Gold catalyzed cycloisomerization of propargylic alcohols and acetates as synthetic strategies to N-heterocycles

Dewi Susanti

2014

Dewi Susanti. (2014). Gold catalyzed cycloisomerization of propargylic alcohols and acetates as synthetic strategies to N-heterocycles. Doctoral thesis, Nanyang Technological University, Singapore.

<https://hdl.handle.net/10356/61849>

<https://doi.org/10.32657/10356/61849>

**NANYANG
TECHNOLOGICAL
UNIVERSITY**

GOLD CATALYZED CYCLOISOMERIZATION OF
PROPARGYLIC ALCOHOLS AND ACETATES AS
SYNTHETIC STRATEGIES TO *N*-HETEROCYCLES

DEWI SUSANTI

**GOLD CATALYZED CYCLOISOMERIZATION OF
PROPARGYLIC ALCOHOLS AND ACETATES AS
SYNTHETIC STRATEGIES TO *N*-HETEROCYCLES**

DEWI SUSANTI

SCHOOL OF PHYSICAL AND MATHEMATICAL SCIENCES

2014

2014

**GOLD CATALYZED CYCLOISOMERIZATION OF
PROPARGYLIC ALCOHOLS AND ACETATES AS
SYNTHETIC STRATEGIES TO *N*-HETEROCYCLES**

DEWI SUSANTI

DEWI SUSANTI

School of Physical and Mathematical Sciences

A thesis submitted to the Nanyang Technological University
in partial fulfillment of the requirement for the degree of
Doctor of Philosophy

2014

ACKNOWLEDGEMENTS

I would like to express my sincere gratitude to my supervisor Assoc. Prof. Wai Hong Chan for his constant support and guidance throughout my research. Since the first day I joined his research group, he has always encouraged me to continue with my passion in chemistry by taking a PhD degree. His advice and willingness to provide feedback to me has helped me to significantly improve my technical, interpersonal, and time management skills. In addition, his wide knowledge of chemistry has given a valuable insight whenever I encountered problems in my research.

I would also like to thank my fellow lab mates, Weidong, Prasath, Reddy, Ton, Ella, Wanteng, Sally, Ciputra, and the undergraduates for providing such a wonderful working environment in the lab. The brainstorming process during our scientific discussion has improved my analytical thinking whilst our casual conversations in the lab have always brightened up my day. I would also like to acknowledge the undergraduate students who have contributed their effort in the projects presented in this thesis, particularly Linda, Sebastian, Richard, Fujiet and Jeffrey. Also, my special thanks to Dave who helps to proofread my writing.

Many thanks go to CBC support staff-Ai Hua and the teaching lab, Ee Ling, Mr. A, Derek, Wen Wei, Dr. Li and Dr Rakesh for their assistance with instrument training/usage such as NMR, LCMS, HRMS, IR and X-ray crystallography. I would also like to thank Celine, Lynette and Wei Ting for their assistance in administrative matters, particularly in issues relating to my qualifying examinations, conference registration and thesis submission. In addition, my gratitude goes to Hendra and Wilson for assisting in the purchasing process of common glassware, chemicals and solvents.

I am grateful to have friends in the CBC building – Joyce, Stephen, Yamakawa, Pei Juan, Gish, Novi, Clarissa, Charmaine, Shaun, Wei Fong, Hui Quan and many others that

have never failed to entertain and support me throughout these 4 years. They have made school a vibrant place to be. I especially enjoyed our lunch, tea, or dinner sessions that have helped me to relax despite the busy lab schedule.

Furthermore, my gratitude also goes to my high school friends, my seniors from Medan and my sports buddies who have fully supported me and have provided a listening ear for all of my complaints. In particular, my special thanks goes to my boyfriend Kelvin Lim who supports and teaches me to always think positively in every difficult situation.

I am also indebted to the Nanyang Research Scholarship (Jan 2010 - Jan 2014) for providing financial support for my PhD degree and providing me the opportunity to attend the overseas conference in Kyoto, Japan.

Lastly, I would like to thank my family members, especially my mother, for their unconditional love and mental support throughout these four years.

TABLE OF CONTENTS

Abstract	v
Publications	vii
Abbreviation.....	viii
Part 1	
Chapter I	Propargylic Alcohols and Acetates in Gold Catalyzed Synthetic Strategies to <i>N</i> -Heterocycles
1.1	Introduction 1
1.2	Gold as a Lewis Acidic Catalyst.....3
1.3	Gold Catalyzed Cycloisomerizations of Propargylic Alcohols6
1.4	Gold Catalyzed Reactions of Propargylic Esters..... 17
1.4.1	1,2-Acyloxy Migration of Propargylic Esters 23
1.4.2	1,3-Acyloxy Migration of Propargylic Esters 27
1.5	Proposed Work 34
Part II	
Chapter II	Gold Catalyzed Tandem 1,3-Migration/[2+2] Cycloaddition of 1,7-Enyne Benzoates to Azabicyclo[4.2.0]oct-5-enes
2.1	Introduction 37
2.2	Results and Discussion..... 38
2.3	Conclusion 51
Chapter III	Silver Acetate Catalyzed Hydroamination of 1-(2- (Sulfonylamino)phenyl)prop-2-yn-1-ols to (Z)-2-Methylene- 1 sulfonylindolin-3-ols
3.1	Introduction 52
3.2	Results and Discussion..... 54

	3.3 Conclusion	61
Chapter IV	Silica Gel-Mediated Hydroamination/Semipinacol Rearrangement of 2-Alkylaminophenylprop-1-yn-3-ols: Synthesis of 2-Oxindoles from Alkynes and 1-(2- Aminophenyl)ketones	
	4.1 Introduction	62
	4.2 Results and Discussion.....	63
	4.3 Conclusion	73
Chapter V	Gold(I) Catalyzed Cycloisomerization and Thermal [4+2] Cycloaddition of 1,9-Diene-4-yne Esters. Efficient Synthesis of 3-Azatricyclo[5.2.1.0 ^{1,5}]dec-8-enes.	
	5.1 Introduction	74
	5.2 Results and Discussion.....	76
	5.3 Conclusion	85
Chapter VI	Concluding Remarks	86
Part III		
Chapter VII	Experimental Section	89
Chapter VIII	References	233

ABSTRACT

The work in this thesis was undertaken at the Division of Chemistry and Biological Chemistry, School of Physical and Mathematical Sciences, Nanyang Technological University from January 2010 to January 2014 under the supervision of Assoc. Prof. Philip Wai Hong Chan.

The work in this thesis has been directed toward the development of new methodologies utilizing propargylic alcohols and acetates in gold catalyzed strategies to potentially synthetically useful *N*-heterocycles. The thesis is divided into three parts:

- ❖ Part I consists of Chapter 1, which provides a brief introduction to the field of gold catalysis and its application toward *N*-heterocycle synthesis from propargylic alcohols and acetates.
- ❖ Part II discusses about establishing novel approaches involving intramolecular cycloisomerization employing nitrogen tethered propargylic alcohols and acetates as the substrate to synthesize *N*-heterocycles. There are four chapters in this section. Chapter II describes tandem 1,3-migration/[2+2] cycloaddition of enantiopure 1,7-enyne benzoates in the presence of a gold(I) complex to form stereochemically well-defined azabicyclo[4.2.0]oct-5-enes. The cycloisomerization process is shown to be regioselective and stereoconvergent. In Chapter III, a further investigation of earlier works on gold catalyzed 1-(2-tosylaminophenyl)prop-2-yn-1-ols to (*Z*)-2-methylene-1-tosylindolin-3-ols is described. In the course of this work, it was found that silver salts could serve as an alternative catalyst to mediate the formation of (*Z*)-2-methylene-1-tosylindolin-3-ols. In this new approach, an expansion of the scope and the synthetic utility of indolin-3-ols for the formation of other indole family of compounds are also presented. Arising from the work described in Chapter III, Chapter IV demonstrates the serendipitous discovery of a method for the

synthesis of 3,3-disubstituted 2-oxindoles from silica-gel mediated hydroamination/semipinacol rearrangement of 2-alkylaminophenylprop-1-yn-3-ol. The synthetic utility of the methodology is exemplified by large-scale preparation of one substrate in excellent yield and recycling of the silica gel up to 8 times without apparent loss of activity. Chapter V introduces tandem gold(I) catalyzed 1,2-acyloxy migration/thermal [4+2] cycloaddition of 1,9-diene-4-yne acetates as an efficient method to 3-azatricyclo[5.2.1.0^{1,5}]dec-8-enes. Lastly, Chapter VI discusses the concluding remarks from Chapter II to Chapter V.

- ❖ Part III contains experimental data (Chapter VII) and references (Chapter VIII) pertaining to this thesis.

PUBLICATIONS

1. “Silica Gel-Mediated Hydroamination/Semipinacol Rearrangement of 2-Alkylaminophenylprop-1-yn-3-ols: Synthesis of 2-Oxindoles from Alkynes and 1-(2-Aminophenyl)ketones”, Susanti, D.; Ng, L. L. R.; Chan, P. W. H. *Adv. Synth. Cat.* **2013**, 356, 353.
2. “Silver Acetate Catalyzed Hydroamination of 1-(2-(Sulfonylamino)phenyl)prop-2-yn-1-ols to (Z)-2-Methylene-1-sulfonylindolin-3-ols”, Susanti, D.; Koh, F.; Kusuma, J. A.; Kothandaraman, P.; Chan, P. W. H. *J. Org. Chem.* **2012**, 77, 7166. (*selected by the editors of Journal of Organic Chemistry as Featured Article*)
3. “Gold-Catalyzed Tandem 1,3-Migration/[2+2] Cycloaddition of 1,7-Enyne Benzoates to Azabicyclo[4.2.0]oct-5-enes”, Rao, W.; Susanti, D.; Chan, P. W. H. *J. Am. Chem. Soc.* **2011**, 133, 15248.
4. “Cyclopropyl Carbinol Rearrangement for Benzo-fused Nitrogen Ring Synthesis”, Kothandaraman, P.; Huang, C.; Susanti, D.; Rao, W.; Chan, P. W. H. *Chem. Eur. J.* **2011**, 17, 10081.
5. “Efficient Synthesis of 3-Acyl-5-hydroxybenzofurans via Copper(II) Triflate-Catalyzed Cycloaddition of Unactivated 1,4-Benzoquinones with 1,3-Dicarbonyl Compounds”, Mothe, S. R. Susanti, D.; Chan, P. W. H. *Tetrahedron Lett.* **2010**, 51, 2136.

ABBREVIATIONS

Å	Angstrom
Ac	acetyl
Ar	aryl
Boc	<i>tert</i> -butyloxycarbonyl
<i>n</i> Bu	<i>n</i> -butyl
Bn	benzyl
Bz	benzoyl
Cbz	benzyloxycarbonyl
Cy	cyclohexyl
DAST	(diethylamino)sulfur trifluoride
DCC	1,3-dicyclohexylcarbodiimide
DCE	1,2-dichloroethane
DFT	density functional theory
DIAD	diisopropyl azodicarboxylate
DMF	<i>N,N</i> -dimethylformamide
DMAP	4-(dimethylamino)pyridine
DMSO	dimethylsulfoxide
d.r.	diastereomeric ratio
DTBM-SEGPPOS	5,5'-bis[di(3,5-di- <i>tert</i> -butyl-4-methoxyphenyl)phosphino]- 4,4'-bi-1,3-benzodioxole
<i>ee</i>	enantiomeric ratio
Et	ethyl
h	hour
Hex	hexyl
HMPA	hexamethylphosphoramide

IBX	2-iodoxybenzoic acid
IPr	1,3-Bis(2,6-diisopropylphenyl)imidazol-2-ylidene
<i>i</i> Pr	isopropyl
JohnPhos	(2-biphenyl)di- <i>tert</i> -butylphosphine
LDA	lithium diisopropylamide
Me	methyl
Mont	montmorillonite
m.p.	melting point
MS	molecular sieves
Ms	methanesulfonyl, mesyl
<i>n</i> Pent	<i>n</i> -pentyl
<i>n</i> Pr	<i>n</i> -propyl
Ns	4-nitrobenzenesulfonyl, nosyl
NMR	nuclear magnetic resonance
Nu	nucleophile
NIS	<i>N</i> -iodosuccinimide
Pic	2-pyridinecarboxylate, picolinate
Piv	pivaloyl
Ph	phenyl
rt	room temperature
TBS	<i>tert</i> -butyldimethylsilyl
<i>t</i> Bu	<i>tert</i> -butyl
TFA	trifluoroacetic acid
TfOH	trifluoromethanesulfonic acid
THF	tetrahydrofuran
TLC	thin layer chromatography

TMS	trimethylsilyl
Ts	<i>p</i> -toluenesulfonyl
XPhos	2-Dicyclohexylphosphino-2',4',6'-triisopropylbiphenyl
xylylBINAP	2,2'-Bis[bis(3,5-dimethylphenyl)phosphino]-1,1'- binaphthyl

Chapter I. Propargylic Alcohols and Acetates in Gold Catalyzed Synthetic Strategies to *N*-Heterocycles

1.1 Introduction

The importance of nitrogen-containing heterocycles is reflected by their presence as a structure in a myriad of natural, pharmaceutical and agrochemical products as well as functional compounds (Figure 1.1).¹ Added to this is their role as synthetic intermediates in a number of industrial processes.² Hence, the discovery and development of atom-economical and ecologically benign synthetic methodologies to nitrogen-containing heterocycles remains a constant pursuit in organic chemistry.

The classical approaches to construct nitrogen-containing heterocycles have normally relied upon C–N bond forming reactions such as nucleophilic substitution or addition under basic or acidic conditions.³ For instance, in 1911, Pictet and Spengler discovered the synthesis of isoquinoline **3** by heating β -phenylethylamine **1** and formaldehyde **2** in the presence of hydrochloric acid (Scheme 1.1).⁴ To date, this reaction has remained one of the most convenient and efficient methods for the synthesis of isoquinolines and various alkaloid frameworks. Nevertheless, several drawbacks in this strategy such as harsh reaction conditions, functional group tolerance and employment of stoichiometric amounts of various reagents have driven the need to develop new synthetic methods to overcome such limitations.

Scheme 1.1 The Pictet-Spengler tetrahydroisoquinoline synthesis.

Figure 1.1 Examples of nitrogen-containing heterocycles of biological and material interest.

Over the years, the development of new synthetic approaches to *N*-heterocycles from readily available and biocompatible substrates and catalysts has continued to receive an immense amount of attention. One strategy has been the cycloisomerization chemistry of propargylic alcohols and esters catalyzed by gold(I) and gold(III) complexes and salts.^{5,6} The transformation has been shown to benefit from the ease of accessing the propargylic substrate and thus the possibility of introducing a wide variety of substitution patterns. In the case of reactions with propargylic alcohols, a further advantage is the ability to form a quaternary carbon centre by using a tertiary alcohol and the formation of H₂O as potentially the only byproduct. Added to this is the opportunity to realize reactions that proceed efficiently under mild conditions by exploiting the highly reactive and chemoselective nature of gold catalysis.⁷ The main focus of this Introduction will be on the advances made in the field of gold catalyzed reactions of propargylic alcohols and esters as strategies for the synthesis of nitrogen-containing heterocycles.

1.2 Gold as a Lewis Acidic Catalyst

Whilst there is a perception that gold is an inert noble metal, the fast growing number of organic transformations catalyzed by gold complexes over the past two decades is a testament to the contrary.⁷ Being naturally more abundant than other robust transition metal catalysts such as palladium, platinum and rhodium, gold has an electronic configuration of [Xe]4f¹⁴5d¹⁰6s¹ with common oxidation states of 0, +1, and +3. Metallic gold with an oxidation state of 0 is an inert metal, but the latter two oxidation states of the metal have been shown to exhibit exceptional Lewis acidity, with an affinity to coordinate to π bonds that cannot be matched by any other metal. This exceptional π acidity, or alkynophilicity, of gold is attributed to the relativistic effect that reaches a maximum in the periodic table with the group 11 metal.^{7t} This chemical property of gold is due to the relativistic contraction of the 6s orbital and expansion of 5d orbitals of the metal that results in it being able to exist as a large diffuse cationic species with a low-lying lowest

unoccupied molecular orbital (LUMO). This “soft” character of gold has been translated into the significant affinity of the metal to “soft” π -systems such as alkynes and their subsequent susceptibility toward intra- or intermolecular attack by a nucleophile under mild reaction conditions (Scheme 1.2).

Scheme 1.2 General reactivity pattern in gold catalyzed nucleophilic addition to C–C multiple bonds.

The alkyne functional group is a relatively weak π -acceptor and strong two electron σ -donor toward gold(I) and gold(III) complexes and salts. That said, high level computational studies of the Au^+ –acetylene complex suggest that there is significant back bonding of the metal centre into the vacant p orbitals of the alkyne moiety.⁸ Based on this theoretical study, an alternative pathway could be envisioned in which the gold would first activate the alkyne unit to give species **A**, which is susceptible toward nucleophilic attack by making it electron deficient (Scheme 1.3). The presence of the metal in the ensuing organogold species **B** would consequently facilitate the trapping of an electrophile to provide the carbonium adduct **C** by stabilizing the incipient cationic species by backbonding from the metal 5d orbitals.

Scheme 1.3 Gold to alkyne backbonding.

Experimental evidence for this theoretical pathway has been provided in a number of subsequent gold catalyzed enyne cycloisomerization studies.⁹ In these investigations, the mechanistic hypothesis of these types of cycloisomerizations was taken a step further with the proposal that such reactions occur through the cationic species **D**, which then evolved to the cyclopropyl intermediate **E** or **G** (Scheme 1.4). As to which species represents the key intermediate in the reaction is still in dispute since evidence for such reactive species has as yet to be realized. Thus far, support for the metal-stabilized cationic species **E** over the typical metal carbenoid **G** has mainly relied on theoretical calculations and experimental observations. Toste and co-workers suggested that the position of this key intermediate could sit somewhere in between the carbocation **E** to carbenoid **G** equilibrium depending on the substituents on the substrate and the ancillary ligand of the gold complex.¹⁰

Scheme 1.4 Mechanistic scenario for gold catalyzed enyne cycloisomerization.

1.3 Gold Catalyzed Cycloisomerizations of Propargylic Alcohols

The first pioneering work on gold catalyzed synthesis of *N*-heterocycles was reported by Utimoto and co-workers in 1987 describing the synthesis of tetrahydropyridines (Scheme 1.5).¹¹ In this study, NaAuCl₄ catalyzed intramolecular hydroamination of alkynyl-1-amines **4** to 2-alkylenepiperidines **5** in a regioselective manner. These newly formed cycloadducts rapidly isomerized to give tetrahydropyridines **6** in 64-92% yield.

Scheme 1.5 Gold(III) catalyzed 6-*exo-dig* cyclization of alkynyl-1-amine.

A decade later after this breakthrough, numerous advancements on gold catalysis have been reported to synthesize a variety of nitrogen-containing heterocyclic molecules.⁷ One of these advancements is the direct substitution of propargylic alcohols in the presence of a gold catalyst to furnish *N*-heterocycles. The classical example of direct nucleophilic substitution of propargylic alcohols is the Nicholas reaction utilizing a stoichiometric amount of [Co₂(CO)₈].¹² Although this method has been shown to be efficient, the generation of excess amount of byproduct in the multistep process has limited its synthetic utility in organic synthesis. In 2005, Campagne and co-workers utilized catalytic amount of NaAuCl₄ to perform Nicholas-type reactions with propargylic alcohols **7** (Scheme 1.6).¹³ This method was found to be applicable to a wide variety of nucleophiles such as arenes, allyltrimethylsilane, alcohols and thiols and afforded the corresponding substitution adducts **8** in 33-97% yield. From a mechanistic point of view, the reaction was posited to involve a carbocation intermediate based on one example showing the racemic substituted adduct **8** (R¹, R³ = Ph, R² = H) was obtained from reaction of the

corresponding enantioenriched propargylic alcohol **7** (96% *ee*, *ee* = enantiomeric excess) with allyltrimethylsilane.

Scheme 1.6 Gold(III) catalyzed direct nucleophilic of propargylic alcohols.

Following this work, Cossy and co-workers reported gold(I) chloride catalyzed cycloisomerization of 1,6-ene-ynamides bearing a propargylic alcohol **9** moiety at room temperature (Scheme 1.7).¹⁴ The reaction mechanism in this study was proposed to involve the stabilized gold carbenoid species **10** that underwent a 1,2-hydride shift to furnish the 2-azabicyclo[3.1.0]hexane framework **11** in 40-61% yield with d.r. values of up to 95:5 (d.r. = diastereomeric ratio).

Scheme 1.7 Gold(I) chloride catalyzed cycloisomerization of hydroxylated 1,6-ene-ynamide.

A similar approach was developed by Shi and co-workers using the $\text{AuPPh}_3\text{Cl}/\text{AgSbF}_6$ catalytic system for the cycloisomerization of epoxy propargylic alcohols **12** to bicyclo ketal products **14** (Scheme 1.8).¹⁵ The reaction was shown to be applicable to secondary and alkyl substituted tertiary epoxy tethered propargylic alcohols. The only exception was phenyl substituted tertiary propargylic alcohols, which were

reported to result in recovery of the starting material in near quantitative yields. Based on deuterium and ^{18}O -labeling experiments, the mechanism of the reaction was posited to proceed *via* Meyer-Schuster rearrangement of the propargylic alcohol followed by ring opening of the ensuing oxirane by the carbonyl oxygen and subsequent addition of the hydroxyl group to the carbonyl carbon centre in **13** to give ketal **14** in 12-56% yield.

Scheme 1.8 Gold(I) catalyzed synthesis of ketal from epoxy propargylic alcohols.

At about the same time, Liang and co-workers reported gold(III) catalyzed tandem allylic amination/intramolecular hydroamination of 1-en-4-yn-3-ols with TsNH_2 to obtain highly substituted pyrroles **18** (Scheme 1.9).¹⁶ In this reaction, an excess amount of the sulfonamide nucleophile (15 equiv) and a high catalyst loading of 20 mol % were required to achieve high product yields. The mechanism was proposed to first involve intermolecular amination of the gold(III) activated propargylic alcohol to afford enynamine **16**. Subsequent intramolecular hydroamination of this adduct followed by isomerization of the ensuing bicyclic intermediate **17** then provided the pyrrole adduct **18** in 25-83% yield. The limitation of this methodology was the need for an aryl substituent at the R^2 position and a cyclic alcohol moiety, in instances where this was not the case, only the allylic amination product **16** with no further cyclization was observed despite prolonged reaction times of 24 h at reflux temperature.

Scheme 1.9 Gold(III) catalyzed tandem allylic amination/intramolecular hydroamination of 1-en-4-yn-3-ols.

Another approach to substituted pyrrole derivatives was demonstrated by the groups of Aponick and Akai (Table 1.1).^{17,18} From easily accessible 1,2-amino alcohols **19**, both groups independently showed the aromatic *N*-heterocycle could be achieved in yields up to 99% using the respective reactive catalytic systems $[\text{P}(t\text{-Bu})_2(o\text{-biphenyl})]\text{AuCl}/\text{AgOTf}$

Table 1.1 Gold(I) catalyzed intramolecular cyclization of propargylic alcohol **19**

Entry	Catalyst	Time	Yield (%)	Ref
1	$[\text{P}(t\text{-Bu})_2(o\text{-biphenyl})]\text{AuCl}$ /AgOTf	0.08-1.3 h	87-99	17
2	$(\text{Ph}_3\text{P})\text{AuCl}/\text{AgNTf}_2$	0.25-9 h	85-98	18

and $(\text{Ph}_3\text{P})\text{AuCl}/\text{AgNTf}_2$ (Table 1.1). Achieved under mild conditions at room temperature or 0 °C, the reactions were also shown to proceed well at catalyst loadings as low as 0.05 mol %.

More recently, a third synthetic strategy to substituted pyrroles from propargylic alcohols was reported by Chan and co-workers.¹⁹ In this work, *N*-substituted *N*-

sulfonylaminobut-3-yn-2-ols **21** were converted to tetrasubstituted pyrroles **22** in 38-98% yield. The mechanistic pathway was surmised to involve a 1,3 sulfonyl shift of the vinyl gold species obtained after the aminocyclization of **21** (Scheme 1.10).

Scheme 1.10 Gold(I) carbene catalyzed tandem aminocyclization/1,3-sulfonyl migration.

Another work directed toward the synthesis of nitrogen-containing heterocycles is the one-pot dual gold(III)-iron(III) catalyzed direct nucleophilic addition of propargylic alcohols **23** to provide 2,3-dihydroisoxazoles **27** reported by Campagne and co-workers (Scheme 1.11).²⁰ By exploiting the different catalytic reactivities between gold(III) and iron(III) along with their compatibilities, this enabled iron(III) to first catalyze the nucleophilic addition of the protected hydroxylamine **24** to the corresponding propargylic alcohol **23** to give the substitution product **25**. Gold(III) catalyzed cycloisomerization of **25** then generated the 2,3-dihydroisoxazole **27** product in 36-86% yield. When the 2,3-dihydroisoxazole **27** was further treated with 1.1 equiv of hydroxylamine and 10 mol % of NaAuCl₄·2H₂O, the disubstituted product **28** was obtained in 74% yield through the addition of the hydroxyl group in the protected hydroxylamine to the alkene moiety of **27**. Based on this experiment, it was surmised that another possible mechanism might have involved addition of the hydroxyl moiety of the hydroxylamine to the alkyne group in **23** to obtain intermediate **26** followed by cyclization to deliver **27**. Although the role of DMAP as co-catalyst is not clear, it was suggested that complexation of DMAP and

gold(III) would break the possible stable coordination between the metal and the hydroxyl group of the hydroxylamine moiety in **25** and hence promote cyclization.

Scheme 1.11 Dual gold(III)–iron(III) catalyzed one pot synthesis of 2,3-dihydroisoxazoles from propargylic alcohols **23** and hydroxylamine **24**.

The following year, Shin and co-workers reported that 5,6-fused azacycles **33** could be accessed from the 1-aminoindane framework **32** (Scheme 1.12).²¹ Starting from nitron containing propargylic alcohols **29**, gold(III) catalyzed redox reaction of the nitron to the alkyne was put forward to generating the gold carbenoid species **30**. It was proposed that a subsequent 1,2-pinacol shift would then provide the gold(III) coordinated enolate **31**, which was thought to undergo subsequent Mannich reaction to give 1-aminoindane **32** in up to 87% yield and d.r. values of up to 15:1. The preference of the observed diastereomer was due to the proposed metal chelation in a chair-like transition state of enolate species **31**. The presence of the vinyl group in the substituent at R^3 position of 1-aminoindane **32** was thought to result in either spontaneous or silica gel mediated Michael addition to afford the 5,6-fused azacycle product **33** in 55-77% yield with d.r. values up to 15:1.

Scheme 1.12 Gold(III) catalyzed tandem intramolecular redox/pinacol/Mannich/Michael reaction of propargylic alcohol **29**.

At about the same time, Chan and co-workers reported the preparation of indenyl-fused indole **36** and 2,3-disubstituted indole derivatives **37** in up to 94% yield through gold(I) catalyzed cycloisomerization of 2-tosylaminophenylprop-1-yn-3-ols **34**.²² The mechanism was proposed to involve *in situ* generation of the indolyl-substituted vinyl gold species **35** on treating with the AuCl/AgOTf/HMPA catalytic system (Scheme 1.13).

Scheme 1.13 Gold(I) catalyzed synthesis of indenyl-fused and indole derivatives.

Following this work, Wang and co-workers showed that gold(I) catalyzed cascade alkylation/iminium trapping of indoles **38** to generate polycyclic indolines **40** with two stereogenic centres in 64-88% yield (Scheme 1.14).²³ In this synthetic strategy, the functional groups including the protected nitrogen moiety and alcohol group at the propargylic position were shown to serve as internal nucleophiles to trap the iminium ion intermediate **39**. The configuration of the quaternary centres was controlled by the stereochemistry of the secondary alcohol and this was demonstrated by one example (R^1 , R^4 = H, R^2 = Me, X = O, R^3 = Boc) in **40** whereby the chirality in the product was retained from the corresponding enantioenriched starting material (81% *ee*).

Scheme 1.14 Gold(I) catalyzed cascade alkylation/iminium trapping.

In a similar manner, Bandini and co-workers reported gold(I) catalyzed cascade reaction of 3-substituted indoles **41** to dihydropyranylindolines **44** and furoindolines **45** in moderate to good yields and with excellent d.r. values of up to 50:1.²⁴ In this work, it was proposed the gold(I) activated alkyne would trigger Friedel-Crafts alkylation at the C3 carbon of the indole unit in either an *exo-dig* or *endo-dig* manner to form the spirovinyl gold intermediates **42** and **43**, respectively. A survey of different gold catalysts revealed that in the presence of gold(I) complex **Au₂**, tetracyclic dihydropyranylindoline **44** was furnished as the only product in 59-86% yield from indoles containing a malonyl tethered propargylic alcohol **41** (Table 1.1, entry 1). On the other hand, the introduction of more flexible side chains by increasing the carbon chain length and changing the tether from a

Table 1.2 Gold(I) catalyzed synthesis of polycyclic indolines

Entry	Catalyst (5 mol %)	Time	Yield		Ref
			44	45	
1	 Au₂	16 h	59-86%	52-76%	24
2	$[(R)\text{-xylylBINAP}(\text{AuBF}_4)_2]$	4-16 h	50-75% (<i>ee</i> > 87%)	-	25
3	$[(S)\text{-DTBM-segphos}(\text{AuOTf})_2]$	4-16 h	-	62-67% (<i>ee</i> > 85%)	25

malonyl to nitrogen-containing group, a switch in regioselectivity was found with the 7-*endo-dig* cyclization product **45** being obtained in 52-76% yield.

In a continuation of this work, the same group revealed that upon treatment of starting indoles **41** with chiral gold(I) complex $[(R)\text{-xylylBINAP}(\text{AuBF}_4)_2]$, chiral adducts of **44** could be obtained as a single regioisomer in 50-75% yield and with *ee* values up to 87% (Table 1.2, entry 2).²⁵ Changing the gold(I) complex to $[(S)\text{-DTBM-segphos}(\text{AuOTf})_2]$ and changing the length of the carbon chain as well as the tether unit containing a nitrogen moiety also gave **45** in 62-67% yield and with *ee* values up to 85% (Table 1.2, entry 3).

Prior to the work of Bandini and co-workers, the group of Liu reported gold(I) catalyzed cascade cyclization/heterolytic fragmentation/elimination reactions of 3-alkynylindoles bearing a diol moiety **46** to 3-allenylindole derivatives **49** in 37-83% yield under mild reaction conditions (Scheme 1.15).²⁶ Mechanistically, the spirovinyl gold intermediate **47** was obtained from 6-*endo-dig* alkylation of the C3 position of the indole

Scheme 1.15 Gold(I) catalyzed cascade cyclization/heterolytic fragmentation and elimination reaction.

to the alkyne in the substrate. It was surmised that further heterolytic fragmentation of **47** resulted in 1,5-indole migration to afford intermediate **48**. Subsequent C-3 allenylation of this vinyl gold species **48** by dehydration and protodeauration furnished the desired product **49**.

In a further exploration of the synthetic strategy to obtain polycyclic fused indoles, Bandini and co-workers showed that 2-(propargylic alcohol)-anilines **50** provided azepino[1,2-*a*]indoles **52** in good to excellent yields of 50-96% (Scheme 1.16).²⁷ Deuterium labeling studies concluded that nucleophilic vinyl gold intermediate **51**, which was obtained through hydroamination/dehydration and insertion, allowed the second cyclization to occur at the carbonyl group tethered to the aniline moiety.

Scheme 1.16 Gold(I) catalyzed synthesis of azepino[1,2-*a*]indoles **50**.

Recently, it was shown that upon changing the carbonyl functionality to a hydroxyl group enabled access not only to oxazino[4,3-*a*]indole derivatives but also the 7-membered ring family of tetrahydro[1,4]-oxazepino[4,3-*a*]indoles **55** depending on the chain length of the corresponding aniline diols **53** (Scheme 1.17).²⁸ Furthermore, the method was applicable to tertiary and secondary propargylic alcohols albeit with the need for higher reaction temperatures in the latter case. In contrast, primary propargylic alcohols led to recovery of the starting material when treated to the same reaction conditions. Although this result suggested the involvement of a carbocationic species, the significant racemization to 16% and 18% *ee* in the products from the corresponding enantiomerically enriched alcohols with *ee* values of 60% ($R^1 = R^2, R^4 = R^5 = \text{H}, R^3 = \text{Me}$)

Scheme 1.17 Gold(I) catalyzed cascade reaction to polycyclic fused indoles.

and 81% ($R^1-R^5 = H$), respectively, led to the speculation of an S_N1 type mechanism *via* an ion pairing. The possible involvement of an ion pair interaction in intermediate **54** was posited to occur between the acidic proton and the counterion of the gold(I) complex.

1.4 Gold Catalyzed Reactions of Propargylic Esters

In 1969, Saucy, Marbet and co-workers showed that the carboxylic ester group at the propargylic position rearranged to allenic acetates in the presence of acetic acid and a silver or copper catalyst.²⁹ Following this work, Ohloff described $ZnCl_2$ mediated cycloisomerization of one example, that of 1,6-enyne ester **56** to carvenone **58** and 2-acetoxy-2-carene **59** in 70% and 5% yield, respectively (Scheme 1.18).³⁰ It was thought that the coordination of the zinc(II) catalyst to the alkene moiety in metal complex **57** initiated the 1,2-acyloxy migration and subsequent cyclization. The drawback of this method, however, was the requirement of a stoichiometric amount of the zinc(II) salt.

Scheme 1.18 $ZnCl_2$ mediated 1,2-acyloxy migration.

In 1984, Rautenstrauch reported palladium(II) catalyzed 1,2-acyloxy migration and cycloisomerization of 1,4-enyne esters **60** to cyclopentenones **63** in 48-89% yield although the efficiency of the reaction was not mentioned (Scheme 1.19).³¹ Various substrates containing different alkyl substituents at the R^1 and R^2 positions were well tolerated with the only exception being those with substitution at the terminal position of the alkene and alkyne. In contrast to Ohloff's proposed mechanism, the coordination of palladium(II) to both the alkene and alkyne functional groups to give **61** was reasoned to

Scheme 1.19 Palladium(II) catalyzed tandem 1,2-acyloxy migration/cycloisomerizations.

initiate the cycloisomerization process to form cyclopentadiene intermediate **62**. As shown in Scheme 1.19, evidence of this diene ring adduct was supported by its trapping with *N*-phenylmaleimide to give Diels-Alder adduct **64**. On the other hand, treating the 1,5 and 1,6-enyne esters of **60** ($n = 2,3$, $\text{R}^1 = \text{alkyl}$, $\text{R}^2 = \text{H}$) with the same catalyst was reported to induce cyclopropanation of the alkene to give the bicyclic product **65** albeit in low yields of 10-40%.

The work by Rautenstrauch represented the first transition metal catalyzed 1,2-acyloxy migration, which has now known as the Rautenstrauch rearrangement. Surprisingly, the synthetic utility of this reaction was neglected in the following three decades until 2003 when Uemura and co-workers reported the ruthenium(II) catalyzed intermolecular cyclopropanation of propargylic acetate **66** with excess amount of styrene **67** (Scheme 1.20).³² In the course of the study, it was shown that AuCl_3 could also catalyze the reaction and furnished the desired cyclopropane **68** in 63% yield *via* tandem 1,2-acyloxy migration/cyclopropanation along with 26% yield of the 1,3-acyloxy migration product **69**.

Scheme 1.20 Tandem 1,2-acyloxy migration/cyclopropanation of propargylic acetate **64**.

Building on this seminal work, a number of groups have subsequently developed other metal-catalyzed synthetic methods featuring 1,2- and 1,3-acyloxy moiety migrations.^{6,33} In these latter investigations, factors such as the nature of the substituents at the propargylic position,³⁴ choice of metal catalyst³⁵ and reaction temperature³⁶ could control which migration pathway was favoured. Although these studies provided insight into the mechanistic premise governing 1,2- and 1,3-acyloxy moiety migrations, these investigations remained inconclusive. In this context, in works focused on the mechanism of the 1,2- and 1,3-acyloxy migrations mediated by gold catalysis,

Scheme 1.21 1,2 and 1,3 acyloxy rearrangement of propargylic ester.

Cavallo and co-workers showed the possible existence of a dynamic equilibrium between the gold carbenoid species **72** and gold activated allene **73** via the gold activated alkyne **70** based on DFT (density functional theory) calculations (Scheme 1.21).³⁷ The 1,2-

acyloxy migration occur either from an initial 1,3-shift to give **73** followed by a retro 1,2-shift of this adduct or through direct 5-*exo-dig* cyclization of the gold coordinated alkyne **70**. On the other hand, a 1,3-migration pathway was calculated to be the result of a direct 6-*endo-dig* cyclization or two sequential 1,2-acyloxy migrations process.

To support the reversibility of a direct 1,2-shift (**70** $\longleftrightarrow$ **72**) and 1,3-shift (**70** $\longleftrightarrow$ **73**), Toste and co-workers described in a study the scrambling of the stereodefined ester group at the propargylic and cyclopropyl positions of the starting material (Scheme 1.22).³⁸ In the study, it was shown that the scrambling of relative stereochemistry of the starting material **75** (R = Ph) at both the propargylic and the cyclopropyl position took place in gold(I) catalyzed transformation of cyclopropyl propargylic ester **75** to cyclopentene **78**. Firstly, the relative stereochemistry of at the propargylic position of the starting material **75** was lost (d.r. = 1:1) within two minutes, suggesting the propargylic ester rearrangement to be fast and reversible. It was calculated that the rearrangement occurred *via* 1,3-acyloxy rearrangement generating the allene species **76**. Upon coordination of the allene with the gold(I) complex, the substituents were forced into the same plane and resulted in the lost of stereochemical information. Secondly, the *cis* stereochemistry at the cyclopropyl position of the substrate **75** was observed to gradually isomerize to the *trans* isomer over a period of an hour. It was posited that this scrambling event occurred *via* the carbocation allenic species **77**. Using the same approach to prove the reversibility of 1,2-acyloxy migration, scrambling of the relative stereochemistry at the carbon proximal to ester group (d.r. = 1:1) of terminal propargylic substrate **75** (R = H) and gradual isomerization from the *cis* to the *trans* isomer of the cyclopropane moiety were found. The organogold species **79** obtained from 1,2-acyloxy shift was further proven by trapping with Ph₂SO and generating the aldehyde **80** although no yield of this product was reported.³⁹

Scheme 1.22 Reversibility of direct 1,2-acyloxy shift and direct 1,3-acyloxy shift.

On the other hand, to further investigate the direct 1,3-acyloxy shift, the same group conducted an ^{18}O -labeling study (Scheme 1.23).³⁸ In this study, subjecting ^{18}O -75 to $\text{PPh}_3\text{AuSbF}_6$ was reported to give ^{18}O -78 as the single product in 76% yield with ^{18}O -atom fully retained at the carbonyl oxygen. It was posited that in the event of a double

Scheme 1.23 ^{18}O -labelling study to prove direct 1,3-acyloxy migration.

1,2-acyloxy migration, the ^{18}O -atom should reside at the oxygen of the ester linkage to the allene moiety in ^{18}O -**82** and furnished product ^{18}O -**83**, which was not observed in this case.

A separate ^{18}O labeling experiment to study the mechanism of 1,2- and 1,3-shifts was performed by Nolan and co-workers in gold(III), gold(I) and platinum(II) catalyzed transformations of propargylic ester ^{18}O -**84** (Scheme 1.24).⁴⁰ This study showed that nearly quantitative transfer of the isotope to the products ^{18}O -**85** and ^{18}O -**86** were

Scheme 1.24 ^{18}O -labelling study by Nolan and co-workers.

obtained from PtCl_2 catalyzed transformation of ^{18}O -**84**, which suggested net 1,2-shift of acyloxy group (Scheme 1.24, Eq 1). On the other hand, upon treating the same starting material ^{18}O -**84** with AuCl_3 or $\text{IPrAuCl}/\text{AgBF}_4$ combination, scrambling of ^{18}O -isotope in the product was found and a mixture of ^{18}O -**85** and/or ^{18}O -**86** and/or ^{18}O -**87** were observed (Scheme 1.24, Eq 2 and 3). These results indicated the random occurrence of a double 1,2-shift and a direct 1,3-shift of the acyloxy group that happened several times before the cyclization took place.

1.4.1. 1,2-Acyloxy Migration of Propargylic Esters

A year after the seminal discovery of gold(III) catalyzed 1,2-acyloxy migrations by Uemura and co-workers,³² further investigations in the field was performed by Fürstner and co-workers.⁴¹ As part of their broader study on platinum(II) catalyzed cycloisomerization of hydroxylated enynes, it was found that the combination of 2 mol % of (Ph₃P)AuCl and AgSbF₆ enabled the acyloxy enyne **88** to undergo tandem 1,2-acyloxy migration (Scheme 1.25). This generated the gold carbenoid species **89**, which was susceptible to cyclopropanation to afford bicyclic enol ester **90**. Further treatment of the reaction mixture with potassium carbonate furnished the bicyclic ketone **91** in 74% overall yield.

Scheme 1.25 Gold(I) catalyzed tandem 1,2-shift/cyclopropanation.

A further insight into Rautenstrauch rearrangement in the synthesis of cyclopentanones³¹ was reported by Toste and co-workers (Scheme 1.26).⁴² The methodology was applicable to various 1,4-enyne esters **92**, furnishing the corresponding product **95** in 45-88% yield. By changing the catalyst from PPh₃AuOTf to PPh₃AuSbF₆, the chirality of the stereodefined starting propargylic pivaloate was transferred to the product with *ee* values up to 97%. Mechanistically similar to Rautenstrauch's report,³¹ the gold(I) catalyst was speculated to activate the alkyne moiety of **92**. This resulted in 1,2-addition of the carbonyl oxygen from propargylic pivaloate to the alkyne bond and

generated the vinyl gold species **93**. The stereoselectivity was explained by the conformation of adduct **93** where the C–O bond was proposed to occupy the orthogonal position to the plane of the alkene unit. Subsequent cyclization afforded cyclopentadiene **94**, which hydrolyzed to cyclopentanone **95**.

Scheme 1.26 Gold(I) catalyzed synthesis of cyclopentanone from 1,4-enyne esters.

Following this work, the same group demonstrated the synthesis of the *N*-containing medium size ring azepines by applying the Rautenstrauch rearrangement and [4+3] annulation of the imines **97** and propargylic benzoates **96** (Scheme 1.27).⁴³ Various imines **97** containing different substituents reacted well with secondary propargylic esters **96** to afford the azepine product **100** as a single diastereomer (> 20:1 d.r.). On the other hand, reaction of the imine with tertiary propargylic esters gave a mixture of diastereomers. In this strategy, the conjugated imine acted as nucleophile-electrophile pair. Addition of the imine to the gold carbenoid species **98**, formed through 1,2-benzyloxy migration of **96**, was described to generate the allyl gold intermediate **99**, which underwent subsequent intramolecular addition to the electrophilic iminium ion and afforded the azepine **100**.

Scheme 1.27 Tandem Rautenstrauch rearrangement/[4+3] annulation of conjugated imine and propargylic benzoate to azepine.

Using an azide instead of conjugated imines in the [4+3] annulation reaction with propargylic esters was recently disclosed by Hu and co-workers as an alternative strategy to obtain azepines **104** in 50-78% yield and with diastereoselectivities up to 20:1 (Scheme 1.28).⁴⁴ The generality of the approach was demonstrated by the reaction of different alkyl and benzyl azides **101** with secondary and tertiary propargylic esters **102**. However,

Scheme 1.28 Tandem Rautenstrauch rearrangement/imine formation/[4+3] annulation of azide and propargylic benzoate to azepine.

this method required an excess amount of the propargylic ester to generate the conjugated imine **103** *in situ* and 10 mol % of the catalyst was added in two batches to efficiently catalyze the reaction.

Furthermore, Toste and co-workers demonstrated that the same PicAuCl_2 catalyst could catalyze [3+3] cycloaddition of propargylic benzoates **105** and azomethine imines **106** (Scheme 1.29).⁴⁵ Stepwise addition of the ylide to the gold carbenoid **107** obtained from 1,2-shift of the acyloxy moiety of **105**, led to the intermediate **108**. Further cyclization of this iminium species gave the tetrahydropyrazine **109** in 41-98% yield and with *cis:trans* selectivities up to 20:1.

Scheme 1.29 Gold(III) catalyzed [3+3] annulation of azomethine imines with propargylic benzoates.

Recently, Liu and co-workers found that propargylic benzoates **110** could undergo [4+2] cycloaddition with nitrosoaryl compounds **111** in the presence of IPrAuCl and AgNTf_2 catalyst combination (Scheme 1.30).⁴⁶ The reaction proceeded smoothly with different propargylic esters and nitrosoarenes providing oxazine **116** in 67-74% yield. In this work, it was proposed that addition of the nitrogen atom of the nitrosoaryl compound

to the alkenyl gold carbenoid species **112** obtained through 1,2-benzyloxy shift of **110** gave oxazetidine **113**. Loss of $[\text{Au}=\text{O}]^+$ from this adduct generated conjugated imine **114**, which tautomerized to the diene **115**. It was suggested that $[\text{Au}=\text{O}]^+$ underwent disproportionation to regenerate the active gold(I) catalyst and molecular oxygen. Subsequent cycloaddition of the diene with the gold(I) activated nitrosoaryl compound gave the oxazine.

Scheme 1.30 Gold(I) catalyzed [4+2] cycloaddition of nitrosoaryl with propargylic ester.

1.4.2. 1,3-Acyloxy Migration of Propargylic Esters

Although the first reported example of gold(III) catalyzed 1,3-migration of the acyloxy group of a propargylic acetate only afforded the corresponding allenyl ester in 26% yield,³² the discovery triggered further studies in this field. In 2005, Zhang and co-workers revealed a new strategy for the synthesis of tetracyclic 2,3-indoline-fused cyclobutanes **120** in 69-98% yield from gold(I) catalyzed 1,3-acyloxy migration of the indole-3-propargylic acetate **117** (Scheme 1.31).⁴⁷ This strategy involved formation of the oxonium vinyl gold species **118** with the gold atom *cis* to the R^2 group. Consequently, this led to the attack of the nucleophilic C3 carbon atom of indole to the oxonium carbon

centre and formation of the lactone intermediate **119**. Formation of this functionalized tetracyclic indoline fused cyclobutane **120** with the *E*-exocyclic alkene stereochemistry was subsequently obtained after attack of the vinyl gold moiety to the iminium ion in the spiro species **119**.

Scheme 1.31 Gold(I) catalyzed tandem 1,3-acyloxy/[2+2] cycloaddition to tetracyclic 2,3-indoline fused cyclobutane.

In 2010, Liu and co-workers reported the synthesis of piperidines **123** in 50-92% yield from gold(III) catalyzed cycloisomerization of *N*-protected propargylic esters **121** (Scheme 1.32).⁴⁸ The allenyl ester **122** obtained *in situ* from 3,3-sigmatropic rearrangement of the acyloxy group in the substrate was activated upon coordination of the allene by the gold(III) catalyst. This further triggered the 6-*endo-dig* cyclization of the allene to furnish the nitrogen-containing ring product **123**. The limitation of this strategy was the poor *cis:trans* isomers albeit good product yields of 50-92% were obtained.

Scheme 1.32 Synthesis of piperidine from tandem gold(III) catalyzed 3,3-rearrangement/hydroamination.

She and co-workers also reported the synthesis of piperidines from gold(I) catalyzed tandem acyloxy migration/intramolecular [3+2] cycloaddition of 1,7-enyne esters **124** (Scheme 1.33).⁴⁹ The cyclization process was reasoned to involve double 1,2-acyloxy migration to form an *in situ* generated dipole **125** which could undergo [3+2] cycloaddition with the alkene moiety of the substrate to provide bridged intermediate **126**. It was shown that product selectivity was determined by the substitution pattern at the R^1

Scheme 1.33 Synthesis of piperidine from gold(I) catalyzed formal [3+2] cycloaddition.

and R³ positions. A methyl substituent at either the R¹ or R³ position in dry CH₂Cl₂ afforded bicyclic adduct **128** in up to 85% yield. On the other hand, when R¹ and R³ = H in the substrate and dry CH₂Cl₂ was employed, this furnished the adduct **128** in a moderate yield of 35%. Experiments with substrates where R¹ and R³ = H conducted in wet dichloromethane were found to give the hydrolyzed product **127** in 61-93% yield.

From enantiopure 1,7-enyne esters, Chan and co-workers demonstrated the synthesis of the piperidine derivatives **132** and **133** as a single diastereo- and enantiomer in up to 97% yield (Scheme 1.34).⁵⁰ In these reactions, the allene acted as a nucleophile instead of an electrophile as described in earlier works, and in doing so, underwent 6-*exo-dig* cyclization to afford intermediate **131**. It was speculated that the electronic and steric factors of the ligand in the gold(I) complex employed controlled the unique selectivity of the product. Reactions with gold(I) carbene **Au₁** was found to be less prone to protodeauration⁵¹ and thus gave the 1,5-acyl shift product **132** from alkyl gold

Scheme 1.34 Gold(I) catalyzed tandem 3,3-rearrangement/6-*exo-trig* cyclization/1,5-acyl migration.

complex **131** in up to 77% yield. On the other hand, the gold(I) phosphine complex **Au₂**, which has been reported to be more susceptible to protodeaurations⁵¹ afforded the deacylated product **133** in up to 97% yield with the assistance of 2 equiv of water.

The same group also showed that by changing the tethered alkene to either a terminal or internal alkyne to give diyne ester **134**, a switch in the mode of reactivity was observed (Scheme 1.35).⁵² In the case of reactions with a pendant terminal alkyne moiety catalyzed by the gold(I) phosphine complex **Au₂**, selective coordination of gold(I) at the terminal alkyne of **135** triggered a concerted 5-*endo-dig* followed by 7-*endo-dig* cyclization by the appropriately placed aryl moiety to furnish the indeno[1,2-*c*]azepine ring system **136** in 44-79% yield (Scheme 1.35, Eq. 1). On the other hand, the gold(I) complex was found to preferentially coordinate to the propargylic position having the ester group in the case of substrates with an internal alkyne, resulting in 1,3-benzyloxy migration and 6-*exo-dig*

Scheme 1.35 Gold catalyzed formation of indeno[1,2-*c*]azepine and azabicyclo[4.2.0]octa-1(8),5-dienes.

cyclization to provide adduct **137** (Scheme 1.35, Eq 2). This active species would then undergo Prins-type cyclization to give the piperidine fused cyclobutene **138** in 45-80% yield.

Prior to the work by Chan and co-workers, the group of Shi demonstrated unusual 5-membered ring cycloadducts could be obtained from 1,6-diyne esters **139** (Scheme 1.36).⁵³ This strategy proved to work for a wide variety of substrates including oxygen tethered 1,6-diyne esters. On the basis of deuterium experiment studies, two mechanistic pathways were deduced. As water was needed as an additive, its attack at the gold(I) activated alkyne containing the ester group was thought to release the AcO^- ion to give allenol **140** (Scheme 1.36, path 1). Another possible pathway was reasoned to involve a 1,3-acyloxy shift and generation of the oxonium intermediate **141** upon allene activation by the gold(I) catalyst (Scheme 1.36, path 2). Hydrolysis of intermediates **140** and **141** delivered the enone **142**, which upon tautomerization provided the gold(I) coordinated

Scheme 1.36 Gold(I) catalyzed synthesis of 3-pyrrolines.

species **143** that underwent subsequent 5-*endo-dig* cyclization to afford the 2,3-disubstituted 3-pyrroline **144** in 35-88% yield.

In the course of their studies on the silver(I) catalyzed cycloisomerization of 1,6-diyne esters to naphthalene adducts, Toste and co-workers found that the strategy was also applicable to pyrrole containing diyne-esters **145** on employing a gold(I) and silver(I) catalyst system (Scheme 1.37).⁵⁴ The reaction involved the *in situ* formation of the allene **146** from 1,3-acyloxy shift of the substrate, which then underwent further 6-*endo-dig* cyclization to provide the indole derivatives **147** in 58% yield.

Scheme 1.37 Gold(I) catalyzed synthesis of nitrogen containing aromatic ketone.

A recent study conducted by Hashmi and co-workers revealed 1,7-enyne esters **148** to undergo 1,5-acyl shift to afford pyrrolidin-2-ones **150** in 42-92% yield (Scheme 1.38). The scope of the reaction included different migrating groups such as the phosphatoxy,⁵⁵ carbonate,⁵⁵ or acyloxy moieties.⁵⁶ The formation of the product involved either a six-membered ring or eight-membered ring intermediate of the vinyl gold species **149**.

Scheme 1.38 Gold(I) catalyzed synthesis of pyrrolidin-2-ones.

More recently, Huang and co-workers demonstrated the synthesis of quinolines **155** in moderate yields of 41-55% from two different pathways (Scheme 1.39).⁵⁷ The first pathway involved 3,3-sigmatropic shift of **151** to generate the allene species **153**, which then underwent 6-*endo-dig* cyclization involving the diazo moieties to the allene bond

Scheme 1.39 Gold(I) catalyzed synthesis of quinolines.

followed by denitrogenation. On the other hand, starting from azide **152**, gold(I) coordination to triple bond was described to trigger 6-*endo-dig* cyclization of the azide. Subsequent denitrogenation and 1,2-hydride shift of the putative gold carbenoid species **154** afforded the quinoline derivative **155**.

1.5 Proposed Work

The work on this thesis will focus on establishing new methodologies to synthesize nitrogen-containing heterocyclic compounds of biological and material interest in an atom-economical and ecologically benign manner from readily available starting materials. This can be achieved by exploring the highly reactive and chemoselective nature of gold catalysis in combination with nitrogen containing propargylic alcohols and esters in an intramolecular manner.

Thus, the first aim of this project is to develop a new protocol on gold catalyzed synthetic method for the construction of azabicyclo[4.2.0]oct-5-enes and 3-azatricyclo[5.2.1.0^{1,5}]dec-8-enes. It was envisaged that 3,3-sigmatropic rearrangement of benzyloxy group in enantiopure 1,7-enyne benzoates **156** would generate the allene intermediate **157**. Selective activation of the alkene moiety by the gold catalyst would trigger [2+2] cycloaddition to give the desired product **158** (Scheme 1.40). On the other hand, 1,6-enyne ester **159** would undergo 1,2-acyloxy migration to form cyclopentadiene intermediate **160** *in situ* followed by a thermal Diels-Alder cyclization to furnish **161** (Scheme 1.41).

Scheme 1.40 Proposed gold catalyzed tandem 3,3-rearrangement/[2+2] cycloaddition.

Scheme 1.41 Proposed gold catalyzed 2,3-rearrangement/thermal Diels-Alder.

In the course of our studies on gold catalyzed reactions of propargylic alcohols, it was found that silver salts could also serve as a possible alternative to third row metal as the catalyst to mediate the construction of the indolin-3-ol derivatives **164** *via* intramolecular hydroamination of 2-aminophenylprop-1-yn-3-ols **34** (Scheme 1.42). From this investigation, during examining the scope of the hydroamination reaction to include alkyl

protected 2-aminophenylprop-1-yn-3-ols **162**, an unexpected reaction leading to the formation of 2-oxindoles **163** in the presence of silica gel is also presented. This latter 2-oxindoles forming reaction was thought to proceed *via* a tandem hydroamination/semipinacol rearrangement of the *N*-alkyl protected substrate.

Scheme 1.42 Proposed formation of indolin-3-ol and 2-oxindole.

Chapter II. Gold Catalyzed Tandem 1,3-Migration/[2+2] Cycloaddition of 1,7-Enyne Benzoates to Azabicyclo[4.2.0]oct-5-enes

2.1 Introduction

Gold catalyzed cyclization of 1,*n*-enyne esters **70** *via* initial 1,3-acyloxy migration to the allenic ester **73** and activation of the allenic moiety in this species through coordination of the metal complex, as shown in Scheme 2.1, path 1 and a number of examples in Chapter 1, is well-documented.^{37,40,47,54,58} On the other hand, a tandem process involving 1,3-*O*-ester migration followed by selective coordination of the gold catalyst to an appropriately placed unactivated alkene rather than the allenic moiety is not known (Scheme 2.1 path 2).⁵⁹ Hence, we envisioned that gold(I) coordinated species **157** generated from this change in selectivity by the metal catalyst might then be more prone to undergo a stepwise [2+2] process and provide synthetically useful bicyclic derivatives fused with a cyclobutane ring. To our knowledge, this mode of reactivity is not observed in 1,*n*-enyne cycloisomerizations because other more generally favored skeletal rearrangements occur.^{6,7,9,34,58,60} Added to this is a recent report showing acyloxy substituted 1,6-enynes derived from dipropargylic amides to be resistant to the gold catalyzed cycloisomerization process.⁶¹ As part of an ongoing program exploring the scope of gold catalysis in heterocyclic synthesis,^{22,62} we disclose herein the details of this chemistry involving Au(I) mediated tandem 1,3-migration/[2+2] cycloaddition of 1,7-enyne benzoates (Scheme 2.1). This process delivers a regioselective and stereoconvergent route to azabicyclo[4.2.0]oct-5-enes, a key class of compounds in synthetic and natural product chemistry,⁶³ that gives the products in good to excellent yields and as a single regio- and diastereomer. The bicyclic ring adducts could also be obtained as a single enantiomers with up to four stereogenic centers, demonstrating the reaction to proceed with efficient transfer of chirality from the enantiopure substrate to the product.

Scheme 2.1 Allene activation or alkene activation in gold catalyzed 1,*n* enyne esters.

2.2 Results and Discussion

All the 1,7-enyne benzoates examined in this work were prepared as shown in Scheme 2.2 – 2.4. The ketone **165** used in the synthesis of the starting material was obtained in house and prepared from the corresponding L- α -amino acid in three steps following literature procedures.⁶⁴ As shown in Scheme 2.2, reaction of enantiopure ketone **165** to a variety of alkynes pretreated with LDA furnished the propargylic alcohol as two diastereomers **166** and **166'** in 70-90% yields and in ratios of up to 4:1. Alternatively, the racemic ketone **165** was subjected to either $c\text{C}_3\text{H}_5\text{MgBr}$ or $\text{C}_5\text{H}_{11}\text{MgBr}$ in THF to afford

Scheme 2.2 Synthesis of propargylic alcohol **166** and **166'** from enantiopure aminoketone **165**.

Scheme 2.3 Synthesis of propargylic alcohol (±)-**166** and (±)-**166'** from racemic 1-tosylaminoketone **165**.

the racemic propargylic alcohols **166** and **166'** in 70-88% yields and in ratios of up to 4:1 (Scheme 2.3). With the major diastereomer of propargylic alcohol **166** in hand (Scheme 2.4), the alcohol moiety was treated with benzoyl chloride, 4-(dimethylamino)pyridine and NEt_3 in CH_2Cl_2 to give propargylic ester **167** in 53-90% yield. This was followed by allylic alkylation of the amine moiety with allyl bromide or cinnamyl bromide in DMF and NaH as the base to give the 1,7-enyne esters **156** in 60-85% yield. The (3*S*,4*S*) absolute configuration of the enantiopure propargylic alcohol **166h** and the relative configuration of the racemic propargylic benzoate **167f** were determined by X-ray crystal structure analysis (Figure 2.1).⁶⁵

Scheme 2.4 Synthesis of 1,7-enyne benzoates **156a-x**.

By using the enantiopure *syn*-1,7-enyne benzoate **156a** as the model substrate, we began our studies by examining a variety of gold complexes as well as PtCl_2 to establish the reaction conditions (Table 2.1). Au(I) complexes **Au₁**, **Au₃**, **Au₅**, **Au₆**, and **Au₇** were

Figure 2.1 ORTEP drawings of (a) **166h** and (b) **167f** with thermal ellipsoids at 50% probability levels.

prepared following the literature procedure⁶⁶ and the structure of **Au₅** was confirmed by X-ray crystallography (Figure 2.2).⁶⁷ This study revealed that treating **156a** with 5 mol % of Au(I) catalyst **Au₂** and 4Å molecular sieves (MS) in (CH₂Cl)₂ at 80 °C for 15 h gave the best result, furnishing **158a** in 82% yield and as a single regio-, diastereo- and enantiomer (entry 1). The (1*R*,4*S*,7*R*) absolute configuration of the cyclobutane-fused piperidine product was determined by X-ray crystallography (Figure 2.3).⁶⁸ Lower product yields were obtained when the reaction was repeated at room temperature, with the more sterically crowded Au(I) complexes **Au₃** or **Au₄** in place of **Au₂** as the catalyst, or in the absence of 4Å MS (entries 2, 3, 8, and 9). The reaction at room temperature also afforded allenene **168a** in 48% yield (entry 3).⁶⁹ In marked contrast, only the allenene was obtained in 77-95% yield when the solvent was changed from (CH₂Cl)₂ to either MeCN, MeNO₂, 1,4-dioxane or toluene (entries 4-7). A survey of other Au(I) and Au(III) complexes as well as PtCl₂ as the catalyst gave similar outcome (entries 10-17). In all but one of these latter experiments, the allenene adduct was again afforded in 63-96% yield.

Table 2.1 Optimization of the reaction conditions^a

Entry	Catalyst	Solvent	Yield (%) ^b	
			158a	168a
1	Au₂	(CH ₂ Cl) ₂	82	-
2 ^c	Au₂	(CH ₂ Cl) ₂	53	-
3 ^d	Au₂	(CH ₂ Cl) ₂	44	48
4	Au₂	MeCN	-	95
5	Au₂	1,4-dioxane	-	88
6	Au₂	MeNO ₂	-	80
7	Au₂	PhMe	-	77
8	Au₃	(CH ₂ Cl) ₂	69	-
9	Au₄	(CH ₂ Cl) ₂	68	-
10	Au₁	(CH ₂ Cl) ₂	-	29 ^e
11	Au₅	(CH ₂ Cl) ₂	-	93
12	Au₆	(CH ₂ Cl) ₂	-	86
13	Au₇	(CH ₂ Cl) ₂	-	83

Table 2.1 (*continued*).

Entry	Catalyst	Solvent	Yield (%) ^b	
			158a	168a
14	Ph ₃ PAuNTf ₂	(CH ₂ Cl) ₂	-	88
15	Au₈	(CH ₂ Cl) ₂	-	95
16	AuBr ₃	(CH ₂ Cl) ₂	-	63
17	PtCl ₂	(CH ₂ Cl) ₂	-	96

^a All reactions were performed at the 0.15 mmol scale with catalyst:**156a** ratio of 1:20 and 4Å MS (150 mg) at 80 °C for 15 h. ^b Isolated yield. ^c The reaction was carried out in the absence of 4Å MS. ^d The reaction was carried out at room temperature for 30 h. ^e Pyrrole **169a** obtained as a byproduct in 20% yield.

(a) **Au₅**

Figure 2.2 ORTEP drawing of Au(I) complex **Au₅** (only the complex cation is shown) with thermal ellipsoids at 50% probability levels.

Figure 2.3 ORTEP drawings of (a) **158a** and (b) **169a** with thermal ellipsoids at 50% probability levels.

In our hands, the analogous reaction of **156a** with the gold(I) carbene complex **Au₁** as the catalyst was the only instance that afforded the pyrrole byproduct **169a** along with **168a**, in 20 and 29% yield, respectively (entry 10). The structure of the aromatic *N*-heterocycle **169a** was also structurally confirmed by X-ray crystallographic analysis (Figure 2.3).⁶⁸

With the optimal conditions in hand, we next sought to evaluate their generality for a series of 1,7-enyne benzoates, and the results are summarized in Table 2.2. These experiments showed that with the Au(I) complex **Au₂** as the catalyst, the conditions proved to be broad and a variety of highly substituted azabicyclo[4.2.0]oct-5-enes could be obtained in 41-90% yield from the corresponding substrates **156b-x**. This hitherto included starting 1,7-enynes containing a thiophene, cyclopropane, OTBS and MeSO₂ moieties (**156d** and **156m**, **156f**, **156n** and **156p**, respectively), showing that such functional groups were well-tolerated under the reaction conditions. Similarly, reactions

Table 2.2 Tandem 1,3-migration/[2+2] cycloaddition of 1,7-enyne benzoates **156b-x** catalyzed by **Au₂**^a

^a All reactions were performed on a 0.15 mmol scale with an **Au₂**:**156** ratio of 1:20 and 4 Å MS (150 mg) at 80 °C for 15-24 h. Values in parentheses denote isolated product yields. ^b The reaction was conducted with the (3*R*,4*S*)-**156a** and 10 mol % **Au₂**. ^c The reaction was conducted with an inseparable 1:1 mixture of diastereomers of the substrate. ^d The reaction was conducted with an inseparable 4:1 mixture of diastereomers of the substrate. ^e The reaction was conducted with an inseparable 3.3:1 mixture of diastereomers of the substrate.

of substrates containing an activated alkene moiety (**156q-x**) were found to proceed well and provide the corresponding bicyclic adducts in excellent yields. More notably, these intramolecular cyclizations also demonstrated that the ring-forming process occurs in a highly selective manner. We found that the [2+2] cycloaddition step to occur regioselectively at the distal 2π component of the *in situ* formed allene moiety, affording the cyclobutane-fused piperidine as the sole product in all the reactions described in Table 2.2. The pyrrolidine regioisomer resulting from [2+2] cycloaddition at the proximal 2π component of the *in situ* formed allene moiety was not observed using NMR analysis of the crude reaction mixtures.⁷⁰ The reaction was additionally shown to give the corresponding products as single diastereomers irrespective of whether it started from a single isomer or a diastereomeric mixture of the substrate. In the case of reactions with **156b-d**, **156g-k** and **156p-x**, the corresponding adducts were also furnished as single enantiomers with up to four stereogenic centers, illustrating efficient transfer of chirality from the enantiopure substrate to the bicyclic product. Moreover, the formation of cyclobutane-fused piperidines as single diastereomers from stereoisomeric starting 1,7-enynes that are presumably epimeric at C3 (**156l**, **156n**, **156o** and **156w**) showed that the transformation is stereoconvergent. This was further exemplified by the Au(I) catalyzed reaction of the (3*R*,4*S*)-**156a**, which also provided (1*R*,4*S*,7*R*)-**158a** in 48% yield. On the other hand, the stereochemistry of the alkene moiety was found to be retained in the product. Substrates containing a *trans*-alkene group (**156q-w**) were found to give the corresponding bicyclo-[4.2.0] adducts having the bridgehead proton and R⁴ group *syn* with respect to each other. In contrast, the reaction of **156x** with a pendant *cis*-alkene moiety gave **158x**, in which the stereochemical relationship between these groups in the product was *anti* and epimeric at C8. The absolute configurations (1*R*,4*S*,7*R*) for **158b** and **158i**, (1*R*,4*S*,7*R*,8*S*) for **158r** and (1*R*,4*R*,7*R*,8*R*) for **158x** were determined on the

Figure 2.4 ORTEP drawings of (a) **158b**, (b) **158i**, (c) **158r** and (d) **158x** with thermal ellipsoids at 50% probability levels.

(a) **158m**

Figure 2.5 ORTEP drawing of (a) **158m** with thermal ellipsoids at 50% probability levels.

basis of X-ray crystal structure measurements (Figures 2.4).⁷¹ Similarly, the relative *syn* diastereochemistry of **158m** was determined by X-ray crystallography (Figure 2.5).⁷²

The mechanistic premise presented in Scheme 2.1 predicts that the Au(I) catalyzed cycloisomerization proceeds through a tandem 3,3-rearrangement/[2+2] cycloaddition pathway involving an allenene intermediate. While the isolation of the allenene **168a** produced by reactions of **156a** under various conditions described in entries 3-7 and 10-17 in Table 2.1 was fortuitous, the result argues in favor of this being the actual intermediate in the Au(I) catalyzed transformation. This argument is further corroborated by the fact that **158a** was furnished in 88% yield when a 1,2-dichloroethane solution containing **168a** was treated with 5 mol % of the Au(I) complex **Au₂** under the conditions depicted in eq 1 in Scheme 2.5. The role of the gold(I) catalyst in triggering the stepwise [2+2] cycloaddition by preferentially coordinating to the unactivated alkene moiety was also shown by first repeating the reaction in the absence of the metal catalyst. This test

led to recovery of only the starting allenene in nearly quantitative yield, mirroring the lack of reactivity observed in thermal [2+2] cycloadditions of allenenes containing an unactivated alkene moiety.⁷³ Moreover, conducting the reaction again for a second time with the gold(I) catalyst and in the presence of D₂O provided *cis*-piperidine **d₁-170a** in 30% yield and with 90% deuterium incorporation (eq 2 Scheme 2.5). On the other hand, resubjecting **158a** to these latter conditions with the gold(I) catalyst and D₂O was found to give the debenzoylated product **171a** in 31% yield (eq 1 Scheme 2.5).

Scheme 2.5 [2+2] Cycloadditions of **168a** Catalyzed by **Au₂**.

A tentative mechanism for the present Au(I) catalyzed reaction to form cyclobutane-fused piperidine is outlined in Scheme 2.6. This could involve activation of the alkyne moiety of the 1,7-enyne substrate by the gold(I) catalyst, resulting in *syn* 1,3-migration of the carboxylic ester group and formation of allenene **168** via **172** and **173**. To avoid unfavorable steric interactions between the gold complex and the substituents on the allene moiety, it is possible that the catalyst then selectively coordinates to the alkene bond of this newly formed allenene intermediate to give the gold activated adduct **157**. This is the active species that undergoes the stepwise [2+2] cycloaddition process involving *anti* addition of the allenic group to the gold coordinated alkene moiety to give

the piperidine adduct **174**.⁷⁴ Subsequent nucleophilic addition of the Au–C(sp³) bond to the carbonyl carbon center of the benzoyl cationic moiety generated from this initial intramolecular cyclization step would then deliver **158** with release of the gold(I) catalyst.⁷⁵ The pyrrole byproduct **169a** could originate from coordination of the gold catalyst to the alkyne unit in **156** or allene moiety in **168** followed by nucleophilic attack of the tethered sulfonamide moiety and a deauration step involving 1,3-migration of the Ts group.⁷⁶ We surmise that the obtained product regioselectivities result from the greater electron-donating ability of the OBz moiety relative to that of the R² group in **168**. This would consequently make the distal 2π component of the allene side chain more nucleophilic in character and therefore more likely to take part in the first step of the

Scheme 2.6 Tentative Mechanism for Tandem 1,3-Migration/[2+2] Cycloaddition of **156** Catalyzed by Au₂.

[2+2] cycloaddition. The observed stereoconvergence leading to a single diastereomer regardless of the stereochemistry at C3 in the substrate could be due to the oxonium species adopting the conformation shown in Scheme 2.6. This would provide optimal orbital alignment and thus overlap between the HOMO of the Au–C(sp³) bond with the LUMO of the carbonyl carbon center, enabling the second C–C bond-forming step of the [2+2] cycloaddition to proceed efficiently. It would also explain the lower reactivities observed in reactions with the *anti* isomer of **156a** and substrates containing this diastereomer (**156l**, **156n**, **156o** and **156w**), since the close proximity of the bulky alkyl gold side chain could significantly restrict the rotational freedom of the benzoyl C–C bond (eq 1 Scheme 2.7). A similar rationale could be applied to account for preferential nucleophilic attack of the Au–C(sp³) bond from below the plane of the benzoyl moiety and the moderate product yield obtained for the reaction of **156x** containing a *cis* alkene unit (eq 2 Scheme 2.7). The formation of the product as a single enantiomer from an enantiopure substrate additionally suggests that neither the starting material nor any of the

Scheme 2.7 Possible conformational states for tandem 1,3-migration/[2+2] cycloaddition of **156** catalyzed by **Au₂**.

putative intermediates are prone to racemization. This consequently allows efficient transfer of the retained chirality at the α -carbon centre to the amino group, giving the enantioselectivities observed at the newly formed stereogenic centers.

2.3 Conclusion

In summary, we have demonstrated gold(I) catalyzed tandem 1,3-migration/[2+2] cycloaddition of 1,7-enyne benzoates to be a regioselective and stereoconvergent strategy for the construction of highly functionalized azabicyclo[4.2.0]oct-5-enes. The reaction has been shown to tolerate a diverse set of 1,7-enyne substrates and furnish stereochemically well-defined cyclobutane-fused piperidines for potential application in natural product synthesis. Our studies suggest that, when allene activation is not possible in 1,*n*-enyne cycloisomerizations involving a 1,3-migration step, the gold catalyst preferentially coordinates to the alkene moiety. This results in bicyclic ring formation *via* a [2+2] cycloaddition pathway, which is not typically favored in 1,*n*-enyne cycloisomerizations.

Chapter III. Silver Acetate Catalyzed Hydroamination of 1-(2-(Sulfonylamino)phenyl)prop-2-yn-1-ols to (Z)-2-Methylene-1 sulfonylindolin-3-ols

3.1 Introduction

The indole ring system is a common structural motif found in a myriad of bioactive natural compounds and pharmaceutical products as well as optoelectronic functional materials.^{22,77-80} Added to this is their utility as substrates in strategies to various synthetically valuable products. While this has led to a number of impressive works to this class of compounds being developed over the years, those that focus on the synthesis of (Z)-2-methylene-1-sulfonylindolin-3-ols have been less well explored.⁷⁹ This is surprising given the potential of this member of the indole family of compounds to serve as a versatile building blocks in organic synthesis and their presence in a number of bioactive natural products.⁸⁰ For this reason, it is desirable to establish new synthetic methods to prepare (Z)-2-methylene-1-sulfonylindolin-3-ols in an efficient manner and with selective control of substitution patterns under mild conditions from acyclic substrates and a catalyst system that are readily accessible, atom-economical and low cost.

Lewis acid catalyzed reactions of unsaturated alcohols with amine nucleophiles have come under increasing scrutiny in recent years as efficient and convenient strategies for *N*-heterocyclic synthesis.^{5,81,82} For example, we described one method to prepare variety of benzo-fused and 2,3-disubstituted indoles that relied on gold(I) catalyzed cycloisomerization of 1-(2-(tosylamino)phenyl)prop-2-yn-1-ols.²² In the course of this work, treatment of the model substrate 1-(2-(tosylamino)phenyl)prop-2-yn-1-ol **34a** ($R^3 = \text{Ts}$, $R^1 = R^2 = \text{H}$), with 5 mol % of IPrAuCl/AgOTf catalyst combination was found to give (Z)-benzylidene-3-phenyl-1-tosylindolin-3-ol **164a** and the desired indenyl-fused indole **175a** in 52% and 5% yield respectively (Scheme 3.1, eq 1). This result prompted

us to investigate the role of silver salts in the catalytic system. By treating **34a** with 5 mol % of AgOTf as the catalyst, we found that (*Z*)-benzylidene-3-phenyl-1-tosylindolin-3-ol **164a** was obtained as the sole product in 45% yield instead of the anticipated indenyl-fused indole **175a** (Scheme 3.1, eq 2).²² In continuation of this study, a significant expansion of this chemistry with the discovery that under the appropriate conditions, simple silver salts can efficiently effect the hydroamination of propargylic alcohols **34a** is reported herein (Scheme 3.1, eq 3).^{83,84} This process will provide a convenient and operationally straightforward synthetic method that provides (*Z*)-2-methylene-1-sulfonylindolin-3-ols in excellent yields for a variety of substrates under mild conditions that did not require the exclusion of air or moisture at room temperature. The application of this catalytic nitrogen ring formation process to the synthesis of other members of the indole family of compounds is also presented.

Scheme 3.1 Silver catalyzed cycloisomerization of 1-(2-(tosylamino)phenyl)prop-2-yn-1-ols **34**.

3.2 Results and Discussion

All 1-((2-sulfonylamino)phenyl)prop-2-yn-1-ols **34** were prepared as illustrated in Scheme 3.2. This initially involved sulfonylation of 2-aminoketone **176** with sulfonyl chloride to give sulfonyl protected 2-aminoketone **177** in near quantitative yield. This was followed by reaction with a variety of substituted alkyne pretreated with LDA to furnish the corresponding 1-((2-sulfonylamino)phenyl)prop-2-yn-1-ols **34** in 64-97% yield.

Scheme 3.2 Synthesis of 1-((2-sulfonylamino)phenyl)prop-2-yn-1-ols **34**

Our studies began by examining the silver catalyzed hydroamination of **34a** to establish the reaction conditions (Table 3.1). This initially revealed that treating a MeCN solution of **34a** contained in an open round bottom flask with 10 mol % of AgOAc at room temperature for 15 min furnished **164a** in near quantitative yield (entry 1). Our studies subsequently showed that a gradual decrease in the catalyst loading of AgOAc from 10 to 5 to 1 mol % also provided the *N*-heterocycle in near quantitative yield albeit with the need for longer reaction times of 1 and 18 h, respectively (entries 2 and 3). A similar outcome was found on changing the solvent from MeCN to PhMe and CH₂Cl₂ or performing the reaction with other inexpensive and readily available silver(I) salts in place of AgOAc as the catalyst (entries 5-6 and 8-13). On the other hand, the analogous reactions with THF as the solvent or AgSbF₆ as the catalyst were found to give a markedly lower product yield of 17 and 27%, respectively (entries 4 and 7). Low product yields were also obtained in control experiments with the Brønsted acid catalysts TfOH and Tf₂NH, whereas AcOH was found to result in the recovery of the substrate in near

quantitative yield (entries 14-16). On the basis of the above results, reaction of **34a** in the presence of 5 mol % of AgOAc in MeCN at room temperature for 1 h contained in an open round-bottom flask was deemed to provide the optimum conditions.

Table 3.1 Optimization of the reaction conditions^a

Entry	Solvent	Catalyst	Yield (%) ^b
1 ^c	MeCN	AgOAc	99
2 ^d	MeCN	AgOAc	99(99) ^e
3 ^f	MeCN	AgOAc	99
4	THF	AgOAc	17
5	PhMe	AgOAc	99
6	CH ₂ Cl ₂	AgOAc	99
7	MeCN	AgSbF ₆	27
8	MeCN	AgBF ₄	94
9 ^g	MeCN	Ag ₂ CO ₃	99
10	MeCN	AgNO ₃	99
11	MeCN	AgOTf	99
12 ^h	MeCN	Ag ₂ O	99
13	MeCN	AgNTf ₂	99

Table 3.1 (*continued*).

Entry	Solvent	Catalyst	Yield (%) ^b
14	MeCN	CH ₃ CO ₂ H	- ⁱ
15	MeCN	TfOH	11
16	MeCN	Tf ₂ NH	11

^a All reactions were performed with 0.2 mmol of **34a** and 5 mol % of catalyst at room temperature for 18 h. ^b ¹H NMR yield with CH₂Br₂ as the internal standard. ^c Reaction performed with 10 mol % catalyst loading for 15 min. ^d Reaction performed with 5 mol % catalyst loading for 1 h. ^e Value in parenthesis denotes isolated product yield. ^f Reaction performed with 1 mol % catalyst loading. ^g Reaction performed with 2.5 mol % catalyst loading. ^h Reaction performed with 2.5 mol % catalyst loading for 4.5 h. ⁱ Recovery of starting material in near quantitative yield.

To define the generality of the present procedure, we next turn our attention to the reactions of a variety of 1-(2-(sulfonylamino)phenyl)prop-2-yn-1-ols and the results are summarized in Table 3.2. In general, these experiments demonstrated that by using AgOAc as the catalyst, the reaction conditions proved to be broad and a wide variety of substituted (Z)-2-methylene-1-sulfonylindolin-3-ols could be furnished in good to excellent yields. In our hands, no other side products arising from 6-*endo-trig* cyclization of the substrate was detected by TLC and ¹H NMR analysis of the crude reaction mixtures. Reactions of **34b-d** with an electron-donating or electron-withdrawing substituent on the aniline ring were shown to be well tolerated and afford the corresponding products **164b-d** in excellent yields of 87-97%. Similarly, starting alcohols with an embedded naphthalene ring moiety (**34e**) or a pendant of electron-withdrawing and electron-donating containing phenyl ring on the carbinol carbon center (**34f-h**) were

Table 3.2 Cycloisomerization of **34b-34y** catalyzed by AgOAc^a

^a Unless otherwise stated, all reactions were performed in MeCN at room temperature for 1 h with 0.2 mmol of **34a** in the presence of 5 mol % of AgOAc. Values in parentheses denote isolated product yields. ^b Reaction time = 1.5 h. ^c Reaction time = 2.5 h. ^d Reaction time = 3 h. ^e Reaction time = 2 h. ^f Recovery of starting material in near quantitative yield.

found to proceed well, furnishing **164e-h** in excellent yields of 92-99%. Likewise, the present procedure was found to work well for substrates **34i-n** where the propargylic carbon centre contained a thiophene, alkyl or cycloalkane moiety or a phenyl group with an electron-withdrawing or electron-donating substituent at the para position. In these reactions, the corresponding (*Z*)-2-methylene-1-sulfonylindolin-3-ol adducts **164i-n** were obtained in 88-99% yield. The presence of a methyl and *n*-butyl group on the respective

carbinol and propargylic carbon centers was found to have no influence on the outcome of the reaction with **164o** afforded in 98% yield. Additionally, substrates with either a pendant terminal alkyne moiety or where the carbinol carbon centre is a secondary alcohol, as in **34p-u**, were found to proceed well and provide **164p-u** in 68-96 % yield. Substrates containing an Ns (**34v**), Ms (**34w**), Ac (**34x**) or Boc (**34y**) instead of a Ts protecting group on the nitrogen center were also examined under the standard conditions. In these experiments, the corresponding *N*-sulfonyl protected products **164v** and **164w** were both obtained in near quantitative yield. In contrast, those with the Ac or Boc protecting group on the nitrogen center were found to be unreactive and resulted in recovery of starting materials in near quantitative yields.

A tentative mechanism for the present Ag(I) catalyzed (*Z*)-2-methylene-1-sulfonylindolin-3-ol forming reaction is illustrated in Scheme 3.3. This could initially involve activation of **34** through coordination of the metal catalyst with the alkyne moiety

Scheme 3.3 Proposed mechanism.

of the substrate to provide the silver(I) coordinated intermediate **178**. This is the active species that undergoes the intramolecular amination process involving *anti* addition of the sulfonamide moiety to the alkyne bond to afford the vinyl silver complex **179**.⁸⁵

Protodemetalation of this putative organosilver complex would then provide **164**. The role of the silver(I) catalyst in triggering the hydroamination process by coordinating to the alkyne moiety of the substrate was supported by repeating the Ag(I) catalyzed reaction of **34a** in the presence of D₂O under the conditions described in Scheme 3.4. This test led to the formation of **d₁-164a** in 99% yield with 55% deuterium incorporation.

Scheme 3.4 Hydroamination of **34a** in the presence of D₂O catalyzed by AgOAc.

Next, the synthetic utility of the (*Z*)-2-methylene-1-sulfonylindolin-3-ols obtained via the Ag(I) catalyzed hydroamination reaction was examined (Scheme 3.5). First, we demonstrated that Brønsted acid catalyzed 1,3-allylic alcohol isomerization (1,3-AAI) of **164a** to the (1*H*-indol-2-yl)methanol **180a** could be achieved in 90% yield in the presence of 5 mol % of *p*-TsOH·H₂O under the conditions depicted in Scheme 3.5, eq 1.⁸⁶ On the other hand, subjecting **164p** to 5 equiv of DAST in dichloromethane from −78 °C to room temperature over 4 h provided the 2-fluoromethylindole **181p** in 56% yield (Scheme 3.5, eq 2). Treating the same starting material to 2 equiv of NIS (*N*-iodosuccinimide) in MeCN at reflux for 1 h gave the 3-iodomethyloxindole **182p** in 87% yield (Scheme 3.5, eq 3).⁸⁷ The structure of 2-fluoromethylindole **181p** and 3-iodomethyloxindole **182p** were determined by X-ray crystallography analysis (Figure 3.1).^{88,89} Finally, the indolin-3-one **183r** could be furnished in 71% yield on exposing the secondary alcohol **164r** to the same conditions of 2 equiv of NIS in MeCN at reflux for 1 h (Scheme 3.5, eq. 4).

Scheme 3.5 Selective transformations of (Z)-2-methylene-1-sulfonylindolin-3-ols **164a**, **164p** and **164r**.

Figure 3.1 ORTEP drawings of (a) **181p** and (b) **182p** with thermal ellipsoids at 50% probability levels.

3.3 Conclusion

In summary, an efficient silver(I) catalyzed synthetic route to (Z)-2-methylene-1-sulfonylindolin-3-ols based on intramolecular hydroamination of 1-(2-(sulfonylamino)phenyl)prop-2-yn-1-ols has been reported. Achieved under mild conditions at room temperature and without the need to exclude air or moisture, the reaction was shown to be applicable to a wide range of alcohol substrates containing electron-withdrawing, electron-donating and sterically demanding functional groups. The synthetic utility of the present method to this partially hydrogenated member of the indole family was also demonstrated in 1,3-AAI, nucleophilic substitution, oxidation and rearrangement reactions.

Chapter IV. Silica Gel-Mediated Hydroamination/Semipinacol Rearrangement of 2-Alkylaminophenylprop-1-yn-3-ols: Synthesis of 2-Oxindoles from Alkynes and 1-(2-Aminophenyl)ketones

4.1 Introduction

The various chemical and physical properties of silica gel have established it an indispensable functional material in chemistry.⁹⁰⁻⁹⁴ This is reflected by its various applications, ranging from its use as the stationary phase in the separation of organic compounds by flash column chromatography⁹¹ to serving as the solid phase support for the metal catalyst in heterogeneous catalysis.⁹² In the case of the former activity, the marginally acidic nature of the native form of silica gel, it has a pH value that is close to neutral, can sometimes make the isolation of compounds containing acid labile functional groups a challenge.⁹³ On the flip side, harnessing this weak Brønsted acid property can also provide the opportunity to devise new silica gel-mediated functional group transformations to various synthetically valuable products.⁹⁴ Herein, we report our discovery of a scalable and recyclable heterogeneous synthetic approach to 3,3-disubstituted 2-oxindoles,^{87,95} a structural motif found in a myriad of bioactive natural products,⁹⁶ in good to excellent yields (Scheme 4.1). The nitrogen-containing ring forming process relies on base-mediated 1,2-addition of an alkyne to a 1-(2-aminophenyl)ketone followed by silica gel-catalyzed hydroamination/semipinacol rearrangement^{84,97} of the resulting propargylic alcohol.^{5,19,22,75i,78a,98} Added to this, the reaction features operational simplicity under conditions that do not require the exclusion of air or moisture at room temperature. The synthetic method also tolerates to a broad range of functional groups that allows for the efficient and atom-economical assembly of a variety of 2-oxindoles from the readily available substrates.

Scheme 4.1 Synthesis of 2-oxindoles from silica gel-mediated cycloisomerization of 2-alkylaminophenylprop-1-yn-3-ols.

4.2 Result and Discussion

The starting material **184** examined in this study were prepared as shown in Scheme 4.2.⁹⁹ This involved protection of the amine moiety of **176** with the corresponding alkyl, benzyl or allyl halide in the presence of K_2CO_3 as the base in DMF at 80°C to furnish the desired **184** in 30-60% yield.

Scheme 4.2 Synthesis of 2-(alkylamino)ketone **184**

A demonstrative example of this methodology is the large-scale addition of phenylacetylene (3.5 equiv) to 2-(methylamino)benzophenone **184a** (1 g, 4.73 mmol) in the presence of LDA (3.5 equiv) shown in Eq 1 in Table 4.1. By directly treating a 5 % EtOAc/nhexane solution in an open round bottom flask containing the crude mixture of this reaction, after aqueous work-up, with silica gel (100 equiv) under ambient conditions at room temperature for 2.5 h, the 2-oxindole product **163a** was obtained in 89% yield. The structure of the 1,2-addition adduct was determined by NMR analysis while that of

(a) **163a**

Figure 4.1 ORTEP drawing 3-benzyl-1-methyl-3-phenylindolin-2-one (**163a**) with thermal ellipsoids at 50% probability levels

the nitrogen-containing heterocycle was confirmed by X-ray crystallography (Figure 4.1).¹⁰⁰ A second illustrative example is the establishment of a recyclable system for the second step of this reaction involving silica gel-mediated cycloisomerization of the 2-alkylaminophenylprop-1-yn-3-ol **162a** (Table 4.1). Addition of silica gel (100 equiv) to the crude mixture, obtained from aqueous work-up of the base-mediated reaction of 0.5 mmol of **184a** and 3.5 equiv of phenylacetylene in 5 % EtOAc/nhexane, contained in an open round bottom flask at room temperature for 2.5 h gave **163a** in 91% yield. The silica gel was removed by filtration and used directly for a further 7 consecutive transformations under the same above mentioned conditions. As shown in cycles 2-8, product yields of 90-94% were achieved for each consecutive conversion with no apparent loss of activity observed albeit longer reaction times of 18 h were required for runs 2-8.

Table 4.1 Large-scale and recyclable silica gel for cycloisomerization of **162a** to **163a**^a

Run	1	2	3	4	5	6	7	8
Yield[%] ^b	94,(91) ^{c,d}	94	94	94	94	90	93	94

^a All reactions were performed with 0.5 mmol of **184a** and 1.75 mmol of phenylacetylene with 3.5 equiv of LDA in THF at $-78\text{ }^{\circ}\text{C}$ -rt for 3 h followed by 3 g of silica in 10 mL of *n*hexane/EtOAc (20:1 v/v) at rt for 18 h. ^b ¹H NMR yield with CH₂Br₂ as the internal standard. ^c Reaction time = 2.5 h. ^d Value in parenthesis denotes isolated yield

The discovery of this unprecedented and yet simple 2-oxindole forming process was serendipitously observed during an attempt to purify the crude mixture obtained from LDA-mediated reaction of **184a** with phenylacetylene by silica gel flash column chromatography. Our initial intentions for preparing the 2-alkylaminophenylprop-1-yn-3-ol substrate had been for a study focused on defining the generality of the silver-catalyzed hydroamination of the *N*-protected π -rich alcohols to the corresponding indolin-3-ols.⁹⁸ The unexpected formation of the 2-oxindole product via a mechanistically interesting redox rearrangement prompted us to further examine and gain a better understanding of the cycloisomerization process (Table 4.2). With this in mind, we first surveyed the analogous transformations mediated by other solid acids in place of silica gel (entries 1-2). This revealed markedly a lower product yield of 40% was obtained when the reaction was repeated with MCM-41 (entry 1).¹⁰¹ In contrast, the analogous reaction mediated by Mont-K10^{102,103} which has a higher acidity^{103c} than silica was found to give a mixture of

Table 4.2 Cycloisomerization of **2a** mediated by various acidic reaction conditions^a

Entry	Acid	Solvent	Yield [%] ^b
1	MCM-41	EtOAc/ <i>n</i> hexane ^c	40
2	Mont-K10	EtOAc/ <i>n</i> hexane ^c	- ^d
3	SiO ₂	<i>n</i> hexane	82
4	SiO ₂	PhMe	80 ^e
5	SiO ₂	CH ₂ Cl ₂	90 ^e
6	SiO ₂	CH ₃ NO ₂	89
7	SiO ₂	EtOAc	- ^f
8	SiO ₂	acetone	- ^f
9	SiO ₂	THF	- ^f
10	<i>p</i> TsOH·H ₂ O ^g	EtOAc/ <i>n</i> hexane ^[c]	- ^h

^a All reactions were performed with 0.5 mmol of **184a** and 1.75 mmol of phenylacetylene with 3.5 equiv of LDA in THF at -78 °C-rt for 3 h followed by the solid acid (3g) in 10 mL of solvent at rt for 24 h. ^b ¹H NMR yield with CH₂Br₂ as the internal standard. ^c Ratio of *n*hexane/EtOAc = 20:1. ^d Mixture of unknown decomposition products obtained based on ¹H NMR and TLC analysis of the crude reaction mixture. ^e Reaction time = 1 h. ^f Starting materials recovered in near quantitative yield. ^g Reaction was performed with 5 mol % of *p*TsOH·H₂O. ^h Compound **185a** was obtained in 38% yield.

unidentifiable decomposition products based on TLC and ^1H NMR analysis (entry 2). These initial findings led us to surmise that the trigger for the present nitrogen-ring forming process could be due to the mildly acidic conditions provided by silica gel. This was further supported by the outcome of control experiments in other solvents or in the presence of a strong Brønsted acid such as $p\text{TsOH}\cdot\text{H}_2\text{O}$ (entries 3-10). Slightly lower product yields of 80-90% were afforded on employing *n*hexane, toluene, dichloromethane or mildly acidic MeNO_2 instead of 5 % $\text{EtOAc}/n\text{hexane}$ as the solvent system (entries 3-6). On the other hand, the propargylic alcohol was only detected by ^1H NMR analysis of the crude mixture when polar solvents, such as EtOAc , acetone and THF, were used as the reaction medium (entries 7-9). With 5 mol % of $p\text{TsOH}\cdot\text{H}_2\text{O}$ as the catalyst in 5 % $\text{EtOAc}/n\text{hexane}$, the reaction was found to furnish the (1*H*-indol-2-yl)methanol **185a** in 38% yield along with a mixture of decomposition products that could not be identified by NMR analysis or mass spectrometry (entry 10).

We next explored the scope of the present 1,2-addition and cycloisomerization reaction with the LDA/silica gel system (Table 4.3). These experiments showed that a series of 3,3-disubstituted 2-oxindoles could be afforded in good to excellent yields from the corresponding 1-(2-aminophenyl)ketones **184a-o** and alkynes. Reactions of 1-(2-aminophenyl)ketones containing an electron-withdrawing (**184b,c**) or electron-donating group (**184d**) on the aniline ring with phenylacetylene were found to proceed well, giving the corresponding 3,3-disubstituted 2-oxindole derivatives in 84-96% yield. The presence of other aryl (**184e-h**), 2-thienyl (**184i**), alkyl (**184j**) or cycloalkyl (**184k-m**) motifs at the carbonyl carbon center of the ketone was found to have no influence on the course of the reaction and on treating with phenylacetylene, furnished **163e-m** in 59-91% yield. Likewise, 1-(2-aminophenyl)ketones with a *N*-benzyl (**184n**) or *N*-allyl (**184o**) instead of

Table 4.3 Cycloisomerization of 2-alkylaminophenylprop-1-yn-3-ols **162b-v** mediated by silica gel^a

^a All reactions were performed with 0.5 mmol of **184** and 1.75 mmol of the alkyne with 3.5 equiv of LDA in THF at $-78\text{ }^{\circ}\text{C}$ to rt for 3 h followed by silica gel (100 equiv) in 10 mL of *n*hexane/EtOAc (20:1 v/v) at rt for 1-18 h. Values in parentheses denote isolated product yield. ^b Reaction conducted at $40\text{ }^{\circ}\text{C}$ for 18 h.

a *N*-methyl protecting group was found to be well tolerated and reaction with phenylacetylene afforded **163n** and **163o** in 88 and 83% yield, respectively. The analogous reactions of **184a** with different alkynes bearing a phenyl group with an electron-donating or electron-withdrawing group at the para position or a sterically demanding 1-naphthalenyl, or 3-ethynylthiophene moiety were also found to provide the corresponding 2-oxindole adducts **163p-t** in 86-98% yield. The only exceptions were the 1,2-addition/cycloisomerization reactions of **184a** with ethynyl cyclopropane or hex-1-yne, which gave **163u** and **163v** in lower yield of 26 and 35%, respectively. The structures of **163g**, **163h**, **163j**, **163p** were determined by X-ray crystal structure measurements (Figure 4.2).¹⁰⁴

While the above results implicate a cyclization pathway involving hydroamination followed by semipinacol rearrangement, to demonstrate this to be the case, the following control experiments were performed (Scheme 4.3). As it was anticipated the propargylic alcohol would lead to the formation of an enammonium cationic species, we reasoned that trapping of this intermediate in an intramolecular manner might be possible on introducing an allyl group, as a substituent in the nitrogen centre. Thus, we first examined the reaction of *N,N*-diallyl protected ketone **184w** with phenylacetylene under the

Scheme 4.3 Control experiments with **184w** and **184a-¹⁸O** mediated by silica gel.

(a) **163g** (b) **163h** (c) **163j** (d) **163p**

Figure 4.2 ORTEP drawings of (a) **163g**, (b) **163h**, (c) **163j**, and (d) **163p** with thermal ellipsoids at 50% probability levels.

conditions described in Scheme 4.3, Eq 1. This test afforded the 3,3-disubstituted 2-oxindole derivative **163w** in 53% yield and corroboration that formation of the nitrogen-containing ring occurs via the posited hydroamination step and involves charge-accelerated 3-aza Cope rearrangement of the allyl group.^{78h} The structures of **163w** was determined by X-ray crystal structure measurements (Figure 4.3).¹⁰⁵ In a second control experiment, the LDA-mediated 1,2-addition of phenylacetylene to **184a**-¹⁸O with an ¹⁸O

content of 55% followed by treatment of the resulting crude mixture with 3 g of silica gel in 5 % EtOAc/*n*hexane under the conditions described in Scheme 4.3, Eq 2 was investigated. The test reaction gave **163a**-¹⁸O in 71% yield and with retention of the ¹⁸O content based on LCMS measurements. This led us to surmise the apparent migration of the carbonyl group in the ketone substrate to the C2 position in the product to occur in an intramolecular manner. It also hinted the semipinacol rearrangement of the presumed formed enammonium cationic intermediate to proceed via an epoxide adduct.

(a) **163w**

Figure 4.3 ORTEP drawing of (a) **163w** with thermal ellipsoids at 50% probability levels

A tentative mechanism for the present LDA-mediated/silica gel-promoted reaction to form 3,3-disubstituted 2-oxindoles is put forward in Scheme 4.4. Using the LDA-mediated 1,2-addition of phenylacetylene to **184a** to form the propargylic alcohol **162a** as a representative example, this could initially involve the activation of the alkyne moiety of this newly formed adduct on exposure to silica gel. As a consequence hydroamination involving nucleophilic attack by the pendant alkylamido group in a 5-*exo-dig* manner might occur to produce the cationic enammonium cycloadduct **186a** and its iminium isomer **186a'**. This is the active species that undergoes the semipinacol rearrangement

process beginning with addition of the alcohol group to the iminium carbon center to give the oxiranium adduct **187a**. This is followed by formation of carbocation at the C3 position to give **188a**, which upon oxidative 1,2-migration of the alkyl group from the C2

Scheme 4.4 Proposed mechanism for the silica gel-mediated cycloisomerization of propargylic alcohols represented by **162a**

to C3 position, would furnish **189a**. Subsequent deprotonation of the resultant oxonium species **189a** would then provide the 2-oxindole product. The lower product yields afforded for reactions with alkyl substituted alkynes such as ethynylcyclopropane and hex-1-yne would be consistent with the lower ability of the pendant group to stabilize a partial positive charge in the course of the 1,2-migration process. The preferential formation of **185a** when the reaction of **162a** was subjected to $p\text{TsOH}\cdot\text{H}_2\text{O}$ could originate from protonation of the alcohol group in **186a** that leads to nucleophilic substitution of the resulting activated adduct at the allylic carbon position by H_2O .^{86a}

4.3 Conclusion

In summary, we have developed an efficient and practical two-step method for the synthesis of 3,3-disubstituted 2-oxindoles from base-mediated 1,2-addition of readily available alkynes to ketones followed by silica gel-promoted cycloisomerization of the resulting crude mixture. Achieved under reaction conditions that are tolerant to air and moisture at room temperature, the potential of our approach to the *N*-heterocycle was also exemplified by the large-scale preparation of one example in excellent yield. Added to this is the development of a recycling system that was shown to be effective for up to 8 cycles. This is notable in view of the current need for more rapid and direct atom economical chemical processes that can make use of low cost and readily available substrates and catalytic systems.

Chapter V. Gold(I) Catalyzed Cycloisomerization and Thermal [4+2] Cycloaddition of 1,9-Diene-4-yne Esters. Efficient Synthesis of 3-Azatricyclo[5.2.1.0^{1,5}]dec-8-enes

5.1 Introduction

Cascade reactions in organic synthesis represents one of the most efficient and atom economical methods for the stereoselective construction of complex molecular frameworks. Indeed, the synthetic approach has witnessed a wide number of impressive methods that have made use of the whole spectrum of chemical transformation combinations.¹⁰⁶ One of these that has attracted particular attention is the incorporation of pericyclic reactions due to their concerted nature, predictability and outstanding control of stereoselectivity.¹⁰⁷

In recent years, gold catalyzed cascade reactions involving pericyclic transformations have been extensively explored.^{6,7,108,109} An example is the synthesis of cyclopentenones *via* gold catalyzed 2,3- or 3,3-sigmatropic rearrangement followed by Nazarov cyclization and hydrolysis of 1,*n*-enynes, as shown in Scheme 5.1.^{42,108g,108i} In the case of 3,3-sigmatropic rearrangement of **190** (Scheme 5.1, path a), the intermediate **191** could undergo electrophilic cyclization to form gold carbenoid species **192**. Further elaboration of this organogold species involving protodeauration and isomerization was shown to form the cyclopentenone **193** when R¹ contained alkyl group.¹⁰⁸ⁱ In contrast, electrocyclic cyclopropanation of **192** furnished polycyclic adduct **194** when R¹ = alkene moiety.^{108g} Moreover, gold catalyzed 2,3-sigmatropic rearrangement of **92**, as shown in Scheme 5.1, path b, was reported to undergo Nazarov-type cyclization to give cyclopentadienyl acetate intermediate **94**, which upon hydrolysis, afforded cyclopentanone **95**.⁴² The trapping of intermediate **94**, obtained from gold catalyzed cascade 2,3-sigmatropic rearrangement/Nazarov-type cyclization,^{60,108} with the tethered alkene, by contrast, is not known. Hence, we envisioned that the diene moiety of the cyclopentadienyl acetate

obtained from 1,2-acyloxy shift may be susceptible to an intramolecular [4+2] cycloaddition with an appropriately placed tethered alkene (Scheme 5.1, path c). As part of an ongoing process exploring the scope of gold catalyzed synthesis of heterocycles, we disclosed herein the details of this chemistry that provides an efficient route to 3-azatricyclo[5.2.1.0^{1,5}]dec-8-enes from 1,9-diene-4-yne.

Scheme 5.1 Reactivities of 1,*n*-enyne esters in gold catalyzed cascade reaction involving pericyclic transformation

5.2 Results and Discussion

The 1,9-diene-4-yne esters examined in this work were prepared as shown in Schemes 4.2 and 4.3. The enyne **195** was synthesized from the corresponding propargylamine in two steps following literature procedures.¹¹⁰ The reaction of enyne **195** with *in situ* generated LDA and vinyl ketone **196** furnished the alcohol **197** in 30-38% yield. Subsequent treatment of the alcohol **197** in dichloromethane with acetic anhydride or benzoyl chloride in the presence of 10 mol % of DMAP and 1.5 equiv of Et₃N for 15 h furnished the 1,9-diene-4-yne esters **159a-b,f-q** in 60-88% yield as shown in Scheme 4.2. Alternatively, 1,9-diene-4-yne esters **159c-e** could be obtained from another synthetic pathway as shown in Scheme 4.3. Treatment of 1,6-enyne **195** with *in situ* generated LDA and aldehyde **199** furnished the alcohol **200** in 50-65% yield. This is followed by oxidation with 2.5 equiv of IBX in DMSO to obtain the corresponding ketone **201**. The reaction of the crude mixture of ketone **201** with 3 equiv of vinylmagnesium chloride in THF at room temperature for 1 hour gave the alcohol **197** in 50-60% yield. Subsequently, protection of the alcohol **197** with 3 equiv of acetic anhydride, 10 mol % of DMAP and 1.5 equiv of NEt₃ in dichloromethane gave **159c-e** in 72-80% yield.

Scheme 4.2 Synthesis of 1,9-diene-4-yne esters **159a-b,f-q** starting from enyne **195**.

Scheme 4.3 Synthesis of 1,9-diene-4-yne esters **159c-e** starting from enyne **195**.

Our study commenced by examining the gold(I) and gold(III) catalyzed cycloisomerization of 1,9-diene-4-yne esters to establish the reaction conditions (Table 5.1). This initial study revealed that treatment of **159a** with 5 mol % of **Au₂** in the presence of 4Å MS in PhMe at 80 °C for 2 h afforded **161a** in 97% yield (entry 1). The structure and relative stereochemistry of 3-azatricyclo[5.2.1.0^{1,5}]dec-8-ene **161a** were ascertained by ¹H NMR spectroscopy and X-ray crystallographic analysis (Figure 5.1).¹¹¹ Our studies subsequently showed that when the reaction was repeated at 50 °C and room temperature, or with the more sterically crowded Au(I) complex **Au₃** in place of **Au₂** as the catalyst, a longer reaction time of 17 h was needed to furnish adduct **161a** in 82-97% yield (entry 2-4). A similar outcome was found upon replacing **Au₂** with Au(I) phosphine complexes **Au₄**, **Au₁₀**, AuPPh₃NTf₂, gold(III) complex **Au₈** or simple gold(I) and gold(III) salts such as AuCl and AuCl₃ (entry 6, 7 and 12-15). In the case of reactions mediated by sterically bulky gold (I) phosphine **Au₉**, gold(I) phosphite **Au₇**, or PtCl₂, a lower product yield was obtained in 50-79% (entry 5, 11 and 16). In contrast, the analogous reaction catalyzed by NHC–gold(I) (NHC = *N*-heterocyclic carbene) complex **Au₁₁** furnished the product in near quantitative yield in 2 h (entry 10). Likewise, other NHC-gold(I) complexes **Au₁** and **Au₆** were found to give a similar result albeit requiring a slightly

longer reaction time of 3 h in the former transformation (entries 8 and 9). Changing the reaction medium from PhMe to THF, MeCN or (CH₂Cl)₂ in the presence of 5 mol % of **Au₁₁** did not provide any improvements (entries 17-19). On the basis of the above results, the reaction of **159a** in the presence of 5 mol % of **Au₁₁** as the catalyst in PhMe at 80 °C for 2 h provided the optimum conditions.

Table 5.1 Optimization of the reaction conditions^a

Entry	Catalyst	Time	Solvent	Yield ^b
1	Au₂	2h	PhMe	97
2	Au₂	17h	PhMe	97 ^d
3	Au₂	17h	PhMe	82 ^c
4	Au₃	17h	PhMe	93
5	Au₉	17h	PhMe	76
6	Au₄	3h	PhMe	93
7	Au₁₀	2h	PhMe	91
8	Au₁	3h	PhMe	99
9	Au₆	2h	PhMe	99
10	Au₁₁	2h	PhMe	99(99) ^e

Table 5.1 *continued*

Entry	Catalyst	Time	Solvent	Yield ^b
11	Au₇	6h	PhMe	79
12	Au₈	5h	PhMe	95
13	AuPPh ₃ NTf ₂	5h	PhMe	95
14	AuCl	5h	PhMe	97
15	AuCl ₃	3h	PhMe	93
16	PtCl ₂	17h	PhMe	50
17	Au₁₁	8h	THF	95
18	Au₁₁	4h	MeCN	91
19	Au₁₁	5h	DCE	76

^a All reactions were performed at the 0.3 mmol scale of **159a** with 5 mol % of catalyst loading and 4Å MS (300 mg) at 80 °C. ^b ¹H NMR yield with CH₂Br₂ as the internal standard. ^c Reaction was carried out at room temperature. ^d Reaction was carried out at 50 °C. ^e Yields in parenthesis denotes isolated yield.

Figure 5.1 ORTEP drawing of **161a** with thermal ellipsoids at 50% probability levels.

Table 5.2 Gold(I) catalyzed cycloisomerization and thermal [4+2] cycloaddition of 1,9-diene-4-yne esters.^a

^a All reactions were performed at the 0.3 mmol scale of **159** with 5 mol % of catalyst loading and 4Å MS (300 mg) at 80 °C for 17 h. Values in parentheses denote isolated product yields. ^b Reaction time = 3 h.

(a) **161h** (b) **161i** (c) **161q**

Figure 5.2 ORTEP drawings of (a) **161h**, (b) **161i** and (c) **161q** with thermal ellipsoids at 50% probability levels.

With the optimal conditions in hand, we next sought to define the generality of the present procedure for a series of 1,9-diene-4-yne esters and the results are summarized in Table 5.2. These experiments showed that with NHC-gold(I) complex **Au₁₁** as the catalyst, the reaction conditions proved to be broadly applicable to a wide variety of substrates **159**, delivering the corresponding substituted 3-azatricyclo[5.2.1.0^{1,5}]dec-8-enes **161** in good to excellent yields of 35-99%. This included starting 1,9-diene-4-yne esters containing a thiophene, furan, OBn moiety at the alkene moiety (**159j**, **159k**, **159n** and **159p**, respectively) showing that such functional groups were well tolerated under the reaction conditions. The analogous reaction with a substrate containing a benzoate (**159b**) instead of an acetoxy migrating group was shown to proceed well and gave the product **161b** in 90% yield. Likewise, the presence of an alkyl (**159c,d**) or benzyl moiety (**159e**) at the carbon centre proximal to ester group was found to react well and furnish **161c-e** in 85-99% yield. In the case of secondary substrates, as in **159f** and **159g**, the reactions were found to proceed well and provide the corresponding cycloadducts **161f** and **161g** in 48% and 67% yield, respectively. The stereochemistry of the alkene moiety in **159h-p** were found to be retained in the products. This was shown in substrates containing *trans* alkene group in **159h-k** and **159o** which were found to give the corresponding 3-azatricyclo[5.2.1.0^{1,5}]dec-8-enes having the bridgehead proton *syn* to the pendant R⁴ group. For reactions with substrates containing a *cis* alkene (**159l-n**, **159p**) moiety, cycloadducts **161l-n** and **161p**, having the bridgehead proton *anti* to the R⁵ functional group, were obtained as a single isomer in 35-91%. The analogous reaction of **159q** with sterically demanding gem disubstituted alkene moiety was also found to give the corresponding cycloadduct **161q** in 88% yield as a single isomer. The relative configuration for **161h**, **161i**, and **161q** were determined on the basis of X-ray crystal structure measurements (Figures 5.2).¹¹²

In addition to the above results, the following control experiment shown in Scheme 5.2 was performed to support the mechanistic premise put forward in Scheme 5.1. In view of the formation for cyclopentadienyl acetate intermediate in the reaction medium, we attempted to isolate the species by examining the cycloisomerization of **159a** in the presence of 5 mol % of **Au₁₁** under the conditions shown in Scheme 5.2 at shorter reaction times. This revealed cyclopentadienyl acetate **160a** was furnished in 74% yield. The structure of this adduct was determined by ¹H and ¹³C NMR spectroscopic analysis. The role of the gold(I) complex in the subsequent [4+2] cycloaddition of the diene moiety in **160a** and the tethered alkene was further tested by subjecting intermediate **160a** at 80 °C in the absence of the metal catalyst. This test revealed that the cycloadduct **161a** could be furnished in 80% yield after 4 h which led us to deduce that thermal [4+2] cycloaddition process was more likely to be operative.

Scheme 5.2 Control experiment of tandem gold catalyzed acyloxy migration of **159a** and thermal [4+2] cycloaddition.

On the basis of the above results, a plausible mechanism for the gold catalyzed cycloisomerization involving the 1,2- or 1,3-acyloxy migration/Nazarov-type cyclization followed by thermal [4+2] cycloaddition is outlined in Scheme 5.4. This could initially involve activation of alkyne moiety in **159** by the gold(I) catalyst to give the gold(I) coordinated complex **202**. This results in either *syn* 1,2- or 1,3-acyloxy migration. In the case of a 1,2-acyloxy shift, the 1,3-dioxin-1-ium intermediate **203** was obtained which would then undergo a concerted C–O bond breaking from the carbon proximal to ester

Scheme 5.4 Tentative mechanism for gold catalyzed 1,2-acyloxy migration/thermal [4+2] cycloaddition of 1,9-diene-4-yne esters **159**

group and Nazarov-type cyclization to give cationic intermediate **205**.⁴² However, we surmise that formation of species **205** involving stepwise C–O bond breaking process of **203** to give **204** could also be likely based on DFT calculations by de Lera and co-workers that showed the possibility of a short-lived cationic intermediate similar to that of **204**.¹¹³ Subsequent deauration of cyclopentenyl gold species **205** would then provide intermediate **160**. Finally, thermal [4+2] cycloaddition of this cyclopentadienyl intermediate with the tethered alkene would furnish 3-azatricyclo[5.2.1.0^{1,5}]dec-8-ene **161**. Alternatively, the realization that the substitution pattern in the product cannot rule out path a in Scheme 5.1, it is also possible that the gold activated alkyne moiety in **202** would undergo *syn* 1,3-acyloxy shift of the carboxylic ester group. This would give the allene intermediate **207** via six membered ring intermediate **206**. Further gold activation of the allene moiety in this allenic adduct would provide **207** and subsequent formation of cationic species **208**. This is the active species that undergoes Nazarov-type cyclization which upon generation of gold carbenoid **209** would then trigger the 1,2-acyloxy shift to afford cationic species **210**. Elimination of gold cationic species gave cyclopentadienyl acetate **160** and subsequent thermal [4+2] cycloaddition furnished the adduct **161**.

5.3 Conclusion

In summary, we have described an efficient tandem gold(I) catalyzed 1,2-acyloxy migration/Nazarov type cyclization/thermal [4+2] cycloaddition of 1,9-diene-4-yne esters towards the formation of 3-azatricyclo[5.2.1.0^{1,5}]dec-8-enes. The method is applicable to diverse set of substrates ranging from tertiary to secondary propargylic acetates with a different substituents at various positions. Our studies suggest that while formation of cyclopentadiene from 1,2-acyloxy migration was known, further thermal [4+2] cycloaddition from the corresponding intermediate was not observed before.

Chapter VI. Concluding Remarks

Gold catalyzed intramolecular based protocols for the synthesis of azabicyclo[4.2.0]oct-5-enes and azatricyclo[5.2.1.0^{1,5}]dec-8-enes have been established (Scheme 6.1 and Scheme 6.3). In addition, silver catalyzed intramolecular cycloisomerization of 1-(2-(sulfonylamino)phenyl)prop-2-yn-1-ols to (Z)-2-methylene-1-sulfonylindolin-3-ols and a new methodology that relies on silica catalyzed intramolecular cycloisomerization of alkyl protected 2-aminophenylprop-1-yn-3-ols to 3,3-disubstituted 2-oxindoles have been realized (Scheme 6.2).

An efficient synthetic method that allows access to azabicyclo[4.2.0]oct-5-enes **158** relying on gold(I) catalyzed tandem 1,3-migration/[2+2] cycloaddition of 1,7-enyne benzoates **156** was described in Chapter II. The reaction was demonstrated to be applicable to a wide variety of starting materials and afforded the product in 41-90% yield and as a single regio- and diastereomer. The cycloisomerization also proceeds with efficient transfer of chirality from the enantiopure substrate to the bicyclo[4.2.0] adduct as a single enantiomer with up to four stereogenic centers. In addition, the reaction was shown to be stereoconvergent since one diastereomer of the adduct was obtained from two different diastereomers of the starting 1,7-enyne benzoate **156**. The mechanism was suggested to involve gold catalyzed 3,3-sigmatropic rearrangement of the benzoate functional group to form the allenene intermediate. This was followed by the selective activation of gold(I) complex to the alkene moiety in the allenene as shown intermediate **157** and promoted the stepwise [2+2] cycloaddition *via* Au-C(sp³) species to construct azabicyclo[4.2.0]oct-5-enes **158**.

In Chapter III, the expansion of previous work on gold(I) catalyzed 1-(2-(sulfonylamino)phenyl)prop-2-yn-1-ols to (Z)-2-methylene-1-sulfonylindolin-3-ols was reported. It was shown that silver salt could effectively replace gold(I) catalyst in mediating the cycloisomerization process at room temperature and furnish the adduct in

Scheme 6.1 Gold catalyzed tandem 1,3-migration/[2+2] cycloaddition of 1,7-ene benzoates to azabicyclo[4.2.0]oct-5-enes

good to excellent yield of 68-99%. The methodology was applicable to a wide range of 1-(2-(sulfonylamino)phenyl)prop-2-yn-1-ols **34** bearing electron-withdrawing, electron-donating and sterically demanding substrate combinations. The mechanism was surmised to undergo intramolecular *5-exo-dig* cyclization of the sulfonamide protected nitrogen unit to the silver activated alkyne moiety and furnished the (*Z*)-2-methylene-1-sulfonylindolin-3-ols **164**. The application of this *N*-heterocyclic ring forming strategy was further exemplified by the synthesis of other members of the indole family. The serendipitous discovery in the process of exploring the generality on the substrate scopes to 2-alkylaminophenylprop-1-yn-3-ol **162** to obtain indolin-3-ols **164** in the silver catalyzed hydroamination strategy has been discussed in Chapter IV. It was found that 2-alkylaminophenylprop-1-yn-3-ols **162**, furnished from LDA-mediated 1,2-addition of alkynes to 1-(2-aminophenyl)ketones, can be converted to a variety of 3,3-disubstituted 2-oxindoles **163** in 26-98% yield by using silica gel in *n*hexane/EtOAc (20:1 v/v) as the reaction medium at room temperature. The mechanism was posited to proceed *via* tandem hydroamination and semipinacol rearrangement. The application of the approach was demonstrated by the large-scale synthesis along with the recycling of the silica gel up to 8 times without significant loss of activity for one example.

Scheme 6.2 Cycloisomerization of propargylic alcohols **162** to 2-oxindoles **163** and propargylic alcohols **34** to indolin-3-ols **164**

In Chapter V, a novel strategy for the synthesis of 3-azatricyclo[5.2.1.0^{1,5}]dec-8-enes **161** from 1,9-diene-4-yne esters **159** was described. It was shown that the synthetic methodology was applicable for a wide variety of substrates bearing different pendant functional groups. The mechanism was proposed to involve gold catalyzed 1,2 or 1,3-sigmatropic rearrangement of the acyloxy group and subsequent Nazarov-type cyclization of substrate **159** to form cyclopentadienyl acetate intermediate **160**. The newly formed cyclic intermediate would then undergo thermal [4+2] cycloaddition to give the product **161** in 35-99% yield.

Scheme 6.3 Cycloisomerization of 1,9-diene-4-yne esters **159** to 3-azatricyclo[5.2.1.0^{1,5}]dec-8-enes **161**

Chapter VII. Experimental Section

7.1 General Remarks

Unless specified, all reagents and starting materials were purchased from commercial sources and used as received. Solvents were purified following standard literature procedures. Analytical thin layer chromatography (TLC) was performed using Merck 60 F254 pre-coated silica gel plate. Visualization was achieved by UV light (254 nm). Flash chromatography was performed using Merck silica gel and gradient solvent system. ^1H spectra was measured on 300, 400 and 500 MHz spectrometer. Chemical shifts (ppm) were recorded with respect to TMS in CDCl_3 . Multiplicities are given as: s (singlet), brs (broad singlet), d (doublet), t (triplet), q (quartet), qn (quintet), m (multiplet), dd (doublet of doublets), dt (doublet of triplets), qd (quartet of doublets), or td (triplet of doublets). The number of protons (n) for a given resonance is indicated by $n\text{H}$. Coupling constants are reported as a J value in Hz. Infrared spectra were recorded on Shimadzu IR Prestige-21 FTIR Spectrometer. High resolution mass spectra (HRMS) were obtained using a LC/HRMS TOF spectrometer using simultaneous electrospray (ESI). Mass spectral data are reported in units of mass to charge (m/z).

7.2 Gold Catalyzed Tandem 1,3-Migration/[2+2] Cycloaddition of 1,7-Enyne

Benzoates to Azabicyclo[4.2.0]oct-5-enes

Synthesis of gold(I) complex **Au₅**

A solution of IPrAuCl (124.2 mg, 0.2 mmol) and DMAP (24.4 mg, 0.2 mmol) in CH₂Cl₂ (2 mL) was added over a solution of AgSbF₆ (68.7 mg, 0.2 mmol) in CH₂Cl₂ (1 mL) at room temperature. After stirring for two hours, the mixture was filtered and washed with CH₂Cl₂ (2 x 2 mL), the resulting solution was evaporated to small volume (ca. 2 mL) and pentane (5 mL) was slowly added resulting in the immediate precipitation of a white solid. The precipitate was filtered and washed with pentane (2 x 5 mL) and dried under vacuum. Complex **Au₅** was obtained as a white, air-stable solid (147mg, 78%). Mp = 230 °C (decompose); ¹H NMR (CDCl₃, 400 MHz): δ 1.26 (d, 12H, *J* = 6.8 Hz), 1.32 (t, 12H, *J* = 6.84 Hz), 2.51-2.57 (m, 4H), 3.00 (s, 6H), 6.45 (d, 2H, *J* = 6.7 Hz), 7.29-7.37 (m, 8H), 7.56 (t, 2H, *J* = 7.8 Hz); ¹³C NMR (CDCl₃, 100 MHz): δ 24.0, 24.6, 28.9, 39.3, 107.7, 124.4, 124.4, 131.2, 133.5, 145.7, 149.1, 155.2, 169.6; IR (NaCl, neat) ν: 2967, 1624, 1549, 1215, 1078 cm⁻¹; HRMS (ESI) calcd. For C₃₄H₄₆N₄Au (M⁺-SbF₆): 707.3388, found: 707.3379.

General Routes for the Preparation of 1,7-Enyne Benzoates

α-tosylamino ketones were synthesized from commercial available L-α-amino acids following literature procedures.⁶⁴

General Procedures for the Preparation of Amino Alcohols **166** and **166'** from Enantiopure α -Tosylamino Ketones

To a solution of ethynylbenzene (3.0 mmol) in THF (15 mL) was added LDA (2.0 M in THF, 1.5 mL, 3.0 mmol) at $-78\text{ }^\circ\text{C}$. The resulting solution was stirred for 1 h at $-78\text{ }^\circ\text{C}$. The α -tosylamino ketone **165** (1 mmol) in THF (2 mL) was subsequently slowly added to the resulting solution at $-78\text{ }^\circ\text{C}$ and the reaction mixture was slowly warmed up to room temperature stirred for 10 h. The reaction mixture was quenched by addition of saturated NH_4Cl (10 mL) and extracted with EtOAc (2 x 30 mL). The combined organic layers were washed with brine (20 mL), dried over MgSO_4 , concentrated under reduced pressure and purified by flash column chromatography on silica gel (eluent: *n*-hexane: ethyl acetate = 7: 1) to give two separated *syn* and *anti* diastereomer.

General Procedure for the Preparation of Racemic Amino Alcohols **166k-l** and **166k'-l'**

To a solution of **165** (1.0 mmol) in THF (10 mL) was added RMgBr ($\text{R} = \text{cC}_3\text{H}_5$ or *n*pentyl) (3.0 mmol) at $0\text{ }^\circ\text{C}$. The resulting solution was stirred for 1 h at $0\text{ }^\circ\text{C}$ and warmed up to room temperature stirred for 10 h. The reaction mixture was quenched by addition of saturated NH_4Cl (10 mL) and extracted with EtOAc (2 x 20 mL). The combined organic layers were washed with brine (15 mL), dried over MgSO_4 , concentrated under reduced pressure and purified by flash column chromatography on silica gel (eluent: *n*-hexane: ethyl acetate = 7: 1) to give two separated *syn* and *anti* diastereomer.

General Procedures for the Preparation 167 from 166.

To a solution of amino alcohols **166** (0.4 mmol) and DMAP (4.88 mg, 0.04 mmol) in CH_2Cl_2 (5 mL) at 0 °C was added BzCl (0.0557 mL, 0.48 mmol) and Et_3N (0.0836 mL, 0.6 mmol). The reaction mixtures was allowed to warm to room temperature and stirred for 15 hours. Upon completion, the reaction mixture was added saturated NaHCO_3 solution (5 mL) and extracted with CH_2Cl_2 (2 x10 mL). The combined organic layer was washed with brine, dried over MgSO_4 , concentrated under reduced pressure and purified by flash column chromatography on silica gel (eluent: *n*-hexane: ethyl acetate = 9: 1) to give the desired product.

General Procedures for the Preparation of 1,7-Enyne benzoates 156a-x from 167.

To a solution of **167** (0.3 mmol) and NaH (60%) (18 mg, 0.45 mmol) in anhydrous DMF (3 mL) at 0 °C was added allyl bromide or cinnamyl bromide (0.45 mmol). The reaction mixtures was allowed to warm to room temperature and stirred for 5 hours. Upon completion, the reaction mixture was quenched with H_2O (10 mL) and extracted with EtOAc (3x10 mL). The combined organic layer was washed with brine, dried over MgSO_4 , concentrated under reduced pressure and purified by flash column chromatography on silica gel (eluent: *n*-hexane: ethyl acetate = 9: 1) to give the desired product.

General Experimental Procedure for Optimizing the Tandem 1,3-Migration/[2+2] Cycloaddition of 1,7-Enyne Benzoates **156a.**

To a solution of 1,7-enyne benzoates **156a** (0.15 mmol) and 4 Å molecular sieves (150 mg) in anhydrous 1,2-dichloroethane (1.5 mL) was added gold(I)/(III) or PtCl₂ catalyst (7.5 μmol) under an argon atmosphere. The reaction mixture was stirred at 80 °C for 15. The reaction mixture then cooled to room temperature and filtered through Celite, washed with CH₂Cl₂, the solvent was removed under reduced pressure. Purification by flash column chromatography on silica gel (*n*-hexane/ EtOAc = 9:1 as eluent) gave the product **158a** or **168a**.

General Experimental Procedure for Gold(I) Complex Au₂ Catalyzed Tandem 1,3-Migration/[2+2] Cycloaddition of 1,7-Enyne Benzoates **156b-x.**

To a solution of 1,7-enyne benzoates **156** (0.15 mmol) and 4 Å molecular sieves (150 mg) in anhydrous 1,2-dichloroethane (1.5 mL) was added gold(I) complex **Au₂** (5.8 mg, 7.5 μmol) under an argon atmosphere. The reaction mixture was stirred at 80 °C for 15-24h. The reaction mixture then cooled to room temperature and filtered through celite, washed with CH₂Cl₂, the solvent was removed under reduced pressure. Purification by flash column chromatography on silica gel (*n*-hexane/ EtOAc = 9:1 as eluent) gave the product **158**.

Procedure for Gold(I) Complex Au_2 Catalyzed [2+2] Cycloaddition of **168a.**

To a solution of allene **168a** (0.15 mmol) and 4 Å molecular sieves (150 mg) in anhydrous 1,2-dichloroethane (1.5 mL) was added gold(I) complex Au_2 (5.8 mg, 7.5 μmol) under an argon atmosphere. The reaction mixture was stirred at 80 °C for 15 h. The reaction mixture then cooled to room temperature and filtered through Celite, washed with CH_2Cl_2 , the solvent was removed under reduced pressure. Purification by flash column chromatography on silica gel (*n*-hexane/ EtOAc = 9:1 as eluent) gave the product **158a** in 88% yield.

Procedure for Gold(I) Complex Au_2 Catalyzed [2+2] cycloaddition of **168a in the Presence of D_2O .**

To a solution of allene **168a** (0.15 mmol) and D_2O (0.75 mmol) in anhydrous 1,2-dichloroethane (1.5 mL) was added gold(I) complex Au_2 (5.8 mg, 7.5 μmol) under an argon atmosphere. The reaction mixture was stirred at 80 °C for 15 h. The reaction mixture then cooled to room temperature and the solvent was removed under reduced pressure. Purification by flash column chromatography on silica gel (*n*-hexane/ EtOAc = 9:1 as eluent) gave the product **d₁-170a** in 30% yield with 90% incorporation.

Procedure for Gold(I) Complex $\mathbf{Au}_2$ Catalyzed Reaction of **158a** in the Presence of $\mathbf{D_2O}$

To a solution of **158a** (0.15 mmol) and D_2O (0.75 mmol) in anhydrous 1,2-dichloroethane (1.5 mL) was added gold(I) complex $\mathbf{Au}_2$ (7.5 μmol) under an argon atmosphere. The reaction mixture was stirred at 80 $^\circ\text{C}$ for 15 h. The reaction mixture then cooled to room temperature and the solvent was removed under reduced pressure. Purification by flash column chromatography on silica gel (*n*hexane/ EtOAc = 9:1 as eluent) gave **171a** in 31% yield.

(*S*)-4-Methyl-*N*-(2-methyl-5-oxoheptan-4-yl)benzenesulfonamide (**165a**)

White solid, mp = 62-63 $^\circ\text{C}$; $[\alpha]_D^{25} +77.1$ (*c* 1.0, CHCl_3); ^1H NMR (CDCl_3 , 300 MHz): δ 0.82-0.89 (m, 9H), 1.24-1.41 (m, 2H), 1.77-1.90 (m, 1H), 2.05-2.18 (m, 1H), 2.36-2.49 (m, 4H), 2.63-2.74 (m, 2H), 3.90 (td, 1H, J = 9.2, 4.3 Hz), 5.40 (d, 1H, J = 8.8 Hz), 7.28 (d, 2H, J = 8.3 Hz), 7.69 (d, 2H, J = 8.3 Hz); ^{13}C NMR (CDCl_3 , 100 MHz): δ 7.46, 21.2, 21.5, 23.2, 24.4, 32.8, 41.4, 59.7, 127.3, 129.6, 136.7, 143.6, 209.5; IR (NaCl, neat) ν : 3289, 3020, 2959, 1719, 1337, 1163 cm^{-1} ; HRMS (ESI) calcd. For $\text{C}_{15}\text{H}_{24}\text{NO}_3\text{S}$ ($\text{M}^+ + \text{H}$): 298.1477, found: 298.1476.

(S)-4-Methyl-N-(4-oxohexan-3-yl)benzenesulfonamide (165b)

White solid, mp = 74-77 °C; $[\alpha]_D^{25} +91.1$ (*c* 1.0, CHCl₃); ¹H NMR (CDCl₃, 500 MHz): δ 0.83-0.90 (m, 6H), 1.53-1.62 (m, 1H), 1.78-1.85 (m, 1H), 2.15-2.23 (m, 1H), 2.41-2.47 (m, 4H), 3.89 (m, 1H), 5.60 (d, 1H, *J* = 7.4 Hz), 7.28 (d, 2H, *J* = 8.2 Hz), 7.70 (d, 2H, *J* = 8.2 Hz); ¹³C NMR (CDCl₃, 125 MHz): δ 7.5, 9.0, 21.5, 25.7, 32.7, 62.1, 127.2, 129.7, 136.8, 143.6, 208.5; IR (NaCl, neat) ν : 3279, 3022, 2957, 1715, 1335, 1090 cm⁻¹; HRMS (ESI) calcd. For C₁₃H₁₉NO₃SNa (M⁺+Na): 292.0983, found: 292.0987.

(S)-4-Methyl-N-(2-methyl-4-oxohexan-3-yl)benzenesulfonamide (165c)

White solid, mp = 120-122 °C; $[\alpha]_D^{25} +118.7$ (*c* 1.0, CHCl₃); ¹H NMR (CDCl₃, 500 MHz): δ 0.67 (d, 3H, *J* = 6.8 Hz), 0.77 (td, 3H, *J* = 6.6, 1.4 Hz), 1.00 (d, 3H, *J* = 6.5 Hz), 2.01-2.08 (m, 2H), 2.30-2.38 (m, 4H), 3.76 (dd, 1H, *J* = 9.0, 6.1 Hz), 5.45 (d, 1H, *J* = 7.6 Hz), 7.23 (d, 2H, *J* = 7.5 Hz), 7.65 (d, 2H, *J* = 7.5 Hz); ¹³C NMR (CDCl₃, 125 MHz): δ 7.5, 16.2, 20.0, 21.5, 30.3, 33.6, 66.1, 127.3, 129.6, 136.6, 143.6, 208.8; IR (NaCl, neat) ν : 3281, 3019, 2970, 1719, 1215, 1092 cm⁻¹; HRMS (ESI) calcd. For C₁₄H₂₃NO₃S (M⁺+H): 285.1399, found: 235.1391.

(S)-4-Methyl-N-(3-oxo-1-phenylpentan-2-yl)benzenesulfonamide (165d)

White solid, mp = 93-95 °C; $[\alpha]_D^{25} +58.6$ (*c* 1.0, CHCl₃); ¹H NMR (CDCl₃, 500 MHz): δ 0.85 (t, 3H, *J* = 7.2 Hz), 2.14-2.22 (m, 1H), 2.29-2.37 (m, 1H), 2.40 (s, 3H), 2.92 (qd, 2H, *J* = 14.0, 6.5 Hz), 4.11 (dd, 1H, *J* = 14.4, 6.6 Hz), 5.36 (d, 1H, *J* = 8.0 Hz), 7.01-7.03 (m, 2H), 7.21-7.23 (m, 5H), 7.58 (d, 2H, *J* = 8.2 Hz); ¹³C NMR (CDCl₃, 125 MHz): δ 7.2, 21.5, 34.0, 38.9, 127.1, 127.2, 128.7, 129.2, 129.7, 135.2, 136.6, 143.6, 208.8; IR (NaCl, neat) ν : 3273, 2970, 1719, 1450, 1333, 1155, 1092 cm⁻¹; HRMS (ESI) calcd. For C₁₈H₂₂NO₃S (M⁺+H): 332.1320, found: 332.1325.

(S)-4-Methyl-N-(3-oxobutan-2-yl)benzenesulfonamide (165e)^{64b}

White solid, mp = 104-105 °C; $[\alpha]_D^{25} +75.1$ (*c* 1.0, CHCl₃), Lit⁴: $[\alpha]_D^{20} +80.0$ (*c* 1.0, CH₂Cl₂); ¹H NMR (CDCl₃, 300 MHz): δ 1.29 (d, 3H, *J* = 7.2 Hz), 2.12 (s, 3H), 2.40 (s, 3H), 3.89-3.94 (m, 1H), 5.91 (d, 1H, *J* = 6.5 Hz), 7.29 (d, 2H, *J* = 8.0 Hz), 7.74 (d, 2H, *J* = 8.0 Hz); ¹³C NMR (CDCl₃, 75 MHz): δ 18.3, 21.4, 26.1, 57.7, 127.0, 129.7, 136.9, 143.6, 206.4.

(S)-4-Methyl-N-(2-oxohexan-3-yl)benzenesulfonamide (165f)

White solid, mp = 68-70 °C; $[\alpha]_D^{25} +103.0$ (*c* 1.0, CHCl₃); ¹H NMR (CDCl₃, 400 MHz): δ 0.82 (t, 3H, *J* = 7.3 Hz), 1.24-1.33 (m, 2H), 1.47-1.55 (m, 1H), 1.65-1.72 (m, 1H), 2.06 (s,

3H), 2.40 (s, 3H), 3.90 (td, 1H, $J = 7.8, 4.6$ Hz), 5.84 (d, 1H, $J = 6.4$ Hz), 7.28 (d, 2H, $J = 8.2$ Hz), 7.72 (d, 2H, $J = 8.0$ Hz); ^{13}C NMR (CDCl_3 , 100 MHz): δ 13.7, 18.1, 21.6, 26.7, 34.0, 62.0, 127.2, 129.8, 137.0, 143.8, 206.6; IR (NaCl, neat) ν : 3273, 2970, 1719, 1333, 1163 cm^{-1} ; HRMS (ESI) calcd. For $\text{C}_{13}\text{H}_{20}\text{NO}_3\text{S}$ ($\text{M}^+ + \text{H}$): 270.1164, found: 270.1167.

(S)-4-Methyl-N-(2-oxo-1-phenylpropyl)benzenesulfonamide (165g)^{64d}

White solid, mp = 161-163 °C; $[\alpha]_{\text{D}}^{25} +293.2$ (c 1.0, CHCl_3), Lit⁶: $[\alpha]_{\text{D}}^{20} +287.6$ (c 0.8, CHCl_3); ^1H NMR (CDCl_3 , 400 MHz): δ 1.98 (s, 3H), 2.33 (s, 3H), 5.02 (d, 1H, $J = 4.8$ Hz), 6.08 (d, 1H, $J = 4.8$ Hz), 7.07-7.11 (m, 4H), 7.19-7.23 (m, 3H), 7.47 (d, 2H, $J = 8.2$ Hz); ^{13}C NMR (CDCl_3 , 100 MHz): δ 21.4, 26.6, 66.4, 126.9, 128.0, 128.7, 129.1, 129.3, 135.0, 137.2, 143.2, 201.8.

(S)-N-(1-Hydroxy-3-oxopentan-2-yl)-4-methylbenzenesulfonamide (165h)

White solid, mp = 129-130 °C; $[\alpha]_{\text{D}}^{25} +54.1$ (c 1.0, CHCl_3); ^1H NMR (CDCl_3 , 400 MHz): δ 0.94 (d, 3H, $J = 7.2$ Hz), 2.32-2.41 (m, 4H), 2.52-2.62 (m, 2H), 3.83-3.91 (m, 3H), 5.94 (d, 1H, $J = 5.6$ Hz), 7.29 (d, 2H, $J = 8.0$ Hz), 7.71 (d, 2H, $J = 8.2$ Hz); ^{13}C NMR (CDCl_3 , 100 MHz): δ 7.4, 21.6, 30.0, 63.0, 63.1, 127.1, 129.9, 136.3, 144.0, 206.8; IR (NaCl, neat) ν : 3505, 3267, 1722, 1344, 1159 cm^{-1} ; HRMS (ESI) calcd. For $\text{C}_{12}\text{H}_{17}\text{NO}_4\text{SNa}$ ($\text{M}^+ + \text{Na}$): 294.0776, found: 294.0781.

(S)-N-(1-(*tert*-Butyldimethylsilyloxy)-3-oxopentan-2-yl)-4-methylbenzenesulfonamide (165i)

Colourless oil; $[\alpha]_D^{25} +49.8$ (*c* 1.0, CHCl₃); ¹H NMR (CDCl₃, 400 MHz): δ -0.01 (s, 6H), 0.81 (s, 9H), 0.93 (t, 3H, *J* = 7.2 Hz), 2.04-2.33 (m, 1H), 2.41 (s, 3H), 2.56-2.66 (m, 1H), 3.65 (dd, 1H, *J* = 10.2, 4.6 Hz), 3.84-3.88 (m, 1H), 3.97 (dd, 1H, *J* = 10.2, 3.4 Hz), 5.61 (d, 1H, *J* = 7.2 Hz), 7.28 (d, 2H, *J* = 8.0 Hz), 7.70 (d, 2H, *J* = 8.2 Hz); ¹³C NMR (CDCl₃, 100 MHz): δ -5.68, -5.60, 7.3, 18.1, 21.5, 25.7, 33.7, 62.6, 64.1, 127.1, 129.8, 136.9, 143.7, 207.4; IR (NaCl, neat) ν : 3273, 2936, 2857, 1719, 1339, 1165, 1092 cm⁻¹; HRMS (ESI) calcd. For C₁₈H₃₂NO₄SSi (M⁺+H): 386.1821, found: 386.1821.

(S)-4-Methyl-N-(1-(methylthio)-4-oxohexan-3-yl)benzenesulfonamide (165j)

White solid, mp = 87-89 °C; $[\alpha]_D^{25} +64.1$ (*c* 1.0, CHCl₃); ¹H NMR (CDCl₃, 400 MHz): δ 0.88 (t, 3H, *J* = 7.3 Hz), 1.67-1.76 (m, 1H), 1.94-2.02 (m, 1H), 2.05 (s, 3H), 2.15-2.25 (m, 1H), 2.41-2.59 (m, 6H), 4.05 (td, 1H, *J* = 8.0, 3.9 Hz), 5.64 (d, 1H, *J* = 7.9 Hz), 7.29 (d, 2H, *J* = 7.9 Hz), 7.70 (d, 2H, *J* = 8.2 Hz); ¹³C NMR (CDCl₃, 100 MHz): δ 7.5, 15.5, 21.5, 29.8, 31.8, 32.9, 60.1, 127.2, 129.7, 136.6, 143.8, 208.3; IR (NaCl, neat) ν : 3273, 2936, 1719, 1333, 1161, 1092 cm⁻¹; HRMS (ESI) calcd. For C₁₄H₂₁NO₃S₂Na (M⁺+Na): 338.0861, found: 338.0869.

4-Methyl-*N*-(6-methyl-3-oxo-1-phenylhept-1-yn-4-yl)benzenesulfonamide (165k)

White solid, mp = 114-116 °C; ^1H NMR (CDCl_3 , 400 MHz): δ 0.93-0.95 (m, 6H), 1.46-1.53 (m, 1H), 1.66-1.73 (m, 1H), 1.85-1.95 (m, 1H), 2.36 (s, 3H), 4.17 (td, 1H, $J = 9.3$, 4.3 Hz), 5.51 (d, 1H, $J = 9.1$ Hz), 7.24 (d, 2H, $J = 8.0$ Hz), 7.37-7.54 (m, 5H), 7.74 (d, 2H, $J = 8.2$ Hz); ^{13}C NMR (CDCl_3 , 100 MHz): δ 21.5, 21.6, 23.1, 24.5, 41.6, 62.1, 85.6, 95.7, 119.2, 127.2, 128.8, 129.8, 131.4, 133.3, 136.9, 143.7, 186.0; IR (NaCl, neat) ν : 3273, 2970, 2201, 1670, 1163 cm^{-1} ; HRMS (ESI) calcd. For $\text{C}_{21}\text{H}_{24}\text{NO}_3\text{S}$ ($\text{M}^+ + \text{H}$): 370.1477, found: 370.1476.

4-Methyl-*N*-(3-oxo-1-phenyl-5-(thiophen-3-yl)pent-4-yn-2-yl)benzenesulfonamide (165l)

Brown solid, mp = 102-104 °C; ^1H NMR (CDCl_3 , 400 MHz): δ 2.36 (s, 3H), 3.19-3.20 (m, 2H), 4.39-4.44 (m, 1H), 5.46 (d, 1H, $J = 8.2$ Hz), 7.15-7.23 (m, 7H), 7.35 (dd, 1H, $J = 5.0$, 3.0 Hz), 7.65 (d, 2H, $J = 8.2$ Hz), 7.78 (d, 1H, $J = 3.0$ Hz); ^{13}C NMR (CDCl_3 , 100 MHz): δ 21.6, 38.7, 63.9, 86.4, 91.9, 118.5, 126.5, 127.0, 127.2, 128.6, 129.8, 129.8, 130.3, 134.7, 135.3, 136.9, 143.6, 184.4; IR (NaCl, neat) ν : 3285, 3019, 2193, 1670, 1215, 1155 cm^{-1} ; HRMS (ESI) calcd. For $\text{C}_{22}\text{H}_{20}\text{NO}_3\text{S}_2$ ($\text{M}^+ + \text{H}$): 410.0885, found: 410.0880.

***N*-((3*S*,4*S*)-3-Ethyl-3-hydroxy-6-methyl-1-phenylhept-1-yn-4-yl)-4-methylbenzenesulfonamide (166a)**

Colourless oil; $[\alpha]_{\text{D}}^{25} -40.2$ (c 1.0, CHCl_3); ^1H NMR (CDCl_3 , 400 MHz): δ 0.69 (d, 3H, J = 6.3 Hz), 0.78 (d, 3H, J = 6.5 Hz), 1.09 (t, 3H, J = 7.3 Hz), 1.36 (t, 2H, J = 11.0 Hz), 1.59-1.73 (m, 3H), 2.38 (s, 3H), 2.80 (s, 1H), 3.59 (t, 1H, J = 8.9 Hz), 5.00 (d, 1H, J = 8.9 Hz), 7.23-7.40 (m, 7H), 7.79 (d, 2H, J = 8.0 Hz); ^{13}C NMR (CDCl_3 , 100 MHz): δ 8.32, 21.3, 21.5, 23.8, 24.4, 30.5, 41.2, 60.2, 74.9, 86.1, 89.6, 122.4, 127.1, 128.3, 128.5, 129.5, 131.8, 138.3, 143.3; IR (NaCl, neat) ν : 3466, 3279, 2957, 2359, 1335, 1159 cm^{-1} ; HRMS (ESI) calcd. For $\text{C}_{23}\text{H}_{28}\text{NO}_2\text{S}$ ($\text{M}^+ - \text{OH}$): 382.1841, found: 382.1846.

***N*-((3*R*,4*S*)-3-Ethyl-3-hydroxy-6-methyl-1-phenylhept-1-yn-4-yl)-4-methylbenzenesulfonamide (166a')**

White solid, mp = 154-156 $^{\circ}\text{C}$; $[\alpha]_{\text{D}}^{25} -46.3$ (c 1.0, CHCl_3); ^1H NMR (CDCl_3 , 400 MHz): δ 0.71 (d, 3H, J = 4.8 Hz), 0.81 (d, 3H, J = 5.0 Hz), 1.07 (t, 3H, J = 7.3 Hz), 1.43-1.51 (m, 3H), 1.67-1.84 (m, 2H), 2.40 (s, 3H), 2.87 (s, 1H), 3.49 (t, 1H, J = 9.0 Hz), 4.95 (d, 1H, J = 9.4 Hz), 7.26-7.40 (m, 7H), 7.80 (d, 2H, J = 8.0 Hz); ^{13}C NMR (CDCl_3 , 100 MHz): δ 8.3, 21.3, 21.5, 23.9, 24.3, 30.4, 41.7, 60.3, 74.9, 86.2, 89.2, 122.2, 127.1, 128.3, 128.6, 129.6, 131.7, 138.4, 143.4; IR (NaCl, neat) ν : 3385, 3140, 2963, 1599, 1315, 1159 cm^{-1} ; HRMS (ESI) calcd. For $\text{C}_{23}\text{H}_{28}\text{NO}_2\text{S}$ ($\text{M}^+ - \text{OH}$): 382.1841, found: 382.1842.

***N*-((3*S*,4*S*)-3-Ethyl-3-hydroxy-6-methyl-1-(*p*-tolyl)hept-1-yn-4-yl)-4-methylbenzene Sulphonamide (166b)**

White solid, mp = 106-108 °C; $[\alpha]_D^{25}$ -39.8 (*c* 1.0, CHCl₃); ¹H NMR (CDCl₃, 400 MHz): δ 0.69 (d, 3H, *J* = 6.2 Hz), 0.78 (d, 3H, *J* = 6.4 Hz), 1.09 (t, 3H, *J* = 7.3 Hz), 1.32-1.43 (m, 2H), 1.59-1.71 (m, 3H), 2.33 (s, 3H), 2.41 (s, 1H), 2.72 (s, 1H), 3.58 (t, 1H, *J* = 8.9 Hz), 4.92 (d, 1H, *J* = 8.9 Hz), 7.09 (d, 2H, *J* = 7.9 Hz), 7.23-7.29 (m, 4H), 7.79 (d, 2H, *J* = 8.1 Hz); ¹³C NMR (CDCl₃, 100 MHz): δ 8.3, 21.3, 21.5, 21.5, 23.8, 24.4, 30.6, 41.2, 60.2, 74.9, 86.2, 88.8, 119.3, 127.1, 129.0, 129.5, 131.7, 138.4, 138.6, 143.3; IR (NaCl, neat) ν : 3480, 3273, 2970, 1451, 1315, 1155 cm⁻¹; HRMS (ESI) calcd. For C₂₄H₃₀NO₂S (M⁺-OH): 396.1997, found: 396.1991.

***N*-((3*S*,4*S*)-3-Ethyl-1-(4-fluorophenyl)-3-hydroxy-6-methylhept-1-yn-4-yl)-4-methylbenzenesulfonamide (166c)**

Yellow oil; $[\alpha]_D^{25}$ -49.9 (*c* 1.0, CHCl₃); ¹H NMR (CDCl₃, 400 MHz): δ 0.67 (d, 3H, *J* = 6.4 Hz), 0.77 (d, 3H, *J* = 6.4 Hz), 1.08 (t, 3H, *J* = 7.3 Hz), 1.29-1.39 (m, 2H), 1.55-1.70 (m, 3H), 2.39 (s, 3H), 2.89 (s, 1H), 3.58 (td, 1H, *J* = 8.8, 1.9 Hz), 5.21 (s, 1H), 6.96 (t, 2H, *J* = 8.6 Hz), 7.24 (d, 2H, *J* = 8.0 Hz), 7.37 (dd, 2H, *J* = 8.5, 5.5 Hz), 7.80 (d, 2H, *J* = 8.1 Hz); ¹³C NMR (CDCl₃, 100 MHz): δ 8.3, 21.2, 21.5, 23.8, 24.4, 30.5, 41.0, 60.0, 74.9, 85.0, 89.4, 115.5 (d, 1C, *J*_{C-F} = 22.1 Hz), 118.5 (d, 1C, *J*_{C-F} = 3.3 Hz), 127.0, 129.5, 133.7 (d, 1C, *J*_{C-F} = 8.4 Hz), 138.3, 143.3, 162.6 (d, 1C, *J*_{C-F} = 247.9 Hz); IR (NaCl, neat) ν :

3370, 3273, 3019, 1495, 1333, 1215, 1155 cm^{-1} ; HRMS (ESI) calcd. For $\text{C}_{23}\text{H}_{27}\text{FNO}_2\text{S}$ ($\text{M}^+ - \text{OH}$): 400.1747, found: 400.1746.

***N*-((3*S*,4*S*)-3-Ethyl-3-hydroxy-6-methyl-1-(thiophen-3-yl)hept-1-yn-4-yl)-4-methylbenzenesulfonamide (166d)**

Yellow solid, mp = 137-139 °C; $[\alpha]_{\text{D}}^{25}$ -40.6 (c 1.0, CHCl_3); ^1H NMR (CDCl_3 , 400 MHz): δ 0.68 (d, 3H, J = 6.4 Hz), 0.77 (d, 3H, J = 6.4 Hz), 1.08 (t, 3H, J = 7.4 Hz), 1.23-1.38 (m, 2H), 1.56-1.72 (m, 3H), 2.39 (s, 3H), 2.80 (s, 1H), 3.57 (td, 1H, J = 11.4, 2.2 Hz), 5.06 (d, 1H, J = 9.0 Hz), 7.06 (dd, 1H, J = 5.0, 1.0 Hz), 7.22-7.28 (m, 3H), 7.41 (dd, 1H, J = 2.9, 1.0 Hz), 7.79 (d, 2H, J = 8.2 Hz); ^{13}C NMR (CDCl_3 , 100 MHz): δ 8.3, 21.3, 21.5, 23.8, 24.4, 30.6, 41.1, 60.2, 75.0, 81.2, 89.2, 121.4, 125.2, 127.1, 129.2, 129.5, 129.9, 138.4, 143.3; IR (NaCl, neat) ν : 3483, 3283, 2228, 1597, 1325, 1157, 1092 cm^{-1} ; HRMS (ESI) calcd. For $\text{C}_{21}\text{H}_{26}\text{NO}_2\text{S}_2$ ($\text{M}^+ - \text{OH}$): 388.1405, found: 388.1403.

($\pm$)-*N*-(5-Hydroxy-2-methyl-5-(phenylethynyl)decan-4-yl)-4-methylbenzenesulfonamide (166e)

Yellow oil; ^1H NMR (CDCl_3 , 400 MHz): δ 0.73 (d, 3H, J = 6.3 Hz), 0.81 (d, 3H, J = 6.5 Hz), 0.88 (t, 3H, J = 7.0 Hz), 1.20-1.67 (m, 11H), 2.38 (s, 3H), 2.73 (s, 1H), 3.56 (t, 1H, J = 8.1 Hz), 4.91 (d, 1H, J = 9.0 Hz), 7.23-7.39 (m, 7H), 7.79 (d, 2H, J = 8.2 Hz); ^{13}C NMR (CDCl_3 , 100 MHz): δ 14.1, 21.3, 21.5, 22.6, 23.6, 23.9, 24.3, 31.9, 37.8, 41.2, 60.5, 74.4, 86.0, 89.8, 122.4, 127.1, 128.3, 128.5, 129.5, 131.8, 138.4, 143.3; IR (NaCl, neat) ν :

3379, 3280, 3019, 2957, 1599, 1329, 1215, 1157 cm^{-1} ; HRMS (ESI) calcd. For $\text{C}_{26}\text{H}_{34}\text{NO}_2\text{S}$ ($\text{M}^+ - \text{OH}$): 424.2310, found: 424.2301.

(±)-*N*-(3-Cyclopropyl-3-hydroxy-6-methyl-1-phenylhept-1-yn-4-yl)-4-methylbenzenesulfonamide (166f)

White solid, mp = 140-142 °C; ^1H NMR (CDCl_3 , 400 MHz): δ 0.48-0.50 (m, 2H), 0.59-0.66 (m, 2H), 0.72 (d, 3H, J = 6.4 Hz), 0.81 (d, 3H, J = 6.6 Hz), 1.12-1.16 (m, 1H), 1.40-1.47 (m, 2H), 1.69-1.73 (m, 1H), 2.40 (s, 3H), 2.65 (s, 1H), 3.69 (td, 1H, J = 9.4, 2.4 Hz), 4.55 (t, 1H, J = 9.2 Hz), 7.25-7.29 (m, 7H), 7.79 (d, 2H, J = 8.2 Hz); ^{13}C NMR (CDCl_3 , 100 MHz): δ 0.9, 3.3, 17.1, 21.2, 21.5, 23.8, 24.3, 41.5, 61.3, 75.7, 86.1, 87.6, 122.2, 127.1, 128.3, 128.6, 129.5, 131.8, 138.4, 143.3; IR (NaCl, neat) ν : 3479, 3273, 2970, 2230, 1491, 1332, 1155 cm^{-1} ; HRMS (ESI) calcd. For $\text{C}_{24}\text{H}_{28}\text{NO}_2\text{S}$ ($\text{M}^+ - \text{OH}$): 394.1841, found: 394.1837.

***N*-((3*S*,4*S*)-4-Ethyl-4-hydroxy-6-phenylhex-5-yn-3-yl)-4-methylbenzenesulfonamide (166g)**

Pale-yellow oil; $[\alpha]_{\text{D}}^{25}$ -47.7 (c 1.0, CHCl_3); ^1H NMR (CDCl_3 , 400 MHz): δ 0.68 (t, 3H, J = 7.4 Hz), 1.08 (t, 3H, J = 7.2 Hz), 1.37-1.49 (m, 1H), 1.62-1.79 (m, 2H), 1.89-1.97 (m, 1H), 2.35 (s, 3H), 2.89 (s, 1H), 3.42 (td, 1H, J = 9.4, 3.0 Hz), 5.17 (d, 1H, J = 9.2 Hz), 7.19-7.38 (m, 7H), 7.79 (d, 2H, J = 8.0 Hz); ^{13}C NMR (CDCl_3 , 100 MHz): δ 8.4, 11.0, 21.5, 24.2, 31.1, 63.4, 74.8, 86.0, 89.6, 122.4, 127.1, 128.2, 128.5, 129.5, 131.8, 138.4,

143.3; IR (NaCl, neat) ν : 3480, 3370, 3019, 1491, 1215 cm^{-1} ; HRMS (ESI) calcd. For $\text{C}_{21}\text{H}_{24}\text{NO}_2\text{S}$ ($\text{M}^+ - \text{OH}$): 354.1528, found: 354.1518.

***N*-((3*S*,4*S*)-4-Ethyl-4-hydroxy-2-methyl-6-phenylhex-5-yn-3-yl)-4-methylbenzenesulfonamide (166h)**

Yellow solid, mp = 124-126 $^{\circ}\text{C}$; $[\alpha]_{\text{D}}^{25}$ -31.4 (c 1.0, CHCl_3); ^1H NMR (CDCl_3 , 400 MHz): δ 0.74 (d, 3H, J = 7.0 Hz), 0.93 (d, 3H, J = 6.8 Hz), 1.07 (t, 3H, J = 7.4 Hz), 1.61-1.70 (m, 1H), 1.76-1.85 (m, 1H), 2.25-2.32 (m, 1H), 2.36 (s, 3H), 2.51 (s, 1H), 3.48 (dd, 1H, J = 10.0, 2.4 Hz), 5.00 (d, 1H, J = 10.0 Hz), 7.20-7.40 (m, 7H), 7.78 (d, 2H, J = 8.3 Hz); ^{13}C NMR (CDCl_3 , 100 MHz): δ 8.4, 17.3, 21.5, 22.6, 28.2, 32.6, 65.4, 74.8, 86.5, 89.7, 122.3, 127.0, 128.3, 128.6, 129.5, 131.8, 139.0, 143.1; IR (NaCl, neat) ν : 3480, 3273, 2970, 2230, 1599, 1491, 1315, 1159 cm^{-1} ; HRMS (ESI) calcd. For $\text{C}_{22}\text{H}_{26}\text{NO}_2\text{S}$ ($\text{M}^+ - \text{OH}$): 368.1684, found: 368.1692.

***N*-((2*S*,3*S*)-3-Ethyl-3-hydroxy-1,5-diphenylpent-4-yn-2-yl)-4-methylbenzenesulfonamide (166i)**

Yellow oil; $[\alpha]_{\text{D}}^{25}$ -4.3 (c 1.0, CHCl_3); ^1H NMR (CDCl_3 , 400 MHz): δ 0.85 (t, 3H, J = 7.4 Hz), 1.77-1.94 (m, 2H), 2.33 (s, 3H), 2.62 (dd, 1H, J = 14.2, 9.3 Hz), 2.96 (s, 1H), 3.33 (dd, 1H, J = 14.2, 4.0 Hz), 3.82 (td, 1H, J = 9.1, 4.0 Hz), 5.10 (d, 1H, J = 9.0 Hz), 6.97-7.08 (m, 7H), 7.25-7.44 (m, 7H); ^{13}C NMR (CDCl_3 , 100 MHz): δ 8.4, 21.5, 31.2, 38.0, 63.6, 75.2, 86.8, 89.2, 122.2, 126.3, 126.7, 128.3, 128.5, 128.6, 129.3, 129.5, 131.9,

137.4, 137.7, 142.8; IR (NaCl, neat) ν : 3480, 3273, 3019, 1491, 1315, 1157 cm^{-1} ; HRMS (ESI) calcd. For $\text{C}_{26}\text{H}_{26}\text{NO}_2\text{S}$ ($\text{M}^+ - \text{OH}$): 416.1684, found: 416.1680.

***N*-((2*S*,3*S*)-3-Hydroxy-3-methyl-5-phenylpent-4-yn-2-yl)-4-methylbenzenesulfonamide (166j)**

Yellow oil; $[\alpha]_{\text{D}}^{25} +5.2$ (c 1.0, CHCl_3); ^1H NMR (CDCl_3 , 400 MHz): δ 1.14 (d, 3H, $J = 6.6$ Hz), 1.51 (s, 3H), 2.35 (s, 3H), 3.07 (s, 1H), 3.41-3.48 (m, 1H), 5.28 (d, 1H, $J = 8.8$ Hz), 7.20-7.36 (m, 7H), 7.78 (d, 2H, $J = 8.0$ Hz); ^{13}C NMR (CDCl_3 , 100 MHz): δ 16.6, 21.5, 26.2, 57.8, 71.0, 85.1, 90.1, 122.1, 127.1, 128.2, 128.6, 129.7, 131.8, 137.6, 143.5; HRMS (ESI) calcd. For $\text{C}_{19}\text{H}_{20}\text{NO}_2\text{S}$ ($\text{M}^+ - \text{OH}$): 326.1215, found: 326.1215.

***N*-((3*S*,4*S*)-3-Hydroxy-3-methyl-1-phenylhept-1-yn-4-yl)-4-methylbenzenesulfonamide (166k)**

Yellow oil; $[\alpha]_{\text{D}}^{25} -30.6$ (c 1.0, CHCl_3); ^1H NMR (CDCl_3 , 400 MHz): δ 0.73 (t, 3H, $J = 7.2$ Hz), 0.87-1.02 (m, 1H), 1.13-1.20 (m, 1H), 1.25-1.47 (m, 1H), 1.52 (s, 3H), 1.82-1.85 (m, 1H), 2.38 (s, 3H), 3.09 (s, 1H), 3.46 (t, 1H, $J = 8.0$ Hz), 5.13 (d, 1H, $J = 8.0$ Hz), 7.24-7.39 (m, 7H), 7.79 (d, 2H, $J = 8.0$ Hz); ^{13}C NMR (CDCl_3 , 100 MHz): δ 13.8, 19.3, 21.5, 25.9, 33.8, 62.2, 71.1, 84.9, 90.9, 122.3, 127.1, 128.3, 128.5, 129.6, 131.8, 138.1, 143.4; IR (NaCl, neat) ν : 3381, 3281, 3019, 2236, 1335, 1215, 1159 cm^{-1} ; HRMS (ESI) calcd. For $\text{C}_{21}\text{H}_{24}\text{NO}_2\text{S}$ ($\text{M}^+ - \text{OH}$): 354.1528, found: 354.1529.

N*-((1*S*)-2-Hydroxy-2-methyl-1,4-diphenylbut-3-yn-1-yl)-4-methylbenzenesul*fonamide (166l)**

Yellow solid; obtained as two diastereomers in a ratio of 3.3:1; mp = 50-53 °C; $[\alpha]_D^{25} +133.4$ (*c* 1.0, CHCl₃); major isomer: ¹H NMR (CDCl₃, 400 MHz): δ 1.59 (s, 3H), 2.17 (s, 1H), 2.27 (s, 3H), 4.41 (d, 1H, *J* = 9.1 Hz), 5.70 (d, 1H, *J* = 8.9 Hz), 6.98 (d, 2H, *J* = 7.9 Hz), 7.11-7.20 (m, 5H), 7.28-7.29 (m, 5H), 7.49 (d, 2H, *J* = 8.0 Hz); ¹³C NMR (CDCl₃, 100 MHz): δ 21.4, 27.4, 65.7, 70.9, 86.3, 89.5, 121.8, 127.1, 127.9, 128.0, 128.3, 128.5, 128.8, 129.2, 131.8, 136.0, 137.2, 143.0; IR (NaCl, neat) ν : 3379, 3279, 3019, 1329, 1215, 1157 cm⁻¹; HRMS (ESI) calcd. For C₂₄H₂₂NO₂S (M⁺-OH): 388.1371, found: 388.1371.

(±)-*N*-(3-Hydroxy-1-phenyl-3-(thiophen-3-ylethynyl)octan-2-yl)-4-methylbenzenesul**fonamide (166m)**

Yellow solid, mp = 147-149 °C; ¹H NMR (CDCl₃, 400 MHz): δ 0.89 (t, 3H, *J* = 6.5 Hz), 1.21-1.39 (m, 4H), 1.59-1.78 (m, 4H), 2.34 (s, 3H), 2.60-2.66 (m, 1H), 2.92 (s, 1H), 3.29 (dd, 1H, *J* = 14.0, 4.2 Hz), 3.78 (td, 1H, *J* = 9.0, 4.2 Hz), 5.13 (dd, 1H, *J* = 17.6, 9.0 Hz), 7.00-7.14 (m, 8H), 7.23-7.25 (m, 1H), 7.39-7.41 (m, 3H); ¹³C NMR (CDCl₃, 100 MHz): δ 14.1, 21.5, 22.6, 23.6, 32.0, 38.1, 38.3, 63.6, 74.7, 81.9, 89.1, 121.2, 125.3, 126.3, 126.8, 128.5, 129.3, 129.5, 130.0, 137.4, 137.7, 142.8; IR (NaCl, neat) ν : 3379, 3279, 3022, 2953, 2232, 1599, 1321, 1157 cm⁻¹; HRMS (ESI) calcd. For C₂₇H₃₀NO₂S₂ (M⁺-OH): 464.1718, found: 464.1722.

***N*-((2*S*)-1-((*tert*-Butyldimethylsilyl)oxy)-3-ethyl-3-hydroxy-5-phenylpent-4-yn-2-yl)-4-methylbenzenesulfonamide (166n)**

Yellow oil; obtained as two diastereomers in a ratio of 1:1; $[\alpha]_{\text{D}}^{25} +7.8$ (*c* 1.0, CHCl_3); ^1H NMR (CDCl_3 , 400 MHz): δ -0.02 (s, 3H), 0.01 (s, 3H), 0.03 (s, 3H), 0.04 (s, 3H), 0.86 (s, 18H), 0.93 (t, 3H, $J = 7.4$ Hz), 0.93 (t, 3H, $J = 7.3$ Hz), 1.54-1.65 (m, 2H), 1.72-1.83 (m, 2H), 2.32 (s, 3H), 2.40 (s, 3H), 3.40-3.44 (m, 2H), 3.66 (dd, 1H, $J = 10.3, 2.4$ Hz), 3.83 (dd, 1H, $J = 10.3, 2.4$ Hz), 3.93 (dd, 1H, $J = 10.2, 7.2$ Hz), 4.23 (s, 1H), 4.42 (d, 1H, $J = 10.2$ Hz), 4.52 (s, 1H), 5.19 (d, 1H, $J = 9.1$ Hz), 5.40 (d, 1H, $J = 9.6$ Hz), 7.17 (d, 2H, $J = 8.1$ Hz), 7.25-7.38 (m, 12H), 7.75-7.78 (m, 4H); ^{13}C NMR (CDCl_3 , 100MHz): δ -5.9, -5.7, -5.7, -5.7, 8.1, 8.4, 18.1, 18.1, 21.5, 21.5, 25.8, 31.4, 32.8, 57.4, 58.5, 64.7, 65.5, 75.2, 75.2, 76.8, 77.2, 77.4, 77.5, 86.0, 88.5, 89.35, 122.3, 122.3, 127.0, 127.1, 128.2, 128.3, 128.5, 128.6, 129.7, 129.7, 131.6, 131.8, 137.6, 138.5, 143.5, 143.5; IR (NaCl, neat) ν : 3381, 3019, 2399, 1339, 1215, 1161 cm^{-1} ; HRMS (ESI) calcd. For $\text{C}_{26}\text{H}_{36}\text{NO}_3\text{SSi}$ ($\text{M}^+ - \text{OH}$): 470.2185, found: 470.2189.

***N*-((2*S*)-3-Ethyl-1,3-dihydroxy-5-phenylpent-4-yn-2-yl)-4-methylbenzenesulfonamide (166o)**

Yellow solid; obtained as two diastereomers in a ratio of 4:1; mp = 100-103 °C; $[\alpha]_{\text{D}}^{25} -13.0$ (*c* 1.0, CHCl_3); major isomer: ^1H NMR (CDCl_3 , 400 MHz): δ 1.04 (t, 3H, $J = 7.4$ Hz), 1.67-1.84 (m, 2H), 2.29 (s, 3H), 3.14 (s, 1H), 3.36-3.44 (m, 1H), 3.71 (s, 1H), 3.81-3.91 (m, 2H), 5.57 (d, 1H, $J = 8.6$ Hz), 7.14 (d, 2H, $J = 8.1$ Hz), 7.26-7.32 (m, 5H), 7.76

(d, 2H, $J = 8.2$ Hz); ^{13}C NMR (CDCl_3 , 100 MHz): δ 8.2, 21.5, 32.7, 59.9, 62.9, 75.1, 86.4, 88.4, 121.9, 127.1, 128.2, 128.7, 129.7, 131.9, 137.4, 143.5; IR (NaCl, neat) ν : 3480, 3370, 3273, 2970, 1599, 1491, 1155 cm^{-1} ; HRMS (ESI) calcd. For $\text{C}_{20}\text{H}_{23}\text{NO}_4\text{SNa}$ ($\text{M}^+ + \text{Na}$): 396.1245, found: 396.1247.

***N*-((3*S*,4*S*)-4-Ethyl-4-hydroxy-1-(methylthio)-6-phenylhex-5-yn-3-yl)-4-methylbenzenesulfonamide (166p)**

Brown oil; $[\alpha]_{\text{D}}^{25} -31.0$ (c 1.0, CHCl_3); ^1H NMR (CDCl_3 , 400 MHz): δ 1.08 (t, 3H, $J = 7.3$ Hz), 1.61-1.83 (m, 3H), 1.94 (s, 3H), 2.16-2.25 (m, 2H), 2.32-2.39 (m, 4H), 2.73 (s, 1H), 3.65 (td, 1H, $J = 9.1, 2.8$ Hz), 5.12 (d, 1H, $J = 9.4$ Hz), 7.23-7.40 (m, 7H), 7.79 (d, 2H, $J = 8.2$ Hz); ^{13}C NMR (CDCl_3 , 100 MHz): δ 8.3, 15.2, 21.5, 30.7, 30.8, 31.6, 60.4, 74.7, 86.5, 89.0, 122.1, 127.1, 128.3, 128.7, 129.7, 131.8, 138.3, 143.5; IR (NaCl, neat) ν : 3370, 3273, 2970, 2230, 1491, 1155 cm^{-1} ; HRMS (ESI) calcd. For $\text{C}_{22}\text{H}_{26}\text{NO}_2\text{S}_2$ ($\text{M}^+ - \text{OH}$): 400.1405, found: 400.1403.

***N*-((3*S*,4*S*)-4-Ethyl-4-hydroxy-1-(methylsulfonyl)-6-phenylhex-5-yn-3-yl)-4-methylbenzenesulfonamide (166q)**

White solid, mp = 98-100 $^{\circ}\text{C}$; $[\alpha]_{\text{D}}^{25} +1.8$ (c 1.0, CHCl_3); ^1H NMR (CDCl_3 , 400 MHz): δ 1.01 (t, 3H, $J = 7.3$ Hz), 1.49-1.58 (m, 1H), 1.67-1.76 (m, 1H), 2.04-2.14 (m, 1H), 2.33 (s, 3H), 2.42-2.51 (m, 2H), 2.86 (s, 3H), 3.14 (t, 2H, $J = 8.2$ Hz), 3.58 (td, 1H, $J = 8.9, 3.9$ Hz), 5.09 (d, 1H, $J = 9.2$ Hz), 7.21 (d, 2H, $J = 8.0$ Hz), 7.28-7.35 (m, 5H), 7.76 (d, 2H, $J = 8.1$ Hz); ^{13}C NMR (CDCl_3 , 100 MHz): δ 8.3, 21.5, 23.7, 32.2, 40.6, 51.5, 59.5, 74.8,

86.9, 88.2, 121.8, 127.1, 128.3, 128.8, 129.7, 131.9, 137.9, 143.7; IR (NaCl, neat) ν : 3370, 3273, 3019, 2230, 1416, 1315, 1215 cm^{-1} ; HRMS (ESI) calcd. For $\text{C}_{22}\text{H}_{26}\text{NO}_4\text{S}_2$ ($\text{M}^+ - \text{OH}$): 432.1303, found: 432.1301.

(3*S*,4*S*)-3-Ethyl-6-methyl-4-(4-methylphenylsulfonamido)-1-phenylhept-1-yn-3-yl

Benzoate (167a)

White solid, mp = 70-72 °C; $[\alpha]_{\text{D}}^{25}$ -37.1 (*c* 1.0, CHCl_3); ^1H NMR (CDCl_3 , 400 MHz): δ 0.80 (d, 3H, J = 6.2 Hz), 0.84 (d, 3H, J = 6.0 Hz), 1.14 (t, 3H, J = 7.3 Hz), 1.32-1.56 (m, 3H), 1.97-2.06 (m, 1H), 2.19-2.34 (m, 4H), 4.19 (t, 1H, J = 9.8 Hz), 5.65 (d, 1H, J = 9.6 Hz), 7.11 (d, 2H, J = 8.0 Hz), 7.26-7.34 (m, 3H), 7.40-7.58 (m, 5H), 7.74 (d, 2H, J = 8.0 Hz), 7.98 (m, 2H, J = 7.8 Hz); ^{13}C NMR (CDCl_3 , 100 MHz): δ 8.7, 21.3, 21.5, 23.9, 24.0, 30.5, 41.5, 57.2, 83.5, 85.5, 88.9, 122.1, 126.8, 128.1, 128.4, 128.7, 129.3, 129.8, 130.3, 132.1, 133.2, 139.3, 142.7, 165.2; IR (NaCl, neat) ν : 3280, 3019, 2230, 1719, 1215 cm^{-1} ; HRMS (ESI) calcd. For $\text{C}_{30}\text{H}_{33}\text{NO}_4\text{SNa}$ ($\text{M}^+ + \text{Na}$): 526.2028, found: 526.2013.

(3*R*,4*S*)-3-Ethyl-6-methyl-4-(4-methylphenylsulfonamido)-1-phenylhept-1-yn-3-yl

benzoate (167a')

Yellow oil; $[\alpha]_{\text{D}}^{25}$ -29.9 (*c* 1.0, CHCl_3); ^1H NMR (CDCl_3 , 400 MHz): δ 0.86 (d, 3H, J = 5.8 Hz), 0.93 (d, 3H, J = 5.6 Hz), 1.00 (t, 3H, J = 7.3 Hz), 1.50-1.70 (m, 3H), 2.02-2.11 (m, 1H), 2.26 (s, 3H), 2.33-2.42 (m, 1H), 4.19 (t, 1H, J = 9.5 Hz), 5.60 (d, 1H, J = 9.6 Hz), 7.07 (d, 2H, J = 8.1 Hz), 7.25-7.53 (m, 8H), 7.73 (d, 2H, J = 8.2 Hz), 7.91 (m, 2H, J = 7.6 Hz); ^{13}C NMR (CDCl_3 , 100 MHz): δ 8.5, 21.4, 21.4, 23.9, 24.2, 28.5, 41.8, 58.3,

84.5, 86.5, 88.0, 122.1, 126.5, 128.2, 128.3, 128.8, 129.3, 129.8, 130.2, 131.9, 133.0, 139.4, 142.6, 165.0; IR (NaCl, neat) ν : 3273, 3019, 2341, 1719, 1451, 1215 cm^{-1} ; HRMS (ESI) calcd. For $\text{C}_{30}\text{H}_{33}\text{NO}_4\text{SNa}$ ($\text{M}^+ + \text{Na}$): 526.2028, found: 526.2025.

(3*S*,4*S*)-3-Ethyl-6-methyl-4-(4-methylphenylsulfonamido)-1-(*p*-tolyl)hept-1-yn-3-yl Benzoate (167b)

White solid, mp = 65-67 °C; $[\alpha]_{\text{D}}^{25}$ -38.2 (*c* 1.0, CHCl_3); ^1H NMR (CDCl_3 , 400 MHz): δ 0.80 (d, 3H, J = 6.2 Hz), 0.85 (d, 3H, J = 5.8 Hz), 1.12 (t, 3H, J = 7.3 Hz), 1.35-1.58 (m, 3H), 1.96-2.03 (m, 1H), 2.19-2.31 (m, 4H), 2.33 (s, 3H), 4.26 (t, 1H, J = 9.4 Hz), 5.78 (d, 1H, J = 9.5 Hz), 7.01-7.11 (m, 4H), 7.29 (d, 2H, J = 8.0 Hz), 7.37-7.54 (m, 3H), 7.73 (d, 2H, J = 8.2 Hz), 7.95 (d, 2H, J = 7.4 Hz); ^{13}C NMR (CDCl_3 , 100 MHz): δ 8.7, 21.4, 21.5, 21.5, 24.0, 24.1, 30.1, 41.5, 57.1, 83.4, 84.9, 89.0, 119.1, 126.8, 128.4, 129.1, 129.3, 129.9, 130.4, 132.0, 133.1, 138.8, 139.2, 142.7, 165.2; IR (NaCl, neat) ν : 3273, 3019, 2230, 1719, 1267, 1215 cm^{-1} ; HRMS (ESI) calcd. For $\text{C}_{31}\text{H}_{35}\text{NO}_4\text{SNa}$ ($\text{M}^+ + \text{Na}$): 540.2185, found: 540.2197.

(3*S*,4*S*)-3-Ethyl-1-(4-fluorophenyl)-6-methyl-4-(4-methylphenylsulfonamido)hept-1-yn-3-yl Benzoate (167c)

White solid, mp = 68-70 °C; $[\alpha]_{\text{D}}^{25}$ -26.9 (*c* 1.0, CHCl_3); ^1H NMR (CDCl_3 , 400 MHz): δ 0.78 (d, 3H, J = 5.8 Hz), 0.83 (d, 3H, J = 5.5 Hz), 1.14 (t, 3H, J = 7.3 Hz), 1.33-1.50 (m, 3H), 1.97-2.03 (m, 1H), 2.22-2.28 (m, 4H), 4.22 (t, 1H, J = 9.9 Hz), 5.96 (d, 1H, J = 5.5

Hz), 6.95 (t, 2H, $J = 8.6$ Hz), 7.10 (d, 2H, $J = 8.0$ Hz), 7.39-7.43 (m, 4H), 7.54 (t, 1H, $J = 7.4$ Hz), 7.74 (d, 2H, $J = 8.2$ Hz), 7.94 (d, 2H, $J = 8.2$ Hz); ^{13}C NMR (CDCl_3 , 100 MHz): δ 8.8, 21.3, 21.4, 23.9, 24.1, 30.3, 41.3, 57.3, 83.4, 85.4, 87.9, 115.4 (d, 1C, $J_{\text{C-F}} = 21.9$), 118.3 (d, 1C, $J_{\text{C-F}} = 3.3$), 126.7, 128.4, 129.3, 129.7, 130.2, 133.2, 134.2 (d, 1C, $J_{\text{C-F}} = 8.5$), 139.4, 142.7, 162.7 (d, 1C, $J_{\text{C-F}} = 248.4$), 165.3; IR (NaCl, neat) ν : 3279, 3022, 2959, 2232, 1722, 1506, 1267, 1094 cm^{-1} ; HRMS (ESI) calcd. For $\text{C}_{30}\text{H}_{32}\text{NO}_4\text{FSNa}$ ($\text{M}^+ + \text{Na}$): 544.1934, found: 544.1935.

(3S,4S)-3-Ethyl-6-methyl-4-(4-methylphenylsulfonamido)-1-(thiophen-3-yl)hept-1-yn-3-yl Benzoate (167d)

Yellow solid, mp = 71-73 °C; $[\alpha]_{\text{D}}^{25} -31.2$ (c 1.0, CHCl_3); ^1H NMR (CDCl_3 , 400 MHz): δ 0.79 (d, 3H, $J = 6.2$ Hz), 0.84 (d, 3H, $J = 5.9$ Hz), 1.13 (t, 3H, $J = 7.3$ Hz), 1.32-1.38 (m, 1H), 1.45-1.54 (m, 2H), 1.96-2.04 (m, 1H), 2.19-2.31 (m, 4H), 4.20 (td, 1H, $J = 9.5, 1.7$ Hz), 5.79 (d, 1H, $J = 9.6$ Hz), 7.08-7.14 (m, 3H), 7.21 (dd, 1H, $J = 5.0, 3.0$ Hz), 7.40-7.48 (m, 3H), 7.55 (t, 1H, $J = 7.5$ Hz), 7.75 (d, 2H, $J = 8.2$ Hz), 7.97 (d, 2H, $J = 7.6$ Hz); ^{13}C NMR (CDCl_3 , 100 MHz): δ 8.8, 21.3, 21.5, 23.9, 24.1, 30.4, 41.3, 57.3, 83.6, 84.1, 85.2, 121.2, 125.1, 126.8, 128.4, 129.3, 129.7, 130.0, 130.2, 130.3, 133.2, 139.3, 142.7, 165.2; IR (NaCl, neat) ν : 3273, 3019, 2230, 1719, 1267, 1215 cm^{-1} ; HRMS (ESI) calcd. For $\text{C}_{28}\text{H}_{31}\text{NO}_4\text{S}_2\text{Na}$ ($\text{M}^+ + \text{Na}$): 532.1592, found: 532.1606.

(±)-2-Methyl-4-(4-methylphenylsulfonamido)-5-(phenylethynyl)decan-5-yl Benzoate (167e)

White solid, mp = 57-59 °C; ^1H NMR (CDCl_3 , 400 MHz): δ 0.85-0.91 (m, 9H), 1.21-1.41(m, 5H), 1.47-1.63 (m, 4H), 1.82-1.90 (m, 1H), 2.12-2.17 (m, 1H), 2.29 (s, 3H), 4.23 (t, 1H, $J = 9.6$ Hz), 5.58 (d, 1H, $J = 9.6$ Hz), 7.12 (d, 2H, $J = 8.1$ Hz), 7.25-7.31 (m, 3H), 7.40-7.45 (m, 4H), 7.56 (t, 1H, $J = 7.5$ Hz), 7.75 (d, 2H, $J = 8.2$ Hz), 7.75 (d, 2H, $J = 7.6$ Hz); ^{13}C NMR (CDCl_3 , 100 MHz): δ 14.0, 21.3, 21.5, 22.5, 23.8, 24.0, 31.6, 37.2, 41.5, 57.4, 83.2, 85.8, 88.7, 122.1, 126.9, 128.2, 128.4, 128.7, 129.4, 129.7, 130.3, 132.1, 133.1, 139.3, 142.8, 165.2; IR (NaCl, neat) ν : 3279, 3019, 2957, 1719, 1315, 1269, 1215 cm^{-1} ; HRMS (ESI) calcd. For $\text{C}_{33}\text{H}_{39}\text{NO}_4\text{SNa}$ ($\text{M}^+ + \text{Na}$): 568.2498, found: 568.2498.

(±)-3-Cyclopropyl-6-methyl-4-(4-methylphenylsulfonamido)-1-phenylhept-1-yn-3-yl Benzoate (167f)

Yellow solid, mp = 140-142 °C; ^1H NMR (CDCl_3 , 400 MHz): δ 0.54-0.74 (m, 3H), 0.80 (d, 3H, $J = 6.1$ Hz), 0.85 (d, 3H, $J = 5.8$ Hz), 0.88-0.96 (m, 1H), 1.46-1.66 (m, 4H), 2.20 (s, 3H), 4.49 (t, 1H, $J = 9.6$ Hz), 6.00 (d, 1H, $J = 9.6$ Hz), 7.00 (d, 2H, $J = 8.1$ Hz), 7.22-7.29 (m, 3H), 7.34-7.38 (m, 4H), 7.49 (t, 1H, $J = 7.3$ Hz), 7.74 (d, 2H, $J = 8.1$ Hz), 7.93 (d, 2H, $J = 7.7$ Hz); ^{13}C NMR (CDCl_3 , 100 MHz): δ 3.0, 3.6, 16.5, 21.4, 21.5, 24.0, 24.2, 41.9, 59.1, 83.0, 85.2, 89.3, 121.9, 126.8, 128.2, 128.3, 128.8, 129.3, 129.8, 130.6, 132.1, 132.9, 139.3, 142.6, 165.1; IR (NaCl, neat) ν : 3279, 3019, 2961, 2232, 1717, 1275, 1215 cm^{-1} ; HRMS (ESI) calcd. For $\text{C}_{31}\text{H}_{33}\text{NO}_4\text{SNa}$ ($\text{M}^+ + \text{Na}$): 538.2028, found: 538.2028.

(3*R*,4*S*)-3-Ethyl-4-(4-methylphenylsulfonamido)-1-phenylhex-1-yn-3-yl Benzoate (167g)

Pale-yellow oil; $[\alpha]_D^{25} -45.3$ (c 1.0, CHCl_3); ^1H NMR (CDCl_3 , 400 MHz): δ 0.82 (t, 3H, $J = 7.4$ Hz), 1.11 (t, 3H, $J = 7.3$ Hz), 1.37-1.48 (m, 1H), 1.85-1.92 (m, 1H), 2.01-2.10 (m, 1H), 2.23-2.32 (m, 4H), 4.08 (td, 1H, $J = 9.7, 2.8$ Hz), 5.63 (d, 1H, $J = 9.6$ Hz), 7.11 (d, 2H, $J = 8.0$ Hz), 7.25-7.32 (m, 3H), 7.39-7.43 (m, 4H), 7.54 (t, 1H, $J = 7.2$ Hz), 7.75 (d, 2H, $J = 8.0$ Hz), 7.97 (d, 2H, $J = 7.8$ Hz); ^{13}C NMR (CDCl_3 , 100 MHz): δ 8.7, 11.1, 21.5, 24.7, 30.3, 60.4, 83.2, 85.6, 88.8, 122.1, 126.9, 128.2, 128.4, 128.7, 129.4, 129.7, 130.3, 132.1, 133.1, 139.1, 142.8, 165.1; IR (NaCl, neat) ν : 3279, 3019, 2359, 1717, 1271, 1215, 1157 cm^{-1} ; HRMS (ESI) calcd. For $\text{C}_{28}\text{H}_{29}\text{NO}_4\text{SNa}$ ($\text{M}^+ + \text{Na}$): 498.1715, found: 498.1719.

(3*S*,4*S*)-3-Ethyl-5-methyl-4-(4-methylphenylsulfonamido)-1-phenylhex-1-yn-3-yl Benzoate (167h)

Colouless solid, mp = 60-63 °C; $[\alpha]_D^{25} -43.0$ (c 1.0, CHCl_3); ^1H NMR (CDCl_3 , 400 MHz): δ 0.87 (d, 3H, $J = 7.0$ Hz), 0.95 (d, 3H, $J = 6.8$ Hz), 1.04 (t, 3H, $J = 7.3$ Hz), 2.05-2.15 (m, 1H), 2.20-2.37 (m, 5H), 4.12 (dd, 1H, $J = 10.0, 2.4$ Hz), 5.48 (s, 1H), 7.18 (d, 2H, $J = 8.0$ Hz), 7.28-7.35 (m, 3H), 7.39-7.45 (m, 4H), 7.56 (t, 1H, $J = 7.4$ Hz), 7.78 (d, 2H, $J = 8.2$ Hz), 7.98 (d, 2H, $J = 8.3$ Hz); ^{13}C NMR (CDCl_3 , 100 MHz): δ 8.5, 17.6, 21.5, 22.8, 28.7, 30.3, 62.5, 83.3, 86.0, 88.7, 122.0, 126.9, 128.3, 128.5, 128.8, 129.5, 129.7, 130.3, 132.0, 133.2, 139.2, 142.9, 165.0; IR (NaCl, neat) ν : 3279, 2967, 2232, 1721,

1269, 1159, 1094 cm^{-1} ; HRMS (ESI) calcd. For $\text{C}_{29}\text{H}_{31}\text{NO}_4\text{SNa}$ ($\text{M}^+ + \text{Na}$): 512.1872, found: 512.1868.

(3*S*,4*S*)-3-Ethyl-4-(4-methylphenylsulfonamido)-1,5-diphenylpent-1-yn-3-yl

Benzoate (167i)

Yellow oil; $[\alpha]_{\text{D}}^{25} -5.8$ (c 1.0, CHCl_3); ^1H NMR (CDCl_3 , 400 MHz): δ 1.15 (t, 3H, $J = 7.3$ Hz), 2.15-2.24 (m, 1H), 2.31 (s, 3H), 2.37-2.46 (m, 1H), 2.68 (dd, 1H, $J = 14.2, 8.4$ Hz), 3.20 (dd, 1H, $J = 14.2, 4.4$ Hz), 4.54 (td, 1H, $J = 9.4, 4.4$ Hz), 5.58 (d, 1H, $J = 9.7$ Hz), 6.99-7.12 (m, 7H), 7.31-7.34 (m, 3H), 7.41-7.57 (m, 7H), 7.96 (d, 2H, $J = 7.5$ Hz); ^{13}C NMR (CDCl_3 , 100 MHz): δ 8.6, 21.4, 30.3, 38.4, 60.1, 83.6, 85.3, 89.2, 122.0, 126.3, 126.6, 128.2, 128.4, 128.4, 128.8, 129.4, 129.6, 129.8, 130.2, 132.2, 133.2, 137.4, 138.5, 142.4, 165.2; IR (NaCl, neat) ν : 3381, 3019, 1715, 1267, 1215 cm^{-1} ; HRMS (ESI) calcd. For $\text{C}_{33}\text{H}_{31}\text{NO}_4\text{SNa}$ ($\text{M}^+ + \text{Na}$): 560.1872, found: 560.1879.

(3*S*,4*S*)-3-Methyl-4-(4-methylphenylsulfonamido)-1-phenylpent-1-yn-3-yl Benzoate (167j)

Colourless oil; $[\alpha]_{\text{D}}^{25} -21.5$ (c 1.0, CHCl_3); ^1H NMR (CDCl_3 , 400 MHz): δ 1.29 (d, 3H, $J = 6.6$ Hz), 1.87 (s, 3H), 2.36 (s, 3H), 3.91-3.98 (m, 1H), 5.05 (d, 1H, $J = 9.6$ Hz), 7.21-7.44 (m, 9H), 7.55 (t, 1H, $J = 7.3$ Hz), 7.79 (d, 2H, $J = 8.1$ Hz), 7.97 (d, 2H, $J = 7.3$ Hz); ^{13}C NMR (CDCl_3 , 100 MHz): δ 17.4, 21.5, 24.0, 56.5, 78.2, 86.0, 87.5, 121.8, 127.1, 128.2, 128.4, 128.8, 129.7, 129.7, 130.4, 132.0, 133.1, 137.9, 143.4, 164.4; IR (NaCl,

neat) ν : 3273, 3019, 1722, 1275, 1215, 1092 cm^{-1} ; HRMS (ESI) calcd. For $\text{C}_{26}\text{H}_{25}\text{NO}_4\text{SNa}$ ($\text{M}^+ + \text{Na}$): 470.1402, found: 470.1407.

(3S,4S)-3-Methyl-4-(4-methylphenylsulfonamido)-1-phenylhept-1-yn-3-yl Benzoate (167k)

Yellow solid, mp = 60-63 $^{\circ}\text{C}$; $[\alpha]_{\text{D}}^{25} -52.7$ (c 1.0, CHCl_3); ^1H NMR (CDCl_3 , 400 MHz): δ 0.84 (t, 3H, $J = 7.3$ Hz), 1.19-1.23 (m, 1H), 1.35-1.40 (m, 1H), 1.46-1.53 (m, 1H), 1.83 (s, 3H), 1.87-1.91 (m, 1H), 2.35 (s, 3H), 4.00 (td, 1H, $J = 9.8, 2.9$ Hz), 4.95 (d, 1H, $J = 9.8$ Hz), 7.19 (d, 2H, $J = 8.0$ Hz), 7.29-7.32 (m, 3H), 7.40-7.45 (m, 4H), 7.56 (t, 1H, $J = 7.4$ Hz), 7.76 (d, 2H, $J = 8.2$ Hz), 7.76 (d, 2H, $J = 7.3$ Hz); ^{13}C NMR (CDCl_3 , 75 MHz): δ 14.0, 19.3, 21.5, 24.6, 34.1, 60.5, 78.7, 86.7, 87.5, 122.0, 126.9, 128.2, 128.3, 128.7, 129.5, 129.7, 130.5, 132.0, 133.0, 138.9, 143.0, 164.7; IR (NaCl, neat) ν : 3273, 3019, 2342, 1721, 1273, 1215, 1159 cm^{-1} ; HRMS (ESI) calcd. For $\text{C}_{28}\text{H}_{29}\text{NO}_4\text{SNa}$ ($\text{M}^+ + \text{Na}$): 498.1715, found: 498.1711.

(1S)-2-Methyl-1-(4-methylphenylsulfonamido)-1,4-diphenylbut-3-yn-2-yl Benzoate (167l)

Yellow solid; obtained as two diastereomers in a ratio of 3.3:1; mp = 168-170 $^{\circ}\text{C}$; $[\alpha]_{\text{D}}^{25} +98.1$ (c 1.0, CHCl_3); major isomer: ^1H NMR (CDCl_3 , 400 MHz): δ 1.91 (s, 3H), 2.20 (s, 3H), 4.90 (d, 1H, $J = 9.0$ Hz), 6.41 (d, 1H, $J = 8.9$ Hz), 6.89 (d, 2H, $J = 8.2$ Hz), 7.14-7.53 (m, 15H), 7.80 (d, 2H, $J = 7.7$ Hz); ^{13}C NMR (CDCl_3 , 100 MHz): δ 21.4, 24.9, 64.7, 77.8, 86.4, 88.2, 121.9, 127.0, 127.8, 128.2, 128.2, 128.7, 128.8, 129.2, 129.6, 130.3, 131.9,

132.0, 133.0, 136.5, 137.3, 142.9, 164.6; IR (NaCl, neat) ν : 3275, 3019, 2359, 1719, 1273, 1215, 1161 cm^{-1} ; HRMS (ESI) calcd. For $\text{C}_{31}\text{H}_{27}\text{NO}_4\text{SNa}$ ($\text{M}^+ + \text{Na}$): 532.1559, found: 532.1556.

($\pm$)-3-(1-(4-Methylphenylsulfonamido)-2-phenylethyl)-1-(thiophen-3-yl)oct-1-yn-3-yl Benzoate (167m)

Yellow solid, mp = 64-66 °C; ^1H NMR (CDCl_3 , 400 MHz): δ 0.84 (t, 3H, J = 6.9 Hz), 1.14-1.27 (m, 4H), 1.43-1.57 (m, 2H), 2.03 (ddd, 1H, J = 25.8, 11.9, 4.8 Hz), 2.31 (s, 3H), 2.40 (ddd, 1H, J = 25.8, 11.9, 4.8 Hz), 2.89 (dd, 1H, J = 14.2, 7.9 Hz), 3.33 (dd, 1H, J = 14.2, 4.3 Hz), 4.38 (ddd, 1H, J = 17.0, 8.0, 4.4 Hz), 7.03 (d, 2H, J = 8.1 Hz), 7.11-7.15 (m, 6H), 7.29 (dd, 1H, J = 5.0, 3.0 Hz), 7.38 (t, 2H, J = 7.7 Hz), 7.45 (d, 2H, J = 8.2 Hz), 7.50-7.56 (m, 2H), 7.82 (d, 2H, J = 7.2 Hz); ^{13}C NMR (CDCl_3 , 75 MHz): δ 14.1, 21.5, 22.5, 23.8, 31.6, 36.8, 38.4, 60.3, 83.2, 84.4, 85.3, 121.1, 125.2, 126.2, 126.7, 128.4, 128.4, 129.4, 129.6, 129.8, 130.2, 133.2, 137.5, 138.6, 142.5, 165.2; IR (NaCl, neat) ν : 3279, 3019, 2951, 1717, 1269, 1215, 1157 cm^{-1} ; HRMS (ESI) calcd. For $\text{C}_{34}\text{H}_{35}\text{NO}_4\text{S}_2\text{Na}$ ($\text{M}^+ + \text{Na}$): 608.1905, found: 608.1900.

(4S)-5-((*tert*-Butyldimethylsilyl)oxy)-3-ethyl-4-(4-methylphenylsulfonamido)-1-phenylpent-1-yn-3-yl Benzoate (167n)

Yellow oil; obtained as two diastereomers in a ratio of 1.15:1; $[\alpha]_{\text{D}}^{25}$ -8.7 (c 1.0, CHCl_3); ^1H NMR (CDCl_3 , 400 MHz): δ -0.05 (s, 3H), -0.04 (s, 3H), -0.03 (s, 3H), -0.02 (s, 3H),

0.81 (s, 9H), 0.84 (s, 9H), 1.09 (t, 3H, $J = 7.3$ Hz), 1.17 (t, 3H, $J = 7.3$ Hz), 2.09-2.19 (m, 2H), 2.27 (s, 3H), 2.29 (s, 3H), 2.32-2.49 (m, 2H), 3.51 (dd, 1H, $J = 10.6, 5.5$ Hz), 3.83 (dd, 1H, $J = 10.6, 5.5$ Hz), 4.00-4.07 (m, 2H), 4.13-4.15 (m, 1H), 4.37-4.41 (s, 1H), 5.63 (d, 1H, $J = 9.3$ Hz), 5.68 (d, 1H, $J = 9.5$ Hz), 7.08-7.14 (m, 4H), 7.08-7.14 (m, 4H), 7.14-7.46 (m, 14H), 7.53-7.56 (m, 2H), 7.71-7.79 (m, 4H), 7.92-7.98 (m, 4H); ^{13}C NMR (CDCl_3 , 100 MHz): δ -5.6, -5.6, 8.6, 8.7, 18.3, 18.3, 21.5, 25.8, 25.9, 28.9, 30.1, 57.3, 58.9, 62.2, 62.6, 81.5, 82.7, 85.7, 85.8, 88.8, 89.1, 122.1, 122.2, 127.0, 127.1, 128.2, 128.3, 128.7, 128.8, 128.9, 129.5, 129.6, 129.7, 129.8, 130.4, 130.6, 130.6, 131.9, 131.9, 132.9, 133.0, 137.9, 138.3, 143.1, 143.1, 164.7, 165.1; IR (NaCl, neat) ν : 3273, 2936, 2230, 1788, 1719, 1450, 1267 cm^{-1} ; HRMS (ESI) calcd. For $\text{C}_{33}\text{H}_{41}\text{NO}_5\text{SSiNa}$ ($\text{M}^+ + \text{Na}$): 614.2372, found: 614.2366.

(2S)-3-Ethyl-2-(4-methylphenylsulfonamido)-5-phenylpent-4-yne-1,3-diyl Dibenzoate (167o)

Yellow solid; obtained as two diastereomers in a ratio of 4:1; mp = 61-64 °C; $[\alpha]_{\text{D}}^{25} -26.2$ (c 1.0, CHCl_3); major isomer: ^1H NMR (CDCl_3 , 400 MHz): δ 1.16 (t, 3H, $J = 7.3$ Hz), 2.15 (s, 3H), 2.27-2.32 (m, 1H), 2.41-2.49 (m, 1H), 4.48-4.70 (m, 3H), 6.12 (d, 1H, $J = 9.6$ Hz), 6.95 (d, 2H, $J = 8.0$ Hz), 7.24-7.55 (m, 11H), 7.70 (d, 2H, $J = 8.2$ Hz), 7.84 (d, 2H, $J = 7.5$ Hz), 7.88 (d, 2H, $J = 7.7$ Hz); ^{13}C NMR (CDCl_3 , 100 MHz): δ 8.5, 21.5, 30.4, 57.1, 64.0, 81.4, 84.6, 89.5, 121.7, 126.7, 128.2, 128.5, 128.9, 129.5, 129.8, 129.8, 132.1, 133.1, 133.4, 138.5, 140.2, 165.1, 166.5; IR (NaCl, neat) ν : 3283, 3015, 2228, 1722, 1715, 1329, 1271, 1161 cm^{-1} ; HRMS (ESI) calcd. For $\text{C}_{34}\text{H}_{31}\text{NO}_6\text{SNa}$ ($\text{M}^+ + \text{Na}$): 604.1770, found: 604.1771.

(3*S*,4*S*)-3-Ethyl-4-(4-methylphenylsulfonamido)-6-(methylsulfonyl)-1-phenylhex-1-yn-3-yl Benzoate (167p)

White solid, mp = 151-153 °C; $[\alpha]_D^{25}$ -42.3 (*c* 0.83, CHCl₃); ¹H NMR (CDCl₃, 400 MHz): δ 1.07 (t, 3H, *J* = 7.2 Hz), 1.91-2.04 (m, 2H), 2.16-2.26 (m, 4H), 2.42-2.49 (m, 1H), 2.88 (s, 3H), 3.15-3.33 (m, 2H), 4.08 (t, 1H, *J* = 8.8 Hz), 6.38 (d, 1H, *J* = 9.3 Hz), 7.03 (d, 2H, *J* = 7.9 Hz), 7.27-7.29 (m, 5H), 7.40-7.48 (m, 2H), 7.54-7.60 (m, 1H), 7.72 (d, 2H, *J* = 8.0 Hz), 7.95 (d, 2H, *J* = 7.6 Hz); ¹³C NMR (CDCl₃, 100 MHz): δ 8.7, 21.5, 24.0, 30.9, 41.2, 51.2, 57.5, 82.6, 84.3, 89.6, 121.6, 127.1, 128.1, 128.5, 129.0, 129.6, 129.9, 130.2, 132.1, 133.6, 138.1, 143.3, 165.5; IR (NaCl, neat) ν : 3273, 3019, 2230, 1719, 1451, 1215 cm⁻¹; HRMS (ESI) calcd. For C₂₉H₃₁NO₆S₂Na (M⁺+Na): 576.1491, found: 576.1497.

(3*S*,4*S*)-4-(*N*-Allyl-4-methylphenylsulfonamido)-3-ethyl-6-methyl-1-phenylhept-1-yn-3-yl Benzoate (156a)

Colourless oil; $[\alpha]_D^{25}$ -86.9 (*c* 1.0, CHCl₃); ¹H NMR (CDCl₃, 400 MHz): δ 0.89 (d, 3H, *J* = 5.7 Hz), 1.00 (d, 3H, *J* = 5.3 Hz), 1.12 (t, 3H, *J* = 7.3 Hz), 1.53-1.63 (m, 2H), 1.99-2.13 (m, 2H), 2.35 (m, 3H), 2.58-2.67 (m, 1H), 4.11-4.26 (m, 2H), 4.96-5.08 (m, 3H), 5.78-5.88 (m, 1H), 7.19 (d, 2H, *J* = 7.9 Hz), 7.26-7.30 (m, 3H), 7.39-7.58 (m, 5H), 7.76 (d, 2H, *J* = 8.0 Hz), 8.01 (m, 2H, *J* = 7.8 Hz); ¹³C NMR (CDCl₃, 100 MHz): δ 8.9, 21.5, 21.8, 23.6, 24.0, 29.2, 37.7, 46.8, 59.7, 84.0, 87.0, 89.3, 116.6, 122.3, 128.1, 128.2, 128.4, 128.7, 129.2, 129.6, 130.9, 131.8, 133.0, 136.4, 137.8, 143.2, 164.1; IR (NaCl, neat) ν :

3019, 2342, 1721, 1267, 1215, 1090 cm^{-1} ; HRMS (ESI) calcd. For $\text{C}_{33}\text{H}_{37}\text{NO}_4\text{SNa}$ ($\text{M}^+ + \text{Na}$): 566.2341, found: 566.2351.

(3*R*,4*S*)-4-(*N*-Allyl-4-methylphenylsulfonamido)-3-ethyl-6-methyl-1-phenylhept-1-yn-3-yl Benzoate (156a')

Colourless oil; $[\alpha]_{\text{D}}^{25} -26.6$ (c 1.0, CHCl_3); ^1H NMR (CDCl_3 , 400 MHz): δ 0.89 (d, 3H, J = 5.8 Hz), 0.94 (d, 3H, J = 7.5 Hz), 1.17 (t, 3H, J = 7.4 Hz), 1.53-1.63 (m, 2H), 2.02 (t, 1H, J = 9.8 Hz), 2.27-2.34 (m, 4H), 2.45-2.51 (m, 1H), 4.22-4.32 (m, 2H), 4.80 (d, 1H, J = 10.7 Hz), 4.95 (d, 1H, J = 10.2 Hz), 5.06 (d, 1H, J = 17.2 Hz), 5.695.79 (m, 1H), 7.17 (d, 2H, J = 8.0 Hz), 7.24-7.30 (m, 3H), 7.39-7.54 (m, 5H), 7.74 (d, 2H, J = 8.0 Hz), 8.07 (m, 2H, J = 7.6 Hz); ^{13}C NMR (CDCl_3 , 100 MHz): δ 8.8, 21.5, 21.6, 23.7, 24.2, 30.6, 38.2, 47.0, 61.0, 81.5, 87.3, 89.0, 116.5, 122.4, 128.0, 128.3, 128.4, 128.7, 129.3, 129.9, 130.8, 131.7, 132.9, 136.2, 138.0, 143.2, 164.7; IR (NaCl, neat) ν : 3019, 2342, 1719, 1333, 1266, 1215, 1026 cm^{-1} ; HRMS (ESI) calcd. For $\text{C}_{33}\text{H}_{37}\text{NO}_4\text{SNa}$ ($\text{M}^+ + \text{Na}$): 566.2341, found: 566.2337.

(3*S*,4*S*)-4-(*N*-Allyl-4-methylphenylsulfonamido)-3-ethyl-6-methyl-1-(*p*-tolyl)hept-1-yn-3-yl Benzoate (156b)

Colourless oil; $[\alpha]_{\text{D}}^{25} -77.0$ (c 1.0, CHCl_3); ^1H NMR (CDCl_3 , 400 MHz): δ 0.88 (d, 3H, J = 5.8 Hz), 0.99 (d, 3H, J = 5.4 Hz), 1.11 (t, 3H, J = 7.4 Hz), 1.54-1.59 (m, 2H), 1.99-2.11 (m, 2H), 2.33 (s, 3H), 2.35 (s, 3H), 2.59-2.65 (m, 1H), 4.12-4.25 (m, 2H), 4.97-5.08 (m,

3H), 5.79-5.87 (m, 1H), 7.09 (d, 2H, $J = 7.9$ Hz), 7.19 (d, 2H, $J = 8.1$ Hz), 7.29 (d, 2H, $J = 7.9$ Hz), 7.44 (t, 3H, $J = 7.6$ Hz), 7.55 (t, 1H, $J = 7.4$ Hz), 7.76 (d, 2H, $J = 8.1$ Hz), 8.02 (d, 2H, $J = 7.6$ Hz); ^{13}C NMR (CDCl_3 , 100 MHz): δ 8.9, 21.5, 21.5, 21.8, 23.7, 24.0, 29.2, 37.8, 46.8, 59.6, 84.1, 86.3, 89.4, 116.6, 119.2, 128.1, 128.4, 129.0, 129.2, 129.6, 130.9, 131.7, 133.0, 136.4, 137.8, 138.9, 143.2, 164.1; IR (NaCl, neat) ν : 2970, 2230, 1724, 1339, 1265 cm^{-1} ; HRMS (ESI) calcd. For $\text{C}_{34}\text{H}_{39}\text{NO}_4\text{SNa}$ ($\text{M}^+ + \text{Na}$): 580.2498, found: 580.2498.

(3*S*,4*S*)-4-(*N*-Allyl-4-methylphenylsulfonamido)-3-ethyl-1-(4-fluorophenyl)-6-methylhept-1-yn-3-yl Benzoate (156c)

Colourless oil; $[\alpha]_{\text{D}}^{25} -75.7$ (c 1.0, CHCl_3); ^1H NMR (CDCl_3 , 400 MHz): δ 0.90 (d, 3H, $J = 5.5$ Hz), 1.01 (d, 3H, $J = 5.2$ Hz), 1.14 (t, 3H, $J = 7.3$ Hz), 1.54-1.57 (m, 2H), 1.98-2.11 (m, 2H), 2.36 (s, 3H), 2.62-2.67 (m, 1H), 4.17-4.19 (m, 2H), 4.92-5.07 (m, 3H), 5.78-5.85 (m, 1H), 6.98 (t, 2H, $J = 8.6$ Hz), 7.19 (d, 2H, $J = 8.1$ Hz), 7.40-7.46 (m, 4H), 7.56 (t, 3H, $J = 7.4$ Hz), 7.76 (d, 2H, $J = 8.2$ Hz), 8.01 (d, 2H, $J = 7.6$ Hz); ^{13}C NMR (CDCl_3 , 100 MHz): δ 9.0, 21.5, 21.8, 23.7, 24.0, 29.2, 37.6, 46.8, 60.0, 83.9, 86.7, 88.4, 115.5 (1C, d, $J_{\text{C-F}} = 22.1$ Hz), 116.6, 118.4 (1C, d, $J_{\text{C-F}} = 3.4$ Hz), 128.1, 128.5, 129.3, 129.5, 130.9, 133.1, 133.9 (1C, d, $J_{\text{C-F}} = 8.4$ Hz), 136.4, 137.9, 143.2, 162.7 (1C, d, $J_{\text{C-F}} = 248.6$ Hz), 164.1; IR (NaCl, neat) ν : 3019, 2959, 1724, 1601, 1506, 1265, 1155 cm^{-1} ; HRMS (ESI) calcd. For $\text{C}_{33}\text{H}_{36}\text{NO}_4\text{FSNa}$ ($\text{M}^+ + \text{Na}$): 584.2247, found: 584.2238.

(3*S*,4*S*)-4-(*N*-allyl-4-methylphenylsulfonamido)-3-ethyl-6-methyl-1-(thiophen-3-yl)hept-1-yn-3-yl Benzoate (156d)

Colourless oil; $[\alpha]_D^{25} -74.7$ (c 1.0, CHCl_3); ^1H NMR (CDCl_3 , 400 MHz): δ 0.88 (d, 3H, $J = 5.8$ Hz), 0.99 (d, 3H, $J = 5.4$ Hz), 1.11 (t, 3H, $J = 7.4$ Hz), 1.51-1.56 (m, 2H), 1.97-2.12 (m, 2H), 2.38 (s, 3H), 2.57-2.66 (m, 1H), 4.17 (d, 2H, $J = 6.1$ Hz), 4.93-5.08 (m, 3H), 5.77-5.87 (m, 1H), 7.09 (d, 2H, $J = 5.0$ Hz), 7.20-7.24 (m, 3H), 7.42-7.46 (m, 3H), 7.56 (t, 1H, $J = 7.4$ Hz), 7.76 (d, 2H, $J = 8.2$ Hz), 8.00 (d, 2H, $J = 7.4$ Hz); ^{13}C NMR (CDCl_3 , 100 MHz): δ 8.9, 215, 21.8, 23.7, 24.0, 29.2, 37.6, 46.8, 59.8, 84.0, 84.6, 86.5, 116.5, 121.3, 125.2, 128.1, 128.4, 129.2, 129.6, 129.6, 130.0, 130.9, 133.0, 136.4, 137.8, 143.2, 164.1; IR (NaCl, neat) ν : 2936, 2230, 1718, 1450, 1267 cm^{-1} ; HRMS (ESI) calcd. For $\text{C}_{31}\text{H}_{35}\text{NO}_4\text{S}_2\text{Na}$ ($\text{M}^+ + \text{Na}$): 572.1905, found: 572.1907.

($\pm$)-4-(*N*-Allyl-4-methylphenylsulfonamido)-2-methyl-5-(phenylethynyl)decan-5-yl Benzoate (156e)

Colourless oil; ^1H NMR (CDCl_3 , 400 MHz): δ 0.85-0.90 (m, 6H), 0.98 (d, 3H, $J = 6.2$ Hz), 1.20-1.29 (m, 5H), 1.51-1.65 (m, 3H), 1.79-1.87 (m, 1H), 2.03 (t, 1H, $J = 12.0$ Hz), 2.35 (s, 3H), 2.44-2.52 (m, 1H), 4.14-4.26 (m, 2H), 4.97-5.10 (m, 3H), 5.83-5.93 (m, 1H), 7.19 (d, 2H, $J = 8.0$ Hz), 7.28-7.46 (m, 6H), 7.56 (t, 1H, $J = 7.4$ Hz), 7.78 (d, 2H, $J = 8.2$ Hz), 8.00 (d, 2H, $J = 7.4$ Hz); ^{13}C NMR (CDCl_3 , 100 MHz): δ 14.1, 21.5, 21.7, 22.4, 23.7, 23.9, 31.6, 36.1, 37.8, 46.9, 60.1, 83.9, 87.2, 89.2, 116.6, 122.3, 128.1, 128.3, 128.4,

128.7, 129.3, 129.6, 130.9, 131.8, 133.0, 136.6, 138.1, 143.1, 164.2; IR (NaCl, neat) ν : 3019, 2957, 1719, 1338, 1267, 1215 cm^{-1} ; HRMS (ESI) calcd. For $\text{C}_{36}\text{H}_{43}\text{NO}_4\text{SNa}$ ($\text{M}^+ + \text{Na}$): 608.2811, found: 608.2818.

($\pm$)-4-(*N*-Allyl-4-methylphenylsulfonamido)-3-cyclopropyl-6-methyl-1-phenylhept-1-yn-3-yl Benzoate (156f)

Colourless oil; ^1H NMR (CDCl_3 , 400 MHz): δ 0.49-0.51 (m, 1H), 0.67-0.69 (m, 2H), 0.87 (d, 3H, $J = 6.4$ Hz), 1.00 (d, 3H, $J = 6.4$ Hz), 1.16-1.21 (m, 1H), 1.51-1.65 (m, 3H), 2.02 (t, 1H, $J = 12.0$ Hz), 2.36 (s, 3H), 4.20-4.21 (m, 2H), 4.97-5.09 (m, 3H), 5.72-5.82 (m, 1H), 7.18-7.46 (m, 10H), 7.56 (t, 1H, $J = 7.2$ Hz), 7.77 (d, 2H, $J = 8.0$ Hz), 8.02 (d, 2H, $J = 7.6$ Hz); ^{13}C NMR (CDCl_3 , 100 MHz): δ 4.4, 4.6, 17.1, 21.5, 21.7, 23.5, 24.0, 38.1, 47.1, 62.7, 83.3, 86.7, 90.2, 116.6, 122.0, 127.9, 128.3, 128.4, 128.8, 129.2, 129.6, 131.2, 131.9, 132.8, 136.4, 138.5, 143.0, 164.00; IR (NaCl, neat) ν : 2956, 2928, 1722, 1339, 1215 cm^{-1} ; HRMS (ESI) calcd. For $\text{C}_{34}\text{H}_{38}\text{NO}_4\text{S}$ ($\text{M}^+ + \text{H}$): 556.2522, found: 556.2524.

(3*S*,4*S*)-4-(*N*-Allyl-4-methylphenylsulfonamido)-3-ethyl-1-phenylhex-1-yn-3-yl Benzoate (156g)

Pale-yellow oil; $[\alpha]_{\text{D}}^{25} -74.5$ (c 1.0, CHCl_3); ^1H NMR (CDCl_3 , 400 MHz): δ 0.86 (t, 3H, $J = 7.2$ Hz), 1.11 (t, 3H, $J = 7.3$ Hz), 1.93-2.03 (m, 2H), 2.12-2.21 (m, 1H), 2.35 (s, 3H), 2.62-2.71 (m, 1H), 4.07-4.16 (m, 2H), 4.80 (d, 1H, $J = 6.2$ Hz), 5.00 (d, 1H, $J = 10.1$ Hz), 5.09 (d, 1H, $J = 17.2$ Hz), 5.90-6.00 (m, 1H), 7.19-7.33 (m, 5H), 7.40-7.46 (m, 4H), 7.55

(t, 1H, $J = 7.3$ Hz), 7.77 (d, 2H, $J = 7.9$ Hz), 7.97 (d, 2H, $J = 7.7$ Hz); ^{13}C NMR (CDCl_3 , 100 MHz): δ 8.9, 11.9, 21.4, 21.5, 29.3, 46.9, 63.1, 84.1, 87.0, 89.2, 116.7, 122.3, 128.1, 128.2, 128.4, 128.7, 129.3, 129.6, 130.8, 131.8, 133.0, 136.2, 137.7, 143.2, 164.2; IR (NaCl, neat) ν : 3017, 2232, 1721, 1341, 1269, 1215 cm^{-1} ; HRMS (ESI) calcd. For $\text{C}_{31}\text{H}_{33}\text{NO}_4\text{SNa}(\text{M}^+ + \text{Na})$: 538.2028, found: 538.2020.

(3*S*,4*S*)-4-(*N*-Allyl-4-methylphenylsulfonamido)-3-ethyl-5-methyl-1-phenylhex-1-yn-3-yl Benzoate (156h)

Yellow oil; $[\alpha]_{\text{D}}^{25} -49.9$ (c 1.0, CHCl_3); ^1H NMR (CDCl_3 , 400 MHz): δ 0.95 (d, 3H, $J = 6.6$ Hz), 1.01 (t, 3H, $J = 7.3$ Hz), 1.16 (d, 3H, $J = 6.6$ Hz), 1.78-1.87 (m, 1H), 2.38 (s, 3H), 2.43-2.53 (m, 1H), 2.66-2.75 (m, 1H), 4.08-4.20 (m, 2H), 4.88 (d, 1H, $J = 10.2$ Hz), 5.04 (d, 1H, $J = 10.2$ Hz), 5.13 (d, 1H, $J = 17.2$ Hz), 5.96-6.06 (m, 1H), 7.24-7.46 (m, 9H), 7.56 (t, 1H, $J = 7.4$ Hz), 7.84 (d, 2H, $J = 8.2$ Hz), 8.06 (d, 2H, $J = 7.6$ Hz); ^{13}C NMR (CDCl_3 , 100 MHz): δ 8.8, 21.3, 21.5, 22.4, 30.0, 30.0, 47.6, 66.3, 85.0, 87.2, 89.0, 117.4, 122.1, 128.3, 128.4, 128.9, 129.2, 129.8, 130.7, 131.8, 133.0, 135.8, 137.8, 143.1, 164.3; IR (NaCl, neat) ν : 3019, 1719, 1337, 1269, 1215 cm^{-1} ; HRMS (ESI) calcd. For $\text{C}_{32}\text{H}_{35}\text{NO}_4\text{SNa}(\text{M}^+ + \text{Na})$: 552.2185, found: 552.2186.

(3*S*,4*S*)-4-(*N*-Allyl-4-methylphenylsulfonamido)-3-ethyl-1,5-diphenylpent-1-yn-3-yl Benzoate (156i)

White solid, mp = 56-58 $^{\circ}\text{C}$; $[\alpha]_{\text{D}}^{25} -54.9$ (c 1.0, CHCl_3); ^1H NMR (CDCl_3 , 400 MHz): δ 1.14 (t, 3H, $J = 7.3$ Hz), 2.34-2.41 (m, 4H), 2.71-2.80 (m, 1H), 3.06 (dd, 1H, $J = 14.6, 8.6$

Hz), 3.43 (dd, 1H, $J = 14.6, 5.0$ Hz), 4.08 (dd, 1H, $J = 16.6, 7.6$ Hz), 4.34 (dd, 1H, $J = 16.6, 4.4$ Hz), 5.00-5.09 (m, 2H), 5.45 (dd, 1H, $J = 8.4, 5.0$ Hz), 5.78-5.88 (m, 1H), 7.03 (d, 2H, $J = 8.2$ Hz), 7.15-7.22 (m, 7H), 7.32-7.56 (m, 8H), 7.89 (d, 2H, $J = 7.6$ Hz); ^{13}C NMR (CDCl_3 , 100 MHz): δ 8.5, 21.5, 29.0, 35.5, 46.9, 62.6, 83.9, 87.0, 89.4, 116.8, 122.2, 126.4, 128.0, 128.3, 128.4, 128.7, 128.8, 129.2, 129.5, 129.6, 130.5, 131.9, 132.9, 136.1, 137.0, 138.5, 142.9, 164.1; IR (NaCl, neat) ν : 3019, 2340, 1722, 1491, 1267, 1215, 1157 cm^{-1} ; HRMS (ESI) calcd. For $\text{C}_{36}\text{H}_{35}\text{NO}_4\text{SNa}$ ($\text{M}^+ + \text{Na}$): 600.2185, found: 600.2184.

(3*S*,4*S*)-4-(*N*-Allyl-4-methylphenylsulfonamido)-3-methyl-1-phenylpent-1-yn-3-yl

Benzoate (156j)

Colourless oil; $[\alpha]_{\text{D}}^{25} -21.2$ (c 1.0, CHCl_3); ^1H NMR (CDCl_3 , 400 MHz): δ 1.29 (d, 3H, $J = 6.9$ Hz), 2.02 (s, 3H), 2.42 (s, 3H), 3.99 (dd, 1H, $J = 16.6, 6.6$ Hz), 4.13 (dd, 1H, $J = 16.5, 5.8$ Hz), 4.54 (q, 1H, $J = 6.9$ Hz), 5.05 (d, 1H, $J = 10.4$ Hz), 5.14 (m, 1H, $J = 17.7$ Hz), 5.92-6.02 (m, 1H), 7.26-7.32 (m, 5H), 7.41-7.46 (m, 4H), 7.56 (t, 1H, $J = 7.4$ Hz), 7.77 (d, 2H, $J = 8.2$ Hz), 8.00 (d, 2H, $J = 7.3$ Hz); ^{13}C NMR (CDCl_3 , 100 MHz): δ 13.7, 21.6, 24.5, 46.8, 60.0, 78.8, 87.0, 88.4, 117.0, 122.1, 127.5, 128.3, 128.4, 128.7, 129.6, 129.7, 130.8, 131.8, 133.0, 136.1, 137.4, 143.4, 164.1; IR (NaCl, neat) ν : 3019, 2230, 1719, 1273, 1215 cm^{-1} ; HRMS (ESI) calcd. For $\text{C}_{29}\text{H}_{29}\text{NO}_4\text{SNa}$ ($\text{M}^+ + \text{Na}$): 510.1715, found: 510.1732.

(3*S*,4*S*)-4-(*N*-Allyl-4-methylphenylsulfonamido)-3-methyl-1-phenylhept-1-yn-3-yl**Benzoate (156k)**

Colourless oil; $[\alpha]_{\text{D}}^{25} -78.8$ (c 1.0, CHCl_3); ^1H NMR (CDCl_3 , 400 MHz): δ 0.93 (t, 3H, $J = 7.3$ Hz), 1.27-1.38 (m, 3H), 1.91-2.03 (m, 4H), 2.38 (s, 3H), 4.15 (d, 2H, $J = 5.9$ Hz), 4.50 (s, 1H), 5.02 (d, 1H, $J = 10.2$ Hz), 5.11 (d, 1H, $J = 17.1$ Hz), 5.84-5.94 (m, 1H), 7.22-7.29 (m, 5H), 7.39-7.46 (m, 4H), 7.56 (t, 1H, $J = 7.4$ Hz), 7.77 (d, 2H, $J = 8.2$ Hz), 8.00 (d, 2H, $J = 7.4$ Hz); ^{13}C NMR (CDCl_3 , 100 MHz): δ 14.2, 20.0, 21.5, 24.9, 46.7, 64.6, 79.0, 87.5, 88.5, 117.1, 122.2, 128.0, 128.3, 128.4, 128.7, 129.4, 129.6, 130.9, 131.8, 133.0, 135.9, 137.8, 143.4, 164.1; HRMS (ESI) calcd. For $\text{C}_{31}\text{H}_{33}\text{NO}_4\text{SNa}$ ($\text{M}^+ + \text{Na}$): 538.2028, found: 538.2028.

(1*S*)-1-(*N*-Allyl-4-methylphenylsulfonamido)-2-methyl-1,4-diphenylbut-3-yn-2-yl**Benzoate (156l)**

Yellow oil; obtained as two diastereomers in a ratio of 4:1; $[\alpha]_{\text{D}}^{25} +39.5$ (c 1.0, CHCl_3); major isomer: ^1H NMR (CDCl_3 , 400 MHz): δ 2.15 (s, 3H), 2.36 (s, 3H), 4.00 (dd, 1H, $J = 16.7, 7.1$ Hz), 4.90 (dd, 1H, $J = 16.7, 5.3$ Hz), 4.88 (d, 1H, $J = 10.2$ Hz), 4.98 (d, 1H, $J = 17.2$ Hz), 5.67-5.76 (m, 2H), 7.14 (d, 2H, $J = 6.8$ Hz), 7.17-7.35 (m, 9H), 7.43-7.48 (m, 2H), 7.65-7.75 (m, 6H); ^{13}C NMR (CDCl_3 , 100 MHz): δ 21.5, 26.6, 40.0, 67.3, 78.2, 87.9, 89.1, 116.5, 122.1, 128.1, 128.3, 128.3, 128.3, 128.8, 129.3, 129.5, 130.1, 131.8, 132.9, 136.0, 136.0, 137.1, 143.4, 164.1; IR (NaCl, neat) ν : 3019, 1724, 1271, 1215, 1161 cm^{-1} ; HRMS (ESI) calcd. For $\text{C}_{34}\text{H}_{31}\text{NO}_4\text{SNa}$ ($\text{M}^+ + \text{Na}$): 572.1872, found: 572.1868.

(±)-3-(1-(*N*-Allyl-4-methylphenylsulfonamido)-2-phenylethyl)-1-(thiophen-3-yl)oct-1-yn-3-yl Benzoate (156m)

Colourless oil; ^1H NMR (CDCl_3 , 400 MHz): δ 0.86 (d, 3H, $J = 5.8$ Hz), 1.28-1.67 (m, 6H), 2.13-2.23 (m, 1H), 2.34 (s, 3H), 2.54-2.61 (m, 1H), 3.07 (dd, 1H, $J = 14.6, 8.6$ Hz), 3.40 (dd, 1H, $J = 14.6, 5.0$ Hz), 4.07 (dd, 1H, $J = 16.6, 7.6$ Hz), 4.33 (dd, 1H, $J = 16.6, 7.6$ Hz), 5.00-5.08 (m, 2H), 5.37 (dd, 1H, $J = 8.0, 5.0$ Hz), 5.78-5.88 (m, 1H), 7.03 (d, 2H, $J = 8.1$ Hz), 7.14-7.29 (m, 9H), 7.39 (t, 2H, $J = 7.7$ Hz), 7.53 (t, 2H, $J = 7.7$ Hz), 7.87 (d, 2H, $J = 7.5$ Hz); ^{13}C NMR (CDCl_3 , 100 MHz): δ 14.1, 21.5, 22.5, 23.6, 31.6, 35.6, 35.8, 47.0, 63.1, 83.6, 84.7, 86.8, 116.8, 121.3, 125.4, 126.4, 127.9, 128.3, 128.7, 129.2, 129.6, 129.6, 129.8, 130.0, 130.6, 133.0, 136.3, 137.2, 138.6, 142.8, 164.2; IR (NaCl, neat) ν : 3019, 2868, 1717, 1267, 1215 cm^{-1} ; HRMS (ESI) calcd. For $\text{C}_{37}\text{H}_{39}\text{NO}_4\text{S}_2\text{Na}$ ($\text{M}^+ + \text{Na}$): 648.2218, found: 648.2212.

(4*S*)-4-(*N*-Allyl-4-methylphenylsulfonamido)-5-((*tert*-butyldimethylsilyl)oxy)-3-ethyl-1-phenylpent-1-yn-3-yl Benzoate (156n)

Colourless oil; obtained as two diastereomers in a ratio of 1:1; $[\alpha]_{\text{D}}^{25} -9.6$ (c 1.0, CHCl_3); ^1H NMR (CDCl_3 , 400 MHz): δ -0.03 (s, 3H), 0.00 (s, 3H), 0.02 (s, 3H), 0.06 (s, 3H), 0.86 (s, 9H), 0.89 (s, 9H), 1.15-1.21 (m, 6H), 2.33-2.69 (m, 10H), 3.98-4.30 (m, 8H), 4.84-5.03 (m, 6H), 5.72-5.87 (m, 2H), 7.19-7.22 (m, 4H), 7.30-7.31 (m, 6H), 7.42-7.46 (m, 8H), 7.53-7.58 (m, 2H), 7.81-7.85 (m, 4H), 8.02 (d, 2H, $J = 7.6$ Hz), 8.06 (d, 2H, $J = 7.6$ Hz);

^{13}C NMR (CDCl_3 , 100 MHz): δ -5.5, -5.4, -5.4, 8.8, 18.5, 21.5, 26.0, 26.0, 29.5, 30.6, 47.5, 61.2, 61.8, 62.8, 64.5, 80.4, 82.2, 86.6, 86.8, 89.1, 89.4, 116.2, 122.2, 128.3, 128.3, 128.4, 128.7, 128.8, 129.3, 129.6, 129.8, 130.7, 130.8, 131.7, 131.9, 133.0, 133.1, 136.2, 137.9, 138.1, 143.0, 164.1, 164.4; IR (NaCl, neat) ν : 2959, 2928, 1727, 1719, 1344, 1265 cm^{-1} ; HRMS (ESI) calcd. For $\text{C}_{36}\text{H}_{45}\text{NO}_5\text{SSiNa}$ ($\text{M}^+ + \text{Na}$): 654.2685, found: 654.2689.

(2*S*)-2-(*N*-Allyl-4-methylphenylsulfonamido)-3-ethyl-5-phenylpent-4-yne-1,3-diyl

Dibenzoate (156o)

Colourless oil; obtained as two diastereomers in a ratio of 4:1; $[\alpha]_{\text{D}}^{25}$ -64.8 (c 1.0, CHCl_3); major isomer: ^1H NMR (CDCl_3 , 400 MHz): δ 1.19 (t, 3H, $J = 7.3$ Hz), 2.22 (s, 3H), 2.30-2.42 (m, 1H), 2.67-2.76 (m, 1H), 4.25-4.30 (m, 2H), 4.74-4.76 (m, 1H), 4.92-5.35 (m, 4H), 5.92-5.96 (m, 1H), 6.99 (d, 2H, $J = 8.0$ Hz), 7.48-7.47 (m, 9H), 7.53-7.58 (m, 2H), 7.72 (d, 2H, $J = 8.2$ Hz), 8.00 (d, 2H, $J = 7.6$ Hz), 8.04 (d, 2H, $J = 7.7$ Hz); ^{13}C NMR (CDCl_3 , 100 MHz): δ 8.8, 21.4, 29.3, 59.9, 62.1, 62.4, 82.2, 85.8, 90.0, 121.8, 127.9, 128.3, 128.3, 128.4, 128.5, 129.0, 129.4, 129.7, 129.8, 129.9, 130.4, 131.9, 131.9, 133.1, 135.7, 143.3, 164.1, 166.4; IR (NaCl, neat) ν : 3063, 3019, 2974, 2232, 1722, 1717, 1269, 1092 cm^{-1} ; HRMS (ESI) calcd. For $\text{C}_{37}\text{H}_{35}\text{NO}_6\text{SNa}$ ($\text{M}^+ + \text{Na}$): 644.2083, found: 644.2084.

(3*S*,4*S*)-4-(*N*-Allyl-4-methylphenylsulfonamido)-3-ethyl-6-(methylsulfonyl)-1-phenylhex-1-yn-3-yl Benzoate (156p)

White solid, mp = 56-58 $^{\circ}\text{C}$; $[\alpha]_{\text{D}}^{25}$ -93.2 (c 1.0, CHCl_3); ^1H NMR (CDCl_3 , 400 MHz): δ 1.04 (t, 3H, $J = 7.3$ Hz), 1.94-2.04 (m, 1H), 2.31 (s, 3H), 2.47-2.59 (m, 3H), 2.90 (s, 3H),

3.14-3.25 (m, 2H), 4.11-4.28 (m, 2H), 4.97 (d, 1H, $J = 8.6$ Hz), 5.11 (d, 1H, $J = 10.0$ Hz), 5.17 (d, 1H, $J = 17.2$ Hz), 5.97-6.02 (m, 1H), 7.18 (d, 2H, $J = 7.9$ Hz), 7.29-7.34 (m, 5H), 7.45 (t, 2H, $J = 7.6$ Hz), 7.57 (t, 1H, $J = 7.4$ Hz), 7.76 (d, 2H, $J = 8.2$ Hz), 8.00 (d, 2H, $J = 7.6$ Hz); ^{13}C NMR (CDCl_3 , 100 MHz): δ 8.9, 20.9, 21.5, 28.9, 41.2, 47.1, 51.9, 60.2, 83.5, 85.8, 90.1, 118.4, 121.6, 128.0, 128.3, 128.6, 129.0, 129.6, 129.7, 130.2, 131.8, 133.4, 135.4, 137.1, 143.8, 164.2; IR (NaCl, neat) ν : 3019, 1724, 1491, 1267, 1215, 1155 cm^{-1} ; HRMS (ESI) calcd. For $\text{C}_{32}\text{H}_{35}\text{NO}_6\text{S}_2\text{Na}$ ($\text{M}^+ + \text{Na}$): 616.1804, found: 616.1794.

(3S,4S)-4-(*N*-Cinnamyl-4-methylphenylsulfonamido)-3-ethyl-1-phenylhex-1-yn-3-yl Benzoate (156q)

Pale-yellow oil; $[\alpha]_{\text{D}}^{25} -70.9$ (c 1.0, CHCl_3); ^1H NMR (CDCl_3 , 400 MHz): δ 0.95 (t, 3H, $J = 7.3$ Hz), 1.14 (t, 3H, $J = 7.4$ Hz), 2.03 (q, 2H, $J = 6.2$ Hz), 2.13-2.23 (m, 1H), 2.27 (s, 3H), 2.64-2.73 (m, 1H), 4.29 (d, 1H, $J = 6.2$ Hz), 4.84 (t, 1H, $J = 5.9$ Hz), 6.14-6.21 (m, 1H), 6.35 (d, 1H, $J = 16.0$ Hz), 7.06-7.10 (m, 4H), 7.16-7.44 (m, 10H), 7.54 (t, 1H, $J = 7.3$ Hz), 7.77 (d, 2H, $J = 8.2$ Hz), 8.01 (d, 2H, $J = 7.6$ Hz); ^{13}C NMR (CDCl_3 , 100 MHz): δ 9.0, 11.9, 21.5, 29.4, 46.5, 63.2, 75.3, 84.0, 87.1, 89.4, 115.0, 122.3, 126.4, 127.6, 128.2, 128.3, 128.5, 128.5, 128.7, 129.3, 129.7, 130.8, 131.9, 133.1, 136.6, 138.0, 143.2, 164.2; IR (NaCl, neat) ν : 3019, 2359, 1719, 1269, 1215 cm^{-1} ; HRMS (ESI) calcd. For $\text{C}_{37}\text{H}_{37}\text{NO}_4\text{SNa}$ ($\text{M}^+ + \text{Na}$): 614.2341, found: 614.2343.

(3*S*,4*S*)-4-(*N*-Cinnamyl-4-methylphenylsulfonamido)-3-ethyl-6-methyl-1-phenylhept-1-yn-3-yl Benzoate (156r)

Yellow oil; $[\alpha]_D^{25} -61.3$ (*c* 1.0, CHCl₃); ¹H NMR (CDCl₃, 400 MHz): δ 0.88 (d, 3H, *J* = 6.6 Hz), 1.03 (d, 3H, *J* = 6.2 Hz), 1.15 (t, 3H, *J* = 7.4 Hz), 1.57-1.72 (m, 2H), 2.03-2.16 (m, 2H), 2.27 (s, 3H), 2.63-2.68 (m, 1H), 4.31-4.37 (m, 2H), 5.02 (d, 1H, *J* = 11.0, 2.0 Hz), 6.08 (dt, 1H, *J* = 16.0, 7.0 Hz), 6.31 (d, 1H, *J* = 16.0 Hz), 7.07-7.12 (m, 4H), 7.17-7.33 (m, 6H), 7.36-7.45 (m, 4H), 7.56 (t, 1H, *J* = 7.4 Hz), 7.77 (d, 2H, *J* = 8.2 Hz), 8.01 (m, 2H, *J* = 7.5 Hz); ¹³C NMR (CDCl₃, 100 MHz): δ 9.0, 21.4, 21.8, 23.9, 24.1, 29.3, 37.9, 46.4, 59.7, 83.9, 87.1, 89.4, 122.3, 126.3, 127.2, 127.6, 128.2, 128.3, 128.5, 128.7, 129.2, 129.6, 130.9, 131.9, 133.1, 136.5, 138.0, 143.2, 164.1; IR (NaCl, neat) ν : 3022, 2959, 2359, 1719, 1491, 1265, 1152 cm⁻¹; HRMS (ESI) calcd. For C₃₉H₄₁NO₄SNa (*M*⁺+Na): 642.2654, found: 642.2662.

(3*S*,4*S*)-4-(*N*-Cinnamyl-4-methylphenylsulfonamido)-3-ethyl-5-methyl-1-phenylhex-1-yn-3-yl Benzoate (156s)

Yellow oil; $[\alpha]_D^{25} -57.9$ (*c* 0.26, CHCl₃); ¹H NMR (CDCl₃, 400 MHz): δ 1.03-1.06 (m, 6H), 1.18 (d, 3H, *J* = 6.6 Hz), 1.81-1.90 (m, 1H), 2.34 (s, 3H), 2.50-2.58 (m, 1H), 2.68-2.76 (m, 1H), 4.24-4.37 (m, 2H), 4.89 (d, 1H, *J* = 10.1 Hz), 6.23-6.31 (m, 1H), 6.41 (d, 1H, *J* = 16.0 Hz), 7.11-7.46 (m, 14H), 7.56 (t, 1H, *J* = 7.5 Hz), 7.83 (d, 2H, *J* = 8.3 Hz), 8.06 (d, 2H, *J* = 7.5 Hz); ¹³C NMR (CDCl₃, 100 MHz): δ 8.9, 21.4, 21.5, 22.3, 30.1, 30.2,

47.3, 66.4, 84.9, 87.4, 89.1, 122.2, 126.4, 126.8, 127.7, 128.4, 128.5, 128.5, 129.0, 129.2, 129.8, 130.7, 131.9, 132.6, 133.1, 136.5, 138.1, 143.1, 164.3; IR (NaCl, neat) ν : 2970, 2230, 1719, 1333, 1267, 1155 cm^{-1} ; HRMS (ESI) calcd. For $\text{C}_{38}\text{H}_{39}\text{NO}_4\text{SNa}$ ($\text{M}^+ + \text{Na}$): 628.2498, found: 628.2485.

(3*S*,4*S*)-4-(*N*-Cinnamyl-4-methylphenylsulfonamido)-3-ethyl-1,5-diphenylpent-1-yn-3-yl Benzoate (156t)

Colourless oil; $[\alpha]_{\text{D}}^{25}$ -67.1 (c 1.0, CHCl_3); ^1H NMR (CDCl_3 , 400 MHz): δ 1.16 (t, 3H, J = 7.3 Hz), 2.28 (s, 3H), 2.34-2.43 (m, 1H), 2.71-2.80 (m, 1H), 3.15 (dd, 1H, J = 14.6, 8.9 Hz), 3.48 (dd, 1H, J = 14.6, 4.7 Hz), 4.33-4.44 (m, 2H), 5.50 (dd, 1H, J = 8.8, 4.8 Hz), 5.88-5.95 (m, 1H), 6.28 (d, 1H, J = 16.0 Hz), 6.95-7.12 (m, 4H), 7.19-7.41 (m, 15H), 7.51-7.55 (m, 3H), 7.90 (d, 2H, J = 7.5 Hz); ^{13}C NMR (CDCl_3 , 100 MHz): δ 8.6, 21.4, 29.2, 35.8, 46.4, 62.6, 83.9, 87.2, 89.6, 122.3, 126.4, 126.9, 127.6, 128.1, 128.3, 128.4, 128.4, 128.7, 128.9, 129.2, 129.6, 129.7, 130.5, 131.8, 132.0, 133.0, 136.4, 137.5, 138.5, 142.9, 164.1; IR (NaCl, neat) ν : 3019, 2229, 1719, 1267, 1215 cm^{-1} ; HRMS (ESI) calcd. For $\text{C}_{42}\text{H}_{39}\text{NO}_4\text{SNa}$ ($\text{M}^+ + \text{Na}$): 676.2498, found: 676.2492.

(3*S*,4*S*)-4-(*N*-Cinnamyl-4-methylphenylsulfonamido)-3-methyl-1-phenylpent-1-yn-3-yl Benzoate (156u)

White solid, mp = 55-58 $^{\circ}\text{C}$; $[\alpha]_{\text{D}}^{25}$ -24.2 (c 1.0, CHCl_3); ^1H NMR (CDCl_3 , 400 MHz): δ 1.40 (d, 3H, J = 6.8 Hz), 2.03 (s, 3H), 2.37 (s, 3H), 4.19-4.29 (m, 2H), 4.60 (q, 1H, J = 6.8 Hz), 6.20 (dt, 1H, J = 16.0, 6.4 Hz), 6.39 (d, 1H, J = 16.0 Hz), 7.10 (d, 1H, J = 7.3 Hz),

7.17-7.32 (m, 8H), 7.40-7.45 (m, 4H), 7.56 (t, 1H, $J = 7.1$ Hz), 7.77 (d, 2H, $J = 8.0$ Hz), 8.00 (d, 2H, $J = 7.9$ Hz); ^{13}C NMR (CDCl_3 , 100 MHz): δ 14.1, 21.5, 24.6, 46.4, 60.0, 78.9, 87.1, 88.7, 122.1, 126.4, 127.0, 127.6, 128.3, 128.4, 128.5, 128.8, 129.6, 129.7, 130.8, 132.0, 132.3, 133.1, 136.6, 137.8, 143.4, 164.2; IR (NaCl, neat) ν : 1726, 1342, 1271, 1155, 1090 cm^{-1} ; HRMS (ESI) calcd. For $\text{C}_{35}\text{H}_{33}\text{NO}_4\text{SNa}$ ($\text{M}^+ + \text{Na}$): 586.2028, found: 586.2033.

(3*S*,4*S*)-4-(*N*-Cinnamyl-4-methylphenylsulfonamido)-3-methyl-1-phenylhept-1-yn-3-yl (156v)

Colourless oil; $[\alpha]_{\text{D}}^{25} -70.7$ (c 1.0, CHCl_3); ^1H NMR (CDCl_3 , 400 MHz): δ 0.95 (t, 3H, $J = 7.3$ Hz), 1.37-1.43 (m, 2H), 1.96-2.00 (m, 5H), 2.31 (s, 3H), 4.26-4.37 (m, 2H), 4.57 (t, 1H, $J = 8.1$ Hz), 6.15 (dt, 1H, $J = 16.0, 6.4$ Hz), 6.38 (d, 1H, $J = 16.0$ Hz), 7.08-7.31 (m, 10H), 7.33-7.45 (m, 4H), 7.55 (t, 1H, $J = 7.3$ Hz), 7.77 (d, 2H, $J = 8.0$ Hz), 8.00 (d, 2H, $J = 7.6$ Hz); ^{13}C NMR (CDCl_3 , 100 MHz): δ 14.3, 20.0, 21.5, 25.1, 30.9, 46.3, 64.6, 79.0, 87.7, 88.7, 122.2, 126.3, 126.8, 127.7, 128.1, 128.3, 128.5, 128.8, 129.4, 129.6, 130.9, 131.9, 132.4, 133.1, 136.5, 138.1, 143.3, 164.1; IR (NaCl, neat) ν : 3021, 2959, 1719, 1271, 1215 cm^{-1} ; HRMS (ESI) calcd. For $\text{C}_{37}\text{H}_{37}\text{NO}_4\text{SNa}$ ($\text{M}^+ + \text{Na}$): 614.2341, found: 614.2349.

(1*S*)-1-(*N*-Cinnamyl-4-methylphenylsulfonamido)-2-methyl-1,4-diphenylbut-3-yn-2-yl Benzoate (156w)

Yellow solid; obtained as two diastereomers in a ratio of 4:1; mp = 61-63 °C; $[\alpha]_D^{25} +0.6$ (*c* 1.0, CHCl₃); major isomer: ¹H NMR (CDCl₃, 400 MHz): δ 2.19 (s, 3H), 2.24 (s, 3H), 4.26 (dd, 1H, *J* = 16.6, 7.0 Hz), 4.46-4.54 (m, 1H), 5.74-5.85 (m, 2H), 6.20 (d, 1H, *J* = 16.0 Hz), 6.90-6.93 (m, 2H), 7.04 (d, 2H, *J* = 8.0 Hz), 7.15-7.25 (m, 3H), 7.27-7.34 (m, 8H), 7.42-7.49 (m, 3H), 7.68 (d, 2H, *J* = 8.2 Hz), 7.74-7.78 (m, 4H); ¹³C NMR (CDCl₃, 100 MHz): δ 21.4, 26.8, 48.7, 67.1, 78.2, 88.0, 89.2, 122.1, 126.2, 126.9, 127.4, 128.2, 128.3, 128.3, 128.4, 128.9, 129.3, 129.5, 130.2, 131.8, 131.9, 133.0, 136.2, 136.5, 137.6, 143.4, 164.1; IR (NaCl, neat) ν : 3019, 1724, 1450, 1271, 1215, 1159 cm⁻¹; HRMS (ESI) calcd. For C₄₀H₃₅NO₄SNa (M⁺+Na): 648.2185, found: 648.2190.

(3*S*,4*S*)-3-Ethyl-5-methyl-4-(4-methyl-*N*-((*Z*)-3-phenylallyl)phenylsulfonamido)-1-phenylhex-1-yn-3-yl Benzoate (156x)

Yellow oil; $[\alpha]_D^{25} -49.0$ (*c* 1.0, CHCl₃); ¹H NMR (CDCl₃, 400 MHz): δ 0.98 (d, 3H, *J* = 6.6 Hz), 1.06 (t, 3H, *J* = 7.2 Hz), 1.17 (d, 3H, *J* = 6.6 Hz), 1.93-2.00 (m, 1H), 2.26-2.40 (m, 4H), 2.73-2.86 (m, 1H), 4.41 (d, 1H, *J* = 17.8 Hz), 4.56 (dd, 1H, *J* = 18.2, 4.7 Hz), 4.89 (d, 1H, *J* = 9.5 Hz), 5.85-5.90 (m, 1H), 6.37 (d, 1H, *J* = 12.0 Hz), 7.11-7.32 (m, 12H), 7.39-7.56 (m, 3H), 7.68 (d, 2H, *J* = 8.0 Hz), 8.02 (d, 2H, *J* = 7.4 Hz); ¹³C NMR (CDCl₃, 100 MHz): δ 8.8, 21.4, 21.5, 22.5, 30.2, 30.2, 43.4, 66.2, 84.7, 87.0, 89.2, 122.0,

127.0, 128.2, 128.3, 128.3, 128.4, 128.6, 128.8, 129.1, 129.3, 129.7, 130.1, 130.7, 131.7, 133.0, 136.4, 137.4, 143.1, 164.3; IR (NaCl, neat) ν : 3019, 1717, 1599, 1491, 1215 cm^{-1} ; HRMS (ESI) calcd. For $\text{C}_{38}\text{H}_{39}\text{NO}_4\text{SNa}$ ($\text{M}^+ + \text{Na}$): 628.2498, found: 628.2503.

(1*R*,4*S*,7*R*)-5-Ethyl-4-isobutyl-7-phenyl-3-tosyl-3-aza-bicyclo[4.2.0]oct-5-en-7-yl

Benzoate (158a)

Colourless solid, mp = 126-128 °C; $[\alpha]_{\text{D}}^{25} +124.7$ (c 1.0, CHCl_3); ^1H NMR (CDCl_3 , 400 MHz): δ 0.97 (d, 3H, J = 6.6 Hz), 1.09-1.15 (m, 6H), 1.46-1.49 (m, 2H), 1.99-2.05 (m, 2H), 2.22-2.34 (m, 5H), 2.76-2.90 (m, 2H), 3.00 (dd, 1H, J = 11.1, 7.8 Hz), 4.02 (dd, 1H, J = 14.0, 6.6 Hz), 4.58 (t, 1H, J = 5.6 Hz), 7.03 (d, 2H, J = 8.0 Hz), 7.26 (s, 5H), 7.37-7.41 (m, 2H), 7.50-7.54 (m, 1H), 7.60 (d, 2H, J = 8.1 Hz), 7.91 (m, 2H, J = 7.6 Hz); ^{13}C NMR (CDCl_3 , 100 MHz): δ 12.2, 21.5, 21.6, 22.6, 24.1, 24.6, 30.9, 38.3, 41.6, 43.3, 53.3, 86.9, 126.9, 127.1, 128.0, 128.2, 128.3, 128.4, 129.3, 129.5, 130.6, 133.0, 133.9, 138.6, 139.1, 142.9, 164.6; IR (NaCl, neat) ν : 3019, 2970, 1719, 1451, 1279, 1215, 1159 cm^{-1} ; HRMS (ESI) calcd. For $\text{C}_{33}\text{H}_{37}\text{NO}_4\text{SNa}$ ($\text{M}^+ + \text{Na}$): 566.2341, found: 566.2347.

(1*R*,4*S*,7*R*)-5-Ethyl-4-isobutyl-7-p-tolyl-3-tosyl-3-azabicyclo[4.2.0]oct-5-en-7-yl**Benzoate (158b)**

Colourless solid, mp = 148-151 °C; $[\alpha]_D^{25} +122.5$ (*c* 1.0, CHCl₃); ¹H NMR (CDCl₃, 400 MHz): δ 0.97 (d, 3H, *J* = 6.5 Hz), 1.10-1.15 (m, 6H), 1.46-1.49 (m, 2H), 1.96-2.05 (m, 2H), 2.24-2.33 (m, 6H), 2.38 (s, 3H), 2.78-2.89 (m, 2H), 2.98 (dd, 1H, *J* = 10.6, 8.0 Hz), 4.00 (dd, 1H, *J* = 13.9, 6.6 Hz), 4.58 (t, 1H, *J* = 6.6 Hz), 7.01-7.16 (m, 6H), 7.38 (t, 2H, *J* = 7.4 Hz), 7.50 (t, 1H, *J* = 7.2 Hz), 7.60 (d, 2H, *J* = 7.9 Hz), 7.97 (m, 2H, *J* = 7.6 Hz); ¹³C NMR (CDCl₃, 100 MHz): δ 12.2, 21.2, 21.4, 21.6, 22.6, 24.2, 24.6, 30.9, 38.4, 41.6, 43.3, 53.3, 86.7, 126.9, 127.2, 128.0, 128.4, 128.9, 129.3, 129.5, 130.7, 133.0, 134.1, 136.1, 137.6, 138.6, 142.8, 164.7; IR (NaCl, neat) ν : 3019, 1719, 1451, 1215, 1155 cm⁻¹; HRMS (ESI) calcd. For C₃₄H₄₀NO₄S (M⁺+H): 558.2678, found: 558.2682.

(1*R*,4*S*,7*R*)-5-Ethyl-7-(4-fluorophenyl)-4-isobutyl-3-tosyl-3-azabicyclo[4.2.0]oct-5-en-7-yl Benzoate (158c)

Colourless solid, mp = 138-139 °C; $[\alpha]_D^{25} +123.2$ (*c* 1.0, CHCl₃); ¹H NMR (CDCl₃, 400 MHz): δ 0.97 (d, 3H, *J* = 6.7 Hz), 1.10 (d, 3H, *J* = 6.4 Hz), 1.15 (t, 3H, *J* = 7.6 Hz), 1.45-1.49 (m, 2H), 1.98-2.06 (m, 2H), 2.24-2.30 (m, 5H), 2.76-2.88 (m, 2H), 2.98 (dd, 1H, *J* = 11.1, 7.8 Hz), 4.03 (dd, 1H, *J* = 14.0, 6.6 Hz), 4.58 (t, 1H, *J* = 6.2 Hz), 6.93 (t, 2H, *J* = 8.6

Hz), 7.04 (d, 2H, $J = 8.0$ Hz), 7.24-7.28 (m, 2H), 7.38-7.42 (m, 2H), 7.51-7.61 (m, 3H), 7.80 (d, 2H, $J = 7.5$ Hz); ^{13}C NMR (CDCl_3 , 100 MHz): δ 12.2, 21.4, 21.5, 22.6, 24.1, 24.6, 31.0, 38.4, 41.6, 43.2, 53.3, 86.1, 115.0 (1C, d, $J_{\text{C-F}} = 21.2$ Hz), 126.9, 128.4, 139.3, 129.3, 129.4, 129.5, 130.4, 133.1, 133.7, 134.8, 134.9, 138.6, 143.0, 162.3 (1C, d, $J_{\text{C-F}} = 245.7$ Hz), 164.6; IR (NaCl, neat) ν : 3021, 2959, 1719, 1508, 1279, 1215 cm^{-1} ; HRMS (ESI) calcd. For $\text{C}_{33}\text{H}_{37}\text{NO}_4\text{SFNa}$ ($\text{M}^+ + \text{H}$): 562.2427, found: 562.2417.

(1*R*,4*S*,7*S*)-5-Ethyl-4-isobutyl-7-(thiophen-3-yl)-3-tosyl-3-azabicyclo[4.2.0]oct-5-en-7-yl Benzoate (158d)

White solid, mp = 129-131 °C; $[\alpha]_{\text{D}}^{25} +73.0$ (c 1.0, CHCl_3); ^1H NMR (CDCl_3 , 400 MHz): δ 0.96 (d, 3H, $J = 6.8$ Hz), 1.09-1.15 (m, 6H), 1.46 (dd, 2H, $J = 7.4, 5.7$ Hz), 2.01-2.16 (m, 2H), 2.20-2.26 (m, 2H), 2.37 (s, 3H), 2.73-2.90 (m, 3H), 4.04 (dd, 1H, $J = 14.0, 6.6$ Hz), 4.57 (t, 1H, $J = 6.2$ Hz), 6.81 (dd, 1H, $J = 3.0, 1.2$ Hz), 7.03 (dd, 1H, $J = 5.0, 1.2$ Hz), 7.13-7.18 (m, 3H), 7.40 (t, 2H, $J = 7.6$ Hz), 7.53 (t, 1H, $J = 7.4$ Hz), 7.65 (d, 2H, $J = 8.2$ Hz), 7.92 (d, 2H, $J = 8.2$ Hz); ^{13}C NMR (CDCl_3 , 100 MHz): δ 12.4, 21.6, 21.6, 22.6, 24.1, 24.6, 31.3, 39.7, 41.7, 43.3, 53.3, 83.4, 124.1, 125.6, 127.0, 127.3, 128.2, 128.4, 129.4, 129.5, 130.6, 133.0, 133.9, 138.7, 140.5, 143.1, 164.6; IR (NaCl, neat) ν : 3022, 2957, 1717, 1450, 1341, 1281, 1159, 1090 cm^{-1} ; HRMS (ESI) calcd. For $\text{C}_{31}\text{H}_{35}\text{NO}_4\text{S}_2\text{Na}$ ($\text{M}^+ + \text{Na}$): 572.1905, found: 572.1903.

(±)-4-Isobutyl-5-pentyl-7-phenyl-3-tosyl-3-azabicyclo[4.2.0]oct-5-en-7-yl Benzoate (158e)

White solid, mp = 113-114 °C; ^1H NMR (CDCl_3 , 400 MHz): δ 0.92-0.98 (m, 6H), 1.08 (d, 3H, J = 6.4 Hz), 1.34-1.49 (m, 8H), 2.01-2.05 (m, 2H), 2.22-2.37 (m, 5H), 2.66-2.74 (m, 1H), 2.87 (dd, 1H, J = 13.9, 10.8 Hz), 2.96 (dd, 1H, J = 11.0, 7.8 Hz), 4.03 (dd, 1H, J = 14.0, 6.6 Hz), 4.53 (t, 1H, J = 5.9 Hz), 7.04 (d, 2H, J = 8.0 Hz), 7.26-7.46 (m, 7H), 7.53 (t, 1H, J = 7.4 Hz), 7.62 (d, 2H, J = 8.2 Hz), 7.92 (d, 2H, J = 7.3 Hz); ^{13}C NMR (CDCl_3 , 100 MHz): δ 14.1, 21.5, 21.6, 22.5, 24.1, 24.6, 26.8, 29.5, 31.1, 31.8, 38.5, 41.7, 43.3, 53.9, 86.9, 126.9, 126.9, 127.4, 127.9, 128.1, 128.4, 129.3, 129.5, 130.6, 133.0, 134.4, 138.6, 139.3, 142.9, 164.6; IR (NaCl, neat) ν : 3019, 2940, 1719, 1339, 1279, 1215 cm^{-1} ; HRMS (ESI) calcd. For $\text{C}_{36}\text{H}_{44}\text{NO}_4\text{S}$ ($\text{M}^+ + \text{H}$): 586.2991, found: 586.2988.

(±)-5-Cyclopropyl-4-isobutyl-7-phenyl-3-tosyl-3-azabicyclo[4.2.0]oct-5-en-7-yl Benzoate (158f)

Colourless solid, mp = 166-169 °C; ^1H NMR (CDCl_3 , 400 MHz): δ 0.26-0.37 (m, 2H), 0.61-0.65 (m, 2H), 0.99 (d, 3H, J = 6.8 Hz), 1.08 (d, 3H, J = 6.4 Hz), 1.39-1.46 (m, 1H), 1.57-1.72 (m, 3H), 1.98-2.07 (m, 1H), 2.16-2.24 (m, 1H), 2.38 (s, 3H), 2.62-2.73 (m, 2H), 2.97 (dd, 1H, J = 14.0, 10.7 Hz), 4.07 (dd, 1H, J = 13.9, 6.6 Hz), 4.38 (d, 1H, J = 10.0 Hz), 7.07-7.27 (m, 7H), 7.40 (t, 2H, J = 7.6 Hz), 7.53 (t, H, J = 7.4 Hz), 7.63 (d, 2H, J =

8.2 Hz), 7.98 (d, 2H, $J = 7.2$ Hz); ^{13}C NMR (CDCl_3 , 100 MHz): δ 4.1, 6.7, 10.9, 21.6, 21.7, 24.2, 24.7, 31.1, 38.9, 42.2, 43.5, 55.6, 87.4, 126.4, 127.0, 127.7, 128.2, 128.4, 129.3, 129.5, 130.9, 133.0, 135.5, 138.8, 140.3, 142.9, 164.9; IR (NaCl, neat) ν : 3019, 1715, 1450, 1281, 1215 cm^{-1} ; HRMS (ESI) calcd. For $\text{C}_{34}\text{H}_{38}\text{NO}_4\text{S}$ (M^++H): 556.2522, found: 556.2526.

(1*R*,4*S*,7*R*)-4,5-Diethyl-7-phenyl-3-tosyl-3-azabicyclo[4.2.0]oct-5-en-7-yl Benzoate (158g)

Colourless oil; $[\alpha]_{\text{D}}^{25} +141.9$ (c 1.0, CHCl_3); ^1H NMR (CDCl_3 , 400 MHz): δ 1.08-1.14 (m, 6H), 1.49-1.61 (m, 1H), 1.88-1.95 (m, 1H), 1.99-2.07 (m, 1H), 2.16-2.21 (m, 1H), 2.23 (s, 3H), 2.38 (t, 1H, $J = 9.4$ Hz), 2.74-2.86 (m, 2H), 2.95 (dd, 1H, $J = 11.0, 7.8$ Hz), 4.06 (dd, 1H, $J = 13.8, 6.6$ Hz), 4.49 (d, 1H, $J = 9.2$ Hz), 7.06 (d, 1H, $J = 8.0$ Hz), 7.27 (s, 5H), 7.40 (t, 1H, $J = 7.6$ Hz), 7.52 (t, 1H, $J = 7.4$ Hz), 7.61 (d, 2H, $J = 8.0$ Hz), 8.01 (d, 2H, $J = 7.7$ Hz); ^{13}C NMR (CDCl_3 , 100 MHz): δ 11.0, 12.5, 21.5, 22.4, 25.5, 31.1, 38.2, 44.0, 56.0, 86.8, 126.8, 127.0, 128.0, 128.2, 128.4, 128.4, 129.3, 129.5, 130.6, 133.0, 134.1, 138.7, 139.3, 142.9, 164.7; IR (NaCl, neat) ν : 3024, 2968, 1719, 1599, 1450, 1159 cm^{-1} ; HRMS (ESI) calcd. For $\text{C}_{31}\text{H}_{33}\text{NO}_4\text{SNa}$ (M^++Na): 538.2028, found: 538.2022.

(1*R*,4*S*,7*R*)-5-Ethyl-4-isopropyl-7-phenyl-3-tosyl-3-azabicyclo[4.2.0]oct-5-en-7-yl**Benzoate (158h)**

Colourless oil; $[\alpha]_{\text{D}}^{25} +144.0$ (*c* 1.0, CHCl_3); ^1H NMR (CDCl_3 , 400 MHz): δ 0.95 (d, 3H, $J = 7.0$ Hz), 1.17 (t, 3H, $J = 7.6$ Hz), 1.25 (d, 3H, $J = 6.7$ Hz), 1.71-1.78 (m, 1H), 2.23-2.29 (m, 6H), 2.88-3.03 (m, 3H), 4.08 (dd, 1H, $J = 14.2, 6.9$ Hz), 4.58 (s, 1H), 7.02 (d, 1H, $J = 8.0$ Hz), 7.27-7.42 (m, 7H), 7.51-7.59 (m, 3H), 7.92 (d, 2H, $J = 7.8$ Hz); ^{13}C NMR (CDCl_3 , 100 MHz): δ 12.8, 18.1, 20.8, 21.5, 22.7, 30.5, 30.5, 38.7, 46.5, 58.2, 86.7, 126.9, 127.0, 127.2, 128.0, 128.2, 128.4, 129.4, 129.5, 130.6, 133.0, 135.3, 138.6, 139.1, 143.0, 164.6; IR (NaCl, neat) ν : 3019, 2230, 1719, 1215 cm^{-1} ; HRMS (ESI) calcd. For $\text{C}_{32}\text{H}_{36}\text{NO}_4\text{S}$ ($\text{M}^+ + \text{H}$): 530.2365, found: 530.2360.

(1*R*,4*S*,7*R*)-4-Benzyl-5-ethyl-7-phenyl-3-tosyl-3-azabicyclo[4.2.0]oct-5-en-7-yl**Benzoate (158i)**

Colourless solid, mp = 149-152 °C; $[\alpha]_{\text{D}}^{25} +71.4$ (*c* 1.0, CHCl_3); ^1H NMR (CDCl_3 , 400 MHz): δ 1.22 (t, 3H, $J = 7.6$ Hz), 2.13 (dd, 2H, $J = 14.3, 8.6$ Hz), 2.19-2.25 (m, 1H), 2.29 (s, 3H), 2.46-2.55 (m, 1H), 2.95-3.06 (m, 3H), 3.15 (dd, 1H, $J = 14.0, 4.8$ Hz), 3.79 (dd, 1H, $J = 13.6, 5.7$ Hz), 4.89 (t, 1H, $J = 5.2$ Hz), 7.06 (d, 2H, $J = 8.1$ Hz), 7.16-7.19 (m, 3H), 7.21-7.24 (m, 2H), 7.29-7.32 (m, 3H), 7.38-7.40 (m, 2H), 7.44-7.59 (m, 5H), 8.01 (d, 2H, $J = 7.1$ Hz); ^{13}C NMR (CDCl_3 , 100 MHz): δ 12.8, 21.5, 23.1, 31.2, 38.6, 39.0, 43.9,

55.0, 87.1, 126.7, 126.8, 127.0, 127.6, 128.1, 128.2, 128.3, 128.5, 129.4, 129.5, 130.0, 130.6, 133.1, 135.5, 137.4, 138.3, 139.1, 142.9, 164.6; IR (NaCl, neat) ν : 3022, 2957, 1719, 1450, 1279, 1157 cm^{-1} ; HRMS (ESI) calcd. For $\text{C}_{36}\text{H}_{35}\text{NO}_4\text{SNa}$ ($\text{M}^+ + \text{Na}$): 600.2185, found: 600.2185.

(1*R*,4*S*,7*R*)-4,5-Dimethyl-7-phenyl-3-tosyl-3-azabicyclo[4.2.0]oct-5-en-7-yl Benzoate (158j)

White solid, mp = 154-157 °C; $[\alpha]_{\text{D}}^{25} +104.2$ (c 1.0, CHCl_3); ^1H NMR (CDCl_3 , 400 MHz): δ 1.38 (d, 3H, J = 6.8 Hz), 1.98 (s, 3H), 2.20-2.43 (m, 5H), 2.80 (dd, 1H, J = 13.3, 10.4 Hz), 3.09 (dd, 1H, J = 11.2, 7.6 Hz), 4.01 (dd, 1H, J = 12.6, 6.3 Hz), 4.51 (q, 1H, J = 6.6 Hz), 7.13 (d, 2H, J = 8.1 Hz), 7.29-7.33 (m, 3H), 7.28-7.55 (m, 5H), 7.62 (d, 2H, J = 8.2 Hz), 7.95 (d, 2H, J = 7.3 Hz); ^{13}C NMR (CDCl_3 , 100 MHz): δ 15.8, 19.5, 21.5, 32.7, 38.3, 43.7, 53.2, 86.7, 123.8, 126.7, 127.0, 128.1, 128.4, 128.4, 129.5, 129.5, 130.6, 133.0, 134.9, 138.7, 139.2, 143.0, 164.7; IR (NaCl, neat) ν : 3021, 1719, 1314, 1281, 1217, 1161 cm^{-1} ; HRMS (ESI) calcd. For $\text{C}_{29}\text{H}_{30}\text{NO}_4\text{S}$ ($\text{M}^+ + \text{H}$): 488.1896, found: 488.1895.

(1*R*,4*S*,7*R*)-5-Methyl-7-phenyl-4-propyl-3-tosyl-3-azabicyclo[4.2.0]oct-5-en-7-yl**Benzoate (158k)**

Colourless oil; $[\alpha]_{\text{D}}^{25} +79.8$ (c 1.0, CHCl_3); ^1H NMR (CDCl_3 , 400 MHz): δ 0.97 (t, 3H, J = 6.9 Hz), 1.48-1.62 (m, 3H), 1.78-1.85 (m, 1H), 1.99 (s, 4H), 2.26-2.34 (m, 4H), 2.81 (dd, 1H, J = 13.8, 10.6 Hz), 3.02 (dd, 1H, J = 11.0, 7.8 Hz), 4.01 (dd, 1H, J = 13.8, 6.4 Hz), 4.00 (t, 1H, J = 5.0 Hz), 7.05 (d, 2H, J = 8.0 Hz), 7.26-7.42 (m, 7H), 7.51-7.60 (m, 3H), 7.94 (d, 2H, J = 7.3 Hz); ^{13}C NMR (CDCl_3 , 100 MHz): δ 14.1, 16.2, 19.6, 21.5, 31.5, 35.0, 38.4, 44.1, 57.7, 86.7, 122.6, 126.7, 127.1, 128.0, 128.2, 128.4, 129.4, 129.5, 130.6, 133.0, 134.9, 138.7, 139.1, 142.9, 164.6; IR (NaCl, neat) ν : 3021, 2959, 1717, 1450, 1280, 1159 cm^{-1} ; HRMS (ESI) calcd. For $\text{C}_{31}\text{H}_{33}\text{NO}_4\text{SNa}$ ($\text{M}^+ + \text{Na}$): 538.2028, found: 538.2022.

(1*R*,4*S*,7*R*)-5-Methyl-4,7-diphenyl-3-tosyl-3-azabicyclo[4.2.0]oct-5-en-7-yl Benzoate (158l)

White solid, mp = 138-140 $^{\circ}\text{C}$; $[\alpha]_{\text{D}}^{25} +83.4$ (c 1.0, CHCl_3); ^1H NMR (CDCl_3 , 400 MHz): δ 1.84 (s, 3H), 2.28 (s, 3H), 2.50-2.61 (m, 2H), 2.92 (dd, 1H, J = 13.2, 10.1 Hz), 3.24 (dd, 1H, J = 11.1, 7.4 Hz), 3.92 (dd, 1H, J = 13.2, 6.4 Hz), 5.50 (s, 1H), 7.02 (d, 2H, J = 8.0 Hz), 7.29-7.43 (m, 12H), 7.52-7.55 (m, 3H), 7.96 (d, 2H, J = 7.3 Hz); ^{13}C NMR (CDCl_3 , 100 MHz): δ 16.5, 21.4, 32.5, 38.5, 43.6, 60.1, 86.8, 121.0, 126.7, 127.1, 127.9, 128.3,

128.5, 128.7, 128.7, 129.3, 129.5, 130.6, 133.1, 137.0, 138.2, 139.0, 139.5, 142.8, 164.7;
 IR (NaCl, neat) ν : 3019, 1719, 1491, 1281, 1157 cm^{-1} ; HRMS (ESI) calcd. For $\text{C}_{34}\text{H}_{32}\text{NO}_4\text{S}$ ($\text{M}^+ + \text{H}$): 550.2052, found: 550.2058.

(±)-4-Benzyl-5-pentyl-7-(thiophen-3-yl)-3-tosyl-3-azabicyclo[4.2.0]oct-5-en-7-yl

Benzoate (158m)

Colourless solid, mp = 130-133 °C; ^1H NMR (CDCl_3 , 400 MHz): δ 0.93 (t, 3H, J = 6.7 Hz), 1.29-1.67 (m, 6H), 2.00-2.22 (m, 3H), 2.37 (s, 3H), 2.43-2.55 (m, 1H), 2.82-2.93 (m, 2H), 3.03 (dd, 1H, J = 14.0, 6.0 Hz), 3.14 (dd, 1H, J = 14.0, 4.6 Hz), 3.80 (dd, 1H, J = 12.9, 6.0 Hz), 4.80 (s, 1H), 6.99-7.26 (m, 10H), 7.45-7.53 (m, 4H), 7.58 (t, 1H, J = 7.6 Hz), 8.01 (d, 2H, J = 8.0 Hz); ^{13}C NMR (CDCl_3 , 100 MHz): δ 14.1, 21.5, 22.6, 27.6, 29.9, 31.7, 31.8, 39.1, 40.2, 43.9, 55.3, 83.8, 123.6, 125.8, 126.2, 126.7, 126.9, 127.0, 128.2, 128.5, 129.5, 130.0, 130.6, 133.2, 136.0, 137.3, 138.4, 140.7, 143.0, 164.7; IR (NaCl, neat) ν : 3019, 2940, 1717, 1450, 1279, 1157 cm^{-1} ; HRMS (ESI) calcd. For $\text{C}_{37}\text{H}_{40}\text{NO}_4\text{S}_2$ ($\text{M}^+ + \text{H}$): 626.2399, found: 626.2398.

(1*R*,4*R*,7*R*)-4-(((*tert*-Butyldimethylsilyl)oxy)methyl)-5-ethyl-7-phenyl-3-tosyl-3-azabicyclo[4.2.0]oct-5-en-7-yl Benzoate (158n)

White solid, mp = 168-169 °C; $[\alpha]_D^{25} +116.1$ (*c* 1.0, CHCl₃); ¹H NMR (CDCl₃, 400 MHz): δ 0.00 (s, 3H), 0.01 (s, 3H), 0.74 (s, 9H), 1.18 (m, 3H, *J* = 7.6 Hz), 2.15-2.24 (m, 6H), 2.97-3.07 (m, 1H), 3.14-3.24 (m, 2H), 3.95 (dd, 1H, *J* = 10.5, 2.4 Hz), 4.01-4.06 (m, 2H), 4.56 (s, 1H), 7.10 (d, 2H, *J* = 8.1 Hz), 7.27-7.44 (m, 7H), 7.52 (t, 1H, *J* = 7.5 Hz), 7.62 (d, 2H, *J* = 8.2 Hz), 7.92 (d, 2H, *J* = 7.5 Hz); ¹³C NMR (CDCl₃, 100 MHz): δ -5.8, -5.6, 13.2, 17.9, 21.5, 22.5, 25.6, 32.0, 38.6, 46.3, 55.2, 65.5, 86.8, 125.8, 126.6, 127.0, 128.0, 128.3, 129.4, 129.6, 130.5, 132.9, 136.3, 138.6, 139.2, 143.0, 164.6; IR (NaCl, neat) ν : 3022, 2957, 1715, 1450, 1215, 1159 cm⁻¹; HRMS (ESI) calcd. For C₃₆H₄₅NO₅SSiNa (M⁺+Na): 654.2685, found: 654.2686.

((1*R*,4*R*,7*R*)-7-(Benzoyloxy)-5-ethyl-7-phenyl-3-tosyl-3-azabicyclo[4.2.0]oct-5-en-4-yl)methyl Benzoate (158o)

Colourless oil; $[\alpha]_D^{25} +72.0$ (*c* 1.0, CHCl₃); ¹H NMR (CDCl₃, 400 MHz): δ 1.23 (t, 3H, *J* = 7.6 Hz), 2.15-2.22 (m, 1H), 2.28-2.45 (m, 5H), 2.89-2.98 (m, 1H), 3.03-3.11 (m, 2H), 4.10 (dd, 1H, *J* = 13.8, 6.6 Hz), 4.59 (dd, 1H, *J* = 11.8, 6.3 Hz), 4.66 (dd, 1H, *J* = 11.8, 2.4 Hz), 4.97 (t, 1H, *J* = 2.9 Hz), 7.08 (d, 2H, *J* = 8.0 Hz), 7.23-7.52 (m, 11H), 7.62 (d, 2H, *J* = 8.1 Hz), 7.88 (d, 2H, *J* = 7.5 Hz), 8.01 (d, 2H, *J* = 7.5 Hz); ¹³C NMR (CDCl₃, 100

MHz): δ 12.9, 21.5, 22.6, 31.5, 38.4, 45.0, 53.3, 65.2, 86.8, 124.7, 126.7, 126.9, 128.2, 128.3, 128.4, 129.5, 129.6, 129.7, 129.8, 129.8, 130.3, 133.0, 133.1, 137.2, 138.2, 138.9, 143.3, 164.6, 166.5; IR (NaCl, neat) ν : 3021, 2968, 1717, 1715, 1601, 1450, 1275, 1161 cm^{-1} ; HRMS (ESI) calcd. For $\text{C}_{37}\text{H}_{35}\text{NO}_6\text{SNa}$ ($\text{M}^+ + \text{Na}$): 644.2083, found: 644.644.2086.

(1*R*,4*S*,7*R*)-5-Ethyl-4-(2-(methylsulfonyl)ethyl)-7-phenyl-3-tosyl-3-azabicyclo[4.2.0]oct-5-en-7-yl Benzoate (158p)

White solid, mp = 209-210 °C; $[\alpha]_{\text{D}}^{25} +133.0$ (c 1.0, CHCl_3); ^1H NMR (CDCl_3 , 400 MHz): δ 1.12 (t, 3H, J = 7.5 Hz), 1.98-2.06 (m, 2H), 2.17-2.29 (m, 4H), 2.38-2.54 (m, 2H), 2.74-2.88 (m, 2H), 2.92-3.04 (m, 4H), 3.40 (t, 3H, J = 7.9 Hz), 4.11 (dd, 1H, J = 14.0, 6.6 Hz), 4.62 (d, 1H, J = 10.7), 7.08 (d, 2H, J = 8.0 Hz), 7.22-7.27 (m, 5H), 7.40 (t, 2H, J = 7.6 Hz), 7.52-7.60 (m, 3H), 7.90 (d, 2H, J = 7.5 Hz); ^{13}C NMR (CDCl_3 , 100 MHz): δ 12.5, 21.6, 22.2, 23.5, 30.8, 38.0, 41.7, 52.0, 53.6, 86.6, 126.8, 126.9, 128.1, 128.3, 128.5, 129.5, 129.6, 130.3, 133.2, 135.4, 137.7, 138.9, 143.6, 164.6; IR (NaCl, neat) ν : 3021, 2957, 1717, 1450, 1281 cm^{-1} ; HRMS (ESI) calcd. For $\text{C}_{32}\text{H}_{36}\text{NO}_6\text{S}_2$ ($\text{M}^+ + \text{H}$): 594.1984, found: 594.1996.

(1*R*,4*S*,7*R*,8*S*)-4,5-Diethyl-7,8-diphenyl-3-tosyl-3-azabicyclo[4.2.0]oct-5-en-7-yl**Benzoate (158q)**

White solid, mp = 80-83 °C; $[\alpha]_D^{25} +90.6$ (*c* 1.0, CHCl₃); ¹H NMR (CDCl₃, 400 MHz): δ 0.97 (t, 3H, *J* = 7.5 Hz), 1.14 (t, 3H, *J* = 7.3 Hz), 1.65-1.76 (m, 1H), 1.87-1.93 (m, 2H), 2.17-2.26 (m, 1H), 2.37-2.43 (m, 1H), 2.53 (s, 3H), 3.19 (dd, 1H, *J* = 13.6, 10.7 Hz), 4.18 (dd, 1H, *J* = 13.7, 6.2 Hz), 4.58 (d, 1H, *J* = 9.0 Hz), 4.64 (d, 1H, *J* = 9.0 Hz), 6.51 (d, 2H, *J* = 7.2 Hz), 6.61 (d, 2H, *J* = 7.6 Hz), 7.00-7.18 (m, 6H), 7.38-7.57 (m, 5H), 7.83 (d, 2H, *J* = 8.0 Hz), 7.97 (d, 2H, *J* = 7.6 Hz); ¹³C NMR (CDCl₃, 100 MHz): δ 11.0, 12.4, 21.7, 22.1, 25.5, 34.9, 43.8, 52.3, 56.8, 93.3, 126.8, 127.2, 127.6, 127.7, 127.9, 128.4, 128.5, 129.5, 129.6, 129.7, 130.8, 131.8, 133.1, 136.6, 137.2, 139.3, 143.0, 165.0; IR (NaCl, neat) ν : 2970, 2936, 1719, 1451, 1159, 1092 cm⁻¹; HRMS (ESI) calcd. For C₃₇H₃₇NO₄SNa (*M*⁺+Na): 614.2341, found: 614.2343.

(1*R*,4*S*,7*R*,8*S*)-5-Ethyl-4-isobutyl-7,8-diphenyl-3-tosyl-3-azabicyclo[4.2.0]oct-5-en-7-yl Benzoate (158r)

White solid, mp = 90-93 °C; $[\alpha]_D^{25} +77.1$ (*c* 1.0, CHCl₃); ¹H NMR (CDCl₃, 400 MHz): δ 0.98-1.02 (m, 6H), 1.11 (d, 3H, *J* = 6.8 Hz), 1.43 (dt, 1H, *J* = 12.2, 1.8 Hz), 1.68 (dt, 1H, *J* = 12.2, 2.1 Hz), 1.87-1.96 (m, 1H), 2.06-2.11 (m, 1H), 2.19-2.28 (m, 1H), 2.45 (dd, 1H, *J* = 9.0, 7.9 Hz), 2.54 (s, 3H), 3.21 (dd, 1H, *J* = 13.8, 10.7 Hz), 4.13 (dd, 1H, *J* = 13.8, 6.3

Hz), 4.58 (d, 1H, $J = 9.2$ Hz), 4.66 (d, 1H, $J = 9.0$ Hz), 6.51 (d, 2H, $J = 7.0$ Hz), 6.57 (d, 2H, $J = 7.6$ Hz), 7.00-7.10 (m, 5H), 7.16 (t, 1H, $J = 7.4$ Hz), 7.39-7.44 (m, 4H), 7.55 (t, 1H, $J = 7.4$ Hz), 7.84 (d, 2H, $J = 8.2$ Hz), 7.97 (m, 2H, $J = 7.5$ Hz); ^{13}C NMR (CDCl_3 , 100 MHz): δ 12.2, 21.6, 21.8, 22.4, 24.2, 24.7, 34.8, 41.5, 43.1, 52.6, 54.3, 93.6, 126.8, 127.4, 127.6, 127.7, 128.0, 128.0, 128.5, 128.6, 129.3, 129.6, 129.8, 130.8, 131.9, 133.1, 136.5, 137.2, 139.2, 143.1, 165.0; IR (NaCl, neat) ν : 2970, 2229, 1719, 1450, 1267, 1155 cm^{-1} ; HRMS (ESI) calcd. For $\text{C}_{39}\text{H}_{41}\text{NO}_4\text{SNa}$ ($\text{M}^+ + \text{Na}$): 642.2654, found: 642.2645.

(1R,4S,7R,8S)-5-Ethyl-4-isopropyl-7,8-diphenyl-3-tosyl-3-azabicyclo[4.2.0]oct-5-en-7-yl Benzoate (158s)

Colourless solid, mp = 163-165 °C; $[\alpha]_{\text{D}}^{25} +176.4$ (c 1.0, CHCl_3); ^1H NMR (CDCl_3 , 400 MHz): δ 1.04 (t, 3H, $J = 7.5$ Hz), 1.09 (d, 3H, $J = 7.0$ Hz), 1.29 (d, 3H, $J = 6.7$ Hz), 1.95-2.04 (m, 1H), 2.08-2.14 (m, 1H), 2.24-2.41 (m, 2H), 2.49 (s, 3H), 3.24 (dd, 1H, $J = 13.9$, 10.6 Hz), 4.16 (dd, 1H, $J = 14.0$, 6.4 Hz), 4.60 (d, 1H, $J = 9.1$ Hz), 6.45 (d, 2H, $J = 7.3$ Hz), 6.66 (d, 2H, $J = 7.6$ Hz), 7.00-7.10 (m, 5H), 7.18 (t, 1H, $J = 7.0$ Hz), 7.37-7.57 (m, 5H), 7.80 (d, 2H, $J = 8.2$ Hz), 7.98 (d, 2H, $J = 7.5$ Hz); ^{13}C NMR (CDCl_3 , 100 MHz): δ 12.8, 17.8, 21.3, 21.7, 22.3, 30.9, 34.5, 46.4, 52.6, 59.3, 93.2, 126.8, 127.4, 127.6, 127.6, 128.0, 128.2, 128.5, 128.6, 129.7, 129.9, 130.7, 130.8, 131.3, 133.1, 136.6, 137.2, 139.2, 143.2, 165.0; IR (NaCl, neat) ν : 3019, 1719, 1450, 1267, 1215 cm^{-1} ; HRMS (ESI) calcd. For $\text{C}_{38}\text{H}_{40}\text{NO}_4\text{S}$ ($\text{M}^+ + \text{H}$): 606.2678, found: 606.2672.

(1*R*,4*S*,7*R*,8*S*)-4-Benzyl-5-ethyl-7,8-diphenyl-3-tosyl-3-azabicyclo[4.2.0]oct-5-en-7-yl**Benzoate (158t)**

Yellow oil; $[\alpha]_{\text{D}}^{25} +36.8$ (*c* 1.0, CHCl_3); ^1H NMR (CDCl_3 , 400 MHz): δ 1.05 (t, 3H, $J = 7.6$ Hz), 2.06-2.16 (m, 1H), 2.37-2.46 (m, 4H), 2.61 (dd, 1H, $J = 17.1, 8.7$ Hz), 2.89 (dd, 1H, $J = 13.8, 10.5$ Hz), 3.04 (dd, 1H, $J = 14.0, 7.9$ Hz), 3.17 (dd, 1H, $J = 14.0, 4.6$ Hz), 3.95 (dd, 1H, $J = 13.8, 6.4$ Hz), 4.45 (d, 1H, $J = 9.2$ Hz), 4.93 (t, 1H, $J = 5.2$ Hz), 6.57 (d, 2H, $J = 6.7$ Hz), 6.76 (d, 2H, $J = 7.2$ Hz), 7.01-7.09 (m, 5H), 7.16-7.25 (m, 8H), 7.45 (t, 2H, $J = 7.6$ Hz), 7.55-7.59 (m, 3H), 8.01 (d, 2H, $J = 7.2$ Hz); ^{13}C NMR (CDCl_3 , 100 MHz): δ 12.6, 21.6, 22.7, 35.4, 39.1, 43.4, 52.9, 56.3, 93.6, 126.5, 126.8, 127.2, 127.7, 127.7, 128.1, 128.3, 128.5, 128.7, 129.6, 129.6, 129.9, 130.8, 130.9, 131.1, 133.2, 136.5, 137.2, 138.0, 138.5, 143.0, 165.1; IR (NaCl, neat) ν : 3026, 1717, 1454, 1277, 1217, 1157 cm^{-1} ; HRMS (ESI) calcd. For $\text{C}_{42}\text{H}_{39}\text{NO}_4\text{SNa}$ ($\text{M}^+ + \text{Na}$): 676.2498, found: 676.2491.

(1*R*,4*S*,7*R*,8*S*)-4,5-Dimethyl-7,8-diphenyl-3-tosyl-3-azabicyclo[4.2.0]oct-5-en-7-yl**Benzoate (158u)**

White solid, mp = 151-152 °C; $[\alpha]_{\text{D}}^{25} +78.3$ (*c* 1.0, CHCl_3); ^1H NMR (CDCl_3 , 400 MHz): δ 1.43 (d, 3H, $J = 6.8$ Hz), 1.64 (d, 3H, $J = 1.4$ Hz), 2.49 (s, 3H), 2.57-2.63 (m, 1H), 3.14 (dd, 1H, $J = 13.3, 10.4$ Hz), 4.15 (dd, 1H, $J = 13.3, 6.1$ Hz), 4.54 (d, 1H, $J = 9.0$ Hz), 4.62 (q, 1H, $J = 6.6$ Hz), 6.61 (d, 2H, $J = 6.6$ Hz), 6.76 (d, 2H, $J = 7.2$ Hz), 7.03-7.11 (m, 5H),

7.18 (t, 1H, $J = 7.4$ Hz), 7.36 (d, 2H, $J = 8.0$ Hz), 7.42 (t, 2H, $J = 7.6$ Hz), 7.55 (t, 1H, $J = 7.4$ Hz), 7.79 (d, 2H, $J = 8.2$ Hz), 7.99 (d, 2H, $J = 7.2$ Hz); ^{13}C NMR (CDCl_3 , 100 MHz): δ 15.3, 19.5, 21.6, 36.3, 43.5, 52.9, 53.8, 93.1, 126.8, 126.9, 127.0, 127.4, 127.7, 127.9, 128.0, 128.5, 128.7, 129.6, 129.8, 130.6, 130.8, 133.1, 136.4, 137.1, 139.0, 143.1, 165.1; IR (NaCl, neat) ν : 3021, 1717, 1458, 1277, 1161 cm^{-1} ; HRMS (ESI) calcd. For $\text{C}_{35}\text{H}_{33}\text{NO}_4\text{SNa}$ ($\text{M}^+ + \text{Na}$): 586.2028, found: 586.2018.

(1*R*,4*S*,7*R*,8*S*)-5-Methyl-7,8-diphenyl-4-propyl-3-tosyl-3-azabicyclo[4.2.0]oct-5-en-7-yl Benzoate (158v)

Yellow solid, mp = 72-74 °C; $[\alpha]_{\text{D}}^{25} +62.9$ (c 1.0, CHCl_3); ^1H NMR (CDCl_3 , 400 MHz): δ 0.99 (t, 3H, $J = 6.6$ Hz), 1.43-1.70 (m, 6H), 1.77-1.82 (m, 1H), 2.34-2.41 (m, 1H), 2.50 (s, 3H), 3.13 (dd, 1H, $J = 13.7, 10.6$ Hz), 4.13 (dd, 1H, $J = 13.7, 6.2$ Hz), 4.49 (d, 1H, $J = 9.0$ Hz), 6.52 (d, 2H, $J = 7.0$ Hz), 6.52 (d, 2H, $J = 7.5$ Hz), 7.00-7.17 (m, 6H), 7.36-7.44 (m, 4H), 7.55 (t, 1H, $J = 7.5$ Hz), 7.81 (d, 2H, $J = 8.2$ Hz), 7.98 (d, 2H, $J = 7.3$ Hz); ^{13}C NMR (CDCl_3 , 100 MHz): δ 14.2, 15.7, 19.6, 21.7, 35.0, 35.2, 44.0, 53.0, 58.3, 93.2, 126.0, 126.9, 127.2, 127.6, 127.7, 128.0, 128.5, 128.6, 129.6, 129.8, 130.6, 130.8, 133.1, 136.3, 137.1, 139.2, 143.1, 165.1; IR (NaCl, neat) ν : 2959, 1716, 1458, 1342, 1159 cm^{-1} ; HRMS (ESI) calcd. For $\text{C}_{37}\text{H}_{37}\text{NO}_4\text{SNa}$ ($\text{M}^+ + \text{Na}$): 614.2341, found: 614.2345.

(1*R*,4*S*,7*R*,8*S*)-5-Methyl-4,7,8-triphenyl-3-tosyl-3-azabicyclo[4.2.0]oct-5-en-7-yl**Benzoate (158w)**

White solid, mp = 168-170 °C; $[\alpha]_{\text{D}}^{25} +125.6$ (c 1.0, CHCl_3); ^1H NMR (CDCl_3 , 400 MHz): δ 1.49 (s, 3H), 2.41 (s, 3H), 2.86 (s, 1H), 3.22 (dd, 1H, $J = 13.0, 10.4$ Hz), 4.04 (dd, 1H, $J = 13.0, 6.1$ Hz), 4.84 (d, 1H, $J = 9.1$ Hz), 5.60 (s, 1H), 6.70 (d, 2H, $J = 6.6$ Hz), 6.92 (d, 2H, $J = 7.6$ Hz), 7.06-7.42 (m, 13H), 7.51-7.60 (m, 5H), 8.00 (d, 2H, $J = 7.8$ Hz); ^{13}C NMR (CDCl_3 , 100 MHz): δ 16.0, 21.6, 36.4, 43.6, 53.0, 60.9, 93.2, 124.1, 127.0, 127.8, 127.8, 127.9, 128.1, 128.2, 128.5, 128.6, 128.8, 129.0, 129.5, 129.7, 130.7, 133.1, 133.1, 136.4, 137.1, 138.4, 139.6, 142.9, 165.2; IR (NaCl, neat) ν : 3022, 1715, 1450, 1215, 1157 cm^{-1} ; HRMS (ESI) calcd. For $\text{C}_{40}\text{H}_{35}\text{NO}_4\text{SNa}$ ($\text{M}^+ + \text{Na}$): 648.2184, found: 648.2182.

(1*R*,4*S*,7*R*,8*R*)-5-Ethyl-4-isopropyl-7,8-diphenyl-3-tosyl-3-azabicyclo[4.2.0]oct-5-en-7-yl Benzoate (158x)

Colourless solid, mp = 159-160 °C; $[\alpha]_{\text{D}}^{25} +72.5$ (c 1.0, CHCl_3); ^1H NMR (CDCl_3 , 400 MHz): δ 0.92 (d, 3H, $J = 6.9$ Hz), 1.22 (d, 3H, $J = 6.6$ Hz), 1.28 (t, 3H, $J = 7.4$ Hz), 2.19-2.22 (m, 4H), 2.32-2.36 (m, 1H), 2.42-2.52 (m, 2H), 3.20-3.29 (m, 1H), 3.55 (dd, 1H, $J = 14.2, 6.8$ Hz), 4.52 (d, 1H, $J = 8.7$ Hz), 4.57 (s, 1H), 6.94 (d, 2H, $J = 7.8$ Hz), 7.06-7.11 (m, 3H), 7.30-7.37 (m, 7H), 7.44-7.51 (m, 5H), 7.74 (d, 2H, $J = 7.8$ Hz); ^{13}C NMR

(CDCl₃, 100 MHz): δ 12.9, 18.4, 21.5, 21.5, 22.8, 30.8, 35.4, 41.9, 51.1, 58.6, 85.9, 126.7, 126.8, 126.9, 127.0, 127.8, 128.0, 128.2, 128.2, 128.8, 129.2, 129.3, 130.2, 132.8, 135.7, 136.1, 138.6, 139.8, 142.9, 163.5; IR (NaCl, neat) ν : 3022, 2968, 1722, 1161 cm⁻¹; HRMS (ESI) calcd. For C₃₈H₄₀NO₄S (M⁺+H): 606.2678, found: 606.2681.

(2*S*,4*S*)-4-(*N*-Allyl-4-methylphenylsulfonamido)-3-ethyl-6-methyl-1-phenylhepta-1,2-dienyl Benzoate (168a)

Colourless oil; $[\alpha]_D^{25}$ -19.9 (*c* 1.0, CHCl₃); ¹H NMR (CDCl₃, 400 MHz): δ 0.79 (d, 3H, *J* = 6.6 Hz), 0.84 (d, 3H, *J* = 6.6 Hz), 1.15 (d, 3H, *J* = 7.2 Hz), 1.47-1.53 (m, 1H), 1.64-1.71 (m, 1H), 2.13-2.23 (m, 1H), 2.35-2.42 (m, 4H), 3.77 (dd, 1H, *J* = 16.4, 6.8 Hz), 3.90 (dd, 1H, *J* = 16.4, 5.2 Hz), 4.52 (dd, 1H, *J* = 8.6, 5.4 Hz), 5.01 (d, 1H, *J* = 9.8 Hz), 5.04 (d, 1H, *J* = 16.2 Hz), 5.68-5.78 (m, 1H), 7.23-7.37 (m, 7H), 7.50 (t, 2H, *J* = 7.7 Hz), 7.63 (t, 1H, *J* = 7.1 Hz), 7.73 (t, 2H, *J* = 6.0 Hz), 8.16 (d, 2H, *J* = 7.8 Hz); ¹³C NMR (CDCl₃, 100 MHz): δ 11.9, 21.5, 22.2, 22.9, 25.1, 25.9, 41.2, 46.5, 59.0, 117.1, 121.5, 124.3, 124.6, 127.5, 127.6, 128.1, 128.6, 128.6, 129.5, 129.6, 130.1, 133.0, 133.5, 135.6, 138.1, 143.3, 164.2, 194.9; IR (NaCl, neat) ν : 3021, 2959, 1950, 1736, 1335, 1265, 1215 cm⁻¹; HRMS (ESI) calcd. For C₃₃H₃₇NO₄SN_a (M⁺+Na): 566.2341, found: 566.2336.

1-Allyl-3-ethyl-2-isobutyl-5-phenyl-4-tosyl-1H-pyrrole (169a)

Colourless solid, mp = 100-102 °C; ^1H NMR (CDCl_3 , 400 MHz): δ 0.93 (d, 6H, J = 6.5 Hz), 1.18 (t, 3H, J = 7.3 Hz), 1.76-1.86 (m, 1H), 2.33 (s, 3H), 2.38 (d, 2H, J = 7.5 Hz), 2.76 (q, 2H, J = 7.3 Hz), 4.16 (d, 2H, J = 1.8 Hz), 4.55 (d, 1H, J = 17.1 Hz), 5.02 (d, 1H, J = 10.4 Hz), 5.57-5.66 (m, 1H), 7.07 (d, 2H, J = 7.9 Hz), 7.12 (d, 2H, J = 7.6 Hz), 7.27-7.38 (m, 5H); ^{13}C NMR (CDCl_3 , 100 MHz): δ 16.5, 18.1, 21.4, 22.5, 29.3, 33.2, 46.7, 116.1, 119.0, 123.0, 126.6, 127.5, 128.7, 128.9, 129.4, 130.8, 131.5, 133.8, 136.2, 141.9, 142.1; IR (NaCl, neat) ν : 3019, 2936, 1453, 1300, 1215, 1138 cm^{-1} ; HRMS (ESI) calcd. For $\text{C}_{26}\text{H}_{31}\text{NO}_2\text{SNa}$ ($\text{M}^+ + \text{Na}$): 444.1973, found: 444.1972.

((3*R*,6*S*)-5-Ethyl-6-isobutyl-3-methyl-1-tosyl-1,2,3,6-tetrahydropyridin-4-yl)(phenyl)-methanone (d₁-170a)

Pale-yellow oil; $[\alpha]_{\text{D}}^{25}$ -12.6 (c 1.0, CHCl_3); ^1H NMR (CDCl_3 , 400 MHz): δ 0.67 (d, 2H, J = 6.6 Hz), 0.87 (t, 3H, J = 7.6 Hz), 0.94-0.98 (m, 6H), 1.36-1.39 (m, 1H), 1.58-1.65 (m, 1H), 1.79-1.91 (m, 2H), 2.04-2.13 (m, 1H), 2.38-2.48 (m, 3H), 2.51 (s, 3H), 2.92 (dd, 1H, J = 14.9, 11.4 Hz), 3.95 (dd, 1H, J = 14.9, 6.3 Hz), 4.38 (d, 1H, J = 10.6 Hz), 7.32-7.55 (m, 7H), 7.81 (d, 2H, J = 8.1 Hz); ^{13}C NMR (CDCl_3 , 100 MHz): δ 12.8, 21.2, 21.7, 24.0, 24.3, 24.6, 29.2, 41.7, 44.6, 52.3, 127.5, 128.6, 129.1, 129.8, 133.4, 135.8, 136.6, 138.3, 139.6, 143.2, 198.7; IR (NaCl, neat) ν : 2961, 1661, 1597, 1449, 1090 cm^{-1} ; HRMS (ESI) calcd. For $\text{C}_{26}\text{H}_{33}\text{DNO}_3\text{S}$ ($\text{M}^+ + \text{H}$): 441.2322, found: 421.2334.

(1*R*,4*S*)-5-Ethylidene-4-isobutyl-7-phenyl-3-tosyl-3-azabicyclo[4.2.0]oct-6-ene (171a)

Colourless oil; *E/Z* ratio = 3.5:1; $[\alpha]_D^{25} +33.2$ (*c* 1.0, CHCl₃); ¹H NMR (CDCl₃, 400 MHz): *E*-isomer: δ 0.89 (d, 3H, *J* = 6.3 Hz), 0.97 (d, 3H, *J* = 6.3 Hz), 1.12-1.14 (m, 1H), 1.55-1.71(m, 2H), 1.83 (d, 3H, *J* = 7.0 Hz), 2.25-2.31 (m, 2H), 2.40 (s, 3H), 2.70 (dd, 1H, *J* = 13.6, 4.0Hz), 3.02 (t, 1H, *J* = 13.6 Hz), 4.20 (dd, 1H, *J* = 13.9, 6.0 Hz), 5.10 (dd, 1H, *J* = 9.8, 5.1 Hz), 5.64 (q, 1H, *J* = 7.0 Hz), 7.19-7.39 (m, 7H), 7.72 (d, 2H, *J* = 8.1 Hz); *Z*-isomer: 2.87 (dd, 1H, *J* = 13.5, 4.2 Hz), 4.66 (t, 1H, *J* = 7.4 Hz), 5.40 (q, 1H, *J* = 6.9 Hz); ¹³C NMR (CDCl₃, 100 MHz): δ 12.8, 21.5, 21.8, 23.5, 24.1, 31.8, 35.8, 41.4, 46.7, 52.8, 120.0, 125.2, 127.2, 128.3, 129.5, 134.2, 135.1, 136.0, 138.9, 139.7, 143.0; IR (NaCl, neat) ν : 3021, 2957, 2399, 1597, 1337, 1157, 1092 cm⁻¹; HRMS (ESI) calcd. for C₂₆H₃₁NO₂SSNa (*M*⁺+Na): 444.1973, found: 444.1992.

7.3 Silver Acetate Catalyzed Hydroamination of 1-(2-(Sulfonylamino)phenyl)prop-2-yn-1-ols to (Z)-2-Methylene-1 sulfonylindolin-3-ols

General Experimental Procedure for the Preparation of 34a-o and 34r-u

To a solution of the appropriate 1-(2-aminophenyl)ketone or aldehyde (1 mmol) in pyridine (0.5 mL) was added *p*-TsCl (0.23 g, 1.2 mmol) at room temperature under an nitrogen atmosphere. The resulting solution was stirred for 4-10 h at room temperature.

On completion, the reaction mixture was quenched by adding H₂O (5 mL), filtered, dried and used directly for the next step. To a stirred solution of diisopropylamine (0.21 mL, 1.5 mmol) in anhydrous THF at –20 °C was added *n*-butyllithium (2.0 M in cyclohexane solution, 0.75 mL, 1.5 mmol) dropwise and the resulting solution was allowed to stirred at the same temperature for 10 min. On lowering the reaction temperature to –78 °C, the appropriate alkyne (1 mmol) was added in a dropwise manner. The resulting mixture was stirred at the same temperature for 1 h. The ketone (0.5 mmol) obtained from the previous step was dissolved in THF (2 mL) and added to the reaction mixture dropwise and allowed to stir for 1 h at the same temperature. The reaction mixture was slowly warmed up to room temperature and stirred for a further 1 h. Upon completion, the reaction mixture was quenched by adding saturated NH₄Cl (10 mL) and extracted with EtOAc (2 x 10 mL). The combined organic layers were washed with brine (20 mL), dried over MgSO₄, and concentrated under reduced pressure. Purification by flash column chromatography on silica gel (10% EtOAc/*n*-hexane) gave the title compound in 64-97% yield.

General Experimental Procedure for the Preparation of 34p,q

To a solution of the appropriate 1-(2-aminophenyl)ketone (1 mmol) in pyridine (0.5 mL) was added *p*-TsCl (0.23 g, 1.2 mmol) at room temperature under nitrogen atmosphere. The resulting solution was stirred for 4-10 h at room temperature. On completion, the reaction mixture was quenched by adding H₂O (5 mL), filtered, dried and used directly for the next step. The solid (0.5 mmol) was dissolved in THF (5 mL) and a solution of

ethynylmagnesium bromide (0.5 M in THF solution, 3 mL, 1.5 mmol) was added at room temperature, brought up to reflux and allowed to stir at this temperature for 3 h. Upon completion, the reaction mixture was cooled to room temperature and quenched by addition of saturated NH_4Cl (10 mL). The reaction mixture was extracted with EtOAc (2 x 10 mL), washed with brine (20 mL), dried over MgSO_4 and concentrated under reduced pressure. Purification by flash column chromatography on silica gel (10% EtOAc/*n*-hexane) gave the title compound in 71-88% yield.

General Experimental Procedure for the Preparation of 34v,w

To a mixture of 2-aminobenzophenone (0.493 g, 2.5 mmol) and pyridine (1.21 mL, 15 mmol) in dichloromethane (10 mL) was added the corresponding $\text{R}^4\text{SO}_2\text{Cl}$ (3 mmol) at 0 °C for 15 minutes. The reaction mixture was then brought up to room temperature and stirred for 4 h. Upon completion, the reaction mixture was quenched with 10% aqueous HCl and extracted with dichloromethane (2 x 10 mL). The combined organic layers were washed with brine (15 mL), dried over MgSO_4 , concentrated under reduced pressure and dried under vacuum to afford the ketone as solid which was used directly for the next step. To a stirred solution of diisopropylamine (0.21 mL, 1.5 mmol) in anhydrous THF at -20 °C was added *n*-butyllithium (2.0 M in cyclohexane solution, 0.75 mL, 1.5 mmol) dropwise and the resulting solution was allowed to stirred at the same temperature for 10 min. On lowering the reaction temperature to -78 °C, the appropriate alkyne (1 mmol) was added in a dropwise manner. The resulting mixture was stirred at the same temperature for 1 h. The ketone (0.5 mmol) obtained from the previous step was dissolved

in THF (2 mL) and added to the reaction mixture dropwise and allowed to stir for 1 h at the same temperature. The reaction mixture was slowly warmed up to room temperature and stirred for a further 1 h. Upon completion, the reaction mixture was quenched by adding saturated NH_4Cl (10 mL) and extracted with EtOAc (2 x 10 mL). The combined organic layers were washed with brine (20 mL), dried over MgSO_4 , and concentrated under reduced pressure. Purification by flash column chromatography on silica gel (15% EtOAc/*n*-hexane) gave the title compound in 83-90% yield.

General Experimental Procedure for the Preparation of **34y**

To a mixture of 2-aminobenzophenone (0.986 g, 5 mmol) and DMAP (0.061g, 0.5 mmol) in CH_2Cl_2 (10 mL) at 0 °C was added Boc_2O (1.378 mL, 6 mmol) and Et_3N (0.766 mL, 5.5 mmol). The reaction mixture was allowed to warm to room temperature and stirred for 15 h. Upon completion, H_2O (10 mL) was added to the reaction mixture and extracted with CH_2Cl_2 (2 x 10 mL). The combined organic layers were washed with brine, dried over MgSO_4 and concentrated under reduced pressure to give the ketone as yellow liquid which was used directly to the next step. To a stirred solution of diisopropylamine (0.15 g, 1.5 mmol) in anhydrous THF at -20 °C was added *n*-butyllithium (2.0 M in cyclohexane solution, 0.75 mL, 1.5 mmol) dropwise and the resulting solution was allowed to stirred at the same temperature for 10 min. On lowering the reaction temperature to -78 °C, the appropriate alkyne (1 mmol) was added in a dropwise manner. The resulting mixture was stirred at the same temperature for 1 h. The ketone (0.5 mmol) obtained from the previous step was dissolved in THF (2 mL) and added to the reaction

mixture dropwise and allowed to stir for 1 h at the same temperature. The reaction mixture was slowly warmed up to room temperature and stirred for a further 1 h. Upon completion, the reaction mixture was quenched by adding saturated NH_4Cl (10 mL) and extracted with EtOAc (2 x 10 mL). The combined organic layers were washed with brine (20 mL), dried over MgSO_4 , and concentrated under reduced pressure. Purification by flash column chromatography on silica gel (12% EtOAc/*n*-hexane) gave the title compound in 25% yield.

General Procedure for Optimizing the Hydroamination of (**34a**)

To a solution of **34a** (0.2 mmol) in the appropriate solvent (2 mL) was added the appropriate catalyst (0.01 mmol). The reaction was stirred at room temperature and monitored by TLC analysis. Upon completion, the reaction mixture was filtered through Celite, washed with CH_2Cl_2 (10 mL) and concentrated under reduced pressure. Purification by flash column chromatography on silica gel (10% EtOAc/*n*-hexane) gave **164a**.

General Procedure for AgOAc Catalyzed Hydroamination of (**34**)

To a solution of **34** (0.2 mmol) in acetonitrile (2 mL) was added AgOAc (0.01 mmol). The reaction was stirred at room temperature and monitored by TLC analysis. Upon

completion, the reaction mixture was filtered through Celite, washed with CH_2Cl_2 (10 mL) and concentrated under reduced pressure. Purification by flash column chromatography on silica gel (10% EtOAc/*n*-hexane) gave **164**.

Procedure for AgOAc Catalyzed Hydroamination of (**34a**) in the Presence of D_2O

To a solution of **34a** (90.7 mg, 0.2 mmol) and D_2O (18 μL , 1 mmol) in anhydrous acetonitrile (2 mL) was added AgOAc (0.01 mmol). The reaction was stirred at room temperature under nitrogen atmosphere and monitored by TLC analysis. Upon completion, the reaction mixture was filtered through Celite, washed with CH_2Cl_2 (10 mL) and concentrated under reduced pressure. Purification by flash column chromatography on silica gel (10% EtOAc/*n*-hexane) gave (**d₁-164a**).

Synthesis of Phenyl(3-phenyl-1-tosyl-1*H*-indol-2-yl)methanol (**180a**)

To a stirred solution of **164a** (90.7 mg, 0.2 mmol) in acetonitrile (2 mL) was added $p\text{-TsOH} \cdot \text{H}_2\text{O}$ (1.9 mg, 0.01 mmol) at atmospheric condition. The reaction mixture was allowed to stir for 3 h at room temperature. Upon completion, the reaction mixture was added H_2O (5 mL), extracted with EtOAc (2 x 10 mL), washed with brine (20 mL), dried over MgSO_4 and concentrated under reduced pressure. Purification by flash column chromatography on silica gel (15% EtOAc/*n*-hexane) gave title compound **180a** as a yellow oil.

Synthesis of 2-(Fluoromethyl)-3-phenyl-1-tosyl-1*H*-indole (**181p**)

To a solution of **164p** (37.7 mg, 0.1 mmol) in dry CH_2Cl_2 (1 mL) at $-78\text{ }^\circ\text{C}$ was added *N,N*-diethylaminosulfur trifluoride (66 μL , 0.5 mmol). After stirring for 1 h at this temperature, the reaction mixture was warmed up to room temperature. After stirring for 3 h at this temperature, the reaction mixture was quenched with saturated aqueous NaHCO_3 (5 mL) dropwise at $0\text{ }^\circ\text{C}$. The reaction mixture was allowed to stir for 5 min at room temperature, extracted with CH_2Cl_2 (3 x 10 mL) and washed with brine (20 mL). The combined organic layers were dried over MgSO_4 and concentrated under reduced pressure. Purification by flash column chromatography on silica gel (5% EtOAc/*n*-hexane) gave the title compound **181p** as a white solid.

Synthesis of 3-(Iodomethyl)-3-phenyl-1-tosylindolin-2-one (**182p**)

To a solution of **164p** (37.7 mg, 0.1 mmol) in anhydrous MeCN (1 mL) was added NIS (45 mg, 0.2 mmol). The reaction mixture was stirred for 1 h at reflux and monitored by TLC analysis. Upon completion, the reaction mixture was cooled to room temperature, quenched by addition of 10% $\text{Na}_2\text{S}_2\text{O}_3 \cdot 5\text{H}_2\text{O}$ (5 mL) and extracted with EtOAc (2x10 mL). The combined organic layers were washed with brine, dried over MgSO_4 and concentrated under reduced pressure. Purification by flash column chromatography on silica gel (5% EtOAc/*n*-hexane) gave the title compound **182p** as white solid.

Synthesis of (Z)-2-Benzylidene-1-tosylindolin-3-one (183r)

To a solution of **164r** (37.7 mg, 0.1 mmol) in MeCN (1 mL) was added NIS (45 mg, 0.2 mmol). The reaction mixture was stirred at reflux for 1 h and monitored by TLC analysis. Upon completion, the reaction mixture was cooled to room temperature, quenched by addition of 10% $\text{Na}_2\text{S}_2\text{O}_3 \cdot 5\text{H}_2\text{O}$ (5 mL) and extracted with EtOAc (2 x 10 mL). The combined organic layers were washed with brine (20 mL), dried over MgSO_4 and concentrated under reduced pressure. Purification by flash column chromatography on silica gel (5% EtOAc/*n*-hexane) gave the title compound as a yellow solid.

N-(2-(1-Hydroxy-1,3-diphenylprop-2-yn-1-yl)phenyl)-4-methylbenzenesulfonamide (**34a**)²²

Yield 90%; wt. 0.204 g; white solid; ^1H NMR (CDCl_3 , 400 MHz): δ 8.89 (1H, brs), 7.58 (1H, d, $J = 7.8$ Hz), 7.52 (1H, d, $J = 8.16$ Hz), 7.40-7.46 (4H, m), 7.31 (2H, d, $J = 8.16$ Hz), 7.23-7.28 (6H, m), 7.14-7.20 (1H, m), 6.93-6.97 (3H, m), 4.24 (1H, brs), 2.23 (3H, s); ^{13}C NMR (CDCl_3 , 100 MHz): δ 143.4, 143.1, 136.3, 136.0, 131.8, 130.9, 129.5, 129.4, 129.0, 128.7, 128.4, 128.1, 127.4, 126.1, 122.8, 122.0, 118.7, 90.0, 89.1, 75.5, 21.5.

***N*-(2-(1-Hydroxy-1,3-diphenylprop-2-yn-1-yl)-4-methylphenyl)-4-methylbenzenesulfonamide (34b)**

Yield 80%; wt. 0.187 g; white solid; m.p. 140-142 °C; ^1H NMR (CDCl_3 , 400 MHz): δ 8.67 (1H, brs), 7.59 (2H, t, $J = 8.8$ Hz), 7.44-7.46 (2H, m), 7.38 (2H, d, $J = 8.24$ Hz), 7.28-7.34 (5H, m), 7.19-7.24 (1H, m), 7.10 (2H, d, $J = 8.04$ Hz), 6.97-7.01 (3H, m), 3.32 (1H, brs), 2.38 (3H, s), 2.30 (3H, s); ^{13}C NMR (CDCl_3 , 100 MHz): δ 143.3, 139.9, 138.0, 136.5, 136.0, 131.8, 130.8, 129.4, 129.3, 129.0, 128.8, 128.4, 127.4, 126.0, 122.8, 121.9, 118.8, 89.9, 89.1, 75.4, 21.5, 21.2; IR (NaCl, neat) ν : 3445, 3019, 2399, 1491, 1159 cm^{-1} ; HRMS (ESI) calcd. for $\text{C}_{29}\text{H}_{26}\text{NO}_3\text{S}$ ($\text{M}^+ + \text{H}$): 468.1655, found: 468.1633.

***N*-(4-Bromo-2-(1-hydroxy-1,3-diphenylprop-2-yn-1-yl)phenyl)-4-methylbenzenesulfonamide (34c)²²**

Yield 96%; wt. 0.256 g; white solid; ^1H NMR (CDCl_3 , 300 MHz): δ 8.54 (1H, brs), 7.68 (2H, td, $J = 7.71, 1.47$ Hz), 7.42-7.45 (2H, m), 7.30-7.36 (8H, m), 7.21 -7.26 (2H, m), 7.03-7.08 (3H, m), 3.35 (1H, brs), 2.35 (3H, s); ^{13}C NMR (CDCl_3 , 75 MHz): δ 143.6, 142.3, 136.2, 135.9, 131.8, 131.5, 130.4, 129.8, 129.5, 129.1, 129.1, 128.4, 127.6, 127.0, 123.1, 122.3, 121.7, 119.2, 89.7, 89.4, 75.1, 21.6.

***N*-(4-Chloro-2-(1-hydroxy-1,3-diphenylprop-2-yn-1-yl)phenyl)-4-methylbenzenesulfonamide (34d)²²**

Yield 94%; wt. 0.229 g; yellow solid; ¹H NMR (CDCl₃, 300 MHz): δ 8.70 (1H, brs), 7.57 (1H, s), 7.42-7.50 (5H, m), 7.23-7.31 (8H, m), 7.14 (1H, dd, J = 8.73, 2.22 Hz), 6.97 (2H, d, J = 8.01 Hz), 3.88 (1H, brs), 2.28 (3H, s); ¹³C NMR (CDCl₃, 75 MHz): δ 143.7, 142.3, 135.9, 134.5, 132.6, 131.8, 129.5, 129.3, 129.2, 128.8, 128.4, 128.2, 127.4, 126.0, 121.6, 120.0, 89.7, 89.1, 75.0, 21.5.

***N*-(3-(1-Hydroxy-1,3-diphenylprop-2-yn-1-yl)naphthalen-2-yl)-4-methylbenzenesulfonamide (34e)²²**

Yield 75%; wt. 0.189 g; pale yellow solid; ¹H NMR ((CD₃)₂CO, 400 MHz): δ 9.31 (1H, brs), 8.35 (1H, s), 7.96 (1H, s), 7.87 (1H, d, J = 8.08, Hz), 7.79 (1H, d, J = 8.16 Hz), 7.46-7.53 (5H, m), 7.36-7.42 (9H, m), 7.23 (1H, s), 7.09 (2H, d, J = 8 Hz), 2.88 (1H, brs), 2.26 (3H, s); ¹³C NMR ((CD₃)₂CO, 100 MHz): δ 143.6, 136.3, 134.1, 133.6, 131.5, 131.4, 129.4, 129.0, 128.9, 128.6, 128.5, 128.2, 128.0, 127.4, 127.2, 126.7, 125.8, 125.1, 122.2, 114.1, 90.6, 88.5, 75.1, 20.4.

***N*-(2-(1-Hydroxy-3-phenyl-1-(*p*-tolyl)prop-2-yn-1-yl)phenyl)-4-methylbenzenesulfonamide (34f)²²**

Yield 82 %; wt. 0.192 g; pale yellow solid; ¹H NMR (CDCl₃, 400 MHz): δ 7.55-7.60 (2H, m), 7.46-7.47 (2H, m), 7.40 (2H, d, *J* = 8.28 Hz), 7.29-7.35 (5H, m), 7.22 (2H, td, *J* = 8.32, 1.4 Hz), 7.11 (2H, d, *J* = 8.08 Hz), 6.97-7.03 (3H, m), 2.38 (3H, s), 2.31 (3H, s); ¹³C NMR (CDCl₃, 100 MHz): δ 143.3, 140.0, 138.0, 136.4, 136.0, 131.8, 130.9, 129.4, 129.3, 129.3, 128.9, 128.9, 128.4, 127.4, 126.0, 122.8, 121.9, 118.8, 90.0, 89.0, 75.4, 21.5, 21.2.

***N*-(2-(1-(4-Chlorophenyl)-1-hydroxy-3-phenylprop-2-yn-1-yl)phenyl)-4-methylbenzenesulfonamide (34g)²²**

Yield 93%; wt. 0.227 g; white solid; ¹H NMR (CDCl₃, 400 MHz): δ 8.56 (1H, brs), 7.70 (2H, td, *J* = 7.92, 1.28 Hz), 7.44 (2H, dd, *J* = 7.84, 1.6 Hz), 7.26-7.36 (8H, m), 7.18 (2H, d, *J* = 8.48 Hz), 7.04-7.07 (3H, m), 3.42 (1H, brs), 2.34 (3H, s); ¹³C NMR (CDCl₃, 100 MHz): δ 143.5, 141.5, 136.3, 136.0, 134.1, 131.8, 130.3, 129.8, 129.4, 129.2, 128.9, 128.6, 128.4, 127.2, 127.0, 123.0, 121.6, 119.3, 89.7, 89.3, 75.1, 21.5.

***N*-(2-(1-(4-Bromophenyl)-1-hydroxy-3-phenylprop-2-yn-1-yl)phenyl)-4-methylbenzenesulfonamide (34h)²²**

Yield 64%; wt. 0.171 g; white solid; ¹H NMR (CDCl₃, 400 MHz): δ 8.57 (1H, brs), 7.71 (2H, t, J = 7.8 Hz), 7.43 (2H, d, J = 6.72 Hz), 7.21-7.34 (10H, m), 7.03-7.07 (3H, m), 3.45 (1H, brs), 2.35 (3H, s); ¹³C NMR (CDCl₃, 100 MHz): δ 143.5, 142.0, 136.3, 136.0, 131.8, 131.6, 130.2, 129.9, 129.4, 129.2, 128.9, 128.4, 127.5, 127.0, 123.0, 122.4, 121.5, 119.2, 89.8, 89.2, 75.2, 21.6.

***N*-(2-(3-(4-Fluorophenyl)-1-hydroxy-1-phenylprop-2-yn-1-yl)phenyl)-4-methylbenzenesulfonamide (34i)²²**

Yield 94%; wt. 0.222 g; white solid; ¹H NMR (CDCl₃, 400 MHz): δ 8.61 (1H, brs), 7.53 (2H, t, J = 7.32 Hz), 7.44-7.47 (4H, m), 7.39 (2H, d, J = 8.16 Hz), 7.32-7.35 (3H, m), 7.22 (2H, t, J = 7.8 Hz), 6.98-7.05 (5H, m), 3.23 (1H, brs), 2.32 (3H, s); ¹³C NMR (CDCl₃, 100 MHz): δ 161.7 (1C, d, J_{C-F} = 249 Hz), 142.7 (1C, d, J_{C-F} = 74.5 Hz), 136.5, 136.0, 133.9, 133.8, 130.6, 129.6, 129.4, 128.7 (1C, d, J_{C-F} = 11 Hz), 128.3, 127.4, 126.0, 122.8, 118.9, 115.6 (1C, d, J_{C-F} = 22 Hz), 89.4, 88.3, 75.5, 21.5.

***N*-(2-(1-Hydroxy-1-phenyl-3-(4-(trifluoromethyl)phenyl)prop-2-yn-1-yl)phenyl)-4-methyl benzenesulfonamide (34j)**

Yield 70%; wt. 0.183 g; yellow solid; m.p. 70-73 °C; ^1H NMR (CDCl_3 , 400 MHz): δ 8.67 (1H, brs), 7.56 (4H, s), 7.46-7.54 (4H, m), 7.33-7.39 (5H, m), 7.22 (1H, t, $J = 7.84$ Hz), 6.98-7.04 (3H, m), 3.67 (1H, brs), 2.31 (3H, s); ^{13}C NMR (CDCl_3 , 100 MHz): δ 143.5, 142.4, 136.5, 136.1, 132.1, 130.5, 129.7, 129.5, 128.8, 128.8, 128.4, 127.3, 126.1, 125.6, 125.3 (1C, q, $J_{\text{C-F}} = 3.6$ Hz), 122.9, 119.0, 92.0, 87.7, 75.5, 21.5; IR (NaCl, neat) ν : 3423, 3019, 2399, 1603, 1493, 1323, 1159, 1092 cm^{-1} ; HRMS (ESI) calcd. for $\text{C}_{29}\text{H}_{23}\text{F}_3\text{NO}_3\text{S}$ ($\text{M}^+ + \text{H}$): 522.1351, found: 522.1360.

***N*-(2-(1-Hydroxy-1-phenyl-3-(*p*-tolyl)prop-2-yn-1-yl)phenyl)-4-methylbenzene sulfonamide (34k)²²**

Yield 88%; wt. 0.206 g; white solid; ^1H NMR (CDCl_3 , 400 MHz): δ 8.73 (1H, brs), 7.56 (2H, dd, $J = 7.84, 16.4$ Hz), 7.44-7.46 (2H, m), 7.29-7.36 (7H, m), 7.19 (1H, t, $J = 7.52$ Hz), 7.10 (2H, d, $J = 7.88$ Hz), 6.96-7.00 (3H, m), 3.53 (1H, brs), 2.33 (3H, s), 2.28 (3H, s); ^{13}C NMR (CDCl_3 , 100 MHz): δ 143.4, 143.0, 139.3, 136.4, 136.0, 131.7, 130.8, 129.4, 129.1, 128.9, 128.6, 128.2, 127.4, 126.1, 122.8, 118.8, 89.5, 89.2, 75.5, 21.6, 21.5.

***N*-(2-(1-Hydroxy-1-phenyl-3-(thiophen-3-yl)prop-2-yn-1-yl)phenyl)-4-methylbenzenesulfonamide (34l)**

Yield 88%; wt. 0.202 g; white solid; m.p. 126-127 °C; ^1H NMR (CDCl_3 , 400 MHz): δ 8.64 (1H, brs), 7.51-7.55 (3H, m), 7.45-7.47 (2H, m), 7.38 (2H, d, $J = 8.24$ Hz), 7.31-7.34 (3H, m), 7.27-7.30 (2H, m), 7.22 (1H, td, $J = 7.12, 1.28$ Hz), 7.13 (1H, d, $J = 4.96$ Hz), 6.97-7.04 (3H, m), 3.31 (1H, brs), 2.32 (3H, s); ^{13}C NMR (CDCl_3 , 75 MHz): δ 162.3, 143.4, 142.8, 136.4, 136.0, 130.7, 129.9, 129.8, 129.4, 128.9, 128.7, 128.2, 127.4, 126.1, 125.6, 122.8, 120.8, 118.8, 89.4, 84.6, 75.6, 21.5; IR (NaCl, neat) ν : 3447, 3019, 2243, 1601, 1493, 1335, 1159, 1092 cm^{-1} ; HRMS (ESI) calcd. for $\text{C}_{26}\text{H}_{22}\text{NO}_3\text{S}_2$ ($\text{M}^+ + \text{H}$): 460.1041, found: 460.1049.

***N*-(2-(3-Cyclopropyl-1-hydroxy-1-phenylprop-2-yn-1-yl)phenyl)-4-methylbenzenesulfonamide (34m)²²**

Yield 80%; wt. 0.167 g; white solid; ^1H NMR (CDCl_3 , 300 MHz): δ 8.58 (1H, brs), 7.50 (2H, d, $J = 8.1$ Hz), 7.25-7.38 (7H, m), 7.18 (1H, td, $J = 7.02, 1.44$ Hz), 7.05 (2H, d, $J = 8.1$ Hz), 6.97 (1H, td, $J = 7.68, 1.11$ Hz), 3.09 (1H, brs), 2.32 (3H, s), 1.28-1.36 (1H, m), 0.75-0.83 (4H, m); ^{13}C NMR (CDCl_3 , 75 MHz): δ 143.3, 143.2, 136.5, 135.8, 131.1, 129.4, 129.3, 128.7, 128.5, 128.0, 127.4, 125.9, 122.7, 118.6, 93.7, 76.4, 75.0, 21.5, 8.5, -0.4.

N*-(2-(1-Hydroxy-1-phenylhept-2-yn-1-yl)phenyl)-4-methylbenzenesulfonamide*(34n)**²²

Yield 80%; wt. 0.173 g; white solid; ¹H NMR (CDCl₃, 300 MHz): δ 8.67 (1H, brs), 7.58 (1H, dd, J = 7.83, 1.41 Hz), 7.51 (1H, d, J = 7.41 Hz), 7.24-7.38 (6H, m), 7.17 (1H, td, J = 8.25, 1.47 Hz), 6.94-7.03 (3H, m), 3.38 (1H, brs), 2.30 (3H, s), 2.27 (2H, t, J = 7.17 Hz), 1.47-1.54 (2H, m), 1.34-1.42 (2H, m), 0.88 (3H, t, J = 7.26 Hz), ¹³C NMR (CDCl₃, 75 MHz): δ 143.5, 143.3, 136.4, 135.8, 131.2, 129.4, 129.3, 128.8, 128.5, 127.9, 127.4, 125.9, 122.7, 118.6, 90.9, 81.4, 75.1, 30.4, 22.1, 21.5, 18.6, 13.6.

***N*-(2-(2-Hydroxyoct-3-yn-2-yl)phenyl)-4-methylbenzenesulfonamide (34o)**

Yield 70%; wt. 0.130 g; colorless oil; ¹H NMR (CDCl₃, 400 MHz): δ 9.19 (1H, brs), 7.76 (2H, d, J = 8.24 Hz), 7.57 (1H, dd, J = 7.88, 1.2 Hz), 7.53 (1H, d, J = 8.2 Hz), 7.16-7.26 (3H, m), 6.99 (1H, t, J = 7.44 Hz), 3.00 (1H, brs), 2.36 (3H, s), 2.26 (2H, t, J = 7 Hz), 1.60 (3H, s), 1.49-1.56 (2H, m), 1.38-1.46 (2H, m), 0.91 (3H, t, J = 7.32 Hz); ¹³C NMR (CDCl₃, 75 MHz): δ 143.7, 137.2, 135.6, 131.9, 129.6, 128.8, 127.4, 127.2, 123.3, 119.7, 87.8, 82.4, 71.9, 31.6, 30.5, 22.0, 21.5, 18.4, 13.6; IR (NaCl, neat) ν : 3453, 3225, 2957, 2932, 2243, 1584, 1495, 1333, 1159, 1092 cm⁻¹; HRMS (ESI) calcd. for C₂₁H₂₆NO₃S (M⁺ + H): 372.1633, found: 372.1652.

N*-(2-(1-Hydroxy-1-phenylprop-2-yn-1-yl)phenyl)-4-methylbenzenesulfonamide*(34p)**^{22,78b}

Yield 88%; wt. 0.166 g; white solid; ¹H NMR (CDCl₃, 400 MHz): δ 8.63 (1H, brs), 7.55 (2H, d, *J* = 6.4 Hz), 7.25-7.40 (7H, m), 7.21 (1H, t, *J* = 8.24 Hz), 7.04 (2H, d, *J* = 7.76 Hz), 6.99 (1H, t, *J* = 7.8 Hz), 3.81 (1H, brs), 2.88 (1H, s), 2.31 (3H, s); ¹³C NMR (CDCl₃, 100 MHz): δ 143.6, 142.4, 136.3, 135.9, 130.3, 129.7, 129.5, 129.0, 128.8, 128.4, 127.4, 126.0, 123.0, 119.0, 84.6, 77.9, 75.0, 21.6.

***N*-(2-(2-Hydroxybut-3-yn-2-yl)phenyl)-4-methylbenzenesulfonamide (34q)**

Yield 71%; wt. 0.112 g; white solid; m.p. 109-110 °C; ¹H NMR (CDCl₃, 300 MHz): δ 9.13 (1H, brs), 7.75 (2H, d, *J* = 8.25 Hz), 7.55 (2H, d, *J* = 8.07 Hz), 7.17-7.25 (3H, m), 7.00 (1H, t, *J* = 7.77 Hz), 3.40 (1H, brs), 2.70 (1H, s), 2.35 (3H, s), 1.67 (3H, s); ¹³C NMR (CDCl₃, 75 MHz): δ 143.8, 137.1, 135.6, 130.8, 129.7, 129.1, 127.3, 127.3, 123.5, 119.9, 85.7, 74.8, 71.6, 31.2, 21.5; IR (NaCl, neat) ν: 3444, 3302, 3021, 2132, 1599, 1584, 1334, 1161, 1092 cm⁻¹; HRMS (ESI) calcd. for C₁₇H₁₇NO₃SN⁺ (M⁺ + Na): 338.0827, found: 338.0810.

***N*-(2-(1-Hydroxy-3-phenylprop-2-yn-1-yl)phenyl)-4-methylbenzenesulfonamide (34r)**

Yield 85%; wt. 0.160 g; pale yellow solid; m.p. 139-141 °C; ^1H NMR (CDCl_3 , 400 MHz): δ 7.69 (2H, d, $J = 7.72$ Hz), 7.56 (1H, d, $J = 7.36$ Hz), 7.42-7.46 (3H, m), 7.26-7.34 (4H, m), 7.11-7.17 (3H, m), 5.52 (1H, s), 2.87 (1H, brs), 2.34 (3H, s); ^{13}C NMR (CDCl_3 , 100 MHz): δ 143.9, 136.7, 135.5, 131.8, 130.9, 129.7, 129.0, 128.4, 127.2, 125.2, 122.8, 121.9, 88.5, 86.4, 63.4, 21.6; IR (NaCl, neat) ν : 3448, 3019, 2230, 1587, 1491, 1331, 1159, 1092 cm^{-1} ; HRMS (ESI) calcd. for $\text{C}_{22}\text{H}_{19}\text{NO}_3\text{SNa}$ ($\text{M}^+ + \text{Na}$): 400.0983, found: 400.0992.

***N*-(2-(1-Hydroxybut-2-yn-1-yl)phenyl)-4-methylbenzenesulfonamide (34s)**

Yield 97%; wt. 0.153 g; white solid; m.p. 128-130 °C; ^1H NMR (CDCl_3 , 400 MHz): δ 7.68 (2H, d, $J = 8.2$ Hz), 7.42-7.47 (2H, m), 7.21-7.26 (3H, m), 7.10 (1H, t, $J = 7.56$ Hz), 5.21 (1H, d, $J = 1.92$ Hz), 2.38 (3H, s), 1.90 (3H, s); ^{13}C NMR (CDCl_3 , 100 MHz): δ 143.9, 136.9, 135.5, 131.2, 129.7, 129.5, 128.2, 127.2, 125.0, 122.7, 85.3, 76.9, 63.2, 21.6, 3.8; IR (NaCl, neat) ν : 3442, 3026, 2399, 1491, 1215, 1159, 1092 cm^{-1} ; HRMS (ESI) calcd. for $\text{C}_{17}\text{H}_{18}\text{NO}_3\text{S}$ ($\text{M}^+ + \text{H}$): 316.1007, found: 316.1005.

***N*-(2-(1-Hydroxyhept-2-yn-1-yl)phenyl)-4-methylbenzenesulfonamide (34t)**

Yield 71%; wt. 0.127 g; yellow solid; m.p. 92-94 °C; ^1H NMR (CDCl_3 , 300 MHz): δ 8.00 (1H, brs), 7.67 (2H, d, $J = 8.22$ Hz), 7.48 (1H, d, $J = 7.44$ Hz), 7.39 (1H, d, $J = 7.92$ Hz), 7.19-7.26 (3H, m), 7.09 (1H, t, $J = 7.29$ Hz), 5.24 (1H, s), 2.89 (1H, brs), 2.36 (3H, s), 2.24 (2H, t, $J = 7.08$ Hz), 1.46-1.54 (2H, m), 1.34-1.44 (2H, m), 0.90 (3H, t, $J = 7.2$ Hz); ^{13}C NMR (CDCl_3 , 75 MHz): δ 143.8, 136.8, 135.4, 131.5, 129.7, 129.4, 128.2, 127.2, 125.1, 122.7, 89.7, 77.8, 62.9, 30.5, 22.0, 21.5, 18.5, 13.6; IR (NaCl, neat) ν : 3566, 3472, 3462, 3312, 3019, 2959, 2934, 1587, 1493, 1458, 1333, 1161, 1092 cm^{-1} ; HRMS (ESI) calcd. for $\text{C}_{20}\text{H}_{24}\text{NO}_3\text{S}$ ($\text{M}^+ + \text{H}$): 358.1477, found: 358.1467.

***N*-(2-(3-Cyclopropyl-1-hydroxyprop-2-yn-1-yl)phenyl)-4-methylbenzenesulfonamide (34u)**

Yield 74%; wt. 0.126 g; white solid; m.p. 116-118 °C; ^1H NMR (CDCl_3 , 300 MHz): δ 7.96 (1H, brs), 7.68 (2H, d, $J = 8.25$ Hz), 7.38-7.44 (2H, m), 7.20-7.26 (3H, m), 7.08 (1H, td, $J = 7.56, 0.87$ Hz), 5.20 (1H, s), 2.71 (1H, brs), 2.37 (3H, s), 1.25-1.32 (1H, m), 0.78-0.83 (2H, m), 0.73-0.76 (2H, m); ^{13}C NMR (CDCl_3 , 75 MHz): δ 143.9, 136.8, 135.5, 131.2, 129.7, 129.4, 128.2, 127.2, 125.0, 122.6, 92.8, 72.9, 63.1, 21.5, 8.4, -0.5; IR (NaCl, neat) ν : 3429, 3019, 2236, 1587, 1491, 1458, 1331, 1277, 1159, 1092 cm^{-1} ; HRMS (ESI) calcd. for $\text{C}_{19}\text{H}_{20}\text{NO}_3\text{S}$ ($\text{M}^+ + \text{H}$): 342.1164, found: 342.1177.

N*-(2-(1-Hydroxy-1,3-diphenylprop-2-yn-1-yl)phenyl)-4-nitrobenzenesulfonamide*(34v)**

Yield: 90%; wt. 0.218 g; yellow solid; m.p. 83-85 °C; ^1H NMR (CDCl_3 , 400 MHz): δ 9.08 (1H, brs); 7.90 (2H, d, J = 8.48 Hz), 7.68 (1H, d, J = 8.12 Hz), 7.60 (1H, d, J = 7.6 Hz), 7.52 (2H, d, J = 8.56 Hz), 7.37 (4H, d, J = 7.24 Hz), 7.22-7.33 (7H, m), 7.07 (1H, t, J = 7.52 Hz), 3.91 (1H, brs); ^{13}C NMR (CDCl_3 , 100 MHz): δ 149.7, 144.8, 142.8, 135.1, 131.7, 131.4, 129.8, 129.4, 129.2, 128.7, 128.5, 128.3, 128.2, 125.9, 124.0, 123.9, 121.5, 119.3, 89.5, 75.6; IR (NaCl, neat) ν : 3453, 3264, 3019, 1605, 1531, 1491, 1348, 1261, 1043 cm^{-1} ; HRMS (ESI) calcd. for $\text{C}_{27}\text{H}_{20}\text{N}_2\text{O}_5\text{SNa}$ ($\text{M}^+ + \text{Na}$): 507.0991 found: 507.0997.

***N*-(2-(1-Hydroxy-1,3-diphenylprop-2-yn-1-yl)phenyl)methanesulfonamide (34w)**

Yield: 83%; wt. 0.157 g; pale yellow solid; m.p. 141-143 °C; ^1H NMR (CDCl_3 , 400 MHz): δ 8.31 (1H, brs), 7.83 (1H, d, J = 7.8 Hz), 7.71 (1H, d, J = 8.08 Hz), 7.57 (2H, d, J = 7.28 Hz), 7.47 (2H, dd, J = 7.52, 1.48 Hz), 7.31-7.40 (7H, m), 7.17 (1H, td, J = 7.72, 0.8 Hz), 3.74 (1H, brs), 2.09 (3H, s); ^{13}C NMR (CDCl_3 , 100 MHz): δ 143.4, 135.9, 132.7, 131.8, 130.0, 129.2, 128.8, 128.5, 128.3, 126.0, 124.0, 121.6, 120.9, 89.6, 89.5, 75.1,

38.0; IR (NaCl, neat) ν : 3447, 3019, 2376, 1395, 1335, 1215, 1043 cm^{-1} ; HRMS (ESI) calcd. for $\text{C}_{22}\text{H}_{20}\text{NO}_3\text{S}$ ($\text{M}^+ + \text{H}$): 378.1164, found: 378.1156.

***N*-(2-(1-Hydroxy-1,3-diphenylprop-2-yn-1-yl)phenyl)acetamide (34x)**

Yield: 76%; wt. 0.130 g; pale yellow solid; m.p. 72-75 $^{\circ}\text{C}$; ^1H NMR (CDCl_3 , 400 MHz): δ 8.68 (1H, brs), 7.96 (1H, d, $J = 8$ Hz), 7.72 (1H, d, $J = 7.48$ Hz), 7.51 (2H, d, $J = 7.12$ Hz), 7.42 (2H, d, $J = 6.68$ Hz), 7.26-7.34 (7H, m), 7.11 (1H, t, $J = 7.48$ Hz), 4.44 (1H, brs), 1.77 (3H, s); ^{13}C NMR (CDCl_3 , 100 MHz): δ 168.3, 143.3, 136.2, 132.8, 131.7, 129.2, 128.9, 128.5, 128.4, 128.1, 128.0, 125.9, 124.2, 123.8, 122.1, 90.1, 88.8, 75.0, 24.3; IR (NaCl, neat) ν : 3564, 3364, 3017, 2359, 1678, 1491, 1215, 1042 cm^{-1} ; HRMS (ESI) calcd. for $\text{C}_{23}\text{H}_{19}\text{NO}_2\text{Na}$ ($\text{M}^+ + \text{Na}$): 364.1313, found: 364.1313.

***tert*-Butyl (2-(1-hydroxy-1,3-diphenylprop-2-yn-1-yl)phenyl)carbamate (34y)**

Yield: 25%; wt. 0.1 g; pale yellow solid; m.p. 67-69 $^{\circ}\text{C}$; ^1H NMR (CDCl_3 , 400 MHz): δ 7.73-7.77 (2H, m), 7.59 (1H, d, $J = 7.68$ Hz), 7.46 (2H, d, $J = 7.56$ Hz), 7.38 (2H, d, $J = 5.76$ Hz), 7.20-7.27 (7H, m), 6.97 (1H, t, $J = 7.56$ Hz), 3.39 (1H, brs), 1.24 (9H, s); ^{13}C NMR (CDCl_3 , 100 MHz): δ 153.0, 143.2, 136.8, 131.8, 129.3, 128.9, 128.4, 128.3, 128.0, 127.7, 126.0, 122.8, 122.1, 90.2, 88.8, 79.8, 75.0, 28.2; IR (NaCl, neat) ν : 3402, 2978, 1719, 1587, 1491, 1159, 1026 cm^{-1} ; HRMS (ESI) calcd. for $\text{C}_{26}\text{H}_{25}\text{NO}_3\text{Na}$ ($\text{M}^+ + \text{Na}$): 422.1732, found: 422.1732.

(Z)-2-Benzylidene-3-phenyl-1-tosylindolin-3-ol (164a)²²

wt. 0.089 g; pale yellow solid; ¹H NMR (CDCl₃, 400 MHz): δ 7.90 (1H, d, *J* = 8.08 Hz), 7.66 (2H, d, *J* = 7.2 Hz), 7.42 (1H, t, *J* = 7.8 Hz), 7.30-7.37 (4H, m), 7.14-7.23 (7H, m), 6.96-7.02 (3H, m), 6.26 (1H, s), 2.28 (3H, s); ¹³C NMR (CDCl₃, 100 MHz): δ 145.4, 144.8, 142.5, 141.9, 138.2, 135.6, 133.0, 130.0, 129.6, 129.4, 128.3, 127.9, 127.9, 127.8, 127.3, 126.9, 126.7, 125.4, 124.8, 119.5, 81.8, 21.6.

(Z)-2-Benzylidene-5-methyl-3-phenyl-1-tosylindolin-3-ol (164b)

wt. 0.091 g; white solid; m.p. 147-148 °C; ¹H NMR (CDCl₃, 400 MHz): δ 7.90 (1H, d, *J* = 8.08 Hz), 7.66 (2H, d, *J* = 7.72 Hz), 7.42 (1H, td, *J* = 8.2, 1.12 Hz), 7.31-7.36 (4H, m), 7.20-7.24 (1H, m), 7.16 (1H, t, *J* = 7.44 Hz), 7.08 (2H, d, *J* = 8.04 Hz), 6.97-7.02 (5H, m), 6.27 (1H, s), 2.29 (3H, s), 2.29 (3H, s); ¹³C NMR (CDCl₃, 100 MHz): δ 145.4, 144.8, 141.9, 139.5, 138.3, 137.0, 135.7, 133.1, 129.9, 129.6, 129.3, 128.6, 128.3, 127.9, 127.7, 126.8, 126.6, 125.3, 124.6, 119.5, 81.8, 21.6, 21.1; IR (NaCl, neat) ν: 3566, 3026, 2872, 1616, 1599, 1449, 1366, 1169, 1086 cm⁻¹; HRMS (ESI) calcd. for C₂₉H₂₅NO₃SNa (M⁺ + Na): 490.1453, found: 490.1465.

(Z)-2-Benzylidene-5-bromo-3-phenyl-1-tosylindolin-3-ol (164c)

wt. 0.093 g; white solid; m.p. 149-151 °C; ^1H NMR (CDCl_3 , 400 MHz): δ 7.92 (1H, d, J = 8.12 Hz), 7.66 (2H, d, J = 7.52 Hz), 7.46 (1H, t, J = 7.4 Hz), 7.19-7.36 (8H, m), 7.06 (4H, t, J = 8.52 Hz), 6.99 (1H, d, J = 7.56 Hz), 6.27 (1H, s), 2.34 (3H, s); ^{13}C NMR (CDCl_3 , 75 MHz): δ 145.0, 145.0, 141.9, 141.7, 135.3, 133.1, 131.0, 130.2, 129.6, 129.4, 128.5, 128.3, 127.9, 126.9, 125.2, 124.8, 121.6, 119.6, 81.6, 21.6; IR (NaCl, neat) ν : 3566, 3026, 2872, 1616, 1599, 1445, 1371, 1171, 1038 cm^{-1} ; HRMS (ESI) calcd. for $\text{C}_{28}\text{H}_{22}\text{BrNO}_3\text{SNa}$ ($\text{M}^+ + \text{Na}$): 554.0401, found: 554.0394.

(Z)-2-Benzylidene-5-chloro-3-phenyl-1-tosylindolin-3-ol (164d)

wt. 0.094 g; yellow solid; m.p. 102-107 °C; ^1H NMR (CDCl_3 , 400 MHz): δ 7.85 (1H, d, J = 8.64 Hz), 7.63 (2H, d, J = 7.48 Hz), 7.32-7.42 (4H, m), 7.22-7.26 (7H, m), 7.09 (2H, d, J = 8.2 Hz), 6.95 (1H, d, J = 2.12 Hz), 6.24 (1H, s), 2.35 (3H, s); ^{13}C NMR (CDCl_3 , 75 MHz): δ 145.1, 144.9, 141.9, 140.4, 140.1, 135.3, 132.8, 132.2, 130.1, 129.6, 128.4, 128.1, 127.9, 127.6, 126.6, 125.5, 125.3, 120.7, 81.7, 21.6; IR (NaCl, neat) ν : 3570, 3026, 2872, 1616, 1599, 1462, 1445, 1371, 1171, 1038 cm^{-1} ; HRMS (ESI) calcd. for $\text{C}_{28}\text{H}_{22}\text{ClNO}_3\text{SNa}$ ($\text{M}^+ + \text{Na}$): 510.0907, found: 510.0893.

(Z)-2-Benzylidene-3-phenyl-1-tosyl-2,3-dihydro-1H-benzo[f]indol-3-ol (164e)

wt. 0.1 g; yellow solid; m.p. 123-125 °C; ^1H NMR (CDCl_3 , 400 MHz): δ 8.31 (1H, s), 7.96 (1H, d, $J = 8.24$ Hz), 7.70 (3H, d, $J = 7.76$ Hz), 7.54 (1H, t, $J = 7.2$ Hz), 7.34-7.47 (6H, m), 7.18-7.27 (6H, m), 6.94 (2H, d, 8.04 Hz), 6.33 (1H, s), 2.25 (3H, s); ^{13}C NMR (CDCl_3 , 100 MHz): δ 145.3, 144.6, 142.2, 139.4, 137.8, 135.7, 134.4, 133.6, 132.1, 129.5, 129.3, 128.4, 128.3, 128.0, 127.8, 127.5, 127.2, 126.9, 125.9, 125.0, 124.0, 116.3, 81.7, 21.5; IR (NaCl, neat) ν : 3570, 3026, 2872, 1616, 1599, 1506, 1445, 1371, 1038 cm^{-1} ; HRMS (ESI) calcd. for $\text{C}_{32}\text{H}_{25}\text{NO}_3\text{SNa}$ ($\text{M}^+ + \text{Na}$): 526.1453, found: 526.1454.

(Z)-2-Benzylidene-3-(p-tolyl)-1-tosylindolin-3-ol (164f)

wt. 0.086 g; white solid; m.p. 145-147 °C; ^1H NMR (CDCl_3 , 400 MHz): δ 7.91 (1H, d, $J = 8.12$ Hz), 7.66 (2H, d, $J = 7.64$ Hz), 7.43 (1H, t, $J = 7.96$ Hz), 7.32-7.38 (4H, m), 7.16-7.24 (2H, m), 7.10 (2H, d, $J = 7.96$ Hz), 7.04 (2H, d, $J = 8$ Hz), 7.00 (3H, d, $J = 8.44$ Hz), 6.27 (1H, s), 2.32 (3H, s), 2.30 (3H, s); ^{13}C NMR (CDCl_3 , 100 MHz): δ 145.4, 144.8, 141.9, 139.5, 138.4, 137.0, 135.7, 133.1, 129.9, 129.6, 129.3, 128.6, 128.3, 127.9, 127.7, 126.8, 126.6, 125.3, 124.6, 119.5, 81.8, 21.6, 21.1; IR (NaCl, neat) ν : 3566, 3016, 2924, 1628, 1597, 1462, 1445, 1368, 1088 cm^{-1} ; HRMS (ESI) calcd. for $\text{C}_{29}\text{H}_{25}\text{NO}_3\text{SNa}$ ($\text{M}^+ + \text{Na}$): 490.1453, found: 490.1457.

(Z)-2-Benzylidene-3-(4-chlorophenyl)-1-tosylindolin-3-ol (164g)

wt. 0.095 g; white solid; m.p. 94-95 °C; ^1H NMR (CDCl_3 , 400 MHz): δ 7.92 (1H, d, J = 8.12 Hz), 7.66 (2H, d, J = 7.64 Hz), 7.46 (1H, t, J = 7.84 Hz), 7.34 (4H, t, J = 7.2 Hz), 7.19-7.27 (3H, m), 7.12-7.17 (4H, m), 7.05 (2H, d, J = 8.04 Hz), 6.99 (1H, d, J = 7.52 Hz), 6.26 (1H, s), 2.33 (3H, s); ^{13}C NMR (CDCl_3 , 100 MHz): δ 145.0, 141.9, 141.1, 137.7, 135.3, 133.3, 133.1, 130.2, 129.6, 129.4, 128.3, 128.1, 128.1, 127.9, 126.9, 125.2, 124.8, 119.6, 81.6, 21.6; IR (NaCl, neat) ν : 3445, 3024, 2924, 1628, 1597, 1489, 1462, 1368, 1071 cm^{-1} ; HRMS (ESI) calcd. for $\text{C}_{28}\text{H}_{22}\text{ClNO}_3\text{SNa}$ ($\text{M}^+ + \text{Na}$): 510.0907, found: 510.0889.

(Z)-2-Benzylidene-3-(4-bromophenyl)-1-tosylindolin-3-ol (164h)

wt. 0.105 g; yellow solid; m.p. 105-107 °C; ^1H NMR (CDCl_3 , 400 MHz): δ 7.91 (1H, d, J = 8.12 Hz), 7.66 (2H, d, J = 7.64 Hz), 7.45 (1H, t, J = 7.96 Hz), 7.18-7.35 (8H, m), 6.98-7.06 (5H, m), 6.28 (1H, s), 2.32 (3H, s); ^{13}C NMR (CDCl_3 , 100 MHz): δ 145.0, 145.0, 141.9, 141.7, 137.6, 135.3, 133.1, 131.0, 130.2, 129.6, 129.4, 128.5, 128.3, 127.9, 127.0, 125.2, 124.8, 121.6, 119.6, 81.6, 21.6; IR (NaCl, neat) ν : 3445, 3019, 2924, 1628, 1597, 1489, 1462, 1370, 1171, 1088, 1011 cm^{-1} ; HRMS (ESI) calcd. for $\text{C}_{28}\text{H}_{22}\text{BrNO}_3\text{SNa}$ ($\text{M}^+ + \text{Na}$): 554.0401, found: 554.0407.

(Z)-2-(4-Fluorobenzylidene)-3-phenyl-1-tosylindolin-3-ol (164i)

wt. 0.083 g; white solid; m.p. 162-163 °C; ^1H NMR (CDCl_3 , 400 MHz): δ 7.90 (1H, d, J = 8.08 Hz), 7.65 (2H, t, J = 7.56 Hz), 7.43 (1H, t, J = 7.8 Hz), 7.36 (2H, d, J = 7.92 Hz), 7.16-7.24 (6H, m), 6.97-7.05 (5H, m), 6.22 (1H, s), 2.31 (3H, s); ^{13}C NMR (CDCl_3 , 100 MHz): δ 160.8 (1C, d, $J_{\text{C-F}}$ = 247 Hz), 145.2, 144.9, 141.8 (1C, d, $J_{\text{C-F}}$ = 62 Hz), 138.2, 133.0, 131.6, 131.4, 131.3, 130.0, 129.4, 128.3, 128.0, 127.4, 126.9, 126.7, 125.4, 123.7, 119.5, 114.8 (1C, d, $J_{\text{C-F}}$ = 21 Hz), 81.8, 21.6; IR (NaCl, neat) ν : 3445, 3019, 2924, 1636, 1603, 1509, 1462, 1171, 1088 cm^{-1} ; HRMS (ESI) calcd. for $\text{C}_{28}\text{H}_{22}\text{FNO}_3\text{SNa}$ ($\text{M}^+ + \text{Na}$): 494.1202, found: 494.1208.

(Z)-3-Phenyl-1-tosyl-2-(4-(trifluoromethyl)benzylidene)indolin-3-ol (164j)

wt. 0.1 g; white solid; m.p. 178-179 °C; ^1H NMR (CDCl_3 , 400 MHz): δ 7.91 (1H, d, J = 8.12 Hz), 7.74 (2H, d, J = 8.08 Hz), 7.56 (2H, d, J = 8.12 Hz), 7.45 (1H, t, J = 7.8 Hz), 7.35 (2H, d, J = 8.04 Hz), 7.18-7.24 (6H, m), 6.99-7.04 (3H, m), 6.27 (1H, s), 2.31 (3H, s); ^{13}C NMR (CDCl_3 , 100 MHz): δ 147.6, 145.1, 142.2, 141.7, 139.4, 137.8, 132.9, 130.2, 129.7, 129.4, 129.4, 128.3, 128.0, 127.5, 127.0, 126.6, 125.4, 124.8 (1C, q, J = 3.71 Hz), 122.8, 119.4, 81.9, 21.6; IR (NaCl, neat) ν : 3564, 3019, 2924, 1659, 1628, 1616, 1597, 1462, 1369, 1323, 1171, 1088, 1019 cm^{-1} ; HRMS (ESI) calcd. for $\text{C}_{29}\text{H}_{22}\text{F}_3\text{NO}_3\text{SNa}$ ($\text{M}^+ + \text{Na}$): 544.1170, found: 544.1183.

(Z)-2-(4-Methylbenzylidene)-3-phenyl-1-tosylindolin-3-ol (164k)

wt. 0.093 g; yellow solid; m.p. 137-139 °C; ^1H NMR (CDCl_3 , 400 MHz): δ 7.92 (1H, d, J = 8.08 Hz), 7.57 (2H, d, J = 7.64 Hz), 7.43 (1H, t, J = 7.76 Hz), 7.37 (2H, d, J = 7.76 Hz), 7.13-7.24 (8H, m), 7.04 (2H, d, J = 7.96 Hz), 6.97 (1H, d, J = 7.52 Hz), 6.22 (1H, s), 2.34 (3H, s), 2.31 (3H, s); ^{13}C NMR (CDCl_3 , 100 MHz): δ 144.8, 144.5, 142.6, 142.0, 138.4, 137.8, 133.1, 132.6, 129.9, 129.6, 129.4, 128.6, 128.4, 127.9, 127.3, 126.8, 126.7, 125.3, 125.1, 119.6, 81.8, 21.6, 21.5; IR (NaCl, neat) ν : 3441, 3019, 2924, 1659, 1628, 1512, 1462, 1369, 1171, 1088, 1015 cm^{-1} ; HRMS (ESI) calcd. for $\text{C}_{29}\text{H}_{25}\text{NO}_3\text{SNa}$ ($\text{M}^+ + \text{Na}$): 490.1453, found: 490.1458.

(Z)-3-Phenyl-2-(thiophen-3-ylmethylene)-1-tosylindolin-3-ol (164l)

wt. 0.091 g; yellow oil; ^1H NMR (CDCl_3 , 300 MHz): δ 7.91 (1H, d, J = 8.07 Hz), 7.71 (1H, d, J = 4.83 Hz), 7.36-7.45 (4H, m), 7.27-7.28 (1H, m), 7.19 (6H, s), 6.96-7.04 (3H, m), 6.32 (1H, s), 2.31 (3H, s); ^{13}C NMR (CDCl_3 , 75 MHz): δ 162.3, 144.8, 144.0, 142.0, 138.4, 136.4, 133.0, 129.9, 129.3, 128.7, 128.4, 127.9, 127.3, 126.9, 126.7, 126.5, 125.4, 124.4, 119.8, 119.5, 81.8, 21.6; IR (NaCl, neat) ν : 3564, 3019, 2870, 1670, 1521, 1464, 1362, 1169, 1087, 1056, 1030 cm^{-1} ; HRMS (ESI) calcd. for $\text{C}_{26}\text{H}_{21}\text{NO}_3\text{S}_2\text{Na}$ ($\text{M}^+ + \text{Na}$): 482.0861, found: 482.0869.

(Z)-2-(Cyclopropylmethylene)-3-phenyl-1-tosylindolin-3-ol (164m)

wt. 0.082 g; yellow solid; m.p. 174-176 °C; ^1H NMR (CDCl_3 , 400 MHz): δ 7.87 (1H, d, J = 8.12 Hz), 7.42 (2H, d, J = 8.16 Hz), 7.38 (1H, t, J = 7.64 Hz), 7.06-7.17 (8H, m), 6.90 (1H, d, J = 7.48 Hz), 4.75 (1H, d, J = 10.44 Hz), 2.40-2.48 (1H, m), 2.32 (3H, s), 0.94-1.00 (1H, m), 0.81-0.88 (1H, m), 0.42-0.48 (1H, m), 0.24-0.30 (1H, m); ^{13}C NMR (CDCl_3 , 100 MHz): δ 144.6, 143.9, 142.8, 142.1, 138.5, 133.3, 133.2, 129.7, 129.4, 128.2, 127.7, 127.0, 126.7, 126.5, 125.2, 119.6, 80.9, 21.6, 12.0, 8.3, 7.7; IR (NaCl, neat) ν : 3568, 3019, 1670, 1636, 1597, 1449, 1364, 1169, 1090, 1018 cm^{-1} ; HRMS (ESI) calcd. for $\text{C}_{25}\text{H}_{23}\text{NO}_3\text{SNa}$ ($\text{M}^+ + \text{Na}$): 440.1296, found: 440.1303.

(Z)-2-Pentylidene-3-phenyl-1-tosylindolin-3-ol (164n)

wt. 0.085 g; yellow oil; ^1H NMR (CDCl_3 , 400 MHz): δ 7.85 (1H, d, J = 8.12 Hz), 7.36-7.40 (3H, m), 7.10-7.18 (6H, m), 7.05 (2H, d, J = 8.4 Hz), 6.92 (1H, d, J = 7.6 Hz), 5.41 (1H, t, J = 8 Hz), 2.58-2.65 (1H, m), 2.50-2.55 (1H, m), 2.32 (3H, s), 1.23-1.35 (4H, m), 0.87 (3H, t, J = 6.8 Hz); ^{13}C NMR (CDCl_3 , 100 MHz): δ 145.3, 144.6, 142.8, 142.1, 138.4, 133.5, 129.7, 129.4, 129.1, 128.1, 127.7, 127.1, 126.7, 126.5, 125.2, 119.4, 81.0, 31.4, 29.0, 22.4, 21.6, 13.9; IR (NaCl, neat) ν : 3547, 3028, 2957, 1670, 1636, 1597, 1449, 1366, 1173, 1090, 1016 cm^{-1} ; HRMS (ESI) calcd. for $\text{C}_{26}\text{H}_{27}\text{NO}_3\text{SNa}$ ($\text{M}^+ + \text{Na}$): 456.1609, found: 456.1619.

(Z)-3-Methyl-2-pentylidene-1-tosylindolin-3-ol (164o)

wt. 0.073 g; yellow oil; ^1H NMR (CDCl_3 , 400 MHz): δ 7.80 (1H, d, $J = 8.08$ Hz), 7.34-7.39 (3H, m), 7.17-7.24 (2H, m), 7.12 (2H, d, $J = 8.12$ Hz), 5.75 (1H, t, $J = 7.2$ Hz), 2.59-2.61 (2H, m), 2.32 (3H, s), 1.36-1.47 (4H, m), 1.07 (3H, s), 0.93 (3H, t, $J = 7.08$ Hz); ^{13}C NMR (CDCl_3 , 100 MHz): δ 144.7, 144.1, 141.2, 138.2, 133.6, 129.5, 129.4, 128.0, 126.4, 124.7, 123.1, 119.6, 76.4, 31.7, 28.9, 26.6, 22.5, 21.5, 14.0; IR (NaCl, neat) ν : 3523, 3019, 2871, 1670, 1521, 1464, 1362, 1171, 1088, 1056, 1030 cm^{-1} ; HRMS (ESI) calcd. for $\text{C}_{21}\text{H}_{25}\text{NO}_3\text{SNa}$ ($\text{M}^+ + \text{Na}$): 394.1453, found: 394.1458.

2-Methylene-3-phenyl-1-tosylindolin-3-ol (164p)

wt. 0.066 g; white solid; m.p. 160-161 $^{\circ}\text{C}$; ^1H NMR (CDCl_3 , 400 MHz): δ 7.97 (1H, d, $J = 8.28$ Hz), 7.59 (2H, d, $J = 8.04$ Hz), 7.37 (1H, t, $J = 7.84$ Hz), 7.01-7.16 (7H, m), 6.92 (2H, d, $J = 7.68$ Hz), 5.88 (1H, s), 4.91 (1H, s), 2.37 (3H, s); ^{13}C NMR (CDCl_3 , 100 MHz): δ 153.4, 144.8, 143.6, 140.9, 135.4, 134.0, 130.3, 129.6, 127.9, 127.4, 127.2, 125.6, 125.5, 125.2, 116.4, 101.6, 80.7, 21.6; IR (NaCl, neat) ν : 3441, 3019, 2924, 1638, 1628, 1601, 1462, 1362, 1171, 1088, 1011 cm^{-1} ; HRMS (ESI) calcd. for $\text{C}_{22}\text{H}_{19}\text{NO}_3\text{SNa}$ ($\text{M}^+ + \text{Na}$): 400.0983, found: 400.0997.

3-Methyl-2-methylene-1-tosylindolin-3-ol (164q)

wt. 0.061 g; colorless oil; ^1H NMR (CDCl_3 , 400 MHz): δ 7.87 (1H, d, $J = 8.24$ Hz), 7.57 (2H, d, $J = 8.12$ Hz), 7.26-7.37 (2H, m), 7.13-7.18 (3H, m), 5.78 (1H, s), 5.14 (1H, s), 2.34 (3H, s), 1.17 (3H, s); ^{13}C NMR (CDCl_3 , 75 MHz): δ 152.8, 144.7, 140.0, 135.4, 134.0, 129.9, 129.4, 127.3, 125.3, 123.3, 116.6, 98.6, 28.9, 21.5; IR (NaCl, neat) ν : 3581, 3019, 2976, 2924, 1659, 1603, 1462, 1360, 1173, 1090 cm^{-1} ; HRMS (ESI) calcd. for $\text{C}_{17}\text{H}_{17}\text{NO}_3\text{SNa}$ ($\text{M}^+ + \text{Na}$): 338.0827, found: 338.0839.

(Z)-2-Benzylidene-1-tosylindolin-3-ol (164r)

wt. 0.065 g; yellow solid; m.p. 122-123 $^{\circ}\text{C}$; ^1H NMR (CDCl_3 , 400 MHz): δ 7.77-7.81 (3H, m), 7.33-7.42 (4H, m), 7.19-7.29 (4H, m), 7.08 (2H, d, $J = 8.12$ Hz), 6.59 (1H, s), 4.84 (1H, s), 2.32 (3H, s); ^{13}C NMR (CDCl_3 , 100 MHz): δ 144.8, 142.5, 141.3, 134.9, 134.8, 133.0, 129.8, 129.7, 129.3, 128.1, 128.0, 126.8, 124.6, 123.6, 120.3, 73.7, 21.6; IR (NaCl, neat) ν : 3447, 3019, 1670, 1636, 1521, 1464, 1368, 1171, 1088, 1056, 1030 cm^{-1} ; HRMS (ESI) calcd. for $\text{C}_{22}\text{H}_{19}\text{NO}_3\text{SNa}$ ($\text{M}^+ + \text{Na}$): 400.0983, found: 400.0981.

(Z)-2-Ethylidene-1-tosylindolin-3-ol (164s)

wt. 0.043 g; yellow oil; ^1H NMR (CDCl_3 , 400 MHz): δ 7.73 (1H, d, $J = 8.08$ Hz), 7.34-7.38 (3H, m), 7.15-7.22 (2H, m), 7.11 (2H, d, $J = 8.08$ Hz), 5.89 (1H, qd, $J = 7.16$, 1.48

Hz), 4.66 (1H, s), 2.33 (3H, s), 2.08 (3H, dd, $J = 7.16, 1.4$ Hz); ^{13}C NMR (CDCl_3 , 100 MHz): δ 144.6, 142.6, 142.3, 135.0, 133.2, 129.6, 129.3, 127.9, 126.5, 124.6, 122.4, 120.2, 72.7, 21.6, 15.0; IR (NaCl, neat) ν : 3422, 3028, 1670, 1636, 1522, 1462, 1358, 1169, 1088, 1055, 1030 cm^{-1} ; HRMS (ESI) calcd. for $\text{C}_{17}\text{H}_{17}\text{NO}_3\text{SNa}$ ($\text{M}^+ + \text{Na}$): 338.0827, found: 338.0820.

(Z)-2-Pentylidene-1-tosylindolin-3-ol (164t)

wt. 0.051 g; white solid; m.p. 117-120 °C; ^1H NMR (CDCl_3 , 400 MHz): δ 7.74 (1H, d, $J = 8.08$ Hz), 7.33-7.39 (3H, m), 7.16-7.23 (2H, m), 7.10 (2H, d, $J = 8.12$ Hz), 5.77 (1H, td, $J = 7.24, 1.16$ Hz), 4.66 (1H, d, $J = 9.84$ Hz), 2.58-2.63 (2H, m), 2.33 (3H, s), 1.39-1.47 (4H, m), 0.93 (3H, t, $J = 7.08$ Hz); ^{13}C NMR (CDCl_3 , 100 MHz): δ 144.6, 142.6, 141.0, 135.0, 133.2, 129.6, 129.3, 128.0, 127.9, 126.5, 124.6, 120.2, 72.7, 31.5, 28.6, 22.5, 21.6, 14.0; IR (NaCl, neat) ν : 3419, 3019, 2871, 1670, 1636, 1522, 1464, 1358, 1169, 1088, 1055, 1030 cm^{-1} ; HRMS (ESI) calcd. for $\text{C}_{20}\text{H}_{23}\text{NO}_3\text{SNa}$ ($\text{M}^+ + \text{Na}$): 380.1296, found: 380.1300.

(Z)-2-(Cyclopropylmethylene)-1-tosylindolin-3-ol (164u)

wt. 0.053 g; white solid; m.p. 97-99 °C; ^1H NMR (CDCl_3 , 400 MHz): δ 7.75 (1H, d, $J = 8.08$ Hz), 7.34-7.39 (3H, m), 7.15-7.22 (2H, m), 7.11 (2H, d, $J = 8.08$ Hz), 5.12 (1H, d, $J = 10.4$ Hz), 4.64 (1H, s), 2.35-2.42 (1H, m), 2.33 (3H, s), 0.95-0.99 (2H, m), 0.51-0.53 (2H, m); ^{13}C NMR (CDCl_3 , 100 MHz): δ 144.6, 142.7, 139.5, 135.0, 133.1, 132.2, 129.6,

129.3, 128.0, 126.5, 124.6, 120.3, 72.7, 21.6, 11.6, 8.0, 8.0. IR (NaCl, neat) ν : 3565, 3019, 2870, 1670, 1521, 1464, 1362, 1169, 1088, 1056, 1030 cm^{-1} ; HRMS (ESI) calcd. for $\text{C}_{19}\text{H}_{19}\text{NO}_3\text{SNa}$ ($\text{M}^+ + \text{Na}$): 364.0983, found: 364.0986.

(Z)-2-Benzylidene-1-((4-nitrophenyl)sulfonyl)-3-phenylindolin-3-ol (164v)

wt. 0.096 g; yellow solid; m.p. 108-110 $^{\circ}\text{C}$; ^1H NMR (CDCl_3 , 400 MHz): δ 7.94 (1H, d, J = 8.12 Hz), 7.87 (2H, d, J = 8.6 Hz), 7.68 (2H, d, J = 7.48 Hz), 7.54 (2H, d, J = 8.64 Hz), 7.49 (1H, t, J = 8.08 Hz), 7.36 (2H, t, J = 7.76 Hz), 7.19-7.29 (4H, m), 7.08-7.15 (5H, m), 6.55 (1H, s), 2.12 (1H, brs); ^{13}C NMR (CDCl_3 , 100 MHz): δ 144.9, 141.8, 141.1, 137.4, 135.2, 130.4, 129.6, 129.4, 128.3, 128.2, 128.0, 127.2, 126.6, 125.6, 124.0, 123.5, 119.1, 82.2; IR (NaCl, neat) ν : 3443, 3022, 1667, 1604, 1530, 1348, 1172, 1063 cm^{-1} ; HRMS (ESI) calcd. for $\text{C}_{27}\text{H}_{20}\text{N}_2\text{O}_5\text{SNa}$ ($\text{M}^+ + \text{Na}$): 507.0991, found: 507.0976.

(Z)-2-Benzylidene-1-(methylsulfonyl)-3-phenylindolin-3-ol (164w)

wt. 0.075 g; pale yellow solid; m.p. 79-81 $^{\circ}\text{C}$; ^1H NMR (CDCl_3 , 400 MHz): δ 7.71 (1H, d, J = 8 Hz), 7.61 (2H, d, J = 7.36 Hz), 7.51 (2H, d, J = 6.68 Hz), 7.43 (1H, t, J = 7.52 Hz), 7.30-7.38 (5H, m), 7.17-7.26 (3H, m), 6.24 (1H, s), 2.88 (1H, brs), 2.72 (3H, s); ^{13}C NMR (CDCl_3 , 100 MHz): δ 145.4, 142.2, 141.7, 138.1, 135.3, 130.4, 129.4, 128.3, 128.1, 128.0,

127.0, 126.8, 125.1, 123.9, 118.4, 82.8, 37.8; IR (NaCl, neat) ν : 3462, 3021, 1602, 1462, 1321, 1215, 1161, 1082 cm^{-1} ; HRMS (ESI) calcd. for $\text{C}_{22}\text{H}_{19}\text{NO}_3\text{SNa}$: 400.0983, found: 400.0984.

(Z)-2-Benzylidene-3-phenyl-1-tosylindolin-3-ol (d_1 -164a)

wt. 0.09 g; white solid; m.p. 163-165 $^{\circ}\text{C}$; ^1H NMR (CDCl_3 , 300 MHz): δ 7.91 (1H, d, J = 8.07 Hz), 7.66 (2H, d, J = 7.53 Hz), 7.30-7.45 (5H, m), 7.14-7.24 (8H, m), 6.96-7.03 (3H, m), 6.26 (0.45H, s), 2.29 (3H, s); ^{13}C NMR (CDCl_3 , 75 MHz): δ 145.4, 144.8, 142.5, 141.9, 138.3, 135.6, 133.1, 130.0, 129.6, 129.4, 128.4, 127.9, 127.9, 127.8, 127.3, 126.9, 126.7, 125.4, 124.8, 119.5, 81.8, 21.6; IR (NaCl, neat) ν : 3526, 3078, 2956, 2860, 1718, 1660, 1598, 1450, 1367, 1186, 1172 cm^{-1} ; HRMS (ESI) calcd. for $\text{C}_{28}\text{H}_{22}\text{DNO}_3\text{SNa}$ (M^+ + Na): 477.1359, found: 477.1361.

Phenyl(3-phenyl-1-tosyl-1H-indol-2-yl)methanol (180a)²²

wt. 81.6 mg; yellow oil; ^1H NMR (CDCl_3 , 400 MHz): δ 8.05 (1H, d, J = 8.4 Hz), 7.49 (2H, d, J = 7.12 Hz), 7.44 (3H, t, J = 7.76 Hz), 7.32-7.38 (4H, m), 7.20-7.26 (7H, m), 7.06 (2H, d, J = 8.2 Hz), 6.30 (1H, d, J = 11.84 Hz), 4.72 (1H, d, J = 11.8 Hz), 2.29 (3H, s); ^{13}C NMR (CDCl_3 , 100 MHz): δ 144.9, 142.5, 137.2, 136.4, 135.3, 132.3, 130.2, 129.7, 128.9, 128.2, 128.2, 127.2, 126.9, 125.7, 125.6, 123.9, 120.7, 114.7, 68.6, 21.6.

2-(Fluoromethyl)-3-phenyl-1-tosyl-1H-indole (181p)

wt. 21.2 mg; white solid; m.p. 111-113 °C ; ^1H NMR (CDCl_3 , 400 MHz): δ 9.25 (1H, d, J = 8.44 Hz), 8.92 (2H, d, J = 8.16 Hz), 8.55 (1H, d, J = 7.8 Hz), 8.41-8.48 (6H, m), 8.21-8.28 (3H, m), 6.72 (2H, d, $J_{\text{H-F}}$ = 48.4 Hz), 3.34 (3H, s); ^{13}C NMR (CDCl_3 , 100 MHz): δ 145.0, 136.4, 135.5, 130.2, 130.1, 129.7, 128.8, 128.4, 127.3, 127.2, 126.5, 123.9, 120.9, 114.9, 73.9 (1C, d, $J_{\text{C-F}}$ = 163.2 Hz), 21.6; IR (NaCl, neat) ν : 3019, 1599, 1497, 1454, 1375, 1279, 1175, 1090, 1053, 1026 cm^{-1} ; HRMS (ESI) calcd. for $\text{C}_{22}\text{H}_{19}\text{FNO}_2\text{S}$ ($\text{M}^+ + \text{H}$): 380.1121, found: 380.1128.

3-(Iodomethyl)-3-phenyl-1-tosylindolin-2-one (182p)

wt. 43.7 mg; white solid; m.p. 148-151 °C; ^1H NMR (CDCl_3 , 400 MHz): δ 8.05 (1H, d, J = 8.24 Hz), 7.98 (2H, d, J = 8.24 Hz), 7.48 (1H, t, J = 8.2 Hz), 7.24-7.32 (9H, m), 3.99 (1H, d, J = 9.92 Hz), 3.53 (1H, d, J = 9.88 Hz), 2.39 (3H, s); ^{13}C NMR (CDCl_3 , 100 MHz): δ 174.8, 145.8, 139.7, 136.6, 134.9, 129.9, 129.8, 129.7, 129.1, 128.6, 128.3, 127.0, 125.1, 114.1, 57.2, 21.7, 9.2; IR (NaCl, neat) ν : 3059, 2962, 1597, 1381, 1176, 575, 544 cm^{-1} ; HRMS (ESI) calcd. for $\text{C}_{22}\text{H}_{19}\text{INO}_3\text{S}$ ($\text{M}^+ + \text{H}$): 504.0130, found: 504.0130.

(Z)-2-Benzylidene-1-tosylindolin-3-one (183r)

wt. 26.7 mg; yellow solid; m.p. 110-112 °C; ^1H NMR (CDCl_3 , 400 MHz): δ 8.14 (1H, d, J = 8.28 Hz), 8.0 (1H, s), 7.87-7.89 (2H, m), 7.61-7.69 (2H, m), 7.42-7.45 (5H, m), 7.25 (1H, t, J = 7.52 Hz), 7.12 (2H, d, J = 8 Hz), 2.32 (3H, s); ^{13}C NMR (CDCl_3 , 100 MHz): δ 183.1, 148.5, 145.2, 136.0, 133.6, 133.1, 133.0, 132.3, 131.3, 130.6, 129.7, 128.1, 127.4, 126.7, 125.6, 124.3, 118.9, 21.6; IR (NaCl, neat) ν : 3019, 1701, 1616, 1474, 1460, 1364, 1119, 1090 cm^{-1} ; HRMS (ESI) calcd. for $\text{C}_{22}\text{H}_{18}\text{NO}_3\text{S}$ ($\text{M}^+ + \text{H}$): 376.1007, found: 376.1012.

7.4 Silica Gel-Mediated Hydroamination/Semipinacol Rearrangement of 2-Alkylaminophenylprop-1-yn-3-ols: Synthesis of 2-Oxindoles from Alkynes and 1-(2-Aminophenyl)ketones

General Procedure for the Synthesis of 1-(2-Alkylaminophenyl)ketones (184a-m)

1-(2-aminophenyl)ketone substrates were purchased from commercial sources or synthesized according to the reported protocols.^{99a} To a solution of 1-(2-aminophenyl)ketone **176** (3 mmol) in DMF (7.5 mL) was added potassium carbonate (0.829 g, 6 mmol) and methyl iodide (0.373 mL, 6 mmol for **184a-m**, **184p-v**), benzyl bromide (0.535 mL, 4.5 mmol for **184n**) or allyl bromide (0.388 mL, 4.5 mmol for **184o**; 1.29 mL, 15 mmol for **184w**). The reaction was stirred at 80 °C and monitored by TLC

analysis until completion. The reaction was quenched with water (10 mL) was added to the reaction mixture. The aqueous layer was extracted with ethyl acetate (15 mL x 3). The combined organic layers were washed with washed with water (15 mL x 3) and brine (15 mL), dried over MgSO_4 and concentrated under reduced pressure. The crude mixture was purified by flash column chromatography on silica gel (2% EtOAc/*n*-hexane) to give the title compound.

Procedure for the Synthesis of ^{18}O -Labelled (2-(Methylamino)phenyl)(phenyl) methanone (184a- ^{18}O**)^{99a,99b}**

To a stirred solution of 2-aminobenzophenone (0.197g, 1 mmol) in THF (19 mL) was added H_2O^{18} (97% ^{18}O atoms, 0.2 mL, 11 mmol) and conc. H_2SO_4 (0.05 mL). The reaction mixture was heated at 50 °C for 16 h. The resulting solution was then extracted with EtOAc (10 mL), washed with water (10 mL), dried over MgSO_4 and evaporated under reduced pressure. The resulting compound was used directly without further purification. To a stirred solution of 1-(2-aminophenyl)ketone **176a- ^{18}O** (1 mmol) in DMF (2.5 mL) was added potassium carbonate (0.276 g, 2 mmol) and methyl iodide (0.125 mL, 2 mmol). The reaction was stirred at 80 °C for 24 h and water (5 mL) was added. The aqueous layer was extracted with ethyl acetate (7.5 mL x 3). The combined organic layers were washed with washed with water (7.5 mL x 3) and brine (7.5 mL), dried over MgSO_4 and concentrated under reduced pressure. The crude mixture was purified by flash column chromatography on silica gel (2% EtOAc/*n*-hexane) to give the title compound.

General Procedure for the Synthesis of 3,3-disubstituted 2-oxindoles (**163**)

To a stirred solution of *in situ* formed LDA (3.5 equiv) in THF (3 mL) at -78 °C was added the appropriate alkyne (3.5 equiv, 1.75 mmol). The resulting reaction mixture was allowed to stir for a further 1 h before the ketone **184** (0.5 mmol) in THF (2 mL) was added to reaction mixture and stirred for 1 h at the same temperature and at room temperature for 1 h. Upon completion, the reaction mixture was quenched with saturated NH₄Cl (15 mL) and extracted with EtOAc (2 x 15 mL). The combined organic layers were washed with brine (20 mL), dried over MgSO₄ and concentrated under reduced pressure. The crude mixture obtained was dissolved in an open round bottom flask with *n*hexane/EtOAc (10 mL, 20:1 v/v) contained and silica gel (100 equiv, 3 g) was added. The reaction mixture was stirred and monitored by TLC analysis until completion. The reaction mixture was filtered, washed with EtOAc (20 mL), concentrated under reduced pressure and purified by flash column chromatography on silica gel (eluent: *n*hexane/EtOAc = 10:1) to give the product **163**.

Procedure for the Large-Scale Synthesis of 3-Benzyl-1-methyl-3-phenylindolin-2-one (**163a**)

To a stirred solution of *in situ* generated LDA (3.5 equiv) in THF (28 mL) at -78 °C was added the phenylacetylene (1.70g, 1.82 mL, 16.6 mmol) in a dropwise manner. The

resulting reaction mixture was allowed to stir for a further 1 h before the ketone **184a** (1g, 4.73 mmol) in THF (19 mL) was added to reaction mixture dropwise and stirred for 1 h at the same temperature and then at room temperature for another 1 h. Upon completion, the reaction mixture was quenched by adding saturated NH_4Cl (50 mL) and extracted with EtOAc (2 x 30 mL). The combined organic layers were washed with brine (50 mL), dried over MgSO_4 and concentrated under reduced pressure. The crude mixture obtained was dissolved in *n*hexane/EtOAc (95 mL, 20:1 v/v) and silica gel (28.38 g, 473 mmol) was added. The reaction mixture was stirred and monitored by TLC analysis until completion. The reaction mixture was filtered, washed with EtOAc (20 mL), concentrated under reduced pressure and purified by flash column chromatography on silica gel (eluent: *n*hexane/EtOAc = 10:1) to give the 2-oxindole **163a** in 89% yield.

Procedure for the Recycling of Silica Gel in the Cycloisomerization of **162a** to **163a**

To a stirred solution of *in situ* generated LDA (3.5 equiv) in THF (3 mL) at -78°C was added phenylacetylene (1.75 mmol, 0.179 g, 0.193 mL) in a dropwise manner. The resulting reaction mixture was allowed to stir for a further 1 h before the ketone **184a** (0.5 mmol, 0.106 g) in THF (2 mL) was added to reaction mixture dropwise and stirred for 1 h at the same temperature and at room temperature for 1 h. Upon completion, the reaction mixture was quenched by adding saturated NH_4Cl (15 mL) and extracted with EtOAc (2 x 15 mL). The combined organic layers were washed with brine (20 mL), dried over MgSO_4 and concentrated under reduced pressure. The crude mixture obtained was dissolved in *n*hexane/EtOAc (10 mL, 20:1 v/v) and silica gel (100 mmol, 3 g) was added. The reaction mixture was stirred and monitored by TLC analysis until completion. The

silica gel was filtered, washed with EtOAc (20 mL) and the filtrate was concentrated under reduced pressure and purified by flash column chromatography on silica gel (eluent: *n*hexane/EtOAc = 10:1) to give the 2-oxindole product. The filtered silica gel was then used directly for the next cycle of the reaction.

(2-(Methylamino)phenyl)(phenyl)methanone (184a)^{99c}

Yield: 51%; yellow solid; ¹H NMR (CDCl₃, 400 MHz): δ 8.53 (1H, brs), 7.58-7.60 (2H, m), 7.38-7.52 (5H, m), 6.74 (1H, d, *J* = 8.48 Hz), 6.53 (1H, t, *J* = 7.16 Hz), 2.96 (3H, s); ¹³C NMR (CDCl₃, 100 MHz): δ 199.4, 152.7, 140.6, 135.5, 135.1, 130.7, 129.0, 128.0, 117.2, 113.6, 111.1, 29.5.

(5-Chloro-2-(methylamino)phenyl)(phenyl)methanone (184b)

Yield: 45%; yellow solid; m.p. 94-97 °C; ¹H NMR (CDCl₃, 500 MHz): δ 8.47(1H, brs), 7.58 (2H, d, *J* = 7.2 Hz), 7.53 (1H, t, *J* = 7.45 Hz), 7.43-7.48 (3H, m), 7.33 (1H, d, *J* = 9 Hz), 6.69 (1H, d, *J* = 9 Hz), 2.94 (3H, d, *J* = 5 Hz); ¹³C NMR (CDCl₃, 125 MHz): δ 198.3, 151.2, 139.8, 134.9, 134.1, 131.1, 129.0, 128.3, 118.3, 117.9, 112.7, 29.6; IR (NaCl, neat) ν: 3445, 3020, 1624, 1566, 1512, 1311, 754, 700 cm⁻¹; HRMS(ESI) calcd for C₁₄H₁₂ClNO (M⁺ + Na): 268.0505, found: 268.0499.

(5-Bromo-2-(methylamino)phenyl)(phenyl)methanone (184c)

Yield: 35%; yellow solid; m.p. 102-104 °C; ^1H NMR (CDCl_3 , 400 MHz): δ 8.48 (1H, brs), 7.55-7.58 (3H, m), 7.49-7.54 (1H, m), 7.42-7.47 (3H, m), 6.62 (1H, d, $J = 9.04$ Hz), 2.91 (3H, d, $J = 5.12$ Hz); ^{13}C NMR (CDCl_3 , 100 MHz): δ 198.2, 151.5, 139.8, 137.5, 137.0, 131.2, 129.0, 128.3, 118.6, 113.2, 105.0, 29.6; IR (NaCl, neat) ν : 3446, 3020, 1624, 1508, 1340 cm^{-1} ; HRMS (ESI) calcd for $\text{C}_{14}\text{H}_{12}\text{BrNO}$ ($\text{M}^+ + \text{H}$): 290.0181, found: 290.0181.

(5-Methyl-2-(methylamino)phenyl)(phenyl)methanone (184d)

Yield: 32%; brown solid; m.p. 66-68 °C; ^1H NMR (CDCl_3 , 400 MHz): δ 8.34 (1H, brs), 7.57-7.60 (2H, m), 7.42-7.52 (3H, m), 7.22-7.25 (2H, m), 6.68 (1H, d, $J = 8.44$ Hz), 2.94 (3H, s), 2.16 (3H, s); ^{13}C NMR (CDCl_3 , 100 MHz): δ 199.2, 150.9, 140.7, 136.2, 135.0, 130.6, 128.9, 128.0, 122.5, 117.1, 111.2, 29.6, 20.2; IR (NaCl, neat) ν : 3350, 3093, 3051, 1633, 1600, 1527, 1315 cm^{-1} ; HRMS (ESI) calcd for $\text{C}_{15}\text{H}_{15}\text{NO}$ ($\text{M}^+ + \text{H}$): 226.1232, found: 226.1233.

(4-Bromophenyl)(2-(methylamino)phenyl)methanone (184e)

Yield: 48%, yellow solid; m.p. 105-106 °C; ^1H NMR (CDCl_3 , 400 MHz): δ 8.51 (1H, brs), 7.57 (2H, d, $J = 8.68$ Hz), 7.39-7.53 (4H, m), 6.75 (1H, d, $J = 8.72$ Hz), 6.54 (1H, t, $J = 7.8$ Hz), 2.97 (3H, s); ^{13}C NMR (CDCl_3 , 100 MHz): δ 198.0, 152.8, 139.4, 135.4, 135.2, 131.4, 130.7, 125.4, 116.9, 113.8, 111.4, 29.6 cm^{-1} ; IR (NaCl, neat) ν : 3327, 3021, 1620, 1574, 1475, 1350; HRMS(ESI) calcd for $\text{C}_{14}\text{H}_{12}\text{BrNO}$ ($\text{M}^+ + \text{H}$): 290.0181, found: 290.0181.

(4-Chlorophenyl)(2-(methylamino)phenyl)methanone (184f)

Yield: 50% ; yellow solid; m.p. 84-86 °C; ^1H NMR (CDCl_3 , 400 MHz): δ 8.49 (1H, brs), 7.51 (2H, d, $J = 8.36$ Hz), 7.37-7.41 (4H, m), 6.72 (1H, d, $J = 8.44$ Hz), 6.52 (1H, t, $J = 7.16$ Hz), 2.92 (3H, d, $J = 5.04$ Hz); ^{13}C NMR (CDCl_3 , 100 MHz): δ 197.8, 152.8, 138.9, 136.9, 135.3, 135.1, 130.5, 128.3, 116.9, 113.8, 111.3, 29.5; IR (NaCl, neat) ν : 3414, 3021, 1622, 1572, 1520, 1475, 1338, 754, 667 cm^{-1} ; HRMS(ESI) calcd for $\text{C}_{14}\text{H}_{12}\text{ClNO}$ ($\text{M}^+ + \text{H}$): 246.0686, found: 246.0690.

(2-(Methylamino)phenyl)(*p*-tolyl)methanone (184g)

Yield: 45%; dark yellow solid; m.p. 58-60 °C; ^1H NMR (CDCl_3 , 400 MHz): δ 8.46 (1H, brs), 7.46-7.50 (3H, m), 7.32-7.36 (1H, m), 7.17-7.19 (2H, m), 6.67 (1H, dd, $J = 8.72, 1.8$ Hz), 6.47-6.51 (1H, m), 2.87 (3H, d, $J = 2.76$ Hz), 2.35 (3H, d, $J = 2.28$ Hz); ^{13}C NMR (CDCl_3 , 100 MHz): δ 197.9, 151.4, 140.0, 136.7, 134.2, 133.7, 128.2, 127.6, 116.4, 112.5, 109.9, 28.3, 20.4 cm^{-1} ; IR (NaCl, neat) ν : 3347, 3026, 3021, 1620, 1574, 1518, 1475, 1336; HRMS(ESI) calcd for $\text{C}_{15}\text{H}_{15}\text{NO}$ ($\text{M}^+ + \text{H}$): 226.1232, found: 226.1230.

(2-(Methylamino)phenyl)(naphthalen-2-yl)methanone (184h)

Yield: 45%; yellow solid; m.p. 105-106 °C; ^1H NMR (CDCl_3 , 400 MHz): δ 8.54 (1H, brs), 8.05 (1H, s), 7.86 (3H, t, $J = 8.36$ Hz), 7.70 (1H, dd, $J = 8.44, 1.56$ Hz), 7.47-7.55 (3H, m), 7.37-7.41 (1H, m), 6.74 (1H, d, $J = 8.56$ Hz), 6.50-6.54 (1H, m), 2.94 (3H, d, $J = 4.8$ Hz); ^{13}C NMR (CDCl_3 , 100 MHz): δ 199.2, 152.8, 137.9, 135.6, 135.1, 134.4, 132.4, 129.7, 129.0, 128.0, 127.8, 127.6, 126.7, 125.9, 117.6, 113.8, 111.2, 29.6; IR (NaCl, neat) ν : 3343, 3019, 1620, 1574, 1425, 1354 cm^{-1} ; HRMS(ESI) calcd for $\text{C}_{18}\text{H}_{15}\text{NO}$ ($\text{M}^+ + \text{H}$): 262.1232, found: 262.1231.

(2-(Methylamino)phenyl)(thiophen-2-yl)methanone (184i)

Yield: 42%; brown oil; ^1H NMR (CDCl_3 , 400 MHz): δ 7.92 (1H, brs), 7.81 (1H, dd, J = 7.92, 1.56 Hz), 7.61 (1H, dd, J = 4.96, 0.92 Hz), 7.52 (1H, dd, J = 3.72, 1.04 Hz), 7.39-7.43 (1H, m), 7.10 (1H, dd, J = 4.92, 3.84 Hz), 6.72 (1H, d, J = 8.48 Hz), 6.62 (1H, td, J = 7.92, 0.72 Hz), 2.91 (3H, s); ^{13}C NMR (CDCl_3 , 100 MHz): δ 189.6, 151.9, 145.1, 134.7, 133.6, 133.4, 132.3, 127.5, 118.1, 114.0, 111.1, 29.6; IR (NaCl, neat) ν : 3368, 3094, 1612, 1570, 1518, 1456, 1323 cm^{-1} ; HRMS(ESI) calcd for $\text{C}_{12}\text{H}_{11}\text{NOS}$ ($\text{M}^+ + \text{H}$): 218.0640, found: 218.0638.

1-(2-(Methylamino)phenyl)ethanone (184j)^{99a}

Yield: 43%; yellow solid; ^1H NMR (CDCl_3 , 400 MHz): δ 8.78 (1H, brs), 7.70 (1H, d, J = 7.96 Hz), 7.36 (1H, t, J = 7.84 Hz), 6.65 (1H, d, J = 8.52 Hz), 6.57 (1H, t, J = 7.28 Hz), 2.87 (3H, d, J = 5 Hz), 2.55 (3H, s); ^{13}C NMR (CDCl_3 , 100 MHz): δ 200.7, 152.0, 135.1, 132.7, 117.6, 113.8, 111.2, 29.3, 27.8.

Cyclohexyl(2-(methylamino)phenyl)methanone (184k)

Yield: 30%; yellow solid; m.p. 53-55 °C; ^1H NMR (CDCl_3 , 400 MHz): δ 8.84 (1H, brs), 7.67 (1H, d, J = 8.04 Hz), 7.24 (1H, t, J = 8 Hz), 6.56 (1H, d, J = 8.52 Hz), 6.47 (1H, t, J

= 7.68 Hz), 3.18 (1H, tt, $J = 11.4, 3.08$ Hz), 2.76 (3H, d, $J = 4.96$ Hz), 1.71-1.75 (4H, m), 1.61-1.64 (1H, m), 1.36-1.46 (2H, m), 1.23-1.33 (2H, m), 1.13-1.20 (1H, m); ^{13}C NMR (CDCl_3 , 100 MHz): δ 206.5, 152.6, 134.8, 131.5, 116.1, 113.8, 111.5, 45.7, 30.1, 29.3, 26.1, 26.1; IR (NaCl, neat) ν : 3318, 3076, 1630, 1570, 1475, 1362, 1327 cm^{-1} ; HRMS(ESI) calcd for $\text{C}_{14}\text{H}_{19}\text{NO}$ ($\text{M}^+ + \text{Na}$): 240.1364, found: 240.1361.

Cyclopentyl(2-(methylamino)phenyl)methanone (184l)

Yield: 60%; yellow oil; ^1H NMR (CDCl_3 , 400 MHz): δ 8.88 (1H, brs), 7.79 (1H, d, $J = 8.24$ Hz), 7.32-7.36 (1H, m), 6.66 (1H, d, $J = 8.68$ Hz), 6.57 (1H, t, $J = 8.24$ Hz), 3.72 (1H, qn, $J = 8.24$ Hz), 2.86 (3H, d, $J = 4.56$ Hz), 1.86-1.91 (4H, m), 1.58-1.76 (4H, m); ^{13}C NMR (CDCl_3 , 100 MHz): δ 205.7, 152.5, 134.7, 132.1, 117.1, 113.9, 111.4, 46.6, 30.7, 29.4, 26.4; IR (NaCl, neat) ν : 3323, 3021, 1632, 1574, 1520, 1475, 1327 cm^{-1} ; HRMS(ESI) calcd for $\text{C}_{13}\text{H}_{17}\text{NO}$ ($\text{M}^+ + \text{H}$): 204.1388, found: 204.1389.

Cyclopropyl(2-(methylamino)phenyl)methanone (184m)

Yield: 41%; yellow oil; ^1H NMR (CDCl_3 , 400 MHz): δ 8.67 (1H, brs), 7.95 (1H, dd, $J = 8.08, 1.48$ Hz), 7.33-7.37 (1H, m), 6.58-6.66 (2H, m), 2.83 (3H, d, $J = 5.08$ Hz), 2.57-2.64 (1H, m), 1.11-1.14 (2H, m), 0.88-0.92 (2H, m); ^{13}C NMR (CDCl_3 , 100 MHz): δ 201.9, 151.6, 134.7, 131.8, 118.4, 114.0, 111.2, 29.3, 17.1, 10.6; IR (NaCl, neat) ν : 3319, 3076, 3007, 1620, 1604, 1566, 1475, 1389 cm^{-1} ; HRMS(ESI) calcd for $\text{C}_{11}\text{H}_{13}\text{NO}$ ($\text{M}^+ + \text{H}$): 176.1075, found: 176.1079.

(2-(Benzylamino)phenyl)(phenyl)methanone (184n)

Yield: 40%; yellow solid; m.p. 65-67 °C; ^1H NMR (CDCl_3 , 400 MHz): δ 9.00 (1H, brs), 7.60-7.63 (2H, m), 7.25-7.53 (11H, m), 6.72 (1H, d, $J = 8.24$ Hz), 6.53-6.57 (1H, m), 4.50 (2H, d, $J = 5.04$ Hz); ^{13}C NMR (CDCl_3 , 100 MHz): δ 199.5, 151.7, 140.5, 138.6, 135.6, 135.0, 130.9, 129.1, 128.8, 128.1, 127.3, 127.2, 117.6, 114.2, 112.1; IR (NaCl, neat) ν : 3332, 3080, 3051, 1622, 1574, 1518, 1456, 1325 cm^{-1} ; HRMS(ESI) calcd for $\text{C}_{20}\text{H}_{17}\text{NO}$ ($\text{M}^+ + \text{H}$): 288.1388, found: 288.1389.

(2-(Allylamino)phenyl)(phenyl)methanone (184o)

Yield: 42%; yellow solid; m.p. 55-57 °C; ^1H NMR (CDCl_3 , 400 MHz): δ 7.59-7.61 (2H, m), 7.42-7.50 (4H, m), 7.34-7.38 (1H, m), 6.74 (1H, d, $J = 8.36$ Hz), 6.52-6.56 (1H, m), 5.95-6.01 (1H, m), 5.32 (1H, dd, $J = 17.2, 1.44$ Hz), 5.20 (1H, dd, $J = 10.36, 1.44$ Hz), 3.93 (2H, t, $J = 5.04$ Hz); ^{13}C NMR (CDCl_3 , 100 MHz): δ 199.4, 151.7, 140.6, 135.5, 134.9, 134.3, 130.8, 129.0, 128.1, 117.4, 116.3, 114.0, 111.9, 45.2; IR (NaCl, neat) ν : 3393, 3094, 3083, 1622, 1572, 1456, 1380 cm^{-1} ; HRMS(ESI) calcd for $\text{C}_{16}\text{H}_{15}\text{NO}$ ($\text{M}^+ + \text{H}$): 238.1232, found: 238.1227.

(2-(Diallylamino)phenyl)(phenyl)methanone (184w)

Yield: 55%; yellow oil; ^1H NMR (CDCl_3 , 400 MHz): δ 7.75-7.77 (2H, m), 7.50-7.55 (1H, m), 7.33-7.41 (4H, m), 7.02-7.07 (2H, m), 5.40-5.50 (2H, m), 4.97-5.01 (4H, m), 3.52 (4H, d, $J = 6.2$ Hz); ^{13}C NMR (CDCl_3 , 100 MHz): δ 198.7, 149.7, 137.8, 134.1, 133.5, 132.8, 130.8, 129.8, 128.1, 121.5, 120.8, 117.7, 55.6; IR (NaCl, neat) ν : 3065, 3011, 1659, 1595, 1483, 1360 cm^{-1} ; HRMS(ESI) calcd for $\text{C}_{19}\text{H}_{19}\text{NO}$ ($\text{M}^+ + \text{H}$): 278.1545, found: 278.1540.

 ^{18}O -Labelled (2-(Methylamino)phenyl)(phenyl)methanone (184a- O^{18})

Yield: 56%; yellow solid; ^1H NMR (CDCl_3 , 400 MHz): δ 8.45 (1H, brs), 7.49-7.51 (2H, m), 7.28-7.42 (5H, m), 6.65 (1H, d, $J = 8.52$ Hz), 6.44 (1H, t, $J = 7.2$ Hz), 2.86 (3H, d, $J = 4.76$ Hz); ^{13}C NMR (CDCl_3 , 100 MHz): δ 199.3, 199.3, 152.7, 140.6, 135.5, 135.1, 130.7, 129.0, 128.0, 117.2, 113.6, 111.1, 29.5; IR (NaCl, neat) ν : 2931, 2893, 1619, 1602, 1555, 1448, 1433, 1244 cm^{-1} ; HRMS(ESI) calcd for $\text{C}_{14}\text{H}_{13}\text{N}^{18}\text{O}$ ($\text{M}^+ + \text{H}$): 214.1118, found: 214.1115.

3-Benzyl-1-methyl-3-phenylindolin-2-one (163a)⁹⁵¹

Reaction time = 2.5 h; white solid; ¹H NMR (CDCl₃, 400 MHz): δ 7.49 (2H, d, J = 7.56 Hz), 7.34 (2H, t, J = 7.04 Hz), 7.28 (1H, d, J = 7.16 Hz), 7.19-7.23 (2H, m), 6.98-7.09 (4H, m), 6.82 (2H, d, J = 6.56 Hz), 6.60 (1H, d, J = 7.8 Hz), 3.69 (1H, d, J = 12.76 Hz), 3.44 (1H, d, J = 12.76 Hz), 2.94 (3H, s); ¹³C NMR (CDCl₃, 75 MHz): δ 177.8, 143.8, 139.9, 135.8, 131.3, 130.1, 128.7, 128.3, 127.5, 127.4, 126.6, 125.6, 122.3, 108.2, 58.4, 44.1, 26.1

3-Benzyl-5-chloro-1-methyl-3-phenylindolin-2-one (163b)

Reaction time = 18 h; yellow solid; m.p. 179-180 °C; ¹H NMR (CDCl₃, 400 MHz): δ 7.44 (2H, d, J = 7.68 Hz), 7.28-7.36 (3H, m), 7.15 (2H, d, J = 10.36 Hz), 7.02 (3H, d, J = 6.96 Hz), 6.83 (2H, d, J = 6.4 Hz), 6.48 (1H, d, J = 8.16 Hz), 3.68 (1H, d, J = 12.8 Hz), 3.40 (1H, d, J = 12.8 Hz), 2.89 (3H, s); ¹³C NMR (CDCl₃, 100 MHz): δ 177.4, 142.4, 139.1, 135.2, 133.2, 130.0, 128.8, 128.2, 127.8, 127.7, 127.6, 127.2, 126.8, 125.7, 109.0, 58.6, 43.9, 26.2; IR (NaCl, neat) ν : 3017, 1703, 1612, 1495, 1470, 1373, 1354, 756, 700 cm⁻¹; HRMS (ESI) calcd for C₂₂H₁₈ClNO (M⁺ + H): 348.1155, found: 348.1147.

3-Benzyl-5-bromo-1-methyl-3-phenylindolin-2-one (163c)

Reaction time = 18 h; yellow solid; m.p. 146-148 °C; ^1H NMR (CDCl_3 , 400 MHz): δ 7.43 (2H, d, $J = 7.32$ Hz), 7.25-7.35 (5H, m), 7.02 (3H, d, $J = 6.48$ Hz), 6.82 (2H, d, $J = 6.2$ Hz), 6.42 (1H, d, $J = 8.04$ Hz), 3.67 (1H, d, $J = 12.8$ Hz), 3.39 (1H, d, $J = 12.76$ Hz), 2.87 (3H, s); ^{13}C NMR (CDCl_3 , 100 MHz): δ 177.3, 142.8, 139.1, 135.2, 133.6, 131.1, 130.0, 128.8, 128.5, 127.8, 127.7, 127.2, 126.8, 114.9, 109.5, 58.6, 43.9, 26.2; IR (NaCl, neat) ν : 3019, 1713, 1611, 1491, 1366, 1350 cm^{-1} ; HRMS (ESI) calcd for $\text{C}_{22}\text{H}_{18}\text{BrNO}$ ($\text{M}^+ + \text{H}$): 392.0650, found: 392.0644.

3-Benzyl-1,5-dimethyl-3-phenylindolin-2-one (163d)

Reaction time = 1 h; yellow solid; m.p. 139-141 °C; ^1H NMR (CDCl_3 , 400 MHz): δ 7.47 (2H, d, $J = 7.4$ Hz), 7.30 (2H, t, $J = 6.84$ Hz), 7.23 (1H, d, $J = 6.72$ Hz), 6.96-6.99 (5H, m), 6.81 (2H, d, $J = 5.92$ Hz), 6.44 (1H, d, $J = 7.72$ Hz), 3.65 (1H, d, $J = 12.68$ Hz), 3.41 (1H, d, $J = 12.68$ Hz), 2.86 (3H, s), 2.32 (3H, s); ^{13}C NMR (CDCl_3 , 100 MHz): δ 177.8, 141.5, 140.1, 135.9, 131.7, 131.5, 130.1, 128.7, 128.5, 127.5, 127.4, 127.4, 126.6, 126.2, 107.8, 58.4, 43.9, 26.1, 21.4; IR (NaCl, neat) ν : 3063, 3017, 1713, 1607, 1489, 1364, 1348 cm^{-1} ; HRMS (ESI) calcd for $\text{C}_{23}\text{H}_{21}\text{NO}$ ($\text{M}^+ + \text{H}$): 328.1701, found: 328.1703.

3-Benzyl-3-(4-bromophenyl)-1-methylindolin-2-one (163e)

Reaction time = 5.5 h; yellow solid; m.p. 194-196 °C; ^1H NMR (CDCl_3 , 400 MHz): δ 7.43 (2H, d, $J = 8.52$ Hz), 7.36 (2H, d, $J = 8.56$ Hz), 7.15-7.23 (2H, m), 6.98-7.09 (4H, m), 6.80 (2H, d, $J = 7.2$ Hz), 6.59 (1H, d, $J = 7.72$ Hz), 3.61 (1H, d, $J = 12.76$ Hz), 3.37 (1H, d, $J = 12.76$ Hz), 2.92 (3H, s); ^{13}C NMR (CDCl_3 , 100 MHz): δ 177.3, 143.7, 138.8, 135.3, 131.7, 130.6, 130.0, 129.2, 128.5, 127.5, 126.7, 125.5, 122.3, 121.7, 108.3, 57.9, 44.1, 26.1; IR (NaCl, neat) ν : 3019, 1707, 1612, 1472, 1375 cm^{-1} ; HRMS (ESI) calcd for $\text{C}_{22}\text{H}_{18}\text{BrNO}$ ($\text{M}^+ + \text{H}$): 392.0650, found: 392.0648.

3-Benzyl-3-(4-chlorophenyl)-1-methylindolin-2-one (163f)

Reaction time = 5.5 h; white solid; m.p. 176-177 °C; ^1H NMR (CDCl_3 , 400 MHz): δ 7.43 (2H, d, $J = 8.52$ Hz), 7.28 (2H, d, $J = 8.56$ Hz), 7.15-7.23 (2H, m), 6.98-7.09 (4H, m), 6.80 (2H, d, $J = 7.08$ Hz), 6.59 (1H, d, $J = 7.76$ Hz), 3.62 (1H, d, $J = 12.76$ Hz), 3.37 (1H, d, $J = 12.76$ Hz), 2.92 (3H, s); ^{13}C NMR (CDCl_3 , 100 MHz): δ 177.4, 143.7, 138.2, 135.4, 133.5, 130.7, 130.0, 128.8, 128.7, 128.5, 127.5, 126.7, 125.5, 122.3, 108.3, 57.8, 44.2, 26.1; IR (NaCl, neat) ν : 3062, 3019, 1707, 1612, 1489, 1350, 779, 758 cm^{-1} ; HRMS (ESI) calcd for $\text{C}_{22}\text{H}_{18}\text{ClNO}$ ($\text{M}^+ + \text{H}$): 348.1155, found: 348.1147.

3-Benzyl-1-methyl-3-(*p*-tolyl)indolin-2-one (163g)

Reaction time = 1 h; white solid; m.p. 150-151 °C; ^1H NMR (CDCl_3 , 400 MHz): δ 7.36 (2H, d, $J = 8.2$ Hz), 7.12-7.19 (4H, m), 6.96-7.06 (4H, m), 6.82 (2H, d, $J = 6.64$ Hz), 6.55 (1H, d, $J = 7.72$ Hz), 3.67 (1H, d, $J = 12.76$ Hz), 3.39 (1H, d, $J = 12.76$ Hz), 2.90 (3H, s), 2.30 (3H, s); ^{13}C NMR (CDCl_3 , 100 MHz): δ 178.0, 143.8, 137.2, 136.8, 135.8, 131.5, 130.1, 129.4, 128.2, 127.5, 127.2, 126.5, 125.5, 122.2, 108.0, 58.1, 44.0, 26.1, 21.1; IR (NaCl, neat) ν : 3017, 1701, 1612, 1454, 1366, 1350 cm^{-1} ; HRMS (ESI) calcd for $\text{C}_{23}\text{H}_{21}\text{NO}$ ($\text{M}^+ + \text{H}$): 328.1701, found: 328.1706.

3-Benzyl-1-methyl-3-(naphthalen-2-yl)indolin-2-one (163h)

Reaction time = 18 h; yellow solid; m.p. 151-153 °C; ^1H NMR (CDCl_3 , 400 MHz): δ 7.91 (1H, d, $J = 1.2$ Hz), 7.78-7.80 (3H, m), 7.58 (1H, dd, $J = 8.68, 1.76$ Hz), 7.41-7.44 (2H, m), 7.19-7.22 (2H, m), 6.98-7.08 (4H, m), 6.85 (2H, d, $J = 6.44$ Hz), 6.59 (1H, d, $J = 7.8$ Hz), 3.79 (1H, d, $J = 12.72$ Hz), 3.53 (1H, d, $J = 12.72$ Hz), 2.94 (3H, s); ^{13}C NMR (CDCl_3 , 100 MHz): δ 177.8, 143.9, 137.2, 135.7, 133.3, 132.7, 131.4, 130.1, 128.4, 128.3, 128.3, 127.5, 126.6, 126.2, 126.2, 126.1, 125.6, 125.5, 122.3, 108.2, 58.5, 43.8, 26.2; IR (NaCl, neat) ν : 3059, 3013, 1712, 1611, 1495, 1470, 1454, 1373 cm^{-1} ; HRMS (ESI) calcd for $\text{C}_{26}\text{H}_{21}\text{NO}$ ($\text{M}^+ + \text{H}$): 364.1701, found: 364.1701.

3-Benzyl-1-methyl-3-(thiophen-2-yl)indolin-2-one (163i)

Reaction time = 1 h; brown solid; m.p. 138-140 °C; ^1H NMR (CDCl_3 , 400 MHz): δ 7.29 (1H, d, $J = 7.32$ Hz), 7.19-7.20 (2H, m), 6.99-7.08 (5H, m), 6.94-6.95 (1H, m), 6.82 (2H, d, $J = 7.12$ Hz), 6.57 (1H, d, $J = 7.72$ Hz), 3.60 (1H, d, $J = 12.88$ Hz), 3.42 (1H, d, $J = 12.88$ Hz), 2.92 (3H, s); ^{13}C NMR (CDCl_3 , 100 MHz): δ 176.6, 143.5, 143.4, 135.2, 130.7, 130.1, 128.7, 127.5, 126.8, 125.4, 125.3, 125.1, 122.3, 108.2, 56.0, 46.4, 26.2; IR (NaCl, neat) ν : 3057, 3028, 1697, 1603, 1470, 1454, 1350 cm^{-1} ; HRMS (ESI) calcd for $\text{C}_{20}\text{H}_{17}\text{NOS}$ ($\text{M}^+ + \text{H}$): 320.1109, found: 320.1111.

3-Benzyl-1,3-dimethylindolin-2-one (163j)

Reaction time = 18 h; white solid; m.p. 94-96 °C; ^1H NMR (CDCl_3 , 400 MHz): δ 7.18 (1H, td, $J = 7.64, 1.04$ Hz), 7.11 (1H, d, $J = 7.24$ Hz), 7.01-7.07 (4H, m), 6.83 (2H, dd, $J = 6.56, 2.56$ Hz), 6.60 (1H, d, $J = 7.76$ Hz), 3.10 (1H, d, $J = 13$ Hz), 2.99 (1H, d, $J = 13.6$ Hz), 2.98 (3H, s), 1.47 (3H, s); ^{13}C NMR (CDCl_3 , 100 MHz): δ 180.0, 143.2, 136.2, 133.0, 129.8, 127.8, 127.5, 126.4, 123.3, 122.1, 107.8, 49.9, 44.6, 25.9, 22.7; IR (NaCl, neat) ν : 3010, 3009, 1705, 1612, 1454, 1350 cm^{-1} ; HRMS (ESI) calcd for $\text{C}_{17}\text{H}_{17}\text{NO}$ ($\text{M}^+ + \text{H}$): 252.1388, found: 252.1382.

3-Benzyl-3-cyclohexyl-1-methylindolin-2-one (163k)

Reaction time = 5 h; orange solid; m.p. 94-96 °C; ^1H NMR (CDCl_3 , 400 MHz): δ 7.30 (1H, d, $J = 7$ Hz), 7.13 (1H, t, $J = 7.28$ Hz), 7.03 (1H, t, $J = 7.08$ Hz), 6.94 (3H, s), 6.74 (2H, d, $J = 5.6$ Hz), 6.47 (1H, d, $J = 7.48$ Hz), 3.16 (1H, d, $J = 13.08$ Hz), 3.11 (1H, d, $J = 12.76$ Hz), 2.84 (3H, s), 2.00-2.05 (1H, m), 1.91-1.94 (1H, m), 1.77-1.79 (1H, m), 1.61 (2H, d, $J = 11.56$ Hz), 1.50 (1H, d, $J = 12.44$ Hz), 1.21-1.34 (4H, m), 1.05-1.11 (1H, m), 0.84-0.93 (1H, m); ^{13}C NMR (CDCl_3 , 100 MHz): δ 179.2, 144.1, 136.4, 130.8, 129.8, 127.6, 127.3, 126.1, 124.2, 121.8, 107.5, 58.5, 45.2, 41.1, 27.9, 27.5, 26.8, 26.4, 26.4, 25.5; IR (NaCl, neat) ν : 3053, 1701, 1602, 1454, 1350 cm^{-1} ; HRMS (ESI) calcd for $\text{C}_{22}\text{H}_{25}\text{NO}$ ($\text{M}^+ + \text{H}$): 320.2014, found: 320.2006.

3-Benzyl-3-cyclopentyl-1-methylindolin-2-one (163l)

Reaction time = 5 h; orange solid; m.p. 98-100 °C; ^1H NMR (CDCl_3 , 400 MHz): δ 7.30 (1H, d, $J = 7.32$ Hz), 7.13 (1H, t, $J = 7.64$ Hz), 6.94-7.03 (4H, m), 6.79-6.82 (2H, m), 6.51 (1H, d, $J = 7.72$ Hz), 3.27 (1H, d, $J = 12.96$ Hz), 3.10 (1H, d, $J = 12.96$ Hz), 2.90 (3H, s), 2.47-2.52 (1H, m), 1.76-1.79 (1H, m), 1.41-1.74 (6H, m), 1.15-1.26 (1H, m); ^{13}C NMR (CDCl_3 , 100 MHz): δ 179.0, 144.0, 136.5, 130.8, 129.7, 127.6, 127.4, 126.1, 124.1, 121.8, 107.5, 56.8, 47.3, 42.6, 27.7, 26.9, 25.7, 25.0, 24.9; IR (NaCl, neat) ν : 3012, 1701, 1610, 1454, 1367 cm^{-1} ; HRMS (ESI) calcd for $\text{C}_{21}\text{H}_{23}\text{NO}$ ($\text{M}^+ + \text{H}$): 306.1858, found: 306.1859.

3-Benzyl-3-cyclopropyl-1-methylindolin-2-one (163m)

Reaction time = 3 h; yellow solid; m.p. 109-111 °C; ^1H NMR (CDCl_3 , 400 MHz): δ 7.14 (1H, td, $J = 7.68, 1.24$ Hz), 7.01-7.06 (4H, m), 6.96 (1H, td, $J = 7.48, 0.84$ Hz), 6.89-6.92 (2H, m), 6.56 (1H, d, $J = 7.76$ Hz), 3.26 (1H, d, $J = 13.16$ Hz), 3.15 (1H, d, $J = 13.16$ Hz), 2.96 (3H, s), 1.36-1.43 (1H, m), 0.47-0.55 (1H, m), 0.32-0.42 (2H, m), 0.06-0.12 (1H, m); ^{13}C NMR (CDCl_3 , 100 MHz): δ 178.8, 143.8, 136.4, 130.0, 129.4, 127.9, 127.5, 126.3, 124.1, 121.7, 107.7, 53.7, 42.8, 25.9, 17.3, 1.7, 0.4; IR (NaCl, neat) ν : 3053, 3009, 1709, 1610, 1454, 1360 cm^{-1} ; HRMS (ESI) calcd for $\text{C}_{19}\text{H}_{19}\text{NO}$ ($\text{M}^+ + \text{H}$): 278.1545, found: 278.1541.

1,3-Dibenzyl-3-phenylindolin-2-one (163n)

Reaction time = 18 h; yellow solid; m.p. 84-86 °C; ^1H NMR (CDCl_3 , 400 MHz): δ 7.51-7.53 (2H, m), 7.26-7.35 (4H, m), 7.01-7.17 (8H, m), 6.91 (2H, d, $J = 6.12$ Hz), 6.64 (2H, d, $J = 6.4$ Hz), 6.39-6.42 (1H, m), 4.84 (1H, d, $J = 16.48$ Hz), 4.48 (1H, d, $J = 16.04$ Hz), 3.80 (1H, d, $J = 12.8$ Hz), 3.50 (1H, d, $J = 13.28$ Hz); ^{13}C NMR (CDCl_3 , 100 MHz): δ 177.8, 143.2, 140.5, 135.9, 135.4, 131.5, 130.6, 128.8, 128.7, 128.3, 128.0, 127.7, 127.3, 126.8, 125.6, 122.4, 109.6, 58.5, 43.8, 43.8; IR (NaCl, neat) ν : 3053, 3009, 1709, 1610, 1493, 1454, 1367, 1350 cm^{-1} ; HRMS (ESI) calcd for $\text{C}_{28}\text{H}_{23}\text{NO}$ ($\text{M}^+ + \text{H}$): 390.1858, found: 390.1859.

1-Allyl-3-benzyl-3-phenylindolin-2-one (163o)

Reaction time = 7 h; yellow solid; m.p. 94-96 °C; ^1H NMR (CDCl_3 , 400 MHz): δ 7.48-7.52 (2H, m), 7.24-7.34 (4H, m), 7.15-7.21 (1H, m), 6.98-7.09 (4H, m), 6.85 (2H, d, J = 6.4 Hz), 6.58 (1H, d, J = 7.76 Hz), 5.30-5.39 (1H, m), 4.90 (1H, dd, J = 10.52, 1.36 Hz), 4.61 (1H, dd, J = 17.4, 0.92 Hz), 4.20-4.26 (1H, m), 3.92-3.98 (1H, m), 3.74 (1H, d, J = 12.68 Hz), 3.45 (1H, d, J = 12.84 Hz); ^{13}C NMR (CDCl_3 , 100 MHz): δ 177.5, 143.2, 140.2, 135.8, 131.5, 131.1, 130.4, 128.8, 128.2, 127.7, 127.6, 127.3, 126.7, 125.5, 122.3, 117.2, 109.3, 58.4, 43.9, 42.3; IR (NaCl, neat) ν : 2955, 2930, 2858, 1715, 1610, 1454, 1350 cm^{-1} ; HRMS (ESI) calcd for $\text{C}_{24}\text{H}_{21}\text{NO}$ ($\text{M}^+ + \text{Na}$): 362.1521, found: 362.1523.

3-(4-Fluorobenzyl)-1-methyl-3-phenylindolin-2-one (163p)

Reaction time = 4 h; yellow solid; m.p. 126-128 °C; ^1H NMR (CDCl_3 , 400 MHz): δ 7.47 (2H, d, J = 7.28 Hz), 7.19-7.35 (5H, m), 7.07 (1H, t, J = 7.56 Hz), 6.77-6.81 (2H, m), 6.69 (2H, t, J = 8.72 Hz), 6.61 (1H, d, J = 7.76 Hz), 3.67 (1H, d, J = 12.92 Hz), 3.38 (1H, d, J = 12.92 Hz), 2.94 (3H, s); ^{13}C NMR (CDCl_3 , 100 MHz): δ 177.7, 160.5 (1C, d, $J_{\text{C-F}}$ = 243 Hz), 143.7, 139.5, 131.5 (1C, d, $J_{\text{C-F}}$ = 7.8 Hz), 131.4, 131.4, 131.1, 128.7, 128.4, 127.5, 127.2, 125.4, 122.3, 114.2 (1C, d, $J_{\text{C-F}}$ = 21 Hz), 108.2, 58.3, 43.1, 26.1; IR (NaCl, neat) ν : 3017, 1699, 1614, 1454, 1325, 1020, 1011 cm^{-1} ; HRMS (ESI) calcd for $\text{C}_{22}\text{H}_{19}\text{FNO}$ ($\text{M}^+ + \text{H}$): 332.1451, found: 332.1450.

1-Methyl-3-phenyl-3-(4-(trifluoromethyl)benzyl)indolin-2-one (163q)

Reaction time = 4 h; yellow solid; m.p. 122-123 °C; ^1H NMR (CDCl_3 , 400 MHz): δ 7.48 (2H, d, $J = 7.48$ Hz), 7.21-7.36 (7H, m), 7.09 (1H, t, $J = 7.44$ Hz), 6.94 (2H, d, $J = 8.04$ Hz), 6.62 (1H, d, $J = 7.92$ Hz), 3.74 (1H, d, $J = 12.72$ Hz), 3.47 (1H, d, $J = 12.72$ Hz), 2.93 (3H, s); ^{13}C NMR (CDCl_3 , 100 MHz): δ 177.4, 143.7, 139.9, 139.3, 130.7, 130.4, 129.0, 128.7, 128.6, 127.7, 127.2, 125.6, 125.4, 124.3 (1C, q, $J_{\text{C-F}} = 2.7$ Hz), 122.9, 122.4, 108.3, 58.1, 43.6, 26.1; IR (NaCl, neat) ν : 3053, 3009, 2920, 1709, 1611, 1493, 1470, 1350, 1126, 1082 cm^{-1} ; HRMS (ESI) calcd for $\text{C}_{23}\text{H}_{18}\text{F}_3\text{NO}$ ($\text{M}^+ + \text{H}$): 382.1419, found: 382.1419.

1-Methyl-3-(4-methylbenzyl)-3-phenylindolin-2-one (163r)

Reaction time = 18 h; yellow solid; m.p. 121-123 °C; ^1H NMR (CDCl_3 , 400 MHz): δ 7.48 (2H, d, $J = 7.52$ Hz), 7.17-7.33 (5H, m), 7.05 (1H, t, $J = 7.28$ Hz), 6.79 (2H, d, $J = 7.76$ Hz), 6.70 (2H, d, $J = 7.8$ Hz), 6.59 (1H, d, $J = 7.92$ Hz), 3.63 (1H, d, $J = 12.84$ Hz), 3.40 (1H, d, $J = 12.84$ Hz), 2.93 (3H, s), 2.16 (3H, s); ^{13}C NMR (CDCl_3 , 100 MHz): δ 177.9, 143.8, 139.9, 136.0, 132.6, 131.4, 129.9, 128.6, 128.2, 128.2, 127.4, 127.3, 125.6, 122.2, 108.1, 58.3, 43.6, 26.1, 21.0; IR (NaCl, neat) ν : 3078, 3053, 3009, 1713, 1612, 1470, 1350 cm^{-1} ; HRMS (ESI) calcd for $\text{C}_{23}\text{H}_{21}\text{NO}$ ($\text{M}^+ + \text{H}$): 328.1701, found: 328.1700.

1-Methyl-3-(naphthalen-1-ylmethyl)-3-phenylindolin-2-one (163s)

Reaction time = 18 h; yellow solid; m.p. 160-162 °C; ^1H NMR (CDCl_3 , 400 MHz): δ 7.94-7.97 (1H, m), 7.64-7.66 (1H, m), 7.55 (3H, t, $J = 8.12$ Hz), 7.20-7.36 (5H, m), 7.00-7.13 (4H, m), 6.80 (1H, t, $J = 7.56$ Hz), 6.46 (1H, d, $J = 7.76$ Hz), 4.18 (1H, d, $J = 13.76$ Hz), 3.98 (1H, d, $J = 13.76$ Hz), 2.86 (3H, s); ^{13}C NMR (CDCl_3 , 100 MHz): δ 178.2, 143.7, 140.1, 133.5, 132.4, 132.4, 130.8, 128.6, 128.3, 128.1, 127.9, 127.5, 127.5, 127.4, 126.3, 125.2, 125.2, 124.6, 124.6, 121.9, 107.9, 58.1, 39.4, 26.2; IR (NaCl, neat) ν : 3051, 3017, 2934, 1712, 1612, 1492, 1352 cm^{-1} ; HRMS (ESI) calcd for $\text{C}_{26}\text{H}_{21}\text{NO}$ ($\text{M}^+ + \text{H}$): 364.1701, found: 364.1698.

1-Methyl-3-phenyl-3-(thiophen-3-ylmethyl)indolin-2-one (163t)

Reaction time = 2 h; brown solid; m.p. 81-84 °C; ^1H NMR (CDCl_3 , 400 MHz): δ 7.47 (2H, d, $J = 7.48$ Hz), 7.22-7.34 (4H, m), 7.15 (1H, d, $J = 7.12$ Hz), 7.07 (1H, t, $J = 7.12$ Hz), 6.92-6.94 (1H, m), 6.66 (1H, d, $J = 7.76$ Hz), 6.63 (1H, d, $J = 2.04$ Hz), 6.44 (1H, d, $J = 4.84$ Hz), 3.67 (1H, d, $J = 13.32$ Hz), 3.49 (1H, d, $J = 13.32$ Hz), 2.98 (3H, s); ^{13}C NMR (CDCl_3 , 100 MHz): δ 178.0, 143.9, 139.4, 136.0, 131.7, 129.1, 128.6, 128.3, 127.5, 127.3, 125.2, 124.1, 123.3, 122.4, 108.2, 57.8, 38.5, 26.2; IR (NaCl, neat) ν : 3015, 1701, 1612, 1454, 1365 cm^{-1} ; HRMS (ESI) calcd for $\text{C}_{20}\text{H}_{17}\text{NOS}$ ($\text{M}^+ + \text{H}$): 320.1109, found: 320.1111.

3-(Cyclopropylmethyl)-1-methyl-3-phenylindolin-2-one (163u)

Reaction time = 18 h; yellow oil; ^1H NMR (CDCl_3 , 400 MHz): δ 7.33-7.36 (3H, m), 7.22-7.31 (4H, m), 7.12 (1H, t, $J = 7.48$ Hz), 6.90 (1H, d, $J = 7.8$ Hz), 3.24 (3H, s), 2.44 (1H, dd, $J = 13.52, 4.8$ Hz), 2.04 (1H, dd, $J = 13.52, 8.36$ Hz), 0.23-0.29 (1H, m), 0.15-0.19 (3H, m), -0.11- -0.06 (1H, m); ^{13}C NMR (CDCl_3 , 75 MHz): δ 178.8, 144.2, 140.4, 132.6, 128.5, 128.1, 127.2, 126.9, 125.1, 122.4, 108.1, 57.0, 42.6, 26.4, 6.5, 4.2, 3.7; IR (NaCl, neat) ν : 3015, 2957, 1701, 1603, 1470, 1350 cm^{-1} ; HRMS (ESI) calcd for $\text{C}_{19}\text{H}_{19}\text{NO}$ ($\text{M}^+ + \text{H}$): 278.1545, found: 278.1541.

1-Methyl-3-pentyl-3-phenylindolin-2-one (163v)

Reaction time = 18 h; yellow liquid; ^1H NMR (CDCl_3 , 400 MHz): δ 7.20-7.37 (7H, m), 7.09-7.13 (1H, m), 6.89 (1H, d, $J = 7.8$ Hz), 3.22 (3H, s), 2.35 (1H, td, $J = 13.28, 4.6$ Hz), 2.18 (1H, td, $J = 12.36, 4.12$ Hz), 1.06-1.29 (6H, m), 0.77-0.81 (3H, m); ^{13}C NMR (CDCl_3 , 100 MHz): δ 178.9, 144.0, 140.5, 132.6, 128.6, 128.2, 127.3, 127.0, 124.8, 122.7, 108.3, 56.9, 38.0, 32.0, 26.5, 24.2, 22.4, 14.1; IR (NaCl, neat) ν : 3061, 3016, 1713, 1612, 1472, 1348 cm^{-1} ; HRMS (ESI) calcd for $\text{C}_{20}\text{H}_{23}\text{NO}$ ($\text{M}^+ + \text{H}$): 294.1858, found: 294.1858.

1,7-Diallyl-3-benzyl-3-phenylindolin-2-one (163w)

Reaction time = 18 h; yellow solid; m.p. 76-78 °C; ^1H NMR (CDCl_3 , 400 MHz): δ 7.45-7.48 (2H, m), 7.32-7.36 (2H, m), 7.27-7.30 (1H, m), 7.19 (1H, dd, $J = 7.36, 1.32$ Hz), 7.00-7.08 (4H, m), 6.93 (1H, dd, $J = 7.76, 1.24$ Hz), 6.88-6.91 (2H, m), 5.83-5.93 (1H, m), 5.56-5.65 (1H, m), 4.87-4.93 (2H, m), 4.43-4.48 (1H, m), 4.15-4.30 (3H, m), 3.80 (1H, d, $J = 12.68$ Hz), 3.44 (1H, d, $J = 12.68$ Hz), 3.27-3.39 (2H, m); ^{13}C NMR (CDCl_3 , 100 MHz): δ 178.5, 141.5, 140.8, 137.6, 135.8, 133.4, 132.6, 132.1, 130.5, 128.8, 127.8, 127.5, 127.2, 126.7, 123.9, 122.5, 121.0, 116.3, 115.3, 57.7, 43.8, 43.2, 35.5; IR (NaCl, neat) ν : 3015, 1701, 1600, 1481, 1358 cm^{-1} ; HRMS (ESI) calcd for $\text{C}_{27}\text{H}_{25}\text{NO}$ ($\text{M}^+ + \text{H}$): 380.2014, found: 380.2016.

 ^{18}O -Labelled 3-Benzyl-1-methyl-3-phenylindolin-2-one (163a- O^{18})

White solid; m.p. 128-130 °C; ^1H NMR (CDCl_3 , 400 MHz): δ 7.48 (2H, d, $J = 7.48$ Hz), 7.26-7.34 (3H, m), 7.19 (2H, t, $J = 7.48$ Hz), 6.97-7.07 (4H, m), 6.82 (2H, d, $J = 6.56$ Hz), 6.57 (1H, d, $J = 7.72$ Hz), 3.69 (1H, d, $J = 12.76$ Hz), 3.43 (1H, d, $J = 12.76$ Hz), 2.92 (3H, s); ^{13}C NMR (CDCl_3 , 100 MHz): δ 177.8, 177.8, 143.8, 139.8, 135.7, 131.3, 130.0, 128.6, 128.2, 127.5, 127.3, 126.5, 125.5, 122.2, 108.1, 58.3, 44.0, 26.1; IR (NaCl, neat) ν : 3053, 3009, 1713, 1697, 1603, 1454, 1366, 1350 cm^{-1} ; HRMS (ESI) calcd for $\text{C}_{22}\text{H}_{19}\text{N}^{18}\text{O}$ ($\text{M}^+ + \text{Na}$): 338.1407, found: 338.1400.

(1-Methyl-3-phenyl-1*H*-indol-2-yl)(phenyl)methanol (185a)

Yellow oil; ^1H NMR (CD_2Cl_2 , 400 MHz): δ 7.63 (1H, d, $J = 7.96$ Hz), 7.49 (2H, d, $J = 7.04$ Hz), 7.43 (2H, t, $J = 7.76$ Hz), 7.25-7.34 (8H, m), 7.11 (1H, t, $J = 7.6$ Hz), 6.34 (1H, s), 3.50 (3H, s), 2.58 (1H, brs); ^{13}C NMR (CDCl_3 , 100 MHz): δ 141.5, 137.7, 135.8, 134.7, 130.1, 128.7, 128.5, 127.3, 126.6, 126.6, 125.9, 122.7, 120.0, 119.9, 117.5, 109.2, 67.4, 31.3 IR (NaCl, neat) ν : 3447, 3061, 3015, 2932, 1330, 1215, 1016 cm^{-1} ; HRMS (ESI) calcd for $\text{C}_{22}\text{H}_{19}\text{NO}$ ($\text{M}^+ + \text{H}$): 314.1545, found: 314.1541.

7.5 Gold(I) Catalyzed Cycloisomerization and Thermal [4+2] Cycloaddition of 1,9-Diene-4-yne Esters. Efficient Synthesis of 3-Azatricyclo[5.2.1.0^{1,5}]dec-8-enes.
General Procedure for The Synthesis of 1,9-Diene-4-yne Esters 159a-b, 159f-q¹¹⁰

1,6-Enyne **195** was synthesized following the literature procedure.^{110a-b} To a stirred solution of **195** (5 mmol) in 20 mL of THF at -78 °C was slowly added *n*-butyllithium (2.0 M in cyclohexane solution, 3.75 mL, 7.5 mmol). The resulting solution was stirred for 45 minutes and the corresponding vinyl ketone **196** (1.5 equiv) was subsequently added in dropwise manner. After 17 h, the reaction mixture was quenched with saturated NH_4Cl (15 mL) and extracted with EtOAc (2 x 20 mL). The combined organic layers

were washed with brine (15 mL), dried over MgSO_4 , concentrated under reduced pressure and purified by flash column chromatography on silica gel (eluent: *n*-hexane: ethyl acetate = 6:1) to give enynyl alcohol **197** in 30-38% yield which, without characterization, was directly employed to the next step. To a solution of enynyl alcohol **197** (1.5 mmol) in CH_2Cl_2 (10 mL) at 0 °C was added DMAP (0.15 mmol, 18.3 mg), BzCl (4.5 mmol, 0.522 mL) or acetic anhydride (4.5 mmol, 0.425 mL) and NEt_3 (2.25 mmol, 0.314 mL). The resulting solution was allowed to stir for 15 h at room temperature. Upon completion, the reaction mixture was quenched with saturated NaHCO_3 solution (10 mL) and extracted with CH_2Cl_2 (2 x 15 mL). The combined organic layer was washed with brine (10 mL), dried over MgSO_4 , concentrated under reduced pressure and purified by flash column chromatography on silica gel (eluent: *n*-hexane: ethyl acetate = 9: 1) to give the desired product **159** in 60-88% yield.

General Procedure for The Synthesis of 1,9-Diene-4-yne Esters **159c-e**

To a stirred solution of **195** (5 mmol) in 20 mL of THF at -78°C was slowly added *n*-butyllithium (2.0 M in cyclohexane solution, 3.75 mL, 7.5 mmol). The resulting solution was stirred for 45 minutes and the corresponding aldehyde **199** (1.5 equiv) was subsequently added in dropwise manner. After 17 h, the reaction mixture was quenched

with saturated NH_4Cl (15 mL) and extracted with EtOAc (2 x 20 mL). The combined organic layers were washed with brine (15 mL), dried over MgSO_4 , concentrated under reduced pressure and purified by flash column chromatography on silica gel (eluent: *n*-hexane: ethyl acetate = 6:1) to give enynyl alcohol **200** in 50-65% yield which, without characterization, was directly employed to the next step. To a stirred solution of **200** (3 mmol) in DMSO (20 mL) was added IBX (2.5 equiv) portionwise and the reaction mixture was stirred for 17 h at room temperature. Subsequently, water (10 mL) and EtOAc (10 mL) were added and the resulting solution was stirred for 15 minutes. After filtration through a pad of Celite, the aqueous layer was extracted with EtOAc (3 x 10 mL). The combined organic layers were washed with water (2 x 10 mL), brine (10 mL), dried over MgSO_4 and concentrated under reduced pressure. The crude mixture was used directly without further purification. To a stirred solution containing crude mixture of **201** was added vinylmagnesium chloride (1.6 M in THF, 5.6 mL, 9 mmol) and stirred for 1 hour. Upon completion, the reaction mixture was quenched with saturated NH_4Cl (10 mL) and extracted with EtOAc (2 x 10 mL). The combined organic layers were washed with brine (10 mL), dried over MgSO_4 , concentrated under reduced pressure and purified by flash column chromatography on silica gel (eluent: *n*-hexane: ethyl acetate = 7:1) to give the alcohol **197** in 50-60% yield which, without characterization, was directly employed to the next step. To a solution of alcohol **197** (1.5 mmol) in CH_2Cl_2 (10 mL) at 0 °C was added DMAP (0.15 mmol, 18.3 mg), acetic anhydride (4.5 mmol, 0.425 mL) and NEt_3 (2.25 mmol, 0.314 mL). The resulting solution was allowed to stir for 15 h at room temperature. Upon completion, the reaction mixture was quenched with saturated NaHCO_3 solution (10 mL) and extracted with CH_2Cl_2 (2 x 15 mL). The combined organic layer was washed with brine (10 mL), dried over MgSO_4 , concentrated under reduced pressure and purified by flash column chromatography on silica gel (eluent: *n*-hexane: ethyl acetate = 9: 1) to give the desired product **159** in 70-90% yield.

General Experimental Procedure for Optimizing Gold(I) Catalyzed Cycloisomerization and Thermal [4+2] Cycloaddition of 1,9-Diene-4-yne Esters.

To a solution of 1,9-diene-4-yne esters **159a** (0.3 mmol) and 4 Å molecular sieves (300 mg) in dry solvent (3 mL) was added gold(I), gold (III) or PtCl₂ catalyst (15 μmol) under an argon atmosphere. The resulting solution was heated at specified temperature and the reaction was monitored by thin layer chromatography. Upon completion, the reaction mixture was cooled to room temperature, filtered through a pad of Celite, washed with EtOAc and the solvent was evaporated under reduced pressure. Purification by flash column chromatography on silica gel (*n*-hexane/ EtOAc = 9:1 as eluent) gave the product **161a**.

General Experimental Procedure for Gold(I) Catalyzed Cycloisomerization and Thermal [4+2] Cycloaddition of 1,9-Diene-4-yne Esters.

To a solution of 1,9-diene-4-yne esters **159** (0.3 mmol) and 4 Å molecular sieves (300 mg) in dry PhMe (3 mL) was added gold(I) complex **Au₁₁** (15 μmol, 13 mg) under an argon atmosphere. The resulting solution was heated 80 °C and the reaction was monitored by thin layer chromatography. Upon completion, the reaction mixture was

cooled to room temperature, filtered through a pad of Celite, washed with EtOAc and the solvent was evaporated under reduced pressure. Purification by flash column chromatography on silica gel (*n*-hexane/ EtOAc = 9:1 as eluent) gave the product **161**.

Procedure for Gold(I) Complex Au_{11} Catalyzed Nazarov-Type Cyclization of 1,9-Diene-4-yne Esters towards the formation of **160a**

To a solution of 1,9-diene-4-yne ester **159a** (0.3 mmol) and 4 Å molecular sieves (300 mg) in anhydrous toluene (3 mL) was added gold(I) complex **Au₁₁** (15 μmol, 13 mg) under an argon atmosphere. The reaction mixture was stirred at 80 °C for 30 minutes. The reaction mixture then cooled to room temperature and filtered through Celite, washed with EtOAc, the solvent was removed under reduced pressure. Purification by flash column chromatography on silica gel (*n*-hexane/ EtOAc = 9:1 as eluent) furnished **160a** in 74% yield.

Procedure for Thermal [4+2] Cyclization of **160a towards the formation of **159a****

A solution of cyclopentadiene **160a** (0.22 mmol, 80.2 mg) and 4 Å molecular sieves (220 mg) in anhydrous PhMe (2 mL) was heated at 80 °C for 4 hours. The reaction mixture then cooled to room temperature and filtered through Celite, washed with EtOAc, the solvent was removed under reduced pressure. Purification by flash column

chromatography on silica gel (*n*-hexane/ EtOAc = 9:1 as eluent) furnished **159a** in 80% yield.

6-((*N*-Allyl-4-methylphenyl)sulfonamido)-3-methylhex-1-en-4-yn-3-yl Acetate (159a)

White solid; m.p. 50-51 °C; ^1H NMR (CDCl_3 , 400 MHz): δ 7.72 (2H, d, J = 8.2 Hz), 7.28 (2H, d, J = 8 Hz), 5.70-5.80 (2H, m), 5.31 (1H, d, J = 17.08 Hz), 5.20-5.24 (2H, m), 5.07 (1H, d, J = 10.4 Hz), 4.18 (2H, s), 3.84 (2H, d, J = 6.36 Hz), 2.41 (3H, s), 1.96 (3H, s), 1.43 (3H, s); ^{13}C NMR (CDCl_3 , 100 MHz): δ 168.6, 143.4, 138.3, 136.2, 131.9, 129.6, 127.7, 120.1, 115.2, 84.3, 79.4, 73.4, 48.9, 36.1, 28.0, 21.6, 21.5; IR (NaCl, neat) ν : 3022, 2401, 1738, 1643, 1597, 1354, 1168, 1045 cm^{-1} ; HRMS(ESI) calcd for $\text{C}_{19}\text{H}_{23}\text{NO}_4\text{S}$ (M^+ + H): 362.1426, found: 362.1429.

6-((*N*-Allyl-4-methylphenyl)sulfonamido)-3-methylhex-1-en-4-yn-3-yl Benzoate (159b)

Yellow oil; ^1H NMR (CDCl_3 , 400 MHz): δ 7.95 (2H, d, J = 7.32 Hz), 7.70 (2H, d, J = 8.24 Hz), 7.54-7.58 (1H, m), 7.44 (2H, t, J = 7.8 Hz), 7.16 (2H, d, J = 8.72 Hz), 5.85 (1H, dd, J = 17.4, 10.56 Hz), 5.71-5.78 (1H, m), 5.31-5.37 (2H, m), 5.20 (1H, d, J = 10.08 Hz), 5.14 (1H, d, J = 10.52 Hz), 4.21 (2H, s), 3.88 (2H, d, J = 6.88 Hz), 2.28 (3H, s), 1.58 (3H, s); ^{13}C NMR (CDCl_3 , 100 MHz): δ 164.2, 143.3, 138.4, 136.2, 133.1, 132.0, 130.7, 129.7, 129.6, 128.5, 127.7, 120.3, 115.6, 84.4, 79.8, 74.4, 49.0, 36.2, 28.2, 21.5; IR (NaCl, neat) ν : 3088, 2987, 2401, 1724, 1643, 1599, 1350, 1163, 1066 cm^{-1} ; HRMS(ESI) calcd for $\text{C}_{24}\text{H}_{25}\text{NO}_4\text{S}$ (M^+ + Na): 446.1402, found: 446.1401.

6-((*N*-Allyl-4-methylphenyl)sulfonamido)-3-cyclopentylhex-1-en-4-yn-3-yl Acetate (159c)

Yellow oil; ^1H NMR (CDCl_3 , 400 MHz): δ 7.72 (2H, d, $J = 8.24$ Hz), 7.27 (2H, d, $J = 8.12$ Hz), 5.63-5.77 (2H, m), 5.30 (1H, dd, $J = 17.04$, 1.2 Hz), 5.22 (1H, d, $J = 10.08$ Hz), 5.14 (1H, d, $J = 17.12$ Hz), 5.10 (1H, d, $J = 10.52$ Hz), 4.23 (2H, s), 3.86 (2H, d, $J = 6.28$ Hz), 2.41 (3H, s), 2.12-2.21 (1H, m), 1.96 (3H, s), 1.46-1.64 (6H, m), 1.32-1.40 (1H, m), 1.16-1.25 (1H, m); ^{13}C NMR (CDCl_3 , 100 MHz): δ 168.5, 143.3, 136.9, 136.5, 132.0, 129.7, 127.5, 120.0, 116.5, 82.6, 80.6, 80.4, 48.8, 48.7, 36.1, 27.6, 25.8, 25.6, 21.6, 21.5; IR (NaCl, neat) ν : 3022, 2360, 1745, 1643, 1598, 1368, 1163, 1093 cm^{-1} ; HRMS(ESI) calcd for $\text{C}_{23}\text{H}_{29}\text{NO}_4\text{S}$ ($\text{M}^+ + \text{Na}$): 438.1715, found: 438.1691.

6-((*N*-Allyl-4-methylphenyl)sulfonamido)-3-cyclohexylhex-1-en-4-yn-3-yl Acetate (159d)

Yellow oil; ^1H NMR (CDCl_3 , 400 MHz): δ 7.72 (2H, d, $J = 8.16$ Hz), 7.27 (2H, d, $J = 8.44$ Hz), 5.69-5.79 (1H, m), 5.57 (1H, dd, $J = 16.96$, 10.64 Hz), 5.31 (1H, d, $J = 17.04$ Hz), 5.22 (1H, d, $J = 10.04$ Hz), 5.12-5.17 (2H, m), 4.24 (2H, s), 3.87 (2H, d, $J = 6.32$ Hz), 2.41 (3H, s), 1.96 (3H, s), 1.56-1.74 (6H, m), 1.03-1.18 (3H, m), 0.81-0.99 (2H, m); ^{13}C NMR (CDCl_3 , 100 MHz): δ 168.4, 143.2, 136.4, 136.3, 132.0, 129.7, 127.5, 120.0, 117.1, 82.3, 81.1, 80.8, 48.7, 46.6, 36.1, 27.1, 26.9, 26.2, 26.0, 26.0, 21.6, 21.5; IR (NaCl, neat) ν : 3024, 2360, 1741, 1643, 1598, 1350, 1155, 1066 cm^{-1} ; HRMS(ESI) calcd for $\text{C}_{24}\text{H}_{31}\text{NO}_4\text{S}$ ($\text{M}^+ + \text{Na}$): 452.1872, found: 452.1854.

6-((*N*-Allyl-4-methylphenyl)sulfonamido)-3-benzylhex-1-en-4-yn-3-yl Acetate (159e)

Colorless oil; ^1H NMR (CDCl_3 , 400 MHz): δ 7.68 (2H, d, $J = 8.24$ Hz), 7.20-7.28 (5H, m), 7.10-7.12 (2H, m), 5.63-5.71 (2H, m), 5.10-5.24 (4H, m), 4.19 (2H, s), 3.76-3.78 (2H, m), 2.97 (1H, d, $J = 13.44$ Hz), 2.92 (1H, d, $J = 13.44$ Hz), 2.37 (3H, s), 1.95 (3H, s); ^{13}C NMR (CDCl_3 , 100 MHz): δ 168.4, 143.3, 137.0, 136.3, 134.7, 131.9, 131.0, 129.7, 127.8, 127.7, 127.1, 120.1, 116.6, 82.9, 81.7, 77.0, 48.8, 46.7, 36.1, 21.7, 21.5; IR (NaCl, neat) ν : 3028, 2425, 1748, 1643, 1597, 1348, 1163, 1092 cm^{-1} ; HRMS(ESI) calcd for $\text{C}_{25}\text{H}_{27}\text{NO}_4\text{S}$ ($\text{M}^+ + \text{Na}$): 460.1559, found: 460.1563.

6-((*N*-Allyl-4-methylphenyl)sulfonamido)hex-1-en-4-yn-3-yl Acetate (159f)

Colorless oil; ^1H NMR (CDCl_3 , 400 MHz): δ 7.71 (2H, d, $J = 8.12$ Hz), 7.28 (2H, d, $J = 7.92$ Hz), 5.58-5.76 (2H, m), 5.19-5.30 (4H, m), 4.15 (2H, s), 3.80 (2H, d, $J = 6.4$ Hz), 2.42 (3H, s), 2.05 (3H, s); ^{13}C NMR (CDCl_3 , 100 MHz): δ 169.3, 143.5, 135.9, 132.4, 131.8, 129.6, 127.7, 120.0, 118.8, 81.1, 79.8, 63.9, 49.1, 36.1, 21.5, 20.9; IR (NaCl, neat) ν : 3087, 2923, 2400, 1741, 1644, 1598, 1349, 1163, 1093 cm^{-1} ; HRMS(ESI) calcd for $\text{C}_{18}\text{H}_{21}\text{NO}_4\text{S}$ ($\text{M}^+ + \text{Na}$): 370.1089, found: 370.1072.

6-((N-Allyl-4-methylphenyl)sulfonamido)-2-methylhex-1-en-4-yn-3-yl Acetate (159g)

Colorless oil; ^1H NMR (CDCl_3 , 400 MHz): δ 7.70 (2H, d, $J = 8.2$ Hz), 7.28 (2H, d, $J = 7.96$ Hz), 5.68-5.76 (1H, m), 5.54 (1H, s), 5.25 (1H, dd, $J = 17.4, 1.12$ Hz), 5.22 (1H, d, $J = 10.32$ Hz), 4.99 (1H, s), 4.90 (1H, s), 4.16 (2H, s), 3.79 (2H, d, $J = 6.4$ Hz), 2.42 (3H, s), 2.06 (3H, s), 1.65 (3H, s); ^{13}C NMR (CDCl_3 , 100 MHz): δ 169.4, 143.5, 139.7, 135.9, 131.8, 129.6, 127.7, 120.0, 114.8, 81.5, 79.2, 66.7, 49.1, 36.1, 21.5, 20.8, 18.1; IR (NaCl, neat) ν : 3022, 2425, 1740, 1651, 1598, 1348, 1163, 1092 cm^{-1} ; HRMS(ESI) calcd for $\text{C}_{19}\text{H}_{23}\text{NO}_4\text{S}$ ($\text{M}^+ + \text{Na}$): 384.1245, found: 384.1261.

6-((N-Cinnamyl-4-methylphenyl)sulfonamido)-3-methylhex-1-en-4-yn-3-yl Acetate (159h)

White solid; m.p. 92-93 $^{\circ}\text{C}$; ^1H NMR (CDCl_3 , 400 MHz): δ 7.74 (2H, d, $J = 8.12$ Hz), 7.21-7.34 (7H, m), 6.63 (1H, d, $J = 15.8$ Hz), 6.04-6.11 (1H, m), 5.74 (1H, dd, $J = 17.12, 10.4$ Hz), 5.21 (1H, d, $J = 17.12$ Hz), 5.08 (1H, d, $J = 10.4$ Hz), 4.21 (2H, s), 4.00 (2H, d, $J = 6.88$ Hz), 2.40 (3H, s), 1.97 (3H, s), 1.45 (3H, s); ^{13}C NMR (CDCl_3 , 100 MHz): δ 168.6, 143.4, 138.4, 136.3, 136.2, 135.2, 129.7, 128.6, 128.0, 127.8, 126.6, 122.8, 115.3, 84.5, 79.5, 73.8, 48.6, 36.3, 28.0, 21.7, 21.5; IR (NaCl, neat) ν : 3086, 2401, 1742, 1643, 1597, 1344, 1155, 1061 cm^{-1} ; HRMS(ESI) calcd for $\text{C}_{25}\text{H}_{27}\text{NO}_4\text{S}$ ($\text{M}^+ + \text{H}$): 438.1739, found: 438.1738.

(*E*)-6-((*N*-(But-2-en-1-yl)-4-methylphenyl)sulfonamido)-3-methylhex-1-en-4-yn-3-yl Acetate (159i)

Yellow oil; ^1H NMR (CDCl_3 , 400 MHz): δ 7.71 (2H, d, $J = 8.24$ Hz), 7.29 (2H, d, $J = 8.72$ Hz), 5.71-5.80 (2H, m), 5.34-5.39 (1H, m), 5.20 (1H, d, $J = 17.4$ Hz), 5.07 (1H, d, $J = 10.52$ Hz), 4.16 (2H, s), 3.76 (2H, d, $J = 6.84$ Hz), 2.40 (3H, s), 1.96 (3H, s), 1.67 (3H, d, $J = 6.84$ Hz), 1.42 (3H, s); ^{13}C NMR (CDCl_3 , 100 MHz): δ 168.6, 143.2, 138.4, 136.3, 131.7, 129.5, 127.7, 124.5, 115.2, 84.0, 79.6, 73.8, 48.3, 35.8, 28.0, 21.6, 21.5, 17.7; IR (NaCl, neat) ν : 3086, 2402, 1742, 1645, 1599, 1348, 1161, 1092 cm^{-1} ; HRMS(ESI) calcd for $\text{C}_{20}\text{H}_{25}\text{NO}_4\text{S}$ ($\text{M}^+ + \text{H}$): 376.1583, found: 376.1588.

(*E*)-3-Methyl-6-((4-methyl-*N*-(3-(thiophen-2-yl)allyl)phenyl)sulfonamido)hex-1-en-4-yn-3-yl Acetate (159j)

Yellow solid; m.p. 77-78 $^{\circ}\text{C}$; ^1H NMR (CDCl_3 , 400 MHz): δ 7.73 (2H, d, $J = 8.16$ Hz), 7.28 (2H, d, $J = 8.12$ Hz), 7.15 (1H, t, $J = 3.2$ Hz), 6.94 (2H, d, $J = 3.24$ Hz), 6.77 (1H, d, $J = 15.6$ Hz), 5.85-5.93 (1H, m), 5.74 (1H, dd, $J = 17.08, 10.36$ Hz), 5.20 (1H, d, $J = 17.12$ Hz), 5.08 (1H, d, $J = 10.4$ Hz), 4.21 (2H, s), 3.96 (2H, d, $J = 6.88$ Hz), 2.41 (3H, s), 1.98 (3H, s), 1.45 (3H, s); ^{13}C NMR (CDCl_3 , 100 MHz): δ 168.6, 143.5, 141.3, 138.3, 136.2, 129.7, 128.3, 127.7, 127.4, 126.2, 124.8, 122.2, 115.3, 84.5, 79.4, 73.8, 48.3, 36.3, 28.0, 21.7, 21.5; IR (NaCl, neat) ν : 2989, 2247, 1742, 1645, 1598, 1348, 1161, 1062 cm^{-1} ; HRMS(ESI) calcd for $\text{C}_{23}\text{H}_{25}\text{NO}_4\text{S}_2$ ($\text{M}^+ + \text{Na}$): 466.1123, found: 466.1129.

(E)-6-((N-(3-(Furan-2-yl)allyl)-4-methylphenyl)sulfonamido)-3-methylhex-1-en-4-yn-3-yl Acetate (159k)

Yellow solid; m.p. 80-83 °C; ^1H NMR (CDCl_3 , 400 MHz): δ 7.74 (2H, d, $J = 8.12$ Hz), 7.27-7.33 (3H, m), 6.46 (1H, d, $J = 15.76$ Hz), 6.35-6.36 (1H, m), 6.23 (1H, d, $J = 3.04$ Hz), 6.00 (1H, dt, $J = 15.72, 6.88$ Hz), 5.74 (1H, dd, $J = 17.12, 10.4$ Hz), 5.19 (1H, d, $J = 17.12$ Hz), 5.08 (1H, d, $J = 10.36$ Hz), 4.21 (2H, s), 3.97 (2H, d, $J = 6.84$ Hz), 2.41 (3H, s), 1.97 (3H, s), 1.44 (3H, s); ^{13}C NMR (CDCl_3 , 100 MHz): δ 168.6, 152.0, 143.4, 142.3, 138.3, 136.2, 129.6, 127.7, 123.3, 121.4, 115.3, 111.3, 108.5, 84.4, 79.4, 73.8, 48.2, 36.3, 28.0, 21.7, 21.5; IR (NaCl, neat) ν : 2934, 1742, 1651, 1597, 1348, 1163, 1065 cm^{-1} ; HRMS(ESI) calcd for $\text{C}_{23}\text{H}_{25}\text{NO}_5\text{S}$ ($\text{M}^+ + \text{Na}$): 450.1351, found: 450.1317.

6-((N-(Cyclohex-2-en-1-yl)-4-methylphenyl)sulfonamido)-3-methylhex-1-en-4-yn-3-yl Acetate (159l)

Colorless oil; ^1H NMR (CDCl_3 , 400 MHz): δ 7.81 (2H, d, $J = 8.24$ Hz), 7.27 (2H, d, $J = 8.24$ Hz), 5.86-5.93 (2H, m), 5.36-5.44 (2H, m), 5.15 (1H, dt, $J = 10.52, 0.92$ Hz), 4.46 (1H, brs), 4.21 (1H, d, $J = 18.76$ Hz), 4.03 (1H, d, $J = 18.8$ Hz), 2.42 (3H, s), 2.01 (3H, s), 1.95-2.00 (2H, m), 1.74-1.77 (3H, m), 1.57-1.58 (4H, m); ^{13}C NMR (CDCl_3 , 100 MHz): δ 168.8, 143.1, 138.6, 138.3, 133.0, 129.6, 127.5, 127.4, 115.4, 83.6, 82.1, 74.2, 54.9, 33.0, 28.1, 27.9, 24.4, 21.8, 21.6, 21.5; IR (NaCl, neat) ν : 3024, 2424, 1738, 1651, 1597, 1366,

1157, 1067 cm^{-1} ; HRMS(ESI) calcd for $\text{C}_{22}\text{H}_{27}\text{NO}_4\text{S}$ ($\text{M}^+ + \text{H}$): 402.1739, found: 402.1740.

(Z)-6-((N-(Hex-2-en-1-yl)-4-methylphenyl)sulfonamido)-3-methylhex-1-en-4-yn-3-yl

Acetate (159m)

Colorless oil; ^1H NMR (CDCl_3 , 400 MHz): δ 7.72 (2H, d, $J = 8.24$ Hz), 7.28 (2H, d, $J = 8.12$ Hz), 5.74 (1H, dd, $J = 17.12, 10.4$ Hz), 5.61-5.67 (1H, m), 5.30-5.37 (1H, m), 5.20 (1H, d, $J = 17.08$ Hz), 5.06 (1H, d, $J = 10.44$ Hz), 4.17 (2H, s), 3.87 (2H, d, $J = 7.24$ Hz), 2.40 (3H, s), 2.07 (2H, q, $J = 7.4$ Hz), 1.95 (3H, s), 1.42 (3H, s), 1.32-1.39 (2H, m), 0.88 (3H, t, $J = 7.36$ Hz); ^{13}C NMR (CDCl_3 , 100 MHz): δ 168.4, 143.2, 138.3, 136.4, 136.0, 129.6, 127.6, 123.1, 115.1, 83.9, 79.7, 73.6, 42.9, 35.7, 29.0, 27.8, 22.6, 21.5, 21.4, 13.6; IR (NaCl, neat) ν : 2959, 2932, 2425, 2247, 1744, 1651, 1597, 1366, 1159, 1067 cm^{-1} ; HRMS(ESI) calcd for $\text{C}_{22}\text{H}_{29}\text{NO}_4\text{S}$ ($\text{M}^+ + \text{Na}$): 426.1715, found: 426.1721.

(Z)-6-((N-(4-(Benzyloxy)but-2-en-1-yl)-4-methylphenyl)sulfonamido)-3-methylhex-1-en-4-yn-3-yl Acetate (159n)

Colorless oil; ^1H NMR (CDCl_3 , 400 MHz): δ 7.71 (2H, d, $J = 8.24$ Hz), 7.25-7.35 (7H, m), 5.82-5.88 (1H, m), 5.72 (1H, dd, $J = 17.4, 10.52$ Hz), 5.52-5.58 (1H, m), 5.18 (1H, d, $J = 17.36$ Hz), 5.05 (1H, d, $J = 10.56$ Hz), 4.49 (2H, s), 4.18 (2H, s), 4.14 (2H, d, $J = 6.44$ Hz), 3.89 (2H, d, $J = 7.32$ Hz), 2.40 (3H, s), 1.93 (3H, s), 1.41 (3H, s); ^{13}C NMR (CDCl_3 ,

100 MHz): δ 168.4, 143.3, 138.1, 138.0, 136.0, 132.0, 129.5, 128.3, 127.6, 127.5, 126.3, 115.2, 84.0, 79.5, 73.6, 72.2, 65.4, 43.1, 36.1, 27.8, 21.5, 21.4; IR (NaCl, neat) ν : 3028, 2862, 2425, 1744, 1643, 1597, 1348, 1161, 1065 cm^{-1} ; HRMS(ESI) calcd for $\text{C}_{27}\text{H}_{31}\text{NO}_5\text{S}$ ($\text{M}^+ + \text{Na}$): 504.1821, found: 504.1829.

(E)-6-((N-(But-2-en-1-yl)-4-methylphenyl)sulfonamido)-3-ethylhex-1-en-4-yn-3-yl Acetate (159o)

Yellow oil; ^1H NMR (CDCl_3 , 400 MHz): δ 7.71 (2H, d, $J = 8.08$ Hz), 7.26 (2H, d, $J = 8.08$ Hz), 5.63-5.76 (2H, m), 5.35-5.39 (1H, m), 5.17 (1H, d, $J = 17.12$ Hz), 5.12 (1H, d, $J = 10.4$ Hz), 4.20 (2H, s), 3.77 (2H, d, $J = 6.84$ Hz), 2.40 (3H, s), 1.97 (3H, s), 1.72-1.78 (1H, m), 1.67 (3H, d, $J = 6.32$ Hz), 1.57-1.62 (1H, m), 0.78 (3H, t, $J = 7.28$ Hz); ^{13}C NMR (CDCl_3 , 100 MHz): δ 168.5, 143.2, 137.2, 131.7, 129.6, 129.6, 127.6, 124.5, 116.3, 82.8, 80.6, 77.9, 48.2, 35.8, 33.6, 21.6, 21.5, 17.7, 8.1; IR (NaCl, neat) ν : 3022, 2401, 1744, 1670, 1597, 1354, 1163, 1016 cm^{-1} ; HRMS(ESI) calcd for $\text{C}_{21}\text{H}_{27}\text{NO}_4\text{S}$ ($\text{M}^+ + \text{H}$): 390.1739, found: 390.1732.

(Z)-6-((N-(4-(Benzyloxy)but-2-en-1-yl)-4-methylphenyl)sulfonamido)-3-ethylhex-1-en-4-yn-3-yl Acetate (159p)

Colorless oil; ^1H NMR (CDCl_3 , 400 MHz): δ 7.71 (2H, d, $J = 8.24$ Hz), 7.26-7.34 (7H, m), 5.81-5.86 (1H, m), 5.62 (1H, dd, $J = 17.4, 10.52$ Hz), 5.54-5.57 (1H, m), 5.16 (1H, d, $J = 17.4$ Hz), 5.10 (1H, d, $J = 10.52$ Hz), 4.48 (2H, s), 4.21 (2H, s), 4.14 (2H, d, $J = 6.4$

Hz), 3.91 (2H, d, $J = 7.32$ Hz), 2.40 (3H, s), 1.94 (3H, s), 1.72-1.77 (1H, m), 1.57-1.63 (1H, m), 0.75-0.79 (3H, m); ^{13}C NMR (CDCl_3 , 100 MHz): δ 168.4, 143.2, 138.0, 137.0, 136.2, 132.0, 129.5, 128.3, 127.6, 127.5, 126.4, 116.2, 82.8, 80.5, 77.6, 72.2, 65.5, 43.1, 36.1, 33.5, 21.5, 21.4, 8.0; IR (NaCl, neat) ν : 3022, 2425, 1740, 1643, 1597, 1348, 1157, 1065 cm^{-1} ; HRMS(ESI) calcd for $\text{C}_{28}\text{H}_{33}\text{NO}_5\text{S}$ ($\text{M}^+ + \text{Na}$): 518.1977, found: 518.1983.

3-Methyl-6-((4-methyl-*N*-(2-methylallyl)phenyl)sulfonamido)hex-1-en-4-yn-3-yl

Acetate (159q)

White solid; m.p. 67-68 °C; ^1H NMR (CDCl_3 , 400 MHz): δ 7.72 (2H, d, $J = 8.28$ Hz), 7.28 (2H, d, $J = 8.24$ Hz), 5.71 (1H, dd, $J = 16.92, 10.08$ Hz), 5.17 (1H, d, $J = 16.92$ Hz), 5.05 (1H, dd, $J = 10.08, 2.76$ Hz), 5.01 (1H, s), 4.97 (1H, s), 4.14 (2H, s), 3.76 (2H, s), 2.40 (3H, s), 1.95 (3H, s), 1.77 (3H, s), 1.39 (3H, s); ^{13}C NMR (CDCl_3 , 100 MHz): δ 168.5, 143.3, 139.1, 138.4, 136.3, 129.6, 127.7, 115.7, 115.2, 84.4, 79.3, 73.7, 52.3, 35.8, 28.0, 21.7, 21.5, 19.7; IR (NaCl, neat) ν : 2980, 2307, 1739, 1644, 1596, 1348, 1153, 1066 cm^{-1} ; HRMS(ESI) calcd for $\text{C}_{20}\text{H}_{25}\text{NO}_4\text{S}$ ($\text{M}^+ + \text{Na}$): 398.1402, found: 398.1390.

2-((*N*-Allyl-4-methylphenyl)sulfonamido)methyl)-5-methylcyclopenta-1,4-dien-1-yl

Acetate (160a)

Yellow oil; ^1H NMR (CDCl_3 , 400 MHz): δ 7.69 (2H, d, $J = 8$ Hz), 7.28 (2H, d, $J = 7.88$ Hz), 6.01 (1H, s), 5.50-5.57 (1H, m), 5.07-5.11 (2H, m), 3.98 (2H, s), 3.72 (2H, d, $J = 6.12$ Hz), 2.80 (2H, s), 2.43 (3H, s), 2.21 (3H, s), 1.79 (3H, s); ^{13}C NMR (CDCl_3 , 100

MHz): δ 168.9, 150.8, 143.2, 137.6, 132.6, 129.6, 127.4, 127.2, 124.4, 118.6, 49.4, 42.1, 37.9, 21.5, 20.4, 12.3; IR (NaCl, neat) ν : 3022, 2872, 1749, 1655, 1495, 1370, 1342, 1211, 1159, 1092, 1015 cm^{-1} ; HRMS(ESI) calcd for $\text{C}_{19}\text{H}_{23}\text{NO}_4\text{S}$ ($\text{M}^+ + \text{H}$): 362.1426, found: 362.1419.

***rac*-(3a*R*,6*R*,7a*R*)-5-Methyl-2-tosyl-1,2,3,6,7,7a-hexahydro-3a,6-methanoisoindol-4-yl Acetate (161a)**

White solid; m.p. 132-135 °C; ^1H NMR (CDCl_3 , 400 MHz): δ 7.69 (2H, d, $J = 8.2$ Hz), 7.30 (2H, d, $J = 8.04$ Hz), 3.80 (1H, t, $J = 9.12$ Hz), 3.36 (1H, d, $J = 10.92$ Hz), 3.27 (1H, d, $J = 10.92$ Hz), 2.75 (1H, t, $J = 10.04$ Hz), 2.67 (1H, brs), 2.43 (3H, s), 2.15 (4H, s), 1.53 (3H, s), 1.47-1.51 (1H, m), 1.33-1.40 (2H, m), 0.84 (1H, d, $J = 8$ Hz); ^{13}C NMR (CDCl_3 , 100 MHz): δ 169.1, 147.3, 143.3, 134.2, 129.6, 127.8, 127.3, 61.4, 53.3, 47.8, 47.2, 46.8, 45.0, 31.3, 21.5, 20.2, 10.8; IR (NaCl, neat) ν : 3026, 1751, 1643, 1597, 1340, 1161, 1032 cm^{-1} ; HRMS(ESI) calcd for $\text{C}_{19}\text{H}_{23}\text{NO}_4\text{S}$ ($\text{M}^+ + \text{H}$): 362.1426, found: 362.1425.

***rac*-(3a*R*,6*R*,7a*R*)-5-Methyl-2-tosyl-1,2,3,6,7,7a-hexahydro-3a,6-methanoisoindol-4-yl Benzoate (161b)**

White solid; m.p. 71-73 °C; ^1H NMR (CDCl_3 , 400 MHz): δ 8.04 (2H, d, $J = 7.68$ Hz), 7.62-7.67 (3H, m), 7.49 (2H, t, $J = 7.52$ Hz), 7.21 (2H, d, $J = 7.76$ Hz), 3.83 (1H, t, $J = 9$

Hz), 3.45 (1H, d, $J = 11.08$ Hz), 3.33 (1H, d, $J = 11.08$ Hz), 2.81 (1H, t, $J = 10.16$ Hz), 2.73 (1H, brs), 2.39 (3H, s), 2.21-2.23 (1H, m), 1.59 (3H, s), 1.53-1.56 (1H, m), 1.42-1.47 (2H, m), 0.94 (1H, d, $J = 8.16$ Hz); ^{13}C NMR (CDCl_3 , 100 MHz): δ 164.8, 147.4, 143.2, 134.2, 133.8, 130.1, 129.6, 128.7, 128.6, 128.2, 127.3, 61.7, 53.4, 48.0, 47.3, 47.0, 45.2, 31.4, 21.5, 11.0; IR (NaCl, neat) ν : 2965, 1734, 1643, 1599, 1342, 1161, 1065 cm^{-1} ; HRMS(ESI) calcd for $\text{C}_{24}\text{H}_{25}\text{NO}_4\text{S}$ ($\text{M}^+ + \text{H}$): 424.1583, found: 424.1584.

***rac*-(3a*R*,6*R*,7a*R*)-5-Cyclopentyl-2-tosyl-1,2,3,6,7,7a-hexahydro-3a,6-methanoisoindol-4-yl Acetate (161c)**

White solid; m.p. 100-103 $^{\circ}\text{C}$; ^1H NMR (CDCl_3 , 400 MHz): δ 7.69 (2H, d, $J = 8.16$ Hz), 7.29 (2H, d, $J = 8.08$ Hz), 3.80 (1H, t, $J = 9$ Hz), 3.35 (1H, d, $J = 10.96$ Hz), 3.26 (1H, d, $J = 10.92$ Hz), 2.80 (1H, brs), 2.75 (1H, t, $J = 10.04$ Hz), 2.44-2.49 (1H, m), 2.42 (3H, s), 2.21-2.23 (1H, m), 2.14 (3H, s), 1.57-1.70 (4H, m), 1.48-1.55 (3H, m), 1.24-1.43 (4H, m), 0.84 (1H, d, $J = 7.28$ Hz); ^{13}C NMR (CDCl_3 , 100 MHz): δ 169.2, 146.5, 143.3, 134.9, 134.2, 129.6, 127.3, 61.4, 53.6, 47.7, 47.3, 44.7, 44.4, 37.2, 32.7, 31.4, 30.6, 25.1, 25.0, 21.5, 20.3; IR (NaCl, neat) ν : 2957, 1753, 1651, 1597, 1344, 1163, 1092 cm^{-1} ; HRMS(ESI) calcd for $\text{C}_{23}\text{H}_{29}\text{NO}_4\text{S}$ ($\text{M}^+ + \text{Na}$): 438.1715, found: 438.1721.

***rac*-(3*aR*,6*R*,7*aR*)-5-Cyclohexyl-2-tosyl-1,2,3,6,7,7*a*-hexahydro-3*a*,6-methanoisindol-4-yl Acetate (161d)**

White solid; m.p. 127-130 °C; ^1H NMR (CDCl_3 , 400 MHz): δ 7.61 (2H, d, $J = 8.12$ Hz), 7.22 (2H, d, $J = 8.16$ Hz), 3.73 (1H, t, $J = 8.92$ Hz), 3.27 (1H, d, $J = 10.92$ Hz), 3.17 (1H, d, $J = 10.92$ Hz), 2.77 (1H, brs), 2.66 (1H, t, $J = 10.04$ Hz), 2.35 (3H, s), 2.12-2.14 (1H, m), 2.07 (3H, s), 2.01-2.03 (1H, m), 1.54-1.61 (3H, m), 1.40-1.47 (3H, m), 1.01-1.34 (7H, m), 0.75 (1H, d, $J = 8.16$ Hz); ^{13}C NMR (CDCl_3 , 100 MHz): δ 169.3, 146.0, 143.3, 136.3, 134.2, 129.6, 127.3, 61.3, 53.6, 47.9, 47.3, 44.5, 44.2, 36.2, 32.7, 31.4, 30.6, 26.2, 26.1, 26.0, 21.5, 20.3; IR (NaCl, neat) ν : 2926, 1755, 1651, 1597, 1344, 1163, 1092 cm^{-1} ; HRMS(ESI) calcd for $\text{C}_{24}\text{H}_{31}\text{NO}_4\text{S}$ ($\text{M}^+ + \text{Na}$): 452.1872, found: 452.1872.

***rac*-(3*aR*,6*R*,7*aR*)-5-Benzyl-2-tosyl-1,2,3,6,7,7*a*-hexahydro-3*a*,6-methanoisindol-4-yl Acetate (161e)**

White solid; m.p. 115-117 °C; ^1H NMR (CDCl_3 , 400 MHz): δ 7.68 (2H, d, $J = 8.2$ Hz), 7.22-7.30 (4H, m), 7.15-7.18 (1H, m), 7.09 (2H, d, $J = 7.04$ Hz), 3.79 (1H, t, $J = 8.76$ Hz), 3.30-3.41 (3H, m), 3.16 (1H, d, $J = 15.36$ Hz), 2.72 (1H, t, $J = 10.04$ Hz), 2.64 (1H, brs), 2.41 (3H, s), 2.19-2.22 (1H, m), 2.10 (3H, s), 1.38-1.43 (2H, m), 1.18-1.23 (1H, m), 0.80 (1H, dd, $J = 8.36, 1.12$ Hz); ^{13}C NMR (CDCl_3 , 100 MHz): δ 169.2, 148.2, 143.4, 138.4, 134.2, 130.4, 129.6, 128.7, 128.4, 127.3, 126.2, 61.5, 53.4, 47.5, 47.3, 46.1, 45.1, 32.1,

31.9, 21.5, 20.2; IR (NaCl, neat) ν : 3026, 2962, 1753, 1664, 1599, 1342, 1163, 1049 cm^{-1} ;
 HRMS(ESI) calcd for $\text{C}_{25}\text{H}_{27}\text{NO}_4\text{S}$ ($\text{M}^+ + \text{H}$): 438.1739, found: 438.1743.

***rac*-(3a*S*,6*R*,7a*R*)-2-Tosyl-1,2,3,6,7,7a-hexahydro-3a,6-methanoisoindol-4-yl Acetate (161f)**

Colorless oil; ^1H NMR (CDCl_3 , 400 MHz): δ 7.71 (2H, d, $J = 8.08$ Hz), 7.31 (2H, d, $J = 8$ Hz), 5.60 (1H, d, $J = 3.16$ Hz), 3.83 (1H, t, $J = 8.84$ Hz), 3.48 (1H, d, $J = 10.84$ Hz), 3.36 (1H, d, $J = 10.88$ Hz), 2.90 (1H, brs), 2.78 (1H, t, $J = 10.08$ Hz), 2.43 (3H, s), 2.14 (3H, s), 1.51-1.56 (1H, m), 1.33-1.44 (3H, m), 0.89 (1H, d, $J = 7.96$ Hz); ^{13}C NMR (CDCl_3 , 100 MHz): δ 168.4, 154.3, 143.4, 129.6, 127.6, 127.3, 116.7, 60.8, 53.4, 48.2, 46.7, 44.1, 43.0, 32.4, 21.5, 20.8; IR (NaCl, neat) ν : 2964, 2872, 1765, 1626, 1597, 1344, 1163, 1092 cm^{-1} ; HRMS(ESI) calcd for $\text{C}_{18}\text{H}_{21}\text{NO}_4\text{S}$ ($\text{M}^+ + \text{Na}$): 370.1089, found: 370.1096.

***rac*-(3a*S*,6*R*,7a*R*)-6-Methyl-2-tosyl-1,2,3,6,7,7a-hexahydro-3a,6-methanoisoindol-4-yl Acetate (161g)**

Colorless oil; ^1H NMR (CDCl_3 , 400 MHz): δ 7.70 (2H, d, $J = 8.2$ Hz), 7.31 (2H, d, $J = 8.08$ Hz), 5.44 (1H, s), 3.82 (1H, t, $J = 8.56$ Hz), 3.44 (1H, d, $J = 10.8$ Hz), 3.31 (1H, d, $J = 10.84$ Hz), 2.81 (1H, t, $J = 10.08$ Hz), 2.43 (3H, s), 2.16-2.19 (1H, m), 2.13 (3H, s), 1.40-1.43 (1H, m), 1.29-1.33 (1H, m), 1.24 (3H, s), 1.21 (1H, d, $J = 7.2$ Hz), 0.90 (1H, d, $J = 8.32$ Hz); ^{13}C NMR (CDCl_3 , 100 MHz): δ 168.2, 153.7, 143.3, 134.2, 129.5, 127.2, 120.6, 61.1, 53.5, 53.4, 51.3, 46.8, 46.7, 39.3, 21.4, 20.7, 19.3; IR (NaCl, neat) ν : 3024,

2954, 1765, 1626, 1597, 1343, 1163, 1047 cm^{-1} ; HRMS(ESI) calcd for $\text{C}_{19}\text{H}_{23}\text{NO}_4\text{S}$ ($\text{M}^+ + \text{H}$): 362.1426, found: 362.1425.

***rac*-(3a*R*,6*S*,7*S*,7a*R*)-5-Methyl-7-phenyl-2-tosyl-1,2,3,6,7,7a-hexahydro-3a,6-methanoisoindol-4-yl Acetate (161h)**

White solid; m.p. 150-153 $^{\circ}\text{C}$; ^1H NMR (CDCl_3 , 400 MHz): δ 7.71 (2H, d, $J = 8.24$ Hz), 7.31 (2H, d, $J = 8$ Hz), 7.11-7.27 (6H, m), 3.87 (1H, t, $J = 9.4$ Hz), 3.41 (1H, d, $J = 10.96$ Hz), 3.34 (1H, d, $J = 10.96$ Hz), 3.22-3.24 (1H, m), 2.95 (1H, t, $J = 9.84$ Hz), 2.82 (1H, brs), 2.68-2.69 (1H, m), 2.43 (3H, s), 2.19 (3H, s), 1.54 (1H, d, $J = 8.4$ Hz), 1.21-1.25 (1H, m), 1.33 (3H, s); ^{13}C NMR (CDCl_3 , 100 MHz): δ 169.2, 148.3, 143.5, 141.4, 134.1, 129.7, 128.2, 127.7, 127.4, 126.4, 126.3, 61.9, 55.9, 53.4, 51.8, 50.1, 49.9, 47.6, 21.6, 20.3, 12.7; IR (NaCl, neat) ν : 3024, 1751, 1674, 1597, 1341, 1161 1055 cm^{-1} ; HRMS(ESI) calcd for $\text{C}_{25}\text{H}_{27}\text{NO}_4\text{S}$ ($\text{M}^+ + \text{H}$): 438.1739, found: 438.1741.

***rac*-(3a*R*,6*S*,7*S*,7a*R*)-5,7-Dimethyl-2-tosyl-1,2,3,6,7,7a-hexahydro-3a,6-methanoisoindol-4-yl Acetate (161i)**

White solid; m.p. 105-107 $^{\circ}\text{C}$; ^1H NMR (CDCl_3 , 400 MHz): δ 7.68 (2H, d, $J = 8.16$ Hz), 7.29 (2H, d, $J = 8.04$ Hz), 3.83 (1H, t, $J = 8.72$ Hz), 3.28 (1H, d, $J = 10.88$ Hz), 3.24 (1H, d, $J = 10.88$ Hz), 2.79 (1H, t, $J = 9.88$ Hz), 2.52 (1H, brs), 2.43 (3H, s), 2.16 (3H, s), 2.02-2.05 (1H, m), 1.73-1.77 (1H, m), 1.61 (3H, s), 1.41 (1H, d, $J = 8.24$ Hz), 1.00 (1H, d, $J = 8.24$ Hz), 0.89 (3H, d, $J = 7$ Hz); ^{13}C NMR (CDCl_3 , 100 MHz): δ 168.8, 147.6, 143.3,

134.2, 129.6, 127.3, 126.2, 61.5, 53.2, 53.0, 51.9, 49.2, 47.5, 41.0, 21.5, 20.2, 18.3, 13.2;
 IR (NaCl, neat) ν : 3024, 1755, 1672, 1597, 1342, 1161, 1043 cm^{-1} ; HRMS(ESI) calcd for $\text{C}_{20}\text{H}_{25}\text{NO}_4\text{S}$ ($\text{M}^+ + \text{H}$): 376.1583, found: 376.1586.

***rac*-(3a*R*,6*S*,7*S*,7a*R*)-5-Methyl-7-(thiophen-2-yl)-2-tosyl-1,2,3,6,7,7a-hexahydro-3a,6-methanoisoindol-4-yl Acetate (161j)**

Yellow solid; m.p. 177-180 °C; ^1H NMR (CDCl_3 , 400 MHz): δ 7.70 (2H, d, $J = 8.24$ Hz), 7.32 (2H, d, $J = 8.24$ Hz), 7.07 (1H, dd, $J = 5.04, 0.92$ Hz), 6.86-6.88 (1H, m), 6.74 (1H, d, $J = 3.68$ Hz), 3.92 (1H, t, $J = 9.6$ Hz), 3.47 (1H, t, $J = 3.68$ Hz), 3.38 (1H, d, $J = 11.44$ Hz), 3.32 (1H, d, $J = 11.48$ Hz), 2.93 (1H, t, $J = 9.6$ Hz), 2.85-2.86 (1H, m), 2.60-2.61 (1H, m), 2.44 (3H, s), 2.19 (3H, s), 1.56 (1H, d, $J = 8.68$ Hz), 1.19-1.21 (4H, m); ^{13}C NMR (CDCl_3 , 100 MHz): δ 169.2, 148.6, 145.8, 143.6, 134.2, 129.8, 127.4, 126.9, 126.6, 123.7, 123.2, 61.7, 56.3, 53.0, 52.7, 49.3, 47.5, 46.9, 21.6, 20.4, 12.6; IR (NaCl, neat) ν : 3024, 1749, 1651, 1344, 1163, 1092 cm^{-1} ; HRMS(ESI) calcd for $\text{C}_{23}\text{H}_{25}\text{NO}_4\text{S}_2$ ($\text{M}^+ + \text{H}$): 444.1303, found: 444.1271.

***rac*-(3a*R*,6*S*,7*S*,7a*R*)-7-(Furan-2-yl)-5-methyl-2-tosyl-1,2,3,6,7,7a-hexahydro-3a,6-methanoisoindol-4-yl Acetate (161k)**

Yellow solid; m.p. 166-168 °C; ^1H NMR (CDCl_3 , 400 MHz): δ 7.70 (2H, d, $J = 8.16$ Hz), 7.31 (2H, d, $J = 8.12$ Hz), 7.25 (1H, d, $J = 1.24$ Hz), 6.21-6.22 (1H, m), 5.92 (1H, d, $J = 3.16$ Hz), 3.91 (1H, t, $J = 8.88$ Hz), 3.38 (1H, d, $J = 10.96$ Hz), 3.30 (1H, d, $J = 11$ Hz),

3.21 (1H, t, $J = 3.72$ Hz), 2.96-2.97 (1H, m), 2.91 (1H, t, $J = 9.92$ Hz), 2.47-2.53 (1H, m), 2.44 (3H, s), 2.17 (3H, s), 1.52-1.54 (1H, m), 1.13-1.15 (4H, m); ^{13}C NMR (CDCl_3 , 100 MHz): δ 169.1, 156.0, 148.0, 143.5, 141.0, 134.1, 129.7, 127.4, 126.5, 110.2, 105.3, 61.5, 53.5, 52.6, 49.8, 48.4, 47.3, 44.6, 21.5, 20.3, 11.5; IR (NaCl, neat) ν : 3125, 2965, 1751, 1670, 1597, 1342, 1161, 1026 cm^{-1} ; HRMS(ESI) calcd for $\text{C}_{23}\text{H}_{25}\text{NO}_5\text{S}$ ($\text{M}^+ + \text{Na}$): 450.1351, found: 450.1321.

***rac*-(2a*S*,2a¹*R*,5*S*,8a*S*)-4-Methyl-1-tosyl-1,2,2a¹,5a,6,7,8,8a-octahydro-5*H*-2a,5-methanobenzo[*cd*]indol-3-yl Acetate (161l)**

White solid; m.p. 118-120 °C; ^1H NMR (CDCl_3 , 400 MHz): δ 7.63 (2H, d, $J = 7.84$ Hz), 7.22 (2H, d, $J = 7.96$ Hz), 3.57-3.64 (1H, m), 3.40 (1H, d, $J = 10.08$ Hz), 2.84 (1H, d, $J = 10.04$ Hz), 2.43 (3H, s), 2.40 (2H, brs), 2.07 (4H, s), 1.91-1.96 (1H, m), 1.79-1.89 (1H, m), 1.60-1.69 (2H, m), 1.56 (1H, brs), 1.53 (3H, s), 1.01-1.27 (2H, m), 0.77-0.88 (1H, m); ^{13}C NMR (CDCl_3 , 100 MHz): δ 168.9, 148.4, 143.2, 134.7, 129.5, 127.7, 127.6, 60.8, 58.0, 53.7, 47.6, 46.2, 46.0, 38.2, 32.1, 29.8, 22.1, 21.5, 20.1, 10.9; IR (NaCl, neat) ν : 2938, 1751, 1651, 1344, 1163, 1092 cm^{-1} HRMS(ESI) calcd for $\text{C}_{22}\text{H}_{27}\text{NO}_4\text{S}$ ($\text{M}^+ + \text{H}$): 402.1739, found: 402.1751.

***rac*-(3a*S*,6*S*,7*R*,7a*R*)-5-Methyl-7-propyl-2-tosyl-1,2,3,6,7,7a-hexahydro-3a,6-methanoisindol-4-yl Acetate (161m)**

Colorless oil; ^1H NMR (CDCl_3 , 400 MHz): δ 7.70 (2H, d, $J = 8.2$ Hz), 7.31 (2H, d, $J = 8.04$ Hz), 3.58 (1H, t, $J = 9.04$ Hz), 3.32 (1H, d, $J = 10.88$ Hz), 3.23 (1H, d, $J = 10.88$ Hz), 2.88 (1H, t, $J = 10.32$ Hz), 2.44 (3H, s), 2.31 (1H, brs), 2.21 (1H, q, $J = 8.96$ Hz), 2.14 (3H, s), 1.58-1.63 (1H, m), 1.54 (3H, s), 1.17-1.38 (5H, m), 1.01 (1H, dd, $J = 8.64$, 1.2 Hz), 0.91 (3H, t, $J = 6.6$ Hz); ^{13}C NMR (CDCl_3 , 100 MHz): δ 169.0, 147.5, 143.3, 134.2, 129.6, 129.2, 127.3, 61.2, 51.6, 48.8, 47.4, 47.2, 44.2, 41.8, 34.1, 22.5, 21.5, 20.2, 14.2, 10.7; IR (NaCl, neat) ν : 3024, 2959, 1755, 1670, 1597, 1165, 1092 cm^{-1} ; HRMS(ESI) calcd for $\text{C}_{22}\text{H}_{29}\text{NO}_4\text{S}$ ($\text{M}^+ + \text{H}$): 404.1896, found: 404.1870.

***rac*-(3a*R*,6*S*,7*R*,7a*R*)-7-((Benzyloxy)methyl)-5-methyl-2-tosyl-1,2,3,6,7,7a-hexahydro-3a,6-methanoisindol-4-yl Acetate (161n)**

Colorless oil; ^1H NMR (CDCl_3 , 400 MHz): δ 7.61 (2H, d, $J = 7.8$ Hz), 7.23-7.41 (7H, m), 4.50 (1H, d, $J = 11.92$ Hz), 4.42 (1H, d, $J = 11.88$ Hz), 3.65 (1H, t, $J = 9.6$ Hz), 3.41 (1H, t, $J = 9.46$ Hz), 3.21-3.32 (3H, m), 2.79 (1H, t, $J = 10.56$ Hz), 2.40 (4H, s), 2.26 (1H, q, $J = 9.16$ Hz), 2.13 (3H, s), 1.96 (1H, q, $J = 8.24$ Hz), 1.54 (3H, s), 1.27 (1H, d, $J = 9.16$ Hz), 0.91 (1H, d, $J = 8.68$ Hz); ^{13}C NMR (CDCl_3 , 100 MHz): δ 168.8, 147.8, 143.2, 137.8, 133.8, 129.4, 128.6, 128.3, 127.8, 127.7, 127.1, 73.2, 71.2, 61.0, 49.3, 48.6, 46.8, 46.6, 44.4, 41.7, 21.4, 20.1, 10.6; IR (NaCl, neat) ν : 3026, 2964, 1759, 1676, 1597, 1344,

1163, 1089 cm^{-1} ; HRMS(ESI) calcd for $\text{C}_{27}\text{H}_{31}\text{NO}_5\text{S}$ ($\text{M}^+ + \text{H}$): 482.2001, found: 482.2013.

***rac*-(3a*R*,6*S*,7*S*,7a*R*)-5-Ethyl-7-methyl-2-tosyl-1,2,3,6,7,7a-hexahydro-3a,6-methanoisindol-4-yl Acetate (161o)**

Colorless oil; ^1H NMR (CDCl_3 , 400 MHz): δ 7.68 (2H, d, $J = 8.16$ Hz), 7.29 (2H, d, $J = 8$ Hz), 3.83 (1H, t, $J = 8.84$ Hz), 3.28 (1H, d, $J = 10.88$ Hz), 3.22 (1H, d, $J = 10.88$ Hz), 2.79 (1H, t, $J = 9.92$ Hz), 2.62 (1H, brs), 2.42 (3H, s), 2.12-2.18 (4H, m), 2.01-2.04 (1H, m), 1.75-1.78 (1H, m), 1.39 (1H, d, $J = 8.2$ Hz), 0.93-1.02 (5H, m), 0.87 (3H, d, $J = 7\text{Hz}$); ^{13}C NMR (CDCl_3 , 100 MHz): δ 169.0, 147.0, 143.4, 134.2, 132.1, 129.7, 127.4, 61.6, 53.2, 51.9, 50.8, 49.7, 47.6, 41.2, 21.6, 20.9, 20.3, 18.6, 12.3; IR (NaCl, neat) ν : 3026, 1759, 1667, 1597, 1344, 1163, 1094 cm^{-1} ; HRMS(ESI) calcd for $\text{C}_{21}\text{H}_{27}\text{NO}_4\text{S}$ ($\text{M}^+ + \text{H}$): 390.1739, found: 390.1737.

***rac*-(3a*R*,6*S*,7*R*,7a*R*)-7-((Benzyloxy)methyl)-5-ethyl-2-tosyl-1,2,3,6,7,7a-hexahydro-3a,6-methanoisindol-4-yl Acetate (161p)**

Colorless oil; ^1H NMR (CDCl_3 , 400 MHz): δ 7.61 (2H, d, $J = 8.24$ Hz), 7.27-7.41 (7H, m), 4.50 (1H, d, $J = 12.36$ Hz), 4.42 (1H, d, $J = 12.36$ Hz), 3.63 (1H, dd, $J = 10.52$, 8.68 Hz), 3.40 (1H, dd, $J = 9.16$, 6.88 Hz), 3.21-3.32 (3H, m), 2.79 (1H, t, $J = 10.56$ Hz), 2.51 (1H, brs), 2.40 (3H, s), 2.29-2.31 (1H, m), 2.12 (3H, s), 1.89-2.05 (3H, m), 1.25 (1H, dd, $J = 8.68$, 1.36 Hz), 0.91-0.96 (4H, m); ^{13}C NMR (CDCl_3 , 100 MHz): δ 169.0, 147.1, 143.2,

137.8, 134.1, 133.9, 129.4, 128.4, 127.8, 127.7, 127.1, 73.2, 71.3, 61.1, 48.7, 47.2, 46.9, 46.2, 45.0, 42.2, 21.4, 20.1, 18.8, 11.9; IR (NaCl, neat) ν : 3026, 2965, 1755, 1670, 1454, 1344, 1161, 1089 cm^{-1} ; HRMS(ESI) calcd for $\text{C}_{28}\text{H}_{33}\text{NO}_5\text{S}$ ($\text{M}^+ + \text{H}$): 496.2158, found: 496.2161.

***rac*-(3a*R*,6*R*,7a*R*)-5,7a-Dimethyl-2-tosyl-1,2,3,6,7,7a-hexahydro-3a,6-methanoisoindol-4-yl Acetate (161q)**

White solid; m.p. 114-116 °C; ^1H NMR (CDCl_3 , 400 MHz): δ 7.69 (2H, d, $J = 8.2$ Hz), 7.29 (2H, d, $J = 8.04$ Hz), 3.49 (1H, d, $J = 9.44$ Hz), 3.37 (1H, d, $J = 10.96$ Hz), 3.25 (1H, d, $J = 10.96$ Hz), 2.97 (1H, d, $J = 9.44$ Hz), 2.58 (1H, brs), 2.42 (3H, s), 2.16 (3H, s), 1.78 (1H, dd, $J = 12.04, 3.44$ Hz), 1.57 (3H, s), 1.41 (1H, d, $J = 8.48$ Hz), 0.93 (1H, dd, $J = 12, 2.72$ Hz), 0.88 (1H, d, $J = 8.44$ Hz), 0.81 (3H, s); ^{13}C NMR (CDCl_3 , 100 MHz): δ 169.4, 147.0, 143.3, 134.2, 129.6, 127.5, 127.2, 126.6, 64.3, 59.7, 50.4, 48.9, 46.7, 46.4, 38.4, 23.7, 21.5, 20.4, 10.5; IR (NaCl, neat) ν : 2965, 1753, 1651, 1597, 1344, 1163, 1092 cm^{-1} ; HRMS(ESI) calcd for $\text{C}_{20}\text{H}_{25}\text{NO}_4\text{S}$ ($\text{M}^+ + \text{Na}$): 398.1402, found: 398.1386.

References

1. (a) Baumann, M.; Baxendale, I. R.; Ley, S. V.; Nikbin, N. *Beilstein J. Org. Chem.* **2011**, 7, 442. (b) Jin, Z. *Nat. Prod. Rep.* **2009**, 26, 363. (c) Michael, J. P. *Nat. Prod. Rep.* **2008**, 25, 166. (d) Fattorusso, E.; Taglialatela-Scafati, O., *Modern alkaloids*. Wiley-VCH: Weinheim, 2008; p 615. (e) Baker, D. D.; Chu, M.; Oza, U.; Rajgarhia, V. *Nat. Prod. Rep.* **2007**, 24, 1225. (f) Aniszewski, T., *Alkaloids-Secrets of Life: Alkaloid Chemistry, Biological Significance, Applications and Ecological Role*. 1st ed.; Elsevier: Boston, 2007; p 316. (g) Banerjee, S.; Hemraj-Benny, T.; Wong, S. S. *Adv. Mater.* **2005**, 17, 17. (h) Balaban, A. T.; Oniciu, D. C.; Katritzky, A. R. *Chem. Rev.* **2004**, 104, 2777. (i) Cordell, G. A.; Quinn-Beattie, M. L.; Farnsworth, N. R. *Phytother. Res.* **2001**, 15, 183.
2. (a) Müller, T. E.; Hultsch, K. C.; Yus, M.; Foubelo, F.; Tada, M. *Chem. Rev.* **2008**, 108, 3795. (b) Nakamura, I.; Yamamoto, Y. *Chem. Rev.* **2004**, 104, 2127. (c) Stanovnik, B.; Svete, J. *Chem. Rev.* **2004**, 104, 2433. (d) Trost, B. M. *Acc. Chem. Res.* **2002**, 35, 695. (e) Schmid, A.; Dordick, J. S.; Hauer, B.; Kiener, A.; Wubbolts, M.; Witholt, B. *Nature* **2001**, 409, 258.
3. (a) Bariwal, J.; Van der Eycken, E. *Chem. Soc. Rev.* **2013**, 42, 9283. (b) Candeias, N. R.; Branco, L. C.; Gois, P. M. P.; Afonso, C. A. M.; Trindade, A. F. *Chem. Rev.* **2009**, 109, 2703. (c) Huisgen, R. *Chem. Pharm. Bull.* **2000**, 48, 757. (d) Mitchinson, A.; Nadin, A. J. *Chem. Soc., Perkin Trans. I*, **1999**, 2553. (e) Nadin, A. J. *Chem. Soc., Perkin Trans. I*, **1998**, 3493. (f) Johannsen, M.; Jørgensen, K. A. *Chem. Rev.* **1998**, 98, 1689.
4. Pictet, A.; Spengler, T. *Ber. Dtsch. Chem. Ges.* **1911**, 44, 2030.
5. (a) Bandini, M.; Cera, G.; Chiarucci, M. *Synthesis* **2012**, 504. (b) Cera, G.; Chiarucci, M.; Bandini, M. *Pure Appl. Chem.* **2012**, 84, 1673. (c) Bauer, E. *Synthesis* **2012**, 1131. (d) Bandini, M. *Angew. Chem. Int. Ed.* **2011**, 50, 994. (e)

- Biannic, B.; Aponick, A. *Eur. J. Org. Chem.* **2011**, 6605. (f) Emer, E.; Sinisi, R.; Capdevila, M. G.; Petruzzello, D.; De Vincentiis, F.; Cozzi, P. G. *Eur. J. Org. Chem.* **2011**, 647. (g) Bandini, M.; Tragni, M. *Org. Biomol. Chem.* **2009**, 7, 1501. (h) Ljungdahl, N.; Kann, N. *Angew. Chem. Int. Ed.* **2009**, 48, 642. (i) Muzart, J. *Tetrahedron* **2008**, 64, 5815. (j) Muzart, J. *Eur. J. Org. Chem.* **2007**, 3077. (k) Muzart, J. *Tetrahedron* **2005**, 61, 4179. (l) Tamaru, Y. *Eur. J. Org. Chem.* **2005**, 2647.
6. (a) Shiroodi, R. K.; Gevorgyan, V. *Chem. Soc. Rev.* **2013**, 42, 4991. (b) Wang, S.; Zhang, G. Zhang, L. *Synlett* **2010**, 692. (c) Marion, N.; Nolan, S. P. *Angew. Chem. Int. Ed.* **2007**, 46, 2750. (d) Marco-Contelles, J.; Soriano, E. *Chem. Eur. J.* **2007**, 13, 1350.
7. (a) Rudolph, M.; Hashmi, A. S. K. *Chem. Soc. Rev.* **2012**, 41, 2448. (b) Pina, C. D.; Falletta, E.; Rossi, M. *Chem. Soc. Rev.* **2012**, 41, 350. (c) Xiao, J.; Li, X. *Angew. Chem. Int. Ed.* **2011**, 50, 7226. (d) Rudolph, M.; Hashmi, A. S. K. *Chem. Commun.* **2011**, 47, 6536. (e) Krause, N.; Winter, C. *Chem. Rev.* **2011**, 111, 1994. (f) Corma, A.; Leyva-Perez, A.; Sabater, M. J. *Chem. Rev.* **2011**, 111, 1657. (g) Bandini, M. *Chem. Soc. Rev.* **2011**, 40, 1358. (h) Shapiro, N. D.; Toste, F. D. *Synlett* **2010**, 675. (i) Hashmi, A. S. K.; Hubbert, C. *Angew. Chem. Int. Ed.* **2010**, 49, 1010. (j) Hashmi, A. S. K. *Angew. Chem. Int. Ed.* **2010**, 49, 5232. (k) Skouta, R.; Li, C.-J. *Tetrahedron* **2008**, 64, 4917. (l) Shen, H. C. *Tetrahedron* **2008**, 64, 3885. (m) Patil, N. T.; Yamamoto, Y. *Chem. Rev.* **2008**, 108, 3395. (n) Lipshutz, B. H.; Yamamoto, Y. *Chem. Rev.* **2008**, 108, 2793. (o) Li, Z.; Brouwer, C.; He, C. *Chem. Rev.* **2008**, 108, 3239. (p) Hashmi, A. S. K.; Rudolph, M. *Chem. Soc. Rev.* **2008**, 37, 1766. (q) Gorin, D. J.; Sherry, B. D.; Toste, F. D. *Chem. Rev.* **2008**, 108, 3351. (r) Jiménez-Núñez, E.; Echavarren, A. M. *Chem. Commun.* **2007**, 333. (s) Hashmi, A. S. K. *Chem. Rev.* **2007**, 107, 3180. (t) Gorin, D. J.; Toste, F. D. *Nature*

- 2007**, 446, 395. (u) Fürstner, A.; Davies, P. W. *Angew. Chem. Int. Ed.* **2007**, 46, 3410. (v) Widenhoefer, R. A.; Han, X. *Eur. J. Org. Chem.* **2006**, 4555. (w) Hashmi, A. S. K.; Hutchings, G. J. *Angew. Chem. Int. Ed.* **2006**, 45, 7896. (x) Hashmi, A. S. K. *Angew. Chem. Int. Ed.* **2005**, 44, 6990.
8. (a) Pyykkö, P. *Angew. Chem. Int. Ed.* **2004**, 43, 4412. (b) Barysz, M.; Pyykkö, P. *Chem. Phys. Lett.* **1998**, 285, 398. (c) Heinemann, C.; Hertwig, R. H.; Wesendrup, R.; Koch, W.; Schwarz, H. *J. Am. Chem. Soc.* **1995**, 117, 495. (d) Irikura, K. K.; Goddard III, W. A. *J. Am. Chem. Soc.* **1994**, 116, 8733.
9. (a) Garayalde, D.; Nevado, C. *ACS Catal.* **2012**, 2, 1462. (b) Soriano, E.; Marco-Contelles, J. *Acc. Chem. Res.* **2009**, 42, 1026. (c) Lee, S. I.; Chatani, N. *Chem. Commun.* **2009**, 371. (d) Fürstner, A. *Chem. Soc. Rev.* **2009**, 38, 3208. (e) Michelet, V.; Toullec, P. Y.; Genet, J. P. *Angew. Chem. Int. Ed.* **2008**, 47, 4268. (f) Jiménez-Núñez, E.; Echavarren, A. M. *Chem. Rev.* **2008**, 108, 3326. (g) Hashmi, A. S. K. *Angew. Chem. Int. Ed.* **2008**, 47, 6754. (h) Zhang, L.; Sun, J.; Kozmin, S. A. *Adv. Synth. Catal.* **2006**, 348, 2271. (i) Nieto-Oberhuber, C.; López, S.; Jiménez-Núñez, E.; Echavarren, A. M. *Chem. Eur. J.* **2006**, 12, 5916. (j) Ma, S.; Yu, S.; Gu, Z. *Angew. Chem. Int. Ed.* **2006**, 45, 200. (k) Echavarren, A. M.; Nevado, C. *Chem. Soc. Rev.* **2004**, 33, 431. (l) Lloyd-Jones, G. C. *Org. Biomol. Chem.* **2003**, 1, 215. (m) Aubert, C.; Buisine, O.; Malacria, M. *Chem. Rev.* **2002**, 102, 813.
10. Benitez, D.; Shapiro, N. D.; Tkatchouk, E.; Wang, Y.; Goddard III, W. A.; Toste, F. D. *Nat. Chem.* **2009**, 1, 482.
11. (a) Fukuda, Y.; Utimoto, K. *Synthesis* **1991**, 975. (b) Fukuda, Y.; Utimoto, K.; Nozaki, H. *Heterocycles* **1987**, 25, 297.
12. (a) Lockwood, R. F.; Nicholas, K. M. *Tetrahedron Lett.* **1977**, 18, 4164. (b) Nicholas, K. M.; Pettit, R. *J. Organomet. Chem.* **1972**, 44, C21.

13. Georgy, M.; Boucard, V.; Campagne, J. M. *J. Am. Chem. Soc.* **2005**, *127*, 14180.
14. Couty, S.; Meyer, C.; Cossy, J. *Angew. Chem. Int. Ed.* **2006**, *45*, 6726.
15. Dai, L. -Z.; Shi, M. *Chem. Eur. J.* **2008**, *14*, 7011.
16. Shu, X.-Z.; Liu, X.-Y.; Xiao, H.-Q.; Ji, K.-G.; Guo, L.-N.; Liang, Y.-M. *Adv. Synth. Catal.* **2008**, *350*, 243.
17. Aponick, A.; Li, C. Y.; Malinge, J.; Marques, E. F. *Org. Lett.* **2009**, *11*, 4624.
18. Egi, M.; Azechi, K.; Akai, S. *Org. Lett.* **2009**, *11*, 5002.
19. Teo, W. T.; Rao, W.; Koh, M. J.; Chan, P. W. H. *J. Org. Chem.* **2013**, *78*, 7508.
20. Debleds, O.; Zotto, C. D.; Vrancken, E.; Campagne, J.-M.; Retailleau, P. *Adv. Synth. Catal.* **2009**, *351*, 1991.
21. Yeom, H. -S.; Lee, Y.; Jeong, J.; So, E.; Hwang, S.; Lee, J. -E.; Lee, S. S.; Shin, S. *Angew. Chem. Int. Ed.* **2010**, *49*, 1611.
22. Kothandaraman, P.; Rao, W.; Foo, S. J.; Chan, P. W. H. *Angew. Chem. Int. Ed.* **2010**, *49*, 4619.
23. Liu, Y.; Xu, W.; Wang, X. *Org. Lett.* **2010**, *12*, 1448.
24. Cera, G.; Crispino, P.; Monari, M.; Bandini, M. *Chem. Commun.* **2011**, *47*, 7803.
25. Cera, G.; Chiarucci, M.; Mazzanti, A.; Mancinelli, M.; Bandini, M. *Org. Lett.* **2012**, *14*, 1350.
26. Li, G.; Liu, Y. *J. Org. Chem.* **2010**, *75*, 3526.
27. Cera, G.; Piscitelli, S.; Chiarucci, M.; Fabrizi, G.; Goggiamani, A.; Ramón, R. S.; Nolan, S. P.; Bandini, M. *Angew. Chem. Int. Ed.* **2012**, *51*, 9891.
28. Chiarucci, M.; Matteucci, E.; Cera, G.; Fabrizi, G.; Bandini, M. *Chem. Asian. J.* **2013**, *8*, 1776.
29. Saucy, G.; Marbet, R.; Lindlar, H.; Isler, O. *Helv. Chim. Acta* **1959**, *42*, 1945.
30. Strickler, H.; Davis, J. B.; Ohloff, G. *Helv. Chim. Acta* **1976**, *59*, 1328.
31. Rautenstrauch, V. *J. Org. Chem* **1984**, *49*, 950.

32. Miki, K.; Ohe, K.; Uemura, S. *J. Org. Chem.* **2003**, *68*, 8505.
33. (a) Zhang, D.-H.; Zhang, Z.; Shi, M. *Chem. Commun.* **2012**, *48*, 10271. (b) Shu, X. -Z.; Shu, D.; Schienebeck, C. M.; Tang, W. *Chem. Soc. Rev.* **2012**, *41*, 7698. (c) Bruneau, C. *Angew. Chem. Int. Ed.* **2005**, *44*, 2328.
34. Garayalde, D.; Gómez-Bengoa, E.; Huang, X.; Goeke, A.; Nevado, C. *J. Am. Chem. Soc.* **2010**, *132*, 4720.
35. Moreau, X.; Goddard, J.-P.; Bernard, M.; Lemièrre, G.; López-Romero, J. M.; Mainetti, E.; Marion, N.; Mouriès, V.; Thorimbert, S.; Fensterbank, L.; Malacria, M. *Adv. Synth. Catal.* **2008**, *350*, 43.
36. Cho, E. J. *Chem. Eur. J.* **2012**, *18*, 4495.
37. Correa, A.; Marion, N.; Fensterbank, L.; Malacria, M.; Nolan, S. P.; Cavallo, L. *Angew. Chem. Int. Ed.* **2008**, *47*, 718.
38. Mauleón, P.; Krinsky, J. L.; Toste, F. D. *J. Am. Chem. Soc.* **2009**, *131*, 4513.
39. Witham, C. A.; Mauleón, P.; Shapiro, N. D.; Sherry, B. D.; Toste, F. D. *J. Am. Chem. Soc.* **2007**, *129*, 5838.
40. Marion, N.; Lemièrre, G.; Correa, A.; Costabile, C.; Ramón, R. S.; Moreau, X.; de Frémont, P.; Dahmane, R.; Hours, A.; Lesage, D.; Tabet, J.-C.; Goddard, J.-P.; Gandon, V.; Cavallo, L.; Fensterbank, L.; Malacria, M.; Nolan, S. P. *Chem. Eur. J.* **2009**, *15*, 3243.
41. Mamane, V.; Gress, T.; Krause, H.; Fürstner, A. *J. Am. Chem. Soc.* **2004**, *126*, 8654.
42. Shi, X.; Gorin, D. J.; Toste, F. D. *J. Am. Chem. Soc.* **2005**, *127*, 5802.
43. Shapiro, N. D.; Toste, F. D. *J. Am. Chem. Soc.* **2008**, *130*, 9244.
44. Liu, H.; Li, X.; Chen, Z.; Hu, W. X. *J. Org. Chem.* **2012**, *77*, 5184.
45. Shapiro, N. D.; Shi, Y.; Toste, F. D. *J. Am. Chem. Soc.* **2009**, *131*, 11654.
46. Pagar, V. V.; Jadhav, A. M.; Liu, R.-S. *J. Am. Chem. Soc.* **2011**, *133*, 20728.

47. Zhang, L. *J. Am. Chem. Soc.* **2005**, *127*, 16804.
48. Huang, J.; Huang, X.; Liu, B. *Org. Biomol. Chem.* **2010**, *8*, 2697.
49. Zheng, H.; Huo, X.; Zhao, C.; Jing, P.; Yang, J.; Fang, B.; She, X. *Org. Lett.* **2011**, *13*, 6448.
50. Rao, W.; Sally; Koh, M. J.; Chan, P. W. H. *J. Org. Chem.* **2013**, *78*, 3183.
51. Wang, W.; Hammond, G. B.; Xu, B. *J. Am. Chem. Soc.* **2012**, *134*, 5697.
52. Rao, W.; Koh, M. J.; Kothandaraman, P.; Chan, P. W. H. *J. Am. Chem. Soc.* **2012**, *134*, 10811.
53. Zhang, D.-H.; Yao, L.-F.; Wei, Y.; Shi, M. *Angew. Chem. Int. Ed.* **2011**, *50*, 2583.
54. Zhao, J.; Hughes, C. O.; Toste, F. D. *J. Am. Chem. Soc.* **2006**, *128*, 7436.
55. Yang, W.; Yu, Y.; Zhang, T.; Hansmann, M. M.; Pflästerer, D.; Hashmi, A. S. K. *Adv. Synth. Catal.* **2013**, *355*, 2037.
56. Hashmi, A. S. K.; Yang, W.; Yu, Y.; Hansmann, M. M.; Rudolph, M.; Rominger, F. *Angew. Chem. Int. Ed.* **2013**, *52*, 1329.
57. Zhu, S.; Wu, L.; Huang, X. *J. Org. Chem.* **2013**, *78*, 9120.
58. (a) Teng, T.-M.; Liu, R.-S. *J. Am. Chem. Soc.* **2010**, *132*, 9298. (b) Luo, T.; Schreiber, S. L. *J. Am. Chem. Soc.* **2009**, *131*, 5667. (c) Luo, T.; Schreiber, S. L. *Angew. Chem., Int. Ed.* **2007**, *46*, 8250. (d) Buzas, A.; Gagosz, F. *J. Am. Chem. Soc.* **2006**, *128*, 12614. (e) Marion, N.; Díez-González, S.; de Frémont, P.; Noble, A. R.; Nolan, S. P. *Angew. Chem., Int. Ed.* **2006**, *45*, 3647.
59. Please see refs 54, 58b and 58c, for the only examples of nucleophilic addition of an allene to an alkyne in gold catalysis.
60. (a) Garayalde, D.; Krüger, K.; Nevado, C. *Angew. Chem., Int. Ed.* **2011**, *50*, 911. (b) Uemura, M.; Watson, I. D. G.; Katsukawa, M.; Toste, F. D. *J. Am. Chem. Soc.* **2009**, *131*, 3464. (c) Watson, I. D. G.; Ritter, S.; Toste, F. D. *J. Am. Chem. Soc.*

- 2009**, *131*, 2056. (d) Gorin, D. J.; Dubé, P.; Toste, F. D. *J. Am. Chem. Soc.* **2006**, *128*, 14480.
61. Hashmi, A. S. K.; Molinari, L.; Rominger, F.; Oeser, T. *Eur. J. Org. Chem.* **2011**, 2256.
62. (a) Sze, E. M. L.; Rao, W.; Koh, M. J.; Chan, P. W. H. *Chem. Eur. J.* **2011**, *17*, 1437. (b) Kothandaraman, P.; Foo, S. J.; Chan, P. W. H. *J. Org. Chem.* **2009**, *74*, 5947. (c) Rao, W.; Chan, P. W. H. *Chem. Eur. J.* **2008**, *14*, 10486.
63. (a) Kashiwada, Y.; Yamazaki, K.; Ikeshiro, Y.; Yamagishi, T.; Fujioka, T.; Mihashi, K.; Mizuki, K.; Cosentino, L. M.; Fowke, K.; Morris-Natschke, S. L.; Lee, K.-H. *Tetrahedron* **2001**, *57*, 1559. (b) Kurata, K.; Taniguchi, K.; Agatsuma, Y.; Suzuki, M. *Phytochemistry* **1998**, *47*, 363. (c) Crimmins, M. T.; Huang, S.; Guise-Zawacki, L. E. *Tetrahedron Lett.* **1996**, *37*, 6519. (d) Piers, E.; Lu, Y.-F. *J. Org. Chem.* **1989**, *54*, 2267.
64. (a) Rao, W.; Kothandaraman, P.; Koh, C. B.; Chan, P. W. H. *Adv. Synth. Catal.* **2010**, *352*, 2521. (b) Unthank, M.G.; Tavassoli, B.; Aggarwal, V. K. *Org. Lett.* **2008**, *10*, 1501. (c) Hill, R. R.; Moore, S. A.; Roberts, D. R. *Photochem. Photobiol.* **2005**, *81*, 1439. (d) Davis, F. A.; Ramachandar, T.; Liu, H. *Org. Lett.* **2004**, *6*, 3393.
65. CCDC 826216 (**166h**) and CCDC 826220 (**167f**) contain the supplementary crystallographic data for this paper. These data can be obtained free of charge from The Cambridge Crystallographic Data Centre via www.ccdc.cam.ac.uk/data_request/cif.
66. (a) López-Carrillo, V.; Echavarren, A. M. *J. Am. Chem. Soc.* **2010**, *132*, 9292. (b) Amijs, C. H. M.; López-Carrillo, V.; Raducan, M.; Pérez-Galán, P.; Ferrer, C.; Echavarren, A. M. *J. Org. Chem.* **2008**, *73*, 7721.

67. CCDC 826221 (**Au₅**) contains the supplementary crystallographic data for this paper. These data can be obtained free of charge from The Cambridge Crystallographic Data Centre via www.ccdc.cam.ac.uk/data_request/cif.
68. CCDC 826214 (**169a**) and 826215 (**158a**) contain the supplementary crystallographic data for this paper. These data can be obtained free of charge from The Cambridge Crystallographic Data Centre via www.ccdc.cam.ac.uk/data_request/cif.
69. Wang, D.; Gautam, L. N. S.; Bollinger, C.; Harris, A.; Li, M.; Shi, X. *Org. Lett.* **2011**, *13*, 2618. (b) Nun, P.; Gaillard, S.; Slawin A. M. Z.; Nolan S. P. *Chem. Comm.* **2010**, *46*, 9113. (c) Bolte, B.; Odabachian, Y.; Gagosz, F. *J. Am. Chem. Soc.* **2010**, *132*, 7294. (d) Lo, V. K.-Y.; Wong, M.-K.; Che, C.-M. *Org. Lett.* **2008**, *10*, 517. (e) Sherry, B. D.; Toste, D. *J. Am. Chem. Soc.* **2004**, *126*, 15978.
70. (a) González, A. Z.; Benitez, D.; Tkatchouk, E.; Goddard III, W. A.; Toste, F. D. *J. Am. Chem. Soc.* **2011**, *133*, 5500. (b) Teller, H.; Flügge, S.; Goddard, R.; Fürstner, A. *Angew. Chem. Int. Ed.* **2010**, *49*, 1949. (c) Luzung, M. R.; Mauleón, P.; Toste, F. D. *J. Am. Chem. Soc.* **2007**, *129*, 12402.
71. CCDC 826218 (**158b**), CCDC 826213 (**158i**), CCDC 826217 (**158r**), CCDC 826222 (**158x**) contain the supplementary crystallographic data for this paper. These data can be obtained free of charge from The Cambridge Crystallographic Data Centre via www.ccdc.cam.ac.uk/data_request/cif.
72. CCDC 826219 (**158m**) contains the supplementary crystallographic data for this paper. These data can be obtained free of charge from The Cambridge Crystallographic Data Centre via www.ccdc.cam.ac.uk/data_request/cif.
73. (a) Ohno, H.; Mizutani, T.; Kadoh, Y.; Aso, A.; Miyamura, K.; Fujii, N.; Tanaka, T. *J. Org. Chem.* **2007**, *72*, 4378. (b) Ohno, H.; Mizutani, T.; Kadoh, Y.; Aso, A.; Miyamura, K.; Fujii, N.; Tanaka, T. *Angew. Chem., Int. Ed.* **2005**, *44*, 5113.

74. (a) Xiao, Y.-P.; Liu, X.-Y.; Che, C.-M.; *Angew. Chem., Int. Ed.* **2011**, *50*, 4937.
(b) LaLonde, R. L.; Brenzovich, Jr. W. E.; Benitez, D.; Tkatchouk, E.; Kelley, K.; Goddard III, W. A.; Toste, F. D. *Chem. Sci.* **2010**, *1*, 226 and references therein.
75. The involvement of an *in situ* formed organogold species containing a Au–C(sp³) bond that participates in a nucleophilic addition reaction has also been recently proposed in Au(I)-catalyzed dimerization of propiolic acid, see: Luo, T.; Dai, M.; Zheng, S.-L.; Schreiber, S. L. *Org. Lett.* **2011**, *13*, 2834.
76. (a) Yeom, H.-S.; So, E.; Shin, S. *Chem. Eur. J.* **2011**, *17*, 1764. (b) Nakamura, I.; Yamagishi, U.; Song, D.; Konta, S.; Yamamoto, Y. *Chem. Asian. J.* **2008**, *3*, 285.
(c) Nakamura, I.; Yamagishi, U.; Song, D.; Konta, S.; Yamamoto, Y. *Angew. Chem. Int. Ed.* **2007**, *46*, 2284.
77. For recent selected reviews, see: (a) Sharma, V.; Kumar, P.; Pathak, D. *J. Heterocycl. Chem.* **2010**, *47*, 491. (b) Kochnowska-Karamyan, A. J.; Hamann, M. T. *Chem. Rev.*, **2010**, *110*, 4489. (c) Barluenga, J.; Rodríguez, F.; Fañanás, F. J. *Chem. Asian J.* **2009**, *4*, 1036. (d) Krüger, K.; Tillack, A.; Beller, M. *Adv. Synth. Catal.* **2008**, *350*, 2153. (e) Humphrey, G. R.; Kuethe, J. T. *Chem. Rev.* **2006**, *106*, 2875. (f) Zeni, G.; Larock, R. C. *Chem. Rev.* **2006**, *106*, 4644. (g) Cacchi, S.; Fabrizi, G. *Chem. Rev.* **2005**, *105*, 2873. (h) Somei, M.; Yamada, F. *Nat. Prod. Rep.* **2005**, *22*, 73. (i) Somei, M.; Yamada, F. *Nat. Prod. Rep.* **2004**, *21*, 278.
78. For selected recent examples, see: (a) Mothe, S. R.; Kothandaraman, P.; Lauw, S. J. L.; Chin, S. M. W.; Chan, P. W. H. *Chem. Eur. J.* **2012**, *18*, 6133. (b) Kothandaraman, P.; Mothe, S. R.; Toh, S. S. M.; Chan, P. W. H. *J. Org. Chem.* **2011**, *76*, 7633. (c) Wetzels, A.; Gagosz, F. *Angew. Chem. Int. Ed.* **2011**, *50*, 7354. (d) Oh, C. H.; Karmakar, S.; Park, H.; Ahn, Y.; Kim, J. W. *J. Am. Chem. Soc.* **2010**, *132*, 1792. (e) Hong, D.; Chen, Z.; Lin, X.; Wang, Y. *Org. Lett.* **2010**, *12*, 4608. (f) Yamane, Y.; Liu, X.; Hamasaki, A.; Ishida, T.; Haruta, M.; Yokoyama,

- T.; Tokunaga, M. *Org. Lett.* **2009**, *11*, 5162. (g) Gabriele, B.; Mancuso, R.; Salerno, G.; Lupinacci, E.; Ruffolo, G.; Costa, M. *J. Org. Chem.* **2008**, *73*, 4971.
- (h) Cariou, K.; Ronan, B.; Mignani, S.; Fensterbank, L.; Malacria, M. *Angew. Chem. Int. Ed.* **2007**, *46*, 1881. (i) Zhang, Y.; Donahue, J. P.; Li, C.-J. *Org. Lett.* **2007**, *9*, 627. (j) Hessian, K. O.; Flynn, B. L. *Org. Lett.* **2006**, *8*, 243. (k) Fayol, A.; Fang, Y.-Q.; Lautens, M. *Org. Lett.* **2006**, *8*, 4203. (l) Alfonsi, M.; Arcadi, A.; Aschi, M.; Bianchi, G.; Marinelli, F. *J. Org. Chem.* **2005**, *70*, 2265. (m) Yue, D.; Larock, R. C. *Org. Lett.* **2004**, *6*, 1037.
79. (a) Chowdhury, C.; Das, B.; Mukherjee, S.; Achari, B. *J. Org. Chem.* **2012**, *77*, 5108. (b) Liu, Y.; McWhorter, W. W., Jr. *J. Org. Chem.* **2003**, *68*, 2618. (c) Rodrigues, I.; Bonnet-Delpon, D.; Bégué, J.-P. *J. Org. Chem.* **2001**, *66*, 2098. (d) Seiler, M.; Schumacher, A.; Lindemann, U.; Barbosa, F.; Giese, B. *Synlett* **1999**, 1588. (e) Zhang, X.; Foote, C. S. *J. Am. Chem. Soc.* **1993**, *115*, 8867. (f) Zhang, X.; Foote, C. S. *J. Org. Chem.* **1993**, *58*, 5524.
80. (a) Wang, F.; Fang, Y.; Zhu, T.; Zhang, M.; Lin, A.; Gu, Q.; Zhu, W. *Tetrahedron* **2008**, *64*, 7986. (b) Segraves, N. L.; Robinson, S. J.; Garcia, D.; Said, S. A.; Fu, X.; Schmitz, F. J.; Pietraszkiewicz, H.; Valeriote, F. A.; Crews, P. *J. Nat. Prod.* **2004**, *67*, 783. (c) Pettit, G. R.; Tan, R.; Herald, D. L.; Cerny, R. L.; Williams, M. D. *J. Org. Chem.* **1994**, *59*, 1593. (d) Wong, S. M.; Musza, L. L.; Kydd, G. C.; Kullnig, R.; Gillum, A. M.; Copper, R. *J. Antibiot.* **1993**, *46*, 545. (e) Matsunaga, K.; Shizuri, Y.; Yammura, S.; Kawai, K.; Furukawa, H. *Tetrahedron Lett.* **1991**, *32*, 6883. (f) Houk, D. R.; Ondeyka, J.; Zink, D. L.; Inamine, E.; Goetz, M. A.; Henses, O. D. *J. Antibiot.* **1988**, *41*, 882. (g) Chang, R. S. L.; Lotti, V. J.; Monaghan, R. L.; Birnbaum, J.; Stapley, E. O.; Goetz, M. A.; Albers-Schonberg, G.; Patchett, A. A.; Liesch, J. M.; Henses, O. D.; Springer, J. P. *Science* **1985**, *230*, 177.

81. For selected recent examples by us, refer to refs 22, 62b, 62c, 64a, 78a, 78b and:
 - (a) Kothandaraman, P.; Huang, C.; Susanti, D.; Rao, W.; Chan, P. W. H. *Chem. Eur. J.* **2011**, *17*, 10081. (b) Zhang, X.; Teo, W. T.; Chan, P. W. H. *J. Organomet. Chem.* **2011**, *696*, 331. (c) Rao, W.; Zhang, X.; Sze, E. M. L.; Chan, P. W. H. *J. Org. Chem.* **2009**, *74*, 1740. (d) Rao, W.; Chan, P. W. H. *Chem. Eur. J.* **2008**, *14*, 10486.

82. For selected examples, refer to refs 16-18, 78h, 78k, and:
 - (a) Ali, S.; Zhu, H.-T.; Xia, X.-F.; Ji, K.-G.; Yang, Y.-F.; Song, X.-R.; Liang, Y.-M. *Org. Lett.* **2011**, *13*, 2598. (b) Yang, F.; Jin, T.; Bao, M.; Yamamoto, Y. *Tetrahedron* **2011**, *67*, 10147. (c) Sharland, C. M.; Singkhonrat, J.; NajeebUllah, M.; Hayes, S. J.; Knight, D. W.; Dunford, D. G. *Tetrahedron Lett.* **2011**, *52*, 2320. (d) Guérinot, A.; Serra-Muns, A.; Gnamm, C.; Bensoussan, C.; Reymond, S.; Cossy, J. *Org. Lett.* **2010**, *12*, 1808. (e) Lu, Y.; Fu, X.; Chen, H.; Du, X.; Jia, X.; Liu, Y. *Adv. Synth. Catal.* **2009**, *351*, 129. (f) Gabriele, B.; Mancuso, R.; Salerno, G.; Ruffolo, G.; Plastina, P. *J. Org. Chem.* **2007**, *72*, 6873.

83. For recent general reviews on silver catalysis see ref 7m and
 - (a) Harmata, M. *Silver in Organic Chemistry*; Wender, P. A., Ed.; Wiley: Hoboken, New Jersey, 2011. (b) Belmont, P.; Parker, E. *Eur. J. Org. Chem.* **2009**, 6075. (c) Yamamoto, Y. *Chem Rev.* **2008**, *108*, 3199. (d) Álvarez-Corral, M.; Muñoz-Dorado, M.; Rodríguez-García, I. *Chem Rev.* **2008**, *108*, 3174. (e) Weibel, J.-M.; Blanc, A.; Pale, P. *Chem Rev.* **2008**, *108*, 3149. (f) Naodovic, M.; Yamamoto, H. *Chem Rev.* **2008**, *108*, 3132.

84. For selected review on hydroamination see refs 2a, 7v and
 - (a) Patil, N. T.; Singh, V. *J. Organomet. Chem.* **2011**, *696*, 419. (b) Taylor, J. G.; Adrio, L. A.; Hii, K. K. *Dalton Trans.* **2010**, *39*, 1171. (c) Hartwig, J. F. *Nature* **2008**, *455*, 314. (d) Chemler, S. R.; Fuller, P. H. *Chem. Soc. Rev.* **2007**, *36*, 1153. (e) Doye, S.;

- Severin, R. *Chem. Soc. Rev.* **2007**, 36, 1407. (f) Hultsch, K. C. *Org. Biomol. Chem.* **2005**, 3, 1819. (g) Odom, A. L. *Dalton Trans.* **2005**, 39, 225. (h) Alonso, F.; Beletskaya, I. P.; Yus, M. *Chem. Rev.* **2004**, 104, 3079. (i) Hartwig, J. F. *Pure. Appl. Chem.* **2004**, 76, 507. (j) Marks, T. J.; Hong, S. *Acc. Chem. Res.* **2004**, 37, 673. (k) Pohlki, F.; Doye, S. *Chem. Soc. Rev.* **2003**, 32, 104. (l) Müller, T. E.; Beller, M. *Chem. Rev.* **1998**, 98, 675.
85. For the evidence of the presence of vinyl silver species by trapping with electrophiles, see: (a) Sai, M.; Matsubara, S. *Org. Lett.* **2011**, 13, 4676. (b) Xu, T.; Mu, X.; Peng, H.; Liu, G. *Angew. Chem. Int. Ed.* **2011**, 50, 8176.
86. For selected recent examples on 1,3-AAI, see: (a) McCubin, J. A.; Voth, S.; Krokhin, O. V. *J. Org. Chem.* **2011**, 76, 8537. (b) Uyanik, M.; Fukatsu, R.; Ishihara, K. *Org. Lett.* **2009**, 11, 3470. (c) Akai, S.; Tanimoto, K.; Kanao, Y.; Egi, M.; Yamamoto, T.; Kita, Y. *Angew. Chem. Int. Ed.* **2006**, 45, 2592. (d) Morrill, C.; Grubbs, H. *J. Am. Chem. Soc.* **2005**, 127, 2842 and the references therein. (e) Narasaka, K.; Kusuma, H.; Hayashi, Y. *Tetrahedron* **1992**, 48, 2059.
87. For NIS mediated 2-oxindole formation, see ref 95i. For selected reviews on the synthesis of oxindoles, see: (a) Singh, G. S.; Desta, Z. Y. *Chem. Rev.* **2012**, 112, 6104. (b) Shen, K.; Liu, X.; Lin, L.; Feng, X. *Chem. Sci.* **2012**, 3, 327. (c) Klein, J. E. M. N.; Taylor, R. J. K. *Eur. J. Org. Chem.* **2011**, 6821. (d) Zhou, F.; Liu, Y.-L.; Zhou, J. *Adv. Synth. Catal.* **2010**, 352, 1381. (e) Trost, B. M.; Brennan, M. K. *Synthesis* **2009**, 3003. (f) Galliford, C. V.; Scheidt, K. A. *Angew. Chem. Int. Ed.* **2007**, 46, 8748. (g) Marti, C.; Carreira, E. M. *Eur. J. Org. Chem.* **2003**, 2209.
88. CCDC 883977 (**181p**) contains the supplementary crystallographic data for this paper. These data can be obtained free of charge from the Cambridge Crystallographic Data Centre via www.ccdc.cam.ac.uk/data_request/cif.

89. CCDC 884750 (**182p**) contains the supplementary crystallographic data for this paper. These data can be obtained free of charge from the Cambridge Crystallographic Data Centre via www.ccdc.cam.ac.uk/data_request/cif.
90. (a) Rimola, A.; Costa, D.; Sodupe, M.; Lambert, J.-F.; Ugliengo, P. *Chem. Rev.* **2013**, *113*, 4216. b) Minakata, S. ; Komatsu, M.; *Chem. Rev.* **2009**, *109*, 711. c) Cariati, E. ; Roberto, D.; Ugo, R. *Chem. Rev.* **2003**, *103*, 3707. d) Clark, J. H. *Acc. Chem. Res.* **2002**, *35*, 791.
91. Armarego, W. L. F.; Chai C. L. L. in *Purification of Laboratory Chemicals*, Butterworth-Heinemann, Massachusetts, 2009.
92. For selected examples, see ref 82c and a) Cui, X.; Shi, F.; Deng, Y. *Chem. Commun.* **2012**, *48*, 7586. b) Liu, P. N.; Xia, F.; Wang, Q. W.; Ren, Y. J.; Chen, J. Q. *Green Chem.* **2010**, *12*, 1049.
93. (a) Shimada, T.; Aoki, K.; Shinoda, Y.; Nakamura, T.; Tokunaga, N.; Inagaki, S.; Hayashi, T. *J. Am. Chem. Soc.* **2003**, *125*, 4688 and references therein. (b) Liu, G.; Cogan, D. A.; Owens, T. D.; Tang, T. P.; Ellman, J. A. *J. Org. Chem.* **1999**, *64*, 1278. (c) Alajarin, M.; Molina, P.; Vidal, A. *Tetrahedron Lett.* **1996**, *37*, 8945. (d) Katritzky, A. R.; Rachwal, S.; Offerman, R. J.; Najzarek, Z.; Yagoub, A. K.; Zhang, Y. *Chem. Ber.* **1990**, *123*, 1545. (e) Pannell, K. H.; Rozell, J. M.; Lii, J.; Tien-Mayr, S.-Y. *Organometallics* **1988**, *7*, 2524. (f) Aoyagi, Y.; Katano, K.; Suguna, H.; Primeau, J.; Chang, L. H.; Hecht, S. M. *J. Am. Chem. Soc.* **1982**, *104*, 5537.
94. For selected examples of silica-gel-mediated reactions, see ref 78h and (a) Liu, L. L.; Chiu, P.; *Chem. Commun.* **2011**, *47*, 3416. (b) Molander, G. A.; Cavalcanti, L. N.; Canturk, B. Pan, P.-S.; Kennedy, L. E. *J. Org. Chem.* **2009**, *74*, 7364. (c) Minakata, S.; Kano, D.; Oderaotoshi, Y.; Komatsu, M. *Angew. Chem. Int. Ed.* **2004**, *43*, 79. (d) Wipf, P.; Aoyama, Y.; Benedum, T. E. *Org. Lett.* **2004**, *6*, 3593.

- (e) Kropp, P. J.; Breton, G. W.; Fields, J. D.; Tung, J. C.; Loomis, B. R. *J. Am. Chem. Soc.* **2000**, *122*, 4280.
95. For recent examples on 3,3-disubstituted 2-oxindole synthesis, see: (a) Guo, J.; Dong, S.; Zhang, Y.; Kuang, Y.; Liu, X.; Lin, L.; Feng, X. *Angew. Chem. Int. Ed.* **2013**, *52*, 10245. (b) Wang, Z.; Zhang, Z.; Yao, Q.; Liu, X.; Cai, Y.; Lin, L.; Feng, X. *Chem. Eur. J.* **2013**, *19*, 8591. (c) Katayev, D.; Jia, Y.-X.; Sharma, A. K.; Banerjee, D.; Besnard, C.; Sunoj, R. B.; Kündig, E. P. *Chem. Eur. J.* **2013**, *19*, 11916. (d) Wei, X.-H.; Li, Y.-M.; Zhou, A.-X.; Yang, T.-T.; Yang, S.-D. *Org. Lett.* **2013**, *15*, 4158. (e) Zhou, M.-B.; Song, R.-J.; Ouyang, X.-H.; Wei, W.-T.; Deng, G.-B.; Li, J.-H. *Chem. Sci.* **2013**, *4*, 2690. (f) Beyer, A.; Buendia, J.; Bolm, C. *Org. Lett.* **2012**, *14*, 3948. (g) Tolstoy, P.; Lee, S. X. Y.; Sparr, C.; Ley, S. V. *Org. Lett.* **2012**, *14*, 4810. (h) Lim, Y. H.; Ong, Q.; Duong, H. A.; Nguyen, T. M.; Johannes, C. W. *Org. Lett.* **2012**, *14*, 5676. (i) Kothandaraman, P.; Koh, B. Q.; Limpanuparb, T.; Hirao, H.; Chan, P. W. H. *Chem. Eur. J.* **2012**, *19*, 1978. (j) Gorokhovik, I.; Neuville, L.; Zhu, J. *Org. Lett.* **2011**, *13*, 5536. (k) Wei, H.-L.; Piou, T.; Dufour, J.; Neuville, L.; Zhu, J. *Org. Lett.* **2011**, *13*, 2244. (l) Jia, Y.-X.; Kündig, E. P. *Angew. Chem. Int. Ed.* **2009**, *48*, 1636. (m) Pinto, A.; Jia, Y.; Neuville, L.; Zhu, J. *Chem. Eur. J.* **2007**, *13*, 961. (n) Kündig, E. P.; Seidel, T. M.; Jia, Y.-X.; Bernardinelli, G. *Angew. Chem. Int. Ed.* **2007**, *46*, 8484.
96. Tsukamoto, S.; Kato, H.; Samizo, M.; Nojiri, Y.; Onuki, H.; Hirota, H.; Ohta, T. *J. Nat. Prod.* **2008**, *71*, 2064.
97. For recent reviews on semipinacol rearrangement, see: (a) Song, Z.-L.; Fan, C.-A.; Tu, Y.-Q. *Chem. Rev.*, **2011**, *111*, 7523. (b) Wang, B.; Tu, Y. Q. *Acc. Chem. Res.*, **2011**, *44*, 1207. (c) Leemans, E.; D'hooghe, M.; Kimpe, N. D. *Chem. Rev.*, **2011**, *111*, 3268. (d) Snape, T. J. *Chem. Soc. Rev.* **2007**, *36*, 1823.

98. Susanti, D.; Koh, F.; Kusuma, J. A.; Kothandaraman, P.; Chan, P. W. H. *J. Org. Chem.* **2012**, *77*, 7166.
99. (a) Counciller, C. M.; Eichman, C. C.; Wray, B. C.; Stambuli, J. P. *Org. Lett.* **2008**, *10*, 1021. (b) Attygalle, A. B.; Ruzicka, J.; Varughese, D.; Bialecki, J. B.; Jafri, S. *J. Mass Spectrom.* **2007**, *42*, 1207. (c) Rousseau, G.; Robert, F.; Landais, Y. *Chem. Eur. J.* **2009**, *15*, 11160.
100. CCDC 951801 (**163a**) contains the supplementary crystallographic data for this paper. These data can be obtained free of charge from The Cambridge Crystallographic Data Centre via www.ccdc.cam.ac.uk/data_request/cif.
101. Refer to ref 94c and: (a) Wilson, K.; Clark, J. H. *Pure Appl. Chem.* **2000**, *72*, 1313; (b) Corma, A. *Curr. Opin. Solid State Mater. Sci.* **1997**, *2*, 63.
102. For selected reviews on clay-catalyzed reactions, see: (a) Climent, M. J.; Corma, A.; Iborra, S. *Chem. Rev.* **2011**, *111*, 1072. (b) Sartori, G.; Maggi, R. *Chem. Rev.* **2006**, *106*, 1077. (c) Thomas, J. K. *Acc. Chem. Res.* **1988**, *21*, 275.
103. For selected examples on clay-catalyzed reactions, see: (a) Motokura, K.; Matsunaga, S.; Miyaji, A.; Sakamoto, Y.; Baba, T. *Org. Lett.* **2010**, *12*, 1508. (b) Abid, M.; Spaeth, A.; Török, B. *Adv. Synth. Catal.* **2006**, *348*, 2191. (c) Abid, M.; Török, B. *Adv. Synth. Catal.* **2005**, *347*, 1797. (d) Farkas, J.; Békássy, S.; Ágai, B.; Hegedüs, M.; Figueras, F. *Synth. Commun.* **2000**, *30*, 2479. (e) Bhaskar, P. M.; Loganathan, D. *Tetrahedron Lett.* **1998**, *39*, 2215.
104. CCDC 951803 (**163g**), CCDC 951800 (**163h**), CCDC 951804 (**163j**), CCDC 951802 (**163p**) contain the supplementary crystallographic data for this paper. These data can be obtained free of charge from The Cambridge Crystallographic Data Centre via www.ccdc.cam.ac.uk/data_request/cif.

105. CCDC 965152 (**163w**) contains the supplementary crystallographic data for this paper. These data can be obtained free of charge from The Cambridge Crystallographic Data Centre via www.ccdc.cam.ac.uk/data_request/cif.
106. (a) Pellissier, H. *Chem. Rev.* **2013**, *113*, 442. (b) Volla, C. M. R.; Atodiresei, I.; Rueping, M. *Chem. Rev.* **2013**, doi: 10.1021/cr400215u. (c) Watson, I. D. G.; Toste, F. D. *Chem. Sci.* **2012**, *3*, 2899. (d) Ruiz, M.; López-Alvarado, P.; Giorgi, G.; Menéndez, J. C. *Chem. Soc. Rev.* **2011**, *40*, 3445. (e) Anderson, E. A. *Org. Biomol. Chem.* **2011**, *9*, 3997. (f) Grondal, C.; Jeanty, M.; Enders, D. *Nat. Chem.* **2010**, *2*, 167. (g) Nicolaou, K. C.; Chen, J. S. *Chem. Soc. Rev.* **2009**, *38*, 2993. (h) Ilardi, E. A.; Stivala, C. E.; Zakarian, A. *Chem. Soc. Rev.* **2009**, *38*, 3133. (i) Enders, D.; Grondal, C.; Hüttl, M. R. M. *Angew. Chem. Int. Ed.* **2007**, *46*, 1570. (j) Guo, H. C.; Ma, J. A. *Angew. Chem. Int. Ed.* **2006**, *45*, 354. (k) Nicolaou, K. C.; Edmonds, D. J.; Bulger, P. G. *Angew. Chem. Int. Ed.* **2006**, *45*, 7134. (l) Tietze, L. F.; Brasche, G.; Gericke, K. *Domino Reactions in Organic Synthesis*. Wiley-VCH, Weinheim, 2006.
107. For recent selected reviews on pericyclic reactions, see: (a) Tius, M. A. *Chem. Soc. Rev.* **2014**, doi: 10.1039/C3CS60333D. (b) Foster, R. A. A.; Willis, M. C. *Chem. Soc. Rev.* **2013**, *42*, 63. (c) Magdesieva, T. V. *Russ. Chem. Rev.* **2013**, *82*, 228. (d) Thompson, S.; Coyne, A. G.; Knipe, P. C.; Smith, M. D. *Chem. Soc. Rev.* **2011**, *40*, 4217. (e) López, F.; Mascareñas, J. L. *Beilstein J. Org. Chem.* **2011**, *7*, 1075. (f) Girling, P. R.; Kiyoi, T.; Whiting, A. *Org. Biomol. Chem.* **2011**, *9*, 3105. (g) Poulin, J.; Grisé-Bard, C. M.; Barriault, L. *Chem. Soc. Rev.* **2009**, *38*, 3092.
108. For selected recent examples on gold catalyzed Nazarov-type cyclization, see: (a) Chen, B.; Fan, W.; Chai, G.; Ma, S. *Org. Lett.* **2012**, *14*, 3616. (b) Lemièrre, G.; Gandon, V.; Cariou, K.; Hours, A.; Fukuyama, T.; Dhimane, A.-L.; Fensterbank, L.; Malacria, M. *J. Am. Chem. Soc.* **2009**, *131*, 2993. (c) Suárez-Pantiga, S.;

- Rubio, E.; Alvarez-Rúa, C.; González, J. M. *Org. Lett.* **2009**, *11*, 13. (d) Lin, G.-Y.; Li, C.-W.; Hung, S.-H.; Liu, R.-S. *Org. Lett.* **2008**, *10*, 5059. (e) Bhunia, S.; Liu, R.-S. *J. Am. Chem. Soc.* **2008**, *130*, 16488. (f) Jin, T.; Yamamoto, Y. *Org. Lett.* **2008**, *10*, 3137. (g) Lemièrre, G.; Gandon, V.; Cariou, K.; Fukuyama, T.; Dhimane, A.-L.; Fensterbank, L.; Malacria, M. *Org. Lett.* **2007**, *9*, 2207. (h) Lee, J. H.; Toste, F. D. *Angew. Chem. Int. Ed.* **2007**, *46*, 912. (i) Zhang, L.; Wang, S.; *J. Am. Chem. Soc.* **2006**, *128*, 1442.
109. For selected examples of gold catalyzed [4+2] cycloaddition examples, see: (a) Fustero, S.; Bello, P.; Miró, J.; Sánchez-Roselló, M.; Maestro, M. A.; González, J.; del Pozo, C. *Chem. Commun.* **2013**, *49*, 1336. (b) Sanjuán, A. M.; García-García, P.; Fernández-Rodríguez, M. A.; Sanz, R. *Adv. Synth. Catal.* **2013**, *355*, 1955. (c) Barluenga, J.; Calleja, J.; Mendoza, A.; Rodríguez, F.; Fañanás, F. J. *Chem. Eur. J.* **2010**, *16*, 7110. (d) Kusama, H.; Karibe, Y.; Onizawa, Y.; Iwasawa, N. *Angew. Chem. Int. Ed.* **2010**, *49*, 4269. (e) Teng, T.-M.; Liu, R.-S. *J. Am. Chem. Soc.* **2010**, *132*, 9298. (f) Alonso, I.; Trillo, B.; López, F.; Montserrat, S.; Ujague, G.; Castedo, L.; Lledós, A.; Mascareñas, J. L. *J. Am. Chem. Soc.* **2009**, *131*, 13020. (g) Li, G.; Zhang, G.; Zhang, L. *J. Am. Chem. Soc.* **2008**, *130*, 3740.
110. (a) Jeong, N.; Kim, D. H.; Choi, J. H. *Chem. Commun.* **2004**, 1134. (b) Benedetti, E.; Simonneau, A.; Hours, A.; Amouris, H.; Penoni, A.; Palmisano, G.; Malacria, M.; Goddard, J.-P.; Fensterbank, L. *Adv. Synth. Catal.* **2011**, *353*, 1908. (c) Cordonnier, M.-C.; Blanc, A.; Pale, P. *Org. Lett.* **2008**, *10*, 1569. (d) Rao, W.; Koh, M. J.; Kothandaraman, P.; Chan, P. W. H. *J. Am. Chem. Soc.* **2012**, *134*, 10811.
111. CCDC 973692 (**161a**) contains the supplementary crystallographic data for this paper. These data can be obtained free of charge from The Cambridge Crystallographic Data Centre via www.ccdc.cam.ac.uk/data_request/cif.

112. CCDC 973689 (**161h**), CCDC 973691 (**161i**), CCDC 973690 (**161q**) contain the supplementary crystallographic data for this paper. These data can be obtained free of charge from The Cambridge Crystallographic Data Centre via www.ccdc.cam.ac.uk/data_request/cif.
113. Faza, O. N. J.; López,, C. S.; Álvarez, R.; de Lera, A. R. *J. Am. Chem. Soc.* **2006**, *128*, 2434.