Enantioselective NHC-Catalysed Redox [4+2]-Hetero-Diels-Alder Reactions using α-Aroyloxyaldehydes and Unsaturated Ketoesters

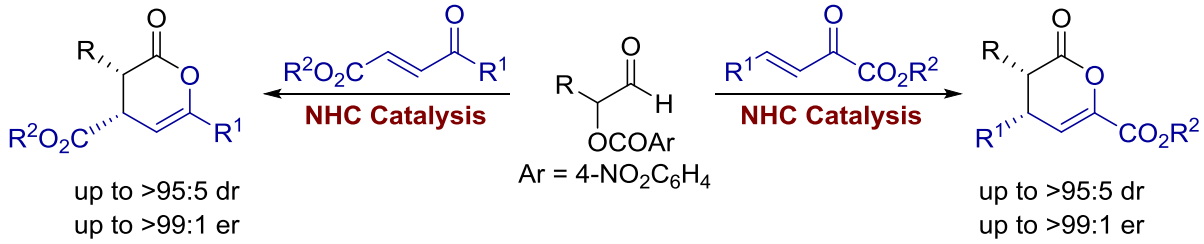
James E. Taylor,[a] Alyn T. Davies,[a] James J. Douglas,[a] Gwydion Churchill,[b] and Andrew D. Smith[a,*]

[a] EaStCHEM, School of Chemistry, University of St Andrews, North Haugh, St Andrews, KY16 9ST, U.K.

[b] AstraZeneca, Process Research and Development, Macclesfield, Cheshire, SK10 2NA, U.K.

E-mail: ads10@st-andrews.ac.uk

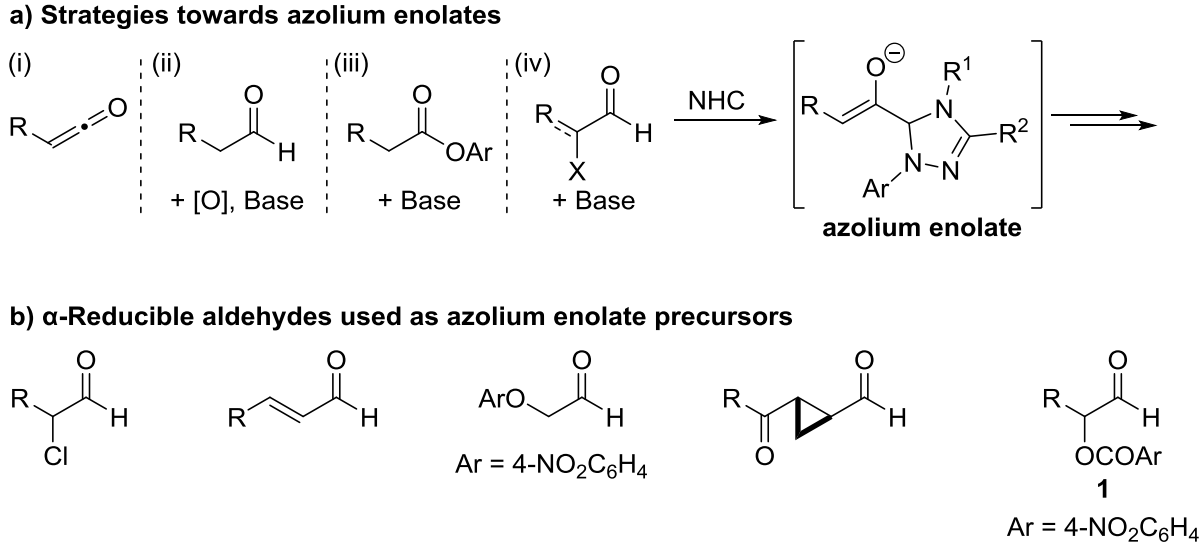
Abstract



N-Heterocyclic carbene (NHC)-catalysed redox [4+2]-hetero-Diels-Alder reactions of α-aroyloxyaldehydes with either β,γ-unsaturated α-ketoesters or α,β-unsaturated γ-ketoesters generates substituted *syn*-dihydropyranones in good yield with excellent enantioselectivity (up to >99:1 er). The product diastereoselectivity is markedly dependent upon the nature of the unsaturated enone substituent. The presence of either electron-neutral or electron-rich aryl substituents gives excellent diastereoselectivity (up to >99:5 dr), while electron-deficient aryl substituents give reduced diastereoselectivity. In these cases, the *syn*-dihydropyranone products are more susceptible to base-promoted epimerisation at the C(4)-position under the reaction conditions, accounting for the lower diastereoselectivity obtained.

1 Introduction

N-Heterocyclic carbenes (NHCs) are versatile organocatalysts that exhibit a wide range of reactivity.[1] Of the multiple activation modes accessible through NHC catalysis, the generation and use of azolium enolates has emerged as a powerful strategy for the enantioselective synthesis of complex small-molecules. A number of methods has been developed for the formation of azolium enolate intermediates (Scheme 1a). For example, addition of an NHC into a substituted ketene directly generates an azolium enolate,[2] while deprotonation of acyl azolium intermediates, themselves generated from either the reaction of NHCs with aldehydes under oxidative conditions[3] or the addition of NHCs into activated carboxylic esters,[4] also leads to enolate formation. Another common strategy for azolium enolate formation is the addition of NHCs into aldehydes bearing α-reducible functional groups, which subsequently undergo a redox process to form the desired enolate.[5-10] Examples of such α-reducible aldehydes include α-chloroaldehydes,[6] enals,[7] α-aryloxyaldehydes,[8] and formyl cyclopropanes[9] (Scheme 1b). We have previously reported that bench-stable α-aroyloxyaldehydes **1** are also efficient redox azolium enolate precursors.[10]

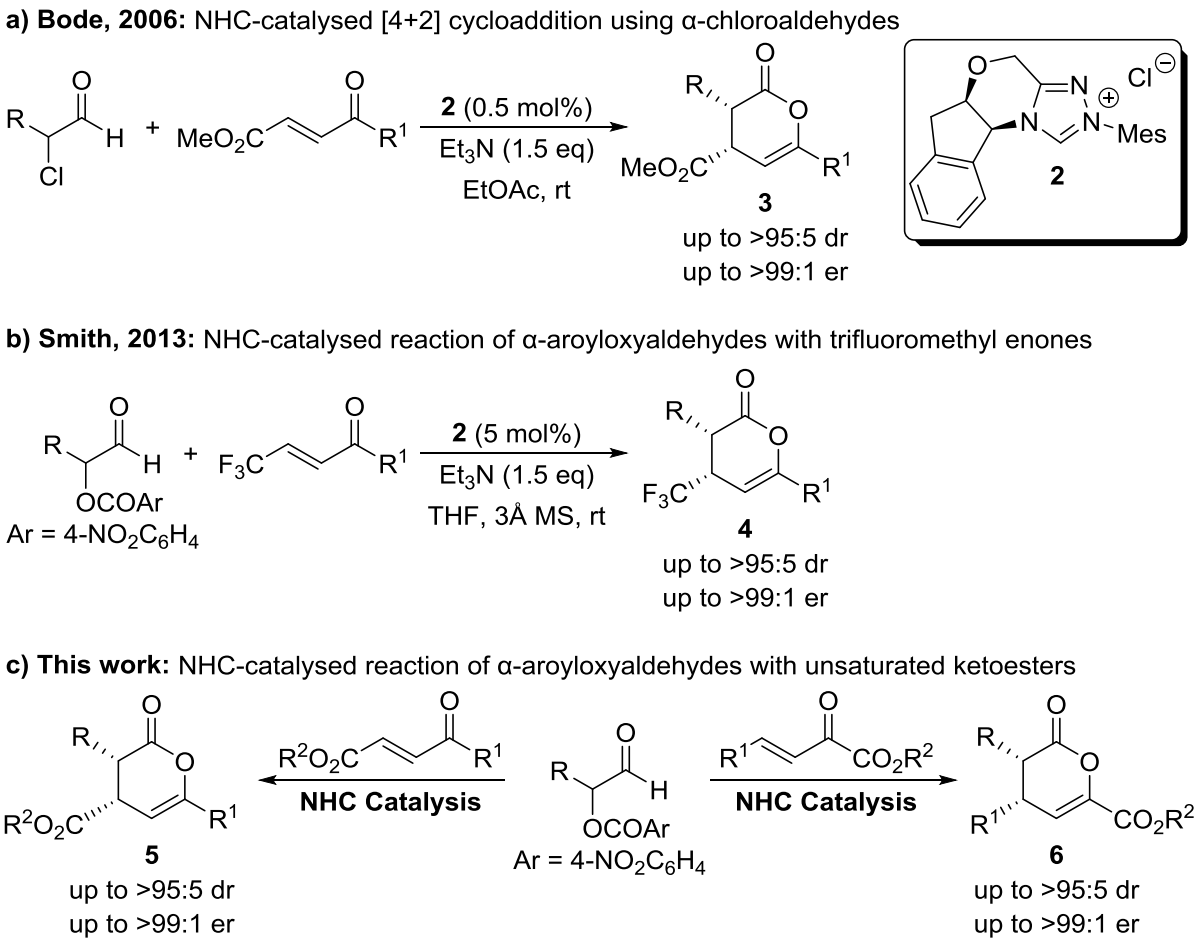


Scheme 1. Generation of azolium enolate intermediates.

Azolium enolates generated from NHCs and α-reducible aldehydes react with a variety of electrophiles to generate a diverse array of products. Of particular relevance is the reaction of azolium enolates with substituted enones in enantioselective [4+2]-hetero-Diels-Alder processes to form stereodefined dihydropyranone products. For example, Bode and co-workers

demonstrated that azolium enolates generated from α-chloroaldehydes react with both β,γ-unsaturated α-ketoesters and α,β-unsaturated γ-ketoesters to form *syn*-dihydropyranones **3** with excellent enantioselectivity (Scheme 2a).[6b] In this case, the use of unsaturated ketoesters bearing either alkyl or electron-neutral/rich aryl substituents generally formed the product dihydropyranones in high diastereoselectivity. Notably, the presence of electron-deficient aryl (4-BrC_6H_4) or heteroaryl (2-furyl) substituents lead to a decrease in diastereoselectivity, although the origin of the reduced dr was not further investigated. This methodology was subsequently extended to the use of the bench-stable sodium bisulfate adducts of α-chloroaldehydes under biphasic conditions, allowing the use of unsubstituted chloroacetaldehyde sodium bisulfite to form dihydropyranones containing a single stereocentre.[6c] The NHC-catalysed redox hetero-Diels-Alder reaction of enals with unsaturated ketoesters has also been reported to proceed with high levels of stereoselectivity.[7d]

α-Aroyloxyaldehydes have previously been used as azolium enolate precursors in NHC-catalysed [4+2]-hetero-Diels-Alder reactions with various trifluoromethyl enones (Scheme 2b)[10b,d] and α,β-unsaturated trichloromethyl ketones[10e] to form functionalised



Scheme 2. NHC-catalysed redox [4+2]-hetero-Diels-Alder reactions.

syn-dihydropyranones **4** with high diastereo- and enantioselectivity. Azolium enolates generated from α-aroyloxyaldehydes also undergo [2+2][10f] and [3+2]-cycloadditions,[10g] as well as enantioselective α-aminations to from *N*-aryl amino acid derivatives.[10c]

Herein, the NHC-catalysed redox hetero-Diels-Alder reaction of bench-stable α-aroyloxyaldehydes with both β,γ-unsaturated α-ketoesters and α,β-unsaturated γ-ketoesters is reported to form *syn*-dihydropyranones (**5** and **6)** with excellent enantioselectivity (Scheme 2c). The effect of various aryl substituents on the unsaturated ketoesters on the reaction diastereoselectivity is assessed, with control experiments performed to determine the origin of the reduced product diastereoselectivity observed in some cases.

2 Results and discussion

2.1 Reaction optimisation

First, the reaction of azolium enolates derived from α-aroyloxyaldehydes[11] with β,γ-unsaturated α-ketoesters was studied. Treating α-aroyloxyaldehyde **7** and α-ketoester **8** with

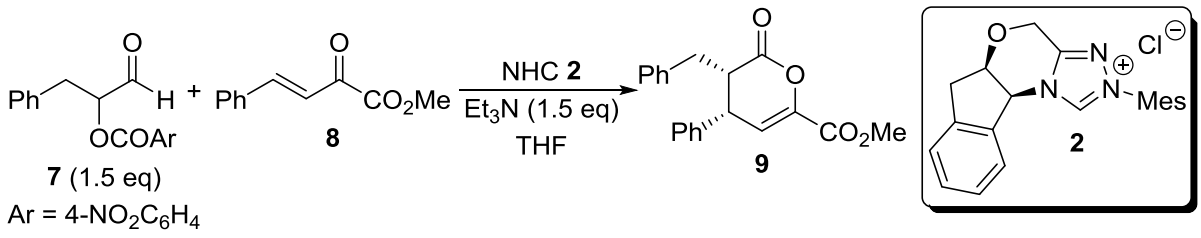
NHC precatalyst **2** (20 mol%) and Et_3N (1.5 eq) in THF at room temperature gave dihydropyranone **9** in a promising 50% yield and 92:8 dr with excellent enantioselectivity (>99:1 er) for the major *syn*-diastereoisomer (Table 1, entry 1).[12] Lowering the catalyst loading led to increased reaction times and decreased diastereoselectivity, although the enantioselectivity for both diastereoisomers was high (Table 1, entries 2 and 3). Decreasing the reaction temperature to –78 °C led to an increase in diastereoselectivity (> 99:1 dr), but gave lower conversion into the desired product (Table 1, entry 4). Starting the reaction at 0 °C and allowing it to warm slowly to room temperature using 10 mol% **2** gave an excellent compromise between reactivity and stereoselectivity, with *syn*-dihydropyranone **9** isolated in 93% yield with >95:5 dr and >99:1 er (Table 1, entry 5). The relative and absolute configuration of the major product was assigned by analogy to that of a known derivative formed during investigation of the reaction substrate scope (*vide infra*).

2.2 Reaction scope with β,γ-unsaturated α-ketoesters

The scope of the NHC-catalysed redox reaction of various α-aroyloxyaldehydes with a range of β,γ-unsaturated α-ketoesters was studied under the previously optimised conditions (Table 2). The reaction worked well with different alkyl α-aroyloxyaldehyde substituents, forming *syn*-dihydropyranones **10** and **11** in good yields with excellent levels of stereoselectivity (up to >95:5 dr and >99:1 er). The reaction with β,γ-unsaturated α-ketoesters bearing electron-rich

Table 1

Reaction optimisation



Entry	NHC (mol%)	T (°C)	Time (h)	Conversion (%)[a,b]	dr[a]	er[c]
1	**2** (20)	rt	5	>90 (50)	92:8	>99:1
2	**2** (10)	rt	12	>90	85:15	N/D
3	**2** (1)	rt	48	>90	76:24	>99:1 (*syn*) >99:1 (*anti*)
4	**2** (10)	–78	12	45	>95:5	N/D

5	**2** (10)	0 to rt	12	>90 (93)	>95:5	>99:1

[a] Determined by ^{1}H NMR analysis of the crude reaction mixture.

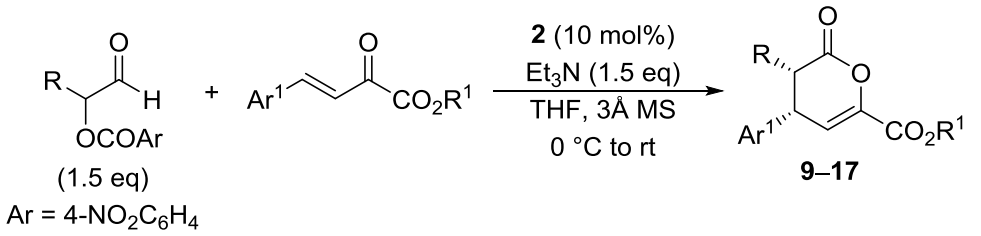
[b] Isolated yield after purification by column chromatography in parentheses.

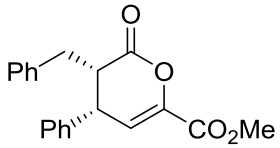
[c] er of major diastereoisomer determined by HPLC analysis.

aromatic substituents (4-MeC_6H_4 and 4-$MeOC_6H_4$) gave dihydropyranones **12-15** in high yields, but with slightly reduced levels of *syn*-diastereoselectivity (≥91:9 dr) compared with the reaction with phenyl substituted α-ketoester **8**. However, in each case the major *syn*-diastereoisomer was formed with high levels of enantioselectivity (≥96:4 er). The relative configuration of *syn*-dihydropyranone **12** could be confirmed through comparison of its spectroscopic data with the literature,[6b] while the absolute configuration was confirmed through comparison of its specific rotation [96:4 er, $[\alpha]_D^{20}$ +299.4 (*c* 0.5, $CHCl_3$)] with the reported value [(3*S*,4*S*)-**12**, 98.5:1.5 er, $[\alpha]_D^{20}$ +310.3 (*c* 1.0, $CHCl_3$)].[6b] The incorporation of a more electron-deficient aryl bromine substituent led to a modest 42% yield of dihydropyranone **16** in a reduced 89:11 dr, although the enantioselectivity remained high (99:1 er). An extended aromatic 2-naphthyl substituent was also successfully incorporated, forming **17** in 48% yield with good stereoselectivity (94:6 dr, >99:1 er).

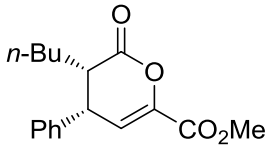
Table 2

Scope of the reaction using β,γ-unsaturated α-ketoesters[a–c]

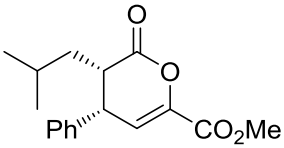




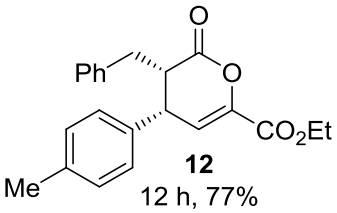
9
12 h, 93%
>95:5 dr, >99:1 er



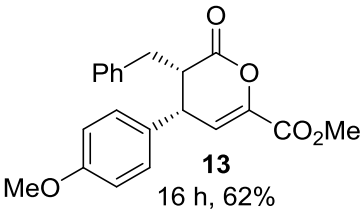
10
3 h, 69%
>95:5 dr, 98:2 er



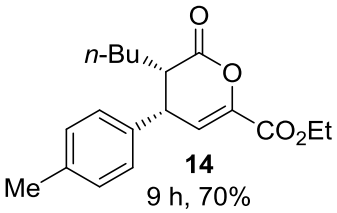
11
24 h, 63%
>95:5 dr, >99:1 er



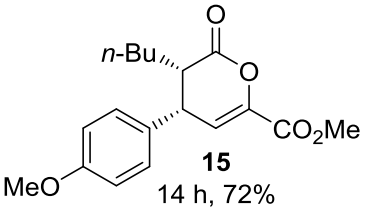
12
12 h, 77%
94:6 dr, 96:4 er



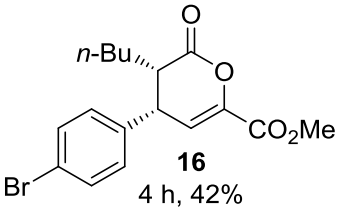
13
16 h, 62%
91:9 dr, >99:1 er



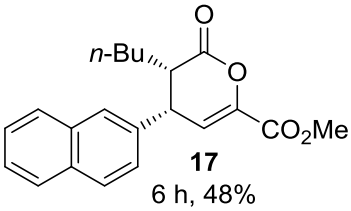
14
9 h, 70%
92:8 dr, >99:1 er



15
14 h, 72%
92:8 dr, >99:1 er



16
4 h, 42%
89:11 dr, 99:1 er



17
6 h, 48%
94:6 dr, >99:1 er

[a] Isolated yields of single diastereoisomers (>95:5 dr) after column chromatography.

[b] dr determined by ^{1}H NMR analysis of the crude reaction mixtures.

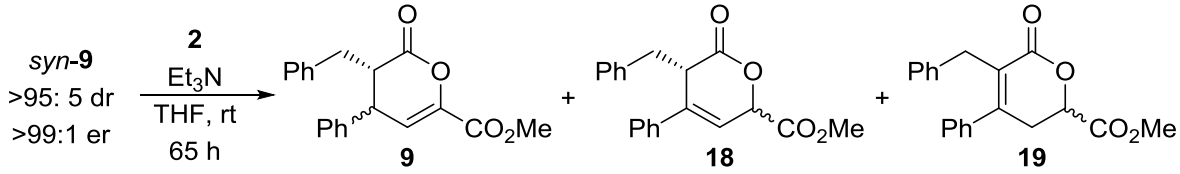
[c] er of major diastereoisomer determined by HPLC analysis.

To investigate the reduced diastereoselectivity observed in certain cases, a series of control experiments was performed (Table 3). Treating isolated *syn*-dihydropyranone **9** (>95:5 dr) with NHC precatalyst **2** (15 mol%) and Et_3N (15 mol%) resulted in epimerisation, returning **9** in 89:11 dr after 65 h at room temperature (Table 3, entry 1). Furthermore, significant amounts of products **18** and **19** arising from double bond isomerisation were also observed, indicating that the initial deprotonation leading to both epimerisation and isomerisation is most likely to occur at the C(4) position in conjugation with the enone.[13,14] The use of Et_3N (15 mol%) alone resulted in reduced amounts of both epimerisation (93:7 dr after 65 h) and isomerisation, suggesting that the free NHC is capable of deprotonating **9** (Table 3, entry 2). Treating **9** with

a stoichiometric amount of Et_3N (1 eq) resulted in increased levels of isomerisation into both **18** and **19** (Table 3, entry 3), while increased reaction times led to further isomerisation and increased epimerisation of the remaining dihydropyranone **9** (Table 3, entry 4). The NHC and base-promoted epimerisation and isomerisation of the product *syn*-dihydropyranones could therefore account for the reduced diastereoselectivity and lower yields obtained in certain instances (Table 2).

Table 3

Investigation into the epimerisation of *syn*-**9**



Entry	**2** (mol%)	Et_3N (mol%)	**9**/**18**/**19**[a]	dr **9**[a]	dr **18**[a]
1	15	15	50:30:20	89:11	59:41
2	–	15	92:8:0	93:7	55:45
3	–	100	48:37:15	94:6	60:40
4[b]	–	100	27:14:59	80:20	52:48

[a] Determined by ^{1}H NMR analysis of the crude reaction mixtures.

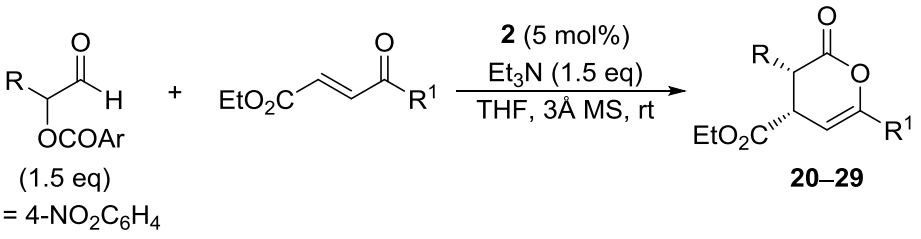
[b] Entry 3 re-subjected to the same conditions for a further 120 h.

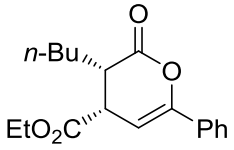
2.3 Reactions with α,β-unsaturated γ-ketoesters

Next, the use of α,β-unsaturated γ-ketoesters in the NHC-catalysed redox process with α-aroyloxyaldehydes was investigated (Table 4). In this case, only 5 mol% NHC precatalyst **2** was required alongside Et_3N (1.5 eq) in THF at room temperature to form the corresponding *syn*-dihydropyranones in high yields and with excellent stereoselectivity. α-Aroyloxyaldehydes bearing alkyl and benzyl substituents were well tolerated, forming products **20**-**22** in high yields with excellent diastereo- and enantioselectivity (>95: 5 dr, >99:1 er). The relative and absolute configuration of **21** was confirmed through comparison of its spectroscopic data and specific rotation [>99:1 er, $[\alpha]_D^{20}$ +173 (*c* 1.05 in $CHCl_3$)] with the literature [>99:1 er, $[\alpha]_D^{20}$ +107 (*c* 0.82, $CHCl_3$)],[6c] with all other products in this series assigned by analogy. The reaction using an α,β-unsaturated γ-ketoester bearing a methyl substituent needed to be heated at 40 °C

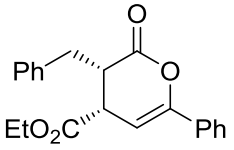
Table 4

Scope of the reaction using α,β-unsaturated γ-ketoesters[a–c]

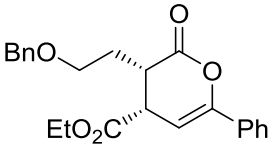




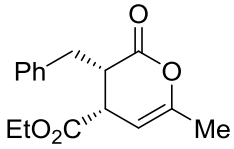
20
5 h, 85%
>95:5 dr, >99:1 er



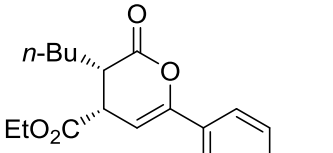
21
2 h, 79%[d]
>95:5 dr, >99:1 er



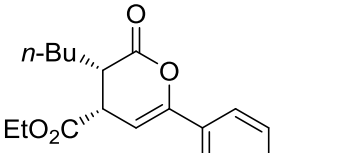
22
9 h, 85%
90:10 dr, >99:1 er



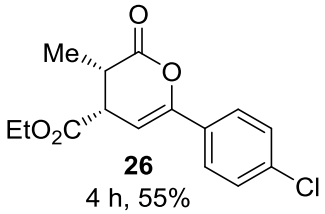
23
7 h, 65%[e]
>95:5 dr, 98.5:1.5 er



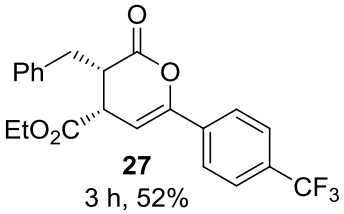
24
6 h, 80%
>95:5 dr, >99:1 er



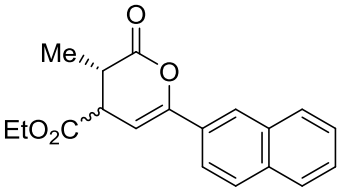
25
6 h, 90%
>95:5 dr, >99:1 er



26
4 h, 55%
80:20 dr, >99:1 er



27
3 h, 52%
80:20 dr, >99:1 er



syn-**28** + *anti*-**29**
24 h, 50:50 dr
syn-**28**: 32%, >99:1 er
anti-**29**: 35%, >99:1 er

[a] Isolated yields of single diastereoisomers (>95:5 dr) after column chromatography.

[b] dr determined by ^{1}H NMR analysis of the crude reaction mixtures.

[c] er of major diastereoisomer determined by HPLC analysis.

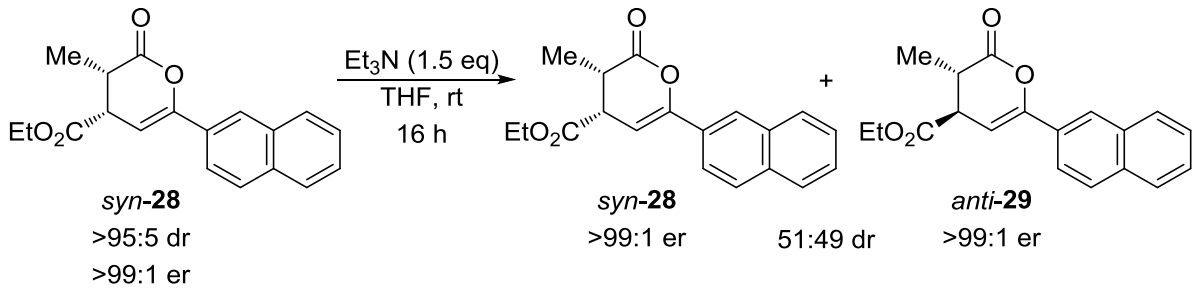
[d] 10 mol% **2** used.

[e] Reaction performed at 40 °C using Cs_2CO_3 instead of Et_3N.

and required the use of Cs_2CO_3 as base to form *syn*-dihydropyranone **23** in 65% yield as a single diastereoisomer in high enantioselectivity. The absolute configuration of **23** could also be confirmed through comparison of its specific rotation [98.5:1.5 er, $[\alpha]_D^{20}$ +271 (*c* 0.32 in $CHCl_3$)] with the literature [>99:1 er, $[\alpha]_D^{20}$ +251 (*c* 0.93, $CHCl_3$)].[6c] The use of α,β-unsaturated γ-ketoester bearing electron-rich aryl substituents worked particularly well, forming *syn*-dihydropyranones **24** and **25** in high yield with excellent levels of stereoselectivity (>95:5 dr,

>99:1 er). However, the incorporation of aryl groups containing electron-withdrawing substituents led to the formation of **26** and **27** in lower yields with reduced diastereoselectivity (80:20 dr), although the enantioselectivity remained high in both cases (>99:1 er). A similar reduction in diastereoselectivity was observed by Bode and co-workers in the related NHC-catalysed redox reaction of an α-chloroaldehyde with an α,β-unsaturated γ-ketoester bearing a 4-bromo substituted aryl ring.[6b] The reaction of a methyl substituted α-aroyloxyaldehyde with a 2-naphthyl substituted α,β-unsaturated γ-ketoester under the previously optimised conditions gave the largest reduction in diastereoselectivity, with *syn*-**28** and *anti*-**29** formed as a 50:50 mixture, although both diastereoisomers were obtained in excellent enantioselectivity (>99:1 er).

The dramatic reduction in diastereoselectivity observed with the 2-naphthyl substituted α,β-unsaturated γ-ketoester was probed by treating isolated *syn*-dihydropyranone **28** (>95:5 dr) with Et_3N (1.5 eq) in THF at room temperature (Scheme 3). After 16 hours, the dihydropyranone had epimerized into a 50:50 mixture of diastereoisomers, with both obtained in >99:1 er. This is consistent with the result from the initial NHC-catalysed process, suggesting that the initially formed *syn*-diastereoisomer is epimerized under the basic reaction conditions. In this case, it is likely that epimerisation occurs at the C(4) position and that the presence of conjugated electron-deficient aryl substituents in the C(6) position increases the propensity for deprotonation, which accounts for the reduced diastereoselectivity observed in these cases. However, selective epimerisation at the C(3) position adjacent to the lactone cannot be unambiguously ruled out.

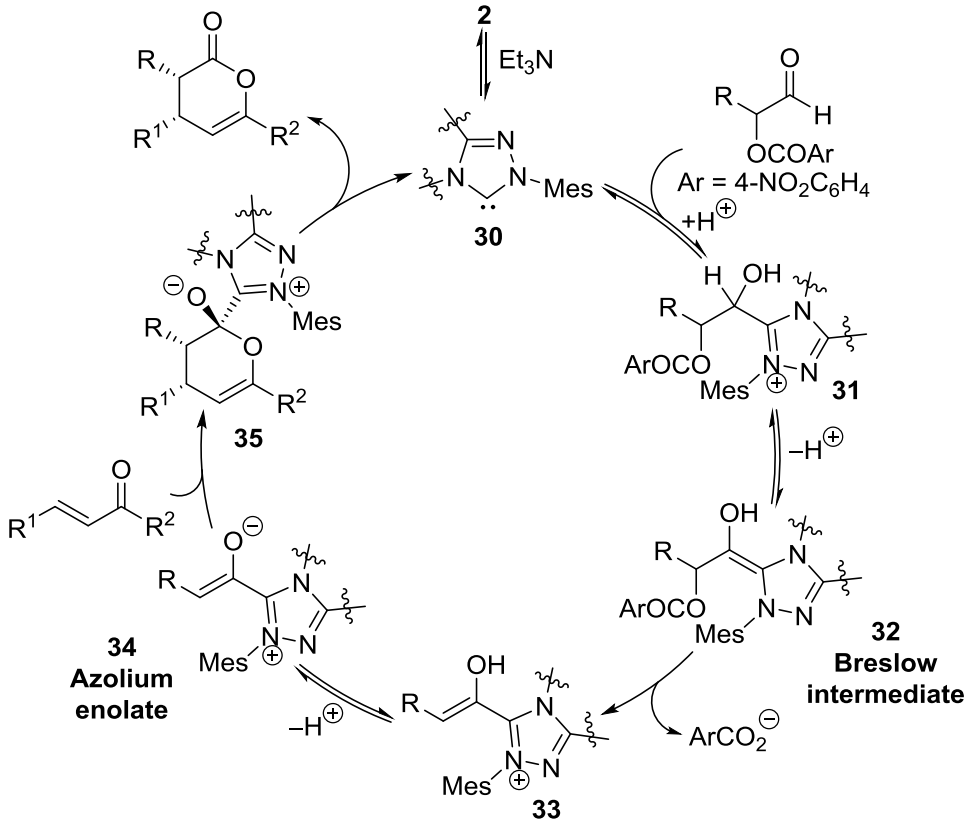


Scheme 3. Base-promoted epimerisation of *syn*-**28**

2.4 Proposed mechanism

The proposed reaction mechanism is shown in Scheme 4. Initially, the catalytically active free NHC is generated through deprotonation of NHC precursor **2**. Nucleophilic addition of the free NHC **30** into the α-aroyloxyaldehyde generates adduct **31**, which is likely to be the

catalytic resting state.[10b] Reversible deprotonation of **31** transiently forms Breslow intermediate **32** that can eliminate 4-nitrobenzoate. The resulting enol **33** can be deprotonated to form the key azolium enolate intermediate **34**, which can undergo an enantioselective asynchronous *endo*-hetero-Diels-Alder reaction with an appropriate unsaturated ketoester. Finally, elimination from intermediate **35** releases the product *syn*-dihydropyranone and regenerates the free NHC catalyst. This mechanistic proposal is consistent with the computational studies from Bode and co-workers on related NHC-catalysed [4+2]-hetero-Diels-Alder processes.[15]



Scheme 4. Proposed reaction mechanism

3 Conclusion

α-Aroyloxyaldehydes are efficient azolium enolate precursors in enantioselective NHC-catalysed [4+2] hetero-Diels-Alder reactions with unsaturated ketoesters. Reactions using either β,γ-unsaturated α-ketoesters or α,β-unsaturated γ-ketoesters form the corresponding *syn*-dihydropyranone products with generally high diastereoselectivity and excellent enantioselectivity. In cases where the unsaturated ketoester bears an electron-deficient aryl substituent, the initially-formed *syn*-dihydropyranones are more susceptible to epimerisation at

the C(4)-position under the reaction conditions, which lowers the observed diastereoselectivity of the products.

4 Experimental

4.1 General

Anhydrous reactions were carried out in flame-dried glassware under an inert atmosphere (N_2 or Ar) using standard vacuum line techniques. Anhydrous THF and Et_2O were obtained after passing through an alumina column (Mbraun SPS-800). Petrol is defined as petroleum ether 40-60 °C. All other solvents and commercial reagents were used as received without further purification. α-Aroyloxyaldehydes were prepared according to previously reported procedures.[10]

Room temperature (rt) refers to 20-25 °C and a temperature of 0 °C was obtained using an ice/water bath. Reaction involving heating were performed using DrySyn blocks and a contact thermocouple. Under reduced pressure refers to the use of a rotary evaporator with vacuum controller.

Analytical thin layer chromatography was performed on pre-coated aluminium plates (Kieselgel 60 F_{254} silica) and visualisation was achieved using ultraviolet light (254 nm) and/or staining with a 1% aqueous $KMnO_4$ solution. Flash column chromatography was performed on Kieselgel 60 silica in the solvent system stated.

Melting points were recorded on an Electrothermal 9100 melting point apparatus, (dec) refers to decomposition. Optical rotations were measured on a Perkin Elmer Precisely/Model-341 polarimeter operating at the sodium D line with a 100 mm path cell at 20 °C.

HPLC analyses were obtained on either a Gilson HPLC consisting of a Gilson 305 pump, Gilson 306 pump, Gilson 811C dynamic mixer, Gilson 805 manometric module, Gilson 401C dilutor, Gilson 213XL sample injector and sample detection was performed with a Gilson 118 UV/vis detector or a Shimadzu HPLC consisting of a DGU-20A5 degasser, LC-20AT liquid chromatography SIL-20AHT autosampler, CMB-20A communications bus module, SPD-M20A diode array detector and a CTO-20A column oven. Separation was achieved using Chiralcel OD-H and OJ-H columns or a Chiralpak AD-H column. All HPLC traces were compared with an authentic racemic spectrum prepared in analogous fashion using (±)-**2**.

Infrared spectra (ν_{max}) were recorded on a Shimadzu IRAffinity-1 Fourier transform IR spectrophotometer using either thin film or solid using Pike MIRacle ATR accessory.

^{1}H, ^{13}C{^{1}H}, and ^{19}F{^{1}H} NMR spectra were acquired on either a Bruker Avance 300 (^{1}H 300 MHz; ^{13}C{^{1}H} 75 MHz; ^{19}F{^{1}H} 282 MHz), a Bruker Avance II 400 (^{1}H 400 MHz; ^{13}C{^{1}H} 100 MHz; ^{19}F{^{1}H} 376 MHz), or a Bruker Ultrashield 500 (^{1}H 500 MHz) spectrometer at room temperature in the deuterated solvent stated. All chemical shifts are quoted in parts per million (ppm) relative to the residual solvent peak. All coupling constants, *J*, are quoted in Hz. Multiplicities are indicated as s (singlet), d (doublet), t (triplet), q (quartet), m (multiplet), and multiples thereof. The abbreviation Ar denotes aromatic and *app* denotes apparent.

High resolution mass spectrometry (*m/z*) data was acquired by electrospray ionisation (ESI), atmospheric pressure chemical ionisation (APCI) or nanospray ionisation (NSI) at the EPSRC UK National Mass Spectrometry Facility at Swansea University.

4.2 General procedure for the synthesis of β,γ-unsaturated α-ketoesters

Part 1: Based upon a literature procedure procedure,[16] KOH (1.5 eq) in MeOH (6 M) was added to a solution of pyruvic acid (1.0 eq), the required aryl aldehyde (1.0 eq) and MeOH (12 M) at 0 °C. The first equivalent of KOH solution was added dropwise over 30 min, the rest was added as one portion. The reaction mixture was heated at 40 °C for 1 h before being cooled to 0 °C and stirred overnight. The precipitate was collected by filtration and washed with cold MeOH (×2) and Et_2O before being dried under vacuum to give the desired β,γ-unsaturated α-ketoacid potassium salt.

Part 2: Based upon a literature procedure procedure,[17] acetyl chloride (11.5 eq) was added dropwise to the appropriate alcohol (0.2 M) at 0 °C before the required potassium salt (1.0 eq) was added. The reaction mixture was warmed to rt and stirred for 2 h before being heated at reflux for 6 h. The solution was cooled to rt, concentrated under reduced pressure and then partitioned between CH_2Cl_2 and H_2O. The layers were separated and the aqueous layer extracted with CH_2Cl_2 (×2). The combined organic phases were washed with a saturated $NaHCO_3$ solution and H_2O before being dried over Na_2SO_4, filtered and concentrated to give the crude β,γ-unsaturated α-ketoester that was purified by column chromatography.

4.2.1 (*E*)-Methyl 2-oxo-4-phenylbut-3-enoate 8

Following General Procedure 4.2 (part 1), KOH (16.8 g, 300 mmol) in MeOH (60 mL), pyruvic acid (13.8 mL, 200 mmol) and benzaldehyde (20.4 mL, 200 mmol) in MeOH (15 mL) were reacted to give potassium (*E*)-2-oxo-4-phenylbut-3-enoate (39.0 g, 91%) as a yellow solid with spectroscopic data in accordance with the literature.[18] mp 246–248 °C {Lit.[18] 248 °C}; ^{1}H

NMR (400 MHz, D_2O) δ_H: 6.78 (1H, d, *J* 15.0, PhCH=C*H*), 7.34–7.42 (3H, m, Ar(3,4,5)*H*), 7.39 (1H, d, *J* 15.0, C PhC*H*=CH), 7.57–7.61 (2H, m, Ar(2,6)*H*).

Following General Procedure 4.2 (part 2), potassium (*E*)-2-oxo-4-phenylbut-3-enoate (7.48 g, 35 mmol) and acetyl chloride (28.6 mL, 402 mmol) in MeOH (200 mL) were reacted. The crude was purified by column chromatography (90:10 petrol : EtOAc), then recrystallised from MeOH to give **8** (1.16 g, 17%) as a yellow crystalline solid with spectroscopic data in accordance with the literature.[18] mp 69–71 °C {Lit.[18] 69–70 °C}; ^{1}H NMR (300 MHz, $CDCl_3$) δ_H: 3.94 (3H, s, OCH_3), 7.38 (1H, d, *J* 16.1, *H*C=C), 7.42–7.49 (3H, m, Ar*H*), 7.61–7.67 (2H, m, Ar*H*), 7.89 (1 H, d, *J* 16.2, *H*C=C).

4.2.2 (*E*)-Ethyl 2-oxo-4-(*p*-tolyl)but-3-enoate 36

Following General Procedure 4.2 (part 1), KOH (1.40 g, 24.9 mmol) in MeOH (5 mL), pyruvic acid (1.15 mL, 16.6 mmol) and *p*-tolualdehyde (1.96 mL, 16.6 mmol) in MeOH (2 mL) were reacted to give potassium (*E*)-2-oxo-4-(*p*-tolyl)but-3-enoate (2.78 g, 12.2 mmol, 73%) as yellow solid, with spectroscopic data in accordance with the literature.[18] mp 242–244 °C (dec); ^{1}H NMR (400 MHz, D_2O) δ_H: 2.28 (3H, s, ArCH_3), 6.74 (1H, d, *J* 16.4, ArCH=C*H*), 7.23 (2H, d, *J* 8.1, Ar*H*), 7.51 (2H, d, *J* 8.2, Ar*H*), 7.59 (1H, d, *J* 16.4, ArC*H*=CH).

Following General Procedure 4.2 (part 2), potassium (*E*)-2-oxo-4-(*p*-tolyl)but-3-enoate (1.00 g, 4.38 mmol) and acetyl chloride (3.58 mL, 50.4 mmol) in ethanol (30 mL) were reacted. The crude was purified by column chromatography (95:5 petrol : EtOAc) to give **36** (0.560 g, 58%) as a yellow solid, with spectroscopic data in accordance with the literature.[17] mp 40–42 °C {Lit.[17] 47–48 °C}; ^{1}H NMR (300 MHz, $CDCl_3$) δ_H: 1.41 (3H, t, *J* 7.1, OCH_2CH_3), 2.40 (3H, s, ArCH_3), 4.39 (2H, q, *J* 7.1, OCH_2CH_3), 7.23 (2H, d, *J* 7.9, Ar*H*), 7.32 (1H, d, *J* 16.1, ArCH=C*H*), 7.53 (2H, d, *J* 8.2, Ar*H*), 7.84 (1H, d, *J* 16.1, ArC*H*=CH).

4.2.3 (*E*)-Methyl 4-(4-methoxyphenyl)-2-oxobut-3-enoate 37

Following General Procedure 4.2 (part 1), KOH (1.11 g, 19.8 mmol) in MeOH (4 mL), pyruvic acid (0.917 mL, 13.2 mmol) and *p*-anisaldehyde (1.80 g, 1.61 mL, 13.2 mmol) in MeOH (1.5 mL) were reacted to give potassium (*E*)-4-(4-methoxyphenyl)-2-oxobut-3-enoate (2.31 g, 72%) as a yellow solid, with spectroscopic data in accordance with the literature.[16] mp 250–252 °C {Lit.[16] 248 °C}; ^{1}H NMR (400 MHz, D_2O) δ_H: 6.66 (1H, d, *J* 16.4, CH=C*H*), 6.95 (2H, d, *J* 8.8, Ar*H*), 7.50–7.69 (3H, m, Ar*H* and C*H*=CH).

Following General Procedure 4.2 (part 2), potassium (*E*)-2-oxo-4-(4-methoxyphenyl)but-3-enoate (2.00 g, 8.19 mmol) and acetyl chloride (6.70 mL, 94.2 mmol) in MeOH (60 mL) were

reacted. The crude was purified by column chromatography (85:15 petrol : EtOAc) to give **37** (1.37 g, 76%) as a yellow crystalline solid, with spectroscopic data in accordance with the literature.[18] mp 95–96 °C {Lit.[18] 99–100 °C}; ^{1}H NMR (300 MHz, $CDCl_3$) δ_H: 3.80 (3H, s, OC*H*$_3$), 3.86 (3H, s, OC*H*$_3$), 6.87 (2H, d, *J* 8.8, Ar*H*), 7.19 (1H, d, *J* 16.0, ArCH=C*H*), 7.54 (2H, d, *J* 8.5, Ar*H*), 7.79 (1H, d, *J* 16.0, ArC*H*=CH).

4.2.4 (*E*)-Methyl 4-(4-fluorophenyl)-2-oxobut-3-enoate 38

Following General Procedure 4.2 (part 1), KOH (1.36 g, 24.2 mmol) in MeOH (6 mL), pyruvic acid (1.12 mL, 16.1 mmol) and 4-fluorobenzaldehyde (2.00 g, 1.73 mL, 16.1 mmol) in MeOH (2 mL) were reacted to give potassium (*E*)-4-(4-fluorophenyl)-2-oxobut-3-enoate (2.67 g, 71%) as a yellow solid, with spectroscopic data in accordance with the literature.[19] mp 205–208 °C (dec); ^{1}H NMR (500 MHz, D_2O) δ_H: 6.73 (1H, d, *J* 16.3, ArCH=C*H*), 7.11 (2H, t, *J* 8.2, ArC(2)*H*), 7.59 (1H, d, *J* 16.4, ArC*H*=CH), 7.64 (2H, dd, *J* 7.4, 5.2, ArC(3)*H*); ^{19}F NMR (376 MHz, D_2O) δ_F: –109.0 (ArC(4)*F*).

Following General Procedure 4.2 (part 2), potassium (*E*)-4-(4-fluorophenyl)-2-oxobut-3-enoate (1.00 g, 4.31 mmol) and acetyl chloride (3.53 mL, 49.6 mmol) in MeOH (40 mL) were reacted. The crude was purified by column chromatography (95:5 petrol : EtOAc) to give (*E*)-methyl 4-(4-fluorophenyl)-2-oxobut-3-enoate (0.320 g, 36%) as a yellow crystalline solid, with spectroscopic data in accordance with the literature.[20] mp 86–87 °C; ν_{max} (solid) 1722 (C=O), 1690 (C=O); ^{1}H NMR (400 MHz, $CDCl_3$) δ_H: 3.87 (3H, s, OC*H*$_3$), 7.06 (2H, t, *J* 8.6, ArC(3)*H*), 7.25 (1H, dd, *J* 16.2, 0.6, CH=C*H*), 7.58 (2H, dd, *J* 8.7, 5.4, ArC(2)*H*), 7.78 (1H, d, *J* 16.1, C*H*=CH); ^{19}F NMR (376 MHz, $CDCl_3$) δ_F: –107.3 (tt, *J* 8.1, 5.5, C(4)*F*); ^{13}C{^{1}H} NMR (101 MHz, $CDCl_3$) δ_C: 53.1 (O*C*H$_3$), 116.4 (d, *J* 22.0, *C*(3)), 120.1 (d, *J* 2.2, ArCH=*C*H), 130.3 (d, *J* 3.1, *C*(1)), 131.2 (d, *J* 8.8, *C*(2)), 147.2 (Ar*C*H=CH), 162.5 (*C*O$_2$), 164.7 (d, *J* 253.9, *C*(4)), 182.1 (CH=CH*C*O); HRMS (NSI$^+$) $C_{11}H_{10}O_3F$ $[M+H]^+$ found 209.0610, requires 209.0608 (+0.7 ppm).

4.2.5 (*E*)-Methyl 4-(4-bromophenyl)-2-oxobut-3-enoate 39

Following General Procedure 4.2 (part 1), KOH (4.55 g, 81.1 mmol) in MeOH (15 mL), pyruvic acid (3.81 mL, 54.1 mmol) and 4-bromobenzaldehyde (10.0 g, 54.1 mmol) in MeOH (15 mL) were reacted to give potassium (*E*)-2-oxo-4-(4-bromophenyl)but-3-enoate (15.9 g, 84%) as a yellow solid, with spectroscopic data in accordance with the literature.[18] mp 240 °C (dec) {Lit.[18] 233 °C}; ^{1}H NMR (400 MHz, D_2O) δ_H: 6.91 (1H, d, *J* 17.1, C(3)*H*), 7.59–7.60 (2H, m, Ar(3,5)*H*), 7.62 (1H, d, *J* 17.1, C(4)*H*), 7.65–7.68 (2H, m, Ar(2,6)*H*).

Following General Procedure 4.2 (part 2), potassium (*E*)-2-oxo-4-(4-bromophenyl)but-3-enoate (2.00 g, 6.82 mmol) and acetyl chloride (5.57 mL, 78.4 mmol) in MeOH (40 mL) were reacted. The crude was purified by column chromatography (95:5 petrol : EtOAc) to give **39** (1.21 g, 66%) as a yellow crystalline solid, with spectroscopic data in accordance with the literature.[18] mp 109–112 °C {Lit.[18] 120 °C}; ^{1}H NMR (400 MHz, $CDCl_3$) δ_H: 3.87 (3H, s, OC*H*$_3$), 7.31 (1H, d, *J* 16.1, ArCH=C*H*), 7.43 (2H, d, *J* 8.5, Ar*H*), 7.50 (2H, d, *J* 8.5, Ar*H*), 7.74 (1H, d, *J* 16.1, ArC*H*=CH).

4.2.6 (*E*)-Methyl 4-(naphthalen-2-yl)-2-oxobut-3-enoate 40

Following General Procedure 4.2 (part 1), KOH (1.08 g, 19.2 mmol) in MeOH (3 mL), pyruvic acid (0.890 mL, 12.8 mmol) and 2-naphthaldehyde (2.00 g, 12.8 mmol) in MeOH (3 mL) were reacted to give potassium (*E*)-4-(naphthalen-2-yl)-2-oxobut-3-enoate (2.46 g, 73%) as a yellow solid, with spectroscopic data in accordance with the literature.[18] mp >320 °C {Lit.[18] 270–272 °C (dec)}; ^{1}H NMR (400 MHz, D_2O) δ_H: 6.85 (1H, d, *J* 16.5, ArCH=C*H*), 7.50 (2H, s, Ar*H*), 7.65–7.74 (2H, m, Ar*H*, and ArC*H*=CH), 7.81–7.86 (3H, m, Ar*H*), 7.99 (1H, s, Ar(1)*H*).

Following General Procedure 4.2 (part 2), potassium (*E*)-4-(naphthalen-2-yl)-2-oxobut-3-enoate (1.00 g, 3.78 mmol) and acetyl chloride (3.08 mL, 43.5 mmol) in MeOH (30 mL) were reacted. The crude was purified by column chromatography (95:5 petrol : EtOAc) to give **40** (0.570 g, 63%) as a yellow solid, with spectroscopic data in accordance with the literature.[18] mp 94–96 °C {Lit.[18] 70–72 °C}; ^{1}H NMR (400 MHz, $CDCl_3$) δ_H: 3.96 (3H, s, OC*H*$_3$), 7.49 (1H, d, *J* 16.1, ArCH=C*H*), 7.52–7.61 (2H, m, Ar*H*), 7.77 (1H, dd, *J* 8.6, 1.8, Ar*H*), 7.84–7.93 (3H, m, Ar*H*), 8.02–8.09 (2H, m, ArC*H*=CH and Ar*H*).

4.3 General procedure for the NHC-catalysed redox hetero-Diels-Alder reaction with β,γ-unsaturated α-ketoesters

The appropriate α-aroyloxyaldehyde (1.5 eq), β,γ-unsaturated α-ketoester (1.0 eq) and NHC precatalyst **2** (10 mol%) were dissolved in anhydrous THF (0.075 M) in a sealed vial containing 3Å molecular sieves. The solution was cooled to 0 °C before Et_3N (1.5 eq.) was added. The reaction stirred, allowing to warm to rt, until complete by TLC analysis. The mixture was diluted with EtOAc and washed successively with 1 M HCl, saturated $NaHCO_3$ and brine. The organic layer was dried with $MgSO_4$, filtered and concentrated under reduced pressure to give the crude product, which was purified by column chromatography.

4.3.1 (3*S*,4*S*)-Methyl 3-benzyl-2-oxo-4-phenyl-3,4-dihydro-2*H*-pyran-6-carboxylate 9

Following General Procedure 4.3, 1-oxo-3-phenylpropan-2-yl 4-nitrobenzoate **7** (50 mg, 0.17 mmol), (*E*)-methyl 2-oxo-4-phenylbut-3-enoate **8** (21.0 mg, 0.11 mmol), NHC precatalyst **2** (4.0 mg, 11 μmol), Et_3N (23 μL, 0.17 mmol) and THF (3 mL) were reacted for 12 h. The crude (>95:5 dr) was purified by column chromatography (90:10 petrol : EtOAc) to give **9** (51 mg, 93%) as a colourless solid. mp 106–107 °C; $[\alpha]_D^{20}$ +398 (*c* 0.23, $CHCl_3$); Chiral HPLC analysis, Chiralpak AD-H (90:10 hexane : IPA, flow rate 1.0 mLmin^{-1}, 254 nm, 30 °C) t_R (*R*,*R*) 18.0 min, t_R (*S*,*S*) 27.8 min, >99:1 er; ν_{max} (KBr, cm^{-1}) 2956, 2925, 1765, 1628, 1664, 1602, 1495, 1435, 1316, 1100; ^{1}H NMR (400 MHz, $CDCl_3$) δ_H: 2.33 (1H, dd, *J* 10.6, 15.8, C(3)C*H*^{A}H^B), 3.16–3.23 (2H, m, C(3)CH^A*H*^{B} and C(3)*H*), 3.55 (1H, t, *J* 6.8, C(4)*H*), 3.77 (3H, OC*H*$_3$), 6.58 (1H, d, *J* 6.7, C(5)*H*), 6.93–7.00 (4H, m, C(3)Ar*H*), 7.15–7.26 (6H, m, C(3)Ar*H* and C(3)CH$_2$Ar*H*); ^{13}C{^{1}H} NMR (75 MHz, $CDCl_3$) δ_C: 32.1 (C(3)C*H*$_2$), 40.6 (C(3)*H*), 44.8 (C(4)*H*), 52.7 (OC*H*$_3$), 118.8 (*C*(5)), 126.8 (C(3)CH$_2$Ar*C*(4)), 128.4 (C(4)Ar*C*(4)), 128.4 (Ar*C*), 128.7 (Ar*C*), 128.9 (Ar*C*), 129.2 (Ar*C*), 135.8 (*C*Ph-1), 138.1 (C(3)CH$_2$Ar*C*(1)), 141.9 (*C*(6)), 161.0 (*C*O$_2$Me), 168.5 (*C*(2)); HRMS (ESI+) $C_{20}H_{22}O_4N$ [M+NH$_4$]$^+$ found 340.1544, requires 340.1543 (+ 0.2 ppm).

4.3.2 (3*S*,4*S*)-Methyl 3-butyl-2-oxo-4-phenyl-3,4-dihydro-2*H*-pyran-6-carboxylate 10

Following General Procedure 4.3, 1-oxohexan-2-yl 4-nitrobenzoate (50 mg, 0.19 mmol), (*E*)-methyl 2-oxo-4-phenylbut-3-enoate **8** (25.2 mg, 0.13 mmol), NHC precatalyst **2** (4.2 mg, 10.0 μmol), Et_3N (28 μL, 0.19 mmol) and THF (3 mL) were reacted for 3 h. The crude (>95:5 dr) was purified by column chromatography (95:5 petrol : EtOAc) to give **10** (26 mg, 69%) as a colourless oil. $[\alpha]_D^{20}$ +156 (*c* 0.15, $CHCl_3$); Chiral HPLC analysis, Chiralpak AD-H (95:5 hexane : IPA, flow rate 1.0 mLmin^{-1}, 220 nm) t_R (*R*,*R*) 16.2 min, t_R (*S*,*S*) 18.3 min, 98:2 er; ν_{max} (ATR, cm^{-1}) 2954, 1773, 1734, 1661, 1454, 1437, 1323, 1259, 1045; ^{1}H NMR (300 MHz, $CDCl_3$) δ_H: 0.81 (3H, t, *J* 7.1, CH$_2$C*H*$_3$), 1.08–1.40 (5H, m, C*H*$_2$ ×2 and C(3)C*H*^{A}H^B), 1.60–1.70 (1H, m, C(3)CH^A*H*^{B}), 2.79 (1H, d, *J* 6.9, C(3)*H*), 3.79 (1H, t, *J* 6.7, C(4)*H*), 3.83 (3H, s, OC*H*$_3$), 6.68 (1H, d, *J* 6.4, C(5)*H*), 7.06 (2H, dt, *J* 1.8, 5.8, ArC(2)*H*), 7.23–7.29 (3H, m, ArC(3)*H* and ArC(4)*H*); ^{13}C{^{1}H} NMR (100 MHz, $CDCl_3$) 13.9 (*C*H$_3$), 22.5 (*C*H$_2$), 26.0 (*C*H$_2$), 29.4 (*C*H$_2$), 41.5 (*C*(4)), 43.4 (*C*(3)), 52.7 (O*C*H$_3$), 118.4 (*C*(5)), 128.1 (*C*PhH-2,6), 128.1 (*C*Ph-4), 129.1 (Ar*C*(3)), 136.0 (Ar*C*(1)), 142.1 (*C*(6)), 161.1 (*C*O$_2$Me), 168.8 (*C*(2)); HRMS (ESI+) $C_{17}H_{24}O_4N$ [M+NH$_4$]$^+$ found 306.1702, requires 306.1700 (+ 0.7 ppm).

4.3.3 (3*S*,4*S*)-Methyl 3-isobutyl-2-oxo-4-phenyl-3,4-dihydro-2*H*-pyran-6-carboxylate 11

Following General Procedure 4.3, 4-methyl-1-oxopentan-2-yl 4-nitrobenzoate **7** (133 mg, 0.50 mmol), (*E*)-methyl 2-oxo-4-phenylbut-3-enoate **8** (63.0 mg, 0.33 mmol), NHC precatalyst **2** (12.0 mg, 33 μmol), Et_3N (70 μL, 0.50 mmol) and THF (5 mL) were reacted for 24 h. The crude (>95:5 dr) was purified by column chromatography (95:5 petrol : EtOAc) to give **11** (60 mg, 63%) as a colourless oil. $[\alpha]_D^{20}$ +279 (*c* 0.14, $CHCl_3$); Chiral HPLC analysis, Chiralpak AD-H (95:5 hexane : IPA, flow rate 1.0 mLmin^{-1}, 220 nm) t_R (*R*,*R*) 11.9 min, t_R (*S*,*S*) 13.0 min, >99:1 er; ν_{max} (KBr, cm^{-1}) 2959, 1769, 1708, 1661, 1317, 1265, 1094, 1082; ^{1}H NMR (300 MHz, $CDCl_3$) δ_H: 0.83 (3H, d, *J* 6.6, C*H*$_3$), 0.88 (3H, d, *J* 6.6, C*H*$_3$), 1.04 (1H, *app* dt, *J* 7.0, 14.0, *i*-BuC*H*), 1.56 (2H, dt, *J* 7.0, 13.9, C(3)C*H*^{A}H^B), 1.72 (1H, dd, *J* 7.0, 14.0, C(3)C*H*$_a$H$_a$), 2.93 (1H, app q, *J* 6.9, C(3)*H*), 3.77 (1H, t, *J* 6.7, C(4)*H*), 3.87 (3H, s, OC*H*$_3$), 6.72 (1H, d, *J* 6.4, C(5)*H*), 7.07–7.10 (2H, dt, *J* 1.8, 5.8, ArC(2)*H*), 7.27–7.34 (3H, m, ArC(3)*H* and ArC(4)*H*); ^{13}C{^{1}H} NMR (100 MHz, $CDCl_3$) δ_C: 22.2 ((*C*H$_3$)$_2$CH), 22.5 ((*C*H$_3$)$_2$CH), 25.2 ((CH$_3$)$_2$*C*H), 35.2 (C(3)*C*H$_2$), 41.2 (*C*(3)), 41.7 (*C*(4)), 52.7 (O*C*H$_3$), 118.4 (*C*(5)), 128.1 (Ar*C*(2)), 128.1 (Ar*C*C(4)), 129.1 (Ar*C*C(3)), 136.0 (Ar*C*(1)), 142.1 (*C*(6)), 161.1 (*C*O$_2$Me), 168.9 (*C*(2)); HRMS (ESI+) $C_{17}H_{24}O_4N$, $[M+NH_4]^+$ found 306.1704; requires 306.1700 (+ 1.4 ppm).

4.3.4 (3*S*,4*S*)-Ethyl 3-benzyl-2-oxo-4-(*p*-tolyl)-3,4-dihydro-2*H*-pyran-6-carboxylate 12

Following General Procedure 4.3, 1-oxo-3-phenylpropan-2-yl 4-nitrobenzoate **7** (202 mg, 0.675 mmol), (*E*)-ethyl 4-(*p*-tolyl)-2-oxobut-3-enoate **36** (98.2 mg, 0.450 mmol), NHC precatalyst **2** (16.6 mg, 45.0 μmol), Et_3N (94.1 μL, 0.675 mmol) and THF (10 mL) were reacted for 12 h. The crude (94:6 dr) was purified by column chromatography (95:5 petrol : EtOAc) to give **12** (122 mg, 77%) as a pale yellow oil, with spectroscopic data in accordance with the literature.[6b] $[\alpha]_D^{20}$ +299.4 (*c* 0.5, $CHCl_3$) {Lit.[6b] $[\alpha]_D^{20}$ +310.3 (*c* 1.0, $CHCl_3$)}; Chiral HPLC analysis, Chiralcel OD-H (90:10 hexane : IPA, flow rate 0.5 mLmin^{-1}, 254 nm, 30 °C) t_R (3*R*,4*R*): 19.7 min, t_R (3*S*,4*S*): 23.5 min, 96:4 er; ν_{max} (film, cm^{-1}) 2981, 1773, 1732; ^{1}H NMR (400 MHz, $CDCl_3$) δ_H: 1.34 (3H, t, *J* 7.1, OCH$_2$C*H*$_3$), 2.36 (3H, s, C(4)ArC(4)C*H*$_3$), 2.43 (1H, dd, *J* 15.8, 10.5, C(3)*H*), 3.22–3.32 (2H, m, C(3)C*H*$_2$), 3.60 (1H, t, *J* 6.8, C(4)*H*), 4.31 (2H, q, *J* 7.1, OC*H*$_2$CH$_3$), 6.66 (1H, d, *J* 6.7, C(5)*H*), 6.93 (2H, d, *J* 8.1, C(3)CH$_2$ArC(2)*H*), 7.09 (2H, d, *J* 6.8, C(4)ArC(2)*H*), 7.16 (2H, d, *J* 7.8, C(4)ArC(3)*H*), 7.21–7.36 (3H, m, C(3)CH$_2$ArC(3)*H* and C(3)CH$_2$ArC(4)*H*); ^{13}C{^{1}H} (100 MHz, $CDCl_3$) δ_C: 14.2 (OCH$_2$*C*H$_3$), 21.1

(C(4)ArC(4)*C*H$_3$), 32.1 (C(3)*C*H$_2$), 40.2 (*C*(4)), 44.9 (*C*(3)), 61.9 (O*C*H$_2$CH$_3$), 118.8 (*C*(5)), 126.7 (C(3)CH$_2$Ar*C*(4)), 128.3 (C(3)CH$_2$Ar*C*(3)), 128.6 (C(3)CH$_2$Ar*C*(2)), 129.0 (C(4)Ar*C*(2)), 129.9 (C(4)Ar*C*(3)), 132.7 (C(4)Ar*C*(1)), 138.1 (C(4)Ar*C*(4)), 138.2 (C(3)CH$_2$Ar*C*(4)), 141.9 (*C*(6)), 160.5 (*C*O$_2$Et), 168.7 (*C*(2)).

4.3.5 (3*S*,4*S*)-Methyl 3-benzyl-4-(4-methoxyphenyl)-2-oxo-3,4-dihydro-2*H*-pyran-6-carboxylate 13

Following General Procedure 4.3, 1-oxo-3-phenylpropan-2-yl 4-nitrobenzoate **7** (202 mg, 0.675 mmol), (*E*)-methyl 4-(4-methoxyphenyl)-2-oxobut-3-enoate **37** (99.1 mg, 0.450 mmol), NHC precatalyst **2** (16.6 mg, 45.0 μmol), Et$_3$N (94.1 μL, 0.675 mmol) and THF (10 mL) were reacted for 16 h. The crude (91:9 dr) was purified by column chromatography (90:10 petrol : EtOAc) to give **13** (98.3 mg, 62%) as a pale yellow oil. $[\alpha]_D^{20}$ +277.3 (*c* 0.5, CHCl$_3$); Chiral HPLC analysis, Chiralcel OD-H (90:10 hexane : IPA, flow rate 0.5 mLmin^{-1}, 220 nm, 30 °C) t_R (3*R*,4*R*): 40.7 min, t_R (3*S*,4*S*): 45.0 min, >99:1 er; ν_{max} (film, cm^{-1}) 2955, 1771, 1734; ^{1}H NMR (300 MHz, CDCl$_3$) δ_H: 2.41 (1H, dd, *J* 15.7, 10.6, C(3)*H*), 3.21–3.30 (2H, m, C(3)C*H*$_2$), 3.58 (1H, t, *J* 6.7, C(4)*H*), 3.80 (3H, s, OC*H*$_3$), 3.84 (3H, s, CO$_2$C*H*$_3$), 6.65 (1H, d, *J* 6.8, C(5)*H*), 6.86 (2H, d, *J* 8.8, C(4)ArC(2)*H*), 6.93 (2H, d, *J* 8.8, C(4)ArC(3)*H*), 7.04–7.11 (2H, m, C(3)CH$_2$ArC(2)*H*), 7.20–7.35 (3H, m, C(3)CH$_2$ArC(3)*H* and C(3)CH$_2$ArC(4)*H*); ^{13}C{^{1}H} NMR (100 MHz, CDCl$_3$) δ_C: 30.9 (C(3)*C*H$_2$), 38.7 (*C*(4)), 43.9 (*C*(3)), 51.6 (CO$_2$*C*H$_3$), 54.3 (C(4)ArC(4)O*C*H$_3$), 113.5 (C(4)Ar*C*(2)), 118.1 (*C*(5)), 125.7 (C(3)CH$_2$Ar*C*(1)), 126.4 (C(4)Ar*C*(1)), 127.6 (C(3)CH$_2$Ar*C*(3)), 127.9 (C(3)CH$_2$Ar*C*(2)), 128.9 (C(4)Ar*C*(3)), 137.1 (C(3)CH$_2$Ar*C*(1)), 140.5 (*C*(6)), 158.5 (C(4)Ar*C*(4)), 160.0 (*C*O$_2$Me), 167.6 (*C*(2)); HRMS (NSI$^+$) $C_{21}H_{24}O_5N_1$ $[M+NH_4]^+$ found 370.1655, requires 370.1649 (+1.6 ppm).

4.3.6 (3*S*,4*S*)-Ethyl 3-butyl-2-oxo-4-(*p*-tolyl)-3,4-dihydro-2*H*-pyran-6-carboxylate 14

Following General Procedure 4.3, 1-oxohexan-2-yl 4-nitrobenzoate (200 mg, 0.750 mmol), (*E*)-ethyl 2-oxo-4-(*p*-tolyl)but-3-enoate **36** (109 mg, 0.500 mmol), NHC precatalyst **2** (18.4 mg, 50.0 μmol), Et$_3$N (105 μL, 0.750 mmol) and THF (10 mL) were reacted for 9 h. The crude (92:8 dr) was purified by column chromatography (95:5 petrol : EtOAc) to give **14** (110 mg, 70%) as a pale yellow oil. $[\alpha]_D^{20}$ +249.2 (*c* 0.5, CHCl$_3$); Chiral HPLC analysis, Chiralpak AD-H (95:5 hexane : IPA, flow rate 1 mLmin^{-1}, 254 nm, 30 °C) t_R (3*S*,4*S*): 11.3 min, t_R (3*R*,4*R*): 13.7 min, >99:1 er; ν_{max} (film, cm^{-1}) 2957, 1773, 1732; ^{1}H NMR (400 MHz, CDCl$_3$) δ_H: 0.78 (3H, t, *J* 7.2, CH$_2$C*H*$_3$), 1.04–1.38 (7H, m, (C*H*$_2$)$_2$ and OCH$_2$C*H*$_3$), 1.54–1.71 (2H, m, C*H*$_2$), 2.24 (3H, s, ArC(4)C*H*$_3$), 2.73 (1H, q, *J* 7.0, C(3)*H*), 3.70 (1H, t, *J* 6.8, C(4)*H*), 4.24 (2H, q, *J*

7.1, OC*H*$_2$CH$_3$), 6.62 (1H, d, *J* 6.4, C(5)*H*), 6.91 (2H, d, *J* 8.1, ArC(2)*H*), 7.04 (2H, d, *J* 7.8, ArC(3)*H*); ^{13}C{^{1}H} NMR (100 MHz, $CDCl_3$) δ_C: 13.9 (OCH$_2$*C*H$_3$), 14.2 (CH$_2$*C*H$_3$), 21.1 (ArC(4)*C*H$_3$), 22.5 (*C*H$_2$), 26.0 (*C*H$_2$), 29.4 (*C*H$_2$), 41.1 (*C*(4)), 43.4 (*C*(3)), 61.9 (O*C*H$_2$CH$_3$), 118.4 (*C*(5)), 127.9 (Ar*C*(2)), 129.8 (Ar*C*(3)), 132.9 (Ar*C*(1)), 137.9 (Ar*C*(4)), 142.1 (*C*(6)), 160.6 (*C*O$_2$Et), 169.0 (*C*(2)); HRMS (NSI$^+$) $C_{19}H_{28}O_4N$ $[M+NH_4]^+$ found 334.2019, requires 334.2013 (+1.8 ppm).

4.3.7 (3*S*,4*S*)-Methyl 3-butyl-4-(4-methoxyphenyl)-2-oxo-3,4-dihydro-2*H*-pyran-6-carboxylate 15

Following General Procedure 4.3, 1-oxohexan-2-yl 4-nitrobenzoate (200 mg, 0.750 mmol), (*E*)-methyl 4-(4-methoxyphenyl)-2-oxobut-3-enoate **37** (110 mg, 0.500 mmol), NHC precatalyst **2** (18.4 mg, 50.0 μmol), Et$_3$N (105 μL, 0.750 mmol) and THF (10 mL) were reacted for 14 h. The crude (92:8 dr) was purified by column chromatography (95:5 petrol : EtOAc) to give **15** (114 mg, 72%) as a pale yellow oil. $[\alpha]_D^{20}$ +245.1 (*c* 0.5, $CHCl_3$); Chiral HPLC analysis, Chiralpak AD-H (90:10 hexane : IPA, flow rate 0.5 mLmin^{-1}, 220 nm, 30 °C) t_R (3*S*,4*S*): 30.5 min, t_R (3*R*,4*R*): 32.6 min, >99:1 er; ν_{max} (film, cm^{-1}) 2955, 1771, 1734; ^{1}H NMR (300 MHz, $CDCl_3$) δ_H: 0.84 (3H, t, *J* 7.1, CH$_2$C*H*$_3$), 1.09–1.43 (5H, m, (C*H*$_2$)$_2$ and C(3)C*H*^{A}H^B), 1.58–1.76 (1H, m, C(3)CH^A*H*^{B}), 2.78 (1H, q, *J* 6.9, C(3)*H*), 3.73–3.80 (4H, m, ArC(4)OC*H*$_3$ and C(4)*H*), 3.85 (3H, s, CO$_2$C*H*$_3$), 6.69 (1H, d, *J* 6.5, C(5)*H*), 6.83 (2H, d, *J* 8.7, ArC(2)*H*), 7.00 (2H, d, *J* 8.7, ArC(3)*H*); ^{13}C{^{1}H} NMR (75 MHz, $CDCl_3$) δ_C: 12.8 (CH$_2$*C*H$_3$), 21.4 (*C*H$_2$), 24.9 (*C*H$_2$), 28.3 (*C*H$_2$), 39.6 (*C*(4)), 42.5 (*C*(3)), 51.6 (CO$_2$*C*H$_3$), 54.3 (ArC(4)O*C*H$_3$), 113.4 (Ar*C*(2)), 117.7 (*C*(5)), 126.7 (Ar*C*(1)), 128.1 (Ar*C*(3)), 140.8 (*C*(6)), 158.3 (Ar*C*(4)), 160.1 (*C*O$_2$Me), 167.9 (*C*(2)); HRMS (NSI$^+$) $C_{18}H_{26}O_5N$ $[M+NH_4]^+$ found 336.1812, requires 336.1805 (+1.9 ppm).

4.3.8 (3*S*,4*S*)-Methyl 4-(4-bromophenyl)-3-butyl-2-oxo-3,4-dihydro-2*H*-pyran-6-carboxylate 16

Following General Procedure 4.3, 1-oxohexan-2-yl-4-nitrobenzoate (200 mg, 0.750 mmol), (*E*)-methyl 4-(4-bromophenyl)-2-oxobut-3-enoate **39** (135 mg, 0.500 mmol), NHC precatalyst **2** (18.4 mg, 50.0 μmol), Et$_3$N (105 μL, 0.750 mmol) and THF (10 mL) were for 4 h. The crude (89:11 dr) was purified by column chromatography (95:5 petrol : EtOAc) to give **16** (77.1 mg, 42%) as a pale yellow oil. $[\alpha]_D^{20}$ +205.3 (*c* 0.5, $CHCl_3$); Chiral HPLC analysis, Chiralpak AD-H (95:5 hexane : IPA, flow rate 1 mLmin^{-1}, 220 nm, 30 °C) t_R (3*S*,4*S*): 15.1 min, t_R (3*R*,4*R*): 17.7 min, 99:1 er; ν_{max} (film, cm^{-1}) 2955, 1773, 1732; ^{1}H NMR (300 MHz, $CDCl_3$) δ_H: 0.78–

1.00 (3H, m, CH_2CH_3), 1.06–1.47 (5H, m, $(CH_2)_2$ and C(3)CH^AH^B), 1.54–1.77 (1H, m, C(3)CH^AH^B), 2.82 (1H, q, *J* 7.0, C(3)*H*), 3.79 (1H, t, *J* 6.7, C(4)*H*), 3.87 (3H, s, ArC(4)OCH_3), 6.67 (1H, d, *J* 6.4, C(5)*H*), 6.97 (2H, d, *J* 8.4, ArC(3)*H*), 7.44 (2H, d, *J* 8.5, ArC(2)*H*); $^{13}C\{^1H\}$ NMR (75 MHz, $CDCl_3$) δ_C: 12.8 (CH_2CH_3), 21.4 (CH_2), 24.9 (CH_2), 28.3 (CH_2), 39.7 (*C*(4)), 42.2 (*C*(3)), 51.7 (CO_2CH_3), 116.6 (*C*(5)), 121.1 (Ar*C*(4)), 128.7 (Ar*C*(3)), 131.3 (Ar*C*(2)), 134.0 (Ar*C*(1)), 141.3 (*C*(6)), 159.8 (CO_2Me), 167.4 (*C*(2)); HRMS (NSI^+) $C_{17}H_{23}BrO_5N$ $[M+NH_4]^+$ found 384.0813, requires 384.0805 (+2.1 ppm).

4.3.9 (3*S*,4*S*)-Methyl 3-butyl-4-(naphthalen-2-yl)-2-oxo-3,4-dihydro-2*H*-pyran-6-carboxylate 17

Following General Procedure 4.3, 1-oxohexan-2-yl 4-nitrobenzoate (200 mg, 0.750 mmol), (*E*)-methyl 4-(naphthalen-2-yl)-2-oxobut-3-enoate **40** (120 mg, 0.500 mmol), NHC precatalyst **2** (18.4 mg, 50.0 μmol), Et_3N (105 μL, 0.750 mmol) and THF (10 mL) were reacted for 6 h. The crude (94:6 dr) was purified by column chromatography (95:5 petrol : EtOAc) to give **17** (81.7 mg, 48%) as a colourless solid. mp 99–101 °C; $[\alpha]_D^{20}$ +297.0 (*c* 0.5, $CHCl_3$); Chiral HPLC analysis, Chiralpak AD-H (95:5 hexane : IPA, flow rate 1 mLmin^{-1}, 254 nm, 30 °C) t_R (3*R*,4*R*): 22.0 min, t_R (3*S*,4*S*): 25.0 min, >99:1 er; ν_{max} (solid) 2951, 1757, 1736; ^1H NMR (400 MHz, $CDCl_3$) δ_H: 0.83 (3H, t, *J* 7.3, CH_2CH_3), 1.11–1.49 (5H, m, $(CH_2)_2$ and C(3)CH^AH^B), 1.63–1.78 (1H, m, C(3)CH^AH^B), 2.90 (1H, q, *J* 7.0, C(3)*H*), 3.88 (3H, s, CO_2CH_3), 3.99 (1H, t, *J* 6.7, C(4)*H*), 6.77 (1H, d, *J* 6.3, C(5)*H*), 7.19 (1H, dd, *J* 8.5, 1.9, Ar*H*), 7.44–7.52 (2H, m, Ar*H*), 7.57 (1H, d, *J* 1.8, ArC(2)*H*), 7.74–7.85 (3H, m, Ar*H*); $^{13}C\{^1H\}$ NMR (75 MHz, $CDCl_3$) δ_C: 12.8 (CH_3CH_2), 21.4 (CH_2), 25.0 (CH_2), 28.4 (CH_2), 40.6 (*C*(4)), 42.4 (*C*(3)), 51.7 (CO_2CH_3), 117.2 (*C*(5)), 124.5 (Ar*C*(8)), 125.3 (Ar*C*), 125.5 (Ar*C*), 126.1 (Ar*C*(2)), 126.6 (Ar*C*(6)), 126.8 (Ar*C*), 127.7 (Ar*C*(2a)), 128.0 (Ar*C*), 131.9 (Ar*C*(1)), 132.4 (Ar*C*(6a)), 141.1 (*C*(5)), 163.3 (CO_2CH_3), 167.7 (*C*(2)); HRMS (NSI^+) $C_{21}H_{26}O_4N_1$ $[M+NH_4]^+$ found 356.1862, requires 356.1856 (+1.6 ppm).

4.4 General procedure for the synthesis of α,β-unsaturated γ-ketoesters

Based upon a literature procedure,[21] periodic acid (1 eq.) was added portionwise to a solution of (+)-diethyl L-tartrate (1 eq.) in anhydrous Et_2O (0.5 M). The solution was stirred at rt for 3 h before being filtered into a dried two-necked round-bottomed flask containing $MgSO_4$ (1.0 g / 7 mL Et_2O), washing with THF (1 mL / 0.8 mL EtO). The resulting solution was cooled to 0 °C before the appropriate phosphorane (1.5 eq.) was added in one portion. The reaction was stirred overnight (*cf.* 16 h), allowing to warm slowly to rt. The reaction was filtered and

concentrated under reduced pressure to give the crude product, which was purified by column chromatography.

4.4.1 (*E*)-Ethyl 4-oxopent-2-enoate 41

Following General Procedure 4.4, periodic acid (0.95 g, 4.2 mmol) and (+)-diethyl L-tartrate (0.72 mL, 4.2 mmol) in Et_2O (8.5 mL) were stirred for 3 h at rt. The reaction was filtered into a two-necked round-bottomed flask containing $MgSO_4$ (1.0 g), washing with THF (10.5 mL), before 1-(triphenylphosphoranylidene)propan-2-one (2.0 g, 6.3 mmol) was added at 0 °C. The crude product was purified by column chromatography (80:20 hexane : Et_2O, R_f 0.24) to give **41** (0.61 g, 68%) as a colourless oil, with spectroscopic data in accordance with the literature.[22] ^{1}H NMR (300 MHz, $CDCl_3$) δ_H: 1.32 (3H, t, *J* 7.2 CH_2CH_3), 2.36 (3H, s, $COCH_3$), 4.26 (2H, q, *J* 7.2, OCH_2), 6.64 (1H, d, *J* 16.1, EtO_2CCH), 7.01 (1H, d, *J* 16.1, CHCOMe).

4.4.2 (*E*)-Ethyl 4-oxo-4-(*p*-tolyl)but-2-enoate 42

Following General Procedure 4.4, periodic acid (0.39 g, 1.7 mmol) and (+)-diethyl L-tartrate (0.35 g, 1.7 mmol) in Et_2O (3.5 mL) were stirred for 3 h at rt. The reaction was filtered into a two-necked round-bottomed flask containing $MgSO_4$ (0.5 g), washing with THF (4.3 mL), before 1-(*p*-tolyl)-2-(triphenylphosphoranylidene)ethanone (1.0 g, 2.5 mmol) was added at 0 °C. The crude product was purified by column chromatography (95:5 petrol : EtOAc, R_f 0.36) to give **42** (0.39 g, 78%) as a yellow oil, with spectroscopic data in accordance with the literature.[21] ^{1}H NMR (300 MHz, $CDCl_3$) δ_H: 1.35 (3H, t, *J* 7.1, CH_2CH_3), 2.44 (3H, s, ArC(4)CH_3), 4.30 (2H, q, *J* 7.1, OCH_2), 6.87 (1H, d, *J* 15.6, EtO_2CCH), 7.31 (2H, d, *J* 8.2, ArC(3,5)*H*), 7.91 (1H, d, *J* 15.5, CHCOAr), 7.91 (1H, d, *J* 8.2, ArC(2,6)*H*).

4.4.3 (*E*)-Ethyl 4-(4-methoxyphenyl)-4-oxobut-2-enoate 43

Following General Procedure 4.4, periodic acid (0.37 g, 1.6 mmol) and (+)-diethyl L-tartrate (0.34 g, 1.6 mmol) in Et_2O (3.2 mL) were stirred for 3 h at rt. The reaction was filtered into a two-necked round-bottomed flask containing $MgSO_4$ (0.5 g), washing with THF (4.1 mL), before 1-(4-methoxyphenyl)-2-(triphenylphosphoranylidene)ethanone (1.0 g, 2.4 mmol) was added at 0 °C. The crude product was purified by column chromatography (70:30 petrol : Et_2O, R_f 0.25) to give **43** (0.48 g, 83%) as a yellow oil, which solidified over time, with spectroscopic data in accordance with the literature.[21] mp 40–42 °C; ^{1}H NMR (300 MHz, $CDCl_3$) δ_H: 1.35 (3H, t, *J* 7.2 CH_2CH_3), 3.90 (3H, s, OCH_3), 4.30 (2H, q, *J* 7.1, OCH_2), 6.87 (1H, d, *J* 15.5, EtO_2CCH), 6.98 (2H, d, *J* 9.0, ArC(3,5)*H*), 7.92 (1H, d, *J* 15.5, CHCOAr), 8.01 (2H, d, *J* 9.0, ArC(2,6)*H*).

4.4.4 (*E*)-Ethyl 4-(4-chlorophenyl)-4-oxobut-2-enoate 44

Following General Procedure 4.4, periodic acid (0.37 g, 1.6 mmol) and (+)-diethyl L-tartrate (0.33 g, 1.6 mmol) in Et_2O (3.2 mL) were stirred for 3 h at rt. The reaction was filtered into a two-necked round-bottomed flask containing $MgSO_4$ (0.5 g), washing with THF (4.0 mL), before 1-(4-chlorophenyl)-2-(triphenylphosphoranylidene)ethanone (1.0 g, 2.4 mmol) was added at 0 °C. The crude product was purified by column chromatography (95:5 petrol : EtOAc, R_f 0.29) to give **44** (0.57 g, 99%) as a yellow solid, with spectroscopic data in accordance with the literature.[21] mp 62–63 ºC; ^{1}H NMR (300 MHz, $CDCl_3$) δ_H: 1.35 (3H, t, *J* 7.1, C*H*$_3$), 4.30 (2H, q, *J* 7.1, OC*H*$_2$), 6.90 (1H, d, *J* 15.5, EtO_2CCH), 7.49 (2H, d, *J* 8.7, ArC(3,5)*H*), 7.87 (1H, d, *J* 15.6, C*H*COAr), 7.95 (1H, d, *J* 8.7, ArC(2,6)*H*).

4.4.5 (*E*)-Ethyl 4-oxo-4-(4-(trifluoromethyl)phenyl)but-2-enoate 45

Following General Procedure 4.4, periodic acid (0.68 g, 3.0 mmol) and (+)-diethyl L-tartrate (0.51 mL, 3.0 mmol) in Et_2O (6.0 mL) were stirred for 3 h at rt. The reaction was filtered into a two-necked round-bottomed flask containing $MgSO_4$ (1.0 g), washing with THF (7.5 mL), before 1-(4-(trifluoromethyl)phenyl)-2-(triphenylphosphoranylidene)ethanone (2.0 g, 4.5 mmol) was added at 0 °C. The crude product was purified by column chromatography (90:10 petrol : Et_2O, R_f 0.24) to **45** (0.85 g, 70%) as a yellow solid. mp 61–63 ºC; ν_{max} (film, cm^{-1}) 1721, 1672, 1630, 1414, 1315, 1294, 1163, 1123, 1111; ^{1}H NMR (300 MHz, $CDCl_3$) δ_H: 1.35 (3H, t, *J* 7.1 C*H*$_3$), 4.31 (2H. q. *J* 7.1, OC*H*$_2$), 6.91 (1H, d, *J* 15.6, EtO_2CCH), 7.78 (2H, d, *J* 8.4, ArC(3,5)*H*), 7.87 (1H, d, *J* 15.5, C*H*COAr), 8.09 (2H, d, *J* 8.3, ArC(2,6)*H*); ^{13}C{^{1}H} NMR (75 MHz, $CDCl_3$) δ_C: 14.3 (CH_3), 61.7 (OCH_2), 123.6 (q, $^1J_{CF}$ 272.8, CF_3), 126.1 (q, $^3J_{CF}$ 3.7, Ar*C*(2)H), 129.3 (Ar*C*(3)H), 133.8 (EtO_2C=*C*H), 135.1 (q, $^2J_{CF}$ 32.8, Ar*C*(1)), 135.7 (C=*C*HCOAr), 139.4 (Ar*C*(4)), 165.4 (*C*O_2Et), 188.9 (*C*OAr); ^{19}F{^{1}H} NMR (282 MHz, $CDCl_3$) δ_F: –63.69 (C*F*$_3$); HRMS (APCI$^+$) $C_{13}H_{12}O_3F_3$ $[M+H]^+$ found 273.0732, requires 273.0733 (–0.4 ppm).

4.4.6 (*E*)-Ethyl 4-(naphthalen-2-yl)-4-oxobut-2-enoate 46

Following General Procedure 4.4, periodic acid (1.06 g, 4.6 mmol) and (+)-diethyl L-tartrate (0.80 mL, 4.6 mmol) in Et_2O (9.0 mL) were stirred for 3 h at rt. The reaction was filtered into a two-necked round-bottomed flask containing $MgSO_4$ (1.5 g), washing with THF (11.5 mL), before 1-(naphthalen-2-yl)-2-(triphenylphosphoranylidene)ethanone (3.00 g, 7.0 mmol) was added at 0 °C. The crude product was purified by column chromatography (80:20 hexane : Et_2O, R_f 0.38) to give **46** (1.24 g, 70%) as a yellow solid. mp 57–59 ºC; ν_{max} (film, cm^{-1}) 1717,

1667, 1624, 1464, 1364, 1304, 1246, 1175, 1123; ^{1}H NMR (300 MHz, $CDCl_3$) δ_H: 1.38 (3H, t, *J* 7.2 C*H*$_3$), 4.33 (2H. q. *J* 7.2, OC*H*$_2$), 6.96 (1H, d, *J* 15.5, EtO$_2$CC*H*), 7.52–7.68 (2H, m, Ar*H*), 7.86–8.10 (4H, m, Ar*H*), 8.09 (1H, d, *J* 15.5, C*H*COAr), 8.46–8.55 (1H, m, Ar*H*); ^{13}C{^{1}H} NMR (75 MHz, $CDCl_3$) δ_C: 14.4 (*C*H$_3$), 61.6 (O*C*H$_2$), 124.2 (Ar*C*), 127.2 (Ar*C*), 128.0 (Ar*C*), 129.1 (Ar*C*), 129.2 (Ar*C*), 129.9 (Ar*C*), 131.3 (Ar*C*), 132.6 (C=*C*CO$_2$), 132.7 (Ar*C*), 134.2 (Ar*C*), 136.0 (Ar*C*), 136.6 (C=*C*CO), 165.9 (*C*O$_2$), 189.4 (*C*O); HRMS (NSI$^+$) $C_{16}H_{15}O_3$ $[M+H]^+$ found 255.1017, requires 255.1016 (+0.5 ppm).

4.5 General procedure for the NHC-catalysed redox hetero-Diels-Alder reaction with α,β-unsaturated γ-ketoesters

The appropriate α-aroyloxyaldehyde (1.5 eq), α,β-unsaturated γ-ketoester (1.0 eq) and NHC precatalyst **2** (5 mol%) were dissolved in anhydrous THF (0.075 M) in a sealed vial containing 3Å molecular sieves. Et_3N (1.5 eq.) was added and the reaction stirred until complete by TLC analysis. The mixture was diluted with EtOAc and washed successively with 1 M HCl, saturated $NaHCO_3$ and brine. The organic layer was dried with $MgSO_4$, filtered and concentrated under reduced pressure to give the crude product, which was purified by column chromatography.

4.5.1 (3*S*,4*S*)-Ethyl 3-butyl-2-oxo-6-phenyl-3,4-dihydro-2*H*-pyran-4-carboxylate 20

Following General Procedure 4.5, 1-oxohexan-2-yl 4-nitrobenzoate (200 mg, 0.75 mmol), (*E*)-ethyl 4-oxo-4-phenylbut-2-enoate (102 mg, 0.500 mmol), NHC precatalyst **2** (18.4 mg, 50.0 μmol), Et_3N (105 μL, 0.75 mmol) and THF (10 mL) were reacted for 5 h. The crude (>95:5 dr) was purified by column chromatography (95:5 petrol : EtOAc) to give **20** (129 mg, 85%) as colourless solid. mp 61–63 °C; $[\alpha]_D^{20}$ +185.5 (*c* 0.5, $CHCl_3$); Chiral HPLC analysis, Chiralcel OJ-H (95:5 hexane : IPA, flow rate 1 mLmin^{-1}, 254 nm, 30 °C) t_R (3*S*,4*S*): 17.2 min, t_R (3*R*,4*R*): 22.3 min, >99:1 er; ν_{max} (solid) 2953 (C-H), 1761 (C=O), 1719 (C=O); ^{1}H NMR (400 MHz, $CDCl_3$) δ_H: 0.91 (3H, t, *J* 7.1, CH$_2$C*H*$_3$), 1.25 (3H, t, *J* 7.1, OCH$_2$C*H*$_3$), 1.31–1.54 (5H, m, (C*H*$_2$)$_2$ and C(3)C*H*^{A}H^B), 1.99–2.13 (1H, m, C(3)CH^A*H*^{B}), 2.68–2.79 (1H, m, C(3)*H*), 3.53 (1H, t, *J* 6.3, C(4)*H*), 4.17 (2H, qd, *J* 7.1, 2.5, OC*H*$_2$CH$_3$), 5.88 (1H, d, *J* 6.5, C(5)*H*), 7.32–7.41 (3H, m, ArC(2)*H* and ArC(4)*H*), 7.61–7.66 (2H, m, ArC(3)*H*); ^{13}C{^{1}H} NMR (100 MHz, $CDCl_3$) δ_C: 12.8 (CH$_2$*C*H$_3$), 13.0 (OCH$_2$*C*H$_3$), 21.5 (*C*H$_2$), 25.8 (*C*H$_2$), 28.3 (*C*H$_2$), 39.5 (*C*(3)), 40.8 (*C*(4)), 60.5 (O*C*H$_2$CH$_3$), 96.9 (*C*(5)), 123.8 (Ar*C*(3)), 127.5 (Ar*C*(2)), 128.4 (Ar*C*(4)), 130.9 (Ar*C*(1)), 151.1 (*C*(6)), 168.2 (*C*(2)), 169.2 (*C*O$_2$Et); HRMS (NSI$^+$) $C_{18}H_{26}O_4N$ $[M+NH_4]^+$ found 320.1864, requires 320.1856 (+2.4 ppm).

4.5.2 (3*S*,4*S*)-Ethyl 3-benzyl-2-oxo-6-phenyl-3,4-dihydro-2*H*-pyran-4-carboxylate 21

Following General Procedure 4.5, 1-oxo-3-phenylpropan-2-yl 4-nitrobenzoate **7** (238 mg, 0.80 mmol), (*E*)-ethyl 4-oxo-4-phenylbut-2-enoate (108 mg, 0.53 mmol), NHC precatalyst **2** (19.5 mg, 53 μmol), Et_3N (0.11 mL, 0.80 mmol) and THF (5 mL) were reacted for 2 h. The crude (>95:5 dr) was purified by column chromatography (95:5 petrol : EtOAc) to give **21** (140 mg, 79%) as a colourless oil, with spectroscopic data in accordance with the literature.[6c] $[\alpha]_D^{20}$ +173.0 (*c* 1.05, $CHCl_3$) {Lit.[6c] +107.2 (*c* 0.82, $CHCl_3$)}; Chiral HPLC analysis Chiralpak AD-H (90:10 hexane : IPA, flow rate 1.0 mLmin^{-1}, 254 nm, 30 °C) >99:1 er; ^{1}H NMR (300 MHz, $CDCl_3$) δ_H: 1.29 (3H, t, *J* 7.1, OCH_2CH_3) 2.77 (1H, dd, *J* 14.2, 10.2, PhC*H*^{A}H^B), 2.97–3.03 (1H, m, C(3)*H*), 3.25 (1H, dd, *J* 6.9, 5.9, C(4)*H*) 3.55 (1H, dd, *J* 14.2, 4.6, PhCH^A*H*^{B}), 4.22 (2H, q, *J* 7.1, OCH_2CH_3), 5.80 (1H, d, *J* 7.0, C(5)*H*), 7.16–7.21 (2H, m, Ar*H*), 7.26–7.40 (6H, m, Ar*H*), 7.60–7.63 (2H, m, Ar*H*).

4.5.3 (3*S*,4*S*)-Ethyl 3-(2-(benzyloxy)ethyl)-2-oxo-6-phenyl-3,4-dihydro-2*H*-pyran-4-carboxylate 22

Following General Procedure 4.5, 4-(benzyloxy)-1-oxobutan-2-yl 4-nitrobenzoate (257 mg, 0.75 mmol), (*E*)-ethyl 4-oxo-4-phenylbut-2-enoate (102 mg, 0.50 mmol), NHC precatalyst **2** (9.2 mg, 25.0 μmol), Et_3N (105 μL, 0.75 mmol) and THF (5 mL) were reacted for 9 h. The crude (90:10 dr) was purified by column chromatography (85:15 petrol : EtOAc, R_f 0.25) to give **22** (161 mg, 85%) as white solid. mp 77–78 °C (hexane); $[\alpha]_D^{20}$ +169.1 (*c* 0.55 in $CHCl_3$); Chiral HPLC analysis, Chiralcel OD-H (95:5 hexane : IPA, flow rate 1 mLmin^{-1}, 254 nm, 30 ºC) t_R (3*R*,4*R*): 23.2 min, t_R (3*S*,4*S*): 25.1 min, >99:1 er; ν_{max} (film, cm^{-1}) 1767 (C=O), 1715 (C=O), 1657 (C=C); ^{1}H NMR (300 MHz, $CDCl_3$) δ_H: 1.23 (3H, t, *J* 7.1, OCH_2CH_3), 1.72–1.83 (1H, m, C(3)C*H*^{A}H^B), 2.37–2.48 (1H, m, C(3)CH^A*H*^{B}), 3.04 (1H, q, *J* 6.7, C(3)*H*), 3.50 (1H, t, *J* 6.5, C(4)*H*), 3.60–3.72 (2H, m, C(3)CH_2CH_2), 4.09–4.20 (2H, m, OCH_2CH_3), 4.50 (2H, d, *J* 2.1, OCH_2Ar), 5.86 (1H, d, *J* 6.9, C(5)*H*), 7.27–7.40 (8H, m, Ar*H*), 7.61–7.66 (2H, m, Ar*H*); ^{13}C{^{1}H} NMR (75 MHz, $CDCl_3$) δ_C: 14.2 (CH_3), 27.8 (CH_2), 37.6 (*C*(3)H), 42.1 (*C*(4)H), 61.7 (OCH_2CH_3), 67.4 (OCH_2CH_2), 73.2 (OCH_2Ph), 98.2 (*C*(5)H), 125.0 (Ar*C*H), 127.8 (Ar*C*H), 128.5 (Ar*C*H), 128.6 (Ar*C*H), 129.6 (Ar*C*H), 132.0 (Ar*C*), 138.2 (Ar*C*), 152.4 (*C*(6)), 169.4 (*C*(2)), 170.4 (CO_2Et); HRMS (NSI$^+$) $C_{23}H_{25}O_5$ $[M+H]^+$ found 381.1697, requires 381.1697 (+0.1 ppm).

4.5.4 (3*S*,4*S*)-Ethyl 3-benzyl-6-methyl-2-oxo-3,4-dihydro-2*H*-pyran-4-carboxylate 23

In a modified procedure, 1-oxo-3-phenylpropan-2-yl 4-nitrobenzoate **7** (196 mg, 0.65 mmol), (*E*)-ethyl 4-oxopent-2-enoate **41** (62 mg, 0.44 mmol), NHC precatalyst **2** (8.0 mg, 21.8 μmol), and Cs_2CO_3 (142 mg, 0.44 mmol) were dissolved in THF (4.4 mL) in a sealed vial and heated at 40 °C for 7 h. The mixture was then diluted with EtOAc and washed successively with 1 M HCl (×2), $NaHCO_3$ (×2), and brine (×2) before being dried over $MgSO_4$ and concentrated under reduced pressure. The crude (>95:5 dr) was purified by column chromatography (95:5 petrol : EtOAc, R_f 0.20) to give **23** (79 mg, 65%) as white solid, with spectroscopic data in accordance to the literature.[6c] mp 88–89 °C (hexane); $[\alpha]_D^{20}$ +270.9 (*c* 0.32 in $CHCl_3$) {Lit.[6c] +250.6 (*c* 0.93, $CHCl_3$)}; Chiral HPLC analysis, Chiralcel AD-H (95:5 hexane : IPA, flow rate 1 mLmin^{-1}, 254 nm, 30 °C) t_R (3*R*,4*R*): 11.0 min, t_R (3*S*,4*S*): 13.2 min, 98.5:1.5 er; ν_{max} (film, cm^{-1}) 1771 (C=O), 1726 (C=O), 1688 (C=C); ^{1}H NMR (300 MHz, $CDCl_3$) δ_H: 1.21 (3H, t, *J* 7.1, OCH_2CH_3), 1.83 (3H, s, C(6)CH_3), 2.61 (1H, dd, *J* 14.3, 10.1, C(3)CH^AH^B), 2.75–2.82 (1H, m, C(3)*H*), 2.92 (1H, t, *J* 6.4, C(4)*H*), 3.42 (1H, dd, *J* 14.2, 4.6, C(3)CH^AH^B), 4.13 (2H, q, *J* 7.2, OCH_2), 4.95 (1H, dd, *J* 6.8, 1.1, C(5)*H*), 7.04–7.10 (2H, m, ArC(2)*H*), 7.12–7.27 (3H, m, ArC(3)*H* and ArC(4)*H*); ^{13}C{^{1}H} NMR (75 MHz, $CDCl_3$) δ_C: 14.2 (CH_2CH_3), 18.9 (CCH_3), 33.3 (CH_2), 40.4 (*C*(3)H), 42.8 (*C*(4)H), 61.5 (OCH_2), 98.7 (*C*(5)H), 126.9 (Ar*C*H), 128.8 (Ar*C*H), 129.1 (Ar*C*H), 138.3 (Ar*C*), 152.4 (*C*(6)), 169.3 (*C*(2)), 170.7 (CO_2Et); HRMS (NSI$^+$) $C_{16}H_{19}O_4$ $[M+H]^+$ found 275.1280, requires 275.1278 (+0.8 ppm).

4.5.5 (3*S*,4*S*)-Ethyl 3-butyl-2-oxo-6-(*p*-tolyl)-3,4-dihydro-2*H*-pyran-4-carboxylate 24

Following General Procedure 4.5, 1-oxohexan-2-yl 4-nitrobenzoate (200 mg, 0.75 mmol), (*E*)-ethyl 4-oxo-4-(*p*-tolyl)but-2-enoate **42** (109 mg, 0.50 mmol), NHC precatalyst **2** (9.2 mg, 25.0 μmol), Et_3N (105 μL, 0.75 mmol) and THF (5 mL) were reacted for 6 h. The crude (>95:5 dr) was purified by column chromatography (90:10 hexane : Et_2O, R_f 0.19) to give **24** (127 mg, 80%) as colourless needles. mp 64–65 °C (hexane); $[\alpha]_D^{20}$ +158.4 (*c* 0.38 in $CHCl_3$); Chiral HPLC analysis, Chiralcel OD-H (95:5 hexane : IPA, flow rate 1 mLmin^{-1}, 254 nm, 30 ºC) t_R (3*S*,4*S*): 8.3 min, t_R (3*R*,4*R*): 9.0 min, >99:1 er; ν_{max} (film, cm^{-1}) 1763 (C=O), 1719 (C=O), 1684 (C=C); ^{1}H NMR (300 MHz, $CDCl_3$) δ_H: 0.91 (3H, t, *J* 7.1, $(CH_2)_3CH_3$), 1.25 (3H, t, *J* 7.2, OCH_2CH_3), 1.31–1.52 (5H, m, C(3)H_aH_b and CH_2 ×2), 1.98–2.15 (1H, m, C(3)H_aH_b), 2.36 (3H, s, ArC(4)CH_3), 2.73 (1H, q, *J* 6.5, C(3)*H*), 3.51 (1H, t, *J* 6.3, C(4)*H*), 4.17 (2H, qd, *J* 7.2, 1.9, OCH_2), 5.82 (1H, d, *J* 6.5, C(5)*H*), 7.18 (2H, d, *J* 8.1, ArC(3)*H*), 7.53 (2H, d, *J* 8.3, ArC(2)*H*); ^{13}C{^{1}H} NMR (75 MHz, $CDCl_3$) δ_C: 14.0 (CH_3), 14.2 (CH_3), 21.4 (CH_3), 22.6

(CH_2), 26.9 (CH_2), 29.5 (CH_2), 40.7 (*C*(3)H), 42.0 (*C*(4)H), 61.6 (OCH_2), 97.1 (*C*(5)H), 124.9 (Ar*C*), 129.2 (Ar*C*H), 129.3 (Ar*C*H), 139.7 (Ar*C*), 152.4 (*C*(6)), 169.6 (*C*(2)), 170.5 (CO_2Et); HRMS (NSI^+) $C_{19}H_{25}O_4$ $[M+H]^+$ found 317.1751, requires 317.1747 (+1.1 ppm).

4.5.6 (3*S*,4*S*)-Ethyl 3-butyl-6-(4-methoxyphenyl)-2-oxo-3,4-dihydro-2*H*-pyran-4-carboxylate 25

Following General Procedure 4.5, 1-oxohexan-2-yl 4-nitrobenzoate (200 mg, 0.75 mmol), (*E*)-ethyl 4-(4-methoxyphenyl)-4-oxobut-2-enoate **43** (117 mg, 0.50 mmol), NHC precatalyst **2** (9.2 mg, 25.0 μmol), Et_3N (105 μL, 0.75 mmol) and THF (5 mL) were reacted for 6 h. The crude (>95:5 dr) was purified by column chromatography (85:15 hexane : Et_2O, R_f 0.17) to give **25** (149 mg, 90%) as white solid. mp 61–62 °C (hexane); $[\alpha]_D^{20}$ +123.6 (*c* 0.39 in $CHCl_3$); Chiral HPLC analysis, Chiralcel OD-H (95:5 hexane : IPA, flow rate 1 mLmin^{-1}, 254 nm, 30 ºC) t_R (3*R*,4*R*): 13.9 min, t_R (3*S*,4*S*): 14.5 min, >99:1 er; ν_{max} (film, cm^{-1}) 1751 (C=O), 1726 (C=O), 1661 (C=C); ^{1}H NMR (300 MHz, $CDCl_3$) δ_H: 0.91 (3H, t, *J* 7.1, CH_2CH_3), 1.25 (3H, t, *J* 7.2, OCH_2CH_3), 1.31–1.49 (5H, m, C(3)H_aH_b), 1.99–2.11 (1H, m, C(3)H_aH_b), 2.72 (1H, q, *J* 6.5, C(3)*H*), 3.50 (1H, t, *J* 6.3, C(4)*H*), 3.82 (3H, s, ArC(4)OCH_3), 4.17 (2H, qd, *J* 7.1, 1.9, OCH_2), 5.74 (1H, d, *J* 6.5, C(5)*H*), 6.89 (2H, d, *J* 8.9, ArC(3)*H*), 7.57 (2H, d, *J* 9.0, ArC(2)*H*); ^{13}C{^{1}H} NMR (75 MHz, $CDCl_3$) δ_C: 14.0 (CH_3), 14.2 (CH_3), 22.6 (CH_2), 26.9 (CH_2), 29.5 (CH_2), 40.8 (*C*(3)H), 41.9 (*C*(4)H), 55.5 (OCH_3), 61.6 (OCH_2), 96.0 (*C*(5)H), 114.0 (Ar*C*), 124.6 (Ar*C*H), 126.4 (Ar*C*H), 152.1 (*C*(6)), 160.7 (Ar*C*), 169.6 (*C*(2)), 170.6 (CO_2Et); HRMS (NSI^+) $C_{19}H_{25}O_5$ $[M+H]^+$ found 333.1699, requires 333.1697 (+0.7 ppm).

4.5.7 (3*S*,4*S*)-Ethyl 6-(4-chlorophenyl)-3-methyl-2-oxo-3,4-dihydro-2*H*-pyran-4-carboxylate 26

Following General Procedure 4.5, 1-oxopropan-2-yl 4-nitrobenzoate (167 mg, 0.75 mmol), (*E*)-ethyl 4-(4-chlorophenyl)-4-oxobut-2-enoate **44** (119 mg, 0.50 mmol), NHC precatalyst **2** (9.2 mg, 25.0 μmol), Et_3N (105 μL, 0.75 mmol) and THF (5 mL) were reacted for 4 h. The crude (80:20 dr) was purified by column chromatography (70:30 hexane : Et_2O, minor-*anti* R_f 0.29, major-*syn* R_f 0.23) to give **26** (81 mg, 55%) as white solid. mp 93–95 °C (hexane); $[\alpha]_D^{20}$ +248.5 (*c* 0.27 in $CHCl_3$); Chiral HPLC analysis, Chiralcel OD-H (95:5 hexane : IPA, flow rate 1 mLmin^{-1}, 254 nm, 30 °C) t_R (3*R*,4*R*): 14.3 min, t_R (3*S*,4*S*): 15.7 min, >99:1 er; ν_{max} (film, cm^{-1}) 1765 (C=O), 1721 (C=O), 1657 (C=C); ^{1}H NMR (300 MHz, $CDCl_3$) δ_H: 1.26 (3H, t, *J* 7.2, OCH_2CH_3), 1.34 (3H, d, *J* 7.0, C(3)CH_3), 2.92 (1H, pent, *J* 6.7, C(3)*H*), 3.44 (1H, t, *J* 6.3, C(4)*H*), 4.19 (2H, qd, *J* 7.1, 3.2, OCH_2), 5.86 (1H, d, *J* 6.6, C(5)*H*), 7.35 (2H, d, *J* 8.7,

ArC(2)*H*), 7.57 (2H, d, *J* 8.8, ArC(3)*H*); $^{13}C\{^{1}H\}$ NMR (75 MHz, $CDCl_3$) δ_C: 12.6 (C(3)*C*H_3), 14.2 (CH_2CH_3), 35.6 (*C*(3)H), 43.8 (*C*(4)H), 61.8 (OCH_2), 98.4 (*C*(5)H), 126.3 (Ar*C*), 128.9 (Ar*C*H), 130.5 (Ar*C*H), 135.6 (Ar*C*), 151.6 (*C*(6)), 169.6 (*C*(2)), 170.2 (CO_2Et); HRMS (NSI^+) $C_{15}H_{16}O_4Cl$ $[N+H]^+$ found 295.0735, requires 295.0732 (+1.1 ppm).

4.5.8 (3*S*,4*S*)-Ethyl 3-benzyl-2-oxo-6-(4-(trifluoromethyl)phenyl)-3,4-dihydro-2*H*-pyran-4-carboxylate 27

Following General Procedure 4.5, 1-oxo-3-phenylpropan-2-yl 4-nitrobenzoate **7** (224 mg, 0.75 mmol), (*E*)-ethyl 4-oxo-4-(4-(trifluoromethyl)phenyl)but-2-enoate **45** (136 mg, 0.50 mmol), NHC precatalyst **2** (18.3 mg, 50.0 μmol), Et_3N (105 μL, 0.75 mmol) and THF (5 mL) were reacted for 3 h. The crude (80:20 dr) was purified by column chromatography (90:10 petrol : EtOAc, major-*syn* R_f 0.16, minor-*anti* R_f 0.09) to give **27** (105 mg, 52%) as white solid. mp 145–147 °C (hexane); $[\alpha]_D^{20}$ +172.9 (*c* 0.31 in $CHCl_3$); Chiral HPLC analysis, Chiralcel OD-H (95:5 hexane : IPA, flow rate 1 mLmin^{-1}, 254 nm, 30 ºC) t_R (3*S*,4*S*): 18.8 min, t_R (3*R*,4*R*): 15.4 min, >99:1 er; ν_{max} (film, cm^{-1}) 1775 (C=O), 1719 (C=O), 1659 (C=C); ^1H NMR (300 MHz, $CDCl_3$) δ_H: 1.30 (3H, t, *J* 7.2, OCH_2CH_3), 2.78 (1H, dd, *J* 14.4, 9.9, C(3)H_aH_b), 2.98–3.06 (1H, m, C(3)*H*), 3.30 (1H, t, *J* 6.4, C(4)*H*), 3.55 (1H, dd, *J* 14.2, 4.7, C(3)H_aH_b), 4.23 (2H, q, *J* 7.2, OCH_2), 5.92 (1H, d, *J* 7.0, C(5)*H*), 7.17–7.19 (2H, m, C(3)CH_2ArC(2)*H*), 7.24–7.36 (3H, m, C(3)CH_2ArC(3)*H* and C(3)CH_2ArC(4)*H*), 7.63 (2H, d, *J* 8.5, C(6)ArC(2)*H*), 7.73 (2H, d, *J* 8.5, C(6)ArC(3)*H*); $^{13}C\{^{1}H\}$ NMR (75 MHz, $CDCl_3$) δ_C: 14.3 (CH_3), 33.3 (CH_2Ph), 40.8 (*C*(3)H), 42.8 (*C*(4)H), 62.0 (OCH_2), 100.3 (*C*(5)H), 124.0 (q, $^1J_{CF}$ 272, CF_3), 125.2 (Ar*C*H), 125.7 (q, $^3J_{CF}$ 3.8, C(6)Ar*C*(3,5)H), 127.1 (Ar*C*H), 129.0 (Ar*C*H), 129.1 (Ar*C*H), 131.4 (q, $^2J_{CF}$ 32.5, C(6)Ar*C*(4)), 135.2 (Ar*C*), 137.9 (Ar*C*), 151.4 (*C*(6)), 168.4 (*C*(2)), 170.0 (CO_2Et); HRMS (NSI^+) $C_{22}H_{23}O_4NF_3$ $[M+NH_4]^+$ found 422.1574, requires 422.1574 (+0.1 ppm).

4.5.9 (3*S*,4*S*)-Ethyl 3-methyl-6-(naphthalen-2-yl)-2-oxo-3,4-dihydro-2*H*-pyran-4-carboxylate 28 and (3*S*,4*R*)-Ethyl 3-methyl-6-(naphthalen-2-yl)-2-oxo-3,4-dihydro-2*H*-pyran-4-carboxylate 29

Following General Procedure 4.5, 1-oxopropan-2-yl 4-nitrobenzoate (167 mg, 0.75 mmol), (*E*)-ethyl 4-(naphthalen-2-yl)-4-oxobut-2-enoate **46** (127 mg, 0.50 mmol), NHC precatalyst **2** (9.2 mg, 25.0 μmol), Et_3N (105 μL, 0.75 mmol) and THF (5 mL) were reacted for 24 h. The crude (50:50 dr) was purified by column chromatography (90:10 petrol : EtOAc, *anti* R_f 0.29, *syn* R_f 0.23) to give *syn*-**28** (49 mg, 32%) as white solid and *anti*-**29** (55 mg, 35%) as white solid. *syn*-**28**: mp 101–103 °C (hexane); $[\alpha]_D^{20}$ +220.3 (*c* 0.34 in $CHCl_3$); Chiral HPLC analysis,

Chiralcel OD-H (95:5 hexane : IPA, flow rate 1 mLmin^{-1}, 254 nm, 30 °C) t_R (3*S*,4*S*): 26.7 min, t_R (3*R*,4*R*): 24.1 min, >99:1 er; ν_{max} (film, cm^{-1}) 1771 (C=O), 1715 (C=O), 1651 (C=C); ^{1}H NMR (300 MHz, $CDCl_3$) δ_H: 1.27 (3H, t, *J* 7.2, OCH_2CH_3), 1.37 (3H, d, *J* 6.9, C(3)CH_3), 2.97 (1H, pent, *J* 6.7, C(3)*H*), 3.49 (1H, t, *J* 6.3, C(4)*H*), 4.15–4.26 (2H, m, OCH_2), 6.02 (1H, d, *J* 6.6, C(5)*H*), 7.48–7.53 (2H, m, Ar*H*), 7.65 (1H, dd, *J* 8.7, 1.9, ArC(2)*H*), 7.78–7.91 (3H, m, Ar*H*), 8.16–8.22 (1H, m, Ar*H*); ^{13}C{^{1}H} NMR (75 MHz, $CDCl_3$) δ_C: 12.7 (C(3)CH_3), 14.2 (CH_2CH_3), 35.7 (*C*(3)H), 43.9 (*C*(4)H), 61.8 (OCH_2), 98.5 (*C*(5)H), 122.1 (Ar*C*H), 124.6 (Ar*C*H), 126.8 (Ar*C*H), 127.1 (Ar*C*H), 127.7 (Ar*C*H), 128.4 (Ar*C*H), 128.8 (Ar*C*H), 129.0 (Ar*C*), 133.1 (Ar*C*), 133.7 (Ar*C*), 152.4 (*C*(6)), 170.0 (*C*(2)), 170.3 (CO_2Et); HRMS (NSI$^+$) $C_{19}H_{19}O_4$ $[M+H]^+$ found 311.1282, requires 311.1278 (+1.3 ppm).

anti-**29**: mp 92–94 °C (hexane); $[\alpha]_D^{20}$ –91.9 (*c* 0.37 in $CHCl_3$); Chiral HPLC analysis, Chiralcel OD-H (95:5 hexane : IPA, flow rate 1 mLmin^{-1}, 254 nm, 30 °C) t_R (3*R*,4*S*): 15.2 min, t_R (3*S*,4*R*): 15.9 min, >99:1 er; ν_{max} (film, cm^{-1}) 1769 (C=O), 1728 (C=O), 1661 (C=C); ^{1}H NMR (300 MHz, $CDCl_3$) δ_H: 1.33 (3H, t, *J* 7.2, OCH_2CH_3), 1.40 (3H, d, *J* 6.9, C(3)CH_3), 3.10–3.20 (1H, m, C(3)*H*), 3.38 (1H, dd, *J* 9.1, 4.0, C(4)*H*), 4.27 (2H, q, *J* 7.2, OCH_2), 5.86 (1H, d, *J* 4.2, C(5)*H*), 7.48–7.53 (2H, m, Ar*H*), 7.65 (1H, dd, *J* 8.7, 1.7, ArC(2)*H*), 7.79–7.93 (3H, m, Ar*H*), 8.15–8.23 (1H, m, Ar*H*); ^{13}C{^{1}H} NMR (75 MHz, $CDCl_3$) δ_C: 14.3 (CH_2CH_3), 15.0 (C(3)CH_3), 35.7 (*C*(3)H), 45.0 (*C*(4)H), 62.0 (OCH_2), 98.0 (*C*(5)H), 122.0 (Ar*C*H), 124.5 (Ar*C*H), 126.8 (Ar*C*H), 127.0 (Ar*C*H), 127.7 (Ar*C*H), 128.4 (Ar*C*H), 128.8 (Ar*C*H), 128.8 (Ar*C*), 133.1 (Ar*C*), 133.7 (Ar*C*), 150.9 (*C*(6)), 170.3 (CO_2Et), 171.5 (*C*(2)); HRMS (NSI$^+$) $C_{19}H_{19}O_4$ $[M+H]^+$ found 311.1282, requires 311.1278 (+1.3 ppm).

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Supplementary data

Supplementary data associated with this article can be found, in the online version, at xxx.

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