Gold-catalyzed intramolecular animation of alcohol pro-electrophiles as novel synthetic strategies to nitrogen heterocycles

Prasath Kothandaraman

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**NANYANG
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UNIVERSITY**

GOLD-CATALYZED INTRAMOLECULAR AMINATION OF
ALCOHOL PRO-ELECTROPHILES AS NOVEL
SYNTHETIC STRATEGIES TO NITROGEN
HETEROCYCLES

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A thesis submitted to the Nanyang Technological University
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Doctor of Philosophy

2011

DEDICATION

I would like to dedicate this thesis to my beloved father V. Kothandaraman and mother K. Vasantha who moulded me as a person and good human being with great love; without my parents I couldn't be able to sail in this life.

I would also like to dedicate this to my beloved aunties Jayalakshmi and Padmavathi who gave their care and heart as well.

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“Friendship hastens help in mishaps like hands picking up dress that slips”

“To love such friends the world desires whose friendship has unbroken ties” –

Thiruvalluvar

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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 December 2007 to March 2011 under the supervision of Asst. Prof. Philip Wai Hong Chan.

The work of this thesis has been directed towards establishing gold-catalyzed intramolecular amination of alcohol pro-electrophiles as novel synthetic strategies to nitrogen heterocycles. This thesis is divided into three parts:

- Part I consists of Chapter I, which gives an introduction to gold catalysis and its application to amination of alcohol pro-electrophiles by a variety of nitrogen nucleophiles.
- Part II is aimed at exploring novel intramolecular-based approaches for *N*-heterocycles employing the highly reactive and chemoselective nature of gold catalysis in combination with alcohol pro-electrophiles containing a tethered nitrogen moiety. Chapter II addressed an efficient gold-catalyzed synthetic route to 1,2-dihydroquinolines based on intramolecular amination of 1-(2-tosylaminophenyl)prop-2-en-1-ols. The method was shown to be applicable to the synthesis of the bioactive tetrahydroquinoline alkaloid (±)-angustureine. In Chapter III is described, a novel strategy to indenyl-fused and 2,3-disubstituted indoles that relied on a gold-catalyzed cycloisomerization reactions of 1-(2-tosylaminophenyl)prop-2-yn-1-ols. Chapter IV detailed the extension of this approach to include the synthesis of indole-2-carbaldehydes via 1,3-allylic alcohol isomerization (1,3-AAI) of (*E*)-2-iodomethylene-3-phenyl-1-tosylindolin-3-ols generated *in situ* from reactions of 1-(2-tosylaminophenyl)prop-2-yn-1-ols with NIS in the presence of a gold catalyst.

In Chapter V, gold-catalyzed tandem ring opening/amination of secondary and tertiary 2-tosylaminophenylcyclopropyl carbinols is introduced as an efficient synthetic route to 2,3-dihydro-1*H*-benzo[*b*]azepines as well as 2-vinylindolines.

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

PUBLICATIONS

1. “Gold-Catalyzed Cycloisomerizations of 1-(2-Tosylaminophenyl)prop-2-yn-1-ols to 1*H*-Indole-2-carbaldehydes and (*E*)-2-(Iodomethylene)indolin-3-ols” **Kothandaraman, P.;** Mothe, S. R.; Toh, S. S. M.; Chan, P. W. H. *J. Org. Chem.* **2011**, DOI: 10.1021/jo201208e. (*selected by the editors of Journal of Organic Chemistry as Featured Article*)
2. “Intramolecular Cyclopropyl Carbinol Rearrangement for Benzofused Nitrogen Ring Synthesis” **Kothandaraman, P.;** Huang, C.; Susanti, D.; Rao, W.; Chan, P. W. H. *Chem. Eur. J.* **2011**, *17*, DOI: 10.1002/chem.201101363.
3. “Rapid Access to Halohydrofurans via Brønsted Acid Catalyzed Hydroxylation/Halocyclization of Cyclopropyl Methanols with Water and Electrophilic Halides” Mothe, S. R.; **Kothandaraman, P.;** Rao, W.; Chan, P. W. H. *J. Org. Chem.* **2011**, *76*, 8, 2521-2531.
4. “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” Rao, W.; **Kothandaraman, P.;** Koh, C. B.; Chan, P. W. H. *Adv. Synth. Catal.* **2010**, *352*, 14-15, 2521.
5. “Gold-Catalyzed Cycloisomerization Reactions of 2-Tosylaminophenylprop-1-yn-3-ols as a Versatile Approach for Indole Synthesis” **Kothandaraman, P.;** Rao, W.; Foo, S. J.; Chan, P. W. H. *Angew. Chem. Int. Ed.* **2010**, *49*, 27, 4619. (*chosen by the Editors of Angewandte Chemie as a “Hot Paper” ; this work has also been highlighted as a Hot Research Topic by the University (NTU) <http://research.ntu.edu.sg/pages/default.aspx> and Received 6th Asian-European Symposium Poster Presentation Award*)

6. "Oxidative Preparation of Aromatic Orthocarboxylates from Aldehydes" Tanabe, H.; He, X.; **Kothandaraman, P.**; Yamane, M. *Synlett*, **2010**, 1190.
7. "Gold- and Silver-Catalyzed Intramolecular Allylic Amination of 2-Tosylaminophenylprop-1-en-3-ols. A Concise Synthesis of (±)-Angustureine" **Kothandaraman, P.**; Foo, S. J.; Chan, P. W. H. *J. Org. Chem.* **2009**, 74, 5947. (*highlighted by Organic Chemistry Portal: <http://www.organic-chemistry.org/abstracts/lit2/637.shtm>*)
8. "Gold- and Silver-Catalyzed Allylic Alkylation of 1,3-Dicarbonyl Compounds with Allylic Alcohols" **Kothandaraman, P.**; Rao, W.; Zhang, X.; Chan, P. W. H. *Tetrahedron* **2009**, 65, 1833. (*invited paper for the Symposia-In-Print series on ["Catalysis using Gold Complexes"](#)*)

ABBREVIATIONS

Ac	acetate
Ar	aryl
BINAP	2,2'-bis(diphenylphosphino)-1,1'-binaphthyl
Boc	<i>tert</i> -butoxycarbonyl
Bu	butyl
Cbz	benzyloxycarbonyl
DCE	1,2-dichloroethane
DMF	dimethylformamide
DMAP	4-(dimethylamino)pyridine
DMSO	dimethylsulfoxide
DMI	1,3-dimethyl-2-imidazolidinone
dr	diastereomeric ratio
ee	enantiomeric excess
Et	ethyl
equiv	equivalent
Fmoc	9-fluorenylmethyloxycarbonyl
h	hour
HMPA	hexamethylphosphoramide
<i>i</i> Pr	isopropyl
IPr	1,3-bis(2,6-diisopropylphenyl)imidazol-2-ylidene
LDA	lithium diisopropylamide
Me	methyl
min	minute
m.p.	melting point

Moz	<i>p</i> -methoxybenzylcarbonyl
Ms	methylsulfonyl
NMR	nuclear magnetic resonance
ⁿ Pr	<i>n</i> -propyl
Nu	nucleophile
NIS	<i>N</i> -iodosuccinimide
Ns	<i>p</i> -nitrophenylsulfonyl
OAc	acetate
OMe	methoxyl
OTf	trifluoromethanesulfonate
Ph	phenyl
<i>p</i> -TsOH	<i>p</i> -toluenesulfonic acid
r.t.	room temperature
TFA	trifluoroacetic acid
TfOH	trifluoromethanesulfonic acid
THF	tetrahydrofuran
TLC	thin layer chromatography
TMS	trimethylsilyl
Ts	<i>p</i> -methylphenylsulfonyl
α	alpha
β	beta
γ	gamma
δ	delta
ε	epsilon
ζ	zeta

Chapter I. Alcohol Pro-electrophiles in Gold-Catalyzed Synthetic Strategies to *N*-Heterocycles

1.1 Introduction

Nitrogen heterocycles are an immensely important class of compounds because of their role as key structural features in a myriad of biomolecules as well as targets of current biological and material interest, selected examples of which are shown in Figure 1.1.¹ In addition, *N*-heterocycles are invaluable building blocks in organic synthesis. Not surprisingly, with this broad spectrum of properties and applications, a diverse array of approaches directed toward *N*-heterocycles synthesis has been established over the years.^{1,2}

Generally, the construction of nitrogen heterocycles has relied upon addition or substitution of a nitrogen nucleophile to a carbon electrophile under acidic or basic conditions.³ For example, Fischer and Jourdan reported in 1883 what is now one of the best known methods for the synthesis of indoles from aryl hydrazines in the presence of pyruvic acid (Scheme 1.1).⁴ Today, this synthetic method is still used in the pharmaceutical industry for the preparation of the triptan-based class of antimigraine drugs.⁵ A main drawback of these synthetic methods, however, has been the need to often employ harsh strong acidic or basic conditions that can lead to limited functional group tolerance and unwanted competitive side reactions. In addition,

Scheme 1.1 The Fischer indole synthesis

Figure 1.1 Examples of nitrogen heterocyclic compounds of biological and material interest

many of these synthetic methods require stoichiometric or excess amounts of various reagents that result in the generation of equivalent quantities of byproducts. In this context, the development of new synthetic methods that can make use of transition metal catalysis has been actively pursued as a strategy to overcome such limitations posed by traditional transformations. Returning to the Fischer indole synthesis, for example, a milder version of this ring forming reaction that relies on the Pd-catalyzed coupling of aryl hydrazines with aryl halides in place of carbonyl compounds as one of the substrates was demonstrated over a century later by Buchwald and co-workers (Scheme 1.2).^{6a}

Scheme 1.2 Palladium-catalyzed Fischer indole synthesis

Recently, the establishing of novel catalytic synthetic routes to nitrogen heterocycles has also explored the use of readily available and more biocompatible substrates and catalysts.^{6b-i} As part of this ongoing program, one synthetic strategy that has received an increase amount of attention has been the use of alcohols as pro-electrophiles in combination with ecologically benign and commercially available gold complexes and salts.⁷ The reactions were shown to benefit from the ease of preparing the alcohol starting material and thus the possibility to introduce a wide variety of substitution patterns. Added to this was the potential to form a quaternary carbon centre by utilizing tertiary alcohols and formation of H₂O as potentially the only side product. By exploiting the highly reactive and chemoselective nature of gold catalysis, the reactions often proceed efficiently under mild conditions. The focal

point of this Introduction will be on the advances made in the development of gold-catalyzed reactions of alcohol as pro-electrophiles with nitrogen nucleophiles as highly efficient and selective methods for C–N bond formation. It will also provide a brief preface on the emergence of gold complexes and salts as powerful and versatile Lewis acidic catalysts for amine synthesis prior to their application to the chemistry of unsaturated alcohols.

1.2 Gold as a Lewis Acidic Catalyst

The chemical view of gold, until recently, was always one of an inert metal of high monetary value. While this is true with regard to metallic gold, recent works have shown complexes and salts of Au(I) and Au(III) to be among one of the most versatile and highly reactive homogeneous as well as heterogeneous catalysts that can efficiently and selectively mediate a wide variety of organic transformations. Indeed, this is witnessed by an exponentially increasing number of reports appearing in the last 25 years describing gold to either match or exhibit catalytic activities superior to more well-established metal catalysts currently in use in organic synthesis.⁸

Located below copper (^{29}Cu) and silver (^{47}Ag) in Group 11 and between platinum (^{78}Pt) and mercury (^{80}Hg) in Period VI in the Periodic Table, both metallic gold (^{79}Au , $Z = 79$; $[\text{Xe}]4f^{14}5d^{10}6s^1$) and a majority of the gold complexes and salts are known to exhibit a high tolerance to air and moisture. The metal itself is also more naturally abundant than palladium, platinum and rhodium, transition metals often chosen as the catalysts in a myriad of organic transformations.^{8q,r} Because of its $5d^{10}6s^1$ electronic configuration, the most common oxidation states of gold are 0, +1 and +3 with respective $d^{10}6s^1$, d^{10} and d^8 configurations. In the case of the latter two oxidation states, complexes and salts of both Au(I) and Au(III) have emerged as exceptionally potent and yet uniquely selective Lewis acids that have a high affinity for π bonds of

alkenes, alkynes and allenes. This π -acidity is linked to relativistic effects that results the contracted and lower in energy lowest unoccupied molecular orbital (LUMO) of the 6s orbital of Au is the primary acceptor of electron density from the highest occupied molecular orbital (HOMO) π orbital of π bonds causes increased π -acidity of cationic gold-complexes, and expansion of the 5d orbitals, and reaches a maximum in the Periodic Table with gold.⁹ As shown in Scheme 1.3, recognition and exploitation of such π -interactions has led to an ever-increasing number of efficient synthetic methods for C–X (X = C, N, O, S) bond formation over the years. This reactivity has also often allowed for such reactions to be accomplished under mild conditions and at low catalyst loadings so as to offset the cost of the metal.

Scheme 1.3 General mechanism for gold-catalyzed addition of nucleophiles to C–C multiple bonds

1.3 Gold-Catalyzed Addition of Nitrogen Nucleophiles to Alkenes, Alkynes and Allenes

In recent years, there has been an increasing number of works documenting gold-catalyzed amination of alkenes, alkynes and allenes as synthetic methods for the preparation of amines and amine derivatives.^{10,11} Although this has led to many synthetic strategies for C–N bond formation, the number of literature examples still remains far fewer than those reported for C–C and C–O bond formations.

The field of gold-catalyzed C–N bond formation first appeared with pioneering studies reported in 1987 by Utimoto and co-workers (Scheme 1.4).¹² In this work, NaAuCl₄ was shown to mediate intramolecular hydroamination of amino alkynes **8** regioselectively in a 6-*exo*-dig manner to give 2-alkylidene-piperidines **9**. These adducts were found to further undergo a rapid isomerization to give the corresponding and more stable tetrahydropyridines **10** in 64-92% yield.

Scheme 1.4 Gold-catalyzed intramolecular hydroamination of alkyne

Following this work, a second notable milestone was that by Tanaka and co-workers who reported the first gold-catalyzed intermolecular hydroamination of aromatic and aliphatic alkynes **11** with aniline derivatives **12** under solvent-free conditions (Scheme 1.5).¹³ The reactions proceeded well and formed the corresponding imines **13** in 28-99% yields with excellent regioselectivity. Notably,

the transformation could be accomplished with a low catalyst loading of 0.01 mol% of $(\text{Ph}_3\text{P})\text{AuMe}$ and 0.05 mol% of $\text{H}_3\text{PW}_{12}\text{O}_{40}$ as an acidic promoter.

Scheme 1.5 Gold(I)-catalyzed hydroamination of alkynes with aniline derivatives

To broaden the synthetic utility of gold-mediated cycloisomerizations of alkynes to nitrogen heterocycles, Li and co-workers demonstrated the double hydroamination of *o*-alkynylanilines **14** with terminal alkynes **15** catalyzed by AuCl_3 with AgOTf as a co-catalyst (Scheme 1.6).¹⁴ The corresponding *N*-vinylindoles **17** were obtained in up to 82% yield at room temperature and in the absence of solvent. Subsequent mechanistic studies revealed that intermolecular hydroamination of **14** with alkyne **15** to give the intermediate **16** proceeded before the intramolecular C–N bond forming step.

Scheme 1.6 Gold(III)-catalyzed double hydroamination of *o*-alkynylaniline **14**

At about the same time, Che and co-workers reported that tandem hydroamination/hydroarylation of **12** and **15** could be accomplished with the gold carbene Au(I) catalyst **20** and AgOTf as a co-catalyst (Scheme 1.7).¹⁵ In this work, the reaction proceeded well and furnished 1,2-dihydroquinolines **18** and quinolines **19** in 42-94% yield under microwave-assisted conditions.

Scheme 1.7 Gold(I)-catalyzed synthesis of 1,2-dihydroquinolines and quinolines

The gold-catalyzed intramolecular allene hydroamination reaction was disclosed in 2004 by Krause and co-workers (Scheme 1.8).¹⁶ Allenes of the type **21** readily cyclized in the presence of AuCl₃ as the catalyst and at loadings as low as 2 mol% at room temperature to give the corresponding 3-pyrrolines **22** in 69-95% yield. More notably, high product diastereomeric ratios (dr) of up to 99:1 were obtained for reactions of **21** where X = H although longer reaction times were required. However, lower product dr values were observed for cycloisomerization of *N*-protected substrates (X = Ms, Ts, Ac, Boc). The mechanism was proposed to proceed via initial coordination of the Au(III) catalyst to the allene moiety of the substrate. This is followed by nucleophilic attack of the amine group to produce 3-pyrrolines **22**, as shown in the inset in Scheme 1.8. It was suggested that prior to the amine attack,

competitive intramolecular coordination of the oxygen atom of *N*-protected allenes could stabilize the zwitterionic complex **23a**, which can further undergo partial isomerisation via single bond rotation to **23b**, was the probable source of the decrease in the diastereoselectivity in these reactions (for Ac = 70:30, Boc = 46:54).

Scheme 1.8 Gold(III)-catalyzed cycloisomerization of α -aminoallenes **21**

Following this work, the gold-catalyzed intermolecular hydroamination of achiral and chiral allenes **24** and **26** with aryl amines **12** with high chirality transfer was reported by Yamamoto and co-workers in 2006 (Scheme 1.9).¹⁷ Allylic amines **25** were obtained in excellent yields up to 96% in the presence of AuBr₃ as the catalyst under mild conditions. The reaction also proceeded for sterically bulky allenes albeit in lower product yields (typically < 35%). However, the scope was demonstrated to be limited as 1,1-disubstituted allenes were found to give either no reaction or a 9% yield in two examples examined. Notably, this approach could provide chiral allylic amines **27** in good yields and with high enantiomeric excess (ee) values of up to 99%

from the corresponding enantioenriched starting allenes **26**. The mechanism was reported to involve the formation of a gold-amine complex **28** prior to coordination of the metal to the allene. This then led to attack from the less hindered π face of the allene and formation of *E*-allyl amine adduct. It was suggested that the possible isomerization may take place through the intermediate **28b** as shown in the inset to give the *E*-allyl amine adduct.

Scheme 1.9 Gold(III)-catalyzed intermolecular hydroamination of allenes

At about the same time, gold-catalyzed inter- and intramolecular hydroamination of unactivated olefins was described by He and co-workers (Scheme 1.10).¹⁸ The reactions of a wide range of unactivated alkenes **29** with ArSO₂NH₂ **30** furnished the desired products **31** in yields of 44-95% in the presence of *in situ* generated Ph₃PAuOTf as the catalyst (eq 1 in Scheme 1.10). To broaden the synthetic utility of this method, it was shown that intermolecular followed by intramolecular

hydroamination of 1,5-dienes **32** with TsNH₂ **30a** provided a one-pot route to pyrrolidine derivatives **33** in good to excellent yields (eq 2 in Scheme 1.10).

Scheme 1.10 Gold(I)-catalyzed inter and intramolecular hydroamination of alkenes

This gold(I)-catalyzed approach could be further extended to intramolecular hydroamination of amino alkenes **34** to afford the corresponding pyrrolidines **35** in excellent yields of up to 99% (eq 3 in Scheme 1.10). In this work, the pyrrolidines were obtained in good yields even with other sources of arylsulfonamide nucleophiles tethered to alkenes. However, the reaction was found to be ineffective with other amine-based nucleophiles such as anilines, carbamates and sulfamates. Subsequent mechanistic studies suggested initial coordination of the gold catalyst to the alkene;

this was then followed by nucleophilic attack of the amide group from the opposite face of the newly formed alkyl gold to give the pyrrolidine products **35**.

More recently, Widenhoefer reported the intramolecular hydroamination of alkenyl carbamates of the type **36** shown in Scheme 1.11 with $\text{Au}[\text{P}(t\text{Bu})_2(o\text{-biphenyl})]\text{Cl}$ **38** as the catalyst and AgOTf as the co-catalyst (Scheme 1.11).¹⁹ In these reactions, the desired 2-methylpyrrolidines **37** were obtained in 59-97% yield. The mechanism was proposed to involve outer-sphere attack of the amine nucleophile onto the gold-bound alkene **36a** followed by protonolysis of the $\text{Au}-\text{C}$ (sp^3) bond to give the pyrrolidines.

Scheme 1.11 Gold(I)-catalyzed intramolecular hydroamination of alkenes **36**

Following these seminal works, an immense amount of effort has also been made toward establishing asymmetric carbon-nitrogen bond formation using gold catalysis. Most notable is that by Toste who showed the first gold(I)-catalyzed enantioselective intramolecular hydroamination of allenes **39** that relied on chiral dinuclear gold(I)-phosphine complex **41** containing a counter ion (Scheme 1.12).²⁰ This gave the corresponding 2-vinylpyrrolidines ($n = 1$) and piperidines ($n = 2$) **40** under mild conditions at room temperature in good to excellent yields and enantiomeric excess (ee) of up to 99%.

Scheme 1.12 Gold(I)-catalyzed asymmetric hydroamination of allenes **39**

1.4 Gold-Catalyzed Amination of Alcohol Pro-electrophiles

While studies on gold-catalyzed amination of alkenes, alkynes and allenes have gathered pace, the analogous amination of alcohols as pro-electrophiles has received attention only in recent years. This approach was first explored by Campagne who reported NaAuCl_4 -catalyzed intermolecular amination of benzylic alcohols **42** with a variety of nitrogen nucleophiles such as TsNH_2 **30a**, 4-nitroaniline **12a**, 2,4-dinitrophenylhydrazine and trimethylsilyl azide (Scheme 1.13).²¹ This gave the corresponding benzylic amine derivatives **43** and **44** in good yields. It was shown that this synthetic approach was also useful for the access of diarylmethylamines using trimethylsilyl azide in a two step amination-reduction sequence. Various aromatic and heterocyclic substrates bearing both electron-donating and electron-withdrawing groups were well tolerated and afforded the desired amine derivatives. However, the method was found to be limited to secondary benzylic alcohol since attempted

amination of primary benzylic alcohol **42a** ($R^2 = H$) with TsNH_2 **30a** was reported to give no reaction. The mechanism was surmised to follow an $\text{S}_{\text{N}}1$ pathway and proceed through formation of the reactive carbocation intermediate **45**.

Scheme 1.13 Gold-catalyzed amination of alcohols **42**

In 2007, Liu demonstrated AuCl_3 could catalyze intermolecular amination of allylic alcohols **46** with TsNH_2 **30a** and ArNH_2 **12** under mild conditions at room temperature (Table 1.1, entry 1). This led to the corresponding allylic amine and allylic amide derivatives **47** and **48** in 29-96% yield. Furthermore, the reaction was shown to proceed well for both cyclic and acyclic allylic alcohols and furnished the desired allylic amines and allylic amides in good yields. However, to achieve high conversions, an excess amount of TsNH_2 **30a** or ArNH_2 **12** (4 equiv) was required. The mechanism of this reaction was believed to involve activation of allylic alcohols via coordination of the gold catalyst with the hydroxyl group undergo elimination to give the allylic cation intermediate. Subsequent nucleophilic attack of the amine afforded the desired allylic amines. The formation of regioisomers from non-symmetric allylic alcohols was reasoned to be consistent with the possible involvement of an allylic carbocationic species.

Table 1.1 Gold-catalyzed amination of allylic alcohols with various amines

$$\text{R}^1\text{-CH(OH)-CH=CH-R}^2 + \text{NH}_2\text{R}^3 \xrightarrow[\text{solvent}]{[\text{Au}]}$$

$$\text{R}^1\text{-CH=CH-CH(NHR}^3\text{)-R}^2 \text{ and/or } \text{R}^1\text{-CH(NHR}^3\text{)-CH=CH-R}^2$$

46 **47** **48**

$\text{R}^1 = \text{alkyl, aryl}$
 $\text{R}^2 = \text{H, alkyl, aryl}$

Entry	[Au]	NH ₂ R ³		Yield (%)	Ref
1	AuCl ₃	TsNH ₂ 30a	ArNH ₂ 12	29-96	22
2	 38 /AgSbF ₆	 49		85-100	23
3	[(PhO) ₃ P]AuCl/AgOTf	NH ₂ SO ₂ Ar 30	ArNH ₂ 12	36-98	24

Following this work, the intermolecular amination of allylic alcohols **46** with cyclic ureas **49** was described by Widenhoefer (Table 1.1, entry 2). In this work, it was reported that the amination proceeded well in the presence of Au[P(*t*-Bu)₂(*o*-biphenyl)]SbF₆ generated *in situ* from reaction of Au[P(*t*-Bu)₂(*o*-biphenyl)]Cl **38** with AgSbF₆ as a co-catalyst. This furnished the corresponding allylic ureas **47** and **48** in 85-100% yield with up to 25:1 γ -regioselectivity. More notably, the amination process was also shown to proceed with primary allylic alcohols such as cinnamyl alcohol and 3-methyl-2-buten-1-ol, affording the α -amination products in respective yields of 85 and 100%. It was suggested that the γ -amination product **47** was obtained via an S_N2'

pathway while the α -aminated adduct **48** was afforded via a putative carbocation intermediate.

More recently, Nájera and co-workers demonstrated that amination of allylic alcohols **46** with ArSO_2NH_2 **30** and ArNH_2 **12** could be achieved in the presence of a gold-phosphite gold complex (Table 1.1, entry 3). The reaction was found to proceed smoothly under mild conditions at room temperature and at catalyst loadings as low as 0.5 mol% of $[(\text{PhO})_3\text{P}]\text{AuCl}$ and 0.5 mol % of AgOTf as a co-catalyst, affording the corresponding γ and α -amino substituted products **47** and **48** in moderate to excellent yields of 36-98%. This was shown to contrast to the analogous reactions catalyzed by AgOTf alone, which were reported to require a significantly higher catalyst loading of 2 mol% and longer reaction times of 24 h. The mechanism was proposed to proceed through π -activation of the double bond of the substrate in a manner similar to that reported by Widenhoefer and co-workers in studies on intermolecular amination of allylic alcohols **46** with cyclic urea **49**. It was reasoned that another route to the α -amination product could be due to the isomerization of the γ -substituted adduct **47** or γ -allylic alcohol substrate.

An intramolecular version of this reaction was communicated at about the same time by the group of Widenhoefer using a gold(I) complex generated *in situ* from reaction of $\text{Au}[\text{P}(t\text{-Bu})_2(o\text{-biphenyl})]\text{Cl}$ **38** with AgSbF_6 as co-catalyst (Scheme 1.14).²⁵ In this work, the desired pyrrolidine ($n = 1$) and piperidine ($n = 2$) derivatives **51** were obtained in yields of 41-99% with high diastereomeric ratios (dr) values of up to 50:1 from the corresponding allylic alcohols **50**. The reaction mechanism was shown to involve *syn* addition of the amino group relative to the departing hydroxyl group.

Scheme 1.14 Gold-catalyzed intramolecular amination of allylic alcohols **50**

Chan reported a synthetic route to pyrrolidines that relied upon tandem ring opening/amination of cyclopropyl methanols **52** with ArSO_2NH_2 **30** and AuOTf generated *in situ* from reaction of AuCl and AgOTf as the catalysts (Scheme 1.15).²⁶ Although a high reaction temperature of 100 °C was required, the reactions proceeded well at catalyst loadings as low as 2 mol% and produced the pyrrolidines **53** in yields of 30-95%. The mechanism was thought to involve activation of the alcohol by the AuCl/AgOTf catalyst, followed by ionization of the starting material, which caused ring opening of the cyclopropane moiety and trapping by the sulfonamide nucleophile. The resultant aminated acyclic intermediate **54** was proposed to undergo subsequent intramolecular hydroamination to give pyrrolidine **53**.

Scheme 1.15 Gold-catalyzed tandem ring opening/amination of cyclopropyl methanols with sulfonamides

In 2008, Liang reported an efficient tandem process involving intermolecular allylic amination/intramolecular hydroamination of 1-en-4-yn-3-ols **55** with TsNH₂ **30a** catalyzed by HAuCl₄·H₂O (Scheme 1.16).²⁷ In this reaction, the corresponding fused pyrroles **57** were obtained in 25-83% yield at room temperature. However, excess amount of the **30a** (up to 15 equiv) along with a high catalyst loading of 20 mol% was required to achieve high product yields. In addition, the reaction proceeded well only for substrates containing a cyclohexane moiety although the reason for this unique reactivity was not explained. Reaction involving one acyclic example of **55** where R¹ = R² = Ph was shown to lead to only the corresponding amination intermediate **56** as the sole product in 89% yield. The mechanism was proposed to proceed via a formal intermolecular allylic amination step followed by intramolecular hydroamination of **56** to form the fused pyrrole **57**.

Scheme 1.16 Gold(III)-catalyzed amination of 1-en-4-yn-3-ols with TsNH₂ **30a**

A similar approach to tetrasubstituted pyrroles **60** was subsequently reported by Liu (Scheme 1.17).²⁸ The reaction relied on (*p*-MeOC₆H₄)₃PAuBF₄, generated *in situ* from (*p*-MeOC₆H₄)₃PAuCl and AgBF₄, to mediate cascade amination/intramolecular hydroamination of (*Z*)-2-en-4-yn-1-ols **58** with TsNH₂ **30a** or 4-nitroaniline **12a**. While 4 equiv of the nitrogen nucleophile **12a** was required to afford pyrroles in

yields up to 84%, the method was applicable to a wide range of enyne alcohols **58**. The only exception was for substrates containing an alkyl substituent ($R^1 = \text{alkyl}$) which were shown to additionally require 2 equiv of $\text{BF}_3 \cdot \text{Et}_2\text{O}$ to furnish the pyrrole derivatives in yields up to 82%.

Scheme 1.17 Gold(I)-catalyzed amination of (Z)-2-en-4-yn-1-ols with amine nucleophiles

Following this work, the groups of Akai and Aponick independently demonstrated that the catalytic systems $\text{Au}[\text{P}(t\text{-Bu})_2(o\text{-biphenyl})]\text{Cl}$ **38** + AgOTf and $(\text{Ph}_3\text{P})\text{AuCl}$ + AgNTf_2 combinations could effect cycloisomerization of β -aminosubstituted propargylic alcohols **61** (Table 1.2). In both synthetic approaches, the reactions proceeded rapidly at catalyst loadings as low as 0.05 mol% and afforded the corresponding pyrrole products **62** in good yields up to 99%. Although no detailed mechanistic studies were conducted, the cyclization process was thought to likely involve initial coordination of the Au(I) catalyst to the alkyne moiety of **61**.

Table 1.2 Gold-catalyzed intramolecular cyclization of propargylic alcohols **61**.

61 **62**

$R^1-R^3 = \text{H, alkyl, aryl}$
 $R = \text{Ts, Boc, Bu, Bn}$

Entry	Catalyst	Yield (%)	Ref
1	$(\text{Ph}_3\text{P})\text{AuCl}/\text{AgNTf}_2$	85-98	29
2	 38 $/\text{AgOTf}$	75-99	30

More recently, as a part of efforts directed toward developing a general method for the direct nucleophilic substitution of propargylic alcohols with a variety of C, N, O and S-based nucleophiles, Campagne demonstrated a synthetic example that led to a propargylic amine **64** (Scheme 1.18).³¹ In this work, $\text{NaAuCl}_4 \cdot 2\text{H}_2\text{O}$ was found to efficiently catalyze the amination of propargylic alcohol **63** with PhSO_2NH_2 **30b** to afford the corresponding amino-substituted product **64** in a moderate yield of 58%.

Scheme 1.18 Gold-catalyzed amination of propargyl alcohol **64** with PhSO_2NH_2 **30b**

1.5 Proposed work

The work of this thesis has been directed toward providing novel synthetic methodologies that enable the delivery of nitrogen ring compounds of biological and materials interest in an efficient and selective manner. This will be accomplished by exploring the highly reactive and chemoselective nature of gold catalysis in combination with inexpensive and readily available alcohol as pro-electrophiles containing a tethered nitrogen nucleophile under operationally straightforward and mild conditions. By establishing intramolecular-based approaches for nitrogen ring synthesis, the new methods will also be developed in a manner that does not require the need for stoichiometric or excess amounts of reagents and subsequent formation of equivalent quantities of byproducts.

Thus, the aim of this project has been to establish new gold-catalyzed protocols for the construction of 1,2-dihydroquinolines, indenyl-fused and 2,3-disubstituted indoles, 2,3-dihydro-1*H*-benzo[*b*]azepines as well as 2-vinylindolines and indole-2-carbaldehydes from alcohols (Figure 1.2). It is envisioned that a synthetic route to 1,2-dihydroquinolines can be developed from 2-tosylaminophenylprop-1-en-3-ols **I**. Replacing the alkene moiety of **I** with an alkyne functional group, the indole ring structure can be prepared via intramolecular cycloisomerization of 1-(2-tosylaminophenyl)prop-2-yn-1-ols **II'**. Through trapping of a putative vinyl gold species in these reactions with an electrophilic iodide source, we reasoned that the extension of this approach to include the synthesis of (*E*)-2-iodomethylene-3-phenyl-1-tosylindolin-3-ols from **II''** could also be developed. On the other hand, if the same reactions were conducted at reflux temperature, we surmised that vinyl iodide derivatives would undergo a further 1,3-allylic alcohol isomerization (1,3-AAI) process and provide an approach to indole-2-carbaldehydes. Finally, by utilizing

secondary **III''** and tertiary 2-tosylaminophenylcyclopropyl carbinols **III'**, we envisioned that this approach could also provide a synthetic route to the respective 2-vinylindolines as well as 2,3-dihydro-1*H*-benzo[*b*]azepines.

Figure 1.2 Gold-catalyzed synthesis of nitrogen heterocyclic compounds from alcohols

Chapter II. Gold-Catalyzed Intramolecular Amination
of 1-(2-tosylaminophenyl)prop-2-en-1-ols. A Concise Synthesis of (±)-
Angustureine

2.1 Introduction

Partially hydrogenated quinolines are an important member of the *N*-heterocyclic family of compounds because of their presence in a myriad of biologically active natural products and therapeutics and ability to serve as versatile building blocks in organic synthesis. Representative examples range from the structurally simple and bioactive (+)-angustureine, peniprequinolone and (–)-galipeine to the architecturally challenging compounds martinelline and (+)-meloscine (Figure 2.1).³² Although this has led to many synthetic methods³³ that has also recently included gold catalyzed

Figure 2.1 Examples of bioactive compounds containing a partial hydrogenated quinoline moiety

reactions,⁸ the reactions have been reported to usually require high temperatures and/or prolonged reaction times. In addition, limited examples demonstrating substrate scope, modest selectivities, and, in many cases, the need for more than stoichiometric amounts of various reagents and additives has lessened their utility in organic synthesis. We envisioned a gold-catalyzed strategy involving the use of alcohol as proelectrophiles^{34,35} would be attractive from a synthetic standpoint as the ease of preparing the starting material provides the possibility to introduce a wide variety of substitution patterns in one step. Added to this is the potential formation of H₂O as the only side product. To our knowledge, while methods for quinoline synthesis from alcohols have been recently described,³⁶ the corresponding studies to 1,2-dihydroquinolines have been thus far limited to two reported literature methods. Lau and co-workers reported the thermolytic electrocyclization of *N*-methyl-2-hydroxyalkylanilines and found the reaction to only proceed at high temperatures (80–180 °C).³⁷ At about the same time, Kobayashi and co-workers showed that intramolecular cyclization of *o*-(1-hydroxy-2-alkenyl)phenyl isocyanides could be accomplished in the presence of BF₃·Et₂O as catalyst at 0 °C.³⁸ However, these methods were shown to give low to good product yields and only applicable to a limited substrate scope. In this regard, it remains a challenge to develop catalytic systems that can effect 1,2-dihydroquinoline formation for a wide variety of alcohol as pro-electrophiles under ambient conditions. In this chapter, a synthetic route to 1,2-dihydroquinolines **66** involving intramolecular amination of 1-(2-tosylaminophenyl)prop-2-en-1-ols **65** catalyzed by AuCl₃ with AgSbF₆ as a cocatalyst under mild conditions at room temperature is described (Scheme 2.1). Uniquely, the reaction was found to only efficiently proceed in the presence of a gold and silver catalyst combination and provide good to excellent product yields up to 91% for a

wide variety of the starting alcohols. The application of this catalytic 1,2-dihydroquinoline formation process to the synthesis of ($\pm$)-angustureine in four steps is also presented.

Scheme 2.1 $\text{AuCl}_3/\text{AgSbF}_6$ -catalyzed intramolecular amination of 1-(2-tosylamino phenyl)prop-2-en-1-ols **65** and its application to the synthesis of ($\pm$)-angustureine

2.2 Results and Discussion

All 1-(2-tosylaminophenyl)prop-2-en-1-ols studied in this work were prepared as shown in Scheme 2.2. This initially involved tosylation of the corresponding 2-aminophenylketone **A** with *p*-TsCl to give the 2-tosylaminophenylketone intermediate **B**. Subsequent treatment of **B** with vinylmagnesium bromide gave the corresponding alcohols **65a-h**. Likewise, condensation of **B** with aromatic aldehydes in the presence of base gave the α,β -unsaturated ketone intermediate **C**. This is followed by reduction of **C** with NaBH_4 in MeOH to afford the corresponding 1-(2-tosylaminophenyl)prop-2-en-1-ols **65i-q**.

Scheme 2.2 Synthesis of 1-(2-tosylaminophenyl)prop-2-en-1-ols

Initially, *N*-(2-(2-hydroxybut-3-en-2-yl)phenyl)-4-methylbenzenesulfonamide **65a** was chosen as the model substrate to establish the reaction conditions (Table 2.1). This revealed that treatment of **65a** with 5 mol% of AuCl_3 and 15 mol% of AgSbF_6 in toluene at room temperature for 1 h gave the best result (Table 2.1, entry 1). Under these conditions, 4-methyl-1-tosyl-1,2-dihydroquinoline **66a** was furnished in 87% yield.

The structure of 1,2-dihydroquinoline **66a** was confirmed by ^1H NMR analysis and X-ray crystal structure determination of three closely related products *vide infra*. Lower product yields of 32-56% were obtained when the reaction was repeated with lower loadings of 5 or 10 mol % of AgSbF_6 or removing the AgCl formed *in situ* prior to use (Table 2.1, entries 2-4). Similarly, a lower product yield of 58% was afforded when the reaction was performed in nitromethane in place of toluene as solvent (Table 2.1, entry 5). In contrast, the analogous reactions in acetonitrile or 1,4-dioxane were found to result in trace product formation and near-quantitative recovery of the starting alcohol **65a** (Table 2.1, entries 6 and 7). An inspection of entries 8-25 in Table 2.1 revealed the reaction also proceeded less effectively with other Lewis and

Table 2.1 Optimization of reaction conditions^a

Entry	Catalyst	Solvent	Time (h)	Yield (%) ^b
1	AuCl ₃ /AgSbF ₆	PhMe	1	87
2	AuCl ₃ /AgSbF ₆	PhMe	4	55 ^c
3	AuCl ₃ /AgSbF ₆	PhMe	4	32 ^d
4	AuCl ₃ /AgSbF ₆	PhMe	16	56 ^e
5	AuCl ₃ /AgSbF ₆	MeNO ₂	16	58
6	AuCl ₃ /AgSbF ₆	MeCN	16	— ^f
7	AuCl ₃ /AgSbF ₆	1,4-dioxane	16	— ^f
8	AuCl ₃ /AgOTf	PhMe	16	72
9	AuCl/AgSbF ₆	PhMe	4	62
10	AuCl/AgOTf	PhMe	4	60
11	Ph ₃ PAuCl/AgSbF ₆	PhMe	6	68
12	AuCl ₃	PhMe	16	15
13	AuCl	PhMe	16	— ^g
14	Ph ₃ PAuCl	PhMe	16	— ^g
15	AgSbF ₆	PhMe	16	— ^g
16	AgOTf	PhMe	16	— ^g
17	Bi(OTf) ₃	PhMe	16	— ^g

Table 2.1 (*continued*)

Entry	Catalyst	Solvent	Time (h)	Yield (%) ^b
18	CuCl ₂	PhMe	16	— ^g
19	Cu(OTf) ₂	PhMe	16	12
20	Yb(OTf) ₃	PhMe	16	7
21	InCl ₃	PhMe	16	11
22	FeCl ₃ ·6H ₂ O	PhMe	16	18
23	BF ₃ ·Et ₂ O	PhMe	16	16
24	<i>p</i> -TsOH·H ₂ O	PhMe	16	13
25	TfOH	PhMe	0.5	— ^h
26	HCl	PhMe	0.5	— ^h

^aAll reactions were performed at room temperature with 0.2 mmol of **65a** in the presence of 5 mol % of catalyst. ^bIsolated yield. ^cReaction performed with 5 mol% of AuCl₃ and 10 mol% of AgSbF₆. ^dReaction performed with 5 mol % of AuCl₃ and 5 mol % of AgSbF₆. ^eReaction performed with 5 mol% of AuCl₃ and 15 mol% of AgSbF₆ with removal of AgCl prior to use. ^fTrace amount refers to less than 1% of product isolated after flash column chromatography. ^gNo reaction based on TLC or ¹H NMR analysis of the crude mixture. ^hMixture of unknown side products furnished based on ¹H NMR analysis of the crude mixture.

Brønsted acid catalysts. In these reactions, the use of AuCl₃ in combination with AgOTf, AuCl with AgOTf or AgSbF₆, or Ph₃PAuCl with AgSbF₆ were the instances that gave slightly lower product yields of 62-72% (Table 2.1, entries 8-11). When AuCl₃, Yb(OTf)₃, Cu(OTf)₂, InCl₃, FeCl₃·6H₂O, BF₃·Et₂O and *p*-TsOH·H₂O were examined as the catalyst, markedly lower product yields of 7-18% were afforded

(Table 2.1, entries 12 and 19-24). However, changing the catalyst to AuCl, Ph₃PAuCl, AgSbF₆, AgOTf, Bi(OTf)₃, or CuCl₂ gave no reaction on the basis of ¹H NMR or TLC analysis of the crude mixtures (Table 2.1, entries 13-18). On the other hand, when TfOH or HCl was employed as a catalyst, the reaction was found to proceed to give a wide variety of side products that could not be separated by flash column chromatography or identified by ¹H NMR analysis of the crude mixtures (Table 2.1, entries 25 and 26). The contrasting catalytic activities observed for the AgSbF₆- and TfOH-mediated reactions provided evidence that the cationic Au(III) complex is the active species (Table 2.1, entries 15 and 25). Additionally, the significantly poorer reactivities found for the respective reactions catalyzed by AuCl₃²² and Bi(OTf)₃³⁹ are noteworthy as these catalysts were recently reported to efficiently mediate the allylation of sulfonamides with allylic alcohols (Table 2.1, entries 12 and 17). Likewise, BF₃·Et₂O, which was found to catalyze the intramolecular cyclization of *o*-(1-hydroxy-2-alkenyl)phenyl isocyanides,³⁸ was shown to be less effective in this study (Table 2.1, entry 23).

To define the scope of the present procedure, reactions of a variety of 1-(2-tosylaminophenyl)prop-2-en-1-ols **65** (Table 2.2) were examined. These experiments showed that with AuCl₃/AgSbF₆, starting alcohols with a methyl- and/or phenyl-substituted terminal alkene moiety gave the corresponding products **66b-d** in excellent yields (Table 2.2, entries 1-3). Similarly, the substrate **65e**, which contains a pendant *m*-toluidine ring unit, underwent the intramolecular allylic amination and afforded **66e** in 86% yield (Table 2.2, entry 4). Likewise, the reaction of *p*-chloroaniline-substituted alcohol **65f** gave **66f** in 59% yield under the standard conditions, the yield of which could be increased to 68% on repeating with CH₂Cl₂ as the solvent at reflux (Table 2.2, entry 5). The present procedure also worked well for

1-(2-tosylaminophenyl)prop-2-en-1-ols containing electron-withdrawing or electron-donating groups at the terminal position of the allylic alcohol moiety, giving **66i-l** in 58-90% yield (Table 2.2, entries 8-11).

Notably, these cyclizations also demonstrated that the electronic nature of the C=C bond could play a role since a gradual decrease in product yields from 78% to 58% was found and longer reaction times from 1 to 4 h were required as the electron-withdrawing ability of the substituent increased on going from **65j** to **65l**. The reactions of substituted 1-(2-tosylaminophenyl)prop-2-en-1-ols **65m** and **65n** bearing a sterically bulky naphthylene and mesitylene group, respectively, were found to proceed well and afford **66m** and **66n** in excellent yields (Table 2.2, entries 12 and 13). However, moderate yields were obtained for intramolecular cyclizations of alcohols with a pendant benzo[*d*][1,3]dioxole group on the allylic moiety or as part of the aniline unit as in **65h** and **65q** (Table 2.2, entries 7 and 16).

On the other hand, reactions of alcohols with pendant *trans* diene functionalities proceeded well when subjected to the standard conditions and gave **66o** and **66p** in good yields (Table 2.2, entries 14 and 15). For the cyclization of **65p**, switching the catalyst to 5 mol% of AuCl and 5 mol% of AgOTf under reflux conditions was required to shorten the reaction time from 24 to 6 h. Reaction of **65g** containing a *p*-nitroaniline unit was found to be ineffective with no product formation detected by ¹H NMR analysis of the crude mixture and near-quantitative recovery of the starting alcohol **65g** (Table 2.2, entry 6).

Table 2.2 AuCl₃/AgSbF₆-catalyzed intramolecular amination of **65b-q**^a

Entry	Alcohol	Product	Yield (%) ^b
1	65b-c		66b , R = Me 89
2	65b-c		66c , R = Ph 87
3	65d-e		66d , R = H 86
4	65d-e		66e , R = Me 86
5	65f-g		66f , R = Cl 68 ^c
6	65f-g		66g , R = NO ₂ - ^d
7	65h		66h 45
8	65i-l		66i , R = Me 90
9	65i-l		66j , R = Br 78 ^e
10	65i-l		66k , R = Cl 62 ^f
11	65i-l		66l , R = F 58 ^f
12	65m		66m 85

Table 2.2 (continued)

Entry	Alcohol	Product	Yield (%) ^b
13	65n	66n	86
14	65o-p	66o , R = Ph	62
15		66p , R = <i>n</i> -Pr	69 ^g
16	65q	66q	42

^aAll reactions were performed in PhMe at room temperature for 1 h with AuCl₃:AgSbF₆:**65** ratio = 1:3:20. ^bIsolated yield. ^cReaction conducted in CH₂Cl₂ as solvent at 40 °C. ^dNo reaction based on ¹H NMR analysis of the crude mixture. ^eReaction conducted for 2 h. ^fReaction conducted for 4 h. ^gReaction conducted with AuCl:AgOTf ratio = 1:1 as catalyst at reflux for 6 h.

At this juncture, it is worthy to highlight the chemoselective nature of the present reaction. Consistent with earlier findings for the intramolecular cyclization of **65a** (entry 1 in Table 2.1), it was found that the 1,2-dihydroquinolines described in Table 2.2 were obtained in 42-90% yields. As shown in Figures 2.3 and 2.4, this was further confirmed by X-ray crystal structure determination of **66b** as well as that for **66c**, **66e**, and **66i**.⁴⁰ On the basis of ¹H NMR analysis of the crude mixtures, possible indole formation arising from competitive intramolecular hydroamination could not be detected under our experimental conditions. Similarly, a competitive Freidel-Crafts alkylation leading to indenenes and dienes was not found. Under the standard conditions, intramolecular cyclization of **65c** was the only instance in which the indene adduct **67** (Figure 2.2), determined by X-ray crystal analysis (Figure 2.5), was also obtained as a minor side product in 3% yield.⁴⁰

Figure 2.2 Structure of indene adduct **67**

(a) **66b** (b) **66c**

Figure 2.3 ORTEP drawing of (a) **66b** and (b) **66c** with thermal ellipsoids at 50% probability levels⁴⁰

(a) **66e** (b) **66i**

Figure 2.4 ORTEP drawing of (a) **66e** and (b) **66i** with thermal ellipsoids at 50% probability levels⁴⁰

Figure 2.5 ORTEP drawing of **67** with thermal ellipsoids at 50% probability levels⁴⁰

Although highly speculative, the mechanistic outline of the present $\text{AuCl}_3/\text{AgSbF}_6$ -catalyzed 1,2-dihydroquinoline forming reaction is depicted in Scheme 2.3. This involves the gold and silver catalyst combination activating the allylic alcohol **65** by coordinating to the hydroxyl functionality. This generates the Au(III)-coordinated intermediate **68** that undergoes elimination to give allylic cation **69** and $[\text{Au}]\text{-OH}$, which releases the metal catalyst by protodemetalation.⁴¹ It is possible that this newly formed cationic species suffers from nucleophilic attack of the sulfonamide group and subsequent formation of the product **66**. The role of the catalyst in facilitating dehydroxylation of the alcohol substrate would account for the moderate yields for the reactions of **65h** and **65q** and no product formation for the cyclization of **65g** (entries 6, 7, and 16 in Table 2). It would not be inconceivable that such interactions are presumably weakened due to competitive coordination with a very electron rich neighbor such as a 1,3-dioxole moiety or a strongly coordinating nitro substituent on the alcohol substrate.

Scheme 2.3 Tentative mechanism for $\text{AuCl}_3/\text{AgSbF}_6$ -catalyzed intramolecular cyclization of 1-(2-tosylaminophenyl)prop-2-en-1-ols **65**

The possible involvement of an allylic carbocation species prior to formation of the new C–N bond is also supported by the reactions of **65r** and its regioisomer **65s**. Under the conditions described in Scheme 2.4, the same 1,2-dihydroquinoline **66r** was afforded in both reactions in comparable yields of 91% and 87% from **65r** and **65s** respectively.

Scheme 2.4 $\text{AuCl}_3/\text{AgSbF}_6$ -catalyzed intramolecular amination of **65r** and **65s**

The origin of the indene side product **67** from **65c** is due to competitive cyclization of this resulting carbocation species by the phenyl group. What remains currently unclear is whether the gold center first coordinates to the C=C bond before hydroxyauration and elimination to give the allylic cation and if subsequent coordination of this intermediate to the catalyst takes place prior to the ring-forming step.⁴² The earlier findings of entries 8-25 in Table 2.1 showing markedly poorer or lack of catalytic activity with other Lewis and Brønsted catalysts would certainly suggest that such interactions to be a possibility.

Having established a synthetic route to 1,2-dihydroquinolines, this new methodology was applied to the synthesis of the biologically active tetrahydroquinoline alkaloid (±)-angustureine.⁴³ As shown in Scheme 2.5, Pd/C-mediated hydrogenation of **66p** in MeOH gave the tetrahydroquinoline **70** in 96% yield. Subsequent treatment of this *N*-tosyl intermediate with a methanolic solution containing excess amounts of magnesium powder furnished the detosylated tetrahydroquinoline **71** in 98% yield.⁴³ⁱ Finally, *N*-methylation of **71** with MeI and K_2CO_3 as a base gave (±)-angustureine in 96% yield.^{43e,h} The ^1H and ^{13}C NMR

spectra of ($\pm$)-angustureine prepared are identical with the corresponding spectra of the authentic natural compound.⁴³

Scheme 2.5 Synthesis of ($\pm$)-angustureine from **66p**

2.3 Conclusion

In summary, gold-catalyzed synthetic route to 1,2-dihydroquinolines based on intramolecular amination of 1-(2-tosylaminophenyl)prop-2-en-1-ols under mild conditions has been developed. These results show the reaction to be applicable to a wide range of α -aryl allylic alcohols containing electron-withdrawing, electron-donating, and sterically demanding substituents. These studies also revealed only the use of a gold and silver catalyst combination to efficiently mediate the present cyclization process. The synthetic utility of the present method to prepare partially hydrogenated class of heterocycles was also demonstrated by further modifying one of dihydroquinolines to the synthesis of the bioactive tetrahydroquinoline alkaloid, ($\pm$)-angustureine.

Chapter III. Gold-Catalyzed Cycloisomerization Reactions of 1-(2-tosylaminophenyl)prop-2-yn-1-ols as a Versatile Approach for Indole Synthesis

3.1 Introduction

Indole derivatives are important cyclic compounds in organic synthesis because of their ability to serve as building blocks for functional materials and as key components in a myriad of bioactive compounds.⁴⁴ For this reason, the establishment of new efficient synthetic methods to prepare this class of *N*-heterocycles, with selective control of substitution patterns, from readily available and simple substrates continues to be actively pursued.^{44,45}

In the previous chapter, it was reported an efficient synthetic route to 1,2-dihydroquinolines **66** involving intramolecular amination of 2-tosylamino phenylprop-1-en-3-ols **65** catalyzed by AuCl₃ with AgSbF₆ as a co-catalyst.⁴⁶ As part of an ongoing program to develop this type of synthetic approach for carbon–nitrogen bond formation,^{7,21-31} it is reasoned that readily available 1-(2-tosylaminophenyl)prop-2-yn-1-ols **72** might also undergo gold-mediated intramolecular cyclization but in a 5-*exo*-dig manner given the exceptional alkynophilicity of the gold catalyst (Scheme 3.1).⁴⁷ The resultant putative indolyl-substituted vinyl gold species **80**⁴⁸ generated would then be susceptible to protodeauration and intramolecular Friedel-Crafts alkylation⁴⁹ or pentadienyl cation cyclization when R¹ = Ar and afford the indenyl-fused indole **73** (route 1 in Scheme 3.1). On the other hand, it was envisaged that a more reactive primary vinyl gold species formed when R¹ = H would be prone to a more rapid protodeauration/1,3-allylic alcohol isomerization (1,3-AAI) process⁵⁰ and provide the (1*H*-indol-2-yl)methanol product **74** (route 2a in Scheme 3.1). In the presence of a strong nucleophile, S_N2' substitution would be expected to give the 2-

alkyl-1*H*-indole adduct **75** preferentially (route 2b in Scheme 3.1). Similarly, it was reasoned for reactions in which $R^1 = \text{CHR}^2\text{R}^3$, a more facile protodeauration and dehydration step would proceed and deliver 2-vinyl-1*H*-indoles of the type **76**, as shown in route 3 in Scheme 3.1.

Scheme 3.1 Design of a vinyl gold approach for indole synthesis

In this chapter, the details of this gold-catalyzed method for the chemoselective synthesis of indenyl-fused and 2,3-disubstituted indoles that makes use of a putative vinyl gold intermediate **80** formed from cyclization of 1-phenyl-1-(2-(tosylamino)phenyl)prop-2-yn-1-ols **72** is disclosed.⁵¹ Although metal-catalyzed 5-*endo*-dig cycloisomerization of *o*-alkynylanilines have been extensively explored methods in indole synthesis,^{45f,51} the analogous 5-*exo*-dig process and dehydrative

cyclizations of substituted propargylic alcohols of the type **72** have remained sparse.^{45c,f,h}

3.2 Results and Discussion

1-(2-Tosylaminophenyl)prop-2-yn-1-ols **72** were prepared as illustrated in Scheme 3.2. This involved tosylation of starting material **A** with *p*-TsCl to furnish intermediate **B**. Subsequent reaction of 2-tosylaminoketone **B** with a variety of substituted alkynes pretreated with LDA or ethynylmagnesium bromide furnished the corresponding 1-(2-tosylaminophenyl)prop-2-yn-1-ols **72**.

Scheme 3.2 Synthesis of 1-(2-tosylaminophenyl)prop-2-yn-1-ols **72**

Initially, the cycloisomerization/Friedel-Crafts alkylation or pentadienyl cation cyclization of **72a** by the use of a variety of Lewis and Brønsted acid catalysts was examined to establish the reaction conditions (Table 3.1). This initial study revealed that treatment of **72a** with 5 mol% of AuCl and 5 mol% AgOTf in toluene at reflux gave the indenyl-fused indole **73a** in 74% yield along with the side product **77**^{52,53} in 25% yield (Table 3.1, entry 1). The structure of indole **73a** was confirmed by ¹H NMR analysis and X-ray crystal structure determination of two closely related products (*vide infra*).^{54,55} Similarly, the structure of α,β -unsaturated byproduct was determined by ¹H NMR analysis and X-ray crystallography (Figure 3.1). Subsequent studies showed that introduction of HMPA resulted in an increase in product yield of **73a** and formation of **74a**⁵⁹ as a side product in 6% yield (Table 3.1, entry 2). By using CaSO₄ to remove water from the reaction and in combination with HMPA,

Table 3.1 Optimization of the reaction conditions^a

Entry	Catalyst	Solvent	Yield (%) ^b			
			73a	74a	77	78
1	AuCl/AgOTf	PhMe	74	-	25	-
2 ^c	AuCl/AgOTf	PhMe	87	6	-	-
3 ^d	AuCl/AgOTf	PhMe	94	-	-	-
4 ^e	AuCl/AgOTf	PhMe	20	-	67	-
5 ^f	AuCl/AgOTf	PhMe	-	-	87	-
6	AuCl/AgOTf	(CH ₂ Cl) ₂	44	-	40	-
7	AuCl/AgOTf	THF	- ^e	-	-	-
8	AuCl/AgOTf	MeCN	-	-	80	-

^aAll reactions were performed with 0.2 mmol of **72a** in the presence of 5 mol % of catalyst (AuCl/AgOTf ratio = 1:1) at reflux for 17 h.

Table 3.1 (*continued*)

Entry	Catalyst	Solvent	Yield (%) ^b			
			73a	74a	77	78
9	AuCl/AgOTf	1,4-dioxane	25	-	55	-
10	AuCl/AgOTf	DMSO	- ^e	-	-	-
11	AuCl/AgSbF ₆	PhMe	65	32	-	-
12	AuCl/AgPF ₆	PhMe	38	-	-	-
13	AuCl ₃ /AgOTf	PhMe	61	24	-	-
14	Ph ₃ PAuCl/AgOTf	PhMe	32 ^g	11	-	-
15	82 /AgOTf	PhMe	38 ^g	26	-	-
16	20 /AgOTf	PhMe	5	-	-	52
17	38 /AgOTf	PhMe	12	10	76	-
18	84 /AgOTf	PhMe	3	-	72	-
19	AuCl	PhMe	42	20	-	-
20	AuCl ₃	PhMe	32	24	-	-
21	Ph ₃ PAuCl	PhMe	17 ^g	12	-	-
22	Ph ₃ PAuNTf ₂	PhMe	14	-	-	47
23	83	PhMe	12 ^g	7	-	-
24	85	PhMe	8	57	-	-
25	PtCl ₂	PhMe	12	-	-	-
26	AgOTf	PhMe	-	45	-	-
27 ^d	AgOTf	PhMe	16	48	-	-
28	FeCl ₃	PhMe	22	-	-	-

^aAll reactions were performed with 0.2 mmol of **72a** in the presence of 5 mol % of catalyst (Au/Ag ratio = 1:1) at reflux for 17 h.

Table 3.1 (*continued*)

Entry	Catalyst	Solvent	Yield (%) ^b			
			73a	74a	77	78
29	Yb(OTf) ₃	PhMe	12	-	-	-
30	Cu(OTf) ₂	PhMe	15	-	-	-
31	InCl ₃	PhMe	21	-	-	-
32	TfOH	PhMe	11	-	-	-
33 ^d	TfOH	PhMe	13	-	-	-
34	<i>p</i> -TSA.H ₂ O	PhMe	- ^h	-	-	-

^aAll reactions were performed with 0.2 mmol of **72a** in the presence of 5 mol % of catalyst at reflux for 17 h. ^bIsolated yield. ^cReaction performed with 20 mol % of HMPA for 2 h. ^dReaction performed with 20 mol % of HMPA and CaSO₄ (35 mg) for 2 h. ^eReaction performed with 20 mol % of DMI and CaSO₄ (35 mg) for 2 h. ^fReaction performed with 20 mol % of DMAP and CaSO₄ (35 mg) for 2 h. ^gRecovery of **72a** in 18-64% yield. ^hMixture of unknown side products furnished based on ¹H NMR analysis of the crude mixture.

formation of **74a** byproduct could be suppressed to give **73a** in 94% yield (Table 3.1, entry 3). By contrast, an inspection of entries 4-10 in Table 3.1 shows that repeating the reaction with DMI or DMAP in place of HMPA or in other solvents was markedly less effective. Similarly, a survey of other Lewis and Brønsted acid catalysts did not provide improved results (Table 3.1, entries 11-34). In these latter reactions, a number of the conditions examined also led to either the recovery of the starting alcohol **72a** in yields up to 64% or gave the (*Z*)-indolin-3-ol **78**⁵⁶ as an additional side product

whose structure was determined by ^1H NMR and X-ray crystallographic analysis (Figure 3.2). More notably, the low catalytic activities observed in reactions mediated by TfOH, AgOTf and other metal triflates also provided evidence to rule out a process promoted by the Brønsted acid and that the cationic Au(I) complex is the active catalytic species (Table 3.1).

(a) **73f** (b) **77**

Figure 3.1 ORTEP drawing of (a) **73f** and (b) **77** with thermal ellipsoids at 50% probability levels^{53,54}

Figure 3.2 ORTEP drawing of (Z)-2-benzylidene-3-phenyl-1-tosylindolin-3-ol **78** with thermal ellipsoids at 50% probability levels⁵⁶

To define the scope of the present procedure, the reactions of a variety of 1-phenyl-1-(2-tosylaminophenyl)prop-2-yn-1-ols **72** were examined (Table 3.2). These experiments showed that with AuCl/AgOTf as the catalyst, starting alcohols **72b-k** and **72m** efficiently underwent the tandem cycloisomerization/Friedel-Crafts alkylation or pentadienyl cation cyclization and gave the corresponding indoles **73b-k** and **73m** in good to excellent yields (Table 3.2, entries 1-10 and 12). The structure of **73f** was also confirmed by X-ray crystal analysis (Figure 3.1)⁵⁴ Under the standard conditions, the reaction of *o,p*-dimethylaniline alcohol **72l** gave a mixture of decomposition products based on TLC and ¹H NMR analysis of the crude mixture (Table 3.2, entry 11).

Table 3.2 Tandem cycloisomerization/Friedel-Crafts alkylation or pentadienyl cation cyclization of **72b-m** catalyzed by AuCl/AgOTf^a

Entry	Substrate	Product	Yield (%) ^b
1	72b-d		73b , R = Me 91
2			73c , R = Cl 86
3			73d , R = Br 87
4	72e		73e , R ¹ = Me, R ² = H 82 ^c 73e' , R ¹ = H, R ² = Me
5	72f-i		73f , R = <i>p</i> -F-C ₆ H ₄ 94
6			73g , R = <i>p</i> -Cl- C ₆ H ₄ 91
7			73h , R = <i>p</i> -OMe-C ₆ H ₄ 46
8			73i , R = <i>p</i> -Me-C ₆ H ₄ 76
9	72j-l		73j , R ¹ = Br, R ² = H 90
10			73k , R ¹ = Cl, R ² = H 86
11			73l , R ¹ = R ² = Me - ^d

Table 3.2 (continued)

Entry	Substrate	Product	Yield (%) ^b
12	<p>72m</p>	<p>73m</p>	82

^aAll reactions were performed with 0.2 mmol of **72** in the presence of 5 mol% of AuCl and AgOTf, 20 mol% of HMPA and CaSO₄ (35 mg) in toluene at reflux for 2 hours. ^bYield of isolated product. ^cIsolated as an inseparable mixture of regioisomers in a 2:1 ratio. ^dMixture of unknown side products obtained based on ¹H NMR analysis of the crude mixture.

Having established the reaction conditions that gave indenyl-fused indoles, the scope of this new methodology for the synthesis of 2,3-disubstituted indoles was examined (Table 3.3). As mentioned earlier, it was anticipated such control of product chemoselectivity could be achieved by varying the nature of the R¹ group on the alkynyl moiety in 1-phenyl-1-(2-(tosylamino)phenyl)prop-2-yn-1-ols **72**. With this in mind, the reaction of the terminal acetylenic alcohols **72n** and **72o** was tested with 5 mol% of AuCl and AgOTf under the standard conditions and found 3-hydroxymethylindoles **74b** and **74c** could be obtained in 77 and 86% yield, respectively (Table 3.3, entries 1 and 2). Under similar conditions, repeating the reaction of **72n** in the presence of MeOH or 2,6-dimethylphenol gave the corresponding 2-methoxymethyl-1*H*-indole **75a** and 2-arylmethylindole **75b** in 82 and 76% yield, respectively (Table 3.3, entries 3-4). Likewise, the reactions of **72p-t** with a alkyl group at the terminal of the acetylenic proceed well and furnished the

Table 3.3 Synthesis of (1*H*-indol-2-yl)methanols **74**, 2-alkyl-1*H*-indoles **75** and 2-vinyl-1*H*-indoles **76** catalyzed by AuCl/AgOTf^a

Entry	Substrate	Product	Yield (%) ^b
1	72n-o	74b , R = H	77
2		74c , R = Me	86
3 ^c	72n	75a	82
4 ^d		75b	76
5	72p-q	76a , R = H	90
6		76b , R = <i>n</i> Pr	80
7	72r-t	76c , <i>n</i> = 1	86
8		76d , <i>n</i> = 3	86
9		76e , <i>n</i> = 4	87

^aAll reactions were performed with 0.2 mmol of **72** in the presence of 5 mol % of AuCl and AgOTf, 20 mol% of HMPA and CaSO₄ (35 mg) in PhMe at reflux for 2 h.

^bIsolated yield. ^cReaction conducted in the presence of 8 equiv of MeOH. ^dReaction conducted in the presence of 8 equiv of 2,6-dimethylphenol.

corresponding 2-vinyl-1*H*-indoles **76a-e** in excellent yields (Table 3.3, entries 5-9). In these latter reactions, the structure of **76e** was also confirmed by X-ray structural analysis (Figure 3.3)⁵⁵ and no other side products were detected by TLC and ¹H NMR analysis of the crude mixtures.

Figure 3.3 ORTEP drawing of 2-(cyclohexyldenemethyl)-3-phenyl-1-tosyl-1*H*-indole (**76e**) with thermal ellipsoids at 50% probability levels⁵⁵

Although the isolation of (*Z*)-indolin-3-ol **78** furnished from reactions of **72a** catalyzed by **20**/AgOTf or Ph₃PAuNTf₂ outlined in entries 16 and 22 in Table 3.1 was fortuitous, the result argues in favour of the mechanism put forward in Scheme 3.1. This was further corroborated by the observation that when a solution of **78** in toluene was treated with 5 mol% of AuCl and AgOTf under the conditions shown in Scheme 3.2, the expected indenyl-fused indole **73a** was obtained in 98% yield. The role of the gold catalyst in facilitating the dehydroxylation step could also be shown by repeating

the reaction in the absence of the metal catalyst, which gave **74a** (see page 43) along with recovery of the starting indolin-3-ol **78** in 10 and 90% yield, respectively.

Scheme 3.2 Gold-catalyzed intramolecular Friedel-Crafts alkylation of **78**

Even though the above results provide evidence for the mechanism outlined in Scheme 3.1, other possible pathways were considered but then discounted based on the following control experiments. As gold carbene species are often proposed in alkyne cycloisomerization reactions mediated by the metal catalyst, the reactions of **72n** with Ph₂SO and styrene catalyzed by AuCl/AgOTf under the standard conditions were first examined.⁵⁷ Analysis of the crude mixtures of these reactions by ¹H NMR spectroscopy revealed no adducts resulting from trapping of such a putative species by Ph₂SO or styrene. This test afforded **74b** in 72-75% yield in both experiments, and led to the rationale that an alternative mechanism for the present reaction involving formation of a gold carbene intermediate was unlikely. Experiments that show the near quantitative recovery of the starting materials for the reactions of **74a**⁵⁹ in the presence or absence of 2,6-dimethylphenol as well as that for **77** exposed to 5 mol % of AuCl/AgOTf under the standard conditions led to also rule out the possibility of indole formation proceeding via intermediates of the type **74** or **77** (see page 43 and 46).

The beneficial effect of added HMPA led to the initial consideration that its role as that of a ligand that moderates the reactivity of Au catalyst through coordination to

the metal centre in a similar manner to that reported for lanthanide salts.⁵⁸ Indeed, this speculation was supported by ^{31}P NMR measurements of an equimolar sample of $\text{AuCl}/\text{AgOTf} + \text{HMPA}$ that shows the phosphorus resonance to shift downfield by $\delta = 3.3$ ppm relative to the respective signal in free HMPA ($\delta = 23.5$ ppm). Further analysis of this mixture by ESI high resolution mass spectrometry also reveals the presence of a peak at m/z 526 that could be assigned to $[\text{AuCl}/\text{AgOTf} + \text{HMPA} + \text{H}]^+$. This evidence is comparable to the data reported for lanthanide HMPA complexes.⁵⁸ However, a marked downfield shift from $\delta = 9.41$ to 10.1 and 10.41 ppm of the NH proton signal in the respective ^1H NMR spectra of **72a** and **72a** + AuCl/AgOTf , presumably resulting from hydrogen-bonding, upon addition of HMPA implies it could also play a dual role in promoting the cycloisomerization process. A lower product yield obtained for the reaction of **72a** catalyzed by AuCl/AgOTf in the absence of HMPA (entry 1 in Table 3.1) would certainly suggest that such interactions are a possibility. In addition to the complex formation between HMPA-Au, HMPA could also involve in stabilizing the cationic intermediates.

3.3 Conclusion

In summary, gold-catalyzed synthetic route to indenyl-fused and 2,3-disubstituted indoles from a common vinyl gold species generated *in situ* from easily accessible propargylic alcohol substrates under mild conditions has been reported. Uniquely, the reactions were found to only proceed efficiently and with complete control of product chemoselectivity for a wide variety of starting alcohols.

Chapter IV. Gold-Catalyzed Cycloisomerizations of 1-(2-Tosylaminophenyl)prop-2-yn-1-ols to 1*H*-Indole-2-carbaldehydes

4.1 Introduction

1*H*-Indole-2-carbaldehydes are immensely important targets in organic synthesis because of their frequent use as building blocks in numerous strategies to natural products and bioactive compounds of current therapeutic interest.⁶⁰ The presence of the vinyl iodide moiety in (*E*)-2-iodomethyleneindolin-3-ols also makes this class of compounds a potentially valuable coupling partner in the field of transition metal-catalyzed cross-coupling reactions.⁶⁶ Generally, synthetic methods to the former has relied upon oxidation or formylation of a pre-functionalized indole substrate while there are no known examples to the latter. In the case of 1*H*-indole-2-carbaldehyde synthesis, this is far from ideal as each step in a stepwise transformations often requires their own set of stoichiometric or excess amounts of various reagents that can lead to equimolar or more amounts of waste products. In this regard, it is therefore surprising to find that single step or one-pot intramolecular strategies to these synthetically useful compounds have not been widely investigated. This is all the more so given the myriad of works to other members of the indole family using this more atom economical synthetic approach.^{44,45,63} Hence, synthetic methods to 1*H*-indole-2-carbaldehydes and (*E*)-2-iodomethylene-indolin-3-ols that can construct both the indole ring and aldehyde or vinyl iodide moiety in a one step or one pot manner from readily available, low cost and simple acyclic substrates are desirable.

Within the emerging field of Lewis acidic gold catalysis,⁸ the *in situ* formation of a putative vinyl gold species is often put forward as a key intermediate in reactions involving alkyne substrates. Evidence for the involvement of this transient

organometallic intermediate was first reported by Hammond and co-workers using ^1H NMR measurements obtained from monitoring the gold-catalyzed intramolecular cycloisomerization of allenoates to γ -lactones.^{48c} Added to this was the synthesis of a γ -iodolactone when the reaction was repeated in the presence of iodine. At about the same time, Fürstner and co-workers described the formation of a vinyl gold intermediate could also be detected by ^1H NMR spectroscopy in a study focused on the rearrangement of 3,3-disubstituted cyclopropenes mediated by of $[\text{Au}(\text{PPh}_3)]\text{NTf}_2$.^{48b} More recently, Hashmi and co-workers unambiguously demonstrated the gold-catalyzed cycloisomerization of *N*-propargyl carboxamides to aromatic oxazoles with $[\text{IPrAu}]\text{OTf}$ s proceeded via a vinyl gold species by isolating and characterizing the organometallic complex by X-ray crystallography.^{48a} Following these seminal works, an increasing number of reports have provided further ^1H NMR spectroscopic or X-ray crystallographic evidence for the involvement of such a reactive species in gold-mediated cross-coupling reactions.⁶² In view of this precedent, we reasoned that a strategy that made use of propargylic 1,3-amino alcohols in the presence of a gold catalyst and electrophilic iodide source would hold promise as a new synthetic approach to 1*H*-indole-2-carbaldehydes.

In the previous chapter, it has been described that propargylic alcohols of the type **72** readily underwent gold-mediated tandem cycloisomerization/1,3-allylic alcohol isomerization (1,3-AAI) to give the corresponding (1*H*-indol-2-yl)methanol products **74** (route a in Scheme 4.1).⁶³ Based on this mechanistic rationale, it was envisioned that if iodination instead of protonation could be achieved in the deauration step,⁶⁴ this would deliver the (*E*)-2-iodomethylene-indolin-3-ol **88**, as shown in route b in Scheme 4.1. Under the Lewis acidic conditions, 1,3-allylic alcohol isomerization (1,3-

AAI) followed by elimination of HI from the resultant iodo(1*H*-indol-2-yl)methanol **89** would be expected to give the indole-2-carbaldehyde adduct **90**.

Scheme 4.1 Gold-catalyzed synthetic approach for indole-2-carbaldehydes **90**

In this chapter, the gold(I) complex **85** in combination with *N*-iodosuccinimide (NIS) can effect tandem cycloisomerization of 1-(2-(tosylaminophenyl)prop-2-yn-1-ols **72** is reported (Scheme 4.2). This process provides a synthetic route to 1*H*-indole-2-carbaldehydes **90** in 70-90% yield for a wide variety of alcoholic substrates under mild and operationally simple conditions.

Scheme 4.2 Gold-catalyzed cycloisomerization/formylation of 1-(2-(Tosylamino)phenyl)prop-2-yn-1-ols **72**

4.2 Results and Discussion

All 1-(2-tosylaminophenyl)prop-2-yn-1-ols **72** studied in this work were prepared as illustrated in Scheme 4.3. This involved tosylation of starting material **A** with *p*-TsCl to furnish intermediate **B** followed by the reaction of 2-tosylaminoketone **B** with ethynylmagnesium bromide to furnish the corresponding 1-(2-Tosylaminophenyl)prop-2-yn-1-ols **72**.

Scheme 4.3 Synthesis of 1-(2-(Tosylamino)phenyl)prop-2-yn-1-ols **72**

With this in mind, the cycloisomerization of *N*-(2-(1-hydroxy-1-phenylprop-2-ynyl)phenyl)-4-methylbenzenesulfonamide **72n** was first examined by a variety of Lewis acid catalysts to establish the reaction conditions. This initially revealed that treatment of **72n** with 5 mol% of the gold(I) complex **85** and 2 equiv of NIS in toluene at room temperature for 0.5 h afforded (*E*)-2-iodomethylene-3-phenyl-1-tosylindolin-3-ol **88a** in 85% yield (Table 4.1, entry 1). The structure of the indolinol **88a** was confirmed by ¹H NMR analysis and X-ray crystallographic determination of

a closely related compound **88c** (see Figure 4.1).⁶⁵ Prolonging the reaction time from 0.5 for 24 h at room temperature was found to have no effect on converting **88a** to the desired 1*H*-indole-2-carbaldehyde product **90**. It has been found that this could be achieved on repeating the reaction in toluene at reflux for 3 h, giving **90** in 90% yield (Table 4.1, entry 2). A further increase in the product yield to 98% was achieved when acetone instead of toluene was employed as solvent (Table 4.1, entry 3). On the other hand, lower product yields of 62-72% were obtained when the reaction was performed in CH₂Cl₂ and 1,2-dichloroethane (Table 4.1, entries 4 and 5). Longer reaction times were also required for the complete consumption of the starting material. Similarly, a survey of other Lewis acidic catalysts did not give improved results (Table 4.1, entries 6-11). In these reactions, either lower product yields along with the formation of (1*H*-indol-2-yl)methanol **74b** as a side product or recovery of the starting alcohol was found. In addition, the reaction with NIS alone with toluene as the solvent led to recovery of the alcohol **72n** in near quantitative yield (Table 4.1, entry 12). Furthermore, the use of iodine in the absence of metal catalyst, which has been reported to catalyze a closely related reaction,^{45h} did not lead to indole-2-carbaldehyde **90** under our conditions.

Table 4.1 Optimization of the reaction condition^a

Entry	Catalyst	Solvent	Time (h)	Yield (%) ^b		
				90a	88a	74b
1 ^c	85	PhMe	0.5	-	85	-
2	85	PhMe	3	90	-	-
3	85	(CH ₃) ₂ CO	2	98	-	-
4	85	CH ₂ Cl ₂	16	62	-	-
5	85	(CH ₂ Cl) ₂	16	72	-	-
6	[Au(PPh ₃)]NTf ₂	(CH ₃) ₂ CO	6	82	-	-
7	83	(CH ₃) ₂ CO	16	85	-	-
8	AuCl/AgOTf	(CH ₃) ₂ CO	16	72	-	-
9	CuOTf ₂	(CH ₃) ₂ CO	16	20	-	25
10	InOTf ₂	(CH ₃) ₂ CO	16	-	-	-
11	AgOTf	(CH ₃) ₂ CO	16	21	-	27
12 ^d	NIS	PhMe	16	-	-	-

^aUnless otherwise stated, all reactions were performed with 0.2 mmol of **72n** in the presence of 5 mol% of catalyst and 0.4 mmol of NIS at reflux for 16 h. ^bIsolated yield.

^cReaction performed with NIS at room temperature. ^dReaction performed at room temperature and led to the near quantitative recovery of the starting material **72n**.

Having established the reaction conditions, the scope of the present method to a variety of terminal propargylic alcohols was examined (Table 4.2). These experiments showed that reaction of alcohols **72u-e** with 5 mol% of gold(I) complex **85** and 2 equiv of NIS as electrophilic source gave the corresponding indole-2-carbaldehyde in good to excellent yields. The reactions of substrates containing an electron-donating group on the aryl ring which were well tolerated and afforded the corresponding products **90b-c** in good yields of 70-75% (Table 4.2, entries 1 and 2). Likewise, the reaction of **72y** with a 3-amido-2-naphthalenyl ring moiety was found to proceed well and furnish the corresponding product **90d** in 78% yield (Table 4.2, entry 5). In contrast, no product formation was observed for reactions of substrates bearing an electron withdrawing group on the aromatic ring **72w-x**, even on prolonged the reaction time to 18 h (Table 4.2, entry 3 and 4). In these reactions, only the *trans* vinyl iodide intermediates **88b** and **88c** were obtained in 98 and 96% yields, respectively. On the other hand, reactions of alcohols **72o** and **72a-δ** with an electron-donating or electron-withdrawing or sterically bulky substituent in the phenyl group on the carbinol carbon furnished the corresponding products **90f-j** in high yields of 82-90% (Table 4.2, entries 7-11). Similarly, the reaction of **72ε** bearing a methyl group at the carbinol carbon was found to lead to the formation of 3-methyl-1-tosyl-1*H*-indole-2-carbaldehyde **90k** in 79% yield at room temperature for 0.5 h (Table 4.2, entry 12). Under the standard reaction conditions, *o,p*-dimethylaniline alcohol **72z** gave a mixture of decomposition products based on TLC and ¹H NMR analysis of the crude mixture (Table, 4.2, entry 6). Similarly, the reaction of the secondary alcohol **72ζ** gave a mixture of decomposition products under the standard conditions. Repeating this reaction at room temperature gave (*E*)-2-iodomethylene-1-tosylindolin-3-one **91** in 78% yield (Table 4.2, entry 13). While this result points to NIS-mediated oxidation

of the hydroxyl group, whether this occurred before or after the cycloisomerization step remains not clear.⁶⁷

Table 4.2 Gold-catalyzed synthesis of indole-2-carbaldehyde **90**^a

Entry	Alcohol	Product	Yield (%) ^b
1	72u-v	90b , R = Me	75
2		90c , R = OMe	70
3	72w-x	88b , R = Cl	98 ^c
4		88c , R = Br	96 ^c
5	72y	90d	78
6	72z	90e	- ^e
7	72o and 72a-β	90f , R = Me	88
8		90g , R = Br	87
9		90h , R = Cl	85

Table 4.2 (continued)

Entry	Alcohol	Product	Yield (%) ^b
10	72γ	90i	90
11	72δ	90j	82
12	72ε	90k	79 ^d
13	72ζ	91	78 ^d

^aUnless otherwise stated, all reactions were performed with 0.26 mmol of **72** in the presence of 5 mol% of gold(I) complex **85** and 0.53 mmol of NIS in acetone at reflux for 2-3 h. ^bIsolated yield. ^cReaction performed at reflux for 18 h. ^dReaction performed at room temperature for 0.5 h. ^eMixture of unknown side products obtained based on ¹H NMR analysis of the crude mixture.

Given that vinyl iodides are invaluable coupling partners in transition metal mediated cross-coupling reactions,⁶⁶ the generality of this approach was further explored as a means to selectively access the intermediate (*E*)-2-iodomethylene-3-phenyl-1-tosylindolin-3-ol **88** in these reactions (Table 4.3). These experiments showed that treating **72** with 5 mol% of the gold(I) complex **85** and 2 equiv of NIS in acetone at room temperature for 0.25 h afford the corresponding (*E*)-2-iodomethylene-3-phenyl-1-tosylindolin-3-ols **88a-d** in 82-99% yield (Table 4.3, entries 1-4). The structure of **88c** was confirmed by X-ray crystal structure analysis (Figure 4.1).⁶⁵

Table 4.3 Gold-catalyzed synthesis of vinyl iodides **88a-d**^a

Entry	Substrate	Product	Yield (%) ^b
1	72n	88a	99
2	72w	88b	98 ^c
3	72x	88c	96 ^c
4	72y	88d	82

^aAll reactions were performed with 0.26 mmol of **72** in the presence of 5 mol% of gold(I) complex **85** and 0.53 mmol of NIS in acetone at room temperature for 0.25 h. ^bIsolated yield. ^cReaction performed for 1 h.

Figure 4.1 ORTEP drawing of **88c** with thermal ellipsoids at 50% probability levels⁶⁵

To demonstrate that (*E*)-2-iodomethylene-3-phenyl-1-tosylindolin-3-ol **88** is the actual intermediate in the Au(I)-catalyzed cyclization of propargylic alcohols of the type **72** to indole-2-carbaldehydes **90**, the control experiments performed as outlined in Scheme 4.4. The role of the gold catalyst in facilitating the 1,3-allylic alcohol isomerization and subsequent process was demonstrated by the formation of **90a** in 98% yield from **88a** under the conditions described in Scheme 4.4, eq 1. This was supported by repeating this experiment in the absence of the gold catalyst showing the recovery of **88a** in near quantitative yield (Scheme 4.4, eq 2). In another experiment, reaction of **74b** with 2 equiv of NIS was also found to lead to the recovery of the starting (1*H*-indol-2-yl)methanol (Scheme 4.4, eq 3).⁶⁷ Along with ¹H NMR analysis of the crude reaction mixture showing the corresponding aldehyde **90** could not be detected, this led to the unlikely possibility of a reaction pathway involving the oxidation of alcohol **74b** with NIS.

Scheme 4.4 Experiments conducted to elucidate the mechanism

4.3 Conclusion

In summary, an efficient synthetic strategy to 1*H*-indole-2-carbaldehydes whereby both the indole and formyl groups are formed from 1,3-AAI of an acyclic alcoholic substrate under mild conditions has been described. On the whole, the reaction was shown to tolerate a variety of starting alcoholic substrate containing electron-donating, electron-withdrawing, and sterically demanding groups. Uniquely, the reactions were also shown to proceed most efficiently with gold catalysts containing a bulky ligand. By controlling the reaction temperature, the chemoselective outcome of the reaction could be fine-tuned to give the (*E*)-2-iodomethylene-3-phenyl-1-tosylindolin-3-ol. This is also noteworthy that iodomethylene indolinols are readily prepared which would be employed as coupling partners in transition metal catalyzed cross coupling reactions.

Chapter V. Cyclopropyl Carbinol Rearrangement for Benzofused Nitrogen Ring Synthesis

5.1 Introduction

Transition metal-catalyzed ring openings of cyclopropanes offer a highly efficient and convenient synthetic route to nitrogen heterocycles.⁶⁸ By exploiting the inherent ring strain in these three-membered cyclic structures, no pre-functionalization is required and the reactions can, in theory, be atom economical and afford minimal waste products. The field has received an immense amount of attention over the years, with a myriad of metal-mediated methods for *N*-heterocycles synthesis being developed.^{68,69} Those that make use of a cyclopropyl carbinol-based strategy, by contrast, have been less widely investigated.⁷⁰ While our group recently delineated one such process that made possible the conversion of cyclopropyl carbinols and aryl sulfonamides to pyrrolidines using gold catalysis, applications to other nitrogen ring systems have remained rare (Scheme 5.1).²⁶

Scheme 5.1 Gold-catalyzed tandem ring opening/amination of cyclopropyl carbinols with sulfonamides

In this context, further exploration of this chemistry led to 2-tosylamino phenylcyclopropyl carbinols **92** (Scheme 5.2). It was reasoned that this reactive class of compounds might also undergo ionization through coordination of the hydroxyl functional group of the substrate with a gold catalyst.^{7,8} The resultant carbocationic

species **96** formed *in situ* would be susceptible to cyclopropyl carbinol rearrangement followed by trapping by the tethered aniline moiety when R^1 = alkyl or aryl and afford the 2,3-dihydro-1*H*-benzo[*b*]azepine product **93** (route a in Scheme 5.2). On the other hand, it was anticipated that a carbocationic species generated from a secondary alcohol containing a disubstituted cyclopropane ring would be prone to a more rapid ring opening process that leads to the formation of the diene **97** (route b in Scheme 5.2).⁷¹ Subsequent gold-mediated intramolecular diene hydroamination, of which there are only a handful of examples of this type of C–N bond forming process in the literature,⁷² would then be expected to deliver the 2-vinyl indoline **94**.⁷³ In this chapter, the details of this chemistry that might offer an approach to these two structurally important bioactive classes of benzofused nitrogen heterocycles are described.^{26,71e} The synthetic approach also provides an alternative method for 2,3-dihydro-1*H*-benzo[*b*]azepine **93** synthesis that does not rely on a ring closing alkene metathesis strategy.⁷⁴

Scheme 5.2 Cyclopropyl carbinol rearrangement for benzofused nitrogen ring synthesis

5.2 Results and Discussion

All 2-tosylaminophenylcyclopropyl carbinols **92** studied in this work were prepared as shown in Scheme 5.3. This initially involved tosylation of the corresponding 2-aminophenylketone **A** with *p*-TsCl to give the 2-tosylaminophenylketone intermediate **B**. The tertiary cyclopropyl carbinols studied in this work were prepared from reaction of the corresponding 2-tosylaminophenylketone **B** with cyclopropyl magnesium bromide as shown in eq 1 in Scheme 5.3. Likewise, cyclopropanation of compound **C** with trimethylsulfoxonium iodide in the presence of base following the literature procedure gave the compound **D**. Subsequent reduction of this cyclopropylketone adduct with NaBH₄ afforded the corresponding secondary cyclopropyl carbinols as

shown in eq 2 in Scheme 5.3.^{78a,b}

Scheme 5.3 Synthesis of 2-tosylaminophenylcyclopropyl carbinols **92**

The cyclopropyl carbinol rearrangement of *N*-(2-(1-cyclopropyl-1-hydroxy ethyl) phenyl)-4-methylbenzene sulfonamide **92a** was examined by a variety of Lewis and Brønsted acid catalysts to establish the reaction conditions (Table 5.1). The best result was obtained by treating **92a** with 5 mol% of (*p*-CF₃C₆H₄)₃PAuCl and 5 mol% of AgOTf in toluene at reflux for 2 h, which gave 5-methyl-1-tosyl-2,3-dihydro-1*H*-benzo[*b*]azepine **93a** in 81% yield (Table 5.1, entry 1). The structure of the 2,3-dihydro-1*H*-benzo[*b*]azepine product was established on the basis of ¹H NMR spectroscopy measurements and X-ray crystallography (Figure 5.1).⁷⁵ By contrast, the reaction in other solvents was markedly less effective (Table 5.1, entries 2-5). Use of CH₂Cl₂ and 1,2-dichloroethane as solvents as well as 1,4-dioxane afforded the vinyl cyclopropane (VCP) byproduct **99** in 24-78% yield (Table 5.1, entries 2-4). Changing the solvent from toluene to MeNO₂ was found to result in no reaction with recovery of the substrate (Table 5.1, entry 5). Similarly, a survey of other Lewis and Brønsted acid catalysts did not provide any improvements (Table 5.1, entries 6-22). In all but one of these latter experiments, the VCP byproduct **99** was again obtained as either the only or major product or no reaction was observed. The analogous reaction of **92a**

catalyzed by 5 mol% of AuCl and 5 mol% of AgOTf in toluene was the only instance in which we found **93a** could be furnished in a high yield of 72% (Table 5.1, entry 7). More notably, the low catalytic activities observed in reactions mediated by TfOH, AgOTf and other metal triflates also provided evidence to rule out a process promoted by the Brønsted acid and that the cationic Au(I) complex is the active catalytic species.

Table 5.1 Optimization of the reaction conditions^a

Entry	Catalyst	Solvent	Yield (%) ^b	
			93a	99
1 ^c	(<i>p</i> -CF ₃ C ₆ H ₄) ₃ PAuCl/AgOTf	PhMe	81	-
2	(<i>p</i> -CF ₃ C ₆ H ₄) ₃ PAuCl/AgOTf	CH ₂ Cl ₂	-	44
3	(<i>p</i> -CF ₃ C ₆ H ₄) ₃ PAuCl/AgOTf	(CH ₂ Cl) ₂	10	78
4	(<i>p</i> -CF ₃ C ₆ H ₄) ₃ PAuCl/AgOTf	1,4-dioxane	18	24
5 ^d	(<i>p</i> -CF ₃ C ₆ H ₄) ₃ PAuCl/AgOTf	MeNO ₂	-	-
6	Ph ₃ PAuCl/AgOTf	PhMe	-	81
7 ^c	AuCl/AgOTf	PhMe	72	-
8	AuCl ₃ /AgOTf	PhMe	10	36
9	(4-CF ₃ C ₆ H ₄) ₃ PAuCl	PhMe	12	-
10 ^d	Ph ₃ PAuCl	PhMe	-	5
11 ^d	AuCl	PhMe	8	-
12 ^d	AuCl ₃	PhMe	-	29
13	AgOTf	PhMe	19	63

Table 5.1 (*continued*)

Entry	Catalyst	Solvent	Yield (%) ^b	
			93a	99
14 ^d	AgSbF ₆	PhMe	-	-
15	Cu(OTf) ₂	PhMe	-	73
16	Yb(OTf) ₃	PhMe	-	53
17	FeCl ₃	PhMe	-	51
18	InCl ₃	PhMe	-	63
19	ZnCl ₂	PhMe	-	76
20	BF ₃ .Et ₂ O	PhMe	-	34
21	<i>p</i> -TsOH.H ₂ O	PhMe	-	60
22	TfOH	PhMe	7	67

^aAll reactions were performed with 0.3 mmol of **92a** in the presence of 5 mol% of catalyst at reflux for 18 h. ^bIsolated yield. ^cReaction performed for 2 h. ^dRecovery of **92a** in 52-80% yield.

Figure 5.1 ORTEP drawing of **93a** with thermal ellipsoids at 50% probability levels⁷⁵

To investigate the scope of this method for the synthesis of benzoazepines, a variety of tertiary 2-tosylaminophenylcyclopropyl carbinols **92** was evaluated and the results are summarized in Table 5.2. In general, fortunately the present reaction was found to be broad, delivering a variety of substituted 2,3-dihydro-1*H*-benzo[*b*]azepines **93** in good to excellent yields. Starting alcohols with a phenyl ring and its derivatives with an electron-withdrawing or electron-donating group at the *para* position were found to proceed well, affording the corresponding benzoazepines **93b-e** in excellent yields of 83-87%. Similarly, 2,3-dihydro-1*H*-benzo[*b*]azepines **93f-j** containing substituents on the benzofused ring structure were obtained in good to excellent yields of 46-92% from the corresponding cyclopropyl carbinols **92f-j**. The structures of **93b** and **93j** were confirmed by X-ray crystallographic analysis (Figure 5.2).⁷⁵ Under the standard conditions, disubstituted cyclopropane **92k** furnished a mixture of decomposition products based on TLC and ¹H NMR analysis of the crude mixture. More notably, the above mentioned reactions also demonstrated the electronic nature of the aniline moiety was found to play role on reactivity. On changing the group at the *para* position of the ring from Me to H to Br to Cl on going from **92f** → **92b** → **92g** → **92h**, product yields gradually decreased.

Table 5.2 (*p*-CF₃C₆H₄)₃PAuCl/AgOTf-catalyzed cyclopropyl carbinol rearrangement of **92b-k**^a

Substrates

Products

^aAll reactions were performed with 0.3 mmol of **92** in the presence of 5 mol% of (*p*-CF₃C₆H₄)₃PAuCl/AgOTf in PhMe at reflux for 2-3 h. ^bValues in parenthesis represent isolated yields (%). ^cReaction performed for 17 h. ^dMixture of unknown side products furnished based on ¹H NMR analysis of the crude mixture.

(a) 93b

(b) 93j

Figure 5.2 ORTEP drawing of (a) **93b** and (b) **93j** with thermal ellipsoids at 50% probability levels⁷⁵

With the reaction conditions to 2,3-dihydro-1*H*-benzo[*b*]azepines established, the synthesis of 2-vinyl indolines **94** were examined (Table 5.3). As shown earlier in Scheme 5.1, it was anticipated such control in product chemoselectivity could be achieved by simply switching from a tertiary to a secondary alcoholic substrate. With this in mind, we first tested the reaction of *N*-(2-(hydroxy(2-phenylcyclopropyl)methyl)phenyl)-4-methylbenzenesulfonamide **92l** with 5 mol% of (*p*-CF₃C₆H₄)₃PAuCl and 5 mol% of AgOTf under the standard conditions and found that (*E*)-2-styryl-1-tosylindoline **94a** could be obtained in 82% yield. Under similar conditions, the reaction with other secondary alcohols **92m-r** containing either an electron-withdrawing, electron-donating or sterically bulky aryl group on the cyclopropane ring gave the corresponding 2-vinyl indoline products **94b-g** in excellent yields of 78-92% yield. In these latter reactions, the *trans* stereochemistry structure of **94g** was also confirmed by X-ray crystal structure analysis (Figure 5.3)⁷⁵ and no other side products were detected by TLC and ¹H NMR analysis of the crude mixtures. In our hands, (*p*-CF₃C₆H₄)₃PAuCl/AgOTf-catalyzed cyclopropyl carbinol rearrangement of secondary alcohols containing a *n*-pentyl group or no substituents on the cyclopropane ring as in **92s** and **92t** were found to be less successful. Despite increasing the reaction time from 2 to 17 h, we found the reaction of **92s** gave **94h** in a low yield of 23% while that of **92t** resulted in a mixture of decomposition products based on TLC and ¹H NMR analysis of the crude mixture.

Table 5.3 (*p*-CF₃C₆H₄)₃PAuCl/AgOTf synthesis of 2-vinyl indolines **94**^a

Substrate	Product
<p>92l, R = Ph 92m, R = <i>p</i>-F-C₆H₄ 92n, R = <i>p</i>-Cl-C₆H₄ 92o, R = <i>p</i>-Br-C₆H₄ 92p, R = <i>p</i>-Me-C₆H₄</p>	<p>94a, R = Ph, (82) 94b, R = <i>p</i>-F-C₆H₄, (78) 94c, R = <i>p</i>-Cl-C₆H₄, (80) 94d, R = <i>p</i>-Br-C₆H₄, (80) 94e, R = <i>p</i>-Me-C₆H₄, (81)</p>
<p>92q</p>	<p>94f, (90)</p>
<p>92r</p>	<p>94g, (92)</p>
<p>92s</p>	<p>94h, (23)^c</p>
<p>92t</p>	<p>94i, (-)^d</p>

^aAll reactions were performed with 0.2 mmol of **92** in the presence of 5 mol% of (4-CF₃C₆H₄)₃PAuCl/AgOTf in PhMe at reflux for 1.5-3 h. ^bValues in parenthesis represent isolated yield (%). ^cReaction performed for 17 h. ^dMixture of unknown side products furnished based on ¹H NMR analysis of the crude mixture.

Figure 5.3 ORTEP drawing of **94g** with thermal ellipsoids at 50% probability levels⁷⁵

In addition to the above results, the following control experiments illustrated in Scheme 5.4 were conducted to provide further support for the mechanism as well as discount the possibility of other pathways. In view of the competitive formation of the VCP side product **99** from reactions of **92a** under certain conditions described in Table 5.1, this intermediate was treated with 5 mol% of (*p*-CF₃C₆H₄)₃PAuCl and 5 mol% of AgOTf under the standard conditions (Scheme 5.4, eq 1). This test resulted only in the recovery of the VCP substrate **99** in near quantitative yield and led to surmise that an alternative pathway for the present reaction involving the intermediate of **99** was unlikely. Interestingly, this contrasted to a previous study by Togni and co-workers who had demonstrated one example of a closely related VCP to readily

Scheme 5.4 (*p*-CF₃C₆H₄)₃PAuCl/AgOTf-catalyzed reactions of dienes **97a** and **97b**

undergo tandem ring opening/intramolecular hydroamination with TsNH₂ **30a** and give the corresponding pyrrolidine adduct in 64% yield.⁷⁶ Indeed, this was further supported by the fact that when a toluene solution containing **921** was treated with 5 mol% of (*p*-CF₃C₆H₄)₃PAuCl/AgOTf under the conditions shown in eq 2 in Scheme 5.4, the disubstituted *trans*-diene **97a**, whose structure was determined by X-ray crystallography (Figure 5.4),⁷⁵ and **94a** were obtained in yields of 62 and 30%, respectively. On retreating compound **97a** under the standard conditions of 5 mol % of (*p*-CF₃C₆H₄)₃PAuCl/AgOTf in toluene at reflux for 1 h, the expected 2-vinyl indoline **94a** was obtained in 84% yield, which is comparable to that furnished from **921** shown in entry 1 in Table 5.3. The reactivities of the secondary alcohols examined

in Table 5.3 additionally suggest the diene formation process to occur in a step wise manner and thus involve a transient carbocationic species. This explains also the poor results with compounds **92s** and **92t** since the ability to stabilize such an intermediate through resonance stabilization would be expected to rapidly diminish on going from **92l-r** $\rightarrow$ **92s** $\rightarrow$ **92t**. For tertiary alcohols, the mechanism put forward in Scheme 5.2 leading to the 2,3-dihydro-1*H*-benzo[*b*]azepines **93** was supported by repeating the cyclopropyl carbinol rearrangement **92b** under the conditions shown in eq 3 in Scheme 5.4 at shorter reaction times. This showed that **93b** along with recovery of the substrate in yields of 58 and 35%, respectively, but not the trisubstituted diene **97b** was obtained. Indeed, this was further corroborated by the fact that the 1,2-dihydroquinoline **100** was afforded in 92% yield when a toluene solution containing a 1:1 *cis/trans* isomeric mixture of **97b**⁷⁷ was subjected to 5 mol % of (*p*-CF₃C₆H₄)₃PAuCl and AgOTf under the conditions shown in eq 4 in Scheme 5.4.

Figure 5.4 ORTEP drawing of **97a** with thermal ellipsoids at 50% probability levels⁷⁵

It is interesting to note that the contrasting product selectivities found in these control experiments additionally provide an insight into the role of steric effects on chemoselectivity in such C–N bond forming processes. As illustrated in Figure 5.5, it was suggested that formation of the C–N bond preferentially proceeds at the internal C=C bond of the diene when R = alkyl or aryl despite the reaction requiring to undergo an unfavourable 5-*endo*-trig pathway. This could be so that unfavourable steric interactions between the metal and R group can be kept to a minimum upon cyclization. On the other hand, such steric interactions are apparently absent when R = H and the hydroamination process, under reflux conditions, can occur at the terminal C=C bond of the diene in a 6-*exo*-trig manner to give the thermodynamically more stable benzofused six-membered nitrogen ring structure. Additionally, the fact that the *trans* isomer of **97b** can also undergo intramolecular hydroamination suggests that Au–C bond formation is further advanced than N–C bond formation in the transition state depicted in Figure 5.5. This would not be inconceivable given that resultant developing carbocationic charge can be stabilized by the allylic moiety.

Figure 5.5 Possible transition states for $(p\text{-CF}_3\text{C}_6\text{H}_4)_3\text{PAuCl}/\text{AgOTf}$ -catalyzed intramolecular hydroaminations of dienes **97a** and **97b**

5.3 Conclusion

In summary, it has been demonstrated for the first time that cyclopropyl carbinol rearrangement is an effective and chemoselective strategy for the construction of benzofused nitrogen heterocycles. The reaction was shown to tolerate a diverse set of alcoholic substrates and proceed efficiently only in the presence of the gold and silver catalyst combination, furnishing 2,3-dihydro-1*H*-benzo[*b*]azepines and 2-vinyl indolines for application in natural product synthesis and as versatile privileged scaffolds in medicinal chemistry. Previous synthetic approaches to these benzofused nitrogen ring compounds have relied on multistep routes; this method is rapid and makes use of starting materials and a catalytic system that is readily available,

ecologically benign and simple. Efforts to further explore the mechanism, scope and synthetic applications of the present reaction are currently underway.

Chapter VI. Concluding Remarks

Gold-catalyzed intramolecular based approaches for the synthesis of 1,2-dihydroquinolines, indenyl-fused and 2,3-disubstituted indoles, indole-2-carbaldehydes and 2,3-dihydro-1*H*-benzo[*b*]azepines as well as 2-vinyl indolines from alcohol substrates have been established (Figure 6.1). An efficient synthetic route to 1,2-dihydroquinolines that relies on AuCl₃/AgSbF₆-catalyzed intramolecular amination of 1-(2-tosylaminophenyl)prop-2-en-1-ols **65** was described in Chapter II. Uniquely, the reactions were found to only proceed rapidly at room temperature in the presence of the gold and silver catalyst combination and produce the 1,2-dihydroquinoline products **66** in yields of 40-91%. The method was shown to be applicable to a broad range of 1-(2-tosylaminophenyl)prop-2-en-1-ols **65** containing electron-withdrawing, electron-donating, and sterically demanding substrate combinations. The mechanism is suggested to involve activation of the alcohol substrate by the AuCl₃/AgSbF₆ catalyst. This is followed by ionization of the starting material, which causes intramolecular nucleophilic addition of the sulfonamide unit to the allylic cation moiety and construction of the 1,2-dihydroquinoline. The utility of this *N*-heterocyclic ring forming strategy as a synthetic tool that makes use of alcohols as pro-electrophiles was exemplified by its application to the synthesis of the bioactive tetrahydroquinoline alkaloid (±)-angustureine.

In Chapter III, a novel strategy to indenyl-fused and 2,3-disubstituted indoles **73** that relied on a gold-catalyzed cycloisomerization reactions of 1-(2-tosylamino phenyl)prop-2-yn-1-ols **72** was described. A putative indolyl-substituted vinyl gold species **87** generated from AuCl/AgOTf catalyzed cyclization of 1-(2-tosylamino phenyl)prop-2-yn-1-ols **72** and afforded the indenyl-fused indole **73** when R = Ar. On

the other hand, (1*H*-indol-2-yl)methanol products **74** were obtained via protodeauration/1,3-allylic alcohol isomerization (1,3-AAI) of **87** when R = H. Similarly, for reactions in which R = alkyl, a more rapid protodeauration and dehydration step proceeded and furnished 2-vinyl-1*H*-indoles in good to excellent yields of up to 90%. This approach was extended and detailed in Chapter IV, to prepare 1*H*-indole-2-carbaldehydes and (*E*)-2-iodomethyleneindolin-3-ols **88** by gold(I)-catalyzed cycloisomerization of 1-(2-tosylaminophenyl)prop-2-yn-1-ols **72** with *N*-iodosuccinimide (NIS). The reactions were shown to be operationally simplistic and proceed efficiently for a wide variety of substrates, affording the corresponding products in good to excellent yields (80-99%). The mechanism is suggested to involve activation of the alkyne moiety of the substrate by the gold(I) catalyst. This triggers intramolecular addition of the tethered aniline moiety to give a vinyl gold intermediate **87**, which undergoes iododeauration with NIS to give the (*E*)-2-iodomethyleneindolin-3-ol **88**. Subsequent 1,3-allylic alcohol isomerization (1,3-AAI) of this vinyl iodide intermediate **88** then gives the 1*H*-indole-2-carbaldehyde **90** at reflux temperature.

In Chapter V, a synthetic method that relies on gold-catalyzed cyclopropyl carbinol rearrangement of 2-tosylaminophenylcyclopropyl carbinols to prepare 2,3-dihydro-1*H*-benzo[*b*]azepines **93** and 2-vinyl indolines **94** was described. The reactions were shown to be chemoselective with the respective secondary and tertiary alcoholic substrates **92** providing the corresponding benzofused five- and seven-membered ring products exclusively. The ring forming process was also found to only proceed in moderate to excellent yields under mild conditions in the presence of the gold and silver catalyst combination. The mechanism is thought to involve activation of the alcohol by the (*p*-CF₃C₆H₄)₃PAuCl/AgOTf catalyst that results in ionization of

the starting material. The resulted tertiary carbocationic intermediate generated in this manner then triggers ring opening of the cyclopropane moiety and trapping by the tethered aniline moiety to give the 2,3-dihydro-1*H*-benzo[*b*]azepine **93**. Cyclopropane ring fragmentation of the secondary carbocationic analogue, on the other hand, results in diene formation followed by subsequent intramolecular hydroamination to afford the 2-vinyl indoline **94**.

Figure 6.1 Gold-catalyzed synthesis of nitrogen heterocyclic compounds from alcohols

Chapter VII. Experimental Section

7.1 General Remarks

All reactions were performed under an argon atmosphere. 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 plate. Visualization was achieved by UV light (254 nm). Flash chromatography was performed using silica gel and gradient solvent system (EtOAc: *n*-hexane as eluant). ^1H and ^{13}C NMR spectra were measured on 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), brs (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 FTIR spectrometer. Solid samples were examined as a thin film between NaCl salt plates. Low resolution mass spectra were determined on a mass spectrometer and reported in units of mass to charge (m/z). High resolution mass spectra (HRMS) were obtained on a LC/HRMS mass spectrometer.

7.2 Gold-Catalyzed Intramolecular Amination of 1-(2-Tosylaminophenyl) prop-2-en-1-ols. A Concise Synthesis of (±)-Angustureine

General Procedure for the Preparation of *N*-Protected Aniline Substituted Allylic Alcohols **65a-h**

To a solution of the appropriate 1-(2-aminophenyl)ketone (1.1 mmol) in pyridine (0.4 mL) was added *p*-toluenesulfonylchloride (1.6 mmol) at room temperature under nitrogen atmosphere. The resulting solution was stirred for 4 h at room temperature. On completion, the reaction mixture was quenched by adding H₂O (5 mL) and filtered. The resulting solid was dried and used directly for the next step. The solid (0.51 mmol) was dissolved in anhydrous THF (8 mL) and a solution of vinyl magnesium bromide (1 M THF solution, 1.5 mmol) was added at room temperature (note: isopropenyl magnesium bromide (0.5 M THF solution, 1.5 mmol) was used for compounds **65b** and **65c**). The resulting mixture was allowed to reflux for 3 h. On completion, the reaction mixture was cooled to room temperature and treated with saturated NH₄Cl solution (7 mL). After additional stirring at room temperature for 10 min, EtOAc (15 mL) was added, and the organic phase was separated. The aqueous phase was further extracted with EtOAc (3 x 5 mL) and the combined organic layers were washed with brine (20 mL), dried over anhydrous Na₂SO₄ and concentrated under reduced pressure. Purification by flash column chromatography on silica gel (eluent: *n*-hexane: EtOAc = 9: 1) gave the compound **65a-h**.

***N*-(2-(2-Hydroxybut-3-en-2-yl)phenyl)-4-methylbenzenesulfonamide (65a)**

White solid; m.p. 141-144 °C; ^1H NMR (CDCl_3 , 300 MHz): δ 9.28 (1H, brs), 7.70 (2H, d, $J = 8.31$ Hz), 7.55 (1H, dd, $J = 1.08, 8.20$ Hz), 7.11-7.26 (4H, m), 6.93-6.99 (1H, m), 5.87 (1H, dd, $J = 10.63, 17.31$ Hz), 5.15 (1H, d, $J = 17.28$ Hz), 5.04 (1H, d, $J = 10.65$ Hz), 2.36 (3H, s), 1.60 (3H, s); ^{13}C NMR (CDCl_3 , 75 MHz): δ 143.5, 142.6, 137.1, 136.5, 132.2, 129.4, 128.6, 127.3, 126.9, 123.2, 119.8, 113.6, 78.6, 28.8, 21.5; IR (NaCl, neat) ν : 3246, 1487, 1386, 1257, 1159, 1091, 756, 667 cm^{-1} ; MS (ESI) m/z 340 $[\text{M}+\text{Na}]^+$; HRMS (ESI) calcd. for $\text{C}_{17}\text{H}_{20}\text{NO}_3\text{S}$ (M^++H): 318.1164, found: 318.1160.

***N*-(2-(2-hydroxy-3-methylbut-3-en-2-yl)phenyl)-4-methylbenzenesulfonamide (65b)**

White solid; m.p. 135-138 °C; ^1H NMR (CDCl_3 , 400 MHz): δ 9.15 (1H, brs), 7.68 (2H, d, $J = 8.10$ Hz), 7.62 (1H, d, $J = 8.18$ Hz), 7.17 (3H, m), 7.11 (1H, d, $J = 7.80$ Hz), 6.94 (1H, t, $J = 7.60$ Hz), 5.18 (1H, s), 4.87 (1H, s), 2.34 (3H, s), 1.63 (3H, s), 1.30 (3H, s); ^{13}C NMR (CDCl_3 , 100 MHz): δ 148.3, 143.4, 136.9, 136.6, 132.1, 129.3, 128.5, 127.5, 127.2, 123.2, 119.7, 111.6, 78.6, 29.0, 21.4, 19.1; IR (NaCl, neat) ν : 3443, 1338, 1215, 1159, 1091, 756, 655 cm^{-1} ; MS (ESI) m/z 354 $[\text{M}+\text{Na}]^+$; HRMS (ESI) calcd. for $\text{C}_{18}\text{H}_{21}\text{NO}_3\text{SNa}$ (M^++Na): 354.1140, found: 354.1148.

***N*-(2-(1-Hydroxy-2-methyl-1-phenylallyl)phenyl)-4-methylbenzenesulfonamide (65c)**

White solid; m.p. 93-98 °C; ^1H NMR (CDCl_3 , 300 MHz): δ 9.32 (1H, brs), 7.68 (1H, d, $J = 8.19$ Hz), 7.49 (2H, d, $J = 8.26$ Hz), 7.19-7.33 (6H, m), 7.11 (2H, d, $J = 8.10$ Hz), 6.80-6.95 (2H, m), 5.04 (1H, s), 4.50 (1H, s); ^{13}C NMR (CDCl_3 , 75 MHz): δ 143.3, 143.2, 137.2, 136.7, 131.6, 130.0, 129.3, 128.7, 128.2, 127.7, 127.4, 127.4, 122.3, 119.2, 117.0, 84.7, 21.6, 20.1; IR (NaCl, neat) ν : 3427, 1490, 1338, 1215, 1159, 756, 665 cm^{-1} ; MS (ESI) m/z 416 $[\text{M}+\text{Na}]^+$; HRMS (ESI) calcd. for $\text{C}_{23}\text{H}_{23}\text{NO}_3\text{SNa}$ (M^++Na): 416.1296, found: 416.1294.

***N*-(2-(1-Hydroxy-1-phenylallyl)phenyl)-4-methylbenzenesulfonamide (65d)**

White solid; m.p. 120-123 °C; ^1H NMR (CDCl_3 , 300 MHz): δ 9.13 (1H, brs), 7.55 (1H, d, $J = 7.98$ Hz), 7.14-7.28 (8H, m), 7.01-7.09 (3H, m), 6.90 (1H, t, $J = 7.31$ Hz), 6.28 (1H, dd, $J = 10.49, 17.11$ Hz), 5.20 (1H, d, $J = 10.53$ Hz), 4.87 (1H, d, $J = 17.1$ Hz), 3.72 (1H, brs), 2.31 (3H, s); ^{13}C NMR (CDCl_3 , 75 MHz): δ 143.2, 142.2, 136.6, 136.1, 132.1, 129.4, 129.0, 128.8, 128.3, 127.5, 127.3, 126.6, 122.5, 118.8, 115.8, 80.9, 21.5; IR (NaCl, neat) ν : 3258, 1490, 1398, 1261, 1157, 1091, 758, 665 cm^{-1} ; MS (ESI) m/z 402 $[\text{M}+\text{Na}]^+$; HRMS (ESI) calcd. for $\text{C}_{22}\text{H}_{21}\text{NO}_3\text{SNa}$ (M^++Na): 402.1140, found: 402.1136.

***N*-(2-(1-Hydroxy-1-phenylallyl)-5-methylphenyl)-4-methylbenzenesulfonamide
(65e)**

White solid; m.p. 158-162 °C; ^1H NMR (CDCl_3 , 300 MHz): δ 8.79 (1H, brs), 7.32 (1H, s), 7.09-7.24 (7H, m), 6.95 (2H, d, $J = 8.09$ Hz), 6.84 (1H, d, $J = 7.94$ Hz), 6.64 (1H, d, $J = 7.86$ Hz), 6.17 (1H, dd, $J = 10.49, 17.1$ Hz), 5.12 (1H, d, $J = 10.53$ Hz), 4.81 (1H, d, $J = 17.09$ Hz), 2.93 (1H, brs), 2.25 (3H, s), 2.17 (3H, s); ^{13}C NMR (CDCl_3 , 75 MHz): δ 143.4, 143.2, 142.3, 138.9, 136.4, 136.4, 129.3, 129.2, 128.8, 128.3, 127.5, 127.3, 126.5, 123.2, 119.7, 115.5, 80.7, 21.5, 21.2; IR (NaCl, neat) ν : 3018, 1508, 1448, 1396, 1215, 1157, 1091, 756, 667 cm^{-1} ; MS (ESI) m/z 416 $[\text{M}+\text{Na}]^+$; HRMS (ESI) calcd. for $\text{C}_{23}\text{H}_{23}\text{NO}_3\text{SNa}$ (M^++Na): 416.1296, found: 416.1297.

***N*-(4-Chloro-2-(1-hydroxy-1-phenylallyl)phenyl)-4-methylbenzenesulfonamide
(65f)**

White solid; m.p. 106-108 °C; ^1H NMR (CDCl_3 , 300 MHz): δ 7.50 (1H, d, $J = 8.75$ Hz), 7.24-7.32 (5H, m), 7.12-7.19 (3H, m), 7.02-7.06 (3H, m), 6.22 (1H, dd, $J = 10.49, 17.09$ Hz), 5.25 (1H, d, $J = 10.27$ Hz), 4.91 (1H, d, $J = 17.08$ Hz), 2.33 (3H, s); ^{13}C NMR (CDCl_3 , 75 MHz): δ 142.3, 141.5, 135.9, 135.3, 133.8, 129.4, 128.8, 128.7, 128.5, 127.9, 127.3, 126.4, 120.2, 116.6, 80.6, 21.5; IR (NaCl, neat) ν : 3446, 1489, 1386, 1330, 1159, 1089, 756 cm^{-1} ; MS (ESI) m/z 436 $[\text{M}+\text{Na}]^+$; HRMS (ESI) calcd. for $\text{C}_{22}\text{H}_{20}\text{NO}_3\text{SNaCl}$ (M^++Na): 436.0750, found: 436.0754.

N*-(2-(1-Hydroxy-1-phenylallyl)-4-nitrophenyl)-4-methylbenzenesulfonamide*(65g)**

Yellow gum; ^1H NMR (CDCl_3 , 400 MHz): δ 9.32 (1H, brs), 8.06-8.01 (2H, m), 7.67 (1H, d, $J = 9.0$ Hz), 7.37-7.25 (5H, m), 7.21 (2H, d, $J = 7.2$ Hz), 7.08 (2H, d, $J = 8.0$ Hz), 6.41 (1H, dd, $J = 10.52, 17.04$ Hz), 5.43 (1H, d, $J = 10.48$ Hz), 5.04 (1H, d, $J = 17.08$ Hz), 3.20 (1H, br s), 2.34 (3H, s); ^{13}C NMR (CDCl_3 , 100 MHz): δ 144.3, 142.5, 142.0, 141.5, 140.8, 135.1, 132.4, 129.6, 128.7, 128.2, 127.3, 126.3, 124.7, 124.3, 117.7, 117.5, 80.6, 21.5; IR (NaCl, neat) ν : 3442, 3020, 1662, 1489, 1390, 1330, 1156, 1086, 756 cm^{-1} ; MS (ESI) m/z 447 $[\text{M}+\text{Na}]^+$; HRMS (ESI) calcd. for $\text{C}_{22}\text{H}_{20}\text{N}_2\text{O}_5\text{SNa}$ (M^++Na): 447.1289, found: 447.1285.

***N*-(6-(2-Hydroxybut-3-en-2-yl)benzo[*d*][1,3]dioxol-5-yl)-4-methylbenzenesulfonamide (65h)**

White solid; m.p. 121-125 $^{\circ}\text{C}$; ^1H NMR (CDCl_3 , 500 MHz): δ 9.00 (1H, brs), 7.69 (2H, d, $J = 8.28$ Hz), 7.22 (2H, d, $J = 8.05$ Hz), 7.19 (1H, s), 6.62 (1H, s), 5.91 (2H, s), 5.81 (1H, dd, $J = 10.62, 17.30$ Hz), 5.15 (1H, d, $J = 17.30$ Hz), 5.01 (1H, d, $J = 10.65$ Hz), 2.38 (3H, s), 1.50 (3H, s); ^{13}C NMR (CDCl_3 , 125 MHz): δ 147.3, 143.5, 142.6, 137.1, 130.8, 129.4, 128.6, 127.4, 126.1, 113.6, 106.8, 102.6, 101.5, 72.1, 29.0, 21.5; IR (NaCl, neat) ν : 3468, 2981, 1625, 1598, 1506, 1487, 1344, 1155, 1041, 921, 756 cm^{-1} ; MS (ESI) m/z 384 $[\text{M}+\text{Na}]^+$; HRMS (ESI) calcd. for $\text{C}_{18}\text{H}_{19}\text{NO}_5\text{SNa}$ ($\text{M}++\text{Na}$): 384.0882, found: 384.0882.

General Experimental Procedure for the Preparation of *N*-Protected Aniline

Substituted Allylic Alcohols (65i)-(65o) and (65q)-(65r)

Aryl aldehyde (1.76 mmol) was added to the solution of 85% KOH in MeOH (10 mL) and H₂O (2 mL) at 0 °C. After dissolution, 1-(2-aminophenyl)ethanone (1.46 mmol) was added over a period of 10 min and the resultant reaction mixture was stirred for 3 h at 0 °C. A solid product found to precipitate was filtered, washed with cold MeOH and dried. The dried solid was used directly for the next step. The solid (1.1 mmol) was dissolved in pyridine (0.4 mL) and *p*-toluenesulfonylchloride (1.6 mmol) was added to the reaction mixture at room temperature under nitrogen atmosphere. The resulting solution was stirred for 4 h at room temperature. On completion, the reaction mixture was quenched by adding H₂O (5 mL) and filtered. The resulting solid was dried and used as such for the next step. The solid (0.39 mmol) was dissolved in MeOH (7 mL) and NaBH₄ (0.59 mmol) was added portion wise to the reaction mixture at 0 °C under a nitrogen atmosphere. The reaction mixture was allowed to stir for 2 h at room temperature. Upon completion, the reaction mixture was quenched with H₂O (2 mL) and the solvent was evaporated under reduced pressure. To the crude mixture was added H₂O (4 mL) and the solution was extracted with EtOAc (7 mL). The aqueous phase was further extracted with

EtOAc (3 x 5 mL) and the combined organic layers were washed with brine (20 mL), dried over anhydrous Na₂SO₄ and concentrated under reduced pressure. Purification by flash column chromatography on silica gel (eluent: *n*-hexane: EtOAc = 9: 1) gave the title compound.

(*E*)-*N*-(2-(1-Hydroxy-3-*p*-tolylallyl)phenyl)-4-methylbenzenesulfonamide (65i)

White solid; m.p. 118-121 °C; ¹H NMR (CDCl₃, 300 MHz): δ 8.32 (1H, brs), 7.63 (2H, d, *J* = 8.29 Hz), 7.51 (1H, dd, *J* = 0.74, 8.09 Hz), 7.02-7.26 (9H, m), 6.45 (1H, d, *J* = 15.70 Hz), 6.09 (1H, dd, *J* = 6.17, 15.87 Hz), 5.25-5.29 (1H, m), 2.50 (1H, d, *J* = 3.28 Hz), 2.35 (3H, s), 2.32 (3H, s); ¹³C NMR (CDCl₃, 75 MHz): δ 143.6, 143.2, 138.0, 135.9, 131.6, 129.5, 129.3, 128.9, 128.3, 127.6, 127.2, 126.6, 124.5, 121.6, 74.8, 21.5, 21.2; IR (NaCl, neat) ν: 3018, 1215, 1159, 756, 667 cm⁻¹; MS (ESI) *m/z* 416 [M+Na]⁺; HRMS (ESI) calcd. for C₂₃H₂₃NO₃SNa (M⁺+Na): 416.1296, found: 416.1292.

(*E*)-*N*-(2-(3-(4-bromophenyl)-1-hydroxyallyl)phenyl)-4-methylbenzenesulfonamide (65j)

White solid; m.p. 117-121 °C; ¹H NMR (CDCl₃, 300 MHz): δ 8.49 (1H, brs), 7.57 (2H, d, *J* = 8.27 Hz), 7.43 (1H, d, *J* = 7.65 Hz), 7.36 (2H, d, *J* = 8.45 Hz), 7.01-7.21

(7H, m), 6.39 (1H, d, $J = 15.45$ Hz), 6.09 (1H, dd, $J = 5.61, 15.9$ Hz), 5.32 (1H, d, $J = 4.98$ Hz), 3.57 (1H, brs), 2.27 (3H, s); ^{13}C NMR (CDCl_3 , 75 MHz): δ 143.7, 136.5, 135.7, 135.2, 131.8, 131.6, 130.0, 129.9, 129.7, 129.5, 128.9, 128.5, 128.2, 128.0, 127.1, 124.7, 121.6, 121.6, 74.1, 21.5; IR (NaCl, neat) ν : 3424, 3018, 1597, 1489, 1330, 1159, 1091, 756, 665 cm^{-1} ; MS (ESI) m/z 480 $[\text{M}+\text{Na}]^+$; HRMS (ESI) calcd. for $\text{C}_{22}\text{H}_{20}\text{NO}_3\text{SNaBr}$ (M^++Na): 480.0245, found: 480.0244.

(*E*)-*N*-(2-(3-(4-chlorophenyl)-1-hydroxyallyl)phenyl)-4-methylbenzenesulfonamide (65k)

White solid; m.p. 118-123 $^{\circ}\text{C}$; ^1H NMR (CDCl_3 , 300 MHz): δ 7.59 (2H, d, $J = 7.97$ Hz), 7.43 (1H, d, $J = 7.96$ Hz), 7.02- 7.26 (9H, m), 6.41 (1H, d, $J = 15.87$ Hz), 6.09 (1H, dd, $J = 5.46, 15.86$ Hz), 5.34 (1H, d, $J = 5.09$ Hz), 2.28 (3H, s); ^{13}C NMR (CDCl_3 , 75 MHz): δ 143.7, 136.5, 135.8, 134.7, 133.4, 132.0, 129.9, 129.6, 129.5, 128.8, 128.6, 128.5, 127.9, 127.2, 124.8, 121.7, 73.9, 21.5; IR (NaCl, neat) ν : 3462, 3018, 1597, 1490, 1332, 1215, 1159, 1091, 756, 667 cm^{-1} ; MS (ESI) m/z 436 $[\text{M}+\text{Na}]^+$; HRMS (ESI) calcd. for $\text{C}_{22}\text{H}_{20}\text{NO}_3\text{SNaCl}$ (M^++Na): 436.0750, found: 436.0752.

(*E*)-*N*-(2-(3-(4-fluorophenyl)-1-hydroxyallyl)phenyl)-4-methylbenzene**sulfonamide (65l)**

Gum liquid; ^1H NMR (CDCl_3 , 300 MHz): δ 7.58 (2H, d, J = 8.20 Hz), 7.35 (1H, d, J = 8.06 Hz), 7.06-7.18 (4H, m), 6.90-6.99 (5H, m), 6.37 (1H, d, J = 15.86 Hz), 6.01 (1H, dd, J = 5.73, 15.89 Hz), 5.84 (1H, brs), 5.33 (1H, d, J = 5.59 Hz), 2.24 (3H, s); ^{13}C NMR (CDCl_3 , 75 MHz): δ 143.2, 137.0, 136.8, 132.5, 129.6, 129.4, 129.2, 128.7, 128.4, 128.3, 128.2, 127.2, 124.2, 121.9, 115.5, 115.2, 73.6, 21.4; IR (NaCl, neat) ν : 3473, 3020, 1600, 1508, 1332, 1228, 1157, 1091, 756, 665 cm^{-1} ; MS (ESI) m/z 420 $[\text{M}+\text{Na}]^+$; HRMS (ESI) calcd. for $\text{C}_{22}\text{H}_{20}\text{NO}_3\text{SNaF}$ (M^++Na): 420.1046, found: 420.1041.

(*E*)-*N*-(2-(1-hydroxy-3-(naphthalen-2-yl)allyl)phenyl)-4-methylbenzene**sulfonamide (65m)**

Yellow solid; m.p. 137-141 $^{\circ}\text{C}$; ^1H NMR (CDCl_3 , 300 MHz): δ 8.53 (1H, brs), 7.72-7.81 (3H, m), 7.60-7.63 (3H, m), 7.42-7.56 (4H, m), 7.14-7.25 (2H, m), 7.02-7.07 (1H, m), 6.94 (2H, d, J = 8.16 Hz), 6.61 (1H, d, J = 15.88 Hz), 6.25 (1H, dd, J = 5.69, 15.89 Hz), 5.36 (1H, d, J = 5.41 Hz), 2.16 (3H, s); ^{13}C NMR (CDCl_3 , 75 MHz): δ 143.6, 136.5, 135.9, 133.6, 133.5, 133.1, 131.6, 131.1, 129.5, 129.4, 128.9, 128.5,

128.1, 128.0, 127.6, 127.2, 127.0, 126.3, 126.1, 124.6, 123.6, 121.5, 74.5, 21.3; IR (NaCl, neat) ν : 3447, 3018, 1597, 1325, 1215, 1157, 1091, 757, 667 cm^{-1} ; MS (ESI) m/z 452 $[\text{M}+\text{Na}]^+$; HRMS (ESI) calcd. for $\text{C}_{26}\text{H}_{23}\text{NO}_3\text{SNa}$ (M^++Na): 452.1296, found: 452.1291.

(*E*)-*N*-(2-(1-hydroxy-3-mesitylallyl)phenyl)-4-methylbenzenesulfonamide (65n)

Yellow solid; m.p. 130-134 $^{\circ}\text{C}$; ^1H NMR(CDCl_3 , 300 MHz): δ 8.32 (1H, brs), 7.61 (2H, d, $J = 8.28$ Hz), 7.48 (1H, d, $J = 8.75$ Hz), 7.16-7.25 (2H, m), 7.04-7.10 (3H, m), 6.85 (2H, s), 6.46 (1H, d, $J = 16.18$ Hz), 5.62 (1H, dd, $J = 6.35, 16.17$ Hz), 5.27 (1H, d, $J = 6.24$ Hz), 2.74 (1H, brs), 2.27 (6H, s), 2.18 (6H, s); ^{13}C NMR (CDCl_3 , 75 MHz): δ 143.7, 136.7, 136.5, 135.8, 133.6, 132.6, 132.2, 129.8, 129.5, 128.8, 128.6, 128.1, 127.1, 124.8, 122.1, 74.6, 21.4, 20.9; IR (NaCl, neat) ν : 3481, 3018, 1598, 1494, 1332, 1159, 1091, 756, 665 cm^{-1} ; MS (ESI) m/z 444 $[\text{M}+\text{Na}]^+$; HRMS (ESI) calcd. for $\text{C}_{25}\text{H}_{27}\text{NO}_3\text{SNa}$ (M^++Na): 444.1609, found: 444.1613.

***N*-(2-((2*E*,4*E*)-1-hydroxy-5-phenylpenta-2,4-dienyl)phenyl)-4-methylbenzenesulfonamide (65o)**

Brown oil; ^1H NMR (CDCl_3 , 300 MHz): δ 8.44 (1H, brs), 7.66 (2H, d, $J = 8.25$ Hz), 7.49 (1H, d, $J = 8.01$ Hz), 7.04-7.39 (10H, m), 6.46-6.65 (2H, m), 6.23-6.31 (1H, m),

5.68 (1H, dd, $J = 6.13, 15.14$ Hz), 5.22 (1H, d, $J = 6.06$ Hz), 3.18 (1H, brs), 2.31 (3H, s); ^{13}C NMR (CDCl_3 , 75 MHz): δ 143.7, 136.9, 136.7, 135.8, 133.7, 132.9, 131.8, 131.7, 129.6, 128.8, 128.7, 128.4, 127.8, 127.7, 127.3, 126.4, 124.6, 121.7, 74.2, 21.5; IR (NaCl, neat) ν : 3253, 3022, 1598, 1494, 1334, 1215, 1159, 1091, 756, 667 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: 428.1303.

(*E*)-*N*-(2-(3-(benzo[d][1,3]dioxol-5-yl)-1-hydroxyallyl)phenyl)-4-methylbenzene sulfonamide (65q)

Yellow solid; m.p. 127-130 $^{\circ}\text{C}$; ^1H NMR(CDCl_3 , 300 MHz): δ 8.48 (1H, brs), 7.61 (2H, d, $J = 8.20$ Hz), 7.49 (1H, d, $J = 8.06$ Hz), 7.0-7.26 (5H, m), 6.69-6.74 (3H, m), 6.36 (1H, d, $J = 15.76$ Hz), 5.91 (1H, dd, $J = 6.21, 15.89$ Hz), 5.93 (2H, s), 5.25 (1H, t, $J = 3.63$ Hz), 3.11 (1H, d, $J = 3.06$ Hz), 2.31 (3H, s); ^{13}C NMR (CDCl_3 , 75 MHz): δ 147.9, 147.5, 143.7, 136.6, 135.7, 131.1, 130.5, 129.6, 128.8, 128.4, 127.2, 127.1, 124.6, 121.7, 121.6, 108.2, 105.8, 101.1, 74.6, 21.5; IR (NaCl, neat) ν : 3018, 1506, 1489, 1215, 1159, 1087, 756, 665 cm^{-1} ; MS (ESI) m/z 446 $[\text{M}+\text{Na}]^+$; HRMS (ESI) calcd. for $\text{C}_{23}\text{H}_{21}\text{NO}_5\text{SNa}$ (M^++Na): 446.1038, found: 446.1039.

(*E*)-*N*-(2-(1-hydroxy-3-phenylallyl)phenyl)-4-methylbenzenesulfonamide (65r)

White solid; m.p. 84-88 °C; ^1H NMR (CDCl_3 , 300 MHz): δ 8.54 (1H, brs), 7.62 (2H, d, $J = 8.27$ Hz), 7.51 (2H, d, $J = 7.89$ Hz), 7.20-7.35 (5H, m), 7.12-7.15 (1H, m), 7.03-7.08 (3H, m), 6.48 (1H, d, $J = 15.96$ Hz), 6.13 (1H, dd, $J = 5.87, 15.89$ Hz), 5.32 (1H, d, $J = 5.6$ Hz), 3.32 (1H, brs), 2.29 (3H, s); ^{13}C NMR (CDCl_3 , 75 MHz): δ 143.69, 136.5, 136.1, 135.8, 131.8, 131.1, 129.5, 129.1, 128.8, 128.5, 128.4, 127.9, 127.2, 126.7, 126.6, 124.6, 121.6, 74.3, 21.5; IR (NaCl, neat) ν : 3253, 3022, 1494, 1398, 1336, 1217, 1159, 1091, 754, 665 cm^{-1} ; MS (ESI) m/z 402 $[\text{M}+\text{Na}]^+$; HRMS (ESI) calcd. for $\text{C}_{22}\text{H}_{21}\text{NO}_3\text{SNa}$ ($\text{M}^+ + \text{Na}$): 402.1140, found: 402.1137.

Experimental Procedure for the Preparation of *N*-(2-((*2E,4E*)-1-Hydroxyocta-2,4-dienyl)phenyl)-4-methylbenzenesulfonamide (65p)

To a solution of the 1-(2-aminophenyl)ethanone (0.88 mmol) in pyridine (0.4 mL) was added *p*-toluenesulfonylchloride (1.06 mmol) at room temperature under nitrogen atmosphere. The resulting solution was stirred for 4 h at room temperature. On

completion, the reaction mixture was quenched by adding H₂O (5 mL) and filtered off. The resulting solid was dried and then used as such for the next step. To a stirred solution of diisopropylamine (0.34g, 3.4 mmol) in anhydrous THF (5 mL) was added butyl lithium (1.6 M Hexane solution; 2.1 mL; 3.4 mmol) at -20 °C as drop wise. The resulting solution was stirred at the same temperature for 30 min, and then the temperature brought up to -78 °C. The solid (0.25 g, 0.86 mmol) obtained was dissolved in anhydrous THF (2 mL), and added to the reaction mixture at the same temperature. The reaction mixture was allowed to stir for additional 1 h. To this reaction mixture was added HMPA (0.46 g, 2.59 mmol) at -78 °C. Followed by (*E*)-hex-2-enal (0.12 g, 1.29 mmol) was added drop wise and the resulting mixture was stirred for additional 30 min. 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 NH₄Cl (10 mL) and extracted with EtOAc (2 x 10 mL). The combined organic layers were washed with brine, dried over Mg₂SO₄, and concentrated under reduced pressure. Purification by flash column chromatography on silica gel (eluent: *n*-hexane: EtOAc = 20: 1) gave 4-methyl-*N*-(2-(2*E*,4*E*)-octa-2,4-dienoylphenyl)benzenesulfonamide compound (274 mg, 86% yield).

4-Methyl-*N*-(2-(2*E*,4*E*)-octa-2,4-dienoylphenyl)benzenesulfonamide (0.74 mmol) was dissolved in MeOH (10 mL) and NaBH₄ (0.87 mmol) was added portion wise at 0 °C under an nitrogen atmosphere. The reaction mixture was allowed to stir for 2 h at room temperature. Upon completion, the reaction mixture was quenched with H₂O (3 mL) and the solvent was evaporated under reduced pressure. To the crude mixture was added H₂O (5 mL) and the solution was extracted with EtOAc (10 mL) and organic phase was separated. The aqueous phase further extracted with EtOAc (3 x 10 mL) and the combined organic layers were washed with brine (20 mL), dried over

anhydrous Na_2SO_4 and concentrated under reduced pressure. Purification by flash column chromatography on silica gel (eluent: *n*-hexane: EtOAc = 9: 1) gave the title Compound (**65p**).

***N*-(2-((2*E*,4*E*)-1-hydroxyocta-2,4-dienyl)phenyl)-4-methylbenzenesulfonamide (**65p**)**

Yellow solid; m.p. 100-103 °C; ^1H NMR (CDCl_3 , 500 MHz): δ 8.31 (1H, brs), 7.65 (2H, d, $J = 8.16$ Hz), 7.48 (1H, d, $J = 8.02$ Hz), 7.18-7.21 (3H, m), 7.0-7.06 (2H, m), 6.07-6.12 (1H, m), 5.86-5.91 (1H, m), 5.67-5.73 (1H, m), 5.42 (1H, dd, $J = 6.65$, 15.15 Hz), 5.07 (1H, d, $J = 6.59$ Hz), 2.37 (3H, s), 2.04 (2H, q), 1.38 (2H, m), 0.89 (3H, t, $J = 7.34$ Hz); ^{13}C NMR (CDCl_3 , 125 MHz): δ 143.6, 136.9, 136.8, 135.7, 132.5, 131.8, 129.7, 129.6, 129.1, 128.7, 128.2, 127.2, 124.6, 121.8, 74.5, 34.8, 22.3, 21.5, 13.7; IR (NaCl, neat) ν : 3481, 3020, 1598, 1494, 1334, 1159, 1091, 756, 665 cm^{-1} ; MS (ESI) m/z 394 $[\text{M}+\text{Na}]^+$; HRMS (ESI) calcd. for $\text{C}_{21}\text{H}_{25}\text{NO}_3\text{SNa}$ (M^++Na): 394.1453, found: 394.1450.

Experimental Procedure for the Preparation of (*E*)-*N*-(2-(3-Hydroxy-3-phenylprop-1-enyl)phenyl)-4-methyl benzenesulfonamide (65s)

To a solution of benzoylmethylene triphenylphosphorane (1.45 mmol) in MeCN (6 mL), a solution of *N*-(2-formylphenyl)-4-methylbenzenesulfonamide^{43f} (0.72 mmol) in the same solvent was added dropwise. The mixture was stirred 16 h at room temperature and then heated at 50 °C for 5 h. The solvent was evaporated off and the residue taken up with EtOAc (10 mL) and HCl 2 M solution (3 mL) to pH 6. The organic layer was separated, dried over Na₂SO₄, filtered and the solvent was evaporated off. The residue was taken for further step to get the title compound **1t**. The residue (0.26 mmol) was dissolved in MeOH (7 mL) and NaBH₄ (0.31 mmol) was added as portion wise to the reaction mixture at 0 °C under the nitrogen atmosphere. The reaction mixture was allowed to stir for 2 h at room temperature. Upon completion, the reaction mixture was quenched with H₂O (2 mL) and the solvent was evaporated under reduced pressure. To the crude was added H₂O (4 mL) and the solution was extracted with EtOAc (10 mL) and phases were separated. The aqueous phases was extracted with EtOAc (3 x 5 mL), the combined organic layers were washed with brine solution and dried over anhydrous Na₂SO₄ and concentrated under reduced pressure. Purification by flash column chromatography on silica gel (eluent: *n*-hexane: EtOAc = 1: 5) gave the title compound.

(*E*)-*N*-(2-(3-hydroxy-3-phenylprop-1-enyl)phenyl)-4-methylbenzenesulfonamide (65s)

White solid; m.p. 147-151 °C; ^1H NMR (CDCl_3 , 400 MHz): δ 7.62 (2H, d, J = 8.24 Hz), 7.28-7.37 (7H, m), 7.09-7.18 (4H, m), 6.99 (1H, brs), 6.56 (1H, d, J = 15.68 Hz), 6.10 (1H, dd, J = 6.04, 15.68 Hz), 5.25 (1H, d, J = 5.4 Hz), 2.58 (1H, brs), 2.36 (3H, s); ^{13}C NMR (CDCl_3 , 100 MHz): δ 143.8, 142.2, 136.3, 135.5, 133.3, 132.0, 129.6, 128.6, 128.5, 127.8, 127.2, 127.0, 126.6, 126.4, 125.5, 124.5, 74.7, 21.5; IR (NaCl, neat) ν : 3251, 3020, 1492, 1398, 1335, 1217, 1160, 1089, 754, 665 cm^{-1} ; MS (ESI) m/z 379 $[\text{M}+\text{H}]^+$; HRMS (ESI) calcd. for $\text{C}_{22}\text{H}_{21}\text{NO}_3\text{SNa}$ ($\text{M}^+ + \text{Na}$): 402.1140, found: 402.1140.

General Experimental Procedure for Optimizing the Lewis and Brønsted Acid-Catalyzed Intramolecular Allylic Amination of *N*-(2-(2-Hydroxybut-3-en-2-yl)phenyl)-4-methylbenzenesulfonamide (65a)

For reactions with a gold/silver catalyst combination, the gold (15 μmol) and silver (47.3 μmol) salts were first stirred in toluene (1.5 mL) at room temperature for 10 min. In all other cases, the catalyst was added to a respective solvent prior to adding the starting materials. A toluene solution (1.5 mL) containing **65a** (0.31 mmol) was added slowly dropwise and the reaction mixture was stirred at room temperature and

monitored to completion by TLC analysis. The crude mixture was concentrated under reduced pressure and purified by flash column chromatography on silica gel (*n*hexane/ EtOAc 20:1 as eluent) to give **66a**.

General procedure for the AuCl₃/AgSbF₆-catalyzed intramolecular allylic amination of **65**

A solution of AuCl₃ (15 μmol) and AgSbF₆ (47.3 μmol) was stirred in toluene (1.5 mL) under an Ar atmosphere at room temperature for 10 minutes. Then a toluene solution (1.5 mL) containing **65** (0.31 mmol) was added slowly as drop wise, and the reaction mixture stirred at room temperature and monitored to completion by TLC analysis. The solvent removed under reduced pressure. Purification by flash column chromatography on silica gel (*n*-hexane/EtOAc 20:1 as eluent) gave **66**.

4-Methyl-1-tosyl-1,2-dihydroquinoline (66a**)**^{33g}

White solid; ¹H NMR (CDCl₃, 400 MHz): δ 7.70 (1H, dd, *J* = 1.36, 8.2 Hz), 7.30 (1H, ddd, *J* = 1.8, 7.8, 7.7 Hz), 7.21-7.26 (3H, m), 7.12 (1H, dd, *J* = 1.36, 7.32 Hz), 7.06 (2H, d, *J* = 7.8 Hz), 5.31 (1H, m), 4.33 (2H, m), 2.33 (3H, s), 1.57 (3H, s); ¹³C NMR

(CDCl₃, 100 MHz): δ 143.1, 136.1, 135.1, 131.6, 131.4, 128.8, 127.8, 127.4, 127.2, 126.7, 123.2, 120.3, 45.3, 21.4, 17.7; MS (ESI) m/z 300 [M+H]⁺.

3,4-Dimethyl-1-tosyl-1,2-dihydroquinoline (66b)

White solid; m.p. 95-97 °C; ¹H NMR(CDCl₃, 500 MHz): δ 7.65 (1H, m), 7.18-7.26 (4H, m), 7.04-7.09 (3H, m), 4.17 (2H, s), 2.32 (3H, s), 1.60 (3H, s), 1.45 (3H, s); ¹³C NMR (CDCl₃, 125 MHz): δ 143.1, 135.8, 134.3, 133.1, 128.6, 127.5, 127.2, 126.8, 126.6, 126.1, 124.6, 122.9, 50.2, 21.4, 17.9, 12.6; IR (NaCl, neat) ν : 3020, 2918, 1597, 1483, 1346, 1215, 1165 cm⁻¹; MS (ESI) m/z 314 [M+H]⁺; HRMS (ESI) calcd. for C₁₈H₂₀NO₂S (M⁺+H): 314.1215, found: 314.1208.

3-Methyl-4-phenyl-1-tosyl-1,2-dihydroquinoline (66c)

White solid; yield 87%; m.p. 184-187 °C; ¹H NMR (CDCl₃, 500 MHz): δ 7.74 (1H, d, J = 7.99 Hz), 7.31 (2H, d, J = 8.04 Hz), 7.22-7.25 (4H, m), 7.12 (2H, d, J = 8.02 Hz), 7.03 (1H, t, J = 7.61 Hz), 6.50 (1H, d, J = 7.77 Hz), 6.43-6.44 (2H, m), 4.42 (2H, s), 2.39 (3H, s), 1.54 (3H, s); ¹³C NMR (CDCl₃, 125 MHz): δ 143.5, 136.9, 136.2, 133.9, 132.5, 132.3, 129.6, 129.1, 129.0, 128.1, 127.1, 127.0, 126.9, 126.6, 125.7, 50.3, 21.4, 18.9; IR (NaCl, neat) ν : 3018, 1481, 1346, 1215, 1165 cm⁻¹; MS (ESI) m/z 376

$[M+H]^+$; HRMS (ESI) calcd. for $C_{23}H_{21}NO_2SNa$ ($M^+ + Na$): 398.1191, found: 398.1196.

4-Phenyl-1-tosyl-1,2-dihydroquinoline (66d)

White solid; m.p. 129-131 °C; 1H NMR ($CDCl_3$, 400 MHz): δ 7.78 (1H, d, $J = 7.97$ Hz), 7.31 (3H, d, $J = 7.99$ Hz), 7.21-7.25 (3H, m), 6.99-7.15 (4H, m), 6.86 (1H, d, $J = 7.68$ Hz), 6.70 (2H, d, $J = 7.61$ Hz), 5.56 (1H, t, $J = 4.39$ Hz), 4.53 (2H, d, $J = 4.40$ Hz), 2.26 (3H, s); ^{13}C NMR ($CDCl_3$, 100 MHz): δ 143.4, 138.7, 138.1, 136.1, 135.5, 130.9, 129.5, 129.0, 128.5, 128.27, 127.9, 127.6, 127.5, 126.6, 126.0, 121.6, 45.5, 21.3; IR (NaCl, neat) ν : 3406, 3028, 1610, 1492, 1348, 1165 cm^{-1} ; MS (ESI) m/z 362 $[M+H]^+$; HRMS (ESI) calcd. for $C_{22}H_{19}NO_2SNa$ ($M^+ + Na$): 384.1034, found: 384.1043.

7-Methyl-4-phenyl-1-tosyl-1,2-dihydroquinoline (66e)

White solid; m.p. 159-164 °C; 1H NMR ($CDCl_3$, 400 MHz): δ 7.61 (1H, s), 7.32 (2H, d, $J = 8.20$ Hz), 7.19-7.25 (3H, m), 7.00 (2H, d, $J = 8.07$ Hz), 6.93 (1H, d, $J = 7.76$ Hz), 6.75 (1H, d, $J = 7.90$ Hz), 6.69 (2H, dd, $J = 1.3, 7.19$ Hz), 5.48 (1H, t, $J = 4.41$ Hz), 4.49 (2H, d, $J = 4.43$ Hz), 2.41 (3H, s), 2.25 (3H, s); ^{13}C NMR ($CDCl_3$, 100 MHz): δ 143.3, 138.6, 138.4, 138.2, 136.2, 135.5, 129.0, 128.5, 128.3, 128.0, 127.9,

127.5, 127.4, 125.8, 120.4, 45.6, 21.4, 21.3; IR (NaCl, neat) ν : 3022, 2922, 1598, 1490, 1348, 1215, 1161 cm^{-1} ; MS (ESI) m/z 376 $[\text{M}+\text{H}]^+$; HRMS (ESI) calcd. for $\text{C}_{23}\text{H}_{21}\text{NO}_2\text{SNa}$ (M^++Na): 398.1191, found: 398.1192.

6-chloro-4-phenyl-1-tosyl-1,2-dihydroquinoline (66f)

White solid; m.p. 167-170 $^{\circ}\text{C}$; ^1H NMR (CDCl_3 , 400 MHz): δ 7.71 (1H, d, $J = 8.58$ Hz), 7.33 (2H, d, $J = 8.21$ Hz), 7.22-7.30 (4H, m), 7.05 (2H, d, $J = 8.05$ Hz), 6.84 (1H, s), 6.68 (2H, d, $J = 7.36$ Hz), 5.60 (1H, t, $J = 4.42$ Hz), 4.52 (2H, d, $J = 4.44$ Hz), 2.28 (3H, s); ^{13}C NMR (CDCl_3 , 100 MHz): δ 143.7, 137.9, 137.3, 135.9, 134.0, 132.4, 132.3, 129.2, 128.9, 128.4, 128.2, 128.1, 127.9, 127.5, 125.8, 122.9, 45.4, 21.3; IR (NaCl, neat) ν : 3421, 2920, 1471, 1354, 1215, 1163 cm^{-1} ; MS (ESI) m/z 396 $[\text{M}+\text{H}]^+$; HRMS (ESI) calcd. for $\text{C}_{22}\text{H}_{18}\text{NO}_2\text{SNaCl}$ (M^++Na): 418.0644, found: 418.0644.

8-methyl-5-tosyl-5,6-dihydro-[1,3]dioxolo[4,5-g]quinoline (66h)

White solid; m.p. 158-161 $^{\circ}\text{C}$; ^1H NMR (CDCl_3 , 500 MHz): δ 7.26 (2H, d, $J = 8.41$ Hz), 7.22 (1H, s), 7.06 (2H, d, $J = 8.04$ Hz), 6.58 (1H, s), 6.00 (2H, s), 5.15 (1H, m), 4.26 (2H, m), 2.34 (3H, s), 1.47 (3H, s); ^{13}C NMR (CDCl_3 , 125 MHz): δ 146.4, 143.1, 135.9, 131.2, 129.4, 128.7, 127.5, 126.4, 118.0, 108.8, 103.1, 101.5, 45.3, 21.4, 17.9;

IR (NaCl, neat) ν : 3022, 2918, 1597, 1483, 1348, 1263, 1161 cm^{-1} ; MS (ESI) m/z 344 $[\text{M}+\text{H}]^+$; HRMS (ESI) calcd. for $\text{C}_{18}\text{H}_{18}\text{NO}_4\text{S}$ (M^++H): 344.0957, found: 344.0960.

2-*p*-Tolyl-1-tosyl-1,2-dihydroquinoline (66i)

White solid; m.p. 124-127 $^{\circ}\text{C}$; ^1H NMR (CDCl_3 , 400 MHz): δ 7.61 (1H, d, $J = 7.95$ Hz), 7.31 (2H, d, $J = 8.21$ Hz), 7.19-7.25 (3H, m), 7.02-7.13 (5H, m), 6.95 (1H, d, $J = 7.4$ Hz), 6.24 (1H, d, $J = 9.57$ Hz), 5.97 (1H, d, $J = 5.86$ Hz), 5.83 (1H, dd, $J = 5.93$, 9.56 Hz), 2.34 (3H, s), 2.25 (3H, s); ^{13}C NMR (CDCl_3 , 100 MHz): δ 143.3, 137.6, 136.2, 135.3, 132.9, 129.1, 128.7, 128.2, 127.7, 127.4, 127.2, 126.7, 126.4, 126.2, 125.4, 56.8, 21.5, 21.0; IR (NaCl, neat) ν : 3022, 1598, 1510, 1483, 1344, 1215, 1166 cm^{-1} ; MS (ESI) m/z 376 $[\text{M}+\text{H}]^+$; HRMS (ESI) calcd. for $\text{C}_{23}\text{H}_{21}\text{NO}_2\text{SNa}$ (M^++Na): 398.1191, found: 398.1192.

2-(4-Bromophenyl)-1-tosyl-1,2-dihydroquinoline (66j)

White solid; m.p. 154-156 $^{\circ}\text{C}$; ^1H NMR (CDCl_3 , 400 MHz): δ 7.65 (1H, d, $J = 7.97$ Hz), 7.33 (4H, t, $J = 8.7$ Hz), 7.23 (3H, d, $J = 8.16$ Hz), 7.10-7.17 (3H, m), 6.98 (1H, d, $J = 7.41$ Hz), 6.30 (1H, d, $J = 9.54$ Hz), 5.98 (1H, d, $J = 5.88$ Hz), 5.85 (1H, dd, $J = 6.01$, 9.51 Hz), 2.36 (3H, s); ^{13}C NMR (CDCl_3 , 100 MHz): δ 143.6, 137.4, 135.9, 132.6, 128.4, 127.6, 126.6, 126.4, 126.0, 125.8, 122.0, 56.2, 21.5; IR (NaCl, neat) ν :

3026, 1597, 1485, 1346, 1215, 1166 cm^{-1} ; MS (ESI) m/z 440 $[\text{M}+\text{H}]^+$; HRMS (ESI) calcd. for $\text{C}_{22}\text{H}_{19}\text{NO}_2\text{SBr}$ (M^++H): 440.0320, found: 440.0318.

2-(4-Chlorophenyl)-1-tosyl-1,2-dihydroquinoline (66k)

While solid; m.p. 128-131 $^{\circ}\text{C}$; ^1H NMR (CDCl_3 , 300 MHz): δ 7.53 (1H, d, $J = 7.91$), 7.11-7.25 (4H, m), 7.04-7.15 (3H, m), 6.98 (3H, d, $J = 8.1$ Hz), 6.87 (1H, dd, $J = 1.53$, 7.41 Hz), 6.19 (1H, d, $J = 9.56$ Hz), 5.89 (1H, d, $J = 5.97$ Hz), 5.74 (1H, dd, $J = 5.94$, 9.54 Hz), 2.25 (3H, s); ^{13}C NMR (CDCl_3 , 75 MHz): δ 143.5, 136.9, 135.9, 133.7, 132.6, 129.1, 128.8, 128.6, 128.4, 127.5, 127.2, 126.6, 126.4, 125.9, 56.2, 21.5; IR (NaCl, neat) ν : 3026, 1597, 1487, 1344, 1215, 1166 cm^{-1} ; MS (ESI) m/z 396 $[\text{M}+\text{H}]^+$; HRMS (ESI) calcd. for $\text{C}_{22}\text{H}_{19}\text{NO}_2\text{SCl}$ (M^++H): 396.0825, found: 396.0827.

2-(4-Fluorophenyl)-1-tosyl-1,2-dihydroquinoline (66l)

Gum liquid; ^1H NMR (CDCl_3 , 400 MHz): δ 7.61 (1H, d, $J = 7.98$ Hz), 7.28-7.33 (4H, m), 7.21 (1H, t, $J = 8.7$ Hz), 7.08-7.15 (3H, m), 6.96 (1H, d, $J = 7.40$), 6.89 (2H, t, $J = 8.66$ Hz), 6.28 (1H, d, $J = 9.57$ Hz), 5.98 (1H, d, $J = 5.90$ Hz), 5.83 (1H, dd, $J = 5.91$, 9.55 Hz), 2.35 (3H, s); ^{13}C NMR (CDCl_3 , 100 MHz): δ 161.2, 143.5, 136.0, 134.0, 132.6, 129.3, 129.2, 129.1, 128.4, 127.6, 127.2, 126.5, 126.3, 126.2, 125.7, 115.4, 115.2, 56.2, 21.5; IR (NaCl, neat) ν : 3018, 2432, 1602, 1508, 1419, 1346, 1215, 1166

cm^{-1} ; MS (ESI) m/z 380 $[\text{M}+\text{H}]^+$; HRMS (ESI) calcd. for $\text{C}_{22}\text{H}_{18}\text{NO}_2\text{SNaF}$ ($\text{M}^+ + \text{Na}$): 402.0940, found: 402.0945.

2-(Naphthalen-2-yl)-1-tosyl-1,2-dihydroquinoline (66m)

Yellow solid; m.p. 142-143 °C; ^1H NMR (CDCl_3 , 300 MHz): δ 7.58-7.76 (6H, m), 7.33-7.40 (4H, m), 7.07-7.19 (4H, m), 6.96 (1H, d, $J = 1.62$, 7.33 Hz), 6.33 (1H, d, $J = 9.60$ Hz), 6.16 (1H, d, $J = 5.86$ Hz), 5.93 (1H, dd, $J = 5.88$, 9.58 Hz), 2.34 (3H, s); ^{13}C NMR (CDCl_3 , 75 MHz): δ 143.4, 136.1, 135.6, 133.0, 132.8, 128.7, 128.4, 128.3, 128.0, 127.7, 127.5, 126.5, 126.3, 126.1, 126.0, 125.9, 125.7, 57.0, 21.5; IR (NaCl, neat) ν : 3018, 1635, 1598, 1483, 1340, 1215, 1166 cm^{-1} ; MS (ESI) m/z 412 $[\text{M}+\text{H}]^+$; HRMS (ESI) calcd. for $\text{C}_{26}\text{H}_{22}\text{NO}_2\text{S}$ ($\text{M}^+ + \text{H}$): 412.1371, found: 412.1373.

2-Mesityl-1-tosyl-1,2-dihydroquinoline (66n)

White solid; m.p. 138-140 °C; ^1H NMR (CDCl_3 , 400 MHz): δ 7.57 (1H, d, $J = 8.12$ Hz), 7.30 (2H, d, $J = 7.92$ Hz), 7.08 (1H, t, $J = 7.50$ Hz), 7.02 (2H, d, $J = 7.93$ Hz), 6.93 (1H, t, $J = 7.33$ Hz), 6.83 (1H, d, $J = 7.23$ Hz), 6.73 (2H, s), 6.42 (1H, d, $J = 2.4$ Hz), 6.08 (1H, d, $J = 9.75$ Hz), 5.44 (1H, dd, $J = 5.09$, 9.76 Hz), 2.25 (3H, s), 2.15 (3H, s), 2.13 (6H, s); ^{13}C NMR (CDCl_3 , 100 MHz): δ 143.5, 137.2, 136.9, 136.3, 135.7, 135.6, 130.3, 129.4, 128.6, 127.2, 126.8, 126.3, 125.1, 124.9, 123.6, 123.3, 56.9, 21.5, 20.8, 20.7; IR (NaCl, neat) ν : 3025, 2970, 2920, 1598, 1487, 1454, 1350,

1215, 1163 cm^{-1} ; MS (ESI) m/z 404 $[\text{M}+\text{H}]^+$; HRMS (ESI) calcd. for $\text{C}_{25}\text{H}_{26}\text{NO}_2\text{S}$ (M^++H): 404.1684, found: 404.1683.

(*E*)-2-Styryl-1-tosyl-1,2-dihydroquinoline (66o)

Gum liquid; ^1H NMR (CDCl_3 , 500 MHz): δ 7.76 (1H, d, $J = 8.04$ Hz), 7.33 (2H, d, $J = 8.28$ Hz), 7.26-7.30 (6H, m), 7.16-7.22 (2H, m), 7.10 (2H, d, $J = 8.0$ Hz), 6.98 (1H, dd, $J = 1.33, 7.50$ Hz), 6.52 (1H, dd, $J = 1.12, 15.86$ Hz), 6.18 (1H, d, $J = 9.52$ Hz), 6.04 (1H, dd, $J = 5.99, 15.85$ Hz), 5.73 (1H, dd, $J = 5.81, 9.51$ Hz), 5.58 (1H, t, $J = 5.70$ Hz), 2.37 (3H, s); ^{13}C NMR (CDCl_3 , 125 MHz): δ 143.4, 136.3, 136.2, 133.0, 132.1, 129.0, 128.4, 128.2, 127.8, 127.5, 127.2, 126.6, 126.4, 125.9, 125.4, 125.2, 55.9, 21.5; IR (NaCl, neat) ν : 3020, 1610, 1483, 1346, 1215, 1166 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: 388.1370.

(*E*)-2-(Pent-1-enyl)-1-tosyl-1,2-dihydroquinoline (66p)

Colourless oil; ^1H NMR (CDCl_3 , 500 MHz): δ 7.69 (1H, d, $J = 8.01$ Hz), 7.22-7.29 (3H, m), 7.12 (1H, t, $J = 7.52$ Hz), 7.04 (2H, d, $J = 8.19$ Hz), 6.92 (1H, d, $J = 8.42$ Hz), 6.05 (1H, d, $J = 9.54$ Hz), 5.57-5.64 (2H, m), 5.26-5.34 (2H, m), 2.32 (3H, s), 1.83-1.92 (2H, m), 1.23-1.28 (2H, m), 0.71 (3H, t, $J = 7.36$ Hz); ^{13}C NMR (CDCl_3 , 125 MHz): δ 143.2, 136.4, 133.8, 133.1, 129.0, 128.6, 127.9, 127.4, 127.2, 126.9,

126.2, 126.2, 125.8, 124.5, 55.9, 34.0, 22.0, 21.5, 13.3; IR (NaCl, neat) ν : 3025, 1596, 1478, 1342, 1216, 1165 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: 354.1526.

2-(Benzo[d][1,3]dioxol-5-yl)-1-tosyl-1,2-dihydroquinoline (66q)

Gum liquid; ^1H NMR(CDCl_3 , 400 MHz): δ 7.62 (1H, d, $J = 7.88$ Hz), 7.30 (2H, d, $J = 8.3$ Hz), 7.07-7.24 (4H, m), 6.95 (1H, dd, $J = 1.56, 7.41$ Hz), 6.77-6.84 (2H, m), 6.64 (1H, d, $J = 8.0$ Hz), 6.25 (1H, d, $J = 9.55$ Hz), 5.91 (1H, d, $J = 5.91$ Hz), 5.87 (2H, s), 5.78 (1H, dd, $J = 5.89, 9.52$ Hz), 2.30 (3H, s); ^{13}C NMR (CDCl_3 , 100 MHz): δ 147.7, 147.3, 143.4, 136.1, 132.7, 132.1, 129.1, 128.5, 128.3, 127.6, 127.2, 126.4, 126.2, 125.5, 121.0, 108.1, 108.3, 101.0, 56.7, 21.5; IR (NaCl, neat) ν : 3027, 1502, 1485, 1340, 1251, 1234, 1166 cm^{-1} ; MS (ESI) m/z 406 $[\text{M}+\text{H}]^+$; HRMS (ESI) calcd. for $\text{C}_{23}\text{H}_{20}\text{NO}_4\text{S}$ (M^++H): 406.1113, found: 406.1115.

2-Phenyl-1-tosyl-1,2-dihydroquinoline (66r)^{33j}

White solid; ^1H NMR (CDCl_3 , 400 MHz): δ 7.62 (1H, d, $J = 7.92$ Hz), 7.32-7.34 (4H, m), 7.17-7.25 (4H, m), 7.0-7.13 (3H, m), 6.95 (1H, d, $J = 7.36$ Hz), 6.26 (1H, d, $J = 9.55$ Hz), 6.01 (1H, d, $J = 5.76$ Hz), 5.86 (1H, dd, $J = 5.88, 9.47$ Hz), 2.34 (3H, s); ^{13}C NMR (CDCl_3 , 100 MHz): δ 143.4, 138.4, 136.1, 132.9, 129.1, 128.6, 128.4, 128.2, 127.9, 127.6, 127.4, 127.2, 126.5, 126.3, 125.5, 56.9, 21.5; MS (ESI) m/z 362 $[\text{M}+\text{H}]^+$.

4-Methyl-*N*-(2-(2-methyl-1*H*-inden-3-yl)phenyl)benzenesulfonamide (67)

White solid; m.p. 143-147 °C; ^1H NMR(CDCl_3 , 400 MHz): δ 7.76 (1H, d, $J = 8.22$ Hz), 7.46 (3H, dd, $J = 8.30, 9.41$ Hz), 7.35-7.29 (1H, m), 7.16-7.07 (6H, m), 6.52 (1H, brs), 6.49 (1H, d, $J = 7.47$ Hz), 3.53 (2H, m), 2.34 (3H, s), 1.83 (3H, s); ^{13}C NMR (CDCl_3 , 100 MHz): δ 145.1, 144.1, 143.7, 142.2, 136.0, 134.8, 134.4, 130.4, 129.4, 128.7, 127.2, 126.4, 125.8, 124.7, 124.5, 123.5, 119.9, 119.0, 42.9, 21.5, 14.6; IR (NaCl, neat) ν : 3270, 3025, 1623, 1340, 1251, 1166, 719 cm^{-1} ; MS (ESI) m/z 376 $[\text{M}+\text{H}]^+$; HRMS (ESI) calcd. for $\text{C}_{23}\text{H}_{22}\text{NO}_2\text{S}$ (M^++H): 376.1371, found: 376.1372.

Experimental Procedure for the Preparation of 2-Pentyl-1-tosyl-1,2,3,4-tetrahydroquinoline (70)

To a solution of **66p** (165 mg; 0.46 mmol) in MeOH (10 mL) was added 10% Pd/C (16.5 mg) under H_2 atmosphere. After the reaction mixture was stirred at room temperature for 3 h, the reaction mixture was filtrated through a celite pad. After removal of the solvent, the residue was purified by flash column chromatography on silica gel (eluent: *n*-hexane: EtOAc = 20: 1) gave the title compound **70** (161 mg, 96% yield).

2-Pentyl-1-tosyl-1,2,3,4-tetrahydroquinoline (70)^{43e,h}

Gum liquid; ^1H NMR (CDCl_3 , 500 MHz): δ 7.74 (1H, d, $J = 8.12$ Hz), 7.36 (2H, d, $J = 8.24$ Hz), 7.20-7.23 (1H, m), 7.14 (2H, d, $J = 8.09$ Hz), 7.08-7.11 (1H, m), 6.96 (1H, d, $J = 7.46$ Hz), 4.23-4.27 (1H, m), 2.38-2.44 (1H, m), 2.36 (3H, s), 1.86-1.92 (1H, m), 1.66-1.74 (1H, m), 1.54-1.61 (1H, m), 1.32-1.41 (4H, m), 1.20-1.27 (4H, m), 0.84 (3H, dd, $J = 6.86, 7.0$ Hz); ^{13}C NMR (CDCl_3 , 125 MHz): δ 143.2, 136.7, 135.2, 132.7, 129.3, 128.2, 127.5, 127.1, 126.5, 125.5, 55.6, 34.3, 31.5, 26.7, 25.5, 23.9, 22.5, 21.5, 14.0; MS (ESI) m/z 358 $[\text{M}+\text{H}]^+$.

Experimental Procedure for the Preparation of 2-Pentyl-1,2,3,4-tetrahydroquinoline (71)⁴³ⁱ

To a solution of the substrate **70** (160 mg, 0.45 mmol) in MeOH (10 mL) was added Mg powder (100 mg, 4.48 mmol). The resulting suspension was allowed to stir at room temperature for 18 h. The reaction mixture was diluted with dichloromethane (10 mL) and poured into 1 M HCl. The organic phase was washed twice with 2 M NaHCO_3 , brine solution and then dried over MgSO_4 and concentrated under reduced pressure. Purification by flash column chromatography on silica gel (eluent: *n*-hexane: EtOAc = 9: 1) gave the title compound **71** (89 mg, 98% yield).

2-Pentyl-1,2,3,4-tetrahydroquinoline (71)^{43e,h}

Colourless oil; ¹H NMR (CDCl₃, 400 MHz): δ 6.94 (2H, d, J = 7.35 Hz), 6.58 (1H, t, J = 7.32 Hz), 6.47 (1H, d, J = 8.12 Hz), 3.77 (1H, brs), 3.21-3.27 (1H, m), 2.70-2.86 (2H, m), 1.93-2.0 (1H, m), 1.55-1.65 (1H, m), 1.32-1.52 (8H, m), 0.93 (3H, t, J = 6.83 Hz); ¹³C NMR (CDCl₃, 100 MHz): δ 144.7, 129.2, 126.7, 121.4, 116.8, 114.0, 51.6, 36.7, 31.9, 28.1, 26.4, 25.4, 22.6, 14.0; MS (ESI) m/z 204 [M+H]⁺.

Experimental Procedure for the Preparation of (±)-Angustureine^{43e,h}

To a solution of **71** (85 mg, 0.41 mmol) and K₂CO₃ (57 mg, 0.41 mmol) in THF (4 mL), was added MeI (0.15 mL, 2.5 mmol) under nitrogen atmosphere. After the reaction mixture was refluxed for 12 h, the reaction was quenched by water. Organic compounds were extracted with CH₂Cl₂ and combined organic layers washed with brine and dried over anhydrous Na₂SO₄. After removal of the solvent, the residue was purified by flash column chromatography on silica gel (eluent: *n*-hexane: EtOAc = 9: 1) gave the title compound (±)-angustureine (87 mg, 96% yield).

1-Methyl-2-pentyl-1,2,3,4-tetrahydroquinoline (±)-angustureine^{43e,h}

Yellow oil; ¹H NMR (CDCl₃, 400 MHz): δ 7.05 (1H, t, J = 7.8 Hz), 6.95 (1H, d, J = 6.88 Hz), 6.55 (1H, t, J = 7.32 Hz), 6.50 (1H, d, J = 8.24 Hz), 3.20-3.24 (1H, m), 2.91 (3H, s), 2.75-2.79 (1H, m), 2.62-2.67 (1H, m), 1.86-1.90 (2H, m), 1.53-1.58 (2H, m), 1.25-1.41 (6H, m), 0.87 (3H, t, J = 6.84 Hz); ¹³C NMR (CDCl₃, 100 MHz): δ 145.4,

128.6, 127.1, 121.9, 115.2, 110.4, 59.0, 38.0, 32.1, 31.2, 25.8, 24.4, 23.6, 22.7, 14.1;
MS (ESI) m/z 218 $[M+H]^+$.

7.3 Gold-Catalyzed Cycloisomerization Reactions of 1-(2-Tosylaminophenyl) prop-2-yn-1-ols as a Versatile Approach for Indole Synthesis

General Experimental Procedure for the Preparation of *N*-Protected Aniline Substituted Propargylic Alcohols (72a)-(72l) and (72p)-(72s)

To a solution of the (2-aminophenyl)(phenyl)methanone (0.88 mmol) in pyridine (0.4 mL) was added *p*-toluenesulfonylchloride (1.06 mmol) at room temperature under nitrogen atmosphere. The resulting solution was stirred for 4 h at room temperature. On completion, the reaction mixture was quenched by adding H₂O (5 mL) and filtered off. The resulting solid was dried and then used as such for the next step. To a stirred solution of diisopropylamine (0.28g, 2.8 mmol) in anhydrous THF (5 mL) was added butyl lithium (1.6 M Hexane solution; 1.8 mL; 2.8 mmol) at $-20\text{ }^{\circ}\text{C}$ as drop wise. The resulting solution was stirred at the same temperature for 10 min, and then the temperature brought up to $-78\text{ }^{\circ}\text{C}$. Followed by the corresponding alkyne (0.18 mL, 1.4 mmol) was added as drop wise. The resulting mixture was stirred at the same temperature for additional 1 h. The solid (0.25 g, 0.711 mmol) obtained was dissolved in anhydrous THF (2 mL), and added to the reaction mixture at the same temperature and allowed to stir for additional 1 h. The reaction mixture was slowly warmed up to room temperature and stirred for a further 1 h. On completion, the reaction mixture was quenched by adding saturated NH₄Cl (10 mL)

and extracted with EtOAc (2 x 10 mL). The combined organic layers were washed with brine, dried over Mg_2SO_4 , and concentrated under reduced pressure. Purification by flash column chromatography on silica gel (eluent: *n*-hexane: EtOAc = 20: 1) gave the title compound.

***N*-(2-(1-Hydroxy-1,3-diphenylprop-2-ynyl)phenyl)-4-ethylbenzenesulfonamide (72a)**

White solid; m.p. 136-140 °C; ^1H NMR (CDCl_3 , 400 MHz): δ 7.54 (2H, t, J = 6.52 Hz), 7.44-7.47 (4H, m), 7.36 (2H, d, J = 8.16 Hz), 7.29-7.34 (6H, m), 7.19 (1H, t, J = 7.28 Hz), 6.97-7.02 (3H, m), 2.30 (3H, s); ^{13}C NMR (CDCl_3 , 100 MHz): δ 143.3, 142.8, 136.4, 136.0, 131.7, 130.6, 129.5, 129.4, 129.0, 128.8, 128.6, 128.3, 128.2, 127.3, 126.0, 122.7, 121.7, 118.8, 89.7, 89.2, 75.5, 21.5; IR (NaCl, neat) ν : 3427, 3338, 2210, 1598, 1490, 1334, 1159, 1091 cm^{-1} ; MS (ESI) m/z 476 $[\text{M}+\text{Na}]^+$; HRMS (ESI) calcd. for $\text{C}_{28}\text{H}_{23}\text{NO}_3\text{SNa}$ (M^++Na): 476.1296, found: 476.1295.

***N*-(2-(1-Hydroxy-3-phenyl-1-*p*-tolylprop-2-ynyl)phenyl)-4-methylbenzenesulfonamide (72b)**

Pale yellow solid; m.p. 138-141 °C; ^1H NMR (CDCl_3 , 400 MHz): δ 8.64 (1H, brs), 7.57 (2H, t, J = 11.2 Hz), 7.44 (2H, dd, J = 1.52, 7.36 Hz), 7.38 (2H, d, J = 8.24 Hz),

7.29-7.34 (5H, m), 7.20 (1H, t, $J = 8.36$ Hz), 7.10 (2H, d, $J = 8.12$ Hz), 6.97-7.02 (3H, m), 3.2 (1H, brs), 2.38 (3H, s), 2.31 (3H, s); ^{13}C NMR (CDCl_3 , 100 MHz): δ 143.3, 139.8, 138.0, 136.4, 135.9, 131.7, 130.7, 129.4, 129.3, 128.9, 128.8, 128.3, 127.4, 125.9, 122.7, 121.8, 118.8, 89.8, 89.1, 75.4, 21.5, 21.2; IR (NaCl, neat) ν : 2953, 1522, 1336, 1159, 1091 cm^{-1} ; MS (ESI) m/z 490 $[\text{M}+\text{Na}]^+$; HRMS (ESI) calcd. for $\text{C}_{29}\text{H}_{25}\text{NO}_3\text{SNa}$ (M^++Na): 490.1453, found: 490.1449.

***N*-(2-(1-(4-Chlorophenyl)-1-hydroxy-3-phenylprop-2-ynyl)phenyl)-4-methylbenzenesulfonamide (72c)**

White solid; m.p. 135-138 $^{\circ}\text{C}$; ^1H NMR (CDCl_3 , 500 MHz): δ 8.69 (1H, brs), 7.72 (2H, t, $J = 8.0$ Hz), 7.46 (2H, d, $J = 8.05$ Hz), 7.27-7.38 (7H, m), 7.19 (3H, m), 7.09 (1H, d, $J = 7.65$ Hz), 7.06 (2H, d, $J = 7.7$ Hz), 3.7 (1H, brs), 2.39 (3H, s); ^{13}C NMR (CDCl_3 , 125 MHz): δ 143.5, 141.5, 136.3, 135.9, 134.0, 131.7, 130.3, 129.8, 129.4, 129.1, 129.0, 128.9, 128.6, 128.4, 128.7, 127.22, 127.0, 125.3, 123.0, 121.5, 119.2, 89.7, 89.3, 75.1, 21.5; IR (NaCl, neat) ν : 3323, 2223, 1598, 1583, 1489, 1400, 1336, 1159, 1091 cm^{-1} ; MS (ESI) m/z 510 $[\text{M}+\text{Na}]^+$; HRMS (ESI) calcd. for $\text{C}_{28}\text{H}_{22}\text{NO}_3\text{SNaCl}$ (M^++Na): 510.0907, found: 510.0911.

***N*-(2-(1-(4-Bromophenyl)-1-hydroxy-3-phenylprop-2-ynyl)phenyl)-4-methylbenzenesulfonamide (72d)**

White solid; m.p. 146-150 °C; ^1H NMR (CDCl_3 , 400 MHz): δ 8.68 (1H, brs), 7.72 (2H, d, $J = 8.52$ Hz), 7.45 (2H, d, $J = 7.92$ Hz), 7.31-7.36 (8H, m), 7.23 (2H, d, $J = 8.56$ Hz), 7.06 (3H, d, $J = 8.08$ Hz), 3.75 (1H, s), 2.36 (3H, s); ^{13}C NMR (CDCl_3 , 100 MHz): δ 143.5, 142.0, 136.2, 135.9, 131.7, 131.5, 130.2, 129.8, 129.4, 129.1, 128.9, 128.4, 127.5, 127.0, 123.0, 122.3, 121.5, 119.2, 89.7, 89.2, 75.1, 21.5; IR (NaCl, neat) ν : 3419, 2223, 1600, 1583, 1490, 1396, 1336, 1159, 1091 cm^{-1} ; MS (ESI) m/z 554 $[\text{M}+\text{Na}]^+$; HRMS (ESI) calcd. for $\text{C}_{28}\text{H}_{23}\text{NO}_3\text{SBr}$ (M^++H): 532.0582, found: 532.0581.

***N*-(2-(1-hydroxy-3-phenyl-1-*m*-tolylprop-2-ynyl)phenyl)-4-methylbenzenesulfonamide (72e)**

Yellolw gum; ^1H NMR (CDCl_3 , 500 MHz): δ 8.80 (1H, brs), 7.65-7.67 (1H, dd, $J = 1.15, 7.8$ Hz), 7.61 (1H, d, $J = 8.05$ Hz), 7.50-7.48 (2H, dd, $J = 1.55, 8.0$ Hz), 7.40-7.32 (6H, m), 7.27 (3H, m), 7.17 (1H, d, $J = 7.45$ Hz), 7.06-7.02 (3H, m), 3.72 (1H, s), 2.34-2.32 (6H, s); ^{13}C NMR (CDCl_3 , 125 MHz): δ 143.3, 142.8, 138.3, 136.3, 135.9, 2.34-2.32 (6H, s);

131.8, 130.8, 129.4, 129.4, 129.0, 128.9, 128.9, 128.5, 128.3, 127.3, 126.6, 123.1, 122.8, 121.9, 118.7, 89.9, 89.1, 75.4, 21.6, 21.5; IR (NaCl, neat) ν : 3325, 3031, 2854, 2224, 1600, 1583, 1492, 1448, 1334, 1159, 1091, 690 cm^{-1} ; HRMS (ESI) calcd. for $\text{C}_{29}\text{H}_{26}\text{NO}_3\text{S}$ ($\text{M}^+ + \text{H}$): 468.1633, found: 468.1632.

***N*-(2-(3-(4-Fluorophenyl)-1-hydroxy-1-phenylprop-2-ynyl)phenyl)-4-methylbenzenesulfonamide (72f)**

White solid; m.p. 158-160 $^{\circ}\text{C}$; ^1H NMR (CDCl_3 , 400 MHz): δ 8.70 (1H, s), 7.51-7.53 (2H, m), 7.41-7.46 (4H, m), 7.31-7.37 (5H, m), 7.18-7.24 (1H, dd, $J = 8.6, 15.8$ Hz), 6.96-7.02 (5H, m), 3.57 (1H, s), 2.30 (3H, s); ^{13}C NMR (CDCl_3 , 100 MHz): δ 161.6 (1C, d, $J_{\text{C-F}} = 250$ Hz), 142.7 (1C, d, $J_{\text{C-F}} = 70$ Hz), 136.4, 135.9, 133.8, 133.7, 130.6, 129.5, 129.4, 128.8 (1C, d, $J_{\text{C-F}} = 16$ Hz), 128.2, 127.3, 126.0, 122.8, 118.8, 117.9, 117.8, 115.8 (1C, d, $J_{\text{C-F}} = 22$ Hz), 89.4, 88.2, 75.4, 21.5; IR (NaCl, neat) ν : 3294, 2221, 1600, 1506, 1490, 1336, 1159, 1091 cm^{-1} ; MS (ESI) m/z 494 [$\text{M} + \text{Na}$] $^+$; HRMS (ESI) calcd. for $\text{C}_{28}\text{H}_{22}\text{NO}_3\text{SNaF}$ ($\text{M}^+ + \text{Na}$): 494.1202, found: 494.1199.

***N*-(2-(3-(4-Chlorophenyl)-1-hydroxy-1-phenylprop-2-ynyl)phenyl)-4-methylbenzenesulfonamide (72g)**

White solid; m.p. 134-138 °C; ^1H NMR (CDCl_3 , 400 MHz): δ 8.70 (1H, brs), 7.50 (2H, d, $J = 8.12$ Hz), 7.43 (2H, dd, $J = 1.6, 7.04$ Hz), 7.31-7.38 (7H, m), 7.24-7.27 (2H, m), 7.18 (1H, t, $J = 8.36$ Hz), 6.96 (3H, m), 3.62 (1H, brs), 2.30 (3H, s); ^{13}C NMR (CDCl_3 , 100 MHz): δ 143.4, 142.6, 136.4, 135.9, 135.1, 133.0, 130.5, 129.5, 129.4, 128.8, 128.7, 128.7, 128.3, 127.3, 126.0, 122.8, 120.3, 118.8, 90.6, 88.0, 75.5, 21.5; IR (NaCl, neat) ν : 3421, 3346, 2223, 1600, 1583, 1490, 1334, 1159, 1091 cm^{-1} ; MS (ESI) m/z 510 $[\text{M}+\text{Na}]^+$; HRMS (ESI) calcd. for $\text{C}_{28}\text{H}_{23}\text{NO}_3\text{SCl}$ (M^++H): 488.1087, found: 488.1089.

***N*-(2-(1-Hydroxy-3-(4-methoxyphenyl)-1-phenylprop-2-ynyl)phenyl)-4-methylbenzenesulfonamide (72h)**

Pale yellow solid; m.p. 158-162 °C; ^1H NMR (CDCl_3 , 300 MHz): δ 8.72 (1H, s), 7.54-7.60 (2H, m), 7.45 (2H, dd, $J = 1.98, 5.49$ Hz), 7.31-7.40 (6H, m), 7.19-7.26 (2H, m), 6.99-7.03 (3H, m), 6.82 (2H, d, $J = 8.79$ Hz), 3.79 (3H, s), 3.45 (1H, s), 2.31 (3H, s); ^{13}C NMR (CDCl_3 , 75 MHz): δ 160.1, 143.3, 142.9, 136.3, 135.9, 133.3, 130.8, 129.4, 128.8, 128.6, 128.1, 127.3, 126.0, 122.7, 118.7, 114.3, 113.8, 89.3, 88.4, 75.5, 55.3, 21.5; IR (NaCl, neat) ν : 3367, 2220, 1604, 1510, 1490, 1332, 1290, 1159, 1091

cm^{-1} ; MS (ESI) m/z 506 $[\text{M}+\text{Na}]^+$; HRMS (ESI) calcd. for $\text{C}_{29}\text{H}_{25}\text{NO}_4\text{SNa}$ (M^++Na): 506.1402, found: 506.1400.

***N*-(2-(1-Hydroxy-1-phenyl-3-*p*-tolylprop-2-ynyl)phenyl)-4-methylbenzene sulfonamide (72i)**

White solid; m.p. 151-155 °C; ^1H NMR (CDCl_3 , 400 MHz): δ 8.71 (1H, brs), 7.53 (2H, dd, $J = 1.95, 15.64$ Hz), 7.44 (2H, dd, $J = 1.68, 6.76$ Hz), 7.29-7.36 (7H, m), 7.17-7.23 (1H, m), 7.09 (2H, d, $J = 7.92$ Hz), 6.98 (3H, d, $J = 8.16$ Hz), 3.45 (1H, brs), 2.33 (3H, s), 2.28 (3H, s); ^{13}C NMR (CDCl_3 , 100 MHz): δ 143.3, 142.9, 139.2, 136.3, 135.9, 131.7, 130.7, 129.4, 129.1, 128.8, 128.6, 128.1, 127.4, 126.0, 122.7, 118.7, 118.7, 89.5, 89.1, 75.5, 21.56, 21.51; IR (NaCl, neat) ν : 3344, 2222, 1600, 1583, 1510, 1490, 1404, 1336, 1159, 1091 cm^{-1} ; MS (ESI) m/z 490 $[\text{M}+\text{Na}]^+$; HRMS (ESI) calcd. for $\text{C}_{29}\text{H}_{25}\text{NO}_3\text{SNa}$ (M^++Na): 490.1453, found: 490.1457.

***N*-(4-Bromo-2-(1-hydroxy-1,3-diphenylprop-2-ynyl)phenyl)-4-methyl benzene sulfonamide (72j)**

White solid; m.p. 151-155 °C; ^1H NMR (CDCl_3 , 400 MHz): δ 8.67 (1H, brs), 7.73 (1H, s), 7.42-7.44 (5H, m), 7.26-7.31 (9H, m), 6.95 (2H, d, $J = 7.72$ Hz), 3.75 (1H, brs), 2.27 (3H, s); ^{13}C NMR (CDCl_3 , 100 MHz): δ 143.7, 142.1, 135.7, 135.0, 132.7, 132.2, 131.8, 129.5, 129.2, 128.8, 128.4, 128.4, 127.3, 125.9, 121.5, 120.2, 115.7,

89.8, 89.6, 89.0, 74.9, 21.5; IR (NaCl, neat) ν : 3304, 2223, 1597, 1487, 1384, 1330, 1159, 1091 cm^{-1} ; MS (ESI) m/z 556 $[\text{M}+\text{Na}]^+$; HRMS (ESI) calcd. for $\text{C}_{28}\text{H}_{22}\text{NO}_3\text{SNa}81\text{Br}$ (M^++Na): 556.0381, found: 556.0378.

***N*-(4-Chloro-2-(1-hydroxy-1,3-diphenylprop-2-ynyl)phenyl)-4-methylbenzene sulfonamide (72k)**

Yellow solid; m.p. 160-164 $^{\circ}\text{C}$; ^1H NMR (CDCl_3 , 400 MHz): δ 7.58 (1H, s), 7.43-7.50 (5H, m), 7.23-7.32 (9H, m), 7.14 (1H, d, $J = 7.2$ Hz), 6.96 (2H, d, $J = 7.76$ Hz), 2.28 (3H, s); ^{13}C NMR (CDCl_3 , 100 MHz): δ 143.6, 142.2, 135.8, 134.5, 132.5, 131.8, 129.5, 129.2, 129.1, 128.8, 128.4, 128.1, 127.3, 125.9, 121.5, 119.9, 89.6, 89.0, 74.9, 21.5; IR (NaCl, neat) ν : 3421, 2926, 2223, 1598, 1487, 1386, 1332, 1161, 1091 cm^{-1} ; MS (ESI) m/z 510 $[\text{M}+\text{Na}]^+$; HRMS (ESI) calcd. for $\text{C}_{28}\text{H}_{22}\text{NO}_3\text{SClNa}$ (M^++Na): 510.0907, found: 510.0901.

***N*-(2-(1-Hydroxy-1,3-diphenylprop-2-ynyl)-4,6-dimethylphenyl)-4-methylbenzenesulfonamide (72l)**

White solid; m.p. 158-161 $^{\circ}\text{C}$; ^1H NMR (CDCl_3 , 400 MHz): δ 7.70 (2H, d, $J = 8.08$ Hz), 7.62 (2H, d, $J = 7.36$ Hz), 7.46-7.48 (2H, m), 7.28-7.41 (6H, m), 7.22 (2H, d, $J = 8.48$ Hz), 7.07 (1H, s), 6.96 (1H, s), 4.36 (1H, s), 2.39 (3H, s), 2.21 (3H, s), 1.91 (3H, s); ^{13}C NMR (CDCl_3 , 100 MHz): δ 144.1, 143.5, 140.0, 138.2, 137.1, 136.4, 132.5,

131.8, 130.5, 129.4, 128.7, 128.4, 128.3, 128.2, 128.0, 127.3, 126.5, 122.2, 91.5, 88.5, 74.7, 21.5, 21.1, 19.6; IR (NaCl, neat) ν : 3408, 1598, 1490, 1473, 1327, 1155, 1091 cm^{-1} ; MS (ESI) m/z 504 $[\text{M}+\text{Na}]^+$; HRMS (ESI) calcd. for $\text{C}_{30}\text{H}_{27}\text{NO}_3\text{SNa}$ (M^++Na): 504.1609, found: 504.1603.

***N*-(3-(1-Hydroxy-1,3-diphenylprop-2-ynyl)naphthalen-2-yl)-4-methylbenzenesulfonamide (72m)**

Pale yellow solid; m.p. 193-197 °C; ^1H NMR ($(\text{CD}_3)_2\text{CO}$, 400 MHz): δ 9.30 (1H, s), 8.35 (1H, s), 7.95 (1H, s), 7.86 (1H, d, $J = 8.08$ Hz), 7.78 (1H, d, $J = 8.2$ Hz), 7.46-7.54 (5H, m), 7.35-7.42 (8H, m), 7.22 (1H, s), 7.08 (2H, d, $J = 8.08$ Hz), 2.85 (1H, s), 2.26 (3H, s); ^{13}C NMR (CDCl_3 , 100 MHz): δ 143.6, 136.2, 134.1, 133.5, 131.5, 131.4, 129.4, 129.0, 128.9, 128.6, 128.5, 128.1, 127.9, 127.4, 127.2, 126.6, 125.8, 125.1, 122.1, 114.0, 90.5, 88.5, 75.0, 20.4; IR (NaCl, neat) ν : 3428, 1521, 1342, 1317, 1159 cm^{-1} ; MS (ESI) m/z 526 $[\text{M}+\text{Na}]^+$; HRMS (ESI) calcd. for $\text{C}_{32}\text{H}_{25}\text{NO}_3\text{SNa}$ (M^++Na): 526.1453, found: 526.1459.

General Experimental Procedure for the Preparation of *N*-Protected Aniline Substituted Propargylic Alcohols (72n)-(72o)

To a solution of the appropriate 1-(2-aminophenyl)ketone (1.1 mmol) in pyridine (0.4 mL) was added *p*-toluenesulfonylchloride (1.6 mmol) at room temperature under

nitrogen atmosphere. The resulting solution was stirred for 4 h at room temperature. On completion, the reaction mixture was quenched by adding H₂O (5 mL) and filtered off. The resulting solid was dried and then used as such for the next step. The solid (0.51 mmol) was dissolved in anhydrous THF (8 mL) and then a solution of ethynylmagnesium bromide for **72n** and **72o** (0.5 M THF solution; 1.5 mmol) was added at room temperature (note: 1-propynyl magnesium bromide (0.5 M THF solution; 1.5 mmol) was used for compound **72p**). The resulting mixture was allowed to reflux for 3 h. On completion, the reaction mixture was cooled to room temperature and treated with saturated NH₄Cl (7 mL). After additional stirring at room temperature for 10 min, EtOAc (15 mL) was added, and phases were separated. The aqueous phases was extracted with EtOAc (3 x 5 mL), the combined organic layers were washed with brine solution and dried over anhydrous Na₂SO₄ and concentrated under reduced pressure. Purification by flash column chromatography on silica gel (eluent: *n*-hexane: EtOAc = 9: 1) gave the title compound.

***N*-(2-(1-Hydroxy-1-phenylprop-2-ynyl)phenyl)-4-methylbenzenesulfonamide
(72n)**

White solid; m.p. 91-94 °C; ¹H NMR (CDCl₃, 400 MHz): δ 8.47 (1H, brs), 7.54 (1H, dd, *J* = 8.32, 12.4 Hz), 7.38 (2H, d, *J* = 6.6 Hz), 7.29-7.36 (5H, m), 7.21 (1H, d, *J* = 7.48 Hz), 7.05 (2H, d, *J* = 8.0 Hz), 6.98 (1H, t, *J* = 7.64 Hz) 3.22 (1H, brs), 2.90 (1H, s), 2.33 (3H, s); ¹³C NMR (CDCl₃, 100 MHz): δ 143.4, 142.2, 136.3, 135.8, 130.1, 129.6, 129.4, 128.8, 128.7, 128.3, 127.3, 125.8, 122.8, 119.0, 84.4, 77.8, 74.9, 21.5;

IR (NaCl, neat) ν : 3302, 2221, 1492, 1334, 1159, 1091 cm^{-1} ; MS (ESI) m/z 400 $[\text{M}+\text{Na}]^+$; HRMS (ESI) calcd. for $\text{C}_{22}\text{H}_{20}\text{NO}_3\text{S}$ (M^++H): 378.1164, found: 378.1163.

***N*-(2-(1-Hydroxy-1-*p*-tolylprop-2-ynyl)phenyl)-4-methylbenzenesulfonamide (72o)**

Yellow gum; ^1H NMR (CDCl_3 , 500 MHz): δ 8.49 (1H, brs), 7.50 (1H, d, $J = 7.5$ Hz), 7.47 (1H, dd, $J = 1.35, 7.85$ Hz), 7.27 (2H, d, $J = 8.3$ Hz), 7.18-7.12 (3H, m), 7.01 (2H, d, $J = 8.1$ Hz), 6.97 (2H, d, $J = 8.15$ Hz), 6.92-6.89 (1H, m), 2.78 (1H, s), 2.29 (3H, s), 2.25 (3H, s); ^{13}C NMR (CDCl_3 , 125 MHz): δ 143.3, 139.4, 138.1, 136.4, 135.8, 130.2, 129.5, 129.3, 128.8, 127.3, 125.7, 122.8, 119.0, 84.6, 77.5, 74.8, 21.5, 21.2; IR (NaCl, neat) ν : 3306, 2218, 1495, 1339, 1162, 1092 cm^{-1} ; MS (ESI) m/z 414 $[\text{M}+\text{Na}]^+$; HRMS (ESI) calcd. for $\text{C}_{23}\text{H}_{21}\text{NO}_3\text{SNa}$ (M^++Na): 414.1140, found: 414.1147.

***N*-(2-(1-Hydroxy-1-phenylbut-2-ynyl)phenyl)-4-methylbenzenesulfonamide (72p)**

White solid; m.p. 135-138 $^{\circ}\text{C}$; ^1H NMR (CDCl_3 , 400 MHz): δ 8.70 (1H, s), 7.59 (1H, dd, $J = 1.2, 7.84$ Hz), 7.54 (1H, d, $J = 8.16$ Hz), 7.39 (2H, dd, $J = 1.48, 7.16$ Hz), 7.28-7.35 (5H, m), 7.20 (1H, t, $J = 7.92$ Hz), 7.05 (2H, d, $J = 8.16$ Hz), 6.99 (1H, t, J

= 7.68 Hz), 3.47 (1H, s), 2.34 (3H, s), 1.93 (3H, s); ^{13}C NMR (CDCl_3 , 100 MHz): δ 143.3, 136.3, 135.8, 131.1, 129.4, 129.3, 128.9, 128.5, 127.9, 127.3, 125.8, 122.6, 118.6, 86.3, 80.5, 75.1, 21.5, 3.9; IR (NaCl, neat) ν : 3327, 2942, 2223, 1600, 1583, 1490, 1334, 1159, 1091 cm^{-1} ; MS (ESI) m/z 414 $[\text{M}+\text{Na}]^+$; HRMS (ESI) calcd. for $\text{C}_{23}\text{H}_{21}\text{NO}_3\text{SNa}$ (M^++Na): 414.1140, found: 414.1140.

***N*-(2-(1-Hydroxy-1-phenylhept-2-ynyl)phenyl)-4-methylbenzenesulfonamide (72q)**

White solid; m.p. 125-128 $^{\circ}\text{C}$; ^1H NMR (CDCl_3 , 300 MHz): δ 8.72 (1H, brs), 7.61 (1H, dd, J = 1.35, 7.85 Hz), 7.39-7.42 (2H, m), 7.27-7.35 (5H, m), 7.24 (1H, t, J = 8.73 Hz), 6.98-7.07 (3H, m), 3.50 (1H, brs), 2.33 (3H, s), 2.30 (2H, t, J = 7.17 Hz), 1.51-1.60 (2H, m), 1.38-1.48 (2H, m), 0.90 (3H, t, J = 7.29 Hz); ^{13}C NMR (CDCl_3 , 75 MHz): δ 143.3, 143.2, 136.5, 135.8, 129.4, 129.2, 128.8, 128.4, 127.8, 127.3, 125.8, 122.6, 118.5, 90.1, 77.5, 75.0, 30.4, 22.0, 21.5, 18.6, 13.5; IR (NaCl, neat) ν : 3566, 3429, 3367, 2960, 2933, 2226, 1600, 1492, 1456, 1334, 1159, 1091 cm^{-1} ; MS (ESI) m/z 456 $[\text{M}+\text{Na}]^+$; HRMS (ESI) calcd. for $\text{C}_{26}\text{H}_{28}\text{NO}_3\text{S}$ (M^++H): 434.1790, found: 434.1794.

***N*-(2-(3-Cyclopropyl-1-hydroxy-1-phenylprop-2-ynyl)phenyl)-4-methylbenzenesulfonamide (72r)**

White solid; m.p. 173-176 °C; ^1H NMR (CDCl_3 , 400 MHz): δ 8.60 (1H, brs), 7.48 (2H, t, $J = 6.12$ Hz), 7.25-7.36 (7H, m), 7.15 (1H, t, $J = 7.8$ Hz), 7.03 (2H, d, $J = 8.08$ Hz), 6.94 (1H, t, $J = 7.68$ Hz), 3.18 (1H, brs), 2.31 (3H, s), 1.28-1.35 (1H, m), 0.73-0.83 (4H, m); ^{13}C NMR (CDCl_3 , 100 MHz): δ 143.3, 143.2, 136.2, 135.7, 131.1, 129.2, 128.7, 127.9, 127.3, 125.9, 122.6, 118.6, 93.7, 76.4, 75.0, 21.5, 8.5; IR (NaCl, neat) ν : 3305, 2235, 1598, 1581, 1490, 1454, 1392, 1334, 1276, 1159, 1089 cm^{-1} ; MS (ESI) m/z 440 $[\text{M}+\text{Na}]^+$; HRMS (ESI) calcd. for $\text{C}_{25}\text{H}_{24}\text{NO}_3\text{S}$ (M^++H): 418.1477, found: 418.1478.

***N*-(2-(3-Cyclopentyl-1-hydroxy-1-phenylprop-2-ynyl)phenyl)-4-methylbenzenesulfonamide (72s)**

White solid; m.p. 132-136 °C; ^1H NMR (CDCl_3 , 500 MHz): δ 8.73 (1H, brs), 7.55 (1H, dd, $J = 1.25, 7.60$ Hz), 7.47 (1H, d, $J = 8.15$ Hz), 7.35 (2H, dd, $J = 1.35, 7.3$ Hz), 7.21-7.29 (5H, m), 7.12 (1H, t, $J = 8.0$ Hz), 6.98 (2H, d, $J = 8.1$ Hz), 6.93 (1H, t, $J = 7.7$ Hz), 3.58 (1H, brs), 2.65-2.70 (1H, m), 2.27 (3H, s), 1.87-1.90 (2H, m), 1.51-1.69 (6H, m); ^{13}C NMR (CDCl_3 , 125 MHz): δ 143.6, 143.3, 136.3, 135.7, 131.3, 129.4, 129.2, 128.7, 128.4, 127.8, 127.3, 125.9, 122.7, 118.5, 94.9, 81.0, 74.9, 33.6, 30.2, 25.0, 21.3; IR (NaCl, neat) ν : 3325, 2962, 2870, 2227, 1600, 1583, 1492, 1456, 1334,

1159, 1091 cm^{-1} ; MS (ESI) m/z 468 $[\text{M}+\text{Na}]^+$; HRMS (ESI) calcd. for $\text{C}_{27}\text{H}_{28}\text{NO}_3\text{S}$ (M^++H): 446.1790, found: 446.1793.

***N*-(2-(3-Cyclohexyl-1-hydroxy-1-phenylprop-2-ynyl)phenyl)-4-methylbenzenesulfonamide (72t)**

White solid; m.p. 110-114 $^{\circ}\text{C}$; ^1H NMR (CDCl_3 , 400 MHz): δ 8.62 (1H, brs), 7.58 (1H, dd, $J = 1.36, 7.84$ Hz), 7.52 (1H, dd, $J = 0.68, 8.16$ Hz), 7.40 (2H, m), 7.29-7.36 (5H, m), 7.19 (1H, t, $J = 8.76$ Hz), 7.06 (2H, d, $J = 8.12$ Hz), 6.98 (1H, t, $J = 7.76$ Hz), 3.09 (1H, brs), 2.48-2.51 (1H, m), 2.35 (3H, s), 1.83-1.85 (2H, m), 1.69-1.71 (2H, m), 1.47-1.53 (3H, m), 1.31-1.34 (3H, m); ^{13}C NMR (CDCl_3 , 100 MHz): δ 143.3, 143.2, 136.4, 135.7, 131.1, 129.4, 129.2, 128.6, 128.4, 127.9, 127.3, 125.9, 122.6, 118.6, 94.8, 81.3, 74.9, 32.2, 29.1, 25.7, 24.8, 21.5; IR (NaCl, neat) ν : 3327, 2931, 2854, 2224, 1600, 1583, 1492, 1448, 1334, 1159, 1091 cm^{-1} ; MS (ESI) m/z 482 $[\text{M}+\text{Na}]^+$; HRMS (ESI) calcd. for $\text{C}_{28}\text{H}_{30}\text{NO}_3\text{S}$ (M^++H): 460.1946, found: 460.1944.

General Procedure for Optimizing the Lewis and Brønsted Acid-Catalyzed Intramolecular Cyclization of 2-Tosylaminophenyl-1-yne-3-ols (72a)

For reactions with a gold/silver catalyst combination, the gold (11 μmol) and silver (11 μmol) catalysts were first stirred in toluene (1.5 mL) at room temperature for 10 minutes. In all other cases, the catalyst was added to a respective solvent prior to adding the starting materials. Then a toluene solution (1.5 mL) containing **72a** (0.22 mmol) was added slowly as drop wise, and the reaction mixture stirred at reflux

temperature and monitored to completion by TLC analysis. The solvent removed under reduced pressure. Purification by flash column chromatography on silica gel (*n*-hexane/EtOAc 20:1 as eluent) gave **73a**.

General Procedure for Gold-Catalyzed Intramolecular Cyclization of 2-Tosylaminophenyl-1-yne-3-ols (**72a**)

A solution of AuCl (11 μ mol), AgOTf (11 μ mol) and CaSO₄ (35 mg) in toluene (1.5 mL) was stirred under an Ar atmosphere at room temperature for 10 min. On completion, HMPA (20 mol %) was added followed by slow dropwise addition of a solution of **72a** (0.22 mmol) in 1.5 mL of toluene (note: 8 equiv of the nucleophile was also added at this point for reactions of **72n** described in entries 3-4 in Table 3). The reaction mixture was then stirred at reflux temperature for 2 h. The solvent was removed under reduced pressure. Purification by flash column chromatography on silica gel (20:1 *n*hexane/EtOAc as eluent) gave the indole product.

6-Phenyl-5-tosyl-5,6-dihydroindeno[2,1-*b*]indole (**73a**)

Off white solid; m.p. 175-180 °C; ¹H NMR (CDCl₃, 300 MHz): δ 8.05-8.11 (1H, m), 7.86-7.90 (1H, m), 7.64 (1H, d, *J* = 7.44 Hz), 7.28-7.41 (3H, m), 7.09-7.26 (9H, m), 6.97 (2H, d, *J* = 8.16 Hz), 5.33 (1H, s), 2.27 (3H, s); ¹³C NMR (CDCl₃, 75 MHz): δ 150.0, 149.0, 144.6, 139.9, 139.0, 136.1, 135.2, 129.6, 128.6, 127.2, 126.9, 125.2, 125.0, 124.3, 124.2, 123.7, 120.0, 119.4, 114.7, 51.4, 21.5; IR (NaCl, neat) ν : 3064, 2960, 2926, 1605, 1597, 1494, 1444, 1373, 1352, 1261, 1188, 1170, 1149, 1120, 1097,

1020, 700 cm^{-1} ; MS (ESI) m/z 436 $[\text{M}+\text{H}]^+$; HRMS (ESI) calcd. for $\text{C}_{28}\text{H}_{21}\text{NO}_2\text{SNa}$ (M^++Na): 458.1191, found: 451.1193.

8-Methyl-6-phenyl-5-tosyl-5,6-dihydroindeno[2,1-*b*]indole (73b):

Colourless gum; ^1H NMR (CDCl_3 , 400 MHz): δ 8.05 (1H, d, $J = 5.28$ Hz), 7.83 (1H, d, $J = 5.44$ Hz), 7.53 (1H, d, $J = 7.52$ Hz), 7.34-7.36 (2H, m), 7.09-7.25 (8H, m), 6.96 (3H, d, $J = 8.16$ Hz), 5.28 (1H, s), 2.30 (3H, s), 2.26 (3H, s); ^{13}C NMR (CDCl_3 , 100 MHz): δ 150.2, 148.4, 144.5, 139.9, 139.3, 135.3, 134.9, 133.3, 129.5, 128.7, 128.6, 127.8, 126.9, 125.9, 124.2, 123.6, 120.03, 119.1, 114.7, 51.4, 21.5, 21.4 ; IR (NaCl, neat) ν : 3062, 2924, 1597, 1494, 1445, 1371, 1170, 1149, 1087, 1041, 869 cm^{-1} ; MS (ESI) m/z 450 $[\text{M}+\text{H}]^+$; HRMS (ESI) calcd. for $\text{C}_{29}\text{H}_{24}\text{NO}_2\text{S}$ (M^++H): 450.1528, found: 450.1528.

8-Chloro-6-phenyl-5-tosyl-5,6-dihydroindeno[2,1-*b*]indole (73c)

Colorless gum; ^1H NMR (CDCl_3 , 400 MHz): δ 8.05-8.07 (1H, m), 7.81-7.83 (1H, m), 7.57 (1H, d, $J = 7.96$ Hz), 7.36-7.39 (2H, m), 7.21-7.30 (4H, m), 7.12 (3H, d, $J = 8.52$ Hz), 7.06 (2H, d, $J = 6.84$ Hz), 6.97 (2H, d, $J = 8.2$ Hz), 5.31 (1H, s), 2.27 (3H, s); ^{13}C NMR (CDCl_3 , 100 MHz): δ 151.5, 148.8, 144.7, 139.8, 138.1, 135.1, 134.7, 130.7,

129.6, 128.8, 128.6, 127.4, 127.2, 126.9, 126.5, 125.5, 124.5, 123.8, 120.1, 119.9, 114.7, 51.4, 21.5; IR (NaCl, neat) ν : 3066, 2962, 2924, 1598, 1492, 1444, 1411, 1373, 1253, 1190, 1172, 1149, 1120, 1089, 1039, 867 cm^{-1} ; MS (ESI) m/z 492 $[\text{M}+\text{Na}]^+$; HRMS (ESI) calcd. for $\text{C}_{28}\text{H}_{21}\text{NO}_2\text{SCl}$ (M^++H): 470.0982, found: 470.0982.

8-Bromo-6-phenyl-5-tosyl-5,6-dihydroindeno[2,1-*b*]indole (73d)

Yellow gum; ^1H NMR (CDCl_3 , 400 MHz): δ 8.05-8.07 (1H, m), 7.81-7.83 (1H, m), 7.50 (1H, d, $J = 8.0$ Hz), 7.43 (1H, dd, $J = 1.60, 8.15$ Hz), 7.36-7.39 (2H, m), 7.22-7.28 (4H, m), 7.13 (2H, d, $J = 8.36$ Hz), 7.07 (2H, d, $J = 6.92$ Hz), 6.97 (2H, d, $J = 8.2$ Hz), 5.31 (1H, s), 2.27 (3H, s); ^{13}C NMR (CDCl_3 , 100 MHz): δ 151.8, 148.8, 144.7, 139.8, 138.0, 135.1, 130.3, 129.6, 128.8, 128.6, 127.3, 126.9, 126.5, 124.5, 123.8, 123.8, 120.5, 119.9, 118.5, 114.7, 51.3, 21.5; IR (NaCl, neat) ν : 3061, 2961, 2926, 1598, 1492, 1444, 1373, 1190, 1170, 1089, 1041, 871 cm^{-1} ; MS (ESI) m/z 536 $[\text{M}+\text{Na}]^+$; HRMS (ESI) calcd. for $\text{C}_{28}\text{H}_{21}\text{NO}_2\text{SBr}$ (M^++H): 516.0456, found: 516.0461.

9-methyl-6-phenyl-5-tosyl-5,6-dihydroindeno[2,1-*b*]indole and 7-methyl-6-phenyl-5-tosyl-5,6-dihydroindeno[2,1-*b*]indole 73e and 73e'

Colourless gum; ^1H NMR (CDCl_3 , 400 MHz): δ 8.07-8.04 (1H, m), 7.99-7.97 (1H, m), 7.91-7.82 (2H, m), 7.55-7.54 (1H, d, $J = 7.06$ Hz), 7.49 (1H, s), 7.45-6.82 (21H, m), 5.35 (1H, s), 5.29 (1H, s), 2.38 (3H, s), 2.33 (4H, s), 2.11 (1H, s); ^{13}C NMR (CDCl_3 , 100 MHz): δ 149.9, 149.2, 147.9, 147.2, 144.5, 144.5, 139.9, 139.7, 139.3, 137.3, 137.0, 136.4, 136.1, 135.2, 135.2, 134.4, 129.8, 129.5, 129.5, 128.8, 128.6, 128.6, 128.3, 127.7, 127.4, 127.1, 127.0, 126.9, 126.8, 126.8, 125.8, 124.6, 124.3, 124.2, 124.1, 123.7, 123.6, 120.3, 120.0, 120.0, 117.2, 114.7, 114.6, 51.1, 50.8, 21.6, 21.4, 21.4, 18.6; IR (NaCl, neat) ν : 3062, 2924, 1597, 1494, 1445, 1371, 1170, 1149, 1087, 1041, 691, 752 cm^{-1} ; MS (ESI) m/z 450 $[\text{M}+\text{H}]^+$; HRMS (ESI) calcd. for $\text{C}_{29}\text{H}_{24}\text{NO}_2\text{S}$ (M^++H): 450.1528, found: 450.1528.

6-(4-Fluorophenyl)-5-tosyl-5,6-dihydroindeno[2,1-*b*]indole (73f)

Yellow solid; m.p. 173-177 $^{\circ}\text{C}$; ^1H NMR (CDCl_3 , 300 MHz): δ 8.0-8.03 (1H, m), 7.76-7.79 (1H, m), 7.56 (1H, d, $J = 7.6$ Hz), 7.21-7.31 (3H, m), 7.13 (2H, $J = 7.83$ Hz), 7.04-7.05 (2H, m), 6.92-6.97 (4H, m), 6.76 (2H, t, $J = 8.61$ Hz), 5.21 (1H, s), 2.19 (3H, s); ^{13}C NMR (CDCl_3 , 75 MHz): δ 149.8, 148.6, 144.8, 140.1, 136.0, 135.3,

134.7, 130.1, 130.0, 129.6, 127.4, 126.7, 125.3, 124.9, 124.5, 124.1, 123.8, 120.0, 119.5, 115.5 (1C, d, J_{C-F} = 21.7 Hz), 114.8, 50.6, 21.5; IR (NaCl, neat) ν : 2926, 2927, 1558, 1541, 1506, 1496, 1442, 1373, 1259, 1168, 1147, 1118,, 1016, 864 cm^{-1} ; MS (ESI) m/z 454 $[\text{M}+\text{H}]^+$; HRMS (ESI) calcd. for $\text{C}_{28}\text{H}_{21}\text{NO}_2\text{SF}$ (M^++H): 454.1277, found: 454.1279.

6-(4-Chlorophenyl)-5-tosyl-5,6-dihydroindeno[2,1-*b*]indole (73g)

Yellow gum; ^1H NMR (CDCl_3 , 300 MHz): δ 8.10-8.13 (1H, m), 7.85-7.88 (1H, m), 7.65 (1H, d, J = 7.41 Hz), 7.30-7.40 (3H, m), 7.20 (2H, J = 8.31 Hz), 7.11-7.14 (4H, m), 6.96 (4H, dd, J = 8.25, 12.78 Hz), 5.27 (1H, s), 2.30 (3H, s); ^{13}C NMR (CDCl_3 , 75 MHz): δ 149.5, 148.3, 144.8, 140.2, 137.5, 136.0, 135.4, 132.8, 129.9, 129.6, 128.7, 127.7, 127.5, 126.5, 125.3, 124.9, 124.5, 124.0, 123.8, 120.0, 119.6, 114.8, 50.6, 21.5; IR (NaCl, neat) ν : 3061, 2965, 2926, 1489, 1444, 1373, 1188, 1170, 1089, 1014, 908 cm^{-1} ; MS (ESI) m/z 470 $[\text{M}+\text{H}]^+$; HRMS (ESI) calcd. for $\text{C}_{28}\text{H}_{21}\text{NO}_2\text{SCl}$ (M^++H): 470.0982, found: 470.0980.

6-(4-Methoxyphenyl)-5-tosyl-5,6-dihydroindeno[2,1-*b*]indole (73h)

White solid; m.p. 247-250 °C; ^1H NMR (CDCl_3 , 400 MHz): δ 8.07-8.09 (1H, m), 7.84-7.86 (1H, m), 7.64 (1H, d, $J = 7.4$ Hz), 7.29-7.38 (3H, m), 7.09-7.24 (4H, m), 6.98-7.00 (4H, m), 6.72 (2H, d, $J = 8.72$ Hz), 5.28 (1H, s), 3.78 (3H, s), 2.26 (3H, s); ^{13}C NMR (CDCl_3 , 100 MHz): δ 158.7, 150.3, 149.2, 144.5, 140.0, 136.0, 135.4, 130.8, 129.6, 129.5, 127.3, 127.2, 126.9, 125.1, 124.9, 124.3, 124.2, 123.7, 119.9, 119.4, 114.7, 114.0, 55.2, 50.7, 21.5; IR (NaCl, neat) ν : 3061, 2965, 2924, 1510, 1442, 1419, 1367, 1174, 1031, 1014 cm^{-1} ; MS (ESI) m/z 488 $[\text{M}+\text{Na}]^+$; HRMS (ESI) calcd. for $\text{C}_{29}\text{H}_{24}\text{NO}_3\text{S}$ (M^++H): 466.1477, found: 466.1479.

6-*p*-Tolyl-5-tosyl-5,6-dihydroindeno[2,1-*b*]indole (73i)

Yellow solid; m.p. 184-188 °C; ^1H NMR (CDCl_3 , 400 MHz): δ 8.07-8.09 (1H, m), 7.85-7.87 (1H, m), 7.66 (1H, d, $J = 7.4$ Hz), 7.29-7.37 (3H, m), 7.09-7.20 (5H, m), 6.95-7.02 (5H, m), 5.28 (1H, s), 2.33 (3H, s), 2.27 (3H, s); ^{13}C NMR (CDCl_3 , 100 MHz): δ 150.1, 149.1, 144.5, 140.0, 136.5, 136.1, 135.8, 135.4, 129.4, 129.3, 128.4, 127.1, 126.9, 125.1, 124.9, 124.2, 123.7, 119.9, 119.4, 114.7, 51.1, 21.5, 21.1; IR (NaCl, neat) ν : 3064, 2967, 2928, 1598, 1510, 1494, 1444, 1371, 1188, 1172, 1087,

1047, 1016, 812 cm^{-1} ; MS (ESI) m/z 472 $[\text{M}+\text{Na}]^+$; HRMS (ESI) calcd. for $\text{C}_{29}\text{H}_{24}\text{NO}_2\text{S}$ (M^++H): 450.1528, found: 450.1528.

2-Bromo-6-phenyl-5-tosyl-5,6-dihydroindeno[2,1-*b*]indole (73j)

Colorless gum; ^1H NMR (CDCl_3 , 400 MHz): δ 7.93 (2H, dd, $J = 1.88, 13.26$ Hz), 7.62 (1H, d, $J = 7.48$ Hz), 7.44 (1H, dd, $J = 2.0, 8.8$ Hz), 7.34 (1H, td, $J = 1.52, 7.16$ Hz), 7.15-7.27 (3H, m), 7.11-7.13 (3H, m), 7.06 (2H, d, $J = 5.92$ Hz), 6.98 (2H, d, $J = 8.2$ Hz), 5.31 (1H, s), 2.29 (3H, s); ^{13}C NMR (CDCl_3 , 100 MHz): δ 150.1, 149.8, 144.9, 138.6, 138.6, 135.4, 134.9, 129.7, 128.7, 128.6, 127.4, 127.1, 127.0, 126.9, 126.7, 125.7, 125.5, 125.0, 122.7, 119.4, 117.2, 116.0, 51.4, 21.5; IR (NaCl, neat) ν : 3066, 2962, 2927, 1598, 1444, 1367, 1190, 1176, 1161, 1099, 1087, 1045, 1016, 700 cm^{-1} ; MS (ESI) m/z 536 $[\text{M}+\text{Na}]^+$; HRMS (ESI) calcd. for $\text{C}_{28}\text{H}_{21}\text{NO}_2\text{SBr}$ (M^++H): 516.0456, found: 516.0464.

2-Chloro-6-phenyl-5-tosyl-5,6-dihydroindeno[2,1-*b*]indole (73k)

Yellow gum; ^1H NMR (CDCl_3 , 300 MHz): δ 8.0 (1H, d, $J = 8.88$ Hz), 7.81 (1H, d, $J = 1.8$ Hz), 7.64 (1H, d, $J = 7.44$ Hz), 7.30-7.33 (2H, m), 7.06-7.25 (9H, m), 6.98 (2H, d, $J = 8.19$ Hz), 5.30 (1H, s), 2.28 (3H, s); ^{13}C NMR (CDCl_3 , 75 MHz): δ 149.8, 144.9, 138.6, 138.2, 135.4, 135.0, 129.6, 129.6, 128.7, 128.6, 127.3, 127.1, 126.9, 125.5,

125.2, 125.0, 124.4, 119.7, 119.4, 115.6, 51.4, 21.5; IR (NaCl, neat) ν : 3061, 2193, 1597, 1494, 1446, 1433, 1371, 1253, 1190, 1174, 1163, 1087, 1047, 862 cm^{-1} ; MS (ESI) m/z 470 $[\text{M}+\text{H}]^+$; HRMS (ESI) calcd. for $\text{C}_{28}\text{H}_{21}\text{NO}_2\text{SCl}$ (M^++H): 470.0982, found: 470.0982.

7-Phenyl-6-tosyl-6,7-dihydrobenzo[*f*]indeno[2,1-*b*]indole (73m)

White solid; m.p. 250-254 $^{\circ}\text{C}$; ^1H NMR (CDCl_3 , 400 MHz): δ 8.54 (1H, s), 8.31 (1H, s), 8.02 (2H, q, $J = 3.96$ Hz), 7.80 (1H, d, $J = 7.32$ Hz), 7.51-7.55 (2H, m), 7.38 (1H, t, $J = 6.96$ Hz), 7.31 (2H, d, $J = 8.36$ Hz), 7.23-7.31 (4H, m), 7.18 (1H, d, $J = 7.24$ Hz), 7.14 (2H, d, $J = 5.8$ Hz), 6.99 (2H, d, $J = 8.24$ Hz), 5.39 (1H, s), 2.26 (3H, s); ^{13}C NMR (CDCl_3 , 100 MHz): δ 152.0, 149.9, 144.6, 139.8, 138.7, 135.9, 135.0, 130.9, 130.7, 129.6, 128.7, 128.5, 128.5, 127.9, 127.7, 127.3, 127.0, 126.8, 125.3, 125.2, 125.1, 124.9, 124.5, 119.6, 117.8, 112.2, 51.9, 21.4; IR (NaCl, neat) ν : 3068, 2962, 2926, 1597, 1452, 1431, 1379, 1174, 1095, 1012, 871 cm^{-1} ; MS (ESI) m/z 508 $[\text{M}+\text{Na}]^+$; HRMS (ESI) calcd. for $\text{C}_{32}\text{H}_{24}\text{NO}_2\text{S}$ (M^++H): 486.1528, found: 486.1532.

Phenyl(3-phenyl-1-tosyl-1*H*-indol-2-yl)methanol (74a)⁵⁹

Yellow oil; ^1H NMR (CDCl_3 , 300 MHz): δ 8.03 (1H, d, $J = 8.34$ Hz), 7.35-7.51 (10H, m), 7.22-7.33 (5H, m), 7.06 (2H, d, $J = 8.16$ Hz), 6.31 (1H, d, $J = 11.85$ Hz), 4.70

(1H, d, J = 11.85 Hz), 2.31 (3H, s); ^{13}C NMR (CDCl_3 , 75 MHz): δ 144.8, 142.4, 137.1, 135.2, 132.3, 130.1, 129.6, 128.8, 128.1, 128.1, 126.8, 125.6, 125.5, 123.8, 120.6, 114.6, 68.5, 21.5; MS (ESI) m/z 476 $[\text{M}+\text{Na}]^+$.

(3-Phenyl-1-tosyl-1*H*-indol-2-yl)methanol (74b)

Yellow solid; m.p. 207-211 °C; ^1H NMR (CDCl_3 , 500 MHz): δ 8.14 (1H, d, J = 8.40 Hz), 7.77 (2H, d, J = 8.25 Hz), 7.46-7.53 (5H, m), 7.34-7.41 (2H, m), 7.21-7.26 (3H, m), 4.84 (2H, d, J = 6.3 Hz), 3.3 (1H, t, J = 6.85 Hz), 2.3 (3H, s); ^{13}C NMR (CDCl_3 , 125 MHz): δ 145.2, 136.1, 135.6, 135.5, 132.1, 130.1, 130.0, 129.3, 128.7, 127.9, 126.5, 125.6, 123.9, 120.5, 114.5, 55.8, 21.6; IR (NaCl, neat) ν : 3526, 2926, 1598, 1494, 1450, 1369, 1188, 1174, 1089, 1051, 1024, 812 cm^{-1} ; MS (ESI) m/z 400 $[\text{M}+\text{Na}]^+$; HRMS (ESI) calcd. for $\text{C}_{22}\text{H}_{19}\text{NO}_3\text{SNa}$ (M^++Na): 400.0983, found: 400.0983.

(3-*p*-Tolyl-1-tosyl-1*H*-indol-2-yl)methanol (74c)

Yellow gum; ^1H NMR (CDCl_3 , 500 MHz): δ 8.14 (1H, d, J = 8.40 Hz), 7.77 (2H, d, J = 8.40 Hz), 7.52 (1H, d, J = 7.8 Hz), 7.40-7.22 (8H, m), 4.84 (2H, d, J = 7.45 Hz), 3.34 (1H, t, J = 7.45 Hz), 2.42 (3H, s), 2.35 (3H, s); ^{13}C NMR (CDCl_3 , 125 MHz): δ 145.1, 137.7, 136.1, 135.6, 135.3, 130.0, 129.9, 129.4, 129.0, 126.5, 125.6, 125.5,

123.8, 120.6, 114.5, 55.9, 21.6, 21.3; IR (NaCl, neat) ν : 3528, 2924, 1597, 1496, 1452, 1367, 1189, 1172, 1089, 1051, 1024, 812 cm^{-1} ; MS (ESI) m/z 414 $[\text{M}+\text{Na}]^+$; HRMS (ESI) calcd. for $\text{C}_{23}\text{H}_{21}\text{NO}_3\text{SNa}$ (M^++Na): 414.1140, found: 414.1142.

2-(Methoxymethyl)-3-phenyl-1-tosyl-1H-indole (75a)

White gum; ^1H NMR (CDCl_3 , 400 MHz): δ 8.21 (1H, d, $J = 8.44$ Hz), 7.97 (2H, d, $J = 8.28$ Hz), 7.50-7.33 (7H, m), 7.24-7.18 (3H, m), 4.73 (2H, s), 3.36 (3H, s), 2.32 (3H, s); ^{13}C NMR (CDCl_3 , 100 MHz): δ 144.5, 136.2, 136.1, 132.8, 132.4, 130.1, 129.5, 129.0, 128.6, 127.8, 127.2, 126.4, 125.4, 123.5, 120.3, 114.8, 64.3, 57.8, 21.5; IR (NaCl, neat) ν : 2926, 1598, 1494, 1450, 1369, 1188, 1174, 1089, 1051, 1024, 812 cm^{-1} ; MS (ESI) m/z 414 $[\text{M}+\text{Na}]^+$; HRMS (ESI) calcd. for $\text{C}_{23}\text{H}_{21}\text{NO}_3\text{S}$ (M^++H): 392.1320, found: 392.1327.

2,6-Dimethyl-4-((3-phenyl-1-tosyl-1H-indol-2-yl)methyl)phenol (75b)

Yellow gum; ^1H NMR (CDCl_3 , 500 MHz): δ 8.27 (1H, d, $J = 8.35$ Hz), 7.47 (1H, d, $J = 7.8$ Hz), 7.42-7.32 (8H, m), 7.27-7.24 (1H, m), 7.01-6.99 (2H, d, $J = 8.25$ Hz), 6.58 (2H, s), 4.46 (1H, s), 4.36 (2H, s), 2.29 (3H, s), 2.06 (6H, s); ^{13}C NMR (CDCl_3 , 125 MHz): δ 150.5, 144.2, 136.6, 136.1, 135.6, 133.0, 130.6, 130.0, 129.7, 129.2, 128.7, 128.4, 127.5, 126.4, 124.5, 124.2, 123.5, 122.6, 119.6, 114.9, 30.9, 21.5, 15.8; IR

(NaCl, neat) ν : 3473, 2960, 2929, 1598, 1494, 1450, 1367, 1261, 1188, 1172, 1149, 1120, 1089, 1051, 1024, 970, 931, 812 cm^{-1} ; MS (ESI) m/z 482 $[\text{M}+\text{H}]^+$; HRMS (ESI) calcd. for $\text{C}_{30}\text{H}_{27}\text{NO}_3\text{SNa}$ ($\text{M}^+ + \text{Na}$): 504.1609, found: 504.1618.

3-Phenyl-1-tosyl-2-vinyl-1*H*-indole (76a)

Yellow gum; ^1H NMR (CDCl_3 , 400 MHz): δ 8.25 (1H, d, $J = 8.4$ Hz), 7.66 (2H, d, $J = 8.24$ Hz), 7.14-7.41 (11H, m), 5.31 (1H, dd, $J = 1.16, 11.44$ Hz), 5.10 (1H, dd, $J = 1.2, 17.64$ Hz), 2.31 (3H, s); ^{13}C NMR (CDCl_3 , 100 MHz): δ 144.7, 136.2, 135.5, 134.7, 133.4, 131.0, 130.1, 129.6, 128.6, 127.3, 126.9, 126.4, 125.2, 124.0, 123.9, 122.2, 120.0, 115.2, 21.6; IR (NaCl, neat) ν : 2958, 2926, 1683, 1598, 1492, 1448, 1373, 1357, 1172, 1149, 1120, 1089, 1035, 1014, 812 cm^{-1} ; MS (ESI) m/z 374 $[\text{M}+\text{H}]^+$; HRMS (ESI) calcd. for $\text{C}_{23}\text{H}_{20}\text{NO}_2\text{S}$ ($\text{M}^+ + \text{H}$): 374.1215, found: 374.1205.

(*E*)-2-(Pent-1-enyl)-3-phenyl-1-tosyl-1*H*-indole (76b)

Yellow gum; ^1H NMR (CDCl_3 , 400 MHz): δ 8.18 (1H, d, $J = 8.24$ Hz), 7.57 (2H, d, $J = 8.24$ Hz), 7.02-7.32 (10H, m), 6.70 (1H, d, $J = 15.96$ Hz), 5.51-5.49 (1H, quintet, $J = 7.08$ Hz), 2.25 (3H, s), 1.94 (2H, q, $J = 7.2$ Hz), 1.18 (2H, sextet), 0.70 (3H, t, $J = 7.36$ Hz); ^{13}C NMR (CDCl_3 , 100 MHz): δ 144.5, 140.1, 136.1, 135.8, 135.1, 133.7, 130.9, 130.2, 129.5, 128.4, 127.0, 126.9, 124.7, 123.7, 122.7, 119.6, 118.9, 115.1,

35.3, 21.9, 21.5, 13.6; IR (NaCl, neat) ν : 2960, 2929, 1598, 1494, 1450, 1367, 1261, 1188, 1172, 1149, 1120, 1089, 1051, 1024, 970, 931, 812 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: 416.1680.

2-(Cyclopropylidenemethyl)-3-phenyl-1-tosyl-1H-indole (76c)

Yellow gum; ^1H NMR (CDCl_3 , 500 MHz): δ 8.27 (1H, d, $J = 8.35$ Hz), 7.58-7.61 (2H, m), 7.49-7.51 (1H, m), 7.30-7.41 (6H, m), 7.20-7.23 (1H, t, $J = 7.45$ Hz), 7.14 (2H, d, $J = 7.85$ Hz), 6.17 (1H, s), 2.66 (2H, m), 2.45 (2H, m), 2.33 (3H, s); ^{13}C NMR (CDCl_3 , 125 MHz): δ 144.5, 138.0, 137.1, 135.3, 132.9, 132.2, 130.8, 130.0, 129.6, 129.5, 129.4, 128.5, 128.1, 127.5, 126.7, 126.5, 125.6, 125.3, 124.0, 119.9, 116.0, 34.4, 28.1, 21.6; IR (NaCl, neat) ν : 2956, 2865, 1716, 1597, 1450, 1367, 1186, 1172, 1091, 1049, 1024, 931, 742, 702 cm^{-1} ; MS (ESI) m/z 400 $[\text{M}+\text{H}]^+$; HRMS (ESI) calcd. for $\text{C}_{25}\text{H}_{22}\text{NO}_2\text{S}$ (M^++H): 400.1371, found: 400.1374.

2-(Cyclopentylidenemethyl)-3-phenyl-1-tosyl-1H-indole (76d)

Pale yellow solid; m.p. 110-115 $^{\circ}\text{C}$; ^1H NMR (CDCl_3 , 400 MHz): δ 8.33 (1H, d, $J = 8.4$ Hz), 7.60 (2H, d, $J = 8.16$ Hz), 7.51 (1H, d, $J = 7.92$ Hz), 7.32-7.38 (5H, m), 7.22-7.25 (2H, m), 7.11 (2H, d, $J = 8.12$ Hz), 6.62 (1H, s), 2.31-2.36 (5H, m), 1.41-1.48 (2H, quintet, $J = 7.0$ Hz), 1.14-1.21 (2H, quintet, $J = 7.04$ Hz), 0.97-1.0 (2H, m);

^{13}C NMR (CDCl_3 , 100 MHz): δ 152.7, 144.4, 136.7, 136.3, 134.5, 134.2, 129.8, 129.3, 129.1, 128.4, 126.8, 126.7, 124.6, 123.6, 122.6, 119.3, 115.0, 110.0, 33.9, 30.8, 25.8, 25.3, 21.5; IR (NaCl, neat) ν : 2958, 2868, 1718, 1598, 1450, 1367, 1186, 1172, 1091, 1049, 1024, 931, 812 cm^{-1} ; MS (ESI) m/z 428 $[\text{M}+\text{H}]^+$; HRMS (ESI) calcd. for $\text{C}_{27}\text{H}_{26}\text{NO}_2\text{S}$ (M^++H): 428.1684, found: 428.1681.

2-(Cyclohexylidenemethyl)-3-phenyl-1H-indole (76e)

White solid; m.p. 147-151 $^{\circ}\text{C}$; ^1H NMR (CDCl_3 , 400 MHz): δ 8.32 (1H, d, J = 8.4 Hz), 7.64 (2H, d, J = 8.28 Hz), 7.51 (1H, d, J = 7.8 Hz), 7.31-7.37 (5H, m), 7.21-7.28 (2H, m), 7.14 (2H, d, J = 8.12 Hz), 6.41 (1H, s), 2.32 (3H, s), 2.15 (2H, t, J = 5.92 Hz), 1.40-1.43 (3H, m), 1.24-1.29 (5H, m); ^{13}C NMR (CDCl_3 , 100 MHz): δ 147.2, 144.4, 136.5, 136.4, 133.9, 133.4, 129.8, 129.5, 129.5, 128.4, 127.0, 126.8, 124.5, 123.5, 122.8, 119.4, 114.7, 111.6, 36.8, 30.01, 27.4, 26.1, 25.4, 21.5; IR (NaCl, neat) ν : 2931, 2854, 1647, 1598, 1494, 1448, 1371, 1355, 1172, 1149, 1120, 1091, 1074, 1049, 1024, 941, 812 cm^{-1} ; MS (ESI) m/z 442 $[\text{M}+\text{H}]^+$; HRMS (ESI) calcd. for $\text{C}_{28}\text{H}_{28}\text{NO}_2\text{S}$ (M^++H): 442.1841, found: 442.1847.

(E)-4-Methyl-N-(2-(3-oxo-1,3-diphenylprop-1-enyl)phenyl)benzenesulfonamide**(77)**

Yellow solid; m.p. 152-155 °C; ^1H NMR (CDCl_3 , 300 MHz): δ 7.78 (2H, dd, $J = 1.41$, 8.49 Hz), 7.62 1H, dd, $J = 0.75$, 8.16 Hz), 7.47-7.52 (1H, m), 7.35-7.43 (5H, m), 7.25-7.29 (2H, m), 7.14-7.22 (5H, m), 6.97 (2H, dd, $J = 1.47$, 8.43 Hz), 6.36 (1H, brs), 6.32 (1H, s), 2.32 (3H, s); ^{13}C NMR (CDCl_3 , 75 MHz): δ 192.4, 149.9, 144.0, 137.3, 136.0, 134.6, 134.5, 133.1, 130.6, 130.0, 129.6, 129.5, 128.9, 128.8, 128.7, 128.5, 128.1, 127.1, 125.4, 123.1, 21.5; IR (NaCl, neat) ν : 2927, 2854, 1653, 1647, 1489, 1448, 1338, 1261, 1165, 1091, 1016 cm^{-1} ; MS (ESI) m/z 454 $[\text{M}+\text{H}]^+$; HRMS (ESI) calcd. for $\text{C}_{28}\text{H}_{24}\text{NO}_3\text{S}$ (M^++H): 454.1477, found: 454.1472.

(Z)-2-benzylidene-3-phenyl-1-tosylindolin-3-ol (78)

Pale yellow solid; m.p. 172-176 °C; ^1H NMR (CDCl_3 , 500 MHz): δ 7.93 (1H, d, $J = 8.1$ Hz), 7.68 (2H, d, $J = 7.5$ Hz), 7.46-7.39 (1H, t, $J = 8.60$ Hz), 7.37-7.33 (4H, m), 7.26-7.17 (7H, m), 7.06 (2H, d, $J = 8.05$ Hz), 7.0-6.98 (1H, dd, $J = 0.65$, 7.55 Hz), 6.26 (1H, s), 2.32 (3H, s); ^{13}C NMR (CDCl_3 , 125 MHz): δ 145.3, 144.8, 142.4, 141.9, 138.2, 135.6, 129.9, 129.6, 129.3, 128.3, 127.9, 127.9, 127.8, 127.3, 126.8, 126.6, 125.3, 124.9, 119.5, 81.8, 21.6; IR (NaCl, neat) ν : 3526, 3078, 2956, 2860, 1718,

1660, 1598, 1450, 1367, 1186, 1172, 1091, 1049, 1024, 931, 812 cm^{-1} ; HRMS (ESI) calcd. for $\text{C}_{28}\text{H}_{23}\text{NO}_3\text{SNa}$ ($\text{M}^+ + \text{Na}$): 476.1296, found: 476.1298

Hexamethylphosphoramide

^{13}C NMR (PhMe- d_8 , 100 MHz): δ 36.4; ^{31}P NMR (PhMe- d_8 , 100 MHz): δ 23.5.

AuCl/AgOTf + HMPA

Yellow oil; ^{13}C NMR (PhMe- d_8 , 100 MHz): δ 36.2; ^{31}P NMR (PhMe- d_8 , 100 MHz): δ 26.8; HRMS (ESI) calcd. for $\text{C}_7\text{H}_{19}\text{AuF}_3\text{N}_3\text{O}_4\text{PS}$ ($\text{M}^+ + \text{H}$): 526.0452, found: 526.0452.

N-(2-(1-Hydroxy-1,3-diphenylprop-2-ynyl)phenyl)-4-ethylbenzenesulfonamide (72a)

^1H NMR (PhMe- d_8 , 500 MHz): δ 9.41 (1H, brs), 8.24-8.26 (1H, dd, $J = 0.75$, 8.15 Hz), 8.02-8.0 (1H, dd, $J = 1.35$, 7.8 Hz), 7.81-7.73 (2H, m), 7.74 (2H, d, $J = 8.25$ Hz), 7.64-7.62 (2H, dd, $J = 1.4$, 7.6 Hz), 7.52-7.09 (8H, m), 7.12-7.09 (1H, dt, $J = 1.0$, 7.75 Hz), 6.91 (2H, d, $J = 8.15$ Hz), 3.27 (1H, brs), 2.29 (3H, s).

N-(2-(1-Hydroxy-1,3-diphenylprop-2-ynyl)phenyl)-4-ethylbenzenesulfonamide (72a) + HMPA

^1H NMR (PhMe- d_8 , 500 MHz): δ 10.09 (1H, brs), 7.96-7.95 (1H, dd, $J = 0.70$, 8.15 Hz), 7.85-7.83 (1H, dd, $J = 1.35$, 7.8 Hz), 7.71-7.69 (2H, m), 7.48 (2H, d, $J = 8.2$ Hz), 7.35-7.33 (2H, m), 7.10-6.94 (8H, m), 6.81-6.78 (1H, dt, $J = 0.95$, 7.70 Hz), 6.60 (2H, d, $J = 8.1$ Hz), 2.36 (14H, d, $J = 9.5$ Hz), 1.86 (3H, s).

N*-(2-(1-Hydroxy-1,3-diphenylprop-2-ynyl)phenyl)-4-ethylbenzenesulfonamide*(72a) + AuCl/AgOTf+ HMPA**

^1H NMR (PhMe-*d*8, 400 MHz): δ 10.42 (1H, s), 7.96-7.94 (1H, d, J = 8.16 Hz), 7.89-7.87 (1H, d, J = 7.8 Hz), 7.77-7.59 (2H, d, J = 7.76 Hz), 7.50 (2H, d, J = 7.92 Hz), 7.36-7.32 (3H, m), 7.12-6.90 (7H, m), 6.82-6.77 (1H, m), 6.62 (2H, d, J = 8.0 Hz), 2.41 (42H, d, J = 9.44 Hz), 1.87 (3H, s).

7.4 Gold(I)-Catalyzed Cycloisomerization of 1-(2-Tosylaminophenyl)prop-2-yn-1-ols to 1*H*-Indole-2-carbaldehydes***N*-(2-(1-Hydroxy-1-phenylprop-2-ynyl)-4-methylphenyl)-4-methylbenzenesulfonamide (72u)**

Yellow solid; m.p. 136-139 °C; ^1H NMR (CDCl_3 , 400 MHz): δ 8.46 (1H, brs), 7.43 (1H, d, J = 8.3 Hz), 7.24-7.36 (8H, m), 7.00 (3H, dd, J = 6.9 Hz, J = 7.7 Hz), 3.77 (1H, s), 2.87 (1H, s), 2.31 (3H, s), 2.24 (3H, s); ^{13}C NMR (CDCl_3 , 100 MHz): δ 143.3, 142.5, 136.4, 133.2, 132.6, 130.3, 130.1, 129.5, 129.4, 128.7, 128.2, 127.4, 125.9, 119.3, 84.7, 77.6, 74.9, 21.5, 20.9; IR (NaCl, neat) ν : 3419, 3305, 3022, 2113, 1647, 1635, 1498, 1392, 1330, 1157, 1091, 844, 813 cm^{-1} ; MS (ESI) m/z 414 $[\text{M}+\text{Na}]^+$; HRMS (ESI) calcd. for $\text{C}_{23}\text{H}_{21}\text{NO}_3\text{SNa}$ (M^++Na): 414.1140, found: 414.1143.

***N*-(2-(1-Hydroxy-1-phenylprop-2-ynyl)-4-methoxyphenyl)-4-methylbenzene sulfonamide (72v)**

Brown solid; m.p. 144-146 °C; ^1H NMR (CDCl_3 , 400 MHz): δ 8.05 (1H, brs), 7.49 (1H, d, $J = 8.8$ Hz), 7.26-7.40 (8H, m), 7.14 (1H, d, $J = 2.8$ Hz), 7.06 (2H, d, $J = 8.8$ Hz), 6.76 (1H, dd, $J = 2.8$ Hz, $J = 8.9$ Hz), 3.73 (3H, s), 3.30 (1H, s), 2.87 (1H, s), 2.35 (3H, s); ^{13}C NMR (CDCl_3 , 100 MHz): δ 155.4, 143.3, 142.2, 136.5, 132.7, 129.4, 128.7, 128.6, 128.3, 127.3, 125.8, 121.6, 115.4, 113.7, 84.6, 77.5, 74.7, 55.4, 21.5; IR (NaCl, neat) ν : 3392, 3292, 3020, 2113, 1153, 1089, 1035, 844, 812 cm^{-1} ; MS (ESI) m/z 430 $[\text{M}+\text{Na}]^+$; HRMS (ESI) calcd. for $\text{C}_{23}\text{H}_{21}\text{NO}_4\text{SNa}$ (M^++Na): 430.1089, found: 430.1082.

***N*-(4-Chloro-2-(1-hydroxy-1-phenylprop-2-ynyl)phenyl)-4-methylbenzene sulfonamide (72w)**

Yellow solid; m.p. 152-154 °C; ^1H NMR (CDCl_3 , 400 MHz): δ 8.52 (1H, brs), 7.57 (1H, s), 7.49 (1H, d, $J = 8.5$ Hz), 7.16-7.36 (8H, m), 7.03 (2H, d, $J = 7.3$ Hz), 3.80 (1H, s), 2.91 (1H, s), 2.33 (3H, s); ^{13}C NMR (CDCl_3 , 100 MHz): δ 143.7, 141.6, 135.8, 134.4, 131.9, 129.5, 129.4, 128.8, 128.7, 128.6, 128.3, 127.3, 125.8, 120.2, 83.8, 78.3, 74.4, 21.5; IR (NaCl, neat) ν : 3406, 3302, 3018, 2113, 1637, 1485, 1332, 1157, 1089, 813 cm^{-1} ; MS (ESI) m/z 434 $[\text{M}+\text{Na}]^+$; HRMS (ESI) calcd. for $\text{C}_{22}\text{H}_{18}\text{ClNO}_3\text{SNa}$ (M^++Na): 434.0594, found: 434.0598.

***N*-(4-Bromo-2-(1-hydroxy-1-phenylprop-2-ynyl)phenyl)-4-methylbenzene
sulfonamide (72x)**

White solid; m.p. 164-166 °C; ^1H NMR (CDCl_3 , 400 MHz): δ 8.46 (1H, brs), 7.72 (1H, d, $J = 2.1$ Hz), 7.44 (1H, d, $J = 8.8$ Hz), 7.26-7.38 (8H, m), 7.04 (2H, d, $J = 8.1$ Hz), 3.58 (1H, s), 2.93 (1H, s), 2.34 (3H, s); ^{13}C NMR (CDCl_3 , 100 MHz): δ 143.8, 141.5, 135.8, 135.0, 132.5, 132.1, 131.5, 129.5, 128.9, 128.6, 127.4, 125.8, 120.5, 115.8, 83.8, 78.4, 74.4, 21.5; IR (NaCl, neat) ν : 3406, 3292, 3018, 2113, 1595, 1481, 1382, 1321, 1153, 1087, 883, 819 cm^{-1} ; MS (ESI) m/z 478 $[\text{M}+\text{Na}]^+$; HRMS (ESI) calcd. for $\text{C}_{22}\text{H}_{18}\text{BrNO}_3\text{SNa}$ (M^++Na): 478.0088, found: 478.0082.

***N*-(3-(1-Hydroxy-1-phenylprop-2-ynyl)naphthalen-2-yl)-4-methylbenzene
sulfonamide (72y)**

Yellow solid; m.p. 200-203 °C; ^1H NMR ($(\text{CD}_3)_2\text{CO}$, 400 MHz): δ 9.18 (1H, brs), 8.30 (1H, s), 7.97 (1H, s), 7.76 (2H, dd, $J = 8.2$ Hz, $J = 12.7$ Hz), 7.43-7.46 (3H, m), 7.31-7.39 (6H, m), 7.07 (2H, dd, $J = 8.1$ Hz), 3.59 (1H, s), 3.06 (1H, s), 2.22 (3H, s); ^{13}C NMR ($(\text{CD}_3)_2\text{CO}$, 100 MHz): δ 143.7, 143.3, 136.2, 134.0, 133.6, 131.0, 129.5, 128.9, 128.7, 128.5, 128.1, 128.0, 127.5, 127.3, 126.7, 125.7, 125.3, 114.2, 85.0, 78.5, 74.6, 20.5; IR (NaCl, neat) ν : 3381, 3294, 3018, 2117, 1633, 1469, 1336, 1155, 1089, 891, 869 cm^{-1} ; MS (ESI) m/z 450 $[\text{M}+\text{Na}]^+$; HRMS (ESI) calcd. for $\text{C}_{26}\text{H}_{21}\text{NO}_3\text{SNa}$ (M^++Na): 450.1140, found: 450.1144.

***N*-(2-(1-Hydroxy-1-phenylprop-2-ynyl)-4,6-dimethylphenyl)-4-methylbenzene sulfonamide (72z)**

White solid; m.p. 74-78 °C; ^1H NMR (CDCl_3 , 300 MHz): δ 7.65 (2H, d, $J = 8.3$ Hz), 7.49 (2H, dd, $J = 1.8$ Hz, $J = 8.2$ Hz), 7.30-7.37 (3H, m), 7.21 (3H, d, $J = 8.1$ Hz), 7.02 (1H, brs), 6.96 (1H, s), 4.48 (1H, s), 2.90 (1H, s), 2.40 (3H, s), 2.23 (3H, s), 1.86 (3H, s); ^{13}C NMR (CDCl_3 , 75 MHz): δ 143.8, 143.6, 139.7, 138.1, 138.0, 136.6, 132.7, 130.2, 129.5, 128.6, 128.4, 128.1, 127.3, 126.3, 86.3, 77.5, 74.4, 21.6, 21.1, 19.5; IR (NaCl, neat) ν : 3419, 3302, 3020, 2112, 1637, 1473, 1381, 1321, 1155, 1091, 813 cm^{-1} ; MS (ESI) m/z 428 $[\text{M}+\text{Na}]^+$; HRMS (ESI) calcd. for $\text{C}_{24}\text{H}_{23}\text{NO}_3\text{SNa}$ ($\text{M}^+ + \text{Na}$): 428.1296, found: 428.1290.

***N*-(2-(1-(4-Bromophenyl)-1-hydroxyprop-2-ynyl)phenyl)-4-methylbenzene sulfonamide (72a)**

Brown solid; m.p. 162-164 °C; ^1H NMR (CDCl_3 , 400 MHz): δ 8.43 (1H, brs), 7.71 (1H, d, $J = 8.2$ Hz), 7.65 (1H, d, $J = 7.8$ Hz), 7.27 (4H, m), 7.14 (2H, d, $J = 8.5$ Hz), 7.07 (3H, d, $J = 8.4$ Hz), 3.48 (1H, s), 2.93 (1H, s), 2.36 (3H, s); ^{13}C NMR (CDCl_3 , 100 MHz): δ 143.6, 141.4, 136.3, 135.9, 131.7, 130.0, 129.6, 129.4, 128.9, 127.3, 127.0, 123.1, 122.6, 119.4, 84.0, 78.3, 74.6, 21.6; IR (NaCl, neat) ν : 3437, 3304, 3018, 2113, 1637, 1492, 1396, 1328, 1159, 1091, 891, 819 cm^{-1} ; MS (ESI) m/z 478

$[M+Na]^+$; HRMS (ESI) calcd. for $C_{22}H_{18}BrNO_3SNa$ (M^++Na): 478.0088, found: 478.0082.

***N*-(2-(1-(4-Chlorophenyl)-1-hydroxyprop-2-ynyl)phenyl)-4-methylbenzene sulfonamide (72 β)**

Yellow solid; m.p. 169-171 °C; 1H NMR ($(CD_3)_2CO$, 300 MHz): δ 9.02 (1H, brs), 7.71 (1H, dd, $J = 1.5$ Hz, $J = 3.8$ Hz), 7.68 (1H, dd, $J = 1.6$ Hz, $J = 4.3$ Hz), 7.34 (2H, d, $J = 8.3$ Hz), 7.32 (1H, d, $J = 1.8$ Hz), 7.27 (4H, d, $J = 5.9$ Hz), 7.14 (2H, d, $J = 8.0$ Hz), 7.03 (1H, td, $J = 1.2$ Hz, $J = 7.7$ Hz), 3.52 (1H, s), 2.33 (3H, s); ^{13}C NMR ($(CD_3)_2CO$, 75 MHz): δ 143.7, 142.6, 136.7, 136.3, 133.4, 130.3, 129.5, 129.4, 128.9, 128.4, 127.3, 126.9, 122.7, 118.4, 84.6, 78.5, 74.1, 20.7; IR (NaCl, neat) ν : 3435, 3292, 3018, 2113, 1490, 1396, 1328, 1159, 1091, 893, 821 cm^{-1} ; MS (ESI) m/z 434 $[M+Na]^+$; HRMS (ESI) calcd. for $C_{22}H_{18}ClNO_3SNa$ (M^++Na): 434.0594, found: 434.0601.

***N*-(2-(1-Hydroxy-1-(naphthalen-2-yl)prop-2-ynyl)phenyl)-4-methylbenzene sulfonamide (72 γ)**

White solid; m.p. 145-151 °C; ^1H NMR (CDCl_3 , 300 MHz): δ 8.64 (1H, brs), 7.80 (2H, d, $J = 6.3$ Hz), 7.69 (4H, dd, $J = 7.5$ Hz, $J = 8.7$ Hz), 7.47-7.68 (2H, m), 7.34 (1H, dd, $J = 1.9$ Hz, $J = 8.7$ Hz), 7.28 (1H, dd, $J = 1.5$ Hz, $J = 7.5$ Hz), 7.06 (2H, d, $J = 8.3$ Hz), 7.02 (1H, dd, $J = 0.9$ Hz, $J = 7.6$ Hz), 6.57 (2H, d, $J = 8.1$ Hz), 3.67 (1H, s), 2.93 (1H, s), 2.15 (3H, s); ^{13}C NMR ($(\text{CD}_3)_2\text{CO}$, 75 MHz): δ 143.3, 140.9, 136.4, 136.3, 133.1, 133.0, 130.6, 129.3, 129.1, 129.0, 128.4, 128.3, 127.6, 126.8, 126.5, 124.0, 123.9, 122.6, 118.1, 84.9, 78.4, 74.6, 20.5; IR (NaCl, neat) ν : 3414, 3304, 3026, 2115, 1647, 1490, 1398, 1332, 1157, 1089, 896, 812 cm^{-1} ; MS (ESI) m/z 450 $[\text{M}+\text{Na}]^+$; HRMS (ESI) calcd. for $\text{C}_{26}\text{H}_{21}\text{NO}_3\text{SNa}$ (M^++Na): 450.1140, found: 450.1142.

***N*-(2-(1-(Biphenyl-4-yl)-1-hydroxyprop-2-ynyl)phenyl)-4-methylbenzene sulfonamide (72 δ)**

White solid; m.p. 145-147 °C; ^1H NMR (CDCl_3 , 300 MHz): δ 8.55 (1H, brs), 7.65 (2H, d, $J = 8.3$ Hz), 7.61 (2H, d, $J = 3.5$ Hz), 7.34-7.59 (9H, m), 7.24 (1H, dd, $J = 1.5$ Hz, $J = 8.7$ Hz), 7.01-7.06 (1H, m), 6.95 (2H, d, $J = 8.1$ Hz), 3.41 (1H, s), 2.93 (1H, s), 2.19 (3H, s); ^{13}C NMR ($(\text{CD}_3)_2\text{CO}$, 75 MHz): δ 143.5, 142.7, 140.4, 140.1, 136.7, 136.4,

130.6, 129.4, 129.3, 129.0, 127.6, 127.1, 126.9, 126.8, 126.2, 122.5, 118.0, 85.0, 78.1, 74.5, 20.4; IR (NaCl, neat) ν : 3419, 3032, 2113, 1490, 1330, 1157, 1089, 837, 812 cm^{-1} ; MS (ESI) m/z 476 $[\text{M}+\text{Na}]^+$; HRMS (ESI) calcd. for $\text{C}_{28}\text{H}_{23}\text{NO}_3\text{SNa}$ (M^++Na): 476.1296, found: 476.1292.

***N*-(2-(2-Hydroxybut-3-yn-2-yl)phenyl)-4-methylbenzenesulfonamide (72 ϵ)**

White solid; m.p. 107-109 °C; ^1H NMR (CDCl_3 , 300 MHz): δ 9.19 (1H, brs), 7.73 (2H, d, $J = 8.3$ Hz), 7.53 (2H, d, $J = 8.0$ Hz), 7.20 (3H, d, $J = 8.3$ Hz), 6.97 (1H, td, $J = 1.0$ Hz, $J = 7.7$ Hz), 3.62 (1H, s), 2.69 (1H, s), 2.34 (3H, s), 1.67 (3H, s); ^{13}C NMR (CDCl_3 , 75 MHz): δ 143.8, 137.0, 135.6, 130.9, 129.7, 129.1, 127.3, 127.2, 123.5, 119.9, 85.7, 74.7, 71.6, 31.2, 21.5; IR (NaCl, neat) ν : 3498, 3307, 3028, 2115, 1635, 1600, 1496, 1375, 1332, 1159, 1091, 871, 813 cm^{-1} ; MS (ESI) m/z 338 $[\text{M}+\text{Na}]^+$; HRMS (ESI) calcd. for $\text{C}_{17}\text{H}_{17}\text{NO}_3\text{SNa}$ (M^++Na): 338.0827, found: 338.0830.

***N*-(2-(1-Hydroxyprop-2-ynyl)phenyl)-4-methylbenzenesulfonamide (72 ζ)**

Yellow oil; ^1H NMR (CDCl_3 , 400 MHz): δ 7.92 (1H, brs), 7.66 (2H, d, $J = 8.0$ Hz), 7.52 (1H, d, $J = 7.6$ Hz), 7.32 (2H, d, $J = 8.0$ Hz), 7.24 (2H, dd, $J = 8.0$ Hz, $J = 13.2$ Hz), 7.13 (1H, t, $J = 7.6$ Hz), 5.33 (1H, d, $J = 2.4$ Hz), 3.61 (1H, brs), 2.64 (1H, d, $J = 2.0$ Hz), 2.35 (3H, s); ^{13}C NMR (CDCl_3 , 100 MHz): δ 144.1, 136.5, 135.2, 131.4, 129.7, 129.6, 128.4, 127.3, 125.6, 123.4, 81.6, 76.4, 62.3, 21.6; IR (NaCl, neat) ν :

3423, 3302, 3020, 2121, 1635, 1492, 1400, 1328, 1159, 1091, 833, 813 cm^{-1} ; MS (ESI) m/z 324 $[\text{M}+\text{Na}]^+$; HRMS (ESI) calcd. for $\text{C}_{16}\text{H}_{15}\text{NO}_3\text{SNa}$ (M^++Na): 324.0670, found: 324.0671.

General Procedure for Optimizing the Lewis Acid-Catalyzed Intramolecular Cyclization of *N*-(2-(1-hydroxy-1-phenylprop-2-ynyl)phenyl)-4-methyl benzene sulfonamide (72n)

For reactions with a gold/silver catalyst combination, the gold (13.2 μmol) and silver (13.2 μmol) catalysts were first stirred in acetone (1 mL) at room temperature for 10 minutes. In all other cases, the catalyst was added to a respective solvent prior to adding the starting materials. Then a solution of *N*-iodosuccinimide (0.53 mmol) in acetone (0.5 mL) was added and stirred for another 10 min at room temperature. Followed by a solution of **72n** (0.26 mmol) in acetone (1 mL) was added slowly as dropwise and the reaction mixture stirred at reflux temperature and monitored to completion by TLC analysis. The solvent removed under reduced pressure. Purification by flash column chromatography on silica gel (*n*-hexane/EtOAc 24:1 as eluent) gave **90a**.

General Procedure for Gold-Catalyzed Intramolecular Cyclization of *N*-(2-(1-hydroxy-1-phenylprop-2-ynyl)phenyl)-4-methylbenzenesulfonamide (72n)

To a solution of [Au] **85** ((13.2 μmol) in acetone (1 mL) was added a solution of *N*-iodosuccinimide (0.53 mmol) in acetone (0.5 mL) and stirred for 10 min at room temperature. Followed by a solution of **72n** (0.26 mmol) in acetone (1 mL) was added slowly as dropwise and the reaction mixture stirred at reflux temperature and monitored to completion by TLC analysis. On completion, the reaction mixture was

quenched by adding 10% Na₂S₂O₃·5H₂O (5 mL) and extracted with EtOAc (2 x 10 mL). The combined organic layers were washed with brine, dried over Mg₂SO₄, and concentrated under reduced pressure. Purification by flash column chromatography on silica gel (*n*-hexane/EtOAc 24:1 as eluent) gave the indole-2-carbaldehyde product **90a**.

3-Phenyl-1-tosyl-1*H*-indole-2-carbaldehyde (**90a**)

Yellow solid; m.p. 147-150 °C; ¹H NMR (CDCl₃, 400 MHz): δ 10.22 (1H, s), 8.30 (1H, d, *J* = 8.5 Hz), 7.83 (2H, d, *J* = 8.3 Hz), 7.52-7.58 (2H, m), 7.45 (5H, m), 7.26 (1H, m), 7.24 (2H, d, *J* = 6.5 Hz), 2.36 (3H, s); ¹³C NMR (CDCl₃, 100 MHz): δ 182.4, 145.3, 138.2, 135.8, 135.2, 132.5, 130.5, 130.4, 129.7, 129.3, 129.2, 129.0, 128.4, 127.2, 124.6, 122.6, 115.7, 21.7; IR (NaCl, neat) ν: 3064, 3030, 2920, 1683, 1598, 1543, 1444, 1369, 1172, 1089, 906, 812 cm⁻¹; MS (ESI) *m/z* 376 [M+H]⁺; HRMS (ESI) calcd. for C₂₂H₁₈NO₃S (M⁺+H): 376.1007, found: 376.1006.

5-Methyl-3-phenyl-1-tosyl-1*H*-indole-2-carbaldehyde (**90b**)

Yellow gum; ¹H NMR (CDCl₃, 400 MHz): δ 10.21 (1H, s), 8.17 (1H, d, *J* = 8.6 Hz), 7.79 (2H, d, *J* = 8.2 Hz), 7.45 (5H, m), 7.36 (1H, d, *J* = 7.0 Hz), 7.22-7.29 (3H, m), 2.38 (3H, s), 2.36 (3H, s); ¹³C NMR (CDCl₃, 100 MHz): δ 182.5, 145.2, 136.5, 135.6, 135.1, 134.6, 132.6, 130.6, 130.5, 129.7, 129.6, 129.5, 129.0, 128.4, 127.2, 122.1, 115.5, 21.7, 21.3; IR (NaCl, neat) ν: 3061, 3026, 2922, 1681, 1597, 1543, 1492, 1369,

1172, 1087, 837, 812 cm^{-1} ; MS (ESI) m/z 390 $[\text{M}+\text{H}]^+$; HRMS (ESI) calcd. for $\text{C}_{23}\text{H}_{20}\text{NO}_3\text{S}$ (M^++H): 390.1164, found: 390.1166.

5-Methoxy-3-phenyl-1-tosyl-1*H*-indole-2-carbaldehyde (90c)

Yellow solid; m.p. 129-132 $^{\circ}\text{C}$; ^1H NMR (CDCl_3 , 400 MHz): δ 10.23 (1H, s), 8.19 (1H, d, $J = 9.2$ Hz), 7.76 (2H, d, $J = 8.3$ Hz), 7.43 (5H, m), 7.22 (2H, d, $J = 8.0$ Hz), 7.16 (1H, dd, $J = 2.6$ Hz, $J = 9.2$ Hz), 6.86 (1H, d, $J = 2.4$ Hz), 3.76 (3H, s), 2.36 (3H, s); ^{13}C NMR (CDCl_3 , 100 MHz): δ 182.6, 157.3, 145.2, 135.4, 134.9, 133.1, 132.8, 130.6, 130.4, 129.7, 128.9, 128.4, 127.1, 119.2, 116.9, 103.4, 55.7, 21.6; IR (NaCl, neat) ν : 3020, 2926, 1681, 1597, 1541, 1492, 1371, 1174, 1087, 812 cm^{-1} ; MS (ESI) m/z 406 $[\text{M}+\text{H}]^+$; HRMS (ESI) calcd. for $\text{C}_{23}\text{H}_{20}\text{NO}_4\text{S}$ (M^++H): 406.1113, found: 406.1115.

3-Phenyl-1-tosyl-1*H*-benzo[*f*]indole-2-carbaldehyde (90d)

Yellow solid; m.p. 172-175 $^{\circ}\text{C}$; ^1H NMR (CDCl_3 , 400 MHz): δ 10.33 (1H, s), 8.71 (1H, s), 8.04 (1H, d, $J = 8.4$ Hz), 7.97 (1H, s), 7.83 (1H, d, $J = 8.3$ Hz), 7.74 (2H, d, $J = 8.3$ Hz), 7.44 (7H, m), 7.16 (2H, d, $J = 8.2$ Hz), 2.30 (3H, s); ^{13}C NMR (CDCl_3 , 100 MHz): δ 183.0, 145.2, 136.4, 135.7, 134.7, 134.3, 133.8, 131.0, 130.6, 130.2, 130.0, 129.7, 129.2, 128.5, 128.4, 127.2, 126.8, 125.5, 122.1, 113.3, 21.6; IR (NaCl, neat) ν : 3030, 2926, 1681, 1593, 1548, 1489, 1363, 1118, 1085, 948, 918, 875, 844, 812 cm^{-1} ;

MS (ESI) m/z 426 $[M+H]^+$; HRMS (ESI) calcd. for $C_{26}H_{20}NO_3S$ (M^++H): 426.1164, found: 426.1161.

3-*p*-Tolyl-1-tosyl-1*H*-indole-2-carbaldehyde (90f)

Yellow solid; m.p. 147-150 °C; 1H NMR ($CDCl_3$, 300 MHz): δ 10.2 (1H, s), 8.29 (1H, d, $J = 8.4$ Hz), 7.82 (2H, d, $J = 8.4$ Hz), 7.52 (2H, d, $J = 7.8$ Hz), 7.32 (2H, d, $J = 8.1$ Hz), 7.23 (5H, m), 2.42 (3H, s), 2.36 (3H, s); ^{13}C NMR ($CDCl_3$, 75 MHz): δ 182.4, 145.2, 139.0, 138.3, 136.1, 135.2, 132.5, 130.4, 129.7, 129.3, 129.1, 127.2, 124.6, 122.7, 115.7, 79.5, 21.6, 21.4; IR (NaCl, neat) ν : 3026, 2922, 1681, 1597, 1544, 1369, 1174, 1089, 920, 812 cm^{-1} ; MS (ESI) m/z 390 $[M+H]^+$; HRMS (ESI) calcd. for $C_{23}H_{20}NO_3S$ (M^++H): 390.1164, found: 390.1166.

3-(4-Bromophenyl)-1-tosyl-1*H*-indole-2-carbaldehyde (90g)

Yellow solid; m.p. 139-141 °C; 1H NMR ($CDCl_3$, 400 MHz): δ 10.31 (1H, s), 8.29 (1H, d, $J = 8.5$ Hz), 7.77 (2H, d, $J = 8.2$ Hz), 7.54 (3H, m), 7.46 (1H, d, $J = 7.4$ Hz), 7.30 (3H, m), 7.23 (2H, d, $J = 8.0$ Hz), 2.36 (3H, s); ^{13}C NMR ($CDCl_3$, 100 MHz): δ 182.6, 145.5, 137.8, 134.8, 133.6, 132.4, 132.1, 131.6, 129.8, 129.4, 129.3, 129.1,

127.1, 124.9, 123.3, 122.3, 115.7, 21.7; IR (NaCl, neat) ν : 3066, 3020, 2922, 1681, 1595, 1539, 1485, 1371, 1172, 1087, 920, 812 cm^{-1} ; MS (ESI) m/z 454 $[\text{M}+\text{H}]^+$; HRMS (ESI) calcd. for $\text{C}_{22}\text{H}_{17}\text{BrNO}_3\text{S}$ (M^++H): 454.0113, found: 454.0115.

3-(4-Chlorophenyl)-1-tosyl-1*H*-indole-2-carbaldehyde (90h)

White solid; m.p. 140-143 $^{\circ}\text{C}$; ^1H NMR (CDCl_3 , 300 MHz): δ 10.31 (1H, s), 8.29 (1H, d, $J = 8.6$ Hz), 7.77 (2H, d, $J = 8.4$ Hz), 7.54 (1H, td, $J = 1.2$ Hz, $J = 8.5$ Hz), 7.38-7.49 (5H, m), 7.29 (1H, d, $J = 7.9$ Hz), 7.23 (1H, d, $J = 9.3$ Hz), 2.36 (3H, s); ^{13}C NMR (CDCl_3 , 75 MHz): δ 182.6, 162.3, 145.5, 137.8, 135.0, 134.8, 133.6, 132.5, 131.8, 129.8, 129.3, 129.1, 128.9, 128.6, 127.1, 124.9, 122.3, 115.7, 21.7; IR (NaCl, neat) ν : 3026, 2922, 1681, 1597, 1541, 1487, 1371, 1174, 1089, 920, 812 cm^{-1} ; MS (ESI) m/z 410 $[\text{M}+\text{H}]^+$; HRMS (ESI) calcd. for $\text{C}_{22}\text{H}_{17}\text{ClNO}_3\text{S}$ (M^++H): 410.0618, found: 410.0619.

3-(Naphthalen-2-yl)-1-tosyl-1*H*-indole-2-carbaldehyde (90i)

Yellow oil; ^1H NMR (CDCl_3 , 300 MHz): δ 10.27 (1H, s), 8.33 (1H, d, $J = 8.5$ Hz), 7.85 (6H, m), 7.50 (5H, m), 7.25 (3H, m), 2.37 (3H, s); ^{13}C NMR (CDCl_3 , 75 MHz):

δ 182.5, 145.3, 138.2, 135.7, 135.3, 133.3, 133.0, 132.7, 130.1, 129.8, 129.4, 129.2, 128.2, 128.0, 127.9, 127.8, 127.3, 126.9, 126.6, 124.7, 122.7, 115.8, 76.6, 21.7; IR (NaCl, neat) ν : 3055, 3020, 2924, 1676, 1598, 1541, 1442, 1369, 1174, 1089, 962, 925, 862, 812 cm^{-1} ; MS (ESI) m/z 426 $[\text{M}+\text{H}]^+$; HRMS (ESI) calcd. for $\text{C}_{26}\text{H}_{20}\text{NO}_3\text{S}$ (M^++H): 426.1164, found: 426.1164.

3-(Biphenyl-4-yl)-1-tosyl-1H-indole-2-carbaldehyde (90j)

Yellow solid; m.p. 137-140 $^{\circ}\text{C}$; ^1H NMR (CDCl_3 , 300 MHz): δ 10.28 (1H, s), 8.31 (1H, d, $J = 8.4$ Hz), 7.82 (2H, d, $J = 8.4$ Hz), 7.71-7.53 (8H, m), 7.44-7.48 (2H, m), 7.29-7.39 (2H, m), 7.24 (2H, d, $J = 8.1$ Hz), 2.37 (3H, s); ^{13}C NMR (CDCl_3 , 75 MHz): δ 182.6, 145.3, 141.8, 140.4, 138.2, 135.3, 135.1, 132.5, 131.0, 129.8, 129.2, 128.9, 127.7, 127.2, 127.1, 127.0, 124.7, 122.7, 115.8, 36.6, 24.7, 21.7; IR (NaCl, neat) ν : 3066, 3030, 2958, 2924, 1683, 1597, 1544, 1508, 1487, 1444, 1371, 1172, 1089, 921, 846, 812 cm^{-1} ; MS (ESI) m/z 452 $[\text{M}+\text{H}]^+$; HRMS (ESI) calcd. for $\text{C}_{28}\text{H}_{22}\text{NO}_3\text{S}$ (M^++H): 452.1320, found: 452.1321.

3-Methyl-1-tosyl-1*H*-indole-2-carbaldehyde (90k)

White solid; m.p. 193-195 °C; ^1H NMR (CDCl_3 , 300 MHz): δ 10.61 (1H, s), 8.20 (1H, d, $J = 8.5$ Hz), 7.55 (3H, d, $J = 8.2$ Hz), 7.50 (1H, dd, $J = 1.1$ Hz, $J = 8.4$ Hz), 7.29 (1H, dd, $J = 0.7$ Hz, $J = 7.9$ Hz), 7.12 (2H, d, $J = 8.1$ Hz), 2.51 (3H, s), 2.30 (3H, s); ^{13}C NMR (CDCl_3 , 75 MHz): δ 185.3, 145.3, 137.5, 134.2, 133.0, 132.1, 130.6, 129.8, 129.1, 126.7, 124.6, 121.6, 115.8, 21.6, 10.5; IR (NaCl, neat) ν : 3057, 2910, 1672, 1595, 1556, 1490, 1444, 1415, 1363, 1172, 1089, 954, 879, 813 cm^{-1} ; MS (ESI) m/z 314 $[\text{M}+\text{H}]^+$; HRMS (ESI) calcd. for $\text{C}_{17}\text{H}_{16}\text{NO}_3\text{S}$ (M^++H): 314.0851, found: 314.0853.

(*E*)-2-(Iodomethylene)-1-tosylindolin-3-one (91)

Brown solid; m.p. 100-103 °C; ^1H NMR (CDCl_3 , 400 MHz): δ 8.27 (1H, s), 8.14 (1H, d, $J = 8.8$ Hz), 7.73 (2H, d, $J = 7.6$ Hz), 7.50 (2H, d, $J = 8.2$ Hz), 7.29 (2H, dd, $J = 7.5$ Hz, $J = 9.8$ Hz), 7.18 (2H, d, $J = 8.0$ Hz), 2.34 (3H, s); ^{13}C NMR (CDCl_3 , 100 MHz): δ 183.3, 146.8, 145.7, 136.9, 135.0, 133.1, 129.9, 127.2, 125.6, 125.0, 124.8, 117.0, 77.2, 21.6; IR (NaCl, neat) ν : 3446, 3095, 1707, 1606, 1458, 1363, 1267, 1199, 1174, 1083, 1016, 981, 943, 846, 821 cm^{-1} ; MS (ESI) m/z 425 $[\text{M}+\text{H}]^+$; HRMS (ESI) calcd. for $\text{C}_{16}\text{H}_{13}\text{INO}_3\text{S}$ (M^++H): 425.9661, found: 425.9668.

General Procedure for Gold-Catalyzed Intramolecular Cyclization of *N*-(2-(1-hydroxy-1-phenylprop-2-ynyl)phenyl)-4-methylbenzenesulfonamide (72**)**

To a solution of [Au] **85** ((13.2 μ mol) in acetone (1 mL) was added a solution of *N*-iodosuccinimide (0.53 mmol) in acetone (0.5 mL) and stirred for 10 min at room temperature. Followed by a solution of **72** (0.26 mmol) in acetone (1 mL) was added slowly as dropwise and the reaction mixture stirred at room temperature and monitored by TLC analysis. On completion, the reaction mixture was quenched by adding 10% Na₂S₂O₃·5H₂O (5 mL) and extracted with EtOAc (2 x 10 mL). The combined organic layers were washed with brine, dried over MgSO₄, and concentrated under reduced pressure. Purification by flash column chromatography on silica gel (*n*-hexane/EtOAc 24:1 as eluent) gave the indole-2-carbaldehyde product.

(*E*)-2-(Iodomethylene)-3-phenyl-1-tosylindolin-3-ol (88a**)**

Yellow solid; m.p. 84-86 °C; ¹H NMR (CDCl₃, 400 MHz): δ 7.91 (1H, d, *J* = 8.3 Hz), 7.58 (2H, d, *J* = 8.2 Hz), 7.31 (2H, d, *J* = 8.2 Hz), 7.24 (2H, d, *J* = 8.1 Hz), 7.12 (3H m), 7.01 (3H, m), 6.95 (1H, d, *J* = 7.5 Hz), 2.65 (1H, s), 2.41 (3H, s); ¹³C NMR (CDCl₃, 100 MHz): δ 148.0, 145.3, 142.3, 139.7, 135.1, 133.6, 130.2, 129.8, 128.2, 127.6, 127.3, 126.0, 125.6, 125.3, 116.6, 82.9, 65.9, 21.7; IR (NaCl, neat) ν : 3446, 3105, 1807, 1624, 1598, 1462, 1365, 1292, 1257, 1172, 1087, 1074, 810 cm⁻¹; MS (ESI) *m/z* 504 [M+H]⁺; HRMS (ESI) calcd. for C₂₂H₁₉INO₃S (M⁺+H): 504.0130, found 504.0135.

(E)-5-Chloro-2-(iodomethylene)-3-phenyl-1-tosylindolin-3-ol (88b)

Yellow solid; m.p. 138-141 °C; ^1H NMR (CDCl_3 , 400 MHz): δ 7.86 (1H, d, J = 8.8 Hz), 7.58 (2H, d, J = 8.0 Hz), 7.14-7.33 (7H, m), 6.98 (2H, d, J = 7.2 Hz), 6.92 (1H, d, J = 1.2 Hz), 2.73 (1H, s), 2.44 (3H, s); ^{13}C NMR (CDCl_3 , 100 MHz): δ 147.7, 145.6, 141.6, 138.3, 136.6, 133.3, 131.3, 130.4, 130.0, 128.4, 127.7, 127.6, 125.5, 125.4, 117.7, 82.7, 66.2, 21.7; IR (NaCl, neat) ν : 3446, 3109, 1637, 1595, 1458, 1363, 1172, 1039, 883, 823 cm^{-1} ; MS (ESI) m/z 537 $[\text{M}+\text{H}]^+$; HRMS (ESI) calcd. for $\text{C}_{22}\text{H}_{18}\text{ClINO}_3\text{S}$ (M^++H): 537.9741, found 537.9744.

(E)-5-Bromo-2-(iodomethylene)-3-phenyl-1-tosylindolin-3-ol (88c)

Yellow solid; m.p. 103-106 °C; ^1H NMR (CDCl_3 , 400 MHz): δ 7.80 (1H, d, J = 8.8 Hz), 7.58 (2H, d, J = 8.2 Hz), 7.42 (1H, dd, J = 1.8 Hz, J = 8.8 Hz), 7.32 (1H, s), 7.14-7.30 (5H, m), 7.06 (1H, d, J = 1.7 Hz), 6.98 (2H, d, J = 7.5 Hz), 2.75 (1H, s), 2.44 (3H, s); ^{13}C NMR (CDCl_3 , 100 MHz): δ 147.6, 145.6, 141.6, 138.8, 136.9, 133.3, 133.2, 130.0, 128.4, 128.3, 127.7, 127.6, 125.4, 118.8, 118.1, 82.6, 66.1, 21.7; IR (NaCl, neat) ν : 3442, 3109, 1633, 1595, 1417, 1361, 1172, 1128, 1076, 1035, 883, 812 cm^{-1} ; MS (ESI) m/z 581 $[\text{M}+\text{H}]^+$; HRMS (ESI) calcd. for $\text{C}_{22}\text{H}_{18}\text{BrINO}_3\text{S}$ (M^++H): 581.9236, found 581.9249.

(E)-2-(Iodomethylene)-3-phenyl-1-tosyl-2,3-dihydro-1H-benzo[f]indol-3-ol (88d)

Yellow solid; m.p. 135-137 °C; ^1H NMR (CDCl_3 , 400 MHz): δ 8.33 (1H, s), 7.88 (1H, d, $J = 8.3$ Hz), 7.62 (3H, t, $J = 8.4$ Hz), 7.32-7.48 (4H, m), 7.12-7.25 (5H, m), 7.05 (2H, d, $J = 7.4$ Hz), 2.90 (1H, s), 2.39 (3H, s); ^{13}C NMR (CDCl_3 , 100 MHz): δ 147.8, 145.4, 142.8, 137.6, 135.3, 134.6, 134.0, 131.6, 129.9, 128.3, 128.2, 128.1, 127.6, 127.4, 127.0, 125.5, 125.2, 113.0, 82.5, 64.5, 21.7; IR (NaCl, neat) ν : 3442, 3105, 1633, 1504, 1489, 1446, 1361, 1170, 1153, 1089, 1047, 947 cm^{-1} ; MS (ESI) m/z 576 $[\text{M}+\text{Na}]^+$; HRMS (ESI) calcd. for $\text{C}_{26}\text{H}_{20}\text{INO}_3\text{SNa}$ (M^++Na): 576.0106, found 576.0103.

7.5 Cyclopropyl Carbinol Rearrangement for Benzofused Nitrogen Ring Synthesis

General Experimental Procedure for the Preparation of 2-Tosylaminophenylcyclopropyl carbinols (**92a-j** and **92t**):

To a solution of the (2-aminophenyl)(phenyl)methanone) (0.88 mmol) in pyridine (0.4 mL) (note: for compound **92t**, 2-aminobenzaldehyde was used) was added *p*-toluenesulfonyl chloride (1.06 mmol) at room temperature under nitrogen atmosphere. The resulting solution was stirred for 4 h at room temperature. On completion, the

reaction mixture was quenched by adding H₂O (5 mL) and filtered off. The resulting solid was washed with *n*-Hexane:EtOAc (20:1) and dried then used as such for the next step. The solid (0.51 mmol) was dissolved in anhydrous THF (8 mL) and then a solution of cyclopropylmagnesium bromide (0.5 M THF solution; 1.5 mmol) was added at room temperature. The resulting mixture was allowed to reflux for 3-4 h. On completion judged by TLC, the reaction mixture was cooled to room temperature and treated with saturated NH₄Cl (7 mL). After additional stirring at room temperature for 10 min, EtOAc (15 mL) was added, and phases were separated. The aqueous phases was extracted with EtOAc (3 x 5 mL), the combined organic layers were washed with brine solution and dried over anhydrous Na₂SO₄ and concentrated under reduced pressure. Purification by flash column chromatography on silica gel (eluent: *n*-hexane: EtOAc = 8:2) gave the title compound.

***N*-(2-(1-Cyclopropyl-1-hydroxyethyl)phenyl)-4-methylbenzenesulfonamide (92a)**

White solid; m.p. 82-84 °C; ¹H NMR (CDCl₃, 300 MHz): δ 10.05 (1H, brs), 7.75 (2H, d, *J* = 8.1 Hz), 7.54 (1H, d, *J* = 8.13 Hz), 7.30 (1H, d, *J* = 7.71 Hz), 7.11-7.25 (3H, m), 6.93 (1H, t, *J* = 7.47 Hz), 2.95 (1H, brs), 2.33 (3H, s), 1.23-1.28 (1H, m), 1.20 (3H, s), 0.54-0.57 (1H, m), 0.41-0.46 (3H, m); ¹³C NMR (CDCl₃, 75 MHz): δ 143.6, 137.0, 136.3, 134.4, 129.6, 127.9, 127.2, 127.1, 123.3, 119.4, 77.6, 26.1, 22.6, 21.4, 3.5, 1.1; IR (KBr) ν: 3431, 3082, 3067, 3007, 2978, 2359, 2332, 1598, 1584, 1497, 1323, 1307, 1208, 1152, 1090, 760, 658 cm⁻¹; MS (ESI) *m/z* 332 [M+H]⁺; HRMS (ESI) calcd. for C₁₈H₂₂NO₃S (M⁺+H): 332.1320, found: 332.1310.

***N*-(2-(Cyclopropyl(hydroxy)(phenyl)methyl)phenyl)-4-methylbenzene
sulfonamide (92b)**

White solid; m.p. 129-132 °C; ^1H NMR (CDCl_3 , 300 MHz): δ 8.81 (1H, brs), 7.70-7.73 (1H, dd, $J = 1.26$, 7.8 Hz), 7.54 (1H, d, $J = 8.15$ Hz), 7.15-7.28 (4H, m), 7.11 (4H, d, $J = 8.34$ Hz), 6.95-7.05 (3H, m), 2.85 (1H, brs), 2.29 (1H, s), 1.51-1.62 (1H, m), 0.49-0.65 (2H, m), 0.28-0.36 (1H, m); 0.17-0.23 (1H, m), ^{13}C NMR (CDCl_3 , 75 MHz): δ 143.0, 142.5, 136.5, 136.0, 133.7, 129.3, 128.7, 128.2, 127.9, 127.2, 126.4, 122.4, 118.4, 79.5, 22.6, 21.4, 2.9, 0.8; IR (KBr) ν : 3429, 3285, 1597, 1584, 1493, 1452, 1321, 1155, 1088 cm^{-1} ; MS (ESI) m/z 394 $[\text{M}+\text{H}]^+$; HRMS (ESI) calcd. for $\text{C}_{23}\text{H}_{24}\text{NO}_3\text{S}$ (M^++H): 394.1477, found: 394.1475.

***N*-(2-((4-Chlorophenyl)(cyclopropyl)(hydroxy)methyl)phenyl)-4-methylbenzene
sulfonamide (92c)**

White solid; m.p. 153-156 °C; ^1H NMR ($(\text{CD}_3)_2\text{CO}$, 300 MHz): δ 9.24 (1H, brs), 7.84-7.81 (1H, dd, $J = 1.23$, 7.8 Hz), 7.69-7.66 (1H, dd, $J = 0.75$, 7.44 Hz), 7.28-7.22 (1H, td, $J = 1.38$, 8.67 Hz), 7.18-7.05 (9H, m), 5.72 (1H, brs), 2.32 (3H, s), 1.63-1.56 (1H, m), 0.57-0.51 (2H, m), 0.27-0.32 (2H, m); ^{13}C NMR ($(\text{CD}_3)_2\text{CO}$, 75 MHz): δ 143.2, 142.7, 137.0, 136.7, 133.9, 132.5, 129.2, 128.6, 128.3, 127.8, 127.7, 126.7, 122.4, 117.9, 78.4, 22.2, 20.6, 1.9, 0.8; IR (KBr) ν : 3420, 3215, 1598, 1584, 1489,

1396, 1379, 1350, 1325, 1281, 1153, 764, 665 cm^{-1} ; MS (ESI) m/z 428 $[\text{M}+\text{H}]^+$; HRMS (ESI) calcd. for $\text{C}_{23}\text{H}_{23}\text{NO}_3\text{SCl}$ (M^++H): 428.1087, found: 428.1086.

***N*-(2-((4-Bromophenyl)(cyclopropyl)(hydroxy)methyl)phenyl)-4-methylbenzenesulfonamide (92d)**

White solid; m.p. 159-162 $^{\circ}\text{C}$; ^1H NMR ($(\text{CD}_3)_2\text{CO}$, 300 MHz): δ 9.25 (1H, brs), 7.84 (1H, d, $J = 7.8$ Hz), 7.69 (1H, d, $J = 8.07$ Hz), 7.33 (2H, d, $J = 8.52$ Hz), 7.27 (1H, t, $J = 7.95$ Hz), 7.16-6.99 (7H, m), 5.72 (1H, brs), 2.33 (3H, s), 1.62-1.57 (1H, m), 0.52-0.54 (2H, m), 0.29-0.31 (2H, m); ^{13}C NMR ($(\text{CD}_3)_2\text{CO}$, 75 MHz): δ 143.3, 143.2, 137.0, 136.7, 133.9, 130.7, 129.3, 128.6, 128.4, 128.1, 126.7, 122.4, 120.8, 117.9, 78.4, 22.2, 20.7, 2.0, 0.9; IR (KBr) ν : 3414, 3213, 1598, 1584, 1483, 1398, 1377, 1350, 1323, 1283, 1153, 1119, 1090, 762, 664 cm^{-1} ; MS (ESI) m/z 472 $[\text{M}+\text{H}]^+$; HRMS (ESI) calcd. for $\text{C}_{23}\text{H}_{23}\text{NO}_3\text{SBr}$ (M^++H): 472.0582, found: 472.0581.

***N*-(2-(Cyclopropyl(hydroxy)(p-tolyl)methyl)phenyl)-4-methylbenzenesulfonamide (92e)**

White solid; m.p. 154-157 °C; ^1H NMR (CDCl_3 , 300 MHz): δ 8.93 (1H, brs), 7.71 (1H, d, $J = 7.8$ Hz), 7.57 (1H, d, $J = 8.1$ Hz), 7.19 (1H, t, $J = 7.26$ Hz), 7.10 (2H, d, $J = 8.22$ Hz), 6.92-7.03 (7H, m), 3.10 (1H, brs), 2.33 (3H, s), 2.28 (3H, s), 1.48-1.57 (1H, m), 0.62-0.47 (2H, m), 0.24-0.30 (1H, m), 0.15-0.21 (1H, m); ^{13}C NMR (CDCl_3 , 75 MHz): δ 143.0, 139.4, 136.7, 136.5, 136.1, 133.9, 129.1, 128.6, 128.5, 128.2, 127.2, 126.3, 122.4, 118.4, 79.5, 22.6, 21.5, 21.1, 3.0, 0.7; IR (KBr) ν : 3431, 3206, 1598, 1583, 1493, 1394, 1325, 1281, 1153, 1091, 762, 669 cm^{-1} ; MS (ESI) m/z 430 $[\text{M}+\text{Na}]^+$; HRMS (ESI) calcd. for $\text{C}_{24}\text{H}_{25}\text{NO}_3\text{SNa}$ (M^++Na): 430.1453, found: 430.1458.

***N*-(2-(Cyclopropyl(hydroxy)(phenyl)methyl)-4-methylphenyl)-4-methylbenzenesulfonamide (92f)**

White solid; m.p. 200-203 °C; ^1H NMR ($(\text{CD}_3)_2\text{CO}$, 300 MHz): δ 9.20 (1H, brs), 7.63 (1H, d, $J = 1.5$ Hz), 7.43 (1H, d, $J = 8.28$ Hz), 7.15-7.30 (5H, m), 7.07 (4H, s), 7.01 (1H, dd, $J = 1.41, 8.28$ Hz), 5.51 (1H, brs), 2.30 (3H, s), 2.26 (3H, s), 1.59-1.68 (1H, m), 0.48-0.59 (2H, m), 0.31-0.37 (2H, m); ^{13}C NMR ($(\text{CD}_3)_2\text{CO}$, 75 MHz): δ 144.9, 143.9, 137.6, 135.4, 134.9, 132.1, 130.2, 129.9, 129.5, 128.7, 128.0, 127.9, 127.2,

118.3, 79.5, 23.1, 21.3, 21.0, 2.9, 1.6; IR (KBr) ν : 3453, 3231, 3082, 3009, 2359, 2330, 1597, 1493, 1446, 1419, 1334, 1319, 1279, 1157, 1091, 758, 662 cm^{-1} ; MS (ESI) m/z 408 $[\text{M}+\text{H}]^+$; HRMS (ESI) calcd. for $\text{C}_{24}\text{H}_{26}\text{NO}_3\text{S}$ (M^++H): 408.1633, found: 408.1633.

***N*-(4-Bromo-2-(cyclopropyl(hydroxy)(phenyl)methyl)phenyl)-4-methylbenzenesulfonamide (92g)**

White solid; m.p. 197-200 $^{\circ}\text{C}$; ^1H NMR ($(\text{CD}_3)_2\text{CO}$, 300 MHz): δ 9.25 (1H, brs), 7.94 (1H, d, $J = 2.31$ Hz), 7.50 (1H, d, $J = 8.76$ Hz), 7.26-7.40 (4H, m), 7.16-7.19 (2H, m), 7.06-7.13 (4H, m), 5.77 (1H, brs), 2.32 (3H, s), 1.61-1.70 (1H, m), 0.55-0.59 (2H, m), 0.27-0.40 (2H, m); ^{13}C NMR ($(\text{CD}_3)_2\text{CO}$, 75 MHz): δ 143.5, 143.0, 136.5, 136.3, 136.1, 131.0, 131.0, 129.4, 127.9, 127.3, 127.1, 126.1, 119.2, 114.5, 78.4, 21.9, 20.4, 1.9, 0.7; IR (KBr) ν : 3445, 3223, 3084, 2358, 2341, 1595, 1572, 1498, 1323, 1228, 1161, 1090, 762, 662 cm^{-1} ; MS (ESI) m/z 472 $[\text{M}+\text{H}]^+$; HRMS (ESI) calcd. for $\text{C}_{23}\text{H}_{22}\text{NO}_3\text{SBrNa}$ (M^++Na): 494.0401, found: 494.0406.

***N*-(4-Chloro-2-(cyclopropyl(hydroxy)(phenyl)methyl)phenyl)-4-methylbenzenesulfonamide (92h)**

Yellow solid; m.p. 190-194 $^{\circ}\text{C}$; ^1H NMR ($(\text{CD}_3)_2\text{CO}$, 300 MHz): δ 9.26 (1H, brs), 7.80 (1H, d, $J = 2.43$ Hz), 7.57 (1H, d, $J = 8.79$ Hz), 7.17-7.36 (6H, m), 7.09 (4H, s), 5.78 (1H, brs), 2.31 (3H, s), 1.60-1.69 (1H, m), 0.55-0.58 (2H, m), 0.29-0.39 (2H,

m); ^{13}C NMR ($(\text{CD}_3)_2\text{CO}$, 75 MHz): δ 143.4, 143.0, 136.3, 136.2, 135.8, 129.4, 128.2, 128.1, 128.0, 127.3, 127.1, 126.9, 126.1, 118.8, 78.5, 22.0, 20.5, 2.0, 0.75; IR (KBr) ν : 3437, 3228, 3084, 2964, 1597, 1576, 1490, 1392, 1336, 1323, 1228, 1190, 764, 662 cm^{-1} ; MS (ESI) m/z 428 $[\text{M}+\text{H}]^+$; HRMS (ESI) calcd. for $\text{C}_{23}\text{H}_{23}\text{NO}_3\text{SCl}$ (M^++H): 428.1087, found: 428.1087.

***N*-(3-(Cyclopropyl(hydroxy)(phenyl)methyl)naphthalen-2-yl)-4-methylbenzene sulfonamide (92i)**

White solid; m.p. 213-216 $^{\circ}\text{C}$; ^1H NMR (CDCl_3 , 400 MHz): δ 8.84 (1H, brs), 8.24 (1H, s), 7.89 (1H, s), 7.79 (1H, d, $J = 7.8$ Hz), 7.68 (1H, d, $J = 7.92$ Hz), 7.45-7.40 (2H, m), 7.29-7.25 (1H, m), 7.21 (2H, t, $J = 7.44$ Hz), 7.12 (2H, d, $J = 7.36$ Hz), 7.07 (2H, d, $J = 8.24$ Hz), 6.91 (2H, d, $J = 8.16$ Hz), 2.85 (1H, brs), 2.24 (3H, s), 1.75-1.68 (1H, m), 0.74-0.59 (2H, m), 0.42-0.36 (1H, m), 0.27-0.21 (1H, m); ^{13}C NMR ($(\text{CD}_3)_2\text{CO}$, 75 MHz): δ 143.1, 141.7, 135.7, 134.2, 133.8, 133.3, 129.2, 128.8, 128.1, 127.9, 127.6, 127.4, 127.3, 127.0, 126.8, 126.3, 125.0, 115.0, 79.5, 22.8, 21.4, 3.1, 0.9; IR (KBr) ν : 3473, 3275, 1595, 1502, 1465, 1446, 1352, 1311, 1161, 1145, 1087, 1031, 1018, 927 cm^{-1} ; MS (ESI) m/z 466 $[\text{M}+\text{Na}]^+$; HRMS (ESI) calcd. for $\text{C}_{27}\text{H}_{25}\text{NO}_3\text{SNa}$ (M^++Na): 466.1453, found: 466.1456.

***N*-(6-(1-Cyclopropyl-1-hydroxyethyl)benzo[d][1,3]dioxol-5-yl)-4-methylbenzene sulfonamide (92j)**

Yellow solid; m.p. 143-147 °C; ^1H NMR (CDCl_3 , 400 MHz): δ 9.80 (1H, brs), 7.73 (2H, d, $J = 8.04$ Hz), 7.24 (2H, d, $J = 8.0$ Hz), 7.16 (1H, s), 6.84 (1H, s), 5.9 (2H, s), 2.70 (1H, brs), 2.37 (3H, s), 1.23-1.17 (1H, m), 1.07 (3H, s), 0.60-0.35 (4H, m); ^{13}C NMR (CDCl_3 , 100 MHz): δ 146.8, 143.7, 143.5, 137.0, 130.3, 129.5, 128.3, 127.2, 106.9, 102.2, 101.3, 76.8, 25.9, 22.8, 21.5, 3.7, 1.0; IR (KBr) ν : 3471, 3209, 3197, 2895, 1627, 1597, 1506, 1489, 1411, 1390, 1344, 1244, 1155, 1091, 1041, 925, 866, 813 cm^{-1} ; MS (ESI) m/z 398 $[\text{M}+\text{Na}]^+$; HRMS (ESI) calcd. for $\text{C}_{19}\text{H}_{21}\text{NO}_5\text{SNa}$ (M^++Na): 398.1038, found: 398.1036.

General Experimental Procedure for the Preparation of *N*-tosylaminophenylcyclopropylmethanols (92k-92s):

Following a slight modification of literature procedures,^{78a,b} alcohols **92k-92s** were prepared. Aryl aldehyde (1.76 mmol) was added to the solution of 40% NaOH in MeOH (10 mL) and H_2O (2 mL) at 0 °C. After dissolution, 1-(2-

aminophenyl)ethanone (1.46 mmol) was added over a period of 10 min and the resultant reaction mixture was stirred for 3 h at 0 °C. A solid product found to precipitate was filtered, washed with cold MeOH and dried. The dried solid was used directly for the next step. The solid (1.1 mmol) was dissolved in pyridine (0.4 mL) and *p*-toluenesulfonylchloride (1.6 mmol) was added to the reaction mixture at room temperature under nitrogen atmosphere. The resulting solution was stirred for 3-4 h at room temperature. On completion, the reaction mixture was quenched by adding H₂O (5 mL) and filtered and washed with hexane:EtOAc (9:1). The resulting solid **A** was dried and used as such for the next step. Dimethylsulfoxide (DMSO) (5 ml) was added drop wise to the solid mixture of NaH (60% in oil, 0.12 g, 3 mmol) and Trimethylsulfoxonium iodide (0.66 g, 3 mmol). After the evolution of hydrogen, the cloudy solution turned clear and was stirred for another 15 minutes followed by the solid **A** (1 mmol) thus obtained from the previous step was added. The reaction mixture was stirred for 20 h. After completion, the reaction was quenched with water, extracted with ethyl acetate, washed with brine and dried over MgSO₄. The solvent was evaporated under reduced pressure to give the product **B** in 65-87% yield. The product **B** (0.3 mmol) was dissolved in MeOH (5 ml) followed by NaBH₄ (0.75 mmol) was added portion-wise. Upon completion, the reaction mixture was quenched with saturated NH₄Cl solution and extracted with ethyl acetate, washed with water and brine solution and dried over Na₂SO₄. The solvent was evaporated under reduced pressure to give the residue. The residue was further subjected to flash chromatography to give title compound **921-s**.

Compound **92k** was prepared by the following procedure: The product **B** (0.51 mmol) was dissolved in anhydrous THF (8 mL) and then a solution of phenylmagnesium chloride (2 M THF solution; 1.5 mmol) was added at room temperature. The resulting

mixture was allowed to reflux for 3-4 h. On completion judged by TLC, the reaction mixture was cooled to room temperature and treated with saturated NH_4Cl (7 mL). After additional stirring at room temperature for 10 min, EtOAc (15 mL) was added, and phases were separated. The aqueous phases was extracted with EtOAc (3 x 5 mL), the combined organic layers were washed with brine solution and dried over anhydrous Na_2SO_4 and concentrated under reduced pressure. Purification by flash column chromatography on silica gel (eluent: *n*-hexane: EtOAc = 8:2) gave the compound **92k**.

***N*-(2-(Hydroxy(phenyl)(2-*p*-tolylcyclopropyl)methyl)phenyl)-4-methylbenzene sulfonamide (92k)**

Colorless liquid; ^1H NMR (CDCl_3 , 500 MHz): δ 8.62 (1H, brs), 7.55-7.50 (2H, m), 7.29-7.23 (3H, m), 7.19-7.16 (3H, m), 7.13 (2H, d, $J = 8.3$ Hz), 7.07 (2H, d, $J = 7.9$ Hz), 6.99-6.93 (5H, m), 2.74 (1H, s), 2.30 (6H, s), 1.80-1.74 (2H, m), 1.13-1.06 (1H, m), 1.04-0.97 (1H, m); ^{13}C NMR (CDCl_3 , 125 MHz): δ 143.4, 143.1, 138.5, 136.5, 136.1, 135.4, 133.3, 129.3, 129.2, 128.9, 128.4, 128.3, 127.4, 127.3, 125.9, 125.8, 122.6, 118.7, 79.1, 34.3, 21.5, 20.9, 19.4, 12.3; IR (NaCl, neat) ν : 3460, 3282, 2870, 1597, 1583, 1516, 1492, 1448, 1402, 1332, 1290, 1157, 1089, 937, 813 cm^{-1} ; MS (ESI) m/z 470 $[\text{M}+\text{H}]^+$; HRMS (ESI) calcd. for $\text{C}_{29}\text{H}_{27}\text{NO}_3\text{SNa}$ ($\text{M}^+ + \text{Na}$): 492.1609, found: 492.1610.

N*-(2-(Hydroxy(2-phenylcyclopropyl)methyl)phenyl)-4-methylbenzene*sulfonamide (92l)**

White solid; m.p. 121-123 °C; ^1H NMR (CDCl_3 , 300 MHz): δ 8.55 (1H, brs), 7.61 (2H, d, $J = 8.25$ Hz), 7.51 (1H, d, $J = 7.98$ Hz), 7.27-7.01 (10H, m), 3.92 (1H, d, $J = 8.55$ Hz), 2.89 (1H, brs), 2.32 (3H, s), 1.95-1.89 (1H, quintet, $J = 4.92$ Hz), 1.34-1.25 (1H, m), 0.79-0.84 (1H, m), 0.69-0.77 (1H, m); ^{13}C NMR (CDCl_3 , 75 MHz): δ 143.6, 141.6, 136.9, 135.9, 132.2, 129.6, 128.7, 128.4, 127.8, 127.0, 126.1, 125.9, 124.7, 122.2, 77.6, 30.9, 28.0, 22.6, 21.5, 13.7; IR (KBr) ν : 3470, 3167, 3071, 2920, 1601, 1585, 1496, 1330, 1157, 1091, 754, 660 cm^{-1} ; MS (ESI) m/z 416 $[\text{M}+\text{Na}]^+$; HRMS (ESI) calcd. for $\text{C}_{23}\text{H}_{23}\text{NO}_3\text{SNa}$ (M^++Na): 416.1296, found: 416.1299.

N*-(2-((2-(4-Fluorophenyl)cyclopropyl)(hydroxy)methyl)phenyl)-4-methylbenzene*sulfonamide (92m)**

White solid; m.p. 130-133 °C; ^1H NMR ($(\text{CD}_3)_2\text{CO}$, 300 MHz): δ 7.64-7.68 (2H, m), 7.53-7.57 (1H, m), 7.21-7.30 (4H, m), 7.01-7.13 (5H, m), 4.17-4.14 (1H, dd, $J = 2.49$, 8.37 Hz), 2.95 (1H, brs), 2.34 (3H, s), 2.05-2.08 (1H, m), 1.18-1.24 (1H, m), 0.86-0.80 (1H, m), 0.71-0.78 (1H, m); ^{13}C NMR ($(\text{CD}_3)_2\text{CO}$, 75 MHz): δ 162.7 (1C, d, $J = 241.5$ Hz), 143.7, 138.5, 138.4, 137.5, 136.3, 133.3, 129.6, 128.0, 127.8, 127.7, 126.9, 124.2, 121.2, 114.9 (1C, d, $J = 21.75$ Hz), 77.0, 29.2, 21.7, 20.5, 12.9; IR (KBr) ν : 3458, 3275, 3261, 3022, 1597, 1587, 1512, 1494, 1458, 1402, 1330, 1159, 1091,

1018, 933, 827 cm^{-1} ; MS (ESI) m/z 434 $[\text{M}+\text{Na}]^+$; HRMS (ESI) calcd. for $\text{C}_{23}\text{H}_{22}\text{NO}_3\text{SNaF}$ (M^++Na): 434.1202, found: 434.1206.

***N*-(2-((2-(4-Chlorophenyl)cyclopropyl)(hydroxy)methyl)phenyl)-4-methylbenzenesulfonamide (92n)**

White solid; m.p. 120-122 $^{\circ}\text{C}$; ^1H NMR ($(\text{CD}_3)_2\text{CO}$, 300 MHz): δ 9.21 (1H, brs), 7.66 (2H, d, $J = 8.25$ Hz), 7.54 (1H, d, $J = 7.5$ Hz), 7.20-7.34 (6H, m), 7.03-7.07 (3H, m), 5.50 (1H, brs), 4.18 (1H, d, $J = 8.31$ Hz), 2.34 (3H, s), 2.03-2.09 (1H, m), 1.20-1.28 (1H, m), 0.83-0.89 (1H, m), 0.73-0.79 (1H, m); ^{13}C NMR ($(\text{CD}_3)_2\text{CO}$, 75 MHz): δ 143.7, 141.6, 137.6, 136.3, 133.3, 130.6, 129.6, 128.1, 128.0, 128.0, 127.7, 126.9, 124.2, 121.3, 76.8, 29.8, 21.8, 20.5, 13.2. IR (KBr) ν : 3466, 3163, 3088, 3067, 3044, 3032, 2916, 1585, 1496, 1458, 1325, 1271, 1157, 1092, 1045 cm^{-1} ; MS (ESI) m/z 450 $[\text{M}+\text{Na}]^+$; HRMS (ESI) calcd. for $\text{C}_{23}\text{H}_{22}\text{NO}_3\text{SNaCl}$ (M^++Na): 450.0907, found: 450.0906.

***N*-(2-((2-(4-Bromophenyl)cyclopropyl)(hydroxy)methyl)phenyl)-4-methylbenzenesulfonamide (92o)**

Colorless gum; ^1H NMR (CDCl_3 , 300 MHz): δ 8.44 (1H, br), 7.63 (2H, d, $J = 7.98$ Hz), 7.47 (1H, d, $J = 7.95$ Hz), 7.37 (2H, d, $J = 8.13$ Hz), 7.05-7.25 (5H, m), 6.92 (2H, d, $J = 8.1$ Hz), 3.99 (1H, d, $J = 8.16$ Hz), 2.77 (1H, brs), 2.35 (3H, s), 1.88-1.94 (1H,

m), 1.20-1.37 (1H, m), 0.74-0.82 (2H, m); ^{13}C NMR (CDCl_3 , 75 MHz): δ 143.7, 140.6, 136.9, 135.9, 132.2, 131.3, 129.6, 128.8, 127.9, 127.7, 127.0, 124.8, 122.3, 119.5, 77.4, 28.1, 22.1, 21.5, 13.7; IR (NaCl, neat) ν : 3251, 2964, 2926, 2399, 1598, 1585, 1492, 1332, 1271, 1159, 1091, 1074, 1043 cm^{-1} ; MS (ESI) m/z 494 $[\text{M}+\text{Na}]^+$; HRMS (ESI) calcd. for $\text{C}_{23}\text{H}_{22}\text{NO}_3\text{SNaBr}$ (M^++Na): 494.0401, found: 494.0391.

***N*-(2-(Hydroxyl(2-*p*-tolylcyclopropyl)methyl)phenyl-4-methylbenzene sulfonamide (92p)**

Colorless liquid; ^1H NMR (CDCl_3 , 300 MHz): δ 8.57 (1H, brs), 7.61 (2H, d, $J = 8.07$ Hz), 7.50 (1H, d, $J = 7.98$ Hz), 7.01-7.22 (7H, m), 6.92 (2H, d, $J = 7.86$ Hz), 3.88 (1H, d, $J = 8.55$ Hz), 2.96 (1H, brs), 2.31 (3H, s), 2.29 (3H, s), 1.84-1.90 (1H, m), 0.83-0.97 (1H, m), 0.73-0.79 (1H, m), 0.61-0.68 (1H, m); ^{13}C NMR (CDCl_3 , 75 MHz): δ 143.6, 138.5, 137.0, 136.0, 135.4, 132.3, 129.6, 129.0, 128.7, 127.8, 127.0, 126.1, 124.7, 122.2, 77.6, 27.8, 22.2, 21.5, 21.0, 13.5; IR (NaCl, neat) ν : 3491, 3246, 2961, 1598, 1585, 1494, 1334, 1286, 1161, 1091, 706 cm^{-1} ; MS (ESI) m/z 430 $[\text{M}+\text{Na}]^+$; HRMS (ESI) calcd. for $\text{C}_{24}\text{H}_{25}\text{NO}_3\text{SNa}$ (M^++Na): 430.1453, found: 430.1450.

***N*-(2-(Hydroxy(2-(naphthalen-2-yl)cyclopropyl)methyl)phenyl)-4-methylbenzene sulfonamide (92q)**

White solid; m.p. 122-125 °C; ^1H NMR (CDCl_3 , 300 MHz): δ 8.56 (1H, brs), 7.70-7.78 (3H, m), 7.59 (2H, d, $J = 8.22$ Hz), 7.37-7.50 (4H, m), 7.11-7.23 (3H, m), 7.01-7.07 (3H, m), 3.97 (1H, d, $J = 8.4$ Hz), 2.94 (1H, brs), 2.25 (3H, s), 2.05-2.11 (1H, m), 1.34-1.43 (1H, m), 0.83-0.95 (1H, m), 0.72-0.78 (1H, m); ^{13}C NMR (CDCl_3 , 75 MHz): δ 143.6, 139.1, 136.9, 135.9, 133.4, 132.5, 132.1, 129.6, 128.7, 128.0, 127.8, 127.6, 127.3, 127.0, 126.1, 125.2, 125.0, 124.8, 124.5, 122.3, 77.5, 28.0, 22.8, 21.4, 13.5; IR (KBr) ν : 3474, 3206, 3051, 1634, 1598, 1585, 1499, 1329, 1160, 1090, 760, 665 cm^{-1} ; MS (ESI) m/z 466 $[\text{M}+\text{Na}]^+$; HRMS (ESI) calcd. for $\text{C}_{27}\text{H}_{25}\text{NO}_3\text{SNa}$ (M^++Na): 466.1453, found: 466.1454.

***N*-(2-(Hydroxyl(2-mesitylcyclopropyl)methyl)phenyl)-4-methylbenzene sulfonamide (92r)**

White solid; m.p. 157-161 °C; ^1H NMR (CDCl_3 , 300 MHz): δ 8.59 (1H, brs), 7.54 (3H, d, $J = 8.16$ Hz), 7.17-7.23 (1H, td, $J = 2.22, 6.84$ Hz), 6.92-7.06 (2H, m), 6.95 (2H, d, $J = 8.07$ Hz), 6.79 (2H, s), 3.91 (1H, d, $J = 7.02$ Hz), 2.97 (1H, brs), 2.31 (6H, s), 2.24 (3H, s), 2.16 (3H, s), 1.54-1.59 (1H, m), 0.95-1.04 (1H, m), 0.47-0.54 (1H, m), 0.26-0.32 (1H, m); ^{13}C NMR (CDCl_3 , 75 MHz): δ 143.6, 138.4, 136.8, 136.0, 135.8,

134.2, 132.4, 129.6, 128.8, 128.6, 128.0, 126.8, 124.6, 122.4, 79.5, 25.7, 21.2, 20.9, 20.8, 19.6, 13.7; IR (KBr) ν : 3501, 3227, 2997, 2953, 2918, 1611, 1597, 1585, 1454, 1377, 1331, 1306, 1157, 1090 cm^{-1} ; MS (ESI) m/z 458 $[\text{M}+\text{Na}]^+$; HRMS (ESI) calcd. for $\text{C}_{26}\text{H}_{29}\text{NO}_3\text{SNa}$ (M^++Na): 458.1766, found: 458.1761.

***N*-(2-(Hydroxy(2-pentylcyclopropyl)methyl)phenyl)-4-methylbenzene sulfonamide (92s)**

White solid; m.p. 86-88 °C; ^1H NMR (CDCl_3 , 300 MHz): δ 8.64(1H, brs), 7.62 (2H, d, $J = 8.22$ Hz), 7.53 (1H, d, $J = 7.98$ Hz), 7.11-7.25 (4H, m), 6.99-7.05 (1H, m), 3.57 (1H, d, $J = 8.58$ Hz), 2.76 (1H, brs), 2.33 (3H, s), 1.29-1.38 (6H, m), 1.10-1.23 (2H, m), 0.87-0.91(3H, m), 0.61-0.68(2H, m), 0.11-0.16(2H, m); ^{13}C NMR (CDCl_3 , 75 MHz): δ 143.6, 137.1, 135.9, 132.5, 129.5, 128.4, 127.7, 127.0, 124.5, 122.2, 78.4, 33.3, 31.7, 29.2, 24.1, 22.6, 21.4, 18.7, 14.1, 10.6; IR (NaCl, neat) ν : 3485, 3260, 3066, 2959, 2854, 1598, 1585, 1494, 1334, 1286, 1163, 1092, 667 cm^{-1} ; MS (ESI) m/z 388 $[\text{M}+\text{H}]^+$; HRMS (ESI) calcd. for $\text{C}_{22}\text{H}_{29}\text{NO}_3\text{SNa}$ (M^++Na): 410.1766, found: 410.1769.

***N*-(2-(Cyclopropyl(hydroxy)methyl)phenyl)-4-methylbenzenesulfonamide (92t)**

Yellow solid; m.p. 98-102 °C; ^1H NMR (CDCl_3 , 400 MHz): δ 8.65 (1H, brs), 7.63 (2H, d, $J = 8.28$ Hz), 7.45 (1H, d, $J = 8.08$ Hz), 7.21-7.15 (4H, m), 7.05 (1H, td, $J = 0.76, 7.56$ Hz), 3.53 (1H, d, $J = 9.12$ Hz), 3.16 (1H, brs), 2.32 (3H, s), 1.07-0.99 (1H,

m), 0.59-0.53 (1H, m), 0.44-0.37 (1H, m), 0.33-0.26 (1H, m), 0.00-0.05 (1H, m); ^{13}C NMR (CDCl_3 , 100 MHz): δ 143.7, 136.9, 135.9, 132.7, 129.5, 128.5, 127.7, 127.0, 124.6, 122.1, 78.4, 21.4, 16.6, 4.2, 3.4; IR (KBr) ν : 3473, 3253, 1597, 1583, 1492, 1400, 1332, 1290, 1159, 1089, 1028, 756 cm^{-1} ; MS (ESI) m/z 318 $[\text{M}+\text{H}]^+$; HRMS (ESI) calcd. for $\text{C}_{17}\text{H}_{20}\text{NO}_3\text{S}$ (M^++H): 318.1164, found: 318.1165.

General Procedure for Optimizing the Lewis and Brønsted Acid-Catalyzed Intramolecular Cyclopropyl Carbinol Rearrangement for Benzofused Nitrogen Ring Synthesis (92a)

For reactions with a gold/silver catalyst combination, the gold (15 μmol) and silver (15 μmol) catalysts were first stirred in toluene (1.5 mL) at room temperature for 10 minutes. In all other cases, the catalyst was added to a respective solvent prior to adding the starting materials. Then a toluene solution (1.5 mL) containing **92a** (0.3 mmol) was added slowly drop wise, and the reaction mixture stirred at reflux temperature and monitored to completion by TLC analysis. The solvent removed under reduced pressure. Purification by flash column chromatography on silica gel (*n*-hexane/EtOAc 20:1 as eluent) gave **93a**.

General Procedure for Gold-Catalyzed Intramolecular Cyclopropyl Carbinol Rearrangement for Benzofused Nitrogen Ring Synthesis (92):

A solution of of $(4\text{-CF}_3\text{C}_6\text{H}_4)_3\text{PAuCl}$ (15 μmol), AgOTf (15 μmol) in toluene (1.5 mL) was stirred under an Ar atmosphere at room temperature for 10 min. On completion, slow dropwise addition of a solution of **92** (0.3 mmol) in 1.5 mL of toluene. The reaction mixture was then stirred at reflux temperature for 2 h. The solvent was removed under reduced pressure. Purification by flash column

chromatography on silica gel (20:1 *n*-hexane/EtOAc as eluent) gave the benzazepine **93** and vinylindoline product **94**.

5-Methyl-1-tosyl-2,3-dihydro-1*H*-benzo[*b*]azepine (93a)^{33g}

¹H NMR (CDCl₃, 300 MHz): δ 7.53 (1H, dd, J = 1.74, 7.23 Hz), 7.43 (2H, d, J = 8.25 Hz), 7.26-7.32 (2H, m), 7.13-7.17 (3H, m), 5.63-5.59 (1H, td, J = 1.38, 6.6 Hz), 4.13 (2H, brs), 2.37 (3H, s), 2.02-2.11 (2H, m), 1.54 (3H, s); ¹³C (CDCl₃, 75 MHz): δ 142.6, 140.8, 137.8, 136.4, 136.2, 131.9, 129.0, 128.2, 127.6, 127.3, 127.1, 125.7, 57.2, 26.3, 22.1, 21.4; MS (ESI) m/z 314 [M+H]⁺.

5-Phenyl-1-tosyl-2,3-dihydro-1*H*-benzo[*b*]azepine (93b)

Yellow solid; m.p. 141-145 °C; ¹H NMR (CDCl₃, 300 MHz): δ 7.61 (1H, d, J = 7.8 Hz), 7.51 (2H, d, J = 8.13 Hz), 7.15-7.33 (5H, m), 6.87-6.95 (5H, m), 6.23 (1H, t, J = 6.90 Hz), 4.23 (2H, br), 2.23-2.30 (2H, m), 2.20 (3H, s); ¹³C NMR (CDCl₃, 75 MHz): δ 142.8, 140.6, 139.4, 137.8, 137.7, 131.3, 130.5, 129.2, 128.2, 127.9, 127.8, 127.8, 127.3, 127.2, 126.6, 57.6, 26.9, 21.3; IR (KBr) ν : 3080, 3051, 2974, 2878, 1487, 1341, 1161 cm⁻¹; MS (ESI) m/z 376 [M+H]⁺; HRMS (ESI) calcd. for C₂₃H₂₂NO₂S (M⁺+H): 376.1371, found: 376.1375.

5-(4-Chlorophenyl)-1-tosyl-2,3-dihydro-1H-benzo[b]azepine (93c)

White solid; m.p. 168-171 °C; ^1H NMR (CDCl_3 , 300 MHz): δ 7.59 (1H, dd, J = 1.19, 7.8 Hz), 7.49 (2H, d, J = 8.22 Hz), 7.22-7.35 (3H, m), 7.16 (2H, d, J = 8.5 Hz), 6.97 (2H, d, J = 8.1 Hz), 6.90 (1H, dd, J = 1.52, 7.64 Hz), 6.82 (2H, d, J = 8.52 Hz), 6.25 (1H, t, J = 6.96 Hz), 4.30 (2H, br), 2.26-2.33 (2H, m), 2.23 (3H, s); ^{13}C NMR (CDCl_3 , 75 MHz): δ 142.9, 141.7, 139.1, 138.9, 137.9, 137.6, 133.1, 131.4, 130.3, 129.2, 129.0, 128.4, 128.1, 128.0, 127.3, 127.0, 57.7, 26.8, 21.3; IR (KBr) ν : 2959, 2933, 2913, 2880, 2856, 1491, 1481, 1342, 1323, 1161, 1111, 1038 cm^{-1} ; MS (ESI) m/z 410 $[\text{M}+\text{H}]^+$; HRMS (ESI) calcd. for $\text{C}_{23}\text{H}_{21}\text{NO}_2\text{SCl}$ (M^++H): 410.0982, found: 410.0984.

5-(4-Bromophenyl)-1-tosyl-2,3-dihydro-1H-benzo[b]azepine (93d)

White solid; m.p. 171-175 °C; ^1H NMR (CDCl_3 , 300 MHz): δ 7.59 (1H, d, J = 7.8 Hz), 7.49 (2H, d, J = 8.16 Hz), 7.23-7.35 (4H, m), 6.97 (2H, d, J = 8.04 Hz), 6.90 (1H, d, J = 7.56 Hz), 6.76 (2H, d, J = 8.4 Hz), 6.26 (1H, t, J = 6.93 Hz), 4.30 (2H, br), 2.28-2.32 (2H, m), 2.23 (3H, s); ^{13}C NMR (CDCl_3 , 75 MHz): δ 142.9, 141.8, 139.4, 139.0, 137.9, 137.6, 131.5, 130.9, 130.2, 129.3, 129.2, 128.5, 128.1, 127.3, 127.1, 121.2,

57.7, 26.8, 21.3; IR (KBr) ν : 2911, 2878, 2365, 2330, 1489, 1442, 1339, 1161 cm^{-1} ;
 MS (ESI) m/z 454 $[\text{M}+\text{H}]^+$; HRMS (ESI) calcd. for $\text{C}_{23}\text{H}_{21}\text{NO}_2\text{SBr}$ (M^++H):
 454.0476, found: 454.0474.

5-*p*-Tolyl-1-tosyl-2,3-dihydro-1*H*-benzo[*b*]azepine (93e)

Yellow solid; m.p. 159-163 $^{\circ}\text{C}$; ^1H NMR (CDCl_3 , 400 MHz): δ 7.61 (1H, d, J = 7.8 Hz), 7.50 (2H, d, J = 7.76 Hz), 7.21-7.33 (2H, m), 6.93-7.00 (4H, m), 6.78 (2H, d, J = 7.44 Hz), 6.18 (1H, t, J = 6.84 Hz), 4.30 (2H, br), 2.33 (3H, s), 2.25-2.27 (2H, m), 2.21 (3H, s); ^{13}C NMR (CDCl_3 , 100 MHz): δ 142.7, 142.6, 139.6, 137.8, 137.7, 137.6, 136.9, 131.3, 130.5, 129.1, 128.5, 128.1, 127.8, 127.7, 127.4, 125.7, 57.7, 26.8, 21.3, 21.1; IR (KBr) ν : 3030, 2958, 2932, 2908, 2879, 2855, 1481, 1441, 1339, 1325, 1163 cm^{-1} ; MS (ESI) m/z 390 $[\text{M}+\text{H}]^+$; HRMS (ESI) calcd. for $\text{C}_{24}\text{H}_{24}\text{NO}_2\text{S}$ (M^++H): 390.1528, found: 390.1530.

7-Methyl-5-phenyl-1-tosyl-2,3-dihydro-1*H*-benzo[*b*]azepine (93f)

White gum; ^1H NMR (CDCl_3 , 400 MHz): δ 7.45-7.51 (3H, m), 7.11-7.25 (4H, m), 6.94 (4H, dd, J = 8.12, 16.8 Hz), 6.72 (1H, d, J = 1.28 Hz), 6.21 (1H, t, J = 6.96 Hz), 4.21 (2H, br), 2.24 (3H, s), 2.21 (3H, s), 2.25-2.17 (2H, m); ^{13}C NMR (CDCl_3 , 100

MHz): δ 143.0, 142.7, 140.5, 139.2, 137.9, 134.9, 131.1, 130.8, 129.1, 129.0, 127.8, 127.8, 127.3, 127.1, 126.4, 57.7, 26.7, 21.3, 21.0; IR (NaCl, neat) ν : 3022, 2926, 2872, 2854, 1492, 1339, 1159 cm^{-1} ; MS (ESI) m/z 390 $[\text{M}+\text{H}]^+$; HRMS (ESI) calcd. for $\text{C}_{24}\text{H}_{24}\text{NO}_2\text{S}$ (M^++H): 390.1528, found: 390.1530.

7-Bromo-5-phenyl-1-tosyl-2,3-dihydro-1H-benzo[b]azepine (93g)

Colorless gum; ^1H NMR (CDCl_3 , 300 MHz): δ 7.41-7.50 (4H, m), 7.15-7.25 (4H, m), 7.06 (1H, d, $J = 2.1$ Hz), 6.97 (2H, d, $J = 8.07$ Hz), 6.86 (2H, dd, $J = 1.2, 7.65$ Hz), 6.27 (1H, t, $J = 6.96$ Hz), 4.22 (2H, br), 2.26-2.35 (2H, m), 2.22 (3H, s); ^{13}C NMR (CDCl_3 , 75 MHz): δ 143.1, 142.0, 141.5, 139.9, 137.5, 136.7, 133.2, 132.9, 131.3, 129.3, 129.0, 128.2, 128.0, 127.7, 127.5, 127.3, 122.0, 57.6, 26.6, 21.3; IR (NaCl, neat) ν : 2928, 2882, 1479, 1447, 1339, 1159, 1084 cm^{-1} ; MS (ESI) m/z 454 $[\text{M}+\text{H}]^+$; HRMS (ESI) calcd. for $\text{C}_{23}\text{H}_{21}\text{NO}_2\text{SBr}$ (M^++H): 454.0476, found: 454.0474.

7-Chloro-5-phenyl-1-tosyl-2,3-dihydro-1H-benzo[b]azepine (93h)

Yellow solid; m.p. 104-107 $^{\circ}\text{C}$; ^1H NMR (CDCl_3 , 300 MHz): δ 7.56 (1H, d, $J = 8.52$ Hz), 7.50 (2H, d, $J = 8.25$ Hz), 7.30-7.16 (4H, m), 6.98 (2H, d, $J = 8.06$ Hz), 6.90 (1H, d, $J = 2.47$ Hz), 6.86-6.83 (2H, dd, $J = 1.26, 7.71$ Hz), 6.27 (1H, t, $J = 6.96$ Hz), 4.23 (2H, br), 2.24-2.31 (2H, m), 2.22 (3H, s); ^{13}C NMR (CDCl_3 , 75 MHz): δ 143.0, 142.0,

141.1, 139.9, 137.5, 136.2, 133.9, 132.6, 130.3, 129.3, 128.3, 128.0, 127.7, 127.7, 127.5, 127.3, 57.6, 26.7, 21.4; IR (KBr) ν : 2918, 2876, 1477, 1340, 1161, 773 cm^{-1} ; MS (ESI) m/z 410 $[\text{M}+\text{H}]^+$; HRMS (ESI) calcd. for $\text{C}_{23}\text{H}_{21}\text{NO}_2\text{SCl}$ (M^++H): 410.0982, found: 410.0988.

5-Phenyl-1-tosyl-2,3-dihydro-1*H*-naphtho[2,3-*b*]azepine (93i)

Yellow gum; ^1H NMR (CDCl_3 , 400 MHz): δ 8.09 (1H, s), 7.87 (1H, d, $J = 7.8$ Hz), 7.64 (1H, d, $J = 7.92$ Hz), 7.51-7.40 (4H, m), 7.38 (1H, s), 7.27-7.18 (3H, m), 6.96-6.93 (4H, m), 6.25 (1H, t, $J = 6.96$ Hz), 4.22 (2H, br), 2.25-2.38 (2H, m), 2.21 (3H, s); ^{13}C NMR (CDCl_3 , 100 MHz): δ 142.9, 142.8, 141.1, 137.8, 137.6, 135.0, 132.8, 132.5, 130.1, 130.0, 129.2, 128.0, 127.9, 127.9, 127.7, 127.4, 127.3, 126.7, 126.5, 125.9, 56.1, 26.7, 21.4; IR (NaCl, neat) ν : 3057, 2954, 2875, 1708, 1666, 1631, 1597, 1492, 1444, 1338, 1159, 1087, 1010, 956 cm^{-1} ; MS (ESI) m/z 426 $[\text{M}+\text{H}]^+$; HRMS (ESI) calcd. for $\text{C}_{27}\text{H}_{24}\text{NO}_2\text{S}$ (M^++H): 426.1528, found: 426.1530.

9-Methyl-5-tosyl-6,7-dihydro-5*H*-[1,3]dioxolo[4',5':4,5]benzo[1,2-*b*]azepine (93j)

Colorless solid; m.p. 165-168 $^{\circ}\text{C}$; ^1H NMR (CDCl_3 , 400 MHz): δ 7.45 (2H, d, $J = 8.24$ Hz), 7.18 (2H, d, $J = 8.12$ Hz), 6.99 (1H, s), 6.57 (1H, s), 6.0 (2H, s), 5.57 (1H, td, $J = 1.28, 6.72$ Hz), 4.37 (2H, brs), 2.38 (3H, s), 2.04 (2H, q, $J = 6.44$ Hz), 1.42 (3H,

s); ^{13}C NMR (CDCl_3 , 100 MHz): δ 147.7, 146.5, 142.6, 137.7, 136.7, 135.2, 129.0, 127.4, 125.1, 112.4, 106.3, 101.7, 58.0, 26.1, 21.9, 21.4; IR (NaCl, neat) ν : 3394, 3020, 2856, 1598, 1483, 1419, 1384, 1336, 1246, 1157, 1085, 966 cm^{-1} ; MS (ESI) m/z 358 $[\text{M}+\text{H}]^+$; HRMS (ESI) calcd. for $\text{C}_{19}\text{H}_{20}\text{NO}_4\text{S}$ (M^++H): 358.1113, found: 358.1115.

(*E*)-2-Styryl-1-tosylindoline (94a)^{73b}

Yellow gum; ^1H NMR (CDCl_3 , 300 MHz): δ 7.68 (1H, d, $J = 8.07$ Hz), 7.62 (2H, d, $J = 8.1$ Hz), 7.20-7.32 (6H, m), 7.15 (2H, d, $J = 7.98$ Hz), 6.99-7.08 (2H, m), 6.71 (1H, d, $J = 15.75$ Hz), 6.19 (1H, dd, $J = 7.08, 15.72$ Hz), 4.93-4.99 (1H, m), 3.12 (1H, dd, $J = 9.57, 16$ Hz), 2.76 (1H, dd, $J = 2.15, 16$ Hz), 2.33 (3H, s); ^{13}C NMR (CDCl_3 , 75 MHz): δ 143.8, 141.4, 136.3, 135.7, 131.1, 129.5, 128.7, 128.4, 127.8, 127.8, 127.2, 126.6, 125.1, 124.3, 116.5, 63.9, 35.5, 21.5; MS (ESI) m/z 376 $[\text{M}+\text{H}]^+$.

(*E*)-2-(4-Fluorostyryl)-1-tosylindoline (94b)

Colorless gum; ^1H NMR (CDCl_3 , 300 MHz): δ 7.68 (1H, d, $J = 8.07$ Hz), 7.62 (2H, d, $J = 8.22$ Hz), 7.20-7.30 (3H, m), 7.16 (2H, d, $J = 8.13$ Hz), 6.93-7.08 (4H, m), 6.68 (1H, d, $J = 15.75$ Hz), 6.12 (1H, dd, $J = 6.99, 15.75$ Hz), 4.91-4.97 (1H, m), 3.11 (1H, dd, $J = 9.6, 16.05$ Hz), 2.74 (1H, dd, $J = 2.7, 16.05$ Hz), 2.34 (3H, s), ^{13}C NMR (CDCl_3 , 75 MHz): δ 162.3 (1C, d, $J_{\text{C-F}} = 241.0$ Hz), 143.8, 141.3, 135.7, 131.1, 129.9, 129.5, 128.2, 128.1, 127.9, 127.1, 125.1, 124.4, 116.6, 115.5 (1C, d, $J_{\text{C-F}} = 22.5$ Hz),

63.7, 35.4, 21.5; IR (NaCl, neat) ν : 2961, 2926, 1601, 1477, 1462, 1354, 1166, 1013 cm^{-1} ; MS (ESI) m/z 394 $[\text{M}+\text{H}]^+$; HRMS (ESI) calcd. for $\text{C}_{23}\text{H}_{21}\text{NO}_2\text{SF}$ (M^++H): 394.1277, found: 394.1278.

(E)-2-(4-Chlorostyryl)-1-tosylindoline (94c)

Yellow gum; ^1H NMR (CDCl_3 , 400 MHz): δ 7.68 (1H, d, $J = 7.68$ Hz), 7.61 (2H, d, $J = 7.71$ Hz), 7.22-7.26 (5H, m), 7.16 (2H, d, $J = 7.53$ Hz), 7.01-7.06 (2H, m), 6.67 (1H, d, $J = 15.84$ Hz), 6.17 (1H, dd, $J = 6.90, 15.81$ Hz), 4.94-4.96 (1H, m), 3.11 (1H, dd, $J = 10.29, 16.09$ Hz), 2.75 (1H, dd, $J = 2.07, 16.3$ Hz), 2.34 (3H, s); ^{13}C NMR (CDCl_3 , 75 MHz): δ 143.9, 141.3, 135.6, 134.8, 133.4, 131.0, 129.9, 129.5, 129.4, 128.6, 127.9, 127.8, 127.1, 125.2, 124.4, 116.6, 63.6, 35.4, 21.5; IR (NaCl, neat) ν : 2924, 2855, 1478, 1460, 1354, 1167 cm^{-1} ; MS (ESI) m/z 410 $[\text{M}+\text{H}]^+$; HRMS (ESI) calcd. for $\text{C}_{23}\text{H}_{21}\text{NO}_2\text{SCl}$ (M^++H): 410.0982, found: 410.0991.

(E)-2-(4-Bromostyryl)-1-tosylindoline (94d)

Brown gum; ^1H NMR (CDCl_3 , 300 MHz): δ 7.68 (1H, d, $J = 7.92$ Hz), 7.62 (2H, d, $J = 8.04$ Hz), 7.41 (2H, d, $J = 8.31$ Hz), 7.02-7.26 (6H, m), 6.66 (1H, d, $J = 15.72$ Hz), 6.19 (1H, dd, $J = 6.9, 15.78$ Hz), 4.91-4.96 (1H, m), 3.11 (1H, dd, $J = 9.54, 16.05$ Hz), 2.74 (1H, d, $J = 16.47$ Hz), 2.34 (3H, s); ^{13}C NMR (CDCl_3 , 75 MHz): δ 143.9, 141.3, 135.6, 135.2, 133.0, 131.5, 129.9, 129.5, 129.6, 128.1, 127.9, 127.1, 125.1, 124.4,

121.5, 116.6, 63.6, 35.4, 21.5; IR (NaCl, neat) ν : 2963, 2926, 2870, 1643, 1487, 1477, 1462, 1354, 1166, 1072, 1028 cm^{-1} ; MS (ESI) m/z 454 $[\text{M}+\text{H}]^+$; HRMS (ESI) calcd. for $\text{C}_{23}\text{H}_{21}\text{NO}_2\text{SBr}$ (M^++H): 454.0476, found: 454.0470.

(E)-2-(4-Methylstyryl)-1-tosylindoline (94e)

Yellow gum; ^1H NMR (CDCl_3 , 300 MHz): δ 7.67 (1H, d, $J = 8.1$ Hz), 7.63 (2H, d, $J = 8.25$ Hz), 6.98-7.25 (9H, m), 6.67 (1H, d, $J = 15.72$ Hz), 6.13-6.06 (1H, dd, $J = 7.23$, 15.75 Hz), 4.92-4.98 (1H, m), 3.11 (1H, dd, $J = 9.57$, 16.07 Hz), 2.75 (1H, dd, $J = 2.63$, 16.04 Hz), 2.33 (3H, s), 2.31 (3H, s), ^{13}C NMR (CDCl_3 , 75 MHz): δ 143.7, 141.4, 137.6, 135.8, 133.5, 131.2, 131.1, 129.5, 129.1, 127.8, 127.6, 127.2, 126.5, 125.1, 124.3, 116.5, 64.0, 35.5, 21.5, 21.2; IR (NaCl, neat) ν : 2963, 2924, 1477, 1460, 1354, 1166 cm^{-1} ; MS (ESI) m/z 390 $[\text{M}+\text{H}]^+$; HRMS (ESI) calcd. for $\text{C}_{24}\text{H}_{24}\text{NO}_2\text{S}$ (M^++H): 390.1528, found: 390.1526.

(E)-2-(2-(Naphthalen-2-yl)vinyl)-1-tosylindoline (94f)

White solid; m.p. 133-138 $^{\circ}\text{C}$; ^1H NMR (CDCl_3 , 300 MHz): δ 7.62-7.78 (7H, m), 7.39-7.49 (3H, m), 7.21-7.25 (1H, m), 7.0-7.15 (4H, m), 6.87 (1H, d, $J = 15.75$ Hz), 6.31 (1H, dd, $J = 7.13$, 15.75 Hz), 5.0-5.05 (1H, m), 3.16 (1H, dd, $J = 9.54$, 15.99 Hz), 2.80 (1H, dd, $J = 2.43$, 16.05 Hz), 2.31 (3H, s); ^{13}C NMR (CDCl_3 , 75 MHz): δ 143.8, 141.4, 135.8, 133.7, 133.5, 133.0, 131.3, 131.1, 129.5, 129.0, 128.0, 128.0, 127.9,

127.6, 127.2, 126.8, 126.2, 125.9, 125.2, 124.3, 123.6, 116.5, 64.0, 35.5, 21.4; IR (NaCl, neat) ν : 2961, 2926, 2855, 1466, 1462, 1398, 1354, 1166, 895 cm^{-1} ; MS (ESI) m/z 426 $[\text{M}+\text{H}]^+$; HRMS (ESI) calcd. for $\text{C}_{27}\text{H}_{24}\text{NO}_2\text{S}$ (M^++H): 426.1528, found: 426.1529.

(*E*)-1-Tosyl-2-(2,4,6-trimethylstyryl)indoline (94g)

White solid; m.p. 113-116 $^{\circ}\text{C}$; ^1H NMR (CDCl_3 , 300 MHz): δ 7.68 (1H, s), 7.65 (2H, d, $J = 8.37$ Hz), 7.16-7.24 (3H, m), 6.98-7.07 (2H, m), 6.82 (2H, s), 6.68 (1H, d, $J = 16.02$ Hz), 5.78 (1H, dd, $J = 6.87, 16.02$ Hz), 4.86-4.93 (1H, m), 3.11 (1H, dd, $J = 9.63, 16.05$ Hz), 2.76 (1H, dd, $J = 3.42, 16.04$ Hz), 2.35 (3H, s), 2.24 (3H, s), 2.22 (6H, s); ^{13}C NMR (CDCl_3 , 75 MHz): δ 143.8, 141.6, 136.2, 135.9, 135.5, 133.6, 133.0, 131.1, 129.6, 128.9, 128.4, 127.8, 127.1, 125.0, 124.4, 116.7, 64.2, 35.7, 21.5, 20.9, 20.7; IR (KBr) ν : 3023, 2955, 2926, 2857, 1480, 1463, 1346, 1331, 1159 cm^{-1} ; MS (ESI) m/z 418 $[\text{M}+\text{H}]^+$; HRMS (ESI) calcd. for $\text{C}_{26}\text{H}_{28}\text{NO}_2\text{S}$ (M^++H): 418.1841, found: 418.1843.

(*E*)-2-(Hept-1-enyl)-1-tosylindoline (94h)

White gum; ^1H NMR (CDCl_3 , 400 MHz): δ 7.63 (1H, d, $J = 8.24$ Hz), 7.60 (2H, d, $J = 8.24$ Hz), 7.22 (1H, d, $J = 7.36$ Hz), 7.18 (2H, d, $J = 8.24$ Hz), 7.05-6.98 (2H, m), 5.80 (1H, quintet, $J = 7.8$ Hz), 5.50 (1H, dd, $J = 7.36, 15.6$ Hz), 4.75-4.71 (1H, m),

2.99 (1H, dd, $J = 9.64, 16.48$ Hz), 2.63 (1H, dd, $J = 2.77, 16.04$ Hz), 2.35 (3H, s), 2.02-1.95 (2H, m), 1.35-1.22 (6H, m), 0.84 (3H, t, $J = 7.1$ Hz); ^{13}C NMR (CDCl_3 , 100 MHz): δ 143.6, 141.4, 135.8, 132.7, 131.4, 129.4, 129.2, 127.6, 127.1, 125.0, 124.2, 116.6, 63.8, 35.5, 31.9, 31.4, 28.5, 22.4, 21.5, 14.0; IR (NaCl, neat) ν : 2959, 2928, 2857, 1477, 1460, 1352, 1167 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: 370.1841.

***N*-(2-(1-Cyclopropylvinyl)phenyl)-4-methylbenzenesulfonamide (99)**

Colorless gum; ^1H NMR (CDCl_3 , 300 MHz): δ 7.65-7.61 (3H, m), 7.18 (2H, d, $J = 8.16$ Hz), 7.03-6.94 (3H, m), 5.12 (1H, s), 4.47 (1H, d, $J = 1.27$ Hz), 2.35 (3H, s), 1.41-1.28 (1H, m), 0.68-0.62 (2H, m), 0.32-0.26 (2H, m); ^{13}C NMR (CDCl_3 , 75 MHz): δ 147.7, 143.8, 136.3, 133.9, 131.7, 129.5, 129.2, 128.2, 127.3, 123.8, 119.3, 113.5, 21.5, 17.0, 6.5; IR (NaCl, neat) ν : 3081, 3065, 3007, 2978, 2359, 2332, 1645, 1574, 1584, 1497, 1323, 1307, 1208, 1166, 1090, 760, 658 cm^{-1} ; MS (ESI) m/z 314 $[\text{M}+\text{H}]^+$; HRMS (ESI) calcd. for $\text{C}_{18}\text{H}_{20}\text{NO}_2\text{S}$ (M^++H): 314.1215, found: 314.1217.

4-Methyl-*N*-(2-(1-phenylbuta-1,3-dienyl)phenyl)benzenesulfonamide (97b)⁷⁷

Yellow oil; ^1H NMR (CDCl_3 , 400 MHz): δ 7.76 (2H, d, $J = 8.2$ Hz), 7.60 (1H, d, $J = 8.2$ Hz), 7.00-7.47 (22H, m), 6.82 (1H, d, $J = 11.0$ Hz), 6.47-5.60 (2H, m), 6.26 (1H,

s), 5.80-5.89 (2H m), 5.40 (1H, d, $J = 16.8$ Hz), 5.24 (2H, t, $J = 8.7$ Hz), 5.10 (1H, d, $J = 10.1$ Hz), 2.37 (3H, s), 2.34 (3H, s); ^{13}C NMR (CDCl_3 , 100 MHz): δ 143.7, 143.6, 139.0, 138.5, 138.1, 137.2, 136.1, 136.0, 136.0, 134.7, 134.3, 133.6, 133.5, 132.6, 131.3, 130.8, 130.8, 129.6, 129.5, 129.4, 129.3, 129.0, 128.9, 128.7, 128.4, 128.2, 127.3, 127.2, 126.3, 125.3, 124.4, 123.0, 120.9, 120.7, 119.8, 21.5; MS (ESI) m/z 376 $[\text{M}+\text{H}]^+$.

4-Methyl-*N*-(2-((1*E*,3*E*)-4-phenylbuta-1,3-dienyl)phenyl)benzenesulfonamide (97a)

Colourless solid; m.p. 168-172 °C; ^1H NMR (CDCl_3 , 400 MHz): δ 7.63 (2H, d, $J = 8.04$ Hz), 7.45-7.40 (3H, m), 7.36 (2H, t, $J = 7.44$ Hz), 7.29-7.16 (6H, m), 6.78-6.43 (5H, m), 2.32 (3H, s); ^{13}C NMR (CDCl_3 , 100 MHz): δ 144.0, 137.0, 136.4, 133.8, 133.0, 132.9, 132.4, 129.6, 128.8, 128.7, 128.2, 127.9, 127.3, 126.9, 126.4, 126.3, 21.5; IR (NaCl, neat) ν : 3261, 3061, 3026, 1670, 1597, 1492, 1448, 1400, 1330, 1161, 1089, 989, 920, 813 cm^{-1} ; MS (ESI) m/z 376 $[\text{M}+\text{H}]^+$; HRMS (ESI) calcd. for $\text{C}_{23}\text{H}_{22}\text{NO}_2\text{S}$ (M^++H): 376.1371, found: 376.1369.

2-Methyl-4-phenyl-1-tosyl-1,2-dihydroquinoline (100)⁷⁷

White solid; ^1H NMR (CDCl_3 , 500 MHz): δ 7.81 (1H, d, $J = 8.04$ Hz), 7.23-7.34 (6H, m), 7.12 (1H, t, $J = 7.5$ Hz), 7.02 (2H, d, $J = 8.0$ Hz), 6.86 (1H, d, $J = 7.7$ Hz), 6.72 (2H, d, $J = 5.9$ Hz), 5.62 (1H, d, $J = 6.0$ Hz), 5.08-5.14 (1H, m), 2.27 (3H, s), 1.20

(3H, d, $J = 6.9$ Hz); ^{13}C NMR (CDCl_3 , 125 MHz): δ 143.3, 138.2, 136.4, 135.9, 133.0, 129.9, 129.0, 128.8, 128.2, 128.0, 127.5, 127.5, 126.5, 125.8, 50.8, 21.4, 19.3; MS (ESI) m/z 398 $[\text{M}+\text{Na}]^+$.

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