Lewis acid-catalyzed reactions of alcohol pro-electrophiles as novel strategies for C-C and C-N bond formation

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**NANYANG
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UNIVERSITY**

LEWIS ACID-CATALYZED REACTIONS OF ALCOHOL
PRO-ELECTROPHILES AS NOVEL STRATEGIES FOR C-C
AND C-N BOND FORMATION

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SCHOOL OF PHYSICAL AND MATHEMATICAL SCIENCES

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ABSTRACT

The work in this thesis was undertaken in Chemistry and Biological Chemistry, School of Physical and Mathematical Sciences in Nanyang Technological University from August 2006 to June 2010 under the supervision of Asst Prof Philip Wai Hong Chan.

The work of this thesis has been directed toward the establishing of new Lewis acid catalyzed reactions of alcohol pro-electrophiles as novel synthetic strategies for C–C and C–N bond formation. This thesis is divided into eight chapters:

- Chapter I give an introduction to recent Lewis acid catalyzed reactions of alcohol pro-electrophiles, including several type of alcohols, such as allylic alcohols, propargylic alcohols, benzylic alcohols and α -cyclopropyl alcohols
- Chapter II is aimed at exploring new synthetic strategies for C–C bond formation employing alcohols as pro-electrophiles. Chapter II addresses the gold-catalyzed allylic alkylation of aromatic and heteroaromatic compounds with allylic alcohols.
- Chapter III, a novel strategy to synthesize highly conjugated indenenes involving an unexpected iron(II) chloride-catalyzed dimerization of 1,1,3-trisubstituted-prop-2-yn-1-ols is described.
- Chapter IV details the gold-catalyzed tandem amination/ring expansion of cyclopropyl methanols with sulfonamides as an expedient route to pyrrolidines. The method was shown to be applicable to a broad range of cyclopropyl methanols and sulfonamide substrates.

- Chapter V, ytterbium(III) triflate-catalyzed ring opening of substituted 1-cyclopropyl-2-propyn-1-ols with sulfonamides as an efficient synthetic route to conjugated enynes is described.
- Chapter VI discloses a new efficient synthetic route to *trans*-2,5-dihydro-1*H*-pyrroles and 1,2-dihydroquinolines that relies on Cu(OTf)₂-catalyzed intramolecular hydroamination of homoallylic aminoalcohols under mild and operationally straightforward conditions.
- Chapter VII contains experimental data pertaining to this thesis.
- Chapter VIII contains references pertaining to this thesis.

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1. “Copper Catalyzed Intramolecular Hydroamination of Homoallylic Aminoalcohols as an Expedient Route to *Trans*-2,5-Dihydro-1*H*-pyrroles and 1,2-Dihydroquinolines” Rao, W.; Kothandaraman, P.; Koh, C. B.; Chan, P. W. H. *Adv. Synth. Catal.* **2010**, 352, 2521.
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ABBREVIATIONS

Å	Ångstrom unit
Ac	acetyl
Boc	<i>tert</i> -butoxycarbonyl
Bu	butyl
Bz	benzoyl
Cbz	benzyloxycarbonyl
DCC	1,3-dicyclohexylcarbodiimide
DCE	1,2-dichloroethane
dppm	diphenylphosphinomethane
DMF	dimethylformamide
DMAP	4-(dimethylamino)pyridine
ee	enantiomeric excess
h	hour
HPLC	high performance liquid chromatography
ⁱ Pr	isopropyl
LDA	lithium diisopropylamide
LG	Leaving group
MCP	Methylenecyclopropane
Me	methyl
min	minute
MS	molecular sieves
Hex	hexyl

NMR	nuclear magnetic resonance
ⁿ Pr	<i>n</i> -propyl
Py	pyridine
Nu	Nucleophile
Ph	phenyl
PG	protecting group
rt	room temperature
Tf	Trifluoromethanesulfonyl
TFA	trifluoroacetic acid
THF	tetrahydrofuran
TLC	Thin layer chromatography
TMS	trimethylsilyl
Ts	<i>p</i> -toluenesulfonyl
VCP	Vinyl cyclopropane

Chapter I. Alcohol Pro-electrophiles in Lewis Acid Catalysis

1.1 Introduction

Lewis acids constitute an important class of catalysts in organic synthesis due to their ability to mediate efficient and selective carbon-carbon and carbon-heteroatom bond formation.¹⁻⁵ Generally, this type of reaction has relied upon the interaction of the Lewis acid catalyst with the π bond of alkenes, alkynes and allenes, and π electrons of heteroatoms.² Among the myriad of works devoted to this area, one synthetic strategy has been the use of alcohol pro-electrophiles in combination with environmentally friendly and readily available Lewis acid catalysts such as Ag, Au, Cu, Fe and Yb.³ The reactions were shown to benefit from ease of preparing the alcohol starting material and thus the possibility to introduce a wide variety of substitution patterns. Added to this is the potential to form a quaternary carbon centre by utilizing tertiary alcohols and formation of H₂O as potentially the only side-product. Although still in its infancy, this Lewis acid-catalyzed approach for the construction of immensely important compounds of current biological and material interest from unsaturated alcohols has attracted an increasing amount of attention.⁴ This has been all the more so due to a recent shift in emphasis in green chemistry for more rapid and direct atom economical chemical processes that can make use of ecologically benign and readily available reagents and catalysts.⁵ The focal point of this introduction will be on recent advances made in this field of organic synthesis directed toward developing Lewis acid-catalyzed reactions of stabilized carbocations, generated from unsaturated alcohols, by a variety of carbon-, nitrogen- and oxygen-based nucleophiles as ecologically friendly and operationally straightforward synthetic methods for C–X (X = C, N, O) bond formation.

1.2 Allylic alcohols

Allylic alkylation reactions represent one of the most powerful and efficient carbon-carbon and carbon-heteroatom bond formation methods in organic synthesis for introducing a C₃ unit.⁶ The attractiveness of this reaction is further underlined by the fact that the C=C bond is also retained in the product that can act as a handle for subsequent functional group transformations. First reported in 1965, an allylic alkylation strategy that has been often relied upon is the Tsuji-Trost reaction involving the coupling of a variety of soft and hard nucleophiles with allylic compounds in the presence of a metal catalyst, typically Pd (Scheme 1.1).⁷ The identity of the allylic electrophiles in these reactions has often been compounds containing functional groups that exhibit good leaving group ability such as halides, carboxylates, carbonates, triflates, phosphates when treated with a catalyst and/or nucleophile.⁸ More recently, attention has also been drawn toward developing Tsuji-Trost type reactions that make use of readily available and inexpensive catalysts and allylic alcohol substrates that are ecologically benign and follow the principles of atom economy.⁵

Scheme 1.1 Tsuji-Trost allylic alkylations.

One of the first examples of a Tsuji-Trost reaction mimic was described by Baba and co-workers who reported allylic alkylation of 1,3-dicarbonyl compounds with allylic alcohols and InCl₃ as the catalyst (Table 1.1, entry 1).⁹ The direct substitution reaction, including one example involving cinnamyl alcohol (R¹ = H and R² = Ph in

Table 1.1), was shown to proceed well under mild conditions at 80 °C for 15 h and furnish the corresponding allylic alkylation products **3** and/or **4** in 75-95% yield.

Table 1.1 Lewis acid-catalyzed allylic alkylation of 1,3-dicarbonyl compounds **2** with allylic alcohols **1**.

Entry	Catalyst	Yield (%)	Ref
1	InCl ₃	75-95	9
2	Bi(OTf) ₃	62-73	10
3	Ln(OTf) _m	51-92	11a
4	Yb(OTf) ₃	72-93	11b
5	FeCl ₃	72-82	12
6	AuCl ₃ /AgSbF ₆	55-96	13

Following this work, Rueping and co-workers reported a Bi(OTf)₃-catalyzed version of this C-C bond formation reaction could be accomplished (Table 1.1, entry 2).¹⁰ Although slightly lower product yields were obtained and only a few examples were examined, the reaction was found to give the allylic alkylation adducts as a single regioisomer and proceed well at a lower catalyst loading of 1 mol % and required a shorter reaction time of 3 h. At about same time, other Lewis acids such as the lanthanum triflates Ln(OTf)_m (Ln = Yb, La, Hf; m = 3, 4) and FeCl₃ were also shown to be good Lewis acid catalysts for the allylic alkylation reaction (Table 1.1,

entries 3-5).^{11,12} Notable among these latter works is that by Ishii and co-workers who disclosed that in their reactions mediated by $\text{La}(\text{OTf})_3$ or $\text{Hf}(\text{OTf})_4$, an even lower catalyst loading of 0.5 mol % and, more importantly, a protocol that did not require the exclusion of air or moisture could be employed to achieve product yields of 51 to 92% (Table 1.1, entry 3).^{11a}

More recently, Chan and co-workers demonstrated the efficient allylic alkylation of 1,3-dicarbonyl compounds with a variety of primary allylic alcohols in addition to cinnamyl alcohol could be accomplished in the presence of AuCl_3 and AgOTf as a co-catalyst (Table 1.1, entry 6).¹³ The corresponding allylic alkylation products were obtained as single regioisomers in excellent yields under mild conditions at room temperature.

The efficiency of allylic alcohols as an allylic alkylation reagent was further demonstrated in Friedel-Crafts reactions by Baba and co-workers (Table 1.2, entry 1).⁹ In their seminal work, InCl_3 was shown to catalyze the allylic alkylation of indole derivatives with allylic alcohols **1** and give the corresponding C-3 allylated indole adducts **6** and/or **7** in excellent yields of 64-78%.

Subsequently, Yadav and co-workers expanded the generality of this intermolecular Friedel-Crafts alkylation reaction to other types of indole and allylic alcohol substrates utilizing InBr_3 as catalyst (Table 1.2, entry 2).¹⁴ Other Lewis acids such as FeCl_3 was also shown to be efficient catalysts for the C-C bond formation process, providing the corresponding Friedel-Crafts allylic alkylation adducts in 56 to 98% yields (Table 1.2, entry 3).¹⁵

Table 1.2 Lewis acid-catalyzed Friedel-Crafts alkylation with allylic alcohols **1**.

Entry	Catalyst	Yield (%)	Ref
1	InCl ₃	64-78	9
2	InBr ₃	85-93	14
3	FeCl ₃	56-98	15

In 2008, Nishizawa and co-workers demonstrated Hg(OTf)₂ could catalyze intramolecular Friedel-Crafts allylic alkylation of primary allylic alcohols **8** under mild conditions at 110 °C (Table 1.3, entry 1).¹⁶ This led to the corresponding tetrahydronaphthalene derivatives **9** in up to 99% yield. The reaction was reported to proceed expediently, requiring reaction times as short as 0.1 h and with a catalyst loading as low as 0.5 mol %. However, a drawback to this methodology was the toxic nature of the mercury salt even at a catalyst loading of 0.5 mol %. In this work, the mechanism was reported not to follow the expected S_N1 pathway and formation of a reactive carbocation intermediate as proposed in allylic alkylations with allylic alcohols described by Baba and others.⁹⁻¹⁵ Instead, a mechanism first involving double bond activation by Hg(OTf)₂ coordination followed by Friedel-Crafts cyclization that resulted in the generation of a organomercuric intermediate was put forward. This newly formed species then underwent a protonation-demercuration step to afford product **9**.

Table 1.3 Metal-catalyzed Friedel-Crafts cyclization of allylic alcohols **8**.

8 catalyst (0.5-10 mol%) **9**

X = CH₂, C(COOEt)₂, NHTs
R = H, alkyl, aryl, OMe, SMe

Entry	Catalyst	X	Yield (%)	Ref
1	Hg(OTf) ₂	CH ₂	30-99	16
2	AgOTf	CH ₂ , NHTs, C(COOEt) ₂	53-90	17

Subsequent studies by the group of Bandini showed that this intramolecular C–C bond forming process could be effected using the less toxic Lewis acid AgOTf under ligand free conditions albeit at a higher catalyst loading of 10 mol % (Table 1.3, entry 2).¹⁷ Under these latter conditions, the desired tetrahydronaphthalenes and tetrahydroquinolines **9** were prepared in up to 90% yield. The mechanism was summarized to proceed in a manner similar to that reported for the analogous Hg(OTf)₂-catalyzed process presented by Nishizawa and co-workers.¹⁶

An asymmetric version of this type of reaction was communicated at about the same time by the same group using a chiral gold(I) complex generated *in situ* from reaction of a chiral ligand with AuCl·Me₂S.¹⁸ In this work, (*S*)-3,5-*t*Bu₂-4-MeO-MeObiphep **12** was found to be the best ligand in terms of stereoinduction and chemical yield with the indole derivatives **11** afforded in 52-87% yield and with up to 96% ee under the conditions shown in Scheme 1.2.

Scheme 1.2 Gold-catalyzed enantioselective allylic alkylation of indoles.

In 2007, Shibasaki and co-workers further demonstrated the versatility of allylic alcohols **1** as allylic alkylation reagents in pioneering works exploring the direct allylic alkylation of sulfonamides **13**, carbamates **14**, and carboxamides **15** (Table 1.4, entry 1).¹⁹ In the presence of $\text{Bi}(\text{OTf})_3$ as catalyst and KPF_6 as a co-catalyst, the C–N bond forming process was demonstrated to proceed smoothly at room temperature, affording the allylic amides **18** and/or **19** in up to 99% yield. Control experiments showed that no product formation could be detected using KPF_6 as the sole catalyst and product yields decreased from 96 to 76% when KPF_6 was removed from the catalytic system.

At about the same time, Liu and co-workers reported that the intermolecular *N*-allylic alkylation reaction could be extended to include aniline substrates **16** by switching the catalyst to AuCl_3 (Table 1.4, entry 2).²⁰ In this work, the desired *N*-allylic sulfonamide and aniline products were obtained in moderate to excellent yields under mild conditions at room temperature.

More recently, intermolecular allylic alkylation of cyclic ureas **17** with allylic alcohols mediated by $\text{Au}[\text{P}(t\text{-Bu})_2(o\text{-biphenyl})]\text{Cl}$ **20** and AgSbF_6 as a co-catalyst was described by Widenhoefer and co-workers (Table 1.4, entry 3).²¹ The corresponding

allylic ureas were furnished in excellent yield of 85-100% and with up to 25:1 γ -regioselectivity.

Table 1.4 Metal-catalyzed allylic amination with allylic alcohols.

$ \begin{array}{c} \text{OH} \\ \\ \text{R}^1\text{---CH---CH=CH---R}^2 \end{array} + \text{NH}_2\text{R}^3 \xrightarrow[\text{solvent}]{\text{catalyst}} \begin{array}{c} \text{NHR}^3 \\ \\ \text{R}^1\text{---CH=CH---CH---R}^2 \end{array} \text{ and/or } \begin{array}{c} \text{NHR}^3 \\ \\ \text{R}^1\text{---CH---CH=CH---R}^2 \end{array} $				
1	13-17	18	19	
$\text{R}^1 = \text{alkyl, aryl}$ $\text{R}^2 = \text{H, alkyl, aryl}$				
Entry	Catalyst	NH_2R^3	Yield (%)	Ref
1	$\text{Bi}(\text{OTf})_3/\text{KPF}_6$	$ \begin{array}{c} \text{O} \\ \\ \text{R}^1\text{---S---NH}_2 \\ \\ \text{O} \end{array} $ 13	55-99	19
		$ \begin{array}{c} \text{O} \\ \\ \text{R}^1\text{O---C---NH}_2 \end{array} $ 14		
		$ \begin{array}{c} \text{O} \\ \\ \text{R}^1\text{---C---NH}_2 \end{array} $ 15		
2	AuCl_3	$ \begin{array}{c} \text{O} \\ \\ \text{R}^1\text{---S---NH}_2 \\ \\ \text{O} \end{array} $ 13	58-96	20
		ArNH_2 16		
3	$ \begin{array}{c} t\text{-Bu} \quad t\text{-Bu} \\ \quad \\ \text{P} \text{---} \text{Au---Cl} \\ \\ \text{C}_6\text{H}_4\text{---C}_6\text{H}_4 \end{array} $ 20 $/\text{AgSbF}_6$	$ \begin{array}{c} \text{O} \\ \\ \text{R}^1\text{---N---CH}_2\text{---CH}_2\text{---NH} \end{array} $ 17	85-100	21

The first example of intramolecular allylic alkylation of unsaturated amino alcohols **21** was communicated in 2008 by Nishizawa and co-workers using $\text{Hg}(\text{OTf})_2$ as catalyst (Scheme 1.3).²² A number of 5, 6 and 7-membered nitrogen-containing

heterocycles **22** were synthesized in 25-99% yield with a catalyst loading as low as 1 mol %.

Scheme 1.3 $\text{Hg}(\text{OTf})_2$ -catalyzed intramolecular amination of amino alcohols **21**.

Following this work, Chan and co-workers extended the scope of this intramolecular reaction to allylic amination of **23** with less toxic AuCl_3 as catalyst and AgSbF_6 as a co-catalyst (Scheme 1.4).²³ In the presence of this gold and silver combination, the intramolecular allylic amination process was shown to proceed smoothly, furnishing the corresponding 1,2-dihydroquinolines **24** in 40-91% yields at room temperature. The synthetic utility of this strategy was further exemplified by its application to the synthesis of the bioactive natural product ($\pm$) angustureine **25**.²⁴

Scheme 1.4 Gold(III)-catalyzed intramolecular allylic amination of **23** and synthesis of natural product ($\pm$) angustureine **25**.

Liang and co-workers demonstrated $\text{HAuCl}_4 \cdot \text{H}_2\text{O}$ -catalyzed cascade intermolecular allylic amination/intramolecular hydroamination of 1-en-4-yn-3-ols **26** with p - TsNH_2 **13a** (Scheme 1.5).²⁵ The reaction was shown to lead to fused

carbocyclic pyrroles **28** via hydroamination of intermediate **27**. However, to achieve high conversions, a high catalyst loading of 20 mol % and an excess amount of *p*-TsNH₂ (15 equiv) was required. Furthermore, the reaction was shown to only proceed well for cyclohexanol substrates although the reason for this unique reactivity was not disclosed.

Scheme 1.5 Gold(III)-catalyzed amination/intramolecular hydroamination of **26**.

A similar approach to tetra-substituted pyrroles **31** based on gold-catalyzed tandem amination/intramolecular hydroamination of (*Z*)-2-en-4-yn-1-ols **29** with *p*-TsNH₂ **13a** or 4-nitroaniline **16a** was described by Liu and co-worker (Scheme 1.6).²⁶ In this work, the *N*-substituted pyrroles **31** were obtained in yields of 40-84% and shown to proceed via the amino-substituted conjugated enyne **30**. The synthetic method was found to require 2 equiv of the nitrogen nucleophile and to be applicable to a wide range of enyne alcohols **29**.

Scheme 1.6 Gold(III)-catalyzed amination/intramolecular hydroamination of **29**.

In 2008, Aponick and co-workers disclosed an efficient method for the synthesis of *cis*-2,6-disubstituted tetrahydropyrans and tetrahydrofurans **33** from monoallylic diols **32** in the presence of cationic Ph_3PAuOTf generated *in situ* from reaction of Ph_3PAuCl and AgOTf (Table 1.5, entry 1).²⁷ The results revealed that a catalyst loading as low as 1 mol % at room temperature and short reaction times of 40 min were reported to give the cyclic adducts **33** up to 97% yield and the thermodynamically more stable *cis*-isomer in both the 2,6-disubstituted tetrahydropyran and 2,5-disubstituted tetrahydrofuran product were formed preferentially. Interestingly, product diastereoselectivities could be further improved up to 25:1 by lowering the reaction temperature from room temperature to -50°C .

Table 1.5 Lewis acid-catalyzed cyclization of monoallylic diols **32**.

Entry	Catalyst	X	n	Yield (%)	Ref
1	$\text{Ph}_3\text{AuCl}/\text{AgOTf}$	O	1, 2	79-99	27
2	FeCl_3	O, NPG	2	51-100	28

More recently, Cossy and co-workers reported that a FeCl_3 -catalyzed version of this cyclization process could also be achieved (Table 1.5, entry 2).²⁸ In this work, the desired *cis*-2,6-disubstituted tetrahydropyrans and *cis*-2,6-disubstituted piperidines **33** (n = 2) were afforded in comparable yields at room temperature. More notably, higher product diastereoselectivities (up to 99:1) were obtained for a number of monoallylic

diol substrates when the iron-mediated system was employed when compared to the analogous reactions using gold catalysis. The source of this improved diastereoselectivity was proposed to be due to epimerization of the *trans* isomer to the thermodynamically more stable *cis* isomer via the zwitterionic species **34** shown in Table 1.5.

1.3 Propargylic Alcohols

The most relied upon synthetic strategy for nucleophilic substitution of propargylic compounds as a method for constructing functionalized propargylic frameworks is the Nicholas reaction (Scheme 1.7).²⁹ Although shown to be efficient, the need for a stoichiometric amount of $[\text{Co}_2(\text{CO})_8]$ and multi-step operation along with the production of excess amount of byproduct at the end of the reaction has lessened the synthetic utility of this functional group transformation in organic synthesis.

Scheme 1.7 Classical Nicholas Colbalt-mediated reaction.

In addressing this challenge, the first catalytic Nicholas-type reaction was reported by Toste and co-workers who showed that direct propargylation of aromatic compounds **36** with variously functionalized propargylic alcohols **35** could be achieved in the presence of $(\text{dppm})\text{Re}(\text{O})\text{Cl}_3$ (dppm = diphenylphosphinomethane) as catalyst (Table 1.6, entry 1).³⁰ The synthetic utility of this Re-catalyzed arene propargylation reaction was further highlighted by its application to the total synthesis

of podophyllotoxin **42** in 7 steps from an advanced intermediate **41** shown in Scheme 1.8.³¹

Table 1.6 Lewis acid-catalyzed substitution reaction of propargylic alcohols **35**.

Entry	Catalyst	NuH	Yield (%)	Ref
1	(dppm)Re(O)Cl ₃	36	65-93	30
2	NaAuCl ₄ ·2H ₂ O	36 37 R ¹ OH R ¹ SH 38 39	33-97	32
3	BiCl ₃	36 37 R ¹ OH R ¹ SH R ¹ SO ₂ NH ₂ 38 39 13	10-94	33
4	FeCl ₃	36 37 R ¹ OH R ¹ SH R ¹ SO ₂ NH ₂ 38 39 13	15-95	34
5	AuCl ₃	36	30-96	35

Scheme 1.8 Re-catalyzed synthesis of natural product **42**.

Following this work, Campagne and co-workers expanded this Nicholas-type transformation to a variety of C-, O- and S-based nucleophiles such as electron-rich arenes **36**, allyltrimethylsilane **37**, alcohols **38** and thiols **39** (Table 1.6, entry 2).³² In this work, the reaction was shown to proceed well and give the corresponding propargylic substituted products **40** in 33-97% yield in the presence of $\text{NaAuCl}_4 \cdot 2\text{H}_2\text{O}$ as catalyst at room temperature.

Subsequently, Zhan and co-workers showed that the propargylic substitution reaction could be accomplished in the presence of inexpensive Lewis acids such as BiCl_3 and FeCl_3 (Table 1.6, entries 3-4).^{33,34} In this work, the corresponding propargylic substituted products were obtained in good to excellent yields under atmospheric conditions and comparable yields was achieved in both the BiCl_3 - and FeCl_3 -catalyzed methods.

By re-examining gold catalysis, Dyker and co-workers further expanded the transformation to arenes and heteroarenes containing electron-rich, electron-deficient and carbonyl group combinations (Table 1.6, entry 5).³⁵ The desired product were furnished in excellent yields in the presence of AuCl_3 as catalyst.

In their work toward developing a route to spirocarbocycles, Zhou and co-workers demonstrated an efficient tandem process involving intramolecular Friedel-Crafts cyclization/hydroarylation of diaryl-substituted tertiary propargylic alcohols **43** catalyzed by $\text{FeCl}_3 \cdot 6\text{H}_2\text{O}$ (Scheme 1.9).³⁶ Without the need to exclude air and moisture, the reaction was shown to lead to the functionalized spirocycles **45** in 68–90% yield. Subsequent mechanistic studies revealed the reaction to initially involve intramolecular Friedel-Crafts cyclization of a putative allenyl carbocation species generated *in situ* from iron-mediated elimination of the hydroxyl functional group. This afforded the allene intermediate **44** that then underwent intramolecular hydroarylation to give the desired spirocarbocycle product **45**.

Scheme 1.9 Synthesis of spirocarbocycle compounds **45**.

Following this work, an efficient tandem process involving the intermolecular Friedel-Crafts alkylation/hydroarylation of tertiary propargylic alcohols **35** with phenols **46** was reported by Chan and co-workers (Scheme 1.10).³⁷ In this reaction, the corresponding 6-indenols **47** were obtained in 34–99% yield albeit at a higher catalyst loading of 10 mol % and long reaction times of 24 h. The mechanism was proposed to proceed via an allene intermediate in a manner similar to that reported by Zhou and co-workers in their iron-catalyzed intramolecular Friedel-Crafts cyclization/hydroarylation of diaryl-substituted tertiary propargylic alcohols **43**.³⁶

Scheme 1.10 Yb(OTf)₃-catalyzed formation of 6-indenols **47**.

At about the same time, Wang and co-workers reported highly functionalized indenenes **50** could be synthesized via tandem reaction of diaryl-substituted tertiary propargylic alcohols **48** and aziridines **49** in the presence of Yb(OTf)₃ as catalyst (Scheme 1.11).³⁸ The corresponding 1-tosylaminoindenenes **50** were obtained in moderate to good yields of 41-79% with a catalyst loading as high as 10 mol %. However, the method was reported to be limited to diaryl-substituted tertiary propargylic alcohols and aryl-substituted aziridines.

Scheme 1.11 Synthesis of 1-tosylamino indenenes **50**.

In 2003, the first example of a three component coupling of anilines **16**, 1-phenylprop-2-yn-1-ol **51** and cyclic and acyclic ketones **52** in the presence of the diruthenium(II,III) catalyst **53** and PtCl₂ as a co-catalyst and NH₄BF₄ as an additive

was communicated by Uemura and co-workers (Scheme 1.12).³⁹ The desired poly-substituted pyrroles **54** were obtained in moderate yields of 44 to 59% when a high catalyst loading of 20 mol % and long reaction times of 100 h were employed. However, this method was shown not to be efficient for internal propargylic alcohol substrates and additives were required to achieve high conversions.

Scheme 1.12 Ru- and Pt-catalyzed three component coupling reaction to synthesis poly-substituted pyrroles **54**.

In 2008, Zhan and co-workers showed that InCl₃ in place of the diruthenium(II,III) catalyst **53** and PtCl₂ as co-catalyst could efficiently mediate the reaction of 1,3-dicarbonyl compounds **2**, anilines **16** and secondary propargylic alcohols **35** (Scheme 1.13).⁴⁰ The poly-substituted pyrroles **55** were obtained in higher yields to those first reported by Uemura in their work using ruthenium and platinum catalysis.³⁹

Scheme 1.13 Synthesis of poly-substituted pyrroles **55**.

More recently, Yoshimatsu and co-workers demonstrated an efficient route for the synthesis of highly functionalized thiazoles and selenazoles **58** from α -sulfanyl- and

α -selanyl propargylic alcohols **56** and thioamides and seleamides **57** in the presence of Sc(OTf)₃ as catalyst (Scheme 1.14).⁴¹ The tandem process was found to proceed smoothly under mild conditions in water, affording the corresponding thiazoles and selenazoles **58** in moderated to excellent yields of 54-100%. However, the method was shown to be limited to aryl-substituted secondary propargylic alcohol substrates.

Scheme 1.14 Sc(OTf)₃-catalyzed synthesis of 4-arylmethylthiazoles and selenazoles

58.

As a part of ongoing program on gold-catalyzed direct substituted reactions of propargylic alcohols, Campagne and co-workers reported that a cascade process involving direct amination/cyclization of propargylic alcohols **35** with *N*-protected hydroxylamine could be accomplished in the presence of a dual iron(III)-gold(III) catalyst system in a one-pot manner (Scheme 1.15).⁴² The first step was shown to involve iron-catalyzed amination of **35** with a binucleophilic Cbz- protected hydroxylamine to afford the intermediate **59**. The second step then involved cyclization of the intermediate **59** on introducing the gold(III) catalyst and DMAP as a co-catalyst to furnish the desired 2,3-dihydroisoxazole **60** in 36-86% yield.

Scheme 1.15 Iron- and gold-catalyzed one-pot two-step formation of 2,3-dihydroisoxazoles **60**.

The first example of AgNO_3 -catalyzed intramolecular cyclization/dehydration of propargylic alcohols **61** to aromatic heterocycles was communicated in 2006 by Knight and co-workers (Table 1.7, entry 1).⁴³ The corresponding pyrroles, furans and thiophenes **62** were furnished in up to 99% yield. However, the method was reported to be limited to internal propargylic alcohols and reactions involving terminal examples were shown to be ineffective.

Table 1.7 Metal-catalyzed intramolecular cyclization of propargylic alcohols **61**.

Entry	Catalyst	Yield (%)	Ref
1	AgNO_3	70-99	43
2	20 / AgOTf	87-99	44
3	$(\text{Ph}_3\text{P})\text{AuCl}/\text{AgNTf}_2$	85-98	45

Following this work, the groups of Akai and Aponick independently reported that the same transformation could be achieved more efficiently by employing gold catalysis (Table 1.7, entries 2-3).^{44,45} The corresponding furan, pyrrole and thiophene adducts **62** was obtained in up to 99% yield under similar reaction conditions. These latter studies also revealed the higher catalytic performance of gold catalysis as the reactions were shown to proceed rapidly at catalyst loadings as low as 0.05 mol %.

Gabriele and co-workers disclosed a synthetic strategy involving intramolecular cyclization/dehydration could also be applied to the synthesis of quinolines from propargylic amino alcohols **63** catalyzed by CuCl_2 (Scheme 1.16).⁴⁶ The corresponding quinolines were obtained in 20-90% yield under mild reaction conditions at 60 or 100 °C.

Scheme 1.16 Synthesis of quinolines **64** from **63**.

More recently, Aponick and co-workers disclosed that the Lewis acidic gold complex $\text{Au}[\text{P}(t\text{-Bu})_2(o\text{-biphenyl})]\text{OTf}$ generated *in situ* from the reaction of **20** with AgOTf could facilitate cascade cyclization of propargylic triols **65** (Scheme 1.17).⁴⁷ Although preparation of the starting propargylic alcohols was reported to require several steps, the method was shown to provide an efficient and convenient route to 1,6-dioxaspiro[4,5]dec-9-ene **66** in excellent yields.

Scheme 1.17 Gold-catalyzed cyclization of propargylic triols **65**.

1.4 Benzylic Alcohols

One of the first examples of Lewis acid-catalyzed reactions of benzylic alcohols was reported by Ishii and co-workers in 2003 (Table 1.8, entry 1).^{11a} In this work, rare earth metal triflate salts were shown to catalyze Friedel-Crafts type benzylation of electron-rich arenes and heteroarenes **36** with secondary benzylic alcohols **67** in good to excellent yields. Among the series of rare-earth metal triflate salts of La, Hf, Sc and Yb investigated, comparative experiments showed that the catalytic performance increased in the order $\text{La}(\text{OTf})_3 < \text{Yb}(\text{OTf})_3 < \text{Sc}(\text{OTf})_3 \leq \text{Hf}(\text{OTf})_4$, although the reasons for these differences in reactivity were not disclosed.

Following this, benzylation of electron-rich arenes or heteroarenes **35** with benzylic alcohols **67** catalyzed by a variety of metal catalysts were reported (Table 1.8, entries 2-6). In 2005, Beller and co-workers demonstrated that FeCl_3 could be used in this transformation (Table 1.8, entry 2).⁴⁸ The benzylated products **68** were obtained in up to 99% yield with excellent regioselectivity and without the need for exclusion of air and moisture. Subsequent studies by the same group disclosed that this transformation could also be accomplished by HAuCl_4 (Table 1.8, entry 3).⁴⁹ To achieve high conversions and product yields, the reaction was found to require temperatures of 50 to 80 °C for both catalytic systems.

Table 1.8 Lewis acid-catalyzed arylation of benzylic alcohols **67**.

$ \begin{array}{ccc} \text{Ar} & + & \begin{array}{c} \text{OH} \\ \\ \text{R}^1 - \text{C} - \text{R}^2 \end{array} & \xrightarrow{\text{catalyst (5-10 mol\%)}} & \begin{array}{c} \text{Ar} \\ \\ \text{R}^1 - \text{C} - \text{R}^2 \end{array} \\ \mathbf{36} & & \mathbf{67} & & \mathbf{68} \\ \text{R}^1\text{-R}^2 = \text{H, alkyl, aryl} & & & & \end{array} $			
Entry	Catalyst	Yield (%)	Ref
1	Ln(OTf) _m	65-99	11a
2	FeCl ₃	37-99	48
3	HAuCl ₄	47-99	49
4	Bi(OTf) ₃	35-95	50
5	InCl ₃	65-91	9
6	InBr ₃	84-92	14

Subsequently, an efficient Bi(OTf)₃-catalyzed version of this transformation was reported by Rueping and co-workers, leading to the corresponding benzylation product **68** in 35-95% yield and with excellent regioselectivity (Table 1.8, entry 4).⁵⁰ Interestingly, reactions of anisole with different benzylating reagents were shown to lead to no product formation when benzyl chloride, bromide or amine was used as the benzylating reagent. In marked contrast, the desired product could be afforded in 91% yield when benzyl alcohol was employed.

Baba and co-workers demonstrated that intermolecular Friedel-Crafts type benzylation of indoles could be achieved in the presence of 5 mol % of InCl₃ as catalyst (Table 1.8, entry 5).⁹ The benzylation reaction was shown to proceed well under mild conditions at 80 °C for 15 h and furnish the indole derivatives in 65-91% yield.

At about the same time, Yadav and co-workers reported this process could be accomplished with InBr_3 as catalyst at room temperature albeit with a higher catalyst loading of 10 mol % (Table 1.8, entry 6).¹⁴ A similar catalytic performance was obtained for the two protocols mediated by InCl_3 and InBr_3 .

In 2001, the first example of catalytic benzylation of allyl silanes with benzylic alcohols in the presence of the boron catalyst $\text{B}(\text{C}_6\text{F}_5)_3$ was reported by Gevorgyan and co-workers (Table 1.9, entry 1).⁵¹ While only 3 benzylic alcohols were examined with allyl silane, the benzylated product **70** was afforded in good to excellent yields under mild conditions at room temperature.

Table 1.9 Lewis acid-catalyzed alkylation of secondary benzylic alcohols **67**.

67 + $\text{NuSiMe}_3 \xrightarrow{\text{catalyst (5 mol\%)}}$ **70**
 $\text{R}^1 = \text{alkyl, aryl}$

Entry	Catalyst	NuSiMe_3	Yield (%)	Ref
1	$\text{B}(\text{C}_6\text{F}_5)_3$		80-90	51
2	InCl_3		46-100	52

Following this work, Baba and co-workers reported this C–C bond formation reaction could be accomplished in the presence of InCl_3 as catalyst (Table 1.9, entry 2).⁵² Although a higher temperature of 80 °C was required for some substrates, the method was found to be applicable to various secondary benzylic alcohols and silyl

nucleophiles such as allyl-, propargyl- and alkynylsilanes. The corresponding allylic alkylation products were achieved in 46-100% yield with short reaction times of 10 to 360 min.

In 2006, Baba and co-workers presented a mild and direct method for the benzylation of 1,3-dicarbonyl compounds **2** with benzylic alcohols **67**, including secondary examples, in the presence of InCl_3 as catalyst (Table 1.10, entry 1).⁹ This gave the corresponding benzylated adducts **71** in 46-99% yield and H_2O as the sole byproduct.

Table 1.10 Lewis acid-catalyzed direct benzylation of dicarbonyl compounds **2**.

Entry	Catalyst	Yield (%)	Ref
1	InCl_3	46-99	9
2	$\text{FeCl}_3 \cdot 6\text{H}_2\text{O}$	81-99	53
3	$\text{Ln}(\text{OTf})_m$	44-99	11a
4	$\text{Bi}(\text{OTf})_3$	58-96	10

Subsequently, Beller and co-workers discovered that $\text{FeCl}_3 \cdot 6\text{H}_2\text{O}$ was also an efficient catalyst for this C-C bond forming process, affording **71** in 81-99% yield (Table 1.10, entry 2).⁵³ However, an excess amount of the 1,3-dicarbonyl compound (up to 10 equiv) was required to achieve high product yields.

Later on, benzylation of 1,3-dicarbonyl compounds with a variety of benzylic alcohols that included both primary and secondary examples was reported by Ishii and co-workers in the presence of lanthanide triflate salts such as $\text{La}(\text{OTf})_3$, $\text{Yb}(\text{OTf})_3$, $\text{Sc}(\text{OTf})_3$, $\text{Hf}(\text{OTf})_4$ (Table 1.10, entry 3).^{11a} The reaction was shown to proceed well and the desired benzylation products were isolated in good to excellent yields and with catalyst loadings as low as 0.5 mol % for all the substrates examined.

Expanding the scope of this approach for the benzylation of 1,3-dicarbonyl compounds to include primary benzylic alcohols was shown to be possible by Rueping and co-workers in 2007 (Table 1.10, entry 4).¹⁰ In this work, $\text{Bi}(\text{OTf})_3$ was found to mediate the benzylation reaction with a variety of primary and secondary alcohols to give the benzylated products **70** in 58-96% yield at 100 °C and with a catalyst loading as low as 1 mol %. Moreover, significantly higher product yields were reported for benzylations with primary benzylic alcohol substrates compared to the analogous reactions catalyzed by the lanthanide triflates.

As a part of an ongoing program on Lewis acid-catalyzed benzylic alkylation reactions utilizing alcohols as pro-electrophiles,^{9,52} Baba and co-workers discovered that benzylic alkylation of enol acetates **72** with benzylic alcohols **67** could be accomplished in the presence of InI_3 , FeBr_3 or GaBr_3 as catalyst (Scheme 1.18).⁵⁴ This gave the expected α -alkylated monocarbonyl ketones and aldehydes **73** in excellent yields but in almost all instances, with no product diastereoselectivity.

Scheme 1.18 Lewis acid-catalyzed benzylic alkylation of enol acetates **72** with **67**.

In 2008, Wang and co-workers communicated that tandem intermolecular benzylation/cyclization/oxidation of amino-substituted benzylic alcohols **74** with β -ketoesters **2** catalyzed by FeCl_3 and ZnCl_2 as a co-catalyst could be accomplished (Scheme 1.19).⁵⁵ A wide range of amino-substituted benzylic alcohols **74** with β -ketoesters **2** were examined under these conditions and found to furnish the corresponding 3-quinolinecarboxylic esters **75** in 59-94% yield. In this work, the presence of a stoichiometric amount of ZnCl_2 as co-catalyst was shown to be essential for the transformation; the desired product **75** was afforded in yields of 57% and 22% when either FeCl_3 or ZnCl_2 were employed as the sole catalyst.

Scheme 1.19 Synthesis of 3-quinolinecarboxylic esters **75**.

In an effort to broaden the synthetic versatility of alcohol pro-electrophiles in Lewis acid-catalyzed C–C bond formations, Ding and co-workers reported the first example of direct cyanation of benzylic alcohols **67** with trimethylsilyl cyanide **76** as the cyanide source catalyzed by InBr_3 (Scheme 1.20).⁵⁶ In this work, the corresponding α -aryl nitriles **77** were afforded in up to 99% yield under mild reaction conditions at room temperature. The utility of this method also shown to provide a straightforward and practical route to several key α -aryl nitrile precursors used in the synthesis of bioactive compounds such as verapamil **78**, cicloprofen **79**, naproxen **80** and indoprofen **81** (Figure 1.1).⁵⁷

Scheme 1.20 InBr₃-catalyzed direct cyanation of alcohols **67** with TMSCN **76**.

Figure 1.1 Some bioactive compounds derivatived from α -aryl nitriles.

1.5 α -Cyclopropyl Alcohols

α -Cyclopropyl alcohols are versatile building blocks in organic synthesis. Brønsted acid HX (X = F, Cl or Br) mediated ring-opening of α -cyclopropyl alcohols **82** to give the corresponding homoallylic halides **83** is well demonstrated (Scheme 1.21).⁵⁸ On the other hand, Lewis acids-catalyzed rearrangement reactions involving α -cyclopropyl alcohols to construct complex frameworks have remained sparse.⁵⁹⁻⁶²

Scheme 1.21 Brønsted acid-promoted rearrangement of α -cyclopropyl alcohols **82**.

In 2001, Doris and co-workers demonstrated that the BF₃·OEt₂-mediated rearrangement of cyclopropyl alcohols **84** could be accomplished (Scheme 1.22).⁵⁹

The corresponding polycyclic cyclobutanes **87** were obtained in excellent yields of 90-97%. However, dihydrobenzoxepin **89** was obtained in 47% yield as the sole example when R^2 was changed from a proton to a Ph group. The proposed mechanism was reasoned to involve formation of the key cyclopropyl carbinyl cationic intermediate **85** generated by $\text{BF}_3 \cdot \text{OEt}_2$ -mediated activation the alcohol functional group of **84**. Ring expansion of this key cationic species was then thought to give the cyclobutyl cation **86** when $R^2 = \text{H}$. Alternatively, ring opening of the same intermediate was thought to give the homoallylic cation **88** when $R^2 = \text{Ph}$. Trapping of these two intermediates by intramolecular hydroxyl group then gave the respective desired polycyclic cyclobutane and 2-phenyl-2,3-dihydrobenzoxepin products **87** and **89**.

Scheme 1.22 $\text{BF}_3 \cdot \text{OEt}_2$ -mediated rearrangement of cyclopropyl carbinols **84**.

The first Lewis acid-mediated benzannulation of chiral aryl(aryl')-2,2-dichlorocyclopropylmethanols (AACMs) **90** involving chirality transfer was reported by Nishi and Tanabe in 2004 (Scheme 1.23).⁶⁰ Chiral α -arylnaphthalenes **93** were achieved in excellent yields up to 97% and with ee (enantiomeric excess) values of > 99%. In this work, TiCl_4 was shown to be the best catalyst in terms of chemical yield

and regio- and enantioselectivity. A possible mechanism was proposed to involve activation of the alcohol substrate by TiCl_4 coordination with the OH functional group that resulted in the generation of the cyclopropyl carbinyl cation intermediate **91**. This was followed by highly regioselective ring-opening/Friedel-Crafts cyclization of this newly formed species and formation of intermediate **92**. Arylation then gave the optically pure α -arylnaphthalene **93** exclusively. The synthetic utility of this methodology was subsequently demonstrated by the synthesis of the natural products justicidin B **94**, retrojusticidin B **95** and dehydrodesoxypodophyllotoxin **96** along with its synthetic analogue 5'-methoxyretrochinensin **97** from non-chiral α -cyclopropyl methanols (Figure 1.2).⁶¹

Scheme 1.23 TiCl_4 -mediated chirality transfer benzannulation of **90**.

Figure 1.2 Natural products **94-96** and synthetic analogue **97**.

In 2007, Liang and co-workers demonstrated *trans*-substituted conjugated enynes **99** could be obtained from regioselective gold-catalyzed ring-opening of 1-cyclopropyl-2-propyn-1-ols **98** with a variety of alcohol nucleophiles (Scheme 1.24).⁶² In this work, tri- and tetra-substituted conjugated enynes **99** were obtained in good yields with complete regio- and stereoselective control even for reactions with terminal alcohol substrates. However, the method was reported to be limited to activated tertiary cyclopropyl propargylic alcohols.

Scheme 1.24 Gold-catalyzed ring-open reaction of **98** with alcohols.

1.6 Proposed work

The work of this thesis has been directed toward providing new synthetic methodologies that enable the construction of compounds of current biological and material interest in an efficient and selective manner. This will be accomplished by exploring the reaction chemistry of inexpensive and readily available alcohol pro-electrophiles with a variety of C- and N-based nucleophiles in the presence of an ecologically benign Lewis acid catalyst under operationally straightforward and mild conditions.

Thus, the aim of this project has been to establish new Lewis acid-catalyzed protocols for the efficient and selective formation of allylic alkylated aromatic and heteroaromatic compounds, indenenes, pyrrolidines, *trans*-2,5-dihydro-1*H*-pyrroles and 1,2-dihydroquinolines and conjugated enynes from their respective alcohol substrates (Figure 1.3). It was envisioned that Friedel-Crafts arene and heteroarene allylic alkylation can be developed in an efficient and regioselective manner from the reaction of the respective aromatic compounds and heteroaromatic nucleophiles and allylic alcohols. Replacing the allylic moiety of the alcohol substrate with a cyclopropane ring, the pyrrolidine framework can be prepared via tandem amination/ring expansion of cyclopropyl methanols with sulfonamides. By utilizing alkynyl substituted tertiary cyclopropyl methanols, we envisioned that this approach could also be fine-tuned to provide a synthetic route to conjugated enynes. This would be achieved by ring-opening of the tertiary cyclopropyl methanol substrates with sulfonamide nucleophiles. In the course of this study on the reactivity of propargylic alcohols, an unexpected process involving the dimerization of these substrates under certain conditions that afforded highly conjugated indenenes is also presented. Finally, intramolecular hydroamination of aminodienes generated *in situ*

from homoallylic 1,2-aminoalcohols and 2-amino-benzyl alcohols will be developed as an expedient route to the *trans*-2,5-dihydro-1*H*-pyrroles and 1,2-dihydroquinolines, respectively.

Figure 1.3 Lewis acid-catalyzed strategies for C–C and C–N bond formation from unsaturated alcohols.

Chapter II. Gold-catalyzed allylic alkylation of aromatic and heteroaromatic compounds with allylic alcohols

2.1 Introduction

The Friedel-Crafts allylic alkylation of aromatic and heteroaromatic compounds is one of the most efficient and powerful carbon-carbon bond forming tools in organic synthesis.⁶³ Among the myriad of works devoted to this reaction, those on developing new methods that make use of inexpensive and readily available electrophiles, mild reaction conditions, simple manipulation, atom economy⁵ and environmentally friendly catalysts have become very topical.^{9,64-75} One such approach is replacing of Friedel-Crafts allylic alkylating reagents such as allylic acetates, carbonates, and halides with allylic alcohols in the presence of a variety of transition metal and Brønsted acid catalysts.⁶⁵ Although shown to be efficient, producing H₂O as the only side product, a drawback of these methods is the use of strongly acidic conditions and a large excess of the arene or heteroarene substrate to achieve moderate to good product regioselectivities. In the case of metal catalysts, there is also the need for high reaction temperatures or introduction of a co-catalyst or additive. It therefore remains a challenge to develop a new catalytic system for this useful carbon-carbon bond forming reaction that exhibits outstanding activity in combination with high selectivities under mild conditions.

In this context, we envisioned that simple gold salts would hold promise as a catalyst for developing a new approach for Friedel-Crafts allylic alkylations of aromatic and heteroaromatic compounds with allylic alcohols. A commercially available reagent, this emerging class of Lewis acid catalysts have been shown to be

versatile in mediating a wide variety of stereoselective C–X (X = C, N, O, S) bond formations in excellent yields under mild conditions.^{2,32,35,49,76-77} Recently, Campagne and co-workers described an efficient gold-catalyzed propargylation of allyl silanes with propargylic alcohols which could be accomplished in good to excellent yields and selectivity.³² Following this seminal work, the groups of Dyker³⁵ and Beller⁴⁹ reported similar gold-catalyzed approaches for the propargylation and benzylation of aromatic and heteroaromatic compounds with propargylic and benzylic alcohols, respectively. To our knowledge, however, the analogous gold-catalyzed allylic alkylation reactions of aromatic and heteroaromatic compounds with allylic alcohols are not known. As part of an ongoing program examining the utility of alcohols as building blocks in organic synthesis,⁷⁵ Herein, we report the allylic alkylation of a wide variety of aromatic and heteroaromatic compounds with allylic alcohols catalyzed by AuCl₃ (Scheme 2.1). The reactions were found to proceed in up to 99% yield and with high regioselectivity under mild conditions.

Scheme 2.1 AuCl₃-catalyzed allylic alkylation of arenes.

2.2 Results and Discussion

Initially, we chose to focus our attentions on the allylic alkylation of 2,6-dimethylphenol **46a** with (*E*)-1,3-bis(4-bromophenyl)prop-2-en-1-ol **100a** by a variety of Lewis and Brønsted acid catalysts to establish the reaction conditions (Table 2.1).

Table 2.1 Optimization of reaction conditions.^a

Entry	Catalyst	46a (equiv)	Solvent	Yield (%) ^b
1	AuCl ₃	4	CH ₂ Cl ₂	99
2	AuCl	4	CH ₂ Cl ₂	81
3	PPh ₃ AuCl	4	CH ₂ Cl ₂	5
4	PPh ₃ AuOTf ^c	4	CH ₂ Cl ₂	21
5	BF ₃ ·Et ₂ O	4	CH ₂ Cl ₂	95
6	InCl ₃	4	CH ₂ Cl ₂	95
7	NaAuCl ₄	4	CH ₂ Cl ₂	98
8	Cu(OTf) ₂	4	CH ₂ Cl ₂	99
9	CuBr ₂	4	CH ₂ Cl ₂	85
10	ZnCl ₂	4	CH ₂ Cl ₂	90
11	AgOTf	4	CH ₂ Cl ₂	48
12	AgSbF ₆	4	CH ₂ Cl ₂	10
13	Yb(OTf) ₃	4	CH ₂ Cl ₂	23
14	<i>p</i> -TsOH·H ₂ O	4	CH ₂ Cl ₂	97
15	TfOH	4	CH ₂ Cl ₂	99
16	AuCl ₃	2	CH ₂ Cl ₂	95

Table 2.1 (*continued*).

Entry	Catalyst	46a (equiv)	Solvent	Yield (%) ^b
17	AuCl ₃	1	CH ₂ Cl ₂	70
18	AuCl ₃	2	C ₆ H ₆	82
19	AuCl ₃	2	THF	67
20	AuCl ₃	2	CH ₃ CN	10
21	- ^d	2	CH ₂ Cl ₂	- ^e

^aAll reactions were performed at rt for 15 h in the presence of 4 Å MS with a catalyst: **100a** ratio = 1: 20. ^bIsolated yields. ^cPrepared *in situ* from reaction of PPh₃AuCl with AgOTf. ^dReaction conducted in the absence of catalyst. ^eNo reaction.

This revealed a CH₂Cl₂ solution of **100a** (1 equiv) and **46a** (4 equiv) at room temperature treated with either 5 mol % of AuCl₃, BF₃.Et₂O, InCl₃, NaAuCl₄, Cu(OTf)₂, *p*-TsOH.H₂O, or TfOH as catalyst for 15 h gave the best result.⁷⁷ In each of these reactions, 4-[(*E*)-1,3-bis(4-bromophenyl) allyl]-2,6-dimethylphenol **101a** was furnished in 95-99% yield and as a single regioisomer based on ¹H NMR analysis (Table 2.1, entries 1, 5-8 and 14-15). However, only AuCl₃ was found to maintain its catalytic activity for all the allylic alcohols studied in this work (see later). Reactions with other Lewis and Brønsted acid catalysts such as AuCl, CuBr₂ and ZnCl₂ were found to proceed in slightly lower product yields of 80-90% (Table 2.1, entries 2, 9-10). In contrast, markedly lower product yields of 5-48% were obtained when the reaction was repeated with either PPh₃AuCl, PPh₃AuOTf, AgOTf, AgSbF₆ or Yb(OTf)₃ as catalyst (Table 2.1, entries 3-4 and 11-13). As anticipated, no reaction

was observed in the absence of a catalyst and both starting materials were recovered in quantitative yields (Table 2.1, entry 21).

Inspection of entries 16-20 in Table 2.1, a comparable product yield of 95% was found when the loading of **46a** was lowered from 4 to 2 equiv under the optimized conditions. On the other hand, a corresponding decrease in product yield was observed on gradually decreasing the loading of **46a** from 2 to 1 equiv. An examination of solvent effects also revealed a similar outcome with lower product yields of 67-82% afforded on changing the solvent from CH₂Cl₂ to either C₆H₆ or THF (Table 2.1, entries 18-19). In contrast, repetition of the reaction with MeCN as solvent gave **101a** in a markedly low product yield of 10% (Table 2.1, entry 20).

To define the scope of the AuCl₃-catalyzed allylic alkylation reactions, we applied this process to a series of substituted electron-rich aromatic and heteroaromatic compounds **46a-b**, **102a-c** and **103** with allylic alcohols **100a-l**. The results are summarized in Tables 2.2-2.5.

As shown in Table 2.2, we first focused our attentions to examining the allylic alkylation of substituted aromatic compounds **46a-b**, **102a-c** and **103** with allylic alcohols **100a-c** bearing electron-withdrawing and electron-donating groups. Under the optimized conditions, we found the reactions of phenols **46a-b** with allylic alcohols **100a-c** to proceed in excellent yields of 91-97% (Table 2.2, entries 1-4). The present procedure was also shown to work well for the allylic alkylations of aryl alkyl ethers **102a-c** with **100a**, which gave the corresponding allylated adducts **101f-h** in good to excellent yields (Table 2.2, entries 5-7). On the other hand, steric effects of the aromatic compound may play a role since an *ortho*-substituted bulky group, such as a methyl group, provided **101i** in moderate yield (Table 2.2, entry 8).

Table 2.2 AuCl₃-catalyzed allylic alkylation of aromatic compounds **46a-b**, **102a-c** and **103** with allylic alcohols **100a-c**.^a

Entry	Substrate	Product	Time (h)	Yield (%) ^b	
1	100b + 46a		101b R = Me	1.5	91
2	100c + 46a		101c R = H	1	91
3	100a + 46b		101d R = Br	1	97
4	100b + 46b		101e R = Me	2	94
5	100a + 102a		101f R = CH ₂ CH=CH ₂	3	91
6	100a + 102b		101g R = Me	1.5	93
7	100a + 102c		101h	2	74
8	100a + 103		101i	3	50

^aAll reactions were performed in CH₂Cl₂ at rt in the presence of 4 Å MS with AuCl₃:

100: **46** or **102** or **103** ratio = 1 : 20 : 80. ^bIsolated yields.

To further investigate the substrate scope of the present AuCl₃-catalyzed procedure, the allylic alkylation of **46a** and **46b** with allylic alcohols containing pendant H, alkyl and aryl combinations as in **100d-l** were examined (Table 2.3). In the presence of 5 mol % AuCl₃, allylated adducts **101j-l** were obtained in near quantitative yields from the respective allylic alkylations of **46a** and **46b** with **100d-f** (Table 2.3, entries 1-3). When the less reactive primary allylic alcohols **100g** and **100h** were employed as the allylating source, the respective allylated adducts **101m** and **101n** were afforded in 51 and 63% yield (Table 2.3, entries 4-5). Although requiring a slightly higher temperature of 40 °C and longer reaction time of 15 h, the product yields obtained in these reactions are comparable to those previously reported.⁷⁸ We found the reaction of **46a** with terminal allylic alcohols **100i** and **100j** to also proceed smoothly and give **101o** and **101p** in yields of 80 and 96%, respectively (Table 2.3, entries 6-7). Likewise, conformationally restricted allylic alcohols **100k** and **100l**, which also contains an additional electrophilic carbonyl group, were shown to be good allylating reagents, affording **101q** and **101r** in 77 and 98% yield, respectively (Table 2.3, entries 8-9). More notably, in the latter case, we found the combined use of **100l** with other Lewis and Brønsted acid catalysts to be less effective (Table 2.4). As shown in Table 2.4, lower product yields of 40-88% were obtained for the allylic alkylation of **46a** with **100l** in the presence of 5 mol % of BF₃·Et₂O, *p*-TsOH, or TfOH as catalyst.⁷⁷ In all cases, no improvements in product yields was also observed on increasing the catalyst loading to 15 mol %. In contrast, attempting the allylation with Cu(OTf)₂, InCl₃, NaAlCl₄, or ZnCl₂ as catalyst gave no reaction and recovery of both starting materials in near quantitative yields. These results differ significantly to our earlier findings for the allylic alkylation of **46a** with **100a** in the presence of the same

Table 2.3 AuCl₃-catalyzed allylic alkylation of **46a-b** with allylic alcohols **100b-l**^a

100d , R = H 100e , R = Bn 100f , R = CH=CH ₂	100g , R = H 100h , R = (CH ₂) ₅ CH ₃	100i , R ¹ = H, R ² = Br 100j , R ¹ = Ph, R ² = H	100k	100l

Entry	Substrate	Product	Time (h)	Yield (%)	
1	100d + 46a		101j	2	97
2	100e + 46b		101k R = CH ₂ Bn	2	99
3	100f + 46b		101l R = CH ₂ CH=CH ₂	2	98
4 ^c	100g + 46b		101m R = H	15	51
5 ^c	100h + 46b		101n	15	63
6	100i + 46a		101o R ¹ = H, R ² = Br	1	80
7	100j + 46a		101p R ¹ = Ph, R ² = H	2	96
8	100k + 46a		101q	1	77
9	100l + 46a		101r	1.5	98

^aAll reactions were performed in CH₂Cl₂ at rt in the presence of 4 Å MS with AuCl₃:**100**: **46** ratio = 1 : 20 : 80. ^bIsolated yields. ^cReaction conducted at 40 °C.

Table 2.4 Lewis and Brønsted acid catalyzed allylation of **46a** with **100l**.^a

Entry	Catalyst	Yield (%) ^b
1	AuCl ₃	98
2	InCl ₃	- ^c
3	Cu(OTf) ₂	- ^c
4	NaAlCl ₄	- ^c
5	ZnCl ₂	- ^c
6	BF ₃ .Et ₂ .O	65
7	TfOH	88
8	<i>p</i> -TsOH.H ₂ O	40

^aAll reactions were performed at rt for 1.5 h in the presence of 4 ÅMS with a catalyst: **100l**: **46a** ratio = 1: 20: 80. ^bIsolated yields.^cNo reaction.

Lewis and Brønsted acid catalysts, which gave product yields comparable to that catalyzed by AuCl₃.

In this work, we also examined the AuCl₃-catalyzed allylic alkylations of heteroaromatic compounds (Table 2.5). By applying our optimized conditions, treatment of **104a** with **100a-c** in the presence of 5 mol % of AuCl₃ gave **101s-u** in excellent yields (Table 2.5, entries 1-3). Under similar conditions, allylic alkylation of the *N*-methyl indole **5b** with **100a** was found to proceed well and furnish **101w** in 95% yield (Table 2.5, entry 5). The reaction of **105a** was the only example where the

use of 1 equiv of the heteroarene substrate gave a low product yield of 30% and an excess (1 mL) was required to achieve **101v** in 67% yield (Table 2.5, entry 4). The ability to access the allylated heteroaromatic adducts efficiently is noteworthy as this class of compounds are commonly used in organic synthesis as building blocks and are prevalent structural units found in a myriad of bioactive natural and pharmaceutical compounds.⁷⁹

Table 2.5 AuCl₃-catalyzed allylic alkylation of heteroaromatic compounds **5b**, **104a**, and **105a** with allylic alcohols **100a-c**.^a

<div style="display: flex; justify-content: space-around; align-items: center;"> <div style="text-align: center;"> <p>104a, X = NH 105a, X = O</p> </div> <div style="text-align: center;"> <p>5b</p> </div> </div>					
Entry	Substrate	Product		Time (h)	Yield (%) ^b
1	100a + 104a		101s R = Br	2	97
2	100b + 104a		101t R = Me	1	93
3	100c + 104a		101u R = H	1.5	95
4 ^c	100a + 105a		101v	4	67
5	5b + 100a		101w	4	95

^aAll reactions were performed in CH₂Cl₂ at rt in the presence of 4 Å MS with AuCl₃:

100: **5** or **104** or **105** ratio = 1 : 20 : 80. ^bIsolated yields. ^cReaction conducted with 1 mL furan **105a**.

At this juncture, we would like to highlight the regioselective nature of the present reaction. Without exception, all the allylic alkylations described in Tables 2.2-2.4 were found to proceed with complete regioselectivity and give the allylic alkylation products as single isomers. Under our experimental conditions, allylic substitution of **46** with **100** was found to proceed solely at the *para*-position of the aromatic substrate, based on ^1H NMR analysis of the crude mixtures. The *ortho*-allylic alkylation product was only afforded when the *para*-position of the arene substrate was substituted as in **101x** (Scheme 2.2). The present protocol was also shown to be regioselective for the allylation of heteroaromatic substrates **5b**, **104a**, **105a** with carbon-carbon bond formation only occurring at the C-2 center of **104a**, **105a** and at the C-3 center of **5a**. Moreover, the highly regioselective nature of the present procedure is further exemplified by carbon-carbon bond formation only occurring at the less sterically-hindered carbon centre of the allylic moiety in reactions with allylic alcohols containing two different substituents as in **100d-l**. This is noteworthy as the use of such allylic alkylation reagents had been anticipated to lead to a mixture of regioisomeric products. In addition, our findings compare favourably with previous works, which reported the analogous allylic alkylations with allylic alcohols using other Lewis and Brønsted acid catalysts gave moderate to good product regioselectivities.

Scheme 2.2 AuCl₃-catalyzed allylic alkylation of **46c** with **100a**.

Although the above experimental results do not provide a clear perspective on the mechanism of the present procedure, we tentatively propose the reaction to proceed in a manner similar to that put forward by Campagne and co-workers. This could involve the hydroxyl group becoming a better leaving group through activation of the allylic alcohol by the gold catalyst. The regioselectivities obtained in these reactions may be due to subsequent attack at the sterically less hindered carbon centre of this presumed activated intermediate.

2.3 Conclusion

In summary, we have demonstrated an efficient and regioselective gold-catalyzed method for the allylic alkylation of aromatic and heteroaromatic compounds that proceeded in good to excellent yields at room temperature. The present protocol is applicable to a variety of electron-rich arenes and heteroarenes and allylic alcohols containing electron-withdrawing and electron-donating, and sterically demanding substrate combinations. While TfOH was found to exhibit comparable catalytic activity in mediating the allylation process, the milder conditions of gold catalysis provides an attractive alternative synthetic approach for this useful carbon-carbon bond forming reaction.

Chapter III. Unexpected Iron(III) Chloride-Catalyzed Dimerization of 1,1,3-Trisubstituted-prop-2-yn-1-ols as an Expedient Route to Highly Conjugated Indenes

3.1 Introduction

In addition to their versatility as building blocks in organic synthesis, indenenes are an important class of carbocycles found in a myriad of compounds of biological and material interest.⁸⁰ Although this has led to many synthetic methods to this important carbocycle,⁸¹ the number of literature examples still remains far fewer than those for structurally related heterocycles such as indoles and benzofurans. Moreover, many of the reported reactions have been shown to require high temperatures and/or prolonged reaction times. In this regard the development of mild and efficient synthetic strategies that can make use of inexpensive and ecologically benign starting materials and catalysts for the synthesis of this class of compounds would be desirable.

Iron complexes have re-emerged as efficient Lewis acid catalysts in a variety of stereoselective C–X (X = C, N, O, S) bond formations in recent years.^{3,82,83} When the electrophile in these reactions is an alcohol,³ they were shown not only to benefit from the nontoxic and inexpensive nature of the ubiquitous Group 8 metal but also the low cost of the substrate and formation of H₂O as potentially the only byproduct. Added to this is the ease of preparing the starting alcohol that provided the possibility to introduce a wide variety of substitution patterns and a quaternary carbon centre through the use of a tertiary alcohol. In an effort to develop such reactions,^{83a, 84} we unexpectedly found propargylic alcohols of the type **106** dimerized and gave the indene products **107** and **108** when treated with FeCl₃ under the mild conditions shown in *route* 1 in Scheme 3.1.⁸⁵ The reactions were also shown to proceed

With complete regioselectivity for substrates with a pendant sterically bulky alkyl group on the carbinol carbon and that such selectivities were dependent on the structural nature of this functional group. Interestingly, although indene formation from propargylic alcohols such as **106** has been described twice before in the literature as shown in *routes 2* and *3* in Scheme 3.1, the structures of **107** and **108** are unprecedented. Additionally, while 1,2- and 1,3-migrations of acetoxy,⁸⁶ indole,^{81h} silyl^{85a} and sulfide⁸⁷ groups in the respective propargylic derivatives have been reported, the apparent 1,3-alkyl group migration observed in this reaction is not known. Herein, we report the discovery of this new iron-catalyzed method for the synthesis of ethynyl-2-vinyl-1*H*-indenes from dimerization of a variety of trisubstituted propargylic alcohols.

Scheme 3.1 $FeCl_3$ -catalyzed formation of ethynyl-2-vinyl-1*H*-indenes from trisubstituted propargylic alcohols.

3.2 Results and discussion

We found that treating a solution of **106a** in CH₂Cl₂ and 4 Å MS with 5 mol % of FeCl₃ at room temperature for 0.5 h gave the best result (Table 3.1, entry 1). Under these conditions, the indenenes **107a** and **108a** were obtained in respective yields of 65% and 7%, comparable to the yields and regioselectivities obtained for the closely-related Au-catalyzed reactions with propargylic acetates and indoles.^{81h,81n} The regiochemistry of both indene products were determined by X-ray single crystal structure analysis (Figure 3.1).⁸⁸ Although requiring a longer reaction time of 2 h, the same yields of **107a** and **108a** were reproduced when the experiment was repeated at -78 °C (Table 3.1, entry 2). In contrast, repeating the reaction in other solvents was found to be markedly less effective (Table 3.1, entries 3-5). When toluene was employed as the solvent, the conjugated enyne side-product **112a** was furnished as the major product in 38% yield and the indene adducts as the minor products (Table 3.1, entry 3). Similarly, performing the reaction in either THF or MeCN was found to result in only recovery of the starting alcohol in yields of 85-95% along with **112a** in 7% yield when THF was used as the solvent (Table 3.1, entries 4-5). On the other hand, an examination of other Lewis and Brønsted acid catalysts revealed that InCl₃, ZnCl₂ and AuCl₃ could also mediate the dimerization of **106a** and give **107a** and **108a** albeit in lower yields of 46-62 and 8-14%, respectively (Table 3.1, entries 6-8). Formation of **112a** in yields of 3-8% was also afforded for the ZnCl₂- and AuCl₃-catalyzed reactions. However, in the absence of a catalyst or switching to the metal triflates Cu(OTf)₂ and Yb(OTf)₃ or Brønsted acids *p*-TsOH or TfOH was found to lead to no reaction based on ¹H NMR and TLC analysis of the crude mixtures (Table 3.1, entries 9-13).

Table 3.1 Optimization of the reaction conditions.^a

Entry	Catalyst	Solvent	Time (h)	Yield (%)		
				107a	108a	112a
1	FeCl ₃	CH ₂ Cl ₂	0.5	65	7	-
2 ^b	FeCl ₃	CH ₂ Cl ₂	0.5	65	7	-
3	FeCl ₃	PhMe	15	23	7	38
4	FeCl ₃	MeCN	15	- ^c	-	-
5	FeCl ₃	THF	15	-	-	7
6	AuCl ₃	CH ₂ Cl ₂	0.5	50	8	3
7	InCl ₃	CH ₂ Cl ₂	0.5	61	11	-
8	ZnCl ₂	CH ₂ Cl ₂	15	46	14	-
9	Cu(OTf) ₂	CH ₂ Cl ₂	15	- ^c	-	-
10	Yb(OTf) ₃	CH ₂ Cl ₂	15	- ^c	-	-
11	<i>p</i> -TsOH	CH ₂ Cl ₂	15	- ^c	-	-
12	TfOH	CH ₂ Cl ₂	15	- ^c	-	-
13	- ^d	CH ₂ Cl ₂	15	- ^c	-	-

^aAll reactions were performed at room temperature with 4 Å MS and catalyst:**106a** ratio of 1:20. ^bReaction conducted at -78 °C. ^cNo reaction.

^dReaction conducted in the absence of a catalyst.

(a) **107a** (b) **108a**

Figure 3.1 ORTEP drawings of (a) **107a** and (b) **108a** with thermal ellipsoids at 50% probability levels.⁸⁸

To define the scope of the present indene forming procedure, we next turned our attentions to the reactions of a variety of propargylic alcohols **106** (Table 3.2). This revealed indene products **107b** and **108b**, and **107c** and **108c** could be furnished in good overall yields from 1-cyclobutylprop-2-yn-1-ols containing an electron-donating group at the acetylenic position. Although requiring a longer reaction time and catalyst loading of 10 mol % at 40 °C, the dimerization process was also shown to be applicable to starting alcohols bearing an electron-withdrawing or thiophene group at this position. Under these slightly modified conditions, the indene adducts **107d** and **107e**, which were also structurally characterized by X-ray crystal analysis (Figure 3.2), were afforded in lower yields of 22 and 24%, respectively. Interestingly, steric effects were also found to play a role since a more bulky *i*-Pr or cyclopentane unit in place of the cyclobutane group at the carbinol position in the starting alcohol were found to lead to no reaction. On the other hand, propargylic alcohols with a pendant (CH₂)_{*n*}CH₃ side chain where *n* = 1, 3 or 5 at the carbinol position as in **106f-h** and **106i** gave the corresponding indene products in good to excellent yields under the standard conditions. The enyne byproduct **112** was also obtained in yields of 3-26% for reactions of **106b** and **106d-g** shown in Table 3.2. More notably, dimerization of propargylic alcohols containing an *i*-Bu, Bn or phenethyl moiety at the carbinol position was shown to proceed with complete regioselectivity. A similar regioselective outcome was also found when we conducted the dimerization of **106n** bearing a homoallylic functional group at the carbinol position of the starting alcohol. In each of these latter reactions, the indene adducts **107j-n** were cleanly afforded as the sole product in yields of 61-78%. The structure of **107l** was also characterized by X-ray crystallographic analysis (Figure 3.2).⁸⁸ No minor products

Table 3.2 Iron(III) chloride-catalyzed dimerization of **106b-n**.^a

Entry	Substrate	Product		
		107	108	112
1	106b	107b (55%)	108b (10%)	112b (6%)
2	106c	107c (64%)	108c (10%)	-
3 ^b	106d	107d (22%)	-	112d (26%)
4 ^c	106e	107e (24%)	-	112e (3%)
5	106f	107f (35%)	108f (35%)	112f (9%)

Table 3.2 (continued).

Entry	Substrate	Product		
		107	108	112
6	106g	107g (55%)	108g (18%)	112g (8%)
7	106h	107h (50%)	108h (15%)	-
8	106i	107i (43%)	108i (35%)	-
9	106j	107j (78%)	-	-
10	106k	107k (73%)	-	-
11	106l	107l (69%)	-	-

Table 3.2 (continued).

Entry	Substrate	Product		
		107	108	112
12	106m	107m (61%)	-	-
13	106n	107n (69%)	-	-

^aAll reactions were performed at room temperature for 0.5 h with 4 Å MS and FeCl₃:**106** ratio = 1:20; values denoted in parenthesis are isolated yields. ^bReaction with 10 mol % FeCl₃ at 40 °C for 24 h. ^cReaction with 10 mol % FeCl₃ at 40 °C for 2 h.

that could be attributed to either the indene regioisomer **108** or enyne byproduct **112** were detected based on TLC and ¹H NMR analysis of the crude mixtures. Finally, varying the alkyl substituent at the carbinol position with a methyl group in place of the cyclobutane group was found to lead to oligomerization of the starting alcohol. Further control experiments also showed that no product formation could be detected for reactions with a proton or phenyl group instead of an alkyl group at the carbinol position of the starting material.

(a) **107e** (b) **107l**

Figure 3.2 ORTEP drawings of (a) **107e** and (b) **107l** with thermal ellipsoids at 50% probability levels.⁸⁸

On the basis of the above results, it appears that the chemo- and regioselective outcome of the reaction are dependent on the behaviour of the Lewis acid catalyst and the alkyl substitution pattern at the carbinol position. Although highly speculative, the apparent 1,3-alkyl group migration in products of the type **107** and **108**,⁸⁹ and the formation of the enyne byproduct **112** led us to propose the mechanism outlined in Scheme 3.2 for the reaction of **106i**. This could involve activation of the alcohol substrate through coordination of the hydroxyl functional group to the FeCl₃ catalyst. This delivers the Fe(III)-coordinated intermediate **113** which undergoes elimination to give the putative alkynyl cation species **114** and its allenic resonance form **115**. Alkoxylation of carbocation **114/115** at the sterically less hindered carbon center by another molecule of **106i** and intramolecular Friedel-Crafts reaction would give the dimer **117**.⁹⁰ The reaction then proceeds via a second putative carbocation species **119** resulting from activation of the hydroxyl group of this newly formed dimer due to coordination to the metal catalyst and elimination of [Fe]-OH. This leads to intramolecular cyclization of the alkyne moiety to the resultant carbocation centre generated and concomitant 1,6-alkyl shift to furnish the cationic allylindene **120**.⁹¹ We surmise that this C–C bond formation and 1,3-migration process could be concerted in character so as to avoid the possible formation of a highly reactive and unstable vinylic cation species.⁹² Deprotonation at the methylene carbon center of the 1,3-migrated alkyl group in this indenyl cation species as shown in Scheme 3.2 would provide the indene regioisomer **107i**. Alternatively, the aryl group in **120** could undergo a 1,4-migration to give the cationic indenyl regioisomer **121**, which deprotonates in a similar manner to that described above to provide the indene product **108i**.

Scheme 3.2 Tentative mechanism for FeCl_3 -catalyzed formation of ethynyl-2-vinyl-1*H*-indenes from trisubstituted propargylic alcohols.

The possible involvement of carbocation intermediates is also supported by our results for the dimerization of enantioenriched **106f**. Under the experimental conditions described in Scheme 3.3, the indene products **107f** and **108f** were both obtained as a racemic mixture in 35% yield. What remains unclear is the origin of the product regioselectivities obtained in the present propargylic alcohol process. One possibility for the complete regioselectivities obtained for reactions of

substrates containing an alkyl group with a bulky *i*Pr or Ph group or terminal C=C bond could be to prevent any unfavourable steric and/or stereoelectronic interactions arising between this group and the migrating aryl group in **120**. However, this is highly speculative and the exact reason(s) responsible for the unique regioselectivities observed require future theoretical and experimental studies.

Scheme 3.3 FeCl₃-catalyzed dimerization of enantioenriched **106f**.

3.3 Conclusion

In conclusion, a novel iron-catalyzed route to highly conjugated indenenes based on dimerization of trisubstituted propargylic alcohols has been reported. This chemoselective carbocycle forming method was shown to proceed under very mild conditions at room temperature and provide product yields and regioselectivities comparable to those reported for the analogous reactions with propargylic acetates and indoles catalyzed by gold salts.^{81h,81n} In reactions where the substrate contained a sterically bulky alkyl group at the carbinol carbon, the indene forming process was also shown to proceed with complete regioselectivity. Moreover, it makes use of alcohol substrates and an iron catalyst that are inexpensive, easily accessible and ecologically benign.

Chapter IV. Gold-Catalyzed Tandem Amination/Ring Expansion of Cyclopropyl Methanols with Sulfonamides as an Expedient Route to Pyrrolidines

4.1 Introduction

Gold complexes have emerged as powerful and versatile Lewis acidic catalysts for stereoselective carbon-nitrogen bond formation in recent years.^{25,32,35,49,76,84d} Generally, this type of reaction relies on interaction of the gold catalyst with the π -bonds of alkenes, alkynes, and allenes. In this regard, the development of new methods that explore the scope of other functional groups in gold-catalyzed reactions has gained momentum. A recent notable advance is that by Campagne, Prim, and co-workers, who showed benzylation and propargylation of anilines, azides, and sulfonamide with benzylic and propargylic alcohols to proceed smoothly in the presence of $\text{NaAuCl}_4 \cdot 2\text{H}_2\text{O}$ as catalyst.^{32,93} Following this seminal work, Liu and co-workers reported a similar efficient AuCl_3 -mediated approach for the allylic alkylation of *p*- TsNH_2 with allylic alcohols.²⁰ More recently, the groups of Liu²⁶ and Liang²⁵ independently described gold-catalyzed tandem amination/intramolecular hydroamination strategies for the synthesis of pyrroles from 1-en-4-yn-3-ols could also be accomplished. In view of these works and on ongoing program on carbon-nitrogen bond formation,⁹⁴ we turned our attention to expanding the scope of alcohols as pre-electrophiles in gold catalysis as the basis for developing new strategies for constructing pyrrolidines.

The pyrrolidine ring motif is a common structural unit found in a myriad of bioactive natural products and pharmaceutically interesting compounds.⁹⁵⁻¹⁰⁰ These include anatoxin,⁹⁶ hyacinthacine C_1 ,⁹⁷ (-)-kainic acid,⁹⁸ oxazolomycin A,⁹⁹ and (+)-preussin (Scheme 4.1),¹⁰⁰ which are reported to exhibit bioactivities ranging from

antiviral to cytotoxic. Hence, developing methods for efficient formation of this saturated nitrogen-containing heterocycle is of immense importance in organic synthesis. Recently, Krause et al.¹⁰¹ and He et al.¹⁰² respectively, described gold-catalyzed cycloisomerization of α -amino allenes and intra- and intermolecular hydroamination of alkenes as mild, efficient, and atom economic strategies⁵ for pyrrolidine ring synthesis. Following these works, Shi et al.¹⁰³ and Togni et al.¹⁰⁴ independently reported that tandem versions of gold-catalyzed hydroaminations involving reactions of methylene cyclopropanes (MCPs) or vinyl cyclopropanes (VCPs) with sulfonamides are also efficient preparative methods. A synthetic approach that also relies on the exceptional activity and mild conditions offered by homogenous gold catalysis but makes use of substituted cyclopropyl methanols as aminocyclization of amino-tethered allylic alcohols has been described,^{3b,3d,105} the reactions usually require relatively high catalyst loadings and additives. In addition, limited examples demonstrating substrate scope and moderate to good regio- and chemoselectivities have lessened their utility in organic synthesis. In this regard, we envisioned that a gold-catalyzed

Scheme 4.1 Examples of bioactive compounds containing a pyrrolidine moiety.

strategy involving the use of substituted cyclopropyl methanols as pro-electrophiles would be attractive from a synthetic standpoint, as the ease of preparing the alcohol starting material provides the possibility to introduce a wide variety of substituents and the potential to form a quaternary carbon center by addition to a tertiary alcohol. Moreover, H₂O is potentially the only side product. Herein we report a convenient synthetic route to pyrrolidine derivatives that involves tandem amination/ring expansion of substituted cyclopropyl methanols and sulfonamides catalyzed by AuCl in the presence of AgOTf as a co-catalyst (Scheme 4.2). The reaction proceeds in good to excellent yields of up to 95% for a wide variety of readily available starting materials.

Scheme 4.2 Gold-catalyzed tandem amination/ring expansion of cyclopropylmethanols with sulfonamides.

4.2 Results and Discussion

First, we chose cyclopropyl(phenyl)methanol **122a** and *p*-TsNH₂ **13a** as model substrates to establish the reaction conditions (Table 4.1). The best result was obtained by treatment of 1 equiv of **122a** and 2 equiv of **13a** with 5 mol % of AuCl and 5 mol % of AgOTf in toluene at 100 °C for 15 h, which furnished **123a** as the sole product in 95% yield (Table 4.1, entry 1). The pyrrolidine product was confirmed by ¹H and ¹³C NMR analysis and X-ray crystal structure determination (Figure 4.1).¹⁰⁷ Notably, a slightly lower yield of 91% could be obtained on lowering the catalyst loa-

Table 4.1 Optimization of reaction conditions.^a

Entry	Catalyst	Solvent	Yield (%) ^b			
			123a	124a	125a	126a
1	AuCl/AgOTf	PhMe	95	-	-	-
2 ^c	AuCl/AgOTf	PhMe	91	-	3	-
3	AuCl/AgOTf	CHCl ₃	40	44	-	-
4	AuCl/AgOTf	(CH ₂ Cl) ₂	67	-	trace	-
5	AuCl/AgOTf	MeCN	-	-	-	33
6	AuCl/AgOTf	THF	-	-	-	-
7	Ph ₃ PAuCl/AgOTf	PhMe	80	-	2	-
8	Ph ₃ PAuCl/AgSbF ₆	PhMe	42	40	trace	-
9	AuCl ₃ /AgOTf	PhMe	72	10	trace	-
10	AuCl	PhMe	-	-	-	-
11	AuCl ₃	PhMe	-	-	-	15
12	AgOTf	PhMe	-	-	-	80
13	FeCl ₃ ·6H ₂ O	PhMe	-	-	-	21
14	Yb(OTf) ₃	PhMe	-	22	-	55
15	Cu(OTf) ₂	PhMe	83	-	trace	-
16	InCl ₃	PhMe	-	-	-	-

Table 4.1 (*continued*).

Entry	Catalyst	Solvent	Yield (%) ^b			
			123a	124a	125a	126a
17	ZnCl ₂	PhMe	-	-	-	-
18	BF ₃ .Et ₂ O	PhMe	-	66	3	-
19	TfOH	PhMe	71	trace	2	-
20 ^d	TfOH	PhMe	87	-	-	-
21	<i>p</i> -TsOH.H ₂ O	PhMe	-	28	-	-
22	TFA	PhMe	-	-	-	29

^aAll reactions were performed at 100 °C for 15 h with catalyst: **122a**: **13a** ratio = 1:20:40. ^bIsolated yield. ^cReaction conducted with a catalyst loading of 2 mol %.

^dReaction conducted with TfOH catalyst loading of 20 mol %.

ding of both AuCl and AgOTf to 2 mol % (Table 4.1, entry 2). In contrast, performing the reaction in other solvents gave **123a** in markedly lower yields and with a variety of side products. Use of chlorinated solvents such as CHCl₃ and 1,2-dichloroethane afforded either (*E*)-4-methyl-*N*-(4-phenylbut-3-enyl)benzene sulfonamide **124a** as the major product in 44% yield or 4-methyl-*N,N*-bis[(*E*)-4-phenylbut-3-enyl]benzenesulfonamide **125a** in a trace amount (Table 4.1, entries 3 and 4). On the other hand, when the solvent was changed to MeCN, *N*-[cyclopropyl-(phenyl)methyl]-4-methylbenzenesulfonamide **126a** was preferentially obtained as the sole product in 33% yield, while the use of THF as solvent resulted in a mixture of side products that could not be identified by ¹H NMR analysis (Table 4.1, entries 5 and 6). The structure of **126a** was confirmed by ¹H NMR analysis and X-ray crystal analysis of a closely related product (see below). Inspection of entries 7-22 in Table 4.1 reveals that

tandem amination/ring expansion of **122a** with **13a** in the presence of other Lewis and Brønsted acids as catalyst are less effective. When Ph_3PAuCl was used in combination with AgOTf or AgSbF_6 , or AuCl_3 with AgOTf , lower product yields of 42-80% were obtained (Table 4.1, entries 7-9). Moreover, in these reactions the use of Ph_3PAuCl and AgOTf resulted in formation of **124a** as a side product while those mediated by $\text{Ph}_3\text{PAuCl}/\text{AgSbF}_6$ or $\text{AuCl}_3/\text{AgOTf}$ gave both **124a** (10-40%) and **125a** (trace) as side products. A similar outcome was found when reactions employing single Lewis acid catalysts such as AuCl , AuCl_3 , AgOTf , $\text{Cu}(\text{OTf})_2$, $\text{FeCl}_3 \cdot 6\text{H}_2\text{O}$, InCl_3 and $\text{Yb}(\text{OTf})_3$ were examined (Table 4.1, entries 10-17). In our hands, reaction with $\text{Cu}(\text{OTf})_2$ as catalyst afforded **123a** in a lower yield of 83% and a trace amount of **125a** (Table 4.1, entry 15). However, the reactions mediated by AuCl_3 , AgOTf , $\text{FeCl}_3 \cdot 6\text{H}_2\text{O}$ and $\text{Yb}(\text{OTf})_3$ were found to preferentially furnished **126a** in 15-80% yield along with a variety of byproducts that could not be identified by ^1H NMR measurements; **124a** was also afforded in 22% yield with $\text{Yb}(\text{OTf})_3$ as catalyst (Table 4.1, entries 11-14). A switch in chemoselectivity was further observed on employing $\text{BF}_3 \cdot \text{Et}_2\text{O}$, which afforded **124a** and **125a** in yields of 66 and 3%, respectively (Table 4.1, entry 18).

We also examined the Brønsted acid catalysts TfOH , $p\text{-TsOH} \cdot \text{H}_2\text{O}$ and TFA (Table 4.1, entries 19-22). The reaction of **122a** with **13a** in the presence of 5 mol % of TfOH as catalyst was the only case in which the desired product **123a** was furnished in 71% yield along with a trace amount of **124a** and **125a** in 2% yield. (Table 4.1, entry 19). Efficient transformation to the product in 87% yield was only achieved when the reaction was repeated with an increased catalyst loading of 20 mol% of TfOH catalyst (Table 4.1, entry 20). Based on recent results of He and co-workers and our earlier findings for the analogous AgOTf -catalyzed reaction (Table

4.1, entry 12), this and the significantly lower concentration of TfOH in 5 mol% of AuCl/AgOTf also provides evidence that the cationic gold(I) complex is the active species.¹⁰⁶ In contrast to the activity exhibited by TfOH, when *p*-TsOH·H₂O was employed as catalyst, the reaction was found to give **124a** exclusively in 28% yield, while **126a** was the only product in 29% yield on changing catalyst to TFA (Table 4.1, entries 21 and 22). In each of these reactions, a wide variety of side products was also obtained which could not be separated by flash column chromatography or identified by ¹H NMR analysis of the crude mixtures.

Figure 4.1 ORTEP drawing of **123a** with thermal ellipsoids at 50% probability levels.¹⁰⁷

To investigate the scope of the AuCl/AgOTf-catalyzed tandem amination/ring-expansion reaction, we applied these conditions to a series of substituted cyclopropyl methanols (Table 4.2). Reactions of substituted cyclopropyl methanols containing a pendant electron-donating group with *p*-TsNH₂ **13a** afforded the corresponding pyrrolidine compounds **123b**, **c** and **123g** in yields of 81-91% (Table 4.2, entries 1, 2,

and 6). Similarly, analogous reactions of **122e** and **122f** containing electron-withdrawing groups with **13a** afforded the corresponding pyrrolidine products **123e** and **123f** in comparable yields of 77-84% (Table 4.2, entries 4 and 5). Substituted cyclopropyl methanols **122h** and **122i** bearing a sterically bulky 2,6-dimethylbenzene or naphthyl group, respectively, were found to be good alcoholic substrates affording good product yields (Table 4.2, entries 7 and 8). Similarly, tertiary substituted cyclopropyl methanols **122k**, **1** gave the corresponding quaternary substituted pyrrolidines **123k**, **1** in 60-68% yield (Table 4.2, entries 10 and 11). More notably, **123m-p** could be obtained in moderate from the respective reactions of **122o-r** with **13a** (Table 4.2, entries 14-17). Although a slightly higher catalyst loading of 10 mol% was required, this demonstrated that the present method is also suitable for unactivated alkylsubstituted cyclopropyl methanols. On the other hand, extreme steric effects of tertiary substituted cyclopropyl methanols may play a role, since two bulky geminal groups, such as two benzene rings, led to preferential provided acyclic but-3-enylsulfonamide **124b** in 81% yield (Table 4.2, entry 12). Strongly electron donating pendant groups such as alkynyl and methoxyphenyl on the alcohol substrate also detrimentally influenced the C–N bond forming process. Both **123f** and **123j**, which was also structurally characterized by X-ray crystal analysis (Figure 4.2).¹⁰⁷ Similarly, reaction of alkyne **122n** with **13a** was found to result in formation of acyclic enyne **124c** as the sole product in 69% yield with a *cis:trans* ratio of 1:1 (Table 4.2, entry 13).¹⁰⁸ Retardation of reaction by a strongly electron-donating substituent on the substrate has also been reported by the group of Shi.¹⁰³ and Hartwig¹⁰⁹ in their approaches to pyrrolidines.

Table 4.2 AuCl/AgOTf-catalyzed tandem amination/ring expansions of **122b-r** with **13a**.^a

Entry	Alcohol	Product	Yield (%) ^b
1		123b , R= Me	81
2	122b-f	123c , R= ^t Bu	91
3		123d , R= OMe	31
4		123e , R= F	84
5		123f , R= Cl	77
6	122g	123g	89
7	122h	123h	70
8	122i	123i	80
9	122j	123j	34
10	122k-l	123k , R= H	60
11		123l , R= F	68
12	122m	124b	81

Table 4.2 (continued).

Entry	Alcohol	Product	Yield (%) ^b
13	122n	124c	69 ^d
14 ^c	122o-p	123m , $n = 7$	50
15 ^c	122o-p	123n , $n = 11$	37
16 ^c	122q-r	123o , $n = 1$	32
17 ^c	122q-r	123p , $n = 2$	44

^aAll reactions were performed at 100 °C for 15 h with catalyst: **122a**: **13a** ratio = 1: 20: 40. ^bIsolated yield. ^cReaction conducted with a catalyst loading of 10 mol %. ^dIsolated as a mixture of *cis:trans* isomers in 1:1 ratio.

To further explore the scope of the AuCl/AgOTf-catalyzed reactions, the tandem amidation/ring expansion of **122a** with a variety of different nitrogen nucleophiles was examined (Table 4.3). Under the standard conditions, reaction of **122a** with benzenesulfonamide **13b** gave **123q** in 84% yield and 4- bromobenzenesulfonamide **13c** gave the corresponding pyrrolidine product **123r** in 68% yield (Table 4.3, entries 1 and 2). In contrast, a markedly lower product yield was obtained when 4-nitrobenzenesulfonamide **13d** was employed as nucleophile, presumably due its significantly lower nucleophilicity (Table 4.3, entry 3). On the other hand, the use of a more nucleophilic sulfonamide such as **13e**, which contains a para-methoxyphenyl

(a) **123f** (b) **123j**

Figure 4.2 ORTEP drawing of (a) **122f** and (b) **123j** with thermal ellipsoids at 50% probability levels.¹⁰⁷

group, was found to result in no reaction on the basis of both TLC and ^1H NMR analysis (Table 4.3, entry 4). In addition, the analogous reactions of **122a** with carbamates such as **14a**, **14b** did not proceed as anticipated. Under the optimized conditions, these reactions were found to afford amidated cyclopropanes **126b** and **126c** as the sole adducts in 85 and 73% yield, respectively (Table 4.3, entries 5 and 6). In both cases, formation of the desired pyrrolidine adduct could not be detected by ^1H NMR analysis on increasing the catalyst loading to 10 mol % or increasing the reaction time to 36 h.

Table 4.3 AuCl/AgOTf-catalyzed reaction of **122a** with **13b-e** and **14a-b**.^a

		13b , R = H	14a , R = <i>t</i> -Bu	
		13c , R = Br	14b , R = Bn	
		13d , R = NO ₂		
		13e , R = OMe		
Entry	Nucleophile	Product		Yield (%) ^b
1	13b		123q , R = H	84
2	13c		123r , R = Br	68
3	13d		123s , R = NO ₂	31
4	13e			- ^c
5	14a		126b , R = <i>t</i> -Bu	85
6	14b		126c , R = Bn	73

^aAll reactions were performed at 100 °C in toluene for 24 h with AuCl/AgOTf: **122a**: **13** or **14** ratio = 1: 20: 40. ^bIsolated yield. ^cNo reaction.

Competitive formation of **124a** and **126a** under certain conditions during the reactions of **122a** with **13a** outlined in Table 4.1 led us to initially speculate on their possible involvement as intermediates in the present AuCl/AgOTf-catalyzed procedure. To support this hypothesis and gain a better understanding of the reaction mechanism, we conducted the following experiments using **122a** and **13a** as probe substrates. Treatment of these starting materials with 5 mol % of AuCl and AgOTf in toluene for 15 h at room temperature gave **126a** as the only product in 95% yield (Table 4.4, entry 1). Under these modified conditions, reactions of **13a** with cyclopropyl methanols bearing electron-withdrawing, electron-donating, and sterically demanding substituents also proceeded in a similar manner at room temperature to give the corresponding substituted cyclopropyl sulfonamides **126d-h** in yields of 61-99% (Table 4.4, entries 2-6). The structure of **126h** was established by X-ray crystallography (Figure 4.3).¹⁰⁷ On the other hand, **124a** was exclusively furnished in 93% yield by the analogous AuCl/AgOTf-catalyzed reaction of **122a** and

Figure 4.3 ORTEP drawing of (a) **126h** with thermal ellipsoids at 50% probability levels.¹⁰⁷

Table 4.4 AuCl/AgOTf-catalyzed aminations of **122a-j** with **13a**.^a

Entry	Alcohol	Product	Yield (%) ^b
1	122a	126a , R = H	95
2	122d	126d , R = OMe	95
3	122e	126e , R = F	87
4	122h	126f	61
5	122i	126g	91
6	122j	126h	99

^aAll reactions were performed at room temperature in toluene for 15 h with AuCl/AgOTf: **122**: **13a** ratio = 1: 20: 40. ^bIsolated yield.

and **13a** at 100 °C for 1 h. In both instances, conversion to **123a** from **124a** in 93% yield and from **126a** in 70% yield was found on re-treating these compounds under the standard conditions of 5 mol % of AuCl and AgOTf in toluene at 100 °C for 15 h (Scheme 4.3).¹¹⁰ In the latter case, monitoring the reaction by ¹H NMR spectroscopy revealed complete conversion of **126a** to a mixture of **123a** and **124a** in a ratio of 1:2 after 1 h. This suggested a pathway by which generation of an intermediate that

closely resembles could precede product formation. The possible involvement of such a species would also account for our findings on the reaction of enantiopure **122a** with **13a**. Under our experimental conditions, pyrrolidine adduct **123a** was obtained as a racemic mixture in 93% yield, as shown in Scheme 4.4.¹¹¹

Scheme 4.3 AuCl/AgOTf-catalyzed conversion to **123a** from **124a** and **126a**.

Scheme 4.4 AuCl/AgOTf-catalyzed tandem amination/ring expansion of enantiopure **122a** with **13a**.

On the basis of the above results, we tentatively propose the present AuCl/AgOTf catalyzed pyrrolidine-forming reaction to proceed by the mechanism outlined in Scheme 4.5, although it is highly speculative. In a manner similar to that put forward by us,^{84d} Campagne et al.³² and Aponick et al.²⁷, we postulate that the gold/silver catalyst combination activates alcohol substrate **122** by coordinating to the oxygen atom. This affords gold(I)-coordinated cyclopropyl methanol **127**, which can undergo elimination to give carbocation intermediate **128** and [Au]-OH, which releases the gold catalyst by protodemetalation. It is possible that this newly formed cationic species could initially react with **13** to produce cyclopropyl sulfonamide **126** (route *a* in Scheme 4.5). However, as the introduced sulfonamide functionality can also be activated by coordination to the catalyst, the C–N bond-forming step may be

reversible, and the carbocation intermediate is reformed as quickly as it is amidated. Alternatively, as shown in *route b* in Scheme 4.5, the amidation step could be skipped altogether, and ring opening of the cyclopropane moiety of **128** followed by trapping with **13** directly furnishes acyclic sulfonamide **124**. Subsequent coordination to the catalyst might be expected to give the gold(I)-activated alkene species **130**, which is the active species that undergoes intramolecular hydroamination to afford the pyrrolidine product. A similar cyclization step was proposed by Shi and co-workers for the gold(I)-catalyzed tandem ring opening/ring-closing hydroamination of MCPs.¹⁰³

Scheme 4.5 Tentative mechanism for AuCl/AgOTf-catalyzed tandem amination/ring expansion of substituted cyclopropylmethanols with sulfonamides.

Although a number of pathways are conceivable, we surmise that the mechanism of the present procedure is likely to proceed *via* ring-opening of the cyclopropane moiety of **128** irrespective of whether the reaction follows *routes a* and *b* or only *route b* in Scheme 4.5. This is supported by our isolating **123a** and **123q** in yields of 47 and 36%, respectively, from the crossover reaction of 1 equiv of **13a** with 1 equiv

of **13b** in the presence of 5 mol % of AuCl/AgOTf under the conditions described in Scheme 4.6. A similar outcome was also obtained on repeating the reaction with 5 mol % of TfOH as catalyst, which furnished **123a** and **123q** in yields of 42 and 31%, respectively. The origin of the *N, N*-substituted sulfonamide side product **125** could be due to the acyclic adduct **124** competing with **13** in trapping the species resulting from fragmentation of **128**. More notably, the manner in which the catalyst can efficiently coordinate to the alcohol substrate and resultant intermediates formed during the tandem C-N bond forming process proposed in Scheme 4.5 seems to be a pivotal aspect of the present procedure. This is evident in a number of experiments examined in this work. First, the role of AgOTf in producing a more electrophilic gold catalyst that can participate in substrate coordination seems to be crucial for the reaction to proceed smoothly, since neither AgOTf nor AuCl was found to be an effective catalyst. Moreover, the outcome of the reaction is influenced by the nature of the solvent: polar solvents such as CHCl₃, 1,2-dichloroethane, MeCN, and THF have a detrimental effect on both product yields and chemoselectivity. This also appears to be operative when such interactions are presumably weakened due to competitive coordination with a very electron rich neighbor on the alcohol substrate or nitrogen nucleophile, such as a methoxyphenyl or alkyne moiety, as in **122d**, **122j**, **122n**, and **122e**. We found that in each of these cases, either markedly lower product yields or the acyclic enyne adduct were obtained or no reaction could be detected. Indeed, this is further supported by the fact that when a solution of toluene containing **126h** was treated with 5 mol % of AuCl/AgOTf at 100 °C for 15 h, the expected pyrrolidine **123j** was obtained in a yield of 37%, comparable to those found for the analogous reactions of **122d** and **122j** (Scheme 4.7).

Scheme 4.6 AuCl/AgOTf-catalyzed ring expansion of **126a** with **13b**.

Scheme 4.7 AuCl/AgOTf-catalyzed ring expansion of **126h**.

4.3 Conclusion

We have described an efficient AuCl/AgOTf-catalyzed strategy for formation of pyrrolidine derivatives, including examples with quaternary centers, starting from substituted cyclopropyl methanols. The method is applicable to a wide range of activated and unactivated substituted cyclopropyl methanol and sulfonamide substrates containing electron-withdrawing, electron-donating, and sterically-demanding substituents. In addition, the gold-catalyzed tandem reaction exhibits excellent catalytic activity at low catalyst loadings. When the reactions were conducted at room temperature, *N*-cyclopropylmethyl sulfonamides were formed chemoselectively. Our studies suggest activation of the substituted cyclopropyl methanol substrate by the gold catalyst, which leads to ionization of the alcohol. This possibly triggers subsequent ring opening of the cyclopropane moiety followed by trapping with the sulfonamide nucleophile to give an acyclic aminated intermediate that undergoes intramolecular hydroamination to form the pyrrolidine product. Our studies revealed that TfOH can also mediate the tandem amidation/ring expansion

process, but the lower product yields and selectivities exhibited by TfOH along with the significantly milder conditions of gold catalysis provides an attractive alternative synthetic approach for the formation of pyrrolidines. While the findings of this study suggest it is unlikely that TfOH potentially generated *in situ* is the true species promoting the reaction, it also demonstrates the care required when interpreting such results, given the similar reactivities exhibited by both gold and Brønsted acid catalysts.

Chapter V. Ytterbium(III) Triflate-Catalyzed Amination of 1-Cyclopropylprop-2-yn-1-ols as an Expedient Route to Conjugated Enynes

5.1 Introduction

Establishing methods to conjugated enynes is currently an active area in organic synthesis due to their frequent use as building blocks in numerous strategies to compounds of biological and material interest.¹¹² While this has led to a myriad of works devoted to this reaction, the number of methods that can install this unsaturated hydrocarbon moiety without competitive formation of undesired regio- and stereoisomers has remained sparse.^{112,113} For this reason, the development of new synthetic routes to conjugated enynes in an efficient and stereoselective manner continues to be actively pursued. In a recent notable advance, Nishibayashi and co-workers demonstrated that *trans*-substituted conjugated enynes could be obtained from regioselective diruthenium(II, III)-catalyzed ring opening of terminal 1-cyclopropyl-2-propyn-1-ols with aniline.^{108a} Following this seminal work, we^{84c} and Liang⁶² showed this atom economical ring opening process, which produces H₂O as potentially the only byproduct, to be applicable to a variety of substituted 1-cyclopropyl-2-propyn-1-ols and sulfonamide and alcohol nucleophiles using gold catalysis. However, this method would also greatly benefit from the use of cheaper and commercially available catalysts, such as lanthanide complexes. To our knowledge, synthetic approaches that explore combining rare earth metals as strong Lewis acidic catalysts¹ with alcohol pro-electrophiles³ have thus far been limited to benzylation and allylation of aromatic and 1,3-dicarbonyl compounds with benzylic and allylic alcohols.¹¹ As part of an ongoing program examining the utility of alcohols as building blocks in organic synthesis,⁸⁴ we report in this work the use of Yb(OTf)₃

for ring opening of substituted 1-cyclopropyl-2-propyn-1-ols with sulfonamides (Scheme 5.1). The conjugated enyne products were afforded in yields and regioselective manner comparable to those reported for the closely related Ru₂- or Au-promoted approaches to this synthetically useful building block.

Scheme 5.1 Regioselective Yb(OTf)₃-catalyzed formation of conjugated enynes from cyclopropylprop-2-yn-1-ols **131**.

5.2 Results and Discussion

Initially, we chose to focus our attentions on the nucleophilic ring opening of 1-cyclopropyl-1,3-diphenylprop-2-yn-1-ol **131a** with *p*-TsNH₂ **13a** by a variety of Lewis and Brønsted acid catalysts to establish the reaction conditions (Table 5.1). This revealed that treating a toluene solution containing 1 equiv of **131a** and 2 equiv of *p*-TsNH₂ **13a** with 5 mol % of Yb(OTf)₃ at 100 °C for 5 h gave the best result (Table 5.1, entry 1). Under these conditions, (*Z*)-*N*-(4,6-diphenylhex-3-en-5-ynyl)-4-methylbenzene sulfonamide **132a** was afforded in 75% yield, comparable to those obtained for the closely related Ru₂- and Au-catalyzed reactions with terminal or activated starting alcohols.^{62,108a} The *cis*-stereochemistry of the conjugated enyne product was confirmed by comparison with NOSEY spectroscopic data of closely related adducts and reported literature values.^{62,108a} In our hands, the dimeric

Table 5.1 Optimization of the reaction conditions.^a

Entry	Catalyst	Solvent	Yield (%) ^b		
			132a	133a	134a
1	Yb(OTf) ₃	PhMe	75	- ^c	- ^c
2	Yb(OTf) ₃	DCE	55	-	28
3	Yb(OTf) ₃	MeCN	- ^c	-	-
4	Yb(OTf) ₃	THF	- ^c	-	-
5	PPh ₃ AuCl/AgOTf	PhMe	62	13	- ^c
6	AuCl/AgOTf	PhMe	73	4	- ^c
7	AuCl	PhMe	- ^d	-	-
8	Cu(OTf) ₂	PhMe	54	-	6
9	AgOTf	PhMe	39	6	- ^c
10	InCl ₃	PhMe	- ^d	-	-
11	FeCl ₃ ·6H ₂ O	PhMe	- ^d	-	-
12	TsOH·H ₂ O	PhMe	- ^d	-	-
13	TfOH	PhMe	23	3	-

^aAll reactions were performed at 100 °C for 5 h with catalyst: **131a**: **13a** ratio of 1: 20: 40. ^bIsolated yield. ^cTrace amount of compound isolated after flash column chromatography. ^dNo reaction.

byproducts **133a** and **134a** were also isolated in trace amounts. Similarly, performing the reaction in and **134a** were also isolated in trace amounts. Similarly, performing the reaction in other solvents was found to be less effective (Table 5.1, entries 2-4). When 1, 2-dichloroethane was employed as the solvent, a lower product yield of 55% along with **134a** in a higher yield of 28% was obtained (Table 5.1, entry 2). On the other hand, TLC and ^1H NMR analysis of crude mixtures of reactions conducted in either MeCN or THF detected only the starting alcohol and sulfonamide, which were recovered in near quantitative yields (Table 5.1, entries 3 and 4). The reactions utilizing gold catalysts such as $\text{PPh}_3\text{AuCl}/\text{AgOTf}$, AuCl/AgOTf and AuCl were examined (Table 5.1, entries 5-7). When Ph_3PAuCl was used in combination with AgOTf , lower product yields of 62% along with **133a** in yield of 13% was obtained (Table 5.1, entry 5). Reaction with the AuCl/AgOTf combination as catalyst afforded **132a** in a yield of 73% that was comparable to that obtained with $\text{Yb}(\text{OTf})_3$ as catalyst (Table 5.1, entry 6). On the other hand, no product were observed and both starting material were recovered in near quantitative yields when AuCl was used as the catalyst (Table 5.1, entry 7). An inspection of entries 8-13 in Table 5.1 also revealed the reaction proceeded less well with other common and commercially available Lewis and Brønsted acid catalysts. In these latter reactions, the use of $\text{Cu}(\text{OTf})_2$ and AgOTf and TfOH resulted in the formation of **132a** in markedly lower yields along with slightly higher yields of either or both **133a** and **134a** (Table 5.1, entries 8 and 9). However, switching the catalyst to InCl_3 , $\text{FeCl}_3 \cdot 6\text{H}_2\text{O}$, or $\text{TsOH} \cdot \text{H}_2\text{O}$ was found to result in no reaction observed on the basis of TLC analysis (Table 5.1, entries 10-12). A low product yield of 23% obtained for the analogous TfOH -mediated reaction also provided evidence that, in the presence of potentially TfOH , the cationic $\text{Yb}(\text{III})$ complex is the catalytically active species (Table 5.1, entry 13).

To define the scope of the present procedure, we next turned our attentions to the reactions of a variety of unactivated 1-cyclopropyl-2-propyn-1-ols with **13a** (Table 5.2). Reactions of substituted 1-cyclopropyl-2-propyn-1-ols containing a pendant electron-withdrawing group on the carbinol carbon with **13a** gave the corresponding conjugated enyne products **132b-d** in yields of 67-70% (Table 5.2, entries 1-3). Similarly, the analogous reaction of **131e**, which contains electron-donating groups at both the alkyne and carbinol carbon centers, with **13a** affords the corresponding product **132e** in 56% yield (Table 5.2, entry 4). Likewise, the substituted 1-cyclopropyl-2-propyn-1-ol **131f** bearing a sterically bulky naphthylene group was found to proceed well and afford **132f** in a good yield (Table 5.2, entry 5). The present procedure was also shown to work well for 1-cyclopropyl-2-propyn-1-ols containing alkyl and aryl substituent combinations, giving **132h** and **132j-l** in 55-73% yield (Table 5.2, entries 7 and 9-11). However, moderate yields were obtained for reactions with alcohols containing a cyclopropane group on the alkyne moiety or a terminal acetylene group as in **131g** and **131i** (Table 5.2, entries 6 and 8). On the other hand, starting alcohols with pendant thiophene functionalities provided the corresponding conjugated enyne products in good yields (Table 5.2, entries 12-14). This is noteworthy as such aromatic ring structures are commonly found in a myriad of bioactive natural and pharmaceutical compounds.¹¹⁴ Under the standard conditions, reaction of **131p** with **13a** was the only case that was found to be ineffective, giving no product formation based on TLC and ¹H NMR analysis and recovery of the starting alcohol in near quantitative yield (Table 5.2, entry 15). A possible reason for this could be due to preferential coordination of the Yb catalyst to the pyridyl moiety that, in turn, prevents activation of the OH functional group.

Table 5.2 Yb(OTf)₃-catalyzed amidation of **131b-p** with **13a**.^a

Entry	Alcohol	Time (h)	Product	Yield (%) ^b
1	131b-e	2	132b , R ¹ = H R ² = F	70
2		2	132c , R ¹ = H R ² = Cl	67
3		4	132d , R ¹ = H R ¹ = Br	68
4		12	132e , R ¹ = Me R ¹ = OMe	56
5	131f	7	132f	70
6	131g-h	2	132g , R = H	30
7		1.5	132h , R = Bn	55
8	131i	5	132i	40
9	131j-k	2	132j , R = OMe n = 3	59
10		3	132k , R = H n = 5	73
11	131l	2	132l	72 ^c
12	131m	3	132m	67

Table 5.2 (*continued*).

Entry	Alcohol	Time (h)	product	Yield (%) ^b
13	131n	4	132n	67
14	131o	2	132o	61
15	131p	24	132p	- ^d

^aAll reactions were performed at 100 °C with Yb(OTf)₃: **131**: **13a**: ratio of 1: 20: 40.

^bIsolated yield. ^cIsolated as a mixture of *Z/E* isomers in a ratio = 83: 17. ^dNo reaction based on TLC and ¹H NMR analysis of the crude mixture.

Depending on the nature of the substituent on the carbinol carbon of the alcohol substrate, the products shown in Table 5.2 were exclusively obtained as either the *Z*-isomer for alkyl or aryl groups on the carbinol carbon in all except one case. Similarly, the *E*-product was furnished for heteroarene groups on the carbinol carbon.¹¹⁵ The *trans*-stereochemistry in **132e** and **132g** and *cis*-stereochemistry in **132m** were also confirmed by NOE analysis. Reaction of **131l** was the only instance in which the corresponding enyne adduct was obtained as a mixture of *Z* and *E* isomers in a ratio of *Z/E* = 83:17 (Table 5.2, entry 11). A similar effect of a bulky substituent at the carbinol carbon of the substrate on product regioselectivity has also been reported in the analogous Ru₂- and Au-mediated approaches.^{62,108a}

Table 5.3 Yb(OTf)₃-catalyzed amidation of **131a** with nitrogen nucleophiles.^a

<div style="display: flex; justify-content: space-around; align-items: center;"><div style="text-align: center;"> <p>13b, R = H 13e, R = OMe 13f, R = Cl</p></div><div style="text-align: center;"> <p>14a</p></div><div style="text-align: center;"> <p>16b</p></div><div style="text-align: center;"> <p>135</p></div></div>					
Entry	NuH	Time (h)	Product	Yield (%) ^b	
1	13b	5	132q , R = H	60	
2	13e	1	132r , R = OMe	80	
3	13f	2	132s , R = Cl	69	
4	14a	24	132t	15	
5	16b	12	132u	31	
6	135	6	136a	62	

^aAll reactions were performed at 100 °C with Yb(OTf)₃: **131a**: NuH: ratio of 1: 20: 40. ^bIsolated yield.

To further explore the scope of the Yb(OTf)₃-catalyzed reactions, the ring opening of **131a** with a variety of different nitrogen nucleophiles was examined (Table 5.3). Under the standard conditions, reaction of **131a** with benzenesulfonamide **13b** afforded **132q** in 60% yield (Table 5.3, entry 1). Under similar conditions, arylsulfonamides **13e** and **13f**, which contain either a *para*-substituted electron-donating or electron-withdrawing group, respectively, were found to be good nitrogen sources, giving the corresponding conjugated enynes **132r** and **132s** in yields of 69–80% (Table 5.3, entries 2 and 3). In contrast, other nitrogen sources such as *tert*-butyl carbamate **14a**, aniline **15b**, and *N*-aminophthalimide **135** were found to be less effective (Table 5.3, entries 4–6). Interestingly, the analogous reaction with **14a** gave the deprotected amino-enyne adduct **132t**, albeit in a markedly lower yield of 15% along with recovery of **131a** in 55% yield (Table 5.3, entry 4). When aniline **15b** was employed as the nucleophile, the reaction was found to proceed to give **132u** in 31% yield along with a mixture of byproducts that could not be identified by ¹H NMR analysis (Table 5.3, entry 5). In addition, reaction of **131a** with a more nucleophilic nitrogen source such as **135** did not proceed as anticipated. Under our experimental conditions, the reaction afforded amino-substituted adduct **136a** as the sole product in 62% yield (Table 5.3, entry 6).

We tentatively propose the present Yb(OTf)₃-catalyzed conjugated enyne forming reaction to proceed by the mechanism outlined in Scheme 5.2, although it is highly speculative. This could involve activation of the alcohol substrate through coordination with the hydroxyl functionality. This delivers an ytterbium(III)-chelated intermediate **137** which can undergo elimination to give a putative carbocation species **138** and [Yb]-OH, which releases the metal catalyst by protodemetalation. It is possible that this newly formed cationic species subsequently undergoes cycloprop-

Scheme 5.2 Tentative Mechanism for $\text{Yb}(\text{OTf})_3$ -Catalyzed Amination of 1-Cyclopropylprop-2-yn-1-ols with Sulfonamides.

ylcarbinol homoallylic rearrangement and trapping with **13** to deliver the enyne **132**.¹¹⁶ The obtained *E/Z* product stereoselectivities could be due to the carbocation intermediate **138** adopting the conformer shown in Scheme 5.2 that would control unfavorable steric interactions between the substituents and cyclopropane ring protons.¹¹⁶ The role of the catalyst in facilitating dehydroxylation of the alcohol substrate would account for our earlier findings showing no product formation for the reaction of **131p** with **13a** (Table 5.2, entry 15). It would not be inconceivable that such interactions are presumably weakened due the introduction of a strongly coordinating pyridine moiety on the alcohol substrate. The origin of the *N*, *N*-aminophthalimide product **136a** could be due to direct attack of this resultant carbocation species by **135** before ring fragmentation could occur. Indeed, this is further supported by the fact that, when a toluene solution containing **131a** was treated with indole under the conditions shown in Scheme 5.3, the indole-substituted

adduct **136b** was obtained in 99% yield. In these reactions, the exclusive formation of **136a** mentioned earlier in entry 6 in Table 5.3 and **136b** suggested that, when a carbocation species such as **138** cannot be regenerated, the cyclopropane moiety is resistant to the ring opening process.

Scheme 5.3 Yb(OTf)₃-catalyzed reaction of **131a** with indole.

5.3 Conclusion

In summary, an efficient ytterbium-catalyzed synthetic route to conjugated enynes based on nucleophilic ring opening of unactivated 1-cyclopropyl-2-propyn-1-ols **131** with arylsulfonamides has been reported. These results show that the reaction tolerates a structurally diverse set of alcohol substrates and complement earlier works with terminal and activated starting alcohols mediated by Ru₂ and Au catalysts. The product yields and regioselectivity obtained are also comparable. In addition, the present method benefits from the use of not only alcohol substrates that can be accessed in one step from commercially available and low cost starting materials but also an ytterbium catalyst that is also less expensive. Our studies suggest Yb(OTf)₃-mediated activation of the substituted 1-cyclopropyl-2-propyn-1-ol substrate that leads to ionization of the alcohol. This possibly triggers subsequent ring opening of the cyclopropane moiety followed by trapping with the sulfonamide nucleophile to give the conjugated enyne product.

Chapter VI. Copper(II) Triflate-Catalyzed Intramolecular Hydroamination of Homoallylic Aminoalcohols as an Expedient Route to *trans*-2,5-Dihydro-1*H*-pyrroles and 1,2-Dihydroquinolines

6.1 Introduction

Intramolecular hydroaminations, the formal addition of a nitrogen and hydrogen atom to unsaturated C–C bonds, mediated typically in the presence of transition metal catalysts provides a convenient synthetic route to nitrogen-containing heterocycles.¹¹⁸⁻¹²² Although this has led to a myriad of studies devoted to this reaction, the majority have been focused on intramolecular hydroamination of amino tethered alkenes, alkynes and allenes.^{118,119,122} In contrast and despite recent notable advances made in metal-mediated intermolecular hydroaminations of dienes,¹²³ synthetic methods reporting the analogous intramolecular version of this reaction with aminodienes have remained sparse.¹²⁰

Over the last decade, the use of alcohol pro-electrophiles in Lewis acid catalyzed C–N bond formation strategies has received an increasing amount of attention.¹²⁴⁻¹²⁶ For example, we recently reported an efficient method for pyrrolidine synthesis based on AuCl/AgOTf catalyzed tandem amination/ring expansion of cyclopropyl methanols with aryl sulfonamides that was thought to putatively proceed via intramolecular hydroamination of an aminoalkene intermediate.^{84c} As part of an ongoing program to develop such reactions,¹²⁵ our discovery that Cu(OTf)₂ can effect intramolecular hydroamination of aminodienes generated *in situ* from the respective homoallylic aminoalcohols **139** and **141** is reported herein (Scheme 6.1). This process delivers an expedient route to *trans*-2,5-dihydro-1*H*-pyrroles **140** and 1,2-dihydroquinolines **142**, which are common building blocks in organic synthesis and

key components in a myriad of bioactive compounds.¹²⁷ The *trans*-pyrrolidine adducts were also obtained with high ee values that demonstrated efficient chirality transfer from the enantioenriched starting materials to the products. In addition, the reactions were accomplished with a readily available and inexpensive copper catalyst that did not need require additives and/or a ligand support or exclusion of air and moisture for reactions leading to the construction of **142**. While copper complexes have recently gained momentum as a potentially more ecologically benign hydroamination catalyst, their synthetic utility has often been offset by the need for additives and/or ligands under inert and moisture-free conditions.¹²¹

Scheme 6.1 Intramolecular hydroamination of homoallylic aminoalcohols catalyzed by $\text{Cu}(\text{OTf})_2$.

6.2 Results and Discussion

We began by examining the intramolecular hydroamination of *cis*-(-)-**139a**, prepared from L-valine in >20:1 dr and 97% ee following literature methods, by a variety of Lewis and Brønsted acid catalysts to establish the reaction conditions (Table 6.1). The structure and *cis* stereochemistry of the starting alcohol was determined by NMR measurements and X-ray crystal structure analysis of a closely

Table 6.1 Optimization of the reaction conditions.^a

Entry	Catalyst	Solvent	Yield (%) ^b	dr ^c
1	Cu(OTf) ₂	(CH ₂ Cl) ₂	70	>20:1 ^d
2 ^e	Cu(OTf) ₂	(CH ₂ Cl) ₂	58	>20:1
3 ^f	Cu(OTf) ₂	(CH ₂ Cl) ₂	- ^g	-
4	Cu(OTf) ₂	PhMe	59	>20:1
5	Cu(OTf) ₂	MeNO ₂	21	>20:1
6	Cu(OTf) ₂	MeCN	- ^g	-
7	Cu(OTf) ₂	THF	- ^g	-
8	Cu(OAc) ₂	(CH ₂ Cl) ₂	- ^g	-
9	CuOTf	(CH ₂ Cl) ₂	- ^g	-
10	CuI	(CH ₂ Cl) ₂	- ^g	-
11	Bi(OTf) ₃	(CH ₂ Cl) ₂	49	>20:1
12	In(OTf) ₃	(CH ₂ Cl) ₂	28	>20:1
13	Sc(OTf) ₃	(CH ₂ Cl) ₂	9	- ^h
14	Yb(OTf) ₃	(CH ₂ Cl) ₂	15	- ^h
15	FeCl ₃	(CH ₂ Cl) ₂	- ⁱ	-
16	AgOTf	(CH ₂ Cl) ₂	48	>20:1
17	AuCl/AgOTf	(CH ₂ Cl) ₂	62	>20:1
18	AuCl ₃ /AgOTf	(CH ₂ Cl) ₂	42	>20:1

Table 6.1 (*continued*).

Entry	Catalyst	Solvent	Yield (%) ^b	dr ^c
19	TfOH	(CH ₂ Cl) ₂	27	- ^h
20 ^e	Tf ₂ NH	(CH ₂ Cl) ₂	22	- ^h

^aAll reactions were performed at 80 °C for 15 h with **139a**:catalyst ratio = 20:1. ^bIsolated yield. ^cDetermination of *trans* product dr was based on ¹H NMR analysis of the crude mixture. ^dProduct obtained in 93% ee based on chiral HPLC analysis. ^eReaction conducted without the exclusion of air or moisture. ^fReaction conducted in the presence of 10 mol % K₂CO₃. ^gNo reaction based on TLC and ¹H NMR analysis and near quantitative recovery of the starting alcohol. ^hProduct dr could not be determined due to overlapping impurity signals in ¹H NMR spectrum of the crude mixture. ⁱstarting material **139a** was decomposed.

related adduct (*vide infra*) (Figure 6.1). This revealed treating *cis*-(-)-**139a** in 1,2-dichloroethane with 5 mol % of Cu(OTf)₂ at 80 °C for 15 h gave the best result, furnishing *trans*-(-)-**140a** as the sole product in 70% yield, >20:1 dr *trans* selectivity and 93% ee (Table 6.1, entry 1). The structure and *trans* stereochemistry of the pyrrolidine product was determined by NMR measurements and X-ray crystal structure analysis of two closely related products (*vide infra*) (Figure 6.1).¹²⁸ Lower product yields were obtained when the reaction was repeated under atmospheric conditions or in PhMe or MeNO₂ as solvent (Table 6.1, entries 2 and 4-5). In contrast, the introduction of a catalytic amount of inorganic base or the use of MeCN or THF as solvent was shown to lead to no reaction and recovery of the starting alcohol

(Table 6.1, entries 3 and 6-7). Similarly, a survey of other Lewis and Brønsted acid catalysts did not give improved results with either lower product yields or no reaction found (Table 6.1, entries 8-20). Notably, the lower catalytic activity observed in reactions in the presence of TfOH and other metal triflates also provided evidence to discount a process mediated solely by the Brønsted acid (Table 6.1, entries 7, 9-16 and 18).¹²⁹⁻¹³⁰

Figure 6.1 ORTEP drawing of (a) **139h** with thermal ellipsoids at 50% probability levels.¹²⁸

To define the scope of the present procedure, we turned our attention to the reactions of a variety of enantioenriched *cis*-1-(tosylamino)pent-4-en-2-ols ranging from 91-99% ee (Table 6.2). The structure, *cis* stereochemistry and (2*S*,3*R*) absolute configuration *cis*-(-)-**139h** was determined by X-ray crystallography (Figure 6.1).¹²⁸ Experiments showed that in the presence of 5 mol % of Cu(OTf)₂ as catalyst, starting alcohols *cis*-(-)-**139b-h** and *cis*-(+)-**139i-j** efficiently underwent the intramolecular hydroamination process and gave the corresponding products *trans*-(+)-**140b-h** and *trans*-(-)-**140i-j** in good to excellent yields. In these reactions, the 2,5-dihydro-1*H*-pyrrole adducts were also obtained with *trans* selectivities up to >99:1 dr and ee values of 91-97% that were comparable to those of the respective substrates and

consistent with our earlier findings for that of *cis*-(-)-**139a**. The structure and *trans* stereochemistry of *trans*-(+)-**140c** and *trans*-(+)-**140g** was determined by X-ray crystallographic analysis (Figure 6.2),¹²⁸ with the absolute configuration being (2*S*,5*S*). Similarly, the structure and *trans* stereochemistry of *trans*-(-)-**140j** was confirmed by X-ray crystallography (Figure 6.2),¹²⁸ with the absolute configuration being (2*R*,5*R*).

Table 6.2 Intramolecular hydroamination of **139b-j** catalyzed by Cu(OTf)₂.^a

Alcohols
139b , R = Me, 99% ee 139c , R = Ph, 7:1 dr, 98% ee	139d , R = Me, 98% ee 139e , R = Et, 98% ee 139f , R = <i>n</i> Pr, 98% ee 139g , R = Bn, 97% ee 139h , R = Ph, 94% ee	139i , R = <i>i</i> Pr, 91% ee 139j , R = Bn, 96% ee
Products
140b , R = Me, (79, >99:1, 97) 140c , R = Ph, (83, >99:1, 96)	140d , R = Me, (60, >13:1, 96) 140e , R = Et, (56, >15:1, 97) 140f , R = <i>n</i> Pr, (52, >20:1, 93) 140g , R = Bn, (71, >20:1, 91) 140h , R = Ph, (65, >99:1, 93)	140i , R = <i>i</i> Pr, (72, >20:1, 91) 140j , R = Bn, (72, >20:1, 96)

^aAll reactions were performed at 80 °C in (CH₂Cl)₂ for 15 h with **139**:Cu(OTf)₂ ratio = 20:1 and values in parenthesis represent isolated yield (%), dr and ee (%) of product. Measurement of *trans* product dr and ee values based on respective ¹H NMR and chiral HPLC analysis of the crude mixture.

(a) **140c**

(b) 140h

(c) 140j

Figure 6.2 ORTEP drawing of (a) **140c**, (b) **140h** and (c) **140j** with thermal ellipsoids at 50% probability levels.¹²⁸

We next sought to assess the scope of this new methodology and with this mind, first tested the reaction of 1-(2-(tosylamino)phenyl)-1-phenylbut-3-en-1-ol **141a** (Table 6.3). This led us to find the cyclization process to proceed well on applying the standard conditions with 5 mol % of Cu(OTf)₂ as catalyst, giving **142a** in 97% yield (Table 6.3, entry 1). Moreover, the same product yield could be reproduced when the reaction was repeated without the exclusion of air and moisture (Table 6.3, entry 2). On the other hand and consistent with our earlier findings for that of *cis*-(-)-**139a**, reactions of **141a** with other solvents and Lewis and Brønsted acids were found to lead to lower yields and/or formation of the diene side product **143** (Table 6.3, entries 3-13). Interestingly, while FeCl₃ and TfOH was among the catalysts examined that resulted in lower products yields (Table 6.3, entries 11-13), their ability to effect cyclization is nonetheless noteworthy given that intramolecular hydroaminations mediated by such Lewis and Brønsted acids have remained sparse. In addition, it contrasts with our earlier results which revealed the same catalysts to be markedly less effective for the reaction of **139a** (entries 18-19 in Table 6.1).

Intramolecular hydroamination of a variety of 1-(2-(tosylamino)phenyl)but-3-en-1-ols **141b-p** was also found to proceed smoothly under these slightly modified conditions (Table 6.4). With 5 mol % of Cu(OTf)₂ as catalyst, these reactions gave the corresponding 1,2-dihydroquinolines **142a-p** in excellent yields. This included one example of a fused tetracycle **142m**. In these reactions, the structure of **142c** was also confirmed by X-ray crystallographic analysis (Figure 6.3).¹²⁸ and no other byproducts were detected by ¹H NMR analysis of the crude mixtures.

Table 6.3 Intramolecular hydroamination of **141a** catalyzed by a variety of Lewis and Brønsted acids.^a

$$\text{141a} \xrightarrow[\text{solvent, 80 } ^\circ\text{C}]{\text{catalyst}} \text{142a} + \text{143}$$

Entry	Catalyst	Solvent	Yield (%) ^b	
			142a	143
1	Cu(OTf) ₂	(CH ₂ Cl) ₂	97	-
2	Cu(OTf) ₂ ^c	(CH ₂ Cl) ₂	97	-
3	Cu(OTf) ₂	PhMe	93	-
4	Cu(OTf) ₂	MeNO ₂	78	-
5	Cu(OTf) ₂	THF	64	30
6	CuOTf	PhMe	- ^d	-
7	CuI	PhMe	- ^d	-
8	AgOTf	PhMe	- ^d	54
9	AuCl/AgOTf	PhMe	89	-
10	Yb(OTf) ₃	PhMe	-	16 ^e
11	FeCl ₃	PhMe	80	-
12	FeCl ₃ ·6H ₂ O	PhMe	80	-
13	TfOH	PhMe	83	-

^aAll reactions were performed at 80 °C for 15 h with **141**:catalyst ratio =

20:1. ^bIsolated yield. ^cReaction conducted under atmospheric conditions.

^dNo reaction and near quantitative recovery of the starting alcohol or 43% in the case of AgOTf. ^eStarting material was also recovered in 56% yield.

Table 6.4 Intramolecular Hydroamination of **141b-p** Catalyzed by Cu(OTf)₂.^a

Entry	Alcohol	Product	Time (h)	Yield (%) ^b
1	141b-d	142b R = Me	6	93
2		142c R = OMe	3	87
3		142d R = Br	4	75
4	141e-f	142e R ¹ = Me R ² = H	3	98
5		142f R ¹ = H R ² = OMe	4	75
6	141g-i	142g R = Me	3	97
7		142h R = Cl	3	91
8		142i R = Br	3	95
9	141j-l	142j R ¹ = Me R ¹ = H	20	93
10		142k R ¹ = cPr R ¹ = Me	6	79
11	141m	142l R ¹ = CCPh R ¹ = Me	2	84
12		142m	3	71
13	141n	142n	4	99
14	141o	142o	4	94

Table 6.4 (continued).

Entry	Alcohol	Product	Time (h)	Yield(%) ^b
15	141p	142p	2	89

^aAll reactions were performed at 80 °C in (CH₂Cl)₂ under atmospheric conditions with **141**:Cu(OTf)₂ ratio = 20:1. ^bIsolated yield.

Figure 6.3 ORTEP drawing of **142c** with thermal ellipsoids at 50% probability levels.¹²⁸

The competitive formation of the diene side product **143** for the cyclizations of **141a** under certain conditions mentioned earlier in Table 6.3 led us to speculate on its possible involvement as an intermediate in the present Cu(OTf)₂ catalyzed reactions. Indeed, this is further supported by the fact that **142a** could be obtained in 99% yield when a 1,2-dichloroethane solution containing **143** was treated with 5 mol % of Cu(OTf)₂ under the standard conditions shown in Scheme 6.2.

Scheme 6.2 Intramolecular hydroamination of aminodiene **143** catalyzed by Cu(OTf)₂.

It is worth noting that the fact that the *trans* isomer of **143** can also undergo intramolecular hydroamination additionally suggests a reaction involving an intermediate that contains an allylbenzylic carbocation moiety. This is evident in a number of control experiments examined in this work that supports the cooperative involvement of the Brønsted acid with Cu(OTf)₂ in the catalytic cycle. First is the ability of TfOH to cyclize both **139a** and **141a** albeit less efficiently. Added to this is the near quantitative recovery of **139a** in reactions with less acidic Cu(I) and (II) salts or polar aprotic solvents such as THF and MeCN or in the presence of 10 mol % K₂CO₃ and lower product yields obtained with other metal triflates shown in Table 6.1.

On the basis of the above results, we tentatively propose the mechanism outlined in Scheme 6.3 for the reaction of *cis*-(-)-**139a**, although it is highly speculative. This could involve activation of the alcohol substrate through coordination of the catalyst with the OH group that results in its elimination and formation of the aminodiene **144**. Further coordination of this newly formed adduct to Cu(OTf)₂, re-generated from [Cu]-OH by protonolysis, gives Cu(II)-activated aminodiene species **145**. The released TfOH leads to protonation of the diene moiety of **145** and formation of resonance stabilized allylic cation **146** that is further stabilized through ion pairing with the resultant -OTf anion formed. This is the active species that undergoes the intramolecular hydroamination process to afford the *trans*-(+)-**140a**.¹³¹ The origin of

the trans selectivity could be due carbocationic species adopting the conformer shown in Scheme 6.3 so that the potential for **144** strain between the substituents in allylic cation **146** can be kept to a minimum. In this manner, this would also allow the possibility of unfavourable transannular strain between the *i*-Pr and Me groups to be avoided upon cyclization. The comparable substrate and product ee values also suggest that neither the starting alcohol nor any of the putative intermediates are prone to racemization. This consequently allows efficient transfer of the retained chirality at the α -carbon centre to the amino group and the high distereoselectivity observed at the newly formed C–N bond.

Scheme 6.3 Tentative mechanism for intramolecular hydroamination of **139a** catalyzed by $\text{Cu}(\text{OTf})_2$.

6.3 Conclusion

In summary, an efficient synthetic strategy for the intramolecular hydroamination of aminodienes generated *in situ* from easily accessible homoallylic alcohols in the

presence of an ecologically benign and low cost copper catalyst has been reported. This provided a practical and operationally simplistic route to enantiopure *trans*-2,5-dihydro-1*H*-pyrroles with high ee values that relied on chirality transfer from enantioenriched substrates as well as 1,2-dihydroquinolines under mild conditions. In the latter case, this included conditions that did not need the exclusion of air or moisture. Our studies revealed that TfOH can also catalyze the intramolecular hydroamination process. However, the lower product yields and selectivities exhibited by the Brønsted acid along with the much milder conditions of copper catalysis provides an attractive alternative synthetic approach for the formation of these *N*-heterocycles. Although the findings of this study imply that it is unlikely that TfOH potentially generated *in situ* alone can promote the reaction, careful attention must also be applied when examining such results.

Chapter VII. Experimental

7.1 General Experimental Section

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 pre-coated silica gel plates. Visualization was achieved by UV light(254 nm). Flash chromatography was performed using silica gel and a gradient solvent system (EtOAc: *n*-hexane as eluant). ^1H and ^{13}C NMR spectra were measured on a Bruker Avance 300, 400, and 500 MHz spectrometers. Chemical shifts (ppm) were recorded with tetramethylsilane (TMS) as the internal reference standard. Multiplicities are given as: s (singlet), br s (broad singlet), d (doublet), t (triplet), dd (doublet of doublets) or m (multiplet). The number of protons (n) for a given resonance is indicated by $n\text{H}$ and coupling constants are reported as a J value in Hz. Infrared spectra were recorded on a Shimadzu IR Prestige-21 FT-IR spectrometer. Solid samples were examined on KBr discs or upon dissolution in CHCl_3 and prepared as a thin film between NaCl salt plates. Low resolution mass spectra were determined on a Finnigan LCQ XP MAX mass spectrometer. High resolution mass spectrometry (HRMS) spectra were obtained on a Finnigan MAT95XP GC/HRMS mass spectrometer. Enantiomeric excess (ee) values were determined by high performance liquid chromatography (HPLC) analysis using Daicel Chirapak OD, AD-H, OD-H, OJ-H, AS-H columns. Optical rotations were measured in CHCl_3 on a polarimeter with a sodium vapor lamp at 589 nm and 10 cm cell (c given in g/100 mL).

7.2 Gold-Catalyzed Allylic Alkylation of Aromatic and Heteroaromatic Compounds with Allylic Alcohols

General procedure for AuCl₃-catalyzed allylation of aromatic and heteroaromatic compounds **5b, **46a-c**, **102a-c**, **103-105****

To a solution of **100** (0.3 mmol), **5b** or **46a-c** or **102a-c** or **103-105** (1.2 mmol) and 4Å molecular sieves (50 mg) in CH₂Cl₂ (2 mL) under an N₂ atmosphere, was added AuCl₃ (5 mol%). The mixture was stirred at room temperature and monitored by TLC analysis. On completion, the reaction mixture was filtered through Celite[®] and washed with CH₂Cl₂ (20 mL). The solvent was removed under reduced pressure and the residue was subjected to purification by flash column chromatography to give the title compound **101**.

(*E*)-4-(1,3-bis(4-bromophenyl)allyl)-2,6-dimethylphenol **101a**

Yellow oil; ¹H NMR (CDCl₃, 400 MHz): δ 2.20 (s, 6H), 4.59 (s, 1H), 4.69 (d, 1H, *J* = 7.3 Hz), 6.22 (d, 1H, *J* = 15.8 Hz), 6.56 (dd, 1H, *J* = 15.8, 7.4 Hz), 6.78 (s, 2H), 7.07 (d, 2H, *J* = 8.3 Hz), 7.21 (d, 2H, *J* = 8.4 Hz), 7.39-7.42 (m, 4H); ¹³C NMR (CDCl₃, 100 MHz): δ 16.1, 52.9, 120.3, 121.1, 123.3, 127.9, 128.6, 130.2, 130.3, 131.6, 131.6, 133.3, 134.2,

136.1, 142.8, 151.0; IR (film) 3462, 1485, 1196, 1070, 1009 cm^{-1} ; HRMS (EI) calcd. for $\text{C}_{23}\text{H}_{19}\text{O}^{79}\text{Br}_1^{81}\text{Br}_1$: 470.9777, found: 470.9795.

(E)-4-(1,3-dip-tolylallyl)-2,6-dimethylphenol 101b

Red-yellow oil; ^1H NMR (CDCl_3 , 400 MHz): δ 2.24 (s, 6H), 2.36 (s, 6H), 4.56 (s, 1H), 4.75 (d, 1H, $J = 7.5$ Hz), 6.33 (d, 1H, $J = 15.8$ Hz), 6.62 (dd, 1H, $J = 15.8, 7.6$ Hz), 6.88 (s, 2H), 7.12-7.32 (m, 8H); ^{13}C NMR (CDCl_3 , 100 MHz): δ 16.0, 21.1, 21.2, 53.1, 123.0, 126.2, 128.5, 128.7, 129.1, 129.2, 130.6, 132.3, 134.7, 135.5, 135.8, 136.9, 141.2, 150.7; IR (film) 3429, 2918, 1589, 1510, 1488, 1198, 804 cm^{-1} ; HRMS (EI) calcd. for $\text{C}_{24}\text{H}_{23}\text{O}$ ($\text{M}^+ - \text{CH}_3$): 327.1749, found: 327.1745.

(E)-4-(1,3-diphenylallyl)-2,6-dimethylphenol 101c

Red-yellow oil; ^1H NMR (CDCl_3 , 400 MHz): δ 2.20 (s, 6H), 4.53 (s, 1H), 4.76 (d, 1H, $J = 7.5$ Hz), 6.32 (d, 1H, $J = 15.8$ Hz), 6.64 (dd, 1H, $J = 15.8, 7.6$ Hz), 6.84 (s, 2H), 7.17-7.38 (m, 10H); ^{13}C NMR (CDCl_3 , 100 MHz): δ 16.1, 53.5, 123.0, 126.3, 126.4, 127.3, 128.5, 128.5, 128.6, 128.8, 131.0, 133.1, 135.2, 137.4, 144.1, 150.8; IR (film) 3464, 3026, 2918, 1580, 1481, 1198, 746, 700 cm^{-1} ; HRMS (EI) calcd. for $\text{C}_{23}\text{H}_{22}\text{O}$: 314.1671, found: 314.1663.

(E)-4-(1,3-Bis(4-bromophenyl)allyl)-2-methylphenol 101d

Yellow oil; ^1H NMR(CDCl_3 , 400 MHz): δ 2.20 (s, 3H), 4.72 (d, 1H, $J = 7.3$ Hz), 4.88 (s, 1H), 6.22 (d, 1H, $J = 15.8$ Hz), 6.56 (dd, 1H, $J = 15.8, 7.4$ Hz), 6.70 (d, 1H, $J = 8.2$ Hz), 6.87 (d, 1H, $J = 8.2$ Hz), 6.92 (s, 1H), 7.06-7.42 (m, 8H); ^{13}C NMR (CDCl_3 , 100 MHz): δ 15.9, 52.8, 115.1, 120.4, 121.2, 124.1, 127.1, 127.9, 130.4, 131.1, 131.6, 131.7, 133.2, 134.8, 136.1, 142.7, 152.6; IR (film) 3394, 2918, 1587, 1485, 1263, 1070, 1009, 818 cm^{-1} ; HRMS (EI) calcd. for $\text{C}_{22}\text{H}_{18}\text{O}^{79}\text{Br}_2$: 455.9719, found: 455.9710.

(E)-4-(1,3-Di-*p*-tolylallyl)-2-methylphenol 101e

Red-yellow oil; ^1H NMR(CDCl_3 , 400 MHz): δ 2.26 (s, 3H), 2.37 (s, 6H), 4.80 (d, 1H, $J = 7.3$ Hz), 4.81 (s, 1H), 6.34 (d, 1H, $J = 15.8$ Hz), 6.63 (dd, 1H, $J = 15.8, 7.5$ Hz), 6.73 (d, 1H, $J = 8.2$ Hz), 6.96-7.33 (m, 10H); ^{13}C NMR (CDCl_3 , 100 MHz): δ 15.9, 21.1, 21.2, 53.1, 114.9, 123.8, 126.3, 127.2, 128.5, 129.2, 129.2, 130.8, 131.2, 132.3, 134.7, 135.9, 136.1, 137.0, 141.1, 152.3; IR (film) 3437, 2932, 1582, 1513, 1199, 801 cm^{-1} ; HRMS (EI) calcd. for $\text{C}_{24}\text{H}_{24}\text{O}$: 328.1827, found: 328.1819.

(E)-4,4'-(3-(4-(Allyloxy)phenyl)prop-1-ene-1,3-diyl)bis(bromobenzene) 101f

Colorless oil; ^1H NMR(CDCl_3 , 400 MHz): δ 4.51 (d, 2H, $J = 5.2\text{Hz}$), 4.77 (d, 1H, $J = 7.3\text{Hz}$), 5.28 (d, 1H, $J = 10.5\text{Hz}$), 5.40 (d, 1H, $J = 16.4\text{Hz}$), 6.00-6.09 (m, 1H), 6.22 (d, 1H, $J = 15.8\text{Hz}$), 6.57 (dd, 1H, $J = 15.8, 7.3\text{Hz}$), 6.87 (d, 2H, $J = 8.6\text{Hz}$), 7.06-7.43 (m, 10H); ^{13}C NMR (CDCl_3 , 100 MHz): δ 52.7, 68.9, 114.9, 117.8, 120.4, 121.2, 127.9, 129.5, 130.4, 130.5, 131.6, 131.7, 133.1, 133.3, 134.8, 136.0, 142.5, 157.4; IR (film) 3026, 1587, 1506, 1485, 1400, 1242, 1177, 1070, 1008 cm^{-1} ; HRMS (EI) calcd. for $\text{C}_{24}\text{H}_{20}\text{O}^{79}\text{Br}_2$: 481.9881, found: 481.9857.

(E)-4,4'-(3-(4-Methoxyphenyl)prop-1-ene-1,3-diyl)bis(bromobenzene) 101g

Yellow oil; ^1H NMR(CDCl_3 , 400 MHz): δ 3.80 (s, 3H), 4.80 (d, 2H, $J = 7.3\text{ Hz}$), 6.24 (d, 1H, $J = 15.8\text{ Hz}$), 6.59 (dd, 1H, $J = 15.8, 7.3\text{Hz}$), 6.87 (d, 2H, $J = 8.4\text{Hz}$), 7.08-7.13 (m, 4H), 7.23 (d, 2H, $J = 8.1\text{Hz}$), 7.41-7.45 (m, 4H); ^{13}C NMR (CDCl_3 , 100 MHz): δ 52.7, 55.3, 114.1, 120.4, 121.2, 127.9, 129.5, 130.4, 130.5, 131.6, 131.7, 133.1, 134.7, 136.0, 142.6, 158.4; IR (film) 1510, 1487, 1265, 1072, 1011, 743 cm^{-1} ; HRMS (ESI) calcd. For $\text{C}_{22}\text{H}_{18}\text{O}^{79}\text{Br}_1^{81}\text{Br}_1\text{Na}$: 480.9602, found: 480.9923.

(E)-5-(1,3-Bis(4-bromophenyl)allyl)benzo[d][1,3]dioxole 101h

Colorless oil; ^1H NMR (CDCl_3 , 400 MHz): δ 4.75 (d, 1H, $J = 7.3$ Hz), 5.94 (s, 2H), 6.25 (d, 1H, $J = 15.8$ Hz), 6.56 (dd, 1H, $J = 15.8, 7.3$ Hz), 6.67 (d, 2H, $J = 6.1$ Hz), 6.77 (d, 1H, $J = 5.9$ Hz), 7.08-7.45 (m, 8H); ^{13}C NMR (CDCl_3 , 100 MHz): δ 53.2, 101.1, 108.3, 109.0, 120.5, 121.3, 121.6, 127.9, 130.3, 130.6, 131.6, 131.7, 132.7, 135.9, 136.5, 142.3, 146.4, 147.9; IR (film) 2915, 1587, 1485, 1233, 1040, 1009 cm^{-1} ; HRMS (EI) calcd. for $\text{C}_{22}\text{H}_{16}\text{O}_2^{79}\text{Br}_2$: 469.9517, found: 469.9518.

(E)-1-(1,3-Bis(4-bromophenyl)allyl)-2,4-dimethylbenzene 101i

Colorless oil; ^1H NMR (CDCl_3 , 400 MHz): δ 2.21 (s, 3H), 2.31 (s, 3H), 4.96 (d, 1H, $J = 6.6$ Hz), 6.11 (d, 1H, $J = 15.8$ Hz), 6.59 (dd, 1H, $J = 15.9, 6.6$ Hz), 6.99-7.44 (m, 11H); ^{13}C NMR (CDCl_3 , 100 MHz): δ 19.6, 20.9, 49.5, 120.3, 121.1, 126.8, 127.8, 128.3, 130.4, 130.6, 131.5, 131.6, 133.0, 136.1, 136.4, 137.6, 141.7; IR (film) 1484, 1400, 1070, 1009, 820, 719 cm^{-1} ; HRMS (EI) calcd. for $\text{C}_{23}\text{H}_{20}^{79}\text{Br}_2$: 453.9926, found: 453.9891.

(E)-2,6-Dimethyl-4-(4-phenylbut-3-en-2-yl)phenol 101j

Pale-yellow oil; ^1H NMR (CDCl_3 , 400 MHz): δ 1.41 (d, 3H, $J = 7.0$ Hz), 2.23 (s, 6H), 3.48-3.54 (m, 1H), 4.49 (s, 1H), 6.32-6.41 (m, 2H), 6.87 (s, 2H), 7.16-7.36 (m, 5H); ^{13}C NMR (CDCl_3 , 100 MHz): δ 16.0, 21.4, 41.8, 123.0, 126.2, 127.0, 127.4, 128.0, 128.5, 135.8, 137.3, 137.7, 150.6; IR (film) 3425, 3029, 1487, 1000, 695 cm^{-1} ; HRMS (EI) calcd. For $\text{C}_{18}\text{H}_{20}\text{O}$: 252.1514, found: 252.1515.

(E)-4-(1,5-Diphenylpent-1-en-3-yl)-2-methylphenol 101k

Red-yellow oil; ^1H NMR (CDCl_3 , 400 MHz): δ 2.05–2.13 (m, 2H), 2.14 (s, 3H), 2.54–2.58 (m, 2H), 3.35 (m, 1H), 4.54 (s, 1H), 6.28–6.40 (m, 2H), 6.73 (d, 1H, $J = 8.1$ Hz), 6.95–6.99 (m, 2H), 7.16–7.35 (m, 10H); ^{13}C NMR (CDCl_3 , 100 MHz): δ 15.9, 33.8, 37.5, 47.8, 115.0, 123.8, 125.8, 126.2, 126.2, 127.1, 128.4, 128.5, 129.3, 130.3, 134.5, 136.4, 137.6, 142.3, 152.3; IR (film) 3395, 3026, 1510, 1449, 1263, 1115, 752, 698 cm^{-1} ; HRMS (EI) calcd. for $\text{C}_{24}\text{H}_{24}\text{O}$: 328.1827, found: 328.1821.

(E)-2-Methyl-4-(1-phenylhexa-1,5-dien-3-yl)phenol 101l

Pale-yellow oil; ^1H NMR (CDCl_3 , 400 MHz): δ 2.24 (s, 3H), 2.54 (t, 2H, $J = 7.3$ Hz), 3.39-3.46 (m, 1H), 4.58 (s, 1H), 4.97-5.07 (m, 2H), 5.69-5.94 (m, 1H), 6.32-6.35 (m, 2H), 6.72 (d, 1H, $J = 8.1$ Hz), 6.94-6.99 (m, 2H), 7.18-7.35 (m, 5H); ^{13}C NMR (CDCl_3 , 100 MHz): δ 15.9, 40.3, 48.1, 114.9, 116.2, 123.7, 126.2, 127.1, 128.5, 129.4, 130.3, 133.9, 136.1, 136.7, 152.2; IR (film) 3429, 2918, 1513, 1449, 1263, 1115, 965, 752 cm^{-1} ; HRMS (EI) calcd. for $\text{C}_{19}\text{H}_{20}\text{O}$: 264.1514, found: 264.1508.

4-Cinnamyl-2-methylphenol 101m

Colorless oil; ^1H NMR (CDCl_3 , 400 MHz): δ 2.23 (s, 3H), 3.45 (d, 2H, $J = 6.6$ Hz), 4.55 (s, 1H), 6.29-6.36 (m, 1H), 6.43 (d, 1H, $J = 15.8$ Hz), 6.71 (d, 1H, $J = 8.1$ Hz), 6.94-7.36 (m, 7H); ^{13}C NMR (CDCl_3 , 100 MHz): δ 15.8, 38.5, 114.9, 123.7, 126.1, 127.0, 127.2, 128.5, 129.8, 130.6, 131.3, 132.3, 137.6, 152.2; IR (film) 3368, 2967, 1597, 1495, 1263, 1206, 1111, 966 cm^{-1} ; HRMS (EI) calcd. For $\text{C}_{16}\text{H}_{16}\text{O}$: 224.1201, found: 224.1198.

(E)-4-(2-Benzylideneoctyl)-2-methylphenol 101n

Colorless oil; ^1H NMR (CDCl_3 , 400 MHz): δ 0.86 (t, 3H, $J = 6.5\text{Hz}$), 1.20-1.29 (m, 6H), 1.43-1.49 (m, 2H), 2.15 (t, 2H, $J = 8.1\text{ Hz}$), 2.24 (s, 3H), 3.38 (s, 2H), 4.61 (s, 1H), 6.28 (s, 1H), 6.70 (d, 1H, $J = 8.1\text{ Hz}$), 6.94-7.32 (m, 7H); ^{13}C NMR (CDCl_3 , 100 MHz): δ 14.1, 15.8, 22.6, 28.2, 29.4, 30.2, 31.6, 43.1, 114.8, 123.5, 126.0, 126.7, 127.6, 128.1, 128.7, 131.7, 132.1, 138.5, 143.3, 152.1; IR (film) 3401, 2926, 2857, 1597, 1496, 1464, 1377, 1261, 1111, 698 cm^{-1} ; HRMS (EI) calcd. for $\text{C}_{22}\text{H}_{28}\text{O}$: 308.2140, found: 308.2142.

(E)-4-(3-(4-Bromophenyl)allyl)-2,6-dimethylphenol 101o

Yellow oil; ^1H NMR (CDCl_3 , 400 MHz): δ 2.22 (s, 6H), 3.39 (d, 2H, $J = 5.3\text{ Hz}$), 4.51 (s, 1H), 6.12-6.37 (m, 2H), 6.83 (s, 2H), 7.20-7.40 (m, 4H); ^{13}C NMR (CDCl_3 , 100 MHz): δ 15.9, 38.6, 120.7, 123.1, 127.7, 128.8, 129.3, 130.9, 131.3, 131.6, 136.5, 150.6; IR (film) 3433, 2918, 1485, 1263, 1196, 1146 cm^{-1} ; HRMS (EI) calcd. for $\text{C}_{17}\text{H}_{17}\text{O}^{79}\text{Br}$: 316.0463, found: 316.0450.

4-(3, 3-Diphenylallyl)-2,6-dimethylphenol 101p

Yellow oil; ^1H NMR(CDCl_3 , 400 MHz): δ 2.21(s, 6H), 3.33(d, 2H, $J = 7.6\text{Hz}$), 4.50 (s, 1H), 6.23 (t, 3H, $J = 7.6\text{Hz}$), 6.79 (s, 2H), 7.17-7.41(m, 10H); ^{13}C NMR (CDCl_3 , 100 MHz): δ 16.0, 35.1, 123.1, 127.0, 127.1, 127.4, 128.0, 128.1, 128.3, 128.5, 130.0, 132.5, 140.0, 141.9, 142.6, 150.5; IR (film) 3443, 2912, 1488, 1257, 1183 cm^{-1} ; HRMS (ESI) calcd. for $\text{C}_{23}\text{H}_{22}\text{ONa}$: 337.1568, found: 337.1594.

4-[(3,4-Dihydronaphthalen-2-yl)(*p*-tolyl)methyl]-2,6-dimethylphenol 101q

Yellow oil; ^1H NMR (CDCl_3 , 400 MHz): δ 2.22 (s, 6H), 2.27 (t, 2H, $J = 8.1\text{ Hz}$), 2.36 (s, 3H), 2.82 (t, 2H, $J = 8.2\text{ Hz}$), 4.54 (s, 1H), 4.74 (s, 1H), 5.97 (d, 1H, $J = 0.7\text{ Hz}$), 6.85 (s, 2H), 6.94 (d, 1H, $J = 6.1\text{ Hz}$), 7.10-7.15 (m, 7H); ^{13}C NMR (CDCl_3 , 100 MHz): δ 16.1, 21.1, 28.0, 28.5, 57.5, 122.7, 125.2, 126.0, 126.4, 126.5, 127.2, 129.0, 129.2, 129.4, 133.8, 134.7, 134.8, 135.8, 139.6, 144.5, 150.7; IR (film) 3464, 2918, 1511, 1480, 1325, 1195, 752 cm^{-1} ; HRMS (EI) calcd. for $\text{C}_{26}\text{H}_{26}\text{O}$: 354.1984, found: 354.1982.

2-(4-Hydroxy-3,5-dimethylphenyl)(phenyl)methylcyclohex-2-enone 101r

Colourless solid; m.p. 174-176 °C; ^1H NMR (CDCl_3 , 400 MHz): δ 1.98-2.04 (m, 2H), 2.17 (s, 6H), 2.37-2.47 (m, 4H), 4.60 (s, 1H), 5.36 (s, 1H), 6.41 (t, 1H, $J = 4.0$ Hz), 6.68 (s, 2H), 7.07-7.27 (m, 5H); ^{13}C NMR (CDCl_3 , 100 MHz): δ 16.1, 22.9, 26.2, 38.7, 48.6, 122.8, 126.1, 128.2, 129.0, 129.1, 133.8, 142.8, 143.1, 147.8, 150.7, 198.2; IR (film) 1670, 1489, 1263, 908, 738 cm^{-1} ; HRMS (ESI) calcd. for $\text{C}_{21}\text{H}_{22}\text{O}_2\text{Na}$: 329.1517, found: 329.1977.

(E)-2-(1,3-Bis(4-bromophenyl)allyl)-1H-pyrrole 101s

Colorless oil; ^1H NMR (CDCl_3 , 400 MHz): δ 4.80 (d, 1H, $J = 7.4$ Hz), 5.94 (s, 1H), 6.16 (dd, 1H, $J = 5.4, 2.6$ Hz), 6.31 (d, 1H, $J = 15.8$ Hz), 6.51 (dd, 1H, $J = 15.8, 7.5$ Hz), 6.71 (s, 1H), 7.10-7.46 (m, 8H), 7.83 (bs, 1H); ^{13}C NMR (CDCl_3 , 100 MHz): δ 47.5, 107.1, 108.6, 117.7, 120.9, 121.4, 128.0, 130.2, 130.5, 131.3, 131.7, 131.9, 132.1, 135.8, 140.9; IR (film) 3442, 1484, 1400, 1070, 1009, 820, 719 cm^{-1} ; HRMS (EI) calcd. for $\text{C}_{19}\text{H}_{15}\text{N}^{79}\text{Br}_2$: 414.9571, found: 414.9555.

(E)-2-(1,3-Di-*p*-tolylallyl)-1*H*-pyrrole 101t

Colorless oil; ^1H NMR (CDCl_3 , 400 MHz): δ 2.37 (s, 3H), 2.39 (s, 3H), 4.85 (d, 1H, $J = 7.5$ Hz), 6.00 (s, 1H), 6.21 (dd, 1H, $J = 5.6, 2.7$ Hz), 6.43 (d, 1H, $J = 15.8$ Hz), 6.57 (dd, 1H, $J = 15.7, 7.5$ Hz), 6.73 (d, 1H, $J = 1.4$ Hz), 7.14-7.32 (m, 8H), 7.87 (bs, 1H); ^{13}C NMR (CDCl_3 , 100 MHz): δ 21.1, 21.2, 47.8, 106.6, 108.4, 117.1, 126.3, 128.4, 129.3, 129.4, 130.4, 131.0, 133.5, 134.4, 136.5, 137.2, 139.3; IR (film) 3429, 3395, 3026, 2918, 1510, 1028, 966, 718 cm^{-1} ; HRMS (EI) calcd. for $\text{C}_{21}\text{H}_{21}\text{N}$: 287.1674, found: 287.1675.

(E)-2-(1,3-Diphenylallyl)-1*H*-pyrrole 101u

Colorless oil; ^1H NMR (CDCl_3 , 400 MHz): δ 4.86 (d, 1H, $J = 7.6$ Hz), 5.97 (s, 1H), 6.17 (dd, 1H, $J = 5.7, 2.8$ Hz), 6.42 (d, 1H, $J = 15.8$ Hz), 6.59 (dd, 1H, $J = 15.8, 7.6$ Hz), 6.70 (d, 1H, $J = 1.4$ Hz), 7.19-7.37 (m, 10H), 7.85 (bs, 1H); ^{13}C NMR (CDCl_3 , 100 MHz): δ 48.2, 106.8, 108.5, 117.3, 126.4, 127.0, 127.5, 128.5, 128.6, 128.8, 131.1, 131.3, 133.1, 137.1, 142.2; IR (film) 3429, 3026, 1487, 1449, 966, 698 cm^{-1} ; HRMS (EI) calcd. for $\text{C}_{19}\text{H}_{17}\text{N}$: 259.1361, found: 259.1355.

(E)-2-(1,3-Bis(4-bromophenyl)allyl)furan 101v

Colorless oil; ^1H NMR (CDCl_3 , 400 MHz): δ 4.84 (d, 1H, $J = 7.2$ Hz), 6.08 (d, 1H, $J = 0.6$ Hz), 6.29-6.34 (m, 2H), 6.51 (dd, 1H, $J = 15.8, 7.2$ Hz), 7.11-7.47 (m, 9H); ^{13}C NMR (CDCl_3 , 100 MHz): δ 47.7, 107.1, 110.3, 121.0, 121.4, 127.9, 129.9, 130.0, 130.9, 131.7, 131.8, 135.7, 139.8, 142.1, 155.1; IR (film) 1583, 1481, 1400, 1075, 1005, 735 cm^{-1} ; HRMS (EI) calcd. for $\text{C}_{19}\text{H}_{14}\text{O}^{79}\text{Br}_2$: 415.9411, found: 415.9411.

(E)-3-(1,3-Bis(4-bromophenyl)allyl)-1-methyl-1H-indole 101w

Yellow oil; ^1H NMR (CDCl_3 , 400 MHz): δ 3.74 (s, 3H), 5.05 (d, 2H, $J = 7.2\text{Hz}$), 6.33 (d, 1H, $J = 15.8\text{Hz}$), 6.65 (dd, 1H, $J = 15.6, 7.2\text{Hz}$), 6.73 (s, 1H), 7.00-7.43 (m, 12H); ^{13}C NMR (CDCl_3 , 100 MHz): δ 32.8, 45.6, 109.4, 116.2, 119.1, 119.7, 120.3, 121.0, 121.9, 126.9, 127.4, 127.9, 129.7, 130.3, 131.5, 131.6, 132.9, 136.2, 137.4, 142.3; IR (film) 1587, 1485, 1009 cm^{-1} ; HRMS (EI) calcd. for $\text{C}_{24}\text{H}_{19}\text{N}^{79}\text{Br}_2$: 478.9884, found: 478.9872.

(E)-2-(1,3-Bis(4-bromophenyl)allyl)-4-methylphenol 101x

Colorless oil; ^1H NMR (CDCl_3 , 400 MHz): δ 2.22 (s, 3H), 4.69 (s, 1H), 4.73 (d, 1H, J = 7.2 Hz), 6.23 (d, 1H, J = 15.8 Hz), 6.57 (dd, 1H, J = 15.8, 7.2 Hz), 6.72 (d, 1H, J = 7.2 Hz), 6.89 (d, 1H, J = 7.3 Hz), 6.93 (s, 1H), 7.08 (d, 2H, J = 8.2 Hz), 7.21-7.43 (m, 6H); ^{13}C NMR (CDCl_3 , 100 MHz): δ 20.7, 47.6, 115.1, 116.0, 120.6, 121.3, 127.9, 128.6, 128.7, 130.1, 130.4, 130.8, 131.6, 131.7, 131.9, 135.9, 141.3, 150.9; IR (film) 3366, 3024, 1494, 1487, 1008 cm^{-1} ; HRMS (EI) calcd. For $\text{C}_{22}\text{H}_{18}\text{O}^{79}\text{Br}_1^{81}\text{Br}_1$: 457.9698, found: 457.96

7.3 Unexpected Iron(III) Chloride-Catalyzed Dimerization of 1,1,3-Trisubstituted prop-2-yn-1-ols as an Expedient Route to Highly Conjugated Indenes

General experimental procedure for the synthesis of propargylic alcohols 106a–n

To a solution of alkyne (0.37 mL, 3.3 mmol, 1.1 equiv.) in THF was added LDA (2.0 M in THF, 2.25 mL, 1.5 equiv.) at -78°C . The resulting solution was stirred for 1 h at -78°C . Then the ketone (0.467 mL, 3 mmol, 1.0 equiv.) in THF (2 mL) was added slowly to the resulting solution at -78°C and stirred at room temperature for 10 h. The reaction mixture was quenched by addition of saturated NH_4Cl (10 mL) and extracted with diethyl ether (2 X 30 mL). The combined organic layers were washed with brine, dried over

MgSO₄ then the solvent was removed under reduced pressure and was purified by column chromatography on silica gel (eluent: hexane: ethyl acetate = 9:1) to give the desired product **106**.

General procedure for the Iron(III)-chloride catalyzed dimerization of propargylic alcohols

To a solution of **106** (0.3 mmol) and 4Å molecular sieves (200 mg) in CH₂Cl₂ (3 mL) under an N₂ atmosphere, was added FeCl₃ (5 mol%). The mixture was stirred at room temperature and monitored by TLC analysis. On completion, the reaction mixture was filtered through Celite and washed with CH₂Cl₂ (20 mL). The solvent was removed under reduced pressure and the residue was subjected to purification by flash column chromatography on silica gel (eluent: hexane: dichloromethane = 20:1 to 10:1) to give the desired product **107**, **108** and **112**.

1-Cyclobutyl-1,3-diphenylprop-2-yn-1-ol **106a**

Colourless oil; ¹H NMR (CDCl₃, 400 MHz): δ 1.77-2.00 (m, 4H), 2.10-2.19 (m, 1H), 2.27-2.37 (m, 1H), 2.45 (s, 1H), 2.80-2.86 (m, 1H), 7.29-7.39 (m, 6H), 7.52-7.54 (m, 2H), 7.67(d, 2H, *J* = 7.6 Hz); ¹³C NMR (CDCl₃, 100 MHz): δ 16.7, 23.3, 23.9, 47.2, 75.5, 86.6, 90.4, 122.7, 125.5, 127.6, 128.1, 128.4, 128.5, 131.9, 143.5; FTIR (NaCl, neat) ν: 3420,

1599, 1489, 1447, 754 cm^{-1} ; MS (ESI) m/z 245 $[\text{M}-\text{OH}]^+$; HRMS (ESI) calcd. For $\text{C}_{19}\text{H}_{17}$ (M^+-OH):245.1330, found:245.1328.

1-Cyclobutyl-1-phenyl-3-p-tolylprop-2-yn-1-ol 106b

Pale-yellow oil; ^1H NMR (CDCl_3 , 400 MHz): δ 1.76-1.95 (m, 4H), 2.12-2.17 (m, 1H), 2.30-2.34 (m, 1H), 2.50 (s, 4H), 2.80-2.84 (m, 1H), 7.12-7.36 (m, 6H), 7.47 (d, 1H, $J = 7.5$ Hz), 7.65 (d, 2H, $J = 7.3$ Hz); ^{13}C NMR (CDCl_3 , 100 MHz): δ 16.7, 21.6, 23.3, 23.9, 47.2, 75.6, 86.8, 89.6, 119.6, 125.6, 127.6, 128.1, 129.1, 131.8, 138.7, 143.6; FTIR (NaCl, neat) ν : 3428, 1508, 1489, 1447, 815 cm^{-1} ; MS (ESI) m/z 259 $[\text{M}-\text{OH}]^+$; HRMS (ESI) calcd. For $\text{C}_{20}\text{H}_{19}$ (M^+-OH):259.1487, found: 259.1485.

1-Cyclobutyl-3-(4-pentylphenyl)-1-phenylprop-2-yn-1-ol 106c

Pale-yellow oil; ^1H NMR (CDCl_3 , 400 MHz): δ 0.92 (t, 3H, $J = 7.0$ Hz), 1.30-1.39 (m, 4H), 1.60-1.67 (m, 2H), 1.77-1.99 (m, 4H), 2.12-2.19 (m, 1H), 2.28-2.37 (m, 1H), 2.47 (s, 1H), 2.63 (t, 1H, $J = 7.8$ Hz), 2.80-2.88 (m, 1H), 7.17 (d, 2H, $J = 8.1$ Hz), 7.28-7.46 (m, 5H), 7.66-7.69 (m, 2H); ^{13}C NMR (CDCl_3 , 100 MHz): δ 14.1, 16.7, 22.6, 23.3, 23.9, 31.0, 31.4, 35.9, 47.2, 75.6, 86.8, 89.6, 119.8, 125.6, 127.6, 128.1, 128.5, 131.8, 143.6, 143.7; FTIR (NaCl, neat) ν : 3435, 3026, 2224, 1601, 1508, 1447, 1265, 1011, 980 cm^{-1} ; MS (ESI) m/z 315 $[\text{M}-\text{OH}]^+$; HRMS (ESI) calcd. For $\text{C}_{24}\text{H}_{27}$ (M^+-OH):315.2113, found:315.2108.

3-(4-Chlorophenyl)-1-cyclobutyl-1-phenylprop-2-yn-1-ol 106d

Pale-yellow oil; ^1H NMR (CDCl_3 , 400 MHz): δ 1.76-1.98 (m, 4H), 2.05-2.17 (m, 1H), 2.23-2.32 (m, 1H), 2.43 (s, 3H), 2.78-2.87 (m, 1H), 7.30-7.45 (m, 7H), 7.62-7.64 (m, 2H); ^{13}C NMR (CDCl_3 , 100 MHz): δ 16.7, 23.2, 23.9, 47.1, 75.5, 85.4, 91.4, 121.2, 125.4, 127.7, 128.2, 128.7, 133.1, 134.6, 143.2; FTIR (NaCl, neat) ν : 3420, 2978, 2231, 1489, 1447, 1092, 1015, 827 cm^{-1} ; MS (ESI) m/z 279 $[\text{M}-\text{OH}]^+$; HRMS (ESI) calcd. For $\text{C}_{19}\text{H}_{16}^{35}\text{Cl}$ (M^+-OH): 279.0941, found: 279.0931.

1-Cyclobutyl-1-phenyl-3-(thiophen-3-yl)prop-2-yn-1-ol 106e

Pale-yellow oil; ^1H NMR (CDCl_3 , 400 MHz): δ 1.75-1.97 (m, 4H), 2.05-2.17 (m, 1H), 2.23-2.33 (m, 1H), 2.40 (s, 1H), 2.78-2.86 (m, 1H), 7.17-7.38 (m, 5H), 7.50-7.52 (m, 1H), 7.63-7.65 (m, 2H); ^{13}C NMR (CDCl_3 , 100 MHz): δ 16.7, 23.2, 23.9, 47.1, 75.5, 81.6, 90.0, 121.7, 125.4, 125.5, 127.6, 128.1, 129.1, 130.1, 143.4; FTIR (NaCl, neat) ν : 3422, 2977, 2223, 1601, 1489, 1358, 1015 cm^{-1} ; MS (ESI) m/z 251 $[\text{M}-\text{OH}]^+$; HRMS (ESI) calcd. For $\text{C}_{17}\text{H}_{15}\text{S}$ (M^+-OH): 251.0894, found: 251.0884.

1,3-Diphenylpent-1-yn-3-ol 106f^{132,133}

Pale-yellow oil; ¹H NMR (CDCl₃, 400 MHz): δ 1.04 (t, 3H, J = 7.4 Hz), 1.97-2.15 (m, 4H), 2.53 (s, 1H), 7.30-7.41 (m, 6H), 7.50-7.53 (m, 2H), 7.70-7.72 (m, 2H); ¹³C NMR (CDCl₃, 100 MHz): δ 9.2, 38.5, 74.4, 86.2, 91.3, 122.7, 125.6, 127.7, 128.2, 128.4, 128.5, 131.8, 144.6; MS (ESI) m/z 219 [M-OH]⁺;

1,3-Diphenylhept-1-yn-3-ol 106g¹³⁴

Pale-yellow oil; ¹H NMR (CDCl₃, 400 MHz): δ 0.90 (t, 3H, J = 7.2 Hz), 1.27-1.59 (m, 4H), 1.94-2.10 (m, 2H), 2.49 (s, 1H), 7.30-7.52 (m, 8H), 7.70-7.72 (m, 2H); ¹³C NMR (CDCl₃, 100 MHz): δ 14.0, 22.7, 27.0, 45.3, 73.8, 86.0, 91.6, 122.7, 125.5, 127.7, 128.2, 128.3, 128.5, 131.8, 144.9; MS (ESI) m/z 247 [M-OH]⁺;

1,3-Diphenylnon-1-yn-3-ol 106h

Pale-yellow solid, m.p. 55-56 °C; ¹H NMR (CDCl₃, 400 MHz): δ 0.86 (t, 3H, J = 6.5Hz), 1.28-1.58 (m, 8H), 1.94-2.09 (m, 2H), 2.50 (s, 1H), 7.30-7.41 (m, 6H), 7.50-7.52 (m, 2H), 7.71 (m, 2H, J = 8.0 Hz); ¹³C NMR (CDCl₃, 100 MHz): δ 14.1, 22.6, 24.8, 29.2, 31.7, 45.6, 73.8, 86.0, 91.7, 122.7, 125.5, 127.7, 128.2, 128.3, 128.5, 131.8, 144.9; FTIR (NaCl, neat) ν : 3383, 1599, 1489, 1447, 1265, 1030 cm⁻¹; MS (ESI) m/z 275 [M-OH]⁺; HRMS (ESI) calcd. For C₂₁H₂₃: 275.1800, found: 275.1795.

3-(Benzo[d][1,3]dioxol-5-yl)-1-phenylpent-1-yn-3-ol 106i

Pale-yellow oil; ^1H NMR (CDCl_3 , 400 MHz): δ 1.01 (t, 3H, $J = 7.4$ Hz), 1.91-2.10 (m, 2H), 2.50 (s, 1H), 5.96 (s, 2H), 6.79 (d, 2H, $J = 8.0$ Hz), 7.17-7.49 (m, 7H); ^{13}C NMR (CDCl_3 , 100 MHz): δ 9.3, 38.5, 74.2, 86.1, 91.3, 101.1, 106.5, 107.7, 119.1, 122.6, 128.3, 128.5, 131.8, 138.7, 147.0, 147.6; FTIR (NaCl, neat) ν : 3433, 1624, 1498, 1179 cm^{-1} ; MS (ESI) m/z 263 $[\text{M}-\text{OH}]^+$; HRMS (ESI) calcd. For $\text{C}_{18}\text{H}_{15}\text{O}_2$ (M^+-OH): 263. 1067, found: 263. 1061.

5-Methyl-1,3-diphenylhex-1-yn-3-ol 106j

Pale-yellow solid, m.p. 59-60 $^{\circ}\text{C}$; ^1H NMR (CDCl_3 , 400 MHz): δ 0.91(d, 3H, $J = 6.2$ Hz), 1.04 (d, 3H, $J = 6.2$ Hz), 1.90-2.05 (m, 3H), 2.47 (s, 1H), 7.30-7.52 (m, 8H), 7.71-7.73 (m, 2H); ^{13}C NMR (CDCl_3 , 100 MHz): δ 24.0, 24.1, 25.3, 53.8, 73.7, 86.3, 92.0, 122.7, 125.5, 127.7, 128.2, 128.4, 128.5, 131.7, 145.4; FTIR (NaCl, neat) ν : 3406, 1599, 1490, 1445, 754 cm^{-1} ; MS (ESI) m/z 247 $[\text{M}-\text{OH}]^+$; HRMS (ESI) calcd. For $\text{C}_{19}\text{H}_{19}$ (M^+-OH): 247.1487, found: 247.1477.

1,2,4-Triphenylbut-3-yn-2-ol 106k

Pale-yellow oil; ^1H NMR (CDCl_3 , 400 MHz): δ 2.53 (s, 1H), 3.24 (s, 2H), 7.24-7.43 (m, 13H), 7.67 (m, 2H, $J = 7.4$ Hz); ^{13}C NMR (CDCl_3 , 100 MHz): δ 52.0, 73.7, 87.4, 91.1, 122.5, 125.7, 127.1, 127.8, 127.9, 128.2, 128.3, 128.6, 131.0, 131.7, 135.9, 144.2; FTIR (NaCl, neat) ν : 3428, 3059, 3028, 2924, 1599, 1491, 1449, 1030, 756, 700 cm^{-1} ; MS (ESI) m/z 281 $[\text{M}-\text{OH}]^+$; HRMS (ESI) calcd. For $\text{C}_{22}\text{H}_{17}(\text{M}^+-\text{OH})$: 281.1330, found: 281.1327.

2-(4-Ethoxyphenyl)-1-phenyl-4-p-tolylbut-3-yn-2-ol 106l

Yellow oil; ^1H NMR (CDCl_3 , 400 MHz): δ 1.42 (t, 3H, $J = 7.0$ Hz), 2.34 (s, 3H), 2.50 (s, 1H), 3.18-3.26 (m, 2H), 4.04 (q, 2H, $J = 7.0$ Hz), 6.85-6.89 (m 2H), 7.11 (d, 2H, $J = 7.9$ Hz), 7.21-7.31 (m, 7H), 7.53-7.57 (m, 2H); ^{13}C NMR (CDCl_3 , 100 MHz): δ 14.9, 21.5, 52.0, 63.5, 73.4, 87.4, 90.6, 114.0, 119.5, 126.9, 127.0, 127.8, 129.1, 131.1, 131.6, 136.2, 136.3, 138.6, 158.5; FTIR (NaCl, neat) ν : 3410, 1609, 1508, 1246, 1175, 818, 700 cm^{-1} ; MS (ESI) m/z 339 $[\text{M}-\text{OH}]^+$; HRMS (ESI) calcd. For $\text{C}_{25}\text{H}_{23}\text{O}(\text{M}^+-\text{OH})$: 339.1749, found: 339.1740.

3,5-Diphenyl-1-p-tolylpent-1-yn-3-ol 106m

Pale-yellow oil; ^1H NMR (CDCl_3 , 400 MHz): δ 2.22-2.38 (m, 5H), 2.52 (s, 1H), 2.75-2.94 (m, 2H), 7.13-7.40 (m, 12H), 7.73 (d, 2H, $J = 7.6$ Hz); ^{13}C NMR (CDCl_3 , 100 MHz): δ 21.5, 31.4, 47.2, 73.7, 86.7, 90.5, 119.5, 125.6, 125.9, 127.8, 128.3, 128.4, 128.5, 129.2, 131.7, 138.8, 141.8, 144.7; FTIR (NaCl, neat) ν : 3430, 3051, 2965, 1612, 1498, 1035 cm^{-1} ; MS (ESI) m/z 309 $[\text{M}-\text{OH}]^+$; HRMS (ESI) calcd. For $\text{C}_{24}\text{H}_{21}$ (M^+-OH): 309.1638, found: 309.1633.

3-(4-Ethoxyphenyl)-1-p-tolylhept-6-en-1-yn-3-ol 106n

Pale-yellow oil; ^1H NMR (CDCl_3 , 500 MHz): δ 1.43 (t, 3H, $J = 6.9$ Hz), 2.06-2.37 (m, 7H), 2.54 (s, 1H), 4.05 (q, 2H, $J = 6.9$ Hz), 4.96 (d, 1H, $J = 10.1$ Hz), 5.04 (d, 1H, $J = 17.1$ Hz), 5.81-5.88 (m, 1H), 6.90 (d, 2H, $J = 8.3$ Hz), 7.14 (d, 2H, $J = 7.7$ Hz), 7.39 (d, 2H, $J = 7.7$ Hz), 7.60 (d, 2H, $J = 8.3$ Hz); ^{13}C NMR (CDCl_3 , 100 MHz): δ 14.9, 21.5, 29.5, 44.5, 63.5, 73.3, 86.4, 90.7, 114.1, 114.7, 119.5, 126.8, 129.1, 131.7, 136.7, 138.3, 138.7, 158.5; FTIR (NaCl, neat) ν : 3435, 2226, 1609, 1508, 1246, 1047, 914 cm^{-1} ; MS (ESI) m/z 303 $[\text{M}-\text{OH}]^+$; HRMS (ESI) calcd. For $\text{C}_{22}\text{H}_{23}\text{O}$ (M^+-OH): 303.1743, found: 303.1739.

1-Cyclobutyl-2-(cyclobutylidene(phenyl)methyl)-1-phenyl-3-(phenylethynyl)-1H-indene 107a⁸⁸

Colourless solid, m.p. 180-181°C; ¹H NMR (CDCl₃, 400 MHz): δ 0.96-0.99 (m, 1H), 1.40-1.59 (m, 3H), 1.72-1.86 (m, 2H), 2.04-2.09 (m, 3H), 2.49-2.57 (m, 1H), 2.71 (t, 2H, $J = 7.6$ Hz), 3.13-3.19 (m, 1H), 6.79 (d, 2H, $J = 5.8$ Hz), 7.00-7.13 (m, 8H), 7.23-7.52 (m, 8H), 7.68 (d, 2H, $J = 7.4$ Hz); ¹³C NMR (CDCl₃, 100 MHz): δ 17.1, 17.3, 23.5, 25.0, 32.0, 32.3, 38.3, 66.4, 84.4, 94.3, 120.3, 122.1, 123.7, 125.0, 125.7, 125.9, 126.2, 126.7, 127.2, 127.6, 127.7, 128.2, 128.3, 128.4, 131.8, 138.5, 140.9, 144.3, 145.9, 149.1, 158.4; FTIR (NaCl, neat) ν : 2980, 1653, 1597, 1511, 1443, 1265 cm⁻¹; MS (ESI) m/z 489 [M+H]⁺; HRMS (ESI) calcd. For C₃₈H₃₃ (M⁺+H): 489.2582, found: 489.2567.

1-Cyclobutyl-2-(cyclobutylidene(p-tolyl)methyl)-1-phenyl-3-(p-tolyethynyl)-1H-indene 107b

Colourless solid, m.p. 87-89 °C; ¹H NMR (CDCl₃, 400 MHz): δ 0.90-0.96 (m, 1H), 1.38-1.57 (m, 3H), 1.67-1.82 (m, 2H), 1.95-2.05 (m, 3H), 2.26 (s, 3H), 2.33 (s, 3H), 2.41-2.49 (m, 1H), 2.68 (s, 2H), 3.08-3.16 (m, 1H), 6.77 (d, 2H, $J = 7.2$ Hz), 6.90-7.03 (m, 7H), 7.11 (d, 2H, $J = 7.8$ Hz), 7.23-7.43 (m, 5H), 7.64 (d, 2H, $J = 7.5$ Hz); ¹³C NMR (CDCl₃, 75

MHz): δ 17.1, 17.3, 21.2, 21.5, 23.5, 25.0, 32.0, 32.2, 38.3, 66.3, 83.8, 94.4, 120.2, 120.6, 122.1, 124.9, 125.6, 126.0, 126.5, 127.2, 127.6, 128.1, 128.3, 129.1, 131.7, 135.3, 135.6, 138.3, 141.1, 144.4, 145.2, 149.1, 158.2; FTIR (NaCl, neat) ν : 2978, 2941, 1651, 1506, 896 cm^{-1} ; MS (ESI) m/z 517 $[\text{M}+1]^+$; HRMS (ESI) calcd. For $\text{C}_{40}\text{H}_{37}(\text{M}^++\text{H})$: 517.2895, found: 517.2894.

1-Cyclobutyl-2-(cyclobutylidene(4-pentylphenyl)methyl)-3-((4-pentylphenyl)ethynyl)-1-phenyl-1H-indene 107c

Yellow oil; ^1H NMR (CDCl_3 , 400 MHz): δ 0.87-1.00 (m, 7H), 1.26-1.44 (m, 10H), 1.32-1.49 (m, 9H), 1.55-1.62 (m, 6H), 1.75-1.85 (m, 2H), 2.05-2.14 (m, 3H), 2.48-2.73 (m, 7H), 3.08-3.19 (m, 1H), 6.77 (d, 2H, $J = 6.6$ Hz), 6.88-6.99 (m, 7H), 7.12-7.44 (m, 7H), 7.66 (d, 1H, $J = 7.4$ Hz); ^{13}C NMR (CDCl_3 , 100 MHz): δ 14.1, 14.1, 17.2, 17.3, 22.6, 22.6, 23.6, 25.1, 31.0, 31.2, 31.5, 31.6, 32.1, 32.3, 35.7, 35.9, 38.4, 66.2, 83.9, 94.5, 120.2, 120.9, 122.1, 124.9, 125.6, 126.0, 126.7, 127.2, 127.6, 128.1, 128.3, 128.5, 131.7, 135.8, 140.3, 141.1, 143.3, 144.4, 145.0, 149.2, 158.2; FTIR (NaCl, neat) ν : 2953, 2928, 1647, 1508, 1456, 752 cm^{-1} ; MS (ESI) m/z 629 $[\text{M}+1]^+$; HRMS (ESI) calcd. For $\text{C}_{48}\text{H}_{53}(\text{M}^++\text{H})$: 629.4147, found: 629.4154.

2-((4-Chlorophenyl)(cyclobutylidene)methyl)-3-((4-chlorophenyl)ethynyl)-1-cyclobutyl-1-phenyl-1H-indene 107d

Pale-yellow solid, m.p. 167-168 °C; ^1H NMR (CDCl_3 , 400 MHz): δ 0.94-1.02 (m, 1H), 1.45-1.66 (m, 3H), 1.71-1.88 (m, 2H), 2.06-2.23 (m, 3H), 2.51-2.77 (m, 3H), 3.16-3.22 (m, 1H), 6.73 (d, 2H, $J = 7.4$ Hz), 6.88-7.06 (m, 7H), 7.25-7.46 (m, 8H), 7.64 (d, 2H, $J = 7.4$ Hz); ^{13}C NMR (CDCl_3 , 100 MHz): δ 17.1, 17.2, 23.4, 25.0, 32.2, 32.3, 38.2, 66.2, 85.2, 93.4, 120.2, 121.9, 122.1, 125.0, 125.8, 125.9, 126.2, 127.3, 127.7, 127.7, 128.2, 128.7, 129.4, 131.5, 132.9, 134.3, 136.8, 140.6, 143.8, 146.6, 149.1, 158.2; FTIR (NaCl, neat) ν : 2998, 2931, 1498, 1321, 1108, 835 cm^{-1} ; MS (ESI) m/z 557 $[\text{M}+1]^+$; HRMS (ESI) calcd. For $\text{C}_{38}\text{H}_{31}^{35}\text{Cl}_2(\text{M}^++\text{H})$: 557.1803, found: 557.1812.

3-((1-Cyclobutyl-1-phenyl-3-(thiophen-3-ylethynyl)-1H-inden-2-yl)(cyclobutylidene)methyl) thiophene 107e⁸⁸

Pale-yellow solid, m.p. 127-129 °C; ^1H NMR (CDCl_3 , 400 MHz): δ 0.95-1.01 (m, 1H), 1.45-1.64 (m, 1H), 1.75-1.86 (m, 4H), 2.05-2.11 (m, 2H), 2.45-2.47 (m, 1H), 2.71-2.79 (m, 1H), 3.24-3.28 (m, 1H), 6.70 (dd, 1H, $J = 5.0, 1.1$ Hz), 6.76 (dd, 1H, $J = 2.8, 1.0$ Hz), 6.80 (dd, 1H, $J = 8.1, 2.0$ Hz), 6.98-7.05 (m, 4H), 7.17 (dd, 1H, $J = 5.0, 1.0$ Hz), 7.27-7.49

(m, 5H), 7.64 (d, 2H, $J = 7.5$ Hz); ^{13}C NMR (CDCl_3 , 100 MHz): δ 17.2, 17.2, 23.6, 25.1, 31.8, 32.5, 38.4, 66.3, 83.8, 89.6, 120.3, 121.2, 121.5, 122.0, 122.6, 123.7, 125.0, 125.3, 125.7, 126.2, 127.2, 127.7, 127.9, 128.3, 128.6, 130.1, 139.4, 141.0, 144.2, 145.7, 149.0, 157.9; FTIR (NaCl, neat) ν : 2977, 2941, 1653, 1636, 777 cm^{-1} ; MS (ESI) m/z 501 $[\text{M}+1]^+$; HRMS (ESI) calcd. For $\text{C}_{34}\text{H}_{29}\text{S}_2$ (M^++H): 501.1711, found: 501.1708.

(*E*)-1-ethyl-1-phenyl-3-(phenylethynyl)-2-(1-phenylprop-1-enyl)-1H-indene 107f

Yellow oil; ^1H NMR (CDCl_3 , 400 MHz): δ 1.07 (t, 3H, $J = 7.6$ Hz), 1.57 (d, 1H, $J = 7.8$ Hz), 2.37-2.44 (m, 2H), 5.75 (q, 1H, $J = 7.0$ Hz), 7.09-7.35 (m, 19H); ^{13}C NMR (CDCl_3 , 100 MHz): δ 13.3, 15.2, 19.6, 58.4, 84.5, 89.8, 119.7, 123.7, 126.3, 126.5, 126.6, 126.6, 127.3, 127.7, 127.7, 128.0, 128.2, 128.3, 129.6, 131.8, 136.0, 139.9, 140.8, 141.5, 143.8, 147.9, 151.3; FTIR (NaCl, neat) ν : 2993, 2921, 1654, 1490, 757 cm^{-1} ; MS (ESI) m/z 437 $[\text{M}+1]^+$; HRMS (ESI) calcd. For $\text{C}_{34}\text{H}_{29}$ (M^++H): 437.2269, found: 437.2243.

(*E*)-1-butyl-1-phenyl-3-(phenylethynyl)-2-(1-phenylpent-1-enyl)-1H-indene 107g

Yellow oil; ^1H NMR (CDCl_3 , 400 MHz): δ 0.70 (t, 3H, $J = 7.4$ Hz), 0.86 (t, 3H, $J = 7.4$ Hz), 1.16-1.30 (m, 4H), 1.38-1.50 (m, 2H), 1.87-1.99 (m, 2H), 2.27-2.32 (m, 2H), 5.68 (t, 1H, $J = 7.4$ Hz), 7.08-7.33 (m, 19H); ^{13}C NMR (CDCl_3 , 100 MHz): δ 13.6, 14.0, 23.0,

23.2, 26.3, 31.1, 31.1, 58.6, 84.4, 90.0, 119.7, 123.6, 123.7, 126.3, 126.4, 126.7, 127.3, 127.7, 127.8, 128.0, 128.2, 129.6, 131.8, 134.5, 135.0, 140.3, 140.5, 140.9, 144.3, 147.9, 151.3; FTIR (NaCl, neat) ν : 3057, 2957, 2928, 2859, 1597, 1489, 1445, 1022, 754 cm^{-1} ; MS (ESI) m/z 493 $[\text{M}+1]^+$; HRMS (ESI) calcd. For $\text{C}_{38}\text{H}_{37}$ (M^++H): 493.2895, found: 493.2887.

(*E*)-1-Hexyl-1-phenyl-3-(phenylethynyl)-2-(1-phenylhept-1-enyl)-1H-indene 107h

Yellow oil; ^1H NMR (CDCl_3 , 400 MHz): δ 0.75(t, 3H, $J = 7.2$ Hz), 0.88 (t, 3H, $J = 7.1$ Hz), 1.02-1.51 (m, 18H), 1.83-2.02 (m, 2H), 2.29 (t, 2H, $J = 7.6$ Hz), 5.68 (t, 1H, $J = 7.5$ Hz), 7.08-7.33 (m, 19H); ^{13}C NMR (CDCl_3 , 100 MHz): δ 13.9, 14.1, 22.5, 22.7, 26.6, 28.9, 29.0, 29.5, 29.8, 31.1, 31.7, 58.5, 84.5, 90.0, 119.7, 123.6, 123.7, 126.3, 126.4, 126.7, 127.3, 127.7, 127.7, 128.0, 128.2, 129.6, 131.8, 134.8, 134.8, 140.3, 140.5, 140.9, 144.3, 147.9, 151.2; FTIR (NaCl, neat) ν : 2955, 2855, 1597, 1489, 1028 cm^{-1} ; MS (ESI) m/z 549 $[\text{M}+1]^+$; HRMS (ESI) calcd. For $\text{C}_{42}\text{H}_{45}$ (M^++H): 549.3521, found: 549.3523.

(*E*)-5-(benzo[*d*][1,3]dioxol-5-yl)-5-ethyl-7-(phenylethynyl)-6-(1-phenylprop-1-enyl)-5H-indeno[5,6-*d*][1,3]dioxole 107i

Colourless solid, m.p. 68-70 °C; ^1H NMR (CDCl_3 , 400 MHz): δ 1.03 (t, 3 H, $J = 7.5$ Hz), 1.60 (d, 3H, $J = 7.0$ Hz), 2.33 (q, 2H, $J = 7.4$ Hz), 5.77 (q, 1H, $J = 7.0$ Hz), 5.88 (d, 2H, $J = 8.1$ Hz), 5.92 (s, 2H), 6.59 (s, 1H), 6.65 (d, 1H, $J = 8.1$ Hz), 6.74 (s, 1H), 6.80 (s, 1H), 6.93 (d, 1H, $J = 8.0$ Hz), 7.09-7.30 (m, 10H); ^{13}C NMR (CDCl_3 , 100 MHz): δ 13.3, 15.2, 19.7, 57.6, 84.4, 89.7, 100.8, 100.9, 101.1, 105.0, 106.9, 107.7, 120.0, 123.5, 126.4, 127.6, 127.8, 127.9, 128.0, 129.6, 131.8, 134.6, 136.0, 137.4, 139.9, 141.0, 145.1, 146.3, 146.5, 147.0, 147.3, 147.4; FTIR (NaCl, neat) ν : 2982, 2937, 1672, 1513, 1235, 824 cm^{-1} ; MS (ESI) m/z 525 $[\text{M}+1]^+$; HRMS (ESI) calcd. For $\text{C}_{36}\text{H}_{29}\text{O}_4$ (M^++H): 525.2066, found: 525.2057.

(*E*)-1-isobutyl-2-(3-methyl-1-phenylbut-1-enyl)-1-phenyl-3-(phenylethynyl)-1H-indene 107j

Pale-yellow oil; ^1H NMR (CDCl_3 , 400 MHz): δ 0.78 (d, 3H, $J = 6.5$ Hz), 0.82 (d, 3H, $J = 6.5$ Hz), 0.87 (d, 3H, $J = 6.5$ Hz), 0.92 (d, 3H, $J = 6.5$ Hz), 1.99-2.09 (m, 1H), 2.18 (d, 2H, $J = 7.3$ Hz), 2.34-2.43 (m, 1H), 5.44 (d, 1H, $J = 10.3$ Hz), 7.07-7.32 (m, 19H); ^{13}C NMR

(CDCl₃, 100 MHz): δ 23.0, 23.1, 23.1, 23.2, 28.0, 35.0, 58.8, 90.0, 120.0, 123.7, 123.7, 126.2, 126.4, 126.7, 126.9, 127.3, 127.7, 127.7, 128.0, 128.1, 129.4, 131.8, 132.2, 139.5, 140.2, 140.8, 142.2, 144.9, 149.2, 150.9; FTIR (NaCl, neat) ν : 2957, 2864, 1636, 1456, 752 cm⁻¹; MS (ESI) m/z 493 [M+1]⁺; HRMS (ESI) calcd. For C₃₈H₃₇ (M⁺+H): 493.2895, found: 493.2884.

(*E*)-1-benzyl-2-(1,2-diphenylvinyl)-1-phenyl-3-(phenylethynyl)-1H-indene 107k

Gray oil; ¹H NMR (CDCl₃, 400 MHz): δ 3.89 (q, 2H, J = 15.8 Hz), 6.64 (s, 1H), 6.75-7.36 (m, 29H); ¹³C NMR (CDCl₃, 100 MHz): δ 32.6, 58.9, 84.8, 89.3, 121.0, 123.5, 123.7, 126.1, 126.7, 126.8, 126.9, 126.9, 127.2, 127.5, 127.8, 127.9, 127.9, 128.1, 128.2, 128.4, 128.5, 129.6, 130.0, 131.9, 132.4, 136.5, 137.1, 139.1, 139.5, 140.4, 143.9, 150.7, 151.2; FTIR (NaCl, neat) ν : 2991, 2918, 2089, 1636, 690 cm⁻¹; MS (ESI) m/z 561 [M+1]⁺; HRMS (ESI) calcd. For C₄₄H₃₃ (M⁺+H): 561.2582, found: 561.2592.

(*E*)-1-benzyl-6-ethoxy-1-(4-ethoxyphenyl)-2-(2-phenyl-1-p-tolylvinyl)-3-(p-tolyethynyl)-1H-indene 107l⁸⁸

Pale-yellow solid, m.p. 191-192 °C; ^1H NMR (CDCl_3 , 400 MHz): δ 1.38-1.52 (m, 6 H), 2.25 (s, 3H), 3.79 (d, 1H, $J = 12.9$ Hz), 3.98-4.05 (m, 5H), 6.51 (s, 1H), 6.66-7.31(m, 25H); ^{13}C NMR (CDCl_3 , 100 MHz): δ 14.9, 15.0, 21.3, 21.5, 42.5, 61.4, 63.4, 63.7, 83.5, 101.0, 109.4, 113.1, 114.9, 120.4, 121.4, 125.5, 126.4, 126.5, 126.7, 127.6, 127.8, 128.6, 128.9, 129.6, 129.7, 130.8, 130.9, 131.8, 136.3, 136.4, 136.6, 136.9, 137.0, 137.6, 137.7, 137.9, 152.2, 154.1, 157.6, 158.8; FTIR (NaCl, neat) ν : 2978, 1651, 1506, 1246, 1045, 816 cm^{-1} ; MS (ESI) m/z 677 $[\text{M}+1]^+$; HRMS (ESI) calcd. For $\text{C}_{50}\text{H}_{45}\text{O}_2$ (M^++H): 677.3420, found: 677.3411.

(*E*)-1-phenethyl-1-phenyl-2-(3-phenyl-1-p-tolylprop-1-enyl)-3-(p-tolyethynyl)-1H-indene 107m

Pale-yellow oil; ^1H NMR (CDCl_3 , 400 MHz): δ 2.26 (s, 3H), 2.30 (s, 3H), 2.65-2.88 (m, 4H), 3.17-3.35 (m, 2H), 5.72 (t, 1H, $J = 7.7$ Hz), 6.84-7.43 (m, 27H); ^{13}C NMR (CDCl_3 , 100 MHz): δ 21.2, 21.5, 28.9, 34.9, 35.1, 58.5, 84.8, 88.7, 119.8, 120.5, 123.9, 125.7, 126.0, 126.6, 126.7, 126.8, 127.4, 128.3, 128.3, 128.4, 128.6, 128.7, 128.7, 129.4, 131.7, 131.9, 135.9, 136.5, 136.6, 137.7, 139.2, 140.7, 140.9, 141.9, 143.8, 149.1, 151.4; FTIR (NaCl, neat) ν : 2962, 2933, 1603, 1588, 1025, 717 cm^{-1} ; MS (ESI) m/z 617 $[\text{M}+\text{H}]^+$; HRMS (ESI) calcd. For $\text{C}_{48}\text{H}_{41}$ (M^++H): 617.3208, found: 617.3201.

(*E*)-1-(but-3-enyl)-6-ethoxy-1-(4-ethoxyphenyl)-3-(p-tolylethynyl)-2-(1-p-tolylpenta-1,4-dienyl)-1H-indene 107n

Pale-brown oil; ^1H NMR (CDCl_3 , 400 MHz): δ 1.33-1.40 (m, 6 H), 1.84-1.91 (m, 1H), 2.19-2.613 (m, 11H), 3.91-4.00 (m, 4H), 4.72-4.92 (m, 4H), 5.60-5.75 (m, 3H), 6.53 (d, 1H, $J = 2.2$ Hz), 6.72-6.80 (m, 3H), 6.98-7.24 (m, 10H), 7.39 (m, 1H, $J = 8.2$ Hz); ^{13}C NMR (CDCl_3 , 100 MHz): δ 14.9, 14.9, 21.2, 21.5, 27.9, 33.3, 35.6, 60.8, 63.4, 63.6, 83.6, 98.2, 109.0, 112.6, 114.3, 114.4, 114.7, 120.5, 121.0, 122.6, 127.1, 128.5, 128.8, 129.9, 131.0, 131.8, 136.0, 136.1, 136.5, 136.7, 137.4, 138.0, 138.8, 153.6, 153.8, 157.4, 158.6; FTIR (NaCl, neat) ν : 2978, 1607, 1508, 1248, 756 cm^{-1} ; MS (ESI) m/z 605 $[\text{M}+1]^+$; HRMS (ESI) calcd. For $\text{C}_{44}\text{H}_{45}\text{O}_2$ (M^++H): 605.3420, found: 605.3413.

3-Cyclobutyl-2-(cyclobutylidene(phenyl)methyl)-1-phenyl-1-(phenylethynyl)-1H-indene 108a⁸⁸

Colourless solid, m.p. 161-163 $^{\circ}\text{C}$; ^1H NMR (CDCl_3 , 400 MHz): δ 1.59-1.85 (m, 3H), 1.90-1.97 (m, 1H), 2.03-2.15 (m, 1H), 2.23-2.38 (m, 3H), 2.54-2.72 (m, 3H), 2.84-2.89 (m, 1H), 3.64-3.73 (m, 1H), 6.93 (d, 2H, $J = 7.2$ Hz), 7.04-7.25 (m, 14H), 7.36-7.39 (m, 2H), 7.60 (d, 2H, $J = 7.5$ Hz); ^{13}C NMR (CDCl_3 , 100 MHz): δ 17.3, 19.2, 27.4, 27.8, 31.6,

32.5, 35.2, 58.4, 84.2, 89.8, 120.7, 123.5, 124.3, 125.7, 126.0, 126.6, 127.3, 127.4, 127.5, 127.6, 127.7, 128.0, 131.7, 139.2, 140.8, 141.2, 144.1, 144.2, 145.0, 150.4; FTIR (NaCl, neat) ν : 2983, 1651, 1489, 754 cm^{-1} ; MS (ESI) m/z 489 $[\text{M}+1]^+$; HRMS (ESI) calcd. For $\text{C}_{38}\text{H}_{33}(\text{M}^++\text{H})$: 489.2582, found: 489.2579.

3-Cyclobutyl-2-(cyclobutylidene(p-tolyl)methyl)-1-phenyl-1-(p-tolylethynyl)-1H-indene 108c

Pale-yellow oil; ^1H NMR (CDCl_3 , 400 MHz): δ 1.61-1.96 (m, 5H), 2.02-2.39 (m, 9H), 2.51-2.66 (m, 3H), 2.83-2.89 (m, 1H), 3.63-3.72 (m, 1H), 6.78 (d, 2H, $J = 7.9$ Hz), 6.93-7.00 (m, 4H), 7.10-7.38 (m, 10H), 7.58 (d, 2H, $J = 7.6$ Hz); ^{13}C NMR (CDCl_3 , 100 MHz): δ 17.2, 19.2, 21.0, 21.4, 27.4, 27.9, 31.5, 32.3, 35.3, 58.4, 84.3, 89.0, 120.5, 120.6, 124.3, 125.9, 126.0, 126.5, 127.3, 127.4, 127.6, 128.1, 128.4, 128.4, 131.6, 135.2, 136.5, 137.3, 140.9, 141.1, 144.0, 144.1, 144.5, 150.4; FTIR (NaCl, neat) ν : 2977, 2237, 1664, 1089, 751 cm^{-1} ; MS (ESI) m/z 517 $[\text{M}+1]^+$; HRMS (ESI) calcd. For $\text{C}_{40}\text{H}_{37}(\text{M}^++\text{H})$: 517.2895, found: 517.2902.

3-Cyclobutyl-2-(cyclobutylidene(4-pentylphenyl)methyl)-1-((4-pentylphenyl)-ethynyl)-1-phenyl-1H-indene 108c

Colourless solid, 90-91 °C; ^1H NMR (CDCl_3 , 400 MHz): δ 0.85-0.92 (m, 6H), 1.25-1.34 (m, 9H), 1.54-1.67 (m, 5H), 1.75-1.96 (m, 2H), 2.04-2.37 (m, 4H), 2.47-2.70 (m, 7H), 2.85-2.87 (m, 1H), 3.63-3.72 (m, 1H), 6.85 (d, 2H, $J = 7.8$ Hz), 6.92-7.36 (m, 14H), 7.59 (d, 2H, $J = 7.6$ Hz); ^{13}C NMR (CDCl_3 , 100 MHz): δ 14.0, 14.1, 17.3, 19.2, 22.5, 22.6, 27.4, 27.8, 30.9, 31.2, 31.4, 31.6, 31.8, 32.4, 35.2, 35.7, 35.8, 58.4, 84.2, 89.0, 120.6, 120.8, 124.3, 125.9, 126.5, 127.2, 127.4, 127.5, 127.6, 127.8, 127.9, 131.5, 136.6, 140.3, 140.9, 141.1, 142.4, 144.0, 144.1, 144.5, 150.5; FTIR (NaCl, neat) ν : 2979, 2918, 2089, 1634, 744 cm^{-1} ; MS (ESI) m/z 629 $[\text{M}+1]^+$; HRMS (ESI) calcd. For $\text{C}_{48}\text{H}_{53}$ (M^++H): 629.4147, found: 629.4145.

(E)-3-ethyl-1-phenyl-1-(phenylethynyl)-2-(1-phenylprop-1-enyl)-1H-indene 108f

Yellow oil; ^1H NMR (CDCl_3 , 400 MHz): δ 0.55 (t, 3H, $J = 7.2$ Hz), 1.49 (d, 1H, $J = 7.1$ Hz), 2.37-2.45 (m, 1H), 2.54-2.62 (m, 1H), 5.82 (q, 1H, $J = 7.1$ Hz), 6.95 (m, 1H, $J = 7.4$ Hz), 7.11-7.33 (m, 17H), 7.52 (m, 1H, $J = 7.4$ Hz); ^{13}C NMR (CDCl_3 , 100 MHz): δ 8.1, 15.6, 28.6, 62.2, 84.2, 98.3, 120.2, 122.1, 122.8, 123.5, 126.0, 126.2, 126.5, 126.8, 127.0,

127.8, 127.9, 128.0, 128.5, 130.1, 130.3, 132.0, 137.5, 139.2, 143.3, 144.3, 151.7, 155.3;
 FTIR (NaCl, neat) ν : 3055, 2968, 1597, 1489, 1443, 1265, 756 cm^{-1} ; MS (ESI) m/z 437
 $[\text{M}+1]^+$; HRMS (ESI) calcd. For $\text{C}_{34}\text{H}_{29}(\text{M}^++\text{H})$: 437.2269, found: 437.2261.

(E)-3-butyl-1-phenyl-1-(phenylethynyl)-2-(1-phenylpent-1-enyl)-1H-indene 108g

Yellow oil; ^1H NMR (CDCl_3 , 400 MHz): δ 0.57-0.88 (m, 7H), 1.15-1.53 (m, 5H), 1.82-1.86 (m, 2H), 2.28-2.37 (m, 1H), 2.43-2.50 (m, 1H), 5.73 (t, 1H, $J = 7.6$ Hz), 6.96 (d, 1H, $J = 7.4$ Hz), 7.10-7.31 (m, 17H), 7.52 (d, 1H, $J = 7.5$ Hz); ^{13}C NMR (CDCl_3 , 100 MHz): δ 13.5, 14.0, 22.8, 23.1, 25.4, 31.3, 35.7, 61.7, 84.2, 98.1, 120.2, 122.0, 122.4, 123.5, 126.1, 126.2, 126.4, 126.7, 127.0, 127.7, 127.9, 128.0, 128.4, 130.2, 132.0, 136.3, 136.4, 139.3, 143.2, 144.2, 152.1, 156.1; FTIR (NaCl, neat) ν : 2957, 2859, 1645, 1488, 1456, 754 cm^{-1} ; MS (ESI) m/z 493 $[\text{M}+1]^+$; HRMS (ESI) calcd. For $\text{C}_{38}\text{H}_{37}(\text{M}^++\text{H})$: 493.2895, found: 493.2894.

(E)-3-Hexyl-1-phenyl-1-(phenylethynyl)-2-(1-phenylhept-1-enyl)-1H-indene 108h

Yellow oil; ^1H NMR (CDCl_3 , 400 MHz): δ 0.76 (t, 3H, $J = 7.3$ Hz), 0.83 (t, 3H, $J = 7.1$ Hz), 0.98-1.26 (m, 14H), 1.84 (q, 2H, $J = 7.2$ Hz), 2.29-2.37 (m, 1H), 2.44-2.50 (m, 1H), 5.72 (t, 1H, $J = 7.6$ Hz), 6.96 (d, 1H, $J = 7.4$ Hz), 7.10-7.31 (m, 17H), 7.52

(d, 1H, $J = 7.5$ Hz); ^{13}C NMR (CDCl_3 , 100 MHz): δ 13.9, 14.1, 22.5, 22.6, 23.1, 29.2, 29.3, 29.8, 31.0, 31.6, 36.0, 61.7, 84.2, 98.1, 120.2, 122.0, 122.4, 123.5, 126.0, 126.2, 126.4, 126.7, 127.0, 127.7, 127.9, 128.0, 128.4, 130.2, 132.0, 136.2, 136.5, 139.3, 143.2, 144.3, 152.1, 156.2; IR (NaCl, neat) ν : 2953, 2926, 2855, 1597, 1493, 1443, 754, 698 cm^{-1} ; MS (ESI) m/z 549 $[\text{M}+1]^+$; HRMS (ESI) calcd. For $\text{C}_{42}\text{H}_{45}$ (M^++H): 549.3521, found: 549.3506.

(*E*)-5-(benzo[*d*][1,3]dioxol-5-yl)-7-ethyl-5-(phenylethynyl)-6-(1-phenylprop-1-enyl)-5H-indeno[5,6-*d*][1,3]dioxole 108i

Yellow solid, m.p. 82-83 °C; ^1H NMR (CDCl_3 , 400 MHz): δ 0.55 (t, 3 H, $J = 7.1$ Hz), 1.50 (d, 3H, $J = 7.1$ Hz), 2.27-2.43 (m, 2H), 5.80 (q, 1H, $J = 7.0$ Hz), 5.87-5.93 (m, 4H), 6.45 (s, 1H), 6.52 (s, 1H), 6.67 (d, 1H, $J = 8.2$ Hz), 6.73 (d, 1H, $J = 7.8$ Hz), 6.98 (s, 1H), 7.16-7.33 (m, 10H); ^{13}C NMR (CDCl_3 , 100 MHz): δ 8.0, 15.6, 29.0, 61.4, 84.0, 98.1, 100.8, 101.0, 101.1, 103.2, 106.9, 108.0, 118.5, 122.2, 123.3, 127.0, 127.8, 127.9, 129.0, 130.3, 132.0, 136.9, 137.4, 138.1, 139.2, 145.9, 145.9, 146.8, 147.0, 147.8, 154.4; FTIR (NaCl, neat) ν : 2975, 2915, 1654, 1527, 1033 cm^{-1} ; MS (ESI) m/z 525 $[\text{M}+1]^+$; HRMS (ESI) calcd. For $\text{C}_{36}\text{H}_{29}\text{O}_4$ (M^++H): 525.2066, found: 525.2062.

(3-Cyclobutylideneprop-1-yne-1,3-diyl)dibenzene 112a

Pale yellow oil; ^1H NMR (CDCl_3 , 400 MHz): δ 2.18-2.16 (m, 2H), 3.07-3.11 (m, 4H), 7.20-7.36 (m, 5H), 7.47-7.55 (m, 4H); ^{13}C NMR (CDCl_3 , 100 MHz): δ 17.5, 33.3, 33.6, 87.1, 93.2, 115.7, 124.0, 126.7, 126.9, 127.9, 128.3, 128.3, 131.5, 137.0, 153.7; IR (NaCl, neat) ν : 2968, 2884, 2199, 1597, 1491, 1447, 1217, 1111, 756, 656 cm^{-1} ; MS (ESI) m/z 245 $[\text{M}+1]^+$; HRMS (ESI) calcd. For $\text{C}_{19}\text{H}_{17}(\text{M}^++\text{H})$: 245.1330, found: 245.1334.

1-(3-Cyclobutylidene-3-phenylprop-1-ynyl)-4-methylbenzene 112b

Pale yellow oil; ^1H NMR (CDCl_3 , 400 MHz): δ 2.08-2.16 (m, 2H), 2.34 (s, 3H), 3.06-3.11 (m, 4H), 7.12 (d, 2H, $J = 7.9$), 7.20-7.39 (m, 5H), 7.54 (d, 2H, $J = 7.6$ Hz); ^{13}C NMR (CDCl_3 , 100 MHz): δ 17.5, 21.5, 33.2, 33.6, 86.3, 93.3, 115.8, 120.9, 126.7, 126.9, 128.2, 129.1, 131.4, 137.0, 137.9, 153.2; IR (NaCl, neat) ν : 2963, 2922, 2195, 1603, 1508, 1447, 1107, 818, 754 cm^{-1} ; MS (ESI) m/z 259 $[\text{M}+1]^+$; HRMS (ESI) calcd. For $\text{C}_{20}\text{H}_{19}(\text{M}^++\text{H})$: 259.1487, found: 259.1497.

1-Chloro-4-(3-cyclobutylidene-3-phenylprop-1-ynyl)benzene 112d

Pale yellow oil; ^1H NMR (CDCl_3 , 400 MHz): δ 2.14-2.22 (m, 2H), 3.10-3.16 (m, 4H), 7.26-7.57 (m, 9H); ^{13}C NMR (CDCl_3 , 100 MHz): δ 17.5, 33.2, 33.6, 88.0, 91.9, 115.5, 122.4, 126.8, 126.8, 128.3, 128.6, 132.6, 133.8, 136.7, 154.2; IR (NaCl, neat) ν : 2966, 2884, 2199, 1593, 1489, 1400, 1092, 1015, 829, 780, 698 cm^{-1} ; MS (ESI) m/z 279 $[\text{M}+1]^+$; HRMS (ESI) calcd. For $\text{C}_{19}\text{H}_{15}^{35}\text{Cl}$ (M^++H): 279.0941, found: 279.0937.

2-(3-Cyclobutylidene-3-phenylprop-1-ynyl)thiophene 112e

Brown oil; ^1H NMR (CDCl_3 , 400 MHz): δ 2.09-2.16 (m, 2H), 3.05-3.11 (m, 4H), 7.15 (d, 1H, $J = 4.9$ Hz), 7.21-7.36 (m, 4H), 7.43 (d, 1H, $J = 2.7$ Hz), 7.52 (d, 2H, $J = 7.8$ Hz); ^{13}C NMR (CDCl_3 , 100 MHz): δ 17.5, 33.2, 33.5, 86.4, 88.0, 115.6, 122.9, 125.2, 126.7, 126.9, 127.8, 128.2, 130.0, 136.9, 153.5; IR (NaCl, neat) ν : 2965, 2884, 1493, 1447, 1110, 783, 754, 627 cm^{-1} ; MS (ESI) m/z 251 $[\text{M}+1]^+$; HRMS (ESI) calcd. For $\text{C}_{17}\text{H}_{15}\text{S}$ (M^++H): 251.0894, found: 251.0891.

(Z)-Pent-3-en-1-yne-1,3-diylidibenzene 112f ¹³⁵

Pale yellow oil; ¹H NMR (CDCl₃, 400 MHz): δ 2.15 (d, 3H, J = 7.0 Hz), 6.54 (q, 1H, J = 7.0 Hz), 7.25-7.37 (m, 6H), 7.53-7.65 (m, 4H); ¹³C NMR (CDCl₃, 100 MHz): δ 17.1, 86.7, 95.6, 123.6, 124.5, 125.9, 127.4, 128.2, 128.3, 131.5, 133.2, 138.3; MS (ESI) m/z 219 [M+1]⁺.

(Z)-Hept-3-en-1-yne-1,3-diylidibenzene 112g

Yellow oil; ¹H NMR (CDCl₃, 400 MHz): δ 1.02 (t, 3H, J = 7.4 Hz), 1.54-1.61(m, 2H), 2.56 (dt, 2H, J = 7.4, 7.4 Hz), 6.47 (t, 1H, J = 7.4 Hz), 7.26-7.37 (m, 6H), 7.52-7.7.74 (m, 2H), 7.66 (d, 2H, J = 7.5 Hz); ¹³C NMR (CDCl₃, 100 MHz): δ 14.0, 22.4, 33.4, 86.9, 95.0, 123.6, 123.6, 126.0, 127.4, 128.2, 128.3, 128.4, 131.5, 138.3, 138.8; IR (NaCl, neat) ν : 2961, 2872, 1491, 1449, 1271, 1026, 756, 700 cm⁻¹; MS (ESI) m/z 247 [M+1]⁺; HRMS (ESI) calcd. For C₁₉H₁₉ (M⁺+H): 247.1487, found: 247.1491.

7.4 Gold-Catalyzed Tandem Amination/Ring Expansion of Cyclopropyl

Methanols with Sulfonamides as an Expedient Route to Pyrrolidines

General Procedure for the AuCl/AgOTf-Catalyzed Tandem Amination/Ring

Expansions of **122** with **13**

A solution of AuCl (0.015 mol) and AgOTf (0.015 mol) was stirred in toluene (1.5 mL) under an Argon atmosphere at room temperature for 1 h. On completion, a toluene solution (1.5 mL) containing **122** (0.3 mmol) and **13** (0.6 mmol) was added to the reaction mixture and stirred at 100 °C and monitored to completion by TLC analysis. The reaction mixture then cooled and the solvent was removed under reduced pressure. Purification by flash column chromatography on silica gel (*n*-hexane: EtOAc = 7: 1 as eluent) gave the title compound **123**.

2-Phenyl-1-tosylpyrrolidine **123a** ^{103,109,136}

Colourless solid; ^1H NMR (CDCl_3 , 400 MHz): δ 1.62-1.70 (m, 1H), 1.78-1.90 (m, 2H), 1.94-2.04 (m, 1H), 2.42 (s, 3H), 3.39-3.45 (m, 1H), 3.59-3.64 (m, 1H), 4.79 (dd, 1H, $J = 7.6, 3.3$ Hz), 7.21-7.30 (m, 7H), 7.67 (d, 2H, $J = 8.2$ Hz); ^{13}C NMR (CDCl_3 , 100 MHz): δ 21.5, 24.0, 35.8, 49.4, 63.3, 126.2, 127.0, 127.5, 128.3, 129.6, 135.2, 143.1, 143.3. MS (ESI) m/z 324 $[\text{M}+\text{Na}]^+$, 302 $[\text{M}+\text{H}]^+$.

2-(4-Methylphenyl)-1-tosylpyrrolidine 123b^{103,109,136}

Colourless solid; ¹H NMR (CDCl₃, 400 MHz): δ 1.62-1.68 (m, 1H), 1.76-1.98 (m, 3H), 2.32 (s, 3H), 2.42 (s, 3H), 3.37-3.43 (m, 1H), 3.58-3.63 (m, 1H), 4.73 (dd, 1H, J = 7.5, 3.4 Hz), 7.10 (d, 2H, J = 7.9 Hz), 7.20 (d, 2H, J = 8.0 Hz), 7.28 (d, 2H, J = 8.0 Hz), 7.67 (d, 2H, J = 8.1 Hz); ¹³C NMR (CDCl₃, 100 MHz): δ 21.1, 21.5, 24.0, 35.8, 49.4, 63.1, 126.1, 127.5, 129.0, 129.6, 135.2, 136.6, 140.1, 143.2; MS (ESI) m/z 338 [M+Na]⁺, 316 [M+H]⁺.

2-(4-*Tert*-butylphenyl)-1-tosylpyrrolidine 123c

Colourless solid; m.p. 96-98 °C; ¹H NMR (CDCl₃, 400 MHz): δ 1.30 (s, 9H), 1.63-1.70 (m, 1H), 1.79-1.99 (m, 3H), 2.41 (s, 3H), 3.41-3.47 (m, 1H), 3.58-3.63 (m, 1H), 4.77 (dd, 1H, J = 7.6, 3.4 Hz), 7.19-7.30 (m, 6H), 7.64 (d, 2H, J = 8.2 Hz); ¹³C NMR (CDCl₃, 100 MHz): δ 21.5, 24.1, 31.4, 34.4, 35.7, 49.3, 63.0, 125.2, 125.9, 127.5, 129.5, 135.4, 139.8, 143.1, 149.8; IR (KBr): 2961, 1341, 1335, 1152, 1105, 1005, 671, 586 cm⁻¹; MS (ESI) m/z 380 [M+Na]⁺; HRMS (ESI) calcd. for C₂₁H₂₇NO₂SNa: 380.1655, found: 380.1786.

2-(4-Methoxyphenyl)-1-tosylpyrrolidine 123d¹⁰⁹

Colourless solid; ¹H NMR (CDCl₃, 400 MHz): δ 1.63-1.69 (m, 1H), 1.75-1.97 (m, 3H), 2.42 (s, 3H), 3.37-3.44 (m, 1H), 3.57-3.62 (m, 1H), 3.79 (s, 3H), 4.73 (dd, 1H, J = 7.4, 3.6

Hz), 6.83 (d, 2H, $J = 8.6$ Hz), 7.21-7.28 (m, 4H), 7.66 (d, 2H, $J = 8.2$ Hz); ^{13}C NMR (CDCl_3 , 100 MHz): δ 21.5, 24.0, 35.8, 49.3, 55.3, 62.8, 113.7, 127.3, 127.5, 129.5, 135.2, 135.2, 143.2, 158.7; MS (ESI) m/z 354 $[\text{M}+\text{Na}]^+$.

2-(4-Fluorophenyl)-1-tosylpyrrolidine 123e¹³⁷

Colourless solid; ^1H NMR (CDCl_3 , 400 MHz): δ 1.62-1.69 (m, 1H), 1.73-1.88 (m, 2H), 1.93-2.04 (m, 1H), 2.42 (s, 3H), 3.37-3.43 (m, 1H), 3.58-3.63 (m, 1H), 4.74 (dd, 1H, $J = 7.6, 3.6$ Hz), 6.97 (t, 2H, $J = 8.7$ Hz), 7.26-7.29 (m, 4H), 7.66 (d, 1H, $J = 8.2$ Hz); ^{13}C NMR (CDCl_3 , 100 MHz): δ 21.5, 23.9, 35.9, 49.4, 62.7, 115.1(d, $J = 21.4$ Hz), 127.5, 127.8 (d, $J = 8.0$ Hz), 129.6, 134.9, 138.9 (d, $J = 2.9$ Hz), 143.5, 162.6 (d, $J = 243.4$ Hz); MS (ESI) m/z 342 $[\text{M}+\text{Na}]^+$.

2-(4-Chlorophenyl)-1-tosylpyrrolidine 123f^{109,137}

Colourless solid; ^1H NMR (CDCl_3 , 400 MHz): δ 1.68-1.87 (m, 3H), 1.95-2.02 (m, 12H), 2.43 (s, 3H), 3.38-3.44 (m, 1H), 3.58-3.63 (m, 1H), 4.72 (dd, 1H, $J = 7.8, 3.7$ Hz), 7.23-7.30 (m, 6H), 7.66 (d, 1H, $J = 8.2$ Hz); ^{13}C NMR (CDCl_3 , 100 MHz): δ 21.5, 24.0, 35.8, 49.4, 62.7, 127.5, 127.6, 128.4, 129.7, 132.8, 134.8, 141.7, 143.5; MS (ESI) m/z 358 $[\text{M}+\text{Na}]^+$.

2-(3,5-Dimethylphenyl)-1-tosylpyrrolidine 123g

Colourless solid; m.p. 77-79 °C; ^1H NMR (CDCl_3 , 400 MHz): δ 1.60-1.67 (m, 1H), 1.76-1.99 (m, 3H), 2.26 (s, 6H), 2.42 (s, 3H), 3.41-3.47 (m, 1H), 3.58-3.63 (m, 1H), 4.72 (dd, 1H, $J = 7.2, 3.2$ Hz), 6.85 (s, 3H), 7.26 (d, 2H, $J = 7.8$ Hz), 7.65 (d, 2H, $J = 8.0$ Hz); ^{13}C NMR (CDCl_3 , 100 MHz): δ 21.4, 21.5, 24.0, 35.9, 49.4, 63.3, 124.0, 127.5, 128.7, 129.5, 135.4, 137.7, 142.9, 143.1; IR (KBr): 1605, 1342, 1157, 1094, 1003, 818, 586 cm^{-1} ; MS (ESI) m/z 352 $[\text{M}+\text{Na}]^+$; HRMS (ESI) calcd. for $\text{C}_{19}\text{H}_{23}\text{NO}_2\text{SNa}$: 352.1342, found: 352.1316.

2-(2,6-Dimethylphenyl)-1-tosylpyrrolidine 123h

Colourless solid; m.p. 154-155 °C; ^1H NMR (CDCl_3 , 400 MHz): δ 1.53-1.61 (m, 1H), 1.89-1.99 (m, 2H), 2.16-2.22 (m, 1H), 2.35 (s, 6H), 2.40 (s, 3H), 3.50-3.57 (m, 1H), 3.82 (t, 1H, $J = 9.8$ Hz), 5.01 (dd, 1H, $J = 9.4, 7.8$ Hz), 6.92-7.03 (m, 3H), 7.20 (d, 2H, $J = 8.0$ Hz), 7.54 (d, 2H, $J = 8.1$ Hz); ^{13}C NMR (CDCl_3 , 100 MHz): δ 20.8, 21.5, 25.5, 32.7, 49.3, 60.4, 126.9, 127.4, 129.3, 135.6, 135.9, 136.9, 143.1; IR (KBr): 1341, 1157, 1086, 989 cm^{-1} ; MS (ESI) m/z 352 $[\text{M}+\text{Na}]^+$; HRMS (ESI) calcd. for $\text{C}_{19}\text{H}_{23}\text{NO}_2\text{SNa}$: 352.1342, found: 352.1319.

2-(Naphthalen-1-yl)-1-tosylpyrrolidine 123i¹⁰³

Colourless solid; ¹H NMR (CDCl₃, 400 MHz): δ 1.71-1.90 (m, 3H), 2.06-2.15 (m, 1H), 2.44 (s, 3H), 3.42-3.49 (m, 1H), 3.77-3.82 (m, 1H), 5.57 (d, 1H, J = 6.8 Hz), 7.32 (d, 2H, J = 8.0 Hz), 7.43-7.54 (m, 3H), 7.66 (d, 1H, J = 8.1 Hz), 7.75-7.92 (m, 5H); ¹³C NMR (CDCl₃, 100 MHz): δ 21.6, 23.9, 34.6, 49.4, 60.7, 122.8, 123.8, 125.4, 125.9, 127.6, 127.6, 129.0, 129.7, 129.9, 133.9, 134.9, 138.2, 143.4; MS (ESI) m/z 374 [M+Na]⁺.

2-(2-Methoxyphenyl)-1-tosylpyrrolidine 123j¹⁰³

Colourless solid; ¹H NMR (CDCl₃, 400 MHz): δ 1.60-1.66 (m, 1H), 1.70-1.92 (m, 3H), 2.43 (s, 3H), 3.31-3.37 (m, 1H), 3.62-3.67 (m, 1H), 3.80 (s, 3H), 5.10 (dd, 1H, J = 7.6, 2.4 Hz), 6.82 (d, 1H, J = 8.2 Hz), 6.93 (t, 1H, J = 7.4 Hz), 7.19-7.31 (m, 3H), 7.43 (d, 1H, J = 7.4 Hz), 7.72 (d, 2H, J = 8.1 Hz); ¹³C NMR (CDCl₃, 100 MHz): δ 21.5, 23.8, 34.0, 49.4, 55.2, 58.8, 110.1, 120.3, 127.3, 127.6, 128.0, 129.5, 131.3, 135.1, 143.1, 155.7; MS (ESI) m/z 354 [M+Na]⁺.

2-Methyl-2-phenyl-1-tosylpyrrolidine 123k¹⁰³

Colourless solid; ¹H NMR (CDCl₃, 400 MHz): δ 1.78-1.89 (m, 5H), 1.94-2.01 (m, 1H), 2.11-2.17 (m, 1H), 2.41 (s, 3H), 3.52-3.58 (m, 1H), 3.68-3.73 (m, 1H), 7.20-7.31 (m, 5H),

7.39 (d, 2H, $J = 7.4$ Hz), 7.58 (d, 2H, $J = 8.2$ Hz); ^{13}C NMR (CDCl_3 , 100 MHz): δ 21.5, 22.5, 26.4, 45.8, 49.8, 69.9, 125.8, 126.6, 127.1, 128.0, 129.3, 138.5, 142.5, 146.5; MS (ESI) m/z 338 $[\text{M}+\text{Na}]^+$.

2-(4-Fluorophenyl)-2-methyl-1-tosylpyrrolidine 123l

Colourless solid; m.p. 109-110 °C; ^1H NMR (CDCl_3 , 400 MHz): δ 1.77-1.90 (m, 5H), 1.94-2.13 (m, 2H), 2.41 (s, 3H), 3.51-3.57 (m, 1H), 3.67-3.72 (m, 1H), 6.93-6.99 (m, 2H), 7.23 (d, 1H, $J = 8.1$ Hz), 7.32-7.38 (m, 2H), 7.58 (d, 2H, $J = 8.2$ Hz); ^{13}C NMR (CDCl_3 , 100 MHz): δ 21.5, 22.4, 26.5, 45.8, 49.8, 69.3, 114.7 (d, $J = 21.1$ Hz), 127.1, 127.5 (d, $J = 7.9$ Hz), 129.3, 138.3, 142.5 (d, $J = 40.5$ Hz), 161.6 (d, $J = 243.6$ Hz); IR (KBr): 2853, 1599, 1508, 1335, 1155, 1005, 665 cm^{-1} ; MS (ESI) m/z 356 $[\text{M}+\text{Na}]^+$; HRMS (ESI) calcd. for $\text{C}_{18}\text{H}_{20}\text{NO}_2\text{FSNa}$: 356.1091, found: 356.1473.

2-Octyl-1-tosylpyrrolidine 123m

Brown oil; ^1H NMR (CDCl_3 , 400 MHz): δ 0.88 (t, 3H, $J = 6.6$ Hz), 1.18-1.28 (m, 12H), 1.42-1.59 (m, 4H), 1.71-1.84 (m, 2H), 2.42 (s, 3H), 3.15-3.21 (m, 1H), 3.33-3.39 (m, 1H), 3.55-3.60 (m, 1H), 7.29 (d, 2H, $J = 8.0$ Hz), 7.71 (d, 2H, $J = 8.2$ Hz); ^{13}C NMR (CDCl_3 , 100 MHz): δ 14.1, 21.5, 22.7, 24.1, 26.2, 29.3, 29.6, 30.6, 31.9, 36.5, 48.9, 60.6, 127.5, 129.6, 135.1, 143.1; IR (KBr): 2924, 1346, 1159, 1094, 816, 664 cm^{-1} ; MS (ESI) m/z 360 $[\text{M}+\text{Na}]^+$; HRMS (ESI) calcd. for $\text{C}_{19}\text{H}_{31}\text{NO}_2\text{SNa}$: 360.1968, found: 360.1846.

2-Dodecyl-1-tosylpyrrolidine 123n:

Yellow oil; ^1H NMR (CDCl_3 , 400 MHz): δ 0.88 (t, 3H, $J = 6.9$ Hz), 1.27 (s, 20H), 1.53-1.62 (m, 4H), 1.72-1.83 (m, 2H), 2.43 (s, 3H), 3.16-3.22 (m, 1H), 3.34-3.40 (m, 1H), 3.56-3.62 (m, 1H), 7.30 (d, 2H, $J = 7.9$ Hz), 7.71 (d, 2H, $J = 8.0$ Hz); ^{13}C NMR (CDCl_3 , 100 MHz): δ 14.1, 21.5, 22.7, 24.1, 26.2, 29.4, 29.6, 29.6, 29.7, 30.7, 31.9, 36.5, 48.9, 60.6, 127.5, 129.6, 135.1, 143.1; IR (KBr) ν : 2922, 2853, 1341, 1157, 1091, 806 cm^{-1} ; MS (ESI) m/z 416 $[\text{M}+\text{Na}]^+$; HRMS (ESI) calcd. for $\text{C}_{23}\text{H}_{39}\text{NO}_2\text{SNa}$: 416.2594, found: 416.3034.

2-Benzyl-1-tosylpyrrolidine 123¹³⁸

Yellow oil; ^1H NMR (CDCl_3 , 400 MHz): δ 1.37-1.52 (m, 2H), 1.59-1.72 (m, 2H), 2.43 (s, 3H), 2.72-2.78 (m, 1H), 3.10-3.16 (m, 1H), 3.23-3.27 (m, 1H), 3.37-3.42 (m, 1H), 3.80-3.85 (m, 1H), 7.20-7.38 (m, 7H), 7.76 (d, 2H, $J = 8.2$ Hz); ^{13}C NMR (CDCl_3 , 100 MHz): δ 21.5, 23.8, 29.9, 42.7, 49.3, 61.6, 126.4, 127.5, 128.4, 129.6, 129.7, 134.7, 138.5, 143.3. IR (KBr) ν : 2974, 1597, 1339, 1153, 1092, 820, 665 cm^{-1} ; MS (ESI) m/z 338 $[\text{M}+\text{Na}]^+$; HRMS (ESI) Calcd. for $\text{C}_{18}\text{H}_{21}\text{NO}_2\text{SNa}$: 338.1185, Found: 338.1328.

2-Phenethyl-1-tosylpyrrolidine 123p

Yellow oil; ^1H NMR (CDCl_3 , 400 MHz): δ 1.43-1.63 (m, 3H), 1.74-1.83 (m, 2H), 2.18-2.26 (m, 1H), 2.41 (s, 3H), 2.60-2.77 (m, 2H), 3.17-3.23 (m, 1H), 3.38-3.44 (m, 1H), 3.55-3.61 (m, 1H), 7.19-7.32 (m, 7H), 7.62 (d, 2H, $J = 8.1$ Hz); ^{13}C NMR (CDCl_3 , 100 MHz): δ 21.5, 24.1, 30.8, 32.4, 37.7, 49.1, 59.8, 125.9, 127.6, 128.4, 128.5, 129.6, 134.7, 141.6, 143.2; MS (ESI) m/z 352 $[\text{M}+\text{Na}]^+$.

2-Phenyl-1-(phenylsulfonyl)pyrrolidine 123q¹⁰³

Colourless solid; ^1H NMR (CDCl_3 , 400 MHz): δ 1.63-2.05 (m, 4H), 3.43-3.49 (m, 1H), 3.61-3.66 (m, 1H), 4.82 (dd, 1H, $J = 7.7, 3.5$ Hz), 7.20-7.30 (m, 5H), 7.46-7.58 (m, 3H), 7.77-7.79 (m, 2H); ^{13}C NMR (CDCl_3 , 100 MHz): δ 24.0, 35.8, 49.4, 63.4, 126.2, 127.1, 127.4, 128.3, 129.0, 132.6, 138.1, 142.9; MS (ESI) m/z 310 $[\text{M}+\text{Na}]^+$.

1-(4-Bromophenylsulfonyl)-2-phenylpyrrolidine 123r

Pale-yellow oil; ^1H NMR (CDCl_3 , 400 MHz): δ 1.70-2.10 (m, 4H), 3.43-3.49 (m, 1H), 3.59-3.64 (m, 1H), 4.79 (dd, 1H, $J = 7.7, 3.6$ Hz), 7.23-7.30 (m, 5H), 7.58 (s, 4H); ^{13}C NMR (CDCl_3 , 100 MHz): δ 24.1, 35.9, 49.4, 63.5, 126.2, 127.2, 127.4, 128.4, 128.9,

132.2, 137.5, 142.5; IR (KBr): 2973, 1347, 1342, 1155, 1114, 692 cm^{-1} ; MS (ESI) m/z 388 $[\text{M}+\text{Na}]^+$; HRMS (ESI) calcd. for $\text{C}_{16}\text{H}_{16}\text{NO}_2^{79}\text{BrSNa}$: 387.9983, found: 387.9975.

1-(4-Nitrophenylsulfonyl)-2-phenylpyrrolidine 123s^{103,109}

White solid; ^1H NMR (CDCl_3 , 400 MHz): δ 1.80-2.22 (m, 4H), 3.43-3.49 (m, 1H), 3.58-3.67 (m, 1H), 4.87 (dd, 1H, $J = 7.8, 4.3$ Hz), 7.16-7.26 (m, 5H), 7.79-7.81 (m, 2H), 8.22-8.24 (m, 2H); ^{13}C NMR (CDCl_3 , 100 MHz): δ 24.3, 36.0, 49.5, 63.7, 124.0, 126.4, 127.5, 128.3, 128.4, 141.8, 144.7, 149.8; MS (ESI) m/z 355 $[\text{M}+\text{Na}]^+$.

(E)-4-Methyl-N-(4-phenylbut-3-enyl)benzenesulfonamide 124^{103,136}

Colourless oil; ^1H NMR (CDCl_3 , 400 MHz): δ 2.36 (q, 2H, $J = 6.8$ Hz), 2.41 (s, 3H), 3.09 (q, 2H, $J = 6.5$ Hz), 4.63 (t, 1H, $J = 5.8$ Hz), 5.94-6.01 (m, 1H), 6.35 (d, 1H, $J = 15.8$ Hz), 7.20-7.31 (m, 7H), 7.75 (d, 2H, $J = 8.2$ Hz); ^{13}C NMR (CDCl_3 , 100 MHz): δ 21.5, 33.0, 42.6, 125.6, 126.1, 127.2, 127.5, 128.6, 129.7, 133.2, 136.8, 137.0, 143.5; MS (ESI) m/z 324 $[\text{M}+\text{Na}]^+$.

N-(4,4-Diphenylbut-3-enyl)-4-methylbenzenesulfonamide 124b^{139,140}

Yellow oil; ^1H NMR (CDCl_3 , 400 MHz): δ 2.26 (q, 2H, $J = 7.1$ Hz), 2.40 (s, 3H), 3.03 (q, 2H, $J = 6.6$ Hz), 4.59 (t, 3H, $J = 6.0$ Hz), 5.90 (t, 1H, $J = 7.4$ Hz), 7.08-7.36 (m, 12H),

7.69 (d, 2H, $J = 8.2$ Hz); ^{13}C NMR (CDCl_3 , 100 MHz): δ 21.6, 29.9, 43.1, 124.6, 127.1, 127.3, 127.3, 127.3, 128.2, 128.4, 129.7, 129.7, 136.9, 139.5, 142.0, 143.4, 144.7; MS (ESI) m/z 400 $[\text{M}+\text{Na}]^+$.

4-Methyl-*N*-(6-*p*-tolylhex-3-en-5-ynyl)benzenesulfonamide 124c

Yellow oil; ^1H NMR (CDCl_3 , 400 MHz): δ 2.28-2.42 (m, 14H), 2.25-2.27 (q, 2H, $J = 6.4$ Hz), 3.03-3.13 (m, 4H), 5.54-5.58 (m, 2H), 5.66-5.83 (m, 3H), 5.94-6.01 (m, 1H), 7.10-7.14 (m, 4H), 7.24-7.32 (m, 8H), 7.73-7.76 (m, 4H); ^{13}C NMR (CDCl_3 , 100 MHz): δ 21.5, 21.5, 30.3, 33.2, 42.2, 42.2, 84.8, 86.7, 89.5, 95.0, 112.6, 113.3, 120.0, 120.0, 127.1, 129.1, 129.1, 129.7, 129.8, 131.4, 131.4, 136.9, 138.0, 138.4, 138.6, 138.9, 143.4, 143.6; IR (KBr): 3291, 2920, 2265, 1327, 1159, 1094, 816 cm^{-1} ; MS (ESI) m/z 362 $[\text{M}+\text{Na}]^+$; HRMS (ESI) calcd. for $\text{C}_{20}\text{H}_{21}\text{NO}_2\text{SNa}$: 362.1185, found: 362.1031.

4-Methyl-*N,N*-bis((*E*)-4-phenylbut-3-enyl)benzenesulfonamide 125a¹⁰³

Colourless oil; ^1H NMR (CDCl_3 , 400 MHz): δ 2.39 (s, 3H), 2.49 (q, 4H, $J = 7.2$ Hz), 3.30 (t, 4H, $J = 7.2$ Hz), 6.05-6.12 (m, 2H), 6.39 (d, 2H, $J = 15.8$ Hz), 7.19-7.29 (m, 12H), 7.71 (d, 2H, $J = 8.3$ Hz); ^{13}C NMR (CDCl_3 , 100 MHz): δ 21.5, 32.7, 48.1, 126.1, 126.2, 127.2, 127.3, 128.5, 129.7, 132.3, 137.2, 143.2. MS (ESI) m/z 454 $[\text{M}+\text{Na}]^+$.

General Procedure for the AuCl/AgOTf-Catalyzed Aminations of 122a, 122d, 122e, 122h, 122i and 122j with 13a

A solution of AuCl (0.015 mol) and AgOTf (0.015 mol) was stirred in toluene (1.5 mL) under an Ar atmosphere at room temperature for 1 h. On completion, a toluene solution (1.5 mL) containing **122** (0.3 mmol) and **13a** (0.6 mmol) was added to the reaction mixture and stirred at room temperature and monitored to completion by TLC analysis. The reaction mixture then cooled and the solvent was removed under reduced pressure. Purification by flash column chromatography on silica gel (*n*-hexane: EtOAc = 7: 1 as eluent) gave the title compound **126**.

***N*-(Cyclopropyl(phenyl)methyl)-4-methylbenzenesulfonamide 126a**

Colourless solid; m.p. 127-128 °C; ¹H NMR (CDCl₃, 400 MHz): δ 0.20-0.30 (m, 2H), 0.43-0.53 (m, 2H), 1.05-1.14 (m, 1H), 2.37 (s, 3H), 3.70 (dd, 1H, *J* = 8.4, 6.0 Hz), 5.16 (d, 1H, *J* = 5.6 Hz), 7.13-7.18 (m, 7H), 7.56 (d, 2H, *J* = 8.1 Hz); ¹³C NMR (CDCl₃, 100 MHz): δ 3.8, 4.5, 18.1, 21.5, 62.5, 126.9, 127.1, 127.4, 128.3, 129.3, 137.8, 140.4, 143.0; IR (KBr): 3250, 2927, 14521, 1346, 1160, 1088, 822 cm⁻¹; MS (ESI) *m/z* 324 [M+Na]⁺; HRMS (ESI) calcd. for C₁₇H₁₉NO₂SNa: 324.1029, found: 324.0650.

***Tert*-butylcyclopropyl(phenyl)methylcarbamate 126b**

Colourless solid; m.p. 71-72 °C; ^1H NMR (CDCl_3 , 400 MHz): δ 0.33-0.60 (m, 4H), 1.05-1.13 (m, 1H), 1.41 (s, 9H), 4.12 (bs, 1H), 5.00 (bs, 1H), 7.22-7.33 (m, 5H); ^{13}C NMR (CDCl_3 , 100 MHz): δ 3.6, 17.3, 28.4, 58.4, 79.4, 126.5, 127.1, 128.1, 128.4, 142.7, 155.4; IR (KBr): 3383, 1680, 1522, 1177, 1017, 878, 754 cm^{-1} ; MS (ESI) m/z 270 $[\text{M}+\text{Na}]^+$; HRMS (ESI) calcd. for $\text{C}_{15}\text{H}_{21}\text{NO}_2\text{Na}$: 270.1465, found: 270.1363.

Benzylcyclopropyl(phenyl)methylcarbamate 126c

Colourless solid; m.p. 60-61 °C; ^1H NMR (CDCl_3 , 400 MHz): δ 0.33-0.61 (m, 4H), 1.11-1.13 (m, 1H), 4.16 (bs, 1H), 4.99-5.11 (m, 2H), 5.26 (bs, 1H), 7.23-7.33 (m, 10H); ^{13}C NMR (CDCl_3 , 100 MHz): δ 3.7, 3.8, 17.2, 59.2, 66.8, 126.5, 127.3, 128.1, 128.5, 136.5, 142.2, 155.9; IR (KBr): 3337, 1682, 1528, 1265, 1040, 878 cm^{-1} ; MS (ESI) m/z 304 $[\text{M}+\text{Na}]^+$; HRMS (ESI) calcd. for $\text{C}_{18}\text{H}_{19}\text{NO}_2\text{Na}$: 304.1308, found: 304.1348.

***N*-(Cyclopropyl(4-methoxyphenyl)methyl)-4-methylbenzenesulfonamide 126d**

Colourless solid; m.p. 124-125 °C; ^1H NMR (CDCl_3 , 400 MHz): δ 0.17-0.26 (m, 2H), 0.38-0.51 (m, 2H), 1.04-1.12 (m, 1H), 2.37 (s, 3H), 3.66 (dd, 1H, J = 8.3, 6.0 Hz), 3.75 (s, 3H), 5.28 (d, 1H, J = 6.6 Hz), 6.69 (d, 2H, J = 8.7 Hz), 7.03 (d, 2H, J = 10.0 Hz), 7.14 (d,

1H, $J = 8.0$ Hz), 7.56 (d, 1H, $J = 8.2$ Hz); ^{13}C NMR (CDCl_3 , 100 MHz): δ 3.6, 4.4, 18.0, 21.5, 55.2, 61.9, 113.6, 127.2, 128.0, 129.2, 132.7, 137.9, 142.9, 158.8; IR (KBr): 3237, 1612, 1514, 1437, 1323, 1155, 1049, 806 cm^{-1} ; MS (ESI) m/z 354 $[\text{M}+\text{Na}]^+$; HRMS (ESI) calcd. for $\text{C}_{18}\text{H}_{21}\text{NO}_3\text{SNa}$: 354.1134, found: 354.1085.

***N*-(Cyclopropyl(4-fluorophenyl)methyl)-4-methylbenzenesulfonamide 126e**

Colourless solid; m.p. 100-102 °C; ^1H NMR (CDCl_3 , 400 MHz): δ 0.16-0.27 (m, 2H), 0.43-0.52 (m, 2H), 1.03-1.09 (m, 1H), 2.38 (s, 3H), 3.66 (dd, 1H, $J = 8.4$, 6.0 Hz), 5.41 (d, 1H, $J = 5.7$ Hz), 6.82-6.86 (m, 2H), 7.07-7.16 (m, 4H), 7.55 (d, 2H, $J = 8.1$ Hz); ^{13}C NMR (CDCl_3 , 100 MHz): δ 3.7, 4.4, 18.1, 21.5, 61.9, 115.0 (d, $J = 21.2$ Hz), 127.1, 128.5 (d, $J = 8.0$ Hz), 129.3, 136.4 (d, $J = 3.2$ Hz), 137.7, 143.2, 162.8 (d, $J = 244.3$ Hz); IR (KBr): 3237, 1612, 1514, 1437, 1242, 1155, 1049, 806 cm^{-1} ; MS (ESI) m/z 342 $[\text{M}+\text{Na}]^+$; HRMS (ESI) calcd. for $\text{C}_{17}\text{H}_{18}\text{NO}_2\text{FSNa}$: 342.0934, found: 342.1003.

***N*-(Cyclopropyl(3,5-dimethylphenyl)methyl)-4-methylbenzenesulfonamide 126f**

Colourless solid; m.p. 104-105 °C; ^1H NMR (CDCl_3 , 400 MHz): δ 0.24-0.31 (m, 2H), 0.41-0.53 (m, 2H), 1.04-1.13 (m, 1H), 2.16 (s, 6H), 2.37 (s, 3H), 3.62 (dd, 1H, $J = 8.4$, 6.1 Hz), 5.15 (d, 1H, $J = 5.9$ Hz), 6.64 (s, 2H), 6.77 (s, 1H), 7.13 (d, 2H, $J = 8.1\text{Hz}$), 7.54 (d, 2H, $J = 8.2$ Hz); ^{13}C NMR (CDCl_3 , 100 MHz): δ 3.7, 4.5, 18.0, 21.2, 21.4, 62.6, 124.7,

127.2, 129.0, 129.1, 137.7, 137.9, 140.2, 142.8; IR (KBr): 3262, 2918, 1431, 1333, 1163, 1096, 1026, 812 cm^{-1} ; MS (ESI) m/z 352 $[\text{M}+\text{Na}]^+$; HRMS (ESI) calcd. for $\text{C}_{19}\text{H}_{23}\text{NO}_2\text{SNa}$: 352.1342, found: 352.1355.

***N*-(Cyclopropyl(naphthalen-1-yl)methyl)-4-methylbenzenesulfonamide 126g**

Colourless solid; m.p. 119-120 $^{\circ}\text{C}$; ^1H NMR (CDCl_3 , 400 MHz): δ 0.20- 0.32 (m, 2H), 0.37-0.53 (m, 2H), 1.34-1.43 (m, 1H), 2.24 (s, 3H), 4.61 (t, 1H, $J = 7.2$ Hz), 5.51 (d, 1H, $J = 6.0$ Hz), 6.89 (d, 2H, $J = 8.2$ Hz), 7.24-7.45 (m, 6H), 7.65 (d, 1H, $J = 8.1$ Hz), 7.44-7.77 (m, 1H), 8.01-8.02 (m, 1H); ^{13}C NMR (CDCl_3 , 100 MHz): δ 3.5, 5.3, 17.4, 21.3, 58.8, 123.2, 125.1, 125.3, 125.5, 126.1, 127.0, 128.1, 128.7, 128.9, 130.7, 133.7, 135.5, 137.5, 142.7; IR (KBr): 3254, 1597, 1508, 1443, 1163, 773 cm^{-1} ; MS (ESI) m/z 374 $[\text{M}+\text{Na}]^+$; HRMS (ESI) calcd. for $\text{C}_{21}\text{H}_{21}\text{NO}_2\text{SNa}$: 374.1191, found: 374.1369.

***N*-(Cyclopropyl(2-methoxyphenyl)methyl)-4-methylbenzenesulfonamide 126h¹⁰⁷**

Colourless solid; m.p. 136-138 $^{\circ}\text{C}$; ^1H NMR (CDCl_3 , 400 MHz): δ 0.19-0.24 (m, 1H), 0.33-0.40 (m, 2H), 0.47-0.53 (m, 1H), 1.28-1.36 (m, 1H), 2.28 (s, 3H), 3.66-3.70 (m, 4H), 5.84 (d, 1H, $J = 9.1$ Hz), 6.60 (d, 1H, $J = 8.2$ Hz), 6.71 (t, 1H, $J = 7.4$ Hz), 6.84-7.10 (m, 4H), 7.45 (d, 2H, $J = 8.2$ Hz); ^{13}C NMR (CDCl_3 , 100 MHz): δ 4.2, 4.9, 16.8, 21.4, 55.1, 61.7, 110.6, 120.4, 126.8, 128.0, 128.4, 128.8, 129.0, 137.9, 142.4, 156.2; IR (KBr): 3281,

2928, 1601, 1497, 1423, 1325, 1159, 762 cm^{-1} ; MS (ESI) m/z 354 $[\text{M}+\text{Na}]^+$; HRMS (ESI) calcd. for $\text{C}_{18}\text{H}_{21}\text{NO}_3\text{SNa}$: 354.1134, found: 354.1089.

7.5 Ytterbium(III) Triflate-Catalyzed Amination of 1-Cyclopropylprop-2-yn-1-ols as an Expedient Route to Conjugated Enynes

Representative Experimental Procedure for Preparation of Trisubstituted 1-Cyclopropyl-2-propyn-1-ols **131** (except for **131g**)

To a solution of alkyne (3.3 mmol) in THF (15 mL) was added LDA (2.0 M in THF, 1.8 mL) at $-78\text{ }^\circ\text{C}$. The resulting solution was stirred for 1 h at prior to slow addition of ketone (3 mmol) in THF (2 mL) at $-78\text{ }^\circ\text{C}$. The reaction mixture was slowly warmed up to room temperature and stirred for a further 10 h. On completion, the reaction mixture was quenched by adding saturated NH_4Cl (10 mL) and extracted with Et_2O (2 x 25 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 (eluent: hexane: ethyl acetate = 9: 1) gave **131**.

131g was prepared according the literature procedure^{108a}

To a solution of ethynylmagnesium bromide (0.5 M THF solution; 12.4 mL, 6.2 mmol) at $0\text{ }^\circ\text{C}$ was added dropwise a solution of cyclopropyl phenyl ketone (0.439 g, 3 mmol) in

diethyl ether (10 mL). The resulting mixture was stirred at room temperature for 15 h. The mixture was treated with saturated NH_4Cl aq. (10 mL). The organic layer was extracted with diethyl ether (10 mL x 3) and the combined organic layer was dried over anhydrous MgSO_4 , and concentrated under reduced pressure. Purification by flash column chromatography on silica gel (eluent: hexane: ethyl acetate = 9: 1) gave **131g** (0.31 g, 60% yield) as a colorless oil.

1-Cyclopropyl-1,3-diphenylprop-2-yn-1-ol **131a**

Pale yellow oil; ^1H NMR (CDCl_3 , 400 MHz): δ 0.59-0.74 (m, 3H), 0.86-0.89 (m, 1H), 1.43-1.49 (m, 1H), 2.54 (s, 1H), 7.24-7.45 (m, 8H), 7.74 (d, 2H, $J = 8.0$ Hz); ^{13}C NMR (CDCl_3 , 100 MHz): δ 2.5, 3.3, 23.9, 75.0, 86.1, 88.9, 122.4, 125.5, 127.7, 128.2, 128.3, 128.6, 131.8, 144.8; MS (ESI) m/z 231 $[\text{M}-\text{OH}]^+$.

1-Cyclopropyl-1-(4-fluorophenyl)-3-phenylprop-2-yn-1-ol **131b**

Yellow oil; ^1H NMR (CDCl_3 , 400 MHz): δ 0.57-0.73 (m, 3H), 0.82-0.88 (m, 1H), 1.40-1.47 (m, 1H), 2.38 (bs, 1H), 7.04-7.09 (m, 2H), 7.30-7.45 (m, 5H), 7.71 (dd, 2H, $J = 3.1$, 5.5 Hz); ^{13}C NMR (CDCl_3 , 100 MHz): δ 2.5, 3.4, 23.9, 74.5, 86.3, 88.6, 115.0 (1C, d, $J_{\text{C-F}} = 21.2$ Hz), 122.2, 127.3 (1C, d, $J_{\text{C-F}} = 8.0$ Hz), 128.4, 128.7, 131.8, 140.6 (1C, d, $J_{\text{C-F}} = 3.0$ Hz), 162.3 (1C, d, $J_{\text{C-F}} = 244.4$ Hz); IR (neat) ν : 3406, 3082, 2226, 1894, 1492, 1225,

1157, 835 cm^{-1} ; MS (ESI) m/z 249 $[\text{M}-\text{OH}]^+$; HRMS (ESI) calcd. for $\text{C}_{18}\text{H}_{14}\text{F}$ (M^+-OH): 249.1080, found: 249.1072.

1-(4-Chlorophenyl)-1-cyclopropyl-3-phenylprop-2-yn-1-ol 131c

Pale yellow oil; ^1H NMR (CDCl_3 , 400 MHz): δ 0.63-0.80 (m, 3H), 0.91-0.96 (m, 1H), 1.43-1.49 (m, 1H), 3.27 (s, 1H), 7.32-7.50 (m, 7H), 7.72 (d, 2H, $J = 8.6$ Hz); ^{13}C NMR (CDCl_3 , 100 MHz): δ 2.7, 3.5, 24.0, 74.6, 86.4, 88.7, 122.3, 127.1, 128.4, 128.5, 128.8, 131.9, 133.5, 143.6; IR (neat) ν : 3390, 3007, 2215, 1489, 1092 cm^{-1} ; MS (ESI) m/z 265 $[\text{M}-\text{OH}]^+$; HRMS (ESI) calcd. for $\text{C}_{18}\text{H}_{14}^{35}\text{Cl}$ (M^+-OH): 265.0784, found: 265.0778.

1-(4-Bromophenyl)-1-cyclopropyl-3-phenylprop-2-yn-1-ol 131d

Pale yellow oil; ^1H NMR (CDCl_3 , 400 MHz): δ 0.62-0.74 (m, 3H), 0.85-0.89 (m, 1H), 1.35-1.45 (m, 1H), 2.67 (s, 1H), 7.32-7.52 (m, 7H), 7.62 (d, 2H, $J = 8.6$ Hz); ^{13}C NMR (CDCl_3 , 100 MHz): δ 2.5, 3.4, 23.9, 74.6, 86.4, 88.3, 121.7, 122.1, 127.3, 128.4, 128.8, 131.3, 131.8, 144.0; IR (neat) ν : 3443, 2228, 1398, 1103 cm^{-1} ; MS (ESI) m/z 309 $[\text{M}-\text{OH}]^+$; HRMS (ESI) calcd. for $\text{C}_{18}\text{H}_{14}^{79}\text{Br}$ (M^+-OH): 309.0279, found: 309.0283.

1-Cyclopropyl-1-(4-methoxyphenyl)-3-*p*-tolylprop-2-yn-1-ol 131e

Pale yellow oil; ^1H NMR (CDCl_3 , 400 MHz): δ 0.62-0.72 (m, 3H), 0.85-0.89 (m, 1H), 1.43-1.50 (m, 1H), 2.36 (s, 3H), 2.59 (bs, 1H), 3.83 (s, 3H), 6.92 (d, 2H, $J = 8.8$ Hz), 7.13 (d, 2H, $J = 7.9$ Hz), 7.35 (d, 2H, $J = 8.0$ Hz), 7.68 (d, 2H, $J = 8.8$ Hz); ^{13}C NMR (CDCl_3 , 100 MHz): δ 2.5, 3.2, 21.5, 23.7, 55.3, 74.6, 86.1, 88.5, 113.5, 119.4, 126.8, 129.1, 131.7, 137.2, 138.7, 159.1; IR (neat) ν : 3410, 2221, 1532, 1045 cm^{-1} ; MS (ESI) m/z 275 $[\text{M}-\text{OH}]^+$; HRMS (ESI) calcd. for $\text{C}_{20}\text{H}_{19}\text{O}$ (M^+-OH): 275.1436, found: 275.1437.

1-Cyclopropyl-3-(6-methoxynaphthalen-2-yl)-1-phenylprop-2-yn-1-ol 131f

Colourless solid; m.p. 85-86 $^{\circ}\text{C}$; ^1H NMR (CDCl_3 , 400 MHz): δ 0.62-0.68 (m, 2H), 0.77-0.81 (m, 1H), 0.93-0.97 (m, 1H), 1.48-1.54 (m, 1H), 2.66 (s, 1H), 3.92 (s, 3H), 7.10 (d, 1H, $J = 2.1$ Hz), 7.17 (dd, 1H, $J = 6.6, 9.0$ Hz), 7.32-7.48 (m, 4H), 7.66-7.70 (m, 2H), 7.80 (d, 2H, $J = 7.3$ Hz), 7.90 (s, 1H); ^{13}C NMR (CDCl_3 , 100 MHz): δ 2.5, 3.4, 23.9, 55.4, 75.1, 86.6, 88.6, 105.8, 117.3, 119.5, 125.5, 126.8, 127.7, 128.3, 128.4, 129.1, 129.3, 131.6, 134.3, 145.0, 158.4; IR (neat) ν : 3449, 2978, 1626, 1258, 1022, 856 cm^{-1} ; MS (ESI) m/z 311 $[\text{M}-\text{OH}]^+$; HRMS (ESI) calcd. for $\text{C}_{23}\text{H}_{19}\text{O}$ (M^+-OH): 311.1436, found: 311.1442.

1-Cyclopropyl-1-phenylprop-2-yn-1-ol 131g^{108a}

Colourless oil; ¹H NMR (CDCl₃, 400 MHz): δ 0.59-0.70 (m, 3H), 0.75-0.82 (m, 1H), 1.36-1.43 (m, 1H), 2.43 (s, 1H), 2.59 (s, 1H), 7.30-7.40 (m, 3H), 7.68 (d, 2H, $J = 7.3$ Hz); ¹³C NMR (CDCl₃, 100 MHz): δ 2.3, 3.2, 23.4, 74.2, 74.3, 83.8, 125.3, 127.9, 128.2, 144.2; MS (ESI) m/z 155 [M-OH]⁺.

1-Cyclopropyl-1,4-diphenylbut-2-yn-1-ol 131h

Pale yellow oil; ¹H NMR (CDCl₃, 400 MHz): δ 0.59-0.67 (m, 3H), 0.78-0.82 (m, 1H), 1.35-1.42 (m, 1H), 2.42 (s, 1H), 3.68 (s, 2H), 7.23-7.38 (m, 8H), 7.68-7.70 (m, 2H); ¹³C NMR (CDCl₃, 100 MHz): δ 2.4, 3.3, 23.8, 25.1, 74.7, 82.3, 84.2, 125.4, 126.7, 127.6, 127.8, 128.2, 128.6, 136.5, 145.1; IR (neat) ν : 3428, 2210, 1645, 1449, 1265, 737 cm⁻¹; MS (ESI) m/z 245 [M-OH]⁺; HRMS (ESI) calcd. for C₁₉H₁₇ (M⁺-OH): 245.1330, found: 245.1333.

1,3-Dicyclopropyl-1-phenylprop-2-yn-1-ol 131i

Pale yellow oil; ¹H NMR (CDCl₃, 400 MHz): δ 0.67-0.81 (m, 8H), 1.24-1.36 (m, 2H), 2.34 (s, 1H), 7.26-7.37 (m, 3H), 7.64 (d, 2H, $J = 7.6$ Hz); ¹³C NMR (CDCl₃, 100 MHz): δ -0.6, 2.3, 3.2, 8.4, 8.5, 23.8, 74.6, 74.9, 90.0, 125.4, 127.5, 128.1, 145.3; IR (NaCl, neat)

ν : 3428, 2234, 1889, 1449, 1362, 1028 cm^{-1} ; MS (ESI) m/z 195 $[\text{M}-\text{OH}]^+$; HRMS (ESI) calcd. for $\text{C}_{15}\text{H}_{15}$ (M^+-OH): 195.1174, found: 195.1165.

1-Cyclopropyl-1-(4-methoxyphenyl)hept-2-yn-1-ol 131j

Pale yellow oil; ^1H NMR (CDCl_3 , 400 MHz): δ 0.57-0.58 (m, 3H), 0.73-0.77 (m, 1H), 0.92 (t, 1H, $J = 7.2$ Hz), 1.31-1.55 (m, 5H), 2.25 (t, 2H, $J = 7.0$ Hz), 2.34 (s, 1H), 3.81 (s, 3H), 6.87-6.90 (m, 2H), 7.57-7.61 (m, 2H); ^{13}C NMR (CDCl_3 , 100 MHz): δ 2.3, 3.1, 13.6, 18.4, 22.0, 23.6, 30.8, 55.3, 74.4, 80.0, 86.8, 113.4, 126.7, 137.7, 159.0; IR (neat) ν : 3460, 2234, 1609, 1510, 1300, 1248, 1177, 1034 cm^{-1} ; MS (ESI) m/z 241 $[\text{M}-\text{OH}]^+$; HRMS (ESI) calcd. for $\text{C}_{17}\text{H}_{21}\text{O}$ (M^+-OH): 241.1592, found: 241.1585.

1-Cyclopropyl-1-phenylnon-2-yn-1-ol 131k

Colourless oil; ^1H NMR (CDCl_3 , 400 MHz): δ 0.47-0.62 (m, 3H), 0.73-0.80 (m, 1H), 0.90 (t, 3H, $J = 7.1$ Hz), 1.24-1.43 (m, 7H), 1.49-1.59 (m, 2H), 2.24 (t, 2H, $J = 7.0$ Hz), 2.36 (s, 1H), 7.26-7.37 (m, 3H), 7.66-7.68 (m, 2H); ^{13}C NMR (CDCl_3 , 100 MHz): δ 2.3, 3.3, 14.1, 18.7, 22.6, 23.7, 28.6, 28.6, 31.3, 74.7, 79.9, 87.0, 125.4, 127.5, 128.1, 145.5; IR (neat) ν : 3442, 2236, 1489, 1028 cm^{-1} ; MS (ESI) m/z 239 $[\text{M}-\text{OH}]^+$; HRMS (ESI) calcd. for $\text{C}_{18}\text{H}_{23}$ (M^+-OH): 239.1800, found: 239.1797.

2-Cyclopropyl-4-*o*-tolylbut-3-yn-2-ol 131l

Pale yellow oil; ^1H NMR (CDCl_3 , 400 MHz): δ 0.50-0.60 (m, 3H), 0.68-0.74 (m, 1H), 1.20-1.28 (m, 1H), 1.70 (s, 3H), 2.20 (bs, 1H), 2.40 (s, 3H), 7.10-7.23 (m, 3H), 7.37 (d, 1H, $J = 7.4$ Hz); ^{13}C NMR (CDCl_3 , 100 MHz): δ 1.9, 2.7, 20.7, 22.1, 30.1, 70.9, 82.7, 93.9, 122.4, 125.5, 128.4, 129.4, 132.1, 140.0; IR (neat) ν : 3393, 2215, 1485, 1368, 1271, 1123, 926 cm^{-1} ; MS (ESI) m/z 183 $[\text{M}-\text{OH}]^+$; HRMS (ESI) calcd. for $\text{C}_{14}\text{H}_{15}$ (M^+-OH): 183.1174, found: 183.1158.

1-Cyclopropyl-3-phenyl-1-(thiophen-2-yl)prop-2-yn-1-ol 131m

Pale brown oil; ^1H NMR (CDCl_3 , 400 MHz): δ 0.67-0.76 (m, 3H), 0.90-0.95 (m, 1H), 1.58-1.64 (m, 1H), 2.69 (s, 1H), 6.99 (dd, 1H, $J = 1.1, 4.8$ Hz), 7.27-7.34 (m, 5H), 7.44-7.46 (m, 2H); ^{13}C NMR (CDCl_3 , 100 MHz): δ 2.9, 3.3, 23.8, 72.5, 85.6, 88.4, 122.2, 124.2, 125.1, 126.5, 128.4, 128.8, 131.9, 149.7; IR (neat) ν : 3412, 2226, 1603, 1489, 1231 cm^{-1} ; MS (ESI) m/z 237 $[\text{M}-\text{OH}]^+$; HRMS (ESI) calcd. for $\text{C}_{16}\text{H}_{13}\text{S}$ (M^+-OH): 237.0738, found: 237.0736.

1-Cyclopropyl-1-phenyl-3-(thiophen-3-yl)prop-2-yn-1-ol 131n

Yellow solid; m.p. 60-61 °C; ^1H NMR (CDCl_3 , 400 MHz): δ 0.57-0.69 (m, 3H), 0.77-0.83 (m, 1H), 1.38-1.45 (m, 1H), 2.46 (s, 1H), 7.07 (d, 1H, $J = 5.0$ Hz), 7.22-7.42 (m, 5H), 7.69 (d, 2H, $J = 8.0$ Hz); ^{13}C NMR (CDCl_3 , 100 MHz): δ 2.5, 3.3, 23.8, 75.0, 81.2, 88.7, 121.4, 125.4, 125.5, 127.8, 128.3, 129.2, 130.0, 144.8; IR (neat) ν : 3422, 2226, 1599, 1449, 1358, 1030 cm^{-1} ; MS (ESI) m/z 237 $[\text{M}-\text{OH}]^+$; HRMS (ESI) calcd. for $\text{C}_{16}\text{H}_{13}\text{S}$ (M^+-OH): 237.0738, found 237.0736.

1-Cyclopropyl-1-(thiophen-2-yl)-3-(thiophen-3-yl)prop-2-yn-1-ol 131o

Pale brown oil; ^1H NMR (CDCl_3 , 400 MHz): δ 0.66-0.75 (m, 3H), 0.87-0.91 (m, 1H), 1.56-1.63 (m, 1H), 2.66 (d, 1H, $J = 3.8$ Hz), 6.99 (dd, 1H, $J = 4.0, 8.1$ Hz), 7.11 (d, 1H, $J = 5.0$ Hz), 7.26-7.28 (m, 3H), 7.46 (d, 1H, $J = 2.8$ Hz); ^{13}C NMR (CDCl_3 , 100 MHz): δ 2.8, 3.3, 23.7, 72.4, 80.8, 88.0, 121.1, 124.1, 125.1, 125.4, 126.5, 129.4, 129.9, 149.6; IR (neat) ν : 3422, 2225, 1522, 1358, 1231, 1028, 999 cm^{-1} ; MS (ESI) m/z 243 $[\text{M}-\text{OH}]^+$; HRMS (ESI) calcd. for $\text{C}_{14}\text{H}_{11}\text{S}_2$ (M^+-OH): 243.0302, found: 243.0378.

1-Cyclopropyl-1-phenyl-3-(pyridin-2-yl)prop-2-yn-1-ol 131p

Colourless solid; m.p. 112-113 °C; ^1H NMR (CDCl_3 , 400 MHz): δ 0.59-0.62 (m, 2H), 0.76-0.80 (m, 1H), 0.86-0.90 (m, 1H), 1.47-1.51 (m, 1H), 3.32 (s, 1H), 7.20-7.43 (m, 5H), 7.61-7.65 (m, 1H), 7.76 (d, 2H, $J = 7.6$ Hz), 8.54 (d, 1H, $J = 4.7$ Hz); ^{13}C NMR (CDCl_3 , 100 MHz): δ 2.5, 3.2, 23.8, 74.3, 85.0, 89.7, 123.1, 125.5, 127.4, 127.8, 128.2, 136.2, 142.7, 144.4, 150.0; IR (neat) ν : 3208, 2226, 1585, 1468, 1429, 1267, 1040 cm^{-1} ; MS (ESI) m/z 250 $[\text{M}+\text{H}]^+$; HRMS (ESI) calcd. for $\text{C}_{17}\text{H}_{16}\text{NO}$ (M^++H): 250.1232, found: 250.1228.

(Z)-N-(4,6-Diphenylhex-3-en-5-ynyl)-4-methylbenzenesulfonamide 132a

Pale yellow oil; ^1H NMR (CDCl_3 , 400 MHz): δ 2.34 (s, 3H), 2.73 (dt, 2H, $J = 6.9, 7.1$ Hz), 3.19 (dt, 2H, $J = 6.6, 6.4$ Hz), 4.76 (t, 1H, $J = 5.9$ Hz), 6.26 (t, 1H, $J = 7.5$ Hz), 7.19 (d, 2H, $J = 8.1$ Hz), 7.29-7.36 (m, 6H), 7.49-7.59 (m, 4H), 7.73 (d, 2H, $J = 8.2$ Hz); ^{13}C NMR (CDCl_3 , 100 MHz): δ 21.5, 31.4, 42.5, 86.0, 95.2, 123.0, 126.1, 126.4, 127.1, 128.0, 128.4, 128.6, 129.7, 131.6, 132.8, 136.8, 137.5, 143.4; IR (neat) ν : 3281, 2924, 1715, 1597, 1489, 1449, 1330, 1159 cm^{-1} ; MS (ESI) m/z 402 $[\text{M}+\text{H}]^+$; HRMS (ESI) calcd. for $\text{C}_{25}\text{H}_{24}\text{NO}_2\text{S}$ (M^++H): 402.1528, found: 402.1529.

(Z)-N-(4-(4-Fluorophenyl)-6-phenylhex-3-en-5-ynyl)-4-methylbenzenesulfonamide**132b**

Pale yellow oil; ^1H NMR (CDCl_3 , 400 MHz): δ 2.36 (s, 3H), 2.73 (dt, 2H, $J = 6.9, 7.1$ Hz), 3.19 (dt, 2H, $J = 6.6, 6.4$ Hz), 4.80 (t, 1H, $J = 6.0$ Hz), 6.22 (t, 1H, $J = 7.4$ Hz), 7.00-7.06 (m, 2H), 7.21 (d, 2H, $J = 8.1$ Hz), 7.35-7.57 (m, 7H), 7.74 (d, 2H, $J = 8.2$ Hz); ^{13}C NMR (CDCl_3 , 100 MHz): δ 21.5, 31.4, 42.4, 85.9, 96.3, 115.3 (1C, d, $J_{\text{C-F}} = 21.5$ Hz), 122.8, 125.2, 127.1, 127.7, 127.8, 128.5, 128.7, 129.7, 131.6, 132.7, 133.6, 133.6, 136.9, 143.4, 162.5 (1C, d, $J_{\text{C-F}} = 245.8$ Hz); IR (NaCl, neat) ν : 3283, 1599, 1506, 1325, 1227, 1159, 1094 cm^{-1} ; MS (ESI) m/z 420 $[\text{M}+\text{H}]^+$; HRMS (ESI) calcd. for $\text{C}_{25}\text{H}_{23}\text{NO}_2\text{SF}$ (M^++H): 420.1434, found: 420.1426.

(Z)-N-(4-(4-Chlorophenyl)-6-phenylhex-3-en-5-ynyl)-4-methylbenzenesulfonamide**132c**

Pale yellow oil; ^1H NMR (CDCl_3 , 400 MHz): δ 2.36 (s, 3H), 2.73 (dt, 2H, $J = 6.9, 7.0$ Hz), 3.19 (dt, 2H, $J = 6.5, 6.4$ Hz), 4.70 (t, 1H, $J = 6.0$ Hz), 6.26 (t, 1H, $J = 7.5$ Hz), 7.21 (d, 2H, $J = 8.0$ Hz), 7.30-7.37 (m, 5H), 7.48-7.52 (m, 4H), 7.73 (d, 2H, $J = 8.2$ Hz); ^{13}C NMR (CDCl_3 , 100 MHz): δ 21.5, 31.5, 42.4, 85.6, 96.5, 122.8, 125.2, 127.1, 127.4, 128.5, 128.5, 128.7, 129.7, 131.6, 133.4, 133.7, 136.0, 136.8, 143.4; IR (NaCl, neat) ν : 3443,

1636, 1489, 1325, 1159, 1092 cm^{-1} ; MS (ESI) m/z 436 $[\text{M}+\text{H}]^+$; HRMS (ESI) calcd. for $\text{C}_{25}\text{H}_{23}\text{NO}_2\text{S}^{35}\text{Cl}$ (M^++H): 436.1138, found: 436.1137.

(Z)-N-(4-(4-Bromophenyl)-6-phenylhex-3-en-5-ynyl)-4-methylbenzenesulfonamide

132d

Brown oil; ^1H NMR (CDCl_3 , 400 MHz): δ 2.35 (s, 3H), 2.72 (dt, 2H, $J = 6.9, 7.1$ Hz), 3.18 (dt, 2H, $J = 6.5, 6.4$ Hz), 5.07 (t, 1H, $J = 6.0$ Hz), 6.29 (t, 1H, $J = 7.4$ Hz), 7.20 (d, 2H, $J = 8.1$ Hz), 7.35-7.51 (m, 9H), 7.74 (d, 2H, $J = 8.2$ Hz); ^{13}C NMR (CDCl_3 , 100 MHz): δ 21.5, 31.5, 42.3, 85.5, 96.5, 121.9, 122.7, 125.3, 127.1, 127.7, 128.5, 128.7, 129.8, 131.5, 131.6, 133.5, 136.4, 136.8, 143.5; IR (NaCl, neat) ν : 3280, 1715, 1597, 1487, 1159, 1011, 816 cm^{-1} ; MS (ESI) m/z 480 $[\text{M}+\text{H}]^+$; HRMS (ESI) calcd. for $\text{C}_{25}\text{H}_{23}\text{NO}_2\text{S}^{79}\text{Br}$ (M^++H): 480.0633, found: 480.0631.

(Z)-N-(4-(4-Methoxyphenyl)-6-*p*-tolylhex-3-en-5-ynyl)-4-methylbenzenesulfonamide

132e

Pale yellow oil; ^1H NMR (CDCl_3 , 400 MHz): δ 2.37 (s, 3H), 2.38 (s, 3H), 2.70 (dt, 2H, $J = 6.9, 7.1$ Hz), 3.18 (dt, 2H, $J = 6.6, 6.3$ Hz), 3.83 (s, 3H), 4.56 (t, 1H, $J = 5.8$ Hz), 6.11 (t, 1H, $J = 7.5$ Hz), 6.88 (d, 2H, $J = 8.8$ Hz), 7.15-7.22 (m, 4H), 7.39 (d, 2H, $J = 8.0$ Hz), 7.51 (d, 2H, $J = 8.8$ Hz), 7.73 (d, 2H, $J = 8.2$ Hz); ^{13}C NMR (CDCl_3 , 100 MHz): δ 21.5,

21.6, 31.3, 42.6, 55.4, 85.6, 96.2, 113.7, 120.0, 125.8, 127.1, 127.3, 129.2, 129.7, 130.2, 130.5, 131.5, 136.9, 138.7, 143.3, 159.5; IR (NaCl, neat) ν : 3419, 1645, 1508, 1159 cm^{-1} ; MS (ESI) m/z 446 $[\text{M}+\text{H}]^+$; HRMS (ESI) calcd. for $\text{C}_{27}\text{H}_{28}\text{NO}_3\text{S}$ (M^++H): 446.1790, found: 446.1771.

(Z)-N-(6-(6-Methoxynaphthalen-2-yl)-4-phenylhex-3-en-5-ynyl)-4 methylbenzenesulfonamide 132f

Pale yellow solid; m.p. 135-137 $^{\circ}\text{C}$; ^1H NMR (CDCl_3 , 400 MHz): δ 2.32 (s, 3H), 2.78 (dt, 2H, $J = 6.9, 7.0$ Hz), 3.22 (dt, 2H, $J = 6.5, 6.4$ Hz), 3.93 (s, 3H), 4.73 (t, 1H, $J = 5.9$ Hz), 6.26 (t, 1H, $J = 7.4$ Hz), 7.13-7.39 (m, 7H), 7.50-7.75 (m, 7H), 7.95 (s, 1H); ^{13}C NMR (CDCl_3 , 100 MHz): δ 21.5, 31.4, 42.5, 55.4, 85.8, 96.9, 105.9, 117.8, 119.6, 126.1, 126.6, 127.0, 127.1, 128.0, 128.5, 128.5, 128.5, 128.9, 129.4, 129.7, 131.4, 132.6, 134.3, 136.9, 137.6, 143.4, 158.5; IR (NaCl, neat) ν : 3275, 1626, 1599, 1327, 1265, 1159, 1030 cm^{-1} ; MS (ESI) m/z 482 $[\text{M}+\text{H}]^+$; HRMS (ESI) calcd. for $\text{C}_{30}\text{H}_{28}\text{NO}_3\text{S}$ (M^++H): 482.1790, found: 482.1795.

(E)-4-Methyl-N-(4-phenylhex-3-en-5-ynyl)benzenesulfonamide 132g

Brown oil; ^1H NMR (CDCl_3 , 400 MHz): δ 2.38 (s, 3H), 2.67 (dt, 2H, $J = 6.9, 7.1$ Hz), 3.15 (dt, 2H, $J = 6.6, 6.4$ Hz), 3.33 (s, 1H), 4.72 (t, 1H, $J = 6.0$ Hz), 6.29 (t, 1H, $J = 7.5$

Hz), 7.23-7.35 (m, 5H), 7.51 (d, 2H, $J = 6.9$ Hz), 7.74 (d, 2H, $J = 8.2$ Hz); ^{13}C NMR (CDCl_3 , 100 MHz): δ 21.5, 31.2, 42.4, 80.3, 84.1, 125.5, 126.0, 127.1, 128.1, 128.4, 129.7, 134.6, 136.8, 136.9, 143.5; IR (NaCl, neat) ν : 3310, 1649, 1325, 1188 cm^{-1} ; MS (ESI) m/z 326 $[\text{M}+\text{H}]^+$; HRMS (ESI) calcd. for $\text{C}_{19}\text{H}_{20}\text{NO}_2\text{S}$ (M^++H): 326.1215, found: 326.1206.

(Z)-N-(4,7-Diphenylhept-3-en-5-ynyl)-4-methylbenzenesulfonamide 132h

Pale yellow oil; ^1H NMR (CDCl_3 , 400 MHz): δ 2.35 (s, 3H), 2.64 (dt, 2H, $J = 7.0, 7.1$ Hz), 3.10 (dt, 2H, $J = 6.6, 6.4$ Hz), 3.85 (s, 2H), 4.76 (t, 1H, $J = 6.0$ Hz), 6.17 (t, 1H, $J = 7.4$ Hz), 7.18-7.39 (m, 10H), 7.52 (d, 2H, $J = 7.2$ Hz), 7.71 (d, 2H, $J = 8.2$ Hz); ^{13}C NMR (CDCl_3 , 100 MHz): δ 21.5, 26.0, 31.2, 42.5, 79.4, 94.7, 126.1, 126.5, 126.8, 127.1, 127.9, 128.0, 128.4, 128.7, 129.7, 132.2, 136.6, 136.8, 137.8, 143.4; IR (NaCl, neat) ν : 3277, 1597, 1452, 1325, 1159 cm^{-1} ; MS (ESI) m/z 416 $[\text{M}+\text{H}]^+$; HRMS (ESI) calcd. for $\text{C}_{26}\text{H}_{26}\text{NO}_2\text{S}$ (M^++H): 416.1684, found: 416.1679.

(Z)-N-(6-Cyclopropyl-4-phenylhex-3-en-5-ynyl)-4-methylbenzenesulfonamide 132i

Pale yellow oil; ^1H NMR (CDCl_3 , 400 MHz): δ 0.77-0.91 (m, 4H), 1.43-1.50 (m, 1H), 2.38 (s, 3H), 2.60 (dt, 2H, $J = 6.9, 7.0$ Hz), 3.11 (dt, 2H, $J = 6.4, 6.3$ Hz), 4.73 (t, 1H, $J = 5.7$ Hz), 6.08 (t, 1H, $J = 7.5$ Hz), 7.22-7.32 (m, 5H), 7.47 (d, 2H, $J = 7.2$ Hz), 7.73 (d, 2H, $J = 8.1$ Hz); ^{13}C NMR (CDCl_3 , 100 MHz): δ 0.4, 9.0, 21.5, 31.0, 42.5, 72.5, 100.8, 126.0,

126.7, 127.1, 127.8, 128.3, 129.7, 131.4, 136.8, 138.0, 143.3; IR (NaCl, neat) ν : 3431, 2236, 1647, 1597, 1449, 1157 cm^{-1} ; MS (ESI) m/z 366 $[\text{M}+\text{H}]^+$; HRMS (ESI) calcd. for $\text{C}_{22}\text{H}_{24}\text{NO}_2\text{S}$ (M^++H): 366.1528, found: 366.1524.

(Z)-N-(4-(4-Methoxyphenyl)dec-3-en-5-ynyl)-4-methylbenzenesulfonamide 132j

Pale yellow oil; ^1H NMR (CDCl_3 , 400 MHz): δ 0.94 (t, 3H, $J = 7.2$ Hz), 1.42-1.51 (m, 2H), 1.55-1.62 (m, 2H), 2.38 (s, 3H), 2.43 (t, 2H, $J = 7.2$ Hz), 2.61 (dt, 2H, $J = 6.8, 7.1$ Hz), 3.11 (dt, 2H, $J = 6.5, 6.2$ Hz), 3.81 (s, 3H), 4.75 (t, 1H, $J = 5.8$ Hz), 6.00 (t, 1H, $J = 7.4$ Hz), 6.83 (d, 2H, $J = 8.8$ Hz), 7.23 (d, 2H, $J = 8.0$ Hz), 7.43 (d, 2H, $J = 8.8$ Hz), 7.73 (d, 2H, $J = 8.2$ Hz); ^{13}C NMR (CDCl_3 , 100 MHz): δ 13.6, 19.3, 21.5, 22.1, 30.9, 42.6, 55.3, 77.4, 97.4, 113.6, 126.2, 127.1, 127.2, 129.3, 129.7, 130.7, 136.9, 143.3, 159.3; IR (NaCl, neat) ν : 3277, 1599, 1252, 1159 cm^{-1} ; MS (ESI) m/z 412 $[\text{M}+\text{H}]^+$; HRMS (ESI) calcd. for $\text{C}_{24}\text{H}_{30}\text{NO}_3\text{S}$ (M^++H): 412.1946, found: 412.1944.

(Z)-4-Methyl-N-(4-phenyldodec-3-en-5-ynyl)benzenesulfonamide 132k

Pale yellow oil; ^1H NMR (CDCl_3 , 400 MHz): δ 0.89 (t, 3H, $J = 7.1$ Hz), 1.26-1.48 (m, 6H), 1.56-1.63 (m, 2H), 2.37 (s, 3H), 2.42 (t, 2H, $J = 7.1$ Hz), 2.63 (dt, 2H, $J = 6.8, 7.1$ Hz), 3.12 (q, 2H, $J = 6.5, 6.2$ Hz), 4.77 (s, 1H), 6.10 (t, 1H, $J = 7.4$ Hz), 7.21-7.32 (m, 5H), 7.49-7.51 (m, 2H), 7.72-7.74 (m, 2H); ^{13}C NMR (CDCl_3 , 100 MHz): δ 14.1, 19.6,

21.5, 22.6, 28.7, 28.8, 31.0, 31.3, 42.5, 77.3, 97.8, 126.0, 126.8, 127.1, 127.7, 128.3, 129.7, 131.2, 136.8, 138.0, 143.3; IR (NaCl, neat) ν : 3445, 1636, 1329, 665 cm^{-1} ; MS (ESI) m/z 410 $[\text{M}+\text{H}]^+$; HRMS (ESI) calcd. for $\text{C}_{25}\text{H}_{32}\text{NO}_2\text{S}$ (M^++H): 410.2154, found: 410.2154.

(Z)-4-Methyl-N-(4-methyl-6-o-tolylhex-3-en-5-ynyl)benzenesulfonamide 132l

Pale yellow oil; ^1H NMR (CDCl_3 , 400 MHz): δ 1.92 (s, 3H), 2.37-2.52 (m, 8H), 2.99-3.09 (m, 2H), 4.79 (t, 1H, $J = 5.8$ Hz), 5.56 (t, 1H, $J = 7.3$ Hz), 7.13-7.39 (m, 6H), 7.74 (d, 2H, $J = 8.2$ Hz); ^{13}C NMR (CDCl_3 , 100 MHz): δ 20.9, 21.5, 23.3, 30.8, 42.5, 92.0, 92.9, 121.8, 123.1, 125.5, 127.1, 128.1, 129.4, 129.8, 131.7, 132.5, 136.9, 140.0, 143.5; IR (NaCl, neat) ν : 3420, 1645, 1456, 1323, 1092, 758 cm^{-1} ; MS (ESI) m/z 354 $[\text{M}+\text{H}]^+$; HRMS (ESI) calcd. for $\text{C}_{21}\text{H}_{24}\text{NO}_2\text{S}$ (M^++H): 354.1528, found: 354.1516.

(E)-4-Methyl-N-(6-phenyl-4-(thiophen-2-yl)hex-3-en-5-ynyl)benzenesulfonamide 132m

Brown oil; ^1H NMR (CDCl_3 , 400 MHz): δ 2.36 (s, 3H), 2.68 (dt, 2H, $J = 6.9, 7.1$ Hz), 3.17 (dt, 2H, $J = 6.6, 6.4$ Hz), 4.63 (t, 1H, $J = 5.9$ Hz), 6.15 (t, 1H, $J = 7.6$ Hz), 6.99 (dd, 1H, $J = 5.0, 3.7$ Hz), 7.18-7.37 (m, 7H), 7.49-7.52 (m, 2H), 7.73 (d, 2H, $J = 8.2$ Hz); ^{13}C NMR (CDCl_3 , 100 MHz): δ 21.5, 31.2, 42.4, 85.0, 95.3, 120.6, 122.7, 124.7, 125.1, 127.1,

128.5, 128.8, 129.8, 130.9, 131.7, 136.8, 142.4, 143.4; IR (NaCl, neat) ν : 3428, 1653, 1325, 1157, 1094 cm^{-1} ; MS (ESI) m/z 408 $[\text{M}+\text{H}]^+$; HRMS (ESI) calcd. for $\text{C}_{23}\text{H}_{22}\text{NO}_2\text{S}_2$ (M^++H): 408.1092, found: 408.1081.

(Z)-4-Methyl-N-(4-phenyl-6-(thiophen-3-yl)hex-3-en-5-ynyl)benzenesulfonamide

132n

Brown oil; ^1H NMR (CDCl_3 , 400 MHz): δ 2.37 (s, 3H), 2.72 (dt, 2H, $J = 6.9, 7.1$ Hz), 3.18 (dt, 2H, $J = 6.6, 6.4$ Hz), 4.79 (t, 1H, $J = 5.8$ Hz), 6.25 (t, 1H, $J = 7.5$ Hz), 7.18-7.36 (m, 7H), 7.52-7.58 (m, 3H), 7.74 (d, 2H, $J = 8.2$ Hz); ^{13}C NMR (CDCl_3 , 100 MHz): δ 21.5, 31.4, 42.5, 85.7, 91.3, 122.0, 125.6, 126.1, 126.3, 127.1, 128.0, 128.4, 129.0, 129.7, 129.9, 132.9, 136.9, 137.5, 143.4; IR (NaCl, neat) ν : 3418, 1636, 1323, 1159, 1093 cm^{-1} ; MS (ESI) m/z 408 $[\text{M}+\text{H}]^+$; HRMS (ESI) calcd. for $\text{C}_{23}\text{H}_{22}\text{NO}_2\text{S}_2$ (M^++H): 408.1092, found: 408.1083.

(E)-4-Methyl-N-(4-(thiophen-2-yl)-6-(thiophen-3-yl)hex-3-en-5-ynyl) benzene-sulfonamide 132o

Brown oil; ^1H NMR (CDCl_3 , 400 MHz): δ 2.37 (s, 3H), 2.67 (dt, 2H, $J = 7.0, 7.2$ Hz), 3.15 (dt, 2H, $J = 6.6, 6.5$ Hz), 4.75 (t, 1H, $J = 5.9$ Hz), 6.15 (t, 1H, $J = 7.6$ Hz), 6.98 (dd,

1H, $J = 4.9, 3.8$ Hz), 7.18-7.33 (m, 6H), 7.54 (dd, 1H, $J = 2.0, 2.9$ Hz), 7.74 (d, 2H, $J = 8.2$ Hz); ^{13}C NMR (CDCl_3 , 100 MHz): δ 21.5, 31.1, 42.4, 84.5, 90.5, 120.7, 121.7, 124.7, 125.1, 125.6, 127.1, 127.4, 129.3, 129.7, 129.8, 130.8, 136.8, 142.3, 143.4; IR (NaCl, neat) ν : 3289, 1651, 1325, 1159, 1094 cm^{-1} ; MS (ESI) m/z 414 $[\text{M}+\text{H}]^+$; HRMS (ESI) calcd. for $\text{C}_{21}\text{H}_{20}\text{NO}_2\text{S}_3$ (M^++H): 414.0656, found: 414.0656.

(Z)-N-(4,6-Diphenylhex-3-en-5-ynyl)benzenesulfonamide 132q

Brown oil; ^1H NMR (CDCl_3 , 400 MHz): δ 2.75 (dt, 2H, $J = 7.0, 7.2$ Hz), 3.21 (dt, 2H, $J = 6.6, 6.4$ Hz), 4.92 (t, 1H, $J = 5.9$ Hz), 6.29 (t, 1H, $J = 7.5$ Hz), 7.28-7.61 (m, 13H), 7.87 (d, 2H, $J = 7.2$ Hz); ^{13}C NMR (CDCl_3 , 100 MHz): δ 31.4, 42.5, 86.0, 96.2, 123.0, 126.1, 126.5, 127.1, 128.0, 128.5, 128.6, 129.1, 131.6, 132.7, 137.5, 139.8; IR (NaCl, neat) ν : 3291, 1589, 1453, 1171, 746 cm^{-1} ; MS (ESI) m/z 388 $[\text{M}+\text{H}]^+$; HRMS (ESI) calcd. for $\text{C}_{24}\text{H}_{22}\text{NO}_2\text{S}$ (M^++H): 388.1371, found: 388.1384.

(Z)-N-(4,6-Diphenylhex-3-en-5-ynyl)-4-methoxybenzenesulfonamide 132r

Brown oil; ^1H NMR (CDCl_3 , 400 MHz): δ 2.74 (dt, 2H, $J = 6.9, 7.1$ Hz), 3.19 (dt, 2H, $J = 6.6, 6.4$ Hz), 3.79 (s, 3H), 4.70 (t, 1H, $J = 5.0$ Hz), 6.27 (t, 1H, $J = 7.5$ Hz), 6.87 (d, 2H, $J = 8.8$ Hz), 7.28-7.37 (m, 6H), 7.50-7.60 (m, 4H), 7.79 (d, 2H, $J = 8.8$ Hz); ^{13}C NMR (CDCl_3 , 100 MHz): δ 31.4, 42.4, 55.6, 86.1, 96.2, 114.3, 123.0, 126.1, 126.3, 128.0, 128.5,

128.6, 129.3, 131.4, 131.6, 133.0, 137.5, 162.8; IR (NaCl, neat) ν : 3273, 1597, 1497, 1325, 1260, 1153 cm^{-1} ; MS (ESI) m/z 417 $[\text{M}+\text{H}]^+$; HRMS (ESI) calcd. for $\text{C}_{25}\text{H}_{24}\text{NO}_3\text{S}$ (M^++H): 418.1477, found: 418.1462.

(Z)-4-Chloro-N-(4,6-diphenylhex-3-en-5-ynyl)benzenesulfonamide 132s

Yellow oil; ^1H NMR (CDCl_3 , 400 MHz): δ 2.75 (dt, 2H, $J = 6.9, 7.1$ Hz), 3.21 (dt, 2H, $J = 6.5, 6.3$ Hz), 5.07 (t, 1H, $J = 5.9$ Hz), 6.27 (t, 1H, $J = 7.5$ Hz), 7.29-7.38 (m, 8H), 7.50-7.60 (m, 4H), 7.77-7.79 (m, 2H); ^{13}C NMR (CDCl_3 , 100 MHz): δ 31.4, 42.5, 77.4, 86.0, 96.3, 122.9, 126.1, 126.6, 128.1, 128.5, 128.7, 129.4, 131.6, 132.5, 137.3, 138.4, 139.1; IR (NaCl, neat) ν : 3289, 1489, 1339, 1161, 1094 cm^{-1} ; MS (ESI) m/z 422 $[\text{M}+\text{H}]^+$; HRMS (ESI) calcd. for $\text{C}_{24}\text{H}_{21}\text{NO}_2\text{S}^{35}\text{Cl}$ (M^++H): 422.0982, found: 422.0943.

(Z)-4,6-Diphenylhex-3-en-5-yn-1-amine 132t

Yellow solid; m.p. 85-87 $^{\circ}\text{C}$; ^1H NMR (CDCl_3 , 400 MHz): δ 2.92 (dt, 2H, $J = 6.8, 7.0$ Hz), 4.27 (t, 2H, $J = 6.5$ Hz), 4.67 (bs, 2H), 6.45 (t, 1H, $J = 7.4$ Hz), 7.28-7.39 (m, 6H), 7.53-7.55 (m, 2H), 7.66-7.68 (m, 2H); ^{13}C NMR (CDCl_3 , 100 MHz): δ 31.2, 64.0, 86.3, 95.9, 123.2, 125.9, 126.1, 127.9, 128.4, 128.4, 131.6, 133.1, 137.8, 156.8; IR (NaCl, neat) ν : 3443, 3418, 1697, 1636, 1339, 1070 cm^{-1} ; MS (ESI) m/z 248 $[\text{M}+\text{H}]^+$; HRMS (ESI) calcd. for $\text{C}_{18}\text{H}_{18}\text{N}$ (M^++H): 248.1439, found: 248.1432.

(Z)-N-(4,6-Diphenylhex-3-en-5-ynyl)benzenamine 132u

Yellow oil; ^1H NMR (CDCl_3 , 400 MHz): δ 2.95 (dt, 2H, $J = 7.0, 7.2$ Hz), 3.40 (t, 2H, $J = 6.8$ Hz), 3.84 (bs, 1H), 6.53 (t, 1H, $J = 7.5$ Hz), 6.68-6.75 (m, 3H), 7.17-7.21 (m, 2H), 7.31-7.55 (m, 8H), 7.71 (d, 2H, $J = 7.3$ Hz); ^{13}C NMR (CDCl_3 , 100 MHz): δ 31.6, 43.3, 86.5, 95.8, 112.8, 117.4, 123.2, 125.7, 126.1, 127.9, 128.4, 128.5, 129.3, 131.7, 134.8, 137.8, 148.2; IR (NaCl, neat) ν : 3410, 1682, 1601, 1506, 1265 cm^{-1} ; MS (ESI) m/z 324 $[\text{M}+\text{H}]^+$; HRMS (ESI) calcd. for $\text{C}_{24}\text{H}_{22}\text{N}$ (M^++H): 324.1752, found: 324.1747.

N,N-bis((Z)-4,6-Diphenylhex-3-en-5-ynyl)-4-methylbenzenesulfonamide 133a

Yellow oil; ^1H NMR (CDCl_3 , 400 MHz): δ 2.30 (s, 3H), 2.89 (dt, 4H, $J = 7.5, 7.4$ Hz), 3.45 (t, 4H, $J = 7.8$ Hz), 6.33 (t, 2H, $J = 7.4$ Hz), 7.12 (d, 2H, $J = 8.1$ Hz), 7.25-7.57 (m, 20H), 7.70 (d, 2H, $J = 8.1$ Hz); ^{13}C NMR (CDCl_3 , 100 MHz): δ 21.5, 30.6, 46.9, 86.2, 96.0, 123.1, 125.9, 126.1, 127.2, 127.8, 128.4, 129.7, 131.6, 133.3, 137.0, 137.6, 143.1; IR (NaCl, neat) ν : 3059, 1489, 1339, 1265, 1159, 733 cm^{-1} ; MS (ESI) m/z 632 $[\text{M}+\text{H}]^+$; HRMS (ESI) calcd. for $\text{C}_{43}\text{H}_{38}\text{NO}_2\text{S}$ (M^++H): 632.2623, found: 632.2619.

((Z)-6-((Z)-4,7-Diphenylhept-3-en-5-ynyloxy)hex-3-en-1-yne-1,3-diyl)dibenzene 134a

Yellow oil; ^1H NMR (CDCl_3 , 400 MHz): δ 2.89 (dt, 2H, $J = 6.8, 7.0$ Hz), 3.70 (t, 2H, $J = 6.6$ Hz), 6.54 (t, 2H, $J = 7.4$ Hz), 7.24-7.66 (m, 10H); ^{13}C NMR (CDCl_3 , 100 MHz): δ 32.0, 69.7, 86.6, 95.6, 123.4, 125.0, 126.1, 127.6, 128.3, 128.4, 128.4, 131.6, 134.6, 138.0; IR (NaCl, neat) ν : 3058, 2926, 2199, 1724, 1489, 1449, 1269, 696 cm^{-1} ; MS (ESI) m/z 479 $[\text{M}+\text{H}]^+$; HRMS (ESI) calcd. for $\text{C}_{36}\text{H}_{30}\text{O}$ (M^++H): 479.2375, found: 479.2368.

2-(1-Cyclopropyl-1,3-diphenylprop-2-ynylamino)isoindoline-1,3-dione 136a

White oil; ^1H NMR (CDCl_3 , 400 MHz): δ 0.46-0.63 (m, 3H), 0.77-0.83 (m, 1H), 1.74-1.80 (m, 1H), 5.48 (s, 1H), 7.29-7.45 (m, 8H), 7.70-7.72 (m, 2H), 7.82-7.85 (m, 2H), 7.99 (d, 2H, $J = 7.3$ Hz); ^{13}C NMR (CDCl_3 , 100 MHz): δ 1.6, 4.0, 20.4, 68.3, 85.9, 88.7, 122.5, 123.4, 127.3, 128.3, 128.3, 128.4, 130.3, 131.6, 134.1, 141.8, 166.5; IR (NaCl, neat) ν : 3445, 1726, 1636, 1375, 712 cm^{-1} ; MS (ESI) m/z 393 $[\text{M}+\text{H}]^+$; HRMS (ESI) calcd. for $\text{C}_{26}\text{H}_{21}\text{N}_2\text{O}_2$ (M^++H): 393.1603, found: 393.1602.

3-(1-Cyclopropyl-1,3-diphenylprop-2-ynyl)-1H-indole 136b

Pale yellow solid; m.p. 65-66 °C; ^1H NMR (CDCl_3 , 400 MHz): δ 0.60-0.78 (m, 2H), 0.86-0.94 (m, 2H), 1.69-1.75 (m, 1H), 6.95-6.99 (mt, 1H), 7.14-7.46 (m, 12H), 7.62-7.64 (m, 2H), 7.95 (s, 1H); ^{13}C NMR (CDCl_3 , 100 MHz): δ 2.6, 3.8, 21.5, 46.1, 84.8, 90.3, 111.1, 119.3, 121.2, 121.4, 122.0, 122.4, 123.7, 125.9, 126.5, 127.2, 127.8, 128.1, 128.2, 131.8, 137.1, 145.7; IR (NaCl, neat) ν : 3414, 1597, 1489, 1335, 1097, 1024 cm^{-1} ; MS (ESI) m/z 348 $[\text{M}+\text{H}]^+$; HRMS (ESI) calcd. for $\text{C}_{26}\text{H}_{22}\text{N}$ (M^++H): 348.1752, found: 348.1749.

7.6 Copper(II) Triflate-Catalyzed Intramolecular Hydroamination of Homoallylic Aminoalcohols as an Expedient Route to *trans*-2,5-Dihydro-1*H*-pyrroles and 1,2-Dihydroquinolines

General Procedure for the Preparation of Enantioenriched 1-(Tosylamino)pent-4-en-2-ols 139a-j

Enantioenriched 1-(tosylamino)pent-4-en-2-ols **139a-j** were prepared following literature procedures.^{141,142} This involved adding 1.32 g (33 mmol) of NaOH and 2.5 g (26.4 mmol) of *p*-toluenesulfonyl chloride to a stirred suspension of the (D)- or (L)-amino acid (11 mmol) in H₂O (25 mL) at room temperature. The reaction mixture was stirred at 60 °C for 6 h, cooled to -5 °C and acidified to pH 1 by the addition of concentrated HCl. The resulting precipitate was then collected by filtration, sequentially washed with cold H₂O and EtOH, and air dried to give the *N*-tosyl protected amino acid as a white solid. A CH₂Cl₂ (12 mL) solution containing the crude *N*-tosyl protected amino acid (3.7 mmol), *N*-methylmorpholine (4.08 mmol), *N,O*-dimethylhydroxylamine hydrochloride salt (4.08 mmol) was then cooled to 0 °C under an argon atmosphere and treated with *N,N*-dicyclohexylcarbodiimide (4.08 mmol). The reaction mixture was stirred at 0 °C for 3 h followed by a further 15 h at room temperature. On completion, the reaction mixture was filtered through Celite® and washed with CH₂Cl₂ (25 mL). The residue was washed with a saturated aqueous solution of NaHCO₃ (2 x 10 mL), 10% aqueous solution of citric acid (2 x 10 mL), brine (10 mL) and dried over MgSO₄. Concentrated under reduced pressure and purification of the resulting crude mixture by flash column chromatography on silica gel (eluent: *n*-hexane: EtOAc =1:1) gave the desired Weinreb amide. A solution of the Weinreb amide (2.1 mmol) in THF (6 mL) was then cooled to 0 °C under an argon atmosphere and treated with a solution of PhMgBr (7.38 mmol) in a dropwise manner over 10 min. The reaction mixture was stirred for 4 h at 0 °C followed by a further 15 h at room temperature. On completion, the reaction mixture was poured into a solution containing EtOAc (35 mL) and 3 M aqueous HCl (35 mL) and the organic layer was sequentially washed with 3 M aqueous HCl solution (2 x 30 mL), H₂O (30 mL), and brine

(30 mL), dried over MgSO_4 and concentrated under reduced pressure. Purification of the resulting crude residue by flash column chromatography on silica gel (eluent: *n*-hexane: EtOAc = 5:1) afforded the desired *N*-tosyl protected amino ketone. The resulting solid was used directly for the next step. Finally, a solution of the *N*-tosyl protected amino ketone (0.6 mmol) in THF (6 mL) was cooled to 0 °C under an argon atmosphere and treated with allyl magnesium chloride (2.0 M THF solution, 1.5 mmol) and stirred for 15 h at room temperature. On completion, the reaction mixture was treated with saturated NH_4Cl (5 mL) and extracted with EtOAc (2 x 15 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: EtOAc = 7:1) to give the title compound. For most cases, the two diastereomers obtained could be separated by flash column chromatography with the major diastereomer used for reaction.

***N*-((3*S*,4*R*)-4-Hydroxy-2-methyl-4-phenylhept-6-en-3-yl)-4-methylbenzenesulfonamide 139a**

White solid; m.p. 107-108 °C; ^1H NMR (CDCl_3 , 400 MHz): δ 0.40 (d, 3H, J = 6.9 Hz), 0.67 (d, 3H, J = 6.7 Hz), 1.39-1.48 (m, 1H), 2.34 (s, 1H), 2.41 (s, 3H), 2.63-2.74 (m, 2H), 3.65 (d, 1H, J = 9.7 Hz), 5.05-5.23 (m, 4H), 7.23-7.35 (m, 7H), 7.83 (d, 1H, J = 8.2 Hz); ^{13}C NMR (CDCl_3 , 100 MHz): δ 16.6, 21.5, 22.6, 28.4, 46.0, 65.8, 79.0, 121.0, 125.2, 126.9, 126.9, 128.5, 129.5, 132.7, 139.7, 143.0, 144.0; IR (NaCl, neat) ν : 3389, 3311, 1416, 1157 cm^{-1} ; MS (ESI) m/z 356 $[\text{M}-\text{OH}]^+$; HRMS (ESI) calcd. for $\text{C}_{21}\text{H}_{26}\text{NO}_2\text{S}$ ($\text{M}^+ - \text{OH}$): 356.1684, found: 356.1693; HPLC: (Chiralcel OJ-H, 5% *i*-PrOH/*n*-hexanes, 0.5

mL/min), t_R (minor) = 22.5 min, t_R (major) = 17.8 min; 97% ee; $[\alpha]_D^{25}$ -7.6° ($c = 1.0$, CHCl_3).

***N*-((3*S*,4*R*)-4-Hydroxy-2-methyl-4-*p*-tolylhept-6-en-3-yl)-4-methylbenzenesulfonamide 139b**

Colorless oil; ^1H NMR (CDCl_3 , 300 MHz): δ 0.41 (d, 3H, $J = 6.9$ Hz), 0.66 (d, 3H, $J = 6.7$ Hz), 1.42-1.50 (m, 1H), 2.28 (s, 1H), 2.33 (s, 3H), 2.41 (s, 3H), 2.58-2.68 (m, 2H), 3.61 (d, 1H, $J = 9.7$ Hz), 5.03-5.29 (m, 4H), 7.13-7.30 (m, 6H), 7.82 (d, 2H, $J = 8.3$ Hz); ^{13}C NMR (CDCl_3 , 75 MHz): δ 16.5, 21.0, 21.5, 22.6, 28.4, 45.9, 78.9, 120.9, 125.1, 126.8, 129.1, 129.5, 132.9, 136.4, 139.7, 140.9, 142.9; IR (NaCl, neat) ν : 3383, 3315, 1512, 1435, 1323, 1094, 1047 cm^{-1} ; MS (ESI) m/z 370 $[\text{M}-\text{OH}]^+$; HRMS (ESI) calcd. for $\text{C}_{22}\text{H}_{28}\text{NO}_2\text{S}$ (M^+-OH): 370.1841, found: 370.1841; HPLC: (Chiralcel AS-H, 5% *i*-PrOH/*n*-hexanes, 0.5 mL/min), t_R (minor) = 33.7 min, t_R (major) = 17.2 min; 99% ee; $[\alpha]_D^{25}$ -4.0° ($c = 1.0$, CHCl_3).

***N*-((3*S*,4*R*)-4-(Biphenyl-4-yl)-4-hydroxy-2-methylhept-6-en-3-yl)-4-methylbenzenesulfonamide 139c**

White solid; m.p. 140-142 °C; ^1H NMR (CDCl_3 , 400 MHz): δ 0.43 (d, 3H, $J = 6.9$ Hz), 0.69 (d, 3H, $J = 6.7$ Hz), 1.49-1.55 (m, 1H), 2.35 (s, 1H), 2.41 (s, 3H), 2.68-2.78 (m, 2H), 3.67 (d, 1H, $J = 9.6$ Hz), 5.06-5.13 (m, 3H), 5.19-5.28 (m, 1H), 7.29-7.61 (m, 11H), 7.83 (d, 1H, $J = 8.2$ Hz); ^{13}C NMR (CDCl_3 , 100 MHz): δ 16.6, 21.5, 22.7, 28.5, 46.0, 65.8, 79.0, 121.2, 125.7, 126.9, 127.1, 127.4, 128.8, 129.5, 132.7, 139.6, 140.5, 143.0, 143.1; IR (NaCl, neat) ν : 3393, 3366, 1416, 1325, 1155, 1094 cm^{-1} ; MS (ESI) m/z 432 $[\text{M}-\text{OH}]^+$; HRMS (ESI) calcd. for $\text{C}_{27}\text{H}_{30}\text{NO}_2\text{S}$ (M^+-OH): 432.1997, found: 432.1996; HPLC: (Chiralcel AS-H, 5 % *i*-PrOH/*n*-hexanes, 5 mL/min), t_R (minor) = 24.6 min, t_R (major) = 15.8 min; 98% ee; $[\alpha]_D^{25}$ -2.4° ($c = 1.0$, CHCl_3).

***N*-((2*S*,3*R*)-3-Hydroxy-3-phenylhex-5-en-2-yl)-4-methylbenzenesulfonamide 139d**

White solid; m.p. 83-85 °C; ^1H NMR (CDCl_3 , 400 MHz): δ 0.62 (d, 3H, $J = 6.7$ Hz), 2.40 (s, 3H), 2.50 (s, 1H), 2.72 (dd, 1H, $J = 5.0, 14.1$ Hz), 2.84 (dd, 1H, $J = 9.4, 14.0$ Hz), 3.60-3.68 (m, 1H), 5.05-5.16 (m, 3H), 5.28-5.40 (m, 1H), 7.22-7.33 (m, 7H), 7.80 (d, 2H, $J = 7.2$ Hz); ^{13}C NMR (CDCl_3 , 100 MHz): δ 16.2, 21.5, 44.3, 57.2, 77.8, 120.4, 125.5, 126.9, 127.0, 128.3, 129.7, 132.9, 138.5, 143.1, 143.3; IR (NaCl, neat) ν : 3389, 3323, 1447, 1332, 1161, 816 cm^{-1} ; MS (ESI) m/z 328 $[\text{M}-\text{OH}]^+$; HRMS (ESI) calcd. for $\text{C}_{19}\text{H}_{22}\text{NO}_2\text{S}$ (M^+-OH): 328.1371, found: 328.1366; HPLC: (Chiralcel OJ-H, 5% *i*-PrOH/*n*-hexanes, 0.5 mL/min), t_R (minor) = 41.6 min, t_R (major) = 30.9 min; 98% ee; $[\alpha]_D^{25}$ -5.9° ($c = 1.0$, CHCl_3).

***N*-((3*S*,4*R*)-4-Hydroxy-4-phenylhept-6-en-3-yl)-4-methylbenzenesulfonamide 139e**

White solid; m.p. 126-127 °C; ^1H NMR (CDCl_3 , 400 MHz): δ 0.41 (t, 3H, $J = 7.4$ Hz), 1.04-1.24 (m, 2H), 2.41 (s, 3H), 2.48 (s, 1H), 2.65-2.76 (m, 2H), 3.54 (dt, 1H, $J = 3.6$, 9.4 Hz), 4.72 (d, 1H, $J = 9.6$ Hz), 5.06-5.13 (m, 2H), 5.26-5.36 (m, 1H), 7.23-7.34 (m, 7H), 7.79 (d, 2H, $J = 8.2$ Hz); ^{13}C NMR (CDCl_3 , 100 MHz): δ 10.7, 21.5, 23.7, 44.9, 63.5, 78.1, 120.5, 125.5, 126.9, 127.0, 128.3, 129.5, 132.9, 139.1, 143.2, 143.4; IR (NaCl, neat) ν : 3385, 3294, 1495, 1447, 1333, 1092, 1009 cm^{-1} ; MS (ESI) m/z 342 $[\text{M}-\text{OH}]^+$; HRMS (ESI) calcd. for $\text{C}_{20}\text{H}_{24}\text{NO}_2\text{S}$ (M^+-OH): 342.1528, found: 342.1530; HPLC: (Chiralcel OJ-H, 5 % *i*-PrOH/*n*-hexanes, 0.5 mL/min), t_R (minor) = 54.1 min, t_R (major) = 24.0 min; 98% ee; $[\alpha]_D^{25}$ -15.7° ($c = 1.0$, CHCl_3).

***N*-((4*S*,5*R*)-5-Hydroxy-5-phenyloct-7-en-4-yl)-4-methylbenzenesulfonamide 139f**

White solid; m.p. 114-115 °C; ^1H NMR (CDCl_3 , 400 MHz): δ 0.49 (t, 3H, $J = 7.2$ Hz), 0.65-0.72 (m, 1H), 0.90-0.99 (m, 1H), 1.05-1.13 (m, 2H), 2.40 (s, 3H), 2.63 (s, 1H), 2.71 (d, 2H, $J = 7.7$ Hz), 3.63 (dt, 1H, $J = 4.3$, 8.0 Hz), 5.00-5.10 (m, 2H), 5.27-5.38 (m, 1H), 7.21-7.34 (m, 7H), 7.80 (d, 2H, $J = 8.2$ Hz); ^{13}C NMR (CDCl_3 , 100 MHz): δ 13.7, 19.1, 21.5, 32.8, 44.9, 61.8, 78.3, 120.2, 125.6, 126.9, 127.0, 128.3, 129.5, 133.0, 139.1, 143.1, 143.4; IR (NaCl, neat) ν : 3499, 3385, 1447, 1331, 1157, 1028 cm^{-1} ; MS (ESI) m/z 356 $[\text{M}-\text{OH}]^+$; HRMS (ESI) calcd. for $\text{C}_{21}\text{H}_{26}\text{NO}_2\text{S}$ (M^+-OH): 356.1684, found: 356.1688;

HPLC: (Chiralcel OJ-H, 5 % *i*-PrOH/*n*-hexanes, 0.5 mL/min), t_R (minor) = 30.5 min, t_R (major) = 17.7 min; 98% ee; $[\alpha]_D^{25}$ -7.8° (c = 1.0, CHCl₃).

***N*-((2*S*,3*R*)-3-Hydroxy-1,3-diphenylhex-5-en-2-yl)-4-methylbenzenesulfonamide 139g**

White solid; m.p. 159-160 °C; ¹H NMR (CDCl₃, 300 MHz): δ 2.30-2.38 (m, 4H), 2.57 (dd, 1H, J = 14.3, 3.1 Hz), 2.71 (s, 1H), 2.89 (d, 2H, J = 7.1 Hz), 4.04 (dt, 1H, J = 9.7, 3.0 Hz), 4.99 (d, 1H, J = 10.9 Hz), 5.09-5.21 (m, 2H), 5.32-5.45 (m, 1H), 6.67 (d, 2H, J = 7.1 Hz), 6.87-6.98 (m, 5H), 7.25-7.47 (m, 7H); ¹³C NMR (CDCl₃, 75 MHz): δ 21.4, 37.0, 45.1, 64.3, 78.5, 120.5, 125.6, 125.8, 126.3, 127.2, 128.2, 128.6, 129.2, 129.4, 133.0, 138.2, 138.6, 142.3, 143.5; IR (NaCl, neat) ν : 3499, 3337, 1495, 1325, 1153, 1057 cm⁻¹; MS (ESI) m/z 404 [M-OH]⁺; HRMS (ESI) calcd. for C₂₅H₂₆NO₂S (M⁺-OH): 404.1684, found: 404.1685; HPLC: (Chiralcel AS-H, 5 % *i*-PrOH/*n*-hexanes, 1 mL/min), t_R (minor) = 52.2 min, t_R (major) = 25.6 min; 97% ee; $[\alpha]_D^{25}$ -9.5° (c = 1.0, CHCl₃).

***N*-((1*S*,2*R*)-2-Hydroxy-1,2-diphenylpent-4-enyl)-4-methylbenzenesulfonamide**

139h¹²⁸

White solid; m.p. 179-180 °C; ¹H NMR (CDCl₃, 300 MHz): δ 2.24 (s, 3H), 2.51 (s, 1H), 2.96-3.09 (m, 2H), 4.55 (d, 1H, J = 7.3 Hz), 5.12 (d, 1H, J = 7.5 Hz), 5.23 (d, 1H, J = 12.8 Hz), 5.37-5.47 (m, 1H), 5.58 (d, 1H, J = 7.3 Hz), 6.59 (d, 2H, J = 7.3 Hz), 6.77-6.92 (m, 5H), 7.05-7.15 (m, 5H), 7.36 (d, 2H, J = 6.2 Hz); ¹³C NMR (CDCl₃, 75 MHz): δ 21.3,

43.8, 65.6, 78.1, 120.9, 125.9, 126.7, 126.8, 127.0, 127.2, 127.9, 128.3, 129.0, 132.8, 136.5, 137.4, 141.8, 142.6; IR (NaCl, neat) ν : 3475, 3321, 1321, 1159, 1088 cm^{-1} ; MS (ESI) m/z 390 $[\text{M}-\text{OH}]^+$; HRMS (ESI) calcd. for $\text{C}_{24}\text{H}_{24}\text{NO}_2\text{S}$ (M^+-OH): 390.1528, found: 390.1534; HPLC: (Chiralcel AS-H, 5 % *i*-PrOH/*n*-hexanes, 1 mL/min), t_R (minor) = 68.8 min, t_R (major) = 45.8 min; 94% ee; $[\alpha]_D^{25}$ -22.4° (c = 1.0, CHCl_3).

***N*-((3R,4S)-4-Hydroxy-2-methyl-4-phenylhept-6-en-3-yl)-4-methylbenzenesulfonamide 139i**

White solid; m.p. 107-108 °C; ^1H NMR (CDCl_3 , 400 MHz): δ 0.40 (d, 3H, J = 6.8 Hz), 0.65 (d, 3H, J = 6.7 Hz), 1.40-1.47 (m, 1H), 2.27 (s, 1H), 2.41 (s, 3H), 2.62-2.74 (m, 2H), 3.64 (d, 1H, J = 9.6 Hz), 4.99-5.20 (m, 4H), 7.24-7.35 (m, 7H), 7.81 (d, 1H, J = 8.1 Hz); ^{13}C NMR (CDCl_3 , 100 MHz): δ 16.6, 21.5, 22.6, 28.4, 46.0, 65.8, 79.1, 121.0, 125.2, 126.9, 126.9, 128.4, 129.5, 132.7, 139.7, 143.0, 144.0; MS (ESI) m/z 356 $[\text{M}-\text{OH}]^+$; HRMS (ESI) calcd. for $\text{C}_{21}\text{H}_{26}\text{NO}_2\text{S}$ (M^+-OH): 356.1684, found: 356.1673; HPLC: (Chiralcel OJ-H, 5 % *i*-PrOH/*n*-hexanes, 0.5 mL/min), t_R (minor) = 18.0 min, t_R (major) = 22.4 min; 91% ee; $[\alpha]_D^{25}$ +6.5° (c = 1.0, CHCl_3).

***N*-((2R,3S)-3-Hydroxy-1,3-diphenylhex-5-en-2-yl)-4-methylbenzenesulfonamide 139j**

White solid; m.p. 159-160 °C; ^1H NMR (CDCl_3 , 400 MHz): δ 2.30-2.35 (m, 4H), 2.57 (dd, 1H, J = 14.3, 3.0 Hz), 2.64 (s, 1H), 2.88 (d, 2H, J = 7.6 Hz), 4.04 (dt, 1H, J = 9.8, 3.0 Hz),

4.79 (d, 1H, $J = 9.6$ Hz), 5.12-5.22 (m, 2H), 5.33-5.43 (m, 1H), 6.68 (d, 2H, $J = 7.4$ Hz), 6.89-6.99 (m, 5H), 7.25-7.41 (m, 3H), 7.37-7.46 (m, 4H); ^{13}C NMR (CDCl_3 , 75 MHz): δ 21.4, 37.0, 45.1, 64.3, 78.5, 120.5, 125.6, 125.8, 126.3, 127.2, 128.2, 128.6, 129.2, 129.4, 133.0, 138.2, 138.6, 142.3, 143.5; IR (NaCl, neat) ν : 3499, 3337, 3026, 1495, 1325, 1153, 1057, 910 cm^{-1} ; MS (ESI) m/z 404 $[\text{M}-\text{OH}]^+$; HRMS (ESI) calcd. for $\text{C}_{25}\text{H}_{26}\text{NO}_2\text{S}$ (M^+-OH): 404.1684, found: 404.1685; HPLC: (Chiralcel AS-H, 5% *i*-PrOH/*n*-hexanes, 1 mL/min), t_R (minor) = 25.8 min, t_R (major) = 52.0 min; 96% ee; $[\alpha]_D^{25} +3.1^\circ$ ($c = 1.0$, CHCl_3).

Representative Experimental Procedure for $\text{Cu}(\text{OTf})_2$ -Catalyzed Intramolecular Hydroamination of Enantioenriched 1-(Tosylamino)pent-4-en-2-ols **139a-j**

To a solution of the enantioenriched 1-(tosylamino)pent-4-en-2-ol (0.3 mmol) in 1,2-dichloroethane (3 mL) was added $\text{Cu}(\text{OTf})_2$ (15 μmol) under an argon atmosphere. The reaction mixture was stirred at 80 $^\circ\text{C}$ and monitored to completion by TLC analysis. 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 **140**.

(2*S*,5*S*)-2-Isopropyl-5-methyl-3-phenyl-1-tosyl-2,5-dihydro-1*H*-pyrrole 140a

Brown oil; ^1H NMR (CDCl_3 , 300 MHz): δ 0.63 (d, 3H, $J = 7.2$ Hz), 0.70 (d, 3H, $J = 6.8$ Hz), 1.42 (d, 3H, $J = 6.5$ Hz), 2.41 (s, 3H), 2.64-2.72 (m, 1H), 4.60-4.68 (m, 1H), 5.24 (s, 1H), 5.71 (s, 1H), 7.27-7.30 (m, 7H), 7.77 (d, 2H, $J = 8.3$ Hz); ^{13}C NMR (CDCl_3 , 75MHz): δ 16.3, 20.2, 20.9, 21.5, 33.3, 63.1, 73.9, 126.7, 126.9, 128.0, 128.5, 129.5, 129.5, 135.7, 139.6, 140.2, 142.7; IR (NaCl, neat) ν : 2967, 1599, 1495, 1339, 1159, 814 cm^{-1} ; MS (ESI) m/z 356 $[\text{M}+\text{H}]^+$; HRMS (ESI) calcd. for $\text{C}_{21}\text{H}_{26}\text{NO}_2\text{S}$ (M^++H): 356.1684, found: 356.1687; HPLC: (Chiralcel OD-H, 3 % *i*-PrOH/*n*-hexanes, 0.3 mL/min), t_R (minor) = 32.1 min, t_R (major) = 39.7 min; 93% ee; $[\alpha]_{\text{D}}^{25} +226.0^\circ$ ($c = 1.0$, CHCl_3).

(2*S*,5*S*)-2-Isopropyl-5-methyl-3-*p*-tolyl-1-tosyl-2,5-dihydro-1*H*-pyrrole 140b

Pale-yellow oil; ^1H NMR (CDCl_3 , 400 MHz): δ 0.56 (d, 3H, $J = 7.2$ Hz), 0.62 (d, 3H, $J = 6.8$ Hz), 1.32 (d, 3H, $J = 6.5$ Hz), 2.25 (s, 3H), 2.32 (s, 3H), 2.54-2.61 (m, 1H), 4.51-4.57 (m, 1H), 5.14 (s, 1H), 5.59 (s, 1H), 7.03-7.20 (m, 6H), 7.69 (d, 2H, $J = 8.3$ Hz); ^{13}C NMR (CDCl_3 , 100 MHz): δ 16.3, 20.2, 20.9, 21.2, 21.5, 33.3, 63.0, 73.8, 126.6, 126.8, 128.7, 129.2, 129.5, 132.7, 137.9, 139.5, 140.2, 142.6; IR (NaCl, neat) ν : 2967, 1599, 1337, 1159, 818 cm^{-1} ; MS (ESI) m/z 370 $[\text{M}+\text{H}]^+$; HRMS (ESI) calcd. for $\text{C}_{22}\text{H}_{28}\text{NO}_2\text{S}$ (M^++H): 370.1841, found: 370.1848; HPLC: (Chiralcel OD-H, 3% *i*-PrOH/*n*-hexanes, 0.3 mL/min), t_R (minor) = 26.3 min, t_R (major) = 28.2 min; 97% ee; $[\alpha]_{\text{D}}^{25} +224.6^\circ$ ($c = 1.0$, CHCl_3).

(2*S*,5*S*)-3-(Biphenyl-4-yl)-2-isopropyl-5-methyl-1-tosyl-2,5-dihydro-1*H*-pyrrole 140c¹²⁸

Gray solid; m.p. 160-161°C; ¹H NMR (CDCl₃, 400 MHz): δ 0.71 (d, 3H, *J* = 7.2 Hz), 0.75 (d, 3H, *J* = 6.8 Hz), 1.44 (d, 3H, *J* = 6.5 Hz), 2.42 (s, 3H), 2.67-2.74 (m, 1H), 4.64-4.70 (m, 1H), 5.29 (dd, 1H, *J* = 2.9, 4.3 Hz), 5.78 (s, 1H), 7.29-7.47 (m, 7H), 7.56-7.61 (m, 4H), 7.80 (d, 2H, *J* = 8.2 Hz); ¹³C NMR (CDCl₃, 100 MHz): δ 16.4, 20.3, 20.9, 21.5, 33.4, 63.1, 73.8, 126.7, 127.0, 127.1, 127.3, 127.5, 128.9, 129.5, 134.5, 139.2, 140.1, 140.4, 140.8, 142.7; IR (NaCl, neat) *v*: 2970, 1599, 1487, 1337, 1159, 1060 cm⁻¹; MS (ESI) *m/z* 432 [M+H]⁺; HRMS (ESI) calcd. for C₂₇H₃₀NO₂S (M⁺+H): 432.1997, found: 432.1979; HPLC: (Chiralcel OD, 3 % *i*-PrOH/*n*-hexanes, 0.5 mL/min), *t_R* (minor) = 19.0 min, *t_R* (major) = 20.7 min; 96% ee; [α]_D²⁵ +304.0° (*c* = 1.0, CHCl₃).

(2*S*,5*S*)-2,5-Dimethyl-3-phenyl-1-tosyl-2,5-dihydro-1*H*-pyrrole 140d

Brown oil; ¹H NMR (CDCl₃, 400 MHz): δ 1.43 (d, 3H, *J* = 6.3 Hz), 1.45 (d, 3H, *J* = 6.4 Hz), 2.41 (s, 3H), 4.70-4.76 (m, 1H), 5.15-5.21 (m, 1H), 5.80 (s, 1H), 7.26-7.36 (m, 7H), 7.80 (d, 2H, *J* = 8.3 Hz); ¹³C NMR (CDCl₃, 100 MHz): δ 20.7, 21.5, 21.5, 62.2, 63.6, 125.4, 126.3, 127.0, 128.2, 128.7, 129.5, 132.9, 139.5, 141.7, 142.8; IR (NaCl, neat) *v*: 2971, 1598, 1493, 1335, 1154 cm⁻¹; MS (ESI) *m/z* 328 [M+H]⁺; HRMS (ESI) calcd. for C₁₉H₂₂NO₂S (M⁺+H): 328.1371, found: 328.1377; HPLC: (Chiralcel OJ-H, 5 % *i*-PrOH/

n-hexanes, 1 mL/min), t_R (minor) = 58.4 min, t_R (major) = 81.9 min; 96% ee; $[\alpha]_D^{25}$ +65.6° (c = 1.0, CHCl₃).

(2*S*,5*S*)-2-Ethyl-5-methyl-3-phenyl-1-tosyl-2,5-dihydro-1*H*-pyrrole 140e

Brown oil; ¹H NMR (CDCl₃, 300 MHz): δ 0.55 (t, 3H, J = 7.3 Hz), 1.43 (d, 3H, J = 6.4 Hz), 1.55-1.65 (m, 1H), 2.30-2.38 (m, 1H), 2.41 (s, 3H), 4.69-4.76 (m, 1H), 5.27 (s, 1H), 5.86 (s, 1H), 7.26-7.75 (m, 7H), 7.79 (d, 2H, J = 8.2 Hz); ¹³C NMR (CDCl₃, 75 MHz): δ 6.5, 21.4, 21.5, 24.5, 63.7, 67.9, 126.4, 126.8, 127.0, 128.2, 128.7, 129.5, 133.2, 138.8, 139.6, 142.7; IR (NaCl, neat) ν : 2970, 1599, 1495, 1338, 1162, 1121, 814, 673 cm⁻¹; MS (ESI) m/z 342 [M+H]⁺; HRMS (ESI) calcd. for C₂₀H₂₄NO₂S (M⁺+H): 342.1528, found: 342.1531; HPLC: (Chiralcel AD-H, 3 % *i*-PrOH/*n*-hexanes, 0.3 mL/min), t_R (minor) = 50.6 min, t_R (major) = 55.0 min; 97% ee; $[\alpha]_D^{25}$ +226.0° (c = 1.0, CHCl₃).

(2*S*,5*S*)-5-Methyl-3-phenyl-2-propyl-1-tosyl-2,5-dihydro-1*H*-pyrrole 140f

Brown oil; ¹H NMR (CDCl₃, 400 MHz): δ 0.61 (t, 3H, J = 7.4 Hz), 0.92-1.05 (m, 2H), 1.44 (d, 3H, J = 6.4 Hz), 1.52-1.62 (m, 1H), 2.15-2.25 (m, 1H), 2.41 (s, 3H), 4.69-4.75 (m, 1H), 5.25 (s, 1H), 5.82 (s, 1H), 7.26-7.36 (m, 7H), 7.79 (d, 2H, J = 8.2 Hz); ¹³C NMR (CDCl₃, 100 MHz): δ 13.7, 15.6, 21.4, 21.5, 33.9, 63.6, 67.5, 126.3, 126.7, 126.8, 128.2, 128.7, 129.5, 133.2, 139.3, 139.6, 142.7; IR (NaCl, neat) ν : 2960, 1599, 1337, 1161 cm⁻¹;

MS (ESI) m/z 356 $[M+H]^+$; HRMS (ESI) calcd. For $C_{21}H_{26}NO_2S$ (M^++H): 356.1684, found: 356.1688; HPLC: (Chiralcel AD-H, 3 % *i*-PrOH/*n*-hexanes, 0.3 mL/min), t_R (minor) = 46.5 min, t_R (major) = 64.5 min; 93% ee; $[\alpha]_D^{25} +240.8^\circ$ ($c = 1.0$, $CHCl_3$).

(2*S*,5*S*)-2-Benzyl-5-methyl-3-phenyl-1-tosyl-2,5-dihydro-1*H*-pyrrole 140g¹²⁸

White solid; m.p. 155-156 °C; 1H NMR ($CDCl_3$, 300 MHz): δ 1.16 (d, 3H, $J = 6.6$ Hz), 2.41(s, 3H), 2.96 (dd, 1H, $J = 13.7, 2.0$ Hz), 3.72 (dd, 1H, $J = 13.7, 4.8$ Hz), 4.00-4.07 (m, 1H), 5.48 (s, 1H), 5.60 (s, 1H), 7.07-7.18 (m, 5H), 7.25-7.38 (m, 7H), 7.82 (d, 2H, $J = 8.3$ Hz); ^{13}C NMR ($CDCl_3$, 75 MHz): δ 19.7, 21.5, 39.0, 63.5, 68.4, 126.3, 126.4, 126.6, 127.5, 127.7, 128.3, 128.9, 129.6, 130.9, 133.1, 136.3, 138.5, 140.7, 142.8; IR (NaCl, neat) ν : 3026, 1601, 1495, 1452, 1339, 1157, 1111, 1076 cm^{-1} ; MS (ESI) m/z 404 $[M+H]^+$; HRMS (ESI) calcd. for $C_{25}H_{26}NO_2S$ (M^++H): 404.1684, found: 404.1678; HPLC: (Chiralcel OD-H, 3 % *i*-PrOH/*n*-hexanes, 0.3 mL/min), t_R (minor) = 36.9 min, t_R (major) = 44.9 min; 91% ee; $[\alpha]_D^{25} +317.5^\circ$ ($c = 1.0$, $CHCl_3$).

(2*S*,5*S*)-5-Methyl-2,3-diphenyl-1-tosyl-2,5-dihydro-1*H*-pyrrole 140h

Gray solid; m.p. 123-124 °C; 1H NMR ($CDCl_3$, 300 MHz): δ 1.71 (d, 3H, $J = 6.3$ Hz), 2.30 (s, 3H), 4.72-4.79 (m, 1H), 6.07 (d, 1H, $J = 4.3$ Hz), 6.14(s, 1H), 6.91-7.23 (m, 14H); ^{13}C NMR ($CDCl_3$, 75 MHz): δ 21.4, 22.7, 62.4, 71.7, 126.3, 126.6, 126.9, 127.9, 128.0,

128.2, 128.4, 128.8, 129.2, 132.3, 137.5, 137.7, 139.7, 141.9; IR (NaCl, neat) ν : 3023, 2958, 1600, 1340, 1150 cm^{-1} ; MS (ESI) m/z 390 $[\text{M}+\text{H}]^+$; HRMS (ESI) calcd. for $\text{C}_{24}\text{H}_{24}\text{NO}_2\text{S} (\text{M}^++\text{H})$: 390.1528, found: 390.1515; HPLC: (Chiralcel OJ-H, 5% *i*-PrOH/*n*-hexanes, 1 mL/min), t_R (minor) = 38.2 min, t_R (major) = 48.5 min; 93% ee; $[\alpha]_D^{25} +58.8^\circ$ ($c = 1.0$, CHCl_3).

(2*R*,5*R*)-2-Isopropyl-5-methyl-3-phenyl-1-tosyl-2,5-dihydro-1*H*-pyrrole 140i

Brown oil; ^1H NMR (CDCl_3 , 400 MHz): δ 0.63 (d, 3H, $J = 7.2$ Hz), 0.70 (d, 3H, $J = 6.8$ Hz), 1.42 (d, 3H, $J = 6.5$ Hz), 2.41 (s, 3H), 2.66-2.71 (m, 1H), 4.61-4.67 (m, 1H), 5.24 (s, 1H), 5.71 (s, 1H), 7.27-7.32 (m, 7H), 7.77 (d, 2H, $J = 8.3$ Hz); ^{13}C NMR (CDCl_3 , 100 MHz): δ 16.3, 20.2, 20.9, 21.5, 33.3, 63.0, 73.8, 126.6, 126.9, 128.0, 128.5, 129.5, 129.5, 135.6, 139.6, 140.1, 142.6; IR (NaCl, neat) ν : 2970, 1599, 1495, 1337, 1159, 814 cm^{-1} ; MS (ESI) m/z 356 $[\text{M}+\text{H}]^+$; HRMS (ESI) calcd. for $\text{C}_{21}\text{H}_{26}\text{NO}_2\text{S} (\text{M}^++\text{H})$: 356.1684, found: 356.1672; HPLC: (Chiralcel OD-H, 3% *i*-PrOH/*n*-hexanes, 0.3 mL/min), t_R (minor) = 31.9 min, t_R (major) = 40.1 min; 91% ee; $[\alpha]_D^{25} -217.9^\circ$ ($c = 1.0$, CHCl_3).

(2*R*,5*R*)-2-Benzyl-5-methyl-3-phenyl-1-tosyl-2,5-dihydro-1*H*-pyrrole 140j¹²⁸

White solid; m.p. 155-156 $^\circ\text{C}$; ^1H NMR (CDCl_3 , 400 MHz): δ 1.16 (d, 3H, $J = 6.6$ Hz), 2.41 (s, 3H), 2.96 (dd, 1H, $J = 13.7, 2.0$ Hz), 3.72 (dd, 1H, $J = 13.7, 4.8$ Hz), 4.00-4.06 (m, 1H), 5.48 (s, 1H), 5.60 (s, 1H), 7.08-7.17 (m, 5H), 7.25-7.40 (m, 7H), 7.82 (d, 2H, $J = 8.3$

Hz); ^{13}C NMR (CDCl_3 , 100 MHz): δ 19.7, 21.5, 39.0, 63.5, 68.4, 126.3, 126.4, 126.6, 127.5, 127.7, 128.3, 128.9, 129.6, 130.9, 133.1, 136.3, 138.5, 140.7, 142.8; MS (ESI) m/z 403 $[\text{M}+\text{H}]^+$; HRMS (ESI) calcd. for $\text{C}_{25}\text{H}_{26}\text{NO}_2\text{S}$ (M^++H): 404.1684, found: 404.1679; HPLC: (Chiralcel OD-H, 3% *i*-PrOH/*n*-hexanes, 0.3 mL/min), t_{R} (minor) = 37.1 min, t_{R} (major) = 46.9 min; 96% ee; $[\alpha]_{\text{D}}^{25}$ -345.3° (c = 1.0, CHCl_3).

General Procedure for the Preparation of 1-(2-(Tosylamino)phenyl)but-3-en-1-ols

141a, 141c, 141e, 141g-j, 141m and 141o

At room temperature, *p*-toluenesulfonyl chloride (1.5 mmol) was added to a solution containing the 1-(2-aminophenyl)ketone (1 mmol) in pyridine (1 mL) under a nitrogen atmosphere and stirred for 10-20 h. On completion, the reaction mixture was quenched by adding H_2O (10 mL), filtered, washed with H_2O (3 x 10 mL) and 10% EA in Hex (10 mL), then was dried under reduced pressure. A THF (6 mL) solution containing the crude solid (0.6 mmol) was then treated with a solution of allyl magnesium chloride (2.0 M THF solution, 1.5 mmol) at room temperature (note: 2-methylallyl magnesium bromide 1.0 M THF solution, 1.5 mmol was used for (**1y**)). The resulting reaction mixture was then stirred for 15 h at room temperature, treated with saturated NH_4Cl (5 mL) and extracted with EtOAc (2 x 15 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: EtOAc = 7:1) to give the title compound.

Procedure for the Preparation of 1-(2-(Tosylamino)phenyl)but-3-en-1-ols **141b, **141d**, **141f**, **141k**, **141l** and **141n**.**

1-(2-(Tosylamino)phenyl)but-3-en-1-ols **141b**, **141d**, **141f**, **141k**, **141l** and **141n** were prepared following literature procedures.^{142,143} This involved adding the anthranilic acid (2 mmol) to a stirred solution of Na₂CO₃ (4.8 mmol) in H₂O (5 mL) heated to 60 °C. The resulting reaction mixture was treated with *p*-toluenesulfonyl chloride (2.42 mmol) and stirred at 70 °C, and stirred for 30 min. The temperature was then raised to 85 °C and the reaction mixture was vacuum filtered while hot. The resulting filtrate was treated with 6 M HCl (1.02 mL) and allowed to cool. The precipitate obtained was isolated by filtration, sequentially washed with 1 M HCl (2 x 10 mL) and H₂O (4 x 10 mL), and dried under vacuum. This afforded the *N*-tosyl protected anthranilic acid adduct, which was used directly for the next step. A CH₂Cl₂ (6 mL) solution containing the *N*-tosyl anthranilic acid (1.5 mmol), *N*-methylmorpholine (1.632 mmol), *N,O*-dimethylhydroxylamine hydrochloride salt (1.632 mmol) was cooled to 0 °C under an argon atmosphere and

treated with *N,N*-dicyclohexylcarbodiimide (1.632 mmol). The reaction mixture was stirred at room temperature for 15 h, filtered through Celite® and washed with CH₂Cl₂ (15 mL). The furnished crude mixture was sequentially washed with a saturated aqueous solution of NaHCO₃ (2 x 10 mL), 10% aqueous citric acid solution (2 x 10 mL) and brine (10 mL) and dried over MgSO₄. Removal of the solvent under reduced pressure and purification of the residue obtained by flash column chromatography on silica gel (eluent: *n*-hexane: EtOAc =1:1) afforded the desired Weinreb amide. A solution of the Weinreb amide (1 mmol) in THF (5 mL) was then cooled to 0 °C under an argon atmosphere and treated with a solution of R⁶MgBr (3.5 mmol) (note: PhC ≡ CLi was used for (**1v**)) in a dropwise manner over 5 min and then stirred at room temperature for 15 h. The reaction mixture was then poured into a solution containing EtOAc (20 mL) and 3 M aqueous HCl (20 mL) and the organic layer was sequentially washed with 3 M aqueous solution of HCl (2 x 15 mL), H₂O (15 mL), brine (15 mL) and dried over MgSO₄. Concentration under reduced pressure and purification by flash column chromatography on silica gel (eluent: *n*-hexane: EtOAc =5:1) gave the desired *N*-tosyl protected amino ketone. Finally, a solution containing the *N*-tosyl protected amino ketone (0.5 mmol) in THF (6 mL) was cooled to 0 °C under an argon atmosphere and treated with allyl magnesium chloride (2.0 M THF solution, 1.5 mmol). The resulting reaction mixture was stirred for 15 h at room temperature, treated with saturated NH₄Cl (5 mL) and extracted with EtOAc (2 x 15 mL). The combined organic layers were washed with brine (10 mL), dried over MgSO₄, concentrated under reduced pressure and purified by flash column chromatography on silica gel (eluent: *n*-hexane: EtOAc = 7:1) to give the title compound.

Procedure for the Preparation of 1-(2-(Tosylamino)phenyl)but-3-en-1-ol 141p

Grubbs II (0.03 mmol) was added to a mixture of *N*-(2-(1-hydroxy-1-phenylbut-3-enyl)phenyl)-4-methylbenzenesulfonamide **141a** (0.60 mmol), allyl benzene (1.2 mmol) in CH₂Cl₂ (8 mL) under a nitrogen atmosphere. The reaction mixture was heated at reflux for 24 h. On completion, the reaction mixture was cooled to room temperature and the solvent was removed under reduced pressure. The crude product was purified by flash chromatography on silica gel (*n*-hexane/EtOAc = 5:1) to give the title compound.

***N*-(2-(1-Hydroxy-1-phenylbut-3-enyl)phenyl)-4-methylbenzenesulfonamide 141a**

Colourless solid; m.p. 124-125 °C; ¹H NMR (CDCl₃, 400 MHz): δ 2.28 (s, 3H), 2.78 (dd, 1H, *J* = 14.0, 7.5 Hz), 3.05 (dd, 1H, *J* = 14.0, 6.9 Hz), 3.21 (s, 1H), 5.23-5.27 (m, 2H), 5.61-5.72 (m, 1H), 6.93-7.01 (m, 3H), 7.12-7.32 (m, 9H), 7.56 (d, 1H, *J* = 8.2 Hz), 9.13 (s, 1H); ¹³C NMR (CDCl₃, 100 MHz): δ 21.5, 47.6, 78.2, 119.1, 122.0, 122.6, 125.5, 127.2, 127.2, 127.3, 128.4, 128.8, 129.3, 132.0, 132.3, 136.2, 137.0, 143.1, 144.7; IR (NaCl, neat) *v*: 3499, 3271, 1493, 1387, 1327, 1088 cm⁻¹; MS (ESI) *m/z* 376 [M-OH]⁺; HRMS (ESI) calcd. for C₂₃H₂₂NO₂S (M⁺-OH): 376.1371, found: 376.1365.

***N*-(2-(1-Hydroxy-1-phenylbut-3-enyl)-4-methylphenyl)-4-methylbenzenesulfonamide 141b**

Colourless solid; m.p. 126-128 °C; ^1H NMR (CDCl_3 , 400 MHz): δ 2.28 (s, 3H), 2.29 (s, 3H), 2.40 (s, 3H), 2.77 (dd, 1H, $J = 14.0, 7.5$ Hz), 3.03 (dd, 1H, $J = 14.0, 6.9$ Hz), 3.11 (s, 1H), 5.23-5.26 (m, 2H), 5.61-5.71 (m, 1H), 6.93-6.99 (m, 3H), 7.10-7.25 (m, 8H), 7.46 (d, 1H, $J = 8.3$ Hz), 8.96 (s, 1H); ^{13}C NMR (CDCl_3 , 100 MHz): δ 21.0, 21.5, 47.7, 78.1, 119.3, 122.0, 125.5, 127.1, 127.2, 127.9, 128.4, 129.2, 129.3, 132.0, 132.4, 134.4, 136.3, 142.9, 144.8; IR (NaCl, neat) ν : 3432, 3331, 1509, 1332, 808 cm^{-1} ; MS (ESI) m/z 390 $[\text{M}-\text{OH}]^+$; HRMS (ESI) calcd. for $\text{C}_{24}\text{H}_{24}\text{NO}_2\text{S}$ (M^+-OH): 390.1528, found: 390.1525.

***N*-(2-(1-Hydroxy-1-phenylbut-3-enyl)-4-methoxyphenyl)-4-methylbenzenesulfonamide 141c**

Colourless solid; m.p. 148-150 °C; ^1H NMR (CDCl_3 , 400 MHz): δ 2.30 (s, 3H), 2.74 (dd, 1H, $J = 14.1, 7.4$ Hz), 2.97 (dd, 1H, $J = 14.0, 6.9$ Hz), 3.13 (s, 1H), 3.74 (s, 3H), 5.21-5.24 (m, 2H), 5.59-5.69 (m, 1H), 6.70-6.73 (m, 1H), 6.85 (d, 1H, $J = 2.8$ Hz), 6.96 (s, 2H, $J = 8.1$ Hz), 7.16-7.26 (m, 7H), 7.52 (d, 1H, $J = 8.9$ Hz), 8.76 (s, 1H); ^{13}C NMR (CDCl_3 , 100 MHz): δ 21.5, 47.6, 55.5, 78.1, 112.2, 114.7, 121.2, 121.9, 125.5, 127.2, 127.2, 128.4, 129.3, 130.0, 132.3, 134.3, 136.3, 142.9, 144.4, 155.1; IR (NaCl, neat) ν : 3492, 3341, 1597, 1333, 1217, 1090 cm^{-1} ; MS (ESI) m/z 406 $[\text{M}-\text{OH}]^+$; HRMS (ESI) calcd. for $\text{C}_{24}\text{H}_{24}\text{NO}_3\text{S}$ (M^+-OH): 406.1477, found: 406.1472.

***N*-(4-Bromo-2-(1-hydroxy-1-phenylbut-3-enyl)phenyl)-4-methylbenzenesulfonamide
141d**

Colourless solid; m.p. 131-133 °C; ^1H NMR (CDCl_3 , 400 MHz): δ 2.39 (s, 3H), 2.78 (dd, 1H, $J = 14.0, 7.3$ Hz), 2.98 (dd, 1H, $J = 14.0, 7.0$ Hz), 3.37 (s, 1H), 5.22-5.26 (m, 2H), 5.59-5.67 (m, 1H), 6.95 (d, 2H, $J = 8.2$ Hz), 7.08 (d, 2H, $J = 8.2$ Hz), 7.18-7.44 (m, 8H), 9.08 (s, 1H); ^{13}C NMR (CDCl_3 , 100 MHz): δ 21.5, 47.5, 77.8, 115.6, 120.5, 122.3, 125.4, 127.2, 127.4, 128.5, 129.4, 130.1, 131.5, 131.7, 134.3, 135.7, 136.1, 143.4, 143.9; IR (NaCl, neat) ν : 3418, 3237, 1643, 1597, 1483, 1315, 1153 cm^{-1} ; MS (ESI) m/z 454 $[\text{M}-\text{OH}]^+$; HRMS (ESI) calcd. for $\text{C}_{23}\text{H}_{21}\text{NO}_2\text{S}^{79}\text{Br}$ (M^+-OH): 454.0476, found: 454.0472.

***N*-(2-(1-Hydroxy-1-phenylbut-3-enyl)-5-methylphenyl)-4-methylbenzenesulfonamide 141e**

Colourless solid; m.p. 153-155 °C; ^1H NMR (CDCl_3 , 400 MHz): δ 2.25 (s, 3H), 2.30 (s, 3H), 2.74 (dd, 1H, $J = 14.0, 7.6$ Hz), 3.01-3.06 (m, 2H), 5.24-5.28 (m, 2H), 5.62-5.73 (m, 1H), 6.81 (d, 1H, $J = 7.9$ Hz), 6.96 (d, 2H, $J = 8.1$ Hz), 7.13-7.26 (m, 8H), 7.39 (s, 1H), 9.04 (s, 1H); ^{13}C NMR (CDCl_3 , 100 MHz): δ 21.2, 21.5, 47.7, 78.0, 119.8, 122.1, 123.3, 125.4, 127.1, 127.2, 128.4, 129.3, 132.4, 136.8, 138.8, 143.0, 144.9; IR (NaCl, neat) ν : 3444, 3319, 1508, 1395, 1333, 1159, 812 cm^{-1} ; MS (ESI) m/z 390 $[\text{M}-\text{OH}]^+$; HRMS (ESI) calcd. for $\text{C}_{24}\text{H}_{24}\text{NO}_2\text{S}$ (M^+-OH): 390.1528, found: 390.1523.

***N*-(2-(1-hydroxy-1-phenylbut-3-enyl)-6-methoxyphenyl)-4-methylbenzenesulfonamide 141f**

Colorless oil; ^1H NMR (CDCl_3 , 500 MHz): δ 2.41 (s, 3H), 3.02 (dd, 1H, $J = 14.2, 6.7$ Hz), 3.22 (s, 3H), 3.29 (dd, 1H, $J = 14.0, 7.6$ Hz), 3.47 (s, 1H), 5.27 (d, 1H, $J = 10.2$ Hz), 5.38 (d, 1H, $J = 16.9$ Hz), 5.71-5.79 (m, 1H), 6.75 (d, 1H, $J = 8.1$ Hz), 6.91 (d, 1H, $J = 7.9$ Hz), 7.08 (t, 1H, $J = 8.1$ Hz), 7.24-7.44 (m, 7H), 7.72 (d, 2H, $J = 8.2$ Hz), 8.21 (s, 1H); ^{13}C NMR (CDCl_3 , 125 MHz): δ 21.5, 46.6, 54.6, 78.3, 111.5, 119.9, 121.8, 125.5, 126.3, 126.6, 127.4, 128.2, 128.7, 132.8, 139.5, 140.4, 142.0, 144.7, 154.2; IR (NaCl, neat) ν : 3458, 3256, 1458, 1327, 1153, 1092 cm^{-1} ; MS (ESI) m/z 406 $[\text{M}-\text{OH}]^+$; HRMS (ESI) calcd. for $\text{C}_{24}\text{H}_{24}\text{NO}_3\text{S}$ (M^+-OH): 406.1477, found: 406.1472.

***N*-(2-(1-Hydroxy-1-p-tolylbut-3-enyl)phenyl)-4-methylbenzenesulfonamide 141g**

Colourless solid; m.p. 141-143 $^{\circ}\text{C}$; ^1H NMR (CDCl_3 , 400 MHz): δ 2.30 (s, 3H), 2.36 (s, 3H), 2.76 (dd, 1H, $J = 14.1, 7.5$ Hz), 3.02 (dd, 1H, $J = 14.0, 7.0$ Hz), 3.10 (s, 1H), 5.23-5.27 (m, 2H), 5.62-5.72 (m, 1H), 6.94-7.08 (m, 7H), 7.15-7.29 (m, 4H), 7.60 (d, 1H, $J = 8.2$ Hz), 9.11 (s, 1H); ^{13}C NMR (CDCl_3 , 100 MHz): δ 21.1, 21.5, 47.6, 78.1, 119.2, 122.0, 122.6, 125.4, 127.2, 127.3, 127.3, 128.7, 129.0, 129.1, 132.2, 132.5, 136.3, 136.8, 137.0,

141.7, 143.0; IR (NaCl, neat) ν : 3524, 3445, 1337, 1159, 1087 cm^{-1} ; MS (ESI) m/z 390 $[\text{M}-\text{OH}]^+$; HRMS (ESI) calcd. for $\text{C}_{24}\text{H}_{24}\text{NO}_2\text{S}$ (M^+-OH): 390.1528, found: 390.1516.

***N*-(2-(1-(4-Chlorophenyl)-1-hydroxybut-3-enyl)phenyl)-4-methylbenzenesulfonamide 141h**

Colourless solid; m.p. 116-117 $^{\circ}\text{C}$; ^1H NMR (CDCl_3 , 400 MHz): δ 2.32 (s, 3H), 2.67 (dd, 1H, $J = 13.8, 7.9$ Hz), 3.04 (dd, 1H, $J = 13.9, 6.0$ Hz), 3.31 (s, 1H), 5.18-5.27 (m, 2H), 5.62-5.72 (m, 1H), 6.97-7.34 (m, 11H), 7.73 (d, 1H, $J = 8.1$ Hz), 9.04 (s, 1H); ^{13}C NMR (CDCl_3 , 100 MHz): δ 21.5, 47.8, 77.8, 119.6, 122.4, 122.9, 126.7, 126.8, 127.2, 128.3, 129.1, 129.2, 131.7, 131.9, 133.1, 136.2, 137.1, 143.2, 143.4; IR (NaCl, neat) ν : 3418, 3242, 1599, 1493, 1400, 1159, 1092 cm^{-1} ; MS (ESI) m/z 410 $[\text{M}-\text{OH}]^+$; HRMS (ESI) calcd. for $\text{C}_{23}\text{H}_{21}\text{NO}_2\text{S}^{35}\text{Cl}$ (M^+-OH): 410.0982, found: 410.0976.

***N*-(2-(1-(4-Bromophenyl)-1-hydroxybut-3-enyl)phenyl)-4-methylbenzenesulfonamide 141i**

Colourless solid; m.p. 133-134 $^{\circ}\text{C}$; ^1H NMR (CDCl_3 , 400 MHz): δ 2.34 (s, 3H), 2.65 (dd, 1H, $J = 14.1, 8.0$ Hz), 3.05 (dd, 1H, $J = 14.1, 6.5$ Hz), 3.17 (s, 1H), 5.25-5.30 (m, 2H), 5.63-5.73 (m, 1H), 6.98-7.07 (m, 5H), 7.14 (d, 2H, $J = 8.2$ Hz), 7.23-7.34 (m, 4H), 7.75

(d, 1H, $J = 8.1\text{Hz}$), 9.00 (s, 1H); ^{13}C NMR (CDCl_3 , 100 MHz): δ 21.5, 47.8, 77.8, 119.7, 121.4, 122.6, 122.8, 126.8, 127.1, 127.1, 129.1, 129.3, 131.3, 131.4, 131.9, 136.2, 137.2, 143.2, 143.9; IR (NaCl, neat) ν : 3526, 3283, 1491, 1396, 1337, 1157, 1091 cm^{-1} ; MS (ESI) m/z 454 $[\text{M-OH}]^+$; HRMS (ESI) calcd. for $\text{C}_{23}\text{H}_{21}\text{NO}_2\text{S}^{79}\text{Br}$ (M^+-OH): 454.0476, found: 454.0453.

***N*-(2-(2-Hydroxypent-4-en-2-yl)phenyl)-4-methylbenzenesulfonamide 141j**

Colourless oil; ^1H NMR (CDCl_3 , 400 MHz): δ 1.45 (s, 3H), 2.32-2.37 (m, 4H), 2.54 (dd, 1H, $J = 14.0, 7.2\text{ Hz}$), 2.85 (s, 1H), 5.00-5.09 (m, 2H), 5.49-5.59 (m, 1H), 6.97-7.21 (m, 5H), 7.59 (d, 1H, $J = 8.2\text{ Hz}$), 7.72 (d, 1H, $J = 8.2\text{ Hz}$), 9.88 (s, 1H); ^{13}C NMR (CDCl_3 , 100 MHz): δ 21.5, 28.9, 46.8, 76.7, 120.2, 120.3, 123.4, 126.8, 127.2, 128.2, 129.6, 132.7, 133.3, 136.5, 137.1, 143.6; IR (NaCl, neat) ν : 3546, 3277, 1599, 1496, 1337, 1042 cm^{-1} ; MS (ESI) m/z 314 $[\text{M-OH}]^+$; HRMS (ESI) calcd. for $\text{C}_{18}\text{H}_{20}\text{NO}_2\text{S}$ (M^+-OH): 314.1215, found: 314.1218.

***N*-(2-(1-Cyclopropyl-1-hydroxybut-3-enyl)-4-methylphenyl)-4-methylbenzenesulfonamide 141k**

Colourless solid; m.p. 141-142 $^{\circ}\text{C}$; ^1H NMR (CDCl_3 , 400 MHz): δ 0.15-0.22 (m, 1H), 0.33-0.51 (m, 3H), 1.20-1.27 (m, 1H), 2.25 (s, 3H), 2.35-2.43 (m, 5H), 2.58 (dd, 1H, $J =$

13.9, 7.6 Hz), 5.04-5.08 (m, 2H), 5.51-5.61 (m, 1H), 6.97(d, 1H, $J = 8.3$ Hz), 7.02 (s, 1H), 7.20 (d, 2H, $J = 8.1$ Hz), 7.46 (d, 1H, $J = 8.3$ Hz), 7.70 (d, 1H, $J = 8.2$ Hz), 9.63 (s, 1H); ^{13}C NMR (CDCl_3 , 100 MHz): δ 0.82, 2.30, 21.0, 21.3, 21.5, 46.6, 77.4, 120.3, 120.4, 127.2, 128.3, 128.7, 129.5, 132.0, 132.8, 134.4, 137.2, 143.4; IR (NaCl, neat) ν : 3447. 3225, 1501, 1333, 1161 cm^{-1} ; MS (ESI) m/z 354 $[\text{M}-\text{OH}]^+$; HRMS (ESI) calcd. for $\text{C}_{21}\text{H}_{24}\text{NO}_2\text{S}$ (M^+-OH): 354.1528, found: 342.1517.

***N*-(2-(3-hydroxy-1-phenylhex-5-en-1-yn-3-yl)-4-methylphenyl)-4-methylbenzenesulfonamide 1411**

Yellow oil; ^1H NMR (CDCl_3 , 400 MHz): δ 2.27 (s, 3H), 2.34 (s, 3H), 2.53 (d, 2H, $J = 7.2$ Hz), 3.27 (s, 1H), 5.09 (d, 1H, $J = 17.1$ Hz), 5.20 (d, 1H, $J = 9.9$ Hz), 5.78-5.89 (m, 1H), 7.04 (d, 1H, $J = 8.2$ Hz), 7.20 (d, 2H, $J = 8.1$ Hz), 7.30-7.51 (m, 9H), 7.76 (d, 2H, $J = 8.2$ Hz), 9.07 (s, 1H); ^{13}C NMR (CDCl_3 , 100 MHz): δ 20.9, 21.5, 47.5, 74.6, 88.0, 89.5, 120.5, 120.8, 121.9, 127.2, 128.4, 128.9, 129.0, 129.7, 130.1, 131.8, 132.2, 133.1, 133.1, 137.3, 143.6; IR (NaCl, neat) ν : 3511, 3278, 2183, 1620, 1597, 1393, 1256, 1090 cm^{-1} ; MS (ESI) m/z 414 $[\text{M}-\text{OH}]^+$; HRMS (ESI) calcd. for $\text{C}_{26}\text{H}_{24}\text{NO}_2\text{S}$ (M^+-OH): 414.1528, found: 414.1520.

***N*-(9-Allyl-9-hydroxy-9*H*-fluoren-1-yl)-4-methylbenzenesulfonamide 141m**

Colourless solid; m.p. 145-146 °C; ^1H NMR (CDCl_3 , 500 MHz): δ 2.34 (s, 3H), 2.41 (s, 1H), 2.55 (dd, 1H, $J = 13.4, 7.0$ Hz), 2.75 (dd, 1H, $J = 13.4, 7.5$ Hz), 4.59 (d, 1H, $J = 17.0$ Hz), 4.68 (d, 1H, $J = 10.2$ Hz), 4.92-5.01 (m, 1H), 7.22-7.52 (m, 8H), 7.15-7.80 (m, 3H); ^{13}C NMR (CDCl_3 , 100 MHz): δ 21.5, 42.5, 83.1, 115.8, 118.3, 119.0, 120.2, 123.3, 127.2, 128.0, 129.2, 129.8, 130.4, 131.3, 134.8, 135.0, 136.7, 138.9, 140.4, 144.1, 147.2; IR (NaCl, neat) ν : 3462, 3291, 1643, 1454, 1329, 1163, 1041 cm^{-1} ; MS (ESI) m/z 374 $[\text{M}-\text{OH}]^+$; HRMS (ESI) calcd. for $\text{C}_{23}\text{H}_{20}\text{NO}_2\text{S}$ (M^+-OH): 374.1215, found: 374.1219.

***N*-(3-(1-Hydroxy-1-phenylbut-3-enyl)naphthalen-2-yl)-4-methylbenzenesulfonamide 141n**

Colourless solid; m.p. 163-165 °C; ^1H NMR (CDCl_3 , 400 MHz): δ 2.20 (s, 3H), 2.90 (dd, 1H, $J = 14.0, 7.4$ Hz), 3.22 (dd, 1H, $J = 13.9, 6.9$ Hz), 3.46 (s, 1H), 5.24-5.29 (m, 2H), 5.67-5.77 (m, 1H), 6.84 (d, 2H, $J = 8.1$ Hz), 7.05 (d, 2H, $J = 8.1$ Hz), 7.23-7.42 (m, 7H), 7.64 (d, 1H, $J = 8.0$ Hz), 7.73 (d, 1H, $J = 7.8$ Hz), 7.81 (s, 1H), 7.89 (s, 1H), 9.19 (s, 1H); ^{13}C NMR (CDCl_3 , 100 MHz): δ 21.4, 47.9, 78.1, 115.3, 122.0, 125.1, 125.5, 126.7, 127.0, 127.0, 127.2, 127.4, 127.9, 128.5, 128.9, 129.3, 132.3, 132.4, 133.2, 134.6, 135.7, 143.2, 144.4; IR (NaCl, neat) ν : 3431, 3256, 1487, 1341, 1387, 1092 cm^{-1} ; MS (ESI) m/z 426 $[\text{M}-\text{OH}]^+$; HRMS (ESI) calcd. for $\text{C}_{27}\text{H}_{24}\text{NO}_2\text{S}$ (M^+-OH): 426.1528, found: 426.1523.

***N*-(2-(1-Hydroxy-3-methyl-1-phenylbut-3-enyl)phenyl)-4-methylbenzenesulfonamide 141o**

Colourless solid; m.p. 119-120 °C; ^1H NMR (CDCl_3 , 400 MHz): δ 1.27 (s, 3H), 2.28 (s, 3H), 2.92 (d, 1H, $J = 11.0$ Hz), 3.04 (d, 1H, $J = 11.0$ Hz), 3.57 (s, 1H), 4.77 (s, 1H), 5.03 (s, 1H), 6.93-7.01 (m, 3H), 7.13-7.17 (m, 3H), 7.23-7.26 (m, 5H), 7.37 (d, 1H, $J = 6.3$ Hz), 7.52 (d, 1H, $J = 6.6$ Hz), 9.07 (s, 1H); ^{13}C NMR (CDCl_3 , 100 MHz): δ 21.5, 24.3, 50.5, 77.0, 117.5, 118.9, 122.4, 125.5, 126.8, 127.1, 127.3, 128.4, 128.7, 129.3, 132.5, 136.2, 136.6, 141.4, 143.0, 144.8; IR (NaCl, neat) ν : 3501, 3296, 1599, 1495, 1398, 1335, 1092 cm^{-1} ; MS (ESI) m/z 390 $[\text{M}-\text{OH}]^+$; HRMS (ESI) calcd. for $\text{C}_{24}\text{H}_{24}\text{NO}_2\text{S}$ (M^+-OH): 390.1528, found: 390.1508.

***(E)*-N-(2-(1-hydroxy-1,5-diphenylpent-3-enyl)phenyl)-4-methylbenzenesulfonamide 141p**

Pale-yellow oil; ^1H NMR (CDCl_3 , 400 MHz): δ 2.26 (s, 3H), 2.75 (dd, 1H, $J = 14.0$, 7.6 Hz), 3.00 (dd, 1H, $J = 14.1$, 6.8 Hz), 3.21 (s, 1H), 3.31 (d, 2H, $J = 6.8$ Hz), 5.35-5.43 (m, 1H), 5.73-5.80 (m, 1H), 6.91-7.31 (m, 17H), 7.56 (d, 1H, $J = 8.2$ Hz), 9.14 (s, 1H); ^{13}C NMR (CDCl_3 , 100 MHz): δ 21.5, 39.2, 46.4, 78.3, 119.0, 122.6, 124.9, 125.5, 126.3, 127.1, 127.3, 127.3, 128.4, 128.6, 128.7, 129.3, 132.1, 136.2, 136.9, 137.0, 139.9, 143.1, 144.8; IR (NaCl, neat) ν : 3466, 3265, 3016, 1599, 1496, 1333, 1217, 935 cm^{-1} ; MS (ESI)

m/z 466 $[M-OH]^+$; HRMS (ESI) calcd. for $C_{30}H_{28}NO_2S$ (M^+-OH): 466.1841, found: 486.1836.

General Procedure for $Cu(OTf)_2$ -Catalyzed Intramolecular Hydroamination of 1-(2-(Tosylamino)phenyl)but-3-en-1-ols **141a-p**

To a solution of 1-(2-(tosylamino)phenyl)but-3-en-1-ol **141** (0.3 mmol) in 1,2-dichloroethane (3 mL) was added $Cu(OTf)_2$ (15 μ mol) under atmospheric conditions. The reaction mixture was stirred at 80 °C and monitored to completion by TLC analysis. The reaction mixture then cooled and the solvent was removed under reduced pressure. Purification by flash column chromatography on silica gel (*n*-hexane/ EtOAc = 7:1 as eluent) gave the product **142**.

2-Methyl-4-phenyl-1-tosyl-1,2-dihydroquinoline **142a**

Colourless solid; m.p. 162-163 °C; 1H NMR ($CDCl_3$, 500 MHz): δ 1.20 (d, 3H, J = 6.9 Hz), 2.27 (s, 3H), 5.08-5.14 (m, 1H), 5.62 (d, 1H, J = 6.0 Hz), 6.72 (d, 2H, J = 5.9 Hz), 6.86 (d, 1H, J = 7.7 Hz), 7.02 (d, 2H, J = 8.0 Hz), 7.12 (t, 1H, J = 7.5 Hz), 7.23-7.34 (m, 6H), 7.81 (d, 1H, J = 8.0 Hz); ^{13}C NMR ($CDCl_3$, 125 MHz): δ 19.3, 21.4, 50.8, 125.8, 126.5, 127.5, 127.5, 128.0, 128.2, 128.8, 129.0, 129.9, 133.0, 135.9, 136.4, 138.2, 143.3; IR (NaCl, neat) ν : 3018, 1477, 1341, 1084, 813 cm^{-1} ; MS (ESI) m/z 398 $[M+Na]^+$; HRMS (ESI) calcd. for $C_{23}H_{21}NO_2SNa$ ($M^+ + Na$): 398.1191, found: 398.1192.

2,6-Dimethyl-4-phenyl-1-tosyl-1,2-dihydroquinoline 142b

Colourless solid; m.p. 158-160 °C; ^1H NMR (CDCl_3 , 300 MHz): δ 1.19 (d, 3H, J = 6.9 Hz), 2.23 (s, 3H), 2.27 (s, 3H), 5.03-5.11(m, 1H), 5.68 (d, 1H, J = 6.0 Hz), 6.64 (s, 1H), 6.71-6.74 (m, 2H), 7.02 (d, 2H, J = 8.1Hz), 7.14 (d, 1H, J = 6.8 Hz), 7.15-7.32 (m, 5H), 7.68 (d, 1H, J = 8.1Hz); ^{13}C NMR (CDCl_3 , 75 MHz): δ 19.2, 21.2, 21.4, 50.7, 126.2, 127.5, 127.5, 128.0, 128.6, 128.7, 129.0, 129.6, 130.4, 135.9, 136.3, 136.5, 138.4, 143.2; IR (NaCl, neat) ν : 3021, 1485, 1342, 1167, 1038, 885 cm^{-1} ; MS (ESI) m/z 390 $[\text{M}+1]^+$; HRMS (ESI) calcd. for $\text{C}_{24}\text{H}_{24}\text{NO}_2\text{S}$ (M^++H): 390.1528, found: 390.1521.

6-Methoxy-2-methyl-4-phenyl-1-tosyl-1,2-dihydroquinoline 142c¹²⁸

Colourless solid; m.p. 146-147 °C; ^1H NMR (CDCl_3 , 300 MHz): δ 1.12 (d, 3H, J = 6.9 Hz), 2.27 (s, 3H), 3.69 (s, 3H), 5.03-5.12 (m, 1H), 5.61(d, 1H, J = 5.9 Hz), 6.38 (d, 1H, J = 2.9 Hz), 6.69-6.72 (m, 2H), 6.88 (dd, 1H, J = 8.8, 2.9 Hz), 7.02 (d, 2H, J = 8.0 Hz), 7.73 (d, 1H, J = 8.8 Hz); ^{13}C NMR (CDCl_3 , 75 MHz): δ 19.2, 21.4, 50.8, 55.4, 111.5, 113.0, 125.8, 127.6, 128.0, 128.1, 128.6, 129.1, 130.1, 131.0, 135.8, 136.4, 138.1, 143.2, 157.9; IR (NaCl, neat) ν : 3019, 1485, 1341, 1092 cm^{-1} ; MS (ESI) m/z 428 $[\text{M}+\text{Na}]^+$; HRMS (ESI) calcd. for $\text{C}_{24}\text{H}_{23}\text{NO}_3\text{SNa}$ (M^++Na): 428.1296, found: 428.1288.

6-Bromo-2-methyl-4-phenyl-1-tosyl-1,2-dihydroquinoline 142d

Colourless solid; m.p. 143-145 °C; ^1H NMR (CDCl_3 , 500 MHz): δ 1.19 (d, 3H, $J = 6.9$ Hz), 2.29 (s, 3H), 5.06-5.15 (m, 1H), 5.65 (d, 1H, $J = 6.0$ Hz), 6.69-6.72 (m, 2H), 6.98 (d, 1H, $J = 2.3$ Hz), 7.06 (d, 2H, $J = 8.1$ Hz), 7.23-7.33 (m, 5H), 7.45 (dd, 1H, $J = 2.3$, 8.6 Hz), 7.69 (d, 1H, $J = 8.6$ Hz); ^{13}C NMR (CDCl_3 , 125 MHz): δ 19.3, 21.4, 50.8, 120.2, 127.4, 127.9, 128.2, 128.5, 128.8, 129.2, 130.4, 131.1, 131.6, 132.1, 135.6, 135.7, 137.4, 143.6; IR (NaCl, neat) ν : 3019, 1474, 1339, 1167, 808 cm^{-1} ; MS (ESI) m/z 454 $[\text{M}+1]^+$; HRMS (ESI) calcd. for $\text{C}_{23}\text{H}_{21}\text{NO}_2\text{S}^{79}\text{Br}$ (M^++H): 454.0476, found: 454.0492.

2,7-Dimethyl-4-phenyl-1-tosyl-1,2-dihydroquinoline 142e

Colourless solid; m.p. 139-140 °C; ^1H NMR (CDCl_3 , 500 MHz): δ 1.19 (d, 3H, $J = 6.9$ Hz), 2.26 (s, 3H), 2.41(s, 3H), 5.04-5.11 (m, 1H), 5.54 (d, 1H, $J = 6.0$ Hz), 6.71-6.75 (m, 3H), 6.93 (d, 1H, $J = 7.8$ Hz), 7.01 (d, 1H, $J = 8.0$ Hz), 7.20-7.31 (m, 5H), 7.63 (s, 1H); ^{13}C NMR (CDCl_3 , 125 MHz): δ 19.3, 21.4, 21.5, 50.8, 125.6, 126.3, 127.2, 127.3, 127.5, 127.5, 127.9, 128.6, 129.0, 129.3, 132.9, 135.9, 136.3, 138.4, 143.2; MS (ESI) m/z 390 $[\text{M}+1]^+$; IR (NaCl, neat) ν : 3024, 1493, 1445, 1344, 1167, 1090 cm^{-1} ; HRMS (ESI) calcd. for $\text{C}_{24}\text{H}_{24}\text{NO}_2\text{S}$ (M^++H): 390.1528, found: 390.1523.

8-Methoxy-2-methyl-4-phenyl-1-tosyl-1,2-dihydroquinoline 142f

Colourless solid; m.p. 165-167 °C; ^1H NMR (CDCl_3 , 400 MHz): δ 1.17 (d, 3H, $J = 6.9$ Hz), 2.26 (s, 3H), 3.95 (s, 3H), 4.90-4.97 (m, 1H), 5.60 (d, 1H, $J = 5.8$ Hz), 6.55 (d, 1H, $J = 7.7$ Hz), 6.85-6.88 (m, 2H), 6.99 (d, 1H, $J = 8.3$ Hz), 7.07-7.14 (m, 3H), 7.23-7.26 (m, 3H), 7.48 (d, 1H, $J = 8.2$ Hz); ^{13}C NMR (CDCl_3 , 100 MHz): δ 18.1, 21.4, 51.0, 56.5, 113.1, 118.2, 121.9, 127.5, 127.5, 127.9, 127.9, 128.7, 129.0, 129.1, 132.0, 136.7, 136.8, 138.1, 143.1, 157.5; IR (NaCl, neat) ν : 3019, 1574, 1476, 1271, 1165, 1076 cm^{-1} ; MS (ESI) m/z 428 $[\text{M}+\text{Na}]^+$; HRMS (ESI) calcd. for $\text{C}_{24}\text{H}_{23}\text{NO}_3\text{SNa}$ (M^++Na): 428.1296, found: 428.1280.

2-Methyl-4-*p*-tolyl-1-tosyl-1,2-dihydroquinoline 142g

Colourless solid; m.p. 149-150 °C; ^1H NMR (CDCl_3 , 400 MHz): δ 1.19 (d, 3H, $J = 6.9$ Hz), 2.27 (s, 3H), 2.34 (s, 3H), 5.06-5.13 (m, 1H), 5.59 (d, 1H, $J = 6.0$ Hz), 6.61 (d, 2H, $J = 7.9$ Hz), 6.86 (d, 1H, $J = 7.7$ Hz), 7.01 (d, 2H, $J = 8.2$ Hz), 7.10-7.13 (m, 5H), 7.25-7.33 (m, 3H), 7.79 (d, 1H, $J = 8.0$ Hz); ^{13}C NMR (CDCl_3 , 100 MHz): δ 19.3, 21.2, 21.4, 50.8, 125.8, 126.4, 127.1, 127.5, 128.1, 128.5, 128.7, 128.8, 129.0, 130.0, 133.0, 135.3, 135.9, 136.3, 137.3, 143.3; IR (NaCl, neat) ν : 3021, 1344, 1167, 1091 cm^{-1} ; MS (ESI) m/z 390 $[\text{M}+1]^+$; HRMS (ESI) calcd. for $\text{C}_{24}\text{H}_{24}\text{NO}_2\text{S}$ (M^++H): 390.1528, found: 390.1527.

4-(4-Chlorophenyl)-2-methyl-1-tosyl-1,2-dihydroquinoline 142h

Colourless solid; m.p. 172-173 °C; ^1H NMR (CDCl_3 , 400 MHz): δ 1.19 (d, 3H, $J = 6.9$ Hz), 2.28 (s, 3H), 5.57-5.14 (m, 1H), 5.61(d, 1H, $J = 6.0$ Hz), 6.66 (d, 2H, $J = 8.3$ Hz), 6.81(d, 1H, $J = 7.8$ Hz), 7.02 (d, 2H, $J = 8.2$ Hz), 7.12-7.37 (m, 6H), 7.81 (d, 1H, $J = 8.0$ Hz); ^{13}C NMR (CDCl_3 , 125 MHz): δ 19.2, 21.4, 50.7, 125.5, 126.6, 127.5, 127.9, 128.2, 128.5, 129.0, 129.0, 129.5, 129.9, 133.0, 133.5, 135.4, 135.8, 136.7, 143.3; IR (NaCl, neat) ν : 3022, 1344, 1165, 1088 cm^{-1} ; MS (ESI) m/z 410 $[\text{M}+1]^+$; HRMS (ESI) calcd. For $\text{C}_{23}\text{H}_{21}\text{NO}_2\text{S}^{35}\text{Cl}$ (M^++H): 410.0982, found: 410.0995.

4-(4-Bromophenyl)-2-methyl-1-tosyl-1,2-dihydroquinoline 142i

Colourless solid; m.p. 164-165 °C; ^1H NMR (CDCl_3 , 400 MHz): δ 1.19 (d, 3H, $J = 6.9$ Hz), 2.28 (s, 3H), 5.07-5.14 (m, 1H), 5.62 (d, 2H, $J = 6.0$ Hz), 6.60 (d, 2H, $J = 8.3$ Hz), 6.82 (d, 1H, $J = 7.7$ Hz), 7.02 (d, 2H, $J = 8.2$ Hz), 7.13 (t, 1H, $J = 7.5$ Hz), 7.26-7.38 (m, 5H), 7.81 (d, 1H, $J = 8.0$ Hz); ^{13}C NMR (CDCl_3 , 100 MHz): δ 19.2, 21.4, 50.7, 121.6, 125.5, 126.6, 127.5, 127.9, 128.5, 129.0, 129.0, 129.4, 130.3, 131.2, 133.0, 135.4, 135.8, 137.2, 143.3; IR (NaCl, neat) ν : 3019, 1485, 1341, 814 cm^{-1} ; MS (ESI) m/z 454 $[\text{M}+1]^+$; HRMS (ESI) calcd. for $\text{C}_{23}\text{H}_{21}\text{NO}_2\text{S}^{79}\text{Br}$ (M^++H): 454.0476, found: 454.0494.

2,4-Dimethyl-1-tosyl-1,2-dihydroquinoline 142j

Colourless solid; m.p. 68-69 °C; ^1H NMR (CDCl_3 , 500 MHz): δ 1.09 (d, 3H, $J = 6.9$ Hz), 1.58 (s, 3H), 2.32 (s, 3H), 4.81-4.87 (m, 1H), 5.37 (d, 1H, $J = 5.8$ Hz), 7.02-7.32 (m, 7H), 7.72 (d, 1H, $J = 8.0$ Hz); ^{13}C NMR (CDCl_3 , 125 MHz): δ 17.7, 19.6, 21.4, 50.7, 123.1, 126.2, 126.6, 127.3, 127.8, 128.3, 128.8, 128.9, 130.5, 132.7, 135.9, 143.1; IR (NaCl, neat) ν : 3012, 1485, 1450, 1344, 1165, 1051 cm^{-1} ; MS (ESI) m/z 336 $[\text{M}+\text{Na}]^+$; HRMS (ESI) calcd. For $\text{C}_{18}\text{H}_{19}\text{NO}_2\text{SNa}$ ($\text{M}^+ + \text{Na}$): 336.1034, found: 336.1035.

4-Cyclopropyl-2,6-dimethyl-1-tosyl-1,2-dihydroquinoline 142k

Colourless solid; m.p. 105-106 °C; ^1H NMR (CDCl_3 , 400 MHz): δ -0.44- -0.38 (m, 1H), 0.00-0.07 (m, 1H), 0.40-0.47 (m, 1H), 0.59-0.65 (m, 1H), 1.07 (d, 3H, $J = 6.8$ Hz), 1.21-1.28 (m, 1H), 2.32 (s, 3H), 2.37 (s, 3H), 4.82-4.88 (m, 1H), 5.33 (dd, 1H, $J = 5.9, 1.5$ Hz), 7.03 (d, 2H, $J = 8.1$ Hz), 7.11(dd, 1H, $J = 8.1, 1.5$ Hz), 7.19-7.24 (m, 3H), 7.59 (d, 1H, $J = 8.1$ Hz); ^{13}C NMR (CDCl_3 , 100 MHz): δ 4.1, 5.6, 11.6, 19.6, 21.4, 50.7, 124.1, 124.9, 127.3, 128.1, 128.4, 128.8, 129.8, 130.3, 134.4, 136.1, 136.2, 143.1; IR (NaCl, neat) ν : 3017, 1487, 1344, 1163, 1094, 1040, 814 cm^{-1} ; MS (ESI) m/z 376 $[\text{M}+\text{Na}]^+$; HRMS (ESI) calcd. for $\text{C}_{21}\text{H}_{23}\text{NO}_2\text{SNa}$ ($\text{M}^+ + \text{Na}$): 376.1347, found: 376.1341.

2,6-Dimethyl-4-(phenylethynyl)-1-tosyl-1,2-dihydroquinoline 142l

Yellow oil; ^1H NMR (CDCl_3 , 400 MHz): δ 1.16 (d, 3H, $J = 6.9$ Hz), 2.29 (s, 3H), 2.38 (s, 3H), 4.93-5.00 (m, 1H), 5.96 (d, 1H, $J = 6.0$ Hz), 7.10 (d, 2H, $J = 8.3$ Hz), 7.17 (dd, 1H, $J = 8.2, 1.7$ Hz), 7.26-7.45 (m, 8H), 7.61 (d, 1H, $J = 8.2$ Hz); ^{13}C NMR (CDCl_3 , 100 MHz): δ 19.2, 21.3, 21.5, 50.9, 84.9, 91.2, 118.3, 122.9, 125.8, 127.2, 127.2, 128.0, 128.4, 128.5, 129.2, 129.6, 129.8, 131.5, 134.5, 135.6, 136.6, 143.6; IR (NaCl, neat) ν : 3021, 1489, 1344, 1159, 1092, 812 cm^{-1} ; MS (ESI) m/z 436 $[\text{M}+\text{Na}]^+$; HRMS (ESI) calcd. for $\text{C}_{26}\text{H}_{23}\text{NO}_2\text{SNa}$ ($\text{M}^+ + \text{Na}$): 436.1347, found: 436.1345.

2-Methyl-3-tosyl-2,3-dihydroindeno[1,2,3-de]quinoline 142m

Pale-yellow oil; ^1H NMR (CDCl_3 , 400 MHz): δ 1.44 (d, 3H, $J = 6.8$ Hz), 2.23 (s, 3H), 5.33-5.39 (m, 1H), 6.29 (d, 1H, $J = 5.0$ Hz), 7.02 (d, 2H, $J = 8.0$ Hz), 7.26-7.45 (m, 6H), 7.55 (d, 1H, $J = 7.5$ Hz), 7.68-7.71 (m, 2H); ^{13}C NMR (CDCl_3 , 100 MHz): δ 21.4, 23.1, 54.9, 116.7, 120.9, 122.0, 122.5, 126.7, 127.1, 128.2, 128.7, 129.4, 129.7, 131.4, 132.2, 135.4, 136.1, 137.0, 141.2, 143.6; IR (NaCl, neat) ν : 3022, 1612, 1595, 1445, 1437, 1163, 812 cm^{-1} ; MS (ESI) m/z 374 $[\text{M}+1]^+$; HRMS (ESI) calcd. for $\text{C}_{23}\text{H}_{20}\text{NO}_2\text{S}$ ($\text{M}^+ + \text{H}$): 374.1215, found: 374.1183.

2-Methyl-4-phenyl-1-tosyl-1,2-dihydrobenzo[g]quinoline 142n

Pale-yellow solid, m.p. 163-164 °C; ^1H NMR (CDCl_3 , 400 MHz): δ 1.25 (d, 3H, $J = 6.9$ Hz), 2.25 (s, 3H), 5.14-5.21 (m, 1H), 5.76 (1H, $J = 6.0$ Hz), 6.81 (d, 1H, $J = 5.8$ Hz), 6.98 (d, 1H, $J = 8.2$ Hz), 7.27-7.49 (m, 8H), 7.60 (d, 1H, $J = 8.1$ Hz), 7.90 (d, 1H, $J = 8.2$ Hz), 8.29 (s, 1H); ^{13}C NMR (CDCl_3 , 100 MHz): δ 19.9, 21.4, 51.0, 126.1, 126.3, 126.6, 127.4, 127.5, 127.7, 128.0, 128.0, 128.1, 128.8, 129.1, 129.2, 130.9, 131.8, 133.0, 136.1, 136.8, 138.5, 143.3. IR (NaCl, neat) ν : 3019, 1493, 1346, 1167, 1094, 1028 cm^{-1} ; MS (ESI) m/z 426 $[\text{M}+1]^+$; HRMS (ESI) calcd. for $\text{C}_{27}\text{H}_{24}\text{NO}_2\text{S}$ (M^++H): 426.1528, found: 426.1531.

2,2-Dimethyl-4-phenyl-1-tosyl-1,2-dihydroquinoline 142o

Colourless solid, m.p. 159-160 °C; ^1H NMR (CDCl_3 , 500 MHz): δ 1.56 (s, 6H), 2.24 (s, 3H), 5.46 (s, 1H), 6.86-6.87 (m, 2H), 6.95 (d, 1H, $J = 7.6$ Hz), 7.02 (d, 2H, $J = 8.0$ Hz), 7.16-7.37 (m, 7H), 7.78 (d, 1H, $J = 8.0$ Hz); ^{13}C NMR (CDCl_3 , 125 MHz): δ 21.4, 28.2, 58.2, 125.4, 126.6, 127.6, 127.7, 127.9, 128.0, 128.7, 129.1, 130.6, 130.9, 133.5, 136.7, 136.9, 137.7, 137.8, 142.9; IR (NaCl, neat) ν : 3021, 1599, 1348, 1159, 1090 cm^{-1} ; MS (ESI) m/z 390 $[\text{M}+1]^+$; HRMS (ESI) calcd. for $\text{C}_{24}\text{H}_{24}\text{NO}_2\text{S}$ (M^++H): 390.1528, found: 390.1529.

2-Phenethyl-4-phenyl-1-tosyl-1,2-dihydroquinoline 142p

Colourless solid, m.p. 155-156 °C; ^1H NMR (CDCl_3 , 400 MHz): δ 1.67-1.82 (m, 2H), 2.26 (s, 3H), 2.74-2.82 (m, 1H), 2.86-2.93 (m, 1H), 4.96-5.01 (m, 1H), 5.69 (d, 1H, J = 6.0 Hz), 6.68 (d, 2H, J = 7.0 Hz), 6.85 (d, 1H, J = 7.7 Hz), 7.00 (d, 2H, J = 8.0 Hz), 7.10-7.35 (m, 12H), 7.82 (d, 1H, J = 8.0 Hz); ^{13}C NMR (CDCl_3 , 100 MHz): δ 21.4, 31.7, 34.3, 54.7, 125.9, 125.9, 126.5, 126.6, 127.5, 127.6, 128.0, 128.4, 128.6, 128.6, 128.8, 129.1, 130.2, 133.1, 135.9, 137.0, 138.2, 141.6, 143.4; IR (NaCl, neat) ν : 3022, 1599, 1450, 1072, 812 cm^{-1} ; MS (ESI) m/z 466 $[\text{M}+1]^+$; HRMS (ESI) calcd. for $\text{C}_{30}\text{H}_{28}\text{NO}_2\text{S}$ (M^++H): 466.1841, found: 466.1838.

4-Methyl-*N*-(2-(1-phenylbuta-1,3-dienyl)phenyl)benzenesulfonamide 143

Yellow oil; ^1H NMR (CDCl_3 , 400 MHz): δ 2.34 (s, 3H), 2.37 (s, 3H), 5.10 (d, 1H, J = 10.1 Hz), 5.24 (t, 2H, J = 8.7 Hz), 5.40 (d, 1H, J = 16.8 Hz), 5.80-5.89 (m, 2H), 6.26 (s, 1H), 6.47-5.60 (m, 2H), 6.82 (d, 1H, J = 11.0 Hz), 7.00-7.47 (m, 22H), 7.60 (d, 1H, J = 8.2 Hz), 7.76 (d, 2H, J = 8.2 Hz); ^{13}C NMR (CDCl_3 , 100 MHz): δ 21.5, 119.8, 120.7, 120.9, 123.0, 124.4, 125.3, 126.3, 127.2, 127.3, 128.2, 128.4, 128.7, 128.9, 129.0, 129.3, 129.4, 129.5, 129.6, 130.8, 130.8, 131.3, 132.6, 133.5, 133.6, 134.3, 134.7, 136.0, 136.0, 136.1, 137.2, 138.1, 138.5, 139.0, 143.6, 143.7; IR (NaCl, neat) ν : 3275, 1491, 1452, 911

cm^{-1} ; MS (ESI) m/z 376 $[\text{M}+1]^+$; HRMS (ESI) calcd. for $\text{C}_{23}\text{H}_{22}\text{NO}_2\text{S}$ (M^++H): 376.1371, found: 376.1359.

Chapter VIII. References

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