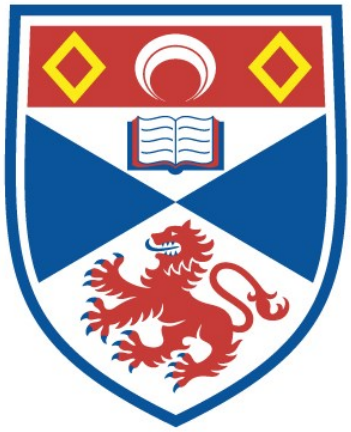
Photocatalytic C(sp³)–C(sp²) radical-polar crossover cross-coupling of styrenyl boronic acids

Jeremy Brals

A thesis submitted for the degree of PhD
at the
University of St Andrews



2023

Declarations

Candidate's declaration

I, Jeremy Brals, do hereby certify that this thesis, submitted for the degree of PhD, which is approximately 74,500 words in length, has been written by me, and that it is the record of work carried out by me, or principally by myself in collaboration with others as acknowledged, and that it has not been submitted in any previous application for any degree. I confirm that any appendices included in my thesis contain only material permitted by the 'Assessment of Postgraduate Research Students' policy.

I was admitted as a research student at the University of St Andrews in September 2019.

I received funding from an organization or institution and have acknowledged the funder(s) in the full text of my thesis.

Date 23/10/2023 Signature of candidate

Supervisor's declaration

I hereby certify that the candidate has fulfilled the conditions of the Resolution and Regulations appropriate for the degree of PhD in the University of St Andrews and that the candidate is qualified to submit this thesis in application for that degree. I confirm that any appendices included in the thesis contain only material permitted by the 'Assessment of Postgraduate Research Students' policy.

Date 23/10/2023 Signature of supervisor

Permission for publication

In submitting this thesis to the University of St Andrews we understand that we are giving permission for it to be made available for use in accordance with the regulations of the University Library for the time being in force, subject to any copyright vested in the work not being affected thereby. We also understand, unless exempt by an award of an embargo as requested below, that the title and the abstract will be published, and that a copy of the work may be made and supplied to any bona fide library or research worker, that this thesis will be electronically accessible for personal or research use and that the library has the right to migrate this thesis into new electronic forms as required to ensure continued access to the thesis.

I, Jeremy Brals, confirm that my thesis does not contain any third-party material that requires copyright clearance.

The following is an agreed request by candidate and supervisor regarding the publication of this thesis:

Printed copy

No embargo on print copy.

Electronic copy

No embargo on electronic copy.

Date 23/10/2023 Signature of candidate

Date 23/10/2023 Signature of supervisor

Underpinning Research Data or Digital Outputs

Candidate's declaration

I, Jeremy Brals, understand that by declaring that I have original research data or digital outputs, I should make every effort in meeting the University's and research funders' requirements on the deposit and sharing of research data or research digital outputs.

Date 23/10/2023 Signature of candidate

Permission for publication of underpinning research data or digital outputs

We understand that for any original research data or digital outputs which are deposited, we are giving permission for them to be made available for use in accordance with the requirements of the University and research funders, for the time being in force.

We also understand that the title and the description will be published, and that the underpinning research data or digital outputs will be electronically accessible for use in accordance with the license specified at the point of deposit, unless exempt by award of an embargo as requested below.

The following is an agreed request by candidate and supervisor regarding the publication of underpinning research data or digital outputs:

No embargo on underpinning research data or digital outputs.

Date 23/10/2023 Signature of candidate

Date 23/10/2023 Signature of supervisor

Acknowledgment

What a crazy thought I had to come abroad, in the middle of nowhere, to do this PhD… Coming to an end, I can only be proud of the hard work, the resilience and the patience that a PhD requires. The retrospective of these four years makes me realise how long and unpredictable the journey has been but also how much I have learnt about myself. This adventure would have certainly been different without the people I met, as well as COVID.

Firstly, I would like to thank Prof. Allan Watson for your constant support and guidance during my PhD. You were always available for chemistry chats as well as making sure I was doing OK. Thank you for your enthusiasm towards good results and your positivity when the chemistry was less successful. Thank you for trusting me and giving me the opportunity to carry out my PhD in your group, and I hope you appreciated working alongside myself as much as I enjoyed your supervision. I also would like to thank Dr. Thomas McGuire, my industrial supervisor at AstraZeneca, for his help and availability during the last four years.

I would like to thank the past members I had the chance to meet during this journey: Thanks to the postdocs Dr. Jamie Fyfe, Dr. Liam McLean and Dr. Aitor Maestro. A big thanks to Dr. Matt West, Dr. Eilidh Sood, and Dr. David Cain, the final year PhD students when I joined the group, they made me feel welcome and helped me to settle in. Then, I would like to thank Dr. Matt Ashford as well as Dr. George Bell, with whom I made lab 337 our home. Finally, I would like to mention Maddison Lovell and Nick D'Arcy-Evans, the two amazing master's students who worked under my supervision.

A special thanks goes to Dr. Eva Israel who dragged me to Scotland. You have been a fantastic friend and my PhD journey would have been so different without you (even if you did leave me for 3-month placement, twice). Thank you for the support, the banter, the French breaks, the speakers, and your friendship in general. I miss the long chats about our lives, foods, plans to open a restaurant, music, French TV, *etc.* during our lunch break, in the lab, in the car commuting, and also every time we were together.

Thank you for being the best friend ever and supported me during this PhD. You made this roller-coaster journey much better and much more enjoyable.

I also would like to thank all the current members of the Watson group. I truly think the group has become a real friendly crew and I am extremely happy to work alongside you. First, Dr. Matt Andrews, you have been a fantastic postdoc and I really enjoyed working with you. Thanks for taking care of the group, thanks for all your precious advices, your willingness to help and your kindness. Kane Bastick for your support and for interrupting my lunches with chemistry chats. Tim Hilton for sharing the desk in front of mine and getting hit as soon as someone wanted to access that damn fridge. Thank you for never stopping moaning no matter the day, the weather or the chemistry. Your positivity and your professionalism in group meetings have improved a lot. A special thank you goes to my friend Marek Varga for the general banter in the lab and in the car. I really appreciated car-pooling (and its jokes) with you even you were always 5 – 8 minutes late. Thanks for always being positive and stressless no matter the situation. I also would like to thank the first year PhD students, Misha Cerna, Tom Richardson and Masha Mazhuga. Masha I really enjoyed working next to you in the lab, you were great company and I will always remember you when listening to Italian music. Misha thanks for the pink hedgehog notebook and Tom, thanks for the fun in the office while we were both writing. I realised you deserved that Banter award.

John Halford-McGuff, my best friend in the lab, a special thanks to you as you are an incredible person. I loved sharing the lab as well as commuting with you and wee Marek. I will keep such good memories from these daily commutes. More than that, I am feeling lucky to work with you. You were always available to help me, support me, advise me, as well as forcing me to run more reactions. You brought a lot to the group and to myself and I am very grateful for this. I also really enjoyed spending time with you and Kasey Killam outside the lab and will always remember that whisky tasting…

Thanks to my friends in the department Dr. Rebecca Craik, and the CPJ group: Callum Adams, Reece Hoogesteger, and Nikki Murdoch. Thank you for the valuable time in 337. Nikki thanks for all the chats we had during our several coffee breaks and for all the laughs we had.

Thanks to my parents, my sister, and the rest of my family for the constant support over the last four years and for visiting me in Scotland. Living abroad did not make things easy but as the French proverb says *loin des yeux, près du coeur*.

Thanks to my best friends aka les Spy for all the fun we had during our weekends, and I wish we had had more. You always cheered me up and the time spent with you always felt like a really enjoyable break, away from the PhD. A special thanks goes to Prunelle, Elisa, Anthonin, Pauline (and Tommy), Chris, Arnold, Kim, and Kaiwei who came to visit me in Scotland. I hope you enjoyed the Scottish experience tour.

Finally, I would like to thank Blair for making the last two years much more enjoyable. My PhD would have been so different without you. Thank you for the constant support during the past two years. I always enjoyed spending time with you and I really loved discovering Scotland. Thank you for all the coffees at Pacamara, the fantastic food, the weekends away, *etc.* A big thank you for everything you did for me, I am feeling very grateful for having you.

Funding

This work was supported by AstraZeneca (Grant number SCH0-XIUA37) and the University of St Andrews.

Research Data/Digital Outputs access statement

Research data underpinning this thesis are available at https://doi.org/10.17630/66a59db2-4d79-4457-b019-b99bfa9c0eff.

Abstract

Organoboron reagents are widely used in organic chemistry due to their versatile reactivity, ubiquity, stability, and low cost. They are commonly employed as coupling partners in cross-coupling reactions, such as the Pd-catalysed Suzuki-Miyaura reaction, which is responsible for 40% of C–C bond formation reactions in the pharmaceutical industry. However, with the development of the photoredox chemistry over the last 15 years, radical-mediated cross-coupling reactions have flourished. Radicals are now easily made from cheap-commercially-available or easy-to-make precursors using visible light irradiation. They can then further react with numerous different coupling partners leading to an extensive range of new cross coupling opportunities, without the requirement for a photocatalyst in some cases. Organoborons have mostly been employed as radical precursors but their use as coupling partners has increased over the past few years.

N-(Acyloxy)phthalimides (NHPI) esters, a class of redox activated ester species, are widely used as alkyl radical precursors owing to their bench-stability and ease of access. Single electron transfer (SET) affords the desired radical through decarboxylation. In this work, we disclose a new method for C–C bond formation between a styrenyl boronic acid and NHPI ester under Ru-mediated photocatalysis. The reaction proceeds smoothly within three hours under blue LED irradiation and affords the desired products in good to excellent yields. The radical addition undergoes unusual polarity-mismatched Giese-type addition to the organoboron coupling partner. A radical polar crossover reaction requires the presence of a redox-active additive to enable the desired bond formation to occur, and proceeds via an unusual boronic acid priming event. This thesis will describe the development and application of this reaction.

PhD Publications

"$Cu(OTf)_2$-mediated cross-coupling of nitriles and *N*-heterocycles with arylboronic acids to generate nitrilium and pyridinium products." N. L. Bell, C. Xu, J. W. B. Fyfe, J. C. Vantourout, J. Brals, S. Chabbra, B. E. Bode, D. B. Cordes, A. M. Z. Slawin, T. M. McGuire, A. J. B. Watson, *Angew. Chem. Int. Ed*. **2021**, *60*, 7935–7940.

"A chemoselective polarity-mismatched photocatalytic $C(sp^3)$–$C(sp^2)$ cross-coupling enabled by synergistic boron activation." J. Brals, T. M. McGuire, A. J. B. Watson, *Angew. Chem. Int. Ed.* **2023**, *62*, e202310462.
This thesis is based upon the above publication.

"Organophotocatalytic radical-polar cross-coupling of styrene boronic acids and redox-active esters" J. Brals, Nicholas D'Arcy-Evans, T. M. McGuire, A. J. B. Watson, *Manuscript accepted, DOI: 10.1055/a-2179-6570.*

Abbreviations

4CzIPN	1,2,3,5-Tetrakis(carbazol-9-yl)-4,6-dicyanobenzene
A	Acceptor
Ac	Acetate
Acr	Acridinium
Aq	Aqueous
Ar	Aromatic
ArTFT	Aryl tetrafluorothianthrenium
ArTT	Aryl thianthrenium
atm	Atmosphere
BDE	Bond dissociation energy
bmim	1-Butyl-3-methylimidazolium
Bn	Benzyl
Boc	*tert*-Butyloxycarbonyl
bpm	2,2'-Bipyrimidine
bpy	2,2'-Bipyridine
Bu	Butyl
cat	Catechol
CFL	Compact fluorescent lamp
COD	1,5-Cyclooctadiene
Cp	Cyclopentadienyl
D	Donor
d.r.	Diastereoisomeric ratio
dan	1,8-Diaminonaphthalene
DCE	1,2-Dichloroethane
DCM	Dichloromethane
dF(CF$_3$)ppy	2-(2,4-Difluorophenyl)-5-(trifluoromethyl)pyridine
DFT	Density functional theory
DIC	*N*,*N'*-Diisopropylcarbodiimide
DIPEA	*N*,*N*-Diisopropylethylamine
DMA	Dimethylacetamide
DMAP	4-Dimethylaminopyridine

DMF	*N*,*N*-Dimethylformamide
DMI	1,3-Dimethyl-2-imidazolidinone
DMSO	Dimethyl sulfoxide
DPEPhos	Bis(2-diphenylphosphinophenyl)ether
dppf	1,1'-Bis(diphenylphosphino)ferrocene
dtbbpy	4,4′-Di-*tert*-butyl-2,2′-dipyridyl
DTBHN	Di-*tert*-butylhyponitrite
e^-	Electron
e.e.	Enantiomeric excess
e.r.	Enantiomeric ratio
EDA	Electron donor acceptor
EDCl	1-Ethyl-3-(3-dimethylaminopropyl)carbodiimide
EDG	Electron-donating group
EnT	Energy transfer
E_{ox}	Oxidation potential
Eq	Equation
equiv.	Equivalent
E_{red}	Reduction potential
EWG	Electron-withdrawing group
EY	Eosin Y
F	Fluorescence
FC	Fluorochem Ltd.
FDA	Food and drug administration
FRET	Förster resonance energy transfer
h	Hours
HAT	Hydrogen atom transfer
HFIP	Hexafluoroisopropanol
HOMO	Highest occupied molecular orbital
HRMS	High resolution mass spectrometry
i-	*iso-*
IC	Internal conversion
IR	Infrared
ISC	Intersystem crossing

LED	Light-emitting diode
LUMO	Lowest occupied molecular orbital
M	Molar
m-	*meta-*
MC	Metal-centred
Me	Methyl
MIDA	*N*-Methyliminodiacetic acid
min	Minutes
MTBE	Methyl *tert*-butyl ether
n-	*neo-*
neop	Neopentylglycol
NFSI	*N*-Fluorobenzenesulfonimide
NHC	*N*-Heterocyclic carbene
NHPI	*N*-Hydroxyphthalimide
NMR	Nuclear magnetic resonance
Nu	Nucleophile
o-	*ortho-*
Ox	Oxidant
P	Phosphorescence
p-	*para-*
PC	Photocatalyst
PC*	Photocatalyst in the excited state
PET	Photoinduced electron transfer
PG	Protecting group
Ph	Phenyl
pin	Pinacol
ppy	2-Phenylpyridine
Pr	Propyl
R6G$^+$	Rhodamine 6G
Red	Reductant
ROS	Reactive oxygen species
rt	Room temperature
s-	*sec-*

SA	Sigma Aldrich Co.
SCE	Saturated calomel electrode
SEO	Single electron oxidation
SER	Single electron reduction
SET	Single electron transfer
SOMO	Singly occupied molecular orbital
t-	*tert-*
TADF	Thermally activated delayed fluorescence
TBAB	Tetrabutylammonium bromide
TBHP	*tert*-Butyl hydroperoxide
TBS	*tert*-Butyldimethylsilyl
TCNHPI	Tetrachlorophthalimide
TEA	Triethylamine
TEMPO	(2,2,6,6-Tetramethylpiperidin-1-yl)oxy
Tf	Triflate
TFA	Trifluoroacetic acid
THF	Tetrahydrofuran
TMB	*N,N,N',N'*-Tetramethylbenzidine
TMG	1,1,3,3-Tetramethylguanidine
TMS	Trimethylsilyl
TS	Transition state
TT	Thianthrenium
UV	Ultraviolet
V	Volt
Vis	Visible
W	Watt
XantPhos	4,5-Bis(diphenylphosphino)-8,9-dimethylxanthene
XAT	Halogen atom transfer

Table of content

1. Introduction

1.1 Photocatalysis

1.1.1 Introduction

Photocatalysis has become a powerful tool to access new synthetic approaches through the generation of reactive radical intermediates.[1,2] For the last two decades, the interest in photocatalysis has soared, highlighting its importance in modern chemistry.[3] Ruthenium and iridium-based photocatalysts are the most commonly employed complexes in photochemistry, since they exhibit excellent photochemical properties.[1,3,4] Firstly, they absorb in the visible spectra, avoiding the use of high energy irradiation (UV), which is incompatible with some functional groups in chemistry. Secondly, they have a long-lived photoexcited states, allowing a bimolecular reaction with another substrate. Finally, by modifying the ligands, the properties of these complexes can be tuned such as attenuating the maximum absorbance or the redox properties,[5] leading to more reducing or more oxidising species ($E_{1/2}(Ru^{II*}/Ru^{I})$ = 0.77 V for $Ru(bpy)_3^{2+}$ whereas $E_{1/2}(Ru^{II*}/Ru^{I})$ = 0.99 V vs. SCE for $Ru(bpm)_3^{2+}$).[1] Over the last decade, improvement within the field has led to the accomplishment of metal-free transformations with the development of organophotocatalysts, which exhibit similar redox properties. The most common photocatalysts used in photochemistry are depicted in Figure *1-1*.[3]

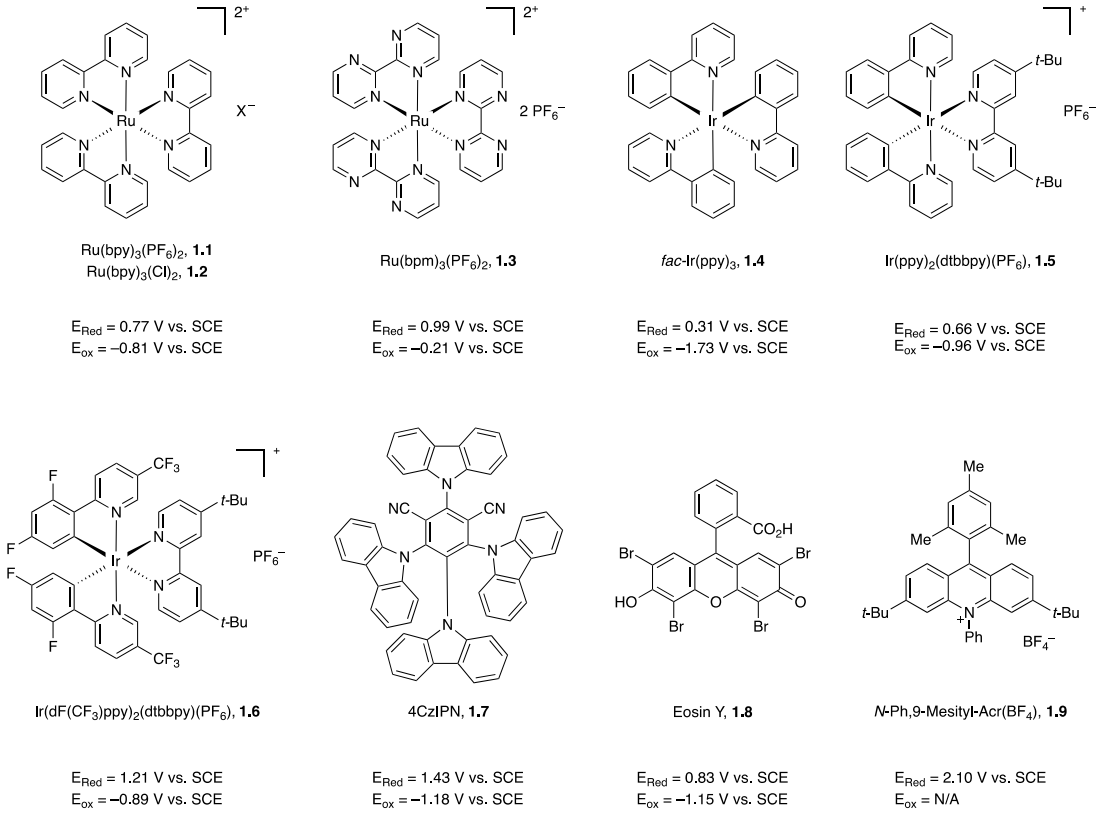


Figure 1-1: Common photocatalysts used in photochemistry.

Subsequently, the development of photocatalysis has led to a variety of bond formations such as C–C,[6] or C–N,[7] C–O,[8] C–S,[9] *etc.*, using either a metal-based[1] or organophotocatalyst,[10] dual catalysis such as combining a photocatalyst and a transition metal,[11,12] or even reactions promoted only by light irradiations such as electron donor acceptor (EDA) complexes.[13]

1.1.2 Fundamentals

After absorption of a photon, activation of organic molecules from the photoexcited catalyst can arise from different processes such as energy transfer (EnT) or single electron transfer (SET).[1,10,14] In some cases, direct hydrogen atom transfer (d-HAT), where the excited photocatalyst abstracts a hydrogen atom from a substrate, can occur but the process remains limited to a few organophotocatalysts (aromatic ketones such as benzophenone, Eosin Y, *etc.*).[15,16]

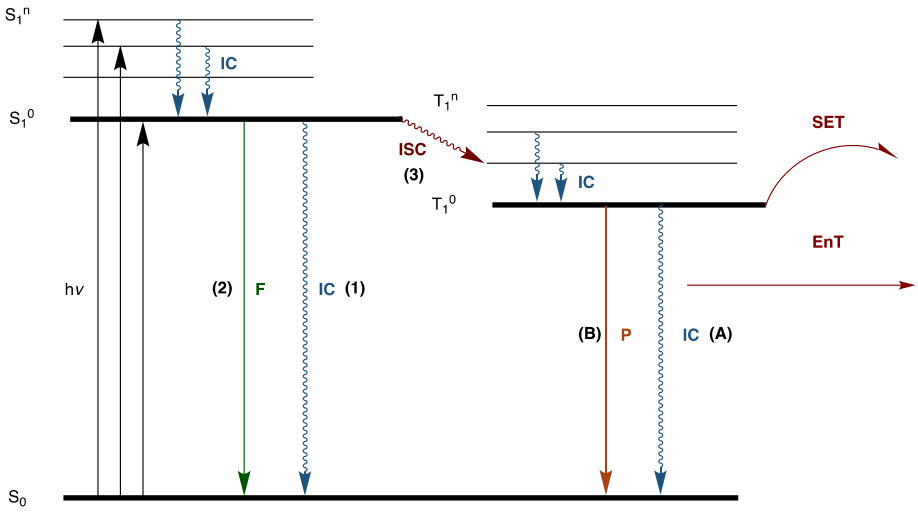


Figure 1-2: Generalised Jablonski diagram of photocatalysts. F = fluorescence, IC = internal conversion, ISC = intersystem crossing, P = phosphorescence.

The fundamental theory can be summarised on a Jablonski diagram, as shown in Figure *1-2*.[1,10,14,17] Upon irradiation at a specific wavelength, the photocatalyst in the ground state absorbs a photon (h*ν*), exciting one electron from the ground state (S_0) to a higher energy excited singlet state (S_1^n). A non-radiative transition (which does not emit a photon), called internal conversion, usually leads the electron to the lowest energy excited singlet state (S_1^0). From there, the electron can undergo different processes: (1) a non-radiative transition where the energy is dispersed through different vibration modes with a loss of heat (IC); (2) a radiative transition between the excited singlet state (S_1^0) to the ground state (S_0), emitting a photon known as fluorescence or (3) the electron can undergo fast intersystem crossing (ISC). The latter corresponds to a non-radiative transition between the excited singlet state (S_1) to the excited triplet state (T_1^n), which are isoenergetic vibrational levels with different spin multiplicity. Internal conversion occurs from a higher excited triplet state (T_1^n) to the lowest energy excited triplet state (T_1^0). The relaxation from T_1^0 to the ground state (S_0) is spin-forbidden (since they have the same spin) leading to a long-lived excited triplet state (T_1^0, 1100 ns for $Ru(bpy)_3^{2+}$). From T_1^0, different processes can occur: (A) a non-radiative transition (IC) to the ground state (S_0); (B) a radiative decay emitting a photon known as phosphorescence or (C) delayed fluorescence where the electron from T_1^0 goes back to S_1^0 (by reverse intersystem crossing in thermally activated delayed fluorescence,[18] known as TADF, or by triplet-triplet annihilation[19]), followed

by delayed fluorescence to the ground state (S_0). Nevertheless, bimolecular processes (involving another substrate) could quench the long-lived T_1^0 of photocatalysts: the electron in the excited triplet state (T_1^0) can undergo single electron transfer (SET) or energy transfer (EnT).

One of the most studied and commonly used photocatalysts is $Ru(bpy)_3^{2+}$.[1,17,20] The HOMO of the complex is centred around the dt_{2g} orbital of the metal whereas the LUMO corresponds to the π* orbital of the ligand (dt_{2g} → π*, λ = 452 nm). The next empty orbital is the metal-centred de_g orbital, which is too high in energy in the case of $Ru(bpy)_3^{2+}$ to be excited under blue LEDs (dt_{2g} → de_g, λ = 350 nm), as depicted in Figure *1-3*. Upon irradiation (λ_{max} = 452 nm), one d-electron from the ground state undergoes metal-to-ligand charge transfer (MLCT) to the π* orbital of the ligand, keeping the same spin, leading to an electron in the excited singlet state (S_1^0). It is worth noting that altering the ligand properties will perturb the molecular orbital energies, leading to potential undesired pathways.[21] Fast intersystem crossing generates the excited triplet state (T_1^0) of the photocatalyst, which has been described as a formal oxidised Ru^{III} species and a reduced bpy ligand ($bpy^{\bullet -}$).[22]

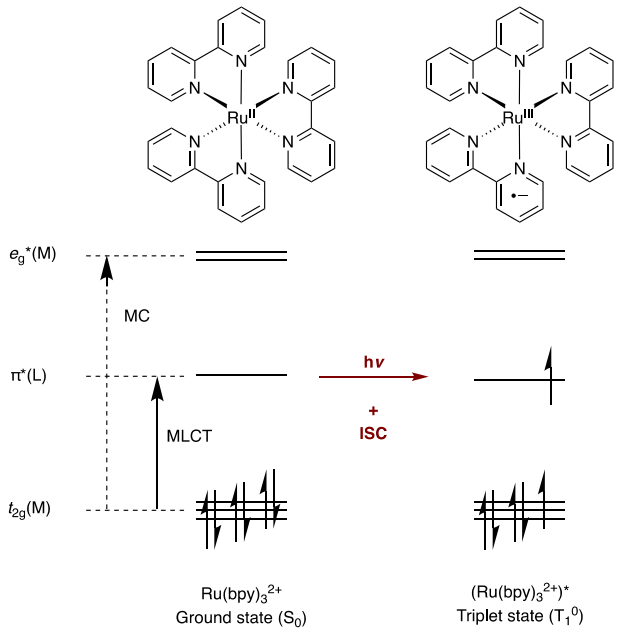


Figure 1-3: Simplified orbital diagram for $Ru(bpy)_3^{2+}$.

1.1.3 Energy transfer

1.1.3.1 Fundamentals

Energy transfer is a bimolecular process referring to a transfer of energy between the long-lived excited triplet state (PC*, T_1^0) of a photocatalyst (donor) and a substrate, also called acceptor (A). Although the excitation of the substrates (usually simple organic molecules) to the excited triplet state (AE, T_1^0) is possible, it usually requires a high-energy photon which can be detrimental for the substrate itself (resulting in degradation). Two non-radiative mechanisms of energy transfer are known: Förster resonance energy transfer (FRET) and Dexter energy transfer, as highlighted in Figure *1-4*.[3,23,24]

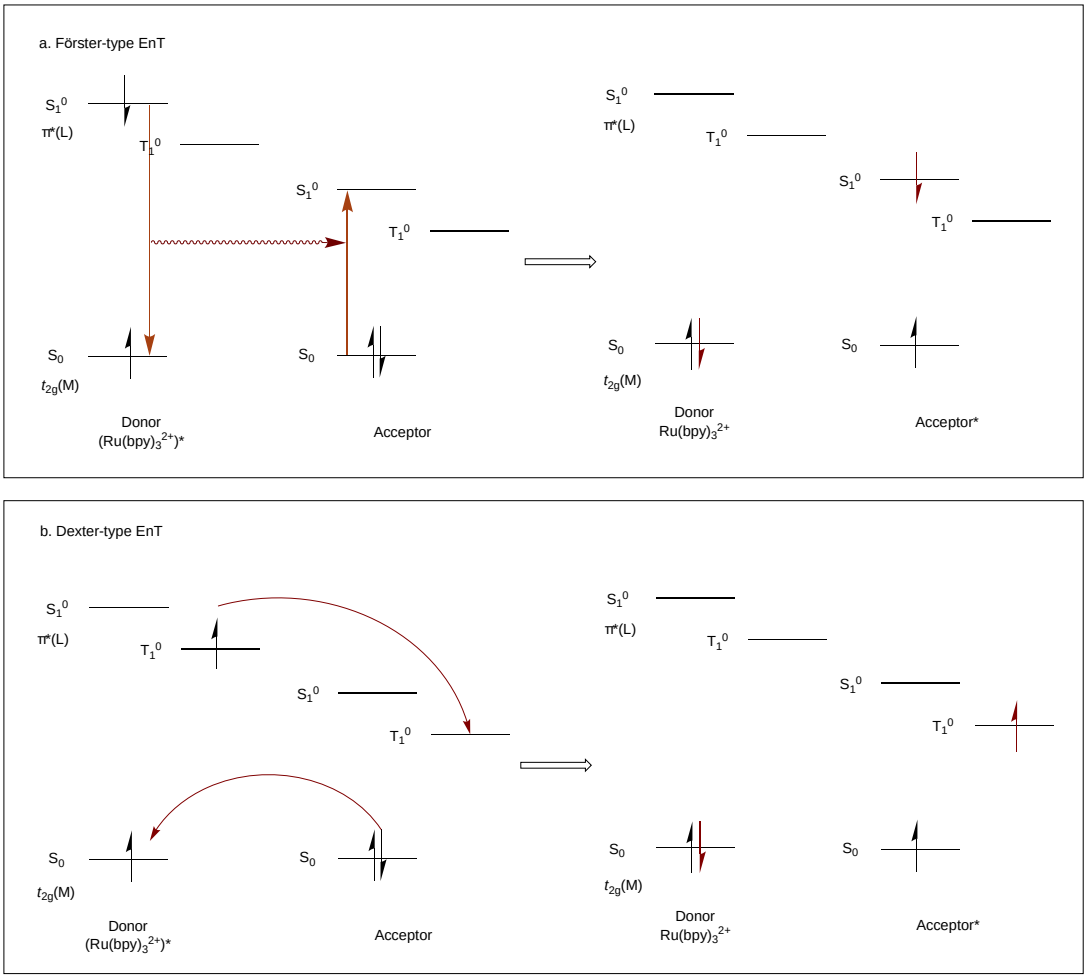


Figure 1-4: Förster and Dexter energy transfer.

The Förster mechanism describes the energy transfer between the excited state of a donor (D*, S_1^0) to an acceptor through a dipole-dipole interaction (Figure *1-4*a).[25,26]

The electron in the excited singlet state oscillates, leading to the formation of a dipole. The dipole generates an electromagnetic field around itself. When an electron from the ground state (S_0) of an acceptor enters the electromagnetic field, the latter oscillates until reaching a resonant interaction state. In this case, the relaxation of the electron in the excited singlet state of the donor (D*, S_1^0) to the ground state (D, S_0) leads to the excitation of an electron from the ground state of the acceptor (A, S_0) to its excited singlet state (A*, S_1^0).[3,23,24] This mechanism is inversely related to the distance between the two electrons but does not require close contact (coulombic interaction) and follows the Wigner's spin conversion rule (stating that the overall spin has to remain the same).

The Dexter energy transfer mechanism describes an intermolecular two electron transfer between a donor (photocatalyst in our case) and an acceptor (Figure *1-4*b).[27–29] This mechanism, also known as triplet-triplet energy transfer relies on two simultaneous electron exchanges where each single transfer occurs between two different energy states, whilst the electron keeps the same spin. The electron from the excited triplet state (D*, T_1^0) of the donor is transferred to the excited triplet state (A*, T_1^0) of the acceptor. On the other hand, an electron from the ground state of the acceptor (A, S_0), is exchanged to the ground state of the donor (D, S_0), keeping the overall spin unchanged. This mechanism requires both the donor and the acceptor to be in very close proximity (orbital overlapping) to occur.[3,23,24] This method is relevant to access the triplet state (A*, T_1^0) of acceptors that are not easy to access otherwise due to inefficient intersystem crossing *e.g.* due to rapid quenching of the excited singlet state.

Glorius and coworkers stated that energy transfer processes induced by a photocatalyst follow a Dexter-type energy transfer mechanism to generate the excited triplet state (A*, T_1^0) of the acceptor.[23,30] The FRET mechanism from the excited singlet state of the donor (D*, S_1^0) to the excited triplet state of the acceptor (A*, T_1^0) would require a change of the spin, forbidden by the Wigner's spin conversion rule.

1.1.3.2 Examples of energy transfer mechanism

Dexter-type energy transfer strategies have been well employed in photochemistry, leading to different types of reactions. Therefore, a broad range of photocatalysts have been found efficient in this process such as Eosin Y, benzophenone, several Ru and Ir-based photocatalysts *etc*., offering a selection of triplet energy values.[3]

Photocatalysed alkene isomerisation ($E \rightarrow Z$) is one of the most commonly reported reactions based on the mentioned energy transfer mechanism.[23,31,32] Although, free rotation around a $C(sp^2)=C(sp^2)$ is usually not appreciable under normal conditions, the use of energy transfer allows the isomerisation of alkenes. The excited triplet state of a photocatalyst (more commonly named photosensitiser in the case of energy transfer, PC*, T_1^0) transfers energy to the excited triplet state of the alkene, leading to an electron exchange between the two species. The photocatalyst relaxes to its ground state (PC*, S_0), whereas an electron populates the LUMO of the alkene ($\pi \rightarrow \pi^*$) thus, decreasing the bond order and allowing the free rotation around the C–C bond, as shown in Figure *1-5*. In both excited singlet and triplet states, the generated diradical species has an energy minimum when the two single-electron orbitals are perpendicular to each other, minimising the Coulombic interaction (Figure *1-5*). Therefore, the electron stays at this energy minimum, which crossed the energy maximum of the ground state (S_0) of the alkene (known as twisted alkene). When the electron relaxes to the ground state, the energy maximum leads to a statistical mixture of (*E*) and (*Z*) diastereoisomers.

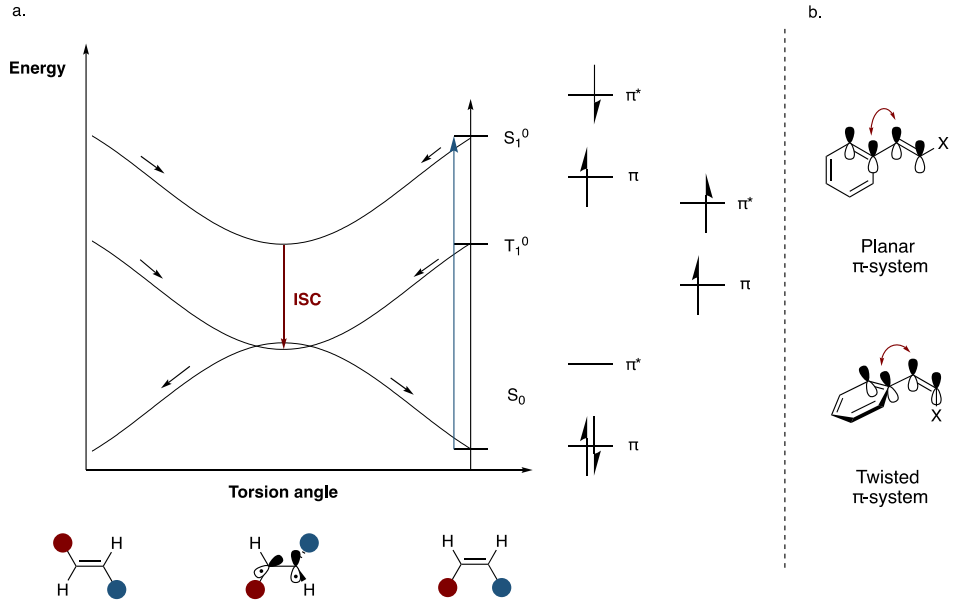
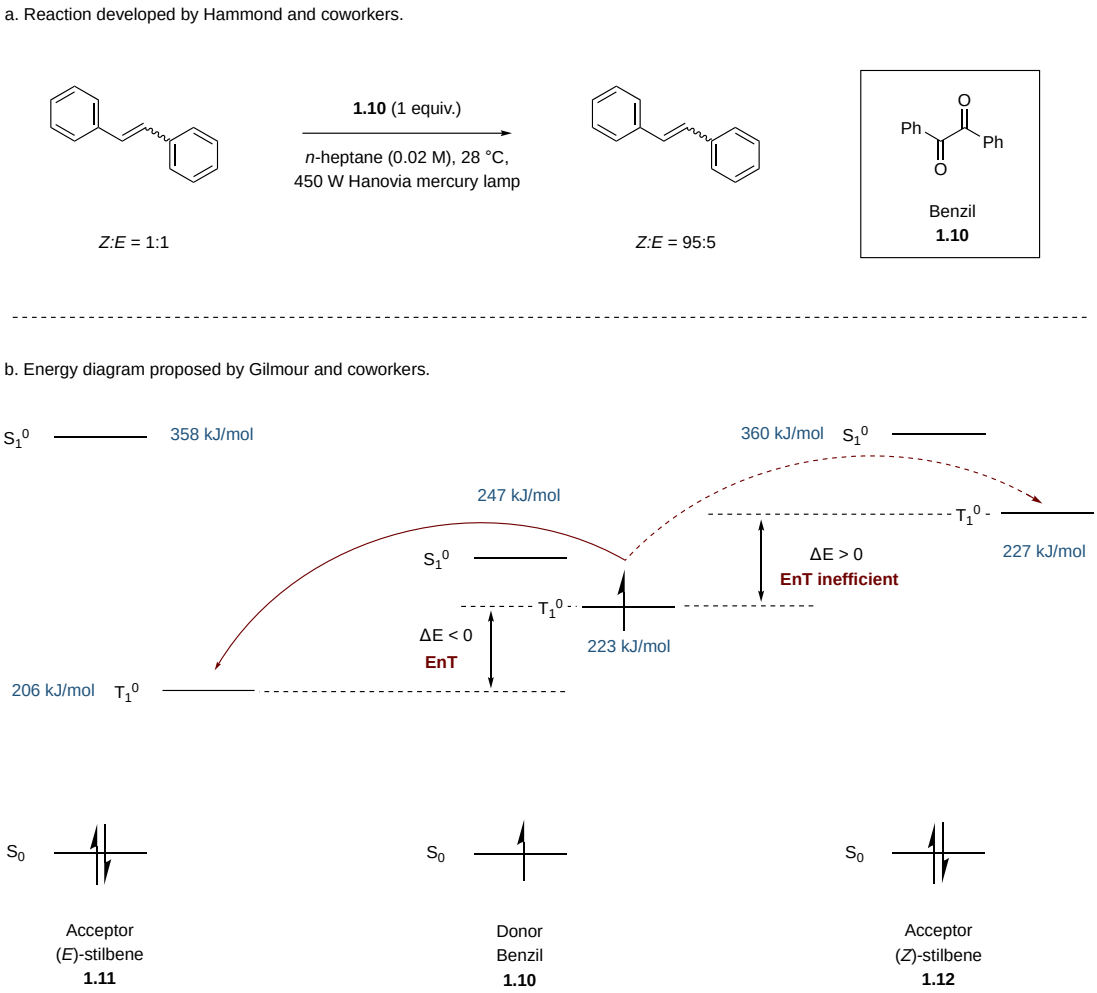


Figure 1-5: Simplified energy surface diagram for *E*:*Z* isomerisation. Blue arrow, sensitisation of the alkene; red arrow, intersystem crossing between S_1^0 and T_1^0; black arrow, movement along the energy surface.

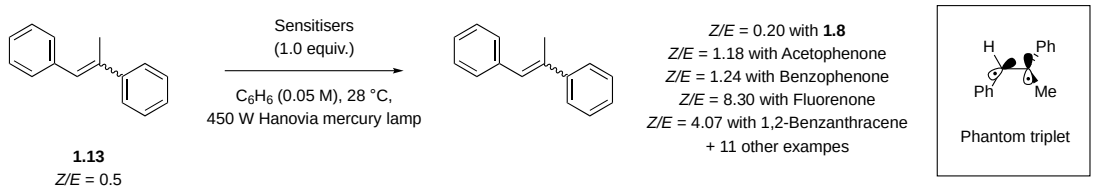
In more complex cases, where the alkene is conjugated to other π systems such as a phenyl substituent or a carbonyl group, the final *E*:*Z* ratio does not display a pure statistical partition, as illustrated by the isomerisation of stilbene using benzil **1.10** reported by Hammond (Scheme *1-1*a).[33] The difference between the excited triplet state energies of the two diastereoisomers leads to a stationary-state ratio. The (*Z*)-diastereoisomer usually exhibits a higher triplet state energy in comparison with the other (*E*)-diastereoisomer (due to improved stabilisation of the double bond), leading to a more difficult sensitisation of the *Z* (vs. the *E*).[34] Gilmour and coworkers described the (*Z*)-alkene as a twisted alkene, leading to lower conjugation between the double bond and the aryl system (vs. the *E*), increasing the energy of the excited states. Thus, after a certain time, when the stationary state is reached, an excess of the (*Z*)-substrate is observed.[35,36] By choosing the sensitiser carefully, where its triplet state energy is in-between the energy of the triplet state of the (*E*)- and the (*Z*)-diastereoisomers, one substrate becomes more reactive than the other, as depicted by Gilmour and coworkers (Scheme *1-1*b).[32] The energy of the triplet state of the (*E*)-stilbene is 206 KJ/mol whereas the energy of the triplet state of the (*Z*)-stilbene is 227 KJ/mol. Thus, the energy transfer between the triplet state of benzil **1.10** (B, T_1^0 at 223 KJ/mol) and the

triplet state of the (*Z*)-stilbene **1.12** (*Z*, T_1^0) is endergonic and unfavoured (ΔE = 4 KJ/mol), whereas the energy transfer between benzil **1.10** (B, T_1^0) and the triplet state of the (*E*)-stilbene **1.11** (*E*, T_1^0) is much more efficient (ΔE = –17 KJ/mol). Although the twisted-like excited triplet state will lead to a statistical partition, when the stationary-state is reached, the (*E*)-diastereoisomer will react much faster toward the energy transfer (vs. the *Z*), enriching the reaction mixture with the (Z)-diastereoisomer.



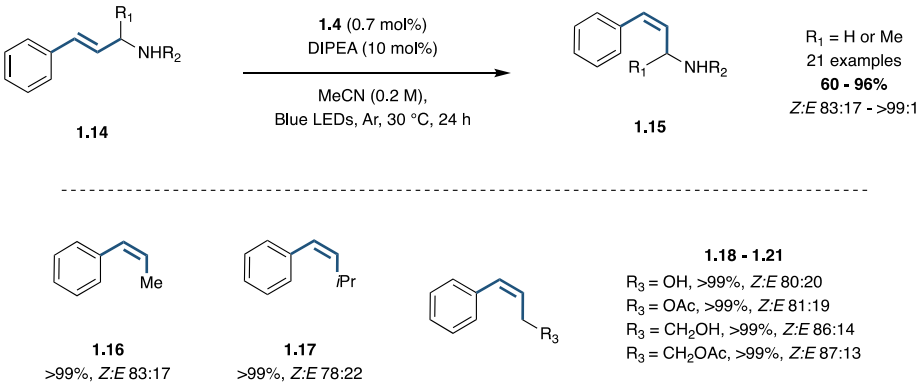
Scheme 1-1: Photomediated isomerisation of stilbene using benzil.

In 1964, Hammond and coworkers reported the *E*:*Z* photochemical isomerisation of different substrates such as 1,2-diphenylpropene **1.13** (Scheme *1-2*).[33] Starting from an isomeric *E*:*Z* mixture of alkenes they subjected to several sensitisers and measured the stationary-state *E*:*Z*. Interestingly, they described the twisted-like excited triplet state as a phantom triplet, arising from a non-vertical excitation. This corresponds to the combination of the excitation of the alkene to the triplet state followed by the rotation of the C–C bond yielding the twisted-like excited triplet state (Figure *1-5*).[37]



Scheme 1-2: Photoisomerisation of 1,2-diphenylpropene by Hammond and coworkers.

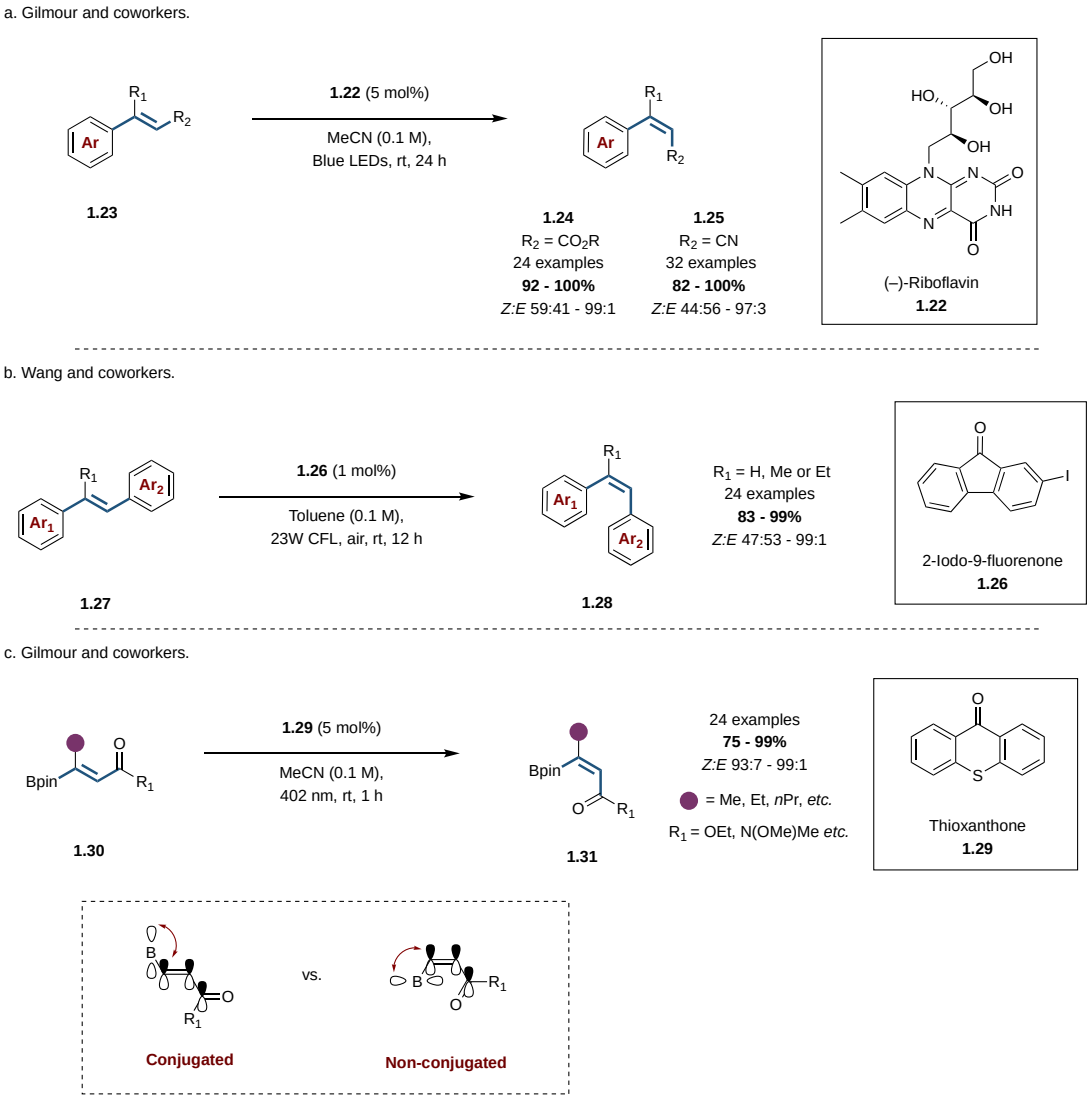
Since the early 60s with the pioneering work of Hammond and others, many methodologies for $E \rightarrow Z$ isomerisation have been developed. A broad range of photocatalysts has been employed, generating the (*Z*)-diastereoisomers of various alkenes. In 2014, Weaver and coworkers developed reaction to access less thermodynamically stable (*Z*)-alkenes using $Ir(ppy)_3$ **1.4** as a photosensitiser, under mild condition (Scheme *1-3*).[38] The reaction underwent good to excellent conversion and excellent isomerization $E \rightarrow Z$ ratio with different cinnamyl-derived amines **1.14**. The reaction tolerated substitution on the *α*-position of the amine (12 examples) and could be employed with other substrates such as *trans-β*-methylstyrene **1.16** or cinnamyl alcohol derivatives **1.18 - 1.21**.



Scheme 1-3: Photocatalysed isomerisation of (*E*)-alkene **1.14**, developed by Weaver and coworkers.

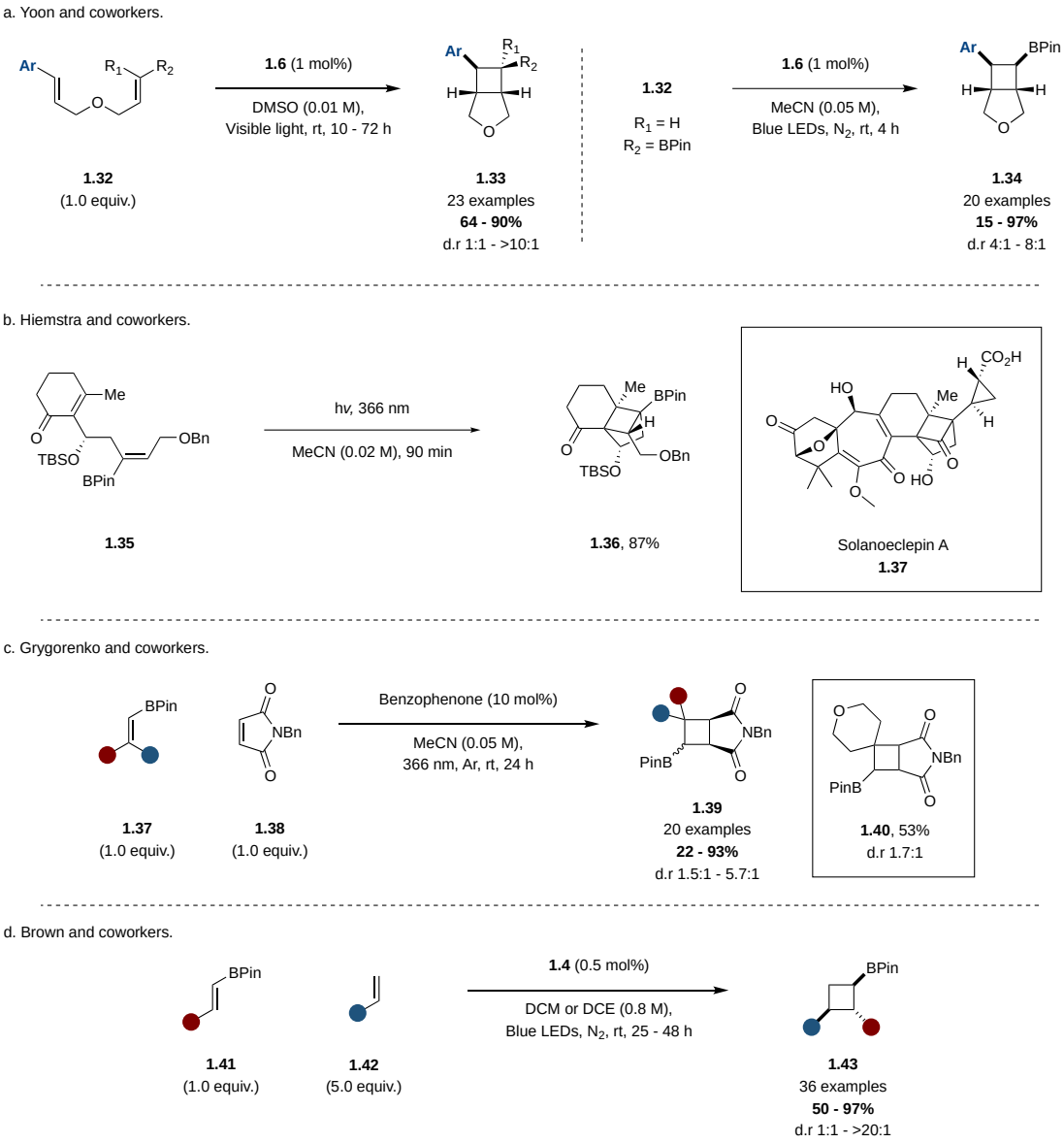
Rueping and coworkers applied this methodology to a two-phase continuous flow system by increasing the affinity of the photocatalyst in a polar phase with an ionic liquid ([bmim][BF_4]).[39] A huge variety of organosensitisers were also found to be highly efficient to achieve $E \rightarrow Z$ isomerisation. The Gilmour lab has strongly

participated in the development of isomerisation chemistry. Over the years, they have reported several methodologies to access (*Z*)-alkenes from a vast range of alkene substrates and using a variety of sensitisers. For instance, (–)-riboflavin **1.22**, commonly known as vitamin B_2, was employed with different olefins **1.23** to afford activated cinnamic esters **1.24**[40] or cinnamonitriles **1.25** (Scheme *1-4*a).[41] Wang and coworkers used 2-iodo-9-fluorenone **1.26** as a sensitiser to yield *Z*-stilbenes **1.28** (Scheme *1-4*b).[42] Finally, Gilmour and coworkers reported a boron-enabled isomerisation of alkene using thioxanthone **1.29** (Scheme *1-4*c). Interestingly, the empty p-orbital of the boron atom is conjugated to the π-system in the case of the (*E*)-alkene **1.30**, whereas it is not the case with the (*Z*)-alkene **1.31**, affording excellent isomerisation ratios after only one hour of reaction.[34]



Scheme 1-4: Different isomerisation methodologies using organosensitisers.

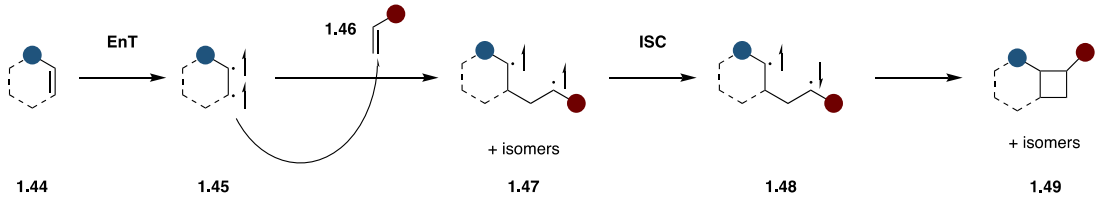
Energy transfer can also be involved in other reactions, such as cycloaddition. For instance, the challenging synthesis of strained cyclobutanes could be overcome through photocatalysed [2+2] cycloadditions.[43,44] Yoon's lab has been focused on the synthesis of these motifs and, in 2012, they reported an intramolecular Ir-mediated reaction of dienes **1.32** enabled by energy transfer to afford complex cyclobutane scaffolds **1.33** (Scheme *1*-5a).[45] In 2015, Cibulka and coworkers reported a similar reaction using flavin derivatives as sensitisers in their metal-free transformation.[46] Yoon and coworkers applied their previous methodology to Bpin-containing dienes **1.32** (where R_1 = H and R_2 = Bpin) to generate Bpin-functionalised 3-oxabicyclo[3.2.0]heptanes **1.34** (Scheme *1*-5a).[47] Although the scope was carried out with boronic acid pinacol esters, the reaction with $B(OH)_2$ (68%), Bneop (75%), and BMIDA (84%) delivered comparable yields. Interestingly, the use of Bdan was found detrimental and only 15% of the product was afforded in this case. The organoboron handle can then be used as a linchpin to access a variety of other functionalities. Hiemstra and coworkers employed an intramolecular [2+2] cycloaddition with Bpin-containing olefin **1.35** in their total synthesis of Solanoeclepin A **1.37** (Scheme *1*-5b).[48]



Scheme 1-5: Different [2+2] cycloaddition processes.

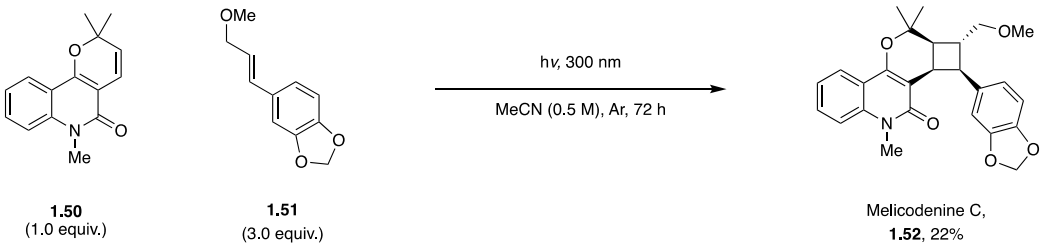
The use of alkenyl boronic esters in intermolecular [2+2]-cycloaddition with a second olefin affords access a variety of B-substituted complex cyclobutane scaffolds. For instance, Grygorenko and coworkers reported metal-free synthesis of 3-azabicyclo[3.2.0]heptane scaffolds **1.39** using alkenyl boronic esters **1.37** and benzophenone as a sensitiser (Scheme *1-5*c).[49] Their methodology allows access to a myriad of spiro cyclic products such as **1.40** obtained with 53% yield (isolated). More recently, Brown and coworkers reported an Ir-photosensitised [2+2]-cycloaddition of alkenyl boronic acid pinacol esters with a variety of alkenes (Scheme *1-5*d).[50] Their investigation revealed energy transfer is more likely happening to the organoboron olefin **1.41**. Their methodology tolerates a good range of different styrenyl Bpin

reagents and affords the desired product **1.43** with good to excellent yields. In some cases, they performed a Brown oxidation to furnish the corresponding alcohols.



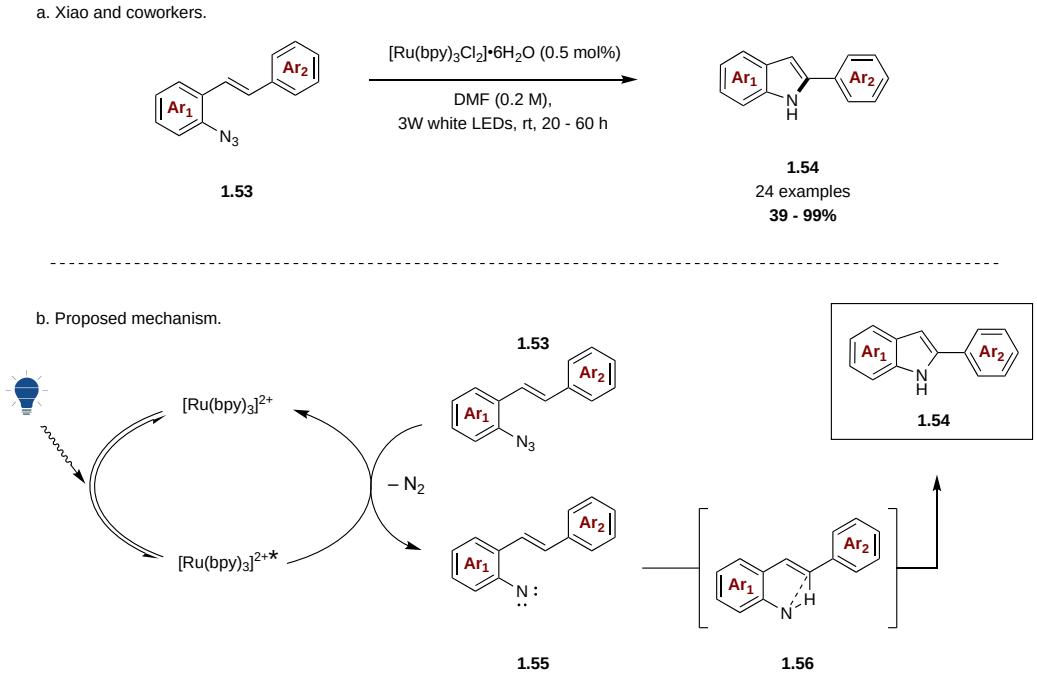
Scheme 1-6: General mechanism for photoinduced [2+2]-cycloaddition.

The reaction starts with triplet-triplet energy transfer between the excited state of the sensitiser and one of the two alkenes, **1.44** in this case (Scheme *1-6*). Since the triplet state **1.45** of the alkene is long-lived, reaction with another alkene **1.46** (intra or intermolecularly) can occur, leading to a 1,4-diradical intermediate **1.47**, with the same spin. ISC of one of the two electrons leads to relaxation from the excited triplet state to the singlet state delivering **1.48**. Subsequent radical recombination yields the [2+2] cycloaddition product **1.49**.[44,51] It is worth noting that in some cases, cycloaddition occurs without a sensitiser; however, this process usually requires a high energy photon to reach the excited triplet state of the alkene. For instance, Quinn and coworkers reported a [2+2] cycloaddition between the two alkenes **1.50** and **1.51** using high energy photons (λ = 300 nm) to access Melicodenine C **1.52**, with only 22% yield, as shown in Scheme *1-7*.[52]



Scheme 1-7: [2+2] Cycloaddition for the synthesis of Melicodenine C.

Energy transfer can also occur with other substrates other than alkenes. For instance, Xiao and coworkers reported the sensitisation of aryl azides **1.53** to afford indoles **1.54**, as illustrated in Scheme *1-8*.[53]

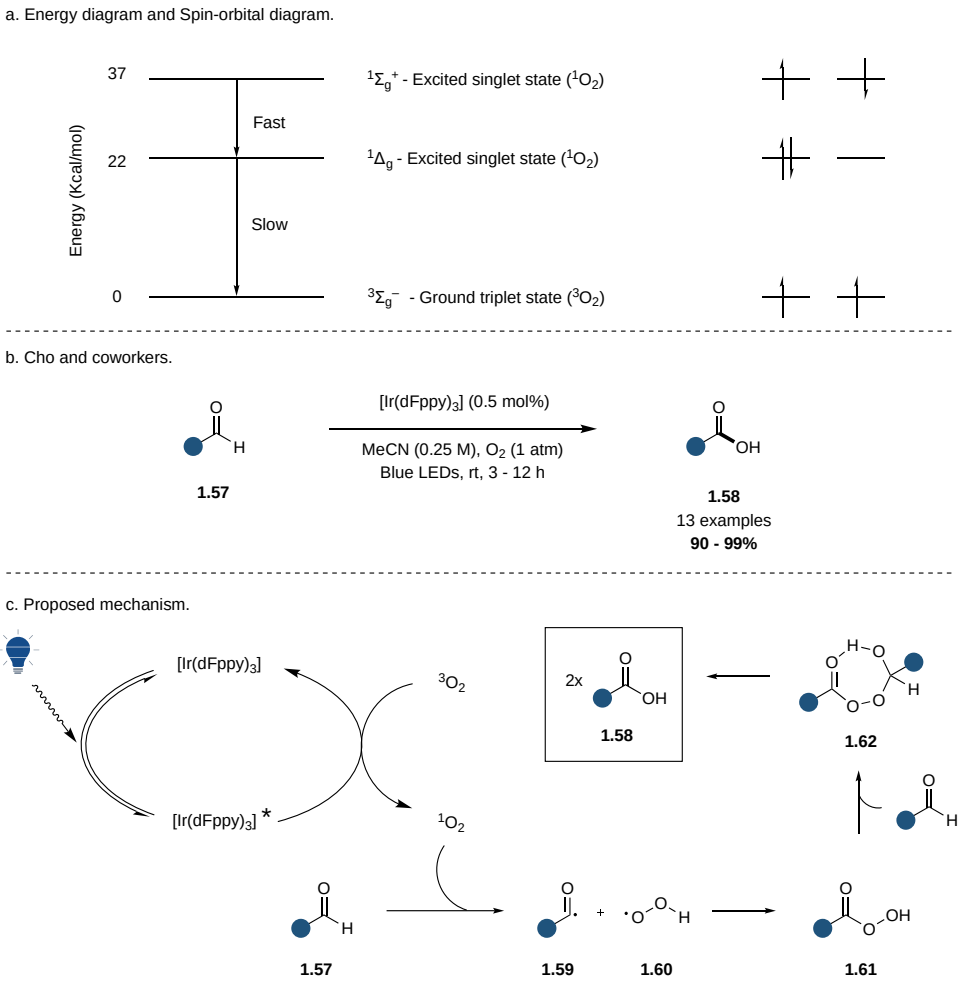


Scheme 1-8: Indole synthesis enabled by energy transfer using aryl azides.

$Ru(bpy)_3^{2+}$ absorbs a photon yielding the excited singlet state. ISC allows the transition from the excited singlet state to the excited triplet state. The long-lived triplet state undergoes energy transfer with the aryl azide **1.53**, populating its triplet state. The release of molecular nitrogen leads to the formation of a nitrene intermediate **1.55**. Concerted nitrene insertion to the alkene **1.56** generates the desired C2-alkylated indole **1.54**. The mechanism was supported by cyclic voltammetry, which revealed a lower reducing potential of the aryl azides **1.53** ($E_{1/2}$ = –1.80 V vs. SCE) than the redox potential of $Ru(bpy)_3^{2+}$ ($E_{1/2}$ = –1.33 V vs. SCE), ruling out a potential single electron transfer mechanism (*vide infra*).

Energy transfer can also be used to generate singlet oxygen from molecular oxygen. Although singlet oxygen can cause damage to biomolecules, it can be employed to incorporate an oxygen atom into substrates. Surprisingly, the ground state of molecular oxygen corresponds to a triplet state where both electrons are populating one π* orbital, with the same spin ($^3\Sigma_g^-$) (see Scheme *1*-9a).[54,55] Energy transfer from a sensitiser leads, in this case, to the formation of excited singlet state, where one electron has its spin flipped. Molecular oxygen has two singlet excited states: $^1\Delta_g$ at 22 kcal/mol and $^3\Sigma_g^+$ at 37 kcal/mol. The states only differ by the position of one electron. In $^1\Delta_g$, the two electrons populate the same π* orbital whereas in $^3\Sigma_g^+$ the two

electrons are in two different π* orbitals. The relaxation of $^3\Sigma_g^+$ to $^1\Delta_g$ is fast since it is spin-allowed, leading to a short-lived $^3\Sigma_g^+$ singlet excited state. However, the $^1\Delta_g$ excited singlet state is considered long-lived since the transition from $^1\Delta_g$ to $^3\Sigma_g^-$ is spin-forbidden. This long-lived excited state can be generated with several sensitisers such as an Ir-based photocatalyst in Cho's methodology.[56] The group developed an aerobic oxidation of a variety of aldehydes **1.57**, using singlet oxygen as depicted in Scheme *1-9*.



Scheme 1-9: a. Energy diagram of molecular oxygen; b. Aerobic oxidation of aldehydes enabled by energy transfer by Cho and coworkers; c. Proposed mechanism.

The reaction tolerated both alkyl and aryl aldehydes and afforded the corresponding carboxylic acids **1.58** with excellent yields. The excited singlet state ($^1O_2$) reacts with the aldehyde **1.57** to afford an acyl radical **1.59** and hydroperoxyl radical **1.60**. The

recombination of the two radicals gives the peracid **1.61** which can react with another equivalent of aldehyde **1.57** furnishing the intermediate **1.62**. Finally, a Bayer–Villiger-type rearrangement generates two molecules of product **1.58**.

1.1.4 SET

1.1.4.1 Fundamentals

Single electron transfer (SET), also known as photoinduced electron transfer (PET) occurs between a photocatalyst in the excited triplet state (PC*, T_1^0) and a substrate, also known as a quencher. Two potential processes can occur depending on the redox properties of the photocatalyst (*vide infra*). The excited triplet state of the photocatalyst (PC*, T_1^0) can undergo either single electron reduction (SER) or single electron oxidation (SEO) with a quencher, as shown in Figure *1-6*. Common photocatalysts, such as $Ru(bpy)_3^{2+}$, can usually undergo both quenching pathways (Figure *1-6*). Single electron reduction (SER) of $Ru(bpy)_3^{2+}$*, T_1^0 with a quencher (called reductant in this case) leads to a +1 reduced $Ru(bpy)_3^+$ (S_0) species. On the other hand, $Ru(bpy)_3^{2+}$*, T_1^0 can undergo single electron oxidation (SEO) with the quencher (named oxidant) and loses the π^* electron to generate an oxidised $Ru(bpy)_3^{3+}$ (S_0) species.

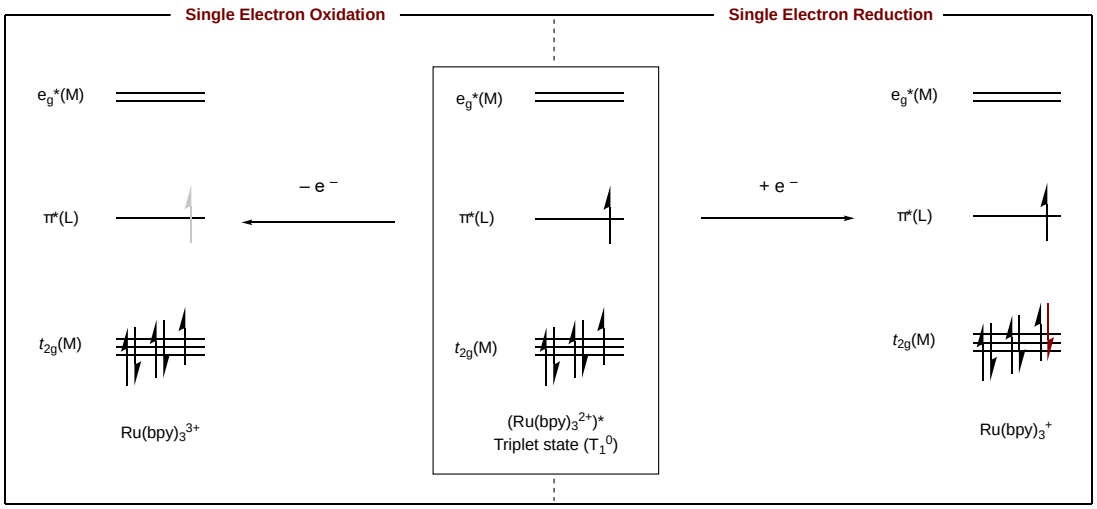


Figure 1-6: Quenching of $Ru(bpy)_3^{2+}$*, T_1^0 through SET.

After generation of either the reduced (reductive quenching) or the oxidised (oxidative quenching) photocatalyst species, another single electron transfer occurs with an

external redox species (or an intermediate) to turn over the photocatalytic cycle and regenerate the photocatalyst in the ground state, as depicted in Scheme *1-10*.

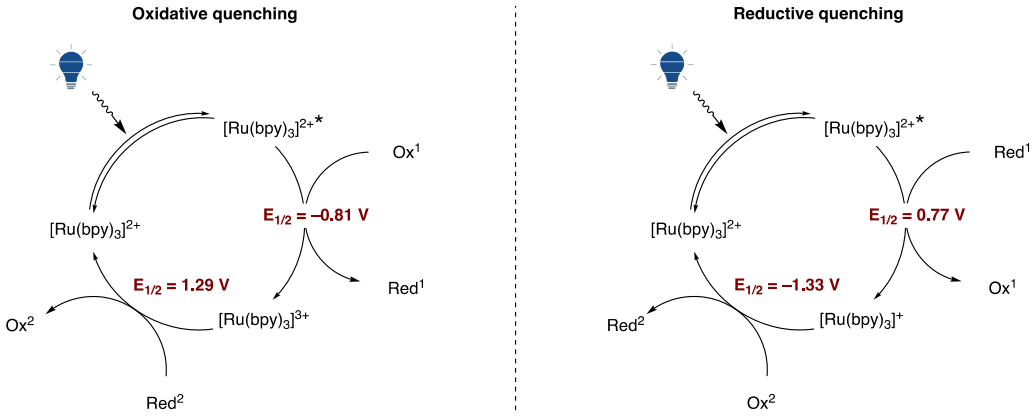
Photoexcited catalysts exhibit more powerful redox properties compared to the corresponding ground state photocatalysts due to the electron distribution of PC*, T_1^0. Each redox couple (Ox_1/Red_1) is characterised by its redox half equation (Eq 1-1) and its redox potential ($E_{1/2}$).

$$Ox_1 + n\ e^- = Red_1 \text{ (Eq 1-1)}$$

$$Ru(bpy)_3^{3+} + e^- = Ru(bpy)_3^{2+} \text{ (Eq 1-2)}$$

$$Ru(bpy)_3^{3+} + e^- = Ru(bpy)_3^{2+*} \text{ (Eq 1-3)}$$

For instance, the redox potential of the Ru^{III}/Ru^{II} described by Eq 1-2 is $E_{1/2}$ = 1.29 V vs. SCE, whereas the redox potential of Ru^{III}/Ru^{II*} (Eq 1-3) is $E_{1/2}$ = −0.81 V vs. SCE. The excited Ru^{II*} is a better reducing agent than the Ru^{II} photocatalyst in its ground state. Similarly, Ru^{II*} is more oxidising than the corresponding Ru^{II} in the ground state. These increased redox properties of an excited state of a photocatalyst form the foundation of SET.

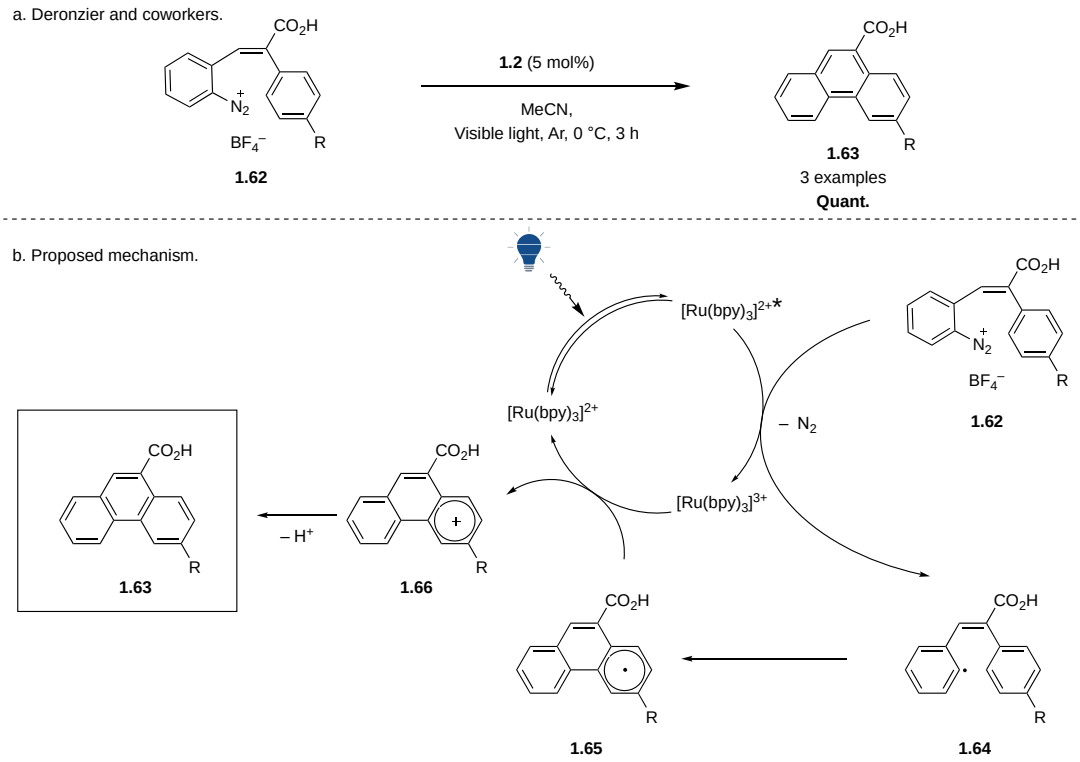


Scheme 1-10: $Ru(bpy)_3^{2+}$ photocatalytic cycles.

1.1.4.2 Example of SET

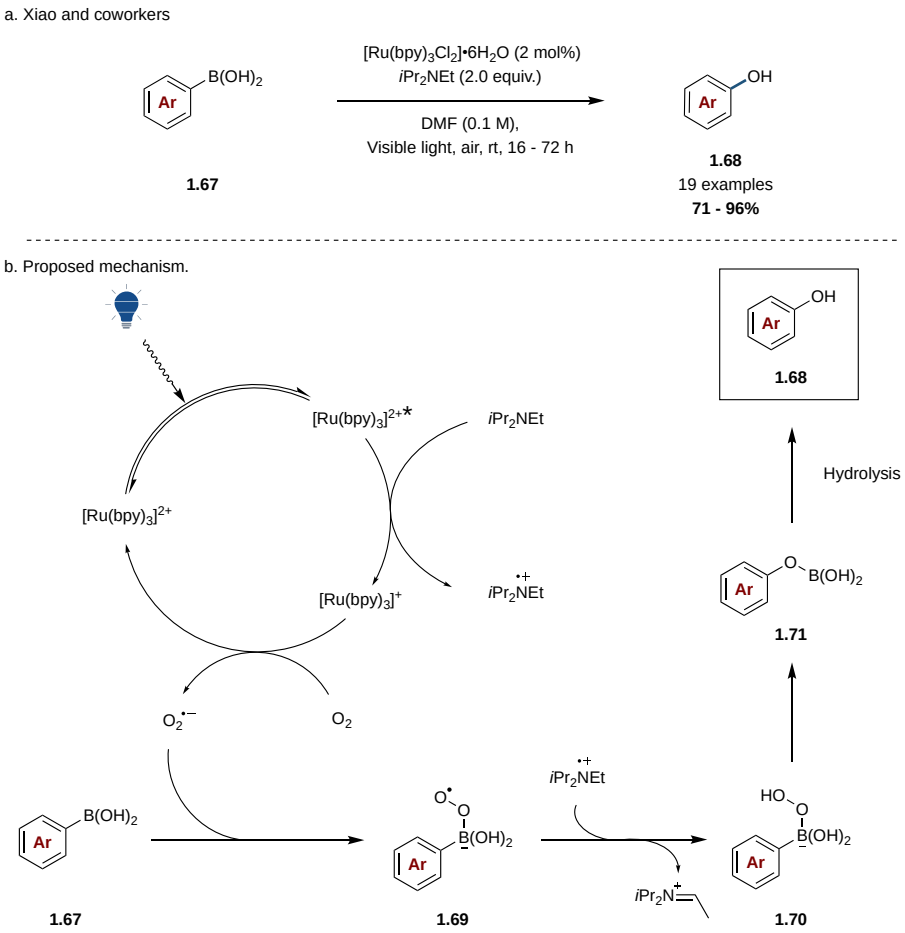
Since the development of photocatalysis, several methodologies reported SET in their mechanisms with both metal-based photocatalysts and organophotocatalysts.

In 1984, Deronzier and coworkers reported one of the first photocatalytic Pschorr reactions mediated by the Ru-based photocatalyst **1.2** using stilbene diazonium salts **1.62** (Scheme *1-11*).[57] They reported an oxidative quenching pathway: upon light irradiation $Ru(bpy_3)^{2+}$* undergoes single electron transfer with **1.62** ($E_{1/2}$ = 0.1 V vs. SCE), furnishing the aryl radical **1.64** after molecular nitrogen release and the oxidised $Ru(bpy_3)^{3+}$ species. Intramolecular radical addition of **1.64** leads to **1.65** which further undergoes single electron oxidation to generate the aryl carbocation **1.66** and the initial $Ru(bpy_3)^{2+}$ photocatalyst in the ground state. Further deprotonation yields the desired product **1.63** with excellent yield. In the absence of photocatalyst, the simple photolysis of **1.62** afforded only 20% of product **1.63**, highlighting the importance of the Ru-mediated photocatalysis.



Scheme 1-11: Photocatalysed Pschorr reaction using diazonium salts.

In 2012, Xiao and coworkers reported an aerobic oxidative hydroxylation of aryl boronic acids **1.67** under photoredox catalysis.[58] The Ru-based methodology proceeds under air and delivers aryl alcohols **1.68** with excellent yields (Scheme *1-12*).

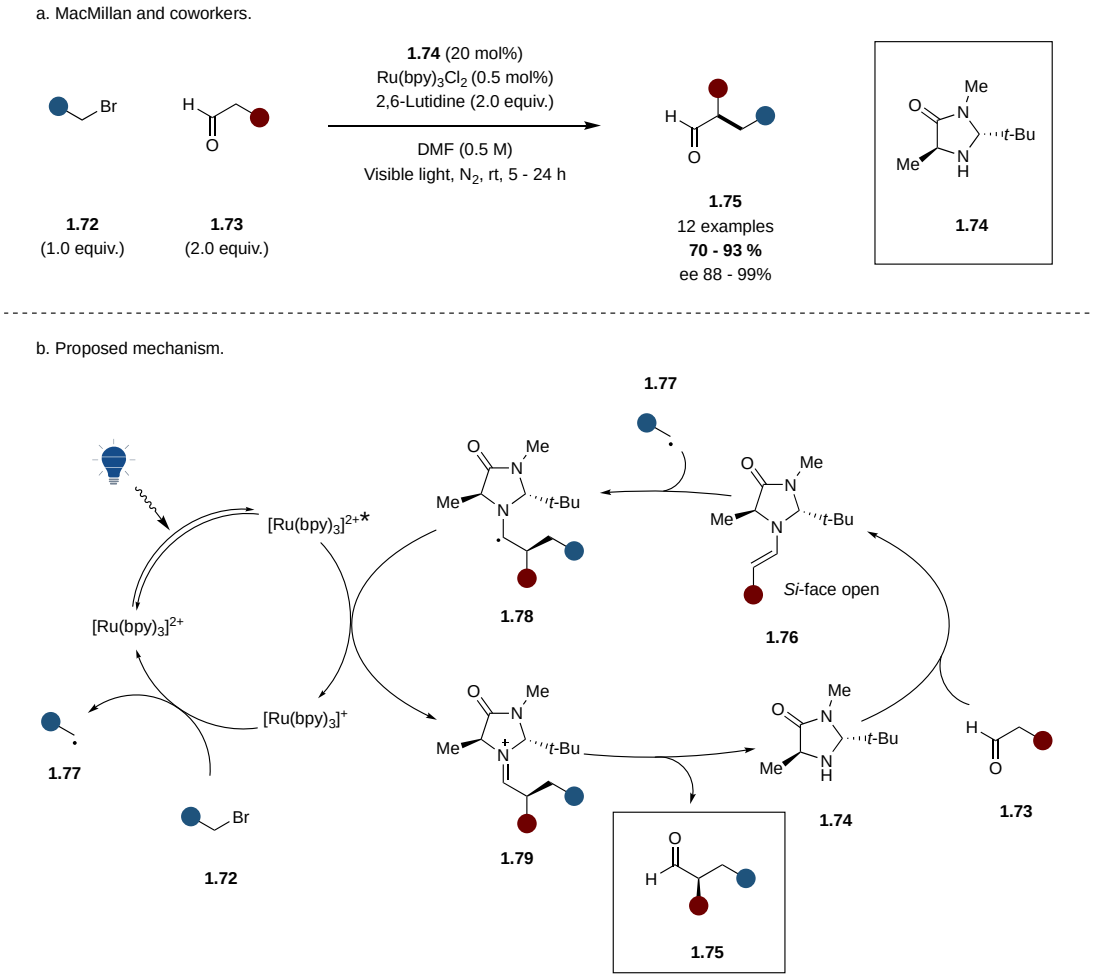


Scheme 1-12: Aerobic oxidative hydroxylation of aryl boronic acids.

In this case, molecular oxygen undergoes single electron reduction with $Ru(bpy)_3^+$, forming the superoxide anion radical ($O_2^{\bullet-}$), which further reacts with aryl boronic acids **1.67** to deliver the radical intermediate **1.69**. HAT (*vide infra*) furnishes **1.70** and subsequent aryl migration yields **1.71**. Final hydrolysis affords the desired aryl alcohols **1.68**. The reaction was also performed with $^{18}O_2$ (1 atm), yielding ^{18}O-labelled alcohols.

1.1.4.3 Combining SET with another methodology: dual catalysis

Photocatalysis is a versatile and powerful tool to access a myriad of chemical transformations. Therefore, the scope of its application could be extended with dual-mediated catalysis between a photocatalyst and a secondary component such as a transition metal or chiral auxiliary, *etc*.[11,12] MacMillan was a pioneer in merging photoredox with organocatalysis leading to enantioselective syntheses.[59] The group reported a visible light-mediated enantioselective alkylation of aldehydes promoted by the *in situ* formation of a chiral enamine, as depicted in Scheme *1-13*.



Scheme 1-13: Enantioselective alkylation of aldehydes mediated by dual catalysis.

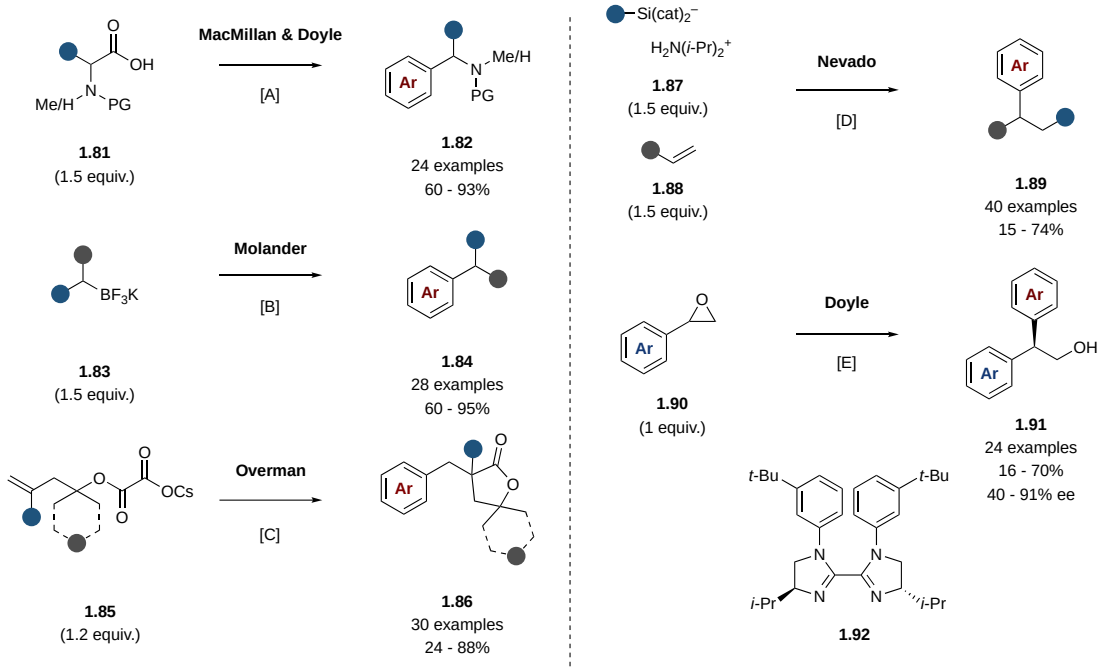
The proposed reaction relies on dual catalysis between an enantiopure imidazolidinone **1.74** and a $Ru(bpy)_3^{2+}$ photocatalyst. Upon irradiation, the photocatalyst absorbs a

photon, generating the excited state of $Ru(bpy)_3^{2+*}$. A sacrificial catalytic amount of **1.76** is used to reduce the excited photocatalyst to $Ru(bpy)_3^{+}$ during the first turnover. The radical precursor **1.72**, which requires one (or two) electron withdrawing substituents, undergoes SET with $Ru(bpy)_3^{+}$ furnishing the electrophilic radical **1.77** and the photocatalyst in its ground state. Simultaneously, the aldehyde **1.73** condenses with **1.74** to form the chiral enamine **1.76**. Addition of the radical **1.77** onto the *Si*-face generates the α-amino radical intermediate **1.78**; further intersection with the photocatalytic cycle affords the iminium species **1.79**. Finally, hydrolysis delivers the desired enantioenriched product **1.75**. The reaction worked well with α-bromomalonates, as well as with ketones, and ester derivatives, leading to excellent yield and enantioselectivity. Since then, this methodology has been extensively applied with a broad range of photocatalysts and organocatalysts.[60–62]

Combining photocatalysis with transition metal catalysis provides another tool to access challenging bond formations.[63] The field of metallophotoredox catalysis has been widely developed over the last decade with a significant variety of transition metals such as Ni,[64] Cu,[65] Co,[66] Au,[67] Fe,[68] *etc*. Combination of photoredox and transition metal catalysis allows to access different oxidation states of the transition metal accessing fundamental steps such as oxidative addition and reductive elimination. Ni has been a privileged transition metal involved in photoredox processes, as highlighted in Scheme *1-14*.[64] For instance, Doyle and MacMillan reported an Ir- and Ni-based dual catalysis, generating C–C bonds from aryl halides **1.80** where the radical precursors are amino acids **1.81**.[69] Furthermore, this methodology could be applied with different radical precursors such as potassium organotrifluoroborates salts **1.83**, as shown by the Molander lab,[70] or homoallylic oxalate salts **1.85**, demonstrated by Overman and coworkers.[71] Nevado and coworkers reported a three-component alkene difunctionalisation of styrenes **1.88** using alkyl silicates **1.87** as radical precursors.[72] The Doyle lab swapped the common dtbbpy ligand to the chiral biimidazoline **1.92** in their coupling reaction between aryl epoxides **1.90** and aryl halides to generate enantioenriched alcohols **1.91** with excellent yields and enantioselectivity.[73]

a. General dual catalysis with aryl halides.

b. Selected examples.



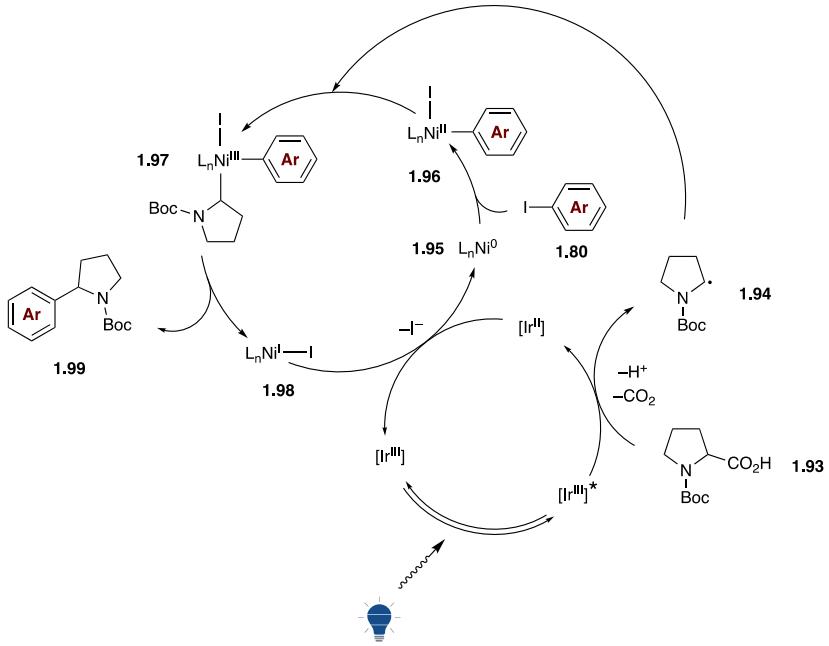
[A]: **1.6** (1 mol%), $NiCl_2$•glyme (10 mol%), dtbbpy (15 mol%), Cs_2CO_3 (1.5 equiv.), DMF (0.02 M), Blue LEDs, Ar, rt, 72 h.
[B]: **1.6** (2.5 mol%), $NiCl_2$•glyme (5 mol%), dtbbpy (5 mol%), Cs_2CO_3 (1.5 equiv.), 1,4-Dioxane (0.05 M), Blue LEDs, N_2, rt, 24 h.
[C]: **1.6** (2 mol%), Ni(dtbbpy)$((H_2O)_4)Cl_2$ (10 mol%), dtbbpy (5 mol%), Benzene:1,4-Dioxane (1:1, 0.03 M), Blue LEDs, N_2, 60 °C, 2 h.
[D]: $Ru(bpy)_3Cl_2$•$6H_2O$ (1 mol%), $NiCl_2$•$6H_2O$ (10 mol%), dtbbpy (15 mol%), DMF (0.1 M), Blue LEDs, N_2, 30 °C, 16 h.
[E]: **1.7** (3 mol%), ArX (2 equiv.), $NiBr_2$•diglyme (10 mol%), **1.92** (10 mol%), $MgCl_2$ (25 mol%), Et_3N (5.0 equiv.), THF (0.05 M), Blue LEDs, N_2, rt, 24 h.

Scheme 1-14: a. General dual photoredox/Ni catalysis for cross-coupling reactions using aryl halides; b. Selected examples.

The metal oxidation state could be altered through different pathways such as interception of the generated radical by the metal generating a +1 oxidised metal complex, or by photoinduced processes.

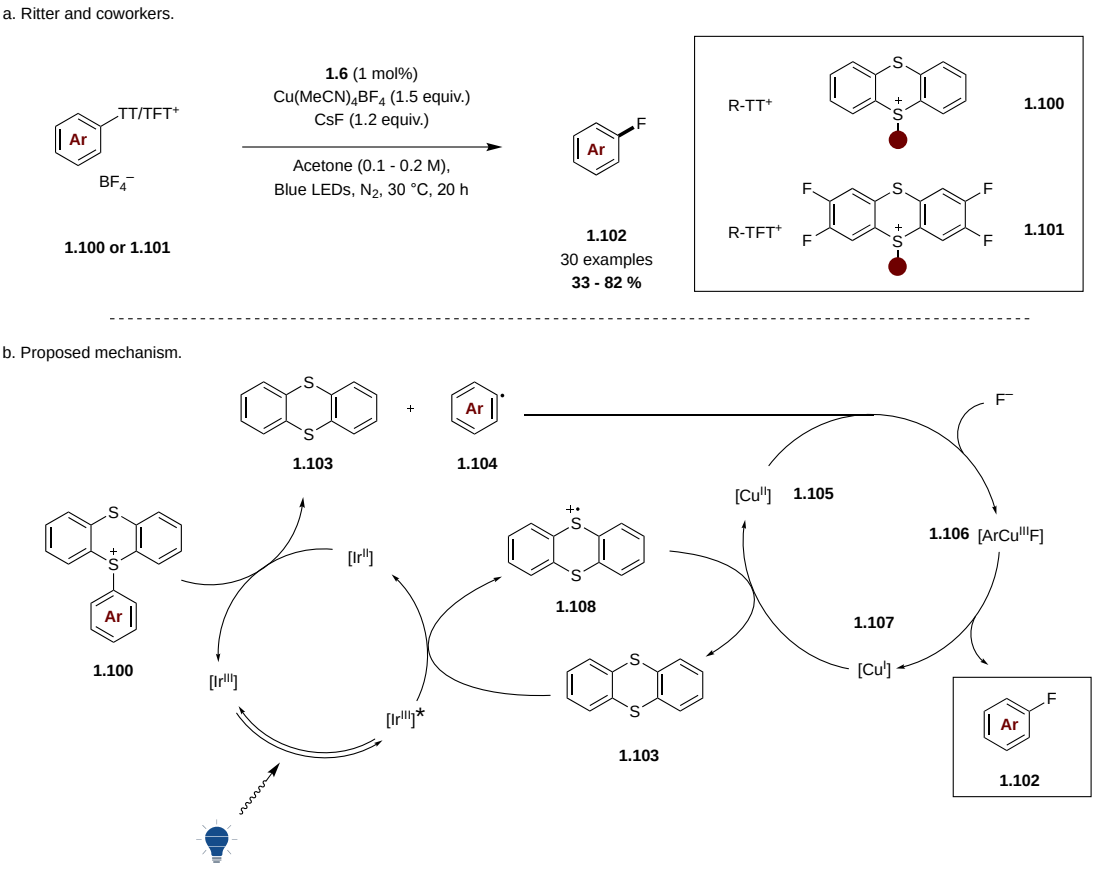
The proposed mechanism of Doyle and MacMillan's coupling reaction between *N*-Boc proline **1.93** and aryl iodide **1.80** is depicted in Scheme *1-15*. This relies on a dual catalysis where the Ir photocatalyst, once excited to its triplet state, decarboxylates amino acids (such as *N*-Boc proline **1.93**) furnishing an α-amino radical **1.94**. At the same time, oxidative addition of aryl iodides **1.80** to Ni^0 catalyst **1.95** generates the

Ni^{II} species **1.96**, which can further intercept the radical **1.94**, leading to the oxidised Ni^{III} species **1.97**. Reductive elimination delivers the reduced Ni^{I} species **1.98** and the desired product **1.99**. A final SET between **1.98** and the Ir^{II} complex regenerates the two catalysts, available for another turnover.



Scheme 1-15: Mechanism proposed by Doyle and MacMillan.

Ritter and coworkers reported a Cu^{I}-mediated fluorination using aryl thianthrenium (ArTT) **1.100** and tetrafluorothianthrenium (ArTFT) salts **1.101** (Scheme *1-16*).[74]



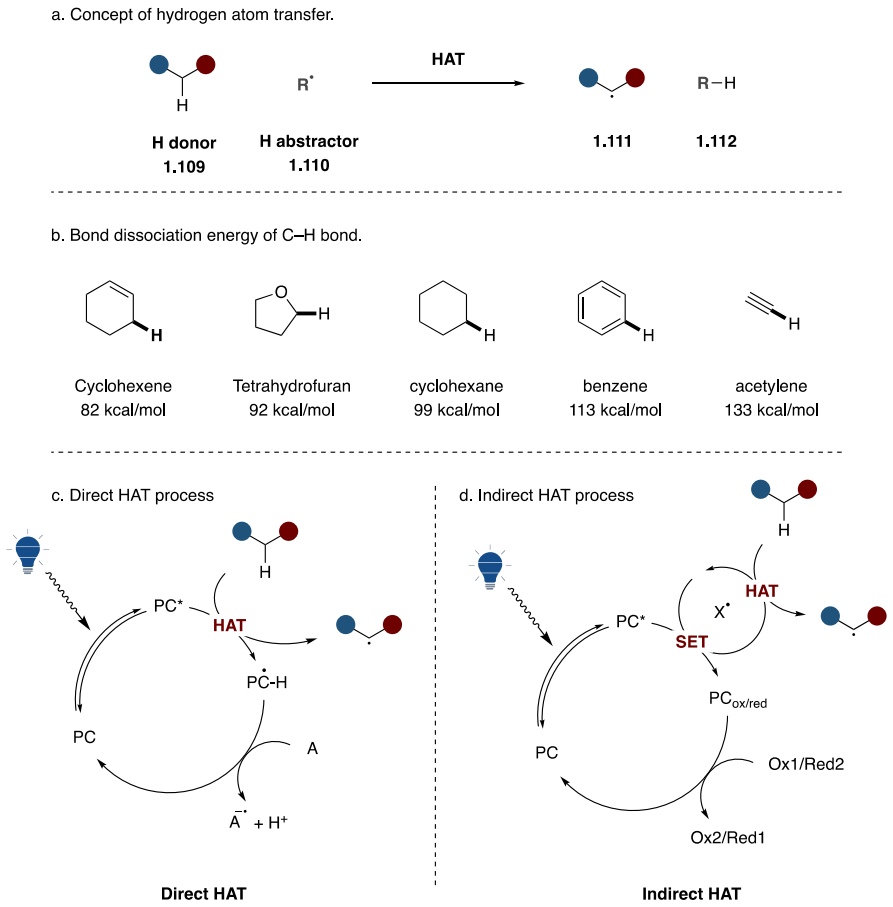
Scheme 1-16: Ir- and Cu-mediated fluorination of aryl thianthrenium salts.

The use of aryl thianthrenium salts has extended over the last decade.[75] Upon irradiation, the Ir^{III} photocatalyst **1.6** absorbs a photon leading, after ISC, to the excited triplet state of the photocatalyst (Ir^{III*}). After a sacrificial turnover of the photocatalyst with **1.100**, the byproduct **1.103** ($E_{1/2}$ ($TT^{\bullet+}$/ TT) = 1.26 V vs. SCE) undergoes single electron transfer with Ir^{III*} to generate the reduced Ir^{II} species ($E_{1/2}$ (Ir^{III*}/Ir^{II}) = 1.21 V vs. SCE) and the radical cation intermediate **1.108**. Single electron reduction of the aryl thianthrenium salt **1.100** (−1.5 V < $E_{1/2}$ ($ArTT^{+}$/ $ArTT^{\bullet}$) < –1.2 V vs. SCE) furnishes the desired aryl radical **1.104** and the byproduct **1.103**. At the same time, single electron oxidation of the Cu^{I} complex **1.107** by **1.108** generates a Cu^{II} species **1.105**, which subsequently intercepts the aryl radical **1.104** and a fluoride furnishing a Cu^{III} species **1.106**. Reductive elimination delivers the desired product **1.102**, regenerating the Cu^{I} catalyst.

Although it was not mentioned in the previous section, it is worth indicating that energy transfer induced by photocatalysts could also be involved in metallophotoredox catalysis.[76–78]

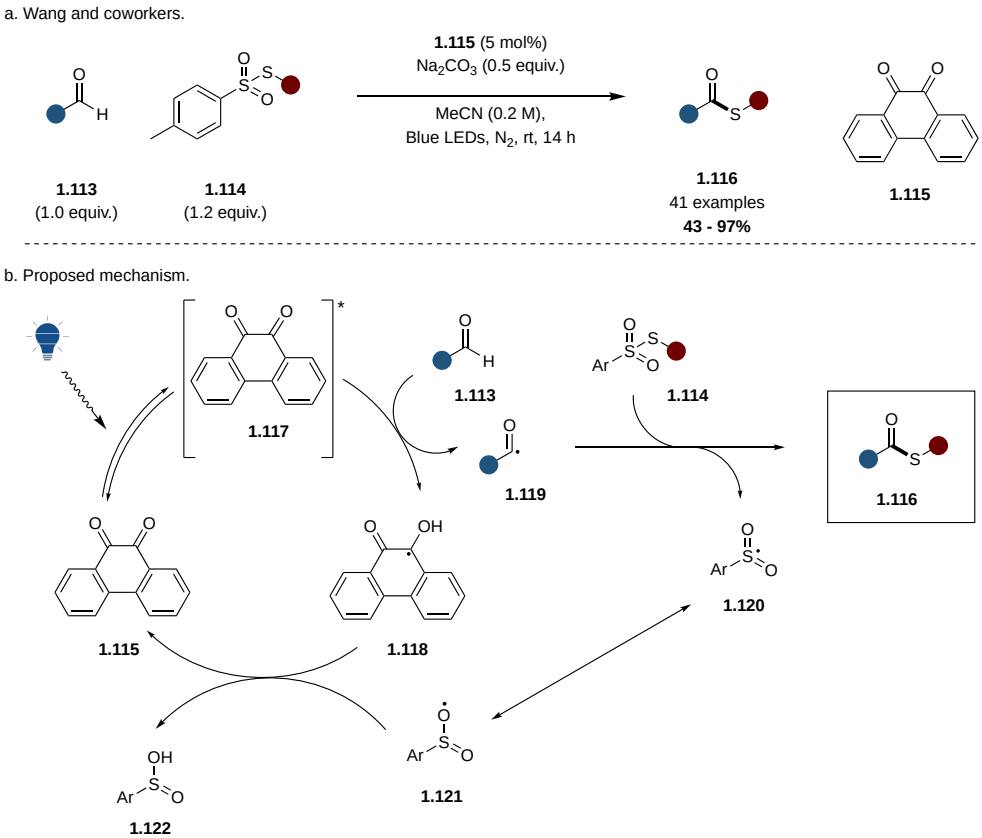
1.1.5 d-HAT

Hydrogen atom transfer (HAT) is a very common elementary step in photocatalysis, leading to the homolytic cleavage of a C–H bond, as depicted in Scheme *1-17*a.[15,16,79] This single step occurs between an H donor **1.109** and a radical H abstractor **1.110**. This process relies on the BDE (bond dissociation energy) of the C–H bond of the H donor, furnishing the radical **1.111**. Generally, the BDE represents the energy required to break apart the A–B bond into two radical species (A–B → A$^{\bullet}$ + B$^{\bullet}$). Thus, a low BDE highlights an easy bond to break. Moreover, a stabilised radical will be easier to form, hence resulting in a lower BDE. In the case of HAT processes, the BDE of C–H bonds is particularly important. For instance, HAT is more probable with cyclohexene (BDE = 82 kcal/mol) or tetrahydrofuran (BDE = 92 kcal/mol), than benzene (BDE = 113 kcal/mol) or acetylene (BDE = 133 kcal/mol) (Scheme *1-17*b).[52]



Scheme 1-17: a. General HAT process; b. Different BDEs of common organic molecules; c. Direct HAT process; d. Indirect HAT process.

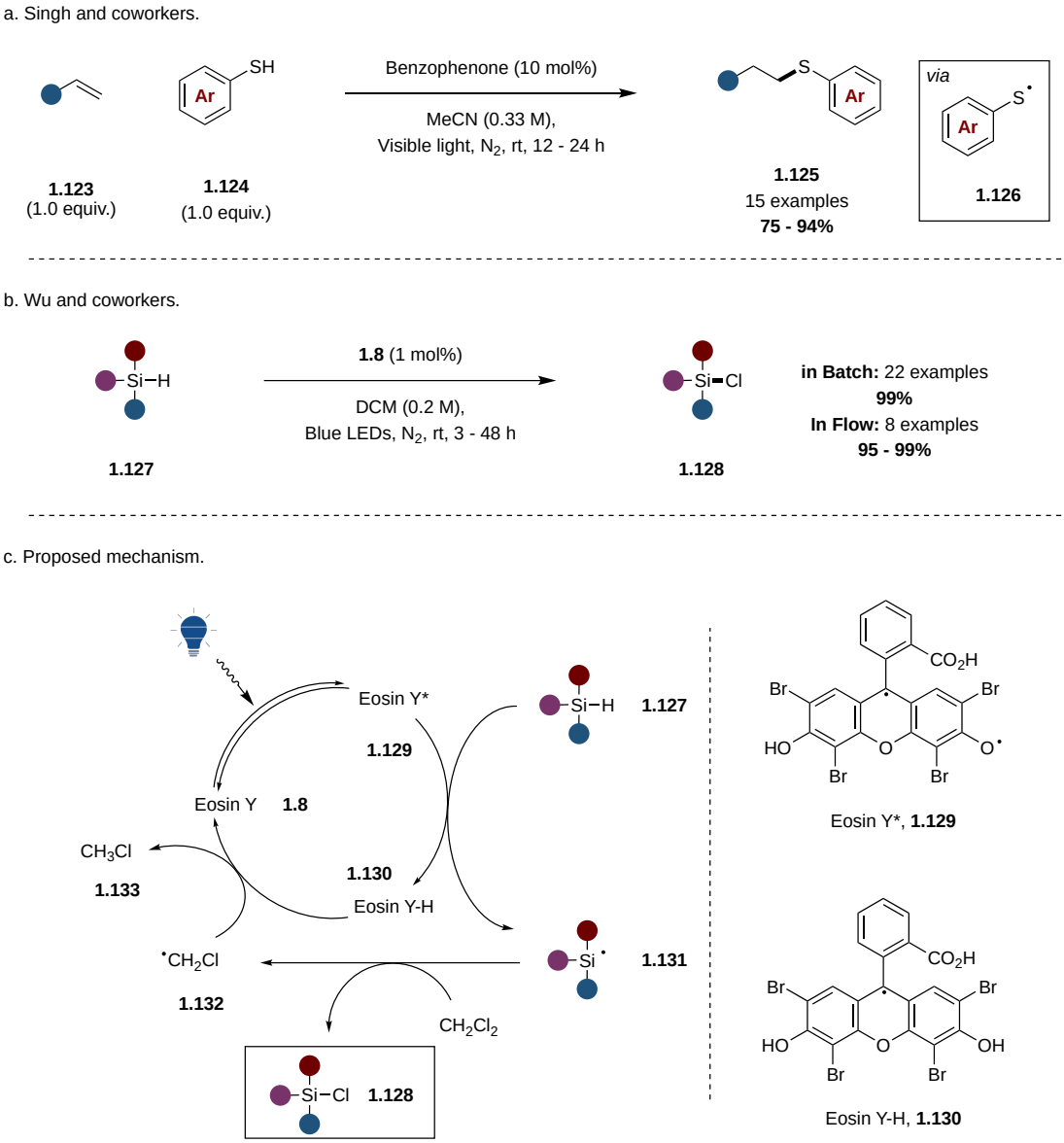
In photocatalysis, different HAT processes have been reported in the literature.[15,16,79] Indeed, HAT could be direct (d-HAT) where the photocatalyst is the H-abstractor and causes the homolytic C–H bond cleavage, as shown in Scheme *1-17*c. On the other hand, HAT could be indirect: the photocatalyst first reacts with a species (additive, second starting material, *etc*.), generating a radical (through a SET in Scheme *1-17*d, but could also come from EnT). Subsequently, HAT takes place between the generated radical and the H donor. Direct HAT requires the photocatalyst to have specific functional groups such as a ketone to be able to abstract the hydrogen atom from the substrate. Metal photocatalysts and some organophotocatalysts such as 4CzIPN can exclusively undergo indirect HAT. Only direct HAT will be discussed in this section, as several examples of indirect HAT have already been disclosed. For instance, Wang and coworkers published visible light-mediated thioester synthesis **1.116** using the diketone-based photocatalyst **1.115** in Scheme *1-18*.[80]



Scheme 1-18: Light-mediated thioesters synthesis developed by Wang and coworkers.

Under blue LEDs, 9,10-phenanthrenequinone **1.115** absorbs a photon to yield the excited species **1.117**, which undergoes the first HAT reaction with the aldehyde starting material **1.113**, leading to the acyl radical **1.119** and the radical **1.118**. The following radical **1.119** attacks the electrophilic thiosulfonate S-ester **1.114** generates the desired product **1.116** and the *S*-radical **1.120**, in resonance with the mesomeric *O*-centred radical **1.121**. A second HAT with **1.118** regenerates the photocatalyst **1.115**, available for another turnover, and sulfinic acid **1.122**. The reaction tolerates aryl and heteroaryl aldehydes, as well as alkyl aldehydes. The reaction was performed with several *S*-thiosulfonates ester such as *S*-aryl, *S*-alkyl, or even amino acid or sugar derived *S*-thiosulfonates esters. Finally, the reaction could be applied to more complex molecules such as steroids.

It is worth noting that HAT processes could also be involved with different bonds than C–H bonds. Singh and coworkers proposed a Giese-type reaction between terminal alkenes **1.123** and aryl thiols (or benzylthiol) **1.124** using benzophenone as a photocatalyst (Scheme *1-19*a).[81] The reaction involves HAT process between aryl thiols and the excited triplet state of benzophenone leading to the *S*-centred radical **1.126**, to yield a variety of thioethers **1.125**.



Scheme 1-19: Different HAT processes involving C–heteroatom bonds.

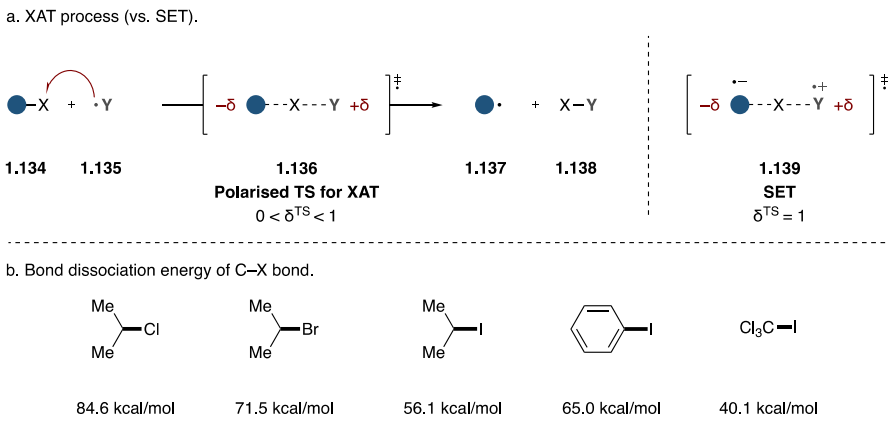
Wu and coworkers reported a homolytic cleavage between a Si–H bond using 1 mol% of Eosin Y **1.8** as photocatalyst (Scheme *1-19*b).[82] Upon absorption of a photon, the excited state **1.129** of Eosin Y undergoes a HAT process with the silane component **1.127**, generating a *Si*-centred radical **1.131** and Eosin Y-H **1.130** (Scheme *1-19*c). The silyl radical intermediate **1.131** subsequently abstracts a chlorine atom from the solvent to yield chlorinated silanes **1.128**, and **1.132**. This process is known as halogen atom transfer (XAT, *vide infra*). The radical species **1.132** undergoes HAT with **1.130**, regenerating the photocatalyst for another turnover. The reaction tolerates several (alkyl and aryl) trisubstituted hydrosilanes, as well as disubstituted or monosubstituted

hydrosilanes, affording the corresponding mono-, di- or trichlorinated products in quantitative yield. The reaction was also successfully applied to flow chemistry with eight examples. Mechanistic investigations such as cyclic voltammetry measurements, or luminescence quenching experiments (Stern–Volmer) ruled out potential SET and EnT. A new absorption peak corresponding to Eosin Y-H radical intermediate **1.130**, which is formed after reaction with silane, was observed in transient absorption spectroscopy, further supporting a HAT mechanism.

1.1.6 Others processes in photocatalysis

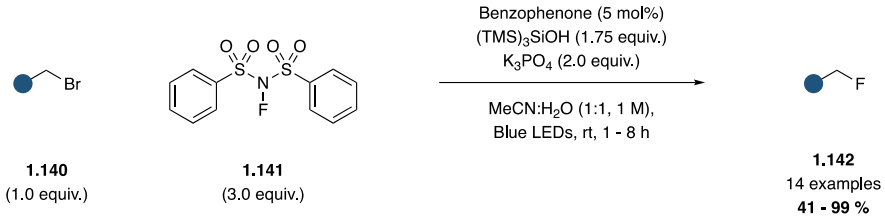
1.1.6.1 XAT process

The halogen atom transfer (XAT) process generates the *C*-centred radical **1.137** through a direct homolytic abstraction of the halogen atom **1.134** by a radical abstractor **1.135** (Scheme *1-20*).[83] Interestingly, a myriad of radical abstractors can be used to trigger the C–X bond cleavage and generate radicals **1.137**. The XAT process is no longer governed by redox potentials, but, unlike SET, relies on bond dissociation energies (BDE), as well as the polarisability of the C–X bond generating a polarised transition state **1.136**. For instance, XAT is more probable with trichloroiodomethane (BDE = 40.1 kcal/mol) or 2-iodopropane (BDE = 56.1 kcal/mol) than the corresponding 2-bromo (BDE = 71.5 kcal/mol) or 2-chloropropane (BDE = 84.6 kcal/mol).[83] It is worth noting that XAT differs from SET by the charge transfer involved of the transition state (**1.136** vs. **1.139**). The charge of the polarised TS for an XAT process varies between 0 and 1 (vs. 1 for a fast SET).



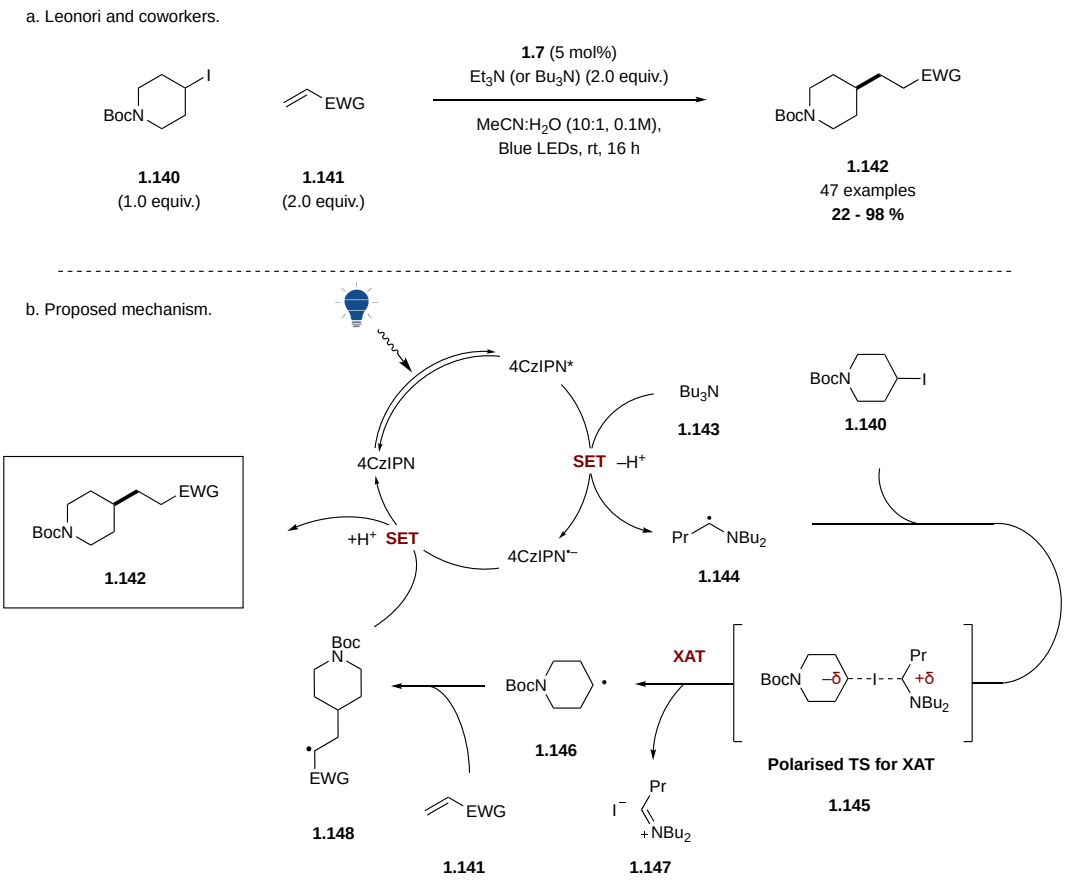
Scheme 1-20: The XAT process.

For instance, MacMillan and coworkers reported the use of tris(trimethylsilyl)silanol and benzophenone as photocatalyst to generate alkyl radicals from the corresponding alkyl bromides **1.140** in the presence of NFSI **1.141**, as shown in Scheme *1-21*.[84]



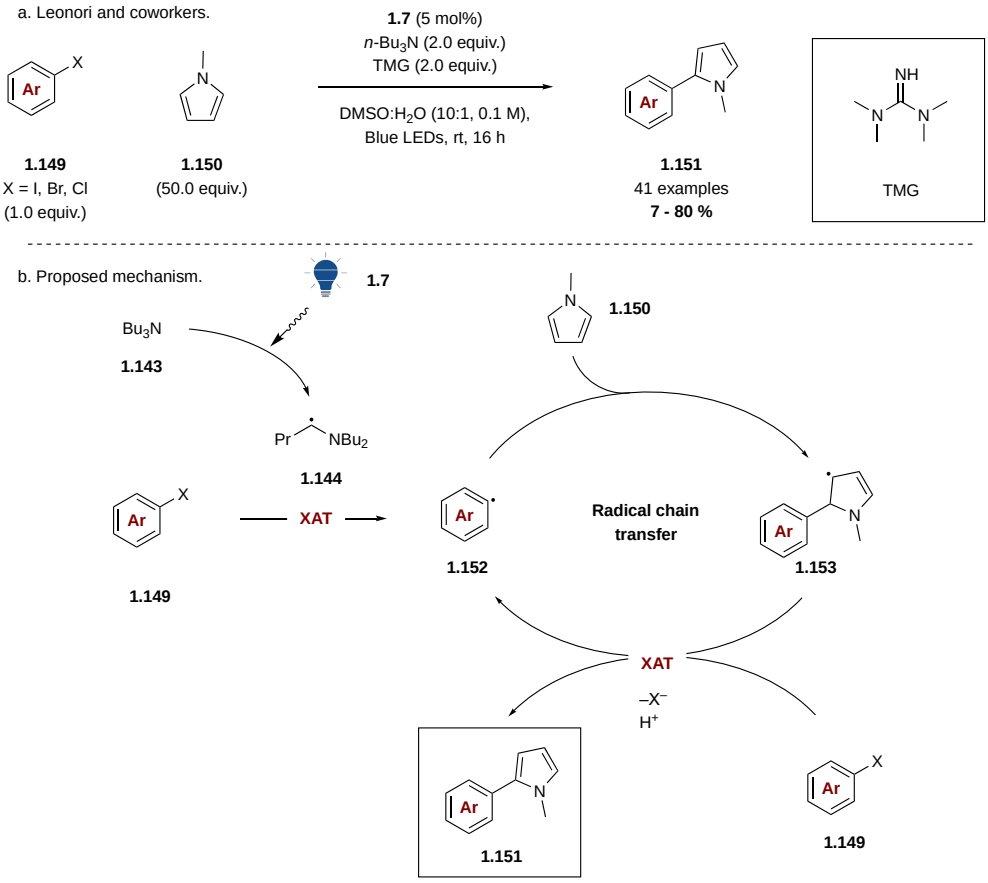
Scheme 1-21: Photocatalysed fluorination of alkyl bromides.

Leonori and coworkers developed a metal-free Giese-type addition of alkyl radicals to electron-poor olefins **1.141** using 4CzIPN under blue LEDs (Scheme *1-22*).[85] The XAT process allows the reduction of alkyl halides **1.140** through a polarised transition state **1.145** that would not be possible through a direct single electron transfer ($E_{1/2}$ = –2.35 V vs. SCE for Boc-protected 4-iodopiperidine **1.140**).[85]



Scheme 1-22: Giese-type addition of alkyl radicals generated by XAT.

Leonori and coworkers proposed the following mechanism: upon excitation, 4CzIPN oxidises the base **1.143**, which after deprotonation, affords the key *α*-amino radical **1.144**. This latter undergoes XAT with the alkyl halide **1.140**, furnishing the alkyl radical **1.146** *in situ*, through the polarised transition state **1.145**. Further interception by a suitable coupling partner such as Michael acceptors **1.141** delivers the radical **1.148**.[85] Finally, SET furnishes the desired product **1.142** and turns over the photocatalyst. Furthermore, XAT processes have been extended to aryl halides. For instance, the Leonori lab developed a coupling reaction between aryl halides **1.149** (iodides, bromides and chlorides) with *N*-methylpyrrole **1.150** (Scheme *1-23*).[86] In this case, 4CzIPN initiates the reaction by a SET with the base to furnish the *α*-amino radical **1.144**. Subsequently, this latter undergoes a XAT process with aryl halides **1.149** to deliver the corresponding aryl radicals **1.152**. Trapping with **1.150** delivers the radical intermediate **1.153**. A radical chain propagation (*vide infra*) is then proposed to occur between the radical **1.153** and the aryl halide starting materials **1.149** to deliver the desired product **1.151** and regenerating the aryl radical **1.152**.



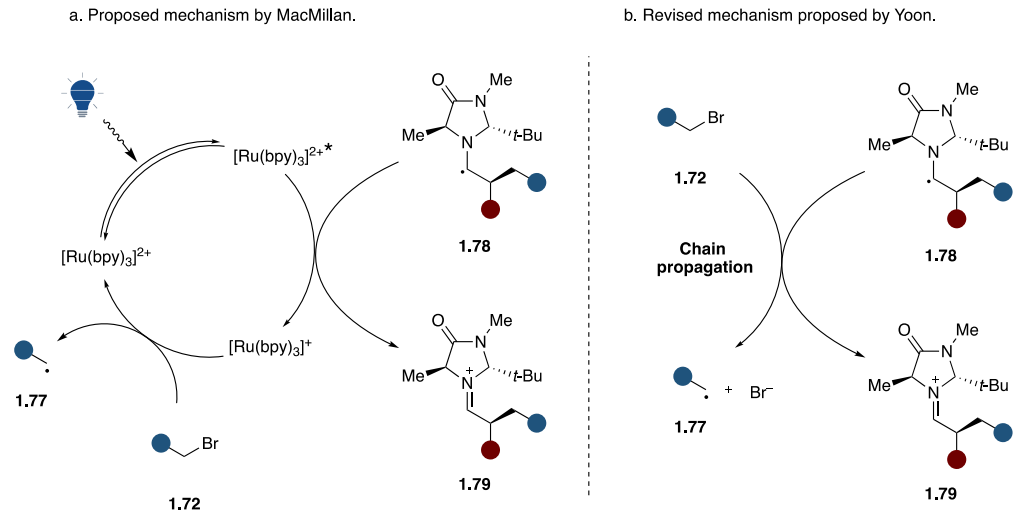
Scheme 1-23: Photoinduced coupling reaction between aryl halides and pyrroles.

1.1.6.2 EDA complexes

Electron donor acceptor (EDA), or charge-transfer complexes, can promote an electron transfer event under light irradiation without the presence of a photocatalyst.[13,87] The complex formation requires an electron-rich component (donor) with low ionisation potential and an electron-poor component (acceptor) with a high electron affinity. When mixing the two components together, they rapidly combine to form an encounter complex, called EDA complex, usually supported by an observable colour change of the reaction mixture. The complex exhibits new properties and a new absorption peak, called the charge-transfer band, at a higher wavelength than the absorption peaks of each component individually. Upon irradiation at this specific wavelength (charge-transfer band), a photoinduced electron transfer occurs between the two components furnishing a radical ion pair [$D^{\bullet+}$ $A^{\bullet-}$], which after dissociation generates free radicals. A few examples will be disclosed (*vide infra*) in this report.

1.1.6.3 Chain propagation

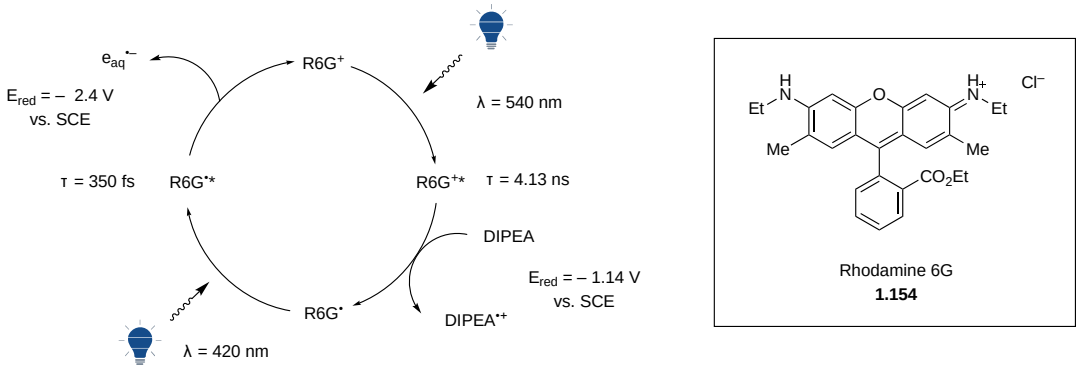
Although EnT and SET are the most commonly encountered photocatalysed processes, the representation of catalytic cycles could be idealistic in some cases. It is often implied that absorption of one photon leads to the formation of one molecule of product. This latter is usually obtained by SET from a radical product intermediate with the reduced/oxidised photocatalyst, closing the catalytic loop. However, in some cases, the radical product intermediate could react with the neutral starting material through a single electron transfer furnishing the product and another starting material radical intermediate.[88] This chain transfer process is often not considered; however, Yoon and coworkers have proven that several photocatalytic methodologies exhibit a significant chain propagation component within the formation of the product. For instance, they disagree with the proposed mechanism depicted by MacMillan and coworkers (Scheme *1-13*) and propose a radical chain propagation after measuring quantum yield and luminescence quenching measurements (Scheme *1-24*).



Scheme 1-24: Proposed and its revised mechanisms.

1.1.6.4 Consecutive photoinduced electron transfer

In the case of SET, the photocatalyst is excited upon absorption of a photon. In the presence of a strong sacrificial electron donor the excited triplet state of the photocatalyst PC* undergoes single electron reduction yielding the reduced $PC^{\bullet-}$ species. Upon absorption of a second photon (different energy), $PC^{\bullet-}$ can undergo excitation generating a very strong reducing $PC^{\bullet-*}$ species.[89] These species are usually short-lived and deactivation processes prevail with bimolecular reactions (through diffusion). In some cases, single electron oxidation of $PC^{\bullet-*}$ regenerates the photocatalyst in the ground state furnishing a 'hydrated' electron. Rhodamine 6G (R6G) **1.154** can absorb two consecutive photons leading to $R6G^{+*}$ (E_{red} = –1.14 V vs. SCE)[10] and subsequently $R6G^{\bullet*}$ (E_{red} = –2.4 V vs. SCE)[90] which exhibits a stronger reducing character (Scheme *1-25*).[91]



Scheme 1-25: Consecutive photoinduced electron transfer with Rhodamine 6G.

1.2 Generalities about organoboron

Organoboron compounds are one of the most important reagents in chemistry and are nowadays involved in a myriad of chemical transformations.[92] The first significant contribution in boron chemistry dates from early 1950 and was carried out by Brown, who devoted his career to the development of organoboranes. Brown was awarded the Nobel Prize in 1979 and left the chemistry world an important named reaction: the Brown oxidation.[93] Since then, the development of organoboron-involved reactions has considerably increased and led to another Nobel prize in this field in 2010 for Suzuki. This award acknowledged his work regarding the use of boronic acids in the Pd-mediated cross-coupling reaction with aryl halides.[94,95] Additionally, other transition metal cross-coupling reactions have been developed with organoborons such as the Chan–Lam reaction,[96,97] and Hayashi reaction.[98] Since their privileged exposure as coupling partners in the Suzuki–Miyaura cross-coupling reaction, organoborons have become one of the most powerful linchpins for synthetic chemists to access challenging bonds such as C–C, C–N, C–O, *etc*. For instance, the well-known Suzuki–Miyaura cross coupling reaction is one of the most used transformations in C–C bond forming reactions in the pharmaceutical[99,100] as well as the agrochemical industries.[101]

Because of their widespread use, organoborons became largely commercially available and usually are not prohibitively expensive. They can be found under different forms as depicted in Figure *1-7* (non-exhaustive list).

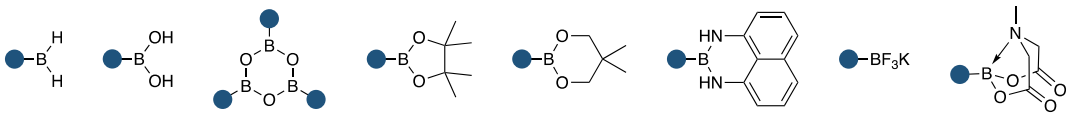


Figure 1-7: Diversity of organoboron compounds.

Due to its three valence electrons, the boron atom binds to three other atoms to form a planar trigonal structure resulting in a sp^2-hybridised boron atom with a perpendicular empty p-orbital. Depending on the boron atom substitution, the resulting molecule exhibits different properties. The most commonly used in organic chemistry are

boranes with three B–C/H bonds **1.155**, boronic acids with two B–OH bonds **1.156** and boronic esters with two B–OR bonds such as pinacol ester **1.158** or neopentyl glycol esters **1.159**. Due to the empty p-orbital, the boron atom exhibits Lewis acidic properties.[102,103] Thus, organoborons can also be found as boronates such as potassium trifluoroborate salts **1.161**. Moreover, another class of organoborons BMIDA (*N*-methyliminodiacetic acid boronic esters) **1.162**, involving electron donation from the nitrogen atom to the empty orbital, leads to very stable organoboron species.

As mentioned previously, the application of organoborons in C–C and C–heteroatom bond formations in synthetic chemistry has been well documented over the last 60 years. In addition to this, organoborons show interesting biological properties and boron-containing drugs have started to appear (Figure *1-8*).[104] In 2003, the FDA approved the first boron-containing drug, which was designed to treat multiple myeloma (bone marrow cancer). Since them a myriad of drugs has been developed such as Ixazomib **1.163** for the treatment multiple myeloma.[105] Tavaborole **1.164** is the first oxaborole antifungal agent approved by FDA in July 2014 and inhibits protein synthesis in the fungus, causing its death.[106] There are several boron-containing drugs waiting for approval such as GSK2878175 **1.166** which could be used as a single-dose treatment for chronic hepatitis C.[107]

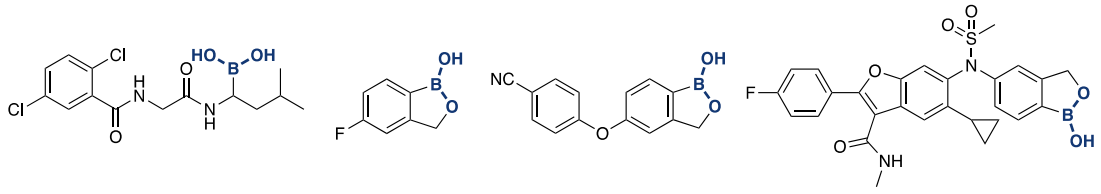


Figure 1-8: Boron-containing drugs.

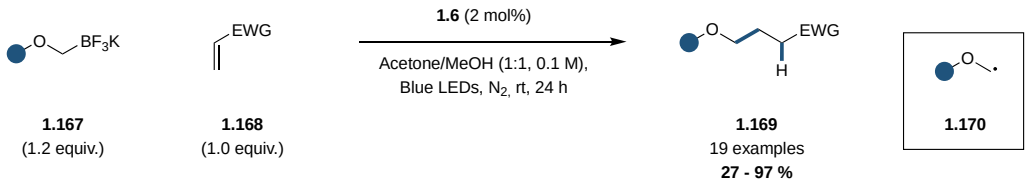
1.3 Use of organoborons in photoredox

With the importance of organoborons in synthetic chemistry and the increasing development of photocatalysis, the merge of the two fields could lead to a powerful toolbox to enable challenging bond formations from a wide organoboron pool.

Different approaches can be considered where organoborons act as radical precursors or radical interceptors.

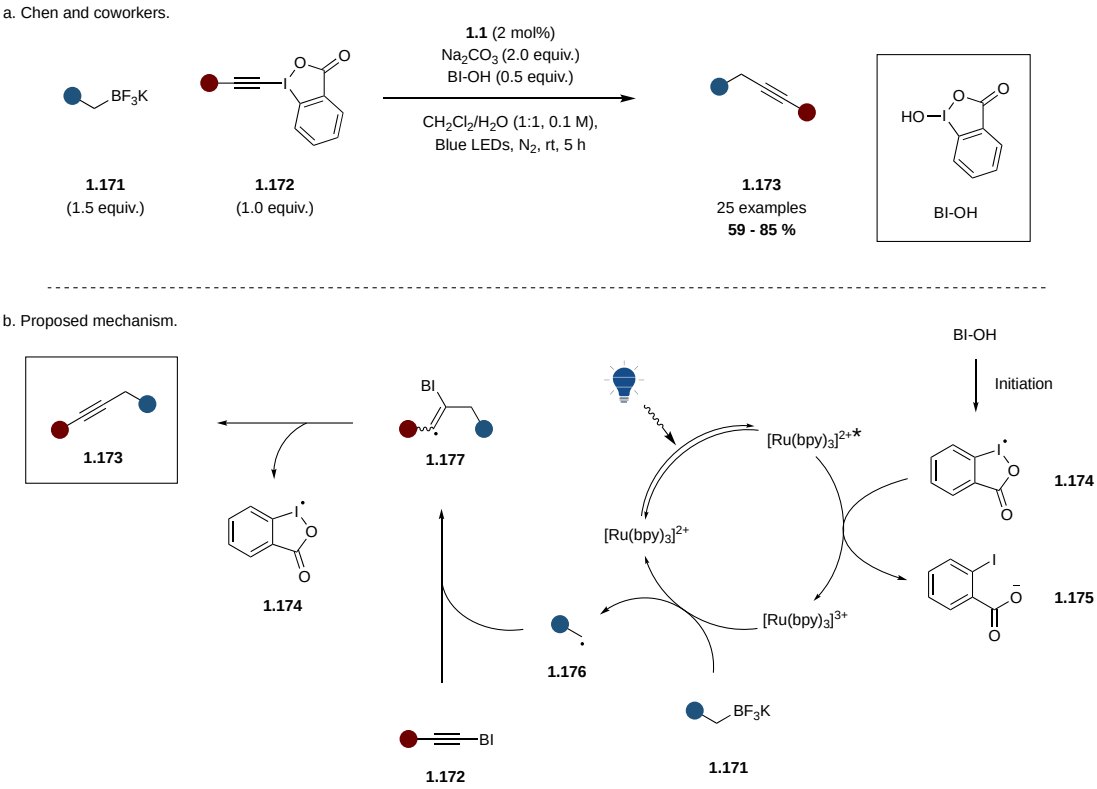
1.3.1 Organoborons as radical precursors

An important contribution of organoborons to the photocatalysis field is to access to new sources of alkyl or aryl radicals. Literature precedent revealed that transition metals such as manganese could lead to homolytic cleavage of C–B(F_3K) bonds furnishing alkyl radicals, supporting the radical behaviour of these species.[108] Consequently, alkyl BF_3Ks have been radical precursors of choice in photocatalysis.[109] In 2013, Akita and coworkers reported an Ir-photocatalysed hydroalkoxymethylation of electron-poor alkenes, as shown in Scheme *1-26*.[110] The methodology requires potassium alkoxymethyltrifluoroborate salts **1.167** to undergo single electron transfer with the excited photocatalyst to generate the alkyl radical **1.170**. This is further intercepted by electron-poor alkenes **1.168** under a Giese-type addition. Although the scope of the reaction was performed under blue LEDs, the benchmark reaction can also occur under sunlight, affording the product with a similar yield.



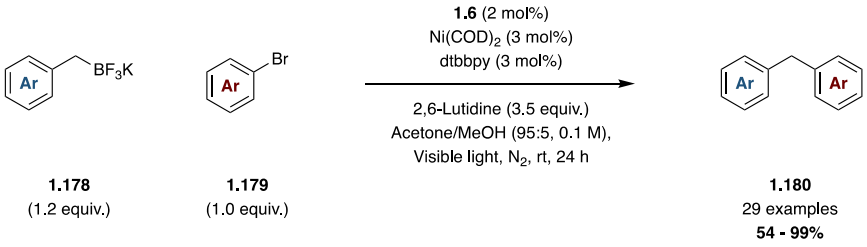
Scheme 1-26: An Ir-photocatalysed hydroalkoxymethylation developed by Akita and coworkers.

In 2014, Chen and coworkers reported a deboronative alkynylation reaction using potassium alkyltrifluoroborate salts **1.171** and alkynyl benziodoxoles **1.172**, as depicted in Scheme *1-27*.[111]



Scheme 1-27: Ru-photoinduced deboronative alkynylations.

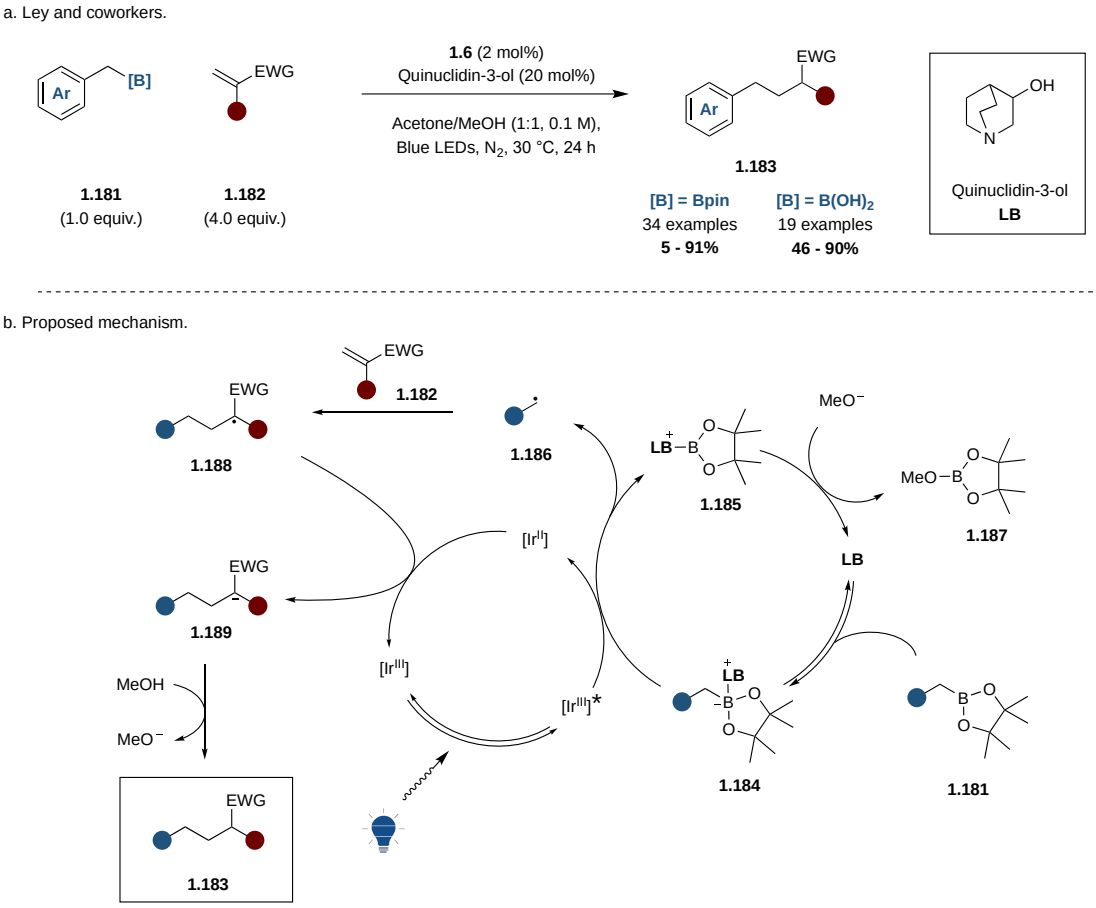
Upon absorption of a photon, the excited $Ru(bpy)_3^{2+}$* undergoes single electron oxidation with the benziodoxole radical **1.174** (or its precursor BI−OH) yielding the oxidised $Ru(bpy)_3^{3+}$ and *o*-iodobenzoic carboxylate **1.175**. Single electron reduction regenerates the photocatalyst and furnishes the desired alkyl radical **1.176** from alkyl BF_3K starting material **1.171**. This later undergoes α-addition to BI-alkyne **1.172** to give a sp^2 alkyl radical **1.177**. Finally, radical *β*-elimination leads to the desired product **1.173** releasing the benziodoxole radical **1.174**. Simultaneously, Molander and coworkers pioneered the use of benzylic BF_3K salts **1.178** as radical precursors in metallophotoredox catalysis (Scheme *1-28*).[112]



Scheme 1-28: Metallophotomediated $C(sp^3)$–$C(sp^2)$ cross-coupling reaction using benzylic BF_3Ks.

This methodology relies on tandem catalysis where the Ir-based photocatalyst generates the benzylic radical through SET prior to interception by the Ni catalyst through a single electron transmetallation.[113] The subsequent reductive elimination releases the cross-coupled product (see Scheme *1-15* for comparable mechanism). This methodology allows the use of C(sp^3)-hybridised nucleophiles in a cross-coupling reaction, whereas they are known to be sluggish and inefficient in the classic 2-electron Suzuki–Miyaura reaction. Indeed, a slower oxidative addition to the Pd complex is usually observed, as well as competing reactions such as β-hydride elimination lowering the efficiency of the coupling reaction. Examination of the reported substrate scope emphasises a great functional group compatibility and an excellent tolerance of a variety of aryl bromides and benzylic BF_3K salts.

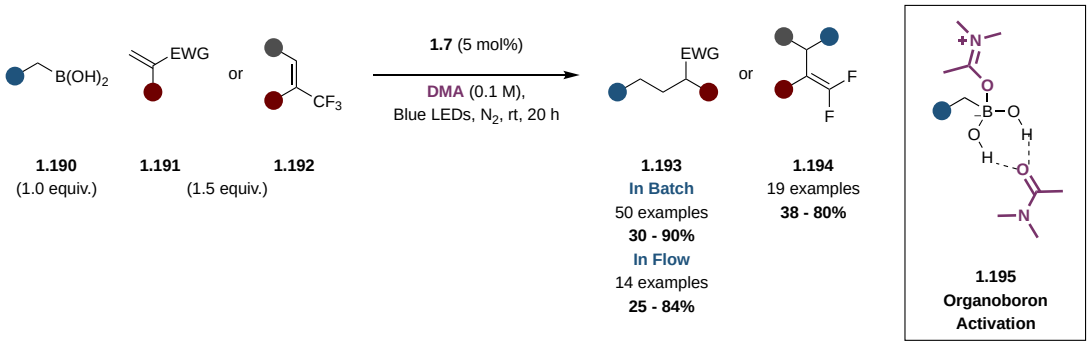
Although several methodologies using alkyl BF_3K salts have populated the field of radical formation, these methods have a drawback: the necessary synthesis of the starting materials from the corresponding alkyl boronic acids or boronic pinacol esters. More general photoredox catalysed radical formations from organoborons have been developed through an *in situ* boronate formation.[114] For instance, Ley and coworkers reported a tandem approach to generate benzylic radical **1.186** from $B(OH)_2$ and Bpin **1.181**, as depicted in Scheme *1-29*.[115] The use of a catalytic Lewis base (quinuclidine-3-ol) furnishes a boronate **1.184**, which can further undergo SET with the photocatalyst.



Scheme 1-29: Lewis base activation of alkyl $B(OH)_2$ and Bpin for the generation of alkyl radicals.

Screening of Lewis bases revealed that quinuclidine-3-ol gave the best result. This base coordinates with the empty p-orbital of the organoboron to form the boronate species **1.184**. Cyclic voltammetry showed that the boronate formation lowers the oxidation potential. 4-Methoxybenzyl boronic acid pinacol ester has a redox potential $E_{1/2}$ = 1.43 V vs. SCE, whereas the addition of one equivalent of DMAP decreases this to $E_{1/2}$ = 0.81 V vs. SCE. SET can occur with the excited state of the photocatalyst ($E_{1/2}$ (Ir^{III*}/Ir^{II})= 1.2 V vs. SCE) furnishing the alkyl radical **1.186** and **1.185**. On one hand, hydrolysis of **1.185** with a methoxide anion regenerates the Lewis base, releasing **1.187**. On the other hand, the alkyl radical **1.186** undergoes a Giese-type addition with an electron-poor alkene **1.182**, furnishing **1.188**. Radical polar crossover through SET leads to the formation of the carbanion **1.189**, which deprotonates methanol to generate the desired product **1.183**. The reaction occurs with both benzylic $B(OH)_2$ and Bpin with good to excellent yields, as well as with alkyl organoborons (10 examples reported). In 2021, Sharma and coworkers reported a solvent assisted activation of

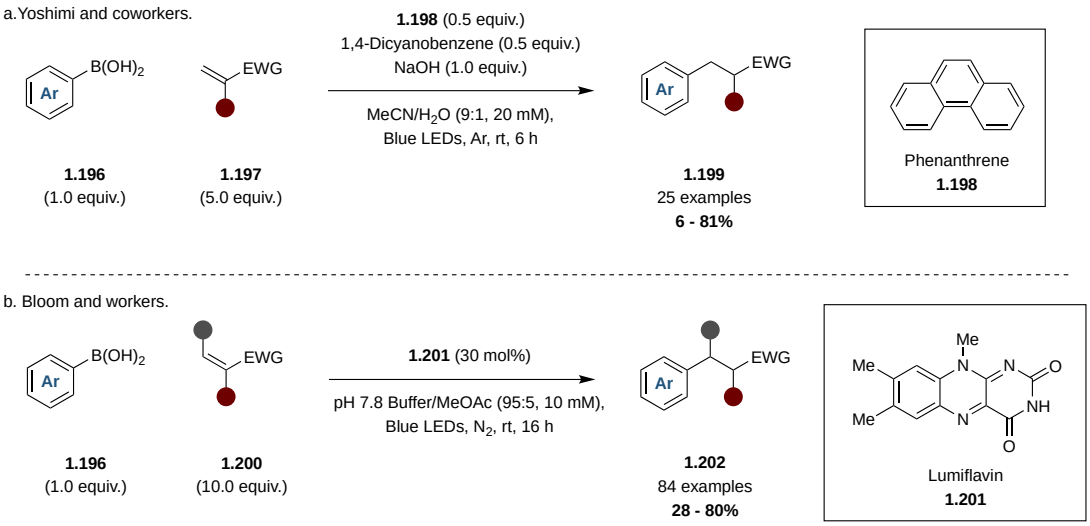
alkyl boronic acids towards the generation of alkyl radicals, as shown in Scheme *1-30*.[116]



Scheme 1-30: Solvent assisted activation of alkyl boronic acids.

The organoboronic acid **1.190** is activated with DMA and forms the complex **1.195** altering the redox potentials and thus promoting SET with 4CzIPN **1.7**. Alkyl radicals were then intercepted with electron-poor alkenes **1.191** under a Giese-type addition to afford products **1.193**. The reaction could be performed in batch as well as in flow affording excellent yields with great functional groups tolerance. Finally, radical addition to trifluoromethyl substituted alkenes **1.192** generates *gem*-difluroalkenes **1.194**. It is worth noting that in this case, the protonation of the carbanion intermediate (comparable to **1.189**) is slower than E_{1cb}-type fluoride elimination.

In 2018, Yoshimi and coworkers reported the formation of aryl radicals from the corresponding aryl boronic acids **1.196** (Scheme *1-31*a).[117] The generated aryl radical undergoes Meerwein type arylation with electron-poor alkenes **1.197**. Similar to both examples above, presence of a base activates the boronic acid through boronate formation, which can subsequently undergo photoinduced SET to generate products **1.199**. Milder conditions have been achieved by Bloom and coworkers in 2020 where strong base was not required.[118] The reaction could be run using a pH buffer with lumiflavin **1.201** as a photocatalyst to deliver the products **1.202** (Scheme *1-31*b).

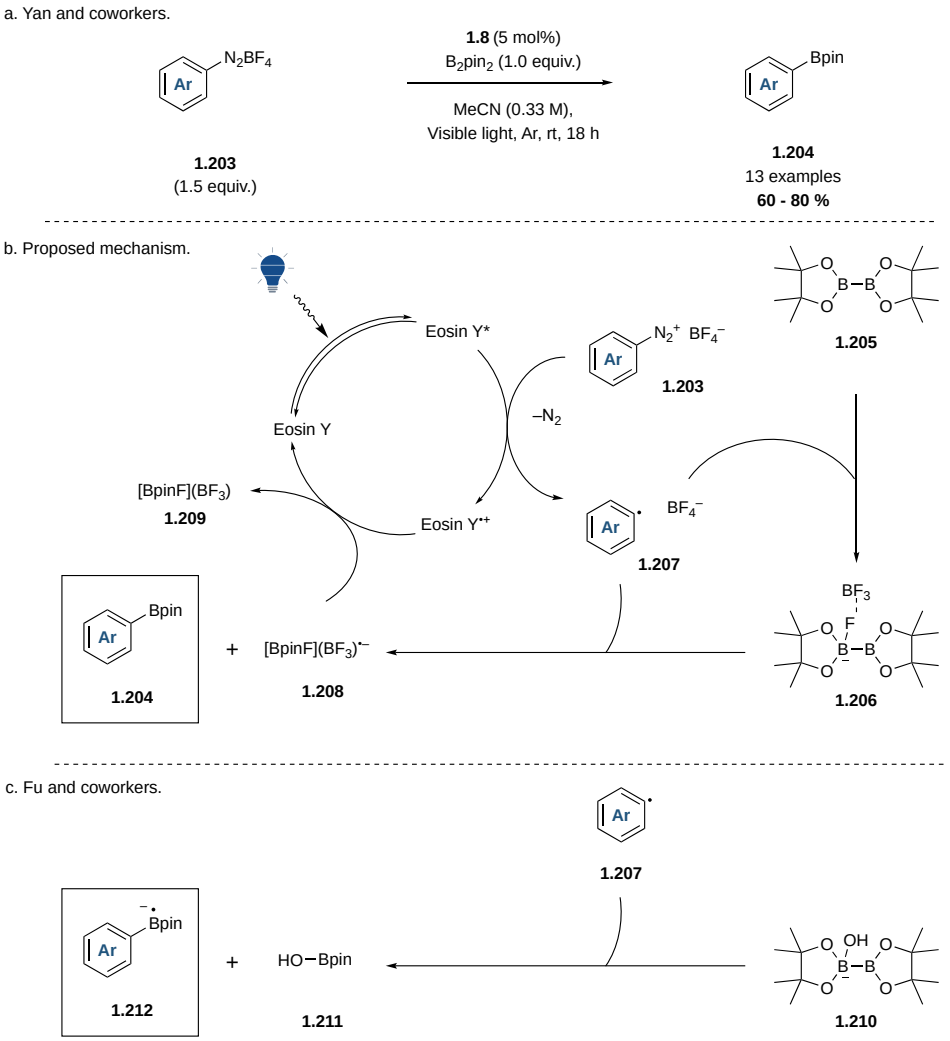


Scheme 1-31: Photo-Meerwein type arylation from aryl boronic acids.

1.3.2 Photocatalysed borylation: intercepting with bis-boronic esters

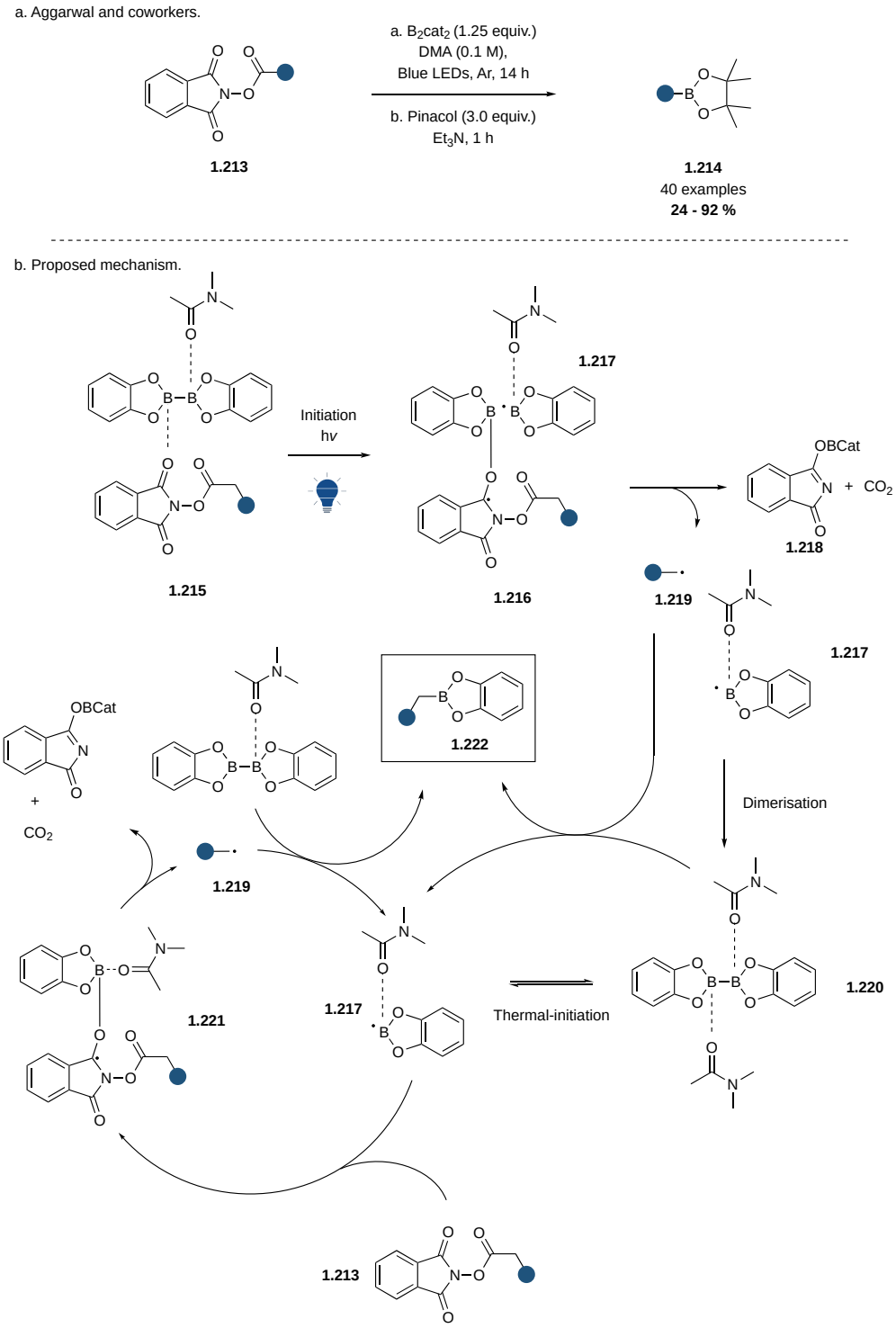
Historically, the access to boron-containing functionalities required harsh conditions and the use of organometallic reagents that could be detrimental to sensitive substrates. Alongside the development of Pd-mediated cross-coupling reactions, the Miyaura borylation made a significant breakthrough.[119] Since then, the number of methodologies to access the organoboron building blocks has soared and photocatalysis can also be employed as a tool to synthesise borylated substrates.[120,121] Interception of radicals with bis-boronic esters such as B_2pin_2 or B_2cat_2, or bis-boronic acid $B_2(OH)_4$ allows selective borylation of a great variety of substrates. In 2012, Yan and coworkers reported an Eosin Y-mediated borylation of aryl diazonium salts **1.203** using B_2Pin_2 **1.205**, as depicted in Scheme *1-32*a.[122] Upon excitation, the photocatalyst allows the generation of an aryl radical **1.1207** by single electron reduction of the starting material **1.203**. Simultaneously, the tetrafluoroborate counteranion (BF_4^-) in presence of B_2pin_2 **1.205** more likely dissociates, generating the active $[B_2Pin_2F](BF_3)^-$ adduct **1.206**. Radical trapping by **1.207** delivers the borylated product **1.204** and a radical intermediate **1.208**. In the formation of the boryl radical intermediate, it remains unclear whether the radical anion is formed on the side product **1.208**, as depicted by Yan's laboratory, or on the boron atom of the product **1.212**, as highlighted by Fu and coworkers in Scheme *1-32*c.[123] In both cases, the radical

intermediate (**1.208** or **1.212**) undergoes single electron oxidation with the photocatalyst furnishing the product **1.204** and the photocatalyst in the ground state.



Scheme 1-32: Photocatalysed borylation of aryl diazonium salts.

Aggarwal and coworkers reported a photoinduced decarboxylative borylation using redox active NHPI esters, as shown in Scheme *1-33*.[124] Similarly, DMA is crucial solvent choice and allows activation of the organoboron species.



Scheme 1-33 : Photoinduced borylation using NHPI esters.

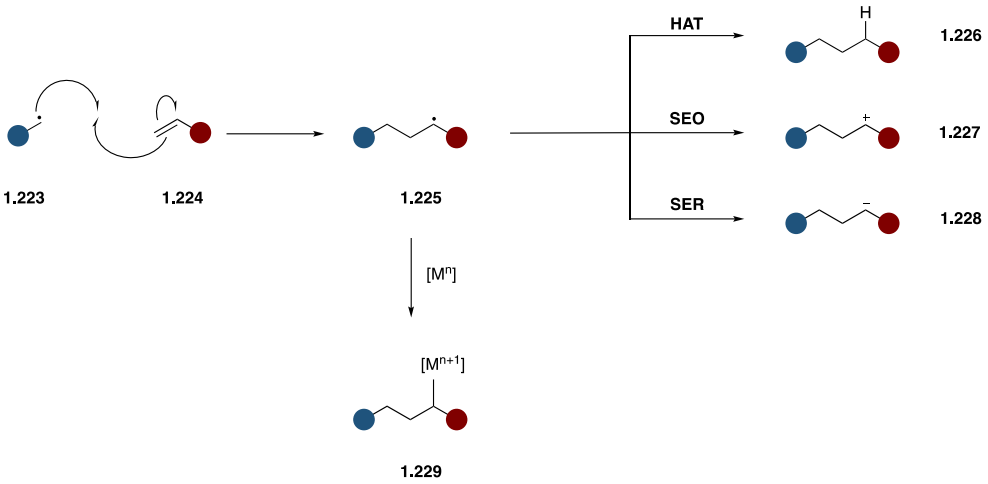
Treatment of the NHPI esters **1.213** with an excess of bis-boronic esters B_2cat_2 in DMA forms a three-component complex **1.215** in low concentration. Upon irradiation, **1.215** absorbs a photon yielding an excited species. Subsequent homolytic cleavage of the B–B bond furnishes two radical species: a DMA-stabilised boryl radical **1.217** and

a *O*-boryl-*N*-hydroxyphthalimide ester radical **1.216**. On one hand, **1.216** undergoes decarboxylation to generate an alkyl radical **1.219**, *O*-boryl phthalimide **1.218** and carbon dioxide. On the other hand, **1.217** dimerises, regenerating the DMA-stabilised B_2cat_2 complex **1.220**. Interception of the alkyl radical **1.219** by **1.220** forms the desired borylated product **1.222** and DMA-stabilised boryl radical **1.217**. A chain propagation mechanism was also postulated where **1.217** reacts with the NHPI ester **1.213** yielding **1.221**, and decarboxylation leads to the formation of the alkyl radical **1.219**. Addition of pinacol (and Et_3N) allows transesterification to more stable boronic acid pinacol esters **1.214**.

1.3.3 Giese-type reaction: intercepting a radical with vinyl organoborons

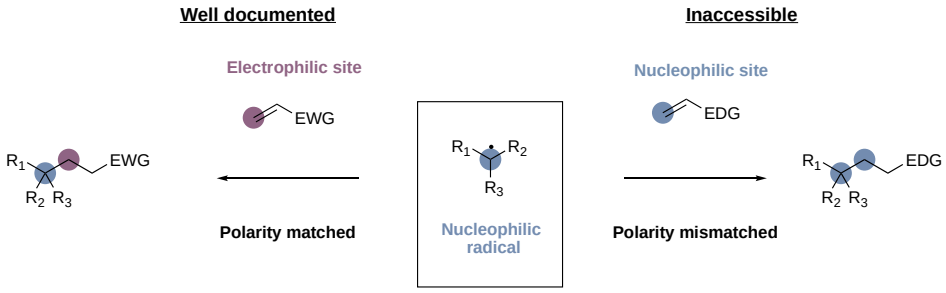
1.3.3.1 Generalities about Giese reaction

Although photochemistry has been in vogue over the last decade, radical addition to olefins has been known for over 40 years. Indeed, in the early 80's Giese pioneered the addition of nucleophilic *C*-centred radicals to Michael acceptors such as methyl acrylate or acrylonitrile, leading to the currently well-known Giese reaction.[125] The reactivity is governed by frontier molecular orbital interactions between the LUMO or HOMO of the alkene component and SOMO orbital of the radical. Alkyl radicals were usually made using toxic and heavy organometallics such as organotins or alkyl mercury salts.[126,127] The current development of photocatalysis affords a variety of ways to access alkyl radicals under mild conditions and, thus, photocatalysed Giese-type reactions have become a reaction of choice.[128,129] Radical addition **1.223** to **1.224** yields the radical intermediate **1.225**, which can undergo different processes as highlighted in Scheme *1-34*: (1) HAT with a H-donor affording **1.226**, (2) single electron oxidation or reduction yielding, respectively, the carbocation **1.227** or the carbanion **1.228**, or (3) interception by a transition metal furnishing the metal complex **1.229**.



Scheme 1-34: Mechanism for radical Giese-type addition to alkenes.

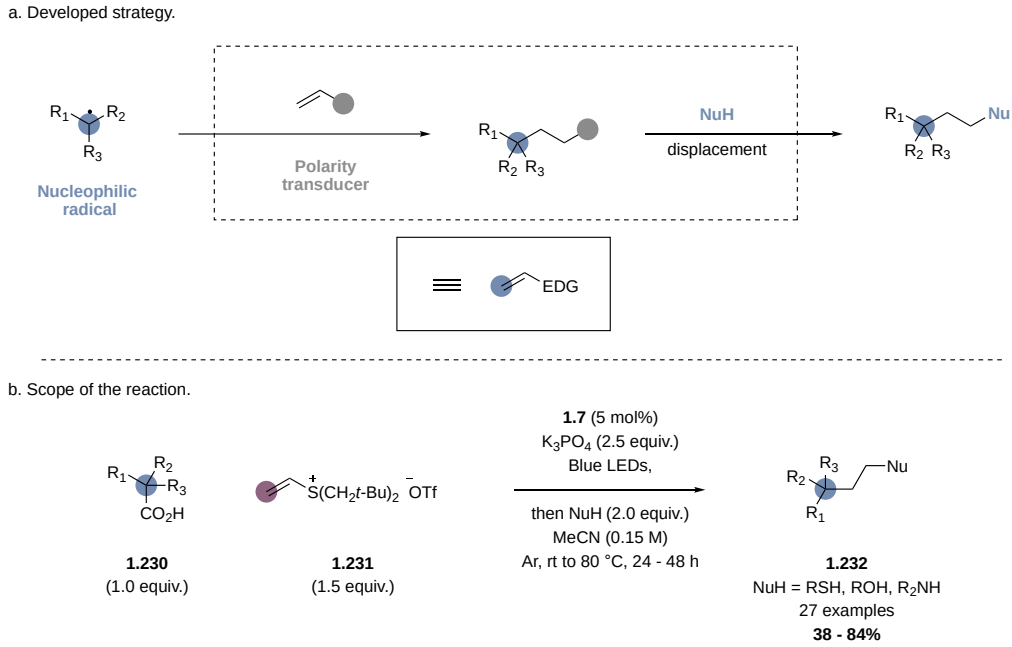
Several examples of Giese-type addition have already been reported previously in this introduction. A clear reactivity pattern can be depicted where a nucleophilic *C*-centred radical reacts with an electron-deficient alkene, as shown in Scheme *1-35*. In this case, the electron-rich SOMO orbital of the radical overlaps with the LUMO of the electron deficient alkene, as well as the HOMO to yield the desired product. The resulting interaction between the LUMO and the SOMO leads to a lower energy orbital, which can interact with the HOMO of the alkene in order to create the new bond.



Scheme 1-35: Polarity-matched and mismatched Giese-type addition.

Therefore, recent development of the reaction allowed broadening of the scope of electron-rich alkenes with electrophilic radicals.[130] New strategies have also been developed to access polarity-mismatched products, as displayed in Scheme *1-36*a. For instance, Silvi and coworkers recently reported a methodology to access a formal polarity-mismatched coupling reaction using vinyl sulfoniums as a polarity transducer in Scheme *1-36*b.[131] The *in situ*-displacement of the sulfonium moiety by a nucleophile

furnishes the formal polarity-mismatched products that could have been obtained with the corresponding electron-rich alkenes. The choice of the redox conditions and the sulfonium salt was crucial to avoid its elimination, giving alkyl styrenes.[132] Decarboxylation of carboxylic acid starting materials **1.230** generates alkyl radicals, further undergoing Giese-type addition to the vinyl sulfonium salt **1.231**. The sulfonium could be displaced with an alcohol, a thiol or an amine affording the desired product **1.232** in good to excellent yields. It is important to note that the reaction still relies on polarity-matched addition to the electrophilic site of the olefin partner.

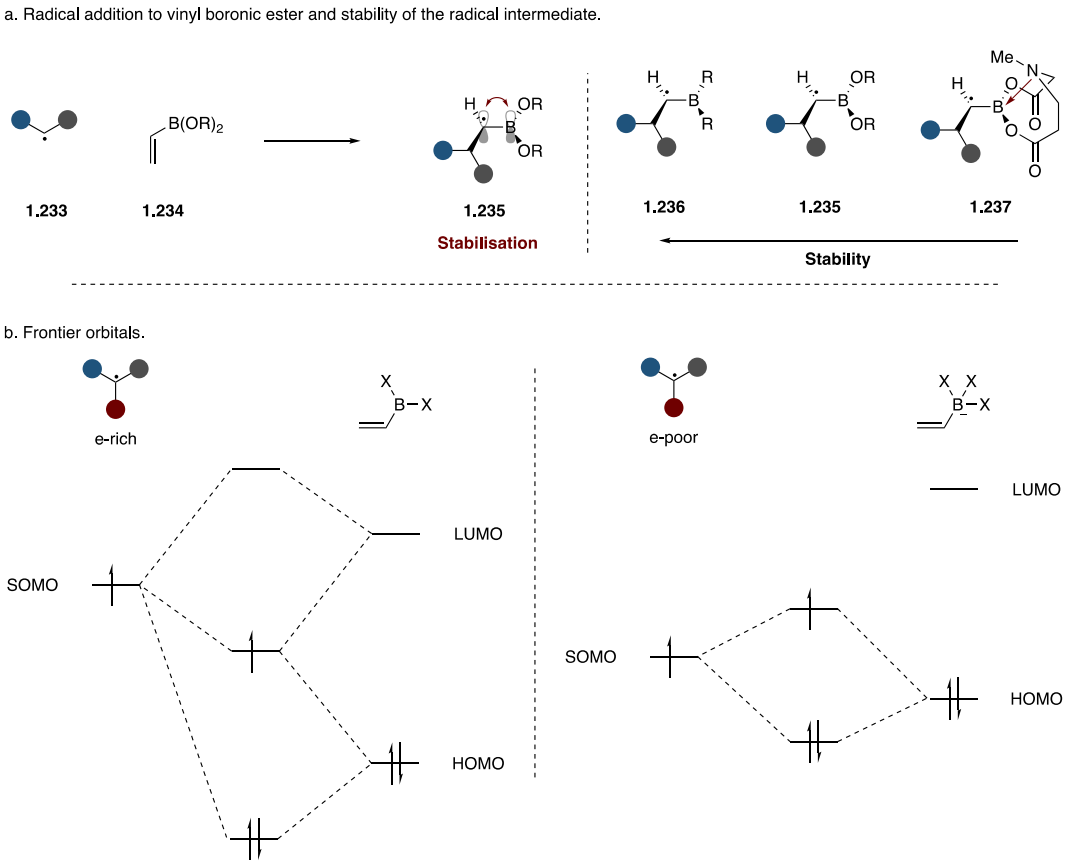


Scheme 1-36: Strategy developed by Silvi and coworkers towards a polarity-mismatched reaction.

1.3.3.2 Use of vinyl Bpin

Introduced by Matteson in the early 60's, the radical **1.233** addition to vinyl organoborons **1.234** generates an α-boryl radical intermediate **1.235** that exhibits interesting stability.[133] The empty p-orbital of the boron atom stabilises the adjacent *C*-centred radical leading to a versatile radical (Scheme *1-37*a). Indeed, Matteson showed that the reaction occurred with both nucleophilic and electrophilic radicals.[134] Consequently, α-boryl radical intermediates have been widely studied, highlighting the important of the substitution on the boron atom, which stabilises the generated

radical intermediate.[135] α-Borane radicals **1.236** are more stabilised than the corresponding α-boronic ester radicals **1.235**, because in the second case, the non-bonding electrons of the oxygen atom increase the electron density of the empty p-orbital of the boron atom, decreasing the hyperconjugation with the radical.[136] Similarly, α-BMIDA radicals **1.237** are less stable α-boryl alkyl radicals since the p-orbital of the boron atom is filled with the nitrogen lone pair of MIDA.[137] Radical addition to alkenyl organoborons has been significantly explored with an increasing interest in photocatalysed methodologies.[138]

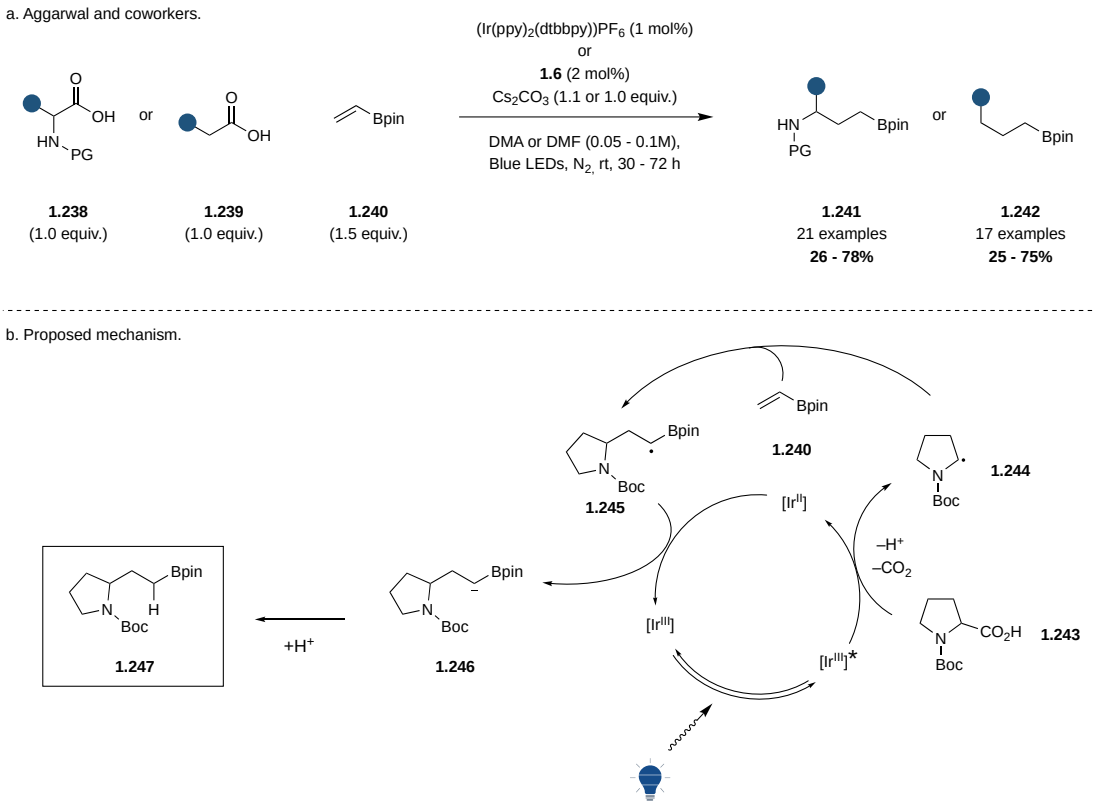


Scheme 1-37: Frontier orbital interactions in Matteson/Giese-type addition.

In most of cases in the Giese-type addition of an electron-rich radical to olefins (such as vinyl organoborons), the SOMO of the radical and the LUMO of the alkene have similar energies to offer significant overlap to allow bond formation (Scheme *1-37*b). Since organoborons exhibit a Lewis acidic character, addition of a base or a nucleophile leads to the formation of a more electron-rich boronate species. In this case, the HOMO of the vinyl organoboronate will display better affinity with electron-

poor SOMO of the radical. Therefore, boronate formation allows tuning of the reactivity towards the radical addition.[139]

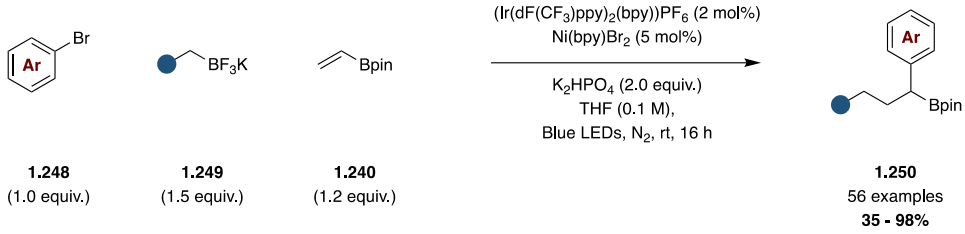
Aggarwal and coworkers reported a photoinduced decarboxylative radical addition to vinyl Bpin **1.240**, depicted in Scheme *1-38*,[140] which was further supplemented by a similar metal-free methodology using Eosin Y as a photocatalyst.[141]



Scheme 1-38: Photoinduced decarboxylative radical additions to vinyl Bpin.

Aggarwal and coworkers proposed the following mechanism: the carboxylic acid starting material, proline **1.243**, in this case, undergoes photoinduced decarboxylation with the excited triplet state of the Ir-based photocatalyst. After deprotonation with base, single electron oxidation leads to the collapse of **1.243**, furnishing a *C*-centred radical **1.244**. Giese-type addition to vinyl Bpin **1.240** generates the α-boryl radical intermediate **1.245**, which subsequently undergoes single electron reduction yielding the α-boryl anion **1.246**. Protonation delivers the desired product **1.247**. The reaction was first performed with protected amino acids **1.238** and furnished the corresponding γ-amino boronic esters **1.241** with good yields. The reaction tolerated both cyclic and aliphatic amino acids with different substitution motifs. They also successfully applied

this methodology to alkyl carboxylic acids **1.239** yielding **1.242** with similar yields. Similarly, Molander and coworkers reported a three-component photoinduced tandem reaction with a Ni catalyst, as shown in Scheme *1-39*.[142] As previously mentioned, the alkyl BF_3K salts **1.249** undergo single electron transfer to generate the alkyl radical. After addition to the olefin **1.240**, the α-boryl radical intermediate is intercepted by one of the Ni species (see Scheme *1-15*). Reductive elimination affords the desired product **1.250**. The expansive scope highlights the tolerance of the reaction towards a variety of radical precursors and aryl halides.



Scheme 1-39: Three-component Giese-type reaction with vinyl Bpin.

1.3.3.3 Use of boron-containing olefins

The alkyl addition to more substituted boron-containing olefins has also been documented. In previous Aggarwal's methodology, five examples were reported, shown in Figure *1-9*, of *α*- and/or *β*-substituted vinyl Bpin (**1.251 – 1.255**), which underwent radical addition with the *α*-amino proline-derivative radical intermediate **1.244**.[140]

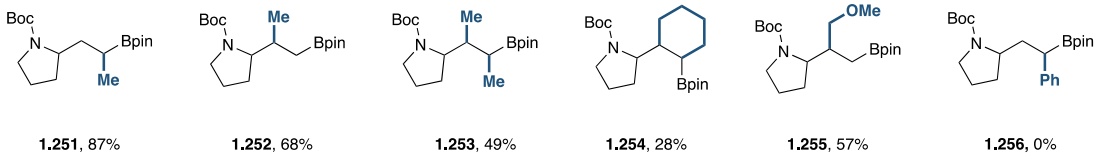
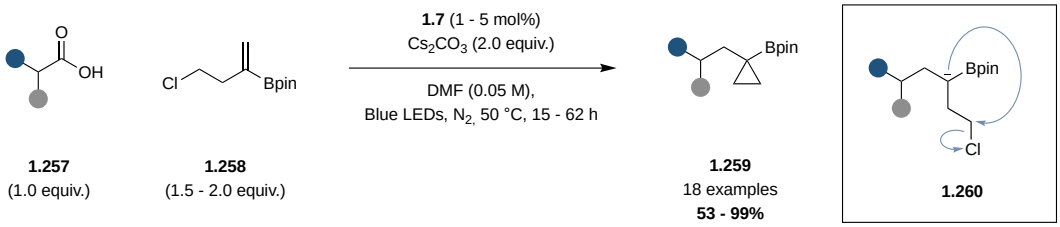


Figure 1-9: Scope of multi-substituted Bpin olefins.

Methyl substitution in either the *α*- or *β*-position afforded the desired products **1.251** and **1.252** with good to excellent yields. Dimethyl-substituted vinyl Bpin underwent radical addition affording **1.253** with a good yield. A cyclohexane backbone **1.254** plummeted the yield of the reaction and phenyl substitution **1.256** was detrimental due to rapid degradation of the starting material under the reaction conditions. In 2018, the

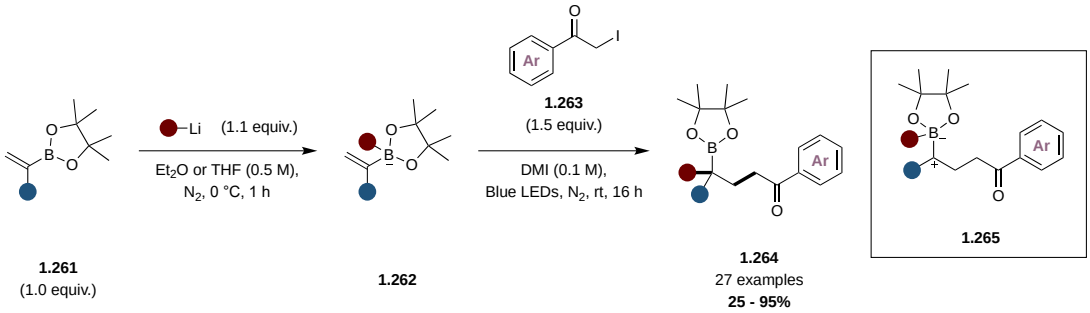
group developed a photoinduced methodology to access Bpin-substituted cyclopropanes using (4-chlorobut-1-en-2-yl)boronic acid pinacol ester **1.258**, as depicted in Scheme *1-40*.[143]



Scheme 1-40: Photoredox-catalysed synthesis of Bpin-functionalised cyclopropanes.

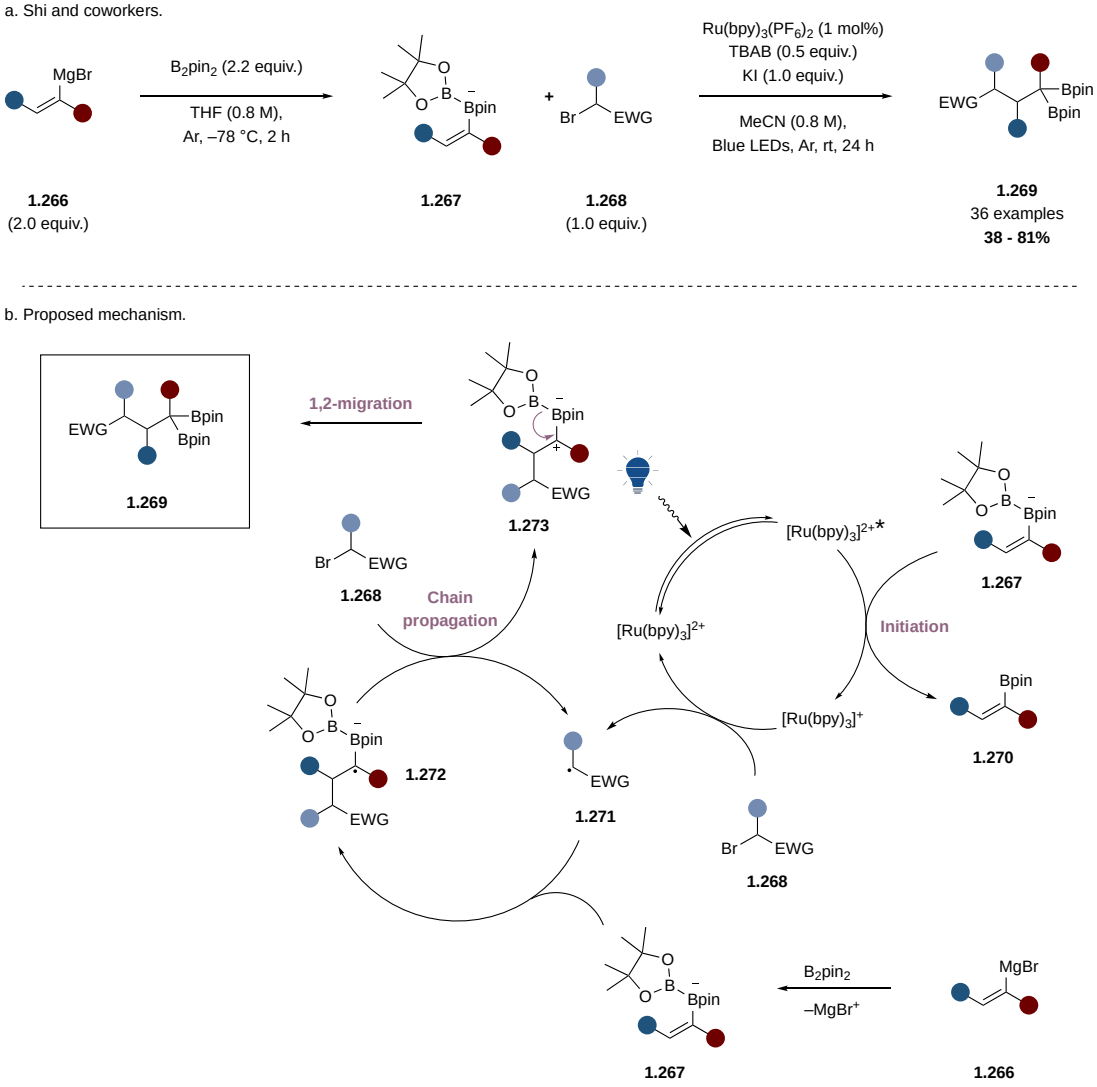
The reaction mechanism is similar to the one mentioned above (see Scheme *1-38*). Single electron reduction of the α-boryl radical intermediate furnishes the α-boryl anion **1.260**. Polar S_N2 displacement of the chloride leads to the formation of the Bpin-substituted cyclopropane products **1.259**. Although a homolytic substitution reaction S_H2 was considered, this hypothesis was ruled out since chlorine is a poor radical leaving group, much poorer than iodine, as reported by Suero and coworkers.[144,145] It is worth noting that the reaction also worked with a broad range of *gem*-disubstituted chloroalkenes and tolerates a diverse range of electron-withdrawing groups including esters, nitrile, primary amides, phosphonate esters, *etc.* as well as aryl substituents.

Electron-rich vinyl boronates has also been used to intercept more electrophilic radicals.[138,146] The initial work in this area used organometallics to generate boronate complexes and radical initiators to afford electrophilic radicals as highlighted by the work of Studer[147] or Renaud.[148] Vinyl boronates can also be used to intercept photoinduced radicals. In 2017, Aggarwal and coworkers reported photocatalysed 1,2-metallate rearrangement where blue LEDs initiate the homolytic cleavage of **1.263** furnishing the *C*-centred radical, as shown in Scheme *1-41*.[149] Boronate formation occurs using vinyl Bpin **1.261** and organolithiums. The electrophilic radical can undergo addition to the vinyl boronate **1.262**. Subsequent single electron oxidation with **1.263** (chain propagation mechanism) affords a carbocation **1.265** which can undergo 1,2-migration to yield the desired boronic ester products **1.264**.



Scheme 1-41: Photoinduced 1,2-metallate rearrangement using vinyl Bpin.

The same idea of 1,2-migration was used by Shi and coworkers in 2019 in their photocatalysed methodology to afford *gem*-bis(boryl)alkanes **1.269** using vinyl boronate complexes **1.267**, in Scheme *1-42*.[150]

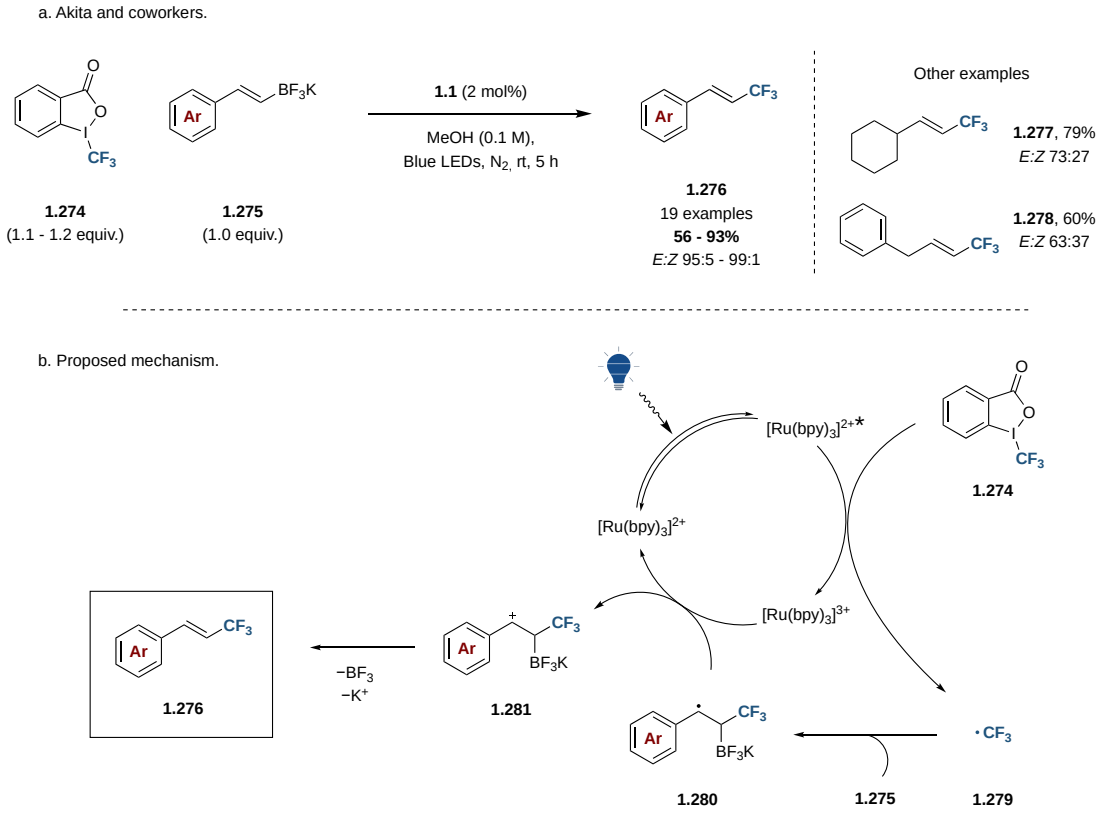


Scheme 1-42: Photocatalysed synthesis of *gem*-bis(boryl)alkanes.

The boronate species **1.267** is made *in situ* using the corresponding Grignard starting material **1.266** and B_2pin_2. Simultaneously, the photocatalyst initiates the formation of the electrophilic radical **1.271** by undergoing single electron reduction of alkyl bromides **1.268** (E_{red} = –1.24 V vs. SCE) after a sacrificial SET with **1.267** (E_{ox} = 0.21 V vs. SCE). Formation of **1.270** was confirmed by GC-MS. Radical addition of **1.271** to **1.267** delivers the radical intermediate **1.272**, which most likely undergoes SET with another equivalent of **1.268** to yield **1.273** through a polar cross-over chain transfer process. 1,2-Boryl migration from the carbocation **1.273** delivers the *gem*-bis(boryl)alkane **1.269**. The reaction tolerates a great variety of different electrophilic radicals with one or two electron withdrawing groups such as esters, amides, ketones or polyfluorinated motifs. The scope of the alkene components is much more limited with only seven examples, of which four are methyl-substituted olefins. The reaction tolerates *gem*-substituted bromophenyl alkenes but was not performed with *β*-bromostyrene.

1.3.3.4 Reaction with styrenyl organoborons

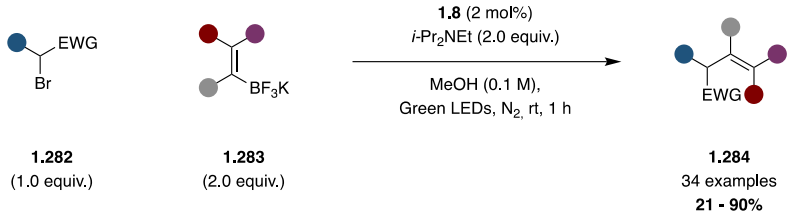
In 2013, Akita and coworkers reported a visible-light-induced trifluoromethylation protocol of styrenyl BF_3K salts, as shown in Scheme *1-43*.[151]



Scheme 1-43: Ru-photocatalysed trifluoromethylation of styrenyl BF_3K salts.

The radical precursor used in this transformation is Togni's reagent **1.274** which can undergo single electron reduction (E_{red} = –1.34 V vs. Cp_2Fe)[152] with Ru-based photocatalyst to furnish the electrophilic $CF_3^{\bullet}$ radical intermediate **1.279**. This latter is then intercepted by styrenyl BF_3K salts **1.275** to form a *β*-boryl radical intermediate **1.280**. Single electron transfer between Ru^{III} and **1.280** regenerates the photocatalyst in the ground state and the carbocation **1.281**. Elimination of the boronate moiety delivers the product **1.276**. Elimination of a *B*-centred radical (boryl radical) in **1.281** has been previously ruled out by Walton and coworkers.[136] Although most of the scope was performed with styrenyl BF_3K salts, the reaction also worked with an alkyl-substituted vinyl BF_3K salt and afforded the desired product **1.277** with a 79% yield.

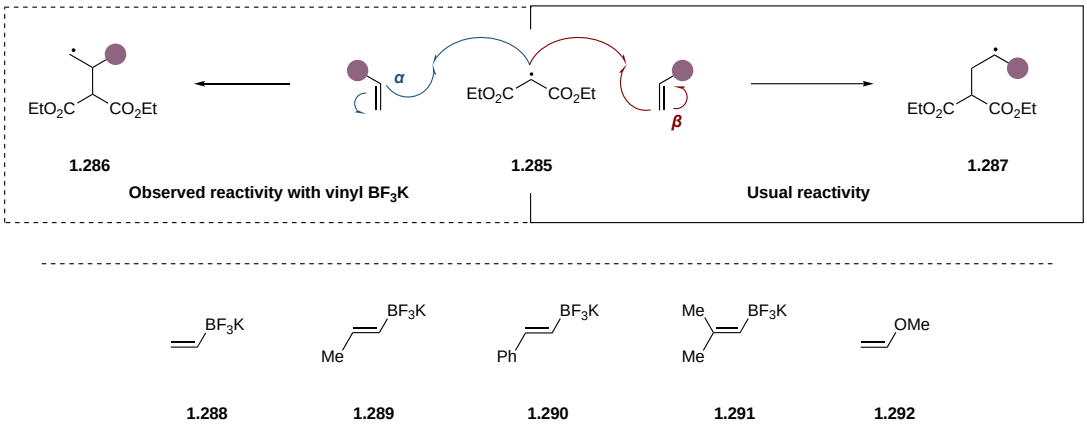
In 2017, Leonori and coworkers reported the use of BF_3K olefin salts **1.282** as coupling partners to afford alkyl-substituted alkenes **1.284**, after elimination of the boron moiety, as drawn in Scheme *1-44*.[153] Interestingly, they also observed that these species exhibit unusual reactivity upon electrophilic radical addition.



Scheme 1-44: Photoinduced electrophilic radical additions to substituted vinyl BF_3K salts.

Upon excitation, the excited triplet state Eosin Y* undergoes single electron oxidation ($E_{1/2}$ $EY^{\bullet+}/EY^{*}$= –1.11 V vs. SCE)[10] with alkyl bromide **1.282** (E_{red} = –0.62 V vs. SCE),[154] generating an electrophilic radical. Radical addition to the vinyl BF_3K salt **1.283** furnishes a similar radical intermediate as **1.280** mentioned in Scheme *1-43*. The radical undergoes *ipso*-addition to the vinyl BF_3K salts and leads to a *β*-boryl radical intermediate. Single electron oxidation yields a carbocation intermediate, triggering the formation of the product **1.284** after the elimination of BF_3.

Interestingly, these examples with vinyl BF_3K salts do not follow the usual Giese-type reaction trend where the radical addition occurs to the *β*-carbon of the olefin. Theoretically, two radical additions can be considered, as highlighted in Scheme *1-45*: (1) addition to the *α*-carbon of the olefin, leading to the radical intermediate **1.286** or (2) addition to the *β*-carbon of the olefin, leading to the radical intermediate **1.287**. In the case of vinyl BF_3K salts, DFT calculations were performed by Leonori and coworkers in order to understand the reactivity of these species.[153] First, the calculation of the ionisation energy ($A_g \rightarrow A^+_g + e^-$) and absolute electronegativity of **1.288** – **1.291** reveals a strong electron-rich character, stronger than the electron-rich methyl vinyl ether **1.292**. Secondly, they studied the radical addition of an electrophilic radical, diethyl malonyl radical **1.285**, to vinyl BF_3K salts by calculating the carbon spin density (in the triplet state) of the two potential radical intermediates **1.286** and **1.287**, as well as the enthalpy of the reaction.

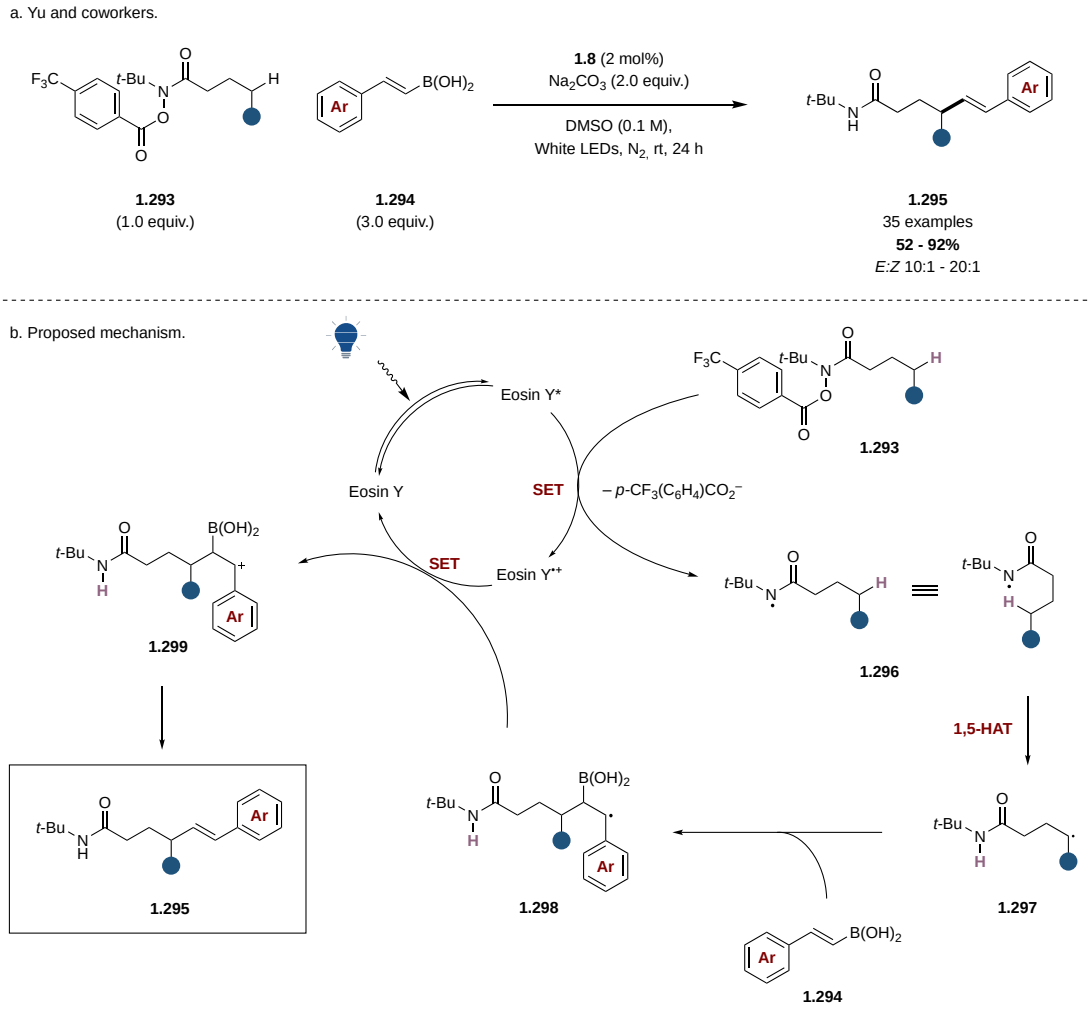


Atomic spin density					
	1.288	**1.289**	**1.290**	**1.291**	**1.292**
α	1.00	0.98	0.83	0.99	0.82
β	0.99	0.90	0.32	0.86	1.01
$-\Delta H_r$ KJ.mol^{-1}					
α	89.5	86.1	113.6	80.3	18.7
β	85.6	72.2	44.8	59.7	57.3

Scheme 1-45: Giese-type addition with vinyl BF_3K salts.

Electrophilic radicals such as **1.285** undergo Giese-type addition with electron-rich olefins such as **1.292**, on the *β*-carbon (vs. *α*-carbon) as suggested by DFT calculation ($-\Delta H_r(\beta) > -\Delta H_r(\alpha)$, in Scheme *1-45*). The calculations for vinyl BF_3K salts reveal a reactivity switch, indicating radical additions to the *α*-carbon rather than the *β*-carbon. Importantly, *β*-carbon vs. *α*-carbon addition to the styrenyl BF_3K salt **1.290** exhibits a very large difference, suggesting additional stabilisation of the benzylic radical intermediate from the adjacent phenyl substituent. Similar reactivity using styrenyl BF_3K salts was observed with non-photoinduced radical processes.[155] Furthermore, recently Meggers and coworkers reported an enantioselective nucleophilic alkenylation of ketones using styrenyl BF_3K salts by merging electrochemistry and asymmetric catalysis.[156]

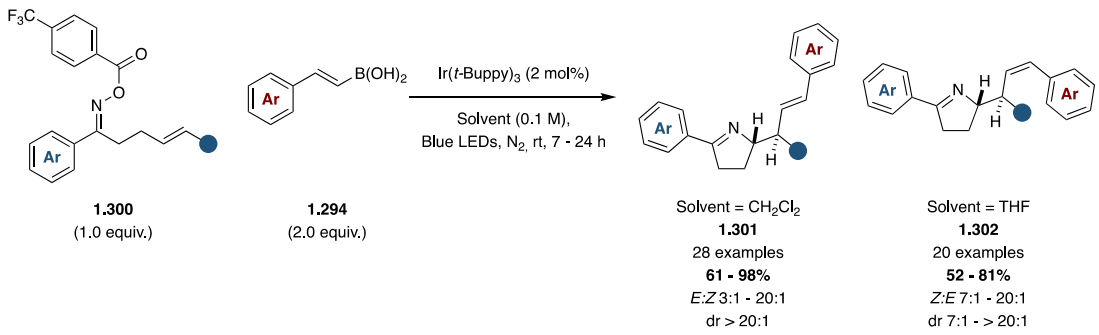
In 2018, Yu and coworkers reported the use of styrenyl boronic acids **1.294** to undergo *α*-carbon addition by a *C*-centred radical **1.297**, as shown in Scheme *1-46*.[157] They developed an Eosin Y-catalysed γ-vinylation of amides using hydroxylamine derivatives **1.293** as radical precursors and styrenyl boronic acids **1.294**.



Scheme 1-46: Photocatalysed γ-vinylation of amides using styrenyl boronic acids.

Hydroxylamine derivatives **1.293** are commonly used as *N*-centred radical precursor due to their weak N–O bond under photoredox conditions.[158] They undergo single electron reduction with the excited triplet state of Eosin Y, furnishing the amidyl radical **1.296** and the corresponding carboxylate anion as byproduct. Subsequently, 1,5-HAT occurs generating the nucleophilic radical **1.297**, which can be intercepted by styrenyl boronic acids **1.294** leading to **1.298**. Single electron oxidation regenerates the photocatalyst in the ground state and the carbocation **1.299**. Elimination of the boronate formed with the carboxylate byproduct delivers the desired product **1.295**. The reaction tolerates primary, secondary, and tertiary C–H bonds and affords the desired product with excellent yield. Both electron-rich and electron-poor styrenyl boronic acids were found suitable for this methodology. The modification of the protecting group on the amide (*t*-Bu) was essential and its change to other substituents such as Ph, or H were found detrimental to the reaction and side reactions were

observed due to the higher electrophilic character of the generated amidyl radical. Electron-withdrawing groups such as Ac or ethyl ester were not as good as the bulky *t*-Bu group. More recently they applied a similar methodology using oxime derivatives **1.300** as iminyl radical precursors (Scheme *1-47*).[159] The reaction now requires an Ir photocatalyst to first trigger the formation of the iminyl radical through a single electron transfer. It undergoes cyclisation to furnish a 1-pyrroline radical intermediate. The subsequent reaction with styrenyl boronic acids 1**.294** leads to the (*E*)-cinnamylpyrroline products **1.301** (see Scheme *1-46*). The reaction afforded excellent diastereoselectivity and exhibited interesting outcomes while changing the solvent. In the case where THF was used, the alkene undergoes isomerisation through energy transfer from the excited triplet state of the Ir photocatalyst to deliver the (*Z*)-products **1.302** (see section 1.1.3). Interestingly, this process does not occur when the reaction is carried out in DCM.

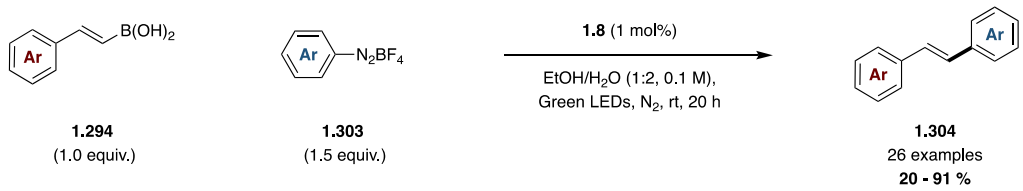


Scheme 1-47: Photocatalysed and solvent-enabled *E:Z* stereodivergent imino-alkenylation of alkenes.

DFT calculations of the different energy levels of both (*E*) and (*Z*)-cinnamylpyrroline products, and the photocatalyst in both solvents revealed different energy gaps between them. In the case of DCM, the energy of the triplet state of the catalyst (56.6 kcal/mol) is too high to transfer energy to the triplet state of the (*E*)-product (48.3 kcal/mol in DCM, $\Delta E = 8.3$ kcal/mol) or the (*Z*)-product (44.2 kcal/mol in DCM, $\Delta E = 12.4$ kcal/mol). Consequently, no energy transfer takes place in DCM. On the other hand, the difference between the triplet state of the catalyst (55.6 kcal/mol) and the products is lower in THF ($\Delta E = 5.9$ kcal/mol with the (*E*)-product and $\Delta E = 11.1$ kcal/mol with the (*Z*)-product), allowing the energy transfer to occur, and thus, furnishing the (*Z*)-product.

Similar reactivity using styrenyl boronic acids was observed with non-photoinduced radical processes, for instance Wu and coworkers reported the synthesis of (*E*)-alkylsulfonyl olefins using alkyl-pyridinium salt (Katritzky salts) and sodium metabisulfite.[160] Their proposed mechanism is very similar as the ones mentioned above and the only difference relates to the organoboron-assisted thermal activation of the Katritzky salts to generate alkyl radicals (vs. photoinduced radical formation).

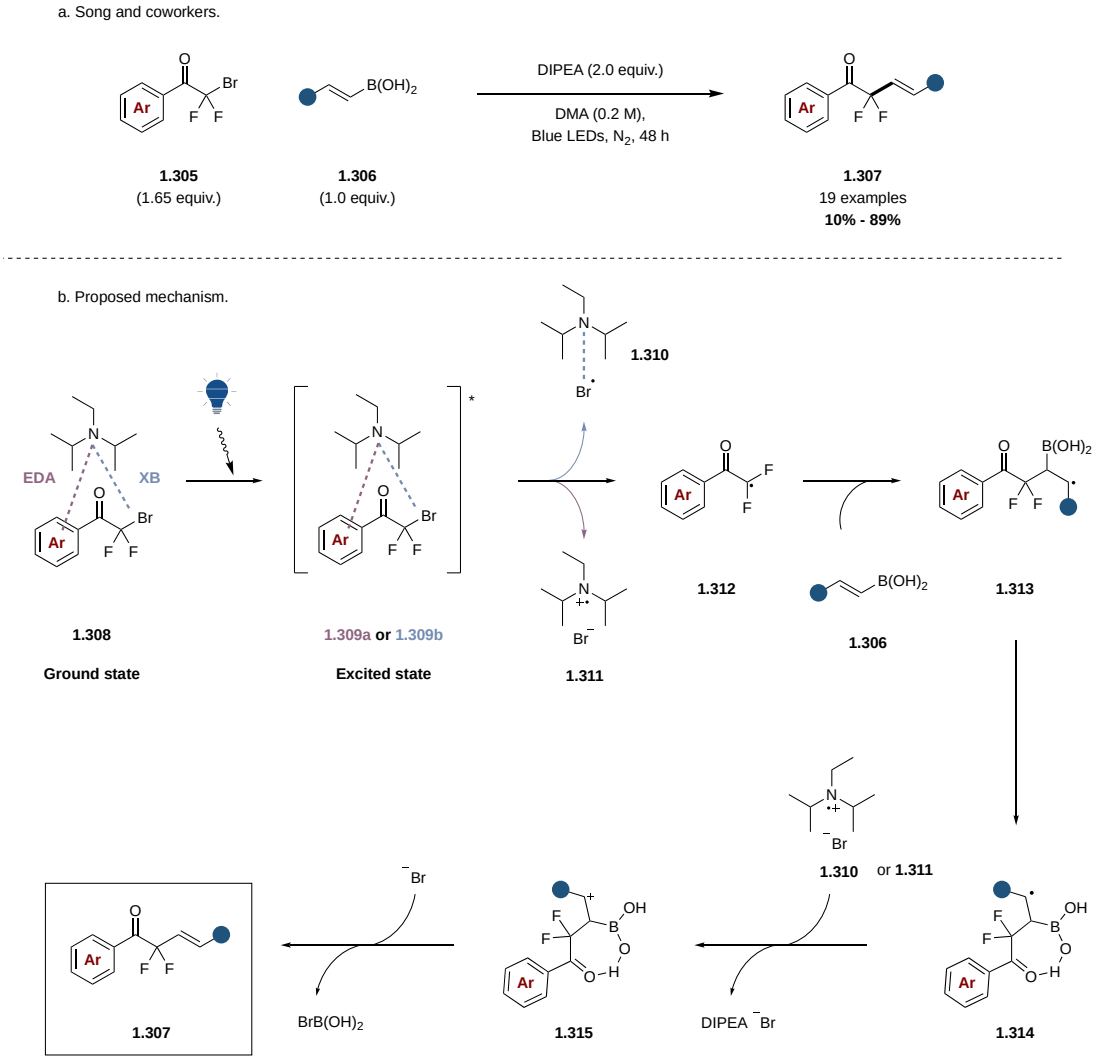
The use of styrenyl boronic acids has been recently employed with other radical precursors. Diazonium salts are common radical precursors of choice to furnish ambiphilic aryl radicals.[161] Wu and coworkers have recently disclosed the use of diazonium salts **1.303** and styrenyl boronic acids **1.294** to afford stilbenes **1.304**, under photoredox conditions (Eosin Y **1.8** and green LEDs), as depicted in Scheme *1-48*.[162]



Scheme 1-48: Photocatalytic coupling reaction between styrenyl boronic acids and aryl diazonium salts.

In 2023, Song and coworkers reported a photoinduced formal Suzuki–Miyaura coupling reaction between α-bromodifluoroacylarenes **1.305** and styrenyl boronic acids **1.306** (Scheme *1-49*).[163] The formation of the electrophilic radical has been postulated to be triggered by either the formation of an electron donor acceptor (EDA) complex where the tertiary amine is the electron donor component and **1.305** plays the electron acceptor component, or halogen bonding (XB) between DIPEA and **1.305**.[164] Upon absorption of a photon, the EDA complex undergoes excitation to yield the excited EDA complex **1.309a**. This subsequently leads to homolytic cleavage after SET furnishing the *C*-centred radical **1.312** and the amminium radical **1.311**. In the case of the XB complex **1.308**, irradiation under visible light furnishes the excited complex intermediate **1.309b**, triggering the homolytic C–Br bond cleavage to the alkyl radical **1.312** and the bromine radical-DIPEA complex **1.310**. The *ipso*-interception of the radical by **1.306** affords the benzylic radical intermediate

1.313, stabilised by hydrogen bonding between the boronic acid moiety and the carbonyl group when it sits in the 7-membered ring intermediate **1.314**. Further single electron oxidation with **1.310** or **1.311** affords the carbocation intermediate **1.315** regenerating DIPEA. Elimination of the boron motif delivers the desired product **1.307**.



Scheme 1-49: Metal-free photocatalysed formal Suzuki–Miyaura reaction using α-bromodifluoroacylarenes.

1.3.4 Miscellaneous – other examples

As highlighted in the previous section, organoborons are commonly used in a broad range of photoinduced transformations due to their versatility towards photoredox

processes. However, the examples mentioned above, relevant to this project, remain non-exhaustive, and several other transformations can be performed under photocatalysed conditions. Although no detailed discussion will be carried out in this section, a number of examples will be presented to emphasise the great diversity of organoborons. Stabilisation of α-boryl radicals has been well discussed (see section 1.3.3.2) and adjacent boron motifs can also be used to generate stabilised radicals: Molander[165] reported a HAT process from **1.316** using a benzophenone derivative as a photocatalyst whereas Charette[166] and Leonori[85] used α-halo boronic esters **1.317** or **1.318** to generate radicals, as illustrated in Figure *1-10*.

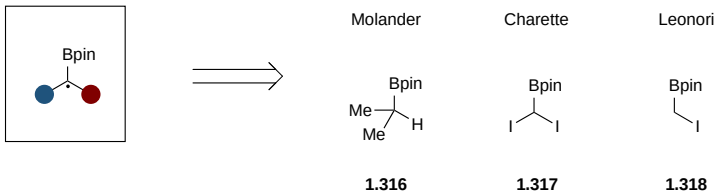
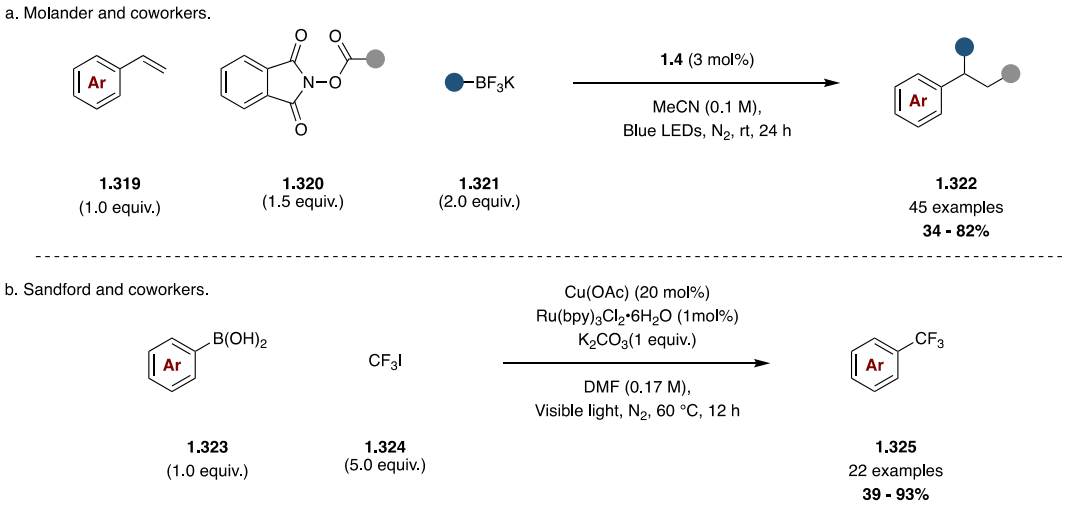


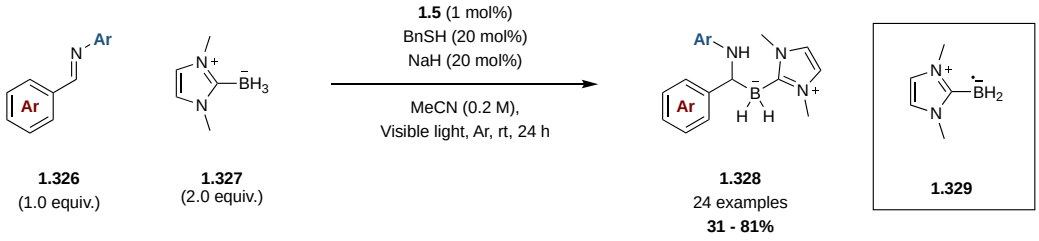
Figure 1-10: Generation of α-boryl radicals.

Organoborons can be used indirectly in photoinduced processes as depicted in Scheme *1-50*. For instance, Molander and coworkers used BF_3K salts **1.321** as nucleophiles in a multicomponent photocatalysed radical/polar crossover 1,2-dicarbofunctionalisation of alkenes to afford substituted alkanes **1.322**.[167] The extended scope tolerates a myriad of different BF_3K salts such as alkynyl, alkenyl, and aryl BF_3K salts. Sandford and coworkers reported a dual Ru-and Cu-catalysis to trifluoromethylate aryl boronic acids **1.323** using trifluoroiodomethane **1.324** as a $CF_3^{\bullet}$ radical source.[168] Transmetalation with the organoboron component followed by reductive elimination delivers the desired products **1.325**.



Scheme 1-50: Indirect use of organoborons in photoinduced processes.

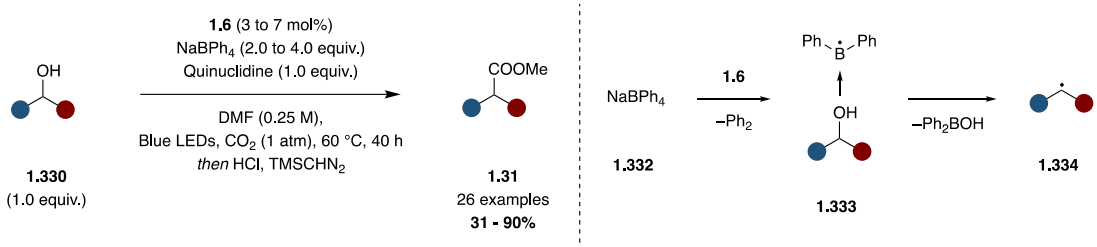
Finally, organoborons can be used to generate *B*-centred (boryl) radicals. These species have only five electrons, resulting in a highly unstable radical species due to the strong electron deficiency of the boron atom. As previously seen in section 1.3.3.2, the use of boronates allows boryl radical formation, which, in this case, have formally seven electrons.[169] For example, bench-stable NHC-boranes **1.327**, are readily used as boryl radical precursors. Although they usually require radical initiators, Zhu and coworkers reported an Ir-based methodology to generate NHC-boryl radical **1.329** from the corresponding NHC-borane **1.327** to hydroborate a variety of imines **1.326**, as shown in Scheme *1-51*.[170] The NHC-boronates **1.328** can then be further transformed into boronic acid pinacol esters in one step synthesis delivering a Bpin linchpin handle.



Scheme 1-51: Photocatalysed hydroboration of imines using NHC-boranes.

Boryl radicals can also be used to activate the homolytic cleavage of certain bonds such as the C–OH bond. Xia and coworkers reported the use of sodium tetraphenylborate **1.332** to generate a diphenyl boryl radical *in situ* which can activate the C–OH bond cleavage, as drawn in Scheme *1-52*.[171] Sodium tetraphenylborate

1.296 undergoes single electron oxidation under the photoredox conditions to afford, after release of a diphenyl molecule, the boryl radical **1.333** which is stabilised by the alcohol starting material **1.330** (or by DMF). This leads to the homolytic cleavage of the C–O bond to deliver the *C*-centred radical **1.334**.



Scheme 1-52: Boryl radical activation of C−OH bonds.

2. Research outline

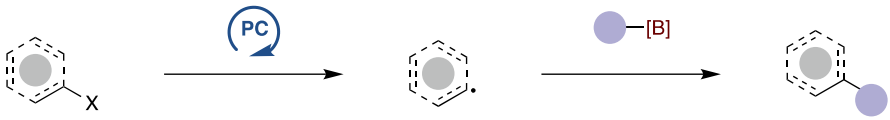
Organoborons are commonly used in the field of chemistry. They are widely commercially available, ubiquitous and often inexpensive. They are employed in a broad range of organic transformations, and are of particular use in metal-catalysed cross-coupling reactions such as Suzuki–Miyaura,[94,95] Chan–Lam,[96,97] or Hayashi[98] reactions.

Over the last 20 years, the development of photocatalysis has unlocked new opportunities within cross-coupling reactions. Indeed, many new reactive intermediates have been generated through photocatalysed radical formation.[3,10] These can be intercepted with Michael acceptors in a Giese-type reaction[128,129] or can be involved in dual catalysis with a transition metal such as Ni or Cu.[11,12]

Although the Suzuki–Miyaura cross-coupling reaction requires the use of palladium, greener methodologies have been developed such as the use of alternative transition metals,[172] solid-supported Pd nanoparticles or more environment-friendly solvents.[173] Using photocatalysis to access C–C bond formations between organoborons and alkyl/aryl halides is a mechanistically feasible proposal and would amount to a metal-free Suzuki–Miyaura-type cross-coupling reaction. Despite the vast development of organoborons in photochemistry, current methodologies tend to use them as radical

precursors more than coupling partners to intercept radicals. Thus, the following project was designed and it is depicted in Scheme *2-1*.

- Generation of *C*-centred radical from a suitable radical precursor and photocatalyst.
- Radical trapping with an organoboron reagent, where the boron moiety is used as a directing handle.
- Obtention of the desired product after elimination of the boron moiety.



Scheme 2-1: Postulated photocatalysed reaction using organoborons.

3. Results and discussion

3.1 From experimental design to hit reaction

The organoborons selected to investigate the postulated photocatalysed reaction were (*E*)-2-phenylvinylboronic (**3.1a**, more commonly named styrenyl boronic acid), phenyl boronic acid (**3.2a**), and their derivatives such as boronic pinacol esters (Bpin, **3.1b** and **3.2b**) or potassium trifluoroborate (BF_3K) salts (**3.1c** and **3.2c**), as depicted in Figure *3-1*.

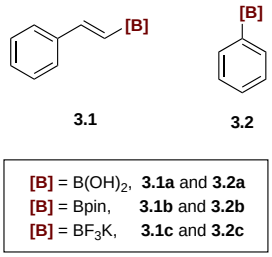


Figure 3-1: Selected organoborons.

The formation of both alkyl and aryl radicals have been well documented for over a decade, highlighting the importance of these reactive intermediates in chemistry.[174,175] Simple and straightforward methods to access radicals using light irradiation have

been well explored, contributing to the soaring development of photochemistry.[3] Thus, based on literature, several radical precursors were selected and applied for the proposed photocatalysed C–C cross-coupling reaction. Aryl or alkyl halides can undergo halogen atom transfer (XAT, see section 1.1.6.1), generating the corresponding radicals (Figure *3-2*).[83] Aryl diazonium (Figure *3-2*)[176,177] or active redox species such as *N*-hydroxyphthalimide (NHPI) esters (Figure *3-2*)[178–180] are commonly employed respectively as aryl or alkyl radical precursors. Examples of radical formation strategies tested for the postulated reaction are depicted in Figure *3-2*.

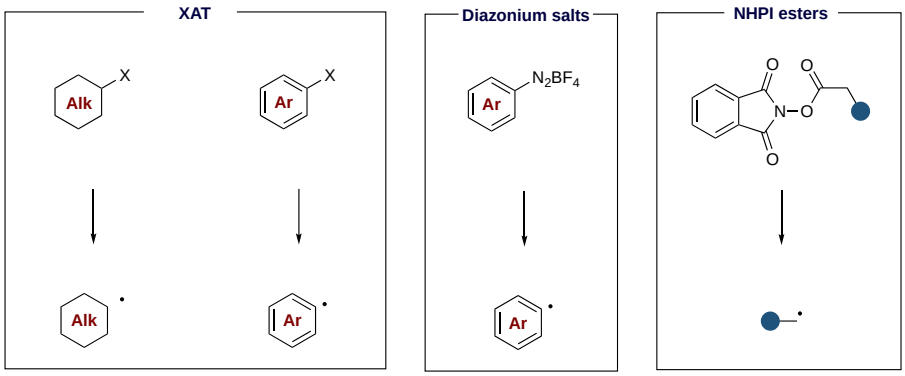
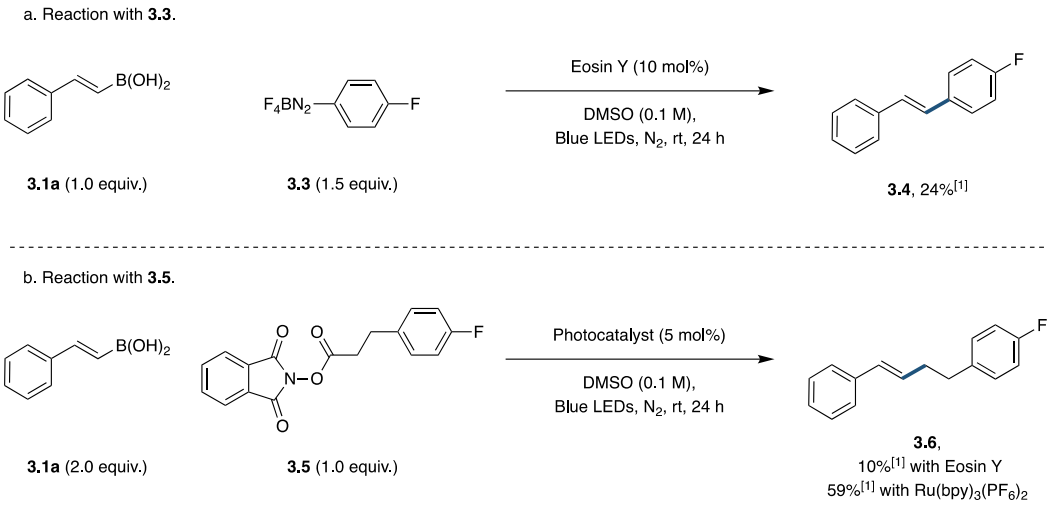


Figure 3-2: Different methodologies considered for radical formations.

XAT processes are an interesting mimic to the Suzuki–Miyaura cross-coupling reaction. The generation of an alkyl radical from the corresponding alkyl halide has been well documented,[83] and several methodologies were trialled. For instance, MacMillan and coworkers used benzophenone and tris(trimethylsilyl)silanol (see Scheme *1-21*)[84], whereas the Leonori lab reported the use of 4CzIPN and a base (see Scheme *1-22*)[85] to generate a *C*-centred radical. These methodologies were applied to the postulated reaction; however, no reaction was observed with **3.1a** – **3.1c** or **3.2a** – **3.2c**. The reaction was then performed with other radical precursors and although no reaction was observed using **3.2a** (or any of its derivatives, **3.2b** and **3.2c**), the reaction with **3.1a** yielded promising results with both diazonium salt **3.3** (Scheme *3-1*a) and NHPI ester **3.5** (Scheme *3-1*b), affording the products **3.4** and **3.6**, respectively.



Scheme 3-1: a. Hit reaction between **3.1a** and aryl diazonium salt **3.3**; b. Hit reaction between **3.1a** and NHPI ester **3.5**.[1] Isolated yields.

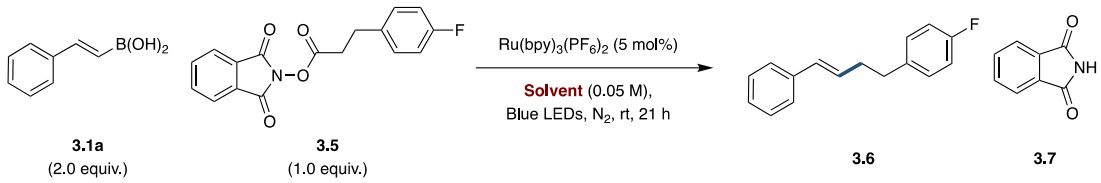
The reaction between styrenyl boronic acid **3.1a** and the fluorinated aryl diazonium salt **3.3** afforded the desired product **3.4** with 24% yield. However, a literature search revealed that the exact same reaction had been reported by Wu and coworkers (see Scheme *1-48*).[162] The reaction between (*E*)-2-phenylvinylboronic **3.1a** and the NHPI ester **3.5** also gave a promising outcome. Pleasingly, the reaction worked and the desired product **3.6** was afforded with 10% yield when Eosin Y was used as the photocatalyst after 24 hours under blue LEDs. Switching the organophotocatalyst for $Ru(bpy)_3(PF_6)_2$ remarkably increased the formation of **3.6** up to 59%. Based on this result, the optimisation was carried out using the NHPI ester **3.5** and $Ru(bpy)_3(PF_6)_2$ as the benchmark reaction.

3.2 Optimisation

3.2.1 Initial optimisation

Once the hit reaction was found, the reaction was optimised and the reaction solvent was the first parameter to be studied (Table *3-1*).

Table 3-1: Solvent screening.



Entry	Solvent	**3.6** (%)[a]	**3.5** (%)[a]
1[b]	DMSO	60	0
2	DMF	35	13
3	Acetone	40	9
4	MeCN	14	57
5	HFIP	0	74
6	2,2,2-Trifluoroethanol	0	83
7	THF	0	88
8	DCM	11	82
9	DCE	0	88
10	PhMe	0	97
11	MTBE	0	92
12	$PhCF_3$	0	90
13[c]	DMSO	59	0

Reaction run on 0.1 mmol scale in dry and degassed solvents. [a] Determined by ^{19}F NMR using 2-fluoro-4-nitrotoluene as an internal standard (added after work up). [b] 99%[a] of **3.7** obtained. [c] Reaction run for three hours.

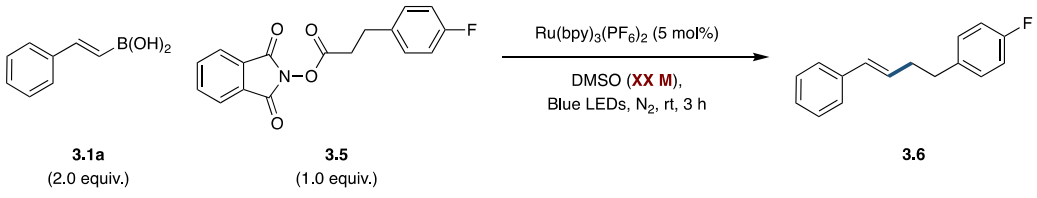
Although a broad range of solvents were tested (Table *3-1*), the reaction outcome was not improved. Polar solvents such as DMSO, DMF or acetone (entries 1 to 3) gave the best results, with DMSO being most effective with 60% of product and full consumption of the NHPI ester **3.5**. Surprisingly, the reaction run in MeCN (entry 4) or fluorinated solvents such as HFIP (entry 5) or 2,2,2-trifluoroethanol (entry 6) gave **3.6** with either very low yield or no product at all. In some cases, the reaction occurred but was not complete after 21 hours (entries 2, 3, and 4). In moderate or non-polar solvents, the reaction did not work (entries 7 to 12), likely due to solubility issues

encountered (**3.1a** precipitated out in these solvents). Decreasing the reaction time to three hours did not significantly affect the yield of the reaction (entry 13) with 59% of product **3.6**.

When the reaction occurred (entries 1 to 4, and 13), the observed poor mass balance (**3.5** + **3.6**) led to the conclusion that the alkyl radical was probably being intercepted by another component in the reaction. Monitoring the crude reaction by ^{19}F NMR spectroscopy revealed no other significant peaks, therefore ruling out the previous hypothesis. Photocatalytic defluorination processes[181,182] have been developed and could compete with the reaction, explaining the poor mass balance obtained. Monitoring the reaction (entry 1) by ^{1}H NMR spectroscopy confirmed the same poor mass balance (**3.5** + **3.6**). Contrastingly full recovery of phthalimide **3.7** was observed, highlighting the quantitative consumption of **3.5** into the alkyl radical (see Section 3.4.1.1 for the formation of the radical). This observation implied potential side reactions occurring under the photocatalytic conditions. The product appeared to be stable under the reaction conditions (see Figure *5-2*). Thus, it was hypothesised that the poor mass balance was likely due to the loss of radical through unknown degradation processes.

The concentration of the reaction was varied as shown in Table *3-2*. Indeed, it was hypothesised that increasing the concentration could lead to an improvement of the reaction, by increasing the probability of bimolecular processes between the alkyl radical and the styrene boronic acid **3.1a**.

Table 3-2: Concentration optimisation.



3.1a (2.0 equiv.) **3.5** (1.0 equiv.) **3.6**

Entry	Concentration (M)	**3.6** (%)[a]	**3.5** (%)[a]
1	0.2	62	2
2	0.1	63 (60)[b]	0
3	0.05	59	0

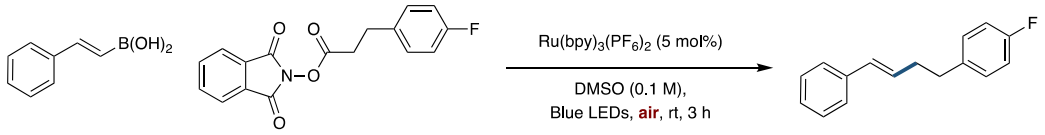
4	0.025	57	1

Reaction run on 0.1 mmol scale in dry and degassed DMSO. [a] Determined by ^{19}F NMR using 2-fluoro-4-nitrotoluene as an internal standard (added after work up). [b] Isolated yield.

Changing the concentration of the reaction mixture from 0.2 M (entry 1) to 0.025 M (entry 4) did not improve the formation of the product **3.6**. In all cases, full consumption of the NHPI ester **3.5** was observed, where only an average of 60% of **3.6** was afforded. The NMR conversion was confirmed with 60% isolated yield in the case of entry 2.

Molecular oxygen can lead to different highly reactive oxygen species (ROS) such as superoxide anion radical ($O_2^{\bullet-}$), hydrogen peroxide (H_2O_2), or singlet oxygen ($^1O_2$), known in biology to cause damage to biomolecules.[183] Those species are also important components in photochemistry and can be useful in incorporating an oxygen atom into a suitable substrate as illustrated in Scheme *1-9*b or Scheme *1-12*. However, molecular oxygen can be detrimental to the reaction by inhibiting the desired reaction through side reactions such as radical trapping or photocatalyst quenching.[184,185] The methodology developed by Xiao and coworkers (Scheme *1-12*)[58] highlights two interesting points: (1) molecular oxygen can compete with the NHPI ester **3.5** in the single electron oxidation of $Ru(bpy_3)^+$; and (2) formation of $O_2^{\bullet-}$ could then be involved in side processes such as hydroxylation of boronic acids, hence rationalising the previous observations on decreased yield and mass balance.

Table 3-3: Atmosphere variation.



3.1a (2.0 equiv.) **3.5** (1.0 equiv.) **3.6**

Entry	Atmosphere	**3.6** (%)[a]	**3.5** (%)[a]
1	N_2	63 (60)[b]	0
2	Air	21	51

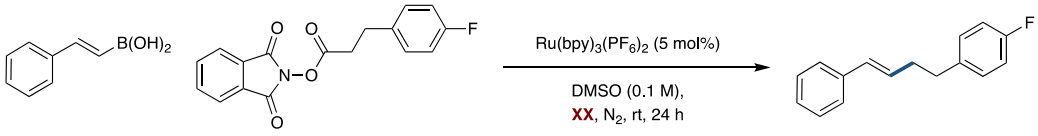
3[c]	Air	23	52

Reaction run on 0.1 mmol scale in dry and degassed DMSO. [a] Determined by ^{19}F NMR using 2-fluoro-4-nitrotoluene as an internal standard (added after work up). [b] Isolated yield. [c] Reaction run in air bubbled through dry DMSO.

Running the reaction under air was found to be detrimental to the reaction, with only 20% of product afforded after three hours (Table *3-3*, entries 2 and 3). The reaction therefore requires an inert atmosphere to avoid any side reactions with molecular oxygen.

To verify that the consumption of **3.5** under blue LED irradiation, the following control experiments were performed, where the reaction was set up under daylight or wrapped in aluminium foil (Table *3-4*).

Table 3-4: Role of blue LEDs.



3.1a (2.0 equiv.) **3.5** (1.0 equiv.) **3.6**

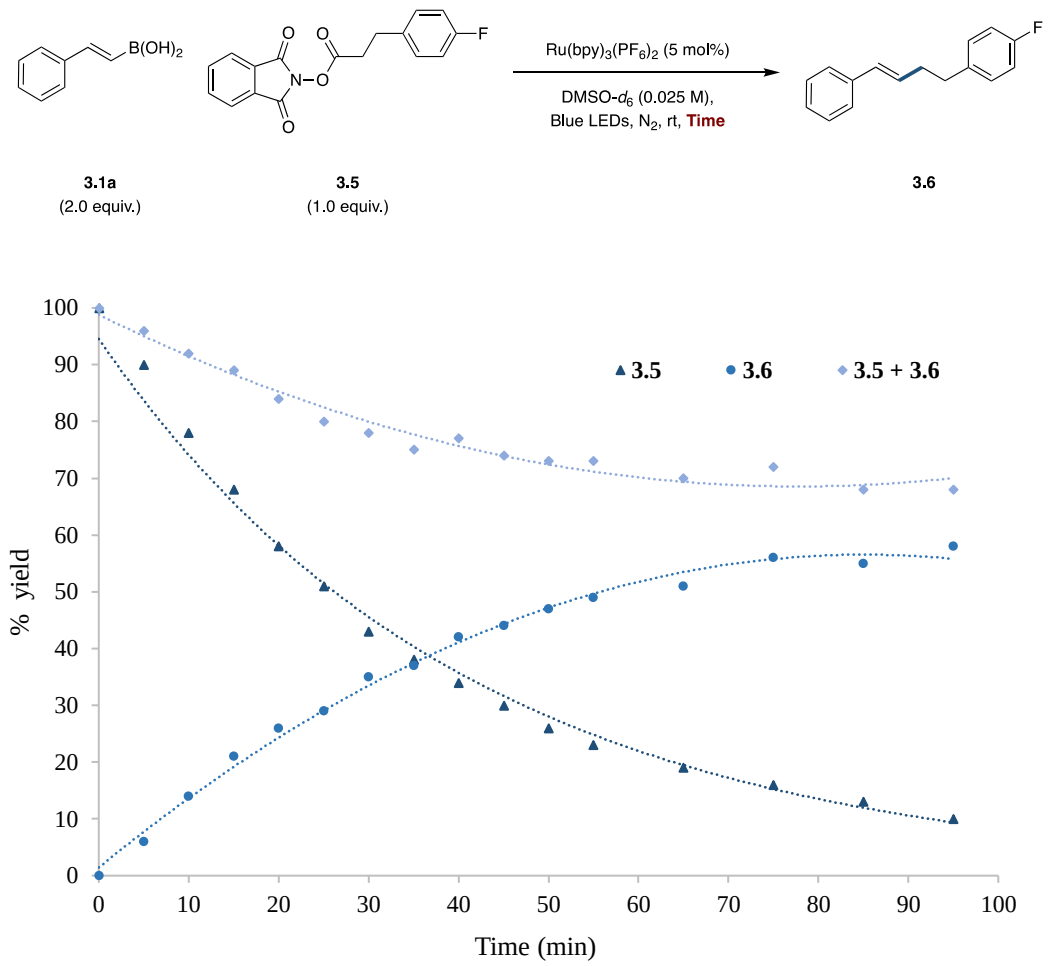
Entry	Conditions	**3.6** (%)[a]	**3.5** (%)[a]
1	Daylight	0	97
2	Dark	0	100

Reaction run on 0.1 mmol scale in dry and degassed DMSO. [a] Determined by ^{19}F NMR using 2-fluoro-4-nitrotoluene as an internal standard (added after work up).

No reaction occurred in both cases and full recovery of the starting material **3.5** was observed, highlighting the importance of the blue LEDs in the alkyl radical formation from **3.5** (*vide infra*).

From previous results, it appeared that the reaction was complete after only three hours. A time study was then carried out with an internal standard.

Figure 3-3: Time study.

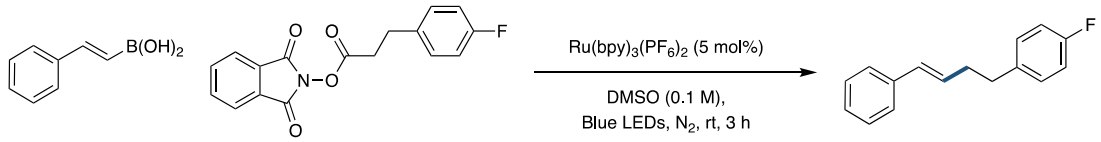


The time labelled in the graph represents the time the sample was irradiated under blue LEDs. It was assumed, based on results from Table *3-4*, that no reaction was occurring under daylight (no reaction promoted by daylight between removing the sample from apparatus to recording the NMR).

After 95 minutes, the reaction was almost complete and less than 10% of the NHPI ester **3.5** was remaining in the reaction mixture. The formation of product **3.6** reached a plateau of approximatively 60% and the mass balance (**3.5** +**3.6**) decreased over the time, reaching 70% recovery of the fluorinated moiety. Notably, a 30% loss of the mass balance was observed after 95 minutes, emphasising potential side reactions. As mentioned previously, no other significant side products were observed on the ^{1}H or ^{19}F NMR of the reaction mixture, suggesting that interception of the alkyl radical with a reaction component does not occur. It was found that under the reaction conditions, both the boronic acid **3.1a** and product **3.6** were stable, implying that decomposition of the alkyl radical is more likely happening after its formation.

It was hypothesised that once the alkyl radical is formed from NHPI ester **3.5,** it may not react fast enough with **3.1a**, and undergoes decomposition. In order to overcome this potential issue, two options were considered: (1) changing the stoichiometry of the reaction to increase the probability of bimolecular collision (Table *3-5*); or (2) slowing down the formation of the alkyl radical.

Table 3-5: Stoichiometry of the reaction.



3.1a (XX equiv.) **3.5** (XX equiv.) **3.6**

Entry	**3.1a** (equiv.)	**3.5** (equiv.)	**3.6** (%)[a]	**3.5** (%)[a]
1	1.0	1.0	31	48
2	1.5	1.0	45	25
3	2.0	1.0	63 (60)[b]	0
4	3.0	1.0	65	0
5	4.0	1.0	67	0
6	5.0	1.0	67	0
7	1.0	2.0	17	57
8	1.0	3.0	24	76

Reaction run on 0.1 mmol scale in dry and degassed DMSO. [a] Determined by ^{19}F NMR using 2-fluoro-4-nitrotoluene as an internal standard (added after work up). [b] Isolated yield.

Increasing the amount of **3.1a** from one to five equivalents (entries 1 to 6) led to an improvement of the formation of **3.6** from 31% to 67%. When the reaction is run with one equivalent (entry 1) or one and half equivalents (entry 2) the reaction efficiency decreased, with remaining starting material **3.5** observed after three hours of reaction. When more than three equivalents were used (entries 4 to 6), heterogeneity of the reaction mixture was observed. Negligible improvement in yield was observed when the number of equivalents of **3.1a** was greater than two thus, in the interest of atom

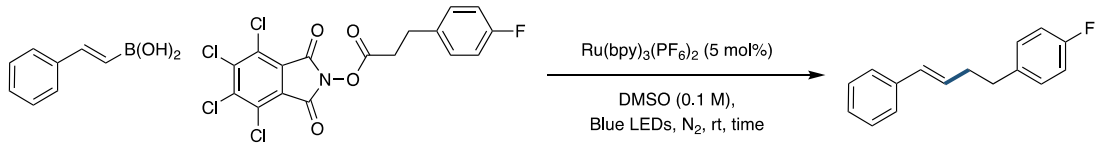
efficiency, two equivalents were used. Finally, switching the stoichiometry of the reagents was ineffective (entries 7 and 8).

To slow down the formation of the alkyl radical, NHPI ester **3.5** was added over an hour using a syringe pump and then the reaction mixture was left to stir for three hours. Full consumption of the starting material and only 57% of the desired product was observed. As the slow addition did not improve the outcome of the reaction, longer addition times were not tried.

3.2.2 Use of tetrachlorophthalimide esters

Tetrachlorophthalimide (TCNHPI) esters are used as an alternative to generate alkyl radicals.[186–188] Bach and coworkers reported the redox potential of TCNHPI esters ($E_{1/2}$ = –0.70 V to –0.54 V vs. SCE)[189] which is higher than the corresponding NHPI ester ($E_{1/2}$ = –1.39 V to –1.28 V vs. SCE).[190] This difference is explained by the four electron-withdrawing chlorines held by the TCNHPI esters, facilitating their reduction. The following TCNHPI ester **3.8** was synthesised and subjected to the reaction condition (Table *3-6*).

Table 3-6: Reaction using TCNHPI ester **3.8**.



3.1a (2.0 equiv.) **3.8** (1.0 equiv.) **3.6**

Entry	Time (h)	**3.6** (%)[a]	**3.8** (%)[a]
1	3	6	87
2	24	24	55

Reaction run on 0.1 mmol scale in dry and degassed DMSO. [a] Determined by ^{19}F NMR using 2-fluoro-4-nitrotoluene as an internal standard (added after work up).

Running the reaction with the NHPI ester **3.8** afforded the desired product with 6% yield after three hours of reaction (entry 1). Increasing the reaction time to 24 hours resulted in 24% of product **3.6** (entry 2) with a poor mass balance (**3.7** + **3.6**) of 79%. Indeed, modifying the redox potential of the NHPI ester will alter the consumption rate of this later, thus changing the rate of the radical formation. However, it was hypothesised that the main issue in the poor mass balance came from side reactions involving the radical species but not from the consumption of the starting material. Since both NHPI esters are yielding the same radical, the same side reactions will occur leading to the same poor mass balance. Different redox active ester species have been used in photochemistry but were not pursued in this study.[191]

3.2.3 Impure batch of styrenyl boronic acid

The results began to appear inconsistent when the reaction was performed with different batches of the boronic acid starting material **3.1a**. Indeed, the optimisation started with an old bottle of (*E*)-2-phenylvinylboronic (**3.1a**) from Sigma Aldrich Co. (SA1, Figure *3-4*). Two new bottles were purchased; one from Sigma Aldrich Co. (SA2) and one from Fluorochem Ltd (FC3, Figure *3-4*).

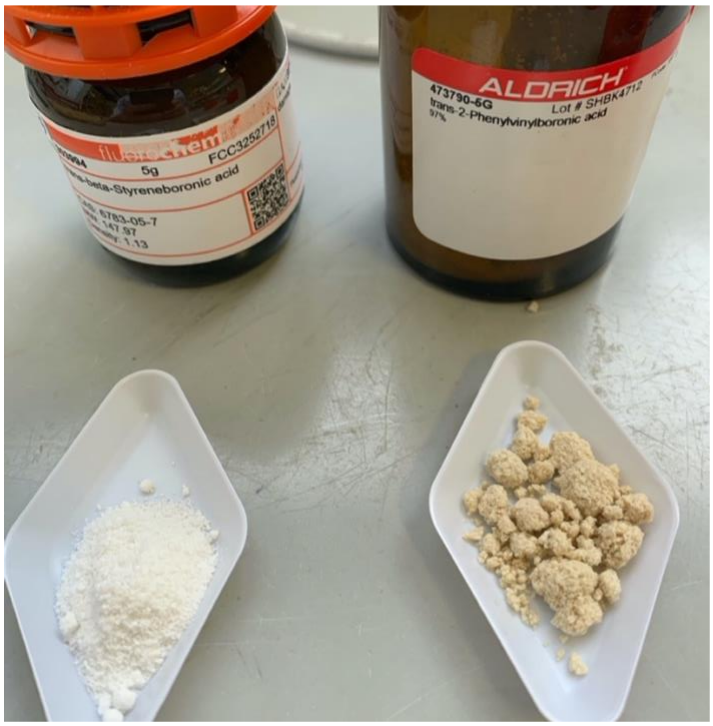
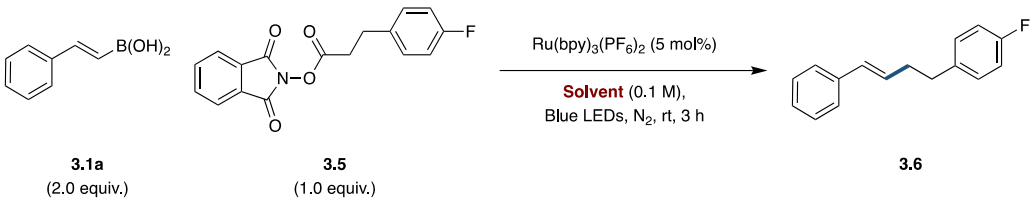


Figure 3-4: Styrenyl boronic acid **3.1a** from FC3 (left) and SA1 (right).

Table 3-7: Reaction with different Styrenyl boronic acid **3.1a** batches.



3.1a (2.0 equiv.) **3.5** (1.0 equiv.) **3.6**

Entry	**3.1a** (batch)	Solvent	**3.6** (%)[a]	**3.5** (%)[a]
1	SA1	DMSO	63 (60)[b]	0
2	SA2	DMSO	3	92
3	FC3	DMSO	8	84
4[c]	FC3	DMSO	7	77
5[d]	FC3	DMSO	31	49
6	FC3	MeCN	0	94
7[e]	FC3	DMSO-d_6	11	82
8	SA1 (1.0 equiv.) FC3 (1.0 equiv.)	DMSO	49	21

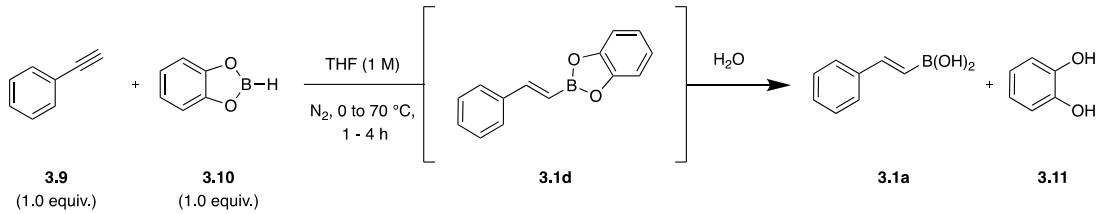
Reaction run on 0.1 mmol scale in dry and degassed DMSO. [a] Determined by ^{19}F NMR using 2-fluoro-4-nitrotoluene as an internal standard (added after work up). [b] Isolated yield. [c] 20 mol% of photocatalyst used. [d] Reaction run for 24 hours. [e] Determined by ^{19}F NMR using 2-fluoro-4-nitrotoluene as an internal standard (added to the reaction mixture).

A significant drop in product formation was observed when the reaction was carried out with the new bottles of starting material **3.1a** (Table *3-7*). Where the standard reaction with the old bottle of **3.1a** (SA1, entry 1) afforded 63% of **3.6**, only 3% and 8% of product were observed respectively with the new Sigma Aldrich bottle (SA2, entry 2) and the Fluorochem bottle (FC3, entry 3). Increasing the loading of photocatalyst to 20 mol% using the FC3 batch (entry 4) yielded only 7% of product, whereas increasing the reaction time to 24 hours (entry 5) afforded 31% of product. Although the reaction seemed to work slightly better after 24 hours, the reaction was found to be irreproducible. Changing solvent to MeCN (entry 7) or monitoring the reaction in DMSO-d_6 (entry 8) led to the same conclusion. Surprisingly, when reacting one equivalent from the old Sigma Aldrich bottle (SA1) and one equivalent from the new Fluorochem bottle (FC3), 49% of **3.6** could be observed after only three hours of

reaction (entry 8). This result suggested that an impurity within the SA1 batch may have been aiding the formation of the product.

3.2.4 Role of catechol

Analysis by ^{1}H NMR spectroscopy of a SA1 sample confirmed the presence of undefined impurities around the aromatic region. Despite the mystery of their origin, different hypotheses were considered: degradation of the starting material over time, contamination from a user, or traces of chemicals used during its synthesis. A literature search revealed different methods to synthesise **3.1a**. The first method was reported by Brown and coworkers in 1975, while studying the hydroboration of alkenes and alkynes using catecholborane **3.10** (Scheme *3-2*).[192]



Scheme 3-2: General synthesis of **3.1a** from phenylacetylene.

Since then, this method has been widely used and is often cited in supplementary informations.[193,194] Thus, ^{1}H NMR spectra stacking with catechol proved the presence of residual traces of catechol **3.11** in the bottle of **3.1a** (Figure *3-5*). Following an inquiry, Sigma Aldrich confirmed that their route to **3.1a** involved hydroboration of **3.9** with catecholborane **3.10** to yield **3.1d**, followed by hydrolysis.

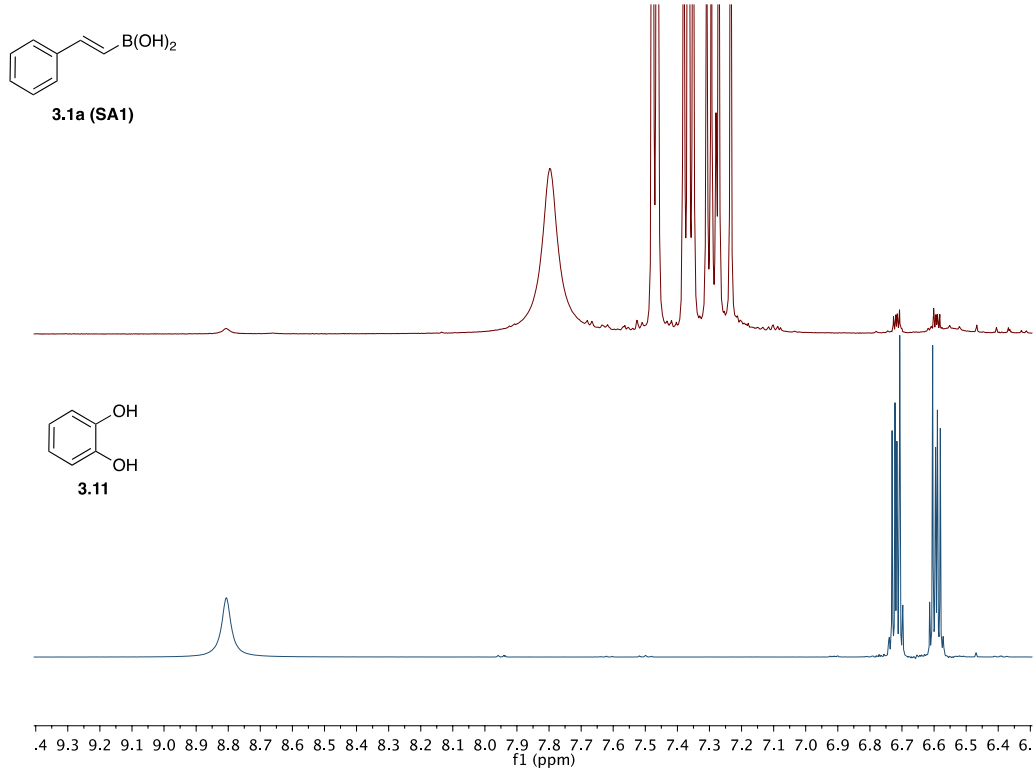
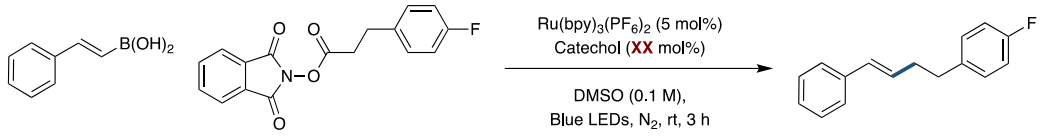


Figure 3-5: Stacked ^{1}H NMR spectra of catechol **3.11** and styrenyl boronic acid **3.1a** (SA1).

To determine whether catechol affected the reaction outcome, a pure batch of **3.1a** was used for the following reaction with exogenous catechol doping. Thus, reactions were run with the Fluorochem bottle of **3.1a** (FC1) and different loadings of catechol **3.11** were added in order to see if the reactivity was restored (Table *3-8*).

Table 3-8: First additive screening.



3.1a (2.0 equiv.) **3.5** (1.0 equiv.) **3.6**

Entry	Catechol (mol%)	**3.6** (%)[a]	**3.5** (%)[a]
1	0	8	84
2[b]	20	64	0
3	20	64	0

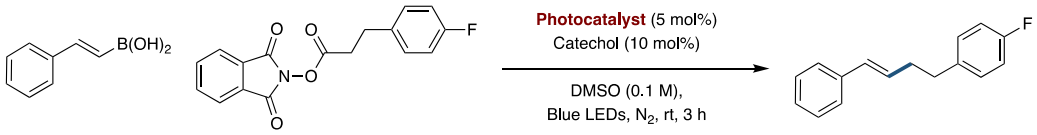
4	10	71	0
5	5	70	0

Reaction run on 0.1 mmol scale in dry and degassed DMSO. [a] Determined by ^{19}F NMR using 2-fluoro-4-nitrotoluene as an internal standard (added after work up). [b] Reaction run for 24 hours.

The reaction was first run with 20 mol% of catechol (Table *3-8*, entry 2), and after 24 hours the reactivity was restored and 64% of **3.6** was obtained, with full consumption of the NHPI ester **3.5**. Decreasing the duration of the reaction to three hours gave a reproducible 64% yield. Finally, reducing the loading of catechol to 10 mol% (entry 4) and 5 mol% (entry 5) afforded 70% yield within three hours.

Following this, different photocatalysts were screened (Table *3-9*).

Table 3-9: Photocatalyst screening.



3.1a (2.0 equiv.) **3.5** (1.0 equiv.) **3.6**

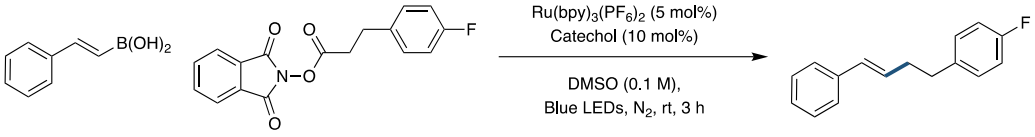
Entry	Photocatalyst	**3.6** (%)[a]	**3.5** (%)[a]
1	None	0	98
2	$Ru(bpy)_3(PF_6)_2$	71	0
3	$Ir(ppy)_3$	63	0
4	$(Ir(dF(CF_3)ppy)_2(dtbpy))PF_6$	8	33
5	4CzIPN	37	0
6	10-Phenylphenothiazine	1	93
7	Eosin Y	10	92
8	Methylene blue	0	95
9	Rose Bengal	27	42
10	Thioxanthen-9-one	0	94

Reaction run on 0.1 mmol scale in dry and degassed DMSO. [a] Determined by ^{19}F NMR using 2-fluoro-4-nitrotoluene as an internal standard (added after work up).

When the reaction was run without any photocatalyst (Table *3-9*, entry 1), no reaction occurred and full recovery of **3.5** was observed. The reaction with $Ru(bpy)_3(PF_6)_2$ gave reproducible 70% yield under the standard conditions (entry 2). Switching the Ru-based photocatalyst to an Ir-based photocatalyst such as $Ir(ppy)_3$ slightly affected the yield and gave 63% of product (entry 3), whereas using $(Ir(dF(CF_3)ppy)_2(dtbpy))PF_6$ plummeted the reaction yield to 8% (entry 4). Common organophotocatalysts were also tested such as 4CzIPN (entry 5) which gave 37% of product after three hours with a very poor mass balance. The use of 10-phenylphenothiazine (entry 6) was detrimental to the reaction with only traces of **3.6** observed. Common organic dyes [195] such as Eosin Y (entry 7), Methylene blue (entry 8) or Rose Bengal (entry 9) did not give promising results and were omitted from the rest of the study. Finally, thioxanthone, another class of photocatalyst, was tested (entry 10) but did not prove to be effective under the standard conditions.[196] The poor performance of these photocatalysts can be explained by their redox properties (*vide infra*). Indeed, NHPI esters undergo single electron reduction with a photo-activated species as long as they are more reducing than the NHPI ester. This will be elaborated upon the next section (see Section 3.4.1.1).

The stoichiometry of the reaction was studied with catalytic amount of catechol added to the reaction (Table *3-10*).

Table 3-10: Stoichiometry screening.



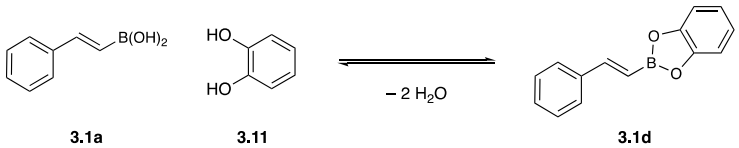
3.1a (XX equiv.) **3.5** (XX equiv.) **3.6**

Entry	**3.1a** (equiv.)	**3.5** (equiv.)	**3.6** (%)[a]	**3.5** (%)[a]
1	1.0	1.0	49	0
2	2.0	1.0	69	0
3	3.0	1.0	67	0
4	4.0	1.0	70	0

5	5.0	1.0	71	0
6	1.0	2.0	62	36
7	1.0	3.0	58	48

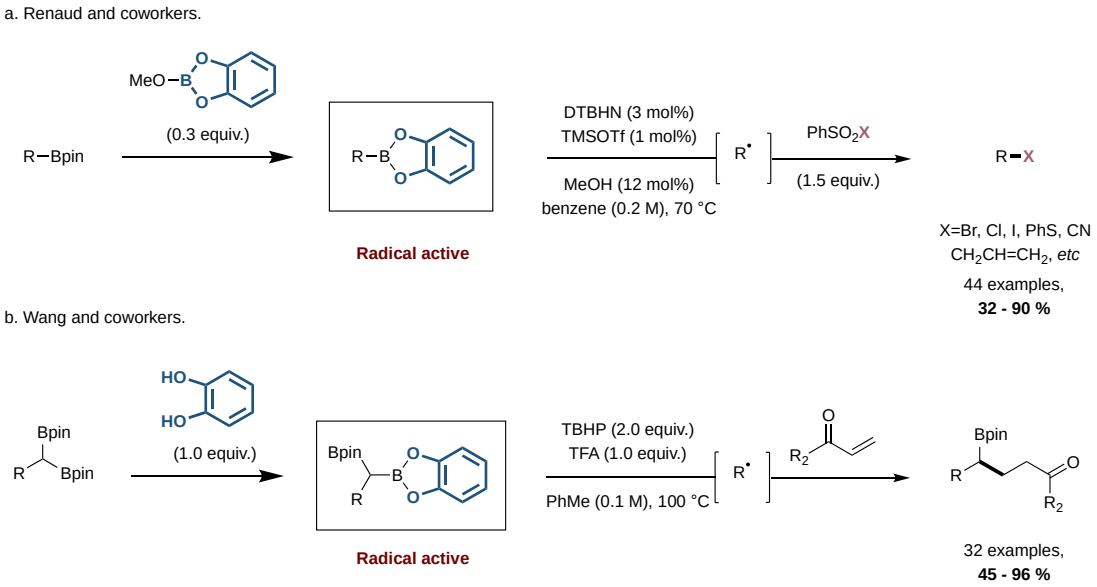
Reaction run in 0.1 mmol scale in dry and degassed DMSO. [a] Determined by ^{19}F NMR using 2-fluoro-4-nitrotoluene as an internal standard (added after work up).

Modifying the stoichiometry of the two starting materials with 10 mol% of catechol led to the same conclusion as the one made from Table *3-5*: two or more equivalents of styrenyl boronic acids **3.1a** gave the best result. From previous experiments, it appeared that catechol was promoting the reaction. It was hypothesised that the catechol could react *in situ* with (*E*)-2-phenylvinylboronic acid **3.1a** to form (*E*)-2-phenylvinylcatechol boronic acid ester **3.1d** (Scheme *3-3*). Further reaction with the NHPI ester **3.5** under the standard conditions would lead to the desired product.



Scheme 3-3: Proposed *in situ* reaction between catechol and trans-styrenyl boronic acid **3.1a**.

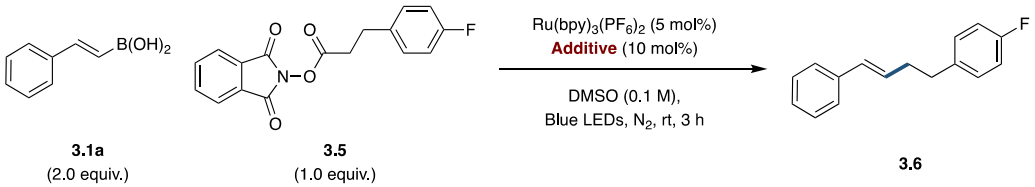
This *in situ* Bcat-formation strategy has been previously reported by Renaud and coworkers in 2020, where an alkyl pinacol boronic ester was subjected to MeOBcat (or *tert*-butyl catechol) to afford, after transesterification, a catechol boronic ester *in situ* (Scheme *3-4*a).[197] This later was employed as an alkyl radical source in a radical chain process, whereas the pinacol boronic ester starting material remained unreactive. Deboronative halogenation, chalcogenation or alkylation were successfully achieved using the corresponding phenyl sulfone and di-*tert*-butylhyponitrite (DTBHN) as radical initiator. This methodology was followed by Wang and coworkers where a similar strategy was used to generate α-boryl radicals from *gem*-diborylalkanes with *tert*-butyl hydroperoxide (TBHP) as a radical initiator (Scheme *3-4*b).[198]



Scheme 3-4: Generation of alkyl radicals from alkyl pinacol boronic esters.

Thus, it was conjectured that modifying the electronic properties of the catechol additive would vary the equilibrium (Scheme *3-3*), therefore promoting the reaction by driving the formation of the catechol ester.[199–201]

Table 3-11: Catechol derivatives screening.



Entry	Additive	**3.6** (%)[a]	**3.5** (%)[a]
1	Catechol	70	0
2	4-Methylcatechol	55	4
3	4-*tert*-Butylcatechol	68	0
4	4-Nitrocatechol	6	77
5	Ethyl 3,4-dihydroxybenzylate	3	87
6	3-Methylcatechol	59	2
7	3-Methoxycatechol	52	0

Reaction run on 0.1 mmol scale in dry and degassed DMSO. [a] Determined by ^{19}F NMR using 2-fluoro-4-nitrotoluene as an internal standard (added after work up).

In order to verify this hypothesis, a variety of catechol derivatives were tested (Table *3-11*). Electron-rich catechols such as 4-methyl (entry 2) or 4-*tert*-butyl (entry 3) gave similar results regarding both the yield of the reaction and recovery of the mass balance, compared to the standard reaction carried out with catechol (entry 1). However, electron-deficient dihydroxybenzenes (entries 4 and 5) were found to be detrimental to the reaction and only traces of product were observed. In these cases, the recovery of the NHPI ester **3.5** was almost complete, leading to the conclusion that the electron-deficient catechols prevent radical formation. Additionally, moving the electron-rich substituent onto the 3-position (entries 6 and 7) did not improve the reaction and similar yields were recorded for the 4-substituted catechols (entries 2 and 3). However, in all the successful cases where the desired product **3.6** was afforded (from 52% in entry 7 to 70% in entry 1), a considerable loss of the alkyl radical was still observed (from 50% to 30%).

As shown in Figure *3-6*, mixing **3.1a** with catechol under the reaction conditions did not form the catechol boronic ester **3.1d** *in situ.* Nevertheless, it is worth noting that the OH peaks from both the boronic acid **3.1a** and from catechol disappeared (Figure *3-6*) suggesting that some kind of interactions such as electron donor acceptor (EDA) complexes between the two starting materials could occur and potentially promote the reaction.

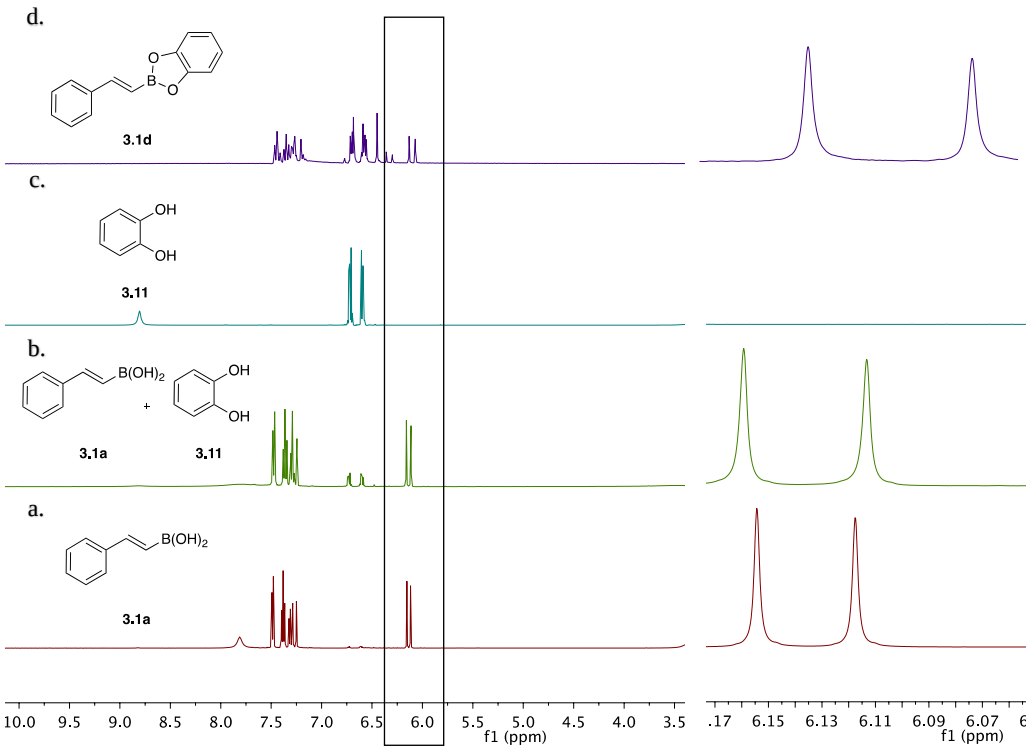
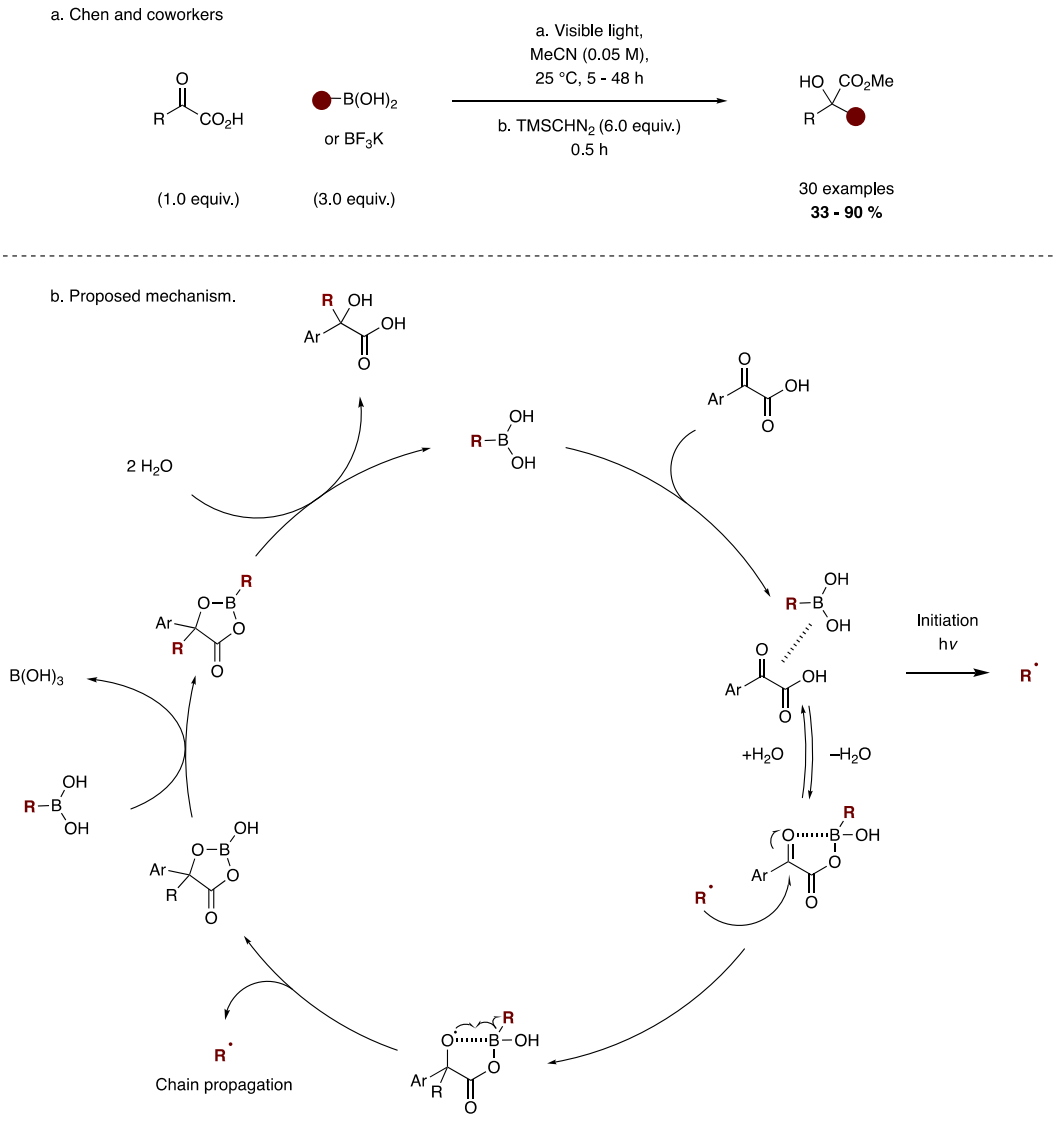


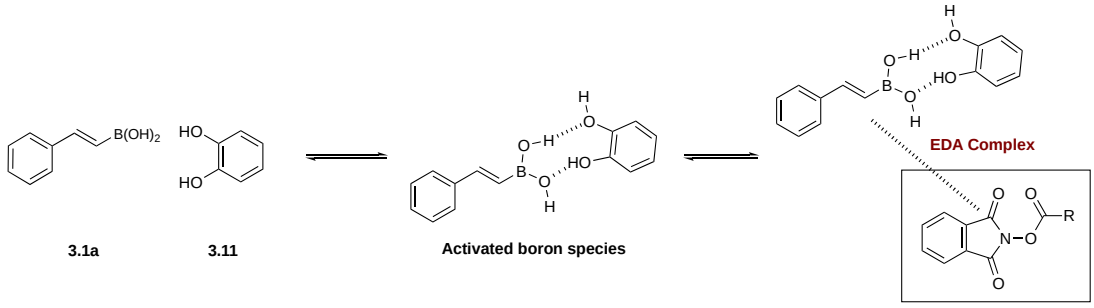
Figure 3-6: Stacked ^{1}H NMR spectra: a) **3.1a**; b) **3.1a** + 10 mol% of **3.11**; c) **3.11**; d) **3.1d**.

Electron donor acceptor (EDA) complexes (see Section 1.1.6.2) involving activated organoboron species have been recently developed.[13,202] Aggarwal and coworkers reported several methodologies using B_2pin_2, activated with *N*,*N*-dimethylacetamide as the donor component and different acceptors such as NHPI esters (see Scheme *1-33*)[124] or *N*-alkylpyridinium salts.[203] More recently, Chen and coworkers reported a radical addition to (hetero)arylketoacids through a chain propagation mechanism, promoted by activation of an alkylboron (Scheme *3-5*).[204]



Scheme 3-5: Radical addition to ketoacids enabled by boron activation.

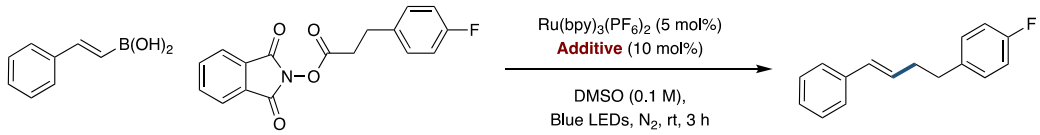
Thus, it was hypothesised that hydrogen bonding between **3.1a** and catechol **3.11** could form an activated organoboron species, which can further promote EDA complex formation with NHPI esters (stabilised by hydrogen bonding and π-stacking), as depicted in Scheme *3-6*.



Scheme 3-6: Hypothesis of hydrogen bonding between **3.1a** and catechol **3.11**.

UV-Vis analysis of mixture of **3.1a**, catechol and NHPI ester **3.5** revealed no significant bathochromic shift, suggesting no clear EDA complex formation (see Section 5.2.3.2). Indeed, the absorption of the potential EDA complex at 456 nm is very weak, ruling out a strong EDA complex effect. A more exhaustive additive screen was performed (Table *3-12*) to determine whether (1) the yield of the reaction and the mass balance could be improved and (2) the role of the additive.

Table 3-12: Additive screening.



3.1a (2.0 equiv.) **3.5** (1.0 equiv.) **3.6**

Entry	Additive	**3.6** (%)[a]	**3.5** (%)[a]
1	Naphthalene-2,3-diol	5	77
2	1,3-Dihydroxybenzene	12	78
3	1,4-Dihydroxybenzene	21	51
4	Phenol	14	72
5	*p*-Benzoquinone	0	90
6	2-Methoxyphenol	21	65
7	1,2-Dimethoxybenzene	12	81
8	1,3-Dimethoxybenzene	15	75
9	1,3,5-Trimethoxybenzene	16	76
10	Anisole	7	56
11	2-Hydroxybenzylalcohol	15	76
12	Salicylic acid	2	90
13	2-Aminophenol	59	0
14	1,2-Phenyldiamine	62	0
15	Naphthalene-2,3-diamine	23	44

16	2-Aminothiophenol	46	12
17	1,2-Benzenedithiol	14	65
18	Aniline	62	12
19	4-Nitroaniline	13	74
20	4-Methoxyaniline	70	0
21	Diphenylamine	64	0
22	Triphenylamine	15	79
23	*N*-Methylaniline	72	0
24	*N*,*N*-Dimethylaniline	75	0
25	Pinacol	10	79
26	Ethylene glycol	9	78
27	(L)-Tartaric acid	4	91
28	Ethylenediamine	20	20
29	Pyridine	21	72
30	DIPEA	25	0
31	DMAP	17	74
32	Urea	10	72
33	Thiourea	16	72
34	Boric acid	8	93

Reaction run on 0.1 mmol scale in dry and degassed DMSO. [a] Determined by ^{19}F NMR using 2-fluoro-4-nitrotoluene as an internal standard (added after work up).

Planar extended aromatic additives such as naphthalene-2,3-diol (entry 1) were tested to determine whether improving the π-stacking interaction between **3.1a**, diol, and the NHPI ester **3.5** could improve the formation of product. However, only 5% of product was observed in this case. To understand the role of the 1,2-diol motif of catechol in the reaction outcome, different regioisomers of catechols were tested such as 1,3- (entry 2) and 1,4-dihydroxybenzene (entry 3). No improvement was observed after three hours of reaction and 12% and 21% of product were afforded, respectively. The

reaction with phenol (entry 4) afforded only 14% of product. These results led to the conclusion that the 1,2-diol motif of catechol was beneficial for the reaction.

Different methyl-capped catechol derivatives were also attempted. The reaction with 2-methoxyphenol (entry 6) gave 21% of product, whereas the reaction with 10 mol% of 1,2- (entry 7) and 1,3-dimethoxybenzene (entry 8) gave 12% and 15% of product respectively. The use of anisole (entry 10) as an additive reduced the yield to 7%, whilst 1,3,5-trimethoxybenzene afforded 16% of product (entry 9). Although the role of catechol remained unknown at this stage, it seemed that the interaction between the 1,2-diol motif of catechol and the boronic acid promoted the reaction, giving the best outcome so far. The reaction was also run with 2-hydroxybenzylalcohol (entry 11) as well as salicylic acid (entry 12), but this did not improve the yield of the reaction and afforded only 15% and 2% of the desired product, respectively. When the reaction was run with 2-aminophenol (entry 13) the yield of the reaction was increased to 59%. Since the presence of an amine re-established the reactivity, different amino-additives were tested. When the reaction was run with 1,2-phenyldiamine (entry 14), 62% of product was obtained after three hours, whereas the use of naphthalene-2,3-diamine (entry 15) gave only 14% of product. 2-Aminothiophenol (entry 16) afforded 46% of product, though the use of a 1,2-dithiol motif shut down the reactivity (entry 17). The use of aniline as an additive (entry 18) re-established the reactivity to 62%, similar to the yield observed with catechol. Electron-poor anilines such as 4-nitroaniline (entry 19) were detrimental to the reaction, while a more electron-rich aniline such as 4-methoxyaniline (entry 20) promoted the reaction. More bulky substituted anilines were less efficient to the reaction (entries 21 and 22) whereas *N*-methylaniline (entry 23) and *N*,*N*-dimethylaniline (entry 24) afforded the best results of the screening with 72% and 75% yields, respectively.

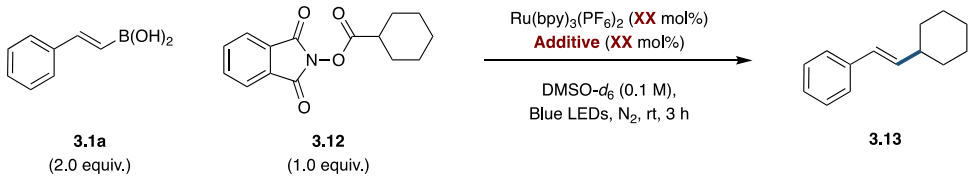
Addition of aliphatic diols such as pinacol (entry 25), ethylene glycol (entry 26), tartaric acid (entry 27) or aliphatic diamines such as ethylenediamine (entry 28) did not improve the reaction. Finally, other additives were also tested such as pyridine (entry 29), DIPEA (entry 30), DMAP (entry 31), urea and thiourea (entries 32 and 33), as well as boric acid (entry 34). However, none of these additives marked an improvement upon *N*,*N*-dimethylaniline.

Although some additives gave good yields, comparable to catechol, mass balance could not be fully tracked throughout these optimisation processes. At this time, the role of the additive remained uncertain; however, this will be revisited in later mechanistic discussions (See Section 3.4).

3.2.5 Second round of optimisation

Since the mass balance remained an issue, the reaction was further investigated with a new NHPI ester: cyclohexane NHPI ester **3.12**. Under standard conditions, **3.12** will yield a secondary alkyl radical, more stable than the primary alkyl radical from **3.5**.[205] This is due to the electron-donating effect from the two alkyl chains that stabilises the radical, leading to a more stable (thus less reactive) radical compared to primary species, less prone to degradation or side reactions.

Table 3-13: Catalyst loading and additives screening.



3.1a (2.0 equiv.) **3.12** (1.0 equiv.) **3.13**

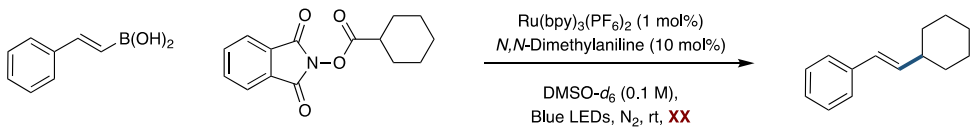
Entry	PC loading (mol%)	Additive (mol%)	**3.13** (%)[a]	**3.12** (%)[a]
1	5	Catechol (10)	82	0
2	5	*N*,*N*-Dimethylaniline (10)	92	0
3	2.5	*N*,*N*-Dimethylaniline (10)	97	0
4	1	*N*,*N*-Dimethylaniline (10)	96 (72)[b]	0
5	1	*N*,*N*-Dimethylaniline (5)	85	10
6	1	None	16	89
7	0	*N*,*N*-Dimethylaniline (10)	0	100
8	1	Catechol (10)	77	0

Reaction run on 0.2 mmol scale in dry and degassed DMSO-d_6. [a] Determined by ^{1}H NMR using 1,3,5-trimethoxybenzene as an internal standard (added after work up). [b] Isolated yield.

When running the reaction with NHPI ester **3.12** (Table *3-13*), an improvement in the formation of the desired product **3.13** using catechol as the additive was noted (entry 1). Full consumption of **3.12** was observed and 82% of product was afforded after three hours of reaction. Changing the additive to *N*,*N*-dimethylaniline (entry 2) further increased the yield to 92% (entry 2). Decreasing the loading of $Ru(bpy)_3(PF_6)_2$ to 2.5 mol% (entry 3) and to 1 mol% (entry 4) gave consistent quantitative ^1H NMR yield, and 72% isolated yield of the product **3.13**. Dropping the loading of *N*,*N*-dimethylaniline to 5 mol% (entry 5) led to a small but noticeable decrease in the formation of the product **3.13**. A final set of control experiments were run: when no additive (entry 6) or no photocatalyst (entry 7) were added, the reaction yield plummeted respectively to 16% and 0%, highlighting the importance of these two components (*vide infra*).

A time study was run using NHPI ester **3.12** and the new set of optimised conditions (Table *3-14*).

Table 3-14: Time study.



3.1a (2.0 equiv.) **3.12** (1.0 equiv.) **3.13**

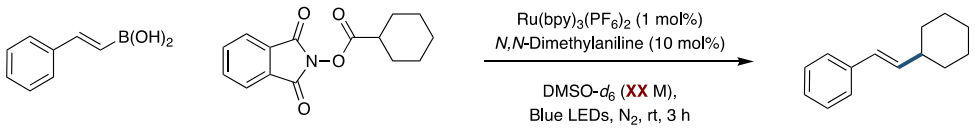
Entry	Time (min)	**3.13** (%)[a]	**3.12** (%)[a]
1	30	60	35
2	60	81	5
3	120	95	0
4	180	96	0

Reaction run on 0.2 mmol scale in dry and degassed DMSO-d_6. [a] Determined by ^1H NMR using 1,3,5-trimethoxybenzene as an internal standard (added after work up).

Running the reaction with the NHPI ester **3.12** confirmed that the reaction exhibits rapid consumption of starting material, yielding quantitative yields within three hours.

A concentration study was also carried out in Table *3-15*. As all the reactions were run in DMSO-d_6 (to monitor the reaction mixture without any potential loss of mass balance during the work-up), increasing the concentration to 0.2 M would save 1 mL of DMSO-d_6 for each reaction run.

Table 3-15: Concentration of the reaction.



3.1a (2.0 equiv.) **3.12** (1.0 equiv.) **3.13**

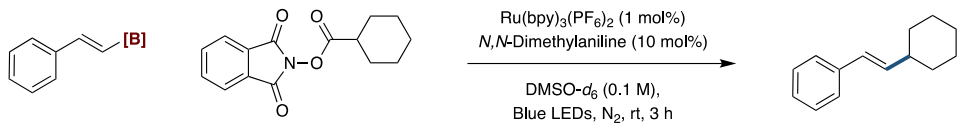
Entry	Scale and Concentration	**3.13** (%)[a]	**3.12** (%)[a]
1	0.1 mmol in 1 mL (0.1 M)	94	0
2	0.2 mmol in 2 mL (0.1 M)	96 (72)[b]	0
3	0.2 mmol in 1 mL (0.2 M)	94 (80)[b]	0

Reaction run in dry and degassed DMSO-d_6. [a] Determined by ^{1}H NMR using 1,3,5-trimethoxybenzene as an internal standard (added after work up). [b] Isolated yield.

Changing the scale of the reaction did not impact the outcome of the reaction (Table *3-15*, entry 1 vs entry 2). Increasing the concentration to 0.2 M led to the same NMR yield; however, afforded a slightly better isolated yield (entry 2 vs. entry 3).

Finally, different styrenyl organoborons were tested under the optimised conditions (Table *3-16*).

Table 3-16: Organoboron screening.



XX (2.0 equiv.) | **3.12** (1.0 equiv.) | **3.13**

Entry	**[B]**	**3.13** (%)[a]	**3.12** (%)[a]
1	$B(OH)_2$ (**3.1a**)	96	0
2	Bpin (**3.1b**)	28	0
3	BF_3K (**3.1c**)	8	0
4	Bcat (**3.1d**)	46	0
5	BMIDA (**3.1e**)	0	23
6	*p*-MeOPhB(OH)$_2$ instead of **3.1a**	0[c]	69
7	(*E*)-Oct-1-en-1-yl boronic acid instead of **3.1a**	0[c]	74

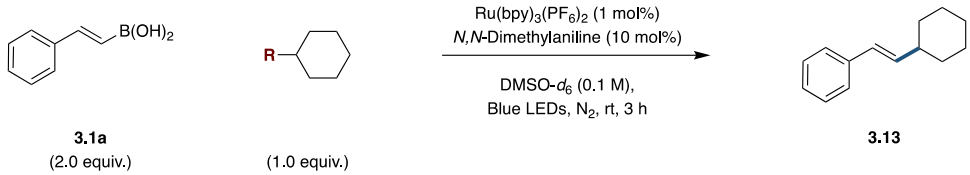
Reaction run on 0.2 mmol scale in dry and degassed DMSO-d_6. [a] Determined by ^{1}H NMR using 1,3,5-trimethoxybenzene as an internal standard (added after work up). [c] Expected products for entries 6 and 7 are different than **3.13** (*vide infra*).

Using styrenyl Bpin **3.1b** (entry 2), full consumption of NHPI ester **3.12** was observed; however, this yielded only 28% of the desired product. This could be explained by the fact that the boron atom in Bpin esters is less electrophilic than in the corresponding boronic acid, which affects the boronate formation step (*vide infra*). Furthermore, running the reaction with styrenyl BF_3K salt **3.1c** led to traces of product (entry 3). When styrenyl Bcat ester **3.1d** was employed as the coupling partner, the reaction gave moderate conversion to product (46%, entry 4). However, **3.1d** is not particularly stable and could easily be hydrolysed *in situ* to the corresponding styrenyl boronic acid **3.1a**, releasing catechol **3.11** which could explain the moderate yield of the reaction. The use of MIDA-protected styrene boronic acid **3.1e** (entry 5) did not afford the desired product **3.13**, nor did the aryl boronic acid (entry 6) or (*E*)-oct-1-en-1-yl boronic acid. The reason for these unsuccessful reactions will be discussed in greater

detail in the next section (see section 3.4). These results highlight the importance of styrenyl boronic acid in the reaction.

Carboxylic acids are also used as radical precursors and offer enhanced atom economy. MacMillan and coworkers were the pioneers in this area using amino acids to generate alkyl radicals *via* a dual Ir/Ni catalytic process (see Scheme *1-15*).[69] Since then, many other methodologies have been developed.[206,207] Thus to overrule this pathway and highlight the importance of the NHPI esters in this designed reaction, control experiments were run with alternative radical precursors (Table *3-17*).

Table 3-17: Role of NHPI esters.



Entry	R	**3.13** (%)[a]	SM (%)[a]
1	COOH	0	95
2	Br	0	100

Reaction run on 0.2 mmol scale in dry and degassed DMSO-d_6. [a] Determined by ^{1}H NMR using 1,3,5-trimethoxybenzene as an internal standard (added after work up).

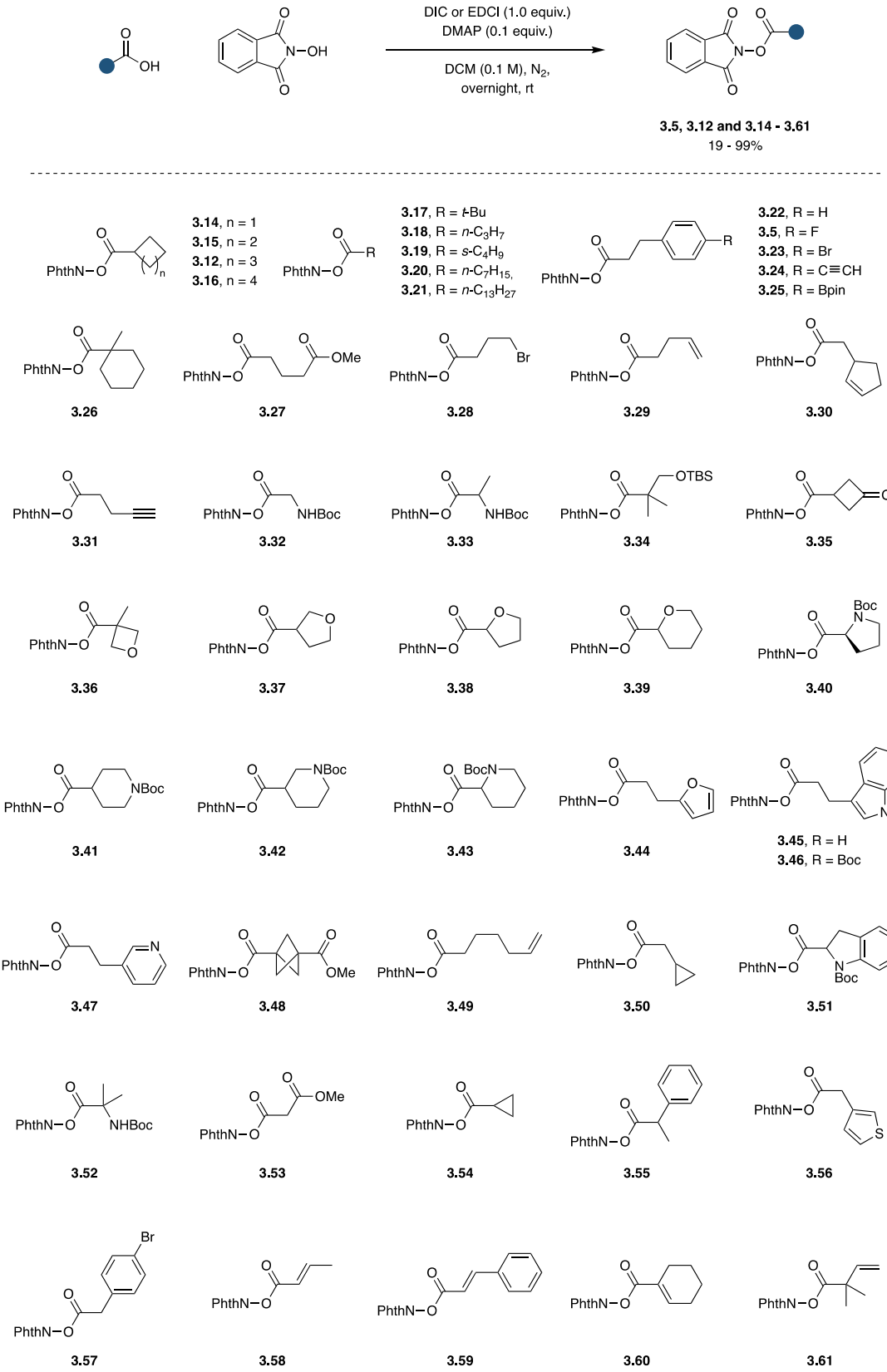
Using the corresponding cyclohexane carboxylic acid (entry 1) did not lead to the formation of the desired product **3.13** and a full recovery of the starting material was obtained (entry 1), ruling out single electron oxidation of the starting material by the photocatalyst and suggesting the reductive quenching of the NHPI ester **3.12** (*vide infra*). Finally, the use of an alkyl halide such as bromocyclohexane was also unproductive.

3.3 Reaction scope

3.3.1 Starting material synthesis

3.3.1.1 NHPI esters

After generating fully optimised conditions, these were then applied to a library of NHPI esters to assess the scope of the reaction. These NHPI esters were readily synthesised in a one-step synthesis from the corresponding carboxylic acid and *N*-hydroxyphthalimide in the presence of a coupling agent such as DIC[208] or EDCl[209] (Scheme *3-7*). Usually, NHPI esters were afforded with good to excellent yields, but in some cases the purification was challenging and was detrimental to the isolated yields (see Section 6).



Scheme 3-7: General synthesis of NHPI Esters.

3.3.1.2 Styrenyl boronic acids

Unfortunately, only a few styrene boronic acid starting materials were commercially available and, in most cases, were very expensive (Figure *3-7*).

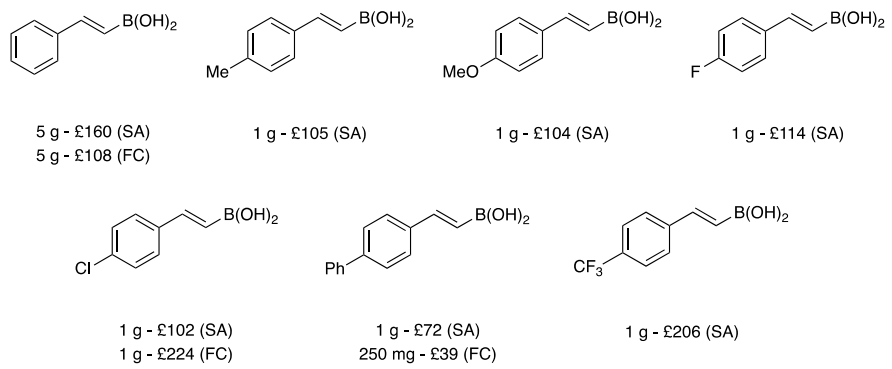
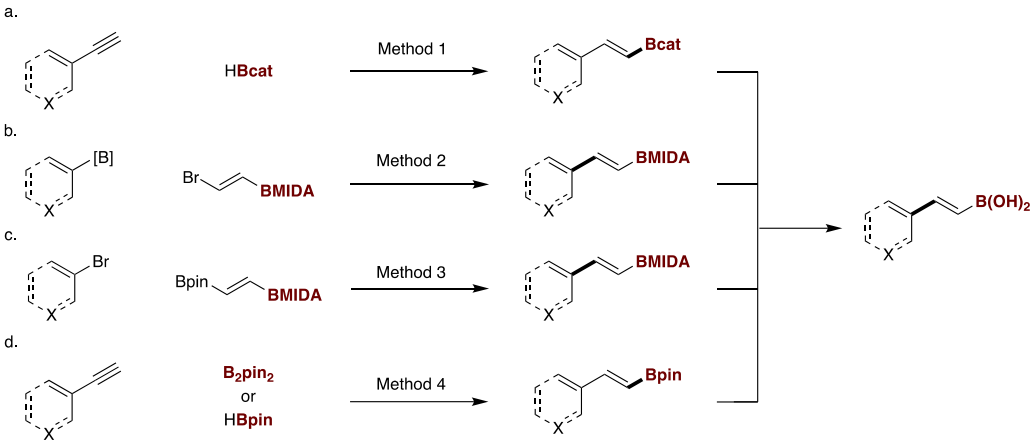


Figure 3-7: Commercially available styrenyl boronic acids. Prices were recorded on 23/05/23. SA: Sigma Aldrich Co. and FC: Fluorochem Ltd.

Although some of styrenyl boronic acids were purchased to expand the scope of the reaction, several substrates had to be synthesised. Based on literature searches, different routes were considered, each yielding alternative organoboron species: Bcat, BMIDA or Bpin. In each case, hydrolysis would afford the desired boronic acid product. The following reactions were considered:

- Hydroboration of a terminal alkyne using catecholborane (method 1, Scheme *3-8*a).
- Suzuki–Miyaura cross-coupling reactions using *trans*-bromo vinyl BMIDA and an (hetero)aryl boronic acid or pinacol ester (method 2, Scheme *3-8*b).
- Suzuki–Miyaura cross-coupling reactions using *trans*-Bpin vinyl BMIDA and an (hetero)aryl halide (method 3, Scheme *3-8*c).
- Metal-mediated hydroboration of a terminal alkyne (method 4, Scheme *3-8*d).



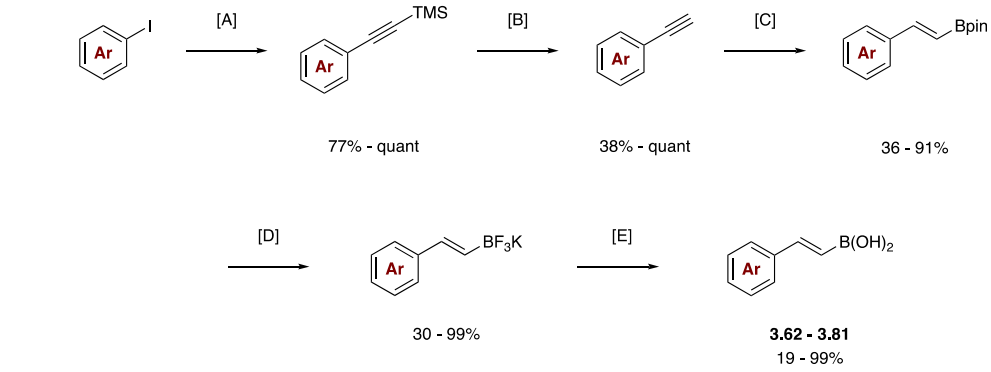
Scheme 3-8: Strategies considered for the synthesis of styrenyl boronic acids.

Hydroboration of alkynes using catechol borane has been reported in the literature.[210,211] Terminal alkynes were subjected to either a 1 M solution of catecholborane in THF or neat catecholborane, followed by hydrolysis. Although product was afforded only in the second case, the reaction worked with a very poor functional group tolerance and separation of the desired product from trace catechol proved challenging. This strategy, therefore, could not be considered as a general method to afford the desired styrenyl boronic acids. Based on previous work in the group, it was hypothesised that a Suzuki–Miyaura cross-coupling reaction between an (hetero)aryl boronic acid and *trans*-bromo vinyl BMIDA (method 2) would be an effective route.[212,213] Unfortunately, although the reaction was successful with moderate yields, purification of highly polar BMIDA products was challenging. Hydrolysis of this MIDA moiety to the corresponding boronic acid was troublesome. For these reasons, this route was also dismissed.

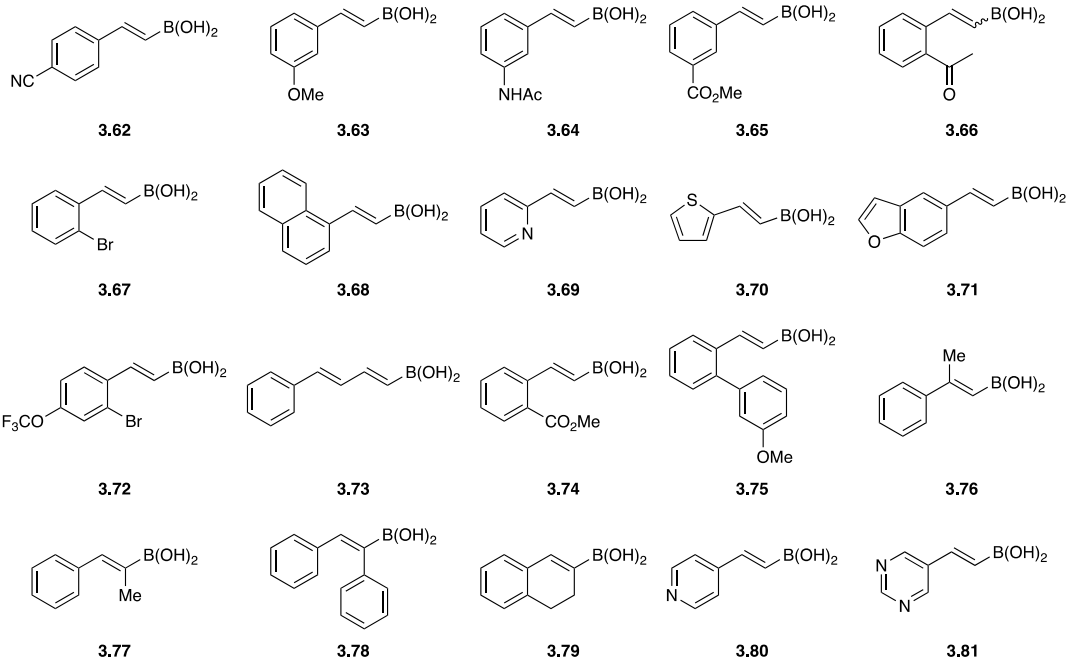
Metal-mediated hydroboration reactions of terminal alkynes delivering stable and easy-to-purify styrenyl boronic pinacol esters have been widely reported in the literature.[214] Different metals could be employed such as zinc,[215] rhodium, silver,[216,217] or copper. After different attempts, a Cu(I)-mediated hydroboration of terminal alkynes using B_2pin_2 was found to be the most efficient way to access to the desired styrenyl boronic pinacol esters (Scheme *3-8*d). However, direct hydrolysis from the boronic pinacol ester to the boronic acid, using for example sodium periodate (commonly reported in SI),[218] failed or gave poor yield. When the reaction worked, the product could not be separated from the pinacol byproduct. Thus, the Bpin product

was first transformed into a BF_3K salt, which can be readily isolated through precipitation. Further hydrolysis would afford the desired starting material with good yield. A summary of the route is depicted in Scheme *3-9*. In the case of commercially available and affordable alkynes, the synthesis started with a Cu-mediated hydroboration, which usually afforded the borylated product in excellent yields.[219–222] Otherwise, the synthesis started with a Sonogashira cross-coupling reaction between TMS-acetylene and the (hetero)aryl iodide (or bromide), followed by TMS deprotection furnishing the desired terminal alkyne. Although some substrates were troublesome, both steps afforded quantitative yield in most cases.

Despite a five-step synthesis to the desired styrenyl boronic acids, the route was robust and gave sufficient yields for use in the reaction. It is worth to note that in some cases, the isolated yield suffered from purification issues. A broad range of (*E*)-styrenyl boronic acids were synthesised using this methodology (Scheme *3-9*). In some cases, synthesis of the Bpin intermediate was afforded using alternative methods such as Miyaura borylation to generate **3.79** (see Section 6).



[A]. TMS-acetylene (1.25 equiv.), $Pd(PPh_3)_2Cl_2$ (1 mol%), CuI (2 mol%), NEt_3 (0.5 M), N_2, overnight, rt.
[B]. K_2CO_3 (2.0 equiv.), MeOH (0.2 M), 1 - 5 h, rt.
[C]. B_2pin_2 (1.1 equiv.), CuCl (5 mol%), DPEPhos (5 mol%), *t*-BuOK (10 mol%), MeOH (2.0 equiv.), THF (0.25 M), N_2, overnight, rt.
[D]. KHF_2 (4.0 equiv.), H_2O (50.0 equiv.), MeOH (0.1 M), 1 - 5 h, rt.
[E]. TMSCl (3.5 equiv.), MeCN:H_2O (4:1, 0.1 M), 1 - 5 h, rt.

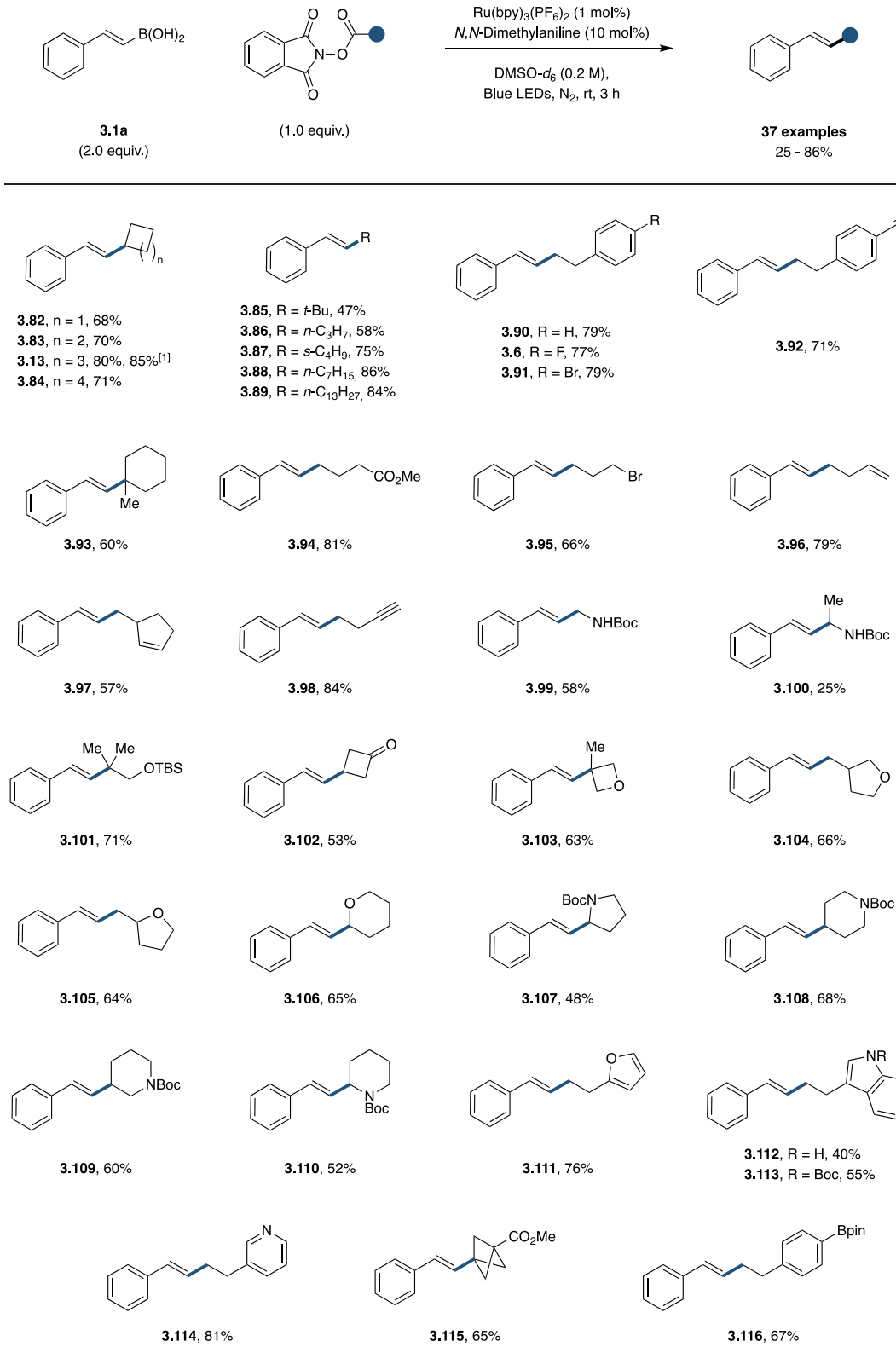


Scheme 3-9: General synthesis of styrenyl boronic acids.

3.3.2 Scope of the reaction

3.3.2.1 NHPI esters

Once starting materials were synthesised, the scope of the reaction was studied, initially through variation of the NHPI esters (Scheme *3-10*).



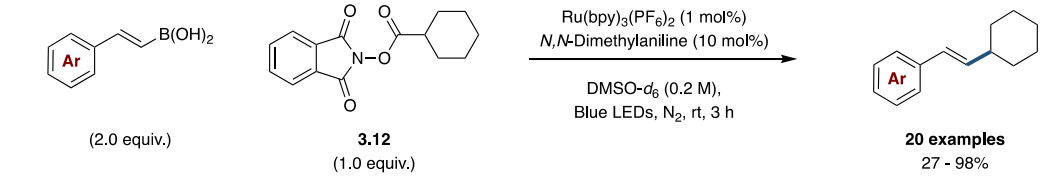
Scheme 3-10: Scope of the reaction: NHPI components.

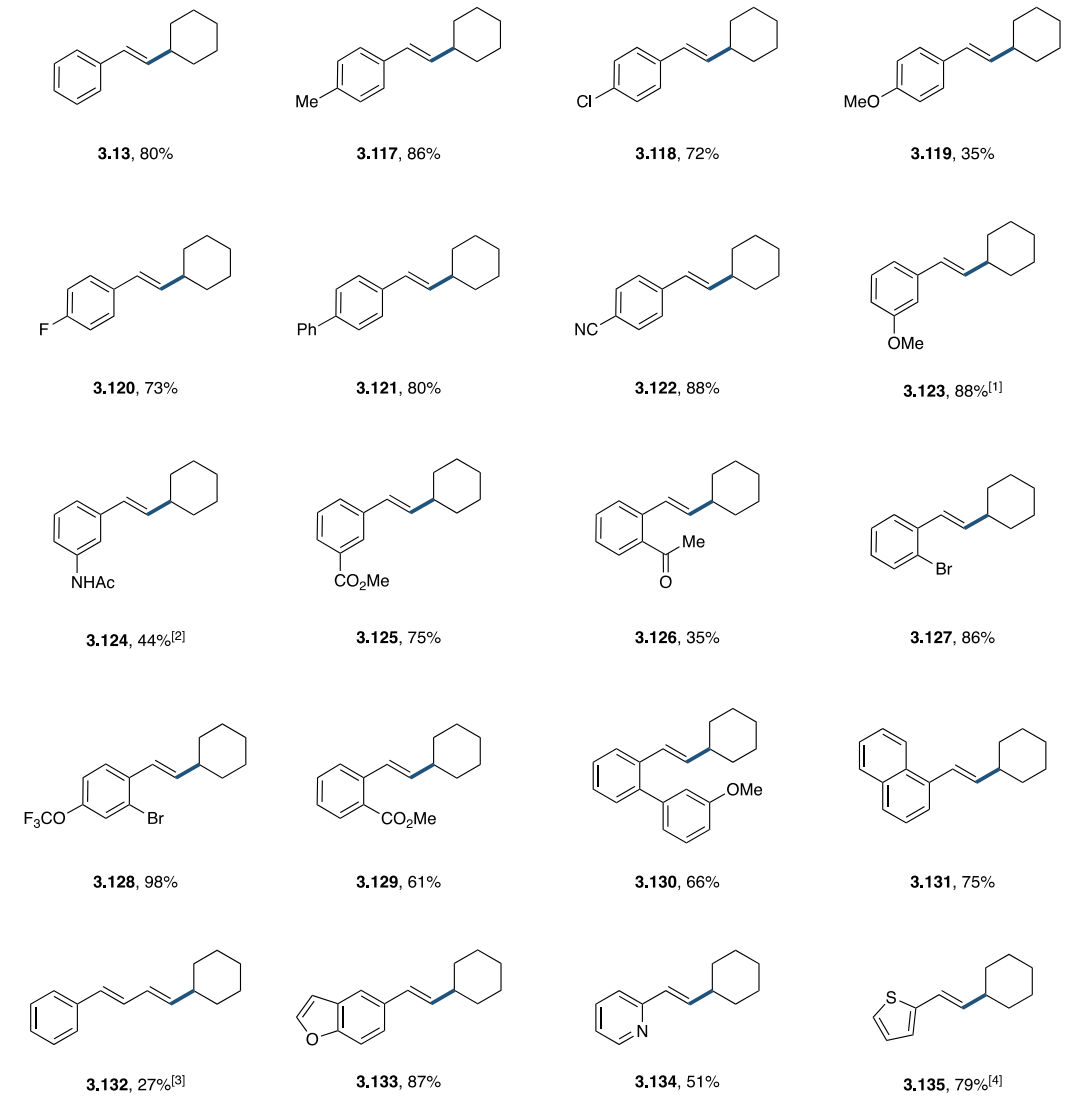
Reaction run on 0.2 mmol scale in dry and degassed DMSO-d_6. Isolated yields. *E:Z* >20:1 unless indicated. [1] Reaction scale up to 8.00 mmol.

The reaction was carried out with a panel of different NHPI esters (Scheme *3-10*). Cyclic NHPI esters from 4- to 7-membered rings (**3.13**, **3.82 – 3.84**, 68% – 80%) afforded the desired product with good to excellent yields. Substrates with altered steric footprints were also tolerated, examples such as *tert*-butyl (**3.85**) and *sec*-butyl (**3.87**) afforded 47% and 75% yields, respectively. Varied alkyl chain lengths were also tolerated from short-chain C3 (**3.86**, 58%), C7 (**3.88**, 86%) and long-chain C13 (**3.89**, 84%). Primary (**3.88 – 3.92**, *etc.*), secondary (**3.82 – 3.84**, *etc.*), and tertiary (**3.85**, **3.93**, **3.101**, *etc.*) radicals generally afforded the desired products with excellent yields. The reaction also tolerated aryl substituents (**3.90 – 3.92**, **3.116**, 67 – 79%). A broad range of functional groups was well tolerated under the reaction conditions such as esters (**3.94** and **3.115**), alkyl bromide (**3.95**), terminal (**3.96**) or internal (**3.97**) alkenes, alkynes (**3.92** and **3.98**), Boc-protected amines (**3.99**, **3.100**, **3107 – 3.110**), protected alcohol (**3.101**), ketone (**3.102**) or ethers (**3.103** and **3.104**). All the substrates afforded the desired products with excellent yield without side reactions. Nucleophilic α-oxo (**3.105** and **3.106**, 64 and 65%), as well as α-amino (**3.99**, **3.100**, **3.107**, and **3.110**, 25 – 58%) radicals were generated under the reaction conditions and reacted with **3.1a** to deliver the desired products in moderate to good yields. It appeared that the reaction is slightly sensitive to steric hinderance. Indeed, a small decrease in yield was observed when running the reaction from 4- (**3.108**) to 3- (**3.109**) to 2-Boc piperidine (**3.110**) yielding 68%, 60% and 52% of product, respectively. Heteroaryl substituents were also tolerated such as furan (**3.111**, 76%), free (**3.112**, 40%) or Boc-protected (**3.113**, 55%) indoles or pyridine (**3.114**, 81%). The strained substituted bicyclo[1.1.1]pentane (**3.115**), a known benzene bioisostere,[223] gave the desired product with 65%. Finally, the incorporation of other synthetic handles for use in further cross-coupling reactions has been considered. An aryl Bpin example (**3.116**) afforded the desired product with 67% yield. The reaction with **3.12** was also suitably scalable, with an 8.00 mmol scale reaction giving excellent yield (1.27 g, 85%).

3.3.2.2 Styrenyl boronic acids

Alternative styrenyl boronic acids were also subjected to the standard conditions, using NHPI ester **3.1a** (Scheme *3-11*).





Scheme 3-11: Scope of the reaction: styrenyl boronic acid components.

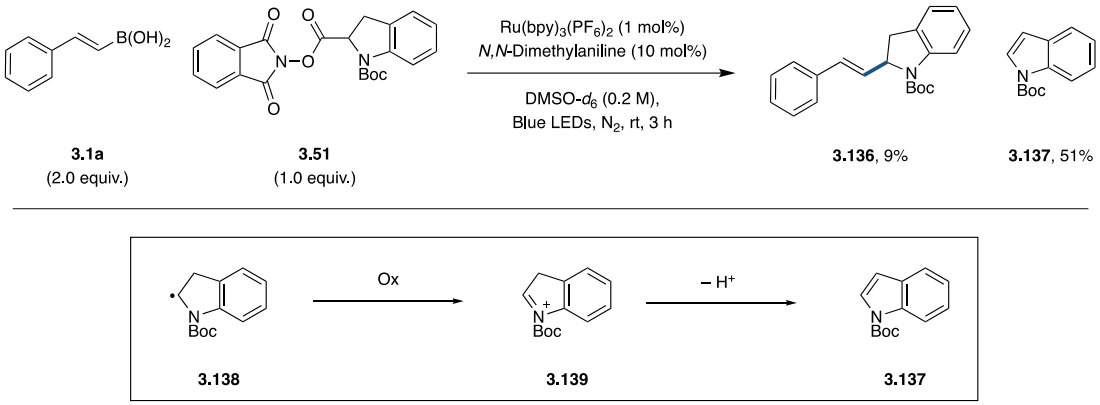
Reaction run on 0.2 mmol scale in dry and degassed DMSO-d_6. Isolated yields. *E*:*Z* >20:1 unless indicated. [1] *E*:*Z* = 16.5:1. [2] *E*:*Z* = 12.5:1. [3] (*E*,*E*):(*Z*,*E*):(*E*,*Z*):(*Z*,*Z*) = 1:1:0.1:0.1. [4] *E*:*Z* = 7.3:1.

The developed methodology tolerated both electron-donating (**3.117**, **3.121**, *etc.*) and electron-withdrawing (**3.118**, **3.120**, *etc.*) substituents, affording comparable yields. Thus, tolyl (**3.117**) or biphenyl (**3.121**) starting materials delivered the desired product with 86% and 80%, respectively. On the other hand, electron-poor *p*-chloro (**3.118**, 72%), *p*-fluoro (**3.120**, 73%) or *p*-cyano (**3.122**, 88%) styrenyl boronic acids were suitable coupling partners. Surprisingly, a very poor yield of 35% was observed when using *p*-methoxy starting material (**3.119**), whereas the reaction performed with *m*-methoxystyrenyl boronic acid afforded the desired product **3.123** with 88% yield. Broad functional group tolerance is also observed for the styrenyl boronic acid moiety, *with meta*-substituted amide (**3.124**, 44%) and ester (**3.125**, 75%) functionalities yielding the desired products with moderate-good yields. Moving the substitution to the *ortho* position afforded the desired product with good to excellent yield: *o*-bromo starting materials (**3.127** and **3.128**) were the best substrates across the scope, affording 86% and 98% yield, respectively. These products are interesting since they could be further employed as cross-coupling partners in reactions such as Suzuki–Miyaura couplings. The ketone substituted example (**3.126**) afforded a poor yield whereas the methyl ester example (**3.129**) restored good reactivity with 61% yield. Bulky substituents on the *ortho* position such as the 3-methoxyphenyl substituted starting material (**3.130**) gave the expected product in good yield. It is worth noting that no side reactions were observed, such as interception of the benzylic radical (or benzylic carbocation, *vide infra*) by nucleophilic substrates (**3.125**, **3.126**, and **3.130**) or protodeboronation of the starting material. Finally, modifying the phenyl ring to a naphthyl group (**3.131**) had little effect on the yield (75%); however, the use of the diene starting material plummeted the reaction yield, where only 27% of product (**3.132**) was observed. Indeed, in this case, the starting material was not very stable and was prone to protodeboronation side reaction, preventing efficient conversion to product. Finally, the reaction with hetereostyrenyl boronic acids such as benzofuran (**3.133**), pyridine (**3.134**), and thiophene (**3.135**) afforded the desired product with good to excellent yield, respectively 87%, 51% and 79%. In most cases, only the *E*-diastereoisomer was obtained after three hours (*E:Z* > 20:1) and only traces (< 1 – 5 %) of the *Z*-diastereoisomer were noticeable by ^{1}H NMR; however, very few examples displayed a higher *E:Z* ratio (< 20:1) such as **3.123**, **3.124**, **3.132** and **3.135**. Photocatalytic isomerisation of (*E*)-alkene to the *Z*-diastereoisomers have been well

documented in the literature (see section 1.1.3.2), it was hypothesised that this process occurred post reaction.[32]

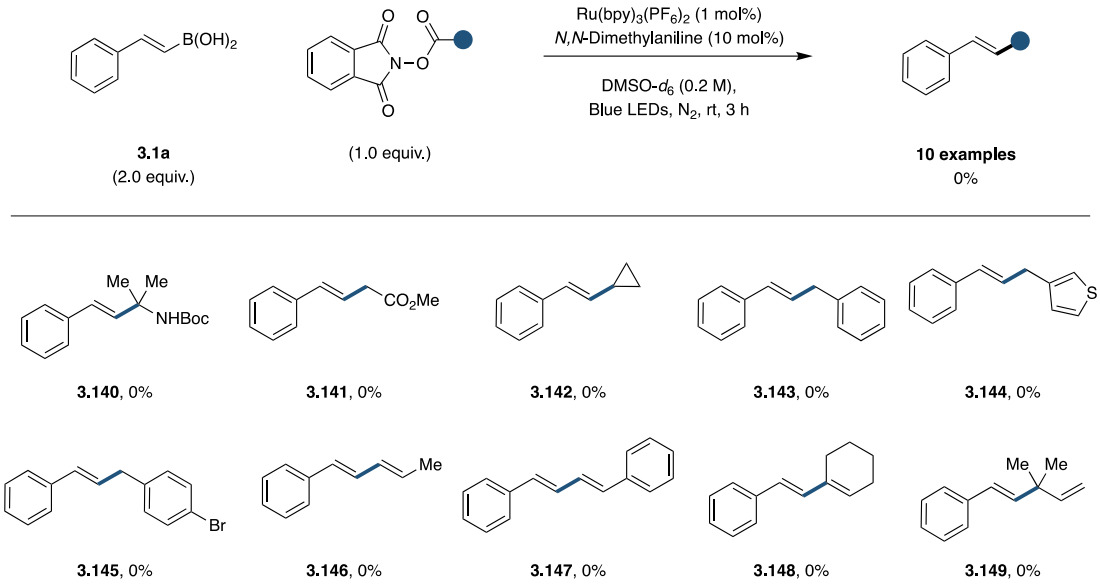
3.3.3 Limitation of the reaction: NHPI ester components

The reaction has some limitations and some NHPI esters were found to be low yielding (Scheme *3-12*) or unreactive (Scheme *3-13*) under the standard conditions.



Scheme 3-12: Developed reaction with the NHPI ester **3.51**.

In the case of the reaction with the NHPI ester **3.51**, only 9% of the desired product **3.136** was afforded (isolated), whereas 51% of Boc-indole **3.137** was isolated. The NHPI ester **3.51** subjected to the reaction conditions furnished the indoline radical **3.138**. Addition to the styrenyl boronic acid **3.1a** delivered the desired product; however, further oxidation of the radical **3.138** resulted in the indoline ammonium species **3.139**, with subsequent rearomatisation affording the indole **3.137**. In some cases, the reaction did not afford the desired product (Scheme *3-13*).



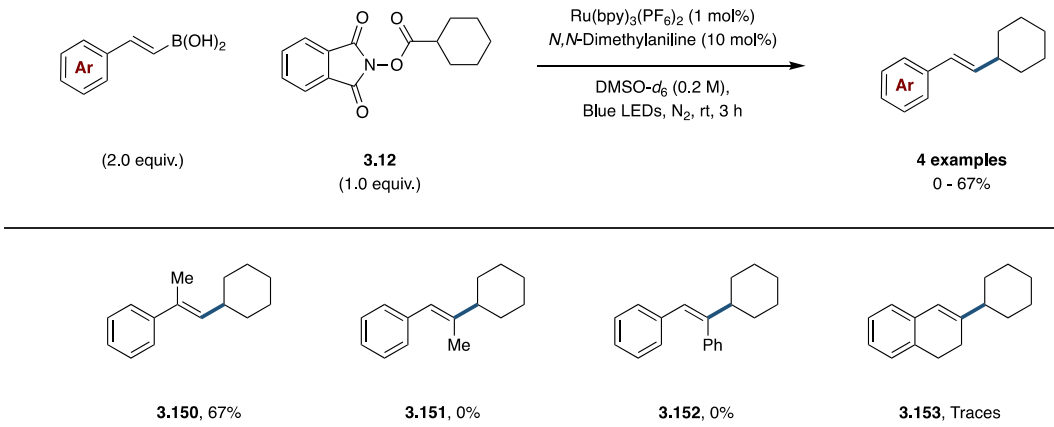
Scheme 3-13: Failed NHPI esters.

The tertiary α-amino substrate **3.52** did not work under the reaction conditions and only trace reactivity was observed (**3.140**). Nevertheless, this result could have been predicted from the decrease observed in the yield between the secondary α-amino substrate (**3.100**, 25%) and the primary α-amino substrate (**3.99**, 58%). NHPI ester **3.53**, which leads to a more electrophilic radical, was fully consumed after three hours but did not yield the desired product **3.141**. The radical is presumed to have undergone degradation, since no identifiable peaks were observed in the NMR of the reaction mixture. Disubstituted **3.53**-like NHPI esters such as cyclopropane[224] or cyclobutane,[225] have been used in the literature, whereas, this specific NHPI ester **3.53** is novel. Cyclopropane NHPI ester **3.54** was found to be unreactive, and only traces of product **3.142** were afforded (< 5%). A darker reaction mixture was observed, whereas a bright red solution is usually obtained, and a significant amount of unreacted starting material was recovered (~ 80%), leading to the hypothesis that a potential catalyst poisoning event occurred. This result was surprising since several publications have reported the use of this NHPI ester.[226] NHPI esters affording benzylic radicals (**3.55**, **3.56**, and **3.57**) were found to be inefficient under the developed reaction conditions. Although full consumption of the NHPI esters was usually observed, only traces (< 10%) of products were afforded (**3.143**, **3.144**, **3.145**, respectively). In some cases, side reactions such as radical homocoupling reactions competed with the desired reaction. Finally, the generation of a sp^2-hybridised radical from NHPI esters **3.58**,

3.59 and **3.60** were unsuccessful under the reaction conditions and no product was observed (**3.146**, **3.147**, **3.148**, respectively). Similarly, König and coworkers reported cinnamic NHPI ester **3.59** as an unreactive substrate in their metal-free, visible-light-mediated, decarboxylative alkylation of biomass-derived molecules.[227] The allylic NHPI ester **3.61** was also subjected to the reaction conditions but the product **3.149** was not afforded (43% of **3.61** was remaining after three hours).

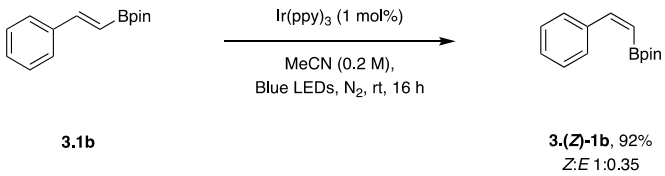
3.3.4 Limitation of the reaction: styrenyl boronic acids

The reaction run with *α*-methyl substituted styrenyl boronic acid **3.76** afforded the desired product **3.150** with 67% yield (Scheme *3-14*). Moving the substitution to the *β*-position was found to be detrimental. In the case of the reaction of **3.77** with **3.12**, no formation of the desired product was observed (**3.151**, 0%) under the standard conditions even though 50% of the NHPI ester was consumed after three hours. In the case of **3.78**, the substrate was found to be very unstable and although only traces of **3.78** were observed in the reaction mixture, no product **3.152** was detected and 60% of the NHPI ester **3.12** remained unreactive. Protodeboronation degraded the styrenyl boronic acid starting material, preventing any potential reaction. Finally, the reaction was attempted with 1,2-dihydronaphthalene boronic acid **3.79** and afforded only traces of product (**3.153**, < 5%), although only 33% of the NHPI ester **3.12** was recovered from the reaction mixture.



Scheme 3-14: Reaction with *α*- and *β*-substituted styrenyl boronic acids.

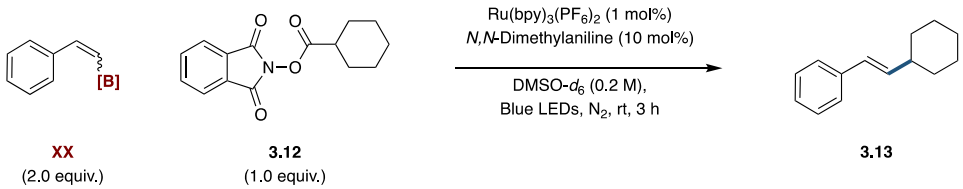
It was hypothesised that the *Z*-diastereoisomer **3.(*Z*)-1a**, subjected to the standard conditions, would still afford the *E*-product **3.13**. Thus, the synthesis of **3.(*Z*)-1a** was attempted: isomerisation of the *E*-diastereoisomer **3.1b** to the *Z*-alkene **3.(*Z*)-1b** using energy transfer as described in section 1.1.3.2 (Scheme *3-15*).[228] The reaction afforded the desired product as a mixture of *Z*:*E* (1:0.35) with excellent yield (92%). Hydrolysis of the Bpin ester to $B(OH)_2$ afforded a mixture of *Z*:*E* diastereoisomers.



Scheme 3-15: Photoinduced isomerization of **3.1b**.

In line with previously observed results (Table *3-16*), running the reaction with the mixture of Bpin esters gave a poor conversion (Table *3-18*, entry 1) where only 13% of product was observed. When the reaction was run with **3.(*Z*)-1a**, the formation of **3.13** dropped down to 34% (entries 2 and 3). In all cases, full consumption of the NHPI ester **3.12** was not observed, leading to the conclusion that the reaction was slower. It is worth noting that **3.(*Z*)-1a** was highly unstable and underwent rapid protodeboronation; side products such as boric acid could be the cause of the reduced reaction rate. No traces of the *Z*-product **3.(*Z*)-13** were observed thus, no further investigations were carried out.

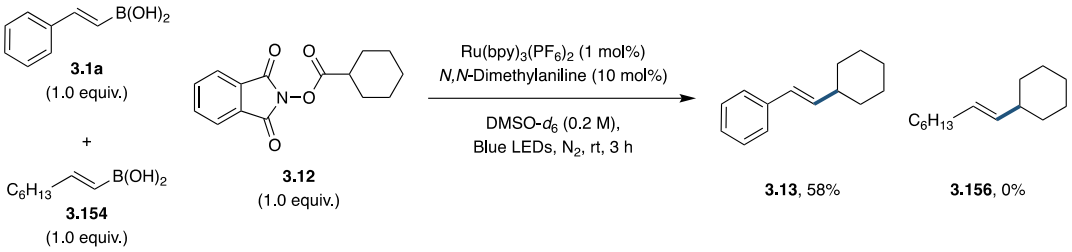
Table 3-18: Reaction with a mixture of *Z*:*E* diastereoisomers.



Entry	**[B]**	Ratio *Z*:*E*	**3.13** (%)[a]	**3.12** (%)[a]
1	Bpin, **3.(*Z*)-1b**	1:0.35	13	40
2	$B(OH)_2$, **3.(*Z*)-1a**	1:1.1	34	64
3[b]	$B(OH)_2$, **3.(*Z*)-1a**	1:1.1	33	49

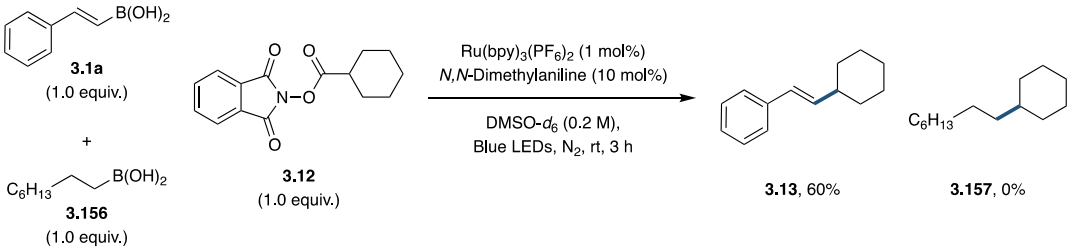
Reaction run in 0.2 mmol scale in dry and degassed DMSO-d_6. [a] Determined by ^{1}H NMR using MTBE as an internal standard (added after reaction). [b] 1.0 equiv. of **3.(*Z*)-1a** used (instead of 2.0 equiv.).

Competition reactions were run with **3.154** and **3.156** and **3.1a** to highlight the chemoselectivity of the reaction towards styrenyl boronic acids (Scheme *3-16* and Scheme *3-17*).



Scheme 3-16: Competition reactions with alkenyl boronic acid, **3.154**.

Running the reaction with one equivalent of styrenyl boronic acid **3.1a** and one equivalent of **3.154** (Scheme *3-16*) gave only one product **3.13** in 58% yield. Although almost full consumption of **3.12** (19% remaining after three hours) was observed, there was no traces of **3.156** in the crude mixture and full recovery of **3.154** was recovered.

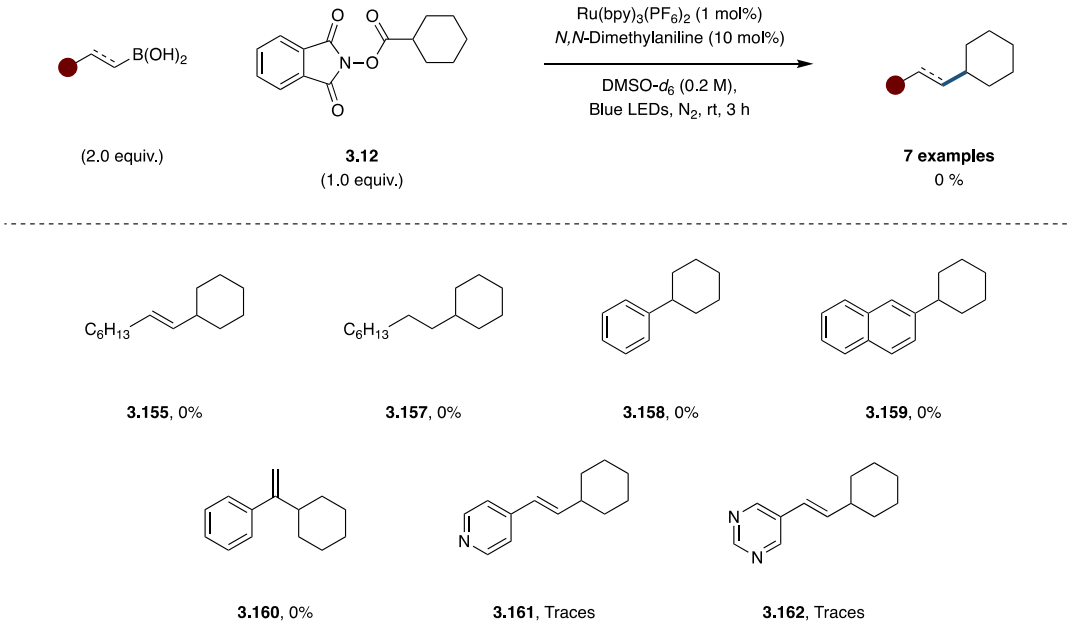


Scheme 3-17: Competition reaction with alkyl boronic acid, **3.156**.

Running the reaction with one equivalent of styrenyl boronic acid **3.1a** and one equivalent of **3.156** (Scheme *3-17*) yielded only one product **3.13** in 60% yield. Although almost full consumption of **3.12** was observed (10% remaining after three hours) there was no traces of **3.157** in the crude mixture and full recovery of **3.156** was recovered.

No traces of product **3.155** and **3.157** were observed, and full recovery of the corresponding organoboron counterparts was afforded. These results emphasised the chemoselectivity towards styrenyl boronic acids, highlighting the importance of an adjacent aryl substituent in stabilising the radical intermediates (see Section 3.4.1.3). Consumption of the NHPI ester **3.12** was slightly reduced in both cases; however, a non-negligible amount of NHPI collapsed to the desired alkyl radical, which potentially followed a degradation pathway.

Moreover, some substrates were found to be unreactive under the reaction conditions (Scheme 3-18).



Scheme 3-18: Failed organoboron components.

In agreement with previous competition reactions (Scheme *3-16* and Scheme *3-17*), running the reaction with two equivalents of **3.154** and **3.156** did not furnish products **3.155** and **3.157**. Aryl boronic acids such as phenyl boronic acid **3.2a** or naphthalene boronic acid were unsuccessful regarding the developed coupling reaction with NHPI ester **3.12** and products **3.158** and **3.159** were not observed, as well as the product **3.160** from a regioisomer of **3.1a**. In some cases, the reaction afforded only traces (<5%) of products **3.161** and **3.162**; however, the starting materials **3.80** and **3.81** were found to be unstable and protodeboronation occurred, disabling the desired reaction.

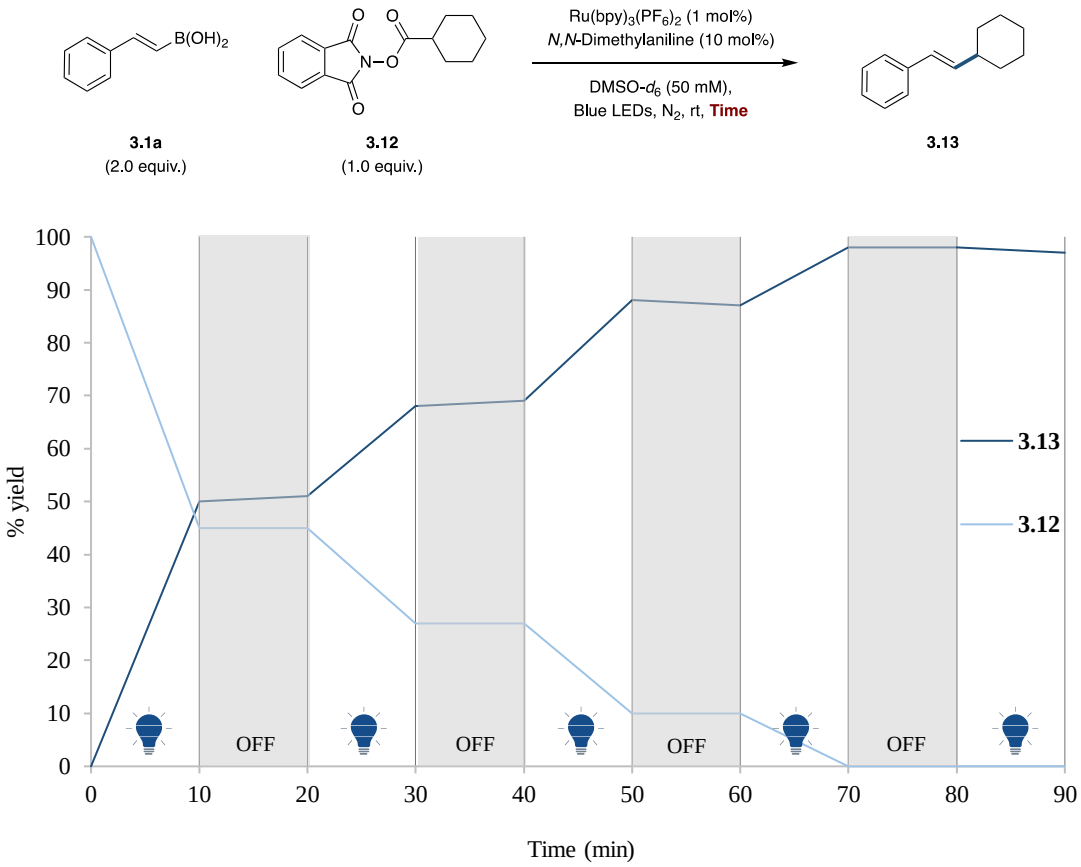
3.4 Mechanistic investigations and control reactions

3.4.1 Mechanism of the reaction

3.4.1.1 Alkyl radical formation

In the first instance, the proposed radical pathway was verified with a number of control experiments. From optimisation reactions, the reaction failed to proceed when no photocatalyst was added (entry 7, Table *3-13*), or when the reaction was not irradiated with blue LEDs (Table *3-4*), highlighting the importance of those two components. Additionally, the following on/off experiment was performed (Scheme *3-19*) and confirmed that the reaction proceeded only when the reaction mixture was irradiated under blue LEDs, disproving an efficient chain propagation mechanism.[84,86]

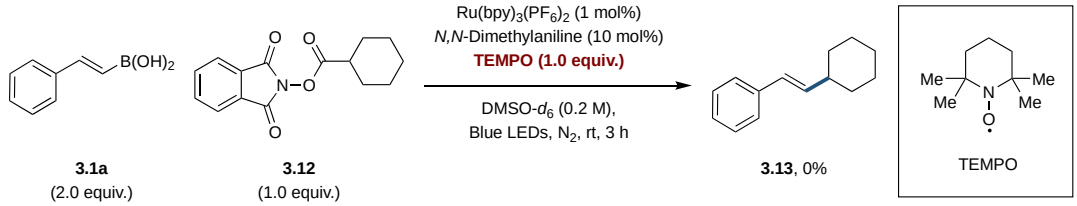
Scheme 3-19: On/Off experiment.



Reaction run in a J. Youngs NMR tube at 50 mM, monitored by ^{1}H NMR using MTBE as an internal standard.

Note: No mechanical stirring was performed during this time study.

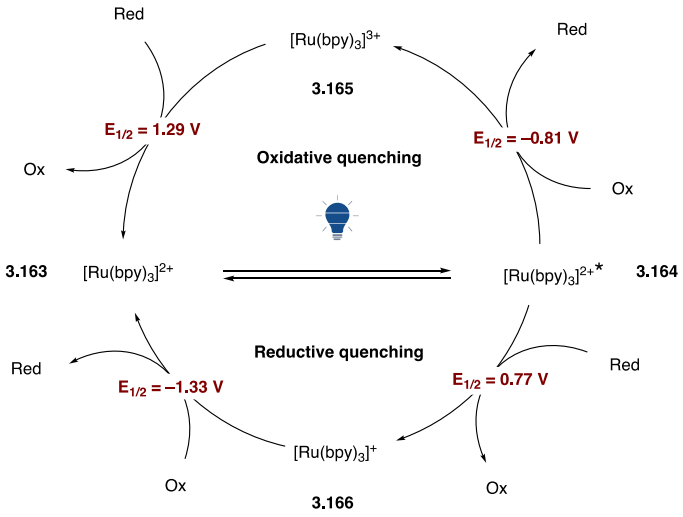
Finally, a common radical trap (TEMPO) was added in order to see if the yield of the reaction would be altered, thus, the reaction was run with one equivalent Scheme *3-20*. The reaction yield fell precipitously and no product was observed under the reaction conditions.



3.1a (2.0 equiv.) **3.12** (1.0 equiv.) **3.13**, 0%

Scheme 3-20: Reaction run with a radical trap: TEMPO.

From previous control experiments, the reaction mechanism likely proceeds through a radical pathway. NHPI esters are active redox species that could be reduced by excited photocatalysts, generating radical intermediates.[178–180] The reaction mixture was irradiated under blue LEDs (λ_{max} = 456 nm), where $Ru(bpy)_3(PF_6)$ absorbs light (λ_{max} = 452 nm). Upon irradiation, $Ru(bpy)_3^{2+}$ **3.163**, in the ground state, absorbs a photon leading to a photoexcited species **3.164** (Scheme *3-21*). This later can either undergo oxidative quenching leading to the oxidised $Ru(bpy)_3^{3+}$ **3.165** ($E_{1/2}$ = –0.81 V vs. SCE) or reductive quenching leading to the reduced species $Ru(bpy)_3^{+}$ **3.166** ($E_{1/2}$ = 0.77 V vs. SCE) (Scheme *3-21*).[1]



Scheme 3-21: Oxidative and reductive quenching pathway of $Ru(bpy)_3^{2+}$ **3.163**.

NHPI esters are involved in a reductive quenching process where they are being reduced by a photocatalyst species.[1] Indeed, NHPI ester **3.12** ($E_{1/2}$ = –1.28 V vs. SCE)[229] could undergo single electron reduction with either $Ru(bpy)_3^{2+*}$ **3.164** (oxidative quenching pathway) or $Ru(bpy)_3^{+}$ **3.166** (reductive quenching pathway). However, in the first case the redox potential of the photocatalyst ($E_{1/2}$ (Ru^{III}/Ru^{II*})) is greater than the redox potential of the NHPI ester ($E_{1/2}$ ($NHPI/NHPI^{\bullet-}$)), preventing the reaction from occurring and thus overruling the oxidative quenching pathway. Upon absorption of a photon, the photoexcited species **3.164** undergoes reductive quenching with an external reductant. Stern–Volmer quenching experiments showed that *N*,*N*-dimethylaniline **3.167** quenched the excited photocatalyst $Ru(bpy)_3^{2+*}$ **3.164** (Figure *3-8*). The additive promotes the single electron reduction of **3.164** to the reduced $Ru(bpy)_3^{+}$ **3.146** species and the amminium radical $PhNMe_2^{\bullet+}$ **3.168**. Thus, the choice of the additive (*N*,*N*-dimethylaniline, **3.167**) was important in promoting the reaction since its redox potential needed to be lower than the redox potential of the photoexcited Ru species ($E_{1/2}$ (Ru^{II*}/Ru^{I}) > $E_{1/2}$ ($PhNMe_2^{\bullet+}$ /$PhNMe_2$)). Literature reports the redox potential of *N*,*N*-dimethylaniline **3.167** ($E_{1/2}$ = 0.76 V vs. SCE),[230] which matches with the Ru photocatalyst. Moreover, neither styrenyl boronic acid **3.1a** nor the NHPI ester **3.12** resulted in the quenching of $Ru(bpy)_3^{2+*}$ **3.164**, highlighting the importance of the presence of *N*,*N*-dimethylaniline **3.167**.

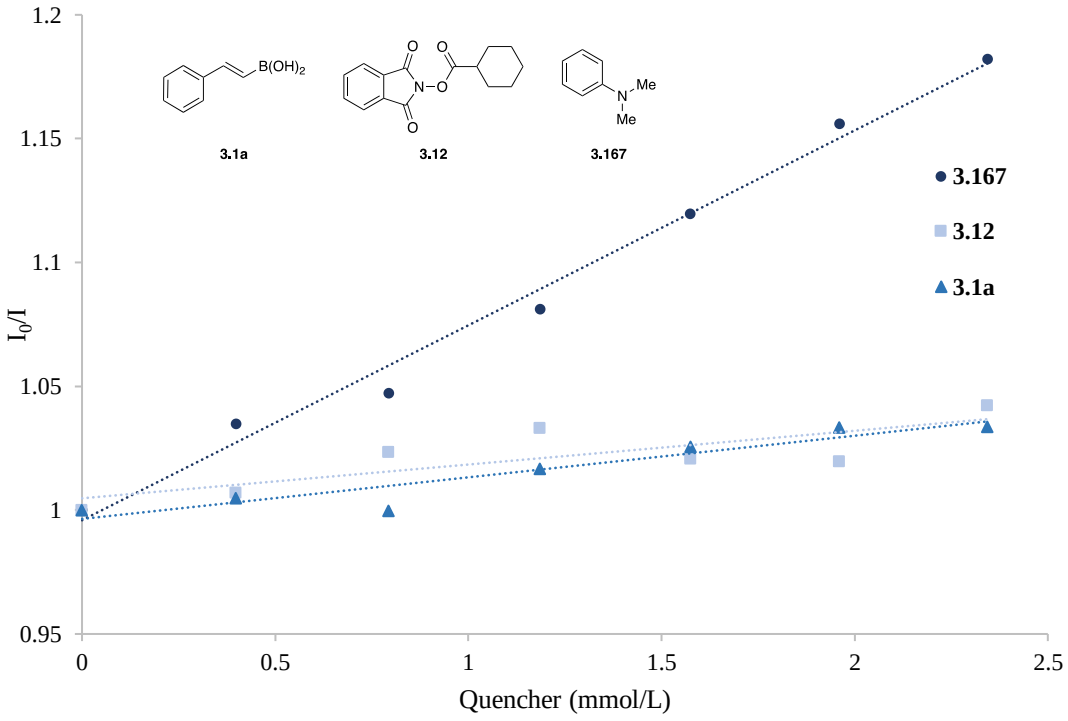
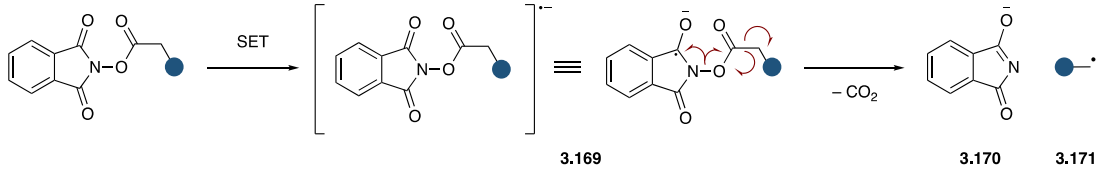


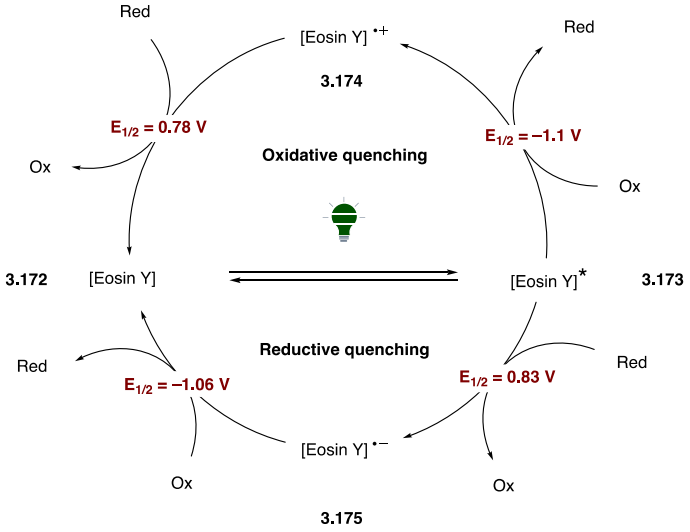
Figure 3-8: Stern–Volmer linearisation.

Hence, the NHPI ester can undergo single electron reduction with $Ru(bpy)_3^+$ **3.166**, regenerating the photocatalyst **3.163** in its ground state and a reduced NHPI ester species **3.169**. This species then irreversibly decarboxylates releasing carbon dioxide, phthalimide anion **3.170** (which after protonation yields phthalimide **3.7**), and the desired alkyl radical **3.171** (Scheme *3-22*).[191]



Scheme 3-22: Decarboxylative reduction of NHPI esters.

The redox properties of the photocatalyst are crucial to promote the reaction and explains why the reaction did not work with several other photocatalysts in Table *3-9*. For instance, looking at the redox potential of Eosin Y (**3.172**, Scheme *3-23*) justified the poor yield observed (entry 7, Table *3-9*).

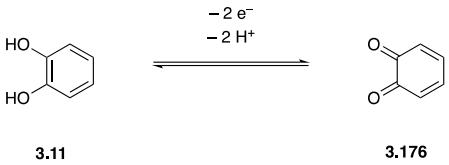


Scheme 3-23: Oxidative and reductive quenching pathway of Eosin Y **3.172**.

Similarly, NHPI esters can undergo single electron transfer with Eosin Y* **3.173** ($E_{1/2}$ ($EY^{\bullet+}/EY^*$) = –1.1 V vs. SCE) or with Eosin $Y^{\bullet-}$ **3.175** ($E_{1/2}$ ($EY/EY^{\bullet-}$) = –1.06 V vs. SCE).[231] The redox potential of NHPI esters do not appear to be in agreement with the reduction potentials of Eosin Y. Thus, $Ru(bpy)_3^+$ **3.176** is more reducing than EY^*

3.173 or $EY^{\bullet -}$ **3.175**, explaining the poor yield of the reaction when Eosin Y was used as photocatalyst.

Looking back at the optimisation (see section 3.2.1), the initial hit was run with catechol **3.11**. Interestingly, catechol has an oxidation potential at 1.21 V vs. Ag/AgCl electrode[232] corresponding to the oxidation to *ortho*-quinone **3.176** (Scheme *3-24*).[233]



Scheme 3-24: Simplified oxidation of catechol.

Despite the different conditions between our reaction conditions and the reported oxidation potential, this latter seems too high to reduce $Ru(bpy)_3^{2+*}$ **3.164** to $Ru(bpy)_3^{+}$ **3.166**. Previous optimisation experiments indicated that catechol promoted the reaction, allowing the reductive quenching of the excited photocatalyst species. This could be explained by the interaction between catechol and styrenyl boronic acid. It has been shown that, in the presence of boronic acid derivatives, catechol is more likely form a boronate species, altering the redox properties of catechol.[234] The boronate formation facilitates the oxidation of catechol by changing the electron density of the oxygen atom. Recently, VanVeller and coworkers reported a 0.9 V decrease in the oxidation of 3,5-di-*tert*-butylcatechol with diphenyl borinic acid (from ~ 0.9 V to ~ 0 V vs. $Ag/AgNO_3$).[235]

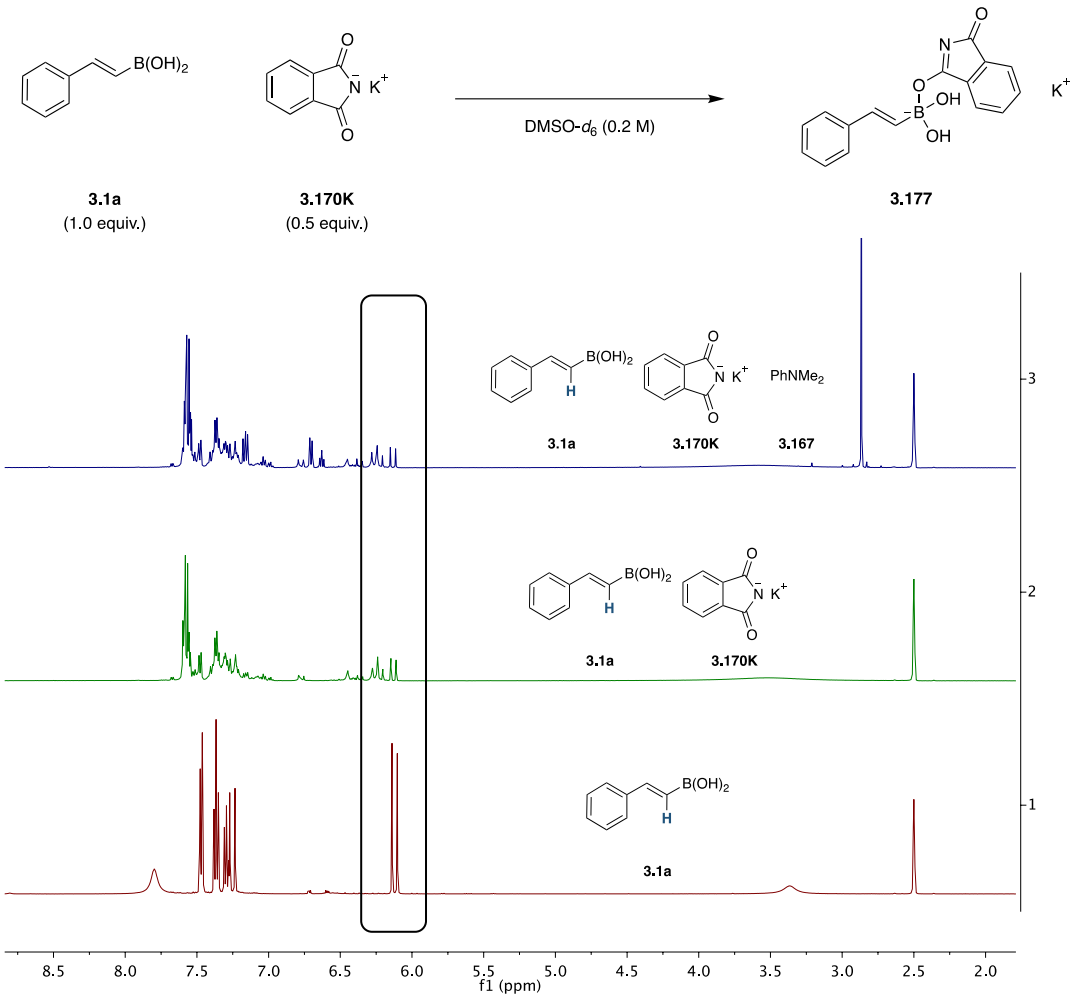
3.4.1.2 Formation of a boronate

Nucleofuge rebound of the phthalimide anion **3.170** with styrenyl boronic acid **3.1a** leads to the *in situ* formation of a styrenyl boronate **3.177**, which can react with the alkyl radical under a Giese-type addition.

The boronate formation was monitored by NMR spectroscopy by stirring styrenyl boronic acid **3.1a** and potassium phthalimide (NPhthK, **3.170K**). Despite a messy ^1H NMR spectrum, highlighting complex interactions between the two starting

materials, ^{11}B NMR spectroscopy confirmed the rapid formation of a boronate species (peak at 0.24 ppm, **3.157**).

Figure 3-9 : ^{1}H NMR spectra. Red: **3.1a**; Green: **3.1a** + **3.170K** (0.5 equiv.); Blue: **1a** + **3.170K** (0.5 equiv.) + **3.167** (5 mol%).



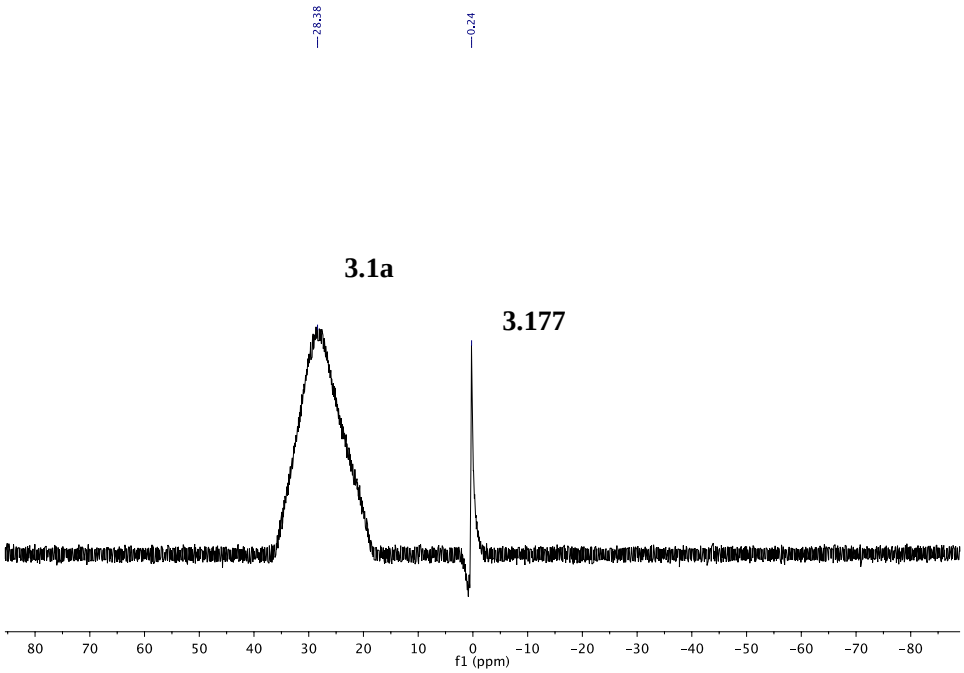
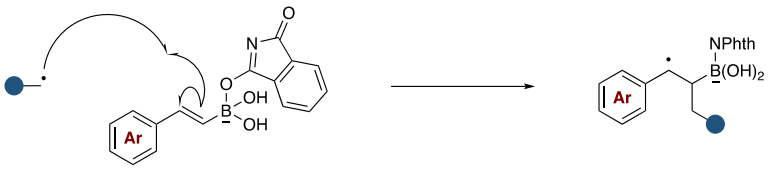


Figure 3-10: ^{11}B NMR of a mixture of **1a** and NPhthK **3.170K** (0.5 equiv.).

The phthalimide rebound, leading to the boronate formation, was found to be important since the reaction did not work with the styrenyl BF_3K salt **3.1c** (Table *3-16*, entry 3) or styrenyl BMIDA **3.1e** (Table *3-16*, entry 5). Meanwhile, styrenyl BF_3K salts could too electron-rich to undergo reaction with nucleophilic radicals (*vide infra*). Interestingly, the reaction only works efficiently with free boronic acids. In 2023, Song and coworkers reported a visible-light mediated coupling reaction between styrenyl boronic acids and α-bromodifluoroacylarenes (see Scheme *1-49*).[163] Styrenyl boronic acid intercepts an electrophilic difluoroacyl radical, affording the same type of product. They proposed two different pathways regarding the formation of the alkyl radical, both involve the formation of a cyclic intermediate, where hydrogen bonding plays a role in its stabilisation (see Scheme *3-5*). The importance of the boronic acid moiety in our developed reaction could result from a similar interaction between **3.1a** and the NHPI ester **3.12**.

3.4.1.3 Interception of the alkyl radical



3.171 3.177 3.178

Scheme 3-25: Interception of the radical by **3.177**.

From the recent examples using styrenyl boronic acids (see section 1.3.3.4), it is not surprising that the alkyl radical undergoes *ipso*-addition to styrenyl boronic acid, and does not follow the usual reactivity observed in the Giese-type addition to alkenyl Bpin (See section 1.3.3.2) generating an α-boryl radical. DFT calculations by Leonori and coworkers (Scheme *1-45*) regarding the styrenyl BF_3K salt reported a huge difference in the reaction enthalpies between the formation of the α-boryl or *β*-boryl radical intermediates.[153] The *ipso*-addition to the styrenyl BF_3K salt generates a benzylic radical intermediate, stabilised by the adjacent aryl group. In our case, the *in situ* formation of a boronate leads to a similar electron-rich coupling partner which obeys the same reactivity (Scheme *3-25*). Thus, **3.171** undergoes *ipso*-addition to **3.177** to furnish the benzylic *β*-boryl radical **3.178**, stabilised by the phenyl group.

Although the Giese reaction is well developed between nucleophilic radicals and electron-poor alkenes (see Scheme *1-35*), the use of vinyl Bpin allows a more tuneable reactivity (see Section 1.3.3.2). In more complex cases, such as the use of styrenyl boronic acids/BF_3K salts exhibiting a strong electron-rich character, electrophilic radicals are used as privileged coupling partners (see Section 1.3.3.4). The polarity-matched reactivity has been illustrated by Akita and coworkers (Scheme *1-43*)[151] with their use of the electrophilic CF_3 radical, by Leonori and coworkers (Scheme *1-44*)[153] reporting the use of malonyl radicals, as well as Song and coworkers (Scheme *1-49*)[163] who used *α*-bromodifluoroacylarenes as radical precursors (Figure *3-11*).

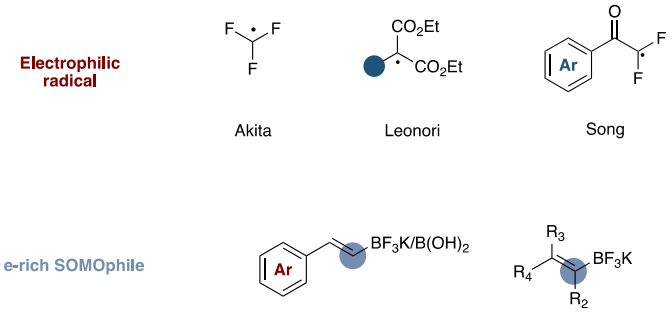
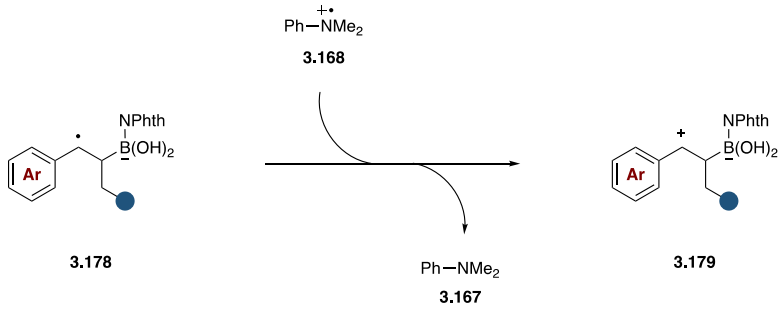


Figure 3-11: Polarity-matched reactivity with electrophilic radicals.

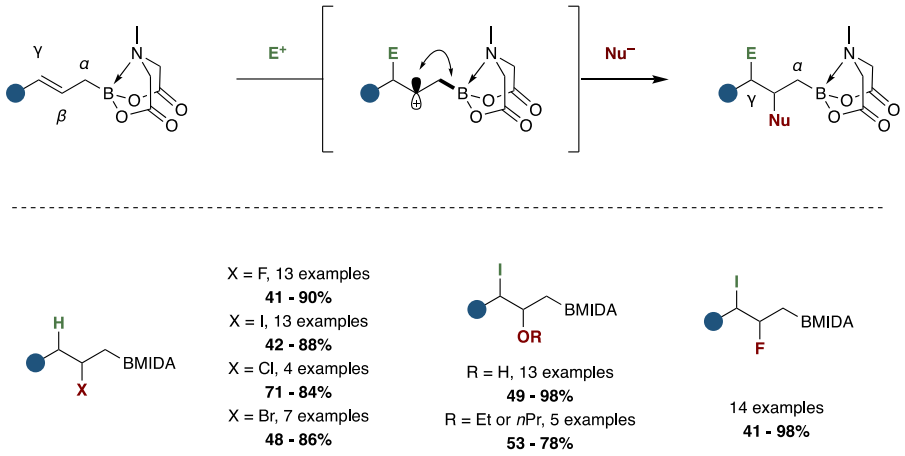
Radical addition to styrenyl boronic acids follows the same polarity-matched reactivity as polar chemistry.[236] A nucleophilic radical reacts with an electrophilic alkene (electron-poor SOMOphile),[236] whereas an electrophilic radical will react with an electron-rich olefin (as explained in Scheme *1-35*). The generation of alkyl radicals **3.171** using NHPI ester **3.12** furnishes nucleophilic radicals that react with the electron-rich SOMOphile **3.177**, highlighting a polarity-mismatched coupling reactivity. This unusual reactivity, although surprising, was also reported by Yu and coworkers (Scheme *1-46*).[157,159] These examples highlight the versatility of styrenyl organoborons, similarly to vinyl Bpin (see section 1.3.3.2), which are able to react with both nucleophilic or electrophilic radicals, as well as ambiphilic aryl radicals (Scheme *1-49*).[162]



Scheme 3-26: Radical-polar crossover.

Finally, oxidative radical-polar crossover of **3.178** affords the carbocation **3.179** (Scheme *3-26*).[237] Single electron oxidation of the benzylic radical most-likely occurs with $PhNMe_2^{\bullet+}$ **3.168**, yielding the benzylic carbocation **3.159** and regenerating the electron shuttle $PhNMe_2$ **3.167**. The oxidation potential of a benzylic radical is approximatively $E_{1/2}$ = 0.37 V vs. SCE,[238] which is lower than $E_{1/2}$

($PhNMe_2^{\bullet+}$/$PhNMe_2$) = 0.76 V vs. SCE. In addition to the stabilisation by the adjacent phenyl group, the carbocation **3.179** is also stabilised by the *β*-boron atom. Recently, Yudin and coworkers reported a *β*-boron stabilisation of carbocation through hyperconjugation from the σ(C−B) bond using MIDA boronates for electrophilic addition to alkenes (Scheme *3-27*).[239]

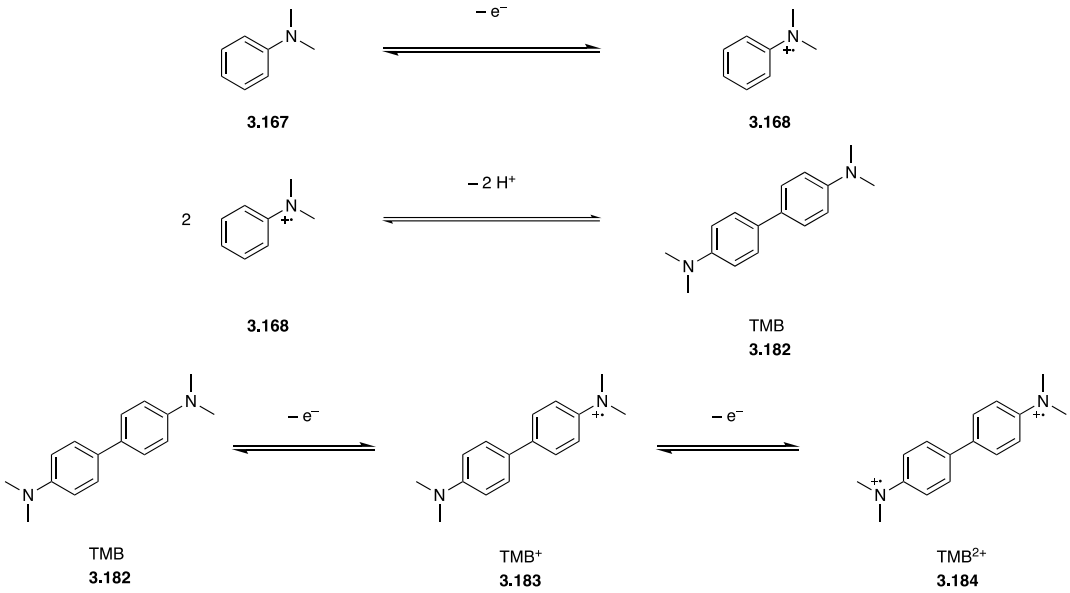


Scheme 3-27: Regioselective addition to alkenes enabled by the *β*-boron effect.

Finally, elimination of the phthalimide-boronate moiety **3.180** yields the desired cross-coupled (*E*)-product **3.181** (Scheme *3-28*).

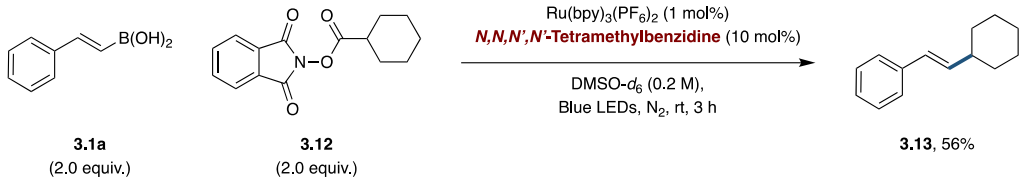
Scheme 3-28: Elimination step yielding the cross-coupled product.

It is worth noting that oxidation of *N,N*-dimethylaniline **3.167** could lead to side products, altering the proposed mechanism. In 1991, Bard and coworkers studied the dimerisation of *N,N*-dimethylaniline **3.167** to *N,N,N',N'*-tetramethylbenzidine (TMB) **3.182** (Scheme *3-29*).[230] The amminium radical $PhNMe_2^{\bullet+}$ **3.168** as classified as a short-lived intermediate and usually undergoes dimerisation. The dimer **3.182** can undergo two consecutive one-electron oxidations furnishing TMB^+ **3.183** and TMB^{2+} **3.184**, respectively. Cyclic voltametry revealed two new oxidation peaks on the second scan, corresponding to the two oxidations of TMB.[240]



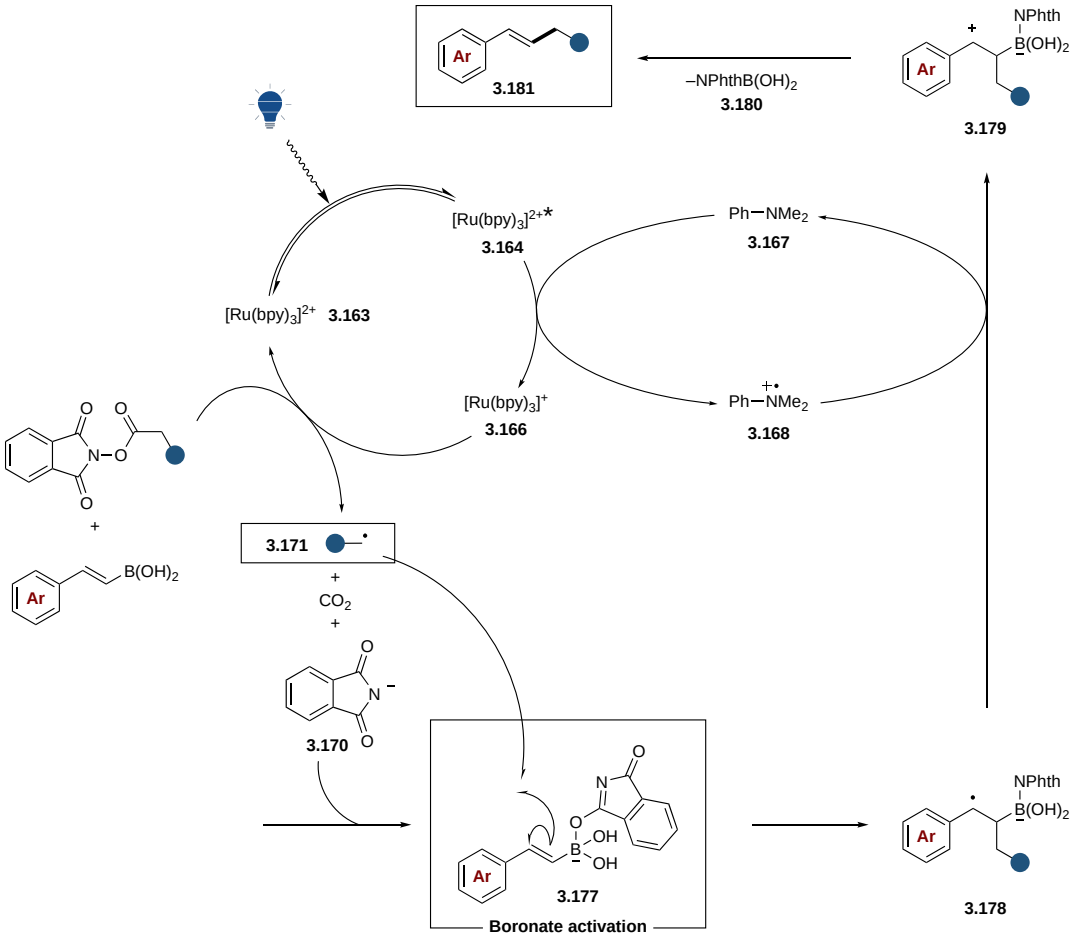
Scheme 3-29: Dimerisation of *N*,*N*-dimethylaniline **3.67**.

N,N,N',N'-tetramethylbenzidine **3.182** was not observed when the reaction was run with 10 mol% of *N*,*N*-dimethylaniline **3.167**. Increasing the amount to one equivalent led to the formation of traces of TMB **3.182**, observed in the crude ^{1}H NMR. Finally, switching the additive to **3.182** afforded the desired product with 56% yield after three hours of reaction (Scheme *3-30*, 45% of NHPI ester **3.12** was found unreacted). Thus, although the formation of TMB is unlikely to occur under our conditions, the reaction can still proceed smoothly with *N,N,N',N'*-tetramethylbenzidine.



Scheme 3-30: Reaction run with 10 mol% of *N*,*N*,*N'*,*N'*-tetramethylbenzidine **3.182**.

Hence, the following mechanism is proposed in Scheme *3-31*:

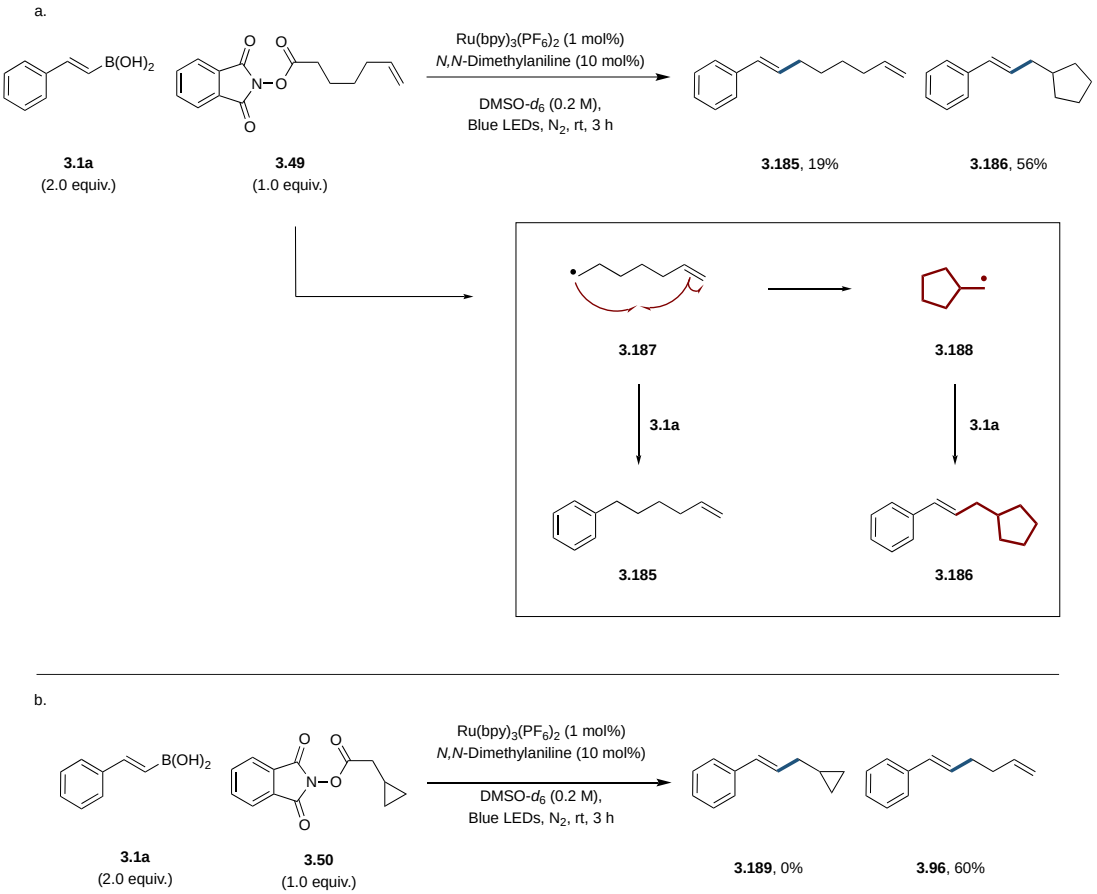


Scheme 3-31: Proposed mechanism. PF_6^- counteranion is omitted for clarity.

The mechanism is also in agreement with similar reactions involving styrenyl boronic acids[162,163] or styrenyl BF_3K salts.[151,156]

3.4.2 Radical clock experiments

The reaction was subjected to two radical clock probes **3.49** and **3.50** (Scheme *3-32*).



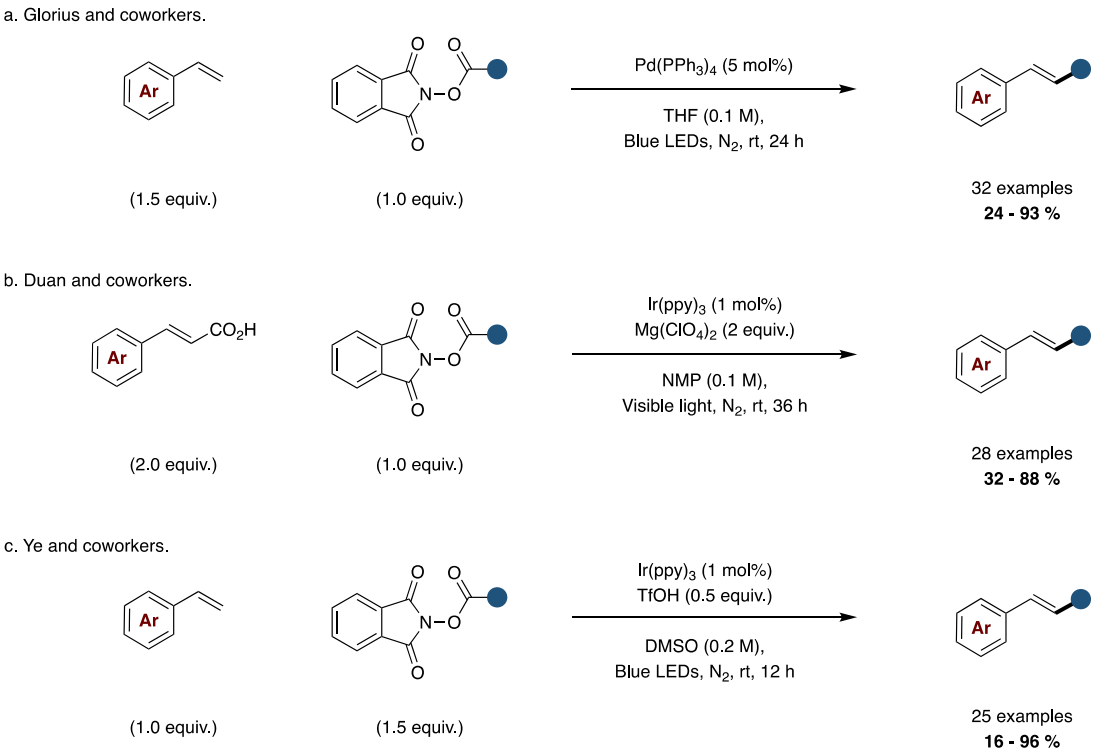
Scheme 3-32: Radical clock probes.

The reaction with the NHPI ester **3.49** gave a mixture of two different products: **3.185**, coming from the alkyl radical **3.187** (19% yield) and the major product of the reaction, **3.186**, obtained in 56% yield (Scheme *3-32*). This later came from radical closure of the primary alkyl radical **3.187** leading to the cyclic alkyl radical **3.188**, which further reacted with **3.1a** to afford the cyclic product **3.186**. The alkyl radical clock **3.187** involved in this 5-exo cyclization has a rate constant in the range of 10^5 s^{-1} at room temperature.[241] The ratio between the two products **3.185** and **3.187** leads to think that the rate of the reaction is close to 10^5 s^{-1} since 19% of **3.185** was observed. Moreover, running the reaction with a methylene cyclopropane NHPI ester **3.50**, afforded the ring-opened product **3.96** with 60% yield. In this case, no cyclopropanyl product **3.189** was observed. Cyclopropylmethyl radical undergoes ring opening with a rate constant

of 7.8×10^7 s^{-1}.[242] These results with radical clock probes **3.49** and **3.50** confirmed the formation of the alkyl radicals and allowed the appreciation of the rate constant of the reaction, which should be in between 10^5 and 10^7 s^{-1}.

3.4.3 Chemoselectivity of the designed reaction

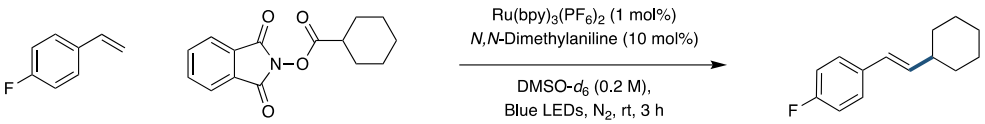
Although alkenes are widely used in photochemistry to intercept radicals, styrenes are increasingly chosen as coupling partners in radical cross-coupling reactions. Based on the work of Myers and coworkers,[243] who reported a Pd-mediated decarboxylative Heck-type olefination of aryl carboxylic acids, Glorius and coworkers developed a photocatalysed Pd-mediated decarboxylative Heck-type coupling reaction using NHPI esters (Scheme *3-33*a).[244] At the same time, Duan and coworkers published a light-mediated dual decarboxylative coupling reaction using NHPI esters and *α,β*-unsaturated carboxylic acids (Scheme *3-33*b).[245] Switching the additive to 0.5 equiv. of trifluoromethanesulfonic acid allowed Ye and coworkers to develop a Heck-type coupling reaction between styrenes and NHPI esters (Scheme *3-33*c).[246]



Scheme 3-33: Reactions between NHPI esters and styrenes.

To highlight the importance of the styrenyl boronic acid in this methodology, control experiments were run with *p*-fluorostyrene (Table *3-19* and Table *3-20*).

Table 3-19: Reactions run with *p*-fluorostyrene **3.190**.



3.190 (2.0 equiv.) **3.12** (1.0 equiv.) **3.120**

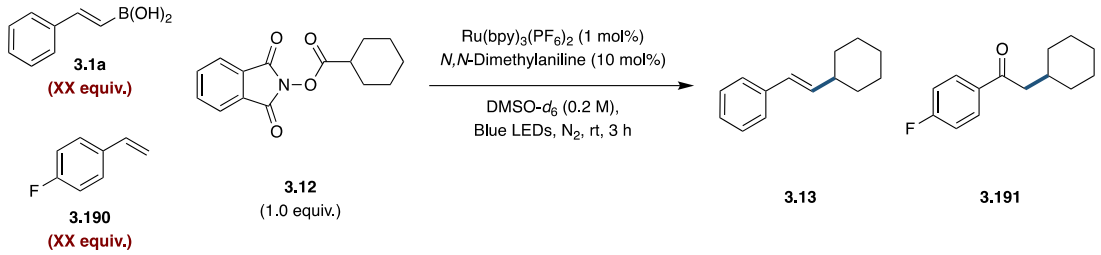
Entry	**3.120** (%)[a]	**3.12** (%)[b]	**3.190** (%)[a]
1	Traces	70	70
2[c]	Traces	0	80
3[d]	0	78	100

Reaction run in 0.2 mmol scale in dry and degassed DMSO-d_6. [a] Determined by ^{1}H NMR using MTBE as an internal standard (added after reaction). [b] Determined by ^{1}H NMR using MTBE as an internal standard (added after work up). [c] Reaction run with 50 mol% of *N*,*N*-dimethylaniline. [d] Reaction run with 20 mol% of $Ru(bpy)_3(PF_6)_2$.

Gratifyingly, running the reaction under the standard conditions with two equivalents of *p*-fluorostyrene **3.190** did not lead to the formation of the Heck-type product or any other byproducts (Table *3-19*). Increasing both the amount of *N*,*N*-dimethylaniline to 50 mol% (entry 2) or the photocatalyst to 20 mol% (entry 3) did not promote the formation of **3.120**. Although consumption of the NHPI ester **3.12** was observed, no addition to styrene **3.190** was detected. Residual peaks on the ^{19}F NMR of the crude mixture revealed the presence of potential byproducts coming from the styrene moiety, but only in traces amount (< 5%).

Competition experiments were run between styrenyl boronic acid **3.1a** and *p*-fluorostyrene **3.190** in Table *3-20*.

Table 3-20: Competition reaction with *p*-fluorostyrene.



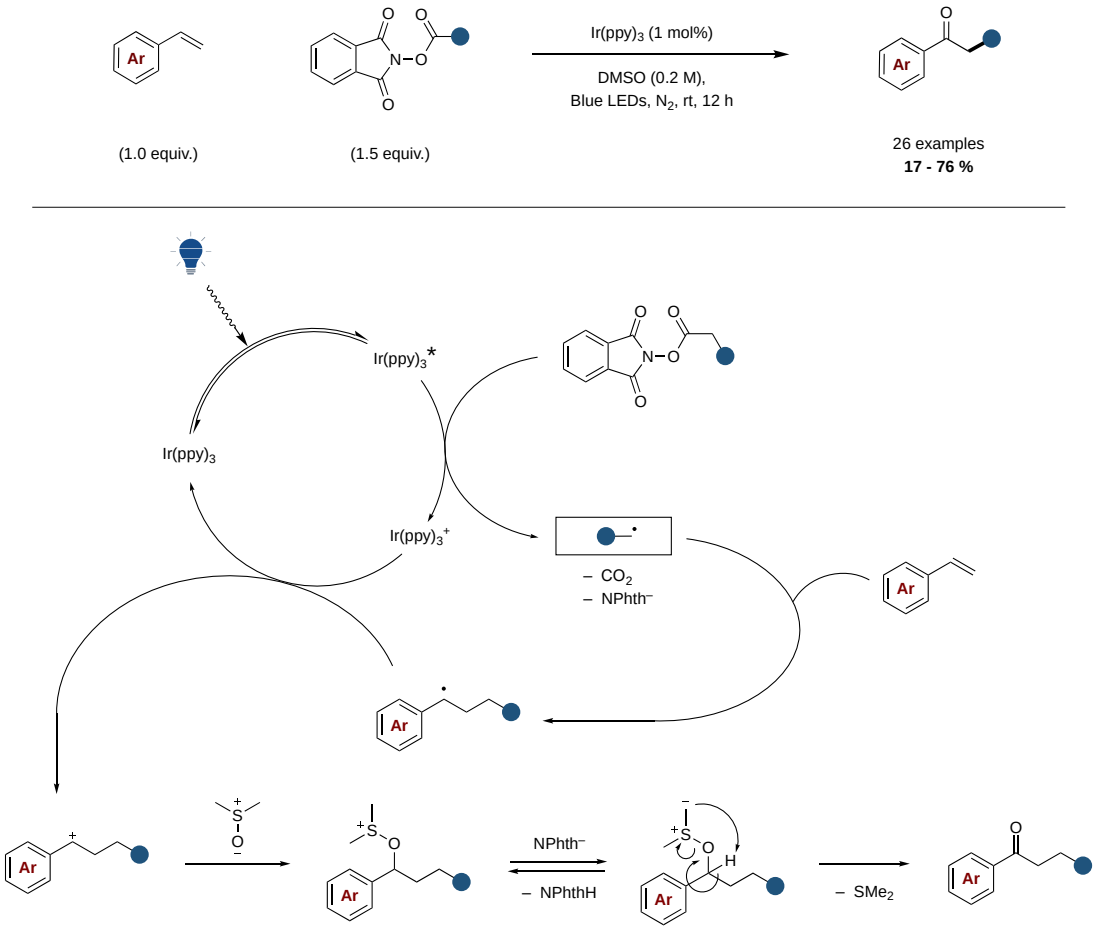
Entry	**3.1a** (equiv.)	**3.190** (equiv.)	**3.13** (%)[a]	**3.191** (%)[a]	**3.12** (%)[b]	**3.190** (%)[a]
1	1	1	35[b]	19	31	50
2[c]	1	1	42[b]	23	0	38
3[d]	1	1	15[b]	10	60	40
4[e]	0	2	-	17	55	71
5[f]	0	2	-	20	45	70

Reaction run in 0.2 mmol scale in dry and degassed DMSO-d_6. [a] Determined by ^{1}H NMR using MTBE as an internal standard (added after reaction). [b] Determined by ^{1}H NMR using MTBE as an internal standard (added after work up). [c] Reaction run with 50 mol% of *N*,*N*-dimethylaniline. [d] Reaction run with 20 mol% of $Ru(bpy)_3(PF_6)_2$. [e] 1.0 equiv. of $PhB(OH)_2$ added. [f] 1.0 equiv. of $B(OH)_3$ added.

Surprisingly, the reaction with one equivalent of each starting material (Table *3-20*, entry 1) led to the formation of an unexpected byproduct **3.191**. Although the structure was confirmed by NMR and HRMS analysis, the origin of its formation was unknown at the time. Increasing the loading of the additive to 50 mol% (entry 2) boosted the consumption of the NHPI **3.12** by increasing the number of turnovers, thus slightly improving the yield of both product **3.13** and the ketone byproduct **3.191**. Moreover, the rise in catalyst loading to 20 mol% (entry 3) did not improve the outcome of the reaction. Finally, switching **3.1a** for phenyl boronic acid (entry 4) or boric acid (entry 5) with 2 equivalents of styrene **3.190** encouraged the formation of the byproduct, whereas it was not observed in the previous table (see Table *3-19*). It was hypothesised that the reaction was promoted by a boronic acid moiety; however, literature search corroborated the formation of this ketone byproduct. Indeed, this transformation is known and proceeds *via* a Kornblum-type oxidation under photoredox conditions.[247] Ye and coworkers disclosed an oxo-alkylation where the radical addition to styrene such as **3.190** generates a benzylic radical. This radical is further oxidised to a benzylic carbocation prior to interception by DMSO (Scheme

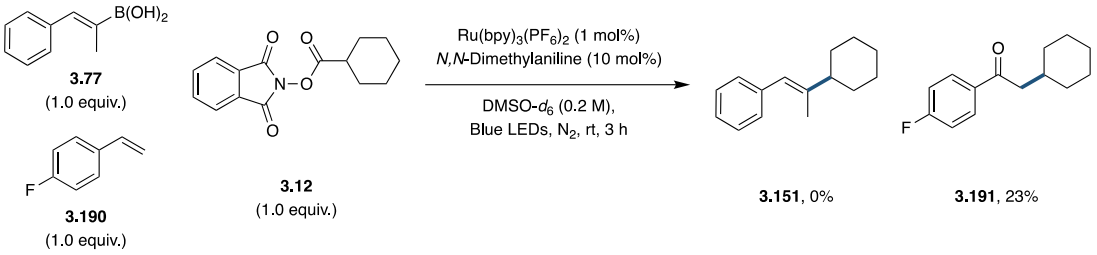
3-34).[246] Subsequent elimination of SMe_2 yields the desired ketone such as **3.191** as in the Kornblum oxidation.

It is worth noting that only traces (< 3%) of (*E*)-1-(2-cyclohexylvinyl)-4-fluorobenzene **3.120** were observed, as well as minor by-products from styrene.



Scheme 3-34: Kornblum-type oxidation developed by Ye.

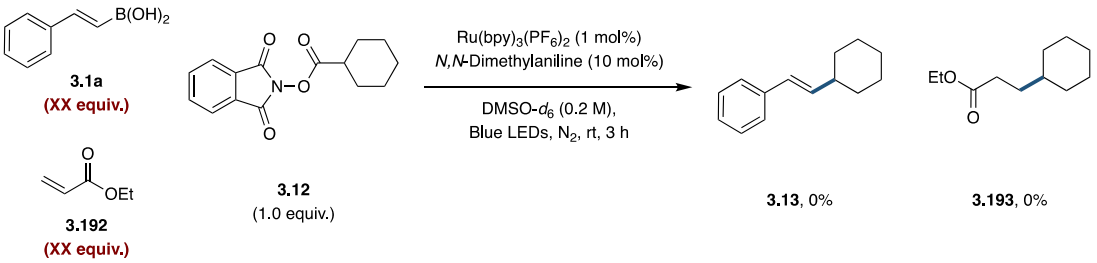
Running the competition experiment with an uncooperative substrate such as **3.77** (Scheme *3-35*), still led to the formation of the Kornblum-type oxidation product **3.191** without promoting the formation of the desired product.



Scheme 3-35: Competition reactions with *p*-fluorostyrene with an unsuccessful styrenyl boronic acid **3.77**.

Competition reactions were run with ethyl acrylate, since it is the most commonly chosen partner for photocatalysed Giese-type reactions (Table *3-21*).[128,129]

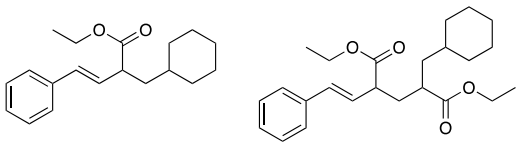
Table 3-21: Competition reactions with ethyl acrylate, **3.192**.



Entry	**3.1a** (equiv.)	**3.192** (equiv.)	**3.13** (%)[a]	**3.193** (%)[a]	**3.12** (%)[a]	**3.192** (%)[a]
1	1	1	18	0	0	0
2	0	2	-	0	51	0
3[a]	0	2	-	0	70	0
4[b]	0	2	-	0	75	0

Reaction run in 0.2 mmol scale in dry and degassed DMSO-d_6. [a] Determined by ^{1}H NMR using MTBE as an internal standard (added after reaction). [b] 1.0 equiv. of $PhB(OH)_2$ added. [c] 1.0 equiv. of $B(OH)_3$ added.

When the reaction was run with one equivalent of **3.1a** and one equivalent of **3.192**, 18% of product **3.13** was observed and no simple Giese-type addition product **3.193** was observed. Nevertheless, different byproducts could be observed by ^{1}H NMR of the crude mixture (entry 1), resulting from a Giese-type addition to ethyl acrylate **3.192** followed by addition to **3.1a**; **3.194** was the main byproduct and was isolated with 16%, whereas **3.195** was only confirmed by HRMS (Figure *3-12*).



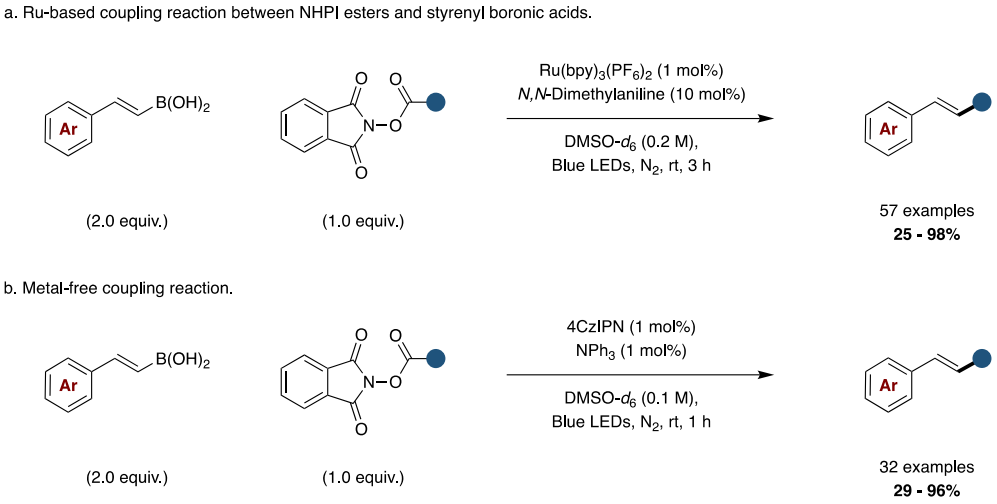
3.194, 16% **3.195**, Traces

Figure 3-12: Observed byproducts.

Adding two equivalents of ethyl acrylate **3.192** and no **3.1a** slowed down the consumption of the NHPI esters, but again, none of the expected Giese-type product was observed (entry 2). Kornblum-type oxidation was not observed under these conditions, even when one equivalent of phenyl boronic acid (entry 3) or boric acid (entry 4) was added.

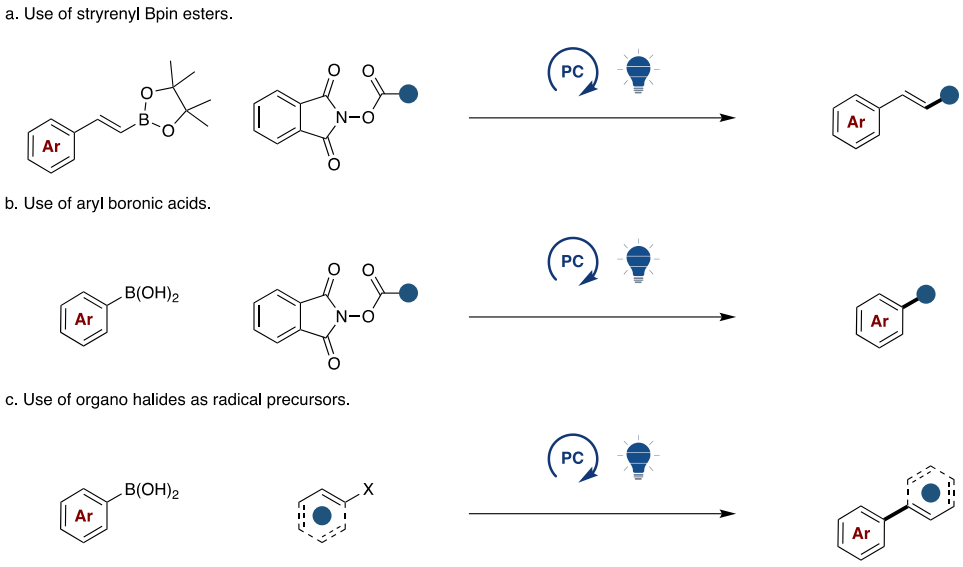
4. Conclusion and outlook

We herein disclose a Ru-based photocatalysed coupling reaction between NHPI esters and styrenyl boronic acids. This methodology expands the use of organoborons as radical interceptors and offers a new tool to access to C–C bond formations. Through an expanded scope, it was demonstrated that the reaction tolerates a broad range of functionalities and affords the desired products with good to excellent yields (Scheme *4-1*a). Although the photoredox-mediated Giese-type reaction to electron-deficient alkenes is well known, a new methodology to enable polarity-mismatched bond formation between a nucleophilic alkyl radicals and electron-rich styrenyl boronic acids through an unusual boronate formation event have been reported. Mechanistic investigations have highlighted the importance of the nucleofuge rebound in the mechanism, leading to the formation of styrene derivatives after elimination of the boronate moiety. The limitations of the reaction were also disclosed and aryl boronic acids, non-conjugated alkenyl boronic acids or heterostyrenyl boronic acids which were prone to protodeboronation, were not suitable coupling partners. Aiming for a metal-free Suzuki–Miyaura coupling reaction, the use of alkyl or aryl halides as radical precursors will require further investigation. However, with the help of an undergraduate master's student, this methodology was further optimised and can now be performed in a transition metal-free environment. Indeed, switching $Ru(bpy)_3(PF_6)_2$ to 4CzIPN, an organophotocatalyst, promotes the reaction with similar outcomes (Scheme *4-1*b).



Scheme 4-1: Developed methodologies.

Several areas of focus could be considered to improve this project. First, it is worthy to note that the synthesis of styrenyl boronic acids was erratic and troublesome. Thus, the development of this methodology to styrenyl Bpin esters would ease the access to starting materials as well as limiting the protodeboronation side reaction (Scheme *4-2*a). Application of the highly-commercially available aryl boronic acids would considerably expand the scope of the reaction and enable a more general $C(sp^2)$–$C(sp^3)$ bond formation (Scheme *4-2*b). With mild reaction conditions and great functional group tolerance, it is envisioned that late functionalisation of more complex molecules would be accessible with our methodology. Finally, switching the NHPI ester radical precursors to aryl/alkyl halides would mimic the Suzuki–Miyaura coupling reaction (Scheme *4-2*c). This could lead to a metal-free version of one of the most used C–C bond formation reactions.



Scheme 4-2: Future work.

5. Experimental section

5.1 General information

Reagents and solvents were obtained from commercial suppliers and were not purified further unless specified. Purification (where specified) was performed following the standard procedures. Chlorotrimethylsilane was dried and distilled over CaH_2. Dry solvents (THF, DCM, Et_2O) were provided by a PureSolv SPS-400-5 solvent purification system and stored over 4 Å molecular sieves.

Reactions were carried out in standard borosilicate glassware, or microwave vials with septum caps. Glassware was either flame-dried under vacuum or allowed to dry in a 180 °C oven for 24 h before use and then purged with vacuum/N_2 cycles. Room temperature was approximately 18 °C. Reactions at elevated temperatures were heated using a sand bath fitted with a temperature probe where the temperature indicated is the temperature of the sand bath. Reactions at low temperature were performed using an ice/water bath (0 °C) or dry ice/acetone bath (–78 °C). Water and/or oxygen-sensitive reactions were carried out in oven-dried glassware under inert atmosphere (N_2) using standard vacuum lines techniques. The light source used was a Kessil LED PR160L-456 nm, referred to as Blue LEDs throughout.

TLC was carried out using Merck aluminium-backed silica plates coated with F_{254} fluorescent indicator, analysed under UV light, and developed using aqueous $KMnO_4$ or ethanolic vanillin solutions, where appropriate. Flash column chromatography performed using silica gel (40–62 μm, Fluorochem).

^{1}H, ^{13}C $\{^{1}H\}$, ^{19}F $\{^{1}H\}$ NMR spectra were recorded by either a Bruker AVII 400 (BBFO probe) or AVIII-HD 500 or AVIII 500 with BBFO+ and Prodigy BBFO probes, respectively, at 400-101-376 MHz or at 500-126-377 MHz respectively. ^{11}B NMR spectra were recorded on a Bruker AV300 spectrometer at 96 MHz or on a Bruker AVII 400 spectrometer at 128 MHz. All spectra were recorded at room

temperature with the deuterated solvents used as a lock for spectra and internal reference ($CDCl_3$: ^1H, 7.26 ppm; ^{13}C, 77.2 ppm; acetone-d_6: ^1H, 2.05 ppm, ^{13}C, 29.8 ppm; d_6-DMSO-d_6: ^1H, 2.50 ppm, ^{13}C, 39.5 ppm; MeCN-d_3: ^1H, 1.94 ppm, ^{13}C, 1.3 ppm). For ^{11}B NMR, samples were run using a standard borosilicate tube and the spectra baselines corrected during processing unless the sample size prevented an acceptable signal-to-noise ratio, where a quartz NMR tube was used. All chemical shifts (δ) are reported in parts per million (ppm) relative to the residual solvent peak, all coupling constants, *J*, are quoted in Hz and refer to $^3J_{HH}$ unless otherwise stated. NMR spectra are reported as follows: chemical shift/ppm (multiplicity, coupling constant(s), number of nuclei). Multiplicity given as app. (apparent), br (broad), s (singlet), d (doublet), t (triplet), q (quartet), quint (quintet), h (hextet), m (multiplet), and combinations thereof. ^{13}C signals adjacent to boron are, in some cases, not observed , due to quadrupolar relaxation or are reported as a broad signal . Signals which overlap with one another are described as multiplets.

IR spectra were recorded using a Shimadzu IT Affinity-1 Fourier transform IR spectrophotometer with a Specac Quest ATR (diamond puck). Spectra were recorded as films (using $CDCl_3$), as solids, or as neat liquids, as specified. Transmittance was recorded with maximal absorption wavenumbers given as cm^{-1}. Steady-state emission, excitation spectra, and time-resolved emission spectra were recorded at 298 K using an Edinburgh Instruments FS5. Samples were irradiated at 468 nm for both steady-state measurements and time-resolved measurements. UV-Vis absorption spectra were recorded using an Agilent Technologies Cary 3500 Series UV-Vis spectrometer. Mass spectra were recorded on a Bruker micrOTOF benchtop ESI with either positive or negative electrospray ionisation or EI using a Thermo Mat 900XP, Double Focussing Hi-resolution mass spectrometer at the University of Edinburgh mass spectrometry facility (SIRCAMS).

5.2 Supplementary information

5.2.1 General procedures

5.2.1.1 Optimisation reactions

General Optimisation Procedure

An oven-dried photoreactor vial, equipped with a Teflon-coated stir bar, was charged with the NHPI ester **XX** (XX mg, XX μmol, XX equiv.), organoboron starting material **XX** (XX mg, XX μmol, XX equiv.), photocatalyst (XX mg, XX μmol, XX mol%), and the additive (XX μL, XX μmol, XX mol%). The vial was then sealed, purged with vacuum-N_2 cycles (3 times), and backfilled with N_2. Degassed dry solvent (XX mL, XX M) was then added. The cap was wrapped with parafilm and the reaction mixture was stirred under blue LEDs (Figure *5-1*) under N_2 for the indicated duration. The reaction was either:

- (1) worked-up: the reaction was partitioned between diethyl ether (5 mL) and brine (5 mL). Organics were extracted with diethyl ether (2 × 10 mL). Organics were combined, washed with brine (15 mL), dried over anhydrous sodium sulfate, filtered, and concentrated *in vacuo* affording the crude mixture. This latter was dissolved in 1.5 mL of $CDCl_3$, internal standard (see table below) was added to the vial. An aliquot of the crude mixture was then analysed by NMR spectroscopy.
- (2) analysed directly: in cases where the reaction was run in DMSO-d_6, internal standard (
- Note: Degassed dry solvents used for the following reactions were obtained after adding 4 Å molecular sieves and bubbling N_2 through for 15 minutes.

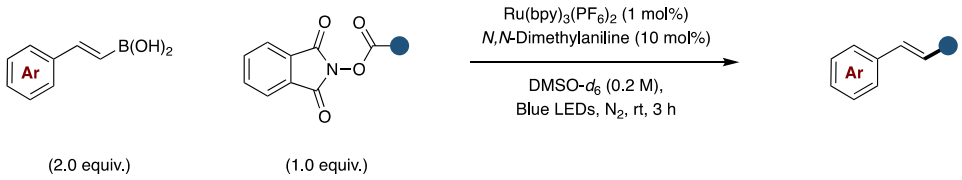
- Table *5-1*) was added directly into the vial. An aliquot of the reaction mixture was then analysed by NMR spectroscopy.
- Analysed both before (1) and after (2) the work-up in some cases (DMSO-d_6 as solvent and MTBE as internal standard).

Note: Degassed dry solvents used for the following reactions were obtained after adding 4 Å molecular sieves and bubbling N_2 through for 15 minutes.

Table 5-1: Different standards used during the optimisation.

Entry	Standard	Nuclei	Reaction scale	**Mass/Volume, µmol, equiv.**
1	2-fluoro-4-nitrotoluene	^{1}H and ^{19}F	100 µmol	15.5 mg, 100 µmol, 1.0 equiv.
2	1,3,5-trimethoxybenzene	^{1}H	200 µmol	11.2 mg, 66.6 µmol, 0.33 equiv.
3	MTBE	^{1}H	200 µmol	8.0 µL, 66.6 µmol, 0.33 equiv.

5.2.1.2 General procedure for the developed reaction



Scheme 5-1: Developed reaction between NHPI esters and styrenyl boronic acids.

General Procedure 1

An oven-dried photoreactor vial, equipped with a Teflon-coated stir bar, was charged with the NHPI ester **XX** (200 µmol, 1.0 equiv.), the styrenyl boronic acid **XX** (400 µmol, 2.0 equiv.), and tris(2,2'-bipyridine)ruthenium hexafluorophosphate (1.7 mg, 2.00 µmol, 1 mol%). The vial was then sealed, purged with N_2-vacuum cycles (3 times), and backfilled with N_2. Degassed dry DMSO-d_6 (1 mL, 0.2 M) was then added followed by *N*,*N*-dimethylaniline (2.5 µL, 20.0 µmol, 10 mol%). The cap was wrapped with parafilm and the reaction mixture was stirred under blue LEDs (Figure *5-1*) under N_2 for three hours. After three hours, the reaction mixture was partitioned between diethyl ether (5 mL) and brine (5 mL). Organics were extracted with diethyl ether (2 × 10 mL). The organic layers were combined, washed with brine (15 mL), dried over anhydrous sodium sulfate, filtered, and concentrated *in vacuo*. The crude residue was purified by flash chromatography (silica gel) using hexane/ethyl acetate or hexane/diethyl ether affording the desired product.

Note: Product *E:Z* ratio was determined by ^{1}H NMR Unless otherwise noted, only the *E* product was observed.

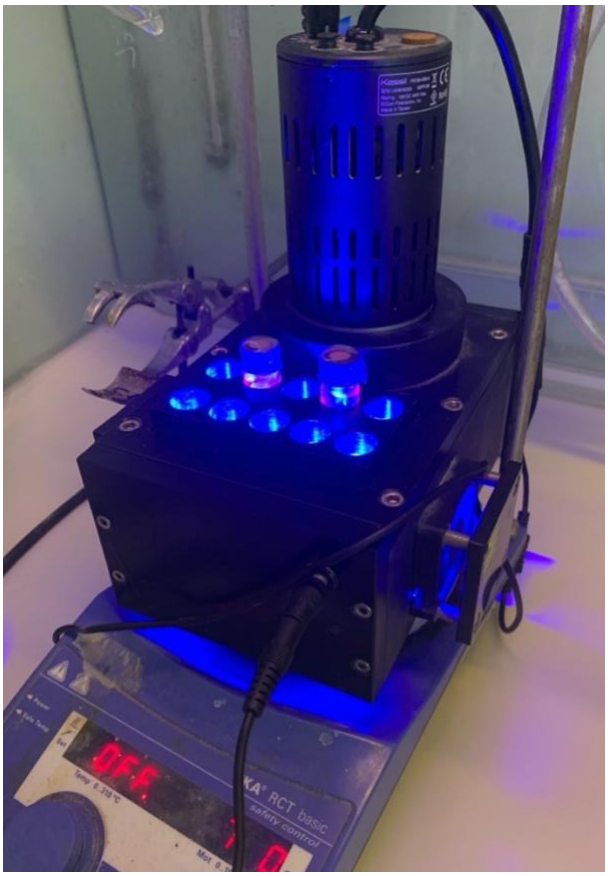


Figure 5-1 : Photoreactor setup.

5.2.2 Optimisation reactions

5.2.2.1 Reaction details for the first round of optimisation with **3.5**

Table 3-1: Solvent screening.

Prepared according to General Optimisation Procedure using the NHPI ester **3.5** (31.3 mg, 100 μmol, 1.0 equiv.), (*E*)-styrenyl boronic acid **3.1a** (29.6 mg, 200 μmol, 2.0 equiv.), and tris(2,2'-bipyridine)ruthenium hexafluorophosphate (4.3 mg, 5.00 μmol, 5 mol%) in the indicated solvent (1 mL, 0.1 M) for 21 hours.

Table 3-2: Concentration optimisation.

Entry	Concentration (M)	**Volume added (mL)**	**3.6** (%)[a]	**3.5** (%)[a]
1	0.2	0.5	62	2
2	0.1	1	63 (60)[b]	0
3	0.05	2	59	0
4	0.025	4	57	1

Reaction run on 0.1 mmol scale in dry and degassed DMSO. [a] Determined by ^{19}F NMR using 2-fluoro-4-nitrotoluene as an internal standard (added after work up). [b] Isolated yield.

Prepared according to General Optimisation Procedure using the NHPI ester **3.5** (31.3 mg, 100 μmol, 1.0 equiv.), (*E*)-styrenyl boronic acid **3.1a** (29.6 mg, 200 μmol, 2.0 equiv.), and tris(2,2'-bipyridine)ruthenium hexafluorophosphate (4.3 mg, 5.00 μmol, 5 mol%) in DMSO (XX mL, XX M).

Table 3-3: Atmosphere variation.

Entry	Atmosphere	**3.6** (%)[a]	**3.5** (%)[a]
1	N_2	63 (60)[b]	0
2	Air	21	51
3[c]	Air	23	52

Reaction run on 0.1 mmol scale in dry and degassed DMSO. [a] Determined by ^{19}F NMR using 2-fluoro-4-nitrotoluene as an internal standard (added after work up). [b] Isolated yield. [c] Reaction run in air bubbled through dry DMSO.

Prepared according to General Optimisation Procedure using the NHPI ester **3.5** (31.3 mg, 100 μmol, 1.0 equiv.), (*E*)-styrenyl boronic acid **3.1a** (29.6 mg, 200 μmol, 2.0 equiv.), and tris(2,2'-bipyridine)ruthenium hexafluorophosphate (4.3 mg, 5.00 μmol, 5 mol%) in DMSO (1 mL, 0.1 M). In this case the vial was left under air and was not purged with N_2-vacuum cycles (3 times). Entry 1 was run with degassed DMSO, whereas entry 2 was run with DMSO with air bubbled through.

Table 3-4: Role of blue LEDs.

Entry	Conditions	**3.6** (%)[a]	**3.5** (%)[a]
1	Daylight	0	97
2	Dark	0	100

Reaction run on 0.1 mmol scale in dry and degassed DMSO. [a] Determined by ^{19}F NMR using 2-fluoro-4-nitrotoluene as an internal standard (added after work up).

Prepared according to General Optimisation Procedure using the NHPI ester **3.5** (31.3 mg, 100 μmol, 1.0 equiv.), (*E*)-styrenyl boronic acid **3.1a** (29.6 mg, 200 μmol, 2.0 equiv.), and tris(2,2'-bipyridine)ruthenium hexafluorophosphate (4.3 mg, 5.00 μmol, 5 mol%) in DMSO (1 mL, 0.1 M) for 24 hours. Entry 1 was run in a fumehood whereas entry 2 was wrapped with aluminium foil.

Figure 3-3: Time study.

Prepared according to General Optimisation Procedure using the NHPI ester **3.5** (31.3 mg, 100 μmol, 1.0 equiv.), (*E*)-styrenyl boronic acid **3.1a** (29.6 mg, 200 μmol, 2.0 equiv.), tris(2,2'-bipyridine)ruthenium hexafluorophosphate (4.3 mg, 5.00 μmol, 5 mol%) in DMSO-d_6 (4 mL, 25 mM). The internal standard $PhCF_3$ (12.2 μL, 100 μmol, 1.0 equiv.) was added. An aliquot was added to a J. Youngs NMR tube and was irradiated under blue LEDs for the indicated time, ^1H NMR was recorded. The NMR tube was then irradiated again *etc.*

Table 3-5: Stoichiometry of the reaction.

Entry	**3.1a** (equiv.)	**Mass of 3.1a** (mg)	**3.5** (equiv.)	**Mass of 3.5** (mg)	**3.6** (%)[a]	**3.5** (%)[a]
1	1	14.8	1	29.6	31	48
2	1.5	22.2	1	29.6	45	25
3	2	29.6	1	29.6	63 (60)[b]	0
4	3	44.4	1	29.6	65	0

5	4	59.2	1	29.6	67	0
6	5	73.5	1	29.6	67	0
7	1	14.8	2	62.7	17	57
8	1	14.8	3	94.0	24	76

Reaction run on 0.1 mmol scale in dry and degassed DMSO. [a] Determined by ^{19}F NMR using 2-fluoro-4-nitrotoluene as an internal standard (added after work up). [b] Isolated yield.

Prepared according to General Optimisation Procedure using the NHPI ester **3.5** (XX mg, XX μmol, XX equiv.), (*E*)-styrenyl boronic acid **3.1a** (XX mg, XX μmol, XX equiv.), and tris(2,2'-bipyridine)ruthenium hexafluorophosphate (4.3 mg, 5.00 μmol, 5 mol%) in DMSO (1 mL, 0.1 M). Entry 1 was run in a fumehood whereas entry 2 was wrapped with aluminium foil.

Table 3-6: Reaction using TCNHPI **ester 3.8**.

Prepared according to General Optimisation Procedure using the NHPI ester **3.8** (45.1 mg, 100 μmol, 1.0 equiv.), (*E*)-styrenyl boronic acid **3.1a** (29.6 mg, 200 μmol, 2.0 equiv.), and tris(2,2'-bipyridine)ruthenium hexafluorophosphate (4.3 mg, 5.00 μmol, 5 mol%) in DMSO (1 mL, 0.1 M) for the indicated time.

Table 3-7: Reaction with different Styrenyl boronic acid 3.1a batches.

Prepared according to General Optimisation Procedure using the NHPI ester **3.5** (31.3 mg, 100 μmol, 1.0 equiv.), (*E*)-styrenyl boronic acid **3.1a** (29.6 mg, 200 μmol, 2.0 equiv.) from the indicated batch, and tris(2,2'-bipyridine)ruthenium hexafluorophosphate (4.3 mg, 5.00 μmol, 5 mol%) in DMSO (1 mL, 0.1 M).

Table 3-8: First additive screening.

Entry	Catechol (mol%)	**Mass of Catechol** (mg)	**3.6** (%)[a]	**3.5** (%)[a]
1	0	0	8	84
2[b]	20	2.2	64	0

3	20	2.2	64	0
4	10	1.1	71	0
5	5	0.6	70	0

Reaction run on 0.1 mmol scale in dry and degassed DMSO. [a] Determined by ^{19}F NMR using 2-fluoro-4-nitrotoluene as an internal standard (added after work up). [b] Reaction run for 24 hours.

Prepared according to General Optimisation Procedure using the NHPI ester **3.5** (31.3 mg, 100 μmol, 1.0 equiv.), (*E*)-styrenyl boronic acid **3.1a** (29.6 mg, 200 μmol, 2.0 equiv.), tris(2,2'-bipyridine)ruthenium hexafluorophosphate (4.3 mg, 5.00 μmol, 5 mol%), and catechol (XX mg, XX μmol, XX mol%) in DMSO (1 mL, 0.1 M) for the indicated time.

Table 3-9: Photocatalyst screening.

Entry	Photocatalyst	**Mass of PC** (mg)	**3.6** (%)[a]	**3.5** (%)[a]
1	None	0	0	98
2	$Ru(bpy)_3(PF_6)_2$	4.3	71	0
3	$Ir(ppy)_3$	3.3	63	0
4	$(Ir(dF(CF_3)ppy)_2(dtbpy))PF_6$	5.6	8	33
5	4-CzIPN	3.4	37	0
6	10-Phenylphenothiazine	1.4	1	93
7	Eosin Y	3.2	10	92
8	Methylene blue	1.7	0	95
9	Rose Bengal	5.1	27	42
10	Thioxanthen-9-one	1.1	0	94

Reaction run on 0.1 mmol scale in dry and degassed DMSO. [a] Determined by ^{19}F NMR using 2-fluoro-4-nitrotoluene as an internal standard (added after work up).

Prepared according to General Optimisation Procedure using the NHPI ester **3.5** (31.3 mg, 100 μmol, 1.0 equiv.), (*E*)-styrenyl boronic acid **3.1a** (29.6 mg, 200 μmol, 2.0 equiv.), photocatalyst (XX mg, 5.00 μmol, 5 mol%), and catechol (1.1 mg, 10.00 μmol, 10 mol%) in DMSO (1 mL, 0.1 M).

Table 3-10: Stoichiometry screening.

Entry	**3.1a** (equiv.)	**Mass of 3.1a** (mg)	**3.5** (equiv.)	**Mass of 3.5** (mg)	**3.6** (%)[a]	**3.5** (%)[a]
1	1	14.8	1	29.6	49	0
2	2	29.6	1	29.6	69	0
3	3	44.4	1	29.6	67	0
4	4	59.2	1	29.6	70	0
5	5	73.5	1	29.6	71	0
6	1	14.8	2	62.7	62	36
7	1	14.8	3	94.0	58	48

Reaction run in 0.1 mmol scale in dry and degassed DMSO. [a] Determined by ^{19}F NMR using 2-fluoro-4-nitrotoluene as an internal standard (added after work up).

Prepared according to General Optimisation Procedure using the NHPI ester **3.5** (XX mg, XX μmol, XX equiv.), (*E*)-styrenyl boronic acid **3.1a** (XX mg, XX μmol, XX equiv.), tris(2,2'-bipyridine)ruthenium hexafluorophosphate (4.3 mg, 5.00 μmol, 5 mol%), and catechol (1.1 mg, 10.00 μmol, 10 mol%) in DMSO (1 mL, 0.1 M).

Table 3-11: Catechol derivatives screening.

Entry	Additive	**Mass** (mg)	**3.6** (%)[a]	**3.5** (%)[a]
1	Catechol	1.1	70	0
2	4-Methylcatechol	1.2	55	4
3	*tert*-Butylcatechol	1.7	68	0

4	4-Nitrocatechol	1.6	6	77
5	Ethyl 3,4-dihydroxybenzylate	1.8	3	87
6	3-Methylcatechol	1.2	59	2
7	3-Methoxycatechol	1.4	52	0

Reaction run on 0.1 mmol scale in dry and degassed DMSO. [a] Determined by ^{19}F NMR using 2-fluoro-4-nitrotoluene as an internal standard (added after work up).

Prepared according to General Optimisation Procedure using the NHPI ester **3.5** (31.3 mg, 100 μmol, 1.0 equiv.), (*E*)-styrenyl boronic acid **3.1a** (29.6 mg, 200 μmol, 2.0 equiv.), tris(2,2'-bipyridine)ruthenium hexafluorophosphate (4.3 mg, 5.00 μmol, 5 mol%), and indicated additive (XX mg, 10.00 μmol, 10 mol%) in DMSO (1 mL, 0.1 M).

Table 3-12: Additive screening.

Entry	Additive	**Mass** (mg)	**3.6** (%)[a]	**3.5** (%)[a]
1	Naphthalene-2,3-diol	1.6	5	77
2	1,3-Dihydroxybenzene	1.1	12	78
3	1,4-Dihydroxybenzene	1.1	21	51
4	Phenol	0.9	14	72
5	*p*-Benzoquinone	1.1	0	90
6	2-Methoxyphenol	1.2	21	65
7	1,2-Dimethoxybenzene	1.4	12	81
8	1,3-Dimethoxybenzene	1.4	15	75
9	1,3,5-Trimethoxybenzene	1.7	16	76
10	Anisole	1.1	7	56
11	2-Hydroxybenzylalcohol	1.2	15	76

12	Salicylic acid	1.4	2	90
13	2-Aminophenol	1.1	59	0
14	1,2-Phenyldiamine	1.1	62	0
15	Naphthalene-2,3-diamine	1.6	23	44
16	2-Aminothiophenol	1.3	46	12
17	1,2-Benzenedithiol	1.4	14	65
18	Aniline	0.9	62	12
19	4-Nitroaniline	1.4	13	74
20	4-Methoxyaniline	1.2	70	0
21	Diphenylamine	1.7	64	0
22	Triphenylamine	2.5	15	79
23	*N*-Methylaniline	1.1	72	0
24	*N*,*N*-Dimethylaniline	1.2	75	0
25	Pinacol	1.2	10	79
26	Ethylene glycol	0.6	9	78
27	(L)-Tartaric acid	1.5	4	91
28	Ethylenediamine	0.6	20	20
29	Pyridine	0.8	21	72
30	DIPEA	1.3	25	0
31	DMAP	1.2	17	74
32	Urea	0.6	10	72
33	Thiourea	0.8	16	72
34	Boric acid	0.6	8	93

Reaction run on 0.1 mmol scale in dry and degassed DMSO. [a] Determined by ^{19}F NMR using 2-fluoro-4-nitrotoluene as an internal standard (added after work up).

Prepared according to General Optimisation Procedure using the NHPI ester **3.5** (31.3 mg, 100 μmol, 1.0 equiv.), (*E*)-styrenyl boronic acid **3.1a** (29.6 mg, 200 μmol, 2.0 equiv.), tris(2,2'-bipyridine)ruthenium hexafluorophosphate (4.3 mg, 5.00 μmol, 5 mol%), and indicated additive (XX mg, 10.00 μmol, 10 mol%) in DMSO (1 mL, 0.1 M).

5.2.2.2 Reaction details for the 2nd round of optimisation with **3.12**

Table 3-13: Catalyst loading and additives screening.

Entry	PC loading (mol%)	**Mass of PC** (mg)	Add. (mol%)	**Mass of Add.** (mg)	**3.13** (%)[a]	**3.12** (%)[a]
1	5	8.5	Catechol (10)	2.2	82	0
2	5	8.5	*N*,*N*-Dimethylaniline (10)	2.5 μL	92	0
3	2.5	4.3	*N*,*N*-Dimethylaniline (10)	2.5 μL	97	0
4	1	1.7	*N*,*N*-Dimethylaniline (10)	2.5 μL	96 (72)[b]	0
5	1	1.7	*N*,*N*-Dimethylaniline (5)	1.5 μL	85	10
6	1	1.7	None	0	16	89
7	0	0	*N*,*N*-Dimethylaniline (10)	2.5 μL	0	100
8	1	1.7	Catechol (10)	2.2	77	0

Reaction run on 0.2 mmol scale in dry and degassed DMSO-d_6. [a] Determined by ^{1}H NMR using 1,3,5-trimethoxybenzene as an internal standard (added after work up). [b] Isolated yield.

Prepared according to General Optimisation Procedure using the NHPI ester **3.12** (54.7 mg, 200 μmol, 1.0 equiv.), (*E*)-styrenyl boronic acid **3.1a** (59.2 mg, 400 μmol, 2.0 equiv.), tris(2,2'-bipyridine)ruthenium hexafluorophosphate (XX mg, XX μmol, XX mol%), and the additive (XX μL, XX μmol, XX mol%) in DMSO-d_6 (2 mL, 0.1 M).

Table 3-14: Time study.

Prepared according to General Optimisation Procedure using the NHPI ester **3.12** (54.7 mg, 200 μmol, 1.0 equiv.), (*E*)-styrenyl boronic acid **3.1a** (59.2 mg, 400 μmol, 2.0 equiv.), tris(2,2'-bipyridine)ruthenium hexafluorophosphate (1.7 mg, 2.00 μmol, 1 mol%), and *N*,*N*-dimethylaniline (2.5 μL, 20.0 μmol, 10 mol%) in DMSO-d_6 (2 mL, 0.1 M) for the indicated time.

Table 3-15: Concentration of the reaction.

Entry	Scale and Concentration	**3.13** (%)[a]	**3.12** (%)[a]
1	0.1 mmol in 1 mL (0.1 M)	94	0
2	0.2 mmol in 2 mL (0.1 M)	96 (72)[b]	0
3	0.2 mmol in 1 mL (0.2 M)	94 (80)[b]	0

Reaction run on 0.2 mmol scale in dry and degassed DMSO-d_6. [a] Determined by ^{1}H NMR using 1,3,5-trimethoxybenzene as an internal standard (added after work up). [b] Isolated yield.

Prepared according to General Optimisation Procedure using the NHPI ester **3.12** (54.7 mg, 200 μmol, 1.0 equiv.), (*E*)-styrenyl boronic acid **3.1a** (59.2 mg, 400 μmol, 2.0 equiv.), tris(2,2'-bipyridine)ruthenium hexafluorophosphate (1.7 mg, 2.00 μmol, 1 mol%), and *N*,*N*-dimethylaniline (2.5 μL, 20.0 μmol, 10 mol%) in DMSO-d_6 (XX mL, XX M).

Table 3-16: Organoboron screening.

Entry	**[B]**	**Mass of [B]** (mg)	**3.13** (%)[a]	**3.12** (%)[a]
1	$B(OH)_2$ (**3.1a**)	59.2	96	0
2	Bpin (**3.1b**)	92.0	28	0
3	BF_3K (**3.1c**)	84.0	8	0
4	Bcat (**3.1d**)	88.2	46	0

5	BMIDA (**3.1e**)	103.6	0	23
6	*p*-MeOPhB(OH)$_2$ instead of **1a**	60.8	0[c]	69
7	(*E*)-Oct-1-en-1-yl boronic acid instead of **1a**	62.4	0[c]	74

Reaction run on 0.2 mmol scale in dry and degassed DMSO-d_6. [a] Determined by ^{1}H NMR using 1,3,5-trimethoxybenzene as an internal standard (added after work up). [c] Expected products for entries 6 and 7 are different than **9** (*vide infra*).

Prepared according to General Optimisation Procedure using the NHPI ester **3.12** (54.7 mg, 200 μmol, 1.0 equiv.), the indicated organoboron starting material (XX mg, 400 μmol, 2.0 equiv.), tris(2,2'-bipyridine)ruthenium hexafluorophosphate (1.7 mg, 2.00 μmol, 1 mol%), and *N,N*-dimethylaniline (2.5 μL, 20.0 μmol, 10 mol%) in DMSO-d_6 (1 mL, 0.2 M).

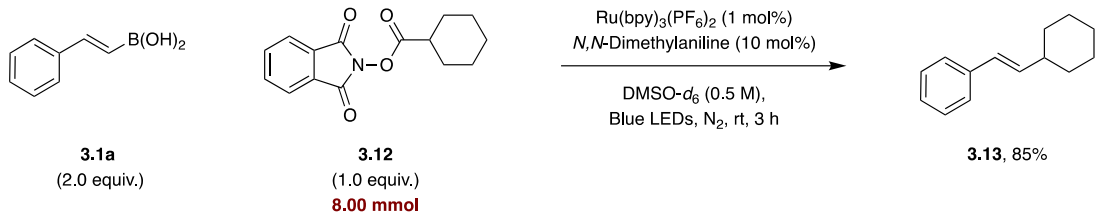
Table 3-17: Role of NHPI esters.

Entry	Substrate	**Mass** (mg)	**3.13** (%)[a]	SM (%)[a]
1	Cyclohexane carboxylic acid	25.6	0	95
2	Bromocyclohexane	32.6	0	100

Reaction run on 0.2 mmol scale in dry and degassed DMSO-d_6. [a] Determined by ^{1}H NMR using 1,3,5-trimethoxybenzene as an internal standard (added after work up).

Prepared according to General Optimisation Procedure using the indicated starting material (XX mg, 200 μmol, 1.0 equiv.), (*E*)-styrenyl boronic acid **3.1a** (59.2 mg, 400 μmol, 2.0 equiv.), tris(2,2'-bipyridine)ruthenium hexafluorophosphate (1.7 mg, 2.00 μmol, 1 mol%), and *N,N*-dimethylaniline (2.5 μL, 20.0 μmol, 10 mol%) in DMSO-d_6 (1 mL, 0.2 M).

5.2.2.3 Reaction scale up



Scheme 5-2: Reaction scale up.

Prepared according to General Procedure 1 using the NHPI ester **3.12** (2.19 g, 8.00 mmol, 1.0 equiv.), (*E*)-2-phenylvinylboronic acid, **3.1a** (2.37 g, 16.00 mmol, 2.0 equiv.), tris(2,2'-bipyridine)ruthenium hexafluorophosphate (68.8 mg, 80.00 µmol, 1 mol%), and *N*,*N*-dimethylaniline (100 µL, 800.0 µmol, 10 mol%) in DMSO-d_6 (16 mL, 0.5 M). The crude residue was purified by flash chromatography (silica gel) with pure hexane affording 1.27 g of a colourless oil as the desired product (85%, *E:Z* > 20:1).

5.2.2.4 Control reactions and mechanistic experiments

Table 3-18: Reaction with a mixture of Z:E diastereoisomers.

Entry	**[B]**	**Mass of [B]** (mg)	Ratio *Z*:*E*	**3.13** (%)[a]	**3.12** (%)[a]
1	Bpin, **3.(*Z*)-1b**	92.0	1:0.35	13	40
2	$B(OH)_2$, **3.(*Z*)-1a**	59.9	1:1.1	34	64
3[b]	$B(OH)_2$, **3.(*Z*)-1a**	29.6	1:1.1	33	49

Reaction run in 0.2 mmol scale in dry and degassed DMSO-d_6. [a] Determined by ^{1}H NMR using MTBE as an internal standard (added after reaction). [b] 1.0 equiv. of **3.(*Z*)-1a** used (instead of 2.0 equiv.).

Prepared according to General Optimisation Procedure using the NHPI ester **3.12** (54.7 mg, 200 µmol, 1.0 equiv.), the indicated organoboron starting material (XX mg, XX µmol, 2.0 equiv.), tris(2,2'-bipyridine)ruthenium hexafluorophosphate (1.7 mg, 2.00 µmol, 1 mol%), and *N*,*N*-dimethylaniline (2.5 µL, 20.0 µmol, 10 mol%) in DMSO-d_6 (1 mL, 0.2 M).

Scheme 3-16: Competition reactions with alkenyl boronic acid**, 3.154**.

Prepared according to General Optimisation Procedure using the NHPI ester **3.12** (54.7 mg, 200 μmol, 1.0 equiv.), (*E*)-styrenyl boronic acid **3.1a** (29.6 mg, 200 μmol, 1.0 equiv.), (*E*)-oct-1-en-1-yl boronic acid **3.154** (31.2 mg, 200 μmol, 1.0 equiv.), tris(2,2'-bipyridine)ruthenium hexafluorophosphate (1.7 mg, 2.00 μmol, 1 mol%), and *N*,*N*-dimethylaniline (2.5 μL, 20.0 μmol, 10 mol%) in DMSO-d_6 (1 mL, 0.2 M). After 3 hours, 58% of product **3.13** was observed and no traces of **3.156** were detected (19% of **3.12** and 100% of **3.154** were recovered).

Scheme 3-17: Competition reaction with alkyl boronic acid, **3.156**.

Prepared according to General Optimisation Procedure using the NHPI ester **3.12** (54.7 mg, 200 μmol, 1.0 equiv.), (*E*)-styrenyl boronic acid **3.1a** (29.6 mg, 200 μmol, 1.0 equiv.), octyl boronic acid **3.156** (31.6 mg, 200 μmol, 1.0 equiv.), tris(2,2'-bipyridine)ruthenium hexafluorophosphate (1.7 mg, 2.00 μmol, 1 mol%), and *N*,*N*-dimethylaniline (2.5 μL, 20.0 μmol, 10 mol%) in DMSO-d_6 (1 mL, 0.2 M). After 3 hours, 60% of product **3.13** was observed and no traces of **3.157** were detected (10% of **3.12** and 100% of **3.156** were recovered).

Scheme 3-19: On/Off experiment.

Prepared according to General Optimisation Procedure using the NHPI ester **3.12** (27.2 mg, 100 μmol, 1.0 equiv.), (*E*)-styrenyl boronic acid **3.1a** (29.6 mg, 200 μmol, 2.0 equiv.), tris(2,2'-bipyridine)ruthenium hexafluorophosphate (0.9 mg, 1.00 μmol, 1 mol%), and *N*,*N*-dimethylaniline (1.5 μL, 10.0 μmol, 10 mol%) in DMSO-d_6 (2 mL, 50 mM). MTBE (4.0 μL, 33.3 μmol, 0.33 equiv.) was added. An aliquot was added to a J. Youngs NMR tube and was irradiated under blue LEDs for ten minutes. ^{1}H NMR was recorded. The NMR tube was left in the fumehood for 10 minutes, before another ^{1}H NMR was recorded. This process was repeated for 90 minutes.

Scheme 3-20: Reaction run with a radical trap: TEMPO.

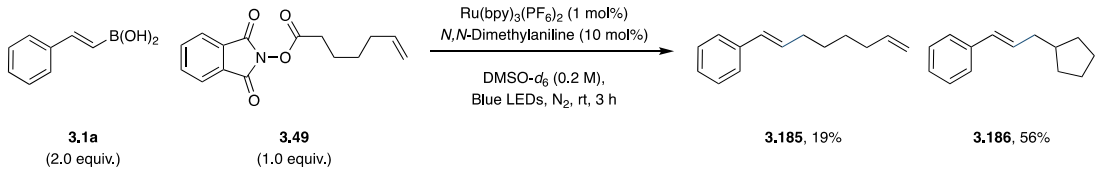
Prepared according to General Optimisation Procedure using 1,3-dioxoisoindolin-2-yl cyclohexanecarboxylate, **3.12** (54.7 mg, 200 μmol, 1.0 equiv.), (*E*)-2-phenylvinylboronic acid **3.1a** (59.2 mg, 400 μmol, 2.0 equiv.), tris(2,2' bipyridine)ruthenium hexafluorophosphate (1.7 mg, 2.00 μmol, 1 mol%), TEMPO

(31.2 mg, 200 μmol, 1.0 equiv.), and *N*,*N*-dimethylaniline (2.5 μL, 20.0 μmol, 10 mol%) in DMSO-d_6 (1 mL, 0.2 M). No traces of product **3.13** were observed and **3.12** was fully recovered (96%).

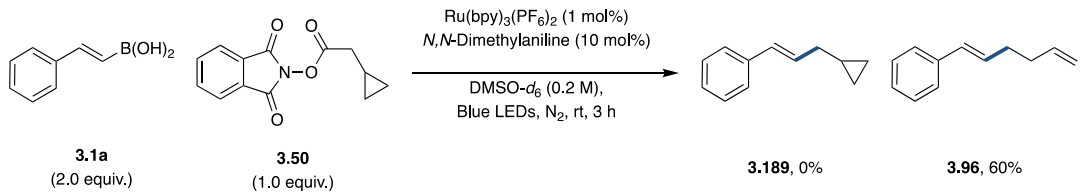
Scheme 3-30: Reaction run with 10 mol% of N,N,N',N'-tetramethylbenzidine **3.182**.

Prepared according to General Optimisation Procedure using 1,3-dioxoisoindolin-2-yl cyclohexanecarboxylate, **3.12** (54.7 mg, 200 μmol, 1.0 equiv.), (*E*)-2-phenylvinylboronic acid **3.1a** (59.2 mg, 400 μmol, 2.0 equiv.), tris(2,2' bipyridine)ruthenium hexafluorophosphate (1.7 mg, 2.00 μmol, 1 mol%), and *N*,*N*,*N'*,*N'*-tetramethylbenzidine **3.182** (4.8 mg, 20.0 μmol, 10 mol%) in DMSO-d_6 (1 mL, 0.2 M). After 3 hours, 56% of product **3.13** was observed with 45% of **3.12** left unreacted.

Scheme 3-32: Radical clock probes.



Prepared according to General Procedure 1 using 1,3-dioxoisoindolin-2-yl hept-6-enoate **3.49** (54.7 mg, 200 μmol, 1.0 equiv.), (*E*)-2-phenylvinylboronic acid **3.1a** (59.2 mg, 400 μmol, 2.0 equiv.), tris(2,2' bipyridine)ruthenium hexafluorophosphate (1.7 mg, 2.00 μmol, 1 mol%), and *N*,*N*-dimethylaniline (2.5 μL, 20.0 μmol, 10 mol%) in DMSO-d_6 (1 mL, 0.2 M). The crude residue was purified by flash chromatography (silica gel) using pure hexane affording 7.2 mg of **3.185** as a colourless oil (19%, *E:Z* > 20:1) and 21.1 mg of **3.186** as a colourless oil (56%, E:Z > 20:1).



Prepared according to General Procedure 1 using 1,3-dioxoisoindolin-2-yl 2-cyclopropylacetate **3.50** (49.0 mg, 200 μmol, 1.0 equiv.), (*E*)-2-phenylvinylboronic acid **3.1a** (59.2 mg, 400 μmol, 2.0 equiv.), tris(2,2' bipyridine)ruthenium

hexafluorophosphate (1.7 mg, 2.00 μmol, 1 mol%), and *N*,*N*-dimethylaniline (2.5 μL, 20.0 μmol, 10 mol%) in DMSO-d_6 (1 mL, 0.2 M). The crude residue was purified by flash chromatography (silica gel) using pure hexane affording 18.9 mg of **3.96** as a colourless oil (60%, *E:Z* > 20:1). No trace of **3.189** was observed.

Table 3-19: Reactions run with p-fluorostyrene **3.190**.

Entry	Mass of PC (mg)	Volume of *N*,*N*-dimethylaniline (μL)	**3.120** (%)[a]	**3.12** (%)[b]	**3.190** (%)[a]
1	1.7	2.5	Traces	70	70
2[c]	1.7	12.7	Traces	0	80
3[d]	34.4	2.5	0	78	100

Reaction run in 0.2 mmol scale in dry and degassed DMSO-d_6. [a] Determined by ^{1}H NMR using MTBE as an internal standard (added after reaction). [b] Determined by ^{1}H NMR using MTBE as an internal standard (added after work up). [c] Reaction run with 50 mol% of *N*,*N*-dimethylaniline. [d] Reaction run with 20 mol% of $Ru(bpy)_3(PF_6)_2$.

Prepared according to General Optimisation Procedure using the NHPI ester **3.12** (54.7 mg, 200 μmol, 1.0 equiv.), *p*-fluorostyrene **3.190** (48 μL, 400 μmol, 2.0 equiv.), tris(2,2'-bipyridine)ruthenium hexafluorophosphate (XX mg, XX μmol, XX mol%), and *N*,*N*-dimethylaniline (XX μL, XX μmol, XX mol%) in DMSO-d_6 (1 mL, 0.2 M).

Table 3-20: Competition reaction with p-fluorostyrene.

Entry	**3.1a** (equiv.)	Mass of **3.1a** (mg)	**3.190** (equiv.)	Volume of **3.190** (μL)	**3.13** (%)[a]	**3.191** (%)[a]	**3.12** (%)[b]	**3.190** (%)[a]
1	1	29.6	1	24	35[b]	19	31	50
2[c]	1	29.6	1	24	42[b]	23	0	38
3[d]	1	29.6	1	24	15[b]	10	60	40
4[e]	0	0	2	48	-	17	55	71
5[f]	0	0	2	48	-	20	45	70

Reaction run in 0.2 mmol scale in dry and degassed DMSO-d_6. [a] Determined by ^{1}H NMR using MTBE as an internal standard (added after reaction). [b] Determined by ^{1}H NMR using MTBE as an internal standard (added after work up). [c] Reaction run with 50 mol% (13 μL) of *N*,*N*-dimethylaniline. [d] Reaction run with 20 mol% (34.4 mg) of $Ru(bpy)_3(PF_6)_2$. [e] 1.0 equiv. (24.4 mg) of $PhB(OH)_2$ added. [f] 1.0 equiv. (12.4 mg) of $B(OH)_3$ added.

Prepared according to General Optimisation Procedure using the NHPI ester **3.12** (54.7 mg, 200 μmol, 1.0 equiv.), (*E*)-2-phenylvinylboronic acid **3.1a** (XX mg, XX μmol, XX equiv.), *p*-fluorostyrene **3.190** (XX μL, XX μmol, XX equiv.), tris(2,2'-bipyridine)ruthenium hexafluorophosphate (1.7 mg, 2.00 μmol, 1 mol%), *N,N*-dimethylaniline (2.5 μL, 20.0 μmol, 10 mol%), and the indicated additive (XX mg, 200 μmol, 1.0 equiv.) in DMSO-d_6 (1 mL, 0.2 M).

Scheme 3-35: Competition reactions with p-fluorostyrene with an unsuccessful styrenyl boronic acid **3.77**.

Prepared according to General Optimisation Procedure using the NHPI ester **3.12** (54.7 mg, 200 μmol, 1.0 equiv.), (*Z*)-(1-phenylprop-1-en-2-yl)boronic acid **3.77** (32.4 mg, 200 μmol, 1.0 equiv.), *p*-fluorostyrene **3.190** (24 μL, 200 μmol, 1.0 equiv.), tris(2,2'-bipyridine)ruthenium hexafluorophosphate (1.7 mg, 2.00 μmol, 1 mol%), and *N,N*-dimethylaniline (2.5 μL, 20.0 μmol, 10 mol%) in DMSO-d_6 (1 mL, 0.2 M). After 3 hours, 23% of product **3.191** was observed and no traces of **3.120** or **3.151** were detected (32% of **3.12** and 40% of **3.190** were recovered).

Table 3-21: Competition reactions with ethyl acrylate, **3.192**.

Entry	**3.1a** (equiv.)	Mass of **3.1a** (mg)	**3.192** (equiv.)	Volume of **3.192** (μL)	**3.13** (%)[a]	**3.193** (%)[a]	**3.12** (%)[a]	**3.192** (%)[a]
1	1	29.6	1	21.7	18	0	0	0
2	0	0	2	43.3	-	0	51	0
3[a]	0	0	2	43.3	-	0	70	0
4[b]	0	0	2	43.3	-	0	75	0

Reaction run in 0.2 mmol scale in dry and degassed DMSO-d_6. [a] Determined by ^{1}H NMR using MTBE as an internal standard (added after reaction). [b] 1.0 equiv. (24.4 mg) of $PhB(OH)_2$ added. [c] 1.0 equiv. (12.4 mg) of $B(OH)_3$ added.

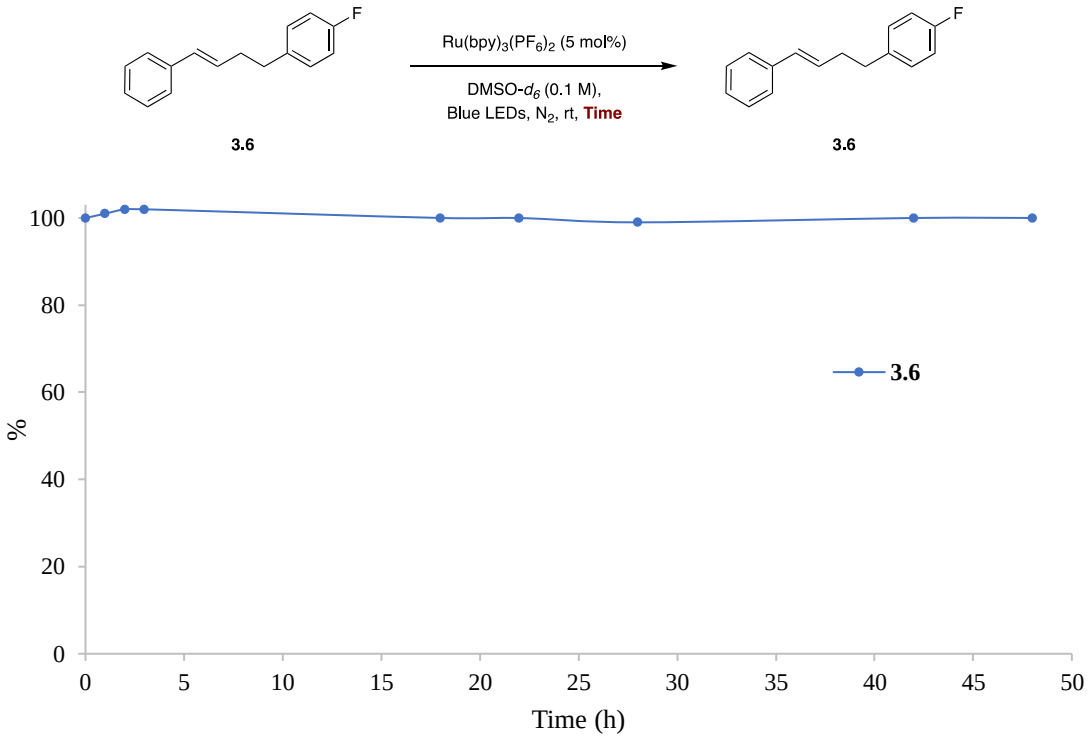
Prepared according to General Optimisation Procedure using the NHPI ester **3.12** (54.7 mg, 200 μmol, 1.0 equiv.), (*E*)-2-phenylvinylboronic acid **3.1a** (XX mg, XX μmol, XX equiv.), ethyl acrylate **3.192** (XX μL, XX μmol, XX equiv.), tris(2,2'-bipyridine)ruthenium hexafluorophosphate (1.7 mg, 2.00 μmol, 1 mol%),

N,*N*-dimethylaniline (2.5 µL, 20.0 µmol, 10 mol%), and the indicated additive (XX mg, 200 µmol, 1.0 equiv.) in DMSO-d_6 (1 mL, 0.2 M).

5.2.3 Miscellaneous

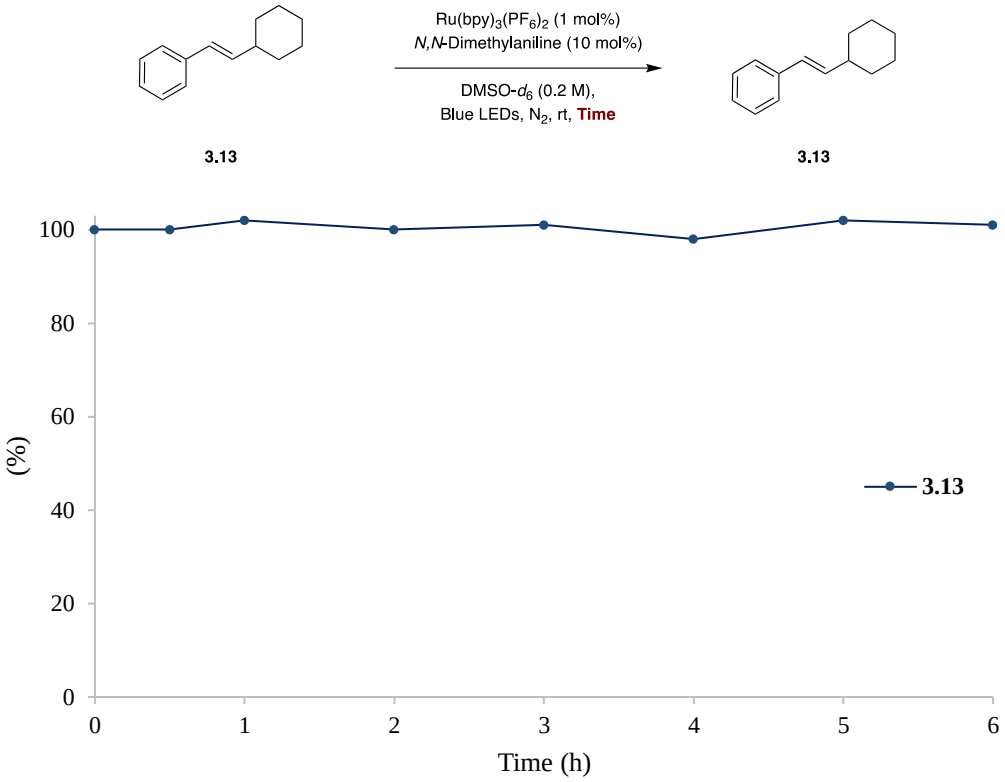
5.2.3.1 Stability of products

Figure 5-2: Stability of **3.6**.



Prepared according to General Optimisation Procedure using (*E*)-1-fluoro-4-(4-phenylbut-3-en-1-yl)benzene **3.6** (22.6 mg, 100 µmol, 1.0 equiv.), tris(2,2'-bipyridine)ruthenium hexafluorophosphate (4.3 mg, 5.00 µmol, 5 mol%) in DMSO-d_6 (1mL, 0.1 M). $PhCF_3$ (12.2 µL, 100 µmol, 1.0 equiv.) was added. An aliquot was added to a J. Youngs NMR tube and was analysed by ^{19}F NMR spectroscopy. The NMR tube was irradiated under blue LEDs for XX hours and ^{19}F NMR was recorded. This process was repeated for 48 hours.

Figure 5-3: Stability of 3.13.

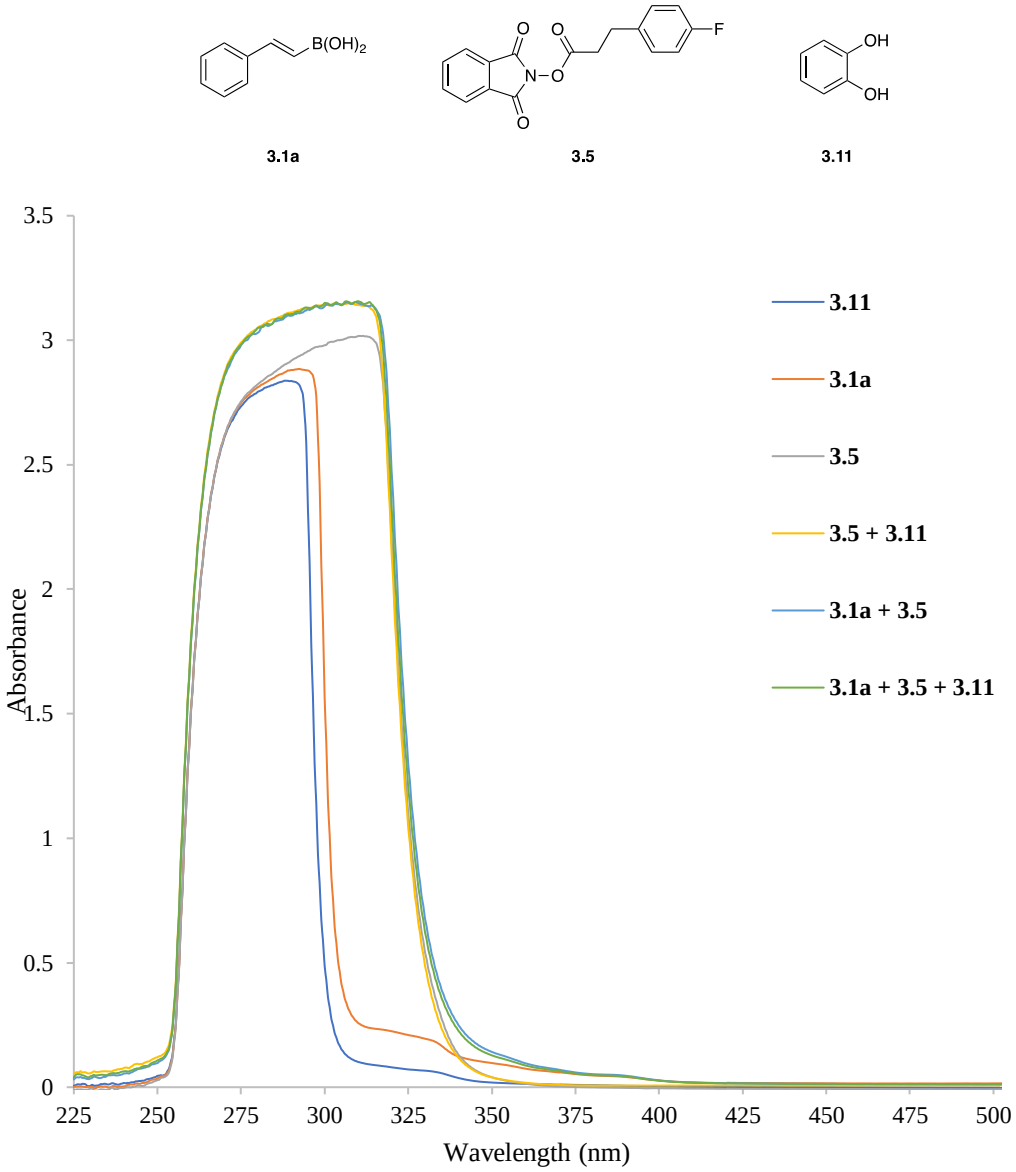


Prepared according to General Optimisation Procedure using (*E*)-(2-cyclohexylvinyl)benzene **3.13** (37.3 mg, 200 µmol, 1.0 equiv.), tris(2,2'-bipyridine)ruthenium hexafluorophosphate (1.7 mg, 2.00 µmol, 1 mol%), and *N*,*N*-dimethylaniline (2.5 µL, 20.0 µmol, 10 mol%) in DMSO-d_6 (2 mL, 0.2 M). MTBE (8.0 µL, 66.6 µmol, 0.33 equiv.) was added. An aliquot was added to a J. Youngs NMR tube and was analysed by ^{1}H NMR spectroscopy. The NMR tube was irradiated under blue LEDs for XX minutes and ^{1}H NMR was recorded. This process was repeated for 6 hours.

5.2.3.2 UV-Vis

Solutions of styrenyl boronic acid **3.1a**, NHPI **3.5**, catechol **3.11**, and combination of them at 10^{-2} M in DMSO was prepared and used for the UV-Vis absorption experiments.

Figure 5-4: UV-Vis absorption with **3.12**.



Solutions of styrenyl boronic acid **3.1a**, NHPI **3.12**, *N*,*N*-dimethylaniline **3.167**, and combination of them at 10^{-1} M in DMSO was prepared and used for the UV-Vis absorption experiments.

Figure 5-5 : UV-Vis absorption with **3.12**.

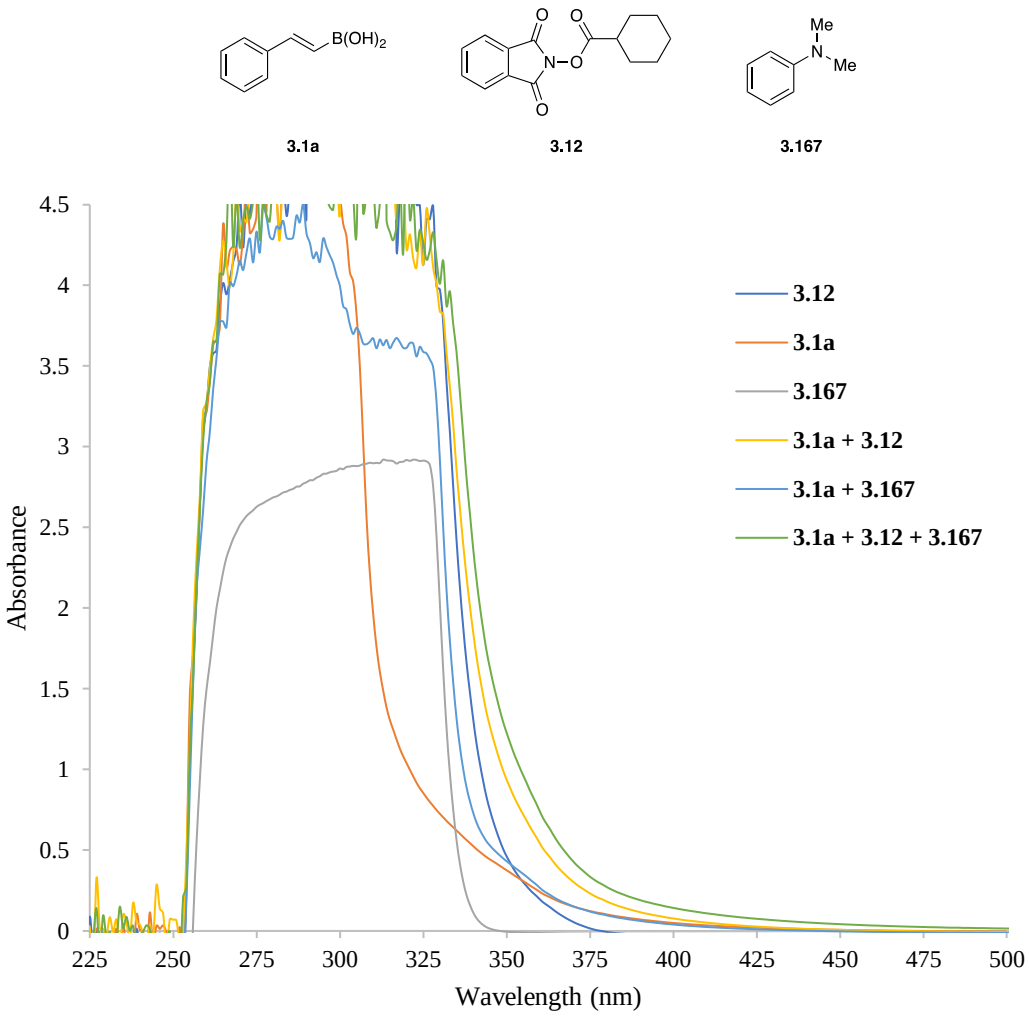
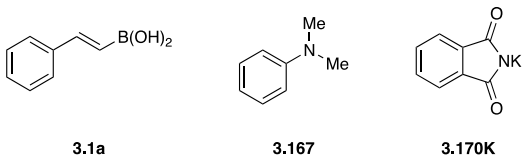
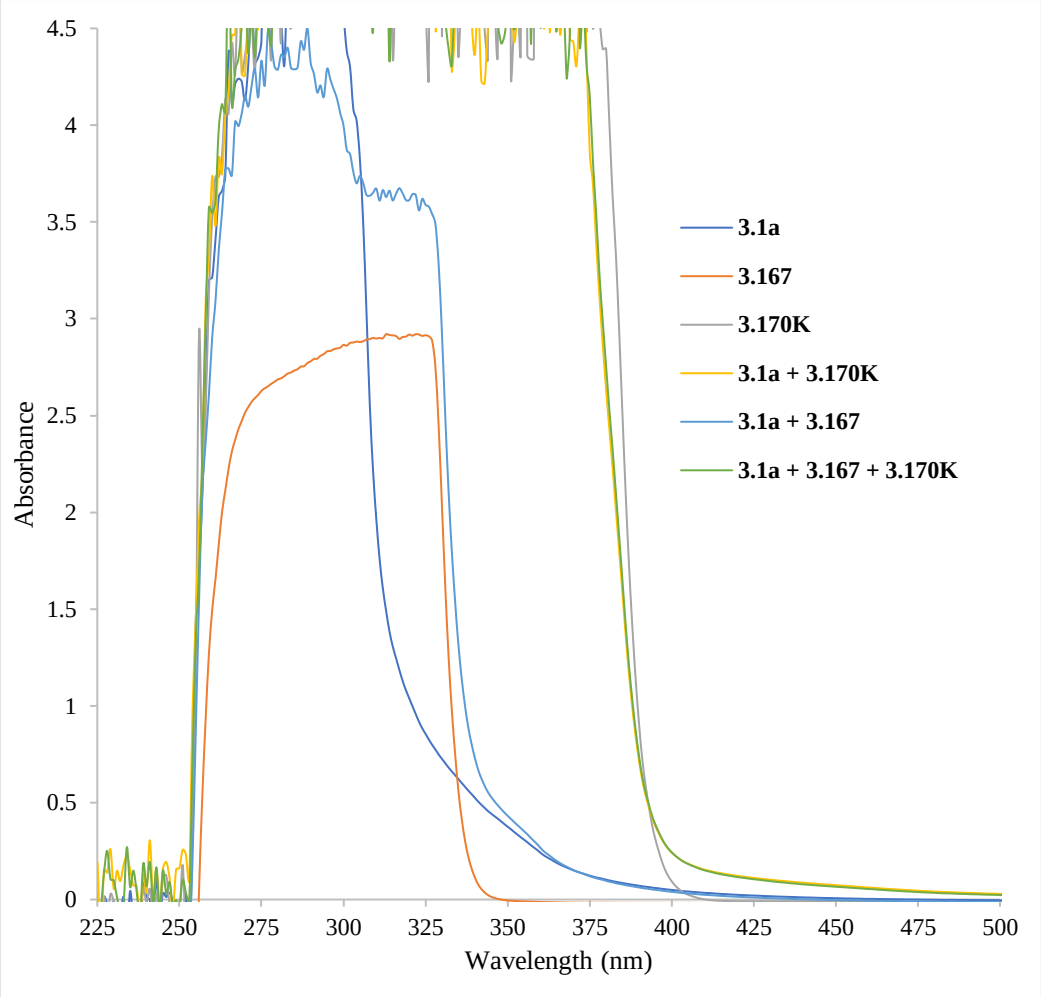


Figure 5-6 : UV-Vis absorption with **3.170K**.





5.2.3.3 Emission quenching and Stern–Volmer linearisation

A stock solution of tris(2,2'-bipyridine)ruthenium hexafluorophosphate at 10^{-5} M in DMSO was prepared and used for all the quenching studies. Quencher solutions of *N*,*N*-dimethylaniline, styrenyl boronic acid, **3.1a**, or cyclohexane NHPI, **3.12** were prepared at 10^{-1} M in DMSO and degassed with N_2 bubbling through for 25 minutes prior their use. The cuvette sealed with a septum was purged with vacuum-N_2 cycles and backfilled with N_2. The solution of photocatalyst was added (2.5 mL) into the cuvette and was degassed with N_2 bubbling through for 25 minutes. Aliquots of quencher solutions were added (10 µL) using a micro-syringe attached through the septum (see apparatus from the literature).[248]

Figure 5-7: Emission quenching using **3.1a**.

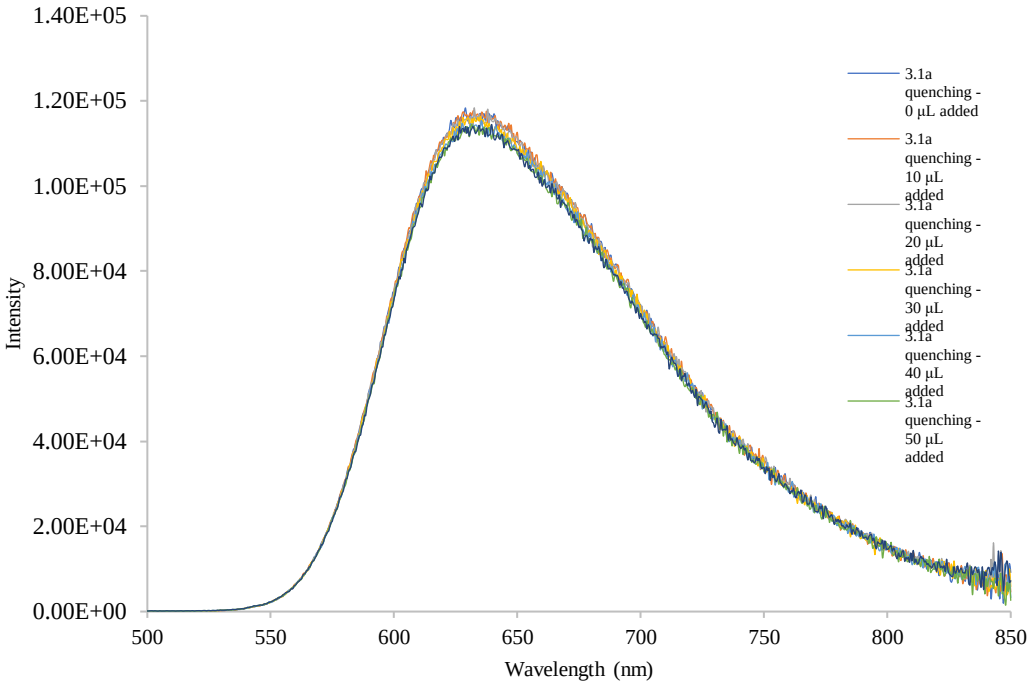


Figure 5-8: Emission quenching using **3.12**.

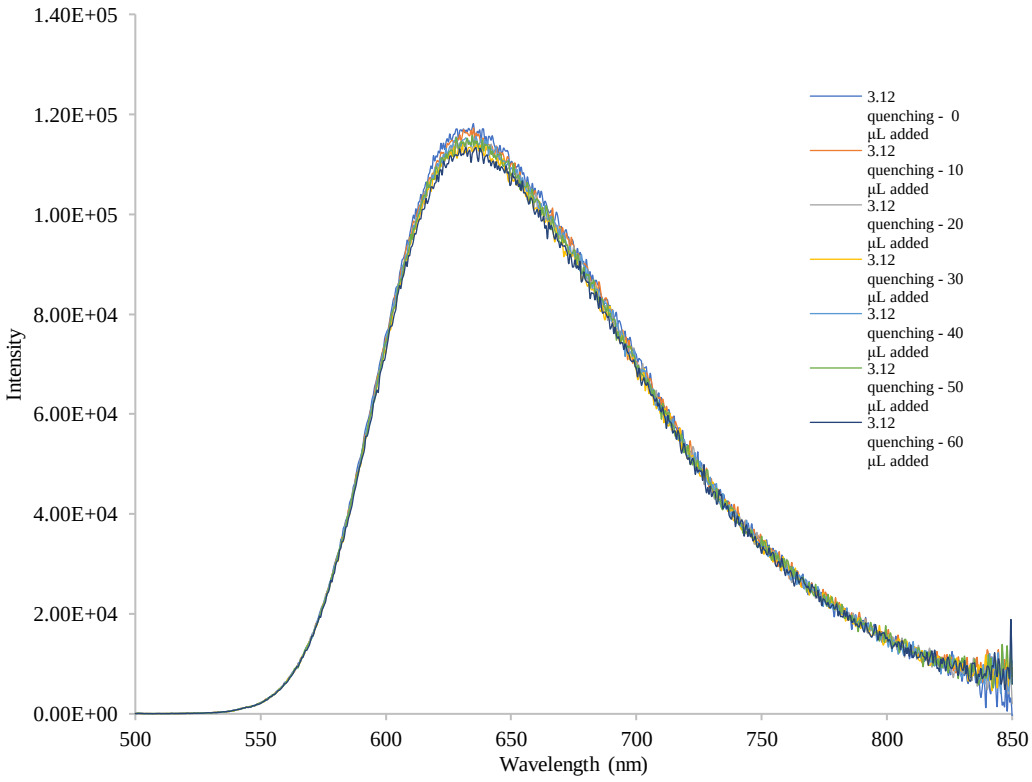
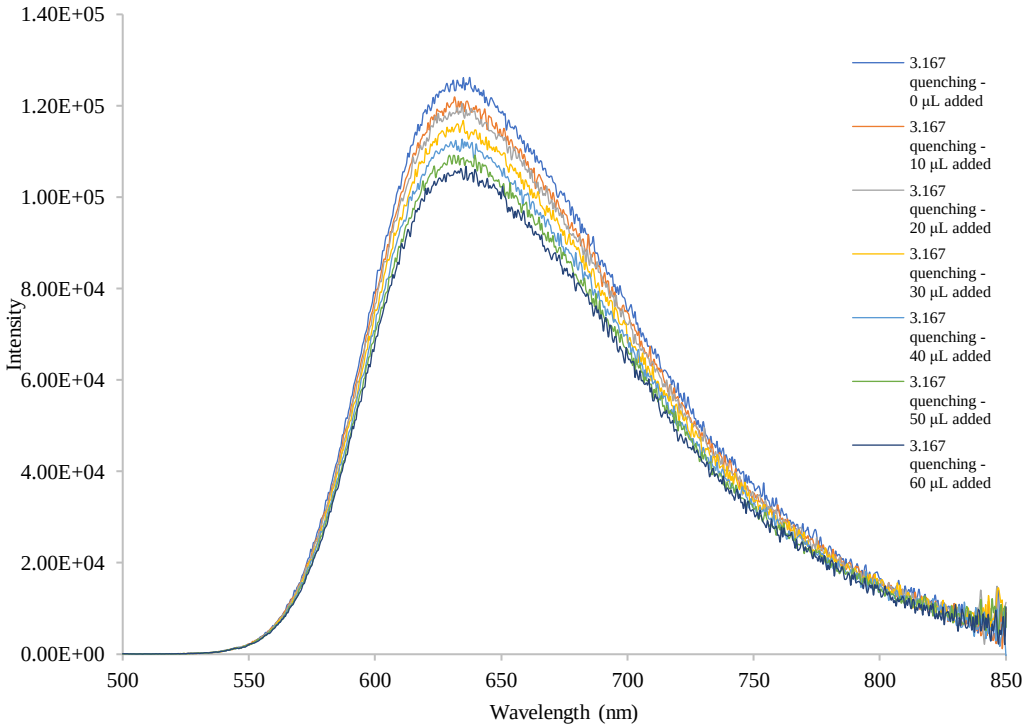


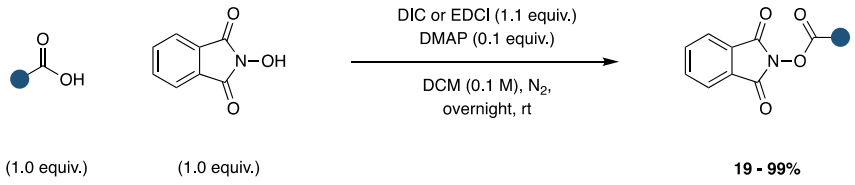
Figure 5-9: Emission quenching using *N*,*N*-dimethylaniline **3.167**.



5.3 Synthesis of starting materials

5.3.1 Synthesis of NHPI esters

NHPI esters were synthesised according to the literature using either DIC (General procedure 2A)[208] or EDCl (General procedure 2B).[209]



Scheme 5-3: General synthesis of NHPI Esters.

General Procedure 2A (DIC)

Prepared according to the literature.[208] A flame-dried three-necked round bottom flask equipped with a Teflon-coated stir bar was charged with *N*-hydroxyphthalimide (1.0 equiv.), 4-dimethylaminopyridine (10 mol%), and the desired carboxylic acid (1.0

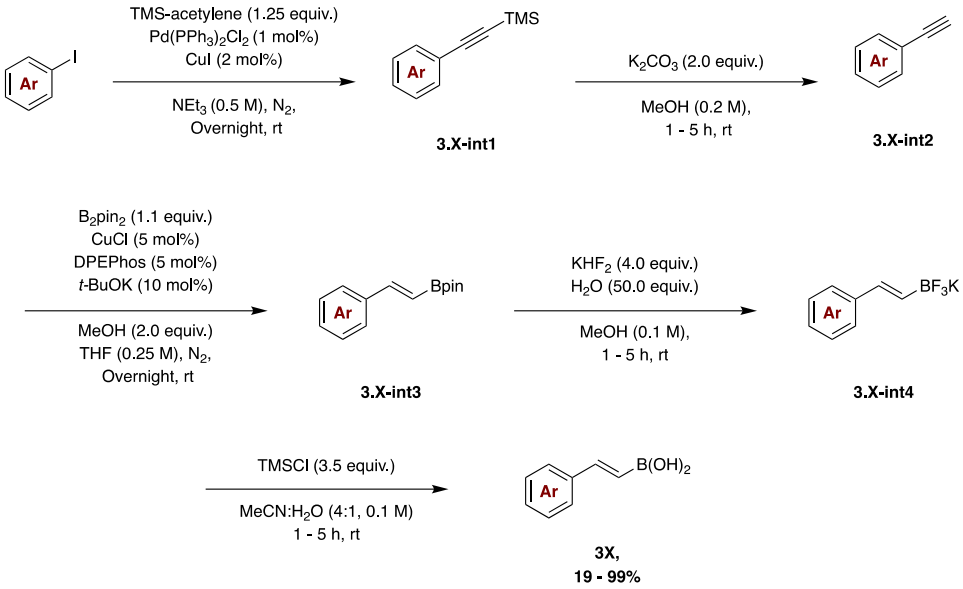
equiv., if solid). The flask was purged using an N_2-vacuum cycle (3 times) and backfilled with N_2. DCM (0.1 M, total volume) was added, followed by the desired carboxylic acid (1.0 equiv., if liquid). *N*,*N'*-Diisopropyl-carbodiimide (1.1 equiv.) was dissolved in DCM and added dropwise to the reaction mixture. The reaction mixture was left to stir overnight at room temperature. Once complete, the reaction mixture was concentrated *in vacuo*. The crude residue was purified by flash chromatography (silica gel) using hexane/ethyl acetate or hexane/diethyl ether.

General Procedure 2B (EDCl)

Prepared according to the literature.[209] A flame-dried three-necked round bottom flask equipped with a Teflon-coated stir bar was charged with the desired carboxylic acid (1.0 equiv., if solid), EDC hydrochloride (1.2 equiv.), and 4-dimethylaminopyridine (10 mol%). The flask was purged using an N_2-vacuum cycle (3 times) and backfilled with N_2. DCM (0.1 M, total volume) was added followed by the desired carboxylic acid (1.0 equiv., if liquid). *N*-Hydroxyphthalimide (1.0 equiv.) was added portionwise to the reaction mixture. The reaction mixture was left to stir overnight at room temperature. Once complete, the reaction mixture was washed with 1 M HCl. The organic layer was washed with brine, dried over sodium sulfate, filtered, and concentrated *in vacuo*. The crude residue was purified by flash chromatography (silica gel) using hexane/ethyl acetate or hexane/diethyl ether.

5.3.2 Synthesis of styrenyl boronic acids

The styrenyl boronic acids were synthesised according to Scheme *5-4*. In the case of a commercially available alkynes, the synthesis started with a Cu-mediated hydroboration.[219–222] Otherwise, the synthesis started with a Sonogashira cross-coupling reaction with the (hetero)aryl iodide (or bromide).



Scheme 5-4: General synthesis of styrenyl boronic acids.

General Procedure 3: Sonogashira cross-coupling reaction

An oven-dried microwave vial equipped with a Teflon-coated stir bar was charged with dichlorobis(triphenylphosphine)palladium (1 mol%), copper iodide (2 mol%), and the desired (hetero)aryl iodide (or bromide) (1.0 equiv., if solid). The vial was then sealed, purged using an N_2-vacuum cycle (3 times), and backfilled with N_2. Triethylamine (0.5 M) was added followed by the desired (hetero)aryl iodide (or bromide) (1.0 equiv., if liquid), and trimethylsilylacetylene (1.25 equiv.). The reaction mixture was left to stir overnight at room temperature. Once complete, the crude mixture was filtered through celite, rinsed with DCM, and the combined organics were concentrated *in vacuo*. The crude residue was purified by flash chromatography (silica gel) using hexane/ethyl acetate or hexane/diethyl ether affording the desired product **3.X-int1**.

General Procedure 4: TMS deprotection

3.X-int1 (1.0 equiv.) was dissolved in MeOH (0.2 M) and potassium carbonate (2.0 equiv.) was added. The reaction mixture was stirred one to five hours at room temperature. Once complete, the volatiles were removed under vacuum. The crude mixture was partitioned between water and DCM and the organics were extracted with DCM. The combined organics were washed with water, dried over sodium sulfate,

filtered, and concentrated *in vacuo*. The crude residue was purified by flash chromatography (silica gel) using hexane/ethyl acetate or hexane/diethyl ether affording the desired product **3.X-int2**.

General Procedure 5: Cu-mediated hydroboration

Prepared according to the literature.[219–222] An oven-dried microwave vial equipped with a Teflon-coated stir bar was charged with copper(I) chloride (5 mol%), potassium *tert*-butoxide (10 mol%), and bis(2-diphenylphosphinophenyl) ether (DPEPhos) (5 mol%). The vial was sealed and purged using an N_2-Vacuum cycles (3 times) and backfilled with N_2. THF (0.25 M, total volume) was added, and the mixture was stirred for 45 minutes at room temperature. Bis(pinacolato)diboron (1.1 equiv.) was dissolved in THF and added *via* syringe. The reaction mixture was then left to stir at room temperature for 30 minutes. The alkyne **3.X-int2** (1.0 equiv.) was dissolved in THF if solid or added directly to the reaction mixture if liquid, followed by MeOH (2.0 equiv.). The reaction mixture was stirred overnight at room temperature. Once complete, the reaction mixture was filtered through a pad of celite, rinsed with DCM, and the combined organics were concentrated *in vacuo*. The crude residue was purified by flash chromatography (silica gel) using hexane/ethyl acetate or hexane/diethyl ether affording the desired product **3.X-int3**.

General Procedure 6: BF_3K Synthesis

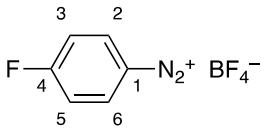
3.X-int3 (1.0 equiv.) was dissolved in MeOH (0.1 M) and potassium hydrogen fluoride (4.0 equiv.) was added. Water (50.0 equiv.) was added dropwise, and the reaction was left to stir for one to five hours at room temperature. The reaction was monitored by ^{11}B NMR and once complete, the mixture was concentrated *in vacuo* and the crude residue was dissolved in hot acetone, filtered, and concentrated *in vacuo.* The white precipitate was then dissolved in acetone and diethyl ether was added to precipitate the salt. The desired product, **3.X-int4** was obtained after filtration.

General Procedure 7: Hydrolysis of BF_3K substrate to styrenyl boronic acid

SX-int4 (1.0 equiv.) was dissolved in a mixture of MeCN and H_2O (4:1, 0.1 M). Freshly distilled chlorotrimethylsilane (3.5 equiv.) was added and the reaction mixture and was left to stir for one to five hours at room temperature, monitoring by ^{11}B NMR spectroscopy. Once complete, the reaction mixture was partitioned between water and ethyl acetate and the organics were extracted with ethyl acetate (3 times). The organic layers were combined, dried over sodium sulfate, filtered, and concentrated *in vacuo* affording the desired product **3.X**. **3.X** was usually obtained as a mixture of the desired product and boroxine, a drop of water was added in order to hydrolyse the boroxine into the boronic acid.

6. Data

4-Fluorobenzenediazonium tetrafluoroborate, **3.3**



An oven-dried vial was purged with vacuum-N_2 cycle (3 times) and backfilled with N_2. Tetrafluoroboric acid, *ca* 50% w/w aq. solution (1.00 mL, 8.00 mmol, 4.0 equiv.) was added, cooled down to 0 °C and 4-fluoroaniline (190 µL, 2.00 mmol, 1.0 equiv.) was then added. A solution of sodium nitrite (140 mg, 2.00 mmol, 1.0 equiv.) in water (2 mL) was cooled down to 0 °C and then added dropwise into the reaction mixture. The reaction was left to stir for four hours under N_2 at 0 °C. The reaction mixture was then filtered and a pale orange solid was recovered. This later was then dissolved in acetone and diethyl ether was then slowly added to precipitate the compound. 77 mg of a white solid was then collected by filtration (28%).

^{1}H NMR (500 MHz, DMSO-d_6) δ 8.87 – 8.72 (m, 2H, H^2 and H^6), 7.98 – 7.80 (m, 2H, H^3 and H^5).

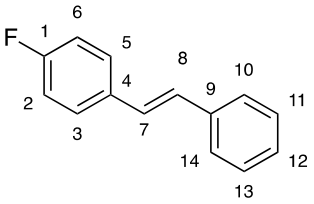
^{13}C NMR (126 MHz, DMSO-d_6) δ 168.4 (d, $^{1}J_{CF}$ = 266.9 Hz, C^4), 137.0 (d, $^{3}J_{CF}$ = 12.3 Hz, C^2 and C^6), 119.4 (d, $^{2}J_{CF}$ = 25.3 Hz, C^3 and C^5), 111.9 (d, $^{4}J_{CF}$ = 2.8 Hz, C^1).

^{11}B NMR (128 MHz, DMSO-d6) δ –1.29.

^{19}F {^{1}H} NMR (376 MHz, DMSO-d_6) δ –87.22 (BF_4), –148.20 (F).

Data are consistent with the literature.[249]

(*E*)-1-Fluoro-4-styrylbenzene, **3.4**



Prepared according to General Procedure 1 using 4-fluorobenzenediazonium tetrafluoroborate **3.3** (42.0 mg, 0.2 mmol, 1.0 equiv.), (*E*)-2-phenylvinylboronic acid **3.1a** (44.4 mg, 0.30 mmol, 1.5 equiv.), and Eosin Y (13.9 mg, 0.02 mmol, 10 mol%) in DMSO (2 mL, 0.1 M). The crude residue was purified by flash chromatography (silica gel) from pure hexane to a mixture of 2% of diethyl ether in hexane affording 9.5 mg of **3.4** as a white solid (24%, *E:Z* > 20:1).

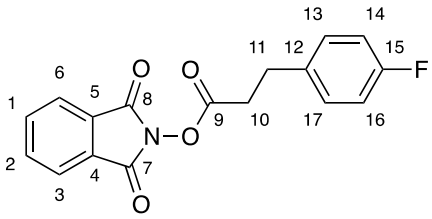
^{1}H NMR (400 MHz, Chloroform-*d*) δ 7.53 – 7.46 (m, 4H, H^{3}, H^{5}, H^{10} and H^{14}), 7.40 – 7.34 (m, 2H, H^{11} and H^{13}), 7.30 – 7.24 (m, 1H, H^{12}), 7.11 – 6.98 (m, 4H, H^{2}, H^{6}, H^{7} and H^{8}).

^{13}C NMR (126 MHz, Chloroform-*d*) δ 162.3 (d, $^{1}J_{CF}$ = 247.1 Hz, C^{1}), 137.1 (C^{9}), 133.5 (d, $^{4}J_{CF}$ = 3.3 Hz, C^{4}), 128.7 (C^{11} and C^{13}), 128.5 (C^{7}), 128.0 (d, $^{3}J_{CF}$ = 7.9 Hz, C^{3} and C^{5}), 127.7 (C^{12}), 127.4 (C^{8}), 126.4 (C^{10} and C^{14}), 115.6 (d, $^{2}J_{CF}$ = 21.6 Hz, C^{2} and C^{6}).

^{19}F {^{1}H} NMR (376 MHz, Chloroform-*d*) δ –114.25.

Data are consistent with the literature.[250]

1,3-Dioxoisoindolin-2-yl 3-(4-fluorophenyl)propanoate, **3.5**



Prepared according to General Procedure 2A using 3-(4-fluorophenyl)propionic acid (1.68 g, 10.00 mmol, 1.0 equiv.), *N*,*N'*-diisopropyl-carbodiimide (1.70 mL, 11 mmol, 1.1 equiv.), 4-dimethylaminopyridine (122 mg, 1 mmol, 10 mol%), and *N*-hydroxyphthalimide (1.80 g, 11 mmol, 1.1 equiv.) in DCM (100 mL, 0.1 M). The crude residue was purified by flash chromatography (silica gel) from pure hexane to a mixture of 12% of ethyl acetate in hexane affording 2.18 g of a white solid consistent with the desired product (70%).

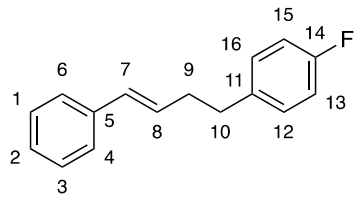
^{1}H NMR (500 MHz, Chloroform-*d*) δ 7.97 – 7.84 (m, 2H, H^{1} and H^{2}), 7.84 – 7.74 (m, 2H, H^{3} and H^{6}), 7.39 – 7.14 (m, 2H, H^{13} and H^{17}), 7.12 – 6.88 (m, 2H, H^{14} and H^{16}), 3.07 (t, *J* = 7.65 Hz, 2H, H^{11}), 2.96 (t, J = 7.63 Hz, 2H, H^{10}).

^{13}C NMR (126 MHz, Chloroform-*d*) δ 168.9 (C^{9}), 162.0 (C^{7} and C^{8}), 161.9 (d, $^{1}J_{CF}$ = 244.5 Hz, C^{15}), 135.0 (C^{1} and C^{2}), 134.9 (broad app. s, C^{12}), 130.0 (d, $^{3}J_{CF}$ = 7.9 Hz, C^{13} and C^{17}), 129.0 (C^{4} and C^{5}), 124.2 (C^{3} and C^{6}), 115.7 (d, $^{2}J_{CF}$ = 21.3 Hz, C^{14} and C^{16}), 33.0 (C^{10}), 29.9 (C^{11}).

^{19}F {^{1}H} NMR (377 MHz, Chloroform-*d*) δ –116.27.

Data are consistent with the literature.[251]

(*E*)-1-Fluoro-4-(4-phenylbut-3-en-1-yl)benzene, **3.6**



Prepared according to General Procedure 1 using 1,3-dioxoisoindolin-2-yl 3-(4-fluorophenyl)propanoate **3.5** (62.7 mg, 200 μmol, 1.0 equiv.), (*E*)-2-phenylvinylboronic acid **3.1a** (59.2 mg, 400 μmol, 2.0 equiv.), tris(2,2'-bipyridine)ruthenium hexafluorophosphate (1.7 mg, 2.00 μmol, 1 mol%), and *N*,*N*-dimethylaniline (2.5 μL, 20.0 μmol, 10 mol%) in DMSO-d_6 (1 mL, 0.2 M). The crude residue was purified by flash chromatography (silica gel) with pure hexane affording 35.0 mg of a white solid as the desired product (77%, *E*:*Z* > 20:1).

^{1}H NMR (400 MHz, Chloroform-*d*) δ 7.36 – 7.27 (m, 4H, H^{1}, H^{3}, H^{4} and H^{6}), 7.24 – 7.19 (m, 1H, H^{2}), 7.19 – 7.12 (m, 2H, H^{12} and H^{16}), 7.05 – 6.92 (m, 2H, H^{13} and H^{15}), 6.41 (dt, *J* = 15.78, 1.44 Hz, 1H, H^{7}), 6.24 (dt, *J* = 15.78, 6.79 Hz, 1H, H^{8}), 2.95 – 2.68 (m, 2H, H^{10}), 2.65 – 2.41 (m, 2H, H^{9}).

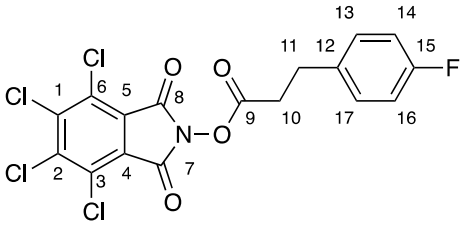
^{13}C NMR (126 MHz, Chloroform-*d*) δ 161.8 (d, $^{1}J_{CF}$ = 243.4 Hz, C^{14}), 138.1 (C^{5}), 137.8 (d, $^{4}J_{CF}$ = 3.3 Hz, C^{11}), 131.1 (C^{7}), 130.3 (d, $^{3}J_{CF}$ = 7.7 Hz, C^{12} and C^{16}), 130.1 (C^{8}), 129.1 (C^{1} and C^{3}), 127.6 (C^{2}), 126.5 (C^{4} and C^{6}), 115.6 (d, $^{2}J_{CF}$ = 21.0 Hz, C^{13} and C^{15}), 35.6 (C^{10}), 35.5 (C^{9}).

^{19}F {^{1}H} NMR (376 MHz, Chloroform-*d*) δ –117.66.

IR (film): 3026, 2926, 2360, 1600, 1508, 1448, 1220, 908, 732 cm^{-1}.

HRMS (EI): *m/z* calculated for $[M]^+$ ($C_{16}H_{15}F$): 226.1152; found 226.1147.

4,5,6,7-Tetrachloro-1,3-dioxoisoindolin-2-yl 3-(4-fluorophenyl)propanoate, **3.8**



Prepared according to General Procedure 2A using 3-(4-fluorophenyl)propionic acid (336 mg, 2.00 mmol, 1.0 equiv.), *N*,*N*′-diisopropyl-carbodiimide (340 µL, 2.20 mmol, 1.1 equiv.), 4-dimethylaminopyridine (24 mg, 200 umol, 10 mol%), and *N*-hydroxytetrachlorophthalimide (602 mg, 2.00 mmol, 1.0 equiv.) in DCM (20 mL, 0.1 M). The crude residue was purified by flash chromatography (silica gel) from pure hexane to a mixture of 12% of ethyl acetate in hexane affording 458 mg of a pale yellow solid consistent with the desired product (51%).

^{1}H NMR (500 MHz, Chloroform-*d*) δ 7.24 – 7.19 (m, 2H, H^{13} and H^{17}), 7.06 – 6.96 (m, 2H, H^{14} and H^{16}), 3.09 – 3.04 (m, 2H, H^{11}), 2.99 – 2.93 (m, 2H, H^{10}).

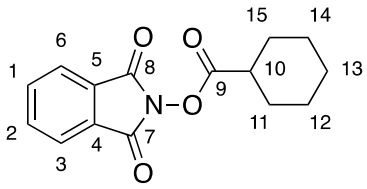
^{13}C NMR (126 MHz, Chloroform-*d*) δ 168.5 (C^{9}), 161.9 (d, $^{1}J_{CF}$ = 244.9 Hz, C^{15}), 157.6 (C^{7} and C^{8}), 141.2 (C^{1} and C^{2}), 134.7 (d, $^{4}J_{CF}$ = 3.24 Hz, C^{12}), 130.6 (C^{4} and C^{5}), 129.9 (d, $^{3}J_{CF}$ = 7.98 Hz, C^{13} and C^{17}), 124.8 (C^{3} and C^{6}), 115.7 (d, $^{2}J_{CF}$ = 21.32 Hz, C^{14} and C^{16}), 32.9 (C^{10}), 29.9 (C^{11}).

^{19}F {^{1}H} NMR (376 MHz, Chloroform-*d*) δ –116.06.

IR (solid): 1820, 1795, 1774, 1735, 1603, 1510, 1417, 1321, 1298, 1215, 1198, 951, 918 cm^{-1}.

HRMS (ESI): *m/z* calculated for $[M + Na]^+$ $(C_{17}H_8NO_4Cl_4FNa)^+$: 471.9083; found 471.9105.

1,3-Dioxoisoindolin-2-yl cyclohexanecarboxylate, **3.12**



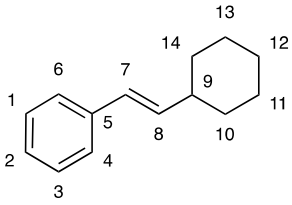
Prepared according to General Procedure 2A using cyclohexanecarboxylic acid (641 mg, 5.00 mmol, 1.0 equiv.), *N,N'*-diisopropyl-carbodiimide (850 µL, 5.50 mmol, 1.1 equiv.), 4-dimethylaminopyridine (61 mg, 500 µmol, 10 mol%), and *N*-hydroxyphthalimide (816 mg, 5.00 mmol, 1.0 equiv.) in DCM (50 mL, 0.1 M). The crude residue was purified by flash chromatography (silica gel) from pure hexane to a mixture of 8% of ethyl acetate in hexane affording 938 mg of a white solid consistent with the desired product (69%).

^{1}H NMR (400 MHz, Chloroform-*d*) δ 7.91 – 7.85 (m, 2H, H^{3} and H^{6}), 7.82 – 7.75 (m, 2H, H^{1} and H^{2}), 2.73 (tt, *J* = 10.89, 3.79 Hz, 1H, H^{10}), 2.15 – 2.03 (m, 2H, H^{11} and H^{15}), 1.90 – 1.72 (m, 2H, H^{12} and H^{14}), 1.73 – 1.62 (m, 3H, H^{11}, H^{13} and H^{15}), 1.46 – 1.22 (m, 3H, H^{12}, H^{13} and H^{14}).

^{13}C NMR (126 MHz, Chloroform-*d*) δ 172.0 (C^{9}), 162.2 (C^{7} and C^{8}), 134.8 (C^{1} and C^{2}), 129.1 (C^{4} and C^{5}), 124.0 (C^{3} and C^{6}), 40.6 (C^{10}), 28.9 (C^{11} and C^{15}), 25.6 (C^{13}), 25.1 (C^{12} and C^{14}).

Data are consistent with the literature.[227]

(*E*)-(2-Cyclohexylvinyl)benzene, **3.13**



Prepared according to General Procedure 7 using 1,3-dioxoisoindolin-2-yl cyclohexanecarboxylate **3.12** (54.7 mg, 200 µmol, 1.0 equiv.), (*E*)-2-phenylvinylboronic acid, **3.1a** (59.2 mg, 400 µmol, 2.0 equiv.), tris(2,2'-bipyridine)ruthenium hexafluorophosphate (1.7 mg, 2.00 µmol, 1 mol%), and

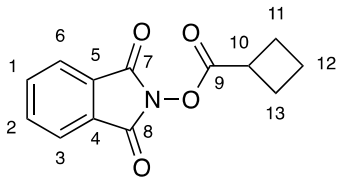
N,*N*-dimethylaniline (2.5 μL, 20.0 μmol, 10 mol%) in DMSO-d_6 (1 mL, 0.2 M). The crude residue was purified by flash chromatography (silica gel) with pure hexane affording 30.1 mg of a colourless oil as the desired product (81%, *E:Z* > 20:1).

^{1}H NMR (500 MHz, Chloroform-*d*) δ 7.37 – 7.33 (m, 2H, H^4 and H^6), 7.31 – 7.27 (m, 2H, H^1 and H^3), 7.21 – 7.16 (m, 1H, H^2), 6.35 (d, *J* = 16.01 Hz, 1H, H^7), 6.18 (dd, *J* = 15.98, 6.96 Hz, 1H, H^8), 2.18 – 2.08 (m, 1H, H^9), 1.86 – 1.74 (m, 4H, H^{10}, H^{11}, H^{13} and H^{14}), 1.72 – 1.65 (m, 1H, H^{12}), 1.39 – 1.25 (m, 2H, H^{11} and H^{13}), 1.25 – 1.14 (m, 3H, H^{10}, H^{12} and H^{14}).

^{13}C NMR (126 MHz, Chloroform-*d*) δ 138.2 (C^5), 137.0 (C^8), 128.6 (C^1 and C^3), 127.3 (C^7), 126.9 (C^2), 126.1 (C^4 and C^6), 41.3 (C^9), 33.1 (C^{10} and C^{14}), 26.3 (C^{12}), 26.2 (C^{11} and C^{13}).

Data are consistent with the literature.[252]

1,3-Dioxoisoindolin-2-yl cyclobutanecarboxylate, **3.14**



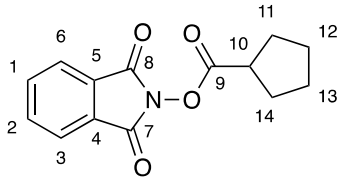
Prepared according to General Procedure 2A using cyclobutanecarboxylic acid (380 μL, 4.00 mmol, 1.0 equiv.), *N*,*N'*-diisopropyl-carbodiimide (680 μL, 4.40 mmol, 1.1 equiv.), 4-dimethylaminopyridine (49 mg, 400 μmol, 10 mol%), and *N*-hydroxyphthalimide (653 mg, 4.00 mmol, 1.0 equiv.) in DCM (40 mL, 0.1 M). The crude residue was purified by flash chromatography (silica gel) from pure hexane to a mixture of 8% of ethyl acetate in hexane affording 855 mg of a white solid consistent with the desired product (87%).

^{1}H NMR (500 MHz, Chloroform-*d*) δ 7.91 – 7.86 (m, 2H, H^3 and H^6), 7.82 – 7.74 (m, 2H, H^1 and H^2), 3.56 – 3.46 (m, 1H, H^{10}), 2.56 – 2.46 (m, 2H, H^{11} and H^{13}), 2.46 – 2.34 (m, 2H, H^{11} and H^{13}), 2.18 – 1.99 (m, 2H, H^{12}).

^{13}C NMR (126 MHz, Chloroform-*d*) δ 171.6 (C^9), 162.2 (C^7 and C^8), 134.9 (C^1 and C^2), 129.1 (C^4 and C^5), 124.1 (C^3 and C^6), 35.1 (C^{10}), 25.5 (C^{11} and C^{13}), 18.9 (C^{12}).

Data are consistent with the literature.[253]

1,3-Dioxoisoindolin-2-yl cyclopentanecarboxylate, **3.15**



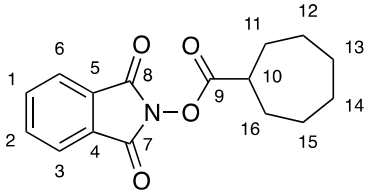
Prepared according to General Procedure 2A using cyclopentanecarboxylic acid (571 mg, 5.00 mmol, 1.0 equiv.), *N*,*N'*-diisopropyl-carbodiimide (850 μL, 5.50 mmol, 1.1 equiv.), 4-dimethylaminopyridine (61 mg, 500 μmol, 10 mol%), and *N*-hydroxyphthalimide (816 mg, 5.00 mmol, 1.0 equiv.) in DCM (50 mL, 0.1 M). The crude residue was purified by flash chromatography (silica gel) from pure hexane to a mixture of 8% of ethyl acetate in hexane affording 871 mg of a white solid consistent with the desired product (67%).

^{1}H NMR (500 MHz, Chloroform-*d*) δ 7.91 – 7.85 (m, 2H, H^3 and H^6), 7.82 – 7.73 (m, 2H, H^1 and H^2), 3.08 – 3.14 (m, 1H, H^{10}), 2.15 – 1.97 (m, 4H, H^{11} and H^{14}), 1.87 – 1.71 (m, 2H, H^{12} and H^{13}), 1.73 – 1.62 (m, 2H, H^{12} and H^{13}).

^{13}C NMR (126 MHz, Chloroform-*d*) δ 173.0 (C^9), 162.3 (C^7 and C^8), 134.8 (C^1 and C^2), 129.1 (C^4 and C^5), 124.0 (C^3 and C^6), 40.8 (C^{10}), 30.4 (C^{11} and C^{14}), 26.1 (C^{12} and C^{13}).

Data are consistent with the literature.[254]

1,3-Dioxoisoindolin-2-yl cycloheptanecarboxylate, **3.16**



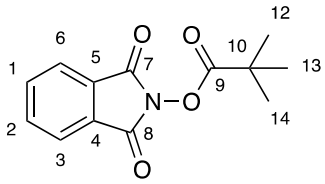
Prepared according to General Procedure 2A using cycloheptanecarboxylic acid (550 μL, 4.00 mmol, 1.0 equiv.), *N*,*N'*-diisopropyl-carbodiimide (680 μL, 4.40 mmol, 1.1 equiv.), 4-dimethylaminopyridine (49 mg, 400 μmol, 10 mol%), and *N*-hydroxyphthalimide (653 mg, 4.00 mmol, 1.0 equiv.) in DCM (40 mL, 0.1 M). The crude residue was purified by flash chromatography (silica gel) from pure hexane to a mixture of 4% of ethyl acetate in hexane affording 742 mg of a white solid consistent with the desired product (65%).

^{1}H NMR (500 MHz, Chloroform-*d*) δ 7.91 – 7.84 (m, 2H, H^{3} and H^{6}), 7.81 – 7.74 (m, 2H, H^{1} and H^{2}), 2.89 (hept, *J* = 4.56 Hz, 1H, H^{10}), 2.18 – 2.09 (m, 2H, H^{11} and H^{16}), 1.93 – 1.82 (m, 2H, H^{11} and H^{16}), 1.85 – 1.77 (m, 2H, H^{12} and H^{15}), 1.66 – 1.51 (m, 6H, H^{12}, H^{13}, H^{14} and H^{15}).

^{13}C NMR (126 MHz, Chloroform-*d*) δ 172.9 (C^{9}), 162.3 (C^{7} and C^{8}), 134.8 (C^{1} and C^{2}), 129.2 (C^{4} and C^{5}), 124.0 (C^{3} and C^{6}), 42.3 (C^{10}), 30.9 (C^{11} and C^{16}), 28.4 (C^{13} and C^{14}), 26.4 (C^{12} and C^{15}).

Data are consistent with the literature.[255]

1,3-Dioxoisoindolin-2-yl pivalate, **3.17**



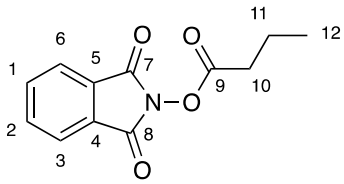
Prepared according to General Procedure 2A using pivalic acid (511 mg, 5.00 mmol, 1.0 equiv.), *N*,*N'*-diisopropyl-carbodiimide (850 μL, 5.50 mmol, 1.1 equiv.), 4-dimethylaminopyridine (61 mg, 500 μmol, 10 mol%), and *N*-hydroxyphthalimide (816 mg, 5.00 mmol, 1.0 equiv.) in DCM (50 mL, 0.1 M). The crude residue was purified by flash chromatography (silica gel) from pure hexane to a mixture of 8% of ethyl acetate in hexane affording 922 mg of a white solid consistent with the desired product (75%).

^{1}H NMR (500 MHz, Chloroform-*d*) δ 7.93 – 7.84 (m, 2H, H^{3} and H^{6}), 7.82 – 7.70 (m, 2H, H^{1} and H^{2}), 1.43 (s, 9H, H^{12}, H^{13} and H^{14}).

^{13}C NMR (126 MHz, Chloroform-*d*) δ 174.5 (C^{9}), 162.2 (C^{7} and C^{8}), 134.8 (C^{1} and C^{2}), 129.2 (C^{4} and C^{5}), 124.0 (C^{3} and C^{6}), 38.5 (C^{10}), 27.2 (C^{12}, C^{13} and C^{14}).

Data are consistent with the literature.[256]

1,3-Dioxoisoindolin-2-yl butyrate, **3.18**



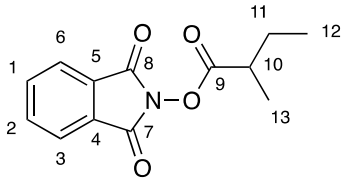
Prepared according to General Procedure 2A using butyric acid (340 μL, 4.00 mmol, 1.0 equiv.), *N*,*N'*-diisopropyl-carbodiimide (680 μL, 4.40 mmol, 1.1 equiv.), 4-dimethylaminopyridine (49 mg, 400 μmol, 10 mol%), and *N*-hydroxyphthalimide (653 mg, 4.00 mmol, 1.0 equiv.) in DCM (40 mL, 0.1 M). The crude residue was purified by flash chromatography (silica gel) from pure hexane to a mixture of 7% of ethyl acetate in hexane affording 561 mg of a colourless oil consistent with the desired product (56%).

^{1}H NMR (500 MHz, Chloroform-*d*) δ 7.91 – 7.86 (m, 2H, H^{3} and H^{6}), 7.81 – 7.76 (m, 2H, H^{1} and H^{2}), 2.65 (t, *J* = 7.31 Hz, 2H, H^{10}), 1.82 (h, *J* = 7.38 Hz, 2H, H^{11}), 1.07 (t, *J* = 7.41 Hz, 3H, H^{12}).

^{13}C NMR (126 MHz, Chloroform-*d*) δ 169.6 (C^{9}), 162.1 (C^{7} and C^{8}), 134.9 (C^{1} and C^{2}), 129.1 (C^{4} and C^{5}), 124.1 (C^{3} and C^{6}), 32.9 (C^{10}), 18.4 (C^{11}), 13.5 (C^{12}).

Data are consistent with the literature.[256]

1,3-Dioxoisoindolin-2-yl 2-methylbutanoate, **3.19**



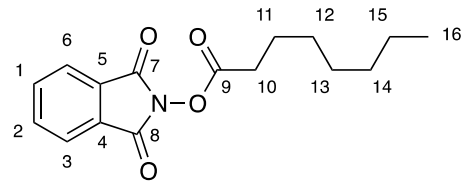
Prepared according to General Procedure 2A using (+/-)-2-methylbutyric acid (550 μL, 5.00 mmol, 1.0 equiv.), *N*,*N'*-diisopropyl-carbodiimide (850 μL, 5.50 mmol, 1.1 equiv.), 4-dimethylaminopyridine (61 mg, 500 μmol, 10 mol%), and *N*-hydroxyphthalimide (816 mg, 5.00 mmol, 1.0 equiv.) in DCM (50 mL, 0.1 M). The crude residue was purified by flash chromatography (silica gel) from pure hexane to a mixture of 6% of ethyl acetate in hexane affording 813 mg of a colourless oil consistent with the desired product (66%).

^{1}H NMR (500 MHz, Chloroform-*d*) δ 7.91 – 7.85 (m, 2H, H^{3} and H^{6}), 7.81 – 7.76 (m, 2H, H^{1} and H^{2}), 2.78 (h, *J* = 7.00 Hz, 1H, H^{10}), 1.92 – 1.80 (m, 1H, H^{11}), 1.75 – 1.64 (m, 1H, H^{11}), 1.35 (d, *J* = 6.94 Hz, 3H, H^{13}), 1.07 (t, *J* = 7.46 Hz, 3H, H^{12}).

^{13}C NMR (126 MHz, Chloroform-*d*) δ 172.8 (C^{9}), 162.2 (C^{7} and C^{8}), 134.8 (C^{1} and C^{2}), 129.1 (C^{4} and C^{5}), 124.0 (C^{3} and C^{6}), 38.7 (C^{10}), 27.0 (C^{11}), 16.6 (C^{13}), 11.4 (C^{12}).

Data are consistent with the literature.[257]

1,3-Dioxoisoindolin-2-yl octanoate, **3.20**



Prepared according to General Procedure 2A using octanoic acid (790 μL, 5.00 mmol, 1.0 equiv.), *N*,*N'*-diisopropyl-carbodiimide (850 μL, 5.50 mmol, 1.1 equiv.), 4-dimethylaminopyridine (61 mg, 500 μmol, 10 mol%), and *N*-hydroxyphthalimide (816 mg, 5.00 mmol, 1.0 equiv.) in DCM (50 mL, 0.1 M). The crude residue was purified by flash chromatography (silica gel) from pure hexane to a mixture of 6% of

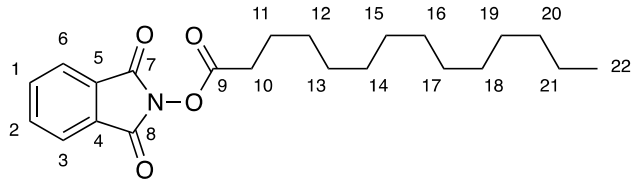
ethyl acetate in hexane affording 1.11 g of a white solid consistent with the desired product (71%).

^{1}H NMR (500 MHz, Chloroform-*d*) δ 7.91 – 7.85 (m, 2H, H^{3} and H^{6}), 7.81 – 7.76 (m, 2H, H^{1} and H^{2}), 2.66 (t, *J* = 7.49 Hz, 2H, H^{10}), 1.78 (p, *J* = 7.53 Hz, 2H, H^{11}), 1.49 – 1.39 (m, 2H, H^{12}), 1.38 – 1.24 (m, 6H, H^{13}, H^{14} and H^{15}), 0.89 (t, *J* = 6.66 Hz, 3H, H^{16}).

^{13}C NMR (126 MHz, Chloroform-*d*) δ 169.8 (C^{9}), 162.2 (C^{7} and C^{8}), 134.9 (C^{1} and C^{2}), 129.1 (C^{4} and C^{5}), 124.1 (C^{3} and C^{6}), 31.7 (C^{13} or C^{14} or C^{15}), 31.1 (C^{10}), 28.9 (C^{12}), 28.9 (C^{13} or C^{14} or C^{15}), 24.8 (C^{11}), 22.7 (C^{13} or C^{14} or C^{15}), 14.2 (C^{16}).

Data are consistent with the literature.[256]

1,3-Dioxoisoindolin-2-yl tetradecanoate, **3.21**



Prepared according to General Procedure 2A using tetradecanoic acid (114 mg, 500 μmol, 1.0 equiv.), *N*,*N*′-diisopropyl-carbodiimide (85 μL, 550 μmol, 1.1 equiv.), 4-dimethylaminopyridine (6 mg, 50.0 μmol, 10 mol%), and *N*-hydroxyphthalimide (89.7 mg, 550 μmol, 1.1 equiv.) in DCM (5 mL, 0.1 M). The crude residue was purified by flash chromatography (silica gel) from pure hexane to a mixture of 3% of ethyl acetate in hexane affording 160 mg of a white solid consistent with the desired product (86%).

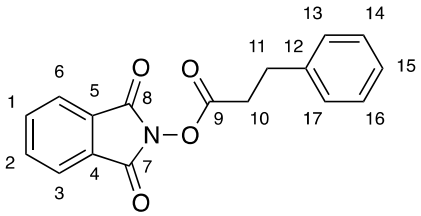
^{1}H NMR (500 MHz, Chloroform-*d*) δ 7.94 – 7.84 (m, 2H, H^{3} and H^{6}), 7.83 – 7.61 (m, 2H, H^{1} and H^{2}), 2.65 (t, *J* = 7.49 Hz, 2H, H^{10}), 1.77 (d, *J* = 7.54 Hz, 2H, H^{11}), 1.47 – 1.39 (m, 2H, H^{12}), 1.36 – 1.19 (m, 18H, H^{13} to H^{21}), 0.87 (t, *J* = 6.86 Hz, 3H, H^{22}).

^{13}C NMR (126 MHz, Chloroform-*d*) δ 169.8 (C^{9}), 162.1 (C^{7} and C^{8}), 134.8 (C^{1} and C^{2}), 129.0 (C^{4} and C^{5}), 124.0 (C^{3} and C^{6}), 32.0, 31.1 (C^{10}), 29.8 298, 29.7, 29.7, 29.5,

29.5, 29.2, 28.9 (C^{12}), 24.8 (C^{11}), 22.8, 14.2 (C^{22}). Alkyl carbons could not be unambiguously assigned.

Data are consistent with the literature.[227]

1,3-Dioxoisoindolin-2-yl 3-phenylpropanoate, **3.22**



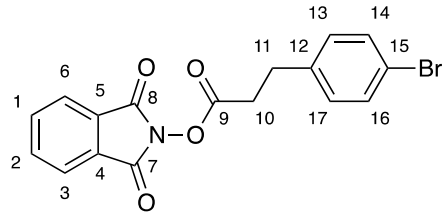
Prepared according to General Procedure 2A using phenylpropanoic acid (751 mg, 5.00 mmol, 1.0 equiv.), *N*,*N'*-diisopropyl-carbodiimide (850 μL, 5.50 mmol, 1.1 equiv.), 4-dimethylaminopyridine (61 mg, 500 μmol, 10 mol%), and *N*-hydroxyphthalimide (816 mg, 5.00 mmol, 1.0 equiv.) in DCM (50 mL, 0.1 M). The crude residue was purified by flash chromatography (silica gel) from pure hexane to a mixture of 10% of ethyl acetate in hexane affording 1.10 g of a white solid consistent with the desired product (75%).

^{1}H NMR (400 MHz, Chloroform-*d*) δ 7.93 – 7.86 (m, 2H, H^3 and H^6), 7.83 – 7.76 (m, 2H, H^1 and H^2), 7.37 – 7.31 (m, 2H, H^{14} and H^{16}), 7.29 – 7.21 (m, 3H, H^{13}, H^{15} and H^{17}), 3.14 – 3.07 (m, 2H, H^{11}), 3.02 – 2.96 (m, 2H, H^{10}).

^{13}C NMR (101 MHz, Chloroform-*d*) δ 169.0 (C^9), 162.0 (C^7 and C^8), 139.3 (C^{12}), 134.9 (C^1 and C^2), 129.0 (C^4 and C^5), 128.8 (C^{14} and C^{16}), 128.4 (C^{13} and C^{17}), 126.8 (C^{15}), 124.1 (C^3 and C^6), 32.8 (C^{10}), 30.7 (C^{11}).

Data are consistent with the literature.[258]

1,3-Dioxoisoindolin-2-yl 3-(4-bromophenyl)propanoate, **3.23**



Prepared according to General Procedure 2A using 3-(4-bromophenyl)propionic acid (916 mg, 4 mmol, 1.0 equiv.), *N,N'*-diisopropyl-carbodiimide (680 µL, 4.40 mmol, 1.1 equiv.), 4-dimethylaminopyridine (49 mg, 400 µmol, 10 mol%), and *N*-hydroxyphthalimide (718 mg, 4.40 mmol, 1.1 equiv.) in DCM (40 mL, 0.1 M). The crude residue was purified by flash chromatography (silica gel) from pure hexane to a mixture of 18% of ethyl acetate in acetate affording 217 mg of a white solid consistent with the desired product (14%).

^{1}H NMR (500 MHz, Chloroform-*d*) δ 7.95 – 7.88 (m, 2H, H^{3} and H^{6}), 7.85 – 7.78 (m, 2H, H^{1} and H^{2}), 7.52 – 7.43 (m, 2H, H^{14} and H^{16}), 7.24 – 7.13 (m, 2H, H^{13} and H^{17}), 3.11 – 3.05 (m, 2H, H^{11}), 3.02 – 2.96 (m, 2H, H^{10}).

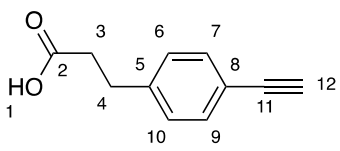
^{13}C NMR (126 MHz, Chloroform-*d*) δ 168.8 (C^{9}), 162.0 (C^{7} and C^{8}), 138.2 (C^{12}), 135.0 (C^{1} and C^{2}), 132.0 (C^{14} and C^{16}), 130.2 (C^{13} and C^{17}), 129.0 (C^{4} and C^{5}), 124.2 (C^{3} and C^{6}), 120.8 (C^{15}), 32.6 (C^{10}), 30.1 (C^{11}).

IR (solid): 1788, 1735, 1610, 1487, 1463, 1450, 1369, 1282, 1186, 1153, 1068, 962 cm^{-1}.

HRMS (ESI): *m/z* calculated for $[M + H]^{+}$ $(C_{17}H_{13}{}^{79}BrNO_4)^{+}$: 374.0022; found = 374.0015.

Data are consistent with the literature.[259]

3-(4-Ethynylphenyl)propanoic acid, **3.24-int1**



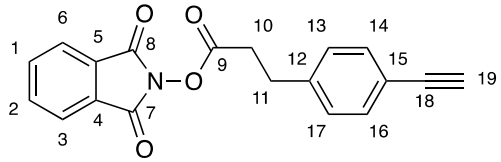
An oven-dried microwave vial was charged with dichlorobis(triphenylphosphine)palladium (14 mg, 20.0 μmol, 1 mol%), copper iodide (8 mg, 40.0 μmol, 2 mol%), and 3-(4-iodophenyl)propanoic acid (250 μL, 2.00 mmol,1 equiv.). The vial was then sealed and purged with vacuum-N_2 cycles (3 times) and backfilled with N_2. Triethylamine (4 mL, 0.5 M) was added followed by trimethylsilylacetylene (260 μL, 2.50 mmol, 1.25 equiv.). The reaction mixture was stirred overnight at room temperature. The crude mixture was partitioned between DCM (20 mL) and an aqueous solution of 1 M NaOH (20 mL). Organic layer was extracted with an aqueous solution of 1 M NaOH (2 × 10 mL). Aqueous layers were combined and acidified with an aqueous solution of 2 M HCl (until pH ~ 2). Organics were extracted with DCM (3 × 15 mL). Organic layers were combined, washed with brine (20 mL), dried over sodium sulfate, filtered, and concentrated *in vacuo* affording 334 mg of a white solid consistent with the desired product (96%).

^{1}H NMR (400 MHz, Chloroform-*d*) δ 7.46 – 7.40 (m, 2H, H^7 and H^9), 7.19 – 7.14 (m, 2H, H^6 and H^{10}), 3.05 (s, 1H, H^{12}), 2.96 (t, *J* = 7.68 Hz, 2H, H^4), 2.71 – 2.65 (m, 2H, H^3). H^1 is not observed.

^{13}C NMR (101 MHz, Chloroform-*d*) δ 178.7 (C^2), 141.2 (C^5), 132.5 (C^7 and C^9), 128.5 (C^6 and C^{10}), 120.3 (C^8), 83.6 (C^{11}), 77.1 (C^{12}), 35.3 (C^3), 30.5 (C^4).

Data are consistent with the literature.[260]

1,3-Dioxoisoindolin-2-yl 3-(4-ethynylphenyl)propanoate, **3.24**



Prepared according to General Procedure 2B using 3-(4-ethynylphenyl)propanoic acid **2.24-int1** (315 mg, 1.81 mmol, 1.0 equiv.), EDC hydrochloride (417 mg, 2.17 mmol, 1.2 equiv.), 4-dimethylaminopyridine (22 mg, 181 μmol, 10 mol%), and *N*-hydroxyphthalimide (295 mg, 1.81 mmol, 1.0 equiv.) in DCM (18 mL, 0.1M). The crude residue was purified by flash chromatography (silica gel) from pure hexane to a

mixture of 30% of diethyl ether in hexane affording 268 mg of a white solid consistent with the desired product (46%).

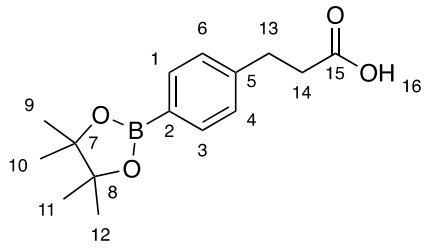
^{1}H NMR (500 MHz, Chloroform-*d*) δ 7.93 – 7.85 (m, 2H, H^{3} and H^{6}), 7.83 – 7.76 (m, 2H, H^{1} and H^{2}), 7.49 – 7.43 (m, 2H, H^{14} and H^{16}), 7.25 – 7.19 (m, 2H, H^{13} and H^{17}), 3.10 (t, *J* = 7.72 Hz, 2H, H^{11}), 3.06 (s, 1H, H^{19}), 3.01 – 2.96 (m, 2H, H^{10}).

^{13}C NMR (126 MHz, Chloroform-*d*) δ 168.8 (C^{9}), 162.0 (C^{7} and C^{8}), 140.1 (C^{12}), 135.0 (C^{1} and C^{2}), 132.6 (C^{14} and C^{16}), 129.0 (C^{4} and C^{5}), 128.5 (C^{13} and C^{17}), 124.2 (C^{3} and C^{6}), 120.7 (C^{15}), 83.6 (C^{18}), 77.2 (C^{19}), 32.5 (C^{10}), 30.5 (C^{11}).

IR (solid): 1845, 1816, 1789, 1739, 1465, 1400, 1371, 1282, 1186, 1138, 1070, 964 cm^{-1}.

HRMS (ESI): *m/z* calculated for $[M + H]^{+}$ $(C_{19}H_{14}NO_4)^{+}$: 320.0917; found = 320.0914.

3-(4-(4,4,5,5-Tetramethyl-1,3,2-dioxaborolan-2-yl)phenyl)propanoic acid, **3.25-int1**



In an oven-dried round bottom flask, charged with a Teflon-coated stir bar, 3-(4-bromophenyl)propionic acid (916 mg, 4.00 mmol, 1.0 equiv.), bis(pinacolato)diboron (1.52 g, 6.00 mmol, 1.5 equiv.), potassium acetate (1.18 g, 12.0 mmol, 3.0 equiv.), and 1,1'-bis(diphenylphosphino)ferrocenepalladium (II) chloride (146 mg, 200 μmol, 5 mol%) were weighed out. The flask was sealed and purged with vacuum-N_2 and backfilled with N_2. Dry and degassed 1,4-dioxane (25 mL, 0.16 M) was added and the reaction mixture was stirred at 90 °C overnight. Once completion was reached, the reaction mixture was concentrated *in vacuo*. The crude residue was partitioned between an aqueous solution of NaOH (2 M, 15 mL) and ethyl acetate (30 mL). Organics were extracted with an aqueous solution of NaOH (2 M, 15 mL). Aqueous layers were combined, acidified (pH ~ 4) with an aqueous solution of HCl (2 M). Organics were extracted with ethyl acetate (3 × 20 mL). Organic layers were

combined, washed with brine (30 mL), dried over sodium sulfate, filtered, and concentrated *in vacuo* affording 1.10 g of a brown solid consistent with the desired product (95%).

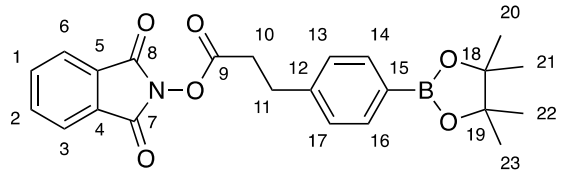
^{1}H NMR (500 MHz, Chloroform-*d*) δ 7.77 – 7.73 (m, 2H, H^{1} and H^{3}), 7.24 – 7.19 (m, 2H, H^{4} and H^{6}), 2.97 (t, *J* = 7.85 Hz, 2H, H^{13}), 2.67 (t, *J* = 7.86 Hz, 2H, H^{14}), 1.33 (s, 12H, H^{9}, H^{10}, H^{11} and H^{12}). H^{16} is not observed.

^{11}B NMR (96 MHz, Chloroform-*d*) δ 30.79.

^{13}C NMR (126 MHz, Chloroform-*d*) δ 178.5 (C^{15}), 143.8 (C^{5}), 135.2 (C^{1} and C^{3}), 127.9 (C^{4} and C^{6}), 83.9 (C^{7} and C^{8}), 35.7 (C^{14}), 31.0 (C^{13}), 25.0 (C^{9}, C^{10}, C^{11} and C^{12}). C^{2} is not observed due to quadrupolar relaxation.

Data are consistent with the literature.[261]

1,3-Dioxoisoindolin-2-yl 3-(4-(4,4,5,5-tetramethyl-1,3,2-dioxaborolan-2-yl)phenyl)propanoate, **3.25**



Prepared according to General Procedure 2B using 3-(4-(4,4,5,5-Tetramethyl-1,3,2-dioxaborolan-2-yl)phenyl)propanoic acid **3.25-int1** (500 mg, 1.81 mmol, 1.0 equiv.), EDC hydrochloride (417 mg, 2.17 mmol, 1.2 equiv.), 4-dimethylaminopyridine (22 mg, 181 μmol, 10 mol%), and *N*-hydroxyphthalimide (295 mg, 1.81 mmol, 1.0 equiv.) in DCM (18 mL, 0.1 M). The crude residue was purified by flash chromatography (silica gel) from pure hexane to a mixture of 40% of diethyl ether in hexane affording 178 mg of white solid consistent with the desired product (23%).

^{1}H NMR (500 MHz, Chloroform-*d*) δ 7.90 – 7.86 (m, 2H, H^{3} and H^{6}), 7.82 – 7.76 (m, 4H, H^{1}, H^{2}, H^{14} and H^{16}), 7.30 – 7.26 (m, 2H, H^{13} and H^{17}), 3.11 (t, *J* = 7.85 Hz, 2H, H^{11}), 3.01 – 2.96 (m, 2H, H^{10}), 1.34 (s, 12H, H^{20}, H^{21}, H^{22} and H^{23}).

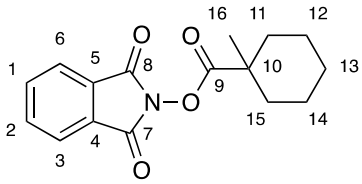
^{11}B NMR (96 MHz, Chloroform-*d*) δ 30.77.

^{13}C NMR (126 MHz, Chloroform-*d*) δ 168.9 (C^9), 162.0 (C^7 and C^8), 142.5 (C^{12}), 135.4 (C^{14} and C^{16}), 134.9 (C^1 and C^2), 129.0 (C^4 and C^5), 127.8 (C^{13} and C^{17}), 124.1 (C^3 and C^6), 83.9 (C^{18} and C^{19}), 32.6 (C^{10}), 30.8 (C^{11}), 25.0 (C^{20}, C^{21}, C^{22} and C^{23}). C^{15} is not observed due to quadrupolar relaxation.

IR (solid): 1822, 1786, 1737, 1610, 1471, 1446, 1371, 1354, 1267, 1190, 1139, 1080 cm^{-1}.

HRMS (ESI): *m/z* calculated for $[M + H]^+$ $(C_{23}H_{25}BNO_6)^+$: 422.1769; found = 422.1777.

1,3-Dioxoisoindolin-2-yl 1-methylcyclohexane-1-carboxylate, **3.26**



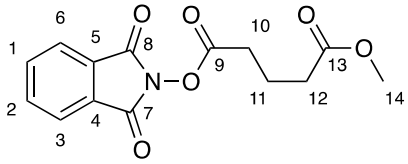
Prepared according to General Procedure 2B using 1-methyl-1-cyclohexanecarboxylic acid (284 mg, 2.00 mmol, 1.0 equiv.), EDC hydrochloride (460 mg, 2.40 mmol, 1.2 equiv.), 4-dimethylaminopyridine (24 mg, 200 μmol, 10 mol%), and *N*-hydroxyphthalimide (326 mg, 2.00 mmol, 1.0 equiv.) in DCM (20 mL, 0.1 M). The crude residue was purified by flash chromatography (silica gel) from pure hexane to a mixture of 4% of ethyl acetate in hexane affording 350 mg of a colourless oil consistent with the desired product (61%).

^{1}H NMR (500 MHz, Chloroform-*d*) δ 7.90 – 7.85 (m, 2H, H^3 and H^6), 7.80 – 7.76 (m, 2H, H^1 and H^2), 2.27 – 2.20 (m, 2H, H^{11} and H^{15}), 1.71 – 1.61 (m, 3H, H^{12}, H^{13} and H^{14}), 1.61 – 1.52 (m, 2H, H^{12} and H^{14}), 1.43 (s, 3H, H^{16}), 1.41 – 1.34 (m, 2H, H^{11} and H^{15}), 1.33 – 1.25 (m, 1H, H^{13}).

^{13}C NMR (126 MHz, Chloroform-*d*) δ 173.8 (C^9), 162.4 (C^7 and C^8), 134.8 (C^1 and C^2), 129.2 (C^4 and C^5), 124.0 (C^3 and C^6), 43.3 (C^{10}), 35.8 (C^{11} and C^{15}), 26.9 (C^{16}), 25.6 (C^{13}), 23.2 (C^{12} and C^{14}).

Data are consistent with the literature.[262]

1,3-Dioxoisoindolin-2-yl methyl glutarate, **3.27**



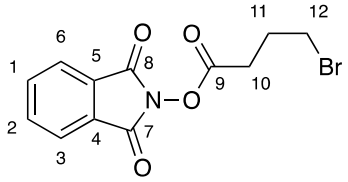
Prepared according to General Procedure 2B using mono-methyl glutarate (250 μL, 2.00 mmol, 1.0 equiv.), EDC hydrochloride (460 mg, 2.40 mmol, 1.2 equiv.), 4-dimethylaminopyridine (24 mg, 200 μmol, 10 mol%), and *N*-hydroxyphthalimide (326 mg, 2.00 mmol, 1.0 equiv.) in DCM (20 mL, 0.1 M). The crude residue was purified by flash chromatography (silica gel) from pure hexane to a mixture of 40% of diethyl ether in hexane affording 467 mg of a white solid consistent with the desired product (80%).

^{1}H NMR (500 MHz, Chloroform-*d*) δ 7.91 – 7.85 (m, 2H, H^{3} and H^{6}), 7.83 – 7.76 (m, 2H, H^{1} and H^{2}), 3.69 (s, 3H, H^{14}), 2.76 (t, *J* = 7.29 Hz, 2H, H^{10}), 2.50 (t, *J* = 7.28 Hz, 2H, H^{12}), 2.10 (p, *J* = 7.31 Hz, 2H, H^{11}).

^{13}C NMR (126 MHz, Chloroform-*d*) δ 173.1 (C^{12}), 169.1 (C^{9}), 162.0 (C^{7} and C^{8}), 134.9 (C^{1} and C^{2}), 129.0 (C^{4} and C^{5}), 124.1 (C^{3} and C^{6}), 51.9 (C^{14}), 32.6 (C^{12}), 30.2 (C^{10}), 19.9 (C^{11}).

Data are consistent with the literature.[263]

1,3-Dioxoisoindolin-2-yl 4-bromobutanoate, **3.28**



Prepared according to General Procedure 2A using 4-bromobutyric acid (835 mg, 5.00 mmol, 1.0 equiv.), *N*,*N*′-diisopropyl-carbodiimide (850 μL, 5.50 mmol, 1.1 equiv.), 4-dimethylaminopyridine (61 mg, 500 μmol, 10 mol%), and *N*-hydroxyphthalimide (816 mg, 5.00 mmol, 1.0 equiv.) in DCM (50 mL, 0.1 M). The crude residue was purified by flash chromatography (silica gel) from pure hexane to a mixture of 9% of

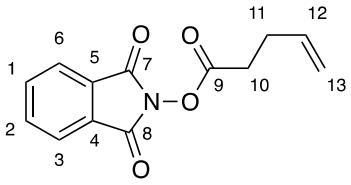
ethyl acetate in hexane affording 865 mg of a white solid consistent with the desired product (55%).

^{1}H NMR (500 MHz, Chloroform-*d*) δ 7.89 – 7.82 (m, 2H, H^{3} and H^{6}), 7.80 – 7.73 (m, 2H, H^{1} and H^{2}), 3.52 (t, *J* = 6.37 Hz, 2H, H^{12}), 2.86 (t, *J* = 7.22 Hz, 2H, H^{10}), 2.30 (p, *J* = 6.79 Hz, 2H, H^{11}).

^{13}C NMR (126 MHz, Chloroform-*d*) δ 168.8 (C^{9}), 161.9 (C^{7} and C^{8}), 134.9 (C^{1} and C^{2}), 128.8 (C^{4} and C^{5}), 124.1 (C^{3} and C^{6}), 31.8 (C^{12}), 29.5 (C^{10}), 27.5 (C^{11}).

Data are consistent with the literature.[255]

1,3-Dioxoisoindolin-2-yl pent-4-enoate, **3.29**



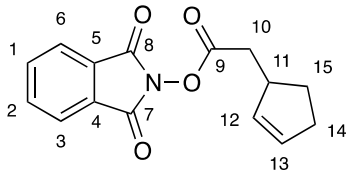
Prepared according to General Procedure 2A using 4-pentenoic acid (410 μL, 4.00 mmol, 1.0 equiv.), *N,N'*-diisopropyl-carbodiimide (680 μL, 4.40 mmol, 1.1 equiv.), 4-dimethylaminopyridine (49 mg, 400 μmol, 10 mol%), and *N*-hydroxyphthalimide (653 mg, 4.00 mmol, 1.0 equiv.) in DCM (40 mL, 0.1 M). The crude residue was purified by flash chromatography (silica gel) from pure hexane to a mixture of 5% of ethyl acetate in hexane affording 610 mg of a colourless oil consistent with the desired product (62%).

^{1}H NMR (500 MHz, Chloroform-*d*) δ 7.91 – 7.86 (m, 2H, H^{3} and H^{6}), 7.81 – 7.75 (m, 2H, H^{1} and H^{2}), 5.88 (ddt, *J* = 16.80, 10.18, 6.44 Hz, 1H, H^{12}), 5.16 (dd, *J* = 17.12, 1.62 Hz, 1H, H^{13}), 5.10 (dd, *J* = 10.25, 1.52 Hz, 1H, H^{13}), 2.78 (t, *J* = 7.45 Hz, 2H, H^{10}), 2.53 (q, *J* = 7.15 Hz, 2H, H^{11}).

^{13}C NMR (126 MHz, Chloroform-*d*) δ 169.1 (C^{9}), 162.1 (C^{7} and C^{8}), 135.3 (C^{12}), 134.9 (C^{1} and C^{2}), 129.0 (C^{4} and C^{5}), 124.1 (C^{3} and C^{6}), 116.8 (C^{13}), 30.5 (C^{10}), 28.6 (C^{11}).

Data are consistent with the literature.[264]

1,3-Dioxoisoindolin-2-yl 2-(cyclopent-2-en-1-yl)acetate, **3.30**



Prepared according to General Procedure 2A using 2-cyclopentene-1-acetic acid (631 mg, 5.00 mmol, 1.0 equiv.), *N*,*N*'-diisopropyl-carbodiimide (850 μL, 5.50 mmol, 1.1 equiv.), 4-dimethylaminopyridine (61 mg, 500 μmol, 10 mol%), and *N*-hydroxyphthalimide (816 mg, 5.00 mmol, 1.0 equiv.) in DCM (50 mL, 0.1 M). The crude residue was purified by flash chromatography (silica gel) from pure hexane to a mixture of 7% of ethyl acetate in hexane affording 550 mg of a beige solid consistent with the desired product (41%).

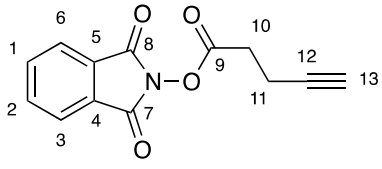
^{1}H NMR (500 MHz, Chloroform-*d*) δ 7.92 – 7.85 (m, 2H, H^3 and H^6), 7.83 – 7.76 (m, 2H, H^1 and H^2), 5.88 – 5.82 (m, 1H, H^{13}), 5.80 – 5.74 (m, 1H, H^{12}), 3.28 – 3.18 (m, 1H, H^{11}), 2.71 (d, *J* = 7.02 Hz, 1H, H^{10}), 2.66 (d, *J* = 7.95 Hz, 1H, H^{10}), 2.50 – 2.38 (m, 1H, H^{14}), 2.41 – 2.29 (m, 1H, H^{14}), 2.29 – 2.19 (m, 1H, H^{15}), 1.65 – 1.54 (m, 1H, H^{15}).

^{13}C NMR (126 MHz, Chloroform-*d*) δ 168.9 (C^9), 162.1 (C^7 and C^8), 134.9 (C^1 and C^2), 132.7 (C^{12}), 132.7 (C^{13}), 129.0 (C^4 and C^5), 124.1 (C^3 and C^6), 42.1 (C^{11}), 37.1 (C^{10}), 32.0 (C^{14}), 29.6 (C^{15}).

IR (film): 1813, 1786, 1738, 1468, 1361, 1186, 1082, 972, 878, 694 cm^{-1}.

HRMS (ESI): *m/z* calculated for $[M + H]^+$ $(C_{15}H_{14}NO_4)^+$: 272.0917; found 272.0915.

1,3-Dioxoisoindolin-2-yl pent-4-ynoate, **3.31**



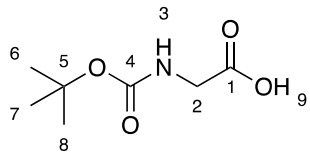
Prepared according to General Procedure 2A using 4-pentynoic acid (491 mg, 5.00 mmol, 1.0 equiv.), *N,N'*-diisopropyl-carbodiimide (850 μL, 5.50 mmol, 1.1 equiv.), 4-dimethylaminopyridine (61 mg, 500 μmol, 10 mol%), and *N*-hydroxyphthalimide (816 mg, 5.00 mmol, 1.0 equiv.) in DCM (50 mL, 0.1 M). The crude residue was purified by flash chromatography (silica gel) from pure hexane to a mixture of 12% of ethyl acetate in hexane affording 571 mg of a white solid consistent with the desired product (47%).

^{1}H NMR (400 MHz, Chloroform-*d*) δ 7.93 – 7.84 (m, 2H, H^{3} and H^{6}), 7.84 – 7.75 (m, 2H, H^{1} and H^{2}), 2.94 (t, *J* = 7.84, 2H, H^{10}), 2.65 (td, *J* = 7.57, 2.68 Hz, 2H, H^{11}), 2.07 (t, *J* = 2.67 Hz, 1H, H^{13}).

^{13}C NMR (176 MHz, Chloroform-*d*) δ 168.1 (C^{9}), 161.9 (C^{7} and C^{8}), 135.0 (C^{1} and C^{2}), 129.0 (C^{4} and C^{5}), 124.2 (C^{3} and C^{6}), 81.0 (C^{12}), 70.2 (C^{13}), 30.5 (C^{10}), 14.3 (C^{11}).

Data are consistent with the literature.[265]

(*tert*-Butoxycarbonyl)glycine, **3.32-int1**



Glycine (601 mg, 8.00 mmol, 1.0 equiv.) and di-*tert*-butyl dicarbonate (2.10 g, 9.60 mmol, 1.2 equiv.) were dissolved in THF (40 mL, 0.2 M), and cooled down to 0 °C. Sodium hydroxide (320 mg, 8.00 mmol, 1.0 equiv.) was dissolved in water (10 mL) and then added dropwise to the reaction mixture at 0 °C. The reaction mixture was slowly warmed up to room temperature and stirred overnight. The volatiles were evaporated under vacuum and the resulting suspension was dissolved in water (40 mL). Organics were extracted with diethyl ether (30 mL). The aqueous layer was acidified with a solution of 1 M of HCl (pH ~ 2). Organics were extracted with diethyl ether (3 × 30 mL), dried over sodium sulfate, filtered, and concentrated *in vacuo* affording 1.40 g of a white solid consistent with the desired product as a mixture of rotamers (99%, 0.6:0.4).

Major rotamer

^{1}H NMR (500 MHz, Chloroform-*d*) δ 9.88 (s, 1H, H^{9}), 5.13 (s, 1H, H^{3}), 3.96 (d, *J* = 5.64 Hz, 2H, H^{2}), 1.45 (s, 9H, H^{6}, H^{7} and H^{8}).

^{13}C NMR (126 MHz, Chloroform-*d*) δ 175.0 (C^{1}), 156.1 (C^{4}), 80.6 (C^{5}), 42.4 (C^{2}), 28.4 (C^{6}, C^{7} and C^{8}).

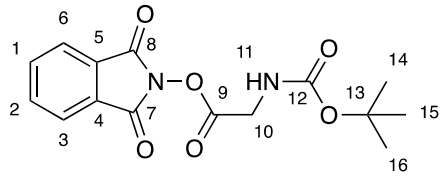
Minor rotamer

^{1}H NMR (500 MHz, Chloroform-*d*) δ 9.88 (s, 1H, H^{9}), 6.83 (s, 1H, H^{3}), 3.89 (d, *J* = 4.91 Hz, 2H, H^{2}), 1.45 (s, 9H, H^{6}, H^{7} and H^{8}).

^{13}C NMR (126 MHz, Chloroform-*d*) δ 174.1(C^{1}), 157.4 (C^{4}), 81.9 (C^{5}), 43.5 (C^{2}), 28.4 (C^{6}, C^{7} and C^{8}).

Data are consistent with the literature.[266]

1,3-Dioxoisoindolin-2-yl (*tert*-butoxycarbonyl)glycinate, **3.32**



Prepared according to General Procedure 2B using (*tert*-butoxycarbonyl)glycine **3.32-int1** (350 mg, 2.00 mmol, 1.0 equiv.), EDC hydrochloride (460 mg, 2.40 mmol, 1.2 equiv.), 4-dimethylaminopyridine (24 mg, 200 μmol, 10 mol%), and *N*-hydroxyphthalimide (326 mg, 2.00 mmol, 1.0 equiv.) in DCM (20 mL, 0.1 M). The crude residue was dissolved with the minimum amount of DCM and hexane was added to precipitate the product, 245 mg of a white solid was recovered after filtration consistent with the desired product as a mixture of rotamers (38%, 0.76:0.24).

Major rotamer

^{1}H NMR (500 MHz, Chloroform-*d*) δ 7.92 – 7.87 (m, 2H, H^{3} and H^{6}), 7.82 – 7.78 (m, 2H, H^{1} and H^{2}), 5.08 (t, *J* = 6.08 Hz, 1H, H^{11}), 4.25 – 4.19 (m, 2H, H^{10}), 1.46 (s, 9H, H^{14}, H^{15} and H^{16}).

^{13}C NMR (126 MHz, Chloroform-*d*) δ 167.3 (C^9), 161.6 (C^7 and C^8), 155.4 (C^{12}), 135.0 (C^1 and C^2), 128.9 (C^4 and C^5), 124.2 (C^3 and C^6), 80.8 (C^{13}), 40.5 (C^{10}), 28.4 (C^{14}, C^{15} and C^{16}).

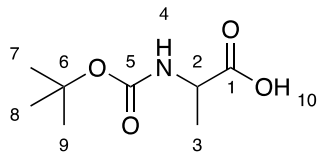
Minor rotamer

^{1}H NMR (500 MHz, Chloroform-*d*) δ 7.92 – 7.87 (m, 2H, H^3 and H^6), 7.82 – 7.78 (m, 2H, H^1 and H^2), 5.20 (s, 1H, H^{11}), 4.36 (d, *J* = 5.94 Hz, 2H, H^{10}), 1.50 (s, 9H, H^{14}, H^{15} and H^{16}).

^{13}C NMR (126 MHz, Chloroform-*d*) δ 167.1 (C^9), 161.6 (C^7 and C^8), 155.2 (C^{12}), 134.3 (C^1 and C^2), 129.3 (C^4 and C^5), 123.5 (C^3 and C^6), 82.0 (C^{13}), 41.9 (C^{10}), 28.1 (C^{14}, C^{15} and C^{16}).

Data are consistent with the literature.[227]

(*tert*-Butoxycarbonyl)alanine, **3.33-int1**



DL-Alanine (713 mg, 8.00 mmol, 1.0 equiv.) and di-*tert*-butyl dicarbonate (2.10 g, 9.60 mmol, 1.2 equiv.) were dissolved in THF (40 mL, 0.2 M), and cooled down to 0 °C. Sodium hydroxide (320 mg, 8.00 mmol, 1.0 equiv.) was dissolved in water (10 mL) and then added dropwise to the reaction mixture at 0 °C. The reaction mixture was slowly warmed up to room temperature and stirred overnight. Volatiles were evaporated under vacuum and the resulting suspension was dissolved in water (40 mL). Organics were extracted with diethyl ether (30 mL). The aqueous layer was acidified with a solution of 1 M of HCl (pH ~ 2). Organics were extracted with diethyl ether (3 × 30 mL), dried over sodium sulfate, filtered, and concentrated *in vacuo* affording 1.50 g of a white solid consistent with the desired product as a mixture of rotamers (99%, 0.62:0.38).

Major rotamer

^{1}H NMR (500 MHz, Chloroform-*d*) δ 10.03 (s, 1H, H^{10}), 5.13 (broad s, 1H, H^{4}), 4.41 – 4.27 (m, 1H, H^{2}), 1.44 (s, 9H, H^{7}, H^{8} and H^{9}), 1.42 (d, *J* = 7.22 Hz, 3H, H^{3}).

^{13}C NMR (126 MHz, Chloroform-*d*) δ 178.1 (C^{1}), 155.6 (C^{5}), 80.4 (C^{6}), 49.2 (C^{2}), 28.4 (C^{7}, C^{8} and C^{9}), 18.5 (C^{3}).

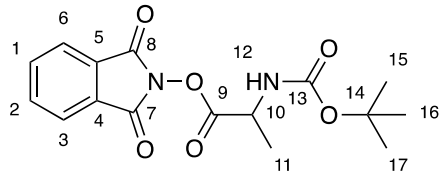
Minor rotamer

^{1}H NMR (500 MHz, Chloroform-*d*) δ 10.03 (s, 1H, H^{10}), 6.67 (broad s, 1H, H^{4}), 4.21 – 4.10 (m, 1H, H^{2}), 1.44 (s, 9H, H^{7}, H^{8} and H^{9}), 1.42 (d, *J* = 7.22 Hz, 3H, H^{3}).

^{13}C NMR (126 MHz, Chloroform-*d*) δ 177.5 (C^{1}), 156.9 (C^{5}), 81.7 (C^{6}), 50.3 (C^{2}), 28.4 (C^{7}, C^{8} and C^{9}), 18.5 (C^{3}).

Data are consistent with the literature.[267]

1,3-Dioxoisoindolin-2-yl (*tert*-butoxycarbonyl)alaninate, **3.33**



Prepared according to General Procedure 2B using (*tert*-butoxycarbonyl)alanine **3.33-int1** (378 mg, 2.00 mmol, 1.0 equiv.), EDC hydrochloride (460 mg, 2.40 mmol, 1.2 equiv.), 4-dimethylaminopyridine (24 mg, 200 μmol, 10 mol%), and *N*-hydroxyphthalimide (326 mg, 2.00 mmol, 1.0 equiv.) in DCM (20 mL, 0.1 M). The crude residue was dissolved with the minimum amount of DCM and hexane was added to precipitate the product, 188 mg of a white solid was recovered after filtration consistent with the desired product as a mixture of rotamers (28%, 0.75:0.25).

Major rotamer

^{1}H NMR (500 MHz, Chloroform-*d*) δ 7.91 – 7.86 (m, 2H, H^{3} and H^{6}), 7.82 – 7.77 (m, 2H, H^{1} and H^{2}), 5.07 (d, *J* = 6.45 Hz, 1H, H^{12}), 4.76 (p, *J* = 7.64 Hz, 1H, H^{10}), 1.62 (d, *J* = 7.24 Hz, 3H, H^{11}), 1.46 (s, 9H, H^{15}, H^{16} and H^{17}).

^{13}C NMR (126 MHz, Chloroform-*d*) δ 170.1 (C^9), 161.7 (C^7 and C^8), 154.8 (C^{13}), 135.0 (C^1 and C^2), 129.0 (C^4 and C^5), 124.2 (C^3 and C^6), 80.7 (C^{14}), 47.8 (C^{10}), 28.4 (C^{15}, C^{16} and C^{17}), 19.0 (C^{11}).

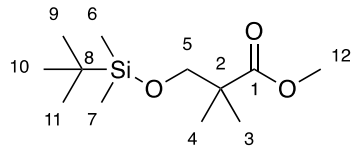
Minor rotamer

^{1}H NMR (500 MHz, Chloroform-*d*) δ 7.91 – 7.86 (m, 2H, H^3 and H^6), 7.82 – 7.77 (m, 2H, H^1 and H^2), 4.82 (broad s, 1H, H^{12}), 4.51 (broad s, 1H, H^{10}), 1.62 (d, *J* = 7.24 Hz, 3H, H^{11}), 1.46 (s, 9H, H^{15}, H^{16} and H^{17}).

^{13}C NMR (126 MHz, Chloroform-*d*) δ 170.1 (C^9), 161.7 (C^7 and C^8), 154.8 (C^{13}), 135.0 (C^1 and C^2), 129.0 (C^4 and C^5), 124.2 (C^3 and C^6), 80.7 (C^{14}), 49.2 (C^{10}), 28.2 (C^{15}, C^{16} and C^{17}), 18.2 (C^{11}).

Data are consistent with the literature.[268]

Methyl 3-((*tert*-butyldimethylsilyl)oxy)-2,2-dimethylpropanoate, **3.34-int1**



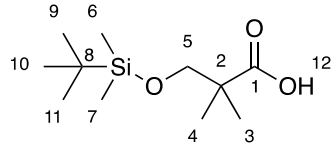
Imidazole (374 mg, 5.50 mmol, 1.1 equiv.) and *tert*-butyldimethylchlorosilane (829 mg, 5.50 mmol, 1.1 equiv.) were dissolved in DMF (20 mL, 0.25 M). Methyl 2,2-dimethyl-3-hydroxypropionate (640 μL, 5.00 mmol, 1.0 equiv.) was then added and the reaction mixture was left to stir overnight. Once completion was reached, the reaction mixture was portioned between brine (50 mL) and ethyl acetate (50 mL). The aqueous layer was extracted with ethyl acetate (2 × 30 mL). Organic layers were combined and washed with brine (50 mL), dried over sodium sulfate, filtered, and concentrated *in vacuo*. The crude residue was purified by flash chromatography (silica gel) from pure hexane to a mixture of 2% of diethyl ether in hexane affording 740 mg of a colourless oil consistent with the desired product (60%).

^{1}H NMR (500 MHz, Chloroform-*d*) δ 3.65 (s, 3H, H^{12}), 3.56 (s, 2H, H^5), 1.14 (s, 6H, H^3 and H^4), 0.86 (s, 9H, H^9, H^{10} and H^{11}), 0.01 (s, 6H, H^6 and H^7).

^{13}C NMR (126 MHz, Chloroform-*d*) δ 177.4 (C^{1}), 70.2 (C^{5}), 51.8 (C^{12}), 45.0 (C^{2}), 25.9 (C^{9}, C^{10} and C^{11}), 22.0 (C^{3} and C^{4}), 18.3 (C^{8}), –5.5 (C^{6} and C^{7}).

Data are consistent with the literature.[269]

3-((*tert*-Butyldimethylsilyl)oxy)-2,2-dimethylpropanoic acid, **3.34-int2**



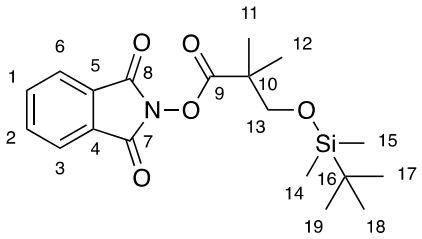
Methyl 3-((*tert*-butyldimethylsilyl)oxy)-2,2-dimethylpropanoate **3.34-int1** (739 mg, 3.00 mmol, 1.0 equiv.) was dissolved in a mixture of THF:H_2O:MeOH (2:2:1, 20 mL, 0.15 M) and cooled down to 0 °C. Lithium hydroxide (216 mg, 9.00 mmol, 3.0 equiv.) was added and the reaction mixture was slowly warmed up to room temperature, and left to stir for 48 hours. The reaction mixture was partitioned between ethyl acetate (30 mL) and water (30 mL). Aqueous layer was acidified with a 1M solution of HCl (pH ~ 2). Organics were extracted with ethyl acetate (3 × 30 mL), combined, dried over sodium sulfate, filtered, and concentrated *in vacuo* affording 535 mg of a colourless oil consistent with the desired product (77%).

^{1}H NMR (500 MHz, Chloroform-*d*) δ 3.59 (s, 2H, H^{5}), 1.18 (s, 6H, H^{3} and H^{4}), 0.89 (s, 9H, H^{9}, H^{10} and H^{11}), 0.07 (s, 6H, H^{6} and H^{7}). H^{12} is not observed.

^{13}C NMR (126 MHz, Chloroform-*d*) δ 181.4 (C^{1}), 69.8 (C^{5}), 44.3 (C^{2}), 25.9 (C^{9}, C^{10} and C^{11}), 22.0 (C^{3} and C^{4}), 18.3 (C^{8}), –5.5 (C^{6} and C^{7}).

Data are consistent with the literature.[269]

1,3-Dioxoisoindolin-2-yl 3-((*tert*-butyldimethylsilyl)oxy)-2,2-dimethylpropanoate, **3.34**



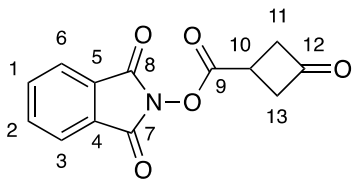
Prepared according to General Procedure 2B using 3-((*tert*-butyldimethylsilyl)oxy)-2,2-dimethylpropanoic acid **3.34-int2** (697 mg, 3.00 mmol, 1.0 equiv.), EDC hydrochloride (690 mg, 3.60 mmol, 1.2 equiv.), 4-dimethylaminopyridine (37 mg, 300 μmol, 10 mol%), and *N*-hydroxyphthalimide (489 mg, 3.00 mmol, 1.0 equiv.) in DCM (30 mL, 0.1 M). The crude residue was purified by flash chromatography (silica gel) from pure hexane to a mixture of 5% of diethyl ether in hexane affording 262 mg of a colourless oil consistent with the desired product (23%).

^{1}H NMR (500 MHz, Chloroform-*d*) δ 7.91 – 7.86 (m, 2H, H^{3} and H^{6}), 7.80 – 7.75 (m, 2H, H^{1} and H^{2}), 3.75 (s, 2H, H^{13}), 1.39 (s, 6H, H^{11} and H^{12}), 0.92 (s, 9H, H^{17}, H^{18} and H^{19}), 0.09 (s, 6H, H^{14} and H^{15}).

^{13}C NMR (126 MHz, Chloroform-*d*) δ 172.9 (C^{9}), 162.1 (C^{7} and C^{8}), 134.7 (C^{1} and C^{2}), 129.2 (C^{4} and C^{5}), 124.0 (C^{3} and C^{6}), 69.3 (C^{13}), 45.0 (C^{10}), 25.9 (C^{17}, C^{18} and C^{19}), 22.0 (C^{11} and C^{12}), 18.4 (C^{16}), –5.5 (C^{14} and C^{15}).

Data are consistent with the literature.[270]

1,3-Dioxoisoindolin-2-yl 3-oxocyclobutane-1-carboxylate, **3.35**



Prepared according to General Procedure 2A using 3-oxocyclobutanecarboxylic acid (456 mg, 4.00 mmol, 1.0 equiv.), *N*,*N*′-diisopropyl-carbodiimide (680 μL, 4.40 mmol, 1.1 equiv.), 4-dimethylaminopyridine (49 mg, 400 μmol, 10 mol%), and *N*-

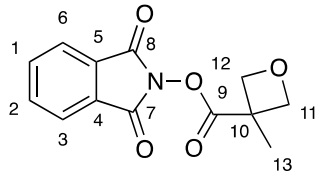
hydroxyphthalimide (653 mg, 4.00 mmol, 1.0 equiv.) in DCM (40 mL, 0.1 M). The crude residue was purified by flash chromatography (silica gel) from pure hexane to a mixture of 18% of ethyl acetate in hexane affording 221 mg of a pale yellow solid consistent with the desired product (21%). It contained some impurities; the compound was used without further purification.

^{1}H NMR (500 MHz, Chloroform-*d*) δ 7.95 – 7.86 (m, 2H, H^{3} and H^{6}), 7.85 – 7.78 (m, 2H, H^{1} and H^{2}), 3.72 – 3.46 (m, 5H, H^{10}, H^{11} and H^{13}).

^{13}C NMR (126 MHz, Chloroform-*d*) δ 201.4 (C^{12}), 170.8 (C^{9}), 161.9 (C^{7} and C^{8}), 135.1 (C^{1} and C^{2}), 129.0 (C^{4} and C^{5}), 124.3 (C^{3} and C^{6}), 52.4 (C^{11} and C^{13}), 25.2 (C^{10}).

Data are consistent with the literature.[271]

1,3-Dioxoisoindolin-2-yl 3-methyloxetane-3-carboxylate, **3.36**



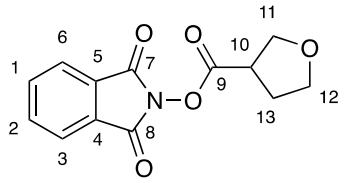
Prepared according to General Procedure 2A using 3-methyloxetane-3-carboxylic acid (232 mg, 2.00 mmol, 1.0 equiv.), *N*,*N'*-diisopropyl-carbodiimide (340 μL, 2.20 mmol, 1.1 equiv.), 4-dimethylaminopyridine (24 mg, 200 μmol, 10 mol%), and *N*-hydroxyphthalimide (326 mg, 2.00 mmol, 1.0 equiv.) in DCM (20 mL, 0.1 M). The crude residue was purified by flash chromatography (silica gel) from pure hexane to a mixture of 25% of ethyl acetate in hexane affording 215 mg of a white solid consistent with the desired product (41%).

^{1}H NMR (500 MHz, Chloroform-*d*) δ 7.91 – 7.86 (m, 2H, H^{3} and H^{6}), 7.82 – 7.77 (m, 2H, H^{1} and H^{2}), 5.16 (d, *J* = 6.25 Hz, 2H, H^{11} and H^{12}), 4.55 (d, *J* = 6.26 Hz, 2H, H^{11} and H^{12}), 1.83 (s, 3H, H^{13}).

^{13}C NMR (126 MHz, Chloroform-*d*) δ 170.6 (C^{9}), 161.9 (C^{7} and C^{8}), 135.0 (C^{1} and C^{2}), 129.0 (C^{4} and C^{5}), 124.2 (C^{3} and C^{6}), 79.1 (C^{11} and C^{12}), 43.4 (C^{10}), 21.5 (C^{13}).

Data are consistent with the literature.[270]

1,3-Dioxoisoindolin-2-yl tetrahydrofuran-3-carboxylate, **3.37**



Prepared according to General Procedure 2B using tetrahydro-3-furoic acid (380 μL, 4.00 mmol, 1.0 equiv.), EDC hydrochloride (920 mg, 4.80 mmol, 1.2 equiv.), 4-dimethylaminopyridine (49 mg, 400 μmol, 10 mol%), and *N*-hydroxyphthalimide (653 mg, 4.00 mmol, 1.0 equiv.) in DCM (40 mL, 0.1 M). The crude residue was purified by flash chromatography (silica gel) from pure hexane to a mixture of 25% of ethyl acetate in hexane affording 612 mg of a white solid consistent with the desired product (59%).

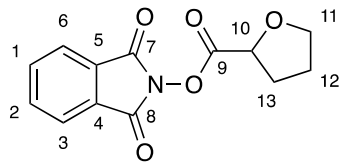
^{1}H NMR (500 MHz, Chloroform-*d*) δ 7.91 – 7.87 (m, 2H, H^3 and H^6), 7.82 – 7.77 (m, 2H, H^1 and H^2), 4.17 – 4.10 (m, 2H, H^{11}), 3.99 – 3.86 (m, 2H, H^{12}), 3.43 – 3.48 (m, 1H, H^{10}), 2.43 – 2.29 (m, 2H, H^{13}).

^{13}C NMR (126 MHz, Chloroform-*d*) δ 170.5 (C^9), 161.9 (C^7 and C^8), 135.0 (C^1 and C^2), 129.0 (C^4 and C^5), 124.1 (C^3 and C^6), 70.1 (C^{11}), 68.4 (C^{12}), 41.0 (C^{10}), 30.0 (C^{13}).

IR (solid): 1805, 1782, 1735, 1649, 1463, 1288, 1186, 1172, 1138, 1062, 970 cm^{-1}.

HRMS (ESI): *m/z* calculated for $[M + H]^+$ $(C_{13}H_{12}NO_5)^+$: 262.0710, found 262.0715.

1,3-Dioxoisoindolin-2-yl tetrahydrofuran-2-carboxylate, **3.38**



Prepared according to General Procedure 2B using tetrahydro-2-furoic acid (380 μL, 4.00 mmol, 1.0 equiv.), EDC hydrochloride (920 mg, 4.80 mmol, 1.2 equiv.), 4-dimethylaminopyridine (49 mg, 400 μmol, 10 mol%), and *N*-hydroxyphthalimide (653 mg, 4.00 mmol, 1.0 equiv.) in DCM (40 mL, 0.1 M). The crude residue was purified by flash chromatography (silica gel) from pure hexane to a mixture of 20% of

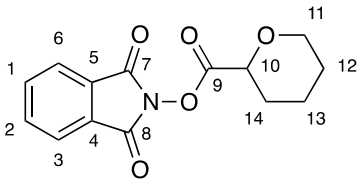
ethyl acetate in hexane affording 563 mg of a white solid consistent with the desired product (69%).

^{1}H NMR (500 MHz, Chloroform-*d*) δ 7.92 – 7.84 (m, 2H, H^{3} and H^{6}), 7.83 – 7.75 (m, 2H, H^{1} and H^{2}), 4.86 (dd, *J* = 8.55, 4.94 Hz, 1H, H^{10}), 4.12 – 4.06 (m, 1H, H^{11}), 4.02 – 3.98 (m, 1H, H^{11}), 2.50 – 2.33 (m, 2H, H^{13}), 2.15 – 1.97 (m, 2H, H^{12}).

^{13}C NMR (126 MHz, Chloroform-*d*) δ 169.9 (C^{9}), 161.8 (C^{7} and C^{8}), 134.9 (C^{1} and C^{2}), 129.0 (C^{4} and C^{5}), 124.1 (C^{3} and C^{6}), 75.1 (C^{10}), 70.0 (C^{11}), 31.0 (C^{13}), 25.2 (C^{12}).

Data are consistent with the literature.[227]

1,3-Dioxoisoindolin-2-yl tetrahydro-2*H*-pyran-2-carboxylate, **3.39**



Prepared according to General Procedure 2B using tetrahydro-2*H*-pyran-2-carboxylic acid (430 μL, 4.00 mmol, 1.0 equiv.), EDC hydrochloride (920 mg, 4.80 mmol, 1.2 equiv.), 4-dimethylaminopyridine (49 mg, 400 μmol, 10 mol%), and *N*-hydroxyphthalimide (653 mg, 4.00 mmol, 1.0 equiv.) in DCM (40 mL, 0.1 M). The crude residue was purified by flash chromatography (silica gel) from pure hexane to a mixture of 20% of ethyl acetate in hexane affording 456 mg of a white solid consistent with the desired product (41%).

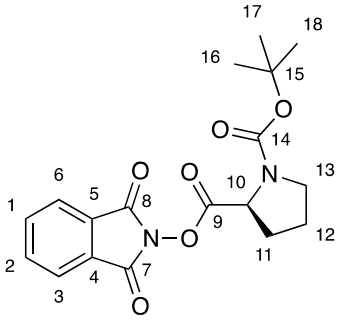
^{1}H NMR (400 MHz, Chloroform-*d*) δ 7.91 – 7.85 (m, 2H, H^{3} and H^{6}), 7.81 – 7.76 (m, 2H, H^{1} and H^{2}), 4.48 (dd, *J* = 9.49, 3.22 Hz, 1H, H^{10}), 4.13 (dt, *J* = 11.73, 3.75 Hz, 1H, H^{11}), 3.65 – 3.56 (m, 1H, H^{11}), 2.18 – 2.08 (m, 1H, H^{14}), 1.99 – 1.88 (m, 2H, H^{13} and H^{14}), 1.76 – 1.63 (m, 2H, H^{12} and H^{13}), 1.63 – 1.58 (m, 1H, H^{12}).

^{13}C NMR (101 MHz, Chloroform-*d*) δ 168.1 (C^{9}), 161.7 (C^{7} and C^{8}), 134.9 (C^{1} and C^{2}), 129.0 (C^{4} and C^{5}), 124.1 (C^{3} and C^{6}), 74.3 (C^{10}), 68.1 (C^{11}), 29.0 (C^{14}), 25.2 (C^{12}), 22.4 (C^{13}).

IR (solid): 1816, 1786, 1734, 1463, 1355, 1213, 1138, 1120, 1093, 1082, 1006, 968 cm^{-1}.

HRMS (ESI): *m/z* calculated for $[M + H]^+$ $(C_{14}H_{14}NO_5)^+$: 276.0866, found 276.0867.

1-(*tert*-Butyl) 2-(1,3-dioxoisoindolin-2-yl) (*S*)-pyrrolidine-1,2-dicarboxylate, **3.40**



Prepared according to General Procedure 2A using *N*-(*tert*-butoxycarbonyl)-L-proline (1.08 g, 5.00 mmol, 1.0 equiv.), *N*,*N*′-diisopropyl-carbodiimide (850 μL, 5.50 mmol, 1.1 equiv.), 4-dimethylaminopyridine (61 mg, 500 μmol, 10 mol%), and *N*-hydroxyphthalimide (816 mg, 5.00 mmol, 1.0 equiv.) in DCM (50 mL, 0.1 M). The crude residue was purified by flash chromatography (silica gel) from pure hexane to a mixture of 20% of ethyl acetate in hexane affording 1.32 g of a white solid consistent with the desired product as a mixture of rotamers (73%, 0.82:018).

Major rotamer

^{1}H NMR (500 MHz, Chloroform-*d*) δ 7.91 – 7.84 (m, 2H, H^3 and H^6), 7.82 – 7.73 (m, 2H, H^1 and H^2), 4.60 (dd, *J* = 8.83, 3.70 Hz, 1H, H^{10}), 3.62 (ddd, *J* = 10.42, 7.86, 4.46 Hz, 1H, H^{13}), 3.48 (dt, *J* = 10.47, 7.48 Hz, 1H, H^{13}), 2.48 – 2.31 (m, 2H, H^{11}), 2.13 – 1.92 (m, 2H, H^{12}), 1.51 (s, 9H, H^{16}, H^{17} and H^{18}).

^{13}C NMR (126 MHz, Chloroform-*d*) δ 169.8 (C^9), 161.8 (C^7 and C^8), 153.6 (C^{14}), 134.9 (C^1 and C^2), 129.0 (C^4 and C^5), 124.1 (C^3 and C^6), 81.2 (C^{15}), 57.3 (C^{10}), 46.4 (C^{13}), 31.5 (C^{11}), 28.2 (C^{16}, C^{17} and C^{18}), 23.7 (C^{12}).

Minor rotamer

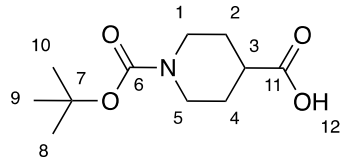
^{1}H NMR (500 MHz, Chloroform-*d*) δ 7.91 – 7.84 (m, 2H, H^3 and H^6), 7.82 – 7.73 (m, 2H, H^1 and H^2), 4.70 (dd, *J* = 7.49, 4.72 Hz, 1H, H^{10}), 3.55 (ddd, *J* = 11.64, 7.89, 4.25

Hz, 1H, H^{13}), 3.42 (dt, *J* = 10.30, 7.55 Hz, 1H, H^{13}), 2.48 – 2.31 (m, 2H, H^{11}), 2.13 – 1.92 (m, 2H, H^{12}), 1.47 (s, 9H, H^{16}, H^{17} and H^{18}).

^{13}C NMR (126 MHz, Chloroform-*d*) δ 169.5 (C^{9}), 161.7 (C^{7} and C^{8}), 154.2 (C^{14}), 134.8 (C^{1} and C^{2}), 129.1 (C^{4} and C^{5}), 124.1 (C^{3} and C^{6}), 80.5 (C^{15}), 57.2 (C^{10}), 46.6 (C^{13}), 30.4 (C^{11}), 28.5 (C^{16}, C^{17} and C^{18}), 24.5 (C^{12}).

Data consistent with the literature.[227]

1-(*tert*-Butoxycarbonyl)piperidine-4-carboxylic acid, **3.41-int1**



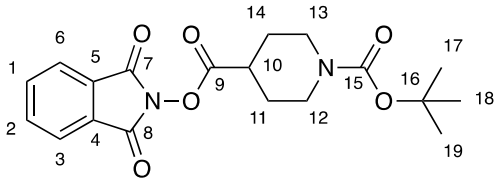
Isonipecotic acid (1.03 g, 8.00 mmol, 1.0 equiv.) was dissolved in 1,4-dioxane (30 mL) and cooled down to 0 °C. 8 mL of a solution of 1 M of sodium hydroxide (1.0 equiv.) were then slowly added. Di-*tert*-butyl dicarbonate (2.10 g, 9.60 mmol, 1.2 equiv.) was dissolved in 1,4-dioxane (10 mL) and was added dropwise at 0 °C. The reaction mixture was slowly warmed up to room temperature and stirred overnight. Volatiles were evaporated under vacuum and the resulting suspension was dissolved in water (40 mL). Organics were extracted with ethyl acetate (2 × 20 mL). The aqueous layer was acidified with a solution of 1 M of HCl (pH ~ 2). The precipitated white solid was filtered, washed with cold water (2 × 20 mL), and dried under vacuum overnight affording 1.51 g of a white solid consistent with the desired product (82%).

^{1}H NMR (500 MHz, Chloroform-*d*) δ 4.02 (broad s, 2H, H^{1} and H^{5}), 2.85 (broad t, *J* = 11.95 Hz, 2H, H^{1} and H^{5}), 2.48 (tt, *J* = 10.96, 3.90 Hz, 1H, H^{3}), 1.90 (broad d, *J* = 13.15 Hz, 2H, H^{2} and H^{4}), 1.74 – 1.51 (m, 2H, H^{2} and H^{4}), 1.45 (s, 9H, H^{8}, H^{9} and H^{10}). H^{12} is not observed.

^{13}C NMR (126 MHz, Chloroform-*d*) δ 180.4 (C^{11}), 154.9 (C^{6}), 79.9 (C^{7}), 43.1 (C^{1} and C^{5}), 40.9 (C^{3}), 28.6 (C^{8}, C^{9} and C^{10}), 27.9 (C^{2} and C^{4}).

Data are consistent with the literature.[272]

1-(*tert*-Butyl) 4-(1,3-dioxoisoindolin-2-yl) piperidine-1,4-dicarboxylate, **3.41**



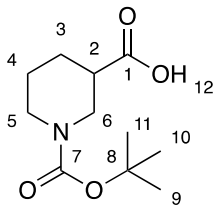
Prepared according to General Procedure 2A using 1-(*tert*-butoxycarbonyl)piperidine-4-carboxylic acid **3.41-int1** (917 mg, 4.00 mmol, 1.0 equiv.), *N*,*N'*-diisopropylcarbodiimide (680 μL, 4.40 mmol, 1.1 equiv.), 4-dimethylaminopyridine (49 mg, 400 μmol, 10 mol%), and *N*-hydroxyphthalimide (653 mg, 4.00 mmol, 1.0 equiv.) in DCM (40 mL, 0.1 M). The crude residue was purified by flash chromatography (silica gel) from pure hexane to a mixture of 25% of ethyl acetate in hexane affording 1.14 g of a beige solid consistent with the desired product (76%).

^{1}H NMR (500 MHz, Chloroform-*d*) δ 7.87 – 7.90 (m, 2H, H^{3} and H^{6}), 7.82 – 7.76 (m, 2H, H^{1} and H^{2}), 4.10 – 3.95 (m, 2H, H^{12} and H^{13}), 3.05 – 2.96 (m, 2H, H^{12} and H^{13}), 2.91 (tt, *J* = 10.40, 3.97 Hz, 1H, H^{10}), 2.10 – 2.02 (m, 2H, H^{11} and H^{14}), 1.89 – 1.79 (m, 2H, H^{11} and H^{14}), 1.46 (s, 9H, H^{17}, H^{18} and H^{19}).

^{13}C NMR (126 MHz, Chloroform-*d*) δ 170.8 (C^{9}), 162.1 (C^{7} and C^{8}), 154.7 (C^{15}), 134.9 (C^{1} and C^{2}), 129.0 (C^{4} and C^{5}), 124.1 (C^{3} and C^{6}), 80.0 (C^{16}), 42.7 (broad, C^{12} and C^{13}), 38.7 (C^{10}), 28.5 (C^{17}, C^{18} and C^{19}), 27.9 (C^{11} and C^{14}).

Data are consistent with the literature.[253]

1-(*tert*-Butoxycarbonyl)piperidine-3-carboxylic acid, **3.42-int1**



3-Piperidinecarboxylic acid (1.03 g, 8.00 mmol, 1.0 equiv.) and di-*tert*-butyl dicarbonate (2.10 g, 9.60 mmol, 1.2 equiv.) were dissolved in THF (40 mL, 0.2 M) and cooled down to 0 °C. Sodium hydroxide (320 mg, 8.00 mmol, 1.0 equiv.) was dissolved in water (10 mL) and then added dropwise to the reaction mixture at 0 °C.

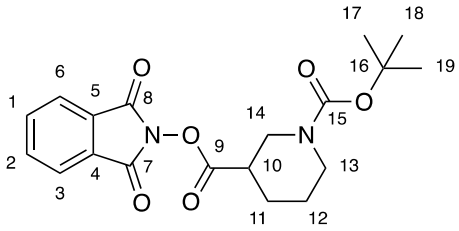
The reaction mixture was slowly warmed up to room temperature and stirred overnight. Volatiles were evaporated under vacuum and the resulting suspension was dissolved in water (40 mL). Organics were extracted with ethyl acetate (2 × 30 mL). The aqueous layer was acidified with a solution of 1 M of HCl (pH ~ 2). Organics were extracted with ethyl acetate (3 × 30 mL), dried over sodium sulfate, filtered, and concentrated *in vacuo* affording 1.84 g of a white solid consistent with the desired product (100%).

^{1}H NMR (500 MHz, Chloroform-*d*) δ 11.13 (broad s, 1H, H^{12}), 4.31 – 3.94 (m, 1H, H^{6}), 3.94 – 3.81 (broad s, 1H, H^{5}), 3.21 – 2.92 (broad s, 1H, H^{6}), 2.89 – 2.78 (m, 1H, H^{5}), 2.54 – 2.40 (m, 1H, H^{2}), 2.12 – 2.00 (m, 1H, H^{3}), 1.75 – 1.67 (m, 1H, H^{4}), 1.66 – 1.57 (m, 1H, H^{3}), 1.52 – 1.46 (m, 1H, H^{4}), 1.45 (s, 9H, H^{9}, H^{10} and H^{11}).

^{13}C NMR (126 MHz, Chloroform-*d*) δ 179.3 (C^{1}), 154.9 (C^{7}), 80.1 (C^{8}), 45.7 (C^{6}), 43.7 (C^{5}), 41.2 (C^{2}), 28.5 (C^{9}, C^{10} and C^{11}), 27.3 (C^{3}), 24.2 (C^{4}).

Data are consistent with the literature.[273]

1-(*tert*-Butyl) 3-(1,3-dioxoisoindolin-2-yl) piperidine-1,3-dicarboxylate, **3.42**



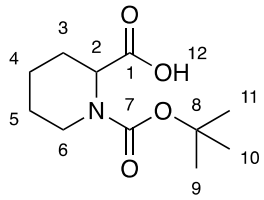
Prepared according to General Procedure 2A using 1-(*tert*-butoxycarbonyl)piperidine-3-carboxylic acid **3.42-int1** (459 mg, 2.00 mmol, 1.0 equiv.), *N*,*N'*-diisopropylcarbodiimide (340 μL, 2.20 mmol, 1.1 equiv.), 4-dimethylaminopyridine (24 mg, 200 μmol, 10 mol%), and *N*-hydroxyphthalimide (326 mg, 2.00 mmol, 1.0 equiv.) in DCM (20 mL, 0.1 M). The crude residue was purified by flash chromatography (silica gel) from pure hexane to a mixture of 20% of ethyl acetate in hexane affording 515 mg of a white solid consistent with the desired product (69%).

^{1}H NMR (500 MHz, Chloroform-*d*) δ 7.92 – 7.83 (m, 2H, H^{3} and H^{6}), 7.83 – 7.66 (m, 2H, H^{1} and H^{2}), 4.30 (m, 1H, H^{14}), 3.95 (d, *J* = 13.27 Hz, 1H, H^{13}), 3.17 (broad s, 1H, H^{14}), 2.96 – 2.79 (m, 2H, H^{10} and H^{13}), 2.36 – 2.21 (m, 1H, H^{11}), 1.87 – 1.74 (m, 2H, H^{11} and H^{12}), 1.60 – 1.50 (m, 1H, H^{12}), 1.46 (s, 9H, H^{17}, H^{18} and H^{19}).

^{13}C NMR (126 MHz, Chloroform-*d*) δ 169.6 (C^{9}), 161.9 (C^{7} and C^{8}), 154.6 (C^{15}), 134.9 (C^{1} and C^{2}), 129.0 (C^{4} and C^{5}), 124.1 (C^{3} and C^{6}), 80.2 (C^{16}), 45.4 (C^{14}), 43.4 (C^{13}), 39.2 (C^{10}), 28.5 (C^{17}, C^{18} and C^{19}), 27.6 (C^{11}), 24.1 (C^{12}).

Data are consistent with the literature.[263]

1-(*tert*-Butoxycarbonyl)piperidine-2-carboxylic acid, **3.43-int1**



Piperidine-2-carboxylic acid (1.03 g, 8.00 mmol, 1.0 equiv.) and di-*tert*-butyl dicarbonate (2.10 g, 9.60 mmol, 1.2 equiv.) were dissolved in THF (40 mL, 0.2 M), and cooled down to 0 °C. Sodium hydroxide (320 mg, 8.00 mmol, 1.0 equiv.) was dissolved in water (10 mL) and then added dropwise to the reaction mixture at 0 °C. The reaction mixture was slowly warmed up to room temperature and stirred overnight. Volatiles were evaporated under vacuum and the resulting suspension was dissolved in water (40 mL). Organics were extracted with ethyl acetate (2 × 20 mL). The aqueous layer was acidified with a solution of 1 M of HCl (pH ~ 2). Organics were extracted with ethyl acetate (3 × 30 mL), dried over sodium sulfate, filtered, and concentrated *in vacuo* affording 1.54 g of a white solid as the desired product as a mixture of rotamers (84%, 0.55:0.45).

Major rotamer

^{1}H NMR (500 MHz, Chloroform-*d*) δ 11.28 (broad s, 1H, H^{12}), 5.01 – 4.88 (m, 1H, H^{2}), 3.97 – 3.85 (m, 1H, H^{6}), 3.05 – 2.93 (m, 1 H, H^{6}), 2.29 – 2.15 (m, 1H, H^{3}), 1.74 – 1.64 (m, 2H, H^{3} and H^{4}), 1.63 – 1.57 (m, 1H, H^{5}), 1.46 (s, 9H, H^{9}, H^{10} and H^{11}), 1.42 – 1.37 (m, 1H, H^{5}), 1.35 – 1.24 (m, 1H, H^{4}).

^{13}C NMR (126 MHz, Chloroform-*d*) δ 178.2 (C^1), 156.3 (C^7), 80.4 (C^8), 53.7 (C^2), 42.2 (C^6), 28.5 (C^9, C^{10} and C^{11}), 26.7 (C^3), 24.9 (C^5), 20.9 (C^4).

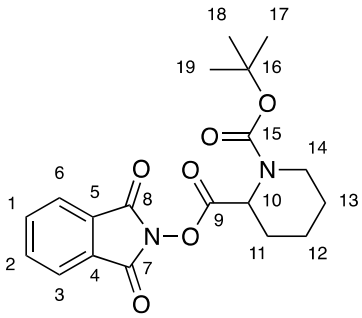
Minor rotamer

^{1}H NMR (500 MHz, Chloroform-*d*) δ 11.28 (broad s, 1H, H^{12}), 4.81 – 4.69 (m, 1H, H^2), 4.07 – 3.98 (m, 1H, H^6), 2.93 – 2.82 (m, 1H, H^6), 2.29 – 2.15 (m, 1H, H^3), 1.74 – 1.64 (m, 2H, H^3 and H^4), 1.63 – 1.57 (m, 1H, H^5), 1.43 (s, 9H, H^9, H^{10} and H^{11}), 1.42 – 1.37 (m, 1H, H^5), 1.35 – 1.24 (m, 1H, H^4).

^{13}C NMR (126 MHz, Chloroform-*d*) δ 178.4 (C^1), 155.6 (C^7), 80.4 (C^8), 54.8 (C^2), 41.2 (C^6), 28.4 (C^9, C^{10} and C^{11}), 26.7 (C^3), 24.6 (C^5), 20.8 (C^4).

Data are consistent with the literature.[274]

1-(*tert*-Butyl) 2-(1,3-dioxoisoindolin-2-yl) piperidine-1,2-dicarboxylate, **3.43**



Prepared according to General Procedure 2A using 1-(*tert*-butoxycarbonyl)piperidine-2-carboxylic acid, **3.43-int1** (459 mg, 2.00 mmol, 1.0 equiv.), *N*,*N'*-diisopropylcarbodiimide (340 μL, 2.20 mmol, 1.1 equiv.), 4-dimethylaminopyridine (24 mg, 200 μmol, 10 mol%), and *N*-hydroxyphthalimide (326 mg, 2.00 mmol, 1.0 equiv.) in DCM (20 mL, 0.1 M). The crude residue was purified by flash chromatography (silica gel) from pure hexane to a mixture of 11% of ethyl acetate in hexane affording 639 mg of a white solid consistent with the desired product as a mixture of rotamers (85%, 0.68:0.32).

Major rotamer

^{1}H NMR (500 MHz, Chloroform-*d*) δ 7.91 – 7.85 (m, 2H, H^{3} and H^{6}), 7.83 – 7.76 (m, 2H, H^{1} and H^{2}), 5.13 (app. d, *J* = 6.13 Hz, 1H) 4.10 – 4.03 (m, 1H, H^{10}), 3.15 – 2.96 (m, 1H, H^{14}), 2.46 – 2.29 (m, 1H, H^{11}), 1.92 – 1.72 (m, 3H, H^{11}, H^{12} and H^{13}), 1.56 – 1.40 (m, 11H, H^{12}, H^{13}, H^{17}, H^{18} and H^{19}).

^{13}C NMR (126 MHz, Chloroform-*d*) δ 168.9 (C^{9}), 161.9 (C^{7} and C^{8}), 155.3 (C^{15}), 134.9 (C^{1} and C^{2}), 129.1 (C^{4} and C^{5}), 124.1 (C^{3} and C^{6}), 81.2 (C^{16}), 53.7 (C^{10}), 41.3 (C^{14}), 28.2 (C^{17}, C^{18} and C^{19}), 27.3 (C^{11}), 24.5 (C^{13}), 20.4 (C^{12}).

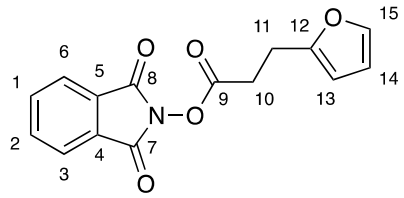
Minor rotamer

^{1}H NMR (500 MHz, Chloroform-*d*) δ 7.91 – 7.85 (m, 2H, H^{3} and H^{6}), 7.83 – 7.76 (m, 2H, H^{1} and H^{2}), 5.38 (broad s, 1H, H^{10}), 4.03 – 3.90 (m, 1H, H^{14}), 3.15 – 2.96 (m, 1H, H^{14}), 2.46 – 2.29 (m, 1H, H^{11}), 1.92 – 1.72 (m, 3H, H^{11}, H^{12} and H^{13}), 1.56 – 1.40 (m, 11H, H^{12}, H^{13}, H^{17}, H^{18} and H^{19}).

^{13}C NMR (126 MHz, Chloroform-*d*) δ 168.7 (C^{9}), 161.9 (C^{7} and C^{8}), 155.5 (C^{15}), 134.9 (C^{1} and C^{2}), 129.1 (C^{4} and C^{5}), 124.1 (C^{3} and C^{6}), 80.7 (C^{16}), 52.7 (C^{10}), 42.3 (C^{14}), 28.4 (C^{17}, C^{18} and C^{19}), 27.3 (C^{11}), 24.9 (C^{13}), 20.7 (C^{12}).

Data are consistent with the literature.[275]

1,3-Dioxoisoindolin-2-yl 3-(furan-2-yl)propanoate, **3.44**



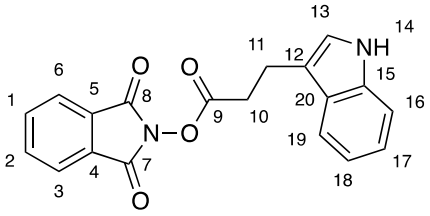
Prepared according to General Procedure 2B using 3-(2-furyl)propionic acid (280 mg, 2.00 mmol, 1.0 equiv.), EDC hydrochloride (460 mg, 2.40 mmol, 1.2 equiv.), 4-dimethylaminopyridine (24 mg, 200 μmol, 10 mol%), and *N*-hydroxyphthalimide (653 mg, 4.00 mmol, 1.0 equiv.) in DCM (40 mL, 0.1 M). The crude residue was dissolved with the minimum amount of DCM and hexane was added to precipitate the product, 410 mg of a white solid was recovered after filtration consistent with the desired product (72%).

^{1}H NMR (500 MHz, Chloroform-*d*) δ 7.92 – 7.83 (m, 2H, H^{3} and H^{6}), 7.83 – 7.74 (m, 2H, H^{1} and H^{2}), 7.34 (dd, *J* = 1.91, 0.87 Hz, 1H, H^{15}), 6.31 (dd, *J* = 3.20, 1.89 Hz, 1H, H^{14}), 6.13 (dd, *J* = 3.16, 0.97 Hz, 1H, H^{13}), 3.11 (t, *J* = 7.95, 7.06 Hz, 2H, H^{11}), 3.05 – 2.98 (m, 2H, H^{10}).

^{13}C NMR (126 MHz, Chloroform-*d*) δ 168.7 (C^{9}), 162.0 (C^{7} and C^{8}), 152.7 (C^{12}), 141.7 (C^{15}), 134.9 (C^{1} and C^{2}), 129.0 (C^{4} and C^{5}), 124.1 (C^{3} and C^{6}), 110.5 (C^{14}), 106.2 (C^{13}), 29.8 (C^{10}), 23.2 (C^{11}).

Data are consistent with the literature.[276]

1,3-Dioxoisoindolin-2-yl 3-(1*H*-indol-3-yl)propanoate, **3.45**



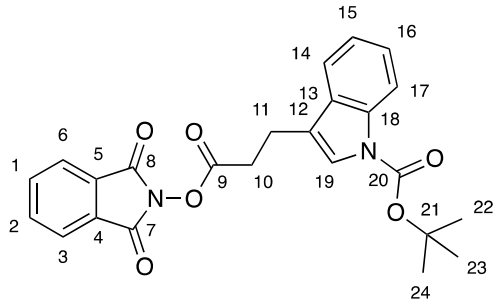
Prepared according to General Procedure 2B using 3-indolepropionic acid (378 mg, 2.00 mmol, 1.0 equiv.), EDC hydrochloride (460 mg, 2.40 mmol, 1.2 equiv.), 4-dimethylaminopyridine (24 mg, 200 μmol, 10 mol%), and *N*-hydroxyphthalimide (653 mg, 4.00 mmol, 1.0 equiv.) in DCM (40 mL, 0.1 M). The crude residue was dissolved with the minimum amount of DCM and hexane was added to precipitate the product, 538 mg of a yellow solid was recovered after filtration consistent with the desired product (77%).

^{1}H NMR (500 MHz, Chloroform-*d*) δ 8.06 (s, 1H, H^{14}), 7.92 – 7.83 (m, 2H, H^{3} and H^{6}), 7.82 – 7.76 (m, 2H, H^{1} and H^{2}), 7.62 (d, *J* = 7.86 Hz, 1H, H^{19}), 7.38 (d, *J* = 8.06 Hz, 1H, H^{16}), 7.24 – 7.19 (m, 1H, H^{17}), 7.18 – 7.11 (m, 2H, H^{13} and H^{18}), 3.26 (t, *J* = 7.55 Hz, 2H, H^{11}), 3.07 (t, *J* = 7.55 Hz, 2H, H^{10}).

^{13}C NMR (126 MHz, Chloroform-*d*) δ 169.4 (C^{9}), 162.1 (C^{7} and C^{8}), 136.4 (C^{15}), 134.9 (C^{1} and C^{2}), 129.0 (C^{4} and C^{5}), 127.1 (C^{20}), 124.1 (C^{3} and C^{6}), 122.3 (C^{17}), 122.1 (C^{13}), 119.6 (C^{18}), 118.6 (C^{19}), 113.8 (C^{12}), 111.4 (C^{16}), 32.0 (C^{10}), 20.5 (C^{11}).

Data are consistent with the literature.[277]

tert-Butyl 3-(3-((1,3-dioxoisoindolin-2-yl)oxy)-3-oxopropyl)-1*H*-indole-1-carboxylate, **3.46**



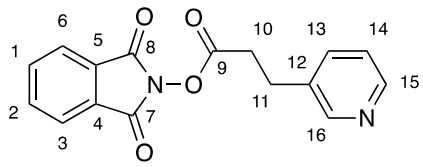
In a round bottom flask, 1,3-dioxoisoindolin-2-yl 3-(1*H*-indol-3-yl)propanoate **3.45** (267 mg, 800 μmol, 1.0 equiv.), di-*tert*-butyl dicarbonate (175 mg, 800 μmol, 1.0 equiv.), and 4-dimethylaminopyridine (5 mg, 40.0 μmol, 5 mol%) were dissolved in THF (8 mL, 0.1M). The reaction mixture was stirred overnight at room temperature. Once completion was reached, the mixture was partitioned between a solution of 1 M of HCl (10 mL) and diethyl ether (20 mL). Aqueous layer was extracted with diethyl ether (2 × 20 mL). Organic layers were combined, dried over sodium sulfate, filtered, and concentrated *in vacuo*. The crude residue was dissolved with the minimum amount of DCM and hexane was added to precipitate the product, 256 mg of a yellow solid was recovered after filtration consistent with the desired product (74%).

^{1}H NMR (500 MHz, Chloroform-*d*) δ 8.23 – 8.10 (m, 1H, H^{17}), 7.92 – 7.86 (m, 2H, H^{3} and H^{6}), 7.83 – 7.76 (m, 2H, H^{1} and H^{2}), 7.55 (ap. d, *J* = 7.74 Hz, 1H, H^{14}), 7.50 (broad s, 1H, H^{19}), 7.37 – 7.32 (m, 1H, H^{16}), 7.30 – 7.24 (m, 1H, H^{15}), 3.22 – 3.17 (m, 2H, H^{11}), 3.11 – 3.06 (m, 2H, H^{10}), 1.68 (s, 9H, H^{22}, H^{23} and H^{24}).

^{13}C NMR (126 MHz, Chloroform-*d*) δ 169.1 (C^{9}), 162.0 (C^{7} and C^{8}), 149.8 (C^{20}), 135.7 (C^{18}), 134.9 (C^{1} and C^{2}), 130.0 (C^{13}), 129.0 (C^{4} and C^{5}), 124.7 (C^{16}), 124.1 (C^{3} and C^{6}), 123.2 (C^{19}), 122.7 (C^{15}), 118.7 (C^{14}), 118.2 (C^{12}), 115.5 (C^{17}), 83.7 (C^{21}), 31.1 (C^{10}), 28.3 (C^{22}, C^{23} and C^{24}), 20.2 (C^{11}).

Data are consistent with the literature.[278]

1,3-Dioxoisoindolin-2-yl 3-(pyridin-3-yl)propanoate, **3.47**



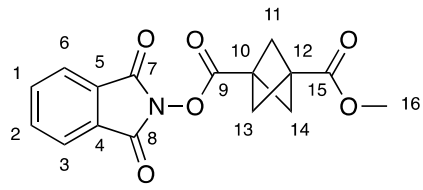
Prepared according to General Procedure 2B using 3-pyridinepropionic acid (302 mg, 2.00 mmol, 1.0 equiv.), EDC hydrochloride (460 mg, 2.40 mmol, 1.2 equiv.), 4-dimethylaminopyridine (24 mg, 200 μmol, 10 mol%), and *N*-hydroxyphthalimide (326 mg, 2.00 mmol, 1.0 equiv.) in DCM (20 mL, 0.1 M). The crude residue was purified by flash chromatography (silica gel) from pure hexane to a mixture of 50% of ethyl acetate in hexane affording 115 mg of white solid consistent with the desired product (19 %).

^{1}H NMR (500 MHz, Chloroform-*d*) δ 8.54 (s, 1H, H^{16}), 8.50 (d, *J* = 4.74 Hz, 1H, H^{15}), 7.89 – 7.84 (m, 2H, H^{3} and H^{6}), 7.80 – 7.74 (m, 2H, H^{1} and H^{2}), 7.60 (dt, *J* = 7.79, 1.97 Hz, 1H, H^{13}), 7.29 – 7.23 (m, 1H, H^{14}), 3.10 (t, *J* = 7.56 Hz, 2H, H^{11}), 2.99 (t, *J* = 7.41 Hz, 2H, H^{10}).

^{13}C NMR (126 MHz, Chloroform-*d*) δ 168.6 (C^{9}), 161.9 (C^{7} and C^{8}), 149.8 (C^{16}), 148.2 (C^{15}), 136.1 (C^{13}), 134.9 (C^{1} and C^{2}), 134.7 (C^{12}), 128.9 (C^{4} and C^{5}), 124.1 (C^{3} and C^{6}), 123.7 (C^{14}), 32.4 (C^{10}), 27.8 (C^{11}).

Data are consistent with the literature.[279]

1-(1,3-Dioxoisoindolin-2-yl) 3-methyl bicyclo[1.1.1]pentane-1,3-dicarboxylate, **3.48**



Prepared according to General Procedure 2B using 3-(methoxycarbonyl)bicyclo[1.1.1]pentane-1-carboxylic acid (510 mg, 3.00 mmol, 1.0 equiv.), EDC hydrochloride (690 mg, 3.60 mmol, 1.2 equiv.) 4-dimethylaminopyridine (37 mg, 300 μmol, 10 mol%), and *N*-hydroxyphthalimide (489 mg, 3.00 mmol, 1.0 equiv.) in DCM (30 mL, 0.1 M). The crude residue was

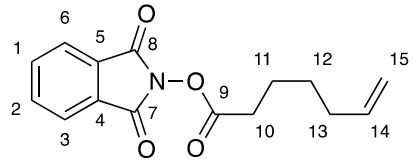
dissolved with the minimum amount of DCM and hexane was added to precipitate the product, 658 mg of a white solid was recovered after filtration consistent with the desired product (70%).

^{1}H NMR (500 MHz, Chloroform-*d*) δ 7.91 – 7.86 (m, 2H, H^{3} and H^{6}), 7.82 – 7.77 (m, 2H, H^{1} and H^{2}), 3.72 (s, 3H, H^{16}), 2.55 (s, 6H, H^{11}, H^{13} and H^{14}).

^{13}C NMR (126 MHz, Chloroform-*d*) δ 169.0 (C^{15}), 164.8 (C^{9}), 161.8 (C^{7} and C^{8}), 135.0 (C^{1} and C^{2}), 129.0 (C^{4} and C^{5}), 124.2 (C^{3} and C^{6}), 53.7 (C^{11}, C^{13} and C^{14}), 52.2 (C^{16}), 38.7 (C^{10} or C^{12}), 35.5 (C^{10} or C^{12}).

Data are consistent with the literature.[280]

1,3-Dioxoisoindolin-2-yl hept-6-enoate, **3.49**



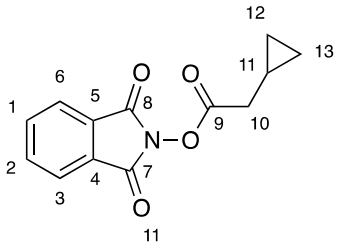
Prepared according to General Procedure 2A using 6-heptenoic acid (270 μL, 2.00 mmol, 1.0 equiv.), *N*,*N*′-diisopropyl-carbodiimide (340 μL, 2.20 mmol, 1.1 equiv.), 4-dimethylaminopyridine (24 mg, 200 μmol, 10 mol%), and *N*-hydroxyphthalimide (326 mg, 2.00 mmol, 1.0 equiv.) in DCM (20 mL, 0.1 M). The crude residue was purified by flash chromatography (silica gel) from pure hexane to a mixture of 4% of ethyl acetate in hexane affording 406 mg of a colourless oils consistent with the desired product (99%).

^{1}H NMR (500 MHz, Chloroform-*d*) δ 7.90 – 7.84 (m, 2H, H^{3} and H^{6}), 7.81 – 7.73 (m, 2H, H^{1} and H^{2}), 5.80 (ddt, *J* = 16.89, 10.11, 6.64 Hz, 1H, H^{14}), 5.03 (dd, *J* = 17.15, 1.81 Hz, 1H, H^{15}), 4.97 (dd, *J* = 10.22, 1.69 Hz, 1H, H^{15}), 2.66 (t, *J* = 7.41 Hz, 2H, H^{10}), 2.11 (app. q, *J* = 7.13 Hz, 2H, H^{13}), 1.79 (p, *J* = 7.48 Hz, 2H, H^{11}), 1.54 (p, *J* = 7.50 Hz, 2H, H^{12}).

^{13}C NMR (126 MHz, Chloroform-*d*) δ 169.6 (C^9), 162.1 (C^7 and C^8), 138.1 (C^{14}), 134.9 (C^1 and C^2), 129.0 (C^4 and C^5), 124.0 (C^3 and C^6), 115.1 (C^{15}), 33.2 (C^{13}), 30.9 (C^{10}), 28.0 (C^{12}), 24.2 (C^{11}).

Data are consistent with the literature.[255]

1,3-Dioxoisoindolin-2-yl 2-cyclopropylacetate, **3.50**



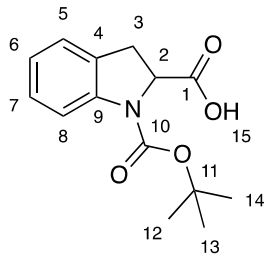
Prepared according to General Procedure 2B using cyclopropylacetic acid (370 μL, 4.00 mmol, 1.0 equiv.), EDC hydrochloride (920 mg, 4.80 mmol, 1.2 equiv.), 4-dimethylaminopyridine (49 mg, 400 μmol, 10 mol%), and *N*-hydroxyphthalimide (653 mg, 4.00 mmol, 1.0 equiv.) in DCM (40 mL, 0.1 M). The crude residue was dissolved with the minimum amount of DCM and hexane was added to precipitate the product, 675 mg of a white solid was recovered after filtration consistent with the desired product (69%).

^{1}H NMR (500 MHz, Chloroform-*d*) δ 7.90 – 7.85 (m, 2H, H^3 and H^6), 7.80 – 7.76 (m, 2H, H^1 and H^2), 2.58 (d, J = 7.11 Hz, 2H, H^{10}), 1.22 – 1.12 (m, 1H, H^{11}), 0.69 – 0.62 (m, 2H, H^{12} and H^{13}), 0.35 – 0.27 (m, 2H, H^{12} and H^{13}).

^{13}C NMR (126 MHz, Chloroform-*d*) δ 169.1 (C^9), 162.1 (C^7 and C^8), 134.9 (C^1 and C^2), 129.0 (C^4 and C^5), 124.0 (C^3 and C^6), 36.1 (C^{10}), 6.6 (C^{11}), 4.7 (C^{12} and C^{13}).

Data are consistent with the literature.[281]

1-(*tert*-Butoxycarbonyl)indoline-2-carboxylic acid, **3.51-int1**



Indoline-2-carboxylic acid (1.31 g, 8.00 mmol, 1.0 equiv.) and di-*tert*-butyl dicarbonate (2.10 g, 9.60 mmol, 1.2 equiv.) were dissolved in THF (40 mL, 0.2 M), and cooled down to 0 °C. Sodium hydroxide (320 mg, 8.00 mmol, 1.0 equiv.) was dissolved in water (10 mL) and then added dropwise to the reaction mixture at 0 °C. The reaction mixture was slowly warmed up to room temperature and stirred overnight. Volatiles were evaporated under vacuum and the resulting suspension was dissolved in water (40 mL). Organics were extracted with diethyl ether (30 mL). The aqueous layer was acidified with a solution of 1 M of HCl (pH ~ 2). Organics were extracted with diethyl ether (3 × 30 mL), dried over sodium sulfate, filtered, and concentrated in *vacuo* affording 1.52 g of a pale brown solid as the desired product as a mixture of rotamers (72%, 0.62:0.38).

Major rotamer:

^{1}H NMR (500 MHz, Chloroform-*d*) δ 11.23 (s, 1H, H^{15}), 7.93 (d, *J* = 8.13 Hz, 1H, H^{8}), 7.23 (t, *J* = 7.86 Hz, 1H, H^{7}), 7.14 (d, *J* = 7.14 Hz, 1H, H^{5}), 6.99 (t, *J* = 7.44 Hz, 1H, H^{6}), 4.89 (dd, *J* = 11.56, 4.66 Hz, 1H, H^{2}), 3.55 (dd, *J* = 16.81, 11.40 Hz, 1H, H^{3}), 3.20 (dd, *J* = 16.71, 5.09 Hz, 1H, H^{3}), 1.54 (s, 9H, H^{12}, H^{13} and H^{14}).

^{13}C NMR (126 MHz, Chloroform-*d*) δ 178.2 (C^{1}), 151.6 (C^{10}), 142.4 (C^{9}), 128.0 (C^{7}), 127.7 (C^{4}), 124.4 (C^{5}), 122.8 (C^{6}), 114.6 (C^{8}), 81.7 (C^{11}), 60.1 (C^{2}), 32.6 (C^{3}), 28.2 (C^{12}, C^{13} and C^{14}).

Minor rotamer:

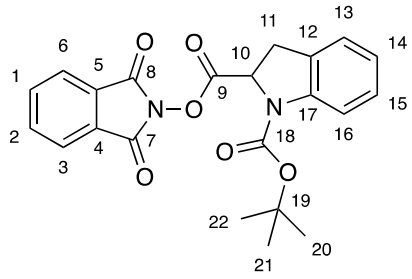
^{1}H NMR (500 MHz, Chloroform-*d*) δ 11.23 (s, 1H, H^{15}), 7.52 (d, *J* = 8.05 Hz, 1H, H^{8}), 7.23 (t, *J* = 7.86 Hz, 1H, H^{7}), 7.14 (d, *J* = 7.14 Hz, 1H, H^{5}), 6.99 (t, *J* = 7.44 Hz, 1H, H^{6}), 5.00 (d, *J* = 11.56 Hz, 1H, H^{2}), 3.55 (dd, *J* = 16.81, 11.40 Hz, 1H, H^{3}), 3.20 (dd, *J* = 16.71, 5.09 Hz, 1H, H^{3}), 1.64 (s, 9H, H^{12}, H^{13} and H^{14}).

^{13}C NMR (126 MHz, Chloroform-*d*) δ 177.5 (C^{1}), 153.1 (C^{10}), 141.3 (C^{9}), 128.8 (C^{7}), 127.9 (C^{4}), 124.9 (C^{5}), 122.8 (C^{6}), 114.7 (C^{8}), 82.9 (C^{11}), 59.9 (C^{2}), 31.7 (C^{3}), 28.4 (C^{12}, C^{13} and C^{14}).

IR (film): 2980, 1703, 1603, 1485, 1465, 1370, 1319, 1252, 1149, 1045, 1020, 907, 727 cm^{-1}.

HRMS: *m/z* calculated for $[M + Na]^{+}$ $(C_{14}H_{17}NO_4Na)^{+}$: 286.1050; found 286.1046.

1-(*tert*-Butyl) 2-(1,3-dioxoisoindolin-2-yl) indoline-1,2-dicarboxylate, **3.51**



Prepared according to General Procedure 2B using 1-(*tert*-butoxycarbonyl)indoline-2-carboxylic acid **3.51-int1** (527 mg, 2.00 mmol, 1.0 equiv.), EDC hydrochloride (460 mg, 2.40 mmol, 1.2 equiv.), 4-dimethylaminopyridine (24 mg, 200 μmol, 10 mol%), and *N*-hydroxyphthalimide (326 mg, 2.00 mmol, 1.0 equiv.) in DCM (20 mL, 0.1 M). The crude residue was purified by flash chromatography (silica gel) from pure hexane to a mixture of 11% of diethyl ether in hexane affording 278 mg of white solid consistent with the desired product (34%).

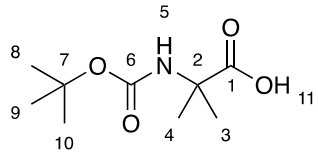
^{1}H NMR (500 MHz, Chloroform-*d*) δ 7.95 – 7.90 (m, 1H, H^{13}), 7.90 – 7.85 (m, 2H, H^{3} and H^{6}), 7.82 – 7.76 (m, 2H, H^{1} and H^{2}), 7.22 (app t, *J* = 7.92 Hz, 1H, H^{14}), 7.19 (app d, *J* = 7.53 Hz, 1H, H^{16}), 6.99 (app t, *J* = 7.45 Hz, 1H, H^{15}), 5.22 (dd, *J* = 11.75, 4.61 Hz, 1H, H^{10}), 3.73 (dd, *J* = 16.83, 11.73 Hz, 1H, H^{11}), 3.53 (dd, *J* = 16.78, 4.72 Hz, 1H, H^{11}), 1.60 (s, 9H, H^{20}, H^{21} and H^{22}).

^{13}C NMR (126 MHz, Chloroform-*d*) δ 168.5 (C^{9}), 161.7 (C^{7} and C^{8}), 151.3 (C^{18}), 142.3 (C^{17}), 135.0 (C^{1} and C^{2}), 129.0 (C^{4} and C^{5}), 128.3 (C^{14}), 127.3 (C^{12}), 124.7 (C^{16}), 124.2 (C^{3} and C^{6}), 123.1 (C^{15}), 114.8 (C^{13}), 82.8 (C^{19}), 58.5 (C^{10}), 33.2 (C^{11}), 28.2(C^{20}, C^{21} and C^{22}).

IR (film): 2978, 2360, 1820, 1790, 1714, 1605, 1529, 1485, 1466, 1383, 1369, 1147, 1086, 982 cm^{-1}.

HRMS: *m/z* calculated for $[M]^+$ $(C_{22}H_{20}N_2O_6)^+$: 408.1316; found 408.1316.

2-((*tert*-Butoxycarbonyl)amino)-2-methylpropanoic acid, **3.52-int1**



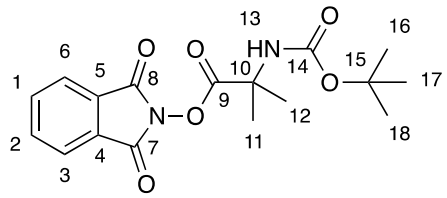
2-Aminoisobutyric acid (825 mg, 8.00 mmol, 1.0 equiv.) and di-*tert*-butyl dicarbonate (2.10 g, 9.60 mmol, 1.2 equiv.) were dissolved in THF (40 mL, 0.2 M), and cooled down to 0 °C. Sodium hydroxide (320 mg, 8.00 mmol, 1.0 equiv.) was dissolved in water (10 mL) and then added dropwise to the reaction mixture at 0 °C. The reaction mixture was slowly warmed up to room temperature and stirred overnight. Volatiles were evaporated under vacuum and the resulting suspension was dissolved in water (40 mL). Organics were extracted with ethyl acetate (2 × 30 mL). The aqueous layer was acidified with a solution of 1 M of HCl (pH ~ 2). Organics were extracted with ethyl acetate (3 × 30 mL), dried over sodium sulfate, filtered, and concentrated *in vacuo* affording 1.57 g of a white solid as the desired product (97%).

^{1}H NMR (500 MHz, Chloroform-*d*) δ 10.48 (s, 1H, H^{11}), 6.39 – 5.12 (m, 1H, H^5), 1.52 (s, 6H, H^3 and H^4), 1.43 (s, 9H, H^8, H^9 and H^{10}).

^{13}C NMR (126 MHz, Chloroform-*d*) δ 180.1 (C^1), 155.2 (C^6), 80.2 (C^7), 56.2 (C^2), 28.4 (C^8, C^9 and C^{10}), 25.4 (C^3 and C^4).

Data are consistent with the literature.[282]

1,3-Dioxoisoindolin-2-yl 2-((*tert*-butoxycarbonyl)amino)-2-methylpropanoate, **3.52**



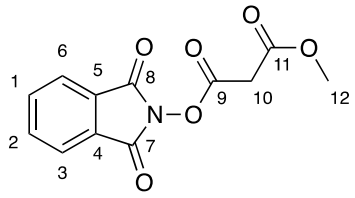
Prepared according to General Procedure 2B using 2-((*tert*-butoxycarbonyl)amino)-2-methylpropanoic acid **3.52** (406 mg, 2.00 mmol, 1.0 equiv.), EDC hydrochloride (460 mg, 2.40 mmol, 1.2 equiv.), 4-dimethylaminopyridine (24 mg, 200 μmol, 10 mol%) *N*-hydroxyphthalimide (653 mg, 4.00 mmol, 1.0 equiv.) in DCM (40 mL, 0.1 M). The crude residue was dissolved with the minimum amount of DCM and hexane was added to precipitate the product, 497 mg of a white solid was recovered after filtration consistent with the desired product (71%).

^{1}H NMR (500 MHz, Chloroform-*d*) δ 7.90 – 7.85 (m, 2H, H^{3} and H^{6}), 7.81 – 7.74 (m, 2H, H^{1} and H^{2}), 5.02 (broad s, 1H, H^{13}), 1.70 (s, 6H, H^{11} and H^{12}), 1.51 (s, 9H, H^{16}, H^{17} and H^{18}).

^{13}C NMR (126 MHz, Chloroform-*d*) δ 171.2 (C^{9}), 161.8 (C^{7} and C^{8}), 154.4 (C^{14}), 134.8 (C^{1} and C^{2}), 129.1 (C^{4} and C^{5}), 124.0 (C^{3} and C^{6}), 80.6 (C^{15}), 55.9 (C^{10}), 28.3 (C^{16}, C^{17} and C^{18}), 25.7 (C^{11} and C^{12}).

Data are consistent with the literature.[283]

1,3-Dioxoisoindolin-2-yl methyl malonate, **3.53**



Prepared according to General Procedure 2A using 3-methoxy-3-oxopropanoic acid (210 μL, 2.00 mmol, 1.0 equiv.), *N*,*N*'-diisopropyl-carbodiimide (340 μL, 2.20 mmol, 1.1 equiv.), 4-dimethylaminopyridine (24 mg, 200 μmol, 10 mol%), and *N*-hydroxyphthalimide (326 mg, 2.00 mmol, 1.0 equiv.) in DCM (20 mL, 0.1 M). The crude residue was purified by flash chromatography (silica gel) from pure hexane to a mixture of 30% of ethyl acetate in hexane affording 290 mg of a white solid consistent with the desired product (55%).

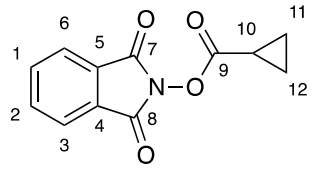
^{1}H NMR (500 MHz, Chloroform-*d*) δ 7.92 – 7.85 (m, 2H, H^{3} and H^{6}), 7.84 – 7.77 (m, 2H, H^{1} and H^{2}), 3.83 (s, 3H, H^{12}), 3.74 (s, 2H, H^{10}).

^{13}C NMR (126 MHz, Chloroform-*d*) δ 164.9 (C^{11}), 162.8 (C^{9}), 161.6 (C^{7} and C^{8}), 135.1 (C^{1} and C^{2}), 128.9 (C^{4} and C^{5}), 124.2 (C^{3} and C^{6}), 53.3 (C^{12}), 38.2 (C^{10}).

IR (film): 1821, 1790, 1735, 1611, 1468, 1439, 1358, 1189, 1136, 1080, 975, 955, 914 cm^{-1}.

HRMS: *m/z* calculated for $[M + Na]^+$ $(C_{12}H_9NO_6Na)^+$: 286.0322; found 286.0318.

1,3-Dioxoisoindolin-2-yl cyclopropanecarboxylate, **3.54**



Prepared according to General Procedure 2A using cyclopropanecarboxylic acid (420 μL, 5.00 mmol, 1.0 equiv.), *N*,*N'*-diisopropyl-carbodiimide (850 μL, 5.50 mmol, 1.1 equiv.), 4-dimethylaminopyridine (61 mg, 500 μmol, 10 mol%), and *N*-hydroxyphthalimide (816 mg, 5.00 mmol, 1.0 equiv.) in DCM (50 mL, 0.1 M). The crude residue was purified by flash chromatography (silica gel) from pure hexane to a mixture of 10% of ethyl acetate in hexane affording 761 mg of a white solid consistent with the desired product (66%).

^{1}H NMR (500 MHz, Chloroform-*d*) δ 7.91 – 7.85 (m, 2H, H^{3} and H^{6}), 7.81 – 7.73 (m, 2H, H^{1} and H^{2}), 1.99 – 1.92 (m, 1H, H^{10}), 1.29 – 1.24 (m, 2H, H^{11} and H^{12}), 1.20 – 1.14 (m, 2H, H^{11} and H^{12}).

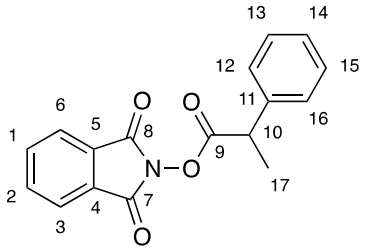
^{13}C NMR (126 MHz, Chloroform-*d*) δ 171.3 (C^{9}), 162.2 (C^{7} and C^{8}), 134.9 (C^{1} and C^{2}), 129.0 (C^{4} and C^{5}), 124.1 (C^{3} and C^{6}), 10.8 (C^{11} and C^{12}), 10.4 (C^{10}).

IR (solid): 1800, 1777, 1746, 1611, 1464, 1430, 1387, 1373, 1287, 1182, 1134, 1113, 1015, 1003, 975, 964, 876, 789, 692 cm^{-1}.

HRMS (ESI): *m/z* calculated for $[M + H]^+$ $(C_{12}H_{10}NO_4)^+$: 232.0604; found 232.0607.

Data consistent with the literature.[257]

1,3-Dioxoisoindolin-2-yl 2-phenylpropanoate, **3.55**



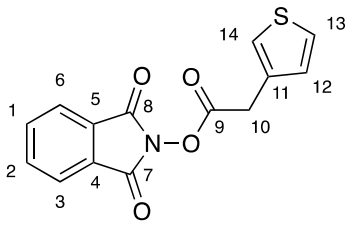
Prepared according to General Procedure 2A using 2-phenylpropionic acid (680 μL, 5.00 mmol, 1.0 equiv.), *N*,*N'*-diisopropyl-carbodiimide (850 μL, 5.50 mmol, 1.1 equiv.), 4-dimethylaminopyridine (61 mg, 500 μmol, 10 mol%), and *N*-hydroxyphthalimide (816 mg, 5.00 mmol, 1.0 equiv.) in DCM (50 mL, 0.1 M). The crude residue was purified by flash chromatography (silica gel) from pure hexane to a mixture of 8% of ethyl acetate in hexane affording 1.08 g of a colourless oil consistent with the desired product (73%).

^{1}H NMR (500 MHz, Chloroform-*d*) δ 7.89 – 7.83 (m, 2H, H^{3} and H^{6}), 7.81 – 7.74 (m, 2H, H^{1} and H^{2}), 7.44 – 7.37 (m, 4H, H^{12}, H^{13}, H^{15} and H^{16}), 7.36 – 7.30 (m, 1H, H^{14}), 4.12 (q, *J* = 7.18 Hz, 1H, H^{10}), 1.68 (d, *J* = 7.22 Hz, 3H, H^{17}).

^{13}C NMR (126 MHz, Chloroform-*d*) δ 170.9 (C^{9}), 162.0 (C^{7} and C^{8}), 138.5 (C^{11}), 134.9 (C^{1} and C^{2}), 129.1 (C^{4}, C^{5}), 129.1 (C^{arom}), 128.0 (C^{14}), 127.7 (C^{arom}), 124.1 (C^{3} and C^{6}), 43.1 (C^{10}), 19.1 (C^{17}).

Data are consistent with the literature.[284]

1,3-Dioxoisoindolin-2-yl 2-(thiophen-3-yl)acetate, **3.56**



Prepared according to General Procedure 2B using 3-thiopheneacetic acid (284 mg, 2.00 mmol, 1.0 equiv.), EDC hydrochloride (460 mg, 2.40 mmol, 1.2 equiv.), 4-dimethylaminopyridine (24 mg, 200 μmol, 10 mol%), and *N*-hydroxyphthalimide (653

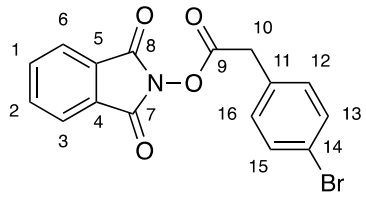
mg, 4.00 mmol, 1.0 equiv.) in DCM (40 mL, 0.1 M). The crude residue was dissolved with the minimum amount of DCM and hexane was added to precipitate the product, 313 mg of a white solid was recovered after filtration consistent with the desired product (54%).

^{1}H NMR (500 MHz, Chloroform-*d*) δ 7.92 – 7.86 (m, 2H, H^{3} and H^{6}), 7.82 – 7.77 (m, 2H, H^{1} and H^{2}), 7.35 (dd, *J* = 4.93, 2.98 Hz, 1H, H^{13}), 7.33 – 7.31 (m, 1H, H^{14}), 7.13 (dd, *J* = 4.99, 1.37 Hz, 1H, H^{12}), 4.03 (s, 2H, H^{10}).

^{13}C NMR (126 MHz, Chloroform-*d*) δ 167.4 (C^{9}), 162.0 (C^{7} and C^{8}), 135.0 (C^{1} and C^{2}), 130.9 (C^{11}), 129.0 (C^{4} and C^{5}), 128.3 (C^{12}), 126.5 (C^{13}), 124.2 (C^{3} and C^{6}), 124.0 (C^{14}), 32.6 (C^{10}).

Data are consistent with the literature.[285]

2-(2-(4-Bromophenyl)acetyl)isoindoline-1,3-dione, **3.57**



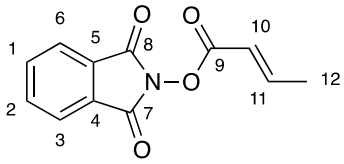
Prepared according to General Procedure 2A using 4-bromophenylacetic acid (1.08 g, 5.00 mmol, 1.0 equiv.), *N,N'*-diisopropyl-carbodiimide (850 µL, 5.50 mmol, 1.1 equiv.), 4-dimethylaminopyridine (61 mg, 500 µmol, 10 mol%), and *N*-hydroxyphthalimide (816 mg, 5.00 mmol, 1.0 equiv.) in DCM (50 mL, 0.1 M). The crude was purified by flash chromatography from pure hexane to a mixture of 12% of ethyl acetate in hexane affording 1.42 g of a white solid consistent with the desired product (79%).

^{1}H NMR (500 MHz, Chloroform-*d*) δ 7.98 – 7.85 (m, 2H, H^{3} and H^{6}), 7.86 – 7.64 (m, 2H, H^{1} and H^{2}), 7.58 – 7.45 (m, 2H, H^{13} and H^{15}), 7.38 – 7.13 (m, 2H, H^{12} and H^{16}), 3.95 (s, 2H, H^{10}).

^{13}C NMR (126 MHz, Chloroform-*d*) δ 167.4 (C^9), 161.9 (C^7 and C^8), 135.0 (C^1 and C^2), 132.1 (C^{13} and C^{15}), 131.1 (C^{12} and C^{16}), 130.6 (C^{11}), 128.9 (C^4 and C^5), 124.2 (C^3 and C^6), 122.1 (C^{14}), 37.3 (C^{10}).

Data consistent with the literature.[285]

1,3-Dioxoisoindolin-2-yl (*E*)-but-2-enoate, **3.58**



Prepared according to General Procedure 2A using 3-butenoic acid (410 μL, 5.00 mmol, 1.0 equiv.), *N*,*N*'-diisopropyl-carbodiimide (850 μL, 5.50 mmol, 1.1 equiv.), 4-dimethylaminopyridine (61 mg, 500 μmol, 10 mol%), and *N*-hydroxyphthalimide (816 mg, 5.00 mmol, 1.0 equiv.) in DCM (50 mL, 0.1 M). The crude residue was purified by flash chromatography (silica gel) from pure hexane to a mixture of 6% of ethyl acetate in hexane affording 468 mg of a white solid consistent with the desired product (40%).

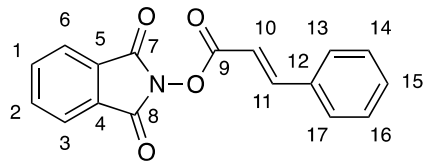
^{1}H NMR (500 MHz, Chloroform-*d*) δ 7.93 – 7.85 (m, 2H, H^3 and H^6), 7.82 – 7.75 (m, 2H, H^1 and H^2), 7.33 (dq, *J* = 15.69, 6.93 Hz, 1H, H^{11}), 6.11 (dq, *J* = 15.63, 1.72 Hz, 1H, H^{10}), 2.02 (dd, *J* = 6.95, 1.73 Hz, 3H, H^{12}).

^{13}C NMR (126 MHz, Chloroform-*d*) δ 162.3 (C^9), 162.3 (C^7 and C^8), 151.4 (C^{11}), 134.9 (C^1 and C^2), 129.1 (C^4 and C^5), 124.1 (C^3 and C^6), 117.2 (C^{10}), 18.9 (C^{12}).

IR (film): 1798, 1774, 1728, 1651, 1470, 1367, 1358, 1313, 1292, 1184, 1172, 1132, 1088, 1084, 972, 878, 786, 704, 519 cm^{-1}.

HRMS (ESI): *m/z* calculated for $[M + H]^+$ $(C_{12}H_{10}NO_4)^+$: 232.0604; found 232.0596.

1,3-Dioxoisoindolin-2-yl cinnamate, **3.59**



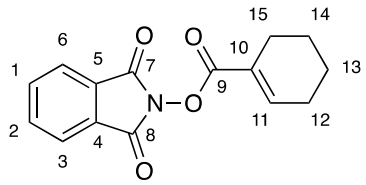
Prepared according to General Procedure 2A using (*E*)-cinnamic acid (741 mg, 5.00 mmol, 1.0 equiv.), *N*,*N*′-diisopropyl-carbodiimide (850 μL, 5.50 mmol, 1.1 equiv.), 4-dimethylaminopyridine (61 mg, 500 μmol, 10 mol%), and *N*-hydroxyphthalimide (816 mg, 5.00 mmol, 1.0 equiv.) in DCM (50 mL, 0.1 M). The crude residue was purified by flash chromatography (silica gel) from pure hexane to a mixture of 10% of ethyl acetate in hexane affording 685 mg of a white solid consistent with the desired product (47%).

^{1}H NMR (500 MHz, Chloroform-*d*) δ 7.97 (d, *J* = 16.05 Hz, 1H, H^{11}), 7.93 – 7.89 (m, 2H, H^{3} and H^{6}), 7.85 – 7.77 (m, 2H, H^{1} and H^{2}), 7.63 – 7.54 (m, 2H, H^{13} and H^{17}), 7.50 – 7.41 (m, 3H, H^{14}, H^{15} and H^{16}), 6.66 (d, *J* = 16.04 Hz, 1H, H^{10}).

^{13}C NMR (126 MHz, Chloroform-*d*) δ 163.2 (C^{9}), 162.2 (C^{7} and C^{8}), 150.1 (C^{11}), 134.9 (C^{1} and C^{2}), 133.7 (C^{12}), 131.7 (C^{15}), 129.3 (C^{14} and C^{16}), 129.1 (C^{4} and C^{5}), 128.8 (C^{13} and C^{17}), 124.1 (C^{3} and C^{6}), 111.8 (C^{10}).

Data are consistent with the literature.[256]

1,3-Dioxoisoindolin-2-yl cyclohex-1-ene-1-carboxylate, **3.60**



Prepared according to General Procedure 2A using 1-cyclohexene-1-carboxylic acid (810 μL, 5.00 mmol, 1.0 equiv.), *N*,*N*′-diisopropyl-carbodiimide (850 μL, 5.50 mmol, 1.1 equiv.), 4-dimethylaminopyridine (61 mg, 500 μmol, 10 mol%), and *N*-hydroxyphthalimide (816 mg, 5.00 mmol, 1.0 equiv.) in DCM (50 mL, 0.1 M). The crude residue was purified by flash chromatography (silica gel) from pure hexane to a

mixture of 7% of ethyl acetate in hexane affording 954 mg of a white solid consistent with the desired product (70%).

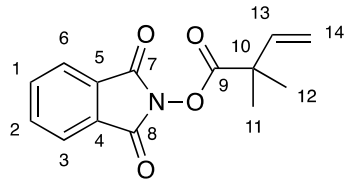
^{1}H NMR (400 MHz, Chloroform-*d*) δ 7.93 – 7.84 (m, 2H, H^{3} and H^{6}), 7.82 – 7.73 (m, 2H, H^{1} and H^{2}), 7.39 (tt, *J* = 3.88, 1.73 Hz, 1H, H^{11}), 2.42 – 2.35 (m, 2H, H^{15}), 2.34 – 2.26 (m, 2H, H^{12}), 1.77 – 1.63 (m, 4H, H^{13} and H^{14}).

^{13}C NMR (126 MHz, Chloroform-*d*) δ 163.1 (C^{9}), 162.5 (C^{7} and C^{8}), 146.0 (C^{11}), 134.8 (C^{1} and C^{2}), 129.2 (C^{4} and C^{5}), 126.3 (C^{10}), 124.0 (C^{3} and C^{6}), 26.4 (C^{12}), 24.1 (C^{15}), 21.8 (C^{14}), 21.1 (C^{13}).

IR (film): 1764, 1744, 1636, 1464, 1356, 1182, 1151, 1134, 1120, 989, 970, 877, 810 cm^{-1}.

HRMS (ESI): *m/z* calculated for $[M + Na]^{+}$ $(C_{15}H_{13}NO_4Na)^{+}$: 294.0742; found = 294.0727.

1,3-Dioxoisoindolin-2-yl 2,2-dimethylbut-3-enoate, **3.61**



Prepared according to General Procedure 2B using 2,2-dimethylbut-3-enoic acid (430 μL, 4.00 mmol, 1.0 equiv.), EDC hydrochloride (920 mg, 4.80 mmol, 1.2 equiv.), 4-dimethylaminopyridine (49 mg, 400 μmol, 10 mol%), and *N*-hydroxyphthalimide (653 mg, 4.00 mmol, 1.0 equiv.) in DCM (40 mL, 0.1 M). The crude residue was purified by flash chromatography (silica gel) from pure hexane to a mixture of 6% of diethyl ether in hexane affording 826 mg of a white solid consistent with the desired product (80%).

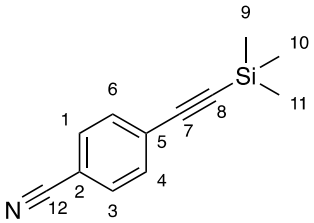
^{1}H NMR (500 MHz, Chloroform-*d*) δ 7.90 – 7.85 (m, 2H, H^{3} and H^{6}), 7.80 – 7.76 (m, 2H, H^{1} and H^{2}), 6.13 (dd, *J* = 17.36, 10.63 Hz, 1H, H^{13}), 5.34 (d, *J* = 17.40 Hz, 1H, H^{14}), 5.25 (d, *J* = 10.65 Hz, 1H, H^{14}), 1.52 (s, 6H, H^{11} and H^{12}).

^{13}C NMR (126 MHz, Chloroform-*d*) δ 172.6 (C^9), 162.1 (C^7 and C^8), 140.3 (C^{13}), 134.8 (C^1 and C^2), 129.1 (C^4 and C^5), 124.0 (C^3 and C^6), 115.0 (C^{14}), 44.6 (C^{10}), 24.9 (C^{11} and C^{12}).

IR (solid): 1809, 1780, 1639, 1608, 1589, 1465, 1363, 1184, 1136, 1053, 1037, 1016 cm^{-1}.

HRMS (ESI): *m/z* calculated for $[M + Na]^+$ $(C_{14}H_{13}NO_4Na)^+$: 282.0737, found 282.0732.

4-((Trimethylsilyl)ethynyl)benzonitrile, **3.62-int1**



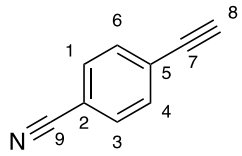
Prepared according to General Procedure 3 using 4-iodobenzonitrile (1.15 g, 5.00 mmol, 1.0 equiv.), dichlorobis(triphenylphosphine)palladium (35 mg, 50.0 μmol, 1 mol%), copper iodide (19 mg, 100 μmol, 2 mol%), and trimethylsilylacetylene (660 μL, 6.25 mmol, 1.25 equiv.) in triethylamine (10 mL, 0.5 M). The crude residue was purified by flash chromatography (silica gel) from pure hexane to a mixture of 3% of ethyl acetate in hexane affording 932 mg of a white solid as the desired product (94%).

^{1}H NMR (500 MHz, Chloroform-*d*) δ 7.61 – 7.57 (m, 2H, H^1 and H^3), 7.56 – 7.51 (m, 2H, H^4 and H^6), 0.26 (s, 9H, H^9, H^{10} and H^{11}).

^{13}C NMR (126 MHz, Chloroform-*d*) δ 132.6 (C^4 and C^6), 132.1 (C^1 and C^3), 128.1 (C^5), 118.6 (C^{12}), 111.9 (C^2), 103.1 (C^7), 99.7 (C^8), –0.1 (C^9, C^{10} and C^{11}).

Data are consistent with the literature.[286]

4-Ethynylbenzonitrile, **3.62-int2**



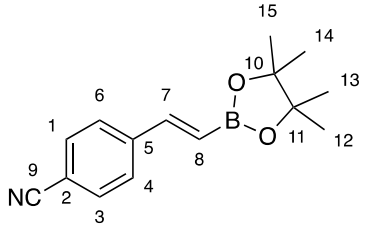
Prepared according to General Procedure 4 using 4-(trimethylsilyl)ethynyl)benzonitrile **3.62-int1** (932 mg, 4.68 mmol, 1.0 equiv.) and potassium carbonate (1.29 g, 9.35 mmol, 2.0 equiv.) in MeOH (23 mL, 0.2 M). The crude residue was purified by flash chromatography (silica gel) from pure hexane to a mixture of 10% of diethyl ether in hexane affording 478 mg of a white solid consistent with the desired product (80%).

^{1}H NMR (500 MHz, Chloroform-*d*) δ 7.63 – 7.60 (m, 2H, H^1 and H^3), 7.59 – 7.55 (m, 2H, H^4 and H^6), 3.30 (s, 1H, H^8).

^{13}C NMR (126 MHz, Chloroform-*d*) δ 132.8 (C^4 and C^6), 132.2 (C^1 and C^3), 127.1 (C^5), 118.4 (C^9), 112.4 (C^2), 82.0 (C^7), 81.7 (C^8).

Data are consistent with the literature.[287]

(*E*)-4-(2-(4,4,5,5-Tetramethyl-1,3,2-dioxaborolan-2-yl)vinyl)benzonitrile, **3.62-int3**



Prepared according to General Procedure 5 using 4-ethynylbenzonitrile **3.62-int2** (191 mg, 1.50 mmol, 1.0 equiv.), copper(I) chloride (7 mg, 75 μmol, 5 mol%), potassium *tert*-butoxide (17 mg, 150 μmol, 10 mol%), bis(2-diphenylphosphinophenyl)ether (DPEPhos) (40 mg, 75 μmol, 5 mol%), bis(pinacolato)diboron (420 mg, 1.65 mmol, 1.1 equiv.), and MeOH (160 μL, 4.00 mmol, 2.0 equiv.) in THF (6 mL, 0.25 M). The crude residue was purified by flash chromatography (silica gel) from pure hexane to a mixture of 10% of diethyl ether in hexane affording 157 mg of a white solid consistent with the desired product (41%).

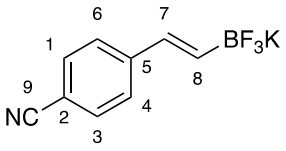
^{1}H NMR (500 MHz, Chloroform-*d*) δ 7.65 – 7.61 (m, 2H, H^{1} and H^{3}), 7.56 – 7.53 (m, 2H, H^{4} and H^{6}), 7.36 (d, *J* = 18.45 Hz, 1H, H^{7}), 6.28 (d, *J* = 18.45 Hz, 1H, H^{8}), 1.32 (s, 12H, H^{12}, H^{13}, H^{14} and H^{15}).

^{11}B NMR (96 MHz, Chloroform-*d*) δ 30.42.

^{13}C NMR (126 MHz, Chloroform-*d*) δ 147.3 (C^{7}), 141.8 (C^{5}), 132.6 (C^{1} and C^{3}), 127.6 (C^{4} and C^{6}), 121.1 (C^{8}), 119.0 (C^{9}), 112.1 (C^{2}), 83.9 (C^{10} and C^{11}), 24.9 (C^{12}, C^{13}, C^{14} and C^{15}).

Data are consistent with literature.[288]

(*E*)-4-(2-(Trifluoro-λ^{4}-boraneyl)vinyl)benzonitrile, potassium salt, **3.62-int4**



Prepared according to General Procedure 6 using (*E*)-4-(2-(4,4,5,5-tetramethyl-1,3,2-dioxaborolan-2-yl)vinyl)benzonitrile **3.62-int3** (250 mg, 1.09 mmol, 1.0 equiv.), potassium hydrogen fluoride (192 mg, 2.46 mmol, 4.0 equiv.), and water (550 μL, 30.8 mmol, 50.0 equiv.) in MeOH (6 mL, 0.1 M). 74 mg of a white solid was obtained after filtration, consistent with the desired product (51%).

^{1}H NMR (500 MHz, Acetone-d_6) δ 7.64 – 7.59 (m, 2H, H^{1} and H^{3}), 7.53 – 7.49 (m, 2H, H^{4} and H^{6}), 6.68 (d, *J* = 18.27 Hz, 1H, H^{7}), 6.57 (dq, *J* = 18.17, 3.36 Hz, 1H, H^{8}).

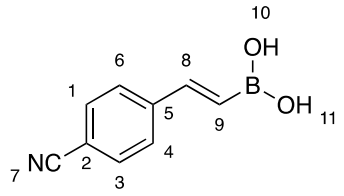
^{11}B NMR (96 MHz, Acetone-d_6) δ 2.74.

^{13}C NMR (126 MHz, Acetone-d_6) δ 146.6 (C^{5}), 132.9 (C^{1} and C^{3}), 132.8 (q, $^{3}J_{CF}$ = 4.1 Hz, C^{7}), 127.1 (C^{4} and C^{6}), 119.9 (C^{9}), 109.4 (C^{2}). C^{8} is not observed.

^{19}F {^{1}H} NMR (376 MHz, Acetone-d_6) δ –142.75.

Data are consistent with the literature.[151]

(*E*)-(4-Cyanostyryl)boronic acid, **3.62**



Prepared according to General Procedure 7 using (*E*)-4-(2-(trifluoro-λ^4-boraneyl)vinyl)benzonitrile, potassium salt, **3.62-int4** (432 mg, 1.84 mmol, 1.0 equiv.) and chlorotrimethylsilane (820 μL, 6.43 mmol, 3.5 equiv.) in MeCN:H_2O (14 mL:3 mL, 0.1 M). 233 mg of a white solid was obtained as the desired product (73%).

^{1}H NMR (500 MHz, DMSO-d_6) δ 7.96 (s, 2H, H^{10} and H^{11}), 7.84 – 7.79 (m, 2H, H^1 and H^3), 7.68 – 7.63 (m, 2H, H^4 and H^6), 7.29 (d, *J* = 18.39 Hz, 1H, H^8), 6.30 (d, *J* = 18.39 Hz, 1H, H^9).

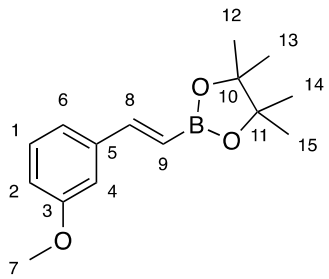
^{11}B NMR (128 MHz, DMSO-d_6) δ 30.67.

^{13}C NMR (126 MHz, DMSO-d_6) δ 143.9 (C^8), 142.1 (C^5), 132.7 (C^1 and C^3), 127.8 (broad, C^9), 127.4 (C^4 and C^6), 118.9 (C^7), 110.5 (C^2).

IR (solid): 1604, 1340, 1323, 1290, 1269, 1230, 1095, 1074, 1039, 997, 987, 958, 931 cm^{-1}.

HRMS (ESI): *m/z* calculated for [M (methyl boronic ester) + Na]$^+$ ($C_{11}H_{12}BNNaO_2$)$^+$: 224.0853; found = 224.0857.

(*E*)-2-(3-Methoxystyryl)-4,4,5,5-tetramethyl-1,3,2-dioxaborolane, **3.63-int3**



Prepared according to General Procedure 5 using 3-methoxyphenylacetylene (640 μL, 5.00 mmol, 1.0 equiv.), copper(I) chloride (25 mg, 250 μmol, 5 mol%), potassium *tert*-butoxide (56 mg, 500 μmol, 10 mol%), bis(2-diphenylphosphinophenyl) ether

(DPEPhos) (135 mg, 250 μmol, 5 mol%), bis(pinacolato)diboron (1.40 g, 5.50 mmol, 1.1 equiv.), and MeOH (410 μL, 10.0 mmol, 2.0 equiv.) in THF (20 mL, 0.25 M). The crude residue was purified by flash chromatography (silica gel) from pure hexane to a mixture of 5% of diethyl ether in hexane affording 1.28 g of a colourless oil consistent with the desired product (98%).

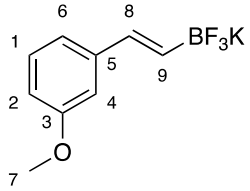
^{1}H NMR (500 MHz, Chloroform-*d*) δ 7.37 (d, *J* = 18.39 Hz, 1H, H^{8}), 7.25 (t, *J* = 7.89 Hz, 1H, H^{1}), 7.08 (dt, *J* = 7.62, 1.26 Hz, 1H, H^{6}), 7.03 (dd, *J* = 2.57, 1.57 Hz, 1H, H^{4}), 6.86 – 6.83 (m, 1H, H^{2}), 6.16 (d, *J* = 18.40 Hz, 1H, H^{9}), 3.80 (s, 3H, H^{7}), 1.31 (s, 12H, H^{12}, H^{13}, H^{14} and H^{15}).

^{11}B NMR (96 MHz, Chloroform-*d*) δ 30.49.

^{13}C NMR (126 MHz, Chloroform-*d*) δ 159.9 (C^{3}), 149.5 (C^{8}), 139.0 (C^{5}), 129.7 (C^{1}), 119.9 (C^{6}), 116.9 (broad, C^{9}), 114.9 (C^{2}), 112.0 (C^{4}), 83.5 (C^{10} and C^{11}), 55.3 (C^{7}), 24.9 (C^{12}, C^{13}, C^{14} and C^{15}).

Data consistent with the literature.[289]

(*E*)-Trifluoro(3-methoxystyryl)-λ^{4}-borane, potassium salt, **3.63-int4**



Prepared according to General Procedure 6 using (*E*)-2-(3-methoxystyryl)-4,4,5,5-tetramethyl-1,3,2-dioxaborolane **3.63-int3** (1.25 g, 4.81 mmol, 1.0 equiv.), potassium hydrogen fluoride (1.50 g, 19.2 mmol, 4.0 equiv.), and water (4.33 mL, 240 mmol, 50.0 equiv.) in MeOH (40 mL, 0.1 M). 827 mg of a white solid was obtained after filtration, consistent with the desired product (72%).

^{1}H NMR (500 MHz, DMSO-d_6) δ 7.15 (t, *J* = 7.85 Hz, 1H, H^{1}), 6.89 (dt, *J* = 7.58, 1.22 Hz, 1H, H^{6}), 6.86 (dd, *J* = 2.65, 1.53 Hz, 1H, H^{4}), 6.68 (ddd, *J* = 8.17, 2.59, 0.96 Hz, 1H, H^{2}), 6.44 (d, *J* = 18.27, 1H, H^{8}), 6.18 (dq, *J* = 18.19, 3.54 Hz, 1H, H^{9}), 3.74 (s, 3H, H^{7}).

^{11}B NMR (96 MHz, DMSO-d_6) δ 2.90.

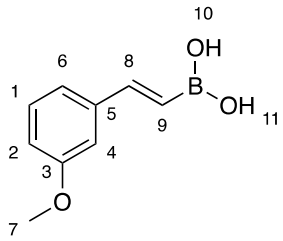
^{13}C NMR (126 MHz, DMSO-d_6) δ 159.4 (C^3), 141.9 (C^5), 139.5 (broad, C^9), 133.1 (q, $^3J_{CF}$ = 4.4 Hz, C^8), 129.2 (C^1), 118.1 (C^6), 111.6 (C^2), 110.4 (C^4), 54.8 (C^7).

^{19}F {^{1}H} NMR (377 MHz, DMSO-d_6) δ –137.84.

IR (solid): 1625, 1600, 1577, 1487, 1463, 1429, 1288, 1265, 1149, 1138, 1232, 1093, 1037, 989 cm^{-1}.

HRMS (ESI): *m/z* calculated for $[M - K]^-$ $(C_9H_9BF_3O)^-$: 201.0705; found = 201.0691.

(*E*)-(3-Methoxystyryl)boronic acid, **3.63**



Prepared according to General Procedure 7 using (*E*)-trifluoro(3-methoxystyryl)-λ^4-borane, potassium salt **3.63-int4** (770 mg, 3.21 mmol, 1.0 equiv.) and chlorotrimethylsilane (1.42 mL, 11.2 mmol, 3.5 equiv.) in MeCN:H_2O (26 mL:6 mL, 0.1 M). 489 mg of a white solid was obtained as a mixture of the desired product and boroxine (86%).

^{1}H NMR (500 MHz, DMSO-d_6) δ 7.81 (s, 2H, H^{10} and H^{11}), 7.28 (t, *J* = 7.89 Hz, 1H, H^1), 7.23 (d, *J* = 18.35 Hz, 1H, H^8), 7.05 (d, *J* = 7.61 Hz, 1H, H^6), 7.01 (t, *J* = 1.98 Hz, 1H, H^4), 6.87 (dd, *J* = 8.18, 2.56 Hz, 1H, H^2), 6.13 (d, *J* = 18.35 Hz, 1H, H^9), 3.77 (s, 3H, H^7).

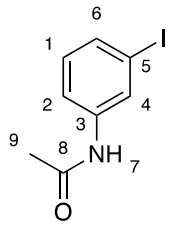
^{11}B NMR (96 MHz, DMSO-d_6) δ 29.49.

^{13}C NMR (126 MHz, DMSO-d_6) δ 159.6 (C^3), 145.8 (C^8), 139.2 (C^5), 129.8 (C^1), 123.6 (broad, C^9), 119.2 (C^6), 114.3 (C^2), 111.6 (C^4), 55.1 (C^7).

IR (solid): 1625, 1593, 1583, 1490, 1350, 1313, 1286, 1249, 1234, 1213, 1153, 989 cm^{-1}.

HRMS (ESI): *m/z* calculated for $[M + H]^+$ $(C_9H_{12}BO_3)^+$: 179.0874; found = 179.0871.

N-(3-iodophenyl)acetamide, **3.64-int0**



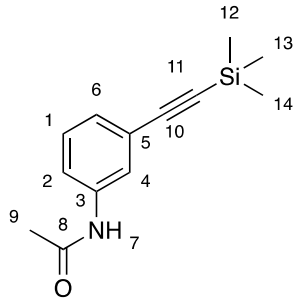
3-Iodoaniline (600 µL, 5.00 mmol, 1.0 equiv.) was dissolved in DCM (25 mL, 0.2 M). Triethylamine (1.39 mL, 10.0 mmol, 2.0 equiv.) was added and the reaction mixture was cooled down to 0 °C. Acetic anhydride (1.42 mL, 15.0 mmol, 3.0 equiv.) was added dropwise at 0 °C and the reaction mixture was left to stir for six hours. Once completion was reached, the reaction mixture was partitioned between DCM (10 mL) and a saturated solution of sodium bicarbonate (20 mL). Organics were extracted with DCM (2 × 15 mL). Organic layers were combined washed with brine (20 mL), dried over sodium sulfate, filtered, and concentrated *in vacuo*. The crude residue was purified by flash chromatography (silica gel) from pure hexane to a mixture of 35% of ethyl acetate in hexane affording 1.27 g of a white solid as the desired product (97%).

^{1}H NMR (500 MHz, Chloroform-*d*) δ 7.91 (t, *J* = 1.88 Hz, 1H, H^{4}), 7.80 (broad s, 1H, H^{7}), 7.49 – 7.43 (m, 1H, H^{2}), 7.42 (dt, *J* = 7.90, 1.28 Hz, 1H, H^{6}), 7.01 (t, *J* = 8.01 Hz, 1H, H^{1}), 2.16 (s, 3H, H^{9}).

^{13}C NMR (126 MHz, Chloroform-*d*) δ 168.9 (C^{8}), 139.2 (C^{6}), 133.4 (C^{3}), 130.6 (C^{4}), 128.8 (C^{1}), 119.3 (C^{5}), 94.2 (C^{2}), 24.7 (C^{9}).

Data are consistent with the literature.[290]

N-(3-((Trimethylsilyl)ethynyl)phenyl)acetamide, **3.64-int1**



Prepared according to General Procedure 3 using *N*-(3-iodophenyl)acetamide **3.64-int0** (1.47 g, 5.63 mmol, 1.0 equiv.), dichlorobis(triphenylphosphine)palladium (39 mg, 56.3 μmol, 1 mol%), copper iodide (21 mg, 113 μmol, 2 mol%), and trimethylsilylacetylene (740 μL, 7.04 mmol, 1.25 equiv.) in triethylamine (12 mL, 0.5 M). The crude residue was purified by flash chromatography (silica gel) from pure hexane to a mixture of 45% of ethyl acetate in hexane affording 1.21 g of a pale-brown solid as the desired product (93%).

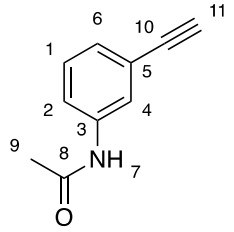
^{1}H NMR (500 MHz, Chloroform-*d*) δ 7.61 (s, 1H, H^{4}), 7.51 – 7.45 (m, 2H, H^{2} and H^{7}), 7.25 – 7.17 (m, 2H, H^{1} and H^{6}), 2.16 (s, 3H, H^{9}), 0.23 (s, 9H, H^{12}, H^{13} and H^{14}).

^{13}C NMR (126 MHz, Chloroform-*d*) δ 168.6 (C^{8}), 137.9 (C^{3}), 129.0 (C^{1}), 128.0 (C^{6}), 123.9 (C^{5}), 123.2 (C^{4}), 120.2 (C^{2}), 104.6 (C^{10}), 94.7 (C^{11}), 24.7 (C^{9}), 0.0 (C^{12}, C^{13} and C^{14}).

IR (film): 2156, 1666, 1606, 1383, 1550, 1483, 1421, 1404, 1371, 1247, 839, 758 cm^{-1}.

HRMS (ESI): *m/z* calculated for $[M + H]^{+}$ $(C_{13}H_{18}NOSi)^{+}$: 232.1152; found = 232.1150.

N-(3-Ethynylphenyl)acetamide, **3.64-int2**



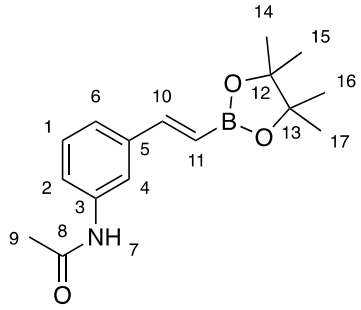
Prepared according to General Procedure 4 using *N*-(3-((trimethylsilyl)ethynyl)phenyl)acetamide **3.64-int1** (1.21 g, 5.23 mmol, 1.0 equiv.) and potassium carbonate (1.45 g, 10.5 mmol, 2.0 equiv.) in MeOH (26 mL, 0.2 M). The crude residue was purified by flash chromatography (silica gel) from pure hexane to a mixture of 35% of ethyl acetate in hexane affording 696 mg of a white solid consistent with the desired product (84%).

^{1}H NMR (500 MHz, Chloroform-*d*) δ 7.68 – 7.59 (m, 2H, H^4 and H^7), 7.55 – 7.51 (m, 1H, H^1), 7.27 – 7.24 (m, 1H, H^2), 7.24 – 7.20 (m, 1H, H^6), 3.06 (s, 1H, H^{11}), 2.17 (s, 3H, H^9).

^{13}C NMR (126 MHz, Chloroform-*d*) δ 168.8 (C^8), 138.1 (C^3), 129.1 (C^2), 128.1 (C^6), 123.4 (C^4), 122.9 (C^5), 120.6 (C^1), 83.3 (C^{10}), 77.6 (C^{11}), 24.7 (C^9).

Data are consistent with the literature.[291]

(*E*)-*N*-(3-(2-(4,4,5,5-Tetramethyl-1,3,2-dioxaborolan-2-yl)vinyl)phenyl)acetamide, **3.64-int3**



Prepared according to General Procedure 5 using *N*-(3-ethynylphenyl)acetamide **3.64-int2** (637 mg, 4.00 mmol, 1.0 equiv.), copper(I) chloride (20 mg, 200 μmol, 5 mol%), potassium *tert*-butoxide (45 mg, 400 μmol, 10 mol%), bis(2-diphenylphosphinophenyl) ether (DPEPhos) (108 mg, 200 umol, 5 mol%), bis(pinacolato)diboron (1.12 g, 4.40 mmol, 1.1 equiv.), and MeOH (320 μL, 8.00 mmol, 2.0 equiv.) in THF (16 mL, 0.25M). The crude residue was purified by flash chromatography (silica gel) from pure hexane to a mixture of 35% of ethyl acetate in hexane affording 819 mg of white solid consistent with the desired product (71%).

^{1}H NMR (500 MHz, Chloroform-*d*) δ 8.20 (broad s, 1H, H^7), 7.58 (t, *J* = 1.92 Hz, 1H, H^4), 7.50 – 7.46 (m, 1H, H^1), 7.31 (d, *J* = 18.41 Hz, 1H, H^{10}), 7.25 – 7.18 (m, 2H, H^2 and H^6), 6.10 (d, *J* = 18.41 Hz, 1H, H^{11}), 2.11 (s, 3H, H^9), 1.28 (s, 12H, H^{14}, H^{15}, H^{16} and H^{17}).

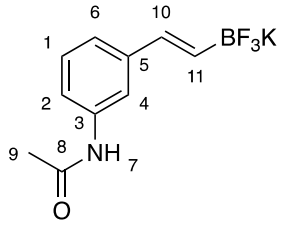
^{11}B NMR (96 MHz, Chloroform-*d*) δ 31.95.

^{13}C NMR (126 MHz, Chloroform-*d*) δ 169.1 (C^8), 149.2 (C^{10}), 138.4 (C^3), 138.2 (C^5), 129.2 (C^2), 122.9 (C^6), 120.7 (C^1), 118.7 (C^4), 117.0 (broad, C^{11}), 83.4 (C^{12} and C^{13}), 24.8 (C^9), 24.5 (C^{14}, C^{15}, C^{16} and C^{17}).

IR (film): 2994, 1666, 1626, 1587, 1483, 1431, 1379, 1372, 1346, 1321, 1248, 1139, 968, 729 cm^{-1}.

HRMS (ESI): *m/z* calculated for $[M + H]^+$ $(C_{16}H_{23}BNO_3)^+$: 288.1765; found = 288.1760.

(*E*)-*N*-(3-(2-(Trifluoro-λ^4-boraneyl)vinyl)phenyl)acetamide, potassium salt, **3.64-int4**



Prepared according to General Procedure 6 using (*E*)-*N*-(3-(2-(4,4,5,5-tetramethyl-1,3,2-dioxaborolan-2-yl)vinyl)phenyl)acetamide **3.64-int3** (800 mg, 2.79 mmol, 1.0 equiv.), potassium hydrogen fluoride (870 mg, 11.1 mmol, 4.0 equiv.), and water (2.51 mL, 139 mmol, 50.0 equiv.) in MeOH (26 mL, 0.1 M). 502 mg of a white solid was obtained after filtration, consistent with the desired product (67%).

^{1}H NMR (500 MHz, DMSO-d_6) δ 9.82 (broad s, 1H, H^7), 7.49 (t, *J* = 1.90 Hz, 1H, H^4), 7.41 – 7.38 (m, 1H, H^2), 7.15 (t, *J* = 7.82 Hz, 1H, H^1), 6.97 (dt, *J* = 7.79, 1.38 Hz, 1H, H^6), 6.41 (d, *J* = 18.14 Hz, 1H, H^{10}), 6.14 (dq, *J* = 18.19, 3.55 Hz, 1H, H^{11}), 2.03 (s, 3H, H^9).

^{11}B NMR (128 MHz, DMSO-d_6) δ 2.62.

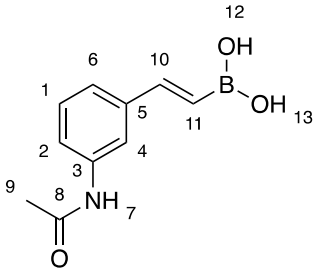
^{13}C NMR (126 MHz, DMSO-d_6) δ 168.2 (C^8), 140.8 (C^5), 139.4 (C^3), 138.9 (broad, C^{11}), 133.1 (q, $^3J_{CF}$ = 4.4 Hz, C^{10}), 128.5 (C^1), 120.5 (C^6), 116.8 (C^2), 116.0 (C^4), 24.1 (C^9).

^{19}F {^{1}H} NMR (377 MHz, DMSO-d_6) δ –137.87.

IR (solid): 1676, 1660, 1583, 1541, 1494, 1423, 1406, 1369, 1307, 1296, 1103, 1074, 1010, 993 cm^{-1}.

HRMS (ESI): *m/z* calculated for $[M - K]^-$ $(C_{10}H_{10}BNOF_3)^-$: 228.0813; found = 228.0822.

(*E*)-(3-Acetamidostyryl)boronic acid, **3.64**



Prepared according to General Procedure 7 using (*E*)-*N*-(3-(2-(trifluoro-λ^4-boraneyl)vinyl) phenyl)acetamide, potassium salt **3.64-int4** (430 mg, 1.61 mmol, 1.0 equiv.) and chlorotrimethylsilane (720 μL, 5.63 mmol, 3.5 equiv.) in MeCN:H_2O (13 mL:3 mL, 0.1 M). 250 mg of a pale-brown solid was obtained (65%) as a mixture of the desired product and protodeboronated product (ratio 2:1).

^{1}H NMR (400 MHz, Acetone-d_6) δ 7.90 (t, *J* = 1.93 Hz, 1H, H^4), 7.54 – 7.51 (m, 1H, H^2), 7.33 (d, *J* = 18.36 Hz, 1H, H^{10}), 7.28 – 7.24 (m, 1H, H^1), 7.20 – 7.16 (m, 1H, H^6), 6.19 (d, *J* = 18.34 Hz, 1H, H^{11}), 2.08 (s, 3H, H^9). H^7, H^{12} and H^{13} are not observed.

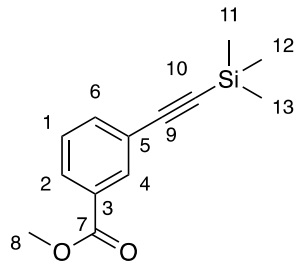
^{11}B NMR (128 MHz, Acetone-d_6) δ 28.75.

^{13}C NMR (126 MHz, Acetone-d_6) δ 168.9 (C^8), 147.5 (C^{10}), 140.8 (C^3), 139.5 (C^5), 129.8 (C^1), 122.7 (C^6), 119.9 (C^2), 117.9 (C^4), 24.3 (C^9). C^{11} is not observed due to quadrupolar relaxation.

IR (film): 2972, 1672, 1556, 1487, 1425, 1371, 1323, 1071, 1045, 879 cm^{-1}.

HRMS (MALDI): *m/z* calculated for $[M + H]^+$ $(C_{10}H_{13}BNO_3)^+$: 206.0983; found = 206.0984.

Methyl 3-((trimethylsilyl)ethynyl)benzoate, **3.65-int1**



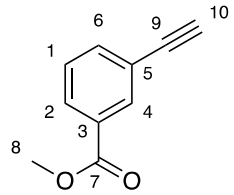
Prepared according to General Procedure 3 using methyl 3-iodobenzoate (1.31 g, 5.00 mmol, 1.0 equiv.), dichlorobis(triphenylphosphine)palladium (35 mg, 50.0 μmol, 1 mol%), copper iodide (19 mg, 100 μmol, 2 mol%), and trimethylsilylacetylene (660 μL, 6.25 mmol, 1.25 equiv.) in triethylamine (10 mL, 0.5 M). The crude residue was purified by flash chromatography (silica gel) from pure hexane to a mixture of 2% of diethyl ether in hexane affording 1.15 g of a pale-yellow solid as the desired product (99%).

^{1}H NMR (500 MHz, Chloroform-*d*) δ 8.15 – 8.12 (m, 1H, H^{4}), 7.97 (dt, *J* = 7.80, 1.52 Hz, 1H, H^{2}), 7.63 (dt, *J* = 7.77, 1.55 Hz, 1H, H^{6}), 7.38 (t, *J* = 7.78 Hz, 1H, H^{1}), 3.92 (s, 3H, H^{8}), 0.26 (s, 9H, H^{11}, H^{12} and H^{13}).

^{13}C NMR (126 MHz, Chloroform-*d*) δ 166.5 (C^{7}), 136.2 (C^{6}), 133.3 (C^{4}), 130.4 (C^{3}), 129.6 (C^{2}), 128.5 (C^{1}), 123.7 (C^{5}), 104.0 (C^{9}), 95.5 (C^{10}), 52.4 (C^{8}), 0.0 (C^{11}, C^{12} and C^{13}).

Data are consistent with the literature.[292]

Methyl 3-ethynylbenzoate, **3.65-int2**



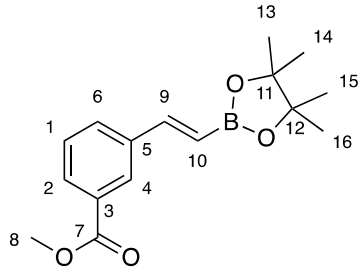
Prepared according to General Procedure 4 using methyl 3-((trimethylsilyl)ethynyl)benzoate **3.65-int1** (1.10 g, 4.73 mmol, 1.0 equiv.) and potassium carbonate (1.31 g, 9.47 mmol, 2.0 equiv.) in MeOH (23 mL, 0.2 M). After work-up 354 mg of a white solid was afforded consistent with the desired product (47%).

^{1}H NMR (500 MHz, Chloroform-*d*) δ 8.16 (t, *J* = 1.76 Hz, 1H, H^{4}), 8.01 (dt, *J* = 7.89, 1.49 Hz, 1H, H^{2}), 7.66 (dt, *J* = 7.69, 1.48 Hz, 1H, H^{6}), 7.40 (t, *J* = 7.77 Hz, 1H, H^{1}), 3.92 (s, 3H, H^{8}), 3.12 (s, 1H, H^{10}).

^{13}C NMR (126 MHz, Chloroform-*d*) δ 166.4 (C^{7}), 136.4 (C^{6}), 133.4 (C^{4}), 130.6 (C^{3}), 129.9 (C^{2}), 128.6 (C^{1}), 122.7 (C^{5}), 82.7 (C^{9}), 78.3 (C^{10}), 52.4 (C^{8}).

Data are consistent with the literature.[293]

Methyl (*E*)-3-(2-(4,4,5,5-tetramethyl-1,3,2-dioxaborolan-2-yl)vinyl)benzoate, **3.65-int3**



Prepared according to General Procedure 5 using methyl 3-ethynylbenzoate **3.65-int3** (641 mg, 4.00 mmol, 1.0 equiv.), copper(I) chloride (20 mg, 200 μmol, 5 mol%), potassium *tert*-butoxide (45 mg, 400 μmol, 10 mol%), bis(2-diphenylphosphinophenyl)ether (DPEPhos) (108 mg, 200 μmol, 5 mol%), bis(pinacolato)diboron (1.12 g, 4.40 mmol, 1.1 equiv.), and MeOH (320 μL, 8.00 mmol, 2.0 equiv.) in THF (16 mL). The crude residue was purified by flash chromatography (silica gel) from pure hexane to a mixture of 10% of diethyl ether in hexane affording 670 mg of a white solid consistent with the desired product (58%).

^{1}H NMR (500 MHz, Chloroform-*d*) δ 8.14 (t, *J* = 1.78 Hz, 1H, H^{4}), 7.93 (dt, *J* = 7.72, 1.45 Hz, 1H, H^{2}), 7.63 (dt, *J* = 7.76, 1.52 Hz, 1H, H^{6}), 7.43 – 7.35 (m, 2H, H^{1} and H^{9}), 6.22 (d, *J* = 18.48 Hz, 1H, H^{10}), 3.88 (s, 3H, H^{8}), 1.29 (s, 12H, H^{13}, H^{14}, H^{15} and H^{16}).

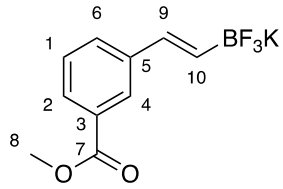
^{11}B NMR (96 MHz, Chloroform-*d*) δ 30.30.

^{13}C NMR (126 MHz, Chloroform-*d*) δ 166.9 (C^7), 148.3 (C^9), 137.9 (C^5), 131.2 (C^6), 130.6 (C^3), 129.8 (C^2), 128.7 (C^1), 128.3 (C^4), 118.0 (broad, C^{10}), 83.5 (C^{11} and C^{12}), 52.2 (C^8), 24.9 (C^{13}, C^{14}, C^{15} and C^{16}).

IR (film): 2551, 1722, 1626, 1379, 1345, 1325, 1288, 1265, 1203, 1141, 970, 848, 748 cm^{-1}.

HRMS (ESI): *m/z* calculated for $[M + H]^+$ $(C_{16}H_{22}BO_4)^+$: 289.1605; found = 289.1602.

Methyl (*E*)-3-(2-(trifluoro-λ^4-boraneyl)vinyl)benzoate, potassium salt, **3.65-int4**



Prepared according to General Procedure 6 using methyl (*E*)-3-(2-(4,4,5,5-tetramethyl-1,3,2-dioxaborolan-2-yl)vinyl)benzoate **3.65-int3** (670 mg, 2.33 mmol, 1.0 equiv.), potassium hydrogen fluoride (726 mg, 9.30 mmol, 4.0 equiv.), and water (2.09 mL, 116 mmol, 50.0 equiv.) in MeOH (22 mL, 0.1 M). 582 mg of a white solid was obtained after filtration, consistent with the desired product (93%).

^{1}H NMR (500 MHz, DMSO-d_6) δ 7.88 (t, *J* = 1.85 Hz, 1H, H^4), 7.71 (dt, *J* = 7.71, 1.50 Hz, 1H, H^2), 7.60 (dt, *J* = 7.83, 1.45 Hz, 1H, H^6), 7.41 (t, *J* = 7.69 Hz, 1H, H^1), 6.53 (d, *J* = 18.19 Hz, 1H, H^9), 6.28 (dq, *J* = 18.22, 3.51 Hz, 1H, H^{10}), 3.85 (s, 3H, H^8).

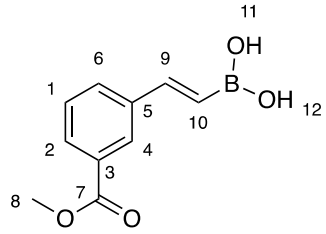
^{11}B NMR (96 MHz, DMSO-d_6) δ 2.86.

^{13}C NMR (126 MHz, DMSO-d_6) δ 166.5 (C^7), 140.8 (C^5), 132.1 (q, $^3J_{CF}$ = 4.5 Hz, C^9), 130.1 (C^6), 129.8 (C^3), 128.8 (C^1), 126.6 (C^2), 125.9 (C^4), 52.1 (C^8). C^{10} is not observed due to quadrupolar relaxation.

^{19}F {^{1}H} NMR (376 MHz, DMSO-d_6) δ –138.11.

Data are consistent with the literature.[294]

(*E*)-(3-(Methoxycarbonyl)styryl)boronic acid, **3.65**



Prepared according to General Procedure 7 using methyl (*E*)-3-(2-(trifluoro-λ^4-boraneyl)vinyl)benzoate, potassium salt **3.65-int4** (500 mg, 1.87 mmol, 1.0 equiv.) and chlorotrimethylsilane (830 μL, 6.53 mmol, 3.5 equiv.) in MeCN:H_2O (15 mL:4 mL, 0.1 M). 251 mg of a white solid was afforded as the desired product (65%) as a mixture of the desired product and boroxine.

^{1}H NMR (500 MHz, DMSO-d_6) δ 8.02 (t, *J* = 1.82 Hz, 1H, H^4), 7.90 (s, 2H, H^{11} and H^{12}), 7.87 (dt, *J* = 7.80, 1.36 Hz, 1H, H^2), 7.74 (dt, *J* = 7.71, 1.50 Hz, 1H, H^6), 7.51 (t, *J* = 7.72 Hz, 1H, H^1), 7.31 (d, *J* = 18.37 Hz, 1H, H^9), 6.22 (d, *J* = 18.38 Hz, 1H, H^{10}), 3.86 (s, 3H, H^8).

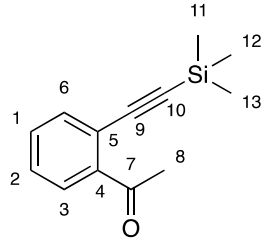
^{11}B NMR (128 MHz, DMSO-d_6) δ 26.62.

^{13}C NMR (126 MHz, DMSO-d_6) δ 166.2 (C^7), 144.6 (C^9), 138.2 (C^5), 131.4 (C^6), 130.2 (C^3), 129.4 (C^1), 129.0 (C^2), 126.9 (C^4), 125.0 (broad, C^{10}), 52.3 (C^8).

IR (solid): 1720, 1705, 1624, 1442, 1355, 1348, 1288, 1226, 1170, 1099, 1078, 989, 844, 744 cm^{-1}.

HRMS (ESI): *m/z* calculated for [M (methyl boronic ester) + H]$^+$ $(C_{12}H_{16}BO_4)^+$: 235.1136; found = 235.1136.

1-(2-((Trimethylsilyl)ethynyl)phenyl)ethan-1-one, **3.66-int1**



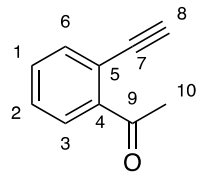
Prepared according to General Procedure 3 using iodoacetophenone (720 μL, 5.00 mmol, 1.0 equiv.), dichlorobis(triphenylphosphine)palladium (35 mg, 50.0 μmol, 1 mol%), copper iodide (19 mg, 100 μmol, 2 mol%), and trimethylsilylacetylene (660 μL, 6.25 mmol, 1.25 equiv.) in triethylamine (10 mL, 0.5 M). The crude residue was purified by flash chromatography (silica gel) from pure hexane to a mixture of 4% of diethyl ether in hexane affording 1.08 g of a yellow oil as the desired product (100%).

^{1}H NMR (500 MHz, Chloroform-*d*) δ 7.68 (ddd, *J* = 7.68, 1.54, 0.55 Hz, 1H, H^{3}), 7.56 (ddd, *J* = 7.61, 1.49, 0.56 Hz, 1H, H^{6}), 7.42 (td, *J* = 7.52, 1.55 Hz, 1H, H^{1}), 7.38 (td, *J* = 7.56, 1.49 Hz, 1H, H^{2}), 2.75 (s, 3H, H^{8}), 0.26 (s, 9H, H^{11}, H^{12} and H^{13}).

^{13}C NMR (126 MHz, Chloroform-*d*) δ 201.0 (C^{7}), 141.7 (C^{4}), 134.4 (C^{6}), 131.3 (C^{1}), 128.7 (C^{2}), 128.6 (C^{3}), 121.5 (C^{5}), 104.0 (C^{9}), 101.3 (C^{10}), 30.3 (C^{8}), –0.2 (C^{11}, C^{12} and C^{13}).

Data are consistent with the literature.[295]

1-(2-Ethynylphenyl)ethan-1-one, **3.66-int2**



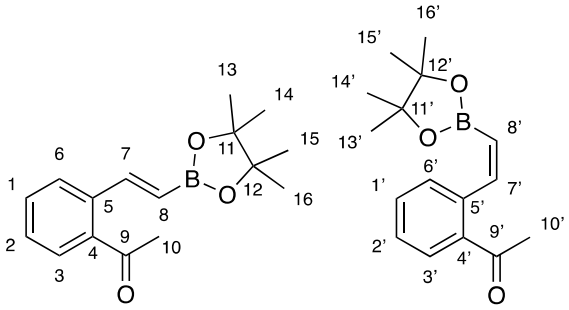
Prepared according to General Procedure 4 using 1-(2-((trimethylsilyl)ethynyl)phenyl)ethan-1-one **3.66-int1** (1.08 g, 5.0 mmol, 1.0 equiv.) and potassium carbonate (1.38 g, 10.0 mmol, 2.0 equiv.) in MeOH (25 mL, 0.2 M). The crude residue was purified by flash chromatography (silica gel) from pure hexane to a mixture of 4% of diethyl ether in hexane affording 276 mg of a pale-yellow oil consistent with the desired product (38%).

^{1}H NMR (500 MHz, Chloroform-*d*) δ 7.70 (dd, *J* = 7.63, 1.51 Hz, 1H, H^{3}), 7.60 (dd, *J* = 7.51, 1.42 Hz, 1H, H^{6}), 7.45 (td, *J* = 7.69, 1.91 Hz, 1H, H^{1}), 7.41 (td, *J* = 6.02, 1.46 Hz, 1H, H^{2}), 3.39 (s, 1H, H^{8}), 2.71 (s, 3H, H^{10}).

^{13}C NMR (126 MHz, Chloroform-*d*) δ 200.3 (C^9), 141.6 (C^4), 134.9 (C^6), 131.4 (C^1), 128.9 (C^2), 128.6 (C^3), 120.5 (C^5), 83.0 (C^8), 82.6 (C^7), 30.0 (C^{10}).

Data are consistent with the literature.[295]

(*E*) and (*Z*)-1-(2-(2-(4,4,5,5-Tetramethyl-1,3,2-dioxaborolan-2-yl)vinyl)phenyl)ethan-1-one, **3.66-int3**



Prepared according to General Procedure 5 using 1-(2-ethynylphenyl)ethan-1-one **3.66-int2** (276 mg, 1.91 mmol, 1.0 equiv.), copper(I) chloride (9 mg, 95.7 μmol, 5 mol%), potassium *tert*-butoxide (21 mg, 191 μmol, 10 mol%), bis(2-diphenylphosphinophenyl)ether (DPEPhos) (52 mg, 95.7 μmol, 5 mol%), bis(pinacolato)diboron (535 mg, 2.11 mmol, 1.1 equiv.), and MeOH (160 μL, 3.83 mmol, 2.0 equiv.) in THF (7 mL, 0.25 M). The crude residue was purified by flash chromatography (silica gel) from pure hexane to a mixture of 10% of diethyl ether in hexane affording 246 mg of a colourless oil consistent with a mixture of *E* and *Z* of the desired product (47%, 0.65:0.35 *Z:E*).

(*E*)-1-(2-(2-(4,4,5,5-Tetramethyl-1,3,2-dioxaborolan-2-yl)vinyl)phenyl)ethan-1-one,

^{1}H NMR (400 MHz, Chloroform-*d*) δ 7.77 (d, *J* = 18.21 Hz, 1H, H^7), 7.67 – 7.59 (m, 2H, H^{arom}), 7.49 – 7.43 (m, 1H, H^{arom}), 7.39 – 7.34 (m, 1H, H^{arom}), 6.06 (d, *J* = 18.21 Hz, 1H, H^8), 2.59 (s, 3H, H^{10}), 1.30 (s, 12H, H^{13}, H^{14}, H^{15} and H^{16}).

^{11}B NMR (96 MHz, Chloroform-*d*) δ 30.91.

^{13}C NMR (126 MHz, Chloroform-*d*) δ 202.2 (C^{9}), 148.1 (C^{7}), 138.4 (C^{4}), 137.8 (C^{5}), 131.7 (C^{arom}), 128.5 (C^{arom}), 128.3 (C^{arom}), 127.9 (C^{arom}), 83.5 (C^{11} and C^{12}), 30.0 (C^{10}), 25.0 (C^{13}, C^{14}, C^{15} and C^{16}). C^{8} is not observed due to quadrupolar relaxation.

(*Z*)-1-(2-(2-(4,4,5,5-Tetramethyl-1,3,2-dioxaborolan-2-yl)vinyl)phenyl)ethan-1-one,

^{1}H NMR (400 MHz, Chloroform-*d*) δ 7.76 – 7.71 (app. d, 1H, $H^{3'}$), 7.67 – 7.59 (m, 1H, $H^{7'}$), 7.43 – 7.40 (m, 2H, $H^{1'}$ and $H^{6'}$), 7.39 – 7.34 (m, 1H, $H^{2'}$), 5.68 (d, *J* = 14.51 Hz, 1H, $H^{8'}$), 2.58 (s, 3H, $H^{10'}$), 1.17 (s, 12H, $H^{13'}$, $H^{14'}$, $H^{15'}$ and $H^{16'}$).

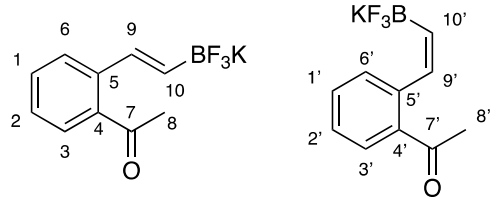
^{11}B NMR (96 MHz, Chloroform-*d*) δ 30.91.

^{13}C NMR (126 MHz, Chloroform-*d*) δ, 201.0 ($C^{9'}$), 149.4 ($C^{7'}$), 139.5 ($C^{5'}$), 137.0 ($C^{4'}$), 131.2 ($C^{1'}$ or $C^{6'}$), 131.1 ($C^{1'}$ or $C^{6'}$), 129.1 ($C^{3'}$), 127.8 ($C^{2'}$), 83.3 ($C^{11'}$ and $C^{12'}$), 29.6 ($C^{10'}$), 24.8 ($C^{13'}$, $C^{14'}$, $C^{15'}$ and $C^{16'}$). $C^{8'}$ is not observed due to quadrupolar relaxation.

IR (film): 2978, 1616, 1564, 1477, 1379, 1371, 1348, 1325, 1249, 1141, 968, 758 cm^{-1}.

HRMS (ESI): *m/z* calculated for $[M + H]^{+}$ $(C_{16}H_{22}BO_3)^{+}$: 273.1656; found = 273.1665.

(*E*) and (*Z*)-1-(2-(2-(Trifluoro-λ^4-boraneyl)vinyl)phenyl)ethan-1-one, potassium salt, **3.66-int4**



Prepared according to General Procedure 6 using the mixture of (*E*) and (*Z*)-1-(2-(2-(4,4,5,5-tetramethyl-1,3,2-dioxaborolan-2-yl)vinyl)phenyl)ethan-1-one **3.66-int3** (275 mg, 1.01 mmol, 1.0 equiv.), potassium hydrogen fluoride (316 mg, 4.04 mmol, 4.0 equiv.), and water (910 μL, 50.5 mmol, 50.0 equiv.) in MeOH (10 mL, 0.1 M). 150 mg of a white solid was obtained after filtration, consistent with a mixture of *E* and *Z* of the desired product (59%, 0.68:0.32 *Z:E*).

(*E*)-1-(2-(2-(Trifluoro-λ^4-boraneyl)vinyl)phenyl)ethan-1-one, potassium salt,

^{1}H NMR (400 MHz, DMSO-d_6) δ, 7.53 (app. d, J = 7.87 Hz, 1H, H^6), 7.51 – 7.43 (m, 1H, H^3), 7.39 (app. t, J = 7.55 Hz, 1H, H^2), 7.24 – 7.15 (m, 1H, H^1), 6.74 (d, J = 18.07 Hz, 1H, H^9), 6.10 (dq, J = 18.09, 3.53 Hz, 1H, H^{10}), 2.47 (s, 3H, H^8).

^{11}B NMR (96 MHz, DMSO-d_6) δ 2.47.

^{13}C NMR (101 MHz, DMSO-d_6) δ 203.7 (C^7), 138.9 (C^5), 138.3 (C^4), 132.9 (q, $^3J_{CF}$ = 4.9 Hz, C^9), 130.5 (C^2), 127.4 (C^3), 126.0 (C^6), 125.6 (C^1), 30.7 (C^8). C^{10} is not observed due to quadrupolar relaxation.

^{19}F {^{1}H} NMR (377 MHz, Chloroform-d) δ –133.30.

(*Z*)-1-(2-(2-(Trifluoro-λ^4-boraneyl)vinyl)phenyl)ethan-1-one, potassium salt,

^{1}H NMR (400 MHz, DMSO-d_6) δ 7.85 (app. d, J = 7.83 Hz, 1H, $H^{6'}$), 7.51 – 7.43 (m, 1H, $H^{3'}$), 7.35 – 7.29 (m, 1H, $H^{1'}$), 7.24 – 7.15 (m, 1H, $H^{2'}$), 6.67 (d, J = 14.99 Hz, 1H, $H^{9'}$), 5.61 (dq, J = 15.03, 5.90 Hz, 1H, $H^{10'}$), 2.47 (s, 3H, $H^{8'}$).

^{11}B NMR (96 MHz, DMSO-d_6) δ 2.47.

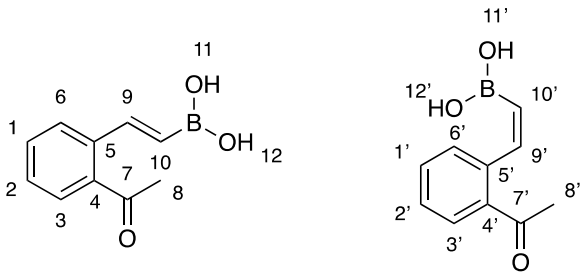
^{13}C NMR (101 MHz, DMSO-d_6) δ 203.1 ($C^{7'}$), 139.8 ($C^{5'}$), 138.1 ($C^{4'}$), 130.6 (q, $^3J_{CF}$ = 4.0 Hz, $C^{9'}$), 130.5 ($C^{6'}$), 129.8 ($C^{1'}$), 126.9 ($C^{3'}$), 125.3 ($C^{2'}$), 30.7 ($C^{8'}$). $C^{10'}$ is not observed due to quadrupolar relaxation.

^{19}F {^{1}H} NMR (377 MHz, Chloroform-d) δ –127.47.

IR (solid): 1611, 1230, 1159, 1053, 1004, 954, 931 cm^{-1}.

HRMS (ESI): m/z calculated for $[M - K]^-$ $(C_{10}H_9BOF_3)^-$: 213.0704; found = 213.0710.

(*E*) and (*Z*)-(2-acetylstyryl)boronic acid, **3.66**



Prepared according to General Procedure 7 using a mixture of (*E*) and (*Z*)-1-(2-(2-(Trifluoro-λ^4-boraneyl)vinyl)phenyl)ethan-1-one, potassium salt **3.66-int4** (463 mg, 1.84 mmol, 1.0 equiv.) and chlorotrimethylsilane (820 μL, 6.43 mmol, 3.5 equiv.) in MeCN:H_2O (15 mL:4 mL, 0.1 M). 86 mg of a pale-yellow solid was obtained as a mixture of *E* and *Z* of the desired product and boroxine (25%, 0.5:0.5 *Z:E*).

(*E*)-(2-acetylstyryl)boronic acid,

^{1}H NMR (500 MHz, Acetonitrile-d_3) δ 7.69 (dd, *J* = 7.79, 1.40 Hz, 1H, H^3), 7.67 (d, *J* = 7.89 Hz, 1H, H^6), 7.62 (d, *J* = 18.17 Hz, 1H, H^9), 7.52 – 7.48 (m, 1H, H^1), 7.42 – 7.40 (m, 1H, H^2), 6.02 (d, *J* = 18.27 Hz, 1H, H^{10}), 5.94 (s, 2H, H^{11} and H^{12}), 2.54 (s, 3H, H^8).

^{11}B NMR (128 MHz, Acetonitrile-d_3) δ 29.07.

^{13}C NMR (126 MHz, Acetonitrile-d_3) δ 203.3 (C^7), 146.7 (C^9), 139.4 (C^5), 138.3 (or 138.2, C^4), 132.4 (C^1), 129.5 (C^3), 129.1(C^2), 128.3 (C^6), 125.7 (broad, C^{10}), 30.3 (or 29.9, C^8).

(*Z*)-(2-acetylstyryl)boronic acid,

^{1}H NMR (500 MHz, Acetonitrile-d_3) δ 7.79 (dd, *J* = 7.69, 1.41 Hz, 1H, H$^{3'}$), 7.47 (dd, *J* = 7.58, 1.40 Hz, 1H, H$^{6'}$), 7.42 – 7.40 (m, 1H, H$^{2'}$), 7.40 – 7.36 (m, 2H, H$^{1'}$ and H$^{9'}$), 5.74 (s, 2H, H$^{11'}$ and H$^{12'}$), 5.66 (d, *J* = 14.71 Hz, 1H, H$^{10'}$), 2.54 (s, 3H, H$^{8'}$).

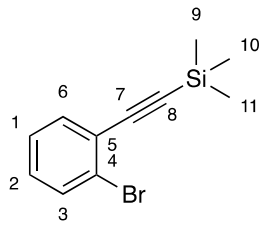
^{11}B NMR (128 MHz, Acetonitrile-d_3) δ 29.07.

^{13}C NMR (126 MHz, Acetonitrile-d_3) δ 202.4 (C$^{7'}$), 145.8 (C$^{9'}$), 140.0 (C$^{5'}$), 138.3 (or 138.2, C$^{4'}$), 132.4 (C$^{6'}$), 130.8 (C$^{1'}$), 130.1 (C$^{3'}$), 128.7 (C$^{2'}$), 125.7 (broad, C$^{10'}$), 30.3 (or 29.9, C$^{8'}$).

IR (film): 3414, 1678, 1616, 1595, 1562, 1475, 1355, 1290, 1253, 1089, 1049, 995 cm^{-1}.

HRMS (ESI): *m/z* calculated for $[M + H]^+$ $(C_{10}H_{12}BO_3)^+$: 191.0874; found = 191.0873.

((2-Bromophenyl)ethynyl)trimethylsilane, **3.67-int1**



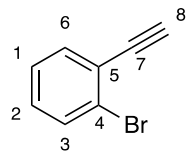
Prepared according to General Procedure 3 using 2-bromoiodobenzene (720 μL, 5.00 mmol, 1.0 equiv.), dichlorobis(triphenylphosphine)palladium (35 mg, 50.0 μmol, 1 mol%), copper iodide (19 mg, 100 μmol, 2 mol%), and trimethylsilylacetylene (660 μL, 6.25 mmol, 1.25 equiv.) in triethylamine (10 mL, 0.5 M). The crude residue was purified by flash chromatography (silica gel) with pure hexane affording 1.20 g of a pale-yellow oil as the desired product (95%).

^{1}H NMR (500 MHz, Chloroform-*d*) δ 7.57 (dd, *J* = 8.09, 1.22 Hz, 1H, H^3), 7.49 (dd, *J* = 7.70, 1.72 Hz, 1H, H^6), 7.24 (td, *J* = 7.59, 1.27 Hz, 1H, H^1), 7.15 (td, *J* = 7.74, 1.73 Hz, 1H, H^2), 0.28 (s, 9H, H^9, H^{10} and H^{11}).

^{13}C NMR (126 MHz, Chloroform-*d*) δ 133.7 (C^6), 132.5 (C^3), 129.7 (C^2), 127.0 (C^1), 125.9 (C^4), 125.4 (C^5), 103.2 (C^7), 99.8 (C^8), 0.0 (C^9, C^{10} and C^{11}).

Data are consistent with the literature.[296]

1-Bromo-2-ethynylbenzene, **3.67-int2**



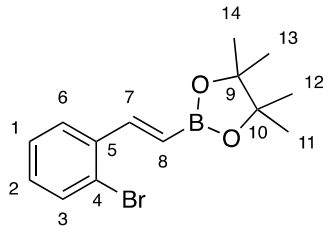
Prepared according to General Procedure 4 using (2-bromophenylethynyl)trimethylsilane **3.67-int1** (1.20 g, 4.74 mmol, 1.0 equiv.) and potassium carbonate (1.31 g, 9.48 mmol, 2.0 equiv.) in MeOH (25 mL, 0.2 M). The crude residue was purified by flash chromatography (silica gel) with pure hexane affording 785 mg of a pale-yellow oil consistent with the desired product (92%).

^{1}H NMR (500 MHz, Chloroform-*d*) δ 7.59 (dd, *J* = 8.03, 1.27 Hz, 1H, H^{3}), 7.53 (dd, *J* = 7.65, 1.75 Hz, 1H, H^{6}), 7.27 (td, *J* = 7.59, 1.29 Hz, 1H, H^{1}), 7.21 (td, *J* = 7.74, 1.76 Hz, 1H, H^{2}), 3.38 (s, 1H, H^{8}).

^{13}C NMR (126 MHz, Chloroform-*d*) δ 134.2 (C^{6}), 132.6 (C^{3}), 130.1 (C^{2}), 127.2 (C^{1}), 125.7 (C^{4}), 124.4 (C^{5}), 82.0 (C^{7}), 81.9 (C^{8}).

Data are consistent with the literature.[296]

(*E*)-2-(2-Bromostyryl)-4,4,5,5-tetramethyl-1,3,2-dioxaborolane, **3.67-int3**



Prepared according to General Procedure 5 using 1-bromo-2-ethynylbenzene **S6-int2** (780 mg, 4.31 mmol, 1.0 equiv.), copper(I) chloride (21 mg, 215 μmol, 5 mol%), potassium *tert*-butoxide (48 mg, 431 μmol, 10 mol%), bis(2-diphenylphosphinophenyl)ether (DPEPhos) (116 mg, 215 μmol, 5 mol%), bis(pinacolato)diboron (1.20 g, 4.74 mmol, 1.1 equiv.), and MeOH (350 μL, 8.62 mmol, 2.0 equiv.) in THF (18 mL, 0.25 M). The crude residue was purified by flash chromatography (silica gel) from pure hexane to a mixture of 3% of diethyl ether in hexane affording 927 mg of a colourless oil consistent with the desired product (70%).

^{1}H NMR (500 MHz, Chloroform-*d*) δ 7.71 (d, *J* = 18.23 Hz, 1H, H^{7}), 7.61 (dd, *J* = 7.83, 1.69 Hz, 1H, H^{6}), 7.55 (dd, *J* = 8.02, 1.24 Hz, 1H, H^{3}), 7.31 – 7.27 (m, 1H, H^{1}),

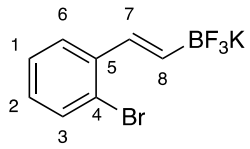
7.14 (td, *J* = 7.75, 1.65 Hz, 2H, H^2), 6.13 (d, *J* = 18.22 Hz, 1H, H^8), 1.32 (s, 12H, H^{11}, H^{12}, H^{13} and H^{14}).

^{11}B NMR (96 MHz, Chloroform-*d*) δ 30.07.

^{13}C NMR (126 MHz, Chloroform-*d*) δ 147.7 (C^7), 137.5 (C^5), 133.2 (C^3), 130.0 (C^2), 127.6 (C^1), 127.4 (C^6), 124.4 (C^4), 120.3 (broad, C^8), 83.6 (C^9 and C^{10}), 25.0 (C^{11}, C^{12}, C^{13} and C^{14}).

Data are consistent with the literature.[297]

(*E*)-(2-Bromostyryl)trifluoro-λ^4-borane, potassium salt, **3.67-int4**



Prepared according to General Procedure 6 using (*E*)-2-(2-bromostyryl)-4,4,5,5-tetramethyl-1,3,2-dioxaborolane **3.67-int3** (900 mg, 2.91 mmol, 1.0 equiv.), potassium hydrogen fluoride (910 mg, 11.7 mmol, 4.0 equiv.), and water (2.62 mL, 146 mmol, 50.0 equiv.) in MeOH (25 mL, 0.1 M). 579 mg of a white solid was obtained after filtration, consistent with the desired product (69%).

^{1}H NMR (500 MHz, DMSO-d_6) δ 7.56 (dd, *J* = 7.87, 1.71 Hz, 1H, H^6), 7.51 (dd, *J* = 7.96, 1.28 Hz, 1H, H^3), 7.28 (td, *J* = 6.85, 0.96 Hz, 1H, H^1), 7.06 (td, *J* = 7.66, 1.69 Hz, 1H, H^2), 6.76 (d, *J* = 17.99 Hz, 1H, H^7), 6.21 (dq, *J* = 18.01, 3.53 Hz, 1H, H^8).

^{11}B NMR (96 MHz, DMSO-d_6) δ 2.66.

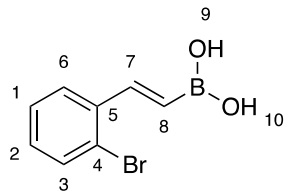
^{13}C NMR (126 MHz, DMSO-d_6) δ 139.3 (C^5), 132.5 (C^3), 131.1 (q, $^3J_{CF}$ = 4.4 Hz, C^7), 127.7 (C^1), 127.7 (C^2), 126.4 (C^6), 122.4 (C^4). C^8 is not observed due to quadrupolar relaxation.

^{19}F {^{1}H} NMR (377 MHz, DMSO-d_6) δ –138.07.

IR (solid): 1579, 1465, 1433, 1290, 1269, 1236, 1159, 1151, 1136, 1095, 1053, 989, 952 cm^{-1}.

HRMS (ESI): *m/z* calculated for $[M - K]^-$ ($C_8H_6B^{79}BrF_3$)$^-$: 248.9703; found = 248.9714.

(*E*)-(2-Bromostyryl)boronic acid, **3.67**



Prepared according to General Procedure 7 using (*E*)-(2-bromostyryl)trifluoro-λ^4-borane potassium salt, **3.67-int4** (500 mg, 1.73 mmol, 1.0 equiv.) and chlorotrimethylsilane (770 μL, 6.06 mmol, 3.5 equiv.) in MeCN:H_2O (14 mL:3 mL, 0.1 M). 360 mg of a white solid was obtained as a mixture of the desired product and boroxine (92%).

^{1}H NMR (500 MHz, DMSO-d_6) δ 7.95 (s, 2H, H^9 and H^{10}), 7.66 (dd, *J* = 7.88, 1.69 Hz, 1H, H^3), 7.62 (dd, *J* = 8.02, 1.22 Hz, 1H, H^6), 7.50 (d, *J* = 18.19 Hz, 1H, H^7), 7.42 – 7.37 (m, 1H, H^1), 7.24 (td, *J* = 7.66, 1.67 Hz, 1H, H^2), 6.12 (d, *J* = 18.16 Hz, 1H, H^8).

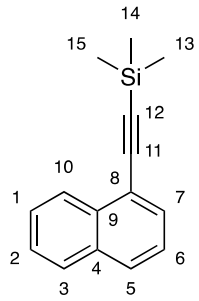
^{11}B NMR (96 MHz, DMSO-d_6) δ 26.85.

^{13}C NMR (126 MHz, DMSO-d_6) δ 143.6 (C^7), 137.2 (C^5), 133.0 (C^6), 130.2 (C^2), 128.2 (C^1), 127.3 (C^3), 123.3 (C^4). C^8 is not observed due to quadrupolar relaxation.

IR (solid): 1606, 1460, 1436, 1363, 1340, 1321, 1290, 1276, 1267, 1195, 1097, 1047 cm^{-1}.

HRMS (ESI): *m/z* calculated for $[M + Na]^+$ $(C_8H_8B^{79}BrO_2Na)^+$: 248.9692; found = 248.9693.

Trimethyl(naphthalen-1-ylethynyl)silane, **3.68-int1**



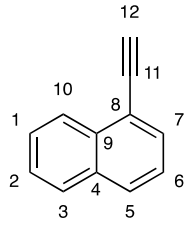
Prepared according to General Procedure 3 using 1-iodonaphthalene (720 μL, 5.00 mmol, 1.0 equiv.), dichlorobis(triphenylphosphine)palladium (35 mg, 50.0 μmol, 1 mol%), copper iodide (19 mg, 100 μmol, 2 mol%), and trimethylsilylacetylene (660 μL, 6.25 mmol, 1.25 equiv.) in triethylamine (10 mL, 0.5 M). The crude residue was purified by flash chromatography (silica gel) with pure hexane affording 1.12 g of a colourless oil as the desired product (100%).

^{1}H NMR (500 MHz, Chloroform-*d*) δ 8.36 (app. d, *J* = 8.32 Hz, 1H, H^{10}), 7.84 (app. t, *J* = 8.70 Hz, 2H, H^{3} and H^{5}), 7.62 – 7.58 (m, 1H, H^{7}), 7.62 – 7.58 (m, 1H, H^{1}), 7.55 – 7.51 (m, 1H, H^{2}), 7.44 – 7.40 (m, 1H, H^{6}), 0.36 (s, 9H, H^{13}, H^{14} and H^{15}).

^{13}C NMR (126 MHz, Chloroform-*d*) δ 133.5 (C^{4} or C^{9}), 133.2 (C^{4} or C^{9}), 130.9 (C^{7}), 129.1 (C^{5}), 128.4 (C^{3}), 127.0 (C^{1}), 126.5 (C^{2}), 126.3 (C^{10}), 125.3 (C^{6}), 120.9 (C^{8}), 103.2 (C^{11}), 99.6 (C^{12}), 0.3 (C^{13}, C^{14} and C^{15}).

Data are consistent with the literature.[298]

1-Ethynylnaphthalene, **3.68-int2**



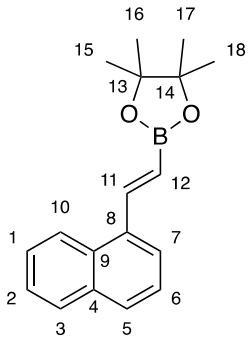
Prepared according to General Procedure 4 using trimethyl(naphthalen-1-ylethynyl)silane **3.68-int1** (1.12 g, 4.99 mmol, 1.0 equiv.) and potassium carbonate (1.38 g, 9.98 mmol, 2.0 equiv.) in MeOH (25 mL, 0.2 M). The crude residue was purified by flash chromatograpghy (silica gel) with pure hexane affording 707 mg of a pale-orange oil consistent with the desired product (64%).

^{1}H NMR (500 MHz, Chloroform-*d*) δ 8.40 (dd, *J* = 8.13, 1.21 Hz, 1H, H^{10}), 7.90 – 7.86 (m, 2H, H^{3} and H^{5}), 7.77 (dd, *J* = 7.08, 1.17 Hz, 1H, H^{7}), 7.61 (ddd, *J* = 8.30, 6.74, 1.35 Hz, 1H, H^{1}), 7.55 (ddd, *J* = 8.21, 6.82, 1.28 Hz, 1H, H^{2}), 7.45 (dd, *J* = 8.27, 7.14 Hz, 1H, H^{6}), 3.50 (s, 1H, H^{12}).

^{13}C NMR (126 MHz, Chloroform-*d*) δ 133.6 (C^4 or C^9), 133.2 (C^4 or C^9), 131.4 (C^7), 129.4 (C^5), 128.4 (C^3), 127.1 (C^1), 126.6 (C^2), 126.2 (C^{10}), 125.2 (C^6), 119.9 (C^8), 82.1 (C^{12}), 81.9 (C^{11}).

Data are consistent with the literature.[299]

(*E*)-4,4,5,5-Tetramethyl-2-(2-(naphthalen-1-yl)vinyl)-1,3,2-dioxaborolane, **3.68-int3**



Prepared according to General Procedure 5 using 1-ethynylnaphthalene **3.68-int2** (700 mg, 4.60 mmol, 1.0 equiv.), copper(I) chloride (23 mg, 230 μmol, 5 mol%), potassium *tert*-butoxide (57 mg, 460 μmol, 10 mol%), bis(2-diphenylphosphinophenyl) ether (DPEPhos) (124 mg, 230 μmol, 5 mol%), bis(pinacolato)diboron (1.28 g, 5.06 mmol, 1.1 equiv.), and MeOH (370 μL, 9.20 mmol, 2.0 equiv.) in THF (18 mL, 0.25 M).The crude residue was purified by flash chromatography (silica gel) from pure hexane to a mixture of 4% of diethyl ether in hexane affording 920 mg of a pale-yellow oil consistent with the desired product (71%).

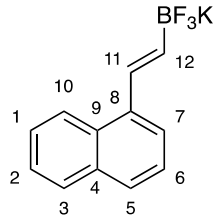
^{1}H NMR (500 MHz, Chloroform-*d*) δ 8.31 – 8.28 (m, 1H, H^{10}), 8.25 (d, *J* = 18.13 Hz, 1H, H^{11}), 7.88 – 7.85 (m, 1H, H^3), 7.83 (dd, *J* = 8.19, 1.08 Hz, 1H, H^5), 7.77 (dt, *J* = 7.22, 0.93 Hz, 1H, H^7), 7.54 (ddd, *J* = 8.44, 6.81, 1.62 Hz, 1H, H^1), 7.52 – 7.50 (m, 1H, H^2), 7.49 – 7.46 (m, 1H, H^6), 6.31 (d, *J* = 18.10 Hz, 1H, H^{12}), 1.37 (s, 12H, H^{15}, H^{16}, H^{17} and H^{18}).

^{11}B NMR (128 MHz, Chloroform-*d*) δ 29.56.

^{13}C NMR (126 MHz, Chloroform-*d*) δ 146.6 (C^{11}), 135.4 (C^{6}), 133.7 (C^{4}), 131.2 (C^{9}), 129.1 (C^{5}), 128.6 (C^{3}), 126.3 (C^{1}), 125.9 (C^{6}), 125.7 (C^{2}), 124.2 (C^{7}), 123.9 (C^{10}), 120.3 (broad, C^{12}), 83.5 (C^{13} and C^{14}), 25.0 (C^{15}, C^{16}, C^{17} and C^{18}).

Data are consistent with the literature.[300]

(*E*)-Trifluoro(2-(naphthalen-1-yl)vinyl)-λ^4-borane, potassium salt, **3.68-int4**



Prepared according to General Procedure 6 using (*E*)-4,4,5,5-tetramethyl-2-(2-(naphthalen-1-yl)vinyl)-1,3,2-dioxaborolane **3.68-int3** (920 mg, 3.28 mmol, 1.0 equiv.), potassium hydrogen fluoride (870 mg, 11.1 mmol, 4.0 equiv.), and water (2.51 mL, 139 mmol, 50.0 equiv.) in MeOH (26 mL, 0.1 M). 710 mg of a white solid was obtained after filtration, consistent with the desired product (98%).

^{1}H NMR (500 MHz, DMSO-d_6) δ 8.18 – 8.14 (m, 1H, H^{10}), 7.89 – 7.85 (m, 1H, H^{3}), 7.72 (d, *J* = 8.09 Hz, 1H, H^{5}), 7.57 (dt, *J* = 7.16, 0.93 Hz, 1H, H^{7}), 7.53 – 7.46 (m, 2H, H^{1} and H^{2}), 7.46 – 7.42 (m, 1H, H^{6}), 7.25 (d, *J* = 17.86 Hz, 1H, H^{11}), 6.25 (dq, *J* = 17.95, 3.54 Hz, 1H, H^{12}).

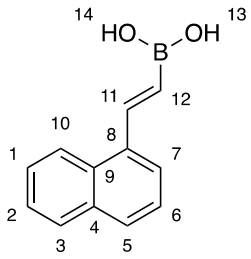
^{11}B NMR (128 MHz, DMSO-d_6) δ 2.52.

^{13}C NMR (126 MHz, DMSO-d_6) δ 143.4 (broad, C^{12}), 138.0 (C^{8}), 133.3 (C^{4}), 130.5 (C^{9}), 129.3 (q, $^{3}J_{CF}$ = 4.5 Hz, C^{11}), 128.3 (C^{3}), 126.0 (C^{5}), 125.9 (C^{6}), 125.6 (C^{1} or C^{2}), 125.4 (C^{1} or C^{2}), 123.6 (C^{10}), 122.2 (C^{7}).

^{19}F {^{1}H} NMR (377 MHz, DMSO-d_6) δ –137.86.

Data are consistent with the literature.[156]

(*E*)-(2-(Naphthalen-1-yl)vinyl)boronic acid, **3.68**



Prepared according to General Procedure 7 using (*E*)-trifluoro(2-(naphthalen-1-yl)vinyl)-λ^4-borane, potassium salt **3.68-int4** (620 mg, 2.38 mmol, 1.0 equiv.) and chlorotrimethylsilane (1.06 mL, 8.34 mmol, 3.5 equiv.) in MeCN:H_2O (20 mL:5 mL, 0.1 M). 326 mg of a white solid was afforded as the desired product (69%) as a mixture of the desired product and boroxine.

^{1}H NMR (500 MHz, DMSO-d_6) δ 8.30 (dd, *J* = 8.55, 1.29 Hz, 1H, H^{10}), 8.15 (d, *J* = 18.19 Hz, 1H, H^{11}), 7.96 (s, 2H, H^{13} and H^{14}), 7.94 (dd, *J* = 7.98, 1.49 Hz, 1H, H^3), 7.89 (d, *J* = 8.14 Hz, 1H H^5), 7.74 (dd, *J* = 7.28, 1.19 Hz, 1H, H^7), 7.61 – 7.56 (m, 1H, H^1), 7.56 – 7.50 (m, 2H, H^2 and H^6), 6.24 (d, *J* = 18.16 Hz, 1H, H^{12}).

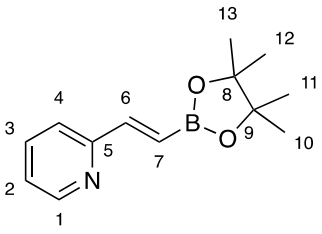
^{11}B NMR (96 MHz, DMSO-d_6) δ 27.88.

^{13}C NMR (126 MHz, DMSO-d_6) δ 142.5 (C^{11}), 135.1 (C^8), 133.4 (C^4), 130.7 (C^9), 128.5 (C^3 and C^5), 126.8 (broad, C^{12}), 126.4 (C^1), 126.0 (C^2 or C^6), 125.8 (C^2 or C^6), 123.4 (C^{10}), 123.3 (C^7).

IR (solid): 1604, 1342, 1317, 1280, 1224, 1192, 1101, 985, 786, 694 cm^{-1}.

HRMS (ESI): *m/z* calculated for $[M + H]^+$ $(C_{12}H_{12}BNO_2)^+$: 199.0924; found = 199.0923.

(*E*)-2-(2-(4,4,5,5-Tetramethyl-1,3,2-dioxaborolan-2-yl)vinyl)pyridine, **3.69-int3**



Prepared according to General Procedure 5 using 2-ethynylpyridine (300 μL, 3.00 mmol, 1.0 equiv.), copper(I) chloride (15 mg, 150 μmol, 5 mol%), potassium *tert*-butoxide (34 mg, 300 μmol, 10 mol%), bis(2-diphenylphosphinophenyl)ether (DPEPhos) (81 mg, 150 μmol, 5 mol%), bis(pinacolato)diboron (838 mg, 3.30 mmol, 1.1 equiv.), and MeOH (240 μL, 6.00 mmol, 2.0 equiv.) in THF (12 mL, 0.1 M). The crude residue was purified by flash chromatography (silica gel) from pure hexane to a mixture of 10% ethyl acetate in hexane affording 545 mg of a colourless oil consistent with the desired product (79%).

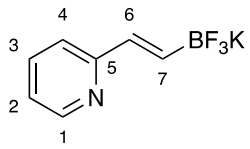
^{1}H NMR (500 MHz, Chloroform-*d*) δ 8.58 (ddd, *J* = 4.81, 1.88, 0.91 Hz, 1H, H^{1}), 7.63 (td, *J* = 7.65, 1.81 Hz, 1H, H^{3}), 7.44 (d, *J* = 18.28 Hz, 1H, H^{6}), 7.38 (dt, *J* = 7.95, 1.07 Hz, 1H, H^{4}), 7.15 (ddd, *J* = 7.53, 4.76, 1.14 Hz, 1H, H^{2}), 6.61 (d, *J* = 18.28 Hz, 1H, H^{7}), 1.29 (s, 12H, H^{10}, H^{11}, H^{12} and H^{13}).

^{11}B NMR (96 MHz, Chloroform-*d*) δ 30.24.

^{13}C NMR (126 MHz, Chloroform-*d*) δ 155.5 (C^{5}), 149.8 (C^{1}), 148.9 (C^{6}), 136.6 (C^{3}), 123.2 (C^{2}), 122.3 (C^{4}), 121.3 (broad, C^{7}), 83.6 (C^{8} and C^{9}), 24.9 (C^{10}, C^{11}, C^{12} and C^{13}).

Data are consistent with the literature.[301]

(*E*)-2-(2-(Trifluoro-λ^{4}-boraneyl)vinyl)pyridine, potassium salt, **3.69-int4**



Prepared according to General Procedure 6 using (*E*)-2-(2-(4,4,5,5-tetramethyl-1,3,2-dioxaborolan-2-yl)vinyl)pyridine **3.69-int3** (855 mg, 3.70 mmol, 1.0 equiv.), potassium hydrogen fluoride (1.16 g, 14.8 mmol, 4.0 equiv.), and water (3.33 mL, 185 mmol, 50.0 equiv.) in MeOH (32 mL, 0.1 M). 472 mg of a white solid was obtained after filtration, consistent with the desired product (60%).

^{1}H NMR (500 MHz, DMSO-d_6) δ 8.42 (ddd, *J* = 4.83, 1.88, 0.92 Hz, 1H, H^{1}), 7.63 (td, *J* = 7.65, 1.87 Hz, 1H, H^{3}), 7.39 – 7.35 (m, 1H, H^{4}), 7.08 (ddd, *J* = 7.42, 4.81, 1.14 Hz, 1H, H^{2}), 6.62 – 6.56 (m, 2H, H^{6} and H^{7}).

^{11}B NMR (96 MHz, DMSO-d_6) δ 2.70.

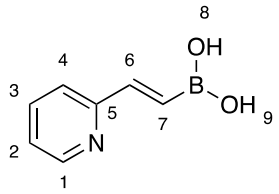
^{13}C NMR (126 MHz, DMSO-d_6) δ 158.2 (C^5), 148.9 (C^1), 143.9 (broad, C^7), 136.1 (C^3), 134.2 (q, $^3J_{CF}$ = 4.3 Hz, C^6), 120.9 (C^2), 119.6 (C^4).

^{19}F {^{1}H} NMR (376 MHz, DMSO-d_6) δ –138.17.

IR (solid): 1585, 1267, 1255, 1244, 1093, 1074, 1053, 1039, 987, 956 cm^{-1}.

HRMS (ESI): *m/z* calculated for $[M - K]^-$ $(C_7H_6NBF_3)^-$: 172.0551; found = 172.0570.

(*E*)-(2-(pyridin-2-yl)vinyl)boronic acid, **3.69**



Prepared according to General Procedure 7 using (*E*)-2-(2-(trifluoro-λ^4-boraneyl)vinyl)pyridine, potassium salt **3.69-int4** (400 mg, 1.90 mmol, 1.0 equiv.) and chlorotrimethylsilane (840 μL, 6.63 mmol, 3.5 equiv.) in MeCN:H_2O (15 mL:4 mL, 0.1 M). The aqueous layer was concentrated *in vacuo* affording 280 mg of a white solid as the desired product (99%).

^{1}H NMR (500 MHz, DMSO-d_6) δ 8.77 (d, *J* = 5.92, 1H, H^1), 8.52 (td, *J* = 7.91, 1.56 Hz, 1H, H^3), 8.24 (d, *J* = 8.15 Hz, 1H, H^4), 7.94 – 7.89 (m, 1H, H^2), 7.47 (d, *J* = 18.47 Hz, 1H, H^6), 6.95 (d, *J* = 18.40 Hz, 1H, H^7).

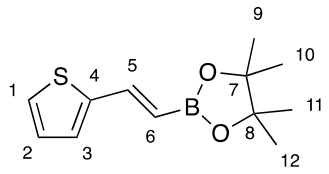
^{11}B NMR (128 MHz, DMSO-d_6) δ 27.43.

^{13}C NMR (126 MHz, DMSO-d_6) δ 149.6 (C^5), 146.0 (C^3), 141.8 (C^1), 137.6 (broad, C^7), 135.6 (C^6), 126.0 (C^2), 124.2 (C^4).

IR (solid): 1606, 1452, 1406, 1357, 1296, 1257, 1219, 1103, 1012, 991, 929 cm^{-1}.

HRMS (ESI): *m/z* calculated for $[M + H]^+$ $(C_7H_9BNO_2)^+$: 150.0720; found = 150.0724.

(*E*)-4,4,5,5-Tetramethyl-2-(2-(thiophen-2-yl)vinyl)-1,3,2-dioxaborolane, **3.70-int3**



Prepared according to General Procedure 5 using 2-ethynylthiophene (500 μL, 5.00 mmol, 1.0 equiv.), copper(I) chloride (25 mg, 250 μmol, 5 mol%), potassium *tert*-butoxide (56 mg, 500 μmol, 10 mol%), bis(2-diphenylphosphinophenyl) ether (DPEPhos) (135 mg, 250 μmol, 5 mol%), bis(pinacolato)diboron (1.40 g, 5.50 mmol, 1.1 equiv.), and MeOH (410 μL, 10.0 mmol, 2.0 equiv.) in THF (20 mL, 0.25 M).The crude residue was purified by flash chromatography (silica gel) from pure hexane to a mixture of 2% of diethyl ether in hexane affording 1.05 g of a pale-yellow oil consistent with the desired product (89%).

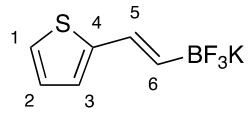
^{1}H NMR (500 MHz, Chloroform-*d*) δ 7.47 (d, *J* = 18.08 Hz, 1H, H^{5}), 7.24 (dd, *J* = 5.04, 1.03 Hz, 1H, H^{1}), 7.09 – 7.06 (m, 1H, H^{3}), 6.98 (dd, *J* = 5.05, 3.58 Hz, 1H, H^{2}), 5.91 (d, *J* = 18.11 Hz, 1H, H^{6}), 1.30 (s, 12H, H^{9}, H^{10}, H^{11} and H^{12}).

^{11}B NMR (128 MHz, Chloroform-*d*) δ 29.83.

^{13}C NMR (126 MHz, Chloroform-*d*) δ 144.0 (C^{4}), 141.9 (C^{5}), 127.9 (C^{3}), 127.8 (C^{2}), 126.4 (C^{1}), 115.9 (broad, C^{6}), 83.5 (C^{7} and C^{8}), 24.9. (C^{9}, C^{10}, C^{11} and C^{12}).

Data are consistent with the literature.[302]

(*E*)-Trifluoro(2-(thiophen-2-yl)vinyl)-λ^{4}-borane, potassium salt, **3.70-int4**



Prepared according to General Procedure 6 using (*E*)-4,4,5,5-tetramethyl-2-(2-(thiophen-2-yl)vinyl)-1,3,2-dioxaborolane **3.70-int3** (1.00 g, 4.23 mmol, 1.0 equiv.), potassium hydrogen fluoride (1.32 g, 16.9 mmol, 4.0 equiv.), and water (3.81 mL, 212 mmol, 50.0 equiv.) in MeOH (42 mL, 0.1 M). 702 mg of a white solid was obtained after filtration, consistent with the desired product (77%).

^{1}H NMR (500 MHz, DMSO-d_6) δ 7.18 (dd, J = 5.06, 1.04 Hz, 1H, H^{1}), 6.91 (dd, J = 5.07, 3.45 Hz, 1H, H^{2}), 6.80 (dd, J = 3.57, 1.13 Hz, 1H, H^{3}), 6.56 (d, J = 17.92 Hz, 1H, H^{5}), 5.89 (dq, J = 17.94, 3.64 Hz, 1H, H^{6}).

^{11}B NMR (128 MHz, DMSO-d_6) δ 2.30.

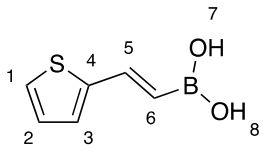
^{13}C NMR (126 MHz, DMSO-d_6) δ 147.3 (C^{4}), 139.8 (broad, C^{6}), 127.3 (C^{2}), 126.4 (q, $^{3}J_{CF}$ = 4.6 Hz, C^{5}), 122.8 (C^{3}), 122.4 (C^{1}).

^{19}F {^{1}H} NMR (377 MHz, DMSO-d_6) δ –138.23.

IR (solid): 1606, 1581, 1290, 1269, 1240, 1220, 1161, 1153, 1093, 1083, 1052, 989 cm^{-1}.

HRMS (ESI): *m/z* calculated for $[M - K]^-$ $(C_6H_5BF_3S)^-$: 177.0163; found = 177.0151.

(*E*)-(2-(Thiophen-2-yl)vinyl)boronic acid, **3.70**



Prepared according to General Procedure 7 using (*E*)-trifluoro(2-(thiophen-2-yl)vinyl)-λ^{4}-borane, potassium salt **3.70-int4** (650 mg, 3.01 mmol, 1.0 equiv.) and chlorotrimethylsilane (1.34 mL, 10.5 mmol, 3.5 equiv.) in MeCN:H_2O (24 mL:6 mL, 0.1 M). 233 mg of a pale-brown solid was afforded as the desired product (50%) as a mixture of the desired product and boroxine.

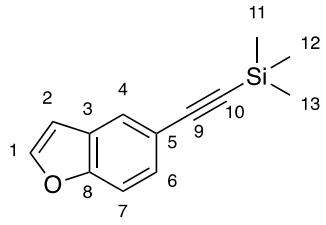
^{1}H NMR (500 MHz, DMSO-d_6) δ 7.46 (d, J = 5.01 Hz, 1H, H^{1}), 7.37 (d, J = 18.07 Hz, 1H, H^{5}), 7.16 – 7.12 (m, 1H, H^{3}), 7.07 – 7.01 (m, 1H, H^{2}), 5.81 (d, J = 18.06 Hz, 1H, H^{6}). H^{7} and H^{8} are not observed.

^{11}B NMR (96 MHz, DMSO-d_6) δ 27.88.

^{13}C NMR (126 MHz, DMSO-d_6) δ 144.0 (C^{4}), 138.7 (C^{5}), 128.1 (C^{2}), 127.6 (C^{3}), 126.3 (C^{1}), 122.7 (broad, C^{6}).

Data are consistent with the literature.[303]

(Benzofuran-5-ylethynyl)trimethylsilane, **3.71-int1**



Prepared according to General Procedure 3 using 5-bromobenzofuran (630 μL, 5.00 mmol, 1.0 equiv.), dichlorobis(triphenylphosphine)palladium (35 mg, 50.0 μmol, 1 mol%), copper iodide (19 mg, 100 μmol, 2 mol%), trimethylsilylacetylene (5.28 mL, 50.0 mmol, 10.0 equiv.), and piperidine (1.48 mL, 15.0 mmol, 3.0 equiv.) in THF (10 mL, 0.5 M). The reaction mixture was stirred for 36 hours at 90 °C. The crude residue was purified by flash chromatography (silica gel) with pure hexane affording 827 mg of a pale-orange oil as the desired product (77%).

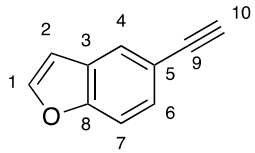
^{1}H NMR (500 MHz, Chloroform-*d*) δ 7.76 (t, *J* = 1.21 Hz, 1H, H^{6}), 7.63 (d, *J* = 2.19 Hz, 1H, H^{1}), 7.44 – 7.43 (m, 2H, H^{4} and H^{7}), 6.73 (d, *J* = 2.29 Hz, 1H, H^{1}), 0.29 (s, 9H, H^{11}, H^{12} and H^{13}).

^{13}C NMR (126 MHz, Chloroform-*d*) δ 154.8 (C^{8}), 145.9 (C^{1}), 128.5 (C^{4}), 127.5 (C^{3}), 125.4 (C^{6}), 117.8 (C^{5}), 111.5 (C^{7}), 106.6 (C^{2}), 105.7 (C^{9}), 92.6 (C^{10}), 0.2 (C^{11}, C^{12} and C^{13}).

IR (film): 2958, 2160, 1539, 1462, 1408, 1328, 1257, 1249, 1201, 1126, 1029, 885, 812 cm^{-1}.

HRMS (MALDI): *m/z* calculated for $[M + H]^{+}$ $(C_{13}H_{15}OSi)^{+}$: 215.0887; found = 215.0886.

5-Ethynylbenzofuran, **3.71-int2**



Prepared according to General Procedure 4 using (benzofuran-5-ylethynyl)trimethylsilane **3.71-int1** (820 mg, 3.83 mmol, 1.0 equiv.) and potassium

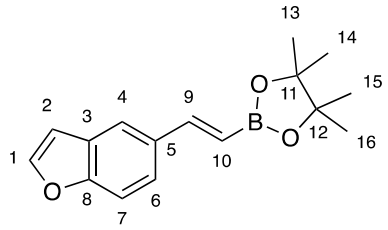
carbonate (1.06 g, 7.65 mmol, 2.0 equiv.) in MeOH (20 mL, 0.2 M). The crude residue was purified by flash chromatograpghy (silica gel) with pure hexane affording 330 mg of a pale-orange oil consistent with the desired product (61%).

^{1}H NMR (400 MHz, Chloroform-*d*) δ 7.77 (t, *J* = 1.03 Hz, 1H, H^{6}), 7.65 (d, *J* = 2.22 Hz, 1H, H^{2}), 7.47 – 7.42 (m, 2H, H^{4} and H^{7}), 6.75 (dd, *J* = 2.23, 0.72 Hz, 1H, H^{1}), 3.04 (s, 1H, H^{10}).

^{13}C NMR (101 MHz, Chloroform-*d*) δ 154.9 (C^{8}), 146.1 (C^{1}), 128.6 (C^{4}), 127.6 (C^{3}), 125.6 (C^{6}), 116.7 (C^{5}), 111.7 (C^{7}), 106.6 (C^{2}), 84.1 (C^{9}), 75.9 (C^{10}).

Data are consistent with the literature.[304]

(*E*)-2-(2-(Benzofuran-5-yl)vinyl)-4,4,5,5-tetramethyl-1,3,2-dioxaborolane, **3.71-int3**



Prepared according to General Procedure 5 using 5-ethynylbenzofuran **3.71-int2** (330 mg, 2.32 mmol, 1.0 equiv.), copper(I) chloride (11 mg, 116 μmol 5 mol%), potassium *tert*-butoxide (26.0 mg, 232 μmol, 10 mol%), bis(2-diphenylphosphinophenyl) ether (DPEPhos) (62.5 mg, 116 μmol, 5 mol%), bis(pinacolato)diboron (648 mg, 2.55 mmol, 1.1 equiv.), and methanol (190 μL, 4.64 mmol, 2.0 equiv.) in THF (10 mL, 0.25 M). The crude residue was purified by flash chromatography (silica gel) from pure hexane to a mixture of 5% of diethyl ether in hexane affording 570 mg of a pale-yellow oil consistent with the desired product (91%).

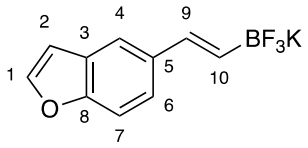
^{1}H NMR (500 MHz, Chloroform-*d*) δ 7.70 (d, *J* = 1.67 Hz, 1H, H^{6}), 7.60 (d, *J* = 2.27 Hz, 1H, H^{1}), 7.51 (d, *J* = 18.21 Hz, 1H, H^{9}), 7.50 – 7.47 (m, 1H, H^{4}), 7.45 (d, *J* = 8.62 Hz, 1H, H^{7}), 6.76 (dd, *J* = 2.25, 0.86 Hz, 1H, H^{2}), 6.16 (d, *J* = 18.38 Hz, 1H, H^{10}), 1.32 (s, 12H, H^{13}, H^{14}, H^{15} and H^{16}).

^{11}B NMR (96 MHz, Chloroform-*d*) δ 30.41.

^{13}C NMR (126 MHz, Chloroform-*d*) δ 155.5 (C^8), 149.9 (C^9), 145.7 (C^1), 132.8 (C^5), 127.8 (C^3), 123.6 (C^4), 120.3 (C^6), 115.1 (broad, C^{10}), 111.6 (C^7), 106.9 (C^2), 83.4 (C^{11} and C^{12}), 24.9 (C^{13}, C^{14}, C^{15} and C^{16}).

Data are consistent with the literature.[300]

(*E*)-(2-(Benzofuran-5-yl)vinyl)trifluoro-λ^4-borane, potassium salt, **3.71-int4**



Prepared according to General Procedure 6 using (*E*)-2-(2-(benzofuran-5-yl)vinyl)-4,4,5,5-tetramethyl-1,3,2-dioxaborolane **3.71-int3** (590 mg, 2.18 mmol, 1.0 equiv.), potassium hydrogen fluoride (682 mg, 8.74 mmol, 4 equiv.), and water (1.97 mL, 109 mmol, 50.0 equiv.) in MeOH (21 mL, 0.1 M). 380 mg of a white solid was obtained after filtration, consistent with the desired product (70%).

^{1}H NMR (500 MHz, DMSO-d_6) δ 7.90 (d, J = 2.18 Hz, 1H, H^1), 7.52 (d, J = 1.70 Hz, 1H, H^4), 7.45 (d, J = 8.54 Hz, 1H, H^7), 7.31 (dd, J = 8.53, 1.74 Hz, 1H, H^6), 6.89 (d, J = 2.14 Hz, 1H, H^2), 6.55 (d, J = 18.10 Hz, 1H, H^9), 6.13 (dq, J = 18.17, 3.51 Hz, 1H, H^{10}).

^{11}B NMR (96 MHz, DMSO-d_6) δ 3.12.

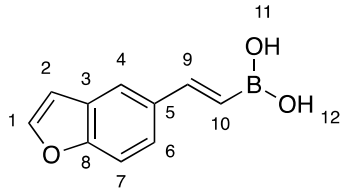
^{13}C NMR (126 MHz, DMSO-d_6) δ 153.3 (C^8), 145.9 (C^1), 137.7 (broad, C^{10}), 135.7 (C^5), 133.0 (q, $^3J_{CF}$ = 4.4 Hz, C^9), 127.4 (C^3), 122.1 (C^6), 117.7 (C^4), 110.9 (C^7), 106.8 (C^2).

^{19}F {^{1}H} NMR (470 MHz, DMSO-d_6) δ –137.58.

IR (solid): 1627, 1537, 1406, 1330, 1309, 1236, 1124, 1093, 1026, 972, 921 cm^{-1}.

HRMS (ESI): *m/z* calculated for $[M - K]^-$ ($C_{10}H_7BF_3O$)$^-$: 211.0549; found = 211.0535.

(*E*)-(2-(Benzofuran-5-yl)vinyl)boronic acid, **3.71**



Prepared according to General Procedure 7 (*E*)-(2-(benzofuran-5-yl)vinyl)trifluoro-λ^4-borane, potassium salt **3.71-int4** (340 mg, 1.36 mmol, 1.0 equiv.) and chlorotrimethylsilane (600 μL, 4.76 mmol, 3.5 equiv.) in MeCN:H_2O (11 mL:3 mL, 0.1 M). 183 mg of a white solid was obtained as a mixture of the desired product and boroxine (72%).

^{1}H NMR (500 MHz, DMSO-d_6) δ 7.99 (d, *J* = 2.22 Hz, 1H, H^1), 7.78 (broad s, 2H, H^{11} and H^{12}), 7.74 (d, *J* = 1.75 Hz, 1H, H^4), 7.57 (d, *J* = 8.51 Hz, 1H, H^7), 7.47 (dd, *J* = 8.60, 1.81 Hz, 1H, H^6), 7.36 (d, *J* = 18.32 Hz, 1H, H^9), 6.97 (d, *J* = 2.19 Hz, 1H, H^2), 6.10 (d, *J* = 18.36 Hz, 1H, H^{10}).

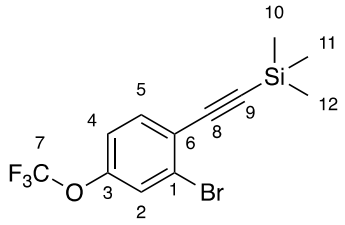
^{11}B NMR (96 MHz, DMSO-d_6) δ 30.24.

^{13}C NMR (126 MHz, DMSO-d_6) δ 154.5 (C^8), 146.7 (C^1), 146.2 (C^9), 133.0 (C^5), 127.7 (C^3), 123.1 (C^6), 121.9 (broad, C^{10}), 119.7 (C^4), 111.5 (C^7), 107.0 (C^2).

IR (solid): 1622, 1589, 1533, 1465, 1442, 1352, 1332, 1307, 1286, 1271, 1255, 1201, 1184, 1124, 1111, 1026, 898 cm^{-1}.

HRMS (ESI): *m/z* calculated for $[M + H]^+$ $(C_{10}H_{10}BO_3)^+$: 189.0717; found = 189.0708.

((2-Bromo-4-(trifluoromethoxy)phenyl)ethynyl)trimethylsilane, **3.72-int1**



Prepared according to General Procedure 3 using 2-bromo-4-(trifluoromethoxy)iodobenzene (830 μL, 5.00 mmol, 1.0 equiv.), dichlorobis(triphenylphosphine)palladium (35 mg, 50.0 μmol, 1 mol%), copper iodide

(19 mg, 100 μmol, 2 mol%), and trimethylsilylacetylene (660 μL, 6.25 mmol, 1.25 equiv.) in triethylamine (10 mL, 0.5 M). The crude residue was purified by flash chromatography (silica gel) from pure hexane to a mixture of 45% of ethyl acetate in hexane affording 1.69 g of a yellow oil as the desired product (100%).

^{1}H NMR (500 MHz, Chloroform-*d*) δ 7.51 (d, *J* = 8.63 Hz, 1H, H^{5}), 7.45 (dd, *J* = 2.45, 1.02 Hz, 1H, H^{2}), 7.11 (ddd, *J* = 8.61, 2.40, 1.05 Hz, 1H, H^{4}), 0.28 (s, 9H, H^{10}, H^{11} and H^{12}).

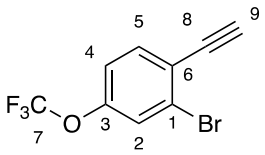
^{13}C NMR (126 MHz, Chloroform-*d*) δ 148.8 (app. d, $^{3}J_{CF}$ = 2.4 Hz, C^{3}), 134.5 (C^{5}), 126.5 (C^{1} or C^{6}), 125.0 (C^{1} or C^{6}), 124.3 (C^{2}), 120.4 (q, $^{1}J_{CF}$ = 258.8 Hz, C^{7}), 119.6 (C^{4}), 101.8 (C^{8}), 101.0 (C^{9}), –0.1 (C^{10}, C^{11} and C^{12}).

^{19}F {^{1}H} NMR (377 MHz, Chloroform-*d*) δ –57.90.

IR (film): 2166, 1595, 1564, 1481, 1247, 1211, 1166, 1043, 941, 839, 759 cm^{-1}.

HRMS (ESI): *m/z* calculated for $[M + H]^{+}$ $(C_{12}H_{13}{}^{79}BrF_3OSi)^{+}$: 336.9866; found = 336.9865.

2-Bromo-1-ethynyl-4-(trifluoromethoxy)benzene, **3.72-int2**



Prepared according to General Procedure 4 using ((2-bromo-4-(trifluoromethoxy)phenyl)ethynyl) trimethylsilane **3.72-int1** (1.69 g, 5.01 mmol, 1.0 equiv.) and potassium carbonate (1.39 g, 10.0 mmol, 2.0 equiv.) in MeOH (25 mL, 0.2 M). The crude residue was purified by flash chromatography (silica gel) with pure hexane affording 809 mg of an orange oil consistent with the desired product (67%).

^{1}H NMR (500 MHz, Chloroform-*d*) δ 7.55 (d, *J* = 8.56 Hz, 1H, H^{5}), 7.48 (dd, *J* = 2.44, 0.98 Hz, 1H, H^{2}), 7.18 – 7.12 (m, 1H, H^{4}), 3.40 (s, 1H, H^{9}).

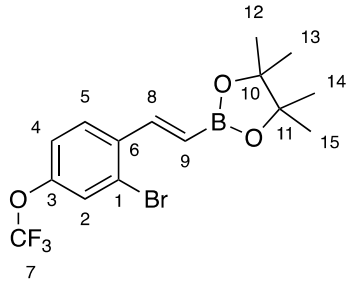
^{13}C NMR (126 MHz, Chloroform-*d*) δ 149.2 (C^{3}), 135.1 (C^{5}), 126.4 (C^{1}), 125.1 (C^{2}), 123.3 (C^{6}), 120.4 (q, $^{1}J_{CF}$ = 259.1 Hz, C^{7}), 119.7 (C^{4}), 82.9 (C^{9}), 80.8 (C^{8}).

^{19}F {^{1}H} NMR (470 MHz, Chloroform-*d*) δ –57.87.

IR (film): 3310, 1569, 1566, 1481, 1249, 1211, 1166, 1043, 912, 825, 144 cm^{-1}.

HRMS (ESI): *m/z* calculated for $[M + H]^+$ $(C_9H_5{}^{79}BrF_3O)^+$: 264.9470; found = 264.9470.

(*E*)-2-(2-Bromo-4-(trifluoromethoxy)styryl)-4,4,5,5-tetramethyl-1,3,2-dioxaborolane, **3.72-int3**



Prepared according to General Procedure 5 using 2-bromo-1-ethynyl-4-(trifluoromethoxy)benzene **3.72-int2** (890 mg, 3.36 mmol, 1.0 equiv.), copper(I) chloride (17 mg, 168 μmol, 5 mol%), potassium *tert*-butoxide (38 mg, 336 μmol, 10 mol%), bis(2-diphenylphosphinophenyl) ether (DPEPhos) (90 mg, 168 μmol, 5 mol%), bis(pinacolato)diboron (938 mg, 3.69 mmol, 1.1 equiv.), and MeOH (270 μL, 6.72 mmol, 2.0 equiv.) in THF (14 mL, 0.25 M). The crude residue was purified by flash chromatography (silica gel) from pure hexane to a mixture of 5% of diethyl ether in hexane affording 889 mg of a pale-yellow oil consistent with the desired product (67%).

^{1}H NMR (500 MHz, Chloroform-*d*) δ 7.64 (d, *J* = 18.23 Hz, 1H, H^8), 7.62 (d, *J* = 8.67 Hz, 1H, H^5), 7.44 (dd, *J* = 2.44, 0.99 Hz, 1H, H^2), 7.18 – 7.15 (m, 1H, H^4), 6.10 (d, *J* = 18.26 Hz, 1H, H^9), 1.32 (s, 12H, H^{12}, H^{13}, H^{14} and H^{15}).

^{11}B NMR (96 MHz, Chloroform-*d*) δ 29.54.

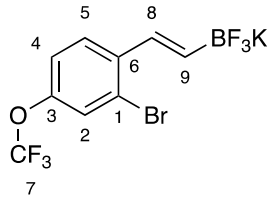
^{13}C NMR (126 MHz, Chloroform-*d*) δ 149.2 (C^3), 146.1 (C^8), 136.4 (C^6), 128.2 (C^5), 125.4 (C^2), 124.3 (C^1), 121.2 (broad, C^9), 120.1 (C^4), 120.1 (q, $^{1}J_{CF}$ = 260.3 Hz, C^7), 83.8 (C^{10} and C^{11}), 25.0 (C^{12}, C^{13}, C^{14} and C^{15}).

^{19}F {^{1}H} NMR (470 MHz, Chloroform-*d*) δ –57.87.

IR (film): 2980, 1622, 1595, 1568, 1479, 1388, 1379, 1371, 1348, 1249, 1213, 1163, 1139, 1111, 991 cm^{-1}.

HRMS (MALDI): *m/z* calculated for $[M + H]^+$ $(C_{15}H_{18}B^{79}BrF_3O_3)^+$: 393.0479; found = 393.0481.

(*E*)-(2-Bromo-4-(trifluoromethoxy)styryl)trifluoro-λ⁴-borane, potassium salt, **3.72-int4**



Prepared according to General Procedure 6 using (*E*)-2-(2-bromo-4-(trifluoromethoxy)styryl)-4,4,5,5-tetramethyl-1,3,2-dioxaborolane **3.72-int3** (890 mg, 2.26 mmol, 1.0 equiv.), potassium hydrogen fluoride (707 mg, 9.06 mmol, 4.0 equiv.), and water (2.04 mL, 113 mmol, 50.0 equiv.) in MeOH (21 mL, 0.1 M). 559 mg of a white solid was obtained after filtration, consistent with the desired product (66%).

^{1}H NMR (500 MHz, DMSO-d_6) δ 7.68 (d, J = 8.71 Hz, 1H, H^5), 7.60 – 7.55 (m, 1H, H^2), 7.37 – 7.29 (m, 1H, H^4), 6.75 (d, J = 17.92 Hz, 1H, H^8), 6.26 (dq, J = 18.03, 3.47 Hz, 1H, H^9).

^{11}B NMR (96 MHz, DMSO-d_6) δ 2.74.

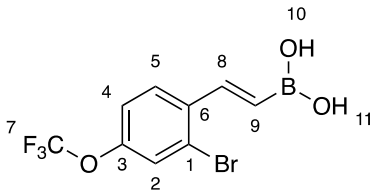
^{13}C NMR (126 MHz, DMSO-d_6) δ 146.3 (C^3), 144.9 (broad, C^9), 139.0 (C^6), 129.8 (q, $^3J_{CF}$ = 4.4 Hz, C^8), 127.5 (C^5), 125.0 (C^2), 122.0 (C^1), 120.5 (C^4), 120.0 (q, $^1J_{CF}$ = 256.7 Hz, C^7).

^{19}F {^{1}H} NMR (376 MHz, DMSO-d_6) δ –57.02, –138.33.

IR (solid): 1629, 1600, 1483, 1309, 1288, 1209, 1159, 1099, 1037, 987, 937 cm^{-1}.

HRMS (ESI): *m/z* calculated for $[M – K]^-$ $(C_9H_5B^{79}BrF_6O)^-$: 332.9528; found = 332.9512.

(*E*)-(2-Bromo-4-(trifluoromethoxy)styryl)boronic acid, **3.72**



Prepared according to General Procedure 7 using (*E*)-(2-bromo-4-(trifluoromethoxy)styryl)trifluoro-λ⁴-borane, potassium salt **3.72-int4** (507 mg, 1.36 mmol, 1.0 equiv.), chlorotrimethylsilane (600 μL, 4.76 mmol, 3.5 equiv.) in MeCN:H_2O (11 mL:3 mL, 0.1 M). 245 mg of a white solid was obtained as a mixture of the desired product and boroxine (58%).

^{1}H NMR (500 MHz, DMSO-d_6) δ 7.94 (s, 2H, H^{10} and H^{11}), 7.78 (d, J = 8.73 Hz, 1H, H^{5}), 7.69 (dd, J = 2.51, 0.93 Hz, 1H, H^{2}), 7.47 (d, J = 18.17 Hz, 1H, H^{8}), 7.43 – 7.40 (m, 1H, H^{4}), 6.15 (d, J = 18.11 Hz, 1H, H^{9}).

^{11}B NMR (96 MHz, DMSO-d_6) δ 30.41.

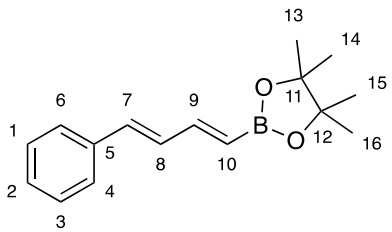
^{13}C NMR (126 MHz, DMSO-d_6) δ 148.0 (C^{3}), 142.1 (C^{8}), 136.8 (C^{6}), 128.8 (broad, C^{9}), 128.6 (C^{5}), 125.3 (C^{2}), 123.3 (C^{1}), 120.8 (C^{4}), 120.0 (q, $^{1}J_{CF}$ = 257.4 Hz, C^{7}).

^{19}F {^{1}H} NMR (470 MHz, DMSO-d_6) δ –56.99.

IR (solid): 1616, 1477, 1363, 1268, 1249, 1209, 1155, 1037, 993, 817 cm^{-1}.

HRMS (ESI): *m/z* calculated for $[M + Na]^-$ $(C_9H_7B^{79}BrF_3O_3Na)^-$: 332.9529; found = 332.9518.

4,4,5,5-Tetramethyl-2-((1*E*,3*E*)-4-phenylbuta-1,3-dien-1-yl)-1,3,2-dioxaborolane, **3.73-int3**



Prepared according to the literature.[305] To a flame-dried flask, purged with vacuum-N_2 cycles, and backfilled with N_2 was added 2,2,6,6-tetramethylpiperidine (660 μL, 3.90 mmol, 1.3 equiv.) in THF (10 mL). The flask was cooled to –78 °C and *n*-BuLi (2.5 M in hexanes, 1.95 mL, 3.90 mmol, 1.3. equiv.) was added dropwise. The mixture was allowed to warm to 0 °C and stirred at 0 °C for one hour. Then a solution of bis(4,4,5,5-tetramethyl-1,3,2-dioxaborolan-2-yl)methane (884 mg, 3.30 mmol, 1.1 equiv.) in THF (5 mL) was added. The reaction vial was allowed to stir for 20 minutes at 0 °C. Then the flask was cooled to –78°C and a solution of cinnamaldehyde (380 μL, 3.00 mmol, 1.0 equiv.) in THF (5 mL) was added. The reaction vial was slowly warmed up to room temperature and left to stir for six hours. The reaction mixture was partitioned between water (20 mL) and diethyl ether (20 mL). The organics were extracted with diethyl ether (3 × 20 mL). The combined organic layers were washed with brine (30 mL), dried over sodium sulfate, and concentrated *in vacuo*. The crude residue was purified by column chromatography (silica gel) from pure hexane to a mixture of 5% of diethyl ether in hexane affording 283 mg of a yellow oil as the desired product (37%).

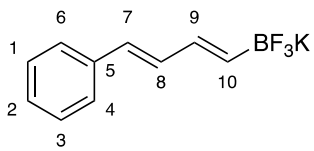
^{1}H NMR (500 MHz, Chloroform-*d*) δ 7.45 – 7.42 (m, 2H, H^4 and H^6), 7.36 – 7.29 (m, 2H, H^1 and H^3), 7.28 – 7.24 (m, 1H, H^2), 7.18 (dd, *J* = 17.60, 10.45 Hz, 1H, H^9), 6.85 (ddd, *J* = 15.58, 10.42, 0.85 Hz, 1H, H^8), 6.70 (d, *J* = 15.58 Hz, 1H, H^7), 5.67 (d, *J* = 17.60 Hz, 1H, H^{10}), 1.30 (s, 12H, H^{13}, H^{14}, H^{15} and H^{16}).

^{11}B NMR (96 MHz, Chloroform-*d*) δ 30.17.

^{13}C NMR (126 MHz, Chloroform-*d*) δ 149.9 (C^9), 136.9 (C^5), 136.3 (C^7), 130.7 (C^8), 128.8 (C^1 and C^3), 128.3 (C^2), 127.0 (C^4 and C^6), 121.3 (broad, C^{10}), 83.4 (C^{11} and C^{12}), 24.9 (C^{13}, C^{14}, C^{15} and C^{16}).

Data are consistent with the literature.[306]

Trifluoro((1*E*,3*E*)-4-phenylbuta-1,3-dien-1-yl)-λ^4-borane, potassium salt, **3.73-int4**



Prepared according to General Procedure 6 using 4,4,5,5-tetramethyl-2-((1*E*,3*E*)-4-phenylbuta-1,3-dien-1-yl)-1,3,2-dioxaborolane **3.73-int3** (286 mg, 1.12 mmol, 1.0 equiv.) potassium hydrogen fluoride (349 mg, 4.47 mmol, 4.0 equiv.), and water (1.01 mL, 55.8 mmol, 50.0 equiv.) in MeOH (11 mL, 0.1 M). 231 mg of a white solid was obtained after filtration, consistent with the desired product (89%).

^{1}H NMR (500 MHz, DMSO-d_6) δ 7.42 – 7.38 (m, 2H, H^{4} and H^{6}), 7.32 – 7.25 (m, 2H, H^{1} and H^{3}), 7.18 – 7.13 (m, 1H, H^{2}), 6.73 (dd, J = 15.67, 10.30 Hz, 1H, H^{8}), 6.32 (d, J = 15.98 Hz, 1H, H^{7}), 6.27 (dd, J = 10.73, 7.03 Hz, 1H, H^{9}), 5.75 (dq, J = 17.38, 3.89 Hz, 1H, H^{10}).

^{11}B NMR (96 MHz, DMSO-d_6) δ 3.55.

^{13}C NMR (126 MHz, DMSO-d_6) δ 146.9 (broad, C^{10}), 138.0 (C^{5}), 134.1 (q, $^{3}J_{CF}$ = 4.5 Hz, C^{9}), 133.9 (C^{8}), 128.6 (C^{1} and C^{3}), 127.2 (C^{7}), 126.6 (C^{2}), 125.8 (C^{4} and C^{6}).

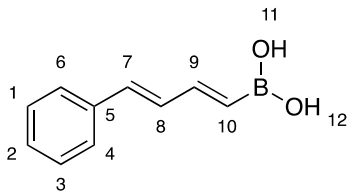
^{19}F {^{1}H} NMR (470 MHz, DMSO-d_6) δ –137.90.

IR (solid): 1597, 1490, 1488, 1388, 1201, 1134, 1091, 954, 840 cm^{-1}.

HRMS (ESI): *m/z* calculated for [M – K]$^{-}$ ($C_{10}H_9BF_3$)$^{-}$: 197.0754; found = 197.0751.

Data are consistent with the literature.[307]

((1*E*,3*E*)-4-Phenylbuta-1,3-dien-1-yl)boronic acid, **3.73**



Prepared according to General Procedure 7 using trifluoro((1*E*,3*E*)-4-phenylbuta-1,3-dien-1-yl)-λ^{4}-borane, potassium salt **3.73-int4** (300 mg, 1.27 mmol, 1.0 equiv.) and chlorotrimethylsilane (560 μL, 4.45 mmol, 3.5 equiv.) in MeCN:H_2O (10 mL:2.5 mL, 0.1 M). 41 mg of a yellow solid was obtained as a mixture of the desired product and boroxine (19%).

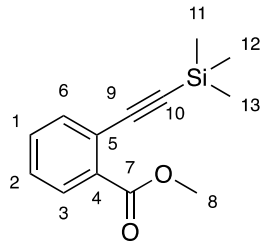
^{1}H NMR (500 MHz, Acetone-d_6) δ 7.53 – 7.47 (m, 2H, H^{4} and H^{6}), 7.38 – 7.31 (m, 2H, H^{1} and H^{3}), 7.29 – 7.22 (m, 1H, H^{2}), 7.16 (dd, *J* = 17.47, 10.42 Hz, 1H, H^{9}), 6.95 (ddd, *J* = 15.68, 10.44, 0.88 Hz, 1H, H^{8}), 6.88 (s, 2H, H^{11} and H^{12}), 6.72 (d, *J* = 15.62 Hz, 1H, H^{7}), 5.73 (d, *J* = 17.46 Hz, 1H, H^{10}).

^{11}B NMR (96 MHz, Acetone-d_6) δ 28.35.

^{13}C NMR (126 MHz, Acetone-d_6) δ 148.0 (C^{9}), 138.0 (C^{5}), 135.5 (C^{7}), 131.9 (C^{8}), 129.5 (C^{1} and C^{3}), 128.8 (C^{2}), 127.5 (C^{4} and C^{6}). C^{10} is not observed due to quadrupolar relaxation.

Data are consistent with the literature.[219]

Methyl 2-((trimethylsilyl)ethynyl)benzoate, **3.74-int1**



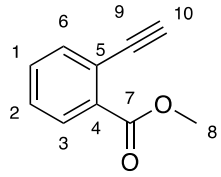
Prepared according to General Procedure 3 using methyl 2-iodobenzoate (1.47 mL, 10.0 mmol, 1.0 equiv.), dichlorobis(triphenylphosphine)palladium (70 mg, 100 μmol, 1 mol%), copper iodide (38 mg, 200 μmol, 2 mol%), and trimethylsilylacetylene (1.32 mL, 12.5 mmol, 1.25 equiv.) in triethylamine (20 mL, 0.5 M). The crude residue was purified by flash chromatography (silica gel) from pure hexane to a mixture of 2% of diethyl ether in hexane affording 2.32 g of a yellow oil as the desired product (100%).

^{1}H NMR (400 MHz, Chloroform-*d*) δ 7.90 (ddd, *J* = 7.78, 1.48, 0.56 Hz, 1H, H^{3}), 7.58 (ddd, *J* = 7.78, 1.44, 0.58 Hz, 1H, H^{6}), 7.44 (td, *J* = 7.58, 1.46 Hz, 1H, H^{1}), 7.36 (td, *J* = 7.70, 1.41 Hz, 1H, H^{2}), 3.92 (s, 3H, H^{8}), 0.27 (s, 9H, H^{11}, H^{12} and H^{13}).

^{13}C NMR (101 MHz, Chloroform-*d*) δ 167.0 (C^{7}), 134.7 (C^{6}), 132.7 (C^{5}), 131.6 (C^{1}), 130.4 (C^{3}), 128.3 (C^{2}), 123.3 (C^{4}), 103.4 (C^{9}), 99.8 (C^{10}), 52.1 (C^{8}), 0.0 (C^{11}, C^{12} and C^{13}).

Data are consistent with the literature.[308]

Methyl 2-ethynylbenzoate, **3.74-int2**



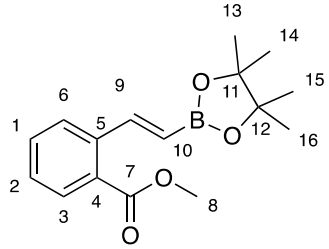
Prepared according to General Procedure 4 using methyl 2-((trimethylsilyl)ethynyl)benzoate **3.74-int1** (2.60 g, 11.2 mmol, 1.0 equiv.) and potassium carbonate (3.09 g, 22.4 mmol, 2.0 equiv.) in MeOH (55 mL, 0.2 M). Organics layers were concentrated *in vacuo* affording 1.32 g of a dark red oil consistent with the desired product (74%).

^{1}H NMR (500 MHz, Chloroform-*d*) δ 7.93 (ddd, *J* = 7.80, 1.46, 0.54 Hz, 1H, H^{3}), 7.62 (dd, *J* = 7.72, 1.14 Hz, 1H, H^{6}), 7.47 (td, *J* = 7.61, 1.46 Hz, 1H, H^{1}), 7.40 (td, *J* = 7.70, 1.37 Hz, 1H, H^{2}), 3.92 (s, 3H, H^{8}), 3.40 (s, 1H, H^{10}).

^{13}C NMR (126 MHz, Chloroform-*d*) δ 166.5 (C^{7}), 135.1 (C^{6}), 132.6 (C^{5}), 131.8 (C^{1}), 130.4 (C^{3}), 128.6 (C^{2}), 122.7 (C^{4}), 82.4 (C^{10}), 82.1 (C^{9}), 52.3 (C^{8}).

Data are consistent with the literature.[308]

Methyl (*E*)-2-(2-(4,4,5,5-tetramethyl-1,3,2-dioxaborolan-2-yl)vinyl)benzoate, **3.74-int3**



Prepared according to General Procedure 5 using methyl 2-ethynylbenzoate **3.74-int2** (1.30 g, 8.12 mmol, 1.0 equiv.), copper(I) chloride (40 mg, 406 μmol, 5 mol%), potassium *tert*-butoxide (91 mg, 812 μmol, 10 mol%), bis(2-diphenylphosphinophenyl) ether (DPEPhos) (219 mg, 406 μmol, 5 mol%), bis(pinacolato)diboron (2.27 g, 8.93 mmol, 1.1 equiv.), and MeOH (660 μL, 16.2

mmol, 2.0 equiv.) in THF (32 mL, 0.25 M). The crude residue was purified by flash chromatography (silica gel) from pure hexane to a mixture of 5% of diethyl ether in hexane affording 2.27 g of a pale-yellow oil consistent with the desired product (97%).

^{1}H NMR (400 MHz, Chloroform-*d*) δ 8.07 (d, *J* = 18.25 Hz, 1H, H^{9}), 7.85 (ddd, *J* = 7.82, 1.47, 0.52 Hz, 1H, H^{3}), 7.63 (ddd, *J* = 7.93, 1.30, 0.63 Hz, 1H, H^{6}), 7.48 (td, *J* = 7.88, 1.45, 1H, H^{1}), 7.33 (td, *J* = 7.59, 1.30 Hz, 1H, H^{2}), 6.07 (d, *J* = 18.23 Hz, 1H, H^{10}), 3.90 (s, 3H, H^{8}), 1.30 (s, 12H, H^{13}, H^{14}, H^{15} and H^{16}).

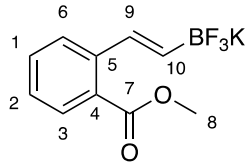
^{11}B NMR (96 MHz, Chloroform-*d*) δ 30.22.

^{13}C NMR (101 MHz, Chloroform-*d*) δ 167.8 (C^{7}), 148.1 (C^{9}), 139.7 (C^{5}), 132.2 (C^{1}), 130.3 (C^{3}), 129.2 (C^{4}), 128.2 (C^{2}), 127.6 (C^{6}), 120.1 (broad, C^{10}), 83.5 (C^{11} and C^{12}), 52.3 (C^{8}), 24.9 (C^{13}, C^{14}, C^{15} and C^{16}).

IR (film): 1720, 1620, 1474, 1381, 1371, 1346, 1325, 1290, 1251, 1205, 1141, 1128, 1076, 955 cm^{-1}.

HRMS (ESI): *m/z* calculated for $[M + K]^{+}$ $(C_{16}H_{21}BO_4K)^{+}$: 327.1173; found = 327.1167.

Methyl (*E*)-2-(2-(trifluoro-λ^4-boraneyl)vinyl)benzoate, potassium salt, **3.74-int4**



Prepared according to General Procedure 6 using (methyl (*E*)-2-(2-(4,4,5,5-tetramethyl-1,3,2-dioxaborolan-2-yl)vinyl)benzoate **3.74-int3** (2.20 g, 7.63 mmol, 1.0 equiv.), potassium hydrogen fluoride (2.39 g, 30.5 mmol, 4.0 equiv.), and water (6.88 mL, 382 mmol, 50.0 equiv.) in MeOH (65 mL, 0.1 M). 3.1 g of a white solid was obtained, consistent with the desired product and residual potassium hydrogen fluoride (147%). No further purification was performed and the crude was taken directly into the next step.

^{1}H NMR (400 MHz, DMSO-d_6) δ 7.61 (dd, J = 8.04, 1.25 Hz, 1H, H^{6}), 7.57 (dd, J = 7.78, 1.44 Hz, 1H, H^{3}), 7.47 – 7.41 (m, 1H, H^{1}), 7.21 (td, J = 7.45, 1.24 Hz, 1H, H^{2}), 6.99 (d, J = 18.07 Hz, 1H, H^{9}), 6.19 (dq, J = 18.09, 3.58 Hz, 1H, H^{10}), 3.80 (s, 3H, H^{8}).

^{11}B NMR (96 MHz, DMSO-d_6) δ 2.74.

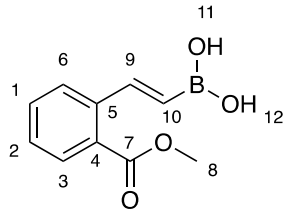
^{13}C NMR (126 MHz, DMSO-d_6) δ 168.3 (C^{7}), 142.8 (broad, C^{10}), 140.5 (C^{5}), 131.3 (C^{1}), 130.2 (q, $^{3}J_{CF}$ = 4.6 Hz, C^{9}), 129.0 (C^{3}), 128.7 (C^{4}), 125.7 (C^{6}), 125.6 (C^{2}), 51.9 (C^{8}).

^{19}F {^{1}H} NMR (376 MHz, DMSO-d_6) δ –137.87.

IR (solid): 1707, 1479, 1438, 1305, 1267, 1232, 1205, 1132, 1078, 997, 928 cm^{-1}.

HRMS (MALDI): *m/z* calculated for [M – K]$^{-}$ ($C_{10}H_9BF_3O_2$)$^{-}$: 229.0639; found = 229.0655.

(*E*)-(2-(methoxycarbonyl)styryl)boronic acid, **3.74**



Prepared according to General Procedure 7 using methyl (*E*)-2-(2-(trifluoro-λ^{4}-boraneyl)vinyl)benzoate, potassium salt **3.74-int4** (190 mg, 709 μmol, 1.0 equiv.) and chlorotrimethylsilane (320 μL, 2.48 mmol, 3.5 equiv.) in MeCN:H_2O (6 mL:1.5 mL, 0.1 M). 120 mg of a white solid was obtained as a mixture of the desired product and boroxine (82%).

^{1}H NMR (500 MHz, DMSO-d_6) δ 7.86 (s, 2H, H^{11} and H^{12}), 7.75 – 7.72 (m, 1H, H^{3}), 7.74 (d, J = 17.92 Hz, 1H, H^{9}), 7.67 (d, J = 7.87 Hz, 1H, H^{6}), 7.57 (t, J = 7.58 Hz, 1H, H^{1}), 7.41 (t, J = 7.53 Hz, 1H, H^{2}), 6.04 (d, J = 18.20 Hz, 1H, H^{10}), 3.84 (s, 3H, H^{8}).

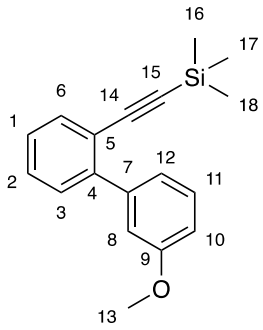
^{11}B NMR (96 MHz, DMSO-d_6) δ 26.65.

^{13}C NMR (126 MHz, DMSO-d_6) δ 167.6 (C^7), 143.7 (C^9), 138.6 (C^5), 132.1 (C^1), 129.6 (C^3), 129.4 (C^4), 128.1 (C^2), 126.8 (C^6), 52.3 (C^8). C^{10} is not observed due to quadrupolar relaxation.

IR (solid): 1722, 1618, 1597, 1568, 1479, 1448, 1435, 1371, 1292, 1249, 1163, 1130, 1074, 987 cm^{-1}.

HRMS (ESI): *m/z* calculated for $[M + H]^+$ $(C_{10}H_{12}BO_4)^+$: 207.0823; found = 207.0826.

((3'-Methoxy-[1,1'-biphenyl]-2-yl)ethynyl)trimethylsilane, **3.75-int1**



An oven-dried microwave vial was charged with 1,1'-bis(diphenylphosphino)ferrocenepalladium chloride (173 mg, 237 μmol, 5 mol%), 3-methoxybenzeneboronic acid (1.44 g, 9.48 mmol, 2.0 equiv.), and potassium phosphate (3.02 g, 14.2 mmol, 3.0 equiv.). The vial was then sealed and purged with vacuum-N_2 cycles (3 times) and backfilled with N_2. Toluene (19 mL, 0.25 M) was added followed by ((2-bromophenyl)ethynyl)trimethylsilane **3.67-int1** (840 μL, 4.74 mmol, 1.0 equiv.) and water (4.27 mL, 237 mmol, 50.0 equiv.). The reaction mixture was stirred for 24 hours at 90 °C. The crude mixture was cooled down, partitioned between ethyl acetate (20 mL) and brine (20 mL). Organics were extracted with ethyl acetate (2 × 20 mL). Organics were combined, washed with brine (20 mL), dried over sodium sulfate, filtered, and concentrated *in vacuo*. The crude residue was purified by flash chromatography (silica gel) from pure hexane to a mixture of 1% of diethyl ether in hexane affording 1.29 g of a yellow oil as the desired product (97%).

^{1}H NMR (500 MHz, Chloroform-*d*) δ 7.61 (dd, *J* = 7.69, 0.71 Hz, 1H, H^6), 7.43 – 7.41 (m, 1H, H^3), 7.39 (td, *J* = 7.39, 1.39 Hz, 1H, H^2), 7.35 (t, *J* = 7.99 Hz, 1H, H^{11}), 7.30

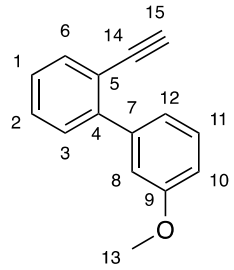
(td, J = 7.59, 1.76 Hz, 1H, H^1), 7.23 – 7.20 (m, 2H, H^8 and H^{12}), 6.95 (ddd, J = 8.23, 2.55, 1.03 Hz, 1H, H^{10}), 3.87 (s, 3H, H^{13}), 0.18 (s, 9H, H^{16}, H^{17} and H^{18}).

^{13}C NMR (126 MHz, Chloroform-*d*) δ 159.2 (C^9), 144.2 (C^4 or C^7), 141.8 (C^4 or C^7), 133.5 (C^6), 129.4 (C^2 or C^3 or C^{11}), 128.9 (C^2 or C^3 or C^{11}), 128.8 (C^2 or C^3 or C^{11}), 127.1 (C^1), 121.9 (C^8 or C^{12}), 121.5 (C^5), 115.1 (C^8 or C^{12}), 113.2 (C^{10}), 104.8 (C^{14}), 97.7 (C^{15}), 55.3 (C^{13}), –0.1 (C^{16}, C^{17} and C^{18}).

IR (neat liquid): 2156, 1602, 1579, 1469, 1438, 1419, 1296, 1247, 1207, 1178, 1053, 1020, 866 cm^{-1}.

HRMS (ESI): *m/z* calculated for $[M + H]^+$ $(C_{28}H_{21}OSi)^+$: 281.1356; found = 281.1356.

2-Ethynyl-3'-methoxy-1,1'-biphenyl, **3.75-int2**



Prepared according to General Procedure 4 using ((3'-methoxy-[1,1'-biphenyl]-2-yl)ethynyl)trimethylsilane **3.75-int1** (1.29 g, 4.60 mmol, 1.0 equiv.) and potassium carbonate (1.27 g, 9.20 mmol, 2.0 equiv.) in MeOH (23 mL, 0.2 M). The crude residue was purified by flash chromatography (silica gel) from pure hexane to a mixture of 10% of diethyl ether in hexane affording 967 mg of a yellow oil consistent with the desired product (100%).

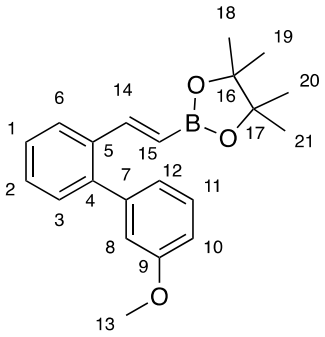
^{1}H NMR (500 MHz, Chloroform-*d*) δ 7.63 (dt, J = 7.76, 1.05 Hz, 1H, H^6), 7.43 – 7.39 (m, 2H, H^2 and H^3), 7.35 (t, J = 8.11 Hz, 1H, H^{11}), 7.31 (ddd, J = 7.67, 6.43, 2.32 Hz, 1H, H^1), 7.21 – 7.14 (m, 2H, H^8 and H^{12}), 6.94 (ddd, J = 8.26, 2.54, 1.06 Hz, 1H, H^{10}), 3.86 (s, 3H, H^{13}), 3.07 (s, 1H, H^{15}).

^{13}C NMR (126 MHz, Chloroform-*d*) δ 159.3 (C^9), 144.4 (C^4), 141.7 (C^7), 134.0 (C^6), 129.7 (C^2 or C^3or C^{11}), 129.2(C^2 or C^3or C^{11}), 129.1 (C^2 or C^3or C^{11}), 127.2 (C^1), 121.8 (C^{12}), 120.5 (C^5), 114.9 (C^8), 113.5 (C^{10}), 83.2 (C^{14}), 80.5 (C^{15}), 55.4 (C^{13}).

IR (neat liquid): 3280, 1602, 1579, 1562, 1496, 1469, 1438, 1317, 1296, 1265, 1209, 1170, 1041, 877 cm^{-1}.

HRMS (ESI): *m/z* calculated for $[M + H]^+$ $(C_{15}H_{13}O)^+$: 209.0960; found = 209.0966.

(*E*)-2-(2-(3'-Methoxy-[1,1'-biphenyl]-2-yl)vinyl)-4,4,5,5-tetramethyl-1,3,2-dioxaborolane, **3.75-int3**



Prepared according to General Procedure 5 using 2-ethynyl-3'-methoxy-1,1'-biphenyl **3.75-int2** (900 mg, 4.32 mmol, 1.0 equiv.), copper(I) chloride (43 mg, 432 μmol, 5 mol%), potassium *tert*-butoxide (97 mg, 864 μmol, 10 mol%), bis(2-diphenylphosphinophenyl) ether (DPEPhos) (233 mg, 432 μmol, 5 mol%), bis(pinacolato)diboron 2.41 g, 9.51 mmol, 1.1 equiv.), and MeOH (700 μL, 17.3 mmol, 2.0 equiv.) in THF (17 mL, 0.25 M). The crude residue was purified by flash chromatography (silica gel) from pure hexane to a mixture of 5% of diethyl ether in hexane affording 1.30 g of a pale-yellow oil consistent with the desired product (90%).

^{1}H NMR (500 MHz, Chloroform-*d*) δ 7.74 – 7.67 (m, 1H, H^6), 7.49 (d, *J* = 18.30 Hz, 1H, H^{14}), 7.38 – 7.33 (m, 4H, H^1, H^2, H^3 and H^{11}), 6.97 (dt, *J* = 7.60, 1.26 Hz, 1H, H^{12}), 6.93 (ddd, *J* = 8.14, 2.60, 0.97 Hz, 1H, H^{10}), 6.93 – 6.89 (m, 1H, H^8), 6.14 (d, *J* = 18.29 Hz, 1H, H^{15}), 3.84 (s, 3H, H^{13}), 1.27 (s, 12H, H^{18}, H^{19}, H^{20} and H^{21}).

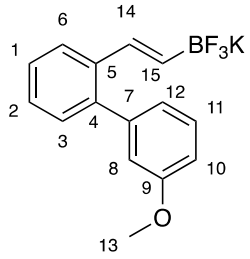
^{11}B NMR (96 MHz, Chloroform-*d*) δ 31.72.

^{13}C NMR (126 MHz, Chloroform-*d*) δ 159.3 (C^9), 148.9 (C^{14}), 142.0 (C^7), 141.3 (C^4), 136.1 (C^5), 130.2 (C^1 or C^2 or C^3), 129.2 (C^{11}), 128.6 (C^1 or C^2 or C^3), 127.7 (C^1 or C^2 or C^3), 126.6 (C^6), 122.5 (C^{12}), 118.1 (broad, C^{15}), 115.2 (C^8), 113.6 (C^{10}), 83.3 (C^{16} and C^{17}), 55.4 (C^{13}), 24.9 (C^{18}, C^{19}, C^{20} and C^{21}).

IR (neat liquid): 1616, 1577, 1467, 1419, 1379, 1371, 1344, 1321, 1267, 1211, 1139, 1043, 968 cm^{-1}.

HRMS (ESI): *m/z* calculated for $[M + H]^+$ $(C_{21}H_{26}BO_3)^+$: 337.1969; found = 337.1967.

(*E*)-Trifluoro(2-(3'-methoxy-[1,1'-biphenyl]-2-yl)vinyl)-λ^4-borane, potassium salt, **3.75-int4**



Prepared according to General Procedure 6 using (*E*)-2-(2-(3'-Methoxy-[1,1'-biphenyl]-2-yl)vinyl)-4,4,5,5-tetramethyl-1,3,2-dioxaborolane **3.75-int3** (1.00 g, 2.97 mmol, 1.0 equiv.), potassium hydrogen fluoride (929 mg, 11.9 mmol, 4.0 equiv.), and water (2.68 mL, 149 mmol, 50.0 equiv.) in MeOH (26 mL, 0.1 M). 408 mg of a white solid was obtained after filtration, consistent with the desired product (43%).

^{1}H NMR (500 MHz, DMSO-d_6) δ 7.59 (dd, *J* = 7.90, 1.31 Hz, 1H, H, H^6), 7.33 (t, *J* = 7.87 Hz, 1H, H^{11}), 7.28 (td, *J* = 8.06, 1.67 Hz, 1H, H^1), 7.18 (td, *J* = 7.29, 1.28 Hz, 1H, H^2), 7.15 (dd, *J* = 7.59, 1.70 Hz, 1H, H^3), 6.91 (ddd, *J* = 8.28, 2.61, 0.97 Hz, 1H, H^{10}), 6.85 (dt, *J* = 7.48, 1.27 Hz, 1H, H^{12}), 6.82 (dd, *J* = 2.66, 1.51 Hz, 1H, H^8), 6.50 (d, *J* = 18.04 Hz, 1H, H^{14}), 6.15 (dq, *J* = 18.10, 3.58 Hz, 1H, H^{15}), 3.77 (s, 3H, H^{13}).

^{11}B NMR (96 MHz, DMSO-d_6) δ 2.89.

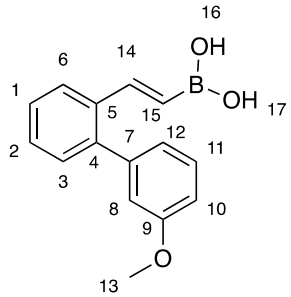
^{13}C NMR (126 MHz, DMSO-d_6) δ 158.8 (C^9), 142.6 (C^7), 140.5 (broad, C^{15}), 139.2 (C^4), 138.0 (C^5), 131.1 (q, $^3J_{CF}$ = 4.7 Hz, C^{14}), 129.7 (C^3), 129.1 (C^{11}), 127.4 (C^1), 125.8 (C^2), 125.0 (C^6), 121.9 (C^{12}), 115.1 (C^8), 112.4 (C^{10}), 55.0 (C^{13}).

^{19}F {^{1}H} NMR (470 MHz, DMSO-d_6) δ –137.53.

IR (solid): 1608, 1579, 1469, 1458, 1421, 1292, 1269, 1234, 1211, 1166, 1089, 1047 cm^{-1}.

HRMS (ESI): *m/z* calculated for $[M - K]^-$ $(C_{15}H_{13}BF_3O)^-$: 277.1017; found = 277.1025.

(*E*)-(2-(3'-Methoxy-[1,1'-biphenyl]-2-yl)vinyl)boronic acid, **3.75**



Prepared according to General Procedure 7 using a mixture of (*E*)-trifluoro(2-(3'-methoxy-[1,1'-biphenyl]-2-yl)vinyl)-λ^4-borane, potassium salt **3.75-int4** (300 mg, 1.05 mmol, 1.0 equiv.) and chlorotrimethylsilane (470 μL, 3.67 mmol, 3.5 equiv.) in MeCN:H_2O (8 mL:2 mL, 0.1 M). 136 mg of a white solid was obtained as the desired product (33%). It contained protodeboronated product, no further purification was caried out (35%).

^{1}H NMR (500 MHz, Acetone-d_6) δ 7.75 – 7.72 (m, 1H, H^6), 7.45 (d, *J* = 18.29 Hz, 1H, H^{14}), 7.43 – 7.28 (m, 4H, H^1, H^2, H^3 and H^{11}), 6.98 – 6.88 (m, 3H, H^8, H^{10} and H^{12}), 6.87 (s, 2H, H^{16} and H^{17}), 6.20 (d, *J* = 18.25 Hz, 1H, H^{15}), 3.83 (s, 3H, H^{13}).

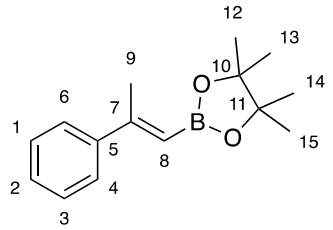
^{11}B NMR (96 MHz, Acetone-d_6) δ 28.75.

^{13}C NMR (126 MHz, Acetone-d_6) δ 160.4 (C^9), 146.5 (C^{14}), 143.0 (C^7), 142.0 (C^4), 137.1 (C^5), 130.9 (C^2 or C^3 or C^{11}), 130.0 (C^2 or C^3 or C^{11}), 129.0 (C^2 or C^3 or C^{11}), 128.5 (C^1), 126.9 (C^6), 122.9 (C^{12}), 116.0 (C^8), 113.7 (C^{10}), 55.5 (C^{13}). C^{14} is not observed due to quadrupolar relaxation.

IR (solid): 1612, 1597, 1577, 1467, 1442, 1419, 1346, 1290, 1267, 1211, 1178, 1045 cm^{-1}.

HRMS (ESI): *m/z* calculated for $[M + H]^+$ $(C_{15}H_{16}BO_3)^+$: 255.1187; found = 255.1182.

(*E*)-4,4,5,5-Tetramethyl-2-(2-phenylprop-1-en-1-yl)-1,3,2-dioxaborolane, **3.76-int3**



Prepared according to the literature.[221] In an oven-dried microwave vial loaded with a Teflon-coated stir bar, copper(I) chloride (10 mg, 100 μmol, 10 mol%), bis(pinacolato)diboron (279 mg, 1.10 mmol, 1.1 equiv.), 4,5-bis(diphenylphosphino)-8,9-dimethylxanthene (XantPhos) (58 mg, 100 μmol, 10 mol%), and potassium *tert*-butoxide (123 mg, 1.10 mmol, 1.1 equiv.) were weighed out. The vial was sealed, purged with N_2-vacuum cycles, and backfilled with N_2. THF (5.00 mL) was added and the mixture was stirred for 10 minutes at room temperature. Phenylacetylene (110 μL, 1.00 mmol, 1.0 equiv.) was added followed by iodomethane (250 μL, 4.00 mmol, 4.0 equiv.). The reaction mixture was stirred overnight at room temperature. The reaction mixture was filtered through a celite pad and the crude residue was purified by flash chromatography (silica gel) from pure hexane to a mixture of 2% of diethyl ether in hexane affording 137 mg of a colourless oil consistent with the desired product (56%).

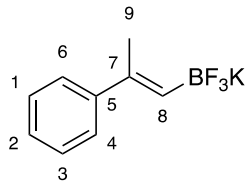
^{1}H NMR (500 MHz, Chloroform-*d*) δ 7.53 – 7.49 (m, 2H, H^4 and H^6), 7.36 – 7.31 (m, 2H, H^1 and H^3), 7.31 – 7.27 (m, 1H, H^2), 5.77 (q, *J* = 0.98 Hz, 1H, H^8), 2.42 (d, *J* = 1.01 Hz, 3H, H^9), 1.32 (s, 12H, H^{12}, H^{13}, H^{14} and H^{15}).

^{11}B NMR (96 MHz, Chloroform-*d*) δ 30.00.

^{13}C NMR (126 MHz, Chloroform-*d*) δ 157.9 (C^7), 143.9 (C^5), 128.3 (C^1 and C^3), 128.0 (C^2), 125.9 (C^4 and C^6), 115.6 (broad, C^8), 83.1 (C^{10} and C^{11}), 25.0 (C^{12}, C^{13}, C^{14} and C^{15}), 20.2 (C^9).

Data are consistent with the literature.[309]

(*E*)-Trifluoro(2-phenylprop-1-en-1-yl)-λ^4-borane, potassium salt, **3.76-int4**



Prepared according to General Procedure 6 using (*E*)-4,4,5,5-tetramethyl-2-(2-phenylprop-1-en-1-yl)-1,3,2-dioxaborolane **3.76-int3** (440 mg, 1.80 mmol, 1.0 equiv.), potassium hydrogen fluoride (563 mg, 7.21 mmol, 4.0 equiv.), and water (1.62 mL, 90.1 mmol, 50.0 equiv.) in MeOH (15 mL, 0.1 M). 311 mg of a white solid was obtained after filtration, consistent with the desired product (77%).

^{1}H NMR (500 MHz, DMSO-d_6) δ 7.36 – 7.33 (m, 2H, H^4 and H^6), 7.26 – 7.21 (m, 2H, H^1 and H^3), 7.13 – 7.08 (m, 1H, H^2), 5.72 (qd, J = 5.07, 1.07 Hz, 1H, H^8), 2.03 (app. s, 3H, H^9).

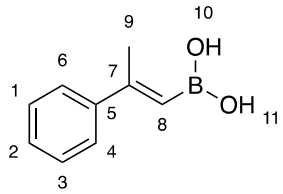
^{13}C NMR (126 MHz, DMSO-d_6) δ 146.0 (C^5), 138.2 (q, $^{3}J_{CF}$ = 4.7 Hz, C^7), 127.8 (C^1 and C^3), 125.4 (C^2), 124.8 (C^4 and C^6), 18.4 (C^9). C^8 is not observed due to quadrupolar relaxation.

^{11}B NMR (96 MHz, DMSO-d_6) δ 2.75.

^{19}F {^{1}H} NMR (376 MHz, DMSO-d_6) δ –132.41.

Data are consistent with the literature.[309]

(*E*)-(2-Phenylprop-1-en-1-yl)boronic acid, **3.76**



Prepared according to General Procedure 7 using (*E*)-trifluoro(2-phenylprop-1-en-1-yl)-λ^4-borane, potassium salt **3.76-int4** (270 mg, 1.20 mmol, 1.0 equiv.) and chlorotrimethylsilane (540 μL, 4.22 mmol, 3.5 equiv.) in MeCN:H_2O (10 mL:3 mL, 0.1 M). 41 mg of a white solid was obtained as a mixture of the desired product and boroxine (21%). It contained 7% of (*E*)-styrylboronic acid (**3.1a**).

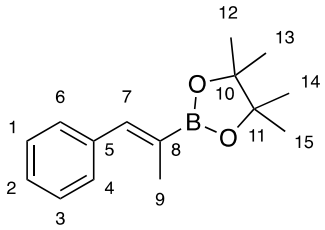
^{1}H NMR (400 MHz, Acetone-d_6) δ 7.56 – 7.48 (m, 2H, H^4 and H^6), 7.39 – 7.32 (m, 2H, H^1 and H^3), 7.31 – 7.23 (m, 1H, H^2), 6.98 (s, 2H, H^{10} and H^{11}), 5.80 (q, J = 1.07 Hz, 1H, H^8), 2.39 (d, J = 1.04 Hz, 3H, H^9).

^{11}B NMR (96 MHz, Acetone-d_6) δ 28.67.

^{13}C NMR (126 MHz, Acetone-d_6) δ 154.2 (C^7), 145.5 (C^5), 129.0 (C^1 and C^3), 128.3 (C^2), 126.4 (C^4 and C^6), 19.8 (C^9). C^8 is not observed due to quadrupolar relaxation.

Data are consistent with the literature.[228]

(*Z*)-4,4,5,5-Tetramethyl-2-(1-phenylprop-1-en-2-yl)-1,3,2-dioxaborolane, **3.77-int3**



Prepared according to the literature.[222] In an oven-dried microwave vial, loaded with a Teflon-coated stir bar, copper(I) chloride (25 mg, 250 μmol, 5 mol%), potassium carbonate (138 mg, 1.00 mmol, 20 mol%), tris(*p*-methoxyphenyl)phosphine (88 mg, 250 μmol, 5 mol%), and bis(pinacolato)diboron (1.52 g, 6.00 mmol, 1.2 equiv.) were weighed out. The vial was sealed and purged with N_2-vacuum cycles, and backfilled with N_2. Et_2O (20 mL, 0.25 M) was added, followed by 1-phenyl-1-propyne (630 μL, 5.00 mmol, 1.0 equiv.) and isopropanol (770 μL, 10.0 mmol, 2.0 equiv.). The reaction mixture was stirred for 16 hours at room temperature. Once completion was reached, the reaction mixture was filtered through a pad of celite, the vial was rinsed with DCM (2 × 20 mL), and concentrated *in vacuo*. The crude residue was purified by flash chromatography (silica gel) from pure hexane to a mixture of 2% of diethyl ether in hexane affording 1.13 g of a colourless oil consistent with the desired product (93%).

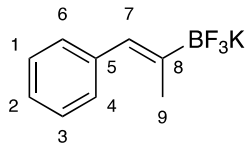
^{1}H NMR (500 MHz, Chloroform-*d*) δ 7.41 – 7.38 (m, 2H, H^4 and H^6), 7.37 – 7.32 (m, 2H, H^1 and H^3), 7.27 – 7.22 (m, 2H, H^2 and H^7), 2.00 (d, *J* = 1.79 Hz, 3H, H^9), 1.32 (s, 12H, H^{12}, H^{13}, H^{14} and H^{15}).

^{11}B NMR (96 MHz, Chloroform-*d*) δ 30.89.

^{13}C NMR (126 MHz, Chloroform-*d*) δ 142.5 (C^7), 138.1 (C^5), 129.5 (C^4 and C^6), 128.2 (C^1 and C^3), 127.2 (C^2), 83.6 (C^{11} and C^{10}), 25.0 (C^{12}, C^{13}, C^{14} and C^{15}), 16.0 (C^9). C^8 is not observed due to quadrupolar relaxation.

Data are consistent with the literature.[310]

(*Z*)-Trifluoro(1-phenylprop-1-en-2-yl)-λ^4-borane, potassium salt, **3.77-int4**



Prepared according to General Procedure 6 using (*Z*)-4,4,5,5-tetramethyl-2-(1-phenylprop-1-en-2-yl)-1,3,2-dioxaborolane **3.77-int3** (1.13 g, 4.63 mmol, 1.0 equiv.), potassium hydrogen fluoride (1.45 g, 18.5 mmol, 4.0 equiv.), and water (4.17 mL, 231 mmol, 50.0 equiv.) in MeOH (46 mL, 0.1 M). 845 mg of a white solid was obtained after filtration, consistent with the desired product (81%).

^{1}H NMR (500 MHz, DMSO-d_6) δ 7.28 – 7.24 (m, 2H, H^1 and H^3), 7.19 – 7.15 (m, 2H, H^4 and H^6), 7.10 – 7.05 (m, 1H, H^2), 6.38 (s, 1H, H^7), 1.71 (d, *J* = 1.72 Hz, 3H, H^9).

^{11}B NMR (96 MHz, DMSO-d_6) δ 3.05.

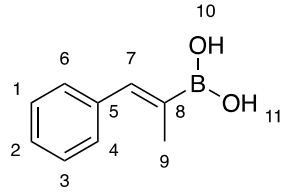
^{13}C NMR (126 MHz, DMSO-d_6) δ 140.6 (C^5), 128.5 (C^4 and C^6), 127.8 (C^1 and C^3), 126.1 (q, $^3J_{CF}$ = 3.1 Hz, C^7), 124.6 (C^2), 16.6 (C^9). C^8 is not observed due to quadrupolar relaxation.

^{19}F {^{1}H} NMR (376 MHz, DMSO-d_6) δ –143.51.

IR (solid): 1489, 1446, 1230, 1217, 1192, 1180, 1035, 1020, 958, 937, 920, 844 cm^{-1}.

HRMS (ESI): *m/z* calculated for [M – K]$^-$ ($C_9H_9BF_3$)$^-$: 185.0754; found = 185.0761.

(*Z*)-(1-Phenylprop-1-en-2-yl)boronic acid, **3.77**



Prepared according to General Procedure 7 using (*Z*)-trifluoro(1-phenylprop-1-en-2-yl)-λ^4-borane, potassium salt **3.77-int4** (800 mg, 3.57 mmol, 1.0 equiv.), and

chlorotrimethylsilane (1.59 mL, 12.5 mmol, 3.5 equiv.) in MeCN:H_2O (28 mL:7 mL, 0.1 M). 436 mg of a white solid was obtained as a mixture of the desired product and boroxine (75%).

^{1}H NMR (500 MHz, DMSO-d_6) δ 7.67 (s, 2H, H^{10} and H^{11}), 7.38 – 7.34 (m, 2H, H^1 and H^3), 7.33 – 7.30 (m, 2H, H^4 and H^6), 7.25 – 7.21 (m, 1H, H^2), 7.12 (d, J = 1.17 Hz, 1H, H^7), 1.88 (d, J = 1.80 Hz, 3H, H^9).

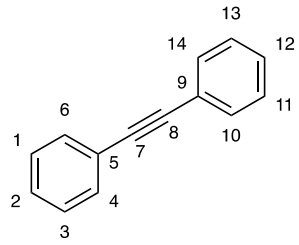
^{11}B NMR (96 MHz, DMSO-d_6) δ 29.26.

^{13}C NMR (126 MHz, DMSO-d_6) δ 139.0 (C^7), 138.2 (C^5), 134.3 (broad, C^8), 129.1 (C^4 and C^6), 128.3 (C^1 and C^3), 126.8 (C^2), 16.3 (C^9).

IR (solid): 1610, 1573, 1489, 1446, 1386, 1359, 1328, 1303, 1263, 1203, 1180, 1099, 1076, 927, 792 cm^{-1}.

HRMS (EI): *m/z* calculated for $[M]^+$ $(C_9H_{11}BNO_2)^+$: 162.0846; found = 162.0852.

1,2-Diphenylethyne, **3.78-int2**



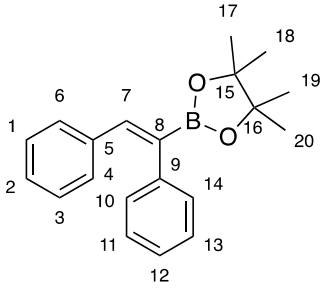
Prepared according to General Procedure 3 using iodobenzene (1.14 mL, 10.0 mmol, 1.0 equiv.), dichlorobis(triphenylphosphine)palladium (70 mg, 100 μmol, 1 mol%), copper iodide (38 mg, 200 μmol, 2 mol%), and phenylacetylene (1.37 mL, 12.5 mmol, 1.25 equiv.) in triethylamine (20 mL, 0.5 M). The crude residue was purified by flash chromatography (silica gel) with pure hexane affording 1.74 g of a yellow solid as the desired product (98%).

^{1}H NMR (400 MHz, Chloroform-d) δ 7.60 – 7.53 (m, 4H, H^4, H^6, H^{10} and H^{14}), 7.43 – 7.34 (m, 6H, H^1, H^2, H^3, H^{11}, H^{12} and H^{13}).

^{13}C NMR (101 MHz, Chloroform-*d*) δ 131.7 (C^{4}, C^{6}, C^{10} and C^{14}), 128.5 (C^{1}, C^{3}, C^{11} and C^{13}), 128.4 (C^{2} and C^{12}), 123.4 (C^{5} and C^{9}), 89.5 (C^{7} and C^{8}).

Data are consistent with the literature.[311]

(*Z*)-2-(1,2-Diphenylvinyl)-4,4,5,5-tetramethyl-1,3,2-dioxaborolane, **3.78-int3**



Prepared according to the literature.[222] In an oven-dried microwave vial, loaded with a Teflon-coated stir bar, copper(I) chloride (42 mg, 421 μmol, 5 mol%), potassium carbonate (233 mg, 1.68 mmol, 20 mol%), tris(*p*-methoxyphenyl)phosphine (148 mg, 421 μmol, 5 mol%), and bis(pinacolato)diboron (2.56 g, 10.1 mmol, 1.2 equiv.) were weighed out. The vial was sealed and purged with N_2-vacuum cycles, and backfilled with N_2. Et_2O (34 mL, 0.25 M) was added, followed by 1,2-diphenylethyne **3.78-int2** (1.50 g, 8.42 mmol, 1.0 equiv.), and isopropanol (770 μL, 16.8 mmol, 2.0 equiv.). The reaction mixture was stirred for 16 hours at room temperature. Once completion was reached, the reaction mixture was filtered through a pad of celite and the vial was rinsed with DCM (2 × 20 mL), and concentrated *in vacuo*. The crude residue was purified by flash chromatography (silica gel) from pure hexane to a mixture of 2% of diethyl ether in hexane affording 1.74 g of a white solid consistent with the desired product (68%).

^{1}H NMR (500 MHz, Chloroform-*d*) δ 7.38 (s, 1H, H^{7}), 7.29 – 7.25 (m, 2H, H^{11} and H^{13}), 7.24 – 7.20 (m, 1H, H^{12}), 7.19 – 7.16 (m, 2H, H^{10} and H^{14}), 7.14 – 7.11 (m, 3H, H^{1}, H^{2} and H^{3}), 7.09 – 7.05 (m, 2H, H^{4} and H^{6}), 1.32 (s, 12H, H^{17}, H^{18}, H^{19} and H^{20}).

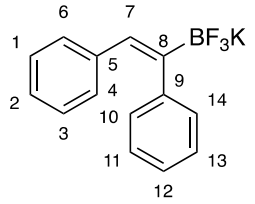
^{11}B NMR (96 MHz, Chloroform-*d*) δ 30.93.

^{13}C NMR (126 MHz, Chloroform-*d*) δ 143.3 (C^{7}), 140.6 (C^{9}), 137.1 (C^{5}), 130.1 (C^{4} and C^{6}), 129.0 (C^{10} and C^{14}), 128.4 (C^{11} and C^{13}), 128.0 (C^{1} and C^{3}), 127.7 (C^{2}), 126.4

(C^{12}), 83.9 (C^{15} and C^{16}), 24.9 (C^{17}, C^{18}, C^{19} and C^{20}). C^8 is not observed due to quadrupolar relaxation.

Data are consistent with the literature.[312]

(*Z*)-(1,2-Diphenylvinyl)trifluoro-λ^4-borane, potassium salt, **3.78-int4**



Prepared according to General Procedure 6 using (*Z*)-2-(1,2-diphenylvinyl)-4,4,5,5-tetramethyl-1,3,2-dioxaborolane **3.78-int3** (1.74 g, 5.68 mmol, 1.0 equiv.), potassium hydrogen fluoride (1.78 g, 22.7 mmol, 4.0 equiv.), and water (5.12 mL, 284 mmol, 50.0 equiv.) in MeOH (56 mL, 0.1 M). 1.21 g of a white solid was obtained after filtration, consistent with the desired product (74%).

^{1}H NMR (400 MHz, DMSO-d_6) δ 7.17 – 7.11 (m, 2H, H^{11} and H^{13}), 7.06 – 7.02 (m, 1H, H^{12}), 7.02 – 6.97 (m, 4H, H^1, H^3, H^{10} and H^{14}), 6.96 – 6.90 (m, 1H, H^2), 6.88 – 6.81 (m, 2H, H^4 and H^6), 6.53 (s, 1H, H^7).

^{11}B NMR (96 MHz, DMSO-d_6) δ 3.02.

^{13}C NMR (101 MHz, DMSO-d_6) δ 146.3 (C^9), 139.6 (C^5), 128.7 (C^4 and C^6), 127.7 (C^1 and C^3 or C^{10} and C^{14}), 127.5 (C^1 and C^3 or C^{10} and C^{14}), 127.4 (broad, C^7), 127.4 (C^{11} and C^{13}), 124.9 (C^2), 124.0 (C^{12}). C^8 is not observed due to quadrupolar relaxation.

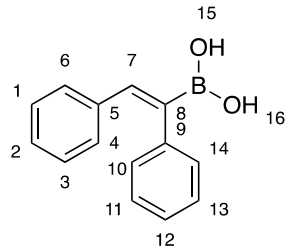
^{19}F {^{1}H} NMR (377 MHz, DMSO-d_6) δ –140.72.

IR (solid): 1593, 1489, 1446, 1198, 1122, 1016, 1097, 1070, 977, 947 cm^{-1}.

HRMS (ESI): *m/z* calculated for $[M - K]^-$ ($C_{14}H_{11}BF_3$)$^-$: 247.0897; found = 247.0913.

Data are consistent with the literature.[313]

(*Z*)-(1,2-Diphenylvinyl)boronic acid, **3.78**



Prepared according to General Procedure 7 using (*Z*)-(1,2-diphenylvinyl)trifluoro-λ^4-borane, potassium salt **3.78-int4** (1.10 g, 3.84 mmol, 1.0 equiv.) and chlorotrimethylsilane (1.71 mL, 13.5 mmol, 3.5 equiv.) in MeCN:H_2O (31 mL:8 mL, 0.1 M). 769 mg of a pale-yellow solid was obtained as a mixture of the desired product and boroxine (89%).

^{1}H NMR (400 MHz, Acetone-d_6) δ 7.38 (s, 1H, H^7), 7.33 – 7.25 (m, 3H, H^{arom}), 7.23 – 7.18 (m, 1H, H^{arom}), 7.13 – 7.09 (m, 4H, H^{arom}), 7.04 – 6.99 (m, 2H, H^4 and H^6), 6.86 (s, 2H, H^{15} and H^{16}).

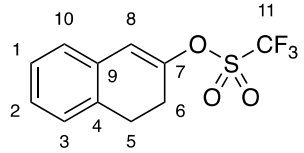
^{11}B NMR (96 MHz, Acetone-d_6) δ 28.48.

^{13}C NMR (101 MHz, Acetone-d_6) δ 143.0 (C^9), 141.1 (C^7), 138.3 (C^5), 130.6 (C^{arom}), 129.4 (C^{arom}), 129.2 (C^{arom}), 128.7 (C^{arom}), 128.1 (C^2 or C^{12}), 126.8 (C^2 or C^{12}). C^8 is not observed due to quadrupolar relaxation.

IR (solid): 3192, 2260, 1678, 1597, 1444, 1406, 1282, 1192, 1074, 997 cm^{-1}.

HRMS: Desired mass not found due to fragmentation/instability of the starting material.

3,4-Dihydronaphthalen-2-yl trifluoromethanesulfonate, **3.79-int0**



In a flame-dried two neck flask, loaded with a Teflon-coated stir bar, potassium *tert*-butoxide (842 mg, 7.50 mmol, 1.5 equiv.) was weighed out. The flask was purged with vacuum-N_2 and backfilled with N_2. THF (30 mL) was added and the reaction mixture

was cooled down to 0 °C. β-Tetralone (731 mg, 5.00 mmol, 1.0 equiv.) was dissolved in THF (10 mL) and added dropwise at 0 °C. The reaction mixture was left to stir for one hour. Finally, *N*-phenylbis(trifluoromethanesulphonimide) (2.14 g, 6.00 mmol, 1.2 equiv.) was dissolved in THF (10 mL) and added dropwise at 0 °C. The reaction was left to stir for four hours. Once completion was reached, the reaction mixture was concentrated *in vacuo*. The crude residue was partitioned between brine (30 mL) and diethyl ether (30 mL). Organics were extracted with diethyl ether (2 × 15 mL). Organic layers were combined, washed with brine (30 mL), dried over sodium sulfate, filtered, and concentrated *in vacuo*. The crude residue was purified by flash chromatography (silica gel) from pure hexane to a mixture of 2% of diethyl ether in hexane affording 1.38 g of a colourless oil consistent with the desired product (99%).

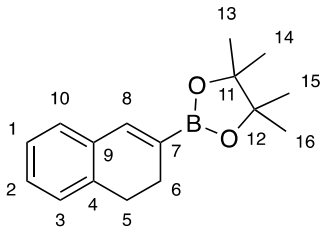
^{1}H NMR (500 MHz, Chloroform-*d*) δ 7.23 – 7.19 (m, 2H, H^{1} and H^{2}), 7.17 – 7.14 (m, 1H, H^{3}), 7.11 – 7.07 (m, 1H, H^{10}), 6.49 (t, *J* = 1.35 Hz, 1H, H^{8}), 3.07 (t, *J* = 8.38 Hz, 2H, H^{5}), 2.70 (td, *J* = 8.41, 1.30 Hz, 2H, H^{6}).

^{13}C NMR (126 MHz, Chloroform-*d*) δ 150.1 (C^{7}), 133.1 (C^{4}), 131.2 (C^{9}), 128.6 (C^{2}), 127.7 (C^{3}), 127.5 (C^{10}), 127.2 (C^{1}), 118.7 (q, $^{1}J_{CF}$ = 320.7 Hz, C^{11}), 118.7 (C^{8}), 28.7 (C^{5}), 26.7 (C^{6}).

^{19}F {^{1}H} NMR (470 MHz, Chloroform-*d*) δ –73.56.

Data are consistent with the literature.[314]

2-(3,4-Dihydronaphthalen-2-yl)-4,4,5,5-tetramethyl-1,3,2-dioxaborolane, **3.79-int3**



Prepared according to the literature.[305] In an oven-dried microwave vial, charged with a Teflon-coated stir bar, 3,4-dihydronaphthalen-2-yl trifluoromethanesulfonate **3.79-int0** (1.20 g, 4.31 mmol, 1.0 equiv.), triphenylphosphine (68 mg, 259 μmol, 6 mol%), bis(triphenylphosphine)palladium (II) chloride (91 mg, 129 μmol, 3 mol%),

bis(pinacolato)diboron (1.20 g, 4.74 mmol, 1.1 equiv.), and potassium acetate (1.27 g, 12.9 mmol, 3.0 equiv.). The vial was sealed and purged with vacuum-N_2 and backfilled with N_2. Dry and degassed 1,4-dioxane (24 mL, 0.2 M) was added and the reaction mixture was stirred at 60 °C overnight. Once completion was reached, the reaction mixture was concentrated *in vacuo*. The crude residue was partitioned between brine (20 mL) and diethyl ether (20 mL). Organics were extracted with diethyl ether (2 × 20 mL). Organic layers were combined, washed with brine (20 mL), dried over sodium sulfate, filtered, and concentrated *in vacuo*. The crude residue was purified by flash chromatography (silica gel) from pure hexane to mixture of 4% of diethyl ether in hexane affording 944 mg of a colourless oil consistent with the desired product (85%).

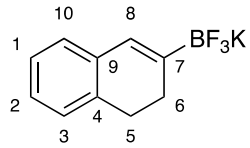
^{1}H NMR (500 MHz, Chloroform-*d*) δ 7.22 (t, *J* = 1.83 Hz, 1H, H^8), 7.18 – 7.15 (m, 2H, H^1 and H^2), 7.14 – 7.09 (m, 2H, H^3 and H^{10}), 2.76 (t, *J* = 8.13 Hz, 2H, H^5), 2.41 (td, *J* = 8.17, 1.79 Hz, 2H, H^6), 1.32 (s, 12H, H^{13}, H^{14}, H^{15} and H^{16}).

^{11}B NMR (96 MHz, Chloroform-*d*) δ 30.85.

^{13}C NMR (126 MHz, Chloroform-*d*) δ 140.6 (C^8), 137.3 (C^4), 133.9 (C^9), 128.1 (C^1 or C^2), 127.6 (C^3), 127.1 (C^{10}), 126.5 (C^1 or C^2), 83.5 (C^{11} and C^{12}), 27.5 (C^5), 25.0 (C^{13}, C^{14}, C^{15} and C^{16}), 24.2 (C^6). C^7 is not observed due to quadrupolar relaxation.

Data are consistent with the literature.[315]

(3,4-Dihydronaphthalen-2-yl)trifluoro-λ^4-borane, potassium salt, **3.79-int4**



Prepared according to General Procedure 6 using 2-(3,4-dihydronaphthalen-2-yl)-4,4,5,5-tetramethyl-1,3,2-dioxaborolane **3.79-int3** (900 mg, 3.51 mmol, 1.0 equiv.), potassium hydrogen fluoride (1.10 g, 14.1 mmol, 4.0 equiv.), and water (3.16 mL, 176 mmol, 50.0 equiv.) in MeOH (35 mL, 0.1 M). 760 mg of a white solid was obtained after filtration, consistent with the desired product (92%).

^{1}H NMR (500 MHz, DMSO-d_6) δ 7.03 (td, J = 7.32, 1.59 Hz, 1H, H^{1}), 7.01 – 6.97 (m, 1H, H^{3}), 6.94 (td, J = 7.28, 1.38 Hz, 1H, H^{2}), 6.86 (dd, J = 7.40, 1.36 Hz, 1H, H^{10}), 6.31 (s, 1H, H^{8}), 2.53 (t, J = 8.11 Hz, 2H, H^{6}), 2.10 (td, J = 7.72, 1.46 Hz, 2H, H^{5}).

^{11}B NMR (96 MHz, DMSO-d_6) δ 2.47.

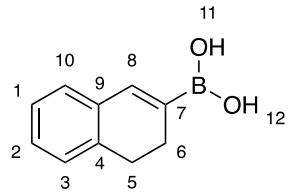
^{13}C NMR (126 MHz, DMSO-d_6) δ 151.3 (broad, C^{7}), 136.2 (C^{4}), 135.2 (C^{9}), 126.9 (C^{3}), 126.0 (C^{1}), 124.8 (q, $^{3}J_{CF}$ = 3.3 Hz, C^{8}), 124.8 (C^{2}), 124.5 (C^{10}), 27.7 (C^{5}), 25.4 (C^{6}).

^{19}F {^{1}H} NMR (377 MHz, DMSO-d_6) δ –142.59.

IR (solid): 1624, 1485, 1448, 1265, 1240, 1197, 1180, 1166, 1103, 999, 966 cm^{-1}.

HRMS (ESI): *m/z* calculated for $[M - K]^-$ $(C_{10}H_9BF_3)^-$: 197.0754; found = 197.0755.

(3,4-Dihydronaphthalen-2-yl)boronic acid, **3.79**



Prepared according to General Procedure 7 using (3,4-dihydronaphthalen-2-yl)trifluoro-λ^{4}-borane, potassium salt **3.79-int4** (650 mg, 2.75 mmol, 1.0 equiv.) and chlorotrimethylsilane (1.22 mL, 9.64 mmol, 3.5 equiv.) in MeCN:H_2O (22 mL:6 mL, 0.1 M). 422 mg of a white solid as was obtained as a mixture of the desired product and boroxine (88%).

^{1}H NMR (400 MHz, DMSO-d_6) δ 7.69 (s, 2H, H^{11} and H^{12}), 7.19 – 7.12 (m, 3H, H^{arom}), 7.11 (t, J = 1.45 Hz, 1H, H^{8}), 7.08 – 7.05 (m, 1H, H^{arom}), 2.63 (t, J = 8.25 Hz, 2H, H^{5}), 2.27 (td, J = 8.10, 1.46 Hz, 2H, H^{6}).

^{11}B NMR (96 MHz, DMSO-d_6) δ 26.50.

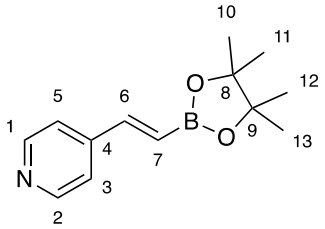
^{13}C NMR (101 MHz, DMSO-d_6) δ 137.2 (C^{8}), 136.4 (C^{4}), 135.7 (broad, C^{7}), 134.0 (C^{9}), 127.5 (C^{arom}), 127.3 (C^{3}), 126.5 (C^{arom}), 126.3 (C^{arom}), 27.1 (C^{5}), 24.3 (C^{6}).

IR (solid): 2929, 1612, 1566, 1450, 1371, 1313, 1282, 1209, 1157, 1112, 992, 904 cm^{-1}.

HRMS (ESI): *m/z* calculated for $[M - H]^-$ $(C_{10}H_{10}BO_2)^-$: 173.0779; found = 173.0775.

Data are consistent with the literature.[316]

(*E*)-4-(2-(4,4,5,5-Tetramethyl-1,3,2-dioxaborolan-2-yl)vinyl)pyridine, **3.80-int3**



Prepared according to General Procedure 5 using 4-ethynylpyridine (516 mg, 5.00 mmol, 1.0 equiv.), copper(I) chloride (25 mg, 250 μmol, 5 mol%), potassium *tert*-butoxide (56 mg, 500 μmol, 10 mol%), bis(2-diphenylphosphinophenyl) ether (DPEPhos) (135 mg, 250 μmol, 5 mol%), bis(pinacolato)diboron (1.40 g, 5.50 mmol, 1.1 equiv.), and MeOH (410 μL, 10.0 mmol, 2.0 equiv.) in THF (20 mL, 0.25 M). 1.05 g of a brown solid was afforded consistent with the desired product (91%). It contained B_2Pin_2 or related adducts.

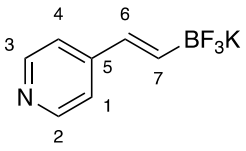
^{1}H NMR (500 MHz, Chloroform-*d*) δ 8.53 – 8.50 (m, 2H, H^1 and H^2), 7.29 – 7.26 (m, 2H, H^3 and H^5), 7.24 (d, *J* = 18.37 Hz, 1H, H^6), 6.32 (d, *J* = 18.41 Hz, 1H, H^7), 1.25 (s, 12H, H^{10}, H^{11}, H^{12} and H^{13}).

^{11}B NMR (128 MHz, Chloroform-*d*) δ 29.89.

^{13}C NMR (126 MHz, Chloroform-*d*) δ 150.0 (C^1 and C^2), 146.4 (C^6), 144.8 (C^4), 122.3 (broad, C^7), 121.3 (C^3 and C^5), 83.8 (C^8 and C^9), 24.8 (C^{10}, C^{11}, C^{12} and C^{13}).

Data are consistent with the literature.[317]

(*E*)-4-(2-(Trifluoro-λ^4-boraneyl)vinyl)pyridine, potassium salt, **3.80-int4**



Prepared according to General Procedure 6 using (*E*)-4-(2-(4,4,5,5-tetramethyl-1,3,2-dioxaborolan-2-yl)vinyl)pyridine, **3.80-int3** (800 mg, 3.46 mmol, 1.0 equiv.), potassium hydrogen fluoride (1.08 g, 13.8 mmol, 4.0 equiv.), and water (3.12 mL, 173

mmol, 50.0 equiv.) in MeOH (32 mL, 0.1 M). 220 mg of a pale-brown solid was obtained after filtration, consistent with the desired product (30%).

^{1}H NMR (500 MHz, DMSO-d_6) δ 8.42 – 8.37 (m, 2H, H^2 and H^3), 7.29 – 7.25 (m, 2H, H^1 and H^4), 6.52 (dq, J = 18.22, 3.31 Hz, 1H, H^7), 6.44 (d, J = 18.30 Hz, 1H, H^6).

^{11}B NMR (128 MHz, DMSO-d_6) δ 2.34.

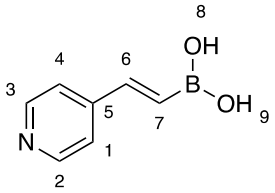
^{13}C NMR (126 MHz, DMSO-d_6) δ 149.6 (C^2 and C^3), 147.2 (C^5), 145.6 (broad, C^7), 131.1 (q, $^{3}J_{CF}$ = 4.5 Hz Hz, C^6), 120.3 (C^1 and C^4).

^{19}F {^{1}H} NMR (377 MHz, DMSO-d_6) δ –138.51.

IR (solid): 1604, 1548, 1425, 1344, 1257, 1238, 1124, 1089, 995, 970 cm^{-1}.

HRMS (ESI): *m/z* calculated for $[M - K]^-$ ($C_7H_6BF_3N)^-$: 172.0551; found = 172.0550.

(*E*)-(2-(Pyridin-4-yl)vinyl)boronic acid, **3.80**



Prepared according to General Procedure 7 using (*E*)-4-(2-(trifluoro-λ^4-boraneyl)vinyl)pyridine, potassium salt **3.80-int4** (200 mg, 948 μmol, 1.0 equiv.) and chlorotrimethylsilane (420 μL, 3.32 mmol, 3.5 equiv.) in MeCN:H_2O (8 mL:2 mL, 0.1 M). The aqueous layer was concentrated *in vacuo* affording 183 mg of a brown solid as the desired product (99%).

^{1}H NMR (400 MHz, DMSO-d_6) δ 8.92 – 8.83 (m, 2H, H^2 and H^3), 8.18 – 8.03 (m, 2H, H^1 and H^4), 7.40 (d, J = 18.37 Hz, 1H, H^6), 6.79 (d, J = 18.35 Hz, 1H, H^7). H^8 and H^9 are not observed.

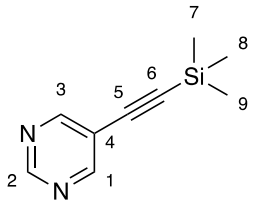
^{11}B NMR (96 MHz, DMSO-d_6) δ 26.10.

^{13}C NMR (101 MHz, DMSO-d_6) δ 153.4 (C^5), 141.9 (C^2 and C^3), 140.5 (C^6), 137.1 (broad, C^7), 124.0 (C^1 and C^4).

IR (solid): 1633, 1591, 1496, 1442, 1406, 1344, 1321, 1294, 1228, 1190, 1116, 936 cm^{-1}.

HRMS (ESI): *m/z* calculated for $[M + H]^+$ $(C_7H_9BNO_2)^+$: 150.0721; found = 150.0720.

5-((Trimethylsilyl)ethynyl)pyrimidine, **3.81-int1**



Prepared according to General Procedure 3 using 5-bromopyrimidine (954 mg, 6.00 mmol, 1.0 equiv.), dichlorobis(triphenylphosphine)palladium (42 mg, 60.0 μmol, 1 mol%), copper iodide (23 mg, 120 μmol, 2 mol%), and trimethylsilylacetylene (6.34 mL, 60.0 mmol, 10.0 equiv.) in triethylamine (12 mL, 0.5 M) at 90 °C. The crude residue was purified by flash chromatography (silica gel) from pure hexane to a mixture of 5% of diethyl ether in hexane affording 1.05 g of a pale-brown oil as the desired product (99%).

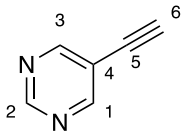
^{1}H NMR (500 MHz, Chloroform-*d*) δ 9.10 (s, 1H, H^2), 8.76 (s, 2H, H^1 and H^3), 0.25 (s, 9H, H^7, H^8 and H^9).

^{13}C NMR (126 MHz, Chloroform-*d*) δ 159.2 (C^1 and C^3), 156.8 (C^2), 119.9 (C^4), 102.9 (C^5), 97.7 (C^6), –0.2 (C^7, C^8 and C^9).

IR (film): 2164, 1541, 1408, 1246, 1184, 908, 860, 840 cm^{-1}.

HRMS (ESI): *m/z* calculated for $[M + H]^+$ $(C_9H_{13}N_2Si)^+$: 177.0843; found = 177.0842.

5-Ethynylpyrimidine, **3.81-int2**



Prepared according to General Procedure 4 using 5-((trimethylsilyl)ethynyl)pyrimidine **3.81-int1** (1.00 g, 5.67 mmol, 1.0 equiv.) and

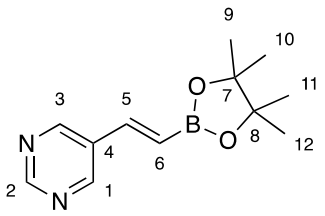
potassium carbonate (1.57 g, 11.3 mmol, 2.0 equiv.) in MeOH (28 mL, 0.2 M). Organics layers were combined, washed with water (20 mL), dried over sodium sulfate, filtered, and concentrated *in vacuo* affording 515 mg of a beige solid consistent with the desired product (87%).

^{1}H NMR (500 MHz, Chloroform-*d*) δ 9.16 (s, 1H, H^{2}), 8.82 (s, 2H, H^{1} and H^{3}), 3.40 (s, 1H, H^{6}).

^{13}C NMR (126 MHz, Chloroform-*d*) δ 159.5 (C^{2}), 157.4 (C^{1} and C^{3}), 118.9 (C^{4}), 84.6 (C^{6}), 77.0 (C^{5}).

Data are consistent with the literature.[318]

(*E*)-5-(2-(4,4,5,5-Tetramethyl-1,3,2-dioxaborolan-2-yl)vinyl)pyrimidine, **3.81-int3**



Prepared according to General Procedure 5 using 5-ethynylpyrimidine **3.81-int2** (800 mg, 7.68 mmol, 1.0 equiv.), copper(I) chloride (38 mg, 384 μmol, 5 mol%), potassium *tert*-butoxide (86 mg, 768 μmol, 10 mol%), bis(2-diphenylphosphinophenyl)ether (DPEPhos) (207 mg, 384 μmol, 5 mol%), bis(pinacolato)diboron (2.15 g, 8.45 mmol, 1.1 equiv.), and MeOH (620 μL, 15.4 mmol, 2.0 equiv.) in THF (30 mL, 0.25 M). The crude residue was purified by flash chromatography (silica gel) from pure hexane to a mixture of 25% of ethyl acetate in hexane affording 1.39 g of a white solid consistent with the desired product (78%). It contained B_2pin_2 or related adducts.

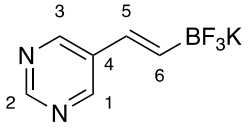
^{1}H NMR (500 MHz, Chloroform-*d*) δ 9.02 (s, 1H, H^{2}), 8.73 (s, 2H, H^{1} and H^{3}), 7.20 (d, J = 18.60 Hz, 1H, H^{5}), 6.25 (d, J = 18.60 Hz, 1H, H^{6}), 1.22 (s, 12H, H^{9}, H^{10}, H^{11} and H^{12}).

^{11}B NMR (96 MHz, Chloroform-*d*) δ 29.67.

^{13}C NMR (126 MHz, Chloroform-*d*) δ 158.1 (C^{2}), 154.8 (C^{1} and C^{3}), 141.8 (C^{5}), 130.8 (C^{4}), 122.0 (broad, C^{6}), 83.8 (C^{7} and C^{8}), 24.7 (C^{9}, C^{10}, C^{11} and C^{12}).

Data are consistent with the literature.[300]

(*E*)-5-(2-(trifluoro-λ^{4}-boraneyl)vinyl)pyrimidine, potassium salt, **3.81-int4**



Prepared according to General Procedure 6 using (*E*)-5-(2-(4,4,5,5-tetramethyl-1,3,2-dioxaborolan-2-yl)vinyl)pyrimidine **S18-int3** (1.35 g, 5.82 mmol, 1.0 equiv.), potassium hydrogen fluoride (1.82 g, 23.3 mmol, 4.0 equiv.), and water (5.24 mL, 291 mmol, 50.0 equiv.) in MeOH (54 mL, 0.1 M). 232 mg of a white solid was obtained after filtration, consistent with the desired product (19%).

^{1}H NMR (500 MHz, Acetone-*d*$_{6}$) δ 8.85 (s, 1H, H^{2}), 8.68 (s, 2H, H^{1} and H^{3}), 6.61 – 6.55 (m, 2H, H^{5} and H^{6}).

^{11}B NMR (96 MHz, Acetone-*d*$_{6}$) δ 2.61.

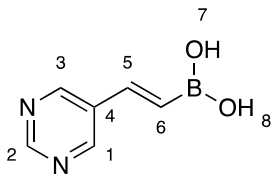
^{13}C NMR (126 MHz, Acetone-*d*$_{6}$) δ 156.7 (C^{2}), 154.3 (C^{1} and C^{3}), 134.7 (C^{4}), 127.0 (q, $^{3}J_{CF}$ = 4.5 Hz, C^{5}). C^{6} is not observed due to quadrupolar relaxation.

^{19}F {^{1}H} NMR (377 MHz, Acetone-*d*$_{6}$) δ –142.74.

IR (solid): 1564, 1450, 1406, 1261, 1232, 1165, 1124, 1076, 991, 952 cm^{-1}.

HRMS (ESI): *m/z* calculated for [M – K]$^{-}$ ($C_6H_5BF_3N_2$)$^{-}$: 173.0503; found = 173.0501.

(*E*)-(2-(Pyrimidin-5-yl)vinyl)boronic acid, **3.81**



Prepared according to General Procedure 7 using (*E*)-5-(2-(trifluoro-λ^4-boraneyl)vinyl)pyrimidine, potassium salt **3.81-int4** (128 mg, 604 μmol, 1.0 equiv.) and chlorotrimethylsilane (270 μL, 2.11 mmol, 3.5 equiv.) in MeCN:H_2O (5 mL:1 mL, 0.1 M). 82 mg of a white solid was obtained as the desired product (91%).

^{1}H NMR (500 MHz, DMSO-d_6) δ 9.11 (s, 1H, H^2), 8.94 (s, 2H, H^1 and H^3), 7.23 (d, *J* = 18.58 Hz, 1H), 6.40 (d, *J* = 18.59 Hz, 1H), 5.88 (s, 2H).

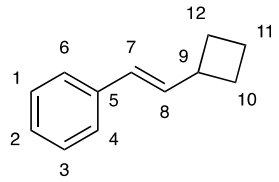
^{11}B NMR (96 MHz, DMSO-d_6) δ 28.54.

^{13}C NMR (126 MHz, DMSO-d_6) δ 157.3 (C^2), 154.7 (C^1 and C^3), 138.8 (C^5), 131.1 (C^4), 128.9 (broad, C^6).

IR (solid): 3209, 1629, 1581, 1521, 1431, 1382, 1361, 1340, 1265, 1251, 1155, 1134, 1097, 997 cm^{-1}.

HRMS (ESI): *m/z* calculated for $[M + H]^+$ $(C_6H_8BN_2O_2)^+$: 151.0673; found = 151.0675.

(*E*)-(2-Cyclobutylvinyl)benzene, **3.82**



Prepared according to General Procedure 1 using 1,3-dioxoisoindolin-2-yl cyclobutanecarboxylate **3.14** (49.0 mg, 200 μmol, 1.0 equiv.), (*E*)-2-phenylvinylboronic acid **3.1a** (59.2 mg, 400 μmol, 2.0 equiv.), tris(2,2'-bipyridine)ruthenium hexafluorophosphate (1.7 mg, 2.00 μmol, 1 mol%), and *N*,*N*-dimethylaniline (2.5 μL, 20.0 μmol, 10 mol%) in DMSO-d_6 (1 mL, 0.2 M). The crude residue was purified by flash chromatography (silica gel) with pure hexane affording 21.4 mg of a colourless oil as the desired product (68%, *E:Z* > 20:1).

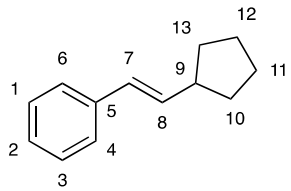
^{1}H NMR (500 MHz, Chloroform-*d*) δ 7.39 – 7.35 (m, 2H, H^4 and H^6), 7.34 – 7.28 (m, 2H, H^1 and H^3), 7.22 – 7.18 (m, 1H, H^2), 6.39 – 6.27 (m, 2H, H^7 and H^8), 3.17 – 3.07

(m, 1H, H^9), 2.25 – 2.14 (m, 2H, H^{10} and H^{12}), 2.03 – 1.91 (m, 3H, H^{10}, H^{11} and H^{12}), 1.91 – 1.79 (m, 1H, H^{11}).

^{13}C NMR (176 MHz, Chloroform-*d*) δ 137.9 (C^5), 135.4 (C^8), 128.6 (C^1 and C^3), 127.7 (C^7), 126.9 (C^2), 126.1 (C^4 and C^6), 38.9 (C^9), 28.9 (C^{10} and C^{12}), 18.7 (C^{11}).

Data are consistent with the literature.[319]

(*E*)-(2-Cyclopentylvinyl)benzene, **3.83**



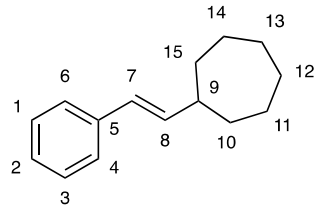
Prepared according to General Procedure 1 using 1,3-dioxoisoindolin-2-yl cyclopentanecarboxylate **3.15** (51.9 mg, 200 μmol, 1.0 equiv.), (*E*)-2-phenylvinylboronic acid **3.1a** (59.2 mg, 400 μmol, 2.0 equiv.), tris(2,2'-bipyridine)ruthenium hexafluorophosphate (1.7 mg, 2.00 μmol, 1 mol%), and *N*,*N*-dimethylaniline (2.5 μL, 20.0 μmol, 10 mol%) in DMSO-d_6 (1 mL, 0.2 M). The crude residue was purified by flash chromatography (silica gel) with pure hexane affording 23.9 mg of a colourless oil as the desired product (70%, *E:Z* = 20:1).

^{1}H NMR (500 MHz, Chloroform-*d*) δ 7.40 – 7.32 (m, 2H, H^4 and H^6), 7.33 – 7.26 (m, 2H, H^1 and H^3), 7.25 – 7.15 (m, 1H, H^2), 6.38 (dd, *J* = 15.83, 0.98 Hz, 1H, H^7), 6.22 (dd, *J* = 15.79, 7.81 Hz, 1H, H^8), 2.67 – 2.56 (m, 1H, H^9), 1.95 – 1.81 (m, 2H, H^{10} and H^{13}), 1.77 – 1.68 (m, 2H, H^{11} and H^{12}), 1.68 – 1.56 (m, 2H, H^{11} and H^{12}), 1.47 – 1.32 (m, 2H, H^{10} and H^{13}).

^{13}C NMR (126 MHz, Chloroform-*d*) δ 138.1 (C^5), 135.8 (C^8), 128.6 (C^1 and C^3), 128.0 (C^7), 126.8 (C^2), 126.0 (C^4 and C^6), 44.0 (C^9), 33.4 (C^{10} and C^{13}), 25.4 (C^{11} and C^{12}).

Data are consistent with the literature.[319]

(*E*)-Styrylcycloheptane, **3.84**



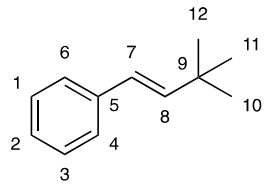
Prepared according to General Procedure 1 using 1,3-Dioxoisoindolin-2-yl cycloheptanecarboxylate **3.16** (57.5 mg, 200 μmol, 1.0 equiv.), (*E*)-2-phenylvinylboronic acid **3.1a** (59.2 mg, 400 μmol, 2.0 equiv.), tris(2,2'-bipyridine)ruthenium hexafluorophosphate (1.7 mg, 2.00 μmol, 1 mol%), and *N*,*N*-dimethylaniline (2.5 μL, 20.0 μmol, 10 mol%) in DMSO-d_6 (1 mL, 0.2 M). The crude residue was purified by flash chromatography (silica gel) with pure hexane affording 28.2 mg of a colourless oil as the desired product (71%, *E:Z* > 20:1).

^{1}H NMR (500 MHz, Chloroform-*d*) δ 7.39 – 7.33 (m, 2H, H^4 and H^6), 7.33 – 7.26 (m, 2H, H^1 and H^3), 7.23 – 7.16 (m, 1H, H^2), 6.34 (d, *J* = 15.93 Hz, 1H, H^7), 6.24 (dd, *J* = 15.87, 7.53 Hz, 1H, H^8), 2.39 – 2.30 (m, 1H, H^9), 1.88 – 1.81 (m, 2H, H^{10} and H^{15}), 1.76 – 1.69 (m, 2H, H^{11} and H^{14}), 1.67 – 1.60 (m, 2H, H^{12} and H^{13}), 1.59 – 1.40 (m, 6H, H^{10}, H^{11}, H^{12}, H^{13}, H^{14} and H^{15}).

^{13}C NMR (126 MHz, Chloroform-*d*) δ 138.2 (C^5), 137.8 (C^8), 128.6 (C^1 and C^3), 126.8 (C^7), 126.8 (C^2), 126.1 (C^4 and C^6), 43.4 (C^9), 34.9 (C^{10} and C^{15}), 28.5 (C^{12} and C^{13}), 26.4 (C^{11} and C^{14}).

Data are consistent with the literature.[320]

(*E*)-(3,3-Dimethylbut-1-en-1-yl)benzene, **3.85**



Prepared according to General Procedure 1 using 1,3-dioxoisoindolin-2-yl pivalate **3.17** (49.4 mg, 200 μmol, 1.0 equiv.), (*E*)-2-phenylvinylboronic acid **3.1a** (59.2 mg, 400 μmol, 2.0 equiv.), tris(2,2'-bipyridine)ruthenium hexafluorophosphate (1.7 mg,

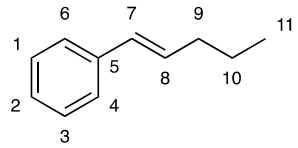
2.00 μmol, 1 mol%), and *N*,*N*-dimethylaniline (2.5 μL, 20.0 μmol, 10 mol%) in DMSO-d_6 (1 mL, 0.2 M). The crude residue was purified by flash chromatography (silica gel) with pure hexane affording 14.8 mg of a colourless oil as the desired product (47%, *E:Z* > 20:1).

^{1}H NMR (500 MHz, Chloroform-*d*) δ 7.42 – 7.37 (m, 2H, H^4 and H^6), 7.32 (s, 2H, H^1 and H^3), 7.24 – 7.19 (m, 1H, H^2), 6.41 – 6.27 (m, 2H, H^7 and H^8), 1.15 (s, 9H, H^{10}, H^{11} and H^{12}).

^{13}C NMR (126 MHz, Chloroform-*d*) δ 142.0 (C^8), 138.2 (C^5), 128.6 (C^1 and C^3), 126.9 (C^2), 126.1 (C^4 and C^6), 124.7 (C^7), 33.5 (C^9), 29.7 (C^{10}, C^{11} and C^{12}).

Data are consistent with the literature.[319]

(*E*)-Pent-1-en-1-ylbenzene, **3.86**



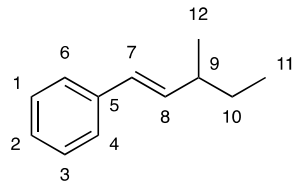
Prepared according to General Procedure 1 using 1,3-dioxoisoindolin-2-yl butyrate **3.18** (46.6 mg, 200 μmol, 1.0 equiv.), (*E*)-2-phenylvinylboronic acid **3.1a** (59.2 mg, 400 μmol, 2.0 equiv.), tris(2,2'-bipyridine)ruthenium hexafluorophosphate (1.7 mg, 2.00 μmol, 1 mol%), and *N*,*N*-dimethylaniline (2.5 μL, 20.0 μmol, 10 mol%) in DMSO-d_6 (1 mL, 0.2 M). The crude residue was purified by flash chromatography (silica gel) with pure hexane affording 16.9 mg of a colourless oil as the desired product (58%, *E:Z* > 20:1).

^{1}H NMR (500 MHz, Chloroform-*d*) δ 7.39 – 7.33 (m, 2H, H^4 and H^6), 7.34 – 7.27 (m, 2H, H^1 and H^3), 7.24 – 7.17 (m, 1H, H^2), 6.40 (dt, *J* = 15.86, 1.52 Hz, 1H, H^7), 6.24 (dt, *J* = 15.79, 6.89 Hz, 1H, H^8), 2.21 (qd, *J* = 7.13, 1.46 Hz, 2H, H^9), 1.51 (h, *J* = 7.26 Hz, 2H, H^{10}), 0.97 (t, *J* = 7.38 Hz, 3H, H^{11}).

^{13}C NMR (126 MHz, Chloroform-*d*) δ 138.1 (C^5), 131.1 (C^8), 130.0 (C^7), 128.6 (C^1 and C^3), 126.9 (C^2), 126.0 (C^4 and C^6), 35.3 (C^9), 22.7 (C^{10}), 13.9 (C^{11}).

Data are consistent with the literature.[321]

(*E*)-(3-Methylpent-1-en-1-yl)benzene, **3.87**



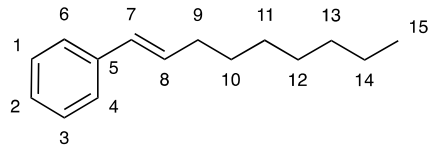
Prepared according to General Procedure 1 using 1,3-dioxoisoindolin-2-yl 2-methylbutanoate **3.19** (49.4 mg, 200 μmol, 1.0 equiv.), (*E*)-2-phenylvinylboronic acid **3.1a** (59.2 mg, 400 μmol, 2.0 equiv.), tris(2,2'-bipyridine)ruthenium hexafluorophosphate (1.7 mg, 2.00 μmol, 1 mol%), and *N*,*N*-dimethylaniline (2.5 μL, 20.0 μmol, 10 mol%) in DMSO-d_6 (1 mL, 0.2 M). The crude residue was purified by flash chromatography (silica gel) with pure hexane affording 24.0 mg of a colourless oil as the desired product (75%, *E:Z* > 20:1).

^{1}H NMR (400 MHz, Chloroform-*d*) δ 7.40 – 7.33 (m, 2H, H^4 and H^6), 7.34 – 7.25 (m, 2H, H^1 and H^3), 7.24 – 7.15 (m, 1H, H^2), 6.35 (broad d, *J* = 15.89 Hz, 1H, H^7), 6.11 (dd, *J* = 15.87, 7.89 Hz, 1H, H^8), 2.27 – 2.15 (m, 1H, H^9), 1.46 – 1.38 (m, 2H, H^{10}), 1.09 (d, *J* = 6.76 Hz, 3H, H^{12}), 0.92 (t, *J* = 7.43 Hz, 3H, H^{11}).

^{13}C NMR (126 MHz, Chloroform-*d*) δ 138.1 (C^5), 136.9 (C^8), 128.6 (C^1 and C^3), 128.2 (C^7), 126.9 (C^2), 126.1 (C^4 and C^6), 39.1 (C^9), 29.9 (C^{10}), 20.4 (C^{12}), 12.0 (C^{11}).

Data are consistent with the literature.[322]

(*E*)-Non-1-en-1-ylbenzene, **3.88**



Prepared according to General Procedure 1 using 1,3-dioxoisoindolin-2-yl octanoate **3.20** (57.9 mg, 200 μmol, 1.0 equiv.), (*E*)-2-phenylvinylboronic acid **3.1a** (59.2 mg, 400 μmol, 2.0 equiv.), tris(2,2'-bipyridine)ruthenium hexafluorophosphate (1.7 mg, 2.00 μmol, 1 mol%), and *N*,*N*-dimethylaniline (2.5 μL, 20.0 μmol, 10 mol%) in DMSO-d_6 (1 mL, 0.2 M). The crude residue was purified by flash chromatography

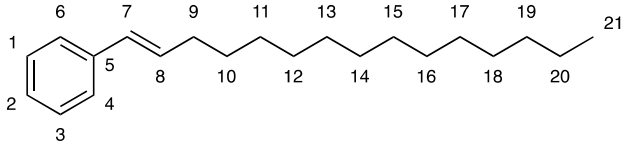
(silica gel) with pure hexane affording 34.6 mg of a colourless oil as the desired product (86%, *E:Z* > 20:1).

^{1}H NMR (400 MHz, Chloroform-*d*) δ 7.37 – 7.33 (m, 2H, H^{4} and H^{6}), 7.32 – 7.27 (m, 2H, H^{1} and H^{3}), 7.22 – 7.16 (m, 1H, H^{2}), 6.41 – 6.32 (d, *J* = 15.95 Hz, 1H, H^{7}), 6.23 (dt, *J* = 15.79, 6.82 Hz, 1H, H^{8}), 2.21 (qd, *J* = 7.17, 1.33 Hz, 2H, H^{9}), 1.52 – 1.41 (m, 2H, H^{10}), 1.41 – 1.23 (m, 8H, H^{11}, H^{12}, H^{13} and H^{14}), 0.89 (t, *J* = 7.09 Hz, 3H, H^{15}).

^{13}C NMR (126 MHz, Chloroform-*d*) δ 138.1 (C^{5}), 131.4 (C^{8}), 129.8 (C^{7}), 128.6 (C^{1} and C^{3}), 126.9 (C^{2}), 126.0 (C^{4} and C^{6}), 33.2 (C^{9}), 32.0 (C^{11} or C^{12} or C^{13} or C^{14}), 29.5 (C^{10}), 29.4 (C^{11} or C^{12} or C^{13} or C^{14}), 29.4 (C^{11} or C^{12} or C^{13} or C^{14}), 22.8 (C^{11} or C^{12} or C^{13} or C^{14}), 14.3 (C^{15}).

Data are consistent with the literature.[321]

(*E*)-Pentadec-1-en-1-ylbenzene, **3.89**



Prepared according to General Procedure 1 using 1,3-dioxoisoindolin-2-yl tetradecanoate **3.21** (74.7 mg, 200 μmol, 1.0 equiv.), (*E*)-2-phenylvinylboronic acid **3.1a** (59.2 mg, 400 μmol, 2.0 equiv.), tris(2,2'-bipyridine)ruthenium hexafluorophosphate (1.7 mg, 2.00 μmol, 1 mol%), and *N*,*N*-dimethylaniline (2.5 μL, 20.0 μmol, 10 mol%) in DMSO-d_6 (1 mL, 0.2 M). The crude residue was purified by flash chromatography (silica gel) with pure hexane affording 48.1 mg of a colourless oil as the desired product (84%, *E:Z* > 20:1).

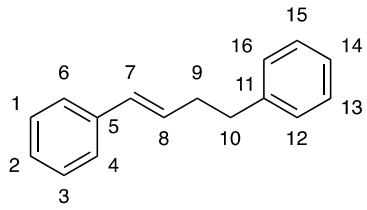
^{1}H NMR (400 MHz, Chloroform-*d*) δ 7.37 – 7.33 (m, 2H, H^{4} and H^{6}), 7.32 – 7.27 (m, 2H, H^{1} and H^{3}), 7.22 – 7.18 (m, 1H, H^{2}), 6.38 (d, *J* = 15.86 Hz, 1H, H^{7}), 6.23 (dt, *J* = 15.80, 6.82 Hz, 1H, H^{8}), 2.24 – 2.17 (m, 2H, H^{9}), 1.51 – 1.42 (m, 2H, H^{10}), 1.27 (m, 20H, from H^{11} to H^{20}), 0.88 (d, *J* = 6.74 Hz, 3H, H^{21}).

^{13}C NMR (126 MHz, Chloroform-*d*) δ 138.1 (C^5), 131.4 (C^8), 129.8 (C^7), 128.6 (C^1 and C^3), 126.9 (C^2), 126.0 (C^4 and C^6), 33.2 (C^9), 32.1, 29.8, 29.8, 29.8, 29.7, 29.5, 29.5, 29.4, 22.9, 14.3 (C^{21}). 2 carbon peaks are missing, the peaks of aliphatic carbon are overlapped between each other.

IR (film): 3024, 2922, 2852, 2358, 2341, 1494, 1465, 1377 cm^{-1}.

HRMS (EI): *m/z* calculated for $[M]^+$ $(C_{21}H_{34})^+$: 286.2655; found 286.2650.

(*E*)-But-1-ene-1,4-diyldibenzene, **3.90**



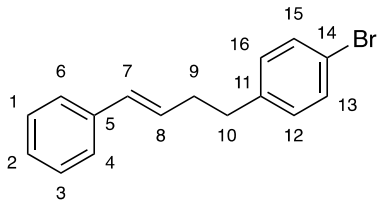
Prepared according to General Procedure 1 using 1,3-dioxoisoindolin-2-yl 3-phenylpropanoate **3.22** (59.1 mg, 200 μmol, 1.0 equiv.), (*E*)-2-phenylvinylboronic acid **3.1a** (59.2 mg, 400 μmol, 2.0 equiv.), tris(2,2'-bipyridine)ruthenium hexafluorophosphate (1.7 mg, 2.00 μmol, 1 mol%), and *N*,*N*-dimethylaniline (2.5 μL, 20.0 μmol, 10 mol%) in DMSO-d_6 (1 mL, 0.2 M). The crude residue was purified by flash chromatography (silica gel) from pure hexane to a mixture of 1% of diethyl ether in hexane affording 32.8 mg of a white solid as the desired product (79%, *E:Z* > 20:1).

^{1}H NMR (500 MHz, Chloroform-d) δ 7.36 – 7.28 (m, 6H, $H^{aromatic}$), 7.25 – 7.17 (m, 4H, H^2, H^{14} and $H^{aromatic}$), 6.42 (d, *J* = 15.84 Hz, 1H, H^7), 6.27 (td, *J* = 15.80, 6.90 Hz, 1H, H^8), 2.83 – 2.75 (m, 2H, H^{10}), 2.57 – 2.51 (m, 2H, H^9).

^{13}C NMR (126 MHz, Chloroform-d) δ 141.9 (C^{11}), 137.8 (C^5), 130.5 (C^7), 130.1 (C^8), 128.6 ($C^{aromatic}$), 128.6 ($C^{aromatic}$), 128.5 ($C^{aromatic}$), 127.1 (C^2 or C^{14}), 126.1 ($C^{aromatic}$), 126.0 (C^2 or C^{14}), 36.0 (C^{10}), 35.0 (C^9).

Data consistent with the literature.[1]

(*E*)-1-Bromo-4-(4-phenylbut-3-en-1-yl)benzene, **3.91**



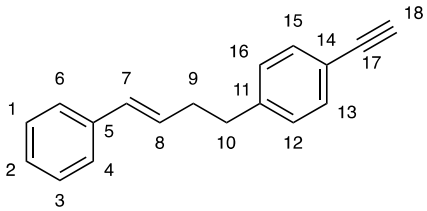
Prepared according to General Procedure 1 using 1,3-dioxoisoindolin-2-yl 3-(4-bromophenyl)propanoate **3.23** (56.1 mg, 150 μmol, 1.0 equiv.), (*E*)-2-phenylvinylboronic acid **3.1a** (44.4 mg, 300 μmol, 2.0 equiv.), tris(2,2'-bipyridine)ruthenium hexafluorophosphate (1.3 mg, 1.50 μmol, 1 mol%), and *N*,*N*-dimethylaniline (2 μL, 15.0 μmol, 10 mol%) in DMSO-d_6 (1 mL, 0.15 M). The crude residue was purified by flash chromatography (silica gel) with pure hexane affording 34.5 mg of a white solid as the desired product (79%, *E:Z* > 20:1).

^{1}H NMR (700 MHz, Chloroform-*d*) δ 7.44 – 7.40 (m, 2H, H^{13} and H^{15}), 7.36 – 7.32 (m, 2H, H^{4} and H^{6}), 7.33 – 7.29 (m, 2H, H^{1} and H^{3}), 7.25 – 7.19 (m, 1H, H^{2}), 7.12 – 7.08 (m, 2H, H^{12} and H^{16}), 6.41 (d, *J* = 15.82 Hz, 1H, H^{7}), 6.23 (dt, *J* = 15.76, 6.87 Hz, 1H, H^{8}), 2.76 (t, *J* = 7.80 Hz, 2H, H^{10}), 2.55 – 2.46 (m, 2H, H^{9}).

^{13}C NMR (176 MHz, Chloroform-*d*) δ 140.8 (C^{11}), 137.7 (C^{5}), 131.5 (C^{13} and C^{15}), 130.9 (C^{7}), 130.4 (C^{12} and C^{16}), 129.5 (C^{8}), 128.6 (C^{1} and C^{3}), 127.2 (C^{2}), 126.1 (C^{4} and C^{6}), 119.8 (C^{14}), 35.4 (C^{10}), 34.8 (C^{9}).

Data are consistent with the literature.[132]

(*E*)-1-Ethynyl-4-(4-phenylbut-3-en-1-yl)benzene, **3.92**



Prepared according to General Procedure 1 using 1,3-dioxoisoindolin-2-yl 3-(4-ethynylphenyl)propanoate **3.24** (31.9 mg, 100 μmol, 1.0 equiv.), (*E*)-2-phenylvinylboronic acid **3.1a** (29.6 mg, 200 μmol, 2.0 equiv.), tris(2,2'-

bipyridine)ruthenium hexafluorophosphate (0.9 mg, 1.00 μmol, 1 mol%), and *N*,*N*-dimethylaniline (1.5 μL, 10.0 μmol, 10 mol%) in DMSO-d_6 (1 mL, 0.2 M). The crude residue was purified by flash chromatography (silica gel) from pure hexane to a mixture of 4% of diethyl ether in hexane affording 16.2 mg of a white solid as the desired product (71%, *E:Z* > 20:1).

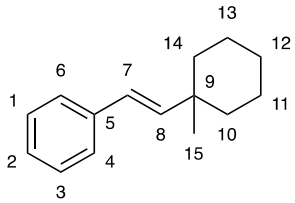
^{1}H NMR (500 MHz, Chloroform-*d*) δ 7.47 – 7.40 (m, 2H, H^{13} and H^{15}), 7.36 – 7.26 (m, 4H, H^1, H^3, H^4 and H^6), 7.24 – 7.18 (m, 1H, H^2), 7.21 – 7.15 (m, 2H, H^{12} and H^{16}), 6.41 (dt, *J* = 15.85, 1.49 Hz, 1H, H^7), 6.23 (dt, *J* = 15.80, 6.85 Hz, 1H, H^8), 3.05 (s, 1H, H^{18}), 2.80 (t, *J* = 8.76 Hz, 2H, H^{10}), 2.57 – 2.48 (m, 2H, H^9).

^{13}C NMR (126 MHz, Chloroform-*d*) δ 142.9 (C^{11}), 137.7 (C^5), 132.3 (C^{13} and C^{15}), 130.8 (C^7), 129.6 (C^8), 128.6 (C^1, C^3, C^{12} and C^{16}), 127.2 (C^2), 126.1 (C^4 and C^6), 119.7 (C^{14}), 83.9 (C^{17}), 76.8 (C^{18}), 35.9 (C^{10}), 34.7 (C^9).

IR (solid): 3277, 1508, 1492, 1448, 1242, 1213, 1176, 1105, 1068, 1020, 991, 979 cm^{-1}.

HRMS (EI): *m/z* calculated for $[M]^+$ ($C_{18}H_{16}$): 232.1246; found 232.1247.

(*E*)-(2-(1-Methylcyclohexyl)vinyl)benzene, **3.93**



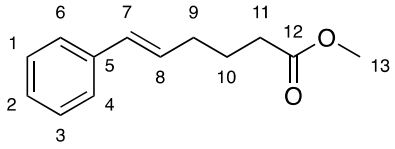
Prepared according to General Procedure 1 using 1,3-dioxoisoindolin-2-yl 1-methylcyclohexane-1-carboxylate **3.26** (57.5 mg, 200 μmol, 1.0 equiv.), (*E*)-2-phenylvinylboronic acid **3.1a** (59.2 mg, 400 μmol, 2.0 equiv.), tris(2,2'-bipyridine)ruthenium hexafluorophosphate (1.7 mg, 2.00 μmol, 1 mol%), and *N*,*N*-dimethylaniline (2.5 μL, 20.0 μmol, 10 mol%) in DMSO-d_6 (1 mL, 0.2 M). The crude residue was purified by flash chromatography (silica gel) with pure hexane affording 23.6 mg of a colourless oil as the desired product (59%, *E:Z* > 20:1).

^{1}H NMR (500 MHz, Chloroform-*d*) δ 7.40 – 7.37 (m, 2H, H^4 and H^6), 7.33 – 7.29 (m, 2H, H^1 and H^3), 7.22 – 7.17 (m, 1H, H^2), 6.34 (d, *J* = 16.38 Hz, 1H, H^7), 6.23 (d, *J* = 16.35 Hz, 1H, H^8), 1.66 – 1.59 (m, 2H, H^{10} and H^{14}), 1.57 – 1.49 (m, 4H, H^{11} and H^{13}), 1.46 – 1.36 (m, 4H, H^{10}, H^{12} and H^{14}), 1.08 (s, 3H, H^{15}).

^{13}C NMR (126 MHz, Chloroform-*d*) δ 141.2 (C^8), 138.4 (C^5), 128.6 (C^1 and C^3), 126.8 (C^2), 126.1 (C^4 and C^6), 126.1 (C^7), 38.1 (C^{10} and C^{14}), 36.3 (C^9), 27.7 (C^{15}), 26.5 (C^{12}), 22.6 (C^{11} and C^{13}).

Data are consistent with the literature.[319]

Methyl (*E*)-6-phenylhex-5-enoate, **3.94**



Prepared according to General Procedure 1 using 1,3-dioxoisoindolin-2-yl methyl glutarate **3.27** (58.3 mg, 200 μmol, 1.0 equiv.), (*E*)-2-phenylvinylboronic acid **3.1a** (59.2 mg, 400 μmol, 2.0 equiv.), tris(2,2'-bipyridine)ruthenium hexafluorophosphate (1.7 mg, 2.00 μmol, 1 mol%), and *N*,*N*-dimethylaniline (2.5 μL, 20.0 μmol, 10 mol%) in DMSO-d_6 (1 mL, 0.2 M). The crude residue was purified by flash chromatography (silica gel) from pure hexane to a mixture of 1% of diethyl ether in hexane affording 33.1 mg of a colourless oil as the desired product (81%, *E:Z* > 20:1).

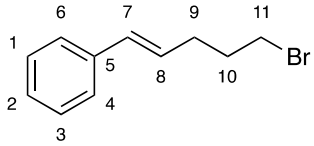
^{1}H NMR (500 MHz, Chloroform-*d*) δ 7.37 – 7.31 (m, 2H, H^4 and H^6), 7.34 – 7.26 (m, 2H, H^1 and H^3), 7.24 – 7.17 (m, 1H, H^2), 6.40 (dt, *J* = 15.81, 1.49 Hz, 1H, H^7), 6.19 (dt, *J* = 15.80, 6.97 Hz, 1H, H^8), 3.67 (s, 3H, H^{13}), 2.38 (t, *J* = 7.51 Hz, 2H, H^{11}), 2.26 (qd, *J* = 7.21, 1.47 Hz, 2H, H^9), 1.83 (p, *J* = 7.41 Hz, 2H, H^{10}).

^{13}C NMR (126 MHz, Chloroform-*d*) δ 174.2 (C^{12}), 137.7 (C^5), 130.9 (C^7), 129.6 (C^8), 128.6 (C^1 and C^3), 127.1 (C^2), 126.1 (C^4 and C^6), 51.6 (C^{13}), 33.5 (C^{11}), 32.5 (C^9), 24.6 (C^{10}).

IR (film): 1734, 1597, 1435, 1363, 1269, 1246, 1196, 1172, 1149, 1022, 962, 742 cm^{-1}.

HRMS (ESI): *m/z* calculated for $[M + Na]^+$ $(C_{13}H_{16}O_2Na)^+$: 227.1042, found 227.1040.

(*E*)-(5-Bromopent-1-en-1-yl)benzene, **3.95**



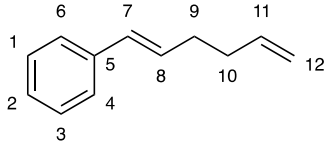
Prepared according to General Procedure 1 using 1,3-dioxoisoindolin-2-yl 4-bromobutanoate **3.28** (62.4 mg, 200 μmol, 1.0 equiv.), (*E*)-2-phenylvinylboronic acid **3.1a** (59.2 mg, 400 μmol, 2.0 equiv.), tris(2,2'-bipyridine)ruthenium hexafluorophosphate (1.7 mg, 2.00 μmol, 1 mol%), and *N*,*N*-dimethylaniline (2.5 μL, 20.0 μmol, 10 mol%) in DMSO-d_6 (1 mL, 0.2 M). The crude residue was purified by flash chromatography (silica gel) with pure hexane affording 37.9 mg of a colourless oil as the desired product (66%, *E:Z* > 20:1).

^{1}H NMR (500 MHz, Chloroform-*d*) δ 7.38 – 7.34 (m, 2H, H^4 and H^6), 7.34 – 7.29 (m, 2H, H^1 and H^3), 7.26 – 7.19 (m, 1H, H^2), 6.46 (d, *J* = 15.82 Hz, 1H, H^7), 6.18 (dt, *J* = 15.84, 7.04 Hz, 1H, H^8), 3.47 (t, *J* = 6.64 Hz, 2H, H^{11}), 2.39 (m, 2H, H^9), 2.05 (p, *J* = 6.74 Hz, 2H, H^{10}).

^{13}C NMR (126 MHz, Chloroform-*d*) δ 137.5 (C^5), 131.4 (C^7), 128.7 (C^1 and C^3), 128.6 (C^8), 127.3 (C^2), 126.1 (C^4 and C^6), 33.4 (C^{11}), 32.3 (C^{10}), 31.4 (C^9).

Data are consistent with the literature.[323]

(*E*)-Hexa-1,5-dien-1-ylbenzene, **3.96**



Prepared according to General Procedure 1 using 1,3-dioxoisoindolin-2-yl pent-4-enoate **3.29** (49.0 mg, 200 μmol, 1.0 equiv.), (*E*)-2-phenylvinylboronic acid **3.1a** (59.2 mg, 400 μmol, 2.0 equiv.), tris(2,2'-bipyridine)ruthenium hexafluorophosphate (1.7

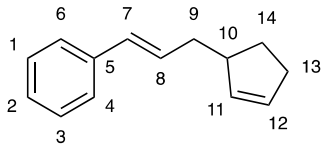
mg, 2.00 μmol, 1 mol%), and *N*,*N*-dimethylaniline (2.5 μL, 20.0 μmol, 10 mol%) in DMSO-d_6 (1 mL, 0.2 M). The crude residue was purified by flash chromatography (silica gel) with pure hexane affording 25.1 mg of a colourless oil as the desired product (79%, *E:Z* > 20:1).

^{1}H NMR (500 MHz, Chloroform-*d*) δ 7.38 – 7.34 (m, 2H, H^4 and H^6), 7.32 – 7.28 (m, 2H, H^1 and H^3), 7.24 – 7.18 (m, 1H, H^2), 6.42 (d, *J* = 15.83 Hz, 1H, H^7), 6.24 (dt, *J* = 15.86, 6.72 Hz, 1H, H^8), 5.88 (ddt, *J* = 16.78, 10.20, 6.50 Hz, 1H, H^{11}), 5.08 (dq, *J* = 17.14, 1.70 Hz, 1H, H^{12}), 5.01 (dq, *J* = 10.20, 1.39 Hz, 1H, H^{12}), 2.38 – 2.30 (m, 2H, H^9), 2.28 – 2.20 (m, 2H, H^{10}).

^{13}C NMR (126 MHz, Chloroform-*d*) δ 138.3 (C^{11}), 137.9 (C^5), 130.3 (C^7), 130.3 (C^8), 128.6 (C^1 and C^3), 127.0 (C^2), 126.1 (C^4 and C^6), 115.1 (C^{12}), 33.7 (C^{10}), 32.6 (C^9).

Data are consistent with the literature.[319]

(*E*)-(3-(Cyclopent-2-en-1-yl)prop-1-en-1-yl)benzene, **3.97**



Prepared according to General Procedure 1 using 1,3-dioxoisoindolin-2-yl 2-(cyclopent-2-en-1-yl)acetate **3.30** (54.3 mg, 200 μmol, 1.0 equiv.), (*E*)-2-phenylvinylboronic acid **3.1a** (59.2 mg, 400 μmol, 2.0 equiv.), tris(2,2'-bipyridine)ruthenium hexafluorophosphate (1.7 mg, 2.00 μmol, 1 mol%), and *N*,*N*-dimethylaniline (2.5 μL, 20.0 μmol, 10 mol%) in DMSO-d_6 (1 mL, 0.2 M). The crude residue was purified by flash chromatography (silica gel) with pure hexane affording 21.0 mg of a colourless oil as the desired product (57%, *E:Z* > 20:1).

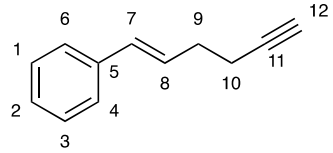
^{1}H NMR (500 MHz, Chloroform-*d*) δ 7.39 – 7.33 (m, 2H, H^4 and H^6), 7.33 – 7.26 (m, 2H, H^1 and H^3), 7.23 – 7.16 (m, 1H, H^2), 6.40 (d, *J* = 15.80 Hz, 1H, H^7), 6.23 (dt, *J* = 15.66, 7.17 Hz, 1H, H^8), 5.80 – 5.64 (m, 2H, H^{11} and H^{12}), 2.88 – 2.77 (m, 1H, H^{10}), 2.42 – 2.14 (m, 4H, H^9 and H^{13}), 2.10 – 2.00 (m, 1H, H^{14}), 1.55 – 1.44 (m, 1H, H^{14}).

^{13}C NMR (126 MHz, Chloroform-*d*) δ 138.0 (C^5), 134.7 (C^{12}), 131.0 (C^7), 130.8 (C^{11}), 129.6 (C^8), 128.6 (C^1 and C^3), 127.0 (C^2), 126.1 (C^4 and C^6), 45.6 (C^{10}), 39.5 (C^9), 32.2 (C^{13}), 29.4 (C^{14}).

IR (film): 3055, 3024, 2924, 2851, 2364, 2357, 1495, 1448, 962, 912, 741, 723, 692 cm^{-1}.

HRMS (EI): *m/z* calculated for $[M]^+$ $(C_{14}H_{16})^+$: 184.1246; found 184.1243.

(*E*)-Hex-1-en-5-yn-1-ylbenzene, **3.98**



Prepared according to General Procedure 1 using 1,3-dioxoisoindolin-2-yl pent-4-ynoate **3.31** (48.6 mg, 200 μmol, 1.0 equiv.), (*E*)-2-phenylvinylboronic acid **3.1a** (59.2 mg, 400 μmol, 2.0 equiv.), tris(2,2'-bipyridine)ruthenium hexafluorophosphate (1.7 mg, 2.00 μmol, 1 mol%), and *N*,*N*-dimethylaniline (2.5 μL, 20.0 μmol, 10 mol%) in DMSO-d_6 (1 mL, 0.2 M). The crude residue was purified by flash chromatography (silica gel) from pure hexane to a mixture of 1% of diethyl ether in hexane affording 25.8 mg of a colourless oil as the desired product (84%, *E:Z* > 20:1).

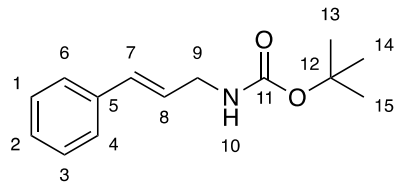
^{1}H NMR (500 MHz, Chloroform-*d*) δ 7.39 – 7.36 (m, 2H, H^4 and H^6), 7.34 – 7.28 (m, 2H, H^1 and H^3), 7.24 – 7.20 (m, 1H, H^2), 6.47 (d, *J* = 15.76 Hz, 1H, H^7), 6.28 (dt, *J* = 15.78, 6.75 Hz, 1H, H^8), 2.49 – 2.43 (m, 2H, H^9), 2.37 (td, *J* = 7.00, 2.02 Hz, 2H, H^{10}), 2.01 (t, *J* = 2.61 Hz, 1H, H^{12}).

^{13}C NMR (126 MHz, Chloroform-*d*) δ 137.5 (C^5), 131.2 (C^7), 128.6 (C^1 and C^3), 128.5 (C^8), 127.3 (C^2), 126.2 (C^4 and C^6), 83.9 (C^{11}), 69.0. (C^{12}), 32.1 (C^9), 18.9 (C^{10}).

IR (film): 3298, 3026, 2912, 1495, 1447, 1433, 1068, 962, 741, 692, 635 cm^{-1}.

HRMS (EI): *m/z* calculated for $[M]^+$ $(C_{12}H_{12})^+$: 156.0933; found 156.0929.

tert-Butyl cinnamylcarbamate, **3.99**



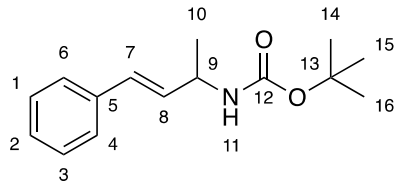
Prepared according to General Procedure 1 using 1,3-dioxoisoindolin-2-yl (*tert*-butoxycarbonyl)glycinate **3.32** (61.4 mg, 200 μmol, 1.0 equiv.), (*E*)-2-phenylvinylboronic acid **3.1a** (59.2 mg, 400 μmol, 2.0 equiv.), tris(2,2'-bipyridine)ruthenium hexafluorophosphate (1.7 mg, 2.00 μmol, 1 mol%), and *N*,*N*-dimethylaniline (2.5 μL, 20.0 μmol, 10 mol%) in DMSO-d_6 (1 mL, 0.2 M). The crude residue was purified by flash chromatography (silica gel) from pure hexane to a mixture of 10% of diethyl ether in hexane affording 27.0 mg of a white solid as the desired product (58%, *E:Z* > 20:1).

^{1}H NMR (500 MHz, Chloroform-*d*) δ 7.37 – 7.34 (m, 2H, H^4 and H^6), 7.33 – 7.29 (m, 2H, H^1 and H^3), 7.25 – 7.21 (m, 1H, H^2), 6.50 (d, *J* = 15.79, 1H, H^7), 6.19 (dt, *J* = 15.69, 6.12 Hz, 1H, H^8), 4.70 (broad s, NH, H^{10}), 3.91 (app. t, *J* = 6.20 Hz, 2H, H^9), 1.47 (s, 9H, H^{13}, H^{14} and H^{15}).

^{13}C NMR (126 MHz, Chloroform-*d*) δ 155.9 (C^{11}), 136.8 (C^5), 131.6 (C^7), 128.7 (C^1 and C^3), 127.7 (C^2), 126.5 (C^4 and C^6), 126.5 (C^8), 79.6 (C^{12}), 42.8 (C^9), 28.5 (C^{13}, C^{14} and C^{15}).

Data are consistent with the literature.[324]

tert-Butyl (*E*)-methyl(4-phenylbut-3-en-2-yl)carbamate, **3.100**



Prepared according to General Procedure 1 using 1,3-dioxoisoindolin-2-yl (*tert*-butoxycarbonyl)alaninate **3.33** (66.9 mg, 200 μmol, 1.0 equiv.), (*E*)-2-phenylvinylboronic acid **3.1a** (59.2 mg, 400 μmol, 2.0 equiv.), tris(2,2'-

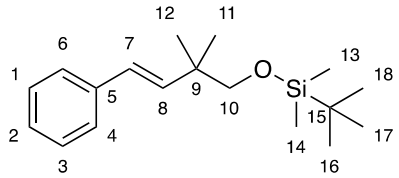
bipyridine)ruthenium hexafluorophosphate (1.7 mg, 2.00 μmol, 1 mol%), and *N*,*N*-dimethylaniline (2.5 μL, 20.0 μmol, 10 mol%) in DMSO-d_6 (1 mL, 0.2 M). The crude residue was purified by flash chromatography (silica gel) from pure hexane to a mixture of 5% of diethyl ether in hexane affording 12.6 mg of a colourless oil as the desired product (25%, *E:Z* > 20:1).

^{1}H NMR (500 MHz, Chloroform-*d*) δ 7.40 – 7.36 (m, 2H, H^4 and H^6), 7.35 – 7.30 (m, 2H, H^1 and H^3), 7.27 – 7.23 (m, 1H, H^2), 6.52 (d, *J* = 16.10 Hz, 1H, H^7), 6.18 (dd, *J* = 15.94, 5.71 Hz, 1H, H^8), 4.57 (broad s, 1H, H^{11}), 4.43 (broad s, 1H, H^9), 1.49 (s, 9H, H^{14}, H^{15} and H^{16}), 1.34 (d, *J* = 6.80 Hz, 2H, H^{10}).

^{13}C NMR (126 MHz, Chloroform-*d*) δ 155.3 (C^{12}), 137.0 (C^5), 131.8 (C^8), 129.3 (C^7), 128.7 (C^1 and C^3), 127.6 (C^2), 126.5 (C^4 and C^6), 79.5 (C^{13}), 48.0 (broad, C^9), 28.6 (C^{14}, C^{15} and C^{16}), 21.3 (C^{10}).

Data are consistent with the literature.[325]

(*E*)-*tert*-Butyl((2,2-dimethyl-4-phenylbut-3-en-1-yl)oxy)dimethylsilane, **3.101**



Prepared according to General Procedure 1 using 1,3-dioxoisoindolin-2-yl 3-((*tert*-butyldimethylsilyl)oxy)-2,2-dimethylpropanoate **3.34** (75.5 mg, 200 μmol, 1.0 equiv.), (*E*)-2-phenylvinylboronic acid **3.1a** (59.2 mg, 400 μmol, 2.0 equiv.), tris(2,2'-bipyridine)ruthenium hexafluorophosphate (1.7 mg, 2.00 μmol, 1 mol%), and *N*,*N*-dimethylaniline (2.5 μL, 20.0 μmol, 10 mol%) in DMSO-d_6 (1 mL, 0.2 M). The crude residue was purified by flash chromatography (silica gel) with pure hexane affording 41.3 mg of a colourless oil as the desired product (71%, *E:Z* > 20:1).

^{1}H NMR (500 MHz, Chloroform-*d*) δ 7.39 – 7.35 (m, 2H, H^4 and H^6), 7.33 – 7.27 (m, 2H, H^1 and H^3), 7.24 – 7.18 (m, 1H, H^2), 6.38 (d, *J* = 16.32 Hz, 1H, H^7), 6.27 (d, *J* =

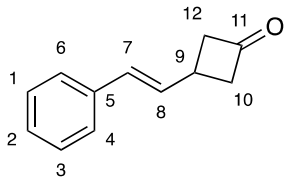
16.30 Hz, 1H, H^8), 3.40 (s, 2H, H^{10}), 1.11 (s, 6H, H^{11} and H^{12}), 0.92 (s, 9H, H^{16}, H^{17} and H^{18}), 0.05 (s, 6H, H^{13} and H^{14}).

^{13}C NMR (126 MHz, Chloroform-*d*) δ 138.3 (C^8), 138.2 (C^5), 128.6 (C^1 and C^3), 126.9 (C^2), 126.9 (C^7), 126.2 (C^4 and C^6), 72.0 (C^{10}), 38.8 (C^9), 26.1(C^{16}, C^{17} and C^{18}), 24.2 (C^{11} and C^{12}), 18.5 (C^{15}), –5.3 (C^{13} and C^{14}).

IR (film): 2954, 2854, 1494, 1471, 1388, 1359, 1249, 1093, 968, 912, 850 cm^{-1}.

HRMS (ESI): *m/z* calculated for $[M + H]^+$ $(C_{18}H_{31}OSi)^+$: 291.21387, found 291.2125.

(*E*)-3-Styrylcyclobutan-1-one, **3.102**



Prepared according to General Procedure 1 using 1,3-dioxoisoindolin-2-yl 3-oxocyclobutane-1-carboxylate **3.35** (51.8 mg, 200 μmol, 1.0 equiv.), (*E*)-2-phenylvinylboronic acid **3.1a** (59.2 mg, 400 μmol, 2.0 equiv.), tris(2,2'-bipyridine)ruthenium hexafluorophosphate (1.7 mg, 2.00 μmol, 1 mol%), and *N*,*N*-dimethylaniline (2.5 μL, 20.0 μmol, 10 mol%) in DMSO-d_6 (1 mL, 0.2 M). The crude residue was purified by flash chromatography (silica gel) with pure hexane affording 21.0 mg of a white solid as the desired product (61%, *E:Z* > 20:1).

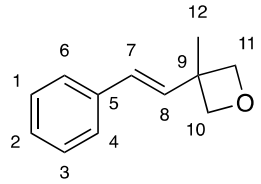
^{1}H NMR (500 MHz, Chloroform-*d*) δ 7.41 – 7.35 (m, 2H, H^4 and H^6), 7.35 – 7.28 (m, 2H, H^1 and H^3), 7.28 – 7.21 (m, 1H, H^2), 6.50 (d, *J* = 15.75 Hz, 1H, H^7), 6.38 (dd, *J* = 15.74, 7.08 Hz, 1H, H^8), 3.37 – 3.29 (m, 2H, H^{10} and H^{12}), 3.29 – 3.20 (m, 1H, H^9), 3.10 – 3.02 (m, 2H, H^{10} and H^{12}).

^{13}C NMR (126 MHz, Chloroform-*d*) δ 207.0 (C^{11}), 136.8 (C^5), 132.2 (C^8), 130.3 (C^7), 128.8 (C^1 and C^3), 127.6 (C^2), 126.2 (C^4 and C^6), 53.5 (C^{10} and C^{12}), 26.8 (C^9).

IR (film): 1769, 1732, 1674, 1599, 1493, 1450, 1377, 1178, 1105, 988, 978, 752, 694 cm^{-1}.

HRMS (ESI): *m/z* calculated for $[M + H]^+$ $(C_{12}H_{13}O)^+$: 173.0960; found 173.0968.

(*E*)-3-Methyl-3-styryloxetane, **3.103**



Prepared according to General Procedure 1 using 1,3-dioxoisoindolin-2-yl 3-methyloxetane-3-carboxylate **3.36** (52.2 mg, 200 μmol, 1.0 equiv.), (*E*)-2-phenylvinylboronic acid **3.1a** (59.2 mg, 400 μmol, 2.0 equiv.), tris(2,2'-bipyridine)ruthenium hexafluorophosphate (1.7 mg, 2.00 μmol, 1 mol%), and *N*,*N*-dimethylaniline (2.5 μL, 20.0 μmol, 10 mol%) in DMSO-d_6 (1 mL, 0.2 M). The crude residue was purified by flash chromatography (silica gel) with pure hexane to 4% of diethyl ether in hexane affording 18.6 mg of a colourless oil as the desired product (63%, *E:Z* > 20:1).

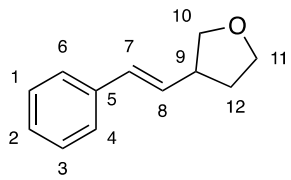
^{1}H NMR (500 MHz, Chloroform-*d*) δ 7.42 – 7.38 (m, 2H, H^4 and H^6), 7.35 – 7.29 (m, 2H, H^1 and H^3), 7.27 – 7.21 (m, 1H, H^2), 6.57 (d, *J* = 16.21 Hz, 1H, H^7), 6.43 (d, *J* = 16.17 Hz, 1H, H^8), 4.73 (d, *J* = 5.59 Hz, 2H, H^{10} and H^{11}), 4.49 (d, *J* = 5.67 Hz, 2H, H^{10} and H^{11}), 1.59 (s, 3H, H^{12}).

^{13}C NMR (126 MHz, Chloroform-*d*) δ 137.1 (C^5), 134.4 (C^7), 128.8 (C^1 and C^3), 128.3 (C^8), 127.6 (C^2), 126.3 (C^4 and C^6), 83.0 (C^{10} and C^{11}), 41.4 (C^9), 23.6 (C^{12}).

IR (film): 2961, 2932, 2866, 1491, 1449, 1379, 978, 912, 827, 746, 731, 692 cm^{-1}.

HRMS (ESI): *m/z* calculated for $[M + Na]^+$ $(C_{12}H_{14}ONa)^+$: 197.0937; found 197.0935.

(*E*)-3-Styryltetrahydrofuran, **3.104**



Prepared according to General Procedure 1 using 1,3-Dioxoisoindolin-2-yl tetrahydrofuran-3-carboxylate. **3.37** (52.2 mg, 200 μmol, 1.0 equiv.), (*E*)-2-phenylvinylboronic acid **3.1a** (59.2 mg, 400 μmol, 2.0 equiv.), tris(2,2'-

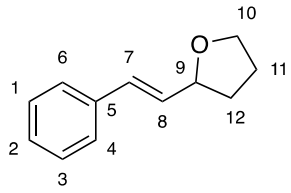
bipyridine)ruthenium hexafluorophosphate (1.7 mg, 2.00 μmol, 1 mol%), and *N,N*-dimethylaniline (2.5 μL, 20.0 μmol, 10 mol%) in DMSO-d_6 (1 mL, 0.2 M). The crude residue was purified by flash chromatography (silica gel) from pure hexane to a mixture of 10% of diethyl ether in hexane affording 23.1 mg of a colourless oil as the desired product (66%, *E:Z* > 20:1).

^{1}H NMR (400 MHz, Chloroform-*d*) δ 7.39 – 7.32 (m, 2H, H^4 and H^6), 7.35 – 7.27 (m, 2H, H^1 and H^3), 7.26 – 7.18 (m, 1H, H^2), 6.46 (d, *J* = 15.73 Hz, 1H, H^7), 6.15 (dd, *J* = 15.77, 8.42 Hz, 1H, H^8), 4.03 – 3.91 (m, 2H, H^{10} and H^{11}), 3.85 (td, *J* = 8.13, 7.18 Hz, 1H, H^{11}), 3.54 (dd, *J* = 8.41, 7.53 Hz, 1H, H^{10}), 3.03 (h, *J* = 7.88 Hz, 1H, H^9), 2.18 (dtd, *J* = 12.22, 7.23, 4.62 Hz, 1H, H^{12}), 1.82 (dq, *J* = 12.28, 7.99 Hz, 1H, H^{12}).

^{13}C NMR (101 MHz, Chloroform-*d*) δ 137.3 (C^5), 130.8 (C^8), 130.6 (C^7), 128.7 (C^1 and C^3), 127.4 (C^2), 126.2 (C^4 and C^6), 73.1 (C^{10}), 68.4 (C^{11}), 43.3 (C^9), 33.4 (C^{12}).

Data are consistent with the literature.[326]

(*E*)-2-Styryltetrahydrofuran, **3.105**



Prepared according to General Procedure 1 using 1,3-dioxoisoindolin-2-yl tetrahydrofuran-2-carboxylate **3.38** (52.2 mg, 200 μmol, 1.0 equiv.), (*E*)-2-phenylvinylboronic acid **3.1a** (59.2 mg, 400 μmol, 2.0 equiv.), tris(2,2'-bipyridine)ruthenium hexafluorophosphate (1.7 mg, 2.00 μmol, 1 mol%), and *N,N*-dimethylaniline (2.5 μL, 20.0 μmol, 10 mol%) in DMSO-d_6 (1 mL, 0.2 M). The crude residue was purified by flash chromatography (silica gel) from pure hexane to a mixture of 10% of diethyl ether in hexane affording 22.3 mg of a colorless oil as the desired product (64%, *E:Z* > 20:1).

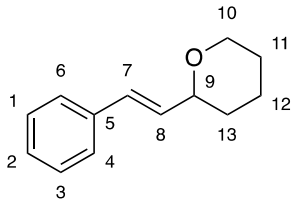
^{1}H NMR (400 MHz, Chloroform-*d*) δ 7.42 – 7.37 (m, 2H, H^4 and H^6), 7.36 – 7.28 (m, 2H, H^1 and H^3), 7.25 – 7.20 (m, 1H, H^2), 6.59 (d, *J* = 15.88 Hz, 1H, H^7), 6.22 (dd, *J* =

15.84, 6.61 Hz, 1H, H^8), 4.48 (m, 1H, H^9), 3.98 (ddd, *J* = 8.31, 7.25, 6.22 Hz, 1H, H^{10}), 3.85 (td, *J* = 7.90, 6.16 Hz, 1H, H^{10}), 2.19 – 2.09 (m, 1H, H^{12}), 2.03 – 1.91 (m, 2H, H^{11}), 1.79 – 1.66 (m, 1H, H^{12}).

^{13}C NMR (101 MHz, Chloroform-*d*) δ 137.0 (C^5), 130.6 (C^8), 130.6 (C^7), 128.6 (C^1 and C^3), 127.6 (C^2), 126.6 (C^4 and C^6), 79.8 (C^9), 68.3 (C^{10}), 32.5 (C^{12}), 26.0 (C^{11}).

Data are consistent with the literature.[327]

(*E*)-2-Styryltetrahydro-2*H*-pyran, **3.106**



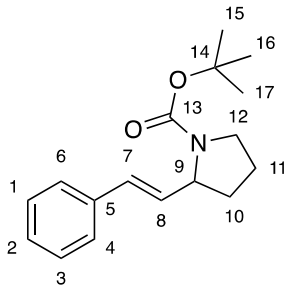
Prepared according to General Procedure 1 using 1,3-dioxoisoindolin-2-yl tetrahydro-2*H*-pyran-2-carboxylate **3.39** (55.1 mg, 200 μmol, 1.0 equiv.), (*E*)-2-phenylvinylboronic acid **3.1a** (59.2 mg, 400 μmol, 2.0 equiv.), tris(2,2'-bipyridine)ruthenium hexafluorophosphate (1.7 mg, 2.00 μmol, 1 mol%), and *N*,*N*-dimethylaniline (2.5 μL, 20.0 μmol, 10 mol%) in DMSO-d_6 (1 mL, 0.2 M). The crude residue was purified by flash chromatography (silica gel) from pure hexane to a mixture of 8% of diethyl ether in hexane affording 24.4 mg of a colorless oil as the desired product (65%, *E:Z* > 20:1).

^{1}H NMR (400 MHz, Chloroform-*d*) δ 7.42 – 7.35 (m, 2H, H^4 and H^6), 7.34 – 7.26 (m, 2H, H^1 and H^3), 7.26 – 7.18 (m, 1H, H^2), 6.59 (dd, *J* = 16.10, 1.37 Hz, 1H, H^7), 6.22 (dd, *J* = 16.03, 5.80 Hz, 1H, H^8), 4.12 – 4.03 (m, 1H, H^{10}), 3.98 (ddt, *J* = 10.63, 5.80, 1.86 Hz, 1H, H^9), 3.55 (td, *J* = 11.58, 2.68 Hz, 1H, H^{10}), 1.95 – 1.84 (m, 1H, H^{12}), 1.80 – 1.70 (m, 1H, H^{13}), 1.68 – 1.54 (m, 3H H^{11} and H^{12}), 1.53 – 1.45 (m, 1H, H^{13}).

^{13}C NMR (101 MHz, Chloroform-*d*) δ 137.1 (C^5), 131.0 (C^8), 129.9 (C^7), 128.6 (C^1 and C^3), 127.6(C^2), 126.5 (C^4 and C^6), 78.2 (C^9), 68.6 (C^{10}), 32.4 (C^{13}), 26.0 (C^{11}), 23.6 (C^{12}).

Data are consistent with the literature.[328]

tert-Butyl (*E*)-2-styrylpyrrolidine-1-carboxylate, **3.107**



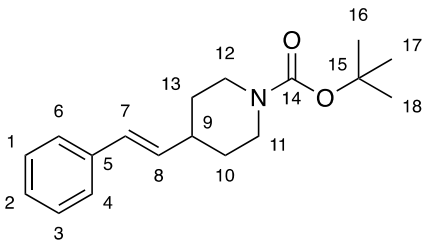
Prepared according to General Procedure 1 using 1-(*tert*-butyl) 2-(1,3-dioxoisoindolin-2-yl) (*S*)-pyrrolidine-1,2-dicarboxylate **3.40** (72.1 mg, 200 μmol, 1.0 equiv.), (*E*)-2-phenylvinylboronic acid **3.1a** (59.2 mg, 400 μmol, 2.0 equiv.), tris(2,2'-bipyridine)ruthenium hexafluorophosphate (1.7 mg, 2.00 μmol, 1 mol%), and *N*,*N*-dimethylaniline (2.5 μL, 20.0 μmol, 10 mol%) in DMSO-d_6 (1 mL, 0.2 M). The crude residue was purified by flash chromatography (silica gel) with pure hexane affording 26.0 mg of a white solid as the desired product (84%, *E*:*Z* > 20:1).

^{1}H NMR (400 MHz, Chloroform-*d*) δ 7.41 – 7.28 (m, 4H, H^1, H^3, H^4 and H^6), 7.28 – 7.20 (m, 1H, H^2), 6.42 (broad d, *J* = 16.02 Hz, 1H, H^7), 6.25 – 6.00 (broad s, 1H, H^8), 4.60 – 4.34 (broad s, 1H, H^9), 3.61 – 3.26 (broad s, 2H, H^{12}), 2.23 – 2.05 (broad s, 1H, H^{10}), 2.00 – 1.85 (m, 2H, H^{11}), 1.85 – 1.78 (m, 1H, H^{10}), 1.47 (broad s, 9H, H^{15}, H^{16} and H^{17}).

^{13}C NMR (176 MHz, Chloroform-*d*) δ 154.9 (C^{13}), 137.2 (C^5), 130.9 (C^8), 129.6 (C^7), 128.7 (C^1 and C^3), 127.4 (C^2), 126.4 (C^4 and C^6), 79.3 (C^{14}), 59.1 (C^9), 46.4 (C^{12}), 32.7 (C^{10}), 28.6 (C^{15}, C^{16} and C^{17}), 23.2 (C^{11}).

Data are consistent with the literature.[244]

tert-Butyl (*E*)-4-styrylpiperidine-1-carboxylate, **3.108**



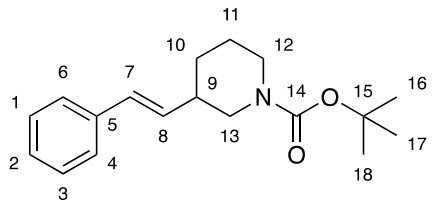
Prepared according to General Procedure 1 using 1-(*tert*-butyl) 4-(1,3-dioxoisoindolin-2-yl) piperidine-1,4-dicarboxylate **3.41** (74.9 mg, 200 μmol, 1.0 equiv.), (*E*)-2-phenylvinylboronic acid **3.1a** (59.2 mg, 400 μmol, 2.0 equiv.), tris(2,2'-bipyridine)ruthenium hexafluorophosphate (1.7 mg, 2.00 μmol, 1 mol%), and *N*,*N*-dimethylaniline (2.5 μL, 20.0 μmol, 10 mol%) in DMSO-d_6 (1 mL, 0.2 M). The crude residue was purified by flash chromatography (silica gel) from pure hexane to a mixture of 6% of diethyl ether in hexane affording 38.9 mg of a white solid as the desired product (68%, *E:Z* > 20:1).

^{1}H NMR (500 MHz, Chloroform-*d*) δ 7.37 – 7.33 (m, 2H, H^4 and H^6), 7.32 – 7.27 (m, 2H, H^1 and H^3), 7.23 – 7.17 (m, 1H, H^2), 6.39 (broad d, *J* = 15.74 Hz, 1H, H^7), 6.15 (dd, *J* = 15.97, 6.89 Hz, 1H, H^8), 4.13 (broad s, 2H, H^{11} and H^{12}), 2.77 (broad s, 2H, H^{11} and H^{12}), 2.35 – 2.22 (m, 1H, H^9), 1.80 – 1.72 (m, 2H, H^{10} and H^{13}), 1.47 (s, 9H, H^{16}, H^{17} and H^{18}), 1.44 – 1.32 (m, 2H, H^{10} and H^{13}).

^{13}C NMR (126 MHz, Chloroform-*d*) δ 155.0 (C^{14}), 137.6 (C^5), 134.5 (C^8), 128.7 (C^1 and C^3), 128.6 (C^7), 127.2 (C^2), 126.2 (C^4 and C^6), 79.5 (C^{15}), 44.0 (broad, C^{11} and C^{12}), 39.5 (C^9), 31.9 (C^{10} and C^{13}), 28.6 (C^{16}, C^{17} and C^{18}).

Data are consistent with the literature.[244]

tert-Butyl (*E*)-3-styrylpiperidine-1-carboxylate, **3.109**



Prepared according to General Procedure 1 using 1-(*tert*-butyl) 3-(1,3-dioxoisoindolin-2-yl) piperidine-1,3-dicarboxylate **3.42** (74.9 mg, 200 μmol, 1.0 equiv.), (*E*)-2-phenylvinylboronic acid **3.1a** (59.2 mg, 400 μmol, 2.0 equiv.), tris(2,2'-bipyridine)ruthenium hexafluorophosphate (1.7 mg, 2.00 μmol, 1 mol%), and *N*,*N*-dimethylaniline (2.5 μL, 20.0 μmol, 10 mol%) in DMSO-d_6 (1 mL, 0.2 M). The crude residue was purified by flash chromatography (silica gel) with pure hexane to a

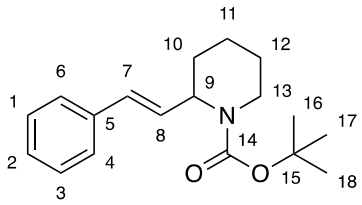
mixture of 5% of diethyl ether in hexane affording 34.7 mg of a colourless oil as the desired product (61%%, *E:Z* > 20:1).

^{1}H NMR (500 MHz, Chloroform-*d*) δ 7.38 – 7.32 (m, 2H, H^4 and H^6), 7.32 – 7.27 (m, 2H, H^1 and H^3), 7.24 – 7.18 (m, 1H, H^2), 6.45 (dd, *J* = 16.09, 1.28 Hz, 1H, H^7), 6.09 (dd, *J* = 16.04, 7.05 Hz, 1H, H^8), 4.14 (broad s, 1H, H^{13}), 4.02 – 3.95 (broad d, *J* = 13.36 Hz, 1H, H^{12}), 2.82 – 2.73 (m, 1H, H^{12}), 2.73 – 2.55 (m, 1H, H^{13}), 2.39 – 2.25 (m, 1H, H^9), 1.98 – 1.87 (m, 1H, H^{10}), 1.74 – 1.67 (m, 1H, H^{11}), 1.55 – 1.48 (m, 1H, H^{11}), 1.47 (s, 9H, H^{16}, H^{17} and H^{18}), 1.42 – 1.33 (m, 1H, H^{10}).

^{13}C NMR (126 MHz, Chloroform-*d*) δ 155.0 (C^{14}), 137.5 (C^5), 131.9 (C^8), 129.9 (C^7), 128.7 (C^1 and C^3), 127.3 (C^2), 126.2 (C^4 and C^6), 79.5 (C^{15}), 49.3 (broad s, C^{13}), 44.3 (broad s, C^{12}), 39.5 (C^9), 31.0 (C^{10}), 28.6 (C^{16}, C^{17} and C^{18}), 24.9 (C^{11}).

Data are consistent with the literature.[319]

tert-Butyl (*E*)-2-styrylpiperidine-1-carboxylate, **3.110**



Prepared according to General Procedure 1 using 1-(*tert*-butyl) 2-(1,3-dioxoisoindolin-2-yl) piperidine-1,2-dicarboxylate **3.43** (74.9 mg, 200 μmol, 1.0 equiv.), (*E*)-2-phenylvinylboronic acid **3.1a** (59.2 mg, 400 μmol, 2.0 equiv.), tris(2,2'-bipyridine)ruthenium hexafluorophosphate (1.7 mg, 2.00 μmol, 1 mol%), and *N*,*N*-dimethylaniline (2.5 μL, 20.0 μmol, 10 mol%) in DMSO-d_6 (1 mL, 0.2 M). The crude residue was purified by flash chromatography (silica gel) from pure hexane to a mixture of 5% of diethyl ether in hexane affording 29.7 mg of a colourless oil as the desired product (52%, *E:Z* > 20:1).

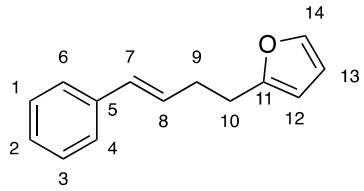
^{1}H NMR (500 MHz, Chloroform-*d*) δ 7.42 – 7.36 (m, 2H, H^4 and H^6), 7.37 – 7.30 (m, 2H, H^1 and H^3), 7.29 – 7.22 (m, 1H, H^2), 6.41 (dd, *J* = 16.14, 1.94 Hz, 1H, H^7), 6.21 (dd, *J* = 16.12, 4.77 Hz, 1H, H^8), 4.99 (broad s, 1H, H^9), 4.07 – 3.96 (m, 1H, H^{13}), 2.99

– 2.89 (m, 1H, H^{13}), 1.90 – 1.83 (m, 1H, H^{10}), 1.83 – 1.74 (m, 1H, H^{10}), 1.69 – 1.66 (m, 1H, H^{12}), 1.66 – 1.62 (m, 1H, H^{11}), 1.62 – 1.55 (m, 1H, H^{11}), 1.50 (s, 9H, H^{16}, H^{17} and H^{18}), 1.48 – 1.44 (m, 1H, H^{12}).

^{13}C NMR (126 MHz, Chloroform-*d*) δ 155.5 (C^{14}), 137.2 (C^{5}), 130.8 (C^{7}), 128.9 (C^{8}), 128.7 (C^{1} and C^{3}), 127.5 (C^{2}), 126.4 (C^{4} and C^{6}), 79.6 (C^{15}), 52.3 (C^{9}), 40.0 (C^{13}), 29.6 (C^{10}), 28.6 (C^{16}, C^{17} and C^{18}), 25.7 (C^{12}), 19.8 (C^{11}).

Data are consistent with the literature.[329]

(*E*)-2-(4-Phenylbut-3-en-1-yl)furan, **3.111**



Prepared according to General Procedure 1 using 1,3-dioxoisoindolin-2-yl 3-(furan-2-yl)propanoate **3.44** (57.1 mg, 200 μmol, 1.0 equiv.), (*E*)-2-phenylvinylboronic acid **3.1a** (59.2 mg, 400 μmol, 2.0 equiv.), tris(2,2'-bipyridine)ruthenium hexafluorophosphate (1.7 mg, 2.00 μmol, 1 mol%), and *N*,*N*-dimethylaniline (2.5 μL, 20.0 μmol, 10 mol%) in DMSO-d_6 (1 mL, 0.2 M). The crude residue was purified by flash chromatography (silica gel) with pure hexane affording 30.1 mg of a colourless oil as the desired product (76%, *E:Z* > 20:1).

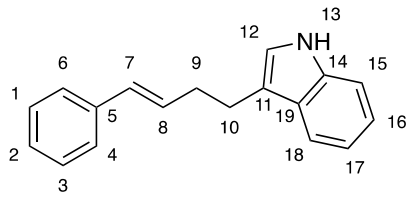
^{1}H NMR (500 MHz, Chloroform-*d*) δ 7.37 – 7.33 (m, 3H, H^{4}, H^{6} and H^{14}), 7.33 – 7.28 (m, 2H, H^{1} and H^{3}), 7.24 – 7.20 (m, 1H, H^{2}), 6.45 (d, *J* = 15.83 Hz, 1H, H^{7}), 6.31 (dd, *J* = 3.14, 1.88 Hz, 1H, H^{13}), 6.26 (dt, *J* = 15.81, 6.84 Hz, 1H, H^{8}), 6.05 (dd, *J* = 3.11, 1.05 Hz, 1H, H^{12}), 2.83 (t, *J* = 7.59 Hz, 2H, H^{10}), 2.62 – 2.54 (m, 2H, H^{9}).

^{13}C NMR (126 MHz, Chloroform-*d*) δ 155.6 (C^{11}), 141.0 (C^{14}), 137.7 (C^{5}), 130.8 (C^{7}), 129.5 (C^{8}), 128.6 (C^{1} and C^{3}), 127.1 (C^{2}), 126.1 (C^{4} and C^{6}), 110.3 (C^{13}), 105.2 (C^{12}), 31.6 (C^{9}), 28.1 (C^{10}).

IR (film): 2918, 2849, 2361, 2339, 1797, 1711, 1597, 1506, 1493, 1447, 1209, 1149, 1006, 962, 921 cm^{-1}.

HRMS (ESI): *m/z* calculated for $[M + Na]^+$ $(C_{14}H_{14}ONa)^+$: 221.0937; found 221.0934.

(*E*)-3-(4-Phenylbut-3-en-1-yl)-1*H*-indole, **3.112**



Prepared according to General Procedure 1 using 1,3-dioxoisoindolin-2-yl 3-(1*H*-indol-3-yl)propanoate **3.45** (66.9 mg, 200 μmol, 1.0 equiv.), (*E*)-2-phenylvinylboronic acid **3.1a** (59.2 mg, 400 μmol, 2.0 equiv.), tris(2,2'-bipyridine)ruthenium hexafluorophosphate (1.7 mg, 2.00 μmol, 1 mol%), and *N*,*N*-dimethylaniline (2.5 μL, 20.0 μmol, 10 mol%) in DMSO-d_6 (1 mL, 0.2 M). The crude residue was purified by flash chromatography (silica gel) from pure hexane to a mixture of 5% of diethyl ether in hexane affording 19.6 mg of a white solid as the desired product (40%, *E:Z* > 20:1).

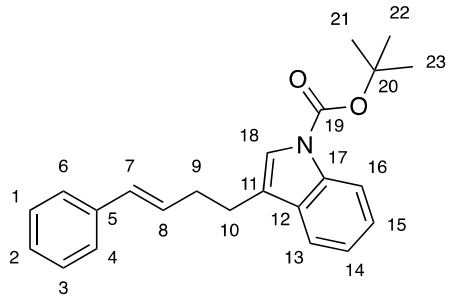
^{1}H NMR (500 MHz, Chloroform-*d*) δ 7.91 (broad s, 1H, H^{13}), 7.70 – 7.63 (m, 1H, H^{18}), 7.40 – 7.33 (m, 3H, H^{4}, H^{6} and H^{15}), 7.34 – 7.26 (m, 2H, H^{1} and H^{3}), 7.26 – 7.18 (m, 2H, H^{2} and H^{16}), 7.18 – 7.11 (m, 1H, H^{17}), 7.03 (d, *J* = 2.26 Hz, 1H, H^{12}), 6.47 (d, *J* = 15.80 Hz, 1H, H^{7}), 6.36 (dt, *J* = 15.81, 6.73 Hz, 1H, H^{8}), 2.99 – 2.93 (m, 2H, H^{10}), 2.69 – 2.61 (m, 2H, H^{9}).

^{13}C NMR (126 MHz, Chloroform-*d*) δ 137.9 (C^{5}), 136.4 (C^{14}), 130.9 (C^{8}), 130.3 (C^{7}), 128.6 (C^{1} and C^{3}), 127.6 (C^{19}), 127.0 (C^{2}), 126.1 (C^{4} and C^{6}), 122.1 (C^{16}), 121.4 (C^{12}), 119.3 (C^{17}), 119.1 (C^{18}), 116.3 (C^{11}), 111.2 (C^{15}), 33.7 (C^{9}), 25.3 (C^{10}).

IR (film): 2918, 2847, 1597, 1491, 1456, 1420, 1339, 1223, 1091, 1028, 1010, 964, 738, 692 cm^{-1}.

HRMS (ESI): *m/z* calculated for $[M + Na]^{+}$ $(C_{18}H_{17}NNa)^{+}$: 270.1253; found 270.1250.

tert-Butyl (*E*)-3-(4-phenylbut-3-en-1-yl)-1*H*-indole-1-carboxylate, **3.113**



Prepared according to General Procedure 1 using *tert*-butyl 3-(3-((1,3-dioxoisoindolin-2-yl)oxy)-3-oxopropyl)-1*H*-indole-1-carboxylate **3.46** (84.1 mg, 200 μmol, 1.0 equiv.), (*E*)-2-phenylvinylboronic acid **3.1a** (59.2 mg, 400 μmol, 2.0 equiv.), tris(2,2'-bipyridine)ruthenium hexafluorophosphate (1.7 mg, 2.00 μmol, 1 mol%), and *N*,*N*-dimethylaniline (2.5 μL, 20.0 μmol, 10 mol%) in DMSO-d_6 (1 mL, 0.2 M). The crude residue was purified by flash chromatography (silica gel) from pure hexane to a mixture of 1% of diethyl ether in hexane affording 38.8 mg of a white solid as the desired product (55%, *E:Z* > 20:1).

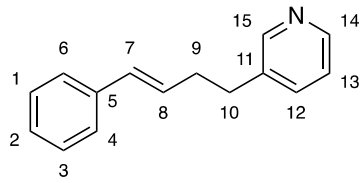
^{1}H NMR (500 MHz, Chloroform-*d*) δ 8.16 (broad s, 1H, H^{16}), 7.60 – 7.56 (m, 1H, H^{13}), 7.43 (broad s, 1H, H^{18}), 7.38 – 7.35 (m, 2H, H^4 and H^6), 7.35 – 7.30 (m, 3H, H^1, H^3 and H^{15}), 7.29 – 7.25 (m, 1H, H^{14}), 7.25 – 7.20 (m, 1H, H^2), 6.49 (d, *J* = 15.83 Hz, 1H, H^7), 6.34 (dt, *J* = 15.72, 6.77 Hz, 1H, H^8), 2.89 (t, *J* = 7.65 Hz, 2H, H^{10}), 2.72 – 2.59 (m, 2H, H^9), 1.68 (s, 9H, H^{21}, H^{22} and H^{23}).

^{13}C NMR (126 MHz, Chloroform-*d*) δ 150.0 (C^{19}), 137.7 (C^5), 135.7 (C^{17}), 130.8 (C^{12}), 130.6 (C^7), 130.1 (C^8), 128.6 (C^1 and C^3), 127.1 (C^2), 126.1 (C^4 and C^6), 124.4 (C^{15}), 122.6 (C^{18} or C^{14}), 122.4 (C^{14} or C^{18}), 120.6 (C^{11}), 119.1 (C^{13}), 115.4 (C^{16}), 83.5 (C^{20}), 32.9 (C^9), 28.4 (C^{21}, C^{22} and C^{23}), 25.1 (C^{10}).

IR (film): 2978, 2930, 1726, 1450, 1367, 1308, 1251, 1223, 11531084, 963, 857, 765 cm^{-1}.

HRMS (EI): *m/z* calculated for $[M]^+$ $(C_{23}H_{25}NO_2)^+$: 347.1880; found 347.1885.

(*E*)-3-(4-Phenylbut-3-en-1-yl)pyridine, **3.114**



Prepared according to General Procedure 1 using 1,3-dioxoisoindolin-2-yl 3-(pyridin-3-yl)propanoate **3.47** (59.3 mg, 200 μmol, 1.0 equiv.), (*E*)-2-phenylvinylboronic acid **3.1a** (59.2 mg, 400 μmol, 2.0 equiv.), tris(2,2'-bipyridine)ruthenium hexafluorophosphate (1.7 mg, 2.00 μmol, 1 mol%), and *N*,*N*-dimethylaniline (2.5 μL, 20.0 μmol, 10 mol%) in DMSO-d_6 (1 mL, 0.2 M). The crude residue was purified by flash chromatography (silica gel) from pure hexane to a mixture of 20% of ethyl acetate in hexane affording 28.1 mg of a colourless oil as the desired product (67%, *E:Z* > 20:1).

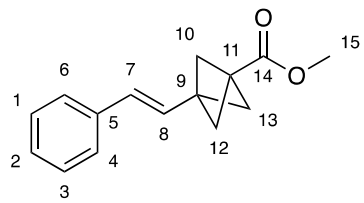
^{1}H NMR (500 MHz, Chloroform-*d*) δ 8.50 (broad s, 2H, H^{14} and H^{15}), 7.54 (dt, *J* = 7.69, 1.74 Hz, 1H, H^{12}), 7.34 – 7.27 (m, 4H, H^1, H^3, H^4 and H^6), 7.26 – 7.22 (m, 1H, H^{13}), 7.22 – 7.18 (m, 1H, H^2), 6.40 (dt, *J* = 15.81, 1.51 Hz, 1H, H^7), 6.22 (dt, *J* = 15.81, 6.90 Hz, 1H, H^8), 2.80 (t, *J* = 8.07 Hz, 2H, H^{10}), 2.54 (dtd, *J* = 8.66, 6.91, 1.44 Hz, 2H, H^9).

^{13}C NMR (126 MHz, Chloroform-*d*) δ 149.9 (C^{15}), 147.4 (C^{14}), 137.5 (C^5), 137.2 (C^{11}), 136.2 (C^{12}), 131.2 (C^7), 129.0 (C^8), 128.7 (C^1 and C^3), 127.3 (C^2), 126.1 (C^4 and C^6), 123.6 (C^{13}), 34.6 (C^9), 33.1 (C^{10}).

IR (film): 1575, 1490, 1477, 1421, 964, 912, 740, 713 cm^{-1}.

HRMS (ESI) *m/z* calculated for $[M + H]^+$ $(C_{15}H_{16}N)^+$: 210.1277, found 210.1277.

Methyl (*E*)-3-styrylbicyclo[1.1.1]pentane-1-carboxylate, **3.115**



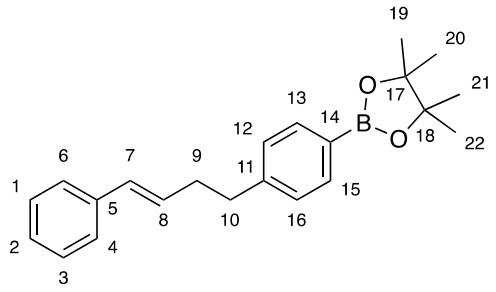
Prepared according to General Procedure 1 using 1-(1,3-dioxoisoindolin-2-yl) 3-methyl bicyclo[1.1.1]pentane-1,3-dicarboxylate **3.48** (63.1 mg, 200 μmol, 1.0 equiv.), (*E*)-2-phenylvinylboronic acid **3.1a** (59.2 mg, 400 μmol, 2.0 equiv.), tris(2,2'-bipyridine)ruthenium hexafluorophosphate (1.7 mg, 2.00 μmol, 1 mol%), and *N,N*-dimethylaniline (2.5 μL, 20.0 μmol, 10 mol%) in DMSO-d_6 (1 mL, 0.2 M). The crude residue was purified by flash chromatography (silica gel) from pure hexane to a mixture of 4% of diethyl ether in hexane affording 30.3 mg of a colourless oil as the desired product (65%, *E:Z* > 20:1).

^{1}H NMR (500 MHz, Chloroform-*d*) δ 7.37 – 7.34 (m, 2H, H^4 and H^6), 7.33 – 7.28 (m, 2H, H^1 and H^3), 7.25 – 7.20 (m, 1H, H^2), 6.37 (d, *J* = 15.93 Hz, 1H, H^7), 6.28 (d, *J* = 15.96 Hz, 1H, H^8), 3.70 (s, 3H, H^{15}), 2.18 (s, 6H, H^{10}, H^{12} and H^{13}).

^{13}C NMR (126 MHz, Chloroform-*d*) δ 170.8 (C^{14}), 136.8 (C^5), 131.2 (C^7), 128.7 (C^1 and C^3), 127.8 (C^2 or C^8), 127.7 (C^2 or C^8), 126.3 (C^4 and C^6), 53.3 (C^{10}, C^{12} and C^{13}), 51.8 (C^{15}), 40.9 (C^9), 37.9 (C^{11}).

Data are consistent with the literature.[319]

(*E*)-4,4,5,5-Tetramethyl-2-(4-(4-phenylbut-3-en-1-yl)phenyl)-1,3,2-dioxaborolane, **3.116**



Prepared according to General Procedure 1 using 1,3-dioxoisoindolin-2-yl 3-(4-(4,4,5,5-tetramethyl-1,3,2-dioxaborolan-2-yl)phenyl)propanoate **3.25** (84.3 mg, 200 μmol, 1.0 equiv.), (*E*)-2-phenylvinylboronic acid **3.1a** (59.2 mg, 400 μmol, 2.0 equiv.), tris(2,2'-bipyridine)ruthenium hexafluorophosphate (1.7 mg, 2.00 μmol, 1 mol%), and *N,N*-dimethylaniline (2.5 μL, 20.0 μmol, 10 mol%) in DMSO-d_6 (1 mL, 0.2 M). The crude residue was purified by flash chromatography (silica gel) from pure

hexane to a mixture of 5% of diethyl ether in hexane affording 44.8 mg of a white solid as the desired product (67%, *E:Z* > 20:1).

^{1}H NMR (400 MHz, Chloroform-*d*) δ 7.82 – 7.77 (m, 2H, H^{13} and H^{15}), 7.39 – 7.30 (m, 4H, H^{1}, H^{3}, H^{4} and H^{6}), 7.30 – 7.26 (m, 2H, H^{12} and H^{16}), 7.26 – 7.21 (m, 1H, H^{2}), 6.45 (dt, *J* = 15.87, 1.46 Hz, 1H, H^{7}), 6.28 (dt, *J* = 15.86, 6.83 Hz, 1H, H^{8}), 2.84 (t, *J* = 7.75 Hz, 2H, H^{10}), 2.62 – 2.52 (m, 2H, H^{9}), 1.37 (s,12H, H^{19}, H^{20}, H^{21} and H^{22}).

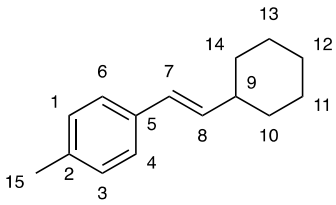
^{11}B NMR (96 MHz, Chloroform-*d*) δ 31.45.

^{13}C NMR (101 MHz, Chloroform-*d*) δ 145.3 (C^{11}), 137.8 (C^{5}), 135.0 (C^{13} and C^{15}), 130.5 (C^{7}), 129.9 (C^{8}), 128.6 (C^{1} and C^{3}), 128.1 (C^{12} and C^{16}), 127.1 (C^{2}), 126.1 (C^{4} and C^{6}), 83.8 (C^{17} and C^{18}), 36.2 (C^{10}), 34.9 (C^{9}), 25.0 (C^{19}, C^{20}, C^{21} and C^{22}). C^{14} is not observed due to quadrupolar relaxation.

IR (film): 2978, 1448, 1610, 1398, 1388, 1357, 1319, 1271, 1165, 1141, 1087, 962 cm^{-1}.

HRMS (ESI): *m/z* calculated for $[M + H]^{+}$ $(C_{22}H_{28}BO_2)^{+}$: 335.2176; found = 335.2171.

(*E*)-1-(2-cyclohexylvinyl)-4-methylbenzene, **3.117**



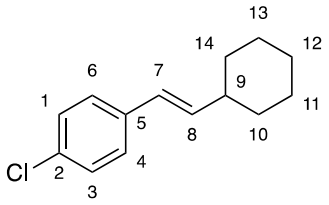
Prepared according to General Procedure 1 using 1,3-dioxoisoindolin-2-yl cyclohexanecarboxylate **3.12** (54.7 mg, 200 μmol, 1.0 equiv.), (*E*)-2-(4-methylphenyl)vinylboronic acid (64.8 mg, 400 μmol, 2.0 equiv.), tris(2,2'-bipyridine)ruthenium hexafluorophosphate (1.7 mg, 2.00 μmol, 1 mol%), and *N*,*N*-dimethylaniline (2.5 μL, 20.0 μmol, 10 mol%) in DMSO-d_6 (1 mL, 0.2 M). The crude residue was purified by flash chromatography (silica gel) with pure hexane affording 29.9 mg of a colourless oil as the desired product (75%, *E:Z* > 20:1).

^{1}H NMR (500 MHz, Chloroform-*d*) δ 7.29 – 7.21 (m, 2H, H^4 and H^6), 7.14 – 7.08 (m, 2H, H^1 and H^3), 6.33 (dd, *J* = 16.06, 1.27 Hz, 1H, H^7), 6.14 (dd, *J* = 15.95, 6.96 Hz, 1H, H^8), 2.34 (s, 3H, H^{15}), 2.17 – 2.08 (m, 1H, H^9), 1.85 – 1.74 (m, 4H, H^{10}, H^{11}, H^{13} and H^{14}), 1.73 – 1.66 (m, 1H, H^{12}), 1.39 – 1.26 (m, 2H, H^{11} and H^{13}), 1.26 – 1.08 (m, 3H, H^{10}, H^{12} and H^{14}).

^{13}C NMR (126 MHz, Chloroform-*d*) δ 136.5 (C^2), 136.0 (C^8), 135.4 (C^5), 129.3 (C^1 and C^3), 127.1 (C^7), 125.9 (C^4 and C^6), 41.3 (C^9), 33.1 (C^{10} and C^{14}), 26.3 (C^{12}), 26.2 (C^{11} and C^{13}), 21.3 (C^{15}).

Data are consistent with the literature.[246]

(*E*)-1-chloro-4-(2-cyclohexylvinyl)benzene, **3.118**



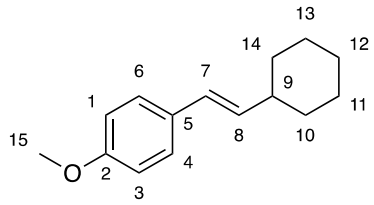
Prepared according to General Procedure 1 using 1,3-dioxoisoindolin-2-yl cyclohexanecarboxylate **3.12** (54.7 mg, 200 μmol, 1.0 equiv.), (*E*)-2-(4-chlorophenyl)vinylboronic acid (73.0 mg, 400 μmol, 2.0 equiv.), tris(2,2'-bipyridine)ruthenium hexafluorophosphate (1.7 mg, 2.00 μmol, 1 mol%), and *N*,*N*-dimethylaniline (2.5 μL, 20.0 μmol, 10 mol%) in DMSO-d_6 (1 mL, 0.2 M). The crude residue was purified by flash chromatography (silica gel) with pure hexane affording 32.0 mg of a colourless oil as the desired product (72%, *E:Z* > 20:1).

^{1}H NMR (500 MHz, Chloroform-*d*) δ 7.36 – 7.21 (m, 4H, H^1, H^3, H^4 and H^6), 6.32 (dd, *J* = 15.94, 1.19 Hz, 1H, H^7), 6.18 (dd, *J* = 15.97, 6.91 Hz, 1H, H^8), 2.20 – 2.10 (m, 1H, H^9), 1.88 – 1.77 (m, 4H, H^{10}, H^{11}, H^{13} and H^{14}), 1.77 – 1.66 (m, 1H, H^{12}), 1.41 – 1.30 (m, 2H, H^{11} and H^{13}), 1.28 – 1.12 (m, 3H, H^{10}, H^{12} and H^{14}).

^{13}C NMR (126 MHz, Chloroform-*d*) δ 137.7 (C^8), 136.7 (C^5), 132.3 (C^2), 128.7 (C^1 and C^3), 127.3 (C^4 and C^6), 126.2 (C^7), 41.3 (C^9), 33.0 (C^{10} and C^{14}), 26.3 (C^{12}), 26.1 (C^{11} and C^{13}).

Data are consistent with the literature.[246]

(*E*)-1-(2-cyclohexylvinyl)-4-methoxybenzene, **3.119**



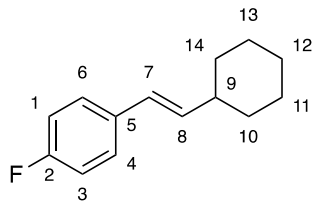
Prepared according to General Procedure 1 using 1,3-dioxoisoindolin-2-yl cyclohexanecarboxylate **3.12** (54.7 mg, 200 μmol, 1.0 equiv.), (*E*)-2-(4-methoxyphenyl)vinylboronic acid (71.2 mg, 400 μmol, 2.0 equiv.), tris(2,2'-bipyridine)ruthenium hexafluorophosphate (1.7 mg, 2.00 μmol, 1 mol%), and *N*,*N*-dimethylaniline (2.5 μL, 20.0 μmol, 10 mol%) in DMSO-d_6 (1 mL, 0.2 M). The crude residue was purified by flash chromatography (silica gel) from pure hexane to 1% of diethyl ether in hexane affording 15.8 mg of a white solid as the desired product (35%, *E:Z* > 20:1).

^{1}H NMR (700 MHz, Chloroform-*d*) δ 7.30 – 7.22 (m, 2H, H^4 and H^6), 6.85 – 6.77 (m, 2H, H^1 and H^3), 6.29 (dd, *J* = 15.99, 1.30 Hz, 1H, H^7), 6.04 (dd, *J* = 15.96, 6.99 Hz, 1H, H^8), 3.80 (s, 3H, H^{15}), 2.14 – 2.05 (m, 1H, H^9), 1.83 – 1.72 (m, 4H, H^{10}, H^{11}, H^{13} and H^{14}), 1.72 – 1.62 (m, 1H, H^{12}), 1.36 – 1.26 (m, 2H, H^{11} and H^{13}), 1.24 – 1.11 (m, 3H, H^{10}, H^{12} and H^{14}).

^{13}C NMR (176 MHz, Chloroform-*d*) δ 158.7 (C^2), 135.0 (C^8), 131.0 (C^5), 127.1 (C^4 and C^6), 126.7 (C^7), 114.0 (C^1 and C^3), 55.4 (C^{15}), 41.3 (C^9), 33.2 (C^{10} and C^{14}), 26.3 (C^{12}), 26.2 (C^{11} and C^{13}).

Data are consistent with the literature.[246]

(*E*)-1-(2-cyclohexylvinyl)-4-fluorobenzene, **3.120**



Prepared according to General Procedure 1 using 1,3-dioxoisoindolin-2-yl cyclohexanecarboxylate **3.12** (54.7 mg, 200 μmol, 1.0 equiv.), (*E*)-2-(4-

fluorophenyl)vinylboronic acid (66.4 mg, 400 μmol, 2.0 equiv.), tris(2,2'-bipyridine)ruthenium hexafluorophosphate (1.7 mg, 2.00 μmol, 1 mol%), *N*,*N*-dimethylaniline (2.5 μL, 20.0 μmol, 10 mol%) in DMSO-d_6 (1 mL, 0.2 M). The crude residue was purified by flash chromatography (silica gel) with pure hexane affording 29.9 mg of a colourless oil as the desired product (73%, *E*:*Z* > 20:1).

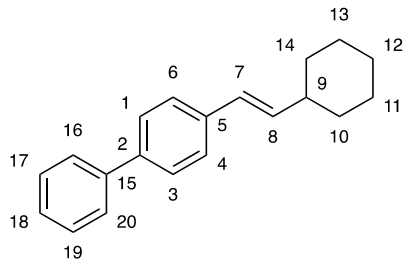
^{1}H NMR (500 MHz, Chloroform-*d*) δ 7.34 – 7.27 (m, 2H, H^4 and H^6), 7.01 – 6.94 (m, 2H, H^1 and H^3), 6.30 (broad d, *J* = 15.97, 1H, H^7), 6.09 (dd, *J* = 15.96, 6.99 Hz, 1H, H^8), 2.17 – 2.07 (m, 1H, H^9), 1.85 – 1.73 (m, 4H, H^{10}, H^{11}, H^{13} and H^{14}), 1.73 – 1.63 (m, 1H, H^{12}), 1.40 – 1.25 (m, 2H, H^{11} and H^{13}), 1.25 – 1.09 (m, 3H, H^{10}, H^{12} and H^{14}).

^{13}C NMR (126 MHz, Chloroform-*d*) δ 162.0 (d, $^{1}J_{CF}$ = 245.4 Hz, C^2), 136.7 (d, $^{5}J_{CF}$ = 2.2 Hz, C^8), 134.3 (d, $^{4}J_{CF}$ = 3.2 Hz, C^5), 127.4 (d, $^{3}J_{CF}$ = 7.8 Hz, C^4 and C^6), 126.2 (C^7), 115.4 (d, $^{2}J_{CF}$ = 21.4 Hz, C^1 and C^3), 41.3 (C^9), 33.1 (C^{10} and C^{14}), 26.3 (C^{12}), 26.2 (C^{11} and C^{13}).

^{19}F {^{1}H} NMR (376 MHz, Chloroform-*d*) δ –116.01.

Data are consistent with the literature.[246]

(*E*)-4-(2-Cyclohexylvinyl)-1,1'-biphenyl, **3.121**



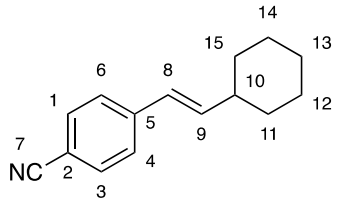
Prepared according to General Procedure 1 using 1,3-dioxoisoindolin-2-yl cyclohexanecarboxylate **3.12** (54.7 mg, 200 μmol, 1.0 equiv.), (*E*)-2-(4-biphenyl)vinylboronic acid (89.6 mg, 400 μmol, 2.0 equiv.), tris(2,2'-bipyridine)ruthenium hexafluorophosphate (1.7 mg, 2.00 μmol, 1 mol%), and *N*,*N*-dimethylaniline (2.5 μL, 20.0 μmol, 10 mol%) in DMSO-d_6 (1 mL, 0.2 M). The crude residue was purified by flash chromatography (silica gel) with pure hexane affording 42.6 mg of a white solid as the desired product (81%, *E*:*Z* > 20:1).

^{1}H NMR (500 MHz, Chloroform-*d*) δ 7.65 – 7.61 (m, 2H, H^{16} and H^{20}), 7.58 – 7.55 (m, 2H, H^{1} and H^{3}), 7.48 – 7.43 (m, 4H, H^{4}, H^{6}, H^{17} and H^{19}), 7.38 – 7.34 (m, 1H, H^{18}), 6.42 (d, *J* = 16.00, 1H, H^{7}), 6.26 (dd, *J* = 15.97, 6.95 Hz, 1H, H^{8}), 2.23 – 2.14 (m, 1H, H^{9}), 1.89 – 1.77 (m, 4H, H^{10}, H^{11}, H^{13} and H^{14}), 1.76 – 1.70 (m, 1H, H^{12}), 1.43 – 1.32 (m, 2H, H^{11} and H^{13}), 1.31 – 1.15 (m, 3H, H^{10}, H^{12} and H^{14}).

^{13}C NMR (126 MHz, Chloroform-*d*) δ 141.0 (C^{2}), 139.6 (C^{15}), 137.3 (C^{5}), 137.2 (C^{8}), 128.9 (C^{17} and C^{19}), 127.3 (C^{1} and C^{3}), 127.2 (C^{18}), 127.0 (C^{16} and C^{20}), 126.9 (C^{7}), 126.5 (C^{4} and C^{6}), 41.4 (C^{9}), 33.1 (C^{10} and C^{14}), 26.3 (C^{12}), 26.2 (C^{11} and C^{13}).

Data are consistent with the literature.[330]

(*E*)-4-(2-Cyclohexylvinyl)benzonitrile, **3.122**



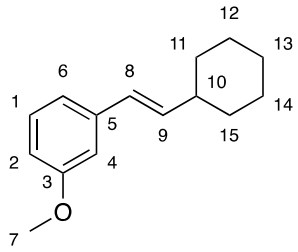
Prepared according to General Procedure 1 using 1,3-dioxoisoindolin-2-yl cyclohexanecarboxylate **3.12** (54.7 mg, 200 μmol, 1.0 equiv.), (*E*)-(4-cyanostyryl)boronic acid **3.62** (69.2 mg, 400 μmol, 2.0 equiv.), tris(2,2'-bipyridine)ruthenium hexafluorophosphate (1.7 mg, 2.00 μmol, 1 mol%), and *N*,*N*-dimethylaniline (2.5 μL, 20.0 μmol, 10 mol%) in DMSO-d_6 (1 mL, 0.2 M). The crude residue was purified by flash chromatography (silica gel) from pure hexane to a mixture of 2% of diethyl ether in hexane affording 36.9 mg of a colourless oil as the desired product (88%, *E:Z* > 20:1).

^{1}H NMR (400 MHz, Chloroform-*d*) δ 7.59 – 7.53 (m, 2H, H^{1} and H^{3}), 7.44 – 7.38 (m, 2H, H^{4} and H^{6}), 6.38 – 6.27 (m, 2H, H^{8} and H^{9}), 2.22 – 2.11 (m, 1H, H^{10}), 1.86 – 1.73 (m, 4H, H^{11}, H^{12}, H^{14} and H^{15}), 1.75 – 1.64 (m, 1H, H^{13}), 1.38 – 1.27 (m, 2H, H^{12} and H^{14}), 1.27 – 1.13 (m, 3H, H^{11}, H^{13} and H^{15}).

^{13}C NMR (101 MHz, Chloroform-*d*) δ 142.8 (C^{5}), 141.1 (C^{9}), 132.4 (C^{1} and C^{3}), 126.5 (C^{4} and C^{6}), 126.1 (C^{8}), 119.3 (C^{7}), 110.0 (C^{2}), 41.4 (C^{10}), 32.8 (C^{11} and C^{15}), 26.2 (C^{13}), 26.0 (C^{12} and C^{14}).

Data are consistent with the literature.[252]

(*E*)-1-(2-Cyclohexylvinyl)-3-methoxybenzene, **3.123**



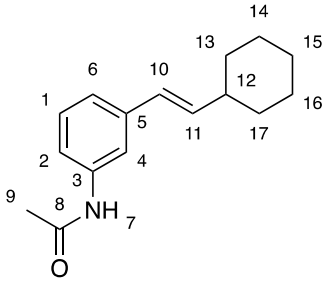
Prepared according to General Procedure 1 using 1,3-dioxoisoindolin-2-yl cyclohexanecarboxylate **3.12** (54.7 mg, 200 μmol, 1.0 equiv.), (*E*)-(3-methoxystyryl)boronic acid **3.63** (71.2 mg, 400 μmol, 2.0 equiv.), tris(2,2'-bipyridine)ruthenium hexafluorophosphate (1.7 mg, 2.00 μmol, 1 mol%), and *N*,*N*-dimethylaniline (2.5 μL, 20.0 μmol, 10 mol%) in DMSO-d_6 (1 mL, 0.2 M). The crude residue was purified by flash chromatography (silica gel) from pure hexane to a mixture of 4% of diethyl ether in hexane affording 37.9 mg of a colourless oil as the desired product (88%, *E:Z* = 20:1.6).

^{1}H NMR (500 MHz, Chloroform-*d*) δ 7.22 (t, *J* = 7.90 Hz, 1H, H^1), 6.99 – 6.94 (m, 1H, H^6), 6.91 (dd, *J* = 2.61, 1.58 Hz, 1H, H^4), 6.76 (ddd, *J* = 8.21, 2.60, 0.94 Hz, 1H, H^2), 6.33 (d, *J* = 15.96 Hz, 1H, H^8), 6.19 (dd, *J* = 15.94, 6.93 Hz, 1H, H^9), 3.82 (s, 3H, H^7), 2.20 – 2.09 (m, 1H, H^{10}), 1.87 – 1.74 (m, 4H, H^{11}, H^{12}, H^{14} and H^{15}), 1.73 – 1.66 (m, 1H, H^{13}), 1.41 – 1.28 (m, 2H, H^{12} and H^{14}), 1.25 – 1.16 (m, 3H, H^{11}, H^{13} and H^{15}).

^{13}C NMR (126 MHz, Chloroform-*d*) δ 159.9 (C^3), 139.7 (C^5), 137.3 (C^9), 129.5 (C^1), 127.2 (C^8), 118.8 (C^6), 112.5 (C^2), 111.3 (C^4), 55.3 (C^7), 41.3 (C^{10}), 33.0 (C^{11} and C^{15}), 26.3 (C^{13}), 26.2 (C^{12} and C^{14}).

Data are consistent with the literature.[331]

(*E*)-*N*-(3-(2-Cyclohexylvinyl)phenyl)acetamide, **3.124**



Prepared according to General Procedure 1 using 1,3-dioxoisoindolin-2-yl cyclohexanecarboxylate **3.12** (27.3 mg, 100 μmol, 1.0 equiv.), (*E*)-(3-acetamidostyryl)boronic acid **3.64** (41.0 mg, 200 μmol, 2.0 equiv.), tris(2,2'-bipyridine)ruthenium hexafluorophosphate (0.9 mg, 1.00 μmol, 1 mol%), and *N*,*N*-dimethylaniline (1.5 μL, 10.0 μmol, 10 mol%) in DMSO-d_6 (1 mL, 0.1 M). The crude residue was purified by flash chromatography (silica gel) from pure hexane to a mixture of 20% of ethyl acetate in hexane affording 10.8 mg of a colourless oil as the desired product (44%, *E:Z* = 20:1.2).

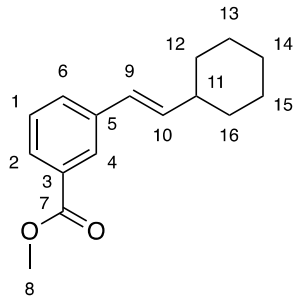
^{1}H NMR (500 MHz, Chloroform-*d*) δ 7.51 (t, *J* = 1.94 Hz, 1H, H^4), 7.30 (dt, *J* = 8.05, 1.62 Hz, 1H, H^2), 7.22 (t, *J* = 7.80 Hz, 1H, H^1), 7.09 (d, *J* = 7.67 Hz, 1H, H^6), 6.30 (d, *J* = 15.98 Hz, 1H, H^{10}), 6.17 (dd, *J* = 15.95, 6.89 Hz, 1H, H^{11}), 2.17 (s, 3H, H^9), 2.14 – 2.07 (m, 1H, H^{12}), 1.83 – 1.73 (m, 4H, H^{13}, H^{14}, H^{16} and H^{17}), 1.71 – 1.64 (m, 1H, H^{15}), 1.35 – 1.24 (m, 2H, H^{14} and H^{16}), 1.23 – 1.12 (m, 3H, H^{13}, H^{15} and H^{17}). H^7 is not observed.

^{13}C NMR (126 MHz, Chloroform-*d*) δ 168.5 (C^8), 139.2 (C^5), 138.2 (C^3), 137.7 (C^{11}), 129.2 (C^1), 126.9 (C^{10}), 122.2 (C^6), 118.3 (C^2), 117.4 (C^4), 41.3 (C^{12}), 33.0 (C^{13} and C^{17}), 26.3 (C^{15}), 26.2 (C^{14} and C^{16}), 24.8 (C^9).

IR (film): 2922, 2848, 1664, 1608, 1585, 1552, 1485, 1444, 1431, 1371, 1319, 1301 cm^{-1}.

HRMS (MALDI): *m/z* calculated for $[M + H]^+$ $(C_{16}H_{22}NO)^+$: 244.1696; found = 244.1696.

Methyl (*E*)-3-(2-cyclohexylvinyl)benzoate, **3.125**



Prepared according to General Procedure 1 using 1,3-dioxoisoindolin-2-yl cyclohexanecarboxylate **3.12** (54.7 mg, 200 μmol, 1.0 equiv.), (*E*)-(3-(methoxycarbonyl)styryl)boronic acid **3.65** (82.4 mg, 400 μmol, 2.0 equiv.), tris(2,2'-bipyridine)ruthenium hexafluorophosphate (1.7 mg, 2.00 μmol, 1 mol%), and *N*,*N*-dimethylaniline (2.5 μL, 20.0 μmol, 10 mol%) in DMSO-d_6 (1 mL, 0.2 M). The crude residue was purified by flash chromatography (silica gel) from pure hexane to a mixture of 2% of diethyl ether in hexane affording 36.7 mg of a colourless oil as the desired product (76%, *E:Z* = 20:1).

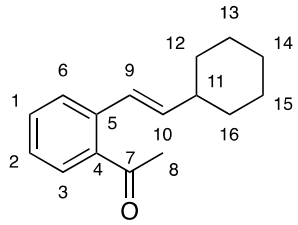
^{1}H NMR (500 MHz, Chloroform-*d*) δ 8.03 (t, *J* = 1.82 Hz, 1H, H^4), 7.85 (dt, *J* = 7.70, 1.40 Hz, 1H, H^2), 7.51 (dt, *J* = 7.68, 1.54 Hz, 1H, H^6), 7.35 (t, *J* = 7.72 Hz, 1H, H^1), 6.37 (dd, *J* = 16.03, 1.13 Hz, 1H, H^9), 6.26 (dd, *J* = 15.98, 6.86 Hz, 1H, H^{10}), 3.9 (s, 3H, H^8) 2.20 – 2.09 (m, 1H, H^{11}), 1.85 – 1.74 (m, 4H, H^{12}, H^{13}, H^{15} and H^{16}), 1.72 – 1.65 (m, 1H, H^{14}), 1.38 – 1.26 (m, 2H, H^{13} and H^{15}), 1.26 – 1.14 (m, 3H, H^{12}, H^{14} and H^{16}).

^{13}C NMR (126 MHz, Chloroform-*d*) δ 167.3 (C^7), 138.5 (C^5), 138.3 (C^{10}), 130.5 (C^6), 130.4 (C^3), 128.6 (C^1), 127.8 (C^2), 127.1 (C^4), 126.4 (C^9), 52.2 (C^8), 41.3 (C^{11}), 33.0 (C^{12} and C^{16}), 26.2 (C^{14}), 26.1 (C^{13} and C^{15}).

IR (film): 2922, 2850, 1720, 1440, 1286, 1265, 1253, 1199, 1105, 964, 748 cm^{-1}.

HRMS (MALDI): *m/z* calculated for [M + Na]$^+$ ($C_{16}H_{20}NaO_2$)$^+$: 267.1356; found = 267.1355.

(*E*)-1-(2-(2-Cyclohexylvinyl)phenyl)ethan-1-one, **3.126**



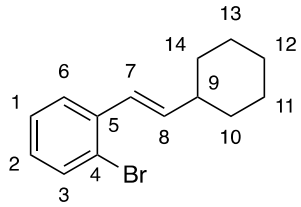
Prepared according to General Procedure 1 using 1,3-dioxoisoindolin-2-yl cyclohexanecarboxylate **3.12** (54.7 mg, 200 μmol, 1.0 equiv.), mixture of (*E*) and (*Z*)-(2-acetylstyryl)boronic acid **3.66** (76.0 mg, 400 μmol, 2.0 equiv.), tris(2,2'-bipyridine)ruthenium hexafluorophosphate (1.7 mg, 2.00 μmol, 1 mol%), and *N*,*N*-dimethylaniline (2.5 μL, 20.0 μmol, 10 mol%) in DMSO-d_6 (1 mL, 0.2 M). The crude residue was purified by flash chromatography (silica gel) from pure hexane to a mixture of 2% of diethyl ether in hexane affording 15.9 mg of a colourless oil as the desired product (35%, *E:Z* > 20:1).

^{1}H NMR (500 MHz, Chloroform-*d*) δ 7.56 (dd, *J* = 7.75, 1.20 Hz, 1H, H^3), 7.53 – 7.48 (m, 1H, H^6), 7.40 (td, *J* = 7.80, 1.39 Hz, 1H, H^1), 7.26 (td, *J* = 7.53, 1.28 Hz, 1H, H^2), 6.81 (d, *J* = 15.93 Hz, 1H, H^9), 6.05 (dd, *J* = 15.85, 6.89 Hz, 1H, H^{10}), 2.56 (s, 3H, H^8), 2.22 – 2.11 (m, 1H, H^{11}), 1.86 – 1.79 (m, 2H, H^{12} and H^{16}), 1.80 – 1.72 (m, 2H, H^{13} and H^{15}), 1.72 – 1.64 (m, 1H, H^{14}), 1.37 – 1.25 (m, 2H, H^{13} and H^{15}), 1.25 – 1.13 (m, 3H, H^{12}, H^{14} and H^{16}).

^{13}C NMR (126 MHz, Chloroform-*d*) δ 203.0 (C^7), 140.2 (C^{10}), 137.9 (C^5), 137.6 (C^4), 131.4 (C^1), 128.6 (C^3), 127.6 (C^6), 126.6 (C^2), 126.1 (C^9), 41.4 (C^{11}), 32.9 (C^{12} and C^{16}), 30.3 (C^8), 26.3 (C^{14}), 26.1 (C^{13} and C^{15}).

Data are consistent with the literature.[332]

(*E*)-1-Bromo-2-(2-cyclohexylvinyl)benzene, **3.127**



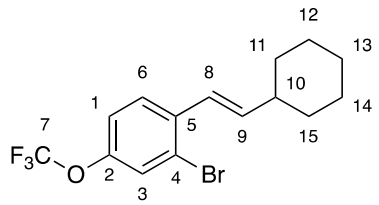
Prepared according to General Procedure 1 using 1,3-dioxoisoindolin-2-yl cyclohexanecarboxylate **3.12** (54.7 mg, 200 μmol, 1.0 equiv.), (*E*)-(2-bromostyryl)boronic acid **3.67** (90.7 mg, 400 μmol, 2.0 equiv.), tris(2,2'-bipyridine)ruthenium hexafluorophosphate (1.7 mg, 2.00 μmol, 1 mol%), and *N*,*N*-dimethylaniline (2.5 μL, 20.0 μmol, 10 mol%) in DMSO-d_6 (1 mL, 0.2 M). The crude residue was purified by flash chromatography (silica gel) with pure hexane affording 45.3 mg of a colourless oil as the desired product (86%, *E:Z* = 20:1.4).

^{1}H NMR (400 MHz, Chloroform-*d*) δ 7.55 – 7.47 (m, 2H, H^3 and H^6), 7.27 – 7.21 (m, 1H, H^1), 7.05 (td, *J* = 7.84, 1.70 Hz, 1H, H^2), 6.68 (d, *J* = 15.82 Hz, 1H, H^7), 6.12 (dd, *J* = 15.85, 6.95 Hz, 1H, H^8), 2.26 – 2.14 (m, 1H, H^9), 1.89 – 1.74 (m, 4H, H^{10}, H^{11}, H^{13} and H^{14}), 1.74 – 1.65 (m, 1H, H^{12}), 1.41 – 1.28 (m, 2H, H^{11} and H^{13}), 1.28 – 1.13 (m, 3H, H^{10}, H^{12} and H^{14}).

^{13}C NMR (101 MHz, Chloroform-*d*) δ 140.0 (C^8), 137.9 (C^5), 132.9 (C^3), 128.2 (C^2), 127.5 (C^1), 126.9 (C^6), 126.4 (C^7), 123.5 (C^4), 41.4 (C^9), 33.0 (C^{10} and C^{14}), 26.3 (C^{12}), 26.1 (C^{11} and C^{13}).

Data are consistent with the literature.[330]

(*E*)-2-Bromo-1-(2-cyclohexylvinyl)-4-(trifluoromethoxy)benzene, **3.128**



Prepared according to General Procedure 1 using 1,3-dioxoisoindolin-2-yl cyclohexanecarboxylate **3.12** (54.7 mg, 200 μmol, 1.0 equiv.), (*E*)-(2-bromo-4-(trifluoromethoxy)styryl)boronic acid **3.72** (124 mg, 400 μmol, 2.0 equiv.),

tris(2,2'-bipyridine)ruthenium hexafluorophosphate (1.7 mg, 2.00 μmol, 1 mol%), and *N,N*-dimethylaniline (2.5 μL, 20.0 μmol, 10 mol%) in DMSO-d_6 (1 mL, 0.2 M). The crude residue was purified by flash chromatography (silica gel) with pure hexane affording 68.3 mg of a colourless oil as the desired product (98%, *E:Z* > 20:1).

^{1}H NMR (400 MHz, Chloroform-*d*) δ 7.50 (d, *J* = 8.66 Hz, 1H, H^6), 7.42 (dd, *J* = 2.43, 1.09 Hz, 1H, H^3), 7.12 (ddt, *J* = 8.73, 2.60, 0.93 Hz, 1H, H^1), 6.63 (dd, *J* = 15.84, 1.37 Hz, 1H, H^8), 6.11 (dd, *J* = 15.85, 6.94 Hz, 1H, H^9), 2.27 – 2.12 (m, 1H, H^{10}), 1.89 – 1.75 (m, 4H, H^{11}, H^{12}, H^{14} and H^{15}), 1.75 – 1.64 (m, 1H, H^{13}), 1.41 – 1.28 (m, 2H, H^{12} and H^{14}), 1.27 – 1.14 (m, 3H, H^{11}, H^{13} and H^{15}).

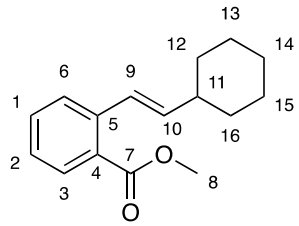
^{13}C NMR (176 MHz, Chloroform-*d*) δ 147.9 (C^2), 141.0 (C^9), 137.0 (C^5), 127.5 (C^6), 125.4 (C^3), 125.3 (C^8), 123.2 (C^4), 120.5 (q, $^1J_{CF}$ = 257.8 Hz, C^7), 120.2 (C^1), 41.4 (C^{10}), 32.9 (C^{11} and C^{15}), 26.2 (C^{13}), 26.1 (C^{12} and C^{14}).

^{19}F {^{1}H} NMR (377 MHz, Chloroform-*d*) δ –58.03.

IR (film): 2924, 2852, 1597, 1448, 1481, 1247, 1213, 1161, 964 cm^{-1}.

HRMS (MALDI): *m/z* calculated for $[M + H]^+$ $(C_{15}H_{17}{}^{79}BrF_3O)^+$: 349.0409; found = 349.0411.

Methyl (*E*)-2-(2-cyclohexylvinyl)benzoate, **3.129**



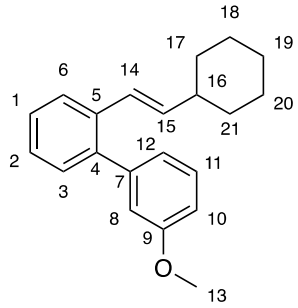
Prepared according to General Procedure 1 using 1,3-dioxoisoindolin-2-yl cyclohexanecarboxylate **3.12** (27.3 mg, 100 μmol, 1.0 equiv.), (*E*)-(2-(methoxycarbonyl)styryl)boronic acid **3.74** (41.2 mg, 200 μmol, 2.0 equiv.), tris(2,2'-bipyridine)ruthenium hexafluorophosphate (0.9 mg, 1.00 μmol, 1 mol%), and *N,N*-dimethylaniline (1.5 μL, 10.0 μmol, 10 mol%) in DMSO-d_6 (1 mL, 0.1 M). The crude residue was purified by flash chromatography (silica gel) with hexane affording 14.8 mg of a colourless oil as the desired product (61%, *E:Z* > 20:1).

^{1}H NMR (500 MHz, Chloroform-*d*) δ 7.84 (dd, *J* = 7.83, 1.48 Hz, 1H, H^{3}), 7.54 (d, *J* = 7.85 Hz, 1H, H^{6}), 7.43 (td, *J* = 7.83, 1.44 Hz, 1H, H^{1}), 7.24 (td, *J* = 6.48, 1.09 Hz, 1H, H^{2}), 7.11 (d, *J* = 15.82 Hz, 1H, H^{9}), 6.09 (dd, *J* = 15.88, 6.85 Hz, 1H, H^{10}), 3.90 (s, 3H, H^{8}), 2.24 – 2.12 (m, 1H, H^{11}), 1.91 – 1.80 (m, 2H, H^{12} and H^{16}), 1.81 – 1.73 (m, 2H, H^{13} and H^{15}), 1.71 – 1.64 (m, 1H, H^{14}), 1.38 – 1.26 (m, 2H, H^{13} and H^{15}), 1.28 – 1.14 (m, 3H, H^{12}, H^{14} and H^{16}).

^{13}C NMR (126 MHz, Chloroform-*d*) δ 168.3 (C^{7}), 140.0 (C^{5}), 139.8 (C^{10}), 132.0 (C^{1}), 130.4 (C^{3}), 128.3 (C^{4}), 127.2 (C^{6}), 126.5 (C^{9}), 126.2 (C^{2}), 52.1 (C^{8}), 41.4 (C^{11}), 33.0 (C^{12} and C^{16}), 26.3 (C^{13} and C^{15}), 26.2 (C^{14}).

Data are consistent with the literature.[333]

(*E*)-2-(2-Cyclohexylvinyl)-3'-methoxy-1,1'-biphenyl, **3.130**



Prepared according to General Procedure 1 using 1,3-dioxoisoindolin-2-yl cyclohexanecarboxylate **3.12** (27.3 mg, 100 μmol, 1.0 equiv.), (*E*)-(2-(3'-Methoxy-[1,1'-biphenyl]-2-yl)vinyl)boronic acid **3.75** (50.8 mg, 200 μmol, 2.0 equiv.), tris(2,2'-bipyridine)ruthenium hexafluorophosphate (0.9 mg, 1.00 μmol, 1 mol%), and *N*,*N*-dimethylaniline (1.5 μL, 10.0 μmol, 10 mol%) in DMSO-d_6 (1 mL, 0.1 M). The crude residue was purified by flash chromatography (silica gel) from pure hexane to a mixture of 3% of diethyl ether in hexane affording 19.2 mg of a white solid as the desired product (66%, *E:Z* > 20:1).

^{1}H NMR (400 MHz, Chloroform-*d*) δ 7.57 (app. d, *J* = 7.52 Hz, 1H, H^{6}), 7.37 – 7.24 (m, 4H, H^{1}, H^{2}, H^{3} and H^{11}), 6.99 – 6.88 (m, 3H, H^{8}, H^{10} and H^{12}), 6.36 (d, *J* = 15.96 Hz, 1H, H^{14}), 6.09 (dd, *J* = 15.92, 7.02 Hz, 1H, H^{15}), 3.84 (s, 3H, H^{13}), 2.12 – 1.99 (m,

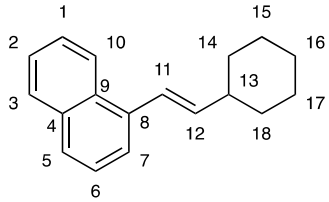
1H, H^6), 1.78 – 1.68 (m, 4H, H^{17}, H^{18}, H^{20} and H^{21}), 1.69 – 1.58 (m, 1H, H^{19}), 1.34 – 1.20 (m, 2H, H^{18} and H^{20}), 1.19 – 1.07 (m, 3H, H^{17}, H^{19} and H^{21}).

^{13}C NMR (101 MHz, Chloroform-*d*) δ 159.3 (C^9), 142.8 (C^7), 140.3 (C^4), 137.9 (C^{15}), 136.2 (C^5), 130.1 (C^2 or C^3), 129.0 (C^{11}), 127.6 (C^1), 126.8 (C^2 or C^3), 126.4 (C^{14}), 125.9 (C^6), 122.5 (C^{12}), 115.3 (C^8), 112.9 (C^{10}), 55.4 (C^{13}), 41.4 (C^{16}), 33.1(C^{17} and C^{21}), 26.3 (C^{19}), 26.1 (C^{18} and C^{20}).

IR (neat liquid): 2922, 1597,1577, 1446, 1423, 1317, 1290, 1276, 1219, 1213, 1176, 1045, 1022, 966 cm^{-1}.

HRMS (ESI): *m/z* calculated for $[M + H]^+$ $(C_{21}H_{25}O)^+$: = 293.1899; found = 293.1898.

(*E*)-1-(2-Cyclohexylvinyl)naphthalene, **3.131**



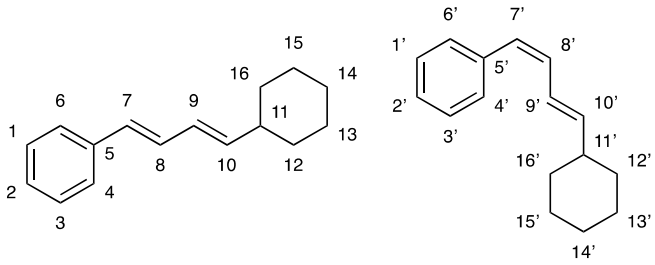
Prepared according to General Procedure 1 using 1,3-dioxoisoindolin-2-yl cyclohexanecarboxylate **3.12** (54.7 mg, 200 μmol, 1.0 equiv.), (*E*)-(2-(naphthalen-1-yl)vinyl)boronic acid **3.68** (79.2 mg, 400 μmol, 2.0 equiv.), tris(2,2'-bipyridine)ruthenium hexafluorophosphate (1.7 mg, 2.00 μmol, 1 mol%), and *N*,*N*-dimethylaniline (2.5 μL, 20.0 μmol, 10 mol%) in DMSO-d_6 (1 mL, 0.2 M). The crude residue was purified by flash chromatography (silica gel) with pure hexane affording 32.8 mg of a colourless oil as the desired product (69%, *E:Z* > 20:1).

^{1}H NMR (500 MHz, Chloroform-*d*) δ 8.19 – 8.11 (m, 1H, H^{10}), 7.84 (dd, *J* = 8.08, 1.57 Hz, 1H, H^3), 7.77 – 7.71 (m, 1H, H^5), 7.57 (dt, *J* = 7.17, 1.00 Hz, 1H, H^7), 7.54 – 7.45 (m, 2H, H^1 and H^2), 7.43 (t, *J* = 7.71 Hz, 1H, H^6), 7.09 (d, *J* = 15.65 Hz, 1H, H^{11}), 6.21 (dd, *J* = 15.69, 6.89 Hz, 1H, H^{12}), 2.33 – 2.21 (m, 1H, H^{13}), 1.96 – 1.88 (m, 2H, H^{14} and H^{18}), 1.87 – 1.78 (m, 2H, H^{15} and H^{17}), 1.77 – 1.68 (m, 1H, H^{16}), 1.44 – 1.33 (m, 2H, H^{15} and H^{17}), 1.33 – 1.22 (m, 3H, H^{14}, H^{16} and H^{18}).

^{13}C NMR (126 MHz, Chloroform-*d*) δ 140.4 (C^{12}), 136.0 (C^{8}), 133.7 (C^{4}), 131.3 (C^{9}), 128.6 (C^{3}), 127.3 (C^{5}), 125.9 (C^{1} or C^{2} or C^{6}), 125.8 (C^{1} or C^{2} or C^{6}), 125.7 (C^{1} or C^{2} or C^{6}), 124.5 (C^{11}), 124.1 (C^{10}), 123.6 (C^{7}), 41.7 (C^{13}), 33.2 (C^{14} and C^{18}), 26.4 (C^{16}), 26.2 (C^{15} and C^{17}).

Data are consistent with the literature.[334]

((1*E*,3*E*) and (1*Z*,3*E*)-4-Cyclohexylbuta-1,3-dien-1-yl)benzene, **3.132**



Prepared according to General Procedure 1 using 1,3-dioxoisoindolin-2-yl cyclohexanecarboxylate **3.12** (27.3 mg, 100 μmol, 1.0 equiv.), ((1*E*,3*E*)-4-phenylbuta-1,3-dien-1-yl)boronic acid **3.73** (34.8 mg, 200 μmol, 2.0 equiv.), tris(2,2'-bipyridine)ruthenium hexafluorophosphate (0.9 mg, 1.00 μmol, 1 mol%), and *N*,*N*-dimethylaniline (1.5 μL, 10.0 μmol, 10 mol%) in DMSO-d_6 (1 mL, 0.1 M). The reaction was not complete and 46% of the NHPI was remaining. The crude residue was purified by flash chromatography (silica gel) with hexane affording 6.1 mg of a colourless oil as a mixture of desired product (27%, ratio EE/ZE/EZ/ZZ: 1:1:0.1:0.1).

Data for (1*E*,3*E*) and (1*Z*,3*E*) as a 1:1 mixture:

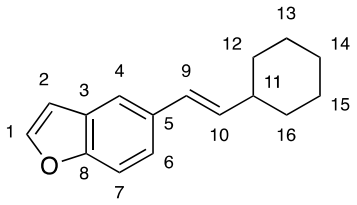
^{1}H NMR (500 MHz, Chloroform-*d*) δ 7.39 – 7.35 (m, 2H, H^{arom}), 7.35 – 7.32 (m, 4H, H^{arom}), 7.31 – 7.27 (m, 2H, H^{arom}), 7.25 – 7.21 (m, 1H, H^{2} or $H^{2'}$), 7.21 – 7.17 (m, 1H, H^{2} or $H^{2'}$), 6.75 (dd, *J* = 15.65, 10.40 Hz, 1H, H^{8}), 6.58 (ddt, *J* = 15.22, 11.07, 1.13 Hz, 1H, $H^{9'}$), 6.45 (d, *J* = 15.59 Hz, 1H, H^{7}), 6.31 (d, *J* = 11.55 Hz, 1H, $H^{7'}$), 6.20 (t, *J* = 11.37 Hz, 1H, $H^{8'}$), 6.21 – 6.14 (m, 1H, H^{9}), 5.82 (dd, *J* = 15.21, 7.06 Hz, 1H, $H^{10'}$), 5.79 (dd, *J* = 15.31, 6.98 Hz, 1H, H^{10}), 2.11 – 2.01 (m, 2H, H^{11} and $H^{11'}$), 1.80 – 1.69 (m, 8H, H^{12}, $H^{12'}$, H^{13}, $H^{13'}$, H^{15}, $H^{15'}$, H^{16} and $H^{16'}$), 1.69 – 1.63 (m, 2H, H^{14}

and $H^{14'}$), 1.37 – 1.22 (m, 4H, H^{13}, $H^{13'}$, H^{15} and $H^{15'}$), 1.22 – 1.08 (m, 6H, H^{12}, $H^{12'}$, H^{13}, H^{14}, $H^{14'}$, H^{16} and $H^{16'}$).

^{13}C NMR (126 MHz, Chloroform-*d*) δ 144.0. ($C^{10'}$), 141.9. (C^{10}), 138.0 (C^{5} or $C^{5'}$), 137.9 (C^{5} or $C^{5'}$), 131.0 ($C^{8'}$), 130.2 (C^{7}), 129.9 (C^{8}), 129.0 (C^{arom}), 128.7 (C^{arom}), 128.3 (C^{arom}), 128.1 (C^{9}), 127.8 ($C^{7'}$), 127.2 (C^{2} or $C^{2'}$), 126.7 (C^{2} or $C^{2'}$), 126.2 (C^{arom}), 124.1 ($C^{9'}$), 41.2 (C^{11} or $C^{11'}$), 41.1 (C^{11} or $C^{11'}$), 33.0 (C^{12} and C^{16} or $C^{12'}$ and $C^{16'}$), 32.9 (C^{12} and C^{16} or $C^{12'}$ and $C^{16'}$), 26.3 (C^{14} or $C^{14'}$), 26.2 (C^{14} or $C^{14'}$), 26.1 (C^{13} and C^{15} or $C^{13'}$ and $C^{15'}$), 26.1 (C^{13} and C^{15} or $C^{13'}$ and $C^{15'}$).

Data (for 1*E*,3*E*) are consistent with the literature.[335]

(*E*)-5-(2-Cyclohexylvinyl)benzofuran, **3.133**



Prepared according to General Procedure 1 using 1,3-dioxoisoindolin-2-yl cyclohexanecarboxylate **3.12** (54.7 mg, 200 μmol, 1.0 equiv.), (*E*)-(2-(benzofuran-5-yl)vinyl)boronic acid **3.71** (75.2 mg, 400 μmol, 2.0 equiv.), tris(2,2'-bipyridine)ruthenium hexafluorophosphate (1.7 mg, 2.00 μmol, 1 mol%), and *N*,*N*-dimethylaniline (2.5 μL, 20.0 μmol, 10 mol%) in DMSO-d_6 (1 mL, 0.2 M). The crude residue was purified by flash chromatography (silica gel) from pure hexane to a mixture of 1% of diethyl ether in hexane affording 39.4 mg of a pale-yellow oil as the desired product (87%, *E:Z* > 20:1).

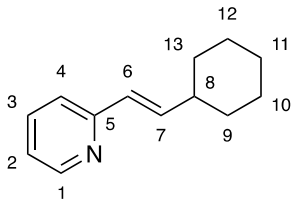
^{1}H NMR (400 MHz, Chloroform-*d*) δ 7.59 (d, *J* = 2.16 Hz, 1H, H^{1}), 7.56 (d, *J* = 1.77 Hz, 1H, H^{4}), 7.43 (dt, *J* = 8.56, 0.83 Hz, 1H, H^{7}), 7.34 (dd, *J* = 8.59, 1.81 Hz, 1H, H^{6}), 6.73 (dd, *J* = 2.21, 0.96 Hz, 1H, H^{2}), 6.45 (dd, *J* = 15.96, 1.27 Hz, 1H, H^{9}), 6.16 (dd, *J* = 15.91, 6.99 Hz, 1H, H^{10}), 2.21 – 2.11 (m, 1H, H^{11}), 1.90 – 1.75 (m, 4H, H^{12}, H^{13}, H^{15} and H^{16}), 1.75 – 1.67 (m, 1H, H^{14}), 1.42 – 1.30 (m, 2H, H^{13} and H^{15}), 1.29 – 1.15 (m, 3H, H^{12}, H^{14} and H^{16}).

^{13}C NMR (101 MHz, Chloroform-*d*) δ 154.4 (C^{8}), 145.4 (C^{1}), 135.9 (C^{10}), 133.3 (C^{5}), 127.8 (C^{3}), 127.4 (C^{9}), 122.7 (C^{6}), 118.5 (C^{4}), 111.3 (C^{7}), 106.7 (C^{2}), 41.3 (C^{11}), 33.2 (C^{12} and C^{16}), 26.3 (C^{14}), 26.2 (C^{13} and C^{15}).

IR (film): 2918, 2845, 1465, 1448, 1440, 1259, 1192, 1122, 1105, 1028, 962, 857 cm^{-1}.

HRMS (EI): *m/z* calculated for $[M]^{+}$ $(C_{16}H_{18}O)^{+}$: 226.1352; found = 226.1350.

(*E*)-2-(2-Cyclohexylvinyl)pyridine, **3.134**



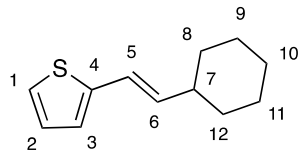
Prepared according to General Procedure 1 using 1,3-dioxoisoindolin-2-yl cyclohexanecarboxylate **3.12** (54.7 mg, 200 μmol, 1.0 equiv.), (*E*)-(2-(pyridin-2-yl)vinyl)boronic acid **3.69** (59.6 mg, 400 μmol, 2.0 equiv.), tris(2,2'-bipyridine)ruthenium hexafluorophosphate (1.7 mg, 2.00 μmol, 1 mol%), and *N*,*N*-dimethylaniline (2.5 μL, 20.0 μmol, 10 mol%) in DMSO-d_6 (1 mL, 0.2 M). The crude residue was purified by flash chromatography (silica gel) from pure hexane to a mixture of 10% of diethyl ether in hexane affording 18.6 mg of a colourless oil as the desired product (51%, *E:Z* > 20:1).

^{1}H NMR (500 MHz, Chloroform-*d*) δ 8.54 – 8.48 (m, 1H, H^{1}), 7.58 (td, *J* = 7.69, 1.88 Hz, 1H, H^{3}), 7.23 (dd, *J* = 7.88, 1.35 Hz, 1H, H^{4}), 7.07 (ddd, *J* = 7.55, 4.88, 1.17 Hz, 1H, H^{2}), 6.69 (dd, *J* = 15.84, 6.95 Hz, 1H, H^{7}), 6.43 (dd, *J* = 15.82, 1.32 Hz, 1H, H^{6}), 2.22 – 2.14 (m, 1H, H^{8}), 1.88 – 1.80 (m, 2H, H^{9} and H^{13}), 1.80 – 1.74 (m, 1H, H^{11}), 1.71 – 1.63 (m, 2H, H^{10} and H^{12}), 1.37 – 1.27 (m, 2H, H^{10} and H^{12}), 1.27 – 1.15 (m, 3H, H^{9}, H^{11} and H^{13}).

^{13}C NMR (126 MHz, Chloroform-*d*) δ 156.4 (C^{5}), 149.5 (C^{1}), 141.6 (C^{7}), 136.5 (C^{3}), 127.5 (C^{6}), 121.6 (C^{2}), 121.2 (C^{4}), 41.1 (C^{8}), 32.7 (C^{9} and H^{13}), 26.2 (C^{11}), 26.1 (C^{10} and C^{12}).

Data are consistent with the literature.[336]

(*E*)-2-(2-Cyclohexylvinyl)thiophene, **3.135**



Prepared according to General Procedure 1 using 1,3-dioxoisoindolin-2-yl cyclohexanecarboxylate **3.12** (54.7 mg, 200 μmol, 1.0 equiv.), (*E*)-(2-(thiophen-2-yl)vinyl)boronic acid **3.70** (61.6 mg, 400 μmol, 2.0 equiv.), tris(2,2'-bipyridine)ruthenium hexafluorophosphate (1.7 mg, 2.00 μmol, 1 mol%), and *N*,*N*-dimethylaniline (2.5 μL, 20.0 μmol, 10 mol%) in DMSO-d_6 (1 mL, 0.2 M). The crude residue was purified by flash chromatography (silica gel) from pure hexane to a mixture of 4% of diethyl ether in hexane affording 30.5 mg of a colourless oil as the desired product (79%, *E:Z* = 20:3).

(*E*)-2-(2-Cyclohexylvinyl)thiophene,

^{1}H NMR (500 MHz, Chloroform-*d*) δ 7.08 (d, *J* = 5.06 Hz, 1H, H^1), 6.93 (dd, *J* = 5.12, 3.47 Hz, 1H, H^2), 6.87 (d, *J* = 3.49 Hz, 1H, H^3), 6.47 (d, *J* = 15.82 Hz, 1H, H^5), 6.04 (dd, *J* = 15.81, 6.91 Hz, 1H, H^6), 2.15 – 2.06 (m, 1H, H^7), 1.85 – 1.73 (m, 4H, H^8, H^9, H^{11} and H^{12}), 1.72 – 1.65 (m, 1H, H^{10}), 1.40 – 1.26 (m, 2H, H^9 and H^{11}), 1.24 – 1.11 (m, 3H, H^8, H^{10} and H^{12}).

^{13}C NMR (126 MHz, Chloroform-*d*) δ 143.6 (C^4), 136.9 (C^6), 127.3 (C^2), 124.3 (C^3), 123.1 (C^1), 120.7 (C^5), 41.1 (C^7), 32.9 (C^8 and C^{12}), 26.3 (C^{10}), 26.1 (C^9 and C^{11}).

Data are consistent with the literature.[331]

(*Z*)-2-(2-Cyclohexylvinyl)thiophene,

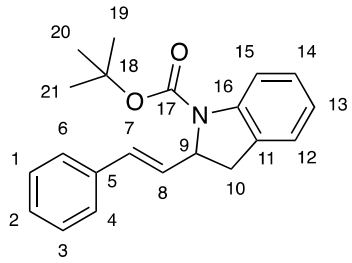
^{1}H NMR (500 MHz, Chloroform-*d*) not reported since mostly overlapped with the *E* product.

^{13}C NMR (126 MHz, Chloroform-*d*) δ 140.6 ($C^{4'}$), 137.1 ($C^{6'}$), 127.2 ($C^{2'}$), 126.8 ($C^{3'}$), 124.9 ($C^{1'}$), 119.9 ($C^{5'}$), 38.1 ($C^{7'}$), 32.9 ($C^{8'}$ and $C^{12'}$), 26.1 ($C^{10'}$), 26.0 ($C^{9'}$ and $C^{11'}$).

tert-Butyl (*E*)-2-styrylindoline-1-carboxylate, **3.136** and *tert*-butyl 1*H*-indole-1-carboxylate, **3.137**

Prepared according to General Procedure 1 using 1-(*tert*-butyl) 2-(1,3-dioxoisoindolin-2-yl) indoline-1,2-dicarboxylate **3.51** (81.7 mg, 200 μmol, 1.0 equiv.), (*E*)-2-phenylvinylboronic acid **3.1a** (59.2 mg, 400 umol, 2.0 equiv.), tris(2,2'-bipyridine)ruthenium hexafluorophosphate (1.7 mg, 2.00 μmol, 1 mol%), and *N*,*N*-dimethylaniline (2.5 μL, 20.0 μmol, 10 mol%) in DMSO-d_6 (1 mL, 0.2 M). The crude residue was purified by flash chromatography (silica gel) from pure hexane to a mixture of 2% of diethyl ether in hexane affording 5.9 mg of **3.136** as a colourless oil (9%, *E:Z* > 20:1) and 22.3 mg of **3.137** as a colourless oil (51%).

tert-Butyl (*E*)-2-styrylindoline-1-carboxylate, **3.136**

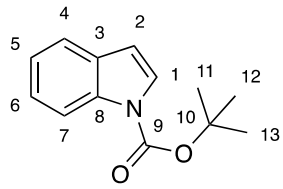


^{1}H NMR (400 MHz, Chloroform-*d*) δ 7.78 (broad s, 1H, H^{15}), 7.35 – 7.32 (m, 2H, H^4 and H^6), 7.31 – 7.26 (m, 2H, H^1 and H^3), 7.24 – 7.17 (m, 2H, H^2 and H^{14}), 7.17 – 7.12 (m, 1H, H^{12}), 6.96 (td, *J* = 7.45, 1.10 Hz, 1H, H^{13}), 6.52 (d, *J* = 15.74 Hz, 1H, H^7), 6.18 (dd, *J* = 15.76, 7.70 Hz, 1H, H^8), 5.08 – 4.96 (m, 1H, H^9), 3.49 (dd, *J* = 16.20, 10.00 Hz, 1H, H^{10}), 2.88 (dd, *J* = 16.17, 2.79 Hz, 1H, H^{10}), 1.52 (s, 9H, H^{19}, H^{20} and H^{21}).

^{13}C NMR (126 MHz, Chloroform-*d*) δ 152.5 (C^{17}), 142.2 (C^{16}), 136.8 (C^5), 130.6 (C^7), 129.3 (C^8), 128.7 (C^1 and C^3), 127.7 (C^2), 127.7 (C^{14}), 126.6 (C^4 and C^6), 125.0 (C^{12}), 122.6 (C^{13}), 115.3 (C^{15}), 81.1 (C^{18}), 61.3 (C^9), 35.1 (C^{10}), 28.6 (C^{19}, C^{20} and C^{21}). C^{11} is missing, it could not be observed (signal too weak).

Data are consistent with the literature.[337]

tert-Butyl 1*H*-indole-1-carboxylate, **3.137**

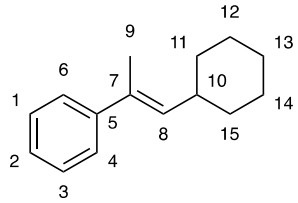


^{1}H NMR (500 MHz, Chloroform-*d*) δ 8.20 – 8.12 (m, 1H, H^{7}), 7.61 (d, *J* = 3.70 Hz, 1H, H^{1}), 7.57 (dt, *J* = 7.66, 1.08 Hz, 1H, H^{4}), 7.34 – 7.30 (m, 1H, H^{6}), 7.26 – 7.21 (m, 1H, H^{5}), 6.58 (d, *J* = 3.74, 1H, H^{2}), 1.68 (s, 9H, H^{11}, H^{12} and H^{13}).

^{13}C NMR (126 MHz, Chloroform-*d*) δ 149.9 (C^{9}), 135.3 (C^{8}), 130.7 (C^{3}), 126.0 (C^{1}), 124.3 (C^{6}), 122.7 (C^{5}), 121.1 (C^{4}), 115.3 (C^{7}), 107.4 (C^{2}), 83.8 (C^{10}), 28.3 (C^{11}, C^{12} and C^{13}).

Data are consistent with the literature.[338]

(*E*)-(1-Cyclohexylprop-1-en-2-yl)benzene, **3.150**



Prepared according to General Procedure 1 using 1,3-dioxoisoindolin-2-yl cyclohexanecarboxylate **3.12** (27.3 mg, 100 μmol, 1.0 equiv.), (*E*)-(2-phenylprop-1-en-1-yl)boronic acid **3.76** (32.4 mg, 200 μmol, 2.0 equiv.), tris(2,2'-bipyridine)ruthenium hexafluorophosphate (0.9 mg, 1.00 μmol, 1 mol%), and *N*,*N*-dimethylaniline (1.5 μL, 10.0 μmol, 10 mol%) in DMSO-d_6 (1 mL, 0.1 M). The crude residue was purified by flash chromatography (silica gel) with hexane affording 15.8 mg of a colourless oil as the desired product (67%, *E:Z* > 20:1). It contained 15% of (*E*)-(2-cyclohexylvinyl)benzene **3.13** from the reaction between (*E*)-styrylboronic acid **3.1a** contained in the starting material. They could not be separated by flash chromatography.

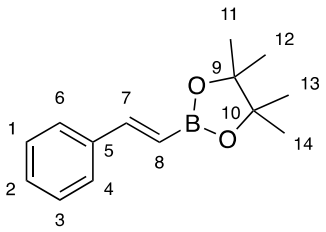
^{1}H NMR (500 MHz, Chloroform-*d*) δ 7.43 – 7.36 (m, 2H, H^{4} and H^{6}), 7.33 – 7.27 (m, 2H, H^{1} and H^{3}), 7.24 – 7.18 (m, 1H, H^{2}), 5.63 (dq, *J* = 9.01, 1.43 Hz, 1H, H^{8}), 2.41 –

2.30 (m, 1H, H^{10}), 2.05 (d, *J* = 1.37 Hz, 3H, H^{9}), 1.81 – 1.64 (m, 5H, H^{11}, H^{12}, H^{13}, H^{14} and H^{15}), 1.40 – 1.28 (m, 2H, H^{12} and H^{14}), 1.24 – 1.09 (m, 3H, H^{11}, H^{13} and H^{15}).

^{13}C NMR (126 MHz, Chloroform-*d*) δ 144.2 (C^{5}), 134.7 (C^{8}), 132.9 (C^{7}), 128.2 (C^{1} and C^{3}), 126.6 (C^{2}), 125.8 (C^{4} and C^{6}), 37.9 (C^{10}), 33.2 (C^{11} and C^{15}), 26.3 (C^{13}), 26.2 (C^{12} and C^{14}), 16.0 (C^{9}).

Data are consistent with the literature.[339]

(*E*)-4,4,5,5-Tetramethyl-2-styryl-1,3,2-dioxaborolane, **3.1b**



Prepared according to General Procedure 5 using phenylacetylene (980 μL, 10.0 mmol, 1.0 equiv.), copper(I) chloride (49 mg, 500 μmol, 5 mol%), potassium *tert*-butoxide (112 mg, 1.00 mmol, 10 mol%), bis(2-diphenylphosphinophenyl)ether (DPEPhos) (269 mg, 500 μmol, 5 mol%), bis(pinacolato)diboron (2.79 g, 11.0 mmol, 1.1 equiv.), and MeOH (810 μL, 20.0 mmol, 2.0 equiv.) in THF (40 mL, 0.25 M). The crude residue was purified by flash chromatography (silica gel) from pure hexane to a mixture of 2% of diethyl ether in hexane affording 2.10 g of a pale-yellow oil consistent with the desired product (91%).

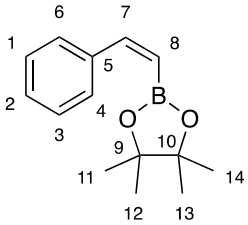
^{1}H NMR (500 MHz, Chloroform-*d*) δ 7.51 – 7.48 (m, 2H, H^{4} and H^{6}), 7.41 (d, *J* = 18.45 Hz, 1H, H^{7}), 7.36 – 7.32 (m, 2H, H^{1} and H^{3}), 7.31 – 7.27 (m, 1H, H^{2}), 6.18 (d, *J* = 18.42 Hz, 1H, H^{8}), 1.32 (s, 12H, H^{11}, H^{12}, H^{13} and H^{14}).

^{11}B NMR (96 MHz, Chloroform-*d*) δ 30.21.

^{13}C NMR (126 MHz, Chloroform-*d*) δ 149.6 (C^{7}), 137.6 (C^{5}), 129.0 (C^{2}), 128.7 (C^{1} and C^{3}), 127.2 (C^{4} and C^{6}), 116.5 (broad, C^{8}), 83.5 (C^{9} and C^{10}), 24.9 (C^{11}, C^{12}, C^{13} and C^{14}).

Data are consistent with the literature.[340]

(*Z*)-4,4,5,5-Tetramethyl-2-styryl-1,3,2-dioxaborolane, **3.(*Z*)-1b**



Prepared according the literature.[228] In an oven-dried microwave vial, loaded with a Teflon-coated stir bar, (*E*)-4,4,5,5-tetramethyl-2-styryl-1,3,2-dioxaborolane **3.1b** (1.00 g, 4.35 mmol, 1.0 equiv.) and tris(2-phenylpyridine)iridium (28.5 mg, 43.5 μmol, 1 mol%) were weighed out. The vial was sealed, purged with vacuum-N_2 cycles (3 times), and backfilled with N_2. Degassed dry MeCN (21 mL, 0.2 M) was then added. The reaction mixture was stirred overnight under blue LEDs under N_2. The reaction mixture was worked-up: it was partitioned between diethyl ether (10 mL) and brine (10 mL). Organics were extracted with diethyl ether (2 × 15 mL). Organics were combined, washed with brine (20 mL), dried over sodium sulfate, filtered, and concentrated *in vacuo*. The crude residue was purified by flash chromatography (silica gel) from hexane to a mixture of 4% of diethyl ether in hexane affording 920 mg of a pale-yellow oil consistent with a mixture of *E* and *Z* of the desired product (92%, 0.74:0.26 *Z:E*).

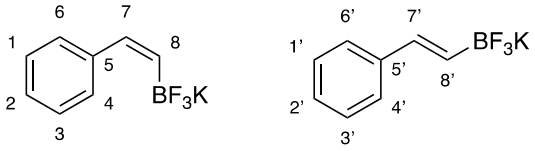
^{1}H NMR (500 MHz, Chloroform-*d*) δ 7.56 – 7.52 (m, 2H, H^4 and H^6), 7.36 – 7.25 (m, 3H, H^1, H^2 and H^3), 7.22 (d, *J* = 15.01 Hz, 1H, H^7), 5.60 (d, *J* = 14.85 Hz, 1H, H^8), 1.30 (s, 12H, H^{11}, H^{12}, H^{13} and H^{14}).

^{11}B NMR (96 MHz, Chloroform-*d*) δ 30.19.

^{13}C NMR (126 MHz, Chloroform-*d*) δ 148.3 (C^7), 138.6 (C^5), 128.7 (C^4 and C^6), 128.1 (C^2), 128.1 (C^1 and C^3), 119.5 (broad, C^8), 83.6 (C^9 and C^{10}), 24 (C^{11}, C^{12}, C^{13} and C^{14}).

Data are consistent with the literature.[341]

(*E*) and (*Z*)-Trifluoro(styryl)-λ^4-borane, potassium salt, **3.(*Z*)-1c**



Prepared according to General Procedure 6 using the mixture of (*E*) and (*Z*)-4,4,5,5-tetramethyl-2-styryl-1,3,2-dioxaborolane **3.(*Z*)-1b** (770 mg, 3.35 mmol, 1.0 equiv.), potassium hydrogen fluoride (1.05 g, 13.4 mmol, 4.0 equiv.), and water (3.01 mL, 167 mmol, 50.0 equiv.) in MeOH (30 mL, 0.1 M). 262 mg of a white solid was obtained after filtration, consistent with a mixture of *E* and *Z* of the desired product (37%, 1:0.95 *Z:E*).

(*Z*)-Trifluoro(styryl)-λ^4-borane, potassium salt, **3.(*Z*)-1c**

^{1}H NMR (500 MHz, DMSO-d_6) δ 7.59 – 7.54 (m, 2H, H^4 and H^6), 7.18 (app. t, J = 7.68 Hz, 2H, H^1 and H^3), 7.08 – 7.05 (m, 1H, H^2), 6.45 (d, J = 15.42 Hz, 1H, H^7), 5.58 (dq, J = 15.17, 6.45 Hz, 1H, H^8).

^{11}B NMR (96 MHz, DMSO-d_6) δ 2.47.

^{13}C NMR (126 MHz, DMSO-d_6) δ 143.2 (broad, C^8), 140.7 (C^5), 135.0 (q, $^3J_{CF}$ = 5.4 Hz, C^7), 128.4 (q, $^5J_{CF}$ = 2.8 Hz, C^4 and C^6), 127.3 (C^1 and C^3), 125.4 (C^2).

^{19}F {^{1}H} NMR (376 MHz, DMSO-d_6) δ –137.79.

Data are consistent with the literature.[342,343]

(*E*)-Trifluoro(styryl)-λ^4-borane, potassium salt, **3.1c**

^{1}H NMR (500 MHz, DMSO-d_6) δ 7.33 – 7.29 (m, 2H, H$^{4'}$ and H$^{6'}$), 7.25 (app. t, J = 7.65 Hz, 2H, H$^{1'}$ and H$^{3'}$), 7.13 – 7.09 (m, 1H, H$^{2'}$), 6.47 (d, J = 18.17 Hz, 1H, H$^{7'}$), 6.19 (dq, J = 18.23, 3.56 Hz, 1H, H$^{8'}$).

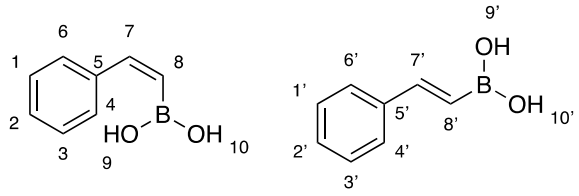
^{11}B NMR (96 MHz, DMSO-d_6) δ 2.47.

^{13}C NMR (126 MHz, DMSO-d_6) δ 140.3 (C$^{5'}$), 138.9 (broad, C$^{8'}$), 133.1 (q, $^3J_{CF}$ = 4.5 Hz, C$^{7'}$), 128.3 (C$^{1'}$ and C$^{3'}$), 125.9 (C$^{2'}$), 125.4 (C$^{4'}$ and C$^{6'}$).

^{19}F {^{1}H} NMR (376 MHz, DMSO-d_6) δ –132.84.

Data are consistent with the literature.[344]

(*E*) and (*Z*)-Styrylboronic acid, **3.(*Z*)-1a**



Prepared according the literature.[342] The mixture of (*E*) and (*Z*)-trifluoro(styryl)-λ^4-borane, potassium salt **3.(*Z*)-1c** (200 mg, 952 μmol, 1.0 equiv.) was dissolved in water (10 mL, 0.1 M). Silica gel (400 mg) was added and the reaction was left to stir for three hours at room temperature. The organics were extracted with diethyl ether (3 × 10 mL). Organic layers were combined, washed with brine (15 mL), dried over sodium sulfate, filtered, and concentrated *in vacuo* affording 126 mg of a white solid consistent with a mixture of *E* and *Z* of the desired product (89%, 1:1.1 *Z:E*).

(*Z*)-Styrylboronic acid, **3.(*Z*)-1a**

^{1}H NMR (500 MHz, Acetone-d_6) δ 7.49 – 7.46 (m, 2H, H^4 and H^6), 7.33 – 7.30 (m, 2H, H^1 and H^3), 7.26 – 7.19 (m, 1H, H^2), 6.98 (s, 2H, H^9 and H^{10}), 6.94 (d, J = 14.78 Hz, 1H, H^7), 5.69 (d, J = 14.95 Hz, 1H, H^8).

^{11}B NMR (96 MHz, Acetone-d_6) δ 29.44.

^{13}C NMR (126 MHz, Acetone-d_6) δ 142.6 (C^7), 140.1 (C^5), 129.3 (C^4 and C^6), 128.6 (C^1 and C^3), 128.2 (C^2). C^8 is not observed due to quadrupolar relaxation.

Data are consistent with the literature.[345]

(*E*)-Styrylboronic acid, **3.1a**

^{1}H NMR (500 MHz, Acetone-d_6) δ 7.52 – 7.49 (m, 2H, $H^{4'}$ and $H^{6'}$), 7.39 (d, J = 18.42 Hz, 1H, $H^{7'}$), 7.37 – 7.33 (m, 2H, $H^{1'}$ and $H^{3'}$), 7.30 – 7.27 (m, 1H, $H^{2'}$),6.90 (s, 2H, $H^{9'}$ and $H^{10'}$), 6.23 (d, J = 18.36 Hz, 1H, $H^{8'}$).

^{11}B NMR (96 MHz, Acetone-d_6) δ 29.44

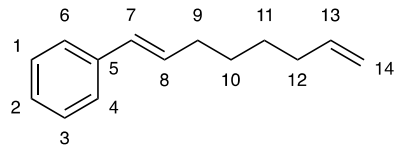
^{13}C NMR (126 MHz, Acetone-d_6) δ 147.5 ($C^{7'}$), 138.9 ($C^{5'}$), 129.5 ($C^{4'}$ and $C^{6'}$), 129.0 ($C^{2'}$), 127.6 ($C^{1'}$ and $C^{3'}$). $C^{8'}$ is not observed due to quadrupolar relaxation.

Data are consistent with the literature.[346]

(*E*)-Octa-1,7-dien-1-ylbenzene, **3.185** and (*E*)-(3-cyclopentylprop-1-en-1-yl)benzene, **3.186**

Prepared according to General Procedure 1 using 1,3-dioxoisoindolin-2-yl hept-6-enoate **3.49** (54.7 mg, 200 μmol, 1 equiv.), *trans*-2-phenylvinylboronic acid **3.1a** (59.2 mg, 400 umol, 2 equiv.), tris(2,2'-bipyridine)ruthenium hexafluorophosphate (1.7 mg, 2.00 μmol, 1 mol%), and *N,N*-dimethylaniline (2.5 μL, 20.0 μmol, 10 mol%) in DMSO-d_6 (1 mL, 0.2 M). The crude residue was purified by flash chromatography (silica gel) with pure hexane affording 7.2 mg of 3.185 as a colourless oil (19%, *E:Z* > 100:1) and 21.1 mg of **3.186** as a colourless oil (56%, *E:Z* > 100:1).

(*E*)-Octa-1,7-dien-1-ylbenzene, **3.185**



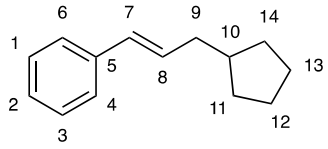
^{1}H NMR (500 MHz, Chloroform-*d*) δ 7.36 – 7.32 (m, 2H, H^4 and H^6), 7.31 – 7.26 (m, 2H, H^1 and H^3), 7.22 – 7.16 (m, 1H, H^2), 6.38 (d, *J* = 15.71 Hz, 1H, H^7), 6.22 (dt, *J* = 15.79, 6.90 Hz, 1H, H^8), 5.82 (ddt, *J* = 16.90, 10.16, 6.64 Hz, 1H, H^{13}), 5.01 (app dq, *J* = 17.10, 1.74 Hz, 1H, H^{14}), 4.95 (ddt, *J* = 10.21, 2.31, 1.25 Hz, 1H, H^{14}), 2.22 (app qd, *J* = 6.96, 1.45 Hz, 2H, H^9), 2.08 (td, *J* = 7.47, 5.87 Hz, 2H, H^{12}), 1.54 – 1.39 (m, 4H, H^{10} and H^{11}).

^{13}C NMR (126 MHz, Chloroform-*d*) δ 139.1 (C^{13}), 138.0 (C^5), 131.1 (C^8), 130.0 (C^7), 128.6 (C^1 and C^3), 126.9 (C^2), 126.0 (C^4 and C^6), 114.5 (C^{14}), 33.8 (C^9), 33.0 (C^{12}), 29.0 (C^{10}), 28.6 (C^{11}).

IR (film): 2924, 2852, 1641, 1493, 1460, 991, 692, 455 cm^{-1}.

HRMS (EI): *m/z* calculated for $[M]^+$ $(C_{14}H_{18})^+$: 186.1403; found 186.1408.

(*E*)-(3-Cyclopentylprop-1-en-1-yl)benzene, **3.186**

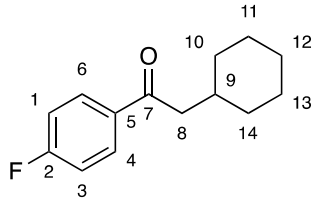


^{1}H NMR (500 MHz, Chloroform-*d*) δ 7.38 – 7.31 (m, 2H, H^{4} and H^{6}), 7.33 – 7.26 (m, 2H, H^{1} and H^{3}), 7.24 – 7.15 (m, 1H, H^{2}), 6.38 (d, *J* = 15.78 Hz, 1H, H^{7}), 6.24 (dt, *J* = 15.69, 7.07 Hz, 1H, H^{8}), 2.22 (dd, *J* = 7.15, 7.24 Hz, 2H, H^{9}), 1.95 (hept, *J* = 7.56 Hz, 1H, H^{10}), 1.83 – 1.72 (m, 2H, H^{11} and H^{14}), 1.71 – 1.59 (m, 2H, H^{12} and H^{13}), 1.59 – 1.46 (m, 2H, H^{12} and H^{13}), 1.25 – 1.14 (m, 2H, H^{11} and H^{14}).

^{13}C NMR (126 MHz, Chloroform-*d*) δ 138.1 (C^{5}), 130.7 (C^{8}), 130.2 (C^{7}), 128.6 (C^{1} and C^{3}), 126.9 (C^{2}), 126.1 (C^{4} and C^{6}), 40.1 (C^{10}), 39.6 (C^{9}), 32.5 (C^{11} and C^{14}), 25.3 (C^{12} and C^{13}).

Data are consistent with the literature.[347]

2-Cyclohexyl-1-(4-fluorophenyl)ethan-1-one, **3.191**



Prepared according to General Procedure 1 using 1,3-dioxoisoindolin-2-yl cyclohexanecarboxylate **3.12** (54.7 mg, 200 μmol, 1.0 equiv.), (*E*)-2-phenylvinylboronic acid **3.1a** (29.6 mg, 200 μmol, 1.0 equiv.), tris(2,2'-bipyridine)ruthenium hexafluorophosphate (1.7 mg, 2.00 μmol, 1 mol%), *p*-fluorostyrene **3.190** (23 μL ,200 μmol, 1.0 equiv.), and *N*,*N*-dimethylaniline (2.5 μL, 20.0 μmol, 10 mol%) in DMSO-d_6 (1 mL, 0.2 M). The crude residue was purified by flash chromatography (silica gel) with pure hexane affording 6.5 mg of a colourless oil as the desired product (16%).

^{1}H NMR (500 MHz, Chloroform-*d*) δ 8.01 – 7.94 (m, 2H, H^{4} and H^{6}), 7.16 – 7.09 (m, 2H, H^{1} and H^{3}), 2.79 (d, *J* = 6.79 Hz, 2H, H^{8}), 2.02 – 1.90 (m, 1H, H^{9}), 1.80 – 1.66 (m, 4H, H^{10}, H^{11}, H^{13} and H^{14}), 1.66 – 1.62 (m, 1H, H^{12}), 1.33 – 1.27 (m, 2H, H^{11} and H^{13}), 1.21 – 1.12 (m, 1H, H^{12}), 1.01 (qd, *J* = 12.31, 3.09 Hz, 2H, H^{10} and H^{14}).

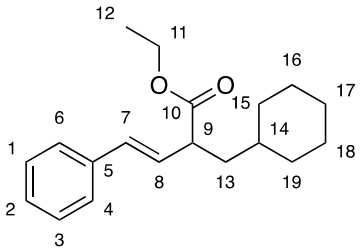
^{13}C NMR (126 MHz, Chloroform-*d*) δ 198.8 (C^{7}), 165.8 (d, $^{1}J_{CF}$ = 254.3 Hz, C^{2}), 134.0 (d, $^{4}J_{CF}$ = 2.9 Hz, C^{5}), 130.9 (d, $^{3}J_{CF}$ = 9.3 Hz, C^{4} and C^{6}), 115.7 (d, $^{2}J_{CF}$ = 21.8 Hz, C^{1} and C^{3}), 46.3 (C^{8}), 34.7 (C^{9}), 33.6 (C^{10} and C^{14}), 26.4 (C^{12}), 26.3 (C^{11} and C^{13}).

^{19}F {^{1}H} NMR (470 MHz, Chloroform-*d*) δ –105.81.

IR (film): 2922, 2850, 1680, 1597, 1506, 1448, 1409, 1354, 1286, 1224, 1193 cm^{-1}.

HRMS (ESI): *m/z* calculated for $[M - H]^{-}$ $(C_{14}H_{16}FO)^{-}$: 219.1190; found = 219.1198.

Ethyl (*E*)-2-(cyclohexylmethyl)-4-phenylbut-3-enoate, **3.194**



Prepared according to General Procedure 1 using the NHPI ester **3.12** (54.7 mg, 200 μmol, 1.0 equiv.), (*E*)-2-phenylvinylboronic acid **3.1a** (29.6 mg, 200 μmol, 1.0 equiv.), ethyl acrylate **3.192** (22 μL, 200 μmol, 1.0 equiv.), tris(2,2'-bipyridine)ruthenium hexafluorophosphate (1.7 mg, 2.00 μmol, 1 mol%), and *N*,*N*-dimethylaniline (2.5 μL, 20.0 μmol, 10 mol%) in DMSO-d_6 (1 mL, 0.2 M). The crude residue was purified by flash chromatography (silica gel) from pure hexane to a mixture of 10% ethyl acetate in hexane affording 6.8 mg of 3.13 as a colourless oil (18%, *E:Z* > 20:1) and 8.9 mg of **3.194** as a colourless oil (16%, *E:Z* > 20:1).

^{1}H NMR (500 MHz, Chloroform-*d*) δ 7.40 – 7.34 (m, 2H, H^{4} and H^{6}), 7.34 – 7.27 (m, 2H, H^{1} and H^{3}), 7.26 – 7.19 (m, 1H, H^{2}), 6.46 (d, *J* = 15.83 Hz, 1H, H^{7}), 6.17 (dd, *J* = 15.87, 8.99 Hz, 1H, H^{8}), 4.22 – 4.10 (m, 2H, H^{11}), 3.32 – 3.24 (m, 1H, H^{9}), 1.79 – 1.60 (m, 6H, H^{13}, H^{15}, H^{16}, H^{17}, H^{18} and H^{19}), 1.55 – 1.46 (m, 1H, H^{13}), 1.27 (t,

J = 7.11 Hz, 3H, H^{12}), 1.27 – 1.11 (m, 4H, H^{14}, H^{16},H^{17} and H^{18}) 1.00 – 0.81 (m, 2H, H^{15} and H^{19}).

^{13}C NMR (126 MHz, Chloroform-*d*) δ 174.6 (C^{10}), 137.1 (C^{5}), 131.9 (C^{7}), 128.7 (C^{1} and C^{3}), 128.4 (C^{8}), 127.6 (C^{2}), 126.5 (C^{4} and C^{6}), 60.7 (C^{11}), 47.3 (C^{9}), 40.4 (C^{13}), 35.2 (C^{14}), 33.5 (C^{15} or C^{19}), 33.0 (C^{15} or C^{19}), 26.7 (C^{17}), 26.3 (C^{16} or C^{18}), 26.3 (C^{16} or C^{18}), 14.4 (C^{12}).

HRMS (ESI): *m/z* calculated for $[M + H]^+$ $(C_{19}H_{27}O_2)^+$: 287.2005, found 287.2007.

7. References

1. C. K. Prier, D. A. Rankic, D. W. C. MacMillan, *Chem. Rev*. **2013**, *113*, 5322–5363.
2. L. Buglioni, F. Raymenants, A. Slattery, S. D. A. Zondag, T. Noël, *Chem. Rev.* **2022**, *122*, 2752–2906.
3. J. D. Bell, J. A. Murphy, *Chem. Soc. Rev*. **2021**, *50*, 9540–9685.
4. A. Juris, V. Balzani, P. Belser, A. von Zelewsky, *Helv. Chim. Acta.***1981**, *64*, 2175–2182.
5. M. H. Shaw, J Twilton, D. W. C. MacMillan, *J. Org. Chem.* **2016**, *81*, 6898–6926.
6. D. Ravelli, S. Protti, M. Fagnoni, *Chem. Rev*. **2016**, *116*, 9850–9913.
7. Y. Zhao, W. Xia, *Chem. Soc. Rev.* **2018**, *47*, 2591–2608.
8. C. Cavedon, P. H. Seeberger, B. Pieber, *Eur. J. Org. Chem*. **2020**,1379–1392.
9. A. Wimmer, B. König, *Beilstein J. Org. Chem*. **2018**, *14*, 54–83.
10. N. A. Romero, D. A. Nicewicz, *Chem. Rev*. **2016**, *116*, 10075–10166.
11. K. L. Skubi, T. R. Blum, T. P. Yoon, *Chem. Rev*. **2016**, *116*, 10035–10074.
12. M. M. Mastandrea, M. A. & Pericàs, *Eur. J. Inorg. Chem*. **2021**, 3421–3431.
13. C. G. S. Lima, T. D. M. Lima, M. Duarte, I. D. Jurberg, M. W. Paixão, *ACS Catal*. **2016**, *6*, 1389–1407.
14. J. W. Tucker, C. R. J. Stephenson, *J. Org. Chem.* **2012**, *77*, 1617–1622.
15. S. Protti, M. Fagnoni, D. Ravelli, *ChemCatChem* **2015**, *7*, 1516–1523.
16. L. Capaldo, D. Ravelli, *Eur. J. Org. Chem.* **2017**, 2056–2071.
17. R. A. Angnes, Z. Li, C. R. D. Correia, G. B. Hammond, *Org. Biomol. Chem*. **2015**, *13*, 9152–9167.
18. T. F. Penfold, F. B. Dias, A. P. Monkman, *Chem. Commun.* **2018**, *54*, 3926–3935.
19. V. G. Krishna, *J. Chem. Phys.* **1967**, 46, 1735–1739.
20. A. Juris, V. Balzani, S. Campagna, P. Belser, A. von Zelewsky, *Coord. Chem. Rev*. **1988**, *84*, 85–277.
21. I. M. Dixo, E. Lebon, P. Sutra, A. Igau, *Chem. Soc. Rev.* **2009**, *38*, 1621–1634.
22. J. K. McCusker, *Acc. Chem. Res*. **2003**, *36*, 876–887.

23. F. Strieth-Kalthoff, M. J. James, M. Teders, L. Pitzer, F. Glorius, *Chem. Soc. Rev.* **2018**, *47*, 7190–7202.
24. Q. Zhou, Y. Zou, L. Lu, W. Xiao, *Angew. Chem. Int. Ed*. **2019**, *58*, 1586–1604.
25. T. Förster, *Ann. Phys*. **1948**, *437*, 55–75.
26. B. Sk, S. Hirata, *Chem. Commun*. **2023**, *59*, 6643–6659.
27. L. D. Dexter. *J. Chem. Phys*. **1953**, *21*, 836–850.
28. S. S.Skourtis, C. Liu, P. Antoniou, A. M. Virshup, D. N. Beratan, *Proc. Natl. Acad. Sci. USA* **2016**, *113*, 8115–8120.
29. Z. Q. You, C. P. Hsu, G. R. Fleming, *J. Chem. Phys*. **2006**, 124, 044506.
30. F. Strieth-Kalthoff, F. Glorius, *Chem* **2020**, *6*, 1888–1903.
31. J. B. Metternich, R. Gilmour, *Synlett* **2016**, *27*, 2541–2552.
32. T. Neveselý, M. Wienhold, J. J. Molloy, R. Gilmour, *Chem. Rev*. **2022**, *122*, 2650–2694.
33. G. S. Hammond, J. Saltiel, A. A. Lamola, N. J. Turro, J. S. Bradshaw, D. O. Cowan, R. C. Counsell, V. Vogt, C. Dalton, *J. Am. Chem. Soc*. **1964**, *86*, 3197–3217.
34. J. J. Molloy, M. Schäfer, M. Wienhold, T. Morack, C. G. Daniliuc, R. Gilmour, *Science* **2020**, *369*, 302–306.
35. J. Saltiel, G. S. Hammond, *J. Am. Chem. Soc*. **1963**, *85*, 2515–2516.
36. R. A. Caldwell, L. Zhou, *J. Am. Chem. Soc*. **1994**, *116*, 2271–2275.
37. J. Saltiel, *J. Am. Chem. Soc*. **1967**, *89*, 1036–1037.
38. K. Singh, S. J. Staig, J. D. Weaver, *J. Am. Chem. Soc*. **2014**, *136*, 5275–5278.
39. D. C. Fabry, M. A. Ronge, M. Rueping, *Chem. Eur. J*. **2015**, *21*, 5350–5354.
40. J. B. Metternich, R. Gilmour, *J. Am. Chem. Soc.* **2015**, *137*, 11254–11257.
41. J. B. Metternich, D. G. Artiukhin, M. C. Holland, M. von Bremen-Kühne, J. Neugebauer, R. Guilmour, *J. Org. Chem*. **2017**, 82, 9955–9977.
42. W. Cai, H. Fan, D. Ding, Y. Zhang, W. Wang, *Chem. Commun*. **2017**, *53*, 12918–12921.
43. D. Sarkar, N. Bera, S. Ghosh, *Eur. J. Org. Chem*. **2020**, 1310–1326.
44. S. Poplata, A. Tröster, Y. Q. Zou, T. Bach, *Chem. Rev*. **2016**, *116*, 9748–9815.
45. Z. Lu, T. P. Yoon, *Angew. Chem. Int. Ed*. **2012**, *51*, 10329–10332.

46. V Mojr, E. Svobodová, K. Straková, T. Neveselý, J Chudoba, H. Dvořáková, R. Cibulka, *Chem. Commun*. **2015**, *51*, 12036–12039.
47. S. O. Scholz, J. B. Kidd, L. Capaldo, N. E. Flikweert, R. M. Littlefield, T. P. Yoon, *Org. Lett*. **2021**, *23*, 3496–3501.
48. R. A. Kleinnijenhuis, B. J. J. Timmer, G. Lutteke, J. M. M. Smit, R. de Gelder, J. H. van Maarseveen, H. Hiemstra, *Chem. Eur. J.* **2016**, *22*, 1266–1269.
49. O. P. Demchuk, O. V. Hryshchuk, B. V. Vashchenko, A. V. Kozytskiy, A. V. Tymtsunik, I. V. Komarov, O. O. Grygorenko, *J. Org. Chem*. **2020**, *85*, 5927–5940.
50. Y. Liu, D. Ni, B. G. Stevenson, V. Tripathy, S. E. Braley, K. Raghavachari, J. R. Swierk, M. K. Brown, *Angew. Chem. Int. Ed*. **2022**, 61, e202200725.
51. D. I. Schuster, G. Lem, N. A. Kaprinidis, *Chem. Rev.* **1993**, 93, 3–22.
52. H. Holla, I. D. Jenkins, J. E. Neve, R. H. Pouwer, N. Pham, S. J. Teague, R. J. Quinn, *Tetrahedron Lett.* **2012**, *53*, 7101–7103.
53. X. D. Xia, J. Xuan, Q. Wang, L. Q. Lu, J. R. Chen, W. J. Xiao, *Adv. Synth. Catal*. **2014**, *356*, 2807–2812.
54. M. C. Derosa, R. J. Crutchley, *Coord. Chem. Rev*. **2002**, *233–234*, 351–371.
55. A. Greer, *Acc. Chem. Res*. **2006**, *39*, 797–804.
56. N. Iqbal, S. Choi, Y. You, E. J. Cho, *Tetrahedron Lett*. **2013**, *54*, 6222–6225.
57. H. Cano-Yelo, A. Deronzier, *J. Chem. Soc. Perkin Trans. 2* ***1984***, 6, 1093–1098
58. Y. Q. Zou, J. R. Chen, X. P. Liu, L. Q. Lu, R. L. Davis, K. A. Jørgensen, W. J. Xiao, *Angew. Chem. Int. Ed*. **2012**, 51, 784–788.
59. D. A. Nicewicz, D. W. C. MacMillan, *Science* **2008**, *322*, 77–80.
60. E. Larionov, M. M. Mastandrea, M. A. Pericas, *ACS Catal*. **2017**, 7, 7008–7013.
61. D. A. Dirocco, T. Rovis, *J. Am. Chem. Soc*. **2012**, *134*, 8094–8097.
62. M. Neumann, S. Füldner, B. König, K. Zeitler, *Angew. Chem. Int. Ed*. **2011**, *50*, 951–954.
63. A. Y. Chan, I. B. Perry, N. B. Bissonnette, B. F. Buksh, G.A. Edwards, L. I. Frye, O. L. Garry, M. N. Lavagnino, B. X. Li, Y. Liang, E. Mao, A. Millet, J. V. Oakley, N. L. Reed, H. A. Sakai, C.P. Seath, D. W. C. MacMillan, *Chem. Rev*. **2022**, *122*, 1485–1542.
64. C. Zhu, H. Yue, L. Chu, M. Rueping, *Chem. Sci*. **2020**, *11*, 4051–4064.

65. Y. Zhang, Q. Wang, Z. Yan, D. Ma, Y. Zheng, *Beilstein J. Org. Chem*. **2021**, *17*, 2520–2542.
66. K. Ram Bajya, S. Selvakumar, *Eur. J. Org. Chem*. **2022**, e202200229.
67. S. Witzel, A. S. K. Hashmi, J. Xie, *Chem. Rev*. **2021**, *121*, 8868–8925.
68. L. H. M. de Groot, A. Ilic, J. Schwarz, K. Wärnmark, *J. Am. Chem. Soc.* **2023**, *145*, 9369–9388.
69. Z. Zuo, D. T. Ahneman, L. Chu, J. A. Terrett, A. G. Doyle, D. W. C. MacMillan, *Science*, **2014**, *345*, 437–440.
70. D. N. Primer, I. Karakaya, J. C. Tellis, G. A. Molander, *J. Am. Chem. Soc.* **2015**, *137*, 2195–2198.
71. N. A. Weires, Y. Slutskyy, L. E. Overman, *Angew. Chem. Int. Ed*. **2019**, *131*, 8649–8653.
72. A. García-Domínguez, R. Mondal, C. Nevado, *Angew. Chem. Int. Ed*. **2019**, *131*, 12414–12418.
73. S. H. Lau, M. A. Borden, T. J. Steiman, L. S. Wang, M. Parasram, A. G. Doyle, *J. Am. Chem. Soc.* **2021**, *143*, 15873–15881.
74. J. Li, J. Chen, R. Sang, W. S. Ham, M. B. Plutschack, F. Berger, S. Chabbra, A. Schnegg, C. Genicot, T. Ritter, *Nat. Chem.* **2020**, *12*, 56–62.
75. H. Meng, M. S. Liu, W. Shu, *Chem. Sci*. 2**022**, *13*, 13690–13707.
76. L. Zhang, E. M. Israel, J. Yan, T. Ritter, Nature Synthesis **2022**, *1*, 376–381.
77. D. R.Heitz, J. C. Tellis, G. A. Molander, *J. Am. Chem. Soc*. **2016**, *138*, 12715–12718.
78. E. R. Welin, C. Le, D. M. Arias-Rotondo, J. K. Mccusker, D. W. C. MacMillan, *Science*, **2017**, *335*, 380–385.
79. L. Capaldo, D. Ravelli, M. Fagnoni, *Chem. Rev*. **2022**, *122*, 1875–1924.
80. Y. Zhang, P. Ji, W. Hu, Y. Wei, H. Huang, W. Wang, *Chem. Eur. J*. **2019**, 25, 8225–8228.
81. M. Singh, A. K. Yadav, L. D. S. Yadav, R. K. P. Singh, *Tetrahedron Lett.* **2017**, *58*, 2206–2208.
82. X. Fan, P. Xiao, Z. Jiao, T. Yang, X. Dai, W. Xu, J. Da Tan, G. Cui, H. Su, W. Fang, J. Wu, *Angew. Chem. Int. Ed*. **2019**, *131*, 12710–12714.
83. F. Juliá, T. Constantin, D. Leonori, *Chem. Rev*. **2022**, 122, 2292–2352.

84. G. H. Lovett, S. Chen, X. S. Xue, K. N. Houk, D. W. C. MacMillan, *J. Am. Chem. Soc*. **2019**, *141*, 20031–20036.
85. T. Constantin, M. Zanini, A. Regni, N. S. Sheikh, F. Juliá, D. Leonori, *Science* **2020**, *367*, 1021–1026.
86. T. Constantin, F. Juliá, N. S. Sheikh, D. Leonori, *Chem. Sci.* **2020**, *11*, 12822–12828.
87. Y. Q. Yuan, S. Majumder, M. H. Yang, S. R. Guo, *Tetrahedron Lett*. **2020**, *61*, 151506.
88. M. A. Cismesia, T. P. Yoon, *Chem. Sci*. **2015**, *6*, 5426–5434.
89. F. Glaser, C. Kerzig, O. S. Wenger, *Angew. Chem. Int. Ed*. **2020**, *59*, 10266–10284.
90. I. Ghosh, B. König, *Angew. Chem. Int. Ed*. **2016**, *55* , 7676–7679.
91. F. Brandl, S. Bergwinkl, C. Allacher, B. Dick, *Chem. Eur. J.* **2020**, *26*, 7946–7954.
92. J. W. B. Fyfe, A. J. B. Watson, *Chem* **2017**, *3*, 31–55.
93. H. C. Brown, B. C. Subba Rao, *J. Am. Chem. Soc*.**1956**, *78*, 5694–5695.
94. A. J. J. Lennox, G. C. Lloyd-Jones, *Chem. Soc. Rev*. **2014**, *43*, 412–443.
95. N. Miyaura, A. Suzuki, *Chem. Rev*. **1995**, *95*, 2457–2483.
96. J. X. Qiao, P. Y. S. Lam, *Synthesis* **2011**, *6*, 829–856.
97. M. J. West, J. W. B. Fyfe, J. C. Vantourout, A. J. B. Watson, *Chem. Rev*. **2019**, *119*,12491–12523
98. T. Hayashi, K. Yamasaki, Chem. Rev. **2003**, *103*, 2829–2844.
99. D. G. Brown, J. Boström, *J. Med. Chem*. **2016**, *59*, 4443–4458.
100. M. J. Buskes, M. J. Blanco, *Molecules* **2020**, *25*, 3493.
101. P. Devendar, R. Y. Qu, W. M. Kang, B. He, G. F. Yang, *J. Agric. Food Chem*. **2018**, *66*, 8914–8934.
102. J. L. Carden, A. Dasgupta, R. L. Melen, *Chem. Soc. Rev*. **2020**, *49*, 1706–1725.
103. V. Nori, F. Pesciaioli, A. Sinibaldi, G. Giorgianni, A. Carlone, *Catalysts* **2022**, *12*, 5.
104. B. C. Das, N. K. Nandwana, S. Das, V. Nandwana, M. A. Shareef, Y. Das, M. Saito, L. M. Weiss, F. Almaguel, N. S. Hosmane, T. Evans, *Molecules* **2022**, *27*, 2615.

105. K. G. Ramirez, *J. Adv. Pract. Oncol*. **2017**, *8*, 401–405.
106. N. Sharma, D. Sharma, D. *J. Pharmacol. Pharmacother*. **2015**, *6*, 236–239.
107. Y. Deng, F. Campbell, K. Han, D. Theodore, M. Deeg, M. Huang, R. Hamatake, S. Lahiri, S. Chen, G. Horvath, S. Manolakopoulos, G. N. Dalekos, G. Papatheodoridis, I. Goulis, T. Banyai, B. Jilma, M. Leivers, *J. Viral Hepat*. **2020**, *27*, 699–708.
108. G. A. Molander, V. Colombel, V. A. Braz. *Org. Lett*. **2011**, *13*, 1852–1855.
109. J. K. Matsui, S. B. Lang, D. R. Heitz, G. A. Molander, *ACS Catal*. **2017**, *7*, 2563–2575.
110. K. Miyazawa, Y. Yasu, T. Koike, M. Akita, *Chem. Commun*. **2013**, *49*, 7249–7251.
111. H. Huang, G. Zhang, L. Gong, S. Zhang, Y. Chen, *J. Am. Chem. Soc*. **2014**, *136*, 2280–2283.
112. J. C. Tellis, D. N. Primer, G. A. Molander, *Science* **2014**, *345*, 433–436.
113. J. C. Tellis, C. B. Kelly, D. N. Primer, M. Jouffroy, N. R. Patel, G. A. Molander, *Acc. Chem. Res*. **2016**, *49*, 1429–1439.
114. V. Corce, C. Ollivier, L. Fensterbank, *Chem. Soc. Rev*. **2022**, *51*, 1470–1510.
115. F. Lima, U. K. Sharma, L. Grunenberg, D. Saha, S. Johannsen, J. Sedelmeier, E. V. Van der Eycken, S. V. Ley, *Angew. Chem. Int. Ed*. **2017**, *129*, 15332–15336.
116. P. Ranjan, S. Pillitteri, G. Coppola, M. Oliva, E. V. Van der Eycken, U. K. Sharma, *ACS Catal*. **2021**, *11*, 10862–10870.
117. Y. Iwata, Y. Tanaka, S. Kubosaki, T. Morita, Y. Yoshimi, *Chem. Commun*. **2018**, *54*, 1257–1260.
118. S. Bloom, M. Chilamari, J. R. Immel, *ACS Catal*. **2020**, *10*, 12727–12737.
119. T. Ishiyama, M. Murata, N. Miyaura, *J. Org. Chem*. **1995**, *60*, 7508–7510.
120. Y. M. Tian, X. N. Guo, H. Braunschweig, U. Radius, T. B. Marder, *Chem. Rev.* **2021**, *121*, 3561–3597.
121. F. W. Friese, A. Studer, *Chem. Sci*. **2019**, *10*, 8503–8518.
122. J. Yu, L. Zhang, G. Yana, *Adv. Synth. Catal*. **2012**, *354*, 2625–2628.
123. M. Jiang, H. Yang, H. Fu, *Org. Lett*. **2016**, *18*, 5248–5251.
124. A. Fawcett, J. Pradeilles, Y. Wang, T. Mutsuga, E. L. Myers, V. K. Aggarwal, *Science* **2017**, *357*, 283–286.

125. B. Giese, *Angew. Chem. Int. Ed. Engl*. **1983**, *22*, 753–764.
126. B. Giese, S. Lachheinl, *Angew. Chem. Int. Ed. Engl*. **1981**, *20*, 967.
127. B. Giese, J. Dupuis, *Angew. Chem. Int. Ed. Engl*. **1983**, *22*, 622–623.
128. D. M. Kitcatt, S. Nicolle, A. L. Lee, *Chem. Soc. Rev*. **2022**, *51*, 1415–1453.
129. A. L. Gant Kanegusuku, J. L. Roizen, *Angew. Chem. Int. Ed*. **2021**, *60*, 21116–21149.
130. Q. Huang, S. R. Suravarapu, P. A. Renaud, *Chem. Sci*. **2021**, *12*, 2225–2230.
131. S. Paul, D. Filippini, M. Silvi, *J. Am. Chem. Soc*. **2023**, *145*, 2773–2778.
132. Y. L. Zhang, L. Yang, J. Wu, C. Zhu, P. Wang, *Org. Lett*. **2020**, *22*, 7768–7772.
133. J. Gresser, J. H. Binks, M. Szwarc, *J. Am. Chem. Soc*. **1959**, *81*, 5004–5005.
134. D. S. Matteson, *J. Am. Chem. Soc*. 1960, 82, 4228–4233.
135. N. Kumar, R. R. Reddy, N. Eghbarieh, A. Masarwa, *Chem. Commun*. **2019**, *56*, 13–25.
136. J. C. Walton, A. J. McCarroll, Q. Chen, B. Carboni, R. Nziengui, *J. Am. Chem. Soc*. **2000**, *122*, 5455–5463.
137. B. Quiclet-Sire, S. Z. Zard, *J. Am. Chem. Soc*. **2015**, *137*, 6762–6765.
138. G. J. Lovinger, J. P. Morken, *Eur. J. Org. Chem*. **2020**, 2362–2368.
139. A. Marotta, C. E. Adams, J. J. Molloy, *Angew. Chem. Int. Ed*. **2022**, e202207067.
140. A. Noble, R. S. Mega, D. Pflästerer, E. L. Myers, V. K. Aggarwal, *Angew. Chem. Int. Ed*. **2018**, *130*, 2177–2181.
141. X. Shu, R. Xu, Q. Ma, S. Liao, *Organic Chemistry Frontiers* **2020**, *7*, 2003–2007.
142. M. W. Campbell, J. S. Compton, C. B. Kelly, G. A. Molander, *J. Am. Chem. Soc*. **2019**, *141*, 20069–20078.
143. C. Shu, R. S. Mega, B. J. Andreassen, A. Noble, V. K. Aggarwal, *Angew. Chem. Int. Ed*. **2018**, *130*, 15656–15660.
144. A. M. del Hoyo, A. G. Herraiz, M. García Suero, *Angew. Chem. Int. Ed*. **2017**, *129*, 1632–1635.
145. A. M. del Hoyo, M. García Suero, *Eur. J. Org. Chem*. **2017**, 2122–2125.
146. T. Taniguchi, *Chem. Eur. J.* **2022**, e202104333.

147. M. Kischkewitz, K. Okamoto, C. Mück-Lichtenfeld, A. Studer, *Science*, **2017**, 355, 936–938.
148. N. D. C. Tappin, M. Gn-Gi-lux, P. Renaud, *Chem. Eur. J.* **2018**, 24, 11498–11502.
149. M. Silvi, C. Sandford, V. K. Aggarwal, *J. Am. Chem. Soc*. **2017**, *139*, 5736–5739.
150. B. Zhao, Z. Li, Y. Wu, Y. Wang, J. Qian, Y. Yuan, Z. Shi, *Angew. Chem. Int. Ed*. **2019**, *131*, 9548–9552.
151. Y. Yasu, T. Koike, M. Akita, *Chem. Commun*. **2013**, 49, 2037–2039.
152. Y. Yasu, T. Koike, M. Akita, *Angew. Chem. Int. Ed*. **2012**, *51*, 9567–9571.
153. D. Fernandez Reina, A. Ruffoni, Y. S. S. Al-Faiyz, J. J. Douglas, N. S. Sheikh, D. Leonori, *ACS Catal*. **2017**, *7*, 4126–4130.
154. H. G. Roth, N. A. Romero, D. A. Nicewicz, *Synlett* **2016**, *27*, 714–723.
155. H. Kim, D. W. C. MacMillan, *J. Am. Chem. Soc*. **2008**, *130*, 398–399.
156. P. Xiong, M. Hemming, S. I. Ivlev, E. Meggers, *J. Am. Chem. Soc*. **2022**, *144*, 6964–6971.
157. H. Chen, L. Guo, S. Yu, *Org. Lett*. **2018**, *20*, 6255–6259.
158. J. Davies, S. P. Morcillo, J. J. Douglas, D. Leonori, *Chem. Eur. J*. **2018**, *24*, 12154–12163.
159. X. Shen, C. Huang, X. A. Yuan, S. Yu, *Angew. Chem. Int. Ed*. **2021**, *60*, 9672–9679.
160. T. Zhu, J. Shen, Y. Sun, J. Wu, *Chem. Commun*. **2021**, *57*, 915–918.
161. D. P. Hari, B. König, *Angew. Chem. Int. Ed*. **2013**, *52*, 4734–4743.
162. T. Meyer, J. X. Xu, J. Rabeah, A. Brückner, X. F. Wu, *ChemPhotoChem* **2020**, *4*, 713–720.
163. C. H. Qu, X. Yan, S. T. Li, J. B. Liu, Z. G. Xu, Z. Z. Chen, D. Y. Tang, H. X. Liu, G. T. Song, *Green Chem*. **2023**, *25*, 3453–3461.
164. G. Cavallo, P. Metrangolo, R. Milani, T. Pilati, A. Priimagi, G. Resnati, G. Terraneo, *Chem. Rev*., **2016**, *116*, 2478–2601.
165. M. W. Campbell, M. Yuan, V. C. Polites, O. Gutierrez, G. A. Molander, *J. Am. Chem. Soc.* **2021**, *143*, 3901–3910.
166. M. Sayes, G. Benoit, A. B. Charette, *Angew. Chem. Int. Ed***.** **2018**, *130*, 13702–13706.

167. M. J. Cabrera-Afonso, A. Sookezian, S. O. Badir, M. El Khatib, G. A. Molander, *Chem. Sci*. **2021**, *12*, 9189–9195.
168. Y. Ye, M. S. Sanford, *J. Am. Chem. Soc*. **2012**, *134*, 9034–9037.
169. T. Taniguchi, *Eur. J. Org. Chem*. **2019**, 6308–6319.
170. N. Zhou, X. A. Yuan, Y. Zhao, J. Xie, C. Zhu, *Angew. Chem. Int. Ed*. **2018**, *130*, 4054–4058.
171. W. D. Li, Y. Wu, S. J. Li, Y. Q. Jiang, Y. L. Li, Y. Lan, J. B. Xia, *J. Am. Chem. Soc.* **2022**, *144*, 8551–8559.
172. F. S. Han, *Chem. Soc. Rev*. **2013**, *42*, 5270–5298.
173. S. E. Hooshmand, B. Heidari, V. Sedghi, R. S. Varma, *Green Chem*. **2019**, *21*, 381–405.
174. S. Crespi, M. Fagnoni, *Chem. Rev*., **2020**, *120*, 9790–9833.
175. N. Kvasovs, V. Gevorgyan, *Chem. Soc. Rev*. **2021**, *50*, 2244–2259.
176. F. Mo, D. Qiu, L. Zhang, J. Wang, *Chem. Rev*. **2021**, *121*, 5741–5829.
177. S. S. Babu, P. Muthuraja, P. Yadav, P. Gopinath, *Adv. Synth. Catal* **2021**, *363*,1782–1809.
178. S. Murarka, *Adv. Synth. Catal.* **2018**, *360*, 1735–1753.
179. X. Zhu, H. Fu, *Chem. Commun*. **2021**, *57*, 9656–9671.
180. S. K. Parida, T. Mandal, S. Das, S. K. Hota, S. De Sarkar, S. Murarka, *ACS Catal*. **2021**, *11*, 1640–1683.
181. M. W. Campbell, V. C. Polites, S. Patel, J. E. Lipson, J. Majhi, G. A. Molander, *J. Am. Chem. Soc*. **2021**, *143*, 19648–19654.
182. N. Sugihara, K. Suzuki, Y. Nishimoto, M. Yasuda, *J. Am. Chem. Soc*. **2021**, *143*, 9308–9313.
183. H. Sies, V. V. Belousov, N. S. Chandel, M. J. Davies, D. P. Jones, G. E. Mann, M. P. Murphy, M. Yamamoto, C. Winterbourn, *Nat. Rev. Mol. Cell. Biol.* **2022**, *23*, 499–515.
184. Y. Nosaka, A. Y. Nosaka, *Chem. Rev*. **2017**, *117*, 11302–11336.
185. C. Bian, A. K. Singh, L. Niu, H. Yi, A. Lei, *Asian J. Org. Chem*. **2017**, *6*, 386–396.
186. J. Wang, T. Qin, T. G. Chen, L. Wimmer, J. T. Edwards, J. Cornella, B. Vokits, S. A. Shaw, P. S. Baran, *Angew. Chem. Int. Ed.* **2016**, *128*, 9828–9831.

187. E. J. Horn, B. R. Rosen, Y. Chen, J. Tang, K. Chen, M. D. Eastgate, P. S. Baran, *Nature* **2016**, *533*, 77–81.
188. E. Le Saux, M. Zanini, P. Melchiorre, *J. Am. Chem. Soc*. **2022**, *144*, 1113–1118.
189. I. Bosque, T. Bach, *ACS Catal*. **2019**, *9*, 9103–9109.
190. K. Okada, K. Okamoto, M. Oda, *J. Am. Chem. Soc*. **1988**, *110*, 8736–8738.
191. Y. Zhang, D. Ma, Z. Zhang, *Arabian J. Chem*. **2022**, *15*, 103922.
192. H. C. Brown, S. K. Gupta, *J. Am. Chem. Soc*. **1975**, *97*, 5249–5255.
193. K. Shirakawa, A. Arase, M. Hoshi, *Synthesis* **2004**, *11*, 1814–1820.
194. K. S. Barbato, Y. Luan, D. Ramella, J. S. Panek, S. E. Schaus, *Org. Lett*. **2015**, *17*, 5812–5815.
195. D. A. Nicewicz, T. M. Nguyen, *ACS Catal*. **2014**, *4*, 355–360.
196. N. F. Nikitas, P. L. Gkizis, C. G. Kokotos, *Org. Biomol. Chem*. **2021**, *19*, 5237–5253.
197. E. André-Joyaux, A. Kuzovlev, N. D. C. Tappin, P. Renaud, *Angew. Chem. Int. Ed*. **2020**, *59*, 13859–13864.
198. C. Wu, Z. Bao, B. Dou, J. Wang, *Chem. Eur. J*. **2021**, *27*, 2294–2298.
199. L. Babcock, R. Pizer, *Inorg. Chem*. **1980**, *19*, 56–61.
200. S. A. Valenzuela, J. R. Howard, H. M. Park, S. Darbha, E. V. Anslyn, *J. Org. Chem*. **2022**, *87*, 15071–15076.
201. R. Pizer, L. Babcock, *Inorg. Chem.* **1977**, *16*, 1677–1681.
202. G. E. M. Crisenza, D. Mazzarella, P. Melchiorre, *J. Am. Chem. Soc*. **2020**, *142*, 5461–5476.
203. J. Wu, L. He, A. Noble, V. K. Aggarwal, *J. Am. Chem. Soc*. **2018**, *140*, 10700–10704.
204. S. Xie, D. Li, H. Huang, F. Zhang, Y. Chen, *J. Am. Chem. Soc*. **2019**, *141*, 16237– 16242.
205. J. Hioe, H. Zipse, *Org. Biomol. Chem*. **2010**, *8*, 3609–3617.
206. L. McMurray, T. M. McGuire, R. L. Howells, *Synthesis* **2020**, *52*, 1719–1737.
207. Y. Jin, H. Fu, *Asian J. Org. Chem.* **2017,** *6*, 68–385.
208. J. Wang, M. Shang, H. Lundberg, K. S. Feu, S. J. Hecker, T. Qin, D. G. Blackmond, P. S. Baran, *ACS Catal*. **2018**, *8*, 9537–9542.

209. J. Brauer, E. Quraishi, L. M. Kammer, T. Opatz, *Chem. Eur. J.* **2021**, *27*, 18168–18174.
210. A. Y. Peng, B. T. Chen, P. J. Chen, *J. Fluor. Chem.* **2013**, *151*, 58–62.
211. R. J. Perner, C. H. Lee, M. Jiang, Y. G. Gu, S. DiDomenico, E. K. Bayburt, K. M. Alexander, K. L. Kohlhaas, M. F. Jarvis, E. L. Kowaluk, S. S. Bhagwat, *Bioorg. Med. Chem. Lett.* **2005**, *15*, 2803–2807.
212. J. W. B. Fyfe, E. Valverde, C. P. Seath, A. R. Kennedy, J. M. Redmond, N. A. Anderson, A. J. B. Watson, *Chem. Eur. J.* **2015**, *21*, 8951–8964.
213. C. W. Muir, J. C. Vantourout, A. Isidro-Llobet, S. J. F. Macdonald, A. J. B. Watson, *Org. Lett.* **2015**, *17*, 6030–6033.
214. S. Rej, A. Das, T. K. Panda, *Adv. Synth. Catal.* **2021**, *363*, 4818–4840.
215. S. Mandal, S. Mandal, K. Geetharani, *Chem Asian J.* **2019**, *14*, 4553–4556.
216. Y. Wang, R. Guan, P. Sivaguru, X. Cong, X. Bi, *Org. Lett.* **2019**, *21*, 4035–4038.
217. R. Mamidala, V. K. Pandey, A. Rit, *Chem. Commun.* **2019**, *55*, 989–992.
218. A. Boelke, L. D. Caspers, B. J. Nachtsheim, *Org. Lett.* **2017**, *19*, 5344–5347.
219. G. Pisella, A. Gagnebin, J. Waser, *Org. Lett.* **2020**, *22*, 3884–3889.
220. J. E. Lee, J. Kwon, J. Yun, *Chem. Commun.* **2008**, *6*, 733–734.
221. R. Alfaro, A. Parra, J. Alemán, J. L. García Ruano, M. Tortosa, *J. Am. Chem. Soc.* **2012**, *134*, 15165–15168.
222. W. Yuan, S. Ma, *Org. Biomol. Chem.* **2012**, *10*, 7266–7268.
223. M. A. M. Subbaiah, N. A. Meanwell, *J. Med. Chem.* **2021**, *64*, 14046–14128.
224. W. Dong, E. Yen-Pon, L. Li, A. Bhattacharjee, A. Jolit, G. A. Molander, *Nat. Chem.* **2022**, *14*, 1068–1077.
225. D. C. Salgueiro, B. K. Chi, I. A. Guzei, P. García-Reynaga, D. J. Weix, *Angew. Chem. Int. Ed.* **2022**, *61*, e202205673.
226. J. J. Mousseau, M. A. Perry, M. W. Bundesmann, G. M. Chinigo, C. Choi, G. Gallego, R. W. Hicklin, S. Hoy, D. C. Limburg, N. W. Sach, Y. Zhang, *ACS Catal.* **2022**, *12*, 600–606.
227. J. Schwarz, B. König, *Green Chem.* **2016**, *18*, 4743–4749.
228. J. J. Molloy, J. B. Metternich, C. G. Daniliuc, A. J. B. Watson, R. Gilmour, *Angew. Chem. Int. Ed.* **2018,** *130*, 3222–3226.

229. G. L. Lackner, K. W. Quasdorf, G. Pratsch, L. E. Overman, *J. Org. Chem*. **2015**, *80*, 6012–6024.
230. H. Yang, D. O. Wipf, A. J. Bard, *J. Electroanal. Chem.* **1992**, *331*, 913-924.
231. V. Srivastava, P. P. Singh, *RSC Adv*. **2017**, *7*, 31377–31392.
232. K. J. Winstanley, A. M. Sayer, D. K. Smith, *Org. Biomol. Chem.* **2006**, *4*, 1760–1767.
233. Q. Lin, Q. Li, C. Batchelor-Mcauley, R. G. Compton, *J. Phys. Chem*. **2015**, *119*, 1489–1495.
234. S. M. Strawbridge, S. J. Green, J. H. R. Tucker, *Chem. Commun*. **2000**, *23*, 2393–2394.
235. Z. M. Robole, K. L. Rahn, B. J. Lampkin, R. K. Anand, B. Vanveller, *J. Org. Chem*. **2019**, *84*, 2346–2350.
236. F. Parsaee, M. C. Senarathna, P. B. Kannangara, S. N. Alexander, P. D. E. Arche, E. R. Welin, *Nat. Rev. Chem*. **2021**, *5*, 486–499.
237. S. Sharma, J. Singh, A. Sharma, *Adv. Synth. Catal*. **2021**, *363*, 3146–3169.
238. D. D. M. Wayner, D. J. McPhee, D. Griller, *J. Am. Chem. Soc*. **1988**, *110*, 132–137.
239. Y. Li, W. X. Fan, S. Luo, A. Trofimova, Y. Liu, J. H. Xue, L. Yang, Q. Li, H. Wang, A. K. Yudin, *J. Am. Chem. Soc*. **2023**, *145*, 7548–7558.
240. F. Cao, J. Kim, A. J. Bard, *J. Am. Chem. Soc*. **2014**, *136*, 18163–18169.
241. C. Walling, A. Cioffari, *J. Am. Chem. Soc*. **1972**, *94*, 6059–6064.
242. M. Newcomb, A. G. Glenn, *J. Am. Chem. Soc*. **1989**, *111*, 275–277.
243. A. G. Myers, D. Tanaka, M. R. Mannion, *J. Am. Chem. Soc*. **2002**, *124*, 11250–11251.
244. M. Koy, F. Sandfort, A. Tlahuext-Aca, L. Quach, C. G. Daniliuc, F. Glorius, *Chem. Eur. J*. **2018**, *24*, 4552–4555.
245. J. J. Zhang, J. C. Yang, L. N. Guo, X. H. Duan, *Chem. Eur. J*. **2017**, *23*, 10259–10263.
246. Z. H. Xia, C. L. Zhang, Z. H. Gao, S. Ye, *Org. Lett*. **2018**, *20*, 3496–3499.
247. G. Kachkovskyi, M. Cieślak, P. Graczyk, P. Zawadzki, J. Kalinowska-Tłuścik, M. Werłos, *Synthesis* **2022**, *54*, 4294–4303.
248. A. Juneau, T. O. Hope, J. Malenfant, M. Mesko, J. McNeill, M. Frenette, *ACS Catal*. **2022**, *12*, 2348–2356.

249. A. D. Lackner, A. Fürstner, *Angew. Chem. Int. Ed*. **2015**, *127*, 13005–13009.
250. G. Cahiez, O. Gager, F Lecomte, *Org. Lett*. **2008**, *10*, 5255–5256.
251. Jin, G. Haug, V. Nguyen, C. Flores-Hansen, H. Arman, O. Larionov, *ACS Catal*. **2019**, *9*, 9764–9774.
252. Y. B. Zhou, Y. Q. Wang, L. C. Ning, Z. C. Ding, W. L. Wang, C. K. Ding, R. H. Li, J. J. Chen, X. Lu, Y. J. Ding, Z. P. Zhan, *J. Am. Chem. Soc*. **2017**, *139*, 3966–3969.
253. J. Cornella, J. Edwards, T. Qin, S. Kawamura, J. Wang, C. M. Pan, R. Gianatassio, M. Schmidt, M. D. Eastgate, P. S. Baran, *J. Am. Chem. Soc*. **2016**, *138*, 2174–2177.
254. K. Huihui, J. Caputo, Z. Melchor, A. Olivares, A. Spiewak, K. Johnson, T. Dibenedetto, S. Kim, L. Ackerman, D. Weix, *J. Am. Chem. Soc*. **2016**, *138*, 5016–5019.
255. W. Zhao, R. P. Wurz, J. C. Peters, G. C. Fu, *J. Am. Chem. Soc*. **2017**, *139*, 12153–12156.
256. X. Xu, J. Sun, Y. Lin, J. Cheng, P. Li, X. Jiang, R., Bai, Y. Xie, *Eur. J. Org. Chem*. **2017**, 7160–7166.
257. P. F. Dai, Y. P. Wang, J. P. Qu, Y. B. Kang, *Org. Lett*. **2021**, *23*, 9360–9364.
258. M. C. Sheikh, S. Takagi, T. Yoshimura, H. Morita, *Tetrahedron* **2010**, *66*, 7272–7278.
259. X. Lu, B. Xiao, L. Liu, Y. Fu, *Chem. Eur. J*. **2016**, *22*, 11161–11164.
260. E. Christiansen, C. Urban, M. Grundmann, M. E. Due-Hansen, E. Hagesaether, J. Schmidt, L. Pardo, S. Ullrich, E. Kostenis, M. Kassack, T. Ulven, *J. Med. Chem*. **2011**, *54*, 6691–6703.
261. M. J. Bu, C. Cai, F. Gallou, B. H. Lipshutz, *Green Chem*. **2018**, *20*, 1233–1237.
262. G. Pratsch, G. L. Lackner, L. E. Overman, *J. Org. Chem*. **2015**, *80*, 6025–6036.
263. X. G. Liu, C. J. Zhou, E. Lin, X. L. Han, S. S. Zhang, Q. Li, H. Wang, *Angew. Chem. Int. Ed*. **2018**, *57*, 13096–13100.
264. S. A. Green, S. Vásquez-Céspedes, R. A. Shenvi, *J. Am. Chem. Soc*. **2018**, *140*, 11317–11324.

265. H. Li, C. Breen, H. Seo, T. Jamison, Y. Q. Fang, M. M. Bio, *Org. Lett*. **2018**, *20*, 1338–1341.
266. C. C. Chen, S. F. Wang, Y. Y. Su, Y. A. Lin, P. C. Lin, *Chem. Asian J*. **2017**, *12*, 1326–1337.
267. E. Garnier-Amblard, S. Mays, R. Arrendale, M. Baillie, A. Bushnev, D. Culver, T. Evers, J. Holt, R. Howard, L. Liebeskind, D. Menaldino, M. Natchus, J. Petros, H Ramaraju, G. P. Reddy, D. Liotta, *ACS Med. Chem. Lett*. **2011**, *2*, 438–443.
268. M. L. Shen, Y. Shen, P. S. Wang, *Org. Lett*. **2019**, *21*, 2993–2997.
269. K. J. Hale, Z. Xiong, L. Wang, S. Manaviazar, R. Mackle, *Org. Lett*. **2015**, *17*, 198–201.
270. Y. Jiang, J. Pan, T. Yang, Y. Zhao, M. J. Koh, *Chem*. **2021**, *7*, 993–1005.
271. A. Tlahuext-Aca, R. A. Garza-Sanchez, M. Schäfer, F. Glorius, *Org. Lett*. **2018**, *20*, 1546–1549.
272. T. Mani, D. Liu, D. Zhou, L. Li, W. E. Knabe, F. Wang, K. Oh, S. Meroueh, *ChemMedChem* **2013**, *8*, 1963–1977.
273. M. C. Grenier, S. Ding, D. Vézina, J. P. Chapleau, W. Tolbert, R. Sherburn, A. Schön, S. Somisetti, C. Abrams, M. Pazgier, A. Finzi, A. B. Smith, *ACS Med. Chem. Lett*. **2020**, *11*, 371–378.
274. A. K. C. Schmidt, C. B. W. Stark, *Org. Lett*. **2011**, *13*, 4164–4167.
275. L. Yu, M. L. Tang, C. M. Si, Z. Meng, Y. Liang, J. Han, X. Sun, *Org. Lett*. **2018**, *20*, 4579–4583.
276. E. Watanabe, Y. Chen, O. May, S. V. Ley, *Chem. Eur. J*. **2020**, *26*, 186–191
277. H. Song, R. Cheng, Q. Q. Min, X. Zhang, *Org. Lett*. **2020**, *22*, 7747–7751.
278. N. Kvasovs, V. Gevorgyan, *Org. Lett.* **2022**, *24*, 4176−4181.
279. F. Sandfort, M. J. O'Neill, J. Cornella, L. Wimmer, P. S. Baran, *Angew. Chem. Int. Ed*. **2017**, *56*, 3319–3323.
280. F. Toriyama, J. Cornella, L. Wimmer, T. G. Chen, D. D. Dixon, G. Creech, P. S. Baran, *J. Am. Chem. Soc.* **2016**, *138*, 11132–11135.
281. T. Qin, L. Malins, J. Edwards, R. Merchant, A. Novak, J. Zhong, R. Mills, M. Yan, C. Yuan, M. Eastgate, P. S. Baran, *Angew. Chem. Int. Ed*. **2017**, *56*, 260–265.
282. D. Balamurugan, K.M. Muraleedharan, *Chem. Eur. J*. **2012**, *18*, 9516–9520.

283. J. T. Correia, G. Piva da Silva, C. M. Kisukuri, E. André, B. Pires, P.S. Carneiro, M. W. Paixão, *J. Org. Chem*. **2020**, *85*, 9820–9834.
284. D. Wang, N. Zhu, P. Chen, Z. Lin, G. Liu, *J. Am. Chem. Soc*. **2017**, *139*, 15632–15635.
285. T. Yang, Y. Jiang, Y. Luo, J. Jun Han Lim, Y. Lan, M. J. Koh, *J. Am. Chem. Soc*. **2020**, *142*, 21410–21419.
286. D. L. Zhu, R. Xu, Q. Wu, H. Y. Li, J. P. Lang, and H. X. Li, *J. Org. Chem*. **2020**, *85*, 9201–9212.
287. M. L. N. Rao, S. S. Islam, *Tetrahedron Lett.* **2021**, *71*, 153051.
288. J. S. Jia, T. X. Wu, Y. J. Fu, Z. R. Hu, H. T. Tang, Y. M. Pan, F. P. Huang, *Adv. Synth. Catal.* **2022**, *364*, 1873–1878.
289. M. Zhong, Y. Gagné, T. O. Hope, X. Pannecoucke, M. Frenette, P. Jubault, T. Poisson, *Angew. Chem. Int. Ed.* **2021**, *60*, 14498–14503.
290. E. J. Linstad, A. L. Vāvere, B. Hu, J. J. Kempinger, S. E. Snyder, S. G. DiMagno, *Org. Biomol. Chem*. **2017**, *15*, 2246–2252.
291. Y. Ly, W. Pu, Q. Chen, Q. Wang, J. Ni, Q. Zhang, *J. Org. Chem*. **2017**, *82*, 8282–8289.
292. D. A. Offermann, J. J. P. McKendrick, J. Sejberg, B. Mo, M. D. Holdom, B. A. Helm, R. J. Leatherbarrow, A. J. Beavil, B. J. Sutton, A. C. Spivey, *J. Org. Chem*. **2012**, *77*, 3197–3214.
293. G. T. Crisp, P. D. Turner, *Tetrahedron* **2000**, *56*, 407–415.
294. S. Liao, A. Porta, X. Cheng, X. Ma, G. Zanoni, L. Zhang, *Angew. Chem. Int. Ed*. **2018**, *130*, 8382–8386.
295. H. Shen, J. Fu, J. Gong, Z. Yang, *Org. Lett*. **2014**, *16*, 5588–5591.
296. C. Körner, P. Starkov, T. D. Sheppard, *J. Am. Chem. Soc*. **2010**, *132*, 5968–5969.
297. C. Morrill, R. H. Grubbs, *J. Org. Chem*. **2003**, *68*, 6031–6034.
298. X. Li, L. Liu, T. Huang, Z. Tang, C. Li, W. Li, T. Zhang, Z. Li, T. Chen, *Org. Lett*. **2021**, *23*, 3304–3309.
299. M. X. He, Z. Y. Mo, Z. Q. Wang, S. Y. Cheng, R. R. Xie, H. T. Tang, Y. M. Pan, *Org. Lett*. **2020**, *22*, 724–728.
300. W. Lu, Z. Shen, *Org. Lett*. **2019**, *21*, 142–146.

301. P. Dominguez-Molano, G. Bru, O. Salvado, R. J. Maza, Jorge J. Carbó, E. Fernández, *Chem. Commun*. **2021**, *57*, 13361–13364.
302. C. Feng, H. Wang, L. Xu, P. Li, *Org. Biomol. Chem*. **2015**, *13*, 7136–7139.
303. S. Liu, L. S. Liebeskind, *J. Am. Chem. Soc*. **2008**, *130*, 6918–6919.
304. P. A. Wender, A. B. Lesser, L. E. Sirois, *Angew. Chem. Int. Ed*. **2012**, *51*, 2736–2740.
305. Y. Liu, D. Ni, M. K. Brown, *J. Am. Chem. Soc*. **2022**, *144*, 18790–18796.
306. C . Zheng, D. Wang, S. S. Stahl, *J. Am. Chem. Soc*. **2012**, *134*, 16496–16499.
307. A. T. Parsons, T.D. Senecal, S.L. Buchwald, *Angew. Chem. Int. Ed*. **2012**, *51*, 2947–2950.
308. K. Norseeda, N. Chaisan, C. Thongsornkleeb, J. Tummatorn, S. Ruchirawat, *J. Org. Chem*. **2019**, *84*, 16222–16236.
309. T. Brégent, J. P. Bouillon, T. Poisson, *Chem. Eur. J*. **2021**, *27*, 13966–13970.
310. Y. Zhao, C. F. Liu, L. Q. H. Lin, A. S. C. Chan, M. J. Koh, *Angew. Chem. Int. Ed*. **2022**, *61*, e2022026.
311. D. P. Ojha, K. R. Prabhu, *Org. Lett*. **2015**, *17*, 18–21.
312. M. Aelterman, M. Sayes, P. Jubault, T. Poisson, *Chem. Eur. J*. **2021**, *27*, 8277–8282.
313. A. Music, C. M. Nuber, Y. Lemke, P. Spieß, D. Didier, *Org. Lett*. **2021**, *23*, 4179–4184.
314. T. Ueda, H. Konishi, K. Manabe, *Org. Lett*. **2012**, *14*, 5370–5373.
315. Y. Hu, W. Sun, T. Zhang, N. Xu, J. Xu, Y. Lan, C. Liu, *Angew. Chem. Int. Ed*. **2019**, *131*, 15960–15965.
316. C. W. Grathwol, N. Wössner, S. Swyter, A. C. Smith, E. Tapavicza, R. K. Hofstetter, A. Bodtke, M. Jung, A. Link, *Beilstein J. Org. Chem*. **2019**, *15*, 2170–2183.
317. Z. Liu, W. Wei, L. Xiong, Q. Feng, Y. Shi, N. Wang, L. Yu, *New J. Chem*. **2017**, *41*, 3172–3176.
318. C. Richardson, C. A. Reed, J. *Org. Chem*. **2007**, *72*, 4750–4755.
319. H. Cao, H. Jiang, H. Feng, J. Mun Chung Kwan, X. Liu, J. Wu, *J. Am. Chem. Soc*. **2018**, *140*, 16360–16367.
320. G. A. Molander, O. A. Argintaru, *Org. Lett*. **2014**, *16*, 1904–1907.

321. S. F. Pizzolato, M. Giannerini, P. H. Bos, M. Fañanás-Mastral, B. L. Feringa, *Chem. Commun*. **2015**, *51*, 8142–8145.
322. N. Kambe, Y. Moriwaki, Y. Fujii, T. Iwasaki, J. Terao, *Org. Lett*. **2011**, *13*, 4656–4659
323. R. Matsubara, T. F. Jamison, *Chem. Asian J*. **2011**, *6*, 1860–1875.
324. B. C. Van Veen, S. M. Wales, J. Clayden, *J. Org. Chem*. **2021**, *86*, 8538–8543.
325. K. Das, R. Shibuya, Y. Nakahara, N. Germain, T. Ohshima, K. Mashima, *Angew. Chem. Int. Ed*. **2012**, *51*, 150–154.
326. D. N. Prada Gori, C. Permingeat Squizatto, P. G. Cornier, C. M.L. Delpiccolo, *J. Org. Chem*. **2018**, *83*, 12798–12805.
327. J. Zhang, Y. Li, R. Xu, Y. Chen, *Angew. Chem. Int. Ed*. **2017**, *129*, 12793–12797.
328. A. Guérinot, A. Serra-Muns, C. Gnamm, C. Bensoussan, S. Reymond, J. Cossy, *Org Lett*. **2010**, *12*, 1808–1811.
329. A. Noble, D. W. C. MacMillan, J. *Am. Chem. Soc*. **2014**, *136*, 11602–11605.
330. J. Hu, B. Cheng, X. Yang, T. P. Loh, *Adv. Synth. Catal.* **2019**, *361*, 4902–4908.
331. D. Zhang, Z. L. Tang, X. H. Ouyang, R. J. Song, J. H. Li, *Chem. Commun*. **2020**, *56*, 14055–14058.
332. S. Yu, S. Liu, Y. Lan, B. Wan, X. Li, *J. Am. Chem. Soc*. **2015**, *137*, 1623–1631.
333. E. M. Woerly, S. M. Banik, E. N. Jacobsen, *J. Am. Chem. Soc*. **2016**, *138*, 13858–13861.
334. H. Y. Wang, L. J. Zhong, G. F. Lv, Y. Li, J. H. Li, *Org. Biomol. Chem*. **2020**, *18*, 5589–5593.
335. M. Zhang, L. Yang, C. Tian, M. Zhou, G. An, G. Li, *Org. Biomol. Chem*. **2019**, *17*, 2258–2264.
336. D. Mao, G. Hong, S. Wu, X. Liu, J. Yu, L. Wang, *Eur. J. Org. Chem*. **2014**, *2014*, 3009–3019.
337. Z. Wang, P. Li, H. Fu, Q. Dai, C. Hu, *Adv. Synth. Catal*. **2019**, *361*, 192–200.
338. S. Minakata, H. Miwa, K. Yamamoto, A. Hirayama, S. Okumura, *J. Am. Chem. Soc*. **2021**, *143*, 4112–4118.

339. A. Krasovskiy, C. Duplais, B. H. Lipshutz, *Org. Lett*. **2010**, *12*, 4742–4744.
340. C. A. Malapit, J. R. Bour, S. R. Laursen, M. S. Sanford, *J. Am. Chem. Soc*. **2019**, *141*, 17322–17330.
341. J. Polášek, J. Paciorek, J. Stošek, H. Semrád, M. Munzarová, C. Mazal, *J. Org. Chem*. **2020**, *85*, 6992–7000.
342. S. Eising, F. Lelivelt, K. M. Bonger, *Angew. Chem. Int. Ed*. **2016**, *128*, 12431–12435.
343. A. Music, A.N. Baumann, P. Spieß, A. Plantefol, T. C. Jagau, D. Didier, *J. Am. Chem. Soc*. **2020**, *142*, 4341–4348.
344. C. Cazorla, E. Métay, M. Lemaire, *Tetrahedron* **2011**, *67*, 8615–8621.
345. H. Huang, C. Yu, X. Li, Y. Zhang, Y. Zhang, X. Chen, P. S. Mariano, H. Xie, W. Wang, *Angew. Chem. Int. Ed*. **2017**, *129*, 8313–8317.
346. D. Haddenham, C. L. Bailey, C. Vu, G. Nepomuceno, S. Eagon, L. Pasumansky, B. Singaram, *Tetrahedron* **2011**, *67*, 576–583.
347. L. L. Anka-Lufford, M. R. Prinsell, D. J. Weix, *J. Org. Chem*. **2012**, *77*, 9989−10000.