Lewis and Brønsted Acid-Mediated Chemistry of Alcohol Pro-electrophiles as Novel Synthetic Strategies for C-X (X = C, N, O) Bond Formation

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DEDICATION

I would like to dedicate my thesis to my beloved father Ashi Reddy and mother Venkatamma for their love, motivation and endless support throughout my life.

I would also like to dedicate this thesis to my loving wife Sumathi and my lovely daughter Vanshika Reddy for their love, care and encouragement.

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ABSTRACT

The work in this thesis was undertaken at the Division of Chemistry and Biological Chemistry, School of Physical and Mathematical Sciences, Nanyang Technological University from August 2008 to June 2012 under the supervision of Asst. Prof. Philip Wai Hong Chan.

The work of this thesis has been directed toward establishing new Lewis and Brønsted acid-catalyzed reactions of alcohol pro-electrophiles as novel synthetic strategies for C–X (X = C, N, O, S) bond formation. This thesis is divided into three parts:

- Part I consists of Chapter I, which gives an introduction of Lewis and Brønsted acid catalyzed reactions of alcohol pro-electrophiles, particularly those containing a pendant activated alcohols such as allylic, propargylic, benzylic and cyclopropylmethyl functional group.
- Part II describes the new strategies developed for C–X (X = C, N, O) bond formation employing alcohols as pro-electrophiles. Chapter II addressed highly efficient synthesis of tri- and tetrasubstituted conjugated enynes from Brønsted acid catalyzed alkoxylation of 1-cyclopropylprop-2-yn-1-ols with alcohols. In Chapter III, a novel strategy to halohydrofurans *via* Brønsted acid-catalyzed hydroxylation/halocyclization of cyclopropyl methanols with water and electrophilic halides is described. Chapter IV represented the silver triflate-catalyzed tandem heterocyclization/alkynylation of 1-((2-tosylamino)aryl)but-2-yne-1,4-diols to 2-alkynyl indoles. In Chapter V, a new method to tri- and tetrasubstituted furans *via* Brønsted acid-catalyzed cycloisomerization of but-2-yne-1,4-diols with or without 1,3-dicarbonyl

compounds is disclosed. Chapter VI detailed silver-catalyzed tandem amination/spiro annulation of 1-(2-(allylamino)phenyl)-4-hydroxy-but-2-yn--1-ones as an expedient approach to 1'-allylspiro[indene-1,2'-indolin]-3'-ones.

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

PUBLICATIONS

1. "Brønsted Acid-Catalyzed Cycloisomerization of But-2-yne-1,4-diols with or without 1,3-Dicarbonyl Compounds to Tri- and Tetrasubstituted Furans", **Mothe, S. R.**; Lauw, S. J. L.; Kothandaraman, P.; Chan, P. W. H. *J. Org. Chem.* **2012**, *77*, 6937.
2. "Silver Triflate-Catalyzed Tandem Heterocyclization/Alkynylation of 1-((2-Tosylamino)aryl)but-2-yne-1,4-diols to 2-Alkynyl Indoles", **Mothe, S. R.**; Kothandaraman, P.; Lauw, S. J. L.; Chin, S. M. W.; Chan, P. W. H. *Chem. Eur. J.* **2012**, *18*, 6133.
3. "Gold-Catalyzed Cycloisomerizations of 1-(2-(Tosylamino)phenyl)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**, *76*, 7633. (*Featured Article and invited by the Editors as the front cover of issue 19*) (*Highlighted by Organic Chemistry Portal*).
4. "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*, 2521.
5. "Efficient Synthesis of 3-Acyl-5-hydroxybenzofurans *via* Copper(II) Triflate-Catalyzed Cycloaddition of Unactivated 1,4-Benzoquinones with 1,3-Dicarbonyl Compounds", **Mothe, S. R.**; Susanti, D.; Chan, P. W. H. *Tetrahedron Lett*. **2010**, *51*, 2136.
6. "Highly Efficient Synthesis of Tri- and Tetrasubstituted Conjugated Enynes from Brønsted Acid-Catalyzed Alkoxylation of 1-Cyclopropylprop-2-yn-1-ols with

Alcohols", **Mothe, S. R.**; Chan, P. W. H. *J. Org. Chem.* **2009**, *74*, 5887. (*Highlighted in SYNFACTS, Synfacts 2009, 11, 1230*).

ABBREVIATIONS

ACS	American Chemical Society
Ar	aryl
BINAPHANE	1,2-bis[(*R*)-4,5-dihydro-3*H*-binaphtho (1,2-*c*:2′,1′-*e*)phosphepino]benzene
Bu	butyl
d	days
Bn	benzyl
DBSA	dodecylbenzenesulfonic acid
DCE	1,2-dichloroethane
DMF	dimethylformamide
DMSO	dimethylsulfoxide
DNBSA	2,4-dinitrobenzenesulfonic acid
dppf	1,1'-bis(diphenylphosphino)ferrocene
dr	diastereomeric ratio
ee	enantiomeric excess
EWG	electron withdrawing group
Et	ethyl
h	hour
HMPA	hexamethylphosphoramide
IBX	2-iodoxybenzoic acid
^{i}Pr	isopropyl
LDA	lithium diisopropylamide
MBH	Morita-Baylis-Hillman
Me	methyl

min	minute
m.p.	melting point
NMR	nuclear magnetic resonance
Nu	nucleophile
NBS	*N*-bromosuccinimide
NCS	*N*-chlorosuccinimide
NIS	*N*-iodosuccinimide
OEt	ethoxy
OMe	methoxy
OTf	trifluoromethanesulfonyl
PG	protecting group
Ph	phenyl
r.t.	room temperature
TFA	trifluoroacetic acid
TfOH	trifluoromethanesulfonic acid
THF	tetrahydrofuran
TLC	thin layer chromatography
TMS	trimethylsilyl
Ts	*p*-toluenesulfonyl

Chapter I. Alcohol Pro-electrophiles in Lewis and Brønsted Acid Catalysis

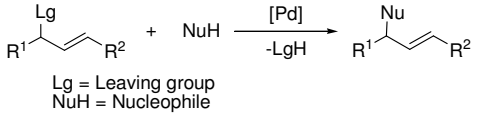
1.1 Introduction

Lewis and Brønsted acids have attracted the attention of the synthetic community because of their ability to efficiently and selectively catalyze carbon-carbon and carbon-heteroatom bond formations.[1-6] For example, Lewis and Brønsted acid catalysts have been found to mediate a number of organic transformations such as the Friedel-Crafts, Diels-Alder, Mukaiyama-Aldol, and Pictet-Spengler reactions and have also been shown to be applicable to large-scale synthesis in the pharmaceutical industry. Another area which has been gaining momentum is the use of alcohol pro-electrophiles in combination with environmentally benign and commercially available Lewis and Brønsted catalysts such as those of Ag, Au, Cu, Fe, *p*-TsOH·H_2O and TfOH.[3] In 2005, the ACS Green Chemistry Institute and global pharmaceutical corporations considered this new concept of C–OH bond activation as a key step in the integration of green chemistry into the pharmaceutical industry.[4] One of the advantages of this synthetic approach is the employment of easily prepared or readily available alcohol substrates that provide the possibility of introducing a wide range of substitution patterns. Added to this is the potential to form a quaternary carbon centre by utilizing tertiary alcohols and the potential of forming H_2O as the only side product.[5] Although these reactions have several practical benefits, the present methodologies still suffer from drawbacks in terms of poor reactivity at low temperatures or in the absence of additives due to the poor leaving group ability of the hydroxyl group.[6] Thus far, improved reactivities have been achieved by utilizing activated alcohols which contain a π-system or "sp^2 equivalent" group adjacent to the hydroxyl moiety. This has hitherto included allylic, propargylic, benzylic and

cyclopropyl functional groups that allow subsequent transformations by stabilizing the putative carbon cationic species formed in these reactions.[6] The focal point of this introduction is on the recent developments made toward Lewis and Brønsted acid-catalyzed reactions of alcohols as pro-electrophiles with a variety of carbon-, nitrogen-, and oxygen-based nucleophiles as efficient and operationally straightforward synthetic methods for the construction of the corresponding C–X (X = C, N, O) bonds.

1.2 Allylic alcohols

Allylic alkylation has proven to be an exceptionally powerful approach to introduce a C_3 unit in organic synthesis.[7] The added attractiveness of this protocol is the retention of the C=C bond in the product that can act as a handle for subsequent functional group transformations. While many traditional allylic alkylation reactions are known in organic synthesis using stoichiometric amount of reagents,[8] a catalytic version was reported by Tsuji and Trost in 1965. In their approach, the allylic functional group introduced *via* the participation of a discrete π-allyl metal complex, typically those of palladium (Scheme 1.1).[9] The drawback of this methodology is the formation of by-products such as the conjugate acids of the halide, triflate, carbonate, carboxylate, acetate or phosphate leaving group that is generated on treating with a catalyst and/or nucleophile.[10] To overcome this disadvantage, much attention has been paid in recent years toward developing Tsuji-Trost type allylic alkylations that make

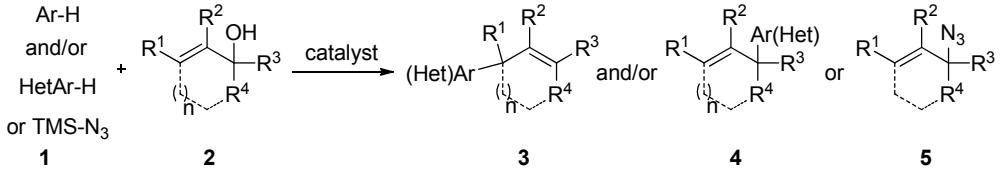


Scheme 1.1 Tsuji-Trost allylic alkylations.

use of ecologically benign and atom economical allylic alcohols as the allylating source.

In 1997, the allylic alkylation was reported by Fukuzawa and co-workers *via* $Sc(OTf)_3$ catalyzed Friedel-Crafts alkylation reaction of allylic alcohols **2** with

Table 1.1 Lewis and Brønsted acid catalyzed intermolecular allylic alkylations.



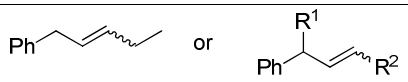
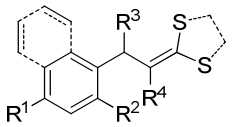
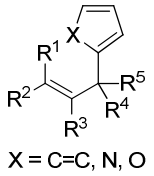
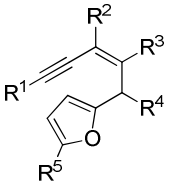
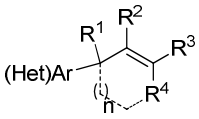
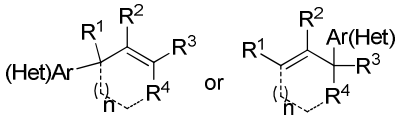
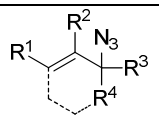
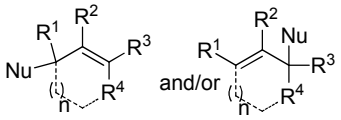
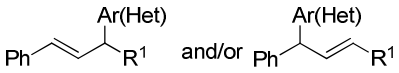
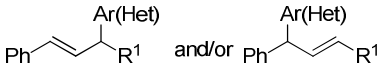
Entry	Catalyst	Product	Yield (%)	Ref
1	$Sc(OTf)_3$		48-95	11
2	$AlCl_3$		50-90	12
3	$AuCl_3$		50-99	14
4	$(Ph_3P)AuNTf_2$		33-91	15
5	$C_6F_5B(OH)_2$		58-99	16
6	$Ca(NTf_2)_2$		68-90	17

Table 1.1 (*Continued*)

Entry	Catalyst	Product	Yield (%)	Ref
7	AgOTf		48-96	19
8	*p*-TsOH·H_2O	 Nu = C, N, O, S, Ar, heteroaromatic	55-84	20
9	TfOH		55-95	21
10	calix[*n*]arene sulfonic acid		60-94	22

benzene **1**, which gave the corresponding products **3** and/or **4** in 48-95% yield with minimal side products (Table 1.1, entry 1).[11] These reactions were shown to proceed well with benzene acting as both the nucleophile and solvent at 115-120 °C. It was shown that the nucleophile always preferred to attack at the less-substituted carbon. In this work, however, only a few aliphatic allylic alcohols were examined and the treatment of cyclic allylic alcohols under the reported conditions was found to not provide any desired product.

Following this pioneering work, Liu and co-workers reported the allylic alkylation of α-hydroxyketene-*S,S*-acetals with various arenes in the presence of $AlCl_3$ (Table 1.1, entry 2).[12] In this work, the involvement of Morita-Baylis-Hillman (MBH) alcohols with an electron-withdrawing group on the C=C bond is particularly noteworthy as it allowed access to the biologically important dihydrocoumarin class of compounds following a sequential Friedel-Crafts alkylation and intramolecular cyclization approach.

Recently, gold complexes have also been demonstrated to be powerful and exceptional catalysts for C–C bond formations.[13] In 2008, Chan and co-workers described $AuCl_3$ mediated allylic alkylation of aromatic and heteroaromatic compounds with allylic alcohols (Table 1.1, entry 3).[14] Under the reported conditions, the reaction was found to proceed well, furnishing the corresponding products in up to 99% yield and with good to excellent regioselectivity at room temperature. By using the Gagosz catalyst $(Ph_3P)AuNTf_2$, Liu and co-workers subsequently disclosed a modified cascade method for the synthesizing of arylated (*Z*)-enones and -enals from enynols and furans (Table 1.1, entry 4).[15] In this work, the corresponding products were obtained in 33-91% yield from gold catalyzed Friedel-Crafts alkylation followed by furan/alkyne cyclizations.

At about the same time, Cubbin and co-workers studied a $C_6F_5B(OH)_2$ mediated version of this C–C bond formation reaction involving allylic alcohols with electron-rich arenes and heteroarenes, giving the desired products in up to 99% yield (Table 1.1, entry 5).[16] The efficiency of this intermolecular cyclization method was exemplified by the ability of $C_6F_5B(OH)_2$ to effect the allylic alkylation of sterically hindered alcohols, the high tolerance of the catalytic system to air and moisture and its solubility in a variety of organic solvents. Added to this, the catalyst was readily recovered from complex mixtures *via* a simple basic extraction. In this work, it was reported that allylic alcohols bearing *p*-FC_6H_4 or cyclohexyl group did not react under the reported standard conditions.

Following this work, Niggemann and co-workers reported that allylic alcohols underwent allylic alkylation with electron-rich arenes at room temperature in the presence of $Ca(NTf_2)_2$, providing the corresponding adducts in good yields (Table 1.1, entry 6).[17] In this work, Bu_4NPF_6 as an additive was shown to be required for the

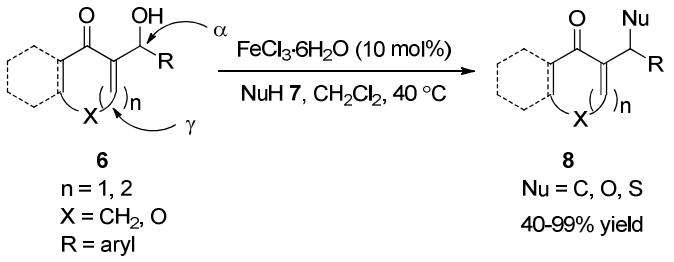
reaction to proceed efficiently. Added to this, the reaction was shown to undergo only intermolecular allylic alkylation. The competitive intramolecular process was not observed as noted in earlier works with other Lewis acids as the catalyst.[18] More recently, Rueping and co-workers demonstrated direct azidation of allylic alcohols with $TMSN_3$ in the presence of AgOTf as the catalyst (Table 1.1, entry 7).[19] The desired products **5** were obtained in up to 96% yield and with up to >20:1 *E*:*Z* and >20:1 α:γ regioselectivity. This synthetic method was shown to provide the synthetically valuable allylic azide intermediates to primary amines, nitrenes and 1,2,3-triazoles.

In addition to Lewis acids, Brønsted acids have also been recently explored as efficient catalysts for the Friedel-Crafts allylation reaction. In 2006, Sanz and co-workers found *p*-$TsOH{\cdot}H_2O$ to be an effective catalyst for the direct Friedel-Crafts allylic alkylation of various arenes and indoles with high product selectivity and yields (Table 1.1, entry 8).[20] The approach was shown to perform well without the need of anhydrous solvents or inert atmosphere. The synthetic utility of this metal-free method made it possible for large scale conversions in an environmentally friendly manner using a readily available and low cost catalyst. A year later, this strategy was extended by Bras and co-workers to include a variety of electron-rich arenes in the presence of a catalytic amount of TfOH (Table 1.1, entry 9).[21] The corresponding allylic alkylated derivatives **3** and/or **4** were afforded in good to excellent yields under solvent free conditions.

Recently, the development of methodologies that use water as a more environmentally friendly solvent system to organic solvents has also received an increasing amount of attention within the field. In 2008, Wang and co-workers reported Friedel-Crafts allylic alkylation of allylic alcohols in water using

calix[*n*]arene sulfonic acid bearing pendant aliphatic chains as recyclable surfactant-type Brønsted acid as the catalyst (Table 1.1, entry 10).[22] In this work, the corresponding allylated aromatic and heteroaromatic products were obtained in 60-94% yield. The advantage of this work was the ability to recover the catalyst up to seven times without significant loss of catalytic activity.

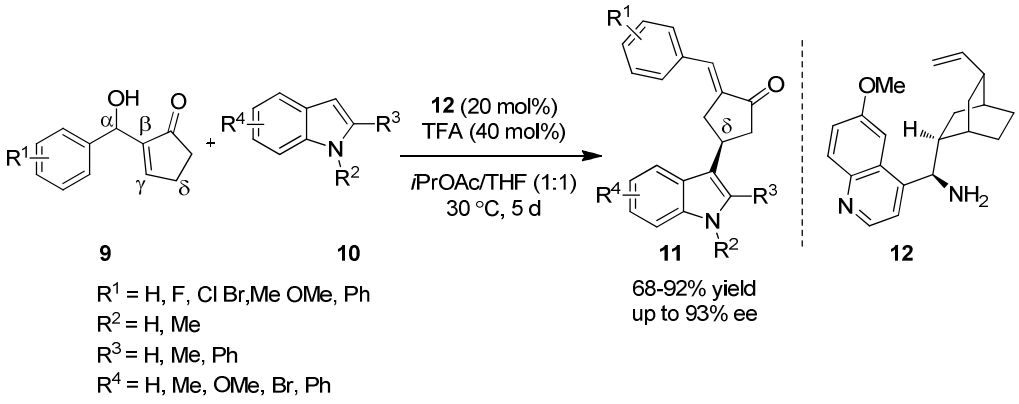
In 2009, Chan and co-workers presented an intermolecular nucleophilic substitution of MBH alcohols **6** with variety of nucleophiles **7** such as 1,3-dicarbonyl compounds, alcohols, thiols, phenols and thiophenols in the presence of $FeCl_3 \cdot 6H_2O$ as the catalyst (Scheme 1.2).[23] The attractiveness of this method was that the substituted cyclic MBH products **8** were afforded with exclusive α-regioselectivity in up to 99% yield under mild conditions that did not need the exclusion of air and moisture. Mechanistically, the reaction was thought to proceed *via* a carbocation intermediate, which was supported by obtaining a racemic allylated product from the reaction of a chiral MBH alcohol substrate (54% ee) and 1,3-dicarbonyl compound.



Scheme 1.2 Iron catalyzed intermolecular nucleophilic substitution of Morita-Baylis-Hillman alcohols **6**.

The following year, Chen and co-workers reported an enantioselective MBH reaction through the use of the chiral organocatalyst derivative **12** in combination with TFA (Scheme 1.3).[24] This synthetic approach provided the products **11** in completely

δ-regiospecific manner in 70-92% yield and with high ee (enantiomeric excess) up to 93% from MBH alcohols **9** and indoles **10**. A drawback of this transformation was the need for an excessive amount of the catalysts and long reaction times of up to 5 days.

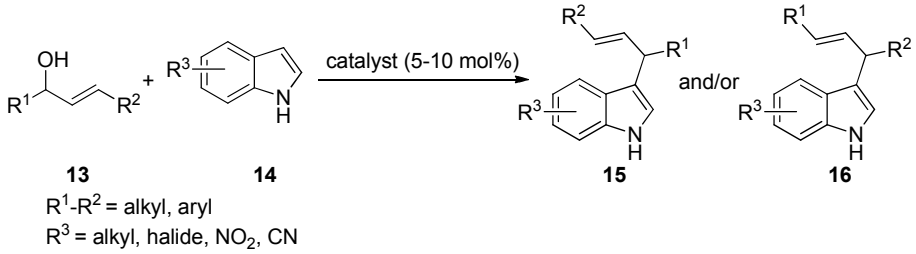


Scheme 1.3 Organocatalytic intermolecular nucleophilic substitution of cyclic Morita-Baylis-Hillman alcohols **9** with indoles **10**.

In 2006, Baba and co-workers designed an $InCl_3$ catalyst system for the direct allylic allylation of indoles **14** with allylic alcohols **13** (Table 1.2, entry 1).[25] In this approach, allylic alkylation of indoles with allylic alcohols proceeded smoothly and furnished the corresponding C-3 allylated indole adducts **15** and/or **16** in good to excellent yields (64-78%). The possibility of other C-2 allylated or allylic amine products were not observed in these reactions.

The generality of this intermolecular C–C bond formation was further explored by Yadav and co-workers *via* $InBr_3$ catalyzed allylic alkylation of indoles with allylic alcohols (Table 1.2, entry 2).[26] Jana and co-workers also made a similar observation in their synthesis of regioselective C-3 allylic indole products from $FeCl_3$ catalyzed allylic allylations (Table 1.2, entry 3).[27] In both these works, the corresponding products **15** and **16** were efficiently synthesized in 56-98% yield.

Table 1.2 Lewis acid catalyzed Friedel-Crafts alkylation with allylic alcohols **13**.



13 **14** **15** **16**

R^1-R^2 = alkyl, aryl

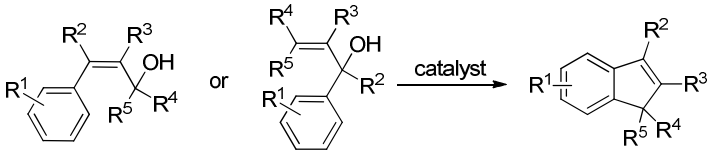
R^3 = alkyl, halide, NO_2, CN

Entry	Catalyst	Yield (%)	Ref
1	$InCl_3$	64-78	25
2	$InBr_3$	85-93	26
3	$FeCl_3$	56-98	27

To construct the indene ring, Li and co-workers developed an efficient method based on the intramolecular Friedel-Crafts allylic alkylation (Table 1.3, entry 1).[28] In their approach, $BF_3{\cdot}Et_2O$ was shown to efficiently catalyze a variety of allylic alcohols of the type **17** under mild conditions and produce the corresponding 3-iodo-1*H*-indene derivatives **19** (R^2 = I) in 55-90% yield, which can act as important precursors for the synthesis of multi-aryl substituted indene derivatives in Suzuki coupling reactions.

In the same year, Liu and co-workers reported intramolecular allylic alkylation of highly substituted allylic alcohols **17** in the presence of $TsOH{\cdot}H_2O$ affording the indene product in yields of 80-99% (Table 1.3, entry 2).[29] This was followed by works by Zhou and co-workers who described intramolecular C–C bond formation reactions *via* $FeCl_3{\cdot}6H_2O$ catalyzed substituted allylic alcohols **18** (Table 1.3, entry 3).[30] These reactions were shown to proceed smoothly under mild conditions and afforded the corresponding substituted indene derivatives in excellent yields of 56-91%.

Table 1.3 Lewis and Brønsted acid catalyzed intramolecular Friedel-Crafts allylic alkylation.



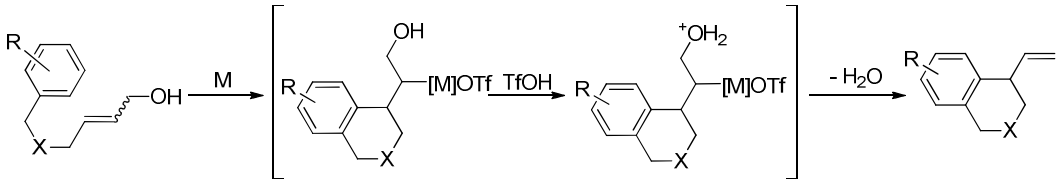
17 **18** **19**

R^1 = H, alkyl, halide
R^2 = H, alkyl, aryl, halide
R^3-R^5 = H, alkyl aryl

Entry	Catalyst	Yield (%)	Ref
1	$BF_3{\cdot}Et_2O$	55-90	28
2	$TsOH{\cdot}H_2O$	80-97	29
3	$FeCl_3{\cdot}6H_2O$	56-93	30

The intramolecular Friedel-Crafts 6-*exo-trig* cyclization of allylic alcohols was also described independently by two groups. In 2008, Nishizawa and co-workers reported the 6-*exo-trig* arylene cyclization that involved the use of allylic alcohols in the presence of catalytic amounts of $Hg(OTf)_2$ with catalyst loading as low as 0.5 mol% (Table 1.4, entry 1).[31] The cyclized 6-membered ring products **23** were obtained with catalytic turnovers of up to 200. In this work, it was postulated that the alkene moiety was initially activated by the catalyst to effect intramolecular Friedel-Crafts 6-*exo-trig* cyclization and give the organomercuric intermediate **21**. Further activation of the allylic hydroxyl group in **21** by TfOH was thought to generate these cationic species **22**, which demercurated to afford the product **23** and regeneration of metal catalyst. A disadvantage of this reaction is the toxic nature of mercury salt despite product yields of up to 99% being obtained.

Table 1.4 Lewis acid catalyzed intramolecular Friedel-Crafts 6-*exo-trig* cyclization of allylic alcohols.



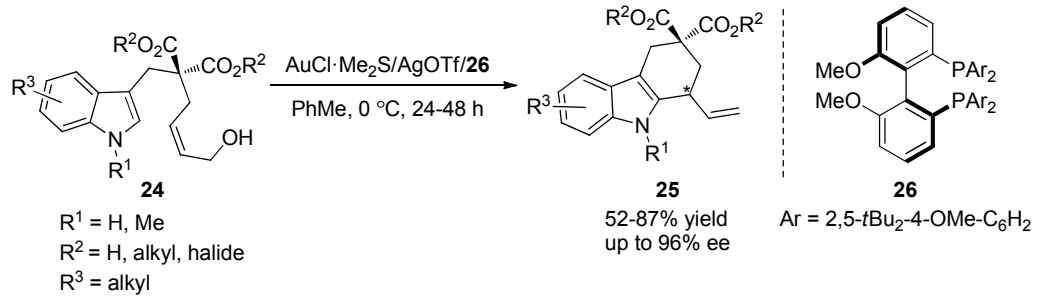
20 **21** **22** **23**

M = Hg, Ag

Entry	[M]	X	Yield (%)	Ref
1	$Hg(OTf)_2$	CH_2	30-99	31
2	AgOTf	CH_2, NHTs, $C(COOEt)_2$	53-90	32

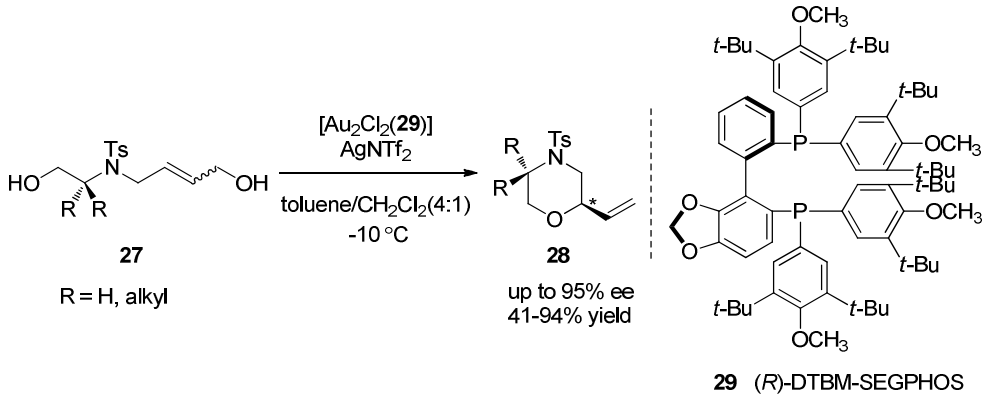
Following this seminal work, Bandini and co-workers showed a AgOTf catalyzed version of this transformation could be realized in comparable product yields (Table 1.4, entry 2).[32] The corresponding functionalized 1-vinyl-1,2,3,4-tetrahydronaphthalene and a 4-vinyl-1,2,3,4-tetrahydroisoquinoline were shown to be obtained with complete regioselectivity except in one example in which a 14:1 mixture of regioisomers were obtained when the *m*-anisolic alcohol substrate was employed. The mechanism of this reaction was hypothesized to proceed in a manner similar to that reported for the $Hg(OTf)_2$ catalyzed transformation.

In 2009, Bandini and co-workers reported the first asymmetric intramolecular Friedel-Crafts 6-*exo-trig* cyclization of allylic alcohols of the type **24** with the $AuCl{\cdot}Me_2S$/AgOTf catalytic system containing the chiral ligand **26** (Scheme 1.4).[33] The method was shown to give the corresponding polycyclic indolyl-containing products **25** in good to excellent yields of 52-87% and with up to 96% ee.



Scheme 1.4 Gold catalyzed enantioselective synthesis of fused indole derivatives.

In 2010, the same group developed enantioselective Au catalyzed intramolecular allylic alkylation of allylic alcohols **27** to functionalized 2-vinyl-morpholines **28** (Scheme 1.5).[34] This substitution reaction was shown to proceed well in the presence of the active chiral gold complex generated *in situ* from the reaction of [Au_2Cl_2(**29**)] and $AgNTf_2$.

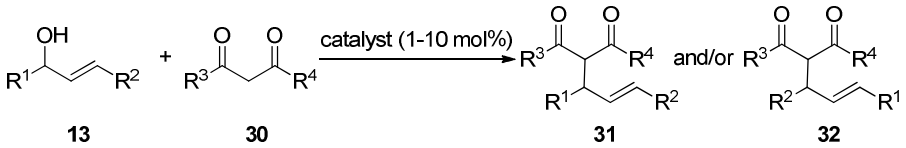


Scheme 1.5 Gold catalyzed enantioselective intramolecular Fridel-Crafts allylation of substituted allylic alcohols **27**.

In addition to the numerous examples in the literature describing the reactions of allylic alcohols with various aromatic compounds, the use of 1,3-dicarbonyl compounds as efficient and powerful nucleophiles in allylic alkylations have been reported (Table 1.5). An $InCl_3$ catalyzed direct allylic alkylation of allylic alcohols **13**

by 1,3-dicarbonyl compounds **30** as nucleophiles was reported by Baba and co-workers (Table 1.5, entry 1).[35] The study showed that the catalytic cycle proceeded well in toluene at 80 °C to provide the corresponding allylic alkylation products **31** and/or **32** in 79-95% yield. Following this work, other catalytic systems that included $Bi(OTf)_3$,[36] $Yb(OTf)_3$,[37] $FeCl_3$[38] and the lanthanum triflates $Ln(OTf)_n$ (Ln = Yb, La, Hf; n = 3, 4)[39] were reported to effect the reaction with similar efficiency, affording the allylated products **31** and/or **32** in 51-93% yield (Table 1.5, entry 2-5).

Table 1.5 Lewis and Brønsted acid catalyzed intermolecular allylic alkylation of 1,3-dicarbonyl compounds **30** with allylic alcohols **13**.



13 **30** **31** **32**

R^1-R^2 = H, alkyl, aryl
R^3-R^4 = alkyl, aryl, alkoxy

Entry	Catalyst	Yield (%)	Ref
1	$InCl_3$	75-95	35
2	$Bi(OTf)_3$	62-73	36
3	$Ln(OTf)_n$	51-92	37
4	$Yb(OTf)_3$	72-93	38
5	$FeCl_3$	72-82	39
6	I_2	51-99	40
7	*p*-TsOH·H_2O	80-72	20

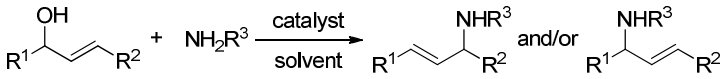
Using molecular iodine as the catalyst, Chan and co-workers developed a direct allylic allylation of 1,3-dicarbonyl compounds with allylic alcohols, providing the

corresponding allylated products in 51-99% yields (Table 1.5, entry 6).[40] The method was shown to be operationally straightforward as it did not need the exclusion of air or moisture.

Sanz and co-workers disclosed a polymer-bound *p*-toluenesulfonic acid catalyzed allylic alkylation of 1,3-dicarbonyl compounds **30** with allylic alcohols **13** (Table 1.5, entry 7).[20] Notably, one advantage of this allylic alkylation methodology was its applicability to large-scale reactions as recovery of the solid acid catalyst was shown to be possible by carrying out a simple filtration. Extension of this method to the allylic amine in 86% yield from the reaction of allylic alcohol **13** and 4-nitrobenzenamine **36** was also demonstrated in one example (Table 1.6, entry 1).[20]

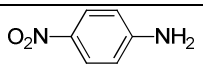
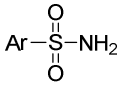
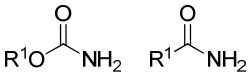
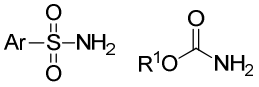
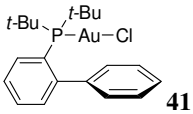
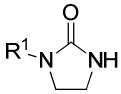
In 2006, Shibasaki and co-workers further exploited this direct allylic amination approach with allylic alcohols **13** by using sulfonamides **37**, carbamates **38** and amides **39** as nucleophiles and $Bi(OTf)_3$ as the catalyst (Table 1.6, entry 2).[41] The substitution reaction was found to require the need to employ KPF_6 as a co-catalyst so as, to afford the corresponding allylic amination adducts **34** and/or **35** in 55-99% yield. Subsequently, Liu and co-workers expanded this intermolecular C–C bond formation approach by showing $AuCl_3$ catalyzed amination with substituted anilines **40** as well as sulfonamides **37** could be achieved (Table 1.6, entry 3).[42] The reactions proceeded under relatively mild conditions in acetonitrile at room temperature to give the desired allylic amine products in good to excellent yields. In addition to the aforementioned metal catalysts, molecular iodine was also investigated as a catalyst in these reactions by Chan and co-workers (Table 1.6, entry 4).[43] In this work, the corresponding amine derivatives were synthesized in good to excellent yields under atmospheric conditions

Table 1.6 Lewis and Brønsted acid catalyzed intermolecular allylic amination with allylic alcohols **13**.



13 **33** **34** **35**

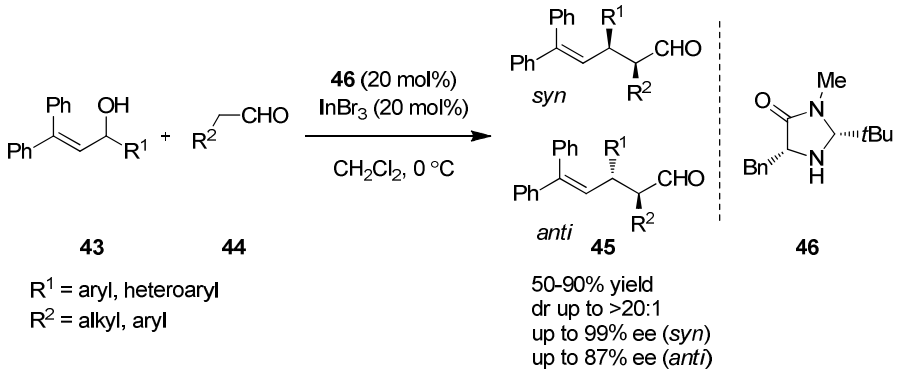
R^1= alkyl, aryl
R^2 = H, alkyl, aryl

Entry	Catalyst	NH_2R^3	Yield (%)	Ref
1	*p*-TsOH·H_2O	 **36**	86	20
2	$Bi(OTf)_3/KPF_6$	 **37**	55-99	41
		 **38** **39**		
3	$AuCl_3$	$TsNH_2$ $ArNH_2$ **37a** **40**	58-96	42
4	I_2	 **37** **38**	61-96	43
5	 **41** /$AgSbF_6$	 **42**	85-100	44

at room temperature. More recently, cyclic ureas **42** were shown to be applicable to the allylic amination process (Table 1.6, entry 5).[44] In this work, the corresponding products were produced in 85-100% yield and with high regioselectivity by

employing [P(*t*-Bu)$_2$(*o*-biphenyl)]AuCl **41** as the catalyst and $AgSbF_6$ as the co-catalyst.

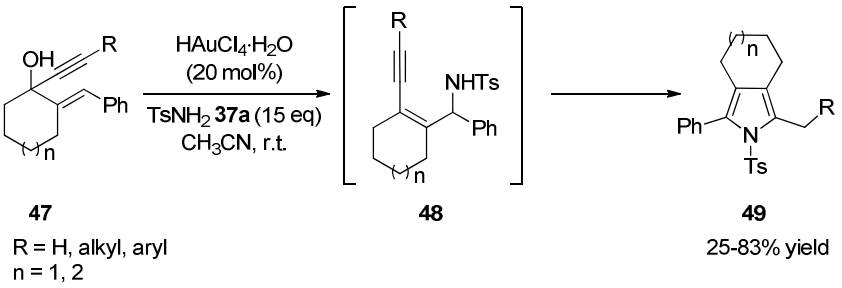
Following this work, Cozzi and co-workers developed a chiral version of the indium catalyzed allylic allylation of aldehydes **44** with allylic alcohols of the type **43** in the presence of the chiral organocatalyst **46** (Scheme 1.6).[45] This robust approach was applied to a wide variety of substrates, providing the corresponding allylated aldehyde derivatives **45** in 50-90% yield and with dr (diastereomeric ratio) values up to >20:1 and up to 99% ee.



Scheme 1.6 Indium catalyzed enantioselective synthesis of substituted allylated aldehyde derivatives **45**.

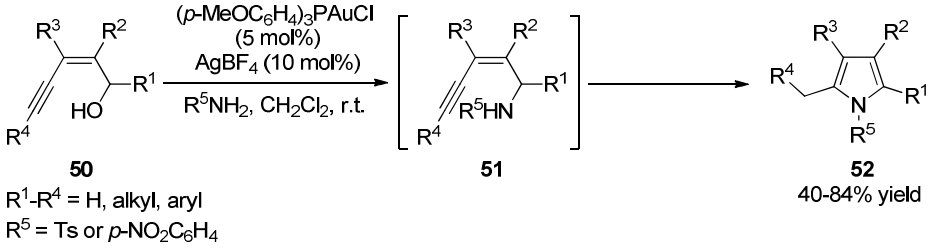
In 2008, an efficient tandem double amination approach to pyrroles involving intermolecular allylic amination/intramolecular hydroamination utilizing allylic alcohols **47** and sulfonamides **37** in the presence of $HAuCl_4 \cdot H_2O$ as the catalyst was demonstrated by Liang and co-workers (Scheme 1.7).[46] The reaction mechanism was reported to proceed *via* an initial amination at the alkene position of the substrate to form the allylic sulfonamide intermediate **48**. Subsequent hydroamination of this adduct followed by aromatization then gave pyrrole derivative **49** in up to 83% yield. A noted drawback was that the method was limited to cyclohexanol substrates **47**.

Furthermore, an excess amount of $TsNH_2$ and a high catalyst loading of 20 mol% of the gold salt was required to achieve high product yields.



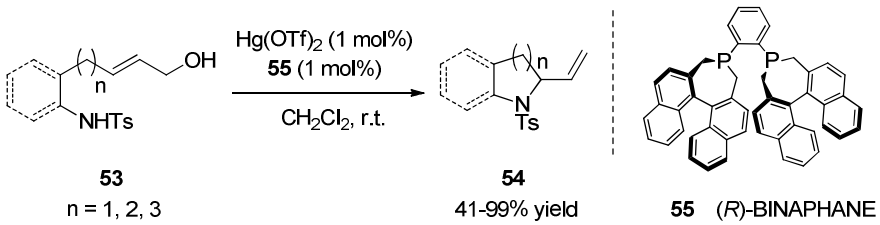
Scheme 1.7 Gold catalyzed tandem intermolecular allylic amination/hydroamination of **47**.

Following this work, a similar approach was carried out by Liu and co-workers towards the synthesis of tetrasubstituted pyrroles **52** by gold catalyzed domino amination/intramolecular hydroamination of (*Z*)-2-en-4-yn-1-ols **50** with 4-nitroaniline **36** or *p*-$TsNH_2$ **37a** (Scheme 1.8).[47] A mechanism was proposed to involve initial amination of the allylic alcohol followed by alkyne hydroamination, delivering the corresponding highly substituted pyrroles in up to 84% yield. This methodology was applied successfully to several substrates using the $(p\text{-}MeOC_6H_4)_3PAuCl/AgBF_4$ catalyst combination at room temperature.



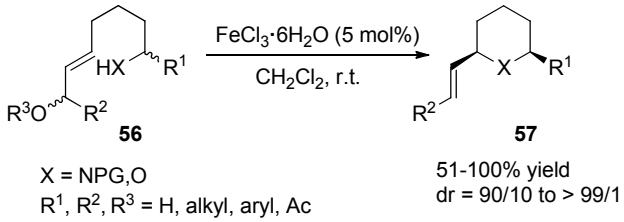
Scheme 1.8 Gold catalyzed tandem synthesis of substituted pyrroles **52**.

Nishizawa and co-workers communicated the first example of intramolecular allylic aminations of *N*-tosylanilinoallylic alcohols **53** using $Hg(OTf)_2$ as catalyst (Scheme 1.9).[48] This practical approach allowed for the synthesis of the corresponding 5 to 7-membered nitrogen-containing heterocycles **54** in 41-99% yield. Two years later, Yamamoto and co-workers developed the enantioselective version of this reaction with the chiral ligand (*R*)-BINAPHANE **55** and $Hg(OTf)_2$ catalyst combination (Scheme 1.9).[49] The cyclization of allylic alcohols with a 1 mol % catalyst loading in mesitylene as the solvent at −30 °C delivered the desired 2-vinyl indoline products in excellent yields of 41-99% and with up to 99% ee.



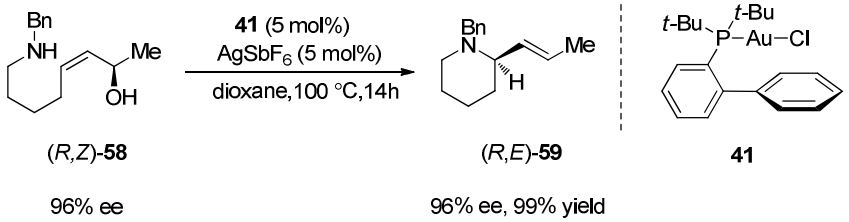
Scheme 1.9 $Hg(OTf)_2$ catalyzed *5-exo-trig* cyclization of anilino sulfonamide allyl alcohol **53**.

Following this work, the diastereoselective hydroamination/hydroalkoxylation of closely related allylic alcohols **56** to the corresponding substituted *cis*-2,6-piperidines and *cis*-2,6-tetrahydropyrans **57** catalyzed by $FeCl_3 \cdot 6H_2O$ was established by Cossy and co-workers (Scheme 1.20).[50] Achieved at room temperature, the approach provided product yields of up to 100% and with high dr values up to >99%.



Scheme 1.20 Fe catalyzed intramolecular cyclization of allyl alcohols **56**.

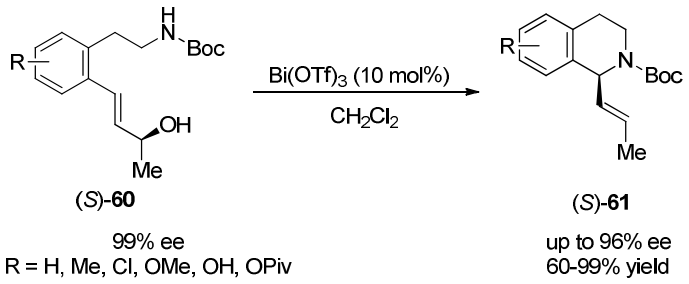
More recently, Widenhoefer and co-workers showed that the formation of enantiopure substituted piperidine derivatives from intramolecular amination of enantioenriched allylic alcohols (*R,Z*)-**58** (96% ee) could be achieved (Scheme 1.21).[51] It was highlighted that the intramolecular substitution of amines to the allylic alcohol occurred with complete 1,3-chirality transfer in the presence of 1:1 mixture of [P(*t*-Bu)$_2$*o*-biphenyl]AuCl as catalyst and $AgSbF_6$ as co-catalyst, furnishing (*R,E*)-**59** in 99% yield and with 96% ee.



Scheme 1.21 Gold catalyzed synthesis of enantioenriched vinylpiperidines **59**.

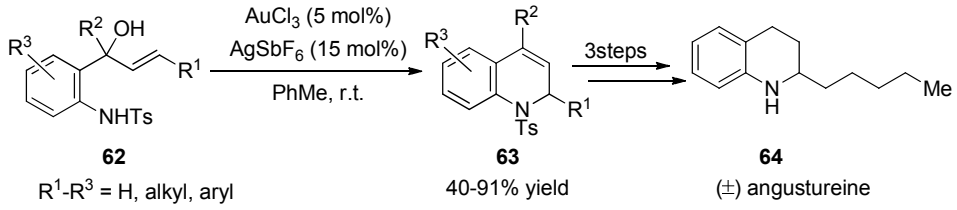
Kawai and co-workers concurrently disclosed that chirality transfer could be accomplished in the intramolecular cyclization of chiral amino allyl alcohols **60** to prepare substituted 1-vinyltetrahydroisoquinoline derivatives **61** (Scheme 1.22).[52] The enantioselective intramolecular nucleophilic substitution catalyzed by $Bi(OTf)_3$ gave the corresponding cyclized products in high yields of 60-99% with 1,3-chirality transfer that led to ee values of up to 96%. The methodology was shown to tolerate a

wide range of aromatic systems and was thought to generate the enantiomeric products *via* a possible syn S_N2' process that was significantly influenced by the substituent on the benzene ring.



Scheme 1.22 Bismuth catalyzed intramolecular amination of allyl alcohol **60**.

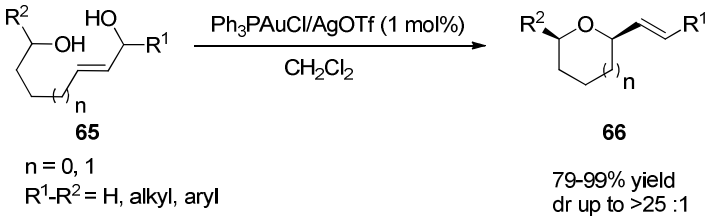
In addition to these works, Chan and co-workers reported the intramolecular C–N bond formation of allylic alcohols **62** in the presence of $AuCl_3/AgSbF_6$ catalyst system at room temperature (Scheme 1.23).[53] This amination process was shown to efficiently undergo a 6-*endo-trig* cyclization in toluene, providing the corresponding 1,2-dihydroquinoline derivatives **63** in moderate to excellent yields. The synthetic utility of this protocol was further exemplified by its application to the synthesis of the bioactive natural product (±) angustureine **64**.



Scheme 1.23 Gold catalyzed intramolecular amination of allylic alcohol **62**.

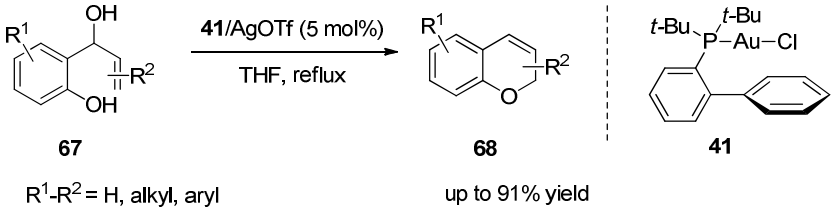
The first example of alcohols act as both the nucleophile and electrophile in the synthesis of *cis*-tetrahydropyrans and *cis*-tetrahydrofurans **66** from monoallylic diols

65 was reported by Aponick and co-workers (Scheme 1.24).[54] The reported $Ph_3PAuCl/AgOTf$ catalyzed alkoxylation method with catalyst loadings as low as 0.1 mol% at −78 °C was shown to proceed smoothly, providing the *O*-heterocyclic adducts in 79-99% yield and with dr values up to > 25:1.



Scheme 1.24 Gold catalyzed intramolecular alkoxylation of allyl alcohol **65**.

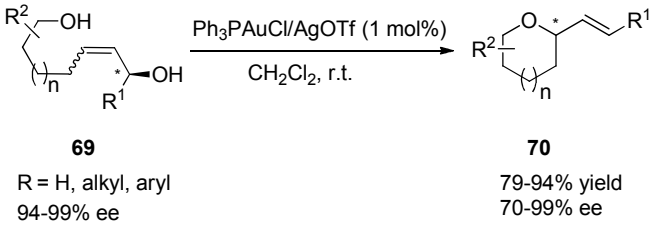
Subsequently the same group successfully implemented an approach involving 6-*endo-trig* cyclization of 2-(1-hydroxyallyl)phenols **67** to various chromenes **68** during studies on gold catalyzed intramolecular alkoxylation of allylic alcohols (Scheme 1.25).[55] This strategy constitutes an efficient method for the synthesis of desired products **68** in up to 91% yield using a 1:1 ratio of [P(*t*-Bu)$_2$(*o*-biphenyl)]AuCl and AgOTf as the catalyst system.



Scheme 1.25 Gold catalyzed intramolecular alkoxylation of allyl alcohol **67**.

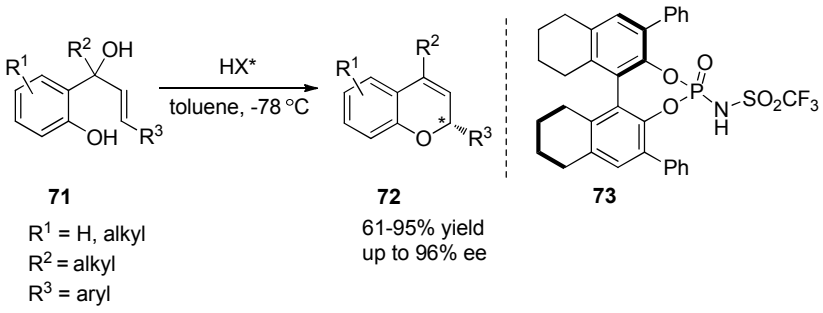
Following this work, the group expanded the intramolecular C–O bond formation strategy to include 1,3-chirality transfer of allylic alcohols of the type **69** to tetrahydropyrans **70** in the presence of $Ph_3PAuCl/AgOTf$ as the catalyst system

(Scheme 1.26).[56] In this work, a notable observation was the marked influence of the olefin geometry of **69** on the stereochemistry of the product **70**.



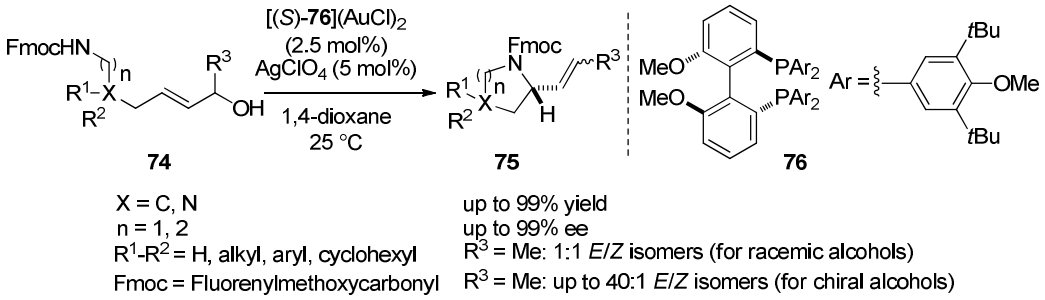
Scheme 1.26 Gold catalyzed chirality transfer reactions of monoallyl diols **69**.

At about the same time, Rueping and co-workers found that *N*-triflylphosphoramide **73** was an efficient chiral Brønsted acid catalyst for the direct intramolecular alkoxylation of 2-(1-hydroxyallyl)phenols **71** in toluene at −78 °C (Scheme 1.27).[57] This synthetic method provided facile access to the enantiomeric substituted chromenes **72** in 61-95% yield and with up to 96% ee. Mechanistically, it was reported that the observed enantiomeric excess of products could have been achieved *via* involvement of a hydrogen bonding network between the phosphoramide moiety of the acid catalyst and hydroxyl moieties of the allylic diol.



Scheme 1.27 Chiral Brønsted acid catalyzed asymmetric alkoxylation of 2-(1-hydroxyallyl)phenols **71**.

More recently, enantioselective gold catalyzed intramolecular dehydrative amination of allylic alcohols **74** was reported by Widenhoefer and co-workers (Scheme 1.28).[58] In this work, the desired substituted vinylpyrrolidine and piperazine derivatives **75** were obtained in up to 99% yield and with 99% ee using the chiral gold complex **76** in the presence of $AgClO_4$ as a co-catalyst under mild conditions at 25 °C. The method was shown to be less effective to *Z*-alkenol and racemic secondary alkenols, which were observed to give the corresponding adducts with ≤5% ee and 1:1 mixture of *E*/*Z* isomers. On the other hand, chiral secondary alkenols were shown to perform well under the reported standard conditions, providing the corresponding cyclic products with high regioselectivity of up to 40:1 and ee values up to 99%.

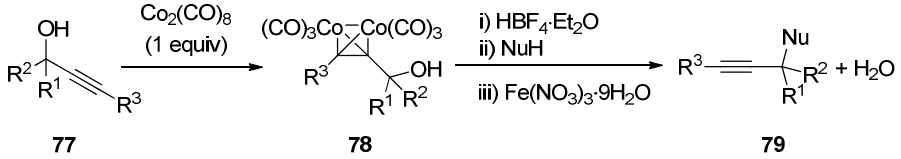


Scheme 1.28 Gold catalyzed enantioselective synthesis of vinylpyrrolidine and piperazine derivatives **75**.

1.3 Propargylic Alcohols

Nucleophilic substitution of propargylic alcohols is useful synthetic strategy in organic synthesis.[141] One strategy for the nucleophilic displacement of propargylic alcohols **77** is the Nicholas reaction (Scheme 1.29).[59] The reaction usually involves the transformation of the alcoholic substrate with $[Co_2(CO)_8]$ to give the corresponding metal-carbonyl-triple bond complex **78** and its subsequent reaction

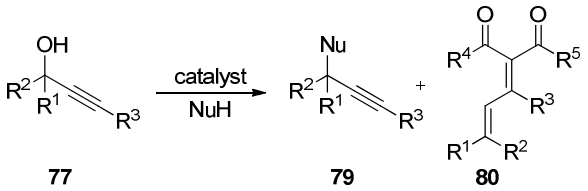
with a variety of nucleophiles. While this transformation has been shown to be efficient, the need for a stoichiometric amount of [$Co_2(CO)_8$] and multi-step operation in addition to the formation of excess amounts of by-products remains its main drawbacks. For this reason, numerous methods have been developed over the years toward an atom economical catalytic version of this reaction.



Scheme 1.29 Nicholas reactions of propargylic compounds.

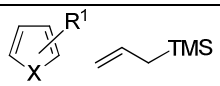
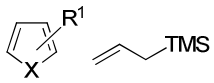
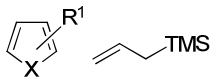
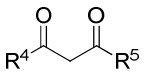
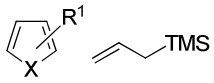
In 2005, a direct nucleophilic substitution of propargylic alcohols was reported by Campagne and co-workers (Table 1.7, entry 1).[60] This reaction was shown to tolerate various nucleophiles, such as arenes **81**, allyltrimethylsilane **82**, alcohols **83** and thiols **84** with $NaAuCl_4 \cdot 2H_2O$ as the catalyst, and afforded the corresponding propargylated derivatives **79** in 33-97% yield. Mechanistically, the reaction was posited to proceed *via* a carbocation intermediate based on observations in one example showing the racemic substituted product was furnished from an enantioenriched propargylic alcohol (96% ee). Following this work, the propargylation of **77** with C-, O-, S-, and N-centered nucleophiles in the presence of $BiCl_3$ under mild conditions at 35 °C was presented by Zhan and co-workers (Table 1.7, entry 2).[61] The method was shown to be applicable to a variety of terminal and internal propargylic alcohols, and provide the products with complete regioselectivity. In the same year, the same group showed $FeCl_3$ was also an efficient catalyst for this nucleophilic substitution reaction and provided the corresponding products in comparable yields of up to 95% (Table 1.7, entry 3).[62]

Table 1.7 Lewis and Brønsted acid catalyzed direct nucleophilic substitution of propargylic alcohols **77**.



77 **79** **80**

R^1-R^2= H, alkyl, aryl
R^3 = H, alkyl, aryl, SPh, SePh
X = C=C, N, O, S

Entry	Catalyst	NuH	Yield (%)	Ref
1	$NaAuCl_4 \cdot 2H_2O$	 **81** **82** R^1OH **83** R^1SH **84**	33-97	60
2	$BiCl_3$	 **81** **82** R^1OH **83** R^1SH **84** $ArSO_2NH_2$ **37**	10-94	61
3	$FeCl_3$	 **81** **82** R^1OH **83** R^1SH **84** $ArSO_2NH_2$ **37**	38-95	62
4	*p*-TsOH·H_2O	 **30**	43-93	63
5	$Sc(OTf)_3$	 **81** **82**	65-100	64

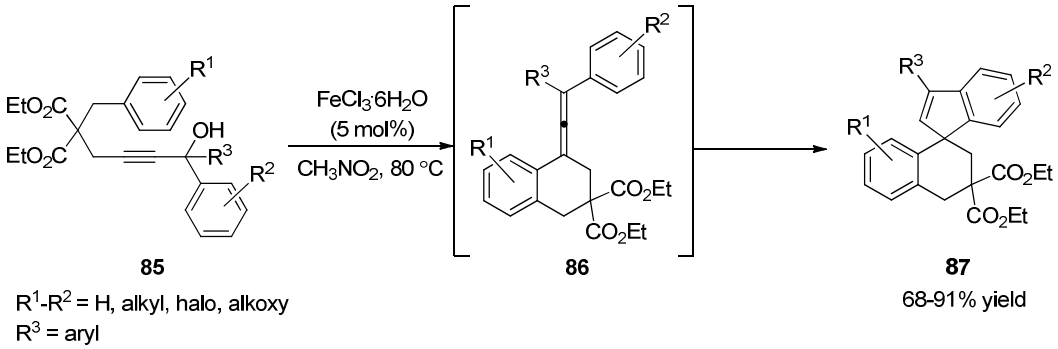
Subsequently, Sanz and co-workers discovered that not only Lewis acids but also simple Brønsted acids to be suitable catalysts for these substitution reactions. In the

presence of a catalytic amount of *p*-TsOH·H_2O, the propargylation reactions were shown to proceed well with 1,3-dicarbonyl compounds **30** as nucleophiles under conditions that did not require the exclusion of air and moisture. This gave the desired propargylic products in moderate to excellent yields (Table 1.7, entry 4).[63] A limitation of this approach, however, was the competitive formation of conjugated diene-dione **80** a side product in reactions with a tertiary propargylic alcohol. It was thought that the by-product could be produced from the condensation of the 1,3-dicarbonyl compound with α,β-unsaturated carbonyl derivative derived from Meyer-Schuster rearrangement.

Yoshimatsu and co-workers disclosed $Sc(OTf)_3$ catalyzed nucleophilc substitution of phenylsulfanyl and selanyl propargylic alcohols (Table 1.7, entry 5).[64] The method provided the desired propargylic products in 65-100% yield with complete regioselectivity. It was noted that when alcohols containing 12-membered cyclic aliphatic system were employed under reported conditions, mixture of allene and enyne products were obtained in 24-51% yield. In this work, it was postulated that the sulfur and selenium functional groups on the propargylic alcohol were necessary to stabilize the putative carbocationic species formed on activation of the substrate by the metal catalyst.

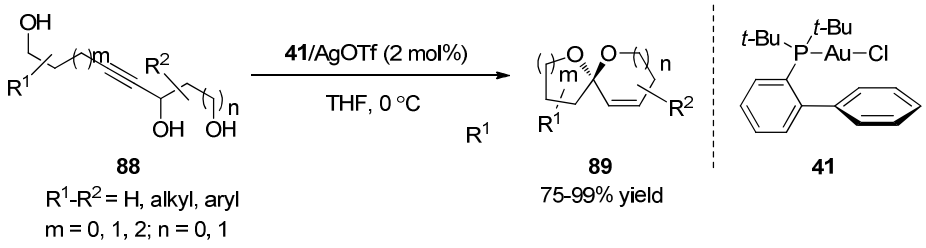
In the same year, Zhou and co-workers demonstrated cascade intramolecular Friedel-Crafts cyclization followed by hydroarylation of diaryl-substituted tertiary propargylic alcohols **85** initiated by $FeCl_3·6H_2O$ (Scheme 1.30).[65] The reactions were found to operate rapidly under mild and operationally straightforward conditions, affording the corresponding spirocarbocycles **87** in 68-91% yield. Mechanistically, it was thought to proceed *via* an initial Friedel-Crafts reaction involving addition of the arene group to the alkyne moiety. This generates the allene intermediate **86** *in situ*

which then undergoes subsequent intramolecular hydroarylation, and formation of the spirocarbocycle **87**.



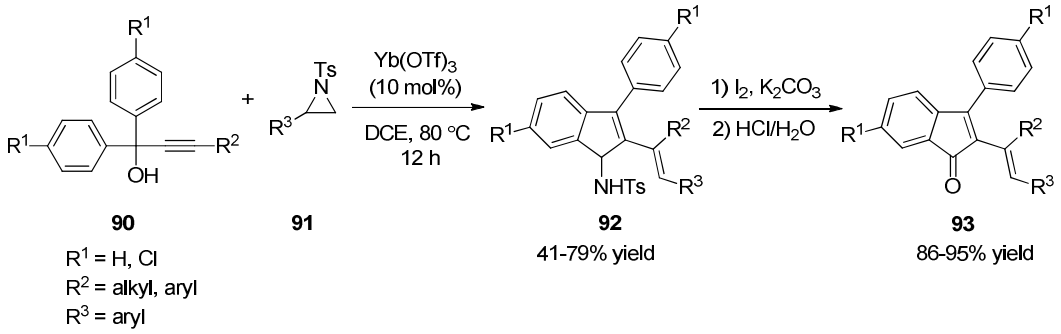
Scheme 1.30 $FeCl_3 \cdot 6H_2O$ catalyzed intramolecular annulation/hydroarylation of propargylic alcohols **85**.

Following this work, Aponick and co-workers reported an efficient tandem intramolecular hydroalkoxylation of substituted propargylic triols **88** to spiroketal derivatives **89** using Au[P(*t*-Bu)$_2$(*o*-biphenyl)]OTf as the active catalyst generated *in situ* from the reaction of **41** and AgOTf (Scheme 1.31).[66] In this work, the corresponding 1,6-dioxaspiro[4.5]dec-9-enes were obtained in excellent yields with a catalyst loading as low as 2 mol %. Relying on one of hydroxyl groups to act as the nucleophile and while the other as the electrophile in the substrate, the work represented the first reported example to synthesize the spiroketals using propargylic triols **88**.



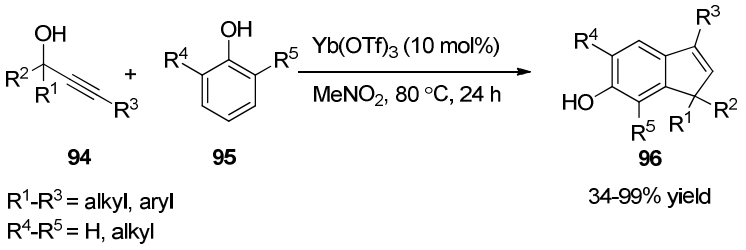
Scheme 1.31 Gold catalyzed tandem synthesis of 1,6-dioxaspiro[4.5]dec-9-enes **89**.

In the same year, a method for the synthesis of highly functionalized indenes **92** from the tandem reactions of aziridines **91** and tertiary propargylic alcohols **90** using $Yb(OTf)_3$ as a catalyst was reported by Lu and co-workers (Scheme 1.32).[67] Under the reported conditions, the desired indene derivatives were produced in 41-79% yield. Further application of the obtained indenes to prepare indenones **93**, powerful therapeutic candidates for the treatment of diabetes, was successfully achieved with I_2/K_2CO_3.



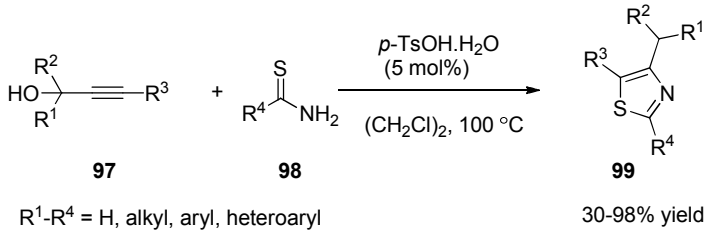
Scheme 1.32 $Yb(OTf)_3$ catalyzed intermolecular tandem reaction of propargylic alcohols **90** and aziridines **91**.

At about the same time, Chan and co-workers demonstrated the preparation of 6-indenols **96** involving an efficient tandem intermolecular Friedel-Crafts alkylation/hydroarylation of tertiary propargylic alcohols **94** with phenols **95** using $Yb(OTf)_3$ as a catalyst (Scheme 1.33).[68] This methodology was found to perform well under mild conditions, while a higher catalyst loading of 10 mol % and long reaction times of 24 h was required, provided the corresponding indene derivatives **96** in 34-99% yield. The mechanism was thought to proceed *via* an allene intermediate formed *in situ* in a manner similar to that reported by Zhou and co-workers for the synthesis of spirocarbocycles **87**.



Scheme 1.33 $Yb(OTf)_3$ catalyzed intermolecular Friedel-Crafts alkylation/hydroarylation of tertiary propargylic alcohols **94**.

Following this work, the same group expanded this intermolecular nucleophilic substitution/cyclization route to highly functionalized thiazoles **99** from the reaction of propargylic alcohols **97** and thioamides **98** in the presence of *p*-TsOH.H_2O as catalyst (Scheme 1.34).[69] This synthetic approach was shown to tolerate a wide variety of secondary and tertiary propargylic alcohols, furnishing the corresponding di- and trisubstituted thiazoles **99** in up to 98% yield. Mechanistically, this intriguing transformation was reported to proceed *via* an allenyl carbocation intermediate that was susceptible to subsequent amide substitution/cyclization to give the resulting cyclized products.



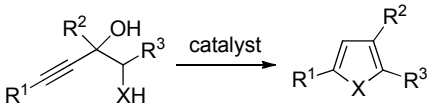
Scheme 1.34 *p*-TsOH.H_2O catalyzed synthesis of substituted thiazoles **99**.

The first example for the synthesis of various N-, O-, S-containing heterocyles *via* $AgNO_3$ catalyzed intramolecular nucleophilic substitution of propargylic alcohols **100** was reported by Knight and co-workers (Table 1.8, entry 1).[70] In this work, the

corresponding pyrrole, furan and thiophene products **101** were obtained in excellent yields up to 70-99%. A drawback of this approach was shown to be that it was limited to internal propargylic alcohols and ineffective for terminal alcohols under the reported conditions.

Subsequent work by the groups of Akai and Aponick demonstrated gold catalyzed intramolecular cyclization of propargylic compounds **100** to various heterocyclic derivatives under mild conditions at 0 °C or room temperature (Table 1.8, entry 2-3).[71-72] The desired pyrrole, furan and thiophene adducts **101** were obtained in up to 99% yield from either [P(*t*-Bu)$_2$(*o*-biphenyl)]AuCl/AgOTf (Aponick) or (Ph$_3$P)AuCl/AgNTf$_2$ (Akai) as the catalyst system. In these later studies, the efficiency of the gold complexes as catalysts was highlighted by the fact that catalyst loadings as low as 0.05 mol% could mediate the reactions.

Table 1.8 Metal catalyzed intramolecular cyclization of propargylic alcohols **100**.



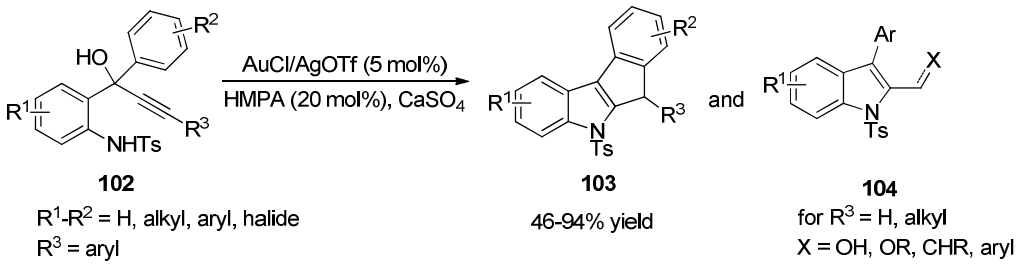
100 **101**

R^1- R^3 = H, alkyl, aryl
X = O, NR, S

Entry	Catalyst	Yield (%)	Ref
1	$AgNO_3$	70-99	70
2	[P(*t*-Bu)$_2$(*o*-biphenyl)]AuCl /AgOTf	87-99	71
3	(Ph$_3$P)AuCl/AgNTf$_2$	85-98	72

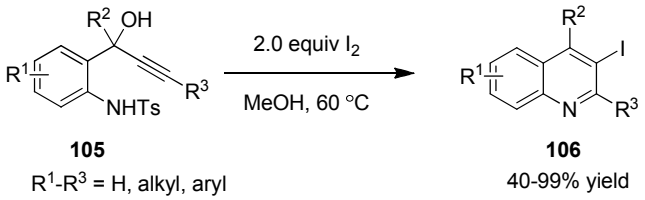
A year later, Chan and co-workers developed a synthetic strategy involving AuCl/AgOTf catalyzed intramolecular tandem cycloisomerization/Friedel-Crafts

alkylation of 2-tosylaminophenylprop-1-yn-3-ols **102** (Scheme 1.35).[73] In this study, HMPA was found to be an effective additive for this reaction to produce a series of indenyl-fused **103** and 2,3-disubstituted indole derivatives **104** in up to 94% yield in a single step operation.



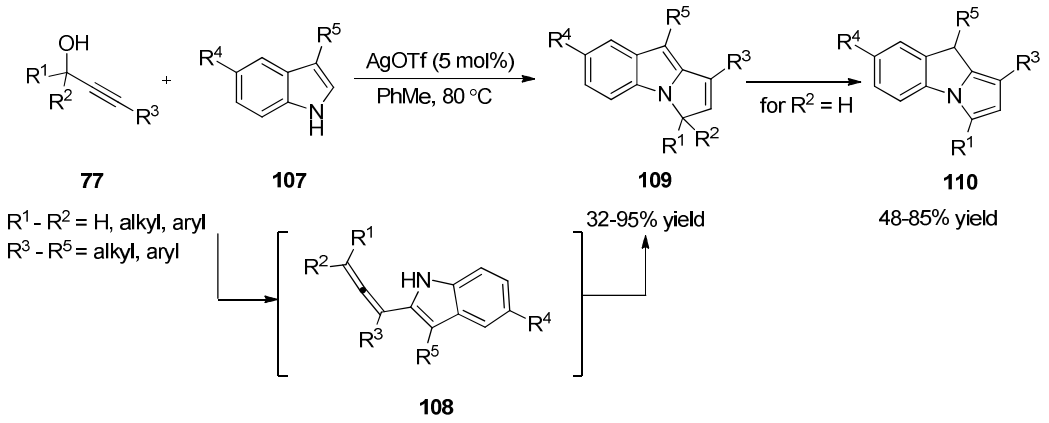
Scheme 1.35 Au catalyzed synthesis of indole derivatives **103** and **104**.

Based on this approach, Liang and co-workers reported the preparation of 3-iodoquinolines **106** *via* I_2 promoted cascade intramolecular *6-endo-dig* iodocyclization of 2-tosylaminophenylprop-1-yn-3-ols **105** (Scheme 1.36).[74] In this reaction, the corresponding iodoquinoline derivatives were produced in moderate to excellent yields with complete regioselectivity. The synthetic utility of this metal-free method was also applied successfully in Pd catalyzed cross coupling reactions to obtain the corresponding functionalized quinoline adducts in excellent yields.



Scheme 1.36 I_2 promoted intramolecular cyclization of 2-tosylaminophenylprop-1-yn-3-ols 103.

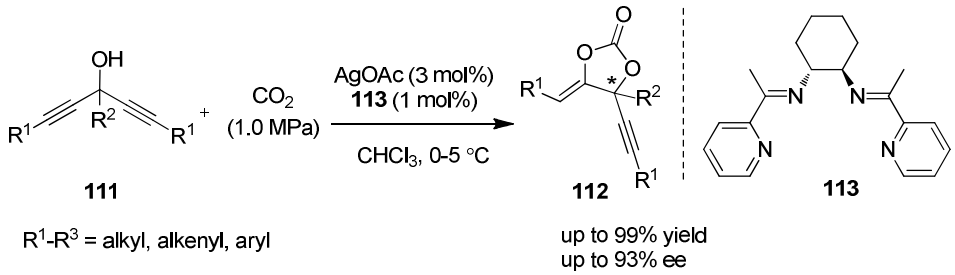
In 2010, an efficient approach for the preparation of N-fused indole derivatives **109** from AgOTf catalyzed propargylic alcohols **77** and substituted 1*H*-indoles **107** was established by Zhan and co-workers (Scheme 1.37).[75] The method was shown to be applicable to a broad range of substrates bearing electron-withdrawing, electron-donating, and sterically demanding substrate combinations. The mechanism was suggested to involve activation of the alcohol by the metal catalyst to form allenyl intermediate **108** followed by a Friedel-Crafts reaction/N–C bond formation process to provide **109**. When R^2 = H, the product **110** was obtained after further isomerization of **109**.



Scheme 1.37 AgOTf catalyzed intermolecular nucleophilic substitution/cyclization of propargyl alcohols **77** and indoles **107**.

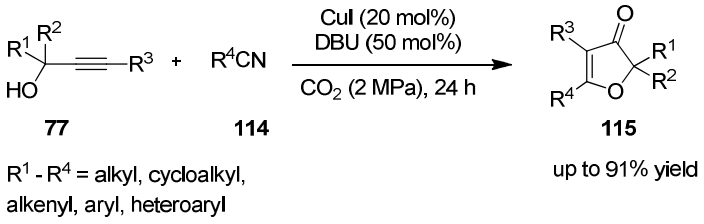
At about the same time, Yamada and co-workers successfully achieved enantioselective carbon dioxide incorporation into bispropargylic alcohols **111** with desymmetrization to get substituted cyclic carbonates **112** in the presence of the AgOAc + **113** catalyst system under mild conditions at 0-5 °C (Scheme 1.38).[76] An interesting feature of this nucleophilic addition reaction is that carbon dioxide acts as both nucleophile and electrophile, affording the corresponding cyclized products **112**

in excellent yields and in up to 93% ee. However, this methodology was shown to be limited to symmetrical bispropargylic alcohols.



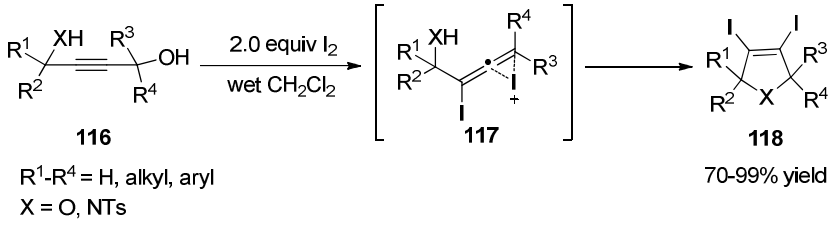
Scheme 1.38 AgOAc catalyzed enantioselective carbon dioxide incorporation of bispropargylic alcohols **111**.

A year later, a CuI catalyzed intermolecular nucleophilic addition reaction of propargylic alcohols **77**, and nitriles **114** and CO_2 for the efficient synthesis of highly substituted 3(*2H*)-furanones **115** in up to 91% yield was reported by Jiang and co-workers (Scheme 1.39).[77] In this transformation, the nitrile was employed as both the reaction solvent and the reactant while the copper salt was noted to play the dual roles of activating alcohol and nitrile. Additionally, water was shown as an efficient additive for the formation of the furanone by assisting in the hydrolyze of the imine to the ketone. However, this approach required the employment of high loadings of the catalyst and base and long reaction time.



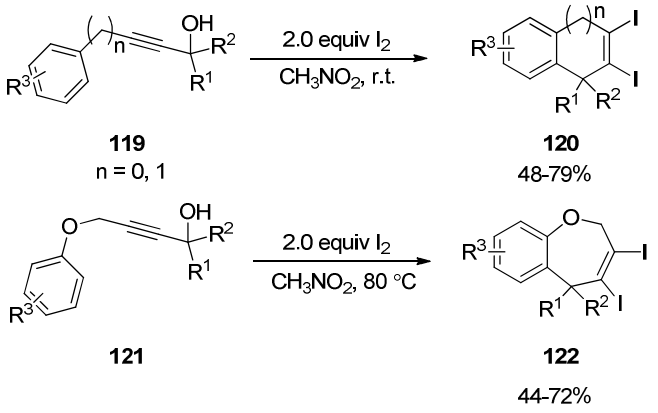
Scheme 1.39 CuI catalyzed synthesis of substituted 3(*2H*)-furanones **115**.

Liang and co-workers designed a method for the preparation of substituted 3,4-diiodoheterocyclics **118** involving I_2 mediated intramolecular hydroalkoxylation/hydroamination of but-2-yne-1,4-diol or 4-aminobut-2-yn-1-ol derivatives **116** (Scheme 1.40).[78] In this work, water was shown to be a very efficient additive in promoting the reaction by allowing the generation of the iodine ion pair from molecular iodine. Mechanistically, the reaction was proposed to proceed *via* activated iodinated allene intermediate **117**. This was followed by intramolecular hydroalkoxylation/hydroamination of **117**, leading to the formation of corresponding diiodoheterocyclic compounds **118** in 70-99% yield.



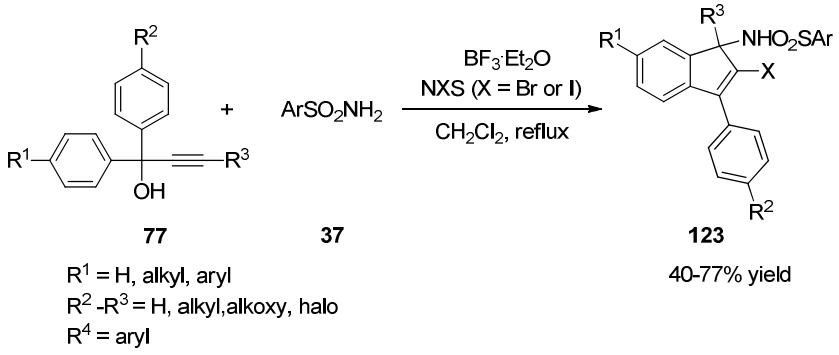
Scheme 1.40 I_2 promoted synthesis of 3,4-diiodoheterocyclics **118**.

In 2011, the same group developed an intramolecular iodocyclization route to diiodinated carbocycles **120** and heterocycles **122** from I_2 promoted reaction of propargyl alcohols based on above approach that replaced the heteroatom in **116** with substituted aromatic ring as in **119/121** (Scheme 1.41).[79] In this work, water was also shown to be necessary for the iodocyclization to proceed efficiently, and give the dihalogenated products in up to 79% yield.



Scheme 1.41 I_2 promoted intramolecular iodocyclization of propargylic alcohols **119** and **121**.

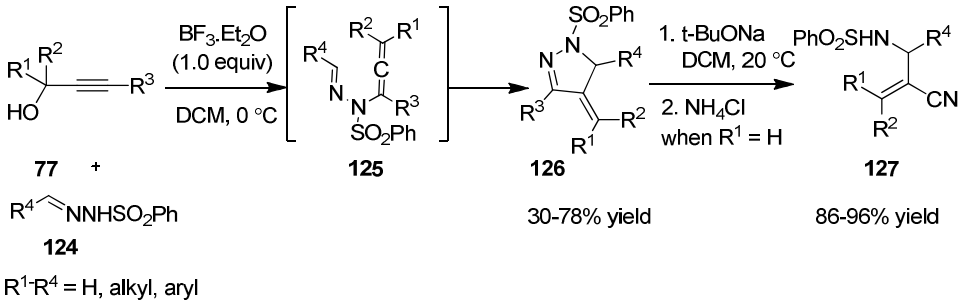
In the same year, NXS (X = Br, I) mediated intermolecular nucleophilic substitution/cyclization of propargylic alcohols **77** with sulfonamides **37** to *N*-(2-iodo/bromoinden-1-yl)arenesulfonamides **123** using $BF_3{\cdot}Et_2O$ as a promoting reagent was reported by Wang and co-workers (Scheme 1.42).[80] While the method was shown to be applicable to only tertiary propargylic alcohols, the corresponding indene adducts were afforded in 40-77% yield.



Scheme 1.42 $BF_3{\cdot}Et_2O$ promoted tandem synthesis of 2-haloindenamines **123.**

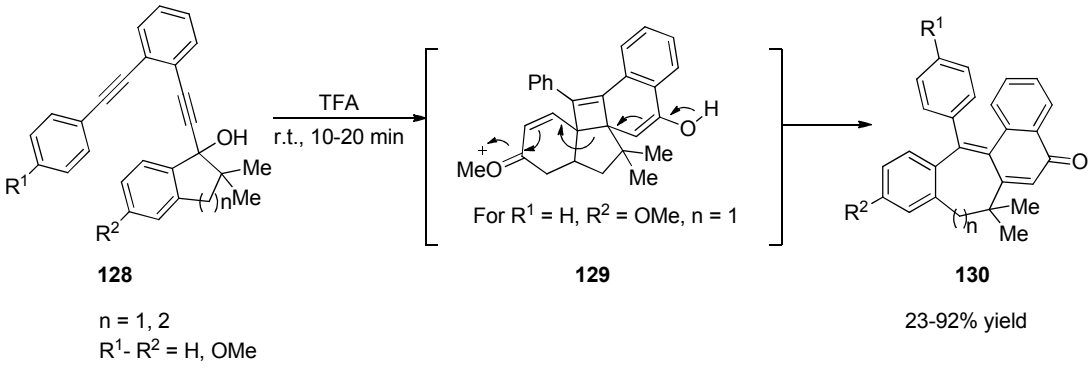
This $BF_3{\cdot}Et_2O$ promoted intermolecular nucleophilic substitution/cyclization reaction of propargylic alcohols **77** and *N*-sulfonylhydrazones **124** to dihydropyrazole

126 was also expanded by the group (Scheme 1.43).[81] In this seminal work, $BF_3{\cdot}Et_2O$ was shown to activate the alcohol substrate followed by amide substitution with *N*-sulfonylhydrazone to form the *N*-sulfonylallenamide **125** as the key intermediate, and its subsequent conversion to the dihydropyrazole derivative. The synthetic utility of this protocol was successfully applied to the preparation of a series of 3,3-diarylacrylonitriles **127** in excellent yields with *t*-BuONa at room temperature.



Scheme 1.43 $BF_3{\cdot}Et_2O$ promoted intermolecular nucleophilic substitution/cyclization of propargylic alcohols **77** and *N*-sulfonylhydrazones **124**.

In 2011, the same group presented a synthetic method for the cycloisomerization of benzannulated enediynyl alcohols **128** to 1,4-naphthoquinone methides **130** with TFA at room temperature (Scheme 1.44).[82] The desired products **130** were obtained in up to 92% yield *via* an unusual two-carbon ring expansion of intermediate **129**. It was noted that when R^2 = OMe, higher product yields were found, presumably due to a more stable putative carbocationic species formed *in situ*.



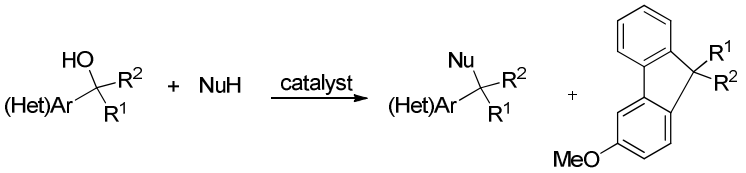
Scheme 1.44 TFA catalyzed tandem cycloisomerization of benzannulated enediynyl alcohols **128**.

1.4 Benzylic Alcohols

One of the most important methods for introducing the benzyl functional group is the direct nucleophilic substitution of benzylic alcohols.[141] In 2005, an efficient approach for the direct arylation of benzylic alcohols **131** to give diarylmethanes and arylheteroarylmethanes **132** using $FeCl_3$ as catalyst was reported by Beller and co-workers (Table 1.9, entry 1).[83] Although the benzylation reported was limited to *o*-xylene **131**, which acted as both the nucleophile and solvent, the method was shown to provide an efficient and convenient route to the corresponding benzylated products in 37-99% yield with 62:38 to 99:1 regioselectivity at 50-80 °C. Following this seminal work, a variety of Lewis and Brønsted acid catalyzed strategies to expand the scope of this reaction have been reported. In 2006, Rueping and co-workers designed a method for the preparation of benzylated adducts from $Bi(OTf)_3$ catalyzed Friedel-Crafts-type benzylation of various arenes and heteroarenes with benzylic alcohols (Table 1.9, entry 2).[84] The benzylated products were obtained in 35-99% yield employing a catalyst loading as low as 0.5 mol%. In this work, two examples of the intramolecular variant of this reaction were shown to work well under the reported

condition and provide the corresponding substituted fluorenes **133**.

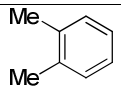
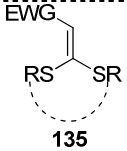
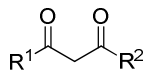
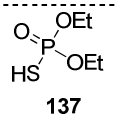
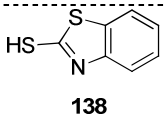
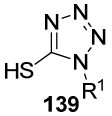
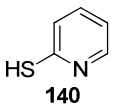
Table 1.9 Lewis and Brønsted acid catalyzed direct nucleophilic substitution of benzylic alcohols **131**.



131 **7** **132** **133**

R^1-R^2 = H, alkyl, aryl

X = C = C, N, O, S

Entry	Catalyst	NuH	Yield (%)	Ref
1	$FeCl_3$	 **134**	37-99	83
2	$Bi(OTf)_3$	 **81**	35-99	84
3	$NaAuCl_4$	R^1NH_2 **33** $TMSN_3$ **1**	63-100	85
4	$BF_3{\cdot}Et_2O$	 **135**	65-95	86
5	DBSA	 **81**  **30** R^1SH **84** R^1NH_2 **33**	62-96	87
6	$NaAuCl_4$	R^1OH **83**	47-96	88
7	$InBr_3$	TMSCN **136**	56-99	89
8	$Ga(OTf)_3$	 **137**  **138**  **139**  **140**	52-94	90

In the same year, Campagne and co-workers described a $NaAuCl_4$ catalyzed version of this intermolecular benzylation with N-nucleophiles such as 4-nitroaniline **36**, tosylamine **37a** and trimethylsilyl azide **1** (Table 1.9, entry 3).[85] Although primary alcohols were found to be ineffective under the reported reaction conditions, secondary benzylic alcohols were found to react well, affording the aminated products in up to quantitative product yields.

Following this work, an efficient method for the synthesis of unsymmetrical ethers from benzylic alcohols **131** and alkyl alcohols **83** utilizing $NaAuCl_4$ as the catalyst was accomplished by Asensio and co-workers (Table 1.9, entry 6).[88] The corresponding ether derivatives were obtained in moderate to excellent yields under mild conditions with a catalyst loading as low as 2 mol %. This study showed that no symmetrical ether byproduct could be detected. Mechanistically, the reaction was assumed to proceed *via* a carbocation intermediate based on the results showing a racemic ether product obtained when a chiral benzylic alcohol substrate was used.

In 2007, $BF_3{\cdot}Et_2O$ mediated intermolecular nucleophilic substitution of benzylic alcohols with α-EWG ketene-(*S*,*S*)-acetals **135** (EWG = CN, COR, $CONH_2$) was demonstrated by Liu and co-workers (Table 1.9, entry 4).[86] The desired benzylated products **132** were obtained in 65-95% yield at room temperature.

At about the same time, Kobayashi and co-workers developed a green method for the direct dehydrative nucleophilic substitution of benzylic alcohols with a variety of nucleophiles in water by employing surfactant-type Brønsted acid DBSA (dodecylbenzenesulfonic acid) as the catalyst (Table 1.9, entry 5).[87] In this work, the DBSA catalyst was shown to promote the reaction efficiently using its surfactant property and strong acidity. The corresponding C-, S- and N-centered benzylated adducts were furnished in up to 96% yield.

One year later, a convenient and efficient route to α-aryl nitriles from direct cyanation of benzylic alcohols with TMSCN **136** was described by Ding and co-workers (Table 1.9, entry 7).[89] The results revealed that with $InBr_3$ as the catalyst, short reaction times at room temperature could be achieved to provide the nitrile products in up to 99% yield. This $InBr_3$ mediated method was shown to produce potentially valuable nitrile derivatives as synthetic intermediates for the preparation of clinically important compounds **141**-**144** (Fig 1.1).

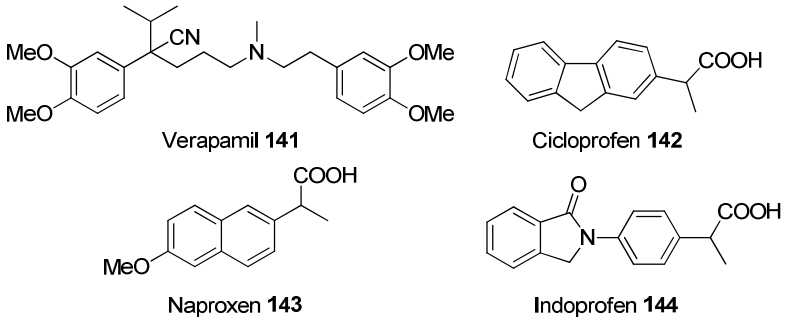
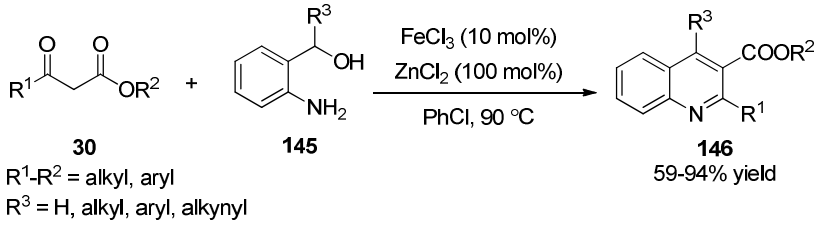


Fig 1.1 Verapamil and α-aryl nitrile derivatives.

Following this work, Wu and co-workers demonstrated the direct nucleophilc substitution of benzylic alcohols utilizing various sulfur nucleophiles and $Ga(OTf)_3$ as the catalyst (Table 1.9, entry 8).[90] This method was found to work well with sulfur nucleophiles such as phosphorothioic acid **137**, phenyltetrazole **139**, and other heteroaromatic thiols **138** and **140,** affording the corresponding thiol derivatives in up to 94% yield, which were very useful due to their application in the preparation of sulfones and utility as substrates in the Julia olefination reaction.

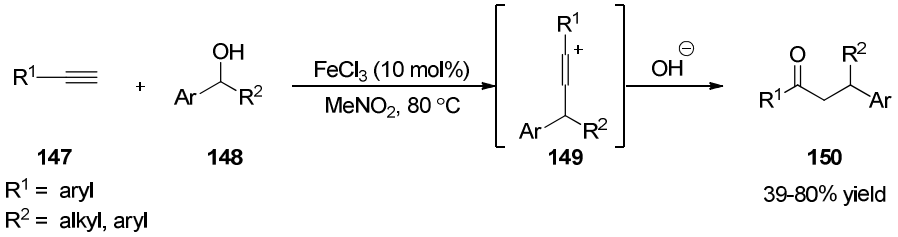
In 2008, Wang and co-workers presented an efficient domino process for the preparation of 3-quinolinecarboxylic ester products **146** involving $FeCl_3/ZnCl_2$ catalyzed intermolecular benzylation/annulation/oxidation of α-amino substituted

2-amino benzylic alcohols **145** with β-ketoesters **30** (Scheme 1.45).[91] In this work, additional control experiments showed that the reaction could not be carried out efficiently by employing either $FeCl_3$ or $ZnCl_2$ alone as the catalyst.



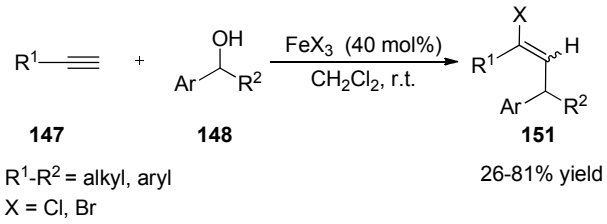
Scheme 1.45 $FeCl_3/ZnCl_2$ catalyzed tandem synthesis of 3-quinolinecarboxylic ester products **146**.

At about the same time, Jana and co-workers broadened the scope of this intermolecular C–C bond formation strategy to terminal aryl acetylenes **147** and benzylic alcohols **148** with $FeCl_3$ as the catalyst (Scheme 1.46).[92] Mechanistically, the benzyl alcohol was surmised to undergo activation *via* metal coordination to the hydroxyl group. This resulted in formation of the benzyl carbocation which then underwent nucleophilic substitution by the aryl acetylene **147**, and provide the vinyl carbon cation **149**. Further attack by the hydroxide ion furnished the corresponding aryl ketone derivatives **150** in moderate to excellent yields.



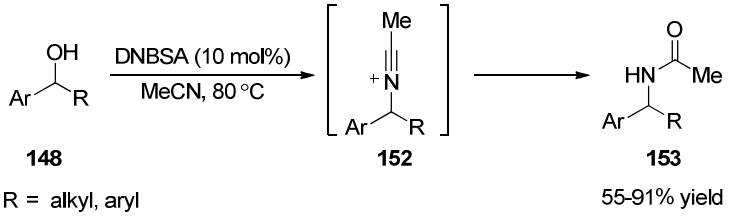
Scheme 1.46 $FeCl_3$ catalyzed tandem synthesis of aryl ketones **150**.

One year later, the same group observed efficient trapping of the vinyl carbocation by Cl^- or Br^- anion from the corresponding Fe(III) salt at room temperature (Scheme 1.47).[93] This afforded the corresponding trisubstituted vinylic halides **151** in up to 81% yield.



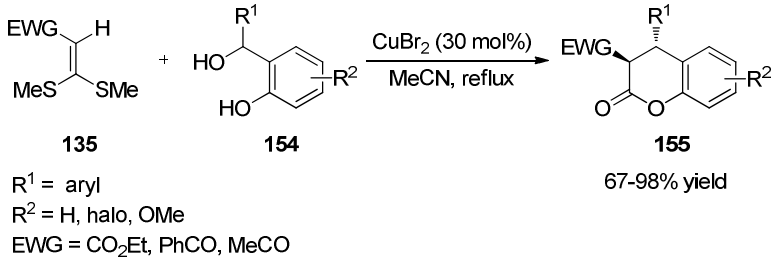
Scheme 1.47 $FeCl_3$ catalyzed tandem synthesis of substituted vinylic halides **151**.

In addition to metal catalysts, Brønsted acids were recently reported to catalyze the nucleophilic substitution reaction of benzylic alcohols efficiently. The tandem DNBSA (2,4-dinitrobenzenesulfonic acid) catalyzed the Ritter-amidation[94] of benzylic alcohols using CH_3CN as both the solvent and reagent was reported by Sanz and co-workers in 2007 (Scheme 1.48).[95] The reaction was thought to proceed *via* carbocation formation followed by sequential CH_3CN attack on the carbocation and trapping of the resultant nitrilium cation **152** by water. This gave the desired *N*-benzylacetamide product **153** in up to 91% yield.



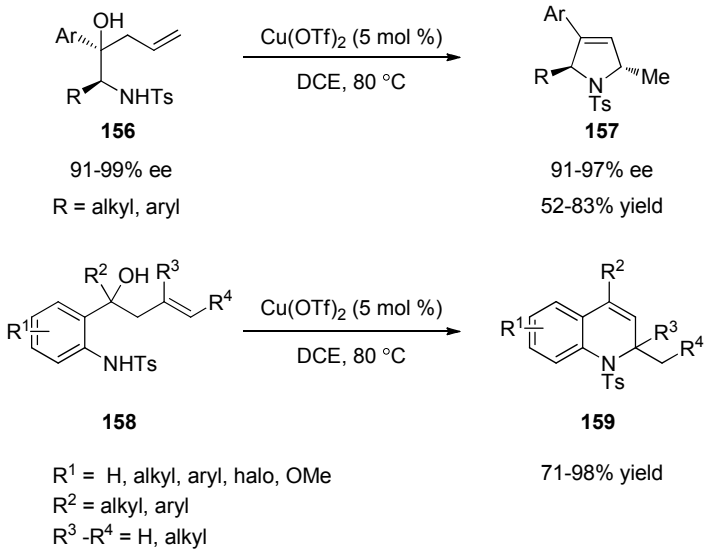
Scheme 1.48 DNBSA catalyzed C–N bond formation strategy.

Following this work, Liu and co-workers developed a route to dihydrocoumarins **155** from $CuBr_2$ catalyzed one-pot reaction of 2-hydroxy benzylic alcohols **154** and ketene dithioacetals **135** (Scheme 1.49).[96] Although a high loading of the catalyst was required in this process, the reaction was found to provide the corresponding cyclized adducts in excellent yields.



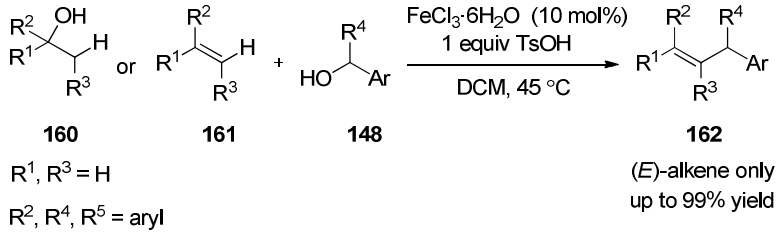
Scheme 1.49 $CuBr_2$ catalyzed one-pot synthesis of dihydrocoumarins **155**.

In 2010, an efficient $Cu(OTf)_2$ catalyzed tandem intramolecular C–N bond formation by hydroamination of homoallylic or α-amino benzylic alcohols was reported by Chan and co-workers (Scheme 1.50).[97] This atom-economical approach was shown to perform well in dichloroethane at 80 °C, providing the corresponding *trans*-2,5-dihydro-1*H*-pyrroles **157** with efficient chirality transfer and 1,2-dihydroquinolines **159** in up to 98% yield. Control experiments conducted in this work showed the reaction proceeds *via* the conjugated diene generated from simple dehydration of **156** or **158**.



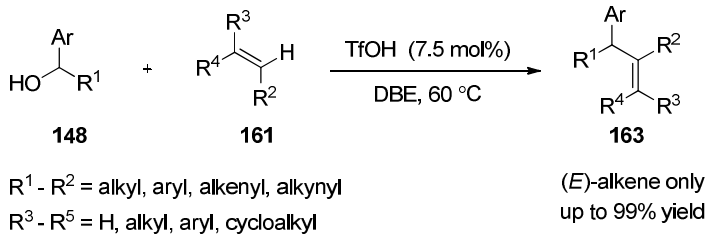
Scheme 1.50 $Cu(OTf)_2$ catalyzed synthesis of *trans*-2,5-dihydro-1*H*-pyrroles **157** and 1,2-dihydroquinolines **159**.

Subsequent studies by Liu and co-workers showed that (*E*)-alkene **162** could be synthesized in highly stereospecific manner *via* direct coupling of alcohols **160** or alkenes **161** with benzylic alcohols **148** employing $FeCl_3 \cdot 6H_2O$ as the catalyst and TfOH as an additive (Scheme 1.51).[98] The potential applicability of this method to large-scale synthesis was also demonstrated in one example in which the gram scale preparation of **162** from **161** where $R^1 = R^4 = Ph$, $R^2 = R^3 = H$, Ar = *p*-ClC_6H_4 was achieved.



Scheme 1.51 $FeCl_3 \cdot 6H_2O$ catalyzed direct coupling of alcohols **160** or alkenes **161** with benzylic alcohols **148**.

At about the same time, Ji and co-workers expanded this sp^3-sp^2 C–C bond formation to the coupling of benzylic alcohols **148** and trisubstituted alkenes **161** utilizing TfOH as a catalyst (Scheme 1.52).[99] This approach was shown to be general for a variety of alcohols and alkenes under metal-free conditions at 60 °C, affording the (*E*)-alkene derivatives **163** exclusively in up to 99% yield.

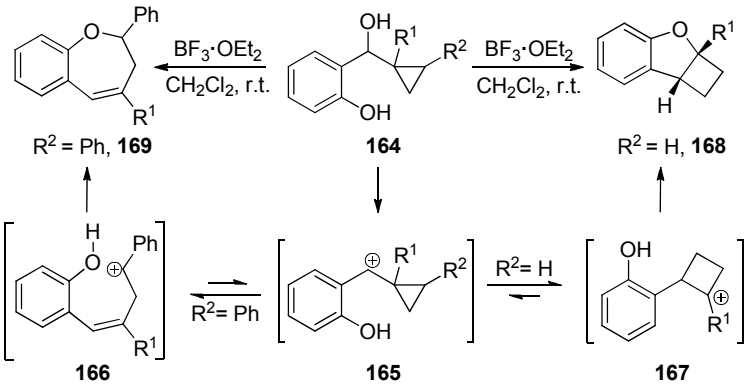


Scheme 1.52 TfOH catalyzed direct coupling of benzyl alcohols **148** with trisubstituted alkenes **161**.

1.5 α-Cyclopropylmethyl Alcohols

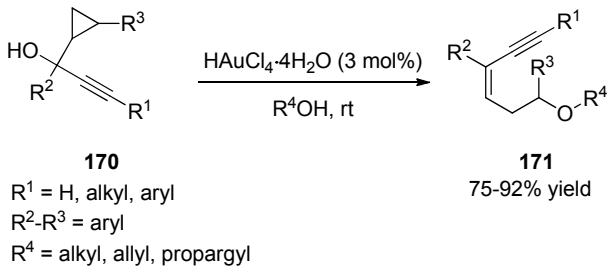
α-Cyclopropyl methanols are important building blocks for the construction of various complex compounds from Lewis and Brønsted acid catalyzed ring-opening and/or rearrangement processes.[100] In a seminal work, $BF_3{\cdot}Et_2O$ promoted intramolecular rearrangement of 2-(cyclopropyl(hydroxy)-methyl)phenols **164** was reported by Doris and co-workers (Scheme 1.53).[101] This provided the polycyclic cyclobutane **168** as the main product when R^2 on the cyclopropyl ring is a proton. On the other hand, the dihydrobenzo[*b*]oxepine was obtained in an example when R^2 was changed from a proton to a Ph group. Mechanistically, the reaction was thought to proceed *via* a common cyclopropylcarbinyl cationic intermediate **165** which underwent a ring expansion to give the cyclobutyl cation **167**. Intramolecular alkoxylation of this intermediate then afforded the desired fused cyclic adducts in 91-97% yield. When R^2 = Ph, the seven-membered oxygen heterocycle **169** was

obtained in 47% yield from rearrangement of cationic species **165** and subsequent alkoxylation of the resultant homoallylic cation **166**.



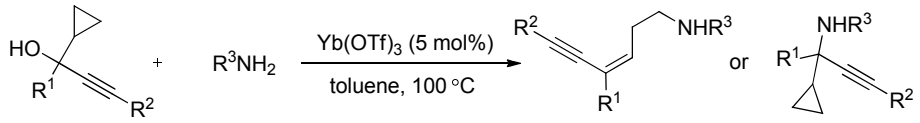
Scheme 1.53 $BF_3{\cdot}OEt_2$ promoted intramolecular rearrangement/alkoxylation of cyclopropylmethyl carbinols **164**.

In 2007, Liang and co-workers reported the preparation of *trans*-substituted conjugated enynes **171** in completely regiospecifically manner from the reaction of 1-cyclopropyl-2-propyn-1-ols **170** and alcohol nucleophiles with $HAuCl_4{\cdot}4H_2O$ as the catalyst (Scheme 1.54).[102] This method was shown to proceed well with a variety of alcohol substrates under mild conditions at room temperature, affording the corresponding tri- and tetrasubstituted conjugated enynes in up to 92% yield. However, the approach was reported to be limited to activated tertiary cyclopropyl propargylic alcohols.



Scheme 1.54 Gold catalyzed ring-opening reaction of **170** with alcohols.

Following this work, Chan and co-workers presented the $Yb(OTf)_3$ catalyzed intermolecular ring opening of substituted 1-cyclopropyl-2-propyn-1-ols **170** with arylsulfonamides for the formation of conjugated enynes **171** (Scheme 1.55).[103] The method was found to proceed in a regioselective manner, providing the corresponding ring-opening products in up to 75% yield. However, either lower product yields or the propargylation adduct **172** was obtained when other N-containing nucleophiles such as aniline, *N*-aminophthalimide and *tert*-butyl carbamate were employed.

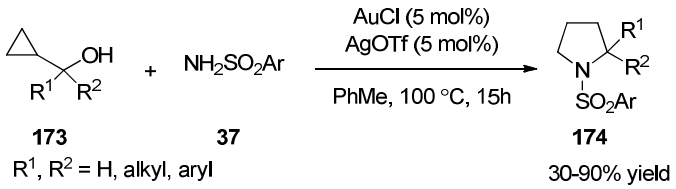


170 **33** **171** **172**

R^1 = H, alkyl, aryl R^3 = Ph, SO_2Ar 30-75% yield
R^2 = alkyl, aryl

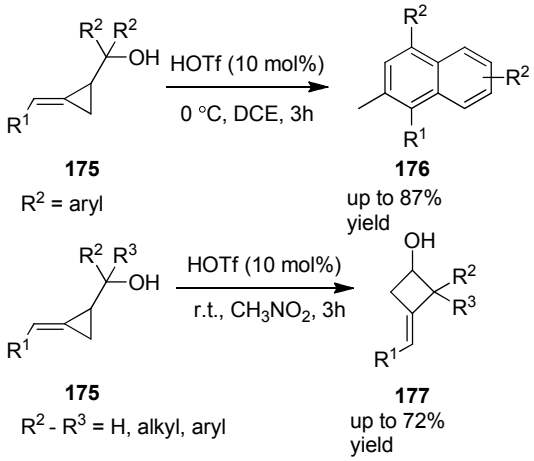
Scheme 1.55 $Yb(OTf)_3$ catalyzed synthesis of conjugated enynes **171a**.

A synthetic protocol for the formation of pyrrolidines **174** from reaction of cyclopropyl substituted benzylic alcohols **173** and sulfonamides **37** in an intermolecular tandem amination/ring expansion version was achieved by Chan and co-workers (Scheme 1.56).[104] This AuCl/AgOTf catalyzed reaction was shown to tolerate a diverse set of alcohol substrates, affording the corresponding N-heterocycles in 30-90% yield, except the secondary alcohols bearing aliphatic group on either R^1 or R^2 giving only 37-50 yields.



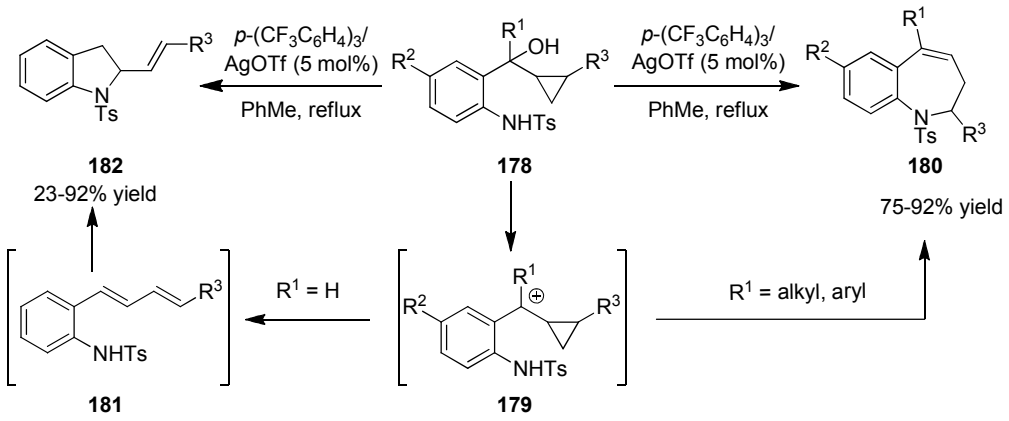
Scheme 1.56 Au catalyzed tandem amination/ring expansion of cyclopropylmethyl alcohols **173**.

In 2010, Shi and co-workers established a method for the synthesis of multi substituted naphthalene **176** and cyclobutanol derivatives **177** from HOTf catalyzed ring opening/rearrangement of methylene cyclopropane alcohols **175** (Scheme 1.57).[105] In this work, the formation of naphthalene products was found to be obtained from a sequential reaction involving a cation-induced ring opening, Friedel-Crafts alkylation followed by aromatization when R^2 = Ar in dichloroethane as the solvent at 0 °C. The cyclobutanol product was afforded from cation-induced ring enlargement process when R^2-R^3 = H, alkyl, aryl in CH_3NO_2 as the solvent at room temperature.



Scheme 1.57 HOTf catalyzed cycloisomerization of methylenecyclopropane alcohols.

One year later, the Chan group demonstrated the gold catalyzed intramolecular ring expansion/cycloisomerization of substituted 2-(cyclopropylmethanol)anilines **178** for the preparation of **180** and **182** derivatives (Scheme 1.58).[106] Mechanistically, the substituent on the carbinol carbon was shown to be an important factor controlling product selectivity through stabilization of cyclopropyl carbocationic species **179** generated from metal catalyzed activation of alcohol group. When $R^1 \neq H$, ring expansion of this cationic species **179** was thought to give the 2,3-dihydro-1*H*-benzo[*b*]azepine derivative **180** in up to 92 % yield. Alternatively, hydroamination of conjugated diene **181** generated from **179** was thought to give 1-tosyl-2-vinylindoline derivative **182** in up to 92% yield when $R^1 = H$.



Scheme 1.58 Gold catalyzed amination/cycloisomerization of 2-(cyclopropyl-methanol)anilines **178**.

1.6 Proposed Work

The work of this thesis has been directed toward providing new synthetic methodologies for the efficient and selective construction of compounds of current biological and material interest. This will be accomplished by investigating ecologically benign inexpensive and readily available Lewis and Brønsted acid

catalyzed reactions of inexpensive and readily available alcohol pro-electrophiles with variety of C-, N- and O-based nucleophiles under operationally straightforward and mild conditions. Thus, the aim of this project has been to establish new Lewis and Brønsted acid-catalyzed protocols for the efficient and selective formation of conjugated enynes, *cis*-halohydrofurans, 2-alkynyl indoles, tri- and tetrasubstituted furans, and 1'-allylspiro[indene-1,2'-indolin]-3'-ones from their respective alcohol substrates (Figure 1.2). It was envisioned that alkoxylation of tertiary cyclopropylmethanols can be achieved in an efficient and completely regioselective manner with a variety of alcohols as nucleophiles. Changing the nucleophile alcohols to water, *cis*-halohydrofuran can be accomplished from one-pot two-step reaction of hydroxylation/halocyclization of secondary and tertiary cyclopropylmethanols in the presence of NXS (X = I, Br, Cl) and Selectfluor and triflic acid as the catalyst. Replacing the cyclopropyl moiety of alcohol substrate with propargylic alcohol, tri- and tetrasubstituted furans can be synthesized *via* tandem isomerization/cyclization of propargylic 1,4-diols and intermolecular nucleophilic substitution/cyclization of propargylic 1,4-diols with 1,3-dicarbonyl compounds respectively. Alternatively, 2-alkynyl indole framework could be achieved from tandem heterocyclization/alkynylation of propargylic 1,4-diols with an appropriately placed aniline moiety. Finally, 1'-allylspiro[indene-1,2'-indolin]-3'-ones were accessed by an intramolecular amination/spiro annulation of 1-(2-(allylamino)phenyl)-4-hydroxy-but--2-yn-1-ones in the presence of silver triflate as the catalyst.

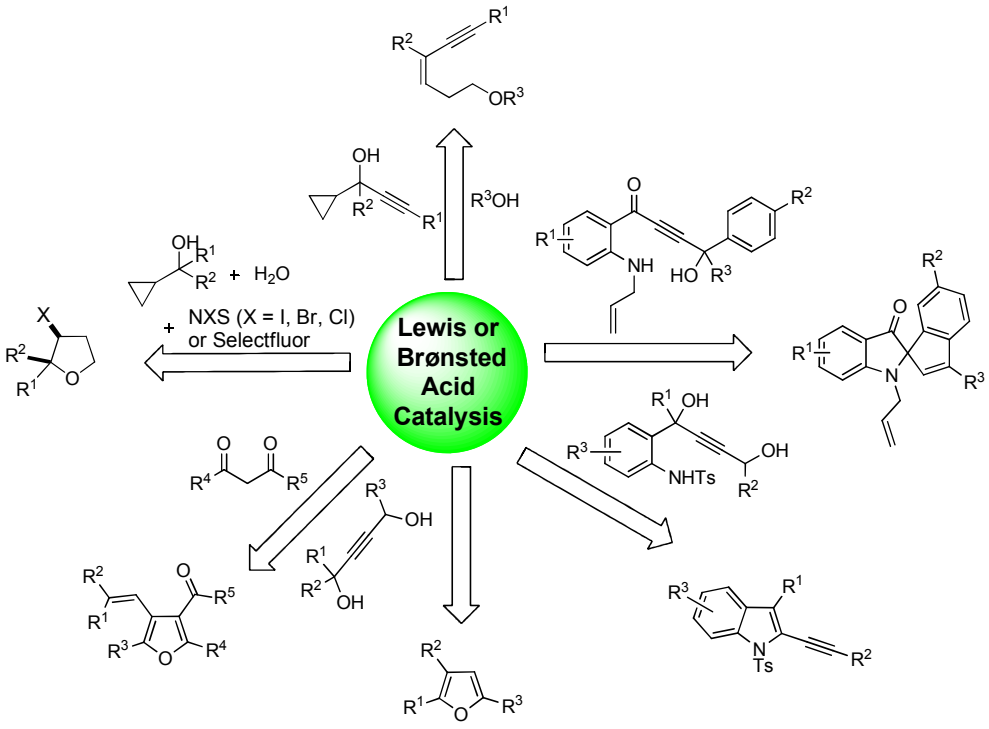


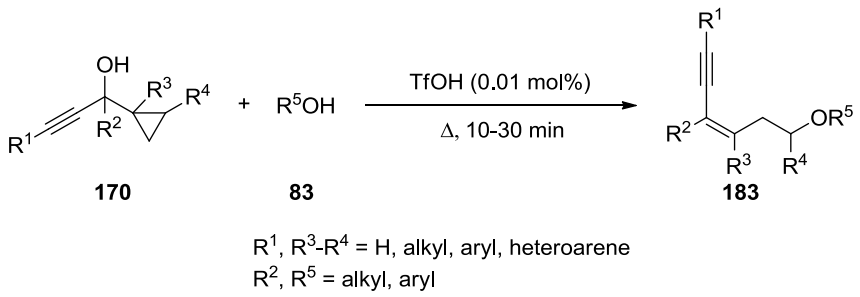
Figure 1.2 Lewis and Brønsted acid catalyzed strategies for C–X (X = C, N, O) bond formation from activated alcohols.

Chapter II. Highly Efficient Synthesis of Tri- and Tetrasubstituted Conjugated Enynes from Brønsted Acid Catalyzed Alkoxylation of 1-Cyclopropylprop-2-yn-1-ols with Alcohols

2.1 Introduction

Conjugated enynes are important targets in organic synthesis because of their demonstrated versatility as intermediates in numerous strategies to compounds of current biological and materials interest. For this reason, simple methods that can install this unsaturated hydrocarbon moiety are highly desirable.[107] This is all the more so if it can be achieved without the competitive formation of undesired regio- and stereoisomers, examples of which remain sparse.[107-109] As mentioned earlier in Sections 1.54 and 1.55 in Chapter I, we[103] and others[101] recently reported one such approach that gave conjugated enynes as single regioisomers from Au or Yb catalyzed ring opening of 1-cyclopropyl-2-propyn-1-ols with *N*- and *O*-centered nucleophiles. These works complemented that previously reported by Nishibayashi and co-workers on diruthenium(II,III) catalyzed ring opening of 1-cyclopropyl-2-propyn-1-ols with aniline.[109] Although all these works were shown to be efficient, producing H_2O as potentially the only byproduct, the potential of this method for scale-up applications has been lessened by the need for high catalyst loadings. Added to this is the cost of the catalyst in reactions mediated by gold and ruthenium and a substrate scope limited to ones containing functional groups that cannot take part in strong metal coordination. In this regard, we envisioned that developing a Brønsted acid catalyzed version of this regioselective enyne forming reaction could hold promise as the basis to re-addressing these shortcomings. An inexpensive and commercially available reagent class that has a high tolerance to air

and moisture, Brønsted acids have been reported to be versatile in mediating a wide variety of organic transformations in excellent yields and with high selectivity.[110] In recent years, this has hitherto included stereoselective Brønsted acid mediated C–X (X=C, N, O, S) bond formation strategies that make use of alcohol pro-electrophiles such as allylic, benzylic, and propargylic alcohols.[111] To our knowledge, however, an efficient Brønsted acid catalyzed protocol for the regioselective synthesis of conjugated enynes from 1-cyclopropyl-2-propyn-1-ols has not been extensively explored.[112] As part of a program examining the utility of alcohols as pro-electrophiles in organic synthesis,[103-104,113] we report herein TfOH catalyzed ring opening of 1-cyclopropyl-2-propyn-1-ols with alcohols (Scheme 2.1).[114] The conjugated enyne products were afforded in excellent yields, high catalyst turnovers, and regioselectivities comparable to those reported for the closely related metal-promoted approaches to this synthetically useful building block.



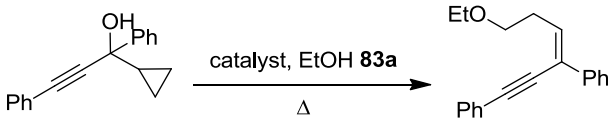
Scheme 2.1 Regioselective TfOH catalyzed synthesis of conjugated enyne from 1-cyclopropyl-2-propyn-1-ols.

2.2 Results and Discussion

All 1-cyclopropyl-2-propyn-1-ols studied in this work were prepared from reaction of the corresponding cyclopropyl ketone and substituted alkyne pretreated with LDA or ethynylmagnesium bromide in place of the alkyne and LDA, or alkynone with

cyclopropylmagnesium bromide following literature procedures.[112] With 1-cyclopropyl-1,3-diphenylprop-2-yn-1-ol **170aa** and EtOH **83a** as the probe substrates, a survey of different reaction conditions initially revealed alkoxylation of **170aa** with a 2mL stock solution of **83a** containing 5 mol % of TfOH at reflux for 15 min gave the best result (Table 2.1, entry 1). Under these conditions, (*Z*)-(6-ethoxyhex-3-en-1-yne-1,3-diyl)dibenzene **183aa** was obtained as the sole product in quantitative yield. The *cis*-stereochemistry of the conjugated enyne product was confirmed by comparison with X-ray crystallographic analysis and NOE spectroscopic data of closely related adducts (vide infra) and reported literature values.[103,109] Our studies subsequently showed that a gradual decrease in the catalyst loading of TfOH from 5 to 1 to 0.1 to 0.01 mol% was found to result in no apparent loss in catalytic activity, and in each of these reactions the same product yield was attained (entries 3-5). On the other hand, further investigations showed that reducing the catalyst loading 2-fold to 0.005 mol% gave **183aa** in a lower yield of 49% (entry 6). Moreover, no product formation could be detected by TLC or ^{1}H NMR analysis of the crude mixture when 0.001 mol% of TfOH was employed, even on extending the reaction time to 20 h (entry 7). Similarly, a lower product yield of 81% was obtained on repeating the reaction with 5 mol% of TfOH at room temperature for 24 h (entry 2). In addition, comparable product yields of 65-75% were afforded when the reaction was repeated with 5 equiv of **83a** in solvents such as toluene, 1,2-dichloroethane, and THF (entries 8-10). Performing the reaction with other inexpensive and commercially available Brønsted acid catalysts was also found to be less effective (entries 11-14). In these latter reactions, the use of 0.01 mol% of Tf_2NH or 5 mol % of *p*-TsOH, TFA, and HCl gave **183aa** in markedly lower yields of 10-55% along with a side product that could not be identified by ^{1}H NMR analysis or low resolution mass spectrometry.

Table 2.1 Optimization of reaction conditions.[a]



170aa **183aa**

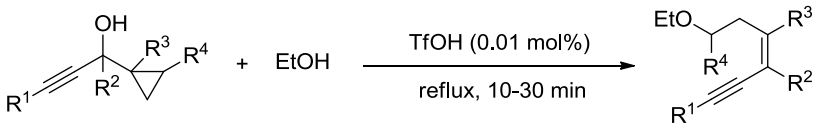
Entry	Catalyst	Catalyst loading (mol%)	Solvent	Yield (%)[b]	Catalyst turnover
1	TfOH	5	-	100	20
2[c]	TfOH	5	-	81	16
3	TfOH	1	-	100	100
4	TfOH	0.1	-	100	1,000
5	TfOH	0.01	-	100	10,000
6	TfOH	0.005	-	49	9,800
7	TfOH	0.001	-	-[d]	-
8[e]	TfOH	0.01	PhMe	75	7,500
9[e]	TfOH	0.01	$(CH_2Cl)_2$	70	7,000
10[e]	TfOH	0.01	THF	65	6,500
11	Tf_2NH	0.01		20	2,000
12[f]	*p*-TsOH	5	-	55	11
13[g]	TFA	5	-	40	8
14[g]	HCl	5	-	10	2

[a]All reactions were performed at reflux for 15 min with 0.2 mmol of **170aa** in 2 mL of **83a**. [b]Yield. [c]Reaction conducted at room temperature for 24 h. [d]No reaction based on TLC or ^{1}H NMR analysis of the crude mixture. [e]Reaction conducted with 5 equiv of **83a**. [f]Reaction conducted for 24 h. [g]Reaction conducted for 2 h.

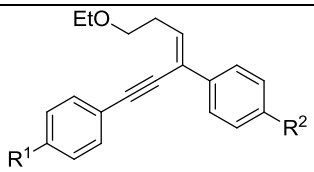
On the basis of the above results, reaction of **170aa** with **83a** in the presence of 0.01 mol % of TfOH at reflux for 15 min was deemed to provide the optimal conditions (entry 5).[116] Under these conditions, a catalyst turnover of 10,000 was also obtained, which to our knowledge is the highest thus far achieved for this reaction. Using these optimized conditions, we were pleased to find that a quantitative product yield of 2.01 g and the same turnover could be reproduced when the reaction was repeated on a large scale with 1.8 g (7.3 mmol) of **170aa**.

To determine the generality of the present procedure, we next turned our attentions to the reactions of a variety of 1-cyclopropyl-2-propyn-1-ols with **83a** (Table 2.2). This revealed that the reactions of substituted 1-cyclopropyl-2-propyn-1-ols containing pendant electron-withdrawing or electron-donating groups with **83a** gave the corresponding conjugated enyne products **183ab-ae** and **183aj-ak** in yields of 88-98% and with turnovers up to 9,800. Similarly, the analogous reactions involving starting alcohols **170af-ag** containing a combination of electron-withdrawing and electron-donating groups with **83a** afforded the corresponding enyne products in comparable yields of 90-92% and with turnovers up to 9,200. More notably, 1-cyclopropyl-2-propyn-1-ols bearing a pyridine or nitrile moiety were found to proceed well under the present conditions and furnish the corresponding conjugated enyne adducts **183ah-ak** in excellent yields and catalyst turnovers. This compares well with our previous works, which reported that a closely related pyridine-containing alcohol substrate was resistant to the ring-opening process with *p*-$TsNH_2$ using ytterbium catalysis.[103] Likewise, substituted 1-cyclopropyl-2-propyn-1-ols **170al-an** and **170az** with a sterically bulky naphthalene group were found to afford **183al-an** and **183az** in excellent yields and catalyst turnovers. A similar outcome was found for reactions of 1-cyclopropyl-2-propyn-1-

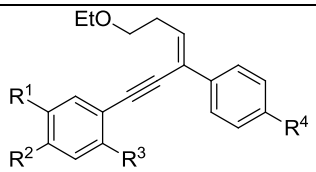
Table 2.2 TfOH catalyzed alkoxylation of **170ab-bd** with **83a**[a]



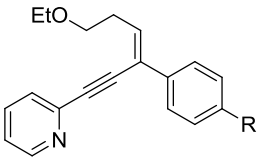
170 **83** **183**



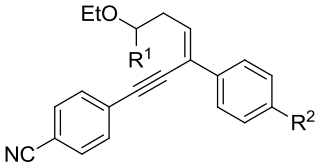
183ab: R^1 = H, R^2 = F (92%, 9,200)
183ac: R^1 = H, R^2 = Cl (95%, 9,500)



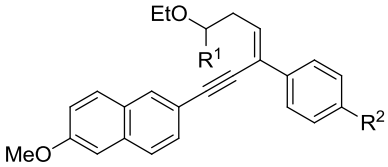
183ad: R^1 = H, R^2 = R^4 = OMe, R^3 = Me (90%, 9,000)
183ae: R^1 = R^2 = R^3 = Me, R^4 = OMe (88%, 8,800)
183af: R^1 = R^3 = H, R^2 = CF_3, R^4 = OMe (90%, 9,000)[b]
183ag: R^1 = H, R^2 = OMe, R^3 = Me, R^4 = F (92%, 9,200)



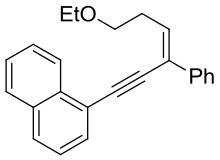
183ah: R = F (91%, 9,100)[c]
183ai: R = OMe (91%, 9,100)[c]



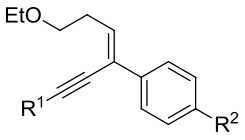
183aj: R^1 = H, R^2 = F (98%, 9,800)[d]
183ak: R^1 = Ph, R^2 = H (91%, 9,100)[d]



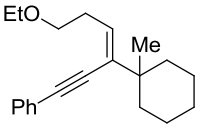
183al: R^1 = H, R^2 = OMe (93%, 9,300)
183am: R^1 = Ph, R^2 = H (90%, 9,000)



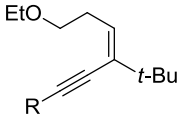
183an: (97%, 9,700)



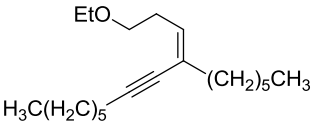
183ao: R^1 = $(CH_2)_5CH_3$, R^2 = Cl (96%, 9,600)
183ap: R^1 = $(CH_2)_3CH_3$, R^2 = H (89%,8,900)



183aq: (92%, 9,200)

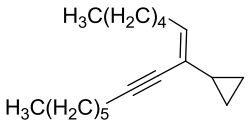


183ar: R = Ph (98%, 9,800)
183as: R = $(CH_2)_5CH_3$ (88%, 8,800)

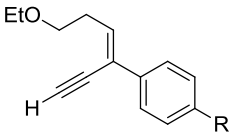


183at: (44%, 4,400)

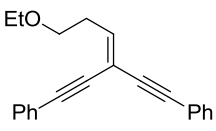
+



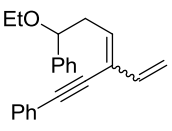
184at: (42%)[e]



183au: R = Cl (85%, 8,500)
183av: R = H (75%, 7,500)

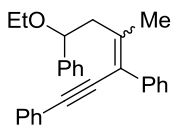


183aw: (96%, 9,600)

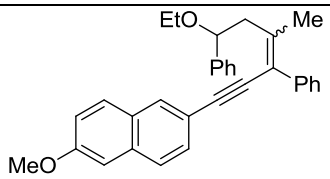


183ax: (92%, 9,200)[f]

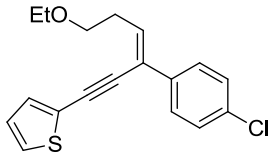
Table 2.2 (*continued*)



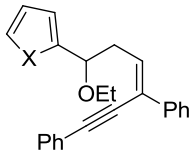
183ay: (95%, 9,500)[g,h]



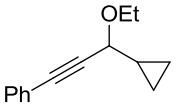
183az: (92%, 9,200)[i,j]



183ba: (89%, 8,900)



183bb: X = O (87%, 8,700)
183bc: X = S (88%, 8,800)[k]



185bd: (91%)

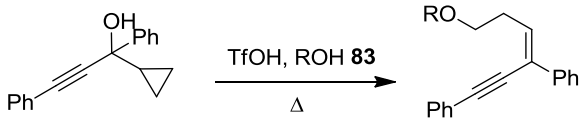
[a]All reactions were performed at reflux for 15 min with 0.2 mmol of **170** in 2 mL of a stock solution of **83a** containing 0.01 mol% of TfOH. Values in parenthesis denote isolated product yields and turnovers. [b]Reaction conducted for 25 min. [c]Reaction conducted for 30 min. [d]Reaction conducted for 20 min. [e]Yield in parentheses denotes that isolated yield for the cyclopropyl enyne side product **184at**. [f]Product obtained as an inseparable 5:1 mixture of *E*/*Z* isomers. [g]Starting alcohol used as a mixture of diastereomers in a ratio = 3:2. [h]Product obtained as an inseparable 3:2 mixture of *E*/*Z*isomers. [i]Starting alcohol used as a mixture of diastereomers in a ratio = 3:1. [j]Product obtained as an inseparable 3:2 mixture of *E*/*Z* isomers. [k]Reaction conducted for 10 min.

-ols containing alkyl groups or both an alkyl and aryl substituent or a terminal alkyne moiety. In these reactions, the corresponding enyne adducts **183ao-av** were furnished in yields of 75-96% and with up to 9,600 turnovers. Reactions of starting alcohols with an alkene or alkyne moiety on the carbinol carbon as in **170aw** and **170ax** were also found to give the corresponding enyne adducts **183aw** and **183ax** in excellent

yields and catalyst turnovers. Similarly, tetrasubstituted conjugated enynes **183ay** and **183az** could be obtained in yields of 95% and 92% and with turnover numbers of 9,500 and 9,200, respectively, for the alkoxylation of 1-cyclopropyl-2-propyn-1-ols **170ay** and **170az** bearing a quaternary carbon centre. Additionally, the present procedure worked well for starting alcohols with a pendant furan or thiophene functionality, providing the corresponding enyne adducts **183ba-bc** in excellent yields and catalyst turnovers. This is noteworthy as such aromatic ring structures are commonly found in bioactive natural and pharmaceutical compounds.[117] As anticipated, reaction of the secondary 1-cyclopropyl-2-propyn-1-ol **170bd** under the standard conditions was the only case that was found to give the ethereal substitution product **185bd** as the sole adduct in 91% yield. A similar outcome in product chemoselectivity leading to preferential formation of the substitution adduct from reaction of a secondary 1-cyclopropyl-2-propyn-1-ol with aniline has also been reported for the analogous Ru_2 catalyzed approach.[109]

In this work, the reaction of **170aa** with a variety of different alcohol nucleophiles was also examined (Table 2.3). Under the standard conditions, reaction of **170aa** with benzyl alcohol **83b** gave the corresponding conjugated enyne adduct **183be** in 80% yield and with a turnover number of 8,000 (entry 1). Similarly, reaction of **170aa** with alcohols bearing a terminal alkene moiety gave **183bf** and **183bg** in 75% and 82% yield and with turnovers of 7,500 and 8,200, respectively (entries 2 and 3). In our hands, comparable product yields and turnovers were also obtained in instances where it was initially envisaged that reactions with nucleophiles containing a sterically demanding group on the R-carbon such as an *i*-Pent, *t*-Bu, and cyclohexyl group as in **83e-g** would detrimentally influence the reactivity of the present procedure (entries 4-6).

Table 2.3 TfOH-catalyzed alkoxylation of **170aa** with **83b-g**.[a]



170aa **183be-bj**

Entry	ROH **83**	Product	Yield	Turnover
1		**183be**, R = Ph	80	8,000
2		**183bf**, R = $CH_2OCH_2CH{=}CH_2$	75	7,500
	83b-d			
3		**183bg** R = $CH{=}CH_2$	82	8,200
4[b]		**183bh**, R = *i*-Pent	86	8,600
5[b]	**83e-f**	**183bi**, R = *t*-Bu	80	8,000
6		**183bj**	76	7,600
	83g			

[a]All reactions were performed at reflux for 20 min with 0.2 mmol of **170aa** in 2 mL of a stock solution of **83** containing 0.01 mol % of TfOH. [b]Reaction conducted for 15 min.

At this juncture, we would like to highlight the chemo- and regioselective nature of the present reaction. Our studies found that the (*Z*)-isomer was obtained as the sole product for all of the reactions described in Table 2.2 where the tertiary starting alcohol contained a pendant internal alkyne moiety. Similarly, the (*E*)-product was furnished exclusively from reactions with substrates containing a terminal alkyne. For reactions affording the tetrasubstituted conjugated enynes **183ay** and **183az**, the *E*:*Z* product selectivities obtained were found to be comparable to the *cis*:*trans* ratios of the respective racemic starting alcohols based on ^{1}H NMR measurements. Reaction of

170ax was the only other example that was found to give the corresponding conjugated enyne **183ax** as an inseparable mixture of *E*/*Z* isomers in a ratio of 5:1. The presence of a bulky substituent on the acetylene moiety of the substrate such as a naphthalene ring as in **170al-an** and **170az** was also found to have no influence on the regioselective outcome of the reaction. In addition, no side products were obtained under our experimental conditions based on ^{1}H NMR analysis of the crude mixtures in all except one case, which is consistent with our earlier findings for the reaction of **170aa** with **83a**. Under our conditions, reaction of **170at** was the only instance that was found to afford **183at** in 44% yield and along with **184at** as a side product in 42% yield. The *cis* stereochemistry in **183aj** was determined by X-ray crystallographic analysis[118] (see Figure 2.1) and NOE measurements, and the *trans* regiochemistry in **183au** was confirmed by NOE analysis.

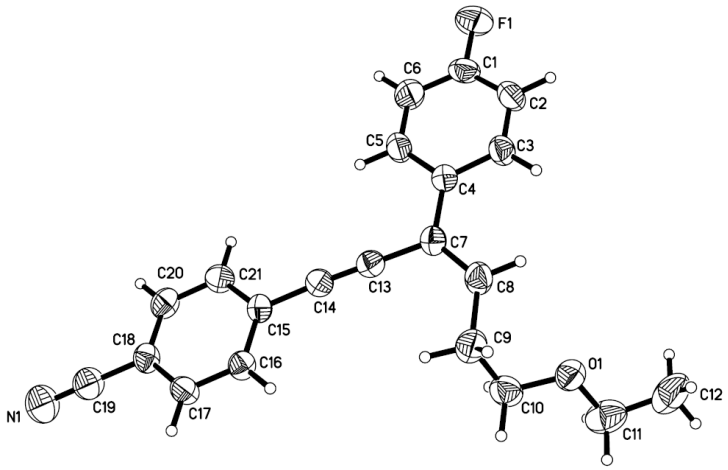
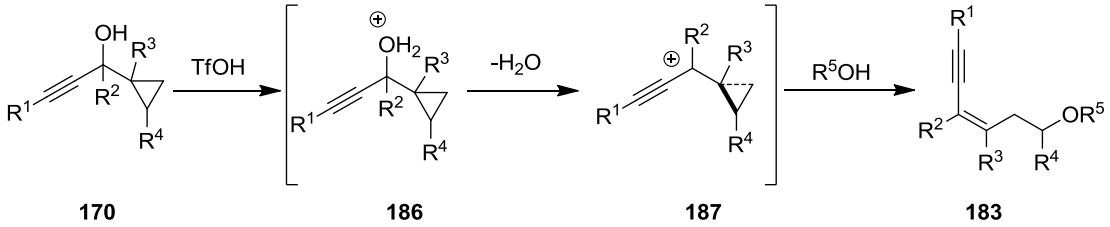


Fig. 2.1 ORTEP drawing of **183aj** with thermal ellipsoids at 50% probability levels.

Although highly speculative, we propose the mechanism of the present reaction to proceed in a manner similar to that reported for the closely related Yb catalyzed amination of 1-cyclopropyl-2-propyn-1-ols with sulfonamides.[103] As outlined in Scheme 2.2, this could involve activation of the alcohol substrate through protonation

of the hydroxyl group by the Brønsted acid. This results in the formation of a protonated intermediate **186**, which can undergo elimination to give a putative carbocation species **187**. It is possible that subsequent cyclopropylcarbinol-homoallylic rearrangement of this newly formed cationic species and trapping with **83** would deliver the enyne **183**.[119] The *E*/*Z* product selectivities obtained when R^3 = H could be due to **187** adopting the conformation shown in Scheme 2.2 with the least amount of unfavorable steric interactions between the substituents and cyclopropane ring.[120] However, for reactions when R^3 = Me that lead to the tetrasubstituted conjugated enyne adduct, such conformational changes may be less favored due to steric interactions between the substituents resulting from rotation of the $C^{\oplus}$–C(cyclopropyl) bond in **187**. For reactions where R^4 = Ph, we postulate that a possible reason for preferential S_N1' attack at the carbon center bearing the substitutent is so that formation of the more sterically hindered tri- or tetrasubstituted enyne adduct can be avoided.[120] The origin of the elimination and ethereal substitution products **184at** and **185bd** could be due to the respective deprotonation and direct attack by **83a** of this resultant carbocation species before ring fragmentation could occur.



Scheme 2.2 Tentative mechanism for TfOH catalyzed alkoxylation of 1-cyclopropyl-2-propyn-1-ols with alcohols.

2.3 Conclusion

In summary, we have presented a Brønsted acid catalyzed method for the nucleophilic ring opening of 1-cyclopropyl-2-propyn-1-ols with alcohols as an expedient route to conjugated enynes. The reaction was shown to be applicable to a wide variety of starting alcohols containing electronic and sterically demanding substrate combinations that complemented the metal-mediated versions of this reaction.[102-103,109] The efficiency of the present operationally straightforward method was exemplified by the excellent product yields and turnover numbers along with complete regioselectivities achieved with a low catalyst loading of 0.01 mol %. Moreover, the approach offers a potential scale-up strategy for the regioselective synthesis of conjugated enynes, which was demonstrated by the large-scale synthesis of one example in quantitative yield and with a high turnover number. This is notable as the present catalytic method makes use of inexpensive and easily accessible alcohol substrates in combination with the low cost and green credentials[43,110-112,113b-c,114] often associated with such metal-free catalytic systems.

Chapter III. Rapid Access to Halohydrofurans via Brønsted Acid-Catalyzed Hydroxylation/Halocyclization of Cyclopropyl Methanols with Water and Electrophilic Halides

3.1 Introduction

Tetrahydrofurans are an important member of the heterocyclic family of compounds due to their presence in a myriad of bioactive natural products[121-125] such as azaspiracid,[122] kadlongirin A,[123] okadaic acid[124] and xyloketal J[125] (Figure 3.1). Because of this and their ability to serve as a versatile building block in organic synthesis, an immense number of efficient and convenient methods to construct this cyclic structure have been developed over the years.[121,125,127] This has hitherto included the halocyclization of homoallylic alcohols in the presence of an electrophilic halide source such NXS and Selectfluor, that provided the corresponding 3-halohydrofuran derivatives.[127] While this synthetic approach was shown to be a powerful and reliable route to the oxygen heterocycle, the reactions were reported to rely on the use of preformed unsaturated alcoholic substrates, which can often require several non-trivial and time consuming steps. In this regard, the establishing of mild and efficient synthetic strategies to this class of furans from inexpensive and commercially available substrates or ones that can be accessed in one step is desirable.

In the previous chapter, we reported an efficient regioselective route to conjugated enynes based on TfOH catalyzed ring-opening of 1-cyclopropyl-2-propyn-1-ols with alcohols.[128] On the basis of these earlier studies, we reasoned that a synthetic approach to 3-halohydrofurans could be achieved through NXS or Selectfluor-mediated

cyclization of a homoallylic alcohol formed *in situ* from Brønsted acid-catalyzed hydroxylative ring-opening of cyclopropyl methanols. While Brønsted acid mediated

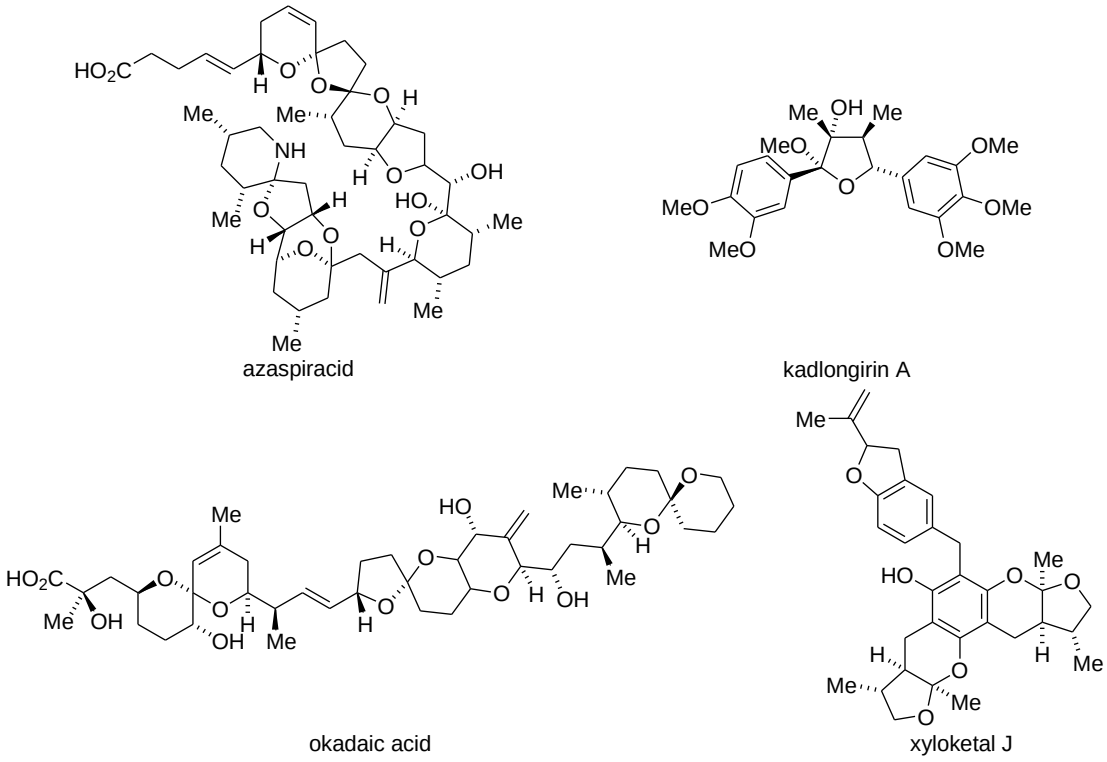
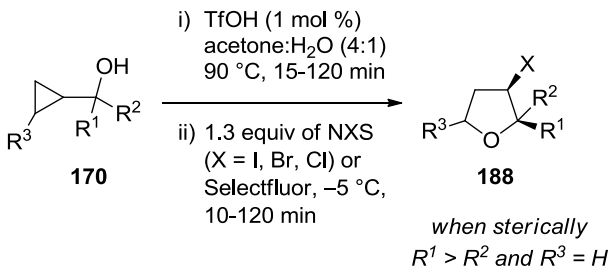


Figure 3.1 Examples of bioactive compounds containing a tetrahydrofuran moiety.

reactions of alcohol pro-electrophiles have come under increasing scrutiny,[111,128-131] to our knowledge those that make use of cyclopropyl methanols have thus far been limited to works describing the synthesis of conjugated enynes mentioned above[128] and homoallylic halides as well as ring expansion and fission reactions.[131] Herein, we report a one-pot, two-step TfOH catalyzed hydroxylation/halocyclization of cyclopropyl methanols with H_2O and NXS or Selectfluor (Scheme 3.1). The 3-halohydrofuran products were obtained in moderate to excellent yields and, in most cases, with preferential *cis* diastereoselectivity.

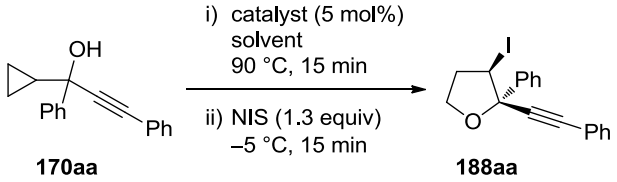


Scheme 3.1 One-pot, two-step halohydrofuran synthesis from ring-opening of cyclopropyl methanols with H_2O followed by halocyclization with an electrophilic halide source.

3.2 Results and Discussion

We chose 1-cyclopropyl-1,3-diphenylprop-2-yn-1-ol (**170aa**) as the probe substrate to establish the reaction conditions (Table 3.1). Initially, this involved treating a solution of **170aa** in 4:1 acetone and H_2O with 5 mol % of TfOH at 90 °C for 15 min followed by 1.3 equiv of NIS at –5 °C for 15 min gave the best result (entry 1). Under these conditions, *cis*-3-iodo-2-phenyl-2-(phenylethynyl)tetrahydrofuran (**188aa**) was obtained in near quantitative yield. The product structure and stereochemistry was determined on the basis of ^{1}H NMR measurements and ^{1}H-^{1}H NOE correlations observed between the H-3 and ortho protons of the phenyl group that implied a *cis* orientation between the I and alkyne moieties in the adduct (see Figure 3.2). The relative *cis* stereochemistry of the 3-iodohydrofuran adduct was also confirmed by X-ray crystallography (see Figure 3.3).[132] As shown in entry 2, a comparable product yield was found on decreasing the catalyst loading from 5 to 1 mol %. However, a marked decrease in product yield was observed on further reducing the catalyst loading from 1 to 0.5 mol % or carrying out the reaction in one step at 90 °C for 15 min (entries 3-4). A similar effect on product yields was observed on lowering the

Table 3.1 Optimization of reaction conditions.[a]



Entry	Catalyst	Solvent	Yield (%)
1	TfOH	acetone:H_2O	99
2	TfOH[b]	acetone:H_2O	99
3	TfOH[c]	acetone:H_2O	55
4	TfOH[d]	acetone:H_2O	42
5[e]	TfOH	acetone:H_2O	85
6[f]	TfOH	acetone:H_2O	52
7	TfOH	THF:H_2O	62
8	TfOH	CH_2Cl_2:H_2O	48
9	Tf_2NH	acetone:H_2O	40
10	TFA	acetone:H_2O	55
11	HCl	acetone:H_2O	25
12	*p*-TsOH·H_2O	acetone:H_2O	45

[a]All reactions were performed with 5 mol % of catalyst in 4:1 of solvent:H_2O at 90 °C for 15 min followed by addition of 1.3 equiv of NIS at –5 °C for 15 min. [b]Reaction conducted with 1 mol % of TfOH. [c]Reaction conducted with 0.5 mol % of TfOH. [d]Reaction conducted with 5 mol % of TfOH and 1.3 equiv of NIS in 4:1 of acetone:H_2O at 90 °C for 15 min. [e]Reaction conducted with 1.1 equiv of NIS. [f]Reaction conducted with 3 equiv of I_2.

amount of NIS from 1.3 to 1.1 equiv or changing the iodide source from NIS to I_2 (entries 5-6). Likewise, changing the organic component of the solvent system from acetone to THF or CH_2Cl_2 was found to lead to lower product yields (entries 7-8). Markedly lower product yields of 25-55% were also obtained on repeating the reaction with other Brønsted acids such as Tf_2NH, TFA, HCl, and *p*-TsOH·H_2O in place of TfOH (entries 9-12). On the basis of these results, reaction of **170aa** in the

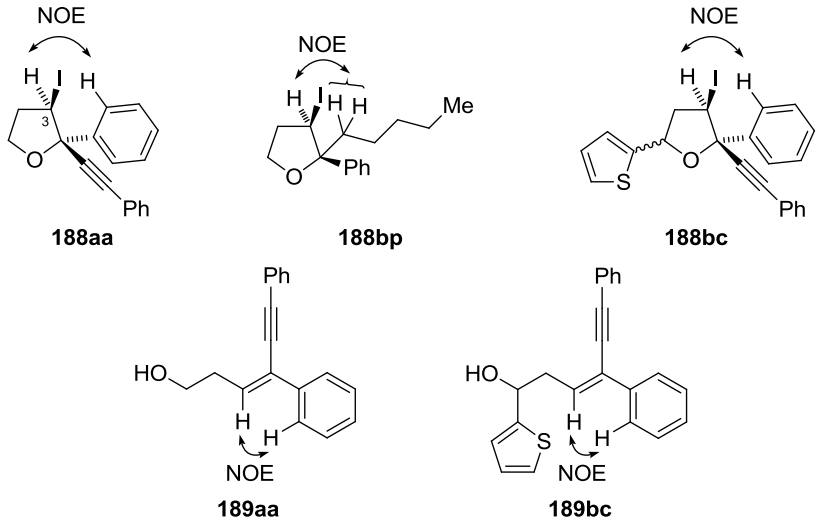


Figure 3.2 ^{1}H-^{1}H NOE analysis of **188aa**, **188bp**, **188bc**, **189aa** and **189bc**.

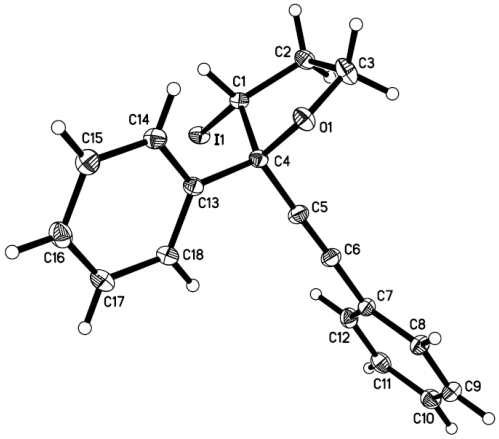
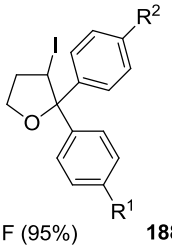


Figure 3.3 ORTEP drawing of **188aa** with thermal ellipsoids at 50% probability levels.

presence of 1 mol % of TfOH in a 4:1 acetone:H_2O solvent system at 90 °C for 15 min followed by 1.3 equiv of NIS at –5 °C for 15 min was deemed to provide the optimal conditions.

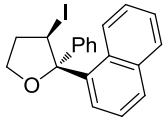
With the optimal conditions established, the generality of the present procedure was next examined and the results are summarized in Table 3.2. Reactions of cyclopropyl methanols with a pendant aryl group at both positions on the carbinol carbon and NIS gave the corresponding 3-iodohydrofurans in excellent yields although a catalyst loading of 5 mol % was required for those containing two electron-deficient aryl substituents (entries 1-11). The analogous reactions involving starting alcohols containing alkyl and aryl substituents on the carbinol carbon and/or cyclopropane ring were also found to afford the corresponding 3-iodohydrofuran products in comparable yields of 83-98% (entries 12-13 and 19-20). Similarly, the present procedure was shown to work well for substituted cyclopropyl methanols containing other bioactively important heteroaryl ring structures[133] and acetylenic groups (entries 14-17 and 21). In these reactions, the corresponding 3-iodohydrofuran adducts **188ba-aw** and **188bc** were furnished in yields of 80-96%. However, we found reaction of the tertiary cyclopropyl methanol **170br** bearing a methyl and terminal alkyne unit to be less effective, affording a mixture of decomposition products that could not be identified by ^{1}H NMR analysis of the crude mixture (entry 18). Similarly, reaction of the secondary cyclopropyl methanol **170bv** with a pentyl side chain on the carbinol carbon was found to result in the near quantitative recovery of the starting alcohol (entry 23). On the other hand, the analogous reaction with the phenyl-substituted secondary alcohol **170bu** was found to proceed well and afford **188bu** in 60% yield albeit at a catalyst loading of 5 mol% (entry 22). This is notable given that the closely related TfOH catalyzed ring-opening of the same substrate with

Table 3.2 TfOH catalyzed hydroxylation/iodocyclization of cyclopropyl methanols **170be-bv**.[a]

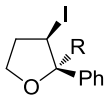


188be: $R^1 = R^2 = F$ (95%)
188bf: $R^1 = R^2 = Cl$ (93%)
188bg: $R^1 = R^2 = Br$ (88%)
188bh: $R^1 = R^2 = H$ (79%)
188bi: $R^1 = R^2 = Me$ (99%)

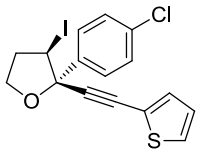
188bj: $R^1 = R^2 = OMe$ (97%)
188bk: $R^1 = Cl$, $R^2 = Me$ (96%)[c]
188bl: $R^1 = Cl$, $R^2 = OMe$ (98%)[d]
188bm: $R^1 = Me$, $R^2 = H$ (98%)[e]
188bn: $R^1 = Ph$, $R^2 = H$ (94%)[f]



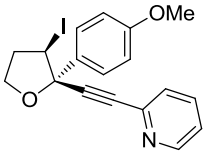
188bo: (80%)



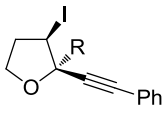
188bp: R = $(CH_2)_4CH_3$ (88%)
188bq: R = $C(CH_3)_3$ (83%)



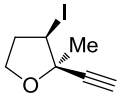
188ba: (96%)



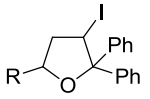
188ai: (92%)



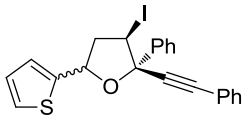
188aq: R = 1-methylcyclohexyl (86%)
188aw: R = C≡CPh (90%)



188br: (-)[g]



188bs: R = Ph (98%)[h]
188bt: R = $(CH_2)_4CH_3$ (94%)[h]



188bc: (80%)[h]

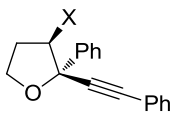
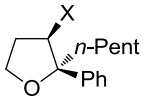
188bu: R = Ph (60%)
188bv: R = $(CH_2)_4CH_3$ (-)[i]

[a]All reactions were performed with 1 mol% of TfOH in 4:1 acetone: H_2O at 90 °C followed by 1.3 equiv of NIS at –5 °C.[134] Values in parenthesis denote isolated product yields. [b]Reaction conducted with 5 mol % of TfOH. [c]Obtained as an inseparable 5:4 mixture of *cis*/*trans* isomers. [d]Obtained as an inseparable 7:4 mixture of *cis*/*trans* isomers. [e]Obtained as an inseparable 3:2 mixture of *cis*/*trans* isomers. [f]Obtained as an inseparable 1:1 mixture of *cis*/*trans* isomers. [g]Mixture of unknown side products afforded based on ^{1}H NMR analysis of the crude mixture. [h]Obtained as an inseparable 5:3 mixture of *cis*/*trans* isomers. [i]No reaction based on TLC and ^{1}H NMR analysis and recovery of the starting alcohol in near quantitative yield.

EtOH was previously reported by us not to be possible, and instead, chemoselectively gave the propargylation product.[128]

In this work, TfOH catalyzed hydroxylative ring-opening of **170aa** and **170bp** followed by halocyclization with other *N*-halosuccinimides and Selectfluor were also examined (Table 3.3). Under the standard conditions, reactions of **170aa** and **170bp** with NBS gave the corresponding 3-bromohalofurans **188bw** and **188bz** in excellent yields (entries 1 and 4). In contrast, the analogous reactions of **170aa** and **170bp** with less electrophilic halide sources such as NCS or Selectfluor were found to lead to moderate product yields (entries 2-3 and 5-6). In the case of the fluorocyclizations, the product yields obtained were found to be comparable to one example reported in a

Table 3.3 TfOH catalyzed hydroxylation/halocyclization of cyclopropyl methanols **170aa** and **170bp**.[a]

Entry	Substrates	Product		Yield (%)
1	**170aa** + NBS		**188bw**, X = Br	85
2	**170aa**+ NCS[b]		**188bx**, X = Cl	35
3	**170aa** + Selectfluor		**188by**, X = F	55
4	**170bp** + NBS		**188bz**, X = Br	82
5	**170bp** + NCS[b]		**188ca**, X = Cl	30
6	**170bp**+ Selectfluor		**189cb** = F	45

[a]All reactions were performed with 1 mol% of TfOH in 4:1 acetone: H_2O at 90 °C followed by 1.3 equiv of the electrophilic halide source at –5 °C.[134]

[b]Reaction conducted at reflux.

seminal work by Gouverneur and co-workers in an analogous reaction with a homoallylic alcohol and Selectfluor.[127a] The structure of **188by** was also confirmed by X-ray crystallographic analysis (see Figure 3.4).[132]

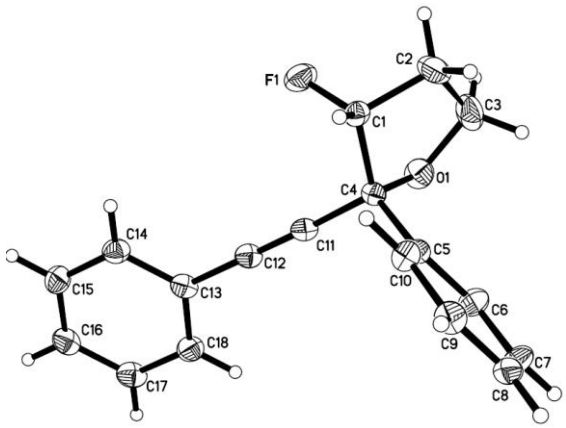
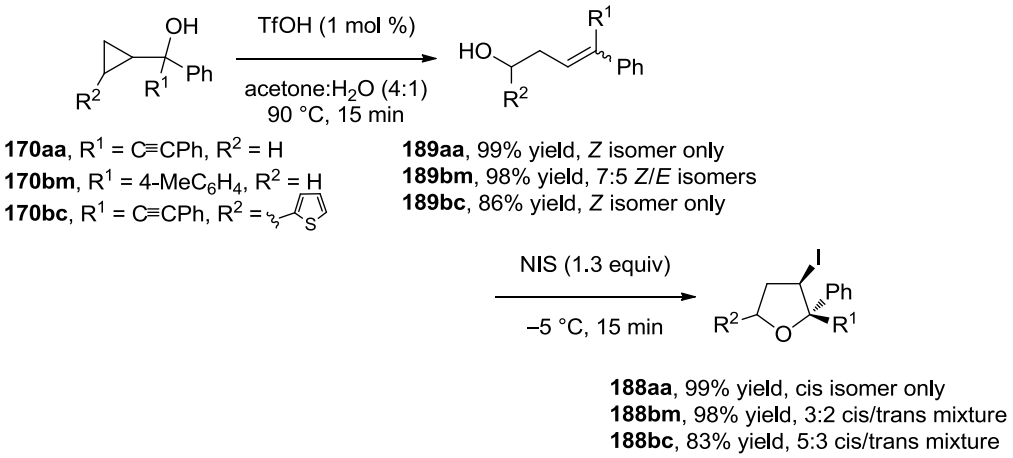


Fig. 3.4 ORTEP drawing of **188by** with thermal ellipsoids at 50% probability levels.

At this juncture, we would like to highlight the diastereoselective nature of the present reaction. In reactions involving substrates in which one of the substituents on the carbinol carbon was significantly more sterically demanding than the other and R^3 = H, the corresponding 3-halohydrofuran derivative was furnished with exclusive cis diastereoselectivity (entries 11-17 and 22 in Table 3.2 and Table 3.3). In addition to our earlier spectroscopic and crystallographic measurements for **188aa** and **188by**, the relative *cis* configurations of **188bo-aw**, **188bu**, **188bw**,**bx**, and **188bz-cb** were determined on the basis of ^{1}H-^{1}H NOE analysis of **188bp**. This revealed ^{1}H-^{1}H NOE correlations could be found between the H-3 and CH_2 of the pentyl group that established a *cis* orientation between the I and Ph substituents of the product (see Figure 2). However, no or close to no diastereoselectivity was observed for hydroxylative ring opening/iodocyclization of starting alcohols containing two slightly different para-substituted aryl groups on the carbinol carbon (entries 7-10 in

Table 3.2). A similar diastereoselective outcome was found for reactions in which the cyclopropane ring of the substrate contained a substituent (entries 19-21 in Table 2). On the other hand, only two out of the four possible product diastereomers were afforded in one of these latter reactions involving a starting alcohol containing two different functional groups on the carbinol carbon (entry 21 in Table 3.2). Although furnished as an inseparable mixture of isomers, the *cis* relationship between the I and alkyne moieties for one of the diastereomers of **188bc** was confirmed on the basis of ^{1}H-^{1}H NOE analysis showing correlations between the H-3 and ortho protons of the phenyl group of the product (see Figure 3.2).

It is evident from the above-mentioned observations that steric effects play an important role in determining the product diastereoselectivities in these reactions. Moreover, the preferential *cis* product selectivities also suggest that the halohydrofuran forming process could follow an anti addition pathway previously reported for endo iodocyclizations of homoallylic alcohols with I_2 or NIS.[135] If this is the case a reaction mechanism that involves *in situ* formation of a (*Z*)-homoallylic alcohol intermediate with the hydroxylative ring-opening and halocyclization steps



Scheme 3.2 TfOH catalyzed hydroxylation/halocyclization of **170aa**, **170bm**, and **170bc** with H_2O and NIS.

proceeding under kinetic control might be anticipated. To support this hypothesis and gain a better understanding of the reaction mechanism, we conducted the following experiments. First is the TfOH catalyzed hydroxylative ring-opening of **170aa**, which was found to give (*Z*)-**188aa** as the sole product in 99% yield under the conditions shown in Scheme 3.2. Similarly, the analogous reaction of **170bc** in the presence of 1 mol % of TfOH under the same conditions was found to furnish **189bc** as a single (*Z*)-stereo- and regioisomer in 86% yield. In both the homoallylic alcohols obtained, the stereochemistry of the C=C bond was confirmed by ^{1}H-^{1}H NOE measurements showing correlations between the alkenyl proton with those at the ortho position of the phenyl group in these adducts (Figure 3.2).[136] Further treating **189aa** and **189bc** with 1.3 equiv of NIS at –5 °C gave the expected iodohydrofurans **188aa** exclusively as the *cis* isomer and **188bc** as an inseparable 5:3 *cis*/*trans* ratio of diastereomers in 99% and 83% yield, respectively. Repeating this sequential stepwise process with **170bm** was shown to give **189bm** as an inseparable 7:5 mixture of (*Z*)/(*E*) isomers in 98% yield. Subsequent iodocyclization with NIS then provided **188bm** as an inseparable 3:2 mixture of *cis*/*trans* diastereomers in 98% yield. In all three cases, the product diastereoselectivities and yields obtained were comparable to the analogous reactions described in entry 2 in Table 3.1 and entries 9 and 21 in Table 3.2. The premise that both the hydroxylative ring-opening and halocyclization steps proceed under kinetic control would be consistent with our findings showing a linear increase in product yields was observed with increasing temperature for the TfOH mediated reaction of **170aa** under the conditions described in Figure 3.5. Indeed, this is further supported by the fact that when the respective solutions of 4:1 acetone:H_2O containing **188aa** and **189aa** were subjected to 1 mol % of TfOH at 90 °C for 24 h, this resulted in both cases in only the recovery of these compounds along with a small

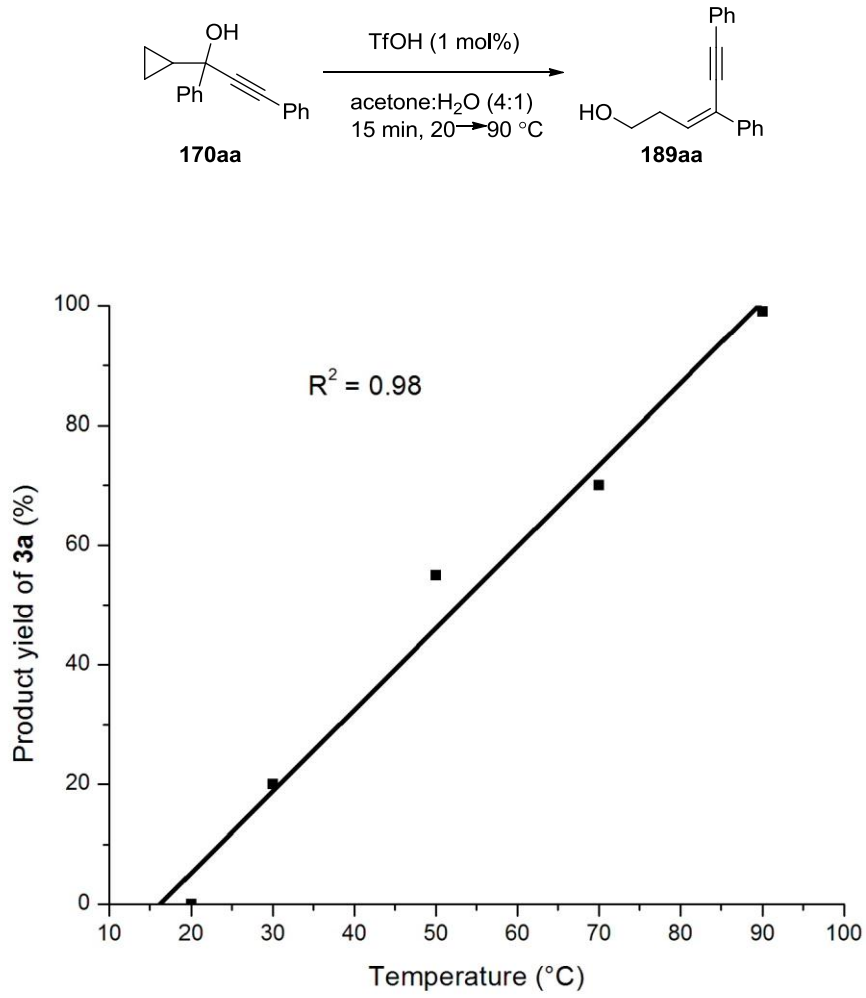
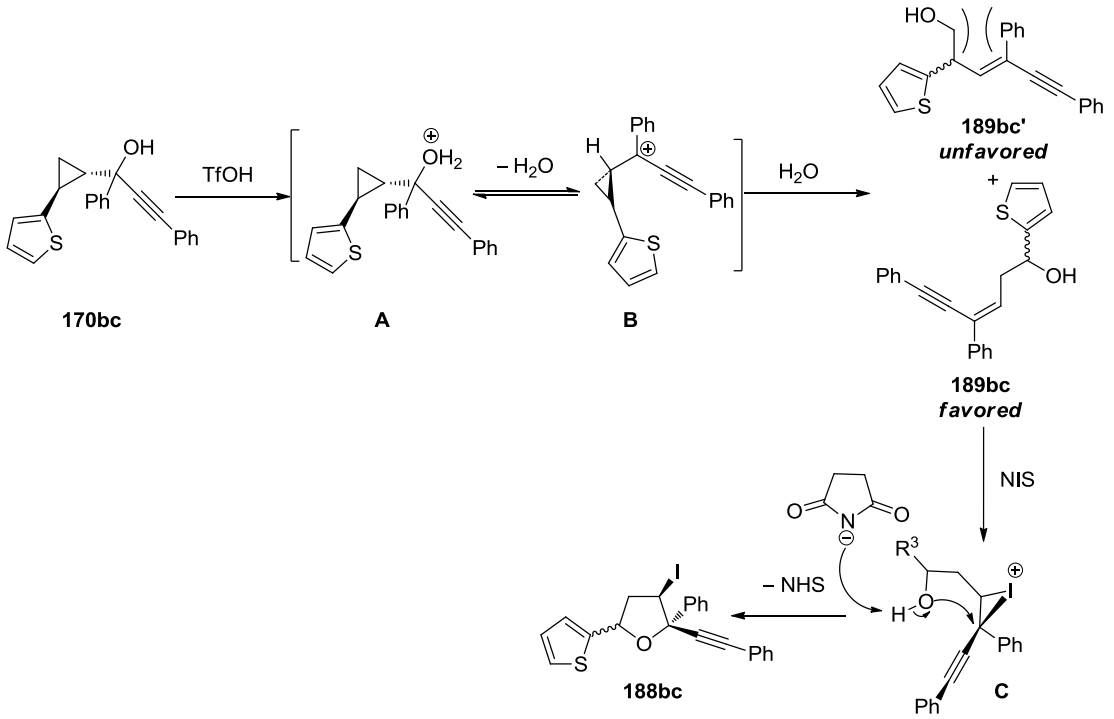


Fig. 3.5 TfOH catalyzed hydroxylative ring-opening of **170aa** to **189aa** at different temperatures

amount of unknown side products based on ^{1}H NMR analysis of the crude reaction mixtures.

On the basis of the above results, we tentatively propose the first step of the present reaction to proceed by the mechanism illustrated in Scheme 3.3 for the hydroxylative ring-opening of **170bc** and iodocyclization with NIS. In a manner similar to that described for the analogous TfOH catalyzed ring-opening of cyclopropyl methanols with alcohols,[128] this could involve dehydration of the substrate by the Brønsted acid to give the putative carbocationic species **B**.[119] While it is possible that this step is

reversible given that the reaction is carried out in the presence of H_2O, subsequent cyclopropylcarbinol-homoallylic rearrangement of this newly formed cationic species and trapping by H_2O would provide the (*Z*)-homoallylic alcohol **189bc**. The second step then involves rapid cyclization of this unsaturated alcohol intermediate from the opposite face of the cationic iodonium moiety in **C** formed on treating with NIS to furnish the 3-halohydrofuran **188bc**.[135] The possible involvement of a carbocationic intermediate would be consistent with our earlier findings showing a marked decrease in product yields as the polarity of the organic component or acidity of the solvent system decreases in control experiments with **170aa** (entries 1-3 and 7-8 in Table 1.1). It would also account for the contrasting activities found for the reactions of the respective tertiary and secondary alcohols **170br** and **170bv** depicted in entries 18 and



Scheme 3.3 Tentative mechanism for TfOH catalyzed hydroxylation/halocyclization of **170bc** with H_2O and NIS.

23 in Table 3.2 since it appears that they cannot efficiently stabilize the resulting cationic charge. We postulate that the *E*/*Z* selectivities observed on forming the homoallylic alcohol intermediate **189bc** could be due to **B** adopting the conformer depicted in Scheme 3.3.[120] This would provide a carbocationic species with the least amount of unfavorable steric interactions between the functional groups and the cyclopropane ring prior to the hydroxylative ring-opening process. For reactions where $R^3 \neq H$ and provided the trisubstituted furan adduct, we surmise that a possible reason for preferential S_N1' attack at the carbon centre bearing the substituent is so that formation of the more sterically demanding primary homoallylic alcohol **189bc**' can be avoided.[120]

3.3 Conclusion

In summary, we have described an efficient one-pot, two-step synthetic route to 3-halohydrofurans based on TfOH catalyzed hydroxylation followed by *N*-halosuccinamide or Selectfluor mediated halocyclization of cyclopropyl methanols. The reaction was shown to be applicable to a wide variety of substrates bearing electronic and sterically demanding substituent combinations. The efficiency of the present mild and operationally straightforward method was demonstrated by the moderate to excellent product yields and, in most cases, with exclusive *cis* selectivity achieved at a low catalyst loading of 1 mol %. Additionally, the present procedure was shown to benefit from reagents and a catalyst that are low cost and commercially available.

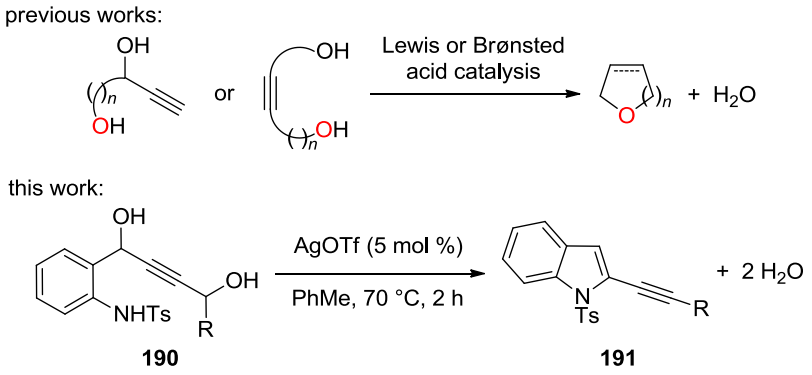
Chapter IV. Silver Triflate-Catalyzed Tandem Heterocyclization/Alkynylation of 1-((2-Tosylamino)aryl)but-2-yne-1,4-diols to 2-Alkynyl Indoles

4.1 Introduction

Indoles are a key structural component in many natural and pharmaceutical products as well as functional materials.[137-139] Because of this, and their ability to serve as a versatile building block in organic synthesis, a myriad of impressive methods for the construction of indole derivatives have been developed over the years.[138] Recently, this has hitherto included transition-metal-catalyzed cross-coupling of an indole with an alkyne, either preformed or generated *in situ*, to access synthetically valuable 2-alkynyl indole derivatives.[139] However, the reactions were shown to require stoichiometric or excess amounts of various reagents, which can lead to equimolar or more amounts of waste products. Added to this is the need to introduce structural elements to direct the C–C bond-forming process to occur regioselectively at the C2 position of the indole ring. For this reason, establishing synthetic methods to this immensely important nitrogen heterocycle in an efficient manner and with control of substitution patterns from readily accessible substrates continues to be actively pursued.

Lewis and Brønsted acid-catalyzed reactions of unsaturated alcohols have emerged over the years as efficient and convenient synthetic strategies for C–C and C–X (X=N, O, S) bond formation.[140-142] For example, we recently reported a method for the synthesis of indenyl-fused and 2,3-disubstituted indoles that relied on the cycloisomerization of 2-tosylaminophenylprop-1-yn-3-ols in the presence of a gold(I) catalyst.[71] We subsequently demonstrated that the synthetic method could be fine-tuned to provide 1*H*-indole-2-carbaldehydes and (*E*)-2-(iodomethylene)indolin-

-3-ols by introducing *N*-iodosuccinimide into the reaction conditions.[138a] Further exploration of this field led us to investigate the potential Lewis acid-catalyzed reactivity of propargylic diols. Thus far, the Lewis and Brønsted acid mediated chemistry of this class of compounds has been reported to give only the oxygen heterocycle and an equimolar amount of H_2O (Scheme 4.1).[142] In contrast, a process involving a Lewis acid triggered C–OH bond activation of a propargylic diol, which results in the formation of an N-heterocycle with the liberation of two molecules of H_2O as potentially the only byproduct is not known. As part of ongoing efforts to



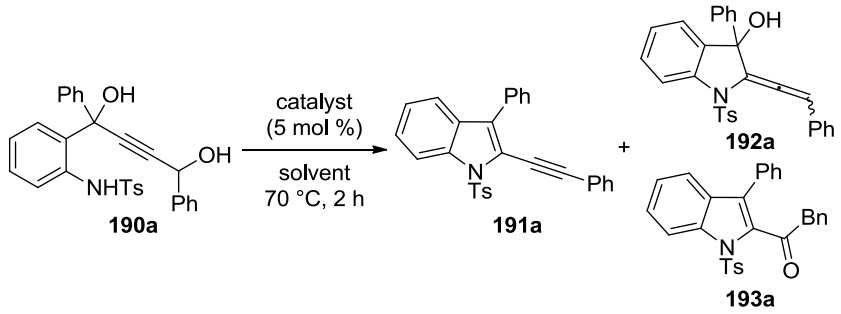
Scheme 4.1 Lewis and Brønsted acid-catalyzed reactivities of propargylic diols.

develop this type of reaction, our discovery that inexpensive, ecologically benign, and readily available simple Ag^I salts can effect tandem heterocyclization/alkynylation of propargylic 1,4-diols of the type **190** with an appropriately placed aniline moiety is reported herein (Scheme 4.1). This provides a convenient route to 2-alkynyl indoles **191** that assembles both the indole ring and alkyne moiety in one step for a wide range of substrates. Achieved under mild conditions, it also represents the first synthetic method for the preparation of this N-heterocycle that does not rely on a cross-coupling strategy.

4.2 Results and Discussion

The 1-((2-tosylamino)aryl)but-2-yne-1,4-diols studied in this work were prepared from the reaction of the corresponding aldehyde and substituted *N*-tosyl-1-(2-amino--phenyl)prop-2-yn-1-ol pretreated with LDA following literature procedures.[143] By using *N*-tosyl-1-(2-aminophenyl)-1,3-diphenyl-prop-2-yn-1-ol **190a** as the probe substrate, we began by examining a variety of Lewis and Brønsted acid catalysts to establish the reaction conditions (Table 4.1). This study initially revealed treating a solution of **190a** in toluene with AgOTf (5 mol%) at room temperature for 7 h gave 3-phenyl-2-(phenylethynyl)-1-tosyl-1*H*-indole **191a** and 3- phenyl-2-(2-phenylvinylid ene)-1-tosyl indolin-3-ol **192a** in 45 and 30% yields, respectively (entry 1). The structure of the 2-alkynyl indole product was determined by ^{1}H NMR spectroscopy and X-ray crystallography (Figure 4.1).[144] Our studies subsequently showed that formation of the 2-vinylidene indolin-3-ol byproduct could be suppressed to give **191a** as the only product in 88% yield by increasing the reaction temperature to 70 °C for 2 h (entry 2). Slightly lower product yields were obtained when the reaction was repeated in the presence of 5 or 10 mol% of Et_3N or K_2CO_3 as well as 1 equiv of the latter inorganic base (entries 3-7). Likewise, changing the solvent from toluene to $MeNO_2$, 1,4-dioxane or 1,2-dichloroethane gave slightly lower product yields of 65–79% (entries 8-10). In contrast, replacing toluene with THF or MeCN as the solvent was found to result in recovery of the substrate in near quantitative yield (entries 11 and 12). Similarly, a survey of other inexpensive silver(I) salts and Lewis acids did not provide any improvements (entries 13-19). Moreover, in reactions where $AgPF_6$, $AgSbF_6$ or $AgBF_4$ was employed as the catalyst, the Meyer–Schuster rearrangement adduct **193a** was also afforded as a side product in 15–55% yield (entries 14-16).[145] The analogous AgOAc mediated reaction was the only instance in

Table 4.1 Optimization of reaction conditions.[a]



Entry	Catalyst	Solvent	Yield (%)[b]		
			191a	**192a**	**193a**
1[c]	AgOTf	PhMe	45	30	-
2	AgOTf	PhMe	88	-	-
3[d]	AgOTf	PhMe	78	-	-
4[e]	AgOTf	PhMe	69	-	-
5[f]	AgOTf	PhMe	86	-	-
6[g]	AgOTf	PhMe	85	-	-
7[h]	AgOTf	PhMe	68	-	-
8	AgOTf	$MeNO_2$	78	-	-
9	AgOTf	1,4-dioxane	79	-	-
10	AgOTf	$(CH_2Cl)_2$	65	-	-
11	AgOTf	THF	-[i]	-	-
12	AgOTf	MeCN	-[i]	-	-
13	$AgNTf_2$	PhMe	38	-	-
14	$AgPF_6$	PhMe	30	-	18
15	$AgSbF_6$	PhMe	20	-	55
16	$AgBF_4$	PhMe	35	-	15

Table 4.1 (*continued*)

Entry	Catalyst	Solvent	Yield (%)[b]		
			191a	**192a**	**193a**
17	AgOAc	PhMe	-[i]	-	-
18	$Cu(OTf)_2$	PhMe	68	-	-
19	$Yb(OTf)_3$	PhMe	50	-	-
20	*p*-TsOH·H_2O	PhMe	-[j]	-	-
21	TFA	PhMe	20	-	-
22	TfOH	PhMe	32	-	-
23	Tf_2NH	PhMe	35	-	-

[a]All reactions were performed at the 0.1 mmol scale with catalyst/**190a** ratio = 1:20 in 4 mL of solvent at 70 °C for 2 h. [b]Isolated yield. [c]Reaction carried out at room temperature for 7 h. [d]Reaction carried out in the presence of 5 mol % of Et_3N. [e]Reaction carried out in the presence of 10 mol % of Et_3N. [f]Reaction carried out in the presence of 5 mol % of K_2CO_3. [g]Reaction carried out in the presence of 10 mol % of K_2CO_3. [h]Reaction carried out in the presence of 1 equiv of K_2CO_3. [i]No reaction based on TLC and ^1H NMR analysis of the crude reaction mixture. [j]Decomposition products obtained based on TLC and ^1H NMR analysis of the crude reaction mixture.

which the substrate was recovered in near quantitative yield (entry 17). Low product yields of 20-35% were additionally afforded in control experiments with the Brønsted acid catalysts TFA, TfOH and Tf_2NH, whereas *p*-TsOH·H_2O led to decomposition of the substrate (entries 20-23). A similar outcome was found when the Brønsted acid mediated reactions were re-examined in a variety of solvents and at

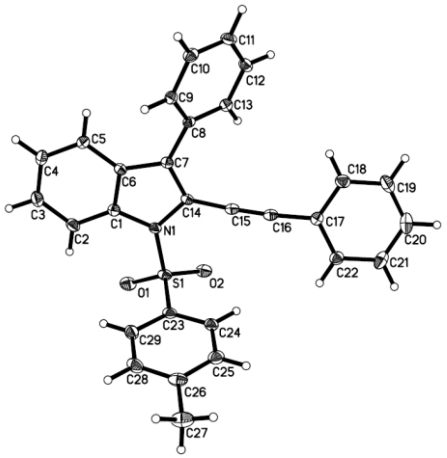
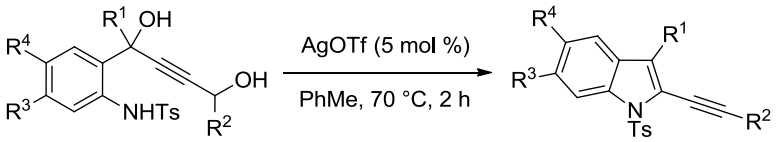


Figure 4.1 ORTEP drawing of **191a** with thermal ellipsoids at 50% probability levels.

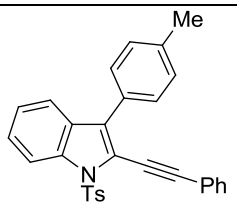
various catalyst loadings and temperatures.[143] Under these various conditions, the 2-alkynyl indole product was furnished in 25-48% yield and/or with recovery of **190a** in up to 68% yield and/or substrate decomposition. Along with the above results of reaction in the presence of a base, the possibility of a hidden Brønsted acid catalyst was shown to be unlikely based on further control experiments with AgOTf at 1 and 5 mol% heated to reflux in 1,2-dichloroethane prior to use or 5 mol% of AgOTf in the presence of 10 mol% of *t*BuCl, which furnished **191a** in low yields of 13-38%.[143, 146] On the basis of the above results, the reaction of **190a** in the presence of AgOTf (5 mol%) in toluene at 70 °C for 2 h provided the optimal conditions.

With the optimized conditions in hand, we next turned to evaluating their generality for a series of propargylic 1,4-diols and the results are summarized in Table 4.2. These reactions demonstrated that by using AgOTf as catalyst, the conditions proved to be broad and a variety of 2-alkynyl indoles could be afforded in good to excellent yields from the corresponding substrates **190b-x**. Starting alcohols with a pendant phenyl moiety and their derivatives with electron-withdrawing or electron-donating groups in the para position at R^1 or R^2 were found to react well, affording **191b-f** in excellent yields of 87-94%. Likewise, 2-alkynyl indoles **191g-m**, containing a

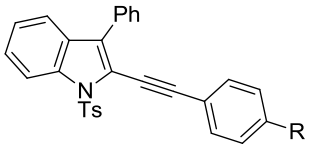
Table 4.2 Tandem heterocyclization/alkynylation of **190b-x** catalyzed by AgOTf.[a]



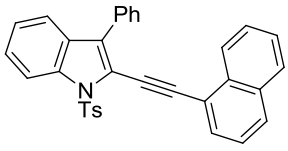
190 **191**



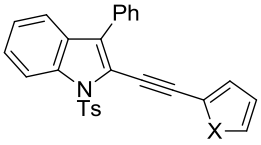
191b: (94%)



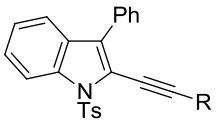
191c: R = F (88%)
191d: R = Cl (87%)
191e: R = Br (89%)
191f: R = OMe (92%)



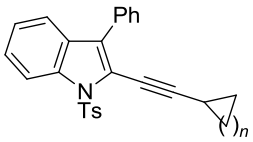
191g: (87%)



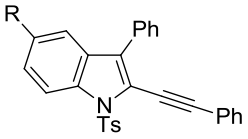
191h: X = O (91%)
191i: X = S (94%)



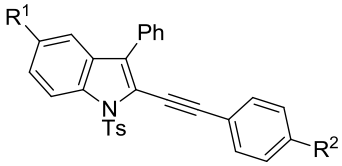
191j: R = *t*Bu (76%)
191k: R = *n*Hex (79%)



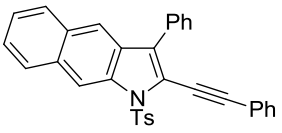
191l: n = 1 (78%)
191m: n = 4 (74%)



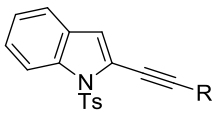
191n: R = Br (80%)
191o: R = Cl (81%)
191p: R = Me (93%)



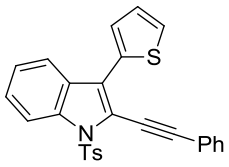
191q: $R^1 = R^2$ = Cl (45%)
191r: R^1 = Cl, R^2 = OMe (91%)



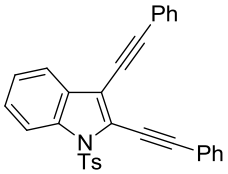
191s: (88%)



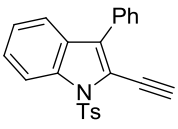
191t: R = Ph (92%)
191u: R = *n*Pent (72%)



191v: (67%)[b]



191w: (61%)[b]



191x: (38%)[c]

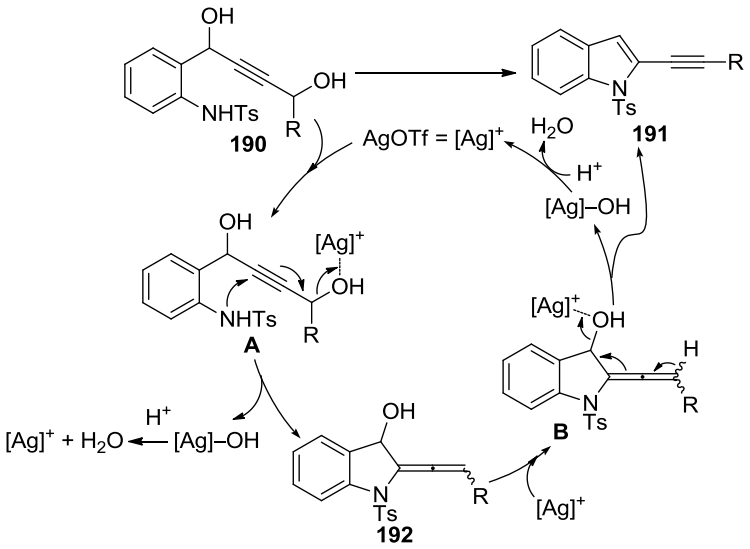
[a]All reactions were performed at the 0.1 mmol scale with AgOTf/**190a** ratio = 1:20 in toluene (4 mL) at 70 °C for 2 h. Values in parenthesis denote isolated product yields. [b]Reaction performed for 0.5 h. [c]Reaction performed at 40 °C for 0.5 h.

1-naphthyl, heteroaryl, alkyl, or cycloalkane substituent on the alkyne side chain, were obtained in excellent yields of 74–94% from the corresponding alcoholic substrates **190g-m**. The presence of an electron-withdrawing or electron-donating

group or benzo-fused ring on the aniline moiety was found to have no influence on the course of the reaction with **191n-p** and **191r-s** obtained in 80–93% yield. Additionally, substrates where both the carbinol carbon centers are secondary alcohols, as in **190t** and **190u**, were found to proceed well and provide **191t** and **191u** in 92 and 72% yields, respectively. This is noteworthy as these adducts cannot be prepared following a cross-coupling approach due to the need for the C3 position of the indole ring to be occupied by a functional group so that the C–C bond-forming process can only occur at the C2 position of the N-heterocyclic substrate.[139] Starting 1,4-diols **190v** and **190w**, with a pendant thiophene or alkyne moiety at R^1, were also found to be well tolerated under the reaction conditions, giving the corresponding 2-alkynyl indoles in respective yields of 67 and 61%. Under the standard conditions, reaction of **190q** in which R^2 = *p*ClC_6H_4 and R^4 = Cl and **190x** where R^2 = H, were the only examples found to give the corresponding 2-alkynyl indoles **191q** and **191x** in lower yields of 45 and 38%, respectively.

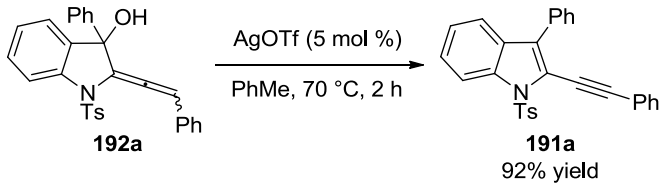
A tentative mechanism for the present Ag^I catalyzed 2-alkynyl indole forming reaction is outlined in Scheme 4.2. This could initially involve activation of **190** through coordination of the metal catalyst with the sterically less hindered secondary alcohol moiety of the substrate to give the silver(I)-coordinated intermediate **A**. It is possible that this could subsequently trigger 5-*exo*-*dig* cyclization of the pendant aniline group to the alkyne moiety and formation of 2-vinylidene indolin-3-ol **192**. Further coordination of this newly formed adduct to AgOTf, which is re-generated from [Ag]–OH by protonolysis and also affords a molecule of H_2O, gives Ag^I-activated allene species **B**. A second C–OH bond activation step that initiates deprotonation of the allene moiety followed by elimination of [Ag]–OH,[147] which

releases the metal catalyst once again by protonolysis, would then provide **191** and another molecule of water.



Scheme 4.2 Proposed reaction pathway for the formation of 2-alkynyl indoles.

While fortuitous, the competitive formation of **192a** for the cyclization of **190a** at room temperature under the conditions mentioned earlier in entry 1, Table 4.1 argues in favor of the mechanism put forward in Scheme 4.2. This argument was further corroborated by the observation that when a solution of **192a** in toluene was treated with 5 mol% of AgOTf under the conditions shown in Scheme 4.3, the expected 2-alkynyl indole **191a** was obtained as the sole product in 92% yield. The role of the silver catalyst in facilitating the two C–OH bond activation steps could also be shown by repeating the reactions of **190a** and **192a** under similar conditions but in the absence of the catalyst. In both instances, this test led to the recovery of the respective starting alcohols in near quantitative yield.



Scheme 4.3 Dehydrative alkynylation of **192a** catalyzed by AgOTf.

4.3 Conclusion

In summary, we have demonstrated for the first time that the silver(I) mediated C–OH bond activation of 1,4-propargylic diols is an effective and chemoselective strategy for the construction of 2-alkynyl indoles. The reaction was shown to tolerate a diverse set of starting alcohols and afford the N-heterocycle for applications in natural product synthesis and medicinal and materials chemistry. Previous methods to this immensely important member of the indole family of compounds have mainly relied on synthetic strategies that require a cross-coupling step and structural elements to regioselectively direct alkynylation to occur at the C2 position of the nitrogen ring. Our approach is rapid, forming the indole ring and alkyne side chain of the N-heterocycle sequentially from a wide variety of starting materials and a catalytic system that are low cost, readily available, and ecologically benign.

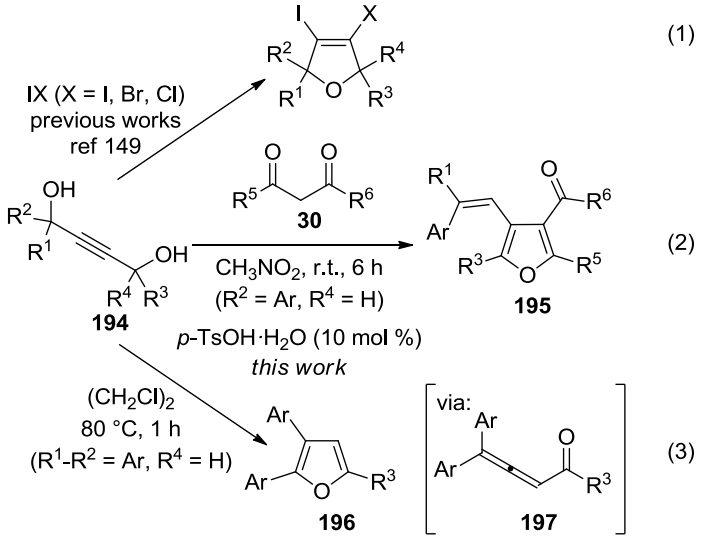
Chapter V. Brønsted Acid-Catalyzed Cycloisomerization of But-2-yne-1,4-diols with or without 1,3-Dicarbonyl Compounds to Tri- and Tetrasubstituted Furans

5.1 Introduction

Furans occupy an important place in the heterocyclic family of compounds because of their prevalence as a key structural component in a myriad of natural and pharmaceutical products and ability to serve as a versatile building block in organic synthesis.[1-2] While this has led to a myriad of impressive approaches for furan synthesis being developed over the years,[148-150] there remains a need for new methods for their construction with selective control substitution of patterns from starting materials and a catalytic system that are readily accessible, atom-economical and low cost.

In the preceding chapter , we have described for the synthesis of 2-alkynyl indoles from 1-((2-tosylamino)aryl)but-2-yne-1,4-diols with AgOTf as the catalyst.[151] Further exploration of this field led us to examine the potential Brønsted acid catalyzed reactivity of readily available propargylic 1,4-diols **194** (Scheme 5.1). Thus far, the synthetic utility of this class of compounds has been reported only in electrophilic halocyclizations in the presence of a stoichiometric amount of a halogen source, such as I_2, to give 3,4-dihalodihydrofurans (Scheme 5.1, eq 1).[152] In contrast, a catalytic cycloisomerization process involving Brønsted acid-induced ionization of a propargylic 1,4-diol, which results in the formation of the aromatic oxygen heterocycle is not known. As part of efforts to develop this type of reaction, we report herein that *p*-TsOH·H_2O can mediate tandem alkylation/cycloisomerization of but-2-yne-1,4-diols **194** with 1,3-dicarbonyl compounds **30** (Scheme 5.1, eq 2). This process provides a convenient synthetic route to tetrasubstituted furans **195** in 42-94%

yield for a wide variety of substrates under mild conditions at room temperature. In the course of this study, our discovery that a synthetic route to 2,3,5-trisubstituted furans **196** in 60-85% yield from *p*-TsOH·H_2O catalyzed dehydrative rearrangement of the starting 1,4-diol under slightly modified reaction conditions is also presented (Scheme 5.1, eq 3). A notable observation we have made for this latter furan forming process is that it occurs via the *in situ* formed allenyl ketone intermediate **197**, the cycloisomerization chemistry of which has been extensively studied under transition metal catalysis.[153]



Scheme 5.1 Design of propargylic 1,4-diol-based approaches for the synthesis of furan derivatives.

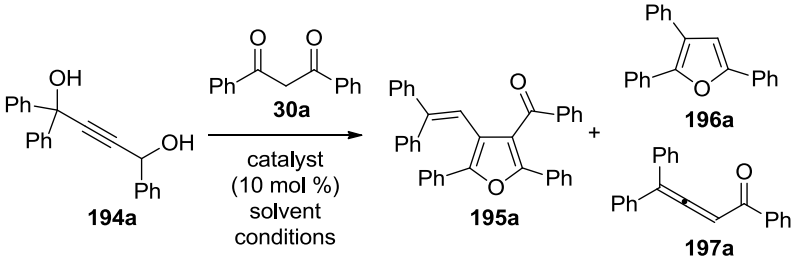
5.2 Results and Discussion

All the but-2-yne-1,4-diols examined in this work were prepared from reaction of the corresponding aldehyde and substituted prop-2-yn-1-ol pretreated with LDA following literature procedures.[154] With 1,1,4-triphenylbut-2-yne-1,4-diol **194a** and 1,3-diphenylpropane-1,3-dione **30a** as the model substrates in hand, we then began by focusing on a variety of Brønsted acid catalysts to test our hypothesis (Table 5.1).

Subjecting **194a** (1 equiv) and **30a** (2 equiv) in $MeNO_2$ with 10 mol % of *p*-TsOH·H_2O at room temperature for 6 h gave the best result (entry 1). Under these conditions, (4-(2,2-diphenylvinyl)-2,5-diphenylfuran-3-yl)(phenyl)methanone **195a** was afforded in 92% yield. The structure of the furan product was determined by ^1H NMR measurements and comparison with the X-ray crystal structure analysis of a closely related adduct (*vide infra*). A lower product yield of 68% was obtained on decreasing the catalyst loading from 10 to 5 mol % (entry 2). Similarly, lower product yields were found on repeating the reaction with TFA, TfOH or Tf_2NH in place of *p*-TsOH·H_2O as the catalyst or employing dichloromethane as the solvent (entries 3-5 and 7). Changing the catalyst from *p*-TsOH·H_2O to HCl or solvent from $MeNO_2$ to 1,4-dioxane were the only instances in which either recovery of the starting material in near quantitative yield or decomposition was found (entries 6 and 8). Unexpectedly, 2,3,5-triphenylfuran **196a** was afforded in 53% yield when $MeNO_2$ was replaced by toluene as the solvent at 80 °C for 1 h due to the heterogeneity of the reaction mixture at room temperature (entry 9). The unprecedented formation of **196a** via a mechanistically intriguing dehydrative rearrangement of **194a** prompted us to additionally examine this transformation more closely to establish a second set of reaction conditions to this class of substituted furans (entries 10-14). This initially showed a comparable yield of the trisubstituted furan was found on repeating the reaction in the absence of the 1,3-dicarbonyl compound (entry 10). Our studies subsequently showed changing the solvent from toluene to 1,2-dichloroethane gave **196a** in 80% yield (entry 11). On the other hand, lower product yields were obtained on replacing toluene with MeCN or $MeNO_2$ as the solvent or reducing the reaction time from 1 h to 30 min (entries 12-14). Reactions with MeCN as solvent or conducted for 30 min also afforded the allenyl ketone byproduct **197a** in 44-54%

yield.[153] On the basis of the above results, reaction of **194a** with **30a** in the presence of 10 mol % of *p*-TsOH·H_2O in $MeNO_2$ at room temperature for 6 h provided the

Table 5.1 Optimization of reaction conditions.[a]



Entry	Catalyst	Solvent	Conditions	Yield (%)		
			(°C)/(h)	**195a**	**196a**	**197a**
1	p-TsOH·H_2O	$MeNO_2$	r.t./6	92	-	-
2[b]	*p*-TsOH·H_2O	$MeNO_2$	r.t./6	68	-	-
3	TfOH	$MeNO_2$	r.t./6	20	-	-
4	TFA	$MeNO_2$	r.t./6	72	-	-
5	Tf_2NH	$MeNO_2$	r.t./6	25	-	-
6	HCl	$MeNO_2$	r.t./6	-[c]	-	-
7	*p*-TsOH·H_2O	CH_2Cl_2	r.t./6	20	-	-
8	*p*-TsOH·H_2O	1,4-dioxane	r.t./6	-[d]	-	-
9	*p*-TsOH·H_2O	PhMe	80/1	-	53	-
10[e]	*p*-TsOH·H_2O	PhMe	80/1	-	58	-
11[e]	*p*-TsOH·H_2O	$(CH_2Cl)_2$	80/1	-	80	-
12[e]	*p*-TsOH·H_2O	$(CH_2Cl)_2$	80/0.5	-	30	54

Table 5.1 (*continued*)

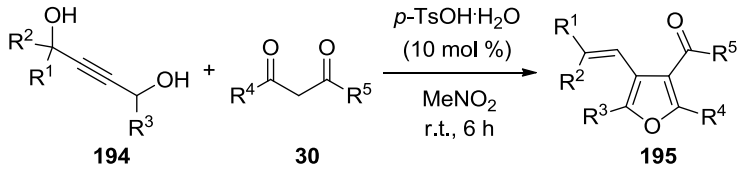
Entry	Catalyst	Solvent	Conditions (°C)/(h)	Yield (%)		
				195a	**196a**	**197a**
13[e]	*p*-TsOH·H_2O	$MeNO_2$	80/1		55	-
14[e]	*p*-TsOH·H_2O	CH_3CN	80/1	-	20	44

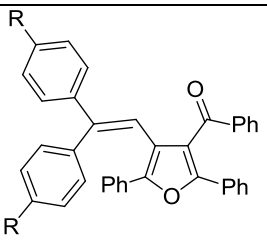
[a]All reactions were performed with **194a**:**30a** ratio = 1:2 and 10 mol % of catalyst. [b]Reaction performed with 5 mol % of catalyst. [c]Mixture of unknown decomposition products obtained based on TLC and ^{1}H NMR analysis of the reaction mixture. [d]No reaction observed based on TLC and ^{1}H NMR analysis of the reaction mixture. [e]Reaction performed in the absence of **30a**.

optimum conditions to the tetrasubstituted furan. On the other hand, reaction of **194a** with 10 mol % of *p*-TsOH·H_2O in 1,2-dichloroethane at 80 °C for 1 h gave the best conditions to the trisubstituted product.

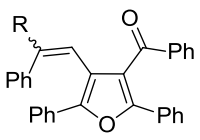
With the two optimized conditions to access tetra- and trisubstituted furans in hand, we first turned to assessing the scope of the bimolecular reaction for a series of 1,3-dicarbonyl compounds and propargylic 1,4-diols (Table 5.2). These experiments showed that with *p*-TsOH·H_2O as the catalyst and $MeNO_2$ as the solvent, the conditions proved to be broad and a variety of tetrasubstituted furans could be furnished in good to excellent yields from the corresponding substrates **194b-r** and **30a-d**. Reactions of starting 1,4-diols **194b-g**, containing para-substituted electron-withdrawing or electron-donating aryl groups at R^1, R^2 and R^3, with **30a** gave **195b-g** and **195j-l** in excellent yields of 78-91%. Replacing the aryl substituent at R^1 with an alkyne moiety was found to have no influence on the course of the reaction with **195h** afforded in 82% yield. Similarly, tetrasubstituted furans **195n-r** with a

Table 5.2 Tandem cycloisomerizations of **194b-r** with **30a-d** catalyzed by *p*-TsOH·H_2O.[a]

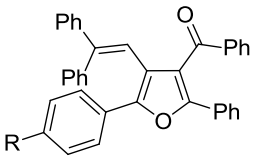




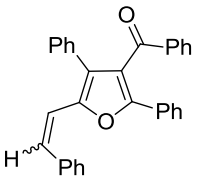
195b: R = F (78%)
195c: R = Cl (83%)
195d: R = Br (86%)
195e: R = Me (80%)



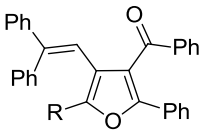
195f: R = *p*-Br(C_6H_4) (83%)[b]
195g: R = *p*-Me(C_6H_4) (85%)[c]
195h: R = C≡CPh (82%)[d]
195i: R = *t*-Bu (42%)[e]



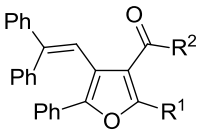
195j: R = F (89%)
195k: R = Br (91%)
195l: R = *t*-Bu (89%)



198m: (45%)[d]



195n: R = 1-napthyl (72%)
195o: R = 2-thiophene (81%)
195p: R = cyclohexyl (85%)
195q: R = Me (74%)
195r: R = *t*-Bu (86%)



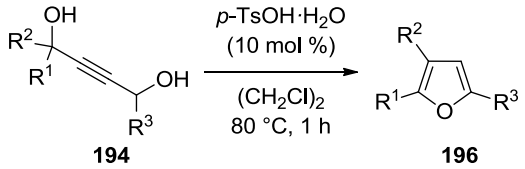
195s: R^1 = Me, R^2 = Ph (83%)
195t: R^1 = R^2 = *p*-MeO(C_6H_4) (94%)
195u: R^1 = R^2 = Me (85%)

[a]All reactions were performed with **194**:**30** ratio = 1:2 and 10 mol% of *p*-TsOH·H_2O in $MeNO_2$ at r.t. for 6 h. Values in parenthesis denote isolated product yields. [b]Product obtained as a 1.3:1 mixture of *E/Z* isomers. [c]Product obtained as a 1.1:1 mixture of *E/Z* isomers. [d]Product obtained as a 1:1 mixture of *E/Z* isomers. [e]Product obtained as a 1:2 mixture of *E/Z* isomers.

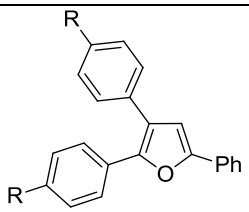
pendant alkyl, cyclohexyl, 1-naphthyl or 2-thiophene functional group at R^3, were obtained in 72-86% yield from the corresponding reactions of starting alcohols **194n-r** with **30a**. This contrasted to the analogous reactions where the phenyl substituent at R^1 was replaced with a *t*-Bu group (**194i**) or both carbinol carbon

centers are secondary alcohols (**194m**) with **30a**. These reactions were the only examples found to give the corresponding furan **195i** and the regiosiomer **198m** in lower yields of 42 and 45%, respectively. On the other hand, reactions of 1,3-dicarbonyl compounds bearing a methyl or Ar group (**30b-d**) with **194a** were found to proceed well and provide **195s-u** in excellent yields. For reactions in which

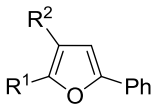
Table 5.3 Tandem cycloisomerizations of **194b-r** catalyzed by *p*-TsOH·H_2O.[a]



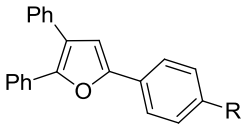
194 **196**



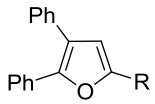
196b: R = F (80%)
196c: R = Cl (80%)
196d: R = Br (81%)
196e: R = Me (79%)



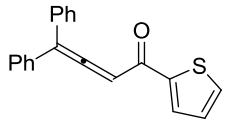
196f': R^1 = Ph, R^2 = *p*-Br(C_6H_4) (83%)[b]
196f": R^1 = *p*-Br(C_6H_4), R^2 = Ph
196g': R^1 = Ph, R^2 = *p*-Me(C_6H_4) (82%)[c]
196g": R^1 = *p*-Me(C_6H_4), R^2 = Ph
196h: R^1 = C≡CPh, R^2 = Ph (-)[d]
196i: R^1 = *t*-Bu, R^2 = Ph (-)[d]



196j: R = F (81%)
196k: R =Br (83%)
196l: R = *t*-Bu (85%)



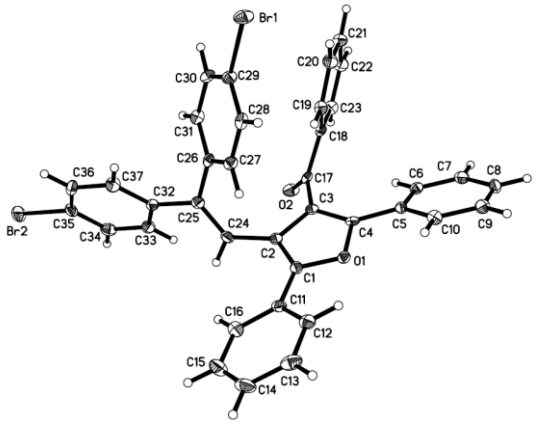
196n: R = 1-napthyl (60%)
196p: R = cyclohexyl (74%)
196q: R = Me (62%)
196r: R = *t*-Bu(82%)



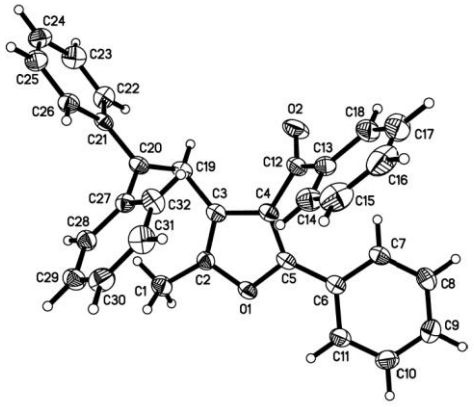
197o: (68%)

[a]All reactions were performed at the 0.16 mmol scale with 10 mol% of *p*-TsOH·H_2O in 1,2-dichloroethane at 80 °C for 1 h. Values in parenthesis denote isolated product yields. [b]Product obtained as a 2.5:1 mixture of regioisomers. [c]Product obtained as a 3.3:1 mixture of regioisomers. [d]Mixture of decomposition products obtained that could not be identified by ^{1}H NMR analysis or mass spectrometry.

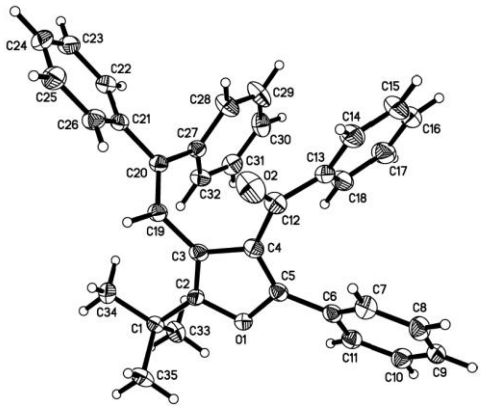
$R^1 \neq R^2$, the tetrasubstituted furan products were also obtained as a mixture of *E*/*Z* isomers in a ratio of up to 2:1 based on ^{1}H NMR measurements of the respective crude mixtures. The structure of the furan products were also determined on the basis of X-ray crystallographic analysis of **195d**, **195q**, **195r** and **198m**.[155]



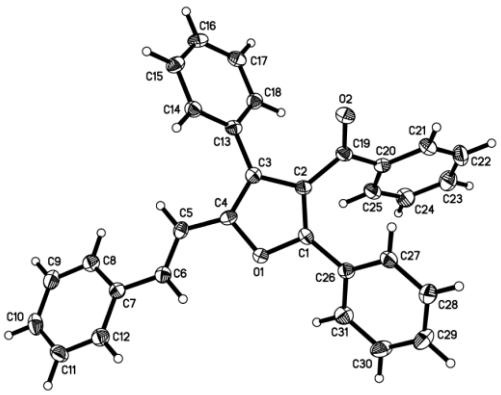
(a) **195d**



(b) **195q**



(c) **195r**

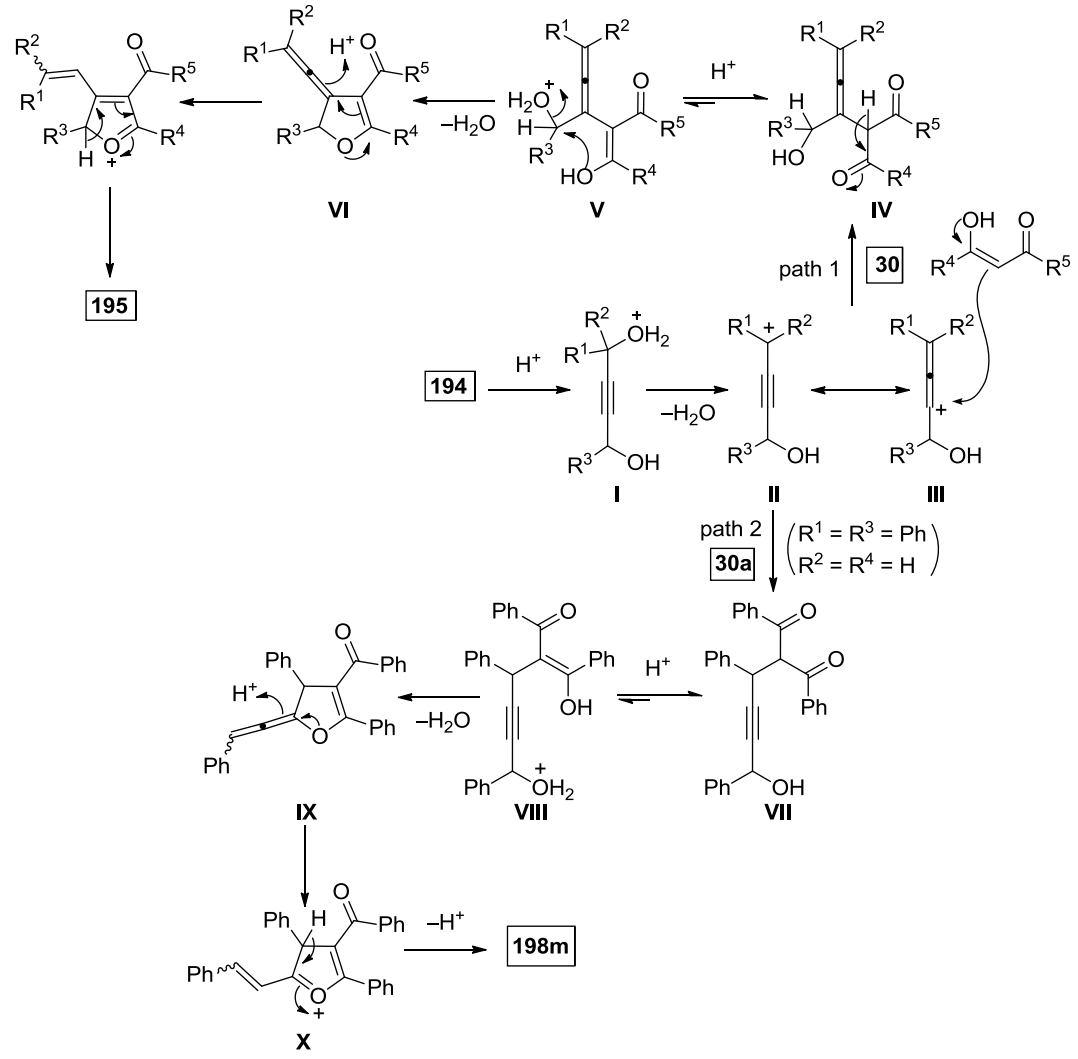


(d) **198m**

Figure 5.1 ORTEP drawing of (a) **195d**, (b) **195q**, (c) **195r** and (d) **198m** with thermal ellipsoids at 50% probability levels.

We next sought to define the scope of the intramolecular reaction with same set of propargylic 1,4-diols compounds **194b-r** and the results are summarized in Table 5.3. Overall, this led us to find the cyclization reactions to proceed well on applying the *p*-TsOH·H_2O catalyzed conditions in 1,2-dichloroethane described in Table 5.1, entry 11. Under these conditions, the corresponding 2,3,5-trisubstituted furans **196b-4g**, **196j-l**, **196n** and **196p-r** were afforded in 60-85% yield. For reactions of **194f** and **194g**, the corresponding 2,3,5-trisubstituted adducts were also obtained as mixture of regioisomers in ratios of up to 3.3:1, comparable to those reported for the metal catalyzed cycloisomerization of allenyl ketones.[156] Reactions of **194h-194i**, **194o** were the only instances in which no product formation was observed. In our hands, reactions of **194h-194i** were found to give a mixture of decomposition products that could not be identified by ^{1}H NMR analysis or mass spectrometry. For **194o**, the allenyl ketone **197o** was the only product obtained in 68% yield, even on prolonging the reaction time to 5 h.

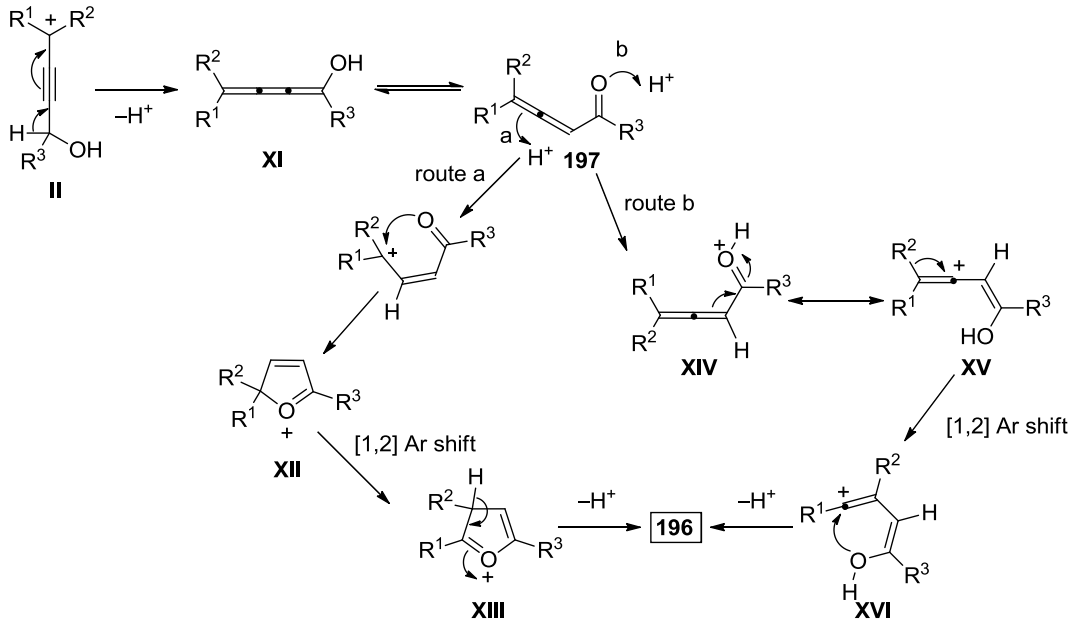
Tentative mechanisms for the present *p*-TsOH·H_2O catalyzed tri- and tetrasubstituted furan forming reactions are outlined in Schemes 5.2 and 5.3. For the formation of tetrasubstituted oxygen heterocycle, this could involve protonation of **194** by the Brønsted acid at the tertiary carbinol oxygen center (Scheme 5.2). This leads to the protonated analogue **I**, which undergoes dehydration to give the alkynyl substituted carbocation **II** and its allenic resonance form **III**. At room temperature, nucleophilic attack at the acetylenic carbon center in **II** or allenic carbon center in **III** by **30** would then to give the alkylated adduct **IV** (Scheme 5.2, path 1). Subsequent isomerization to its enolate form and protonation of the remaining hydroxyl moiety by *p*-TsOH·H_2O would provide cationic tautomer **V**. Intramolecular nucleophilic substitution of the enolic oxygen onto the protonated hydroxyl group of this newly



Scheme 5.2 Tentative mechanism for *p*-TsOH·H_2O catalyzed cycloisomerization/ condensation of **194** in the presence of **30**.

formed species followed by aromatization of the resulting hydrofuran **VI** obtained would then deliver the tetrasubstituted furan **195**. In these reactions, trapping at the sterically less hindered carbon center of the putative ionized species **II** or **III** could be one possible reason for the obtained product regioselectivities.[157] Such a pathway would limit any unfavorable steric interactions between the substituents of the tertiary carbocationic center and the incoming carbon nucleophile. The regioisomer **198m** from **194m** with could be due to the direct alkylation by **30a** of a presumably more

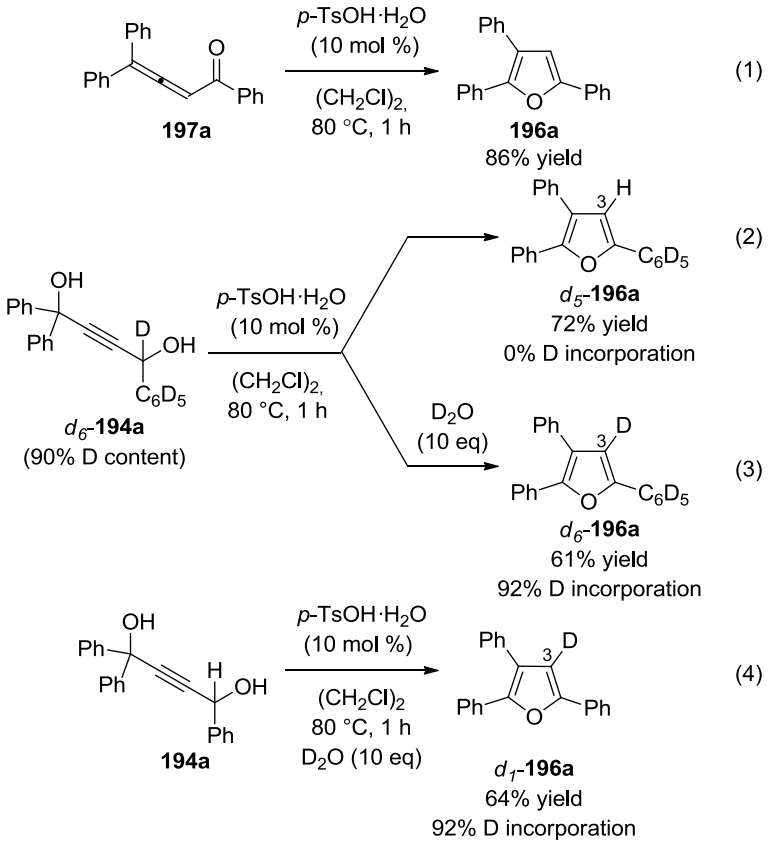
reactive carbocationic species of **II** generated from the secondary 1,4-diol **194m** (Scheme 2, path 2).[158] This would give the propargylic adduct **VII**, which can isomerize to its enolate form and protonate at the remaining hydroxyl moiety by *p*-TsOH·H_2O to form cationic tautomer **VIII**. Cyclization of this cationic intermediate involving nucleophilic substitution of the enolic oxygen onto the protonated hydroxyl group would give **IX**, which can undergo aromatization via **X** to afford **198m**.



Scheme 5.3 Tentative mechanism for cycloisomerization of **194** catalyzed by *p*-TsOH·H_2O.

At 80 °C, it is thought that deprotonation of **II** preferentially occurs at the secondary carbinol carbon center to give the cumulenol **XI** that readily isomerizes to the allenyl ketone **197** (Scheme 5.3).[159] In a manner similar to that reported for the analogous metal catalyzed allenoate/allenyl ketone cyclizations,[153] this is followed by intramolecular addition of the carbonyl oxygen onto the allene moiety of the adduct triggered by the Brønsted acidic conditions (Scheme 5.3, route a). A [1,2]-aryl shift[153d] of the resultant cyclic oxonium intermediate **XII** would give **XIII**, which then

aromatizes to provide the 2,3,5-trisubstituted furan **196**. Alternatively, the allenyl ketone **197** could isomerize to the corresponding vinyl cationic species **XV** via **XIV**, which would then undergo a [1,2]-aryl shift to give the disubstituted variant **XVI** (Scheme 5.3, route b). Cycloaddition involving attack of the enolic hydroxyl group onto the carbocationic carbon center of this species followed by deprotonation would then give **196**. The obtained product selectivities of up to 3.3:1 could be due to competition between R^1 and R^2 when $R^1 \neq R^2$. The decomposition of **194h-194i** could be due to either the alkyl or alkynyl substituents on the tertiary carbinol carbon being unable to sufficiently stabilize the carbocation formed *in situ* that resulted a number of side reactions.



Scheme 5.4 Control experiments with **194a**, *d*$_6$-**194a** and **197a** catalyzed by *p*-TsOH·H_2O.

To demonstrate that the allenyl ketone **197** is the actual intermediate that leads to the formation of the trisubstituted adduct, we first examined the reaction of **197a** with 10 mol % of *p*-TsOH·H_2O in 1,2-dichloroethane at 80 °C for 1 h (Scheme 5.4, eq 1). This afforded **196a** in 86% yield, comparable to that directly obtained from **194a** as described in Table 5.1, entry 11. The mechanistic premise put forward in Scheme 5.3 for the formation of the allenyl ketone **197** via the cumenol **XI** was also supported by the following deuterium labeling experiments (Scheme 5.4, eq 2-4). Exposing a solution of d_6-**194a** in 1,2-dichloroethane with *p*-TsOH·H_2O (10 mol %) under the conditions shown in Scheme 5.4, eq 2 gave d_5-**196a** in 72% yield but with no retention of D content at C3 in the product, as determined by both ^{1}H NMR analysis and GC-MS measurements (Scheme 5.4, eq 2). In contrast, repeating the reactions of d_6-**194a** and **194a** with 10 equiv of D_2O afforded d_6-**196a** and d_1-**196a** in 61% and 64% yield and with a D content of 92%, incorporated at C3 of the adduct based on ^{1}H NMR analysis and GC-MS measurements (Scheme 5.4, eq 3 and 4).

5.3 Conclusion

In summary, an efficient Brønsted acid catalyzed synthetic route to tetrasubstituted furans from but-2-yne-1,4-diols and 1,3-dicarbonyl compounds under mild conditions at room temperature has been reported. The intriguing reactivities of the propargylic 1,4-diol at an elevated reaction temperature of 80 °C was also discovered and exploited to prepare the 2,3,5-trisubstituted class of furans. By judiciously applying one of these two reaction temperatures and solvent medium, our studies showed that a divergence in product selectivity was possible. Efforts to explore the scope and synthetic applications of the present reactions are currently underway and will be reported in due course.

Chapter VI. Silver-Catalyzed Cycloisomerization of 1-(2-(Allylamino)phenyl)-4-hydroxy-but-2-yn-1-ones to 1'-Allylspiro[indene-1,2'-indolin]-3'-ones

6.1 Introduction

The 3-oxindole is present in many biologically active compounds.[160] For example, the indole structure can be found in the alkaloid natural products aristotelone,[161] fluorocurine,[162] rauniticine pseudoindoxyl[163] and diketopiperazine[164] (Figure 6.1). Likewise, indenes are important synthetic targets as they are found in a myriad of bioactive natural products and their role as privileged scaffolds in bioactive pharmaceuticals (Figure 6.1).[165] Added to this is their ability to serve as versatile building blocks for functional materials[166] and utility as ligands in metallocene-based olefin polymerization catalysts.[167] For this reason, the synthesis of these two

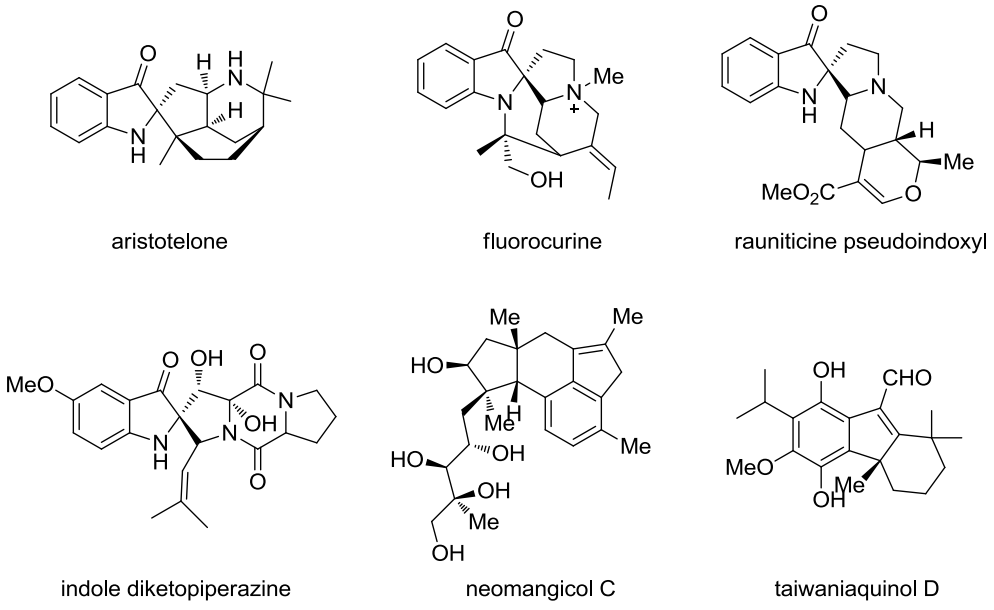
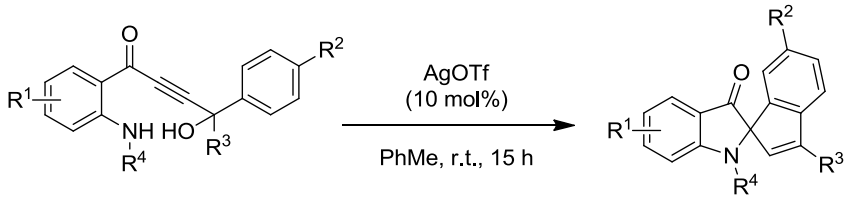


Figure 6.1 Examples of pseudoindoxyl alkaloids and indene natural products.

members of the respective N-heterocyclic family of compounds has attracted the attention of synthetic community with many elegant methods being developed over the years[168]

In the course of our studies exploring the utility of unsaturated alcohols in organic synthesis,[169] we became interested in the potential Lewis acid-catalyzed reactivity of 4-(2-aminophenyl)but-2-yn-1-ols containing a ketone at the benzylic carbon center (Scheme 6.1). To our knowledge, the cycloisomerization chemistry of this class of substrates has so far not been widely investigated. As part of our efforts to develop this type of reaction, our discovery that inexpensive, ecologically benign and readily available simple silver (I) salts can effect tandem heterocyclization/arylation of 1-(2-(allylamino)phenyl)-4-hydroxy-but-2-yn-1-ones. This process provides a convenient route to 1'-allylspiro[indene-1,2'-indolin]-3'-ones in good to excellent yields up to 94% for a wide variety of substrates under mild conditions.[170]



199 **200**

R^1 = H, Cl, Br, Me, OMe
R^2 = H, F, Cl, Br, Me, OMe
R^3 = alkyl, aryl
R^4 = Me, Bn, allyl

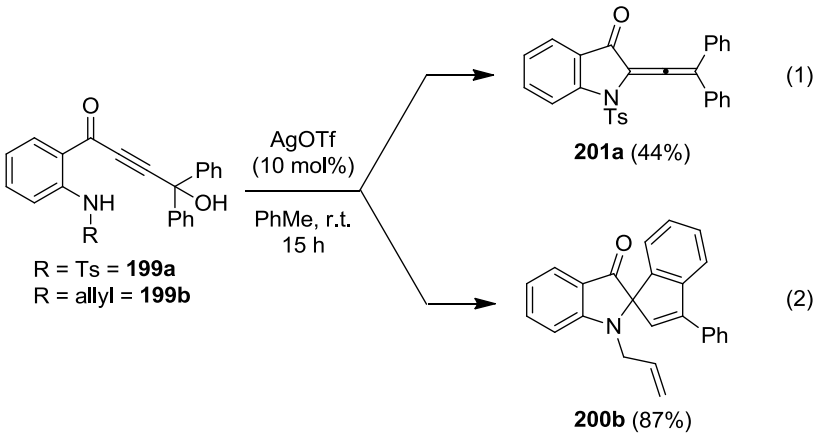
Scheme 6.1 AgOTf catalyzed reactivities

1-(2-(allylamino)phenyl)-4-hydroxy-but-2-yn-1-ones.

6.2 Results and Discussion

All the 1-(2-(allylamino)phenyl)-4-hydroxy-but-2-yn-1-ones examined in this work were prepared from reaction of the corresponding 2-(allylamino)benzaldehyde and

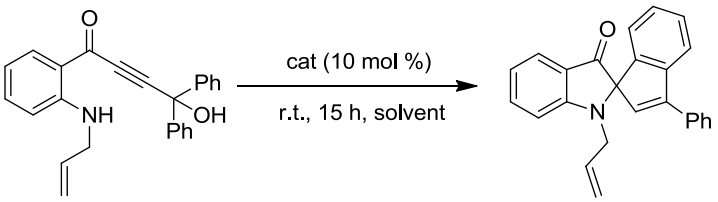
substituted prop-2-yn-1-ol pretreated with LDA followed by MnO_2 oxidation following literature procedures.[154] This initially revealed treating the probe substrate *N*-(2-(4-hydroxy-4,4-diphenylbut-2-ynoyl)phenyl)-4-methyl-benzenesulfonamide (**199a**) with 10 mol % of AgOTf in toluene at room temperature for 15 h gave the allene **201a** as the only product in 44% yield. Further continued heating of the reaction for 12 h at 80 ^{o}C did not produce any cyclization products (Scheme 6.2, eq. 1). This could be due to steric repulsions between the phenyl and tosyl group hindering the cyclization step. On the other hand, repeating the reaction with **199b** in which the protecting group is an allylic moiety, gave **200b** in 87% yield (Scheme 6.2, eq. 2). The structure of the spirocyclic product was determined by ^{1}H NMR and X-ray



Scheme 6.2 AgOTf catalyzed reactivities of N-protected 1-(2--(amino)phenyl)-4-hydroxy-but-2-yn-1-ones.

crystallography of a closely related adduct (*vide infra*). We next turned our attention to examining the cycloisomerization of **199b** in the presence of a variety of Lewis and Brønsted acid catalysts to establish the reaction conditions. The results are summarized in Table 6.1. A lower product yield of 35% was obtained on repeating the reaction with $AgSbF_6$ as the catalyst (entry 1). Changing the catalyst from AgOTf to

Table 6.1 Optimization of reaction conditions.[a]



199b **200b**

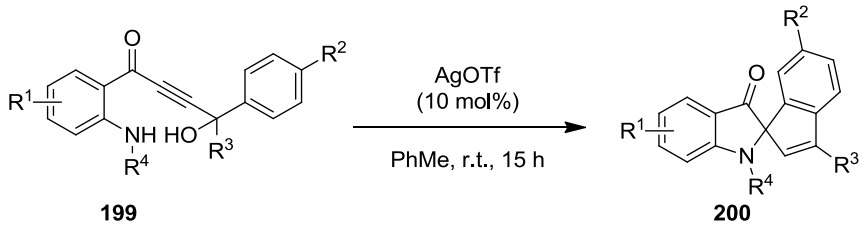
Entry	Catalyst	Solvent	Yield (%)[b]
1	$AgSbF_6$	PhMe	35
2	AgOTf	CH_2Cl_2	72
3	AgOTf	1,4-dioxane	-[c]
4	AgOTf	CH_3CN	-[c]
5	AgOTf	CH_3NO_2	81
6	$AgBF_4$	PhMe	-[c]
7	AgOAc	PhMe	-[c]
8	$AgN(Tf)_2$	PhMe	-[c]
9	$Cu(OTf)_2$	PhMe	-[d]
10	$Yb(OTf)_3$	PhMe	-[d]
11	TfOH	PhMe	-[e]
12	Tf_2NH	PhMe	-[e]

[a]All reactions were performed at the 0.14 mmol scale with 10 mol% of catalyst at r.t. for 15 h. [b]Isolated yield. [c]No reaction based on TLC and ^{1}H NMR analysis of crude reaction mixture. [d]Trace amount of product obtained based on TLC and ^{1}H NMR analysis of crude reaction mixture. [e]Mixture of decomposition products obtained based on TLC and ^{1}H NMR analysis of crude reaction mixture.

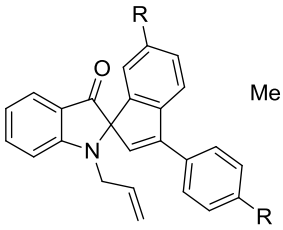
$AgBF_4$, AgOAc or $AgN(Tf)_2$ or solvent from toluene to 1,4-dioxane or CH_3CN were instances in which no reaction was observed based on TLC and ^1H NMR analysis of crude mixture. In these reactions, the starting material was recovered in near quantitative yield (entries 3-4 and 6-8). Similarly, performing the reaction with $Cu(OTf)_2$ or $Yb(OTf)_3$ or Brønsted acids like TfOH or Tf_2NH afforded either trace amount of product based on TLC analysis or decomposition (entries 9-12). On the other hand changing the solvent from toluene to dichloromethane or CH_3NO_2 gave **200b** in 72 and 81% yield, respectively (entries 2 and 5). On the basis of the above results, reaction of **199b** in the presence of 10 mol % of AgOTf in toluene at room temperature for 15 h provided the optimal conditions.

To establish the generality of the present protocol, next we examined various 1-(2-(allylamino)phenyl)-4-hydroxy-but-2-yn-1-one derivatives **199c-w** and results are presented in Table 6.2. These reactions demonstrated that with AgOTf as a catalyst, a variety of substituted 1-(2-(allylamino)phenyl)-4-hydroxy-but-2-yn-1-ones bearing alkyl, aryl, heteroaryl and halide groups provided the corresponding products **200c-w** in yields of 80-94%. Starting alcohols with an electron-withdrawing or electron-donating group on the phenyl moieties at the carbinol carbon center were found to react well, furnishing **200c-g** in excellent yields of 80-89%. Similarly, spiro[indene-1,2'-indolin]-3'-ones **200h-t** bearing a combination of electron-withdrawing and electron-donating groups at either the para or ortho position of the aniline moiety and *tert*-alcoholic carbon were afforded in comparable yields of 80-94% from the corresponding alcoholic substrates **199h-t**. More notably, reaction of **199u** containing a bulky *t*-butyl group at R^3 was found to proceed well, leading to the product **200u** in yield of 87% yield albeit requiring a higher temperature. As anticipated, starting alcohols with a thiophene or tolyl group at R^3 were found to

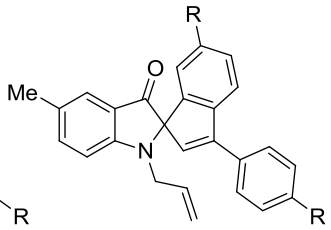
Table 6.2 Silver catalyzed tandem heterocyclization /arylation of 1-(2-(allylamino)--phenyl)-4-hydroxy-but-2-yn-1-ones **199c-y**.[a]



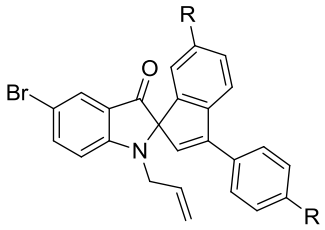
199 **200**



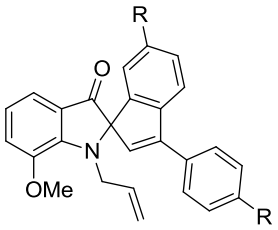
200c: R = F (82%)
200d: R = Cl (83%)
200e: R = Br (80%)
200f: R = Me (88%)
200g: R = OMe (89%)



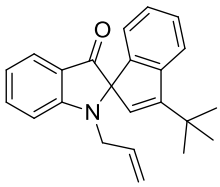
200h: R = H (90%)
200i: R = Cl (82%)
200j: R = Br (84%)
200k: R = Me (92%)
200l: R = OMe (94%)



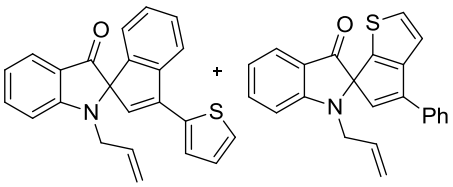
200m: R = H (85%)
200n: R = Cl (80%)
200o: R = Br (81%)
200p: R = Me (86%)
200q: R = OMe (87%)



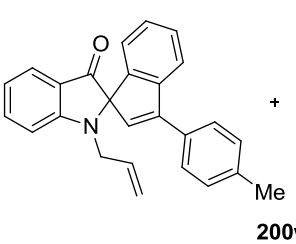
200r: R = H (88%)
200s: R = Br (83%)
200t: R = Me (86%)

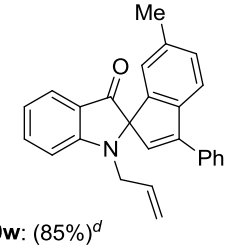


200u: (87%)[b]

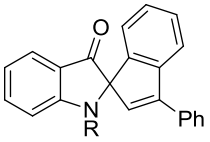


200v: (85%)[c]





200w: (85%)[d]



200x: R = Me (82%)
200y: R =Bn (84%)

[a]All reactions were performed with 10 mol% of AgOTf at r.t. for 15 h. Values in parenthesis denote isolated product yields. [b]Reaction was carried out at 100 °C for 5 h. [c]Product obtained as a 1:1 mixture of regioisomers based on ^{1}H NMR analysis of the reaction mixture. [d]Product obtained as a 1:0.55 mixture of regioisomers based on ^{1}H NMR analysis of the reaction mixture.

result in mixture of regioisomers with **200v** and **200w** obtained in yields of 85 % and a ratio of up to 1:1. The presence of other N-protecting groups such as Me or Bn was no influence on the course of the reaction with **200x-y** obtained in yields of 82-84%. The structure of **200d** was also confirmed by X-ray crystal structure analysis (Figure 6.2).[171]

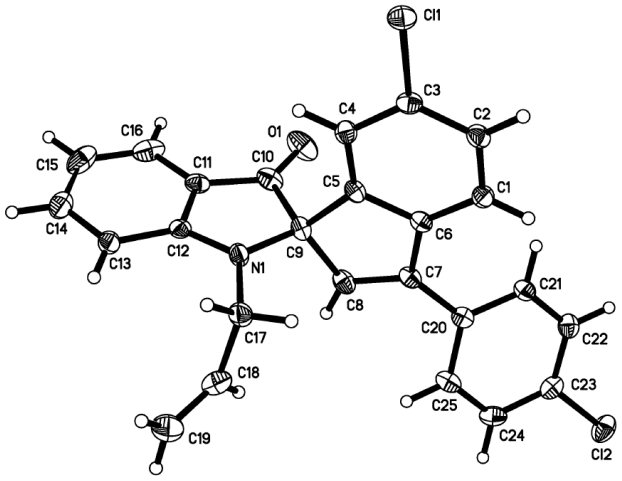
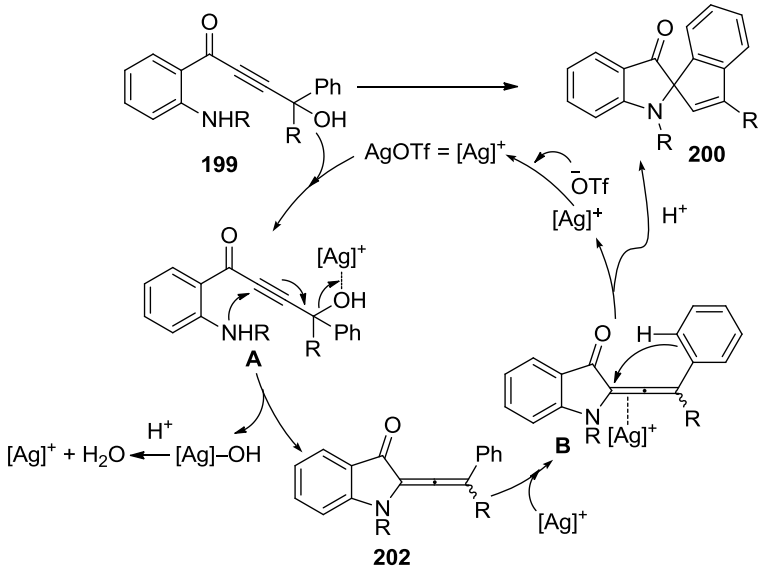


Figure 6.2 ORTEP drawing of **200d** with thermal ellipsoids at 50% probability levels.

A tentative mechanism for the present Ag(I) catalyzed spiro[indene-1,2'-indolin]-3'--one forming reaction is illustrated in Scheme 6.3. This could initially involve activation of the OH group of **199** by coordination of silver catalyst to deliver intermediate **A**. Subsequent 5-*exo*-*dig* cyclization by nucleophilic attack of the pendant aniline group to the alkyne moiety would then give the allene intermediate **202**. This newly formed allene species further undergo coordination to AgOTf, re-generated from [Ag]-OH by protonolysis to afford Ag(I) activated allene intermediate **B**. Intramolecular hydroarylation of the indole C2 center in **B** by the remaining pendant aryl ring followed by re-aromatization and a final protodemetalation step would provide the spiro product **200**.



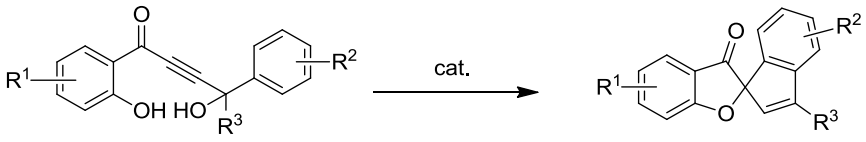
Scheme 6.3 Proposed reaction pathway for the formation of spiro[indene-1,2'-indolin]-3'-ones.

6.3 Conclusion

In summary, we have demonstrated an operationally straightforward and practical method for the efficient synthesis of pseudoindoxyl and indene skeletons in one molecule from silver-catalyzed cycloisomerization of 1-(2-(allylamino)phenyl)-4--hydroxy-but-2-yn-1-ones. The transformation was shown to be applicable to a diverse range of starting alcohols bearing electronic and sterically demanding substituents combinations. Additionally, the method proceeds under mild conditions at room temperature and produce H_2O as potentially the only side product.

Chapter VII. Future Work

As described in Chapter VI, we have developed an efficient synthetic approach to prepare 1-(2-(allylamino)-phenyl)-4-hydroxy-but-2-yn-1-ones from silver(I) catalyzed cycloisomerization of 1-(2-(allylamino)phenyl)-4-hydroxy-but-2-yn-1-ones. Spirocyclic benzofuranones are biologically important targets and have been reported to be efficient inhibitors of the human peptidyl prolyl *cis/trans* isomerase Pin1.[172] Griseofulvin family of compounds, which have been reported to known as an orally active antimycotic drug,[173] display *inter alia* anti-inflammatory[174] and herbicidal activity[175] and aromatase inhibition.[176] These interesting spirocyclic benzofuranone containing compounds **204** can be potentially occurred from tandem cycloisomerization of 4-hydroxy-1-(2-hydroxyphenyl)-4,4-di-phenylbut-2-yn-1-ones **203** in the presence of Lewis or Brønsted acid catalyzed conditions that in the similar way of Chapter VI (Scheme 7.1).



203 **204**

Scheme 7.1 Lewis or Brønsted acid catalyzed cycloisomerization of 4-hydroxy-1-(2-hydroxyphenyl)-4,4-di-phenylbut-2-yn-1-ones **203**.

Celecoxib is a non-steroidal ant-inflammatory drug (NSAID) and selective COX-2 inhibitor have been used in the treatment of osteoarthritis, rheumatoid arthritis, acute pain.[177] Recent studies showed that some members of the NSAID class have anti-cancer activity. One of these compounds, 2,5-dimethyl-celecoxib, which was shown to have no inhibitory COX-2 activity, was found to display stronger

anti-cancer activity than celecoxib. Based on these studies, we aim to prepare compounds containing both the spirobenzofuaranone and pyrazole moieties to enhance antitumor activity (Figure 7.1).

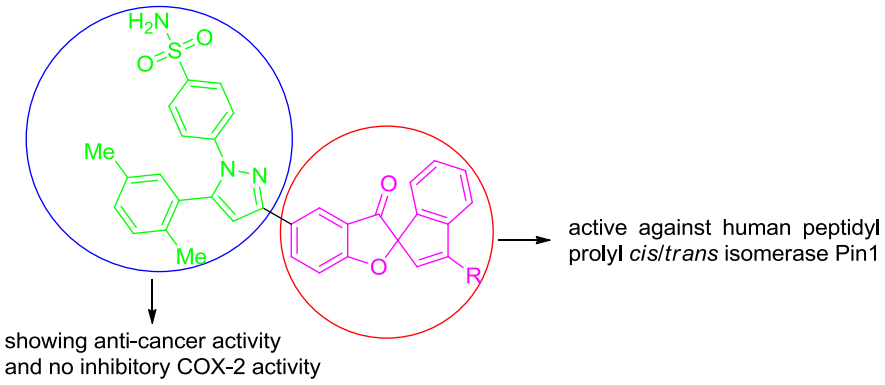
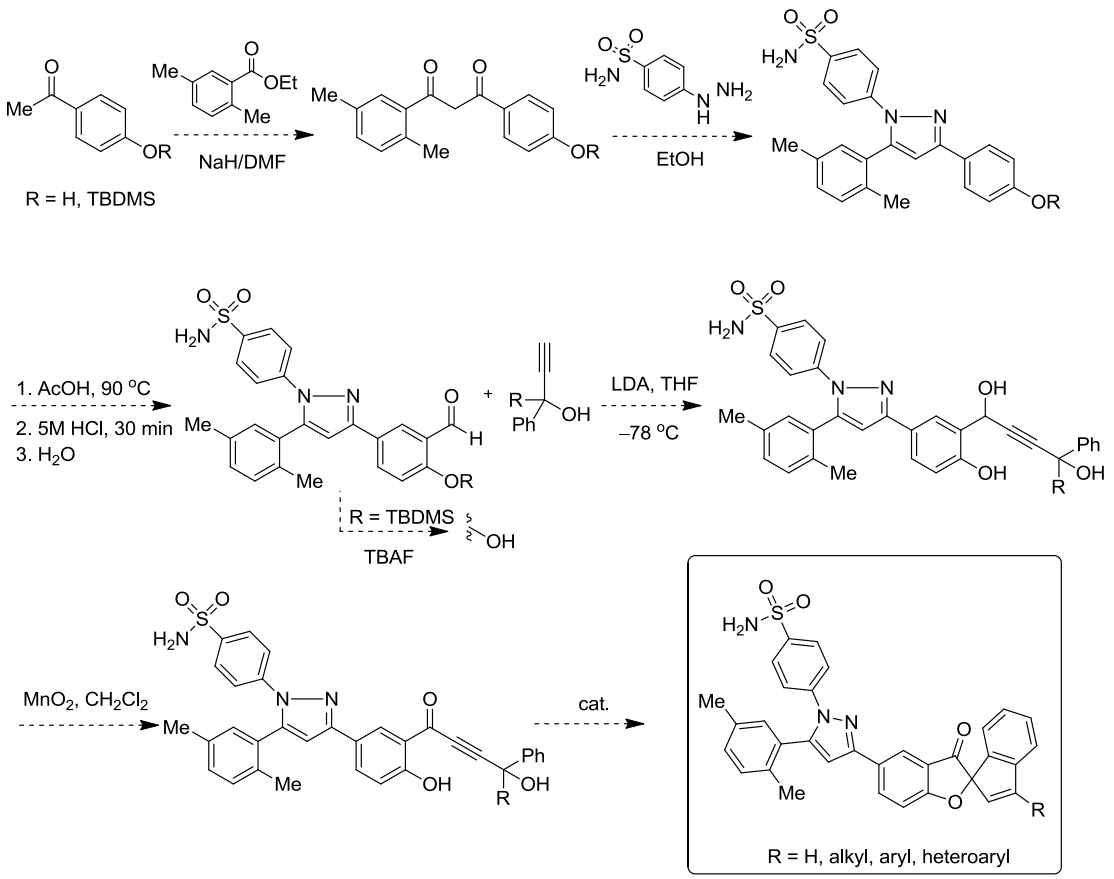


Figure 7.1: 4-(5-(2,5-dimethylphenyl)-3-(3-oxo-3H-spiro[benzofuran-2,1'-inden]-5--yl-1*H*-pyrazol-1-yl)benzenesulfonamide derivatives

Proposed Synthetic Scheme:



Chapter VIII. Concluding Remarks

Lewis and Brønsted acid catalyzed inter and intramolecular based protocols for the efficient and selective formation of conjugated enynes, *cis*-halohydrofurans, 2-alkynyl indoles, tri- and tetrasubstituted furans, and spiro-3-oxindoles from the corresponding alcohol substrates have been established (Figure 6.1). A triflic acid catalyzed ring opening of a wide variety of 1-cyclopropyl-2-propyn-1-ols with alcohols **170** as an efficient synthetic route to conjugated enynes **183** is reported in Chapter II. The reaction was operationally straightforward and accomplished in good to excellent yields (44-100%), high catalyst turnovers (up to 10,000), and with complete regioselectivity under mild conditions with a low catalyst loading of 0.01 mol %. The mechanism is suggested to involve protonation of the alcohol substrate by the TfOH

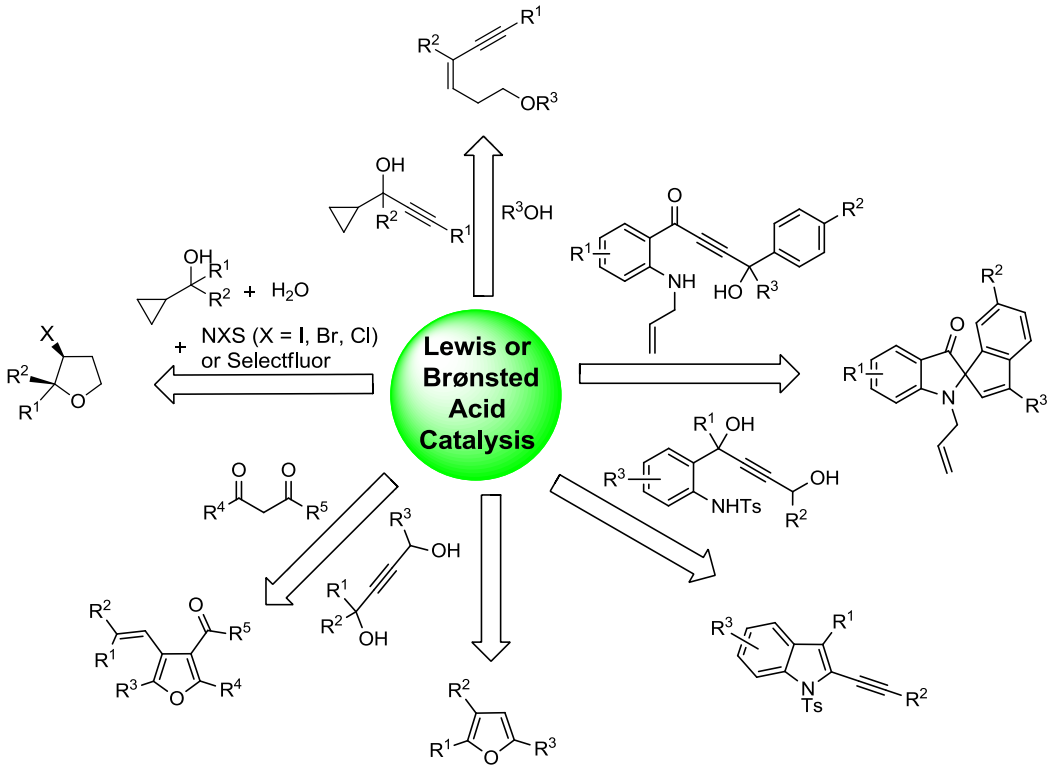


Figure 6.1 Lewis and Brønsted acid catalyzed strategies for C–X (X = C, N, O) bond formation from activated alcohols.

catalyst, followed by ionization of the starting material. This causes ring opening of the cyclopropane moiety and trapping by the alcohol nucleophile to give the conjugated enyne product. In Chapter-III, this approach was extended to prepare 3-halohydrofurans **188** by TfOH catalyzed hydroxylation/halocyclization of cyclopropyl methanols **170** with H_2O and N-halosuccinimide (NXS, X = 1, Br, Cl) or Selectfluor. The reactions proceed rapidly under mild and operationally straightforward conditions with a catalyst loading as low as 1 mol % and afford the 3-halohydrofuran products in moderate to excellent yields and, in most cases, with preferential *cis* diastereoselectivity. The mechanism is suggested to involve protonation of the alcohol substrate by the Brønsted acid catalyst and ionization of the starting material. This results in ring-opening of the cyclopropane moiety and *in situ* formation of a homoallylic alcohol intermediate, which undergoes subsequent intramolecular halocyclization on treating with the electrophilic halide source to give the halohydrofuran. The observed *cis* product selectivity is thought to be determined by the reaction proceeding through an *in situ* generated unsaturated alcohol intermediate that contains a (*Z*)-alkene moiety under the kinetically controlled conditions.

In Chapter IV, a synthetic method that relies on silver(I) mediated C–OH bond activation of 1,4-propargylic diols **190** to construct 2-alkynyl indoles **191** was reported. Previous methods to this immensely important member of the indole family of compounds have mainly relied on synthetic strategies that require a cross-coupling step and structural elements to regioselectively direct alkynylation to occur at the C2 position of the nitrogen ring. The attractiveness of the present synthetic approach lies in the fact that both the indole ring and alkyne side chain of the N-heterocycle are sequentially formed from a starting material and catalytic system that are low cost,

readily available and ecologically benign. In Chapter VI, this novel synthetic method was extended to the synthesis of spiro-3-oxindoles **200** *via* silver(I) catalyzed cycloisomerization of 1-(2-(allylamino)phenyl)-4- hydroxyl-but-2-yn-1-ones **199**. The method was shown to be applicable to a diverse set of alcohols containing electron-withdrawing, electron-donating, and sterically demanding functional groups. The method was shown to proceed under mild conditions at room temperature, affording the corresponding products in good to excellent yields (80-94%).

A Brønsted acid catalyzed method to prepare tri- and tetrasubstituted furans efficiently from cycloisomerization of but-2-yne-1,4-diols **194** with or without 1,3-dicarbonyl compounds was described in Chapter V. By taking advantage of the orthogonal modes of reactivity of the alcoholic substrate through slight modification of the reaction conditions, a divergence in product selectivity was observed. At room temperature, *p*-TsOH·H_2O mediated tandem alkylation/cycloisomerization of the propargylic 1,4-diol with the *β*-dicarbonyl compound **30** was found to selectively occur to provide the tetrasubstituted furan product **195**. On the other hand, increasing the reaction temperature to 80 °C was discovered to result in preferential *p*-TsOH·H_2O catalyzed dehydrative rearrangement of the unsaturated alcohol and formation of the 2,3,5-trisubstituted furan adduct **196**.

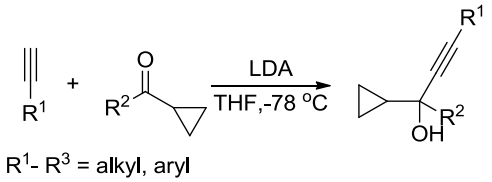
Chapter IX. Experimental Section

7.1 General Remarks

Unless specified, all reagents and starting materials were purchased from commercial sources and used as received. Cyclopropyldiphenyl methanol (**170bh**) was purchased from commercial sources and used as received. Solvents were purified following standard literature procedures. Analytical thin layer chromatography (TLC) was performed using Merck 60 F254 pre-coated silica gel plate. Visualization was achieved by UV light (254 nm). Flash chromatography was performed using Merck silica gel and gradient solvent system (EtOAc: n-hexane as eluant). ^{1}H spectra was measured on 300, 400 and 500 MHz spectrometer. Chemical shifts (ppm) were recorded with respect to TMS in $CDCl_3$. Multiplicities are given as: s (singlet), bs (broad singlet), d (doublet), dt (doublet of triplet), t (triplet), bt (broad triplet), q (quartet), aq (apparent quartet), dd (doublet of doublets), dddd (doublet of doublets of doublets of doublets), aquin (apparent quintet), or m (multiplet). The number of protons (*n*) for a given resonance is indicated by *n*H. Coupling constants are reported in Hz. Infrared spectra were recorded on Shimadzu IR Prestige-21 FTIR Spectrometer. High resolution mass spectra (HRMS) were obtained using a LC/HRMS TOF spectrometer using simultaneous electrospray (ESI). Mass spectral data are reported in units of mass to charge (*m*/*z*).

7.2 Highly Efficient Synthesis of Tri- and Tetrasubstituted Conjugated Enynes from Brønsted Acid-Catalyzed Alkoxylation of 1-Cyclopropylprop-2-yn-1-ols with Alcohols

Representative Experimental Procedure for Preparation of Substituted 1-Cyclopro--pyl-2-1-Cyclo-propyl-2-propyn-1-ols (170aa)-(170ap) and (170aw) & (170ay)-(170bd):



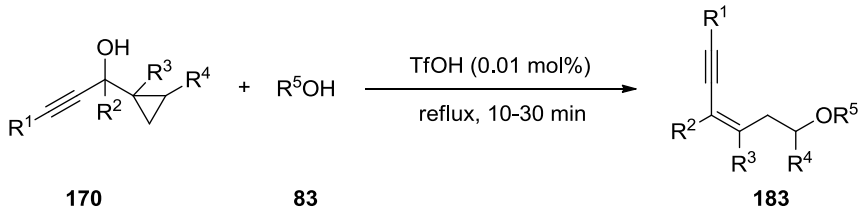
To a solution of alkyne (3 mmol, 1.0 equiv.) in THF was added LDA (2.0 M in THF, 2.25 mL, 1.5 equiv.) at –78 °C. The resulting solution was stirred for a further 1 h at –78 °C prior to slow addition of the cyclopropyl ketone (3 mmol, 1.0 equiv.) in THF (2 mL). The resulting reaction mixture was warmed up to room temperature and stirred for a further 10 h. On completion, the reaction mixture was quenched by addition of saturated NH_4Cl (10 mL) and extracted with diethyl ether (2 x 30 mL). The combined organic layers were washed with brine (20 mL), dried over Mg_2SO_4, concentrated under reduced pressure, and purified by flash column chromatography on silica gel (eluent: *n*-hexane: ethyl acetate = 9: 1) to give the title compound.

Representative Experimental Procedure for Preparation of Substituted 1- Cyclopro--pyl-2-1-Cyclo-propyl-2-propyn-1-ols (170aq)-(170av) and (170ax) & (170ay):

For (**170aq**)-(**170at**):[109] To a solution of cyclopropylmagnesium bromide (0.5 M THF solution; 3.3 mL, 1.6 mmol) in THF (5 mL) at 0 °C was added dropwise a solution of ketone (1.3 mmol) in THF (3 mL). For (**170au**)-(**170av**): To a solution of ethynylmagnesium bromide (0.5 M THF solution; 12.4 mL, 6.2 mmol) in THF (5 mL) at

0 °C was added dropwise a solution of cyclopropyl ketone (3 mmol) in diethyl ether (10 mL). For (**170ax**): To a solution of vinylmagnesium bromide (1.0 M THF solution; 0.6 mL, 0.54 mmol) in THF (3 mL) at 0 °C was added dropwise a solution of cyclopropyl ketone (0.36 mmol) in THF (2 mL). The resulting mixture was stirred at room temperature for 15 h. The mixture was treated with saturated NH_4Cl aq. (10 mL). The organic layer was extracted with diethyl ether (10 mL x 3). The combined organic layers were dried over anhydrous $MgSO_4$, and concentrated under reduced pressure. Purification by flash column chromatography on silica gel (eluent: *n*-hexane: EtOAc = 9: 1) gave the title compound.

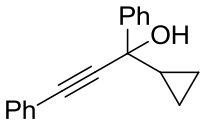
Representative Experimental Procedure for TfOH Catalyzed Preparation of Conjugated Enynes 183



170 **83** **183**

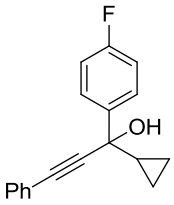
To round bottom flask containing **170** (0.2 mmol) was added TfOH (0. 01 mol%) in the form of 2 mL of a 10^{-5} M of TfOH stock solution in **83** under a nitrogen atmosphere at room temperature. The reaction mixture was stirred at reflux and monitored to completion by TLC analysis. The crude mixture was quenched with water, extracted with EtOAc (3 x 10 mL), and concentrated under reduced pressure. Purification by flash column chromatography on silica gel (eluent: *n*-hexane: EtOAc = 19: 1) furnished the title compound **183**.

Cyclopropyl-1,3-diphenylprop-2-yn-1-ol 170aa[103,104]



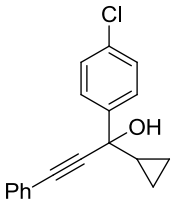
Yield: 65%; white solid; m.p. 69-71 ºC; ^{1}H NMR ($CDCl_3$, 500 MHz): δ 7.76-7.74 (m, 2H), 7.46-7.25 (m, 8H), 2.54 (s, 1H), 1.49-1.44 (m, 1H), 0.90-0.85 (m, 1H), 0.75-0.60 (m, 3H); ^{13}C NMR ($CDCl_3$, 125 MHz): δ 144.9, 131.9, 128.6, 128.4, 128.3, 127.8, 125.59, 122.5, 89.1, 86.1, 75.0, 23.9, 3.4, 2.6.

1-Cyclopropyl-1-(4-fluorophenyl)-3-phenylprop-2-yn-1-ol 170ab[103,104]



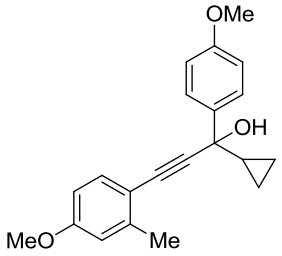
Yield: 80%; pale yellow oil; ^{1}H NMR ($CDCl_3$, 500 MHz): δ 7.72-7.68 (m, 2H), 7.44-7.25 (m, 5H), 7.07-7.03(m, 2H), 1.61-1.39 (m, 1H), 0.87-0.56 (m, 4H); ^{13}C NMR ($CDCl_3$, 125 MHz): δ 163.3, 161.3, 140.6, 131.8, 128.7, 128.3, 127.2, 122.1, 115.0 (d, 1C, *JC-F* = 83.2 Hz), 88.6, 86.2, 74.5, 23.9, 3.3, 2.4.

1-(4-Chlorophenyl)-1-cyclopropyl-3-phenylprop-2-yn-1-ol 170ac[103,104]



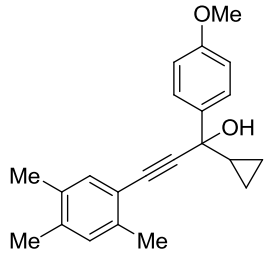
Yield: 78%; pale yellow oil; ^{1}H NMR ($CDCl_3$, 500 MHz): δ 7.70-7.28 (m, 9H), 2.5 (s, 1H), 1.45-1.43 (m, 1H), 0.89-0.63 (m, 4H); $_{13}$C NMR ($CDCl_3$, 125 MHz): δ 143.3, 133.5, 131.8, 128.7, 128.37, 128.34, 126.9, 122.1, 88.3, 86.3, 74.5, 23.9, 3.4, 2.4.

1-Cyclopropyl-3-(4-methoxy-2-methylphenyl)-1-(4-methoxyphenyl)prop-2-yn-1-ol 170ad



Yield: 68%; pale yellow oil; ^{1}H NMR ($CDCl_3$, 500 MHz): δ 7.67 (d, 2H, *J* = 8.7 Hz), 7.33 (d, 1H, *J* = 8.4 Hz), 6.91 (d, 2H, *J* = 8.7 Hz), 6.73 (d, 1H, *J* = 1.9 Hz), 6.66 (dd, 1H, *J* = 8.4, 2.3 Hz), 3.82 (s, 3H), 3.79 (s, 3H), 2.46 (d, 1H, *J* = 3.5 Hz), 1.42-1.48 (m, 1H), 0.84-0.88 (m, 1H), 0.65-0.68 (m, 1H), 0.57-0.62 (m, 2H): ^{13}C NMR ($CDCl_3$, 125 MHz): δ 159.6, 159.0, 142.0, 137.5, 133.5, 126.8, 115.1, 114.6, 113.4, 111.2, 91.7, 84.8, 77.4, 77.1, 76.9, 74.9, 55.3, 55.2, 23.8, 21.1. 2.6, 2.2; IR (neat, cm-1): 3419, 3018, 2399, 1635, 1508, 1419, 1215, 1037, 927, 756, 669; HRMS ESI): calcd for $C_{21}H_{22}O_3Na$ 345.1467, found 345.1469.

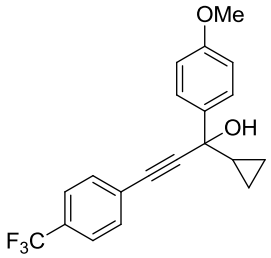
1-Cyclopropyl-1-(4-methoxyphenyl)-3-(2,4,5-trimethylphenyl)prop-2-yn-1-ol 170ae



Yield: 70%; pale yellow oil; ^{1}H NMR ($CDCl_3$, 500 MHz): δ 7.68 (d, 2H, *J* = 8.6 Hz), 7.18 (s, 1H), 6.97 (s, 1H), 6.91 (d, 2H, *J* = 8.7 Hz), 3.82 (s, 3H), 2.5 (s, 1H), 2.36 (s, 3H), 2.22 (s, 3H), 2.19 (s, 3H), 1.48-1.43 (m, 1H), 0.90-0.86 (m, 1H), 0.70-0.66 (m, 1H), 0.61-0.54 (m, 2H); ^{13}C NMR ($CDCl_3$, 125 MHz): δ 159.0, 137.4, 137.3, 133.7,

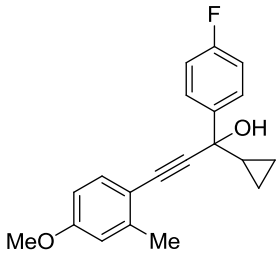
133.1, 130.8, 126.7, 119.3, 113.4, 91.8, 85.2, 75.0, 55.3, 23.7, 20.2, 19.6, 19.0, 3.2, 2.5; IR (neat, cm-1): 3419, 3018, 2399, 1635, 1508, 1215, 927, 756, 669; HRMS (ESI): calcd for $C_{22}H_{25}O_2$ 321.1855, found 321.1859.

1-Cyclopropyl-3-(4-(trifluoromethyl)phenyl)-1-(4-methoxyphenyl)prop-2-yn-1-ol 170af



Yield: 72%; pale yellow oil; ^{1}H NMR ($CDCl_3$, 500 MHz): δ 7.65 (d, 2H, *J* = 8.6 Hz), 7.55 (q, 4H, *J* = 8.2 Hz), 6.92 (d, 2H, *J* = 8.6 Hz), 3.82 (s, 3H), 2.5 (s, 1H), 1.50-1.45(m, 1H), 0.82-0.81 (m, 1H), 0.68-0.61 (m, 2H); ^{13}C NMR ($CDCl_3$, 125 MHz): δ 159.2, 136.5, 132.0, 130.1, 126.7, 126.2, 125.27, 125.24, 113.6, 91.8, 84.4, 74.4, 55.3, 23.5, 3.1, 2.4; IR (neat, cm-1): 3421, 3018, 2399, 1635, 1323, 1215, 756, 669; HRMS (ESI): calcd for $C_{20}H_{18}F_3O_2$ 347.1259, found 347.1258.

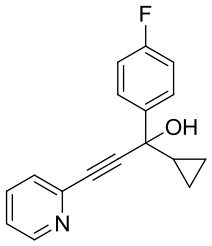
1-Cyclopropyl-1-(4-fluorophenyl)-3-(4-methoxy-2-methylphenyl)prop-2-yn-1-ol 170ag



Yield: 75%; pale yellow oil; ^{1}H NMR ($CDCl_3$, 500 MHz): δ 7.73-7.70 (m, 2H), 7.33 (d, 1H, *J* = 8.5 Hz), 7.07-7.04 (m, 2H), 6.74-6.66 (m, 2H), 3.79 (s, 3H), 2.50 (s, 1H),

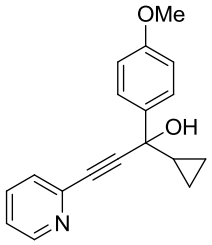
2.40 (s, 3H), 1.45-1.40 (m, 1H), 0.90-0.84 (m, 1H), 0.73-0.68 (m, 1H), 0.64-0.56 (m, 2H); ^{13}C NMR ($CDCl_3$, 125 MHz): δ 163.2, 161.3, 159.8, 142.0, 141.0, 133.5, 127.3 (d, 1C, $J_{C\text{-}F}$ = 32.3 Hz), 114.9 (t, 1C, $J_{C\text{-}F}$ = 81.1 Hz), 114.2, 111.2, 91.0, 85.2, 74.8, 55.2, 23.9, 21.0, 3.4, 2.5; IR (neat, cm-1): 3419, 3018, 2399, 1604, 1421, 1215, 927, 756, 669; HRMS (ESI): calcd for $C_{20}H_{19}FO_2Na$ 333.1267, found 333.1257.

1-Cyclopropyl-1-(4-fluorophenyl)-3-(pyridin-2-yl)prop-2-yn-1-ol 170ah



Yield: 72%; white solid; m.p. 132-234 ^{o}C; ^{1}H NMR ($CDCl_3$, 500 MHz): δ 8.56 (d, 1H, J = 4.2), 7.75 (q, 2H, J = 5.5), 7.66 (t, 1H, J = 7.1), 7.43 (d, 1H, J = 7.7), 7.25 (t, 1H, J = 6.1), 7.06 (t, 2H, J = 8.6), 3.41 (s, 1H), 1.45-1.50 (m, 1H), 0.87-0.90 (m, 1H), 0.76-0.79 (m, 1H), 0.59-0.66 (m, 2H): ^{13}C NMR ($CDCl_3$, 125 MHz): δ 163.2, 161.2, 149.7, 142.4, 140.5, 136.3, 127.4 (t, 1C, $J_{C\text{-}F}$ = 41.6) 123.1, 114.8 (d, 1C, $J_{C\text{-}F}$ =85), 90.08, 84.7, 73.6, 23.8, 3.1, 2.5; IR (neat, cm^{-1}): 3419, 3018, 2399, 1651, 1215, 927, 756, 669: HRMS (ESI): calcd for $C_{17}H_{15}FNO$ 268.1138, found 267.1136.

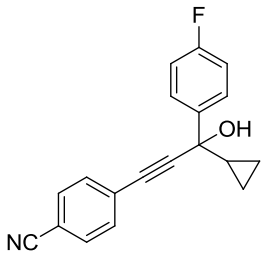
1-Cyclopropyl-1-(4-methoxyphenyl)-3-(pyridin-2-yl)prop-2-yn-1-ol 170ai



Yield: 69%; light brown solid; m.p. 84-86 ^{o}C; ^{1}H NMR ($CDCl_3$, 500 MHz): δ 8.53-8.52 (m, 1H), 7.68-7.66 (m, 2H), 7.63-7.59 (m,1H), 7.39 (d, 1H, J = 7.8), 7.25-7.19 (m, 1H),

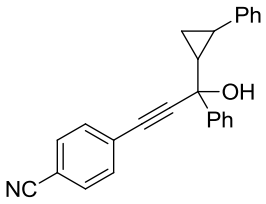
6.90-6.87 (m, 2H), 6.90-6.87 (m, 2H), 3.79 (s, 3H), 3.41 (s, 1H), 1.50-1.44 (m, 1H), 0.86-0.82 (m, 1H), 0.74-0.71 (m, 1H), 0.61-0.55 (m, 2H); ^{13}C NMR ($CDCl_3$, 125 MHz): δ 159.0, 149.8, 142.7, 136.8, 136.2, 127.2, 126.9, 123.0, 113.4, 90.4, 84.6, 73.7, 55.2, 23.6, 3.0, 2.4; IR (neat, cm^{-1}): 3421, 3018, 2399, 1635, 1419, 1215, 927, 756, 669: HRMS (ESI): calcd for $C_{18}H_{18}NO_2$ 280.1338, found 280.1340.

4-(3-Cyclopropyl-3-(4-fluorophenyl)-3-hydroxyprop-1-ynyl)benzonitrile 170aj



Yield: 70%; off white solid; m.p. 78-80 ^{o}C; ^{1}H NMR ($CDCl_3$, 500 MHz): δ 7.67 (q, 2H, J = 5.3), 7.6-7.5 (m, 4H), 7.06 (t, 1H, J = 8.6), 2.56 (s, 1H), 1.47-1.42 (m, 1H), 0.82-0.78 (m, 1H), 0.71-0.60 m, 2H); ^{13}C NMR ($CDCl_3$, 125 MHz): δ 163.3, 161.4, 139.9, 132.3, 132.0, 127.20 (t, 1C, $J_{C\text{-}F}$ = 31.5), 118.3, 115.1 (d, 1C $J_{C\text{-}F}$ = 84.9), 112.0, 93.4, 84.3, 74.2, 23.7, 3.3, 2.4; IR (neat, cm^{-1}): 3419, 3018, 2399, 1506, 1423, 1215, 927, 756, 669: HRMS (ESI): calcd for $C_{19}H_{15}FNO$ 292.1138, found 292.1142.

4-(3-Hydroxy-3-phenyl-3-(2-phenylcyclopropyl)prop-1-ynyl)benzonitrile 170ak

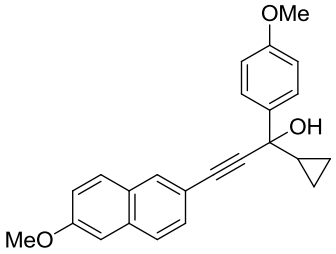


Yield: 68%; colorless oil; ^{1}H NMR ($CDCl_3$, 500 MHz): δ 7.78 (d, 2H, J = 7.4), 7.65-7.58 (m, 4H), 7.47-7.14 (m, 8H), 2.93 (s, 1H), 2.48-2.44 (m, 1H), 1.85-1.81 (m, 1H), 1.45-1.41 (m, 1H), 1.14-1.11 (m, 1H); ^{13}C NMR ($CDCl_3$, 125 MHz): δ 143.9, 141.7, 132.4, 132.1, 128.5, 128.4, 128.1, 127.2, 126.2, 125.9, 125.4, 118.3, 112.0, 94.1, 84.5, 74.1, 34.5, 20.7,

13.4; IR (neat, cm^{-1}): 3427, 3018, 2399, 1643, 1215, 927, 756, 669: HRMS (ESI): calcd for $C_{25}H_{19}NONa$ 372.1364, found 372.1350.

1-Cyclopropyl-3-(2-methoxynaphthalen-6-yl)-1-(4-methoxyphenyl)prop-2-yn-1-ol

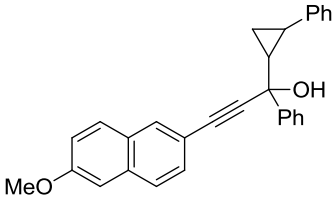
170al



Yield: 67%; white solid; m.p. 95-97 ^{o}C; ^{1}H NMR ($CDCl_3$, 500 MHz): δ 7.88 (s, 1H), 7.71-7.65 (m, 4H), 7.44 (dd, 1H, J = 1.4, J = 8.4), 7.16-7.09 (m, 2H), 6.93 (d, 2H, J = 8.8), 3.92 (s, 3H), 3.83 (s, 3H), 2.56 (s, 1H), 1.51-1.46 (m, 1H), 0.92-0.86 (m, 1H), 0.75-0.71 (m, 1H), 0.66-0.58 (m, 2H); ^{13}C NMR ($CDCl_3$, 125 MHz): δ 159.1, 158.3, 137.2, 134.2, 131.5, 129.3, 129.0, 128.3, 126.8, 119.5, 117.3, 113.5, 105.8, 88.8, 86.4, 74.6, 55.36, 55.33, 23.8, 3.2, 2.5; IR (neat, cm^{-1}): 3427, 3304, 3018, 2358, 1645, 1489, 1215, 1093, 756, 669: HRMS (ESI): calcd for $C_{24}H_{22}O_3Na$ 381.1467, found 381.1451.

3-(2-Methoxynaphthalen-6-yl)-1-phenyl-1-(2-phenylcyclopropyl)prop-2-yn-1-ol

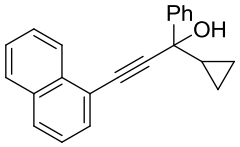
170am



Yield: 66%; pale yellow oil; ^{1}H NMR ($CDCl_3$, 500 MHz): δ 7.97 (s, 1H), 7.86 (d, 2H, J = 7.4), 7.74-7.71 (m, 2H), 7.54-7.44 (m, 4H), 7.39-7.12 (m, 7H), 3.96 (s, 3H), 2.45-2.42 (m, 1H), 1.88-1.83 (m, 1H), 1.66-1.62 (m, 1H), 1.17-1.12 (m, 1H); ^{13}C NMR ($CDCl_3$, 125 MHz): δ 158.4, 144.7, 141.8, 134.3, 131.7, 129.3, 129.0, 128.5, 128.4, 128.3, 127.9,

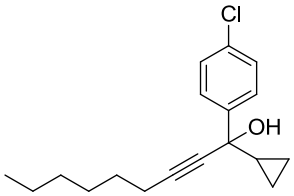
126.9, 126.5, 125.8, 125.5, 119.5, 117.1, 105.8, 89.0, 87.0, 74.2, 55.3, 34.3, 21.5, 12.2; IR (neat, cm^{-1}): 3419, 3018, 2399, 1635, 1215, 756, 669: HRMS (ESI): calcd for $C_{29}H_{25}O2$ 405.1855, found 405.1864.

1-Cyclopropyl-3-(naphthalen-1-yl)-1-phenylprop-2-yn-1-ol 170an



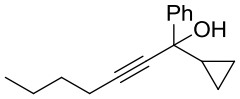
Yield: 85%; light brown Color oil; ^{1}H NMR ($CDCl_3$, 400 MHz): δ 8.28 (d, 1H, J = 8.1), 7.86-7.33 (m, 11H), 2.66 (s, 1H), 1.58-1.53 (m, 1H), 1.02-0.82 (m, 2H), 0.72-0.67 (m, 2H); ^{13}C NMR ($CDCl_3$, 100 MHz): δ 144.8, 133.3, 133.1, 130.9, 129.0, 128.35, 128.32, 127.8, 126.9, 126.4, 125.9, 125.5, 125.1, 120.0, 93.9, 84.2, 75.3, 23.9, 3.4, 2.6; IR (neat, cm^{-1}): 3415, 3018, 1215, 756, 699, 667: HRMS (ESI): calcd for $C_{22}H_{19}O$ 299.1436, found 299.1422.

1-(4-Chlorophenyl)-1-cyclopropylnon-2-yn-1-ol 170ao



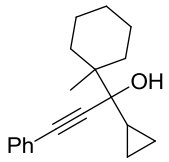
Yield: 65%; pale yellow oil; ^{1}H NMR ($CDCl_3$, 500 MHz): δ 7.59 (d, 2H, J = 8.5), 7.31 (d, 2H, J = 8.5), 2.34 (s, 1H), 2.23 (t, 2H, J = 7.05), 1.48-1.56 (m, 2H), 1.26-1.41 (m, 7H), 0.89 (*t*, 3H, J = 6.9), 0.74-0.77 (m, 1H), 0.50-0.60 (m, 3H); ^{13}C NMR ($CDCl_3$, 125 MHz): δ 128.16, 126.90, 87.36, 79.43, 74.29, 31.27, 28.58, 28.53, 23.77, 22.55, 18.6, 14.0, 3.3, 2.3; IR (neat, cm^{-1}): 3419, 3018, 2931, 2399, 1645, 1215, 756, 669: HRMS (ESI): calcd for $C_{18}H_{24}ClO$ 291.1516, found 291.1527.

1-cyclopropyl-1-phenylhept-2-yn-1-ol 170ap



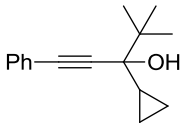
Yield: 60%; colorless oil; ^{1}H NMR ($CDCl_3$, 500 MHz): δ 7.66 (d, 2H, J = 7.8), 7.35-7.22 (m, 3H), 2.25 (s, 1H), 2.23 (t, 2H, J = 7.0), 1.53-1.47 (m, 2H), 1.44-1.37 (m, 2H), 1.34-1.29 (m, 1H), 0.91 (t, 3H, J = 7.2), 0.78-0.74 (m, 1H), 0.60-0.46 (m, 3H); ^{13}C NMR ($CDCl_3$, 125 MHz): δ 145.5, 128.0, 127.4, 125.4, 86.8, 79.9, 74.7, 30.8, 23.7, 22.0, 18.3, 13.6, 3.2, 2.3; IR (neat, cm^{-1}): 3410, 3019, 1215, 1030, 758, 699, 669: HRMS (ESI): calcd for $C_{16}H_{20}ONa$ 251.1412, found 251.1408.

1-Cyclopropyl-1-(1-methylcyclohexyl)-3-phenylprop-2-yn-1-ol 170aq



Yield: 78%; light yellow color oil; ^{1}H NMR ($CDCl_3$, 500 MHz): δ 7.40-7.25 (m, 5H), 1.91 (s, 1H), 1.77-1.60 (m, 7H), 1.58-1.39 (m, 2H), 1.33-1.25 (m, 1H), 1.16 (s, 3H), 1.14-1.09 (m, 1H), 0.68-0.56 (m, 3H), 0.47-0.41 (m, 1H); ^{13}C NMR ($CDCl_3$, 125 MHz): δ 131.6, 128.2, 128.1, 122.9, 88.8, 85.8, 80.3, 42.4, 32.4, 31.5, 26.3, 22.1, 22.0, 17.9, 15.7, 4.6, 0.5; IR (neat, cm^{-1}): 3415, 3018, 1215, 759, 699, 667: HRMS (ESI): calcd for $C_{19}H_{25}O$ 269.1905, found 269.1918.

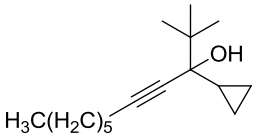
3-Cyclopropyl-4,4-dimethyl-1-phenylpent-1-yn-3-ol 170ar



Yield: 82%; colorless oil; ^{1}H NMR ($CDCl_3$, 500 MHz): δ 7.41-7.28 (m, 5H), 1.93 (s, 1H), 1.32-1.26 (m, 1H), 1.16 (s, 9H), 0.68-0.58 (m, 3H), 0.49-0.41 (m, 1H); ^{13}C NMR ($CDCl_3$,

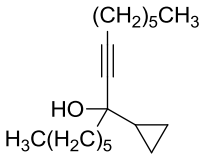
125 MHz): δ 131.6, 128.26, 128.21, 122.8, 88.7, 85.4, 79.3, 39.7, 25.7, 16.3, 4.6, 0.7; IR (neat, cm^{-1}): 3425, 3018, 1215, 757, 699, 667: HRMS (ESI): calcd for $C_{16}H_{20}ONa$ 251.1412, found 251.1421.

3-Cyclopropyl-2,2-dimethylundec-4-yn-3-ol 170as



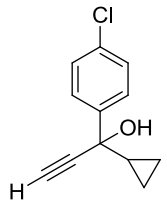
Yield: 80%; colorless oil; ^1H NMR ($CDCl_3$, 500 MHz): δ 2.17 (t, 2H, J = 6.9), 1.75 (s, 1H), 1.50-1.44 (m, 2H), 1.40-1.15 (m, 7H), 1.08 (s, 9H), 0.89 (t, 3H, J = 6.9), 0.55-0.52 (m, 3H), 0.39-0.34 (m, 1H); ^{13}C NMR ($CDCl_3$, 125 MHz): δ 85.8, 79.08, 79.00, 39.4, 31.2, 28.7, 28.5, 25.6, 22.5, 18.5, 16.1, 14.0, 4.6, 0.5; IR (neat, cm^{-1}): 3419, 3018, 2921, 2299, 1645, 1215, 756, 667: HRMS (ESI): calcd for $C_{16}H_{29}O$ 237.2218, found 237.2217.

-Cyclopropylpentadec-8-yn-7-ol 170at



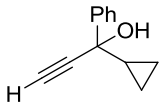
Yield: 75%; colorless oil; ^1H NMR ($CDCl_3$, 500 MHz): δ 2.08 (t, 2H, J = 6.9), 2.04 (s, 1H), 1.66-1.60 (m, 2H), 1.48-1.17 (m, 16H), 1.00-0.94 (m, 1H), 0.83-0.80 (m, 6H), 0.50-0.28 (m, 4H); ^{13}C NMR ($CDCl_3$, 125 MHz): δ 85.2, 79.8, 73.3, 67.8, 43.2, 31.8, 31.2, 29.5, 28.7, 28.4, 25.5, 24.5, 22.6, 22.5, 20.8, 18.4, 14.0, 13.9, 2.8, 0.6; IR (neat, cm^{-1}): 3421, 3018, 2928, 2358, 1634, 1215, 1109, 757, 669: HRMS (ESI): calcd for $C_{18}H_{33}O$ 265.2531, found 265.2536.

1-(4-Chlorophenyl)-1-cyclopropylprop-2-yn-1-ol 170au



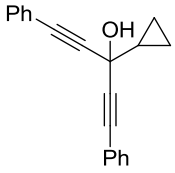
Yield:70%; brown oil; ^{1}H NMR ($CDCl_3$, 500 MHz): δ 7.62-7.60 (m, 2H), 7.36-7.33 (m, 2H), 2.87 (s, 1H), 2.61 (s, 1H), 1.37-1.31 (m, 1H), 0.83-0.75 (m, 1H), 0.68-0.54 (m, 3H); ^{13}C NMR ($CDCl_3$, 125 MHz): δ 142.8, 133.5, 128.3, 126.9, 83.3, 74.4, 73.8, 23.4, 3.2, 2.3; HRMS (ESI): calcd for $C_{12}H_{12}ClO$ 207.0577, found 207.0579.

1-Cyclopropyl-1-phenylprop-2-yn-1-ol 170av



Yield: 87%; brown color oil; ^{1}H NMR ($CDCl_3$, 500 MHz): δ 7.68 (d, 2H, J = 8.0), 7.38-7.29 (m, 3H), 2.58 (s, 1H), 2.45 (s, 1H), 1.41-1.36 (m, 1H), 0.80-0.78 (m, 1H), 0.68-0.56 (m, 3H); ^{13}C NMR ($CDCl_3$, 125 MHz): δ 144.2, 128.2, 127.8, 125.3, 83.8, 74.2, 74.1, 23.4, 3.2, 2.2; IR (neat, cm^{-1}): 3435, 3018, 1643, 1215, 756, 460: HRMS (ESI): calcd for $C_{12}H_{13}O$ 173.0966, found 173.0960.

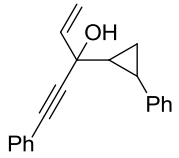
3-Cyclopropyl-1,5-diphenylpenta-1,4-diyn-3-ol 170aw



Yield: 86%; colorless oil; ^{1}H NMR ($CDCl_3$, 500 MHz): δ 7.49-7.25 (m, 10H), 2.71 (s, 1H), 1.71-1.62 (m, 1H), 0.85-0.82 (m, 2H), 0.70-0.66 (m, 2H); ^{13}C NMR ($CDCl_3$, 125 MHz): δ 131.9, 128.7, 128.2, 122.0, 87.6, 83.6, 66.4, 22.5, 2.7; IR (neat, cm^{-1}): 3421,

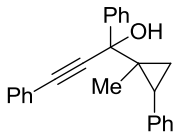
3018, 2399, 1635, 1323; 1215, 756, 669: HRMS (ESI): calcd for $C_{20}H_{16}ONa$ 295.1099, found 295.1085.

5-Phenyl-3-(2-phenylcyclopropyl)pent-1-en-4-yn-3-ol 170ax



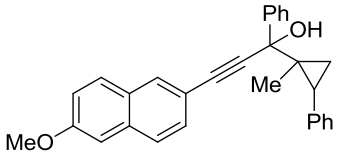
Yield: 74%; pale yellow oil; ^{1}H NMR ($CDCl_3$, 500 MHz): δ 7.46-7.12 (m, 10H), 6.13-6.07 (m, 1H), 5.64 (d, 1H, J = 17.0 Hz), 5.24 (d, 1H, J = 10.2 Hz), 2.33-2.29 (m, 1H), 2.24 (s, 1H), 1.61-1.56 (m, 1H), 1.28-1.25 (m, 1H), 1.03-0.87 (m, 1H); ^{13}C NMR ($CDCl_3$, 125 MHz): δ 142.0, 140.2, 131.8, 129.9, 128.6, 128.3, 126.2, 125.7, 122.2, 114.5, 87.7, 86.4, 72.8, 32.0, 20.0, 12.7; IR (neat, cm^{-1}): 3419, 3018, 2398, 1645, 1215, 757, 665: HRMS (ESI): calcd for $C_{20}H_{19}O$ 275.1436, found 275.1425.

1-(1-Methyl-2-phenylcyclopropyl)-1,3-diphenylprop-2-yn-1-ol 170ay



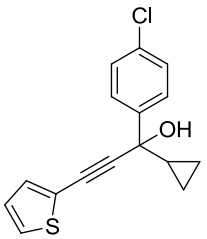
Yield: 85%; pale yellow color oil: mixture of diastereomers A: B = 3: 2; ^{1}H NMR ($CDCl_3$, 400 MHz): δ 7.83-7.20 (m, 26H), 2.93-2.86 (m, 1H), 2.57 (s, 1H, diastereomer A), 2.56 (s, 1H, diastereomer B), 1.77-1.73 (m, 1H, diastereomer B), 1.65-1.61 (m, 1H, diasteriomer A), 0.99-0.94 (m, 1H), 0.79 (s, 3H, diastereomer A), 0.73 (s, 3H, diastereomer B); ^{13}C NMR ($CDCl_3$, 100 MHz): δ 143.49, 143.47, 139.2, 139.1, 129.3, 129.2, 128.6, 128.45, 128.41, 128.07, 128.04, 127.84, 127.80, 126.4, 125.9, 122.58, 122.56, 91.0, 90.9, 85.9, 85.8, 77.3, 76.33, 76.31, 31.7, 31.6, 26.0, 25.3, 15.7, 15.6, 15.5, 14.5; IR (neat, cm^{-1}): 3415, 3019, 1215, 757, 668: HRMS (ESI): calcd for $C_{25}H_{23}O$ 339.1749, found 339.1744.

3-(6-Methoxynaphthalen-2-yl)-1-(1-methyl-2-phenylcyclopropyl)-1-phenylprop-2-yn-1-ol 170az



Yield: 82%; pale yellow color oil: mixture of diastereomers A: B = 3: 2; ^{1}H NMR ($CDCl_3$, 400 MHz): δ 7.91-7.07 (m, 32H), 3.879 (s, 3H, diastereomer B), 3.875 (s, 3H, diastereomer A), 2.91-2.84 (m, 1H), 2.61 (s, 2H), 1.74-1.70 (m, 1H, diastereomer B), 1.63-1.59 (m, 1H, diastereomer A), 0.95-0.90 (m, 1H), 0.75 (s, 3H, diastereomer A), 0.69 (s, 3H, diastereomer B); ^{13}C NMR ($CDCl_3$, 100 MHz): δ 158.43, 158.42, 143.65, 143.60, 139.27, 139.21, 134.3, 131.6, 129.3, 129.2, 129.1, 129.0, 128.46, 128.44, 128.3, 128.1, 128.0, 127.8, 127.7, 126.9, 126.8, 126.6, 126.4, 126.3, 125.9, 119.58, 119.55, 117.3, 105.8, 90.6, 90.5, 86.4, 86.3, 77.3, 76.4, 76.3, 55.3, 31.8, 31.7, 26.1, 25.3, 15.7, 15.6, 15.5, 14.6, 14.2; IR (neat, cm^{-1}): 3417, 3019, 1215, 756, 668: HRMS (ESI): calcd for $C_{30}H_{27}O_2$ 419.2011, found 419.2020.

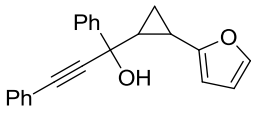
1-(4-Chlorophenyl)-1-cyclopropyl-3-(thiophen-2-yl)prop-2-yn-1-ol 170ba



Yield: 65%; pale yellow oil; ^{1}H NMR ($CDCl_3$, 500 MHz): δ 7.66-7.63 (m, 2H), 7.459-7.451 (m, 1H), 7.35-7.26 (m, 3H), 7.10-7.09 (m, 1H), 2.49 (s, 1H), 1.43-1.37 (m, 1H), 0.85-0.81 (m, 1H), 0.71-0.67 (m, 1H), 0.63-0.57 (m, 2H); ^{13}C NMR ($CDCl_3$, 125 MHz): δ 143.4, 133.5, 129.9, 129.3, 128.3, 127.0, 125.5, 121.1, 88.2, 81.4, 74.4, 23.8, 3.3, 2.5; IR (neat, cm^{-1}): 3585, 3419, 3018, 2399, 1489, 1215, 1091, 1033, 927, 756,

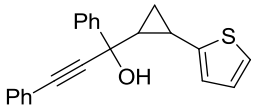
669: HRMS (ESI): calcd for $C_{16}H_{14}ClOS$ 289.0454, found 289.0455.

1-(2-(Furan-2-yl)cyclopropyl)-1,3-diphenylprop-2-yn-1-ol 170bb



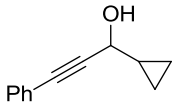
Yield: 60%; colorless oil; ^{1}H NMR ($CDCl_3$, 500 MHz): δ 7.78-7.77 (m, 2H), 7.51-7.25 (m, 9H), 6.28 (q, 1H, J = 1.8), 6.02 (d, 1H, J = 3.1), 2.72 (s, 1H), 2.53-2.49 (m, 1H), 1.92-1.88 (m, 1H), 1.36-1.32 (m, 1H), 1.14-1.10 (m, 1H); ^{13}C NMR ($CDCl_3$, 125 MHz): δ 155.5, 144.2, 140.7, 131.8, 128.7, 128.4, 127.9, 125.4, 122.1, 110.3, 104,1, 88.6, 86.7, 74.2, 32.4, 14.2, 11.59; IR (neat, cm^{-1}): 3419, 3018, 2092, 1639, 1521, 1423, 1215, 927, 765, 669: HRMS (ESI): calcd for $C_{22}H1_9O_2$ 315.1385, found 315.1397.

1,3-Diphenyl-1-(2-(thiophen-2-yl)cyclopropyl)prop-2-yn-1-ol 170bc



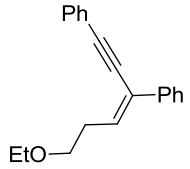
Yield: 83%; light brown color oil; ^{1}H NMR ($CDCl_3$, 400 MHz): δ 7.80-7.78 (m, 2H), 7.51-7.33 (m, 8H), 7.05-6.71 (m, 3H), 2.66 (s, 1H), 2.52-2.48 (m, 1H), 1.83-1.78 (m, 1H), 1.62-1.57 (m, 1H), 1.16-1.09 (m, 1H); ^{13}C NMR ($CDCl_3$, 100 MHz): δ 146.1, 144.3, 131.9, 128.8, 128.46, 128.43, 128.0, 126.8, 125.4, 123.3, 122.7, 122.2, 89.1, 86.6, 73.7, 35.0, 16.6, 13.2 ; IR (neat, cm^{-1}): 3415, 3018, 1489, 1446, 1215, 1029, 756, 669, 449: HRMS (ESI): calcd for $C_{22}H_{19}OS$ 331.1157, found 331.1168.

1-Cyclopropyl-3-phenylprop-2-yn-1-ol 170bd



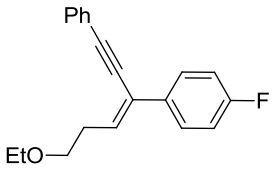
Yield: 80%; light yellow color oil; ^{1}H NMR ($CDCl_3$, 500 MHz): δ 7.39-7.37 (m, 2H), 7.27-7.25 (m, 3H), 4.40 (t, 1H, *J* = 5.5), 2.07 (d, 1H, *J* = 5.2), 1.35-1.27 (m, 1H), 0.60-0.45 (m, 4H); ^{13}C NMR ($CDCl_3$, 125 MHz): δ 131.7, 128.4, 128.2, 122.5, 87.8, 85.0, 66.2, 17.2 3.3, 1.6; IR (neat, cm^{-1}): 3415, 3018, 1215, 1027, 756, 667: HRMS (ESI): calcd for $C_{12}H_{13}O$ 173.0966, found 173.0974.

(*Z*)-6-Ethoxy-1,3-diphenylhex-3-en-1-yne 183aa



Colorless oil; ^{1}H NMR ($CDCl_3$, 300 MHz): δ 7.71-7.68 (m, 2H), 7.57-7.53 (m, 2H), 7.40-7.30 (m, 6H), 6.55 (t, 1H, *J* = 7.3), 3.64 (t, 2H, *J* = 6.7), 3.57 (q, 2H, *J* = 7.0), 2.90 (q, 2H, *J* = 6.8), 1.25 (t, 3H, *J* = 6.9); ^{13}C NMR ($CDCl_3$, 75 MHz): δ 138.0, 134.6, 131.5, 128.39, 128.38, 128.31, 127.6, 126.0, 124.9, 123.4, 95.5, 86.6, 69.4, 66.2, 32.0, 15.2; IR (neat, cm^{-1}): 3419, 3018, 2399, 1645, 1215, 756, 669: HRMS (ESI): calcd for $C_{20}H_{21}O$ 277.1592.0, found 277.1605.

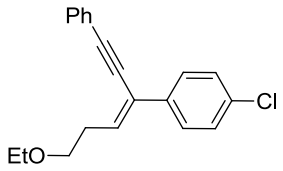
(*Z*)-1-(6-Ethoxy-1-phenylhex-3-en-1-yn-3-yl)-4-fluorobenzene 183ab



Colorless oil; ^{1}H NMR ($CDCl_3$, 500 MHz): δ 7.66-7.63 (m, 2H), 7.54-7.53 (m, 2H), 7.37-7.35 (m, 3H), 7.05 (t, 2H, *J* = 8.6 Hz), 6.47 (t, 1H, *J* = 7.3 Hz) 3.63 (t, 2H, *J* =

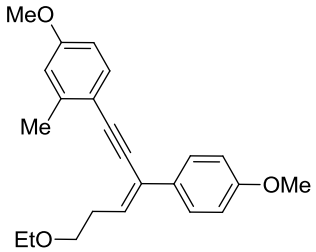
6.7 Hz), 3.56 (q, 2H, *J* = 7.0 Hz), 2.88 (q, 2H, *J* = 6.9 Hz), 1.25 (t, 3H, *J* = 7.0 Hz); ^{13}C NMR ($CDCl_3$, 125 MHz): δ 163.4, 161.4, 134.4, 134.2, 134.1, 131.5, 128.4, 127.7 (d, 1C, $J_{C\text{-}F}$ = 32.2 Hz), 123.8, 123.2, 115.3 (d, 1C, $J_{C\text{-}F}$ = 85.5 Hz), 95.7, 86.3, 69.4, 66.2, 32.0, 15.2; IR (neat, cm^{-1}): 3437, 2866, 1602, 1506, 1232, 1109, 833, 754, 460; HRMS (ESI): calcd for $C_{20}H_{20}OF$ 295.1498, found 295.1493.

(*Z*)-1-Chloro-4-(6-ethoxy-1-phenylhex-3-en-1-yn-3-yl)benzene 183ac



Colorless oil; ^{1}H NMR ($CDCl_3$, 500 MHz): δ 7.61-7.52 (m, 4H), 7.37-7.32 (m, 5H), 6.52 (t, 1H, *J* = 7.3 Hz) 3.63 (t, 2H, *J* = 6.7 Hz), 3.56 (q, 2H, *J* = 7.0 Hz), 2.88 (q, 2H, *J* = 6.8 Hz), 1.24 (t, 3H, *J* = 7.0 Hz); ^{13}C NMR ($CDCl_3$, 125 MHz): δ 136.5, 135.1, 133.4, 131.5, 128.5, 128.49, 128.43, 127.3, 123.8, 123.1, 95.9, 86.1, 69.3, 66.2, 32.0, 15.2; IR (neat, cm^{-1}): 3439, 3018, 1643, 1489, 1215, 1095, 756, 464; HRMS (ESI): calcd for $C_{20}H_{20}OCl$ 311.1203, found 311.1208.

1-((*Z*)-6-Ethoxy-1-(4-methoxy-2-methylphenyl)hex-3-en-1-yn-3-yl)-4-methoxybenzene 183ad

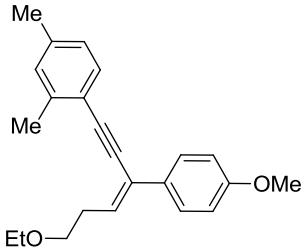


Yellow oil; ^{1}H NMR ($CDCl_3$, 500 MHz): δ 7.61 (d, 2H, *J* = 8.5 Hz), 7.42 (d, 1H, *J* = 8.4 Hz), 6.9 (d, 2H, *J* = 2.7 Hz), 6.78-6.70 (m, 2H), 6.37 (t, 1H, *J* = 7.3 Hz), 3.82 (s, 3H), 3.81 (s, 3H), 3.61 (t, 3H, *J* = 6.8 Hz), 3.53 (q, 2H, *J* = 7.0 Hz), 2.84 (q, 2H, *J* =

7.0 Hz), 2.49 (s, 3H), 1.23 (t, 3H, *J* = 7.0 Hz); ^{13}C NMR ($CDCl_3$, 125 MHz): δ 159.6, 159.2, 141.7, 133.3, 131.5, 131.0, 127.2, 124.7, 115.6, 115.1, 113.7, 113.3, 94.5, 89.3, 69.6, 66.1, 55.3, 55.2, 32.0, 21.3, 15.2; IR (neat, cm^{-1}): 3419, 3018, 2399, 1602, 1508, 1215, 116, 1035, 929, 756, 669; HRMS (ESI): calcd for $C_{23}H_{27}O_3$ 351.1960, found 351.1961.

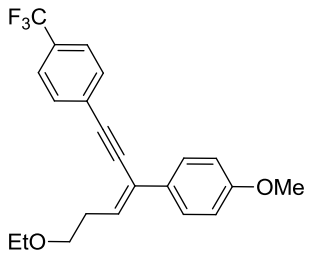
1-((*Z*)-6-Ethoxy-3-(4-methoxyphenyl)hex-3-en-1-ynyl)-2,4,5-trimethylbenzene

183ae



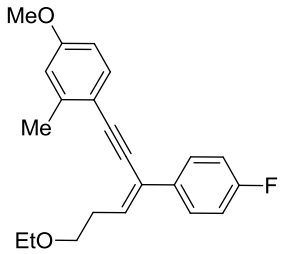
Pale yellow oil; ^{1}H NMR ($CDCl_3$, 500 MHz): δ 7.63-7.60 (m, 2H), 7.27 (s, 1H), 7.00 (s, 1H), 6.90-6.87 (m, 2H), 6.38 (t, 1H, *J* = 7.3 Hz), 3.82 (s, 3H), 3.61 (t, 2H, *J* = 6.8 Hz), 3.54 (q, 2H, *J* = 7.2 Hz), 2.85 (q, 2H, *J* = 6.9 Hz), 2.43 (s, 3H), 2.24 (s, 3H), 2.22 (s, 3H), 1.22 (t, 3H, *J* = 7.0 Hz); ^{13}C NMR ($CDCl_3$, 125 MHz): δ 159.2, 137.2, 137.1, 133.7, 132.9, 131.8, 131.0, 130.9, 127.2, 124.7, 120.4, 113.71, 94.8, 89.6, 69.6, 66.1, 55.3, 32.0, 20.4, 19.7, 19.0, 15.2; IR (neat, cm^{-1}): 3419, 3018, 2358, 1600, 1215, 1109, 927, 756, 669; HRMS (ESI): calcd for $C_{24}H_{29}O_2$ 349.2168, found 349.2169.

1-((*Z*)-6-Ethoxy-3-(4-methoxyphenyl)hex-3-en-1-ynyl)-4-(trifluoromethyl)--benzene 183af



Pale yellow oil; ^{1}H NMR ($CDCl_3$, 500 MHz): δ 7.62-7.56 (m, 6H), 6.90-6.88 (m, 2H), 6.45 (t, 1H, J = 7.3 Hz), 3.82 (s, 3H), 3.61 (t, 2H, J = 6.7 Hz), 3.54 (q, 2H, J = 7.0 Hz), 2.84 (q, 2H, J = 6.9 Hz), 1.22 (t, 3H, J = 7.0 Hz); ^{13}C NMR ($CDCl_3$, 125 MHz): δ 159.4, 134.0, 131.7, 130.3, 127.2, 127.1, 125.3, 125.28, 125. 25, 123.8, 113.8, 93.8, 89.2, 69.4, 66.2, 55.3, 32.0, 15.2; IR (neat, cm^{-1}): 3419, 3018, 2399, 1600, 1519, 1323, 1215, 1132, 927, 756, 669; HRMS (ESI): calcd for $C_{22}H_{22}F_3O_2$ 375.1572, found 375.1559.

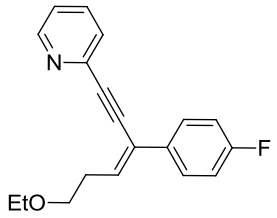
1-((*Z*)-6-Ethoxy-1-(4-methoxy-2-methylphenyl)hex-3-en-1-yn-3-yl)-4-fluorobenzene 183ag



Pale yellow oil; ^{1}H NMR ($CDCl_3$, 500 MHz): δ 7.66-7.62 (m, 2H), 7.42 (d, 1H, J = 8.5 Hz), 7.06-7.02 (m, 2H), 6.78-6.71 (m, 2H), 6.40 (t, 1H, J = 7.3 Hz), 3.81 (s, 3H), 3.61 (t, 2H, J = 6.7 Hz), 3.54 (q, 2H, J = 7.0 Hz), 2.85 (q, 2H, J = 6.9 Hz), 2.48 (s, 3H), 1.22 (t, 3H, J = 7.0 Hz); ^{13}C NMR ($CDCl_3$, 125 MHz): δ 163.3, 161.4, 159.7, 141.7, 134.5 (d, 1C, $J_{C\text{-}F}$ =12.2 Hz), 133.3(d, 1C, $J_{C\text{-}F}$ = 30.1), 127.70 (d, 1C, $J_{C\text{-}F}$ =

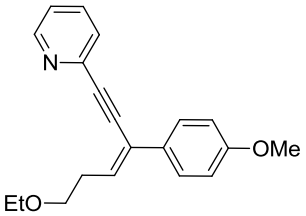
31.9 Hz), 124.3, 115.4, 115.2 (d, 1C, $J_{C\text{-}F}$ = 30.9 Hz), 115.0, 111.3, 94.8, 88.9, 69.4, 66.2, 55.2, 32.0, 21.3, 15.2; IR (neat, cm^{-1}): 3421, 3018, 2399, 1602, 1508, 1423, 1215, 927, 769, 756, 669; HRMS (ESI): calcd for $C_{22}H_{23}FO_2Na$ 361.1580, found 361.1584.

2-((*Z*)-6-Ethoxy-3-(4-fluorophenyl)hex-3-en-1-ynyl)pyridine 183ah



Pale yellow oil; ^{1}H NMR ($CDCl_3$, 500 MHz): δ 8.60 (dq, 1H, *J* = 4.9, 0.9 Hz), 7.67-7.62 (m, 3H), 7.50 (dt, 1H, *J* = 7.8, 0.9 Hz), 7.25-7.23 (m, 1H), 7.05-7.01 (m, 2H), 6.55 (t, 1H, *J* = 7.3 Hz), 3.61 (t, 2H, *J* = 6.4 Hz), 3.53 (q, 2H, *J* = 7.0 Hz), 2.88 (q, 2H, *J* = 6.7 Hz), 1.21 (t, 3H, *J* = 7.0 Hz); ^{13}C NMR ($CDCl_3$, 125 MHz): δ 163.4, 161.4, 150.1, 143.3, 136.5, 136.1, 133.6 (d, 1C, $J_{C\text{-}F}$ = 12.1 Hz), 127.70 (d, 1C, $J_{C\text{-}F}$ = 32.1 Hz), 127.2, 123.1, 123.8, 115.2 (d, 1C, $J_{C\text{-}F}$ = 86.0 Hz), 94.8, 86.1, 69.3, 66.2, 32.1, 15.2; IR (neat, cm^{-1}): 3419, 3018, 2399, 1647, 1429, 1215, 927, 756, 669; HRMS (ESI): calcd for $C_{19}H_{19}FNO$ 296.1451, found 295.1449.

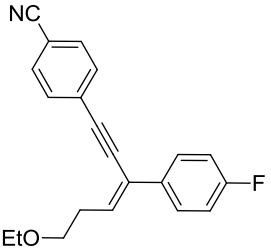
2-((*Z*)-6-Ethoxy-3-(4-methoxyphenyl)hex-3-en-1-ynyl)pyridine 183ai



Light brown oil; ^{1}H NMR ($CDCl_3$, 500 MHz): δ 8.61 (d, 1H, *J* = 4.3 Hz), 7.67-7.59 (m, 3H), 7.49 (d, 1H, *J* = 7.8 Hz), 7.23-7.21 (m, 1H), 6.87 (d, 2H, *J* = 8.7 Hz), 6.50 (t,

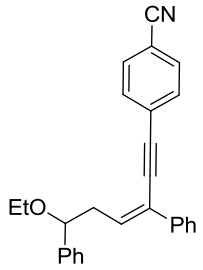
1H, *J* = 7.3 Hz), 3.8 (s, 3H), 3.60 (t, 2H, *J* = 6.6 Hz), 3.52 (q, 2H, *J* = 7.0 Hz), 2.87 (q, 2H, *J* = 6.8 Hz), 1.21 (t, 3H, *J* = 7.0 Hz); ^{13}C NMR ($CDCl_3$, 125 MHz): δ 159.3, 150.1, 143.6, 136.1, 134.8, 130.2, 127.29, 127.24, 123.5, 122.7, 113.7, 94.4, 86.6, 69.5, 66.2, 55.3, 32.0, 15.2; IR (neat, cm^{-1}): 3417, 3018, 2399, 1635, 1510, 1429, 1215, 927, 756, 669, 445; HRMS (ESI): calcd for $C_{20}H_{22}NO_2$ 308.1651, found 308.1650.

4-((*Z*)-6-Ethoxy-3-(4-fluorophenyl)hex-3-en-1-ynyl)benzonitrile 183aj



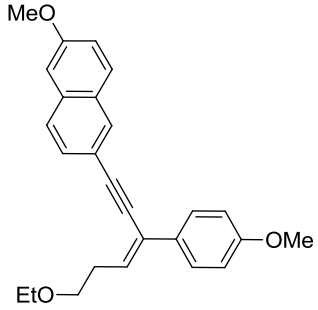
White solid; m.p. 47-49 °C; ^{1}H NMR ($CDCl_3$, 500 MHz): δ 7.64-7.57 (m, 6H), 7.04 (t, 2H, *J* = 8.5 Hz), 6.52 (t, 1H, *J* = 7.3 Hz), 3.61 (t, 3H, *J* = 6.6 Hz), 3.54 (q, 2H, *J* = 6.9 Hz), 2.83 (q, 2H, *J* = 6.8 Hz), 1.22 (t, 3H, *J* = 6.9 Hz); ^{13}C NMR ($CDCl_3$, 125 MHz): δ 163.5, 161.5, 136.5, 133.6, 132.1 (d, 1C, $J_{C\text{-}F}$ = 38.3 Hz), 128.0, 127.6 (d, 1C, $J_{C\text{-}F}$ = 32.2 Hz), 123.3, 118.4, 115.3 (d, 1C, $J_{C\text{-}F}$ = 86.2 Hz), 111.6, 93.8, 90.7, 69.2, 66.3, 32.1, 15.2; IR (neat, cm^{-1}): 3421, 3018, 2399, 1635, 1215, 927, 756, 669, 505: HRMS (ESI): calcd for $C_{21}H_{19}FNO$ 320.1451, found 320.1456.

4-((*Z*)-6-Ethoxy-3,6-diphenylhex-3-en-1-ynyl)benzonitrile 183ak



Pale yellow oil; ^{1}H NMR ($CDCl_3$, 500 MHz): δ 7.79-7.42 (m, 6H), 7.39-7.29 (m, 8H), 6.57 (t, 1H, J = 7.3 Hz), 4.48-4.45 (m, 1H), 3.48-3.37 (m 2H), 3.07-2.94 (m, 2H), 1.22 (t, 3H, J = 6.9 Hz); ^{13}C NMR ($CDCl_3$, 125 MHz): δ 142.2, 137.6, 136.3, 132.07, 132.04, 128.53, 128.50, 128.2, 127.9, 127.7, 126.5, 126.0, 124.5, 118.5, 111.5, 93.6, 91.2, 81.3, 64.3, 40.2, 15.4; IR (neat, cm^{-1}): 3419, 3018, 2399, 1635, 1215, 756, 669; HRMS (ESI): calcd for $C_{27}H_{24}NO$ 378.1858, found 378.1849.

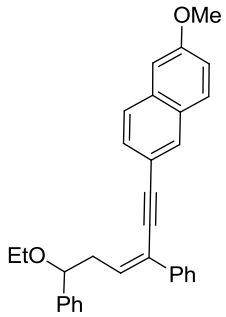
2-((*Z*)-6-Ethoxy-3-(4-methoxyphenyl)hex-3-en-1-ynyl)-6-methoxynaphthalene 183al



Yellow oil; ^{1}H NMR ($CDCl_3$, 500 MHz): δ 7.96 (s, 1H), 7.70 (t, 2H, J = 8.4 Hz), 7.64 (d, 2H, J = 8.7 Hz), 7.17-7.11 (m, 2H), 6.91 (d, 2H, J = 8.7 Hz), 6.42 (t, 1H, J = 7.3 Hz), 3.93 (s, 3H), 3.83 (s, 3H), 3.64 (t, 2H, J = 6.8 Hz), 3.56 (q, 2H, J = 6.9 Hz), 2.90 (q, 2H, J = 6.9 Hz), 1.24 (t, 3H, J =7.0 Hz); ^{13}C NMR ($CDCl_3$, 125 MHz): □ 159.2, 158.3, 134.1, 132.4, 131.1, 130.8, 129.3, 129.0, 128.5, 127.2, 126.8, 124.3, 119.4, 118.3, 105.8, 96.0, 86.4, 69.6, 66.2, 55.3, 32.0, 15.2; IR (neat, cm^{-1}): 3419, 3018,

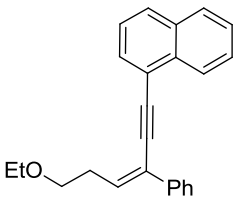
2399, 1635, 1419, 1215, 927, 756, 669; HRMS (ESI): calcd for $C_{26}H_{26}O_3Na$ 409.1780, found 409.1772.

2-((*Z*)-6-Ethoxy-3,6-diphenylhex-3-en-1-ynyl)-6-methoxynaphthalene 183am



Pale yellow oil; ^{1}H NMR ($CDCl_3$, 500 MHz): δ 7.96 (s, 1H), 7.73-7.68 (m, 4H), 7.54-7.52 (m, 1H), 7.44-7.37 (m, 6H), 7.33-7.30 (m, 2H), 7.19 (dd, 1H, J = 8.9, 2.5 Hz), 7.13 (d, 1H, J =2.3 Hz), 6.52 (t, 1H, J = 7.3 Hz), 4.51 (t, 1H, J = 6.7 Hz), 3.94 (s, 3H), 3.51-3.40 (m, 2H), 3.14-3.02 (m, 2H), 1.25 (t, 3H, J = 6.9 Hz); ^{13}C NMR ($CDCl_3$, 125 MHz): δ 158.3, 142.5, 138.3, 134.2, 134.1, 131.2, 129.3, 129.0, 128.5, 128.47, 128.4, 127.7, 127.6, 126.8, 126.6, 126.1, 125.1, 119.4, 118.3, 105.8, 96.2, 86.4, 81.6, 64.3, 55.3, 40.1, 15.4; IR (neat, cm^{-1}): 3421, 3018, 2399, 1647, 1215, 756, 669; HRMS (ESI): calcd for $C_{31}H_{29}O_2$ 433.2168, found 433.2177.

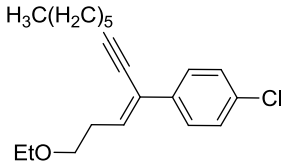
(*Z*)-1-(6-Ethoxy-3-phenylhex-3-en-1-ynyl)naphthalene 183an



Colorless oil; ^{1}H NMR ($CDCl_3$, 500 MHz): δ 8.41 (d, 1H, J = 8.3 Hz) 7.85-7.28 (m, 11H), 6.58 (t, 1H, J = 7.3 Hz) 3.66 (t, 2H, J = 6.7 Hz), 3.55 (q, 2H, J = 7.0 Hz), 2.98 (q, 2H, J = 6.9 Hz), 1.23 (t, 3H, J = 7.0 Hz); ^{13}C NMR ($CDCl_3$, 125 MHz): δ 138.2,

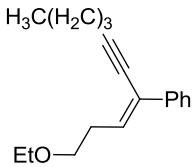
134.9, 133.29, 133.25, 130.6, 128.8, 128.5, 128.3, 127.7, 126.9, 126.4, 126.3, 126.2, 125.3, 125.2, 121.1, 93.7, 91.5, 69.5, 66.3, 32.2, 15.3; IR (neat, cm^{-1}): 3439, 3019, 1215, 756, 669; HRMS (ESI): calcd for $C_{24}H_{23}O$ 327.1749, found 327.1743.

1-Chloro-4-((*Z*)-1-ethoxydodec-3-en-5-yn-4-yl)benzene 183ao



Pale yellow oil; ^{1}H NMR ($CDCl_3$, 300 MHz): δ 7.56-7.55 (m, 2H, *J*= 8.5 Hz), 7.30 (d, 2H, *J* = 8.6 Hz), 6.38 (t, 1H, *J* = 7.2 Hz), 3.60-3.50 (m, 4H), 2.77 (q, 2H, *J* = 6.9 Hz), 2.4 (t, 2H, *J* = 7.0 Hz), 1.68-1.58 (m, 2H), 1.53-1.45 (m, 2H), 1.43-1.31 (m, 4H), 1.24 (t, 3H, *J* = 7.0 Hz), 0.93 (t, 3H, *J* = 6.7 Hz); ^{13}C NMR ($CDCl_3$, 75 MHz): δ 137.1, 133.3, 133.0, 128.2, 127.2, 124.2, 97.2, 69.4, 66.1, 31.8, 31.3, 28.8, 28.6, 22.5, 19.5, 15.2, 14.0; IR (neat, cm^{-1}): 3419, 3018, 2929, 2358, 1645, 1215, 1109, 756, 669; HRMS (ESI): calcd for $C_{20}H_{28}ClO$ 319.1829, found 319.1843.

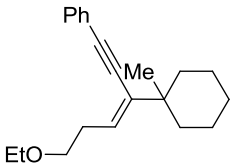
(*Z*)-(1-Ethoxydec-3-en-5-yn-4-yl)benzene 183ap



Colorless oil; ^{1}H NMR ($CDCl_3$, 500 MHz): δ 7.59-7.21 (m, 5H), 6.37 (t, 1H, *J* = 7.2 Hz) 3.55 (t, 2H, *J* = 6.8 Hz), 3.52 (q, 2H, *J* = 7.0 Hz), 2.76 (q, 2H, *J* = 7.0 Hz), 2.45 (t, 2H *J* = 7.0 Hz), 1.62-1.57 (m, 2H), 1.52-1.45 (m, 2H), 1.22 (t, 3H, *J* = 7.0 Hz), 0.94 (t, 3H, *J* = 7.2 Hz); ^{13}C NMR ($CDCl_3$, 125 MHz): δ 138.6, 132.8, 128.2, 128.0, 127.7, 127.3, 126.1, 126.0, 125.3, 96.7, 77.6, 69.5, 66.1, 31.8, 31.0, 22.0, 19.3, 15.2, 13.6; IR (neat, cm^{-1}): 3435, 2960, 1493, 1216, 1105, 756, 694, 667; HRMS (ESI): calcd for

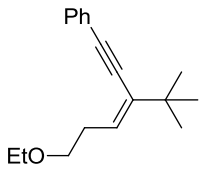
$C_{18}H_{25}O$ 257.1905, found 257.1904.

(*Z*)-(6-Ethoxy-3-(1-methylcyclohexyl)hex-3-en-1-ynyl)benzene 183aq



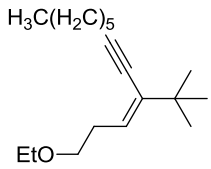
Colorless oil; ^{1}H NMR ($CDCl_3$, 400 MHz): δ 7.44-7.24 (m, 5H), 5.82 (t, 1H, J = 7.1 Hz) 3.52-3.48 (m, 4H), 2.71 (q, 2H, J = 7.0 Hz), 1.83-1.39 (m, 10H), 1.20 (t, 3H, J = 6.9 Hz), 1.11 (s, 3H); ^{13}C NMR ($CDCl_3$, 100 MHz): δ 133.7, 131.3, 131.0, 128.2, 127.7, 124.0, 94.7, 87.5, 69.8, 66.0, 38.6, 36.8, 31.5, 26.3, 22.4, 15.2; IR (neat, cm^{-1}): 3429, 3018, 1656, 1489, 1215, 1095, 757, 464; HRMS (ESI): calcd for $C_{21}H_{29}O$ 297.2218, found 297.2226.

(*Z*)-(3-*Tert*-butyl-6-ethoxyhex-3-en-1-ynyl)benzene 183ar



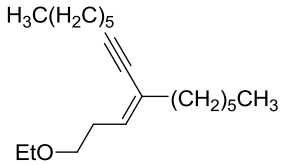
Colorless oil; ^{1}H NMR ($CDCl_3$, 400 MHz): δ 7.43-7.26 (m, 5H), 5.78 (t, 1H, J = 7.1 Hz) 3.51-3.46 (m, 4H), 2.64 (q, 2H, J = 7.0 Hz), 1.19 (t, 3H, J = 7.0 Hz); ^{13}C NMR ($CDCl_3$, 125 MHz): δ 134.7, 131.3, 129.4, 128.2, 127.8, 123.9, 95.2, 87.3, 69.8, 66.0, 35.7, 31.4, 29.4, 15.2; IR (neat, cm^{-1}): 3419, 3018, 1643, 1490, 1215, 1095, 756; HRMS (ESI): calcd for $C_{18}H_{25}O$ 257.1905, found 257.1906.

(*Z*)-4-Tert-Butyl-1-ethoxydodec-3-en-5-yne 183as



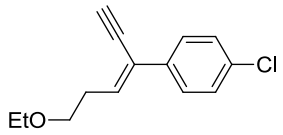
Pale yellow oil; ^{1}H NMR ($CDCl_3$, 400 MHz): δ 5.57 (t, 1H, J = 7.0 Hz), 3.44-3.35 (m, 4H), 2.50 (q, 2H, J = 7.0 Hz), 2.29 (t, 2H, J = 6.9 Hz), 1.55-1.18 (m, 8H), 1.13 (t, 3H, J = 7.0 Hz), 1.02 (s, 9H), 0.82 (t, 3H, J = 6.6 Hz); ^{13}C NMR ($CDCl_3$, 100 MHz): δ 135.2, 127.2, 96.0, 77.9, 69.9, 65.9, 35.6, 31.3, 31.1, 29.2, 28.9, 28.5, 22.5, 19.5, 15.2, 14.0; IR (neat, cm^{-1}): 3422, 3018, 2925, 2358, 1645, 1215, 1109, 756, 667; HRMS (ESI): calcd for $C_{18}H_{33}O$ 265.2531, found 265.2541.

(*Z*)-9-(3-Ethoxypropylidene)pentadec-7-yne 183at



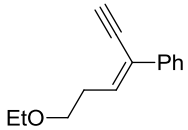
Pale yellow oil; ^{1}H NMR ($CDCl_3$, 500 MHz): δ 5.55 (t, 1H, J = 7.1 Hz), 3.46 (q, 2H, J = 7.0 Hz), 3.39 (t, 2H, J = 7.0 Hz), 2.49 (q, 2H, J = 7.0 Hz), 2.29 (t, 2H, J = 7.0 Hz), 2.02 (t, 2H, J = 7.4 Hz), 1.51-1.22 (m, 16H), 1.15 (t, 3H, J = 7.0 Hz), 0.86-0.81 (m, 6H); ^{13}C NMR ($CDCl_3$, 125 MHz): δ 131.3, 125.4, 94.7, 78.9, 69.8, 65.9, 37.5, 31.7, 31.3, 30.9, 28.9, 28.6, 28.5, 28.4, 22.6, 22.5, 19.5, 15.2, 14.09, 14.04; IR (neat, cm^{-1}): 3419, 3018, 2928, 2358, 1645, 1215, 1109, 756, 667; HRMS (ESI): calcd for $C_{20}H_{37}O$ 293.2844, found 293.2846.

1-Chloro-4-((*E*)-6-ethoxyhex-3-en-1-yn-3-yl)benzene 183au



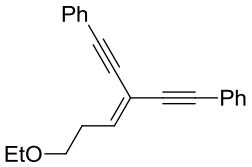
Yellow oil; ^{1}H NMR ($CDCl_3$, 300 MHz): δ 7.57-7.52 (m, 2H), 7.33-7.28 (m, 2H), 6.56 (t, 1H, J = 7.3 Hz), 3.6-3.5 (m, 4H), 3.3 (s, 1H), 2.80 (q, 2H, J = 6.7 Hz), 1.24 (t, 3H, J = 7.0 Hz); ^{13}C NMR ($CDCl_3$, 75 MHz): δ 136.8, 135.9, 133.4, 128.4, 127.2, 122.9, 83.7, 80.2, 69.1, 66.2, 31.9, 15.2; IR (neat, cm^{-1}): 3419, 3018, 2399, 1645, 1419, 1215, 1111, 927, 756, 669; HRMS (ESI): calcd for $C_{14}H_{16}ClO$ 235.0890, found 235.0894.

(*E*)-(6-Ethoxyhex-3-en-1-yn-3-yl)benzene 183av



Colorless oil; ^{1}H NMR ($CDCl_3$, 400 MHz): δ 7.82 (d, 2H, J = 7.8 Hz), 7.62-7.26 (m, 3H), 6.56 (t, 1H, J = 7.3 Hz), 3.60-3.50 (m, 4H), 3.35 (s, 1H), 2.81 (q, 2H, J = 6.8 Hz), 1.23 (t, 3H, J = 7.0 Hz); ^{13}C NMR ($CDCl_3$, 100 MHz): δ 137.5, 136.4, 128.3, 127.7, 125.9, 124.0, 83.4, 80.7, 69.3, 66.2, 31.9, 15.2; IR (neat, cm^{-1}): 3435, 2870, 1643, 1215, 1109, 756; HRMS (ESI): calcd for $C_{14}H_{17}O$ 201.1279, found 201.1278.

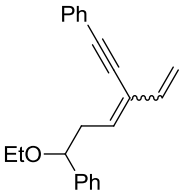
(3-(3-Ethoxypropylidene)penta-1,4-diyne-1,5-diyl)dibenzene 183aw



Colorless oil; ^{1}H NMR ($CDCl_3$, 500 MHz): δ 7.63-7.39 (m, 10H), 6.60 (t, 1H, J = 7.4 Hz) 3.65 (t, 2H, J = 6.6 Hz), 3.63 (q, 2H, J = 6.9 Hz), 2.88 (q, 2H, J = 6.9 Hz), 1.30 (t,

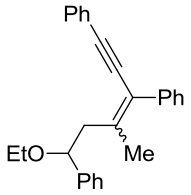
3H, J = 6.9 Hz); ^{13}C NMR ($CDCl_3$, 125 MHz): δ 145.5, 131.6, 128.5, 128.3, 128.2, 122.9, 122.8, 107.0, 93.2, 87.2, 86.9, 84.6, 68.9, 66.2, 31.6, 15.2; IR (neat, cm^{-1}): 3421, 3018, 2399, 1647, 1215, 756, 669; HRMS (ESI): calcd for $C_{22}H_{20}ONa$ 323.1412, found 323.1414.

(*Z*)-(6-Ethoxy-3-vinylhex-3-en-1-yne-1,6-diyl)dibenzene 183ax



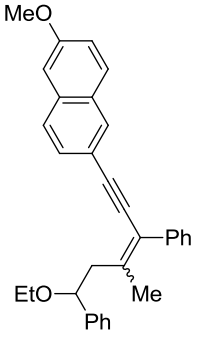
Pale yellow oil; mixture of *E*/*Z* isomers = 5: 1; ^{1}H NMR ($CDCl_3$, 500 MHz): δ 7.40-7.18 (m, 13H), 6.55-6.50 (m, 1H, *E* or *Z* diastereomer), 6.30-6.24 (m, 1H, *E* or *Z* diastereomer), 6.03 (t, 1H, J = 7.4 Hz, *E* or *Z* diastereomer), 5.93 (t, 1H, J = 7.3 Hz, *E* or *Z* diastereomer), 5.71 (d, 1H, J = 16.7 Hz, *E* or *Z* diastereomer), 5.58 (d, 1H, J = 16.9 Hz, *E* or *Z* diastereomer), 5.22 (d, 1H, J = 9.9 Hz, *E* or *Z* diastereomer), 5.10 (d, 1H, J = 10.2 Hz, *E* or *Z* diastereomer), 4.30 (t, 1H, J = 6.8 Hz, *E* or *Z* diastereomer), 4.23 (t, 1H, J = 6.7 Hz, *E* or *Z* diastereomer), 3.36-3.26 (m, 2H), 2.87-2.69 (m, 2H, *E* or *Z* diastereomer), 2.61-2.55 (m, 2H, *E* or *Z* diastereomer), 1.11 (t, 3H, J = 7.0 Hz); ^{13}C NMR ($CDCl_3$, 125 MHz): δ 142.3, 137.6, 136.5, 135.8, 131.5, 130.4, 128.49, 128.40, 128.3, 128.2, 128.0, 127.5, 126.5, 124.8, 123.3, 115.3, 96.2, 84.0, 81.3, 81.2, 64.2, 39.4, 15.3, 1.0: IR (neat, cm^{-1}): 3419, 3018, 2375, 1636, 1215, 756, 669; HRMS (ESI): calcd for $C_{22}H_{23}O$ 303.1749, found 303.1737.

(6-Ethoxy-4-methyl-6-phenylhex-3-en-1-yne-1,3-diyl)dibenzene 183ay



Colorless oil: mixture of *E*/*Z* isomers = 5: 1; ^{1}H NMR ($CDCl_3$, 400 MHz): δ 7.32-7.03 (m, 24H), 4.61 (t, 1H, *J* = 6.9, diastereomer A), 4.29 (q, 0.5H, *J* = 5.8, diastereomer B), 3.41-3.15 (m, 3H), 2.95-2.85 (m, 2H, diastereomer A), 2.61-2.34 (m, 1H, diastereomer B), 2.16 (s, 1.7H, diastereomer B), 1.66 (s, 3H, diastereomer A), 1.11 (t, 3H, *J* = 6.9, diastereomer A), 1.06 (t, 3H, *J* = 7.0, diastereomer B) ; ^{13}C NMR ($CDCl_3$, 100 MHz): δ 144.6, 143.7, 142.6, 142.4, 139.3, 139.2, 131.3, 129.3, 129.1, 128.3, 128.27, 128.26, 128.22, 128.12, 128.10, 127.7, 127.5, 127.4, 126.9, 126.8, 126.6, 126.4, 124.0, 121.4, 120.9, 93.4, 93.0, 90.4, 90.2, 81.7, 80.6, 64.3, 64.2, 46.2, 43.2, 22.1, 21.5, 15.4, 15.3; IR (neat, cm^{-1}): 3419, 3019, 1595, 1215, 1097, 759, 701, 667: HRMS (ESI): calcd for $C_{27}H_{27}O$ 367.2062, found 367.2075.

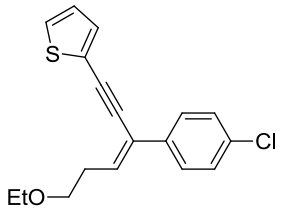
2-(6-Ethoxy-4-methyl-3,6-diphenylhex-3-en-1-ynyl)-6-methoxynaphthalene 183az



Colorless oil; mixture of *E*/*Z* isomers = 3: 1; ^{1}H NMR ($CDCl_3$, 400 MHz): δ 7.74-6.97 (m, 23H), 4.64 (t, 1H, *J* = 6.9 Hz, *E* or *Z* diastereomer), 4.30 (q, 1H, *J* = 5.9 Hz, *E* or *Z* diastereomer), 3.81 (s, 3H, *E* or *Z* diastereomer), 3.80 (s, 3H, *E* or *Z* diastereomer),

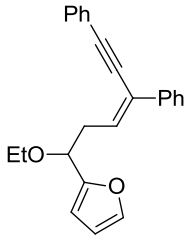
3.42-3.16 (m, 3H), 2.98-2.90 (m, 2H, *E* or *Z* diastereomer), 2.63-2.36 (m, 2H, *E* or *Z* diastereomer), 2.20 (s, 3H, *E* or *Z* diastereomer), 1.68 (s, 3H, *E* or *Z* diastereomer), 1.11 (t, 3H, *J* = 7.0 Hz, *E* or *Z* diastereomer), 1.06 (t, 3H, *J* = 6.9 Hz, *E* or *Z* diastereomer); ^{13}C NMR ($CDCl_3$, 100 MHz): δ 158.17, 158.13, 144.5, 143.4, 142.7, 142.4, 139.4, 139.3, 133.8, 130.76, 130.70, 129.3, 129.2, 129.1, 129.05, 129.02, 128.5, 128.3, 128.2, 128.14, 128.111, 127.5, 127.4, 126.9, 126.8, 126.7, 126.69, 126.66, 126.4, 121.6, 121.1, 119.3, 119.2, 118.9, 105.86, 105.83, 93.9 (*E* or *Z* diastereomer), 93.6 (*E* or *Z* diastereomer), 90.2 (*E* or *Z* diastereomer), 89.9 (*E* or *Z* diastereomer), 81.8, 80.7, 77.2, 64.3, 64.2, 55.3, 46.3, 43.3, 22.1, 21.5, 15.4, 15.3 ; IR (neat, cm^{-1}): 3419, 3019, 1601, 1215, 748, 701, 668; HRMS (ESI): calcd for $C_{32}H_{31}O_2$ 447.2324, found 447.2328.

2-((*Z*)-3-(4-Chlorophenyl)-6-ethoxyhex-3-en-1-ynyl)thiophene 183ba



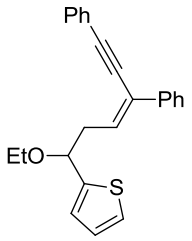
Pale yellow oil; ^{1}H NMR ($CDCl_3$, 500 MHz): δ 7.58-7.56 (m, 2H), 7.51-7.50 (m, 1H), 7.32-7.30 (m, 3H), 7.18-7.17 (m, 1H), 6.48 (t, 1H, *J* = 7.3 Hz), 3.60 (t, 2H, *J* = 6.6 Hz), 3.54 (q, 2H, *J* = 7.0 Hz), 2.83 (q, 2H, *J* = 6.8 Hz), 1.22 (t, 3H, *J* = 7.0 Hz); ^{13}C NMR ($CDCl_3$, 125 MHz): δ 136.5, 135.0, 133.4, 129.8, 128.6, 128.4, 127.3, 125.5, 123.8, 122.1, 90.9, 85.6, 69.3, 66.2, 32.0, 15.2; IR (neat, cm^{-1}): 3684, 3018, 2399, 1521, 1421, 1215, 756, 669; HRMS (ESI): calcd for $C_{18}H_{17}ClOSNa$ 339.0586, found 339.0576.

(*Z*)-2-(1-Ethoxy-4,6-diphenylhex-3-en-5-ynyl)furan 183bb



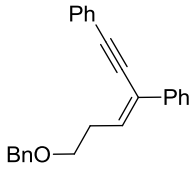
Pale yellow oil; ^{1}H NMR ($CDCl_3$, 500 MHz): δ 7.66-7.55 (m, 4H), 7.44-7.28 (m, 7H), 6.47 (t, 1H, J = 7.3 Hz), 6.37-6.35 (m, 2H), 4.55 (t, 1H, J = 6.9 Hz), 3.60-3.48 (m, 2H), 3.19-3.16 (m, 2H), 1.24 (t, 3H, J = 6.9 Hz); ^{13}C NMR ($CDCl_3$, 125 MHz): δ 154.4, 142.3, 138.0, 133.4, 131.5, 128.38, 128.36, 128.3, 127.6, 126.1, 125.2, 123.3, 110.0, 107.7, 95.7, 86.5, 74.1, 64.3, 36.1, 15.3; IR (neat, cm^{-1}): 3419, 3018, 2399, 2092, 1639, 1423, 1215, 927, 777, 744, 669; HRMS (ESI): calcd for $C_{24}H_{23}O_2$ 343.1698, found 343.1711.

(*Z*)-2-(1-Ethoxy-4,6-diphenylhex-3-en-5-ynyl)thiophene 183bc



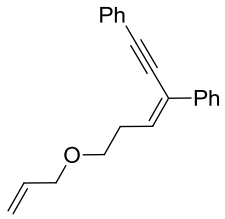
Light brown oil; ^{1}H NMR ($CDCl_3$, 400 MHz): δ 7.64 (d, 2H, J = 7.3 Hz), 7.53-7.26 (m, 9H), 7.01-6.96 (m, 2H), 6.48 (t, 1H, J = 7.3 Hz), 4.74 (t, 1H, J = 6.7 Hz), 3.59-3.42 (m, 2H), 3.19-3.04 (m, 2H), 1.22 (t, 3H, J = 7.0 Hz); ^{13}C NMR ($CDCl_3$, 100 MHz): δ 146.4, 138.1, 133.6, 131.6, 128.4, 128.38, 128.34, 127.7, 126.4, 126.1, 125.3, 124.9, 123.3, 95.7, 86.6, 76.9, 64.3, 40.1, 15.3; IR (neat, cm^{-1}): 3417, 3018, 1643, 1215, 756, 453; HRMS (ESI): calcd for $C_{24}H_{23}OS$ 359.1470, found 359.1472.

(*Z*)-6-(Benzyloxy)-1,3-diphenylhex-3-en-1-yne: Yellow oil 183be



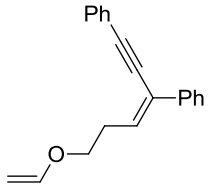
Colorless oil; ^{1}H NMR ($CDCl_3$, 300 MHz): δ 7.77-7.74 (m, 2H), 7.62-7.58 (m, 2H), 7.46-7.32 (m, 12H), 6.61 (t, 1H, *J* = 7.3), 4.64 (s, 2H), 3.76 (t, 2H, *J* = 6.6), 3.01 (q, 2H, *J* = 6.7); ^{13}C NMR ($CDCl_3$, 75 MHz): δ 138.5, 138.1, 134.6, 131.6, 128.49, 128.46, 128.41, 127.86, 127.80, 127.7, 127.6, 126.1, 125.1, 123.4, 95.7, 86.7, 72.9, 69.2, 32.1; IR (neat, cm^{-1}): 3427, 3018, 2399, 1637, 1423, 1215, 927, 756, 669: HRMS (ESI): calcd for $C_{25}H_{23}O$ 339.1749, found 339.1751.

(*Z*)-6-(2-(Allyloxy)ethoxy)-1,3-diphenylhex-3-en-1-yne 183bf



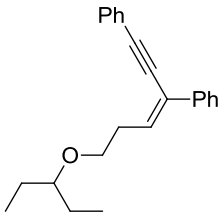
Pale yellow oil; ^{1}H NMR ($CDCl_3$, 300 MHz): δ 7.72 (d, 2H, *J* = 7.2 Hz), 7.59-7.56 (m, 2H), 7.42-7.32 (m, 6H), 6.57 (t, 1H, *J* = 7.3 Hz), 6.03-5.90 (m, 1H), 5.35-5.20 (m, 2H), 4.08 (d, 2H, *J* = 5.6 Hz), 3.75-3.64 (m, 6H), 2.94 (q, 2H, *J* = 6.9 Hz); ^{13}C NMR ($CDCl_3$, 75 MHz): δ 138.0, 134.8, 134.5, 131.5, 128.4, 128.3, 127.6, 126.0, 124.9, 123.4, 117.1, 95.6, 86.6, 72.3, 70.2, 69.4, 31.9; IR (neat, cm^{-1}): 3419, 3018, 2399, 1647, 1215, 1122, 929, 756, 669; HRMS (ESI): calcd for $C_{23}H_{25}O_2$ 333.1855, found 333.1853.

(*Z*)-(6-(Vinyloxy)hex-3-en-1-yne-1,3-diyl)dibenzene 183bg



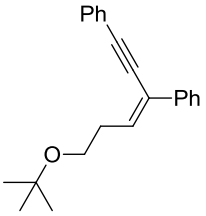
Pale yellow oil; ^{1}H NMR ($CDCl_3$, 300 MHz): δ 7.72-7.69 (m, 2H), 7.59-7.53 (m, 2H), 7.41-7.30 (m, 6H), 6.56 (t, 1H, J = 7.3 Hz), 5.98-5.91 (m, 1H), 5.37-5.20 (m, 2H), 4.06 (dt, 2H, J = 9.3, 1.3 Hz), 3.67 (t, 2H, J = 6.7 Hz), 2.92 (q, 2H, J = 6.8 Hz); ^{13}C NMR ($CDCl_3$, 75 MHz): δ 138.0, 134.8, 134.5, 131.5, 128.41, 128.40, 128.3, 127.6, 126.0, 125.0, 123.4, 117.0, 95.6, 86.6, 71.9, 69.2, 32.0; IR (neat, cm^{-1}): 3419, 3018, 2399, 1647, 1215, 927, 756, 669; HRMS (ESI): calcd for $C_{21}H_{21}O$ 289.1592, found 289.1595.

(*Z*)-6-(Pentan-3-yloxy)-1,3-diphenylhex-3-en-1-yne 183bh



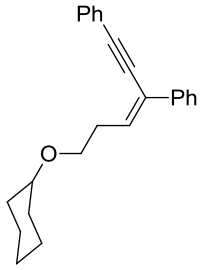
Pale yellow oil; ^{1}H NMR ($CDCl_3$, 300 MHz): δ 7.68 (d, 2H, J = 7.2 Hz), 7.54 (m, 2H), 7.40-7.29 (m, 6H), 6.58 (t, 1H, J = 7.3 Hz), 3.65 (t, 2H, J = 6.7 Hz), 3.23-3.16 (m, 1H), 2.87 (q, 2H, J = 6.8 Hz), 1.63-150 (m, 4H), 0.94 (t, 6H, J = 7.4 Hz); ^{13}C NMR ($CDCl_3$, 75 MHz): δ 138.1, 135.1, 131.5, 128.4, 128.3, 128.2, 127.6, 126.0, 124.7, 123.4, 95.5, 86.7, 82.0, 67.8, 32.5, 26.1, 9.7; IR (neat, cm^{-1}): 3419, 3018, 2399, 1647, 1419, 1215, 927, 756, 669; HRMS (ESI): calcd for $C_{23}H_{27}O$ 319.2062, found 319.2056.

(*Z*)-6-tert-Butoxy-1,3-diphenylhex-3-en-1-yne 183bi



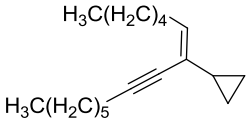
Pale yellow oil; ^{1}H NMR ($CDCl_3$, 300 MHz): δ 7.72-7.69 (m, 2H), 7.58-7.55 (m, 2H), 7.42-7.30 (m, 6H), 6.57 (t, 1H, *J* =7.3 Hz), 3.58 (t, 2H, *J* = 6.8 Hz), 2.85 (q, 2H, *J* = 7.0 Hz), 1.26 (s, 9H); ^{13}C NMR ($CDCl_3$, 75 MHz): δ 138.2, 135.2, 131.5, 128.4, 128.3, 128.2, 127.6, 126.0, 124.6, 123.5, 95.4, 86.7, 72.9, 60.8, 32.9, 27.6; IR (neat, cm^{-1}): 3419, 3018, 2399, 1635, 1215, 756, 669; HRMS (ESI): calcd for $C_{22}H_{25}O$ 305.1905, found 305.1896.

(*Z*)-6-(Cyclohexyloxy)-1,3-diphenylhex-3-en-1-yne 183bj



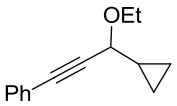
Pale yellow oil; ^{1}H NMR ($CDCl_3$, 300 MHz): δ 7.73-7.70 (m, 2H), 7.59-7.54 (m, 2H), 7.42-7.31 (m, 6H), 6.58 (t, 1H, *J* = 7.3 Hz), 3.69 (t, 2H, *J* = 6.7 Hz), 3.36-3.29 (m, 1H), 2.90 (q, 2H, *J* = 6.9 Hz), 2.00-1.97 (m, 2H), 1.79-1.78 (m, 2H), 1.58-1.55 (m, 1H), 1.41-1.24 (m, 5H); ^{13}C NMR ($CDCl_3$, 75 MHz): δ 138.1, 135.0, 131.5, 128.4, 128.3, 128.2, 127.6, 126.0, 124.7, 123.4, 95.5, 86.7, 76.6, 66.7, 32.5, 32.3, 25.8, 24.2; IR (neat, cm^{-1}): 3419, 3018, 2399, 1647, 1419, 1215, 927 756, 669; HRMS (ESI): calcd for $C_{24}H_{27}O$ 331.2062, found 331.2072.

(*Z*)-Pentadec-6-en-8-yn-7-ylcyclopropane 184at



Pale yellow oil; ^{1}H NMR ($CDCl_3$, 500 MHz): δ 5.71 (t, 1H, J = 7.3 Hz), 2.32-2-18 (m, 4H), 1.54-1.24 (m, 15H), 0.90-0.86 (m, 6H), 0.65-0.53 (m, 4H); ^{13}C NMR ($CDCl_3$, 125 MHz): δ 134.4, 125.2, 94.5, 75.7, 31.5, 31.3, 30.4, 29.0, 28.9, 28.4, 22.59, 22.56, 19.3, 16.2, 14.0, 5.3, 4.9; IR (neat, cm^{-1}): 3421, 3018, 2928, 2358, 1634, 1215, 1109, 757, 669; HRMS (ESI): calcd for $C_{18}H_{31}$ 247.2426, found 247.2437.

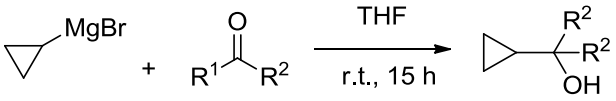
(3-Cyclopropyl-3-ethoxyprop-1-ynyl)benzene 185bd



Light yellow oil; ^{1}H NMR ($CDCl_3$, 300 MHz): δ 7.43-7.24 (m, 5H), 4.12 (d, 1H, J = 8.4 Hz), 3.90-3.80 (m, 1H) 3.59-3.47 (m, 1H), 1.29-1.18 (m, 2H), 0.59-0.45 (m, 2H); ^{13}C NMR ($CDCl_3$, 75 MHz): δ 131.7, 131.4, 128.29, 128.24, 122.7, 86.5, 85.5, 73.2, 64.1, 15.2, 15.1, 3.1, 1.9; IR (neat, cm^{-1}): 3439, 3019, 1490, 1215, 1077, 753, 691, 667; HRMS (ESI): calcd for $C_{14}H_{17}O$ 201.1279, found 201.1273.

7.3 Rapid Access to Halohydrofurans via Brønsted Acid-Catalyzed Hydroxylation/Halocyclization of Cyclopropyl Methanols with Water and Electrophilic Halides

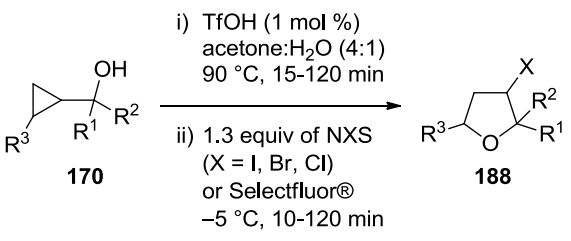
Representative Experimental Procedure for Preparation of Substituted Cyclopropyl methanols (170be)-(170bn)[103,104]



R^1- R^3 = H, alkyl, aryl

To a solution of cyclopropylmagnesium bromide (0.5 M THF solution; 3.3 mL, 1.6 mmol) in THF (5 mL) at 0 °C was added dropwise a solution of ketone or aldehyde (1.3 mmol) in THF (3 mL). The resulting mixture was stirred at room temperature for 15 h. The mixture was treated with saturated NH_4Cl aq. (50 mL). The organic layer was extracted with Et_2O (2 x 25 mL). The combined organic layers were dried over anhydrous $MgSO_4$ and concentrated under reduced pressure. Purification by flash column chromatography on silica gel (eluent: *n*-hexane:EtOAc = 9:1) gave the title compound.

Representative Procedure for TfOH-Catalyzed, *N*-Halosuccinimide or Selectfluor®-Mediated Synthesis of 3-Halohydrofurans 188

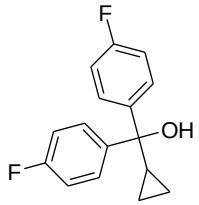


R^1- R^3 = H, alkyl, alkynyl
aryl, heteroaryl

To a round bottom flask containing **170** (0.2 mmol) in acetone:H_2O (4:1, 4 mL) was

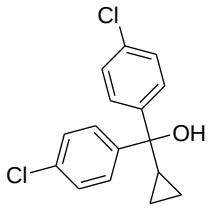
added TfOH (2 μmol) under a nitrogen atmosphere at room temperature. The reaction mixture was stirred at 90 °C and monitored to completion by TLC analysis. The reaction mixture was brought to –5 °C and a solution of NXS or Selectfluor® (0.26 mmol) in acetone (2 mL) was added. The resultant reaction mixture was then stirred at the same temperature and monitored to completion by TLC analysis. The reaction mixture was quenched with 10 % aq solution of $Na_2S_2O_3$ (10 mL), extracted with EtOAc (3 x 10 mL), and concentrated under reduced pressure. Purification by flash column chromatography on silica gel (eluent: *n*-hexane/EtOAc = 19:1) gave the title compound.

Cyclopropylbis(4-fluorophenyl)methanol 170be



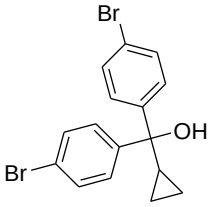
Yield: 80%; colorless oil; ^{1}H NMR ($CDCl_3$, 400 MHz): δ 7.42-7.37 (m, 4H), 7.02-6.96 (m, 4H), 1.88 (s, 1H), 1.60-1.53 (m, 1H), 0.63-0.58 (m, 2H), 0.47-0.43 (m, 2H); ^{13}C NMR ($CDCl_3$, 100 MHz): δ 163.1, 160.6, 142.8 (d, 1C, $J_{C\text{-}F}$ = 12.4 Hz), 128.59 (d, 1C, $J_{C\text{-}F}$ = 31.8 Hz), 114.8 (d, 1C, $J_{C\text{-}F}$ = 84.1 Hz), 21.8, 1.8; IR (neat, cm^{-1}): 3334, 3018, 1604, 1506, 1215, 1159, 837, 752, 669, 518: HRMS (ESI): calcd for $C_{16}H_{15}OF_2$ 261.1091, found 261.1086.

Bis(4-chlorophenyl)(cyclopropyl)methanol 170bf



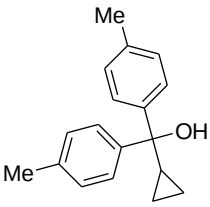
Yield: 85%; colorless oil: ^{1}H NMR ($CDCl_3$, 400 MHz): δ 7.36-7.27 (m, 8H), 1.87 (s, 1H), 1.58-1.51 (m, 1H), 0.63-0.58 (m, 2H), 0.46-0.42 (m, 2H); ^{13}C NMR ($CDCl_3$, 100 MHz): δ 145.2, 133.1, 128.2, 128.1, 76.5, 21.5, 1.8; IR (neat, cm^{-1}): 3431, 1635, 1215, 821, 752, 669, 526; HRMS (ESI): calcd for $C_{16}H_{15}OCl_2$ 293.0500, found 293.0493.

Bis(4-bromophenyl)(cyclopropyl)methanol 170bg



Yield: 78%; colorless oil; ^{1}H NMR ($CDCl_3$, 300 MHz): δ 7.45-7.27 (m, 8H), 1.91 (s, 1H), 1.59-1.49 (m, 1H), 0.63-0.57 (m, 2H), 0.47-0.41 (m, 2H); ^{13}C NMR ($CDCl_3$, 75 MHz): δ 145.7, 131.1, 128.6, 121.3, 21.4, 1.8; IR (neat, cm^{-1}): 3587, 3442, 3018, 1485, 1215, 1010, 761, 669, 522; HRMS (ESI): calcd for $C_{16}H_{15}OBr_2$ 380.9490, found 380.9502.

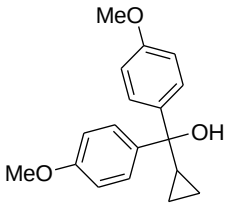
Cyclopropyldi-*p*-tolylmethanol 170bi



Yield: 82%; colorless oil; ^{1}H NMR ($CDCl_3$, 300 MHz): δ 7.35 (d, 4H, J = 8.1 Hz),

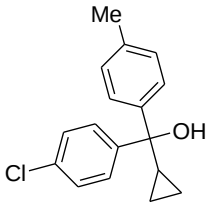
7.14 (d, 4H, *J* = 7.9 Hz), 2.34 (s, 6H), 1.84 (s, 1H), 1.65-1.33 (m, 1H), 0.61-0.53 (m, 2H), 0.50-0.47 (m, 2H); ^{13}C NMR ($CDCl_3$, 75 MHz): δ 144.5, 136.5, 128.6, 126.7, 76.8, 21.6, 21.0, 1.7; IR (neat, cm^{-1}): 3585, 3442, 3018, 2399, 1508, 1215, 1022, 815, 752, 669, 572, 499: HRMS (ESI): calcd for $C_{18}H_{21}O$ 253.1592, found 253.1586.

Cyclopropylbis(4-methoxyphenyl)methanol 170bj



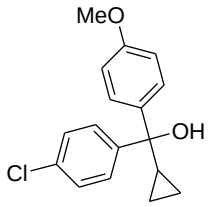
Yield: 87%; colorless oil; ^{1}H NMR ($CDCl_3$, 300 MHz): δ 7.38-7.33 (m, 4H), 6.86-6.81 (m, 4H), 3.79 (s, 6H), 1.94 (s, 1H), 1.64-1.44 (m, 1H), 0.64-0.46 (m, 2H), 0.42-0.29 (m, 2H); ^{13}C NMR ($CDCl_3$, 75 MHz): δ 158.4, 139.7, 128.0, 113.1, 76.6, 55.2, 21.8, 1.7; IR (neat, cm^{-1}): 3541, 3431, 3018, 1635, 1508, 1215, 1035, 779, 671, 522; HRMS (ESI): calcd for $C_{18}H_{21}O_3$ 285.1491, found 285.1494.

(4-Chlorophenyl)(cyclopropyl)(*p*-tolyl)methanol 170bk



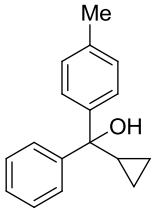
Yield: 76%; colorless oil; ^{1}H NMR ($CDCl_3$, 400 MHz): δ 7.35-7.10 (m, 8H), 2.32 (s, 3H), 1.85 (s, 1H), 1.58-1.51 (m, 1H), 0.63-0.39 (m, 4H); ^{13}C NMR ($CDCl_3$, 100 MHz): δ 146.0, 143.9, 137.0, 132.7, 128.8, 128.2, 127.9, 126.8, 76.7, 21.5, 21.0, 2.0, 1.5; IR (neat, cm^{-1}): 3008, 1489, 1215, 1091, 1014, 819, 756, 667, 509; HRMS (ESI): calcd for $C_{17}H_{18}OCl$ 273.1046, found 273.1041.

(4-Chlorophenyl)(cyclopropyl)(4-methoxyphenyl)methanol 170bl



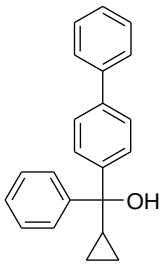
Yield: 84%; light brown oil; ^{1}H NMR ($CDCl_3$, 400 MHz): δ 7.27-7.15 (m, 6H), 6.7 (d, 2H, J = 8.5 Hz), 3.6 (s, 3H), 2.13 (s, 1H), 1.49-1.42 (m, 1H), 0.55-0.34 (m, 4H); ^{13}C NMR ($CDCl_3$, 100 MHz): δ 158.7, 146.1, 139.1, 132.6, 128.2, 127.9, 113.3, 76.5, 55.2, 21.7, 2.1, 1.4; IR (neat, cm^{-1}): 3585, 3446, 1608, 1510, 1249, 1176, 831, 586, 499; HRMS (ESI): calcd for $C_{17}H_{18}O_2Cl$ 289.0995, found 289.0989.

Cyclopropyl(phenyl)(*p*-tolyl)methanol 170bm



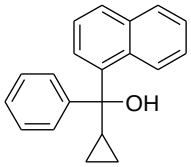
Yield: 84%; colorless oil; ^{1}H NMR ($CDCl_3$, 400 MHz): δ 7.33 (d, 2H, J = 7.8 Hz), 7.22-7.09 (m, 5H), 7.00 (d, 2H, J = 7.8 Hz), 2.21 (s, 3H), 1.83 (s, 1H), 1.51-1.44 (m, 1H), 0.49-0.35 (m, 4H); ^{13}C NMR ($CDCl_3$, 100 MHz): δ 147.5, 144.4, 136.6, 128.7, 127.9, 126.98, 126.92, 126.8, 77.0, 21.7, 21.1, 1.9, 1.7; IR (neat, cm^{-1}): 3356, 3010, 1647, 1510, 1446, 1215, 981, 815, 752, 667, 514; HRMS (ESI): calcd for $C_{17}H_{19}O$ 239.1436, found 239.1430.

Cyclopropyl(phenyl)(4-biphenyl)methanol 170bn



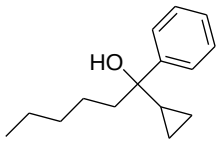
Yield: 68%; white solid; m.p. 92-94 ^{o}C; ^{1}H NMR ($CDCl_3$, 300 MHz): δ 7.50-7.24 (m, 14H), 1.93 (s, 1H), 1.71-1.62 (m, 1H), 0.65-0.58 (m, 2H), 0.54-0.49 (m, 2H); ^{13}C NMR ($CDCl_3$, 75 MHz): δ 147.2, 146.3, 140.8, 139.8, 128.7, 128.0, 127.3, 127.2, 127.0, 126.8, 126.6, 21.6, 1.85, 1.83; IR (neat, cm^{-1}): 3392, 3018, 1645, 1487, 1446, 1215, 1031, 839, 748, 700, 667, 628, 622, 514, 499; HRMS (ESI): calcd for $C_{22}H_{20}ONa$ 323.1412, found 323.1404.

Cyclopropyl(naphthalen-1-yl)(phenyl)methanol 170bo



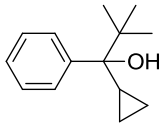
Yield: 70%; white solid; m.p. 111-113 ^{o}C; ^{1}H NMR ($CDCl_3$, 400 MHz): δ 7.29 (d, 1H, J = 7.0 Hz), 8.01 (d, 1H, J = 8.6 Hz), 7.89 (t, 2H, J = 8.9 Hz), 7.61-7.23 (m, 8H), 2.23 (s, 1H), 1.80-1.77 (m, 1H), 0.80-0.50 (m, 4H); ^{13}C NMR ($CDCl_3$, 100 MHz): δ 146.9, 142.1, 135.0, 131.0, 129.1, 128.8, 128.0, 127.4, 126.7, 126.1, 125.4, 125.3, 125.2, 124.7, 77.7, 23.2, 2.3, 2.2; IR (neat, cm^{-1}): 3435, 3018, 1639, 1215, 758, 669, 499; HRMS (ESI): calcd for $C_{20}H_{19}O$ 275.1436, found 275.1435.

1-Cyclopropyl-1-phenylhexan-1-ol 170bp



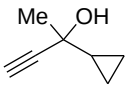
Yield: 76%; colorless oil; ^{1}H NMR ($CDCl_3$, 400 MHz): δ 7.38-7.12 (m, 5H), 1.89-1.63 (m, 2H), 1.44 (s, 1H), 1.21-1.03 (m, 7H), 0.76-0.73 (m, 3H), 0.39 (q, 2H, J = 7.0 Hz), 0.30-0.17 (m, 2H); ^{13}C NMR ($CDCl_3$, 100 MHz): δ 146.5, 128.1, 127.9, 126.5, 125.5, 75.0, 42.3, 32.3, 23.3, 22.5, 21.8, 14.0, 1.4, 0.7: IR (neat, cm^{-1}): 3369, 3012, 2933, 2870, 2399, 1645, 1446, 1215, 1029, 914, 752, 702, 667, 518: HRMS (ESI): calcd for $C_{15}H_{23}O$ 219.1749, found 219.1753

1-Cyclopropyl-2,2-dimethyl-1-phenylpropan-1-ol 170bq



Yield: 72%; light brown oil; ^{1}H NMR ($CDCl_3$, 400 MHz): δ 7.51-7.20 (m, 5H), 1.71-1.67 (m, 1H), 1.25 (s, 1H), 0.98 (s, 9H), 0.82-0.72 (m, 1H), 0.65-0.58 (m, 1H), 0.38-0.31 (m, 1H), –0.04-–0.11 (m, 1H); ^{13}C NMR ($CDCl_3$, 100 MHz): δ 146.0, 127.5, 126.8, 126.2, 78.2, 39.3, 26.0, 16.4, 4.1, 0.3; IR (neat, cm^{-1}): 2976, 1481, 1215, 1145, 773, 704, 667, 470; HRMS (ESI): calcd for $C_{14}H_{21}O$ 205.1592, found 205.1600.

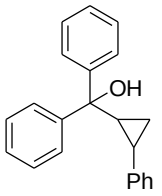
2-Cyclopropylbut-3-yn-2-ol 170br



Yield: 72%; colorless oil; ^{1}H NMR ($CDCl_3$, 400 MHz): δ 2.36 (s, 1H), 2.28 (bs, 1H), 1.57 (s, 3H), 1.19-1.07 (m, 1H), 0.64-0.46 (m, 4H); ^{13}C NMR ($CDCl_3$, 100 MHz): δ 84.9, 71.6, 69.8, 29.6, 21.6, 2.4, 1.5: IR (neat, cm^{-1}): 3369, 1446, 1215, 921, 756, 702,

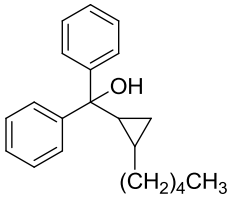
669, 518: HRMS (ESI): calcd for $C_7H_{11}O$ 111.0810, found 111.0809

Diphenyl(2-phenylcyclopropyl)methanol 170bs



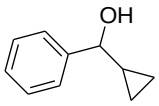
Yield: 82%; colorless oil; ^{1}H NMR ($CDCl_3$, 400 MHz): δ 7.29-7.00 (m, 13H), 6.93 (d, 2H, J = 7.7 Hz), 1.97-1.92 (m, 2H), 1.76-1.71 (m, 1H), 1.11-1.06 (m, 1H), 0.90-0.86 (m, 1H); ^{13}C NMR ($CDCl_3$, 100 MHz): δ 147.4, 147.0, 142.6, 128.5, 128.27, 128.20, 127.4, 127.2, 126.7, 126.2, 125.7, 77.4, 33.5, 20.4, 12.0; IR (neat, cm^{-1}): 3437, 3018, 1643, 1215, 772, 700, 636; HRMS (ESI): calcd for $C_{22}H_{21}O$ 301.1592, found 301.1601.

(2-Pentylcyclopropyl)diphenylmethanol 170bt



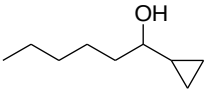
Yield: 78%; colorless oil; ^{1}H NMR ($CDCl_3$, 400 MHz): δ 7.44-7.39 (m, 4H), 7.31-7.21 (m, 6H), 1.86 (s, 1H), 1.40-1.20 (m, 9H), 0.85-0.81 (m, 4H), 0.66-0.62 (m,1H), 0.40-0.36 (m, 1H); ^{13}C NMR ($CDCl_3$, 100 MHz): δ 147.5, 147.3, 127.9, 127.8, 127.0, 126.9, 126.8, 126.6, 77.2, 33.7, 31.6, 29.4, 29.0, 22.6, 15.2, 14.0, 9.1; IR (neat, cm^{-1}): 3437, 3018, 2399, 1639, 1215, 927, 771, 669; HRMS (ESI): calcd for $C_{21}H_{27}O$ 295.2062, found 295.2061.

Cyclopropyl(phenyl)methanol 170bu



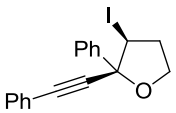
Yield: 83%; colorless oil; ^{1}H NMR ($CDCl_3$, 400 MHz): δ 7.42-7.27 (m, 5H), 3.97 (d, 1H, J = 8.2 Hz), 2.77 (s, 1H), 1.23-1.15 (m, 1H), 0.65-0.48 (m, 4H); ^{13}C NMR ($CDCl_3$, 100 MHz): δ 144.0, 128.3, 127.4, 126.1, 78.4, 19.1, 3.7, 2.8; IR (neat, cm^{-1}): 3435, 3014,1633, 1492, 1452, 1215, 1026, 921, 769, 669: HRMS (ESI): calcd for $C_{10}H_{13}O$ 149.0966, found 149.0968.

1-Cyclopropylhexan-1-ol 170bv



Yield: 79%; colorless oil; ^{1}H NMR ($CDCl_3$, 400 MHz): δ 2.86-2.81 (m, 1H), 1.61-1.55 (m, 3H), 1.46-1.24 (m, 6H),0.91-0.85 (m, 4H), 0.52-0.45 (m, 2H), 0.27-0.18 (m, 2H); ^{13}C NMR ($CDCl_3$, 100 MHz): δ 76.9, 37.2, 31.9, 25.4, 22.6, 18.0, 14.0, 2.7, 2.4: IR (neat, cm^{-1}): 3352, 1449, 1215, 914, 757, 667, 519: HRMS (ESI): calcd for $C_9H_{19}O$ 143.1436, found 143.1442

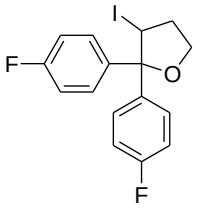
***Cis*-tetrahydro-3-iodo-2-phenyl-2-(2-phenylethynyl)furan 188aa**



White solid; m.p. 117-119 °C; ^{1}H NMR ($CDCl_3$, 500 MHz): δ 7.77-7.55 (m, 4H), 7.41-7.34 (m, 6H), 4.33-4.29 (m, 1H), 4.20 (aq, 1H, J = 7.4 Hz), 4.11 (t, 1H, J = 8.7 Hz), 2.70-2.65 (m, 2H); ^{13}C NMR ($CDCl_3$, 125 MHz): δ 139.2, 131.9, 128.7, 128.5, 128.33, 128.31, 126.0, 122.3, 88.7, 88.3, 85.5, 67.1, 37.8, 33.1; IR (neat, cm^{-1}): 3464, 3431, 3016, 1635, 1490, 1215, 1026, 752, 667, 532; HRMS (ESI): calcd for $C_{18}H_{16}OI$

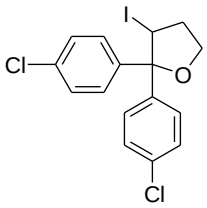
375.0246, found 375.0258.

2,2-Bis(4-fluorophenyl)-tetrahydro-3-iodofuran 188be



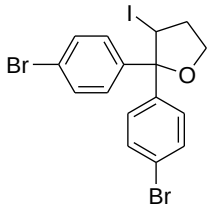
Reaction time (min): step 1/2 (90/15); white solid; m.p. 91-93 ^{o}C; ^{1}H NMR ($CDCl_3$, 400 MHz): δ 7.51-7.35 (m, 4H), 7.02-6.94 (m, 4H), 5.23 (dd, 1H, J = 4.7, 3.0 Hz), 4.43 (aq, 1H, J = 7.9 Hz), 4.05-4.00 (m, 1H), 2.55-2.45 (m, 2H); ^{13}C NMR ($CDCl_3$, 100 MHz): δ 163.1, 162.9, 160.7, 160.4, 142.1, 138.4, 127.6 (d, 1C, J_{C-F} = 32.2 Hz), 127.0 (d, 1C, J_{C-F} = 31.8 Hz), 115.7, 115.5, 114.7, 114.5, 90.4, 65.9, 38.3, 35.2; IR (neat, cm^{-1}): 3018, 1600, 1506, 1215, 1159, 1047, 833, 744, 669, 559, 513; HRMS (ESI): calcd for $C_{16}H_{14}OIF_2$ 387.0057, found 387.0076.

2,2-Bis(4-chlorophenyl)-tetrahydro-3-iodofuran 188bf



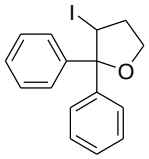
Reaction time (min): step 1/2 (120/15); light brown oil; ^{1}H NMR ($CDCl_3$, 400 MHz): δ 7.38 (d, 2H, J = 8.5 Hz), 7.26-7.16 (m, 6H), 5.14-5.12 (m, 1H), 4.35 (aq, 1H, J = 8.0 Hz), 3.97-3.92 (m,1H), 2.45-2.33 (m, 2H); ^{13}C NMR ($CDCl_3$, 100 MHz): δ 144.5, 140.9, 133.4, 133.0, 128.9, 128.0, 127.2, 126.6, 90.5, 65.9, 38.2, 34.5; IR (neat, cm^{-1}): 3462, 1635, 1215, 752, 669, 522; HRMS (ESI): calcd for $C_{16}H_{14}OCl_2I$ 418.9466, found 418.9478.

2,2-Bis(4-bromophenyl)-tetrahydro-3-iodofuran 188bg



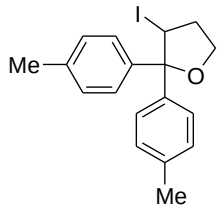
Reaction time (min): step 1/2 (120/15); light brown solid; m.p. 160-162 ^{o}C; ^{1}H NMR ($CDCl_3$, 400 MHz): δ 7.44-7.36 (m, 6H), 7.27 (d, 2H, J = 8.5 Hz), 5.19 (dd, 1H, J = 4.8, 2.4 Hz), 4.42 (aq, 1H, J = 8.0 Hz), 4.04-3.99 (m, 1H), 2.53-2.42 (m, 2H); ^{13}C NMR ($CDCl_3$, 100 MHz): δ 144.9, 141.4, 131.9, 130.9, 127.5, 127.0, 121.6, 121.2, 90.6, 65.9, 38.2, 34.2; IR (neat, cm^{-1}): 3333, 3018, 1635, 1215, 783, 669, 524; HRMS (ESI): calcd for $C_{16}H_{14}OIBr_2$ 508.8436, found 508.8446.

Tetrahydro-3-iodo-2,2-diphenylfuran 188bh



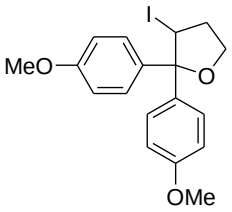
Reaction time (min): step 1/2 (30/20); pale yellow solid; m.p. 83-85 ^{o}C; ^{1}H NMR ($CDCl_3$, 400 MHz): δ 7.54 (d, 2H, J = 7.4 Hz), 7.44 (d, 2H, J = 7.3 Hz), 7.31-7.15 (m, 6H), 5.32-5.30 (m, 1H), 4.43 (aq, 1H, J = 8.0 Hz), 4.07-4.02 (m, 1H), 2.52-2.41 (m, 2H); ^{13}C NMR ($CDCl_3$, 100 MHz): δ 146.5, 142.6, 128.7, 127.7, 127.3, 127.0, 125.8, 125.2, 91.2, 65.6, 38.3, 36.0; IR (neat, cm^{-1}): 3300, 3018, 1489, 1448, 1215, 1029, 752, 669, 518: HRMS (ESI): calcd for $C_{16}H_{16}OI$ 351.0246, found 351.0230.

Tetrahydro-3-iodo-2,2-di-*p*-tolylfuran 188bi



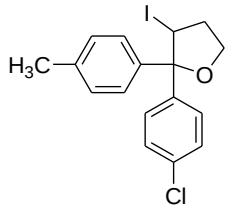
Reaction time (min): step 1/2 (15/20); colorless oil; ^{1}H NMR ($CDCl_3$, 300 MHz): δ 7.41 (d, 2H, J = 8.1 Hz), 7.32 (d, 2H, J = 8.1 Hz), 7.10-7.05 (m, 4H), 5.28 (bt, 1H, J = 3.6 Hz), 4.41 (aq, 1H, J = 7.9 Hz), 4.10-3.96 (m, 1H), 2.51-2.44 (m, 2H), 2.279 (s, 3H), 2.271 (s, 3H); ^{13}C NMR ($CDCl_3$, 75 MHz): δ 143.8, 139.9, 136.8, 136.4, 129.3, 128.4, 125.6, 125.1,91.1, 65.5, 38.4, 36.5, 21.1, 20.9; IR (neat, cm^{-1}): 3334, 3018, 1651, 1215, 748, 669, 513; HRMS (ESI): calcd for $C_{18}H_{20}OI$ 379.0559, found 379.0555.

Tetrahydro-3-iodo-2,2-bis(4-methoxyphenyl)furan 188bj



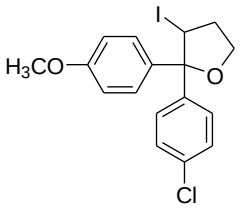
Reaction time (min): step 1/2 (20/15); brown oil; ^{1}H NMR ($CDCl_3$, 400 MHz): δ 7.44 (d, 2H, J = 8.7 Hz), 7.34 (d, 2H, J = 8.7 Hz), 6.85-6.79 (m, 4H), 5.26 (bt, 1H, J = 3.8 Hz), 4.41 (aq, 1H, J = 7.8 Hz), 4.04-3.99 (m, 1H), 3.77 (s, 3H), 3.76 (s, 3H), 2.53-2.48 (m, 2H); ^{13}C NMR ($CDCl_3$, 100 MHz): δ 158.6, 158.3, 139.3, 134.9, 127.0, 126.4, 113.9, 112.9, 90.6, 65.7, 55.2, 55.1, 38.5, 36.7; IR (neat, cm^{-1}): 3242, 1606, 1508, 1174, 1033, 833, 688, 524; HRMS (ESI): calcd for $C_{18}H_{20}O_3I$ 411.0457, found 411.0461.

2-(4-Chlorophenyl)-tetrahydro-3-iodo-2-p-tolylfuran 188bk



Reaction time (min): step 1/2 (60/15); pale yellow oil; dr ratio = 5:4; ^{1}H NMR ($CDCl_3$, 400 MHz): δ 7.46 (d, 1H, J = 8.4 Hz), 7.37-7.06 (m, 7H), 5.25-5.23 (m, 1H, *cis* or *trans* isomer), 5.22-5.20 (m, 1H, *cis* or *trans* isomer), 4.43-4.35 (m, 1H), 4.04-3.98 (m, 1H), 2.49-2.40 (m, 2H), 2.279 (s, 1H, *cis* or *trans* isomer), 2.271 (s, 1H, *cis* or *trans* isomer); ^{13}C NMR ($CDCl_3$, 100 MHz): δ 145.2, 143.2, 141.5, 139.2, 137.2, 136.8, 133.1, 132.6, 129.5, 128.8, 128.5, 127.9, 127.2, 126.7, 125.6, 125.0, 90.8, 65.77 (*cis* or *trans* isomer), 65.71 (*cis* or *trans* isomer), 38.4 (*cis* or *trans* isomer), 38.2 (*cis* or *trans* isomer), 35.5 (*cis* or *trans* isomer), 35.4 (*cis* or *trans* isomer), 21.1 (*cis* or *trans* isomer), 20.9 (*cis* or *trans* isomer); IR (neat, cm^{-1}):3496, 1635, 1215, 752, 499; HRMS (ESI): calcd for $C_{17}H_{17}OClI$ 399.0013, found 399.0016.

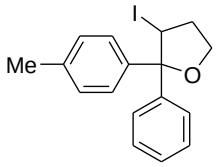
2-(4-Chlorophenyl)-tetrahydro-3-iodo-2-(4-methoxyphenyl)furan 188bl



Reaction time (min): step 1/2 (60/15); brown color oil; dr ratio = 7:4; ^{1}H NMR ($CDCl_3$, 300 MHz): δ 7.46-7.20 (m, 6H), 6.83-677 (m, 2H), 5.23-5.18 (m, 1H), 4.42-4.34 (m, 1H), 4.04-3.96 (m, 1H), 3.75 (s, 3H, *cis* or *trans* isomer), 3.74 (s, 3H, *cis* or *trans* isomer), 2.52-2.41 (m, 2H); ^{13}C NMR ($CDCl_3$, 75 MHz): δ 158.8, 158.5, 145.3, 134.2, 133.1, 132.6, 128.8, 127.8, 127.2, 127.0, 126.7, 126.4, 114.1, 113.1, 90.6, 65.8 (*cis* or *trans* isomer), 65.7 (*cis* or *trans* isomer), 55.2 (*cis* or *trans* isomer), 55.1 (*cis* or

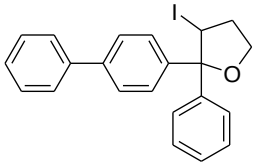
trans isomer), 38.4 (*cis* or *trans* isomer), 38.3 (*cis* or *trans* isomer), 35.8 (*cis* or *trans* isomer), 35.4 (*cis* or *trans* isomer); IR (neat, cm^{-1}): 3435, 3018, 1606, 1508, 1251, 1215, 1033, 759, 669; HRMS (ESI): calcd for $C_{17}H_{17}O_2ClI$ 414.9962, found 414.9964.

Tetrahydro-3-iodo-2-phenyl-2-p-tolylfuran 188bm



Reaction time (min): step 1/2 (15/10); colorless oil; dr ratio = 3:2; ^1H NMR ($CDCl_3$, 300 MHz): δ 7.44-6.98 (m, 9H), 5.18 (bt, 1H, J = 3.3 Hz), 4.34 (aq, 1H, *J* = 8.0 Hz), 4.02-3.95 (m, 1H), 2.40-2.32 (m, 2H), 2.20 (s, 3H, *cis* or *trans* isomer), 2.19 (s, 3H, *cis* or *trans* isomer); ^{13}C NMR ($CDCl_3$, 75 MHz): δ 144.3, 144.1, 141.3, 140.9, 137.0, 136.4, 129.4, 128.7, 128.4, 127.7, 127.2, 126.8, 125.99, 125.96, 125.0, 91.0, 65.1, 57.0 (*cis* or *trans* isomer), 56.9 (*cis* or *trans* isomer), 36.45 (*cis* or *trans* isomer) 36.42 (*cis* or *trans* isomer), 21.0 (*cis* or *trans* isomer), 20.9 (*cis* or *trans* isomer); IR (neat, cm^{-1}): 3400, 3392, 3018, 1647, 1215, 756, 669, 518, 497; HRMS (ESI): calcd for $C_{17}H_{18}OI$ 365.0402, found 365.0389.

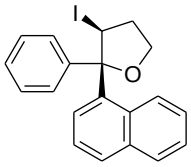
2-(4-Biphenyl)-tetrahydro-3-iodo-2-phenylfuran 188bn



Reaction time (min): step 1/2 (60/15); off white solid; m.p. 134-136 ^oC; dr ratio = 1:1; ^1H NMR ($CDCl_3$, 400 MHz): δ 7.60-7.17 (m, 14H), 5.34-5.31 (m, 1H), 4.45 (aq, 1H, *J* = 7.9 Hz), 4.12-4.04 (m, 1H), 2.54-2.45 (m, 2H); ^{13}C NMR ($CDCl_3$, 100 MHz): δ

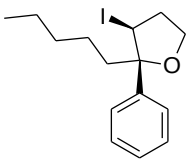
146.4, 145.5, 142.7, 141.7, 140.7, 140.4, 140.1, 139.6, 128.8, 128.7, 128.6, 127.8, 127.45, 127.43, 127.3, 127.2, 127.09, 127.04, 126.4, 126.2, 125.8, 125.7, 125.2, 91.24 (*cis* or *trans* isomer), 91.21 (*cis* or *trans* isomer), 65.7, 38.3, 35.97 (*cis* or *trans* isomer), 35.94 (*cis* or *trans* isomer); IR (neat, cm^{-1}): 3018, 1215, 759, 669, 511; HRMS (ESI): calcd for $C_{22}H_{20}OI$ 427.0559, found 427.0558.

Cis-tetrahydro-3-iodo-2-(naphthalen-1-yl)-2-phenylfuran 188bo



Reaction time (min): step 1/2 (120/60); brown solid; m.p. 116-118 ^{o}C; ^{1}H NMR ($CDCl_3$, 400 MHz): δ 8.17-8.08 (m, 2H), 7.82-7.49 (m, 5H), 7.36-7.12 (m, 5H), 5.77 (d, 1H, J = 5.3 Hz), 4.46 (aq, 1H, J = 8.1 Hz), 4.11-4.06 (m, 1H), 2.89-2.65 (m, 2H); ^{13}C NMR ($CDCl_3$, 100 MHz): δ 141.4, 134.1, 129.9, 128.9, 128.7, 128.3, 127.2, 126.3, 125.6, 125.2, 125.0, 124.65, 124.61, 92.3, 65.3, 39.2, 35.3; IR (neat, cm^{-1}): 3419, 3018, 1645, 1215, 761, 669, 499; HRMS (ESI): calcd for $C_{20}H_{18}OI$ 401.0402, found 401.0421.

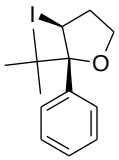
Cis-tetrahydro-3-iodo-2-pentyl-2-phenylfuran 188bp



Reaction time (min): step 1/2 (30/10); colorless oil; ^{1}H NMR ($CDCl_3$, 400 MHz): δ 7.40-7.25 (m, 5H), 4.63 (dd, 1H, J = 5.8, 3.8 Hz), 4.22 (aq, 1H, J = 7.9 Hz), 4.02 (dt, 1H, J = 8.2, 4.0 Hz), 2.47-2.31 (m, 2H), 2.01-1.90 (m, 2H), 1.27-1.14 (m, 5H), 0.89-0.80 (m, 4H); ^{13}C NMR ($CDCl_3$, 75 MHz): δ 142.7, 128.3, 126.9, 125.2, 88.1, 66.0,

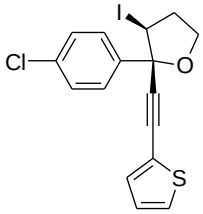
44.2, 38.3, 37.8, 32.0, 24.6, 22.5, 14.0; IR (neat, cm^{-1}): 3018, 1215, 752, 513; HRMS (ESI): calcd for $C_{15}H_{22}OI$ 345.0715, found 345.0732.

Cis-2-_tert_-butyl-tetrahydro-3-iodo-2-phenylfuran 188bq



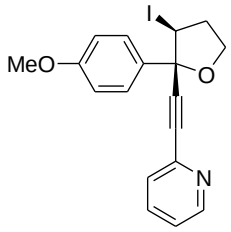
Reaction time: step 1/2 (120/60); colorless oil; ^1H NMR ($CDCl_3$, 300 MHz): δ 7.62-7.14 (m, 5H), 4.60 (dd, 1H, J = 7.7, 6.7 Hz), 3.94-3.83 (m, 2H), 2.61-2.43 (m, 1H), 2.17-2.01 (m, 1H), 0.94 (s, 9H); ^{13}C NMR ($CDCl_3$, 75 MHz): δ 142.1, 128.8, 126.8, 126.4.2, 90.4, 66.2, 40.7, 38.9, 27.2, 27.0; IR (neat, cm^{-1}): 3541, 3018, 1635, 1215, 771, 669, 559, 514; HRMS (ESI): calcd for $C_{14}H_{20}OI$ 331.0559, found 331.0565.

Cis-2-(4-chlorophenyl)-tetrahydro-3-iodo-2-(2-(thiophen-2-yl)ethynyl)furan 188ba



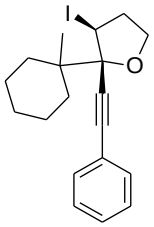
Reaction time (min): step 1/2 (20/30); pale yellow oil; ^1H NMR ($CDCl_3$, 400 MHz): δ 7.61 (d, 2H, J = 8.5 Hz) 7.47-7.11 (m, 5H), 4.22-4.06 (m, 2H), 3.93 (t, 1H, J = 8.8 Hz), 2.61-2.54 (m, 2H); ^{13}C NMR ($CDCl_3$, 100 MHz): δ 137.8, 134.4, 130.0, 129.7, 128.4, 127.5, 125.4, 121.1, 87.3, 85.1, 84.1, 67.1, 37.7, 32.7; IR (neat, cm^{-1}): 3412, 3018, 2399, 1645, 1215, 1031, 927, 744, 669, 624, 522; HRMS (ESI): calcd for $C_{16}H_{13}OSClI$ 414.9420, found 414.9402.

***Cis*-2-(2-(tetrahydro-3-iodo-2-(4-methoxyphenyl)furan-2-yl)ethynyl)pyridine 188ai**



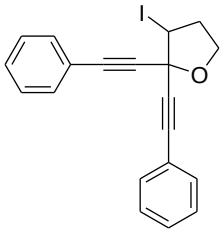
Reaction time (min): step 1/2 (30/15); light brown oil; ^{1}H NMR ($CDCl_3$, 300 MHz): δ 8.63-8.61 (m, 1H), 7.70-7.52 (m, 4H), 7.27-7.22 (m,1H), 6.92-6.87(m, 2H), 4.34-4.27 (m, 1H), 4.21-4.05 (m, 2H), 3.81 (s, 3H), 2.73-2.65 (m, 2H); ^{13}C NMR ($CDCl_3$, 100 MHz): δ 159.8, 150.1, 142.6, 136.1, 130.6, 127.7, 127.4, 123.2, 113.6, 88.2, 87.7, 85.3, 67.1, 55.3, 37.6, 32.5; IR (neat, cm^{-1}): 3367, 3018, 1510, 1465, 1215, 1174, 1029, 752, 667, 511; HRMS (ESI): calcd for $C_{18}H_{17}NO_2I$ 406.0304, found 406.0306.

***Cis*-tetrahydro-3-iodo-2-(1-methylcyclohexyl)-2-(2-phenylethynyl)furan 188aq**



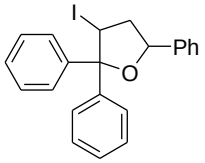
Reaction time (min): step 1/2 (30/10);colorless oil; ^{1}H NMR ($CDCl_3$, 400 MHz): δ 7.54-7.31 (m, 5H), 4.36 (t, 1H, J = 8.3 Hz), 4.03 (aq, 1H, J = 7.6 Hz), 3.80 (aq, 1H, J = 7.4 Hz), 2.59-2.53 (m, 2H), 1.88-1.24 (m, 8H), 1.20 (s, 3H), 0.97-0.88 (m, 2H); ^{13}C NMR ($CDCl_3$, 100 MHz): δ 131.7, 128.3, 128.2, 122.9, 89.9, 89.7, 88.6, 66.5, 41.8, 40.3, 33.3, 31.9, 26.0, 22.1, 22.0, 21.9, 18.4; IR (neat, cm^{-1}): 3018, 2933, 2399, 1215, 1035, 927, 781, 736, 669, 507; HRMS (ESI): calcd for $C_{19}H_{24}OI$ 395.0872, found 395.0878.

Tetrahydro-3-iodo-2,2-bis(2-phenylethynyl)furan 188aw



Reaction time (min): step 1/2 (30/60); light brown oil; ^{1}H NMR ($CDCl_3$, 400 MHz): δ 7.56-7.49 (m, 4H), 7.34-7.25 (m, 6H), 4.53 (t, 1H, J = 7.3 Hz), 4.26-4.09 (m, 2H), 2.86-2.77 (m, 1H), 2.62-2.53 (m, 1H); ^{13}C NMR ($CDCl_3$, 100 MHz): δ 132.0, 129.0, 128.9, 128.29, 128.27, 121.8, 121.7, 86.7, 86.6, 84.9, 84.4, 66.9, 37.2, 30.8; IR (neat, cm^{-1}): 3356, 3018, 1490, 1215, 752, 669, 513; HRMS (ESI): calcd for $C_{20}H_{16}OI$ 399.0246, found 399.0257.

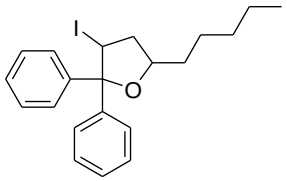
Tetrahydro-3-iodo-2,2,5-triphenylfuran 188bs



Reaction time (min): step 1/2 (15/15); pale yellow solid; m.p. 122-124 ^{o}C; dr ratio = 1:0.6; ^{1}H NMR ($CDCl_3$, 400 MHz): δ 7.55-7.46 (m, 5H), 7.37-7.09 (m, 19H), 5.67 (dd, 1H, J = 8.6, 6.1 Hz, *cis* or *trans* isomer), 5.42 (bt, 1H, J = 4.1 Hz, *cis* or *trans* isomer), 5.29 (bt, 1H, J = 5.7 Hz, *cis* or *trans* isomer), 4.90 (t, 1H, J = 7.4 Hz, *cis* or *trans* isomer), 3.00 (a quin, 1H, J = 7.1 Hz, *cis* or *trans* isomer), 2.76-2.70 (m, 1H, *cis* or *trans* isomer), 2.67-2.60 (m, 1H, *cis* or *trans* isomer), 2.45-2.38 (m, 1H, *cis* or *trans* isomer); ^{13}C NMR ($CDCl_3$, 100 MHz): δ 147.4, 146.8, 144.6, 142.6, 141.39, 141.34, 128.7, 128.5, 128.4, 127.76, 127.71, 127.6, 127.4, 127.3, 127.1, 126.6, 126.43, 126.41, 126.3, 126.2, 126.1, 91.8 (*cis* or *trans* isomer), 90.9 (*cis* or *trans* isomer), 81.6 (*cis* or *trans* isomer), 78.3 (*cis* or *trans* isomer), 46.79 (*cis* or *trans* isomer), 46.74 (*cis*

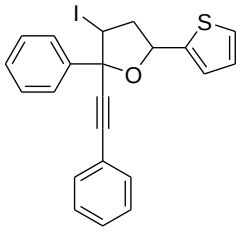
or *trans* isomer), 35.1 (*cis* or *trans* isomer), 33.2 (*cis* or *trans* isomer); IR (neat, cm^{-1}): 3417, 3018, 1631, 1448, 1215, 1049, 929, 774, 700, 669; HRMS (ESI): calcd for $C_{22}H_{19}OINa$ 449.0378, found 449.0388.

Tetrahydro-3-iodo-5-pentyl-2,2-diphenylfuran 188bt



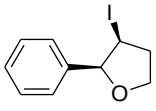
Reaction time (min): step 1/2 (15/30); colorless oil; dr ratio = 1:0.6; ^{1}H NMR ($CDCl_3$, 300 MHz): δ 7.51-7.47 (m, 3H), 7.36-7.08 (m, 13H), 5.38 (dd, 1H, *J* = 4.8, 1.7 Hz, *cis* or *trans* isomer), 5.20 (dd, 1H, *J* = 6.6, 4.5 Hz, *cis* or *trans* isomer), 4.67-4.58 (m, 1H, *cis* or *trans* isomer), 3.91 (a quin 1H, *J* = 6.8 Hz, *cis* or *trans* isomer), 2.65 (vquin, 1H, *J* = 7.02 Hz, *cis* or *trans* isomer), 2.49 (dddd, 1H, *J* = 5.7, 1.9, 5.7, 1.9 Hz, *cis* or *trans* isomer), 2.37-2.29 (m, 1H, *cis* or *trans* isomer), 2.07-1.93 (m, 2H), 1.72-1.64 (m, 2H), 1.49-1.45 (m, 2H), 1.39-1.18 (m, 8H), 0.87-0.80 (m, 5H); ^{13}C NMR ($CDCl_3$, 75 MHz): δ 147.5, 146.9, 145.2, 143.0, 128.5, 128.3, 127.6, 127.5, 127.3, 127.1, 127.0, 126.8, 126.2, 125.9, 125.7, 125.4, 91.0 (*cis* or *trans* isomer), 90.1 (*cis* or *trans* isomer), 79.6 (*cis* or *trans* isomer), 77.4 (*cis* or *trans* isomer), 44.5 (*cis* or *trans* isomer), 44.1 (*cis* or *trans* isomer), 37.1, 35.9 (*cis* or *trans* isomer), 35.8 (*cis* or *trans* isomer), 34.0, 31.82 (*cis* or *trans* isomer), 31.80 (*cis* or *trans* isomer), 26.2 (*cis* or *trans* isomer), 26.1 (*cis* or *trans* isomer), 22.65 (*cis* or *trans* isomer), 22.61 (*cis* or *trans* isomer), 14.07 (*cis* or *trans* isomer), 14.02 (*cis* or *trans* isomer), 1.0; IR (neat, cm^{-1}): 3435, 2100, 1633, 1215, 771, 669; HRMS (ESI): calcd for $C_{21}H_{26}OI$ 421.1028, found 421.1016.

Tetrahydro-3-iodo-2-phenyl-2-(2-phenylethynyl)-5-(thiophen-2-yl)furan 188bc



Reaction time (min): step 1/2 (15/30); light brown solid; m.p. 71-73 ^{o}C dr ratio = 1:0.6; ^{1}H NMR ($CDCl_3$, 500 MHz): δ 7.82-7.77 (m, 2H), 7.57-7.54 (m, 2H), 7.41-6.78 (m, 9H), 5.57 (dd, 1H, J = 8.8, 7.1 Hz, *cis* or *trans* isomer), 5.51 (dd, 1H, J = 9.5, 6.2 Hz, *cis* or *trans* isomer), 4.28-4.21 (m, 1H), 3.09-2.94 (m, 2H); ^{13}C NMR ($CDCl_3$, 75 MHz): δ 151.4, 145.0, 139.3, 139.0, 136.4, 131.88, 131.85, 128.8, 128.7, 128.6, 128.35, 128.31, 126.7, 126.6, 126.25, 126.22, 125.9, 125.5, 122.4, 122.2, 89.8 (*cis* or *trans* isomer), 89.5 (*cis* or *trans* isomer), 89.2, (*cis* or *trans* isomer), 88.9 (*cis* or *trans* isomer), 86.0 (*cis* or *trans* isomer), 85.9 (*cis* or *trans* isomer), 77.9 (*cis* or *trans* isomer), 77.5 (*cis* or *trans* isomer), 47.6 (*cis* or *trans* isomer), 47.2 (*cis* or *trans* isomer), 32.2 (*cis* or *trans* isomer), 31.7 (*cis* or *trans* isomer); IR (neat, cm^{-1}): 3388, 3018, 1647, 1215, 759, 669, 518; HRMS (ESI): calcd for $C_{22}H_{18}OSI$ 457.0123, found 457.0143.

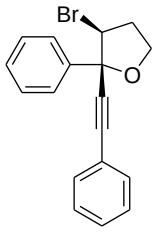
***Cis*-tetrahydro-3-iodo-2-phenylfuran 188bu**



Reaction time (min): step 1/2 (120/15); yellow oil; ^{1}H NMR ($CDCl_3$, 400 MHz): δ 7.41-7.25 (m, 5H), 5.15 (d, 1H, J = 6.3 Hz), 4.21-4.09 (m, 2H), 4.03 (aq, 1H, J = 6.5 Hz), 2.60-2.54 (m, 1H), 2.42-2.34 (m, 1H); ^{13}C NMR ($CDCl_3$, 100 MHz): δ 128.6, 128.5, 128.1, 126.4, 126.0, 89.8, 68.0, 38.3, 27.0; IR (neat, cm^{-1}): 3415, 3018, 1643,

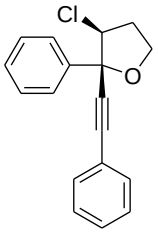
1215, 756, 669, 497; HRMS (ESI): calcd for $C_{10}H_{12}OI$ 274.9933, found 274.9943.

Cis-3-bromo-tetrahydro-2-phenyl-2-(2-phenylethynyl)furan 188bw



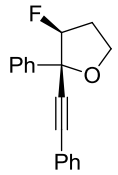
Reaction time (min): step 1/2 (15/20); white solid; m.p. 95-97 ^{o}C; ^{1}H NMR ($CDCl_3$, 300 MHz): δ 7.73 (d, 2H, J = 6.6 Hz), 7.54-7.25 (m, 8H), 4.41-4.33 (m, 1H), 4.26-4.14 (m, 2H), 2.71-2.51 (m, 2H); ^{13}C NMR ($CDCl_3$, 75 MHz): δ 139.8, 131.9, 128.6, 128.4, 128.3, 128.2, 125.7, 122.3, 88.6, 87.1, 84.6, 66.2, 55.6, 35.5; IR (neat, cm^{-1}): 3435, 3018, 1645, 1215, 1039, 779, 669, 524, 503; HRMS (ESI): calcd for $C_{18}H_{16}OBr$ 327.0385, found 327.0383.

Cis-3-chloro-tetrahydro-2-phenyl-2-(2-phenylethynyl)furan 188bx



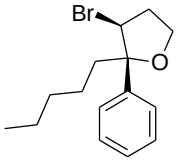
Reaction time (min): step 1/2 (15/120); white solid; m.p. 70-72 ^{o}C; ^{1}H NMR ($CDCl_3$, 300 MHz): δ 7.63-7.42 (m, 4H), 7.34-7.17 (m, 6H), 4.34-4.27 (m, 1H), 4.19-4.07 (m, 2H), 2.56-2.32 (m, 2H); ^{13}C NMR ($CDCl_3$, 75 MHz): δ 140.1, 131.9, 128.6, 128.4, 128.3, 128.2, 125.5, 122.4, 88.6, 86.4, 84.5, 65.8, 65.1, 34.7; IR (neat, cm^{-1}): 3018, 1215, 756, 669, 514; HRMS (ESI): calcd for $C_{18}H_{16}OCl$ 283.0890, found 283.0882.

Cis-3-fluoro-tetrahydro-2-phenyl-2-(2-phenylethynyl)furan 188by



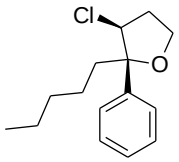
Reaction time (min): step 1/2 (15/120); white solid; m.p 80-82 ^{o}C; ^{1}H NMR ($CDCl_3$, 400 MHz): δ 7.61 (d, 2H, J = 7.4 Hz) 7.49-7.26 (m, 8H), 5.15-5.01 (m, 1H), 4.40 (aq, 1H, J = 8.2 Hz), 4.28-4.20 (m, 1H), 2.35-2.12 (m, 2H); ^{13}C NMR ($CDCl_3$, 125 MHz): δ 140.9, 131.9, 128.5, 128.1, 125.3, 122.4, 99.1, 97.6, 87.5, 86.25 (d, 1C, J_{C-F} = 24.1 Hz), 83.9 (d, 1C, J_{C-F} = 76.1 Hz), 66.7, 31.2 (d, 1C, J_{C-F} = 84.5 Hz), 30.9; IR (neat, cm^{-1}): 3466, 1718, 1280, 1215, 1051, 752, 669; HRMS (ESI): calcd for $C_{18}H_{16}OF$ 267.1185, found 267.1196.

Cis-3-bromo-tetrahydro-2-pentyl-2-phenylfuran 188bz



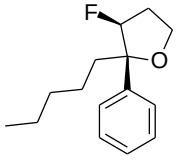
Reaction time (min): step 1/2 (30/15); colorless oil; ^{1}H NMR ($CDCl_3$, 300 MHz): δ 7.33-7.20 (m, 5H), 4.63 (dd, 1H, J = 5.3, 2.8 Hz), 4.21 (aq, 1H, J = 8.3 Hz), 4.02 (dt, 1H, J = 8.3, 3.6 Hz), 2.36-2.19 (m, 2H), 2.04-1.81 (m, 2H), 1.26-1.16 (m, 5H), 0.88-0.75 (m, 4H); ^{13}C NMR ($CDCl_3$, 75 MHz): δ 143.5, 128.3, 127.0, 125.1, 88.8, 65.4, 59.3, 40.4, 36.2, 32.0, 24.2, 22.4, 13.9; IR (neat, cm^{-1}): 3435, 3018, 1645, 1215, 752, 669; HRMS (ESI): calcd for $C_{15}H_{22}OBr$ 297.0854, found 297.0858.

Cis-3-chloro-tetrahydro-2-pentyl-2-phenylfuran 188ca



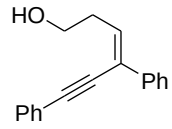
Reaction time (min): step 1/2 (30/120); light brown oil; ^{1}H NMR ($CDCl_3$, 300 MHz): δ 7.27-7.14 (m, 5H), 4.50 (dd, 1H, J = 5.2, 2.6 Hz), 4.14 (aq, 1H, J = 8.2 Hz), 3.96 (dt, 1H, J = 8.4, 3.7 Hz), 2.30-1.80 (m, 4H), 1.18-1.12 (m, 5H), 0.87-0.69 (m, 4H); ^{13}C NMR ($CDCl_3$, 125 MHz): δ 143.9, 128.3, 127.0, 125.1, 89.3, 67.0, 65.1, 38.2, 35.5, 32.1, 23.9, 22.4, 14.0; IR (neat, cm^{-1}): 3435, 3018, 1635, 1219, 785, 667, 590, 503; HRMS (ESI): calcd for $C_{15}H_{22}OCl$ 253.1359, found 253.1350.

Cis-3-fluoro-tetrahydro-2-pentyl-2-phenylfuran 188cb



Reaction time (min): step 1/2 (30/60); colorless oil; ^{1}H NMR ($CDCl_3$, 300 MHz): δ 7.34-7.23 (m, 5H), 5.28-5.09 (m, 1H), 4.19 (aq, 1H, J = 8.4 Hz), 4.04-3.86 (m, 1H), 2.42-1.80 (m, 4H), 1.19-1.17 (m, 5H), 0.92-0.76 (m, 4H); ^{13}C NMR ($CDCl_3$, 75 MHz): δ 142.4, 128.2, 127.0, 125.4, 99.6, 97.2, 89.9 (d, 1C, $J_{C\text{-}F}$ = 75.1 Hz), 65.4, 35.5 (d, 1C, $J_{C\text{-}F}$ = 31.9 Hz), 32.2, 31.8, 31.6, 23.5, 22.4, 13.9; IR (neat, cm^{-1}): 3018, 1215, 759, 665, 524; HRMS (ESI): calcd for $C_{15}H_{22}OF$ 237.1655, found 237.1651.

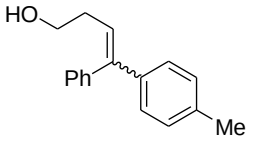
(_Z_)-4,6-Diphenylhex-3-en-5-yn-1-ol 189aa



Colorless oil; ^{1}H NMR ($CDCl_3$, 300 MHz): δ 7.22 (d, 2H, J = 7.2 Hz), 7.58-7.29 (m,

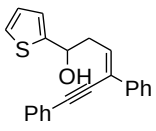
8H), 6.53 (t, 1H, *J* = 7.4 Hz), 3.86 (t, 2H, *J* = 6.4 Hz), 2.89 (q, 2H, *J* = 6.6 Hz), 2.15 (s, 1H); ^{13}C NMR ($CDCl_3$, 75 MHz): δ 137.9, 134.0, 131.6, 128.46, 128.44, 127.8, 126.1, 125.7, 123.2, 95.7, 86.5, 71.8, 62.0, 34.9; IR (neat, cm^{-1}): 3419, 3018, 2399, 1645, 756, 667; HRMS (ESI): calcd for $C_{18}H_{17}O$ 249.1279, found 249.1288.

4-Phenyl-4-*p*-tolylbut-3-en-1-ol 189bm



Colorless oil; mixture of *E*/*Z* isomers = 7:5; ^{1}H NMR ($CDCl_3$, 300 MHz): δ 7.29-6.95 (m, 9H), 6.00-5.95 (m, 1H), 3.62-3.57 (m, 2H), 2.34-2.24 (m, 2H), 2.28 (s, 3H, *E* or *Z* diastereomer), 2.22 (s, 3H, *E* or *Z* diastereomer), 1.62 (bs, 1H); ^{13}C NMR ($CDCl_3$, 75 MHz): δ 162.3, 144.2, 144.1, 142.6, 140.0, 139.6, 136.9, 136.7, 129.88, 129.80, 128.9, 128.8, 128.2, 128.1, 127.3, 127.1, 127.08, 127.05, 125.0, 124.3, 62.6, 33.4 (*E* or *Z* diastereomer), 33.3 (*E* or *Z* diastereomer), 21.2 (*E* or *Z* diastereomer), 21.0 (*E* or *Z* diastereomer); IR (neat, cm^{-1}): 3435, 3018, 2325, 1642, 756, 669; HRMS (ESI): calcd for $C_{17}H_{19}O$ 239.1436, found 239.1438.

(*Z*)-4,6-Diphenyl-1-(thiophen-2-yl)hex-3-en-5-yn-1-ol 189bc

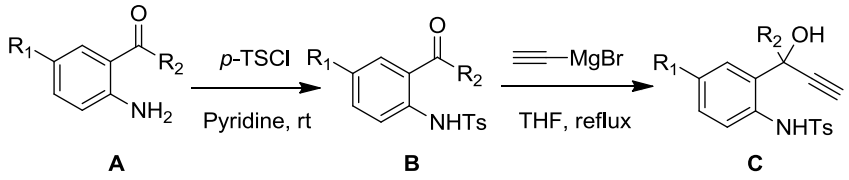


Pale yellow color oil; ^{1}H NMR ($CDCl_3$, 500 MHz): δ 7.65-7.51 (m, 4H), 7.36-7.23 (m, 7H), 7.04-6.96 (m, 2H), 6.50 (t, 1H, *J* = 7.4 Hz), 5.19 (t, 1H, *J* = 6.4 Hz), 3.17-3.13 (m, 2H), 2.15 (bs, 1H); ^{13}C NMR ($CDCl_3$, 125 MHz): δ 147.9, 137.8, 132.6, 131.6, 128.48, 128.44, 128.42, 127.9, 126.7, 126.3, 126.1, 124.8, 123.8, 123.1, 96.0, 86.4, 69.9, 41.1; IR (neat, cm^{-1}): 3415, 3018, 2325, 1645, 757, 669; HRMS (ESI):

calcd for $C_{22}H_{19}OS$ 331.1157, found 331.1165.

7.4 Silver Triflate-Catalyzed Tandem Heterocyclization/Alkynylation of 1-((2-Tosylamino)aryl)but-2-yne-1,4-diols to 2-Alkynyl Indoles

Representative Experimental Procedure for the Preparation of Substituted *N*-(2-(1-Hydroxyprop-2- yn-1-yl)phenyl)-4-methylbenzenesulfonamide Derivatives (C)[128,138a,140]

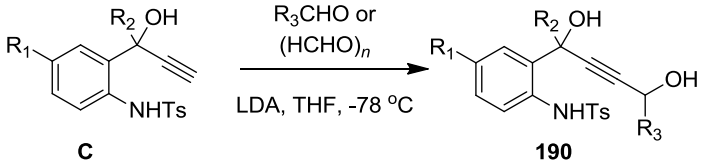


R_1 = H, Me, Cl, Br

R_2 = H, aryl, heteroaryl, alkynyl

To a solution of the appropriate 1-(2-aminophenyl) ketone or aldehyde (A, 2.5 mmol) in pyridine (2 mL) was added *p*-TsCl (3.8 mmol) at room temperature. The resulting solution was stirred for 4 h at room temperature. On completion, the reaction mixture was quenched by addition of H_2O (5 mL) and filtered. The resulting solid (B) was dried and used directly for the next step. The solid (1.4 mmol) was dissolved in anhydrous THF (5 mL), and a solution of ethynylmagnesium bromide (0.5 M THF solution; 4.2 mmol) was added at room temperature. The resulting mixture was allowed to reflux for 3 h. On completion, the reaction mixture was cooled to room temperature, quenched with saturated NH_4Cl (10 mL) and extracted with EtOAc (2 x 10 mL). The combined organic layers were washed with water, brine solution, 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 (C).

Experimental Procedure for Preparation of Substituted *N*-(2-(1,4-Dihydroxybut-2- yn-1-yl)phenyl)-4-methylbenzenesulfonamides (190a)-(190u) & (19ov)



R_1 = H, Me, Cl, Br
R_2 = H, aryl, heteroaryl, alkynyl
R_3 = H, Ph, aryl, hetroaryl
acyclic alkyl, cyclic alkyl

To a solution of diisopropylamine (0.47g, 4.6 mmol) in anhydrous THF (5 mL) was added butyl lithium (1.6 M hexane solution; 2.9 mL; 4.6 mmol) at −78 °C in a dropwise manner. The resulting solution was stirred for 1 h prior to slow addition of the corresponding *N*-(2-(1-hydroxy-1-phenylprop-2-yn-1-yl)phenyl)-4-methylbenzenesulfonamide (C)[135a] (0.50g, 1.3 mmol) in THF at −78 °C. The resulting mixture was stirred at same temperature for 1 h. The corresponding aldehyde (0.21g, 2.0 mmol) in THF (2 mL) was added to the reaction mixture and allowed to stir for a further 1h at same temperature. For **190x:** Suspension of paraformaldehyde in THF (2 mL) was added to the reaction mixture and allowed to stir for a further 1h at same temperature. The resulting mixture was slowly warmed up to room temperature and continued the stirring for a further 3-5 h. On completion, the reaction mixture was quenched by adding saturated NH_4Cl (50 mL) and extracted with EtOAc (2 x 25 mL). The combined organic layers were washed with water, brine, dried over Na_2SO_4 and concentrated under reduced pressure. Purification by flash column chromatography on silica gel (eluent: *n*-hexane:EtOAc = 7.5:2.5) gave the title compound (**190**).

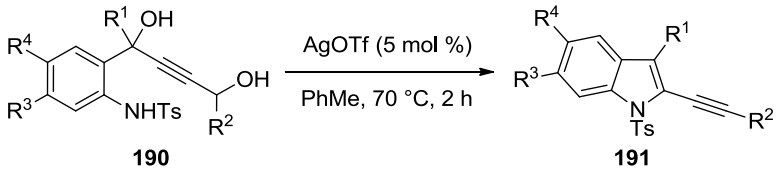
Representative Experimental Procedure to Assess the Deliberate Hidden Brønsted Acid Catalysis of *N*-Tosyl-1-(2-aminophenyl)-1,3-diphenyl-prop-2-yn-1-ol (191a) in 1,2-Dichloroethane[146a]

For a 0.1 mmol scale reaction, AgOTf (5 mol%) was added to 1,2-dichloroethane (1 mL) and heated with stirring to 90 °C for 3 h. The solution was cooled to room temperature and a solution of **190a** in toluene (3 mL) was added drop wise to the reaction solution and continued stirring at 70 °C for 2 h. On completion, the reaction mixture was brought to room temperature and concentrated under reduced pressure. Purification by flash column chromatography on silica gel (eluent: *n*-hexane:EtOAc = 9:1) gave the title compound.

Representative Experimental Procedure to Assess the Deliberate Hidden Brønsted Acid Catalysis of *N*-Tosyl-1-(2-aminophenyl)-1,3-diphenyl-prop-2-yn-1-ol (191a) with *t*-BuCl[146a]

To a solution of AgOTf (5 mol %) in toluene (2 mL), *t*-BuCl (10 mol %) was added dropwise with syringe and stirred for 10 min. A solution of **190a** (0.1 mmol) in toluene (2 mL) was then added drop wise and continued stirring at 70 °C for 2 h. On completion, the reaction mixture was brought to room temperature and concentrated under reduced pressure. Purification by flash column chromatography on silica gel (eluent: *n*-hexane:EtOAc = 9:1) gave the title compound.

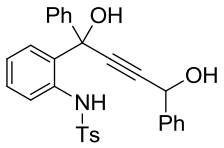
General Experimental Procedure for Silver Triflate-Catalyzed Reactions of Substituted 2-Alkynyl-1-tosyl-1*H*-indoles (191a)-(191x)



190 **191**

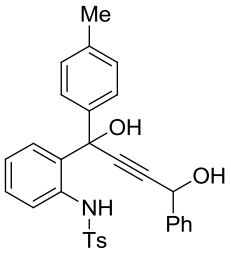
To a solution of AgOTf (5 mol %) in anhydrous toluene (2 mL) at room temperature was added dropwise a solution of the propargylic 1,4-diol 1a (0.1 mmol) in toluene (2 mL). The resulting mixture was stirred at 70 °C for 2 h and monitored by TLC analysis. On completion, the reaction mixture was brought to room temperature 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-(1,4-dihydroxy-1,4-diphenylbut-2-yn-1-yl)phenyl)-4-methylbenzenesulfona--mide 190a**



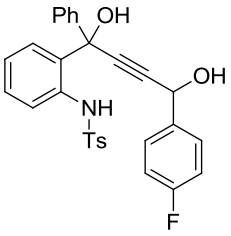
Yield: 85%; white solid; m.p. 152-154 ^{o}C; dr ratio = 1:1; ^{1}H NMR ($CDCl_3$, 400 MHz): δ 8.65 (s, 1H, A or B diastereomer), 8.61 (s, 1H, A or B diastereomer), 7.52-7.28 (m, 14H), 7.21 (t, 1H, J = 7.7 Hz), 7.15-7.12 (m, 2H), 6.97 (t, 1H, J = 7.5 Hz), 5.60 (s, 1H, A or B diastereomer), 5.59 (s, 1H, A or B diastereomer), 3.61 (s, 1H), 2.96 (d, 1H, J = 5.7 Hz), 2.89 (d, 1H, J = 5.6 Hz), 2.38 (s, 3H); ^{13}C NMR ($CDCl_3$, 75 MHz): δ 143.5, 142.5, 139.8, 136.0, 135.9, 131.3, 131.2, 129.5, 129.4, 128.7, 128.67, 128.60, 128.4, 128.2, 127.3, 126.7, 126.2, 126.1, 123.0, 119.2, 88.9, 87.4, 74.9, 64.4, 21.5; IR (neat, cm^{-1}): 3628, 3018, 2399, 1532, 1215, 1045, 927, 771, 669: HRMS (ESI): calcd for $C_{29}H_{26}NO_4S$ 484.1583, found 484.1574.

***N*-(2-(1,4-dihydroxy-4-phenyl-1-(p-tolyl)but-2-yn-1-yl)phenyl)-4-methylbenzene--sulfonamide 190b**



Yield: 71%; white soild; 99-101 ^{o}C; dr ratio = 6:5; ^{1}H NMR ($CDCl_3$, 500 MHz): δ 8.84 (s, 1H, A or B diastereomer), 8.80 (s, 1H, A or B diastereomer), 7.38-7.21 (m, 11H), 7.13-6.85 (m, 6H), 5.40 (s, 1H, A or B diastereomer), 5.36 (s, 1H, A or B diastereomer), 4.65 (bs, 1H, A or B diastereomer), 4.60 (bs, 1H, A or B diastereomer), 3.73 (bs, 1H), 2.31 (s, 3H), 2.288 (s, 3H, A or B diastereomer), 2.282 (s, 3H, A or B diastereomer); ^{13}C NMR ($CDCl_3$, 125 MHz): δ 143.5, 143.4, 139.8, 139.7, 137.9, 137.8, 136.6, 136.5, 135.96, 135.90, 131.4, 131.3, 129.47, 129.43, 129.28, 129.23, 128.86, 128.82, 128.65, 128.63, 128.4, 127.3, 126.8, 126.09, 126.01, 123.1, 123.0, 119.1, 119.0, 88.6, 87.7, 74.85, 74.81, 64.46, 64.42, 21.5, 21.2; IR (neat, cm^{-1}): 3687, 3018, 1215, 929, 752, 746, 669, 574: HRMS (ESI): calcd for $C_{30}H_{28}NO_4S$ 498.1739, found 498.1746.

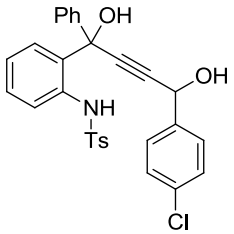
***N*-(2-(4-(4-fluorophenyl)-1,4-dihydroxy-1-phenylbut-2-yn-1-yl)phenyl)-4-methylbenzenesulfonamide 190c**



Yield: 57%; white solid; m.p. 111-113 ^{o}C; dr ratio = 1:1; ^{1}H NMR ($CDCl_3$, 300 MHz): δ 8.87 (s, 1H, A or B diastereomer), 8.85 (s, 1H, A or B diastereomer), 7.37-6.85 (m,

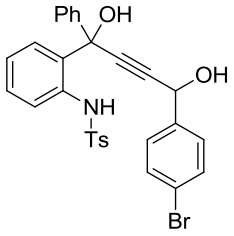
17H), 5.38 (s, 1H, A or B diastereomer), 5.34 (s, 1H, A or B diastereomer), 4.89 (bs, 1H), 3.95 (bs, 1H), 2.28 (s, 3H); ^{13}C NMR ($CDCl_3$, 75 MHz): δ 164.2, 160.9, 143.68, 143.65, 142.5, 136.5, 136.4, 135.9, 135.8, 135.6, 131.3, 131.2, 129.5, 129.3, 128.8, 128.78, 128.72, 128.6, 128.2, 127.2, 126.17, 126.12, 123.18, 123.11, 119.2, 119.1, 115.57, 115.55, 115.29, 115.26, 88.5, 88.7, 77.3, 74.9, 74.8, 63.7, 21.5; IR (neat, cm^{-1}): 3275, 3018, 1508, 1215, 1157, 756, 669: HRMS (ESI): calcd for $C_{29}H_{24}NO_4SFNa$ 524.1308, found 524.1301.

_N_-(2-(4-(4-chlorophenyl)-1,4-dihydroxy-1-phenylbut-2-yn-1-yl)phenyl)-4-methylbenzenesulfonamide 190d



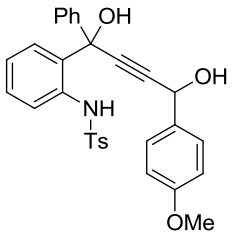
Yield: 60%; pale yellow soil; m.p. 64-66 ^{o}C; dr ratio = 1:1; ^{1}H NMR ($CDCl_3$, 500 MHz): δ 8.87 (bs, 1H), 7.36-6.85 (m, 17H), 5.37 (s, 1H, A or B diastereomer), 5.32 9s, 1H, A or B diastereomer), 4.92 (bs, 1H), 2.29 (s, 3H, A or B diastereomer), 2.28 (s, 3H, A or B diastereomer); ^{13}C NMR ($CDCl_3$, 125 MHz): δ 143.7, 143.6, 142.5, 138.33, 138.30, 136.4, 136.3, 135.9, 135.8, 134.13, 134.10, 131.3, 131.2, 129.62, 129.61, 129.4, 128.8, 128.78, 128.72, 128.69, 128.61, 128.27, 128.24, 128.20, 128.1, 127.2, 126.19, 126.13, 123.2, 123.1, 119.2, 119.1, 88.2, 87.8, 77.3, 74.9, 74.8, 63.7, 63.6, 21.5; IR (neat, cm^{-1}): 3307, 3018, 2399, 1490, 1336, 1288, 1215, 1091, 1014, 752, 700, 565: HRMS (ESI): calcd for $C_{29}H_{25}NO_4SCl$ 518.1193, found 518.1175.

_N_-(2-(4-(4-bromophenyl)-1,4-dihydroxy-1-phenylbut-2-yn-1-yl)phenyl)-4-methylbenzenesulfonamide 190e



Yield: 62%; off white solid; m.p. 78-80 ^{o}C; dr ratio = 1:1; ^{1}H NMR ($CDCl_3$, 400 MHz): δ 8.84 (bs, 1H), 7.36-6.86 (m, 17H), 5.37 (s, 1H, A or B diastereomer), 5.33 (s, 1H, A or B diastereomer), 4.74 (bs, 1H), 4.28 (bs, 1H), 2.30 (s, 3H); ^{13}C NMR ($CDCl_3$, 100 MHz): δ 143.69, 143.67, 142.4, 138.84, 138.81, 136.5, 136.4, 135.9, 135.8, 131.67, 131.64, 131.4, 131.3, 129.63, 129.61, 129.4, 128.8, 128.7, 128.6, 128.5, 128.4, 128.3, 128.2, 127.2, 126.2, 126.1, 123.2, 123.1, 122.37, 122.34, 119.3, 119.2, 88.2, 87.8, 77.3, 74.89, 74.85, 63.74, 63.71, 21.5; IR (neat, cm^{-1}): 3446, 3307, 3018, 2399, 1492, 1332, 1215, 1159, 1091, 1010, 927, 759, 669: HRMS (ESI): calcd for $C_{29}H_{25}NO_4SBr$ 564.0667, found 564.0652.

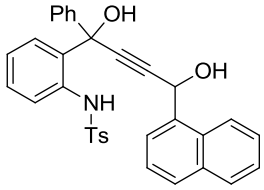
_N_-(2-(1,4-dihydroxy-4-(4-methoxyphenyl)-1-phenylbut-2-yn-1-yl)phenyl)-4-methylbenzenesulfonamide 190f



Yield: 64%; yellow oil; dr ratio = 6:5; ^{1}H NMR ($CDCl_3$, 300 MHz): δ 8.86 (s, 1H, A or B diastereomer), 8.84 (s, 1H, A or B diastereomer), 7.41-6.73 (m, 17H), 5.35 (s, 1H, A or B diastereomer), 5.31 (s, 1H, A or B diastereomer), 4.87 (bs, 1H, A or B diastereomer), 4.83 (bs, 1H, A or B diastereomer), 3.699 (s, 3H, A or B diastereomer),

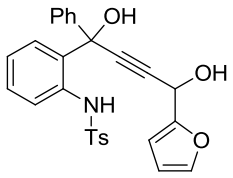
3.691 (A or B diastereomer), 3.61 (bs, 1H), 2.27 (s, 3H); ^{13}C NMR ($CDCl_3$, 75 MHz): δ 159.5, 143.5, 143.4, 142.7, 136.4, 135.96, 135.91, 132.1, 131.1, 129.5, 129.3, 128.8, 128.5, 128.2, 128.0, 127.2, 126.1, 126.0, 123.0, 122.9, 119.0, 118.9, 114.0, 88.9, 87.4, 77.3, 76.7, 74.8, 64.0, 55.3, 21.5; IR (neat, cm^{-1}): 3446, 2399, 1512, 1336, 1215, 1159, 927, 761, 669, 628: HRMS (ESI): calcd for $C_{30}H_{28}NO_5S$ 514.1688, found 514.1703.

_N_-(2-(1,4-dihydroxy-4-(naphthalen-1-yl)-1-phenylbut-2-yn-1-yl)phenyl)-4-methylbenzenesulfonamide 190g



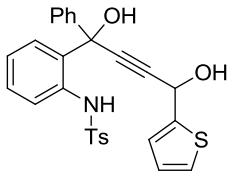
Yield: 55%; white solid; m.p. 142-144 ^{o}C; dr ratio = 3:2.2; ^{1}H NMR ($CDCl_3$+MeOD, 500 MHz): δ 8.20 (m, 1H), 7.84-7.67 (m, 3H), 7.46-72 (m, 13H), 7.13-6.80 (m, 4H), 6.12 (s, 1H, A or B diastereomer), 6.09 (s, 1H, A or B diastereomer), 2.62 (bs, 1H), 2.279 (s, 3H, A or B diastereomer), 2.273 (s, 3H, A or B diastereomer); ^{13}C NMR ($CDCl_3$+MeOD, 1255 MHz): δ 143.46, 143.42, 143.17, 143.14, 136.4, 136.3, 135.9, 135.3, 133.9, 131.2, 131.1, 130.46, 130.43, 129.48, 129.45, 129.1, 129.0, 128.8, 128.66, 128.64, 128.4, 128.3, 127.85, 127.83, 127.2, 126.3, 126.0, 125.9, 125.8, 125.28, 125.23, 124.6, 124.5, 123.9, 122.7, 122.6, 118.6, 118.4, 88.4, 88.18, 88.11, 74.6, 62.37, 62.34, 21.4; IR (neat, cm^{-1}): 3018, 2399, 1506, 1215, 929, 771, 750, 669: HRMS (ESI): calcd for $C_{33}H_{27}NO_4SNa$ 556.1559, found 556.1539.

***N*-(2-(4-(furan-2-yl)-1,4-dihydroxy-1-phenylbut-2-yn-1-yl)phenyl)-4-methylbenzenesulfonamide 190h**



Yield: 65%; brown oil; dr ratio = 1:1; ^{1}H NMR ($CDCl_3$, 400 MHz): δ 8.82 (d, 1H, A or B diastereomer), 8.80 (s, 1H, A or B diastereomer), 7.44-7.24 (m, 10H), 7.14 (t, 1H, *J* = 7.4 Hz), 7.02 (t, 2H, J = 7.1 Hz), 6.92 (t, 1H, *J* = 7.4 Hz), 6.32-6.24 (m, 2 H), 5.46 (s, 1H, A or B diastereomer), 5.43 (s, 1H, A or B diastereomer), 4.75 (bs, 1H), 3.78 (bs, 1H), 2.29 (s, 3H); ^{13}C NMR ($CDCl_3$, 100 MHz): δ 152.17, 152.15, 143.55, 143.52, 143.0, 142.5, 136.4, 136.3, 135.9, 135.8, 131.0, 130.9, 129.5, 129.3, 128.8, 128.5, 128.19, 128.16, 127.3, 126.1, 126.0, 123.07, 123.02, 119.1, 119.0, 110.53, 110.51, 108.2, 86.7, 86.3, 74.86, 74.83, 58.0, 21.5; IR (neat, cm^{-1}): 3018, 2399, 1215, 927, 759, 669, 626: HRMS (ESI): calcd for $C_{27}H_{24}NO_5S$ 474.1375, found 474.1383.

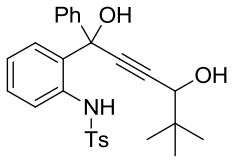
***N*-(2-(1,4-dihydroxy-1-phenyl-4-(thiophen-2-yl)but-2-yn-1-yl)phenyl)-4-methylbenzenesulfonamide 19oi**



Yield: 67%; pale yellow solid; m.p. 157-159 ^{o}C; dr ratio = 6:5; ^{1}H NMR (MeOD, 400 MHz): δ 7.70 (t, 1H, *J* = 8.2 Hz), 7.50 (d, 1H, *J* = 8.2 Hz), 7.38-7.24 (m, 8H), 7.18 (t, 1H, *J* = 7.5 Hz), 7.07-6.91 (m, 5H), 5.73 (s, 1H), 2.29 (s, 3H, A or B diastereomer), 2.28 (s, 3H, A or B diastereomer); ^{13}C NMR (MeOD, 100 MHz): δ 144.95, 143.8, 143.6, 136.0, 135.9, 131.1, 131.0, 129.1, 128.9, 128.6, 128.0, 127.4, 127.0, 126.1, 125.63, 125.60, 125.4, 125.3, 125.0, 122.2, 117.6, 87.9, 86.4, 74.3, 59.2, 20.0; IR

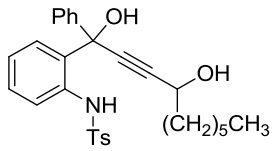
(neat, cm^{-1}): 3687, 3018, 2399, 1521, 1338, 1215, 929, 761, 669, 626: HRMS (ESI): calcd for $C_{27}H_{24}NO_4S_2$ 490.1147, found 490.1136.

_N_-(2-(1,4-dihydroxy-5,5-dimethyl-1-phenylhex-2-yn-1-yl)phenyl)-4-methylbenzenesulfonamide 190j



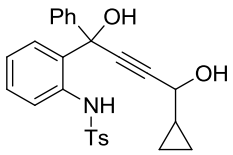
Yield: 58%; colorless oil; dr ratio = 1:1; ^{1}H NMR ($CDCl_3$+MeOD, 500 MHz): δ 9.13 (bs, 1H, A or B diastereomer), 9.10 (bs, 1H, A or B diastereomer), 7.57 (d, 1H, J = 7.7 Hz, A or B diastereomer), 7.47 (d, 1H, J = 7.7 Hz, A or B diastereomer), 7.41-7.27 (m, 8H), 7.14 (t, 1H, J = 7.6 Hz), 7.03 (t, 2H, J = 8.7 Hz), 6.97-6.92 (m, 1H), 4.05 (s, 1H, A or B diastereomer), 4.04 (s, 1H, A or B diastereomer), 2.82 (bs, 1H), 2.31 (s, 3H, A or B diastereomer), 2.30 (s, 3H, A or B diastereomer), 0.94 (s, 9H, A or B diastereomer), 0.92 (s, 9H, A or B diastereomer); ^{13}C NMR ($CDCl_3$+MeOD, 125 MHz): δ 143.5, 143.4, 136.4, 136.3, 135.87, 135.80, 131.3, 129.46, 129.44, 129.0, 128.76, 128.72, 128.36, 128.34, 127.75, 127.72, 127.2, 125.9, 125.8, 122.69, 122.65, 118.5, 118.4, 88.6, 86.8, 74.5, 71.0, 70.9, 35.97, 35.95, 25.3, 25.2, 21.4; IR (neat, cm^{-1}): 3618, 3446, 3018, 2399, 1521, 1215, 1045, 927, 756, 669: HRMS (ESI): calcd for $C_{27}H_{30}NO_4S$ 464.1896, found 464.1880.

_N_-(2-(1,4-dihydroxy-1-phenyldec-2-yn-1-yl)phenyl)-4-methylbenzenesulfonamide 190k



Yield: 63%; pale yellow oil; dr ratio = 6:5; ^{1}H NMR ($CDCl_3$, 400 MHz): δ 8.92 (s, 1H, A or B diastereomer), 8.86 (s, 1H, A or B diastereomer), 7.45-7.23 (m, 9H), 7.12 (t, 1H, J = 7.7 Hz), 7.02 (t, 2H, J = 8.1 Hz), 6.92 (q, 1H, J = 7.1Hz), 5.15 (bs, 1H, A or B diastereomer), 5.13 (bs, 1H, A or B diastereomer), 4.37-4.29 (m, 1H), 3.58 (bs, 1H), 2.30 (s, 3H, A or B diastereomer), 2.29 (s, 3H, A or B diastereomer), 1.64-1.58 (m, 2H), 1.28-1.19 (m, 8H), 0.85 (t, 3H, J = 6.8 Hz); ^{13}C NMR ($CDCl_3$, 100 MHz): δ 143.5, 143.4, 142.99, 142.98, 136.5, 136.4, 135.9, 135.8, 131.4, 131.3, 129.54, 129.52, 129.2, 128.7, 128.4, 128.0, 127.9, 127.2, 126.1, 126.0, 122.97, 122.92, 119.0, 118.9, 90.1, 90.0, 85.9, 85.8, 77.3, 74.7, 74.6, 62.4, 37.2, 37.1, 31.7, 28.8, 25.14, 25.12, 22.55, 22.51, 14.1; IR (neat, cm^{-1}): 3676, 3273, 2927, 2858, 2399, 1600, 1492, 1332, 1215, 1159, 1091, 929, 777, 669: HRMS (ESI): calcd for $C_{25}H_{26}NO_4S$ 436.1583, found 436.1589.

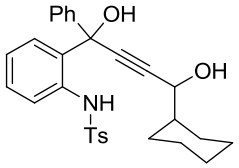
_N_-(2-(4-cyclopropyl-1,4-dihydroxy-1-phenylbut-2-yn-1-yl)phenyl)-4-methylbenzenesulfonamide 190l



Yield: 58%; colorless oil; dr ratio = 6:5; ^{1}H NMR ($CDCl_3$, 500 MHz): δ 8.86 (s, 1H, A or B diastereomer), 8.82 (s, 1H, A or B diastereomer), 7.42-7.24 (m, 9H), 7.13 (t, 1H, J = 7.7 Hz), 7.03 (t, 2H, J = 7.4 Hz), 6.93 (q, 1H, J = 6.9 Hz), 4.90 (bs, 1H), 4.19 (d,

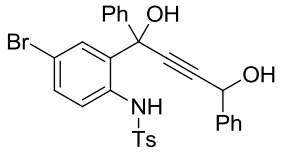
1H, *J* = 6.6 Hz, A or B diastereomer), 4.15 (d, 1H, *J* = 6.6 Hz, A or B diastereomer), 3.43 (bs, 1H), 2.31 (s, 3H, A or B diastereomer), 2.30 (s, 3H, A or B diastereomer), 1.17-1.14 (m, 1H), 0.46-0.25 (m, 4H); ^{13}C NMR ($CDCl_3$, 125 MHz): δ 143.5, 143.4, 142.8, 136.5, 136.4, 135.94, 135.90, 131.27, 131.21, 129.5, 129.2, 128.77, 128.72, 128.5, 128.08, 128.04, 127.2, 126.1, 126.0, 122.97, 122.93, 119.0, 118.9, 86.0, 86.0, 74.75, 74.71, 65.69, 65.66, 21.5, 16.8, 16.7, 3.34, 3.30, 1.8, 1.7; IR (neat, cm^{-1}): 3018, 2399, 1338, 1215, 1029, 769, 756, 669: HRMS (ESI): calcd for $C_{26}H_{26}NO_4S$ 448.1583, found 448.1575.

_N_-(2-(4-cyclohexyl-1,4-dihydroxy-1-phenylbut-2-yn-1-yl)phenyl)-4-methylbenzenesulfonamide 190m



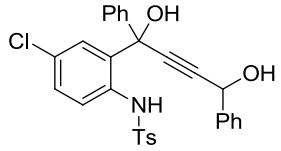
Yield: 59%; white solid; m.p. 115-117 ^{o}C; dr ratio = 3:2; ^{1}H NMR ($CDCl_3$, 400 MHz): δ 8.89 (s, 1H, A or B diastereomer), 8.85 (s, 1H, A or B diastereomer), 7.46-7.24 (m, 9H), 7.13 (t, 1H, *J* = 7.7 Hz), 7.02 (t, 2H, *J* = 7.7 Hz), 6.94-6.89 (m, 1H), 4.94 (bs, 1H), 4.16 (d, 1H, *J* = 6.1 Hz, A or B diastereomer), 4.13 (d, 1H, *J* = 6.1 Hz, A or B diastereomer), 3.35 (bs, 1H), 2.30 (s, 3H, A or B diastereomer), 2.29 (s, 3H, A or B diastereomer), 1.72-1.43 (m, 6H), 1.16-0.87 (m, 5H); ^{13}C NMR ($CDCl_3$, 100 MHz): δ 143.48, 143.45, 143.0, 136.6, 136.4, 135.95, 135.90, 131.4, 131.3, 129.53, 129.51, 129.2, 128.7, 128.4, 128.0, 127.9, 127.2, 126.1, 126.0, 122.95, 122.90, 119.0, 118.9, 89.2, 86.75, 86.73, 77.3, 74.8, 74.7, 67.1, 43.8, 43.7, 28.6, 28.08, 28.04, 26.3, 25.7, 21.5; IR (neat, cm^{-1}): 3419, 3018, 2399, 1635, 1336, 1215, 1159, 929, 756, 669: HRMS (ESI): calcd for $C_{29}H_{32}NO_4S$ 490.2052, found 490.2064.

***N*-(4-bromo-2-(1,4-dihydroxy-1,4-diphenylbut-2-yn-1-yl)phenyl)-4-methylbenzenesulfonamide 190n**



Yield: 61%; pale yellow oil; dr ratio = 1:1; ^{1}H NMR ($CDCl_3$, 400 MHz): δ 8.79 (bs, 1H, A or B diastereomer), 8.76 (bs, 1H, A or B diastereomer), 7.57-6.97 (m, 17H), 5.42 (s, 1H, A or B diastereomer), 5.36 (s, 1H, A or B diastereomer), 4.97 (bs, 1H), 3.75 (bs, 1H), 2.29 (s, 3H, A or B diastereomer), 2.28 (s, 3H, A or B diastereomer); ^{13}C NMR ($CDCl_3$, 100 MHz): δ 143.8, 143.7, 141.98, 141.95, 139.68, 139.61, 135.9, 135.8, 135.0, 134.9, 133.18, 133.10, 132.1, 131.5, 131.0, 129.64, 129.61, 128.8, 128.7, 128.5,9, 128.54, 128.39, 128.33, 127.2, 126.75, 126.72, 126.0, 125.9, 120.5, 120.4, 116.0, 115.9, 89.29, 89.22, 86.9, 74.37, 74.31, 64.4, 64.3, 21.5; IR (neat, cm^{-1}): 3018, 2399, 1215, 1161, 927, 769, 756, 669: HRMS (ESI): calcd for $C_{29}H_{25}NO_4SBr$ 562.0688, found 562.0690.

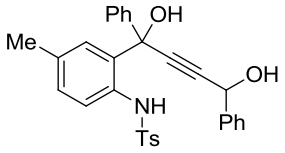
***N*-(4-chloro-2-(1,4-dihydroxy-1,4-diphenylbut-2-yn-1-yl)phenyl)-4-methylbenzenesulfonamide 190o**



Yield: 52%; pale yellow solid; m.p. 151-153 ^{o}C; dr ratio = 7:5; ^{1}H NMR ($CDCl_3$, 300 MHz): δ 8.79 (bs, 1H), 7.40-7.05 (m, 15H), 6.98 (t, 2H, J = 7.7 Hz), 5.39 (s, 1H, A or B diastereomer), 5.34 (s, 1H, A or B diastereomer), 5.08 (bs, 1H), 3.81 (bs, 1H), 2.28 (s, 3H, A or B diastereomer), 2.27 (s, 3H, A or B diastereomer); ^{13}C NMR ($CDCl_3$, 75 MHz): δ 143.84, 143.80, 142.0, 141.9, 139.6, 139.5, 136.0, 135.9, 134.49, 134.43,

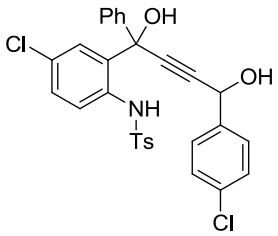
133.0, 132.9, 129.64, 129.62, 129.1, 128.78, 128.71, 128.58, 128.52, 128.4, 128.3, 127.2, 126.75, 126.73, 126.0, 125.9, 120.3, 120.2, 89.1, 86.9, 77.3, 74.46, 74.40, 64.4, 64.3, 21.5; IR (neat, cm^{-1}): 3435, 3018, 1645, 1215, 1039, 779, 669, 524, 503: HRMS (ESI): calcd for $C_{29}H_{25}NO_4SCl$ 518.1193, found 518.1176.

***N*-(2-(1,4-dihydroxy-1,4-diphenylbut-2-yn-1-yl)-4-methylphenyl)-4-methylbenzenesulfonamide 190p**



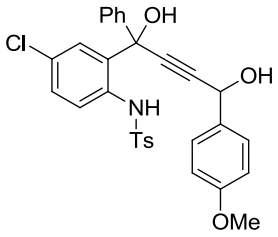
Yield: 67%; pale yellow oil; dr ratio = 1:1; ^{1}H NMR ($CDCl_3$, 400 MHz): δ 8.70 (s, 1H, A or B diastereomer), 8.66 (s, 1H, A or B diastereomer), 7.39-7.19 (m, 14H), 7.02-6.91 (m, 3H), 5.43 (s, 1H, A or B diastereomer), 5.37 (s, 1H, A or B diastereomer), 4.80 (bs, 1H), 3.78 (bs, 1H), 2.28 (s, 3H, A or B diastereomer), 2.27 (s, 3H, A or B diastereomer), 2.12 (s, 3H, A or B diastereomer), 2.11 (s, 3H, A or B diastereomer); ^{13}C NMR ($CDCl_3$, 100 MHz): δ 143.4, 143.3, 142.8, 140.0, 139.9, 136.6, 136.5, 133.3, 133.2, 132.7, 132.6, 131.4, 131.2, 129.7, 129.53, 129.50, 128.64, 128.62, 128. 5, 128.4, 128.3, 128.1, 128.0, 127.2, 126.8, 126.7, 126.1, 126.0, 119.4, 119.3, 88.8, 88.7, 87.7, 77.3, 74.88, 74.81, 64.4, 64.3, 21.5, 20.86, 20.82; IR (neat, cm^{-1}): 3018, 2399, 1521, 1217, 927, 771, 669, 626: HRMS (ESI): calcd for $C_{30}H_{28}NO_4S$ 498.1739, found 498.1729.

***N*-(4-chloro-2-(4-(4-chlorophenyl)-1,4-dihydroxy-1-phenylbut-2-yn-1-yl)phenyl)-4-methylbenzenesulfonamide 190q**



Yield: 49%; yellow solid; m.p. 83-85 ^{o}C; dr ratio = 6:5; ^{1}H NMR ($CDCl_3$, 300 MHz): δ 8.74 (bs, 1H), 7.36-7.20 (m, 13H), 7.11-7.02 (m, 3H), 5.44 (s, 1H, A or B diastereomer), 5.39 (s, 1H, A or B diastereomer), 4.90 (bs, 1H), 3.85 (bs, 1H), 2.33 (s, 3H, A or B diastereomer), 2.32 (s, 3H, A or B diastereomer); ^{13}C NMR ($CDCl_3$, 75 MHz): δ 143.94, 143.91, 141.7, 138.2, 138.1, 136.2, 136.0, 134.5, 134.4, 134.3, 134.2, 133.1, 133.0, 129.6, 129.2, 128.8, 128.7, 128.6, 128.57, 128.52, 128.07, 128.05, 127.2, 126.07, 126.02, 120.6, 120.4, 88.7, 87.1, 77.2, 74.4, 74.3, 63.7, 63.6, 21.5; IR (neat, cm^{-1}): 3628, 3018, 2399, 1521, 1215, 1045, 927, 769, 669: HRMS (ESI): calcd for $C_{29}H_{24}NO_4SCl_2$ 552.0803, found 552.0786.

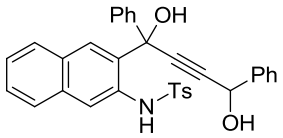
***N*-(4-chloro-2-(1,4-dihydroxy-4-(4-methoxyphenyl)-1-phenylbut-2-yn-1-yl)phenyl)-4-methylbenzenesulfonamide 190r**



Yield: 62%; colorless oil; dr ratio = 1:1; ^{1}H NMR ($CDCl_3$, 400 MHz): δ 8.84 (s, 1H, A or B diastereomer), 8.82 (s, 1H, A or B diastereomer), 7.43-7.20 (m, 11H), 7.09-7.06 (m, 1H), 6.98 (t, 2H, J = 8.7), 6.78-6.73 (m, 2H), 5.33 (s, 1H, A or B diastereomer), 5.28 (s, 1H, A or B diastereomer), 3.95 (bs, 1H), 3.69 (s, 3H, A or B diastereomer),

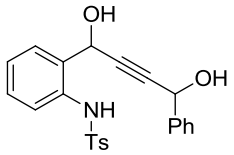
3.68 (A or B diastereomer), 2.28 (s, 3H, 1H, A or B diastereomer), 2.27 (s, 3H, 1H, A or B diastereomer); ^{13}C NMR ($CDCl_3$, 100 MHz): δ 159.6, 159.5, 143.8, 143.7, 142.1, 142.0, 135.9, 135.8, 134.5, 134.4, 132.98, 132.92, 132.0, 131.9, 129.62, 129.61, 129.1, 128.8, 128.76, 128.70, 128.29, 128.25, 128.22, 127.2, 125.99, 125.91, 120.1, 120.0, 114.1, 114.0, 89.36, 89.31, 86.8, 77.3, 74.4, 74.3, 64.0, 63.9, 55.32, 55.31, 21.5; IR (neat, cm^{-1}): 3419, 3018, 1487, 1215, 1031, 763, 667: HRMS (ESI): calcd for $C_{30}H_{27}NO_5SCl$ 548.1298, found 548.1307.

_N_-(3-(1,4-dihydroxy-1,4-diphenylbut-2-yn-1-yl)naphthalen-2-yl)-4-methylbenzenesulfonamide 190s



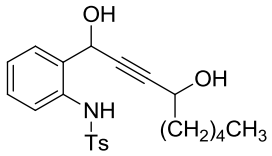
Yield: 66%; yellow oil; dr ratio = 1:1; ^{1}H NMR ($CDCl_3$, 300 MHz): δ 8.84 (bs, 1H), 7.94 (d, 1H, J = 8.6), 7.71 (s, 1H), 7.57-6.85 (m, 18H), 5.47 (s, 1H, A or B diastereomer), 5.38 (s, 1H, A or B diastereomer), 5.06 (bs, 1H), 2.28 (s, 3H); ^{13}C NMR ($CDCl_3$, 75 MHz): δ 162.3, 143.56, 143.50, 142.4, 139.9, 139.8, 136.0, 135.8, 133.4, 133.3, 131.1, 129.4, 129.06, 129.01, 128.6, 128.5, 128.4, 128.1, 127.3, 127.1, 126.9, 126.8, 126.0, 125.9, 125.2, 115.8, 115.6, 89.28, 89.21, 87.6, 74.9, 74.8, 64.5, 21.4; IR (neat, cm^{-1}): 3743, 3018, 2399, 1506, 1215, 929, 769, 667: HRMS (ESI): calcd for $C_{33}H_{28}NO_4S$ 534.1739, found 534.1744.

_N_-(2-(1,4-dihydroxy-4-phenylbut-2-yn-1-yl)phenyl)-4-methylbenzenesulfonamide 190t



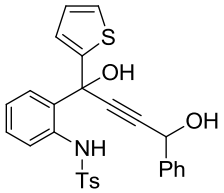
Yield: 65%; brown oil; dr ratio = 1:1; ^{1}H NMR ($CDCl_3$, 400 MHz): δ 8.10 (bs, 1H), 7.63-7.60 (m, 2H), 7.45-7.00 (m, 11H), 5.43 (s, 1H, A or B diastereomer), 5.40 (s, 1H, A or B diastereomer), 4.24 (bs, 1H), 2.295 (s, 3H, A or B diastereomer), 2.290 (s, 3H, A or B diastereomer); ^{13}C NMR ($CDCl_3$, 100 MHz): δ 144.0, 139.9, 136.55, 136.53, 135.19, 135.15, 131.6, 131.5, 129.7, 129.4, 128.68, 128.65, 128.5, 128.44, 128.42, 127.2, 126.8, 126.7, 125.59, 125.55, 123.1, 123.0, 87.8, 84.5, 77.3, 64.37, 64.32, 62.56, 62.52, 21.5; IR (neat, cm^{-1}): 3419, 3018, 2399, 1635,, 1215, 1161, 1091, 777, 669: HRMS (ESI): calcd for $C_{23}H_{22}NO_4S$ 408.1270, found 408.1290.

_N_-(2-(1,4-dihydroxynon-2-yn-1-yl)phenyl)-4-methylbenzenesulfonamide 190u



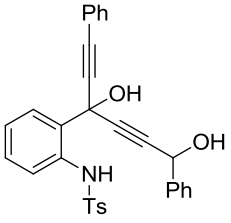
Yield: 63%; colorless oil; dr ratio = 1:1; ^{1}H NMR ($CDCl_3$, 300 MHz): δ 8.11 (bs, 1H), 7.69 (d, 2H, J = 8.0 Hz), 7.46 (t, 1H, J = 6.4 Hz), 7.21-7.05 (m, 5H), 5.38 (s, 1H), 4.39 (t, 1H, J = 6.3 Hz), 2.35 (s, 3H), 1.69-1.25 (m, 8H), 0.85 (t, 3H, J = 6.7 Hz); ^{13}C NMR ($CDCl_3$, 75 MHz): δ 162.3, 143.9, 136.7, 135.29, 135.26, 131.6, 131.5, 129.7, 129.4, 128.4, 127.2, 125.4, 125.3, 123.0, 122.9, 89.46, 89.41, 82.6, 82.5, 62.5, 62.4, 62.39, 62.37, 37.39, 37.35, 31.3, 24.8, 22.5, 21.5, 14.0; IR (neat, cm^{-1}): 3439, 3018, 2399, 2088, 1635, 1423, 1338, 1215, 1161, 1091, 927, 771, 669; HRMS (ESI): calcd for $C_{22}H_{28}NO_4S$ 402.1739, found 402.1723.

***N*-(2-(1,4-dihydroxy-4-phenyl-1-(thiophen-2-yl)but-2-yn-1-yl)phenyl)-4-methylbenzenesulfonamide 190v**



Yield: 75%; light yellow foam; dr ratio = 1:1; ^{1}H NMR ($CDCl_3$, 400 MHz): δ 8.91 (bs, 1H), 7.55-7.50 (m, 2H), 7.43-7.23 (m, 8H), 7.18-7.08 (m, 3H), 6.93-6.80 (m, 3H), 5.47 (s, 1H, A or B diastereomer), 5.45 (s, 1H, A or B diastereomer), 2.32 (s, 3H); ^{13}C NMR ($CDCl_3$, 100 MHz): δ 147.54, 147.51, 143.64, 143.61, 139.6, 136.8, 136.7, 135.98, 135.94, 130.9, 130.8, 129.6, 128.69, 128.67, 128.4, 128.35, 128.30, 127.3, 126.82, 128.81, 126.6, 126.5, 126.18, 126.10, 123.3, 123.2, 119.4, 119.2, 88.1, 88.0, 87.0, 72.65, 72.63, 64.4, 64.3, 21.5; IR (neat, cm^{-1}): 3412, 3018, 2399, 1492, 1332, 1215, 1159, 1091, 756: HRMS (ESI): calcd for $C_{27}H_{23}NO_4S_2Na$ 512.0966, found 512.0965.

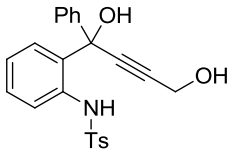
***N*-(2-(3,6-dihydroxy-1,6-diphenylhexa-1,4-diyn-3-yl)phenyl)-4-methylbenzenesulfonamide 190w**



Yield: 58%; brown oil; dr ratio = 2:1; ^{1}H NMR ($CDCl_3$, 400 MHz): δ 7.82-7.79 (m, 3H), 7.55-6.99 (m, 15H), 5.58 (s, 1H, A or B diastereomer), 5.55 (s, 1H, A or B diastereomer), 2.30 (s, 3H); ^{13}C NMR ($CDCl_3$, 100 MHz): δ 143.7, 139.77, 139.70, 137.4, 137.3, 135.9, 131.9, 129.9, 129.6, 129.1, 128.7, 128.6, 128.47, 128.44, 128.3, 127.8, 127.4, 126.9, 126.8, 123.6, 123.5, 121.4, 119.7, 86.9, 86.4, 85.0, 65.7, 64.48,

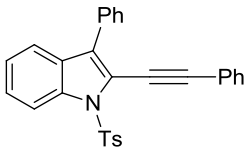
64.40, 21.5; IR (neat, cm^{-1}): 3633, 3018, 2399, 1532, 1215, 1040, 927, 669: HRMS (ESI): calcd for $C_{31}H_{26}NO_4S$ 508.1583, found 508.1567.

_N_-(2-(1,4-dihydroxy-1-phenylbut-2-yn-1-yl)phenyl)-4-methylbenzenesulfonamide 190x



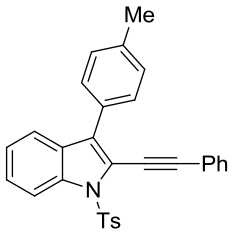
Yield: 55%; brown oil; ^1H NMR ($CDCl_3$, 500 MHz): δ 8.69 (bs, 1H), 7.44-7.30 (m, 9H), 7.18-7.15 (m, 2H), 7.11 (d, 1H, J = 8.0 Hz), 6.96-6.93 (m, 1H), 4.29 (s, 1H), 2.35 (s, 3H); ^{13}C NMR ($CDCl_3$, 125 MHz): δ 143.5, 142.4, 136.8, 136.0, 131.4, 129.5, 129.4, 128.7, 128.6, 128.3, 127.2, 126.2, 123.1, 119.4, 87.4, 86.4, 74.8, 51.0, 21.5; IR (neat, cm^{-1}): 3628, 3018, 2380, 1530, 1215, 927, 769, 669: HRMS (ESI): calcd for $C_{23}H_{22}NO_4S$ 408.1270, found 408.1275.

3-Phenyl-2-(phenylethynyl)-1-tosyl-1*H*-indole 191a



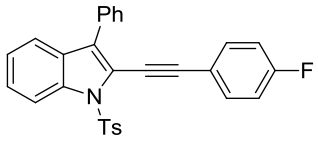
Light brown solid; m.p. 183-185 ^oC; ^1H NMR ($CDCl_3$, 300 MHz): δ 8.37 (d, 1H, J = 8.4 Hz), 7.93 (d, 2H, J = 8.1 Hz), 7.74-7.65 (m, 3H), 7.53-7.25 (m, 11H), 7.21 (d, 1H, J = 8.1 Hz), 2.33 (s, 3H); ^{13}C NMR ($CDCl_3$, 75 MHz): δ 145.0, 136.5, 135.8, 132.1, 131.3, 129.7, 129.6, 129.5, 128.7, 128.47, 128.42, 127.9, 127.1, 126.3, 124.0, 122.7, 120.3, 117.4, 114.8, 98.5, 81.1, 21.6; IR (neat, cm^{-1}): 3446, 3018, 2399, 1598, 1444, 1373, 1215, 1176, 1149, 1089, 1047, 1024, 927, 771, 574: HRMS (ESI): calcd for $C_{29}H_{22}NO_2S$ 448.1371, found 448.1375.

2-(Phenylethynyl)-3-(*p*-tolyl)-1-tosyl-1*H*-indole 191b



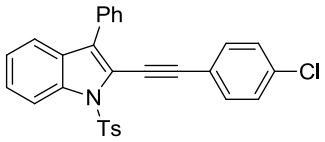
White solid; m.p. 234-236 ^{o}C; ^{1}H NMR ($CDCl_3$, 500 MHz): δ 8.35 (d, 1H, J = 8.5 Hz), 7.92 (d, 2H, J = 8.3 Hz), 7.67-7.27 (m, 12H), 7.20 (d, 2H, J = 8.3 Hz), 2.43 (s, 3H), 2.33 (s, 3H); ^{13}C NMR ($CDCl_3$, 125 MHz): δ 144.9, 137.8, 136.6, 135.8, 131.3, 129.7, 129.6, 129.3, 129.1, 128.7, 128.5, 128.4, 127.1, 126.2, 123.9, 122.8, 120.4, 117.2, 114.8, 98.5, 81.3, 21.6, 21.4; IR (neat, cm^{-1}): 3670, 3019, 1516, 1423, 1215, 1043, 927, 744, 669: HRMS (ESI): calcd for $C_{30}H_{24}NO_2S$ 462.1528, found 462.1528.

2-((4-Fluorophenyl)ethynyl)-3-phenyl-1-tosyl-1*H*-indole 191c



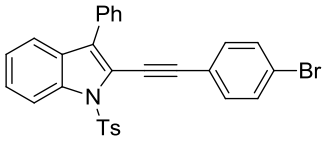
White solid; m.p. 172-174 ^{o}C; ^{1}H NMR ($CDCl_3$, 500 MHz): δ 8.26 (d, 1H, J = 8.5 Hz), 7.81 (d, 2H, J = 8.4 Hz), 7.63-7.56 (m, 3H), 7.44-7.30 (m, 6H), 7.21 (t, 1H, J = 7.5 Hz), 7.12 (d, 2H, J = 8.2 Hz), 6.99-6.96 (m, 2H), 2.24 (s, 3H); ^{13}C NMR ($CDCl_3$, 125 MHz): δ 163.8, 161.8, 145.0, 136.5, 135.8, 133.3 (d, 1C, $J_{C\text{-}F}$ = 28.2 Hz), 132.1, 129.8, 129.7, 129.4 (t, 1C, $J_{C\text{-}F}$ = 16.6 Hz), 128.0, 127.1, 126.4, 124.1, 120.3, 118.8 (d, 1C, $J_{C\text{-}F}$ = 13.7 Hz), 117.3, 115.9, 115.8, 114.8, 97.4, 80.9, 21.6; IR (neat, cm^{-1}): 3743, 2347, 1600, 1373, 1215, 1091, 927, 837, 752, 669, 574: HRMS (ESI): calcd for $C_{29}H_{21}NO_2SF$ 466.1277, found 466.1293.

2-((4-Chlorophenyl)ethynyl)-3-phenyl-1-tosyl-1*H*-indole 191d



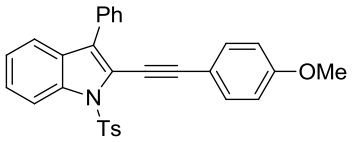
Pale yellow solid; m.p. 152-154 ^{o}C; ^{1}H NMR ($CDCl_3$, 400 MHz): δ 8.25 (d, 1H, J = 8.4 Hz), 7.80 (d, 2H, J = 8.2 Hz), 7.62-7.15 (m, 12H), 7.10 (d, 2H, J = 8.1 Hz), 2.22 (s, 3H); ^{13}C NMR ($CDCl_3$, 100 MHz): δ 145.0, 136.5, 135.7, 134.7, 132.4, 132.0, 130.0, 129.7, 129.4, 128.8, 128.4, 128.3, 128.0, 127.0, 126.4, 124.0, 121.1, 120.3, 117.0, 114.8, 97.3, 82.1, 21.5; IR (neat, cm^{-1}): 3018, 2399, 1487, 1373, 1215, 1174, 1089, 1022, 927, 769, 669: HRMS (ESI): calcd for $C_{29}H_{21}NO_2SCl$ 482.0982, found 482.0977.

2-((4-Bromophenyl)ethynyl)-3-phenyl-1-tosyl-1*H*-indole 191e



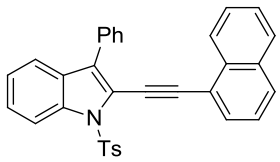
White solid; m.p. 134-136 ^{o}C; ^{1}H NMR ($CDCl_3$, 400 MHz): δ 8.34 (d, 1H, J = 8.4 Hz), 7.88 (d, 2H, J = 8.3 Hz), 7.70-7.27 (m, 12H), 7.19 (d, 2H, J = 8.2 Hz), 2.31 (s, 3H); ^{13}C NMR ($CDCl_3$, 100 MHz): δ 145.1, 136.6, 135.7, 132.7, 132.0, 131.8, 130.1, 129.8, 129.4, 128.4, 128.3, 128.1, 127.0, 126.5, 124.1, 123.1, 121.6, 120.4, 117.1, 114.8, 97.4, 82.3, 77.2, 21.6; IR (neat, cm^{-1}): 3431, 3018, 2399, 1483, 1373, 1269, 1215, 1176, 1149, 1089, 1047, 1010, 927, 752, 669, 574: HRMS (ESI): calcd for $C_{29}H_{21}NO_2SBr$ 526.0476, found 526.0472.

2-((4-Methoxyphenyl)ethynyl)-3-phenyl-1-tosyl-1*H*-indole 191f



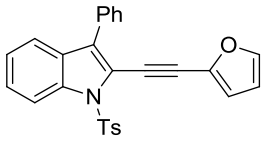
White solid; m.p. 141-143 ^{o}C; ^{1}H NMR ($CDCl_3$, 300 MHz): δ 8.26 (d, 1H, J = 8.4 Hz), 7.82 (d, 2H, J = 8.3 Hz), 7.64-7.13 (m, 10H), 7.09 (d, 2H, J = 8.1 Hz), 6.81-6.78 (m, 2H), 3.72 (s, 3H), 2.20 (s, 3H); ^{13}C NMR ($CDCl_3$, 75 MHz): δ 160.1, 144.9, 136.5, 135.9, 132.9, 132.3, 129.7, 129.6, 129.4, 128.8, 128.5, 128.4, 127.8, 127.1, 126.1, 124.0, 120.2, 117.9, 114.8, 114.2, 98.8, 79.9, 77.2, 55.3, 21.6; IR (neat, cm^{-1}): 3018, 2206, 1604, 1510, 1444, 1373, 1249, 1215, 1174, 1149, 1024, 927, 759, 669: HRMS (ESI): calcd for $C_{30}H_{24}NO_3S$ 478.1477, found 478.1462.

2-(Naphthalen-1-ylethynyl)-3-phenyl-1-tosyl-1*H*-indole 191g



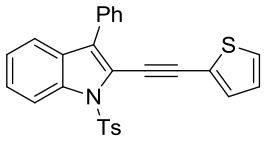
Colorless oil; ^{1}H NMR ($CDCl_3$, 500 MHz): δ 8.39-8.36 (m, 2H), 7.97 (d, 2H, J = 8.3 Hz), 7.87-7.76 (m, 5H), 7.68 (d, 1H, J = 7.9 Hz), 7.56-7.45 (m, 7H), 7.32 (t, 1H, J = 7.4 Hz), 7.17 (d, 2H, J = 8.2 Hz), 2.30 (s, 3H); ^{13}C NMR ($CDCl_3$, 125 MHz): δ 145.0, 136.5, 135.7, 133.1, 132.3, 130.7, 130.2, 129.8, 129.7, 129.2, 128.6, 128.5, 128.2, 128.0, 127.1, 127.0, 126.6, 126.4, 125.3, 124.1, 120.5, 120.3, 117.8, 114.9, 97.3, 85.6, 21.5; IR (neat, cm^{-1}): 3018, 2399, 1483, 1373, 1269, 1215, 1047, 929, 752, 669: HRMS (ESI): calcd for $C_{33}H_{24}NO_2S$ 498.1528, found 498.1515.

2-(Furan-2-ylethynyl)-3-phenyl-1-tosyl-1*H*-indole 191h



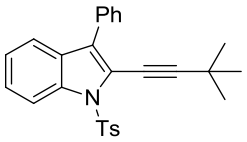
Pale yellow solid; m.p. 165-167 ^{o}C; ^{1}H NMR ($CDCl_3$, 500 MHz): δ 8.27 (d, 1H, J = 8.5 Hz), 7.85 (d, 2H, J = 8.2 Hz), 7.60-7.20 (m, 9H), 7.15 (d, 2H, J = 8.2 Hz), 6.63 (d, 1H, J = 3.3 Hz), 6.379-6.373 (m, 1H), 2.26 (s, 3H); ^{13}C NMR ($CDCl_3$, 125 MHz): δ 145.1, 144.3, 136.75, 136.70, 135.6, 131.8, 130.3, 129.8, 129.3, 128.5, 128.2, 128.0, 127.3, 126.6, 124.0, 120.5, 116.6, 116.5, 114.8, 111.2, 88.4, 84.8, 21.6; IR (neat, cm^{-1}): 3689, 3018, 2399, 1326, 1215, 927, 771, 669: HRMS (ESI): calcd for $C_{27}H_{20}NO_3S$ 438.1164, found 438.1172.

3-Phenyl-2-(thiophen-2-ylethynyl)-1-tosyl-1*H*-indole 191i



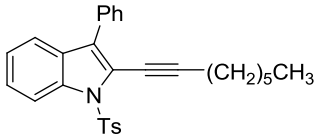
White solid; m.p. 175-177 ^{o}C; ^{1}H NMR ($CDCl_3$, 400 MHz): δ 8.26 (d, 1H, J = 8.4 Hz), 7.81 (d, 2H, J = 8.0 Hz), 7.60-6.90 (m, 13H), 2.21 (s, 3H); ^{13}C NMR ($CDCl_3$, 100 MHz): δ 145.1, 136.7, 135.7, 132.5, 132.0, 129.8, 129.6, 129.4, 128.5, 128.37, 128.34, 128.0, 127.3, 127.2, 126.4, 124.1, 122.6, 120.4, 117.1, 114.8, 92.1, 84.7, 21.6; IR (neat, cm^{-1}): 3018, 2399, 1215, 927, 771, 669: HRMS (ESI): calcd for $C_{27}H_{20}NO_2S_2$ 454.0935, found 454.0947.

2-(3,3-Dimethylbut-1-yn-1-yl)-3-phenyl-1-tosyl-1*H*-indole 191j



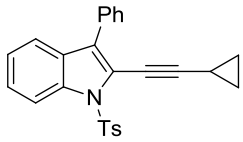
Colorless oil; ^{1}H NMR ($CDCl_3$, 500 MHz): δ 8.33 (d, 1H, J = 8.5 Hz), 7.89 (d, 2H, J = 8.3 Hz), 7.67-7.25 (m, 8H), 7.22 (d, 2H, J = 8.1 Hz), 2.35 (s, 3H), 1.33 (s, 9H); ^{13}C NMR ($CDCl_3$, 125 MHz): δ 144.8, 136.19, 136.10, 132.3, 129.6, 129.3, 128.35, 128.32, 128.1, 127.6, 127.1, 125.8, 123.7, 120.0, 117.9, 114.8, 107.8, 70.6, 30.2, 28.5, 21.68; IR (neat, cm^{-1}): 3687, 3018, 1215, 927, 775, 746, 669, 574: HRMS (ESI): calcd for $C_{27}H_{26}NO_2S$ 428.1684, found 428.1683.

2-(Oct-1-yn-1-yl)-3-phenyl-1-tosyl-1*H*-indole 191k



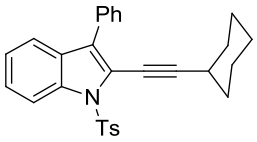
Light brown oil; ^{1}H NMR ($CDCl_3$, 400 MHz): δ 8.23 (d, 1H, J = 8.4 Hz), 7.79 (d, 2H, J = 8.1 Hz), 7.55-7.11 (m, 10H), 2.39 (t, 2H, J = 7.0 Hz), 2.26 (s, 3H), 1.55-1.48 (m, 2H), 1.36-1.17 (m, 6H), 0.80 (t, 3H, J = 6.5 Hz); ^{13}C NMR ($CDCl_3$, 100 MHz): δ 144.8, 136.1, 136.0, 132.3, 129.6, 129.4, 128.6, 128.4, 128.3, 127.6, 127.1, 125.8, 123.8, 120.0, 118.1, 114.8, 100.6, 71.6, 31.4, 28.6, 28.1, 22.5, 21.6, 20.0, 14.1; IR (neat, cm^{-1}): 3676, 3018, 2399, 1521, 1215, 1176, 1045, 927, 756, 669: HRMS (ESI): calcd for $C_{25}H_{22}NO_2S$ 400.1371, found 400.1378.

2-(Cyclopropylethynyl)-3-phenyl-1-tosyl-1*H*-indole 191l



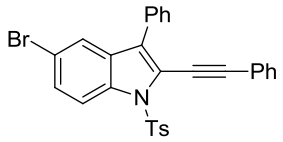
Brown solid; m.p. 70-72 ^{o}C; ^{1}H NMR ($CDCl_3$, 400 MHz): δ 8.30 (d, 1H, J = 8.4 Hz), 7.86 (d, 2H, J = 8.2 Hz), 7.62-7.20 (m, 10H), 2.33 (s, 3H), 1.54-1.47 (m, 1H), 0.92-0.83 (m, 4H); ^{13}C NMR ($CDCl_3$, 100 MHz): δ 144.8, 136.1, 136.0, 132.3, 129.6, 129.3, 128.6, 128.4, 128.3, 127.6, 127.1, 125.8, 123.8, 120.0, 118.0, 114.7, 103.5, 66.7, 21.6, 8.7, 0.8; IR (neat, cm^{-1}): 3410, 3018, 1635, 1215, 767, 752, 669: HRMS (ESI): calcd for $C_{26}H_{22}NO_2S$ 412.1371, found 412.1380.

2-(Cyclohexylethynyl)-3-phenyl-1-tosyl-1*H*-indole 191m



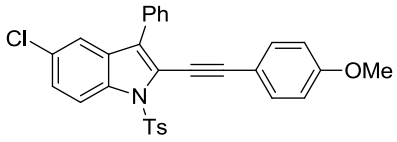
White solid; m.p. 126-128 ^{o}C; ^{1}H NMR ($CDCl_3$, 400 MHz): δ 8.31 (d, 1H, J = 8.4 Hz), 7.89 (d, 2H, J = 8.2 Hz), 7.65-7.20 (m, 10H), 2.71-2.67 (m, 1H), 2.34 (s, 3H), 1.87-1.70 (m, 4H), 1.61-1.32 (m, 6H); ^{13}C NMR ($CDCl_3$, 100 MHz): δ 144.8, 136.1, 136.0, 132.3, 129.6, 129.4, 128.5, 128.4, 128.2, 127.6, 127.1, 125.8, 123.8, 120.0, 118.1, 114.8, 104.2, 71.7, 31.9, 30.1, 25.8, 24.7, 21.6; IR (neat, cm^{-1}): 3427, 3018, 2399, 1645, 1215, 927, 756, 669: HRMS (ESI): calcd for $C_{29}H_{28}NO_2S$ 454.1841, found 454.1842.

5-Bromo-3-phenyl-2-(phenylethynyl)-1-tosyl-1*H*-indole 191n



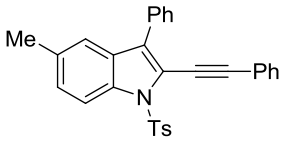
White solid; m.p. 173-175 ^{o}C; ^{1}H NMR ($CDCl_3$, 300 MHz): δ 8.24 (d, 1H, J = 8.9 Hz), 7.91 (d, 2H, J = 8.3 Hz), 7.77-7.37 (m, 12H), 7.23 (d, 2H, J = 8.1 Hz), 2.34 (s, 3H); ^{13}C NMR ($CDCl_3$, 100 MHz): δ 145.3, 135.5, 135.1, 131.5, 131.4, 130.1, 129.9, 129.3, 129.1, 129.0, 128.68, 128.60, 128.5, 128.2, 127.1, 122.8, 122.4, 118.5, 117.6, 116.3, 99.2, 80.6, 21.6; IR (neat, cm^{-1}): 3460, 3018, 2399, 1647, 1215, 927, 752, 669, 582: HRMS (ESI): calcd for $C_{29}H_{21}NO_2SBr$ 526.0476, found 526.0461.

5-Chloro-3-phenyl-2-(phenylethynyl)-1-tosyl-1*H*-indole 191o



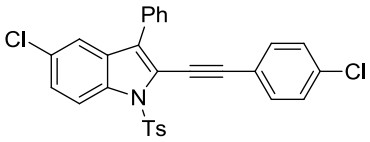
Light brown oil; ^{1}H NMR ($CDCl_3$, 400 MHz): δ 8.27 (d, 1H, J = 8.9 Hz), 7.88 (d, 2H, J = 8.3 Hz), 7.67 (d, 2H, J = 7.2 Hz), 7.60-7.34 (m, 7H), 7.20 (d, 2H, J = 8.1 Hz), 6.90 (d, 2H, J = 8.7 Hz), 3.82 (s, 3H), 2.32 (s, 3H); ^{13}C NMR ($CDCl_3$, 100 MHz): δ 160.2, 145.2, 135.5, 134.7, 133.0, 131.7, 129.9, 129.87, 129.80, 129.3, 128.5, 128.1, 127.9, 127.1, 126.1, 119.6, 119.1, 115.9, 114.5, 114.2, 99.5, 79.5, 55.3, 21.6; IR (neat, cm^{-1}): 3018, 2208, 1604, 1510, 1442, 1371, 1249, 1215, 1172, 1161, 1091, 1024, 771, 667: HRMS (ESI): calcd for $C_{30}H_{23}NO_3SCl$ 512.1087, found 512.1083.

5-Methyl-3-phenyl-2-(phenylethynyl)-1-tosyl-1*H*-indole 191p



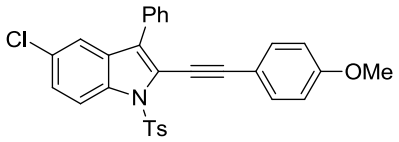
White solid; m.p. 170-172 ^{o}C; ^{1}H NMR ($CDCl_3$, 400 MHz): δ 8.2 (d, 1H, J = 8.6 Hz), 7.89 (d, 2H, J = 8.3 Hz), 7.71 (d, 2H, J = 7.2 Hz), 7.52-7.22 (m, 10H), 7.17 (d, 2H, J = 8.2 Hz), 2.40 (s, 3H), 2.29 (s, 3H); ^{13}C NMR ($CDCl_3$, 100 MHz): δ 144.9, 135.8, 134.8, 133.8, 132.3, 131.3, 129.7, 129.6, 129.5, 128.7, 128.6, 128.5, 128.4, 127.9, 127.8, 127.1, 122.8, 120.0, 117.5, 114.6, 98.4, 81.3, 21.6, 21.3; IR (neat, cm^{-1}): IR (neat, cm^{-1}): 3687, 3019, 2399, 11598, 1217, 1176, 927, 771, 667: HRMS (ESI): calcd for $C_{30}H_{24}NO_2S$ 462.1528, found 462.1531.

5-Chloro-2-((4-chlorophenyl)ethynyl)-3-phenyl-1-tosyl-1*H*-indole 191q



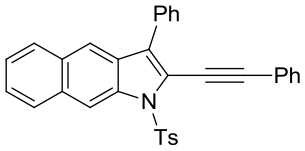
Light brown oil; ^{1}H NMR ($CDCl_3$, 400 MHz): δ 8.27 (d, 1H, J = 8.9 Hz), 7.86 (d, 2H, J = 8.3 Hz), 7.66-7.33 (m, 10H), 7.25 (s, 1H), 7.22 (d, 1H, J = 8.1 Hz), 2.35 (s, 3H); ^{13}C NMR ($CDCl_3$, 100 MHz): δ 145.6, 135.6, 135.3, 135.0, 132.7, 131.6, 130.3, 130.1, 129.8, 129.5, 129.3, 129.1, 128.8, 128.5, 127.2, 126.8, 121.1, 120.0, 118.5, 116.1, 98.1, 21.8; IR (neat, cm^{-1}): 3419, 3018, 1215, 769, 750, 669: HRMS (ESI): calcd for $C_{29}H_{20}NO_2SCl_2$ 516.0592, found 516.0576.

5-Chloro-2-((4-methoxyphenyl)ethynyl)-3-phenyl-1-tosyl-1*H*-indole 191r



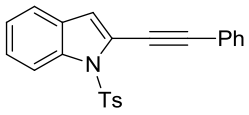
Light brown oil; ^{1}H NMR ($CDCl_3$, 400 MHz): δ 8.27 (d, 1H, J = 8.9 Hz), 7.88 (d, 2H, J = 8.3 Hz), 7.67 (d, 2H, J = 7.2 Hz), 7.60-7.34 (m, 7H), 7.20 (d, 2H, J = 8.1 Hz), 6.90 (d, 2H, J = 8.7 Hz), 3.82 (s, 3H), 2.32 (s, 3H); ^{13}C NMR ($CDCl_3$, 100 MHz): δ 160.2, 145.2, 135.5, 134.7, 133.0, 131.7, 129.9, 129.87, 129.80, 129.3, 128.5, 128.1, 127.9, 127.1, 126.1, 119.6, 119.1, 115.9, 114.5, 114.2, 99.5, 79.5, 55.3, 21.6; IR (neat, cm^{-1}): 3018, 2208, 1604, 1510, 1442, 1371, 1249, 1215, 1172, 1161, 1091, 1024, 771, 667: HRMS (ESI): calcd for $C_{30}H_{23}NO_3SCl$ 512.1087, found 512.1083.

3-Phenyl-2-(phenylethynyl)-1-tosyl-1*H*-benzo[*f*]indole 191s



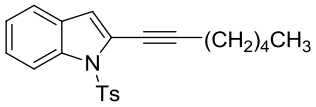
Brown oil; ^{1}H NMR ($CDCl_3$, 500 MHz): δ 8.80 (s, 1H), 8.09 (s, 1H), 8.06 (d, 1H, J = 8.3 Hz), 7.92-7.86 (m, 3H), 7.81 (d, 2H, J = 7.5 Hz), 7.56-7.25 (m, 10H), 7.16 (d, 2H, J = 8.1 Hz), 2.30 (s, 3H); ^{13}C NMR ($CDCl_3$, 125 MHz): δ 144.9, 135.7, 135.5, 132.4, 132.3, 132.0, 131.5, 130.8, 129.8, 129.7, 129.5, 129.08, 129.01, 128.53, 129.52, 128.2, 128.1, 127.1, 125.6, 125.0, 122.5, 120.0, 118.5, 112.0, 99.7, 81.3, 21.5; IR (neat, cm^{-1}): 3689, 3018, 2399, 1338, 1215, 927, 771, 669: HRMS (ESI): calcd for $C_{33}H_{24}NO_2S$ 498.1528, found 498.1534.

2-(Phenylethynyl)-1-tosyl-1*H*-indole 191t



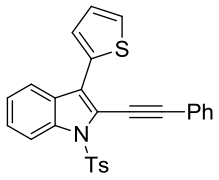
Brown oil; ^{1}H NMR ($CDCl_3$, 500 MHz): δ 8.26 (d, 1H, *J* = 8.5 Hz), 7.86 (d, 2H, *J* = 8.3 Hz), 7.65-7.63 (m, 2H), 7.48 (d, 1H, *J* = 7.8 Hz), 7.41-7.23 (m, 5H), 7.18 (d, 2H, *J* = 8.2 Hz), 6.92 (s, 1H), 2.31 (s, 3H); ^{13}C NMR ($CDCl_3$, 125 MHz): δ 145.0, 136.6, 135.7, 131.5, 129.7, 129.0, 128.9, 128.5, 127.0, 125.9, 123.9, 122.5, 121.0, 120.9, 116.8, 114.7, 96.7, 80.6, 21.6; IR (neat, cm^{-1}): 3743,3019, 2399, 1506, 1215, 1176, 927, 756, 669: HRMS (ESI): calcd for $C_{23}H_{18}NO_2S$ 372.1058, found 372.1048.

2-(Hept-1-yn-1-yl)-1-tosyl-1*H*-indole 191u



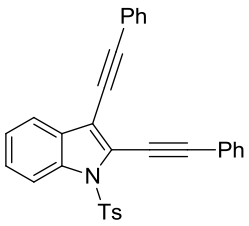
Pale yellow oil; ^{1}H NMR ($CDCl_3$, 400 MHz): δ 8.21 (d, 1H, *J* = 8.4 Hz), 7.83 (d, 2H, J = 8.2 Hz), 7.43 (d, 1H, *J* = 7.7 Hz), 7.33 (t, 1H, *J* = 7.7 Hz), 7.25-7.19 (m, 3H), 675 (s, 1H), 1.72-1.56 (m, 2H), 1.52-1.25 (m, 4H), 0.94 (t, 3H, *J* = 7.2 Hz); ^{13}C NMR ($CDCl_3$, 100 MHz): δ 144.8, 136.2, 135.9, 129.6, 129.0, 127.0, 125.4, 123.6, 121.5, 120.7, 116.1, 114.6, 98.7, 71.6, 31.1, 28.0, 22.2, 21.6, 19.9, 14.0; IR (neat, cm^{-1}): 3419, 3018, 2399, 1635, 1521, 1446, 1375, 1215, 1176, 1122, 1091, 927, 777, 669; HRMS (ESI): calcd for $C_{22}H_{24}NO_2S$ 366.1528, found 366.1526.

2-(Phenylethynyl)-3-(thiophen-2-yl)-1-tosyl-1H-indole 191v



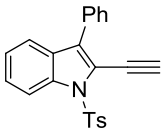
Light yellow oil; ^{1}H NMR ($CDCl_3$, 500 MHz): δ 8.35 (d, 1H, J = 8.5 Hz), 7.92-7.64 (m, 6H), 7.46-7.17 (m, 9H), 2.31 (s, 3H); ^{13}C NMR ($CDCl_3$, 125 MHz): δ 145.1, 136.5, 135.7, 133.6, 131.4, 129.8, 129.0, 128.5, 127.7, 127.1, 126.5, 125.7, 124.2, 123.0, 122.7, 120.5, 117.0, 114.8, 100.9, 81.4, 21.6; IR (neat, cm^{-1}): 3018, 2399, 1215, 925, 771, 669: HRMS (ESI): calcd for $C_{27}H_{20}NO_2S_2$ 454.0935, found 454.0952.

2,3-bis(Phenylethynyl)-1-tosyl-1H-indole 191w



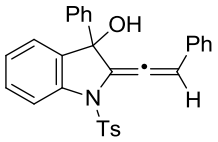
Light yellow oil; ^{1}H NMR ($CDCl_3$, 500 MHz): δ 8.27 (d, 1H, J = 8.5 Hz), 7.89 (d, 2H, J = 8.3 Hz), 7.70-7.57 (m, 5H), 7.45-7.33 (m, 8H), 7.21 (d, 2H, J = 8.1 Hz), 2.33 (s, 3H); ^{13}C NMR ($CDCl_3$, 125 MHz): δ 145.3, 135.7, 135.4, 131.66, 131.63, 129.8, 129.2, 129.1, 128.5, 128.4, 127.1, 126.7, 124.3, 123.5, 123.0, 122.5, 120.4, 114.7, 112.4, 101.5, 97.8, 80.7, 80.1, 21.6; IR (neat, cm^{-1}): 3446, 3018, 2389, 1590, 1440, 1373, 1215, 1176, 1089, 1042, 1024, 927, 771, 574: HRMS (ESI): calcd for $C_{31}H_{22}NO_2S$ 472.1371, found 472.1375.

2-ethynyl-3-phenyl-1-tosyl-1H-indole 191x



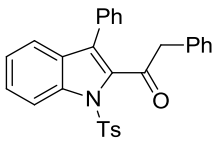
Light brown oil; ^{1}H NMR ($CDCl_3$, 500 MHz): δ 8.31 (d, 1H, J = 8.5 Hz), 7.91 (d, 2H, J = 8.3 Hz), 7.63-7.37 (m, 7H), 7.30-7.23 (m, 3H), 3.61 (s, 1H), 2.36 (s, 3H); ^{13}C NMR ($CDCl_3$, 125 MHz): δ 145.1, 139.5, 136.2, 135.6, 131.6, 131.5, 129.8, 129.4, 128.5, 128.1, 127.2, 126.7, 124.0, 122.5, 120.5, 114.9, 87.0, 21.6; IR (neat, cm^{-1}): 3445, 3018, 2399, 1515, 1420, 1373, 1215, 1157, 1145, 1024, 925, 771, 574: HRMS (ESI): calcd for $C_{23}H_{18}NO_2S$ 372.1058, found 372.1068.

3-Phenyl-2-(2-phenylvinylidene)-1-tosylindolin-3-ol 192a



Brown solid; m.p. 124-126 ^{o}C; ^{1}H NMR ($CDCl_3$, 400 MHz): δ 7.95 (d, 1H, J = 8.2 Hz), 7.55 (d, 2H, J = 8.1 Hz), 7.37-7.02 (m, 15H), 6.77 (s, 1H), 2.33 (s, 1H), 2.30 (s, 3H); ^{13}C NMR ($CDCl_3$, 125 MHz): δ 196.0, 144.6, 143.2, 140.6, 134.6, 133.9, 133.2, 129.6, 128.6, 128.4, 127.99, 127.92, 127.6, 127.4, 125.5, 125.2, 125.0, 122.6, 109.1, 108.8, 108.6, 81.9, 21.6; IR (neat, cm^{-1}): 3419, 3018, 2399, 1635, 1336, 1215, 1145, 929, 777, 669: HRMS (ESI): calcd for $C_{29}H_{24}NO_3S$ 466.1477, found 466.1495.

2-Phenyl-1-(3-phenyl-1-tosyl-1*H*-indol-2-yl)ethanone 193a

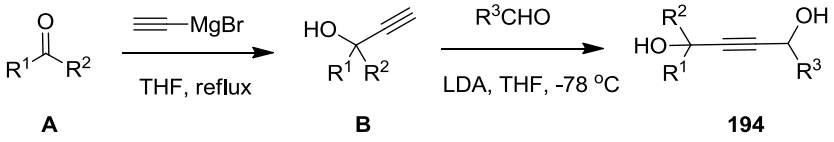


Pale yellow oil; ^{1}H NMR ($CDCl_3$, 500 MHz): δ 8.12 (d, 1H, J = 8.4 Hz), 7.81 (d, 2H,

J = 8.2 Hz), 7.43-7.01 (m, 15H), 4.13 (s, 2H), 2.31 (s, 3H); ^{13}C NMR ($CDCl_3$, 125 MHz): δ 195.8, 145.3, 136.1, 134.2, 133.6, 133.2, 130.6, 129.9, 129.84, 129.81, 129.6, 128.4, 128.37, 128.32, 127.5, 127.2, 126.9, 126.7, 124.5, 121.3, 115.1, 51.6, 21.6; IR (neat, cm^{-1}): 3435, 3018, 1645, 1215, 779, 669, 524: HRMS (ESI): calcd for $C_{29}H_{24}NO_3S$ 466.1477, found 466.1482.

7.5 Brønsted Acid-Catalyzed Cycloisomerization of But-2-yne-1,4-diols with or without 1,3-Dicarbonyl Compounds to Tri- and Tetrasubstituted Furans

Experimental Procedure for Preparation of Substituted but-2-yne-1,4-diols (194a)-(1954)[151,152]



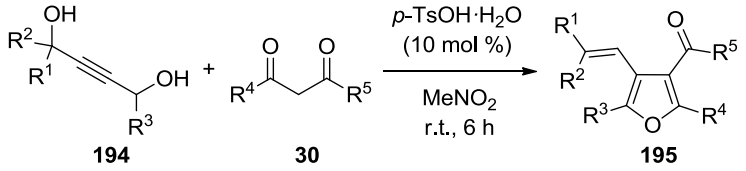
A **B** **194**

R^1 = alkyl, alkynyl, aryl, heteroaryl
R^2 = H, alkyl, alkynyl, aryl, heteroaryl
R^3 = alkyl, aryl, heteroaryl

To a solution of ketone or aldehyde (**A**) (0.5, 2.7 mmol) in THF (5 mL) was added drop wise ethynylmagnesium bromide (0.5 M THF solution; 2.9 mL; 3.5 mmol) at room temperature. The resulting solution was stirred for a further 1-10 h at same temperature. On completion, the reaction mixture was quenched by adding saturated NH_4Cl (50 mL) and extracted with EtOAc (2 x 25 mL). The combined organic layers were washed with water, brine, dried over Na_2SO_4 and concentrated under reduced pressure. Purification by flash column chromatography on silica gel (eluent: *n*-hexane:EtOAc = 9:1) gave the intermediate (**B**). To a solution of diisopropylamine (0.47g, 4.6 mmol) in anhydrous THF (5 mL) was added butyl lithium (1.6 M hexane solution; 2.9 mL; 4.6 mmol) at −78 °C in a dropwise manner. The resulting solution

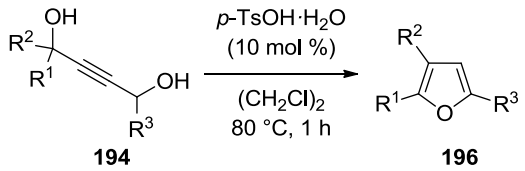
was stirred for 1 h prior to slow addition of the corresponding alkynol (**B**) (0.50g, 1.3 mmol) in THF at −78 °C. The resulting mixture was stirred at same temperature for 1 h. The corresponding aldehyde (0.21g, 2.0 mmol) in THF (2 mL) was added to the reaction mixture and allowed to stir for a further 1h at same temperature. On completion, the reaction mixture was quenched by adding saturated NH_4Cl (50 mL) and extracted with EtOAc (2 x 25 mL). The combined organic layers were washed with water, brine, dried over Na_2SO_4 and concentrated under reduced pressure. Purification by flash column chromatography on silica gel (eluent: *n*-hexane:EtOAc = 8:2) gave the title compound (**194**).

Representative Procedure for Brønsted Acid-Catalyzed Intermolecular Reactions of (194) with (30)



To a solution of *p*-TsOH·H_2O (16 μmol) in $MeNO_2$ (2 mL) at room temperature was added dropwise the propargylic 1,4-diol **194** (0.16 mmol) and 1,3-dicarbonyl compound 2 (0.3 mmol) dissolved in $MeNO_2$ (2 mL). The resulting mixture was stirred at room temperature for 6 h and monitored by TLC analysis. The solvent was concentrated under reduced pressure. Purification by flash column chromatography on silica gel (eluent: *n*-hexane:EtOAc = 9:1) gave the tetrasubstituted furan **195**.

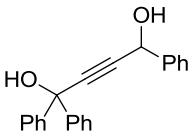
Representative Procedure for Brønsted Acid-Catalyzed Intramolecular Reactions of (194)



194 **196**

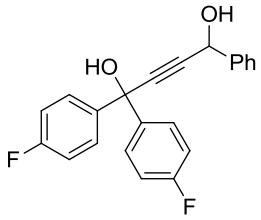
To a solution of *p*-TsOH·H_2O (16 μmol) in 1,2-dichloroethane (2 mL) at room temperature was added dropwise the propargylic 1,4-diol **194** (0.16 mmol) dissolved in 1,2-dichloroethane (2 mL). The resulting mixture was stirred at 80 ºC for 1 h and monitored by TLC analysis. On completion, the reaction mixture was cooled down to room temperature and concentrated under reduced pressure. Purification by flash column chromatography on silica gel (eluent: *n*-hexane:EtOAc = 9:1) gave the trisubstituted furan **196**.

1,1,4-Triphenylbut-2-yne-1,4-diol 194a



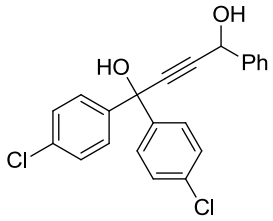
Yield: 85%; white solid; m.p. 139-141 ^{o}C; ^{1}H NMR (CD_3OD, 300 MHz): δ 7.61-7.55 (m, 6H), 7.36-7.15 (m, 9H), 5.57 (s, 1H); ^{13}C NMR (CD_3OD, 75 MHz): δ 145.7, 141.3, 128.1, 127.7, 127.6, 127.0, 126.5, 125.8, 88.8, 86.7, 73.7, 63.7; IR (neat, cm^{-1}): 3419, 3018, 2399, 1635, 1556, 1419, 1215, 1004, 927, 771, 669; HRMS (ESI): calcd for $C_{22}H_{19}O_2$ 315.1385, found 315.1378.

1,1-bis(4-Fluorophenyl)-4-phenylbut-2-yne-1,4-diol 194b



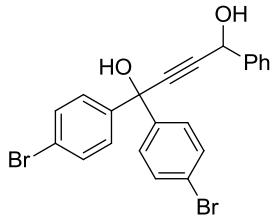
Yield: 69%; light brown solid; m.p. 131-133 ^{o}C; ^{1}H NMR ($CDCl_3$+CD_3OD, 400 MHz): δ 7.54-7.50 (m, 5H), 7.38-7.28 (m, 3H), 7.21-7.17 (m, 1H), 6.99-6.94 (m, 4H), 5.53 (s, 1H), 2.68 (bs, 2H); ^{13}C NMR ($CDCl_3$+CD_3OD, 100 MHz): δ 163.5, 160.9, 140.9, 140.5, 129.3, 129.2, 128.5, 128.3, 127.8, 127.7, 126.5, 115.3, 115.09, 115.05, 114.8, 114.6, 88.7, 87.0, 73.0, 64.0; IR (neat, cm^{-1}): 3442, 3018, 2399, 1645, 1602, 1521, 1473, 1423, 1338, 1215, 1097, 1014, 927, 758, 669, 624; HRMS (ESI): calcd for $C_{22}H_{17}O_2F_2$ 351.1197, found 351.1214.

1,1-bis(4-Chlorophenyl)-4-phenylbut-2-yne-1,4-diol 194c



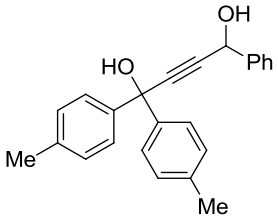
Yield: 75%; white solid; m.p. 120-122 ^{o}C; ^{1}H NMR ($CDCl_3$, 400 MHz): δ 7.45-7.42 (m, 6H), 7.37-7.32 (m, 3H), 7.25-7.22 (m, 4H), 5.50 (s, 1H), 3.47 (bs, 1H), 2.82 (bs, 1H); ^{13}C NMR ($CDCl_3$, 100 MHz): δ 142.84, 142.82, 139.9, 133.9, 128.8, 128.7, 128.5, 127.3, 126.6, 88.4, 87.5, 73.5, 64.6; IR (neat, cm^{-1}): 3446, 3018, 2399, 1489, 1404, 1215, 1093, 1014, 927, 775, 669; HRMS (ESI): calcd for $C_{22}H_{17}O_2Cl_2$ 383.0606, found 383.0594.

1,1-bis(4-Bromophenyl)-4-phenylbut-2-yne-1,4-diol 194d



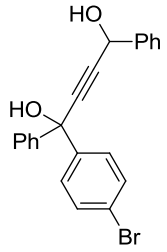
Yield: 78%; off white solid; m.p. 133-135 ^{o}C; ^{1}H NMR ($CDCl_3$, 400 MHz): δ 7.41-7.23 (m, 13H), 5.44 (s, 1H), 3.86 (bs, 1H), 3.20 (bs, 1H); ^{13}C NMR ($CDCl_3$, 100 MHz): δ 143.34, 143.31, 139.8, 131.5, 128.8, 128.7, 128.5, 127.7, 127.67, 126.6, 125.6, 122.1, 88.3, 87.4, 73.6, 64.5; IR (neat, cm^{-1}): 3419, 3018, 2399, 2088, 1635, 1516, 1417, 1215, 1010, 927, 771, 669; HRMS (ESI): calcd for $C_{22}H_{17}O_2Br_2$ 470.9595, found 470.9602.

4-Phenyl-1,1-di*p*-tolylbut-2-yne-1,4-diol 194e



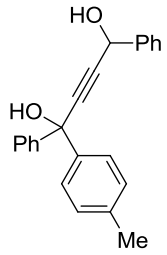
Yield: 81%; light brown solid; m.p. 140-142 ^{o}C; ^{1}H NMR ($CDCl_3$, 400 MHz): δ 7.54-7.52 (m, 2H), 7.47 (d, 4H, J = 8.2 Hz), 7.39-7.33 (m, 3H), 7.12 (d, 4H, J = 8.0), 5.56 (s, 1H), 3.04 (bs, 1H), 2.61 (bs, 1H), 2.32 (s, 6H); ^{13}C NMR ($CDCl_3$, 100 MHz): δ 142.0, 140.3, 137.4, 128.9, 128.6, 128.4, 126.7, 125.9, 89.6, 86.6, 74.2, 64.7, 21.0; IR (neat, cm^{-1}): 3419, 3018, 2399, 2088, 1637, 1560, 1516, 1473, 1419, 1215, 927, 771, 669; HRMS (ESI): calcd for $C_{24}H_{23}O_2$ 343.1698, found 343.1690.

1-(4-Bromophenyl)-1,4-diphenylbut-2-yne-1,4-diol 194f



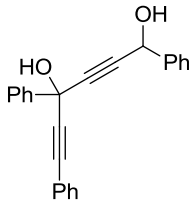
Yield: 76%; yellow solid; m.p. 109-111 ^{o}C; dr ratio = 1:1; ^{1}H NMR ($CDCl_3$, 400 MHz): δ 7.53-7.24 (m, 14H), 5.50 (s, 1H, A or B diastereomer), 5.49 (s, 1H, A or B diastereomer), 3.40 (bs, 1H), 2.80 (bs, 1H); ^{13}C NMR ($CDCl_3$, 100 MHz): δ 144.2, 143.8, 140.0, 131.3, 128.7, 128.6, 128.4, 128.0, 127.8, 126.6, 125.9, 121.8, 88.8, 87.2, 74.0, 64.6; IR (neat, cm^{-1}): 3446, 3018, 2399, 1635, 1521, 1473, 1419, 1215, 1010, 927, 756, 669; HRMS (ESI): calcd for $C_{22}H_{18}O_2Br$ 393.0490, found 393.0481.

1,4-Diphenyl-1-p-tolylbut-2-yne-1,4-diol 194g



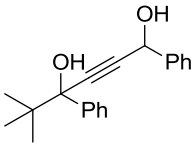
Yield: 75%; white solid; m.p. 123-125 ^{o}C; ^{1}H NMR ($CDCl_3$, 300 MHz): δ 7.56-7.23 (m, 12H), 7.10 (d, 2H, J = 7.7 Hz), 5.52 (s, 1H), 3.13 (bs, 1H), 2.65 (bs, 1H), 2.29 (s, 3H); ^{13}C NMR ($CDCl_3$, 100 MHz): δ 144.8, 141.9, 140.3, 137.5, 129.0, 128.6, 128.4, 128.2, 127.7, 126.7, 126.0, 89.5, 86.8, 74.3, 64.6, 21.0; IR (neat, cm^{-1}): 3439, 3018, 2088, 1637, 1508, 1419, 1215, 1016, 927, 758, 669; HRMS (ESI): calcd for $C_{23}H_{21}O_2$ 329.1542, found 329.1541.

1,4,6-Triphenylhexa-2,5-diyne-1,4-diol 194h



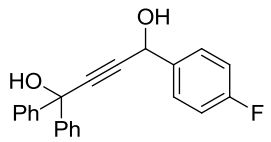
Yield: 82%; light brown solid; m.p. 129-131 ^{o}C; ^{1}H NMR ($CDCl_3$+CD_3OD, 500 MHz): δ 7.86-7.84 (m, 2H), 7.56-7.29 (m, 13H), 5.53 (s, 1H, A or B diastereomer), 5.52 (s, 1H, A or B diastereomer), 3.32 (bs, 2H); ^{13}C NMR ($CDCl_3$+CD_3OD, 125 MHz): δ 142.0, 140.3, 131.5, 128.5, 128.3, 128.2, 128.1, 128.0, 126.6, 126.5, 125.7, 122.0, 89.2, 86.3, 84.5, 84.3, 84.2, 64.8, 63.8, 63.7; IR (neat, cm^{-1}): 3018, 2399, 1516, 1419, 1215, 927, 769, 669; HRMS (ESI): calcd for $C_{24}H_{19}O_2$ 339.1385, found 339.1387.

5,5-Dimethyl-1,4-diphenylhex-2-yne-1,4-diol 194i



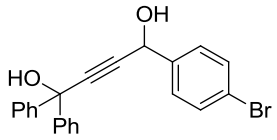
Yield: 79%; colorless oil; inseparable mixture with benzylic alcohol (1:1 ratio); ^{1}H NMR ($CDCl_3$, 400 MHz): δ 7.57-7.51 (m, 4H), 7.37-7.23 (m, 6H, (4H, benzylic)), 5.50 (s, 1H), 4.60 (s, 2H, (benzylic)), 2.83 (bs, 1H), 2.75 (bs, 1H), 0.99 (s, 9H); ^{13}C NMR ($CDCl_3$, 100 MHz): δ 141.9, 140.8, 140.6, 128.6, 128.5, 128.3, 127.6, 127.4, 127.1, 127.0, 126.6, 89.8, 85.5, 78.9, 65.2, 64.6, 39.5, 25.4; IR (neat, cm^{-1}): 3383, 3014, 2972, 2401, 1953, 1726, 1600, 1492, 1454, 1392, 1215, 1136, 1078, 1001, 906, 756, 700, 667; HRMS (ESI): calcd for $C_{20}H_{23}O_2$ 295.1698, found 295.1686.

4-(4-Fluorophenyl)-1,1-diphenylbut-2-yne-1,4-diol 194j



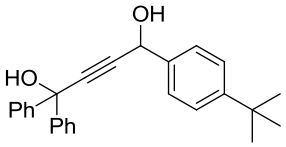
Yield: 71%; off white solid; m.p. 113-115 ^{o}C; ^{1}H NMR ($CDCl_3$, 500 MHz): δ 7.53-7.51 (m, 4H), 7.41-7.38 (m, 2H), 7.29-7.21 (m, 6H), 6.97 (t, 2H, J = 8.6 Hz), 5.42 (s, 1H), 3.54 (bs, 1H), 3.19 (bs, 1H); ^{13}C NMR ($CDCl_3$, 125 MHz): δ 163.8, 161.8, 144.7 (d, 1C, J_{C-F} = 10.1 Hz), 136.2 (d, 1C, J_{C-F} = 11.4 Hz), 128.78, 128.71, 128.5, 128.0, 126.1, 115.7, 115.5, 89.7, 86.8, 74.6, 64.0; IR (neat, cm^{-1}): 3421, 3018, 2399, 1635, 1508, 1419, 1215, 1014, 927, 771, 669; HRMS (ESI): calcd for $C_{22}H_{18}O_2F$ 333.1291, found 333.1279.

4-(4-Bromophenyl)-1,1-diphenylbut-2-yne-1,4-diol 194k



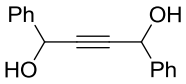
Yield: 73%; light brown solid; m.p. 166-168 ^{o}C; ^{1}H NMR ($CDCl_3$+CD_3OD, 500 MHz): δ 7.58-7.55 (m, 4H), 7.48-7.40 (m, 4H), 7.31-7.19 (m, 6H), 5.49 (s, 1H); ^{13}C NMR ($CDCl_3$+CD_3OD, 125 MHz): δ 145.15, 145.10, 139.9, 131.6, 131.58, 131.55, 128.6, 128.5, 128.3, 128.2, 127.8, 127.6, 126.0, 125.97, 125.95, 122.1, 89.4, 86.3, 74.0, 63.4; IR (neat, cm^{-1}): 3419, 3018, 2399, 2088, 1635, 1521, 1419, 1215, 1010, 927, 771, 669; HRMS (ESI): calcd for $C_{22}H_{18}O_2Br$ 393.0490, found 393.0487.

4-(4-*tert*-Butylphenyl)-1,1-diphenylbut-2-yne-1,4-diol 194l



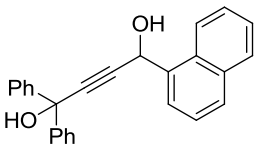
Yield: 78%; white solid; m.p. 162-164 ^{o}C; ^{1}H NMR ($CDCl_3$+CD_3OD, 400 MHz): δ 7.59 (d, 4H, J = 7.3 Hz), 7.46 (d, 2H, J = 7.8 Hz), 7.38 (d, 2H, J = 7.8Hz) 7.29-7.21 (m, 6H) 5.50 (s, 1H), 1.30 (s, 9H); ^{13}C NMR ($CDCl_3$+CD_3OD, 100 MHz): δ 151.2, 145.2, 145.1, 137.6, 128.1, 127.4, 126.5, 126.02, 126.00, 125.4, 89.0, 86.8, 74.0, 63.8, 34.5, 31.2; IR (neat, cm^{-1}): 3439, 3018, 2399, 1635, 1419, 1215, 927, 771, 669; HRMS (ESI): calcd for $C_{26}H_{27}O_2$ 371.2011, found 371.2013.

1,4-Diphenylbut-2-yne-1,4-diol 194m



Yield: 87%; light brown solid; m.p. 117-119 ^{o}C; ^{1}H NMR ($CDCl_3$+CD_3OD, 400 MHz): δ 7.52 (d, 4H, J = 7.2 Hz), 7.35-7.26 (m, 6H), 5.47 (s, 2H), 3.32 (bs, 2H); ^{13}C NMR ($CDCl_3$+CD_3OD, 100 MHz): δ 140.6, 128.4, 128.1, 126.63, 126.62, 86.1, 86.0, 63.9; IR (neat, cm^{-1}): 3585, 3018, 2399, 1653, 1521, 1456, 1419, 1338, 1217, 1122, 1014, 927, 771, 698, 669; HRMS (ESI): calcd for $C_{16}H_{15}O_2$ 239.1072, found 239.1082.

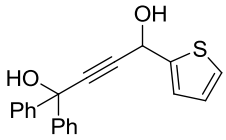
4-(Naphthalen-1-yl)-1,1-diphenylbut-2-yne-1,4-diol 194n



Yield: 71%; white solid; m.p. 121-123 ^{o}C; ^{1}H NMR ($CDCl_3$, 500 MHz): δ 8.22-7.82 (m, 2H), 7.80 (d, 1H, J = 8.2 Hz), 7.74 (d, 1H, J = 7.0 Hz), 7.56-7.46 (m, 6H), 7.37 (t,

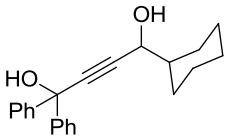
1H, *J* = 7.6 Hz), 7.25-7.18 (m, 6H), 6.12 (s, 1H); ^{13}C NMR ($CDCl_3$, 125 MHz): δ 144.6, 144.5, 135.2, 133.9, 130.4, 129.3, 128.6, 128.2, 127.6, 126.3, 125.9, 125.8, 125.1, 124.6, 123.9, 89.8, 86.8, 74.4, 62.9; IR (neat, cm^{-1}): 3439, 3018, 2399, 2088, 1633, 1519, 1423, 1215, 1014, 927, 771, 669; HRMS (ESI): calcd for $C_{26}H_{21}O_2$ 365.1542, found 365.1545.

1,1-Diphenyl-4-(thiophen-2-yl)but-2-yne-1,4-diol 194o



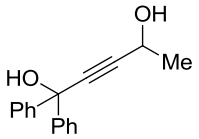
Yield: 82%; pale yellow solid; m.p. 156-158 ^{o}C; ^{1}H NMR ($CDCl_3$+CD_3OD, 500 MHz): δ 7.62-7.58 (m, 4H), 7.31-7.21 (m, 7H), 7.14 (bd, 1H, *J* = 3.4 Hz), 6.95-6.94 (m, 1H), 5.73 (s, 1H), 3.04 (bs, 2H); ^{13}C NMR ($CDCl_3$+CD_3OD, 125 MHz): δ 145.1, 145.0, 144.8, 128.2, 127.6, 126.8, 126.1, 126.0, 125.8, 125.5, 88.4, 86.1, 74.0, 59.8; IR (neat, cm^{-1}): 3441, 3018, 2399, 2088, 1635, 1516, 1419, 1215, 1014, 927, 771, 669; HRMS (ESI): calcd for $C_{20}H_{17}O_2S$ 321.0949, found 321.0965.

4-Cyclohexyl-1,1-diphenylbut-2-yne-1,4-diol 194p



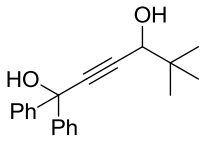
Yield: 86%; white solid; m.p. 141-143 ^{o}C; ^{1}H NMR ($CDCl_3$, 400 MHz): δ 7.58 (d, 4H, *J* = 7.6 Hz), 7.32-7.22 (m, 6H), 4.26 (d, 1H, *J* = 5.9 Hz), 3.18 (bs, 1H), 2.19 (bs, 1H), 1.86-1.58 (m, 5H), 1.28-1.01 (m, 6H); ^{13}C NMR ($CDCl_3$, 100 MHz): δ 144.9, 128.2, 127.6, 125.9, 88.3, 87.4, 74.4, 67.2, 44.1, 28.6, 28.1, 26.4, 25.87, 25.84; IR (neat, cm^{-1}): 3446, 3018, 2399, 1647, 1521, 1419, 1338, 1215, 1016, 927, 771, 669; HRMS (ESI): calcd for $C_{22}H_{25}O_2$ 321.1855, found 321.1870.

1,1-Diphenylpent-2-yne-1,4-diol 194q



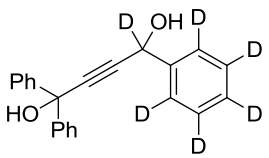
Yield: 80%; white solid; m.p. 109-111 ^{o}C; ^{1}H NMR ($CDCl_3$, 400 MHz): δ 7.55 (d, 4H, J = 7.1 Hz), 7.30-7.20 (m, 6H), 4.56 (q, 1H, J = 6.6 Hz), 3.47 (bs, 1H), 2.92 (bs, 1H), 1.44 (d, 3H, J = 6.6 Hz); ^{13}C NMR ($CDCl_3$, 100 MHz): δ 144.8, 128.2, 127.7, 126.01, 126.00, 89.0, 86.7, 74.2, 58.4, 24.0; IR (neat, cm^{-1}): 3419, 3018, 2397, 1645, 1489, 1448, 1328, 1215, 1020, 925, 758, 669; HRMS (ESI): calcd for $C_{17}H_{17}O_2$ 253.1229, found 253.1227.

5,5-Dimethyl-1,1-diphenylhex-2-yne-1,4-diol 194r



Yield: 82%; off white solid; m.p. 163-165 ^{o}C; ^{1}H NMR ($CDCl_3$+CD_3OD, 400 MHz): δ 7.58-7.22 (m, 10H), 4.10 (s, 1H), 3.63 (bs, 2H), 1.01 (s, 9H); ^{13}C NMR ($CDCl_3$+CD_3OD, 100 MHz): δ 145.4, 145.3, 127.9, 127.3, 126.5, 125.89, 125.87, 88.1, 86.6, 73.9, 70.8, 35.9, 25.2; IR (neat, cm^{-1}): 3689, 3018, 2962, 2397, 1521, 1419, 1215, 1004, 927, 769, 667; HRMS (ESI): calcd for $C_{20}H_{23}O_2$ 295.1698, found 295.1706.

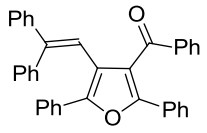
1,1,-Triphenylbut-2-yne-1,4-diol *d_6*-194a



Yield: 81%; white solid; m.p. 141-143 ^{o}C; ^{1}H NMR ($CDCl_3$+CD_3OD, 400 MHz): δ

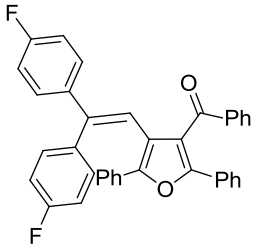
7.59 (d, 4H, *J* = 7.6 Hz), 7.30-7.20 (m, 6H), 3.2 (bs, 2H); ^{13}C NMR ($CDCl_3$+CD_3OD, 100 MHz): δ 145.18, 145.12, 140.4, 128.0, 127.4, 125.96, 125.94, 89.0, 86.6, 77.3, 73.9; IR (neat, cm^{-1}): 3446, 3018, 2399, 1635, 1521, 1423, 1215, 1029, 927, 771, 669; HRMS (ESI): calcd for C_{22} $^{1}H_{14}$ $^{2}H_5O_2$ 320.1699, found 320.1686.

(4-(2,2-Diphenylvinyl)-2,5-diphenylfuran-3-yl)(phenyl)methanone 195a



Yellow solid; m.p. 124-126 ^{o}C; ^{1}H NMR ($CDCl_3$, 400 MHz): δ 7.89-7.87 (m, 2H), 7.55-7.20 (m, 16H), 7.10-6.90 (m, 7H), 6.74 (s, 1H); ^{13}C NMR ($CDCl_3$, 100 MHz): δ 191.1, 152.3, 149.6, 146.6, 142.8, 138.8, 137.1, 132.7, 130.66, 130.61, 129.8, 129.5, 128.79, 128.71, 128.5, 128.3, 128.2, 128.0, 127.95, 127.90, 127.8, 127.7, 127.1, 127.0, 125.5, 122.7, 121.0, 118.1; IR (neat, cm^{-1}): 3018, 1734, 1653, 1597, 1483, 1446, 1327, 1215, 1074, 1026, 898, 758, 669; HRMS (ESI): calcd for $C_{37}H_{26}O_2Na$ 525.1831, found 525.1830.

(4-(2,2-bis(4-Fluorophenyl)vinyl)-2,5-diphenylfuran-3-yl)(phenyl)methanone 195b

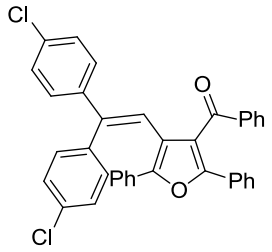


Yellow solid; m.p. 173-175 ^{o}C; ^{1}H NMR ($CDCl_3$, 400 MHz): δ 7.86-7.84 (m, 2H), 7.54-6.84 (m, 20H), 6.75 (s, 1H), 6.62 (t, 1H, *J* = 8.7 Hz); ^{13}C NMR ($CDCl_3$, 100 MHz): δ 191.1, 163.8, 163.4, 161.4, 161.0, 152.4, 152.3, 149.8, 149.7, 145.5 (d, 1C,

$J_{C\text{-}F}$ = 14.2 Hz), 142.6, 138.9, (d, 1C, $J_{C\text{-}F}$ = 12.2 Hz), 138.6, 137.1, 136.7, 134.8, 132.9, 132.7, 132.4, 132.3, 130.58 (d, 1C, $J_{C\text{-}F}$ = 24.6 Hz), 129.9, 129.8, 129.7, 129.49, 129.41, 128.84, 128.83, 128.7, 128.6, 128.5, 128.3, 128.2, 128.1, 128.0, 127.96, 127.93 (d, 1C, $J_{C\text{-}F}$ = 10.0 Hz), 127.2, 127.1, 125.5, 122.6, 122.5, 120.8, 118.1, 118.0, 115.0, 114.9, 114.8, 114.7; IR (neat, cm^{-1}): 3392, 3018, 2397, 1647, 1506, 1444, 1328, 1215, 898, 756; HRMS (ESI): calcd for $C_{37}H_{24}O_2F_2Na$ 561.1642, found 561.1631.

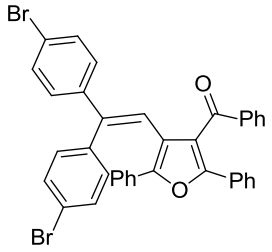
(4-(2,2-bis(4-Chlorophenyl)vinyl)-2,5-diphenylfuran-3-yl)(phenyl)methanone

195c



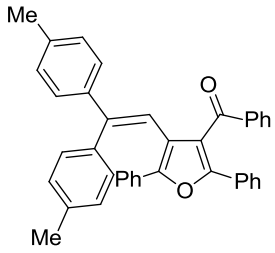
Pale yellow solid; m.p. 195-197 ^oC; ^1H NMR ($CDCl_3$, 400 MHz): δ 7.82 (d, 2H, J = 7.4 Hz), 7.49-7.17 (m, 15H), 7.08 (d, 2H, J = 8.4 Hz), 6.87 (d, 2H, J = 8.4 Hz), 6.81 (d, 2H, J = 8.4 Hz), 6.77 (s, 1H); ^{13}C NMR ($CDCl_3$, 100 MHz): δ 191.0, 152.4, 150.1, 144.1, 140.7, 137.0, 136.4, 134.0, 133.8, 132.9, 131.8, 130.3, 129.6, 129.5, 129.2, 128.8, 128.6, 128.39, 128.31, 128.25, 128.1, 128.0, 127.1, 125.5, 122.3, 120.5, 118.9; IR (neat, cm^{-1}): 3442, 3018, 2399, 1647, 1506, 1490, 1417, 1338, 1215, 1091, 1014, 927, 777, 669; HRMS (ESI): calcd for $C_{37}H_{25}O_2Cl_2$ 571.1232, found 571.1252.

(4-(2,2-bis(4-Bromophenyl)vinyl)-2,5-diphenylfuran-3-yl)(phenyl)methanone 195d



Pale yellow solid; m.p. 209-211 ^{o}C; ^{1}H NMR ($CDCl_3$, 400 MHz): δ 7.82 (d, 2H, J = 7.6 Hz), 7.80-7.17 (m, 15H), 7.01 (dd, 4H, J = 8.0, 6.5 Hz), 6.79 (s, 1H), 6.75 (d, 2H, J = 8.3 Hz); ^{13}C NMR ($CDCl_3$, 100 MHz): δ 191.0, 152.4, 150.1, 144.2, 141.1, 137.4, 136.4, 132.9, 132.1, 131.3, 131.1, 130.3, 129.8, 129.5, 129.2, 128.8, 128.6, 128.3, 128.17, 128.10, 127.2, 125.5, 122.3, 122.2, 120.4, 119.0; IR (neat, cm^{-1}): 3680, 3018, 2399, 1653, 1597, 1521, 1489, 1419, 1328, 1215, 1070, 1010, 929, 908, 756, 667; HRMS (ESI): calcd for $C_{37}H_{25}O_2Br_2$ 659.0221, found 659.0221.

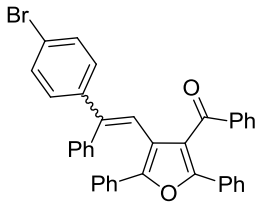
(4-(2,2-di-*p*-Tolylvinyl)-2,5-diphenylfuran-3-yl)(phenyl)methanone 195e



Pale yellow solid; m.p. 176-178 ^{o}C; ^{1}H NMR ($CDCl_3$, 500 MHz): δ 7.91 (d, 2H, J = 7.4 Hz), 7.51-7.37 (m, 7H), 7.34 (t, 1H, J = 7.4 Hz), 7.22-7.18 (m, 5H), 7.07 (dd, 4H, J = 17.7, 8.1 Hz), 6.81 (d, 2H, J = 8.0 Hz), 6.74 (d, 2H, J = 7.9 Hz), 6.70 (s, 1H), 2.35 (s, 3H), 2.13 (s, 3H); ^{13}C NMR ($CDCl_3$, 125 MHz): δ 191.0, 152.0, 149.7, 146.4, 140.2, 137.5, 137.2, 136.9, 136.0, 132.4, 130.7, 130.6, 129.8, 129.6, 128.79, 128.72, 128.5, 128.4, 128.29, 128.25, 127.8, 127.7, 127.2, 127.1, 125.4, 122.7, 121.4, 116.8, 21.2, 21.1; IR (neat, cm^{-1}): 3018, 2399, 1653, 1598, 1516, 1419, 1336, 1215, 1026,

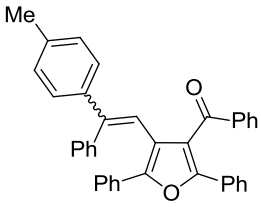
929, 771, 669; HRMS (ESI): calcd for $C_{39}H_{31}O_2$ 531.2324, found 531.2321.

(4-(2-(4-Bromophenyl)-2-phenylvinyl)-2,5-diphenylfuran-3-yl)(phenyl)metha--none 195f



Pale yellow solid; m.p. 155-157 ^{o}C; *E*/*Z* ratio = 1.3:1; ^{1}H NMR ($CDCl_3$, 400 MHz): δ 7.86 (d, 2H, *J* = 8.2 Hz), 7.53-7.31 (m, 9H), 7.29-7.16 (m, 8H), 7.05-6.76 (m, 5H), 6.71 (s, 1H); ^{13}C NMR ($CDCl_3$, 100 MHz): δ 191.1 (1C, *E* or *Z* isomer), 191.0 (1C, *E* or *Z* isomer), 152.5, 152.3, 150.0, 149.7, 145.49, 145.40, 142.2, 141.7, 138.2, 137.9, 137.0, 136.4, 132.8, 132.7, 132.2, 131.1, 131.0, 130.5, 130.4, 129.8, 129.6, 129.4, 129.3, 128.8, 128.6, 128.5, 128.2, 128.1, 128.08, 128.02, 127.9, 127.16, 127.11, 125.5, 121.98, 121.95, 120.75, 120.72, 118.6, 118.4; IR (neat, cm^{-1}): 3442, 3018, 2399, 1653, 1521, 1419, 1338, 1215, 1026, 927, 769, 669; HRMS (ESI): calcd for $C_{37}H_{25}O_2BrNa$ 603.0936, found 603.0942.

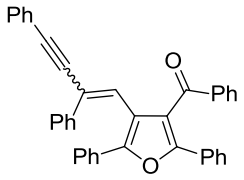
(2,5-Diphenyl-4-(2-phenyl-2-(*p*-tolyl)vinyl)furan-3-yl)(phenyl)methanone 195g



Pale yellow solid; m.p. 161-163 ^{o}C; *E*/*Z* ratio = 1.1:1; ^{1}H NMR ($CDCl_3$, 400 MHz): δ 7.89-7.37 (m, 9H), 7.35-7.12 (m, 9H), 7.06-6.95 (m, 3H), 6.90 (d, 1H, *J* = 6.9 Hz), 6.79 (d, 1H, *J* = 8.0 Hz), 6.72 (s, 1H), 6.70 (d, 1H, *J* = 5.0 Hz). 2.32 (s, 3H, *E* or *Z* isomer), 2.10 (s, 3H, *E* or *Z* isomer); ^{13}C NMR ($CDCl_3$, 100 MHz): δ 191.1 (1C, *E* or

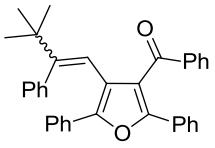
Z isomer), 191.0 (1C, *E* or *Z* isomer), 152.2, 152.1, 149.8, 149.5, 146.58, 146.52, 143.07, 143.05, 138.9, 137.6, 137.3, 137.2, 136.8, 135.9, 132.6, 130.67, 130.61, 129.88, 129.83, 129.5, 128.78, 128.73, 128.57, 128.50, 128.4, 128.3, 128.26, 128.23, 128.21, 127.99, 127.94, 127.8, 127.76, 127.74, 127.1, 127.0, 125.5, 122.8, 122.6, 121.3, 121.0, 117.5, 117.3; IR (neat, cm^{-1}): 3419, 3018, 2399, 1647, 1506, 1338, 1215, 927, 771, 669; HRMS (ESI): calcd for $C_{38}H_{28}O_2Na$ 539.1987, found 539.1994.

(4-(2,4-Diphenylbut-1-en-3-yn-1-yl)-2,5-diphenylfuran-3-yl)(phenyl)methanone 195h



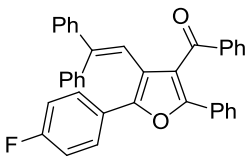
Yellow solid; m.p. 118-120 ^{o}C; *E*/*Z* ratio = 1:1; ^{1}H NMR ($CDCl_3$, 400 MHz): δ 7.85-7.73 (m, 4H), 7.53-7.16 (m, 19H), 7.06-6.94 (m, 3H); ^{13}C NMR ($CDCl_3$, 100 MHz): δ 192.1 (1C, *E* or *Z* isomer), 190.9 (1C, *E* or *Z* isomer), 153.3, 152.7, 149.9, 149.7, 138.4, 137.9, 136.7, 136.4, 132.8, 132.7, 131.67, 131.61, 130.6, 130.2, 129.9, 129.6, 129.3, 129.0, 128.85, 128.81, 128.7, 128.6, 128.39, 128.34, 128.29, 128.24, 128.21, 128.1, 128.09, 128.03, 128.00, 127.9, 127.8, 127.4, 127.2, 127.1, 126.3, 126.2, 125.9, 125.1, 123.2, 122.9, 122.4, 119.9, 119.3, 98.0, 91.2, 89.9, 87.7; IR (neat, cm^{-1}): 3442, 3018, 2399, 1653, 1489, 1215, 1026, 927, 773, 669; HRMS (ESI): calcd for $C_{39}H_{27}O_2$ 527.2011, found 527.2006.

(4-(3,3-Dimethyl-2-phenylbut-1-en-1-yl)-2,5-diphenylfuran-3-yl)(phenyl)metha--none 195i



Pale yellow solid; m.p. 145-147 ^{o}C; *E*/*Z* ratio = 1:2; ^{1}H NMR ($CDCl_3$, 400 MHz): δ 7.84 (d, 1H, *J* = 7.4 Hz), 7.76 (d, 2H, *J* = 7.4 Hz), 7.67 (d, 1H, *J* = 7.2 Hz), 7.45-7.02 (m, 25H), 6.81 (d, 2H, *J* = 6.9 Hz), 6.50 (s, 1H, *E* or *Z* isomer), 6.11 (s, 1H, *E* or *Z* isomer), 1.35 (s, 9H, *E* or *Z* isomer), 1.14 (s, 9H, *E* or *Z* isomer); ^{13}C NMR ($CDCl_3$, 100 MHz): δ 193.9 (1C, *E* or *Z* isomer), 193.7 (1C, *E* or *Z* isomer), 156.2, 152.3, 151.3, 150.4, 147.8, 146.9, 145.9, 141.3, 137.39, 137.35, 133.4, 133.3, 132.0, 131.9, 129.8, 129.78, 129.71, 129.5, 129.4, 129.2, 129.1, 128.6, 128.5, 128.4, 128.32, 128.30, 128.2, 128.0, 127.9, 127.8, 127.5, 127.24, 127.21, 126.8, 126.3, 126.2, 125.8, 122.3, 121.6, 116.0, 110.6, 37.1, 36.0, 30.9, 29.7; IR (neat, cm^{-1}): 3414, 3018, 2399, 1653, 1521, 1419, 1325, 1215, 1020, 927, 779, 669; HRMS (ESI): calcd for $C_{35}H_{31}O_2$ 483.2324, found 483.2326.

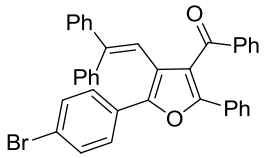
(4-(2,2-Diphenylvinyl)-5-(4-fluorophenyl)-2-phenylfuran-3-yl)(phenyl)methanone 195j



Pale yellow solid; m.p. 143-145 ^{o}C; ^{1}H NMR ($CDCl_3$, 400 MHz): δ 7.81 (dd, 2H, *J* = 8.5, 5.4 Hz), 7.56 (d, 2H, *J* = 7.7 Hz), 7.50-7.48 (m, 2H), 7.40 (t, 1H, *J* = 7.2 Hz), 7.25-6.96 (m, 15H), 6.89 (d, 2H, *J* = 7.3 Hz), 6.69 (s, 1H); ^{13}C NMR ($CDCl_3$, 100 MHz): δ 191.1, 163.6, 161.1, 152.2, 148.7, 146.9, 142.7, 138.8, 137.0, 132.7, 130.5,

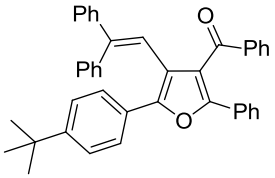
129.8, 129.4, 128.5, 128.0 (d, 1C, $J_{C\text{-}F}$ = 26.1 Hz), 128.00, 127.86, 127.81, 127.7, 127.4, 127.3, 127.0, 126.9 (d, 1C, $J_{C\text{-}F}$ = 16.8 Hz), 126, 122.7, 120.6, 117.7, 115.9, 115.7; IR (neat, cm^{-1}): 3419, 3018, 2399, 1653, 1516, 1417, 1328, 1215, 927, 769, 669; HRMS (ESI): calcd for $C_{37}H_{26}O_2F$ 521.1917, found 521.1916.

(5-(4-Bromophenyl)-4-(2,2-diphenylvinyl)-2-phenylfuran-3-yl)(phenyl)metha--none 195k



Pale yellow solid; m.p. 181-183 ^oC; ^1H NMR ($CDCl_3$, 400 MHz): δ 7.72 (d, 2H, J = 8.5 Hz), 7.56-7.49 (m, 7H), 7.41 (t, 1H, J = 7.3 Hz), 7.27-7.20 (m, 7H), 7.11-6.97 (m, 5H), 6.89 (d, 2H, J = 7.0 Hz), 6.69 (s, 1H); ^{13}C NMR ($CDCl_3$, 100 MHz): δ 191.0, 152.5, 148.5, 147.1, 142.6, 138.7, 137.0, 132.8, 131.9, 130.5, 129.8, 129.4, 129.3, 128.6, 128.3, 128.2, 128.08, 128.01, 127.9, 127.8, 127.0, 126.9, 122.8, 121.8, 121.5, 117.5; IR (neat, cm^{-1}): 3446, 3018, 2399, 1653, 1521, 1479, 1419, 1215, 1008, 927, 771, 669; HRMS (ESI): calcd for $C_{37}H_{26}O_2Br$ 581.1116, found 581.1128.

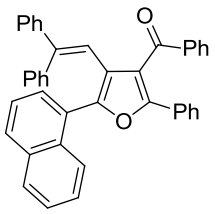
(5-(4-(*tert*-Butyl)phenyl)-4-(2,2-diphenylvinyl)-2-phenylfuran-3-yl)(phenyl)meth--anone 195l



Yellow oil; ^1H NMR ($CDCl_3$, 300 MHz): δ 7.81 (d, 2H, J = 8.5 Hz), 7.53-7.36 (m, 7H), 7.24-7.18 (m, 8H), 7.09-6.88 (m, 7H), 6.72 (s, 1H), 1.34 (s, 9H); ^{13}C NMR ($CDCl_3$, 75 MHz): δ 191.1, 152.0, 151.1, 149.9, 146.3, 142.9, 138.8, 137.1, 132.6,

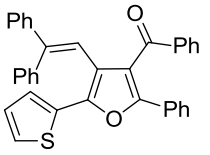
130.6, 129.8, 129.6, 128.4, 128.28, 128.23, 127.9, 127.8, 127.77, 127.70, 127.0, 125.7, 125.3, 122.6, 120.4, 118.3, 34.7, 31.2; IR (neat, cm^{-1}): 3419, 3016, 2399, 1651, 1598, 1519, 1489, 1423, 1319, 1215, 927, 781; HRMS (ESI): calcd for $C_{41}H_{35}O_2$ 559.2637, found 559.2644.

(4-(2,2-Diphenylvinyl)-5-(naphthalen-1-yl)-2-phenylfuran-3-yl)(phenyl)metha--none 195n



Brown oil; ^1H NMR ($CDCl_3$, 400 MHz): δ 8.06-8.03 (m, 1H), 7.83-7.79 (m, 4H), 7.53-7.6.79 (m, 20H), 6.66 (s, 1H), 6.61-6.59 (m, 2H); ^{13}C NMR ($CDCl_3$, 100 MHz): δ 192.0, 152.8, 150.2, 146.3, 142.8, 139.2, 137.1, 133.8, 133.1, 131.0, 130.1, 130.0, 129.7, 129.5, 129.2, 128.7, 128.4, 128.3, 128.27, 128.23, 128.0, 127.8, 127.7, 127.6, 127.5, 127.4, 127.2, 126.9, 126.3, 126.0, 125.9, 125.1, 122.8, 122.4, 117.2; IR (neat, cm^{-1}): 3439, 3018, 2399, 1651, 1489, 1446, 1323, 1215, 1132, 1074, 898, 756, 696, 669; HRMS (ESI): calcd for $C_{41}H_{29}O_2$ 553. 2168, found 553.2161.

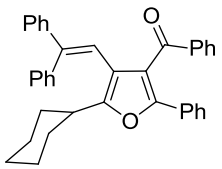
(4-(2,2-Diphenylvinyl)-2-phenyl-5-(thiophen-2-yl)furan-3-yl)(phenyl)methanone 195o



Yellow oil; ^1H NMR ($CDCl_3$, 400 MHz): δ 7.87 (d, 2H, J = 7.5 Hz), 7.48-7.27 (m, 13H), 7.22 (d, 1H, J = 5.0 Hz), 7.13-6.91 (m, 6H), 6.87 (d, 2H, J = 7.3 Hz); ^{13}C NMR

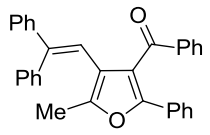
($CDCl_3$, 100 MHz): δ 193.6, 150.4, 148.5, 142.7, 142.2, 141.0, 137.2, 133.7, 132.1, 129.8, 129.6, 128.8, 128.5, 128.4, 128.3, 128.2, 128.0, 127.8, 127.6, 127.4, 127.3, 126.2, 125.7, 121.7, 121.0, 112.9; IR (neat, cm^{-1}): 3394, 3018, 2399, 1654, 1597, 1490, 1446, 1215, 929, 906, 767, 669; HRMS (ESI): calcd for $C_{35}H_{25}O_2S$ 509.1575, found 509.1594.

(5-Cyclohexyl-4-(2,2-diphenylvinyl)-2-phenylfuran-3-yl)(phenyl)methanone 195p



Yellow oil; ^1H NMR ($CDCl_3$, 400 MHz): δ 7.70 (d, 2H, J = 7.5 Hz), 7.40-7.02 (m, 18H), 6.60 (s, 1H), 2.53-2.46 (m, 1H), 1.74-1.47 (m, 7H), 1.25-1.13 (m, 3H); ^{13}C NMR ($CDCl_3$, 100 MHz): δ 192.3, 156.4, 151.4, 145.2, 143.1, 139.8, 137.3, 132.8, 130.8, 129.9, 128.2, 128.1, 128.0, 127.9, 127.5, 127.3, 126.7, 121.6, 118.3, 117.8, 36.6, 30.9, 26.3, 25.8; IR (neat, cm^{-1}): 3446, 3018, 2399, 2308, 1647, 1506, 1338, 1215, 927, 767, 669; HRMS (ESI): calcd for $C_{37}H_{33}O_2$ 509.2481, found 509.2474.

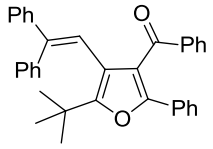
(4-(2,2-Diphenylvinyl)-5-methyl-2-phenylfuran-3-yl)(phenyl)methanone 195q



Pale yellow solid; m.p. 143-145 ^oC; ^1H NMR ($CDCl_3$, 400 MHz): δ 7.75 (d, 2H, J = 7.1 Hz), 7.43-7.37 (m, 3H), 7.29-7.07 (m, 15H), 6.56 (s, 1H), 1.91 (s, 3H); ^{13}C NMR ($CDCl_3$, 100 MHz): δ 192.4, 151.6, 148.9, 145.4, 143.0, 140.0, 137.3, 132.9, 130.6, 129.9, 129.7, 128.2, 128.19, 128.17, 128.0, 127.9, 127.5, 127.2, 126.6, 121.8, 120.0, 117.7, 12.5; IR (neat, cm^{-1}): 3018, 2399, 1653, 1597, 1489, 1215, 1074, 1022, 929,

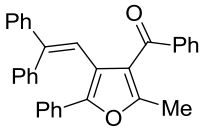
771, 669; HRMS (ESI): calcd for $C_{32}H_{25}O_2$ 441.1855, found 441.1855.

(5-(*tert*-Butyl)-4-(2,2-diphenylvinyl)-2-phenylfuran-3-yl)(phenyl)methanone 195r



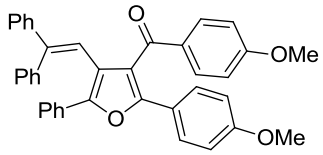
Pale yellow solid; m.p. 125-127 ^{o}C; ^{1}H NMR ($CDCl_3$, 500 MHz): δ 7.47 (d, 2H, J = 7.1 Hz), 7.39-7.33 (m, 3H), 7.23-7.11 (m, 8H), 7.04-6.92 (m, 7H), 6.69 (s, 1H), 1.44 (s, 9H); ^{13}C NMR ($CDCl_3$, 125 MHz): δ 191.5, 158.4, 150.8, 144.6, 143.3, 139.1, 137.4, 132.3, 130.8, 129.9, 129.7, 128.2, 128.1, 128.0, 127.9, 127.8, 127.6, 127.46, 127.42, 126.9, 122.2, 119.1, 117.9, 34.3, 29.3; IR (neat, cm^{-1}): 3419, 3016, 2972, 2432, 2399, 1651, 1598, 1519, 1489, 1423, 1319, 1215, 1074, 1028, 927, 781, 667; HRMS (ESI): calcd for $C_{35}H_{31}O_2$ 483.2324, found 483.2324.

(4-(2,2-Diphenylvinyl)-2-methyl-5-phenylfuran-3-yl)(phenyl)methanone 195s



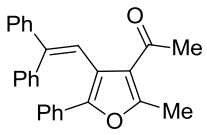
Yellow solid; m.p. 108-110 ^{o}C; ^{1}H NMR ($CDCl_3$, 400 MHz): δ 7.77 (d, 2H, J = 7.2 Hz), 7.47-7.22 (m, 11H), 7.10-7.01 (m, 5H), 6.83 (d, 2H, J = 7.0 Hz), 6.75 (s, 1H), 2.20 (s, 3H); ^{13}C NMR ($CDCl_3$, 100 MHz): δ 190.6, 154.7, 148.8, 145.8, 142.9, 139.0, 137.9, 132.3, 130.8, 129.77, 129.74, 128.7, 128.2, 128.0, 127.9, 127.8, 127.7, 127.6, 127.5, 125.3, 122.8, 119.2, 118.4, 31.6; IR (neat, cm^{-1}): 3018, 2399, 1647, 1521, 1419, 1215, 927, 771, 669; HRMS (ESI): calcd for $C_{32}H_{25}O_2$ 441.1855, found 441.1866.

(4-(2,2-Diphenylvinyl)-2-(4-methoxyphenyl)-5-phenylfuran-3-yl)(4-methoxyphenyl)methanone 195t



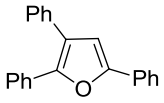
Yield 94 %; yellow oil; ^{1}H NMR ($CDCl_3$, 400 MHz): δ 7.83 (d, 2H, J = 7.2 Hz), 7.53-7.45 (m, 4H), 7.38 (t, 2H, J = 7.6 Hz), 7.30-7.13 (m, 6H), 7.01-6.88 (m, 5H), 6.75 (s, 1H), 6.74-6.69 (m, 4H), 3.80 (s, 3H), 3.73 (s, 3H); ^{13}C NMR ($CDCl_3$, 100 MHz): δ 189.9, 163.2, 159.7, 152.0, 149.0, 146.4, 142.9, 138.9, 132.2, 130.8, 130.6, 130.2, 128.7, 128.5, 128.3, 128.0, 127.7, 127.6, 125.4, 122.5, 121.7, 120.9, 118.2, 113.7, 113.2, 55.4, 55.2; IR (neat, cm^{-1}): 3680, 3441, 3018, 2839, 2399, 1645, 1598, 1500, 1419, 1334, 1255, 1215, 1170, 1136, 1029, 927, 900, 767, 669; HRMS (ESI): calcd for $C_{39}H_{31}O_4$ 563.2222, found 563.2226.

1-(4-(2,2-Diphenylvinyl)-2-methyl-5-phenylfuran-3-yl)ethanone 195u



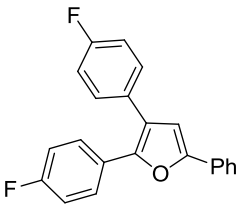
Pale yellow oil; ^{1}H NMR ($CDCl_3$, 400 MHz): δ 77.60 (d, 2H, J = 7.3 Hz), 7.39-7.19 (m, 8H), 7.14-7.05 (m, 3H), 6.92 (s, 1H), 6.91-6.89 (m, 2H), 2.48 (s, 3H), 2.29 (s, 3H); ^{13}C NMR ($CDCl_3$, 100 MHz): δ 195.2, 156.4, 148.1, 146.2, 142.6, 139.1, 130.6, 130.0, 128.4, 128.3, 128.2, 127.9, 127.7, 127.49, 127.40, 125.5, 124.2, 118.9, 117.8, 30.5, 14.4; IR (neat, cm^{-1}): 3442, 3018, 2399, 1668, 1516, 1444, 1361, 1215, 1118, 927, 771, 669; HRMS (ESI): calcd for $C_{27}H_{23}O_2$ 379.1698, found 379.1697.

2,3,5-Triphenylfuran 196a



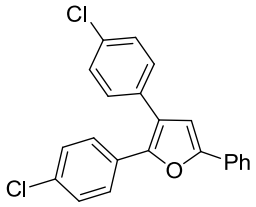
Pale yellow solid; m.p. 91-93 ^{o}C; ^{1}H NMR ($CDCl_3$, 400 MHz): δ 7.77 (d, 2H, J = 7.8 Hz), 7.61 (d, 2H, J = 8.0 Hz), 7.47-7.24 (m, 11H), 6.81 (s, 1H); ^{13}C NMR ($CDCl_3$, 100 MHz): δ 152.5, 147.9, 134.3, 131.1, 130.5, 128.76, 128.72, 128.6, 128.4, 127.54, 127.51, 127.3, 126.1, 124.5, 123.8, 109.4; IR (neat, cm^{-1}): 3439, 3018, 2962, 2399, 1635, 1556, 1419, 1261, 1215, 1097, 1014, 929, 775, 698, 669; HRMS (ESI): calcd for $C_{22}H_{17}O$ 297.1279, found 297.1291.

2,3-bis(4-Fluorophenyl)-5-phenylfuran 196b



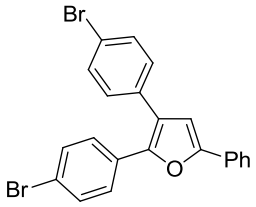
Pale yellow oil; ^{1}H NMR ($CDCl_3$, 400 MHz): δ 7.75 (d, 2H, J = 7.6 Hz), 7.55-7.37 (m, 6H), 7.29 (t, 1H, J = 7.4 Hz), 7.08 (t, 2H, J = 8.6 Hz), 7.01 (t, 2H, J = 8.7 Hz), 6.76 (s, 1H); ^{13}C NMR ($CDCl_3$, 100 MHz): δ 163.4, 160.9, 152.6, 147.0, 130.3, 130.2, 128.7, 127.9 (d, 1C, $J_{C\text{-}F}$ = 31.8 Hz), 127.6, 123.8, 123.2, 115.8, 115.6, 115.4, 109.2; IR (neat, cm^{-1}): 3442, 3018, 2399, 1653, 1521, 1473, 1419, 1338, 1217, 1014, 927, 958, 669; HRMS (ESI): calcd for $C_{22}H_{15}OF_2$ 333.1091, found 333.1085.

2,3-bis(4-Chlorophenyl)-5-phenylfuran 196c



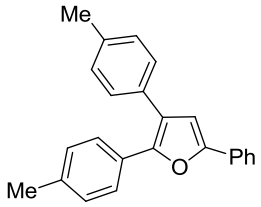
Yellow solid; m.p. 128-130 ^{o}C; ^{1}H NMR ($CDCl_3$, 400 MHz): δ 7.74 (d, 2H, J = 7.4 Hz), 7.51 (d, 2H, J = 8.6 Hz), 7.42 (t, 2H, J = 7.6 Hz), 7.36 (s, 4H), 7.32-7.25 (m, 3H), 6.76 (s, 1H); ^{13}C NMR ($CDCl_3$, 100 MHz): δ 153.0, 146.9, 133.46, 133.43, 132.4, 130.1, 129.9, 129.2, 129.0, 128.8, 128.7, 127.8, 127.3, 123.8, 123.7, 109.1; IR (neat, cm^{-1}): 3018, 2854, 2399, 1489, 1261, 1215, 1093, 1014, 952, 931, 831, 775, 669; HRMS (ESI): calcd for $C_{22}H_{15}OCl_2$ 365.0500, found 365.0512.

2,3-bis(4-Chlorophenyl)-5-phenylfuran 196d



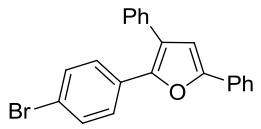
Yellow solid; m.p. 154-156 ^{o}C; ^{1}H NMR ($CDCl_3$, 400 MHz): δ 7.74 (d, 2H, J = 7.4 Hz), 7.52 (d, 2H, J = 8.3 Hz), 7.43-7.40 (m, 6H), 7.32-7.28 (m, 3H), 6.76 (s, 1H); ^{13}C NMR ($CDCl_3$, 100 MHz): δ 153.1, 146.9, 132.9, 132.0, 131.7, 130.2, 130.1, 129.6, 128.8, 127.9, 127.5, 123.9, 121.6, 121.5, 109.1; IR (neat, cm^{-1}): 3439, 3018, 2399, 2104, 1635, 1516, 1419, 1215, 1010, 927, 754, 669; HRMS (ESI): calcd for $C_{22}H_{14}OBr_2Na$ 474.9309, found 474.9297.

5-Phenyl-2,3-di-*p*-tolylfuran 196e



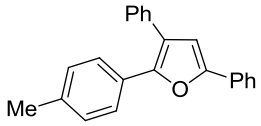
Pale yellow oil; ^{1}H NMR ($CDCl_3$, 500 MHz): δ 7.75 (d, 2H, J = 7.2 Hz), 7.51 (d, 2H, J = 8.2 Hz), 7.40 (t, 2H, J = 7.7 Hz), 7.35 (d, 2H, J = 8.0 Hz), 7.28 (d, 1H, J = 7.4 Hz), 7.19 (d, 2H, J = 7.8 Hz), 7.12 (d, 2H, J = 8.0 Hz), 6.78 (s, 1H), 2.39 (s, 3H), 2.34 (s, 3H); ^{13}C NMR ($CDCl_3$, 125 MHz): δ 152.1, 148.0, 137.3, 136.8, 131.4, 130.8, 130.6, 129.3, 129.0, 128.7, 128.5, 127.3, 126.0, 123.8, 123.7, 109.4, 21.3, 21.2; IR (neat, cm^{-1}): 3676, 3018, 1602, 1512, 1472, 1419, 1252, 1215, 1097, 1017, 929, 757, 669; HRMS (ESI): calcd for $C_{24}H_{21}O$ 325.1592, found 325.1579.

2-(4-Bromophenyl)-3,5-diphenylfuran 196f



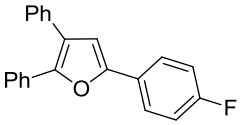
Yellow oil; regioisomeric ratio = 2.5:1; ^{1}H NMR ($CDCl_3$, 400 MHz): δ 7.76 (d, 2H, J = 7.9 Hz), 7.60-7.27 (m, 12H), 6.80 (s, 1H, A or B isomer), 6.78 (s, 1H, A or B isomer); ^{13}C NMR ($CDCl_3$, 100 MHz): δ 152.8, 148.1, 146.7, 134.0, 133.2, 131.8, 131.5, 130.8, 130.3, 129.9, 128.8, 128.7, 128.6, 128.5, 127.79, 127.75, 127.70, 127.5, 127.4, 126.2, 125.1, 123.88, 123.85, 121.3, 109.6, 108.9; IR (neat, cm^{-1}): 3444, 3018, 2399, 1716, 1506, 1417, 1338, 1215, 929, 771, 669; HRMS (ESI): calcd for $C_{22}H_{16}OBr$ 375.0385, found 375.0383.

3,5-Diphenyl-2-(p-tolyl)furan 196g



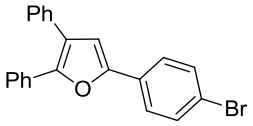
Brown solid; m.p. 142-144 ^{o}C; regioisomeric ratio = 3.3:1; ^{1}H NMR ($CDCl_3$, 400 MHz): δ 7.76 (d, 2H, J = 7.9 Hz), 7.62 (d, 1H, J = 7.7 Hz), 7.50-7.45 (m, 1H), 7.40 (t, 2H, J = 7.6 Hz), 7.36 (d, 2H, J = 7.9 Hz), 7.32-7.18 (m, 6H), 7.12 (d, 1H, J = 8.0 Hz, A or B isomer), 6.80 (s, 1H, A or B isomer), 6.79 (s, 1H, A or B isomer), 2.39 (s, 1H, A or B isomer), 2.34 (s, 1H, A or B isomer); ^{13}C NMR ($CDCl_3$, 100 MHz): δ 152.4, 147.7, 137.0, 131.3, 131.2, 130.6, 129.4, 129.1, 128.7, 128.68, 128.64, 128.5, 128.3, 127.4, 127.3, 126.1, 126.0, 124.5, 123.8, 123.7, 109.5, 109.3, 21.2; IR (neat, cm^{-1}): 3676, 3018, 1602, 1512, 1489, 1419, 1261, 1215, 1097, 1020, 929, 756, 669; HRMS (ESI): calcd for $C_{23}H_{19}O$ 311.1436, found 311.1425.

5-(4-Fluorophenyl)-2,3-diphenylfuran 196j



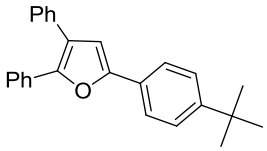
Pale yellow oil; ^{1}H NMR ($CDCl_3$, 500 MHz): δ 7.75-7.71 (m, 2H), 7.60-7.59 (m, 2H), 7.47-7.24 (m, 8H), 7.14-7.09 (m, 2H), 6.75 (s, 1H); ^{13}C NMR ($CDCl_3$, 125 MHz): δ 163.4, 161.4, 151.9, 148.1, 134.3, 131.2, 128.9, 128.8, 128.6, 127.7, 127.5, 127.1 (d, 1C, $J_{C\text{-}F}$ = 13.1 Hz), 126.3, 125.8, 125.7, 124.7, 116.1, 115.9, 109.3; IR (neat, cm^{-1}): 3419, 3018, 2962, 2399, 1653, 1604, 1498, 1442, 1261, 1215, 1157, 1097, 1012, 952, 933, 837, 756, 696, 669; HRMS (ESI): calcd for $C_{22}H_{16}OF$ 315.1185, found 315.1180.

5-(4-Bromophenyl)-2,3-diphenylfuran 196k



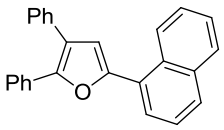
Pale yellow oil; ^{1}H NMR ($CDCl_3$, 400 MHz): δ 7.62-7.57 (m, 4H), 7.53 (d, 2H, J = 8.4 Hz), 7.45 (d, 2H, J = 7.2 Hz), 7.40-7.23 (m, 6H), 6.81 (s, 1H); ^{13}C NMR ($CDCl_3$, 100 MHz): δ 151.4, 148.2, 134.0, 131.9, 130.8, 129.4, 128.7, 128.6, 128.4, 127.7, 127.4, 126.1, 125.2, 124.6, 121.2, 110.0; IR (neat, cm^{-1}): 3439, 3018, 2962, 2399, 2088, 1637, 1521, 1485, 1419, 1261, 1215, 1097, 1008, 929, 779, 669; HRMS (ESI): calcd for $C_{22}H_{16}OBr$ 375.0385, found 375.0385.

5-(4-tert-Butylphenyl)-2,3-diphenylfuran 196l



Yellow solid; m.p. 104-106 ^{o}C; ^{1}H NMR ($CDCl_3$, 300 MHz): δ 7.70 (d, 2H, J = 8.4 Hz), 7.61-7.59 (m, 2H), 7.48-7.23 (m, 10H), 6.76 (s, 1H), 1.35 (s, 9H); ^{13}C NMR ($CDCl_3$, 75 MHz): δ 152.8, 150.6, 147.5, 134.4, 131.2, 128.7, 128.6, 128.3, 127.8, 127.3, 127.2, 126.0, 125.6, 124.4, 123.6, 108.9, 34.6, 31.2; IR (neat, cm^{-1}): 3419, 3018, 2399, 1647, 1506, 1456, 1338, 1215, 927, 771, 669; HRMS (ESI): calcd for $C_{26}H_{25}O$ 353.1905, found 353.1900.

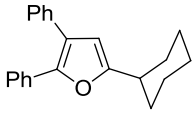
5-(Naphthalen-1-yl)-2,3-diphenylfuran 196n



Pale yellow oil; ^{1}H NMR ($CDCl_3$, 500 MHz): δ 8.58 (d, 1H, J = 8.4 Hz), 7.91 (d, 1H,

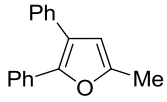
J = 7.5 Hz), 7.87-7.85 (m, 2H), 7.66 (d, 2H, *J* = 7.3 Hz), 7.58-7.51 (m, 5H), 7.41 (t, 2H, *J* = 7.4 Hz), 7.36-7.24 (m, 4H), 6.90 (s, 1H); ^{13}C NMR ($CDCl_3$, 125 MHz): δ 152.2, 148.3, 134.3, 134.0, 131.1, 130.2, 128.8, 128.75, 128.70, 128.6, 128.4, 128.1, 127.5, 127.3, 126.7, 126.2, 126.09, 126.01, 125.5, 125.3, 124.2, 113.7; IR (neat, cm^{-1}): 3018, 2399, 1600, 1502, 1442, 1215, 1097, 1016, 923, 777, 696, 669; HRMS (ESI): calcd for $C_{26}H_{19}O$ 347.1436, found 347.1432.

5-Cyclohexyl-2,3-diphenylfuran 196p



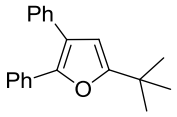
Pale yellow oil; ^{1}H NMR ($CDCl_3$, 400 MHz): δ 7.52-7.40 (m, 4H), 7.35-7.24 (m, 5H), 7.21-7.17 (m, 1H), 6.13 (s, 1H), 2.73-2.66 (m, 1H), 2.13-1.71 (m, 5H), 1.52-1.25 (m, 5H); ^{13}C NMR ($CDCl_3$, 100 MHz): δ 160.0, 146.2, 134.9, 131.6, 128.6, 128.5, 128.2, 126.9, 126.8, 125.9, 122.7, 107.4, 37.2, 31.5, 26.1, 25.9; IR (neat, cm^{-1}): 3446, 3018, 2399, 1647, 1516, 1417, 1338, 1215, 1014, 927, 775, 669; HRMS (ESI): calcd for $C_{22}H_{23}O$ 303.1749, found 303.1736.

5-Methyl-2,3-diphenylfuran 196q



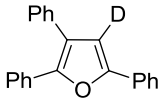
Pale yellow oil; ^{1}H NMR ($CDCl_3$, 400 MHz): δ 7.50 (d, 2H, *J* = 7.5 Hz), 7.40-7.19 (m, 8H), 6.15 (s, 1H), 2.38 (s, 3H); ^{13}C NMR ($CDCl_3$, 125 MHz): δ 151.3, 146.7, 134.7, 131.4, 128.58, 128.55, 128.3, 127.0, 126.9, 125.9, 123.1, 110.1, 13.5; IR (neat, cm^{-1}): 3419, 3018, 2343, 1637, 1521, 1419, 1328, 1215, 925, 771, 669; HRMS (ESI): calcd for $C_{17}H_{15}O$ 235.1123, found 235.1118.

5-(*tert*-Butyl)-2,3-diphenylfuran 196r



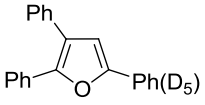
Pale yellow oil; ^{1}H NMR ($CDCl_3$, 400 MHz): δ 7.52 (d, 2H, J = 7.4 Hz), 7.42 (d, 2H, J = 7.2 Hz), 7.33 (bt, 2H, J = 7.2 Hz), 7.26, (bt, 3H, J = 7.8 Hz), 7.19 (d, 1H, J = 7.0 Hz), 6.12 (s, 1H), 1.36 (s, 9H); ^{13}C NMR ($CDCl_3$, 100 MHz): δ 163.2, 146.2, 134.9, 131.7, 128.6, 128.5, 128.2, 126.9, 126.8, 125.9, 122.6, 106.6, 32.7, 29.1 IR (neat, cm^{-1}): 3419, 3018, 2399, 1647, 1521, 1419, 1338, 1215, 927, 771, 669; HRMS (ESI): calcd for $C_{20}H_{21}O$ 277.1592, found 277.1602.

2,3,5-Triphenylfuran *d_1*-196a



Yellow solid; m.p. 94-96 ^{o}C; ^{1}H NMR ($CDCl_3$, 400 MHz): δ 7.78 (d, 2H, J = 7.7 Hz), 7.62 (d, 2H, J = 7.4 Hz), 7.48-7.25 (m, 11H); ^{13}C NMR ($CDCl_3$, 125 MHz): δ 152.5, 147.9, 134.3, 131.1, 130.5, 128.76, 128.71, 128.6, 128.4, 127.53, 127.51, 127.3, 126.1, 124.4, 123.8, 109.4; IR (neat, cm^{-1}): 3439, 3018, 2962, 2399, 1635, 1556, 1419, 1261, 1215, 1097, 1014, 929, 775, 698, 669; HRMS (ESI): calcd for C_{22} $^{1}H_{16}$ ^{2}HO 298.1342, found 298.1332.

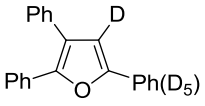
2,3,5-Triphenylfuran *d_5*-196a



Yellow solid; m.p. 91-93 ^{o}C; ^{1}H NMR ($CDCl_3$, 500 MHz): δ 7.61-746 (m, 4H), 7.38 (t, 2H, J = 7.4 Hz), 7.34-7.24 (m, 4H), 6.81 (s, 1H); ^{13}C NMR ($CDCl_3$, 125 MHz): δ

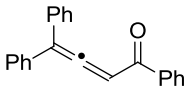
152.5, 147.8, 134.3, 131.1, 130.3, 128.7, 128.6, 128.4, 128.2, 128.0, 127.5, 127.3, 126.1, 124.5, 123.6, 114.6, 109.4; IR (neat, cm^{-1}): 3446, 3018, 2399, 1602, 1516, 1419, 1215, 1022, 927, 775, 669; HRMS (ESI): calcd for $C_{22}\,{}^{1}H_{12}\,{}^{2}H_5O$ 302.1593, found 302.1604.

2,3,5-Triphenylfuran *d_6*-196a



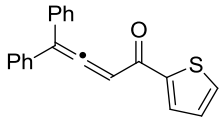
Pale yellow oil; ^{1}H NMR ($CDCl_3$, 500 MHz): δ 7.62-7.46 (m, 4H), 7.40-7.23 (m, 6H); ^{13}C NMR ($CDCl_3$, 75 MHz): δ 147.8, 134.3, 131.1, 130.3, 128.7, 128.6, 128.4, 128.2, 127.9, 127.4, 127.3, 126.1, 124.4, 123.4, 123.0, 109.4; IR (neat, cm^{-1}): 3421, 3018, 2926, 2399, 1602, 1502, 1477, 1442, 1379, 1213, 1099, 1022, 954, 779, 694, 669; HRMS (ESI): calcd for $C_{22}\,{}^{1}H_{11}\,{}^{2}H_6O$ 303.1656, found 303.1659.

1,4,4-Triphenylbuta-2,3-dien-1-one 197a



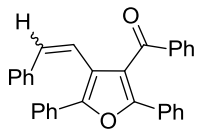
Brown color oil; ^{1}H NMR ($CDCl_3$, 400 MHz): δ 7.82 (d, 2H, J = 7.7 Hz), 7.50 (t, 1H, J = 7.3 Hz), 7.39-7.25 (m, 12H), 6.80 (s, 1H); ^{13}C NMR ($CDCl_3$, 100 MHz): δ 216.1, 191.5, 137.4, 134.2, 132.7, 128.76, 128.72, 128.6, 128.34, 128.33, 113.7, 96.5; IR (neat, cm^{-1}): 3439, 3018, 2399, 1635, 1521, 1419, 1259, 1215, 1097, 1016, 927, 848, 771, 669; HRMS (ESI): calcd for $C_{22}H_{17}O$ 297.1279, found 297.1292.

4,4-Diphenyl-1-(thiophen-2-yl)buta-2,3-dien-1-one 197o



Brown color oil; ^{1}H NMR ($CDCl_3$, 400 MHz): δ 7.799-7.790 (m, 1H), 7.60 (bd, 1H, *J* = 4.9 Hz), 7.40-7.34 (m, 10H), 7.05 (bt, 1H, *J* = 4.3 Hz), 6.77 (s, 1H); ^{13}C NMR ($CDCl_3$, 100 MHz): δ 214.8, 181.9, 143.0, 134.0, 133.8, 132.6, 128.7, 128.6, 128.4, 127.9, 127.1, 114.5, 96.8; IR (neat, cm^{-1}): 3439, 3018, 2399, 1625, 1521, 1416, 1242, 1215, 1095, 1011, 927, 771, 669; HRMS (ESI): calcd for $C_{20}H_{15}OS$ 303.0844, found 303.0856

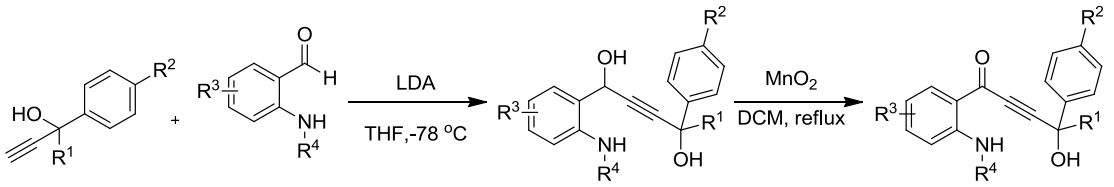
(2,5-diphenyl-4-styrylfuran-3-yl)(phenyl)methanone 198m



Pale yellow solid; m.p. 146-148 ^{o}C; *E*/*Z* ratio = 1:1; ^{1}H NMR ($CDCl_3$, 400 MHz): δ 7.84-7.81 (m, 2H), 7.68 (d, 1H, *J* = 7.1 Hz), 7.61 (d, 1H, *J* = 7.1 Hz), 7.48 (d, 2H, *J* = 7.6 Hz), 7.42-7.15 (m, 14H), 6.98 (d, 1H, *J* = 16.1 Hz), 6.65 (d, 1H, *J* = 12.5 Hz, *E* or *Z* isomer), 6.37 (d, 1H, *J* = 12.5 Hz, *E* or *Z* isomer); ^{13}C NMR ($CDCl_3$, 100 MHz): δ 193.6 (1C, *E* or *Z* isomer), 193.3 (1C, *E* or *Z* isomer), 151.6, 148.4, 137.2, 136.8, 133.47, 133.42, 131.5, 129.8, 129.6, 129.5, 129.1, 128.8, 128.7, 128.6, 128.5, 128.4, 128.38, 128.35, 127.97, 127.92, 127.5, 126.59, 126.52, 126.0, 122.8, 115.3, 114.4; IR (neat, cm^{-1}): 3442, 3018, 2399, 1635, 1521, 1417, 1338, 1215, 927, 771, 669; HRMS (ESI): calcd for $C_{31}H_{23}O_2$ 427.1698, found 427.1706.

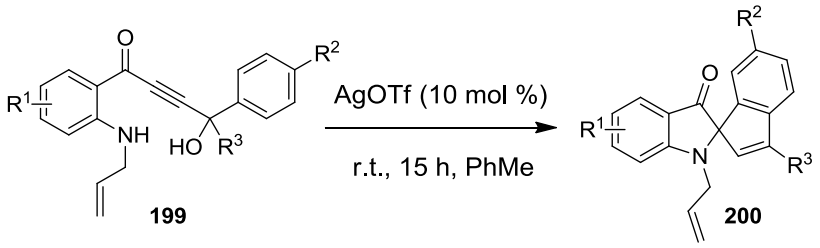
7.6 Silver-Catalyzed Cycloisomerization of 1-(2-(Allylamino)phenyl)-4-hydroxy-but-2-yn-1-ones to 1'-Allylspiro[indene-1,2'-indolin]-3'-ones

Representative Experimental Procedure for Preparation of Substituted 1-(2-(Amino)phenyl)-4-hydroxy-but-2-yn-1-ones (199a)-(199y)[138a,152,153]



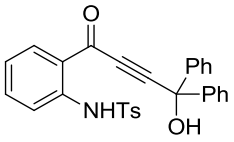
To a solution of diisopropylamine (0.47g, 4.6 mmol) in anhydrous THF (5 mL) was added butyl lithium (1.6 M hexane solution; 2.9 mL; 4.6 mmol) at −78 °C in a dropwise manner. The resulting solution was stirred for 1 h prior to slow addition of the corresponding propargyl alcohol (0.50g, 1.3 mmol) in THF at −78 °C. The resulting mixture was stirred at same temperature for 1 h. The corresponding aminoaldehyde (0.21g, 2.0 mmol) in THF (2 mL) was added to the reaction mixture and allowed to stir for a further 1h at same temperature. The resulting mixture was slowly warmed up to room temperature and continued the stirring for a further 3-5 h. On completion, the reaction mixture was quenched by adding saturated NH_4Cl (50 mL) and extracted with EtOAc (2 x 25 mL). The combined organic layers were washed with water, brine, dried over Na_2SO_4 and concentrated under reduced pressure. To the obtained crude, MnO_2 (1.17g, 13.5 mmol) was added in dichloromethane (10 mL) and stirred at reflux for 15-30 min. On completion, the reaction mixture was filtered through celite and washed with dichloromethane (2 x 15 mL). The organic layer was concentrated under reduced pressure and the obtained crude product was purified by flash column chromatography on silica gel (eluent: *n*-hexane:EtOAc = 7.5:2.5) gave the title compound (**199**).

Representative Experimental Procedure for Preparation of Substituted Spiro[indene-1,2'-indolin]-3'-one



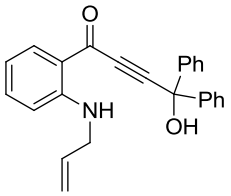
To a solution of AgOTf (16 μmol) in toluene (2 mL) at room temperature was added dropwise the 1-(amino)phenyl)-4-hydroxy-but-2-yn-1-one **199** (0.16 mmol) dissolved in toluene (2 mL). The resulting mixture was stirred at room temperature for 15 h and monitored by TLC analysis. The solvent was concentrated under reduced pressure. Purification by flash column chromatography on silica gel (eluent: *n*-hexane:EtOAc = 9:1) gave the tetrasubstituted furan **200**.

***N*-(2-(4-Hydroxy-4,4-diphenylbut-2-ynoyl)phenyl)-4-methylbenzenesulfonamide 199a**



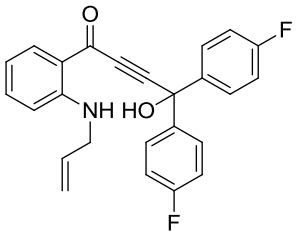
Yield: 78%: pale yellow solid; m.p. 151-153 ^{o}C; ^{1}H NMR (400 MHz, $CDCl_3$) δ 11.08 (s, 1H), 8.11 (d, 1H, *J* = 7.8 Hz), 7.68 (d, 2H, J = 8.1 Hz), 7.59 (d, 5H, *J* = 7.9 Hz), 7.42-7.25 (m, 7H), 7.17 (d, 2H, *J* = 8.1 Hz), 6.99 (t, 1H, *J* = 7.6 Hz), 3.74 (s, 1H), 2.29 (s, 3H); ^{13}C NMR ($CDCl_3$, 100 MHz): δ 180.2, 144.3, 143.2, 140.8, 136.2, 136.0, 135.0, 129.8, 128.6, 128.4, 127.3, 126.0, 122.7, 122.0, 118.0, 97.8, 83.8, 74.7, 21.5; IR (neat, cm^{-1}): 3442, 3018, 2399, 1620, 1490, 1404, 1246, 1215, 1159, 1091, 921, 777, 669; HRMS (ESI): calcd for $C_{29}H_{23}NO_4SNa$ 504.1245, found 504.1260

1-(2-(Allylamino)phenyl)-4-hydroxy-4,4-diphenylbut-2-yn-1-one 199b



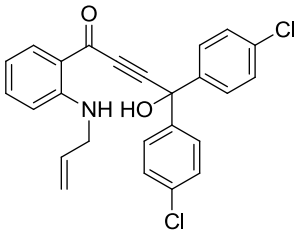
Yield: 75%: orange solid; m.p. 101-103 ^{o}C; ^{1}H NMR (300 MHz, $CDCl_3$) δ 8.86 (bs, 1H), 8.05 (dd, 1H, J = 1.4, 8.1 Hz), 7.64-7.21 (m, 11H), 6.64-6.53 (m, 2H), 5.94-5.82 (m, 1H), 5.21 (dddd, 2H, J = 1.3, 17.2, 1.3, 10.3 Hz), 3.87-3.84 (m, 2H), 3.62 (bs, 1H); ^{13}C NMR ($CDCl_3$, 75 MHz): δ 178.8, 151.8, 143.7, 136.1, 135.3, 133.8, 128.5, 128.1, 126.1, 118.3, 116.3, 115.0, 111.8, 95.0, 84.8, 74.7, 44.9; IR (neat, cm^{-1}): 3581, 3018, 2399, 2214, 1616, 1589, 1571, 1517, 1421, 1249, 1215, 1163, 927, 756, 669; HRMS (ESI): calcd for $C_{25}H_{22}NO_2$ 368.1651, found 368.1658.

1-(2-(Allylamino)phenyl)-4,4-bis(4-fluorophenyl)-4-hydroxybut-2-yn-1-one 199c



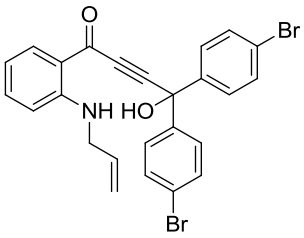
Yield: 70%; yellow solid; m.p. 78-80 ^{o}C; ^{1}H NMR ($CDCl_3$, 400 MHz): δ 8.90 (bs, 1H), 8.03 (dd, 1H, J = 1.52, 8.08 Hz), 7.64-7.00 (m, 9H), 6.68-6.58 (m, 2H), 5.97-5.87 (m, 1H), 5.30-5.18 (m, 2H), 3.93-3.89 (m, 2H), 3.32 (bs, 1H); ^{13}C NMR ($CDCl_3$, 100 MHz): δ 178.6, 163.7, 161.2, 151.8, 143.5, 139.6, 136.2, 135.1, 133.7, 128.6, 128.3, 128.1 (1C, $J_{C\text{-}F}$ = 32.5), 126.0, 118.2, 116.4, 115.4, 115.2, 114.9, 111.8, 94.3, 84.9, 74.2, 44.9; IR (neat, cm^{-1}): 3682, 3018, 2399, 1616, 1573, 1517, 1421, 1249, 1215, 1159, 927, 757, 669; HRMS (ESI): calcd for $C_{25}H_{20}NO_2F_2$ 404.1462, found 404.1456.

1-(2-(Allylamino)phenyl)-4,4-bis(4-chlorophenyl)-4-hydroxybut-2-yn-1-one 199d



Yield: 75%; brown solid; m.p. 117-119 ^{o}C; ^{1}H NMR ($CDCl_3$, 500 MHz): δ 8.83 (bs, 1H), 7.97-7.95 (m, 1H), 7.55 (d, 4H, J = 8.6 Hz), 7.37-7.29 (m, 5H), 6.67 (d, 1H, J = 8.6 Hz), 6.57 (t, 1H, J = 7.5 Hz), 5.94-5.86 (m, 1H), 5.28 (d, 1H, J = 17.2 Hz), 5.21 (d, 1H, J = 10.3 Hz), 4.16 (bs, 1H), 3.88 (bt, 2H, J = 5.2 HZ), 3.32 (bs, 1H); ^{13}C NMR ($CDCl_3$, 125 MHz): δ 178.5, 152.0, 142.0, 136.4, 135.1, 134.2, 133.6, 128.7, 127.5, 118.0, 116.4, 115.0, 111.9, 94.0, 85.0, 73.7, 44.9; IR (neat, cm^{-1}): 3684, 3018, 2399, 1616, 1517, 1421, 1215, 1093, 1012, 927, 769, 669; HRMS (ESI): calcd for $C_{25}H_{20}NO_2Cl_2$ 436.0871, found 436.0884.

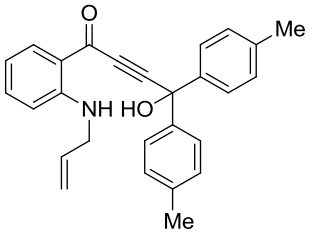
1-(2-(Allylamino)phenyl)-4,4-bis(4-bromophenyl)-4-hydroxybut-2-yn-1-one 199e



Yield: 71%: orange solid; m.p. 134-136 ^{o}C; ^{1}H NMR (400 MHz, $CDCl_3$) δ 8.84 (s, 1H), 7.95 (d, 1H, J = 7.4 Hz), 7.46-7.44 (m, 8H), 7.35 (t, 1H, J = 7.6 Hz), 6.67 (d, 1H, J = 8.6 Hz), 6.58 (t, 1H, J = 7.5 Hz), 5.95-5.85 (m, 1H), 5.28 (d, 1H, J = 17.1 Hz), 5.20 (d, 1H, J = 10.4 Hz), 3.89 (bt, 2H, J = 5.2 Hz), 3.82 (bs, 1H); ^{13}C NMR ($CDCl_3$, 100 MHz): δ 178.4, 151.9, 142.4, 136.4, 135.0, 133.6, 131.7, 127.8, 122.5, 118.0, 116.4, 115.0, 111.9, 93.5, 85.1, 73.8, 44.9; IR (neat, cm^{-1}): 3018, 2399, 1616, 1571, 1517, 1421, 1215, 1163, 1010, 927, 771, 669; HRMS (ESI): calcd for

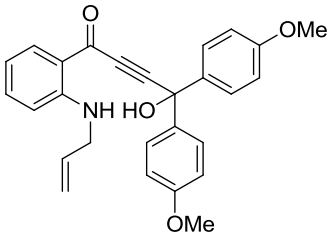
$C_{25}H_{20}NO_2Br_2$ 523.9861, found 523.9873.

1-(2-(Allylamino)phenyl)-4-hydroxy-4,4-di-p-tolylbut-2-yn-1-one 199f



Yield: 78%: brown gummy; ^{1}H NMR (400 MHz, $CDCl_3$) δ 8.92 (bt, 1H, *J* = 5.0 Hz), 8.09 (dd, 1H, *J* = 1.5, 8.0 Hz), 7.54 (d, 4H, *J* = 8.2 Hz), 7.39-7.34 (m, 1H), 7.17 (d, 4H, *J* = 8.0 Hz), 6.68 (d, 1H, *J* = 8.5 Hz), 6.61 (t, 1H, *J* = 7.5 Hz), 5.95-5.88 (m, 1H), 5.31-5.19 (m, 2H), 3.92-3.90 (m, 2H), 3.27 (bs, 1H), 2.34 (s, 6H); ^{13}C NMR ($CDCl_3$, 100 MHz): δ 178.9, 151.8, 141.0, 137.8, 136.0, 135.2, 133.8, 129.1, 126.0, 118.4, 116.3, 114.9, 111.8, 95.2, 84.6, 74.5, 44.9, 21.1; IR (neat, cm^{-1}): 3682, 3018, 2399, 2212, 1616, 1581, 1517, 1421, 1249, 1215, 927, 756, 669; HRMS (ESI): calcd for $C_{27}H_{26}NO_2$ 396.1964, found 396.1974.

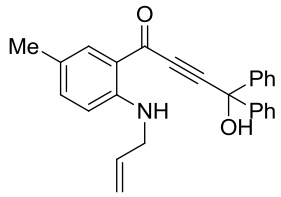
1-(2-(Allylamino)phenyl)-4-hydroxy-4,4-bis(4-methoxyphenyl)but-2-yn-1-one 199g



Yield: 75%: yellow solid; m.p. 79-79 ^{o}C; ^{1}H NMR (400 MHz, $CDCl_3$) δ 8.91 (bs, 1H), 8.07-8.03 (m, 1H), 7.54 (d, 4H, *J* = 8.8 Hz), 7.44-7.34 (m, 1H), 6.90-6.86 (m, 4H), 6.68 (d, 1H, *J* = 8.6 Hz), 6.60 (t, 1H, *J* = 7.5 Hz), 5.97-5.87 (m, 1H), 5.30-5.18 (m, 2H), 3.91 (bs, 2H), 3.79 (s, 6H); ^{13}C NMR ($CDCl_3$, 100 MHz): δ 178.9, 159.3, 151.8,

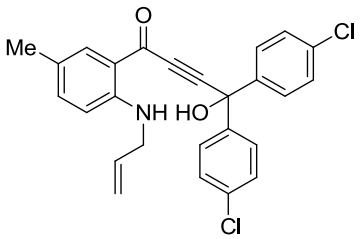
141.8, 136.1, 136.0, 135.2, 133.8, 133.3, 131.9, 127.9, 127.5, 118.3, 116.3, 114.9, 113.7, 111.8, 95.3, 84.5, 74.0, 55.3, 44.9; IR (neat, cm^{-1}): 3682, 3018, 2837, 2399, 2212, 1701, 1616, 1571, 1508, 1419, 1249, 1217, 1174, 1033, 927, 833, 753, 667; HRMS (ESI): calcd for $C_{27}H_{26}NO_4$ 428.1862, found 428.1867.

1-(2-(Allylamino)-5-methylphenyl)-4-hydroxy-4,4-diphenylbut-2-yn-1-one 199h



Yield: 69%: orange solid; m.p. 126-128 ^oC; ^1H NMR (400 MHz, $CDCl_3$) δ 8.75 (bs, 1H), 7.81 (bs, 1H), 7.66-7.17 (m, 11H), 6.60 (d, 1H, *J* = 8.6 Hz), 5.95-5.85 (m, 1H), 5.27 (d, 1H, *J* = 17.2 Hz), 5.18 (d, 1H, *J* = 10.3 Hz), 3.89-3.86 (m, 2H), 3.27 (bs, 1H), 2.17 (s, 3H); ^{13}C NMR ($CDCl_3$, 100 MHz): δ 178.5, 150.0, 143.8, 137.5, 134.6, 134.0, 128.5, 128.1, 126.1, 123.8, 118.2, 116.2, 111.9, 94.5, 85.0, 74.7, 45.0, 20.1; IR (neat, cm^{-1}): 3502, 3018, 2399, 1635, 1521, 1215, 767, 669; HRMS (ESI): calcd for $C_{26}H_{24}NO_2$ 382.1807, found 382.1807.

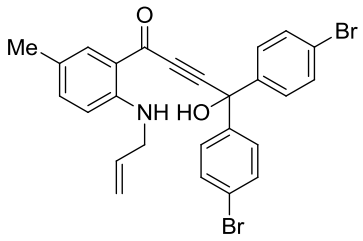
1-(2-(Allylamino)-5-methylphenyl)-4,4-bis(4-chlorophenyl)-4-hydroxybut-2-yn-1-one 199i



Yield: 66%: orange solid; m.p. 135-137 ^oC; ^1H NMR (400 MHz, $CDCl_3$) δ 8.70 (bs, 1H), 7.69 (bs, 1H), 7.55 (d, 4H, *J* = 8.4 Hz), 7.32 (d, 4H, *J* = 8.4 Hz), 7.20 (d, 1H, *J* =

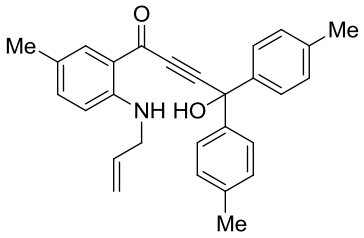
8.6 Hz), 6.60 (d, 1H, *J* = 8.7 Hz), 5.94-5.85 (m, 1H), 5.26 (d, 1H, *J* = 17.2 Hz), 5.19 (d, 1H, *J* = 10.3 Hz), 3.89-3.87 (m, 2H), 3.77 (bs, 1H), 2.17 (s, 3H); ^{13}C NMR ($CDCl_3$, 100 MHz): δ 178.2, 150.2, 142.0, 137.8, 134.39, 134.31, 133.9, 128.7, 127.5, 123.9, 118.0, 116.2, 112.0, 93.5, 85.3, 73.7, 44.9, 20.2; IR (neat, cm^{-1}): 3448, 3018, 2399, 1629, 1570, 1521, 1431, 1255, 1215, 1093, 927, 771, 669; HRMS (ESI): calcd for $C_{26}H_{22}NO_2Cl_2$ 450.1028, found 450.1028.

1-(2-(Allylamino)-5-methylphenyl)-4,4-bis(4-bromophenyl)-4-hydroxybut-2-yn-1-one 199j



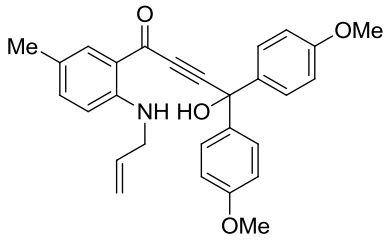
Yield: 63%: orange solid; m.p. 137-139 ^{o}C; ^{1}H NMR (400 MHz, $CDCl_3$) δ 8.71 (bt, 1H, *J* = 5.1 Hz), 7.69 (bs, 1H), 7.50-7.45 (m, 8H), 7.20 (d, 1H, *J* = 8.6 Hz), 6.61 (d, 1H, *J* = 8.6 Hz), 5.95-5.85 (m, 1H), 5.27 (d, 1H, *J* = 17.2 Hz), 5.19 (d, 1H, *J* = 10.3 Hz), 3.88 (bt, 2H, *J* = 5.0 Hz), 3.76 (bs, 1H), 2.17 (s, 3H); ^{13}C NMR ($CDCl_3$, 100 MHz): δ 178.1, 150.2, 142.5, 137.8, 134.3, 133.9, 131.6, 127.8, 123.9, 122.5, 118.0, 116.3, 112.0, 93.3, 85.3, 73.8, 45.0, 20.2; HRMS (ESI): calcd for $C_{26}H_{22}NO_2Br_2$ 538.0017, found 538.0023.

1-(2-(Allylamino)-5-methylphenyl)-4-hydroxy-4,4-di-p-tolylbut-2-yn-1-one 199k



Yield: 76%: yellow solid; m.p. 146-148 ^{o}C; ^{1}H NMR (400 MHz, $CDCl_3$) δ 8.75 (bs, 1H), 7.81 (bs, 1H), 7.52 (d, 4H, *J* = 8.1 Hz), 7.19-7.14 (m, 5H), 6.59 (d, 1H, *J* = 8.6 Hz), 5.95-5.86 (m, 1H), 5.27 (d, 1H, *J* = 17.2 Hz), 5.18 (d, 1H, *J* = 10.3 Hz), 3.88 (bt, 2H, *J* = 5.2 Hz), 3.10 (bs, 1H), 2.32 (s, 6H), 2.18 (s, 3H); ^{13}C NMR ($CDCl_3$, 100 MHz): δ 178.7, 150.0, 141.1, 137.8, 137.4, 134.7, 134.1, 129.1, 126.0, 123.7, 118.3, 116.1, 111.9, 94.9, 84.8, 74.5, 45.0, 21.1, 20.1; IR (neat, cm^{-1}): 3446, 3018, 2399, 1627, 1612, 1521, 1429, 758, 669; HRMS (ESI): calcd for $C_{28}H_{28}NO_2$ 410.2120, found 410.2118.

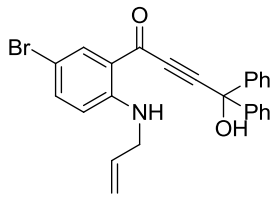
1-(2-(allylamino)-5-methylphenyl)-4-hydroxy-4,4-bis(4-methoxyphenyl)but-2-yn-1-one 199l



Yield: 76%: yellow gummy; ^{1}H NMR (400 MHz, $CDCl_3$) δ 8.75 (bs, 1H), 7.81 (bs, 1H), 7.55 (d, 4H, *J* = 8.6 Hz), 7.19 (d, 1H, *J* = 8.6 Hz), 6.88 (d, 4H, *J* = 8.7 Hz), 6.60 (d, 1H, *J* = 8.6 Hz), 5.95-5.86 (m, 1H), 5.28 (d, 1H, *J* = 17.2 Hz), 5.18 (d, 1H, *J* = 10.3 Hz), 3.89 (bt, 2H, *J* = 5.0 Hz), 3.79 (s, 6H), 3.07 (bs, 1H), 2.19 (s, 3H); ^{13}C NMR ($CDCl_3$, 100 MHz): δ 178.6, 159.3, 150.0, 137.4, 136.2, 134.6, 134.0, 127.4, 123.7, 118.2, 116.1, 113.7, 111.8, 94.9, 84.7, 74.0, 55.3, 44.9, 20.1; HRMS (ESI): calcd for

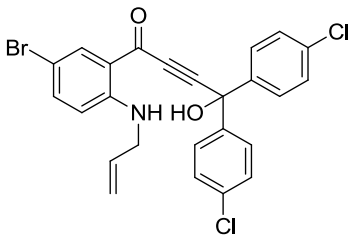
$C_{28}H_{28}NO_4$ 442.2018, found 442.2029.

1-(2-(Allylamino)-5-bromophenyl)-4-hydroxy-4,4-diphenylbut-2-yn-1-one 199m



Yield: 65%: orange solid; ^{1}H NMR (300 MHz, $CDCl_3$) δ 8.85 (bs, 1H), 8.14 (d, 1H, *J* = 2.3 Hz), 7.64-7.23 (m, 11H), 6.56 (d, 1H, *J* = 9.1 Hz), 5.93-5.81 (m, 1H), 5.26-5.16 (m, 2H), 3.87 (bd, 2H, *J* = 4.7 Hz); ^{13}C NMR ($CDCl_3$, 75 MHz): δ 177.8, 150.5, 143.5, 138.6, 136.9, 133.3, 128.6, 128.5, 128.2, 126.0, 119.6, 116.6, 113.9, 106.0, 95.7, 84.2, 74.7, 45.0; IR (neat, cm^{-1}): 3581, 3018, 2399, 2216, 1614, 1508, 1450, 1215, 925, 756, 669; HRMS (ESI): calcd for $C_{25}H_{21}NO_2Br$ 446.0756, found 446.0766.

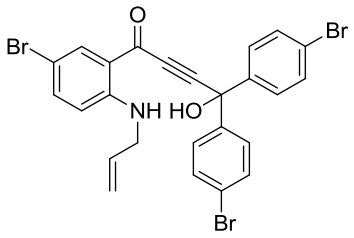
1-(2-(Allylamino)-5-bromophenyl)-4,4-bis(4-chlorophenyl)-4-hydroxybut-2-yn-1-one 199n



Yield: 63%: orange gummy; ^{1}H NMR (300 MHz, $CDCl_3$) δ 8.84 (bs, 1H), 8.04 (d, 1H, *J* = 2.4 Hz), 7.56-7.33 (m, 9H), 6.59 (d, 1H, *J* = 9.1 Hz), 5.95-5.82 (m, 1H), 5.29-5.18 (m, 2H), 3.89 (bt, 2H, *J* = 5.3 Hz), 3.35 (bs, 1H); ^{13}C NMR ($CDCl_3$, 125 MHz): δ 177.3, 150.6, 141.7, 138.8, 136.7, 134.5, 133.1, 128.8, 127.4, 121.4, 119.4, 119.0, 116.7, 114.1, 106.1, 94.1, 84.6, 73.8, 45.0; HRMS (ESI): calcd for $C_{25}H_{19}NO_2\,Cl_2Br$

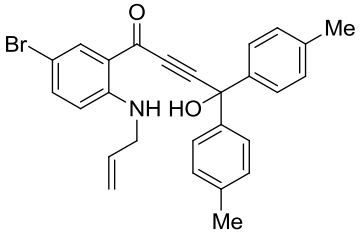
513.9976, found 513.9973.

1-(2-(Allylamino)-5-bromophenyl)-4,4-bis(4-bromophenyl)-4-hydroxybut-2-yn-1-one 199o



Yield: 61%: orange gummy; ^{1}H NMR (300 MHz, $CDCl_3$) δ 8.83 (bs, 1H), 8.02 (bd, 1H, *J* = 2.2 Hz), 7.51-7.37 (m, 9H), 6.58 (d, 1H, *J* = 9.1 Hz), 5.94-5.82 (m, 1H), 5.29-5.19 (m, 2H), 3.88 (bt, 2H, *J* = 5.2 Hz), 3.66 (bs, 1H); ^{13}C NMR ($CDCl_3$, 100 MHz): δ 177.4, 150.6, 142.2, 138.8, 136.7, 133.1, 131.8, 131.7, 127.7, 122.7, 119.3, 116.7, 114.0, 106.1, 94.2, 84.5, 73.9, 45.0; HRMS (ESI): calcd for $C_{25}H_{19}NO_2Br_3$ 601.8966, found 601.8959.

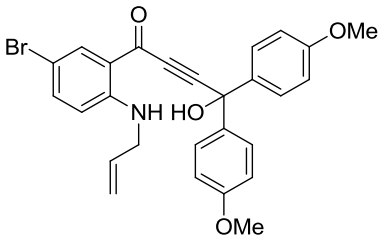
1-(2-(Allylamino)-5-bromophenyl)-4-hydroxy-4,4-di-p-tolylbut-2-yn-1-one 199p



Yield: 65%: yellow solid; m.p. 129-131 ^{o}C; ^{1}H NMR (400 MHz, $CDCl_3$) δ 8.88 (bs, 1H), 8.14 (bd, 1H, *J* = 2.1 Hz), 7.51 (d, 4H, *J* = 8.1 Hz), 7.39 (dd, 1H, *J* = 2.1, 9.1 Hz), 7.18 (d, 4H, *J* = 8.0 Hz), 6.57 (d, 1H, *J* = 9.0 Hz), 5.93-5.83 (m, 1H), 5.26 (d, 1H, *J* = 17.2 Hz), 5.20 (d, 1H, *J* = 10.3 Hz), 3.87 (bt, 2H, *J* = 5.4 Hz), 3.09 (bs, 1H), 2.33 (s, 6H); ^{13}C NMR ($CDCl_3$, 100 MHz): δ 177.8, 150.5, 140.7, 138.5, 138.0, 136.9, 133.3, 129.2, 129.1, 126.0, 119.7, 116.6, 113.9, 106.0, 95.9, 84.0, 74.5, 45.0, 21.1; IR

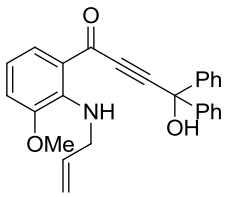
(neat, cm^{-1}): 3446, 3018, 2399, 1614, 1508, 1215, 1033, 756, 669; HRMS (ESI): calcd for $C_{27}H_{25}NO_2Br$ 474.1069, found 474.1085.

1-(2-(Allylamino)-5-bromophenyl)-4-hydroxy-4,4-bis(4-methoxyphenyl)but-2-yn-1-one 199q



Yield: 64%: yellow solid; m.p. 141-143 ^oC; ^1H NMR (300 MHz, $CDCl_3$) δ 8.87 (bs, 1H), 8.13 (bd, 1H, J = 2.4 Hz), 7.54-7.49 (m, 4H), 7.40 (dd, 1H, J = 9.0, 2.3 Hz), 6.91-6.85 (m, 4H), 6.57 (d, 1H, J = 9.0 Hz), 5.95-5.82 (m, 1H), 5.27-5.17 (m, 2H), 3.88 (bt, 2H, J = 5.3 Hz), 3.79 (s, 6H), 3.10 (bs, 1H); ^{13}C NMR ($CDCl_3$, 75 MHz): δ 177.8, 159.4, 150.5, 138.5, 136.9, 135.9, 133.3, 127.4, 119.7, 116.6, 113.9, 113.8, 113.7, 106.0, 96.0, 84.0, 74.0, 55.3, 44.9; IR (neat, cm^{-1}): 3446, 3018, 2399, 1614, 1508, 1215, 1033, 756, 669; HRMS (ESI): calcd for $C_{27}H_{25}NO_4Br$ 506.0967, found 506.0969.

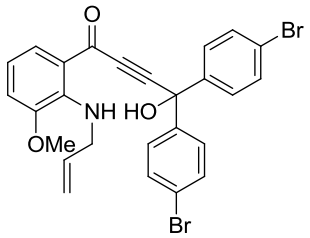
1-(2-(Allylamino)-3-methoxyphenyl)-4-hydroxy-4,4-diphenylbut-2-yn-1-one 199r



Yield: 75%: orange gummy; ^1H NMR (400 MHz, $CDCl_3$) δ 8.83 (bs, 1H), 7.73-7.24 (m, 11H), 6.89 (d, 1H, J = 7.7 Hz), 6.59 (t, 1H, J = 7.9 Hz), 5.97-5.87 (m, 1H), 5.21 (d, 1H, J = 17.1 Hz), 5.09 (d, 1H, J = 10.2 Hz), 4.22 (bd, 2H, J = 5.3 Hz), 3.77 (s,

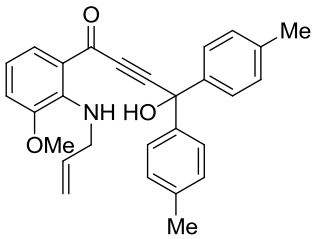
3H), 3.23 (bs, 1H); ^{13}C NMR ($CDCl_3$, 100 MHz): δ 178.7, 149.5, 144.5, 143.6, 136.4, 128.5, 128.1, 127.2, 126.1, 120.8, 117.0, 115.6, 115.2, 94.6, 85.3, 74.7, 56.0, 48.7; HRMS (ESI): calcd for $C_{26}H_{24}NO_3$ 398.1756, found 398.1749.

1-(2-(Allylamino)-3-methoxyphenyl)-4,4-bis(4-bromophenyl)-4-hydroxybut-2-yn-1-one 199s



Yield: 67%: orange gummy; ^{1}H NMR (400 MHz, $CDCl_3$) δ 8.82 (bs, 1H), 7.62 (d, 1H, J = 8.2 Hz), 7.46 (s, 8H), 6.89 (d, 1H, J = 7.7 Hz), 6.58 (t, 1H, J = 7.9 Hz), 5.96-5.87 (m, 1H), 5.21 (d, 1H, J = 17.1 Hz), 5.09 (d, 1H, J = 10.2 Hz), 4.23 (bd, 2H, J = 5.3 Hz), 3.78 (s, 3H), 3.49 (bs, 1H); ^{13}C NMR ($CDCl_3$, 100 MHz): δ 178.2, 149.5, 144.7, 142.4, 136.3, 131.7, 127.7, 126.9, 122.5, 120.4, 117.0, 115.6, 115.3, 93.2, 85.6, 73.8, 56.0, 48.7; HRMS (ESI): calcd for $C_{26}H_{22}NO_3Br_2$ 553.9966, found 553.9980.

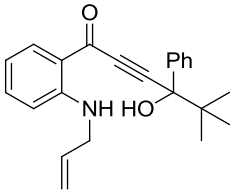
1-(2-(Allylamino)-3-methoxyphenyl)-4-hydroxy-4,4-di-p-tolylbut-2-yn-1-one 199t



Yield: 69%: orange gummy; ^{1}H NMR (400 MHz, $CDCl_3$) δ 8.81 (bs, 1H), 7.73 (d, 1H, J = 8.1 Hz), 7.50 (d, 4H, J = 8.0 Hz), 7.15 (d, 4H, J = 7.9 Hz), 6.88 (d, 1H, J = 7.7 Hz), 6.58 (t, 1H, J = 7.9 Hz), 5.96-5.87 (m, 1H), 5.21 (d, 1H, J = 17.1 Hz), 5.08 (d, 1H, J = 10.2 Hz), 4.21 (bd, 2H, J = 5.4 Hz), 3.77 (s, 3H), 3.16 (bs, 1H), 2.32 (s,

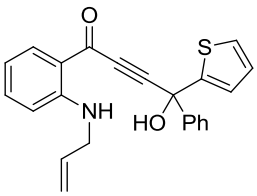
6H); ^{13}C NMR ($CDCl_3$, 100 MHz): δ 178.9, 149.5, 144.5, 141.0, 137.8, 136.4, 129.1, 127.3, 126.0, 120.9, 117.0, 115.6, 115.2, 95.1, 85.1, 74.5, 56.0, 48.7, 21.1; HRMS (ESI): calcd for $C_{28}H_{28}NO_3$ 426.2069, found 426.2081.

1-(2-(Allylamino)phenyl)-4-hydroxy-5,5-dimethyl-4-phenylhex-2-yn-1-one 199u



Yield: 73%: orange solid; m.p. 83-85 ^{o}C; ^{1}H NMR (400 MHz, $CDCl_3$) δ 8.92 (bs, 1H), 8.14 (d, 1H, *J* = 7.9 Hz), 7.65 (d, 2H, *J* = 7.2 Hz), 7.40-7.29 (m, 4H), 6.70-6.64 (m, 2H), 5.98-5.89 (m, 1H), 5.31 (d, 1H, *J* = 17.2 Hz), 5.21 (d, 1H, *J* = 10.2 Hz), 3.92 (bt, 2H, *J* = 5.2 Hz), 2.53 (s, 1H), 1.09 (s, 9H); ^{13}C NMR ($CDCl_3$, 100 MHz): δ 179.0, 151.8, 140.9, 135.9, 135.1, 133.8, 127.8, 127.5, 127.3, 118.4, 116.3, 114.9, 111.8, 95.9, 84.0, 79.3, 44.9, 39.9, 25.5; IR (neat, cm^{-1}): 3442, 3018, 2399, 2210, 1616, 1573, 1517, 1419, 1249, 1215, 1163, 927, 769, 669; HRMS (ESI): calcd for $C_{23}H_{26}NO_2$ 348.1964, found 348.1973.

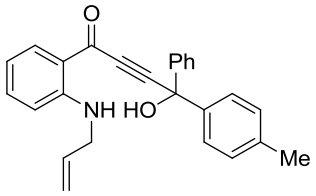
1-(2-(Allylamino)phenyl)-4-hydroxy-4-phenyl-4-(thiophen-2-yl)but-2-yn-1-one 199v



Yield: 77%: yellow solid; m.p. 76-78 ^{o}C; ^{1}H NMR (400 MHz, $CDCl_3$) δ 8.88 (bs, 1H), 8.05 (d, 1H, *J* = 8.0 Hz), 7.73 (d, 2H, *J* = 7.3 Hz), 7.39-7.27 (m, 5H), 7.14 (bd, 1H, *J* = 3.2 Hz), 6.93 (bt, 1H, *J* = 4.3 Hz), 6.67-6.58 (m, 2H), 5.95-5.86 (m, 1H), 5.28 (d,

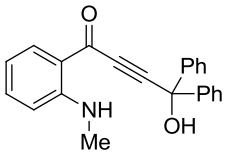
1H, *J* = 17.1 Hz), 5.19 (d, 1H, *J* = 10.3 Hz), 3.89 (bt, 2H, *J* = 5.2 Hz), 3.53 (s, 1H); ^{13}C NMR ($CDCl_3$, 100 MHz): δ 178.5, 151.8, 148.5, 142.9, 136.1, 135.2, 133.7, 128.48, 128.45, 126.6, 126.3, 125.8, 125.7, 118.2, 116.3, 114.9, 111.8, 93.6, 83.8, 72.0, 44.8; IR (neat, cm^{-1}): 3568, 3018, 2399, 2216, 1616, 1573, 1517, 1421, 1319, 1249, 1215, 1163, 927, 767, 669; HRMS (ESI): calcd for $C_{23}H_{20}NO_2S$ 374.1215, found 374.1226.

1-(2-(Allylamino)phenyl)-4-hydroxy-4-phenyl-4-(p-tolyl)but-2-yn-1-one 199w



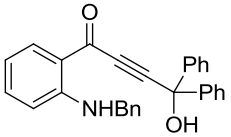
Yield: 74%: yellow gummy; ^{1}H NMR (400 MHz, $CDCl_3$) δ 8.89 (bs, 1H), 8.06 (d, 1H, *J* = 7.9 Hz), 7.63 (d, 2H, *J* = 7.4 Hz), 7.51 (d, 2H, *J* = 7.9 Hz), 7.36-7.23 (m, 4H), 7.15 (d, 2H, *J* = 7.8 Hz), 6.66 (d, 1H, *J* = 8.5 Hz), 6.58 (t, 1H, *J* = 7.5 Hz), 5.95-5.86 (m, 1H), 5.28 (d, 1H, *J* = 17.2 Hz), 5.19 (d, 1H, *J* = 10.3 Hz), 3.89 (bs, 2H), 3.32 (bs, 1H), 2.32 (s, 3H); ^{13}C NMR ($CDCl_3$, 100 MHz): δ 178.8, 151.8, 143.8, 140.9, 137.9, 136.0, 135.3, 133.8, 129.1, 128.4, 128.0, 126.1, 126.0, 118.3, 116.3, 114.9, 111.8, 95.0, 84.7, 74.6, 44.9, 21.1; IR (neat, cm^{-1}): 3442, 3018, 2399, 1612, 1506, 1485, 1321, 1215, 999, 769, 669; HRMS (ESI): calcd for $C_{26}H_{24}NO_2$ 382.1807, found 382.1788.

4-Hydroxy-1-(2-(methylamino)phenyl)-4,4-diphenylbut-2-yn-1-one 199x



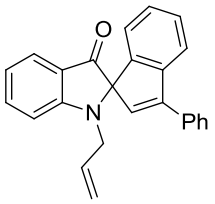
Yield: 73%: yellow gummy; ^{1}H NMR (400 MHz, $CDCl_3$) δ 8.67 (bs, 1H), 8.04 (d, 1H, J = 8.0 Hz), 7.64 (d, 4H, J = 7.3 Hz), 7.40-7.26 (m, 7H), 6.67 (d, 1H, J = 8.6 Hz), 6.58 (t, 1H, J = 7.5 Hz), 3.36 (bs, 1H), 2.92 (d, 3H, J = 5.0 Hz); ^{13}C NMR ($CDCl_3$, 100 MHz): δ 178.6, 152.8, 143.7, 136.2, 135.2, 128.5, 128.1, 126.1, 118.2, 114.6, 111.0, 94.6, 84.8, 74.7, 29.3; HRMS (ESI): calcd for $C_{23}H_{20}NO_2$ 342.1494, found 342.1499.

1-(2-(Benzylamino)phenyl)-4-hydroxy-4,4-diphenylbut-2-yn-1-one 199y



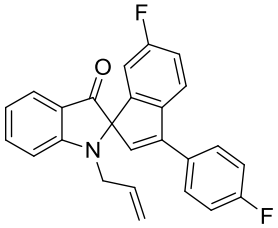
Yield: 76%: yellow solid; m.p. 120-122 ^{o}C; ^{1}H NMR (500 MHz, $CDCl_3$) δ 9.18 (bs, 1H), 8.08 (d, 1H, J = 7.8 Hz), 7.64 (bd, 4H, J = 7.4 Hz), 7.36-7.23 (m, 12H), 6.63-6.57 (m, 2H), 4.47 (bd, 2H, J = 5.5 Hz), 3.29 (bs, 1H); ^{13}C NMR ($CDCl_3$, 125 MHz): δ 178.9, 151.8, 143.7, 138.1, 136.2, 135.3, 128.7, 128.5, 128.2, 127.3, 126.9, 126.1, 118.5, 115.2, 112.0, 94.8, 84.8, 74.7, 46.7; IR (neat, cm^{-1}): 3421, 3018, 2399, 1662, 1616, 1517, 1423, 1215, 927, 756, 669; HRMS (ESI): calcd for $C_{29}H_{24}NO_2$ 418.1807, found 418.1819.

1'-Allyl-3-phenylspiro[indene-1,2'-indolin]-3'-one 200b



Yellow gummy; ^{1}H NMR ($CDCl_3$, 400 MHz): δ 7.59-7.24 (m, 9H), 7.10 (t, 1H, J = 7.2 Hz), 7.01 (d, 1H, J = 7.2 Hz), 6.84 (d, 1H, J = 8.2 Hz), 6.69 (t, 1H, J = 7.2 Hz), 5.99 (s, 1H), 5.69-5.61 (m, 1H), 5.10 (d, 1H, J = 17.2 Hz), 5.03 (d, 1H, J = 10.1 Hz), 3.70 (dd, 1H, J = 16.5, 4.1 Hz), 3.49 (dd, 1H, J = 16.6, 5.0 Hz); ^{13}C NMR ($CDCl_3$, 100 MHz): δ 197.1, 161.1, 150.0, 144.2, 142.3, 137.6, 134.5, 134.2, 129.3, 128.7, 128.6, 128.5, 127.7, 126.6, 125.6, 122.4, 121.7, 121.5, 117.1, 116.8, 109.8, 83.3, 46.6; IR (neat, cm^{-1}): 3446, 3018, 2399, 1701, 1612, 1485, 1321, 1259, 1215, 1029, 1001, 927, 756, 667, 683; HRMS (ESI): calcd for $C_{25}H_{20}NO$ 350.1545, found 350.1559.

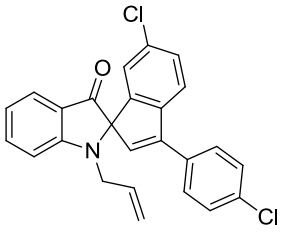
1'-Allyl-6-fluoro-3-(4-fluorophenyl)spiro[indene-1,2'-indolin]-3'-one 200c



Yellow gummy; ^{1}H NMR ($CDCl_3$, 400 MHz): δ 7.67-7.49 (m, 5H), 7.35 (td, 1H, J = 1.0, 7.5 Hz), 7.21-7.08 (m, 3H), 6.93 (d, 1H, J = 8.3 Hz), 6.81-6.77 (m, 1H), 6.05 (s, 1H), 5.80-5.71 (m, 1H), 5.19-5.10 (m, 2H) 3.81-3.75 (dtdt, 1H, J = 1.6, 5.2, 1.6, 5.2 Hz), 3.59-3.52 (dtdt, 1H, J = 1.4, 5.7, 1.4, 5.6 Hz); ^{13}C NMR ($CDCl_3$, 100 MHz): δ 196.9, 164.1, 161.6, 161.1, 148.9, 144.0, 142.3, 137.7, 134.2, 130.6 (1C, $J_{C\text{-}F}$ = 12.8 Hz), 129.4 (1C, $J_{C\text{-}F}$ = 32.5 Hz), 128.8, 126.7, 125.6, 122.4, 121.6, 121.3, 117.2, 116.8, 115.7, 115.5, 109.8, 83.3, 46.6; IR (neat, cm^{-1}): 3435, 3018, 1645, 1215, 1039,

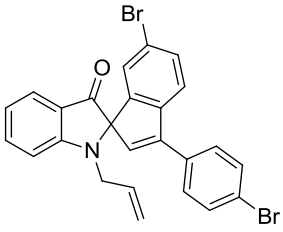
779, 669, 524, 503: HRMS (ESI): calcd for $C_{25}H_{18}NOF_2$ 386.1356, found 386.1340.

1'-Allyl-6-chloro-3-(4-chlorophenyl)spiro[indene-1,2'-indolin]-3'-one 200d



Yellow solid; m.p. 146-148 ^{o}C; ^{1}H NMR ($CDCl_3$, 300 MHz): δ 7.67 (d, 1H, J = 7.6 Hz), 7.55-7.30 (m, 7H), 7.07 (bd, 1H, J = 1.6 Hz), 6.94 (d, 1H, J = 8.3 Hz), 6.81 (t, 1H, J = 7.4 Hz), 6.09 (s, 1H), 5.82-5.70 (m, 1H), 5.19-5.11 (m, 2H), 3.84 (dd, 1H, J = 5.2, 16.6 Hz), 3.58 (dd, 1H, J = 16.6, 5.6 Hz); ^{13}C NMR ($CDCl_3$, 75 MHz): δ 195.8, 161.0, 148.0, 144.2, 142.3, 137.9, 134.6, 133.9, 132.9, 132.5, 130.1, 129.0, 128.9, 128.8, 125.7, 123.0, 122.0, 121.4, 117.6, 117.1, 109.9, 82.9, 46.7; IR (neat, cm^{-1}): 3442, 3018, 2399, 1701, 1612, 1485, 1323, 1215, 1091, 929, 771, 669; HRMS (ESI): calcd for $C_{25}H_{18}NOCl_2$ 418.0765, found 418.0776.

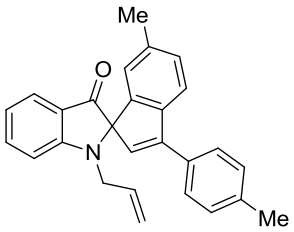
1'-Allyl-6-bromo-3-(4-bromophenyl)spiro[indene-1,2'-indolin]-3'-one 200e



Yellow gummy; ^{1}H NMR ($CDCl_3$, 400 MHz): δ 7.66-7.44 (m, 7H), 7.34 (d, 1H, J = 8.1 Hz), 7.21 (bd, 1H, J = 1.6 Hz), 6.93 (d, 1H, J = 8.3 Hz), 6.81 (t, 1H, J = 7.4 Hz), 6.08 (s, 1H), 5.80-5.70 (m, 1H) 5.18-5.10 (m, 2H), 3.83 (dd, 1H, J = 16.6, 5.3 Hz), 3.56 (dd, 1H, J = 16.6, 5.7 Hz); ^{13}C NMR ($CDCl_3$, 100 MHz): δ 195.7, 161.0, 148.1, 144.4, 142.7, 138.0, 133.9, 132.8, 131.9, 131.8, 130.2, 129.1, 125.8, 122.8, 122.4,

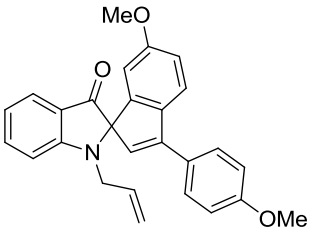
121.4, 120.9, 117.6, 117.2, 109.9, 83.0, 46.7; IR (neat, cm^{-1}): 3446, 3018, 2399, 1699, 1612, 1483, 1323, 1215, 927, 758, 669; HRMS (ESI): calcd for $C_{25}H_{18}NOBr_2$ 505.9755, found 505.9759.

1'-Allyl-6-methyl-3-(*p*-tolyl)spiro[indene-1,2'-indolin]-3'-one 200f



Yellow gummy; ^{1}H NMR ($CDCl_3$, 400 MHz): δ 7.68 (d, 1H, J = 7.4 Hz), 7.55-7.49 (m, 3H), 7.45 (d, 1H, J = 7.7 Hz), 7.28-6.89 (m, 5H), 6.78 (t, 1H, J = 7.3 Hz), 5.98 (s, 1H), 5.81-5.71 (m, 1H) 5.20 (dd, 1H, J = 17.1, 1.4 Hz), 5.13 (dd, 1H, J = 10.2, 1.4 Hz), 3.81-3.52 (m, 2H), 2.42 (s, 3H), 2.31 (s, 3H); ^{13}C NMR ($CDCl_3$, 100 MHz): δ 197.5, 161.0, 149.8, 142.6, 141.7, 138.3, 137.5, 136.5, 134.4, 131.8, 129.35, 129.30, 127.6, 127.5, 125.5, 123.2, 121.6, 121.2, 117.0, 116.8, 109.8, 83.1, 46.5, 21.37, 21.36; IR (neat, cm^{-1}): 3018, 2399, 1701, 1614, 1487, 1321, 1215, 1001, 927, 771, 669; HRMS (ESI): calcd for $C_{27}H_{24}NO$ 378.1858, found 378.1856.

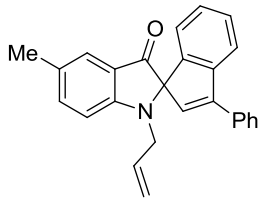
1'-Allyl-6-methoxy-3-(4-methoxyphenyl)spiro[indene-1,2'-indolin]-3'-one 200g



Yellow gummy; ^{1}H NMR ($CDCl_3$, 400 MHz): δ 7.67 (d, 1H, J = 7.6 Hz), 7.59 (d, 2H, J = 8.6 Hz), 7.50 (t, 1H, J = 7.6 Hz), 7.45 (d, 1H, J = 8.4 Hz), 6.99-6.84 (m, 4H), 6.78 (t, 1H, J = 7.4 Hz), 6.65 (bd, 1H, J = 2.2 Hz), 5.88 (s, 1H), 5.80-5.71 (m, 1H), 5.20 (d,

1H, *J* = 17.0 Hz), 5.12 (d, 1H, *J* = 10.2 Hz), 3.86 (s, 3H), 3.80-3.54 (m, 2H), 3.76 (s, 3H); ^{13}C NMR ($CDCl_3$, 100 MHz): δ 197.5, 161.0, 159.8, 159.0, 149.1, 144.3, 137.6, 137.1, 134.3, 128.8, 127.3, 125.7, 125.5, 122.0, 121.5, 117.1, 116.8, 114.0, 113.6, 109.8, 109.2, 83.0, 55.6, 55.3, 46.5; IR (neat, cm^{-1}): 3446, 3018, 2837, 2399, 1699, 1612, 1508, 1485, 1321, 1247, 1031, 927, 771, 667; HRMS (ESI): calcd for $C_{27}H_{24}NO_3$ 410.1756, found 410.1756.

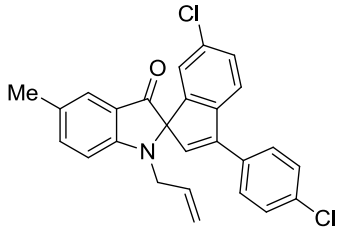
1'-Allyl-5'-methyl-3-phenylspiro[indene-1,2'-indolin]-3'-one 200h



Yellow gummy; ^{1}H NMR ($CDCl_3$, 400 MHz): δ 7.63 (d, 2H, *J* = 7.2 Hz), 7.53 (d, 1H, *J* = 7.6 Hz), 7.45-7.29 (m, 6H), 7.20 (t, 1H, *J* = 7.4 Hz), 7.06 (d, 1H, *J* = 7.4 Hz), 6.84 (d, 1H, *J* = 8.4 Hz), 6.07 (s, 1H), 5.77-5.68 (m, 1H), 5.16 (d, 1H, *J* = 17.1 Hz), 5.08 (d, 1H, *J* = 10.2 Hz), 3.75 (dd, 1H, *J* = 16.6, 5.2 Hz), 3.53 (dd, 1H, *J* = 16.6, 5.6 Hz); ^{13}C NMR ($CDCl_3$, 100 MHz): δ 196.9, 159.7, 149.8, 144.2, 142.6, 139.0, 134.6, 134.5, 129.6, 128.7, 128.6, 128.5, 127.7, 126.63, 126.61, 125.0, 122.4, 121.8, 121.4, 116.7, 109.8, 83.7, 46.8, 20.4; IR (neat, cm^{-1}): 3446, 3018, 2399, 1701, 1622, 1492, 1215, 927, 756; HRMS (ESI): calcd for $C_{26}H_{22}NO$ 364.1701, found 364.1693.

1'-Allyl-6-chloro-3-(4-chlorohenyl)-5'-methylspiro[indene-1,2'-indolin]-3'-one

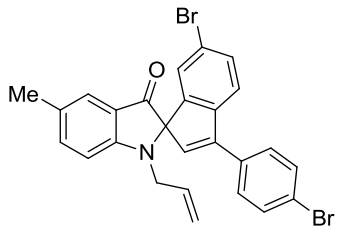
200i



Yellow gummy; ^{1}H NMR ($CDCl_3$, 400 MHz): δ 7.52 (d, 2H, J = 8.4 Hz), 7.45-7.28 (m, 6H), 7.05 (bd, 1H, J = 1.5 Hz), 6.86 (d, 1H, J = 8.4 Hz), 6.08 (s, 1H), 5.79-5.69 (m, 1H), 5.16-5.08 (m, 2H), 3.79 (dd, 1H, J = 16.6, 5.3 Hz), 3.54 (dd, 1H, J = 16.6, 5.6 Hz); ^{13}C NMR ($CDCl_3$, 100 MHz): δ 195.7, 159.6, 147.8, 144.4, 142.3, 139.3, 134.5, 134.2, 132.8, 132.5, 130.4, 128.9, 128.89, 128.85, 127.1, 125.2, 122.9, 122.0, 121.5, 117.0, 109.9, 83.3, 46.9, 20.3; IR (neat, cm^{-1}): 3446, 3018, 2399, 1697, 1624, 1498, 1215, 1091, 927, 767, 669; HRMS (ESI): calcd for $C_{26}H_{20}NOCl_2$ 432.0922, found 432.0932.

1'-Allyl-6-bromo-3-(4-bromophenyl)-5'-methylspiro[indene-1,2'-indolin]-3'-one

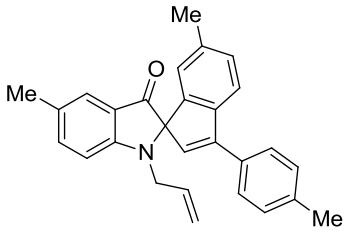
200j



Yellow gummy; ^{1}H NMR ($CDCl_3$, 400 MHz): δ 7.58 (d, 2H, J = 8.3 Hz), 7.47-7.31 (m, 6H), 7.19 (s, 1H), 6.86 (d, 1H, J = 8.4 Hz), 6.07 (s, 1H), 5.79-5.70 (m, 1H), 5.16 (s, 1H), 5.11 (d, 1H, J = 11.2 Hz), 3.80 (dd, 1H, J = 5.2, 16.6 Hz), 3.53 (dd, 1H, J = 16.6, 5.6 Hz); ^{13}C NMR ($CDCl_3$, 100 MHz): δ 195.6, 159.6, 147.9, 144.6, 142.6, 139.4, 134.1, 132.9, 131.9, 131.7, 130.5, 129.1, 127.1, 125.7, 125.2, 122.7, 122.4,

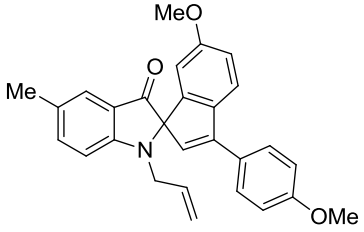
121.5, 120.8, 117.0, 109.9, 83.3, 46.9, 20.3; IR (neat, cm^{-1}): 3441, 3018, 2399, 1624 1498, 1215, 927, 769, 669; HRMS (ESI): calcd for $C_{26}H_{20}NOBr_2$ 519.9912, found 519.9905.

1'-Allyl-5',6-dimethyl-3-(*p*-tolyl)spiro[indene-1,2'-indolin]-3'-one 200k



Yellow gummy; ^1H NMR ($CDCl_3$, 400 MHz): δ 7.53 (d, 2H, J = 7.9 Hz), 7.46 (s, 1H), 7.42 (d, 1H, J = 7.7 Hz), 7.33-7.22 (m, 3H), 7.12 (d, 1H, J = 7.7 Hz), 6.86 (s, 1H), 6.83 (d, 1H, J = 8.4 Hz), 5.96 (s, 1H), 5.78-5.68 (m, 1H), 5.16 (d, 1H, J = 17.1 Hz), 5.08 (d, 1H, J = 10.2 Hz), 3.75 (dd, 1H, J = 16.7, 5.3 Hz), 3.51 (dd, 1H, J = 16.6, 5.5 Hz), 2.38 (s, 3H), 2.29 (s, 3H), 2.27 (s, 3H); ^{13}C NMR ($CDCl_3$, 100 MHz): δ 197.5, 159.7, 149.6, 142.9, 141.7, 138.9, 138.3, 136.5, 134.6, 131.9, 129.3, 127.9, 127.5, 126.4, 125.0, 123.2, 121.8, 121.2, 116.6, 109.7, 83.5, 46.7, 21.4, 21.3, 20.3; IR (neat, cm^{-1}): 3442, 3018, 2399, 1691, 1624, 1500, 1419, 1215, 927, 771, 669; HRMS (ESI): calcd for $C_{28}H_{26}NO$ 392.2014, found 392.2015.

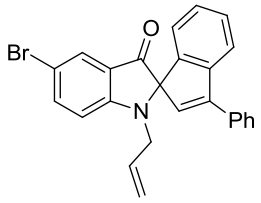
1'-Allyl-6-methoxy-3-(4-methoxyphenyl)-5'-methylspiro[indene-1,2'-indolin]-3'-one 200l



Yellow gummy; ^1H NMR ($CDCl_3$, 400 MHz): δ 7.58 (d, 2H, J = 8.5 Hz), 7.46-7.33

(m, 3H), 6.98 (d, 2H, *J* = 8.6 Hz), 6.86-6.82 (m, 2H), 6.63 (bd, 1H, *J* = 2.2 Hz), 5.88 (s, 1H), 5.80-5.70 (m, 1H) 5.19 (d, 1H, *J* = 17.1 Hz), 5.10 (d, 1H, *J* = 10.2 Hz), 3.85 (s, 3H), 3.76-3.51 (m, 5H); ^{13}C NMR ($CDCl_3$, 100 MHz): δ 197.4, 159.7, 159.6, 159.0, 148.9, 144.5, 138.9, 137.1, 134.5, 128.8, 127.3, 126.5, 126.0, 125.0, 121.9, 121.6, 116.6, 113.9, 113.5, 109.7, 109.2, 83.4, 55.5, 55.3, 46.7, 20.3; IR (neat, cm^{-1}): 3446, 3018, 2399, 1689, 1624, 1500, 1429, 1215, 927, 769, 669; HRMS (ESI): calcd for $C_{28}H_{26}NO_3$ 424.1913, found 424.1924.

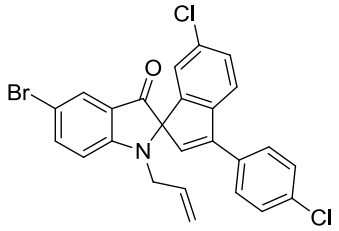
1'-Allyl-5'-bromo-3-phenylspiro[indene-1,2'-indolin]-3'-one 200m



Yellow gummy; ^{1}H NMR ($CDCl_3$, 400 MHz): δ 7.75 (bd, 1H, *J* = 2.0 Hz), 7.63-7.32 (m, 8H), 7.18 (t, 1H, *J* = 7.3 Hz), 7.06 (d, 1H, *J* = 7.3 Hz), 6.81 (d, 1H, *J* = 8.7 Hz), 6.04 (s, 1H), 5.76-5.66 (m, 1H), 5.17-5.09 (m, 2H) 3.76-3.50 (m, 2H); ^{13}C NMR ($CDCl_3$, 100 MHz): δ 195.7, 159.6, 150.4, 144.1, 141.9, 140.0, 134.3, 133.7, 129.0, 128.7, 128.6, 127.9, 127.6, 126.8, 123.2, 122.4, 121.6, 117.2, 111.5, 109.5, 83.6, 46.5; IR (neat, cm^{-1}): 3682, 3018, 2399, 1703, 1606, 1477, 1427, 1305, 1259, 1217, 1168, 1107, 1001, 929, 771, 667; HRMS (ESI): calcd for $C_{25}H_{19}NOBr$ 428.0650, found 428.0654.

1'-Allyl-5'-bromo-6-chloro-3-(4-chlorophenyl)spiro[indene-1,2'-indolin]-3'-one

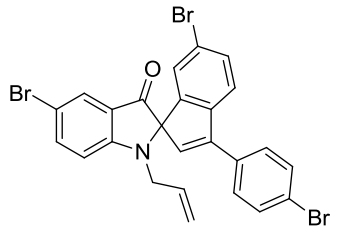
200n



Yellow gummy; ^{1}H NMR ($CDCl_3$, 400 MHz): δ 7.76 (bd, 1H, J = 1.9 Hz), 7.59 (dd, 1H, J = 8.7, 1.9 Hz), 7.53-7.32 (m, 6H), 7.05 (bd, 1H, J = 1.6 Hz), 6.84 (d, 1H, J = 8.7 Hz), 6.05 (s, 1H), 5.78-5.68 (m, 1H), 5.18-5.13 (m, 2H), 3.80 (dd, 1H, J = 16.7, 5.3 Hz), 3.55 (dd, 1H, J = 17.7, 4.7 Hz); ^{13}C NMR ($CDCl_3$, 100 MHz): δ 194.5, 159.6, 148.7, 143.6, 142.1, 140.4, 134.8, 133.4, 133.1, 132.2, 129.4, 129.1, 129.0, 128.8, 128.0, 122.97, 122.92, 122.2, 117.5, 111.5, 109.9, 83.2, 46.7; IR (neat, cm^{-1}): 3442, 3018, 2399, 1606, 1521, 1419, 1215, 929, 769, 669; HRMS (ESI): calcd for $C_{25}H_{17}NOCl_2Br$ 495.9871, found 495.9861.

1'-Allyl-5'-bromo-6-bromo-3-(4-bromophenyl)spiro[indene-1,2'-indolin]-3'-one

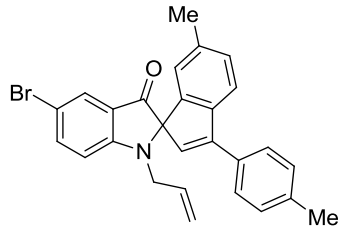
200o



Yellow gummy; ^{1}H NMR ($CDCl_3$, 400 MHz): δ 7.76 (bd, 1H, J = 2.0 Hz), 7.60-7.43 (m, 6H), 7.35 (d, 1H, J = 8.1 Hz), 7.20 (bd, 1H, J = 1.6 Hz), 6.84 (d, 1H, J = 8.7 Hz), 6.05 (s, 1H), 5.77-5.68 (m, 1H), 5.18-5.13 (m, 2H), 3.80 (dd, 1H, J = 16.7, 5.3 Hz), 3.54 (dd, 1H, J = 16.6, 5.6 Hz); ^{13}C NMR ($CDCl_3$, 100 MHz): δ 194.4, 159.6, 148.5, 143.9, 142.5, 140.4, 133.4, 132.6, 132.08, 132.02, 129.4, 129.1, 128.0, 125.7, 122.99,

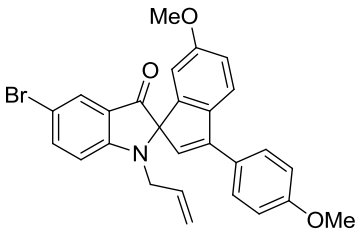
122.91, 122.6, 121.1, 117.5, 111.5, 110.0, 83.2, 46.7; IR (neat, cm^{-1}): 3496, 3018, 2399, 1707, 1606, 1477, 1427, 1215, 929, 771, 669; HRMS (ESI): calcd for $C_{25}H_{17}NOBr_3$ 583.8860, found 583.8885.

1'-Allyl-5'-bromo-6-methyl-3-(*p*-tolyl)spiro[indene-1,2'-indolin]-3'-one 200p



Yield 88 %; yellow gummy; ^{1}H NMR ($CDCl_3$, 400 MHz): δ 7.75 (bd, 1H, J = 2.0 Hz), 7.55-7.50 (m, 3H), 7.42 (d, 1H, J = 7.7 Hz), 7.26-7.23 (m, 2H), 7.14 (d, 1H, J = 7.7 Hz), 6.85 (s, 1H), 6.80 (d, 1H, J = 8.7 Hz), 5.93 (s, 1H), 5.75-5.66 (m, 1H), 5.17-5.10 (m, 2H), 3.74 (dd, 1H, J = 16.7, 5.3 Hz), 3.52 (dd, 1H, J = 16.7, 5.6 Hz); ^{13}C NMR ($CDCl_3$, 100 MHz): δ 196.2, 159.6, 150.2, 142.1, 141.6, 139.9, 138.5, 136.7, 133.9, 131.6, 129.5, 129.3, 127.8, 127.5, 126.8, 123.2, 123.1, 121.3, 117.1, 111.4, 109.3, 83.4, 46.5, 21.39, 21.37; IR (neat, cm^{-1}): 3446, 3018, 2399, 1705, 1608, 1477, 1429, 1215, 1002, 927, 771, 669; HRMS (ESI): calcd for $C_{27}H_{23}NOBr$ 456.0963, found 456.0969.

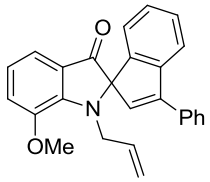
1'-Allyl-5'-bromo-6-methoxy-3-(4-methoxyphenyl)spiro[indene-1,2'-indolin]-3'-one 200q



Yellow gummy; ^{1}H NMR ($CDCl_3$, 400 MHz): δ 7.76 (bd, 1H, J = 1.9 Hz), 7.58-7.54

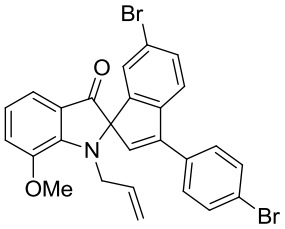
(m, 3H), 7.46 (d, 1H, J = 8.4 Hz), 6.99-6.79 (m, 4H), 6.63 (bd, 1H, J = 2.3 Hz), 5.86 (s, 1H), 5.78-5.68 (m, 1H), 5.20-5.11 (m, 2H), 3.85 (s, 3H), 3.79-3.52 (m, 5H); ^{13}C NMR ($CDCl_3$, 100 MHz): δ 196.2, 159.9, 159.6, 159.1, 149.6, 143.8, 140.0, 136.9, 133.8, 128.8, 127.8, 127.0, 125.0, 123.0, 122.1, 117.1, 114.0, 113.7, 111.4, 109.4, 109.2, 83.3, 55.6, 55.3, 46.5; IR (neat, cm^{-1}): 3622, 3018, 2399, 1701, 1608, 1508, 1477, 1247, 1215, 927, 769, 669; HRMS (ESI): calcd for $C_{27}H_{23}NO_3Br$ 488.0861, found 488.0857.

1'-Allyl-7'-methoxy-3-phenylspiro[indene-1,2'-indolin]-3'-one 200r



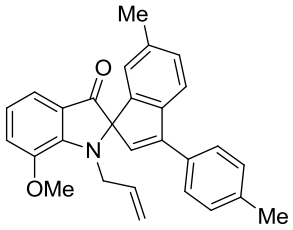
Yellow gummy; ^{1}H NMR ($CDCl_3$, 300 MHz): δ 7.63-6.98 (m, 11H), 6.69 (t, 1H, J = 7.7 Hz), 6.08 (s, 1H), 5.94-5.81 (m, 1H), 4.94-4.88 (m, 2H), 4.38-4.31 (m, 1H), 3.88 (s, 3H), 3.67-3.59 (m, 1H); ^{13}C NMR ($CDCl_3$, 75 MHz): δ 197.3, 162.3, 151.8, 149.3, 147.3, 144.3, 142.6, 136.9, 134.7, 129.8, 128.6, 128.3, 127.6, 126.4, 123.3, 122.6, 121.3, 118.0, 117.5, 117.4, 115.6, 55.7, 48.5; IR (neat, cm^{-1}): 3442, 3018, 2399, 1697, 1606, 1502, 1246, 1215, 1002, 927, 769, 669, 624; HRMS (ESI): calcd for $C_{26}H_{22}NO_2$ 380.1651, found 380.1654.

1'-Allyl-6-bromo-3-(4-bromophenyl)-7'-methoxyspiro[indene-1,2'-indolin]-3'-one 200s



Yellow gummy; ^{1}H NMR ($CDCl_3$, 400 MHz): δ 7.59 (d, 2H, J = 8.2 Hz), 7.47-7.25 (m, 6H), 7.02 (d, 1H, J = 7.6 Hz), 6.73 (t, 1H, J = 7.7 Hz), 6.09 (s, 1H), 5.92-5.83 (m, 1H), 4.96 (d, 1H, J = 10.2 Hz), 4.92 (d, 1H, J = 17.0 Hz), 4.41 (dd, 1H, J = 16.0, 5.2 Hz), 3.89 (s, 3H), 3.63 (dd, 1H, J = 16.0, 6.4 Hz); ^{13}C NMR ($CDCl_3$, 100 MHz): δ 196.0, 151.7, 147.4, 144.7, 142.7, 136.7, 133.0, 131.9, 131.6, 130.8, 129.1, 126.0, 123.0, 122.6, 122.3, 120.7, 118.3, 118.0, 117.6, 115.9, 83.5, 55.8, 48.8; IR (neat, cm^{-1}): 3446, 3018, 2399, 1697, 1606, 1506, 1213, 925, 758, 669; HRMS (ESI): calcd for $C_{26}H_{20}NO_2Br_2$ 535.9861, found 535.9862.

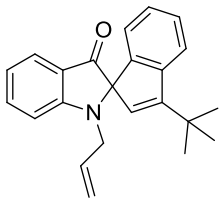
1'-Allyl-7'-methoxy-6-methyl-3-(*p*-tolyl)spiro[indene-1,2'-indolin]-3'-one 200t



Yellow gummy; ^{1}H NMR ($CDCl_3$, 400 MHz): δ 7.52 (d, 2H, J = 7.8 Hz), 7.41 (d, 1H, J = 7.7 Hz), 7.28-7.23 (m, 3H), 7.13 (d, 1H, J = 7.7 Hz), 6.99 (d, 1H, J = 7.6 Hz), 6.91 (s, 1H), 6.68 (t, 1H, J = 7.7 Hz), 5.92 (s, 1H), 5.91-5.83 (m, 1H), 4.94 (s, 1H), 4.91 (d, 1H, J = 9.0 Hz), 4.36 (dd, 1H, J = 16.0, 5.2 Hz), 3.87 (s, 3H), 3.60 (dd, 1H, J = 16.0, 6.4 Hz), 2.40 (s, 3H), 2.29 (s, 3H); ^{13}C NMR ($CDCl_3$, 100 MHz): δ 197.8, 151.8, 149.1, 147.3, 142.9, 141.7, 138.1, 137.1, 136.4, 132.0, 129.27, 129.21, 128.1,

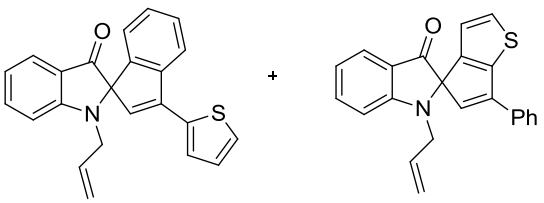
127.5, 123.4, 123.2, 121.0, 117.9, 117.5, 117.3, 115.6, 83.7, 55.7, 48.4, 21.3; IR (neat, cm^{-1}): 3446, 3018, 2399, 1695, 1606, 1508, 1215, 771, 669; HRMS (ESI): calcd for $C_{28}H_{26}NO_2$ 408.1964, found 408.1958.

1'-Allyl-3-(tert-butyl)spiro[indene-1,2'-indolin]-3'-one 200u



Yellow gummy; ^1H NMR ($CDCl_3$, 400 MHz): δ 7.62 (d, 1H, J = 7.6 Hz), 7.60 (d, 1H, J = 7.6 Hz), 7.48 (t, 1H, J = 7.6 Hz), 7.28 (t, 1H, J = 7.5 Hz), 7.08 (t, 1H, J = 7.4 Hz), 7.00 (d, 1H, J = 7.4 Hz), 6.88 (d, 1H, J = 8.3 Hz), 6.73 (t, 1H, J = 7.4 Hz), 5.75-5.66 (m, 1H), 5.65 (s, 1H), 5.14 (d, 1H, J = 17.1 Hz), 5.08 (d, 1H, J = 10.2 Hz), 3.68 (dd, 1H, J = 16.6, 5.2 Hz), 3.47 (dd, 1H, J = 16.6, 5.8 Hz); ^{13}C NMR ($CDCl_3$, 100 MHz): δ 197.7, 160.9, 159.3, 144.4, 143.0, 137.4, 134.4, 128.3, 125.8, 125.4, 125.3, 122.9, 122.2, 121.7, 116.9, 116.8, 109.7, 82.5, 46.3, 33.6, 29.2; IR (neat, cm^{-1}): 3446, 3018, 2968, 2399, 1701, 1612, 1485, 1321, 1215, 1002, 925, 756; HRMS (ESI): calcd for $C_{23}H_{24}NO$ 330.1858, found 330.1873.

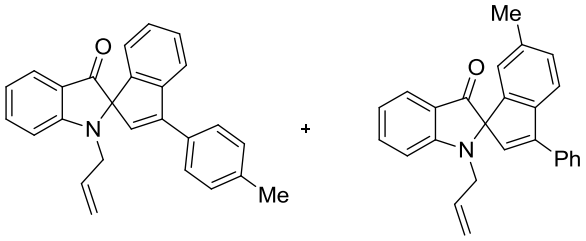
1'-Allyl-3-(thiophen-2-yl)spiro[indene-1,2'-indolin]-3'-one 200v



Brown gummy; mixture of regioisomeric ratio = 1:1; ^1H NMR ($CDCl_3$, 400 MHz): δ 7.76-7.30 (m, 8H), 6.92 (d, 1H, J = 8.3 Hz), 6.80-6.77 (m, 2H), 6.27 (s, 1H, A or B regioisomer), 6.27 (s, 1H, A or B regioisomer), 5.81-5.71 (m, 1H), 5.20 (dd, 1H, J =

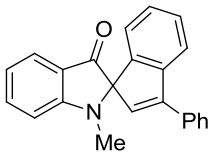
17.1, 1.3 Hz), 5.13 (dd, 1H, *J* = 10.2, 1.2 Hz), 3.77 (dd, 1H, *J* = 16.6, 5.2 Hz), 3.66 (dd, 1H, *J* = 16.6, 5.6 Hz); ^{13}C NMR ($CDCl_3$, 100 MHz): δ 195.6, 160.5, 146.4, 145.1, 144.9, 137.6, 134.0, 132.8, 128.8, 128.7, 127.8, 127.5, 126.3, 125.5, 121.7, 120.6, 117.0, 116.8, 110.0, 80.7, 46.6; IR (neat, cm^{-1}): 3495, 3016, 2399, 1699, 1612, 1483, 1321, 1215, 997, 927, 769, 669; HRMS (ESI): calcd for $C_{23}H_{18}NOS$ 356.1109, found 356.1120.

1'-Allyl-3-(*p*-tolyl)spiro[indene-1,2'-indolin]-3'-one 200w



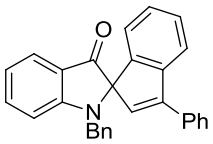
Yellow gummy; Mixture of regioisomeric ratio = 1:0.55; ^{1}H NMR ($CDCl_3$, 400 MHz): δ 7.68-7.32 (m, 7H), 7.28-6.90 (m, 4H), 6.78 (t, 1H, *J* = 7.4 Hz), 6.04 (s, 1H, A or B regioisomer), 6.02 (s, 1H, A or B regioisomer), 5.81-5.70 (m, 1H), 5.20-5.09 (m, 2H), 3.82-3.74 (m, 1H), 3.57 (dd, 1H, *J* = 16.8, 4.9 Hz); ^{13}C NMR ($CDCl_3$, 100 MHz): δ 197.4, 161.0, 149.9, 144.4, 142.6, 142.4, 141.5, 138.4, 137.6, 136.6, 134.7, 134.37, 134.31, 131.6, 129.39, 129.34, 128.7, 128.69, 128.62, 128.4, 128.2, 127.6, 127.5, 126.5, 125.6, 123.2, 122.4, 121.7, 121.6, 121.5, 121.2, 117.1, 117.0, 116.8, 109.85, 109.81, 83.3, 83.1, 46.5, 21.3; IR (neat, cm^{-1}): 3481, 3018, 2399, 1701, 1612, 1487, 1321, 1215, 1001, 927, 771, 669; HRMS (ESI): calcd for $C_{26}H_{22}NO$ 364.1701, found 364.1705.

1'-Methyl-3-phenylspiro[indene-1,2'-indolin]-3'-one 200x



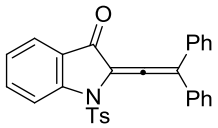
Yellow gummy; ^{1}H NMR ($CDCl_3$, 400 MHz): δ 7.67-7.38 (m, 8H), 7.34 (t, 1H, J = 7.5 Hz), 7.18 (t, 1H, J = 7.4 Hz), 7.04 (d, 1H, J = 7.4 Hz), 6.92 (d, 1H, J = 8.2 Hz), 6.77 (t, 1H, J = 7.4 Hz), 6.08 (s, 1H), 2.74 (s, 3H); ^{13}C NMR ($CDCl_3$, 100 MHz): δ 197.2, 161.7, 150.4, 144.1, 142.0, 137.8, 134.5, 129.1, 128.7, 128.6, 128.5, 127.7, 126.6, 125.6, 122.1, 121.69, 121.61, 117.0, 109.1, 83.4, 29.0; IR (neat, cm^{-1}): 3442, 3018, 2399, 1695, 1614, 1489, 1321, 1215, 993, 767, 669; HRMS (ESI): calcd for $C_{23}H_{18}NO$ 324.1388, found 324.1404.

1'-Benzyl-3-phenylspiro[indene-1,2'-indolin]-3'-one 200y



Yellow gummy; ^{1}H NMR ($CDCl_3$, 400 MHz): δ 7.69 (dd, 1H, J = 7.8, 0.8 Hz), 7.53-7.09 (m, 15H), 6.81-6.77 (m, 2H), 6.02 (s, 1H), 4.40 (d, 1H, J = 16.1 Hz), 4.09 (d, 1H, J = 16.1 Hz); ^{13}C NMR ($CDCl_3$, 100 MHz): δ 197.1, 161.4, 149.9, 144.2, 142.2, 138.0, 137.7, 134.4, 129.4, 128.7, 128.6, 128.5, 128.4, 127.7, 127.3, 127.0, 126.6, 125.6, 122.3, 122.0, 121.5, 117.5, 110.1, 83.6, 48.2; IR (neat, cm^{-1}): 3481, 3018, 2399, 1699, 1612, 1483, 1321, 1215, 1002, 771, 669; HRMS (ESI): calcd for $C_{29}H_{22}NO$ 400.1701, found 400.1721.

2-(2,2-Diphenylvinylidene)-1-tosylindolin-3-one 201a



Yield 78 %; yellow solid; ^{1}H NMR ($CDCl_3$, 500 MHz): δ 8.22 (d, 1H, J = 8.4 Hz), 7.76 (d, 1H, J = 7.6 Hz), 7.70-7.22 (m, 14H), 6.76 (d, 2H, J = 8.1 Hz), 2.22 (s, 3H); ^{13}C NMR ($CDCl_3$, 125 MHz): δ 201.3, 183.7, 149.0, 144.7, 136.7, 134.8, 133.3, 129.48, 129.42, 129.1, 128.6, 127.2, 125.4, 124.6, 124.5, 124.3, 116.1, 111.3, 21.5; HRMS (ESI): calcd for $C_{29}H_{22}NO_3S$ 464.1320, found 464.1331.

Chapter VIII. References

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