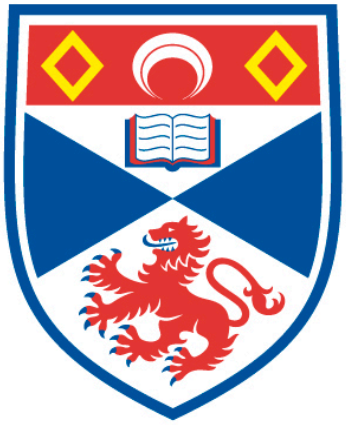
DESIGN AND STUDY OF NOVEL GOLD COMPLEXES FOR EFFICIENT CATALYTIC PROCESS TOWARDS THE ACTIVATION OF ALKYNES

Danila Gasperini

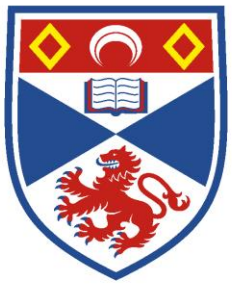
A Thesis Submitted for the Degree of PhD
at the
University of St Andrews



2018

Design and study of novel gold complexes for efficient catalytic processes towards the activation of alkynes

Danila Gasperini



University of
St Andrews

This thesis is submitted in partial fulfilment for the degree of PhD
at the University of St Andrews

May 2018

1. Candidate's declarations:

I, Danila Gasperini, do hereby certify that this thesis, submitted for the degree of PhD, which is approximately 69,900 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 was admitted as a research student at the University of St Andrews in April 2014.

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

Date 5 February 2018 Signature of candidate: .....

2. 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.

Date 5 February 2018 Signature of supervisor: .....

3. 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, Danila Gasperini, 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

Embargo on all of print copy for a period of 2 years on the following ground(s):

- Publication would preclude future publication

Supporting statement for printed embargo request

I intend to publish my thesis.

Electronic copy

Embargo on all of electronic copy for a period of 2 years on the following ground(s):

- Publication would preclude future publication

Supporting statement for electronic embargo request

I intend to publish my thesis.

Title and Abstract

- I agree to the title and abstract being published.

Date 5 February 2018 Signature of candidate: .....

Date 5 February 2018 Signature of supervisor: .....

Underpinning Research Data or Digital Outputs

Candidate's declaration

I, Danila Gasperini, 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 5 February 2018 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:

Embargo on all of electronic files for a period of 2 years on the following ground(s):

- Publication would preclude future publication

Supporting statement for embargo request

I intend to publish my thesis.

Date 5 February 2018 Signature of candidate: .....

Date 5 February 2018 Signature of supervisor: .....

To my Mother, and about time…

Acknowledgements

This thesis has been a great journey. Many people have contributed to make it happen. Primarily Andy who provided support and supervision until the end of the PhD. Thanks to Steve, for the opportunity of starting the degree, and working on gold.

It was not easy, but I have enjoyed learning and expanding the boundaries of my knowledge around the chemistry of the pretty metal.

A great thank goes to Dr. Alba Collado, who helped me at start and taught me the right tools to a better understanding of organometallic chemistry. Rik Veenboer, I loved the useful and animated discussions about chemistry and life and appreciated the support during this 4 years. Thanks also to ErPi, Caro, Enry, Dady, Marcel, José, Bellecaviglie who have helped going on until the submission with proof-readings, pints and useful suggestions. The ADS group was wonderful, they have welcomed me greatly and helped me continuing working, before and after the darkest moments. In particular, Stefania, Jason, Nassilia, Aileen, Mark, James, Claire, Tom, Steph, Jude and all those who contributed with chats and smiles to my everyday in the lab.

Thanks to my best friends, Rossana, Antonello, Gaia, Alessandra, Roberta lights in the dark. All the great people that accompanied me during this 4 years in this little village: Mausi, Leo, Guy, Flavio, Rob, Lorena, MariaG you have always been close and supported my decisions and crazy moments. The Parisian people whose optimism will never leave me, Neus, Doina, Andreas, Nika, Vaizanne. The volleyball people, in Dundee and St Andrews and referees in Bologna, with whom I shared victories and losses. We never gave up.

To my family, who kept me alive and breathing. To Lachicca and Vadzim, beloved siblings, you have always cheered me up. To Chiara, I wouldn't have arrived here today without you, and I am glad I was with you in the most difficult hours of our life. To my dad, thanks for supporting me and everyday understanding.

To my mother, who is the real engine of all this, thank you.

Mi manchi tanto. Mi hai regalato amore e la faccia tosta per continuare fino alla fine. Sei la mia Speranza, ogni giorno. Spero questa dedica arrivi fino a te.

Published work and author contributions

Some of the work reported in this thesis has been published as peer-reviewed journal articles as described below. Unless stated otherwise, the work reported is all my own work and I was the primary researcher on the projects.

Chapter 2.

Based on data reported in the following publications:

S. Dupuy, D. Gasperini, S. P. Nolan, *ACS Catal.* 2015, **5**, 6918-6921;
S. Dupuy contributed with some preliminary catalytic results and wrote the manuscript.

D. Gasperini, L. Maggi, S. Dupuy, R. M. P. Veenboer, D. B. Cordes, A. M. Z. Slawin and S. P. Nolan, *Adv. Synth. Catal.*, 2016, **358**, 3857-3862;
L. Maggi and R. M. P. Veenboer contributed with synthesis of starting materials, S. Dupuy contributed with some preliminary catalytic results, D.B. Cordes carried out the X-ray diffraction analyses.

Chapter 3.

This chapter presented data intended for the following publication:

D. Gasperini, S. V. C. Vummaleti, A. Poater, L. Cavallo, D. B. Cordes, A. M. Z. Slawin and S. P. Nolan "Dinuclear gold carboxylate and their involvement into the hydrocarboxylation of alkynes" *manuscript in preparation*.
S. V. C. Vummaleti contributed with computational data, D. B. Cordes carried out the X-ray diffraction analyses.

Chapter 4.

This chapter presented data intended for the following publication:

D. Gasperini, M. D. Greenhalgh, R. Imad, S. Siddiqui, A. Malik, F. Arshad, M. I. Choudhary, D. B. Cordes, A. M. Z. Slawin, S. P. Nolan and A. D. Smith "Synthesis and characterisation of Au(I) and Au(III)-isothiourea complexes and their catalytic and biological activity" *manuscript in preparation.*

R. Imad, S. Siddiqui, A. Malik, F. Arshad contributed with the biological analyses, D. B. Cordes carried out X-ray diffraction analyses, M.D. Greenhalgh contributed to update and proof-read the manuscript.

Chapter 6.

Based on data reported in the following publications

D. Gasperini, A. Collado, A. Goméz-Suárez, D. B. Cordes, A. M. Z. Slawin and S. P. Nolan, *Chem. Eur. J.*, 2015, **21**, 5403-5412;

A. Collado contributed with some experimental initial results, A. Collado and A. Goméz-Suárez proof-read the manuscript, D. B. Cordes, A. M. Z. Slawin carried out X-ray diffraction analyses.

Some unpublished results are intended for the following publication:

D. Gasperini, R. M. P. Veenboer, P. B. Webb, S. V. C. Vummaleti, A. Poater, L. Cavallo, D. B. Cordes, A. M. Z. Slawin and S. P. Nolan "Organogold(III) species: studies into their formation and their reductive elimination" *manuscript in preparation*.

P. B. Webb contributed with IR study and kinetic data, S. V. C. Vummaleti contributed with computational data, D. B. Cordes carried out X-ray diffraction analyses.

Other articles were also published as a result of collaborative efforts and were not included in this thesis:

R. M. P. Veenboer, D. Gasperini, F. Nahra, D. B. Cordes, A. M. Z. Slawin, C. S. J. Cazin and S. P. Nolan, *Organometallics*, 2017, **36**, 3645-3653

A. Collado, S. R. Patrick, D. Gasperini, S. Meiries and S. P. Nolan, *Beilstein J. Org. Chem.*, 2015, **11**, 1809-1814.

A. Gómez-Suárez, D. Gasperini, S. V. C. Vummaleti, A. Poater, L. Cavallo, S. P. Nolan, *ACS Catal.*, 2014, **4**, 2701-2705

Abstract

Gold has emerged as valuable tool for chemists. The physico-chemical properties of the metal centre make it exceptionally prone to activate multiple bonds, such as alkynes and alkenes. Thus, its utility in catalysis has been exploited together with the synthesis of suitable catalysts to allow new, efficient transformations, and the understanding of their intrinsic mechanisms. Reported in this thesis are efforts to this goal, such as the design and study of new Au(I) and Au(III) complexes towards functionalisation of alkynes.

The development of new catalytic systems is tackled in Chapter 2. An efficient method for the intermolecular hydrocarboxylation of alkynes catalysed by dinuclear Au-NHC species to access diverse vinyl esters in excellent yield and stereoselectivity is described. The successful methodology is followed by the straightforward intramolecular hydrocarboxylation of alkynoic acids to allow the stereoselective and regioselective synthesis of γ-, δ- and ε-lactones in high yield.

Initial mechanistic studies into the hydrocarboxylation of alkynes are shown in Chapter 3. The discovery and characterisation of novel dinuclear gold carboxylates species is described, and their role in the catalytic inter- and intramolecular process is investigated.

Chapter 4 highlights the synthesis of novel Au complexes bearing chiral isothiourea ligands. Neutral and heteroleptic Au(I) and Au(III) species are obtained in excellent yield, and their solution and solid-state behaviour studied, together with their electronic and steric properties. Further testing towards activation and functionalisation of alkynes and propargylic derivatives are shown.

Dual catalytic processes involving Au and isothiourea catalysts are presented in Chapter 5. Attempts towards Lewis acid/Lewis base activation of multiple bond derivatives and activated esters towards the formation of new C-C bonds is described.

The synthesis of organogold compounds, bearing NHC ligands, is described in Chapter 6. Through deprotonation of C(sp^3)-H bonds, a series of stable gold(I) complexes was synthesised and found to be suitable synthons to different gold species. Finally, the redox chemistry of organogold species is explored.

List of abbreviations

$\%V_{bur}$ - percent of buried volume

4-DMAP - 4-dimethylaminopyridine

Å - Angstrom

Ac - acetyl

acac - acetylacetonate

AO - atomic orbital

APCI - atmospheric pressure chemical ionisation

BAr^F - tetrakis[3,5-bis(trifluoromethyl)phenyl]borate

BINAP - (1,1′-binaphthalene-2,2′-diyl)bis(diphenylphosphine)

Bn - benzyl

BPPFA - *N*,*N*-dialkyl-1-[2,1'-bis(diphenylphosphino)ferrocenyl]ethylamine

BTM - benzotetramisole

cat. - catalyst

CIP - carbon/charcoal adsorption

COD - 1,5-cyclooctadiene

COSY - correlation spectroscopy

CPME - cyclopentyl methyl ether

CSA - camphorsulfonic acid

CSTR - continuous-stirred tank reactor

d - days

DABCO - 1,4-diazabicyclo[2.2.2]octane

DBN - 1,5-diazabicyclo[4.3.0]non-5-ene

DBU - 1,8-diazabicyclo[5.4.0]undec-7-ene

DCC - dicyclohexylcarbodiimide

DCE - dichloroethane

dept - distortionless enhancement by polarisation transfer

DFT - density functional theory

DHPB - 3,4-dihydro-2*H*-pyrimido[2,1-b]benzothiazole

DMF - *N*,*N*-dimethylformamide

DMSO - dimethyl sulfoxide

ESI - electron spray ionisation

eV - electronvolt

FABA - tetrakis(pentafluorophenyl)borate

FTIR - Fourier-transform infrared spectroscopy

h - hours

HBTM - homobenzotetramisole

HMBC - heteronuclear multiple bond correlation

HOMO - highest occupied molecular orbital

HRMS - high resolution mass spectrometry

HSQC - heteronuclear single quantum correlation

Hz - Hertz

i - *ipso*

IAd - 1,3-bis(adamantyl)imidazole-2-ylidene

IMes - 1,3-bis(mesityl)imidazol-2-ylidene

IPent - 1,3-bis(2,6-bis(1-ethylpropyl)phenyl)imidazol-2-ylidene

IPr - 1,3-bis(2,6-di*iso*propylphenyl)imidazol-2-ylidene

IPr* - 1,3-bis(2,6-bis(diphenylmethyl)-4-methylphenyl)imidazol-2-ylidene

IPr^{Cl} - 4,5-dichloro-1,3-bis(2,6-di*iso*propylphenyl)imidazol-2-ylidene

I*t*Bu - 1,3-bis(*tert*-butyl)imidazol-2-ylidene

ITU - isothiourea

LB - Lewis base

LUMO - lowest occupied molecular orbital

m - *meta*

m.p. - melting point

MBO - Mayer bond order

Me - methyl

mg - milligram

min - minutes

mL - millilitre

Ms - mesyl

NBS - *N*-bromo succinimide

NHC - N-heteocyclic carbenes

NMI - 1-methylimidazole

NMR - nuclear magnetic resonance

NOESY - nuclear Overhauser effect spectroscopy

NSI - nanospray ionisation

Nu - nucleophile

o - *ortho*

o/n - overnight

OA - oxidative addition

ORG - organocatalyst

p - *para*

PCC - pyridinium chlorochromate

Pin - pinacol

PNB - *para*-nitrobenzoate

PNP - *para*-nitrophenol

ppm - part par million

py - pyridine

Pybox - pyridine bis(oxazoline)

r.t. - room temperature

RDS - rate determining step

RE - reductive elimination

s - seconds

S - singlet

SIMes - 1,3-bis(2,6-di*iso*propylphenyl)imidazolin-2-ylidene

SIPr - 1,3-bis(mesityl)imidazolin-2-ylidene

SOMO - singly occupied molecular orbital

t - time

T - triplet/Temperature

TBAF - tetra-*n*-butylammonium floride

TBDMS - *tert*-buthyldimethylsilyl

TEP - Tolman electronic parameter

Tf - triflyl

THF - tetrahydrofuran

THT - tetrahydrothiophene

TIPS - triisopropylsilyl

TM - transition metal

tmg - tetramethyl guanidine

TOF - turn-over frequency

TON - turn-over number

Ts - tosyl

TS - transition state

dppe - 1,2-bis(diphenylphosphino)ethane

dpfam - *N,N'*-bis[2-(diphenylphosphino)phenyl]amidinate

dppf - 1,1'-ferrocenediyl-bis(diphenylphosphine)

CAAC - cyclic (alkyl)(amino)carbenes

Table of Contents

1. Gold, the "king of metals" 1

1.1. Why is gold special? 2

1.2. Ligand effect to gold complexes 5

1.3. Mononuclear and dinuclear organogold(I) and -gold(III) compounds 14

1.4. *N*-Au(I) and *N*-Au(III) compounds 22

1.5. O-Au(I) compounds 28

1.6. From sleeping beauty, to "gold rush"! 34

1.7. Aims and objectives 44

1.8. Bibliography 44

2. Hydrocarboxylation of alkynes catalysed by dinuclear Au(I)-NHC complexes . 59

2.1. Introduction 59

2.2. Intermolecular gold(I)-catalysed hydrocarboxylation of internal alkynes 64

2.3. Intramolecular cyclisation of alkynoic acids 73

2.4. Conclusions and perspectives 82

2.5. Experimental 83

2.6. Bibliography 98

3. Probing the mechanism of the hydrocarboxylation of alkynes 103

3.1. Introduction 103

3.2. Results and discussion 107

3.3. Conclusions and perspectives 139

3.4. Experimental 140

3.5. Bibliography 145

4. When gold meets isothiourea: synthesis, characterization and activity of Au(I) and Au(III) isothiourea complexes 150

4.1. Introduction 150

4.2. Results and discussion 153

4.3. Stoichiometric and catalytic reactivity of Au ITU complexes 171

4.4. Conclusions and perspectives 178

4.5. Experimental 179

4.6. Bibliography 197

5. Dual catalysis towards the activation of alkyne derivatives 202

5.1. Introduction 202

5.2. Aims and objectives 210

5.3. Activation of alkynes 211

5.4. Propargylic alkynes synthesis and activation 216

5.5. Conclusions and perspectives 225

5.6. Experimental 226

5.7. Bibliography 235

6. Synthesis and application of organogold species 240

6.1. Introduction 240

6.2. From side products to valuable synthons 242

6.3. Reactivity of acetonyl-Au(I) NHC complexes 253

6.4. Reductive elimination from C(sp^3)-Au compounds 260

6.5. Conclusions and perspectives 267

6.6. Experimental 268

6.7. Bibliography 283

7. Conclusions 291

1. Gold, the “king of metals”

Gold has been known for millennia. First discovered as shining nuggets, it quickly became a symbol of power, richness and beauty for every human culture. This “noble” metal is resistant to corrosion, but ductile and malleable, thus its widespread use in jewellery and art.

Gold and silver coins were soon utilised as practical currency. The concept of gold standard monetary system arose and was used until the 1970s. It is highly conductive, which made it appealing for electronic industry.[1] Gold metal is non-toxic and approved as a food additive, while gold complexes are noxious;[2] *e.g.* auranofin, or gold(I)-thiolate drugs, are used for the treatment of symptoms of rheumatoid arthritis.[3]

It is mainly supplied from aurous or argentous ores, found in Australia, South America, Russia, and South Africa. Other supplies come from platinum-group metal rich ores,[4] or from recovery of industrial wastes, particularly electronic scraps.[5] Gold in its metallic form can be obtained through gravity concentration, chlorination, cyanide leaching, and carbon/charcoal adsorption (CIP).[6] A fine powder is obtained and shaped conveniently.

However, the environmental impact of these metallurgic processes poses enormous issues, and their replacements are cost prohibitive, and less advantageous (*e.g.* non-cyanide lixiviants,[7] biological treatment of wastes).[8] The quest for more benign methods to obtain gold is still open.

Gold(0) can be further processed to chloride complexes in higher oxidation states (Figure 1.1); by treatment with hydrochloric acid, and chlorine gas, an aqueous solution of $HAuCl_4$ is formed.[9] If sodium or potassium salts are present in the mixture, the corresponding $NaAuCl_4$, or $KAuCl_4$ salts are obtained and commercially available as hydrates. Reaction of metallic gold with Cl_2 forms $AuCl_3$, which upon loss of chlorine lead to metastable AuCl. The latter promptly disproportionates to Au(0), and $AuCl_3$. Stable Au(I) complexes, with formula $[AuCl(PR_3)]$, and $[AuCl(SR_2)]$, are formed by reduction of $HAuCl_4$ with phosphines (PR_3), or dialkyl sulfides (SMe_2, THT).[10]

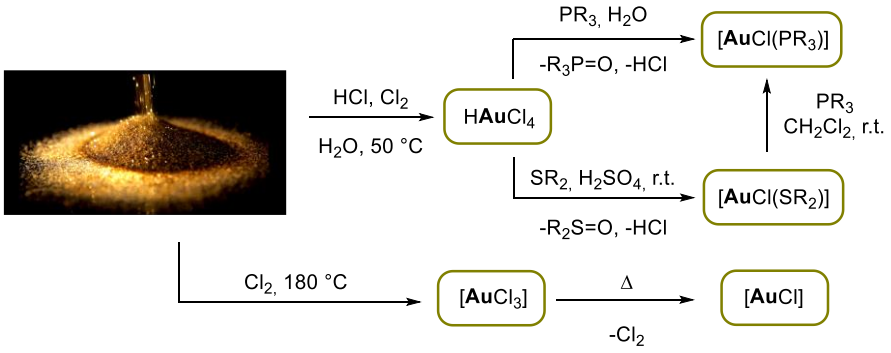


Figure 1.1. Simplified processing of Au(0) to Au(III) and Au(I) salts and complexes.

These are the main precursors of highly functionalised gold compounds, whose development, design and understanding have evolved rapidly in the last century, with the first examples of organogold compounds dating back to 1907.[11] The catalytic properties of the metal centre have been recognised, and an exponential number of reports have appeared in both homogeneous and heterogeneous catalysis.[12] Research interests in gold arise from the macroscopic, and electronic properties of this late transition metal with an overview of this field following.

1.1. Why is gold special?

The bright yellow transition metal can be found in the periodic table along with the group 11 elements, copper, silver and röntgenium. With an atomic number Z = 79, gold has one stable isotope, ^{197}Au, with nuclear spin s = 3/2. It appears most commonly in the +1 and +3 oxidation states, other than Au(0), corresponding respectively to the ground state electronic configurations [Xe]4f^{14}5d^{10}, and [Xe]4f^{14}5d^{8}. Although less common, the oxidation states of -1 (auride, CsAu),[13] +2,[14] +5 (AuF_6^-)[15] have also been found. Compared to Cu, and Ag, Au shows a higher ionization potential (9.22 eV *vs* 7.57 eV for Ag), together with the highest electronegativity among transition metals (χ = 2.4 *vs* χ = 1.9 for Cu and Ag). For decades this abnormal behaviour was explained by extending the concept of the lanthanide contraction to 5d metals (the effect of filling 4f shell before 6s, and 6p); this abstraction was not sufficient for a full description of the maximum observed for the metal and was thus expanded through relativistic terms.[16] The contributions of this phenomenon in chemistry can be explained as referring to electrons whose velocity approaches the speed of light (*c*) when moving close to heavy nuclei (Z > 50);[17] thus the mass of an electron increases considerably when v approaches *c*, following the mass

correction to the relativistic one-electron equation of Dirac.[18] This correction is shown in Equation 1.1 where m_0 is the non-relativistic term, with v = speed of electron, and c = speed of light (~3×10^8 m/s). In non-relativistic terms c = ∞, thus v/c ≈ 0, and corrections to the mass is negligible.

$$m = \frac{m_0}{\sqrt{1-(v/c)^2}}$$

Equation 1.1. Relativistic effect of electron speed on mass.

For a given atom, the average radial velocity of the 1s electrons is $\langle v_r \rangle$ = Z. The expression v/c thus becomes Z/c (137 Hartree atomic unit = c). For Au, with Z = 79 will give 79/137 = 0.5766, thus the electron in 1s orbital moves at ~58% of c.

The increment on the mass of the electron implies a decrease of the Bohr radius, caused by an inverse proportionality to its mass, as shown in Equation 1.2, where $\hbar \approx 1.054\times10^{34}$ J·s, e = electron charge ≈ 1.60×10^{-19} C and m_e = mass of electron.

$$a_0 = \frac{4\pi e_0 \hbar^2}{m_e Z e^2}$$

Equation 1.2. Bohr radius equation.

Therefore, the radius of the 1s orbital for Au will be reduced by roughly 20%. A final contraction will occur for all s orbitals; however, a decreased effect is seen by valence shell orbitals, because of the dominant core contraction (Figure 1.2).[19] The same effect can be seen to a lesser extent for p orbitals. A direct effect of the closest proximity of these electrons in s and p orbitals to the nucleus manifests itself in the increased first-ionization, electronegativity, and electron affinity of the atom considered.

The second consequence of the relativistic effect is spin-orbit splitting, which considers not only the quantum numbers l and s, but the vector sum J (J = L + S). Thus, for p orbitals with quantum number L = 1, J is 1/2 and 3/2, while for d orbitals with L = 2, J becomes 3/2 and 5/2 (Figure 1.2). An indirect effect of the relativism observed for heavy elements is the radial expansion of d and f orbitals which are destabilised energetically as a consequence of an increased shielding by the electrons in the contracted s orbitals.

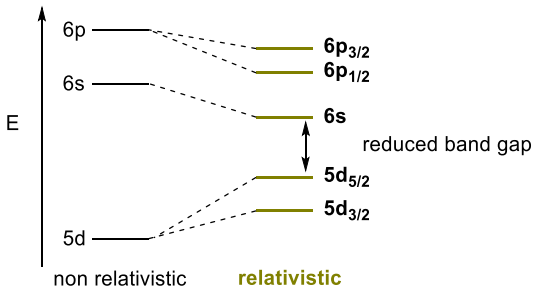


Figure 1.2. General orbital scheme for Au without (NR), and with (R) relativistic effect.

The golden/yellow colour of metallic gold might be caused by the small band gap between the full 5d and the half-filled 6s Fermi level (Figure 1.2): gold will absorb in the visible blue-violet region and emit in the red-yellow.[18]

The relativistic effects lead to reduced atomic radii, as found for Au(I) cations in gold complexes, which was calculated to be smaller than Ag(I) species (1.25 *vs* 1.33 Å).[20] This effect was shown also for Au(III),[21] while it is less pronounced for Au(0) and Ag(0). Higher oxidation states can therefore be accessed more easily for gold; that can also be explained in relativistic term because of the fine spin-orbit splitting of 5d orbitals which allows hybrid orbitals to form, and interact in stronger bonds.[22] The same is true for Au(II) complexes, which often contain a pair of tightly bound gold atoms with a typical dumb-bell shape $[Au(II)\text{-}Au(II)]^{4+}$. Very few examples of mononuclear Au(II) complexes are known.[23] The destabilization of 5d orbitals has been proposed as an explanation of aurophilic interactions, such as short Au(I)-Au(I) bonds typically around 3 Å.[24] More detailed theoretical calculations however, do not attribute this effect to orbital rehybridisation, but to dispersion forces, for which a full explanation has not yet been found.[25] The calculated energy for these metallophilic attractions is around 29-46 $kJ \cdot mol^{-1}$,[26] comparable to hydrogen bonding forces.

The energy orbital diagram (Figure 1.2) can also explain the molecular structure of Au(I) compounds, which are d^{10} species with 14 electrons. Because of the smaller energy gap between 5d and 6s mixing of atomic orbitals needs to be considered; mixing of gold AO $5d_z^2$, and 6s orbitals gives two molecular orbitals, referred to as Ψ_1, and Ψ_2. The electron pair residing in the $5d_z^2$ orbital can occupy Ψ_1, whose lobes are in the xy-plane away from the ligands. Further hybridization of Ψ_2 with $6p_z$ gives two orbitals with lobes concentrated along the z-axis, which can then accept electron pairs from the ligands and

form the linear geometry usually observed for Au(I) complexes (Figure 1.3).[27] However few examples of tricoordinated Au(I) complexes are known.[28]

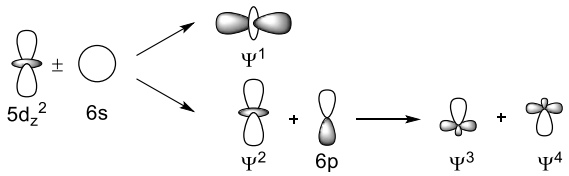


Figure 1.3. Formation of hybrid orbitals from mixing of atomic orbitals s, p and d.

Au(III), a d^8 species with 16 electrons that is isoelectronic to Pt(II), forms square planar structures.[29] Through studies on electronic structures of square planar complexes, the orbital energies for the 5d shell was found to be $d_{x^2-y^2} >> d_{z^2} > d_{xz}, d_{yz} > d_{xy}$.[30] These orbitals were shown to have some ligand character, forming MO that point towards the square vertices.[27] DFT calculations on the stability of AuX_4^- highlight the tendency to 4 coordination mode, over a 3 coordination (*e.g.* AuX_3 are usually found as dimers).[31]

1.2. Ligand effect to gold complexes

The contraction of 6s orbitals strongly impacts Au-L, or Au-X bonds (generally L = PR_3, NHC, while X is a 2 e^- donor), usually strengthening this interaction, because of a low-lying lowest-unoccupied molecular orbital (LUMO).[16] By tuning L, a diverse number of organometallic complexes has been explored. The knowledge gained from studying these species allowed the synthesis of both more stable and more reactive species, breaking the dichotomy of the terms stability *vs* reactivity. Considering the plethora of compounds that can coordinate to Au, such as phosphines, N-heterocyclic carbenes (NHC) as well as *N*-centred Lewis bases, judicious choice of the ligand appears to be of strong relevance.[32] A discussion of their properties will follow. Moreover, the bonding within gold complexes containing C, N and O compounds will be reviewed.

1.2.1. N-heterocyclic carbenes

Since their discovery, carbenes are one of the most investigated reactive species in organic chemistry.[33] Carbenes are neutral species with a divalent C(0) atom with an electron sextet in the valence shell.[35] The 2s and 2p orbitals in the carbon atom can exist in different energetic levels depending on: 1) the geometry of the carbene; 2) the mesomeric and inductive effect of substituents around the carbon atom; 3) steric effects.

Linear carbenes are less stable, where 4 electrons sit in sp hybridised orbitals, while 2 electrons are in degenerate non-bonding p orbitals (p_x, and p_y). Bending the carbene breaks degeneracy, and the carbon atom becomes sp^2 hybridised, with a p_y orbital, called also p_π, almost unchanged; while p_x, called σ, assumes partial s character, and decreases in energy.[34] Thus, the non-bonding electrons can occupy sp^2 and p_π orbitals, a triplet state T, or pair in the σ orbital, a singlet state S.

Substituents around the carbon significantly affect the ground state configuration of a carbene (Figure 1.4); σ-electron withdrawing substituents more electronegative than carbon ($\chi > 2.5$) stabilise the HOMO by an inductive effect, favouring the singlet state. π-Electron-donating ligands stabilise the carbene by a mesomeric effect, allowing π-donation of the lone-pair from the substituents to the empty p_π orbital.

This is commonly observed in cyclic diaminocarbenes and carbenes with at least one α-amino substituent. These are given the generic name N-heterocyclic carbenes (NHC), which assume a pivotal role among the singlet carbenes, since the isolation in 1991 by Arduengo of the first free NHC compound, 1,3-bis(adamantyl)imidazole-2-ylidene (IAd) (Figure 1.4).[35]

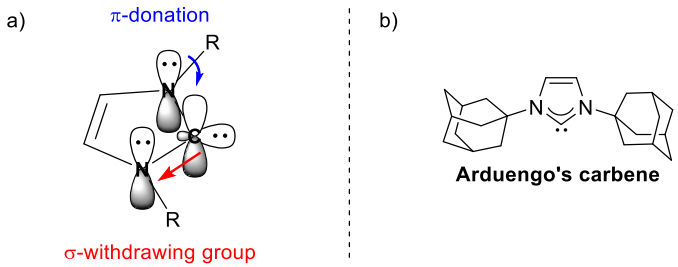


Figure 1.4. a) Substituent effect to the stability of an NHC; b) Arduengo's carbene, first stable NHC isolated.[35]

Considering the structure of imidazolylidenes, resonance forms can be drawn to best describe these interactions (Figure 1.5, a).[36] These species display carbenic rather than ylidic nature, as confirmed by DFT calculations,[37] and spectroscopic analyses.[38] The important resonance structures makes NHC electron-rich nucleophiles, whereas other carbenes are typically considered electrophilic. In general, most NHC are isolable, although sensitive to H_2O and electrophiles.[39]

With these intriguing characteristics, a number of NHC ligands bearing variations on the original scaffold have been reported (Figure 1.5, b);[40,41,42] other than the aforementioned imidazolylidenes, other structures such as imidazolidinylidenes, thiazolylidenes,

oxazolylidenes, triazolylidenes, and pyrrolylidenes.[36a] The most commonly encountered architecture in literature, and the one used in this work, displays a five-membered ring skeleton, however expanded carbenes are known. Sterically demanding *N*-substituents, and backbone substituents have a stabilising effect to the carbene, however this plays a minor role compared to electronic stabilisation.

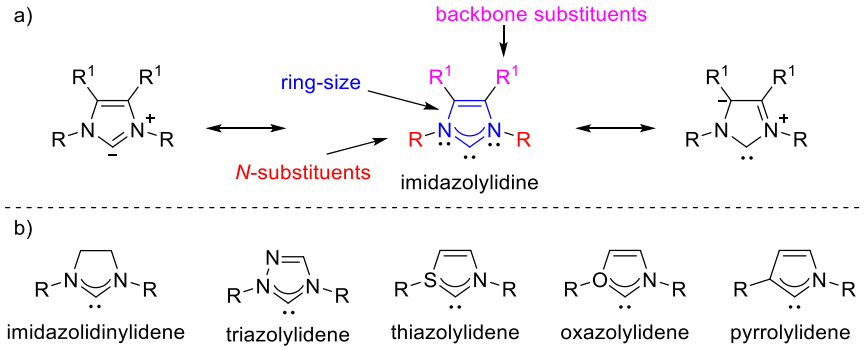


Figure 1.5. a) Resonance structures for imidazolylidene, and detail into its skeleton; b) most encountered NHCs.

1.2.1.1. Synthesis of NHCs

Free carbenes can be obtained through several routes (Figure 1.6). The most common methodology involves the deprotonation of azolium salts with a suitable base, such as K_2CO_3, NaH, KO*t*Bu or KHMDS.[43] The acidity of the salts is quite important: imidazolium salts usually shows pK_a in DMSO ranging from 16-24.[44] Imidazolinium salts are slightly less acidic compared to their unsaturated analogues (pK_a in DMSO for SIPr = 21.5 *vs* IPr = 21.1), while triazolium salts are even more acidic (pK_a in H_2O = 16-19).[45] Other interesting procedures rely on decarboxylation of NHC-CO_2 adducts,[46] desulfurisation of thioureas with potassium in boiling THF[47] or vacuum-pyrolysis under removal of volatile leaving groups.[48]

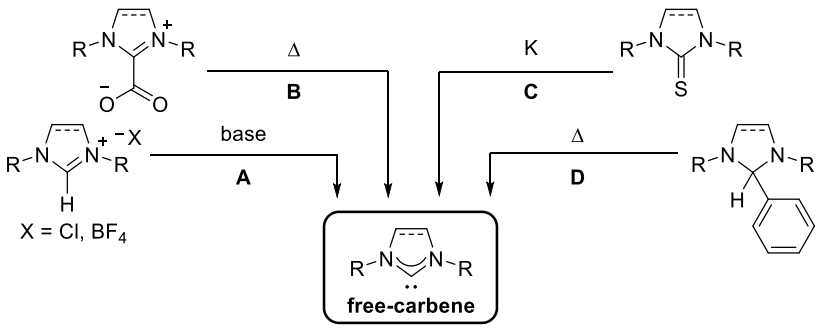
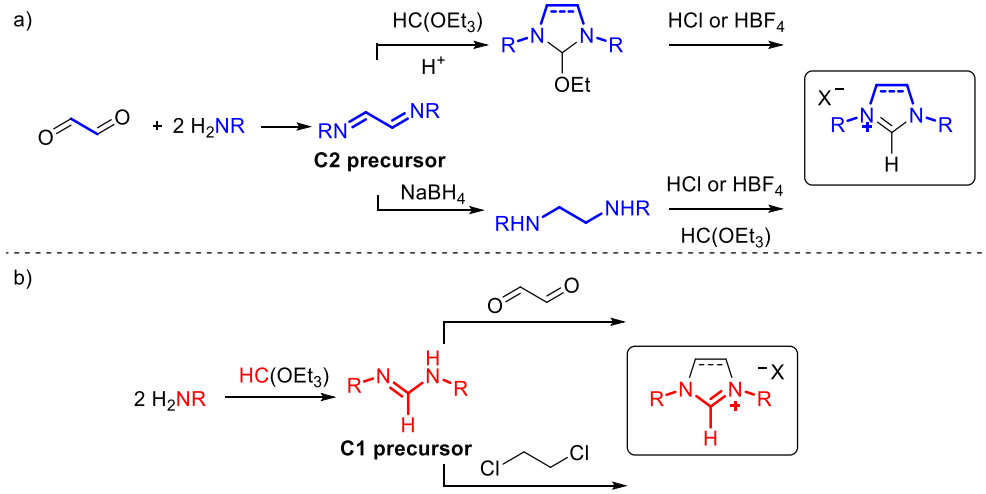


Figure 1.6. Major pathways for the formation of free-carbenes: A) deprotonation;[43] B) decarboxylation;[46] C) desulfurisation;[47] D) vacuum-pyrolysis.[48]

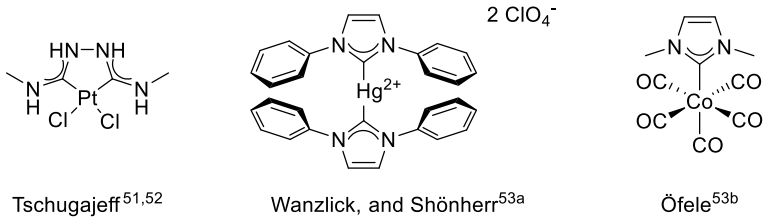
Imidazolium, and imidazolidinium salts, can be readily synthesised *via* (Scheme 1.1):[49] a) ring-closure reactions from a C2 unit, pre-backbone precursor; b) ring-closure reactions from formamidine, C1 pre-carbenic precursor. The former proceeds through formation 1,4-diaza-1,3-butadiene compound from glyoxal and the chosen amine, and cyclisation with chloromethyl ether, triethyl orthoformate, or paraformaldehyde in presence of acid to form the imidazolium salt. Reduction of the diimines with $NaBH_4$, followed by condensation with C1 precursors will lead to imidazolidinylidenes (Scheme 1.1, a). In the second route, formamidine, a pre-carbenic precursor, is formed from ethyl orthoformate, and a primary amine; subsequent cyclisation with glyoxal leads to imidazolium salts, while 1,2-dichloroethane gives the saturated NHC (b).[50]



Scheme 1.1. General synthesis of imidazolium and imidazolidinium salts from: a) ring closure from C2 units;[49] b) ring-closure from a formamidine C1 precursor.[50]

1.2.1.2. Au-NHC coordination

The first examples of M-NHC carbenes, was reported by Tschugajeff in 1925.[51] The authors reported the formation of a red salt from a reaction with tetrakis(methylisocyanide)Pt(II) complex with hydrazine. The structure of this carbene-Pt complex was only recognised in 1970, and isolated as the chloride complex (Figure 1.7).[52] Further studies, in 1968 by Wanzlick, Shönherr and Öfele into the synthesis of Cr(O) and Hg(II) carbene complexes,[53] opened the way for the exciting fusion of metal-carbene chemistry that still exists today.



Tschugajeff[51,52] Wanzlick, and Shönherr[53a] Öfele[53b]

Figure 1.7. First metal NHC complexes.

The nature of metal carbene interactions can be described by considering their molecular orbital contributions, as the sum of σ and π interactions between the sp^2 and p orbitals from the ligand and metal centred d orbitals.[54] Three contributions have to be considered (Figure 1.8): 1) σ-donation from the carbene lone electron pair to the d_z^2 orbital of the metal (a); 2) backdonation of the metal d_{xz}, and d_{yz} orbitals to the empty p_π orbital of the NHC, with a contribution of ~ 20% of the total attractive interaction (b);[55] 3) for electron-deficient metals a contribution of π-donation from filled, and empty p orbital of the ligand to d-orbital of the metal (c).[56]

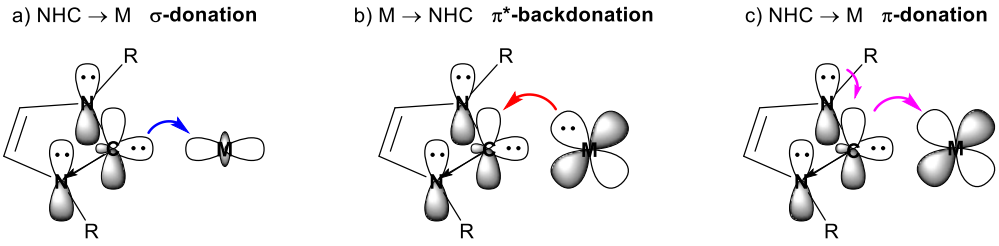
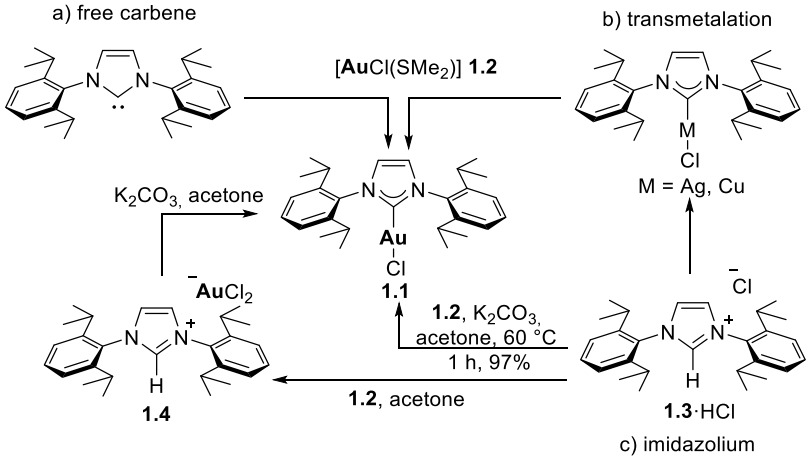


Figure 1.8. Metal-NHC bond contributions.

The gold NHC bond can be described according to the molecular orbital diagram presented in Figure 1.8. For Au(I) it has been described as a three-centre four-electron hyperbond, formed by donation of electron density from ancillary and auxiliary ligands to the vacant 6s orbital centred on the metal. Higher contribution of backbonding in Au-NHC was found for neutral complexes, such as [AuCl(NHC)], with values of π-acceptance of around 50% of σ-contributions.[57] When complexes with strong π-acceptors, *e.g.* CO^-, or CN^- were considered, backbonding contributions decreased by 10 fold, however these were still important.[58]

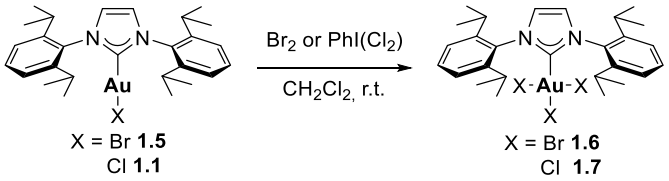
[AuCl(NHC)] complexes are among the most investigated organogold compounds,[59] and the most used species in catalysis.[59c] Complex [AuCl(IPr)] (**1.1**) can be synthesised through (Scheme 1.2); a) the generation of a free carbene, subsequently reacted with a gold source, [AuCl(SMe_2)] (**1.2**);[59c] b) the carbene transfer route from Ag-,[60] or Cu-[61]

NHC precursors; c) from **1.2**, and imidazolium salt IPr·HCl (**1.3**·HCl) in presence of an equimolar amount of a weak base, K_2CO_3.[62] The latter was found to be the most useful route to access these complexes. These reactions were demonstrated to proceed *via* [IPr·H][$AuCl_2$] (**1.4**) species when reacting **1.3**·HCl, and the gold precursor **1.2**. Abstraction of the proton with an equivalent of base from the imidazolium moiety delivers the desired organogold complex.



Scheme 1.2. Synthesis of **1.1** through: a) free carbene;[59c] b) transmetalation;[60,61] c) imidazolium routes.[62]

The use of NHC ligands to stabilise Au(III) complexes is also known (Scheme 1.3) as demonstrated by neutral complexes of the kind [AuX_3(IPr)], where X = Br (**1.6**) or Cl (**1.7**).[59d,63] They have been synthesised through reaction of **1.1** or [AuBr(IPr)] (**1.5**) with oxidants, usually elemental bromine or iodosobenzene dichloride compounds.



Scheme 1.3. Synthesis of [AuX_3(IPr)] complexes **1.6**, and **1.7** (X = Br, Cl).[59d,63]

Further details of Au(I)- and Au(III)-NHC complexes will be covered in sections 1.3, 1.4 and 1.5. The high stabilising effect that ligand can impart to the gold centre allowed sensitive species, such as [AuF(IPr)],[64] [AuH(IPr)],[65] [AuCl(biphenyl)(IPr)][66] to be accessible and isolable.

1.2.1.3. Electronic and Steric Properties of NHC Ligands

The utility of M-NHC complexes in catalysis are highly dependent on their peculiar electronic and steric properties. Among the methods used to define the bonding arrangement in M-NHC complexes (Section 1.2.1.2), the quantification using Tolman electronic parameter (TEP) gives a measure of the electron-donating ability of a ligand to a metal centre (Figure 1.9).[67] Initially proposed to study tertiary phosphines, the method involves measurement of the vibrational stretching frequency of a carbonyl ligand, C≡O ($\nu_{C\equiv O}$), by IR spectroscopy. In a [Ni(L)$(CO)_3$] complex, where L is usually an NHC or phosphine, the spectator ligand L is electron-donating resulting in an electron-rich metal centre. Considering a carbonyl ligand in a *trans* or *cis* position to L, strong backdonation from the d orbital of the electron rich metal centre to the π* anti-bonding orbital of the carbonyl results in weakening of the carbon oxygen bond. Measurement of the $\nu_{C\equiv O}$ stretching frequency allows the actual π-donor ability of the metal centre to be extrapolated, and consequently gives a measure of the ligand donor ability. The lower the observed $\nu_{C\equiv O}$ compared to unbound CO (2143 cm^{-1}), the stronger is the σ-donating ability of the ligand. Generally, NHCs are better σ-electron-donors than phosphines and phosphites, with values ranging from 2058-2048 cm^{-1} for NHCs *vs* 2210-2056 cm^{-1} for PR_3.

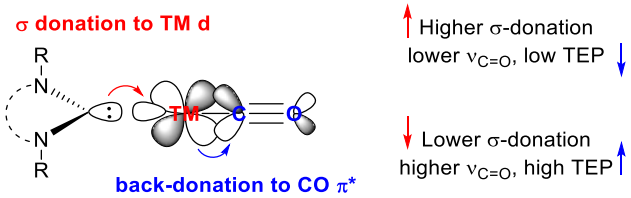


Figure 1.9. Description of TEP concept.

The limitations of this method include the toxicity of $Ni(CO)_4$ complexes, required to synthesise $[NiCl(CO)_3]$ species. Less toxic variants, such as $[IrCl(L)(CO)_2]$ and $[RhCl(L)(CO)_2]$, are known and linear regression is necessary to link these systems to the Ni complexes (Equation 1.3).[68]

$$TEP = 0.847\nu_{av}(CO)[Ir] + 336\ cm^{-1}$$

Equation 1.3. Expression to calculate TEP for Ir systems corrected based on linear regression.[68]

Together with the accepted σ-donor nature of NHC ligands, studies on their π-behaviour are of relevance. Examples of π-donor capacity have been shown.[69] More interesting, the π-accepting nature of NHCs, which accounts for higher contribution to bonding, has been demonstrated with theoretical, and experimental studies. Bielawski and co-workers synthesised [RhCl(COD)(NHC)] complexes, with modified NHCs presenting an IR handle in the backbone, *e.g.* isonitrile (Figure 1.10).[70] Replacement of COD with CO, a strong π-acceptor ligand, led to $[RhCl(CO)_2(NHC)]$ species; the $\nu_{C\equiv N}$ frequencies of the isonitrile group for the latter shifted to higher values indicating a degree of π-acceptance for the NHC ligand, higher in 1st *vs* the 2nd series of Rh complexes.

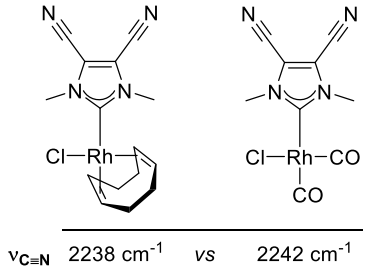


Figure 1.10. Analysis of π-acceptor nature of NHCs: IR studies on Rh NHC complexes.[70]

Nolan's research group analysed the NMR spectra of a series of $[PtCl_2(S(O)Me_2)(NHC)]$ complexes (Figure 1.11).[71] The δ_{Pt} shifts, and $^1J_{Pt\text{-}C}$, were observed; interestingly lower δ_{Pt}, and $^1J_{Pt\text{-}C}$ were found for complexes bearing saturated NHCs. These results, if considering that the other ligands to Pt are not π-acceptors, suggest that for the more

electron-donating saturated NHC ligands (*e.g.* SIPr) the degree of π-acceptance from the metal centre is higher compared to unsaturated NHCs (*e.g.* IPr).

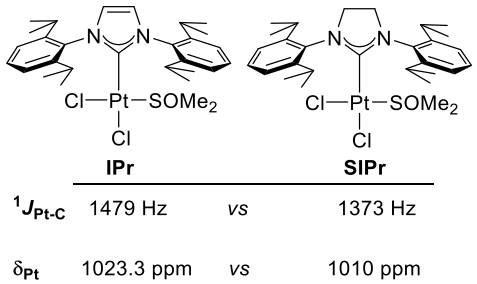


Figure 1.11. Analysis of π-acceptor nature of NHCs: NMR analysis on Pt complexes.[71]

Other studies on phosphinidene-NHC adducts, [NHC-PPh] showed that SIPr species had a higher rotational energy than IPr derivatives (Figure 1.12).[72] Moreover SIPr-PPh showed significant double bond character between P and C, supporting the hypothesis of a stronger M-C bond, thus stronger π-acceptance for the saturated analogue.

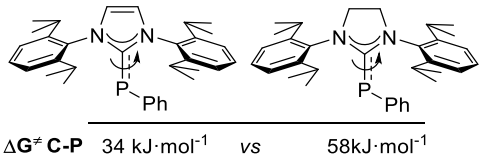


Figure 1.12. Analysis of π-acceptor nature of NHCs: rotational barriers for phopshinidene-NHC adducts.[72]

Alkyl *N*-substituents tend to give more electron-donating NHCs than their aromatic congeners and they possess different steric demand and flexibility, as the case of sterically hindered IAd and I*t*Bu ligands.[73] Substitution of the C^4 and C^5 position affects the electronic properties of the ligand, albeit to a lesser extent than the steric properties.[74]

Concerning their steric properties, NHCs and phosphines cannot be directly related through Tolman's "cone angle", Θ.[67] This measure defines steric properties for symmetric phosphines as the apex angle of a cylindrical cone, delimited by the Van der Waals radii of the external substituent atoms, and centred at 2.28 Å away from the P atom. While this model represents C_3 symmetrical shaped PR_3 well, it fails to describe the local C_2 symmetrical NHC ligands. A key parameter was proposed by Nolan and Cavallo,[75] as the "percent of buried volume" ($\%V_{bur}$) and defined as the percentage of volume of a sphere occupied by a ligand (Figure 1.13). The sphere refers to a defined radius around the metal centre, and the volume of the sphere represents the potential space occupied by the ligand within the sphere radius.

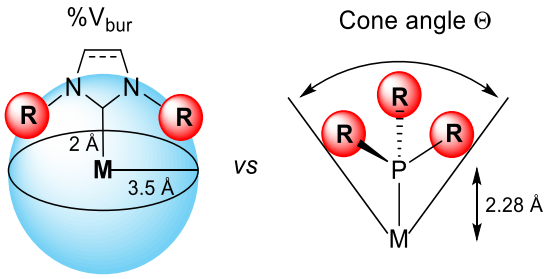


Figure 1.13. $\%V_{bur}$ and Tolman cone angle to calculate the steric parameters of NHCs and phosphines.

A study of $\%V_{bur}$ for Cu(I), Ag(I) and Au(I)-NHC linear species, not affected greatly by steric encumberment, showed the values obtained for the different metal complexes data were similar. The validity of the method was demonstrated for phosphine complexes.[75a] Initial $\%V_{bur}$ calculations were exempt of flexibility, or rigidity of the ligand around the metal centre, therefore giving a snapshot of NHC and phosphine metal complexes rather than the entire picture. Further refinement of this model now considers the dynamic behaviour of the M-NHC complex in order to better represent the real role of the species in catalysis.[76]

1.3. Mononuclear and dinuclear organogold(I) and -gold(III) compounds

As continuation of the exploration of the chemistry of Au-C bonds, presented in section 1.2.1, the chemistry of organogold compounds has proven extremely diverse, with Au-NHC bonds being one example of species bearing a C-Au bond. The study of such species gives a deeper understanding of precursors and intermediates of the many gold-catalysed transformations, helping to rationalise reaction mechanisms.

1.3.1. Mononuclear and dinuclear C(sp)-Au(I) complexes

Gold is considered a soft Lewis acid. In particular $Au(I)^+$, which is a large and diffuse cation has shown great affinity for π-systems,[77] such as alkynes, alkenes, allenes, in agreement with HSAB theory.[78] In particular coordination of alkynes to $[Au(IPr)]^+$ can occur in 2 different modes: i) π-coordination, better described by η^2 hapticity, of the metal centre to the triple bond as observed in $[Au(\eta^2\text{-PhC}\equiv\text{CPh})(IPr)][BF_4]$ (**1.9**) or ii) σ-coordination of gold with terminal alkynes [Au(C≡CPh)(IPr)] (**1.10**) (Figure 1.14).

The two complexes differ significantly in the orbital arrangement that forms the alkyne-Au(I) bond (Figure 1.14). The interaction in **1.9** can be described through the Dewar-Chatt-Duncanson model;[79] the major contributions to bonding are the σ and π interactions between the gold centre and π orbitals of the alkyne. In complex **1.10** interaction between C(sp) hybridized orbital to the d_z^2 orbital forms the σ-bond. This description defines the natural difference in bond strength of **1.9** *vs* **1.10**: alkynes bound through π-coordination to the metal centre are easily displaced in solution, while σ-acetylide-Au neutral species containing phosphines, and NHC ligands are highly stable.

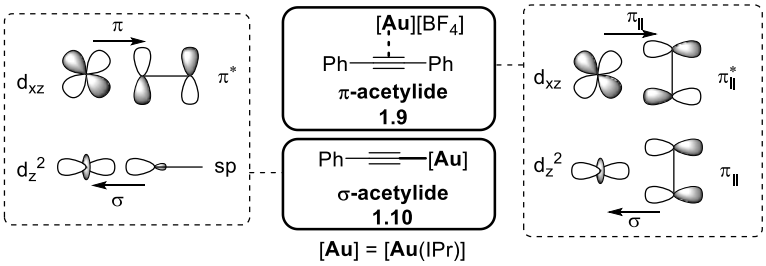


Figure 1.14. Major contributions (σ and π backbonding) to orbital interactions in σ- and π-acetylide-Au(I) species.

1.10, and related complexes of general formula [Au(C≡CR)(L)] (L = NHC, PR_3) can be synthesised in the following ways (Figure 1.15). Method i) uses ligand metathesis from [AuCl(L)] precursors with ethynyl Grignard reagents,[80] or acetylene and a strong base.[81] Alternatively ii) requires protonolysis of [Au(OH)(NHC)] complexes (Section 1.5.1) to access mononuclear, dinuclear and even trinuclear acetylide species;[82] only one example of phosphine ligand substitution by NHC represented in iii) has been reported to date.[83]

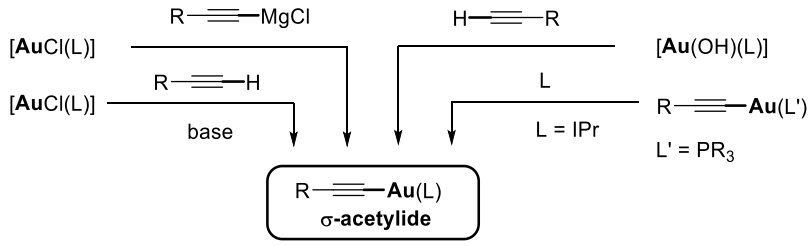
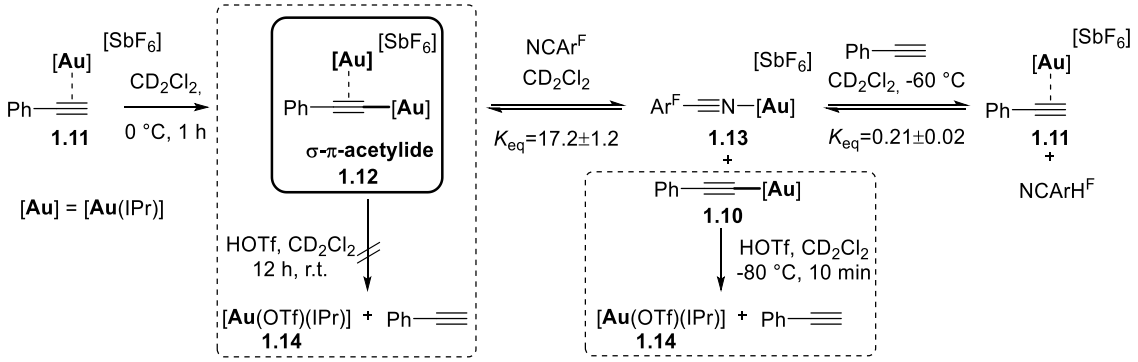


Figure 1.15. General scheme for the synthesis of σ-acetylide-Au(I) complexes; i) ligand metathesis;[80,81] ii) protonolysis;[82] iii) ligand displacement.[83]

Involvement of σ-acetylide-Au(I) complexes have been suggested for alkynylation of arenes,[84] and heterocycles,[85] such as indoles,[86] thiophenes,[87] furans,[88] and anilines.[89] C(sp)-H cleavage was observed from η^2-acetylide species bearing terminal alkynes (**1.11**) to σ-π-acetylide-Au(I) species (**1.12**) (Scheme 1.4).[90] Treatment of the species

[{Au(IPr)}$_2$(η^1,η^2-C≡CC$_4$H$_4$R)][SbF$_6$] with NCAr^F, showed displacement of the η^2-coordinated Au species to form the cationic [Au(IPr)(NCAr^F)][SbF$_6$] (**1.13**), and **1.10** σ-acetylide-Au(I) species with a K_{eq} = 17.2±1.2. Complex **1.13** reacted slowly with phenylacetylene (K_{eq} = 0.21 ± 0.02) to form the π-complex **1.11**, to reiterate the higher affinity of Au to form σ- instead of π-complexes with alkynes. Moreover, σ-π-acetylide **1.12** was resistant to protodeauration, with no conversion when treated with HOTf after 12 h, differently from the σ-acetylide **1.10** which promptly released phenylacetylene, and [Au(OTf)(IPr)] (**1.14**).



Scheme 1.4. Synthesis of **1.12**, and it reactivity towards nitriles;[90] in the dashed box reactivity of **1.12**, and **1.10** towards protodeauration.

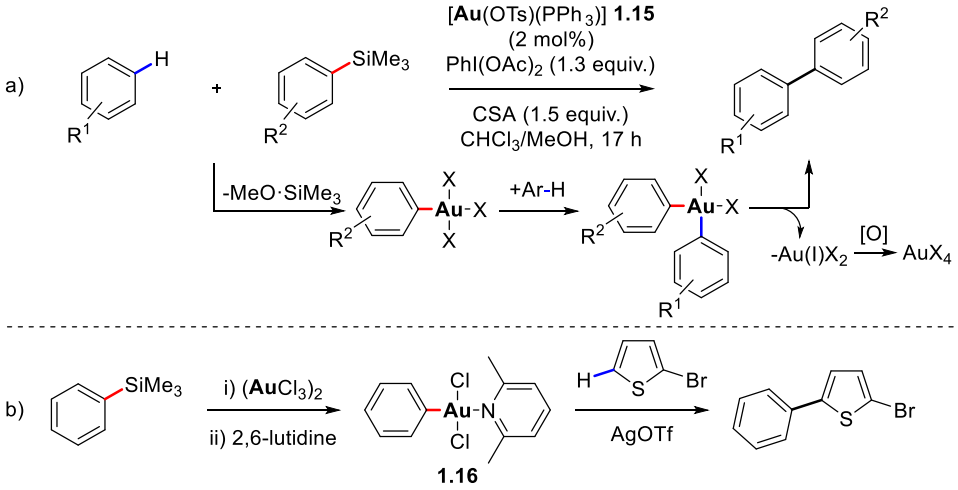
Alternative synthetic routes to **1.12** involve: i) reaction of cationic complexes [Au(IPr)(NCCH$_3$)][SbF$_6$] with 2 equiv. of terminal acetylene;[91] ii) dinuclear gold hydroxide (Section 1.5.2) with a stoichiometric amount of alkyne;[92] iii) addition of a gold(I) σ-acetylide species to an activated [AuCl(IPr)] **1.1** precursor.[93] These species have been postulated as reaction intermediates,[94] and questioned as catalytic dead-end species,[95] because of their reluctance to undergo protodeauration and their role in trapping active gold species [Au(L)]$^+$. However, they have shown to be suitable pre-catalysts for transformation involving diynes (Scheme 1.25).[93,96]

1.3.2. Mononuclear C(sp^2)-Au(I), and Au(III) complexes

The chemistry of Au bound to C(sp^2) atoms is more diverse. Among the most studied C(sp^2)-H bond activation by Au(I), or Au(III) is the functionalisation of arenes.[97] Initial results of stoichiometric reactions were reported in 1931. Reaction of AuCl$_3$ in benzene or PhMe, led to the formation of aryl-Au(III) species, and subsequent decomposition into AuCl, and functionalized aryl-Cl bond.[98] Further applications in catalytic cross-coupling

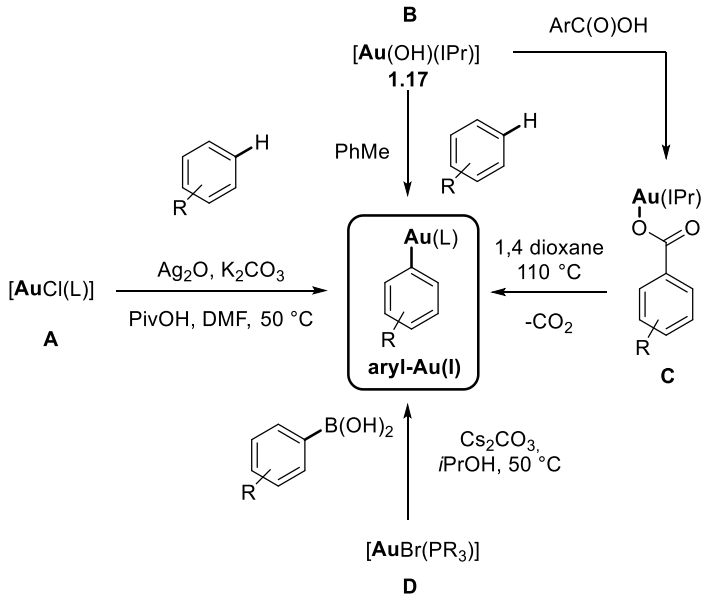
processes gold catalysed were reported: Russel *et al.* reported the oxidative arylation of arenes with arylsilanes catalysed by [Au(OTs)(PPh$_3$)] (**1.15**) (Scheme 1.5, a).[99] Initial oxidation to Au(III), and further C-Si auration took place; this step proceeded faster than the 2nd step of C-H auration. Further reductive elimination released the C-C coupled product and Au(I). Reoxidation of the species closed the catalytic cycle.

A full mechanistic study disclosed a wealth of relevant information.[100] The formation of aryl-Au(III) species (**1.16**) by C-Si auration was demonstrated through stoichiometric experiments, while **1.16** reductively eliminated the product after a second arylation step confirming the predominant C-Si *vs* C-H auration (Scheme 1.5, b).



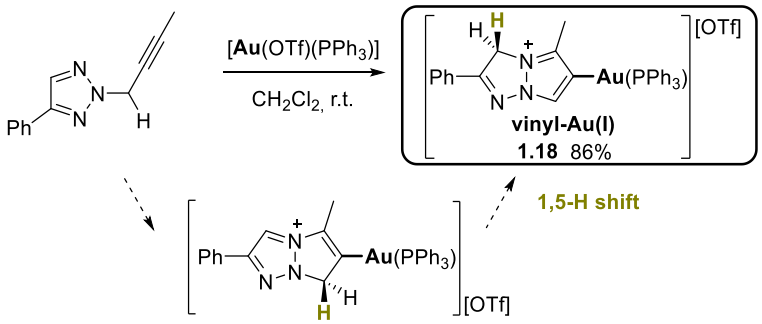
Scheme 1.5. a) Catalytic oxidative arylation of arenes with arylsilanes by **1.15**;[99] b) stoichiometric experiments to **1.16**, followed by C(sp^2)-H functionalisation to product.[100]

However, other than this example of C-Si auration, aryl-Au(I) species have been synthesised mainly through C-H activation, and C-B transmetalation (Scheme 1.6). The first method was employed by Larossa, reacting [AuCl(L)] (L = PPh$_3$, PEt$_3$, PtBu$_3$, P(OPh)$_3$, IPr) with electron-deficient arenes, in presence of Ag$_2$O, K$_2$CO$_3$, and PivOH, the latter possibly aiding the concerted metalation deprotonation pathway (**A**).[101] Similar results were shown by Nolan and co-workers, through protonolysis of [Au(OH)(IPr)] (**1.17**) with suitable acidic arenes,[102] or though decarboxylation of carboxylic acids (**B**, **C**).[103] Transmetalation from boronic acids to [AuBr(PR$_3$)] was reported as a robust process to achieve σ-bound aryl-gold(I) species (**D**).[104]



Scheme 1.6. Synthesis of aryl-Au(I) complexes from: a) C-H auration from [AuCl(L)];[101] b) C-H auration from **1.17**;[102] c) decarboxylation from carboxylate-Au(I);[103] d) C-B transmetalation from [AuBr(PR_3)].[104]

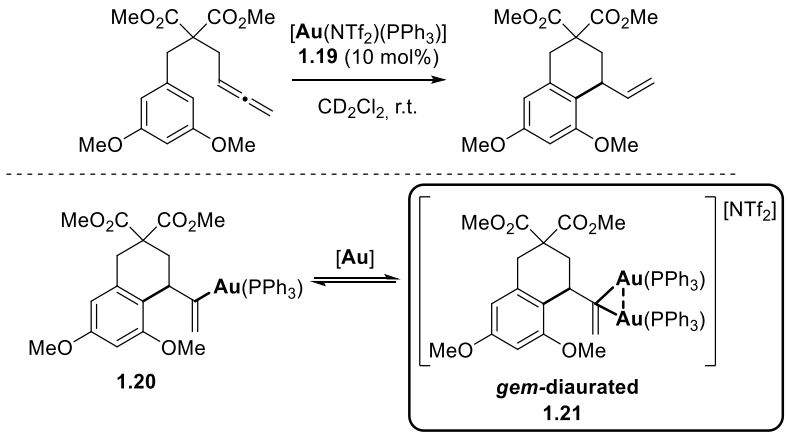
Another class of organogold species are vinyl-Au(I) complexes. Several examples are known, and their solid structures have been elucidated.[105] Mainly found as intermediate in Au(I) catalysed processes, although isolable, these complexes tend to decompose easily under acidic conditions, which explains the ease of protodeauration from these species.[106] Chen *et. al* described the formation of a stable C(sp^2)-Au species through triazole-alkyne 5-*endo*-dig cyclisation (Scheme 1.7).[107] The incredible high stability of complex **1.18** was attributed to the highly electron-deficient triazolium heterocycle, as **1.18** did not decompose in the presence of HOTf even after 12 h.



Scheme 1.7. Vinyl-Au(I) species **1.18** formed by triazole-alkyne 5-*endo*-dig cyclisation.[107]

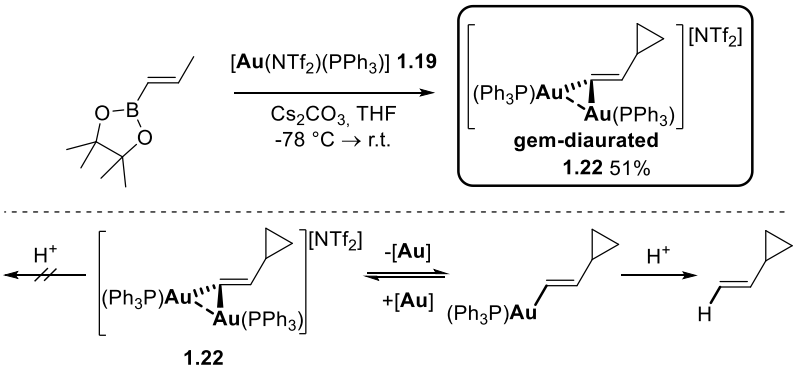
A second Au centre can be trapped by vinyl- or aryl-Au(I) compounds, to form the so called geminally diaurated, or *gem*-diaurated species. These complexes started to attract attention when Gagné and co-workers described the mechanism of hydroarylation of

allenes catalysed by [Au(NTf$_2$)(PPh$_3$)] (**1.19**) complex (Scheme 1.8).[106b] Stoichiometric experiments showed the formation of a vinyl-Au(I) species (**1.20**), which upon treatment with a second equivalent of Au^+ precursors formed a dinuclear species (**1.21**) that was characterised in solution.[108]



Scheme 1.8. Vinyl-Au(I) and *gem*-diaurated species found in the hydroarylation of allenes.[108]

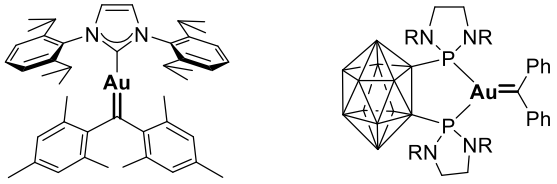
The interaction in **1.21** was described as a three-centre two-electron species: similar species have been synthesised, and characterised.[92,109] An excellent report by Fürstner's research group, highlighted the difficult associated with *gem*-diaurated systems and showed that the right conditions need to be applied.[110] Subjecting vinyl-borane to an equivalent of **1.19**, gave a gem-diaurated species (**1.22**) (Scheme 1.9). This species was not prone to reaction with acids, thus prior dissociation to reform a vinyl-Au species was proposed as necessary to permit protodemetalation.



Scheme 1.9. Synthesis of **1.22** from **1.19**, dissociation into vinyl-Au(I), thus protodeauration.[110]

Gold compounds have been shown to be able to transfer carbene groups, formed through reaction with diazo compounds to organic substrates,[111] and Au-carbenoid species have been postulated as plausible intermediates in several transformation.[112] Few ylide-type

Au-carbenes have been actually synthesised,[113] however, two carbene-Au complexes have been recognized and characterised by the research groups of Straub,[114] and Bourissou (Figure 1.16).[115] The former utilised [Au(NTf$_2$)(IPr*)] complex, reacted with dimesityldiazomethane to produce the [Au(CMes)$_2$(IPr*)] (**1.23**) complex, with partial double bond character Au=CMes$_2$, due to gold-carbene π*-backbonding. The second example reacted *o*-carborane diphosphine (DPCb) Au(I) species with diphenyldiazomethane; backdonation and π-bonding from the [Au(DPCb)]$^+$ species stabilised the carbene (**1.24**).



1.23
Straub[114]

1.24 R = *i*Pr
Bourissou[115]

Figure 1.16. Stable carbene-Au(I) complexes **1.23**,[114] and **1.24**.[115]

1.3.3. Mononuclear and dinuclear C(sp^3)-Au(I) complexes

Alkyl-Au(I) complexes have been widely used as pre-catalysts for Au-catalysed reactions. With general formula [Au(CR$_3$)(L)] (L = PPh$_3$, IPr), these compounds are formed through (Figure 1.17); a) transmetalation of [AuCl(L)] precursors with lithium,[116] magnesium,[116a] zinc, [117] silver[118] organometallic species; b) direct auration of oxo-,[119] alkoxo-[120], carboxo-,[121] hydroxo-Au(I)[102] complexes with organic substrates; c) reactions of [AuCl(L)] with silyl-enol ethers, in presence of CsF, specifically for ketonyl-Au(I) complexes.[122]

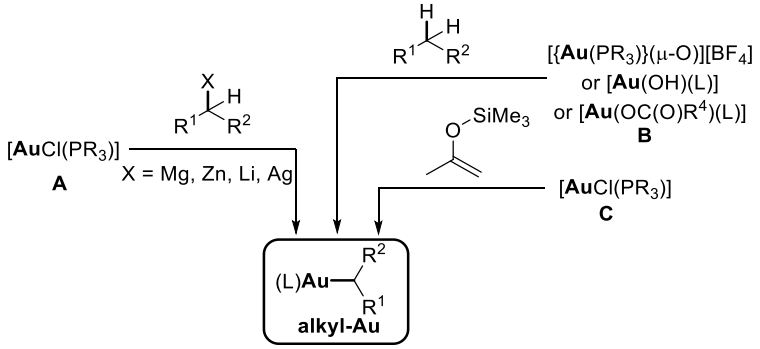
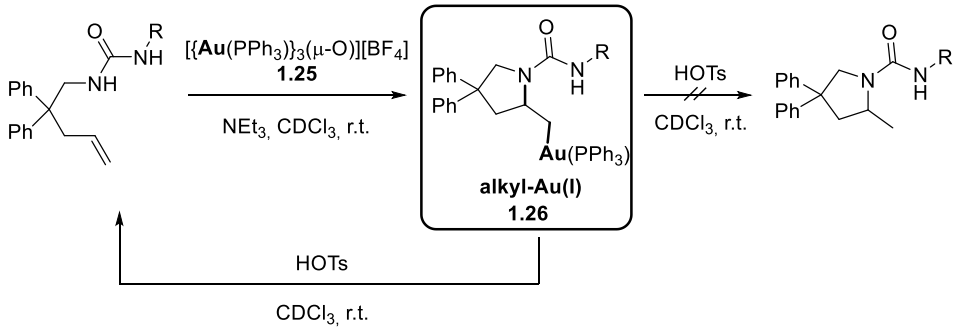


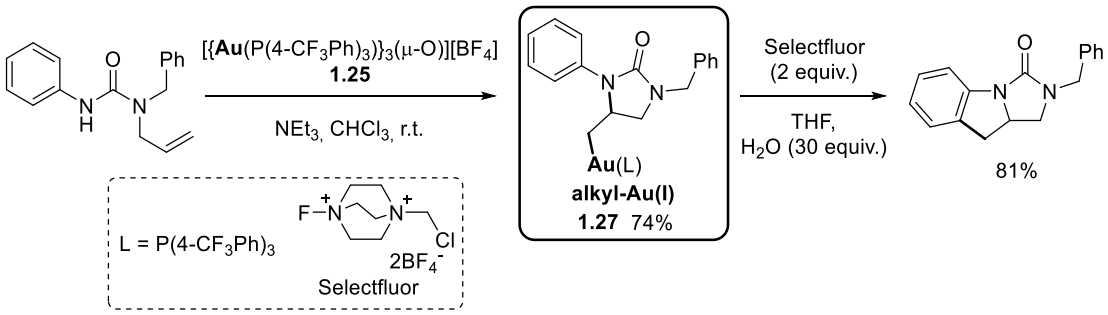
Figure 1.17. General synthesis of alkyl-Au(I) complexes: a) transmetalation with organometallic complexes;[116-118] b) auration;[102,119-121] c) auration to ketonyl-Au(I) complexes.[122]

Several organic substrates could be activated, *e.g.* nitriles, ketones, chloroform, cyanoacetates. Among these, [Au(CH_3)(L)] (L = PPh_3, IPr) [117, 118b, 123] have been recognised as catalyst precursors, mainly because of the ease of activation of the complex and the silver-free methodology (section 1.6.1).[124] Examples of alkyl-gold intermediates were isolated by the group of Toste[125] and Zhang.[126] The former studied the intramolecular aminoauration of alkenes, with successful isolation of alkyl-Au(I) species **1.25** by reacting the tethered alkene with [{Au(PPh_3)}$_3$(μ-O)][BF_4] (**1.26**) (Scheme 1.10). Attempts to protodeaurate the species however resulted mainly in reversible retroaminoauration under catalytic conditions.



Scheme 1.10. Synthesis of alkyl-Au(I) species; Toste's work on intramolecular aminoauration of alkenes and attempt of protodeauration of **1.26**.[125]

Zhang's research group isolated complex **1.27** when studying the gold-catalysed intramolecular [3+2] annulation of *N*,*N*-dialkyl-*N*'-phenylurea derivatives (Scheme 1.11).[126] This alkyl-Au(I) complex further reacted with starting material to deliver the product in high yield. Moreover, it could be utilised as a catalyst for the reaction, and together with its ease of protodemetalation, the author suggested that **1.27** is a plausible reaction intermediate.



Scheme 1.11. Zhang's work on intramolecular [3+2] annulation of urea derivatives, and protodeauration to product of **1.27**.[126]

The possibility of β-H elimination from alkyl-Au(I) complexes to form [AuH(IPr)] complexes has been explored.[127] The feasibility of this common reaction in transition-metal catalysis, was ruled out for ethyl- and methyl-Au(I) NHC species, which showed significant reaction rates for the process to deliver hydride-Au(I) NHC complexes. This process was only feasible at T above 200 °C, well-beyond the usual thermal stability of the majority of gold complexes.

1.4. *N*-Au(I) and *N*-Au(III) compounds

Historically, one of the first gold mixtures found, and one of the most explosive was obtained from the combination of $AuCl_3$, and NH_3,[128] this mixture often called *aurum fulminans*, or "fulminating gold". It results in a polymeric species, with the closest formula hypothesised to be $_{\infty}[Au(\mu\text{-}NH_2)(\mu\text{-}NH_3)_2]Cl$. Other than this powerful explosive, new stable and less dangerous complexes with *N*-Au bonds have been synthesised, and among the rich coordination chemistry of gold the use of nitrogen ligands has been widely exploited.[129]

1.4.1. *N*-Au(I) complexes

N-Au(I) complexes are formed less readily with respect to C-Au(I) ones, due to the highly soft character of the Au(I) centre, which prefers to coordinate with softer atoms, *e.g.* P or S. However, examples of stable Au(I) heteroleptic complexes bearing N(sp^3) coordinating ligands were found, with general formula [Au(N_L)(L)] (N_L is the N containing ligand, while L is the spectator ligand, mainly tertiary phosphines or NHC). Both primary, secondary, and tertiary amines were tolerated, and their complexes reported.[130] The main synthetic routes to access these species were; i) reaction of [AuCl(PPh_3)] (**1.28**) with primary or secondary amines in the presence of Ag salts (AgX = BF_4, CF_3SO_4) or strong bases (NaOH) (Route **A**, Figure 1.18, a);[130a,130c,131] ii) by ligand displacement starting from [Au(acac)(PPh_3)] (**1.29**), and ammonium salts (Route **B**);[130e] or iii) by protonolysis of a Brønsted basic precursor, such as **1.17** with a primary or secondary amine (Route **C**).[130d] Selected representative examples are shown in Figure 1.18, b.

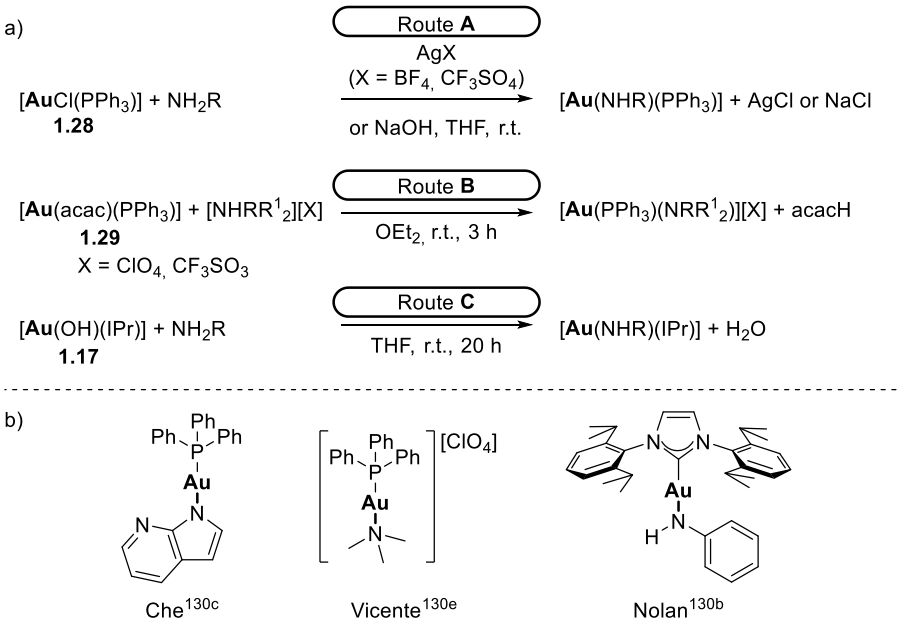
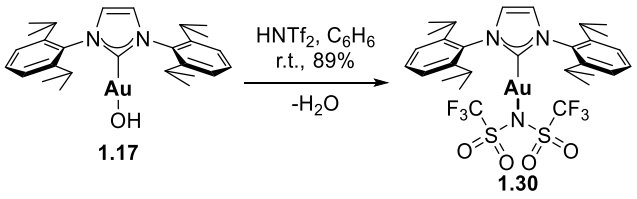


Figure 1.18. a) Routes **A**, **B**, **C** for the synthesis of heteroleptic complexes of the kind [Au(N_L)(L)] and [Au(N_L)(L)][X];[130,131] b) representative examples N(sp^3)-Au complexes.[130b,c,e]

Gagosz and co-workers reported the synthesis of a stable heteroleptic triflimide-complexes [Au(NTf_2)(L)] (Scheme 1.12).[132] Several precursors bearing diverse spectator ligands were well tolerated, such as phosphines, NHC and cyclic (alkyl)(amino)carbenes (CAAC),[133] and yielded the triflimide-Au(I) complexes. These were assessed mainly *via* route **A**; through route **C**, such as protonolysis of **1.17** with $HNTf_2$, complex [Au(NTf_2)(IPr)] (**1.30**) was obtained.[102] The inner-sphere counterion was easily displaced to activate suitable substrates, thus the complexes have been shown to be able pre-catalysts in Au(I) catalysed reactions.[134]



Scheme 1.12. Synthesis of **1.30** from complex **1.17** *via* protonolysis.[102]

Less active species containing a N-Au bond were reported by Hammond in 2014, of the kind [Au(Pht)(L)] (Figure 1.19).[135] These complexes formed by reacting [AuCl(L)] with potassium phtalamide, were not active in solution. However Brønsted acid activation of [Au(Pht)(PPh_3)] (**1.31**) with $HCTf_3$, released the active species $[Au(L)]^+$, which

efficiently catalysed the intermolecular hydroamination reactions, addition of X-H (C, O, N) to alkenes, and alkynes.[136]

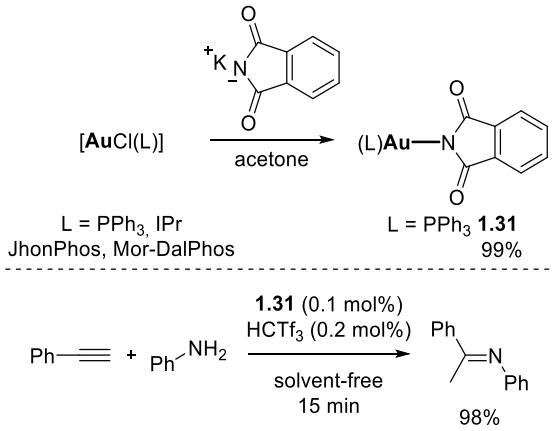
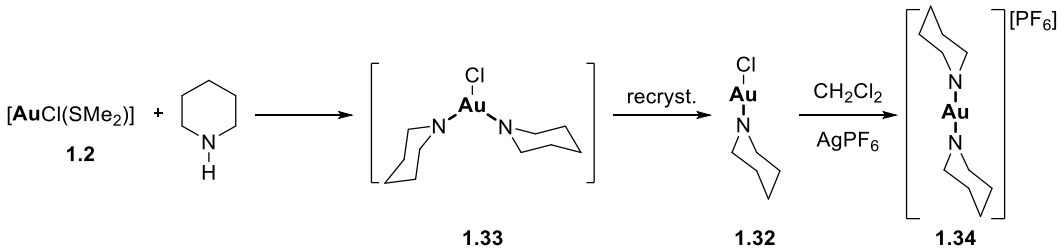


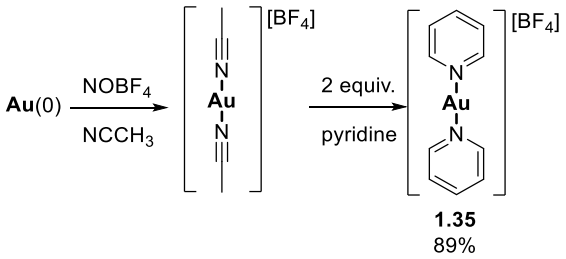
Figure 1.19. Phtalamide-Au(I) complexes synthesis, and activation for the intermolecular hydroamination of alkynes.[136]

Few neutral Au(I) complexes bearing an aliphatic amine have been reported, although the synthesis of piperidine-Au(I) (**1.32**) with formula [AuCl(piperidine)] was disclosed in 1977 (Scheme 1.13).[137] The complex was postulated to derive from [AuCl(piperidine)$_2$] (**1.33**), formed from [AuCl(SMe$_2$)] **1.2**, and an excess of piperidine; complex **1.33** was compared to [AuCl(PPh$_3$)$_2$] tricoordinated complex,[138] but it was characterised solely by elemental analysis. Formation of **1.32**, confirmed by X-ray analysis of suitable crystals, showed low stability, and when further reacted with $AgPF_6$ formed the homoleptic [Au(piperidine)$_2$][PF$_6$] (**1.34**) complex.



Scheme 1.13. Synthesis of **1.32**, and **1.34** from **1.2**, and excess of piperidine.[137]

More reports discussed the synthesis of complexes with N(sp^2) donor ligands to Au(I), with pyridine and its derivatives being the most studied compounds.[139] Of interest, the homoleptic pyridine-Au(I) complex (**1.35**) reported by Corbo *et al.*, was synthesised from oxidation of metallic gold, to form a nitrile-Au(I) intermediate that promptly reacted with pyridine (Scheme 1.14).[140]



Scheme 1.14. Synthesis of heteroleptic pyridine complex **1.34**.[140]

Other N(sp^2) non-aromatic ligands bound to Au(I) have appeared in the literature; Coetzee *et al.* reported the synthesis of ylideneamine-Au(I) complexes (Figure 1.20).[130d] The heteroleptic compound **1.36** was formed by ligand exchange from [Au(NO_3)(I*t*Bu)], and ylideneamine. Similar structures were reported by Schneider in 1997 such as tetramethylguanidine-Au(I) compounds $[Au(tmg)(PPh_3)]^+$ (**1.37**), and [AuX(tmg)] (X = Cl, Br) (**1.38**),[141] and their solution and solid state behaviour was studied. The NMR spectra in $CDCl_3$ showed that **1.38** existed in equilibrium with the heteroleptic species $[Au(tmg)_2][AuBr_2]$ (**1.39**).

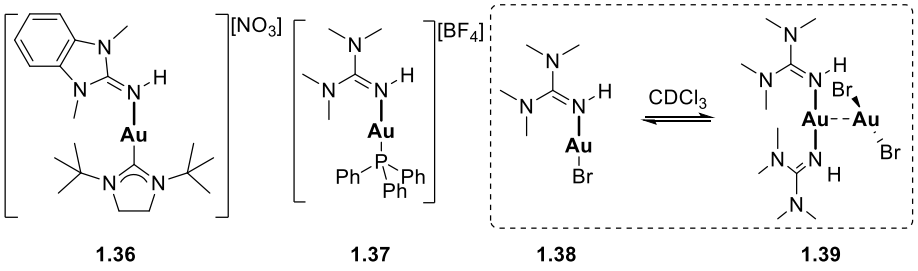


Figure 1.20. Ylideneamine-Au(I) **1.36** by Coetzee *et al.*;[130d] tetramethylguanidine-Au(I) cationic and neutral complexes reported by Schneider.[141]

Several dinuclear or multinuclear Au compounds with N(sp^2) coordinating ligands were synthesised and extensively reviewed.[129a] Among those, two examples are reported in Figure 1.21 such as binuclear benzimidazolethiolate Au complex,[142] and tetranuclear guanidinate Au(I) species.[143] One example of a chiral ligand to Au(I) was reported by Peters in 2015 (Figure 1.21, b). The dinuclear planar chiral ferrocenyl-oxazolidinone Au(I) complex (**1.40**) was oxidised in presence of $[AuCl(SMe_2)]$ **1.2** to form the corresponding Au(II) chiral complex **1.41**.[144]

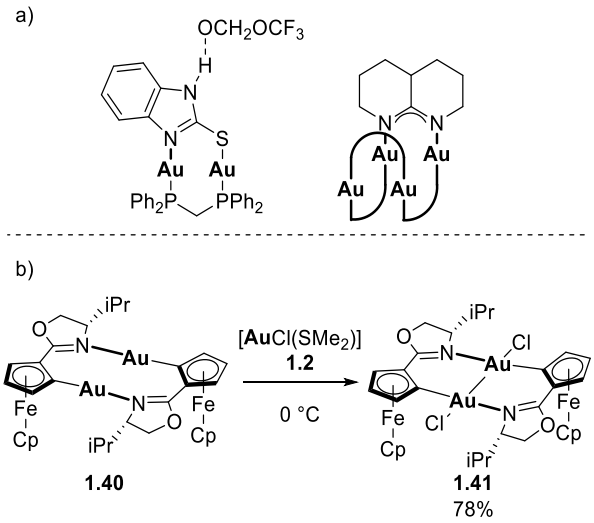


Figure 1.21. a) Selected multinuclear N(sp^2)-Au(I) compounds;[142,143] b) dinuclear Au(I), and Au(II) planar chiral ferrocenyl complexes.[144]

Finally, nitrile species are the best example of *N*(sp)-Au complexes. These can be easily formed *via* oxidation of Au(0) with a nitrosonium salt, $NOBF_4$, in the presence of nitriles, producing $[Au(NCR)_2][BF_4]$ as observed in Scheme 1.14.[145] Stable complexes were found when benzonitrile was used, in presence of $NOBF_4$ salt, as stable $[Au(NCPh)_2][BF_4]$ species.[146] The benzonitrile ligands were demonstrated to be readily displaced by PPh_3 in the presence of a base, forming $[Au(PPh_3)(NCPh)][BF_4]$.[147] This species was not isolated, however similar structures with formula $[Au(L)(NCCH_3)][X]$ were studied, and obtained from [AuCl(L)],[139d,148] by halide abstraction, or from [Au(L)(OH)] and by protonolysis.[149] For example, **1.42**, and **1.43** are among the most commonly used nitrile-Au(I) complexes bearing bulky monophosphinobiaryl ligand, or IPr (Figure 1.22). These have shown great success as precursors in gold-catalysed reactions, *e.g.* cyclisation of enynes.[150]

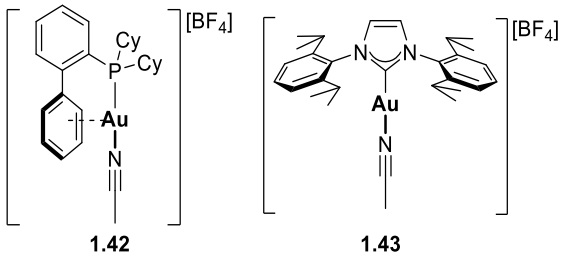


Figure 1.22. Examples of nitrile-Au(I) complexes with biphenyl-phosphane,[148] and NHC ligands.[139d,149]

The ligand strength of N-based ligands have been studied by Zhdanko and Maier;[151] the authors determined by ^1H and ^{31}P NMR spectroscopy the affinity scale of a number of

mononuclear complexes, such as $[Au(L)(NCCH_3)]^+$ (Figure 1.23). The nucleophiles used for the dissociation experiments were compared, and the ligand exchange equilibrium constant calculated. When **1.44** was used, a general trend was found; nitriles and alkynes were weakly coordinating to the metal centre, while OTf^- and 4-DMAP showed moderate coordination abilities. Phosphines, chlorides and hydroxides anions strongly coordinated to the $[Au(L)]^+$ unit.

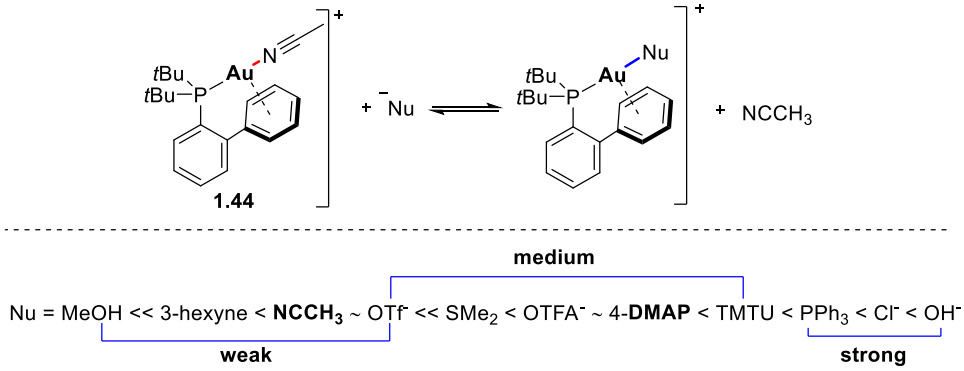


Figure 1.23. Affinity scale of anions for **1.44** and coordinating abilities.[151]

1.4.2. *N*-Au(III) complexes

As with Au(I), primary,[152] secondary[130f,153] and tertiary[154] amines can coordinate to Au(III). The most studied well-defined *N*-Au(III) species are based on pyridine (py) or aromatic derivatives;[155] bidentate (*N*,*O*),[156] pincer (C^N^C),[157] porphyrin,[158] and salen[159] ligands are among the most used, with some catalytic activity demonstrated.[160]

A recent study of the coordination chemistry of $[AuCl_3(py)]$ complex (**1.45**) through natural bond order (NBO) analysis described the delocalisation of the lone pair of the pyridine N atom into the empty orbitals of the metal centre, and the $AuCl_3$ fragment.[161] These studies showed a substantial depletion of charge along the N-Au bond, thus suggesting that electrostatic contributions rather than covalent ones. Moreover, the pyridine ligands were shown to be a strong σ-donor and poor π-acceptor.

These ligands have been shown to confer high efficiency to the catalytic systems, other than increased stability. An example is the phenol synthesis reported by Hashmi research laboratories (Figure 1.24);[162] monodentate and bidentate pyridine-Au(I) complexes **1.45**, and **1.46** showed higher conversions to the final product, compared to $AuCl_3$,[163] allowing access to different scaffolds, which were not accessible with the Au salt.

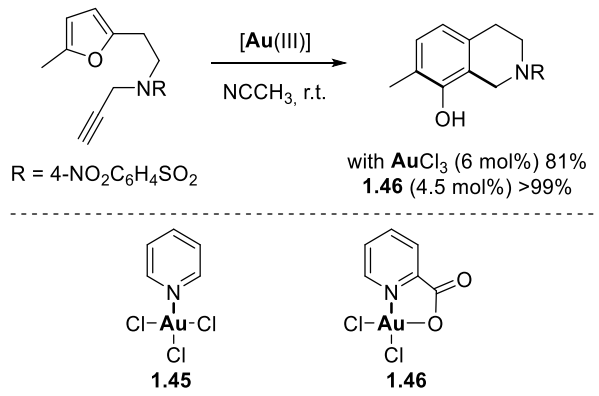


Figure 1.24. Hashmi phenol synthesis enhanced by well-defined pyridine-Au(III) complexes.[162,163]

The synthesis of Au(III) species bearing a multidentate ligand (C^N^C), with a N donor enabled the trapping of elusive species, such as Au-H (**1.47**),[164] Au-CO (**1.48**)[165] compounds reported by Bochmann and co-workers from hydroxide- (**1.49**) and alkoxide-Au(III) (**1.50**) precursors (Figure 1.25).[166]

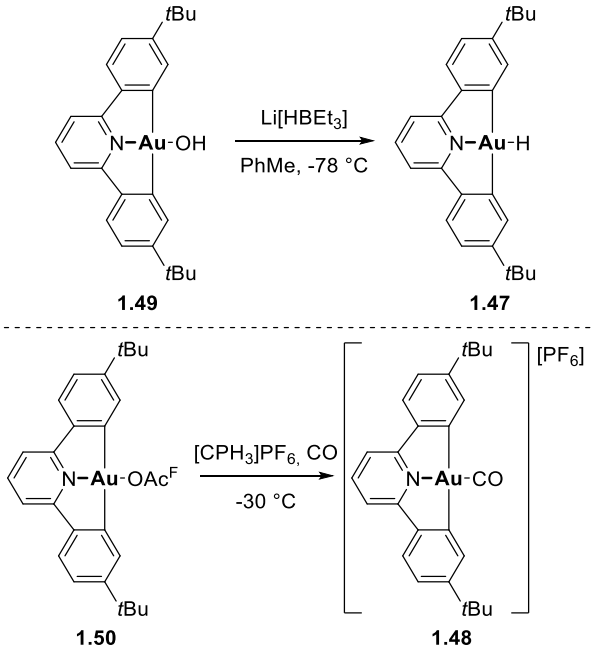


Figure 1.25. Complexes **1.47** and **1.48** bearing C^N^C ligands reported by Bochmann and co-workers.[164,165]

1.5. O-Au(I) compounds

Generally Au shows lower affinity for O atoms, due to the mismatch between the soft late-transition metal (diffused atomic radii, low oxidation states) and the hard nature of O bases (small radii, high electronegativity).[78] However, several compounds containing a

O-Au bond were reported, and studied: these species are postulated to be highly reactive, thus their uses as precursors of organometallic compounds, or as pre-catalysts in homogeneous catalysis were developed.[167] Nowadays, their technological applications, *e.g.* gold deposition processes, are widely explored.[168] Mainly anionic ligands, of the kind OH^-, OR'^-, O^{2-}, and many others[169] are reported to ligate to Au(I) complexes. The range of Au(III) species with an oxygen-donating ligand were expanded more probably due to the higher stability of such species, but they will not be discussed herein.[129b]

1.5.1. Mononuclear Au(I)-OH, Au(I)-OR' species

The first hydroxide-Au(I) species observed were the neutral complexes [Au(OH)] and [Au(OH)($NCCH_3$)],[170] formed by hydrolysis of Au(I) species in aqueous acetonitrile. Disproportionation into Au(0), and Au(III) was not observed. Although their solid-state structures have not been confirmed yet, the feasibility of hydroxide as suitable ligand to Au(I) was confirmed. No examples of [Au(OH)(PPh_3)] have been characterised yet.[151]
In 2007 Nolan's research group in collaboration with Maseras' reported the formation of enones and enals from alkynes, catalysed by Au(I) complexes (Figure 1.26).[171] During computational studies the possible involvement of a [Au(OH)(IPr)] (**1.17**) synthon was postulated to form from **1.1**, the chloride precursor in the presence of $AgSbF_6$ salt. **1.17** was hypothesised to be the catalytically active species involved in the assisted SN_2' addition of OH^- to propargylic acetates.

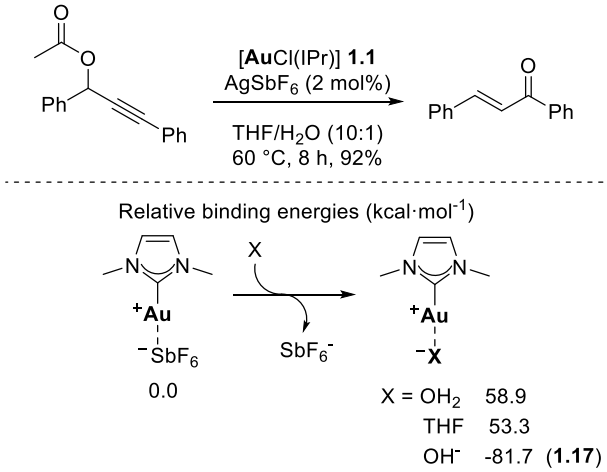
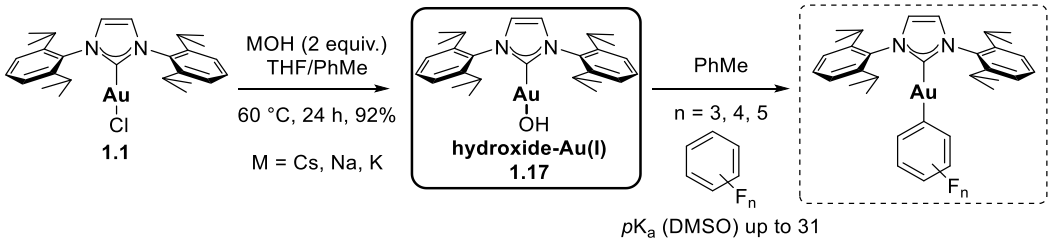


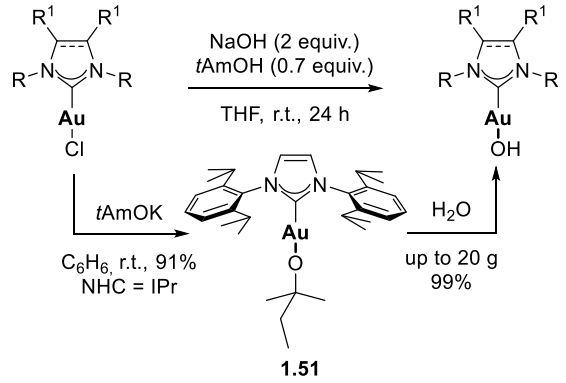
Figure 1.26. Au(I)-catalysed formation of enones and enals.[171] Relative binding energies (kcal·mol^{-1}) to Au(I) of H_2O, THF and OH^- units.

Further effort upon the isolation of the energetically favoured species were undertaken, and in 2010 the first report of hydroxide-Au(I) NHC species was reported (Scheme 1.15).[102] Initially **1.17** was synthesised through reaction of **1.1** precursor in presence of a base, of the kind MOH ($CsOH \cdot H_2O$, NaOH or KOH) in THF/PhMe mixtures. This species was utilised to access several organogold species through a silver-free protonolysis procedure; Au(I)-OH reacted with fluoroarenes with a p*K*a (DMSO) < p*K*a (DMSO) of water (31.4). Thus, reaction with pentafluorobenzene (p*K*a (DMSO) = 23.1), and 1,2,4,5-tetrafluorobenzene (p*K*a (DMSO) = 29.0) were successful, but the complex did not react with 1,3,5-trifluorobenzene (p*K*a (DMSO) = 31.5).[102]



Scheme 1.15. Synthesis of **1.17**, and protonolysis reactions with fluoroarenes.[102]

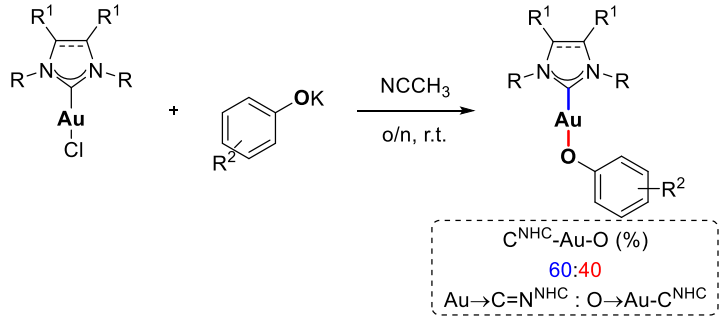
Further improved synthetic methods were reported for the synthesis of various [Au(OH)(NHC)], at larger scale, in a silver-free process.[172] Among the viable routes, [Au(OH)(IPr)] was obtained in up to 20 g through the synthesis of [Au(O*t*Am)(IPr)] intermediate (**1.51**), isolated in 91% yield by reaction of Cl-Au(I) precursors with NaOH/*t*AmOH mixture and further hydrolysis (Scheme 1.16).[148,173]



Scheme 1.16. Improved synthesis of **1.17** through formation of **1.51**.[172]

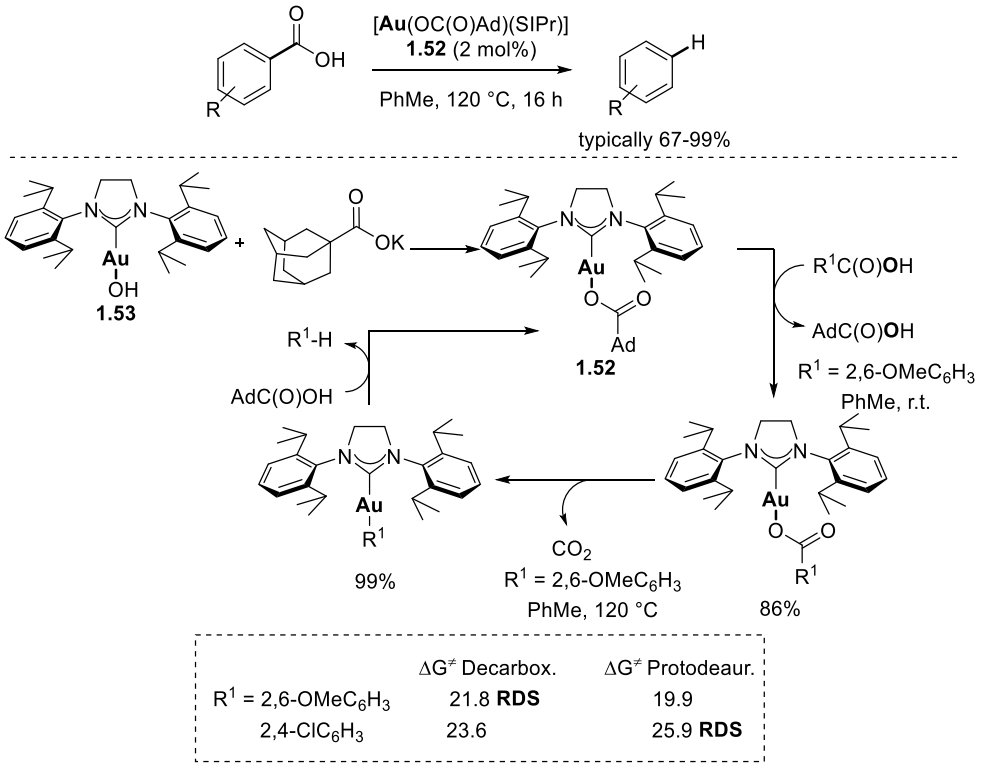
Alkoxide-Au(I) species were initially isolated with phosphine ancillary ligands in 1991,[120a] and further found active in the catalytic Knoevenagel condensation of benzaldehyde, and active methylene compounds, such as alkyl cyanoacetate or acetophenone.[120b] Further studies into these species were performed by Hashmi and co-

workers; the authors isolated phenoxide-Au(I) species bearing NHC ligands (Scheme 1.17).[174] Studies on the coordination of the oxygen ligands to the $[Au(NHC)]^+$ fragment showed that the main contributions over the three-centre four-electrons hyperbond came from Au-carbene interactions (d→π* or d→p_z*, the latter for saturated SIPr ligand), and Au-O interactions. The species formed were sensitive to high temperature, and moderately active in hydration of alkynes.



Scheme 1.17. Synthesis of phenolate-Au(I) NHC species. Highlighted Au-$C_{carbene}$ and Au-O interactions.[174]

Furthermore, carboxylate-Au(I) $[Au(OC(O)CH_3)(R_2\text{-imy})]$ species were reported by Schneider and co-workers, and as with the case of hydroxide- and alkoxide-Au(I) species, these were found to be good pre-catalysts for 3-hexyne hydration.[175] Further studies on catalytic protodecarboxylation of carboxylic acids were conducted by Nolan and co-workers.[176] The synthesis of arenes from carboxylic acids through extrusion of CO_2 was explored by catalysis with [Au(OC(O)Ad)(SIPr)] (**1.52**) (Scheme 1.18). The catalyst was formed by protonolysis of hydroxide-Au (**1.53**) with 1-adamantanecarboxylic acid.[103] The mechanism of the reaction was found to proceed through activation of the acid starting material, followed by stepwise decarboxylation to form an aryl-Au(I) compound. The latter was found to be the rate determining step (RDS) of the catalytic cycle when carboxylic acid with $pK_a \geq 4.8$ were used. Further protodeauration to reform the active **1.52**, and release of the product closed the catalytic cycle. This step was found rate limiting at high concentration of catalyst or when electron-deficient acids were used.[177]



Scheme 1.18. Catalytic Au(I)-protodecarboxylation of carboxylic acids, and proposed reaction mechanism with isolated intermediates;[176] highlighted the calculated energy barriers (kcal·mol^{-1}) for decarboxylation, and protodeauration steps.

1.5.2. Dinuclear and multinuclear Au(I)-OH, Au(I)-O species

The tendency of gold to form Au···Au "aurophilic" interactions favours the formation of multinuclear aggregates of oxonium-Au(I) species. For example [{Au(PPh_3)}$_3$(μ-O)][BF_4] **1.25** was found to be trimeric in the solid state (Figure 1.27).[178] This species can be accessed by reacting [AuX(PPh_3)] (X = Cl, Br) with Ag_2O, and $NaBF_4$.

The possible formation of dinuclear O-Au(I) species was therefore targeted (Figure 1.27), as represented by [{Au(PPh_3)}$_2$(OR)][BF_4] (**1.54**) (OR = 8-quinolinyl bidentate ligand).[179] This species showed fluxional behaviour in solution, while the solid-state structure unequivocally highlighted the non-equivalency of the two Au atoms. One was bound to the oxygen, while the second mainly to the nitrogen with short interactions with the oxygen atom.

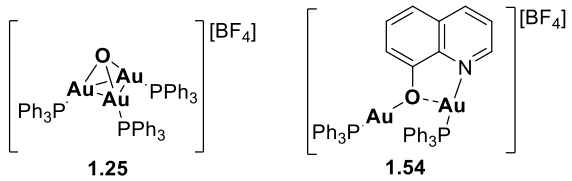
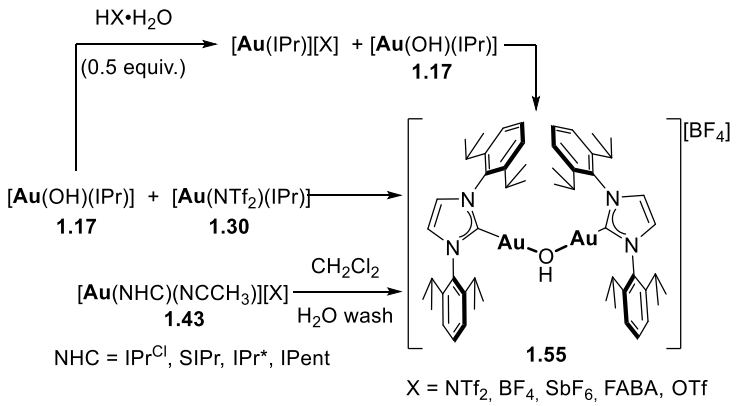


Figure 1.27. Examples of trinuclear,[178] and dinuclear phosphine oxonium-Au(I) species.[179]

Following these results, a dinuclear hydroxide-Au(I) species [{Au(IPr)}$_2$(μ-OH)][BF_4] (**1.55**) was reported by Nolan and co-workers (Scheme 1.19).[180] Complex **1.55** is the only dinuclear hydroxide-Au(I) species fully characterised in both solution and the solid state. This species was formed quantitatively by reaction of stoichiometric amounts of aqueous HBF_4 with **1.17**. Excess acid led to the formation of a possible [Au(IPr)][BF_4] species that could not be isolated, due to its high instability in dry form. However recent findings allowed the synthesis and characterisation of [$Au(IPr^{Cl})$]$^+$ fragment as stable species of the kind [$Au(IPr^{Cl})(F\text{-}BF_3)$].[181] The dinuclear species **1.55** showed two equivalent Au(I) species, and a distance between the Au atoms of 3.746(1) Å, indicates that possible "aurophilic" interactions do not stabilise this species. Mayer Bond Order (MBO) analysis showed that the O-Au bonds were affected by the dinuclear aggregation with a decrease in bond order compared to the mononuclear congener (0.60 *vs* 1.16). However, the values for O-H bond were similar for **1.55** and **1.17**, of 0.86 *vs* 0.92, respectively.[182] Non-negligible interactions (0.14) was found between the [Au(IPr)] fragments, with donation of the $\sigma_{Au\text{-}carbene}$ bond into an empty p_z acceptor of the other [Au(IPr)] unit.

The species can be seen as an *ensemble* of Brønsted base, [Au(OH)(IPr)] **1.17** and Lewis acid, [Au(IPr)][BF_4] fragments; **1.55** was accessed also from [Au(NTf_2)(IPr)] **1.30**, and **1.17** (Scheme 1.19). The cationic compound [Au(IPr)($NCCH_3$)][BF_4] (**1.43**) could be transformed into **1.55** simply by dissolving the precursor in an organic solvent (CH_2Cl_2) in the excess of H_2O.[183] The formation of trinuclear species [{Au(IPr)}$_3$(μ-O)][X] was found energetically unfavoured from **1.55**, while the formation of aquo complex of the kind of [Au(IPr)(OH_2)]$^+$ was considered in water, thus still not isolated neither fully characterised.



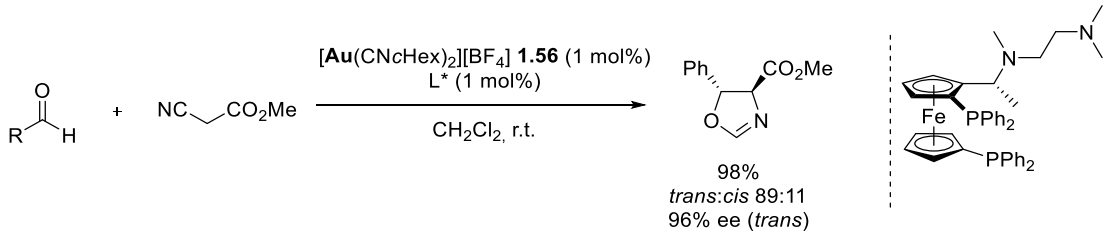
Scheme 1.19. Syntheses of dinuclear hydroxide-Au(I) species.[180-183]

Differently for carbenes, the hydrate-Au(I) phosphine complex was characterised and its structure observed in solid-state as $[Au(OH_2)(PPh_3)][OTf_2]$.[184] Further recrystallisation of the hydrate-Au(I) species and analysis on the crystals showed formation of a tetrameric structures, such as $[\{Au(PPh_3)\}_2(\mu^2\text{-}OH_2)_2][(OTf)_2]$.

1.6. From sleeping beauty, to "gold rush"!

Despite the intriguing properties of gold, its catalytic activity remained hidden, due to the misconception of its inertness. It was considered "catalytically dead" until 1973, when Bond and co-workers found that fine gold particles supported on silica catalyses the hydrogenation of olefins.[186] In the 1990's other heterogeneous reactions based on Au catalysts appeared, *e.g.* CO oxidation at low temperature,[186] or acetylene hydrochlorination.[187]

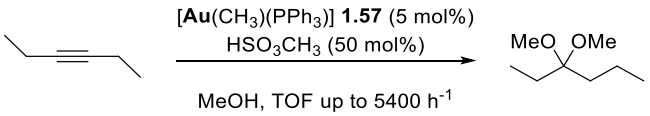
Around the same time, the bis-nitrile-Au(I) complex, $[Au(CN\textit{c}Hex)_2][BF_4]$ (**1.56**), with a chiral ferrocenylphosphine ligand (BPPFA) performed marvellously in the catalytic asymmetric aldol reaction of aldehydes, and isocyanates (Scheme 1.20).[188] The resultant oxazolines were obtained in high enantioselectivity (ee > 90%), and stereoselectivity (*trans*-product > 97%), and could be further functionalised to obtain valuable α-aminoacids. Ito, Hayashi and Sawamura's work in this area is considered a milestone in gold catalysis.



Scheme 1.20. Au(I)-catalysed asymmetric aldol reaction.[188]

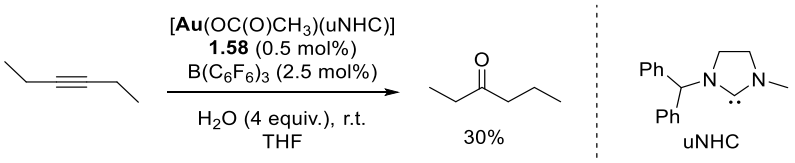
Gold became a powerful tool in homogeneous catalysis. Simple gold salts were used as catalysts, such as AuCl, $AuCl_3$ or $XAuCl_4$ (X = H, Na), and further derivatisation to well-defined complexes led to enhanced performances, diversified reaction modes, and most importantly increased stability of the catalyst. As widely discussed in the previous sections, a range of [AuX(L)], or [Au(L)(L')][X] complexes, where L is usually a phosphine, NHC or *N*-coordinating ligand, have been synthesised. It is general believed that, upon either ligand displacement or protonolysis of the ligands a coordinatively unsaturated 12 e^- species of the kind $[Au(L)]^+$ (L = PR_3 or NHC)[189] will form. This species is often believed to be the major active catalytic species in homogeneous reaction, with its great affinity for multiple bonds, such as alkynes, allenes and olefins.

Among the first reports towards this reactivity mode, in 1998 Teles and co-workers employed well-defined Au(I) pre-catalysts for the formation of acetals from alkynes (Scheme 1.21).[124] The authors improved the catalyst efficiency by tuning the ancillary ligand to Au. Using posphines, arsine, phosphites led to the combination of $[Au(CH_3)(PPh_3)]$ (**1.57**) and HSO_3CH_3 that showed turn-over frequency (TOF) values up to 5400 h^{-1} for the addition of methanol to propyne.



Scheme 1.21. Acetalisation of 3-hexyne catalysed by **1.57**.

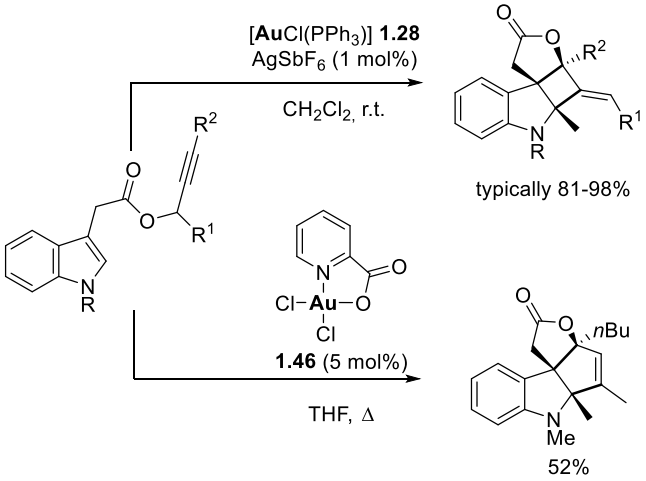
Addition of H_2O to alkynes was tested next, with Herrmann and co-workers showing in 2003 the use of an acetate-Au(I) complex bearing an unsymmetrical NHC (**1.58**), which was found to be moderately active in this transformation (Scheme 1.22).[175]



Scheme 1.22. First acetate-Au(I)-NHC catalysed hydration of alkynes

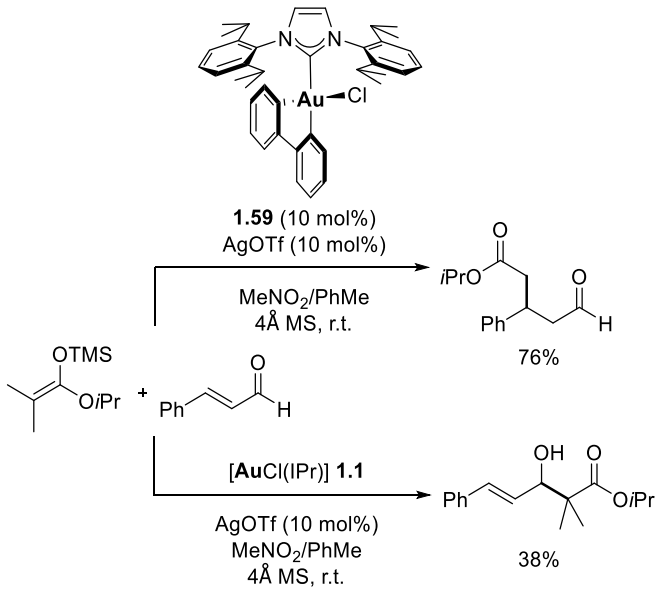
The use of well-defined Au(III) catalysts is less developed that Au(I), however many complexes were achieved.[190] As showed by Hashmi and co-workers, the synthesis of phenol could be achieved both in the presence of Au(III) salts, and well-defined pyridine-Au(III) pre-catalyst that enhanced the reaction performance (Section 1.4.2, Figure 1.24).[162a,163]

Furthermore, the oxidation state of the gold centre has a profound impact on the reaction outcome. The tandem catalysed 3,3-rearrangement/[2+2] cycloaddition of propargylic esters proceeded to tetracyclic cyclobutene products when chloride-Au(I) species **1.28** was used (Scheme 1.23).[191] When dichloro(pyridine-2-carboxylato)Au(III) complex **1.46** was used instead, the [3+2]-cycloaddition product formed.[192]



Scheme 1.23. Au(I) *vs* Au(III) pre-catalyst for the cycloaddition of propargylic esters.[191,192]

Biphenylene-Au(III) NHC complex **1.59** (Scheme 1.24) was utilised by Toste and co-workers to perform the 1,4-addition of ketene acetals to cinnamaldehyde, while when a mixture of [AuCl(IPr)] **1.1**, and AgOTf was tested in the same reaction the 1,2-addition product was obtained.[66]



Scheme 1.24. 1,4- *vs* 1,2-addition of ketene to cinnamaldehyde by Au(III) and Au(I) complexes.[66]

The selected few examples reported herein are among many others,[12a,193] and clearly show the role that gold has assumed as an extremely valuable tool in homogeneous catalysis. Some important effects that are related to gold-catalysis will be described next.

1.6.1. "Silver effect" in Au catalysis

When [AuCl(L)] complexes are used, usually chlorine ligand displacement has to occur to release the active catalyst in solution. The most commonly used halide scavengers are silver salts of the kind AgX (X = BF_4, SbF_6, NTf_2, OTs, OTf, FABA). Their role in catalysis is significant as recognised by Shi and co-workers,[194] who categorised the effect of using silver salts in Au-catalysed transformations into three main categories:

1. "Genuine" Au catalysis, where the presence of the Ag salt does not influence the outcome of the reaction (Figure 1.28, a);[195]
2. Bimetallic Au/Ag catalysis, where the combination of the two metal salts was necessary to ensure conversions (Figure 1.28, b), the two metal catalysts are usually not active alone in the transformation;[196]
3. Silver assisted Au catalysis, where usually Ag is not active in the reaction, and the Au catalyst appear moderately active, while the combination of both metals enhances reactivity (Figure 1.28, c).[197]

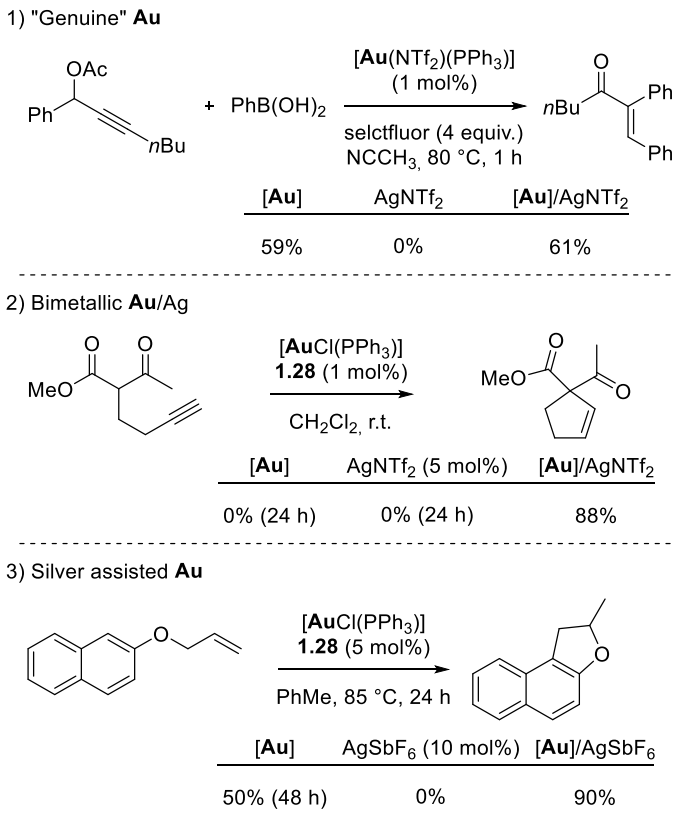


Figure 1.28. Examples of "silver" effect to gold catalysis: a) oxidative coupling between propargylic acetates and boronic acids;[195] b) cyclisation of acetylenic dicarbonyl compounds;[196] c) synthesis of dihydrobenzofurans.[197]

The authors verified their hypothesis based on comparative results with the Au/Ag mixture and the plausible active gold species formed in situ with Ag salts and filtered over celite© ([Au] column in Figure 1.28). An alternative explanation of the phenomenon was postulated by Yu and co-workers, who proposed that in presence of hygroscopic silver salts, the formation of oxo- and hydroxo-Au(I) complexes had to be considered.[184] These species formed in solution of Au/Ag mixtures, in presence of H_2O, and could be isolated after filtration over celite© (section 1.5). However, dinuclear and trinuclear Au complexes of this kind have been showed to be active pre-catalysts, thus the "silver" effect persists.

Interestingly, Echavarren's research group discovered that treatment of chloride-Au(I) JohnPhos complex **1.60** with 1 or more equiv. of AgX (X = NTf_2, OTf, BF_4, SbF_6) in CD_2Cl_2 lead to the prompt formation of a dichloride bridged Au(I) complex, [{Au(JohnPhos)$_2$}(μ-Cl)][X] **1.61** (Figure 1.29, a).[198] Further filtration over celite© of the dinuclear species **1.61** led to a trimetallic complex **1.62** with two Au atoms, and a Ag

atom,[199] which further suggested that the filtration over celite© is not the best way to assess what effect silver can have over a catalytic system.

An analogous complex to **1.61** formed in the cycloisomerisation of 1,6 enynes catalysed by a chloride-Au(I) phosphine-oxide catalyst **1.63** (Figure 1.29, b);[200] the dinuclear-Au(I) chloride was speculated to form when low amounts of a Ag salt was present in the mixture. Thus, when doubling the amount of silver salt in the mixture, the yield of product increased, which supported the off-cycle role of the dichloride bridged-Au(I) species.

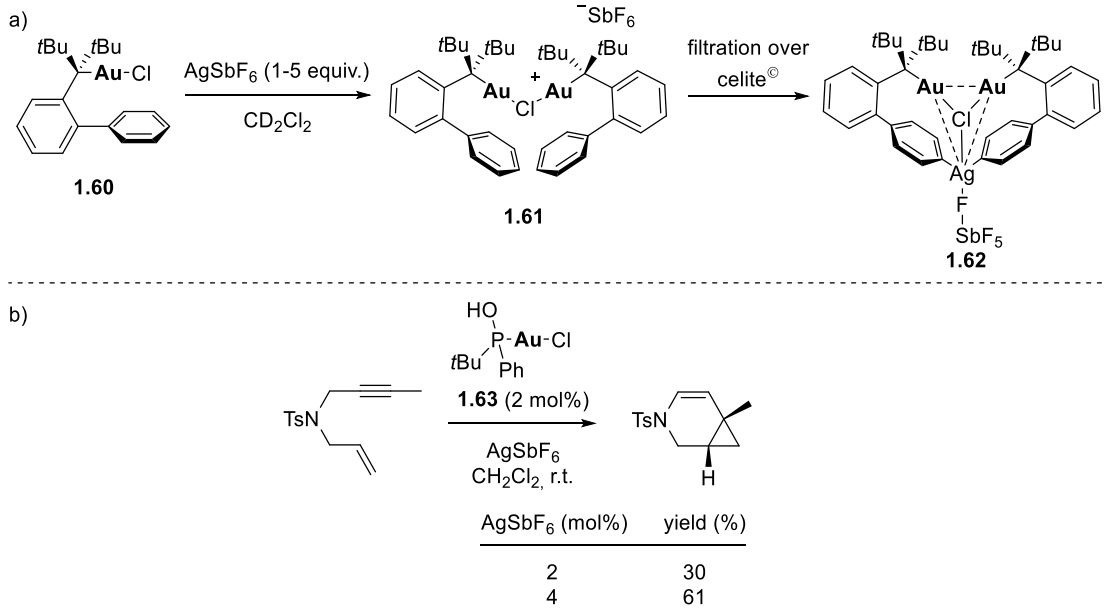


Figure 1.29. a) Formation of dichloride-Au(I) complexes, and formation of trimetallic system;[198,199] b) involvement of dichloride-Au(I) complexes in the cycloisomerisation of 1,6-enynes.[200]

Valuable alternative substitutive halide abstractors are Cu,[201] or other Lewis acids and main group salts,[202] whose effect in catalysis have to be assessed by precise control experiments. More interesting access to $[Au(L)]^+$ species *via* protonolysis of viable precursors decreased the complexity of the problem by eliminating the use of external salts/co-catalysts.

1.6.2. Counterion effect in Au catalysis

Another important effect in gold catalysis is the so called "counterion effect".[203] This effect strongly drives the behaviour of $[Au(L)]^+$ species whose coordination in solution it is of importance to ensure effective activation of substrates. Moreover the spatial location of the counterion around the metal centre in solution can provide information about the

catalyst and intermediates of a process. Interestingly, Macchioni and co-workers have investigated, using spectroscopic and computational tools, the structure of cationic η^2-alkene and η^2-alkyne Au complexes, bearing NHC and phosphine ligands.[204] When analysing cationic alkene- and alkyne-Au(I) phosphine complexes, the weakly coordinating BF_4 counterion was unambiguously found nearby the π-system, far-away from the metal. The specific location of other weakly coordinating counterions was found to depend on the ancillary ligands.

Furthermore, effects of the counterion in catalysis have been found mainly when strongly coordinating counterions are present in solution. A good example of this effect was found by Davies and co-workers who reported the Au(I) catalysed ring expansion of alkynyl aziridines to pyrroles (Figure 1.30).[205] When [AuCl(PPh_3)] was mixed with AgOTs, complex [Au(OTs)(PPh_3)] was formed with the basic OTs^- leading preferentially to rearomatisation and formation of 2,5-disubstituted pyrroles. However when AgOTf was used giving the more electrophilic [Au(OTf)(PPh_3)], this led preferentially to 1,2-shift, prior to rearomatisation, thus forming the 2,4 disubstituted product. The different basicity of the counterions in solution was used to explain the observed divergent pathways.

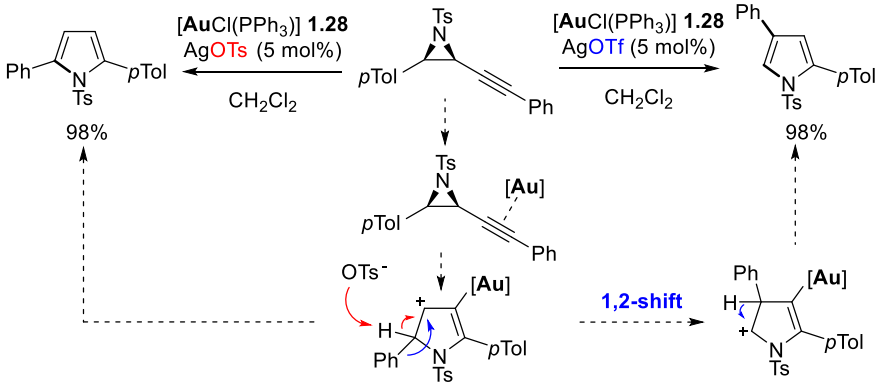
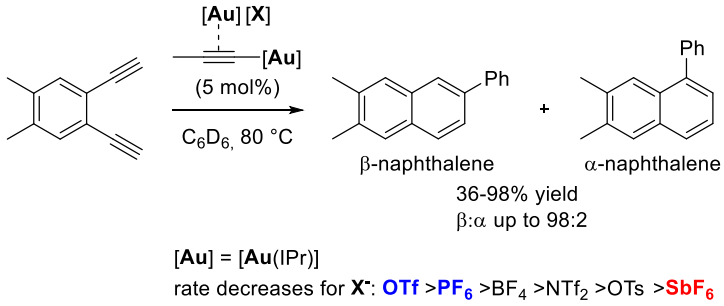


Figure 1.30. Synthesis of pyrroles *via* tandem ring-opening/Wagner-Meerwein Au(I) catalysed process, OTs *vs* OTf.[205]

Another interesting effect related to the choice of the counterion was reported for the cyclisation of diynes to β-naphthalenes and α-naphthalenes (Scheme 1.25).[93] For this transformation the authors used σ-π-propyne digold(I) NHC precursors as instant pre-catalysts; these species allowed fast activation of more acidic substrates, such as diynes, by acetylide exchange driven by release of volatile propyne. The rate of the reaction was strongly influenced by the precursor counterion: fast reaction rate to full conversion of products were observed when in presence of OTf and PF_6 anions, whilst less than 20%

conversion was observed when dinuclear complex with SbF_6 as counterion was used. The coordination of the counterions to $[Au(L)]^+$ species was influential for the reaction outcome.



Scheme 1.25. Cyclisation of diynes to naphthalenes by σ-π-propyne digold(I) NHC catalysts.[93]

1.6.3. Dinuclear Au catalysis

The last example (Scheme 1.25) falls mainly into the category of dual catalysis, which has become a hot topic in gold catalysis.[206] After the seminal work of Houk and Toste on the cycloisomerisation of 1,5-allenynes catalysed by $[\{Au(PPh_3)\}_3(\mu\text{-}O)][BF_4]$ **1.25** complex,[94a] many other examples have appeared in the literature,[91,106b,207] which consisted of the dual activation of a substrate by two molecules of a metal to perform the process. However, it is not easy to prove that two metal centres are involved in the catalytic cycle: several intermediates have been described, as pre-catalysts, or reaction intermediates, as discussed in section 1.3, and their involvement in catalysis have been questioned widely.[95,208]

As a highlight of this interesting branch of chemistry the work on the cyclisation of naphthalenes, and its mechanistic understanding will be reported, since it covers the major points of dual activation by Au complexes. The synthesis of naphthalenes, successful with the use of dinuclear gold species (Scheme 1.25), was initially performed using $[Au(NTf_2)(IPr)]$ **1.30** complexes.[94b] By varying the reaction conditions, the selectivity towards α- and β-naphthalenes could be tuned (Figure 1.31, a). Notably, under conditions that require high catalyst loading and low temperatures, the formation of the α-products was favoured; while the presence of basic additives favoured the β-naphthalene formation.

Mechanistic investigation showed that complex **1.30** was in equilibrium with the acetylide-Au(I) species **1.64**, and the diyne (Figure 1.31, b). When **1.64** was heated in

benzene, with no additional catalyst, no conversion was observed. The same fate was found when diyne and **1.64** were mixed in benzene at 80 °C. Catalytic addition of the Gagosz complex **1.30** to the latter mixture led to full conversion into β-naphthalene product. Thus, reaction of **1.64** with **1.30** was found to be faster compared to the reaction of **1.64** with diyne. This explains why in the presence of bases the equilibrium was shifted toward species **1.64**.

Further analysis on possible intermediates allowed to the isolatation of vinyl-Au(I) species **1.65** and *gem*-diaurated species **1.66** (Figure 1.31, c). Interestingly, the former catalysed the preferential formation of α-naphthalenes, with only 5 mol% of the β-product found, presumably because of favoured protodemetalation of diynes to **1.64**. The *gem*-diaurated species catalysed the reaction, even in absence of additional catalyst.

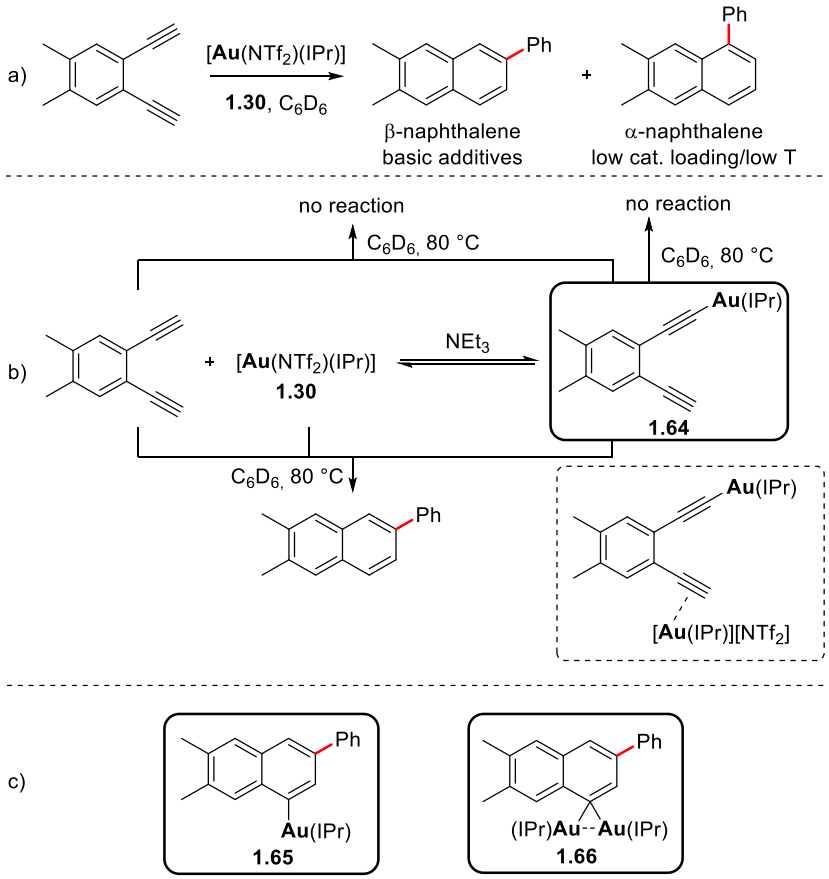


Figure 1.31. a) Switch on selectivity for the formation of naphtalenes from diyne with **1.30**; b) equilibrium between diyne, **1.30** and acetylide-Au(I) **1.64**; c) vinyl-Au(I) **1.65**, and *gem*-diaurated species **1.66**.

A mechanism was thus postulated (Figure 1.32). Complex **1.30** reacted with diyne to form aryl-Au(I) species **1.67**; ligand exchange with a second diyne molecule produced acetylide-Au(I) species **1.64** and started the catalytic cycle for β-naphthalenes. A second

Au species, derived from **1.30**, activated the second alkyne moiety in the diyne by π-coordination; nucleophilic attack from the acetylide-Au(I) species to the activated π-alkyne generated a vinylidene species that was further intercepted by benzene. Following ring expansion, vinyl-Au(I) **1.65** formed, in equilibrium with the off-cycle *gem*-diaurated **1.66**. Final protodeauration released the β-product and reformed the acetylide species **1.64** in solution.

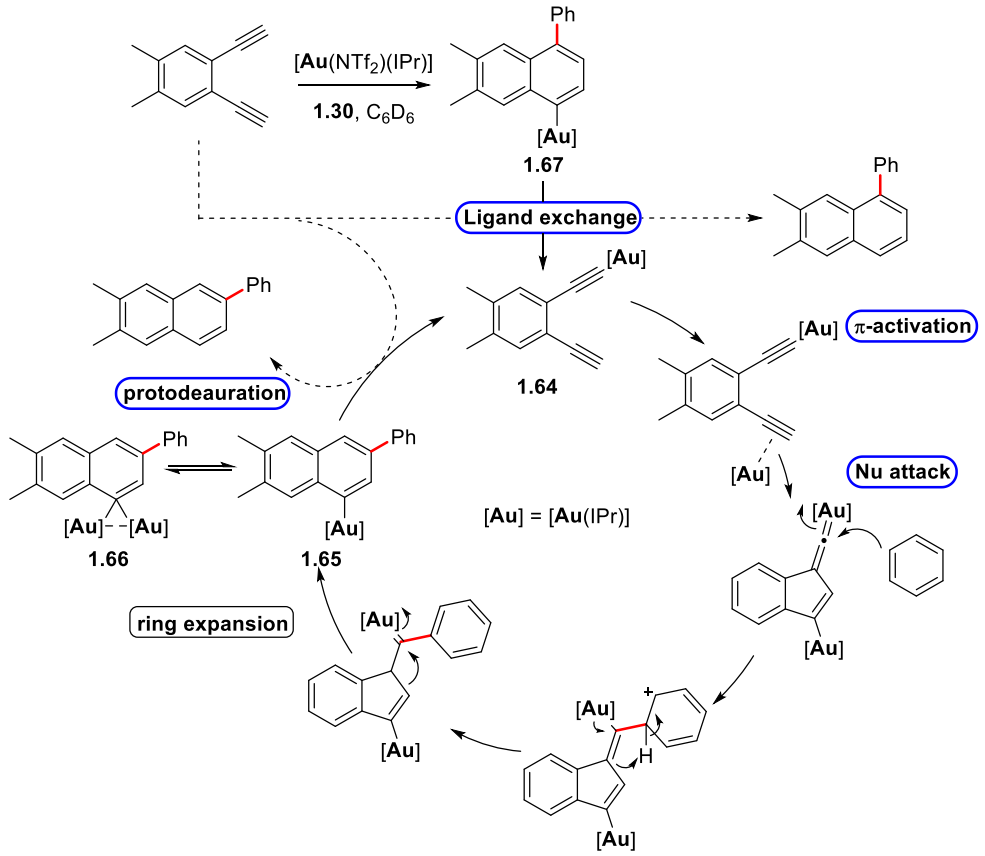


Figure 1.32. Proposed mechanistic cycle: highlighted the major elementary step for gold(I) catalysed hydrofunctionalisation of alkynes.

This reaction mechanism was postulated to be general for the cyclisation of diynes.[209] Other Au-catalysed reactions may be different from Figure 1.32, however, the fundamental elementary steps apply for the majority of Au-catalysed transformation. Among others of interest to this thesis, the hydrofunctionalisation of alkynes, such as the addition of Nu-H to triple bonds mainly proceeds through the following steps: pre-catalyst activation, alkyne activation, nucleophilic attack and protodeauration. The rate of each step can vary in every process, depending on the substrates, catalyst precursors and

reaction conditions, and needs to be assessed individually for a final understanding of the Au(I)-catalysed transformation and its reaction mechanism.

1.7. Aims and objectives

At the onset of this project the use of dinuclear species was set to evaluate and develop new catalytic methodologies. The use of dinuclear gold hydroxide NHC species **1.55** was utilised to perform inter- and intramolecular hydrocarboxylation of alkynes. Further investigation of the reaction mechanism was pursued to explore whether the reaction was a dinuclear process, and to define reaction intermediates which may be involved in the catalytic cycle.

The importance of exploring new gold catalyst was thus pursued by exploring the behaviour of gold complexes with chiral Lewis bases. The synthesis of chiral complexes with a N-Au bond were one of the aims of the project, together with the development of enantioselective transformation of alkynes and derivatives. Further investigation of dual catalysis Au/Lewis bases processes was explored.

Finally, C-Au coordination complexes were examined by isolation and characterisation of organogold NHC derivatives. The application of organogold derivatives as valuable "silver-free" catalysts precursors was investigated through stoichiometric and catalytic experiments, together with the study of their redox chemistry.

1.8. Bibliography

1. P. Goodman, *Gold Bull.*, 2002, **35**, 21-26.

2. S. P. Pricker, *Gold Bull.*, 1996, **29**, 53-60.

3. W. F. Kean and I. R. L. Kean, *Inflammopharmacology*, 2008, **16**, 112-125.

4. P. B. Kettler, *Org. Process Res. Dev.*, 2003, **7**, 342-354.

5. J. Cui and L. Zhang, *J. Hazard. Mater.*, 2008, **158**, 228-256.

6. J. O. Mardsen and I. C. House, *The Chemistry of Gold Extraction*, Society for Mining, Metallurgy and Exploration, Inc., Littleton, Colorado, 2nd edn., 2006.

7. C. Abbruzzese, P. Fornari, R. Massidda, F. Vegliò and S. Ubaldini, *Hydrometallurgy*, 1995, **39**, 265-276.

8. a) A. Akcil, *Biotechnol. Adv.*, 2003, **21**, 501-511; b) J. B. Mosher and L. Figueroa, *Miner. Eng.*, 1996, **9**, 573-581.

9. S. King, J. Massicot and A. McDonagh, *Metals*, 2015, **5**, 1454.

10. A. Ericson, L. I. Elding and S. K. C. Elmroth, *J. Chem. Soc., Dalton Trans.*, 1997, 1159-1164.

11. W. J. Pope and C. S. Gibson, *J. Chem. Soc., Trans.*, 1907, **91**, 2061-2066.

12. a) A. S. K. Hashmi, *Chem. Rev.*, 2007, **107**, 3180-3211; b) B. K. Min and C. M. Friend, *Chem. Rev.*, 2007, **107**, 2709-2724; c) R. Ciriminna, E. Falletta, C. Della Pina, J. H. Teles and M. Pagliaro, *Angew. Chem., Int. Ed.*, 2016, **55**, 14210-14217.

13. A. Sommer, *Nature*, 1943, **152**, 215.

14. A. Laguna and M. Laguna, *Coord. Chem. Rev.*, 1999, **193**, 837-856.

15. N. Bartlett, *Gold Bull.*, 1998, **31**, 22-25.

16. D. J. Gorin and F. D. Toste, *Nature*, 2007, **446**, 395-403.

17. a) D. R. McKelvey, *J. Chem. Ed.*, 1983, **60**, 112; b) K. S. Pitzer, *Acc. Chem. Res.*, 1979, **12**, 271-276.

18. P. Pyykkö and J. P. Desclaux, *Acc. Chem. Res.*, 1979, **12**, 276-281.

19. E. J. Baerends, W. H. E. Schwarz, P. Schwerdtfeger and J. G. Snijders, *J. Phys. B: At., Mol. Opt. Phys*, 1990, **23**, 3225.

20. A. Bayler, A. Schier, G. A. Bowmaker and H. Schmidbaur, *J. Am. Chem. Soc.*, 1996, **118**, 7006-7007.

21. U. M. Tripathi, A. Bauer and H. Schmidbaur, *J. Chem. Soc., Dalton Trans.*, 1997, 2865-2868.

22. H. Schmidbaur, S. Cronje, B. Djordjevic and O. Schuster, *Chem. Phys.*, 2005, **311**, 151-161.

23. a) A. MacCragh and W. S. Koski, *J. Am. Chem. Soc.*, 1965, **87**, 2496-2497; b) S. H. Elder, G. M. Lucier, F. J. Hollander and N. Bartlett, *J. Am. Chem. Soc.*, 1997, **119**, 1020-1026; c) A. J. Blake, J. A. Greig, A. J. Holder, T. I. Hyde, A. Taylor and M. Schröder, *Angew. Chem., Int. Ed. Engl.*, 1990, **29**, 197-198; d) S. Seidel and K. Seppelt, *Science*, 2000, **290**, 117-118; e) S. Preiß, C. Förster, S. Otto, M. Bauer, P. Müller, D. Hinderberger, H. Hashemi Haeri, L. Carella and K. Heinze, *Nature Chem.*, 2017, **9**, 1249.

24. a) H. Schmidbaur, W. Graf and G. Müller, *Angew. Chem., Int. Ed. Engl.*, 1988, **27**, 417-419; b) W. Schneider, A. Bauer and H. Schmidbaur, *Organometallics*, 1996, **15**, 5445-5446.

25. P. Pyykkö, *Angew. Chem., Int. Ed.*, 2004, **43**, 4412-4456.

26. J. J. Rehr, E. Zaremba and W. Kohn, *Phys. Rev. B*, 1975, **12**, 2062-2066.

27. S. A. Cotton, in *Chemistry of Precious Metals*, Springer Netherlands, Dordrecht, 1997, pp. 273-327.

28. M. Joost, A. Zeineddine, L. Estévez, S. Mallet−Ladeira, K. Miqueu, A. Amgoune and D. Bourissou, *J. Am. Chem. Soc.*, 2014, **136**, 14654-14657.

29. A. Leyva-Pérez and A. Corma, *Angew. Chem., Int. Ed.*, 2012, **51**, 614-635.

30. W. R. Mason and H. B. Gray, *J. Am. Chem. Soc.*, 1968, **90**, 5721-5729; J. Börgel, M. G. Campbell and T. Ritter, *J. Chem. Ed.*, 2016, **93**, 118-121.

31. P. Schwerdtfeger, *J. Am. Chem. Soc.*, 1989, **111**, 7261-7262.

32. D. J. Gorin, B. D. Sherry and F. D. Toste, *Chem. Rev.*, 2008, **108**, 3351-3378.

33. D. Bourissou, O. Guerret, F. P. Gabbaï and G. Bertrand, *Chem. Rev.*, 2000, **100**, 39-92.

34. R. Hoffmann, G. D. Zeiss and G. W. Van Dine, *J. Am. Chem. Soc.*, 1968, **90**, 1485-1499.

35. A. J. Arduengo, R. L. Harlow and M. Kline, *J. Am. Chem. Soc.*, 1991, **113**, 361-363.

36. a) T. Dröge and F. Glorius, *Angew. Chem., Int. Ed.*, 2010, **49**, 6940-6952; b) T. Höltzl, V. T. Ngan, M. T. Nguyen and T. Veszprémi, *Chem. Phys. Lett.*, 2009, **481**, 54-57.

37. D. A. Dixon and A. J. Arduengo, *J. Phys. Chem.*, 1991, **95**, 4180-4182.

38. a) A. J. Arduengo, H. Bock, H. Chen, M. Denk, D. A. Dixon, J. C. Green, W. A. Herrmann, N. L. Jones, M. Wagner and R. West, *J. Am. Chem. Soc.*, 1994, **116**, 6641-6649; b) A. J. Arduengo, D. A. Dixon, K. K. Kumashiro, C. Lee, W. P. Power and K. W. Zilm, *J. Am. Chem. Soc.*, 1994, **116**, 6361-6367.

39. O. Hollóczki, P. Terleczky, D. Szieberth, G. Mourgas, D. Gudat and L. Nyulászi, *J. Am. Chem. Soc.*, 2011, **133**, 780-789.

40. D. Enders, K. Breuer, G. Raabe, J. Runsink, J. H. Teles, J.-P. Melder, K. Ebel and S. Brode, *Angew. Chem., Int. Ed. Engl.*, 1995, **34**, 1021-1023.

41. V. Lavallo, Y. Canac, C. Präsang, B. Donnadieu and G. Bertrand, *Angew. Chem., Int. Ed.*, 2005, **44**, 5705-5709.

42. G. Altenhoff, R. Goddard, C. W. Lehmann and F. Glorius, *Angew. Chem., Int. Ed.*, 2003, **42**, 3690-3693.

43. P. de Frémont, N. Marion and S. P. Nolan, *Coord. Chem. Rev.*, 2009, **253**, 862-892.

44. a) R. W. Alder, P. R. Allen and S. J. Williams, *J. Chem. Soc., Chem. Commun.*, 1995, 1267-1268; b) Y.-J. Kim and A. Streitwieser, *J. Am. Chem. Soc.*, 2002, **124**, 5757-5761; c) Y. Chu, H. Deng and J.-P. Cheng, *J. Org. Chem.*, 2007, **72**, 7790-7793.

45. R. S. Massey, C. J. Collett, A. G. Lindsay, A. D. Smith and A. C. O'Donoghue, *J. Am. Chem. Soc.*, 2012, **134**, 20421-20432.

46. A. M. Voutchkova, L. N. Appelhans, A. R. Chianese and R. H. Crabtree, *J. Am. Chem. Soc.*, 2005, **127**, 17624-17625.

47. N. Kuhn and T. Kratz, *Synthesis*, 1993, **1993**, 561-562.

48. G. W. Nyce, S. Csihony, R. M. Waymouth and J. L. Hedrick, *Chem. Eur. J.*, 2004, **10**, 4073-4079.

49. L. Benhamou, E. Chardon, G. Lavigne, S. Bellemin-Laponnaz and V. César, *Chem. Rev.*, 2011, **111**, 2705-2733.

50. K. M. Kuhn and R. H. Grubbs, *Org. Lett.*, 2008, **10**, 2075-2077.

51. L. Tschugajeff, M. Skanawy-Grigorjewa, A. Posnjak and M. Skanawy-Grigorjewa, *Z. Anorg. All. Chem.*, 1925, **148**, 37-42.

52. A. Burke, A. L. Balch and J. H. Enemark, *J. Am. Chem. Soc.*, 1970, **92**, 2555-2557.

53. a) H. W. Wanzlick and H. J. Schönherr, *Angew. Chem.*, 1968, **80**, 154-154; b) K. Öfele, *J. Organomet. Chem.*, 1968, **12**, P42-P43.

54. H. Jacobsen, A. Correa, A. Poater, C. Costabile and L. Cavallo, *Coord. Chem. Rev.*, 2009, **253**, 687-703.

55. a) A. Comas-Vives and J. N. Harvey, *Eur. J. Inorg. Chem.*, 2011, **2011**, 5025-5035; b) X. Hu, I. Castro-Rodriguez, K. Olsen and K. Meyer, *Organometallics*, 2004, **23**, 755-764; c) D. Nemcsok, K. Wichmann and G. Frenking, *Organometallics*, 2004, **23**, 3640-3646.

56. H. Jacobsen, A. Correa, C. Costabile and L. Cavallo, *J. Organomet. Chem.*, 2006, **691**, 4350-4358.

57. D. Marchione, L. Belpassi, G. Bistoni, A. Macchioni, F. Tarantelli and D. Zuccaccia, *Organometallics*, 2014, **33**, 4200-4208.

58. G. Ciancaleoni, N. Scafuri, G. Bistoni, A. Macchioni, F. Tarantelli, D. Zuccaccia and L. Belpassi, *Inorg. Chem.*, 2014, **53**, 9907-9916.

59. a) S. Gaillard, C. S. J. Cazin and S. P. Nolan, *Acc. Chem. Res.*, 2011, **45**, 778-787; b) S. P. Nolan, *Acc. Chem. Res.*, 2010, **44**, 91-100; c) P. de Frémont, N. M. Scott, E. D. Stevens and S. P. Nolan, *Organometallics*, 2005, **24**, 2411-2418; d) P. de Frémont, R. Singh, E. D. Stevens, J. L. Petersen and S. P. Nolan, *Organometallics*, 2007, **26**, 1376-1385.

60. H. M. J. Wang and I. J. B. Lin, *Organometallics*, 1998, **17**, 972-975.

61. M. R. L. Furst and C. S. J. Cazin, *Chem. Commun.*, 2010, **46**, 6924-6925.

62. A. Collado, A. Gómez-Suárez, A. R. Martin, A. M. Z. Slawin and S. P. Nolan, *Chem. Commun.*, 2013, **49**, 5541-5543.

63. S. Gaillard, A. M. Z. Slawin, A. T. Bonura, E. D. Stevens and S. P. Nolan, *Organometallics*, 2010, **29**, 394-402.

64. D. S. Laitar, P. Müller, T. G. Gray and J. P. Sadighi, *Organometallics*, 2005, **24**, 4503-4505.

65. E. Y. Tsui, P. Müller and J. P. Sadighi, *Angew. Chem., Int. Ed.*, 2008, **47**, 8937-8940.

66. C.-Y. Wu, T. Horibe, C. B. Jacobsen and F. D. Toste, *Nature*, 2015, **517**, 449-454.

67. C. A. Tolman, *Chem. Rev.*, 1977, **77**, 313-348.

68. a) A. R. Chianese, X. Li, M. C. Janzen, J. W. Faller and R. H. Crabtree, *Organometallics*, 2003, **22**, 1663-1667; b) R. A. Kelly III, H. Clavier, S. Giudice, N. M. Scott, E. D. Stevens, J. Bordner, I. Samardjiev, C. D. Hoff, L. Cavallo and S. P. Nolan, *Organometallics*, 2008, **27**, 202-210.

69. N. M. Scott, R. Dorta, E. D. Stevens, A. Correa, L. Cavallo and S. P. Nolan, *J. Am. Chem. Soc.*, 2005, **127**, 3516-3526.

70. D. M. Khramov, V. M. Lynch and C. W. Bielawski, *Organometallics*, 2007, **26**, 6042-6049.

71. S. Fantasia, J. L. Petersen, H. Jacobsen, L. Cavallo and S. P. Nolan, *Organometallics*, 2007, **26**, 5880-5889.

72. O. Back, M. Henry-Ellinger, C. D. Martin, D. Martin and G. Bertrand, *Angew. Chem., Int. Ed.*, 2013, **52**, 2939-2943.

73. R. Dorta, E. D. Stevens, C. D. Hoff and S. P. Nolan, *J. Am. Chem. Soc.*, 2003, **125**, 10490-10491.

74. a) J. Huang, H.-J. Schanz, E. D. Stevens and S. P. Nolan, *Organometallics*, 1999, **18**, 2370-2375; b) K. E. Krahulic, G. D. Enright, M. Parvez and R. Roesler, *J. Am. Chem. Soc.*, 2005, **127**, 4142-4143.

75. a) H. Clavier and S. P. Nolan, *Chem. Commun.*, 2010, **46**, 841-861; b) A. Poater, B. Cosenza, A. Correa, S. Giudice, F. Ragone, V. Scarano and L. Cavallo, *Eur. J. Inorg. Chem.*, 2009, **2009**, 1759-1766.

76. F. Ragone, A. Poater and L. Cavallo, *J. Am. Chem. Soc.*, 2010, **132**, 4249-4258.

77. A. Fürstner and P. W. Davies, *Angew. Chem., Int. Ed.*, 2007, **46**, 3410-3449.

78. R. G. Pearson, *J. Am. Chem. Soc.*, 1963, **85**, 3533-3539.

79. J. Chatt and L. A. Duncanson, *J. Chem. Soc.*, 1953, 2939-2947.

80. S. Singh, S. S. Kumar, V. Jancik, H. W. Roesky, H.-G. Schmidt and M. Noltemeyer, *Eur. J. Inorg. Chem.*, 2005, **2005**, 3057-3062.

81. a) R. J. Cross, M. F. Davidson and A. J. McLennan, *J. Organomet. Chem.*, 1984, **265**, c37-c39; b) H.-Y. Chao, W. Lu, Y. Li, M. C. W. Chan, C.-M. Che, K.-K. Cheung and N. Zhu, *J. Am. Chem. Soc.*, 2002, **124**, 14696-14706; c) I. R. Whittall, M. G. Humphrey, S. Houbrechts, A. Persoons and D. C. R. Hockless, *Organometallics*, 1996, **15**, 5738-5745.

82. G. C. Fortman, A. Poater, J. W. Levell, S. Gaillard, A. M. Z. Slawin, I. D. W. Samuel, L. Cavallo and S. P. Nolan, *Dalton Trans.*, 2010, **39**, 10382-10390.

83. O. Fujimura, K. Fukunaga, T. Honma, T. Machida and T. Takahashi, (Ube Industries, Ltd., Japan). Application: WO2006080515, 2006, p. 102 pp.

84. T. de Haro and C. Nevado, *J. Am. Chem. Soc.*, 2010, **132**, 1512-1513.

85. J. P. Brand, C. Chevalley, R. Scopelliti and J. Waser, *Chem. Eur. J.*, 2012, **18**, 5655-5666.

86. J. P. Brand, J. Charpentier and J. Waser, *Angew. Chem., Int. Ed.*, 2009, **48**, 9346-9349.

87. J. P. Brand and J. Waser, *Angew. Chem.*, 2010, **122**, 7462-7465.

88. Y. Li, J. P. Brand and J. Waser, *Angew. Chem., Int. Ed.*, 2013, **52**, 6743-6747.

89. J. P. Brand and J. Waser, *Org. Lett.*, 2012, **14**, 744-747.

90. T. J. Brown and R. A. Widenhoefer, *Organometallics*, 2011, **30**, 6003-6009.

91. A. Grirrane, H. Garcia, A. Corma and E. Álvarez, *ACS Catal.*, 2011, **1**, 1647-1653.

92. A. Gómez-Suárez, S. Dupuy, A. M. Z. Slawin and S. P. Nolan, *Angew. Chem., Int. Ed.*, 2013, **52**, 938-942.

93. A. S. K. Hashmi, T. Lauterbach, P. Nösel, M. H. Vilhelmsen, M. Rudolph and F. Rominger, *Chem. Eur. J.*, 2013, **19**, 1058-1065.

94. a) P. H.-Y. Cheong, P. Morganelli, M. R. Luzung, K. N. Houk and F. D. Toste, *J. Am. Chem. Soc.*, 2008, **130**, 4517-4526; b) A. S. K. Hashmi, I. Braun, M. Rudolph and F. Rominger, *Organometallics*, 2012, **31**, 644-661.

95. A. Simonneau, F. Jaroschik, D. Lesage, M. Karanik, R. Guillot, M. Malacria, J.-C. Tabet, J.-P. Goddard, L. Fensterbank, V. Gandon and Y. Gimbert, *Chem. Sci.*, 2011, **2**, 2417-2422.

96. P. Nösel, T. Lauterbach, M. Rudolph, F. Rominger and A. S. K. Hashmi, *Chem. Eur. J.*, 2013, **19**, 8634-8641.

97. S. Kramer, *Chem. Eur. J.*, 2016, **22**, 15584-15598.

98. M. S. Kharasch and H. S. Isbell, *J. Am. Chem. Soc.*, 1931, **53**, 3053-3059.

99. L. T. Ball, G. C. Lloyd-Jones and C. A. Russell, *Science*, 2012, **337**, 1644-1648.

100. L. T. Ball, G. C. Lloyd-Jones and C. A. Russell, *J. Am. Chem. Soc.*, 2014, **136**, 254-264.

101. P. Lu, T. C. Boorman, A. M. Z. Slawin and I. Larrosa, *J. Am. Chem. Soc.*, 2010, **132**, 5580-5581.

102. S. Gaillard, A. M. Z. Slawin and S. P. Nolan, *Chem. Commun.*, 2010, **46**, 2742-2744.

103. S. Dupuy, F. Lazreg, A. M. Z. Slawin, C. S. J. Cazin and S. P. Nolan, *Chem. Commun.*, 2011, **47**, 5455-5457.

104. D. V. Partyka, M. Zeller, A. D. Hunter and T. G. Gray, *Angew. Chem., Int. Ed.*, 2006, **45**, 8188-8191.

105. a) F. Mohr, L. R. Falvello and M. Laguna, *Eur. J. Inorg. Chem.*, 2006, **2006**, 833-838; b) L.-P. Liu, B. Xu, M. S. Mashuta and G. B. Hammond, *J. Am. Chem. Soc.*, 2008, **130**, 17642-17643; c) A. S. K. Hashmi, A. M. Schuster and F. Rominger, *Angew. Chem., Int. Ed.*, 2009, **48**, 8247-8249; d) Y. Shi, S. D. Ramgren and S. A. Blum, *Organometallics*, 2009, **28**, 1275-1277.

106. a) X. Zeng, R. Kinjo, B. Donnadieu and G. Bertrand, *Angew. Chem., Int. Ed.*, 2010, **49**, 942-945; b) D. Weber, M. A. Tarselli and M. R. Gagné, *Angew. Chem., Int. Ed.*, 2009, **48**, 5733-5736.

107. Y. Chen, D. Wang, J. L. Petersen, N. G. Akhmedov and X. Shi, *Chem. Commun.*, 2010, **46**, 6147-6149.

108. D. Weber and M. R. Gagné, *Chem. Sci.*, 2013, **4**, 335-338.

109. a) J. E. Heckler, M. Zeller, A. D. Hunter and T. G. Gray, *Angew. Chem., Int. Ed.*, 2012, **51**, 5924-5928; b) T. N. Hooper, M. Green and C. A. Russell, *Chem. Commun.*, 2010, **46**, 2313-2315; c) A. S. K. Hashmi, I. Braun, P. Nösel, J. Schädlich, M. Wieteck, M. Rudolph and F. Rominger, *Angew. Chem., Int. Ed.*, 2012, **51**, 4456-4460.

110. G. Seidel, C. W. Lehmann and A. Fürstner, *Angew. Chem., Int. Ed.*, 2010, **49**, 8466-8470.

111. M. R. Fructos, M. M. Diaz-Requejo and P. J. Perez, *Chem. Commun.*, 2016, **52**, 7326-7335.

112. H. V. Adcock, T. Langer and P. W. Davies, *Chem. Eur. J.*, 2014, **20**, 7262-7266.

113. a) G. Seidel and A. Fürstner, *Angew. Chem., Int. Ed.*, 2014, **53**, 4807-4811; b) R. E. M. Brooner and R. A. Widenhoefer, *Chem. Commun.*, 2014, **50**, 2420-2423; c) M. Fañanás-Mastral and F. Aznar, *Organometallics*, 2009, **28**, 666-668.

114. M. W. Hussong, F. Rominger, P. Krämer and B. F. Straub, *Angew. Chem., Int. Ed.*, 2014, **53**, 9372-9375.

115. M. Joost, L. Estévez, S. Mallet-Ladeira, K. Miqueu, A. Amgoune and D. Bourissou, *Angew. Chem., Int. Ed.*, 2014, **53**, 14512-14516.

116. a) K. I. Grandberg and V. P. Dyadchenko, *J. Organomet. Chem.*, 1994, **474**, 1-21; b) Y. T. Struchkov, Y. L. Slovokhotov, D. N. Kravtsov, T. V. Baukova, E. G. Perevalova and K. J. Grandberg, *J. Organomet. Chem.*, 1988, **338**, 269-280.

117. V. J. Scott, J. A. Labinger and J. E. Bercaw, *Organometallics*, 2010, **29**, 4090-4096.

118. a) J. Vicente, M.-D. Bermúdez, M.-P. Carrillo and P. G. Jones, *J. Organomet. Chem.*, 1993, **456**, 305-312; b) M. V. Baker, P. J. Barnard, S. K. Brayshaw, J. L. Hickey, B. W. Skelton and A. H. White, *Dalton Trans.*, 2005, 37-43; c) D. Fan, E. Meléndez, J. D. Ranford, P. F. Lee and J. J. Vittal, *J. Organomet. Chem.*, 2004, **689**, 2969-2974.

119. E. I. Smyslova, E. G. Perevalova, V. P. Dyadchenko, K. I. Grandberg, Y. L. Slovokhotov and Y. T. Struchkov, *J. Organomet. Chem.*, 1981, **215**, 269-279.

120. a) S. Komiya, M. Iwata, T. Sone and A. Fukuoka, *J. Chem. Soc., Chem. Commun.*, 1992, 1109-1110; b) S. Komiya, T. Sone, Y. Usui, M. Hirano and A. Fukuoka, *Gold Bull.*, 1996, **29**, 131-136.

121. F. Cocco, M. A. Cinellu, G. Minghetti, A. Zucca, S. Stoccoro, L. Maiore and M. Manassero, *Organometallics*, 2010, **29**, 1064-1066.

122. a) Y. Ito, M. Inouye, M. Suginome and M. Murakami, *J. Organomet. Chem.*, 1988, **342**, C41-C44; b) M. Masahiro, I. Masahiko, S. Michinori and I. Yoshihiko, *Bull. Chem. Soc. J.*, 1988, **61**, 3649-3652.

123. A. Tamaki and J. K. Kochi, *J. Organomet. Chem.*, 1973, **61**, 441-450.

124. J. H. Teles, S. Brode and M. Chabanas, *Angew. Chem., Int. Ed.*, 1998, **37**, 1415-1418.

125. R. L. LaLonde, J. W. E. Brenzovich, D. Benitez, E. Tkatchouk, K. Kelley, I. I. I. W. A. Goddard and F. D. Toste, *Chem. Sci.*, 2010, **1**, 226-233.

126. G. Zhang, Y. Luo, Y. Wang and L. Zhang, *Angew. Chem., Int. Ed.*, 2011, **50**, 4450-4454.

127. G. Klatt, R. Xu, M. Pernpointner, L. Molinari, T. Quang Hung, F. Rominger, A. S. K. Hashmi and H. Köppel, *Chem. Eur. J.*, 2013, **19**, 3954-3961.

128. G. Steinhauser, J. Evers, S. Jakob, T. M. Klapötke and G. Oehlinger, *Gold Bull.*, 2008, **41**, 305-317.

129. a) H. E. Abdou, A. A. Mohamed and J. P. Fackler, in *Gold Chemistry*, Wiley-VCH Verlag GmbH & Co. KGaA, 2009, pp. 1-45; b) M. A. Cinellu, in *Gold Chemistry*, Wiley-VCH Verlag GmbH & Co. KGaA, 2009, pp. 47-92.

130. a) K. Angermaier and H. Schmidbaur, *J. Chem. Soc., Dalton Trans.*, 1995, 559-564; b) A. Gómez-Suárez, D. J. Nelson, D. G. Thompson, D. B. Cordes, D. Graham, A. M. Z. Slawin and S. P. Nolan, *Beilstein J. Org. Chem.*, 2013, **9**, 2216-2223; c) C.-K. Chan, C.-X. Guo, K.-K. Cheung, D. Li and C.-M. Che, *J. Chem. Soc., Dalton Trans.*, 1994, 3677-3682; d) J. Coetzee, S. Cronje, L. Dobrzanska, H. G. Raubenheimer, G. Joone, M. J. Nell and H. C. Hoppe, *Dalton Trans.*, 2011, **40**, 1471-1483; e) J. Vicente, M.-T. Chicote, R. Guerrero and P. G. Jones, *J. Chem. Soc., Dalton Trans.*, 1995, 1251-

1254; f) H. Duan, S. Sengupta, J. L. Petersen, N. G. Akhmedov and X. Shi, *J. Am. Chem. Soc.*, 2009, **131**, 12100-12102.

131. R. Faggiani, H. E. Howard-Lock, C. J. L. Lock and M. A. Turner, *Can. J. Chem.*, 1987, **65**, 1568-1575.

132. L. Ricard and F. Gagosz, *Organometallics*, 2007, **26**, 4704-4707.

133. A. S. Romanov and M. Bochmann, *Organometallics*, 2015, **34**, 2439-2454.

134. a) N. Mézailles, L. Ricard and F. Gagosz, *Org. Lett.*, 2005, **7**, 4133-4136; b) A. Leyva and A. Corma, *J. Org. Chem.*, 2009, **74**, 2067-2074.

135. S. J. B. Price, M. J. DiMartino, D. T. Hill, R. Kuroda, M. A. Mazid and P. J. Sadler, *Inorg. Chem.*, 1985, **24**, 3425-3434.

136. J. Han, N. Shimizu, Z. Lu, H. Amii, G. B. Hammond and B. Xu, *Org. Lett.*, 2014, **16**, 3500-3503.

137. J. J. Guy, P. G. Jones, M. J. Mays and G. M. Sheldrick, *J. Chem. Soc., Dalton Trans.*, 1977, 8-10.

138. N. C. Baenziger, K. M. Dittemore and J. R. Doyle, *Inorg. Chem.*, 1974, **13**, 805-811.

139. a) M. Munakata, S.-G. Yan, M. Maekawa, M. Akiyama and S. Kitagawa, *J. Chem. Soc., Dalton Trans.*, 1997, 4257-4262; b) F. Bonati, A. Burini, B. R. Pietroni and B. Bovio, *J. Organomet. Chem.*, 1985, **296**, 301-313; c) E. J. Fernández, A. Laguna, J. M. López-de-Luzuriaga, M. Monge, M. Montiel, M. E. Olmos, J. Pérez and M. Rodríguez-Castillo, *Gold Bull.*, 2007, **40**, 172-183; d) P. de Frémont, N. Marion and S. P. Nolan, *J. Organomet. Chem.*, 2009, **694**, 551-560; e) M. Theil, P. Jutzi, B. Neumann, A. Stammler and H.-G. Stammler, *J. Organomet. Chem.*, 2002, **662**, 34-42; f) C. K. Mirabell, R. K. Johnson, D. T. Hill, L. F. Faucette, G. R. Girard, G. Y. Kuo, C. M. Sung and S. T. Crooke, *J. Med. Chem.*, 1986, **29**, 218-223.

140. R. Corbo, G. F. Ryan, M. A. Haghighatbin, C. F. Hogan, D. J. D. Wilson, M. D. Hulett, P. J. Barnard and J. L. Dutton, *Inorg. Chem.*, 2016, **55**, 2830-2839.

141. W. Schneider, A. Bauer, A. Schier and H. Schmidbaur, *Chem. Ber.*, 1997, **130**, 1417-1422.

142. J. Schneider, Y.-A. Lee, J. Pérez, W. W. Brennessel, C. Flaschenriem and R. Eisenberg, *Inorg. Chem.*, 2008, **47**, 957-968.

143. A. A. Mohamed, A. P. Mayer, H. E. Abdou, M. D. Irwin, L. M. Pérez and J. P. Fackler, *Inorg. Chem.*, 2007, **46**, 11165-11172.

144. M. Ayerbe Garcia, W. Frey, M. R. Ringenberg, M. Schwilk and R. Peters, *Chem. Commun.*, 2015, **51**, 16806-16809.

145. G. Bergerhoff, *Z. Anorg. Allg. Chem.*, 1964, **327**, 139-142.

146. D. Michael, P. Mingos and J. Yau, *J. Organomet. Chem.*, 1994, **479**, c16-c17.

147. J. Yau and D. Michael P. Mingos, *J. Chem. Soc., Dalton Trans.*, 1997, 1103-1112.

148. E. Herrero-Gómez, C. Nieto-Oberhuber, S. López, J. Benet-Buchholz and A. M. Echavarren, *Angew. Chem., Int. Ed.*, 2006, **45**, 5455-5459.

149. R. M. P. Veenboer, D. Gasperini, F. Nahra, D. B. Cordes, A. M. Z. Slawin, C. S. J. Cazin and S. P. Nolan, *Organometallics*, 2017, **36**, 3645-3653.

150. a) C. Nieto-Oberhuber, M. P. Muñoz, S. López, E. Jiménez-Núñez, C. Nevado, E. Herrero-Gómez, M. Raducan and A. M. Echavarren, *Chem. Eur. J.*, 2006, **12**, 1677-1693; b) C. Ferrer and A. M. Echavarren, *Angew. Chem., Int. Ed.*, 2006, **45**, 1105-1109; c) C. Nieto-Oberhuber, S. López, M. P. Muñoz, D. J. Cárdenas, E. Buñuel, C. Nevado and A. M. Echavarren, *Angew. Chem., Int. Ed.*, 2005, **44**, 6146-6148.

151. A. Zhdanko, M. Ströbele and M. E. Maier, *Chem. Eur. J.*, 2012, **18**, 14732-14744.

152. a) B. P. Block and J. C. Bailar, *J. Am. Chem. Soc.*, 1951, **73**, 4722-4725; b) G. Nardin, L. Randaccio, G. Annibale, G. Natile and B. Pitteri, *J. Chem. Soc., Dalton Trans.*, 1980, 220-223; c) R. C. Elder and J. W. Watkins, *Inorg. Chem.*, 1986, **25**, 223-226.

153. a) E. Kimura, Y. Kurogi and T. Takahashi, *Inorg. Chem.*, 1991, **30**, 4117-4121; b) M. P. Suh, I. S. Kim, B. Y. Shim, D. Hong and T.-S. Yoon, *Inorg. Chem.*, 1996, **35**, 3595-3598.

154. C. F. Weick and F. Basolo, *Inorg. Chem.*, 1966, **5**, 576-582.

155. a) H. N. Adams, W. Hiller and J. Strähle, *Z. Anorg. Allg. Chem.*, 1982, **485**, 81-91; b) W. Conzelmann, W. Hiller, J. Strähle and G. M. Sheldrick, *Z. Anorg. Allg. Chem.*, 1984, **512**, 169-176; c) H.-N. Adams and J. Strähle, *Z. Anorg. Allg. Chem.*, 1982, **485**, 65-80; d) J. Vicente, M.-T. Chicote, S. Huertas, M. C. Ramírez de Arellano and P. G. Jones, *Eur. J. Inorg. Chem.*, 1998, **1998**, 511-516; e) L. G. Kuz'mina, A. A. Bagatur'yants, A. V. Churakov and J. A. K. Howard, *Chem. Commun.*, 2001, 1394-1395.

156. A. Dar, K. Moss, S. M. Cottrill, R. V. Parish, C. A. McAuliffe, R. G. Pritchard, B. Beagley and J. Sandbank, *J. Chem. Soc., Dalton Trans.*, 1992, 1907-1913.

157. N. Savjani, D.-A. Roşca, M. Schormann and M. Bochmann, *Angew. Chem., Int. Ed.*, 2013, **52**, 874-877.

158. C.-Y. Zhou, P. W. H. Chan and C.-M. Che, *Org. Lett.*, 2006, **8**, 325-328.

159. a) V. K.-Y. Lo, Y. Liu, M.-K. Wong and C.-M. Che, *Org. Lett.*, 2006, **8**, 1529-1532; b) C. Gonzalez-Arellano, A. Corma, M. Iglesias and F. Sanchez, *Chem. Commun.*, 2005, 1990-1992.

160. a) K. Kato, T. Kobayashi, T. Fujinami, S. Motodate, T. Kusakabe, T. Mochida and H. Akita, *Synlett*, 2008, 1081-1085; b) J. P. Reeds, A. C. Whitwood, M. P. Healy and I. J. S. Fairlamb, *Chem. Commun.*, 2010, **46**, 2046-2048; c) V. K.-Y. Lo, K. K.-Y. Kung, M.-K. Wong and C.-M. Che, *J. Organomet. Chem.*, 2009, **694**, 583-591.

161. S. Radenkovic, M. Antic, N. D. Savic and B. D. Glisic, *New J. Chem.*, 2017, **41**, 12407-12415.

162. a) A. S. K. Hashmi, J. P. Weyrauch, M. Rudolph and E. Kurpejović, *Angew. Chem., Int. Ed.*, 2004, **43**, 6545-6547; b) M. Pažický, A. Loos, M. J. Ferreira, D. Serra, N. Vinokurov, F. Rominger, C. Jäkel, A. S. K. Hashmi and M. Limbach, *Organometallics*, 2010, **29**, 4448-4458.

163. A. S. K. Hashmi, T. M. Frost and J. W. Bats, *J. Am. Chem. Soc.*, 2000, **122**, 11553-11554.

164. D.-A. Roşca, D. A. Smith, D. L. Hughes and M. Bochmann, *Angew. Chem., Int. Ed.*, 2012, **51**, 10643-10646.

165. D.-A. Roşca, J. Fernandez-Cestau, J. Morris, J. A. Wright and M. Bochmann, *Sci. Adv.*, 2015, **1**.

166. M. Bortoluzzi, E. De Faveri, S. Daniele and B. Pitteri, *Eur. J. Inorg. Chem.*, 2006, **2006**, 3393-3399.

167. M. A. Cinellu and G. Minghetti, *Gold Bull.*, 2002, **35**, 11-20.

168. J. P. Bravo-Vasquez and R. H. Hill, *Polyhedron*, 2000, **19**, 343-349.

169. a) J.-C. Wang, M. N. I. Khan and J. P. Fackler, Jnr, *Acta Crystallogr. Sec. C*, 1989, **45**, 1008-1010; b) M. Brill, F. Nahra, A. Gómez-Herrera, C. Zinser, D. B. Cordes, A. M. Z. Slawin and S. P. Nolan, *ChemCatChem*, 2017, **9**, 117-120; c) A. Collado, A. Gomez-Suarez, P. B. Webb, H. Kruger, M. Buhl, D. B. Cordes, A. M. Z. Slawin and S. P. Nolan, *Chem. Commun.*, 2014, **50**, 11321-11324.

170. R. Kissner, G. Welti and G. Geier, *J. Chem. Soc., Dalton Trans.*, 1997, 1773-1778.

171. N. Marion, P. Carlqvist, R. Gealageas, P. de Frémont, F. Maseras and S. P. Nolan, *Chem. Eur. J.*, 2007, **13**, 6437-6451.

172. a) A. Gomez-Suarez, R. S. Ramon, A. M. Z. Slawin and S. P. Nolan, *Dalton Trans.*, 2012, **41**, 5461-5463; b) S. R. Patrick, A. Gómez-Suárez, A. M. Z. Slawin and S. P. Nolan, *Organometallics*, 2014, **33**, 421-424.

173. F. Nahra, S. R. Patrick, A. Collado and S. P. Nolan, *Polyhedron*, 2014, **84**, 59-62.

174. N. Ibrahim, M. H. Vilhelmsen, M. Pernpointner, F. Rominger and A. S. K. Hashmi, *Organometallics*, 2013, **32**, 2576-2583.

175. S. K. Schneider, W. A. Herrmann and E. Herdtweck, *Z. Anorg. Allg. Chem.*, 2003, **629**, 2363-2370.

176. S. Dupuy and S. P. Nolan, *Chem. Eur. J.*, 2013, **19**, 14034-14038.

177. S. Dupuy, L. Crawford, M. Bühl and S. P. Nolan, *Chem. Eur. J.*, 2015, **21**, 3399-3408.

178. A. N. Nesmeyanov, E. G. Perevalova, Y. T. Struchkov, M. Y. Antipin, K. I. Grandberg and V. P. Dyadhenko, *J. Organomet. Chem.*, 1980, **201**, 343-349.

179. A. Kolb, P. Bissinger and H. Schmidbauer, *Inorg. Chem.*, 1993, **32**, 5132-5135.

180. S. Gaillard, J. Bosson, R. S. Ramón, P. Nun, A. M. Z. Slawin and S. P. Nolan, *Chem. Eur. J.*, 2010, **16**, 13729-13740.

181. R. M. P. Veenboer, A. Collado, S. Dupuy, T. Lebl, L. Falivene, L. Cavallo, D. B. Cordes, A. M. Z. Slawin, C. S. J. Cazin and S. P. Nolan, *Organometallics*, 2017, **36**, 2861-2869.

182. R. S. Ramón, S. Gaillard, A. Poater, L. Cavallo, A. M. Z. Slawin and S. P. Nolan, *Chem. Eur. J.*, 2011, **17**, 1238-1246.

183. A. Gómez-Suárez, Y. Oonishi, S. Meiries and S. P. Nolan, *Organometallics*, 2013, **32**, 1106-1111.

184. Y. Tang and B. Yu, *RSC Adv.*, 2012, **2**, 12686-12689.

185. G. C. Bond, P. A. Sermon, G. Webb, D. A. Buchanan and P. B. Wells, *J. Chem. Soc., Chem. Commun.*, 1973, 444b-445.

186. M. Okumura, S. Nakamura, S. Tsubota, T. Nakamura, M. Azuma and M. Haruta, *Catal. Lett.*, 1998, **51**, 53-58.

187. B. Nkosi, M. D. Adams, N. J. Coville and G. J. Hutchings, *J. Catal.*, 1991, **128**, 378-386.

188. Y. Ito, M. Sawamura and T. Hayashi, *J. Am. Chem. Soc.*, 1986, **108**, 6405-6406.

189. A. S. K. Hashmi, *Catal. Today*, 2007, **122**, 211-214.

190. a) D. Aguilar, M. Contel, R. Navarro and E. P. Urriolabeitia, *Organometallics*, 2007, **26**, 4604-4611; b) B. Jacques, D. Hueber, S. Hameury, P. Braunstein, P. Pale, A. Blanc and P. de Frémont, *Organometallics*, 2014, **33**, 2326-2335; c) E. Tomás-Mendivil, P. Y. Toullec, J. Borge, S. Conejero, V. Michelet and V. Cadierno, *ACS Catal.*, 2013, **3**, 3086-3098.

191. L. Zhang, *J. Am. Chem. Soc.*, 2005, **127**, 16804-16805.

192. G. Zhang, V. J. Catalano and L. Zhang, *J. Am. Chem. Soc.*, 2007, **129**, 11358-11359.

193. A. S. K. Hashmi and G. J. Hutchings, *Angew. Chem., Int. Ed.*, 2006, **45**, 7896-7936.

194. D. Wang, R. Cai, S. Sharma, J. Jirak, S. K. Thummanapelli, N. G. Akhmedov, H. Zhang, X. Liu, J. L. Petersen and X. Shi, *J. Am. Chem. Soc.*, 2012, **134**, 9012-9019.

195. G. Zhang, Y. Peng, L. Cui and L. Zhang, *Angew. Chem., Int. Ed.*, 2009, **48**, 3112-3115.

196. S. T. Staben, J. J. Kennedy-Smith and F. D. Toste, *Angew. Chem., Int. Ed.*, 2004, **43**, 5350-5352.

197. N. W. Reich, C.-G. Yang, Z. Shi and C. He, *Synlett*, 2006, **2006**, 1278-1280.

198. A. Homs, I. Escofet and A. M. Echavarren, *Org. Lett.*, 2013, **15**, 5782-5785.

199. Y. Zhu, C. S. Day, L. Zhang, K. J. Hauser and A. C. Jones, *Chem. Eur. J.*, 2013, **19**, 12264-12271.

200. F. Schröder, C. Tugny, E. Salanouve, H. Clavier, L. Giordano, D. Moraleda, Y. Gimbert, V. Mouriès-Mansuy, J.-P. Goddard and L. Fensterbank, *Organometallics*, 2014, **33**, 4051-4056.

201. A. Guérinot, W. Fang, M. Sircoglou, C. Bour, S. Bezzenine-Lafollée and V. Gandon, *Angew. Chem., Int. Ed.*, 2013, **52**, 5848-5852.

202. W. Fang, M. Presset, A. Guérinot, C. Bour, S. Bezzenine-Lafollée and V. Gandon, *Chem. Eur. J.*, 2014, **20**, 5439-5446.

203. M. Jia and M. Bandini, *ACS Catal.*, 2015, **5**, 1638-1652.

204. a) D. Zuccaccia, L. Belpassi, F. Tarantelli and A. Macchioni, *J. Am. Chem. Soc.*, 2009, **131**, 3170-3171; b) D. Zuccaccia, L. Belpassi, A. Macchioni and F. Tarantelli, *Eur. J. Inorg. Chem.*, 2013, **2013**, 4121-4135.

205. P. W. Davies and N. Martin, *Org. Lett.*, 2009, **11**, 2293-2296.

206. a) A. Gómez-Suárez and S. P. Nolan, *Angew. Chem., Int. Ed.*, 2012, **51**, 8156-8159; b) A. S. K. Hashmi, *Acc. Chem. Res.*, 2014, **47**, 864-876.

207. a) Y. Oonishi, A. Gómez-Suárez, A. R. Martin and S. P. Nolan, *Angew. Chem., Int. Ed.*, 2013, **52**, 9767-9771; b) Y. Odabachian, X. F. Le Goff and F. Gagosz, *Chem. Eur. J.*, 2009, **15**, 8966-8970.

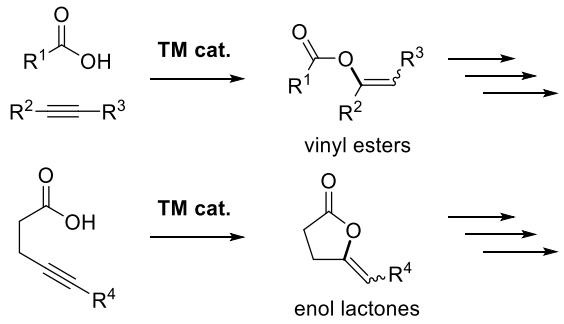
208. A. Zhdanko and M. E. Maier, *Chem. Eur. J.*, 2014, **20**, 1918-1930.

209. M. M. Hansmann, M. Rudolph, F. Rominger and A. S. K. Hashmi, *Angew. Chem., Int. Ed.*, 2013, **52**, 2593-2598.

2. Hydrocarboxylation of alkynes catalysed by dinuclear Au(I)-NHC complexes

2.1. Introduction

The transition metal catalysed hydrocarboxylation of alkynes, *e.g.* the inter- or intramolecular addition of widely available carboxylic acids[1] to alkynes, represents an efficient route to access vinyl esters and enol lactones (Scheme 2.1).[2] These substrates are highly versatile building blocks in organic synthesis,[3] widely used industrially in polymerization processes,[4] and valuable reagents in a variety of synthetic transformations.[5]

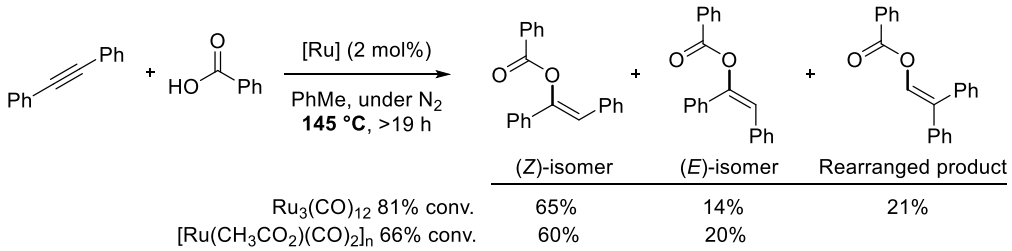


Scheme 2.1. General scheme for the TM-catalysed hydrocarboxylation of alkynes to vinyl esters, lactones, and further derivatisation.

Examples of intermolecular addition of carboxylic acids into alkynes catalysed by metal catalysts have been reported to date, with ruthenium,[6] and palladium[7] being the most commonly encountered. These reports describe the activation of the multiple bond by Lewis acids followed by outer-sphere addition of carboxylate ions,[6a] with few exceptions.[6b] Addition into unactivated internal alkynes has been shown to be more challenging than into terminal alkynes; some catalysts that are active with the latter are completely ineffective with internal alkynes,[8] and those which are able to operate have a limited scope[7b,9] or require harsh reaction conditions, such as high temperature and high catalyst loadings.[6b,6d]

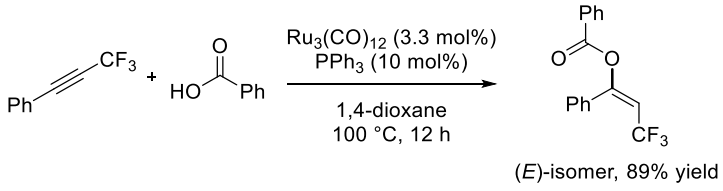
Of note, Shvo, Rotem and co-workers studied extensively the ruthenium-catalysed hydrocarboxylation of alkynes, and in 1983 reported examples of aromatic and aliphatic carboxylic acid addition to internal alkynes (Scheme 2.2).[6b-c] The reaction was performed

in the presence of dodecacarbonylruthenium(0), $Ru_3(CO)_{12}$, or polymeric ruthenium complexes bearing bridging carboxylate ligands, $[Ru(CH_3CO_2)(CO)_2]_n$. This reaction needed high temperatures, 145 °C, to proceed to conversion. Moreover, this method suffered of low stereoselectivity depending on the alkyne and/or acid used; for example, when diphenylacetylene was reacted with benzoic acid, a mixture of (*Z*)- and (*E*)-vinyl benzoates were formed in 4.5:1 and 3:1 ratios when $Ru_3(CO)_{12}$ or $[Ru(CH_3CO_2)(CO)_2]_n$ were used, respectively. The isomeric ratio was reversed when acetic acid was used. Interestingly, a third product was observed, a rearranged vinylbenzoate isomer. It was suggested that this product originated from dissociation of a C-O bond in a vinyl-Ru intermediate, forming a benzylic carbocation, which underwent subsequent rearrangement by 1,2-migration of a phenyl group.[6b] The amount of rearranged vinyl ester was higher when using more acidic carboxylic acid substrates, consistent with enhanced proclivity of the carboxylate to undergo dissociation from the vinyl-Ru intermediate.



Scheme 2.2. Shvo and Rotem's hydrocarboxylation of internal alkynes catalysed by Ru complexes.[6c]

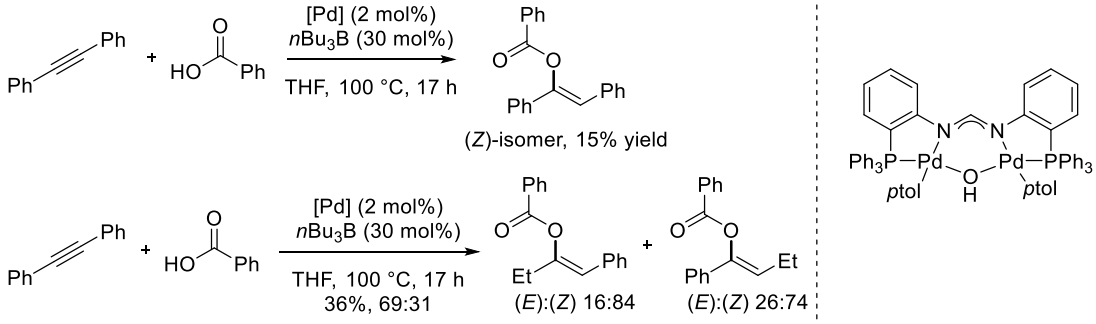
Another interesting example of intermolecular addition to internal alkynes was reported by Kawatsura and Itoh (Scheme 2.3);[6f] the authors used catalytic amounts of $Ru_3(CO)_{12}$ and PPh_3 and succeeded in obtaining the trifluoromethyl group substituted enol esters with high regioselectivity and complete stereoselectivity for the (*E*)-product.



Scheme 2.3. Carboxylic acid addition to trifluoromethyl substituted internal alkynes.[6f]

Tsukada reported in 2011 that hydrocarboxylation of internal alkynes, catalysed by a dinuclear palladium complex with a bridging *N,N'*-bis[2-(diphenylphosphino)phenyl]amidinate (dpfam) ligand (Scheme 2.4),[7a] allowed the

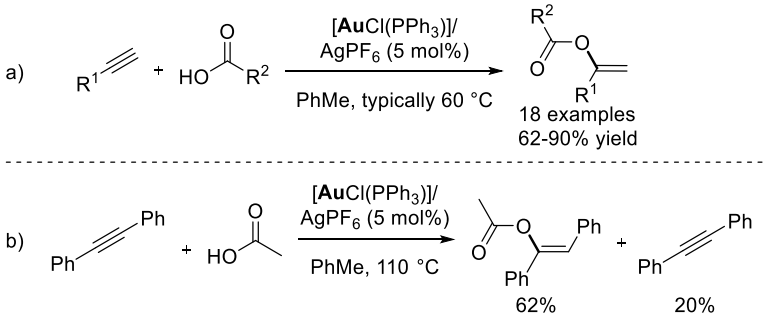
reaction scope to be expanded to unsymmetrical internal alkynes, however with low regioselectivity and low yield of a mixture of (*E*) and (*Z*)-isomers.



Scheme 2.4. Dinuclear Pd-OH catalysed hydrocarboxylation of symmetrical and unsymmetrical internal alkynes.[7a]

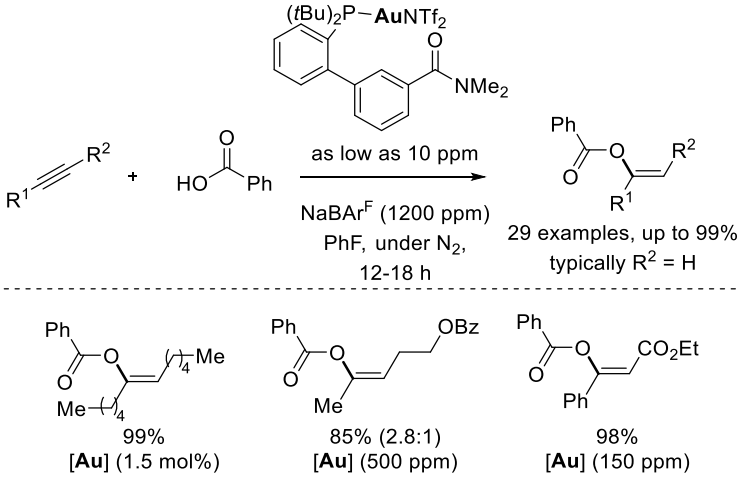
With its high affinity for π-systems, gold(I) cations have been shown to be uniquely effective in the addition of nucleophiles to unsaturated systems such as alkynes or allenes. Examples of the intermolecular addition of carboxylic acids to alkynes catalysed by gold(I) remain scarce; Schimdbaur and co-workers, while exploring the hydration of alkynes, could detect traces of 3-hexene 3-acetate (6.2%) by reacting acetic acid with 3-hexyne in tetrahydrofuran at 60 °C using (triphenylphosphine)gold(I) pentafluoropropionate, [Au(OC(O)C_6F_5)(PPh_3)] (0.134 mol%), and boron trifluoride etherate co-catalyst (5.25 mol%).[10] However, adventitious traces of H_2O preferentially add to the aliphatic alkyne under their reaction conditions, leading to the ketone 3-hexanone.

In 2010, Chary *et al*. reported the hydrocarboxylation of alkynes using 5 mol% of [AuCl(PPh_3)]/$AgPF_6$ (Scheme 2.5).[11] This methodology was applied to various terminal alkynes but was only demonstrated with four internal alkynes, with incomplete conversion and moderate yield of vinyl ester when using diphenylacetylene.



Scheme 2.5. Chary's hydrocarboxylation of internal alkynes;[11] a) general reaction scheme; b) reaction with diphenylacetylene and acetic acid.

Zhang and co-workers described a ligand-directed nucleophilic addition to gold-activated terminal alkynes (Scheme 2.6).[12] The use of tailored ancillary phosphine ligand allowed efficient reactions with high TONs and catalyst loadings as low as 10 ppm, however the reaction required an inert atmosphere. The addition to internal alkynes, although effective, was demonstrated with only three substrates.

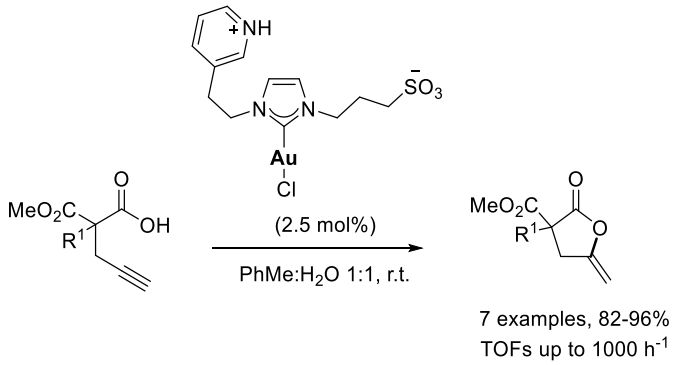


Scheme 2.6. Zhang and co-worker's strategy for efficient gold-catalysed hydrocarboxylation of alkynes; highlight of the three examples with internal alkynes.[12]

These reports clearly showed the need to find a suitable methodology to afford a general procedure for an intermolecular hydrocarboxylation of internal alkynes. In line with Zhang's work, highly efficient catalysts have to be found. Furthermore, regioselectivity and stereoselectivity must be controlled to provide highly valuable products.

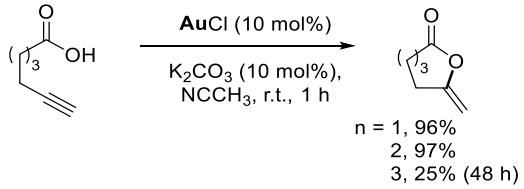
Compared to the intermolecular reaction, numerous reports have described the cyclisation of alkynoic acids to give enol lactones; efficient approaches that rely on the use of a transition-metal catalysts such as Pd,[13] Rh,[14] Hg,[15] Cu,[16] Ag[17] complexes are known. Among others, Au(I)- or Au(III)-catalysed cyclisation reactions have proven highly effective;[13a, 18] however, gold-based systems still show some drawbacks: i) the use of high catalyst loading; ii) the need of additives, such as co-catalysts and bases in stoichiometric or catalytic quantities, iii) the lack of regio- and stereocontrol, with competitive *exo*- and *endo*-cyclisation.

Noteworthy, among the best results are reported by Conejero, Michelet and Cadierno who used water soluble Au(I) and Au(III) NHC complexes. These species were able to catalyse the cyclisation of alkynoic acids in high yield and high TOF, however the system was only shown to be suitable for the cyclisation of γ-alkylidene lactones (Scheme 2.7).[18e]



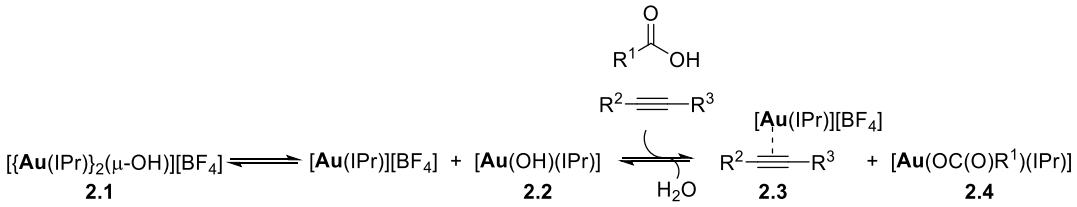
Scheme 2.7. Water soluble Au(I) NHC catalysed cyclisation of alkynoic acids.[18e]

Moreover, while the synthesis of γ- and δ-lactones is well documented, the synthesis of ε-lactones through cyclisation reactions still remained scarce.[13h,19] Among the few methods which report the synthesis of these lactones, the best result was achieved with gold salts, as reported by Pale and co-workers.[18g] In this example, 10 mol% of AuCl and a catalytic amount of K_2CO_3 was used to enable the cyclisation of alkynoic acids (Scheme 2.8). The synthesis of caprolactone (n = 3) was achieved in 25% yield, only after a prolonged reaction time (48 h).



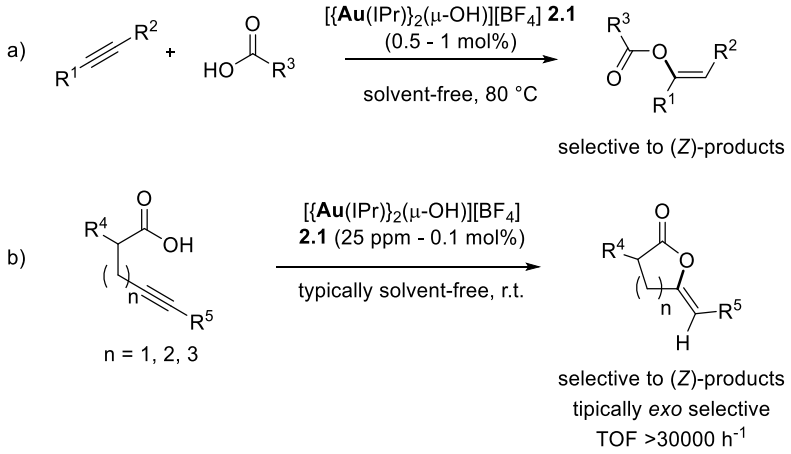
Scheme 2.8. Cyclisation of alkynoic acids by AuCl and K_2CO_3 reported by Pale and co-workers.[18g]

With the aim of improving and developing straightforward and atom-economical synthetic methodologies, the use of [{Au(IPr)}$_2$(μ-OH)][BF_4] (**2.1**),[20] a dinuclear complex bearing an NHC ligand (section 1.5.2), was envisioned to accomplish the inter- and intramolecular addition of carboxylic acids to alkynes. The catalyst had already been found to be effective for the hydrophenoxylation of alkynes,[21] demonstrating the suitability of the bifunctional gold system for the addition of oxygen nucleophiles to alkynes. The catalyst can dissociate into a Lewis acid, [Au(IPr)][BF_4],[22] and Brønsted base, [Au(OH)(IPr)][23] (**2.2**), which are proposed to activate the electrophile and pro-nucleophile, respectively (Scheme 2.9). Specifically, it can be envisioned that formation of π-alkyne-Au(I) (**2.3**) and carboxylate-Au(I) complex (**2.4**) can be used to initiate the catalytic cycle.



Scheme 2.9. Dissociation of dinuclear complex **2.1** and activation of carboxylic acid and alkyne.

To the best of our knowledge, at the time of this study no report of a highly efficient and broadly applicable hydrocarboxylation of internal alkynes using Au(I) NHC catalysts was available. Thus, the process was explored with the use of dinuclear catalyst **2.1**. The reaction conditions were studied to fulfill some basic principles of green chemistry, such as low catalyst loading, atom-economical procedure with a practical work-up. The inter- and intramolecular hydrocarboxylation of internal and terminal alkynes was targeted, in which reaction conditions were varied to optimise for high yield, regioselectivity and stereoselectivity (Scheme 2.10). These strategies proved successful and the results are presented herein.



Scheme 2.10. General scheme for the a) inter- and b) intramolecular hydrocarboxylation of alkynes catalysed by dinuclear gold complex **2.1**.

2.2. Intermolecular gold(I)-catalysed hydrocarboxylation of internal alkynes

2.2.1. First findings: reaction optimisation

Regarding the intermolecular hydrocarboxylation of alkynes, initial screenings were performed by reacting selected model substrates, such as diphenylacetylene (**2.5**) and

bulky 2,6-dimethoxybenzoic acid (**2.6**). The addition of acid to internal alkyne in a 1:1.1 ratio, at 85 °C in PhMe (1 M) in the presence of 2 mol% of [{Au(IPr)}$_2$(μ-OH)][BF$_4$] **2.1** gave complete conversion to (*Z*)-vinyl ester **2.7** as a single stereoisomer, after 16 h (Figure 2.1). Various gold catalysts were examined; dinuclear catalyst bearing a saturated NHC ligand, [{Au(SIPr)}$_2$(μ-OH)][BF$_4$] (**2.8**)[24] performed poorly giving only 34% conversion after the same reaction time. [Au(OH)(IPr)] **2.2** (4 mol%) showed 40% conversion after 16 h.

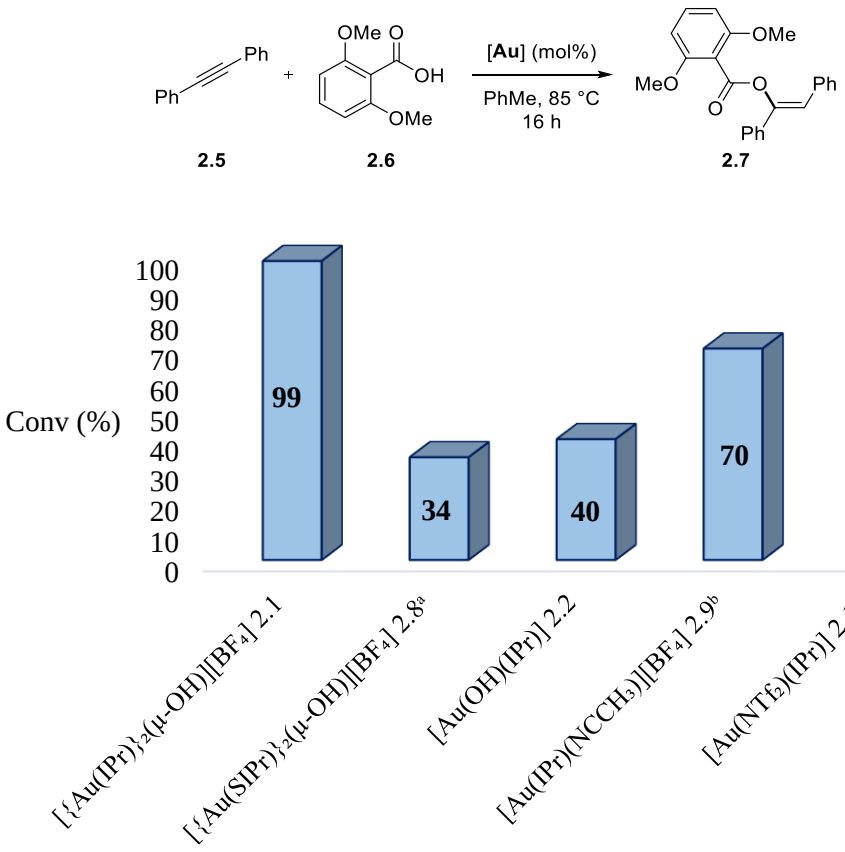
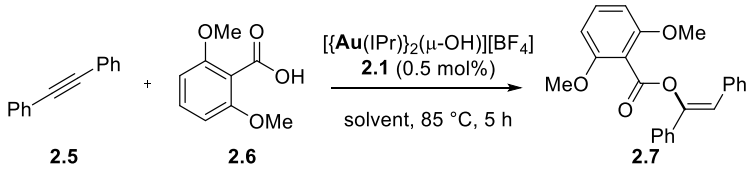


Figure 2.1. Catalyst optimisation. Reaction conditions: **2.5** (0.55 mmol), **2.6** (0.5 mmol), [Au] (2 mol% dinuclear complexes, 4 mol% mononuclear complexes), PhMe (1 M), 85 °C, 16 h, conversion determined by GC (%); [a] 24 h; [b] 15% of alkyne hydration. Initial optimisation studies were performed by Dr. Stephanie Dupuy.

High conversion, 70%, was obtained using [Au(IPr)(NCCH$_3$)][BF$_4$] (**2.9**),[25] although longer reaction times were required and the desired vinyl ester was formed along with 15% of a ketone side-product from the hydration of **2.5** (Figure 2.1). Cationic Gagosz complex [Au(NTf$_2$)(IPr)][26] (**2.10**) alone failed to catalyze the hydrocarboxylation of **2.5**.

These results showed that the best catalyst for this transformation was dinuclear catalyst **2.1**.

The solvent was found to have a large influence on the outcome of the reaction (Figure 2.2). When the catalyst loading of **2.1** was lowered to 0.5 mol%, and the reaction performed in PhMe, a dramatic decrease in conversion was observed (18%). The reaction did not show significant conversion when performed in 1,4-dioxane (4%), whilst no conversion was observed in $NCCH_3$, DMF and THF. Low conversions were also observed with chlorinated solvents, *e.g.* with 1,2-DCE (23%). Finally, the best results were obtained under solvent-free conditions, with full conversion after 5 h. When the reaction was performed with a 1:1 alkyne to acid ratio (**2.5**:**2.6**) at 80 °C, 75% conversion could still be obtained after 5 h. After 10 h the reaction was complete affording (*Z*)-vinyl ester **2.7** in 93% yield without traces of hydration side-product.



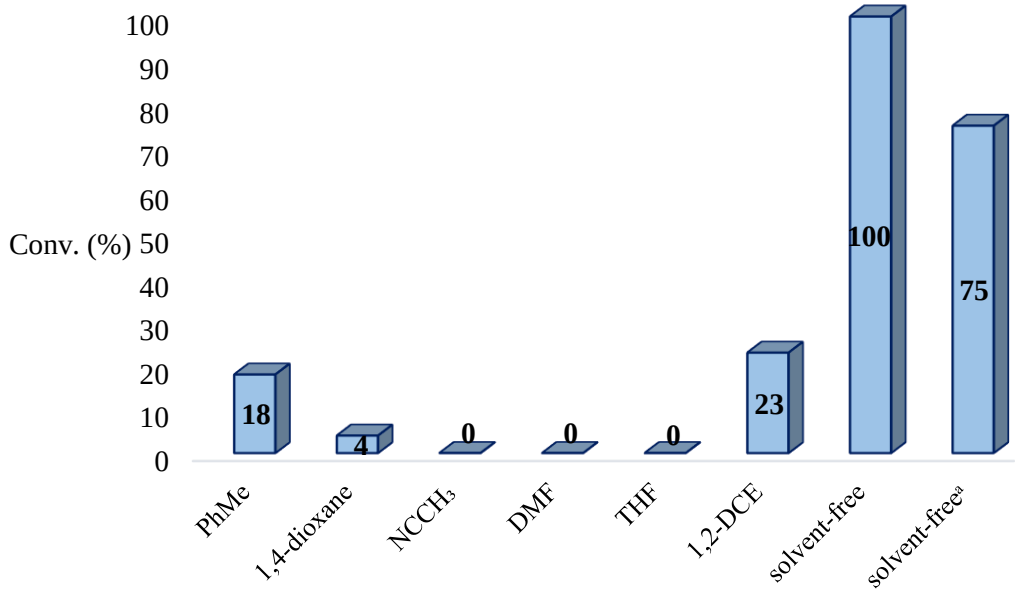
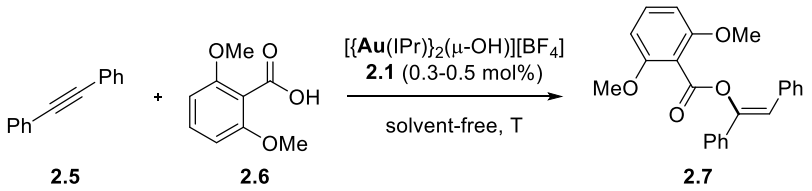


Figure 2.2. Solvent optimisation. Reaction conditions: **2.5** (0.65 mmol), **2.6** (0.5 mmol), **2.1** (0.5 mol%), solvent (1 M) or solvent-free, 85 °C, 1h, conversions determined by GC (%); [a] **2.5** (0.5 mmol), 80 °C.

Finally, variation of reaction temperature and catalyst loading was invesigated (Figure 2.3). Reducing the temperature to 60 °C significantly lowered the yield; 30% and 20%

conversions were observed when 0.5 or 0.3 mol% of **2.1** were used. When the reaction was performed at 80 °C, with a decreased catalyst loading of 0.3 mol%, the product was formed in 60% conversion, providing lower conversion to that observed using 0.5 mol% catalyst loading after the same reaction time (75%). The importance of a dinuclear catalyst was confirmed: by reacting a mixture of [Au(OH)(IPr)] **2.2** and [Au(IPr)(NCCH$_3$)][BF$_4$] **2.9** (total amount of 1 mol%) was found to fully convert the starting materials after 16 h, similarly to the reaction performed with digold hydroxide **2.1** (0.5 mol%) after 5 h.



2.5 **2.6** **2.7**

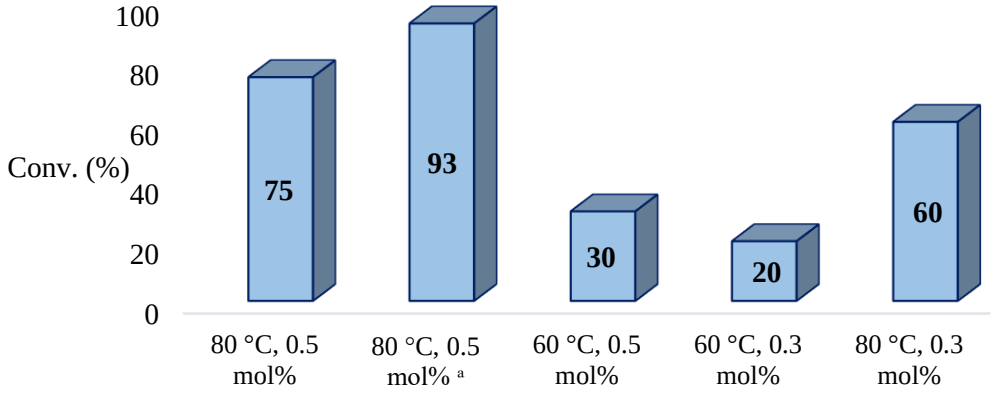


Figure 2.3. Temperature and catalyst loading optimisation. Reaction conditions: **2.5** (0.5 mmol), **2.6** (0.5 mmol), **2.1** (0.3-0.5 mol%), solvent-free, 5 h, T (60-80 °C), conversion determined by GC (%); [a] **2.2** (0.5 mol%) + **2.9** (0.5 mol%), 16 h.

To reduce the environmental impact and to ensure full conversion of starting materials, the reaction was carried out under solvent-free conditions. The catalyst loading was kept at 0.5 mol%. Moreover, the alkyne to acid ratio was kept to 1:1, to allow for a very simple and economical work-up procedure; indeed, just by adding pentane to the crude mixture and by filtering through a short plug of MgSO$_4$, the pure vinyl esters could be isolated. Purification by column chromatography was not needed for this process. The reaction was robust and could be performed in air.

2.2.2. Results and discussion of the intermolecular hydrocarboxylation of alkynes

With the optimal conditions in hand, the scope of the reaction was explored. The methodology was found to be broadly applicable to carboxylic acids and diphenylacetylene **2.5** (Figure 2.4). A diverse range of (*Z*)-diphenylvinyl benzoates could be synthesised with complete stereoselectivity of the alkene, in good to excellent yields. Benzoic acid could be reacted with the alkyne, to yield product **2.11** in 94%. Electron-rich benzoic acids were reactive for this transformation; tertiary amines in the *ortho*-position or methoxy group in the *para*-position to the aryl ring yielded products **2.12** and **2.13** in 93% and 90%. Moreover, electron-rich *ortho*-disubstituted benzoic acid reacted smoothly to yield **2.14** in 97% after 15 h. Halide substituents, F and Br, were well tolerated; 4-bromobenzoate **2.15** was obtained pure in 90% yield. *Ortho*-substituted fluoro and bromo esters **2.16** and **2.17** were isolated in 94% and 90% yield, respectively, with a lower reaction time required for **2.17**. The same effect was observed when 3-bromobenzoic acid was reacted with diphenylacetylene **2.5**, with full conversions into **2.18** after 10 h. Nitro-substituted benzoic acids afforded **2.19** and **2.20**, with > 99% and 74% yield. The reaction time for the latter could be reduced to even lower time, and the reaction fully converted after 5 h. Pleasingly, heteroaryl carboxylic acids such as 2-picolinic acid and furoic acid led to isolation of vinyl esters **2.21** and **2.22** in good yield. A slight increase of temperature to 110 °C was needed when 2-picolinic acid was used to ensure full conversion of the starting materials to vinyl ester **2.22**.

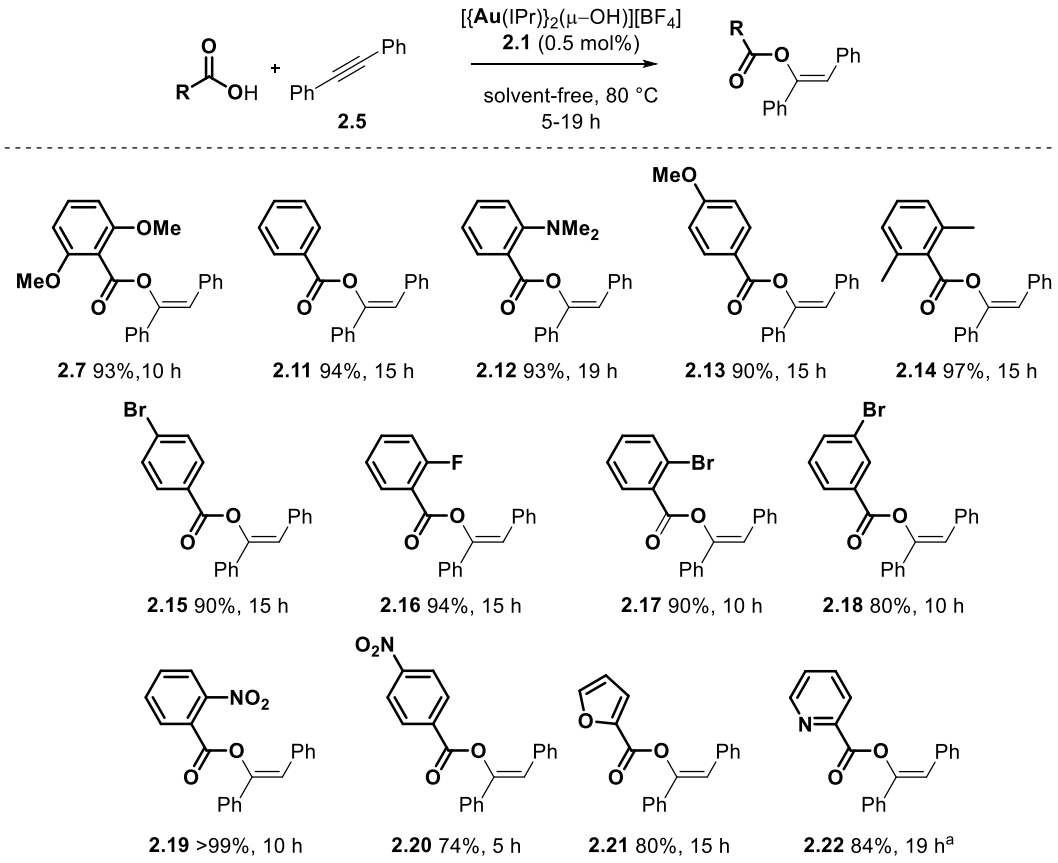


Figure 2.4. Scope of the reaction with substituted benzoic acids. Reaction conditions: **2.5** (0.5 mmol), carboxylic acid (0.5 mmol), **2.1** (0.5 mol%), 80 °C, solvent-free, 5-19 h; Isolated yield, average of two runs; [a] 110 °C.

A current limitation of the method was that the use of 3-picolinic acid provided no conversion to the desired product, despite increasing the reaction temperature and the catalyst loading.

The methodology could be extended to vinyl carboxylic acids (Figure 2.5), such as acrylic acid and cinnamic acid, providing access to **2.23** and **2.24**, in short reaction times (5 h), and with excellent yields (94-95%). The reaction showed complete chemoselectivity, which is notable considering the fact that acrylic acid is known to undergo polymerization very easily.[4] The reaction was applied to several aliphatic carboxylic acids; by reacting formic acid with diphenylacetylene **2.5** the product **2.25** formed much faster, most likely due to its enhanced nucleophilicity. Product **2.25** was obtained without any loss of stereoselectivity and in 80% after 2 h. Acetic acid reacted promptly with **2.5** on a 10 mmol scale (1.78 g of **2.5**), to yield 2.19 g of vinyl acetate **2.26** in 92% isolated yield after 4 h. Compound **2.26** was not found to polymerise to polyvinyl acetate under the optimised

conditions, demonstrating the robustness of the process. Noteworthy, this method provides an improvement on the existing procedure, where vinyl acetate was obtained in only 62% yield.[11] Pivalic acid was subjected to the reaction conditions with 80% yield to **2.27** after 16 h. Other functional groups were tolerated for aliphatic acids, with levulinic acid reacting to provide **2.28** in 89% isolated yield. The use of trifluoroacetic acid did not provide the desired vinyl ester, instead giving a complex mixture of compounds.

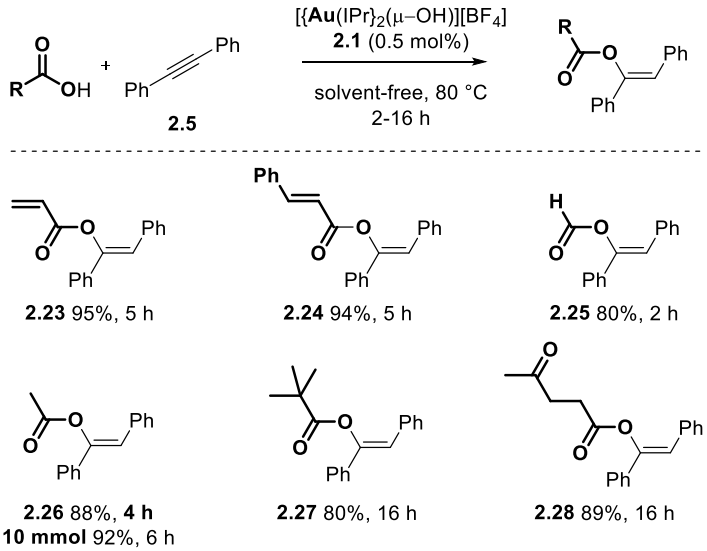


Figure 2.5. Variation on carboxylic acids. Reaction conditions: **2.5** (0.5 mmol), carboxylic acid (0.5 mmol), **2.1** (0.5 mol%), 80 °C, solvent-free, 2-16 h; isolated yield, average of two runs.

Encouraged by these results, the reactivity of both symmetrical and unsymmetrical alkynes with benzoic acid was examined (Figure 2.6). Under the optimised conditions, both 4-octyne and DMAD were successfully converted, again with complete stereoselectivity, to the corresponding **2.29** and **2.30** in high yields. Good to complete regioselectivity was observed using unsymmetrical alkynes, with the addition of the carboxylic acid occurring at the most electrophilic carbon of the triple bond in each case. Remarkably, the reactions of both phenylpropyne and 1,3-diphenyl-1-propyne afforded the vinyl esters **2.31** and **2.32** in 99% and 86% yield with complete regio- and stereoselectivity. Benzyl-2-butynyl ether was fully converted into **2.33** in > 99% isolated yield after 19 h. Ethyl phenylpropiolate reacted promptly with benzoic acid to **2.34** after 6 h, with complete regioselectivity. Diaryl-substituted alkyne underwent hydrocarboxylation to **2.35** with good regioselectivity in 8.5 h. Complete chemoselectivity was obtained when using an enyne substrate, with good regioselective addition (4:1), with full conversion into vinyl ester **2.36** in high yield.

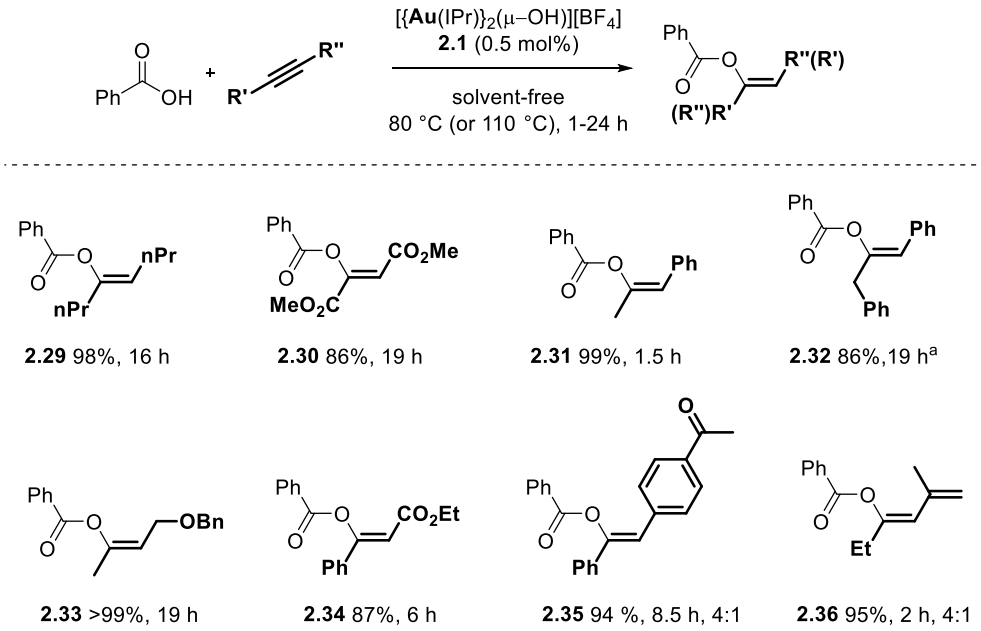


Figure 2.6. Scope of the reaction with unsymmetrically substituted alkynes. Reaction conditions: internal alkyne (0.5 mmol), benzoic acid (0.5 mmol), **2.1** (0.5 mol%), 80 °C, solvent-free, 1.5-19 h; isolated yield, average of two runs; [a] 1 mol%.

Limitations of this method included internal alkynes bearing *ortho* substituents on the aryl ring (Figure 2.7), with no conversion into product observed in any example when using benzoic acid. The steric congestion around the triple bond might impede the reaction by preventing coordination to the gold catalyst. Unsymmetrical alkynes bearing a substituent (-Cl, -OMe, -BPin) in the *para*-position of one of the aryl groups were also found to not undergo conversion into product. Moreover, heteroaryl internal alkynes (pyridine or thiophene) did not react under the optimised reaction conditions, probably due to poisonous binding of the gold catalyst to the N- or S- atoms.

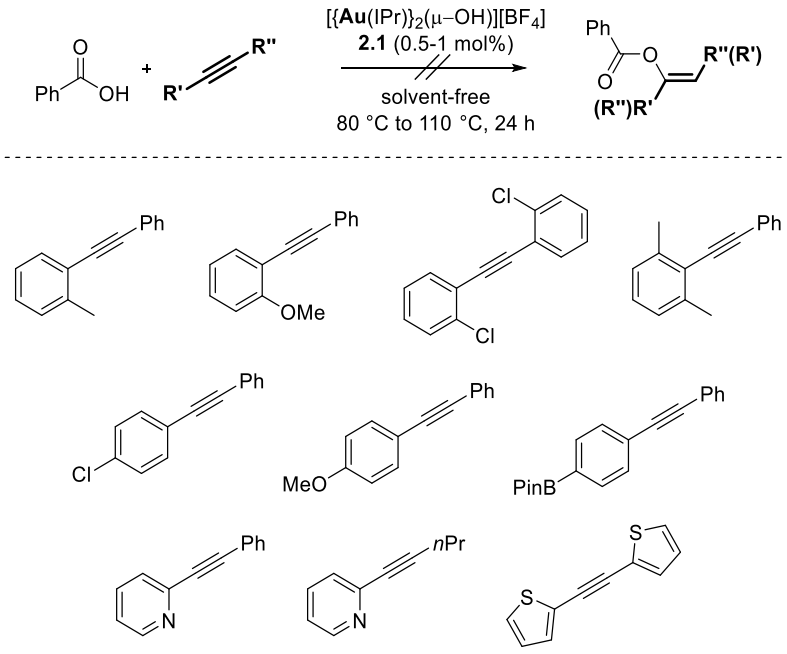
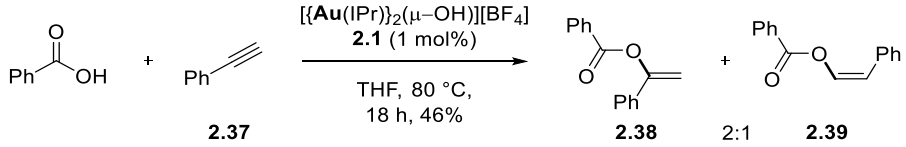


Figure 2.7. Limitations of the process: unreactive alkyne substrates. Reaction conditions: internal alkyne (0.5 mmol), benzoic acid (0.5 mmol), **2.1** (1 mol%), 80 °C or 110 °C, solvent-free, 24 h.

It is worth mentioning the results obtained for terminal alkynes (Scheme 2.11); by reacting phenylacetylene **2.37** with benzoic acid, no conversion was observed after 18 h under the optimised reaction conditions. By increasing the catalyst loading to 1 mol% and conducting the reaction in THF (1 M) at 80 °C, partial conversion into the Markovnikov **2.38** and anti-Markovnikov **2.39** products were obtained (2:1 ratio, 46% isolated yield). However, with other solvents such as PhMe, CH_2Cl_2 or $NCCH_3$, only trace conversion was found. In addition, the use of [Au(OH)(IPr)] **2.2** also failed to catalyse the reaction under the optimised reaction conditions.



Scheme 2.11. Hydrocarboxylation of phenylacetylene using benzoic acid to give **2.38** and **2.39**. Reaction conditions: **2.37** (0.5 mmol), benzoic acid (0.5 mmol), **2.1** (1 mol%), THF (1 M), 80 °C, 18 h.

Finally, the recyclability of the catalyst was assessed (Figure 2.8). Formic acid and diphenylacetylene **2.5** (0.5 mmol of each) reacted rapidly in the presence of dinuclear gold complex **2.1** to afford vinyl ester **2.25**. Upon completion of the reaction, fresh starting materials were iteratively added in 0.5 mmol portions. Following this protocol,

6.5 mmol of **2.5** was converted to **2.25** using just 2.5 μmol of **2.1**, affording an unprecedented high TON of 2610.

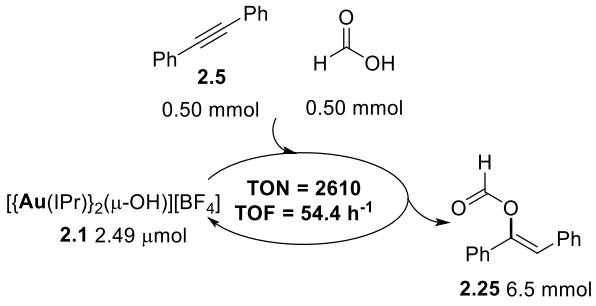


Figure 2.8. Recyclability experiment into the hydrocarboxylation of **2.5** using formic acid to give **2.25**. Reaction conditions: **2.5**, formic acid, **2.1** (0.5 mol%), 80 °C, solvent-free, 48 h.

2.3. Intramolecular cyclisation of alkynoic acids

2.3.1. Cyclisation of alkynoic acids: reaction optimisation

The study of intramolecular reactions was started by subjecting 4-pentynoic acid (**2.40**) to various Au(I)-NHC catalysts in PhMe (Figure 2.9). The reaction was performed at r.t. following previous literature reports.[18e,18g] Using 0.5 mol% catalyst loading of dinuclear gold complex **2.1**, 64% conversion into lactone **2.41** was observed by ^{1}H NMR spectroscopy after only 30 minutes. Other dinuclear complexes, bearing NHC ligands (SIPr and IPr^{Cl}), showed lower conversions to **2.41**. Using 1 mol% of the mononuclear gold complex [Au(OH)(IPr)]**2.2** (in order to provide the same metal loading) a conversion of 60% was observed after the same reaction time. Cyclisation occurred in both cases with complete *exo*-regioselectivity, whilst the formation of the *endo*-cyclised product (**2.42**), which is also favoured by Baldwin's rules,[27] was not observed. Alkynoic acid **2.40** was further reacted with catalysts **2.1** (0.2 mol%) or **2.2** (0.4 mol%) using solvent-free conditions, with complete cyclisation into lactone **2.41** achieved within 5 min. Under the same reaction conditions, cationic [Au(IPr)(NCCH$_3$)][BF$_4$] **2.9** gave 50% conversion.

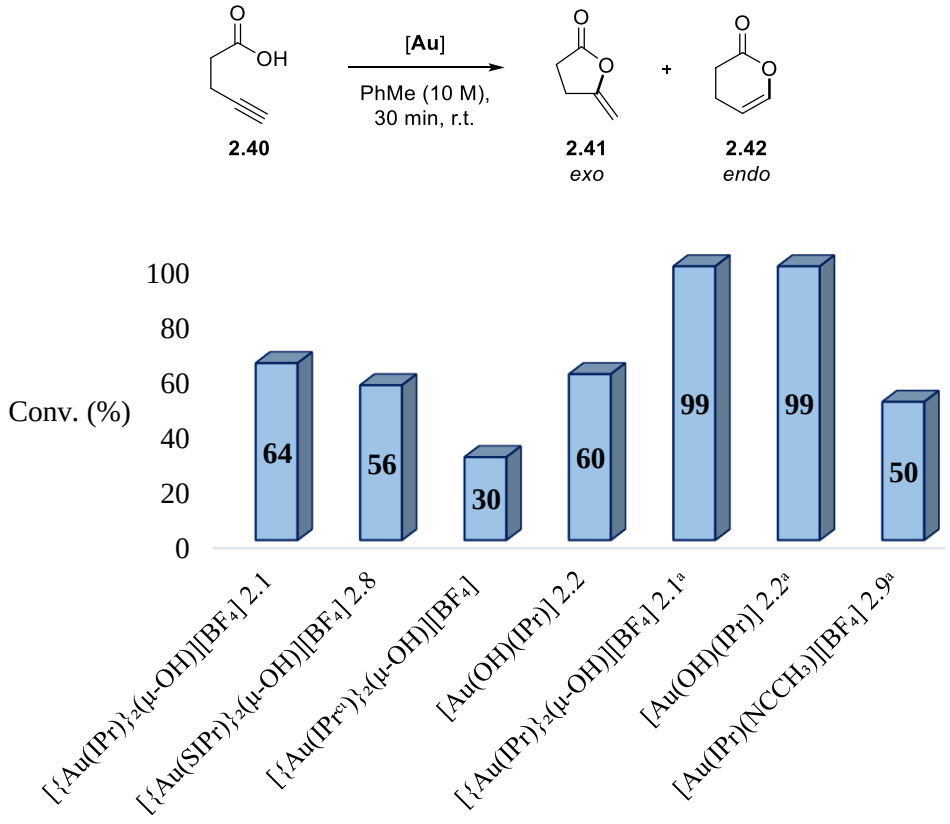


Figure 2.9. Catalyst optimisation. Reaction conditions: **2.40** (0.5 mmol), PhMe (10 M), r.t., [Au] (0.5-1 mol%), 30 min, conversions calculated by ^{1}H NMR spectroscopy, by using pivalaldehyde as internal standard (10 µL, 0.092 mmol); no traces of **2.42** were detected; [a] solvent-free, [Au] (0.2-0.4 mol%), 5 min. Initial tests performed by Dr. Stephanie Dupuy.

Further investigating the effect of solvent, solvent-free conditions provided the best conversion in the shortest time (Figure 2.10); other than PhMe, chlorinated solvents gave good conversions within 5 minutes, with the best result found with $CHCl_3$ up to 88%, however still not comparable with the solvent-free conditions (> 99%). THF provided very low conversions (18%).

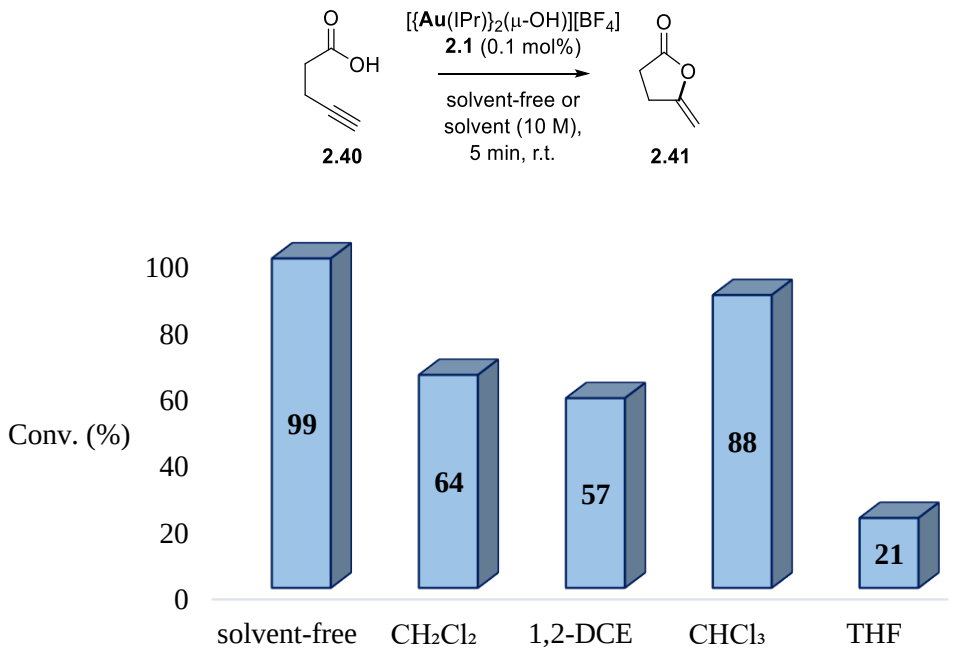


Figure 2.10. Solvent optimisation. Reaction conditions: **2.40** (0.5 mmol), r.t., solvent-free or solvent (10 M), **2.1** (0.1 mol%), 1 h, conversions calculated by ^{1}H NMR spectroscopy, by using pivalaldehyde as internal standard (10 μL, 0.092 mmol); no traces of **2.42** were detected.

Next variation of the gold pre-catalyst and catalyst loading was investigated. By reducing the catalyst loading of **2.2** to 0.2 mol%, full conversion of **2.40** was observed within 5 min (Figure 2.11). The Au(I) acetonyl complex, [Au($CH_2C(O)CH_3$)(IPr)] (**2.43**) (see chapter 6), was found to be a suitable pre-catalyst for the transformation; the alkynoic acid allowed for protonolysis of the pre-catalyst, which enabled full conversion at 0.2 mol% after 1 h. The Au(I)-chloride species [AuCl(IPr)] (**2.44**),[28] was suitable for the cyclisation of 4-pentynoic acid **2.40**, however lower conversion (76%) was obtained compared to dinuclear complex **2.1** and mononuclear neutral precursors **2.2** or **2.43**. Gold pre-catalysts **2.1**, **2.2** and **2.43** had proven to be highly efficient for this transformation, thus the catalyst loadings were decreased even further. Dinuclear complex **2.1**, provided > 99% formation of **2.41** after 1 h at 100 ppm loading, whilst mononuclear complex **2.2** (200 ppm) provided 78% after the same reaction time. In contrast, reducing the catalyst loading of complex **2.43** (100 ppm) gave only 12% conversion after 1 h. Pleasingly, with only 25 ppm (2.5×10^{-5} mol%) of **2.1**, full conversion into enol-lactone **2.41** was found within 1 h, providing an isolated yield of 92%. 5-Hexynoic acid **2.45** was next tested. Dinuclear gold complex **2.1** well performed to full conversion to δ-lactone **2.46** at just 0.1 mol% catalyst loading under solvent-free conditions within 1h. [Au(OH)(IPr)] **2.2**

provided **2.46** in 40% conversion after 1 h, again confirming dinuclear gold complex **2.1** as optimal for this transformation.

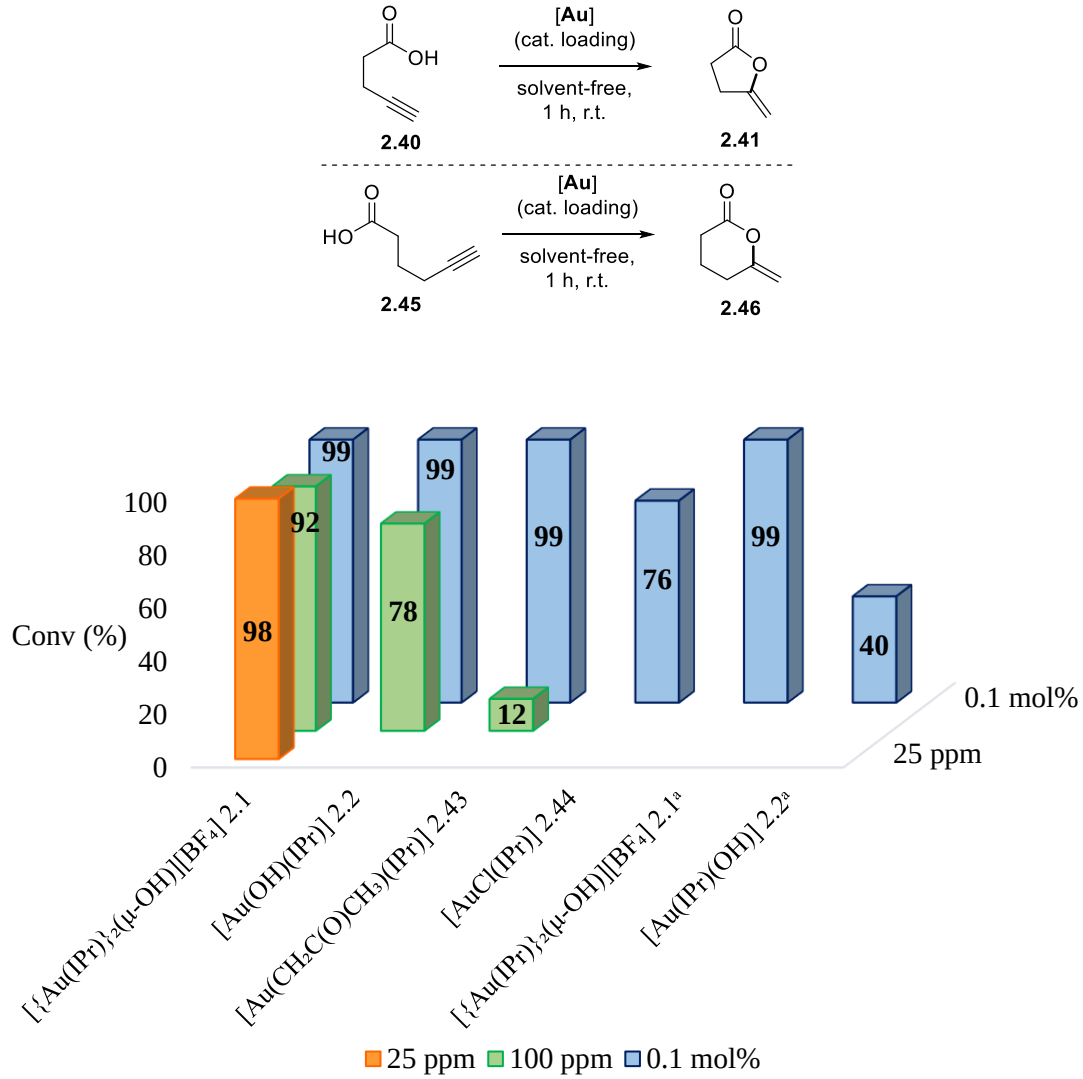


Figure 2.11. Variation of catalyst and catalyst loading. Reaction conditions: **2.40** (0.5 mmol), r.t., solvent-free, [Au] (25 ppm to 0.2 mol%), 1 h; [a] **2.45** (0.5 mmol), r.t., solvent-free, [Au] (0.1-0.2 mol%), 1 h; conversions calculated by ^{1}H NMR spectroscopy, by using pivalaldehyde as internal standard (10 μL, 0.092 mmol). Stock solutions in CH_2Cl_2 were prepared for 100 ppm, 200 ppm and 25 ppm from 0.1 mol% ($0.25\cdot10^{-3}$ M) of **2.1**, 0.2 mol% ($0.5\cdot10^{-3}$ M) of **2.2** and 0.2 mol% ($0.5\cdot10^{-3}$ M) of **2.43**.

Having found the best conditions for 4-pentynoic acid and 5-hexynoic acid cyclisation (solvent-free, **2.1** dinuclear catalyst at low catalyst loadings), the cyclisation of 6-heptynoic acid **2.47** was explored (Figure 2.12). Reacting the alkynoic acid **2.47** under the optimised conditions, using a higher catalyst loading of **2.1** (0.5 mol%), cyclisation to give **2.48** occurred, but only at low conversion (18%). The formation of unidentified products was found by ^{1}H NMR spectroscopy, tentatively assigned as dimers or

oligomers (top orange blocks in the figure), the formation of which would be entropically favoured at high concentration in the absence of solvent. Increasing the temperature to 65 °C while performing the reaction in sealed vessels did not lead to any improvement, both in terms of conversion and quantity of undesired products. The reaction was next performed in a range of solvents, in the hope of favouring the intramolecular pathway over the polymerisation pathway. The first trial was performed in PhMe (0.5 M) which proved successful for the cyclisation of γ-alkynoic acids; however, in this case the reaction did not proceed, and the starting material was recovered. By using ethereal solvents, such as cyclopentylmethylether (CPME) (0.1 M), 36% conversion into caprolactone **2.48** was observed, but unwanted products were still present in the crude mixture. Similar results were obtained by using 1,2-DCE (0.25 M) with full consumption of **2.47**, but low conversion into product (45%). THF (0.25 M) was found not suitable for this transformation with similar results to the use of solvent-free conditions. Upon increasing the reaction temperature to 80 °C in CPME or 1,2-DCE (0.25 M) the highest conversions to **2.48** were observed (55% and 78%, respectively), while side-products were still obtained.

Pleasingly, a clean conversion (39%) of **2.47** into the ε-lactone **2.48** could be achieved in CH_2Cl_2 (0.25 M) at 65°C with a catalyst loading of 0.5 mol% (Figure 2.12). The temperature had high impact to the reaction outcome; when the reaction was performed in CH_2Cl_2 (0.25 M) for 50 °C a four-fold decrease in conversion to **2.48** (13%) was observed.

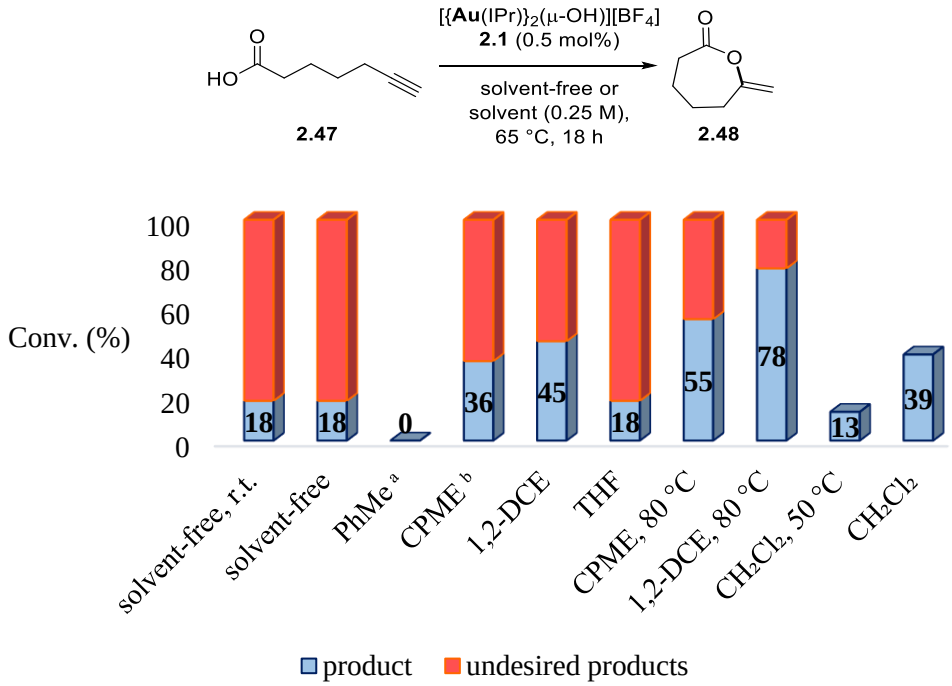


Figure 2.12. Solvent and temperature optimisation. Reaction conditions:**2.47** (0.5 mmol), solvent (0.25 M) or solvent-free, **2.1** (0.5 mol%), 65 °C unless otherwise stated, 18 h, sealed vessels; conversions calculated by ^{1}H NMR spectroscopy, by using pivalaldehyde as internal standard (10 μL, 0.092 mmol); [a] PhMe (0.5 M); [b] CPME (0.1 M).

By increasing the catalyst loading of **2.1** to 1 mol% and performing the reaction in CH_2Cl_2 (0.25 M), 73% conversion was observed after 5 h, and full conversions after 18 h (Figure 2.13). Pleasingly, even higher dilution (0.1 M) also led to the same conversions after 5 h, with caprolactone **2.48** isolated in 78% yield. Under the same reaction conditions, using 2 mol% of [Au(OH)(IPr)] **2.2** did not give satisfactory results, with low conversions and the formation of side-products observed. The same was found for cationic catalyst **2.9**, which gave similar conversion to **2.1**, without decrease of side-products. Chloride-Au(I) **2.44** was not active for this transformation, whilst [Au($CH_2C(O)CH_3$)(IPr)] **2.43** provided similar conversions to **2.2**, along with formation of side-products.

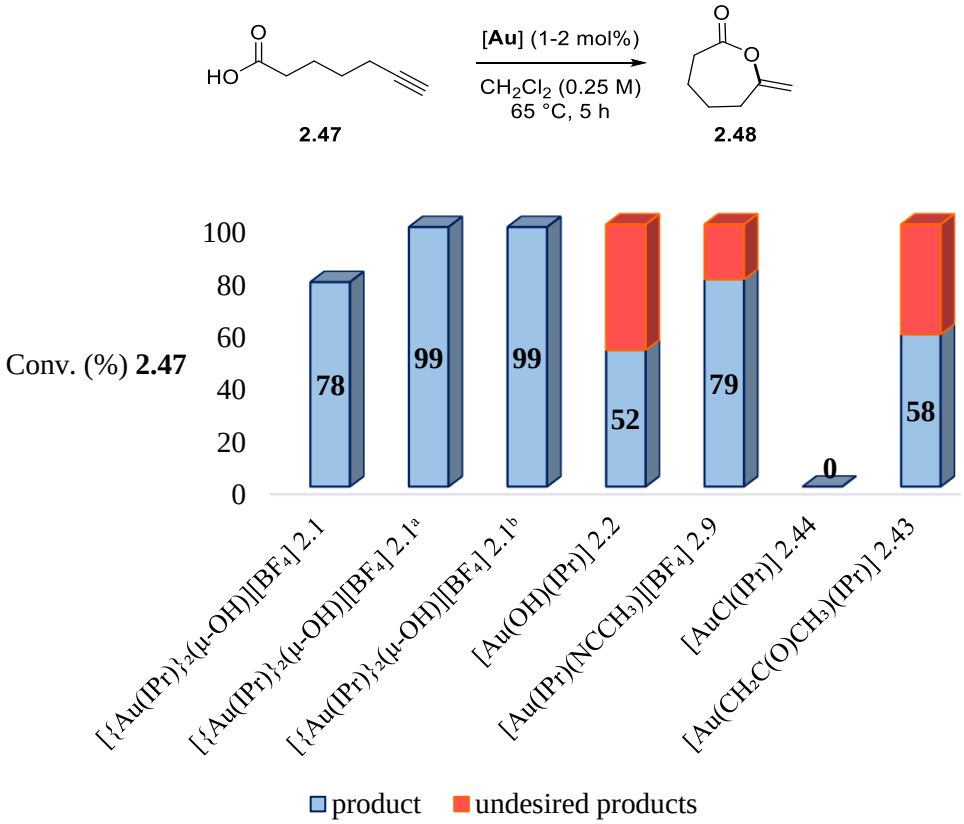


Figure 2.13. Catalyst optimisation. Reaction conditions: **2.47** (0.5 mmol), CH_2Cl_2 (0.25 M), **2.1** (1-2 mol%), 65 °C, 5 h, sealed vessels; conversion calculated by ^{1}H NMR spectroscopy, by using pivalaldehyde as internal standard (10 µL, 0.092 mmol); [a] 18 h; [b] CH_2Cl_2 (0.1 M).

2.3.2. Scope and limitations of the cyclisation of alkynoic acids

Having optimised the reaction conditions, the reactant's versatility was explored. Dinuclear gold complex **2.1** was found to outperform mononuclear complexes for the cyclisation of 4-pentynoic acid **2.40** and 5-hexynoic acid **2.45**, and thus it was chosen as optimal catalyst for the investigation of substrate scope. The catalyst loading of **2.1** was varied from 25 ppm to 0.1 mol%, depending on the substrate. The transformation could be applied to differently substituted alkynoic acids with good to excellent isolated yields (from 86 to 98%). The process was found to be highly stereoselective, furnishing (*Z*)-isomers in all cases. Furthermore, a convenient filtration through a short plug of silica, afforded the final lactones in high purity.

Product **2.49** was isolated in 95% yield with a catalyst loading of only 100 ppm, after 1 h (Figure 2.14). An internal alkyne bearing a phenyl group was also converted in excellent yield under the reaction condition (**2.50**). In both of these examples, substitution at the α-

position with an ester was used to enhance reaction conversion, potentially due to the Thorpe-Ingold effect that forces the reacting termini, the carboxylic acid and the alkyne, to be in closer proximity.[29] High regioselectivity for the *exo*-cyclisation was also observed for these substrates. Exceptions were found when internal alkynes bearing a methyl group were used, as in the case of product **2.51** and **2.52** derived from β-alkynoic malonate, for which the 6-*endo*-dig reaction was competitive with the 5-*exo*-dig cyclisation, as previously reported for alkynoic substrates bearing alkyl substituents.[18e,18h] Thus, products **2.51** and **2.52** were isolated in 94% and 98% yield with *exo*:*endo* ratios of 7:1 and 4:1, respectively. Interestingly, when using 0.2 mol% of **2.2** as pre-catalyst for the formation of **2.51**, the ratio between *exo* and *endo* products was reversed to 1:1.7 *exo*:*endo*. In contrast, for the cyclisation of **2.52** pre-catalyst **2.2** gave the same *exo*:*endo* ratio as dinuclear hydroxide **2.1**.

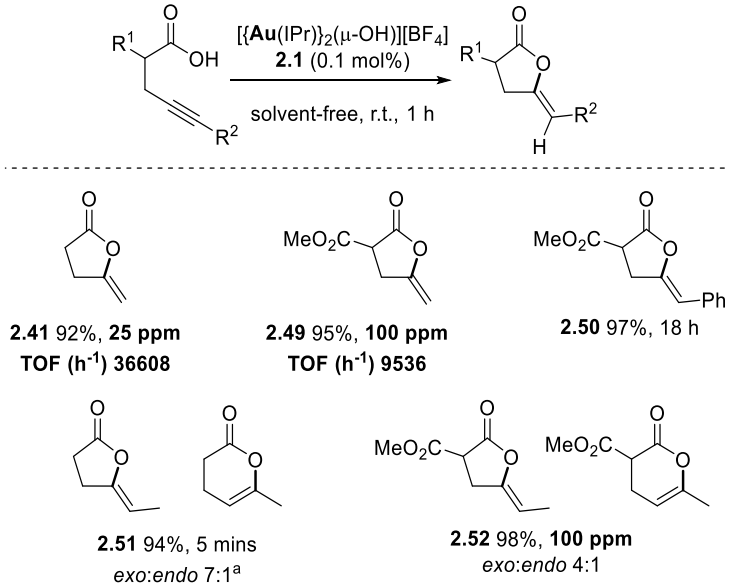


Figure 2.14. Cyclisation to γ-lactones. Reaction conditions: alkynoic acid (0.5 mmol), **2.1** (0.1 mol%), r.t., isolated yield; [a] *exo*:*endo* 1:1.7 with **2.2** (0.2 mol%). The synthesis of the starting materials, where not commercially available, was performed by Lorenzo Maggi.

Under the optimal reaction conditions, the cyclisation process was found to be extremely efficient: the cyclisation of **2.40** into **2.41** occurred with a TOF of greater than 36000 h^{-1}, higher than the best result reported in literature (667 h^{-1}).[18e] Moreover, the conversion into **2.49** showed a TOF of 9538 h^{-1} *vs* 1000 h^{-1} reported by Michelet, Conejero, Cadierno and co-workers.[18e]

The cyclisation of hexynoic acid derivatives proved successful with product **2.46** being isolated from 5-hexynoic acid in 94% yield within 1 h (Figure 2.15). A methyl substituent at the terminal position of the alkynoic acid had no influence on the selectivity of *exo*:*endo* cyclisation, with **2.53** was formed within 5 min and isolated in 92% yield, however the temperature had to be increased to 65 °C to obtain high conversion. Internal alkynes with a bromine, a phenyl group and a *p*-NO_2 aryl substituent were all suitable substrates for this transformation yielding products **2.54**, **2.55** and **2.56** from 86 to 98%. α-Ester substituted hexynoic acids were also reacted: terminal alkynes and internal alkynes could be subjected to the cyclisation conditions, affording products **2.57**, **2.58** and **2.59** in good to excellent yields. Moreover, aryl substituents on the alkyne were well-tolerated giving **2.60** (90%), **2.61** (88%) and **2.62** (97%). To obtain full conversion into **2.61** and **2.62**, the reaction temperature was increased to 65 °C, which allowed a decrease the reaction time to 5 min. Furthermore **2.61** was obtained using only 100 ppm catalyst loading.

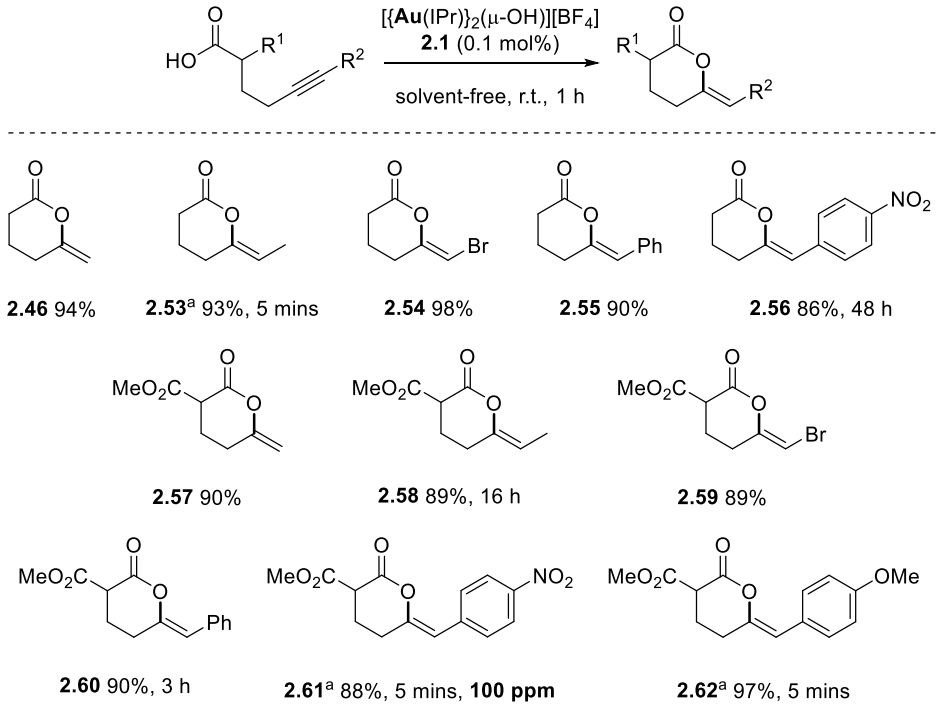


Figure 2.15. Cyclisation to δ-lactones. Reaction conditions: alkynoic acid (0.25-0.5 mmol), **2.1** (0.1 mol%), r.t., 1 h, isolated yield; [a] 65 °C. The cyclisation of these substrates was performed by Lorenzo Maggi.

Finally, the reaction scope for 6-heptynoic acids was explored (Figure 2.16). Other than caprolactone **2.48** (78% yield), full conversion to give ε-lactones **2.63** and **2.64** was observed under the optimised reaction conditions. Compound **2.63** was obtained in 91% isolated yield by increasing the catalyst loading to 2 mol%. The process tolerated a

bromine substituent in the terminal position of the alkyne, affording **2.64** in 80% isolated yield using 2 mol% of the pre-catalyst after 24h.

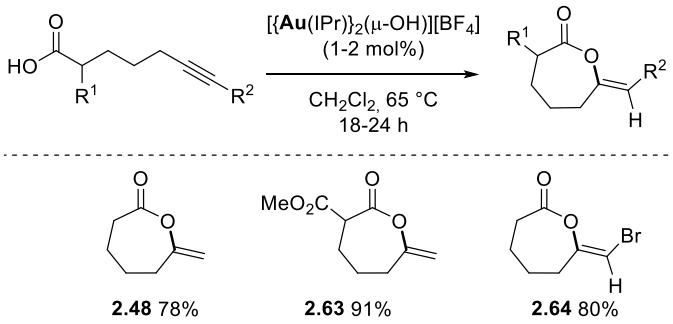


Figure 2.16. Cyclisation to ε-lactones. Reaction conditions: alkynoic acid (0.125-0.25 mmol), **2.1** (1-2 mol%), 65 °C, CH_2Cl_2 (0.25 M), 18-24 h, isolated yield.

The process afforded the (*Z*)-stereoisomers, as confirmed by single diffraction X-ray analysis of suitable crystals of **2.64** (Figure 2.17).[30]

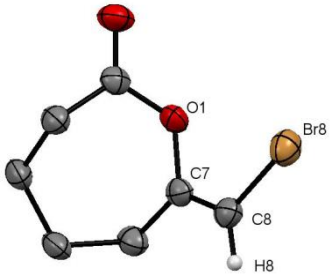


Figure 2.17. Thermal ellipsoid representation of **2.64** at 50% probability. Most of H atoms were omitted for clarity.

Aryl substituents (Ph, 4-$OMeC_6H_4$, 4-$NO_2C_6H_4$) in the terminal position of 6-hexynoic acids did not cyclise under the optimised reaction conditions. 7-Octynoic acid was also found to be unsuitable for the cyclisation, with full conversion of the substrate to give a complex mixture of products observed upon subjecting it to the Au(I) catalyst **2.1**.

2.4. Conclusions

A straightforward and highly efficient methodology for the intermolecular hydrocarboxylation of internal alkynes catalysed by a digold hydroxide complex was developed. 27 Examples of aryl and alkyl substituted vinyl esters were accessed in good to high yields using low catalyst loadings (0.5 mol%). The process showed high chemo- and regioselectivity, furnishing (*Z*)-products exclusively. The use of solvent-free

conditions is the highlight of this strategy: this methodology constitutes an atom-economical alternative to existing routes by providing a practical, operationally simple, and scalable method, with an easy work-up procedure.

Limitations of the methodology have been explored, and mostly involved to the choice of substituents on the alkyne. Moreover, initial application of the dinuclear gold catalyst to terminal alkyne showed only low conversion, suggesting that further studies would be required for optimisation of this system.

Furthermore, dinuclear gold catalyst could efficiently catalyse the cyclisation of alkynoic acids into γ-, δ- and ε-lactones. The process provided access to a wide range of molecules in a highly regio- and stereoselective manner, as confirmed by X-ray analysis and NMR spectroscopy. The methodology satisfied the most important principles of green chemistry, such as prevention for the need of additives, use of solvent-free conditions, and extremely low catalyst loadings, as low as 25 ppm. The mild reaction conditions compared to previous methodologies open the way to explore even more complex structures.

Noteworthily, the use of dinuclear gold complex was necessary for the intermolecular reaction, where mononuclear gold complexes poorly performed under the chosen reaction conditions. With regards to the intramolecular reaction, mononuclear gold complexes could perform under the chosen reaction conditions, however showed different *exo*:*endo* selectivity depending on the substrate and the catalyst loading. The use of dinuclear gold complex was necessary to perform cyclisation to ε-lactones. A deeper understanding of the reaction mechanism for these transformations, which highlights the use of the different catalysts, is presented in chapter 3.

2.5. Experimental

Unless otherwise stated, all solvents and reagents were used as purchased and all reactions were performed under air. NMR spectra were recorded on 700, 500, 400 and 300 MHz spectrometers at room temperature in $CDCl_3$ and C_6D_6. Chemical shifts (δ) are reported in parts par millions (ppm) downfield to tetramethylsilane and referenced to the residual protiated solvent peak (δ = 7.26 ppm for $CDCl_3$ and δ = 7.16 ppm for C_6D_6 in ^1H NMR spectroscopy experiments and δ = 77.16 ppm for $CDCl_3$ δ = 128.06 ppm for C_6D_6 in $^{13}C\{^1H\}$ NMR spectroscopy experiments). Multiplicity are indicated by: s = singlet, d =

doublet, t = triplet, br = broad signal, m = multiplet), coupling constants (*J*) in Hz and integration. For the assignment of the stereochemistry of the reported compounds, nuclear Overhauser effect spectroscopy (NOESY) experiments were also performed. For the assignment of the ^{1}H and $^{13}C\{^{1}H\}$ NMR spectra of gold complexes correlation spectroscopy (COSY), heteronuclear single-quantum correlation spectroscopy (HSQC) and heteronuclear multiple-bond correlation spectroscopy (HMBC) experiments were also performed. Thin-layer chromatography (TLC) analyses were performed on MACHEREY-NAGEL glass plates (7.5×2.5 cm) coated with silica gel, using a combination of petroleum ether or pentane and diethyl ether or ethyl acetate as eluents. TLC plates were visualized using UV light (235 nm). Flash chromatography was performed on silica gel 60 Å pore diameter and 40-63 μm particle sizes. High-resolution mass spectrometry was performed by the EPSRC National Mass Spectrometry Service Centre (NMSSC) (Grove Building Extn., Swansea University, Singleton Park, Swansea, SA2 8PP, U.K.).

$[\{Au(NHC)\}_2(\mu\text{-}OH)][BF_4]$ (NHC = IPr **2.1**, SIPr **2.8**, IPr^{Cl}), [Au(OH)(IPr)] **2.2**, $[Au(IPr)(NCCH_3)][BF_4]$ **2.9**, $[Au(NTf_2)(IPr)]$ **2.10**, $[Au(CH_2C(O)CH_3)(IPr)]$ **2.43** and [AuCl(IPr)] **2.44** were synthesised according to literature reports.[31,32,25a,28,33] Acid, alkynes and alkynoic acids used commercially available: the synthesis of alkynoic acids not commercially available was performed by Lorenzo Maggi and Dr. Richard Veenboer.

2.5.1. General procedures for the synthesis of vinyl esters GP1:

In a scintillation vial, alkyne (0.5 mmol), carboxylic acid (1 equiv.) and $[\{Au(IPr)\}_2(\mu\text{-}OH)][BF_4]$ **2.1** (0.5 mol%), were stirred neat at 80 °C. The reaction was monitored by ^{1}H NMR or GC until complete disappearance of the alkyne. After the reaction was completed the mixture was diluted with Et_2O (~1 mL), filtered through a short plug of silica and concentrated under vacuum. If acid was still present the mixture was quenched with $NaOH_{(aq)}$ (1 M, 2 mL) and extracted with Et_2O (3×3 mL). Further washing with pentane (3×5 mL) were performed to afford the corresponding product. The product was precipitated upon addition of pentane (3×5 mL).

(*Z*)-1,2-Diphenylvinyl 2,6-dimethoxybenzoate (**2.7**): vinyl ester **2.7** was synthesised following GP1 using 2,6-dimethoxy benzoic acid (91.1 mg, 0.5 mmol), diphenylacetylene

(89.1 mg, 0.5 mmol), and [{Au(IPr)}$_2$(μ-OH)][BF_4] **2.1** (3.2 mg, 0.5 mol%, 2,5 μmol). The reaction was stirred for 10 h at 80 °C. The pure product was obtained as an off-white solid (168.1 mg, 93%). ^{1}H NMR (500 MHz, $CDCl_3$) δ = 7.81 (d, *J* = 7.6, 2H, *o*-H phenyl), 7.70 (d, *J* = 7.5, 2H, *o*-H phenyl), 7.41 (m, 2H, *p*-H phenyl + *p*-H 2,6-dimethoxy phenyl), 7.39 – 7.30 (m, 5H, H_{Ar}), 7.26 (t, *J* = 7.3, 1H, *p*-H), 6.71 (s, 1H, C=CH), 6.61 (d, *J*=8.4, 2H, *m*-H 2,6-dimethoxy phenyl), 3.83 (s, 3H, OCH_3). ^{13}C{^{1}H} NMR (101 MHz, $CDCl_3$) δ = 164.5 (CO), 157.8 (C=CH), 147.0 (Cq), 136.2 (Cq), 134.3 (Cq), 131.7 (Cq), 129.5 (*o*-CH phenyl), 128.5 (Cq), 128.8 (CH_{Ar}), 128.2 (*p*-CH phenyl + *p*-CH 2,6-dimethoxy phenyl), 127.5 (*p*-CH), 125.8 (*o*-CH phenyl), 117.7 (C=CH), 112.4 (Cq), 103.9 (*m*-CH 2,6-dimethoxy phenyl), 55.8 (OCH_3). HRMS (NSI) Calcd (%) for $C_{23}H_{21}O_4$ ($M+H^+$) 361.1434, found 361.1435.

(*Z*)-1,2-Diphenylvinyl benzoate (**2.11**): vinyl ester **2.11** was synthesised following GP1 using benzoic acid (61.1 mg, 0.5 mmol), diphenylacetylene (89.1 mg, 0.5 mmol), and [{Au(IPr)}$_2$(μ-OH)][BF_4] **2.1** (3.2 mg, 0.5 mol%, 2.5 μmol). The reaction was stirred for 15 h at 80 °C. The pure product was obtained as an off-white solid (141.2 mg, 94%) whose NMR data were consistent to those reported in the literature.[35] ^{1}H NMR (500 MHz, $CDCl_3$) δ = 8.28 – 8.22 (m, 2H, H_{Ar}), 7.71 – 7.65 (m, 1H, H_{Ar}), 7.63 – 7.58 (m, 2H, H_{Ar}), 7.58 – 7.53 (m, 4H, H_{Ar}), 7.41 – 7.35 (m, 2H, H_{Ar}), 7.31 – 7.26 (m, 2H, H_{Ar}), 7.24 – 7.20 (m, 1H, H_{Ar}), 6.82 (s, 1H, C=CH).^{13}C{^{1}H} NMR (126 MHz, $CDCl_3$) δ = 164.4 (C=O), 146.7 (Cq), 135.8 (Cq), 134.4 (Cq), 133.9 (CH_{Ar}), 130.4 (CH_{Ar}), 129.3 (CH_{Ar}), 128.9 (CH_{Ar}), 128.9 (CH_{Ar}), 128.8 (CH_{Ar}), 128.8 (CH_{Ar}), 128.7 (CH_{Ar}), 127.8 (CH_{Ar}), 124.9 (C=CH), 117.3. m.p. = 120.6-121.8 °C.

(*Z*)-1,2-Diphenylvinyl 2-(dimethylamino)benzoate (**2.12**): vinyl ester **2.12** was synthesised following GP1 using 2-dimethylamino benzoic acid (82.6 mg, 0.5 mmol), diphenylacetylene (89.1 mg, 0.5 mmol), and [{Au(IPr)}$_2$(μ-OH)][BF_4] **2.1** (3.2 mg, 0.5 mol%, 2.5 μmol). The reaction was stirred for 19 h at 80 °C. The pure product was obtained as a green oil (158.7 mg, 93%). ^{1}H NMR (400 MHz, $CDCl_3$) δ = 8.20 (dd, *J* = 7.9, 1.7, 1H, *o*-CH), 7.69 – 7.62 (m, 2H, H_{Ar}), 7.62 – 7.58 (m, 2H), 7.46 (ddd, *J* = 8.4, 7.1, 1.7, 1H, *p*-CH), 7.40 – 7.34 (m, 2H), 7.34 – 7.27 (m, 3H), 7.24 – 7.18 (m, 1H), 7.03 (dd, *J* = 8.5, 1.1, 1H, *o*-CH $N(CH_3)_2$), 6.95 (ddd, *J* = 8.1, 7.1, 1.1, 1H, *p*-CH $N(CH_3)_2$), 6.81 (s, 1H, C=CH), 2.75 (s, 6H, $N(CH_3)_2$).^{13}C{^{1}H} NMR (101 MHz, $CDCl_3$) δ = 164.1

(C=O), 154.1 (Cq), 147.0 (C=CH), 136.2 (Cq), 134.6 (Cq), 133.4 (*p*-CH), 132.5 (*o*-CH), 128.9 (CH_{Ar}), 128.6 (CH_{Ar}), 128.47 (CH_{Ar}), 127.4 (CH_{Ar}), 124.9 (CH_{Ar}), 118.5 (*p*-CH $N(CH_3)_2$), 118.1 (Cq), 117.3 (C-$N(CH_3)_2$), 117.2 (C=CH), 43.8 ($N(CH_3)_2$). HRMS (NSI) Calcd (%) for $C_{23}H_{22}NO_2$ ($M+H^+$) 344.1645, found 344.1646.

(*Z*)-1,2-Diphenylvinyl 4-methoxybenzoate (**2.13**): vinyl ester **2.13** was synthesised following GP1 using 4-methoxy benzoic acid (76.1 mg, 0.5 mmol), diphenylacetylene (89.1 mg, 0.5 mmol), and [{Au(IPr)}$_2$(μ-OH)][BF_4] **2.1** (3.2 mg, 0.5 mol%, 2.5 μmol). The reaction was stirred for 15 h at 110 °C. The pure product was obtained as an off-white solid (152 mg, 92%) whose NMR data were consistent to those reported in the literature.[35] ^{1}H NMR (500 MHz, $CDCl_3$) δ = 8.22 – 8.17 (m, 2H, H_{Ar}), 7.62 – 7.56 (m, 2H, H_{Ar}), 7.57 – 7.52 (m, 2H, H_{Ar}), 7.40 – 7.34 (m, 3H, H_{Ar}), 7.34 – 7.27 (m, 3H, H_{Ar}), 7.23 – 7.18 (m, 3H), 7.04 – 7.00 (m, 2H,), 6.79 (s, 1H, C=CH), 3.91 (s, 3H, OCH_3).^{13}C{^{1}H} NMR (101 MHz, $CDCl_3$) δ = 164.5 (C=O), 157.8 (C=CH), 147.0 (Cq), 136.2 (Cq), 134.3 (Cq), 131.7 (Cq), 129.6 (CH_{Ar}), 128.5 (CH_{Ar}), 128.4 (CH_{Ar}), 128.3 (CH_{Ar}), 127.5 (CH_{Ar}), 125.9 (CH_{Ar}), 117.7 (C=CH), 112.5 (CH_{Ar}), 103.9 (CH_{Ar}), 55.9 (OCH_3).

(*Z*)-1,2-Diphenylvinyl 2,6-dimethylbenzoate (**2.14**): vinyl ester **2.14** was synthesised following GP1 using 2,6-dimethyl benzoic acid (75.1 mg, 0.5 mmol, 1 equiv.), diphenylacetylene (89.1 mg, 0.5 mmol), and [{Au(IPr)}$_2$(μ-OH)][BF_4] **2.1** (3.2 mg, 0.5 mol%, 2.5 μmol). The reaction was stirred for 15 h at 80 °C. The pure product was obtained as a green oil (159.3 mg, 97%). ^{1}H NMR (400 MHz, $CDCl_3$) δ = 7.71 – 7.62 (m, 2H. H_{Ar}), 7.55 – 7.48 (m, 2H, H_{Ar}), 7.45 – 7.35 (m, 3H, H_{Ar}), 7.32 – 7.26 (m, 2H, *p*-H 2,6-dimethyl phenyl + H_{Ar}), 7.09 – 7.02 (m, 2H, *m*-CH 2,6-dimethyl phenyl), 6.71 (s, 1H, C=CH), 2.24 (d, *J* = 0.7, 6H, CH_3). ^{13}C{^{1}H} NMR (101 MHz, $CDCl_3$) δ = 167.8 (CO), 147.8 (C=CH), 136.6 (Cq), 134.4 (Cq), 132.3 (Cq), 130.1 (CH_{Ar}), 129.2 (CH_{Ar}), 128.8 (CH_{Ar}), 128.7 (CH_{Ar}), 128.5 (*p*-CH 2,6-dimethyl phenyl), 128.3 (CH_{Ar}), 127.8 (*m*-CH 2,6-dimethyl phenyl), 126.2 (CH_{Ar}), 118.5 (CH_{Ar}), 20.8 (CH_3). HRMS (NSI) Calcd (%) for $C_{23}H_{21}O_2$ ($M+H^+$) 329.1536, found 329.1536.

(*Z*)-1,2-Diphenylvinyl 4-bromobenzoate (**2.15**): vinyl ester **2.15** was synthesised following GP1 using 4-bromobenzoic acid (100.5 mg, 0.5 mmol), diphenylacetylene (89.1 mg, 0.5 mmol), and [{Au(IPr)}$_2$(μ-OH)][BF_4] **2.1** (3.2 mg, 0.5 mol%, 2.5 μmol).

The reaction was stirred for 15 h at 110 °C. The pure product was obtained as an off-white powder (170.7 mg, 90%). ^{1}H NMR (400 MHz $CDCl_3$) δ = 8.12 – 8.07 (m, 2H, H_{Ar}), 7.72 – 7.67 (m, 2H, H_{Ar}), 7.60 – 7.54 (m, 2H, H_{Ar}), 7.54 – 7.49 (m, 2H, H_{Ar}), 7.42 – 7.32 (m, 3H, H_{Ar}), 7.32 – 7.26 (m, 2H, H_{Ar}), 7.25 – 7.19 (m, 1H, H_{Ar}), 6.81 (s, 1H, C=CH). ^{13}C{^{1}H} NMR (101 MHz, $CDCl_3$) δ = 163.7 (CO), 146.6 (C=CH), 135.5 (Cq), 134.2 (Cq), 132.3 (Cq), 131.8 (CH_{Ar}), 129.3 (C_{Ar}), 128.9 (CH_{Ar}), 128.8 (CH_{Ar}), 128.7 (CH_{Ar}), 128.2 (CH_{Ar}), 127.9 (CH_{Ar}), 124.9 (CH_{Ar}), 117.4 (C=CH). HRMS (ESI) Calcd (%) for $C_{21}H_{16}O_2Br$ ($M+H^+$) 379.0328, found 379.0332.

(*Z*)-1,2-Diphenylvinyl 2-fluorobenzoate (**2.16**): vinyl ester **2.16** was synthesised following GP1 using 2-fluoro benzoic acid (70.1 mg, 0.5 mmol), diphenylacetylene (89.1 mg, 0.5 mmol), and [{Au(IPr)}$_2$(μ-OH)][BF_4] **2.1** (3.2 mg, 0.5 mol%, 2.5 μmol). The reaction was stirred for 15 h at 80 °C. The pure product was obtained as an off-white powder (95.5 mg, 60%). ^{1}H NMR (500 MHz, $CDCl_3$) δ = 8.09 (td, *J* = 7.6, 1.9, 1H, *o*-H 2-F-phenyl), 7.67 – 7.52 (m, 5H, H_{Ar}), 7.43 – 7.34 (m, 3H, H_{Ar}), 7.34 – 7.27 (m, 6H, H_{Ar}), 7.26 – 7.20 (m, 1H, H_{Ar}), 6.80 (s, 1H, C=CH). ^{13}C{^{1}H} NMR (101 MHz, $CDCl_3$) δ = 162.1 (C=O), 146.6 (C=CH), 135.6 (CH_{Ar}), 135.5 (Cq), 134.3 (Cq), 132.9 (*o*-CH 2-F-phenyl), 128.9 (CH_{Ar}), 128.8 (CH_{Ar}), 128.8 (CH_{Ar}), 128.7 (CH_{Ar}), 127.8 (CH_{Ar}), 125.1 (CH_{Ar}), 124.5 (CH_{Ar}), 124.4 (CH_{Ar}), 117.6 (CH_{Ar}), 117.3 (C=CH). ^{19}F{^{1}H} NMR (282 MHz, $CDCl_3$) δ = -107.44. HRMS (ESI) Calcd (%) for $C_{21}H_{16}FO_2$ ($M+H^+$) 319.1130, found 319.1129.

(*Z*)-1,2-Diphenylvinyl 2-bromobenzoate (**2.17**): vinyl ester **2.17** was synthesised following GP1 using 2-bromo benzoic acid (100.5 mg, 0.5 mmol, 1 equiv.), diphenylacetylene (89.1 mg, 0.5 mmol), and [{Au(IPr)}$_2$(μ-OH)][BF_4] **2.1** (3.2 mg, 0.5 mol%, 2.5 μmol). The reaction was stirred for 10 h at 80 °C. The pure product was obtained as an off-white powder (170.5 mg, 90%). ^{1}H NMR (400 MHz, $CDCl_3$) δ = 8.12 – 8.07 (m, 1H, *o*-CH (C_6H_5)CO_2), 7.77 – 7.74 (m, 1H, *p*-CH (C_6H_5)CO_2), 7.67 – 7.62 (m, 2H, *m*-CH (C_6H_5)CO_2), 7.56 – 7.52 (m, 2H, CH_{Ar}), 7.49 – 7.29 (m, 7H, CH_{Ar}), 7.26 – 7.21 (m, 1H, CH_{Ar}), 6.81 (s, 1H, C=CH). ^{13}C{^{1}H} NMR (101 MHz, $CDCl_3$) δ = 163.3 (CO), 146.7 (C=CH), 135.6 (Cq), 135.2 (*p*-CH (C_6H_5)CO_2), 134.2 (Cq), 133.6 (CH_{Ar}), 132.3 (*o*-CH (C_6H_5)CO_2), 130.6 (Cq), 128.9 (CH_{Ar}), 128.8 (CH_{Ar}), 128.7 (CH_{Ar}), 127.9

(CH_{Ar}), 127.5 (CH_{Ar}), 125.2 (*m*-CH (C_6H_5)CO_2), 122.9 (CH_{Ar}), 117.6 (C=CH). HRMS (NSI) Calcd (%) for $C_{21}H_{16}O_2Br$ ($M+H^+$) 379.0328, found 379.0332.

(*Z*)-1,2-Diphenylvinyl 3-bromobenzoate (**2.18**): vinyl ester **2.18**was synthesised following GP1 using 3-bromo benzoic acid (100.5 mg, 0.5 mmol), diphenylacetylene (89.1 mg, 0.5 mmol), and [{Au(IPr)}$_2$(μ-OH)][BF_4] **2.1** (3.2 mg, 0.5 mol%, 2.5 μmol). The reaction was stirred for 10 h at 80 °C. The pure product was obtained as an off-white powder (152 mg, 80%). ^{1}H NMR (500 MHz, $CDCl_3$) δ = 8.37 (t, *J* = 1.8, 1H, *o*-H (C_6H_5)CO_2), 8.16 (dt, *J* = 7.8, 1.3, 1H, *o*-H (C_6H_5)CO_2), 7.80 (ddd, *J* = 8.0, 2.0, 1.1, 1H, *p*-H (C_6H_5)CO_2), 7.60 – 7.55 (m, 2H, H_{Ar}), 7.53 – 7.49 (m, 2H, H_{Ar}), 7.43 (t, *J* = 7.9, 1H, *m*-H (C_6H_5)CO_2), 7.40 – 7.33 (m, 3H, H_{Ar}), 7.32 – 7.27 (m, 2H, H_{Ar}), 7.25 – 7.20 (m, 1H, H_{Ar}), 6.82 (s, 1H, C=CH).^{13}C{^{1}H} NMR (126 MHz, $CDCl_3$) δ = 163.2 (CO), 146.5 (C=CH), 136.9 (*p*-CH (C_6H_5)CO_2), 135.4 (Cq), 134.2 (Cq), 133.3 (*o*-CH (C_6H_5)CO_2), 131.2 (Cq), 130.5 (*m*-CH (C_6H_5)CO_2), 128.9 (CH_{Ar}), 128.9 (*o*-CH (C_6H_5)CO_2), 128.9 (CH_{Ar}), 128.8 (CH_{Ar}), 128.8 (CH_{Ar}), 127.9 (CH_{Ar}), 124.9 (CH_{Ar}), 123.0 (Cq), 117.4 (C=CH). HRMS (NSI) Calcd (%) for $C_{21}H_{16}O_2Br$ ($M+H^+$) 379.0328, found 379.0333.

(*Z*)-1,2-Diphenylvinyl 2-nitrobenzoate (**2.19**): vinyl ester **2.19** was synthesised following GP1 using 2-nitro benzoic acid (83.6 mg, 0.5 mmol, 1 equiv.), diphenylacetylene (89.1 mg, 0.5 mmol), and [{Au(IPr)}$_2$(μ-OH)][BF_4] **2.1** (3.2 mg, 0.5 mol%, 2.5 μmol). The reaction was stirred for 10 h at 80 °C. The pure product was obtained as an off-white powder (172 mg, 99%). ^{1}H NMR (400 MHz, $CDCl_3$) δ = 7.91 – 7.88 (m, 1H, H_{Ar}), 7.83 – 7.80 (m, 1H, H_{Ar}), 7.72 – 7.68 (m, 2H, H_{Ar}), 7.67 – 7.63 (m, 2H, H_{Ar}), 7.51 – 7.46 (m, 2H, H_{Ar}), 7.46 – 7.40 (m, 2H, H_{Ar}), 7.40 – 7.35 (m, 1H, H_{Ar}), 7.35 – 7.30 (m, 2H, H_{Ar}), 7.31 – 7.22 (m, 1H, H_{Ar}), 6.80 (s, 1H, C=CH). ^{13}C{^{1}H} NMR (101 MHz, $CDCl_3$) δ = 162.4 (CO), 146.8 (C=CH), 135.1 (Cq), 134.0 (Cq), 132.8 (Cq), 132.6 (CH_{Ar}), 130.8(CH_{Ar}), 130.1 (Cq), 129.1 (CH_{Ar}), 129.0 (CH_{Ar}), 128.8 (CH_{Ar}), 128.7 (CH_{Ar}), 128.0 (CH_{Ar}), 125.9 (Cq), 125.4 (CH_{Ar}), 124.2 (CH_{Ar}), 118.1 (C=CH), 110.1 (Cq). HRMS (NSI) Calcd (%) for $C_{21}H_{16}O_4N$ (M+H) 346.1074, found 346.1073.

(*Z*)-1,2-Diphenylvinyl 4-nitrobenzoate (**2.20**): vinyl ester **2.20** was synthesised following GP1 using 4-nitrobenzoic acid (83.6 mg, 0.5 mmol, 1 equiv.), diphenylacetylene (89.1 mg, 0.5 mmol), and [{Au(IPr)}$_2$(μ-OH)][BF_4] **2.1** (3.2 mg, 0.5 mol%, 2.5 μmol). The reaction was stirred for 5 h at 110 °C. The pure product was obtained as a yellow powder

(170.7 mg, 74%). ^{1}H NMR (400 MHz $CDCl_3$) δ = 8.42 – 8.36 (m, 4H, *o*,*m*-H *p*-NO_2 phenyl), 7.60 – 7.55 (m, 2H, H_{Ar}), 7.52 – 7.48 (m, 2H, H_{Ar}), 7.43 – 7.33 (m, 3H, H_{Ar}), 7.32 – 7.26 (m, 2H, H_{Ar}, 7.25 – 7.20 (m, 1H, H_{Ar}), 6.85 (s, 1H, C=CH). $^{13}C\{^{1}H\}$ NMR (101 MHz, $CDCl_3$) δ = 162.6 (CO), 151.2 (C=CH), 146.4 (Cq), 135.2 (Cq), 134.6 (Cq), 134.0 (Cq), 131.5 (CH_{Ar}), 129.1 (CH_{Ar}), 128.9 (CH_{Ar}), 128.8 (CH_{Ar}), 128.8 (CH_{Ar}), 128.1 (CH_{Ar}), 124.9 (CH_{Ar}), 124.1 (CH_{Ar}), 117.6 (C=CH). HRMS (ESI) Calcd (%) for $C_{21}H_{16}O_4N$ ($M+H^+$) 346.1074, found 346.1073.

(*Z*)-1,2-Diphenylvinyl furan-2-carboxylate (**2.21**): vinyl ester **2.21** was synthesised following GP1 using furoic acid (56 mg, 0.5 mmol), diphenylacetylene (89.1 mg, 0.5 mmol), and $[\{Au(IPr)\}_2(\mu\text{-}OH)][BF_4]$ **2.1** (3.2 mg, 0.5 mol%, 2.5 μmol). The reaction was stirred for 15 h at 80 °C. The pure product was obtained as an off-white powder (120.5 mg, 83%). ^{1}H NMR (500 MHz, $CDCl_3$) δ = 7.68 (dd, *J* = 27.4, 1.7, 1H, CH^5 furan), 7.59 (d, *J* = 7.6, 1H, H_{Ar}), 7.56 (d, *J* = 7.8, 2H, H_{Ar}), 7.44 (d, *J* = 3.5, 1H, H_{Ar}), 7.38 (t, *J* = 7.5, 1H, C^4H furan), 7.36 – 7.29 (m, 2H), 7.25 – 7.20 (m, 1H, H_{Ar}), 6.80 (s, 1H, C=CH), 6.60 (ddt, *J* = 31.5, 3.0, 1.3, 1H, C^3H furan). $^{13}C\{^{1}H\}$ NMR (126 MHz, $CDCl_3$) δ = 162.9 (C=O), 156.2 (C=CH), 147.6 (C^5H furan), 145.9 (Cq), 144.0 (Cq), 135.5 (CH_{Ar}), 134.2 (CH_{Ar}), 131.7 (CH_{Ar}), 128.9 (CH_{Ar}), 128.8 (CH_{Ar}), 128.7 (C^4H furan), 124.9 (CH_{Ar}), 120.2 (Cq), 119.8 (CH_{Ar}), 117.6 (C=CH), 112.4 (C^3H furan). HRMS (NSI) Calcd (%) for $C_{19}H_{15}O_3$ ($M+H^+$) 291.1016, found 291.1017.

(*Z*)-1,2-Diphenylvinyl picolinate (**2.22**): vinyl ester **2.22** was synthesised following **GP1**using picolinic acid (80 mg, 0.65 mmol, 1.3 equiv.), diphenylacetylene (89.1 mg, 0.5 mmol), and $[\{Au(IPr)\}_2(\mu\text{-}OH)][BF_4]$ **2.1** (6.4 mg, 1 mol%, 5 μmol). The reaction was stirred for 24 h at 110 °C. The pure product was obtained as an off-white powder (126.6 mg, 84%). ^{1}H NMR (300 MHz, $CDCl_3$) δ = 8.90 (ddd, *J* = 4.7, 1.8, 0.9, 1H, H *m*-pyr), 8.23 (dt, *J* = 7.8, 1.1, 1H, H *o*-pyr), 7.91 (td, *J* = 7.7, 1.8, 1H, H *p*-pyr), 7.67 – 7.50 (m, 8H, H_{Ar}), 7.44 – 7.21 (m, 6H, H_{Ar}), 7.23 – 7.15 (m, 1H, H_{Ar}), 6.84 (s, 1H, C=CH). $^{13}C\{^{1}H\}$ NMR(75 MHz, $CDCl_3$) δ = 163.2 (C=O), 150.4 (CH *m*-pyr), 147.4 (Cq), 146.8 (Cq), 137.4 (CH_{Ar}), 135.4 (CH_{Ar}), 134.2 (CH_{Ar}), 131.7 (CH_{Ar}), 129.0 (CH_{Ar}), 128.8 (CH_{Ar}), 128.7 (CH_{Ar}), 128.5 (CH_{Ar}), 128.4 (CH_{Ar}), 127.8 (CH_{Ar}), 127.6 (CH_{Ar}), 126.0 (CH_{Ar}), 125.0 (CH_{Ar}), 123.4 (CH_{Ar}), 117.3 (C=CH). HRMS (NSI) Calcd (%) for $C_{20}H_{16}O_2N$ ($M+H^+$) 302.1176, found 302.1177.

(*Z*)-1,2-Diphenylvinyl acrylate (**2.23**): vinyl ester **2.23** was synthesised following GP1 using acrylic acid (36 mg, 0.5 mmol), diphenylacetylene (89.1 mg, 0.5 mmol), and [{Au(IPr)}$_2$(μ-OH)][BF$_4$] **2.1** (3.2 mg, 0.5 mol%, 2.5 μmol). The reaction was stirred for 5 h at 80 °C. The pure product was obtained as an off-white powder (118.9 mg, 89%). ^{1}H NMR (300 MHz, $CDCl_3$) δ = 7.53 (tt, *J* = 8.2, 1.5, 5H, H_{Ar}), 7.45 – 7.22 (m, 6H, H_{Ar}), 6.74 (s, 1H, C=CH), 6.65 (dd, *J* = 17.3, 1.3, 1H, CH_2=CH *trans*), 6.38 (dd, *J* = 17.3, 10.4, 1H, CH_2=CH), 6.07 (dd, *J* = 10.4, 1.3, 1H, CH_2=C *cis*). ^{13}C{^{1}H} NMR (101 MHz, $CDCl_3$) δ = 163.8 (C=O), 146.4 (Cq), 135.6 (Cq), 134.3 (C=CH), 133.2 (CH_2=CH), 128.9 (CH_{Ar}), 128.8 (CH_{Ar}), 128.8 (CH_{Ar}), 128.7 (CH_{Ar}), 127.8 (CH_2=CH), 124.9 (CH_{Ar}), 117.1 (C=CH). HRMS (NSI) Calcd (%) for $C_{17}H_{15}O_2$ (M+H$^+$) 251.1067, found 251.1068.

(*Z*)-1,2-Diphenylvinyl cinnamate (**2.24**): vinyl ester **2.24** was synthesised following **GP1** using cinnamic acid (74.1 mg, 0.5 mmol), diphenylacetylene (89.1 mg, 0.5 mmol), and [{Au(IPr)}$_2$(μ-OH)][BF$_4$] **2.1** (3.2 mg, 0.5 mol%, 2.5 μmol). The reaction was stirred for 5 h at 80 °C. The pure product was obtained as an off-white powder (153.4 mg, 94%). ^{1}H NMR (400 MHz, $CDCl_3$) δ = 7.83 (d, *J* = 16.0, 1H, CH=CHCO), 7.60 – 7.42 (m, 7H, H_{Ar}), 7.41 – 7.21 (m, 8H, H_{Ar}), 7.19 – 7.12 (m, 1H, H_{Ar}), 6.69 (s, 1H, C=CH), 6.63 (d, *J* = 16.0, 1H, CH=CHCO).^{13}C{^{1}H} NMR(101 MHz, $CDCl_3$) δ = 164.7 (CO), 147.3 (CH=CHCO), 146.6 (Cq), 135.8 (Cq), 134.4 (Cq), 134.2 (C=CH), 131.7 (CH_{Ar}), 131.0 (CH_{Ar}), 129.2 (CH_{Ar}), 128.9 (CH_{Ar}), 128.8 (CH_{Ar}), 128.7 (CH_{Ar}), 128.5 (CH_{Ar}), 127.8 (CH_{Ar}), 124.9 (CH_{Ar}), 117.1 (C=CH), 116.9 (CH=CHCO).HRMS (NSI) Calcd (%) for $C_{23}H_{19}O_2$ (M+H$^+$) 327.1385, found 327.1384.

(*Z*)-1,2-Diphenylvinyl formate (**2.25**): vinyl ester **2.25** was synthesised following GP1 using formic acid (46 mg, 1 mmol), diphenylacetylene (178.2 mg, 1mmol), and [{Au(IPr)}$_2$(μ-OH)][BF$_4$] **2.1** (6.4 mg, 0.5 mol%, 5 μmol). The reaction was stirred for 2 h at 80 °C. The pure product was obtained as an off-white powder (201.6 mg, 90%). ^{1}H NMR (400 MHz, $CDCl_3$) δ = 8.21 (d, *J* = 0.5, 1H, C(O)H), 7.60 – 7.52 (m, 4H, *o*-H phenyl), 7.46 – 7.33 (m, 5H, H_{Ar}, *p*,*m*-H phenyl), 7.32 – 7.27 (m, 1H, *m*-H phenyl), 6.78 (s, 1H, C=CH).^{13}C{^{1}H} NMR (101 MHz, $CDCl_3$) δ = 159.5 (C=O), 146.0 (C=CH), 134.9 (Cq), 133.6 (Cq), 129.2 (CH_{Ar}, 4C), 128.9 (CH_{Ar}, 2C), 128.9 (CH_{Ar}, 2C), 128.1 (CH_{Ar}), 125.1 (CH_{Ar}), 117.2 (C=CH). HRMS (APCI) Calcd (%) for $C_{15}H_{16}O_2N$ (M+NH_4^+) 242.1176, found 242.1177.

(*Z*)-1,2-Diphenylvinyl acetate (**2.26**): vinyl ester **2.26** was synthesised following GP1 using acetic acid (60.1 mg, 1 mmol), diphenylacetylene (178.2 mg, 1 mmol), and [{Au(IPr)}$_2$(μ-OH)][BF$_4$] **2.1** (6.4 mg, 0.5 mol%, 5 μmol). The reaction was stirred for 4 h at 80 °C. The pure product was obtained as an off-white powder (209.4 mg, 88%) whose NMR data were consistent to those reported in the literature.[6b] The synthesis of compound **2.26** was scaled (10 mmol) following the general procedure. The reaction was stirred for 6 h at 80 °C and after work-up the pure product was obtained in 92% yield (2.193 g). ^{1}H NMR (400 MHz, $CDCl_3$) δ = 7.56 – 7.50 (m, 4H, H_{Ar}), 7.42 – 7.31 (m, 5H, H_{Ar}), 7.30 – 7.24 (m, 1H, H_{Ar}), 6.72 (s, 1H, C=CH), 2.32 (s, 3H, CH_3). ^{13}C{^{1}H} NMR (101 MHz, $CDCl_3$) δ = 168.6 (C=O), 146.6 (C=CH), 135.5 (Cq), 134.4 (Cq), 128.7 (CH_{Ar}), 128.6 (CH_{Ar}), 127.7 (CH_{Ar}), 124.8 (CH_{Ar}), 116.8 (C=CH), 21.1 (CH_3); m.p. =96.4-98.2 °C

(*Z*)-1,2-Diphenylvinyl pivalate (**2.27**): vinyl ester **2.27** was synthesised following GP1 using pivalic acid (51.1 mg, 0.5 mmol), diphenylacetylene (89.1 mg, 0.5 mmol), and [{Au(IPr)}$_2$(μ-OH)][BF$_4$] **2.1** (3.2 mg, 0.5 mol%, 2.5 μmol). The reaction was stirred for 16 h at 80 °C. The pure product was obtained as an off-white powder (112.06 mg, 80%) whose NMR data were consistent to those found in literature.[6b] ^{1}H NMR (200 MHz, $CDCl_3$) δ = 7.53-7.25 (m, 10 H), 6.69 (s, 1 H), 1.32 (s, 9 H). ^{13}C{^{1}H} NMR (50 MHz, $CDCl_3$) δ = 175.7 (C=O), 146.9 (C=CH), 136.1 (Cq), 134.3 (Cq), 128.7 (CH_{Ar}), 128.5 (CH_{Ar}), 128.4 (CH_{Ar}), 128.2 (CH_{Ar}), 127.4 (CH_{Ar}), 124.8 (CH_{Ar}), 117.13 (C=CH), 39.0 ($C(CH_3)_3$), 27.2 ($C(CH_3)_3$).

(*Z*)-1,2-Diphenylvinyl 4-oxopentanoate (**2.28**): vinyl ester **2.28** was synthesised following GP1 using levulinic acid (58.1 mg, 0.5 mmol), diphenylacetylene (89.1 mg, 0.5 mmol), and [{Au(IPr)}$_2$(μ-OH)][BF$_4$] **2.1** (3.2 mg, 0.5 mol%, 2.5 μmol). The reaction was stirred for 5 h at 80 °C. The pure product was obtained as an off-white powder (131.1 mg, 89%). ^{1}H NMR (400 MHz, $CDCl_3$) δ = 7.59 – 7.53 (m, 2H, H_{Ar}), 7.55 – 7.47 (m, 2H, H_{Ar}), 7.44 – 7.27 (m, 6H, H_{Ar}), 6.70 (s, 1H, C=CH), 2.88 (ddd, *J* = 6.9, 5.8, 1.2, 2H, CH_2), 2.80 (ddd, *J* = 7.1, 5.8, 1.2, 2H, CH_2), 2.18 (s, 3H, CH_3). ^{13}C{^{1}H} NMR (101 MHz, $CDCl_3$) δ = 206.2 ($COCH_3$), 170.8 (C=O), 146.7 (C=CH), 135.6 (Cq), 134.4 (Cq), 128.9 (CH_{Ar}), 128.8 (CH_{Ar}), 128.8 (CH_{Ar}), 128.7 (CH_{Ar}), 127.8 (CH_{Ar}), 124.9 (CH_{Ar}), 116.9 (CH_{Ar}), 37.8 (CH_2), 29.9 (CH_3), 28.2 (CH_2). HRMS (NSI) Calcd (%) for $C_{19}H_{19}O_3$ ($M+H^+$) 295.1334, found 295.1333.

(*Z*)-Oct-4-en-4-yl benzoate (**2.29**): vinyl ester **2.29** was synthesised following GP1 using benzoic acid (61.1 mg, 0.5 mmol), 4-octyne (55.1 mg, 0.5 mmol), and [{Au(IPr)}$_2$(μ-OH)][BF_4] **2.1** (3.2 mg, 0.5 mol%, 2.5 μmol). The reaction was stirred for 16 h at 80 °C.The pure product was obtained as a green oil (113.9 mg, 98%) whose NMR data were consistent to those reported in the literature.[7a] ^{1}H NMR (400 MHz, $CDCl_3$) δ = 8.13 – 8.09 (m, 2H, *o*-H phenyl), 7.60 (ddt, *J* = 7.9, 6.9, 1.4, 1H, *p*-H phenyl), 7.51 – 7.44 (m, 2H, *m*-H phenyl), 5.11 (tt, *J* = 7.3, 1.0, 1H, C=CH), 2.32 – 2.24 (m, 2H, $CH_2CH_2CH_3$), 1.95 (qt, *J* = 7.4, 1.1, 1H, C=CHCH_2), 1.52 (h, *J* = 7.4, 2H, $CH_2CH_2CH_3$), 1.38 (h, *J* = 7.3, 2H, $CH_2CH_2CH_3$), 0.94 (t, *J* = 7.4, 3H, CH_3), 0.88 (t, *J* = 7.4, 3H, CH_3). $^{13}C\{^1H\}$ NMR (126 MHz, $CDCl_3$) δ = 164.6 (C=O), 148.6 (C=CH), 133.8 (Cq), 133.3 (CH_{Ar}), 130.3(CH_{Ar}), 130.1(CH_{Ar}), 130.0(CH_{Ar}), 128.6(CH_{Ar}), 116.7 (C=CH)), 35.7 (CH_2), 27.59 (CH_2), 22.5 (CH_2), 20.1 (CH_2), 13.9 (CH_3), 13.7 (CH_3).

(*Z*)-Dimethyl 2-(benzoyloxy)fumarate (**2.30**): vinyl ester **2.30** was synthesised following GP1 using benzoic acid (61.1 mg, 0.5 mmol), dimethyl acetylenedicarboxylate (71.06 mg, 0.5 mmol), and [{Au(IPr)}$_2$(μ-OH)][BF_4] **2.1** (3.2 mg, 0.5 mol%, 2.5 μmol). The reaction was stirred for 19 h at 80 °C. The pure product was obtained as a yellow oil (125.8 mg, 86%) whose NMR data were consistent to those reported in the literature.[6b] ^{1}H NMR (300 MHz, $CDCl_3$) δ = 8.22 – 8.05 (m, 2H, *o*-H phenyl), 7.69 – 7.59 (m, 1H, *p*-CH phenyl), 7.55 – 7.46 (m, 2H, *m*-H phenyl), 6.79 (s, 1H, C=CH), 3.86 (s, 3H, OCH_3), 3.72 (s, 3H, OCH_3). $^{13}C\{^1H\}$ NMR (75 MHz, $CDCl_3$) δ = 163.9 (C=O), 163.3 (C=O), 161.8 (C=O), 147.1 (C=CH), 134.2 (Cq), 130.6 (CH_{Ar}), 128.8 (CH_{Ar}), 128.3 (CH_{Ar}), 117.3 (C=CH), 53.4 (CH_3), 52.3 (CH_3).

(*Z*)-1-Phenylprop-1-en-2-yl benzoate (**2.31**): vinyl ester **2.31** was synthesised following GP1 using benzoic acid (61.1 mg, 0.5 mmol), 1-propyn-1-yl-benzene (58.1 mg, 0.5 mmol), and [{Au(IPr)}$_2$(μ-OH)][BF_4] **2.1** (3,2 mg, 0.5 mol%, 2.5 μmol). The reaction was stirred for 1.5 h at 80 °C.The pure product was obtained as an off-white powder (118 mg, 99%) whose NMR data were consistent to those reported in the literature.[7a] ^{1}H NMR (400 MHz, $CDCl_3$) δ = 8.16 – 8.11 (m, 2H, CH_{Ar}), 7.66 – 7.58 (m, 1H, CH_{Ar}), 7.53 – 7.48 (m, 3H, CH_{Ar}), 7.41 – 7.37 (m, 2H, CH_{Ar}), 7.25 – 7.20 (m, 2H), 7.18 – 7.13 (m, 1H, CH_{Ar}), 6.07 (s, 1H, C=CH), 2.21 (d, *J* = 1.0, 3H, CH_3). $^{13}C\{^1H\}$ NMR (101 MHz, $CDCl_3$) δ = 164.3 (C=O), 146.5 (C=CH), 134.5 (Cq), 133.8 (Cq), 133.6 (Cq), 130.3 (CH_{Ar}), 130.2

(CH_{Ar}), 129.7 (CH_{Ar}), 128.7 (CH_{Ar}), 128.6 (CH_{Ar}), 128.5 (CH_{Ar}), 128.3 (CH_{Ar}), 127.1 (CH_{Ar}), 124.4 (CH_{Ar}), 117.0 (C=CH), 20.9 (CH_3).

(*Z*)-1,3-Diphenylprop-1-en-2-yl benzoate (**2.32**): vinyl ester **2.32** was synthesised following GP1 using benzoic acid (30.5 mg, 0.25 mmol, 1 equiv.), 1,3-diphenyl-1-propyne (63.8 mg, 0.25 mmol), and [{Au(IPr)}$_2$(μ-OH)][BF_4] **2.1** (3.2 mg, 1 mol%, 2.5 μmol). The reaction was stirred for 19 h at 80 °C. The pure product was obtained as an off-white powder (70.9 mg, 89%) whose NMR data were consistent to those reported in the literature.[35] ^{1}H NMR (400 MHz, $CDCl_3$) δ = 8.07 – 8.02 (m, 2H, H_{Ar}), 7.54 – 7.44 (m, 2H, H_{Ar}), 7.41 – 7.35 (m, 2H, H_{Ar}), 7.34 – 7.30 (m, 4H, H_{Ar}), 7.21 (ddd, *J* = 8.1, 7.1, 1.0, 2H, H_{Ar}), 7.18 – 7.12 (m, 1H, H_{Ar}), 6.06 (s, 1H, C=CH), 3.84 (d, *J*=1.0, 2H, CH_2C=C). ^{13}C{^{1}H} NMR (101 MHz, $CDCl_3$) δ = 164.4 (C=O), 149.0 (C=CH), 137.2 (Cq), 134.2 (Cq), 133.6 (Cq), 130.2 (CH_{Ar}), 129.6 (CH_{Ar}), 129.4 (CH_{Ar}), 128.7 (CH_{Ar}), 128.7 (CH_{Ar}), 128.5 (CH_{Ar}), 127.3 (CH_{Ar}), 126.9 (CH_{Ar}), 117.9 (C=CH), 40.9 (CH_2).

(*Z*)-4-(Benzyloxy)but-2-en-2-yl benzoate (**2.33**): vinyl ester **2.33** was synthesised following GP1 using benzoic acid (61.1 mg, 0.5 mmol), benzyl-1-propynyl ether (73.1 mg, 0.5 mmol), and [{Au(IPr)}$_2$(μ-OH)][BF_4] **2.1** (3.2 mg, 0.5 mol%, 2.5 μmol). The reaction was stirred for 16 h at 80 °C. The pure product was obtained as a brown oil (140 mg, >99%). ^{1}H NMR (400 MHz, $CDCl_3$) δ = 8.07 – 8.02 (m, 2H, *o*-H phenyl), 7.64 – 7.57 (m, 1H, *p*-H phenyl), 7.50 – 7.43 (m, 2H, *m*-H phenyl), 7.40 – 7.18 (m, 5H, H Benzyl), 5.39 (tq, *J* = 6.8, 1.1, 1H, C=CH), 4.47 (s, 2H, $OCH_2(C_6H_5)$), 4.03 (dq, *J* = 6.8, 1.1, 2H, C=CHCH_2), 2.06 (q, *J* = 1.1, 3H, CH_3). ^{13}C{^{1}H} NMR (101 MHz, $CDCl_3$) δ = 164.4 (C=O), 148.5 (Cq), 138.3 (Cq), 133.6 (CH_{Ar}), 130.1 (CH_{Ar}), 129.5 (CH_{Ar}), 128.6 (CH_{Ar}), 128.5 (CH_{Ar}), 128.4 (CH_{Ar}), 127.9 (CH_{Ar}), 127.7 (CH_{Ar}), 127.1 (CH_{Ar}), 114.3 (C=CH), 72.2 ($OCH_2(C_6H_5)$), 64.2 (C=CHCH_2), 19.95 (CH_3). HRMS (NSI) Calcd (%) for $C_{18}H_{22}O_3N$ ($M+NH_4^+$) 300.1594, found 300.1590.

(*Z*)-3-Ethoxy-3-oxo-1-phenylprop-1-en-1-yl benzoate (**2.34**): vinyl ester **2.34** was synthesised following GP1 using benzoic acid (61.1 mg, 0.5 mmol), ethyl phenylpropiolate (87.1 mg, 0.5 mmol), and [{Au(IPr)}$_2$(μ-OH)][BF_4] **2.1** (3.2 mg, 0.5 mol%, 2.5 μmol). The reaction was stirred for 6 h at 80 °C. The pure product was obtained as an off-white powder (128.9 mg, 87%) whose NMR data were consistent to those reported in the literature.[36] ^{1}H NMR (400 MHz $CDCl_3$) δ = 8.27 – 8.20 (m, 2H, H_{Ar}), 7.68

– 7.62 (m, 4H, H_{Ar}), 7.56 – 7.50 (m, 2H, H_{Ar}), 7.45 – 7.37 (m, 2H, H_{Ar}), 6.38 (s, 1H, C=CH), 4.13 (q, *J* = 7.1, 2H, CH_2CH_3), 1.15 (t, *J* = 7.1, 2H, CH_2CH_3). $^{13}C\{^1H\}$ NMR (101 MHz, $CDCl_3$) δ = 163.8 (C=O), 163.6 (C=O), 157.6 (C=CH), 133.5 (Cq), 133.85 (Cq), 133.3 (CH_{Ar}), 130.2 (CH_{Ar}), 128.5 (CH_{Ar}), 125.8 (CH_{Ar}), 125.8 (CH_{Ar}), 106.7 (C=CH), 60.4 (CH_2), 20.98 (CH_3).

2-(4-Acetylphenyl)-1-phenylvinyl benzoate (**2.35**): vinyl ester **2.35** was synthesised following GP1 using benzoic acid (61.1 mg, 0.5 mmol), 4'-phenylethynyl acetophenone (110.1 mg, 0.5 mmol), and $[\{Au(IPr)\}_2(\mu\text{-}OH)][BF_4]$ **2.1** (3.2 mg, 0.5 mol%, 2.5 μmol). The reaction was stirred for 8.5 h at 80 °C. The desired products were obtained as a mixture of regioisomers (4:1) as a brown/orange powder (160.9 mg, 94%). ^1H NMR (400 MHz, $CDCl_3$) δ = 8.24 (ddd, *J* = 8.5, 2.9, 1.3, 8H, H_{Ar}), 7.99 – 7.94 (m, 2H, H_{Ar}), 7.89 – 7.84 (m, 5H, H_{Ar}), 7.73 – 7.66 (m, 6H, H_{Ar}), 7.66 – 7.51 (m, 22H, H_{Ar}), 7.42 – 7.35 (m, 8H, H_{Ar}), 7.34 – 7.27 (m, 2H, H_{Ar}), 7.26 – 7.21 (m, 1H, H_{Ar}), 6.92 (s, 1H, C=CH), 6.85 (s, 3H, C=CH), 2.60 (s, 3H, $COCH_3$), 2.55 (s, 8H, $COCH_3$). $^{13}C\{^1H\}$ NMR (101 MHz, $CDCl_3$) δ = 197.6 ($COCH_3$), 164.3 (CO_2Ph minor), 164.2 (CO_2Ph major), 148.8 (Cq), 145.7 (Cq), 140.3 (Cq), 139.2 (Cq), 136.9 (Cq), 135.9 (Cq), 135.3 (Cq), 134.2 (CH_{Ar}), 133.9 (Cq), 130.4 (CH_{Ar}), 129.4 (CH_{Ar}), 129.1 (CH_{Ar}), 129.0 (CH_{Ar}), 128.9 (CH_{Ar}), 128.9 (CH_{Ar}), 128.8 (CH_{Ar}), 128.4 (CH_{Ar}), 125.2 (CH_{Ar}), 124.9 (CH_{Ar}), 119.5 (C=CH minor), 116.3 (C=CH major), 26.8 ($COCH_3$ minor), 26.7 ($COCH_3$ major). HRMS (NSI) Calcd (%) for $C_{23}H_{19}O_3$ ($M+H^+$) 343.1329, found 343.1330.

2-Methylhexa-1,3-dien-3-yl benzoate (**2.36**): vinyl ester **2.36** was synthesised following GP1 using benzoic acid (61.1 mg, 0.5 mmol, 1 equiv.), 1-hexen-3-yne-2-methyl (47.1 mg, 0.5 mmol), and $[\{Au(IPr)\}_2(\mu\text{-}OH)][BF_4]$ **2.1** (3.2mg, 0.5 mol%, 2.5 μmol). The reaction was stirred for 2 h at 80 °C. The desired products were obtained as a mixture of regioisomers (4:1) as a brown oil (102.7 mg, 95%). ^1H NMR (300 MHz, $CDCl_3$) δ = 8.21 – 8.15 (m, 2H, H_{Ar}), 8.14 – 8.08 (m, 6H, H_{Ar}), 7.61 (ddt, *J* = 6.8, 5.6, 1.3, 3H, H_{Ar}c), 7.53 – 7.44 (m, 8H, H_{Ar}), 5.70 (d, *J* = 1.0, 2H, C=CH major), 5.54 (t, *J* = 7.3, 1H, C=CH minor), 4.94 (dd, *J* = 34.6, 21.7, 10H, CH_2), 2.45 – 2.35 (m, 5H, CH_2CH_3), 2.16 – 2.02 (m, 2H, CH_2CH_3), 1.98 (d, *J* = 1.1, 3H, CH_2=CCH_3), 1.86 (dd, *J* = 1.5, 0.8, 8H, CH_2=CCH_3), 1.12 (t, *J* = 7.5, 8H, CH_3 major), 1.02 (t, *J* = 7.6, 3H, CH_3 minor).$^{13}C\{^1H\}$ NMR (101 MHz, $CDCl_3$) δ = 164.7 (CO), 164.4 (CO), 150.3 (Cq), 146.9 (Cq), 139.2

(Cq), 136.9 (Cq), 133.5 (CH_{Ar}), 133.4 (CH_{Ar}), 130.2 (CH_{Ar}), 130.1 (CH_{Ar}), 130.0 (CH_{Ar}), 129.8 (CH_{Ar}), 129.5 (CH_{Ar}), 128.7 (CH_{Ar}), 128.6 (CH_{Ar}), 121.1 (C=CH minor), 117.6 (C=CH major), 116.8 ($C=CH_2$ major), 111.84 ($C=CH_2$ minor), 27.6, 22.2, 19.8, 19.7, 13.6 (CH_3 minor), 11.6 (CH_3 major). HRMS (NSI) Calcd (%) for $C_{14}H_{17}O_2$ ($M+H^+$) 217.1223, found 217.1228.

α-Benzoyloxystyrene (**2.38**) and (*Z*)-β-benzoyloxystyrene (**2.39**): vinylesters **2.38** and **2.39** were synthesised following a variation of **GP1** with phenylacetylene (0.5 mmol), benzoic acid (0.5 mmol) and **2.1** (12.7 mg, 2 mol%, 10 μmol) in THF at 80 °C. Partial conversion into products, as inseparable isomers mixture 2:1, was found after 18 h reaction (53 mg, 46%) whose NMR data were consistent to those found in literature.[6b] ^{1}H NMR (300 MHz, $CDCl_3$) δ = 8.27 – 8.12 (m, 4H, H_{Ar}), 7.66 (ddt, *J* = 11.0, 6.7, 1.5 Hz, 3H,H_{Ar}), 7.58 – 7.49 (m, 7H, H_{Ar}), 7.48 – 7.26 (m, 6H, H_{Ar}), 5.87 (d, *J* = 7.2 Hz, 1H, **2.39**), 5.61 (d, *J* = 2.2 Hz, 1H, **2.38**), 5.18 (d, *J* = 2.2 Hz, 1H, **2.38**).

2.5.2. General procedure for the gold(I)-catalysed cyclisation of alkynoic acids GP2:

In a scintillation vial, the alkynoic acid (0.25-1 mmol) and [{Au(IPr)}$_2$(μ-OH)][BF_4] **2.1** (25 ppm-1 mol%) or [Au(OH)(IPr)] **2.2** (0.2 mol%), were stirred in absence of solvent or in CH_2Cl_2 at room temperature or 65 °C (400 rpm). The reaction was monitored by ^{1}H NMR spectroscopy or GC until complete cyclisation of the alkynoic acid (5 min-48 h). After the reaction was completed the mixture was diluted with Et_2O or pentane (1 mL), filtered through a short plug of $MgSO_4$ and concentrated under vacuum. The residue was then purified by pentane washing (3×5mL) to afford the corresponding product.

5-Methylenedihydrofuran-2(3*H*)-one (**2.41**): γ-lactone **2.41** was synthesised following GP2 with 4-pentynoic acid (49.1 mg, 0.5 mmol) catalysed by **2.1**, stock solution from 0.1 mol% ($5\cdot10^{-4}$ M) of **2.1** (0.64 mg in 10 mL of CH_2Cl_2) to 25 ppm, $1.25\cdot10^{-5}$mmol, 25 μL of the stock solution) afforded product **2.41** (44.9 mg, 92%) after 5 mins as a colourless oil whose NMR data are consistent with those reported in literature.[18e] ^{1}H NMR (400 MHz, $CDCl_3$) δ = 4.77–4.72 (m, 1H, $C=CH_2$), 4.34–4.27 (m, 1H, $C=CH_2$), 2.92–2.83 (m, 2H, CH_2), 2.72–2.62 (m, 2H, CH_2). ^{13}C{^{1}H} NMR (100 MHz, $CDCl_3$) δ = 175.0 (C=O), 155.7 ($C=CH_2$), 88.9 ($C=CH_2$), 28.1 (CH_2), 25.2 (CH_2).

6-Methylenetetrahydro-2*H*-pyran-2-one (**2.46**): δ-lactone **2.46** was synthesised following GP2 from 5-hexynoic acid (49.1 mg, 0.5 mmol) catalysed by **2.1** (0.1 mol%, 0.64 mg) afforded, after 1 h, product **2.46** (52.7 mg, 94%) as a colourless oil whose NMR data are consistent with those reported in literature.[18g] ^{1}H NMR (400 MHz, $CDCl_3$) δ = 4.64 (dt, *J* = 1.5, 0.8, 1H, CH), 4.29 (q, *J* = 1.3, 1H, CH), 2.63 (t, *J* = 6.8, 2H, CH_2), 2.51–2.44 (m, 2H, CH_2), 1.87 (p, *J* = 6.7, 2H, CH_2). ^{13}C{^{1}H} NMR (126 MHz, $CDCl_3$) δ = 168.2 (C=O), 155.3 (C=CH_2), 93.8 (C=CH_2), 30.3 (CH_2), 26.8 (CH_2), 18.6 (CH_2).

7-Methyleneoxepan-2-one (**2.48**): ε-lactone **2.48** was synthesised following GP2 from 6-heptynoic acid (31.5 mg, 0.25 mmol) catalysed by **2.1** (3.19 mg, 1 mol%) afforded, after 5 h at 65 °C in CH_2Cl_2 (0.25 M), product **2.48** (24.6 mg, 78%) as a colourless oil, whose NMR data were consistent with those reported in literature.[18g] ^{1}H NMR (400 MHz, $CDCl_3$) δ = 4.83 (d, *J* = 1.3, 1H), 4.69 (d, *J* = 1.2, 1H), 2.61 (ddd, *J* = 7.9, 3.2, 1.8, 2H), 2.36 (ddd, *J* = 6.5, 4.3, 2.3, 2H), 1.81 (dt, *J* = 6.4, 3.0, 4H). ^{13}C{^{1}H} NMR (101 MHz, $CDCl_3$) δ = 172.8, 157.8, 102.5, 33.9, 32.9, 29.3, 23.1.

methyl 5-methylene-2-oxotetrahydrofuran-3-carboxylate (**2.49**): γ-lactone **2.49** was synthesised following GP2 from dimethyl 2-(prop-2-yn-1-yl) malonate (39.0 mg, 0.25 mmol) catalysed by **1a**, stock solution from 0.1 mol% ($2.5\cdot10^{-4}$ M) of **2.1** (0.313 mg in 10 mL of CH_2Cl_2) to 100 ppm ($2.5\cdot10^{-5}$ mmol) 1 mL of the stock solution, afforded product **2.49** (37.2 mg, 95%) as a pale yellow oil whose NMR data are consistent with those reported in literature.[37] ^{1}H NMR (400 MHz, $CDCl_3$) δ = 4.81 (ddd, *J* = 2.9, 2.3, 1.8, 1H, C=CH_2), 4.40 (ddd, *J* = 2.9, 2.0, 1.6, 1H, C=CH_2), 3.82 (s, 3H, OCH_3), 3.79–3.72 (m, 1H, CH_2), 3.30 (ddt, *J* = 16.6, 7.7, 2.2, 1H, CH_2), 3.09 (ddt, *J* = 16.6, 10.4, 1.7, 1H, CH_2). ^{13}C{^{1}H} NMR (100 MHz, $CDCl_3$) δ = 169.6 (C=O), 167.4 (C=O), 153.2 (Cq), 90.0 (CH_2), 53.5 (OCH_3), 46.3 (CH), 29.5 (CH_2).

Methyl (*Z*)-5-benzylidene-2-oxotetrahydrofuran-3-carboxylate (**2.50**): γ-lactone **2.50** was synthesised following GP2 from 2-(methoxycarbonyl)-5-phenylpent-4-ynoic acid (58.1 mg, 0.25 mmol) catalysed by **2.1** (0.1 mol%, 0.32 mg) afforded, after 18 h, product **2.50** (56.5 mg, 97%) as a brown oil whose NMR data are consistent with those reported in literature.[18d] ^{1}H NMR (500 MHz, $CDCl_3$) δ = 7.57–7.51 (m, 2H, H_{Ar}), 7.33 (dd, *J* = 8.4, 7.0, 2H, H_{Ar}), 7.26–7.19 (m, 1H, H_{Ar}), 5.63 (s, 1H, C=CH), 3.87–3.77 (m, 3H, CH_3), 3.48 (ddd, *J* = 16.6, 7.7, 2.0, 1H, CH_2), 3.25 (ddd, *J* = 16.6, 10.4, 1.5, 2H, CH_2). ^{13}C{^{1}H} NMR

(101 MHz, $CDCl_3$) δ = 169.7 (C=O), 167.4 (C=O), 145.5 (C=CH), 133.5 (Cq), 128.7 (CH_{Ar}), 128.6 (CH_{Ar}), 127.3 (CH_{Ar}), 106.0 (C=CH), 53.6 (OCH_3), 45.4 (CH), 30.7 (CH_2).

(*Z*)-5-Ethylidenedihydrofuran-2(3*H*)-one and 6-methyl-3,4-dihydro-2*H*-pyran-2-one (**2.51**): γ-lactone **2.51** was synthesised following GP2 from 5-hexynoic acid (56.1 mg, 0.5 mmol) catalysed by **2.1** (0.1 mol%, 0.64 mg) afforded *exo* and *endo* mixture of **2.51** (52.7 mg, 94%) in a ratio of 7:1 after 5 min as a colourless oil, whose NMR data are consistent with those reported in literature.[14b] *Exo* and *endo* products **2.51** were synthesised using **2.2** (0.2 mol%, 0.60 mg) and were obtained in a 1:1.7 ratio. ^{1}H NMR (500 MHz, $CDCl_3$) δ = 5.02–4.96 (m, 1H, *endo*), 4.60 (qt, *J* = 6.9, 1.8, 7H, *exo*), 2.79 (tp, *J* = 8.6, 1.8, 14H, *exo*), 2.68–2.59 (m, 14H, *exo*), 2.56 (t, *J*=7.6, 1H, *endo*), 2.27 (dddt, *J* = 7.6, 6.1, 4.3, 2.0, 1H, *endo*), 1.87 (q, *J* = 1.7, 1H, *endo*), 1.65 (dt, *J*=6.9, 2.0, 25H, CH_3). ^{13}C{^{1}H} NMR (126 MHz, $CDCl_3$) δ = 175.3 (C=O), 169.3 (C=O), 150.0 (C=CH), 148.4 (C=CH), 99.9 (C=CH), 99.2 (C=CH), 40.9 (CH_2), 28.4 (CH_2), 28.1 (CH_2), 24.9 (CH_2), 18.8 (CH_3), 18.7 (CH_3), 10.4 (CH_3).

Methyl (*Z*)-5-ethylidene-2-oxotetrahydrofuran-3-carboxylate and methyl 6-methyl-2-oxo-3,4-dihydro-2H-pyran-3-carboxylate (**2.52**): γ-lactone **2.52** was synthesised following GP2 from 2-(methoxycarbonyl)hex-4-ynoic acid (42.5 mg, 0.25 mmol) catalysed by **2.1**, stock solution from 0.1 mol% ($2.5\cdot10^{-4}$ M) of **2.1** (0.313 mg in 10 mL of CH_2Cl_2) to 100 ppm, $2.5\cdot10^{-5}$ mmol, 1 mL of the stock solution afforded, after 5 min, *exo*:*endo* products in a 4:1 ratio (41.7 mg, 98%) as a colourless oil.^{1}H NMR (500 MHz, $CDCl_3$) δ = 5.02 (td, *J* = 4.4, 1.2, 1H, *endo*), 4.71 (qt, *J* = 6.9, 1.8, 4H, *exo*), 3.81 (s, 11H, *exo* and *endo*), 3.79 (s, 3H, *exo*), 3.72 (dd, *J* = 10.4, 7.9, 4H, *exo*), 3.55 (dd, *J* = 8.6, 7.0, 1H, 4d), 3.28–3.19 (m, 3H, *exo*), 3.02 (ddp, *J* = 15.3, 10.4, 1.6, 4H, *exo*), 2.74 (dddd, *J* = 16.9, 8.5, 4.2, 2.0, 1H, *endo*), 2.52–2.42 (m, 1H, *endo*), 1.89 (q, *J* = 1.7, 3H, *endo*), 1.68 (dt, *J* = 6.9, 1.9, 11H, 4d). ^{13}C{^{1}H} NMR (126 MHz, $CDCl_3$) δ = 169.9 (*exo*), 168.8 (*endo*), 167.7 (*exo*), 165.3 (*endo*), 150.4 (*endo*), 145.9 (*exo*), 100.6 (*exo*), 98.8 (*endo*), 53.4 (*exo*), 53.1 (*endo*), 46.3 (*exo*), 45.6 (*endo*), 29.4 (*exo*), 22.5 (*endo*), 18.6 (*endo*), 10.6 (*exo*). HRMS (GC/cIMS) Calcd (%) for $C_8H_{14}NO_4$ ($M+NH_4^+$) 188.0923, found 188.0926.

Methyl 7-methylene-2-oxooxepane-3-carboxylate (**2.63**): ε-lactone **2.63** was synthesised following GP2 from 2-(methoxycarbonyl) hept-6-ynoic acid (23.0 mg, 0.125 mmol) catalysed by **2.1** (3.2 mg, 2 mol%,) afforded, after 24 h at 65 °C in CH_2Cl_2 (0.25 M),

product **2.63** (21.1 mg, 91%) as a colourless viscous oil. ^{1}H NMR (400 MHz, C_6D_6) δ = 4.46 (d, *J* = 1.3, 1H, CH_2), 4.11 (t, *J* = 0.9, 1H, CH), 3.45 (dd, *J* = 10.0, 3.6, 1H, CH_2), 3.37 (s, 3H, OCH_3), 1.81–1.62 (m, 3H, CH_2), 1.60–1.51 (m, 1H, CH_2), 1.27 (dtt, *J* = 14.2, 6.1, 4.1, 1H, CH_2), 0.99 – 0.85 (m, 1H, CH_2). ^{13}C{^{1}H} NMR (101 MHz, C_6D_6) δ = 169.0 (C=O), 168.1 (C=O), 157.3 (C=CH), 102.8 (C=CH), 52.1 (OCH_3), 49.6 (CH), 32.0(CH_2), 26.7(CH_2), 25.6(CH_2). HRMS (FTMS/pNSI) Calcd (%) for $C_9H_{13}O_4$ $[M+H]^+$ 185.0808, found 185.0806.

(*Z*)-7-(Bromomethylene)oxepan-2-one (**2.64**): ε-lactone **2.64** was synthesised following GP2 from 7-bromohept-6-ynoic acid (50.6 mg, 0.25 mmol) catalysed by **2.1** (6.37 mg, 2 mol%) afforded, after 24 h at 65 °C in CH_2Cl_2 (0.25 M), product **2.64** (41.0 mg, 80%) as an off-white solid. ^{1}H NMR (500 MHz, C_6D_6) δ = 5.04 (s, 1H, C=CH), 2.03–1.95 (m, 2H, CH_2), 1.63–1.54 (m, 3H, CH_2), 1.06–0.99 (m, 3H, CH_2), 0.92–0.86 (m, 3H, CH_2). ^{13}C{^{1}H} NMR (126 MHz, C_6D_6) δ = 169.6 (C=O), 153.7 (C=CH), 93.0 (C=CH), 33.7 (CH_2), 32.2 (CH_2), 32.1 (CH_2), 28.7 (CH_2), 22.3 (CH_2). HRMS (FTMS/pNSI) Calcd (%) for $C_8H_{13}O_2NBr$ $[M+NH_4]^+$ 222.0124, found 222.0126; m.p. = 67.5-68.3 °C. Suitable crystals were grown by slow diffusion of hexane into a saturated solution of **2.64** in Et_2O.

2.6. Bibliography

1. L. J. Gooßen, N. Rodríguez and K. Gooßen, *Angew. Chem., Int. Ed.*, 2008, **47**, 3100-3120.

2. a) F. Alonso, I. P. Beletskaya and M. Yus, *Chem. Rev.*, 2004, **104**, 3079-3160; b) M. Beller, J. Seayad, A. Tillack and H. Jiao, *Angew. Chem., Int. Ed.*, 2004, **43**, 3368-3398.

3. a) K. Tani and Y. Kataoka, in *Catalytic Heterofunctionalization*, Wiley-VCH Verlag GmbH, 2001, pp. 171-216; b) R. C. Larock and W. W. Leong, *Comprehensive Organic Synthesis*, Pergamon Press, Oxford, 1991.

4. a) H. Arakawa, M. Aresta, J. N. Armor, M. A. Barteau, E. J. Beckman, A. T. Bell, J. E. Bercaw, C. Creutz, E. Dinjus, D. A. Dixon, K. Domen, D. L. DuBois, J. Eckert, E. Fujita, D. H. Gibson, W. A. Goddard, D. W. Goodman, J. Keller, G. J. Kubas, H. H. Kung, J. E. Lyons, L. E. Manzer, T. J. Marks, K. Morokuma, K. M. Nicholas, R. Periana,

L. Que, J. Rostrup-Nielson, W. M. H. Sachtler, L. D. Schmidt, A. Sen, G. A. Somorjai, P. C. Stair, B. R. Stults and W. Tumas, *Chem. Rev.*, 2001, **101**, 953-996; b) F. Simal, A. Demonceau and A. F. Noels, *Angew. Chem. Int. Ed.*, 1999, **38**, 538-540.

5. a) C. Bruneau, M. Neveux, Z. Kabouche, C. Ruppin and P. H. Dixneuf, *Synlett*, 1991, 755-763; b) M. Kawasaki, M. Goto, S. Kawabata and T. Kometani, *Tetrahedron: Asymmetry*, 2001, **12**, 585-596; c) W. B. Motherwell and L. R. Roberts, *J. Chem. Soc., Chem. Commun.*, 1992, 1582-1583; d) Y. F. Wang, J. J. Lalonde, M. Momongan, D. E. Bergbreiter and C. H. Wong, *J. Am. Chem. Soc.*, 1988, **110**, 7200-7205; e) K. E. Koenig, G. L. Bachman and B. D. Vineyard, *J. Org. Chem.*, 1980, **45**, 2362-2365; f) C. Bruneau and P. H. Dixneuf, *Chem. Commun.*, 1997, 507-512; g) T. Kano, K. Sasaki and K. Maruoka, *Org. Lett.*, 2005, **7**, 1347-1349; h) K. D. Otley and J. A. Ellman, *Org. Lett.*, 2015, **17**, 1332-1335; i) G. A. Grasa, R. M. Kissling and S. P. Nolan, *Org. Lett.*, 2002, **4**, 3583-3586; j) Y. Hatamoto, S. Sakaguchi and Y. Ishii, *Org. Lett.*, 2004, **6**, 4623-4625.

6. a) T. Mitsudo, Y. Hori, Y. Yamakawa and Y. Watanabe, *J. Org. Chem.*, 1987, **52**, 2230-2239; b) M. Rotem and Y. Shvo, *J. Organomet. Chem.*, 1993, **448**, 189-204; c) M. Rotem and Y. Shvo, *Organometallics*, 1983, **2**, 1689-1691; d) C. Ruppin and P. H. Dixneuf, *Tetrahedron Lett.*, 1986, **27**, 6323-6324; e) L. J. Goossen, J. Paetzold and D. Koley, *Chem. Commun.*, 2003, 706-707; f) M. Kawatsura, J. Namioka, K. Kajita, M. Yamamoto, H. Tsuji and T. Itoh, *Org. Lett.*, 2011, **13**, 3285-3287.

7. a) N. Tsukada, A. Takahashi and Y. Inoue, *Tetrahedron Lett.*, 2011, **52**, 248-250; b) T. Wakabayashi, Y. Ishii, T. Murata, Y. Mizobe and M. Hidai, *Tetrahedron Lett.*, 1995, **36**, 5585-5588.

8. a) S. Saha, T. Ghatak, B. Saha, H. Doucet and J. K. Bera, *Organometallics*, 2012, **31**, 5500-5505; b) M. Nishiumi, H. Miura, K. Wada, S. Hosokawa and M. Inoue, *Adv. Synth. Cat.*, 2010, **352**, 3045-3052.

9. S. Karabulut, B. Ö. Öztürk and Y. İmamoğlu, *J. Organomet. Chem.*, 2010, **695**, 2161-2166.

10. P. Roembke, H. Schmidbaur, S. Cronje and H. Raubenheimer, *J. Mol. Cat. A.: Chem.*, 2004, **212**, 35-42.

11. B. C. Chary and S. Kim, *J. Org. Chem.*, 2010, **75**, 7928-7931.

12. Y. Wang, Z. Wang, Y. Li, G. Wu, Z. Cao and L. Zhang, *Nat. Commun.*, 2014, **5**, 3470-3478.

13. a) E. Genin, P. Y. Toullec, S. Antoniotti, C. Brancour, J.-P. Genêt and V. Michelet, *J. Am. Chem. Soc.*, 2006, **128**, 3112-3113; b) D. Bouyssi, J. Gore and G. Balme, *Tetrahedron Lett.*, 1992, **33**, 2811-2814; c) A. Arcadi, A. Burini, S. Cacchi, M. Delmastro, F. Marinelli and B. R. Pietroni, *J. Org. Chem.*, 1992, **57**, 976-982; d) J. Garcia-Alvarez, J. Diez and C. Vidal, *Green Chem.*, 2012, **14**, 3190-3196; e) R. Rossi, F. Bellina, M. Biagetti, A. Catanese and L. Mannina, *Tetrahedron Lett.*, 2000, **41**, 5281-5286; f) N. Nebra, J. Monot, R. Shaw, B. Martin-Vaca and D. Bourissou, *ACS Catal.*, 2013, **3**, 2930-2934; g) R. Rossi, F. Bellina, C. Bechini, L. Mannina and P. Vergamini, *Tetrahedron*, 1998, **54**, 135-156; h) T. Wakabayashi, Y. Ishii, K. Ishikawa and M. Hidai, *Angew. Chem., Int. Ed. Engl.*, 1996, **35**, 2123-2124.

14. a) T. B. Marder, D. M. T. Chan, W. C. Fultz, J. C. Calabrese and D. Milstein, *J. Chem. Soc., Chem. Commun.*, 1987, 1885-1887; b) D. M. T. Chan, T. B. Marder, D. Milstein and N. J. Taylor, *J. Am. Chem. Soc.*, 1987, **109**, 6385-6388.

15. A. Jellal, J. Grimaldi and M. Santelli, *Tetrahedron Lett.*, 1984, **25**, 3179-3182.

16. C. Sun, Y. Fang, S. Li, Y. Zhang, Q. Zhao, S. Zhu and C. Li, *Org. Lett.*, 2009, **11**, 4084-4087.

17. a) P. Pale and J. Chuche, *Tetrahedron Lett.*, 1987, **28**, 6447-6448; b) J. A. Marshall, M. A. Wolf and E. M. Wallace, *J. Org. Chem.*, 1997, **62**, 367-371; c) V. Dalla and P. Pale, *New J. Chem.*, 1999, **23**, 803-805.

18. a) M. J. Rodriguez-Alvarez, C. Vidal, J. Diez and J. Garcia-Alvarez, *Chem. Commun.*, 2014, **50**, 12927-12929; b) C. A. Sperger and A. Fiksdahl, *J. Org. Chem.*, 2010, **75**, 4542-4553; c) T. Luo, M. Dai, S.-L. Zheng and S. L. Schreiber, *Org. Lett.*, 2011, **13**, 2834-2836; d) E. Tomás-Mendivil, P. Y. Toullec, J. Díez, S. Conejero, V. Michelet and V. Cadierno, *Org. Lett.*, 2012, **14**, 2520-2523; e) E. Tomás-Mendivil, P. Y. Toullec, J. Borge, S. Conejero, V. Michelet and V. Cadierno, *ACS Catal.*, 2013, **3**, 3086-3098; f) M. Ferré, X. Cattoën, M. WongChiMan and R. Pleixats, *ChemCatChem*, 2016, **8**, 2824-2831; g) H. Harkat, J.-M. Weibel and P. Pale, *Tetrahedron Lett.*, 2006, **47**, 6273-6276; h) H. Harkat, A. Y. Dembelé, J.-M. Weibel, A. Blanc and P. Pale, *Tetrahedron*, 2009, **65**, 1871-1879.

19. a) H. Imagawa, Y. Fujikawa, A. Tsuchihiro, A. Kinoshita, T. Yoshinaga, H. Takao and M. Nishizawa, *Synlett*, 2006, 639-641; b) N. Á. Espinosa-Jalapa, D. Ke, N. Nebra, L.

Le Goanvic, S. Mallet-Ladeira, J. Monot, B. Martin-Vaca and D. Bourissou, *ACS Catal.*, 2014, **4**, 3605-3611.

20. S. Gaillard, J. Bosson, R. S. Ramón, P. Nun, A. M. Z. Slawin and S. P. Nolan, *Chem. Eur. J.*, 2010, **16**, 13729-13740.

21. Y. Oonishi, A. Gómez-Suárez, A. R. Martin and S. P. Nolan, *Angew. Chem. Int. Ed.*, 2013, **125**, 9949-9953.

22. R. M. P. Veenboer, A. Collado, S. Dupuy, T. Lebl, L. Falivene, L. Cavallo, D. B. Cordes, A. M. Z. Slawin, C. S. J. Cazin and S. P. Nolan, *Organometallics*, 2017, **36**, 2861-2869.

23. S. Gaillard, A. M. Z. Slawin and S. P. Nolan, *Chem. Commun.*, 2010, **46**, 2742-2744.

24. A. Gómez-Suárez, Y. Oonishi, S. Meiries and S. P. Nolan, *Organometallics*, 2013, **32**, 1106-1111.

25. a) P. de Frémont, N. Marion and S. P. Nolan, *J. Organomet. Chem.*, 2009, **694**, 551-560; b) R. M. P. Veenboer, D. Gasperini, F. Nahra, D. B. Cordes, A. M. Z. Slawin, C. S. J. Cazin and S. P. Nolan, *Organometallics*, 2017, **36**, 3645-3653.

26. L. Ricard and F. Gagosz, *Organometallics*, 2007, **26**, 4704-4707.

27. J. E. Baldwin, *J. Chem. Soc., Chem. Commun.*, 1976, 734-736.

28. A. Collado, A. Gómez-Suárez, A. R. Martin, A. M. Z. Slawin and S. P. Nolan, *Chem. Commun.*, 2013, **49**, 5541-5543.

29. a) R. M. Beesley, C. K. Ingold and J. F. Thorpe, *J. Chem. Soc., Trans.*, 1915, **107**, 1080-1106; b) C. K. Ingold, *J. Chem. Soc., Trans.*, 1921, **119**, 305-329.

30. CCDC = CCDC 1471000 contain the supplementary crystallographic data for **2.64**. These data can be obtained free of charge from The Cambridge Crystallographic Data Centre *via* https://www.ccdc.cam.ac.uk/structures/;

31. R. S. Ramón, S. Gaillard, A. Poater, L. Cavallo, A. M. Z. Slawin and S. P. Nolan, *Chem. Eur. J.*, 2011, **17**, 1238-1246.

32. A. Gómez-Suárez, R. S. Ramon, A. M. Z. Slawin and S. P. Nolan, *Dalton Trans.*, 2012, **41**, 5461-5463.

33. D. Gasperini, A. Collado, A. Goméz-Suárez, D. B. Cordes, A. M. Z. Slawin and S. P. Nolan, *Chem. Eur. J.*, 2015, **21**, 5403-5412.

34. J. Schranck, A. Tlili, H. Neumann, P. G. Alsabeh, M. Stradiotto and M. Beller, *Chem. Eur. J.*, 2012, **18**, 15592-15597.

35. W. M. Muir, P. D. Ritchie and D. J. Lyman, *J. Org. Chem.*, 1966, **31**, 3790-3793.

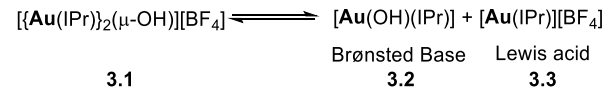
36. W.-J. Yoo and C.-J. Li, *J. Org. Chem.*, 2006, **71**, 6266-6268.

37. A. Nagendiran, O. Verho, C. Haller, E. V. Johnston and J.-E. Bäckvall, *J. Org. Chem.*, 2014, **79**, 1399-1405.

3. Probing the mechanism of the hydrocarboxylation of alkynes

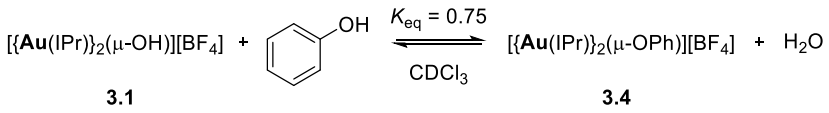
3.1. Introduction

Once the scope and limitations of the hydroacyloxylation (inter- and intramolecular) of alkynes were disclosed (Chapter 2), the mechanism of the reactions were investigated further. As already mentioned, a dual mechanism was hypothesised for the reactions analysed in the presence of a [{Au(IPr)}$_2$(μ-OH)][BF$_4$] (**3.1**); this species is believed to dissociate in solution into monocoordinated complexes,[1] a Brønsted base [Au(OH)(IPr)] (**3.2**)[2] and a Lewis acid species [Au(IPr)][BF$_4$] (**3.3**)[3] (Scheme 3.1).



Scheme 3.1. Dissociation of **3.1** into **3.2** and **3.3**.[1]

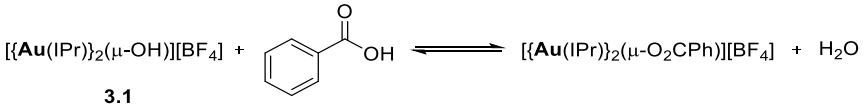
The dissociation of **3.1** in water to form [{Au(IPr)}$_2$(μ-O)][BF$_4$] Brønsted base, and H_3O^+ was discarded, because of the high barrier of 47.0 kcal mol^{-1} that needs to be overcome.[1] Previous reports into the hydrophenoxylation of alkynes showed, however, that a 3rd species might be involved in the catalytic cycle.[4] This hypothesis was confirmed by the isolation of a dinuclear gold phenolate compound [{Au(IPr)}$_2$(μ-OPh)][BF$_4$] (**3.4**),[4] which was in equilibrium with **3.1**, and phenol, with a K_{eq} = 0.75 ± 0.06, calculated in $CDCl_3$ at 298 K (Scheme 3.2).[5] Under catalytic conditions, such as with a large excess of phenol, the formation of **3.4** might be relevant, and most likely part of the pre-equilibrium of the catalytic cycle, acting as a catalyst "reservoir".



Scheme 3.2. Equilibrium between **3.1**, phenol and **3.4**.

Dinuclear gold phenolate **3.4** was prone to decomposition, and strictly anhydrous conditions had to be utilised for its isolation and use in the catalytic system.

A similar species, of the kind [{Au(IPr)}$_2$(μ-O$_2$CPh)][BF$_4$] (Scheme 3.3), was therefore envisaged as possibly involved in the catalytic cycle for the intermolecular hydroacyloxylation of internal alkynes.[6]



Scheme 3.3. Hypothesised formation of dinuclear gold carboxylate from **3.1**.

The use of carboxylate moieties as bridging ligands to metals is known. The carboxylate ion RCO^{2-} can coordinate in a number of different ways (Figure 3.1): a) as a monodentate ligand; b) as a chelating ligand, c) as a bridging bidentate ligand in different configurations (*syn-syn*, *anti-syn*, or *anti-anti*).[7]

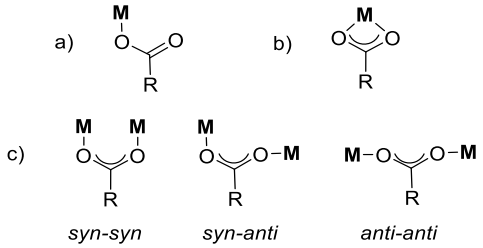
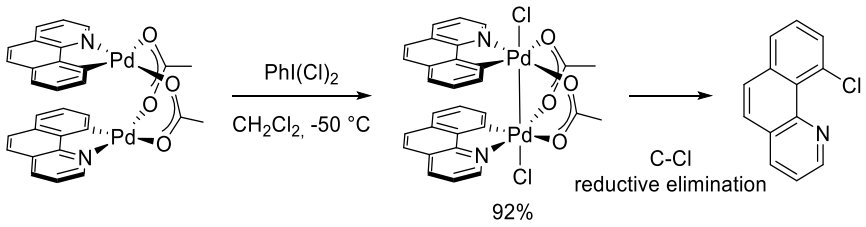


Figure 3.1. Mode of coordination of carboxylate ligands to metals:[7] a) monodentate; b) chelating; c) bridging bidentate ligand.

Concerning the bridging bidentate ligands (Figure 3.1, c), several examples have been reported where simple salts showed bridging coordination of the carboxylates; for example the commercially available [(CuO$_2$CCH$_3$)$_2$]$_n$, a dinuclear polymer, used for CuAAC.[8] [Pd$_3$(μ^2-OAc)$_6$] is another example of a carboxylate complex, whose structure with a bidentate acetate ligand was defined by solution analysis,[9] and finally proved in the solid state.[10] Its uses in catalysis are widespread,[11] and its chemistry in solution has been analysed to achieve the best performances in catalytic reactions.[12] Bridging carboxylate systems were observed in metal proteins, *e.g.* bacterial multicomponent monoxygenases;[13] these enzymes catalyse the oxidation of hydrocarbons by functionalisation of O$_2$.[14] Their binding site was studied, and characterised as having a dinuclear Fe(II) core with bridging acetate ligands. The bridging ligand was believed to be essential in mammalian proteins.[15]

Interesting well-defined complexes have been reported to date for Pd, Ru,[16] Os,[16a,17] Rh,[18] Mn, Fe,[19] Cu,[20] Ag[21]. Their chemistry was investigated, but some of these complexes date

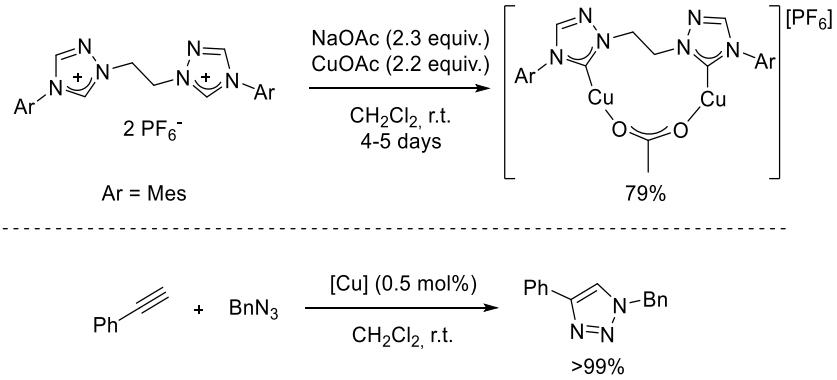
back to the 60s and 70s, when elucidation of their structures was the main interest.[22] Concerning palladium, in 2009 Ritter reported the oxidation of Pd(II) species to supramolecular Pd(III) compounds,[23,24] and the species promptly reductively eliminated to form C-Cl bond (Scheme 3.4).[25]



Scheme 3.4. Dinuclear Pd dicarboxylate complexes, and their oxidation as reported by Ritter and co-workers.[23]

Ruthenium η^2-carboxylate species were studied intensively by Shvo,[16b] who exploited them in the Ru catalysed hydrocarboxylation of terminal, and internal alkynes.[26] Other examples in the hydroformylation reaction are also known.[27]

The chemistry of copper carboxylate with supporting ancillary ligands has also been explored, first by Straub's group.[28,29] The authors reported an active catalyst in the copper catalysed azide-alkyne cycloaddition reaction (Cu-AAC) where two copper catalysts were linked by bis-triazolylidene ligand, and an acetate ligand (Scheme 3.5).

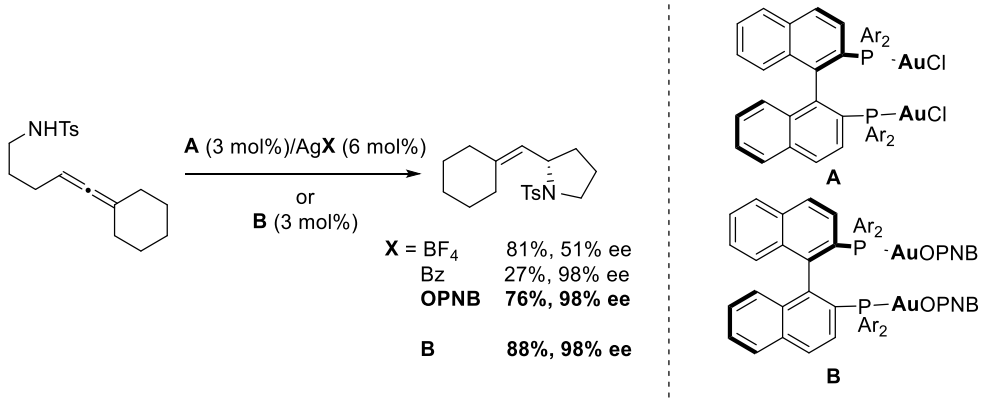


Scheme 3.5. Straub's dinuclear copper catalyst, and further application in the CuAAC.[28,29]

Further interesting findings came from Sadighi and co-workers, who reported on the insertion of CO_2 into $[\{Cu(IPr)\}_2(\mu\text{-}H)][BF_4]$ to obtain $[\{Cu(IPr)\}_2(\mu\text{-}O_2CH)][BF_4]$.[30]

To our knowledge, no examples of organometallic digold complexes bearing a bridging carboxylate moiety have been reported in the literature. Despite the knowledge of mononuclear carboxylate species,[31] there is only mention of dinuclear gold carboxylate species.[1,32] A dinuclear gold species bearing monodentate carboxylate ligands was used

by Toste and co-workers who investigated the Au(I) catalysed enantioselective hydroamination of allenes (Scheme 3.6).[33] A massive counter-ion effect[34] (section 1.6.2) was observed in this transformation: by using a benzoate anion, instead of a weakly coordinating BF_4, the enantioselectivity of the reaction increased dramatically, from 51% to 98% ee. Further increase in yield was obtained using a 4-nitrophenolbenzoate.



Scheme 3.6. Hydroamination of allenes reported by Toste and co-workers.[33]

This reaction was investigated by Lee and Kang who suggested that a dinuclear gold species with a bidentate carboxylate was involved as reaction intermediate (Figure 3.2, a).[35] The authors calculated that such a structure might be in equilibrium with the cationic complex after dissociation of the benzoate ligand. The latter is invoked as fundamental to ensure enantiocontrol of the reaction (b). However, the proposed dinuclear structure was never observed.

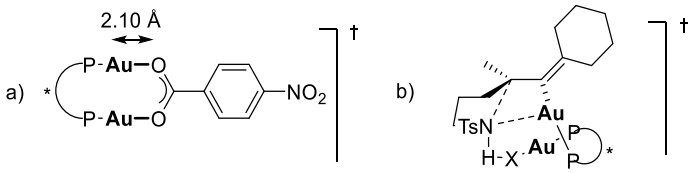
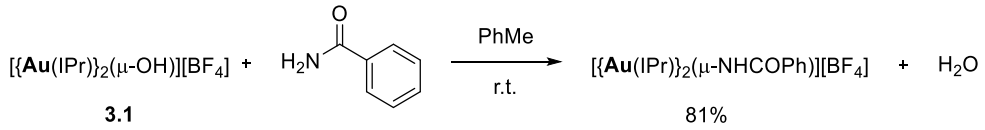


Figure 3.2. a) Computed dinuclear structure; b) transition state towards the S isomer (X = OC(O)(4-$NO_2C_6H_4$).[35]

The second mention of a digold acetate complex was reported by Nolan, and co-workers, however, the findings were not supported by experimental results.[1] In the same manuscript, the authors also isolated and characterised an amido dinuclear complex [{Au(IPr)}$_2$(μ-NHCOPh)][BF_4] (Scheme 3.7). This was found to be poorly active in the catalytic hydration of cyanides to amides, and it is a possible off-cycle species derived from product poisoning of the catalyst. The formation of this species was important to further define the dual activation nature of **3.1**.



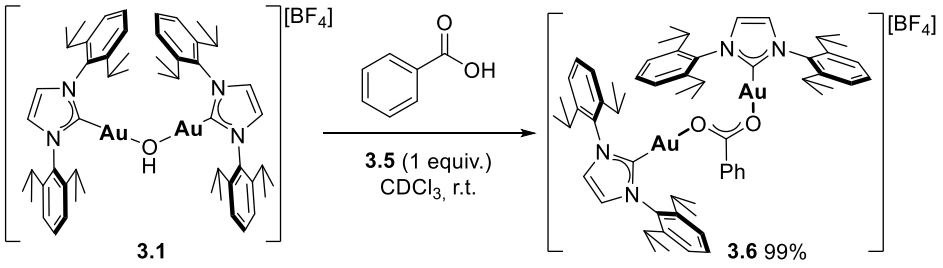
Scheme 3.7. Synthesis of dinuclear benzamido complex by Nolan and co-workers.[1]

With these premises, the formation of a dinuclear gold carboxylate complex from **3.1** was explored (Scheme 3.3). The possible involvement of the dinuclear species into the inter- and intramolecular hydrocarboxylation of alkynes was studied by means of stoichiometric, catalytic, kinetic and computational analysis; the results are discussed herein.

3.2. Results and discussion

3.2.1. Synthesis and characterisation of digold carboxylate complexes

Initial stoichiometric reactions were performed; by mixing digold hydroxide (**3.1**) with an equimolar amount of benzoic acid (**3.5**), in dry $CDCl_3$ and anhydrous conditions, the immediate formation of a new species was identified by ^{1}H NMR (Scheme 3.8). Full characterisation by NMR, and IR spectroscopy allowed us to identify the species as a dinuclear gold carboxylate [{Au(IPr)}$_2$(μ-O_2CPh)][BF_4] (**3.6**).



Scheme 3.8. Synthesis of **3.6** from **3.1**.

Intrigued by the formation of this species we investigated further into its chemistry. **3.6** could be obtained by reacting the dinuclear precursor **3.1** under air, and using technical grade solvents, such as CH_2Cl_2, PhMe, benzene, bromobenzene, THF. When subjected to these reaction conditions **3.1** was always converted in >99%. Even by grinding [{Au(IPr)}$_2$(μ-OH)][BF_4] with an equimolar amount of acid **3.5**, the formation of **3.6** could be observed by FTIR (ATR), and later confirmed by ^{1}H NMR spectroscopy ($CDCl_3$).

Analysis of the ^{1}H NMR spectra of **3.6** showed indicative signals; a 2:1 ratio between [Au(IPr)] units and benzoate signals was found, validating that the benzoate was coordinated to two gold centres. The aromatic signals of the benzoate group at 7.89, 7.22, and 7.19 ppm, shifted downfield compared to the free acid, and to the equivalent mononuclear gold carboxylate complex [Au(OC(O)Ph)(IPr)] (**3.7**) (the values for the latter were at 7.41, 7.27, and 6.88 ppm in $CDCl_3$).[36] Moreover, the $^{13}C\{^{1}H\}$ NMR spectrum showed an upfield shift of the carbenic signal of δ_C = 162.0 ppm for **3.6** compared to δ_C = 168.7 ppm for **3.7**, while closer to that of **3.1** with δ_C = 162.6 ppm. The FTIR (ATR) analysis showed the characteristic symmetrical, and asymmetrical stretching frequencies of O-C-O at 1525, and 1469 cm^{-1},[16b] in line with the frequency of carboxylate anions, while shorter wavenumbers compared to the carboxylate-Au(I) **3.7** (~ 1600-1650 cm^{-1}). Suitable crystals for X-ray diffraction analysis were grown by slow diffusion of pentane into a saturated solution of **3.6** in CH_2Cl_2. The thermal ellipsoid representation in Figure 3.3, validate the hypothesised bridging mode coordination of the carboxylate ion with the two [Au(IPr)] fragments. The crystallographic representation indicated that a *syn-anti* configuration of the metal-ligand fragments is preferred in the solid state, probably to accommodate the fragments around the carboxylate. The *syn-anti* preferential configuration of this complex prevents possible aurophilic interactions between the Au centres.

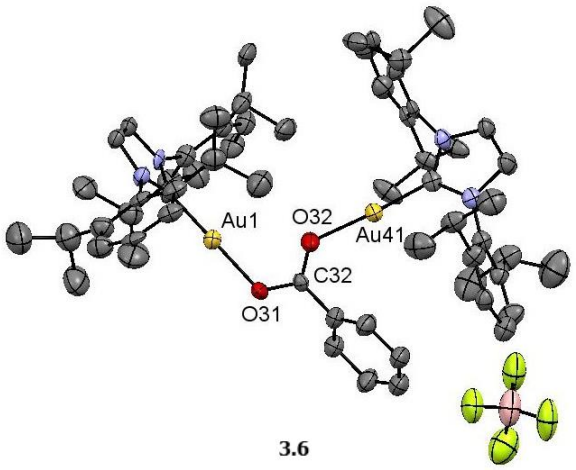


Figure 3.3. Thermal ellipsoid representation of **3.6** showing 50% probability. Most of H atom were omitted for clarity: Au-O 2.045(14) Å, 2.058(17) Å; Au-C 1.90(2) Å, 1.93(3) Å; C-Au-O 179.7(7)°, 176.2(7)°; O-C-O 117.7(18)°.

Each fragment showed the usual linear structure adopted for Au(I) complexes with a $C_{carbene}$-Au-O angle of 179.7(7)° and 176.2(7)°.[36] The angle O-C-O of 117.7(18)° is narrower compared to that of a typical carboxylic acid (~ 125°), and to that of **3.7** (128°).[36] Considering the bond length, the O-Au bonds distances are of 2.045(14), and 2.058(17) Å, in line with the computed structure by Lee and Kang (Figure 3.2).[35] Au-$C_{carbene}$ bonds are 1.90(2), and 1.93(3) Å, which were slightly shorter than in **3.1**,[37] and carboxylate-Au(I) **3.7**.[38]

The generality of this method was expanded to other carboxylic acids (Figure 3.4). Overall, full conversions to the dinuclear carboxylate species were observed and the dinuclear species were successfully isolated by simple removal of the solvent followed by recrystallization from a mixture of dichloromethane and pentane. Substitution in the *para* position of the benzoic acid, such as 4-methoxybenzoic acid and 4-bromobenzoic acid were well tolerated and yielded products **3.8** and **3.9** in 80% yield after 1 h. Glacial acetic acid was suitable under the reaction conditions and was readily converted, in presence of **3.1**, into complex **3.10** in 88% yield. The use of pivalic acid lead to the formation of a clear set of signals assigned to [{Au(IPr)}$_2${μ-O_2C(C(CH_3)$_3$)}][BF_4] (**3.11**) in 80% yield.

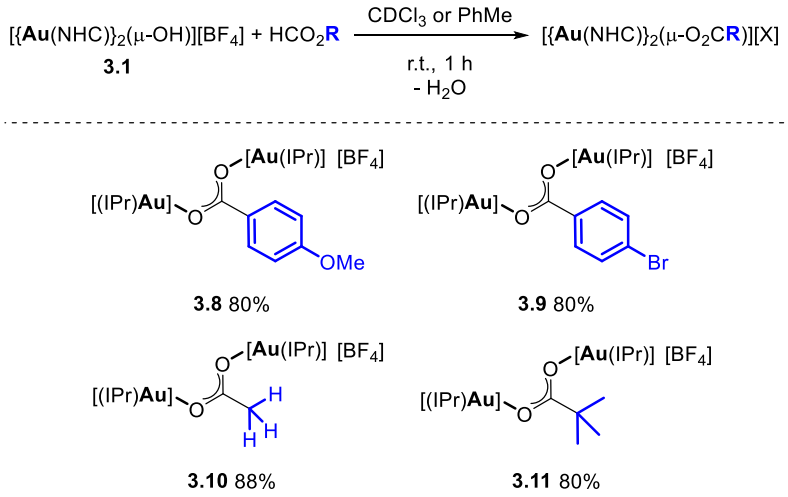


Figure 3.4. Synthesis of dinuclear gold carboxylate complexes: variation of carboxylic acids.

4-Nitrobenzoic acid seemed suitable to convert into the desired dinuclear species, however, a broad set of signals was obtained in this case. The same features were observed with other acids, such as salicylic acid, picolinic acid, levulinic acid, 2-furoic acid, and 2-thiophenecarboxylic acid, although full conversion of **3.1** was observed in all cases. Most likely, the broad signals indicate that different coordination mode of the metal

centre to the carboxylic moiety can be in action leading to an equilibrium in solution, which is not discernible on the NMR timescale.

4-*N*,*N*-dimethylaminobenzoic acid reacted with **3.1** to afford a mixture of unidentified complexes, probably due to the amine moiety which could compete for coordination. Terephthalic acid was reacted with 2 equiv. of [{Au(IPr)}$_2$(μ-OH)][BF$_4$] **3.1**, but did not lead to the targeted tetranuclear gold complex, probably due to the high steric hindrance around the carboxylic moiety. The crude ^{1}H NMR showed one species; however attempt to isolation led to **3.1** being recovered, consistent with labile coordination of the acid compared to OH$^-$ anion. Attempts to isolate species containing trifluoroacetic acid were unsuccessful; full conversion of **3.1** was observed, but still broad signals were detected by ^{1}H NMR. The ^{19}F{^{1}H} NMR of the mixture showed three different peaks, other than the characteristic set of signals of the counterion BF$_4$, which suggested that different fluorinated species were present in the reaction mixture. Attempts to synthesise the formic acid equivalent were not successful either: the mixture obtained was homoleptic complex [Au(IPr)$_2$][BF$_4$], and a second species assigned by ^{1}H NMR as [Au(OC(O)H)(IPr)].

The synthesis of the dinuclear complexes could be expanded to different weakly coordinating counterions, such as SbF$_6$, and FABA (Figure 3.5). By reacting the precursors [{Au(IPr)}$_2$(μ-OH)][SbF$_6$], and [{Au(IPr)}$_2$(μ-OH)][FABA][1] with benzoic acid, the corresponding benzoate analogues **3.12**, and **3.13** were obtained in 82%, and 40% yield, respectively. The higher solubility of the latter was most likely the cause of the lower yield obtained. The synthesis could be expanded to the use of other NHC dinuclear complexes such as [{Au(IPent)}$_2$(μ-OH)][BF$_4$],[39] and the product [{Au(IPent)}$_2$(μ-O$_2$CPh)][BF$_4$] (**3.14**) was obtained in 82% yield.

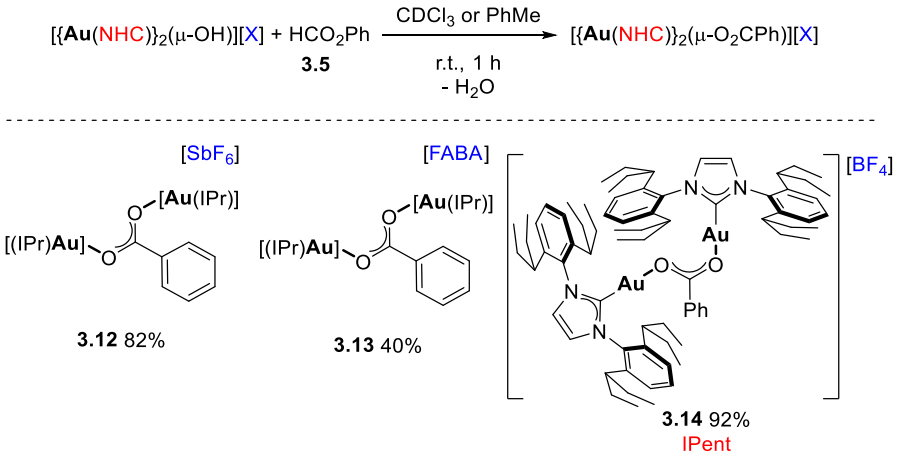


Figure 3.5. Synthesis of dinuclear gold carboxylate complexes: variation of counterions and NHCs.

The synthetical methodology could not be applied to IPr^{Cl}, and SIPr containing dinuclear precursors; full conversion of [{Au(NHC)}$_2$(μ-OH)][BF_4] into a mixture of species was observed when mixing it with benzoic acid **3.5**. Among those, the major species was assigned as [Au(OC(O)Ph)(NHC)].

Full characterisation of the complexes was performed by NMR, and IR spectroscopy (Table 3.1). The dinuclear gold carboxylate species displayed similar features as the carboxylate complex **3.6**; the ^{13}C signal of the carboxylate moiety shifted slightly downfield compared to the signal of the corresponding carboxylic acid, ranging from 179.5 to 184.6 ppm (entries 2, 3, 5, 6). The carbene signals were in line with **3.6**, and **3.1**, with an upfield shift compared to monogold carboxylate species.[38] The FTIR (ATR) signals showed the characteristic peaks for symmetrical, and asymmetrical frequencies, from 1508 to 1589 cm^{-1}, as seen for carboxylate anions, and following the trend of **3.6**.

Table 3.1. Relevant spectroscopic data for dinuclear gold carboxylate complexes.[a]

Entry	Complex	O-C-O (ppm)	$C_{carbene}$ (ppm)	ν_{OCO}*sym*/*asym* (cm^{-1})
1	**3.8**	[b]	162.2	1522/1508
2	**3.9**	179.5	161.6	1579/1529
3	**3.10**	184.6	162.9	1593/1456
4	**3.11**	[b]	162.7	1514/1469
5	**3.12**	180.1	162.1	1527/1519
6	**3.13**	180.1	162.1	1589/1520
7	**3.14**	[b]	162.3	1543/1458

[a] $^{13}C\{^1H\}$ NMR deptq ($CDCl_3$); FTIR (ATR); [b] not visible by 2D NMR at ~0.1 M.

Suitable crystals of all complexes were grown by slow diffusion of pentane into a saturated solution of the complexes in CH_2Cl_2 (Figure 6).

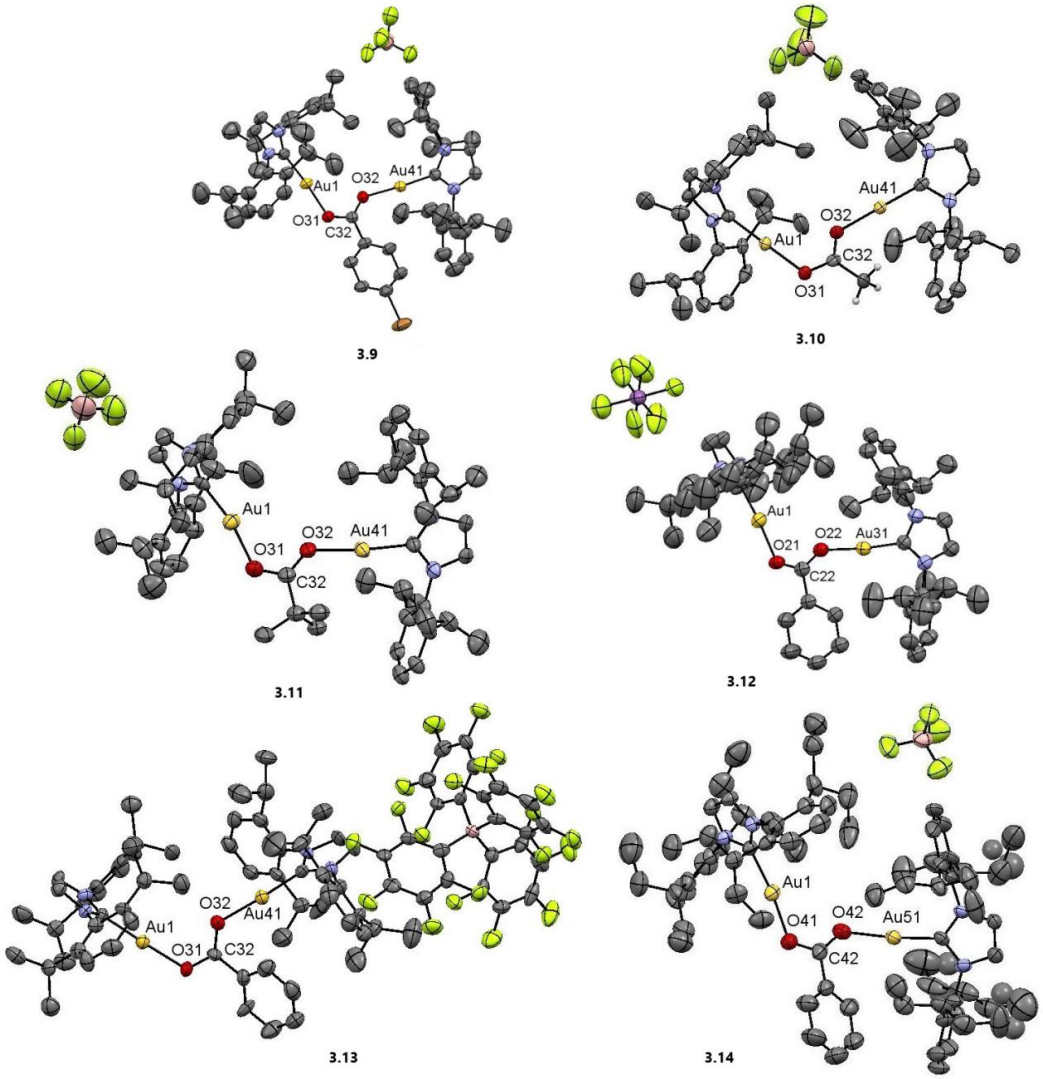


Figure 3.6. Thermal ellipsoid representation of **3.9**, **3.10**, **3.11**, **3.12**, **3.13**, **3.14** showing 50% probability. Most of H atoms were omitted. The structure of **3.8** was obtained but the structure was not refined therefore disorder did not allow to obtain a pretty picture.

The Au-$C_{carbene}$ bonds within all complexes were in line with what found for **3.6** and the monogold carboxylate species (Table 3.2).[36,38] The species showed shorter Au-O bonds with values ranging from 1.940(12) Å to 1.980(11) Å *vs* 2.045(14), and 2.058(17) Å for **3.6** (Figure 3.3). The angle O-C-O was found to be around 120°, similar to that of a carboxylic acid, and consistent with digold carboxylate **3.6**. The $C_{carbene}$-Au-O angles were slightly deviated from linearity ranging from 168.5(9)-178.2(3)°; this effect might be due to the steric repulsion between the NHC ligands, thus pushing to bend the C-Au-O bond slightly from linearity.

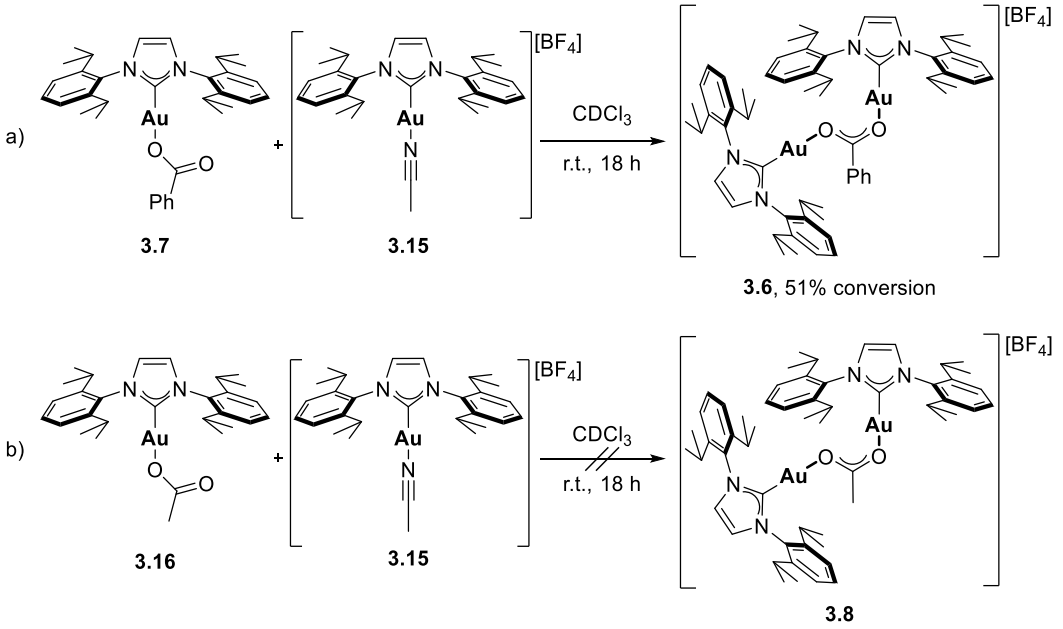
Table 3.2. Main crystallographic data for dinuclear gold carboxylate complexes.[a]

Entry	Complex	Au-$C_{carbene}$ (Å)	Au-O (Å)	O-C-O (°)	$C_{carbene}$-Au-O (°)
1	**3.9**	1.949(13) 1.97(2)	2.061(9) 2.060(13)	119.6(13)	174.6(6) 176.2(5)
2	**3.10**	1.961(7) 1.951(8)	2.064(5) 2.030(5)	120.5(7)	178.2(3) 177.3(3)
3	**3.11**	1.90(4) 2.00(3)	2.07(3) 2.068(19)	118(4)	168.5(9) 171.8(13)
4	**3.12**	1.980(11) 1.961(12)	2.035(8) 2.036(9)	122.5(10)	174.7(5) 174.0(4)
5	**3.13**	1.941(11) 1.945(14)	2.041(7) 2.047(10)	122.8(11)	175.3(4) 175.6(5)
6	**3.14**	1.967(9) 1.940(12)	1.047(7) 2.069(10)	121.1(10)	171.2(3) 174.4(3)

[a] The values for **3.8** were not the final CIF values, thus the data are not reported.

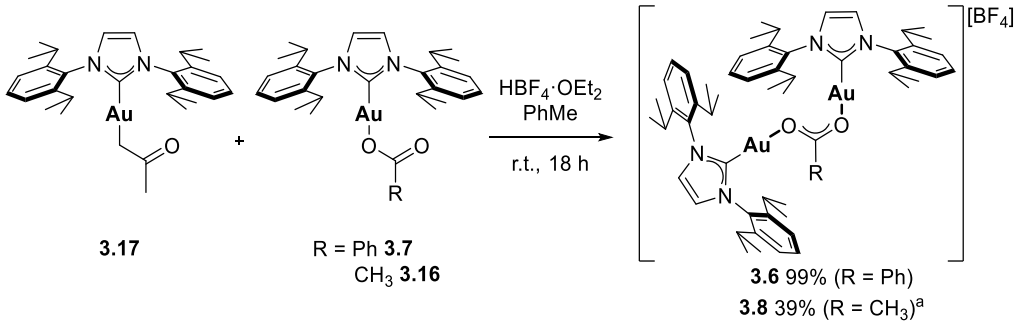
Attempts to synthesise dinuclear gold carboxylate species from mononuclear complexes were performed. Initially, [Au(OC(O)Ph)(IPr)] (**3.7**) and [Au(IPr)(NCCH$_3$)][BF$_4$] (**3.15**) were reacted in dry CDCl$_3$, and 51% conversion into **3.6** was observed after 18 h (Scheme 3.9, a). No further conversion was observed by leaving the reaction for longer times, and decomposition occurred after 48 h. Most likely competitive coordination between acetonitrile, and the oxygen atom in **3.7** for [Au(IPr)]$^+$ resulted in equilibrium, that did not allow further conversion.

A different outcome was observed when reacting [Au(OC(O)CH$_3$)(IPr)] (**3.16**), and **3.15** (Scheme 3.9, b); a mixture of unidentified species was seen by ^{1}H NMR, however one signal was found by ^{19}F{^{1}H} NMR, to account for one BF$_4$ counterion in the mixture. Attempt to isolate the species were unsuccessful, with main decomposition after drying the solvent. Possible coordination with the solvent might be invoked as well.[40]



Scheme 3.9. Synthesis of dinuclear gold carboxylate from: a) **3.7**, and **3.15**; b) **3.16**, and **3.15**.

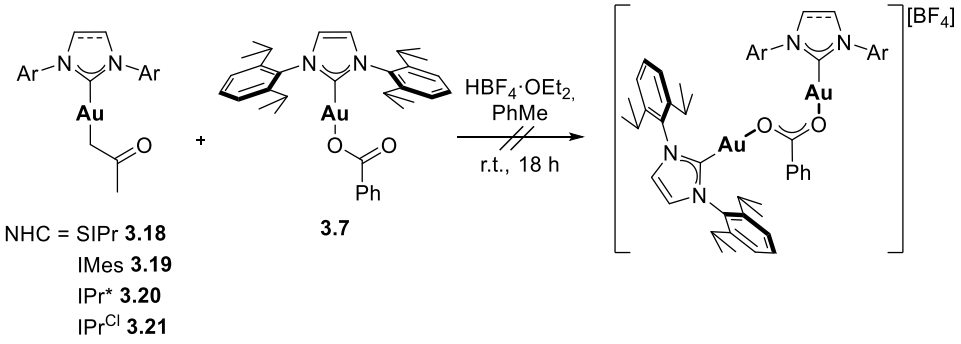
The dinuclear gold carboxylate could be isolated by reacting **3.7** and [Au($CH_2C(O)CH_3$)(IPr)] (**3.17**).[36] First activation of **3.17** with an equimolar amount of $HBF_4 \cdot OEt_2$ in PhMe, was followed by addition of **3.7** (Scheme 3.10). The reaction was stirred for an hour, and the product **3.6** obtained in full conversion after pentane recrystallisation (99% isolated yield). However, when **3.7**, was replaced by **3.16**, [Au($OC(O)CH_3$)(IPr)], the reaction did not proceed to completion, with only 39% conversion into **3.8** observed by ^{1}H NMR.



Scheme 3.10. Reaction of **3.17** with **3.7**, or **3.16** to digold carboxylate **3.6**, and **3.8**; [a] ^{1}H NMR conversion using 1,3,5-trimethoxybenzene as internal standard.

Interestingly, the latter methodology was attempted to obtain cross-over species by reacting [Au($CH_2C(O)CH_3$)(NHC)] bearing different ancillary ligands with **3.7** (Scheme 3.11). [Au($CH_2C(O)CH_3$)(SIPr)] (**3.18**) was activated with $HBF_4 \cdot OEt_2$ complex in PhMe. Subsequent addition of [Au(OC(O)Ph)(IPr)] **3.7** led to immediate decomposition into a

purple solution. Similarly, prompt degradation was observed when acetonyl-Au(I) complex **3.19**, bearing IMes as ancillary ligand, was reacted with an equimolar amount of **3.7**. Reactions of [Au($CH_2C(O)CH_3$)(IPr*)] (**3.20**), and [Au($CH_2C(O)CH_3$)(IPr^{Cl})] (**3.21**) when reacted with **3.7**, after activation, showed a complex series of peaks by ^1H NMR, with major component unreacted gold carboxylate compound. Notably this reaction might produce, by ligand scrambling, three statistically relevant dinuclear complexes (NHC-IPr, IPr-IPr, NHC-NHC);[4] however, **3.6** was not observed under the reaction conditions, suggesting that dinuclear gold complexes did not form under the chosen reaction conditions.



Scheme 3.11. Attempts to synthesise cross-over dinuclear gold carboxylate species.

3.2.2. Intermolecular considerations: stoichiometric reactivity of digold carboxylate complexes

Once the synthesis and characterisation of the dinuclear gold carboxylate complexes, together with limitations, were assessed, focus turned to the understanding the role of these species in the catalytic intermolecular hydrocarboxylation of alkynes. Considering the possible reaction mechanism, three main reaction steps can be envisaged (Figure 3.7):

1. pre-equilibrium, such as the activation of pre-catalyst/pre-catalysts. **3.1**/**3.10** in presence of diphenylacetylene (**3.22**), and acetic acid (**3.23**) form a π-alkyne-Au(I) (**3.24**), and carboxylate-Au(I) (**3.16**) species (Figure 3.7, a).[41] In the presence of an excess of acid **3.23**, under catalytic conditions, a possible acid/base pair might be formed; species of this kind have been invoked by Gagné and co-workers, from interaction of [Au($OC(O)CH_3$)(PPh_3)], and acetic acid.[42] Thus, coordination such as **3.16**·X (X = $HOC(O)CH_3$) might be considered;
2. nucleophilic attack of the Brønsted basic species in an antiperiplanar fashion to the activated alkyne to form vinyl-Au(I) intermediate **I** or **III** (Figure 3.7, b).[43] This step

is believed to be reversible.[44] Intermediate **I**, exhibiting a Au-O interaction, have been postulated by Vidhani[45] and Nolan.[5,46] Species **I** can equilibrate with **II**, where coordination of the second Au species might aid proton shuffle, and help the nucleophilic attack, as suggested by Lee and Khang.[35] Intermediate **III** might be in equilibrium with the *gem*-diaurated species **IV**, most likely believed to be an off-cycle species for Au catalysed processes.[44a, 47]

3. protodeauration, aided by H_2O or acid, to reform the active species, and release the product (**3.25**) in solution (Figure 3.7, c).[5] The (*Z*)-configuration of **3.25** supports the *anti*-nucleophilic attack into the activated alkyne.

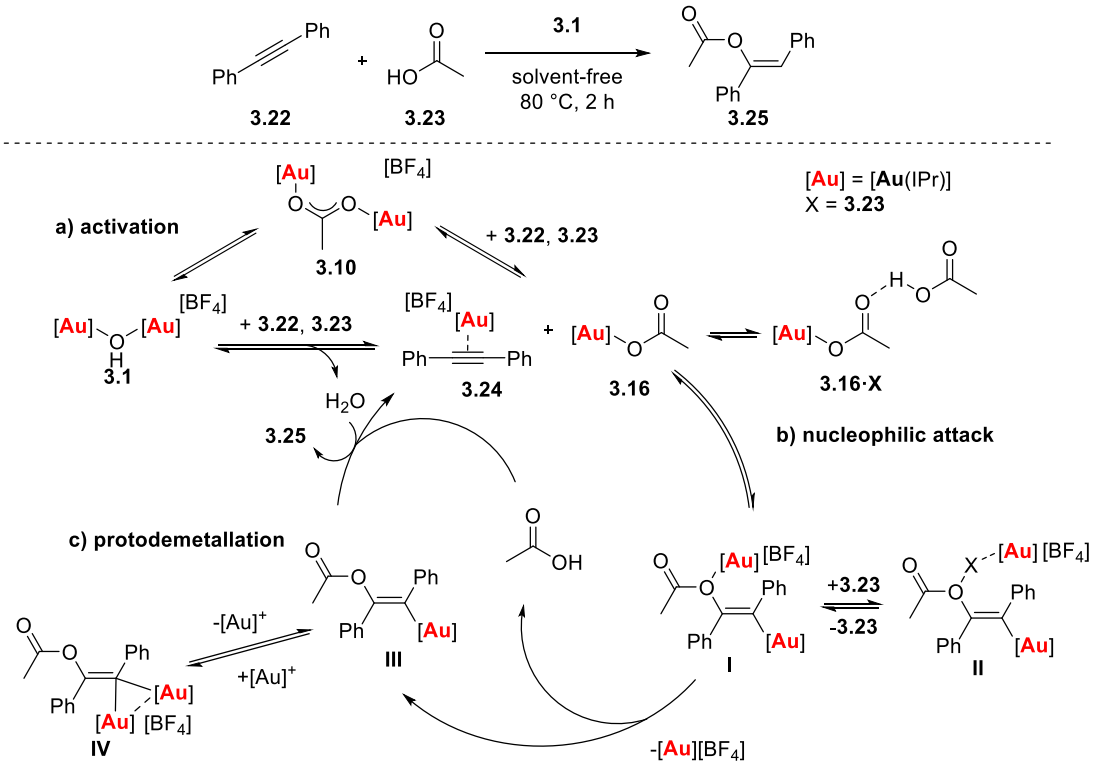
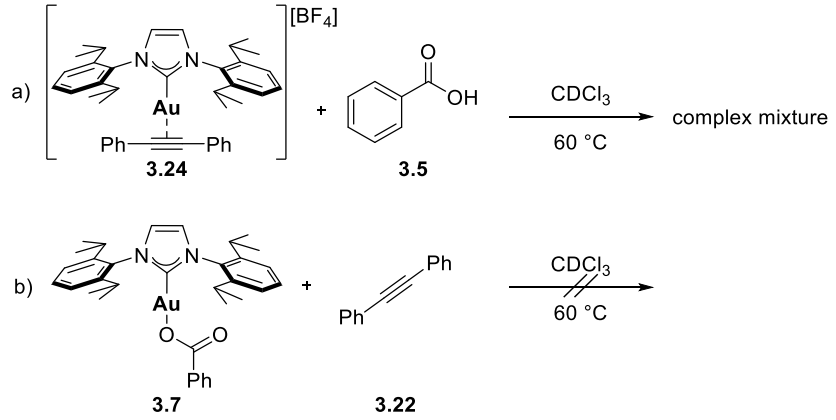


Figure 3.7. Initial mechanistic hypothesis for the intermolecular hydroacyloxylation of alkynes.

Several questions had to be addressed: is the digold carboxylate an off- or in-cycle species? Is it a pre-catalyst resting state? What is the role of acid in the reaction mechanism? Can we envisage what is the RDS of this transformation? Is it a dinuclear process? To investigate these questions initial testing were performed on π-alkyne- and carboxylate-Au(I) intermediates.

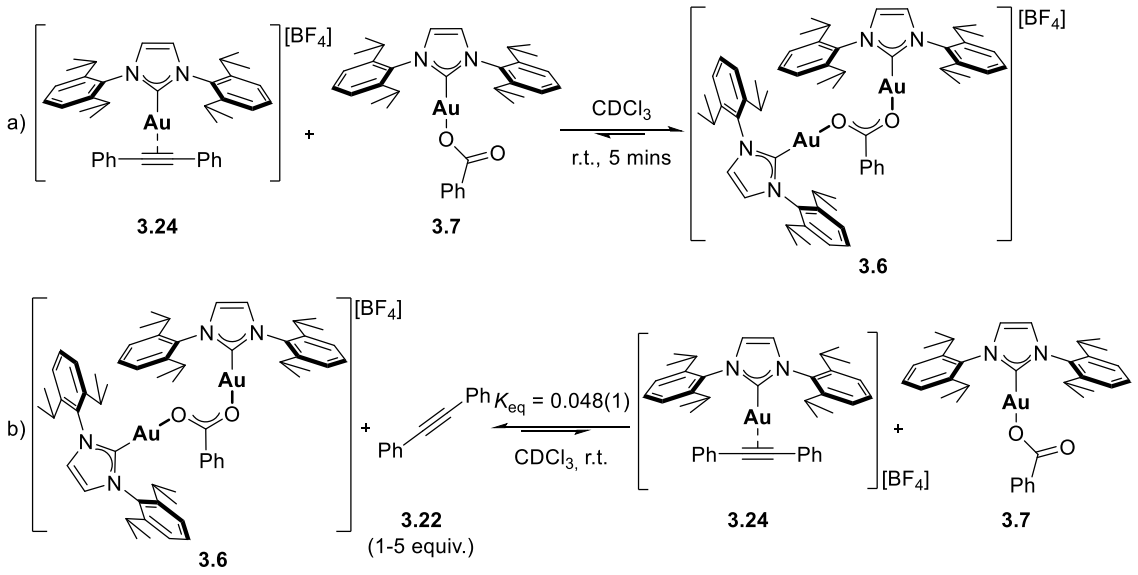
By reacting the π-alkyne complex **3.24** with benzoic acid **3.5** (Scheme 3.12, a) no insertion was observed in $CDCl_3$ at r.t.; decomposition of **3.24** was found by heating the

reaction for 18 h at 60 °C. Mononuclear carboxylate-Au(I) **3.7** did not insert into diphenylacetylene **3.22** at r.t. or by heating at 60 °C (Scheme 3.12, b). Only starting material was recovered over time.



Scheme 3.12. Attempt to reactivity of a) **3.24**, with benzoic acid **3.5**; b) **3.7** with diphenylacetylene **3.22**.

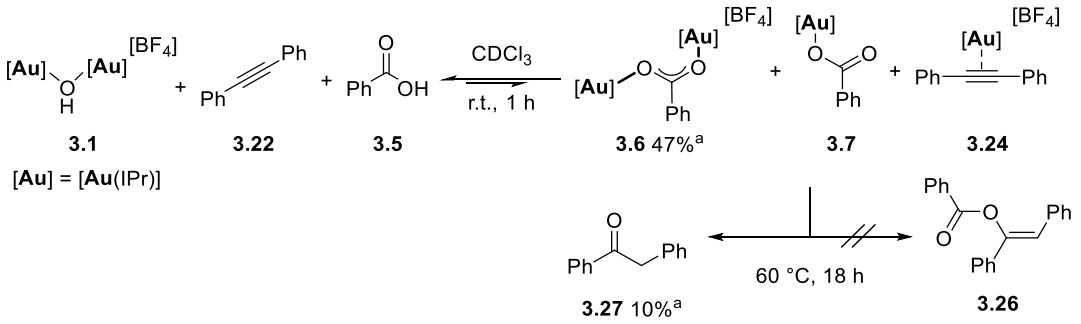
However, mixing complexes **3.24** and **3.7** in $CDCl_3$ for 5 mins at r.t. showed formation of **3.6** (Scheme 3.13, a). The species were in equilibrium, as demonstrated by performing the reverse reaction (b). Reacting **3.6** in the presence of 1, 2, 3, and 5 equiv. of diphenylacetylene **3.22** in $CDCl_3$, immediately showed formation of **3.7**, and **3.24**. A K_{eq} of 0.048 ± 0.001 was calculated, indicating an equilibrium shifted to the left, therefore to **3.6** and the alkyne **3.22**.



Scheme 3.13. a) Equilibrium between **3.24**, **3.7** to **3.6**; b) reverse reaction, and K_{eq} in $CDCl_3$ ($12 \cdot 10^{-3}$ M).

Digold hydroxide **3.1** was reacted with an equimolar amount of alkyne **3.22**, and benzoic acid **3.5** in $CDCl_3$ (Scheme 3.14); full consumption of the starting complex **3.1** occurred

after 1 h to form **3.6** in 47% conversion (^{1}H NMR conversion). Traces of π-alkyne **3.24**, and carboxylate-Au(I) **3.7** were observed, but not quantified because of the superimposition with other signals in the reaction mixture. By heating the reaction for 18 h at 60 °C, no traces of vinyl ester product were observed, while formation of $[Au(IPr)_2][BF_4]$ species was spotted. Hydration of diphenylacetylene was found, with 10% conversion to ketone **3.27**.



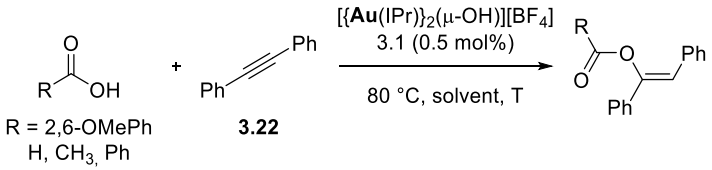
Scheme 3.14. Stoichiometric reaction of **3.1**, with **3.22** and **3.5**; [a] ^{1}H NMR conversion using 1,3,5-trimethoxybenzene as internal standard.

The reluctance to form the product under the reaction conditions, and the competitive hydration reaction suggested that: i) $CDCl_3$ was not a good solvent to mimic the optimised reaction conditions; ii) the O-C bond formation might be reversible, and if formed might re-equilibrate to starting materials; iii) the hydration reaction competes with hydrocarboxylation, probably due to water formation as by-product of **3.1** activation.

Considering the reaction optimisation (Chapter 2), the unsuitability of the solvent (i) was found to be a crucial factor (Table 3.3). As already noticed, when using 2,6-dimethoxyphenyl acetic acid, and diphenyl acetylene (entries 1-3) full conversion was observed in solvent-free conditions, while moving to 1,2-DCE, and PhMe showed >23% conversion for the same transformation after 5 h.

Other acids were therefore screened; with formic acid as the alkyne reaction partner, the reaction catalysed by **3.1** in $CDCl_3$ gave product in 44% conversion after 18 h (Table 3.3, entry 4) vs > 99% yield in solvent-free conditions (entry 5). When moving to d^6-benzene, or d^5-bromobenzene (entries 6, 7) ~70% conversion was obtained after 18 h. If acetic acid, or benzoic acid (entries 8, 9) were used in the presence of **3.1**, less than 2% conversion to product was observed after 24 h in $CDCl_3$. Benzene and bromobenzene were suitable solvents to convert acetic acid, and **3.22** to the corresponding vinyl ester with up to 70% conversion after 24 h (entries 10, 11).

Table 3.3. Solvent effect to the digold hydroxide catalysed hydrocarboxylation of diphenylacetylene.

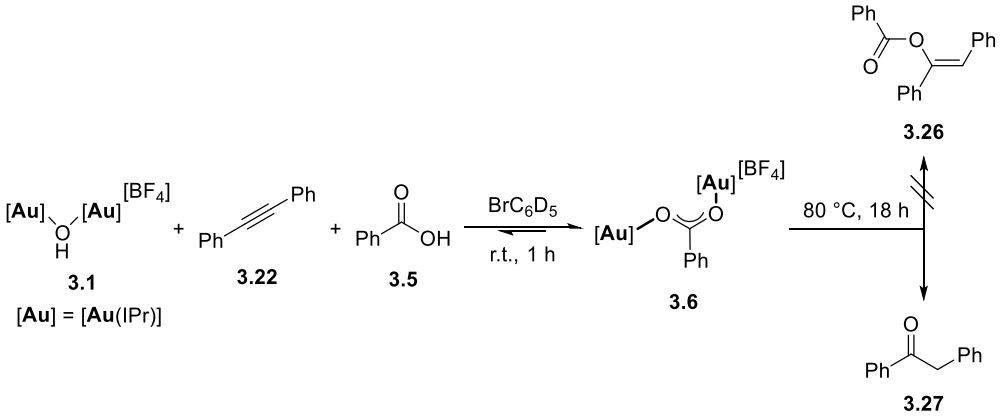


Entry	R	Solvent (M)	time (h)	Conv. (%)[a]
1	2,6-OMePh	solvent-free	5	>99[b]
2	2,6-OMePh	1,2-DCE	5	23[b]
3	2,6-OMePh	PhMe	5	18[b]
4	H	$CDCl_3$	18	44
5	H	solvent-free	1	>99
6	H	C_6D_6	18	69
7	H	BrC_6D_5	18	70
8	CH_3	$CDCl_3$[c]	24	<2
9	Ph	$CDCl_3$[c]	24	<2
10	CH_3	C_6D_6	24	70
11	CH_3	BrC_6D_5	24	66

Reaction conditions: **3.22** (1 mmol), acid (1 equiv.), **3.1** (0.5 mol%), neat, 80 °C; [a] conversion calculated by ^{1}H NMR, using 1,3,5-trimethoxybenzene as internal standard; [b] 1:1.3 **3.22** to acid ratio; [c] 60 °C.

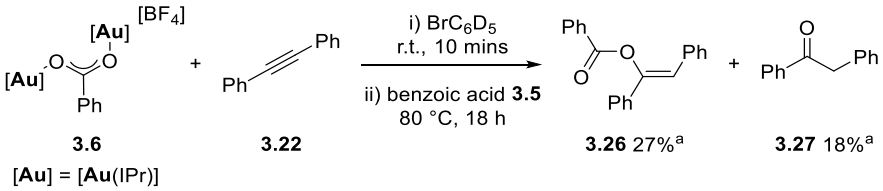
As the reaction is highly solvent dependent,[48] further studies were carried out in d^5-bromobenzene to better mimic the reaction conditions. As already stated, **3.6** was obtained by reacting **3.1**, and the chosen carboxylic acid in this solvent. Benzene was not chosen due to the high insolubility of the cationic complexes in this medium.

Dinuclear gold hydroxide **3.1** was therefore reacted in presence of diphenylacetylene **3.22** and benzoic acid **3.5** in d^5-bromobenzene (Scheme 3.15); a 1:1.3 ratio between **3.6**, and **3.1** was observed after 10 min, with full conversion into **3.6** after 30 min. Monoaurated intermediates **3.24**, and **3.7** were not recognised in the reaction mixture. By heating the reaction to 80 °C no conversion into product was observed after 18 h. In this case, as observed with $CDCl_3$, 24% of hydration product **3.27** was found, supporting the faster competitive hydration reaction.



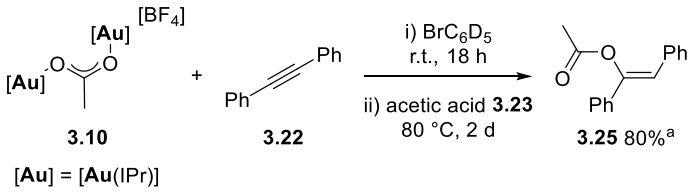
Scheme 3.15. Stoichiometric reaction of **3.1** with **3.22**, and **3.5** in bromobenzene.

Reaction of **3.6**, with **3.22** in d^5-bromobenzene was followed by ^{1}H NMR (Scheme 3.16). Monogold intermediates **3.7** and **3.24** were not present in solution; by adding 1 equiv. of benzoic acid **3.24**, 27% conversion into product **3.26**, together with 18% of **3.27**, was observed after 18 h at 80 °C. Traces of **3.6** were still visible in the reaction mixture.



Scheme 3.16. Stoichiometric reaction of **3.6** in bromobenzene. [a] ^{1}H NMR conversion using 1,3,5-trimethoxybenzene as internal standard.

Dinuclear gold acetate **3.10** was subjected to the same reaction conditions as above in d^5-bromobenzene (Scheme 3.17). The reaction did not show any conversion into π-alkyne **3.24** or acetate-Au(I) **3.16** after 18 h at r.t.; however, upon addition of equimolar amount of acetic acid, and by heating up to 80 °C for 2 days, 80% conversion into product **3.25** was found.



Scheme 3.17. Stoichiometric reaction of **3.10** in bromobenzene. [a] ^{1}H NMR conversion using 1,3,5-trimethoxybenzene as internal standard.

The experiments performed so far can be summarised as follows:

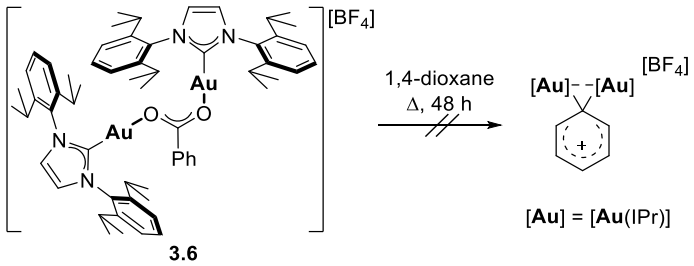
a) the formation of dinuclear carboxylate species was observed under the stoichiometric reaction conditions, as confirmed by grinding experiment, and stoichiometric experiments in d^5-bromobenzene;

b) the solvent had a major impact in the reaction; when $CDCl_3$ was used as the solvent the involvement of off-cycle species might prevent the reaction from proceeding by trapping catalytic active gold species;

c) when stoichiometric reactions of dinuclear species with alkyne and acids were performed in bromobenzene, digold hydroxide **3.1**, and digold carboxylate complexes **3.6** and **3.10** behaved differently. Formation of product could be observed when using **3.6**, and **3.10** while competitive hydration occurred when complex **3.1** was used; release of H_2O from **3.1** activation might explain the reaction outcome and be the major difference between the complexes.

A final attempt to form a vinyl-Au(I) species was investigated. [AuCl(IPr)] complex was activated with an equimolar amount of AgOTf in CH_2Cl_2 at r.t., and addition of vinyl-ester **3.26** to the reaction mixture. However, analysis of the species showed formation of [Au(OTf)(IPr)],[49] with no sign of coordination of Au to the alkene.

Other stoichiometric reactions showed that complex **3.6** does not decompose under the reaction conditions.[38] Decarboxylation attempts were performed, by heating complex **3.6** in 1,4-dioxane at 110 °C for 48 h (Scheme 3.18). No sign of conversions of the starting material were observed, but slow decomposition of complex **3.6** was observed over time with release of benzoic acid.



Scheme 3.18. Attempt of decarboxylation of **3.6**.

3.2.2.1. Mechanistic studies under catalytic conditions

With these results in hand, a deeper understanding of the reaction profile was explored by kinetic analysis. However, the problem of finding suitable conditions that resemble the catalytic process was not easy to solve. The use of $CDCl_3$ or other chlorinated solvents

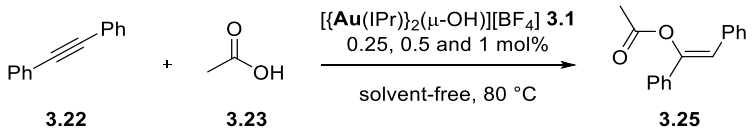
had to be avoided, because of low conversions (>10%) of starting material and the reaction could not be performed in d^5-bromobenzene or d^6-benzene, because the reaction time varied greatly from the solvent-free conditions with longer times needed. Furthermore, the impracticability of using *in situ* NMR analysis at 80 °C for more than 24 h was also considered.

An attempt to follow the reaction under solvent-free conditions in an NMR tube, by heating up the instrument probe at 80 °C and by using a D_2O capillary to enable proper lock and shim of the sample was undertaken; however, broad signals in the ^1H NMR did not allow proper integration.

Moreover, IR techniques would not have been diagnostic due to the presence of several peaks around the carboxylate region.

Therefore, the reaction was performed in solvent-free conditions, by including an internal standard (1,4-dinitrobenzene) in the reaction. Approximation of the concentration was carried out by considering that at 80 °C the reaction became homogeneous, and that 2 mmol of sample, occupied 1 mL volume in a graduated vial of 4 mL (15×45 mm). The data obtained were calculated by considering three values of concentration with a ± 0.1 mL on the volume considered. A few sampling points were taken, to ensure that the volume in the vial did not vary significantly. Each sample was thus analysed by ^1H NMR in $CDCl_3$, to quench the reaction.

By using this assumption, the reaction of acetic acid **3.23** and diphenylacetylene **3.22** was monitored (Figure 3.8). The amount of **3.1** was varied from 0.25 mol% to 1 mol%.



3.22 **3.23** **3.25**

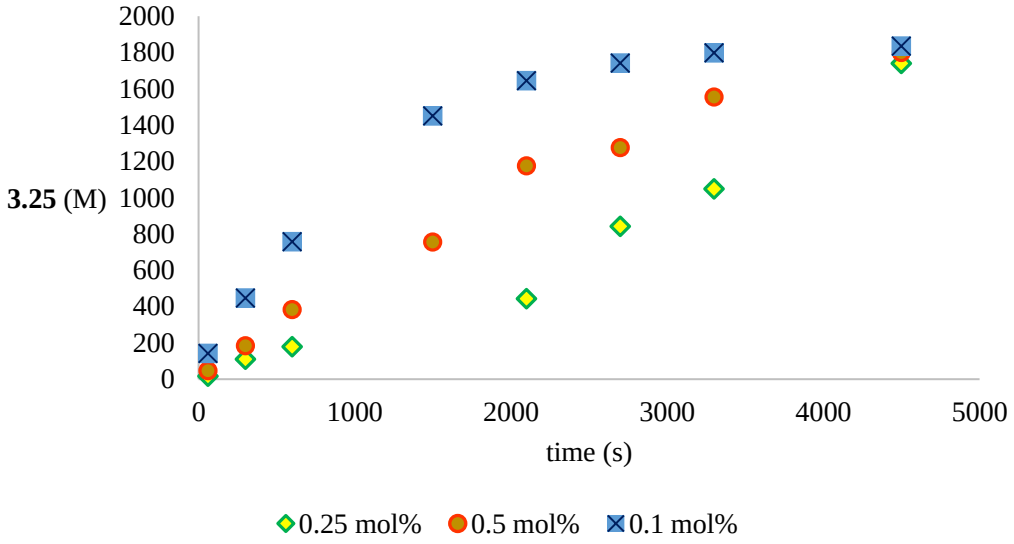


Figure 3.8. Conversion of **3.23** and **3.22** into **3.25** by varying the catalyst loading of **3.1**. Reaction conditions: acetic acid (1 mmol), diphenylacetylene (1 mmol), [Au] (0.25, 0.5 and 1 mol%), 1,4-dinitrobenzene (5 mg), solvent-free, 80 °C, 400 rpm, 4 mL vial (15×45 mm); every run is an average of 3 runs; concentration of **3.23** at t^0= 2000 M.

The calculation of the order in catalyst, could be performed by using a visual method described by Jordi Bures.[50] The concentration of product (y-axes) was plotted *vs* the normalised time scale (x-axis) (Figure 3.9). The latter values were obtained by multiplying the time scale (s) per concentration of catalyst (M) raised to a parameter (α), which describes the order in catalyst. This allows the data obtained to be superimposed, and the extent of this overlapping does describe the value of the order in catalyst. Thus α = 0.6 best fit the order in **3.1**, that was found to be pseudo half-order to dinuclear catalyst. Therefore, we can define that the reaction is assumed to be pseudo-first order in catalyst when **3.1** was utilised under solvent-free conditions.

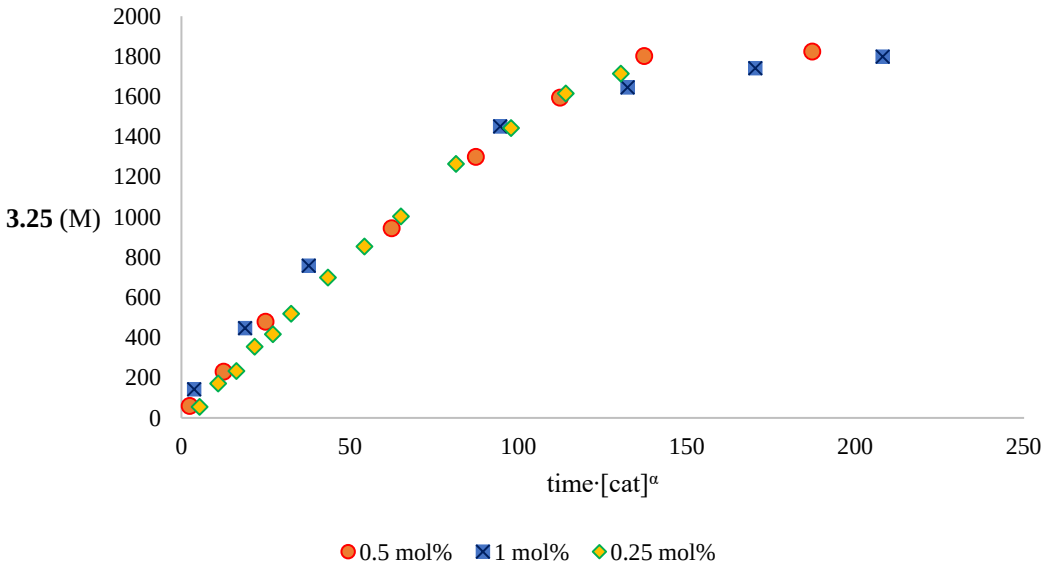
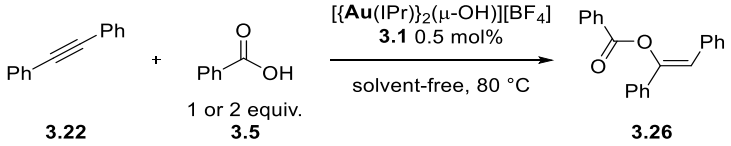


Figure 3.9. Calculation catalyst order (**3.1**) by plotting the concentration of **3.25** (M) *vs* normalised time over [cat]$^{\alpha}$; Concentration of **3.23** at t^0 = 2000 M. A good overlap of the curves at $\alpha = 0.6$ was observed for concentration of **3.23** t^0 = 2500 M and t^0 = 1666 M.

As visible from Figure 3.10, decreased overlapping occurred at higher conversions. This result might be due to the approximation chosen, or to a variation in catalyst order at low concentration of substrates. It is possible that off-cycle intermediates, like *gem*-diaurated species, might occur at higher conversions, thus consume catalytically active $[Au(IPr)]^+$. Attempt to calculate the order in acid were performed, however, by increasing the amount of acetic acid **3.23**, the approximation of the concentration in the vial varied greatly: therefore, even by including the surplus volume due to the increased amount of acid, meaningful data could not be obtained.

However, conversions into vinyl acetate **3.26** from reaction of **3.5** (1 and 2 equiv.) and **3.22** catalysed by **3.1** were followed (Figure 3.10). The data showed that the excess of benzoic acid **3.5** was benign for the transformation, with full conversion into product obtained after 5 hours. With a 1:1 ratio alkyne **3.22** to acid **3.5** the conversion was 73% after the same reaction time.



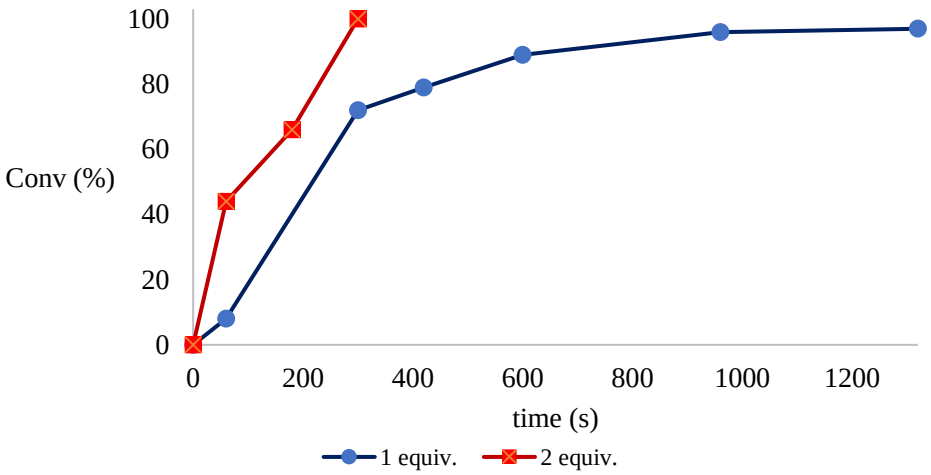


Figure 3.10. Conversion of **3.22** and **3.5** into **3.26** with **3.1**. Reaction conditions: benzoic acid (0.25 and 0.5 mmol), diphenylacetylene (0.25 mmol), **3.1** (0.5 mol%), solvent-free, 80 °C, 400 rpm; conversions measured by using pivalaldehyde (10 μL) as internal standard; every data is an average of 2 runs.

Competitive experiments under catalytic conditions were performed by using a mixture of carboxylic acids (Figure 3.11). Diphenylacetylene **3.22** was mixed with 1 equiv. of benzoic acid **3.5**, and 1 equiv. of 4-methoxybenzoic acid **3.28**, with 0.5 mol% of catalyst **3.1**. After 18 h at 80 °C in the absence of solvent, product **3.26**, and product **3.29**, (*Z*)-1,2-diphenylvinyl-4-methoxybenzoate, were formed in 54% and 17% conversions, respectively, whose sum is represented in the graph (71%). The result can be explained by considering competitive formation of digold carboxylate species, **3.6** and **3.8** when reacting **3.1** with the carboxylic acids **3.5** and **3.28** [pK_a (H_2O) **3.5** = 4.2, pK_a (H_2O) **3.28** = 4.7]. Activation of **3.28** will lead to formation of product **3.29**.

When the reaction was performed with an equimolar ratio between benzoic acid **3.5**, alkyne **3.22**, and 4-bromobenzoic acid (**3.30**), the reaction showed formation of **3.26**, in 75%, while no traces of the vinyl ester deriver from **3.30** were visible in solution (Figure 3.11). Complex **3.1** will preferentially react with the less acidic **3.5**, instead of **3.30**; thus activation of the latter did not occur. The only product for the reaction was **3.26**.

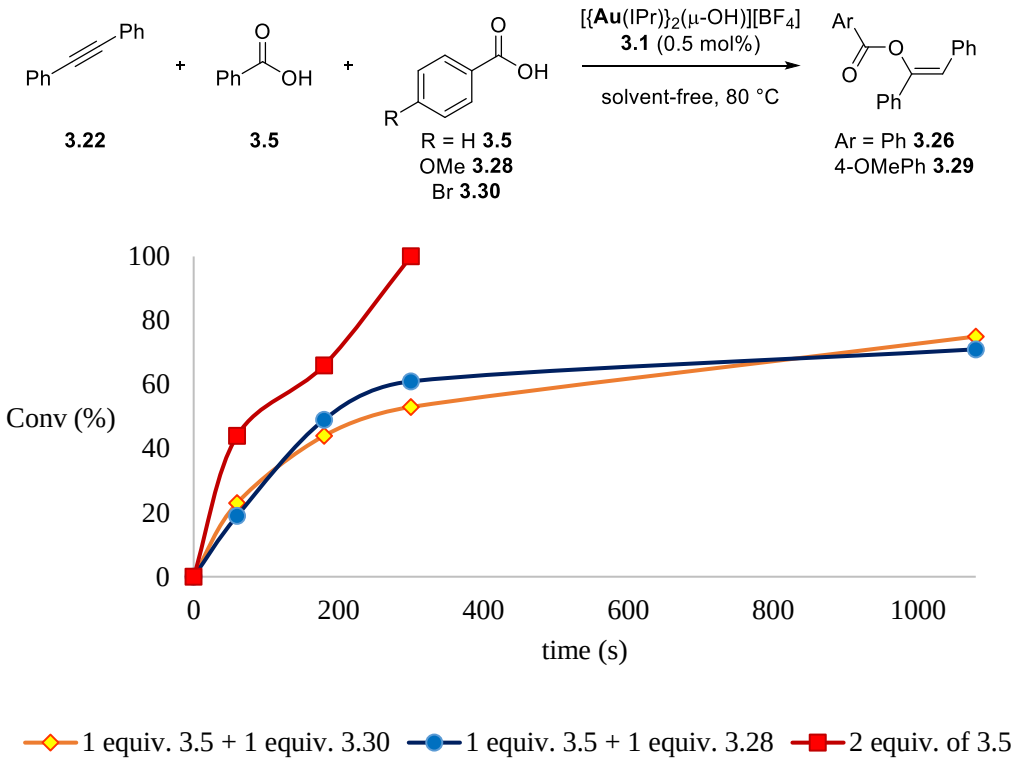


Figure 3.11. Competitive experiments. Reaction conditions: benzoic acid **3.5** (1 mmol), diphenylacetylene **3.22** (1 mmol), 4-substituted benzoic acid (R = OMe **3.28**, Br **3.30**, 1 equiv.), **3.1** (0.5 mol%), solvent-free, 80 °C, 400 rpm; conversions measured by using pivalaldehyde (10 μL) as internal standard; every run is an average of 2 runs.

Lower conversions to products after 18 h were observed when compared to the reaction performed with 2 equiv. of benzoic acid, which reliably gave conversion of > 99% after 5 h. The conversions observed were however higher after a short 1 h reaction time when compared to that observed with only 1 equiv. of benzoic acid (20% *vs* 8%, Figure 3.10). At higher reaction time, the conversions dropped compared to the results with one or two equiv. of benzoic acid; it is speculated that off-cycle species may become important at this stage of the transformation, thus impeding the reaction to proceed further.

Thus, the reaction between **3.5** and **3.22** was performed with 0.5 mol% of **3.1**, and a catalytic amount of acid additive, **3.28** or **3.30** (Figure 3.12). The reaction profiles were similar in both cases, and the formation of solely **3.26** was observed. The conversions were higher compared to the reaction with 1 equiv. of benzoic acid **3.5** at low reaction time (27% *vs* 8%). However, the conversions decreased at longer reaction times, as noticed in the case of equimolar amount of acids (Figure 3.11).

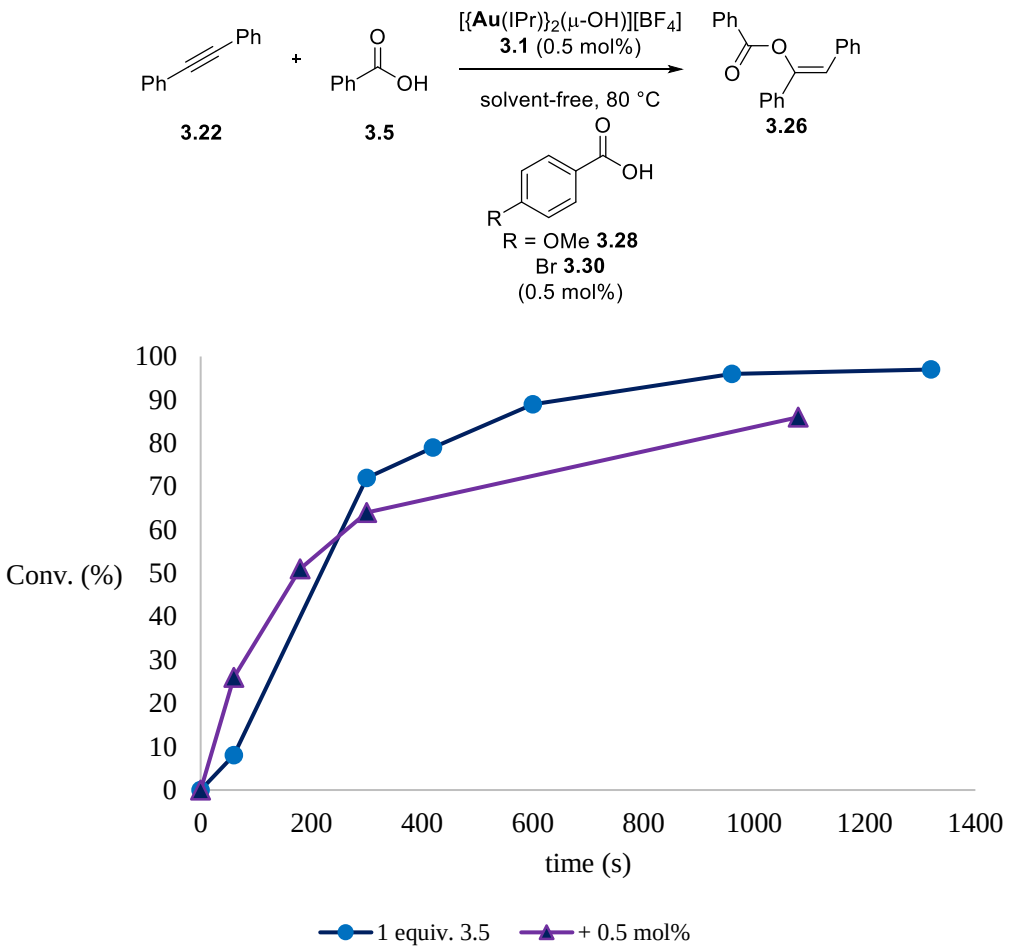
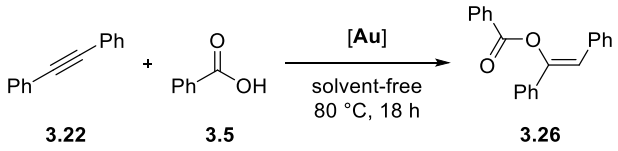


Figure 3.12. Competitive experiment with acid additive. Reaction conditions: benzoic acid **3.5** (1 mmol), diphenylacetylene **3.22** (1 mmol), **3.28** or **3.30** (R = OMe, Br, 0.5 mol%), **3.1** (0.5 mol%), solvent-free, 80 °C, 400 rpm; conversions calculated by using pivalaldehyde (10 μL) as internal standard; every run is an average of 2 runs.

3.2.2.2. Catalytic activity of digold carboxylate complexes

The hydrocarboxylation of diphenylacetylene was tested with the dinuclear carboxylate gold species. Reaction of **3.22** and **3.5** was followed by sampling the reaction at regular interval (Figure 3.13). All the dinuclear pre-catalysts proceeded to product **3.26** with >60% conversion after 7 h, comparable to that obtained with **3.1**. By using **3.6** a slower conversion to **3.26** was found at high reaction time. Of interest, varying the outer-sphere counterion in the dinuclear gold carboxylate led to a decrease in conversion following the order $BF_4 \approx SbF_6 <$ FABA. Pre-catalyst [{Au(IPr)}$_2$(μ-O_2CPh)][FABA] **3.13** showed the highest conversion among the series of complexes tested, outperforming **3.1**. The substituent on the bridging ligand in the *para* position of the aryl ring (R = Br, OMe) did

not affect the conversions; however, compared with the results with R = H, the conversions increased in the order H ≈ Br < OMe. [{Au(IPr)}$_2${μ-O$_2$C(C(CH$_3$)$_3$)}][BF$_4$] **3.11** showed a slower conversion for the first 90 min; afterwards, it became a competitive catalyst. Dinuclear gold acetate **3.10** showed similar conversions to **3.1**.



3.22 **3.5** **3.26**

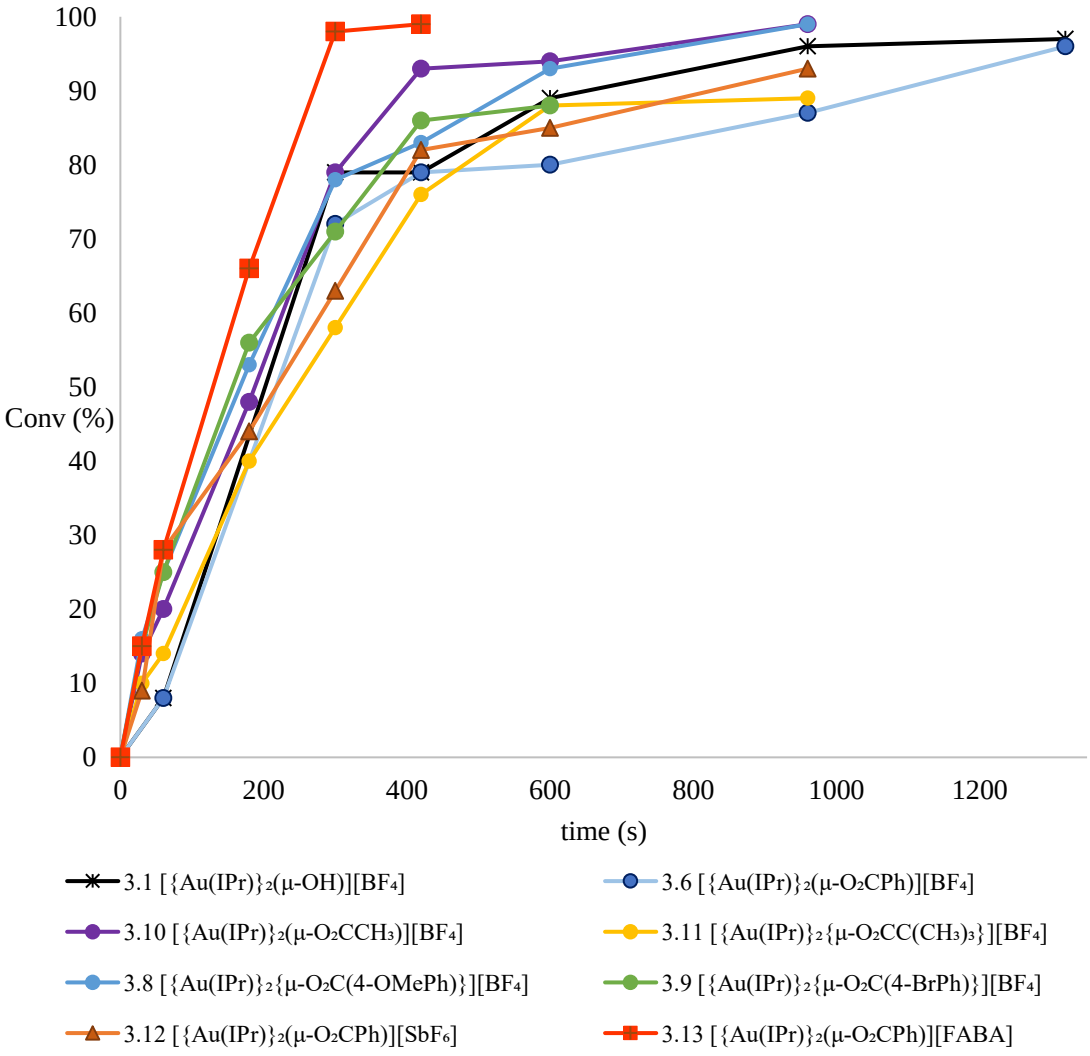


Figure 3.13. Hydrocarboxylation of **3.22** with **3.5** into **3.26** catalysed by dinuclear gold complexes. Reaction conditions: benzoic acid **3.5** (0.25 mmol), diphenylacetylene **3.22** (0.25 mmol), [Au] (0.5 mol%), solvent-free, 80 °C, 400 rpm; conversions were analysed by ^{1}H NMR by using 1,3,5-trimethoxybenzene (5 mg) as internal standard; average of 2 runs for each catalyst.

Further studies into the catalytic activity of the complexes were made. The direct comparison with the hydrophenoxylation of internal alkynes was immediate.[4] The reaction of phenol **3.31** and diphenylacetylene **3.22** was performed with 0.5 mol% of the new dinuclear gold carboxylate complexes (Figure 3.14), in PhMe at 110 °C. The results were compared to what was obtained with digold hydroxide **3.1**. All the complexes were active in the transformation, with full conversion into product **3.32** after 40-90 min. As shown by the graph, digold carboxylate **3.6** outperformed **3.1** under the reaction condition, with > 99% conversion into **3.32** after 40 min reaction *vs* 60 min found for digold hydroxide **3.1**. Interestingly digold acetate **3.10** was the poorest catalysts, but still showed full conversion after 90 min.

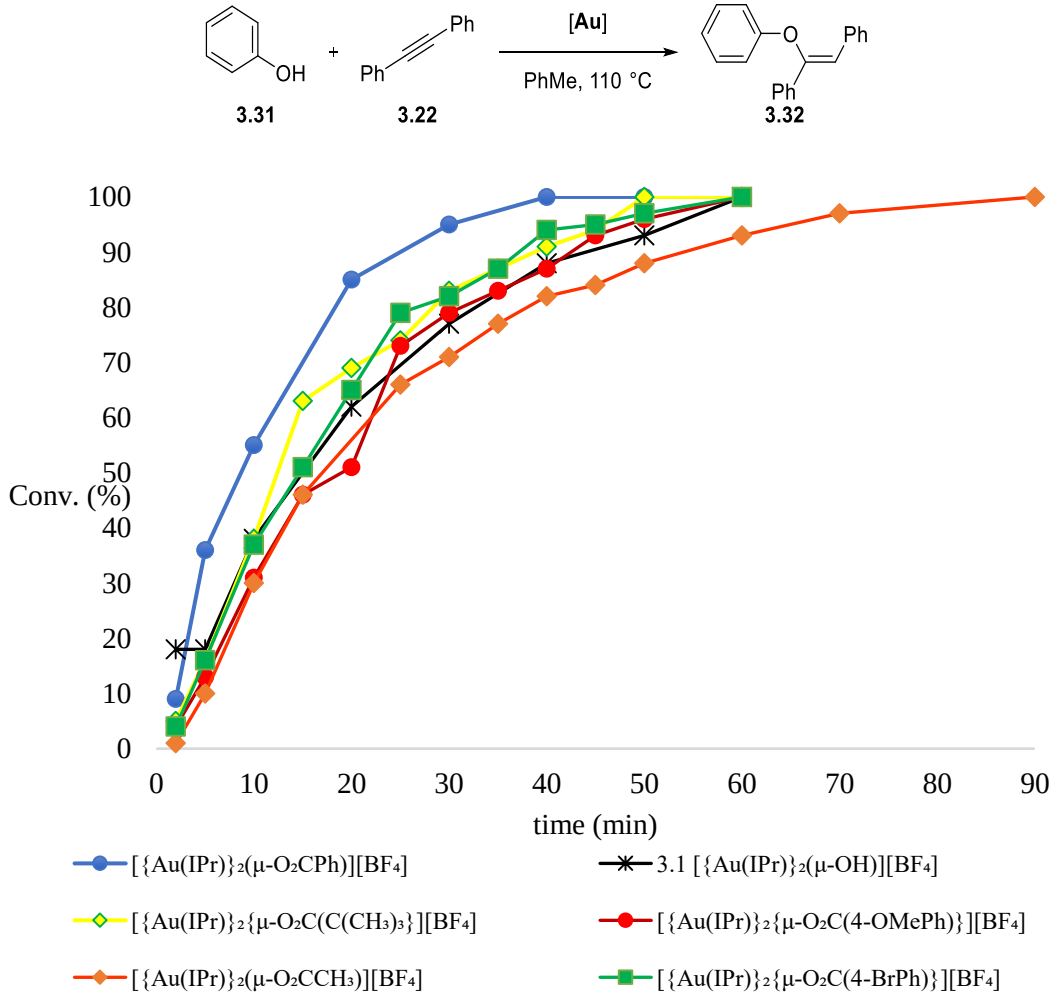


Figure 3.14. Comparison of reaction profile of the hydrophenoxylation of alkynes catalysed by dinuclear gold complexes. Reaction conditions phenol **3.31** (0.5 mmol), diphenylacetylene **3.22** (0.55 mmol, 1.1 equiv.), PhMe (0.5 M), 80 °C; every run is an average of 2 runs.

3.2.2.3. Computational analysis

To help shed light into the reaction mechanism we turned to computational calculations; the energy of intermediates and possible transition states for the reaction of acetic acid **3.23** and diphenylacetylene **3.22** catalysed by dinuclear gold hydroxide **3.1** were calculated (Figure 3.15). The solvent of choice was benzene that best reflected the stoichiometric reactions, and the catalytic conditions. On the basis of the kinetics and thermodynamic analysis presented, the formation of **3.24** and **3.16**, such as the π-alkyne-Au(I) and acetate-Au(I) complex, from digold hydroxide **3.1** mainly arises from cleavage by alkyne (15.6 kcal·mol^{-1}). The cleavage of the pre-catalyst through acetic acid **3.23** was found to be of 23.3 kcal·mol^{-1}, higher than that from the alkyne and therefore less likely to occur. However, the same step from the hydrophenoxylation of alkynes for the activation of **3.1** through phenol was found to be lower (15.5 kcal·mol^{-1}),[5] maybe due to the different solvent used for the calculations (benzene *vs* $CDCl_3$). From this, it can be assumed that the most likely pathway to form dinuclear carboxylate **3.10** will arise from **3.1** through **3.24** and **3.16**. The formation of **3.10** digold acetate is rather facile from these species, by overcoming a barrier of 8.3 kcal·mol^{-1} and releasing an alkyne molecule (**3.22**). The reverse barrier from **3.10** to **3.24** and **3.16** is of 14.5 kcal·mol^{-1}. The formation of the dimer is quite reversible, as observed in the calculated pathways from dinuclear phenoxide species in the hydrophenoxylation of alkynes.[5] This species does not appear to be an off-cycle intermediate for the catalytic cycle from **3.1**, which reiterates the results obtained by stoichiometric, catalytic and kinetic experiments. The next step calculated was the formation of C-O between **3.24** and **3.16** to give intermediate **II**. This step requires the overcoming of a barrier of 11.7 kcal·mol^{-1}, which is 3.4 kcal·mol^{-1} higher in energy the transition state **3.24**+**3.16**→**3.10**. This step is however lower than the activation of **3.1**→**3.24**+**3.16** of 3.9 kcal·mol^{-1}. The result suggested the reversibility of the C-O process, which cannot be the RDS of the reaction from **3.1**.

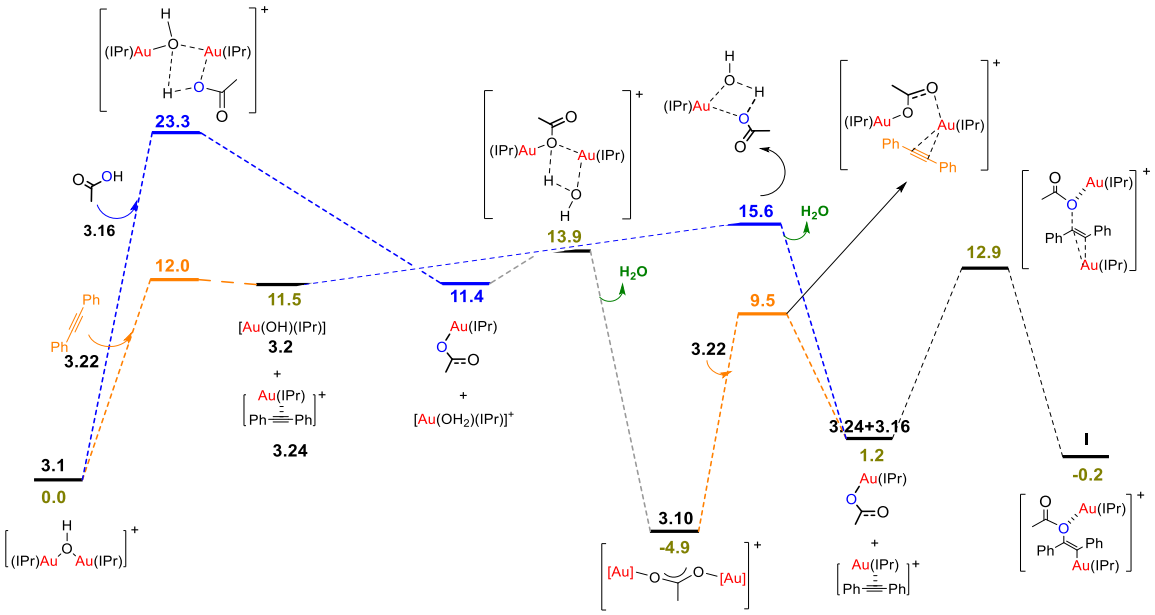


Figure 3.15. Calculated kinetic and thermodynamics analysis for the hydroacyloxylation of alkynes. These results were performed by Sai V. C. Vummaleti.

3.2.2.4. Proposed mechanistic cycle

In summary, the formation of dinuclear gold carboxylate complexes was verified; the species promptly form in catalytic, and stoichiometric conditions. Moreover, dinuclear gold carboxylate complexes were suitable pre-catalysts for the intermolecular hydrocarboxylation of alkynes. The formation of **3.10** from precursor **3.1** was found to be energetically favoured, and the major pathway when reacting acetic acid **3.23** with digold hydroxide **3.1**. The role of the acid might be described as an activator of the pre-catalyst **3.1**, to form the dinuclear complex and further dissociate into the catalytic active species. Attempted kinetic analysis described a pseudo-first order for the catalysed acetic acid **3.23** addition into diphenylacetylene **3.22** by **3.1**. This data suggested that a mononuclear species will be involved in the rate-determining step for the reaction; comparison with literature data suggest it being the protodeauration.[5,47a] However, dinuclear activation of substrates cannot be ruled out, which support the high conversion, and the extreme efficiency of dinuclear gold catalysts.

The mechanistic cycle for the gold catalysed intermolecular cyclisation of diphenylacetylene **3.22** and benzoic acid **3.5** can be updated (Figure 3.16).

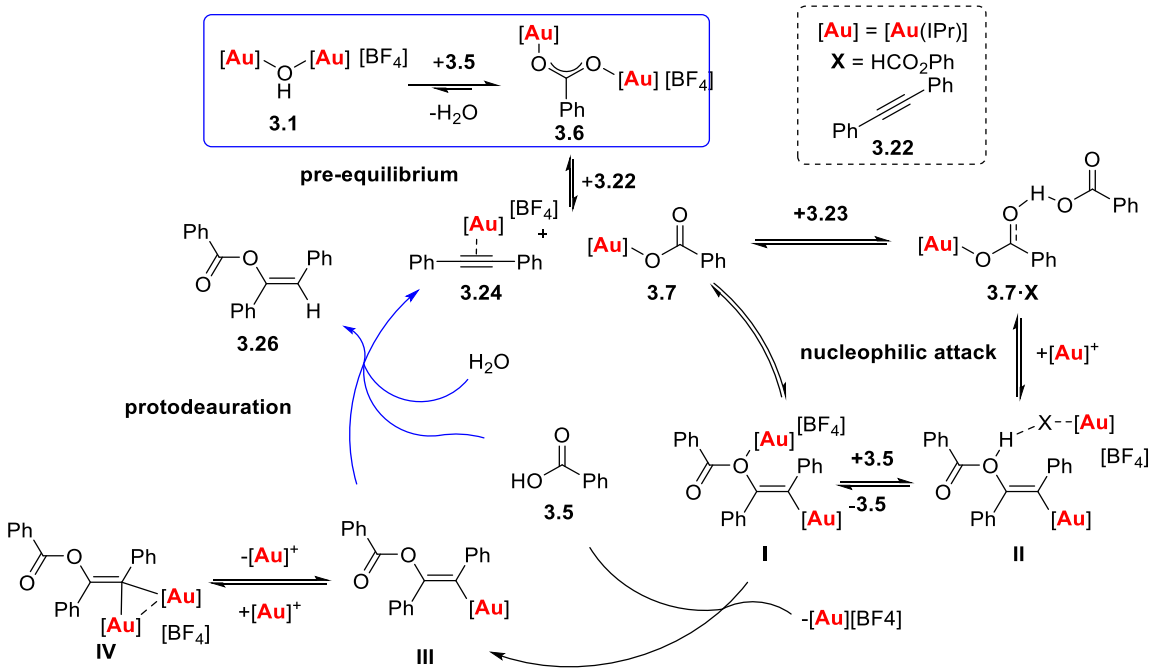
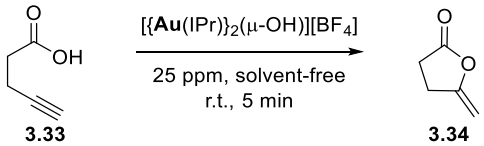


Figure 3.16. Postulated mechanistic cycles.

The pre-equilibrium step included the formation of **3.6** from **3.1** in presence benzoic acid **3.5**. Activation of **3.6** with diphenylacetylene (**3.22**) led to π-alkyne- (**3.24**), and carboxylate-Au(I) (**3.7**) species. **3.7**·X (X = $HOC(O)CH_3$) might be considered in presence of excess acid. Nucleophilic attack in an *anti*-periplanar fashion will occur to form species **I/II**, where the species **3.7/3.7**·X act as proton shuffle to aid the C-O bond formation.[51] Formation of vinyl-Au(I) **III** from **I/II**, in equilibrium with **IV**, followed protodeauration aided either by acid, H_2O or acid, led to product **3.26**, and reform active catalyst $[Au(IPr)]^+$.

3.2.3. Intramolecular considerations

The mechanism of the intramolecular hydroacyloxylation of alkynes catalysed by digold hydroxide **3.1** was explored next (Scheme 3.19).



Scheme 3.19. Intramolecular hydroacyloxylation of alkynoic acid **3.33** to γ-lactone **3.34**.

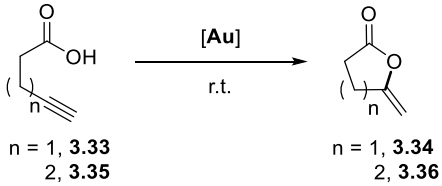
Differently from the intermolecular reaction, the cyclisation of **3.33** into **3.34** was found to be catalysed efficiently by monoaurated complexes, such as **3.2** [Au(OH)(IPr)].

The conversions were similar to the results obtained with **3.1** but dependent on the substrates used. Table 3.4 summarises the data obtained for the cyclisation of 4-pentynoic acid **3.33** and 5-hexynoic acid **3.35**. The data showed that for the cyclisation of **3.33** to γ-lactone **3.34**, the best performing catalysts in solvent-free conditions were **3.1** and **3.2** with a catalyst loading as low as 0.2 mol% and 0.4 mol%, respectively (Table 3.4, entries 1, 2). A comparison with a lower performing catalyst, [Au(IPr)(NCCH$_3$)][BF$_4$] **3.15**, (which afforded only 50% conversion after 5 mins of reaction, entry 3), showed that the presence of the Brønsted basic moiety has a major role in the catalysis. However, the mononuclear complex **3.15** still performed well for this transformation at low catalyst loading after 5 min reaction.

By lowering the catalyst loading to 100 ppm for **3.1** (Table 3.4, entry 5), and 200 ppm for **3.2** (entry 6), the dinuclear precursor **3.1** was found to be very efficient for this transformation. It should be noted that the use of CHCl$_3$ was not deleterious for the reaction (entry 4) affording 88% conversion at 0.1 mol% catalyst loading of **3.1** after 5 min, which will come in useful for future kinetic experiments. The dinuclear gold carboxylate complexes **3.6** and **3.10** were tested at low catalyst loading (entries 7, 8) but showed lower conversion (67–78%) by performing the reaction in solvent-free conditions after 24 h.

The use of dinuclear complexes was then found more efficient for 5-hexynoic acids (Table 3.4, entries 9, 10), where **3.1** catalysed full conversions of **3.35** into δ-lactone **3.36** after 1 h, while **3.2** showed only 40% conversions.

Table 3.4. Catalyst effect on the cyclisation of alkynoic acids **3.33** and **3.35.**



n = 1, **3.33**
2, **3.35**

n = 1, **3.34**
2, **3.36**

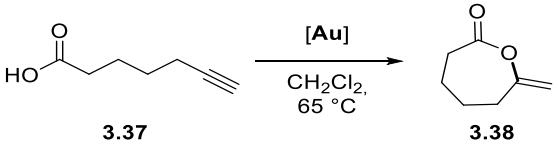
Entry	[Au]	Cat. loading (mol%)	n	Solvent (M)	t (h)	Conv (%)[a]
1	**3.1**	0.2	1	solvent-free	5 min	>99
2	**3.2**	0.4	1	solvent-free	5 min	>99
3	**3.15**	0.4	1	solvent-free	5 min	50
4	**3.1**	0.1	1	$CHCl_3$ (10)	5 min	88
5	**3.1**	100 ppm	1	solvent-free	1	92
6	**3.2**	200 ppm	1	solvent-free	1	78
7	**3.6**	100 ppm	1	solvent-free	24	65
8	**3.10**	100 ppm	1	solvent-free	24	67
9	**3.1**	0.1	2	solvent-free	1	>99
10	**3.2**	0.2	2	solvent-free	1	40

Reaction conditions: **3.33** (0.5 mmol) or **3.35** (0.5 mmol), r.t., [Au] 100 ppm-0.4 mol%, conversions calculated by ^{1}H NMR spectroscopy using pivalaldehyde as internal standard (10 μL); [b] A stock solution in CH_2Cl_2 was prepared for 100 ppm and 200 ppm from 0.1 mol% ($0.25\cdot10^{-3}$ M) of **3.1**, 0.2 mol% ($0.5\cdot10^{-3}$ M) of **3.2**; the amount required at the right concentration (100 and 200 ppm) was collected and dried under vacuum.

Similar results as obtained for 6-hexynoic acid, were found for the cyclization of heptynoic acid **3.37** into ε-caprolactone **3.38** (Table 3.5). This reaction was found generally more challenging and had to be performed in CH_2Cl_2 at 65 °C in sealed vessels to decrease polymerization.

In this case the use of dinuclear gold species was found necessary (Table 3.5, entries 1, 2), and the catalyst loading needed to be > 1 mol%; a catalyst loading of 0.5 mol% for **3.1** showed only 13% conversion after 18 h at 50 °C (entry 3). **3.2** was found less active for this transformation (entry 4), as well as less regioselective, with formation of dimers and polymers in the reaction mixture. Surprisingly, dinuclear carboxylate behaved very well for the cyclisation of heptynoic acid (entry 5), with a low catalyst loading of **3.6** at 0.5 mol% showing full conversion into **3.40**. By decreasing the catalyst loading as low as 0.1 mol% the cyclisation could be performed after 5 h with 65% conversions for **3.6** (entry 6). **3.10** outperformed all the catalysts showing 81% conversions after 5 h at 0.1 mol% catalyst loading (entry 7).

Table 3.5. Catalyst effect on the cyclisation of **3.37**.

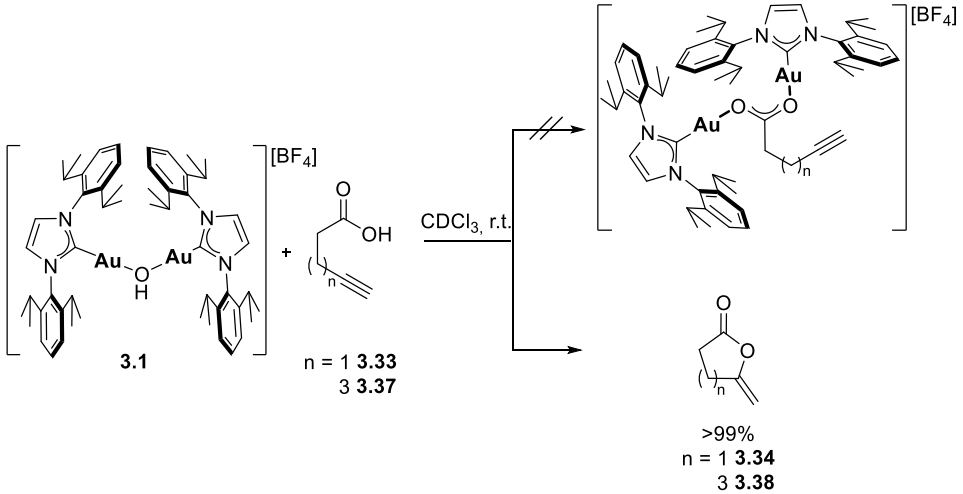


3.37 **3.38**

Entry	[Au]	Cat. loading (mol%)	Solvent (0.25 M)	T (°C)	t (h)	Conv (%)[a]
1	**3.1**	1	CH_2Cl_2	65	5	78
2	**3.1**	1	CH_2Cl_2	65	18	>99
3	**3.1**	0.5	CH_2Cl_2	50	18	13
4	**3.2**	2	CH_2Cl_2	65	5	52[b]
5	**3.6**	0.5	CH_2Cl_2	65	5	99
6	**3.6**	0.1	CH_2Cl_2	65	5	65
7	**3.10**	0.1	CH_2Cl_2	65	5	81

[a] Reaction conditions: 7-heptynoic acid **3.37** (0.5 mmol), [Au] 0.5–2 mol%, CH_2Cl_2 (0.25 M), 65 °C in sealed vessels; ^{1}H NMR conversions calculated using pivalaldehyde as internal standard (10 µL, 0.092 mmol); [b] side-products formation confirmed by ^{1}H NMR spectroscopy and tentatively assigned as dimers or polymers of 7-heptynoic acid.

Initial stoichiometric studies were performed to see whether a dinuclear species could be isolated from alkynoic acids (Scheme 3.20). However, reacting **3.33** or **3.37** with an equimolar amount of **3.1** in $CDCl_3$ at r.t. showed no traces of the desired intermediate and full conversion to the cyclised products was obtained. Decomposition was observed for the gold species, with formation of a golden mirror on the NMR tube walls.



Scheme 3.20. Attempt to isolate dinuclear gold carboxylate from alkynoic acids and **3.1**.

Therefore, in order to obtain some evidence into the mechanism, we monitored the conversion of **3.33** into **3.34** catalysed by different concentration of **3.1**, ranging from 200 to 1000 ppm, in $CDCl_3$ (Figure 3.17). The kinetic experiments were set up in an oven-dried NMR tube. The NMR tube was filled with 10 µL of pivalaldehyde as the internal

standard and 4-pentynoic acid **3.33**. The t^0 was set using 500 µL of $CDCl_3$. After t^0, 100 µL of the catalyst stock solution for each concentration of the catalyst were added and the analysis started.

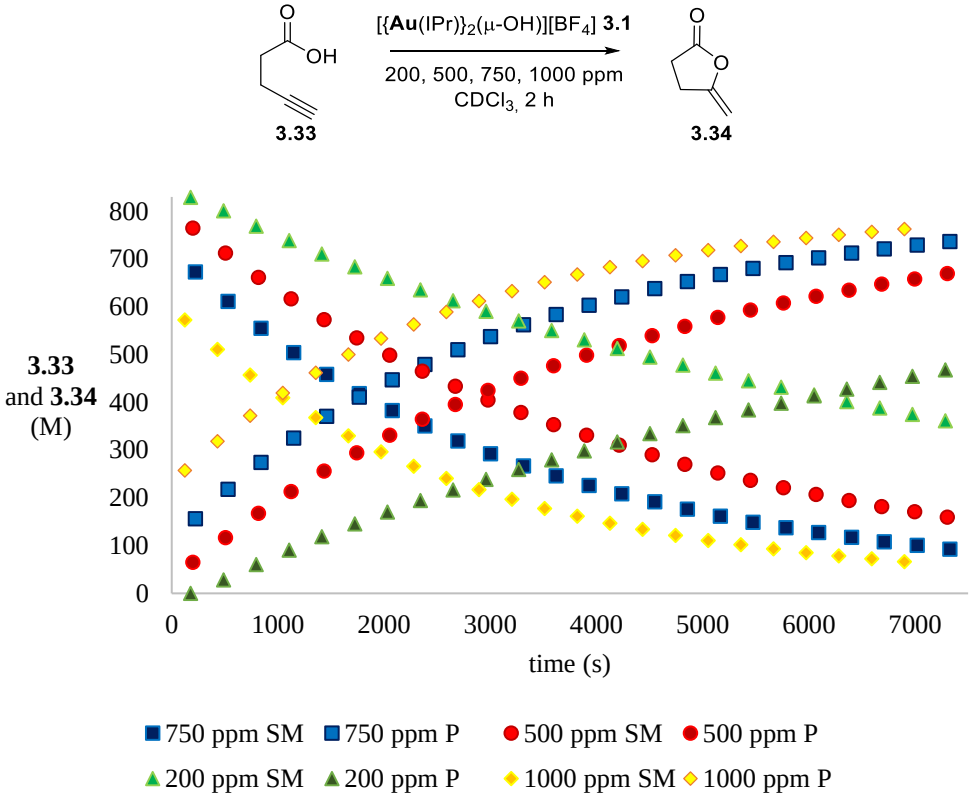


Figure 3.17. Conversions of starting material and product over time at different catalyst concentrations. Experiment conditions: **3.33** (0.5 mmol), pivalaldehyde (0.092 µmol), final concentration of the NMR tube 0.83 M. **3.1** stock solution was prepared by increasing the concentration from 200 ppm ($1 \cdot 10^{-4}$ mmol, 1.23 M), 500 ppm ($2.5 \cdot 10^{-4}$ mmol, 3.08 M), 750 ppm ($3.75 \cdot 10^{-4}$ mmol, 4.62 M) to 1000 ppm ($5 \cdot 10^{-4}$ mmol, 6.16 M) catalyst loading.

By calculating the natural logarithm of the substrate concentration at t^0 (C^0) *vs* the concentration at t^x (C), and by plotting the data obtained at each catalyst loading (200–1000 ppm) *vs* time (s), the rate equation for each curve could be obtained (Figure 3.18). The R^2 values were ~1 for each plot, describing a very good fit to the data.

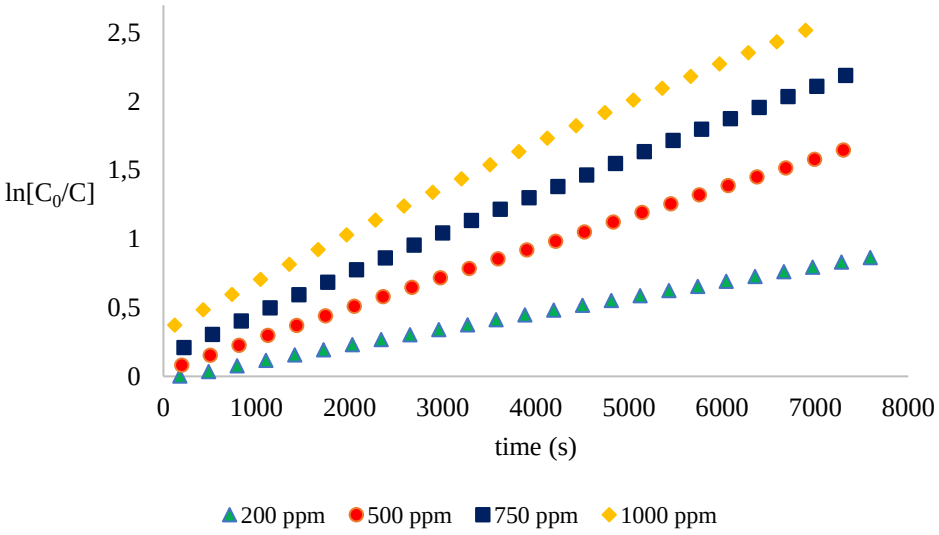


Figure 3.18. Calculation of k_{obs}: $ln(C^0/C)$ *vs* time.

The reaction exhibited first-order dependence to **3.1**. By plotting the rate constant (k_{obs}) *vs* catalyst concentration, the order dependence with respect to the catalyst felt into a first-order dependence, with slight deviation at lower catalyst loading that might suggest a more complex picture (Figure 3.19).

Cat. loading **3.1** (ppm)	k_{obs} (s^{-1})
200	$1.16 \cdot 10^{-04}$
500	$2.33 \cdot 10^{-04}$
750	$2.78 \cdot 10^{-04}$
1000	$3.17 \cdot 10^{-04}$

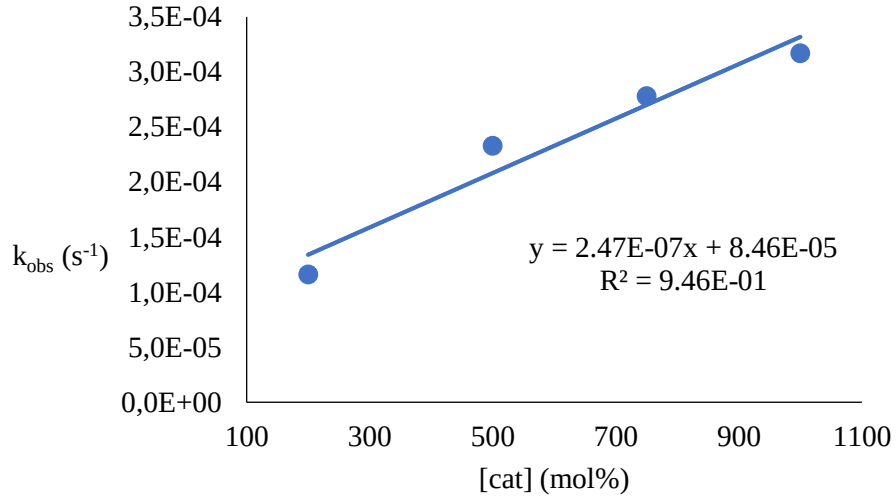
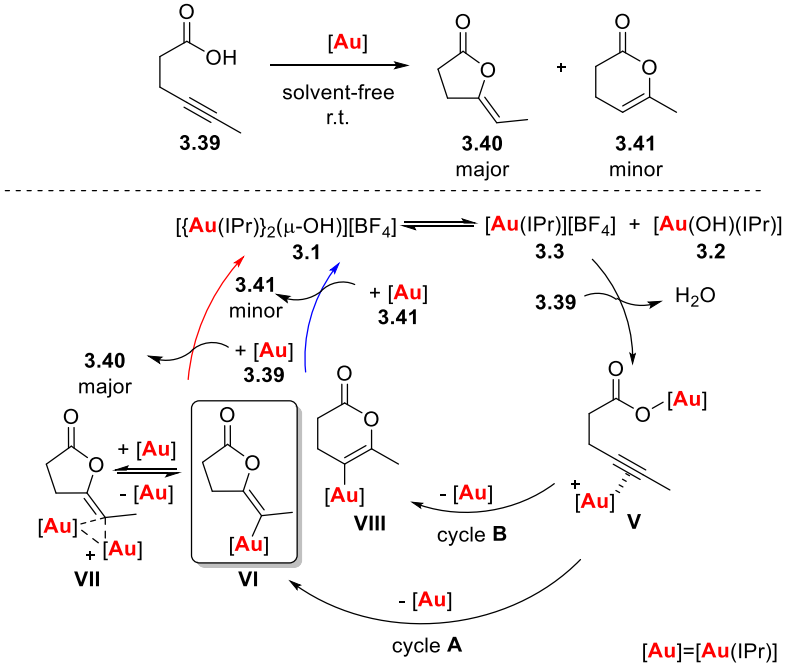


Figure 3.19. Calculation of catalyst order of **3.1**.

As these initial results suggest, cooperative catalysis might not be operative for this intramolecular transformation,[47a] and preliminary kinetics results might not allow full comprehension of the dominant pathway. Therefore, firm conclusions apropos the catalytic cycle for the cyclisation of alkynoic acids cannot be stated, and several possibilities might be considered (Scheme 3.21). However, the consideration of dissociation of **3.1** into **3.2** and **3.3** does help to rationalise the high conversions obtained using **3.2** as a sole pre-catalyst (Table 3.4). As seen from the catalytic test and the kinetic experiments, the results at low catalyst loadings (< 200 ppm) were not as efficient when the reaction was performed with **3.2**. The kinetic experiments showed a slight deviation from linearity when < 200 ppm of **3.1** were utilised (Figure 3.19); this result might be due to a switch of mechanism, probably a dual catalytic pathway. Finally, the results showed how dinuclear Au(I) complex **3.1**, **3.6** and **3.10** were essential for the synthesis of ε-lactones, suggesting that a dual catalysis mechanism might be most likely to drive the reaction to completion in a regioselective fashion. As highlighted in Scheme 3.21, the mechanism for the *exo*- or *endo*-cyclisation of hex-4-ynoic acid (**3.39**) was postulated.[52] The major pathway will be the one pictured as cycle A where *exo*-cyclisation will lead to the major species **3.40**, after protodeauration. The minor pathway, cycle B, will instead lead to the minor *endo*-product **3.41**.



Scheme 3.21. Postulated catalytic cycle for the cyclisation of **3.39** into **3.40** and **3.41**.

3.3. Conclusion and perspective

An initial analysis into the hydroacyloxylation of alkynes was performed. The formation of dinuclear gold carboxylate species can be envisaged to form under the reaction conditions. The complexes were obtained in good yield and fully characterised by NMR and IR spectroscopy. Their structures were confirmed by X-ray analysis. These species were competent pre-catalysts for the intermolecular hydrocarboxylation of alkynes; moreover, they are competent in performing other catalytic processes, such as the hydrophenoxylation of alkynes together with the intramolecular version of the hydrocarboxylation process. Further advances in the use and application of the novel digold carboxylate species might be helpful to explore new reactivity modes and have a further insight into their role in catalysis.

Mechanistic investigations into the dinuclear gold catalysed hydrocarboxylation of alkynes were performed. Initial stoichiometric reactions were followed in deuterated solvent to mimic at best the reaction conditions. However, the reaction did not proceed in $CDCl_3$, for which case the formation of the dinuclear species might be a resting state of the catalyst or the formation of an off-cycle species might interfere with the catalytic cycle. In deuterated bromobenzene the results showed that formation of the dinuclear species is favoured, and the species does not seem to be a resting state of the catalyst. These species might be in equilibrium with pre-catalyst **3.1** in presence of acid, thus allowing activation of the pre-nucleophile. The kinetics of the transformation was studied; an attempt to follow the reaction in neat conditions was presented, which suggested a pseudo-first order in catalyst for the intermolecular hydrocarboxylation of alkynes. An insight through computational analysis suggested that activation of the digold carboxylate from **3.1** is the energetically favoured pathway. Further information about the protodeauration step by computational analysis will follow.

The cyclisation of alkynoic acids was studied; no intermediate could be recognised by stoichiometric tests, the reaction profile was followed by kinetic analysis in $CDCl_3$ and showed a clean 1^{st} order kinetic for the reaction, suggesting a mononuclear metal centre being involved in the RDS step of the reaction.

3.4. Experimental

Unless otherwise stated, all solvents and reagents were used as purchased and all reactions were performed under air. Anhydrous CH_2Cl_2, THF, and PhMe were obtained from an MBraun SPS-800 system. All other solvents and commercial reagents were used as received without further purification unless otherwise stated. Room temperature (r.t.) refers to 20–25 °C. ^1H, $^{13}C\{^1H\}$, $^{19}F\{^1H\}$ NMR spectra were recorded on Bruker Avance 500-300 MHz NMR spectrometers. In $CDCl_3$ and C_6D_6, ^1H and $^{13}C\{^1H\}$ NMR chemical shifts are reported relative to $CHCl_3$, C_6H_6 at 7.26 ppm and 7.16 ppm, 77.16 ppm and 128.06 ppm respectively. In BrC_6D_5, ^1H and $^{13}C\{^1H\}$ NMR chemical shifts are reported relative to C_6H_6 at 7.16 ppm and 128.06. For the assignment of the ^1H and $^{13}C\{^1H\}$ NMR spectra 2D NMR (COSY, HSQC, HMBC) experiments were also performed. Coupling constants (*J*) are reported in Hertz (Hz). Multiplicities are indicated by: br s (broad singlet), s (singlet), d (doublet), t (triplet), q (quartet) and m (multiplet). Infrared spectra (νmax) were recorded on a Shimadzu IRAffinity-1 Fourier transform IR spectrophotometer using either thin film or solid using Pike MIRacle ATR accessory. Analysis was carried out using Shimadzu IRsolution v1.50 and only characteristic peaks are reported. Elemental analyses were performed by Stephen Boyer, at London Metropolitan University. Geometry optimizations were performed at the GGA level with the Gaussian09 set of programs using the BP86 functional of Becke and Perdew.[53-55] The electronic configuration of the molecular systems was described with the standard split-valance basis set with a polarization function of Ahlrichs and co-workers for main-group atoms (SVP keyword in Gaussian).[56] For Au, the small-core, quasi relativistic Stuttgart/Dresden effective core potential, with the associated triple-ζ-valence basis set contracted was used (standard SDD keyword in Gaussian09).[57] No symmetry constraint was used in the geometry optimizations, and the final geometries were confirmed to be maximum or minimum potential energy structures through frequency calculations. The reported energies were obtained via single-point calculations on the BP86 optimized geometries using the M06 functional and triple-ζ basis set for main-group atoms (TZVP keyword in Gaussian09).[58,59] The influence of the solvent (benzene) was included in these single-point energy calculations by using the polarization continuum solvation model PCM.[59] Since entropic contribution calculated within the ideal gas approximation at P = 1 atm is exaggerating the expected values for the dissociative steps in the condensed

phase, all the thermochemical analyses were performed at P = 1354 atm.[60,61] [{Au(NHC)}$_2$(μ-OH)][X] (NHC = IPr, SIPr, IPr^{Cl}, IPent, X = BF_4, SbF_6, FABA) [Au(OH)(IPr)] **3.2**, [Au(IPr)(NCCH$_3$)][BF_4] **3.15**, [Au(OC(O)R)(IPr)] (R = Ph **3.7**, CH_3 **3.16**), [Au(IPr)(η^{2}PhC≡CPh)][BF_4] **3.24** were synthesised according to literature reports.[1,4,36,38-39,62] [Au($CH_2C(O)CH_3$)(NHC)] (NHC = IPr **3.17**, SIPr **3.18**, IMes **3.19**, IPr***3.20**, IPr^{Cl} **3.21**) are reported in chapter 6 of this thesis.[36] For full characterisation of **3.25**, **3.26**, **3.27**, **3.34**, **3.36**, **3.38** see chapter 2. **3.26** ^{1}H NMR (500 MHz, C_6D_6) δ = 8.19 – 8.13 (m, 2H), 7.60 – 7.56 (m, 2H), 7.55 – 7.50 (m, 2H), 7.11 – 6.92 (m, 10H), 6.70 (s, 1H); **3.25** ^{1}H NMR (500 MHz, C_6D_6) δ = 7.51 – 7.45 (m, 2H), 7.45 – 7.41 (m, 2H), 7.21 – 7.11 (m, 13H), 7.10 – 7.04 (m, 2H), 6.54 (s, 1H), 1.76 (s, 3H); **3.7** ^{1}H NMR (400 MHz, C_6D_6) δ = 8.37 – 8.26 (m, 2H), 7.04 (d, *J* = 7.7 Hz, 4H), 7.00 – 6.94 (m, 4H), 6.26 (s, 2H), 2.57 (dp, *J* = 14.1, 6.9 Hz, 4H), 1.51 (d, *J* = 6.9 Hz, 11H), 1.07 (d, *J* = 6.9 Hz, 12H); **3.16** ^{1}H NMR (400 MHz, C_6D_6) δ = 7.16 (p, *J* = 1.1 Hz, 58H), 7.02 (d, *J* = 7.7 Hz, 4H), 6.24 (s, 2H), 2.55 (h, *J* = 7.1 Hz, 4H), 1.89 (s, 3H), 1.49 (d, *J* = 6.9 Hz, 13H), 1.05 (d, *J* = 6.9 Hz, 12H).

3.4.1. General procedure for the synthesis of dinuclear gold carboxylate complexes GP1:

[{Au(NHC)}$_2$(μ-OH)][X] **3.1** (1 equiv.) was mixed with the chosen carboxylic acid (1 equiv.) and stirred in $CDCl_3$ (0.6 mL) at room temperature. At mixing time full conversion into [{Au(NHC)}$_2$(μ-O_2CR)][X] was observed. The crude mixture was filtered through a pad of celite© and washed with dichloromethane (~ 4 mL). The solvent was reduced under vacuum and the product precipitated by addition of pentane. C_6D_6, PhMe, BrC_6D_5, THF were tolerated to perform the transformation.

[{Au(IPr)}$_2$(μ-O_2CPh)][BF_4] **3.6** was prepared according to GP1. The compound was obtained by mixing [{Au(IPr)}$_2$(μ-OH)][BF_4] **3.1** (100 mg, 0.078 mmol) and benzoic acid (9.6 mg, 0.078 mmol) in $CDCl_3$ (0.6 mL). After solvent drying and recrystallisation, a colourless solid was collected in 89% isolated yield (95.9 mg). ^{1}H NMR (400 MHz, $CDCl_3$) δ = 7.53 (t, *J* = 7.8, 4H, *p*-CH IPr), 7.44 – 7.39 (m, 2H, *o*-CH carboxylate), 7.33 (s, 4H, CH imidazole), 7.29 – 7.25 (m, 9H, *m*-CH IPr and *p*-CH carboxylate), 6.88 (t, *J* = 7.9, 2H, *m*-CH carboxylate), 2.44 (hept, *J* = 7.0, 8H, $CH(CH_3)_2$), 1.21 (d, *J* = 6.9, 24H,

$CH(CH_3)_2$), 1.12 (d, *J* = 6.9, 24H, $CH(CH_3)_2$). ^{1}H NMR (400 MHz, BrC_6D_5) δ = 7.65 – 7.53 (m, 10H), 7.40 (d, *J* = 7.7 Hz, 9H), 7.34 – 7.21 (m, 7H), 6.87 (t, *J* = 7.8 Hz, 2H), 2.78 (hept, *J* = 7.0 Hz, 8H), 1.43 (dd, *J* = 13.4, 6.8 Hz, 48H). ^{13}C{^{1}H} NMR (126 MHz, $CDCl_3$) δ = 180.1 (CO_2Ph), 162.0 ($C_{carbene}$), 145.7 (Cq), 133.9 (Cq), 133.8 (Cq), 131.7 (*p*-CH carboxylate), 131.1 (*p*-CH IPr), 128.2 (*m*-CH carboxylate), 128.0 (*o*-CH carboxylate), 124.6 (*m*-CH IPr), 124.4 (CH imidazole), 28.9 ($CH(CH_3)_2$), 24.6 ($CH(CH_3)_2$), 24.0 ($CH(CH_3)_2$). ^{19}F{^{1}H} NMR (377 MHz, $CDCl_3$) δ = -154.42, -154.47. FTIR (ATR) ν = 2960, 2926 (C-H), 1589, 1543 (C=O), 1458 cm^{-1}; elemental anal. calcd. for $C_{61}H_{77}O_2Au_2N_4BF_4$ (1382.07 $g \cdot mol^{-1}$) (%): C 53.13; H 5.63; N 4.06; found: C 53.03; H 5.59; N 4.11.

$[\{Au(IPr)\}_2(\mu\text{-}O_2C^4\text{-}OMeC_6H_4)][BF_4]$ **3.8** was prepared according to GP1. The compound was obtained by mixing $[\{Au(IPr)\}_2(\mu\text{-}OH)][BF_4]$ **3.1** (40 mg, 0.037 mmol) and 4-methoxybenzoic acid (5.7 mg, 0.037 mmol) in $CDCl_3$ (0.6 mL). After solvent drying and recrystallisation, a colourless solid was collected in 80% isolated yield (41.7 mg). ^{1}H NMR (400 MHz, $CDCl_3$) δ = 7.52 (q, *J* = 7.2, 6.6 Hz, 4H, *p*-CH IPr), 7.49 – 7.43 (m, 2H, *o*-CH carboxylate), 7.32 (s, 4H, CH imidazole), 7.31 – 7.20 (m, 8H, *m*-CH IPr), 6.35 (d, *J* = 8.5 Hz, 2H, *m*-CH carboxylate), 3.79 (s, 3H, OMe), 2.45 (p, *J* = 6.8 Hz, 8H, $CH(CH_3)_2$), 1.21 (d, *J* = 6.9 Hz, 24H, $CH(CH_3)_2$), 1.13 (d, *J* = 6.9 Hz, 24H, $CH(CH_3)_2$). ^{13}C{^{1}H} NMR (101 MHz, $CDCl_3$) δ = 162.3 ($C_{carbene}$), 145.7 (Cq), 133.9 (Cq), 131.0 (*p*-CH IPr), 130.6 (*m*-CH carboxylate), 124.6 (*m*-CH IPr), 124.4 (CH imidazole), 113.5 (o-CH carboxylate), 55.5 (OMe), 28.9 ($CH(CH_3)_2$), 24.6 ($CH(CH_3)_2$), 24.0 ($CH(CH_3)_2$). ^{19}F{^{1}H} NMR (376 MHz, $CDCl_3$) δ = -154.30, -154.25. FTIR (ATR) ν = 2960 (C-H), 1604, 1522, 1508 (C=O), 1408.04 cm^{-1}; element. anal. calcd. for $C_{62}H_{79}O_3Au_2N_4BF_4$ (1411.10 $g \cdot mol^{-1}$) (%): C 52.85; H 5.65; N 3.98; found: C 52.92; H 5.43; N 4.06.

$[\{Au(IPr)\}_2(\mu\text{-}O_2C^4\text{-}BrC_6H_4)][BF_4]$ **3.9** was prepared according to GP1. The compound was obtained by mixing $[\{Au(IPr)\}_2(\mu\text{-}OH)][BF_4]$ **3.1** (20 mg, 0.015 mmol) and 4-bromobenzoic acid (4.73 mg, 0.015 mmol) in $CDCl_3$ (0.6 mL). After solvent drying and recrystallisation, a colourless solid was collected in 80% isolated yield (18.3 mg). ^{1}H NMR (400 MHz, $CDCl_3$) δ = 7.56 (t, *J* = 7.8 Hz, 2H, *p*-CH IPr), 7.33 (s, 2H, CH imidazole), 7.27 (dd, *J* = 8.2, 5.9 Hz, 8H, *m*-CH IPr), 6.98 – 6.92 (m, 2H, *m*-CH carboxylate, *o*-CH carboxylate), 2.51 – 2.35 (m, *J* = 6.9 Hz, 8H, $CH(CH_3)_2$), 1.21 (d, *J* =

6.9 Hz, 24H, $CH(CH_3)_2$), 1.11 (d, *J* = 6.8 Hz, 24H, $CH(CH_3)_2$). $^{13}C\{^1H\}$ NMR (101 MHz, $CDCl_3$) δ = 179.5 (O-C-O), 161.6 ($C_{carbene}$), 145.7 (Cq), 133.8 (Cq), 131.4 (*m*-CH carboxylate), 131.1 (*p*-CH IPr), 129.4 (*o*-CH carboxylate), 124.7 (*m*-CH IPr), 124.4 (CH imidazole), 28.9 ($CH(CH_3)_2$), 24.7 ($CH(CH_3)_2$), 24.0 ($CH(CH_3)_2$). $^{19}F\{^1H\}$ NMR (376 MHz, $CDCl_3$) δ = -154.30, -154.25. FTIR (ATR) ν = 2961, 1579 (OCO), 1529 (C=O), 1412 cm^{-1}; element. anal. calcd. for $C_{62}H_{79}O_3Au_2N_4BF_4$ (1460.97 g·mol^{-1}) (%): C 50.25; H 5.25; N 3.84; found: C 49.99; H 5.09; N 3.87.

[[{Au(IPr)}$_2$(μ-O_2CCH_3)][BF_4] **3.10** was prepared according to GP1. The compound was obtained by mixing [{Au(IPr)}$_2$(μ-OH)][BF_4] **3.1** (80 mg, 0.06 mmol) and acetic acid (3.6 μL, 0.06 mmol) in $CDCl_3$ (0.6 mL). After solvent drying and recrystallisation, a white solid was collected in 95% isolated yield (75.4 mg). ^1H NMR (500 MHz, $CDCl_3$) δ = 7.47 (t, *J* = 7.8 Hz, 4H, *p*-CH IPr), 7.37 (s, 4H, CH imidazole), 7.24 (d, *J* = 7.9 Hz, 8H, *m*-CH IPr), 2.42 (hept, *J* = 6.8 Hz, 8H, $CH(CH_3)_2$), 1.29 (d, *J* = 4.2 Hz, 3H, CH_3), 1.21 (d, *J* = 6.8 Hz, 24H, $CH(CH_3)_2$), 1.15 (d, *J* = 6.9 Hz, 24H, $CH(CH_3)_2$). ^1H NMR (500 MHz, C_6D_6) δ = 7.19 (s, 4H), 7.13 (d, *J* = 7.8 Hz, 3H), 6.95 (d, *J* = 7.8 Hz, 8H), 2.32 (h, *J* = 7.0 Hz, 8H), 1.01 (dd, *J* = 25.6, 6.9 Hz, 51H), 0.78 (s, 3H). $^{13}C\{^1H\}$ NMR (101 MHz, $CDCl_3$) δ = 184.6 (O-C-O), 162.9 ($C_{carbene}$), 145.8 (Cq), 133.8 (Cq), 130.9 (*p*-CH IPr), 124.5 (*m*-CH IPr), 124.3 (CH imidazole), 28.8 ($CH(CH_3)_2$), 25.1 (CH_3), 24.6 ($CH(CH_3)_2$), 24.1 ($CH(CH_3)_2$). $^{19}F\{^1H\}$ NMR (470 MHz, $CDCl_3$) δ = -154.36, -154.31. FTIR (ATR) ν = 2962 (C-H), 1539 (C=O), 1456 cm^{-1}; element. anal. calcd. for $C_{62}H_{79}O_3Au_2N_4BF_4$ (1319.55 g·mol^{-1}) (%): C 51.07; H 5.74; N 4.25; found: C 51.15; H 5.69; N 4.34.

[[{Au(IPr)}$_2${μ-O_2($C(CH_3)_3$)][BF_4] **3.11** was prepared according to GP1. The compound was obtained by mixing [{Au(IPr)}$_2$(μ-OH)][BF_4] **3.1** (30 mg, 0.023 mmol) and pivalic acid (2.4 mg, 0.023 mmol) in $CDCl_3$ (0.6 mL). After solvent drying and recrystallisation, a colourless solid was collected in 80% isolated yield (25.1 mg). ^1H NMR (400 MHz, $CDCl_3$) δ = 7.50 (td, *J* = 7.8, 3.6 Hz, 4H, *p*-CH imidazole), 7.34 (s, 4H, CH imidazole), 7.29 – 7.25 (m, 6H, *m*-CH IPr), 7.23 (d, *J* = 7.7 Hz, 2H, *m*-CH IPr), 2.54 – 2.35 (m, 8H, $CH(CH_3)_2$), 1.26 – 1.07 (m, 48H, $CH(CH_3)_2$), 0.72 (d, *J* = 3.1 Hz, 9H, $C(CH_3)_3$). $^{13}C\{^1H\}$ NMR (101 MHz, $CDCl_3$) δ = 162.7 ($C_{carbene}$), 145.7 (Cq), 133.9 (Cq), 130.9 (*p*-CH IPr), 124.6 (*m*-CH IPr), 124.4 (CH imidazole), 124.3 (*m*-CH IPr), 28.8 ($CH(CH_3)_2$), 28.8 ($C(CH_3)_3$), 28.2 ($C(CH_3)_3$), 24.6 ($CH(CH_3)_3$), 24.2 ($CH(CH_3)_2$), 24.0 ($CH(CH_3)_2$).

$^{19}F\{^{1}H\}$ NMR (376 MHz, $CDCl_3$) δ = -154.34, -154.28. FTIR (ATR) = 2960 (C-H), 1514 (C=O), 1469, 1456, 1053 cm^{-1}; element. anal. calcd. for $C_{62}H_{79}O_3Au_2N_4BF_4$ (1362.08 $g \cdot mol^{-1}$) (%): C 52.14; H 6.01; N 4.12; found: C 52.06; H 5.95; N 4.17.

$[\{Au(IPr)\}_2(\mu\text{-}O_2CPh)][SbF_6]$ **3.12** was prepared according to GP1. The compound was obtained by mixing $[\{Au(IPr)\}_2(\mu\text{-}OH)][SbF_6]$ (40 mg, 0.06 mmol) and benzoic acid (3.6 mg, 0.06 mmol) in $CDCl_3$ (0.6 mL). After solvent drying and recrystallisation, a colourless solid was collected in 82% isolated yield (75.3 mg). ^{1}H NMR (400 MHz, $CDCl_3$) δ = 7.54 (t, *J* = 7.8, 4H, *p*-CH IPr), 7.44 – 7.39 (m, 2H, *o*-CH carboxylate), 7.27 (d, *J* = 8.0, 10H, CH imidazole and *m*-CH carboxylate), 6.88 (t, *J* = 7.7, 2H, *m*-CH IPr and *p*-CH carboxylate), 2.44 (hept, *J* = 7.0, 8H, $CH(CH_3)_2$), 1.21 (d, *J* = 6.9, 25H, $CH(CH_3)_2$), 1.12 (d, *J* = 6.9, 23H, $CH(CH_3)_2$). $^{13}C\{^{1}H\}$ NMR (126 MHz, $CDCl_3$) δ = 180.1 (CO_2Ph), 162.1 ($C_{carbene}$), 145.7 (Cq), 133.9 (Cq), 133.8 (Cq), 131.7 (*m*-CH IPr), 131.1 (*p*-CH IPr), 128.3 (*m*-CH carboxylate), 128.0 (*o*-CH carboxylate), 124.5 (CH imidazole and *p*-CH carboxylate), 28.9 ($CH(CH_3)_2$), 24.6 ($CH(CH_3)_2$), 24.0 ($CH(CH_3)_2$). $^{19}F\{^{1}H\}$ NMR (376 MHz, $CDCl_3$) δ = -154.04, -154.09, -156.43. FTIR (ATR) ν = 2960 (C=O), 1589, 1520 (C=O), 1414 cm^{-1}; element. anal. calcd. for $C_{61}H_{80}O_2Au_2N_4SbF_6$ (1531.02 $g \cdot mol^{-1}$) (%): C 47.95; H 5.08; N 3.67; found: C 47.86; H 4.89; N 3.82.

$[\{Au(IPr)\}_2(\mu\text{-}O_2CPh)][FABA]$ **3.13** was prepared according to GP1. The compound was obtained by mixing $[\{Au(IPr)\}_2(\mu\text{-}OH)][FABA]$ (20 mg, 0.016 mmol) and benzoic acid (1.9 mg, 0.016 mmol) in $CDCl_3$ (0.6 mL). After solvent drying and recrystallisation, a colourless solid was collected in 40% isolated yield (12.6 mg). ^{1}H NMR (400 MHz, $CDCl_3$) δ = 7.54 (t, *J* = 7.8, 4H, *p*-CH IPr), 7.44 – 7.39 (m, 2H, *o*-CH carboxylate), 7.27 (d, *J* = 8.0, 10H, CH imidazole and *m*-CH carboxylate), 6.88 (t, *J* = 7.7, 2H, *m*-CH IPr and *p*-CH carboxylate), 2.44 (hept, *J* = 7.0, 8H, $CH(CH_3)_2$), 1.21 (d, *J* = 6.9, 25H, $CH(CH_3)_2$), 1.12 (d, *J* = 6.9, 23H, $CH(CH_3)_2$). $^{13}C\{^{1}H\}$ NMR (126 MHz, $CDCl_3$) δ = 180.1 (CO_2Ph), 162.1 ($C_{carbene}$), 145.7 (Cq), 133.9 (Cq), 133.8 (Cq), 131.7 (*m*-CH IPr), 131.1 (*p*-CH IPr), 128.3 (*m*-CH carboxylate), 128.0 (*o*-CH carboxylate), 124.5 (CH imidazole, and *p*-CH carboxylate), 28.9 ($CH(CH_3)_2$), 24.6 ($CH(CH_3)_2$), 24.0 ($CH(CH_3)_2$). $^{19}F\{^{1}H\}$ NMR (376 MHz, $CDCl_3$) δ = -132.61 (d, *J* = 17.4 Hz), -163.46 (t, *J* = 20.6), -167.05 (t, *J* = 19.7 Hz). FTIR (ATR) ν = 2965 (C-H), 1643, 1527, 1512 (C=O), 1461 cm^{-}

[1]; element. anal. calcd. for $C_{85}H_{77}O_2Au_2N_4BF_{20}$ (1974.31 g·mol^{-1}) (%): C 51.79; H 3.94; N 2.84; found: C 51.66; H 3.85; N 3.02.

[{Au(IPent)}$_2$(μ-O_2CPh)][BF_4] **3.14** was prepared according to GP1. The compound was obtained by mixing [{Au(IPent)}$_2$(μ-OH)][BF_4] (20 mg, 0.016 mmol) and benzoic acid (1.9 mg, 0.016 mmol) in $CDCl_3$ (0.6 mL). After solvent drying and recrystallisation, a colourless solid was collected in 92% isolated yield (8.9 mg). ^{1}H NMR (400 MHz, $CDCl_3$) δ = 7.55 (t, *J* = 7.8 Hz, 4H, *p*-CH IPr), 7.36 – 7.31 (m, 2H, *o*-CH carboxylate), 7.20 (d, *J* = 7.8 Hz, 5H, *m*-CH carboxylate + *m*-CH IPr), 7.14 (s, 4H, CH imidazole), 6.82 (t, *J* = 7.7 Hz, 2H, *m*-CH IPr), 2.02 (p, *J* = 7.3 Hz, 8H, $CH(CH_3)_2$), 1.60 (dp, *J* = 21.9, 7.1 Hz, 24H, $CH(CH_3)_2$), 1.46 (dt, *J* = 14.3, 7.4 Hz, 8H, $CH_2(CH_3)_3$), 0.73 (dt, *J* = 28.4, 7.4 Hz, 62H, $CH(CH_3)_2$ + $CH_2(CH_3)_3$ + $CH_2(CH_3)_3$). ^{13}C{^{1}H} NMR (101 MHz, $CDCl_3$) δ = 162.3 ($C_{carbene}$), 143.4 (Cq), 136.4 (Cq), 131.6 (*m*-CH IPr), 130.7 (*p*-CH IPr), 128.2 (*m*-CH carboxylate), 127.9 (*o*-CH carboxylate), 124.9 (CH imidazole), 124.8 (*p*-CH carboxylate), 42.9 ($CH_2(CH_3)_3$), 28.5 (CH_3), 29.3 (CH_3), 12.9 (CH_3), 12.6 (CH_3). ^{19}F{^{1}H} NMR (376 MHz, $CDCl_3$) δ = -154.25, -154.20. FTIR (ATR) ν = 2960, 2926, 2872 (C-H), 1543 (C-O), 1458, 1417 cm^{-1} Anal. Calcd. For $C_{77}H_{112}O_2Au_2N_4BF_4$ (1606.51 g·mol^{-1}) (%): C 57.68; H 6.85; N 3.49; found: C 57.59; H 6.93; N 3.55.

3.5. Bibliography

1. R. S. Ramón, S. Gaillard, A. Poater, L. Cavallo, A. M. Z. Slawin and S. P. Nolan, *Chem. Eur. J.*, 2011, **17**, 1238-1246.

2. S. Gaillard, A. M. Z. Slawin and S. P. Nolan, *Chem. Commun.*, 2010, **46**, 2742-2744.

3. R. M. P. Veenboer, A. Collado, S. Dupuy, T. Lebl, L. Falivene, L. Cavallo, D. B. Cordes, A. M. Z. Slawin, C. S. J. Cazin and S. P. Nolan, *Organometallics*, 2017, **36**, 2861-2869.

4. Y. Oonishi, A. Gómez-Suárez, A. R. Martin and S. P. Nolan, *Angew. Chem., Int. Ed.*, 2013, **52**, 9767-9771.

5. A. Gómez-Suárez, Y. Oonishi, A. R. Martin, S. V. C. Vummaleti, D. J. Nelson, D. B. Cordes, A. M. Z. Slawin, L. Cavallo, S. P. Nolan and A. Poater, *Chem. Eur. J.*, 2016, **22**, 1125-1132.

6. S. Dupuy, D. Gasperini and S. P. Nolan, *ACS Catal.*, 2015, **5**, 6918-6921.

7. G. B. Deacon and R. J. Phillips, *Coord. Chem. Rev.*, 1980, **33**, 227-250.

8. C. Shao, G. Cheng, D. Su, J. Xu, X. Wang and Y. Hu, *Adv. Synth. Cat.*, 2010, **352**, 1587-1592.

9. T. A. Stephenson, S. M. Morehouse, A. R. Powell, J. P. Heffer and G. Wilkinson, *J. Chem. Soc. (Resumed)*, 1965, 3632-3640.

10. A. C. Skapski and M. L. Smart, *J. Chem. Soc. D: Chem. Commun.*, 1970, 658b-659.

11. A. R. Dick, K. L. Hull and M. S. Sanford, *J. Am. Chem. Soc.*, 2004, **126**, 2300-2301.

12. R. B. Bedford, J. G. Bowen, R. B. Davidson, M. F. Haddow, A. E. Seymour-Julen, H. A. Sparkes and R. L. Webster, *Angew. Chem., Int. Ed.*, 2015, **54**, 6591-6594.

13. L. H. Do and S. J. Lippard, *J. Am. Chem. Soc.*, 2011, **133**, 10568-10581.

14. a) A. C. Rosenzweig, C. A. Frederick, S. J. Lippard and P. Nordlund, *Nature*, 1993, **366**, 537; b) A. C. Rosenzweig and S. J. Lippard, *Acc. Chem. Res.*, 1994, **27**, 229-236.

15. a) R. K. Behan and S. J. Lippard, *Biochem.*, 2010, **49**, 9679-9681; b) P. Nordlund and P. Reichard, *Ann. Rev. Biochem.*, 2006, **75**, 681-706.

16. a) G. R. Crooks, B. F. G. Johnson, J. Lewis, I. G. Williams and G. Gamlen, *J. Chem. Soc. A; In., Phys., Theor.*, 1969, 2761-2766; b) M. Rotem, I. Goldberg, U. Shmueli and Y. Shvo, *J. Organomet. Chem.*, 1986, **314**, 185-212.

17. J. G. Bullitt and F. A. Cotton, *Inorg. Chim. Acta*, 1971, **5**, 406-412.

18. Y. B. Koh and G. G. Christoph, *Inorg. Chem.*, 1978, **17**, 2590-2596.

19. V. Paredes-García, D. Venegas-Yazigi, R. O. Latorre and E. Spodine, *Polyhedron*, 2006, **25**, 2026-2032.

20. P. D. Harvey, M. Drouin and T. Zhang, *Inorg. Chem.*, 1997, **36**, 4998-5005.

21. T. S. A. Hor, S. P. Neo, C. S. Tan, T. C. W. Mak, K. W. P. Leung and R. J. Wang, *Inorg. Chem.*, 1992, **31**, 4510-4516.

22. A. Grodzicki, I. Łakomska, P. Piszczek, I. Szymańska and E. Szłyk, *Coord. Chem. Rev.*, 2005, **249**, 2232-2258.

23. D. C. Powers and T. Ritter, *Nature Chem.*, 2009, **1**, 302.

24. M. G. Campbell, D. C. Powers, J. Raynaud, M. J. Graham, P. Xie, E. Lee and T. Ritter, *Nature Chem.*, 2011, **3**, 949.

25. D. C. Powers, D. Benitez, E. Tkatchouk, W. A. Goddard and T. Ritter, *J. Am. Chem. Soc.*, 2010, **132**, 14092-14103.

26. M. Rotem and Y. Shvo, *J. Organomet. Chem.*, 1993, **448**, 189-204.

27. P. Kalck, M. Siani, J. Jenck, B. Peyrille and Y. Peres, *J. Mol. Catal.*, 1991, **67**, 19-27.

28. R. Berg, J. Straub, E. Schreiner, S. Mader, F. Rominger and B. F. Straub, *Adv. Synth. Catal.*, 2012, **354**, 3445-3450.

29. A. Makarem, R. Berg, F. Rominger and B. F. Straub, *Angew. Chem., Int. Ed.*, 2015, **54**, 7431-7435.

30. C. M. Wyss, B. K. Tate, J. Bacsa, T. G. Gray and J. P. Sadighi, *Angew. Chem., Int. Ed.*, 2013, **52**, 12920-12923.

31. P. Roembke, H. Schmidbaur, S. Cronje and H. Raubenheimer, *J. Mol. Catal. A: Chem.*, 2004, **212**, 35-42.

32. P. M. N. Low, Z.-Y. Zhang, T. C. W. Mak and T. S. A. Hor, *J. Organomet. Chem.*, 1997, **539**, 45-51.

33. R. L. LaLonde, B. D. Sherry, E. J. Kang and F. D. Toste, *J. Am. Chem. Soc.*, 2007, **129**, 2452-2453.

34. M. Jia and M. Bandini, *ACS Catal.*, 2015, **5**, 1638-1652.

35. J. H. Kim, S.-W. Park, S. R. Park, S. Lee and E. J. Kang, *Chem. As. J.*, 2011, **6**, 1982-1986.

36. D. Gasperini, A. Collado, A. Goméz-Suárez, D. B. Cordes, A. M. Z. Slawin and S. P. Nolan, *Chem. Eur. J.*, 2015, **21**, 5403-5412.

37. S. Gaillard, J. Bosson, R. S. Ramón, P. Nun, A. M. Z. Slawin and S. P. Nolan, *Chem. Eur. J.*, 2010, **16**, 13729-13740.

38. S. Dupuy, F. Lazreg, A. M. Z. Slawin, C. S. J. Cazin and S. P. Nolan, *Chem. Commun.*, 2011, **47**, 5455-5457.

39. A. Gómez-Suárez, Y. Oonishi, S. Meiries and S. P. Nolan, *Organometallics*, 2013, **32**, 1106-1111.

40. A. Zhdanko, M. Ströbele and M. E. Maier, *Chem. Eur. J.*, 2012, **18**, 14732-14744.

41. H. Schmidbaur and A. Schier, *Organometallics*, 2010, **29**, 2-23.

42. D. Weber, T. D. Jones, L. L. Adduci and M. R. Gagné, *Angew. Chem., Int. Ed.*, 2012, **51**, 2452-2456.

43. a) L.-P. Liu, B. Xu, M. S. Mashuta and G. B. Hammond, *J. Am. Chem. Soc.*, 2008, **130**, 17642-17643; b) A. S. K. Hashmi, A. M. Schuster, S. Gaillard, L. Cavallo, A. Poater and S. P. Nolan, *Organometallics*, 2011, **30**, 6328-6337; c) A. S. K. Hashmi, A. M. Schuster and F. Rominger, *Angew. Chem., Int. Ed.*, 2009, **48**, 8247-8249; d) A. S. K. Hashmi, T. D. Ramamurthi and F. Rominger, *Adv. Synth. Catal.*, 2010, **352**, 971-975.

44. a) T. J. Brown, D. Weber, M. R. Gagné and R. A. Widenhoefer, *J. Am. Chem. Soc.*, 2012, **134**, 9134-9137; b) R. L. LaLonde, J. W. E. Brenzovich, D. Benitez, E. Tkatchouk, K. Kelley, I. I. I. W. A. Goddard and F. D. Toste, *Chem. Sci.*, 2010, **1**, 226-233; c) Y. Shi, K. E. Roth, S. D. Ramgren and S. A. Blum, *J. Am. Chem. Soc.*, 2009, **131**, 18022-18023.

45. D. V. Vidhani, J. W. Cran, M. E. Krafft, M. Manoharan and I. V. Alabugin, *J. Org. Chem.*, 2013, **78**, 2059-2073.

46. A. Gómez-Suárez, D. Gasperini, S. V. C. Vummaleti, A. Poater, L. Cavallo and S. P. Nolan, *ACS Catal.*, 2014, **4**, 2701-2705.

47. a) A. Zhdanko and M. E. Maier, *Chem. Eur. J.*, 2014, **20**, 1918-1930; b) G. Seidel, C. W. Lehmann and A. Fürstner, *Angew. Chem., Int. Ed.*, 2010, **49**, 8466-8470.

48. E. Álvarez, D. Miguel, P. García-García, M. A. Fernández-Rodríguez, F. Rodríguez and R. Sanz, *Beilstein J. Org. Chem.*, 2011, **7**, 786-793.

49. E. Y. Tsui, P. Müller and J. P. Sadighi, *Angew. Chem., Int. Ed.*, 2008, **47**, 8937-8940.

50. J. Burés, *Angew. Chem., Int. Ed.*, 2016, **55**, 2028-2031.

51. M. Gatto, P. Belanzoni, L. Belpassi, L. Biasiolo, A. Del Zotto, F. Tarantelli and D. Zuccaccia, *ACS Catal.*, 2016, 7363-7376.

52. J. E. Baldwin, *J. Chem. Soc., Chem. Commun.*, 1976, 734-736.

53. Becke, A. D. *Phys. Rev. A*, 1988, **38**, 3098-3100.

54. Perdew, J. P. *Phys. Rev. B*, 1986, **34**, 7406-7406.

55. Perdew, J. P. *Phys. Rev. B*, 1986, **33**, 8822-8824.

56. Schafer, A.; Horn, H.; Ahlrichs, R. *J. Chem. Phys.*, 1992, **97**, 2571-2577.

57. Haussermann, U.; Dolg, M.; Stoll, H.; Preuss, H.; Schwerdtfeger, P.; Pitzer, R. M. *Molecul. Phys.*, 1993, **78**, 1211-1224.

58. Barone, V.; Cossi, M. *J. Phys. Chem. A*, 1998, **102**, 1995-2001.

59. Tomasi, J.; Persico, M. *Chem. Rev.*, 1994, **94**, 2027-2094.

60. Martin, R. L.; Hay, P. J.; Pratt, L. R. *J. Phys. Chem. A.*, 1998, **102**, 3565-3573.

61. Poater, A.; Pump, E.; Vummaleti, S. V. C.; Cavallo, L. *J. Chem Theory Comput.*, 2014, **10**, 4442-4448.

62. L. Ricard and F. Gagosz, *Organometallics*, 2007, **26**, 4704-4707.

4. When gold meets isothiourea: synthesis, characterization, and activity of Au(I) and Au(III) isothiourea complexes

4.1. Introduction

Pursuing the synthesis of new Au complexes, the attention moved from oxygen based ligands to its predecessor in the periodic table: nitrogen.

As highlighted in Chapter 1, the antiproliferative, and antitumoral behaviour of *N*-Au complexes has increased attention into the design of suitable metallodrug candidates.[1] In particular, the bio-uptake, cytotoxicity, and pharmacokinetics of *N*-Au drugs have been considered.[2] Moreover the possible involvement of such species as intermediates in C-N bond-forming reactions has been described.[3] These complexes have also demonstrated interesting luminescent properties.[4]

The use of nitrogen ligands has been reported for Au(I), Au(II), and Au(III) complexes. Notably, the coordination of sp^2 hybridised nitrogen-based ligands to this soft metal centre has been explored (section 1.4). For example pyridine based compounds, which include bidentate (*N*,*O*) ligands, and pincer ligands, impart good stability to the metal centre leading to enhanced reactivity, and more efficient catalytic systems. In contrast, there are very few literature reports on the use of *non*-aromatic *N*-based ligands, such as guanidines,[5] benzimidazolethiolates,[6] and ylideneamines,[7] which bind to the metal centre through the sp^2 hybridised *N* atom (Chapter 1, Figure 1.20). These species demonstrated poor stability, therefore their applications were not fully explored.

We envisaged the use of isothiourea (ITU) motifs (Figure 4.1), such as tetramisole·HCl ((*S*)-**4.1**·HCl), (*S*)-BTM ((*S*)-**4.2**), DHPB (**4.3**), and (2*S*,3*R*)-HyperBTM ((2*S*,3*R*)-**4.4**), with a *N* donor atom could led to stable well-defined complexes. Moreover, the presence of a stereogenic centre within ITUs (*S*)-**4.1**·HCl, **4.2**, and **4.4** would allow for the generation of chiral complexes, with potentially exciting applications in enantioselective catalysis.

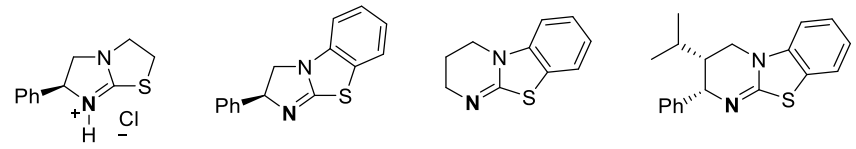


Figure 4.1. Isothiourea motifs used in this work.

Herein is described the successful synthesis and characterization of a range of cationic, and neutral Au(I) ITU species, and the evaluation of their chemistry. Furthermore, the preparation of novel chiral Au(III) ITU complexes was accomplished. An evaluation of the electronic and steric properties of ITUs as ligands for metal complexes is addressed, with studies exploring their stoichiometric, and catalytic behaviour. The synthesis of Ir(I) ITU complexes is also evaluated.

4.1.1. Isothioureas

A brief introduction to isothiourea (ITU) motifs is essential. They are organic Lewis bases,[8] that function as electron-pair donors. These species are nucleophilic, donating their lone pairs to initiate a reaction, by net charge transfer toward the accepting molecule.[9] Isothioureas are known mainly as organocatalysts, with their use widespread, and advanced since the seminal work of Birman in 2006.[10] This concept will be expanded in chapter 5.

Together with their congeners, guanidines, and amidines, isothioureas can be categorised as weak bases,[11] due to the ability of their protonated form to delocalise the positive charge over two nitrogen atoms (Figure 4.2, a). Consideration of their orbital description, in particular by overlap between the nitrogen atom lone pair that sits in an sp^2 hybridised orbital, and the adjacent p-system, accounts for their behaviour (Figure 4.2, b).[12]

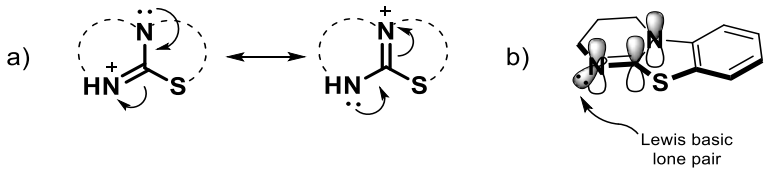


Figure 4.2. a) Protonated ITU resonance structures; b) orbital descriptions of delocalisation in ITU.

Brønsted basicity can be used as a physicochemical descriptor of isothioureas,[13] although their Lewis basicity toward *C* electrophiles has been considered in detail. Mayr and co-workers[14] compared the basicity, and nucleophilicity of ITUs to other organic bases,

through measuring rate and equilibrium constants for the reaction of isothioureas with benzhydrylium ions to give thiouronium tetrafluoroborate salts (Figure 4.3). They compared the data with 4-DMAP, DBU, DBN, NMI, and other bases. Isothioureas were found to be less nucleophilic compared to DABCO, or 4-DMAP, but more nucleophilic than NMI. The nucleophilicity of isothioureas was found to be dependent on the ring size (ring **1**), and substitution pattern (C^3, C^4); an initial decrease in basicity was found for 6 membered ring HBTM compared to 5 membered ring BTM. Substituents at the C^3 position, as found in HyperBTM **4.4**, had a beneficial effect and enhanced the efficiency, and activity of **4.4** in catalysis.[15]

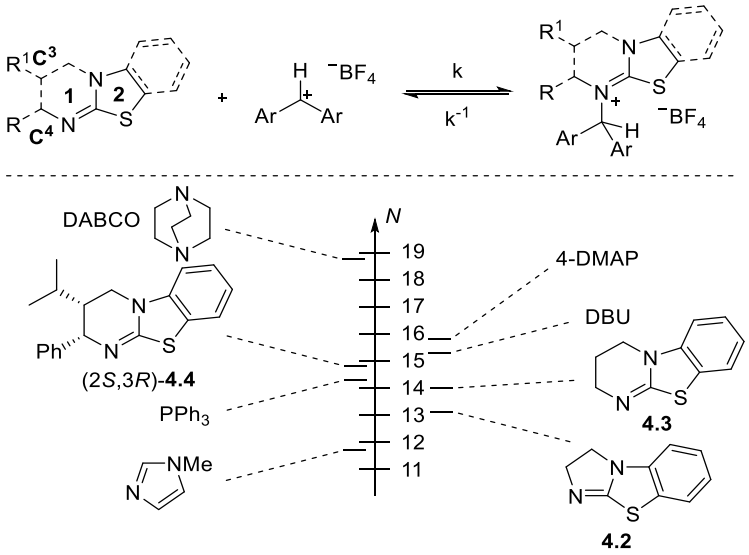
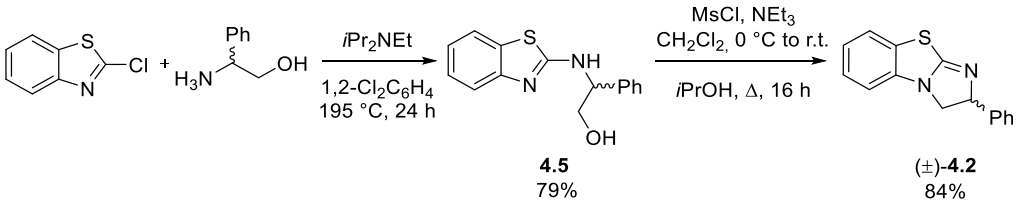


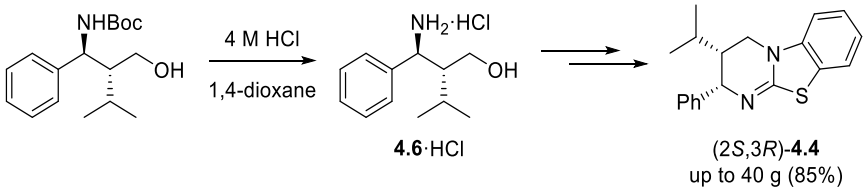
Figure 4.3. Equilibrium reaction of isothiourea, benzhydrilium ion, and thioronium salts; scale of nucleophilicity of most common organic bases, including isothioureas **4.2**, and **4.3**, and (2*S*,3*R*)-**4.4**.

The commercial availability of tetramisole salt **4.1**·HCl,[16] and the ease of synthesis of other isothiourea Lewis bases, make them attractive catalysts, and a good target for *N*-based ligands. The synthesis of BTM **4.2** can be easily pursued by reacting commercially available 2-chlorobenzothiazole with 2-phenyl glycinol ((*R*), or (*S*)) at high temperature (195 °C) (Scheme 4.1).[17] The process resulted in clean formation of intermediate **4.5**, that is further cyclised by addition of a slight excess of methanesulfonyl chloride, to yield **4.2**.



Scheme 4.1. Synthesis of (±)-**4.2**.[17] Reaction condition: 2-phenyl glycinol (1.05 equiv.), *i*Pr_2NEt (4 equiv.), 1,2-ClC_6H_4 (2 M); MsCl (1.2 equiv.), NEt_3 (4 equiv.), CH_2Cl_2 (0.1 M), *i*PrOH (xs).

The synthesis of DHPB **4.3**, an achiral isothiourea,[18] uses a similar route to that of **4.2**, with 3-amino-1-propanol as starting material, followed by subsequent cyclisation.[19] Further advancement of catalyst design led to the synthesis of HBTM-2.1, or (2*S*,3*R*)-HyperBTM (2*S*,3*R*)-**4.4**.[19] The synthesis of **4.6**·HCl, was necessary prior to coupling with chlorobenzotetramisole (Scheme 4.2). Therefore, cyclisation proceeded in a similar fashion to scheme 1, affording (2*S*,3*R*)-**4.4** in 85% isolated yield.

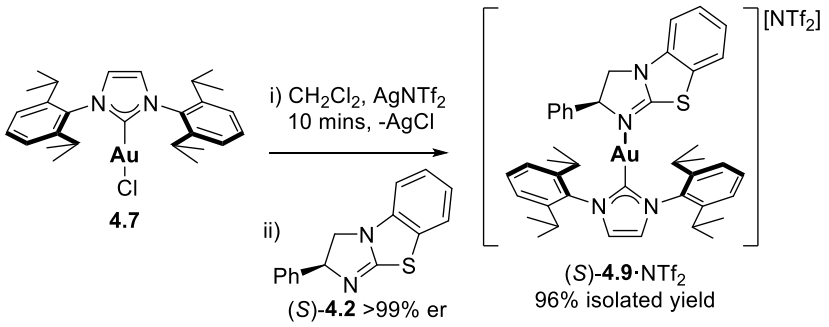


Scheme 4.2. Synthesis of **4.8**·HCl salt for the formation of (2*S*,3*R*)-**4.4**.[19]

4.2. Results and discussion

4.2.1. Synthesis of cationic Au(I) ITU complexes

The synthesis of cationic heteroleptic Au(I) ITU species was first explored. Easily-accessible [AuCl(L)] (L = IPr **4.7**, PPh_3 **4.8**) complexes bearing NHC,[20] and tertiary phosphine ligands, were used as a starting point. Initial testing was made by mixing **4.7** with (*S*)-**4.2** in a 1:1 ratio, in acetone. In the presence of a weak base K_2CO_3 (1 equiv.), the reaction did not proceed even at higher temperature, as observed by ^{1}H NMR spectroscopy ($CDCl_3$). However, by dissolving **4.7** in CH_2Cl_2 in the presence of an halide abstractor and (*S*)-**4.2**, rapid and complete conversion to a new species was observed (Scheme 4.3). This species was fully identified by spectroscopic techniques as [Au(IPr){(*S*)-BTM}][NTf_2] ((*S*)-**4.9**·NTf_2).



Scheme 4.3. Synthesis of (*S*)-**4.6**·NTf_2 complex from **4.5**, and (*S*)-**4.2**.

Using this synthetic route, a series of cationic complexes was synthesised in excellent yields (ranging from 82 to >99% isolated yield) (Figure 4.4). The procedure was applied to (2*S*,3*R*)-**4.4** to isolate (2*S*,3*R*)-**4.10**·NTf_2 in 93% yield. The counterion could be exchanged from triflimide to tetrafluoroborate by using $AgBF_4$ as halide abstractor. Both enantiomers of **4.2**, and **4.4** were used to isolate **4.9**·BF_4, and **4.10**·BF_4 in excellent yields (up to >99%).

The procedure was extended to PPh_3 based complexes by variation of the Au(I) source (Figure 4.4). **4.8** [$AuCl(PPh_3)$], was treated with $AgNTf_2$, or $AgBF_4$; after addition of enantiopure (*S*)-**4.2**, or (*R*)-**4.2**, pure enantiomers of **4.11**·NTf_2, and **4.11**·BF_4 were obtained. Au(I) phosphine complexes of (2*S*,3*R*)-**4.4**, and (2*R*,3*S*)-**4.4** were further isolated as (2*S*,3*R*)-**4.12**·X, and (2*R*,3*S*)-**4.12**·X in up to >99% yield (X = NTf_2, BF_4). The straightforward synthetic procedure required simple filtration through a plug of Celite©, and recrystallization from pentane to afford the pure, air-, and moisture-stable microcrystalline products, which showed no decomposition after several months on the bench.

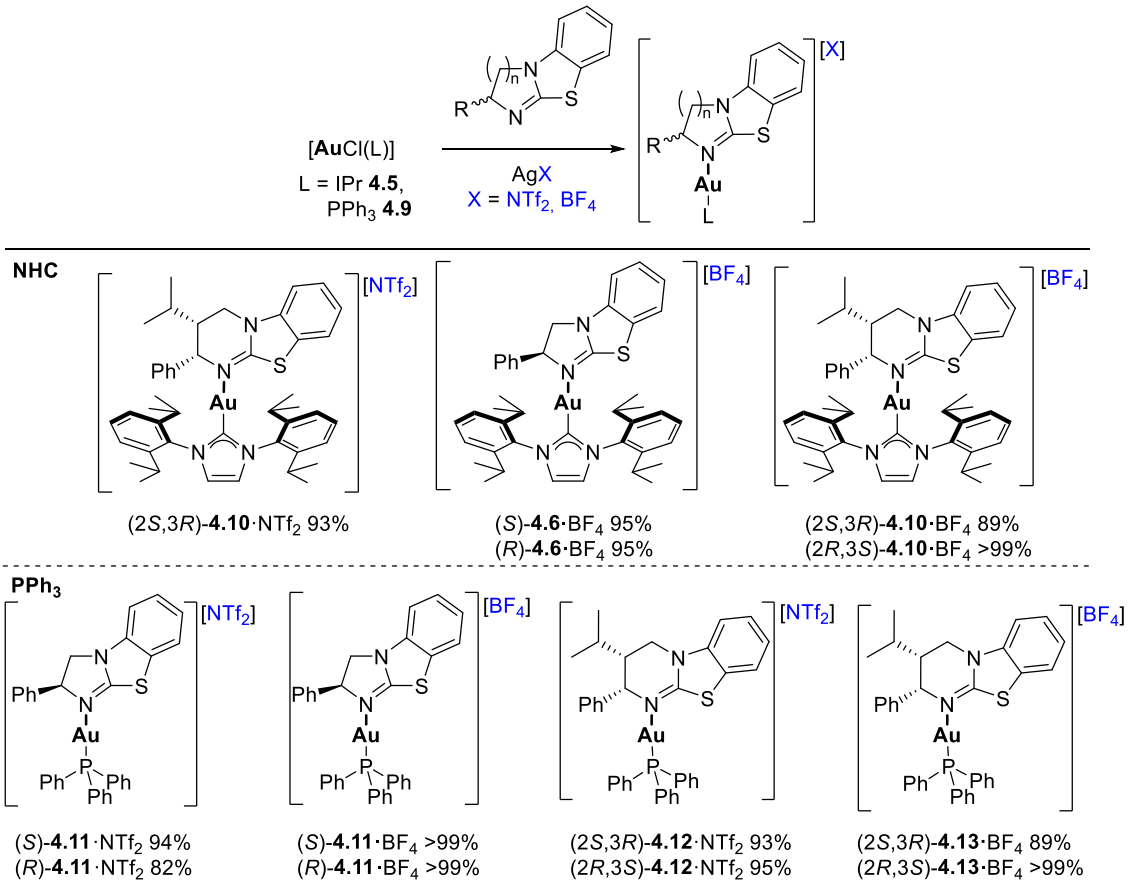
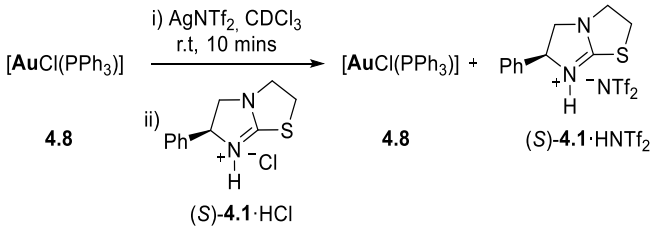


Figure 4.4. Synthesis of heteroleptic complexes from **4.7**, and **4.8** neutral precursors. Reaction conditions: [AuCl(L)] (0.2 mmol), AgX (X = NTf_2, BF_4, 1 equiv.), CH_2Cl_2 (0.1 M), 10 mins, r.t., ITU (**4.2** or **4.4**) (1 equiv.), r.t., 10 mins.

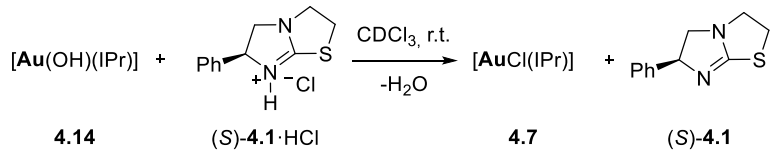
Attempts to react [AuCl(L)] with tetramisole·HCl were next performed. **4.8** was reacted in a 1:1 ratio with (*S*)-**4.1**·HCl, and $AgNTf_2$ in $CDCl_3$ at r.t.; counterion exchange forming (*S*)-**4.1**·$HNTf_2$ was observed by ^{1}H NMR and ^{19}F NMR, with [AuCl(PPh_3)] recovered (Scheme 4.4).



Scheme 4.4. Attempt of reactivity of (*S*)-**4.1**·HCl.

[Au(OH)(IPr)] (**4.14**) Brønsted basic complex was investigated to deprotonate (*S*)-**4.1**·HCl, by releasing H_2O *in situ*. As highlighted in section 1.5.1, this species was able to deprotonate CH bond (pK_a (DMSO) = 29/31).[21] When reacting **4.14** with tetramisole

salt, in $CDCl_3$ formation of [AuCl(IPr)] **4.7**, the thermodynamically favoured product, was observed, and tetramisole free base released in solution (Scheme 4.5).



Scheme 4.5. Reaction of Brønsted basic **4.14** with (*S*)-**4.1**·HCl.

Due to the "non-innocent" role of silver[22] in gold catalysis,[23] an alternative method for the synthesis of these complexes was explored. Specifically, the synthesis of NHC complexes was targeted. Initially, the well-defined precursor [Au(NTf_2)(IPr)] (**4.15**) bearing a labile inner-sphere counterion was used.[24] Complex **4.15** reacted easily in chlorinated solvents, or THF with isothioureas **4.2**, and **4.4** to isolate enantiopure compounds (Figure 4.5). In terms of yield, the process did not differ from the analogous system with **4.2** and $AgNTf_2$, with excellent results (96-99% isolated yields). In addition, [Au(NTf_2)(IPr^{Cl})] (**4.16**) was used for the synthesis of both [Au(IPr^{Cl}){(S)-BTM}][NTf_2] ((*S*)-**4.17**·NTf_2), and [Au(IPr^{Cl}){(2S,3R)-HyperBTM}][NTf_2] ((2S,3R)-**4.18**·NTf_2), in 96% and 99%, respectively. Unfortunately, other triflimide complexes bearing NHC ligands, such as [Au(NTf_2)(SIPr)], and [Au(NTf_2)(IPr*)] did not provide the expected heteroleptic complexes, and resulted in complex mixture of unreacted ITU, and a number of Au species, which promptly decompose to show a gold mirror in the NMR tube.

The scope of the synthetic route was further expanded to cationic Au complex precursors: [Au(IPr)($NCCH_3$)][BF_4] (**4.19**)[25] allowed formation of the BF_4 adduct of (*S*)-**4.9**·BF_4 in 99% isolated yield, with liberation of acetonitrile as the only by-product (Figure 4.5). The same procedure could also be applied to (2*S*,3*R*)-**4.4** to obtain (2*S*,3*R*)-**4.10**·BF_4 in >99% yield. When attempting this approach with [Au(IPr^{Cl})($NCCH_3$)][BF_4], and (2*S*,3*R*)-**4.4** in CH_2Cl_2 no conversion of the starting materials was observed.

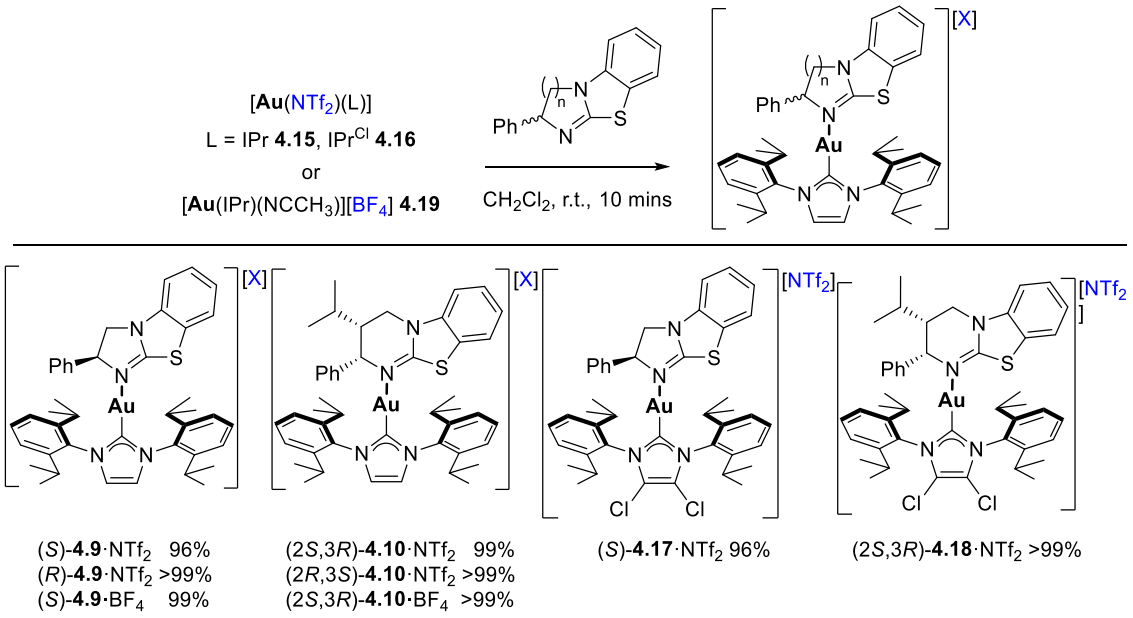
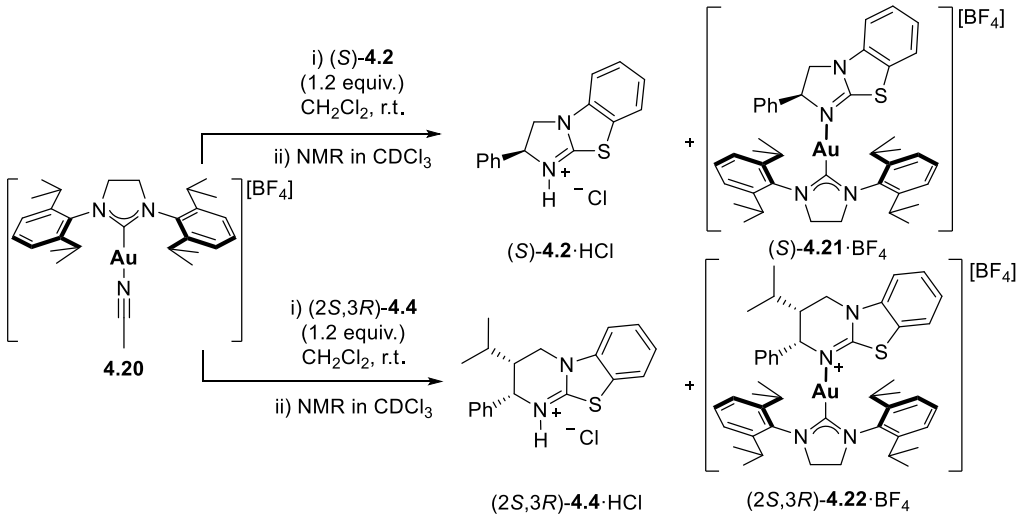


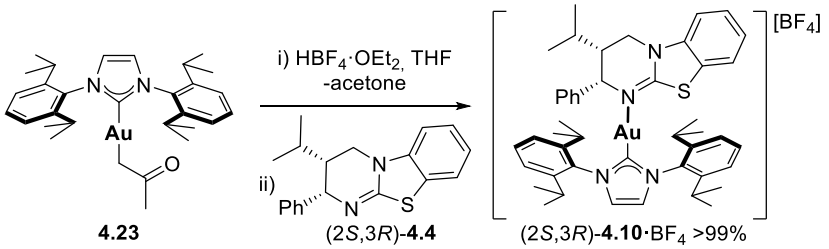
Figure 4.5. Synthesis of heteroleptic compounds from **4.15**, **4.16**, and **4.19** precursors. [Au(NTf$_2$)(L)], or [Au(IPr)(NCCH$_3$)][BF$_4$] (0.15-0.2 mmol), CH$_2$Cl$_2$,or THF (0.1 M), **4.2**, or **4.4** (1 equiv.), r.t., 1 h.

The behaviour of [Au(SIPr)(NCCH$_3$)][BF$_4$] (**4.20**), was investigated. Reacting the complex with a slight excess of either (*S*)-**4.2** and (2*S*,3*R*)-**4.4** (1.2 equiv.) in either chlorinated solvents (CH$_2$Cl$_2$, CDCl$_3$), or PhMe, displayed formation of the corresponding ITU salt, (*S*)-**4.2**·HCl and (2*S*,3*R*)-**4.4**·HCl, and Au complexes [Au(SIPr)(ITU)][BF$_4$] (*S*)-**4.21**·BF$_4$ and (2*S*,3*R*)-**4.22**·BF$_4$ (Scheme 4.6). A second non-identified Au(I) NHC complex was found in the reaction mixture in a 1:4 ratio to (2*S*,3*R*)-**4.22**·BF$_4$.



Scheme 4.6. Major species obtained reacting **4.20** with (*S*)-**4.2**, or (2*S*,3*R*)-**4.4**.

It is noteworthy that **4.15**, **4.16** and **4.19** could be synthesised *via* a silver-free route, by protonolysis of the [Au($CH_2C(O)CH_3$)(IPr)] (**4.23**) (chapter 6).[26] The same complex was thus envisaged as precursor of Au(I) ITU species, through activation with $HBF_4 \cdot OEt_2$ to release acetone in solution (Scheme 4.7). The activated species was further reacted with (2*S*,3*R*)-**4.4** to obtain (2*S*,3*R*)-**4.10**·BF_4 in >99% yield. The reaction was performed in THF, whilst the use of PhMe, or chlorinated solvents gave no trace of the heteroleptic complex but a mixture of products.



Scheme 4.7. Synthesis of (2*S*,3*R*)-**4.10**·BF_4 from **4.23**. Reaction conditions: [Au($CH_2C(O)CH_3$)(IPr)] (0.05 mmol), $HBF_4 \cdot OEt_2$ (1 equiv.), (2*S*,3*R*)-**4.4** (0.05 mmol), THF (0.023 M), r.t., 10 mins.

4.2.1.1. Characterisation of heteroleptic cationic Au(I) ITU complexes

Several distinguishing features of the heteroleptic cationic Au(I) ITU complexes were observed by NMR ($CDCl_3$), and IR spectroscopy (Figure 4.6):

1. δ_H chemical shifts of N^1-CHC_6H_5 were found upfield for [Au(NHC)(ITU)][NTf_2] complexes *vs* 5.68 ppm for (*S*)-**4.2**,[17b] and 4.94 ppm for (2*S*,3*R*)-**4.4**;[19]
2. δ_H chemical shifts of N^1-CHC_6H_5 moved downfield for [Au(PPh_3)(ITU)][NTf_2] complexes *vs* the free Lewis bases. This might be due to the different σ-donation to metal between phosphine, and NHC ligands, which is stronger for the latter.[27a] The counterion might play a role, as observed by Zuccaccia and co-workers;[27b] by analysing phosphane-gold species the authors observed that the counterion resided close to the metal centre *vs* NHC-gold complexes where the anion was found near the imidazole ligand. An interaction between the counterion and the proton under analysis can be envisaged, in phosphane-Au-ITU complexes, to be responsible for the change in electronic environment, therefore the observed deshielded chemical shift.
3. δ_C resonance frequencies of N^1=**C**-N^2 shifted downfield within all complexes in comparison to the parent free Lewis base, with 166.8 ppm for (*S*)-**4.2**, and 158.5 ppm for (2*S*,3*R*)-**4.4**. The deshielded values are consistent with higher delocalisation of positive charge in the ITU ligands when bound to Au;

4. lower $\nu_{C=N}$ stretching frequencies of N^1=C-N^2 bond for [Au(L)(ITU)][NTf_2] (L = NHC, PPh_3) compared to literature values for (*S*)-**4.2** of 1593 cm^{-1},[28] and for (2*S*,3*R*)-**4.4** of 1627 cm^{-1},[29] therefore consistent with the higher delocalisation along the C-N bonds. Moreover, this effect indicates π-acceptance of ITU from the metal centre.

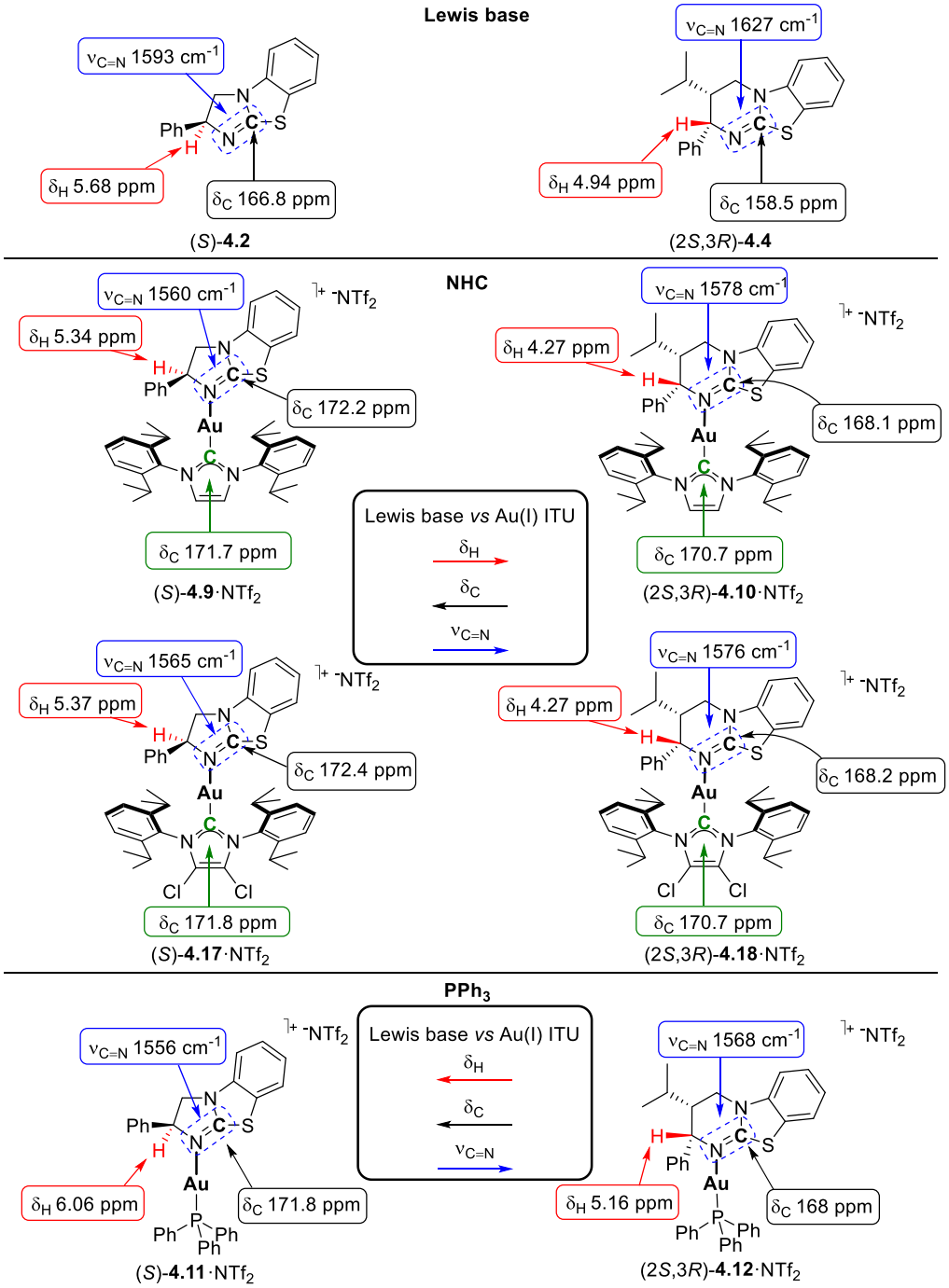


Figure 4.6. Relevant NMR and IR data for heteroleptic species: ^{1}H NMR, $^{13}C\{^1H\}$ NMR udeft ($CDCl_3$); FTIR (ATR).

These general trends were found for all the complexes synthesised, and substantial variations were not observed when changing counterion.

Other details were noticed in the spectroscopic features of heteroleptic Au(I) ITU complexes, such as the CH signals of the *i*propyl groups of the NHC ligands in complexes bearing the (2*S*,3*R*)-HyperBTM. These signals appeared as a double septuplet, consistent with an asymmetric environment around the metal centre. Moreover, the δ_C of the carbenic carbon for unsaturated NHC-based compounds, was observed in the 170.7-171.8 ppm range (Figure 4.6). This value is downfield compared to homoleptic Au(I) NHC species, in which the carbon for IPr appeared around 159 ppm.[30] Further comparison with ylideneamine Au(I) NHC complexes where the carbene was found at 165.6 ppm (CD_2Cl_2),[7] displayed the shielded nature of the carbon atom.

The data obtained for [Au(SIPr)(NCCH$_3$)][BF$_4$] were found to be in accordance with other Au(I) ITU heteroleptic complexes (Figure 4.7); the value for N^1-CHC$_6$H$_5$ showed an upfield shift compared to the free Lewis bases (*S*)-**4.2** and (2*S*,3*R*)-**4.4** with values of 5.24, and 4.16 ppm for (*S*)-**4.21**·BF$_4$, and (2S,3R)-**4.22**·BF$_4$, respectively. While δ_C values for N^1=**C**-N^2 followed the trend of [Au(NHC)(ITU)][X] compounds, the carbenic carbon shifted to higher chemical shift, indicative of saturated N-heterocyclic carbenes. The data of 193.4, and 192.5 ppm, are slightly upfield compared to [Au(SIPr)$_2$][BF$_4$] (206.5 ppm), and downfield compared to [Au(SIPr)(ICy)][BF$_4$] (180.1 ppm).[31]

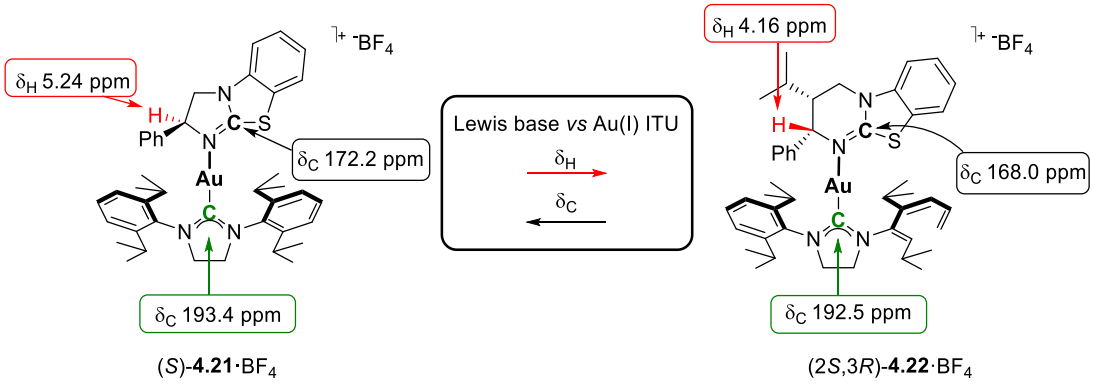


Figure 4.7. Relevant NMR data for [Au(SIPr)(ITU)[BF$_4$]: ^{1}H NMR, ^{13}C{^{1}H} udeft NMR ($CDCl_3$).

The structure of complex (2*R*,3*S*)-**4.10**·NTf$_2$ was unambiguously established by X-ray diffraction analysis (Figure 4.8).[32] The isothiourea binds as expected through the *N*^{1} atom, and the complex is arranged with a linear geometry (*N*^{1}-Au-C angle of 176.2(5)°). The Au-*N*^{1} bond (2.053(11) Å) was found to be longer than the data found for ylideneamine complexes,[7] but in a similar range to amide,[4b] and imido Au(I) complexes.[24] The Au-C

distance of 1.979(13) Å is similar to that of ylideneamine complexes bearing an NHC,[7] and to cationic NHC complexes,[25] but shorter than Au(I) homoleptic NHC species.[30b] The N^1-C, and C-N^2 distances of 1.288(16), and 1.367(18) Å, reveal a lengthening of the N^1-C bond, and a shortening of the C-N^2 bond relative to (2*R*,3*S*)-**4.4**, where N^1-C = 1.279(4) Å, and C-N^2 = 1.386(4) Å.[19] These observations are consistent with delocalisation of the positive charge into the ligand, and together with lower $\nu_{C=N}$ stretching frequencies support the π-acceptance role of ITU from the metal centre.

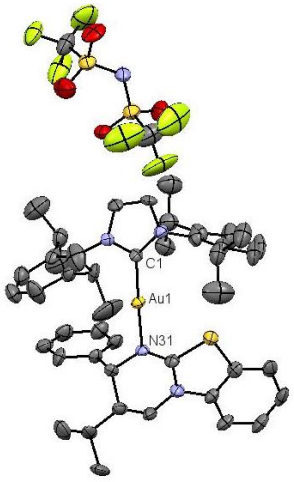


Figure 4.8. Thermal ellipsoid representation of (2*R*,3*S*)-**4.10**·NTf_2. Most H atoms have been omitted for clarity. Significant distances (Å), and angles (°): Au-N^1 2.053(11) Å, Au-C 1.979(13) Å, N^1-Au-C 176.2(5)°, S-C-N^1-Au 4.1(15)°. Two conformers were found in the crystal lattice.

4.2.2. Synthesis and characterisation of neutral Au(I) ITU complexes

Further studies probed the formation of neutral chiral Au(I) ITU complexes. Mixing [AuCl(SMe_2)] (**4.24**) and (*S*)-**4.2** in acetone, resulted in no conversion after 3 days at r.t., and 60 °C, as displayed by ^{1}H NMR. However, by switching to THF, and heating the mixture at 60 °C, [AuCl{(*S*)-BTM}] ((*S*)-**4.25**) was prepared in >99% isolated yield within 1 h (Figure 4.9). The method was applied using (*R*)-**4.2** to obtain enantiopure (*R*)-**4.25** in excellent yield. When (2*S*,3*R*)-**4.4** and (2*R*,3*S*)-**4.4** were reacted under the reaction conditions, complex (2*S*,3*R*)-**4.26** and its enantiomer (2*R*,3*S*)-**4.26**, were obtained in quantitative yield. The synthesis of racemic (±)-**4.26** was scaled to 200 mg (0.67 mmol) with high recovery of product.

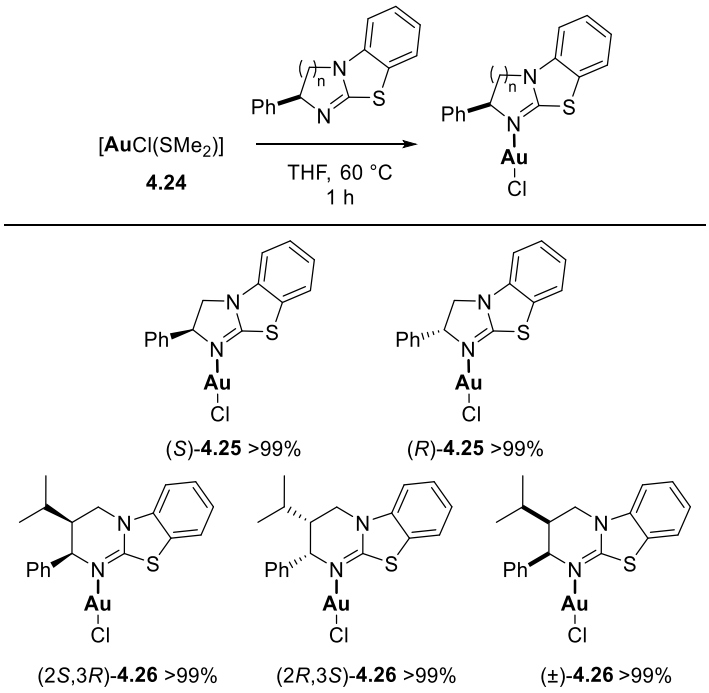
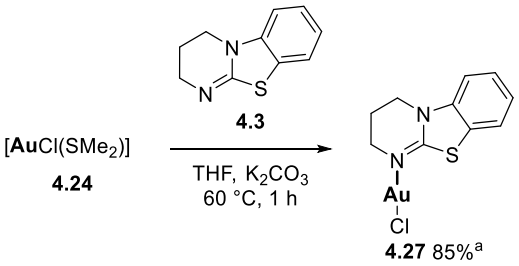


Figure 4.9. Synthesis of neutral Au(I) ITU complexes. Reaction conditions: [AuCl(SMe$_2$)] (0.5 mmol), ITU (1 equiv.), THF (0.1 M), 60 °C, 1 h.

By mixing **4.24** with achiral derivative **4.3**, under the optimised reaction conditions, complex **4.27** was obtained in 85% after 16 h (Scheme 4.8). The use of K_2CO_3 was important for the reaction to proceed. Without base, substantial decomposition was observed.



Scheme 4.8. Synthesis of **4.27** from **4.24**. Reaction conditions: [AuCl(SMe$_2$)] (0.5 mmol), **4.3** (1 equiv.), K_2CO_3 (1 equiv.), THF, or acetone (0.1 M), 60 °C, 16 h; [a] ^{1}H NMR conversions.

The salt, (*S*)-**4.1**·HCl was also tested under the optimised reaction conditions, however reaction with [AuCl(SMe$_2$)] in acetone, or THF in presence of K_2CO_3 at 60 °C did not provide the expected product, with decomposition to golden mirror.

The formation of neutral Au(I) species was confirmed by NMR, and IR spectroscopic analysis. As observed for the heteroleptic complexes, a general trend was found within the chloride Au(I) ITU family (Figure 4.10):

1. δ_H chemical shifts of N^1-CHC_6H_5, or N^1-CH_2in $CDCl_3$ were deshielded compared to the free bases;
2. δ_C resonances of N^1=**C**-N^2 were strongly shielded compared to (*S*)-**4.2**, and (2*S*,3*R*)-**4.4**, with values of 139.8 ppm for (*S*)-**4.25**, and 140.4 ppm for (2*S*,3*R*)-**4.26** *vs* 166.8 ppm for (*S*)-**4.2**, and 158.5 ppm for (2*S*,3*R*)-**4.4**. These values were in contrast to what observed for the heteroleptic species (Figure 4.6). This opposite effect is difficult to interpret if based only on NMR signals. Most likely the presence of *trans* X ligand (Cl), which functions solely as an electron-donor, might increase the strength of the *N*-Au bond (σ, and π interactions), thus influencing the N^1-C, and C-N^2 bonds, shortening the latter, and shielding δ_C;
3. $\nu_{C=N}$ were shown to follow the same trend as the heteroleptic species, with lower frequencies *vs* Lewis bases, ranging from 1564-1580 cm^{-1}, confirming a longer N^1-C bond.

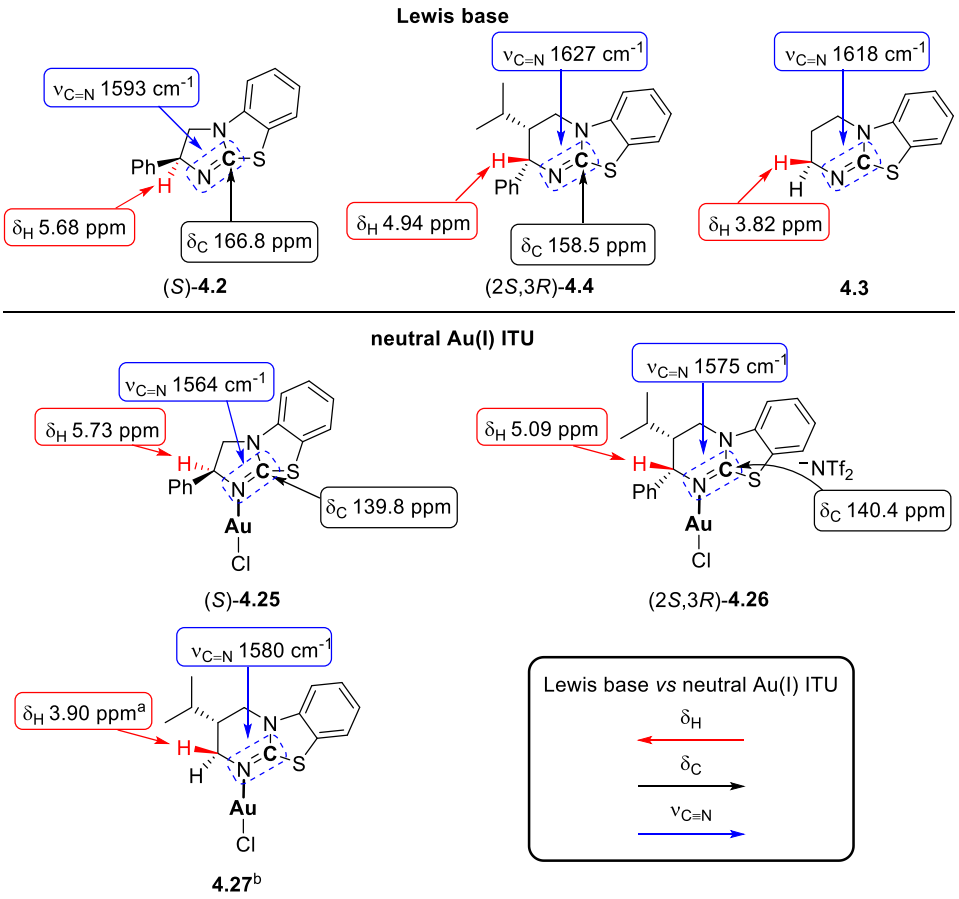


Figure 4.10. Relevant spectroscopic data for neutral Au(I) ITU complexes. ^{1}H NMR, $^{13}C\{^1H\}$ udeft NMR ($CDCl_3$); [c] FTIR (ATR); NIR; [a] δ(-CH_2-*N*); [b] The complex was not sufficiently soluble for analysis.

Colourless crystals of (*R*)-**4.25** and **4.27** were grown by slow diffusion of pentane or hexane into a saturated solution of CH_2Cl_2, and their structures were unambiguously determined by X-ray diffraction analysis (Figure 4.11).[35] The N^1-Au-Cl axes were virtually linear, ranging between 178.7−179.5°. The bond length for N^1-C, and C-N^2 varied significantly in (*S*)-**4.25** *vs* (2*R*,3*S*)-**4.10**·NTf_2 (Figure 4.8); N^1-C lengthened greatly, 1.31(2) *vs* 1.29(1) Å, while the C-N^2 bond shortened to 1.34(2) *vs* 1.36(18) Å. This effect is even more noticeable if compared to the Lewis base (2*S*,3*R*)-**4.4** (N^1-C = 1.279(4) Å and C-N^2 = 1.386(4) Å). The Au-N^1 distances were shorter than in the case of (2*R*,3*S*)-**4.10**·NTf_2; 2.02(1) Å for (*S*)-**4.25** and 2.021(9) Å for **4.27**, while 2.05(1) Å for the heteroleptic complex.

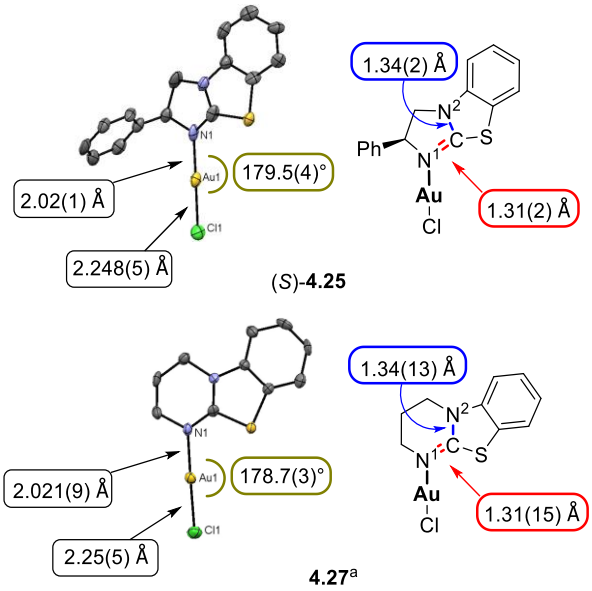


Figure 4.11. Thermal ellipsoid representation of (*S*)-**4.25**, **4.27** showing 50% probability, and schematic representation of [AuCl(ITU)]. Most of the H atoms were omitted for clarity, and major bond length (Å), and angles (°) highlighted; [a] two conformer were found in the crystal lattice of **4.27**.

Suitable crystals were grown also for (2*S*,3*S*)-**4.26**, and (±)-**4.26**, and analysed by X-ray crystallography (Figure 4.12).[36] The main noticeable features in this case are related to the structural arrangement of the complexes; a cation-anion arrangement, $[Au(HyperBTM)_2][AuCl_2]$ is visible both in the enantioenriched, and racemic form. The ion pairs possessed short intermolecular Au(I)···Au(I) interactions of 3.1131(6) Å for (2*R*,3*S*)-**4.26**, and 3.0215(6) Å for (±)-**4.26**.[37]A similar rearrangement was found in the literature for guanidine Au(I) complexes, reported by Schneider *et al.*.[5] Moreover, a head-

to-tail arrangement was visible for (2*R*,3*S*)-**4.26**, while the head-to-head arrangement was found in (±)-**4.26**.

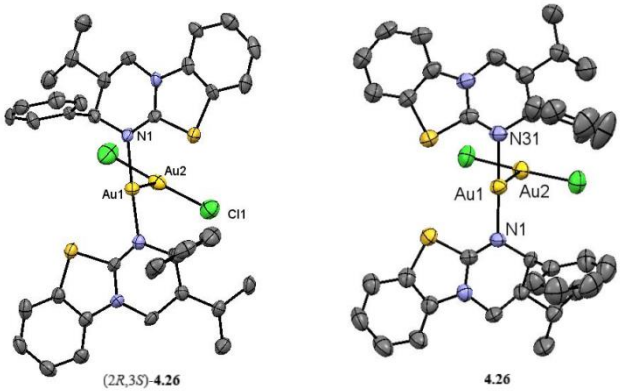


Figure 4.12. Thermal ellipsoid representation of (2*R*,3*S*)-**4.26**, (±)-**4.26** showing 50% probability. Most of the H atoms were omitted for clarity.

However, the solid-state arrangement did not reflect the behaviour of these Au(I) complexes in solution; to support this hypothesis, the ^{1}H NMR spectra of the complexes in $CDCl_3$, showed a single species at 298 K, thus it is postulated that the rearrangement does not happen in solution, or that it happens faster than the NMR acquisition time scale. Furthermore, another interesting peculiarity of (2*R*,3*S*)-**4.26** concerns on the N^1-C, and C-N^2 bond length. In this case C-N^2 was found to be the shortest, with a value of 1.29(14) Å, while N^1-C bond was 1.48(13) Å. Complex (±)-**4.26** followed the trend of (*S*)-**4.25** and **4.27**, with N^1-C = 1.28(6) Å, and C-N^2 = 1.35(8) Å.

4.2.3. Synthesis and characterisation of Au(III) ITU complexes

Following these findings, we sought to explore the synthesis of Au(III) species. By subjecting (*S*)-**4.25** to stoichiometric and sub-stoichiometric amounts of elemental Br_2, formation of several species was observed by ^{1}H NMR spectroscopy ($CDCl_3$). Moreover, the mixture decomposed over time.

The use of hypervalent iodine was next investigated due to the ease of handling and straightforward synthesis of these oxidants,[40] and the literature precedent for the oxidation of Au(I) complexes.[30b,41] Complexes (*S*)-**4.25**, (2*S*,3*R*)-**4.26** and their enantiomers were reacted with iodobenzenediacetate, $PhI(OAc)_2$, in $CDCl_3$ however no substantial conversion of the starting material was observed at various temperatures (up to 60°C), although decomposition of the oxidant into

iodobenzene was noted. In contrast, the use of 1.2 equiv. of iodobenzene dichloride, $PhI(Cl)_2$, led to full conversion of (*S*)-**4.25**, and (2*S*,3*R*)-**4.26** to give Au(III) analogues [$AuCl_3${(2*S*,3*R*)-HyperBTM}] ((2*S*,3*R*)-**4.29**), and [$AuCl_3${(*S*)-BTM}] ((*S*)-**4.28**) as beautiful magenta and purple coloured complexes in excellent yield (96-99%) (Figure 4.13). The synthesis of the enantiomeric complexes, (*R*)-**4.28**, and (2*R*,3*S*)-**4.29**, was also achieved in equally high yield. To the best of our knowledge these complexes represent the first isolated chiral Au(III) species containing an sp^2-hybridised *N*-based monodentate ligand.

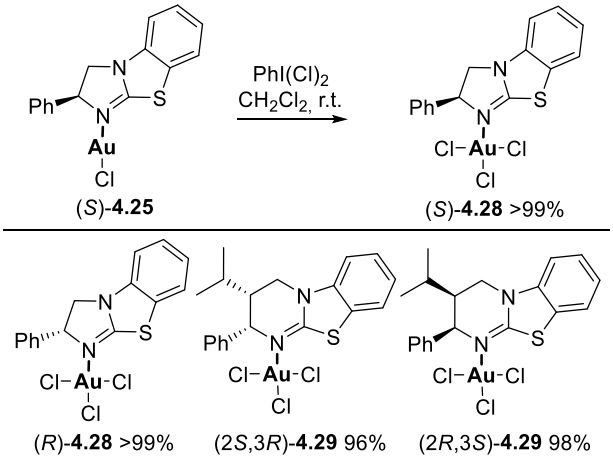
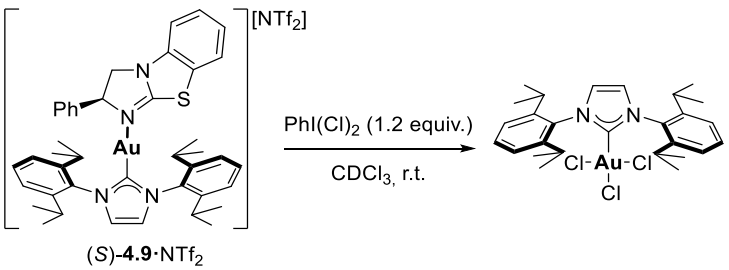


Figure 4.13. Reaction conditions: **4.25**, or **4.26** (0.16 mmol), $PhI(Cl)_2$ (1.2 equiv.), CH_2Cl_2 (0.08 M), 16 h, under inert conditions.

Unfortunately, the oxidation of [AuCl(DHPB)] **4.27** resulted in the formation of a complex mixture of products. When subjecting heteroleptic Au(I) complex, (*S*)-**4.9**·NTf_2 to the optimised reaction conditions, with $PhI(Cl)_2$ (1.2 equiv.) as oxidant, a complex mixture of Au(I) and Au(III) species were observed by ^1H NMR spectroscopy (Scheme 4.9), with [$AuCl_3$(IPr)] being the major one.[42]



Scheme 4.9. Oxidation of (*S*)-**4.9**·NTf_2 with $PhI(Cl)_2$.

The spectroscopic features of the Au(III) ITU complexes were analysed; as observed in Figure 4.14, the complexes followed the trend of chloride-Au(I) ITU complexes

compared to the free Lewis bases (*S*)-**4.2** and (2*S*,3*R*)-**4.4**. Downfield δ_H chemical shifts were observed for N^1-CH-C_6H_5 of 6.36 ppm for (*S*)-**4.28**, and 5.32 ppm for (2*S*,3*R*)-**4.29**. The carbon chemical shift of N^1=**C**-N^2 for (*S*)-**4.28** and (2*S*,3*R*)-**4.29**, was at 138.2 and 139.0 ppm, respectively. The N^1=C-N^2 bond stretching frequencies appeared at 1560 cm^{-1} and 1574 cm^{-1} for Au(III), following the trend of heteroleptic species (Figure 4.6), and neutral Au(I) species (Figure 4.10).

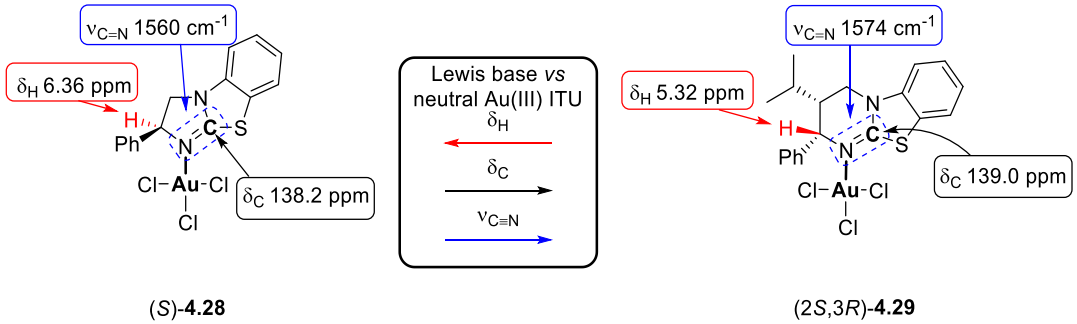


Figure 4.14. Significant spectroscopic data for Au(III) ITU complexes: ^{1}H NMR, $^{13}C\{^1H\}$ udeft NMR ($CDCl_3$); [c] FTIR (ATR), NIR (CH_2Cl_2).

Colourless crystals of (*S*)-**4.28**, and (2*R*,3*S*)-**4.29** were grown by slow diffusion of pentane into a saturated solution of CH_2Cl_2, and their structures were unambiguously determined by X-ray diffraction analysis (Figure 4.15).[43] The square planar geometry was observed for Au(III) complexes with angles ranging from 88.79 to 87.55° (Table 4.1, entries 1, 2). A cation-anion arrangement, like that found for **4.26** (Figure 4.12), was observed in the solid-state structure (*S*)-**4.28**, where the counterion is $AuCl_4$. As for the case of Au(I) neutral ITU complexes, the possible arrangement of (*S*)-**4.28** in solution might vary from the solid state one, as observed by the ^{1}H NMR in $CDCl_3$ at 298K showed no substantial ligand scrambling.

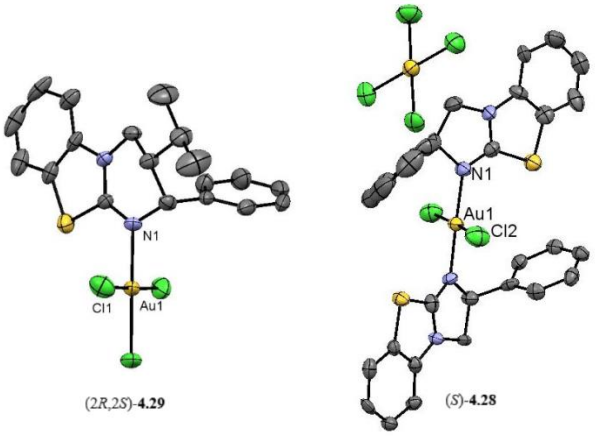


Figure 4.15. Thermal ellipsoid representation of (2*R*,3*S*)-**4.29**, and (*S*)-**4.28** showing 50% probability. Most of the H atoms were omitted for clarity.

Table 4.1. Significant crystallographic data for Au(III) ITU complexes.

Entry	Complex	N-Au-Cl(deg)	Au-N (Å)	N^1-C (Å)	C-N^2(Å)
1	(*S*)-**4.28**	89.4(3) 89.2(3)	1.988(11) 1.992(10)	1.323(18) 1.306(22)	1.321(18) 1.310(17)
2	(2*R*,3*S*)-**4.29**[a]	87.73(15)	2.022(5)	1.294(7)	1.341(8)

[a]Two molecules were found in the crystal lattice of (2*R*,3*S*)-**4.29**.

4.2.3. Steric considerations

Considering the importance of calculating steric and electronic parameters (*S* and *E*) for organometallic complexes (section 1.2.1.3), the percent buried volume (%V_{Bur})[44] using the easily handled *SambVca* tool[45,9,46] was calculated for the neutral Au(I) complexes. The chloride-Au(I) model gave satisfactory results for the analysis of NHC, and phosphine based Au complexes, in particular for monodentate ligands.[44] %V_{Bur} values of 27.5% for (*R*)-**4.25**, 28.7% for (2*R*,3*S*)-**4.26**, and 25.1% for **4.27** were obtained. The ITU ligands appeared similar to the least sterically hindered NHC ligands, and smaller than phosphines (NHC ranging from 26-51%, with imidazole being 18.8%, PR_3 ranging from 38-64%).[45,47] The space filling maps are shown in Figure 4.16.

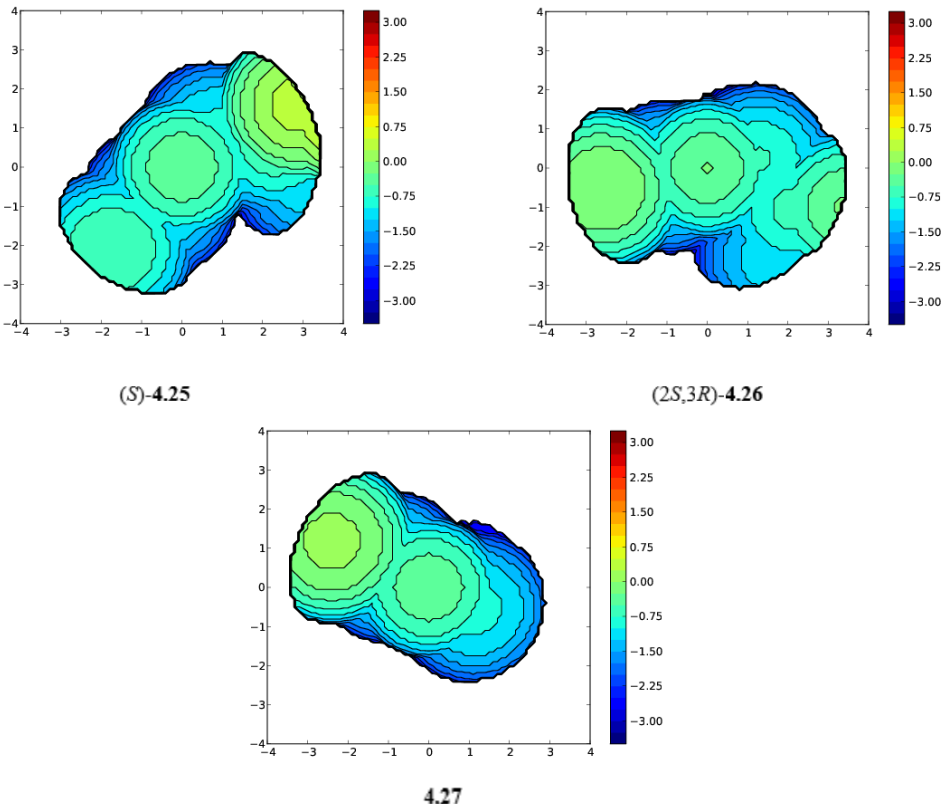
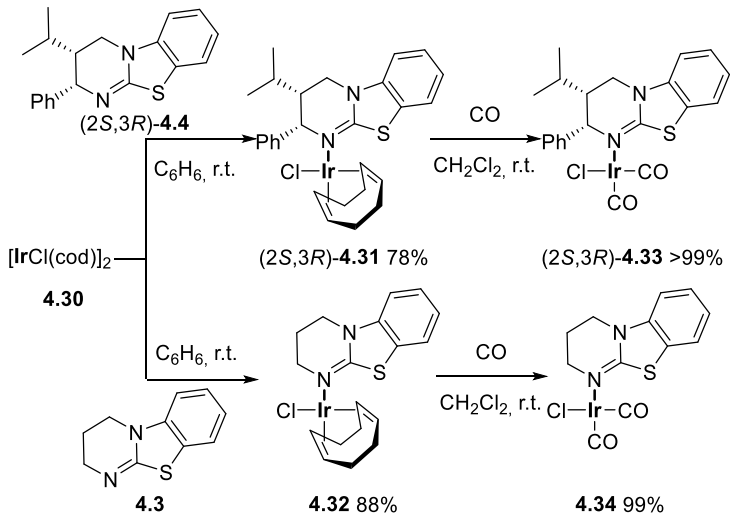


Figure 4.16. Space Filling models for (*S*)-**4.25**, (2*S*,3*R*)-**4.26**, **4.27**.

4.2.4. Electronic considerations: synthesis of Ir(I) ITU complexes

Initial attempts at Tolman Electronic Parameter (TEP) calculations were made.[48] To obtain TEP values for these ligands, the synthesis of Ir(I) ITU complexes was targeted. Reacting $[IrCl(COD)]_2$ (**4.30**) with 2.4 equiv. of (2*S*,3*R*)-**4.4**, or **4.3** in C_6H_6,[49] gave mono-coordinated complexes, [IrCl{(2S,3R)-HyperBTM}(COD)] ((2*S*,3*R*)-**4.31**) and [IrCl(DHPB)(COD)] (**4.32**), as yellow bench-stable solids in good yield (Scheme 4.10). Attempts to react (*S*)-**4.2** with **4.30** resulted in a complex mixture of products.

The Ir(COD) complexes (2*S*,3*R*)-**4.31,** and **4.32** were then reacted with 1 atm of carbon monoxide to form [IrCl{(2*S*,3*R*)-HyperBTM}$(CO)_2$] ((2*S*,3*R*)-**4.33**), and [IrCl(DHPB)$(CO)_2$] (**4.34**), as off-white bench-stable solids in excellent yield (Scheme 4.10).



Scheme 4.10. Synthesis of Ir(I) ITU complexes.

Crystals of (2*S*,3*R*)-**4.31** were grown by slow diffusion of pentane into a saturated CH_2Cl_2 solution (Figure 4.17).[50] The Ir-N^1 distance in (2*S*,3*R*)-**4.31** was 2.104(8) Å, longer than that observed for the Au(I), and Au(III) neutral complexes. The N^1-C, and C-N^2 bonds were 1.257(13), and 1.365(13) Å, respectively. These values were consistent with those found for neutral Au complexes.

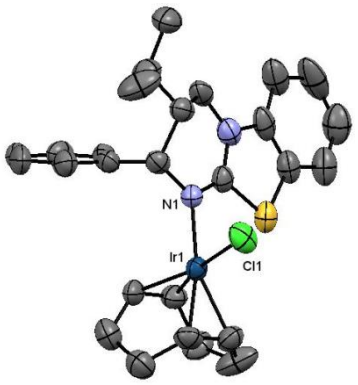


Figure 4.17. Thermal ellipsoid representation of (2*S*,3*R*)-**4.31** showing 50% probability. Significant distances (Å) and angles (°) are: Ir-N^1 2.104(8) Å, N^1-C^1.257(13) Å, C-N^2 1.365(13) Å, N^1-Ir-Cl 87.0(2)°.

The infra-red spectra signals of (2*S*,3*R*)-**4.33**, and **4.34** were performed, and their $\nu_{(CO)av}$ calculated, to obtain TEP values of (2*S*,3*R*)-**4.4**, and **4.3** ligands (Table 4.2). The TEPs were calculated by using 2 different linear regression equations reported respectively by Crabtree,[51] and Nolan,[49] assuming similar behaviour of the σ-donor ITU ligands to carbenes, and phosphines. The values calculated for (2*S*,3*R*)-**4.33** were 2052, and 2048 cm^{-1} (entry 1); 2044, and 2038 cm^{-1} for **4.34** (entry 2). These values suggest that ITUs

were more electron-donating to the metal centre than NHC, or PR_3 ligands, whose TEP values were 2051 cm^{-1} for IPr,[49] and 2069 $cm^{-1}$for PPh_3.[51]

Table 4.2. Main electronic parameters for $[IrCl(ITU)(CO)_2]$ complexes.

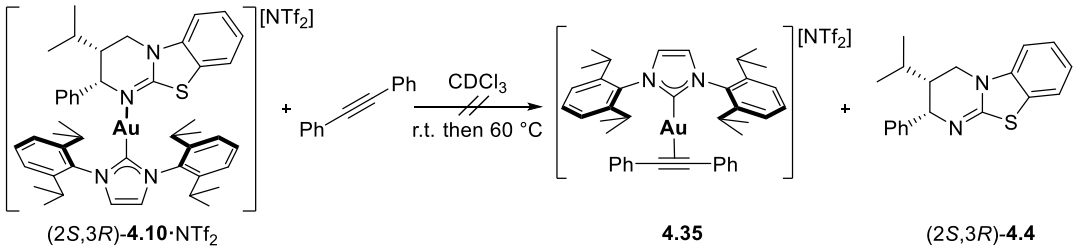
Entry	Complex	ν_{CO}[a] (cm^{-1})	$\nu_{(CO)av}$(cm^{-1})	TEP [b](cm^{-1})	TEP [c](cm^{-1})
1	(2*S*,3*R*)-**4.33**	2062 1981	2021	2052	2048
2	**4.34**	2052 1967	2010	2044	2038

[a]FTIR (ATR); [b]calculated using the equation TEP = 0.722[$\nu_{(CO)av}$[Ir]]+593 cm^{-1};[51c]calculated using the equation TEP = 0.847[$\nu_{(CO)av}$[Ir]]+336 cm^{-1}.[49]

4.3. Stoichiometric and catalytic reactivity of Au ITU complexes

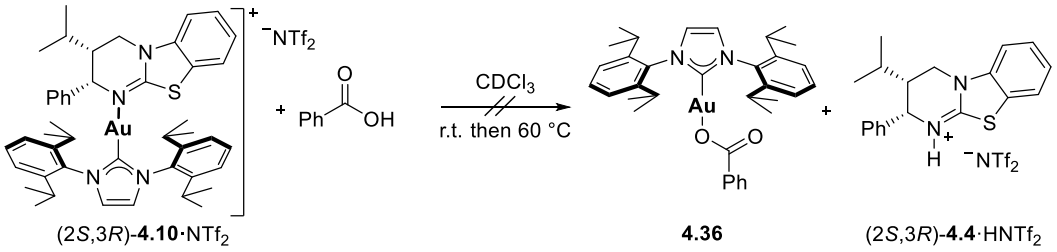
4.3.1. Stoichiometric reactions

Initial stoichiometric experiments were performed for a deeper understanding of the reactivity, and further functionalisation of the Au(I) heteroleptic, and neutral complexes into valuable Au(I) pre-catalysts. Initial attempts to insert alkynes into the N-Au bond were performed (Scheme 4.11). By reacting (2*S*,3*R*)-**4.10**·NTf_2 with an equimolar amount of diphenylacetylene in $CDCl_3$ no conversion of starting materials was found, even after heating the reaction at reflux. No traces of π-activated complex **4.35** were visible by ^1H NMR spectroscopy.



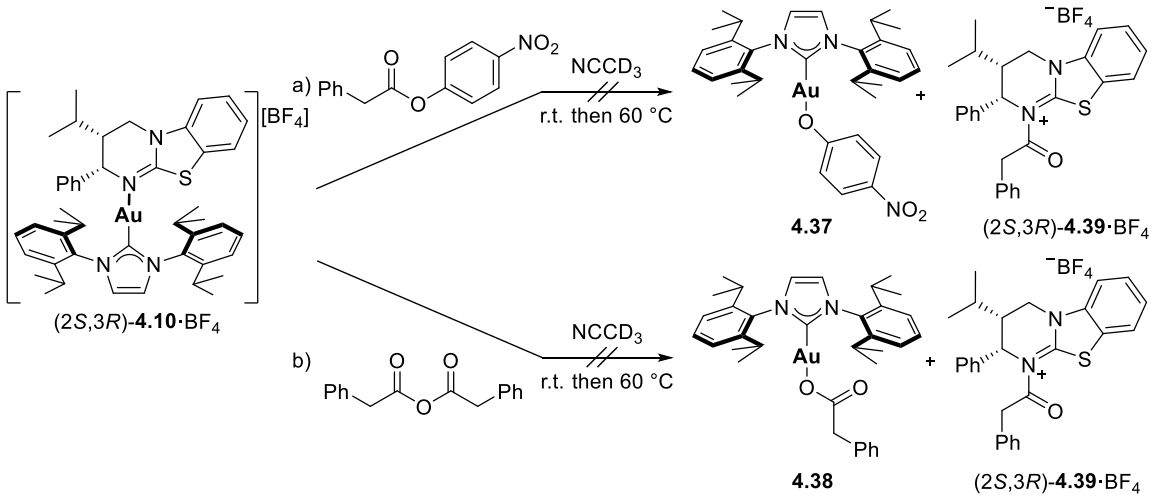
Scheme 4.11. Attempt of alkyne insertion into (2*S*,3*R*)-**4.10**·NTf_2.

The N-Au(I) bond was also not susceptible to reaction with organic acids (Scheme 4.12), with treatment of (2*S*,3*R*)-**4.10**·NTf_2 with benzoic acid in a 1:1 ratio providing no change to the starting Au(I) complex, and carboxylic acid.



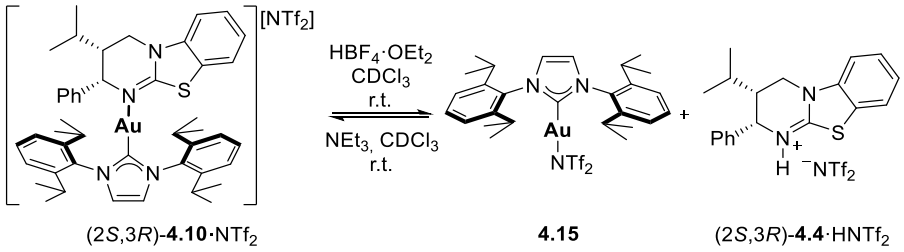
Scheme 4.12. Attempt of formation of carboxylate-Au(I) complexes from (2*S*,3*R*)-**4.10**·NTf_2 and benzoic acid.

Furthermore, treatment of (2*S*,3*R*)-**4.10**·BF_4 with either 1 equiv. of 4-nitrophenyl 2-phenylacetate (Scheme 4.13, a), or 2-phenylacetic anhydride (Scheme 4.13, b) resulted in no formation of phenolate (**4.37**),[52] carboxylate (**4.38**), nor acylated ITU salt ((2*S*,3*R*)-**4.39**·BF_4) at either r.t., or 60 °C. These experiments suggested that even in the presence of a coordinating solvent, such as acetonitrile, no appreciable N-Au bond cleavage is possible under these conditions.



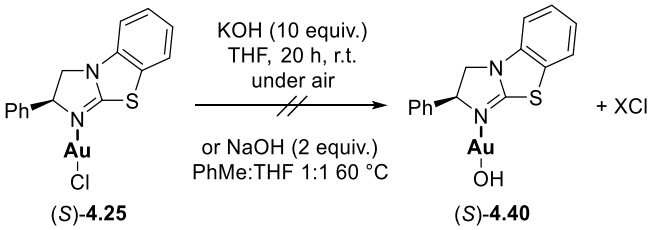
Scheme 4.13. Reaction of (2*S*,3*R*)-**4.10**·BF_4 with a) esters, b) anhydrides.

However, the heteroleptic complexes could be activated by strong mineral acids, such as HBF_4·OEt_2 complex (Scheme 4.14), with this result explored further for the formation of active species for use in catalysis (see section 4.3.2). The equilibrium could be restored to the left by adding triethylamine to the mixture of **4.15**, and (2*S*,3*R*)-**4.4**·HBF_4.



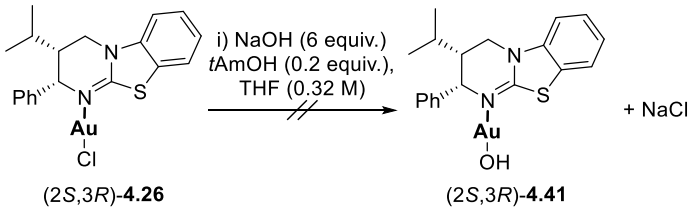
Scheme 4.14. Activation of (2*S*,3*R*)-**4.10**·NTf_2 with strong acids, and reverse.

The use of strong bases was also suitable for the dissociation of complex (2*S*,3*R*)-**4.10**·NTf_2. Treatment with 1 equiv. of KOH solution in THF (0.1 M), led to the release of (2*S*,3*R*)-**4.4** into the reaction mixture. The reaction, followed by ^{1}H NMR, showed a 1:1.6 mixture of (2*S*,3*R*)-**4.10**·NTf_2 to (2*S*,3*R*)-**4.4**, along with the formation of [AuCl(IPr)] **4.5**, which might form in chlorinated media. No traces of [Au(OH)(IPr)] **4.14** were observed. The stoichiometric reactivity of neutral complexes was next explored. Functionalisation of the chlorinated species into more reactive complexes was targeted, but disproportionation of the Au(I) species to metallic gold was the major outcome of the reactions in the chosen conditions. Initial formation of the hydroxide species was tested, by following reported reaction conditions.[21,53] (*S*)-**4.25** was reacted with an excess of KOH in THF solution (0.1 M) under air, as well as by using NaOH (2 equiv.) in a PhMe:THF 1:1 solvent mixture (0.1 M) at 60 °C (Scheme 4.15). The complex was not stable under these conditions, and (*S*)-**4.2** was released into solution, with no trace of the homogeneous complex (*S*)-**4.40** observed by ^{1}H NMR.



Scheme 4.15. Trials of functionalisation of (*S*)-**4.25** into (*S*)-**4.40**.

The reaction of (2*S*,3*R*)-**4.26** with NaOH (6 equiv.), and *t*AmOH (0.2 equiv.) in THF was also attempted under anhydrous conditions (Scheme 4.16).[54] Traces of starting material, and free Lewis base (*S*)-**4.2** were observed, but decomposition was the main pathway.

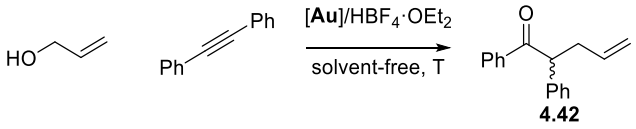


Scheme 4.16. Attempt of functionalisation of (2*S*,3*R*)-**4.26** in dry conditions.

The results however were not surprising due to the highly sensitive nature of (2*S*,3*R*)-**4.41** species if formed; hydroxide-Au(I) complexes are elusive species (section 1.5.1), with few being reported.[55] Final attempts to synthesise, and isolate an homoleptic species $[Au(ITU)_2][X]$ were performed by activation of (*S*)-**4.25** with $AgBF_4$ salts followed by the addition of BTM. Although conversion of starting material was observed, several unidentified species were formed in solution, the structures of which could not be easily interpreted.

4.3.2. Catalytic testing of Au ITU complexes

Having prepared, and characterised Au(I), and Au(III)-ITU complexes, they were tested in model catalytic transformations. Initial studies probed the hydroalkoxylation/Claisen rearrangement[56] of allyl alcohol, and diphenylacetylene to give homoallylic ketone **4.42** (Scheme 4.17).



Scheme 4.17. Au(I)-catalysed hydroalkoxylation/Claisen rearrangement of alkynes.

The heteroleptic, and neutral Au(I) species (2*S*,3*R*)-**4.10**·NTf_2 and (2*S*,3*R*)-**4.26** were used as pre-catalysts, and activated *in situ*. The results were compared to the state of the art (Table 4.3, entry 1), using $[Au(NTf_2)(IPr^{Cl})]$ **4.16**, which provides ketone **4.42** in 99% yield within 20 min at 120 °C. The use of (2*S*,3*R*)-**4.10**·NTf_2 (0.5 mol%), activated with HBF_4·OEt_2, gave full conversion of the starting materials into ketone **4.42** in 99% yield within 5 h. Racemic product was obtained, consistent with the formation, and operation of the presumed active species **4.15**, with the released ITU salt exerting no effect on the stereodetermining step of the transformation. The effect of reducing the temperature from 120 to 60 °C was performed for the reaction with (2*S*,3*R*)-**4.10**·NTf_2 and (2*S*,3*R*)-

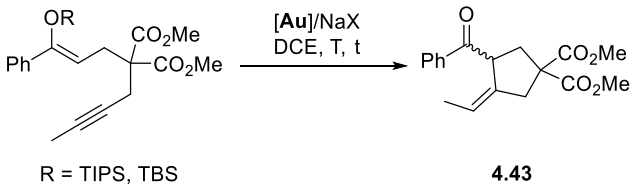
4.12·BF_4. In both cases the product was obtained in ~50% yield after 72 h, however again in racemic form (entries 3, 4). As an alternative, the use of a neutral chiral Au(I) species was tested (entry 5). However, complex (2*S*,3*R*)-**4.26**, activated *in situ* with $NaBAr^F$, showed no activity for this specific transformation. This result is consistent with literature reports,[56-57] where chloride-Au(I) complexes were inactive for this reaction.

Table 4.3. Au(I) catalysed hydroalkoxylation/Claisen rearrangement of internal alkynes.

Entry	[Au] (0.5 mol%)	HBF_4·OEt_2 (mol%)	T (°C)	t (h)	**4.42** (%)[b]
1	**4.16**	-	120	20 mins	99
2	(2*S*,3*R*)-**4.10**·NTf_2	0.5	120	5	99
3	(2*S*,3*R*)-**4.10**·NTf_2	0.5	60	72	52
4	(2*S*,3*R*)-**4.12**·BF_4	0.5	60	72	54
5	(2*S*,3*R*)-**4.26**	1[d]	60	72	-

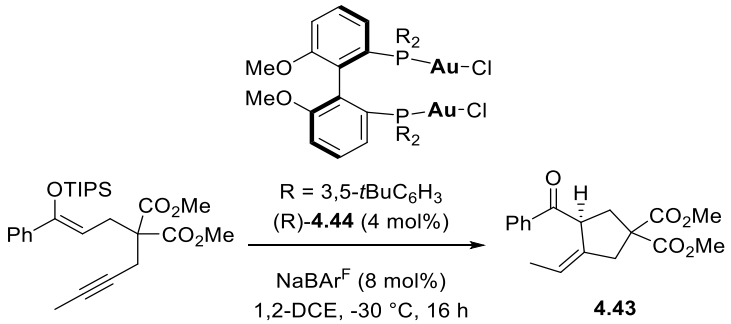
[a]Reaction conditions: diphenylacetylene (0.25 mmol), allyl alcohol (0.75 mmol), [Au] (0.5 mol%), HBF_4·OEt_2 (0.5 mol%), solvent-free; [b] isolated yield; [c] 0.2 mol%.[56d] $NaBAr^F$ (1 mol%).

Further tests in catalysis were directed towards the Au catalysed rearrangement of silyloxyenyne into ketone **4.43** (Scheme 4.18).[58]



Scheme 4.18. Au catalysed silyloxyenynes rearrangement to ketones.

We compared the results obtained to the state of the art reported by Toste and co-workers,[58] in which **4.43** was obtained in 86% yield (86% ee) by using a chiral dinuclear gold complex (*R*)-**4.44** activated by $NaBAr^F$ (Scheme 4.19, Table 4, entry 1).



Scheme 4.19. State of the art for the cyclisation of silyloxyenynes.

At -30 and 0°C, (2*S*,3*R*)-**4.26**, following activation with $NaBF_4$, did not show any traces of the rearrangement of TIPSO-enol substrates (Table 4.4, entries 2, 3), while at reflux the product **4.43** could be isolated in 74% isolated yield after 48 h (entry 4). By switching to a TBSO-enol, 17% conversion was observed after 16 h reaction at -30 °C (entry 5), while the major product of the reaction in this case was the desilylated starting material. However, even at this low reaction temperature no enantioinduction was detected.

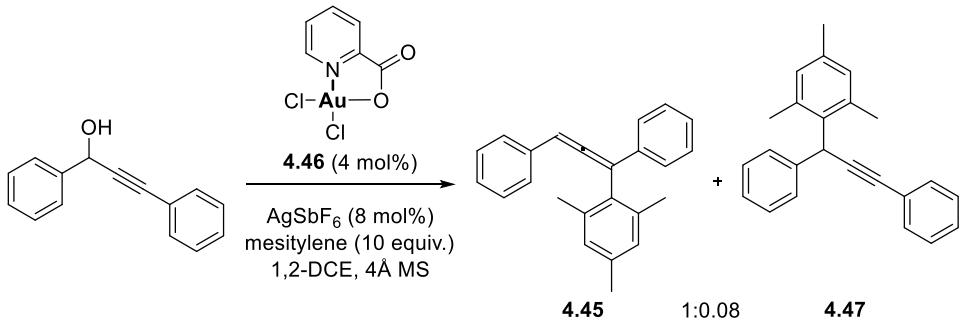
Table 4.4. Rearrangement of silyloxyenynes by Au(I).

Entry	[Au] (4 mol%)[a]	NaX (8 mol%)	T (°C)	t (h)	**4.43** (%)[b]
1	(*R*)-**4.44**	$NaBAr^F$	-30	16	(86)[c]
2	(2*S*,3*R*)-**4.26**	$NaBF_4$	-30	16	0
3	(2*S*,3*R*)-**4.26**	$NaBF_4$	0	16	0
4	(2*S*,3*R*)-**4.26**	$NaBF_4$	84	48	76 (74)[c]
5	(2*S*,3*R*)-**4.26**	$NaBAr^F$	-30	16	17[d]

[a] Reaction conditions: silyloxyenynes (0.04 mmol), (2*S*,3*R*)-**4.26** (10 mol%), $NaBF_4$ (8 mol%), 1,2-DCE (0.02 M); [b] conversions measured by ^{1}H NMR; [c] isolated yield between parenthesis; [d] the reaction was performed with diethyl (*Z*)-2-(but-2-yn-1-yl)-2-(3-((*tert*-butyldimethylsilyl)oxy)-3-phenylallyl)malonate (0.04 mmol), and the major product was the desilylated starting material.

We next tested catalysis using square planar Au(III) ITU complexes. The chosen test reaction was the Friedel/Craft arylation of propargylic alcohols to allenes **4.45**.

The reaction was reported by Li and co-workers (Scheme 4.20);[59] the authors used Au(III) pyridine based bidentate ligand **4.46**, which was activated by $AgSbF_6$. A mixture of C^1 **4.47**, and C^3 **4.45** substitution products were obtained, with formation of the allene as the major product.



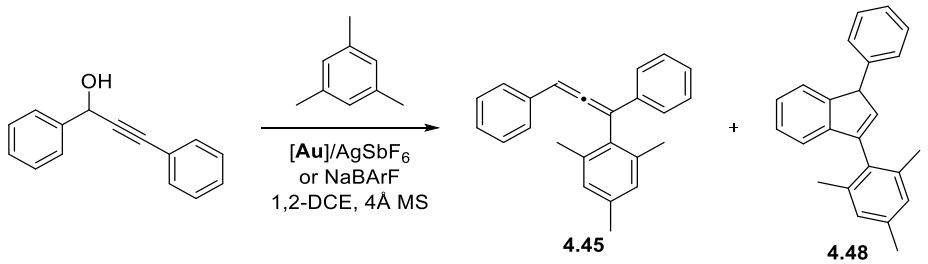
Scheme 4.20. State of the art for the Au(III)-catalysed Friedel/Craft arylation of propargylic alkynes.

Pleasingly, (*S*)-**4.28**, and (2*S*,3*R*)-**4.29** were active in the Friedel-Crafts arylation of alkyne to form allene **4.45** in high efficiency.[59] By using (*S*)-**4.28**, and $AgSbF_6$ (Table 4.5, entries 1, 2), the product was obtained in good to moderate conversions at 50 °C.

Activation using a sodium salt was optimal, and starting material was fully converted to product after 20 mins at r.t., by using (*S*)-**4.28**, or (2*S*,3*R*)-**4.29** (entries 5, 6).

Selective formation of allene **4.45** was obtained in each case, with no direct substitution at C^1 of the propargylic alkyne to give **4.47**.[60] However, no enantioinduction was observed. Neither Na, nor Ag salts alone were active for this transformation (Table 5, entries 3, 7), while formation of **4.45** was achieved only in the presence of a Au source, indicating the catalytic activity of the metal centre in this process (entry 4). Interestingly, formation of a side-product, 3-mesityl-1-phenyl-1H-indene (**4.48**), was also observed in the reaction using (*S*)-**4.28** activated with $AgSbF_6$ after prolonged reaction times at 50 °C. The product might form after Friedel/Craft arylation, through a Nazarov cyclisation, as reported in literature.[61]

Table 4.5. Friedel-Crafts arylation of alkynes by Au(III) catalysis.

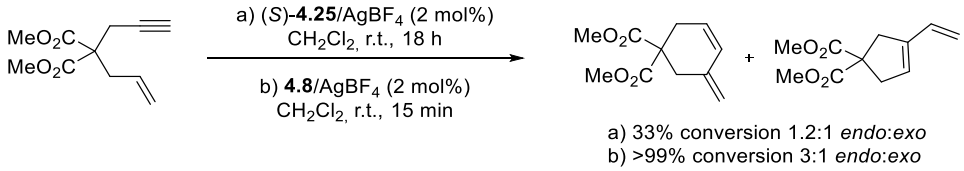


Entry	[Au] (4 mol%)[a]	Na/Ag salt (8 mol%)	T (°C)	t (min)	**4.45** (%)[b]
1	**4.46**	$AgSbF_6$	50	17	87
2	(*S*)-**4.28**	$AgSbF_6$	50	20	83
3	(*S*)-**4.28**	$AgSbF_6$	50	960	57(43)[c]
4	-	$AgSbF_6$	50	20	-
5	(*S*)-**4.28**	-	50	20	-
6	(*S*)-**4.28**	$NaBAr^F$	r.t.	20	100
7	(2*S*,3*R*)-**4.29**	$NaBAr^F$	r.t.	20	100
8	-	$NaBAr^F$	50	20	-

[a] Reaction conditions: 1,3-diphenylprop-2-yn-1-ol (0.1 mmol); mesitylene (7 equiv.); [Au] (4 mol%); $NaBAr^F$, or $AgSbF_6$ (8 mol%); 1,2-DCE (1.5 mL); [b] conversions measured by ^{1}H NMR; [c] isolated yield for 3-mesityl-1-phenyl-1*H*-indene; [d] the reaction was performed also at r.t. with the same results as the one at 50 °C.

The complexes showed some limitations in terms of enantioinduction, most likely due to the remoteness of the chiral ligands to the reactive site. However, their reactivity toward the tested reactions was remarkable, leading to high conversion, in some instances outperforming reported data in literature. To test whether the complexes reported herein could be active for cycloisomerization reactions the well-explored Au(I)-catalysed

cycloaddition of 1,6-enynes was tested.[62] By reacting dimethyl 2-allyl-2-(prop-2-yn-malonate), in the presence of 2 mol% of (*S*)-**4.25** [AuCl{(*S*)-BTM}], and $AgBF_4$ (2 mol%) the reaction proceeded to 33% conversion to give the *endo* and *exo* cyclization products in a 1.2:1 ratio (Scheme 4.21, a). Leaving the reaction for longer reaction times resulted in visible decomposition of the gold catalyst. For comparison, the results with **4.8** [$AuCl(PPh_3)$], showed full conversion after 15 minutes reaction and a 3:1 *endo*:*exo* product ratio (Scheme 4.21, b).[62]



Scheme 4.21. Cycloaddition of 1,6-enynes by Au(I) catalysis.

4.4. Conclusions and perspectives

The synthesis of chiral Au(I), and Au(III) catalysts was achieved by exploiting point chiral organic motifs, isothioureas. The complexes were obtained in good to excellent yield and characterised using spectroscopic analysis. Their structures were confirmed by X-ray crystallography analysis. The reactivity of the newly synthesised complexes was explored; stoichiometric reactions showed that careful conditions must be found to functionalise these complexes, while strong acid, or base activation might release the Au pre-catalyst *in situ*. Their activity was studied in benchmark gold catalysed reactions, in general leading to good activity of the complexes, and good conversions into the targeted products. Future screening of the steric environment, and ligand design should shape these complexes to their optimal performance.

In addition, the newly synthesised heteroleptic, and neutral Au(I) and Au(III)-isothiourea complexes were tested for their biological activity by collaborators. Testing *in vitro* showed high activity against breast cancer cell line MCF-7, and cervical cancer cell line HeLa. Some of the complexes however proved cytotoxic, in particular the heteroleptic complexes with a PPh_3 ancillary ligand. The inhibition of tumour relevant enzymes, β-glucuronidase, and phosphodiesterase, by the Au(III) ITU complexes was also investigated. (*S*)-**4.11**·BF_4 showed 50% inhibition of β-glucuronidase activity at 0.11 μM, compared to standard D-saccharic acid 1,4 lactone with IC_{50} = 47.5 μM.

The synthesis of chiral Ir(I) ITU complexes was also achieved. Their use as asymmetric catalysts might be of interest for further applications.[63] Initial investigations into the transfer hydrogenation of acetophenone was tested using 2 mol% (2*S*,3*R*)-**4.31**, and 5 mol% KOH in *i*PrOH: the reaction gave low conversion (<10%) after 3 days reaction at reflux.[64] Thus, we can envisage that activation with an halide abstractor in the presence of a labile inner sphere counter-ion might be important to form an active species *in situ* to achieve higher conversions.[65]

Future possible research interests around the newly synthesised complexes might be through the use of computational analysis. DFT analysis could help shed light on Au-ITU coordination. This would enhance fundamental understanding of Au coordination chemistry and provide insights into the association/dissociation of the ITU ligands from the metal centre to inspire further applications in catalysis.

4.5. Experimental

Unless otherwise stated, all solvents and reagents were used as purchased and all reactions were performed under air. Anhydrous CH_2Cl_2, Et_2O, THF, and PhMe were obtained from an MBraun SPS-800 system. All other solvents and commercial reagents were used as received without further purification unless otherwise stated. Room temperature (r.t.) refers to 20–25 °C. ^{1}H, $^{13}C\{^{1}H\}$ $^{19}F\{^{1}H\}$ NMR, and $^{31}P\{^{1}H\}$ NMR spectra were recorded on Bruker Avance 500-300 MHz NMR spectrometers. In $CDCl_3$, ^{1}H, and $^{13}C\{^{1}H\}$ NMR chemical shifts are reported relative to $CHCl_3$ at 7.26 ppm and 77.16 ppm, respectively. For the assignment of the ^{1}H, and $^{13}C\{^{1}H\}$ NMR spectra 2D NMR (COSY, HSQC, HMBC) experiments were also performed. Coupling constants (*J*) are reported in Hertz (Hz). Multiplicities are indicated by: br s (broad singlet), s (singlet), d (doublet), t (triplet), q (quartet), and m (multiplet). Infrared spectra (νmax) were recorded on a Shimadzu IRAffinity-1 Fourier transform IR spectrophotometer using either thin film or solid using Pike MIRacle ATR accessory. Analysis was carried out using Shimadzu IRsolution v1.50 and only characteristic peaks are reported. 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. Analytical thin layer chromatography was performed on pre-coated aluminium plates (Kieselgel 60 F254 silica). Plates were visualised under UV light (254 nm) or by staining with $KMnO_4$ followed by heating. Flash column chromatography was

performed on Kieselgel 60 silica in the solvent system stated under a positive pressure of compressed air or on a Biotage® IsoleraTM 4, using Biotage® Snap Ultra or Biotage® KP Sil columns under the solvent system stated. HPLC analyses were obtained on a Shimadzu HPLC consisting of a DGU-20A5 degasser, LC-20AT liquid chromatography SIL-20AHT autosampler, CMB-20A communications bus module, SPDM20A diode array detector, and a CTO-20A column oven that allows the temperature to be set from 25–40 °C. Separation was achieved using Chiralcel OD-H or Chiralpak AD-H columns. Elemental analyses were performed by Stephen Boyer, at London Metropolitan University. [AuCl(SMe)$_2$] **4.24**,[66] [AuCl(L)] (L = IPr **4.7**, PPh$_3$ **4.8**),[67] (*S*)-**4.2** ((*R*)-**4.2**),[19] **4.3**,[19] (2*S*,3*R*)-**4.4** ((2*R*,3*S*)-**4.4**),[19] PhI(Cl)$_2$,[68] [Au(OH)(IPr)] **4.14**,[69] [Au(NTf$_2$)(L)][24] (L = IPr **4.15**, IPr^{Cl} **4.16**), [Au(L)(NCCH$_3$)][BF$_4$] (L = IPr **4.19**, SIPr = **4.20**),[53] [Au(CH$_2$C(O)CH$_3$)(IPr)] **4.23**,[26] 1,3-diphenylprop-2-yn-1-ol,[70] dimethyl (*Z*)-2-(but-2-yn-1-yl)-2-(3-phenyl-3-((triisopropylsilyl)oxy)allyl)malonate, and dimethyl (*Z*)-2-(but-2-yn-1-yl)-2-(3-((*tert*-butyldimethylsilyl)oxy)-3-phenylallyl)malonate,[58] were synthesised according to literature reports, and as reported in chapters 2, 3, 6. Allyl alcohol, diphenylacetylene, mesitylene, [IrCl(COD)]$_2$ **4.30**, PhI(OAc)$_2$ were commercially available.

4.5.1. General synthesis of heteroleptic Au(I) complexes

GP1: [AuCl(IPr)] (**4.7**) or [AuCl(PPh$_3$)] (**4.8**) (0.2 mmol), and AgBF$_4$ or AgNTf$_2$ (1 equiv.) were dissolved in CH$_2$Cl$_2$ (0.1 M) and stirred at r.t. for 10 mins. The ITU ((*S*)-**4.2**, (*R*)-**4.2**, (2*S*,3*R*)-**4.4**, and (2*S*,3*R*)-**4.4**, 1 equiv.) was added, and the reaction stirred for 10 mins at the same temperature. The solvent was removed under vacuum and the resulting solid dissolved in CH$_2$Cl$_2$ (2-3 mL). The solution was concentrated (~1 mL) and the product precipitated by addition of pentane (~10 mL). The precipitate was collected by filtration, washed with pentane (3×5 mL) and dried under vacuum, affording the corresponding complexes as colourless solids in good to excellent yields

GP2: [Au(NTf$_2$)(NHC)] (**4.15**, **4.16**) or [Au(NHC)(NCCH$_3$)][BF$_4$] (**4.19**, **4.20**) (0.2 mmol) were dissolved in CH$_2$Cl$_2$ or THF (0.1 M), and ITU (1 equiv.; 1.2 equiv. for **4.20**) was added. The reaction stirred at r.t. for 1-16 h. The solvent was removed under vacuum and the resulting solid dissolved in CH$_2$Cl$_2$ (2-3 mL). The solution was concentrated (~ 1

mL) and the product precipitated by addition of pentane (~ 10 mL). The precipitate was collected by filtration, washed with pentane (3×5 mL), and dried under vacuum, affording the corresponding complexes as colourless solids in good to excellent yields.

[Au(IPr){(*S*)-BTM}][NTf_2] ((*S*)-**4.9**·NTf_2) and [Au(IPr){(*R*)-BTM}][NTf_2] ((*R*)-**4.9**·NTf_2): complex (*S*)-**4.5**·NTf_2 was synthesised following GP1 using **4.7** (124.2 mg, 0.2 mmol), $AgNTf_2$ (77.6 mg, 0.2 mmol, 1 equiv.), (*S*)-**4.2** (50.4 mg, 0.2 mmol, 1 equiv.) in CH_2Cl_2 (1 mL). The reaction was stirred for 10 mins at r.t. The mixture was concentrated, and the product precipitated to obtain (*S*)-**4.9**·NTf_2 as a white solid in 96% yield (214.7 mg, 0.196 mmol). Complexes (*S*)-**4.9**·NTf_2, and (*R*)-**4.9**·NTf_2 were synthesised also following GP2 using **4.15** (129.9 mg, 0.15 mmol), (*S*)-**4.2** or (*R*)-**4.2** (37.8 mg, 0.15 mmol, 1 equiv.) in THF (1.5 mL). The reaction was stirred for 10 mins at r.t. The mixture was concentrated, and the product precipitated to obtain (*S*)-**4.9**·NTf_2 and (*R*)-**4.9**·NTf_2 as colourless solids in 96% (161.1 mg) and >99% yield (167.8 mg). ^{1}H NMR (500 MHz, $CDCl_3$) δ = 7.53 (t, *J* = 7.8, 2H, C_{Ar}IPr), 7.41 (d, *J* = 8.0, 1H, C_{Ar}ITU), 7.34 – 7.22 (m, 7H, $CH_{backbone}$IPr/C_{Ar}ITU), 7.14 (t, *J* = 7.6, 3H, C_{Ar}IPr/C_{Ar}ITU), 6.92 (d, *J* = 7.7, 3H, C_{Ar}IPr/C_{Ar}ITU), 5.34 (dd, *J* = 10.8, 8.2, 1H, CHPh), 4.51 (t, *J* = 10.5, 1H, CH_{2cis}), 3.81 (dd, *J* = 10.2, 8.3, 1H, CH_{2trans}), 2.44 – 2.29 (m, *J* = 7.0, 4H, CH*i*Pr), 1.18 (dd, *J* = 6.8, 1.9, 12H, CH_3*i*Pr), 1.14 (d, *J*=6.9, 6H, CH_3*i*Pr), 1.09 (d, *J*=6.9, 6H, CH_3*i*Pr). ^{13}C{^{1}H} NMR (126 MHz, $CDCl_3$) δ = 172.2 (C=N), 171.7($C_{carbene}$), 145.6 (Cq), 139.7 (Cq), 135.5 (Cq), 133.3 (Cq), 131.1 (C_{Ar}IPr), 129.3 (C_{Ar}ITU), 128.8 (C_{Ar}ITU), 128.3 (C_{Ar}ITU), 126.4 (C_{Ar}IPr), 125.3 (Cq), 124.4 ($CH_{backbone}$IPr/C_{Ar}ITU), 124.2 (C_{Ar}ITU), 123.7 (C_{Ar}IPr), 121.3 (Cq), 118.8 (Cq), 111.3 (C_{Ar}ITU), 74.3 (CHPh), 52.8 (CH_2), 28.9 (CH*i*Pr), 24.7 (CH_3*i*Pr), 24.0 (CH_3*i*Pr), 23.9 (CH_3*i*Pr). ^{19}F{^{1}H} NMR (471 MHz, $CDCl_3$) δ -78.73. FTIR (ATR) ν = 1560 (C=N) cm^{-1}.

[Au(IPr){(*S*)-BTM}][NTf_2] $[\alpha]_D^{20}$ -6.0°(c 0.1, $CHCl_3$) elemental analysis calcd (%): C 47.27; H 4.33; N 6.26; found: C 44.71; H 4.15; N 5.98.

[Au(IPr){(*R*)-BTM}][NTf_2] $[\alpha]_D^{20}$ +5.5°(c 0.1, $CHCl_3$) elemental analysis calcd (%):C 47.27; H 4.33; N 6.26; found: C 44.79; H 4.09; N 6.07.

[Au(IPr){(*S*)-BTM}][BF_4] ((*S*)-**4.9**·BF_4) and [Au(IPr){(R)-BTM}][BF_4] ((*R*)-**4.9**·BF_4): complexes (*S*)-**4.9**·BF_4 and [Au(IPr){(*R*)-BTM}][BF_4] ((*R*)-**4.9**·BF_4) were synthesised

following GP1 using **4.7** (124.2 mg, 0.2 mmol), $AgBF_4$ (28.9 mg, 0.2 mmol, 1 equiv.), (*S*)-**4.2** or (*R*)-**4.2** (50.41 mg, 0.2 mmol, 1 equiv.) in CH_2Cl_2 (1 mL). The reaction was stirred for 10 mins at r.t. The mixture was concentrated, and the product precipitated to obtain (*S*)-**4.9**·BF_4 and (*R*)-**4.9**·BF_4 as white solids in 95% yield (175.8 mg). Complex (*S*)-**4.9**·BF_4 was synthesised also following GP2 using **4.15** (107.1 mg, 0.15 mmol), (*S*)-**4.2** (37.8 mg, 0.15 mmol, 1 equiv.) in THF (1.5 mL). The reaction was stirred for 10 mins at r.t. The mixture was concentrated and the product precipitated to obtain (*S*)-**4.9**·BF_4 as a colourless solid in 99% yield (137.4 mg). ^{1}H NMR (500 MHz, $CDCl_3$) δ = 7.49 (t, *J* = 7.8, 1H, C_{Ar}IPr), 7.37 (d, *J* = 8.0, 0H), 7.22 (dd, *J* = 7.6, 4.2, 2H), 7.18 (s, 1H), 7.08 (t, *J* = 7.7, 2H), 6.96 (d, *J* = 8.0, 1H), 6.90 (d, *J* = 7.3, 1H), 5.33 (dd, *J* = 10.8, 8.3, 1H), 4.59 (t, *J* = 10.6, 1H), 3.78 (dd, *J* = 10.4, 8.3, 1H), 2.39 – 2.27 (m, *J* = 7.0, 2H), 1.19 – 1.02 (m, 12H). ^{13}C{^{1}H} NMR (126 MHz, $CDCl_3$) δ = 172.1(C=N), 171.7($C_{carbene}$), 145.6(Cq), 139.9(Cq), 135.6(Cq), 133.4(Cq), 131.1(C_{Ar}IPr), 129.2(C_{Ar}ITU), 128.7(C_{Ar}ITU), 128.4(C_{Ar}ITU), 126.4(C_{Ar}IPr), 125.2(Cq), 124.4($CH_{backbone}$IPr/C_{Ar}ITU), 124.2(C_{Ar}ITU), 124.1(C_{Ar}IPr), 123.6(Cq), 111.5(C_{Ar}ITU), 74.3(CHPh), 52.8(CH_2), 28.8(CH*i*Pr), 24.7(CH_3*i*Pr), 24.0(CH_3*i*Pr). ^{19}F{^{1}H} NMR (470 MHz, $CDCl_3$) δ = -153.85, -153.91. FTIR (ATR) ν = 1558 (C=N) cm^{-1}.

[Au(IPr){(*S*)-BTM}][BF_4][α]$_D^{20}$ -6.9°(c = 0.1, $CHCl_3$) elemental analysis calcd (%): C 54.55; H 5.23; N 6.06; found: C 54.46; H 5.37; N 5.96.

[Au(IPr){(*R*)-BTM}][BF_4] [α]$_D^{20}$ +5.5°(c = 0.1, $CHCl_3$) elemental analysis calcd (%):C 54.55; H 5.23; N 6.06; found: C 54.38; H 5.34; N 5.99.

[Au(IPr){(2*S*,3*R*)-HyperBTM}][NTf_2] ((2*S*,3*R*)-**4.10**·NTf_2) and [Au(IPr){(2*R*,3*S*)-HyperBTM}][NTf_2] ((2*R*,3*S*)-**4.10**·NTf_2): complex (2*S*,3*R*)-**4.10**·NTf_2) was synthesised following GP1 using **4.7** (124.2 mg, 0.2 mmol), $AgNTf_2$ (77.6 mg, 0.2 mmol, 1 equiv.), (*2S*,3*R*)-**4.4** (61.7 mg, 0.2 mmol, 1 equiv.) in CH_2Cl_2 (1 mL). The reaction was stirred for 10 min at r.t. The mixture was concentrated, and the product precipitated to obtain (2*S*,3*R*)-**4.10**·NTf_2 as a colourless solid in 93% yield (218.4 mg). Complexes (2*S*,3*R*)-**4.10**·NTf_2 and (2*R*,3*S*)-**4.10**·NTf_2 were synthesised also following GP2 using **4.15** (129.9 mg, 0.15 mmol), (*2S*,3*R*)-**4.4** or (*2R*,3*S*)-**4.4** (46.2 mg, 0.15 mmol, 1 equiv.) in THF (1.5 mL). The reaction was stirred for 10 mins at r.t. The mixture was concentrated, and the

product precipitated to obtain (2*S*,3*R*)-**4.10**·NTf_2 and (2*R*,3*S*)-**4.10**·NTf_2 as colourless solids in 99% (174.4 mg) and > 99% yield (176.1 mg). ^{1}H NMR (500 MHz, $CDCl_3$) δ = 7.52 (t, *J* = 7.8 Hz, 2H, H_{Ar}IPr), 7.33 (td, *J* = 7.8, 1.3 Hz, 1H, H_{Ar}ITU), 7.30 – 7.23 (m, 3H, $H_{backbone}$IPr/H_{Ar}ITU), 7.23 – 7.16 (m, 5H, H_{Ar}ITU), 7.11 (t, *J* = 7.6 Hz, 3H, H_{Ar}IPr), 7.03 (d, *J* = 8.1 Hz, 1H, H_{Ar}ITU), 6.62 – 6.56 (m, 2H, H_{Ar}IPr), 4.24 (dd, *J* = 4.7, 1.5 Hz, 1H, CHPh), 3.86 (ddd, *J* = 12.5, 5.1, 1.7 Hz, 1H, CH_{2cis}), 3.25 (t, *J* = 12.3 Hz, 1H, CH_{2trans}), 2.32 (dp, *J* = 27.2, 6.9 Hz, 4H, CH*i*Pr), 1.89 (ddt, *J* = 12.3, 9.4, 4.8 Hz, 1H, $CH(CH_3)_2$), 1.17 – 1.10 (m, 19H, CH_3*i*Pr), 1.07 (q, *J* = 5.4, 4.7 Hz, 1H, CH-$CH(CH_3)_2$) 0.92 (t, *J* = 6.9 Hz, 9H, CH_3*i*Pr, $CH(CH_3)_2$), 0.69 (d, *J* = 6.7 Hz, 3H, $CH(CH_3)_2$). ^{13}C{^{1}H} NMR (126 MHz, $CDCl_3$) δ = 170.6($C_{carbene}$), 167.9 (C=N), 145.9 (Cq), 139.7 (Cq), 137.8 (Cq), 133.7 (Cq), 130.9 (C_{Ar}ITU), 129.0 (C_{Ar}IPr), 128.6 (C_{Ar}ITU), 128.5 (C_{Ar}ITU), 127.9 (C_{Ar}ITU), 127.8 (C_{Ar}ITU), 127.3 (C_{Ar}IPr), 124.8 (C_{Ar}ITU), 124.5 (C_{Ar}ITU), 124.3 (C_{Ar}ITU), 124.3 ($CH_{backbone}$IPr), 122.2 (C_{Ar}ITU), 120.8 (Cq), 110.6 (C_{Ar}ITU), 64.8 (CHPh), 41.6 (CH_2), 41.2 ($CH(CH_3)_2$), 28.9 ($CH(CH_3)_2$), 26.8 (CH*i*Pr), 24.6 (CH_3*i*Pr), 24.4 (CH_3*i*Pr), 24.1 (CH_3*i*Pr), 24.0 (CH_3*i*Pr), 21.6 (CH_3*i*Pr), 19.7 (CH-$CH(CH_3)_2$). ^{19}F{^{1}H} NMR (377 MHz, $CDCl_3$) δ = -78.72. FTIR (ATR) ν = 1600, 1577 (C=N) cm^{-1}.

[Au(IPr){(2*S*,3*R*)-HyperBTM}][NTf_2] $[\alpha]_D^{20}$ +9.0°(c = 0.1, $CHCl_3$) elemental analysis calcd (%): C 49.10; H 4.81; N 5.96; found: C 49.20; H 4.91; N 6.05.

[Au(IPr){(2*R*,3*S*)-HyperBTM}][NTf_2][$\alpha]_D^{20}$ -10.00°(c = 0.1, $CHCl_3$) elemental analysis calcd (%):C 49.10; H 4.81; N 5.96; found: C 49.22; H 4.89; N 6.03.

[Au(IPr){(2*S*,3*R*)-HyperBTM}][BF_4] ((2*S*,3*R*)-**4.10**·BF_4) and [Au(IPr){(2*R*,3*S*)-HyperBTM}][BF_4] ((2*R*,3*S*)-**4.10**·BF_4): complexes (2*S*,3*R*)-**4.10**·BF_4) and (2*R*,3*S*)-**4.10**·BF_4 were synthesised following GP1 using **4.7** (124.2 mg, 0.2 mmol), $AgBF_4$ (28.9 mg, 0.2 mmol, 1 equiv.), (*2S*,3*R*)-**4.4** or (2*R*,3*S*)-**4.4** (61.7 mg, 0.2 mmol, 1 equiv.) in CH_2Cl_2 (1 mL). The reaction was stirred for 10 min at r.t. The mixture was concentrated, and the product precipitated to obtain (2*S*,3*R*)-**4.10**·BF_4 and (2*R*,3*S*)-**4.10**·BF_4 as colourless solids in 89% (174.7 mg) and 99% yield (194.4 mg). Complex (2*S*,3*R*)-**4.10**·BF_4 was synthesised also following GP2 using **4.19** (107.1 mg, 0.15 mmol), (*2S*,3*R*)-**4.4** (46.2 mg, 0.15 mmol, 1 equiv.) in THF (1.5 mL). The reaction was stirred for 10 mins at r.t. The mixture was concentrated, and the product precipitated to obtain (2*S*,3*R*)-

4.10·BF_4 as a colourless solid in > 99% yield (146.3 mg). ^{1}H NMR (500 MHz, $CDCl_3$) δ = 7.59 (t, *J* = 7.8, 2H, H_{Ar}IPr), 7.41 (t, *J* = 8.1, 1H, H_{Ar}ITU), 7.33 (s, *J* = 9.8, 7.9, 2H, $H_{backbone}$IPr), 7.30 – 7.20 (m, 2H, H_{Ar}ITU), 7.17 (td, *J* = 9.1, 8.1, 2.9, 3H, H_{Ar}IPr/H_{Ar}ITU), 6.65 (d, *J* = 7.6, 2H, H_{Ar}ITU), 4.31 (d, *J* = 4.5, 1H, CHPh), 3.97 (dd, *J* = 12.7, 5.0, 1H, CH_2), 3.33 (t, *J* = 12.4, 1H, CH_2), 2.39 (dhept, *J* = 27.2, 6.7, 4H, CH*i*Pr), 1.95 (ddt, *J* = 13.5, 9.5, 4.7, 1H, $CH(CH_3)_2$), 1.38 – 1.10 (m, 21H, CH_3*i*Pr), 0.98 (t, *J* = 6.6, 9H, CH_3*i*Pr/ $CH(CH_3)_2$), 0.77 (d, *J* = 6.6, 3H, $CH(CH_3)_2$). ^{13}C{^{1}H} NMR (126 MHz, $CDCl_3$) δ 170.4 ($C_{carbene}$), 167.8 (C=N), 145.9 (Cq), 139.7 (Cq), 137.8 (Cq), 133.8 (Cq), 130.9 (C_{Ar}IPr), 128.9 (C_{Ar}IPr), 128.5 (C_{Ar}ITU), 127.9 (C_{Ar}IPr), 127.3 (C_{Ar}ITU), 124.8 (C_{Ar}ITU), 124.5 ($CH_{backbone}$IPr), 124.3 (C_{Ar}ITU), 122.2 (C_{Ar}ITU), 120.8 (C_{Ar}ITU), 110.8 (C_{Ar}ITU), 64.8 (CHPh), 41.7 (CH_2), 41.2 ($CH(CH_3)_2$), 28.9 (CH*i*Pr), 28.8 (CH*i*Pr), 26.8 ($CH(CH(CH_3)_2)$), 24.6 (CH_3*i*Pr), 24.4 (CH_3*i*Pr), 24.2 (CH_3*i*Pr), 24.0 (CH_3*i*Pr), 22.4 (CH_3*i*Pr), 21.6 ($CH(CH_3)_2$), 19.7 ($CH(CH_3)_2$). ^{19}F{^{1}H} NMR (470 MHz, $CDCl_3$) δ = -154.03, -154.08. FTIR (ATR) ν = 1599, 1575 (C=N) cm^{-1}.

[Au(IPr){(2*S*,3*R*)-HyperBTM}][BF_4] $[\alpha]_D^{20}$ +11.2°(c = 0.1, $CHCl_3$) elemental analysis calcd (%): C 56.33; H 5.76; N 5.71; found: C 56.12; H 5.89; N 5.67.

[Au(IPr){(2*R*,3*S*)-HyperBTM}][BF_4] $[\alpha]_D^{20}$ -10.2°(c = 0.1, $CHCl_3$) elemental analysis calcd (%): C 56.33; H 5.76; N 5.71; found: C 56.18; H 5.89; N 5.68.

[Au(PPh_3){(*S*)-BTM}][NTf_2] ((*S*)-**4.11**·NTf_2) and [Au(PPh_3){(*R*)-BTM}][NTf_2] ((*R*)-**4.11**·NTf_2): complexes (*S*)-**4.11**·NTf_2 and (*R*)-**4.11**·$NTf_2$was synthesised following GP1 using **4.8** (98.9 mg, 0.2 mmol), $AgNTf_2$ (77.6 mg, 0.2 mmol, 1 equiv.), (*S*)-**4.2** or (*R*)-**4.2** (50.4 mg, 0.2 mmol, 1 equiv.) in CH_2Cl_2 (1 mL). The reaction was stirred for 10 min at r.t. The mixture was concentrated, and the product precipitated to obtain (*S*)-**4.11**·NTf_2 and (*R*)-**4.11**·NTf_2 as colourless solids in 94% (186.4 mg) and 82% yield (162.6 mg). ^{1}H NMR (500 MHz, $CDCl_3$) δ = 7.59 – 7.50 (m, 5H, $H_{Ar}PPh_3$), 7.50 – 7.39 (m, 10H, $H_{Ar}PPh_3$/H_{Ar}ITU), 7.29 (dd, *J* = 13.8, 7.8 Hz, 6H, $H_{Ar}PPh_3$), 7.21 (t, *J* = 7.8 Hz, 1H, H_{Ar}ITU), 7.08 (d, *J* = 8.0 Hz, 1H, H_{Ar}ITU), 6.01 (dd, *J* = 10.7, 8.7 Hz, 1H, CHPh), 4.81 (t, *J* = 10.3 Hz, 1H, CH_{2cis}), 4.12 (t, *J* = 9.3 Hz, 1H, CH_{2trans}). ^{13}C{^{1}H} NMR (126 MHz, $CDCl_3$) δ = 171.6 (C=N), 140.9 (Cq), 135.8 (Cq), 134.2 (C_{Ar}), 134.1 (C_{Ar}), 132.6 (C_{Ar}), 129.7 (C_{Ar}), 129.6 (C_{Ar}), 129.5 (C_{Ar}), 129.2 (C_{Ar}), 128.3 (C_{Ar}), 127.6 (C_{Ar}), 127.5

(C_{Ar}ITU), 127.1 (C_{Ar}), 126.0 (C_{Ar}), 124.2 (C_{Ar}ITU), 123.8 (C_{Ar}), 121.4 (Cq), 118.8 (Cq), 111.4 (C_{Ar}ITU), 74.5 (CHPh), 52.9 (CH_2). $^{19}F\{^1H\}$ NMR (471 MHz, $CDCl_3$) δ = -78.66. $^{31}P\{^1H\}$ NMR (202 MHz, $CDCl_3$) δ = 31.36. FTIR (ATR) ν = 1556 (C=N) cm^{-1}.

[Au(PPh_3){(*S*)-BTM}][NTf_2] $[\alpha]_D^{20}$ -6.5°(c = 0.1, $CHCl_3$) elemental analysis calcd (%): C 42.39; H 2.74; N 4.24; found: C 42.27; H 2.57; N 4.42.

[Au(PPh_3){(*R*)-BTM}][NTf_2] $[\alpha]_D^{20}$ +6.6°(c = 0.1, $CHCl_3$) elemental analysis calcd (%):C 42.39; H 2.74; N 4.24; found: C 42.33; H 2.59; N 4.47.

[Au(PPh_3){(*S*)-BTM}][BF_4] (*S*)-**4.11**·BF_4, and [Au(PPh_3){(R)-BTM}][BF_4] (*R*)-**4.11**·BF_4: complexes (*S*)-**4.11**·BF_4 and (*R*)-**4.11**·BF_4 was synthesised following GP1 using **4.8** (98.9 mg, 0.2 mmol), $AgBF_4$ (28.9 mg, 0.2 mmol, 1 equiv.), (*S*)-**4.2** or (*R*)-**4.2** (50.4 mg, 0.2 mmol, 1 equiv.) in CH_2Cl_2 (1 mL). The reaction was stirred for 10 min at r.t. The mixture was concentrated, and the product precipitated to obtain (*S*)-**4.11**·BF_4 and (*R*)-**4.11**·BF_4 as colourless solids in 99% yield (198.0 mg, 0.198 mmol). ^1H NMR (300 MHz, $CDCl_3$) δ = 7.64 – 7.11 (m, 24H, $HPPh_3$/H_{Ar}ITU), 6.06 (dd, *J* = 10.7, 8.7 Hz, 1H, CHPh), 4.96 (t, *J* = 10.5 Hz, 1H, CH_{2cis}), 4.14 (t, *J* = 9.5 Hz, 1H, CH_{2trans}). $^{13}C\{^1H\}$ NMR (126 MHz, $CDCl_3$) δ = 171.8 (C=N), 141.0 (Cq), 135.7 (Cq), 134.1 (C_{Ar}), 134.0 (C_{Ar}), 132.6 (C_{Ar}), 129.7 (C_{Ar}), 129.6 (C_{Ar}), 129.4 (C_{Ar}), 129.0 (C_{Ar}), 128.3 (C_{Ar}), 127.6 (C_{Ar}), 127.5 (C_{Ar}), 125.9 (Cq), 124.1 (C_{Ar}), 123.9 (C_{Ar}), 111.6 (C_{Ar}ITU), 74.4 (CHPh), 52.9 (CH_2). $^{19}F\{^1H\}$ NMR (282 MHz, $CDCl_3$) δ = -153.31, -153.36. $^{31}P\{^1H\}$ NMR (121 MHz, $CDCl_3$) δ = 31.36. FTIR (ATR) ν = 1597, 1570 (C=N) cm^{-1}.

[Au(PPh_3){(*S*)-BTM}][BF_4] $[\alpha]_D^{20}$ -5.8°(c = 0.1, $CHCl_3$) elemental analysis calcd (%): C 49.69; H 3.41; N 3.51; found C 49.37; H 3.19; N 3.39.

[Au(PPh_3){(*R*)-BTM}][BF_4] $[\alpha]_D^{20}$ +5.0°(c = 0.1, $CHCl_3$) elemental analysis calcd (%): C 49.69; H 3.41; N 3.51; found C 49.39; H 3.21; N 3.41.

[Au(PPh_3){(2*S*,3*R*)-HyperBTM}][NTf_2] (2*S*,3*R*)-**4.12**·NTf_2 and [Au(PPh_3){(2*R*,3*S*)-HyperBTM}][NTf_2] (2*R*,3*S*)-**4.12**·NTf_2: complexes (2*S*,3*R*)-**4.12**·BF_4 and (2*R*,3*S*)-**4.12**·NTf_2were synthesised following GP1 using **4.8** (124.2 mg, 0.2 mmol), $AgNTf_2$ (77.6 mg, 0.2 mmol, 1 equiv.), (*2S*,3*R*)-**4.4** or (2*R*,3*S*)-**4.4** (61.7 mg, 0.2 mmol, 1 equiv.) in CH_2Cl_2 (1 mL). The reaction was stirred for 10 min at r.t. The mixture was concentrated,

and the product precipitated to obtain (2*S*,3*R*)-**4.12**·BF_4 and (2*R*,3*S*)-**4.12**·NTf_2 as colourless solids in 93% (194.9 mg) and 95% yield (199.1 mg). ^{1}H NMR (500 MHz, $CDCl_3$) δ = 7.61 – 7.52 (m, 4H), 7.48 (dp, *J* = 8.1, 3.0 Hz, 7H), 7.45 – 7.37 (m, 3H), 7.36 – 7.27 (m, 6H), 5.18 – 5.06 (m, 1H), 4.20 (ddd, *J* = 12.5, 5.2, 1.6 Hz, 1H), 3.64 (t, *J* = 11.9 Hz, 1H), 2.29 (dd, *J* = 10.4, 5.8 Hz, 1H), 1.63 (s, 5H), 1.44 – 1.36 (m, 1H), 1.16 (d, *J* = 6.5 Hz, 3H), 0.91 (d, *J* = 6.7 Hz, 3H). ^{13}C{^{1}H} NMR (101 MHz, $CDCl_3$) δ = 166.8 (C=N, assigned *via* 2D ^{1}H,^{13}C-gs-HMBC) 139.8 (Cq), 139.2 (Cq), 134.2 (C_{Ar}), 134.0 (C_{Ar}), 132.7 (C_{Ar}), 129.8 (C_{Ar}), 129.7 (C_{Ar}), 129.3 (C_{Ar}), 128.8 (C_{Ar}), 128.1 (C_{Ar}ITU), 127.9 (C_{Ar}), 127.5 (C_{Ar}), 126.9 (C_{Ar}), 125.0 (C_{Ar}), 122.6 (C_{Ar}), 121.1 (C_{Ar}), 110.9 (C_{Ar}ITU), 42.3 (CH_2), 41.1 ($CH(CH_3)_2$), 27.2 ($CH(CH(CH_3)_2)$), 21.9 ($CH(CH_3)_2$), 19.8 ($CH(CH_3)_2$). ^{19}F{^{1}H} NMR (470 MHz, $CDCl_3$) δ = -78.65. ^{31}P{^{1}H} NMR (202 MHz, $CDCl_3$) δ = 30.17. FTIR (ATR) ν = 1568, 1568 (C=N) cm^{-1}. The compound failed elemental analysis after several attempts.

[Au(PPh_3){(2*S*,3*R*)-HyperBTM}][NTf_2] $[\alpha]_D^{20}$ +9.5° (c = 0.1, $CHCl_3$).

[Au(PPh_3){(2*R*,3*S*)-HyperBTM}][NTf_2] $[\alpha]_D^{20}$ -9.6° (c = 0.1, $CHCl_3$).

[Au(PPh_3){(2*S*,3*R*)-HyperBTM}][BF_4] ((2*S*,3*R*)-**4.12**·BF_4) and [Au(PPh_3){(2*R*,3*S*)-HyperBTM}][BF_4] ((2*R*,3*S*)-**4.12**·BF_4): complexes (2*S*,3*R*)-**4.12**·BF_4 and (2*R*,3*S*)-**4.12**·BF_4were synthesised following GP1 using **4.8** (124.2 mg, 0.2 mmol), $AgBF_4$ (28.9 mg, 0.2 mmol, 1 equiv.), (*2S*,3*R*)-**4.4** or (2*R*,3*S*)-**4.4** (61.7 mg, 0.2 mmol, 1 equiv.) in CH_2Cl_2 (1 mL). The reaction was stirred for 10 min at r.t. The mixture was concentrated, and the product precipitated to obtain (2*S*,3*R*)-**4.12**·BF_4 and (2*R*,3*S*)-**4.12**·BF_4 as colourless solids in 89% (152.0 mg) and >99% yield (169.2 mg). ^{1}H NMR (400 MHz, $CDCl_3$) δ = 7.65 – 7.54 (m, 4H, H_{Ar}), 7.54 – 7.43 (m, 7H, H_{Ar}), 7.41 (dd, *J* = 5.0, 1.9, 3H, H_{Ar}), 7.31 (dddd, *J* = 14.1, 7.1, 3.9, 1.9, 10H, H_{Ar}), 5.16 (d, *J* = 4.6, 1H, CHPh), 4.26 (ddd, *J* = 12.7, 5.2, 1.6, 1H, CH_{2cis}), 3.69 (dd, *J* = 12.6, 11.2, 1H, CH_{2trans}), 2.31 (ddt, *J* = 11.1, 8.5, 4.9, 1H, CH*i*Pr), 1.50 – 1.36 (m, 1H, $CH(CH(CH_3)_2)$), 1.14 (d, *J* = 6.5, 3H, $CH(CH_3)_2$), 0.91 (d, *J* = 6.7 Hz, 3H, $CH(CH_3)_2$). ^{13}C{^{1}H} NMR (101 MHz, $CDCl_3$) δ = 168.0 (C=N), 139.8 (Cq), 139.3 (Cq), 134.0 (C_{Ar}), 133.9 (C_{Ar}), 132.6 (C_{Ar}), 132.6 (C_{Ar}), 129.7 (C_{Ar}), 129.6 (C_{Ar}), 129.2 (C_{Ar}), 128.7 (C_{Ar}), 128.1 (C_{Ar}), 127.9 (C_{Ar}), 127.4 (C_{Ar}), 126.8 (C_{Ar}), 125.0 (C_{Ar}), 122.7 (C_{Ar}), 120.6 (Cq), 111.1 (C_{Ar}), 64.7 (CHPh), 42.1 (CH_2),

41.0 (CH*i*Pr), 27.1 (CH(CH(CH_3)$_2$), 22.3 (CH(CH_3)$_2$), 19.6 (CH(CH_3)$_2$). $^{19}F\{^1H\}$ NMR (377 MHz, $CDCl_3$) δ = -153.50, -153.55. $^{31}P\{^1H\}$ NMR (162 MHz, $CDCl_3$) δ = 30.15. FTIR (ATR) ν = 1599, 1570 (C=N) cm^{-1}.

[Au(PPh_3){(2*S*,3*R*)-HyperBTM}][BF_4] $[\alpha]_D^{20}$ +11.2°(c = 0.1, $CHCl_3$) elemental analysis calcd (%):C 52.01; H 4.13; N 3.28; found: C 52.16; H 4.22; N 3.24.

[Au(PPh_3){(2*R*,3*S*)-HyperBTM}][BF_4] $[\alpha]_D^{20}$ -10.2°(c = 0.1, $CHCl_3$) elemental analysis calcd (%): C 52.01; H 4.13; N 3.28; found: C 52.25; H 4.21; N 3.29.

[Au(IPr^{Cl}){(*S*)-BTM}][NTf_2] ((*S*)-**4.17**·NTf_2): complex (*S*)-**4.17**·NTf_2 was synthesised following GP2 using **4.16** (187.1 mg, 0.15 mmol), (*S*)-**4.2** (37.8 mg, 0.15 mmol, 1 equiv.) in CH_2Cl_2 (1.5 mL). The reaction was stirred for 10 min at r.t. The mixture was concentrated, and the product precipitated to obtain (*S*)-**4.17**·NTf_2 and as colourless solids in 96% (227.9 mg). ^1H NMR (400 MHz, $CDCl_3$) δ = 7.63 (t, *J* = 7.8 Hz, 2H, $H_{Ar}IPr^{Cl}$), 7.44 (dd, *J* = 8.1, 1.1 Hz, 1H), 7.37 – 7.30 (m, 4H), 7.27 – 7.21 (m, 1H), 7.16 (t, *J* = 7.6 Hz, 3H), 6.95 (t, *J* = 8.3 Hz, 3H, H_{Ar}ITU), 5.37 (dd, *J* = 10.8, 8.3 Hz, 1H, CHPh), 4.59 (t, *J* = 10.6 Hz, 1H, CH_{2cis}), 3.87 – 3.77 (m, 1H, CH_{2trans}), 2.48 – 2.08 (m, 4H, CH*i*Pr), 1.25 (dd, *J* = 6.9, 2.0 Hz, 12H, CH_3*i*Pr), 1.18 (d, *J* = 6.9 Hz, 6H, CH_3*i*Pr), 1.12 (d, *J* = 6.9 Hz, 6H, CH_3*i*Pr). $^{13}C\{^1H\}$ NMR (126 MHz, $CDCl_3$) δ = 172.3 (C=N), 171.8 ($C_{carbene}$), 146.1 (Cq), 139.8 (Cq), 135.4 (Cq), 132.2 ($C_{Ar}IPr^{Cl}$), 130.5 (Cq), 129.3 (C_{Ar}), 128.9 (C_{Ar}), 128.4 (C_{Ar}), 126.4 (C_{Ar}ITU), 125.2 (C_{Ar}), 125.0 (C_{Ar}), 124.9 (C_{Ar}), 124.3 (C_{Ar}), 123.7 (C_{Ar}), 121.3 (C_{Ar}), 119.9 (C_{Ar}), 118.8 (C_{Ar}), 111.4 (C_{Ar}ITU), 74.3 (CHPh), 52.9 (CH_2), 29.3 (CH*i*Pr), 24.6 (CH(CH_3)$_2$), 23.6 (CH(CH_3)$_2$), 23.5 (CH(CH_3)$_2$); ^{19}F NMR (377 MHz, $CDCl_3$) δ = -78.71; FTIR (ATR) ν = 1568 (C=N) cm^{-1}.

[Au(*S*-BTM))(IPr^{Cl})][NTf_2] $[\alpha]_D^{20}$ -4.0°(c = 0.1, $CHCl_3$) elemental analysis calcd (%): C 44.49; H 3.99; N 5.90; found: C 44.32; H 3.99; N 5.82.

[Au(IPr^{Cl}){(2*S*,3*R*)-HyperBTM}][NTf_2] ((2*S*,3*R*)-**4.18**·NTf_2): Complex (2*S*,3*R*)-**4.18**·NTf_2 was synthesised following GP2 using **4.16** (187.1 mg, 0.15 mmol), (*2S*,3*R*)-**4.4** (46.2 mg, 0.15 mmol, 1 equiv.) in CH_2Cl_2 (1.5 mL). The reaction was stirred for 10 min at r.t. The mixture was concentrated, and the product precipitated to obtain (2*S*,3*R*)-**4.18**·NTf_2 as colourless solid in 99% (174.4 mg). ^1H NMR (400 MHz, $CDCl_3$) δ = 7.69

(t, *J* = 7.8 Hz, 2H, H_{Ar}), 7.49 – 7.30 (m, 6H, H_{Ar}), 7.33 – 7.10 (m, 6H, H_{Ar}), 6.72 – 6.57 (m, 2H, H_{Ar}), 4.27 (d, *J* = 4.5 Hz, 1H, CHPh), 4.02 – 3.91 (m, 1H, CH_{2cis}), 3.33 (t, *J* = 12.4 Hz, 1H, CH_{2trans}), 2.30 (dp, *J* = 25.0, 6.8 Hz, 4H, CH*i*Pr), 1.98 (ddt, *J* = 13.5, 9.3, 4.9 Hz, 1H, $CH(CH_3)_2$), 1.36 – 1.15 (m, 9H, CH_3*i*Pr/$CH(CH(CH_3)_2)$), 0.99 (dd, *J* = 6.7, 3.2 Hz, 4H CH_3*i*Pr/$CH(CH_3)_2$), 0.76 (d, *J* = 6.6 Hz, 3H, $CH(CH_3)_2$). $^{13}C\{^1H\}$ NMR (126 MHz, $CDCl_3$) δ = 170.7 ($C_{carbene}$), 168.1 (C=N), 146.4 (Cq), 139.7 (Cq), 137.8 (Cq), 132.0 (C_{Ar}), 130.9 (C_{Ar}), 129.1 (C_{Ar}), 128.6 (C_{Ar}), 127.9 (C_{Ar}), 127.3 (C_{Ar}), 125.0 (C_{Ar}), 125.0 (C_{Ar}), 124.9 (C_{Ar}), 122.3 (C_{Ar}), 121.4 (Cq), 120.6 (C_{Ar}), 120.0 (C_{Ar}), 118.8 (Cq), 110.9 (C_{Ar}), 64.9 (CHPh), 41.6 (CH_2), 41.1 ($CH(CH_3)_2$), 29.3 (CH*i*Pr), 26.8 ($CH(CH(CH_3)_2$), 24.7 (CH_3*i*Pr), 24.4 (CH_3*i*Pr), 23.7 (CH_3*i*Pr), 23.6 (CH_3*i*Pr), 21.6 ($CH(CH_3)_2$), 19.6 ($CH(CH_3)_2$). $^{19}F\{^1H\}$ NMR (377 MHz, $CDCl_3$) δ = -78.67. FTIR (ATR) ν = 1575, 1560 (C=N) cm^{-1}.

[Au(2*S*,3*R*-HyperBTM))(IPr^{Cl})][NTf_2] $[\alpha]_D^{20}$ +8.6° (c = 0.1, $CHCl_3$) elemental analysis calcd (%): C 46.34; H 4.46; N 5.63; found: C 46.25; H 4.48; N 5.51.

[Au(SIPr){(*S*)-BTM}][NTf_2] ((*S*)-**4.21**·NTf_2) and (*S*)-**4.2**·HCl: Complex (*S*)-**4.22**·NTf_2 was synthesised following GP2 using **4.20** (107.5 mg, 0.15 mmol), (*S*)-**4.2** (45.4 mg, 0.18 mmol, 1.2 equiv.) in CH_2Cl_2 (1.5 mL). The reaction was stirred for 10 min at r.t. The mixture was concentrated, and the product precipitated to obtain a mixture (207 mg recovered) of (*S*)-**4.21**·NTf_2 and (*S*)-**4.2**·HCl as colourless solids. ^1H NMR (500 MHz, $CDCl_3$) δ = 9.18 (s, 1H, N-H ITU salt), 7.63 (dd, *J* = 8.1, 1.0 Hz, 1H, Ar), 7.50 (ddd, *J* = 8.4, 7.5, 1.1 Hz, 1H, Ar), 7.45 (t, *J* = 7.8 Hz, 2H, Ar), 7.43 – 7.29 (m, 10H, Ar), 7.24 – 7.17 (m, 6H, Ar), 7.16 – 7.10 (m, 3H, Ar), 6.97 (dd, *J* = 8.1, 1.1 Hz, 1H, Ar), 6.88 – 6.83 (m, 2H, Ar), 6.00 – 5.91 (m, 1H, CHPh ITU salt), 5.24 (dd, *J* = 10.8, 8.2 Hz, 1H, CHPh ITU), 5.10 (t, *J* = 10.9 Hz, 1H, CH_2 ITU salt), 4.51 (t, *J* = 10.6 Hz, 1H, CH_2 ITU), 4.30 (dd, *J* = 11.0, 8.3 Hz, 1H, CH_2 ITU salt), 4.14 (s, 4H, CH_2 backbone), 4.06 (s, 1H, CH_2 backbone unknown), 3.82 (dd, *J* = 10.4, 8.2 Hz, 1H, CH_2 ITU), 3.05 (p, *J* = 6.9 Hz, 1H, unknown CH*i*Pr), 2.93 (dp, *J* = 8.6, 6.8 Hz, 4H, CH*i*Pr), 1.40 (dd, *J* = 6.8, 1.6 Hz, 2H), 1.35 – 1.27 (m, 17H), 1.27 – 1.23 (m, 11H), 1.13 (d, *J* = 6.9 Hz, 6H). $^{13}C\{^1H\}$ NMR (126 MHz, $CDCl_3$) δ = 193.3 ($C_{carbene}$), 172.2 (ITU), 169.9(ITU salt), 146.7 (Cq), 139.6 (Cq), 137.0 (Cq), 135.4 (Cq),134.1 (Cq), 133.5 (Cq), 130.3 (C_{Ar}), 130.1 (C_{Ar}), 129.5 (C_{Ar}), 129.5 (C_{Ar}), 129.3 (C_{Ar}), 128.9 (C_{Ar}),128.8 (C_{Ar}),128.4 (C_{Ar}),127.4 (C_{Ar}),126.4

(C_{Ar}),126.3 (C_{Ar}),125.8 (C_{Ar}),125.4 (C_{Ar}), 124.7 (C_{Ar}),124.7 (C_{Ar}),124.2 (C_{Ar}), 124.0 (C_{Ar}), 123.7 (C_{Ar}), 113.1 (C_{Ar}), 111.4 (C_{Ar}), 74.2 (CHPh ITU), 66.9 (CHPh ITU salt), 53.9 ($CH_{2\ backbone}$), 53.6 (unknown $CH_{2\ backbone}$), 53.3 (CH_2 ITU salt), 52.7 (CH_2 ITU), 34.2, 28.9 (CH*i*Pr), 25.3, 24.2, 24.0, 22.5, 14.2.$^{19}F\{^1H\}$ NMR (471 MHz, $CDCl_3$) δ = -151.75, -151.70, -149.75, -149.69, -149.33, -149.26, -149.19. FTIR (ATR) ν = 2962, 1598, 1577 (C=N), 1492, 1460 cm^{-1}.

[Au(SIPr){(2*S*,3*R*)-HyperBTM}][NTf_2] ((2*S*,3*R*)-**4.22**·NTf_2) and (2*S*,3*R*)-**4.4**·HCl: complex (2*S*,3*R*)-**4.22**·NTf_2 was synthesised following GP2 using **4.20** (107.46 mg, 0.15 mmol), (*2S*,3*R*)-**4.4** (55.53 mg, 0.3 mmol, 1.2 equiv.) in THF (1.5 mL). The reaction was stirred for 10 min at r.t. The mixture was concentrated, and the product precipitated to obtain a mixture (200 mg recovered) of (2*S*,3*R*)-**4.22**·NTf_2 and (2*S*,3*R*)-**4.4**·HCl as colourless solids: ^1H NMR (500 MHz, $CDCl_3$) δ = 9.59 (d, *J* = 4.8 Hz, 1H, N-H ITU), 7.68 – 7.56 (m, 3H, H_{Ar}), 7.50 (t, *J* = 7.8 Hz, 2H, H_{Ar}), 7.43 (ddd, *J* = 8.3, 6.6, 1.9 Hz, 1H, H_{Ar}), 7.41 – 7.27 (m, 6H, H_{Ar}), 7.25 – 7.14 (m, 5H, H_{Ar}), 7.12 – 7.03 (m, 3H, H_{Ar}), 6.62 – 6.51 (m, 2H, H_{Ar}), 5.13 (td, *J* = 4.7, 1.4 Hz, 1H, CHPh ITU salt), 4.44 (ddd, *J* = 13.1, 5.0, 1.5 Hz, 1H, CH_2), 4.19 (s, 4H, SIPr CH_2 backbone), 4.16 (dd, *J* = 4.7, 1.5 Hz, 1H, CHPh ITU), 4.06 (s, 1H, unknown Au species), 3.94 – 3.90 (m, 1H, ITU CH_2), 3.80 (dd, *J* = 13.1, 11.9 Hz, 1H, CH_2 ITU salt), 3.30 (t, *J* = 12.4 Hz, 1H, CH_2 ITU), 2.94 (dp, *J* = 25.4, 6.8 Hz, 3H, CH*i*Pr Au species), 2.23 (ddt, *J* = 11.9, 9.5, 4.7 Hz, 1H, $CH(CH_3)_2$ ITU), 1.89 (ddt, *J* = 12.3, 9.5, 4.8 Hz, 1H, $CH(CH_3)_2$ ITU salt), 1.44 – 1.18 (m, 30H), 1.14 (d, *J* = 6.5 Hz, 3H), 1.02 – 0.95 (m, 6H), 0.95 – 0.84 (m, 10H), 0.75 (d, *J* = 6.7 Hz, 3H). $^{13}C\{^1H\}$ NMR (126 MHz, $CDCl_3$) δ = 14.18, 19.70, 21.49, 21.67, 22.45, 24.08, 24.18, 24.33, 24.77, 25.17, 25.26, 26.57, 26.79, 28.92 (CH*i*Pr), 29.00, 34.22, 40.73 ($CH(CH_3)_2$ ITU salt), 41.14 ($CH(CH_3)_2$ ITU), 41.66 (ITU CH_2), 43.37 (ITU salt CH_2), 53.96 ($CH_{2\ backbone}$), 57.04 (CHPh ITU salt), 64.61 (CHPh ITU), 110.65 (C_{Ar}), 113.01 (C_{Ar}), 120.95 (C_{Ar}), 122.19 (C_{Ar}), 122.28 (C_{Ar}), 122.98 (C_{Ar}), 124.59 (C_{Ar}), 124.65 (C_{Ar}), 124.79 (C_{Ar}), 126.44 (C_{Ar}), 127.29 (C_{Ar}), 127.36 (C_{Ar}), 127.74 (C_{Ar}), 128.49 (C_{Ar}), 128.73 (C_{Ar}), 128.96 (C_{Ar}), 129.16 (C_{Ar}), 129.32 (C_{Ar}), 130.00 (C_{Ar}), 134.02 (Cq), 135.89 (Cq), 137.69 (Cq), 138.09 (Cq), 139.69 (Cq), 146.64 (Cq), 147.11 (Cq), 164.26 (ITU salt), 167.96 (ITU), 192.49 ($C_{carbene}$). $^{19}F\{^1H\}$ NMR (471 MHz, $CDCl_3$) δ = -152.14, -152.09, -149.78, -149.57, -149.26. FTIR (ATR) ν = 2960.7, 1614.4, 1589.9, 1577.8 (C=N), 1506, 1462 cm^{-1}.

4.5.2. General procedure for synthesis of neutral Au(I) complexes

GP3: [AuCl(SMe$_2$)] **4.24** (0.5 mmol) and ITU ((*S*)-**4.2**, (*R*)-**4.2**, (2*S*,3*R*)-**4.4**, (2*S*,3*R*)-**4.4**, **4.3**, 1 equiv.) were dissolved in THF (0.1 M) and stirred at 60 °C for 1-16h. The solvent was removed under vacuum and the resulting solid dissolved in CH_2Cl_2 (2-3 mL). The solution was concentrated (~ 1 mL) and the product precipitated by addition of pentane (~ 10 mL). The precipitate was collected by filtration, washed with pentane (3×5 mL) and dried under vacuum, affording the corresponding complexes as colourless solids in good to excellent yields.

[AuCl{(*S*)-BTM}] ((*S*)-**4.25**) and [AuCl{(*R*)-BTM}] ((*R*)-**4.25**): omplexes (*S*)-**4.25** and (*R*)-**4.25** were synthesised following GP3 using **4.24** (147.3 mg, 0.5 mmol), (*S*)-**4.2** or (*R*)-**4.2** (126.2 mg, 0.5 mmol, 1 equiv.) in THF (5 mL, 0.1 M). The reaction was stirred for 1 h at 60 °C. The mixture was concentrated, and the product precipitated to obtain (*S*)-**4.25** and (*R*)-**4.25** as colourless solids in > 99% (239.9 mg). ^{1}H NMR (400 MHz, $CDCl_3$) δ = 7.51 (dd, *J* = 8.0, 1.1, 1H, H_{Ar}), 7.44 – 7.34 (m, 6H, H_{Ar}), 7.21 (td, *J* = 7.8, 1.1, 1H, H_{Ar}), 6.92 (dd, *J* = 8.0, 1.1, 1H, H_{Ar}), 5.74 (dd, *J* = 10.7, 7.9, 1H, CHPh), 4.54 (t, *J* = 10.2, 1H, CH_{2cis}) 4.02 (dd, *J* = 9.7, 7.9, 1H, CH_{2trans}). ^{13}C{^{1}H} NMR (126 MHz, $CDCl_3$) δ = 139.8 (C=N), 135.9 (Cq), 129.3 (C_{Ar}), 129.1 (C_{Ar}), 127.9 (C_{Ar}), 126.6 (C_{Ar}), 125.8 (Cq), 123.9 (C_{Ar}), 123.8 (C_{Ar}), 110.3 (C_{Ar}), 75.1 (CHPh), 52.5 (CH_2). FTIR (ATR) ν = 1564 (C=N) cm^{-1}.

[AuCl{(*S*)-BTM}] $[\alpha]_D^{20}$ -7.9°(c = 0.1, $CHCl_3$) elemental analysis calcd (%): C 37.17; H 2.50; N 5.78; found: C 35.53; H 2.35; N 5.54.

[AuCl{(*R*)-BTM}] $[\alpha]_D^{20}$ +17.0°(c = 0.1, $CHCl_3$) elemental analysis calcd (%):C 37.17; H 2.50; N 5.78; found: C 35.60; H 3.51; N 5.63.

[AuCl{(2*S*,3*R*)-HyperBTM}] ((2*S*,3*R*)-**4.26**), [AuCl{(2*R*,3*S*)-HyperBTM}] ((2*R*,3*S*)-**4.26**) and [AuCl(HyperBTM)] ((±)-**4.26**): complexes (2*R*,3*S*)-**4.26**, (2*R*,3*S*)-**4.26**, and (±)-**4.26** were synthesised following GP3 using **4.24** (147.27 mg, 0.5 mmol), (2*S*,3*R*)-**4.4** or (2*R*,3*S*)-**4.4** (154.2 mg, 0.5 mmol, 1 equiv.) in THF (5 mL, 0.1 M). The reaction was stirred for 1 h at 60 °C. The mixture was concentrated, and the product precipitated to obtain (2*R*,3*S*)-**4.26**, (2*R*,3*S*)-**4.26** and (±)-**4.26** as colourless solids in > 99% (269.5 mg).

^{1}H NMR (500 MHz, $CDCl_3$) δ = 7.48 (dd, *J* = 7.9, 1.2, 1H, H_{Ar}), 7.40 (td, *J* = 7.8, 1.2, 1H, H_{Ar}), 7.34 (dd, *J* = 5.2, 2.0, 3H, H_{Ar}), 7.26 (s, 5H, H_{Ar}), 7.10 (dd, *J* = 7.2, 2.4, 2H, H_{Ar}), 7.07 – 7.04 (m, 1H, H_{Ar}), 5.09 (dd, *J* = 4.3, 1.7, 1H, CHPh), 3.97 (ddd, *J* = 12.1, 4.9, 1.6, 2H, CH_2), 3.47 – 3.38 (m, 2H CH_2, CH), 2.14 (ddd, *J* = 17.3, 9.1, 4.3, 1H, CH), 1.19 (d, *J* = 6.4, 3H, CH_3), 0.89 (d, *J* = 6.7, 3H, CH_3). ^{13}C{^{1}H} NMR (126 MHz, $CDCl_3$) δ = 140.4 (C=N), 137.4 (Cq), 128.9 (Cq), 128.5 (C_{Ar}), 127.7 (C_{Ar}), 127.1 (Cq), 124.3 (C_{Ar}), 122.4 (C_{Ar}), 121.4 (C_{Ar}), 109.9 (C_{Ar}), 109.8 (C_{Ar}), 66.1 (CHPh), 41.8 (CH), 41.6 ($CH(CH_3)_2$), 26.9 (CH_2), 21.7 (CH_3), 20.0 (CH_3). FTIR (ATR) ν = 1575 (C=N) cm^{-1}.

[AuCl{(2*S*,3*R*)-HyperBTM}] $[\alpha]_D^{20}$ +18.1°(c = 0.1, $CHCl_3$) elemental analysis calcd (%):C 42.19; H 3.73; N 5.18; found: C 42.17; H 3.76; N 5.26.

[AuCl{(2*R*,3*S*)-HyperBTM}] $[\alpha]_D^{20}$ -14.9°(c = 0.1, $CHCl_3$) elemental analysis calcd (%): C 42.19; H 3.73; N 5.18; found: C 42.15; H 3.71; N 5.22.

[AuCl(DHPB)] (**4.27**): complex **4.27** were synthesised following GP3 using **4.24** (147.3 mg, 0.5 mmol), **4.3** (95.3 mg, 0.5 mmol, 1 equiv.) in THF (7 mL, 0.01 M), with K_2CO_3 (69.3 mg, 0.5 mmol, 1 equiv.). The reaction was stirred for 16 h at 60 °C. The mixture was concentrated, and the product precipitated to obtain **4.27** as colourless solids in 85% conversions measured by ^{1}H NMR (158.5 mg of off-white solid was recovered). Due to the highly insoluble nature of the compound (not soluble in the most common deuterated NMR solvent, neither DMSO, D_2O), its characterization was not possible in solution (one ^{1}H NMR spectra could be obtained in low resolution). The characterization of the complex was based on elemental analysis, FTIR (ATR), NIR data, and UV-vis spectra. Its structure was fully analysed by X-ray diffraction analysis. The presence of Au-Au aurophilic interactions might decrease the solubility of the complex, as already noticed in the solution behavior of [AuCl(THT)].[71] ^{1}H NMR (400 MHz, $CDCl_3$) δ = 7.42 (d, *J* = 8.1 Hz, 1H, H_{Ar}), 7.39 – 7.32 (m, 1H, H_{Ar}), 7.21 (td, *J* = 7.7, 1.0 Hz, 1H, H_{Ar}), 6.99 (d, *J* = 8.1 Hz, 1H, H_{Ar}), 3.90 (t, *J* = 6.1 Hz, 2H, N^1-CH_2), 3.87 – 3.80 (m, 2H, N^2-CH_2), 2.21 (p, *J* = 5.9 Hz, 2H, CH_2). FTIR (ATR) ν = 1575 (C=N) cm^{-1}. Elemental analysis calcd (%): C 28.42; H 2.38; N 6.63; found: C 28.37; H 2.31; N 6.60.

4.5.3. General procedure for synthesis of neutral Au(III) ITU complexes

GP4: [AuCl(ITU)] (0.16 mmol) and $PhI(Cl)_2$ (1.2 equiv.) were dissolved in CH_2Cl_2 (0.08 M) and stirred at r.t. for 16h. The solvent was removed under vacuum and the resulting solid dissolved in CH_2Cl_2 (2-3 mL). The solution was concentrated (~1 mL) and the product precipitated by addition of pentane (~10 mL). The precipitate was collected by filtration, washed with pentane (3×5 mL) and dried under vacuum, affording the corresponding complexes as purple and magenta solids in good to excellent yields.

[$AuCl_3${(*S*)-BTM}] ((*S*)-**4.28**) and [$AuCl_3${(*R*)-BTM}] ((*R*)-**4.28**): complexes (*S*)-**4.28** and (*R*)-**4.28** were synthesised following GP4 using (*S*)-**4.25** or (*R*)-**4.25** (77.5 mg, 0.16 mmol), $PhICl_2$ (52.8 mg, 0.192 mmol, 1.2 equiv.) in CH_2Cl_2 (2 mL, 0.08 M). The reaction was stirred for 1 h at r.t. The mixture was concentrated, and the product precipitated to obtain (*S*)-**4.25** and (*R*)-**4.25** as purple solids in >99% (88.1 mg). ^{1}H NMR (300 MHz, $CDCl_3$) δ = 7.62 (d, *J* = 7.9, 1H, H_{Ar}), 7.53 – 7.42 (m, 7H, H_{Ar}), 7.33 (dd, *J* = 7.8, 1.2, 1H, H_{Ar}), 7.07 (d, *J* = 7.8, 1H, H_{Ar}), 6.36 (dd, *J* = 11.0, 8.3, 1H, CHPh), 4.70 (dd, *J* = 11.0, 9.9, 1H, CH_{2trans}), 4.16 (dd, *J* = 9.9, 8.3, 1H, CH_{2cis}). ^{13}C{^{1}H} NMR (101 MHz, $CDCl_3$) δ = 138.2 (C=N), 129.9 (Cq), 129.8 (Cq), 128.7 (C_{Ar}), 128.4 (C_{Ar}), 127.6 (C_{Ar}), 127.5 (C_{Ar}), 125.1 (C_{Ar}), 123.9 (C_{Ar}), 123.8 (C_{Ar}), 111.7 (C_{Ar}), 111.1 (C_{Ar}), 73.4 (CHPh), 52.5 (CH_2). FTIR (ATR) ν = 1570(C=N) cm^{-1}.

[$AuCl_3${(*S*)-BTM}] $[\alpha]_D^{20}$ -16.87° (c = $4\cdot10^{-2}$, $CHCl_3$) elemental analysis calcd (%): C 32.42; H 2.18; N 5.04; found: C 32.36; H 2.07; N 5.17.

[$AuCl_3${(*R*)-BTM}] $[\alpha]_D^{20}$ +15° (c = $4\cdot10^{-2}$, $CHCl_3$) elemental analysis calcd (%): C 32.42; H 2.18; N 5.04; found: C 32.28; H 2.07; N 4.98.

[$AuCl_3${(2*S*,3*R*)-HyperBTM}] ((2*S*,3*R*)-**4.29**) and [$AuCl_3${(2*R*,3*S*)-HyperBTM}] ((2*R*,3*S*)-**4.29**): complexes (2*S*,3*R*)-**4.29** and (2*R*,3*S*)-**4.29** were synthesised following GP4 using (2*S*,3*R*)-**4.26** and (2*R*,3*S*)-**4.26** (86.4 mg, 0.16 mmol), $PhICl_2$ (52.8 mg, 0.192 mmol, 1.2 equiv.) in CH_2Cl_2 (2 mL, 0.08 M). The reaction was stirred for 1 h at r.t. The mixture was concentrated, and the product precipitated to obtain (2*S*,3*R*)-**4.29**, (2*R*,3*S*)-**4.29** as magenta solids in 96% (93.9 mg) and 98% (95.9 mg). ^{1}H NMR (500 MHz, $CDCl_3$) δ = 7.61 (dd, *J* = 7.9, 1.2 Hz, 1H, H_{Ar}), 7.50 (ddd, *J* = 8.2, 7.6, 1.2 Hz, 1H, H_{Ar}), 7.40 –

7.32 (m, 5H, H_{Ar}), 7.23 – 7.16 (m, 4H, H_{Ar}), 5.32 (dd, *J* = 4.4, 1.5 Hz, 1H, H_{Ar}), 4.17 (ddd, *J* = 12.3, 4.9, 1.6 Hz, 1H, CHPh), 3.66 (t, *J* = 12.4 Hz, 1H, CH_2), 2.41 – 2.32 (m, 2H, CH_2, CH), 1.40 (dp, *J* = 9.4, 6.5 Hz, 1H, CH), 1.24 (d, *J* = 6.5 Hz, 3H, CH_3), 0.90 (d, *J* = 6.7 Hz, 4H, CH_3). $^{13}C\{^1H\}$ NMR (101 MHz, $CDCl_3$) δ = 139.5 (C=N), 137.6 (Cq), 135.0 (Cq), 130.4 (C_{Ar}), 129.2 (C_{Ar}), 129.0 (C_{Ar}), 128.5 (C_{Ar}), 127.9 (C_{Ar}), 127.8 (C_{Ar}), 125.5 (C_{Ar}), 122.7 (C_{Ar}), 121.8 (C_{Ar}), 111.0 (C_{Ar}), 66.7 (CHPh), 43.7 (CH_2), 42.5 ($CH(CH_3)_2$), 27.2 (CH), 21.8 (CH_3), 20.1 (CH_3). FTIR (ATR) ν = 1573 (C=N) cm^{-1}.

[$AuCl_3$\{(2*S*,3*R*)-HyperBTM\}] $[\alpha]_D^{20}$ -16.87° (c = $4 \cdot 10^{-2}$, $CHCl_3$) elemental analysis calcd (%): C 37.30; H 3.30; N 4.58; found: C 37.6; H 3.33; N 4.61.

[$AuCl_3$\{(2*R*,3*S*)-HyperBTM\}] $[\alpha]_D^{20}$ -16.87° (c = $4 \cdot 10^{-2}$, $CHCl_3$) elemental analysis calcd (%): C 37.30; H 3.30; N 4.58; found: C 37.6; H 3.33; N 4.61.

4.5.4. General procedure for the synthesis of Ir(I) ITU complexes

GP5: A benzene solution (0.8 mL) of ITU ((2*S*,3*R*)-**4.4**, **4.3**, 2.4 equiv.) (0.16 mmol, 2.4 equiv.) was added dropwise to a benzene solution (0.5 mL) of $[Ir(COD)Cl]_2$ **4.30** (46.4 mg, 0.07 mmol). The reaction was stirred overnight, and the formation of a yellow precipitate was observed. The solid was collected, washed with pentane (2×5 mL), and dried under vacuum to provide the products as yellow solids.

GP6: A dichloromethane solution (3/4 mL) of [IrCl(ITU)(COD)] (20/30 mg) was placed under 1 atm of CO. The reaction was stirred until a colour change from bright yellow to very pale yellow was observed, ~10 min. The solvent was removed under reduced pressure. Hexane was added, and the collected precipitate was washed with pentane (2×5 mL) and dried under vacuum to give the corresponding product as pale-yellow solids.

[IrCl\{(2*S*,3*R*)-HyperBTM\}(COD)] ((2*S*,3*R*)-**4.31**): complex (2S,3R)-**4.31** was synthesised following GP5 using (2*S*,3*R*)-**4.4** (49.3 mg, 0.16 mmol, 2.4 equiv.), **4.30** (46.4 mg, 0.07 mmol) in C_6H_6 (0.8 + 0.5 mL). The reaction was stirred for 16 h at r.t. The mixture was concentrated, and the product precipitated to obtain (2*S*,3*R*)-**4.31** as yellow solid in 78% (72.9 mg). ^1H NMR (500 MHz, $CDCl_3$) δ = 7.47 (dd, *J* = 7.8, 1.1 Hz, 1H, H_{Ar}), 7.34 – 7.28 (m, 4H, H_{Ar}), 7.19 – 7.12 (m, 3H, H_{Ar}), 6.95 (d, *J* = 8.0 Hz, 1H, H_{Ar}), 5.03 (dd, *J* = 4.4, 1.6 Hz, 1H, CHPh), 4.55 (s, 1H, CH_{cod}), 4.13 (dd, *J* = 14.3, 7.2 Hz, 1H,

CH_{cod}), 3.91 (ddd, *J* = 11.8, 5.2, 1.8 Hz, 1H, CH_2), 3.39 (t, *J* = 12.2 Hz, 1H, CH_2), 3.27 (td, *J* = 7.3, 3.2 Hz, 1H, CH_{cod}), 2.74 (s, 1H, CH_{cod}), 2.33 – 2.16 (m, 3H, CH_{2cod}), 2.11 (td, *J* = 12.6, 11.6, 6.6 Hz, 1H, CH_{2cod}), 1.88 (s, 1H, CH_{2cod}), 1.52 (dd, *J* = 9.3, 5.5 Hz, 1H, CH_{2cod}), 1.38 (d, *J* = 18.1 Hz, 1H, CH_{2cod}), 1.35 – 1.11 (m, 2H, $CHCH(CH_3)_2$/$CH(CH_3)_2$), 0.94 – 0.78 (m, 5H, $CH(CH_3)_2$). $^{13}C\{^1H\}$ NMR (126 MHz, $CDCl_3$) δ = 162.5 (C=N), 140.5 (Cq), 138.9 (Cq), 128.7 (C_{Ar}), 128.4 (C_{Ar}), 128.2 (C_{Ar}), 127.8 (C_{Ar}), 126.5 (C_{Ar}), 123.7 (C_{Ar}), 123.2 (C_{Ar}), 122.1 (C_{Ar}), 108.8 (C_{Ar}), 71.4 (CHPh), 67.0 (CH_{cod}), 64.5(CH_{cod}), 58.6(CH_{cod}), 57.4 (CH_{cod}), 42.2 (CH_{2ITU}), 41.9 ($CH(CH_3)_2$), 32.9(CH_{2cod}), 31.9 (CH_{2cod}), 31.8 (CH_{2cod}), 30.3 (CH_{2cod}), 26.9 (CH), 21.9 (CH_3), 20.1 (CH_3). FTIR (ATR) ν = 1612(C=N) cm^{-1}.

[IrCl{(2*S*,3*R*)-HyperBTM}(COD)] $[\alpha]_D^{20}$ +3.0° (c = $1 \cdot 10^{-3}$, $CHCl_3$) elemental analysis calcd (%): C 51.65; H 5.68; N 4.15; found: C 51.57; H 5.49; N 4.24.

[IrCl(DHPB)(COD)] (**4.32**): complex **4.32** was synthesised following GP5 using **4.3** (33.8 mg, 0.16 mmol, 2.4 equiv.), **4.30** (50 mg, 0.07 mmol) in C_6H_6 (0.8 + 0.5 mL). The reaction was stirred for 16 h at r.t. The mixture was concentrated, and the product precipitated to obtain **4.32** as a yellow solid in 88% (72.3 mg). ^1H NMR (500 MHz, $CDCl_3$) δ = 7.36 (dt, *J* = 7.8, 1.8 Hz, 1H, H_{Ar}), 7.24 (td, *J* = 7.8, 1.3 Hz, 1H, H_{Ar}), 7.08 (t, *J* = 7.7 Hz, 1H, H_{Ar}), 6.85 (d, *J* = 8.0 Hz, 1H, H_{Ar}), 4.37 (s, 2H, CH_{cod}), 3.81 (t, *J* = 6.1 Hz, 2H, N^1-CH_2), 3.64 – 3.53 (m, 2H, N^2-CH_2), 3.49 – 3.39 (m, 2H, CH_{2cod}), 2.26 (td, *J* = 7.1, 3.4 Hz, 4H, CH_{2cod}), 2.12 (p, *J* = 5.9 Hz, 2H, CH_2ITU), 1.63 – 1.52 (m, 2H, CH_{2cod}), 1.44 (q, *J* = 9.6, 6.6 Hz, 2H, CH_{2cod}). $^{13}C\{^1H\}$ NMR (126 MHz, $CDCl_3$) δ = 162.1 (C=N), 140.3 (Cq), 126.4 (C_{Ar}), 123.1 (C_{Ar}), 122.9 (C_{Ar}), 122.6 (Cq), 121.9 (C_{Ar}), 108.4 (C_{Ar}), 69.9 (CH_{cod}), 58.1 (CH_{cod}), 48.1 (N^2-CH_2), 41.7 (N^1-CH_2), 32.3 (CH_{2cod}), 31.4 (CH_{2cod}), 20.3 (CH_2ITU). FTIR (ATR) ν = 1604, 1579 (C=N) cm^{-1}; elemental analysis calcd (%): C 41.09; H 4.22; N 5.32; found: C 40.15; H 4.36; N 5.42.

[IrCl{(2*S*,3*R*)-HyperBTM}$(CO)_2$] ((2*S*,3*R*)-**4.33**): complex (2S,3R)-**4.33** was synthesised following GP6 using (2*S*,3*R*)-**4.31** (25.4 mg, 0.04 mmol), CO (1 atm) in CH_2Cl_2 (3 mL). The reaction was stirred for 1 h at r.t. The mixture was concentrated, and the product precipitated to obtain (2*S*,3*R*)-**4.33** as pale-yellow solid in 99% (20 mg). ^1H NMR (500 MHz, $CDCl_3$) δ = 7.50 (d, *J* = 7.8 Hz, 1H, H_{Ar}), 7.43 – 7.31 (m, 4H, H_{Ar}), 7.24 (d, *J* = 7.7 Hz, 1H, H_{Ar}), 7.16 (dd, *J* = 7.4, 2.1 Hz, 2H, H_{Ar}), 7.07 (d, *J* = 8.1 Hz, 1H, H_{Ar}),

5.17 (dd, *J* = 4.6, 1.7 Hz, 1H, CHPh), 4.01 (ddd, *J* = 12.0, 5.1, 1.8 Hz, 1H, CH_2), 3.49 (t, *J* = 12.3 Hz, 1H, CH_2), 2.29 – 2.16 (m, 1H, $CH(CH_3)_2$), 1.33 (dq, *J* = 9.4, 6.5 Hz, 1H, $CH(CH(CH_3)_2)$), 1.21 (d, *J* = 6.4 Hz, 3H, $CH(CH_3)_2$), 0.87 (d, *J* = 6.7 Hz, 4H, $CH(CH_3)_2$). $^{13}C\{^1H\}$ NMR (126 MHz, $CDCl_3$) δ = 170.8(CO), 167.0 (CO), 166.5 (C=N), 140.1 (Cq), 138.0 (Cq), 129.0 (C_{Ar}), 128.5 (C_{Ar}), 128.2 (C_{Ar}), 128.1 (C_{Ar}), 127.1 (C_{Ar}), 124.1 (C_{Ar}), 122.8 (Cq), 122.3 (C_{Ar}), 109.7 (C_{Ar}), 64.1 (CHPh), 42.1 (CH_2), 42.1 ($CH(CH_3)_2$), 27.2 ($CH(CH(CH_3)_2$), 21.7 ($CH(CH_3)_2$), 20.1 ($CH(CH_3)_2$). FTIR (ATR) ν = 2061 (CO_{sym}), 1980 (CO_{asym}), 1602, 1577 (C=N) cm^{-1}.

[IrCl{(2*S*,3*R*)-HyperBTM}$(CO)_2$] $[\alpha]_D^{20}$ +4.1°(c = $1\cdot10^{-3}$, $CHCl_3$) elemental analysis calcd (%): C 30.41; H 2.13; N 5.91; found: C 30.54; H 2.24; N 5.84.

[IrCl(DHPB)$(CO)_2$] (**4.34**): complex **4.34** was synthesised following GP6 using **4.32** (25 mg, 0.045 mmol), CO (1 atm) in CH_2Cl_2 (3 mL). The reaction was stirred for 1 h at r.t. The mixture was concentrated, and the product precipitated to obtain **4.34** as a pale-yellow solid in 99% (21.1 mg, 0.044 mmol). ^1H NMR (400 MHz, $CDCl_3$) δ = 7.43 (dd, *J* = 7.8, 1.2 Hz, 1H, C_{Ar}), 7.34 (td, *J* = 7.8, 1.2 Hz, 1H), 7.19 (td, *J* = 7.7, 1.1 Hz, 1H, C_{Ar}), 7.00 (d, *J* = 8.0 Hz, 1H, C_{Ar}), 3.92 (t, *J* = 6.1 Hz, 2H, N^1-CH_2,C_{Ar}), 3.76 – 3.67 (m, 2H, N^2-CH_2), 2.22 (p, *J* = 6.0 Hz, 2H, CH_2). $^{13}C\{^1H\}$ NMR (101 MHz, $CDCl_3$) δ = 170.8 (CO), 167.4 (CO),167.3 (C=N), 140.1 (Cq), 128.8 (Cq), 127.0 (C_{Ar}), 123.9 (C_{Ar}), 122.0 (C_{Ar}), 110.1 (C_{Ar}), 109.5 (C_{Ar}), 48.2 (N^2-CH_2), 42.2 (N^1-CH_2), 20.0 (CH_2). FTIR (ATR) ν = 2052 (CO_{sym}), 1967 (CO_{asym}), 1589, 1577 (C=N) cm^{-1}; elemental analysis calcd (%): C 30.41; H 2.13; N 5.91; found: C 30.54; H 2.24; N 5.84.

4.5.5. Au(I) catalysed hydroalkoxylation/Claisen rearrangement of allylic alcohol and alkyne to γ-δ unsaturated ketones

In a scintillation vial, diphenylacetylene, allylic alcohol (3 equiv.) and [Au] (0.2 or 0.5 mol%), were stirred neat at 120 °C. The reaction was monitored by TLC until complete disappearance of the alkyne was confirmed (1-21 h). After the reaction was completed the mixture was diluted with CH_2Cl_2, filtered through a short plug of silica and concentrated under vacuum. The residue was then purified by flash column chromatography on silica gel to afford the corresponding product 1,2-diphenylpent-4-en-1-one **4.42**, whose data were consistent to those reported in literature.[56] ^1H NMR (300

MHz, $CDCl_3$) δ = 7.94 – 7.87 (m, 2H), 7.47 – 7.39 (m, 1H), 7.38 – 7.29 (m, 2H), 7.26 – 7.23 (m, 2H), 7.23 – 7.19 (m, 2H), 7.20 – 7.11 (m, 1H), 5.70 (ddt, *J* = 17.1, 10.2, 6.9 Hz, 1H), 4.99 (dq, *J* = 17.1, 1.6 Hz, 1H), 4.92 (ddt, *J* = 10.2, 2.0, 1.1 Hz, 1H), 4.58 (t, *J* = 7.3 Hz, 1H), 2.91 (dddt, *J* = 14.5, 8.0, 6.9, 1.2 Hz, 1H), 2.52 (dtt, *J* = 14.1, 6.9, 1.3 Hz, 1H). Chiral HPLC analysis, OD-H (99:1 hexane:*i*PrOH, flow rate 1.0 $mL \cdot min^{-1}$, 220 nm, 30 °C), tr: 5.425 min, 6.726 min, racemic.

4.5.6. Au(I) catalysed rearrangement of silyloxyenynes

[AuCl{(2S,3R)-HyperBTM}] (4-10 mol%) and $NaBAr^F$ or $NaBF_4$(8-30 mol%) was dissolved in 1,2-dichloroethane (1,2-DCE, 0.1 M), and stir at r.t. for 15 mins. The mixture was cooled at -30°C, and a solution of diethyl (*Z*)-2-(but-2-yn-1-yl)-2-(3-phenyl-3-((triisopropylsilyl)oxy)allyl)malonate (18.9 mg, 0.04 mmol) in 1,2-DCE (0.02 M) was transferred to the catalyst mixture. The solution was stirred, and warmed up at r.t., then at 84 °C until almost full consumption of the starting material as indicated by TLC (48 hours). The solution was concentrated and purified on silica gel (EtOAc:hexane, 10:90) to afford dimethyl (*E*)-3-benzoyl-4-ethylidenecyclopentane-1,1-dicarboxylate **4.43** as a pale yellow viscous oil (10 mg, 74%) whose data were consistent to those reported in literature:[58] ^{1}H NMR (300 MHz, $CDCl_3$) δ = 8.01 (d, *J* = 7.6 Hz, 2H), 7.59 (t, *J* = 7.4 Hz, 1H), 7.50 (t, *J* = 7.9 Hz, 2H), 5.60 (q, *J* = 6.3 Hz, 1H), 4.57 (t, *J* = 8.5 Hz, 1H), 3.77 (s, 3H), 3.71 (s, 3H), 3.28 – 3.11 (m, 4-12 1H), 3.05 – 2.83 (m, 2H), 2.26 (dd, *J* = 13.2, 8.1 Hz, 1H), 1.40 (d, *J* = 6.8 Hz, 3H); HPLC: enantiomeric excess determined by HPLC with a Chiralpak IB column (99.5:0.5 hexanes:*i*PrOH, 1.0 ml/min, 254 nm); tr = 20.1 min, 26.3 min, racemic.

4.5.7. Au(III) catalysed synthesis of allenes

In a scintillation vial, [$AuCl_3$(ITU)] (4 mol%), and $NaBAr^F$, or $AgSbF_6$ (8 mol%) were added, and stirred in 1,2-DCE (0.4 M) in presence of 4Å MS under N_2 atmosphere. Mesitylene (7 equiv.) was then added, and the solution stirred at r.t. for 5 min. After this time, a solution of propargylic alcohol (0.1 mmol) in 1,2-DCE (0.08 M) was added dropwise and the reaction mixture was heated at 50 °C for 20 min to afford the product (1-mesitylpropa-1,2-diene-1,3-diyl)dibenzene **4.45**, which was obtained in 90% isolated yield as a colourless oil (27.9 mg) whose data were consistent to those reported in

literature: ^{1}H NMR (300 MHz, $CDCl_3$) δ = 7.31-7.12 (m, 10H), 6.86 (bs, 2H), 6.51 (s, 1H), 2.23 (s, 3H), 2.18 (s, 6H). Chiral HPLC analysis, AD-H (99.1:0.1 hexane:*i*PrOH, flow rate 1.0 mL·min^{-1} , 220 nm, 30 °C), tr: 4.285 min, 4.523 min, racemic.

4.6. Bibliography

1. a) L. Ronconi, L. Giovagnini, C. Marzano, F. Bettìo, R. Graziani, G. Pilloni and D. Fregona, *Inorg. Chem.*, 2005, **44**, 1867-1881; b) E. R. T. Tiekink, *Inflammopharmacology*, 2008, **16**, 138-142; c) B. Bertrand and A. Casini, *Dalton Trans.*, 2014, **43**, 4209-4219.
2. P. Calamai, S. Carotti, A. Guerri, L. Messori, E. Mini, P. Orioli and G. Paolo Speroni, *J. Inorg. Biochem.*, 1997, **66**, 103-109.
3. M. W. Johnson, S. L. Shevick, F. D. Toste and R. G. Bergman, *Chem. Sci.*, 2013, **4**, 1023-1027.
4. a) Y. A. Lee and R. Eisenberg, *J. Am. Chem. Soc.*, 2003, **125**, 7778-7779; b) A. Gómez-Suárez, D. J. Nelson, D. G. Thompson, D. B. Cordes, D. Graham, A. M. Z. Slawin and S. P. Nolan, *Beilstein J. Org. Chem.*, 2013, **9**, 2216-2223.
5. W. Schneider, A. Bauer, A. Schier and H. Schmidbaur, *Chem. Ber.*, 1997, **130**, 1417-1422.
6. J. Schneider, Y.-A. Lee, J. Pérez, W. W. Brennessel, C. Flaschenriem and R. Eisenberg, *Inorg. Chem.*, 2008, **47**, 957-968.
7. J. Coetzee, S. Cronje, L. Dobrzanska, H. G. Raubenheimer, G. Joone, M. J. Nell and H. C. Hoppe, *Dalton Trans.*, 2011, **40**, 1471-1483.
8. G. N. Lewis, *Chemical Catalogue, New York*, 1923.
9. S. E. Denmark and G. L. Beutner, *Angew. Chem., Int. Ed.*, 2008, **47**, 1560-1638.
10. V. B. Birman, H. Jiang, X. Li, L. Guo and E. W. Uffman, *J. Am. Chem. Soc.*, 2006, **128**, 6536-6537.
11. T. Ishikawa, *Superbases for Organic Synthesis: Guanidines, Amidines, Phosphazenes and Related Organocatalysts*, Wiley, Chippenham, 2009.
12. a) M. P. Coles, *Chem. Commun.*, 2009, 3659-3676; b) J. E. Taylor, S. D. Bull and J. M. J. Williams, *Chem. Soc. Rev.*, 2012, **41**, 2109-2121.
13. J. Váňa, M. Sedlák and J. Hanusek, *J. Org. Chem.*, 2010, **75**, 3729-3736.

14. B. Maji, C. Joannesse, T. A. Nigst, A. D. Smith and H. Mayr, *J. Org. Chem.*, 2011, **76**, 5104-5112.

15. a) Y. Zhang and V. B. Birman, *Adv. Synth. Catal.*, 2009, **351**, 2525-2529; b) D. Belmessieri, C. Joannesse, P. A. Woods, C. MacGregor, C. Jones, C. D. Campbell, C. P. Johnston, N. Duguet, C. Concellon, R. A. Bragg and A. D. Smith, *Org. Biomol. Chem.*, 2011, **9**, 559-570.

16. D. Thienpont, O. F. J. Vanparijs, A. H. M. Raeymaekers, J. Vandenberk, P. J. A. Demoen, F. T. N. Allewijn, R. P. H. Marsboom, C. J. E. Niemegeers, K. H. L. Schellekens and P. A. J. Janssen, *Nature*, 1966, **209**, 1084.

17. a) V. B. Birman and X. Li, *Org. Lett.*, 2006, **8**, 1351-1354; b) D. S. B. Daniels, S. R. Smith, T. Lebl, P. Shapland and A. D. Smith, *Synthesis*, 2015, **47**, 34-41.

18. a) M. Kobayashi and S. Okamoto, *Tetrahedron Lett.*, 2006, **47**, 4347-4350; b) V. B. Birman, X. Li and Z. Han, *Org. Lett.*, 2007, **9**, 37-40.

19. L. C. Morrill, J. Douglas, T. Lebl, A. M. Z. Slawin, D. J. Fox and A. D. Smith, *Chem. Sci.*, 2013, **4**, 4146-4155.

20. M. Albrecht, *Angew. Chem., Int. Ed.*, 2015, **54**, 5822-5822.

21. S. Gaillard, A. M. Z. Slawin and S. P. Nolan, *Chem. Commun.*, 2010, **46**, 2742-2744.

22. D. Weber and M. R. Gagné, *Org. Lett.*, 2009, **11**, 4962-4965.

23. a) D. Wang, R. Cai, S. Sharma, J. Jirak, S. K. Thummanapelli, N. G. Akhmedov, H. Zhang, X. Liu, J. L. Petersen and X. Shi, *J. Am. Chem. Soc.*, 2012, **134**, 9012-9019; b) Z. Lu, J. Han, G. B. Hammond and B. Xu, *Org. Lett.*, 2015, **17**, 4534-4537.

24. L. Ricard and F. Gagosz, *Organometallics*, 2007, **26**, 4704-4707.

25. P. de Fremont, E. D. Stevens, M. R. Fructos, M. Mar Diaz-Requejo, P. J. Perez and S. P. Nolan, *Chem. Commun.*, 2006, 2045-2047.

26. D. Gasperini, A. Collado, A. Goméz-Suárez, D. B. Cordes, A. M. Z. Slawin and S. P. Nolan, *Chem. Eur. J.*, 2015, **21**, 5403-5412.

27. a) D. J. Nelson and S. P. Nolan, *Chem. Soc. Rev.*, 2013, **42**, 6723-6753; b) D. Zuccaccia, L. Belpassi, A. Macchioni and F. Tarantelli, *Eur. J. Inorg. Chem.*, 2013, **2013**, 4121-4135.

28. X. Yang, G. Lu and V. B. Birman, *Org. Lett.*, 2010, **12**, 892-895.

29. C. Joannesse, C. P. Johnston, C. Concellón, C. Simal, D. Philp and A. D. Smith, *Angew. Chem., Int. Ed.*, 2009, **48**, 8914-8918.

30. a) S. Gaillard, P. Nun, A. M. Z. Slawin and S. P. Nolan, *Organometallics*, 2010, **29**, 5402-5408; b) A. Collado, J. Bohnenberger, M.-J. Oliva-Madrid, P. Nun, D. B. Cordes, A. M. Z. Slawin and S. P. Nolan, *Eur. J. Inorg. Chem.*, 2016, **2016**, 4111-4122.

31. F. Lazreg, D. B. Cordes, A. M. Z. Slawin and C. S. J. Cazin, *Organometallics*, 2015, **34**, 419-425.

32. CCDC 1587865 ((2*R*,3*S*)-**4.10**·NTf_2) contains the supplementary crystallographic data for this paper. These data can be obtained free of charge from The Cambridge Crystallographic Data Centre via https://www.ccdc.cam.ac.uk/structures/

33. a) R. Narayanaswamy, M. A. Young, E. Parkhurst, M. Ouellette, M. E. Kerr, D. M. Ho, R. C. Elder, A. E. Bruce and M. R. M. Bruce, *Inorg. Chem.*, 1993, **32**, 2506-2517; b) H.-Y. Chao, W. Lu, Y. Li, M. C. W. Chan, C.-M. Che, K.-K. Cheung and N. Zhu, *J. Am. Chem. Soc.*, 2002, **124**, 14696-14706.

34. T. E. Müller, S. W.-K. Choi, D. M. P. Mingos, D. Murphy, D. J. Williams and V. Wing-Wah Yam, *J. Organomet. Chem.*, 1994, **484**, 209-224.

35. CCDC 1587862 (**4.27**), CCDC 1587863 ((*S*)-**4.25**) contain the supplementary crystallographic data for this paper. These data can be obtained free of charge from The Cambridge Crystallographic Data Centre *via* https://www.ccdc.cam.ac.uk/structures/;

36. CCDC 1587864 ((2*R*,3*S*)-**4.26**), and CCDC 1587861 ((±)-**4.26**) contain the supplementary crystallographic data for this paper. These data can be obtained free of charge from The Cambridge Crystallographic Data Centre *via*https://www.ccdc.cam.ac.uk/structures/;

37. H. Schmidbaur, W. Graf and G. Müller, *Angew. Chem., Int. Ed. Engl.*, 1988, **27**, 417-419.

38. C. Kutal, *Coord. Chem. Rev.*, 1990, **99**, 213-252.

39. The newly synthesised complexes were *non*-emissive in the visible region in both solution, and solid state, thus emission properties were not studied further

40. A. Yoshimura and V. V. Zhdankin, *Chem. Rev.*, 2016, **116**, 3328-3435.

41. a) L. T. Ball, G. C. Lloyd-Jones and C. A. Russell, *J. Am. Chem. Soc.*, 2014, **136**, 254-264; b) T. de Haro and C. Nevado, *J. Am. Chem. Soc.*, 2010, **132**, 1512-1513.

42. S. Gaillard, A. M. Z. Slawin, A. T. Bonura, E. D. Stevens and S. P. Nolan, *Organometallics*, 2010, **29**, 394-402.

43. CCDC 1587867 ((*R*)-**4.28**), CCDC 1587866 ((2R,2S)-**4.29**) contain the supplementary crystallographic data for this paper. These data can be obtained free of charge from The Cambridge Crystallographic Data Centre *via* https://www.ccdc.cam.ac.uk/structures/;

44. H. Clavier and S. P. Nolan, *Chem. Commun.*, 2010, **46**, 841-861.

45. A. Poater, B. Cosenza, A. Correa, S. Giudice, F. Ragone, V. Scarano and L. Cavallo, *Eur. J. Inorg. Chem.*, 2009, **2009**, 1759-1766.

46. L. Falivene, R. Credendino, A. Poater, A. Petta, L. Serra, R. Oliva, V. Scarano and L. Cavallo, *Organometallics*, 2016, **35**, 2286-2293.

47. It is to notice that the $\%V_{Bur}$ values are obtained from solid-state crystal structures, therefore careful comparison between the solid and solution coordination environment around the metal centre must be considered.

48. a) G. Ciancaleoni, L. Biasiolo, G. Bistoni, A. Macchioni, F. Tarantelli, D. Zuccaccia and L. Belpassi, *Chem. Eur. J.*, 2015, **21**, 2467-2473; b) G. Ciancaleoni, N. Scafuri, G. Bistoni, A. Macchioni, F. Tarantelli, D. Zuccaccia and L. Belpassi, *Inorg. Chem.*, 2014, **53**, 9907-9916; c) D. Setiawan, R. Kalescky, E. Kraka and D. Cremer, *Inorg. Chem.*, 2016, **55**, 2332-2344.

49. R. A. Kelly Iii, H. Clavier, S. Giudice, N. M. Scott, E. D. Stevens, J. Bordner, I. Samardjiev, C. D. Hoff, L. Cavallo and S. P. Nolan, *Organometallics*, 2008, **27**, 202-210.

50. CCDC 1587868 ((2*S*,3*R*)-**4.31**) contain the supplementary crystallographic data for this paper. These data can be obtained free of charge from The Cambridge Crystallographic Data Centre *via* https://www.ccdc.cam.ac.uk/structures/

51. A. R. Chianese, X. Li, M. C. Janzen, J. W. Faller and R. H. Crabtree, *Organometallics*, 2003, **22**, 1663-1667.

52. N. Ibrahim, M. H. Vilhelmsen, M. Pernpointner, F. Rominger and A. S. K. Hashmi, *Organometallics*, 2013, **32**, 2576-2583.

53. A. Gomez-Suarez, R. S. Ramon, A. M. Z. Slawin and S. P. Nolan, *Dalton Trans.*, 2012, **41**, 5461-5463.

54. F. Nahra, S. R. Patrick, A. Collado and S. P. Nolan, *Polyhedron*, 2014, **84**, 59-62.

55. S. R. Patrick, A. Gómez-Suárez, A. M. Z. Slawin and S. P. Nolan, *Organometallics*, 2014, **33**, 421-424.

56. A. Gómez-Suárez, D. Gasperini, S. V. C. Vummaleti, A. Poater, L. Cavallo and S. P. Nolan, *ACS Catal.*, 2014, **4**, 2701-2705.

57. J. M. Ketcham, B. Biannic and A. Aponick, *Chem. Commun.*, 2013, **49**, 4157-4159.

58. J.-F. Brazeau, S. Zhang, I. Colomer, B. K. Corkey and F. D. Toste, *J. Am. Chem. Soc.*, 2012, **134**, 2742-2749.

59. C.-F. Xu, M. Xu, L.-Q. Yang and C.-Y. Li, *J. Org. Chem.*, 2012, **77**, 3010-3016.

60. a) M. Georgy, V. Boucard and J.-M. Campagne, *J. Am. Chem. Soc.*, 2005, **127**, 14180-14181; b) M. Georgy, V. Boucard, O. Debleds, C. D. Zotto and J.-M. Campagne, *Tetrahedron*, 2009, **65**, 1758-1766.

61. N. Morita, M. Miyamoto, A. Yoda, M. Yamamoto, S. Ban, Y. Hashimoto and O. Tamura, *Tetrahedron Lett.*, 2016, **57**, 4460-4463.

62. C. Nieto-Oberhuber, M. P. Muñoz, E. Buñuel, C. Nevado, D. J. Cárdenas and A. M. Echavarren, *Angew. Chem., Int. Ed.*, 2004, **43**, 2402-2406.

63. T. L. Church and P. G. Andersson, *Coord. Chem. Rev.*, 2008, **252**, 513-531.

64. A. O. Ogweno, S. O. Ojwach and M. P. Akerman, *Dalton Trans.*, 2014, **43**, 1228-1237.

65. R. H. Crabtree, H. Felkin and G. E. Morris, *J. Organomet. Chem.*, 1977, **141**, 205-215.

66. T. E. Müller, J. C. Green, D. M. P. Mingos, C. M. McPartlin, C. Whittingham, D. J. Williams and T. M. Woodroffe, *J. Organomet. Chem.*, 1998, **551**, 313-330.

67. A. Collado, A. Gomez-Suarez, A. R. Martin, A. M. Z. Slawin and S. P. Nolan, *Chem. Commun.*, 2013, **49**, 5541-5543.

68. X.-F. Zhao and C. Zhang, *Synthesis*, 2007, **2007**, 551-557.

69. P. de Frémont, N. Marion and S. P. Nolan, *J. Organomet. Chem.*, 2009, **694**, 551-560.

70. Q. Yao, L. Kong, F. Zhang, X. Tao and Y. Li, *Adv. Synth. Catal.*, 2017, **359**, 3079-3084.

71. S. Ahrland, K. Dreisch, B. Norén and Å. Oskarsson, *Mater. Chem. Phys.*, 1993, **35**, 281-289.

5. Dual catalysis towards the activation of alkyne derivatives

5.1. Introduction

Catalysis is a powerful method that chemists rely on to target new reactions and synthesize new molecules. Its advancement proceeds daily in the academic and industrial community.

Other than transition metal catalysis, as presented in Chapter 2, the use of enzymes,[1] heterogeneous catalysts,[2] and organocatalysts[3] is becoming widespread. The latter has seen a successful development by relying on the practical use of organic molecules, their ready availability, usually at low costs and low toxicity. They have become powerful tools for the synthesis of substrates with high enantiocontrol.[4]

Further to their individual use as catalysts,[5] the combination of transition metal catalysis and organocatalysis has been widely explored over the last 20 years.[6] Advantages of this approach include the possibility to enable new reaction modes that are not accessible by the sole use of either transition metals or organocatalysts, the potential improvement of the efficiency of a reaction, and the broadening of its scope. However, the compatibility of the catalysts needs to be carefully considered or reactivity may be compromised. Judicious choice of the catalytic system is therefore of fundamental importance.

There are three main established ways through which the transition metal and organocatalytic cycles can interact (Figure 5.1):[7]

a) cooperative catalysis in which the metal centre and organic catalysts both activate substrates in the same catalytic cycle (Figure 5.1, a);

b) synergistic catalysis, where substrates A and B are activated simultaneously by the two catalysts, in two separate catalytic cycles, and then react to yield the product (Figure 5.1, b);[8]

c) sequential or relay catalysis where an intermediate, formed after the first catalytic cycle, is envisaged to react in a second catalytic cycle (Figure 5.1, c). The transformation is defined sequential if the reaction conditions need to be tuned for each catalytic cycle, while relay if the conditions remain the same.

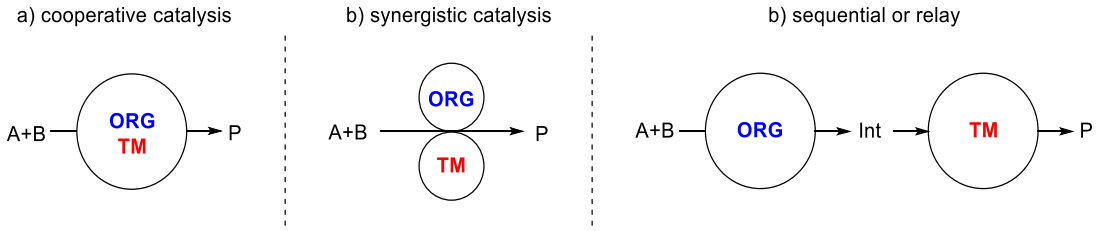


Figure 5.1. Schematic description of dual transition metal (TM)/organocatalyst (ORG) catalysis: a) cooperative catalysis; b) synergistic catalysis; c) sequential or relay catalysis.

A range of metal catalysts have been used alongside organocatalysts in dual catalytic processes. The organocatalytic species which have been reported in literature for this purpose can be divided into four main categories (Figure 5.2):[9] a) Lewis acids, such as secondary and tertiary amines; b) Brønsted acids, phosphoric acids and thioureas; c) Brønsted bases, for example cinchona alkaloids; d) Lewis bases, such as isothiourea, NHCs.[10] Bifunctional catalysts are included within these sets.[11]

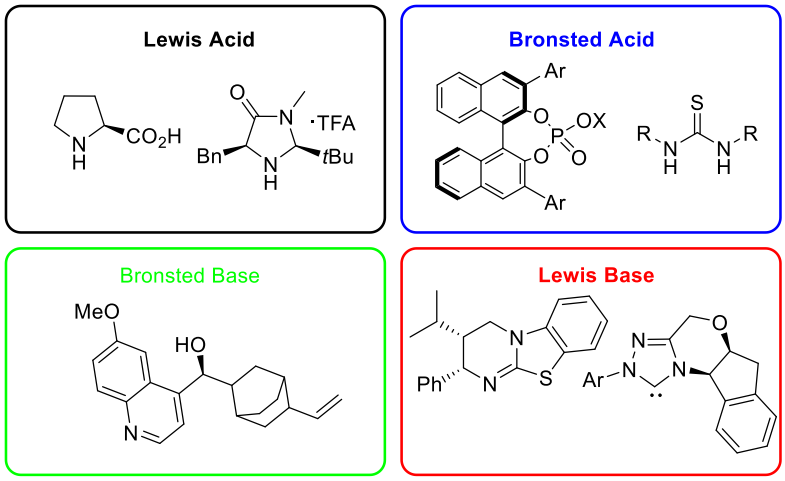


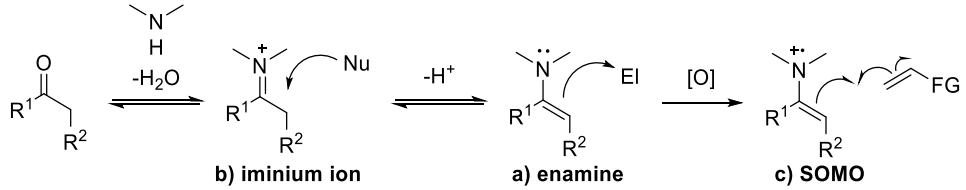
Figure 5.2. Main categories of organocatalysts with illustrative examples.

5.1.1. Lewis base catalysis

Lewis bases can donate a pair of electrons to activate a substrate molecule and enable its reactivity. The activation modes can be categorised in:

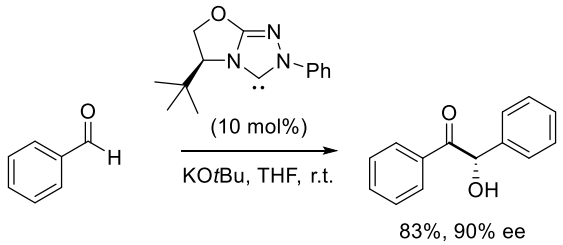
1. enamine catalysis,[12] through condensation of a secondary amine with a carbonyl moiety, formation of iminium cation and tautomerisation to generate a nucleophilic intermediate which will react with electrophiles (Scheme 5.1, a). This reaction mode has been largely applied to enantioselective aldol reactions and carbonyl α-functionalisation processes;[12-13]

2. iminium catalysis,[14] which involves the formation of an iminium ion *in situ* through a secondary amine reacting with a carbonyl group, as for enamines, followed by nucleophilic attack (Scheme 5.1, b). Its use is widespread for Diels-Alder reactions;[15]
3. Singly occupied molecular orbital (SOMO) activation,[16] which works through the generation of a radical cation *via* one electron oxidation of an electron rich enamine, formed as before (Scheme 5.1, c). The highly reactive radical cation can be trapped by radical addition to form α-functionalised molecules, therefore its use in α-allylation reactions.



Scheme 5.1. Simplified example of iminium, enamine and SOMO activation.

4. carbene catalysis; NHCs as described in section 1.2.1, have been shown to be also suitable organocatalysts,[17] with the most common uses involving the formation of reactive acyl anion equivalents with aldehydes. These intermediates can react with aldehydes or α,β-unsaturated substrates, and undergo *umpolung* reaction, *e.g.* benzoin reactions (Scheme 5.2).[18]

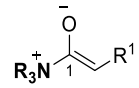


Scheme 5.2. Bicyclic chiral triazolium salt catalysed benzoin reaction.[18]

5. acyl ammonium, ammonium enolates catalysis of which a description follows.

5.1.1.1. Ammonium enolate chemistry

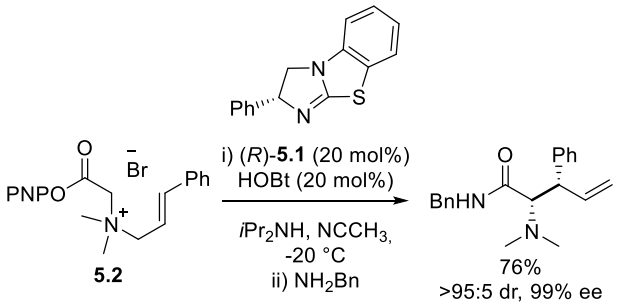
Chiral isothioureas (ITU), examined in section 4.1.1, have been widely employed for a number of transformations.[19,20] Their main activation pathway is the formation of C^1 ammonium enolates (Figure 5.3); the tertiary amine can covalently bind *via* acyl substitution to esters or anhydrides.



C^1 ammonium enolate

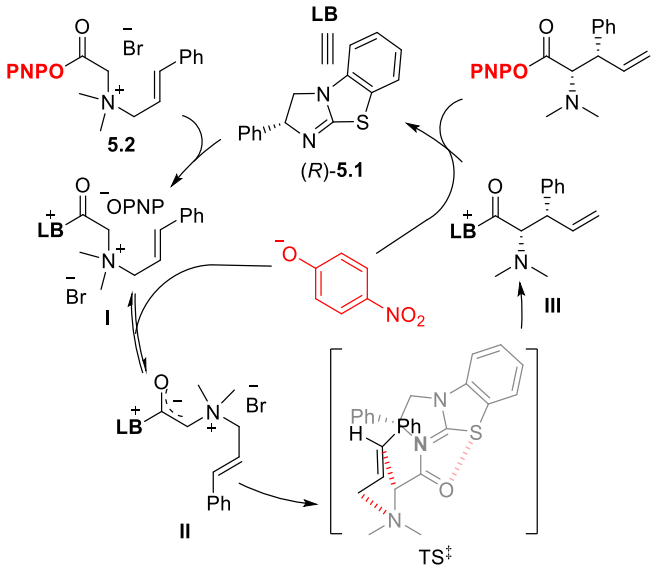
Figure 5.3. C^1 ammonium enolate derived from electrophilic substrates and chiral ITU.

Among the possible precursors, activated aryl esters are attractive for the ease of synthesis and availability of the substrates; moreover, it was shown that the phenolate formed *in situ* is able to act as an external nucleophile and enable catalyst turnover. The work of Smith's group in the [2,3] rearrangement of allylic ammonium ylides catalysed by (*R*)-BTM ((*R*)-**5.1**) was the first example of the successful application of this strategy in isothiourea catalysis (Scheme 5.3).[21]



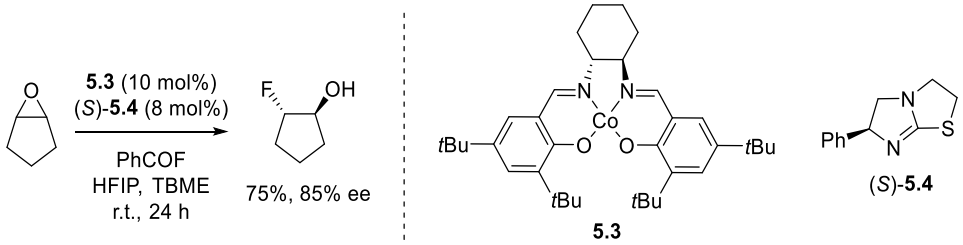
Scheme 5.3. [2,3] rearrangement of allylic ammonium ylides via isothiourea catalysis.[21]

Studies into the mechanism of this reaction found that initial activation of the ammonium salt **5.2** by (*R*)-**5.1** gave intermediate **I** (Scheme 5.4).[22] Reversible deprotonation of **I** by the phenolate released in solution resulted in formation of reactive intermediate **II**. Subsequent rearrangement occurred in an enantioselective fashion (**TS**‡); the origin of the enantioselectivity arises from stabilizing $n_0 \rightarrow \sigma^*_{C\text{-}S}$ interactions between the S atom of the catalyst and the O atom of the acylated substrate.[23] These S···O interactions, together with the Ph substituent in the isothiourea placed in a pseudoaxial position, act as a conformational lock, leading to high facial selectivity for the following rearrangement. Final "rebound" of the phenolate from **III** released the product, which was further functionalised in solution by external nucleophiles.



Scheme 5.4. Mechanistic pathway for [2,3] rearrangement via isothiourea activation of 4-nitrophenol esters.[22] External turnover highlighted.

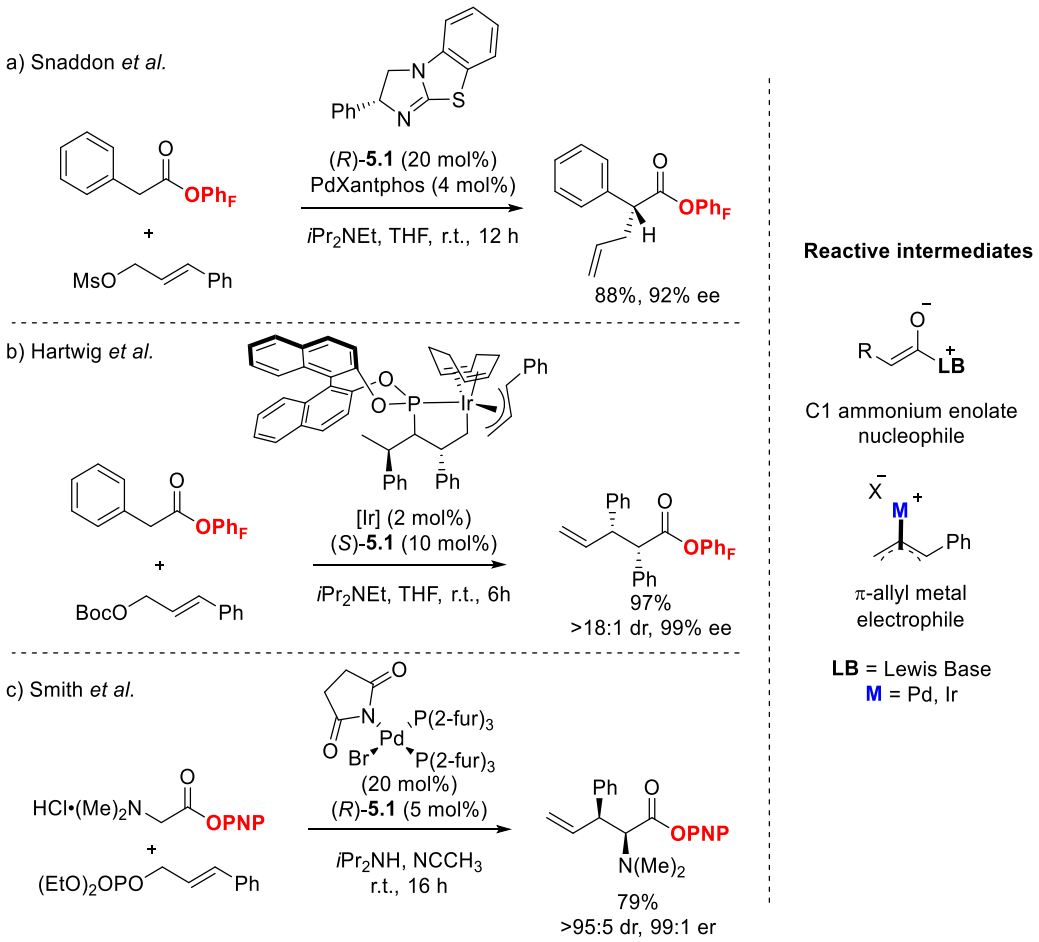
While isothioureas have been extensively explored as Lewis base catalysts in organocatalytic applications, few examples are known where the Lewis base cooperatively activated substrates together with a metal centre. In 2010 Doyle used a combination of a Co(II)-(salen) (**5.3**) Lewis acid and (-)-tetramisole ((*S*)-**5.4**) in a co-catalysed desymmetrization of epoxides by nucleophilic fluorination (Scheme 5.5).[24] In this report the authors suggested a possible non-poisoning axial binding of the isothiourea to the metal centre, although mechanistic studies could not prove the hypothesised involvement of the Lewis base.[25]



Scheme 5.5. Doyle's desymmetrization of epoxides via nucleophilic fluorination.[25]

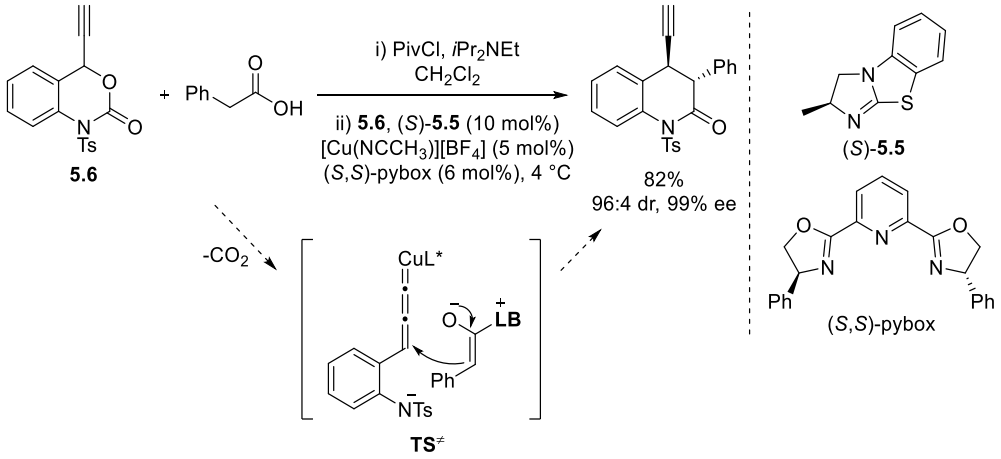
The recent work of Snaddon[26] and Hartwig[27] in the α-allylic functionalisation of aryl acetic acid esters to homoallylic esters, showed the use of well-defined Pd and Ir complexes combined with the Lewis base (Scheme 5.6, a and b). Smith and co-workers expanded the research in dual catalysis with Pd and ITU (Scheme 5.6, c); the authors reported the synthesis of α-amino acids derivatives through allylic amination followed by

[2,3]-sigmatropic rearrangement.[28] Again for this transformation the use of a well-defined Pd(II) source was necessary to ensure compatibility with the basic (*R*)-**5.1** under the reported reaction conditions. The latter reports successfully used external turnover from phenolates generated *in situ* to achieve catalyst turnover.



Scheme 5.6. Relay palladium/isothiourea catalysis and reactive intermediates; a) Snaddon and b) Hartwig α-allylation;[26,27] c) Smith allylic amination/[2,3] rearrangement.[28]

In a similar mechanism, the synergistic cooperative catalysis of $[Cu(NCCH_3)_4][BF_4]$/pybox and (*S*)-MeBTM ((*S*)-**5.5**), was shown to be effective in the synthesis of 3,4-dihydroquinolin-2-ones (Scheme 5.7). This reaction was developed concurrently by Gong[29] as well as Cao and Wu.[30] The authors suggested the generation of a Cu-allenylidene species from decarboxylation of dihydrobenzooxazinones (**5.6**); this species could be trapped by an enamine, formed by isothiourea activation of the anhydride. Catalyst turnover was achieved by the secondary amine released after the decarboxylative activation of the substrate.

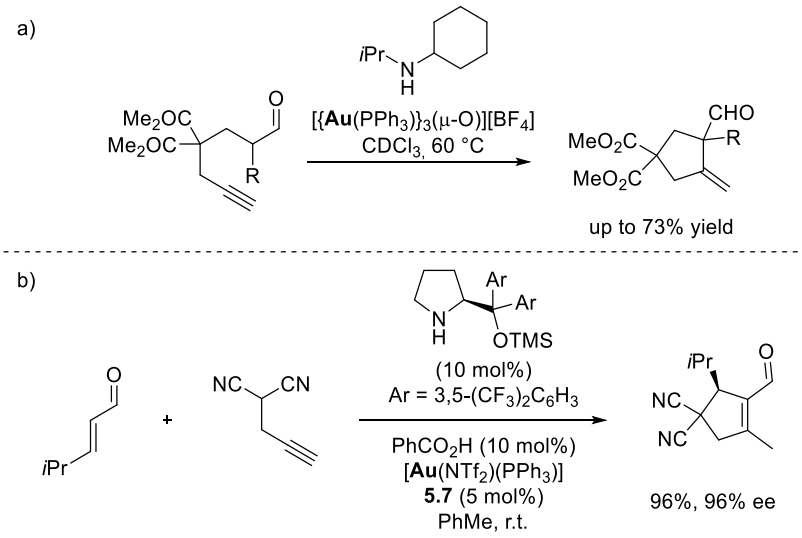


Scheme 5.7. Copper/isothiourea sequential catalysis.[29,30]

5.1.2. Dual gold/organocatalysis reactions

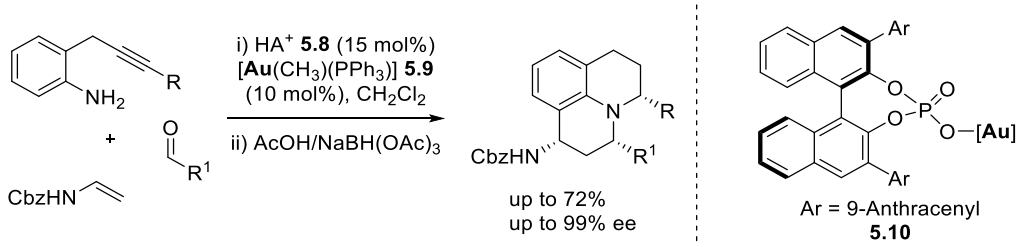
The chemistry of gold towards π-activation of multiple bonds has also been exploited in combination with organocatalysts.[31] Early examples from the literature has shown the cooperation of mainly secondary amines and Au(I) well defined complexes, with few exceptions.[32]

In 2008 the Kirsch group described 5-*exo*-dig cyclisation of aldehydes by nucleophilic attack of an enamine, formed *in situ* with a secondary amine, to Au activated terminal alkyne (Scheme 5.8, a).[33] The enantioselective equivalent of this transformation followed; Jørgensen and co-workers reported a proline and [Au(NTf_2)(PPh_3)] (**5.7**) catalysed cascade iminium/enamine/Au(I) reaction, through formation of a Kirsch type adduct (Scheme 5.8, b).[34] The products obtained were highly enantioenriched cyclopentenes (up to 96% ee).



Scheme 5.8. a) Kirsch's 5-*exo*-dig cyclisation of aldehydes;[33] b) cascade iminium/enamine/Au(I) reaction from Jørgensen and co-workers.[34]

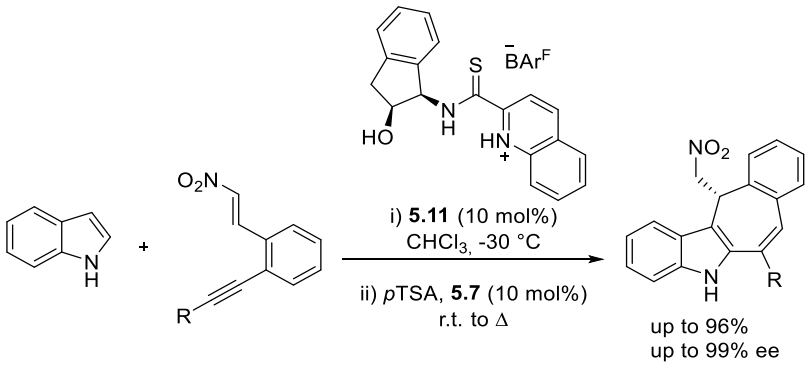
Gold therefore assumed a prominent role in tandem transformation; a series of reactions by Dixon,[35] Gong,[36] Che,[37] together with others,[38] reported the use of Brønsted acids together with well-defined gold complexes. In particular, Gong and co-workers studied a three component coupling combining [4+2] cyclisation, hydroamination and reduction, with the use of chiral phosphoric acid (**5.8**) and [Au(CH_3)(PPh_3)] (**5.9**) complex (Scheme 5.9).[39] ^{31}P NMR studies confirmed that a gold phosphate catalyst (**5.10**) formed by reaction of **5.7** and **5.8**, the metal precursor. **5.9** was hypothesised to be involved in the catalytic cycle. Indeed, the formation of a *non*-poisoning interaction between the metal centre and the organocatalyst such as in **5.10** could be beneficial for the reaction outcome.



Scheme 5.9. Three components coupling by Gong and co-workers.[39]

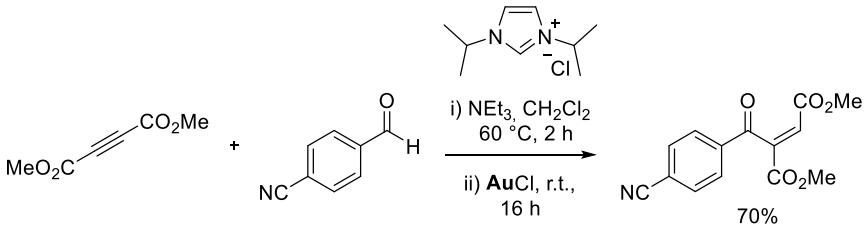
Hydrogen-bonding catalysts have been reported to be compatible with gold catalysts by Jørgensen and Enders' research groups.[40] Enders used this strategy to synthesise a 7-membered ring containing tetracyclic indole derivative with excellent enantioinduction (Scheme 5.10).[40c] The catalysts of choice were a chiral tertiary-amine thiourea catalyst

(**5.11**) and [Au(NTf$_2$)(PPh$_3$)] **5.7**. Addition of *p*TSA was necessary to avoid catalyst decomposition and to enable high catalyst turnover.



Scheme 5.10. Enantioselective synthesis of tetracyclic indoles.[40c]

Finally, a few examples have been reported that utilise both NHC and gold catalysts; in particular the seminal work of Adamo and co-workers (Scheme 5.11).[41] The authors showed how intermolecular hydroacylation reactions can be conducted by cooperative NHC activation of electron-poor aldehydes, and Au(I) coordination into activated alkynes to access chalcones with moderate to good yields. However, the generality of the methodology was not fully expanded.



Scheme 5.11. Adamo's cooperative NHC/Au catalysis.[41]

5.2. Aim and objectives

At the onset of this project, few reports in the literature dealt with the study of cooperative gold Lewis acids and Lewis bases. Therefore, the main aim of the project was to study this concept and its limitations. The dual process can be seen as the activation of suitable starting materials (**IV**), followed by synergistic Au/Lewis base activation (**V**). The nucleophilic enolate attack into activated electrophile (**VI**) could afford enantioselective product (**VII**) and release the active catalysts (Figure 5.4).

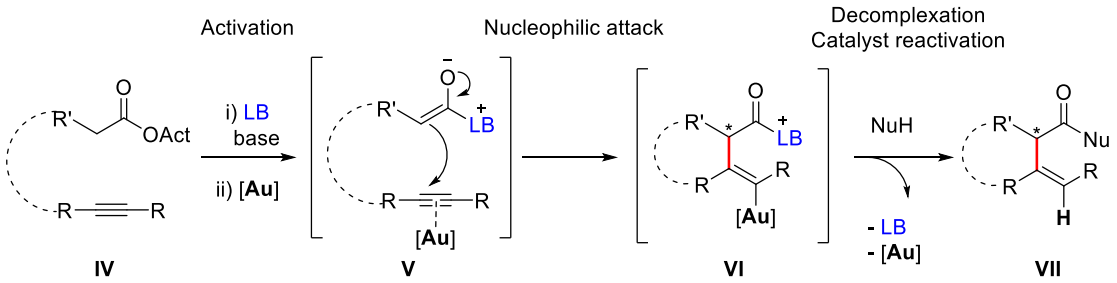


Figure 5.4. Hypothesised pathways for isothiourea/gold catalysis.

The synthesis of the substrates and the design of new synthetical targets will be tackled first. The attempts in catalytic application for dual catalysis with Au/Lewis bases system will follow. Other π-Lewis acids were utilised to obtain reactivity and will be introduced in due course.

5.3. Activation of alkynes

The proposed dual process towards the addition of ammonium enolates into activated alkynes utilised structures containing an ester and an alkyne. The different patterns targeted for this aim were (Figure 5.5): a) phenylacetic anhydrides and alkynes; b) tethered alkyne-esters.

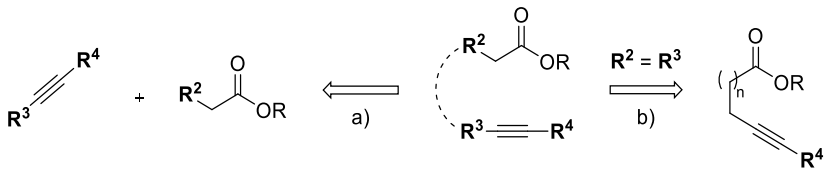


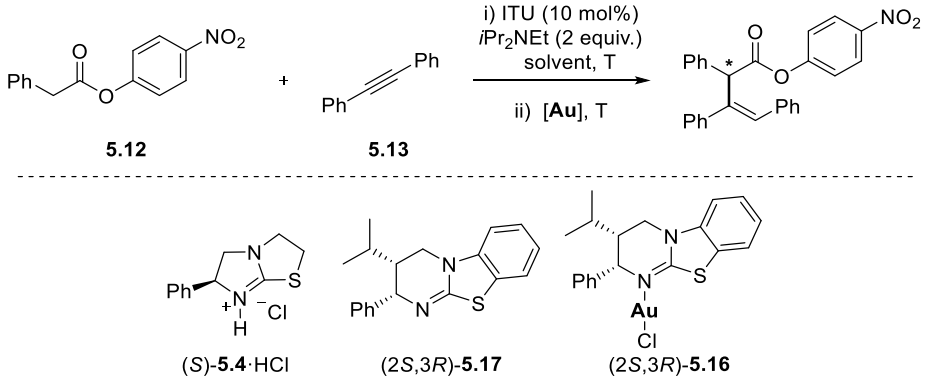
Figure 5.5. Targeted substrates for cooperative transition metal/organocatalysis reactions.

5.3.1. Intermolecular reactions

Initial dual activation intermolecular trials were performed by reacting 4-nitrophenol 2-phenylacetic acid (**5.12**) and diphenylacetylene (**5.13**). Substrate **5.12** was reacted with 10 mol% of (*S*)-tetramisole·HCl (*S*)-**5.4**·HCl (10 mol%) and *i*Pr$_2$NEt in NCCH$_3$ (Table 1, entry 1). After 10 min, a mixture of **5.13** and 5 mol% of [Au(NTf$_2$)(IPr)] **5.14** in NCCH$_3$ was added to the solution. The reaction was stirred for 18 h at r.t., but no conversion of the starting materials was observed. Heating the mixture up to 80 °C for 2 days still resulted in no conversion of the starting materials, and additionally gave catalyst decomposition.

A mixture of [AuCl(PPh$_3$)] (**5.15**) and AgOTs, was next tested (Table 5.1, entry 2). By following the same order of addition of reagents, the mixture was stirred at r.t., then at 80 °C, with no significant conversion of **5.12** and **5.13**. Possible catalyst poisoning was therefore hypothesised under these reaction conditions. The reaction was attempted in the presence of [AuCl{(2*S*,3*R*)-HyperBTM}] ((2*S*,3*R*)-**5.16**) (Chapter 4) and (2*S*,3*R*)-HyperBTM ((2*S*,3*R*)-**5.17**) as the Lewis base. The gold(I) catalyst was activated with NaBAr^F, and the reaction was performed in CH_2Cl_2 and set up at 0 °C, then stirred at 80 °C overnight (entry 3). Starting materials were recovered in the reaction mixture, together with 1,2-diphenylethan-1-one, the ketone derived from hydration of **5.13**.[42] This result suggested that an active gold species might form in solution, but the C-C bond formation is less favourable than addition of water to the triple bond.[43]

Table 5.1. Intermolecular reaction of activated esters and alkynes.

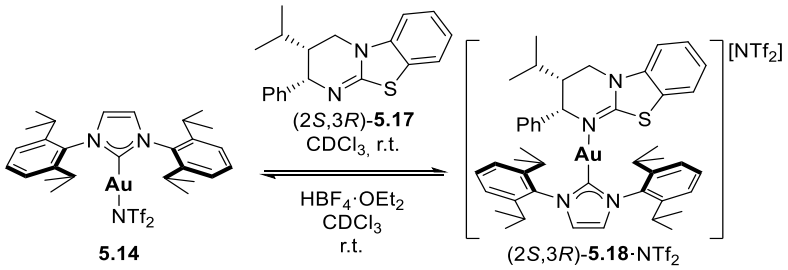


Entry	ITU (mol%)	Solvent	Lewis acid (mol%)	T (°C)	Conv. (%)
1	(*S*)-**5.5**·HCl	$NCCH_3$	**5.14** (5)	r.t. to 80	/
2	(*S*)-**5.5**·HCl	$NCCH_3$	**5.15**/AgOTs (5)	r.t. to 80	/
3	(2*S*,3*R*)-**5.17**[a]	CH_2Cl_2	(2*S*,3*R*)-**5.16** NaBARF (10)	0 to 80 °C	[b]

Reaction conditions: **5.12** (0.1 mmol), **5.13** (0.1 mmol), solvent (0.05 M), *i*Pr$_2$NEt (2 equiv.); [a] *i*Pr$_2$NEt (1 equiv.), dry CH_2Cl_2 (0.015 M), 48-72 h; [b] alkyne hydration.

As observed in chapter 4, a mixture of triflimide-Au(I) **5.14** and isothiourea (2*S*,3*R*)-**5.17**, led to heteroleptic complex [Au(IPr){(2*S*,3*R*)-HyperBTM}][NTf_2] ((2*S*,3*R*)-**5.18**·BF_4) (Scheme 5.12). This complex could be activated *in situ* with tetrafluoroboric acid diethyl ether solution to reform the active **5.2** species *in situ*; however, in the chosen reaction conditions, the presence of base is necessary to ensure formation of the ammonium

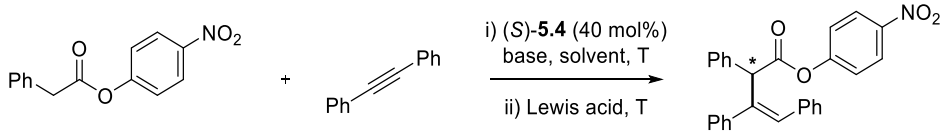
enolate reactive species. Therefore, for the targeted reaction the self-quenching of the catalyst might prevent activation of the organic substrates.



Scheme 5.12. Formation of heteroleptic complex (2*S*,3*R*)-**5.18**·NTf_2 from **5.14** and (2*S*,3*R*)-**5.17**.

The chosen Lewis acid seemed not suitable for the desired transformation, so the use of different salts was investigated next;[44] however, when **5.12** and **5.13** were reacted in presence of (*S*)-**5.4**·HCl (40 mol%) with $FeCl_3$, $Cu(OTf)_2$, Ag_2O, $In(OTf)_3$ or $ZnCl_2$ (20 mol%) the mixture failed to show any conversion of starting material (Table 5.2, entries 1-6). Variation of the base from organic *i*Pr_2NEt to inorganic base K_2CO_3 did not change the outcome.

Table 5.2. Intermolecular reaction of activated esters and alkynes: variation of Lewis acid.



5.12 **5.13**

Entry	Base (equiv.)	Solvent	Lewis acid	T (°C	Conv (%)
1	*i*Pr_2NEt (2)[a]	CH_2Cl_2	$FeCl_3$	0 to 50	/
2	*i*Pr_2NEt (2)	CH_2Cl_2	$Cu(OTf)_2$	0 to 50	/
3	*i*Pr_2NEt (2)	CH_2Cl_2	Ag_2O	0 to 50	/
4	K_2CO_3 (1)	1,2-DCE	$In(OTf)_3$	0 to 80	/
5	K_2CO_3 (1)	1,2-DCE	$ZnCl_2$	0 to 80	/
6	K_2CO_3 (1)	1,2-DCE	$ZnCl_2$	0 to 80	/

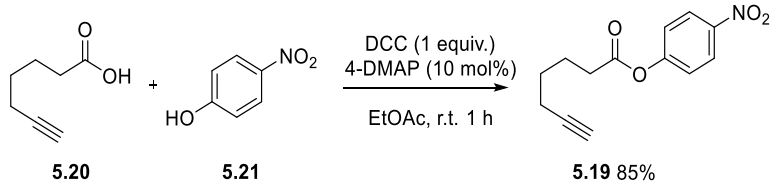
Reaction conditions: **5.12** (0.1 mmol), **5.13** (0.1 mmol), solvent (0.014 M), base (1-2 equiv.), (*S*)-**5.4**·HCl (40 mol%), Lewis acid (20 mol%), 48 h; [a] (*S*)-**5.4**·HCl (30 mol%).

5.3.2. Intramolecular cyclisation

The entropically favoured intramolecular cyclisation of tethered alkyne-ester substrates was targeted next.

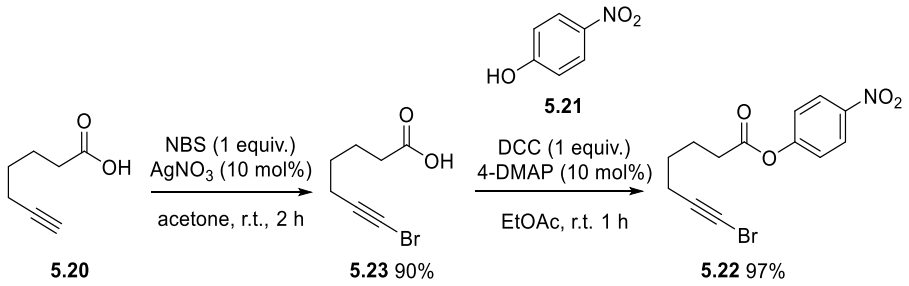
Suitable substrates, such as 4-nitrophenyl hept-6-ynoate (**5.19**) was synthesised from commercially available 6-heptynoic acid (**5.20**), and 4-nitrophenol (PNPOH, **5.21**) by

ester coupling promoted by DCC, and co-catalysed by 4-DMAP (10 mol%) (Scheme 5.13). After initial addition at 0 °C in EtOAc, the reaction was stirred at r.t. for 1 h and the crude mixture recrystallised to yield 85% of **5.19**.



Scheme 5.13. Synthesis of **5.19** from **5.20** and **5.21**.

4-Nitrophenyl 7-bromohept-6-ynoate (**5.22**) was synthesised in a 2 steps sequence: initial bromination of **5.20**, with NBS and $AgNO_3$ (10 mol%) in acetone, gave **5.23** in 90% yield (Scheme 5.14). Subsequent DCC ester coupling, resulted in 97% isolated yield for **5.22**.

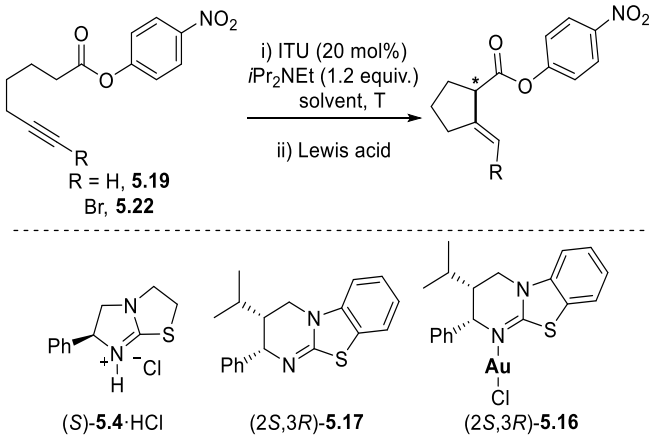


Scheme 5.14. Synthesis of **5.22** from **5.21** *via* **5.23**.

Initial dual catalysis attempts were performed by activation of **5.19**; a solution of the substrate in $NCCH_3$ was treated with (*S*)-**5.4**·HCl (20 mol%) and 1.2 equiv. of *i*Pr_2NEt. After 1 h at r.t. complex [Au(NTf_2)(IPr)] **5.14** (2 mol%) was added to the reaction mixture, and the reaction followed by ^{1}H NMR (Table 5.3, entry 1). **5.19** did not convert under the reaction conditions, even upon heating up the reaction to 80 °C. [AuCl(IPr)] **5.15** was activated *via* AgX (X = BF_4, OTf) and added to a mixture of **5.19** and ITU in $NCCH_3$ (Table 5.3, entries 2, 3). Even after prolonged reaction time and varying the temperature from r.t. to reflux, no successful conversion of the tethered alkyne-ester was observed. When varying the solvent to PhMe, and then with the [Au(IPr)($NCCH_3$)][BF_4] cationic complex (**5.24**), **5.19** was found unreacted (entry 4). Triflimide-Au(I) complex **5.14** (5 mol%) was tested in the absence of ITU, in the presence of *i*Pr_2NH (1.2 equiv.) however no conversion was observed (entry 5). Attempts to activate (2*S*,3*R*)-**5.16** (10 mol%) with $NaBAr^F$ (20 mol%) for the same transformation in the presence of (2*S*,3*R*)-**5.17**, resulted in no conversion of starting material (entry 6). In($OTf)_3$ (20 mol%) failed

to catalyse the reaction when moving to substrate **5.22** in the presence of (*S*)-**5.4**·HCl (entry 7).

Table 5.3. Intermolecular dual-catalysed cyclisation of alkyne-esters moieties.



Entry	ITU	Solvent	Lewis acid (mol%)	T (°C)	R	Conv. (%)
1	(*S*)-**5.4**·HCl	$NCCH_3$	**5.14** (2)	r.t. to 80	H	/
2	(*S*)-**5.4**·HCl	$NCCH_3$	**5.15**/$AgBF_4$ (5)	-20 to r.t. to 80	H	/
3	(*S*)-**5.4**·HCl	$NCCH_3$[a]	**5.15** (5)/AgOTs (20)	r.t. to 80	H	/
4	(*S*)-**5.4**·HCl	PhMe[a]	**5.24** (5)	r.t. to 80	H	/
5	-	$NCCH_3$[b]	**5.14** (5)	r.t. to 80	H	/
6	(2*S*,3*R*)-**5.17**	$NCCH_3$[c]	(2*S*,3*R*)-**5.16** (10) $NaBAr^F$ (20)	0 to 80 °C	H	[d]
7	(*S*)-**5.4**·HCl[a]	1,2-DCE[e]	$In(OTf)_3$ (20)	0 °C to 80	Br	/

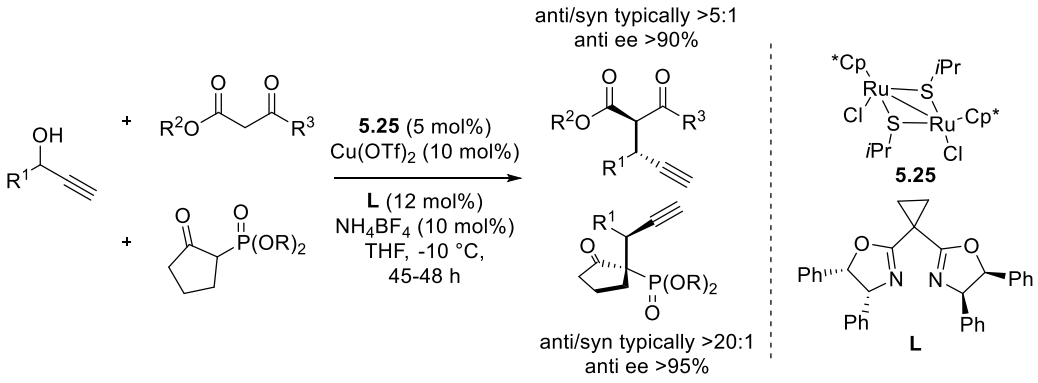
Reaction conditions: **5.19** or **5.22** (0.1 mmol), solvent (0.014 M), *i*Pr$_2$NEt (1.2 equiv.), ITU (20 mol%), Lewis acid (2-20 mol%); [a] *i*Pr$_2$NEt (2 equiv.), 48 h; [b] *i*Pr$_2$NH (1.2 equiv.) $NCCH_3$ (0.05 M) [c] (2*S*,3*R*)-**5.3** (40 mol%), *i*Pr$_2$NEt (1 equiv.); [d] decomposition observed; [e] K_2CO_3 (1 equiv.).

As observed for the intermolecular attempts, no reactivity was found when intramolecular cyclisations were tested. The unsuitability of the Au(I) catalyst and the isothiourea organocatalysts might be one of the possible explanation of low reactivity; interactions between the catalysts might lead to self-quenching processes, which will switch off the metal/ITU activity in solution. The low reactivity of the substrates was considered as

another plausible effect to impede reactivity, therefore other organic motifs were explored.

5.4. Propargylic alkynes synthesis and activation

The next synthons of interest were propargylic alcohols, and derivatives.[45] Transition metals activation of these substrates have been studied extensively by Nishibayashi, Nakamura and co-workers. The authors used several catalytic systems to activate these organic molecules towards nucleophilic addition, *e.g.* addition of enolates into propargylic alcohols (Scheme 5.15).[46] The best results were achieved when thiolate bridged diruthenium complexes (**5.25**) were used. The success of the catalysts relied on the formation of Ru-allenylidene intermediates, which were electrophilic at the C^1 position.[47] The concept was expanded as shown in section 5.1.1 to copper species (Scheme 5.7), which might form the same active intermediate and allow nucleophilic attack to propargylic compounds.[48]



Scheme 5.15. Nishibayashi contributions to the activation of propargylic alcohols.

Few examples are reported with gold,[49] and we successfully utilised Au(III)-ITU catalysts to achieve dehydrative arylation reactions to propargylic alcohols to generate trisubstituted allenes (section 4.3.3).[50] The Lewis acid metal centre is believed to be involved in the dehydrative activation of the alcohol together with coordination to the alkyne. The chemistry of Pd(0) towards propargylic compounds, acetates or carbonates, was of interests, because of the suitability of the metal centre with ITU bases.[51] When reacting propargylic derivatives with Pd(0) precursors formation of π-propargyl (**VIII**), σ-propargyl (IX) and σ-allenyl (**X**) Pd(II) intermediates can occur, whose structures are in equilibrium (Figure 5.6). Further nucleophilic attack depends on the nature of the latter;

a soft nucleophile (β-ketoesters, or malonates) will preferentially attack the C^2 of **VIII**, while a hard nucleophile will attack the C^1 or C^3 position of **IX** and/or **X**. This strategy has been utilised extensively with soft nucleophiles by Tsuji and co-workers to form dehydrofurans.[52]

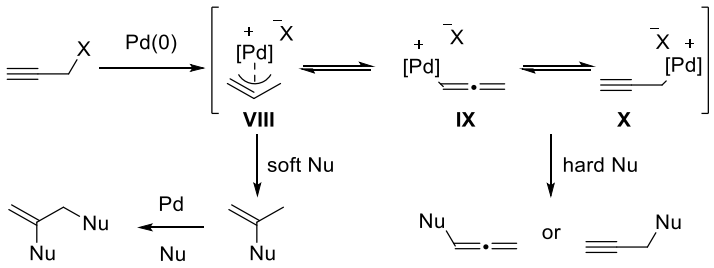


Figure 5.6. Activation of propargylic derivatives by Pd(0) and subsequent nucleophilic attack.

Within these premises, the use of Au, Cu and Pd precursors was set to explore dual catalytic processes with isothiourea organocatalysts for the functionalisation of propargylic derivatives.

5.4.1. Synthesis of propargylic compounds

The synthesis of propargylic alcohols and derivatives was tackled (Figure 5.7). The chosen motifs were: a) propargylic alcohols or derivatives and activated esters; b) benzoxazinones.

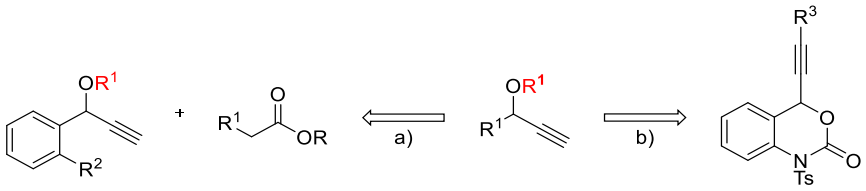
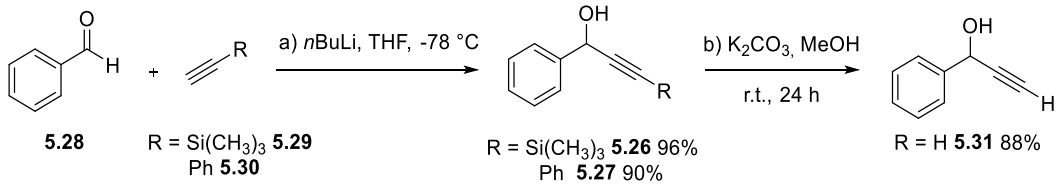


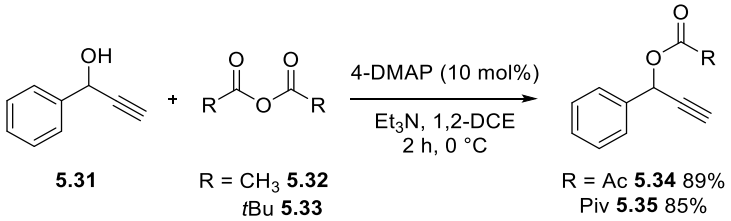
Figure 5.7. Targeted propargylic derivatives.

Terminal and internal propargylic alcohols were easily synthesised by lithium acetylide addition to aldehydes. Compounds **5.26** and **5.27** were obtained from commercially available benzaldehyde (**5.28**) and trimethylsilane acetylene (**5.29**) or phenylacetylene (**5.30**) in 96% and 90% isolated yield, respectively (Scheme 5.16, a). **5.26** was further deprotected to obtain 1-phenylprop-2-yn-1-ol (**5.31**) in 88% isolated yield (b).



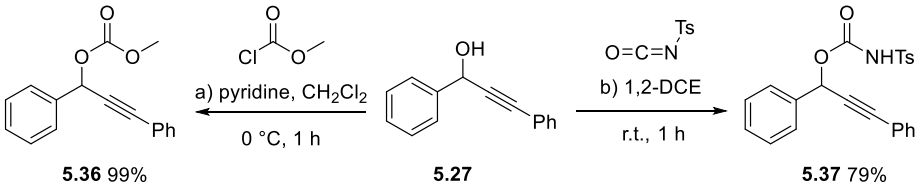
Scheme 5.16. Synthesis of propargylic alcohols **5.26**, **5.27** and **5.31**.

When treating **5.31** with acetic (**5.32**) or pivalic anhydrides (**5.33**) conversions into propargylic acetate (**5.34**) and pivalate (**5.35**) were obtained, and the products isolated in 89 and 85% yield (Scheme 5.17).



Scheme 5.17. Synthesis of **5.34** and **5.35** from **5.31**.

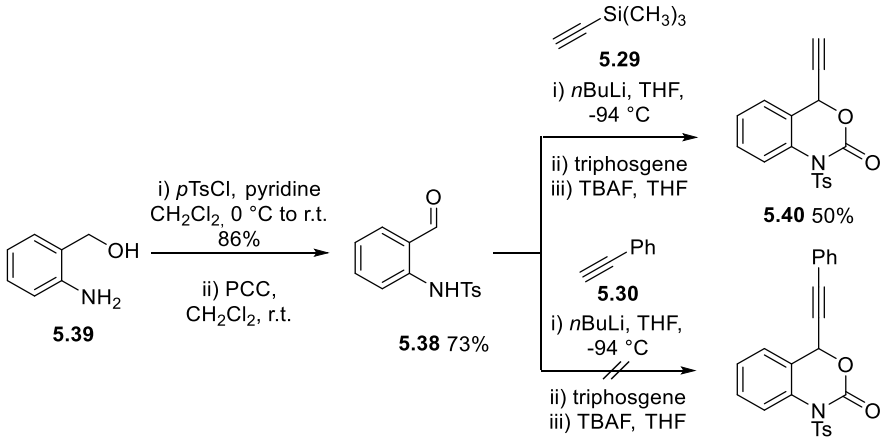
The synthesis of carbonate and carbamides was performed for **5.27**; reaction with methyl-chloroformate, in presence of stoichiometric amount of pyridine, led to **5.36** in 99% yield (Scheme 5.18, a). The formation of **5.37** was instead achieved by reaction of **5.27** with *p*toluensulfonyl isocyanate, in 1,2-dichloroethane (b). The product was obtained in 79% isolated yield by simple evaporation of the solvent.



Scheme 5.18. Synthesis of carbonate (**5.36**) and carbamate (**5.37**) derivatives from **5.27**.

N-(2-Formylphenyl)-4-methylbenzenesulfonamide (**5.38**) was synthesised from commercially available *N*-(2-(hydroxymethyl)phenyl)-4-methylbenzenesulfonamide (**5.39**) through amine protection with *p*TsCl, catalysed by pyridine; after oxidation with pyridinium chlorochromate, under rigorously anhydrous conditions to avoid overoxidation, **5.38** was isolated in 73% yield (Scheme 5.19). By following the literature procedure,[30] **5.38** was treated with trimethylsilyl lithium acetylide, at -94 °C in THF; further cyclisation with a solution of triphosgene in THF, and deprotection with TBAF,

led to recovered **5.40** in 50% yield. When phenyl acetylene **5.30** was used instead of **5.29**, only decomposition was observed.



Scheme 5.19. Synthesis of ethynyl benzoxazinanone **5.40** from **5.38**.

5.4.2. Propargylic derivatives functionalisation

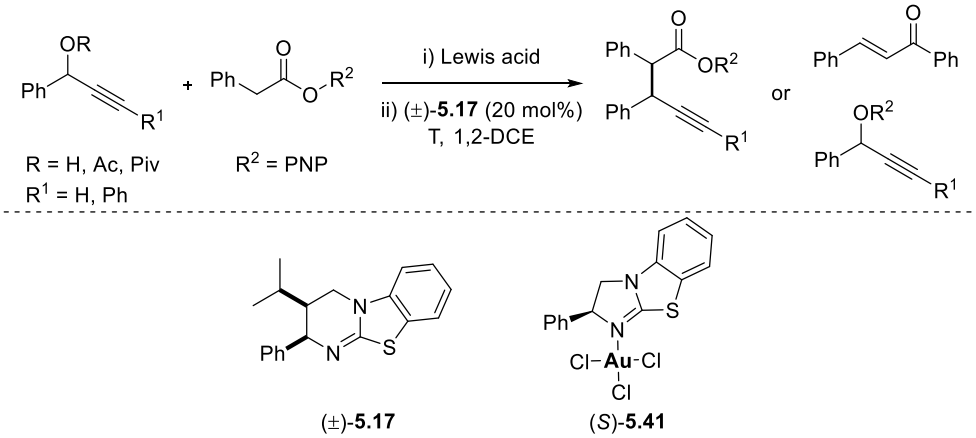
Initial investigations to react propargylic derivatives and phenylacetic esters were undertaken; a solution of 1-phenylprop-2-yn-1-ol (**5.31**) in 1,2-dichloroethane was subjected to a Au(III) source [$AuCl_3${(*S*)-BTM}] ((*S*)-**5.41**) activated with $NaBAr^F$, following the successful results obtained for the Friedel/Crafts arylation of propargylic alcohols to allenes (section 4.3.2).[49b] After 1 h at r.t., 4-nitrophenyl acetic ester **5.12,** and isothiourea (±)-HyperBTM (±)-**5.17** (20 mol%) were added to the mixture, together with Cs_2CO_3 (40 mol%) (Table 5.4, entry 1). The reaction was followed by tlc until disappearance of propargylic alkyne after 18 h, at r.t.. The analysis of the crude showed full conversion of the starting materials to a complex mixture of unidentified products, as indicated by NMR spectroscopy. Column chromatography of the crude mixture did not allow any significant understanding of the products formed. No traces of phenol addition into the propargylic alkyne was observed, as well as no trace of the targeted product.

Propargylic derivative **5.27**, with a Ph substituted internal alkyne, was also tested (Table 5.4, entry 2). Under similar reaction conditions to the above, and after heating the reaction to 50 °C, full conversion of starting materials was observed. However, in this case the crude mixture was too complex to analyse. Purification led to substantial decomposition, which was related to the formation of phenol in solution, derived from **5.12**. Thus, phenyl acetic anhydride **5.42** was reacted with **5.27**, in presence of 4 mol% of (*S*)-**5.41**, again

forming a mixture of products (entry 3). No traces of Meyer-Shuster rearranged product were formed when reacting propargylic alcohols.[53]

When using propargylic pivalate **5.35**, with phenylacetic ester **5.12**, the reaction showed similar conversions into several products even after heating up to reflux (Table 5.4, entry 4). Furthermore, recovery of the starting material **5.34**, propargylic acetate, was found when $Cu(OTf)_2$/(±)-BINAP combination was used instead of Au Lewis acid (entry 5).

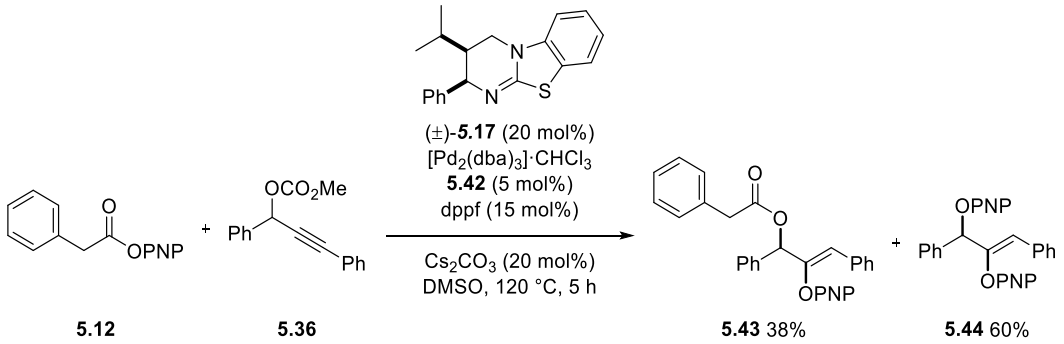
Table 5.4. Intermolecular enol addition to propargylic compounds.



Entry	Lewis acid (mol%)	R	R^1	R^2	T (°C)	Conv. (%)
1	(*S*)-**5.41** (4)/$NaBAr^F$ (8)	H	H	PNP	r.t.	mix.
2	(*S*)-**5.41** (4)/$NaBAr^F$ (8)	H	Ph	PNP	50	mix.
3	(*S*)-**5.41** (4)/$NaBAr^F$ (8)	H	Ph	$OC(O)CH_2Ph$	50	mix.
4	(*S*)-**5.41** (4)/$NaBAr^F$ (8)	Piv	H	PNP	84	mix.
5	$Cu(OTf)_2$ (10)/(±)BINAP (20)	Ac	H	PNP	84	[a]

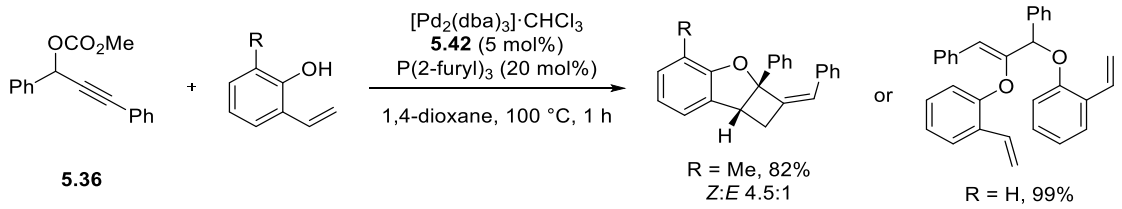
Reaction conditions: propargylic derivative **5.31**, **5.27**, **5.35** and **5.34** (0.1 mmol), **5.12** (0.1 mmol), solvent (0.02 M), Cs_2CO_3 (40 mol%), **5.**(±)-**3** (20 mol%), [Au] or [Cu] (4-10 mol%), $NaBAr^F$ (8 mol%) or (±)-BINAP (20 mol%), 18-48 h; [a] starting material recovered.

Clearer results were found when moving to Pd sources. Propargylic carbonate **5.36** was reacted with 2 equiv. of 4-nitrophenyl acetic acid **5.12**, in the presence of 5 mol% of $[Pd_2(dba)_3]\cdot CHCl_3$ (**5.42**), 1,1'-ferrocenediyl-bis(diphenylphosphine) ligand (dppf, 15 mol%), and (±)-**5.17** in DMSO solution at 120 °C (Scheme 5.20). After 5 h full conversion of starting materials was observed. The products recovered were analysed and fully characterised as **5.43** and **5.44**, and isolated in 38% and 60% yield, respectively.



Scheme 5.20. Initial results from palladium catalysed activation of propargylic carbonates.

Similar structures to **5.44** were reported by Yoshida and co-workers,[54] that explored a [2+2] cycloaddition of propargylic carbonates with 2-vinyl phenols, catalysed by complex **5.42** (Scheme 5.21). When phenols without substitution in the *ortho* position were used, regioselective formation of the diphenoxy substituted allylic compounds similar to **5.44** was observed.



Scheme 5.21. [2+2] cycloaddition from propargyl carbonates activated by palladium.[54]

Crystals were grown by slow evaporation of pentane into a CH_2Cl_2 saturated solution of **5.43** and analysed by X-ray crystallography. The structure obtained confirmed the arrangement of the synthesised structure as hypothesised by NMR and IR spectroscopy (Figure 5.8).

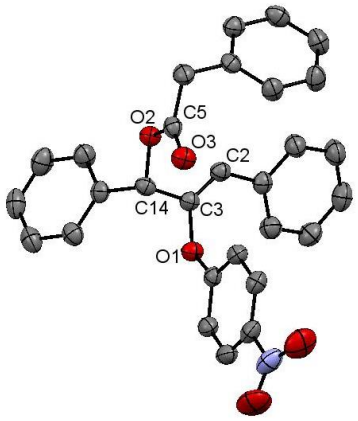


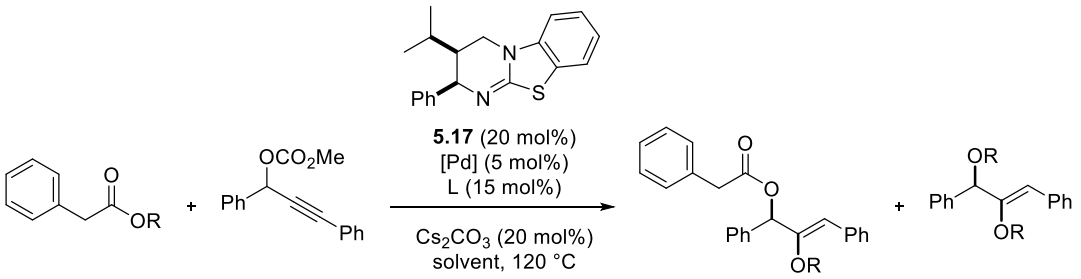
Figure 5.8. Thermal ellipsoid representation of **5.43** showing 50% probability. Most of H atoms were omitted for clarity.

Product **5.43** was unprecedented, and was probably formed from addition of the acid, formed by decomposition of **5.12** in solution, into a propargylic Pd intermediate. The addition of the enol into the activated Pd(II) propargylic species seemed therefore not to be favoured under the reaction conditions.

To see whether this product could be formed in regioselective and enantioselective fashion, the reaction was explored further (Table 5.5). When using THF, at 65 °C, under the same catalytic amount of Pd/ligand/ITU/base, **5.43** and **5.44** were isolated in 59% and 18% yield, respectively (entry 1). However, the reaction needed 5 days to proceed to substantial conversion, with a 1:1 ratio of propargylic carbonate **5.36** and 4-nitrophenyl acetic acid **5.12**. In an attempt to speed up the reaction, P(2-furyl)$_3$ ligand was used and mixed in a 1:3 ratio with the palladium precursor [$Pd_2(dba)_3$]·$CHCl_3$ **5.42** (entry 2); after 5 h 30 min a 1:1 ratio between **5.43** and **5.44** was observed. These results suggested that a more active Pd species could be formed by using monodentate ligands, however the different regioselectivity observed with the 2 ligands was not clear. These reactions were performed with (2*S*,3*R*)-**5.17**, however no enantioinduction was found for product **5.43** neither for **5.44**. The role of the isothiourea was analysed; by performing the reaction in absence of the organocatalyst, the products were formed with a 60% conversion of the starting materials, and **5.44** was the major product (entry 3). Other catalysts, such as [$Pd(PPh_3)_4$] or $Pd(OAc)_2/PPh_3$, were not active under the reaction conditions, and no conversion into desired products was observed after stirring overnight in THF at 65 °C (entries 4, 5).

Interestingly, the reaction could be performed also with 3,5(bistrifluoromethyl)phenyl 2-phenylacetate starting material; even if full conversions was observed by crude ^{1}H NMR into a 1:1 mixture after 18 h reaction at 65 °C, products **5.45** and **5.46** were isolated in 19% and 42% yield (Table 5.5, entry 6). By decreasing the temperature to 50 °C, 72% conversion of the starting materials was observed (entry 7). Reaction of other activated esters or anhydrides did not lead to any conversion to the products, but mainly mixtures of starting materials and decomposition (entries 8, 10). It was interesting to observe that in the presence of 3 Å MS (entry 11) the reaction did not proceed at r.t., with no conversion of starting materials.

Table 5.5. Reaction optimisation for the palladium catalysed activation of propargylic carbonates.



5.36 **A** **B**

R = PNP **5.43** **5.44**

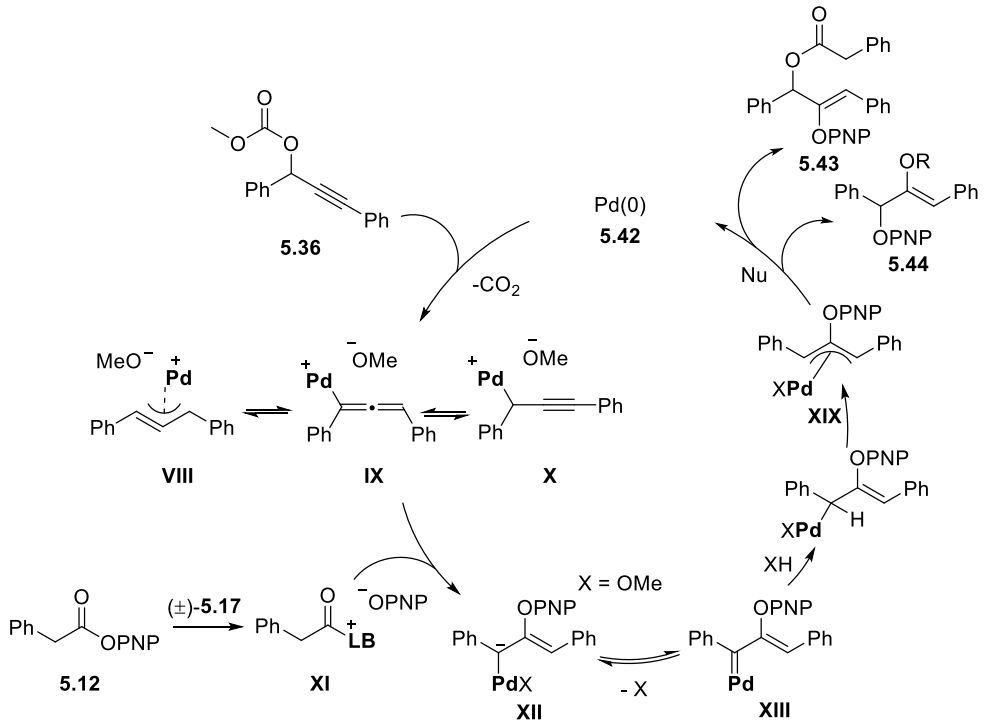
3,5-$(CF_3)_2C_6H$ **5.45** **5.46**

Entry	[Pd]	Ligand	ITU	R	T (°C)	Ratio[a] **A**:**B**
1	**5.42**	dppe	(2*S*,3*R*)-**5.17**	PNP	65	(59:18)[b]
2	**5.42**	P(2-furyl)$_3$	(2*S*,3*R*)-**5.17**	PNP	65	1:1[c]
3	**5.42**	P(2-furyl)$_3$	-	PNP	65	1:2.3[d]
4	[Pd(PPh_3)$_4$]	-	(±)-**5.17**	PNP	65	0:0[e]
5	[Pd(OAc)$_2$]	PPh_3	(±)-**5.17**	PNP	65	0:0[e]
6	**5.42**	P(2-furyl)$_3$	(±)-**5.17**	3,5-$(CF_3)_2C_6H_3$	65	1:1(19:42)[e]
7	**5.42**	P(2-furyl)$_3$	(±)-**5.17**	3,5-$(CF_3)_2C_6H_3$	50	1:1[e, f]
8	**5.42**	dppf	(±)-**5.17**	TCP	65	0:0[e]
9	**5.42**	P(2-furyl)$_3$	(±)-**5.17**	C_6F_5	65	0:0[e]
10	**5.42**	dppf	(±)-**5.17**	$COCH_2Ph$	65	0:0[e]
11	**5.42**	dppe	(±)-**5.17**	PNP	65	0:0[e, g]

Reaction conditions: **5.36** (0.1 mmol), phenylacetic esters (0.1-0.2 mmol), [Pd] (5 mol%), ligand (15 mol%), (±)-**5.17** (20 mol%), 5 h 30 min to 120 h; [a] isolated yield between parenthesis, conversions calculated by ^{1}H NMR with 1,4-dinitrobenzene (5 mg) as internal standard; [b] 120 h; [c] 5 h 30 min; [d] 60% conversion of starting materials; [e] 18 h; [f] 72% conversions of starting materials into **5.45**:**5.46**; [g] 3Å MS.

The results obtained can be explained by considering the proposed reaction mechanism (Scheme 5.22). Decarboxylative activation of **5.36** can be envisaged in the presence of Pd source **5.42**, with the formation of a σ-propargyl or σ-allenyl, or π-propargyl palladium(II) intermediates (**VIII**, **IX**, **X**). The methoxide counterion might act as an internal base. Moreover, reaction of **5.12** and (±)-**5.17** can form an ammonium enolate intermediate (**XI**) and release the phenoxide *in situ*. Therefore, nucleophilic attack of the phenoxide can be envisaged to form species **XII**, in equilibrium with a Pd carbene species (**XIII**). After protonation, this species can form a π-allyl species **XIV**, which can be attacked by a second nucleophile, either a second phenoxide or a carboxylate formed in situ by decomposition of the activated ester. The presence of H_2O might play a crucial role in this reaction, helping formation of the carboxylate, therefore explaining the results

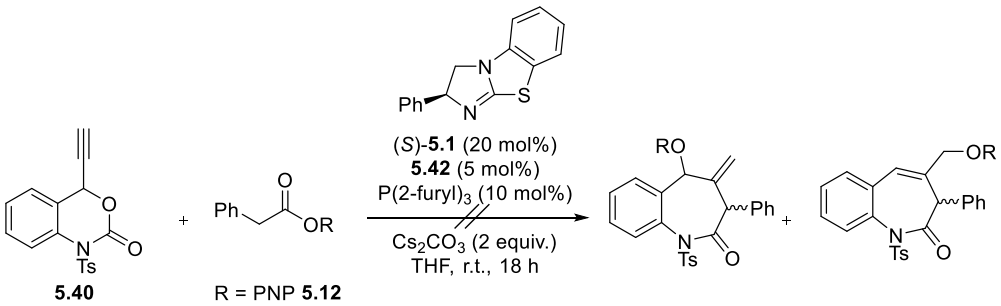
in the presence of molecular sieves. The role of the ITU in the reaction conditions is not clear, and it might be that the formation of an ammonium enolate does not occur under the reaction conditions, and an external base, such as the methoxide, attacks the ester instead.



Scheme 5.22. Possible mechanism for palladium catalysed reaction of **5.36** and **5.12** to **5.43** and **5.44**.

The interest on the new species obtained, and on the possible mechanism of formation, was expanded to reactions with ethynyl benzoxazinone **5.40** (Scheme 5.19). As already mentioned these species were found active towards activation with copper complexes, and the compatibility of Cu salts with isothioureas shown to be feasible (Scheme 7).[29-30] Thus, Pd activation of **5.40** was explored. Initial attempt to react **5.40** with phenylacetic esters **5.12** were performed (Scheme 5.23); the reaction was conducted in presence of the $[Pd_2(dba)_3]\cdot CHCl_3$ source (5 mol%), and P(2-furyl)$_3$ as ligand (10 mol%). Cs_2CO_3 (2 equiv.) and (*S*)-BTM (*S*)-**5.1** (20 mol%) were added sequentially, together with the activated esters **5.12**. The reaction showed full conversion of **5.40** after 18 h reaction at r.t., indicating a prompt reaction of benzoxazinone with the metal source. However, attempt to analyse the crude reaction mixture by ^{1}H NMR were unsuccessful due to the complex mixture obtained. Attempted purification of the reaction mixture by column chromatography led to further decomposition. Reaction of **5.40** and **5.12** was performed in presence of other Pd sources or of other bases, however the same outcome was

obtained. When using 3,5-bis(trifluoromethyl)phenyl 2-phenylacetate, mainly starting material was observed under the reaction conditions shown in Scheme 23. Unfortunately, by reacting other activated esters or phenylacetic acid mainly complex mixtures of products were obtained, followed by decomposition after column chromatography.



Scheme 5.23. Initial attempts in reaction of ethynyl benzoxazinone. Reaction condition: **5.40** (0.1 mmol), phenylacetic acid or phenylacetic esters (0.15-0.2 mmol), THF, Cs_2CO_3 (0.2 mmol), 5.1 (20 mol%), r.t., 18 h.

5.5. Conclusions and perspectives

The challenging cooperative catalysis of Au/ITU was explored. Under the chosen reaction conditions, the targeted products could not be achieved. A possible future target to tackle the cooperative catalysis might be a careful choice of the reaction conditions to allow the transformation to happen; possible self-quenching might be involved between Au(I) or Au(III) catalysts and Lewis base ITU. The use of other Lewis acid was explored but did not result in substantial conversion of the starting materials. The research around the dual Pd/ITU activation of propargylic alkynes gave some intriguing results; the synthesis of functionalised ester **5.43** and vinyl phenol **5.44** was explored, however low regioselectivity towards **5.43** was found. An attempted reaction mechanism was proposed after screening the reaction conditions, which suggested that a solely Pd catalysed mechanism was in operation for the transformation of propargylic carbonate with phenylacetic ester.

The choice of suitable substrates seems necessary in any future work. Interesting potential target starting materials might include a latent nucleophile, capable of turning over the Lewis base catalyst. This would decrease the complexity of the reaction and lead to an effective strategy for dual Lewis acid/Lewis base catalysis. The synthesis of new synthetic targets together with a deeper understanding of the reaction mechanism, and optimal

catalyst conditions will hopefully allow cooperative Au/ITU catalysis to the realisation of new catalytic process.

5.6. Experimental

Unless otherwise stated, all solvents and reagents were used as purchased and all reactions were performed under air. Anhydrous CH_2Cl_2, Et_2O, THF, and PhMe were obtained from an MBraun SPS-800 system. All other solvents and commercial reagents were used as received without further purification unless otherwise stated. Room temperature (r.t.) refers to 20–25 °C. Temperatures of 0 °C were obtained using ice/water. ^{1}H, $^{13}C\{^{1}H\}$ $^{19}F\{^{1}H\}$ NMR and $^{31}P\{^{1}H\}$ NMR spectra were recorded on Bruker Avance 500-300 MHz NMR spectrometers. In $CDCl_3$, ^{1}H and $^{13}C\{^{1}H\}$ NMR chemical shifts are reported relative to $CDCl_3$ at 7.26 ppm and 77.16 ppm, respectively. For the assignment of the ^{1}H and $^{13}C\{^{1}H\}$ NMR spectra 2D NMR (COSY, HSQC, HMBC) experiments were also performed. Coupling constants (*J*) are reported in Hertz (Hz). Multiplicities are indicated by: br s (broad singlet), s (singlet), d (doublet), t (triplet), q (quartet) and m (multiplet). For the assignment of the stereochemistry of the reported compounds, nuclear Overhauser effect spectroscopy (NOESY) experiments were also performed. Infrared spectra (νmax) were recorded on a Shimadzu IRAffinity-1 Fourier transform IR spectrophotometer using either thin film or solid using Pike MIRacle ATR accessory. Analysis was carried out using Shimadzu IRsolution v1.50 and only characteristic peaks are reported. Analytical thin layer chromatography was performed on pre-coated aluminium plates (Kieselgel 60 F254 silica). Plates were visualised under UV light (254 nm) or by staining with $KMnO_4$ followed by heating. Flash column chromatography was performed on Kieselgel 60 silica in the solvent system stated under a positive pressure of compressed air or on a Biotage® IsoleraTM 4, using Biotage® Snap Ultra or Biotage® KP Sil columns under the solvent system stated. HPLC analyses were obtained on a Shimadzu HPLC consisting of a DGU-20A5 degasser, LC-20AT liquid chromatography SIL-20AHT autosampler, CMB-20A communications bus module, SPDM20A diode array detector and a CTO-20A column oven that allows the temperature to be set from 25–40 °C. Separation was achieved using Chiralcel OD-H or Chiralpak AD-H columns.

5.5.1. General procedure for the synthesis of phenylacetic esters GP1:

The titled carboxylic acid (200/400 mg, 1.0 equiv.), substituted phenol (1 equiv.) were added sequentially to a flame-dried round-bottom flask and solubilised in EtOAc or dry CH_2Cl_2 (10 mL) at r. t. under an atmosphere of nitrogen. The reaction was cooled to 0 °C using an ice bath. DCC (1.1 equiv.) and 4-DMAP (0.1 equiv.) were added sequentially. The reaction was allowed to warm to room temperature and stirred for 2 hours. AcOH (1.5 mL) or aq. HCl (3 N, 2.0 mL) was added and the reaction placed in a freezer (–20 °C) for 6 h The resulting suspension was filtered over celite© and the residue washed with ice-cold EtOAc or CH_2Cl_2. The combined filtrates were successively washed with sat. aq. $NaHCO_3$, before being dried ($MgSO_4$) and concentrated under reduced pressure. The residue was purified by column chromatography with EtOAc:Petroleum Ether mixture 1:5)

4-Nitrophenyl 2-phenylacetate (**5.12**): Prepared according to GP1. The title compounds was obtained (2.78 g, 10 mmol, > 99%) as an off-white solid following purification by column chromatography, whose data where consistent to those reported in literature:[55] ^{1}H NMR (400 MHz, $CDCl_3$) δ = 8.25 (d, *J* = 9.2 Hz, 2H), 7.44 – 7.31 (m, 5H), 7.26 (t, *J* = 4.6 Hz, 2H), 3.90 (s, 2H).

2,4,6-Trichlorophenyl-2-phenylacetate: Prepared according to GP1. The title compound was obtained (270 mg, 0.85 mmol, 57%) as a colourless oil following purification by column chromatography whose data are consistent to those reported in literature:[26] ^{1}H NMR (400 MHz, $CDCl_3$): δ = 7.37–7.20 (m, 7H), 3.89 (s, 2H).

2,3,5,6-Tetraflourophenyl 2-phenylacetate: Prepared according to GP1. The title compounds was obtained (489.9 mg, 1.68 mmol, 58%) as an off-white solid following purification by column chromatography, whose data were consistent to those reported in literature:[26] ^{1}H NMR (400 MHz, CDCl3): δ = 7.48–7.28 (m, 5H), 6.96 (m, 1H), 3.96 (s, 2H); ^{19}F{^{1}H} NMR (376 MHz, CDCl3): δ = -138.76 – -139.35 (m), -152.23 – -153.98 (m).

Pentafluorophenyl 2-phenylacetate: prepared according to GP1. The title compound was obtained (184.1 mg, 0.6 mmol, 41%) as a colourless oil following purification by column

chromatography, whose data were consistent to those reported in literature:[56] ^{1}H NMR (300 MHz, $CDCl_3$) δ = 7.45 – 7.27 (m, 5H), 3.97 (s, 2H); $^{19}F\{^{1}H\}$ NMR (282 MHz, $CDCl_3$) δ = -152.40 – -152.72 (m), -157.82 (t, *J* = 21.7 Hz), -162.13 – -162.42 (m).

3,5-Bis(trifluoromethyl)phenyl 2-phenylacetate: prepared according to GP1. The title compounds was obtained (184.06 mg, 0.6 mmol, 41%) as a colourless oil following purification by column chromatography: ^{1}H NMR (400 MHz, $CDCl_3$) δ = 7.76 – 7.73 (m, 1H, H_{Ar}), 7.57 (t, *J* = 0.9 Hz, 2H, H_{Ar}), 7.44 – 7.32 (m, 4H, H_{Ar}), 3.91 (s, 2H, CH_2); $^{19}F\{^{1}H\}$ NMR (377 MHz, $CDCl_3$) δ = -62.94; $^{13}C\{^{1}H\}$ NMR (101 MHz, $CDCl_3$) δ = 169.3 (CO), 151.3 (Cq), 133.0 (d, $^{2}J_{CF}$ = 34.1 Hz), 129.4 (C_{Ar}), 129.0 (C_{Ar}), 126.9 (C_{Ar}), 122.8 (d, $^{1}J_{CF}$ = 273.0 Hz), 122.5 (d, $^{3}J_{CF}$ = 4.0 Hz), 121.5 (m), 41.3 (CH_2). FTIR (ATR) ν = 1774 (CO), 1462, 1369, 1276 cm^{-1}. LRMS (ESI) Calcd (%) for $C_{16}H_9F_6O_2$ ($M\text{-}H^+$) 347.0585, found 347.0583.

4-Nitrophenyl hept-6-ynoate (**5.19**): prepared according GP1. The title compound was obtained (187.9, 0.76 mmol, 76%) as an off-white solid by following purification by column chromatography. ^{1}H NMR (400 MHz,$CDCl_3$) δ = 8.31 – 8.24 (m, 2H, H_{Ar}), 7.31 – 7.26 (m, 2H, H_{Ar}), 2.65 (t, *J* = 7.4 Hz, 2H, CH_2), 2.28 (td, *J* = 7.0, 2.7 Hz, 2H, CH_2), 1.99 (t, *J* = 2.7 Hz, 1H, C≡CH), 1.90 (p, *J* = 7.4 Hz, 2H, CH_2), 1.71 – 1.62 (m, 2H, CH_2); $^{13}C\{^{1}H\}$ NMR (101 MHz, $CDCl_3$) δ = 171.0 (CO), 155.5 (Cq), 125.3 (CAr), 122.5 (CAr), 83.8 (C≡CH), 69.1 (C≡CH), 33.9 (CH_2CO), 27.8 (CH_2-CH_2), 23.9 (CH_2-CH_2), 18.3 ($CH_2C{\equiv}CH$); FTIR (ATR) ν = 1759, 1517, 1346 cm^{-1}; m.p. 58.3 – 58.9 °C.

4-Nitrophenyl 7-bromohept-6-ynoate (**5.22**): prepared according GP1. The title compound was obtained (530.0 mg, 1.62 mmol, 81%) as an off-white solid by following purification by column chromatography. ^{1}H NMR (500 MHz, $CDCl_3$) δ = 8.32 – 8.27 (m, 2H, H_{Ar}), 7.33 – 7.29 (m, 1H, H_{Ar}), 2.66 (t, *J* = 7.4 Hz, 2H, CH_2), 2.32 (d, *J* = 6.9 Hz, 2H, CH_2), 1.95 – 1.85 (m, 2H, CH_2), 1.71 – 1.64 (m, 2H, CH_2); $^{13}C\{^{1}H\}$ NMR (126 MHz, $CDCl_3$) δ = 170.9 (CO), 155.5 (Cq), 145.4 (C_{Ar}), 125.3 (C_{Ar}), 122.5 (C_{Ar}), 79.5 (C≡CBr), 38.7 (C≡CBr), 33.9 (CH_2CO), 27.6 (CH_2-CH_2), 23.9 (CH_2-CH_2), 19.5 (CH_2). FTIR (ATR) ν = 1761, 1514, 1344 cm^{-1}; m.p. >330 °C.

2-Phenylacetic anhydride: the compound was synthesised by following the reported literature conditions.[57] To a solution of phenylacetic acid (1g, 7.32 mmol, 1.0 equiv) in

PhMe (0.37 M in acid) at r.t. was added DCC (755,2 g, 3.66 mmol, 0.55 equiv) and the reaction stirred for 15 min. The reaction was filtered through celite© (PhMe) and concentrated under reduced pressure to give crude reaction mixture. Product was purified by recrystallisation (Et_2O) and obtained as an off-white solid (6.68 mmol 1.7 g, 91%). ^1H NMR (400 MHz, $CDCl_3$) δ = 7.32–7.38 (6H, m, H_{Ar}), 7.23–7.25 (4H, m, H_{Ar}), 3.76 (4H, s, $2CH_2$).

5.5.2. General procedure to the deprotection of trimethylsilane GP2:

The ethynyl silane (up to 2 mmol) was dissolved in MeOH (0.036 M) and K_2CO_3 (30 equiv.) was added. The reaction was stirred at r.t. for 1 h. The products were purified by column chromatography (eluent hexanes:EtOAc 10:1).

1-Phenylprop-2-yn-1-ol (**5.31**): prepared according to GP2. The compound was obtained (466.8 mg, 3.53 mmol, 88%) as a yellow oil whose data were consistent to those reported in literature.[58] ^1H NMR (400 MHz, $CDCl_3$) δ 7.60 – 7.52 (m, 2H), 7.44 – 7.31 (m, 3H), 5.48 (d, *J* = 2.2 Hz, 1H), 2.68 (d, *J* = 2.2 Hz, 1H), 2.06 (br s, 1H).

5.5.3. General procedure for the synthesis of propargylic alkynes GP3:

To a solution of ethynyltrimethylsilane (491.1 mg, 5mmol) or phenylacetylene (510.7 mg, 5 mmol) in THF (20 mL), was added 4.2 mL *n*BuLi (10.4 mmol, 2.5 M in hexane) at -30 °C over 5min. The solution was stirred for 30 min, then the flask was cooled to -78 °C, and 1.0g benzaldehyde (9.4 mmol) was added dropwise. After 30 min the reaction was quenched by the addition of sat. aq. NH_4Cl (15 mL). The aqueous phase was extracted with OEt_2 (3×30 mL). The combined organic layers were then washed with brine, dried over anhydrous sodium sulfate and filtered. After removing the solvent, the residue was purified by column chromatography on silica gel (eluent Petroleum ether:EtOAc 10:1).

1-Phenyl-3-(trimethylsilyl)prop-2-yn-1-ol (**5.26**): prepared according to GP5. The compound was obtained (980.8 mg, 4.8 mmol, 96%) as a yellow oil whose data were consistent to those reported in literature.[59] ^1H NMR (300 MHz, $CDCl_3$) δ = 7.66 (d, *J* = 7.8 Hz, 2H, H_{Ar}), 7.38 (m, 3 H, H_{Ar}), 7.52 (d, *J* = 7.8 Hz, 2H, H_{Ar}), 7.28—7.39 (m, 3 H, H_{Ar}), 5.42 (s, 1 H, CH), 2.63 (brs, 1 H, OH), 0.20 (s, 9 H, $3CH_3$).

1,3-Diphenylprop-2-yn-1-ol (**5.27**): prepared according to GP5. The compound was obtained (937.2 mg, 4.5 mmol, 90%) as a yellow oil, whose data were consistent to those reported in literature.[60] ^{1}H NMR (400 MHz, $CDCl_3$) δ = 7.63-7.65(d, *J* = 7.5 Hz, 2H, H_{Ar}), 7.50-7.52 (m, 2H, H_{Ar}), 7.31-7.50 (m, 6H, H_{Ar}), 5.71 (s, 1H, CH), 2.78 (s, 1H, OH).

5.5.4. General procedure for the synthesis of propargylic derivatives GP4:

a) The chosen anhydride (1.5 equiv.) or methylchloroformate (1.2 equiv.), was added to a mixture of propargylic alcohol (2.35 mmol) in CH_2Cl_2 (0.6 M) was added at 0 °C, together with 4-DMAP (10 mol%) and NEt_3 (1.5 equiv.) then the reaction mixture was warmed to room temperature and stirred for 2 h. The reaction was quenched with water (15 mL) and extracted with CH_2Cl_2 (3×15 mL). The combined organic layers were washed with brine, dried with $MgSO_4$, filtered, and evaporated to give the crude product. The crude product was purified by flash column chromatography on silica gel (EtOAc/hexane) to give the corresponding propargylic ester.

b) To a dry 50 mL 1-necked round-bottomed flask containing propargylic alcohol (1 mmol) was loaded into a dry round bottomed flask and dissolved in 20 mL of 1,2-DCE (5 mL), TsNCO (1 equiv.) dropwise via syringe over 5 min at room temperature. After complete addition the reaction was allowed to stir at room temperature for 1 hour. The solvent was then stripped off to provide the product. Further drying of this oil under vacuum produced a white solid which was used in subsequent transformations without any further purification.

1,3-Diphenylprop-2-yn-1-yl acetate (**5.34**): prepared following GP4.a. The compound was obtained (525.6 mg, 89%) as a yellow oil whose data were consistent to those found in literature.[59] ^{1}H NMR (400 MHz, $CDCl_3$): δ = 7.55–7.52 (m, 2H, H_{Ar}), 7.41–7.38 (m, 3H, H_{Ar}), 6.46 (d, *J* = 2.3 Hz, 1H, CH), 2.66 (d, *J* = 2.3 Hz, C≡CH), 2.11 (s, 3H, CH_3).

1-Phenylprop-2-yn-1-yl pivalate (**5.35**): prepared following GP4.a. The compound was obtained (432.6 mg, 2 mmol, 85%) as a yellow oil, whose data were consistent to those found in literature.[61] ^{1}H NMR (300 MHz, $CDCl_3$) δ = 7.50-7.53 (m, 2H, H_{Ar}), 7.36-7.39 (m, 3H, H_{Ar}), 6.43 (d, *J* = 2.3 Hz, 1H, CH), 2.62 (d, *J* = 2.3 Hz, 1H, C≡CH), 1.23 (s, 9H, $3CH_3$).

1,3-Diphenylprop-2-yn-1-yl methyl carbonate (**5.36**): prepared following GP4.a. The compound was obtained (134.4 mg, 0.5 mmol, 99%) as an colourless oil, whose data were consistent to those found in literature.[62] ^{1}H NMR (400 MHz, $CDCl_3$) δ = 7.63−7.61 (m, 2H, H_{Ar}), 7.49−7.47 (m, 2H, H_{Ar}), 7.44−7.39 (m, 3H, H_{Ar}), 7.34−7.29 (m, 3H, H_{Ar}), 6.53 (s, 1H, CH), 3.82 (s, 3H, CH_3).

1,3-Diphenylprop-2-yn-1-yl tosylcarbamate (**5.37**): prepared following GP4.b. The compound was obtained (405.4 mg, 79%) as an off-white solid, which data were consistent to those reported in literature.[63] ^{1}H NMR (500 MHz, $CDCl_3$) δ = 7.85 – 7.79 (m, 2H, H_{Ar}), 7.56 (dd, *J* = 7.8, 1.5 Hz, 2H, H_{Ar}), 7.39 – 7.28 (m, 4H, H_{Ar}), 7.28 – 7.23 (m, 8H, H_{Ar}), 7.14 – 7.09 (m, 2H, H_{Ar}), 5.57 (d, *J* = 9.2 Hz, 1H, CH), 4.83 (d, *J* = 9.2 Hz, 1H, NH), 2.33 (s, 3H, CH_3).

5.5.5. General procedure of synthesis benzoxazin-2one GP5:

To a solution of 2-aminobenzylalcohol **5.39** (1.23 g, 0.010 mol) in dichloromethane (10 mL), and pyridine (1 mL, 0.013 mol) was added TsCl (2.29 g, 0.012 mol) and the mixture was refluxed for 12 h. The solution was allowed to cool to room temperature and washed with hydrochloric acid (20 mL, 1 mol/L), brine (3×10 mL), and dried over $MgSO_4$. After removal of the solvent, the residue was crystallized from CH_2Cl_2/PhMe to give *N*-Ts 2-aminobenzylic alcohol (2.4 g, 86% yield). A suspension of PCC (2.6 g, 12 mmol) in dry CH_2Cl_2 (40 mL) and benzylalcohol (2.1 g, 8.0 mmol) in the same solvent (80 mL) was stirred at r.t. for 3 h. The raw product *N*-(2-formylphenyl)-4-methylbenzenesulfonamide (**5.38**) was crystallized from $CHCl_3$/EtOH (1:5, 24 ml) to yield the off-white solid (1.6 g, 5.8 mmol,73%), whose data were consistent to those reported in literature.[64] ^{1}H NMR (400 MHz, $CDCl_3$) δ = 10.77 (s, 1H, COH), 9.82 (s, 1H, NH), 7.76 (d, *J* = 8.3 Hz, 2H, H_{Ar}), 7.68 (d, *J* = 8.4 Hz, 1H, H_{Ar}), 7.59 (dd, *J* = 7.7, 1.5 Hz, 1H, H_{Ar}), 7.53 – 7.47 (m, 1H, H_{Ar}), 7.23 (d, *J* = 8.1 Hz, 2H, H_{Ar}), 7.16 (td, *J* = 7.6, 0.9 Hz, 1H, H_{Ar}), 2.36 (s, 3H, CH_3).

Under argon atmosphere, an oven dried 250 mL three-necked flask, equipped with a 100 mL pressure-equalizing dropping funnel, was charged with trimethylsilylacetylene (0.93 mL, 6.6 mmol) and anhydrous THF (20 mL). The solution was cooled to -94 °C (liquid N_2/acetone bath). *n*BuLi (2.64 mL, 2.5 M in hexane, 6.6 mmol) was added to the solution

dropwise over a period of 15 min. The reaction was then stirred at -94 °C for 30 min and the *N*-(2-formylphenyl)-4-methylbenzenesulfonamide **5.38** (825 mg, 3 mmol) was added. The reaction was stirred for 2 h at the same temperature. After this interval, a solution of triphosgene (888 mg, 3 mmol) in anhydrous THF (10 mL) was added dropwise over a period of 2 h. The yellow solution was maintained at -94 °C for 1 h, and the reaction was then carefully quenched by dropwise addition of H_2O over a period of 15 min. The resulting yellow solution was allowed to warm to r.t. After extraction with CH_2Cl_2 (3×15mL), the organic phase was separated, washed with brine, dried over $MgSO_4$, filtered and concentrated. The residue was purified by flash silica gel chromatography (Petrol ether/EtOAc/CH_2Cl_2= 20:1:1) to afford the title compound trimethylsilanylethynyl-benzoxazinanone (**5.40**) as a yellow solid. The compound was charged into a dry 100 mL flask along with anhydrous THF (20 mL). The flask was then cooled to -78 ºC and TBAF (2 mL, 2 mmol, 1.0 M solution in THF) was added dropwise. The resulting solution was stirred for 5 min at -78 ºC. The reaction was quenched with H_2O. The resulting red solution was allowed to warm to room temperature. The organic phase was separated, and aqueous phases were extracted with CH_2Cl_2 (3×15mL). The combined organic layers were washed with brine, dried over $MgSO_4$, filtered, and concentrated. The residue was purified by flash silica gel chromatography (Petrol ether/EtOAc/CH_2Cl_2= 25:1:1) to afford the title compound as white solid.

4-Ethynyl-1-tosyl-1,4-dihydro-2*H*-benzo[d][1,3]oxazin-2-one (**5.40**): prepared following GP5. The compound was obtained (330 mg, 1 mmol, 50% yield) as an off-white solid, whose data were consistent to those reported in literature. ^{1}H NMR (400 MHz, $CDCl_3$) δ = 8.24–7.84 (m, 2H, H_{Ar}), 7.61 (s, 1H, H_{Ar}), 7.53–7.29 (m, 4H, H_{Ar}), 7.26 (s, 1H, H_{Ar}), 5.85 (s, 1H, CH), 2.85 (s, 1H, C≡CH), 2.43 (s, 3H, CH_3).

5.5.6. Synthesis of vinyl esters and vinyl phenols:

In a scintillation vial propargylic carbonate or acetate (from 0.1-0.2 mmol) was dissolved in anhydrous THF. ITU (20 mol%), base (20 mol%) and the ester (1-2 equiv.) were added sequentially and the mixture was stirred at r.t. for 5 mins. Therefore Pd (5 mol%) and L (15-20 mol%) were added and the mixture stirred at 65 °C for 6-24 h. The reaction was monitored by tlc or by ^{1}H NMR until complete disappearance of the propargylic moiety was confirmed. After the reaction was completed the mixture was diluted with THF, filtered through a short plug of silica and concentrated under vacuum. The residue was then purified by flash column chromatography on silica gel using a solvent gradient (99:1 to 97:3 petrol:EtOAc) to afford the corresponding product.

(*E*)-4,4'-((1,3-Diphenylprop-2-ene-1,2-diyl)bis(oxy))bis(nitrobenzene) (**5.43**): the compound was synthesised using 4-nitrophenyl 2-phenylacetate **5.12** (0.144 mmol, 1.2 equiv.), propargylic carbonate **5.36** (31.96 mg, 0.12 mmol), and $[Pd_2(dba)_3]\cdot CHCl_3$ (6.2 mg, 5 mol%, $6\cdot10^{-3}$ mmol), dppf (9.9 mg, 15 mol%, $1.8\cdot10^{-2}$ mmol), (2*S*,3*R*)-HyperBTM (7.4 mg, 20 mol%, $2.4\cdot10^{-2}$ mmol) and Cs_2CO_3 (7.8 mg, 20 mol%, $2.4\cdot10^{-2}$ mmol). The reaction was stirred for 24 h at 65 °C. The crude product was purified by column chromatography to yield the desired product as a colourless oil (17 mg, 38 %). ^{1}H NMR (400 MHz, $CDCl_3$) δ = 8.09 – 8.02 (m, 2H, H_{Ar}), 7.35 (s, 5H, H_{Ar}), 7.33 – 7.27 (m, 2H, H_{Ar}), 7.25 – 7.14 (m, 3H, H_{Ar}), 6.99 – 6.94 (m, 2H, H_{Ar}), 6.38 (s, 1H, CHO), 6.23 (s, 1H, CH), 3.62 (s, 2H, CH_2); ^{13}C{^{1}H} NMR (126 MHz, $CDCl_3$) δ = 170.2 (CO), 160.8 (Cq), 147.2 (Cq), 143.5 (C_{Ar}), 136.4 (C_{Ar}), 134.9 (C_{Ar}), 133.3 (C_{Ar}), 132.5 (C_{Ar}), 130.7 (C_{Ar}), 129.4 (C_{Ar}), 129.12 (C_{Ar}), 128.9 (C_{Ar}), 128.8 (C_{Ar}), 128.7 (C_{Ar}), 128.5 (C_{Ar}), 128.4 (C_{Ar}), 127.5 (C_{Ar}), 127.5 (C_{Ar}), 126.0 (C_{Ar}), 125.5 (C_{Ar}), 119.2 (C=C), 116.0 (C=C), 75.4 (=CH), 41.7 (CH). FTIR (ATR) ν = 3028, 2923, 1737 (CO), 1589 (NO_2), 1338 cm^{-1}; m.p. 112.8 – 113.7 °C. HPLC: enantiomeric excess determined by HPLC with a Chiralpak AD-H column (95:5 hexanes:*i*PrOH, 1.0 ml/min, 254 nm); tr = 35.8 min, 40.7 min, racemic. LRMS (ESI+) Calcd (%) $C_{29}H_{23}NO_5$ (M-NO_2) 465.1576, found 420.1720.

(*E*)-4,4'-((1,3-Diphenylprop-2-ene-1,2-diyl)bis(oxy))bis(nitrobenzene) (**5.44**): the compound was synthesised using 4-nitrophenyl 2-phenylacetate **5.12** (37.1 mg, 0.144 mmol, 1.2 equiv.), propargylic carbonate **5.36** (31.9 mg, 0.12 mmol), and

$[Pd_2(dba)_3]\cdot CHCl_3$ (5 mol%, $6\cdot10^{-3}$ mmol, 6.21 mg), dppf (15 mol%, $1.8\cdot10^{-2}$ mmol, 9.9 mg), (2*S*,3*R*)-HyperBTM (20 mol%, $2.4\cdot10^{-2}$ mmol, 7.40 mg) and Cs_2CO_3 (20 mol%, $2.4\cdot10^{-2}$ mmol, 7.82 mg). The reaction was stirred for 24 h at 65 °C. The crude product was purified by column chromatography to yield the desired product as a colourless oil (36.9 mg, 67 %).^{1}H NMR (500 MHz, $CDCl_3$) δ = 8.14 – 8.05 (m, 4H, H_{Ar}), 7.47 – 7.42 (m, 2H, H_{Ar}), 7.42 – 7.33 (m, 5H, H_{Ar}), 7.24 – 7.17 (m, 3H, H_{Ar}), 7.03 – 6.98 (m, 2H, H_{Ar}), 6.93 – 6.87 (m, 2H, H_{Ar}), 6.49 (s, 1H, CHO), 5.86 (s, 1H, CH). $^{13}C\{^1H\}$ NMR (126 MHz, $CDCl_3$) δ = 162.2 (Cq), 160.9 (Cq), 147.5 (Cq), 142.8 (Cq), 142.2 (Cq), 136.2 (C_{Ar}), 132.3 (C_{Ar}), 129.3 (C_{Ar}), 129.2 (C_{Ar}), 129.2 (C_{Ar}), 128.8 (C_{Ar}), 128.7 (C_{Ar}), 127.0 (C_{Ar}), 126.0 (C_{Ar}), 125.9 (C_{Ar}), 120.2 (C_{Ar}), 116.1 (C=C), 115.9 (C=C), 81.2 (CH); FTIR (ATR) ν = 1587, 1510, 1489 (NO_2) cm^{-1}; m.p. 101.1 – 101.4 °C. HPLC: enantiomeric excess determined by HPLC with a Chiralpak AD-H column (96:4 hexanes : *i*PrOH, 1.0 ml/min, 254 nm); tr = 42.38 min, 48.17 min, racemic.

(*Z*)-5,5'-((1,3-Diphenylprop-2-ene-1,2-diyl)bis(oxy))bis(1,3-bis(trifluoromethyl)benzene) (**5.45**): the compound was synthesised using 3,5-bis(trifluoromethyl)phenyl 2-phenylacetate (0.2, 2 equiv.), propargylic carbonate **5.36** (26.6 mg, 0.1 mmol), and $[Pd_2(dba)_3]\cdot CHCl_3$ (5 mol%, $5\cdot10^{-3}$ mmol, 5.1 mg), P(2-furyl)$_3$ (20 mol%, $2\cdot10^{-2}$ mmol, 4.64 mg), (±)-HyperBTM (20 mol%, $2\cdot10^{-2}$ mmol, 5.8 mg) and Cs_2CO_3 (20 mol%, $2\cdot10^{-2}$ mmol, 6.51 mg). The reaction was stirred for 16 h at 65 °C. The crude product was purified by column chromatography to yield the desired product as a colourless oil (27 mg, 42 %) ^{1}H NMR (500 MHz, $CDCl_3$) δ = 7.52 – 7.45 (m, 4H, H_{Ar}), 7.45 – 7.35 (m, 7H, H_{Ar}), 7.31 – 7.19 (m, 5H, H_{Ar}), 6.57 (s, 1H, CHO), 5.89 (s, 1H, CH). $^{13}C\{^1H\}$ NMR (126 MHz, $CDCl_3$) δ = 157.8 (Cq), 156.5 (Cq), 147.4 (Cq), 135.9 (Cq), 132.9 (C_{Ar}, $^2J_{CF}$ = 20.89 Hz), 132.3 (C_{Ar}), 129.3 (C_{Ar}), 129.2 (C_{Ar}), 129.1 (C_{Ar}), 128.0 (CF $^1J_{CF}$ = 231.29 Hz), 128.8 (C_{Ar}), 124.1 (C_{Ar} $^3J_{CF}$ = 16.35 Hz), 121.9 (C_{Ar} $^3J_{CF}$ = 16.35 Hz), 120.7 (C_{Ar}), 119.1 (C_{Ar}), 116.6 (C=C), 116.2 (C=C), 115.4 (CAr $^4J_{CF}$ = 4.29 Hz), 81.6 (CH). $^{19}F\{^1H\}$ NMR (471 MHz, $CDCl_3$) δ -63.17, -63.20. FTIR (ATR): 1612, 1465, 1373, 1274 cm^{-1}. LRMS (ESI+) Calcd (%) for $C_{31}H_{24}F_6O_4$ (M+H_2O) 574.1579, found 574.1573.

(*Z*)-2-(3,5-Bis(trifluoromethyl)phenoxy)-1,3-diphenylallyl 2-phenylacetate (**5.46**): the compound was synthesised using 3,5-bis(trifluoromethyl)phenyl 2-phenylacetate (0.2

mmol, 2 equiv.), propargylic carbonate **5.36** (26.6 mg, 0.1 mmol), and $[Pd_2(dba)_3]\cdot CHCl_3$ (5 mol%, $5\cdot10^{-3}$ mmol, 5.1 mg), P(2-furyl)$_3$ (20 mol%, $2\cdot10^{-2}$ mmol, 4.6 mg), (±)-HyperBTM (20 mol%, $2\cdot10^{-2}$ mmol, 5.8 mg) and Cs_2CO_3 (20 mol%, $2\cdot10^{-2}$ mmol, 6.5 mg). The reaction was stirred for 16 h at 65 °C. The crude product was purified by flash column chromatography using a solvent gradient (99:1, petrol:ethyl acetate) to yield the desired product as a colourless oil (10 mg, 19%): ^{1}H NMR (500 MHz, $CDCl_3$) δ = 7.44 (s, 1H, H_{Ar}), 7.34 – 7.27 (m, 10H, H_{Ar}), 7.24 – 7.15 (m, 5H, H_{Ar}), 6.37 (s, 1H, CHO), 6.24 (s, 1H, CH), 3.62 (d, *J* = 1.7, 2H, CH_2). ^{13}C{^{1}H} NMR (126 MHz, $CDCl_3$) δ = 170.1 (CO), 156.5 (Cq), 147.3 (Cq), 136.4 (C_{Ar}), 132.9 (C_{Ar} $^{3}J_{CF}$ = 33.81 Hz), 132.9 (C_{Ar} $^{2}J_{CF}$ = 116.33 Hz), 132.5 (C_{Ar}), 129.4 (C_{Ar}), 129.1 (C_{Ar}), 128.9 (C=CH), 128.8 (C_{Ar}), 128.7 (C_{Ar}), 128.4 (C_{Ar}), 127.5 (C_{Ar}), 127.3 (C_{Ar}), 123.0 (CF $^{1}J_{CF}$ = 271 Hz), 119.5 (C=CH), 116.5 (C_{Ar}), 116.1 (C_{Ar} $^{4}J_{CF}$ = 4.40 Hz), 75.3 (CHO), 41.6 (CH_2); ^{19}F{^{1}H} NMR (471 MHz, $CDCl_3$) δ = -62.97 FTIR (ATR) ν = 2198, 2031, 1745 (CO), 1610, 1490 cm^{-1}.

5.7. Bibliography

1. V. L. Schramm, *Chem. Rev.*, 2006, **106**, 3029-3030.
2. R. Schlögl, *Angew. Chem. Int. Ed.*, 2015, **54**, 3465-3520.
3. P. I. Dalko and L. Moisan, *Angew. Chem. Int. Ed.*, 2004, **43**, 5138-5175.
4. P. I. Dalko and L. Moisan, *Angew. Chem. Int. Ed.*, 2001, **40**, 3726-3748.
5. O. Pàmies and J.-E. Bäckvall, *Chem. Rev.*, 2003, **103**, 3247-3262.
6. a) C. Zhong and X. Shi, *Eur J. Org. Chem.*, 2010, **2010**, 2999-3025; b) Z. Shao and H. Zhang, *Chem. Soc. Rev.*, 2009, **38**, 2745-2755.
7. Z. Du and Z. Shao, *Chem. Soc. Rev.*, 2013, **42**, 1337-1378.
8. S. P. Simonovich, J. F. Van Humbeck and D. W. C. MacMillan, *Chem. Sci.*, 2012, **3**, 58-61.
9. J. Seayad and B. List, *Org. Biomol. Chem.*, 2005, **3**, 719-724.
10. S. E. Denmark and G. L. Beutner, *Angew. Chem. Int. Ed.*, 2008, **47**, 1560-1638.
11. S. H. McCooey and S. J. Connon, *Angew. Chem.*, 2005, **117**, 6525-6528.
12. S. Mukherjee, J. W. Yang, S. Hoffmann and B. List, *Chem. Rev.*, 2007, **107**, 5471-5569.
13. B. List, R. A. Lerner and C. F. Barbas, *J. Am. Chem. Soc.*, 2000, **122**, 2395-2396.
14. A. Erkkilä, I. Majander and P. M. Pihko, *Chem. Rev.*, 2007, **107**, 5416-5470.

15. G. M. Lelais and D. W. C. MacMillan, *Aldrichima Acta*, 2006, **39**, 79–87.

16. T. D. Beeson, A. Mastracchio, J.-B. Hong, K. Ashton and D. W. C. MacMillan, *Science*, 2007, **316**, 582-585.

17. a) D. Enders and T. Balensiefer, *Acc. Chem. Res.*, 2004, **37**, 534-541; b) D. Enders, O. Niemeier and A. Henseler, *Chem. Rev.*, 2007, **107**, 5606-5655; c) G. A. Grasa, R. M. Kissling and S. P. Nolan, *Org. Lett.*, 2002, **4**, 3583-3586.

18. D. Enders and U. Kallfass, *Angew. Chem. Int. Ed.*, 2002, **41**, 1743-1745.

19. a) V. B. Birman, H. Jiang, X. Li, L. Guo and E. W. Uffman, *J. Am. Chem. Soc.*, 2006, **128**, 6536-6537; b) K. N. Van, L. C. Morrill, A. D. Smith and D. Romo, in *Lewis Base Catalysis in Organic Synthesis*, Wiley-VCH Verlag GmbH & Co. KGaA, 2016, pp. 527-654.

20. V. B. Birman, X. Li and Z. Han, *Org. Lett.*, 2007, **9**, 37-40.

21. T. H. West, D. S. B. Daniels, A. M. Z. Slawin and A. D. Smith, *J. Am. Chem. Soc.*, 2014, **136**, 4476-4479.

22. T. H. West, D. M. Walden, J. E. Taylor, A. C. Brueckner, R. C. Johnston, P. H.-Y. Cheong, G. C. Lloyd-Jones and A. D. Smith, *J. Am. Chem. Soc.*, 2017, **139**, 4366-4375.

23. a) M. E. Abbasov, B. M. Hudson, D. J. Tantillo and D. Romo, *J. Am. Chem. Soc.*, 2014, **136**, 4492-4495; b) P. Liu, X. Yang, V. B. Birman and K. N. Houk, *Org. Lett.*, 2012, **14**, 3288-3291; c) E. R. T. Robinson, D. M. Walden, C. Fallan, M. D. Greenhalgh, P. H.-Y. Cheong and A. D. Smith, *Chem. Sci.*, 2016, **7**, 6919-6927.

24. J. A. Kalow and A. G. Doyle, *J. Am. Chem. Soc.*, 2010, **132**, 3268-3269.

25. J. A. Kalow and A. G. Doyle, *J. Am. Chem. Soc.*, 2011, **133**, 16001-16012.

26. K. J. Schwarz, J. L. Amos, J. C. Klein, D. T. Do and T. N. Snaddon, *J. Am. Chem. Soc.*, 2016, **138**, 5214-5217.

27. X. Jiang, J. J. Beiger and J. F. Hartwig, *J. Am. Chem. Soc.*, 2017, **139**, 87-90.

28. S. S. M. Spoehrle, T. H. West, J. E. Taylor, A. M. Z. Slawin and A. D. Smith, *J. Am. Chem. Soc.*, 2017, **139**, 11895-11902.

29. J. Song, Z.-J. Zhang and L.-Z. Gong, *Angew. Chem. Int. Ed.*, 2017, **56**, 5212-5216.

30. X. Lu, L. Ge, C. Cheng, J. Chen, W. Cao and X. Wu, *Chem. Eur. J.*, 2017, **23**, 7689-7693.

31. a) A. S. K. Hashmi and C. Hubbert, *Angew. Chem. Int. Ed.*, 2010, **49**, 1010-1012; b) C. C. J. Loh and D. Enders, *Chem. Eur. J.*, 2012, **18**, 10212-10225.

32. D. M. Barber, H. Sanganee and D. J. Dixon, *Chem. Commun.*, 2011, **47**, 4379-4381.

33. J. T. Binder, B. Crone, T. T. Haug, H. Menz and S. F. Kirsch, *Org. Lett.*, 2008, **10**, 1025-1028.

34. K. L. Jensen, P. T. Franke, C. Arróniz, S. Kobbelgaard and K. A. Jørgensen, *Chem. Eur. J.*, 2010, **16**, 1750-1753.

35. M. E. Muratore, C. A. Holloway, A. W. Pilling, R. I. Storer, G. Trevitt and D. J. Dixon, *J. Am. Chem. Soc.*, 2009, **131**, 10796-10797.

36. Z.-Y. Han, H. Xiao, X.-H. Chen and L.-Z. Gong, *J. Am. Chem. Soc.*, 2009, **131**, 9182-9183.

37. X.-Y. Liu and C.-M. Che, *Org. Lett.*, 2009, **11**, 4204-4207.

38. V. Belting and N. Krause, *Org. Lett.*, 2006, **8**, 4489-4492.

39. C. Wang, Z.-Y. Han, H.-W. Luo and L.-Z. Gong, *Org. Lett.*, 2010, **12**, 2266-2269.

40. a) D. Monge, K. L. Jensen, P. T. Franke, L. Lykke and K. A. Jørgensen, *Chem. Eur. J.*, 2010, **16**, 9478-9484; b) C. C. J. Loh, J. Badorrek, G. Raabe and D. Enders, *Chem. Eur. J.*, 2011, **17**, 13409-13414.

41. M. F. A. Adamo, G. Bellini and S. Suresh, *Tetrahedron*, 2011, **67**, 5784-5788.

42. N. Marion, R. S. Ramón and S. P. Nolan, *J. Am. Chem. Soc.*, 2009, **131**, 448-449.

43. C. M. Krauter, A. S. K. Hashmi and M. Pernpointner, *ChemCatChem*, 2010, **2**, 1226-1230.

44. M. G. Capdevila, F. Benfatti, L. Zoli, M. Stenta and P. G. Cozzi, *Chem. Eur. J.*, 2010, **16**, 11237-11241.

45. a) M. Dryzhakov, E. Richmond and J. Moran, *Synthesis*, 2016, **48**, 935-959; b) H. Yamamoto, in *Comprehensive Organic Synthesis*, ed. I. Fleming, Pergamon, Oxford, 1991, pp. 81-98.

46. a) Y. Nishibayashi, M. D. Milton, Y. Inada, M. Yoshikawa, I. Wakiji, M. Hidai and S. Uemura, *Chem. Eur. J.*, 2005, **11**, 1433-1451; b) Y. Nishibayashi, I. Wakiji and M. Hidai, *J. Am. Chem. Soc.*, 2000, **122**, 11019-11020; c) Y. Nishibayashi, I. Wakiji, Y. Ishii, S. Uemura and M. Hidai, *J. Am. Chem. Soc.*, 2001, **123**, 3393-3394; d) Y. Inada, Y. Nishibayashi and S. Uemura, *Angew. Chem. Int. Ed.*, 2005, **44**, 7715-7717; e) K.

Motoyama, M. Ikeda, Y. Miyake and Y. Nishibayashi, *Organometallics*, 2012, **31**, 3426-3430.

47. S. C. Ammal, N. Yoshikai, Y. Inada, Y. Nishibayashi and E. Nakamura, *J. Am. Chem. Soc.*, 2005, **127**, 9428-9438.

48. a) M. Ikeda, Y. Miyake and Y. Nishibayashi, *Angew. Chem. Int. Ed.*, 2010, **49**, 7289-7293; b) A. Yoshida, G. Hattori, Y. Miyake and Y. Nishibayashi, *Org. Lett.*, 2011, **13**, 2460-2463.

49. a) M. Georgy, V. Boucard and J.-M. Campagne, *J. Am. Chem. Soc.*, 2005, **127**, 14180-14181; b) M. Georgy, V. Boucard, O. Debleds, C. D. Zotto and J.-M. Campagne, *Tetrahedron*, 2009, **65**, 1758-1766; c) A. Arcadi, M. Alfonsi, M. Chiarini and F. Marinelli, *J. Organomet. Chem.*, 2009, **694**, 576-582.

50. C.-F. Xu, M. Xu, L.-Q. Yang and C.-Y. Li, *J. Org. Chem.*, 2012, **77**, 3010-3016.

51. J. Tsuji and T. Mandai, *Angew. Chem. Int. Ed. Engl.*, 1996, **34**, 2589-2612.

52. a) I. Minami, M. Yuhara, H. Watanabe and J. Tsuji, *J. Organomet. Chem.*, 1987, **334**, 225-242; b) J. Tsuji, H. Watanabe, I. Minami and I. Shimizu, *J. Am. Chem. Soc.*, 1985, **107**, 2196-2198.

53. R. S. Ramón, S. Gaillard, A. M. Z. Slawin, A. Porta, A. D'Alfonso, G. Zanoni and S. P. Nolan, *Organometallics*, 2010, **29**, 3665-3668.

54. M. Yoshida, S. Ohno and K. Namba, *Angew. Chem. Int. Ed.*, 2013, **52**, 13597-13600.

55. A. J. Harnoy, I. Rosenbaum, E. Tirosh, Y. Ebenstein, R. Shaharabani, R. Beck and R. J. Amir, *J. Am. Chem. Soc.*, 2014, **136**, 7531-7534.

56. F. Damkaci and P. DeShong, *J. Am. Chem. Soc.*, 2003, **125**, 4408-4409.

57. L. C. Morrill, L. A. Ledingham, J.-P. Couturier, J. Bickel, A. D. Harper, C. Fallan and A. D. Smith, *Org. Biomol. Chem.*, 2014, **12**, 624-636.

58. L. Burroughs, L. Eccleshare, J. Ritchie, O. Kulkarni, B. Lygo, S. Woodward and W. Lewis, *Angew. Chem. Int. Ed.*, 2015, **54**, 10648-10651.

59. N. Sakai, H. Hori and Y. Ogiwara, *Eur J. Org. Chem.*, 2015, **2015**, 1905-1909.

60. X. Zhang, W. T. Teo, Sally and P. W. H. Chan, *J. Org. Chem.*, 2010, **75**, 6290-6293.

61. E. Rettenmeier, A. M. Schuster, M. Rudolph, F. Rominger, C. A. Gade and A. S. K. Hashmi, *Angew. Chem. Int. Ed.*, 2013, **52**, 5880-5884.

62. R. Shen, J. Yang, S. Zhu, C. Chen and L. Wu, *Adv. Synth. Catal.*, 2015, **357**, 1259-1269.

63. S. K. Alamsetti, A. K. Å. Persson and J.-E. Bäckvall, *Org. Lett.*, 2014, **16**, 1434-1437.

64. T. Zhang, Z. Qi, X. Zhang, L. Wu and X. Li, *Chem. Eur. J.*, 2014, **20**, 3283-3287.

6. Synthesis and application of organogold species

6.1. Introduction

C-H bonds are abundant in organic molecules. However, their high thermodynamic stability has posed the challenge of low chemical reactivity. A way to activate these is through reaction with transition metals to form more reactive species, such as C-M bonds, which can be followed by less energetically demanding functionalisation.[1] C-H bond functionalisation reactions have become powerful synthetic tools to access molecular complexity in a straightforward, and economical fashion. By using catalytic methods, prefunctionalisation steps can be avoided leading to potentially less wasteful processes. Researchers working in the field of homogeneous, and heterogeneous gold chemistry have realised the reactivity of this metal for C-H activation. Along with the alkynophilicity of gold for the π-activation of unsaturated substrates,[2] examples of C(sp^1)-H, C(sp^2)-H and C(sp^3)-H bond functionalisation have been used to enable catalytic organic transformations.[3] The study of intermediates in these transformations becomes necessary to achieve a better understanding about requirements of suitable gold systems for these processes.

As highlighted in chapter 1 (section 1.3.1), species containing C(sp)-Au bonds are readily formed from terminal alkynes (Figure 6.1, a).[4] C(sp^2)-Au species, such as vinyl-gold, aryl-gold and carbenoid species (section 1.3.2), can be formed from arenes, indoles, furans and oxazoles, *etc.* (Figure 6.1, b).[5,6] C(sp^3)-H bonds are however less acidic,[7] with representative pK_a values in water for methane (56) *vs* ethylene (44), and acetylene (25),[8] thus are less prone to activation. Catalytic reactions that involve C(sp^3)-Au intermediates are far less common.[9] Despite this, many stable C(sp^3)-Au complexes have been prepared, and characterised (Figure 6.1, c and d).[10]

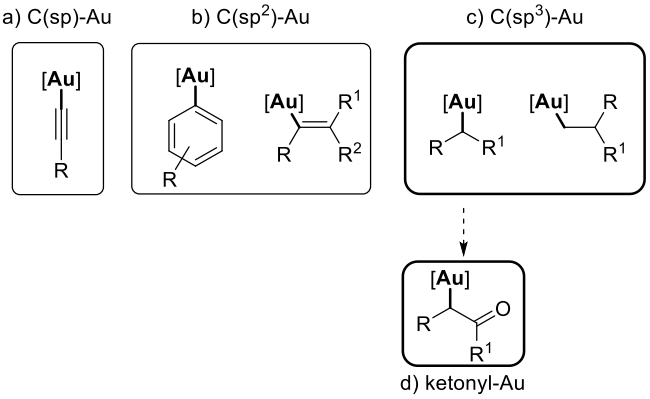


Figure 6.1. Organogold complexes: a) acetylide-Au;[4] b) aryl-, vinyl-Au;[5,6] c) alkyl-Au;[9,10] d) ketonyl-Au.[10]

It is easier to deprotonate C(sp^3)-H in ketones; thus organometallic C-enolates, or ketonyl complexes,[11] have been recognised as interesting compounds (Figure 6.1, d)[12] and proposed to be involved as short-lived intermediates in organic transformations.[9b,13] A range of synthetic methodologies have been used to form these metal-ketonyl derivatives,[11,14] with a range of transition metals, such as Rh, Ni, Pt, Pd and Au.[11,14c,14e,14g,15] The most commonly used procedures to synthesise these species include: i) oxidative addition of α-halogenated carbonyl compounds (Figure 6.2, route **A**),[16] or epoxides (route **B**)[17] to organometallic compounds; ii) transmetalation reactions using Hg salts (route **C**),[11,18] or reactions of main-group enolates with electrophilic metal centers;[13a,19] iii) reactions of carbonyl compounds with metal-hydroxides,[20] or metal-chloride complexes in the presence of bases, such as Ag_2O, KOH, and NaOH (route **D**).[14c,21]

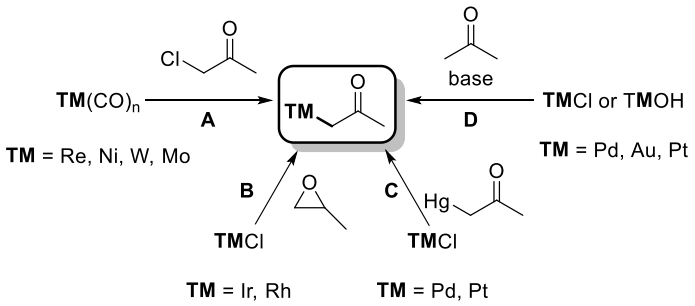


Figure 6.2. General methods for the synthesis of acetonyl-metal complexes. Routes **A** and **B**) oxidative addition;[16,17] route **C**) transmetalation;[11,13a,18-19] route **D)** direct C(sp^3)-H metalation.[14c,20-21]

With regard to gold (section 1.3.3), it is worth reporting some ketonyl-Au complexes that are of relevance to the work presented in this chapter. The synthesis of ketonyl-Au(III) complexes *via* auration of acetone was reported in 1989 by Vicente (Figure 6.3, a).[22] The

authors showed that an ancillary bidentate ligand, bound to the metal centre could promote the formation of an acetonyl-gold complex. Cinellu isolated the structure of an acetonyl-Au(III) complex bearing a *C*,*N*-cyclometalated ligand in 1996.[23] Ketonyl-Au(III) complexes, bearing a 2-phenylpyridine (ppy) chelating ligand, were reported by Fan in 2004.[24] Furthermore, Ito synthesised and fully characterised stable ketonyl-, and homoketonyl-Au(I) complexes bearing triphenylphosphine as ancillary ligand, through addition of silylated vinyl ethers or epoxides to [AuCl(PPh_3)] (Figure 6.3, b).[25] Crystal structures of acetonyl-Au(I) phosphine complexes, and analogues were reported by the groups of Kuzmina, and Laguna.[9b,26]

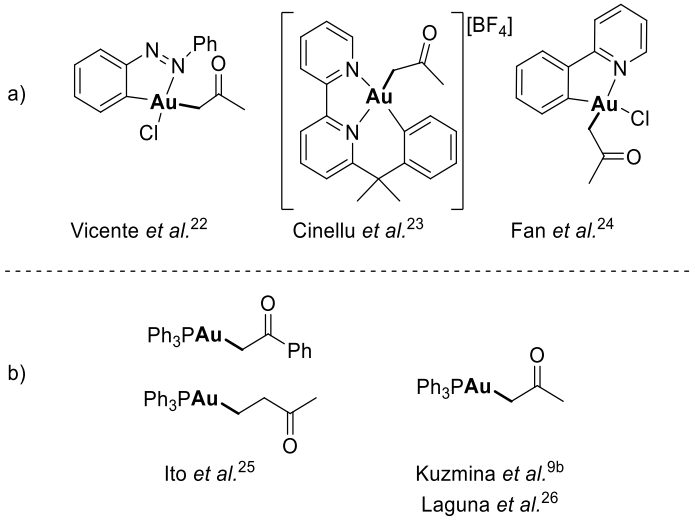


Figure 6.3. Examples of a) acetonyl-Au(III), and b) ketonyl-Au(I) complexes.

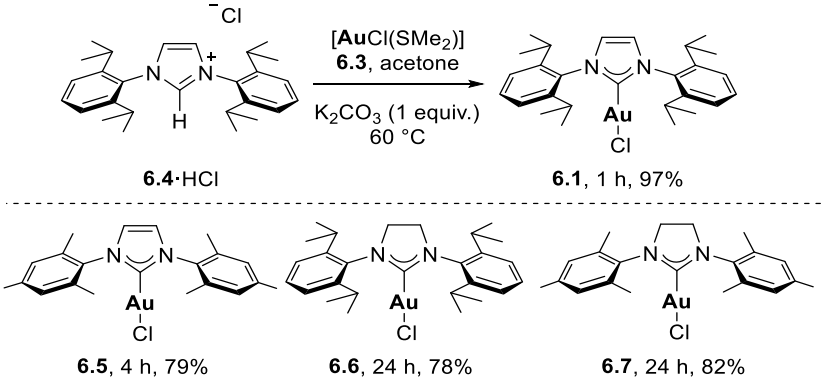
To the best of our knowledge, at the time of this study no examples of ketonyl-Au compounds bearing N-heterocyclic carbenes had been reported. Herein, the *serendipitous* discovery of acetonyl-gold(I) NHC complexes, and the stoichiometric and catalytic study of their reactivity is disclosed. To complement the family of low molecular weight C(sp^3)-Au species, examples of acetophenone-, and acetonitrile-Au complexes are reported together with their characterisation. Initial insights into the redox chemistry of these complexes are also discussed.

6.2. From side products to valuable synthons

Among gold complexes, [AuCl(IPr)] (**6.1**), [Au(OH)(IPr)] (**6.2**), and analogous complexes bearing different NHC ligands are recognised as valuable precursors for several organogold derivatives (section 1.2.1).[27] Concerning the synthesis of **6.1**, a

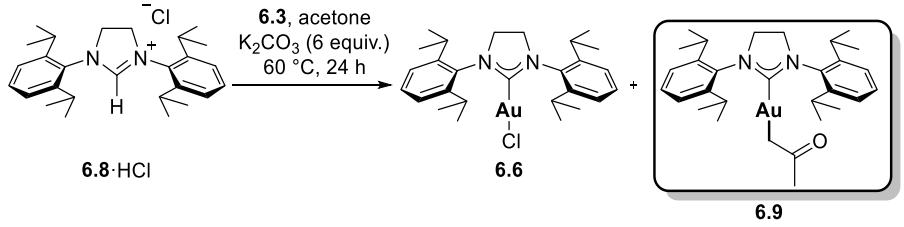
number of synthethic routes have been developed (see Scheme 1.2): a) the generation of a free carbene, followed by reaction with a gold source, [AuCl(SMe$_2$)] (**6.3**);[28] b) the carbene transfer route from a Ag-,[29] or Cu-NHC[30] precursors; c) the reaction of **6.3** with an imidazolium salt, such as IPr·HCl (**6.4**·HCl) in the presence of an equimolar amount a of weak inorganic base, K_2CO_3.[31]

The third method, starting from an imidazolium salt is the most straightforward route to access several [AuCl(NHC)] complexes (Scheme 6.1). The reaction is usually performed in acetone at 60 °C, with the reaction time dependant on the nature of the NHC·HCl being used. For example, under the same reaction conditions, **6.1** and [AuCl(IMes)] (**6.5**) are obtained in 1 h and 4 h respectively, while the synthesis of the saturated analogues [AuCl(SIPr)] (**6.6**), and [AuCl(SIMes)] (**6.7**) require 24 h.



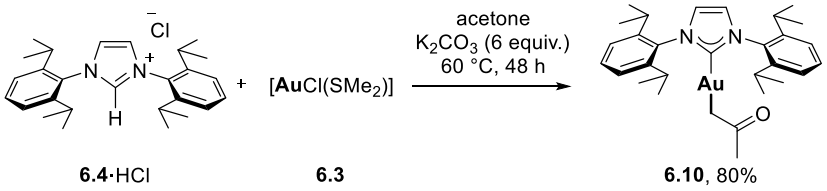
Scheme 6.1. Straightforward procedure to [AuCl(NHC)] complexes from NHC·HCl salts.

In an effort to reduce the reaction time for the synthesis of chloride-gold(I) complexes bearing saturated NHC ligands, a large excess of K_2CO_3 (6 equiv.) was added to the reaction mixture. When SIPr·HCl (**6.8**·HCl) was reacted with **6.3** and an excess of base, a mixture of complexes was obtained (Scheme 6.2); [AuCl(SIPr)] **6.6**, and a new Au(I)-SIPr derivative were obtained in a 1.3:1 ratio. ^{1}H and ^{13}C{^{1}H} NMR spectroscopic analysis of the mixture allowed characterisation of the new species as [Au(CH$_2$C(O)CH$_3$)(SIPr)] (**6.9**).



Scheme 6.2. Synthesis of **6.9** from **6.8**·HCl salt.

The synthesis of the derivative bearing the unsaturated and commercially available IPr·HCl (**6.4**·HCl) salt was explored next. Equimolar amounts of **6.4**·HCl, and [AuCl(SMe$_2$)] **6.3** were stirred in acetone at 60 °C in the presence of 6 equiv. of K_2CO_3. After 48 h, full conversion to [Au($CH_2C(O)CH_3$)(IPr)] (**6.10**) was obtained, with product isolated in 80% yield as a colourless solid (Scheme 6.3).



6.4·HCl **6.3** **6.10**, 80%

Scheme 6.3. Synthesis of **6.10** from **6.4**·HCl.

The new air and moisture stable complex **6.10** was fully characterised by NMR and IR spectroscopy, elemental analysis and single-crystal X-ray diffraction studies. The ^{1}H NMR spectrum in $CDCl_3$ showed a singlet at 2.06 ppm corresponding to the -CH_2 group, and a singlet at 1.54 ppm that was assigned to the -CH_3 moiety, indicating the effective functionalisation of acetone. The $^{13}C\{^1H\}$ NMR spectrum showed the carboxyl peak at 212.13 ppm. The FTIR (ATR) spectrum of **6.10** showed a strong absorption band at 1643 cm^{-1}, corresponding to the stretching frequency of the carbonyl group, ν_{CO}, in agreement with previously reported acetonyl-Au compounds.[22c]

Suitable crystals for X-ray diffraction analysis were grown by slow diffusion of pentane into a saturated solution of **6.10** in CH_2Cl_2 (Figure 6.4).[32] The structure of the complex displays a linear geometry, usual for Au(I) complexes,[25a] with a $C_{carbene}$-Au-CH_2 angle of 175.7(3)°. The Au-$C_{carbene}$ distance of 2.024(7) Å lies in the typical range for gold(I) species bearing NHC ligands.[25a,27] Other relevant distances are Au-CH_2 of 2.091(9) Å, CH_2-CO, 1.456(12) Å and C=O, 1.230(11) Å, in agreement with previously reported Au-acetonyl complexes.[24-25,27]

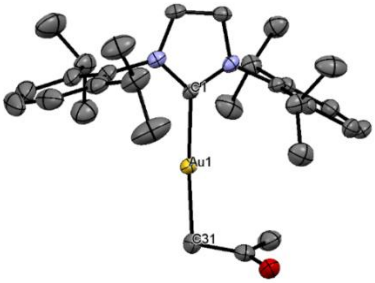
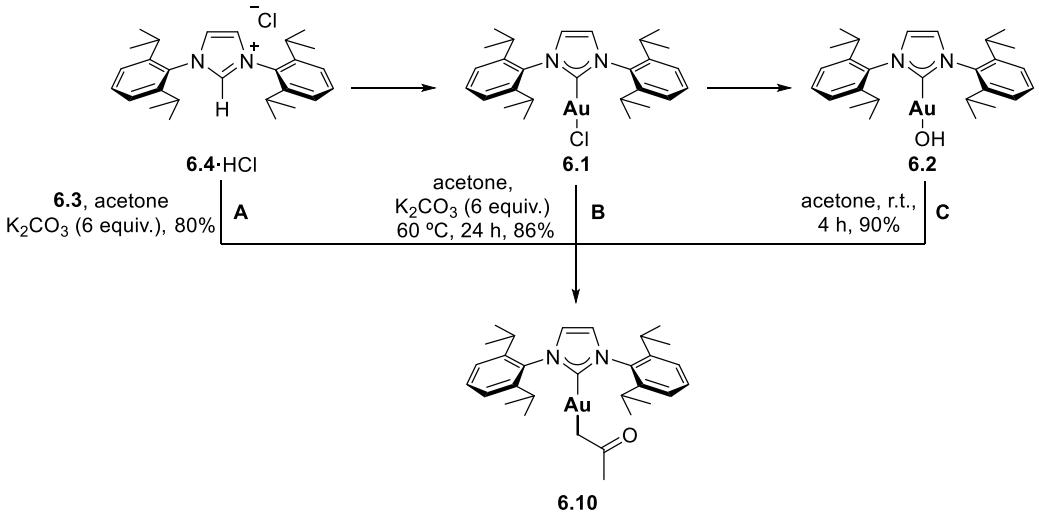


Figure 6.4. Thermal ellipsoid representation of **6.10** showing 50% probability. All H atoms were omitted for clarity. Selected bond angles (°), and lengths (Å): C1-Au-C31 175.7(3)°; Au-C1 2.024(7) Å; Au-C31 of 2.091(9) Å; C31-32 1.456(12) Å, C32-O32 of 1.230(11) Å.

Different synthetic approaches to access the acetonyl-Au(I) complexes became the main target.[66] Using IPr·HCl, **6.4**·HCl, as the proligand, the addition of KOH (6 equiv.) provided **6.10** in 47% after 48 h. In contrast the use of NEt_3 (6 equiv.) provided only **6.1**, the chloride-Au(I) derivative. K_2CO_3 was therefore chosen as the best base to promote this transformation (Scheme 6.4, route **A**).

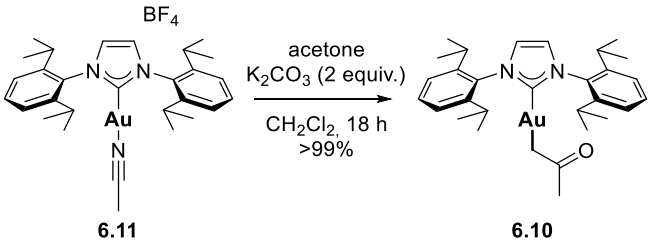
The accessibility of **6.10** was investigated starting from the well-defined [AuCl(IPr)] complex **6.1**. Treatment of **6.1** with 6 equiv. of K_2CO_3 in acetone at 60 °C gave full conversion to the acetonyl complex **6.10** after 24 h (Scheme 6.4, route **B**). The complex was isolated in 84% yield, which correspond to an overall yield of 81% including the preparation of [AuCl(IPr)] from [AuCl(SMe_2)].[31]

[Au($CH_2C(O)CH_3$)(IPr)] was also obtained in 90% yield by protonolysis of [Au(OH)(IPr)] **6.2**, in acetone at r.t. for 4 h (Scheme 6.4, route **C**). The use of an external base was not required under these reaction conditions, due to the Brønsted basic hydroxide ligand on the gold centre in **6.2**.[4,33] An overall yield of 86% was obtained, when taking into account the preparation of [Au(OH)(IPr)].[33,34]



Scheme 6.4. Synthetic routes towards **6.10**: routes **A**, **B** and **C**.

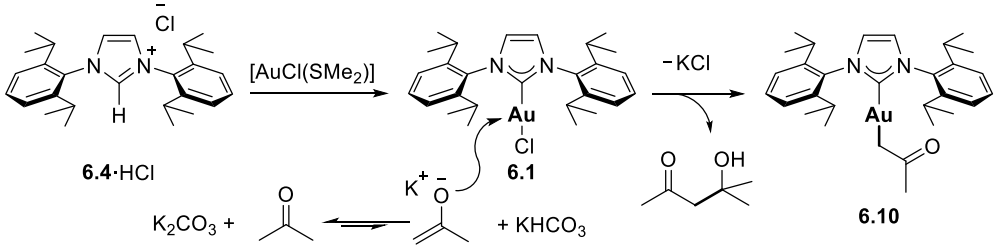
The acetonyl complex **6.10** could also be obtained by reaction of [Au(IPr)(NCCH$_3$)][BF$_4$] (**6.11**)[35] with an excess of acetone in CH_2Cl_2 in presence of 2 equiv. of K_2CO_3 (Scheme 6.5). Complex **6.11** was fully converted into **6.10** at r.t. after 18 h reaction.



Scheme 6.5. Synthesis of **6.10** from **6.11**.

The mechanism for the formation of the acetonyl complex was proposed; following route **A** (Scheme 6.4) the initial formation of [AuCl(IPr)] **6.1** was observed by ^{1}H NMR spectroscopy. From this species, route **A** and **B** proceed most likely *via* the same mechanism (Scheme 6.6); the large excess of K_2CO_3 would promote the deprotonation of acetone generating the corresponding enolate, which would react with the soft electrophilic gold centre, affording **6.10** and KCl. This hypothesis was supported by the identification of the product of the base promoted aldol condensation of acetone, 4-hydroxy-4-methyl-2-pentanone, in the reaction mixture, which was easily removed by pentane washes. No gold complexes arising from the reaction of this side product to gold were observed under the reaction conditions. As further support of the hypothesis, the formation of **6.10** was not observed when NEt_3 was used as base, suggesting that formation of KCl may provide a driving force for this reaction.

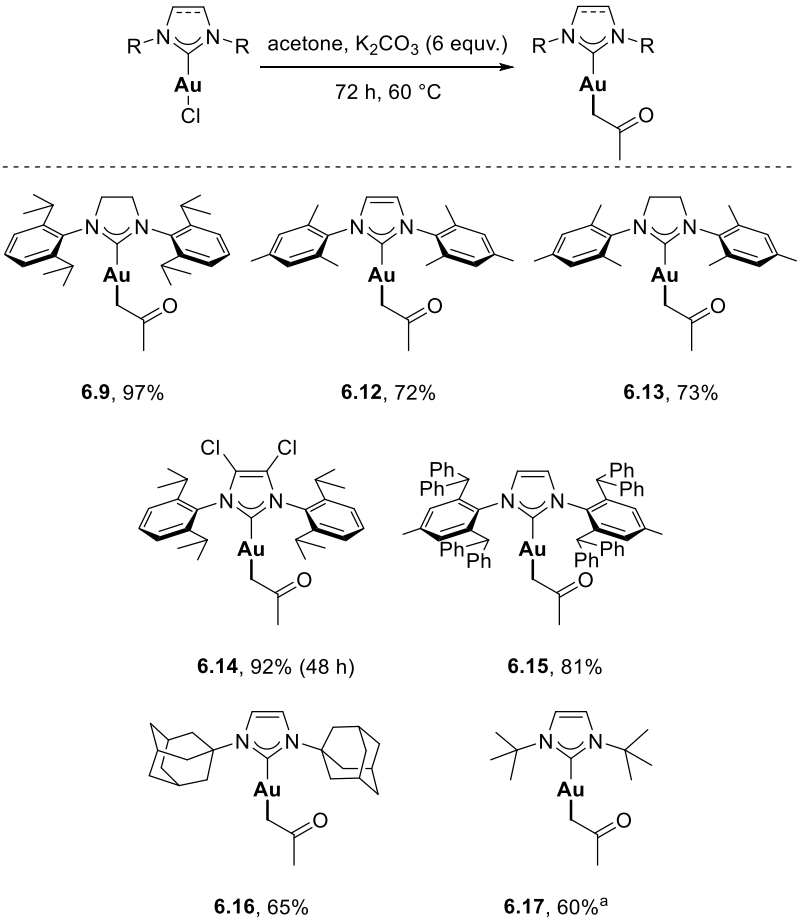
Concerning route **C** (Scheme 6.4), [Au(OH)(IPr)] (**6.2**) has been shown to deprotonate species with pK_a up to 31 (DMSO),[33] and therefore is expected that the Brønsted basic gold centre will be capable of deprotonating acetone (pK_a DMSO = 26.5)[8] to provide **6.10** and water.



Scheme 6.5. Proposed reaction mechanism for the synthesis of **6.10**.

The preparation of various ketonyl-Au derivatives was explored next. Initially, acetonyl-Au derivatives bearing NHC ligands, with a variety of electronic and steric properties were synthesised. When following route **A** (Scheme 6.4), unsuccessful results were obtained for SIPr·HCl and SIMes·HCl: performing the reactions under the optimised conditions (6 equiv. of K_2CO_3, acetone, 60 °C, 6 days) led to a mixture of chloride- and acetonyl-Au species 1:1 ratio and 1:2 ratios with SIPr and SIMes, respectively.

In these cases, it was found that route **B** (Scheme 6.4) was a more suitable synthethic methodology. This approach was convenient as [AuCl(NHC)] complexes where either readily accessible or commercially available.[27,31] This route was preferred over route **C**, as the synthesis and isolation of some [Au(OH)(NHC)] derivatives required inert conditions,[36] moreover reducing the number of synthetic steps. Thus, several [Au($CH_2C(O)CH_3$)(NHC)] derivatives bearing SIPr (**6.9**), IMes (**6.12**), SIMes (**6.13**), IPr^{Cl} (**6.14**), IPr* (**6.15**), IAd (**6.16**) and I*t*Bu (**6.17**) were synthesised (Scheme 6.7). All complexes were obtained in good to excellent yields (65–97%). The reaction times were usually 72 h, however compound **6.14** was obtained after 48 h.



Scheme 6.7. Family of acetonyl-Au(I) NHC complexes; [a]10 equiv. of K_2CO_3.

The complexes were fully characterised by NMR spectroscopy (Table 6.1). The ^{1}H NMR spectra of the complexes in $CDCl_3$ showed two diagnostic singlets corresponding to the -CH_2 and -CH_3 moieties of the acetonyl group. In the case of complexes **6.9**–**6.15**, bearing *N*-aryl substituted NHC ligands, these signals appeared in the range of 1.99−2.33 ppm for the -CH_2 group, and 1.44−1.67 ppm for the -CH_3 group (entries 1-6). These resonances are significantly shifted downfield for the complexes bearing *N*-alkyl substituents **6.16** and **6.17** (2.64−2.62 ppm for -CH_2 group; 2.21−2.20 ppm for -CH_3 group), with these ligand representing the most electron-donating of this series of NHC derivatives (entries 7, 8).[37] The ^{13}C{^{1}H} NMR spectra of complexes **6.9**–**6.15** showed the presence of two characteristic peaks, such as the carbenic carbon atom ranging from 186.55–212.01 ppm, and the carbonyl signal ranging from 212.12–213.07 ppm.

The IR analysis showed strong adsorption bands around 1650 cm^{-1} corresponding to the C=O stretching frequency of the functionalised acetone.[22]

Table 6.1. NMR, and IR spectroscopic data for **6.9**–**6.17**.

Entry	Complex	$\delta(CH_2)$(ppm)[a]	$\delta(CH_3)$(ppm)[a]	$\delta(C_{carbene})$(ppm)[b]	ν_{CO} (cm^{-1}) [c]
1	**6.10**	2.06	1.53	193.06	1643
2	**6.9**	1.99	1.44	212.01	1643
3	**6.12**	2.10	1.64	191.31	1643
4	**6.13**	2.02	1.54	211.58	1645
5	**6.14**	2.06	1.52	193.01	1651
6	**6.15**	2.33	1.67	192.61	1651
7	**6.16**	2.64	2.21	186.55	1643
8	**6.17**	2.62	2.20	188.05	1618

[a] ^{1}H NMR ($CDCl_3$); [b] $^{13}C\{^{1}H\}$ deptq NMR ($CDCl_3$); [c] FTIR (ATR).

Single crystals of complexes **6.9**, **6.12**, **6.14**, **6.15** and **6.16** were grown by slow diffusion of pentane into saturated CH_2Cl_2 or THF solutions.[38] Their structures were unambiguously characterised by X-ray diffraction analysis (Figure 6.5).

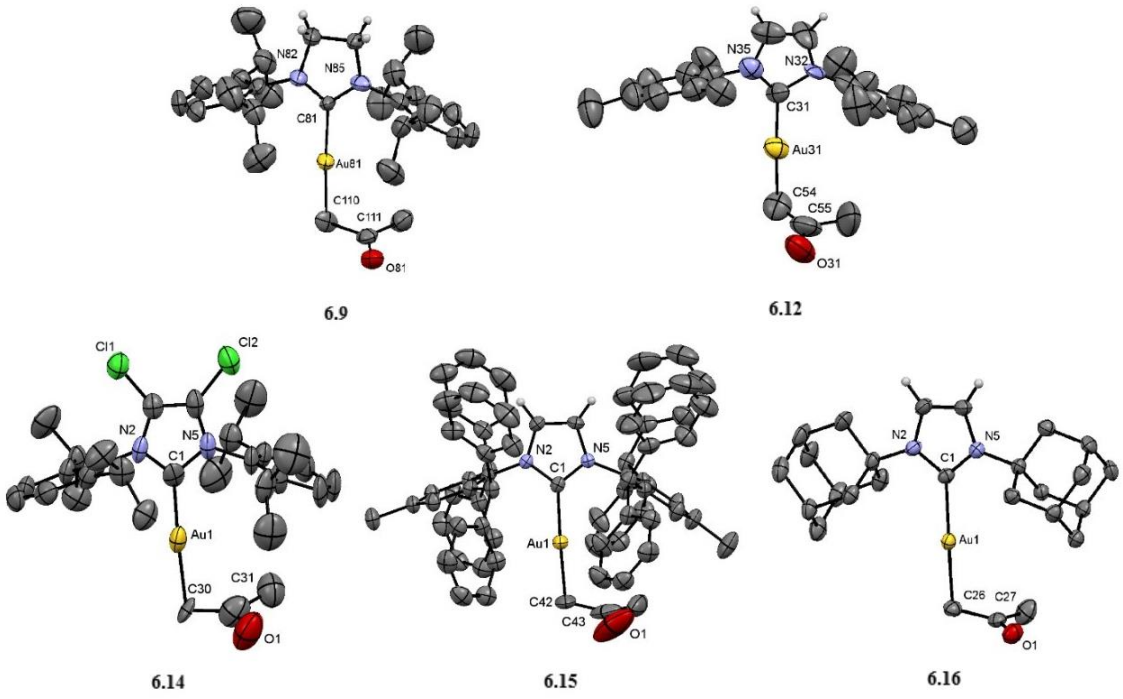


Figure 6.5. Thermal ellipsoid representations of **6.9**, **6.12**, **6.14**, **6.15**, and **6.16** showing 50% probability. Most of the H atoms were omitted for clarity. Two independent molecules were found in the crystal lattice of **6.12**, and **6.15**; while 4 independent molecules were found in **6.9**. In these three cases, the thermal ellipsoid representation of one of the molecules is shown in the Figure.

The compounds showed characteristic Au(I) linear geometry (Table 6.2). The Au-$C_{carbene}$, and Au-CH_2 distances were around 2 Å, with the former slightly shorter than the latter. Compound **6.14**, [Au($CH_2C(O)CH_3$)(IPr^{Cl})], deviated slightly from the trend observed for the other acetonyl-Au complexes with a longer Au-CH_2 bond of 2.222(9) Å (entry 4). Interestingly, the angles between Au-CH_2-C(O) varied from the expected angle of 109.5° of a C(sp^3); whilst in **6.12** Au-CH_2-C(O) was of 110° (entry 3), an angle of 94.7° was found in complex **6.14** (entry 4), deviating greatly from the expected value. This deviation was found to be common in other acetonyl compounds found in literature.[22b,22c,25a] The flattening of Au-CH_2-C(O) angle might suggest that a partial rehybridisation of the C(sp^3) to C(sp^2) might occur, which might reflect into the Au-C bond, decreasing the σ-interaction, while increasing π-ones. The CH_2-C(O) bond length in **6.14** was of 1.497(16) Å (entry 4), shorter compared to the same value for acetone (~1.52 Å), which might support the rehybridization of the C atom. In contrast the CH_2-C(O) bond length in **6.12** was found to be even shorter (1.45(3) Å and 1.38(4) Å), while the C atom retained the tetrahedral geometry (entry 3).

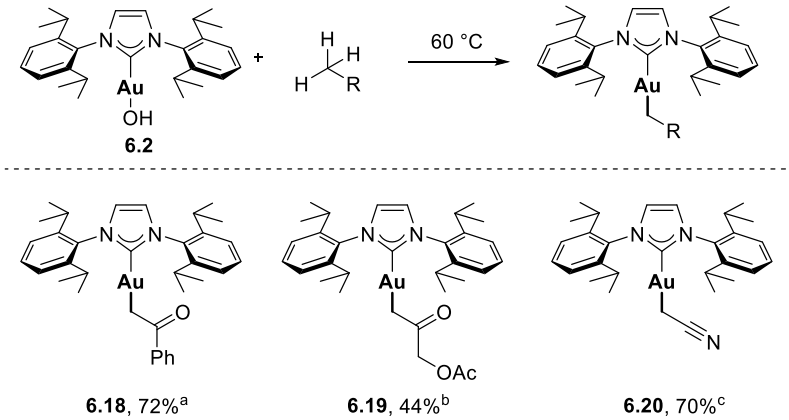
Table 6.2. Significant X-ray crystallographic data: angles (deg), and length (Å)

Entry	Complex	C_{carb}-Au-CH_2 (°)	Au-CH_2-C (°)	Au-CH_2 (Å)	CH_2-C(O) (Å)
1	**6.10**	175.7(3)	103.1(5)	2.091(9)	1.456(12)
2[a]	**6.9**	174.4(4) 179.4(4)	101.9(8) 103.0(6)	2.054(10) 2.111(12)	1.445(16) 1.531(18)
3[a]	**6.12**	176.2(8) 177.3(9)	110(2)	2.06(3) 2.10(3)	1.45(3) 1.38(4)
4	**6.14**	176.3(3)	94.9(7)	2.222(9)	1.497(16)
5[a]	**6.15**	177.4(3) 179.4(3)	107.0(7) 107.1(6)	2.096(9)	1.453(15) 1.464(14)
6	**6.16**	178.62(17)	105.7(7)	2.083(5)	1.467(6)

[a]Several molecules were found in the crystal lattice of the complexes: ranges of distances, and angles obtained is shown.

6.2.1. Synthesis, and characterisation of ketonyl-, and cyanomethyl-Au(I) derivatives

Deprotonation of other organic molecules was tested next (Scheme 6.8). For these studies, [Au(OH)(IPr)] **6.2** was chosen as gold precursors to accelerate the reaction times. Acetophenone (pK_a (DMSO) = 24.7)[39] was reacted in a 1.1:1 ratio with **6.2** in THF at 60 °C. After 24 h, the formation of a new species was observed. The ketonyl-Au(I) species [Au($CH_2C(O)Ph$)(IPr)] (**6.18**) was isolated in 72% yield. In the ^1H NMR spectra (C_6D_6), characteristic downfield signal of the CH_2 protons for the ketonyl ligand were observed at 2.46 ppm *vs* to 2.10 ppm for the CH_3 of acetophenone. To the same extent the functionalisation of acetoxyacetone was targeted. The reaction of **6.2** and acetoxyacetone was performed in THF and showed full conversion of starting material, however different complexes were formed. The targeted complex [Au($CH_2C(O)CH_2OAc$)(IPr)] (**6.19**) was determined to be the major product, with the other products probably arising from the functionalisation of the other CH_3 group. Following recrystallisation with THF/pentane, **6.19** was obtained in 44% isolated yield. Pleasingly the deprotonation of acetonitrile (pK_a (DMSO) = 31.3)[39] could be achieved by using it as solvent of the reaction, to give product **6.20** in 70% yield after heating at reflux for 20 h.



Scheme 6.8. Functionalisation of other organic molecules.[a] THF, 24 h;[b] C_6D_6, 18 h;[c] 80 °C, $NCCH_3$, 20 h

The structure of **6.18** and **6.20** were unambiguously characterised by X-ray diffraction analysis of single crystals grown by slow diffusion of pentane into a saturated CH_2Cl_2 solution (Figure 6.6). The bond lengths and angles follow the trend observed for the acetonyl-Au complexes (Table 6.2).[22b,22c,25a] It is of interest to point out that the flattening of Au-CH_2-C angle in **6.18** of 103.98°, similar to what observed for **6.14**, whilst an angle

of 109.12° was observed in **6.20**. Partial orbital rehybridization of the C atom bound to the metal centre might occur in **6.18** as observed for the acetonyl complex **6.14**.

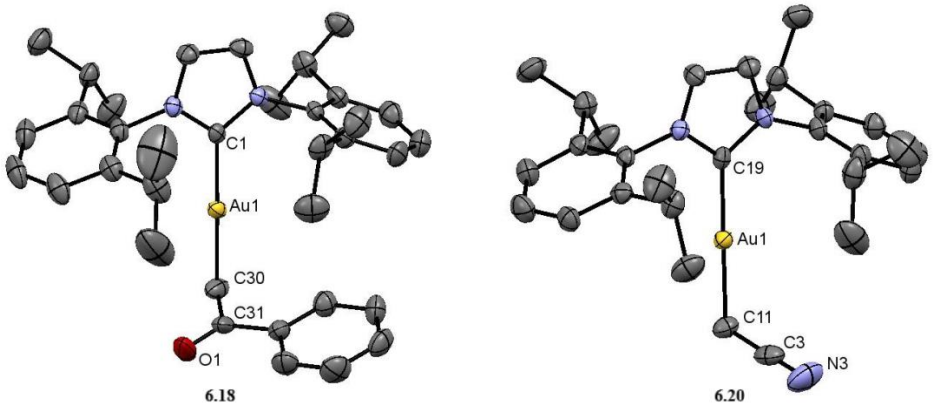
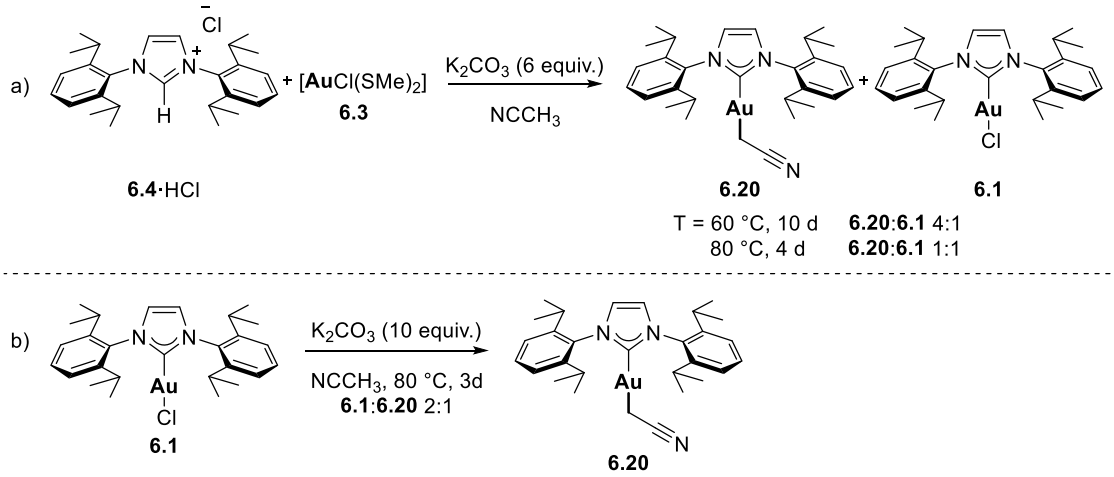


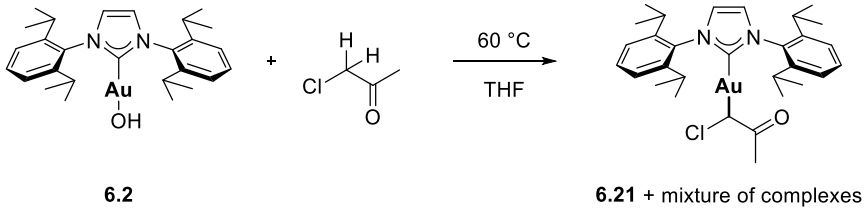
Figure 6.6. Thermal ellipsoid representation of **6.18**, and **6.20** showing 50% probability. All H atoms were omitted for clarity. Selected bond angles (deg), and lengths (Å). **6.18**: C1-Au-C30 179.64(13)°; Au-C30 of 2.094(3) Å; C31-O1 of 1.227(4) Å; **6.20** (2 molecules were found in the unit cell): C19-Au-C11 176.77°; Au-C11 2.112 Å; Au-C11-C3 110.47°.

The formation of **6.20** is interesting. Few examples of cyanomethyl-gold(I) compounds were found in the literature, in all cases bearing phosphines as ancillary ligands.[40] Intrigued by **6.20**, it was tested whether the same complex could be obtained from IPr·HCl, **6.4**·HCl, and [AuCl(SMe$_2$)], **6.3** (Scheme 6.9, a). The reaction, in $NCCH_3$, with K_2CO_3 was followed for 10 days at 60 °C, showing formation of complexes **6.20** and **6.1** in a 4:1 ratio. By increasing the reaction temperature to 80 °C and heating up for 4 days, a 1:1 ratio of **6.20**:**6.1** was obtained suggesting that a stronger base might be needed to reach full conversion of the starting materials. Unfortunately, **6.1** could not be fully converted into pure **6.20** (Scheme 6.9, b); after 3 days at 80 °C, 2:1 mixture of chloride-, and cyanomethyl-Au(I) complex was observed, which did not vary further over time.



Scheme 6.9. Formation of **6.20** from a) **6.4**·HCl, and **6.3**; b) **6.1**. The reactions were performed in collaboration with Dr. Alba Collado.

Chloroacetone was reacted with **6.2** (Scheme 6.10); full conversion of the starting material was observed however a mixture of products was formed. The possible functionalised product **6.21** was found as major compound and was characterised in the reaction mixture. Functionalisation of the CH_2 was observed, probably due to the electron-withdrawing effect of the Cl atom, which decreases the pK_a of the methylene protons.



Scheme 6.10. Deprotonation of chloroacetone with **6.2**.

6.3. Reactivity of acetonyl-Au(I) NHCcomplexes

6.3.1. Stoichiometric reactivity of acetonyl-Au(I)complexes

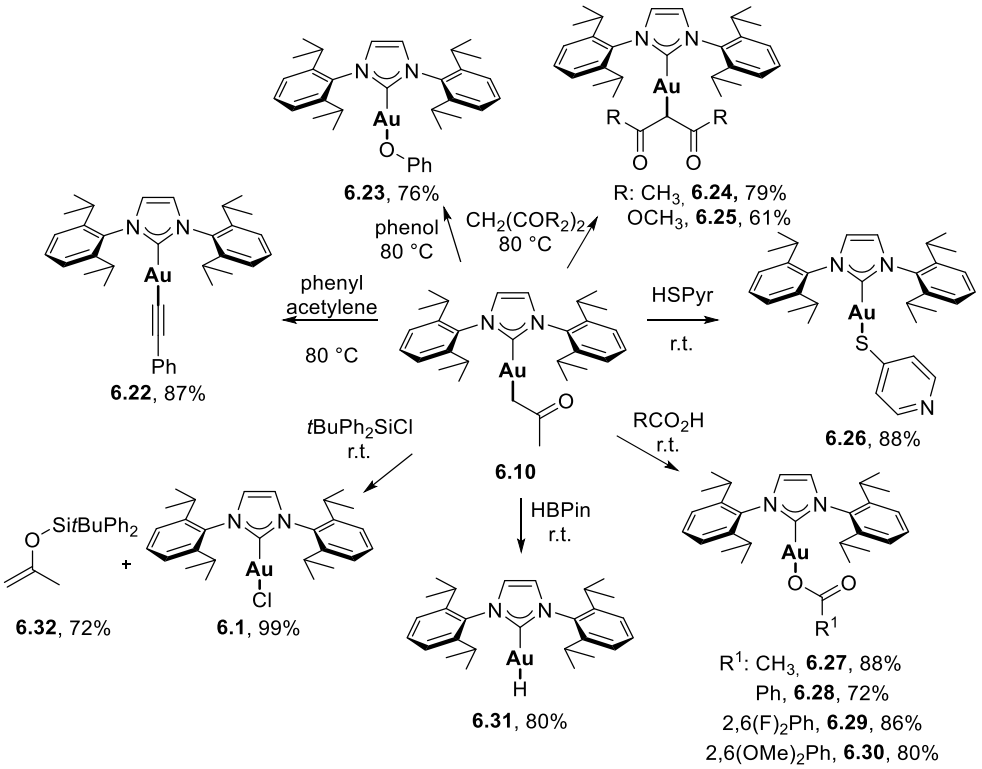
The reactivity of **6.10** was explored first (Scheme 6.11). Protonolysis reactions using organic acids, of known pK_a (DMSO) values,[39] were performed to gauge its basicity.[33] It is notable that acetone would be the only by-product, which could be easily removed from the reaction mixture by evaporation. Deprotonation of fluoroarene C-H bonds, such as pentafluorobenzene and 1,3,5-trifluorobenzene, (pK_a (DMSO) = 29-31.5), in toluene at 100 °C, to obtain [Au($C_6F_nH_{5-n}$)(IPr)] (n=3, 5) was unsuccessful.

In contrast, reaction with phenylacetylene (pK_a (DMSO) = 28.8) led to isolable acetylide-Au(I) complex **6.22** in 87% yield, after heating **6.10** with the alkyne at 80 °C for 24 h (Scheme 6.11). **6.10** was next reacted with phenol (pK_a (DMSO) = 18) at 80 °C to synthesise the corresponding phenolate-Au(I) derivative **6.23** in 76% isolated yield. The result is noteworthy as an alternative protocol to the previously reported synthesis of gold-phenolates.[41] Acetylacetone and dimethoxy malonate (pK_a (DMSO) ~13-16) reacted with **6.10** at 80 °C to give **6.24** and **6.25**[33] in 79% and 61% yield, respectively.

Using more acidic substrates (pK_a < 10), a large number of organogold species were synthesised at r.t. (Scheme 6.11). Indeed, **6.10** reacted with 4-mercaptopyridine, affording **6.26** in 88% yield; the interest of such gold(I) derivatives is derived on their biological activity towards cancer cell lines.[42] The acetate-Au(I) complex [Au(OC(O)CH_3)(IPr)] (**6.27**) was easily obtained in good yield (88%) by treatment of **6.10** with 1 equiv. of acetic acid. The same procedure was applied to benzoic acid to obtain **6.28** in 72% isolated yield. Substituents in the *ortho*-position of the benzoic acid, both electron-withdrawing and electron-donating groups were well tolerated and compounds **6.29** and **6.30** could be isolated in 86% and 80% yield, respectively. Carboxylate-Au(I) derivatives have been used as well-defined pre-catalysts and proposed as intermediates in carboxylation/decarboxylation reactions.[5b,43]

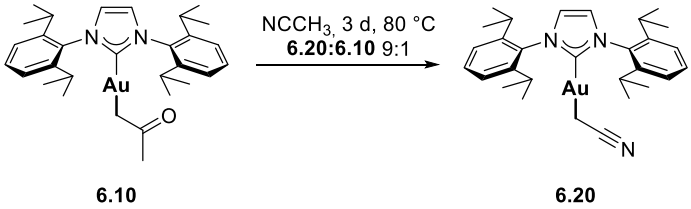
Using an excess of pinacolborane as a hydride source, [Au(H)(IPr)] (**6.31**) was obtained in 80% yield.[44] This reaction was carried out under an argon atmosphere due to the high reactivity of H-Au complexes. **6.10** was finally reacted with *t*$BuPh_2SiCl$, affording the chloride-Au(I) complex **6.1** in 99% yield, and silyl enol ether **6.32** in 72% yields (Scheme 6.11).

Furthermore, suitable single crystals for X-ray diffraction analysis of the new complexes **6.23**, **6.26** and **6.29** were obtained.[45]



Scheme 6.11. Reaction wheel of **6.10**.

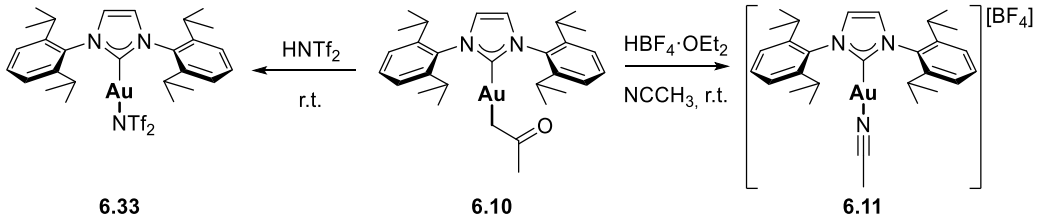
Protonolysis of **6.10** could also be used to access cyanomethyl complex **6.20** (Scheme 6.12). The reaction was followed by ^{1}H NMR and showed conversion into the targeted complex in a 9:1 ratio with the starting material after 3 d at reflux in acetonitrile. As seen in scheme 6.9 and scheme 6.10, a stronger Brønsted base might be needed to drive this reaction to completion. However, it is of note that the formation of **6.20** proceeds to a certain extent, reiterating the Brønsted basicity of the acetonyl complex.



Scheme 6.12. Synthesis of **6.20** from **6.10**.

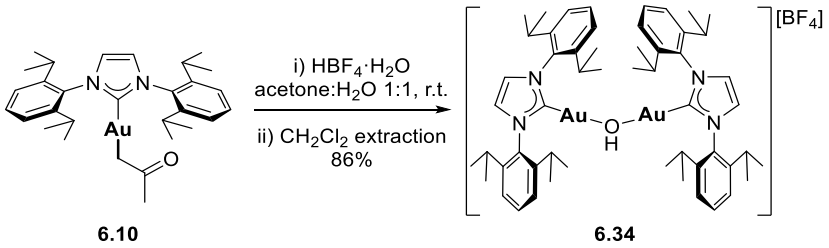
Interestingly, **6.10** provided also access to well-defined pre-catalyst which have found numerous applications in Au(I)-catalysed reactions (Scheme 6.13); [Au(NTf$_2$)(IPr)] (**6.33**)[46] was accessed in good yield (89%) by using trifluoromethanesulfonic acid (HNTf$_2$). Moreover, [Au(IPr)(NCCH$_3$)][BF$_4$] (**6.11**) could be accessed by reacting complex **6.10** with tetrafluoroborate diethyl ether complex (HBF$_4$·OEt$_2$) in acetonitrile.[47]

These routes provide alternative silver-free protocols to access these pre-catalysts, of interest to avoid silver contaminants which might affect catalytic processes.



Scheme 6.13. Synthesis of relevant Au(I) NHC pre-catalysts **6.33**, and **6.11,** from **6.10** and acids.

Finally, complex **6.10** could be used to access dinuclear gold species such as [{Au(IPr)}$_2$(μ-OH)][BF$_4$] (**6.34**), the importance of which was discussed in section 1.5.2. The simple procedure involved the treatment of the acetonyl-Au(I) complex with tetrafluoroboric acid solution ($HBF_4 \cdot H_2O$, 48% wt in H_2O) in acetone:water (1:1) for 1 h (Scheme 6.14). Extraction with CH_2Cl_2, filtration through a short plug of celite and recrystallisation led to isolation of the pure digold species **6.34** in 86% yield.



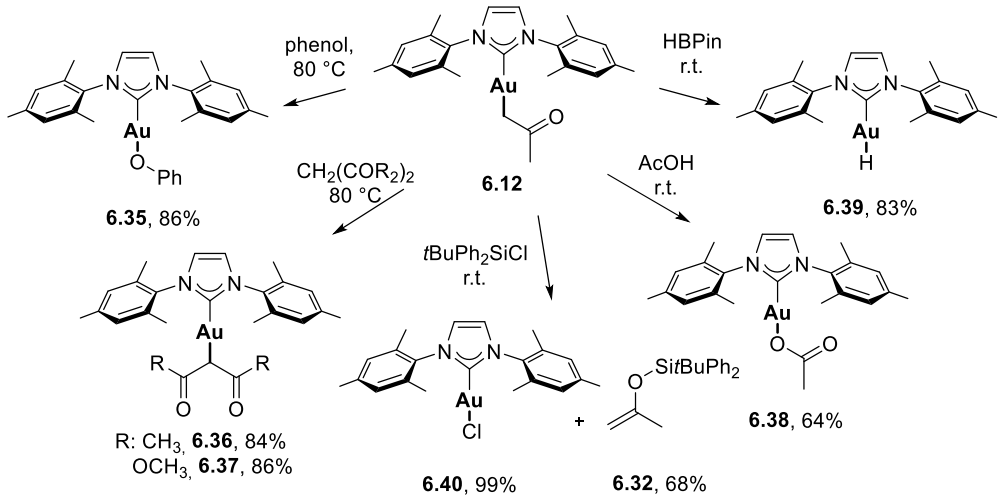
Scheme 6.14. Synthesis of dinuclear gold hydroxide **6.34** from **6.10**.

Next, the stoichiometric reactivity of [Au($CH_2C(O)CH_3$)(IMes)] (**6.12**) was assessed; this complex was of particular interest as Au(I)\IMes complexes have been less developed compared to IPr analogues. This may be due to the lower stability of IMes complexes, for example [Au(OH)(IMes)] is air and moisture sensitive, while [Au(OH)(IPr)] **6.2** can be prepared on a multi-gram scale, and stored under air.[48] In contrast, acetonyl-Au(I) IMes **6.12** is a stable complex, easily synthesised using technical grade solvents, and can be handled under air.

The basicity of [Au($CH_2C(O)CH_3$)(IMes)] was evaluated by reacting it with different organic molecules bearing acidic protons. **6.12** did not react with phenylacetylene (pK_a (DMSO) = 28.8), suggesting a less basic character of the IMes derivative compared to the IPr analogue **6.10**. Therefore, more acidic substrates than alkynes were tested (Scheme 6.15). Indeed, **6.12** reacted with phenol, forming the corresponding gold-phenolate

complex **6.35** in 86% yield. Reaction of **6.12** with acetylacetone, and dimethoxy malonate, at 80 °C, afforded **6.36** and **6.37** in high yields. Furthermore, acetic acid was reacted with **6.12** to give **6.38** in 64% isolated yield.

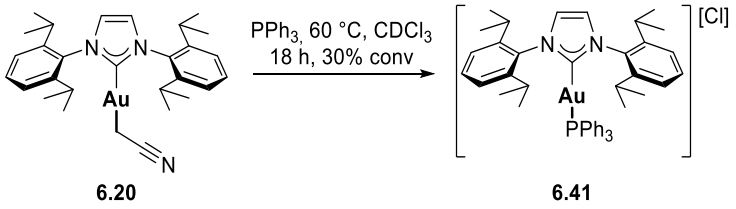
Treatment of **6.12** with an excess of pinacol borane afforded [Au(H)(IMes)] (**6.39**) which was isolated in high yield (83%).[49] As seen for [Au(H)(IPr)] **6.31**, the reaction required an inert atmosphere, and the Au-H complex was stored under argon. **6.12** reacted smoothly with *t*BuPh$_2$SiCl affording [AuCl(IMes)] (**6.40**), and the corresponding substituted silyl enol ether **6.32** (Scheme 6.15).



Scheme 6.15. Reaction wheel of **6.12**.

Suitable crystals for X-ray diffraction analysis were obtained for complexes **6.35**, **6.37** and **6.38**.[50]

Protonolysis reactions of cyanomethyl complex **6.20** were performed next; the species however showed no reactivity with terminal alkynes, phenols or organic acids. Partial ligand exchange was observed in the presence of triphenylphosphine (Scheme 6.16), with formation of the cationic heteroleptic complex [Au(IPr)(PPh$_3$)][Cl] (**6.41**)[51] in 30% conversion after 18 h in refluxing $CDCl_3$ solution.



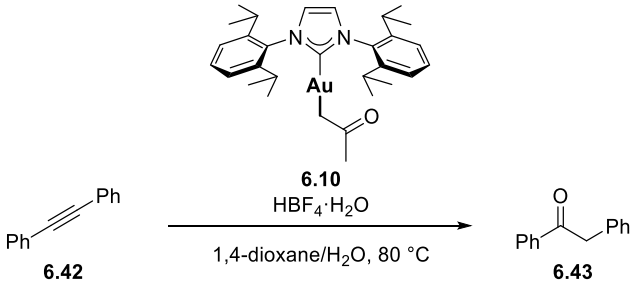
Scheme 6.16. Ligand exchange at **6.20**.

6.3.2. Catalytic Reactivity of acetonyl-Au(I) NHC complexes

The hydration of alkynes to form ketones[52] and the rearrangement of propargylic acetates to form substituted indenes,[53] were selected to test the activity of acetonyl-Au(I) complexes. These reactions are believed to be initiated by the active species $[Au(NHC)]^+$. This species was postulated to form *in situ* by reacting $[Au(CH_2C(O)CH_3)(NHC)]$ with a protic acid.[52,53] Therefore, the catalytic reactions can be performed without requiring the use of expensive and hygroscopic silver salts AgX (X = OTf, BF_4, SbF_6, PF_6) (section 1.6.1),[54] which might also interfere with the performance of the gold catalyst, or indeed act as active catalyst in the same transformation.[55]

Hydration of diphenylacetylene **6.42** to ketone **6.43** was attempted first using 1 mol% of **6.10** (Table 6.3, entry 1). No hydration was observed. However, when a 1:1 ratio of **6.10** and $HBF_4 \cdot H_2O$ was used 80% conversion of **6.42** to give 1,2-diphenylethanone **6.43** was observed after 2 h (entry 2), with full conversion obtained after 4 h (entry 3). When 2 equiv. of acid were used with respect to the acetonyl complex, full conversion was observed after 2 h (entry 4).[52,56] Significantly when diphenylacetylene **6.42** was treated with $HBF_4 \cdot H_2O$ (1 mol%), no traces of **6.43** were observed, indicating the catalytic competence of gold in this reaction (entry 5).

Table 6.3. Hydration of diphenylacetylene with **6.10**, and $HBF_4 \cdot H_2O$



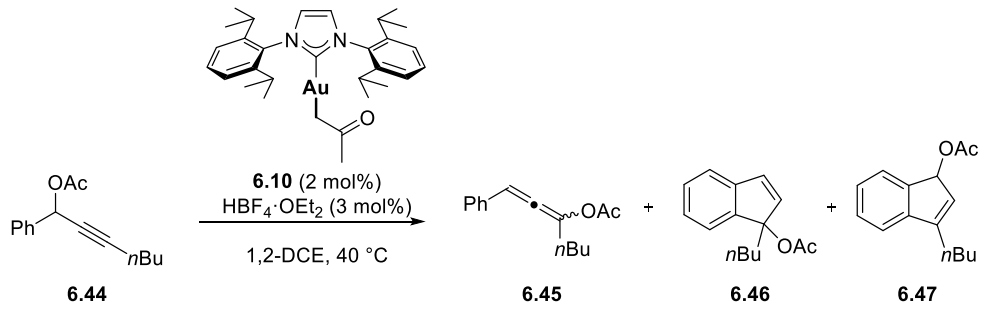
Entry	**6.10**:$HBF_4 \cdot H_2O$ (mol%)	time (h)	Conv. (%)
1	1:0	2	0
2	1:1	2	80
3	1:1	4	>99
4	1:2	2	>99
5	0:1	2	0

Reaction conditions: [a] **6.42** (0.5 mmol), 1,4-dioxane/water (2:1, 1 mL), conversions measured by GC.

Furthermore, cationic gold complexes exhibit high catalytic activity in the intramolecular rearrangement-hydroarylation of propargylic acetates, showing different reactivity depending on the reaction conditions; indeed, under anhydrous conditions, activation of the alkyne, followed by migration of the acetate group, provides allenes which can further undergo rearrangement to form indenes.[53] In contrast, in the presence of water the reaction provides selective formation of conjugated enones.[57]

The catalytic behaviour of **6.10** was therefore tested in this transformation, following *in situ* activation with $HBF_4 \cdot OEt_2$ (Table 6.4). Reaction of propargylic acetate **6.44**, in the presence of **6.10**, and $HBF_4 \cdot OEt_2$ (1:1.5 ratio), led to quantitative formation of the substituted allene **6.45** after just 15 min (entry 1). Upon leaving the reaction 24 h, conversion into a 40:60 ratio of 1,1-disubstituted indene (**6.46**), and 1,3-disubstituted indene (**6.47**) was observed (entry 2). Longer reaction times (48 h) led to the sole formation of indene **6.47**, indicating that this is the thermodynamic product (entry 3). **6.10** was found to be less active compared to the hydroxide-Au(I) derivative **6.2**.[57c] However, the difference in reactivity permitted isolation of the initially-formed allene **6.45**, or the thermodynamic indene **6.47**, by tuning the reaction time.

Table 6.4. Transformation of propargylic acetates into substituted allenes and indenes



Entry	time	**6.45**:**6.46**:**6.47**	Conv. (%)
1	15 min	1:0:0	**6.45** >99[b]
2	24 h	0:0.6:1	**6.46** 40:**6.47** 60[c]
3	48 h	0:0:1	**6.47** >99[c]

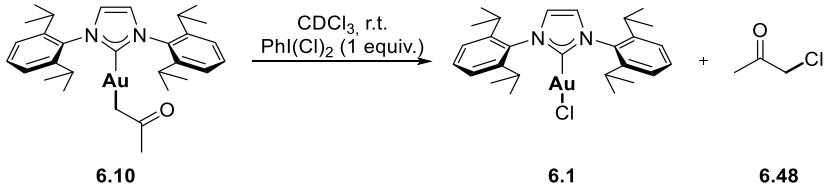
Reaction conditions: [a] propargylic alcohol **6.44** (0.5 mmol), **6.10** (2 mol%), $HBF_4 \cdot OEt_2$ (3 mol%), DCE (10 mL); [b] conversion was calculated by ^{1}H NMR, using pivalaldehyde as internal standard (0.5 mmol);[c] conversions and ratio between **6.46**, and **6.47** were determined by GC analysis, and confirmed by ^{1}H NMR spectroscopy.

6.4. Reductive elimination from C(sp^3)-Au compounds

6.4.1. Formation of C(sp^3)-Au(III) derivatives

The oxidation of acetonyl-Au(I) species was explored, due to the increasing interest of organogold(III) compounds[58] and their involvement in catalysis.[59] Initial attempt to oxidise **6.10** were performed in the presence of hypervalent iodine.[60] As shown in Chapter 4, and following literature precedents, the ease of handling and preparation of these oxidants makes them good candidates to explore higher oxidation chemistry of this metal centre.[5d,61]

By reacting **6.10** with 1 equiv. of $PhI(Cl)_2$ in $CDCl_3$, full conversion of the acetonyl species to [AuCl(IPr)] **6.1** was observed (83% yield), together with chloroacetone (**6.48**) which was identified by comparison with an authentic sample (Scheme 6.17). Iodobenzene was also recovered in the reaction mixture. The same reaction could be performed in CH_2Cl_2, or C_6D_6, and showed the formation of functionalised product **6.48** and the chloride-Au species **6.1** in both cases.



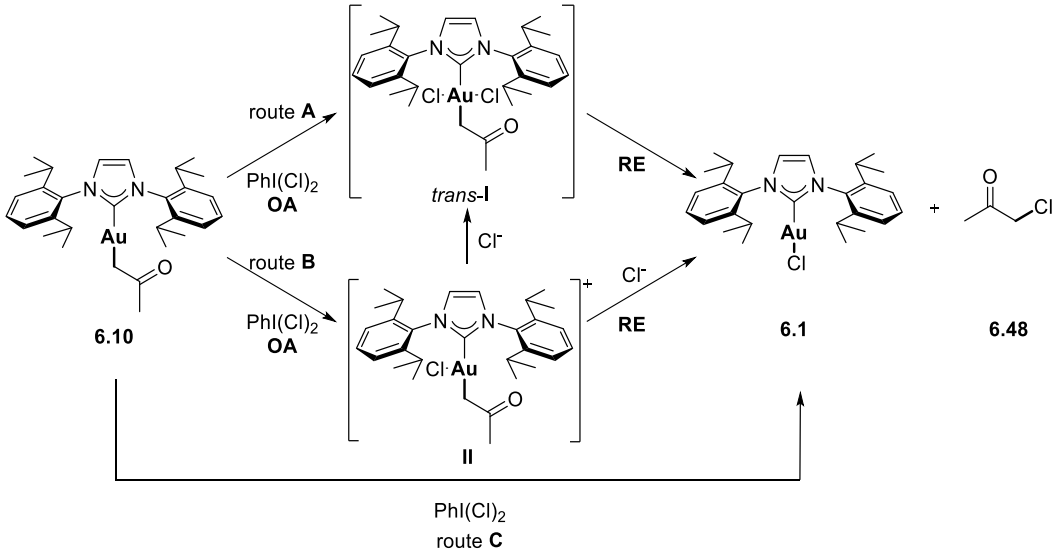
6.10 **6.1** **6.48**

Scheme 6.17. Reaction of **6.10** with $PhI(Cl)_2$.

On a single occasion, when the reaction was performed in CH_2Cl_2, the presence of a highly deshielded species was identified. The diagnostic signal for the *i*Pr CH proton of the NHC appeared at 2.87 ppm ($CDCl_3$), which in comparison to the same proton in **6.10** (2.56 ppm) and to reported signals for [$AuCl_3$(IPr)] (2.85 ppm, $CDCl_3$),[62] was attributed to a possible [$AuCl_2(CH_2C(O)CH_3)$(IPr)] complex (*trans*-**I**) (Scheme 6.18). This organogold(III) species could be formed by concerted (route **A**), or stepwise (route **B**) oxidative addition of $PhI(Cl)_2$ to [$Au(CH_2C(O)CH_3)$(IPr)] **6.10**, to form a *trans* or *cis* dichloride-Au(III) species. Attempts to isolate the organogold(III) complex were unsuccessful, probably due to the high reactivity of species *trans*-**I**, as found for the transient *trans*-[AuI_2(Me)(IPr)] species reported by Bercaw and Labinger.[63] Based on this precedent, the formation of the *trans*-intermediate under the reaction conditions was assumed. However, the intermediacy of the *cis*-Au(III) complex cannot be ruled out.

Indeed, similar species were isolated by Toste and co-workers,[64] of formula $[AuF_2(alkyl)(IPr)]$.

Following these literature findings, it was postulated whether a transient tricoordinate organogold(III) species, like **II**, could be the intermediate for the formation of *trans*-**I**, *via* a stepwise mechanism (route **B**). Reductive elimination could therefore occur either from *trans*-**I** of **II**, forming **6.1** and functionalised acetone **6.48** in either case. The possibility of ligand exchange with the oxidant also cannot be ruled out,[65] with reductive elimination taking place from hypervalent iodine acetonyl intermediate (Scheme 6.18, route **C**). However, the observation of traces of possible Au(III) species by ^{1}H NMR spectroscopy support the likely operation of either route **A** or **B**.

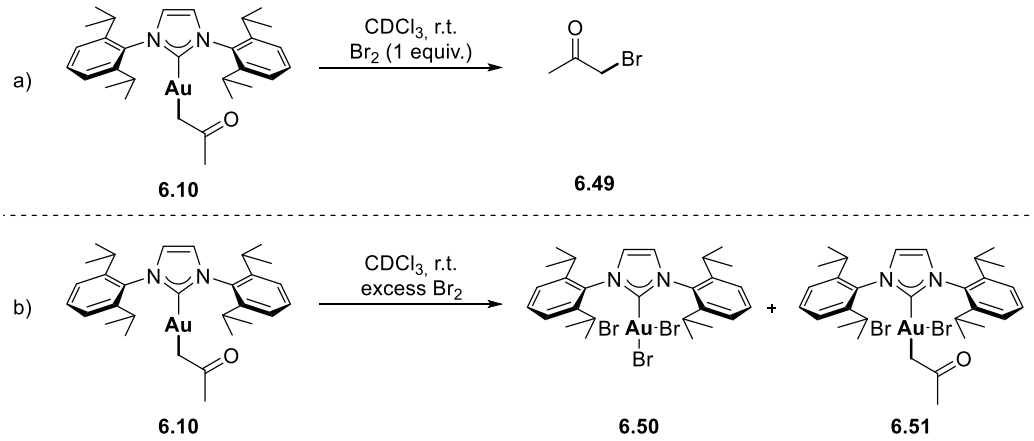


Scheme 6.18. Possible mechanism for the formation of the functionalised product **6.49** from **6.10**; OA = oxidative addition, RE = reductive elimination. Route **A**: concerted mechanism; route **B**: stepwise mechanism; route **C**: ligand-exchange.

The formation of a C(sp^3)-X bond through reductive elimination was explored further.[3b] Therefore, **6.10** was reacted with an equimolar amount of elemental Br_2 (Scheme 6.19, a): the reaction showed a slow release of bromoacetone **6.49**, and the possible formation of an organogold(III) species, which was difficult to isolate and characterise, as observed for the reaction with $PhI(Cl)_2$ (Scheme 6.18). Attempts to analyse the mixture by solvent evaporation and recrystallisation revealed **6.10** as the only Au containing species.

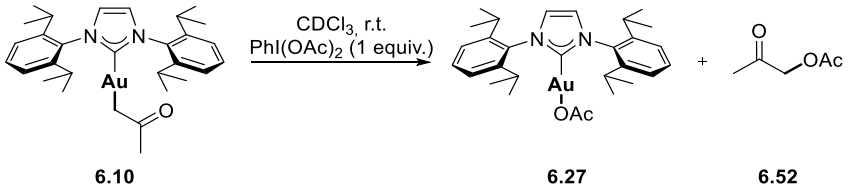
Reacting **6.10** with an excess of Br_2 led to the formation of two major Au(III) species, a $[AuBr_3(IPr)]$ (**6.50**)[66] and a second species which was characterised in the mixture as $[AuBr_2(CH_2C(O)CH_3)(IPr)]$ (**6.51**) (Scheme 6.19, b). This species was not the same as

what formed when **6.10** was reacted with an equimolar amount of Br_2, so it is likely the species observed previously was a transient intermediate or the stereoisomer of [$AuBr_2(CH_2C(O)CH_3)(IPr)$]. Any attempt to isolate this species failed, with the prompt release of bromoacetone, and the isolation of [$AuBr_3(IPr)$] **6.50**.



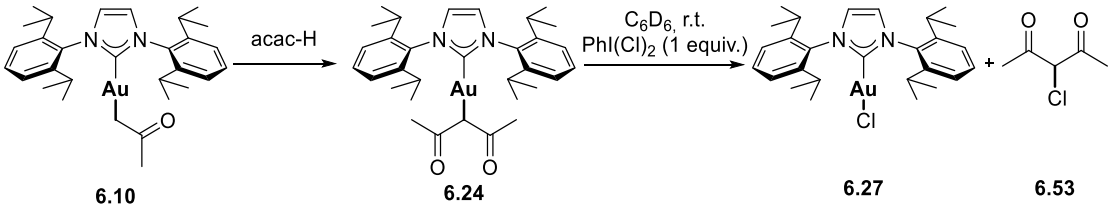
Scheme 6.19. Oxidation reaction of **6.10** with Br_2: a) stoichiometric amount, and b) excess of oxidant.

6.10 was also reacted with an equimolar amount of $PhI(OAc)_2$ in $CDCl_3$ (Scheme 6.20). After 5 min the reaction was analysed by ^1H NMR spectroscopy and showed the formation of [$Au(OC(O)CH_3)(IPr)$] (**6.27**) (86% isolated yield) and acetoxyacetone **6.52**. The formation of **6.27** was obtained with similar results in CH_2Cl_2, while in C_6D_6 the reaction was slower. No traces of organogold(III) species were observed for this transformation, thus, as highlighted in scheme 19, the possible direct cleavage of the Au-CH_2 bond without involvement of an organogold(III) species cannot be ruled out.



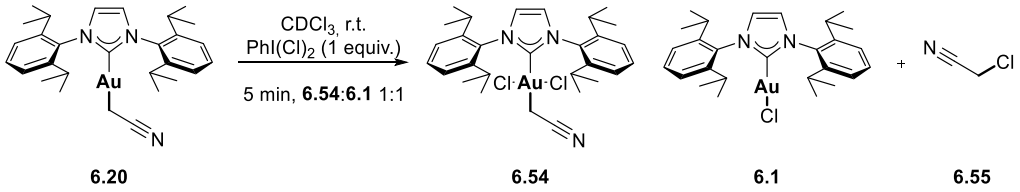
Scheme 6.20. Formation of functionalised acetoxyacetone **6.53** from **6.10**, and $PhI(OAc)_2$.

The oxidation of [Au(acac)(IPr)] **6.24** (acac = acetylacetonate), synthesised from **6.10** (Scheme 6.12), was attempted (Scheme 6.21). Reaction with an equimolar amount of $PhI(Cl)_2$ in C_6D_6 showed the formation of α-chloro acetylacetone (**6.53**) after 5 min, together with [AuCl(IPr)] in a 1:1.6 ratio with the starting material [Au(acac)(IPr)] **6.24**. No traces of an organogold(III) intermediate were found in this case.



Scheme 6.21. Formation of α-chloro acetylacetone **6.54** from **6.24**, and $PhI(Cl)_2$.

The reactivity of cyanomethyl species **6.20** toward oxidation was explored (Scheme 6.22). By reacting **6.20** with an equimolar amount of $PhI(Cl)_2$ yielded a 1:1 mixture of $[AuCl_2(CH_2CN)(IPr)]$ (**6.54**) and [AuCl(IPr)] **6.1**, together with release of chloroacetonitrile (**6.55**).



Scheme 6.22. Oxidative addition/reductive elimination from **6.20** to **6.55**.

Pleasingly, single crystals of **6.54** were grown by slow diffusion of pentane into a $CDCl_3$ saturated solution, and the structure of $[AuCl_2(CH_2CN)(IPr)]$ was unambiguously assigned by X-ray diffraction analysis (Figure 6.7). The crystals used for the analysis, were subjected to ^1H NMR spectroscopy ($CDCl_3$), and underwent prompt decomposition into **6.1**, and **6.55**.

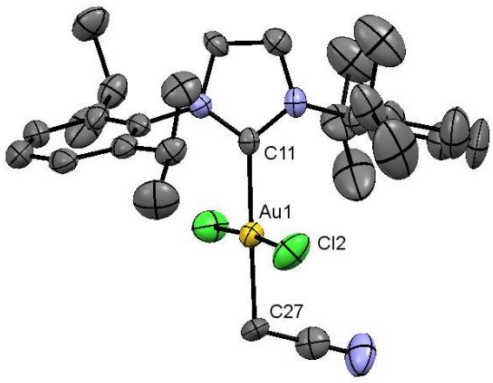
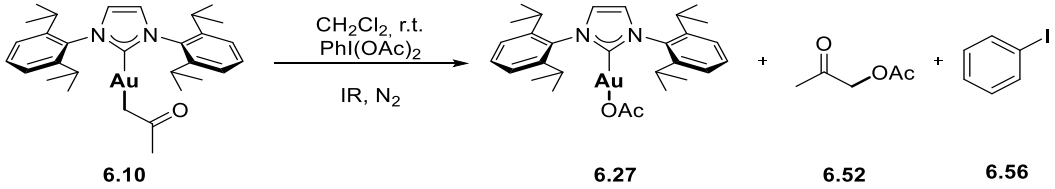


Figure 6.7. Thermal ellipsoid representation of **6.54** showing 50% probability.

6.4.2. Kinetics of the reaction of $[Au(CH_2C(O)CH_3)(IPr)]$ with $PhI(OAc)_2$

To gain further insight into the reaction of **6.10** with $PhI(OAc)_2$, *in situ* IR analyses were performed (Scheme 6.23). A solution of **6.10** $[Au(CH_2C(O)CH_3)(IPr)]$ in CH_2Cl_2 was

transferred by syringe to a continuous stirred-tank reactor (CSTR), fitted with spectroscopic windows (CaF_2) and under a continuous stream of N_2. During the collection of IR data, a series of solutions of $PhI(OAc)_2$ in CH_2Cl_2 were injected into the CSTR.



6.10 **6.27** **6.52** **6.56**

Scheme 6.23. Solution of **6.10** and $PhI(OAc)_2$ in CH_2Cl_2 injected into the CTRS. Formation of products **6.27**, **6.52** and **6.56** observed over time by IR.

Infrared spectra were plotted against: i) a background recorded immediately after the addition of $PhI(OAc)_2$ to the reaction vessel and ii) the solvent (Figure 6.8). Extensive overlap observed in the reaction spectra complicated concentration determination using integrated absorption. For this reason, integrated absorption coefficients were not measured. Rather, absorption coefficients for **6.10**, $PhI(OAc)_2$, PhI (**6.56**), and acetoxy acetone **6.52** were determined from peak heights using a linear baseline, as a function of the concentration of standard solutions.

Figure 6.8 shows a collection of spectra recorded as a function of time following the addition of the oxidant to a solution of the Au(I) complex, overlaid to authentic samples. The formation of acetoxyacetone **6.52**, and PhI **6.56** was observed. However, the acetate region could not be deconvoluted with any degree of accuracy, although changes in the absorption profile do reflect the formation of [Au(OC(O)CH_3)(IPr)] **6.27**. Moreover, given the seemingly identical rates of formation of **6.52**, and **6.56**, the identification of an Au(III) intermediate, if present, was unlikely at this time resolution.

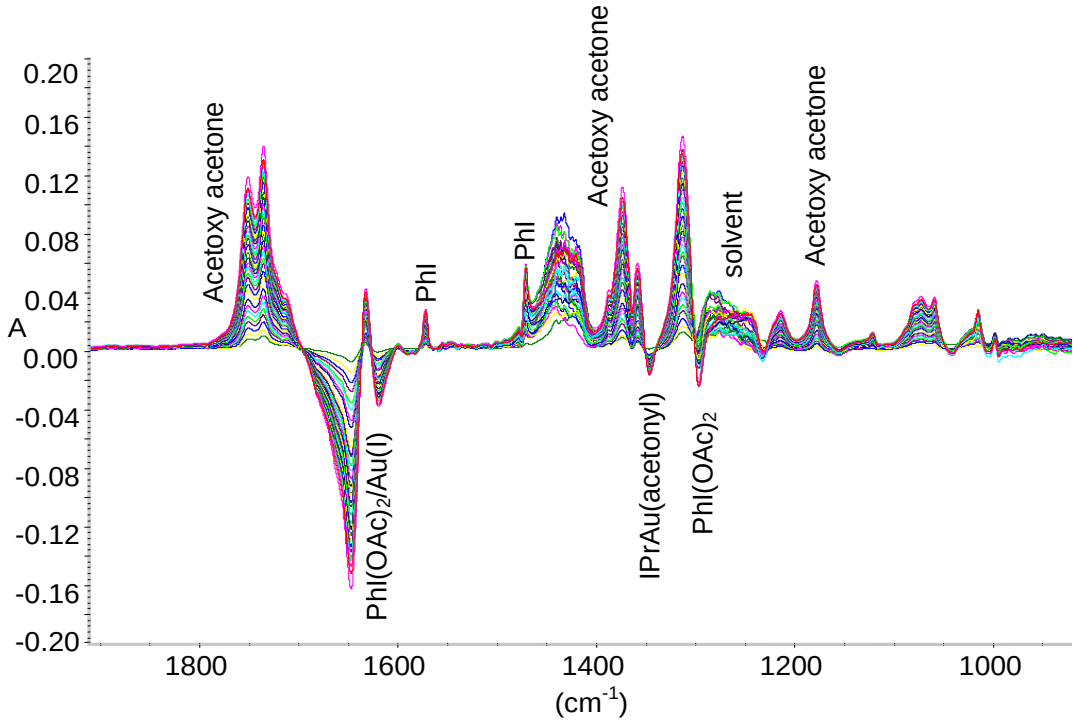


Figure 6.8. Spectra recorded for the reaction between **6.10**, and $PhI(OAc)_2$ to form acetoxyacetone **6.53**. These analyses were performed by Paul Webb.

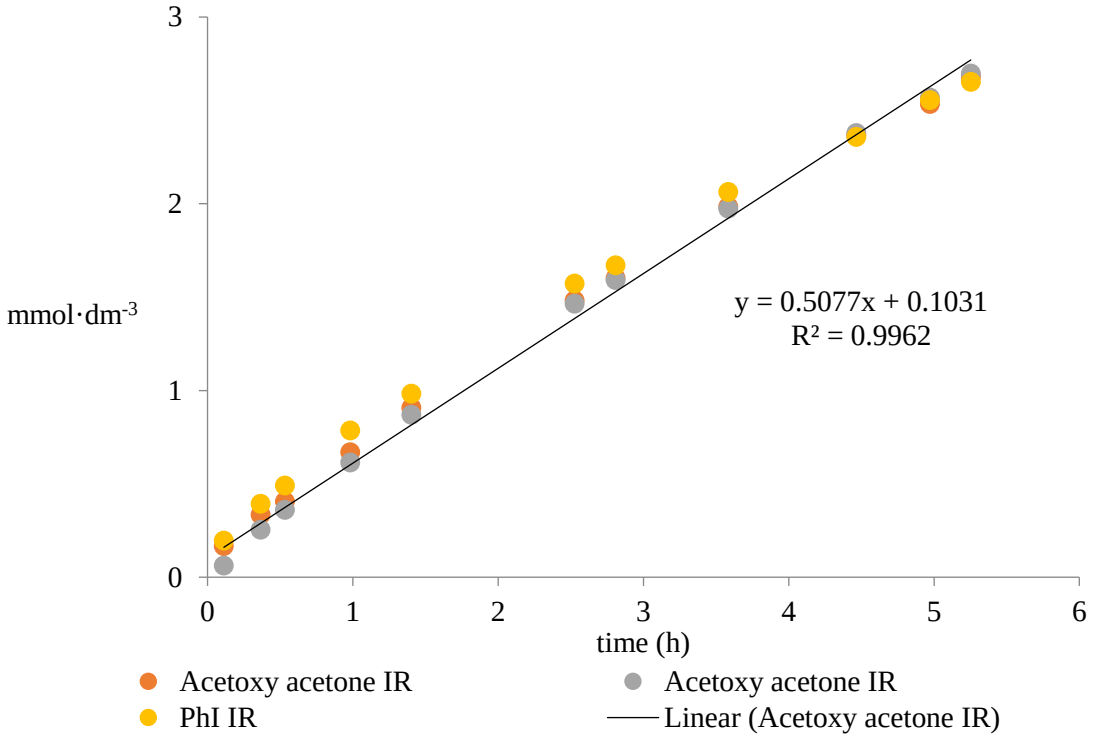


Figure 6.9. Kinetic data for the conversions of **6.10** and $PhI(OAc)_2$ into **6.52**, **6.56**, and **6.27**. These analyses were performed by Paul Webb.

To a first approximation, the kinetic profile for the rate of formation of **6.52**, and **6.56** appears to be zero order in starting materials, although the reaction was more rapid in the early stages (Figure 6.9). The calculated data for PhI were not as accurate, due to partial decomposition of the oxidant at the inlet source.

From this data, it was assumed that the formation of the product is independent of the concentration of the starting materials. Therefore, intermediates might be involved in this transformation, thus ruling out the formation of the product through solely ligand exchange *via* the oxidant. Possible involvement of an organogold(III) species could be envisaged for this transformation, accounting for the results obtained with other oxidants. However, the stepwise or concerted mechanism cannot be discerned *via* this method because no traces of intermediate could be identified in the reaction mixture.

6.4.3. Computational data on the mechanism of formation of C(sp^3)-X bonds

The two major pathways for the formation of α-chloro acetone **6.48** from **6.10** with $PhI(Cl)_2$ (Scheme 6.18) were calculated: i) the oxidative addition pathway, Au(I) → Au(III) (Figure 10, green lines); ii) ligand exchange (Figure 10, black lines).

Initial coordination of the hypervalent iodine reagent to the metal centre was calculated with for the formation of organogold(III) intermediates **II**. From intermediate **II**, the two pathways deviate. The oxidative addition pathway (green lines) was calculated to undergo intramolecular ligand exchange through a three-centres metallocycle giving, after geometrical distorsion, organogold(III) intermediate **IV**, followed by elimination of iodobenzene and the formation of *cis*-[$AuCl_2(CH_2C(O)CH_3)$(IPr)] intermediate **V**. From this intermediate reductive elimination could occur to release α-chloroacetone **6.48** and chloride-Au(I) species **6.1**.

The second pathway, which involves ligand-exchange to the hypervalent iodine to form intermediate **III**, was found to be more energetically demanding: the exergonic step from **II→III** was found to be 14.8 kcal·mol^{-1} higher than the formation of intermediate **IV**. However, the barrier to product formation from **III** was found to be only 20 kcal·mol^{-1}.

The highest barrier calculated in the oxidative addition/reductive elimination pathway was found to be the reductive elimination of α-chloroacetone **6.48** from intermediate **V**, with a barrier of 33 kcal·mol^{-1} (**V→6.48**). Alternatively, the reductive elimination of Cl_2 from **V** to reform **6.10** and PhI was calculated to require a barrier of 70 kcal·mol^{-1}, thus

the organogold(III) intermediate **V** will preferentially form the product **6.48**, instead of releasing Cl_2 and **6.10**.

Following the results obtained, it was shown that the formation of organogold(III) species is energetically favoured for this process under the chosen reaction conditions.

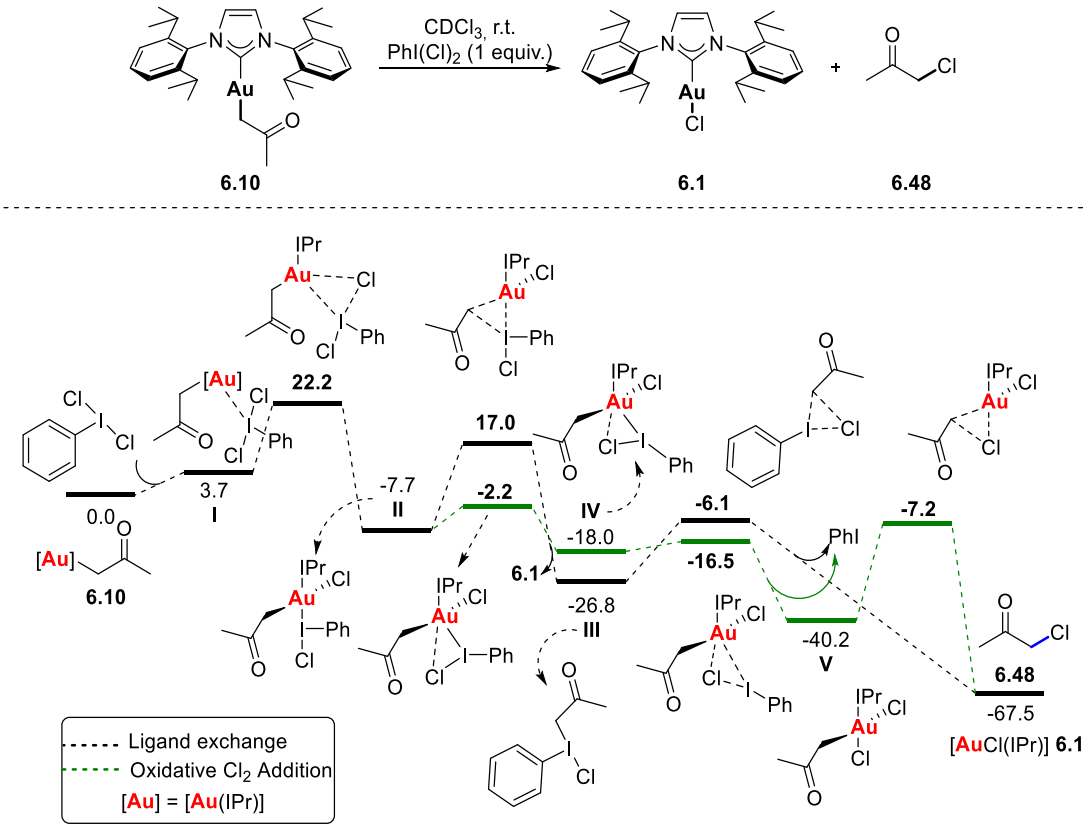


Figure 6.10. Computational calculations for ligand exchange (black line), and oxidative addition/reductive elimination (green line) pathways. Computational analyses were performed by Sai V. C. Vummaleti.

6.5. Conclusions and perspectives

The synthesis of acetonyl-Au(I) complexes was achieved, thus confirming the ability of gold precursor to deprotonate C(sp^3)-H bonds. The new family of complexes was fully described, and expanded to other small molecules, such as acetophenone, acetonitrile and acetoxyacetone were successful.

Originally identified as side-products in the synthesis of [AuCl(NHC)] complexes, these species, in particular [Au($CH_2C(O)CH_3$)(IPr)] **6.10** and [Au($CH_2C(O)CH_3$)(IMes)] **6.12**, were found to be good precursors for the synthesis of a range of catalytically relevant complexes, such as [Au(NTf_2)(NHC)], [Au(NHC)($NCCH_3$)][BF_4], [Au(OPh)(NHC)], [Au($OC(O)CH_3$)(NHC)], [{Au(IPr)}$_2$(μ-OH)][BF_4] species, in addition to biologically

relevant examples, *e.g.* [Au(S-pyr)(IPr)]. It is noteworthy that these complexes could be synthesised through straightforward procedures in a silver-free methodology, with the release of acetone as sole by-product of the reaction. In fact, this methodology has already been applied by Zuccaccia's research group for the synthesis of [Au(OTs)(IPr)] by protonolysis of the acetonyl-Au(I) precursor **6.10**.[67]

Moreover, following the publication of the acetonyl-Au(I), two interesting investigations have been reported on polynuclear Au, and Au-Ag clusters for the activation of C(sp^3)-H bonds, with detailed study on their synthesis, and application in catalytic processes.[68]

The synthesis of a cyanomethyl-Au(I) complex **6.20**, bearing an NHC ligand, was the first of this kind. This complex did not react with organic and inorganic acids. Further analysis into the activation of small molecules containing C(sp^3)-H, together with deeper experimental and computational studies around the nature of C(sp^3)-Au bonding, is highly desirable and will help to a further understanding of the C(sp^3)-Au complexes.

The redox chemistry of acetonyl, and cyanomethyl complexes was also explored. The formation of functionalised C(sp^3)-X bonds was observed by treating ketonyl- or cyanomethyl-Au(I) species with external oxidants, such as iodobenzene dichloride or elemental bromine. Organogold(III) intermediates were postulated to form, under the reaction conditions, by oxidative addition to the gold(I) complexes, which was supported by kinetic data, through flow IR, and computational analysis. Moreover, [$AuCl_2(CH_2CN)$(IPr)] was isolated, and the structure confirmed by single crystal X-ray crystallographic analysis. The formation of these intermediate supported the hypothesis that the formation of C(sp^3)-X bonds proceeded through oxidative addition of Au(I), followed by reductive elimination from Au(III) intermediate. Computational studies supported the operation of this pathway over an alternative ligand exchange mechanism. Further isolation of intermediates is of importance to fully understand the mechanism of the functionalisation of C(sp^3)-H bonds, and further applications in catalytic reactions is highly desirable.

6.6. Experimental

Unless otherwise stated, all solvents, and reagents were used as purchased and all reactions were performed under air. NMR spectra were recorded on 500 and 300 MHz spectrometers at r.t. in $CDCl_3$ or C_6D_6. Chemical shifts (δ) are reported in ppm, relative

to the solvent residual peak $CDCl_3$ (7.26 ppm for ^1H and 77.16 ppm for ^{13}C) and C_6D_6 (7.16 ppm for ^1H and 128.06 ppm for ^{13}C). Multiplicity are indicated by: s = singlet, d = doublet, t = triplet, br = broad signal, m = multiplet), coupling constants (*J*) in Hz and integration. For the assignment of the ^1H and $^{13}C\{^1H\}$ deptq NMR spectra of gold complexes COSY, HSQC and HMBC experiments were also performed. Elemental analysis were performed by Stephen Boyer, at London Metropolitan University. Crystals were grown by slow diffusion of pentane into a saturated CH_2Cl_2/THF/$CDCl_3$ solution. FTIR (ATR) spectra were recorded on a Shimadzu spectrophotometer. FTIR (ATR) for IR studies, Nicolet Avatar, 4 cm^{-1} resolution, 128 scans; CSTR, fitted with spectroscopic windows (CaF_2, Parr). Geometry optimizations were performed at the GGA level with the Gaussian09 set of programs using the BP86 functional of Becke and Perdew.[69-71] The electronic configuration of the molecular systems was described with the standard split-valance basis set with a polarization function of Ahlrichs and co-workers for main-group atoms (SVP keyword in Gaussian).[72] For Au, the small-core, quasi relativistic Stuttgart/Dresden effective core potential, with the associated triple-ζ-valence basis set contracted was used (standard SDD keyword in Gaussian09).[73] No symmetry constraint was used in the geometry optimizations, and the final geometries were confirmed to be maximum or minimum potential energy structures through frequency calculations. The reported energies were obtained via single-point calculations on the BP86 optimized geometries using the M06 functional and triple-ζ basis set for main-group atoms (TZVP keyword in Gaussian09).[74,75] The influence of the solvent (CH_2Cl_2) was included in these single-point energy calculations by using the polarization continuum solvation model PCM.[75] Since entropic contribution calculated within the ideal gas approximation at P= 1 atm is exaggerating the expected values for the dissociative steps in the condensed phase, all the thermochemical analyses were performed at P= 1354 atm.[76,77]

[AuCl(NHC)] **6.1**, [Au(OH)(IPr)] **6.2**, $PhI(Cl)_2$,1-phenylhept-2-yn-1-yl acetate (**6.45**) were synthesised according to literature procedures.[36,78] All the other reagents were commercially available, and used as purchased.

6.6.1. Preparation of [Au(CH_2R)(NHC)]

GP1: A mixture of NHC·HCl (1 equiv.), [AuCl(SMe_2)] (1 equiv.) and K_2CO_3 (6 equiv.) in acetone was stirred for 48−72 h at 60 °C. The solution was then filtered through a pad of Celite®, the solvent removed under vacuum. The resulting solid was dissolved in the minimum amount of CH_2Cl_2 and precipitated by addition of pentane. The precipitate was collected by filtration, washed with pentane, and dried under vacuum, affording the corresponding [Au($CH_2C(O)CH_3$)(NHC)] as a microcrystalline colourless solid.

GP2: A mixture of [AuCl(NHC)] (1 equiv.) and K_2CO_3 (6 equiv.) in acetone as stirred at 60 °C for 24−72 h. The solution was then filtered through a pad of Celite®, the solvent removed under vacuum. The resulting solid was dissolved in the minimum amount of CH_2Cl_2 and precipitated by addition of pentane. The precipitate was collected by filtration, washed with pentane and dried under vacuum, affording the corresponding [Au($CH_2C(O)CH_3$)(NHC)] as a microcrystalline colourless solid.

GP3: [Au(OH)(IPr)] (400 mg, 0.66 mmol, 1 equiv.) was dissolved in acetone, acetonitrile or THF (5 mL) and stirred for 4-20 h at r.t.–80 °C. The procedure for **6.18**, **6.19**, **6.21** proceeded by addition of 1.1 equiv. of the chosen ketone. The solvent was then removed under vacuum. The resulting solid was dissolved in the minimum amount of CH_2Cl_2 (2−3 mL) and precipitated by addition of pentane (~10 mL). The precipitate was collected by filtration, washed with pentane (3×5 mL) and dried under vacuum, affording the corresponding [Au(CH_2R)(IPr)] as a microcrystalline colourless solid.

[Au($CH_2C(O)CH_3$)(IPr)] (**6.10**): complex **6.10** was synthesised following GP1 using IPr·HCl (800 mg, 1.82 mmol, 1 equiv.), [AuCl(SMe_2)] (554.4 mg, 1.82 mmol, 1 equiv.), K_2CO_3 (1.51 g, 10.92 mmol, 6 equiv.) in acetone (10 mL). The reaction was stirred for 48 h at 60 °C. The desired product was obtained as a colourless solid in 80% yield (968.5 mg). Complex **6.10** was also synthesised following GP2 using [AuCl(IPr)] (200 mg, 0.32 mmol, 1 equiv.), and K_2CO_3 (1.51 g, 10.92 mmol, 6 equiv.) in acetone (5 mL). The reaction was stirred for 24 h at 60 °C. The desired product was obtained as a colourless solid in 84% yield (173.8 mg). ^{1}H NMR (500 MHz, $CDCl_3$) δ = 7.49 (t, *J* = 7.8 Hz, 2H, H_{Ar} IPr), 7.28 (d, *J* = 7.8 Hz, 4H, H_{Ar} IPr), 7.13 (s, 2H, H imidazole IPr), 2.56 (sept, *J* = 6.9 Hz, 4H, $CH(CH_3)_2$), 2.06 (s, 2H, CH_2), 1.53 (s, 3H, CH_3), 1.32 (d, *J* = 6.9 Hz, 12H,

$CH(CH_3)_2$), 1.21 (d, *J* = 6.9 Hz, 12H, $CH(CH_3)_2$); $^{13}C\{^1H\}$ NMR (126 MHz, $CDCl_3$): δ = 212.1 (C=O), 193.1 ($C_{carbene}$), 145.8 (CH_{Ar} IPr), 134.4 (CH_{Ar} IPr), 130.5 (CH_{Ar} IPr), 124.4 (CH_{Ar} IPr), 124.1 (CH_{Ar} IPr), 122.8 (CH imidazole IPr), 40.7 (CH_2), 29.5 (CH_3), 28.9 ($CH(CH_3)_2$), 24.5 ($CH(CH_3)_2$), 24.1 ($CH(CH_3)_2$); elemental analysis calcd (%): C 55.98 H 6.58, N 4.35; found: C 55.97, H 6.38, N 4.37; FTIR (ATR) ν = 1643 (CO) cm^{-1}.

[$Au(CH_2C(O)CH_3)$(SIPr)] (**6.9**): complex **6.9** was synthesised following GP2 using [AuCl(SIPr)] (100 mg, 0.16 mmol, 1 equiv.) and K_2CO_3 (138.9 mg, 0.96 mmol, 6 equiv.) in acetone (2 mL). The reaction was stirred for 72 h at 60 °C. The desired product was obtained as a colourless solid in 97% yield (100 mg). ^1H NMR (300 MHz,$CDCl_3$) δ = 7.40 (dd, *J* = 8.3, 7.2 Hz, 2H, H_{Ar} SIPr), 7.23 (d, *J* = 7.7 Hz, 4H, H_{Ar} SIPr), 4.00 (s, 4H, H imidazole SIPr), 3.06 (sept, *J* = 6.9 Hz, 4H, $CH(CH_3)_2$), 1.99 (d, *J* = 0.9 Hz, 2H, CH_2), 1.44 (s, 3H, CH_3), 1.39 (d, *J* = 6.8 Hz, 12H, $CH(CH_3)_2$), 1.33 (d, *J* = 7.0 Hz, 12H, $CH(CH_3)_2$); $^{13}C\{^1H\}$ NMR (126 MHz, $CDCl_3$) δ = 212.4 (C=O), 212.0 ($C_{carbene}$), 146.8 (CH_{Ar} SIPr), 134.5 (CH_{Ar} SIPr), 129.7 (CH_{Ar} SIPr), 124.5 (CH_{Ar} SIPr), 53.7 (CH_2 imidazole SIPr), 41.0 (CH_2), 29.4 ($CH(CH_3)_2$), 29.1 (CH_3), 25.1 (CH_3), 24.2 (CH_3); elemental analysis calcd (%): C 55.88, H 6.79, N 4.42; found: C 55.90, H 6.72, N 4.35; FTIR (ATR) ν = 1643 (CO) cm^{-1}.

[$Au(CH_2C(O)CH_3)$(IMes)] (**6.12**): complex **6.12** was synthesised following GP1 using IMes·HCl (197.7 mg, 0.58 mmol, 1 equiv.), [$AuCl(SMe_2)$] (170.8 mg, 0.58 mmol, 1 equiv.), K_2CO_3 (480 mg, 3.48 mmol, 6 equiv.) in acetone (10 mL). The reaction was stirred for 72 h at 60 °C. The desired product was obtained as a colourless solid in 68% yield (291.3 mg). Complex **6.12** was also synthesised following GP2 using [AuCl(IMes)] (200 mg, 0.373 mmol, 1 equiv.) and K_2CO_3 (308.9 mg, 2.24 mmol, 6 equiv.) in acetone (2 mL). The reaction was stirred for 72 h at 60 °C. The desired product was obtained as a white solid in 73% yield (151.6 mg). ^1H NMR (500 MHz, $CDCl_3$) δ = 7.04 (s, 2H, H imidazole IMes), 7.00 (s, 4H, H_{Ar} IMes), 2.34 (s, 6H, CH_3*p*-CH_3 IMes), 2.10 (s, 12H, CH_3 IMes), 2.09 (s, 3H, CH_2) 1.64 (s, 3H, CH_3). $^{13}C\{^1H\}$ NMR (126 MHz, $CDCl_3$) δ = 212.5 (C=O), 191.3 ($C_{carbene}$), 139.5 (CH_{Ar} IMes), 134.9 (CH_{Ar} IMes), 129.3 (CH_{Ar} IMes), 41.1 (CH_2), 29.4 (CH_3), 21.3 (*p*-CH_3 IMes), 17.9 (CH_3 IMes); elemental analysis calcd (%): C 51.60, H 5.16, N 5.16; found: C 51.62, H 5.23, N 5.02; FTIR (ATR) ν = 1643 (CO), cm^{-1}.

[Au($CH_2C(O)CH_3$)(SIMes)] (**6.13**): complex **6.13** was synthesised following GP2 using [AuCl(SIMes)] (170.8 mg, 0.58 mmol, 1 equiv.), and K_2CO_3 (480.5 mg, 3.48 mmol, 6 equiv.) in acetone (2 mL). The reaction was stirred for 72 h at 60 °C. The desired product was obtained as a colourless solid in 73% yield (237.3 mg). ^{1}H NMR (400 MHz, $CDCl_3$) δ = 6.95 (s, 4H, CH_{Ar} SIMes), 3.92 (s, 4H, H_2 imidazole SIMes), 2.31 (s, 12H, CH_3 SIMes), 2.29 (s, 6H, *p*-CH_3 SIMes), 2.02 (d, *J* = 0.8 Hz, 2H, CH_2), 1.54 (s, 3H, CH_3). $^{13}C\{^1H\}$ NMR (101 MHz, $CDCl_3$) δ = 212.5 (C=O), 211.6 ($C_{carbene}$), 138.7 (CH_{Ar} SIMes), 135.8 (CH_{Ar} SIMes), 135.1 (CH_{Ar} SIMes), 129.6 (CH_{Ar} SIMes), 50.9 (CH_2 imidazole SIMes), 41.4 (CH_2), 29.3 (CH_3), 21.2 (*p*-CH_3 SIMes), 18.2 (CH_3 SIMes); elemental analysis calcd (%): C 51.43, H 5.58, N 5.00; found: C 51.35, H 5.71, N 4.97; FTIR (ATR) ν = 1645 (CO) cm^{-1}.

[Au($CH_2C(O)CH_3$)(IPr^{Cl})] (**6.14**): complex **6.14** was synthesised following GP2 using [AuCl(IPr^{Cl})] (100 mg, 0.145 mmol, 1 equiv.), and K_2CO_3 (120.2 mg, 0.870 mmol, 6 equiv.) in acetone (2 mL). The reaction was stirred for 48 h at 60 °C. The desired product was obtained as a colourless solid in 81% yield (83.2 mg). ^{1}H NMR (500 MHz, $CDCl_3$) δ = 7.54 (t, *J* = 7.7 Hz, 2H, H_{Ar} IPr^{Cl}), 7.31 (d, *J* = 7.8 Hz, 4H, H_{Ar} IPr^{Cl}), 2.46 (2.45 (sept, *J* = 6.8 Hz, 4H, $CH(CH_3)_2$), 2.06 (s, 2H, CH_2), 1.52 (s, 3H, CH_3), 1.32 (d, *J* = 6.8 Hz, 12H, $CH(CH_3)_2$), 1.25 (d, *J* = 6.9 Hz, 12H, $CH(CH_3)_2$). $^{13}C\{^1H\}$ NMR (126 MHz, $CDCl_3$) δ = 212.1 (C=O), 193.0 ($C_{carbene}$), 146.3 (CH_{Ar} IPr^{Cl}), 131.4 (CH_{Ar} IPr^{Cl}), 124.5 (CH_{Ar} IPr^{Cl}), 118.9 (CH_{Ar} IPr^{Cl}), 39.8 (CH_2), 29.6 (CH_3), 29.2 ($CH(CH_3)_2$), 24.6 ($CH(CH_3)_2$), 23.6 ($CH(CH_3)_2$); elemental analysis calcd (%): C 50.64, H 5.53, N 3.94; found: C 50.52, H 5.47, N 3.99; FTIR (ATR) ν = 1651 (CO) cm^{-1}.

[Au($CH_2C(O)CH_3$)(IPr*)] (**6.15**): Complex **6.15** was synthesised following **GP2** using [AuCl(IPr*)] (50 mg, 0.044 mmol, 1 equiv.), and K_2CO_3 (36.2 mg, 0.264 mmol, 6 equiv.) in acetone (2 mL). The reaction was stirred for 72 h at 60 °C. The desired product was obtained as a colourless solid in 92% yield (43.5 mg). ^{1}H NMR (500 MHz, $CDCl_3$) δ = 7.25 – 7.09 (m, 26H, H_{Ar} IPr*), 6.91 – 6.84 (m, 14H), 5.77 (s, 2H, H imidazole IPr*), 5.32 (s, 4H, $CH(Ph)_2$), 2.33 (s, 2H, CH_2), 2.23 (s, 6H, *p*-CH_3 IPr*), 1.67 (s, 3H, CH_3). $^{13}C\{^1H\}$ NMR (126 MHz, $CDCl_3$) δ = 212.5 (C=O), 192.6 ($C_{carbene}$), 142.8 (CH_{Ar} IPr*), 141.1 (CH_{Ar} IPr*), 139.9 (CH_{Ar} IPr*), 134.1 (CH_{Ar} IPr*), 130.1 (CH_{Ar} IPr*), 129.8 (CH_{Ar} IPr*), 129.5 (CH_{Ar} IPr*), 128.6 (CH_{Ar} IPr*), 128.4 (CH_{Ar} IPr*), 126.7 (CH_{Ar} IPr*), 126.7

(CH_{Ar} IPr*), 123.1 (CH imidazole IPr*), 51.3 ($CH(Ph)_2$), 41.4 (CH_2), 29.9 (CH_3), 21.9 (*p*-CH_3 IPr*); elemental analysis calcd (%): C 74.09, H 5.27, N 2.40; found: C 73.97, H 5.22, N 2.47. FTIR (ATR) ν = 1651 (CO) cm^{-1}.

[Au($CH_2C(O)CH_3$)(IAd)] (**6.16**): complex **6.16** was synthesised following GP2 using [AuCl(IAd)] (50 mg, 0.088 mmol, 1 equiv.), and K_2CO_3 (72.9 mg, 0.527 mmol, 6 equiv.) in acetone (2 mL). The reaction was stirred for 72 h at 60 °C. The desired product was obtained as a colourless solid in 84% yield (43.2 mg). ^{1}H NMR (300 MHz, $CDCl_3$) δ = 7.02 (s, 2H, H imidazole IAd), 2.64 (s, 2H, CH_2), 2.53 (d, *J* = 3.0 Hz, 13H. CH IAd), 2.25 (s, 6H, CH_2 IAd), 2.21 (s, 3H, CH_3), 1.76 (d, *J* = 3.2 Hz, 14H, CH IAd). $^{13}C\{^1H\}$ NMR (126 MHz, $CDCl_3$) δ = 213.1 (C=O), 186.5 (C carbene), 115.1 (CH imidazole IAd), 58.9 (CH IAd), 44.4 (CH IAd), 39.5 (CH IAd), 38.1(CH_2), 36.0 (CH IAd), 30.0 (CH_2 IAd), 29.6 (CH_3); elemental analysis calcd (%): C 52.88, H 6.32, N 4.74; found: C 52.78, H 6.27, N 4.63; FTIR (ATR) ν = 1643 (CO) cm^{-1}.

[Au($CH_2C(O)CH_3$)(I*t*Bu)] (**6.17**): complex **6.17** was synthesised following GP2 using [AuCl(I*t*Bu)] (25 mg, 0.06 mmol, 1 equiv.), and K_2CO_3 (83.7 mg, 0.6 mmol, 10 equiv.) in acetone (2 mL). The reaction was stirred for 72 h at 60 °C. The desired product was obtained as a colourless solid in 60% yield (15.7 mg, 0.036 mmol).^{1}H NMR (300 MHz, $CDCl_3$) δ = 7.01 (s, 2H, H imidazole I*t*Bu), 2.62 (q, *J* = 0.9 Hz, 2H, CH_2), 2.20 (t, *J* = 0.9 Hz, 3H, CH_3), 1.83 (s, 17H, $C(CH_3)_3$). $^{13}C\{^1H\}$ NMR (75 MHz, $CDCl_3$) δ = 213.1 (C=O), 188.1 ($C_{carbene}$), 115.9 (CH imidazole I*t*Bu), 58.6 ($C(CH_3)_3$ I*t*Bu), 38.7 (CH_2), 31.9 ($C(CH_3)_3$ I*t*Bu), 29.6 (CH_3); FTIR (ATR) ν = 1618 (CO) cm^{-1}.

[Au($CH_2C(O)Ph$)(IPr)] (**6.18**): complex **6.18** was synthesised following using GP3 reacting acetophenone (42.59 µL, 0.365 mmol, 1.1 equiv.), and [Au(OH)(IPr)] (200 mg, 0.332 mmol, 1 equiv.) in THF (2 mL). The reaction was stirred for 24 h at 60 °C. The desired product was obtained as a colourless solid in 72% yield (167.8 mg). ^{1}H NMR (500 MHz, $CDCl_3$) δ = 7.56 (dd, *J* = 8.2, 1.2 Hz, 2H, H Ph), 7.47 (t, *J* = 7.8 Hz, 1H, CH_{Ar} IPr), 7.22 (d, *J* = 7.8 Hz, 3H, H_{Ar} IPr, H Ph), 7.09 (s, 2H, H imidazole), 7.08 (s, 2H, H Ph), 2.50 (p, *J* = 6.9 Hz, 4H, $CH(CH_3)_2$), 2.46 (s, 2H, CH_2), 1.19 (d, *J* = 6.9 Hz, 12H, $CH(CH_3)_2$), 1.17 (d, *J* = 6.9 Hz, 12H, $CH(CH_3)_2$). $^{13}C\{^1H\}$ NMR (126 MHz, $CDCl_3$) δ = 204.5 (C=O), 192.6 ($C_{carbene}$), 145.7 (Cq IPr), 140.5 (Cq Ph), 134.4 (Cq IPr), 130.4 (Cq IPr),129.6 (CH_{Ar} Ph), 127.6 (CH_{Ar} Ph), 127.4 (CH_{Ar} Ph), 124.1 (CH_{Ar} IPr), 122.8 (CH

imidazole IPr), 36.2 (CH_2), 28.8 ($CH(CH_3)_2$), 24.4 ($CH(CH_3)_2$), 24.1 ($CH(CH_3)_2$); elemental analysis calcd (%): C 59.65, H 6.15, N 3.98; found: C 59.78, H 6.27, N 4.03; FTIR (ATR) ν = 1624 (CO) cm^{-1}.

[Au($CH_2C(O)CH_2OAc$)(IPr)] (**6.19**): complex **6.19** was synthesised following using GP3 reacting acetoxyacetone (3.94 μL, 0.036 mmol, 1.1 equiv.), and [Au(OH)(IPr)] (20 mg, 0.033 mmol, 1 equiv.) in C_6D_6 (2 mL). The reaction was stirred for 18 h at 60 °C. The desired product was obtained as a colourless solid in 44% yield (10.1 mg). ^{1}H NMR (400 MHz, $CDCl_3$) δ = 7.49 (t, *J* = 7.8 Hz, 2H), 7.29 (d, *J* = 7.8 Hz, 4H), 7.13 (s, 2H), 4.02 (s, 2H, CH_2OAc), 2.54 (p, *J* = 6.8 Hz, 4H, $CH(CH_3)_2$ IPr), 2.08 (s, 2H, CH_2-Au), 1.97 (s, 3H, CH_3), 1.31 (d, *J* = 6.9 Hz, 12H, $CH(CH_3)_2$ IPr), 1.21 (d, *J* = 6.9 Hz, 12H, $CH(CH_3)_2$ IPr). $^{13}C\{^1H\}$ NMR (101 MHz, $CDCl_3$) δ = 206.44 (C=O), 192.2 ($C_{carbene}$), 170.6 (C=O, Ac), 145.8 (Cq IPr),134.3 (Cq IPr), 130.6 (Cq IPr), 124.2 (CH_{Ar} IPr), 122.9 (CH imidazole IPr), 67.4 (CH_2), 35.6 (CH_2-Au), 28.9 ($CH(CH_3)_2$), 24.5 ($CH(CH_3)_2$), 24.1 ($CH(CH_3)_2$), 21.1 (CH_3).

[Au(CH_2CN)(IPr)] (**6.20**): Complex **6.20** was synthesised following using **GP3**, reacting [Au(OH)(IPr)] (32.50 mg, 0.053 mmol) in $NCCH_3$ (2 mL). The reaction was stirred for 20 h at 80 °C. The desired product was obtained as a colourless solid in 90% yield (30.4 mg). ^{1}H NMR (400 MHz, C_6D_6) δ = 7.21 (dd, *J* = 8.3, 7.3 Hz, 1H, *p*-H_{Ar} IPr), 7.07 (d, *J* = 7.7 Hz, 1H, *m*-H_{Ar} IPr), 6.36 (s, 2H, H imidazole), 2.57 (h, *J* = 6.9 Hz, 4H, $CH(CH_3)_2$), 1.45 (d, *J* = 6.8 Hz, 12H, $CH(CH_3)_2$), 1.20 (s, 2H, CH_2), 1.08 (d, *J* = 6.9 Hz, 12H, $CH(CH_3)_2$). $^{13}C\{^1H\}$ NMR (101 MHz, C_6D_6) δ = 193.6 ($C_{carbene}$), 145.8 (Cq IPr), 130.8 (*p*-CH_{Ar} IPr), 127.6 (Cq IPr), 124.3 (*m*-C_{Ar} IPr), 122.8 (CH imidazole IPr), 29.0 ($CH(CH_3)_2$), 24.7 ($CH(CH_3)_2$), 23.9 ($CH(CH_3)_2$), -2.1 (CH_2); elemental analysis calcd (%): C 55.68, H 6.12, N 6.72; found: C 55.41, H 6.17, N 6.22; FTIR (ATR) ν = 2196.92 (C≡N), 1471.69/1458.18 cm^{-1}.

[Au($CH(Cl)C(O)CH_3$)(IPr)] (**6.21**): Complex **6.21** was synthesised following using **GP3**, reacting chloroacetone (3.4 mg, 0.036 mmol, 1.1 equiv.), [Au(OH)(IPr)] (20 mg, 0.033 mmol, 1 equiv.) in C_6D_6 (2 mL). The reaction was stirred for 48 h at 60 °C. The desired product was characterised in the reaction mixture: ^{1}H NMR (300 MHz, C_6D_6) δ = 7.25–7.14 (m, 11H, H_{Ar} IPr), 7.08–6.98 (m, 6H, H_{Ar} IPr), 6.32 (d, *J* = 1.5 Hz, 3H, H imidazole), 4.54 (d, *J* = 0.7 Hz, 1H, CHCl), 3.59 (s, 1H), 3.22 (s, 3H), 2.59 (s, 1H), 2.56 – 2.44 (m,

5H, $CH(CH_3)_2$), 1.71 (d, *J* = 0.6 Hz, 3H, CH_3), 1.52 (s, 4H), 1.41 (dd, *J* = 6.8, 2.3 Hz, 18H, $CH(CH_3)_2$), 1.06 (d, *J* = 6.9 Hz, 19H, $CH(CH_3)_2$); $^{13}C\{^1H\}$ NMR (126 MHz, C_6D_6) δ = 202.4, 201.9 (C=O), 198.4, 193.3, 190.3 ($C_{carbene}$), 145.8, 134.6, 134.4, 130.9, 130.8, 128.3, 128.2, 124.3, 124.3, 124.3, 122.8 (CH imidazole), 122.6, 66.7 (CH), 48.3, 47.9, 35.9, 29.0 ($CH(CH_3)_2$), 26.6, 26.1 (CH_3), 24.7 ($CH(CH_3)_2$), 23.9 ($CH(CH_3)_2$).

6.6.2. Reactivity studies of [Au($CH_2C(O)CH_3$)(NHC)] species

GP4: [Au($CH_2C(O)CH_3$)(NHC)] (**6.10** or **6.12**) (1 equiv.) and R-H (1.5 equiv.) were dissolved in THF, C_6D_6 or $CDCl_3$ (1 mL) and stirred at 80 °C. For **6.12** the addition of R-H was performed at 0°C. The solvent was removed under vacuum, and the resulting solid dissolved in CH_2Cl_2 (2-3 mL). The solution was concentrated (~1 mL) and the product precipitated by addition of pentane (~10 mL). The precipitate was collected by filtration, washed with pentane (3×5 mL) and dried under vacuum, affording the corresponding [Au(R)(IPr)] complexes as colourless solids in good to excellent yields.

GP5: [Au($CH_2C(O)CH_3$)(IPr)] (**6.10** or **6.12**) (1 equiv.) and R-H (1.1 equiv.) were dissolved in THF, C_6D_6 or $CDCl_3$ (1 mL) and stirred at r.t.. For **6.12** the addition of R-H was performed at 0°C. The solvent was removed under vacuum and the resulting solid dissolved in CH_2Cl_2 (2−3 mL). The solution was concentrated (~1 mL), and the product precipitated by addition of pentane (~10 mL). The precipitate was collected by filtration, washed with pentane (3×5 mL) and dried under vacuum, affording the corresponding [Au(R)(IPr)] complexes as white solids in good to excellent yields.

GP6: [Au($CH_2C(O)CH_3$)(NHC)] (**6.10** or **6.12**) (1 equiv.) and pinacol borane (2 equiv.) were dissolved in C_6D_6 (1 mL), and stirred at r.t. under argon atmosphere. For **6.12** the addition of R-H was performed at 0°C. The solvent was then removed under vacuum, and the resulting solid dissolved in C_6D_6 (2−3 mL). The solution was concentrated (~1 mL), and the product precipitated by addition of hexane (~10 mL). The precipitate was collected by filtration, washed with pentane (3 × 5 mL), and dried under vacuum, affording the corresponding [Au(H)(NHC)] as colourless solids in good to excellent yields.

[Au(C≡CPh)(IPr)] (**6.22**): complex **6.22** was synthesised following GP4 using [Au($CH_2C(O)CH_3$)(IPr)] (**6.10**) (14.8 mg, 0.023 mmol, 1 equiv.), phenylacetylene (2.82 µL, 0.025 mmol, 1.1 equiv.) in C_6D_6 (1 mL). The reaction was stirred for 24 h at 80 °C. The mixture was concentrated, and the product precipitated to obtain a colourless solid in 87% yield (13.7 mg) whose data were consistent to those found in literature.[33] ^{1}H NMR (400 MHz, $CDCl_3$) δ = 7.49 (t, *J* = 7.8 Hz, 2H, H_{Ar} Ph), 7.32 – 7.28 (m, 4H, H_{Ar} IPr), 7.12 (s, 2H, CH imidazole IPr), 7.12 – 7.02 (m, 3H, H_{Ar} Ph), 2.60 (sept, *J* = 6.9 Hz, 4H, $CH(CH_3)_2$), 1.38 (d, *J* = 6.9 Hz, 12H, $CH(CH_3)_2$), 1.21 (d, *J* = 6.9 Hz, 12H, $CH(CH_3)_2$).

[Au(OPh)(IPr)] (**6.23**): complex [Au(OPh)(IPr)] (**6.23**) was synthesised following GP4 using [Au($CH_2C(O)CH_3$)(IPr)] (**6.10**) (25 mg, 0.039 mmol, 1 equiv.), phenol (5.5 mg, 0.058 mmol, 1.5 equiv.) in C_6D_6 (1 mL). The reaction was stirred for 24 h at 80 °C. The mixture was concentrated, and the product precipitated to obtain a colourless solid in 76% yield (19.9 mg) whose data were consistent to those found in literature.[41] ^{1}H NMR (500 MHz, C_6D_6) δ = 7.25 (t, *J* = 7.8 Hz, 2H, *p*-H_{Ar} IPr), 7.05 (d, *J* = 7.8 Hz, 4H, *m*-H_{Ar} IPr), 6.88 – 6.82 (m, 3H, *m*- and *p*-HPh), 6.74 (tt, *J* = 7.2, 1.2 Hz, 2H, *o*-HPh), 6.23 (s, 2H, H imidazole), 2.50 (hept, *J* = 6.9 Hz, 4H, $CH(CH_3)_2$), 1.31 (d, *J* = 6.9 Hz, 12H, $CH(CH_3)_2$), 1.02 (d, *J* = 6.9 Hz, 12H, $CH(CH_3)_2$).

[Au($CH(COCH_3)_2$)(IPr)] (**6.24**): complex **6.24** was synthesised following GP4 using [Au($CH_2C(O)CH_3$)(IPr)] (**6.10**) (200 mg, 0.31 mmol, 1 equiv.), acetylacetone (31.16 mg, 0.31 mmol, 1 equiv.) in THF (1 mL). The reaction was stirred for 72 h at 60 °C. The mixture was concentrated, and the product precipitated to obtain a colourless solid in 79% yield (167.5 mg, 0.245 mmol). ^{1}H NMR (500 MHz, $CDCl_3$) δ = 7.51 (t, *J* = 7.8 Hz, 2H, CH aromatic IPr), 7.29 (d, *J* = 7.8 Hz, 4H, CH aromatic IPr), 7.19 (s, 2H, CH imidazole IPr), 3.90 (s, 1H, CH), 2.50 (sept, *J* = 6.9 Hz, 4H, $CH(CH_3)_2$), 1.73 (s, 6H, CH_3), 1.29 (d, *J* = 6.9 Hz, 12H, $CH(CH_3)_2$), 1.22 (d, *J* = 6.9 Hz, 12H, $CH(CH_3)_2$). $^{13}C\{^1H\}$ NMR (126 MHz, $CDCl_3$) δ = 202.0 (C=O), 186.5 ($C_{carbene}$), 145.7 (Cq), 133.9 (Cq), 130.8 (CH_{Ar}), 124.4 (CH_{Ar}), 124.3 (CH_{Ar}), 123.2 (NCH), 71.7 (CH), 30.5 ($COCH_3$), 28.9 ($CH(CH_3)_2$), 24.5 ($CH(CH_3)_2$), 24.2 ($CH(CH_3)_2$); elemental analysis calcd (%): C 56.14; H 6.33; N 4.09; found: C 55.91; H 6.41; N 4.13.

[Au($CH(CO_2CH_3)_2$)(IPr)] (**6.25**): complex **6.25** was synthesised following GP4 using [Au($CH_2C(O)CH_3$)(IPr)] (**6.10**) (24.8 mg, 0.039 mmol, 1 equiv.), dimethoxy malonate

(7.9 mg, 0.058 mmol, 1.5 equiv.) in C_6D_6 (1 mL). The reaction was stirred for 96 h at 80 °C. The mixture was concentrated, and the product precipitated to obtain a colourless solid in 61% yield (16.84 mg) whose data were consistent to those reported in literature.[331] ^{1}H NMR (400 MHz, C_6D_6) δ = 7.20 (d, *J* = 7.8 Hz, 2H, *p*-H_{Ar} IPr), 7.04 (d, *J* = 7.7 Hz, 4H, *m*-H_{Ar} IPr), 6.23 (s, 2H, H imidazole), 3.79 (s, 1H, CH), 3.36 (s, 6H, OCH_3), 2.48 (sept, *J* = 6.9 Hz, 4H, $CH(CH_3)_2$), 1.42 (d, *J* = 6.9 Hz, 12H, $CH(CH_3)_2$), 1.06 (d, *J* = 6.9 Hz, 12H, $CH(CH_3)_2$).

[Au(S-pyr)(IPr)] (**6.26**): complex **6.26** was synthesised following GP5 using [$Au(CH_2C(O)CH_3)$(IPr)] (**6.10**) (30 mg, 0.047 mmol, 1 equiv.), 4-mercapto-pyridine (5.7 g, 0.051 mmol, 1.1 equiv.) in C_6D_6 (1 mL). The reaction was stirred for 24 h at r.t.. The mixture was concentrated, and the product precipitated to obtain a colourless solid in 88% yield (28.6 mg). ^{1}H NMR (400 MHz, $CDCl_3$) δ = 7.83 – 7.78 (m, 2H, H pyridine), 7.57 (t, *J* = 7.8 Hz, 2H, H_{Ar} IPr), 7.34 (d, *J* = 7.8 Hz, 4H, H_{Ar} IPr), 7.22 (s, 2H, H imidazole IPr), 6.69 – 6.64 (m, 2H, H pyridine), 2.61 (sept, *J* = 6.9 Hz, 4H, $CH(CH_3)_2$), 1.33 (d, *J* = 6.9 Hz, 12H, $CH(CH_3)_2$), 1.24 (d, *J* = 6.9 Hz, 12H, $CH(CH_3)_2$). $^{13}C\{^1H\}$ NMR (101 MHz, $CDCl_3$) δ = 185.9 ($C_{carbene}$), 157.6 (Cq), 147.4 (Cq), 146.1 (CH_{Ar}), 134.1 (CH_{Ar}), 130.9 (CH_{Ar}), 126.9 (CH_{Ar}), 124.4 (CH_{Ar}), 123.1 (CH_{Ar}), 29.0 ($CH(CH_3)_2$), 24.6 ($CH(CH_3)_2$), 24.2 ($CH(CH_3)_2$); elemental analysis calcd (%): C 55.25; H 5.80; N 6.04; found: C 55.14; H 5.72; N 6.09.

[$Au(OC(O)CH_3)$(IPr)] (**6.27**): complex **6.27** was synthesised following GP5 using [$Au(CH_2C(O)CH_3)$(IPr)] (**6.10**) (9.7 mg, 0.015 mmol, 1 equiv.), acetic acid (0.48 µL, 0.016 mmol, 1.1 equiv.) in $CDCl_3$ (0.5 mL). The reaction was stirred for 24 h at r.t..The mixture was concentrated, and the product precipitated to obtain a colourless solid in 88% yield (8.6 mg) whose data were consistent to those reported in literature.[33] ^{1}H NMR (300 MHz, $CDCl_3$) δ = 7.55 – 7.43 (m, 2H, *p*-H_{Ar} IPr), 7.29 (d, *J* = 7.8 Hz, 4H, *p*-H_{Ar} IPr), 7.18 (s, 2H, H imidazole), 2.55 (sept, *J* = 6.9 Hz, 4H, $CH(CH_3)_2$), 1.77 (s, 3H, CH_3), 1.37 (d, *J* = 6.9 Hz, 12H, $CH(CH_3)_2$), 1.22 (d, *J* = 6.9 Hz, 12H, $CH(CH_3)_2$).

[$Au(OC(O)Ph)$(IPr)] (**6.28**): complex **6.28** was synthesised following **GP5** using [$Au(CH_2C(O)CH_3)$(IPr)] (**6.10**) (50.2 mg, 0.078 mmol, 1 equiv.), benzoic acid (9.5 mg, 0.078 mmol, 1 equiv.) in $CDCl_3$ (0.5 mL). The reaction was stirred for 24 h at r.t..The mixture was concentrated, and the product precipitated to obtain a colourless solid in 72%

yield (39.8 mg, 0.056 mmol). ^{1}H NMR (500 MHz, $CDCl_3$) δ = 7.88 (dt, *J* = 7.1 Hz, 1.5 Hz, 2H, H_{Ar}), 7.50 (t, *J* = 7.8 Hz, 2H, H_{Ar}), 7.33 – 7.27 (m, 6H, H_{Ar}), 7.25 – 7.20 (m, 2H, H_{Ar}), 7.19 (s, 2H, H imidazole IPr), 2.60 (sept, *J* = 6.8 Hz, 4H, $CH(CH_3)_2$), 1.42 (d, *J* = 6.9 Hz, 12H, $CH(CH_3)_2$), 1.23 (d, *J* = 6.9 Hz, 12H, $CH(CH_3)_2$). ^{13}C{^{1}H} NMR (126 MHz, $CDCl_3$) δ = 171.2 ($C_{carbene}$), 168.7 (C=O), 145.8 (Cq IPr), 134.2 (Cq IPr), 130.8 (Cq), 130.3 (CH_{Ar}), 129.8 (CH_{Ar}), 127.5 (CH_{Ar}), 124.4 (CH_{Ar}), 123.3 (CH_{Ar}), 29.1 ($CH(CH_3)_2$), 24.6 ($CH(CH_3)_2$), 24.3 ($CH(CH_3)_2$); elemental analysis calcd (%): C 57.79; H 5.85; N 3.96; found: C 57.66; H 5.95; N 4.06.

[Au{OC(O)Ph(2,6-F_2)}(IPr)] (**6.29**): complex **6.29** was synthesised following GP5 using [Au($CH_2C(O)CH_3$)(IPr)] (**6.10**) (50.2 mg, 0.078 mmol, 1 equiv.), 2,6-difluorobenzoic acid (12.3 g, 0.078 mmol, 1 equiv.) in $CDCl_3$ (0.5 mL). The reaction was stirred for 18 h at r.t.. The mixture was concentrated, and the product precipitated to obtain a colourless solid in 86% yield (50.1 mg, 0.067 mmol). ^{1}H NMR (500 MHz, $CDCl_3$) δ = 7.51 (t, *J* = 7.8 Hz, 2H, *p*-H_{Ar} IPr), 7.30 (d, *J* = 7.8 Hz, 4H, *m*-H_{Ar} IPr), 7.20 (s, 2H), 7.07 (ddd, *J* = 8.4, 6.3, 2.2 Hz, 1H, *p*-H_{Ar} Ph), 6.70 (dd, *J* = 8.3, 7.1 Hz, 2H, *m*-H_{Ar} IPr), 2.57 (sept, *J* = 6.9 Hz, 4H, $CH(CH_3)_2$), 1.38 (d, *J* = 6.8 Hz, 12H, $CH(CH_3)_2$), 1.22 (d, *J* = 6.9 Hz, 12H, $CH(CH_3)_2$) ^{13}C{^{1}H} NMR (126 MHz, $CDCl_3$) δ = 167.8 (C=O), 165.7 ($C_{carbene}$), 160.5 (d, $^{2}J_{CF}$ = 8.5), 158.5 (d, $^{2}J_{CF}$ = 8.4), 145.7 (Cq IPr), 134.1 (Cq IPr), 130.9 (CH_{Ar}), 129.1 (t, $^{3}J_{CF}$ = 9.8), 124.4 (CH_{Ar}), 123.4 (CH_{Ar}), 112.1 (dd, $^{3}J_{CF}$ = 21.3, 3.6), 111.2 (dd, $^{3}J_{CF}$ = 20.7, 15.1 29.03 ($CH(CH_3)_2$), 24.5 ($CH(CH_3)_2$), 24.3 ($CH(CH_3)_2$). ^{19}F{^{1}H} NMR (471 MHz, $CDCl_3$) δ = -112.53; elemental analysis calcd (%): C 54.99; H 5.29; N 3.77; found: C 54.86; H 5.37; N 3.84.

[Au{OC(O)Ph(2,6-OMe)}(IPr)] (**6.30**): complex **6.30** was synthesised following GP5 using [Au($CH_2C(O)CH_3$)(IPr)] (**6.10**) (15 mg, 0.023 mmol, 1 equiv.), 2,6-dimethoxybenzoic acid (4.3 mg, 0.023 mmol, 1 equiv.) in $CDCl_3$ (0.5 mL). The reaction was stirred for 48 h at r.t..The mixture was concentrated, and the product precipitated to obtain a colourless solid in 80% yield (14.2 mg) whose data were consistent to those found in literature.[5b] ^{1}H NMR (400 MHz, $CDCl_3$) δ = 7.50 (t, *J* = 7.8 Hz, 2H, *p*-H_{Ar} IPr), 7.29 (d, *J* = 7.8 Hz, 4H, *m*-H_{Ar} IPr), 7.18 (s, 2H, H imidazole IPr), 6.99 (t, *J* = 8.3 Hz, 1H, *p*-H_{Ar} Ph), 6.35 (d, *J* = 8.4 Hz, 2H, *m*-H_{Ar} Ph), 3.63 (s, 6H, OCH_3), 2.59 (sept, *J* = 6.9 Hz,

4H, $CH(CH_3)_2$), 1.39 (d, *J* = 6.9 Hz, 12H, $CH(CH_3)_2$), 1.22 (d, *J* = 6.9 Hz, 12H, $CH(CH_3)_2$).

[Au(H)(IPr)] (**6.31**): complex **6.31** was synthesised following **GP6** using [Au($CH_2C(O)CH_3$)(IPr)] (**2a**) (30 mg, 0.047 mmol, 1 equiv.), pinacol borane (11.9 mg, 0.047 mmol, 1 equiv.) in C_6D_6 (0.5 mL). The reaction was stirred for 18 h at r.t.. The mixture was concentrated, and the product precipitated to afford **6.31** as a colourless solid in 88% yield (24.3 mg) whose data were consistent to those found in literature.[44] ^{1}H NMR (400 MHz, C_6D_6) δ = 7.23 (t, *J* = 7.5 Hz, 2H, *p*-H_{Ar} IPr), 7.08 (d, *J* = 7.7 Hz, 4H, *m*-H_{Ar} IPr), 6.30 (s, 2H, H imidazole IPr), 5.09 (s, 1H, Au-H), 2.67 (sept, *J* = 6.9 Hz, 4H, $CH(CH_3)_2$), 1.48 (d, *J* = 6.9 Hz, 12H, $CH(CH_3)_2$), 1.10 (d, *J* = 6.9 Hz, 12H, $CH(CH_3)_2$).$^{13}C\{^1H\}$ NMR (101 MHz, C_6D_6) δ = 203.1 (NCAu) [Carbene peak assigned by 2D ^{1}H,^{13}C-gs-HMBC], 145.9 (Cq), 135.1 (Cq), 130.5 (CH_{Ar}), 124.1 (CH_{Ar}), 122.4 (CH imidazole), 29.1 ($CH(CH_3)_2$), 24.9 ($CH(CH_3)_2$), 23.9 ($CH(CH_3)_2$).

[AuCl(IPr)] (**6.1**): complex **6.1** was synthesised following GP5 using [Au($CH_2C(O)CH_3$)(IPr)] (**6.10**) (100 mg, 0.15 mmol, 1 equiv.), *t*$BuPh_2SiCl$ (42.8 mg, 0.15 mmol, 1 equiv.) in C_6D_6 (0.5 mL). The reaction was stirred for 24 h at r.t. The mixture was concentrated, and the product precipitated to afford a colourless solid in 99% yield (76 mg) whose data were consistent to those found in literature.[31] ^{1}H NMR (400 MHz, $CDCl_3$): δ = 7.50 (t, *J* = 7.8 Hz, 2H, H_{Ar} IPr), 7.29 (d, *J* = 7.8 Hz, 4H, H_{Ar} IPr), 7.17 (s, 2H, H_{Ar} IPr), 2.56 (sept, *J* = 6.9 Hz, 4H, $CH(CH_3)_2$), 1.34 (d, *J* = 6.9 Hz, 12H, $CH(CH_3)_2$), 1.22 (d, *J* = 6.9 Hz, 12H, $CH(CH_3)_2$).

tert-Butyldiphenyl(prop-1-en-2-yloxy)silane (**6.32**): the compound was synthesised following GP5 and recovered as a colourless oil in 72% yield (26.3 mg) whose data were consistent to those found in literature.[79] ^{1}H NMR (500 MHz, $CDCl_3$): δ = 7.79 – 7.75 (m, 4H), 7.48 – 7.39 (m, 6H), 3.99 – 3.98 (m, 1H), 3.86 (d, *J* = 0.8 Hz, 1H), 1.86 (d, *J* = 1.0 Hz, 3H), 1.08 (s, 9H). $^{13}C\{^1H\}$ NMR (126 MHz, $CDCl_3$): δ = 155.8 (Cq), 135.6 (C_{Ar}), 133.4 (C_{Ar}), 129.9 (C_{Ar}), 127.7 (CO), 92.5 (CH_2), 26.7 (CH_3), 22.9 (CH_3).

[Au(NTf_2)(IPr)] (**6.33**): complex **6.33** was synthesised following GP5 using [Au($CH_2C(O)CH_3$)(IPr)] (**6.10**) (8.7 mg, 0.013 mmol, 1 equiv.), triflimide (4.14 mg, 0.015 mmol, 1.1 equiv.) in C_6D_6 (0.5 mL). The reaction was stirred for 5 min at r.t.. The

mixture was concentrated, and the product precipitated to afford a colourless solid in 89% yield (10.39 mg) whose data were consistent to those found in literature.[46] ^{1}H NMR (300 MHz, $CDCl_3$): δ = 7.55 – 7.48 (m, 2H, CH aromatic IPr), 7.29 (d, *J* = 7.8 Hz, 4H, CH aromatic IPr), 7.24 (s, 2H, CH imidazole IPr), 2.45 (sept, *J* = 6.9 Hz, 4H, $CH(CH_3)_2$), 1.29 (d, *J* = 6.9 Hz, 12H, $CH(CH_3)_2$), 1.21 (d, *J* = 6.9 Hz, 12H, $CH(CH_3)_2$).

[Au(OPh)(IMes)] (**6.35**): complex **6.35** was synthesised following GP4 using [Au($CH_2C(O)CH_3$)(IMes)] (**6.12**) (29.5 mg, 0.053 mmol, 1 equiv.), phenol (5.5 mg, 0.058 mmol, 1.1 equiv.) in C_6D_6 (1 mL). The reaction was stirred for 18 h at 80 °C. The crude was concentrated, and the product precipitated to afford a colourless solid in 72% yield (22.5 mg). ^{1}H NMR (500 MHz, C_6D_6) δ = 7.21 – 7.17 (m, 2H, H_{Ar}), 6.98 – 6.92 (m, 5H, H_{Ar}), 6.76 (tt, *J* = 7.1 Hz, 1.2 Hz, 2H, H_{Ar}), 6.71 (s, 4H, H_{Ar}), 5.94 (s, 2H, CH imidazole), 2.13 (s, 6H, *p*-CH_3), 1.87 (s, 12H, *o*-CH_3); $^{13}C\{^1H\}$ NMR (126 MHz, C_6D_6): δ = 169.8 ($C_{carbene}$), 168.9 (Cq), 139.7 (*m*-C), 134.9 (*p*-C), 129.6 (*i*-C), 128.9 (CH_{Ar}), 121.5 (CH imidazole), 119.5 (CH_{Ar}), 114.9 (CH_{Ar}), 21.1 (*p*-CH_3), 17.7 (*o*-CH_3); elemental analysis calcd (%): C 54.55, H 4.92, N 4.71; found: C 54.54, H 4.97, N 4.83.

[Au{$CH(C(O)CH_3)_2$}(IMes)] (1,3-dimesityl-2,3-dihydro-1H-imidazol-2-yl)(2,4-dioxopentan-3-yl)gold (**6.36**): complex **6.36** was synthesised following GP5 using [Au($CH_2C(O)CH_3$)(IMes)] (**6.12**) (29.7 mg, 0.053 mmol, 1 equiv.), acetylacetone (8.1 mg, 0.08 mmol, 1.5 equiv.) in C_6D_6 (1 mL). The reaction was stirred for 16 h at 80 °C. The crude was concentrated, and the product precipitated to afford a colourless solid in 84% yield (26.8 mg) whose data were consistent to those found in literature.[80] ^{1}H NMR (400 MHz, $CDCl_3$) δ = 7.10 (s, 2H, H imidazole), 7.01 (d, *J* = 0.7 Hz, 4H, *m*-H_{Ar} IPr), 3.94 (t, *J* = 0.7 Hz, 1H, $CH(COCH_3)_2$), 2.35 (s, 6H, *p*-CH_3), 2.08 (s, 12H, *o*-CH_3), 1.83 (d, *J* = 0.6 Hz, 6H, $CH(COCH_3)_2$).

[Au{$CH(C(O)OCH_3)_2$}(IMes)] **(6.37**): complex **6.37** was synthesised following **GP5** using [Au($CH_2C(O)CH_3$)(IMes)] (**6.12**) (44,1 mg, 0.079 mmol, 1 equiv.), dimethoxymalonate (15.7 mg, 0.119 mmol, 1.5 equiv.) in C_6D_6 (1 mL). The reaction was stirred for 72 h at 80 °C. The crude was concentrated, and the product precipitated to afford a colourless solid in 86% (42.9 mg). ^{1}H NMR (500 MHz, $CDCl_3$) δ = 7.07 (s, 2H, H imidazole), 6.99 (s, 4H, *m*-H_{Ar} IMes), 3.37 (s, 6H, OCH_3), 3.28 (s, 1H, CH), 2.34 (s, 6H, *p*-CH_3), 2.09 (s, 12H, *o*-CH_3). $^{13}C\{^1H\}$ NMR (126 MHz, $CDCl_3$) δ = 185.2 ($C_{carbene}$),

172.9 (C=O), 139.4 (*m*-CH_{Ar} IPr), 134.9 (*p*-CH_{Ar} IPr), 129.3 (*i*-C), 122.1 (CH imidazole), 50.3 (OCH_3), 43.0 (CH), 21.2 (*p*-CH_3), 18.1 (*o*-CH_3); elemental analysis calcd (%): C 49.37, H 4.94, N 4.43; found: C 49.27, H 5.00, N 4.43.

[Au(OC(O)CH_3)(IMes)] (**6.38**): complex **6.38** was synthesised following **GP5** using [Au(CH_2C(O)CH_3)(IMes)] (**6.12**) (49 mg, 0.088 mmol, 1 equiv.), acetic acid (5.80 mg, 0.088 mmol, 1 equiv.) in $CDCl_3$ (1 mL). The reaction was stirred for 1 h at r.t.. The crude was concentrated, and the product precipitated to afford **6.40** as a colourless solid in 64% yield (31.3 mg). ^{1}H NMR (400 MHz, $CDCl_3$) δ = 7.09 (s, 2H, H imidazole), 7.00 – 6.99 (m, 4H, H_{Ar}), 2.34 (s, 6H, *p*-CH_3), 2.12 (s, 12H, *o*-CH_3), 1.82 (s, 3H, CH_3). ^{13}C{^{1}H} NMR (101 MHz, $CDCl_3$) δ = 176.9 (C=O), 166.7 ($C_{carbene}$), 139.8 (Cq), 134.8 (Cq), 129.6 (CH_{Ar}), 122.4 (CH imidazole), 23.9 ($COCH_3$), 21.3 (*p*-CH_3), 17.9 (*o*-CH_3); elemental analysis calcd (%): C 49.29, H 4.89, N 5.00; found: C 49.20, H 4.79, N 5.08.

[Au(H)(IMes)] (**6.39**): complex **6.39** was synthesised following GP6 using [Au(CH_2C(O)CH_3)(IMes)] (**6.12**) (40 mg, 0.072 mmol, 1 equiv.), pinacol borane (18.32 mg, 0.143 mmol, 2 equiv.) in C_6D_6 (0.5 mL). The reaction was stirred for 17 h at r.t.. The crude was concentrated, and the product precipitated as a colourless solid in 83% yield (29.9 mg) whose data were consistent to those found in literature.[49] ^{1}H NMR (500 MHz, C_6D_6) δ = 6.71 – 6.67 (m, 4H, H_{Ar}), 6.02 (s, 2H, H imidazole), 5.28 (s, 1H, Au-H), 2.08 (s, 6H, *p*-CH_3), 2.03 (s, 12H, *o*-CH_3). ^{13}C{^{1}H} NMR (101 MHz, C_6D_6) δ = 203.1 ($C_{carbene}$) [Carbene peak assigned by 2D ^{1}H,^{13}C-gs-HMBC], 139.0 (*m*-C), 135.9 (*p*-C), 134.9 (*i*-C), 129.5 (CH_{Ar}), 121.3 (CH imidazole), 21.1 (*p*-CH_3), 17.9 (*o*-CH_3); elemental analysis calcd (%): C 50.20, H 5.02, N 5.58; found: C 50.08, H 4.94, N 5.58.

[AuCl(IMes)] (**6.40**): complex **6.40** was formed by reacting [Au(CH_2C(O)CH_3)(IMes)] (**6.12**) (100 mg, 0.179 mmol, 1 equiv.) with *t*BuPh$_2$SiCl (49.2 mg, 0.179 mmol, 1 equiv.) in C_6D_6 (1 mL). The reaction was stirred for 17 h at r.t.. The crude mixture was concentrated, and the product precipitated to yield the desired product as a colourless solid in 99% (95.3 mg) whose data were consistent to those found in literature.[6] ^{1}H NMR (400 MHz, $CDCl_3$) δ = 7.09 (s, 2H, H imidazole), 6.99 (s, 4H, H_{Ar}), 2.34 (s, 6H, *p*-CH_3), 2.10 (s, 12H, *o*-CH_3).

1,2-Diphenylethanone (**6.43**): compound **6.43** was synthesised following the reported procedure.[52] Compound **6.10** (3.21 mg, 1 mol%, $5 \cdot 10^{-3}$ μmol), diphenylacetylene (**6.43**) (0.5 mmol, 89.11 mg, 1 equiv.) then 1 mL from a solution of $HBF_4 \cdot H_2O$ (0.48 wt.%) in 1,4-dioxane/water solution (2:1, 1 mL) were used. The compound was analysed (data reported in chapter 3), and the data were consistent to those reported in literature.[10]

1-Phenylhepta-1,2-dien-3-yl-acetate (**6.45**): compound **6.45** was synthesised using **6.10** (0.010 mmol, 6.4 mg, 2 mol%), propargylic acetate (0.5 mmol, 115.1 mg, 1 equiv.) and 1 mL of a solution (0.2 M) of $HBF_4 \cdot OEt_2$ (0.51-0.57 wt%, 0.015 mmol, 2.04 μL, 3 mol%) in 1,2-dichloroethane (10 mL). The mixture was heated at 40 °C. The compound was analysed by ^{1}H NMR after 15 min reaction.[57b] ^{1}H NMR (400 MHz, $CDCl_3$) δ 7.45-7.40 (m, 2H, H_{Ar}), 7.36-7.30 (m, 2H, H_{Ar}), 7.26- 7.20 (m, 1H, H_{Ar}), 6.59 (t, *J* = 3.1 Hz, 1H, CH), 2.37-2.31 (m, 2H, CH_2), 2.15 (s, 3H, CH_3), 1.51-1.34 (m, 4H, CH_2), 0.90 (t, *J* = 7.1 Hz, 3H, CH_2CH_3).

1-Butyl-1H-inden-1-yl-acetate (**6.46**): compound **6.46** was synthesised using **6.10** (0.010 mmol, 6.4 mg, 2 mol%), propargylic acetate (0.5 mmol, 115.0 mg, 1 equiv.), and $HBF_4 \cdot OEt_2$ (0.51-0.57 wt%, 0.015 mmol, 2.04 μL, 3 mol%) in 1,2-dichloroethane (10 mL). The compound was analysed by GC after 24 h reaction. The product formation was confirmed by ^{1}H NMR analysis.[53] ^{1}H NMR (300 MHz, $CDCl_3$) δ = 7.35 (d, *J* = 7.2 Hz, 1H, H_{Ar}), 7.24–7.14 (m, 2H, H_{Ar}), 7.21–7.18 (m, 1H, H_{Ar}), 6.70 (d, *J* = 5.7 Hz, 1H, CArCH=CH), 6.56 (d, *J* = 5.7 Hz, 1H, CArCH=CH), 2.22 (dt, *J* = 12.6, 4.5 Hz, 1H, CCH_2CH_2), 1.99 (s, 3H, OAc), 1.93 (dt, *J* = 12.6, 4.5 Hz, 1H, CCH_2CH_2), 1.32–1.19 (m, 4H, $CH_2CH_2CH_3$), 0.83 ppm (t, *J* = 7.5 Hz, 3H, CH_2CH_3).

3-Butyl-1H-inden-1-yl acetate (**6.47**): compound **6.47** was synthesised using **6.10** (0.010 mmol, 6.4 mg, 2 mol%), propargylic acetate (0.5 mmol, 115.0 mg, 1 equiv.), and $HBF_4 \cdot OEt_2$ (0.51-0.57 wt%, 0.015 mmol, 2.04 μL, 3 mol%) in 1,2-dichloroethane (10 mL). The compound was analysed by GC after 48 h reaction. The product formation was confirmed by ^{1}H NMR analysis.[57c] ^{1}H NMR (400 MHz, $CDCl_3$) δ = 7.44 (d, *J* = 7.3 Hz, 1H, H_{Ar}), 7.35–7.30 (m, 1H, H_{Ar}), 7.25 (d, *J* = 7.2 Hz, 1H, H_{Ar}), 7.21 (dt, J = 7.3,0.9 Hz, 1H, H_{Ar}), 6.19 (m, 1H, CH), 6.05 (m, 1H, CHOAc), 2.51–2.45 (m, 2H, CH_2), 2.15 (s, 3H, CH_3Ac), 1.70–1.62 (m, 2H, $CH_2CH_2CH_3$), 1.49–1.39 (m, 2H, $CH_2CH_2CH_3$), 0.97 (t, *J* = 7.3 Hz, 3H, CH_3).

6.6.3. Preparation of organogold(III) species

$[AuBr_2(CH_2C(O)CH_3)(IPr)]$ (**6.51**): compound **6.51** was synthesised by using **6.10** (0.03 mmol, 20 mg), and a drop of elemental Br_2 in $CDCl_3$ (0.6 mL). The compound was characterised in the mixture together with $[AuBr_3(IPr)]$.[66] ^{1}H NMR (500 MHz, $CDCl_3$) δ = 7.46 (t, *J* = 7.8 Hz, 2H, H_{Ar} IPr), 7.42 (t, *J* = 7.8 Hz, 2H, H_{Ar} **6.51**), 7.28 (d, *J* = 4.9 Hz, 3H, H_{Ar} IPr), 7.24 (d, *J* = 7.8 Hz, 5H, H_{Ar}**6.51**), 7.19 (d, *J* = 1.2 Hz, 3H, H imidazole), 4.23 (s), 4.10 (s), 3.82 (s, 1H, CH_2Br), 3.34 (pd, *J* = 6.7, 2.1 Hz, 1H), 2.97 – 2.83 (m, 10H, $CH(CH_3)_2$ IPr, 6.51, CH_2Br), 2.29 (s, 2H, CH_3), 1.62 (s, 3H, CH_3 6.51), 1.33 (dd, *J* = 12.5, 6.6 Hz, 24H, $CH(CH_3)_2$), 1.19 (d, *J* = 6.6 Hz, 2H), 1.04 (dd, *J* = 7.9, 6.8 Hz, 24H, $CH(CH_3)_2$). $^{13}C\{^1H\}$ NMR (126 MHz, $CDCl_3$) δ = 208.3 (C=O bromoacetone), 199.9 ($C_{carbene}$), 177.8 (C=O), 146.1 (Cq **6.51**), 146.0 (Cq), 133.7 (Cq **6.51**), 132.76 (Cq), 131.86 (CH_{Ar}), 131.1 (CH_{Ar} **6.51**), 126.4 (CH_{Ar}), 125.3, 124.4, 37.7, 35.0 (CH_2Br), 31.2, 29.3, 29.0, 27.3, 26.8 (CH_3), 26.7, 23.2, 22.9.

$[AuCl_2(CH_2CN)(IPr)]$ (**6.54**): compound **6.54** was synthesised by using **6.10** (0.03 mmol, 20 mg), and a drop of elemental Br_2 in $CDCl_3$ (0.6 mL). The compound was characterised in the mixture together with [AuCl(IPr)]. ^{1}H NMR (400 MHz, $CDCl_3$) δ 7.74 – 7.67 (m, 6H, H_{Ar}), 7.61 – 7.47 (m, 6H), 7.39 – 7.33 (m, 9H, H_{Ar} **6.1**, **6.54**), 7.33 – 7.24 (m, 10H, H_{Ar} + Himidazole **6.1**), 7.19 (s, 6H, H_{Ar}), 7.17 (s, 2H, Himidazole **6.54**), 7.14 – 7.07 (m, 1H, H_{Ar}), 4.29 (s, 1H), 4.10 (s, 2H, **6.55**), 2.83 (dp, *J* = 13.5, 6.8 Hz, 4H, C<u>H</u>$(CH_3)_2$ **6.54**), 2.56 (p, *J* = 6.9 Hz, 4H, C<u>H</u>$(CH_3)_2$ **6.1**), 1.99 (s, 2H, CH_2 **6.54**), 1.44 – 1.29 (m, 36H, $CH(C\underline{H}_3)_2$ **6.1**, **6.54**), 1.24 – 1.11 (m, 36H, $CH(C\underline{H}_3)_2$ **6.1**, **6.54**). $^{13}C\{^1H\}$ NMR (101 MHz, $CDCl_3$) δ = 175.5 ($C_{carbene}$ **6.1**), 174.7 ($C_{carbene}$ **6.54**), 146.2 (CqIPr **6.54**), 145.8 (CqIPr **6.1**), 137.6, 134.1 (CH_{Ar} **6.1**), 133.1 (CH_{Ar} **6.1**), 132.0, 131.3, 130.9, 130.4, 127.6 (Cq **6.1**), 126.4, 125.3, 124.9 (*m*-CH_{Ar} **6.1**), 124.5, 124.3, 123.8 (CHimidazole **6.1**), 29.2 ($CH(CH_3)_2$ **6.1**), 28.9 ($CH(CH_3)_2$ **6.54**), 26.7, 26.6, 24.7 ($CH(CH_3)_2$ **6.1**), 24.6 ($CH(CH_3)_2$ **6.1**), 23.2, 22.9, 8.3 (CH_2 **6.54**).

6.7. Bibliography

1. J. A. Labinger and J. E. Bercaw, *Nature*, 2002, **417**, 507.
2. A. S. K. Hashmi, *Chem. Rev.*, 2007, **107**, 3180-3211.

3. a) T. C. Boorman and I. Larrosa, *Chem. Soc. Rev.*, 2011, **40**, 1910-1925; b) M. Joost, A. Amgoune and D. Bourissou, *Angew. Chem. Int. Ed.*, 2015, **54**, 15022-15045.

4. G. C. Fortman, A. Poater, J. W. Levell, S. Gaillard, A. M. Z. Slawin, I. D. W. Samuel, L. Cavallo and S. P. Nolan, *Dalton Trans.*, 2010, **39**, 10382-10390.

5. a) A. S. K. Hashmi, T. D. Ramamurthi and F. Rominger, *Adv. Synth. Catal.*, 2010, **352**, 971-975; b) S. Dupuy, F. Lazreg, A. M. Z. Slawin, C. S. J. Cazin and S. P. Nolan, *Chem. Commun.*, 2011, **47**, 5455-5457; c) S. Dupuy, L. Crawford, M. Bühl, A. M. Z. Slawin and S. P. Nolan, *Adv. Synth. Catal.*, 2012, **354**, 2380-2386; d) L. T. Ball, G. C. Lloyd-Jones and C. A. Russell, *J. Am. Chem. Soc.*, 2014, **136**, 254-264; e) Q. Wu, C. Du, Y. Huang, X. Liu, Z. Long, F. Song and J. You, *Chem. Sci.*, 2015, **6**, 288-293; f) F. Rekhroukh, C. Blons, L. Estevez, S. Mallet-Ladeira, K. Miqueu, A. Amgoune and D. Bourissou, *Chem. Sci.*, 2017, **8**, 4539-4545.

6. a) C. González-Arellano, A. Abad, A. Corma, H. García, M. Iglesias and F. Sánchez, *Angew. Chem. Int. Ed.*, 2007, **46**, 1536-1538; b) P. Li, L. Wang, M. Wang and F. You, *Eur. J. Org. Chem.*, 2008, **2008**, 5946-5951; c) P. W. Davies and N. Martin, *Org. Lett.*, 2009, **11**, 2293-2296; d) M. D. Santos and P. W. Davies, *Chem. Commun.*, 2014, **50**, 6001-6004; e) G. Xu, C. Zhu, W. Gu, J. Li and J. Sun, *Angew. Chem., Int. Ed.*, 2015, **54**, 883-887; f) M. R. Fructos, M. M. Diaz-Requejo and P. J. Perez, *Chem. Commun.*, 2016, **52**, 7326-7335; g) S. Kramer, *Chem. Eur. J.*, 2016, **22**, 15584-15598.

7. M. B. Smith and J. March, *March's Advanced Organic Chemistry: Reactions, Mechanisms, and Structure*, Wiley-Interscience, 2007.

8. F. G. Bordwell, *Acc. Chem. Res.*, 1988, **21**, 456-463.

9. a) C. J. Jones, D. Taube, V. R. Ziatdinov, R. A. Periana, R. J. Nielsen, J. Oxgaard and W. A. Goddard, *Angew. Chem., Int. Ed.*, 2004, **43**, 4626-4629; b) A. S. K. Hashmi, S. Schäfer, M. Wölfle, C. Diez Gil, P. Fischer, A. Laguna, M. C. Blanco and M. C. Gimeno, *Angew. Chem., Int. Ed.*, 2007, **46**, 6184-6187; c) M. R. Fructos, P. de Frémont, S. P. Nolan, M. M. Díaz-Requejo and P. J. Pérez, *Organometallics*, 2006, **25**, 2237-2241; d) S. Bhunia and R.-S. Liu, *J. Am. Chem. Soc.*, 2008, **130**, 16488-16489.

10. a) H. Schmidbauer, *Gold: Chemistry, Biochemistry and Technology*, Wiley, 1999; b) S. Patai and Z. Rappoport, *The Chemistry of Organic Derivatives of Gold and Silver*, Wiley, 1999.

11. J. Vicente, A. Arcas, J. M. Fernández-Hernández and D. Bautista, *Organometallics*, 2001, **20**, 2767-2774.

12. a) D. Seebach, *Angew. Chem. Int. Ed. Engl.*, 1988, **27**, 1624-1654; b) L. R. Domingo and J. Andrés, in *PATAI'S Chemistry of Functional Groups*, John Wiley & Sons, Ltd, 2009.

13. a) G. A. Slough, R. G. Bergman and C. H. Heathcock, *J. Am. Chem. Soc.*, 1989, **111**, 938-949; b) D. A. Culkin and J. F. Hartwig, *Acc. Chem. Res.*, 2003, **36**, 234-245; c) G. Chen, F. Y. Kwong, H. O. Chan, W.-Y. Yu and A. S. C. Chan, *Chem. Commun.*, 2006, 1413-1415; d) M. Henrion, M. J. Chetcuti and V. Ritleng, *Chem. Commun.*, 2014, **50**, 4624-4627.

14. a) G. B. Shul'pin, G. V. Nizova and A. E. Shilov, *J. Chem. Soc., Chem. Commun.*, 1983, 671-672; b) G. V. Nizova, M. V. Serdobov, A. T. Nikitaev and G. B. Shul'pin, *J. Organomet. Chem.*, 1984, **275**, 139-144; c) J. Vicente, J. A. Abad, M.-T. Chicote, M.-D. Abrisqueta, J.-A. Lorca and M. C. Ramírez de Arellano, *Organometallics*, 1998, **17**, 1564-1568; d) K. Matsumoto and M. Ochiai, *Coord. Chem. Rev.*, 2002, **231**, 229-238; e) H.-W. F. Boke C. de Pater, Kees Goubitz, Jan Fraanje, Peter H.M. Budzelaar, Anton W. Gal, Kees Vrieze, *Inorg. Chim. Acta*, 2005, **358**, 431-436; f) M. Feller, A. Karton, G. Leitus, J. M. L. Martin and D. Milstein, *J. Am. Chem. Soc.*, 2006, **128**, 12400-12401; g) A. A. Vicente J., Fernandez-Hernandez J.M., *Organometallics*, 2007, 6155-6169; h) J. Vicente, in *PATAI'S Chemistry of Functional Groups*, John Wiley & Sons, Ltd, 2009.

15. a) E. R. Burkhardt, R. G. Bergman and C. H. Heathcock, *Organometallics*, 1990, **9**, 30-44; b) C. R. Barone, S. de Pinto, L. Maresca, G. Natile and C. Pacifico, *Inorg. Chim. Acta*, 2012, **383**, 13-19.

16. a) J. J. Doney, R. G. Bergman and C. H. Heathcock, *J. Am. Chem. Soc.*, 1985, **107**, 3724-3726; b) T. Hirao, S. Nagata, Y. Yamana and T. Agawa, *Tetrahedron Lett.*, 1985, **26**, 5061-5064; c) E. R. Burkhardt, J. J. Doney, R. G. Bergman and C. H. Heathcock, *J. Am. Chem. Soc.*, 1987, **109**, 2022-2039.

17. D. Milstein, *Acc. Chem. Res.*, 1984, **17**, 221-226.

18. a) J. Vicente, A. Arcas, J. M. Fernandez-Hernandez, A. Sironi and N. Masciocchi, *Chem. Commun.*, 2005, 1267-1269; b) J. Vicente, A. Arcas, J. M. Fernández-Hernández and D. Bautista, *Organometallics*, 2006, **25**, 4404-4413.

19. G. H. Posner and C. M. Lentz, *J. Am. Chem. Soc.*, 1979, **101**, 934-946.

20. a) D. P. Arnold and M. A. Bennett, *J. Organomet. Chem.*, 1980, **199**, 119-135; b) B. J. Truscott, D. J. Nelson, C. Lujan, A. M. Z. Slawin and S. P. Nolan, *Chem. Eur. J.*, 2013, **19**, 7904-7916.

21. M. A. Cairns, K. R. Dixon and M. A. R. Smith, *J. Organomet. Chem.*, 1977, **135**, C33-C34.

22. a) J. Vicente, M.-D. Bermudez, M.-T. Chicote and M.-J. Sanchez-Santano, *J. Chem. Soc., Chem. Commun.*, 1989, 141-142; b) J. Vicente, M. D. Bermudez, J. Escribano, M. P. Carrillo and P. G. Jones, *J. Chem. Soc., Dalton Trans.*, 1990, 3083-3089; c) J. Vicente, M.-D. Bermúdez, M.-P. Carrillo and P. G. Jones, *J. Organomet. Chem.*, 1993, **456**, 305-312.

23. a) M. A. Cinellu, A. Zucca, S. Stoccoro, G. Minghetti, M. Manassero and M. Sansoni, *J. Chem. Soc., Dalton Trans.*, 1996, 4217-4225; b) F. Cocco, M. A. Cinellu, G. Minghetti, A. Zucca, S. Stoccoro, L. Maiore and M. Manassero, *Organometallics*, 2010, **29**, 1064-1066.

24. D. Fan, E. Meléndez, J. D. Ranford, P. F. Lee and J. J. Vittal, *J. Organomet. Chem.*, 2004, **689**, 2969-2974.

25. a) Y. Ito, M. Inouye, M. Suginome and M. Murakami, *J. Organomet. Chem.*, 1988, **342**, C41-C44; b) M. Murakami, M. Inouye, M. Suginome and Y. Ito, *Bull. Chem. Soc. Japan*, 1988, **61**, 3649-3652.

26. a) L.G. Kuzmina, *Koord. Khim. (Coord. Chem.)*, 1994, **20**, 540-546; b) F. Mohr, L. R. Falvello and M. Laguna, *Eur. J. Inorg. Chem.*, 2006, **2006**, 833-838.

27. P. de Frémont, N. M. Scott, E. D. Stevens and S. P. Nolan, *Organometallics*, 2005, **24**, 2411-2418.

28. S. P. Nolan, *Acc. Chem. Res.*, 2010, **44**, 91-100.

29. H. M. J. Wang and I. J. B. Lin, *Organometallics*, 1998, **17**, 972-975.

30. M. R. L. Furst and C. S. J. Cazin, *Chem. Commun.*, 2010, **46**, 6924-6925.

31. A. Collado, A. Gomez-Suarez, A. R. Martin, A. M. Z. Slawin and S. P. Nolan, *Chem. Commun.*, 2013, **49**, 5541-5543.

32. CCDC = CCDC 1039059 (**6.10**) contains the supplementary crystallographic data for this paper. These data can be obtained free of charge from The Cambridge Crystallographic Data Centre *via* https://www.ccdc.cam.ac.uk/structures/;

33. S. Gaillard, A. M. Z. Slawin and S. P. Nolan, *Chem. Commun.*, 2010, **46**, 2742-2744.

34. F. Nahra, S. R. Patrick, A. Collado and S. P. Nolan, *Polyhedron*, 2014, **84**, 59-62.

35. P. de Frémont, N. Marion and S. P. Nolan, *J. Organomet. Chem.*, 2009, **694**, 551-560.

36. S. R. Patrick, A. Gómez-Suárez, A. M. Z. Slawin and S. P. Nolan, *Organometallics*, 2014, **33**, 421-424.

37. D. J. Nelson and S. P. Nolan, *Chem. Soc. Rev.*, 2013, **42**, 6723-6753.

38. CCDC = CCDC 1039060 (**6.9**), CCDC 1039061 (**6.12**), CCDC 1039062 (**6.14**), CCDC 1039063 (**6.15**), and CCDC 1039064 (**6.16**) contain the supplementary crystallographic data for this paper. These data can be obtained free of charge from The Cambridge Crystallographic Data Centre *via* https://www.ccdc.cam.ac.uk/structures/;

39. W. S. Matthews, J. E. Bares, J. E. Bartmess, F. G. Bordwell, F. J. Cornforth, G. E. Drucker, Z. Margolin, R. J. McCallum, G. J. McCollum and N. R. Vanier, *J. Am. Chem. Soc.*, 1975, **97**, 7006-7014.

40. a) J. Vicente, M.-T. Chicote and M.-C. Lagunas, *Helv. Chim. Acta*, 1999, **82**, 1202-1210; b) D. Emeljanenko, A. Peters, V. Vitske, E. Kaifer and H.-J. Himmel, *Eur. J. Inorg. Chem.*, 2010, **2010**, 4783-4789.

41. a) J. D. Egbert, A. M. Z. Slawin and S. P. Nolan, *Organometallics*, 2013, **32**, 2271-2274; b) N. Ibrahim, M. H. Vilhelmsen, M. Pernpointner, F. Rominger and A. S. K. Hashmi, *Organometallics*, 2013, **32**, 2576-2583.

42. a) M. V. Baker, P. J. Barnard, S. J. Berners-Price, S. K. Brayshaw, J. L. Hickey, B. W. Skelton and A. H. White, *J. Organomet. Chem.*, 2005, **690**, 5625-5635; b) E. Schuh, C. Pflüger, A. Citta, A. Folda, M. P. Rigobello, A. Bindoli, A. Casini and F. Mohr, *J. Med. Chem.*, 2012, **55**, 5518-5528.

43. a) S. K. Schneider, W. A. Herrmann and E. Herdtweck, *Z. Anorg. Allg. Chem.*, 2003, **629**, 2363-2370; b) S. Dupuy and S. P. Nolan, *Chem. Eur. J.*, 2013, **19**, 14034-14038.

44. E. Y. Tsui, P. Müller and J. P. Sadighi, *Angew. Chem. Int. Ed.*, 2008, **47**, 8937-8940.

45. CCDC = CCDC 1039066 (**6.23**), CCDC 1039068 (**6.24**), and CCDC 103970 (**6.25**) contain the supplementary crystallographic data for this paper. These data can be

obtained free of charge from The Cambridge Crystallographic Data Centre *via* https://www.ccdc.cam.ac.uk/structures/;

46. L. Ricard and F. Gagosz, *Organometallics*, 2007, **26**, 4704-4707.

47. R. M. P. Veenboer, D. Gasperini, F. Nahra, D. B. Cordes, A. M. Z. Slawin, C. S. J. Cazin and S. P. Nolan, *Organometallics*, 2017, **36**, 3645-3653.

48. S. R. Patrick, A. Gómez-Suárez, A. M. Z. Slawin and S. P. Nolan, *Organometallics*, 2013, **33**, 421-424.

49. H. Lv, J.-H. Zhan, Y.-B. Cai, Y. Yu, B. Wang and J.-L. Zhang, *J. Am. Chem. Soc.*, 2012, **134**, 16216-16227.

50. CCDC = CCDC 1039065 (**6.35**), CCDC 1039067 (**6.37**), and CCDC 1039069 (**6.38**) contain the supplementary crystallographic data for this paper. These data can be obtained free of charge from The Cambridge Crystallographic Data Centre *via* https://www.ccdc.cam.ac.uk/structures/;

51. A. Zhdanko, M. Ströbele and M. E. Maier, *Chem. Eur. J.*, 2012, **18**, 14732-14744.

52. S. B. Gaillard, J.; Ramon, R.S.; Nun, P.; Slawin, A.M; Nolan, S.P., *Chem. Eur. J.*, 2010, **16**, 13729-13740.

53. N. Marion, S. Díez-González, P. de Frémont, A. R. Noble and S. P. Nolan, *Angew. Chem., Int. Ed.*, 2006, **45**, 3647-3650.

54. H. S. a. A. Schier, *Z. Naturforsch.*, 2011, **66b**, 329-350.

55. a) A. S. K. Hashmi, in *Silver in Organic Chemistry*, John Wiley & Sons, Inc., 2010, pp. 357-379; b) X. Giner, C. Nájera, G. Kovács, A. Lledós and G. Ujaque, *Adv. Synth. Catal.*, 2011, **353**, 3451-3466; c) X. Giner, P. Trillo and C. Nájera, *J. Organomet. Chem.*, 2011, **696**, 357-361.

56. P. Nun, R. S. Ramón, S. Gaillard and S. P. Nolan, *J. Organomet. Chem.*, 2011, **696**, 7-11.

57. a) N. Marion, P. Carlqvist, R. Gealageas, P. de Frémont, F. Maseras and S. P. Nolan, *Chem. Eur. J.*, 2007, **13**, 6437-6451; b) P. Nun, S. Gaillard, A. M. Z. Slawin and S. P. Nolan, *Chem. Commun.*, 2010, **46**, 9113-9115; c) P. Nun, S. Gaillard, A. Poater, L. Cavallo and S. P. Nolan, *Org. Biomol. Chem.*, 2011, **9**, 101-104; d) A. Gómez-Suárez, R. S. Ramón, O. Songis, A. M. Z. Slawin, C. S. J. Cazin and S. P. Nolan, *Organometallics*, 2011, **30**, 5463-5470.

58. a) C.-Y. Wu, T. Horibe, C. B. Jacobsen and F. D. Toste, *Nature*, 2015, **517**, 449-454; b) F. Rekhroukh, R. Brousses, A. Amgoune and D. Bourissou, *Angew. Chem., Int. Ed.*, 2015, **54**, 1266-1269; c) M. Joost, L. Estévez, K. Miqueu, A. Amgoune and D. Bourissou, *Angew. Chem. Int. Ed.*, 2015, **54**, 5236-5240; d) M. S. Winston, W. J. Wolf and F. D. Toste, *J. Am. Chem. Soc.*, 2014, **136**, 7777-7782.

59. A. Maity, A. N. Sulicz, N. Deligonul, M. Zeller, A. D. Hunter and T. G. Gray, *Chem. Sci.*, 2015, **6**, 981-986.

60. A. Yoshimura and V. V. Zhdankin, *Chem. Rev.*, 2016, **116**, 3328-3435.

61. a) T. de Haro and C. Nevado, *J. Am. Chem. Soc.*, 2010, **132**, 1512-1513; b) A. Collado, J. Bohnenberger, M.-J. Oliva-Madrid, P. Nun, D. B. Cordes, A. M. Z. Slawin and S. P. Nolan, *Eur. J. Inorg. Chem.*, 2016, **2016**, 4111-4122.

62. S. Gaillard, A. M. Z. Slawin, A. T. Bonura, E. D. Stevens and S. P. Nolan, *Organometallics*, 2010, **29**, 394-402.

63. V. J. Scott, J. A. Labinger and J. E. Bercaw, *Organometallics*, 2010, **29**, 4090-4096.

64. a) N. P. Mankad and F. D. Toste, *J. Am. Chem. Soc.*, 2010, **132**, 12859-12861; b) N. P. Mankad and F. D. Toste, *Chem. Sci.*, 2012, **3**, 72-76.

65. J. P. Brand, C. Chevalley, R. Scopelliti and J. Waser, *Chem. Eur. J.*, 2012, **18**, 5655-5666.

66. P. de Frémont, R. Singh, E. D. Stevens, J. L. Petersen and S. P. Nolan, *Organometallics*, 2007, **26**, 1376-1385.

67. M. Gatto, P. Belanzoni, L. Belpassi, L. Biasiolo, A. Del Zotto, F. Tarantelli and D. Zuccaccia, *ACS Catal.*, 2016, **6**, 7363-7376.

68. a) E. S. Smirnova, J. M. Muñoz Molina, A. Johnson, N. A. G. Bandeira, C. Bo and A. M. Echavarren, *Angew. Chem., Int. Ed.*, 2016, **55**, 7487-7491; b) X.-L. Pei, Y. Yang, Z. Lei, S.-S. Chang, Z.-J. Guan, X.-K. Wan, T.-B. Wen and Q.-M. Wang, *J. Am. Chem. Soc.*, 2015, **137**, 5520-5525.

69. Becke, A. D. *Phys. Rev. A*, 1988, **38**, 3098-3100.

70. Perdew, J. P. *Phys. Rev. B*, 1986, **34**, 7406-7406.

71. Perdew, J. P. *Phys. Rev. B*, 1986, **33**, 8822-8824.

72. Schafer, A.; Horn, H.; Ahlrichs, R. *J. Chem. Phys.*, 1992, **97**, 2571-2577.

73. Haussermann, U.; Dolg, M.; Stoll, H.; Preuss, H.; Schwerdtfeger, P.; Pitzer, R. M. *Molecul. Phys.*, 1993, **78**, 1211-1224.

74. Barone, V.; Cossi, M. *J. Phys. Chem. A*, 1998, **102**, 1995-2001.

75. Tomasi, J.; Persico, M. *Chem. Rev.*, 1994, **94**, 2027-2094.

76. Martin, R. L.; Hay, P. J.; Pratt, L. R. *J. Phys. Chem. A.*, 1998, **102**, 3565-3573.

77. Poater, A.; Pump, E.; Vummaleti, S. V. C.; Cavallo, L. *J. Chem Theory Comput.*, 2014, **10**, 4442-4448.

78. a) J. Yu and C. Zhang, *Synthesis*, 2009, 2324-2328; b) C.-M. Ting, Y.-L. Hsu and R.-S. Liu, *Chem. Commun.*, 2012, **48**, 6577-6579.

79. K. Mikami, Y. Kawakami, K. Akiyama and K. Aikawa, *J. Am. Chem. Soc.*, 2007, **129**, 12950-12951.

80. A. Fedorov, M.-E. Moret and P. Chen, *J. Am. Chem. Soc.*, 2008, **130**, 8880-8881.

7. Conclusions

At the onset of the work developed in this thesis, the intermolecular hydrocarboxylation of internal alkynes was scarce in literature and not fully explored. A general and efficient procedure for the addition of carboxylic acids to alkynes was developed under solvent-free conditions. (*Z*)-vinyl esters were synthesised in good to excellent yields (74-99%) and in a complete stereoselective fashion. The straightforward methodology required the use of a dinuclear hydroxide Au NHC catalyst, [{Au(IPr)}$_2$(μ-OH)][BF_4], in low catalyst loading (0.5-1 mol%). The reaction tolerated different substituents on the acids, from aliphatic to aromatic groups, while it was limited in term of diversity into the alkyne substrates. Recyclability tests were assessed, which allowed the transformation of formic acid and diphenylacetylene into (*Z*)-1,2-diphenylvinyl formate with a high TON (2610). The use of a dinuclear hydroxide Au(I) NHC complex was found suitable for the functionalisation of alkynoic acids, improving existing methods and expanding the substrate scope. Under solvent-free conditions and at r.t., γ- and δ-lactones were obtained in excellent yields (up to 98%) and excellent stereoselectivity. With catalyst loading of [{Au(IPr)}$_2$(μ-OH)][BF_4] as low as 25 ppm, the cyclisation of 4-pentynoic acid was found to occur with the highest TOF reported so far for this transformation (36608 h^{-1}). ε-Lactones were synthesised, from 78% to 91% yield, by slight variation of the reaction conditions.

Initial stoichiometric studies into the intermolecular hydrocarboxylation of alkynes, showed that when reacting digold hydroxide with benzoic acid, a dinuclear benzoate Au-NHC complex, [{Au(IPr)}$_2$(μ-O_2CPh)][BF_4] was formed. Dinuclear carboxylate Au species were underexplored in literature, thus diverse complexes were synthesised with moderate to excellent yield (40-92%), by variation of carboxylic acids and counterions, while limitations were found when varying the spectator ligand. The dinuclear gold carboxylate species were found to be optimal precursors for the inter- and intramolecular hydrocarboxylation of alkynes, as well as for the hydrophenoxylation of alkynes. As confirmed by stoichiometric and catalytic studies these species must form to initiate the catalytic cycle. Subsequent studies on the reaction mechanism suggested that a

mononuclear species is involved in the RDS of both addition of carboxylic acid to alkynes, and cyclisation of alkynoic acids.

Pursuing the further design of gold catalysts, the synthesis of novel heteroleptic chiral Au(I)-ITU complexes was explored when reacting cationic or neutral Au(I) precursors with isothiourea compounds. Further reaction of [AuCl(SMe_2)] with ITU in THF at 60 °C allowed access to enantiomerically enriched [AuCl(ITU)] complexes in excellent yield (> 99%). The neutral Au(I)-ITU compounds were oxidised under mild conditions to prepare one of the very few chiral Au(III) complexes reported in literature, [$AuCl_3$(ITU)] (96-99%). The heteroleptic and neutral Au complexes were fully characterised in solution via NMR, IR and absorption spectroscopy, together with X-ray crystallographic analyses. Further refinement of steric and parameters with calculation of $\%V_{bur}$ in the range between 25.1-28.7% showed that ITU have similar values to NHC and phosphine ligands. Next, the synthesis of [IrCl(CO)(ITU)] was achieved in high yield (99%) and calculation of TEP showed the high σ-donor properties of ITU ligands compared to carbenes and phosphines.
The heteroleptic Au ITU complexes showed good activity towards the hydroalkoxylation/Claisen rearrangement of alkynes and allylic alcohols, with comparable reaction yield to the literature report. Rearrangement of silyloxyenyne was tested in the presence of [AuCl{(2*S*,3*R*)-HyperBTM}], and by optimising the reported reaction conditions, cyclisation of the starting material was obtained in 74% yield. Au(III)-ITU complexes were found to be good precursors for the arylation of propargylic alkynes, with high regioselectivity and conversions into allenes. Unfortunately, no enantioinduction was observed for all of these processes, showing limitations of the complexes.

The role of ITU and Au catalysts in dual catalytic processes was explored for the activation of alkynes and esters towards C-C bond forming reactions. Intra- and intermolecular attempts of reaction of alkynes and esters, or tethered alkyne-ester substrates were found to be extremely challenging, with no substrate conversion when isothiourea and Au precursors were used. Subsequent attempts to functionalise more reactive substrates, such as propargylic derivatives, failed to give any tangible results, under similar reaction conditions, suggesting catalyst poisoning. However, when

subjecting propargylic carbonates and phenylacetic esters to Pd precursors in combination with ITU, a vinyl phenol and homoallylic ester were found. The formation of the homoallylic ester was unprecedented, and explored; however the process was not enantioselective, and the ITU was not needed to obtain the product.

Furthermore, the synthesis of acetonyl-Au(I) NHC species, [Au($CH_2C(O)CH_3$)(NHC)] was developed from [AuCl(NHC)] or [Au(OH)(NHC)] complexes in excess of acetone. The synthetic methodology was expanded to ketones and acetonitrile for the deprotonation of C(sp^3)-H bond. The acetonyl-Au(I) NHC species were shown to be optimal precursors for a range of mono- and dinuclear Au(I) complexes. Moreover, complex [Au($CH_2C(O)CH_3$)(IPr)] was activated in situ with $HBF_4 \cdot OEt_2$ to catalyse the hydration of ketones, and the transformation of propargylic alkynes to allenes and indenes.

The oxidation of organogold species was tested, with fast elimination of the organic moiety and formation of functionalised C(sp^3)-X bonds. An oxidative addition/reductive elimination pathway towards the functionalisation of C(sp^3)-H bond was suggested and supported by kinetic and computational analyses. To further confirm the involvement of Au(III) species, oxidation of [Au(CH_2CN)(IPr)] with $PhI(Cl)_2$ promptly formed [$AuCl_2$(CH_2CN)(IPr)] complex, as confirmed by X-ray crystallographic analysis, which decomposed to [AuCl(IPr)] and chloroacetonitrile.