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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School of Physical and Mathematical Sciences

A thesis submitted to the Nanyang Technological University in partial fulfillment of

the requirement for the degree of Doctor of Philosophy

2012
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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<td>Conclusion</td>
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<td>Experimental Section</td>
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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


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

(Highlighted in SYNFACTS, Synfacts 2009, 11, 1230).
<table>
<thead>
<tr>
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<th>Definition</th>
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<tr>
<td>ACS</td>
<td>American Chemical Society</td>
</tr>
<tr>
<td>Ar</td>
<td>aryl</td>
</tr>
<tr>
<td>BINAPHANE</td>
<td>1,2-bis([(R)-4,5\text{-dihydro-}3H\text{-binaphtho}(1,2-c:2',1'-e)phosphepino]\text{benzene}</td>
</tr>
<tr>
<td>Bu</td>
<td>butyl</td>
</tr>
<tr>
<td>d</td>
<td>days</td>
</tr>
<tr>
<td>Bn</td>
<td>benzyl</td>
</tr>
<tr>
<td>DBSA</td>
<td>dodecylbenzenesulfonic acid</td>
</tr>
<tr>
<td>DCE</td>
<td>1,2-dichloroethane</td>
</tr>
<tr>
<td>DMF</td>
<td>dimethylformamide</td>
</tr>
<tr>
<td>DMSO</td>
<td>dimethylsulfoxide</td>
</tr>
<tr>
<td>DNBSA</td>
<td>2,4-dinitrobenzenesulfonic acid</td>
</tr>
<tr>
<td>dppf</td>
<td>1,1'-bis(diphenylphosphino)ferrocene</td>
</tr>
<tr>
<td>dr</td>
<td>diastereomeric ratio</td>
</tr>
<tr>
<td>ee</td>
<td>enantiomeric excess</td>
</tr>
<tr>
<td>EWG</td>
<td>electron withdrawing group</td>
</tr>
<tr>
<td>Et</td>
<td>ethyl</td>
</tr>
<tr>
<td>h</td>
<td>hour</td>
</tr>
<tr>
<td>HMPA</td>
<td>hexamethylphosphoramide</td>
</tr>
<tr>
<td>IBX</td>
<td>2-iodoxybenzoic acid</td>
</tr>
<tr>
<td>'Pr</td>
<td>isopropyl</td>
</tr>
<tr>
<td>LDA</td>
<td>lithium diisopropylamide</td>
</tr>
<tr>
<td>MBH</td>
<td>Morita-Baylis-Hillman</td>
</tr>
<tr>
<td>Me</td>
<td>methyl</td>
</tr>
<tr>
<td>Abbreviation</td>
<td>Full Form</td>
</tr>
<tr>
<td>--------------</td>
<td>-----------</td>
</tr>
<tr>
<td>min</td>
<td>minute</td>
</tr>
<tr>
<td>m.p.</td>
<td>melting point</td>
</tr>
<tr>
<td>NMR</td>
<td>nuclear magnetic resonance</td>
</tr>
<tr>
<td>Nu</td>
<td>nucleophile</td>
</tr>
<tr>
<td>NBS</td>
<td>N-bromosuccinimide</td>
</tr>
<tr>
<td>NCS</td>
<td>N-chlorosuccinimide</td>
</tr>
<tr>
<td>NIS</td>
<td>N-iodosuccinimide</td>
</tr>
<tr>
<td>OEt</td>
<td>ethoxy</td>
</tr>
<tr>
<td>OMe</td>
<td>methoxy</td>
</tr>
<tr>
<td>OTf</td>
<td>trifluoromethanesulfonyl</td>
</tr>
<tr>
<td>PG</td>
<td>protecting group</td>
</tr>
<tr>
<td>Ph</td>
<td>phenyl</td>
</tr>
<tr>
<td>r.t.</td>
<td>room temperature</td>
</tr>
<tr>
<td>TFA</td>
<td>trifluoroacetic acid</td>
</tr>
<tr>
<td>TfOH</td>
<td>trifluoromethanesulfonic acid</td>
</tr>
<tr>
<td>THF</td>
<td>tetrahydrofuran</td>
</tr>
<tr>
<td>TLC</td>
<td>thin layer chromatography</td>
</tr>
<tr>
<td>TMS</td>
<td>trimethylsilyl</td>
</tr>
<tr>
<td>Ts</td>
<td>p-toluenesulfonyl</td>
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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.\textsuperscript{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\textsubscript{2}O and TfOH.\textsuperscript{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.\textsuperscript{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\textsubscript{2}O as the only side product.\textsuperscript{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.\textsuperscript{6} Thus far, improved reactivities have been achieved by utilizing activated alcohols which contain a π-system or “sp\textsuperscript{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. 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\textsubscript{3} unit in organic synthesis.\textsuperscript{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,\textsuperscript{8} a catalytic version was reported by Tsuji and Trost in 1965. In their approach, the allylic functional group introduced \textit{via} the participation of a discrete $\pi$-allyl metal complex, typically those of palladium (Scheme 1.1).\textsuperscript{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.\textsuperscript{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.](image-url)
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 with

Table 1.1 Lewis and Brønsted acid catalyzed intermolecular allylic alkylations.

<table>
<thead>
<tr>
<th>Entry</th>
<th>Catalyst</th>
<th>Product</th>
<th>Yield (%)</th>
<th>Ref</th>
</tr>
</thead>
<tbody>
<tr>
<td>1</td>
<td>Sc(OTf)$_3$</td>
<td></td>
<td>48-95</td>
<td>11</td>
</tr>
<tr>
<td>2</td>
<td>AlCl$_3$</td>
<td></td>
<td>50-90</td>
<td>12</td>
</tr>
<tr>
<td>3</td>
<td>AuCl$_3$</td>
<td></td>
<td>50-99</td>
<td>14</td>
</tr>
<tr>
<td>4</td>
<td>(Ph$_3$P)AuNTf$_2$</td>
<td></td>
<td>33-91</td>
<td>15</td>
</tr>
<tr>
<td>5</td>
<td>C$_6$F$_3$B(OH)$_2$</td>
<td></td>
<td>58-99</td>
<td>16</td>
</tr>
<tr>
<td>6</td>
<td>Ca(NTf)$_2$</td>
<td></td>
<td>68-90</td>
<td>17</td>
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</table>
Table 1.1 (Continued)

<table>
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<tr>
<th>Entry</th>
<th>Catalyst</th>
<th>Product</th>
<th>Yield (%)</th>
<th>Ref</th>
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<tr>
<td>7</td>
<td>AgOTf</td>
<td><img src="https://example.com" alt="Image" /></td>
<td>48-96</td>
<td>19</td>
</tr>
<tr>
<td>8</td>
<td>p-TsOH·H₂O</td>
<td><img src="https://example.com" alt="Image" /></td>
<td>55-84</td>
<td>20</td>
</tr>
<tr>
<td>9</td>
<td>TfOH</td>
<td><img src="https://example.com" alt="Image" /></td>
<td>55-95</td>
<td>21</td>
</tr>
<tr>
<td>10</td>
<td>calix[n]arene sulfonic acid</td>
<td><img src="https://example.com" alt="Image" /></td>
<td>60-94</td>
<td>22</td>
</tr>
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</table>

benzene 1, which gave the corresponding products 3 and/or 4 in 48-95% yield with minimal side products (Table 1.1, entry 1).

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 AlCl₃ (Table 1.1, entry 2).

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. 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). 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$_3$P)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). 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 CsF$_3$B(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). The efficiency of this intermolecular cyclization method was exemplified by the ability of CsF$_3$B(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$_6$H$_4$ 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). In this work, Bu$_4$NPF$_6$ 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. 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). The desired products 5 were obtained in up to 96% yield and with up to >20:1 $E:Z$ and >20:1 $\alpha:\gamma$ 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·H$_2$O 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). 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). 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). 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\(_3\)-6H\(_2\)O as the catalyst (Scheme 1.2). 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](image)

**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). 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.

\[ \begin{align*} 
\text{Scheme 1.3 Organocatalytic intermolecular nucleophilic substitution of cyclic} \\
\text{Morita-Baylis-Hillman alcohols 9 with indoles 10.} 
\end{align*} \]

In 2006, Baba and co-workers designed an InCl₃ 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 InBr₃ 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 FeCl₃ 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.

![Lewis acid catalyzed Friedel-Crafts alkylation with allylic alcohols](image)

<table>
<thead>
<tr>
<th>Entry</th>
<th>Catalyst</th>
<th>Yield (%)</th>
<th>Ref</th>
</tr>
</thead>
<tbody>
<tr>
<td>1</td>
<td>InCl₃</td>
<td>64-78</td>
<td>25</td>
</tr>
<tr>
<td>2</td>
<td>InBr₃</td>
<td>85-93</td>
<td>26</td>
</tr>
<tr>
<td>3</td>
<td>FeCl₃</td>
<td>56-98</td>
<td>27</td>
</tr>
</tbody>
</table>

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). In their approach, BF₃·Et₂O was shown to efficiently catalyze a variety of allylic alcohols of the type under mild conditions and produce the corresponding 3-iodo-1H-indene derivatives 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·H₂O affording the indene product in yields of 80-99% (Table 1.3, entry 2). This was followed by works by Zhou and co-workers who described intramolecular C–C bond formation reactions via FeCl₃·6H₂O catalyzed substituted allylic alcohols 18 (Table 1.3, entry 3). 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.

![Chemical Structures](image)

<table>
<thead>
<tr>
<th>Entry</th>
<th>Catalyst</th>
<th>Yield (%)</th>
<th>Ref</th>
</tr>
</thead>
<tbody>
<tr>
<td>1</td>
<td>BF₃·Et₂O</td>
<td>55-90</td>
<td>28</td>
</tr>
<tr>
<td>2</td>
<td>TsOH·H₂O</td>
<td>80-97</td>
<td>29</td>
</tr>
<tr>
<td>3</td>
<td>FeCl₃·6H₂O</td>
<td>56-93</td>
<td>30</td>
</tr>
</tbody>
</table>

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). 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.

![Diagram of cyclization reaction]

<table>
<thead>
<tr>
<th>Entry</th>
<th>[M]</th>
<th>X</th>
<th>Yield (%)</th>
<th>Ref</th>
</tr>
</thead>
<tbody>
<tr>
<td>1</td>
<td>Hg(OTf)₂</td>
<td>CH₂</td>
<td>30-99</td>
<td>31</td>
</tr>
<tr>
<td>2</td>
<td>AgOTf</td>
<td>CH₂, NHTs,</td>
<td>53-90</td>
<td>32</td>
</tr>
<tr>
<td></td>
<td></td>
<td>C(COEt)₂</td>
<td></td>
<td></td>
</tr>
</tbody>
</table>

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).

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·Me₂S/AgOTf catalytic system containing the chiral ligand 26 (Scheme 1.4).

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). 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$_2$Cl$_2$(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). 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, Yb(OTf)₃, FeCl₃ and the lanthanum triflates Ln(OTf)ₙ (Ln = Yb, La, Hf; n = 3, 4) 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.

<table>
<thead>
<tr>
<th>Entry</th>
<th>Catalyst</th>
<th>Yield (%)</th>
<th>Ref</th>
</tr>
</thead>
<tbody>
<tr>
<td>1</td>
<td>InCl₃</td>
<td>75-95</td>
<td>35</td>
</tr>
<tr>
<td>2</td>
<td>Bi(OTf)₃</td>
<td>62-73</td>
<td>36</td>
</tr>
<tr>
<td>3</td>
<td>Ln(OTf)ₙ</td>
<td>51-92</td>
<td>37</td>
</tr>
<tr>
<td>4</td>
<td>Yb(OTf)₃</td>
<td>72-93</td>
<td>38</td>
</tr>
<tr>
<td>5</td>
<td>FeCl₃</td>
<td>72-82</td>
<td>39</td>
</tr>
<tr>
<td>6</td>
<td>I₂</td>
<td>51-99</td>
<td>40</td>
</tr>
<tr>
<td>7</td>
<td>p-TsOH-H₂O</td>
<td>80-72</td>
<td>20</td>
</tr>
</tbody>
</table>

Using molecular iodine as the catalyst, Chan and co-workers developed a direct allylic alkylation of 1,3-dicarbonyl compounds with allylic alcohols, providing the
corresponding allylated products in 51-99% yields (Table 1.5, entry 6). 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). 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).

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). The substitution reaction was found to require the need to employ KPF₆ 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 AuCl₃ catalyzed amination with substituted anilines 40 as well as sulfonamides 37 could be achieved (Table 1.6, entry 3). 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). 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.

\[
\begin{align*}
\text{R}^1 &= \text{alkyl, aryl} \\
\text{R}^2 &= \text{H, alkyl, aryl}
\end{align*}
\]

<table>
<thead>
<tr>
<th>Entry</th>
<th>Catalyst</th>
<th>NH$_2$R$^3$</th>
<th>Yield (%)</th>
<th>Ref</th>
</tr>
</thead>
<tbody>
<tr>
<td>1</td>
<td>$p$-TsOH·H$_2$O</td>
<td></td>
<td>86</td>
<td>20</td>
</tr>
<tr>
<td>2</td>
<td>Bi(OTf)$_3$/KPF$_6$</td>
<td></td>
<td>55-99</td>
<td>41</td>
</tr>
<tr>
<td>3</td>
<td>AuCl$_3$</td>
<td>TsNH$_2$</td>
<td>58-96</td>
<td>42</td>
</tr>
<tr>
<td>4</td>
<td>I$_2$</td>
<td>ArNH$_2$</td>
<td>61-96</td>
<td>43</td>
</tr>
<tr>
<td>5</td>
<td>$^{t}$Bu$_2$P$^{t}$AuCl</td>
<td></td>
<td>85-100</td>
<td>44</td>
</tr>
</tbody>
</table>

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 $[\text{P}(t\text{-Bu})_2(\text{o-biphenyl})]\text{AuCl}$ 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 alkylation of aldehydes 44 with allylic alcohols of the type 43 in the presence of the chiral organocatalyst 46 (Scheme 1.6). 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.

\[
\begin{align*}
\text{Ph} - \text{OH} + \text{R}^2 - \text{CHO} &\rightarrow \text{Ph} - \text{R}^1 - \text{CHO} \\
&\quad \text{InBr}_3 (20 \text{ mol%}) \\
&\quad \text{Me} - \text{N} - \text{tBu} \\
&\quad \text{50-90% yield} \\
&\quad \text{dr up to >20:1} \\
&\quad \text{up to 99% ee (syn)} \\
&\quad \text{up to 87% ee (anti)}
\end{align*}
\]

\textbf{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$_6$·H$_2$O as the catalyst was demonstrated by Liang and co-workers (Scheme 1.7). 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 TsNH₂ 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.](image)

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-TsNH₂ 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-MeOC₆H₄)₃PAuCl/AgBF₄ catalyst combination at room temperature.

![Scheme 1.8 Gold catalyzed tandem synthesis of substituted pyrroles 52.](image)
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). 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). 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$_3$·6H$_2$O was established by Cossy and co-workers (Scheme 1.20). 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 \([\text{P}(t\text{-Bu})_2\text{o-biphenyl}]\text{AuCl}\) as catalyst and \(\text{AgSbF}_6\) 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 \(\text{Bi(OTf)}_3\) 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 $S_N2^\prime$ 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). This amination process was shown to efficiently undergo a $\beta$-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). The reported Ph$_3$PAuCl/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). 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$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$_3$PAuCl/AgOTf as the catalyst system.
In this work, a notable observation was the marked influence of the olefin geometry of 69 on the stereochemistry of the product 70.

\[
\text{Scheme 1.26 Gold catalyzed chirality transfer reactions of monoallyl diols 69.}
\]

At about the same time, Rueping and co-workers found that N-triflylphosphoramidate 73 was an efficient chiral Brønsted acid catalyst for the direct intramolecular alkoxylation of 2-(1-hydroxyallyl)phenols 71 in toluene at $-78^\circ$C (Scheme 1.27). 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 phosphoramidate moiety of the acid catalyst and hydroxyl moieties of the allylic diol.

\[
\text{Scheme 1.27 Chiral Brønsted acid catalyzed asymmetric alkoxylation of 2-(1-hydroxyallyl)phenols 71.}
\]
More recently, enantioselective gold catalyzed intramolecular dehydrative amination of allylic alcohols 74 was reported by Widenhoefer and co-workers (Scheme 1.28). 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 AgClO₄ 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. One strategy for the nucleophilic displacement of propargylic alcohols 77 is the Nicholas reaction (Scheme 1.29). The reaction usually involves the transformation of the alcoholic substrate with [Co₂(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 \([\text{Co}_2(\text{CO})_8]\) 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).\(^6^0\) This reaction was shown to tolerate various nucleophiles, such as arenes \(81\), allyltrimethylsilane \(82\), alcohols \(83\) and thiols \(84\) with NaAuCl\(_4\)·2H\(_2\)O 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).\(^6^1\) 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 \(\text{FeCl}_3\) 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).\(^6^2\)
Table 1.7 Lewis and Brønsted acid catalyzed direct nucleophilic substitution of propargylic alcohols 77.

![reaction scheme]

<table>
<thead>
<tr>
<th>Entry</th>
<th>Catalyst</th>
<th>NuH</th>
<th>Yield (%)</th>
<th>Ref</th>
</tr>
</thead>
<tbody>
<tr>
<td>1</td>
<td>NaAuCl₄·2H₂O</td>
<td></td>
<td>33-97</td>
<td>60</td>
</tr>
<tr>
<td>2</td>
<td>BiCl₃</td>
<td></td>
<td>10-94</td>
<td>61</td>
</tr>
<tr>
<td>3</td>
<td>FeCl₃</td>
<td></td>
<td>38-95</td>
<td>62</td>
</tr>
<tr>
<td>4</td>
<td>p-TsOH·H₂O</td>
<td></td>
<td>43-93</td>
<td>63</td>
</tr>
<tr>
<td>5</td>
<td>Sc(OTf)₃</td>
<td></td>
<td>65-100</td>
<td>64</td>
</tr>
</tbody>
</table>

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$_2$O, 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). 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 $\alpha\beta$-unsaturated carbonyl derivative derived from Meyer-Schuster rearrangement.

Yoshimatsu and co-workers disclosed Sc(OTf)$_3$ catalyzed nucleophilic substitution of phenylsulfanyl and selanyl propargylic alcohols (Table 1.7, entry 5). 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$_2$O (Scheme 1.30). 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.

\[
\text{Scheme 1.30} \quad \text{FeCl}_3\cdot6\text{H}_2\text{O} \text{ catalyzed intramolecular annulation/hydroarylation of propargylic alcohols 85.}
\]

Following this work, Aponick and co-workers reported an efficient tandem intramolecular hydroalkoxylation of substituted propargylic triols 88 to spiroketal derivatives 89 using \text{Au[P(t-Bu)\_2(o-biphenyl)]OTf} as the active catalyst generated \textit{in situ} from the reaction of 41 and AgOTf (Scheme 1.31).\textsuperscript{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 spiroketalts using propargylic triols 88.

\[
\text{Scheme 1.31} \quad \text{Gold catalyzed tandem synthesis of 1,6-dioxaspiro[4.5]dec-9-enes 89.}
\]
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$_2$CO$_3$.

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

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.H₂O 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.H₂O catalyzed synthesis of substituted thiazoles 99.

The first example for the synthesis of various N-, O-, S-containing heterocycles via AgNO₃ 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 \( \text{101} \) 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 \( \text{100} \) to various heterocyclic derivatives under mild conditions at 0 °C or room temperature (Table 1.8, entry 2-3). The desired pyrrole, furan and thiophene adducts \( \text{101} \) were obtained in up to 99\% yield from either \([P(t\text{-Bu})_2(o\text{-biphenyl})]\text{AuCl/AgOTf}\) (Aponick) or \((\text{Ph}_3\text{P})\text{AuCl/AgNTf}_2\) (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 \( \text{100} \).

<table>
<thead>
<tr>
<th>Entry</th>
<th>Catalyst</th>
<th>Yield (%)</th>
<th>Ref</th>
</tr>
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<tr>
<td>1</td>
<td>AgNO(_3)</td>
<td>70-99</td>
<td>70</td>
</tr>
<tr>
<td>2</td>
<td>([P(t\text{-Bu})_2(o\text{-biphenyl})]\text{AuCl/AgOTf})</td>
<td>87-99</td>
<td>71</td>
</tr>
<tr>
<td>3</td>
<td>((\text{Ph}_3\text{P})\text{AuCl/AgNTf}_2)</td>
<td>85-98</td>
<td>72</td>
</tr>
</tbody>
</table>

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). 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-idoquinolines 106 via I$_2$ promoted cascade intramolecular 6-endo-dig iodocyclization of 2-tosylaminophenylprop-1-yn-3-ols 105 (Scheme 1.36). 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 1H-indoles 107 was established by Zhan and co-workers (Scheme 1.37). 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 R² = 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). 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 CO₂ 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). 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). 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.](image)

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). 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 \( \text{I}_2 \) promoted intramolecular iodocyclization of propargylic alcohols 119 and 121.

In the same year, NXS (\( X = \text{Br}, \text{I} \)) mediated intermolecular nucleophilic substitution/cyclization of propargylic alcohols 77 with sulfonamides 37 to \( N-(2\text{-iodo/bromoinden-1-yl})\)arenesulfonamides 123 using \( \text{BF}_3\cdot\text{Et}_2\text{O} \) as a promoting reagent was reported by Wang and co-workers (Scheme 1.42).\(^8\) 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 \( \text{BF}_3\cdot\text{Et}_2\text{O} \) promoted tandem synthesis of 2-haloindenamines 123.

This \( \text{BF}_3\cdot\text{Et}_2\text{O} \) 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). In this seminal work, BF3·Et2O 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 BF3·Et2O promoted intermolecular nucleophilic substitution/cyclization of propargylic alcohols 77 and N-sulfonylhydrazones 124.](image)

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). 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=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. In 2005, an efficient approach for the direct arylation of benzylic alcohols to give diarylmethanes and arylheteroarylmethanes using FeCl₃ as catalyst was reported by Beller and co-workers (Table 1.9, entry 1). Although the benzylation reported was limited to o-xylene, 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). 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.

<table>
<thead>
<tr>
<th>Entry</th>
<th>Catalyst</th>
<th>NuH</th>
<th>Yield (%)</th>
<th>Ref</th>
</tr>
</thead>
<tbody>
<tr>
<td>1</td>
<td>FeCl₃</td>
<td>Me</td>
<td>37-99</td>
<td>83</td>
</tr>
<tr>
<td>2</td>
<td>Bi(OTf)₃</td>
<td></td>
<td>35-99</td>
<td>84</td>
</tr>
<tr>
<td>3</td>
<td>NaAuCl₄</td>
<td>R¹NH₂</td>
<td>63-100</td>
<td>85</td>
</tr>
<tr>
<td>4</td>
<td>BF₃·Et₂O</td>
<td></td>
<td>65-95</td>
<td>86</td>
</tr>
<tr>
<td>5</td>
<td>DBSA</td>
<td></td>
<td>62-96</td>
<td>87</td>
</tr>
<tr>
<td>6</td>
<td>NaAuCl₄</td>
<td>R¹CH</td>
<td>47-96</td>
<td>88</td>
</tr>
<tr>
<td>7</td>
<td>InBr₃</td>
<td></td>
<td>56-99</td>
<td>89</td>
</tr>
<tr>
<td>8</td>
<td>Ga(OTf)₃</td>
<td></td>
<td>52-94</td>
<td>90</td>
</tr>
</tbody>
</table>
In the same year, Campagne and co-workers described a NaAuCl₄ 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). 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 NaAuCl₄ as the catalyst was accomplished by Asensio and co-workers (Table 1.9, entry 6). 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, BF₃·Et₂O mediated intermolecular nucleophilic substitution of benzylic alcohols with α-EWG ketene-(S,S)-acetals 135 (EWG = CN, COR, CONH₂) was demonstrated by Liu and co-workers (Table 1.9, entry 4). 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). 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). The results revealed that with InBr₃ as the catalyst, short reaction times at room temperature could be achieved to provide the nitrile products in up to 99% yield. This InBr₃ 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.](image)

Following this work, Wu and co-workers demonstrated the direct nucleophilic substitution of benzylic alcohols utilizing various sulfur nucleophiles and Ga(OTf)₃ as the catalyst (Table 1.9, entry 8). 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 FeCl₃/ZnCl₂ catalyzed intermolecular benzoylation/annulation/oxidation of α-amino substituted
2-amino benzylic alcohols 145 with β-ketoesters 30 (Scheme 1.45). In this work, additional control experiments showed that the reaction could not be carried out efficiently by employing either FeCl₃ or ZnCl₂ alone as the catalyst.

Scheme 1.45 FeCl₃/ZnCl₂ 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 FeCl₃ as the catalyst (Scheme 1.46). 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 FeCl₃ 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). This afforded the corresponding trisubstituted vinyllic halides 151 in up to 81% yield.

\[
\begin{align*}
R_1 & \equiv & & \text{FeX}_3 (40 \text{ mol%}) & & \text{CH}_2\text{Cl}_2, \text{ r.t.} & & X = \text{Cl, Br} \\
& & & & & & \\
& & & & & & \\
R_1 & \text{-} & R_2 & = & \text{alkyl, aryl} & & \\
147 & & & & & & 26-81\% \text{ yield}
\end{align*}
\]

**Scheme 1.47** FeCl₃ catalyzed tandem synthesis of substituted vinyllic 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 of benzylic alcohols using CH₃CN as both the solvent and reagent was reported by Sanz and co-workers in 2007 (Scheme 1.48). The reaction was thought to proceed via carbocation formation followed by sequential CH₃CN 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.

\[
\begin{align*}
\text{Me} & & & & & & \text{HN} \equiv \text{Me} \\
\text{Me} & & & & & & \text{HN} \equiv \text{Me} \\
152 & & & & & & 55-91\% \text{ yield}
\end{align*}
\]

**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.](image)

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-1H-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$_3$·6H$_2$O as the catalyst and TfOH as an additive (Scheme 1.51). 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 $R^1 = R^4 = \text{Ph}$, $R^2 = R^3 = \text{H}$, Ar = $p$-ClC$_6$H$_4$ was achieved.

Scheme 1.51 FeCl$_3$·6H$_2$O 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).\(^9\) 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 benzylic 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.\(^10\) In a seminal work, BF\(_3\)-Et\(_2\)O promoted intramolecular rearrangement of 2-(cyclopropyl(hydroxy)-methyl)phenols 164 was reported by Doris and co-workers (Scheme 1.53).\(^11\) 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 BF₃·OEt₂ 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 HAuCl₄·4H₂O as the catalyst (Scheme 1.54). 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). 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.

\[
\begin{align*}
\text{HO} & \quad \text{R}^1 \quad \text{R}^2 \\
\text{Yb(OTf)}_3 (5 \text{ mol}) & \quad \text{toluene, 100 °C} \\
\text{R}^3 \text{NH}_2 & \quad \text{R}^1 \quad \text{R}^3 \\
\text{or} & \quad \text{R}^1 \quad \text{R}^2 \\
\text{R}^1 & = \text{H, alkyl, aryl} \\
\text{R}^2 & = \text{alkyl, aryl} \\
\text{R}^3 & = \text{Ph, SO₂Ar}
\end{align*}
\]

**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). 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 R¹ or R² 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 R² = Ar in dichloroethane as the solvent at 0 °C. The cyclobutanol product was afforded from cation-induced ring enlargement process when R²-R³ = H, alkyl, aryl in CH₃NO₂ 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). 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-1H-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 \( R^1 = H \).

\[
\begin{align*}
\text{Scheme 1.58 Gold catalyzed amination/cycloisomerization of 2-(cyclopropyl-}
\text{methanol)anilines 178.}
\end{align*}
\]

**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.\textsuperscript{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.\textsuperscript{107-109} As mentioned earlier in Sections 1.54 and 1.55 in Chapter I, we\textsuperscript{103} and others\textsuperscript{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 \textit{N}- and \textit{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.\textsuperscript{109} Although all these works were shown to be efficient, producing \textit{H}$_2$\textit{O} 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. 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. 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. As part of a program examining the utility of alcohols as pro-electrophiles in organic synthesis, we report herein TfOH catalyzed ring
opening of 1-cyclopropyl-2-propyn-1-ols with alcohols (Scheme 2.1). 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](image)

**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.\textsuperscript{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-yn-1-yl)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.\textsuperscript{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 \textsuperscript{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\textsubscript{2}NH 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 \textsuperscript{1}H NMR analysis or low resolution mass spectrometry.
Table 2.1 Optimization of reaction conditions.$^a$

![Chemical structure](image)

<table>
<thead>
<tr>
<th>Entry</th>
<th>Catalyst</th>
<th>Catalyst loading (mol%)</th>
<th>Solvent</th>
<th>Yield (%)$^b$</th>
<th>Catalyst turnover</th>
</tr>
</thead>
<tbody>
<tr>
<td>1</td>
<td>TfOH</td>
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<td>-</td>
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</tr>
<tr>
<td>2$^c$</td>
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<td>-</td>
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<td>100</td>
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<td>-</td>
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<td>9,800</td>
</tr>
<tr>
<td>7</td>
<td>TfOH</td>
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<td>-</td>
<td>-$^d$</td>
<td>-</td>
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<tr>
<td>8$^e$</td>
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<td>PhMe</td>
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<td>(CH₂Cl)₂</td>
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<td>10$^e$</td>
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<td>p-TsOH</td>
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<td>-</td>
<td>55</td>
<td>11</td>
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<td>13$^g$</td>
<td>TFA</td>
<td>5</td>
<td>-</td>
<td>40</td>
<td>8</td>
</tr>
<tr>
<td>14$^g$</td>
<td>HCl</td>
<td>5</td>
<td>-</td>
<td>10</td>
<td>2</td>
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</tbody>
</table>

$^a$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). 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-TsNH₂ using ytterbium catalysis. 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

| 183ab | R¹ = H, R² = F (92%, 9,200) |
| 183ac | R¹ = H, R² = Cl (95%, 9,500) |
| 183ad | R¹ = H, R² = R⁴ = OMe, R³ = Me (90%, 9,000) |
| 183ae | R¹ = R² = R³ = Me, R⁴ = OMe (88%, 8,800) |
| 183af | R¹ = R² = H, R² = CF₃, R⁴ = OMe (90%, 9,000) |
| 183ag | R¹ = H, R² = OMe, R³ = Me, R⁴ = F (92%, 9,200) |

| 183ah | R = F (91%, 9,100) |
| 183ai | R = OMe (91%, 9,100) |
| 183aj | R¹ = H, R² = F (98%, 9,800) |
| 183ak | R¹ = Ph, R² = H (91%, 9,100) |
| 183al | R¹ = H, R² = OMe (93%, 9,300) |
| 183am | R¹ = Ph, R² = H (90%, 9,000) |

| 183an | (97%, 9,700) |
| 183ao | R¹ = (CH₂)₃CH₂, R² = Cl (96%, 9,600) |
| 183ap | R¹ = (CH₂)₃CH₂, R² = H (89%, 8,900) |

| 183ar | R = Ph (98%, 9,800) |
| 183as | R = (CH₂)₃CH₂ (88%, 8,800) |

| 183at | (44%, 4,400) |
| 183au | R = Cl (85%, 8,500) |
| 183av | R = H (75%, 7,500) |

| 183aw | (96%, 9,600) |
| 183ax | (92%, 9,200) |

| 183aq | (92%, 9,200) |
| 183at | (44%, 4,400) |
| 183b | H₃C(H₂C)₅ |
| 183c | H₃C(H₂C)₅ |

Chapter II

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Table 2.2 (continued)

<table>
<thead>
<tr>
<th>Reaction Conditions</th>
<th>Yields/Turnovers</th>
</tr>
</thead>
<tbody>
<tr>
<td>183ay: Me = Et</td>
<td>(95%, 9,500)</td>
</tr>
<tr>
<td>183az: Me = Ph</td>
<td>(92%, 9,200)</td>
</tr>
<tr>
<td>183ba: Me = Cl</td>
<td>(89%, 8,900)</td>
</tr>
<tr>
<td>183bb: X = O</td>
<td>(87%, 8,700)</td>
</tr>
<tr>
<td>183bc: X = S</td>
<td>(88%, 8,800)</td>
</tr>
<tr>
<td>185bd</td>
<td>(91%)</td>
</tr>
</tbody>
</table>

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. Reaction conducted for 25 min. Reaction conducted for 30 min. Reaction conducted for 20 min. Yield in parentheses denotes that isolated yield for the cyclopropyl enyne side product 184at. Product obtained as an inseparable 5:1 mixture of E/Z isomers. Starting alcohol used as a mixture of diastereomers in a ratio = 3:2. Product obtained as an inseparable 3:2 mixture of E/Z isomers. Starting alcohol used as a mixture of diastereomers in a ratio = 3:1. Product obtained as an inseparable 3:2 mixture of E/Z isomers. Reaction conducted for 10 min.

-oils 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-be in excellent yields and catalyst turnovers. This is noteworthy as such aromatic ring structures are commonly found in bioactive natural and pharmaceutical compounds.\(^\text{117}\) 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.\(^\text{109}\)

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. 

![Chemical structure](image)

<table>
<thead>
<tr>
<th>Entry</th>
<th>ROH 83</th>
<th>Product</th>
<th>Yield</th>
<th>Turnover</th>
</tr>
</thead>
<tbody>
<tr>
<td>1</td>
<td>83b-d</td>
<td>183be, R = Ph</td>
<td>80</td>
<td>8,000</td>
</tr>
<tr>
<td>2</td>
<td>R-OH</td>
<td>183bf, R =</td>
<td>75</td>
<td>7,500</td>
</tr>
<tr>
<td>3</td>
<td>83b-d</td>
<td>CH2OCH2CH=CH2</td>
<td></td>
<td></td>
</tr>
<tr>
<td>4b</td>
<td>ROH</td>
<td>183bh, R = i-Pent</td>
<td>86</td>
<td>8,600</td>
</tr>
<tr>
<td>5b</td>
<td>83e-f</td>
<td>183bi, R = t-Bu</td>
<td>80</td>
<td>8,000</td>
</tr>
<tr>
<td>6</td>
<td>R-OH</td>
<td>183bj</td>
<td>76</td>
<td>7,600</td>
</tr>
</tbody>
</table>

\( ^a \) 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
was the only other example that was found to give the corresponding conjugated enyne 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 1H 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 (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.](image)

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. 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.\textsuperscript{119} The \textit{E}/\textit{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.\textsuperscript{120} However, for reactions when \(R^3 = \text{Me}\) 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 \(\text{C}^\oplus - \text{C(cyclopropyl)}\) bond in 187. For reactions where \(R^4 = \text{Ph}\), we postulate that a possible reason for preferential \(S\text{N}1’\) attack at the carbon center bearing the substituent is so that formation of the more sterically hindered tri- or tetrasubstituted enyne adduct can be avoided.\textsuperscript{120} The origin of the elimination and ethereal substitution products 184 at and 185 bd 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](image)

\textbf{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. 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 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\textsuperscript{121-125} such as azaspiracid,\textsuperscript{122} kadlongirin A,\textsuperscript{123} okadaic acid\textsuperscript{124} and xyloketal J\textsuperscript{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.\textsuperscript{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.\textsuperscript{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.\textsuperscript{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 reactions of alcohol pro-electrophiles have come under increasing scrutiny,\textsuperscript{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\textsuperscript{128} and homoallylic halides as well as ring expansion and fission reactions.\textsuperscript{131} Herein, we report a one-pot, two-step TfOH catalyzed hydroxylation/halocyclization of cyclopropyl methanols with H$_2$O 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.

\begin{figure}[h]
\centering
\includegraphics[width=\textwidth]{example.png}
\caption{Examples of bioactive compounds containing a tetrahydrofuran moiety.}
\end{figure}
Scheme 3.1 One-pot, two-step halohydrofuran synthesis from ring-opening of cyclopropyl methanols with H$_2$O 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$_2$O 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). 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

<table>
<thead>
<tr>
<th>Entry</th>
<th>Catalyst</th>
<th>Solvent</th>
<th>Yield (%)</th>
</tr>
</thead>
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<tr>
<td>1</td>
<td>TfOH</td>
<td>acetone:H₂O</td>
<td>99</td>
</tr>
<tr>
<td>2</td>
<td>TfOH b</td>
<td>acetone:H₂O</td>
<td>99</td>
</tr>
<tr>
<td>3</td>
<td>TfOH c</td>
<td>acetone:H₂O</td>
<td>55</td>
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<td>4</td>
<td>TfOH d</td>
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<td>42</td>
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<td>5 e</td>
<td>TfOH</td>
<td>acetone:H₂O</td>
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<td>TfOH</td>
<td>THF:H₂O</td>
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<tr>
<td>8</td>
<td>TfOH</td>
<td>CH₂Cl₂:H₂O</td>
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<tr>
<td>9</td>
<td>Tf₂NH</td>
<td>acetone:H₂O</td>
<td>40</td>
</tr>
<tr>
<td>10</td>
<td>TFA</td>
<td>acetone:H₂O</td>
<td>55</td>
</tr>
<tr>
<td>11</td>
<td>HCl</td>
<td>acetone:H₂O</td>
<td>25</td>
</tr>
<tr>
<td>12</td>
<td>p-TsOH·H₂O</td>
<td>acetone:H₂O</td>
<td>45</td>
</tr>
</tbody>
</table>

a All reactions were performed with 5 mol % of catalyst in 4:1 of solvent:H₂O 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:H₂O at 90 °C for 15 min. e Reaction conducted with 1.1 equiv of NIS. f Reaction conducted with 3 equiv of I₂.
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$_2$Cl$_2$ 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$_2$NH, TFA, HCl, and $p$-TsOH·H$_2$O 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:H₂O 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 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 \(^1\text{H} \) 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.$^a$

<table>
<thead>
<tr>
<th>Compound</th>
<th>$R^1$</th>
<th>$R^2$</th>
<th>Yield (%)</th>
</tr>
</thead>
<tbody>
<tr>
<td>188be</td>
<td>$R^1 = R^2 = F$</td>
<td>95%</td>
<td></td>
</tr>
<tr>
<td>188bf</td>
<td>$R^1 = R^2 = Cl$</td>
<td>93%</td>
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<tr>
<td>188bg</td>
<td>$R^1 = R^2 = Br$</td>
<td>88%</td>
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<td>188bh</td>
<td>$R^1 = R^2 = H$</td>
<td>79%</td>
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<tr>
<td>188bi</td>
<td>$R^1 = R^2 = Me$</td>
<td>99%</td>
<td></td>
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<tr>
<td>188bj</td>
<td>$R^1 = R^2 = OMe$</td>
<td>97%</td>
<td></td>
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<td>188bk</td>
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</tr>
<tr>
<td>188bm</td>
<td>$R^1 = Me, R^2 = H$</td>
<td>98%</td>
<td></td>
</tr>
<tr>
<td>188bn</td>
<td>$R^1 = Ph, R^2 = H$</td>
<td>94%</td>
<td></td>
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</tbody>
</table>

$^a$All reactions were performed with 1 mol% of TfOH in 4:1 acetone: H$_2$O 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.\textsuperscript{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>
<thead>
<tr>
<th>Entry</th>
<th>Substrates</th>
<th>Product</th>
<th>Yield (%)</th>
</tr>
</thead>
<tbody>
<tr>
<td>1</td>
<td>170aa + NBS</td>
<td>188bw, X = Br</td>
<td>85</td>
</tr>
<tr>
<td>2</td>
<td>170aa + NCS\textsuperscript{b}</td>
<td>188bx, X = Cl</td>
<td>35</td>
</tr>
<tr>
<td>3</td>
<td>170aa + Selectfluor</td>
<td>188by, X = F</td>
<td>55</td>
</tr>
<tr>
<td>4</td>
<td>170bp + NBS</td>
<td>188bz, X = Br</td>
<td>82</td>
</tr>
<tr>
<td>5</td>
<td>170bp + NCS\textsuperscript{b}</td>
<td>188ca, X = Cl</td>
<td>30</td>
</tr>
<tr>
<td>6</td>
<td>170bp + Selectfluor</td>
<td>189cb = F</td>
<td>45</td>
</tr>
</tbody>
</table>

\textsuperscript{a} All reactions were performed with 1 mol\% of TfOH in 4:1 acetone: H\textsubscript{2}O at 90 °C followed by 1.3 equiv of the electrophilic halide source at −5 °C.\textsuperscript{134}

\textsuperscript{b} Reaction conducted at reflux.
seminal work by Gouverneur and co-workers in an analogous reaction with a homoallylic alcohol and Selectfluor.\textsuperscript{127a} The structure of 188by was also confirmed by X-ray crystallographic analysis (see Figure 3.4).\textsuperscript{132}

![ORTEP drawing of 188by with thermal ellipsoids at 50% probability levels.](image)

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 \( ^1H-^1H \) NOE analysis of 188bp. This revealed \( ^1H-^1H \) 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 1H-1H 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 I₂ or NIS. 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

\[ \text{Scheme 3.2 TfOH catalyzed hydroxylation/halocyclization of 170aa, 170bm, and 170bc with H₂O and NIS.} \]
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).\textsuperscript{136} Further treating 189aa and 189bc with 1.3 equiv of NIS at $-5 \degree C$ 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$_2$O 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
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 170aa to 189aa at different temperatures.

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

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$_2$O, subsequent cyclopropylcarbinol-homoallylic rearrangement of this newly formed cationic species and trapping by H$_2$O 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. 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$_2$O and NIS.](image-url)
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 R³ \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.\textsuperscript{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.\textsuperscript{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.\textsuperscript{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.\textsuperscript{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.\textsuperscript{71} We subsequently demonstrated that the synthetic method could be fine-tuned to provide 1H-indole-2-carbaldehydes and (E)-2-(iodomethylene)indolin-
-3-ols by introducing $N$-iodosuccinimide into the reaction conditions.\textsuperscript{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$_2$O (Scheme 4.1).\textsuperscript{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$_2$O as potentially the only byproduct is not known. As part of ongoing efforts to
devvelop this type of reaction, our discovery that inexpensive, ecologically benign, and readily available simple Ag$^+$ 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.

\textbf{Scheme 4.1} Lewis and Brønsted acid-catalyzed reactivities of propargylic diols.
4.2 Results and Discussion

The 1-((2-tosylamino)aryl)but-2-yn-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.\textsuperscript{143} By using \(N\)-tosyl-1-(2-aminophenyl)-1,3-diphenyl-prop-2-yn-1-ol \textbf{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 \textbf{190a} in toluene with AgOTf (5 mol\%) at room temperature for 7 h gave 3-phenyl-2-(phenylethynyl)-1-tosyl-1H-indole \textbf{191a} and 3-phenyl-2-(2-phenylvinylidene)-1-tosyl indolin-3-ol \textbf{192a} in 45 and 30\% yields, respectively (entry 1). The structure of the 2-alkynyl indole product was determined by \textsuperscript{1}H NMR spectroscopy and X-ray crystallography (Figure 4.1).\textsuperscript{144} Our studies subsequently showed that formation of the 2-vinylidene indolin-3-ol byproduct could be suppressed to give \textbf{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\textsubscript{3}N or K\textsubscript{2}CO\textsubscript{3} as well as 1 equiv of the latter inorganic base (entries 3-7). Likewise, changing the solvent from toluene to MeNO\textsubscript{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\textsubscript{6}, AgSbF\textsubscript{6} or AgBF\textsubscript{4} was employed as the catalyst, the Meyer–Schuster rearrangement adduct \textbf{193a} was also afforded as a side product in 15–55\% yield (entries 14-16).\textsuperscript{145} The analogous AgOAc mediated reaction was the only instance in
**Table 4.1** Optimization of reaction conditions.$^a$

![Diagram](image_url)

<table>
<thead>
<tr>
<th>Entry</th>
<th>Catalyst</th>
<th>Solvent</th>
<th>Yield (%)$^b$</th>
</tr>
</thead>
<tbody>
<tr>
<td></td>
<td></td>
<td></td>
<td>191a</td>
</tr>
<tr>
<td>1$^c$</td>
<td>AgOTf</td>
<td>PhMe</td>
<td>45</td>
</tr>
<tr>
<td>2</td>
<td>AgOTf</td>
<td>PhMe</td>
<td>88</td>
</tr>
<tr>
<td>3$^d$</td>
<td>AgOTf</td>
<td>PhMe</td>
<td>78</td>
</tr>
<tr>
<td>4$^e$</td>
<td>AgOTf</td>
<td>PhMe</td>
<td>69</td>
</tr>
<tr>
<td>5$^f$</td>
<td>AgOTf</td>
<td>PhMe</td>
<td>86</td>
</tr>
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<td>6$^g$</td>
<td>AgOTf</td>
<td>PhMe</td>
<td>85</td>
</tr>
<tr>
<td>7$^h$</td>
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<td>PhMe</td>
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<td>MeNO$_2$</td>
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</tr>
<tr>
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<td>AgOTf</td>
<td>1,4-dioxane</td>
<td>79</td>
</tr>
<tr>
<td>10</td>
<td>AgOTf</td>
<td>(CH$_2$Cl)$_2$</td>
<td>65</td>
</tr>
<tr>
<td>11</td>
<td>AgOTf</td>
<td>THF</td>
<td>-$^i$</td>
</tr>
<tr>
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<td>AgOTf</td>
<td>MeCN</td>
<td>-$^i$</td>
</tr>
<tr>
<td>13</td>
<td>AgNTf$_2$</td>
<td>PhMe</td>
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</tr>
<tr>
<td>16</td>
<td>AgBF$_4$</td>
<td>PhMe</td>
<td>35</td>
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</table>

$^a$ Reaction performed at 70 °C for 2 h under optimized conditions.
$^b$ Yields are based on isolated product.
$^c$ Reaction conducted under nitrogen atmosphere.
$^d$ Reaction performed in the absence of solvent.
$^e$ Reaction conducted in the presence of 10 mol% of catalyst.
$^f$ Reaction performed in the presence of 10 mol% of additive.
$^g$ Reaction conducted in the presence of 10 mol% of solvent.
$^h$ Reaction conducted in the presence of 10 mol% of catalyst.
$^i$ Reaction conducted in the presence of 10 mol% of solvent.

81
Table 4.1 (continued)

<table>
<thead>
<tr>
<th>Entry</th>
<th>Catalyst</th>
<th>Solvent</th>
<th>Yield (%)$^b$</th>
</tr>
</thead>
<tbody>
<tr>
<td></td>
<td></td>
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<td>191a</td>
</tr>
<tr>
<td>17</td>
<td>AgOAc</td>
<td>PhMe</td>
<td>-</td>
</tr>
<tr>
<td>18</td>
<td>Cu(OTf)$_2$</td>
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<td>68</td>
</tr>
<tr>
<td>19</td>
<td>Yb(OTf)$_3$</td>
<td>PhMe</td>
<td>50</td>
</tr>
<tr>
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<td>$p$-TsOH·H$_2$O</td>
<td>PhMe</td>
<td>-</td>
</tr>
<tr>
<td>21</td>
<td>TFA</td>
<td>PhMe</td>
<td>20</td>
</tr>
<tr>
<td>22</td>
<td>TfOH</td>
<td>PhMe</td>
<td>32</td>
</tr>
<tr>
<td>23</td>
<td>Tf$_2$NH</td>
<td>PhMe</td>
<td>35</td>
</tr>
</tbody>
</table>

$^a$All reactions were performed at the 0.1 mmol scale with catalyst/$\text{190a}$ 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$_3$N. $^e$Reaction carried out in the presence of 10 mol % of Et$_3$N. $^f$Reaction carried out in the presence of 5 mol % of K$_2$CO$_3$. $^g$Reaction carried out in the presence of 10 mol % of K$_2$CO$_3$. $^h$Reaction carried out in the presence of 1 equiv of K$_2$CO$_3$. $^i$No reaction based on TLC and $^j$H NMR analysis of the crude reaction mixture. $^j$Decomposition products obtained based on TLC and $^l$H 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$_2$NH, whereas $p$-TsOH·H$_2$O 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. 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 tBuCl, which furnished 191a in low yields of 13-38%. 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 R1 or R2 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.

<table>
<thead>
<tr>
<th>Product</th>
<th>Reaction Conditions</th>
<th>Isolated Yield (%)</th>
</tr>
</thead>
<tbody>
<tr>
<td>191b</td>
<td>R = F (88%)</td>
<td>94%</td>
</tr>
<tr>
<td>191c</td>
<td>R = Cl (87%)</td>
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<tr>
<td>191d</td>
<td>R = Br (89%)</td>
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<tr>
<td>191e</td>
<td>R = OMe (92%)</td>
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</tr>
<tr>
<td>191f</td>
<td>X = O (91%)</td>
<td></td>
</tr>
<tr>
<td>191g</td>
<td>X = S (94%)</td>
<td></td>
</tr>
<tr>
<td>191h</td>
<td>R = iBu (76%)</td>
<td></td>
</tr>
<tr>
<td>191i</td>
<td>R = nHex (79%)</td>
<td></td>
</tr>
<tr>
<td>191j</td>
<td>R = Br (80%)</td>
<td></td>
</tr>
<tr>
<td>191k</td>
<td>R = Cl (81%)</td>
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</tr>
<tr>
<td>191l</td>
<td>R = Me (93%)</td>
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<td>191m</td>
<td>R = Ph (92%)</td>
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</tr>
<tr>
<td>191n</td>
<td>R = nPent (72%)</td>
<td></td>
</tr>
<tr>
<td>191o</td>
<td>R = Ph (92%)</td>
<td></td>
</tr>
<tr>
<td>191p</td>
<td>R = nPent (72%)</td>
<td></td>
</tr>
<tr>
<td>191q</td>
<td>R = Cl, R = OMe</td>
<td>45%</td>
</tr>
<tr>
<td>191r</td>
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<td>R = Cl, R = OMe</td>
<td>88%</td>
</tr>
<tr>
<td>191t</td>
<td>R = Ph, R = nPent</td>
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</tr>
<tr>
<td>191u</td>
<td>R = Ph, R = nPent</td>
<td>61%</td>
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<tr>
<td>191v</td>
<td>R = Ph, R = nPent</td>
<td>38%</td>
</tr>
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</table>

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.

Reaction performed for 0.5 h. 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. Starting 1,4-diols 190v and 190w, with a pendant thiophene or alkyne moiety at R1, 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 R2 = pClC6H4 and R4 = Cl and 190x where R2 = 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 AgI 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 H2O, gives AgI-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
Chapter IV

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

![Proposed reaction pathway for the formation of 2-alkynyl indoles.](image)

**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.
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-yn-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.\textsuperscript{1,2} While this has led to a myriad of impressive approaches for furan synthesis being developed over the years,\textsuperscript{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-yn-1,4-diols with AgOTf as the catalyst.\textsuperscript{151} Further exploration of this field led us to examine the potential Brønsted acid catalyzed reactivity of readily available propargylic 1,4-diols \textbf{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\textsubscript{2}, to give 3,4-dihalodihydrofurans (Scheme 5.1, eq 1).\textsuperscript{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 \textit{p}-TsOH.H\textsubscript{2}O can mediate tandem alkylation/cycloisomerization of but-2-yn-1,4-diols \textbf{194} with 1,3-dicarbonyl compounds \textbf{30} (Scheme 5.1, eq 2). This process provides a convenient synthetic route to tetrasubstituted furans \textbf{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-H₂O 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 MeNO2 with 10 mol % of p-TsOH·H2O 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 Tf2NH in place of p-TsOH·H2O as the catalyst or employing dichloromethane as the solvent (entries 3-5 and 7). Changing the catalyst from p-TsOH·H2O to HCl or solvent from MeNO2 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 MeNO2 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 MeNO2 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. On the basis of the above results, reaction of 194a with 30a in the presence of 10 mol % of p-TsOH·H2O in MeNO2 at room temperature for 6 h provided the

Table 5.1 Optimization of reaction conditions.

<table>
<thead>
<tr>
<th>Entry</th>
<th>Catalyst</th>
<th>Solvent</th>
<th>Conditions</th>
<th>Yield (%)</th>
<th>195a</th>
<th>196a</th>
<th>197a</th>
</tr>
</thead>
<tbody>
<tr>
<td>1</td>
<td>p-TsOH·H2O</td>
<td>MeNO2</td>
<td>r.t./6</td>
<td>92</td>
<td>-</td>
<td>-</td>
<td></td>
</tr>
<tr>
<td>2b</td>
<td>p-TsOH·H2O</td>
<td>MeNO2</td>
<td>r.t./6</td>
<td>68</td>
<td>-</td>
<td>-</td>
<td></td>
</tr>
<tr>
<td>3</td>
<td>TfOH</td>
<td>MeNO2</td>
<td>r.t./6</td>
<td>20</td>
<td>-</td>
<td>-</td>
<td></td>
</tr>
<tr>
<td>4</td>
<td>TFA</td>
<td>MeNO2</td>
<td>r.t./6</td>
<td>72</td>
<td>-</td>
<td>-</td>
<td></td>
</tr>
<tr>
<td>5</td>
<td>Tf2NH</td>
<td>MeNO2</td>
<td>r.t./6</td>
<td>25</td>
<td>-</td>
<td>-</td>
<td></td>
</tr>
<tr>
<td>6</td>
<td>HCl</td>
<td>MeNO2</td>
<td>r.t./6</td>
<td>-c</td>
<td>-</td>
<td>-</td>
<td></td>
</tr>
<tr>
<td>7</td>
<td>p-TsOH·H2O</td>
<td>CH2Cl2</td>
<td>r.t./6</td>
<td>20</td>
<td>-</td>
<td>-</td>
<td></td>
</tr>
<tr>
<td>8</td>
<td>p-TsOH·H2O</td>
<td>1,4-dioxane</td>
<td>r.t./6</td>
<td>-d</td>
<td>-</td>
<td>-</td>
<td></td>
</tr>
<tr>
<td>9</td>
<td>p-TsOH·H2O</td>
<td>PhMe</td>
<td>80/1</td>
<td>-</td>
<td>53</td>
<td>-</td>
<td></td>
</tr>
<tr>
<td>10c</td>
<td>p-TsOH·H2O</td>
<td>PhMe</td>
<td>80/1</td>
<td>-</td>
<td>58</td>
<td>-</td>
<td></td>
</tr>
<tr>
<td>11c</td>
<td>p-TsOH·H2O</td>
<td>(CH2Cl)2</td>
<td>80/1</td>
<td>-</td>
<td>80</td>
<td>-</td>
<td></td>
</tr>
<tr>
<td>12c</td>
<td>p-TsOH·H2O</td>
<td>(CH2Cl)2</td>
<td>80/0.5</td>
<td>-</td>
<td>30</td>
<td>54</td>
<td></td>
</tr>
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</table>
optimum conditions to the tetrasubstituted furan. On the other hand, reaction of 194a with 10 mol % of p-TsOH·H₂O 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·H₂O as the catalyst and MeNO₂ 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 R¹, R² and R³, with 30a gave 195b-g and 195j-l in excellent yields of 78-91%. Replacing the aryl substituent at R¹ 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 5.1 (continued)

<table>
<thead>
<tr>
<th>Entry</th>
<th>Catalyst</th>
<th>Solvent</th>
<th>Conditions</th>
<th>Yield (%)</th>
<th>195a</th>
<th>196a</th>
<th>197a</th>
</tr>
</thead>
<tbody>
<tr>
<td>13f</td>
<td>p-TsOH·H₂O</td>
<td>MeNO₂</td>
<td>80/1</td>
<td>55</td>
<td>-</td>
<td></td>
<td></td>
</tr>
<tr>
<td>14f</td>
<td>p-TsOH·H₂O</td>
<td>CH₃CN</td>
<td>80/1</td>
<td>-</td>
<td>20</td>
<td>44</td>
<td></td>
</tr>
</tbody>
</table>

"All reactions were performed with 194a:30a ratio = 1:2 and 10 mol % of catalyst.

³Reaction performed with 5 mol % of catalyst. ⁴Mixture of unknown decomposition products obtained based on TLC and ¹H NMR analysis of the reaction mixture. ⁵No reaction observed based on TLC and ¹H NMR analysis of the reaction mixture.

⁶Reaction performed in the absence of 30a."
Table 5.2 Tandem cycloisomerizations of 194b-r with 30a-d catalyzed by $p$-TsOH·H$_2$O.$^a$

![Diagram of cycloisomerization reaction]

All reactions were performed with 194:30 ratio = 1:2 and 10 mol% of $p$-TsOH·H$_2$O 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.

$^a$All reactions were performed with 194:30 ratio = 1:2 and 10 mol% of $p$-TsOH·H$_2$O 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·H₂O.²

<table>
<thead>
<tr>
<th></th>
<th>R²</th>
<th>R³</th>
<th>R⁴</th>
<th>R⁵</th>
<th></th>
<th>R⁶</th>
<th>R⁷</th>
<th>R⁸</th>
<th>R⁹</th>
</tr>
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<tbody>
<tr>
<td>196b</td>
<td>R = F (80%)</td>
<td>196c</td>
<td>R = Cl (80%)</td>
<td>196d</td>
<td>R = Br (81%)</td>
<td>196e</td>
<td>R = Me (79%)</td>
<td></td>
<td></td>
</tr>
<tr>
<td>196f</td>
<td>R¹ = Ph, R² = p-Br(C₆H₄) (83%)</td>
<td>196f</td>
<td>R¹ = Ph, R² = p-Br(C₆H₄) (83%)</td>
<td>196g</td>
<td>R¹ = Ph, R² = p-Me(C₆H₄) (82%)</td>
<td>196h</td>
<td>R¹ = C=CPH, R² = Ph (-)²</td>
<td></td>
<td></td>
</tr>
<tr>
<td>196i</td>
<td>R¹ = t-Bu, R² = Ph (-)²</td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>196j</td>
<td>R = F (81%)</td>
<td>196k</td>
<td>R = Br (83%)</td>
<td>196l</td>
<td>R = t-Bu (85%)</td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>196m</td>
<td>R = 1-naphthyl (80%)</td>
<td>196n</td>
<td>R = cyclohexyl (74%)</td>
<td>196o</td>
<td>R = Me (62%)</td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>196p</td>
<td>R = t-Bu (62%)</td>
<td></td>
<td></td>
<td></td>
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</tr>
</tbody>
</table>

²All reactions were performed at the 0.16 mmol scale with 10 mol% of p-TsOH·H₂O in 1,2-dichloroethane at 80 °C for 1 h. Values in parenthesis denote isolated product yields. ³Product obtained as a 2.5:1 mixture of regioisomers. ⁴Product obtained as a 3.3:1 mixture of regioisomers. ⁵Mixture of decomposition products obtained that could not be identified by ¹H NMR analysis or mass spectrometry.
R¹ \neq R², 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.\(^{155}\)

![Figure 5.1 ORTEP drawing of (a) 195d, (b) 195q, (c) 195r and (d) 198m with thermal ellipsoids at 50% probability levels.](image-url)
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_{2}O 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.\textsuperscript{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 \textsuperscript{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_{2}O 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_{2}O 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$_2$O 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. 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 \( \text{II} \) generated from the secondary 1,4-diol \( 194m \) (Scheme 2, path 2). This would give the propargylic adduct \( \text{VII} \), which can isomerize to its enolate form and protonate at the remaining hydroxyl moiety by \( p\text{-TsOH-H}_2\text{O} \) to form cationic tautomer \( \text{VIII} \). Cyclization of this cationic intermediate involving nucleophilic substitution of the enolic oxygen onto the protonated hydroxyl group would give \( \text{IX} \), which can undergo aromatization via \( \text{X} \) to afford \( 198m \).

\[ \text{Scheme 5.3 Tentative mechanism for cycloisomerization of 194 catalyzed by} \]

\[ p\text{-TsOH-H}_2\text{O}. \]

At 80 °C, it is thought that deprotonation of \( \text{II} \) preferentially occurs at the secondary carbinol carbon center to give the cumulenol \( \text{XI} \) that readily isomerizes to the allenyl ketone \( 197 \) (Scheme 5.3). In a manner similar to that reported for the analogous metal catalyzed allenoate/allenyl ketone cyclizations, 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 of the resultant cyclic oxonium intermediate \( \text{XII} \) would give \( \text{XIII} \), 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$_2$O.
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·H₂O 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 \textit{d}_6-194a in 1,2-dichloroethane with p-TsOH·H₂O (10 mol %) under the conditions shown in Scheme 5.4, eq 2 gave \textit{d}_5-196a in 72% yield but with no retention of D content at C3 in the product, as determined by both \textit{^1}H NMR analysis and GC-MS measurements (Scheme 5.4, eq 2). In contrast, repeating the reactions of \textit{d}_6-194a and 194a with 10 equiv of D₂O afforded \textit{d}_6-196a and \textit{d}_1-196a in 61% and 64% yield and with a D content of 92%, incorporated at C3 of the adduct based on \textit{^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. For example, the indole structure can be found in the alkaloid natural products aristotelone, fluorocurine, rauniticine pseudoindoxyl and diketopiperazine (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). Added to this is their ability to serve as versatile building blocks for functional materials and utility as ligands in metalloocene-based olefin polymerization catalysts. For this reason, the synthesis of these two

![Chemical structures](image)

*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.\textsuperscript{168}

In the course of our studies exploring the utility of unsaturated alcohols in organic synthesis,\textsuperscript{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.\textsuperscript{170}

![Scheme 6.1 AgOTf catalyzed reactivities](image)

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 MnO₂ 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 °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 ¹H NMR and X-ray 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 AgSbF₆ as the catalyst (entry 1). Changing the catalyst from AgOTf to

![Scheme 6.2](image_url)
Table 6.1 Optimization of reaction conditions.\textsuperscript{a}

\begin{table}[h]
\centering
\begin{tabular}{llll}
\hline
Entry & Catalyst & Solvent & Yield (%)\textsuperscript{b} \\
\hline
1 & AgSbF\textsubscript{6} & PhMe & 35 \\
2 & AgOTf & CH\textsubscript{2}Cl\textsubscript{2} & 72 \\
3 & AgOTf & 1,4-dioxane & \textsuperscript{c} \\
4 & AgOTf & CH\textsubscript{3}CN & \textsuperscript{c} \\
5 & AgOTf & CH\textsubscript{3}NO\textsubscript{2} & 81 \\
6 & AgBF\textsubscript{4} & PhMe & \textsuperscript{c} \\
7 & AgOAc & PhMe & \textsuperscript{c} \\
8 & AgN(Tf)\textsubscript{2} & PhMe & \textsuperscript{c} \\
9 & Cu(OTf)\textsubscript{2} & PhMe & \textsuperscript{d} \\
10 & Yb(OTf)\textsubscript{3} & PhMe & \textsuperscript{d} \\
11 & TfOH & PhMe & \textsuperscript{e} \\
12 & Tf\textsubscript{2}NH & PhMe & \textsuperscript{e} \\
\hline
\end{tabular}
\end{table}

\textsuperscript{a}All reactions were performed at the 0.14 mmol scale with 10 mol\% of catalyst at r.t. for 15 h. \textsuperscript{b}Isolated yield. \textsuperscript{c}No reaction based on TLC and \textsuperscript{1}H NMR analysis of crude reaction mixture. \textsuperscript{d}Trace amount of product obtained based on TLC and \textsuperscript{1}H NMR analysis of crude reaction mixture. \textsuperscript{e}Mixture of decomposition products obtained based on TLC and \textsuperscript{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$_3$CN were instances in which no reaction was observed based on TLC and $^1$H 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$_2$NH 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$_3$NO$_2$ 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.\(^a\)

<table>
<thead>
<tr>
<th>Product</th>
<th>R</th>
<th>Yield (%)</th>
</tr>
</thead>
<tbody>
<tr>
<td>200c</td>
<td>R = F</td>
<td>82%</td>
</tr>
<tr>
<td>200d</td>
<td>R = Cl</td>
<td>83%</td>
</tr>
<tr>
<td>200e</td>
<td>R = Br</td>
<td>80%</td>
</tr>
<tr>
<td>200f</td>
<td>R = Me</td>
<td>88%</td>
</tr>
<tr>
<td>200g</td>
<td>R = OMe</td>
<td>89%</td>
</tr>
<tr>
<td>200h</td>
<td>R = H</td>
<td>90%</td>
</tr>
<tr>
<td>200i</td>
<td>R = Cl</td>
<td>82%</td>
</tr>
<tr>
<td>200j</td>
<td>R = Br</td>
<td>84%</td>
</tr>
<tr>
<td>200k</td>
<td>R = Me</td>
<td>92%</td>
</tr>
<tr>
<td>200l</td>
<td>R = OMe</td>
<td>94%</td>
</tr>
<tr>
<td>200m</td>
<td>R = H</td>
<td>85%</td>
</tr>
<tr>
<td>200n</td>
<td>R = Cl</td>
<td>80%</td>
</tr>
<tr>
<td>200o</td>
<td>R = Br</td>
<td>81%</td>
</tr>
<tr>
<td>200p</td>
<td>R = Me</td>
<td>86%</td>
</tr>
<tr>
<td>200q</td>
<td>R = OMe</td>
<td>87%</td>
</tr>
<tr>
<td>200r</td>
<td>R = H</td>
<td>88%</td>
</tr>
<tr>
<td>200s</td>
<td>R = Br</td>
<td>83%</td>
</tr>
<tr>
<td>200t</td>
<td>R = Me</td>
<td>86%</td>
</tr>
<tr>
<td>200u</td>
<td>(87%)(^b)</td>
<td></td>
</tr>
<tr>
<td>200v</td>
<td>(85%)(^c)</td>
<td></td>
</tr>
<tr>
<td>200w</td>
<td>(85%)(^d)</td>
<td></td>
</tr>
<tr>
<td>200x</td>
<td>R = Me</td>
<td>82%</td>
</tr>
<tr>
<td>200y</td>
<td>R = Br</td>
<td>84%</td>
</tr>
</tbody>
</table>

\(^a\)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).\textsuperscript{171}

\begin{figure}[h]
\centering
\includegraphics[width=\textwidth]{200d_ortep.png}
\caption{ORTEP drawing of 200d with thermal ellipsoids at 50% probability levels.}
\end{figure}

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$_2$O 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. Griseofulvin family of compounds, which have been reported to be known as an orally active antimycotic drug, display inter alia anti-inflammatory and herbicidal activity and aromatase inhibition. These interesting spirocyclic benzofuranone containing compounds can be potentially occurred from tandem cycloisomerization of 4-hydroxy-1-(2-hydroxyphenyl)-4,4-di-phenylbut-2-yn-1-ones in the presence of Lewis or Brønsted acid catalyzed conditions that in the similar way of Chapter VI (Scheme 7.1).

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

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. 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 spirobenzofuranone 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-1H-pyrazol-1-yl)benzenesulfonamide derivatives
Proposed Synthetic Scheme:

1. AcOH, 90 °C
2. 5M HCl, 30 min
3. H₂O

R = TBDMS

TBAF

MnO₂, CH₂Cl₂
cat.

R = H, alkyl, aryl, heteroaryl
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](image)

*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 H2O and N-halosuccinimide (NXS, X = I, 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-H2O 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-H2O 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 ($m/z$).
Chapter IX

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-Cyclopropyl-2-1-Cyclo-propyl-2-propyn-1-ols (170aa)-(170ap) and (170aw) & (170ay)-(170bd):

\[
\begin{align*}
\text{R}_1^1, \text{R}_3^3 = \text{alkyl, aryl} \\
\text{LDA} & \quad \text{THF, } -78 \degree C \quad \text{O} \\
\text{R}_1^1 & \quad + \quad \text{R}_2^2 \quad \rightarrow \quad \text{R}_1^1 \quad \text{R}_2^2 \quad \text{OH}^2
\end{align*}
\]

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 \(-78 \degree C\). The resulting solution was stirred for a further 1 h at \(-78 \degree C\) 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\(_4\)Cl (10 mL) and extracted with diethyl ether (2 x 30 mL). The combined organic layers were washed with brine (20 mL), dried over Mg\(_2\)SO\(_4\), 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- Cyclopropyl-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 \degree 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 NH₄Cl aq. (10 mL). The organic layer was extracted with diethyl ether (10 mL x 3). The combined organic layers were dried over anhydrous MgSO₄, 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**

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\textsuperscript{103,104}

\[
\text{Ph} \equiv \text{OH}
\]

Yield: 65%; white solid; m.p. 69-71 ºC; \(^1^H\) NMR (CDCl\(_3\), 500 MHz): \(\delta\) 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): \(\delta\) 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.

\textbf{1-Cyclopropyl-1-(4-fluorophenyl)-3-phenylprop-2-yn-1-ol 170ab\textsuperscript{103,104}}

\[
\text{Ph} \equiv \text{OH}
\]

Yield: 80%; pale yellow oil; \(^1^H\) NMR (CDCl\(_3\), 500 MHz): \(\delta\) 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): \(\delta\) 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.

\textbf{1-(4-Chlorophenyl)-1-cyclopropyl-3-phenylprop-2-yn-1-ol 170ac\textsuperscript{103,104}}

\[
\text{Ph} \equiv \text{OH}
\]

Yield: 78%; pale yellow oil; \(^1^H\) NMR (CDCl\(_3\), 500 MHz): \(\delta\) 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): \(\delta\) 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

Yield: 68%; pale yellow oil; \( ^1 \)H NMR (CDCl\(_3\), 500 MHz): \( \delta \) 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): \( \delta \) 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\(_3\)Na 345.1467, found 345.1469.

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

Yield: 70%; pale yellow oil; \( ^1 \)H NMR (CDCl\(_3\), 500 MHz): \( \delta \) 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): \( \delta \) 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

Yield: 72%; pale yellow oil; \(^1^H\) NMR (CDCl\(_3\), 500 MHz): \(\delta\) 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): \(\delta\) 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\(_3\)O\(_2\) 347.1259, found 347.1258.

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

Yield: 75%; pale yellow oil; \(^1^H\) NMR (CDCl\(_3\), 500 MHz): \(\delta\) 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): $\delta$ 163.2, 161.3, 159.8, 142.0, 141.0, 133.5, 127.3 (d, 1C, $J_{C-F} = 32.3$ Hz), 114.9 (t, 1C, $J_{C-F} = 81.1$ 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$_{19}$FONa 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 °C; $^1$H NMR (CDCl$_3$, 500 MHz): $\delta$ 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): $\delta$ 163.2, 161.2, 149.7, 142.4, 140.5, 136.3, 127.4 (t, 1C, $J_{C-F} = 41.6$) 123.1, 114.8 (d, 1C, $J_{C-F} = 85$), 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 °C; $^1$H NMR (CDCl$_3$, 500 MHz): $\delta$ 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): $\delta$ 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$_{18}$N$_2$O$_2$ 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 °C; $^1$H NMR (CDCl$_3$, 500 MHz): $\delta$ 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): $\delta$ 163.3, 161.4, 139.9, 132.3, 132.0, 127.20 (t, 1C, $J_{C,F}$ = 31.5), 118.3, 115.1 (d, 1C $J_{C,F}$ = 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): $\delta$ 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): $\delta$ 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): calcld 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 °C; \(^1\)H NMR (CDCl\(_3\), 500 MHz): \(\delta\) 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): \(\delta\) 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): calcld for C\(_{24}\)H\(_{22}\)O\(_3\)Na 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): \(\delta\) 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): \(\delta\) 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\(_{25}\)O\(_2\) 405.1855, found 405.1864.

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

![Chemical structure](image)

Yield: 85%; light brown Color oil; \(^1\)H NMR (CDCl\(_3\), 400 MHz): \(\delta\) 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): \(\delta\) 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-cyclopropynon-2-yn-1-ol 170ao

![Chemical structure](image)

Yield: 65%; pale yellow oil; \(^1\)H NMR (CDCl\(_3\), 500 MHz): \(\delta\) 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): \(\delta\) 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): $\delta$ 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): $\delta$ 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-methylocyclohexyl)-3-phenylprop-2-yn-1-ol 170aq

Yield: 78%; light yellow color oil; $^1$H NMR (CDCl$_3$, 500 MHz): $\delta$ 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): $\delta$ 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): $\delta$ 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): $\delta$ 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.
125 MHz): $\delta$ 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

\[
\begin{align*}
&\text{Yield: 80%; colorless oil; }^1\text{H NMR (CDCl}_3, 500 MHz): \delta 2.17 (t, 2H, J = 6.9), 1.75 (s, 1H), 1.50-1.44 (m, 2H), 1.40-1.15 (m, 7H), 1.08 (s, 9H), 0.89 (t, 3H, J = 6.9), 0.55-0.52 (m, 3H), 0.39-0.34 (m, 1H); \quad ^{13}\text{C NMR (CDCl}_3, 125 MHz): \delta 85.8, 79.08, 79.00, 39.4, 31.2, 28.7, 28.5, 25.6, 22.5, 18.5, 16.1, 14.0, 4.6, 0.5; \quad \text{IR (neat, cm}^{-1}\text{): 3419, 3018, 2921, 2299, 1645, 1215, 756, 667: HRMS (ESI): calcd for C}_{16}\text{H}_{29}\text{O 237.2218, found 237.2217.}
\end{align*}
\]

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

\[
\begin{align*}
&\text{Yield: 75%; colorless oil; }^1\text{H NMR (CDCl}_3, 500 MHz): \delta 2.08 (t, 2H, J = 6.9), 2.04 (s, 1H), 1.66-1.60 (m, 2H), 1.48-1.17 (m, 16H), 1.00-0.94 (m, 1H), 0.83-0.80 (m, 6H), 0.50-0.28 (m, 4H); \quad ^{13}\text{C NMR (CDCl}_3, 125 MHz): \delta 85.2, 79.8, 73.3, 67.8, 43.2, 31.8, 31.2, 29.5, 28.7, 28.4, 25.5, 24.5, 22.6, 22.5, 20.8, 18.4, 14.0, 13.9, 2.8, 0.6; \quad \text{IR (neat, cm}^{-1}\text{): 3421, 3018, 2928, 2358, 1634, 1215, 1109, 757, 669: HRMS (ESI): calcd for C}_{18}\text{H}_{33}\text{O 265.2531, found 265.2536.}
\end{align*}
\]
1-(4-Chlorophenyl)-1-cyclopropylprop-2-yn-1-ol 170au

Yield: 70%; brown oil; $^1$H NMR (CDCl$_3$, 500 MHz): $\delta$ 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): $\delta$ 142.8, 133.5, 128.3, 126.9, 83.3, 74.4, 73.8, 23.4, 3.2, 2.3; HRMS (ESI): calcld 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): $\delta$ 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): $\delta$ 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): calcld 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): $\delta$ 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): $\delta$ 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): $\delta$ 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): $\delta$ 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): $\delta$ 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, diastereomer 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): $\delta$ 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.

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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): $\delta$ 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): $\delta$ 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): $\delta$ 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): $\delta$ 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,
Chapter IX

669: HRMS (ESI): calcd for C_{16}H_{14}ClO_{3} 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): \(\delta\) 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): \(\delta\) 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}H_{19}O_{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): \(\delta\) 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): \(\delta\) 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

\[
\text{Ph} \quad \text{OH}
\]

Yield: 80%; light yellow color oil; \(^1\)H NMR (CDCl\(_3\), 500 MHz): \(\delta\) 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): \(\delta\) 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-ynyl) -4-fluorobenzene 183ab

\[
\text{Ph} \quad \text{EtO} \\
\text{C} \text{C} \quad \text{F}
\]

Colorless oil; \(^1\)H NMR (CDCl\(_3\), 300 MHz): \(\delta\) 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): \(\delta\) 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

\[
\text{Ph} \quad \text{EtO} \\
\text{C} \text{C} \quad \text{F}
\]

Colorless oil; \(^1\)H NMR (CDCl\(_3\), 500 MHz): \(\delta\) 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, $J_{C-F}$ = 32.2 Hz), 123.8, 123.2, 115.3 (d, 1C, $J_{C-F}$ = 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

![Structure](image)

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

![Structure](image)

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 = 6.7 Hz), 1.25 (t, 3H, J = 7.0 Hz), 0.98 (d, 3H, J = 6.7 Hz); $^{13}$C NMR (CDCl$_3$, 125 MHz): δ 163.0, 161.3, 138.4, 134.1, 131.9, 128.4, 127.2, 123.1, 122.8, 115.4, 95.5, 86.0, 69.3, 66.2, 32.0, 17.9, 15.2; IR (neat, cm$^{-1}$): 3436, 2866, 1602, 1505, 1231, 1109, 832, 755, 460; HRMS (ESI): calcd for C$_{20}$H$_{20}$OCl 295.1498, found 295.1493.
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): $\delta$ 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): $\delta$ 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, 927, 756, 669; HRMS (ESI): calcd for C$_{22}$H$_{22}$F$_3$O$_2$ 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): $\delta$ 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): $\delta$ 163.3, 161.4, 159.7, 141.7, 134.5 (d, 1C, $J_{CF} = $12.2 Hz), 133.3(d, 1C, $J_{CF} = $30.1), 127.70 (d, 1C, $J_{CF} = $
31.9 Hz), 124.3, 115.4, 115.2 (d, 1C, $J_{C-F} = 30.9$ 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$_2$Na 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): $\delta$ 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): $\delta$ 163.4, 161.4, 150.1, 143.3, 136.5, 136.1, 133.6 (d, 1C, $J_{C-F} = 12.1$ Hz), 127.70 (d, 1C, $J_{C-F} = 32.1$ Hz), 127.2, 123.1, 123.8, 115.2 (d, 1C, $J_{C-F} = 86.0$ 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$_{19}$FO$_2$Na 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): $\delta$ 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): \(\delta\) 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

![Chemical structure](image)

White solid; m.p. 47-49 °C; \(^1\)H NMR (CDCl\(_3\), 500 MHz): \(\delta\) 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): \(\delta\) 163.5, 161.5, 136.5, 133.6, 132.1 (d, 1C, J\(_{C,F}\) = 38.3 Hz), 128.0, 127.6 (d, 1C, J\(_{C,F}\) = 32.2 Hz), 123.3, 118.4, 115.3 (d, 1C, J\(_{C,F}\) = 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): $\delta$ 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): $\delta$ 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$_3$ 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): $\delta$ 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): $\square$ 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$_3$Na 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): $\delta$ 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): $\delta$ 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): $\delta$ 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): $\delta$ 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_{3} 327.1749, found 327.1743.

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

\[
\begin{align*}
\text{H}_3\text{C(H}_2\text{)C} & \\
\text{EtO} & \\
\text{Cl} & \\
\end{align*}
\]

Pale yellow oil; \textsuperscript{1}H NMR (CDCl\textsubscript{3}, 300 MHz): \(\delta\) 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); \textsuperscript{13}C NMR (CDCl\textsubscript{3}, 75 MHz): \(\delta\) 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\textsubscript{20}H\textsubscript{18}ClO 319.1829, found 319.1843.

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

\[
\begin{align*}
\text{H}_3\text{C(H}_2\text{)C} & \\
\text{EtO} & \\
\text{Ph} & \\
\end{align*}
\]

Colorless oil; \textsuperscript{1}H NMR (CDCl\textsubscript{3}, 500 MHz): \(\delta\) 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); \textsuperscript{13}C NMR (CDCl\textsubscript{3}, 125 MHz): \(\delta\) 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): $\delta$ 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): $\delta$ 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): $\delta$ 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): $\delta$ 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): $\delta$ 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): $\delta$ 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, 2928, 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): $\delta$ 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): $\delta$ 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): $\delta$ 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): $\delta$ 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): $\delta$ 7.82 (d, 2H, $J = 7.8$ Hz), 7.62-7.26 (m, 10H), 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): $\delta$ 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): $\delta$ 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): $\delta$ 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): $\delta$ 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): $\delta$ 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-ynyl-1,3-diyl)dibenzene 183ay

Colorless oil; mixture of E/Z isomers = 5:1; $^1$H NMR (CDCl$_3$, 400 MHz): $\delta$ 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): $\delta$ 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, 127.4, 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): $\delta$ 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), 3.80 (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); 13C NMR (CDCl3, 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 C32H31O2 447.2324, found 447.2328.

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

Pale yellow oil; 1H NMR (CDCl3, 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); 13C NMR (CDCl3, 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 C18H17ClO3Na 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): $\delta$ 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): $\delta$ 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, 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): $\delta$ 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): $\delta$ 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): $\delta$ 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): $\delta$ 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$_3$ 339.1749, found 339.1751.

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

Pale yellow oil; $^1$H NMR (CDCl$_3$, 300 MHz): $\delta$ 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): $\delta$ 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-(Vinyl oxy)hex-3-en-1-yne-1,3-diyl) dibenzene 183bg

Pale yellow oil; $^1$H NMR (CDCl$_3$, 300 MHz): $\delta$ 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): $\delta$ 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): $\delta$ 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): $\delta$ 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): $\delta$ 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): $\delta$ 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): $\delta$ 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): $\delta$ 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): $\delta$ 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): $\delta$ 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): $\delta$ 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)$^{103,104}$

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$_4$Cl aq. (50 mL). The organic layer was extracted with Et$_2$O (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

To a round bottom flask containing 170 (0.2 mmol) in acetone:H$_2$O (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 Na₂S₂O₃ (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**

\[
\begin{align*}
\text{F} & \quad \text{OH} \\
\text{F} & \quad \text{F}
\end{align*}
\]

Yield: 80%; colorless oil; \(^1\)H NMR (CDCl₃, 400 MHz): \(\delta\) 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 (CDCl₃, 100 MHz): \(\delta\) 163.1, 160.6, 142.8 (d, 1C, \(J_{C-F} = 12.4\) Hz), 128.59 (d, 1C, \(J_{C-F} = 31.8\) Hz), 114.8 (d, 1C, \(J_{C-F} = 84.1\) Hz), 21.8, 1.8; IR (neat, cm\(^{-1}\)): 3334, 3018, 1604, 1506, 1215, 1159, 837, 752, 669, 518; HRMS (ESI): calcd for C₁₆H₁₅OF₂ 261.1091, found 261.1086.
Bis(4-chlorophenyl)(cyclopropyl)methanol 170bf

Yield: 85%; colorless oil: $^1$H NMR (CDCl$_3$, 400 MHz): $\delta$ 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): $\delta$ 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): $\delta$ 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): $\delta$ 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): $\delta$ 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): \( \delta \) 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

![Structure](image)

Yield: 87%; colorless oil; \(^1\)H NMR (CDCl\(_3\), 300 MHz): \( \delta \) 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): \( \delta \) 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

![Structure](image)

Yield: 76%; colorless oil; \(^1\)H NMR (CDCl\(_3\), 400 MHz): \( \delta \) 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): \( \delta \) 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\(_{15}\)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): $\delta$ 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): $\delta$ 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$_2$Cl 289.0995, found 289.0989.

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

Yield: 84%; colorless oil; $^1$H NMR (CDCl$_3$, 400 MHz): $\delta$ 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): $\delta$ 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 °C; $^1$H NMR (CDCl$_3$, 300 MHz): $\delta$ 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): $\delta$ 147.2, 146.3, 140.8, 139.8, 128.7, 128.0, 127.3, 127.2, 127.0, 126.8, 126.6, 121.5, 1031, 839, 748, 700, 667, 628, 621, 514, 506; IR (neat, cm$^{-1}$): 3392, 3018, 1645, 1487, 1446, 1215, 1031, 839, 748, 700, 667, 628, 621, 514, 499; HRMS (ESI): calcd for C$_{22}$H$_{20}$NOa 323.1412, found 323.1404.

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

Yield: 70%; white solid; m.p. 111-113 °C; $^1$H NMR (CDCl$_3$, 400 MHz): $\delta$ 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): $\delta$ 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): $\delta$ 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): $\delta$ 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): $\delta$ 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): $\delta$ 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): $\delta$ 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): $\delta$ 84.9, 71.6, 69.8, 29.6, 21.6, 2.4, 1.5; IR (neat, cm$^{-1}$): 3369, 1446, 1215, 921, 756, 702,
Diphenyl(2-phenylcyclopropyl)methanol 170bs

Yield: 82%; colorless oil; $^1$H NMR (CDCl$_3$, 400 MHz): $\delta$ 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): $\delta$ 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): $\delta$ 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): $\delta$ 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

\[
\text{\includegraphics[width=2cm]{cyclopropylphenylmethanol.png}}
\]

Yield: 83%; colorless; \(^1\)H NMR (CDCl\(_3\), 400 MHz): \(\delta 7.42-7.27\) (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): \(\delta 144.0, 128.3, 127.4, 126.1, 78.4, 19.1, 3.7, 2.8\); 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

\[
\text{\includegraphics[width=2cm]{cyclopropylhexanol.png}}
\]

Yield: 79%; colorless; \(^1\)H NMR (CDCl\(_3\), 400 MHz): \(\delta 2.86-2.81\) (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): \(\delta 76.9, 37.2, 31.9, 25.4, 22.6, 18.0, 14.0, 2.7, 2.4\); IR (neat, cm\(^{-1}\)): 3352, 1449, 1215, 914, 757, 667, 519; HRMS (ESI): calcd for C\(_9\)H\(_{19}\)O 143.1436, found 143.1442

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

\[
\text{\includegraphics[width=2cm]{cis-tetrahydroiodofuran.png}}
\]

White solid; m.p. 117-119 °C; \(^1\)H NMR (CDCl\(_3\), 500 MHz): \(\delta 7.77-7.55\) (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): \(\delta 139.2, 131.9, 128.7, 128.5, 128.33, 128.31, 126.0, 122.3, 88.7, 88.3, 85.5, 67.1, 37.8, 33.1\); IR (neat, cm\(^{-1}\)): 3464, 3431, 3016, 1635, 1490, 1215, 1026, 752, 667, 532; HRMS (ESI): calcd for C\(_{18}\)H\(_{16}\)OI
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375.0246, found 375.0258.

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

![Chemical Structure]

Reaction time (min): step 1/2 (90/15); white solid; m.p. 91-93 °C; \(^1\)H NMR (CDCl\(_3\), 400 MHz): \(\delta\) 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); \(^1^3\)C NMR (CDCl\(_3\), 100 MHz): \(\delta\) 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, 752, 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

![Chemical Structure]

Reaction time (min): step 1/2 (120/15); light brown oil; \(^1\)H NMR (CDCl\(_3\), 400 MHz): \(\delta\) 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); \(^1^3\)C NMR (CDCl\(_3\), 100 MHz): \(\delta\) 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\(_2\)I 418.9466, found 418.9478.
2,2-Bis(4-bromophenyl)-tetrahydro-3-iodofuran 188bg

![Chemical Structure]

Reaction time (min): step 1/2 (120/15); light brown solid; m.p. 160-162 °C; $^1$H NMR (CDCl$_3$, 400 MHz): $\delta$ 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): $\delta$ 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

![Chemical Structure]

Reaction time (min): step 1/2 (30/20); pale yellow solid; m.p. 83-85 °C; $^1$H NMR (CDCl$_3$, 400 MHz): $\delta$ 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): $\delta$ 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

![Structure of tetrahydro-3-iodo-2,2-di-p-tolylfuran 188bi](image)

Reaction time (min): step 1/2 (15/20); colorless oil; \(^1\)H NMR (CDCl\(_3\), 300 MHz): \(\delta\) 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): \(\delta\) 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, 1251, 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

![Structure of tetrahydro-3-iodo-2,2-bis(4-methoxyphenyl)furan 188bj](image)

Reaction time (min): step 1/2 (20/15); brown oil; \(^1\)H NMR (CDCl\(_3\), 400 MHz): \(\delta\) 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): \(\delta\) 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\(_3\)I 411.0457, found 411.0461.

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

\[
\begin{align*}
&\text{H}_3C-\begin{array}{c}
\text{Cl} \\
\text{O}
\end{array} \\
&\begin{array}{c}
\text{Cl} \\
\text{H}
\end{array}
\end{align*}
\]

Reaction time (min): step 1/2 (60/15); pale yellow oil; dr ratio = 5:4; \(^1\)H NMR (CDCl\(_3\), 400 MHz): \(\delta 7.46 (d, 1H, J = 8.4 \text{ 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): \(\delta 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): caled for C\(_{17}\)H\(_{17}\)OClI 399.0013, found 399.0016.

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

\[
\begin{align*}
&\text{H}_3CO-\begin{array}{c}
\text{Cl} \\
\text{O}
\end{array} \\
&\begin{array}{c}
\text{Cl} \\
\text{H}
\end{array}
\end{align*}
\]

Reaction time (min): step 1/2 (60/15); brown color oil; dr ratio = 7:4; \(^1\)H NMR (CDCl\(_3\), 300 MHz): \(\delta 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): \(\delta 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\(_{17}H_{17}O_2\)ClI 414.9962, found 414.9964.

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

![Structure](image)

Reaction time (min): step 1/2 (15/10); colorless oil; dr ratio = 3:2; \(^1\)H NMR (CDCl\(_3\), 300 MHz): \(\delta\) 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): \(\delta\) 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**

![Structure](image)

Reaction time (min): step 1/2 (60/15); off white solid; m.p. 134-136 °C; dr ratio = 1:1; \(^1\)H NMR (CDCl\(_3\), 400 MHz): \(\delta\) 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): \(\delta\)
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 C₂₂H₂₀OI 427.0559, found 427.0558.

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

\[
\text{\begin{center}
\includegraphics[width=0.3\textwidth]{cistrifuran_188bo.png}
\end{center}}
\]

Reaction time (min): step 1/2 (120/60); brown solid; m.p. 116-118 °C; ᵃ¹H NMR (CDCl₃, 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); ᵃ¹³C NMR (CDCl₃, 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 C₂₀H₁₈IO 401.0402, found 401.0421.

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

\[
\text{\begin{center}
\includegraphics[width=0.3\textwidth]{cistrifuran_188bp.png}
\end{center}}
\]

Reaction time (min): step 1/2 (30/10); colorless oil; ᵃ¹H NMR (CDCl₃, 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); ᵃ¹³C NMR (CDCl₃, 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**

![Structure of 188bq]

Reaction time: step 1/2 (120/60); colorless oil; \(^1\)H NMR (CDCl\(_3\), 300 MHz): \(\delta\) 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): \(\delta\) 142.1, 128.8, 126.8, 126.4, 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**

![Structure of 188ba]

Reaction time (min): step 1/2 (20/30); pale yellow oil; \(^1\)H NMR (CDCl\(_3\), 400 MHz): \(\delta\) 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): \(\delta\) 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.
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*Cis*-2-(2-(tetrahydro-3-iodo-2-(4-methoxyphenyl)furan-2-yl)ethynyl)pyridine

188ai

![Structure of 188ai](image)

Reaction time (min): step 1/2 (30/15); light brown oil; $^1$H NMR (CDCl$_3$, 300 MHz): $\delta$ 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): $\delta$ 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$_2$I 406.0304, found 406.0306.

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

![Structure of 188aq](image)

Reaction time (min): step 1/2 (30/10); colorless oil; $^1$H NMR (CDCl$_3$, 400 MHz): $\delta$ 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): $\delta$ 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

\[
\begin{array}{c}
\text{Reaction time (min): step 1/2 (30/60); light brown oil; } ^1\text{H NMR (CDCl}_3, 400 \text{ MHz): } \delta \nolimits 7.56-7.49 (m, 4H), 7.34-7.25 (m, 6H), 4.53 (t, 1H, } J = 7.3 \text{ Hz), 4.26-4.09 (m, 2H), 2.86-2.77 (m, 1H), 2.62-2.53 (m, 1H); ^{13}\text{C NMR (CDCl}_3, 100 \text{ MHz): } \delta \nolimits 132.0, 129.0, 128.9, 128.29, 128.27, 121.8, 121.7, 86.7, 86.6, 84.9, 84.4, 66.9, 37.2, 30.8; \text{ IR (neat, cm}^{-1}) : 3356, 3018, 1490, 1215, 752, 669, 513; \text{ HRMS (ESI): calcd for C}_{20}\text{H}_{16}\text{O}I 399.0246, \text{ found 399.0257.}
\end{array}
\]

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

\[
\begin{array}{c}
\text{Reaction time (min): step 1/2 (15/15); pale yellow solid; m.p. 122-124 } \degree \text{C; dr ratio = 1:0.6; } ^1\text{H NMR (CDCl}_3, 400 \text{ MHz): } \delta \nolimits 7.55-7.46 (m, 5H), 7.37-7.09 (m, 19H), 5.67 (dd, 1H, } J = 8.6, 6.1 \text{ Hz, cis or trans isomer), 5.42 (bt, 1H, } J = 4.1 \text{ Hz, cis or trans isomer), 5.29 (bt, 1H, } J = 5.7 \text{ Hz, cis or trans isomer), 4.90 (t, 1H, } J = 7.4 \text{ Hz, cis or trans isomer), 3.00 (a quin, 1H, } J = 7.1 \text{ Hz, cis or trans isomer), 2.76-2.70 (m, 1H, cis or trans isomer), 2.67-2.60 (m, 1H, cis or trans isomer), 2.45-2.38 (m, 1H, cis or trans isomer); ^{13}\text{C NMR (CDCl}_3, 100 \text{ MHz): } \delta \nolimits 147.4, 146.8, 144.6, 142.6, 141.39, 141.34, 128.7, 128.5, 128.4, 127.76, 127.71, 127.6, 127.4, 127.3, 127.1, 126.6, 126.43, 126.41, 126.3, 126.2, 126.1, 91.8 (cis or trans isomer), 90.9 (cis or trans isomer), 81.6 (cis or trans isomer), 78.3 (cis or trans isomer), 46.79 (cis or trans isomer), 46.74 (cis}
\end{array}
\]
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**

![Tetrahydro-3-iodo-5-pentyl-2,2-diphenylfuran](image)

Reaction time (min): step 1/2 (15/30); colorless oil; dr ratio = 1:0.6; \(^1\)H NMR (CDCl\(_3\), 300 MHz): \(\delta\) 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): \(\delta\) 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 °C dr ratio = 1:0.6; $^1$H NMR (CDCl$_3$, 500 MHz): $\delta$ 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): $\delta$ 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): $\delta$ 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): $\delta$ 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,
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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**

![Cis-3-bromo-tetrahydro-2-phenyl-2-(2-phenylethynyl)furan 188bw](image)

Reaction time (min): step 1/2 (15/20); white solid; m.p. 95-97 °C; $^1$H NMR (CDCl$_3$, 300 MHz): $\delta$ 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): $\delta$ 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, 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**

![Cis-3-chloro-tetrahydro-2-phenyl-2-(2-phenylethynyl)furan 188bx](image)

Reaction time (min): step 1/2 (15/120); white solid; m.p. 70-72 °C; $^1$H NMR (CDCl$_3$, 300 MHz): $\delta$ 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): $\delta$ 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

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

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

![Chemical structure image]

Reaction time (min): step 1/2 (30/120); light brown oil; $^1$H NMR (CDCl$_3$, 300 MHz): $\delta$ 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): $\delta$ 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

![Chemical structure image]

Reaction time (min): step 1/2 (30/60); colorless oil; $^1$H NMR (CDCl$_3$, 300 MHz): $\delta$ 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): $\delta$ 142.4, 128.2, 127.0, 125.4, 99.6, 97.2, 89.9 (d, 1C, $J_{C,F} = 75.1$ Hz), 65.4, 35.5 (d, 1C, $J_{C,F} = 31.9$ 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

![Chemical structure image]

Colorless oil; $^1$H NMR (CDCl$_3$, 300 MHz): $\delta$ 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): $\delta$ 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): $\delta$ 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): $\delta$ 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): $\delta$ 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): $\delta$ 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}O_{3}S 331.1157, found 331.1165.

7.4 Silver Triflate-Catalyzed Tandem Heterocyclization/Alkynylation of 1-((2-Tosylamino)aryl)but-2-yn-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)\textsuperscript{128,138a,140}

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\textsubscript{2}O (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\textsubscript{4}Cl (10 mL) and extracted with EtOAc (2 x 10 mL). The combined organic layers were washed with water, brine solution, dried over anhydrous Na\textsubscript{2}SO\textsubscript{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 \( N-(2-(1,4\text{-Dihydroxybut-2-yn-1-yl})phenyl)-4\text{-methylbenzenesulfonamides} \) (190a)-(190u) & (19ov)

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 \(-78^\circ\text{C}\) in a dropwise manner. The resulting solution was stirred for 1 h prior to slow addition of the corresponding \( N-(2-(1\text{-hydroxy-1-phenylprop-2-yn-1-yl})phenyl)-4\text{-methylbenzenesulfonamide} \) (C)\textsuperscript{135a} (0.50g, 1.3 mmol) in THF at \(-78^\circ\text{C}\). 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 \( \text{NH}_4\text{Cl} \) (50 mL) and extracted with EtOAc (2 x 25 mL). The combined organic layers were washed with water, brine, dried over \( \text{Na}_2\text{SO}_4 \) and concentrated under reduced pressure. Purification by flash column chromatography on silica gel (eluent: \( n\text{-hexane}:\text{EtOAc} = 7.5:2.5 \)) 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-1H-indoles (191a)-(191x)

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-methylbenzenesulfonamide 190a

Yield: 85%; white solid; m.p. 152-154 °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$_4$S 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 solid; 99-101 °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$_4$S 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 °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): $\delta$ 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, 766. HRMS (ESI): calcd for C$_{29}$H$_{24}$NO$_4$SFNa 524.1308, found 524.1301.

$N$-(2-(4-(4-chlorophenyl)-1,4-dihydroxy-1-phenylbut-2-yn-1-yl)phenyl)-4-methylbenzenesulfonylamide 190d

\[
\text{Ph} \quad \text{OH} \\
\text{NH} \\
\text{Ts} \\
\text{Cl} \\
\text{OH}
\]

Yield: 60%; pale yellow soil; m.p. 64-66 °C; dr ratio = 1:1; $^1$H NMR (CDCl$_3$, 500 MHz): $\delta$ 8.87 (bs, 1H), 7.36-6.85 (m, 17H), 5.37 (s, 1H, A or B diastereomer), 5.32 (s, 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): $\delta$ 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$_{24}$NO$_4$SCl 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 °C; dr ratio = 1:1; \(^1\)H NMR (CDCl\(_3\), 400 MHz): \(\delta\) 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): \(\delta\) 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\(_4\)SBr 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): \(\delta\) 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), 3.581 (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$_5$S 514.1688, found 514.1703.

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

![Diagram of the molecule]

Yield: 55%; white solid; m.p. 142-144 °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), 7.46-7.2 (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$_5$SNa 556.1559, found 556.1539.
\[ N-(2-(4-(furan-2-yl)-1,4-dihydroxy-1-phenylbut-2-yn-1-yl)phenyl)-4-methylbenzenesulfonamide \]
\[ \text{190h} \]

Yield: 65%; brown oil; dr ratio = 1:1; \(^1\)H NMR (CDCl\(_3\), 400 MHz): \(\delta\) 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, 2H), 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): \(\delta\) 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\(_5\)S 474.1375, found 474.1383.

\[ N-(2-(1,4-dihydroxy-1-phenyl-4-(thiophen-2-yl)but-2-yn-1-yl)phenyl)-4-methylbenzenesulfonamide \]
\[ \text{190i} \]

Yield: 67%; pale yellow solid; m.p. 157-159 °C; dr ratio = 6:5; \(^1\)H NMR (MeOD, 400 MHz): \(\delta\) 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): \(\delta\) 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$_4$S$_2$ 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): $\delta$ 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): $\delta$ 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$_4$S 464.1896, found 464.1880.
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*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): $\delta$ 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, $J = 7.1$ Hz), 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): $\delta$ 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$_4$S 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): $\delta$ 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, \( J = 6.6 \text{ Hz, A or B diastereomer} \), 4.15 (d, 1H, \( J = 6.6 \text{ Hz, A or B diastereomer} \)),
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): \( \delta \) 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\(_4\)S
448.1583, found 448.1575.

\[ \text{N-(2-(4-cyclohexyl-1,4-dihydroxy-1-phenylbut-2-yn-1-yl)phenyl)-4-methylbenzenesulfonamide 190m} \]

Yield: 59%; white solid; m.p. 115-117 °C; dr ratio = 3:2; \(^1\)H NMR (CDCl\(_3\), 400 MHz):
\( \delta \) 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, \( J = 7.7 \text{ Hz} \)), 7.02 (t, 2H, \( J = 7.7 \text{ Hz} \)), 6.94-6.89 (m, 1H), 4.94 (bs, 1H),
4.16 (d, 1H, \( J = 6.1 \text{ Hz, A or B diastereomer} \)), 4.13 (d, 1H, \( J = 6.1 \text{ Hz, A or B diastereomer} \)),
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): \( \delta \) 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\(_4\)S 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): \(\delta\) 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): \(\delta\) 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, 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\(_4\)SBr 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 °C; dr ratio = 7:5; \(^1\)H NMR (CDCl\(_3\), 300 MHz): \(\delta\) 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): \(\delta\) 143.84, 143.80, 142.0, 141.9, 139.6, 139.5, 136.0, 135.9, 134.49, 134.43,
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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\(_4\)SCl 518.1193, found 518.1176.

\(N-(2-(1,4\text{-dihydroxy-1,4-diphenylbut-2-yn-1-yl})-4\text{-methylphenyl})-4\text{-methylbenzenesulfonamide} 190p\)

Yield: 67%; pale yellow oil; dr ratio = 1:1; \(^1\)H NMR (CDCl\(_3\), 400 MHz): \(\delta\) 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): \(\delta\) 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\(_4\)S 498.1739, found 498.1729.
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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 °C; dr ratio = 6:5; \(^1\)H NMR (CDCl\(_3\), 300 MHz): \(\delta\) 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): \(\delta\) 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\(_4\)SCl\(_2\) 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): \(\delta\) 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), 3.62 (s, 3H, A or B diastereomer), 3.58 (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): $\delta$ 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$_5$SCl 548.1298, found 548.1307.

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

![Chemical Structure](image)

Yield: 66%; yellow oil; dr ratio = 1:1; $^1$H NMR (CDCl$_3$, 300 MHz): $\delta$ 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): $\delta$ 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$_4$S 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$_4$S 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$_{23}$H$_{28}$NO$_4$S 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$_4$S$_2$Na 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\(_4\)S 508.1583, found 508.1567.

\[ \text{N-(2-(1,4-dihydroxy-1-phenylbut-2-yn-1-yl)phenyl)-4-methylbenzenesulfonamide} \]

190x

Yield: 55%; brown oil; \(^1\)H NMR (CDCl\(_3\), 500 MHz): \(\delta\) 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): \(\delta\) 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\(_4\)S 408.1270, found 408.1275.

\[ \text{3-Phenyl-2-(phenylethynyl)-1-tosyl-1H-indole} \]

191a

Light brown solid; m.p. 183-185 °C; \(^1\)H NMR (CDCl\(_3\), 300 MHz): \(\delta\) 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): \(\delta\) 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\(_{23}\)NO\(_2\)S 448.1371, found 448.1375.
2-(Phenylethynyl)-3-(p-tolyl)-1-tosyl-1H-indole 191b

White solid; m.p. 234-236 °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$_2$S 462.1528, found 462.1528.

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

White solid; m.p. 172-174 °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, $J_{C,F} = 28.2$ Hz), 132.1, 129.8, 129.7, 129.4 (t, 1C, $J_{C,F} = 16.6$ Hz), 128.0, 127.1, 126.4, 124.1, 120.3, 118.8 (d, 1C, $J_{C,F} = 13.7$ 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$_2$SF 466.1277, found 466.1293.
2-((4-Chlorophenyl)ethynyl)-3-phenyl-1-tosyl-1H-indole 191d

Pale yellow solid; m.p. 152-154 °C; $^1$H NMR (CDCl$_3$, 400 MHz): $\delta$ 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): $\delta$ 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, 1149, 1089, 1022, 927, 769, 669; HRMS (ESI): calcd for C$_{29}$H$_{21}$NO$_2$SCl 482.0982, found 482.0977.

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

White solid; m.p. 134-136 °C; $^1$H NMR (CDCl$_3$, 400 MHz): $\delta$ 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): $\delta$ 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$_2$SBr 526.0476, found 526.0472.
2-((4-Methoxyphenyl)ethynyl)-3-phenyl-1-tosyl-1H-indole 191f

![Chemical Structure](image1)

White solid; m.p. 141-143 °C; $^1$H NMR (CDCl$_3$, 300 MHz): $\delta$ 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): $\delta$ 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$_3$S 478.1477, found 478.1462.

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

![Chemical Structure](image2)

Colorless oil; $^1$H NMR (CDCl$_3$, 500 MHz): $\delta$ 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): $\delta$ 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$_2$S 498.1528, found 498.1515.
2-(Furan-2-yethynyl)-3-phenyl-1-tosyl-1H-indole 191h

Pale yellow solid; m.p. 165-167 °C; $^1$H NMR (CDCl$_3$, 500 MHz): $\delta$ 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): $\delta$ 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$_3$S 438.1164, found 438.1172.

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

White solid; m.p. 175-177 °C; $^1$H NMR (CDCl$_3$, 400 MHz): $\delta$ 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): $\delta$ 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$_2$S$_2$ 454.0935, found 454.0947.
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2-(3,3-Dimethylbut-1-yn-1-yl)-3-phenyl-1-tosyl-1H-indole 191j

![Chemical Structure]

Colorless oil; $^1$H NMR (CDCl$_3$, 500 MHz): $\delta$ 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): $\delta$ 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): calcld for C$_{27}$H$_{26}$NO$_2$S 428.1684, found 428.1683.

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

![Chemical Structure]

Light brown oil; $^1$H NMR (CDCl$_3$, 400 MHz): $\delta$ 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): $\delta$ 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): calcld for C$_{25}$H$_{22}$NO$_2$S 400.1371, found 400.1378.
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2-(Cyclopropylethynyl)-3-phenyl-1-tosyl-1H-indole 191

Brown solid; m.p. 70-72 °C; $^1$H NMR (CDCl$_3$, 400 MHz): $\delta$ 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): $\delta$ 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$_2$S 412.1371, found 412.1380.

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

White solid; m.p. 126-128 °C; $^1$H NMR (CDCl$_3$, 400 MHz): $\delta$ 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): $\delta$ 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$_2$S 454.1841, found 454.1842.
5-Bromo-3-phenyl-2-(phenylethynyl)-1-tosyl-1H-indole 191n

![Chemical Structure](image)

White solid; m.p. 173-175 °C; \(^1\)H NMR (CDCl\(_3\), 300 MHz): \(\delta 8.24\) (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); \(^1^3\)C NMR (CDCl\(_3\), 100 MHz): \(\delta 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\(_2\)SBr 526.0476, found 526.0461.

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

![Chemical Structure](image)

Light brown oil; \(^1\)H NMR (CDCl\(_3\), 400 MHz): \(\delta 8.27\) (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); \(^1^3\)C NMR (CDCl\(_3\), 100 MHz): \(\delta 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\(_3\)SCl 512.1087, found 512.1083.
5-Methyl-3-phenyl-2-(phenylethynyl)-1-tosyl-1H-indole 191p

White solid; m.p. 170-172 °C; 1H NMR (CDCl₃, 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); 13C NMR (CDCl₃, 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 C₃₀H₂₄NO₂S 462.1528, found 462.1531.

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

Light brown oil; 1H NMR (CDCl₃, 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); 13C NMR (CDCl₃, 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 C₂₉H₂₀NO₂SCl₂ 516.0592, found 516.0576.
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5-Chloro-2-((4-methoxyphenyl)ethynyl)-3-phenyl-1-tosyl-1H-indole 191r

Light brown oil; $^1$H NMR (CDCl$_3$, 400 MHz): $\delta$ 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): $\delta$ 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$_3$SCl 512.1087, found 512.1083.

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

Brown oil; $^1$H NMR (CDCl$_3$, 500 MHz): $\delta$ 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): $\delta$ 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$_2$S 498.1528, found 498.1534.
2-(Phenylethynyl)-1-tosyl-1H-indole 191t

Brown oil; $^1$H NMR (CDCl$_3$, 500 MHz): $\delta$ 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): $\delta$ 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, 927, 756, 669; HRMS (ESI): calcd for C$_{23}$H$_{18}$NO$_2$S 372.1058, found 372.1048.

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

Pale yellow oil; $^1$H NMR (CDCl$_3$, 400 MHz): $\delta$ 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): $\delta$ 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$_2$S 366.1528, found 366.1526.
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2-(Phenylethynyl)-3-(thiophen-2-yl)-1-tosyl-1H-indole 191v

![Structure](image)

Light yellow oil; $^1$H NMR (CDCl$_3$, 500 MHz): $\delta$ 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): $\delta$ 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$_2$S$_2$ 454.0935, found 454.0952.

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

![Structure](image)

Light yellow oil; $^1$H NMR (CDCl$_3$, 500 MHz): $\delta$ 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): $\delta$ 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$_2$S 472.1371, found 472.1375.
2-ethynyl-3-phenyl-1-tosyl-1H-indole 191x

![Structure](image)

Light brown oil; $^1$H NMR (CDCl$_3$, 500 MHz): $\delta$ 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): $\delta$ 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$_2$S 372.1058, found 372.1068.

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

![Structure](image)

Brown solid; m.p. 124-126 °C; $^1$H NMR (CDCl$_3$, 400 MHz): $\delta$ 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): $\delta$ 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$_3$S 466.1477, found 466.1495.

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

![Structure](image)

Pale yellow oil; $^1$H NMR (CDCl$_3$, 500 MHz): $\delta$ 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}\text{C} \text{NMR (CDCl}_3, 125 \text{ MHz)}: \delta 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; \text{IR (neat, cm}^{-1}): 3435, 3018, 1645, 1215, 779, 669, 524; \text{HRMS (ESI): calcd for } C_{29}H_{24}NO_3S 466.1477, \text{ 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)\(^{151,152}\)

![Chemical Structure](image)

\(R^1 = \text{alkyl, alkynyl, aryl, heteroaryl}\)
\(R^2 = \text{H, alkyl, alkynyl, aryl, heteroaryl}\)
\(R^3 = \text{alkyl, aryl, heteroaryl}\)

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 \(\text{NH}_4\text{Cl (50 mL)}\) and extracted with EtOAc (2 x 25 mL). The combined organic layers were washed with water, brine, dried over \(\text{Na}_2\text{SO}_4\) 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 \(-78^\circ\text{C}\) in a dropwise manner. The resulting solution
was stirred for 1 h prior to slow addition of the corresponding alkynol (B) (0.50 g, 1.3 mmol) in THF at −78 °C. The resulting mixture was stirred at same temperature for 1 h. The corresponding aldehyde (0.21 g, 2.0 mmol) in THF (2 mL) was added to the reaction mixture and allowed to stir for a further 1 h at same temperature. On completion, the reaction mixture was quenched by adding saturated NH₄Cl (50 mL) and extracted with EtOAc (2 x 25 mL). The combined organic layers were washed with water, brine, dried over Na₂SO₄ 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·H₂O (16 μmol) in MeNO₂ (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 MeNO₂ (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)

To a solution of \( p\text{-TsOH\cdot H}_2\text{O} \) (16 \( \mu \text{mol} \)) 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 °C 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 °C; \(^1\)H NMR (CD\(_3\)OD, 300 MHz): \( \delta \) 7.61-7.55 (m, 6H), 7.36-7.15 (m, 9H), 5.57 (s, 1H); \(^{13}\)C NMR (CD\(_3\)OD, 75 MHz): \( \delta \) 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 °C; $^1$H NMR (CDCl$_3$+CD$_3$OD, 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$_3$OD, 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$_2$F$_2$ 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 °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, 758, 669; HRMS (ESI): calcd for C$_{22}$H$_{17}$O$_2$Cl$_2$ 383.0606, found 383.0594.
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1,1-bis(4-Bromophenyl)-4-phenylbut-2-yne-1,4-diol 194d

![Chemical structure image]

Yield: 78%; off white solid; m.p. 133-135 °C; $^1$H NMR (CDCl$_3$, 400 MHz): $\delta$ 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): $\delta$ 143.34, 143.31, 139.8, 131.5, 128.8, 128.7, 128.5, 127.7, 127.6, 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$_2$Br$_2$ 470.9595, found 470.9602.

4-Phenyl-1,1-dip-tolylbut-2-yne-1,4-diol 194e

![Chemical structure image]

Yield: 81%; light brown solid; m.p. 140-142 °C; $^1$H NMR (CDCl$_3$, 400 MHz): $\delta$ 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): $\delta$ 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 °C; dr ratio = 1:1; \(^1^H\) NMR (CDCl\(_3\), 400 MHz): \(\delta\) 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): \(\delta\) 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\(_2\)Br 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 °C; \(^1^H\) NMR (CDCl\(_3\), 300 MHz): \(\delta\) 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): \(\delta\) 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 °C; $^1$H NMR (CDCl$_3$+CD$_3$OD, 500 MHz): $\delta$ 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$_3$OD, 125 MHz): $\delta$ 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-diphenylhexa-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): $\delta$ 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): $\delta$ 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 °C; \(^1\)H NMR (CDCl\(_3\), 500 MHz): \(\delta\) 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): \(\delta\) 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\(_2\)F 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 °C; \(^1\)H NMR (CDCl\(_3\)+CD\(_3\)OD, 500 MHz): \(\delta\) 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\(_3\)OD, 125 MHz): \(\delta\) 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\(_2\)Br 393.0490, found 393.0487.
4-(4-tert-Butylphenyl)-1,1-diphenylbut-2-yn-1,4-diol 194l

Yield: 78%; white solid; m.p. 162-164 °C; $^1$H NMR (CDCl$_3$+CD$_3$OD, 400 MHz): δ 7.59 (d, 4H, $J = 7.3$ Hz), 7.46 (d, 2H, $J = 7.8$ Hz), 7.38 (d, 2H, $J = 7.8$Hz) 7.29-7.21 (m, 6H) 5.50 (s, 1H), 1.30 (s, 9H); $^{13}$C NMR (CDCl$_3$+CD$_3$OD, 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-yn-1,4-diol 194m

Yield: 87%; light brown solid; m.p. 117-119 °C; $^1$H NMR (CDCl$_3$+CD$_3$OD, 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$_3$OD, 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-yn-1,4-diol 194n

Yield: 71%; white solid; m.p. 121-123 °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): $\delta$
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 °C; $^1$H NMR (CDCl$_3$+CD$_3$OD, 500
MHz): $\delta$ 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$_3$OD, 125 MHz): $\delta$
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$_2$S 321.0949, found 321.0965.

4-Cyclohexyl-1,1-diphenylbut-2-yne-1,4-diol 194p

Yield: 86%; white solid; m.p. 141-143 °C; $^1$H NMR (CDCl$_3$, 400 MHz): $\delta$
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): $\delta$
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-ylene-1,4-diol 194q

Yield: 80%; white solid; m.p. 109-111 °C; \(^1\)H NMR (CDCl\(_3\), 400 MHz): \(\delta\) 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): \(\delta\) 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-ylene-1,4-diol 194r

Yield: 82%; off white solid; m.p. 163-165 °C; \(^1\)H NMR (CDCl\(_3\)+CD\(_3\)OD, 400 MHz): \(\delta\) 7.58-7.22 (m, 10H), 4.10 (s, 1H), 3.63 (bs, 2H), 1.01 (s, 9H); \(^{13}\)C NMR (CDCl\(_3\)+CD\(_3\)OD, 100 MHz): \(\delta\) 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, 1645, 1489, 1448, 1328, 1215, 1004, 927, 769, 667; HRMS (ESI): calcd for C\(_{20}\)H\(_{23}\)O\(_2\) 295.1698, found 295.1706.

1,1,-Triphenylbut-2-ylene-1,4-diol \(d_6\)-194a

Yield: 81%; white solid; m.p. 141-143 °C; \(^1\)H NMR (CDCl\(_3\)+CD\(_3\)OD, 400 MHz): \(\delta\)
7.59 (d, 4H, \( J = 7.6 \text{ Hz} \)), 7.30-7.20 (m, 6H), 3.2 (bs, 2H); \(^{13}\)C NMR (CDCl\(_3\)+CD\(_3\)OD, 100 MHz): \( \delta \) 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\(_{22}\)H\(_{14}\)O\(_2\) 320.1699, found 320.1686.

(4-(2,2-Diphenylvinyl)-2,5-diphenylfuran-3-yl)(phenyl)methanone 195a

![Diagram of 195a](image)

Yellow solid; m.p. 124-126 °C; \(^1\)H NMR (CDCl\(_3\), 400 MHz): \( \delta \) 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): \( \delta \) 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\(_2\)Na 525.1831, found 525.1830.

(4-(2,2-bis(4-Fluorophenyl)vinyl)-2,5-diphenylfuran-3-yl)(phenyl)methanone 195b

![Diagram of 195b](image)

Yellow solid; m.p. 173-175 °C; \(^1\)H NMR (CDCl\(_3\), 400 MHz): \( \delta \) 7.86-7.84 (m, 2H), 7.54-6.84 (m, 20H), 6.75 (s, 1H), 6.62 (t, 1H, \( J = 8.7 \text{ Hz} \)); \(^{13}\)C NMR (CDCl\(_3\), 100 MHz): \( \delta \) 191.1, 163.8, 163.4, 161.4, 161.0, 152.4, 152.3, 149.8, 149.7, 145.5 (d, 1C,
\( J_{CF} = 14.2 \text{ Hz} \), 142.6, 138.9, (d, 1C, \( J_{CF} = 12.2 \text{ Hz} \)), 138.6, 137.1, 136.7, 134.8, 132.9, 132.7, 132.4, 132.3, 130.58 (d, 1C, \( J_{CF} = 24.6 \text{ Hz} \)), 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, \( J_{CF} = 10.0 \text{ Hz} \)), 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, \( \text{cm}^{-1} \)): 3392, 3018, 2397, 1647, 1506, 1444, 1328, 1215, 898, 756; HRMS (ESI): calcd for \( \text{C}_{37}\text{H}_{24}\text{O}_{2}\text{F}_{2}\text{Na} \) 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 \( ^{\circ}\text{C} \); \( ^1\text{H} \) NMR (CDCl\(_3\), 400 MHz): \( \delta \) 7.82 (d, 2H, \( J = 7.4 \text{ Hz} \)), 7.49-7.17 (m, 15H), 7.08 (d, 2H, \( J = 8.4 \text{ Hz} \)), 6.87 (d, 2H, \( J = 8.4 \text{ Hz} \)), 6.81 (d, 2H, \( J = 8.4 \text{ Hz} \)), 6.77 (s, 1H); \( ^{13}\text{C} \) NMR (CDCl\(_3\), 100 MHz): \( \delta \) 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, \( \text{cm}^{-1} \)): 3442, 3018, 2399, 1647, 1506, 1490, 1417, 1338, 1215, 1091, 1014, 927, 777, 669; HRMS (ESI): calcd for \( \text{C}_{37}\text{H}_{25}\text{O}_{2}\text{Cl}_{2} \) 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 °C; $^1$H NMR (CDCl$_3$, 400 MHz): $\delta$ 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): $\delta$ 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, 129.2, 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$_2$Br$_2$ 659.0221, found 659.0221.

(4-(2,2-di-p-Tolylinyl)-2,5-diphenylfuran-3-yl)(phenyl)methanone 195e

Pale yellow solid; m.p. 176-178 °C; $^1$H NMR (CDCl$_3$, 500 MHz): $\delta$ 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): $\delta$ 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)methanone 195f

Pale yellow solid; m.p. 155-157 °C; E/Z ratio = 1.3:1; $^1$H NMR (CDCl$_3$, 400 MHz): $\delta$
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): $\delta$ 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_{2}BrNa 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 °C; E/Z ratio = 1.1:1; $^1$H NMR (CDCl$_3$, 400 MHz): $\delta$
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): $\delta$ 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\(_2\)Na 539.1987, found 539.1994.

\((4\text{-}(2,4\text{-Diphenylbut-1-en-3-yn-1-yl})\text{-}2,5\text{-diphenylfuran-3-yl})(\text{phenyl})\text{methanone}

195h

\[
\begin{array}{c}
\text{Ph} \\
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Yellow solid; m.p. 118-120 °C; E/Z ratio = 1:1; \(^1\)H NMR (CDCl\(_3\), 400 MHz): \(\delta\) 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): \(\delta\) 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)methanone 195i

![Chemical structure of 195i](image)

Pale yellow solid; m.p. 145-147 °C; E/Z ratio = 1:2; $^1$H NMR (CDCl₃, 400 MHz): $\delta$ 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 (CDCl₃, 100 MHz): $\delta$ 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, 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 C₃₅H₃₁O₂ 483.2324, found 483.2326.

(4-(2,2-Diphenylvinyl)-5-(4-fluorophenyl)-2-phenylfuran-3-yl)(phenyl)methanone 195j

![Chemical structure of 195j](image)

Pale yellow solid; m.p. 143-145 °C; $^1$H NMR (CDCl₃, 400 MHz): $\delta$ 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 (CDCl₃, 100 MHz): $\delta$ 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, $J_{C,F} = 26.1$ Hz), 128.00, 127.86, 127.81, 127.7, 127.4, 127.3, 127.0, 126.9 (d, 1C, $J_{C,F} = 16.8$ 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 $C_{37}H_{26}O_{2}F$ 521.1917, found 521.1916.

(5-(4-Bromophenyl)-4-(2,2-diphenylvinyl)-2-phenylfuran-3-yl)(phenyl)methanone 195k

Pale yellow solid; m.p. 181-183 °C; $^1$H NMR (CDCl$_3$, 400 MHz): $\delta$ 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): $\delta$ 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 $C_{37}H_{26}O_{2}Br$ 581.1116, found 581.1128.

(5-(4-(tert-Butyl)phenyl)-4-(2,2-diphenylvinyl)-2-phenylfuran-3-yl)(phenyl)methanone 195l

Yellow oil; $^1$H NMR (CDCl$_3$, 300 MHz): $\delta$ 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): $\delta$ 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 C₄₁H₃₅O₂ 559.2637, found 559.2644.

(4-(2,2-Diphenylyvinyl)-5-(naphthalen-1-yl)-2-phenylfuran-3-yl)(phenyl)methanone 195n

Brown oil; \(^1\)H NMR (CDCl₃, 400 MHz): \(\delta\) 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); \(^1^3\)C NMR (CDCl₃, 100 MHz): \(\delta\) 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 C₄₁H₃₅O₂ 553.2168, found 553.2161.

(4-(2,2-Diphenylyvinyl)-2-phenyl-5-(thiophen-2-yl)furan-3-yl)(phenyl)methanone 195o

Yellow oil; \(^1\)H NMR (CDCl₃, 400 MHz): \(\delta\) 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); \(^1^3\)C NMR
(CDCl$_3$, 100 MHz): $\delta$ 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, 128.0, 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$_{30}$O$_2$S 509.1575, found 509.1594.

(5-Cyclohexyl-4-(2,2-diphenylyvinyl)-2-phenylfuran-3-yl)(phenyl)methanone 195p

Yellow oil; $^1$H NMR (CDCl$_3$, 400 MHz): $\delta$ 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): $\delta$ 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$_2$S 509.2481, found 509.2474.

(4-(2,2-Diphenylyvinyl)-5-methyl-2-phenylfuran-3-yl)(phenyl)methanone 195q

Pale yellow solid; m.p. 143-145 °C; $^1$H NMR (CDCl$_3$, 400 MHz): $\delta$ 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): $\delta$ 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\textsubscript{32}H\textsubscript{25}O\textsubscript{2} 441.1855, found 441.1855.

(5-(\textit{tert}-Butyl)-4-(2,2-diphenylvinyl)-2-phenylfuran-3-yl)(phenyl)methanone 195r

Pale yellow solid; m.p. 125-127 °C; \textsuperscript{1}H NMR (CDCl\textsubscript{3}, 500 MHz): \( \delta \) 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); \textsuperscript{13}C NMR (CDCl\textsubscript{3}, 125 MHz): \( \delta \) 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\textsuperscript{-1}): 3419, 3016, 2972, 2432, 2399, 1651, 1598, 1519, 1489, 1423, 1319, 1215, 1074, 1028, 927, 781, 667; HRMS (ESI): calcd for C\textsubscript{35}H\textsubscript{31}O\textsubscript{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 °C; \textsuperscript{1}H NMR (CDCl\textsubscript{3}, 400 MHz): \( \delta \) 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); \textsuperscript{13}C NMR (CDCl\textsubscript{3}, 100 MHz): \( \delta \) 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\textsuperscript{-1}): 3018, 2399, 1647, 1521, 1419, 1215, 927, 771, 669; HRMS (ESI): calcd for C\textsubscript{32}H\textsubscript{25}O\textsubscript{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): \(\delta\) 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): \(\delta\) 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): \(\delta\) 7.76 (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): \(\delta\) 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

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Ph
\[\text{\textcircled{O}}\]
Ph
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Pale yellow solid; m.p. 91-93 °C; $^1$H NMR (CDCl$_3$, 400 MHz): $\delta$ 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): $\delta$ 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

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F
\[\text{\textcircled{O}}\]
F
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Pale yellow oil; $^1$H NMR (CDCl$_3$, 400 MHz): $\delta$ 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): $\delta$ 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 °C; $^1$H NMR (CDCl$_3$, 400 MHz): $\delta$ 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): $\delta$ 153.0, 146.9, 133.46, 133.43, 132.4, 130.1, 129.9, 129.2, 129.0, 128.8, 128.7, 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 °C; $^1$H NMR (CDCl$_3$, 400 MHz): $\delta$ 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): $\delta$ 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$_2$Na 474.9309, found 474.9297.
**5-Phenyl-2,3-di-p-tolylfuran 196e**

![Structure](image)

Pale yellow oil; $^1$H NMR (CDCl$_3$, 500 MHz): $\delta$ 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): $\delta$ 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): $\delta$ 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): $\delta$ 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

![Structure](image)

Brown solid; m.p. 142-144 °C; regioisomeric ratio = 3.3:1; $^1$H NMR (CDCl$_3$, 400 MHz): $\delta$ 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): $\delta$ 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, 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

![Structure](image)

Pale yellow oil; $^1$H NMR (CDCl$_3$, 500 MHz): $\delta$ 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): $\delta$ 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, $J_{C,F} = 13.1$ 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$_{23}$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): $\delta$ 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): $\delta$ 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, 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 $^\circ$C; $^1$H NMR (CDCl$_3$, 300 MHz): $\delta$ 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): $\delta$ 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): $\delta$ 8.58 (d, 1H, $J = 8.4$ Hz), 7.91 (d, 1H,
$J = 7.5 \text{ Hz}$, 7.87-7.85 (m, 2H), 7.66 (d, 2H, $J = 7.3 \text{ Hz}$), 7.58-7.51 (m, 5H), 7.41 (t, 2H, $J = 7.4 \text{ Hz}$), 7.36-7.24 (m, 4H), 6.90 (s, 1H); $^{13}$C NMR (CDCl$_3$, 125 MHz): $\delta$ 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): $\delta$ 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): $\delta$ 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, 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): $\delta$ 7.50 (d, 2H, $J = 7.5 \text{ Hz}$), 7.40-7.19 (m, 8H), 6.15 (s, 1H), 2.38 (s, 3H); $^{13}$C NMR (CDCl$_3$, 125 MHz): $\delta$ 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): $\delta$ 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): $\delta$ 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 °C; $^1$H NMR (CDCl$_3$, 400 MHz): $\delta$ 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): $\delta$ 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, 1647, 1521, 1419, 1338, 1215, 927, 771, 669; HRMS (ESI): calcd for C$_{22}$ $^1$H$_{16}$ $^2$HO 298.1342, found 298.1332.

2,3,5-Triphenylfuran $d_3$-196a

Yellow solid; m.p. 91-93 °C; $^1$H NMR (CDCl$_3$, 500 MHz): $\delta$ 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): $\delta$
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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\(_{22}\)H\(_{12}\)\(^{2}\)H\(_2\)O 302.1593, found 302.1604.

**2,3,5-Triphenylfuran \(d_6\)-196a**

![Image of 2,3,5-Triphenylfuran](image)

Pale yellow oil; \(^1\)H NMR (CDCl\(_3\), 500 MHz): \(\delta\) 7.62-7.46 (m, 4H), 7.40-7.23 (m, 6H); \(^{13}\)C NMR (CDCl\(_3\), 75 MHz): \(\delta\) 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\(_{22}\)H\(_{11}\)\(^{2}\)H\(_6\)O 303.1656, found 303.1659.

**1,4,4-Triphenylbuta-2,3-dien-1-one 197a**

![Image of 1,4,4-Triphenylbuta-2,3-dien-1-one](image)

Brown color oil; \(^1\)H NMR (CDCl\(_3\), 400 MHz): \(\delta\) 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): \(\delta\) 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): $\delta$ 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): $\delta$ 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 °C; $E/Z$ ratio = 1:1; $^1$H NMR (CDCl$_3$, 400 MHz): $\delta$ 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): $\delta$ 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)\textsuperscript{138a,152,153}

\[
\begin{array}{c}
\text{HO} & \text{R}^2 & \text{NH} \\
\text{R}^1 & \text{NH} & \text{OH} \\
\end{array}
\]

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\textsubscript{4}Cl (50 mL) and extracted with EtOAc (2 x 25 mL). The combined organic layers were washed with water, brine, dried over Na\textsubscript{2}SO\textsubscript{4} and concentrated under reduced pressure. To the obtained crude, MnO\textsubscript{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: \textit{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 °C; 1H NMR (400 MHz, CDCl3) 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); 13C NMR (CDCl3, 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 C29H23NO4SNa 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 °C; ¹H NMR (300 MHz, CDCl₃) 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); ¹³C NMR (CDCl₃, 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 C₂₅H₂₂NO₂ 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 °C; ¹H NMR (CDCl₃, 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); ¹³C NMR (CDCl₃, 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, Jₐ=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 C₂₅H₂₀NO₂F₂ 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 °C; $^1$H NMR (CDCl$_3$, 500 MHz): $\delta$ 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): $\delta$ 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, 1571, 1421, 1215, 1093, 1012, 927, 769, 669; HRMS (ESI): calcd for C$_{25}$H$_{20}$NO$_2$Cl$_2$ 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 °C; $^1$H NMR (400 MHz, CDCl$_3$) $\delta$ 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): $\delta$ 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
C₂₅H₂₀NO₂Br₂ 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; ¹H NMR (400 MHz, CDCl₃) 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); ¹³C NMR (CDCl₃, 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 C₂₇H₂₆NO 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 °C; ¹H NMR (400 MHz, CDCl₃) 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); ¹³C NMR (CDCl₃, 100 MHz): δ 178.9, 159.3, 151.8,
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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

![Structure of 199h]

Yield: 69%: orange solid; m.p. 126-128 °C; \(^1\)H NMR (400 MHz, CDCl\(_3\)) \(\delta\) 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): \(\delta\) 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

![Structure of 199i]

Yield: 66%: orange solid; m.p. 135-137 °C; \(^1\)H NMR (400 MHz, CDCl\(_3\)) \(\delta\) 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 =

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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): $\delta$ 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$_2$Cl$_2$ 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 °C; $^1$H NMR (400 MHz, CDCl$_3$) $\delta$ 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): $\delta$ 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$_2$Br$_2$ 538.0017, found 538.0023.
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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 °C; $^1$H NMR (400 MHz, CDCl₃) $\delta$ 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 (CDCl₃, 100 MHz): $\delta$ 178.7, 150.0, 141.1, 137.4, 137.8, 137.9, 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 C₉₂H₈₂NO₂ 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, CDCl₃) $\delta$ 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 (CDCl₃, 100 MHz): $\delta$ 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$_3$) $\delta$ 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): $\delta$ 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$_2$Br 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$_3$) $\delta$ 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): $\delta$ 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$_2$Br
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$_3$) $\delta$ 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): $\delta$ 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$_2$Br$_3$ 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 °C; $^1$H NMR (400 MHz, CDCl$_3$) $\delta$ 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): $\delta$ 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$_2$Br 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 °C; $^1$H NMR (300 MHz, CDCl$_3$) $\delta$ 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): $\delta$ 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$_4$Br 506.0967, found 506.0969.

1-(2-(Allylamino)-3-methoxyphenyl)-4-hydroxy-4,4-diphenylbut-2-yn-1-one 199r

Yield: 75%: orange gummy; $^1$H NMR (400 MHz, CDCl$_3$) $\delta$ 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): $\delta$ 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$_3$) $\delta$ 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): $\delta$ 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$_3$Br$_2$ 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$_3$) $\delta$ 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,
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6H); $^{13}$C NMR (CDCl$_3$, 100 MHz): $\delta$ 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

![Structural formula]

Yield: 73%: orange solid; m.p. 83-85 °C; $^{1}$H NMR (400 MHz, CDCl$_3$) $\delta$ 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): $\delta$ 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

![Structural formula]

Yield: 77%: yellow solid; m.p. 76-78 °C; $^{1}$H NMR (400 MHz, CDCl$_3$) $\delta$ 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); 13C NMR (CDCl₃, 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 C₂₃H₂₀NO₂S 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; ¹H NMR (400 MHz, CDCl₃) 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); 13C NMR (CDCl₃, 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 C₂₆H₂₄NO₂ 382.1807, found 382.1788.
Chapter IX

4-Hydroxy-1-(2-(methylamino)phenyl)-4,4-diphenylbut-2-yn-1-one 199x

Yield: 73%: yellow gummy; $^1$H NMR (400 MHz, CDCl$_3$) $\delta$ 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): $\delta$ 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 °C; $^1$H NMR (500 MHz, CDCl$_3$) $\delta$ 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): $\delta$ 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.

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1'-Allyl-3-phenylspiro[indene-1,2'-indolin]-3'-one 200b

Yellow gummy; \(^1\)H NMR (CDCl\(_3\), 400 MHz): \(\delta\) 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): \(\delta\) 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, 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): \(\delta\) 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 (dtbt, 1H, \(J = 1.6, 5.2, 1.6, 5.2\) Hz), 3.59-3.52 (dtbt, 1H, \(J = 1.4, 5.7, 1.4, 5.6\) Hz); \(^{13}\)C NMR (CDCl\(_3\), 100 MHz): \(\delta\) 196.9, 164.1, 161.6, 148.9, 144.0, 142.3, 137.7, 134.2, 130.6 (1C, \(J_{C,F} = 12.8\) Hz), 129.4 (1C, \(J_{C,F} = 32.5\) 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}NOCl_2 418.0765, found 418.0776.

1'-Allyl-6-chloro-3-(4-chlorophenyl)spiro[indene-1,2'-indolin]-3'-one 200d

Yellow solid; m.p. 146-148 °C; \(^1\)H NMR (CDCl\(_3\), 300 MHz): \(\delta 7.67 (d, 1H, J = 7.6\) 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): \(\delta 195.8, 161.0, 148.0, 144.2, 142.3, 137.9, 134.6, 133.9, 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): \(\delta 7.66-7.44 (m, 7H), 7.34 (d, 1H, J = 8.1\) 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): \(\delta 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

![Image of molecule](image1)

Yellow gummy; $^1$H NMR (CDCl$_3$, 400 MHz): $\delta$ 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): $\delta$ 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

![Image of molecule](image2)

Yellow gummy; $^1$H NMR (CDCl$_3$, 400 MHz): $\delta$ 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); 13C NMR (CDCl₃, 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 C₂₇H₂₄NO₃ 410.1756, found 410.1756.

1'-Allyl-5'-methyl-3-phenylspiro[indene-1,2'-indolin]-3'-one 200h

![Chemical Structure](image_url)

Yellow gummy; 1H NMR (CDCl₃, 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); 13C NMR (CDCl₃, 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 C₂₆H₂₂NO 364.1701, found 364.1693.
1'-Allyl-6-chloro-3-(4-chlorophenyl)-5'-methylspiro[indene-1,2'-indolin]-3'-one

200i

Yellow gummy; $^1$H NMR (CDCl$_3$, 400 MHz): $\delta$ 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): $\delta$ 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): $\delta$ 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): $\delta$ 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 C₂₆H₂₀NOBr₂ 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 (CDCl₃, 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); ¹³C NMR (CDCl₃, 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 C₂₈H₂₆NO 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 (CDCl₃, 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): \( \delta \) 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

![Structure](image)

Yellow gummy; \(^1\)H NMR (CDCl\(_3\), 400 MHz): \( \delta \) 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): \( \delta \) 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

Yellow gummy; \( ^1H \) NMR (CDCl\(_3\), 400 MHz): \( \delta \) 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): \( \delta \) 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\(_2\)Br 495.9871, found 495.9861.

1'-Allyl-5'-bromo-6-bromo-3-(4-bromophenyl)spiro[indene-1,2'-indolin]-3'-one

Yellow gummy; \( ^1H \) NMR (CDCl\(_3\), 400 MHz): \( \delta \) 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): \( \delta \) 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,
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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\(_{23}\)H\(_{17}\)NOBr, 583.8860, found 583.8885.

1'-Allyl-5'-bromo-6-methyl-3-(p-tolyl)spiro[indene-1,2'-indolin]-3'-one 200p

![Chemical structure of 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): \(\delta \) 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): \(\delta \) 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

![Chemical structure of 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): \(\delta \) 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): $\delta$ 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, 1277, 1215, 927, 769, 669; HRMS (ESI): calcd for C$_{27}$H$_{23}$NO$_3$Br 488.0861, found 488.0857.

$1'$-Allyl-7'$'$-methoxy-3-phenylspiro[indene-1,2'$'$-indolin]-3'$'$-one 200r

![Chemical Structure](image)

Yellow gummy; $^1$H NMR (CDCl$_3$, 300 MHz): $\delta$ 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): $\delta$ 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, 1701, 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; ¹H NMR (CDCl₃, 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); ¹³C NMR (CDCl₃, 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 C₂₆H₂₀NO₂Br₂ 535.9861, found 535.9862.

1'-Allyl-7'-methoxy-6-methyl-3-(p-tolyl)spiro[indene-1,2'-indolin]-3'-one 200t

Yellow gummy; ¹H NMR (CDCl₃, 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); ¹³C NMR (CDCl₃, 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; \(^1\)H NMR (CDCl\(_3\), 400 MHz): \(\delta\) 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): \(\delta\) 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; \(^1\)H NMR (CDCl\(_3\), 400 MHz): \(\delta\) 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, \(J = 263\).
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): $\delta$ 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): $\delta$ 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): $\delta$ 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): $\delta$ 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): $\delta$ 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, 1695, 1489, 1321, 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): $\delta$ 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): $\delta$ 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): $\delta$ 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): $\delta$ 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): calcld for C$_{29}$H$_{22}$NO$_3$S 464.1320, found 464.1331.
Chapter VIII. References


44. Mukherjee, P.; Widenhoefer, R. S. Org. Lett. 2010, 12, 1184.


112. Liang and co-workers reported one example of *p*-TsOH catalyzed alkoxylation of a 1-cyclopropyl-2-propyn-1-ol with MeOH that gave the corresponding conjugated enyne product in 58% yield; see ref 102.


116. The reaction of 170aa with 83a in the presence of 0.01 mol% of TfOH at reflux for 15 min was repeated 3 times to ensure the accuracy and reproducibility of the reported yield of 183aa.


118. CCDC 720922 contains the supplementary crystallographic data for this paper. These data can be obtained free of charge from The Cambridge Crystallographic Data Centre via www.ccdc.cam.ac.uk/data_request/cif.

119. The involvement of a cyclopropylmethyl carbocation formed in situ has also been proposed for the catalytic hydroamination of methylenecyclopropanes; see:


130. For selected recent works by us on Brønsted and Lewis acid-catalyzed reactions with alcohol pro-electrophiles, see refs 53, 73, 103 and 104.

131. For reviews on Brønsted acid-catalyzed reactions of cyclopropyl alcohols, see:


132. The crystallographic coordinates have been deposited with the Cambridge Crystallographic Data Centre; deposition nos. 791026 and 797214. These data can be obtained free of charge from The Cambridge crystallographic Data Centre, 12 Union Rd., Cambridge CB2 1EZ, UK or via www.ccdc.cam.ac.uk/data_request/cif.

133. For selected reviews, see refs 121c and 121e and 117c.

134. Please refer to the Experimental Section for the reaction times.

135. For similar product diastereoselectivities resulting from anti addition process reported in endo iodocyclizations of homoallylic alcohols with I$_2$ or NIS, see ref 118g and references therein and refs 127a, 127d, 127e, and 127g-127j.

136. Assignment of the (Z)-stereochemistry was also based on comparison with NMR data reported for closely related conjugated enynes, please refer to refs 102, 109, and 125.


143. Please refer to Supplementary Information for further details.

144. CCDC-844472 (191a) contains the supplementary crystallographic data for this paper. These data can be obtained free of charge from The Cambridge Crystallographic Data Centre via [www.ccdc.cam.ac.uk/data_request/cif](http://www.ccdc.cam.ac.uk/data_request/cif).


Chapter X


152. See ref 78, 142a, 142c and: Kruglov, A. A. Zh. Obshch. Khim. 1937, 7, 2605.


154. Refer to refs 138a, 151, and 152.
155. CCDC 869791 and 888682-888684 contains the supplementary crystallographic data for this paper. These data can be obtained free of charge from The Cambridge Crystallographic Data Centre via www.ccdc.cam.ac.uk/data_request/cif.

156. See refs 153b-153c, 153e and 153g for a comparison of product regioselectivities.


169. See refs 68, 69, 73, 97, 138a and 140.


171. CCDC 844472 contains the supplementary crystallographic data for this paper. These data can be obtained free of charge from The Cambridge Crystallographic Data Centre via [www.ccdc.cam.ac.uk/data_request/cif](http://www.ccdc.cam.ac.uk/data_request/cif).


175. Gates, P. S.; Baldwin, D.; Wilson, C. A.; Gillon, J. Herbicidal
