Gold(I)-Catalyzed 6-endo-dig Hydrative Cyclization of Alkyne-Tethered Ynamide: Access to 1,6-Dihydropyridin-2(3H)-ones

Abstract

Hydrative cyclization of 5-yne-ynamides in the presence of Echavarren’s catalyst and PTSA-H₂O at room temperature affords an array of novel 1,6-dihydropyridin-2(3H)-one derivatives. Isomerization, epoxidation, and hydrogenation of the double bond and insertion of an extended π-conjugate system into the pyridinone skeleton has been successfully accomplished. Formation of new C–C bonds at the periphery of 1,6-dihydropyridin-2(3H)-one yields highly substituted pyridinone derivatives.
Gold(I)-Catalyzed 6-endo-Dig Hydrative Cyclization of an Alkyne-Tethered Ynamide: Access to 1,6-Dihydropyridin-2(3H)ones

Nayan Ghosh, Sanatan Nayak, and Akhila K. Sahoo*[(a)]
3.1. Introduction

Alkynes (1) are versatile building blocks in organic synthesis. Its presence is widely seen in natural products, pharmaceuticals, agrochemicals, as well as materials. Moreover, the heteroatom-substituted alkynes (2) provide opportunity creating an additional functionality in the molecule. Among various heteroatom-substituted alkynes, the directly N-linked alkynes i.e. ynamines 3 (Figure 3.1) is especially an important species possessing broad synthetic utility. The electron-donation ability of nitrogen atom in ynamines strongly polarizes the triple bond and makes the alkynes more reactive over the non heteroatom-substituted alkynes. As a result, ynamines are usually sensitive towards nucleophiles especially to water. This hydrolytic instability therefore causes the difficulties in preparation, handling, and stability of ynamines.

![Figure 3.1: Different type of alkynes](image)

To broaden the synthetic utility of ynamines, it is therefore necessary to improve the stability of ynamines. The incorporation of an electron-withdrawing protecting group on nitrogen would diminish the electron density of N-atom. This would resist the inherent delocalization of N-lone pair to alkyne moiety, thereby enhancing the stability of ynamines. These molecules are classified as *electron-deficient ynamines named as ynamides*. Few representative examples of ynamides 4–6 are shown in Figure 3.2.

![Figure 3.2: Representative example of ynamides](image)

In general, the α-carbon center adjacent to nitrogen in yamide 4 is electrophilic and the β-carbon center is nucleophilic. As a result, regioselective addition of nucleophiles to yamide is possible. Furthermore, the inherent polarization of triple bond in ynamides allows regioselective activation of π-bond by a Lewis/Brønsted acid or transition-metal to the formation of *keteniminium ion* intermediate 8 (Scheme 3.1). Finally, the addition of...
nucleophile to 8 followed by replacement of metal-carbon bond of 9 by an electrophile delivers highly substituted enamines 10 (Scheme 3.1).

Scheme 3.1: General reactivity of ynamides towards nucleophiles

Taking advantage of high polarizability of triple bond in ynamide, a large variety of transformations has been demonstrated by different research groups. Intra and intermolecular cyclization of different π-tethered ynamide, intermolecular oxidation, nucleophilic addition to ynamide, cycloaddition, and dimerization has been reported in the recent past.¹b

3.2. Precedents

Owing to the polarization of triple bond, ynamides can be regioselectively activated by an π-acid to induce the addition of a variety of oxygen-, nitrogen, or carbon-containing nucleophiles at the α position to the nitrogen atom.

3.2.1. Inter and Intramolecular Addition of Nucleophiles to Ynamides

The Hashmi group reported the preparation of highly functionalized cyclopentadienes from propargyl carboxylates 11 and ynamides 4 in the presence of gold-catalyst. The reaction proceeds with the formation of active gold carbonoid intermediate 12 involving the 1,2-carboxylate shift of 11. The nucleophilic attack of ynamide 4 to intermediate 12 led to the desired cyclopentadienes 13 (Scheme 3.2).³a

Scheme 3.2: Intermolecular cyclization of ynamides and propargyl carboxylates

The reaction between carboxylic acids and various aryl substituted ynamides 14 under palladium(II) catalyst afforded α-acyloxy enamide 15 (Scheme 3.3). Activation of triple bond of ynamide 14 by Pd-catalyst followed by regioselective attack of acid at the α-position of activated complex produced the desired product 15.³b
Scheme 3.3: Hydroacyloxylation of ynamides

A highly regio- and stereo-selective hydrofluorination of ynamide has been reported by Evani and Thibodeau groups. The reaction between ynamide 4 and hydrofluoric acid at −50 °C quickly delivered α-fluoroenamide 16 (Scheme 3.4). 3c

Scheme 3.4: Hydrofluorination of ynamides

A highly regioselective Au(I)-catalyzed hydroamination of ynamide with aniline is developed by Skrydstrup group. 3d The aromatic amine 17 underwent hydroamination on ynamide 4 produces 18 (eq 1, Scheme 3.5). Interestingly, the reaction between nitrogen or oxygen nucleophile 20 and conjugated ynamide 19 delivered the highly functionalized heteroaryl 21 or 22 (eq 2, Scheme 3.5). 3e

Scheme 3.5: Addition of aryl amine and water to ynamides

The bis(trifluoromethane)sulfonamide assists the Friedel-Crafts type attack of furan-derivatives 23 to ynamide 4 producing the highly substituted enamine 24 (Scheme 3.6). 3f

Scheme 3.6: Addition of furan to ynamides
The gold-catalyzed 5-endo-dig cyclization followed by allyl rearrangement of ortho-O-allylaryl substituted ynamide 25 allowed the synthesis of highly substituted benzo[b]furan 28. The reaction initiates with the activation of triple bond by gold catalyst. The nucleophilic attack of oxygen atom to the activated triple bond of 26 delivers 27. The 1,3-allyl migration of 27 produce 28 (Scheme 3.7).

**Scheme 3.7:** Gold(I)-catalyzed 5-endo-dig-cyclization/rearrangement of ortho-O-allylaryl substituted ynamide

Hsung group reported the synthesis of 2-amino substituted indoles 32 from o-halo substituted ynamide 29. The reaction involves the palladium-catalyzed Buchwald coupling of halo-group of 29 with amine 30 followed by intramolecular cyclization of o-amino substituted ynamide 31 in a single-pot (Scheme 3.8).

**Scheme 3.8:** Synthesis of 2-amino substituted indole

Furthermore, Hsung group disclosed the Rh(I)-catalyzed cyclization demethylation of o-anisole-substituted ynamide 33 for the synthesis of 2-amino substituted benzofuran derivatives 35 (Scheme 3.9).

**Scheme 3.9:** Rhodium(I)-catalyzed cyclization/demethylation of o-anisole-substituted ynamide

The Brønsted acid-catalyzed highly regioselective intramolecular cyclization of arene-ynamide 36 has been described by Hsung group. The Friedel-Crafts attack of aryl-moiety
to the *in situ* generated active keteniminium intermediate from 36 furnishes the desired dihydroamino-naphthalene derivative 37 (Scheme 3.10). This methodology has successfully been employed for the synthesis of 10-desbromoarborescidine A (38) and 11-desbromoarborescidine C (39) (Scheme 3.10).

**Scheme 3.10:** Intermolecular cyclization of arene-ynamides

3.2.2 Dimerization of Ynamides

Taking the advantage of ambivalent nature of ynamides, Skrydstrup group reported the gold-catalyzed dimerization of ynamides 40. This method delivers highly substituted cyclopentadiene derivative 41 (Scheme 3.11). The reaction proceeds with the involvement of active intermediate 42 (Scheme 3.11).

**Scheme 3.11:** Dimerization of ynamides

3.2.3. Intramolecular Oxidation of Ynamide

The triple bond of ynamides readily undergoes oxidition with the influence of external oxidants sulfoxide, quinoline-N-oxide or pyridine-N-oxide.

The Liu group recently reported the synthesis of peripheral substituted 2-aminofurans 45 from ene-ynamides 43 (Scheme 3.12). The oxide transfer from quinoline-N-oxide 46 to the ynamide triple bond 43 generates the gold carbenoid intermediate 44 *in situ*; the oxa-

**Scheme 3.12:** Intermolecular oxidation and cyclization of ynamides via gold catalyst
Nazarov cyclization of 44 finally delivers 45 (Scheme 3.12).\textsuperscript{6a}

The 1,2-difunctionalization of ynamides is accomplished, when ynamides 4 reacted with imine-$N$-oxide 47 in the presence of Au-catalyst. The oxide transfer from $N$-oxide 47 to the Au-activated ynamide forms the Au-carbenoid species 48 \textit{in situ}. The nucleophilic attack of imine-nitrogen 49 to 48 followed by hydrolysis gives 50 (Scheme 3.13).\textsuperscript{6b}

\begin{equation}
\text{Scheme 3.13: 1,2-Difunctionalization of ynamides}
\end{equation}

The highly substituted oxazole derivatives 54 were synthesized involving gold-catalyzed [3+2] cycloaddition between ynamides 4 and pyridine-$N$-aminide 51. The nucleophilic attack of aminide 51 to the gold-activated ynamides followed by elimination of pyridine from 52 lead to Au-carbenoid 53; cyclization of 53 then furnished oxazole 54 (Scheme 3.14).\textsuperscript{6c}

\begin{equation}
\text{Scheme 3.14: Intermolecular reaction between ynamides and pyridine-$N$-aminide}
\end{equation}

The Zhang group reported the synthesis of $\alpha,\beta$-unsaturated amidines 58 from activated ynamides 55 and iminopyridinium ylides 56 under the influence of gold catalyst. The

\begin{equation}
\text{Scheme 3.15: Intermolecular nitrene transfer to activated ynamides}
\end{equation}
nitrene transfer from iminopyridinium ylides 56 to ynamides 55 followed by 1,2-hydride shift allows the formation of 58 (Scheme 3.15).

The oxidation of differently substituted ynamides 4 with pyridine-N-oxide under gold catalyst lead to α-ketoimides 60 and α,β-unsaturated imides 61 (Scheme 3.16).

![Scheme 3.16: Intermolecular oxidation of ynamides.](image)

In 2008, Hsung and co-worker reported RuO₂/NaIO₄ assisted oxidation of ynamides 4 to the preparation of α-ketoimides 60 (Scheme 3.17). Later in 2011, Li group accomplished the synthesis of α-ketoimides 60 from 4 under the influence of diphenyl sulfoxide oxidant and gold-catalyst (Scheme 3.17).

![Scheme 3.17: Oxidation of ynamides with external oxidant](image)

3.2.4. Cycloaddition Reaction of π-Tethered Ynamides

The π-tethered ynamides: ene-ynamides or allene-ynamides or enyne-ynamides undergo intra and intermolecular cyclization under the influence of transition metal catalysts.

The Liu group demonstrated the gold-catalyzed [4+2] and [2+2+2] cycloadditions of ynamides with alkenes. The terminal aryl substituted ynamides 4 underwent [4+2] cycloaddition with alkene 62 forming dihyronaphthalene derivatives 63 (Scheme 3.18). Similarly, [2+2+2] cycloaddition of terminally unsubstituted ynamides with two molecules of alkenes afforded cyclohexene derivatives 64 (Scheme 3.18).
**Scheme 3.18:** Gold-catalyzed [4+2] and [2+2+2] cycloadditions of ynamides

The Malacria and co-workers have shown the synthesis of N-containing heterocycles 67 through the silver-catalyzed cycloisomerization of allene-ynamides 65 (Scheme 3.19). This reaction proceeds through the activation of triple bond by silver catalyst followed by 6-endo-dig cyclization of allene to the α-carbon of keteniminium intermediate 66 and isomerization sequence (Scheme 3.19). 7b

**Scheme 3.19:** Intramolecular cyclization of allene-ynamides

The Malacria and Crossy groups independently reported the platinum and gold-catalyzed cycloisomerization of ene-ynamides. A formal [2+2] cycloaddition of ene-ynamide 68 provides cyclobutyl fused bicyclic derivative 69; hydrolysis of 69 in the presence of moisture forms the cyclic ketone moiety 70 (Scheme 3.20). 7c,d

**Scheme 3.20:** Cycloisomerization of ene-ynamides

Intermolecular [2+2+2] cycloaddition between diynes/ynamides/yne-ynamides and alkyne have successfully been explored by different research groups (Scheme 3.21). For instance: Tanaka group reported the Rh-catalyzed [2+2+2] cycloaddition between diynes 71 and ynamides 72 for the synthesis of anilides 73 (eq 1, Scheme 3.21). 7e Similarly, Rh-catalyzed [2+2+2] cycloaddition of yne-ynamides 74 with alkyne 75 afforded indolines 76 (eq 2, Scheme 3.21). 7f
Scheme 3.21: Intermolecular [2+2+2] cycloaddition reaction of ynamides

The Ru-catalyzed [2+2] cycloaddition of ynamides 4 with alkenes 77 gave aminocyclobutenes 78 (eq 1, Scheme 3.22). Recently, Danheiser group demonstrated the synthesis of aminocyclobutenones 80 involving the Ru-catalyzed cycloaddition between ynamides 4 and ketenes 79 (eq 2, Scheme 3.22).

Scheme 3.22: [2+2] cycloaddition of ynamides

The conjugated enyne- and dienes-ynamides readily undergo intramolecular [4+2]-cyclo-

Scheme 3.23: Intramolecular [4+2] cycloaddition reaction of conjugated enyne- and dienes-ynamides
addition reaction. BHT (butylated hydroxyl toluene) mediated intramolecular [4+2] cycloaddition of enyne-ynamides 81 gave indolines 82 (eq 1, Scheme 3.23).\textsuperscript{7} The Witulski group reported Rh-catalyzed cycloaddition of diene tethered ynamides 83 to afford tetrahydroindoles 84 in good yield (eq 2, Scheme 3.23).\textsuperscript{7k}

From these observations it is quite clear that different type of transformations on ynamides have thoroughly been investigated over the decades.\textsuperscript{1} A close look on all these transformations suggest that the reactivity of unactivated yne-tethered ynamides to the external nucleophile is limited.\textsuperscript{8} Despite the ambivalent nature of ynamides, regioselective attack of the nucleophile followed by cyclization to the tethered-alkyne moiety is so far unexplored.

3.3. Motivation and Design Plan

Our inherent interest in the development of novel Au-catalyzed transformations\textsuperscript{9,10} inspired us to apply the concept of hydrative cyclization of N-tethered-1,n-diynes 85 to 5-yn-ynamides 87 in the presence of Au-catalyst. The transition-metal catalyzed hydrative cyclizations of 1,n-diynes is well established (Scheme 3.24).\textsuperscript{11}

![Scheme 3.24: Oxidation of N-tethered 1,n-diynes via transition-metal catalyst](image)

We envisioned that preferential attack of a foreign nucleophile such as H\textsubscript{2}O to the α-carbon atom of the keteniminium intermediate 88 generated from 5-yn ynamide 87 would trigger 6-endo-dig cyclization of the β-carbon atom of the keteniminium-π-bond to the TsN-propargyl-alkyne-activated species, followed by protodeauration and tautomerization to afford the dihydropyridinone moiety 89 as depicted in Scheme 3.25. The

![Scheme 3.25: Proposed mode of reactivity of 5-yn-ynamide](image)
dihydropyridinone structural motif is present in a wide array of naturally occurring alkaloids and pharmaceutically important molecules.¹²

3.4. Results and Discussion

3.4.1. Reaction Optimization

Table 3.1: Synthesis of various substituted 87ᵃ,b

| 87a, R = H, 78% | 87b, R = CH₃, 76% | 87c, R = OMe, 83% | 87d, R = F, 63% | 87e, R = Cl, 69% | 87f, R = Br, 76% | 87g, R = I, 62% |
| 87h, 65% | 87i, 73% | 87j, R = OMe, 64% | 87k, R = Br, 56% | 87l, R = I, 63% |

| 87m, 75% | 87n, 56% | 87o, 53% | 87p, 71% | 87q, 72% |
| 87r, 78% | 87s, 70% | 87t, 53% | 87u, 66% | 87v, 75% |

| 87w, 75% | 87x, 57% | 87y, 64% | 87z, 93% |

ⁿReactions were carried out using 87” (1.0 mmol), 87”’ (1.2 mmol), CuSO₄·5H₂O (0.10 mmol), 1,10-phenanthroline (0.20 mmol) and K₃PO₄ (2.0 mmol) in dry toluene (5.0 mL) at 60–65 °C. ‡Isolated yields.
To test the feasibility of the reaction, we investigated the Au-catalyzed hydrative cyclization of 87a first. Following the reported procedure, the precursors 87 and 92 were prepared in moderate to good yields as shown in Table 3.1 and Table 3.2. 13

**Table 3.2: Synthesis of various substituted 92a,b**

<table>
<thead>
<tr>
<th>Compound</th>
<th>Yield (%)</th>
</tr>
</thead>
<tbody>
<tr>
<td>92a</td>
<td>74%</td>
</tr>
<tr>
<td>92b</td>
<td>61%</td>
</tr>
<tr>
<td>92c</td>
<td>68%</td>
</tr>
<tr>
<td>92d, R = COOMe</td>
<td>76%</td>
</tr>
<tr>
<td>92e, R = CF3</td>
<td>67%</td>
</tr>
<tr>
<td>92f</td>
<td>75%</td>
</tr>
<tr>
<td>92g</td>
<td>62%</td>
</tr>
<tr>
<td>92h</td>
<td>50%</td>
</tr>
<tr>
<td>92i</td>
<td>56%</td>
</tr>
</tbody>
</table>

Reactions were carried out using 87"" (1.0 mmol), 92"""" (1.2 mmol), CuSO₄·5H₂O (0.10 mmol), 1,10-phenanthroline (0.20 mmol) and K₃PO₄ (2.0 mmol) in dry toluene (5.0 mL) at 60–65 °C. bIsolated yields.

Table 3.3 summarizes the details of the optimization studies. Reaction of substrate 87a with Echavarren’s catalyst 14 (A; 5.0 mol %) and H₂O (1.0 equiv) in 1,4-dioxane at room temperature (rt) lead to a complex reaction mixture with the complete consumption of the precursor (entry 1). To our delight, use of PTSA·H₂O (1.0 equiv) instead of H₂O produced a mixture of inseparable cyclized product 89a and di-hydration product 91a in 3:1 ratio in 45% yield; the mono-hydration product 90a was also obtained in 40% yield (entry 2). The combined yield of 89a and 91a was increased to 63%, when PTSA·H₂O (2.0 equiv) was employed in the reaction (entry 3). Surprisingly, the hydrative cyclization of 87a in the presence of PTSA·H₂O (2.5 equiv) proceeded well, forming 89a in 91% yield; although a trace amount of 90a was detected by 1H NMR spectrum of the crude reaction mixture (entry 4). The structure of 89a was confirmed by detailed spectroscopic analysis and X-ray crystallographic studies (Figure 3.3). 15 The lower loading of catalyst A (3.0 mol % instead of 5.0 mol %) did not show pronounced effect in the product yield, delivering 89% of 89a.
(entry 5). Screening of other Au-catalysts (entries 6–10) revealed that catalyst A was uniquely effective (entries 4 and 5). Solvent effect was next examined; for example: THF and toluene were found moderate (entries 11 and 12). Unfortunately, the reaction in acetonitrile lead to the decomposition of the precursor 87a (entry 13). The products 89a

**Table 3.3: Reaction optimization**

<table>
<thead>
<tr>
<th>Entry</th>
<th>Catalyst</th>
<th>Additive</th>
<th>Solvent</th>
<th>Time (h)</th>
<th>Yields (%)</th>
</tr>
</thead>
<tbody>
<tr>
<td>1</td>
<td>A (5.0)</td>
<td>H₂O (1.0)</td>
<td>dioxane</td>
<td>4</td>
<td>90a</td>
</tr>
<tr>
<td>2</td>
<td>A (5.0)</td>
<td>PTSA·H₂O</td>
<td>dioxane</td>
<td>4</td>
<td>40 45 (3:1)</td>
</tr>
<tr>
<td>3</td>
<td>A (5.0)</td>
<td>PTSA·H₂O</td>
<td>dioxane</td>
<td>4</td>
<td>20 63 (3:1)</td>
</tr>
<tr>
<td>4</td>
<td>A (5.0)</td>
<td>PTSA·H₂O(2.5)</td>
<td>dioxane</td>
<td>4</td>
<td>6 91 (1:0)</td>
</tr>
<tr>
<td>5</td>
<td>A (3.0)</td>
<td>PTSA·H₂O(2.5)</td>
<td>dioxane</td>
<td>4</td>
<td>89 (1:0)</td>
</tr>
<tr>
<td>6</td>
<td>B (5.0)</td>
<td>PTSA·H₂O(2.5)</td>
<td>dioxane</td>
<td>4</td>
<td>22 71 (9:1)</td>
</tr>
<tr>
<td>7</td>
<td>C (5.0)</td>
<td>PTSA·H₂O(2.5)</td>
<td>dioxane</td>
<td>4</td>
<td>19 70 (1:2)</td>
</tr>
<tr>
<td>8</td>
<td>D (5.0)</td>
<td>PTSA·H₂O(2.5)</td>
<td>dioxane</td>
<td>4</td>
<td>18 68 (3:1)</td>
</tr>
<tr>
<td>9</td>
<td>E (5.0)</td>
<td>PTSA·H₂O(2.5)</td>
<td>dioxane</td>
<td>4</td>
<td>43 31 (1:3)</td>
</tr>
<tr>
<td>10</td>
<td>F (5.0)</td>
<td>PTSA·H₂O(2.5)</td>
<td>dioxane</td>
<td>4</td>
<td>22 65 (6:1)</td>
</tr>
<tr>
<td>11</td>
<td>A (5.0)</td>
<td>PTSA·H₂O(2.5)</td>
<td>THF</td>
<td>4</td>
<td>15 73 (3:1)</td>
</tr>
<tr>
<td>12</td>
<td>A (5.0)</td>
<td>PTSA·H₂O(2.5)</td>
<td>toluene</td>
<td>4</td>
<td>28 60 (9:1)</td>
</tr>
<tr>
<td>13</td>
<td>A (5.0)</td>
<td>PTSA·H₂O(2.5)</td>
<td>acetonitrile</td>
<td>4</td>
<td>90a</td>
</tr>
<tr>
<td>14</td>
<td>A (5.0)</td>
<td>PTSA·H₂O(2.5)</td>
<td>dioxane</td>
<td>2</td>
<td>37 48 (1:0)</td>
</tr>
<tr>
<td>15</td>
<td>In(OTf)₂</td>
<td>PTSA·H₂O(2.5)</td>
<td>THF</td>
<td>4</td>
<td>65 29 (1:0)</td>
</tr>
<tr>
<td>16</td>
<td>Cu(OTf)₂</td>
<td>PTSA·H₂O(2.5)</td>
<td>THF</td>
<td>4</td>
<td>68 15 (1:0)</td>
</tr>
<tr>
<td>17</td>
<td>Pd(OAc)₂</td>
<td>PTSA·H₂O(2.5)</td>
<td>dioxane</td>
<td>4</td>
<td>99 90a</td>
</tr>
<tr>
<td>18</td>
<td>–</td>
<td>H₂O (1.0)</td>
<td>dioxane</td>
<td>4</td>
<td>98 90a</td>
</tr>
</tbody>
</table>

*Reactions were carried out using 87a (0.2 mmol), solvent (3.0 mL). †Isolated yields. ‡Complex reaction profile. §Decomposition of 87a occurred. ‡Reaction was heated at 60 °C for 2 h. †Catalyst (5 mol %) used. ‡90a was isolated. Tf = trifluromethanesulfonyl. PTSA = p-toluenesulfonic acid.
(48%) and 90a (37%) were cleanly isolated, when the reaction was conducted at 60 °C in 1,4-dioxane for 2 h (entry 14). Attempt to cyclize 87a in the presence of In(OTf)₂ or Cu(OTf)₂ turned moderate, forming 90a as major product (entries 15 and 16). Decomposition of precursor 87a was observed, when Pd(OAc)₂ was used as catalyst (entry 17). Surprisingly, 87a underwent mono-hydration with PTSA·H₂O (2.5 equiv) in dioxane at rt in 30 minutes (entry 18), justifying the participation of reactive keteniminium intermediate. Thus, the occurrence of highly selective 6-endo-dig hydrative cyclization of 87a under the influence of the mixture of Au-catalyst and PTSA·H₂O in the formation of pyridinone 89a appears interesting and noteworthy.

**Table 3.4:** Screening of different sulfonic acids<sup>a,b</sup>

<table>
<thead>
<tr>
<th>entry</th>
<th>Additive (2.5 equiv)</th>
<th>Solvent</th>
<th>Yields</th>
</tr>
</thead>
<tbody>
<tr>
<td></td>
<td>89a (%)</td>
<td>90a (%)</td>
<td></td>
</tr>
<tr>
<td>1</td>
<td>methanesulfonic acid</td>
<td>dioxane</td>
<td>87a decomposed</td>
</tr>
<tr>
<td>2</td>
<td>methanesulfonic acid and water (2.0 equiv)</td>
<td>dioxane</td>
<td>87a decomposed</td>
</tr>
<tr>
<td>3</td>
<td>camphorsulfonic acid</td>
<td>dioxane</td>
<td>No reaction</td>
</tr>
<tr>
<td>4</td>
<td>camphorsulfonic acid and water (2.0 equiv)</td>
<td>dioxane</td>
<td>0 : &lt;10</td>
</tr>
</tbody>
</table>

<sup>a</sup>Reactions were carried out using 87a (0.2 mmol), 1,4-dioxane (3.0 mL) at rt.

The compound 87a was decomposed when reacted with methanesulfonic acid or methanesulfonic acid in the presence of water and catalyst A (entries 1 and 2, Table 3.4). Whereas reaction with camphorsulfonic acid did not affect 87a (entry 3); the reaction between 87a and camphorsulfonic acid in the presence of water produced a little amount of mono-hydration product 90a (entry 4). From this observation, we believe PTSA is solely responsible in the generation of keteniminium intermediate.

### 3.4.2. Reaction Scope

The substrate generality of this reaction is investigated under the optimized catalytic conditions, shown in entry 5 in Table 3.3. The results are summarized in Table 3.5. As observed in the optimization studies, the electronically neutral phenyl ring bearing substrate 87a gave the cyclization product 89a in 89% yield. The electron donating
Hydrative Cyclization

groups, such as \( p\text{-Me} \) and \( p\text{-OMe} \) on arene did not affect the reaction efficiency and furnished the desired 1,6-dihydropyridin-2(3\( H \))-one derivatives \( \text{89b} \) and \( \text{89c} \) in good yields. The \( N \)-heterocyclic dihydropyridinone products \( \text{89d–g} \) were isolated in lucrative yields from the corresponding electron-withdrawing halo group containing precursors \( \text{87d–g} \). The Au-catalyzed hydrative cyclization of \( \text{meta} \)-substituted arene in 5-yneynamide \( \text{87h} \) resulted the desired product \( \text{89h} \) in 83\% yield. The electron-donating methyl- or the methoxy-groups and the electron-withdrawing bromo- or iodo-groups at the \( \text{ortho} \)-position on arene rings did not affect the reaction efficiency and the desired products \( \text{89i–l} \) were isolated in good yields. X-Ray diffraction data elucidates the structure of \( \text{89k} \) (Figure 3.3).\(^{15}\) Similarly, the naphthyl-bearing product \( \text{89m} \) was isolated in 76\% yield. Gratifyingly, this reaction delivered the 2-thienyl and \( N \)-protected 3-indolyl substituted 1,6-dihydropyridin-2(3\( H \))-one products \( \text{89n} \) and \( \text{89o} \), respectively with ease. Similarly, substrate \( \text{87p} \) produced \( \text{89p} \) in moderate yield. The precursors \( \text{87q–s} \) having two electron-donating methyl or methoxy groups on arenes in \( m\text{-,}\text{m-}l\text{-}p\text{-,}p\text{-,o-} \) positions successfully underwent hydrative cyclization yielding the corresponding \( \text{89q–s} \) in good yields. However, the di-\( \text{ortho} \)-methoxy substituted \( \text{87t} \) resulted moderate amount of \( \text{89t} \); even though the reaction continued for prolonged time, incomplete conversion of starting material was observed along with the isolation of the mono-hydration product \( \text{90t} \).\(^{16}\) The steric effect of two \( \text{ortho} \)-OMe groups on aryl ring hinders the effective hydrative cyclization, as a result \( \text{89t} \) was obtained in low yield. Examination of alkyl substituents at the \( N \)-propargyl alkyne terminus was next studied. Gratifyingly, various 4-alkyl-3-phenyl substituted 1,6-dihydro-pyridin-2(3\( H \))-ones \( \text{89u–w} \) were synthesized in excellent yields. The pyridinones \( \text{89x} \) and \( \text{89y} \) were successfully isolated in 74\% and 81\% yield, respectively, from the substrates bearing alkyl group at the alkyne terminus of ynamide side. Interestingly, the presence of alkyl-group at both side of the alkyne terminus did not affect the hydrative cyclization, producing the desired \( \text{89z} \) in 83\% yield.

We next examined the effect of substituents on the aryl-group at the \( \text{TsN} \)-alkyne-terminus keeping the phenyl group at the \( \text{TsN} \)-propargyl-alkyne terminus fixed. The results are described in Table 3.6. Thus, substrates \( \text{92a–e} \) with electron-withdrawing groups on aryl ring underwent cyclization efficiently and the desired products \( \text{93a–e} \) were produced in moderate to good yields. Ester, keto and nitro functional groups did not affect the reaction efficiency and the product yields. Similarly, hydrative cyclization of \( \text{92f} \) having electron-rich 3,5-dimethylphenyl substituted \( \text{TsN} \)-ynamide gave \( \text{93f} \) in good yield. The presence of electron-withdrawing and/or –donating groups on the aryl rings at both the alkyne
Table 3.5: Hydrative cyclization of yne-ynamides$^{a,b}$

<table>
<thead>
<tr>
<th>R$^1$</th>
<th>R$^2$</th>
<th>Product</th>
<th>Yield</th>
</tr>
</thead>
<tbody>
<tr>
<td>H</td>
<td>Ts</td>
<td>89a (89%)</td>
<td></td>
</tr>
<tr>
<td>CH$_3$</td>
<td>Ts</td>
<td>89b (79%)</td>
<td></td>
</tr>
<tr>
<td>OMe</td>
<td>Ts</td>
<td>89c (85%)</td>
<td></td>
</tr>
<tr>
<td>F</td>
<td>Ts</td>
<td>89d (76%)$^c$</td>
<td></td>
</tr>
<tr>
<td>Cl</td>
<td>Ts</td>
<td>89e (65%)</td>
<td></td>
</tr>
<tr>
<td>Br</td>
<td>Ts</td>
<td>89f (74%)</td>
<td></td>
</tr>
<tr>
<td>I</td>
<td>Ts</td>
<td>89g (73%)$^c$</td>
<td></td>
</tr>
<tr>
<td>CH$_3$</td>
<td>Ts</td>
<td>89h (83%)$^c$</td>
<td></td>
</tr>
<tr>
<td>OMe</td>
<td>Ts</td>
<td>89i (76%)</td>
<td></td>
</tr>
<tr>
<td></td>
<td></td>
<td>89 (77%)</td>
<td></td>
</tr>
<tr>
<td></td>
<td></td>
<td>89o (65%)</td>
<td></td>
</tr>
<tr>
<td>O</td>
<td>Ts</td>
<td>89p (65%)</td>
<td></td>
</tr>
<tr>
<td>Me</td>
<td>Ts</td>
<td>89q (76%)</td>
<td></td>
</tr>
<tr>
<td>Me</td>
<td>Ts</td>
<td>89r (82%)</td>
<td></td>
</tr>
<tr>
<td>OMe</td>
<td>Ts</td>
<td>89s (75%)</td>
<td></td>
</tr>
<tr>
<td></td>
<td></td>
<td>89t (59%)</td>
<td></td>
</tr>
<tr>
<td></td>
<td></td>
<td>89u (84%)</td>
<td></td>
</tr>
<tr>
<td></td>
<td></td>
<td>89v (86%)</td>
<td></td>
</tr>
<tr>
<td></td>
<td></td>
<td>89w (30%)</td>
<td></td>
</tr>
<tr>
<td></td>
<td></td>
<td>89x (74%)$^d$</td>
<td></td>
</tr>
<tr>
<td></td>
<td></td>
<td>89y (81%)$^d$</td>
<td></td>
</tr>
<tr>
<td></td>
<td></td>
<td>89z (83%)$^d$</td>
<td></td>
</tr>
</tbody>
</table>

$^a$Reactions were carried out using 87 (0.25 mmol), catalyst A (3.0 mol %), PTSA·H$_2$O (0.63 mmol) in 1,4-dioxane (3.0 mL) at room temperature for 4 h. $^b$Isolated yields. $^c$A minor amount of the inseparable dihydration product is detected along with the cyclization product. $^d$Reaction completed in 2 h.
terminus of 92 did not affect the reaction outcome, delivering the desired cyclization products 93g and 93h in 69% and 81% yields, respectively. The yield of the cyclized product 93i, obtained from the substrate bearing the thienyl and p-CIC₆H₄ groups at both the alkyne terminus, was excellent.

**Figure 3.3:** ORTEP diagrams of 89a and 89k.

This methodology demonstrates the synthesis of 1,6-dihydropyridin-2(3H)-ones with broad substrate scope in tolerating various functionalities and protecting groups. Next, we

**Table 3.6:** Hydrative cyclization of yne-ynamides

<table>
<thead>
<tr>
<th>Catalyst</th>
<th>Products</th>
</tr>
</thead>
<tbody>
<tr>
<td>A (3.0 mol%)</td>
<td>93&lt;br&gt;(83%)&lt;sup&gt;a&lt;/sup&gt;</td>
</tr>
<tr>
<td>PTSA·H₂O (0.63 mmol)</td>
<td>93b&lt;br&gt;(72%)&lt;sup&gt;b&lt;/sup&gt;</td>
</tr>
<tr>
<td>1,4-dioxane</td>
<td>93c&lt;br&gt;(82%)&lt;sup&gt;b&lt;/sup&gt;</td>
</tr>
<tr>
<td>rt, 4 h</td>
<td>93d&lt;br&gt;(67%)&lt;sup&gt;b&lt;/sup&gt;</td>
</tr>
<tr>
<td></td>
<td>93e&lt;br&gt;(83%)&lt;sup&gt;b&lt;/sup&gt;</td>
</tr>
<tr>
<td></td>
<td>93f&lt;br&gt;(72%)&lt;sup&gt;c&lt;/sup&gt;</td>
</tr>
<tr>
<td></td>
<td>93g&lt;br&gt;(69%)&lt;sup&gt;c&lt;/sup&gt;</td>
</tr>
<tr>
<td></td>
<td>93h&lt;br&gt;(81%)&lt;sup&gt;c&lt;/sup&gt;</td>
</tr>
<tr>
<td></td>
<td>93i&lt;br&gt;(87%)&lt;sup&gt;c&lt;/sup&gt;</td>
</tr>
</tbody>
</table>

<sup>a</sup>Reactions were carried out using 92 (0.25 mmol), catalyst A (3.0 mol %), PTSA·H₂O (0.63 mmol) in 1,4-dioxane (3.0 mL) at room temperature. <sup>b</sup>Isolated yields. <sup>c</sup>A minor amount of the inseparable dihydration product is detected along with the cyclization product.
envisioned isomerization of the non-conjugated double bond to a conjugated double bond considering the advantage of the acidic proton at the 3-position. Pleasingly compound 89a was converted to 94a (92% yield) upon refluxing with Et$_3$N in EtOAc (Table 3.7). Under the identical conditions 89g, 89i and 89o were smoothly isomerized to the corresponding products 94g, 94i and 94o, respectively. The results are shown in Table 3.7. The conjugated double bond in pyridinone derivatives could be useful for the preparation of optically active analogs via asymmetric hydrogenation, complex structural entities by the Diel’s-Alder reaction, and extended π-conjugated systems through oxidative dehydrogenative coupling of the aryl moieties.

**Table 3.7. Isomerization of the non-conjugated double bond$^{a,b}$**

![Diagram of isomerization reaction]

$^a$Reactions were carried out using 89 (0.25 mmol) and Et$_3$N (1.0 mmol) in ethyl acetate (2.0 mL) at 110 °C. $^b$Isolated yields.

We next turned our attention to explore the C–O bond forming reactions on 89a. Epoxidation on 89a with m-CPBA gave the desired product 95 in 92% yield (Scheme 3.26). Furthermore, hydrogenation of 89a was smoothly conducted with H$_2$/Pd–C in EtOAc and the product cis-96 was exclusively obtained in excellent yield. Similarly, the isomerized compound 94a under the identical hydrogenation condition gave cis-96. The cis-stereochemistry of compound 96 was confirmed by X-ray crystallographic analysis (Figure 3.4).$^{13}$

**Scheme 3.26. Epoxidation and hydrogenation of dihydropyridinones**
The iodo-group in the molecular template 1,6-dihydropyridin-2(3H)-ones was successfully employed to introduce extended π-conjugated systems via Suzuki and Sonogashira reactions (Scheme 3.27). For instance: Suzuki reaction of 94g with PhB(OH)₂ under

Figure 3.4: ORTEP diagrams of 96.

Pd(OAc)₂ and Na₂CO₃ in DMF/H₂O delivered 97 in 91% yield. An excellent yield of the Sonogashira product 98 was obtained from 94g and phenyl acetylene.

Scheme 3.27. Synthesis of extended π-conjugated systems.

Formation of new C–C bonds at the periphery of the 1,6-dihydropyridin-2(3H)-one derivative would generate highly substituted six-membered dihydropyridinone derivatives. We therefore envisioned the reaction of 89k with an electrophile in the presence of a strong base. Abstraction of the acidic-3H proton by LDA generated the corresponding allylic anion, and subsequent isomerization and attack of the allylic anion to p-bromobenzaldehyde afforded 99 in 62% yield (eq. 1).
We next investigated the incorporation of a modifiable functional group, for example, an ester-moiety, into the 1,6-dihydropyridin-2(3H)-one skeleton. The precursor 100 required for this study was readily prepared from 87″a and ethyl 3-bromopropiolate. Hydrative cyclization of 100 under the catalyst A (3.0 mol%), PTSA·H₂O (2.5 equiv) in acetonitrile at rt afforded the isomerized product 101, albeit in moderate yield (Scheme 3.28).

Hydrogenation of 101 with H₂/Pd–C in EtOAc provided quantitative amount of cis-102; X-ray crystallographic analysis confirms its structure. Compound 102 can be further used for the synthesis of various analogs of cis-femoxetine and cis-paroxetine drugs, indicating the broad scope of application of this synthetic strategy.

Scheme 3.28. Synthesis of ester-substituted dihydropyridinone derivative.

3.4.3. Mechanistic Studies

The formation of 90a as the side product in the hydrative cyclization of 87a indicated the participation of this active intermediate in this reaction. To validate this presumption, substrate 90a was prepared from 87″a and phenylacetic acid through EDC coupling. Unfortunately, reaction of 90a under the optimized conditions (entry 5, Table 3.2) did not afford the cyclized product 89a even in trace amounts, ruling out the possible involvement

Scheme 3.29. Plausible Reaction Mechanism
of 90a as intermediate in the synthesis of 89a (Scheme 3.29).

The plausible reaction pathway for this cyclization is outlined in Scheme 3.30. Although the actual role of PTSA·H₂O is yet to be established, however, on the basis of the observations in the optimization studies (entry 18, Table 3.2), it appears the catalyst A and PTSA·H₂O react with compound 87a and generates the intermediate 88.³² Attack of ArSO₂⁻ to 88 and subsequent 6-endo-dig cyclization of the enolate 106 to the Au(I)-activated TsN-propargyl triple bond affords the cyclic vinyl-Au species 107 which undergoes tautomerization, hydrolysis and proto-deauration to yield the desired product 89a. Finally, the cationic Au complex is regenerated for use in the next catalytic cycle. The mono and di-hydration side products 90a and 91a are presumably obtained from intermediate 106.

Scheme 3.30. Proposed catalytic cycle.

3.5. Conclusion

In summary, we have shown a novel synthetic route to 1,6-dihydropyridin-2(3H)-ones through hydrative cyclization of the easily accessible 5-yne-ynamides in the presence of Echavarren’s catalyst and PTSA·H₂O at room temperature. The proposed reaction proceeds easily to afford the product in good to excellent yields and exhibits broad substrate scope; moreover various functional groups are tolerated. Isomerization, epoxidation, and hydrogenation of the double bond are successfully demonstrated.
Sonogashira and Suzuki reactions of the iodo-group help in the introduction of an extended $\pi$-conjugated system into the pyridinone skeleton. Investigations aimed at applying this methodology for the synthesis of complex molecular frameworks and understanding the mechanistic details are underway.

### 3.6. Future Work

Nitrogen-containing six-membered heterocycles are found in many biologically active natural products and are useful motif for the construction of complex molecular frameworks. Dihydropiperidine derivatives, obtained from this strategy, can be applied for the synthesis of cis analogues of femoxetine and paroxetine drug derivatives (113) (Scheme 3.31). Paroxetine hydrochloride is used for the treatment of depression, anxiety and panic disorder.

![Scheme 3.31: Synthetic strategy of Paroxetine and Femoxetine](image-url)
3.7. Experimental

3.7.1. General Experimental Information

See page 45 in Chapter 2.

3.7.2. Materials

For purification of dry solvent: see page 46 in chapter 2. Catalyst A (99.9 %), B (99.9 %), C (99.9 %), IPrAuCl (99.9 %), Ph₃PAuCl (99.9 %), In(OTf)₂, Pd(OAc)₂, PdCl₂(PPh₃)₂, and Sc(OTf)₃ were purchased from Sigma Aldrich Ltd. and used as received. Silver salts such as AgSbF₆ and AgNTf₂ were purchased from Sigma Aldrich Ltd. and used as received. PTSA·H₂O, PhB(OH)₂, m-CPBA, Pd-C, phenyl acetylene and 4-bromo benzaldehyde were purchased from Sigma Aldrich Ltd. and used as received. PPh₃, DEAD, CuSO₄·H₂O, 1.10-phenanthroline, K₃PO₄, Na₂CO₃ were purchased from Merck. The aryl iodides used for reactions were purchased from Merck. Trimethylsilyl acetylene, n-butyl lithium (1.6 M in THF), and TBAF (1.0 M in THF) were purchased from Sigma Aldrich Ltd and used. Analytical and spectral data of all those known compounds are exactly matching with the reported values.

3.7.3. Experimental Procedure

\[ TSH\overset{\text{87'}}{\rightarrow} \overset{\text{2.0 mol % PdCl₂(PPh₃)₂}}{\text{Et₃N (3 equiv), rt, 4 h}} \rightarrow \overset{\text{87''}}{\text{Ar¹}} + \overset{\text{87''/92''}}{\text{Ar²}} \]

\[ \overset{\text{87''/92''}}{\text{Ar²}} \rightarrow \overset{\text{QuSO₄·H₂O (10 mol %), 1,10-phenanthroline (20 mol %)}}{\text{K₃PO₄ (2 equiv), toluene 60-65 °C, 6-8 h}} \rightarrow \overset{\text{87/92}}{\text{Ar¹}} \]

Compound 87’ was prepared based on two known synthetic steps staring from the commercially available tosyl amine. First step involves the –Boc protection of the tosylamine. Mitsunobu reaction between N-Boc-protected tosylamine with the propargyl alcohol in the presence of triphenyl phosphine (Ph₃P) and diethyl azodicarboxylate (DEAD) in THF followed by N-Boc deprotection with TFA delivers 87’.

Following the reported procedure, substrate 87 was prepared from 87’ in two simple synthetic steps. Sonogashira reaction between 87’ and aryl iodides provides 87” in good to excellent yields. Finally, Cu-catalyzed C–N bond formations between 87” and 1-bromo-2-arylacetylene 87’’’ afford the precursor 87 in overall good yields.
Hydrative Cyclization

General Procedure for the Synthesis of 87” (GP 1):

To a solution of substrate 87’ (1.0 mmol), PdCl₂(PPh₃)₂ (0.02 mmol) and CuI (0.04 mmol) in THF (5.0 mL) were added aryl iodide (1.3 mmol) and Et₃N (3.0 mmol) successively under an argon atmosphere. The resulting mixture was stirred at room temperature for 4 h. The crude reaction mixture was filtered through a small pad of Celite and concentrated under the reduced pressure. The crude residue was purified using column chromatography on silica gel to afford 87”.

General Procedure for the Synthesis of 87 (GP 2):¹³

A solution of 87” (1.0 mmol), CuSO₄·5H₂O (0.10 mmol), 1,10-phenanthroline (0.20 mmol) and K₃PO₄ (2.0 mmol) in dry toluene (5.0 mL) was stirred in a Schlenck tube. The 1-bromo-2-arylacetylene (87’’’a) was subsequently introduced into the Schlenck tube. The reaction mixture was heated at 70 °C under the nitrogen atmosphere. The progress of the reaction was monitored periodically by TLC. Upon completion, the reaction mixture was cooled to room temperature and diluted with dichloromethane (10 mL). The crude mixture was filtered through a small pad of Celite and concentrated under the reduced pressure. The crude residue was purified using column chromatography on silica gel to provide 87.

Compounds 87”a-t, 87’’’a and 92”’a-i were prepared following the reported procedures.²¹²²

3.7.4. Spectra and Analytical data

4-Methyl-N-(phenylethynyl)-N-(3-phenylprop-2-ynyl)benzenesulfonamide (87a):

![Chemical structure](87a)

Pale yellow solid (720 mg, 78% yield). mp = 63–64 °C. Rₓ = 0.57 (4:1 hexane/EtOAc); [Silica, UV and I₂]. ¹H NMR (400 MHz, CDCl₃) δ 7.93 (d, J = 8.4 Hz, 2H), 7.45–7.37 (m, 2H), 7.34–7.25 (m, 8H), 7.18 (d, J = 8.4 Hz, 2H), 4.57 (s, 2H), 2.40 (s, 3H). ¹³C NMR (101 MHz, CDCl₃) δ 144.9, 134.3, 131.7, 131.6, 129.6, 128.6, 128.3, 128.2, 128.0, 122.6, 122.0, 86.5, 82.0, 81.2, 71.2, 42.9, 21.6. IR (KBr) νmax 2235, 1597, 1489, 1442, 1361, 1170, 1157 cm⁻¹. HRMS (ESI) for C₂₄H₁₉NO₂SNa (M+Na)⁺: calcd 408.1034, found 408.1032.

4-Methyl-N-(phenylethynyl)-N-(3-(p-tolyl)prop-2-yn-1-yl)benzenesulfonamide (87b):

![Chemical structure](87b)

Yellow crystalline solid (725 mg, 76% yield). mp = 65–66 °C. Rₓ = 0.60 (4:1 hexane/EtOAc); [Silica, UV and I₂]. ¹H NMR (400 MHz, CDCl₃) δ 7.93 (d, J = 8.0 Hz, 2H), 7.40 (br t, J = 8.2 Hz, 2H), 7.30 (s, 5H), 7.07 (br s, 4H), 4.56 (s, 2H), 2.37 (s, 3H), 2.34 (s, 3H). ¹³C NMR (101 MHz, CDCl₃) δ 144.9, 138.8, 134.3,
131.6, 129.6, 128.9, 128.3, 128.0, 122.7, 119.0, 86.7, 82.1, 80.5, 71.2, 43.0, 21.6, 21.5. IR (KBr) \( \nu_{\text{max}} \) 2235, 1597, 1423, 1168, 1037 cm\(^{-1}\). MS (EI) \( m/z \) (%) 400 (M\(^+\) + 1, 100), 345 (22). Anal. calcd for C\(_{12}\)H\(_{12}\)NO\(_2\)S: C, 75.16; H, 5.30; N, 3.51. Found: C, 75.08; H, 5.41; N, 3.58.

N-(3-(4-Methoxyphenyl)prop-2-yn-1-yl)-4-methyl-N-(phenylethynyl)benzenesulfonamide (87c):

Yellow crystalline solid (822 mg, 83% yield). mp = 63–64 °C. \( R_f = 0.44 \) (19:1 hexane/EtOAc); [Silica, UV and I\(_2\)]. \(^1\)H NMR (400 MHz, CDCl\(_3\)) \( \delta \) 7.94 (d, \( J = 8.4 \) Hz, 2H), 7.45–7.38 (m, 2H), 7.36–7.27 (m, 5H), 7.14 (d, \( J = 8.8 \) Hz, 2H), 6.79 (d, \( J = 8.8 \) Hz, 2H), 4.56 (s, 2H), 3.80 (s, 3H), 2.38 (s, 3H). \(^{13}\)C NMR (101 MHz, CDCl\(_3\)) \( \delta \) 159.7, 144.8, 134.2, 133.1, 131.4, 129.5, 128.2, 128.1, 127.9, 122.6, 114.0, 113.7, 86.4, 82.0, 79.7, 71.0, 55.2, 42.9, 21.5. IR (KBr) \( \nu_{\text{max}} \) 2233, 1604, 1510, 1367, 1249, 1168, 1111 cm\(^{-1}\). MS (EI) \( m/z \) (%) 416 (M\(^+\) + 1, 100), 356 (28), 242 (35), 186 (45). Anal. calcd for C\(_{25}\)H\(_{21}\)NO\(_3\)S: C, 72.27; H, 5.09; N, 3.37. Found: C, 72.16; H, 5.15; N, 3.31.

N-(3-(4-Fluorophenyl)prop-2-yn-1-yl)-4-methyl-N-(phenylethynyl)benzenesulfonamide (87d):

Colorless solid (609 mg, 63% yield). mp = 88–89 °C. \( R_f = 0.56 \) (4:1 hexane/EtOAc); [Silica, UV and I\(_2\)]. \(^1\)H NMR (400 MHz, CDCl\(_3\)) \( \delta \) 7.94 (d, \( J = 8.4 \) Hz, 2H), 7.45–7.36 (m, 2H), 7.35–7.29 (m, 5H), 7.22–7.14 (m, 2H), 7.02–6.93 (m, 2H), 4.57 (s, 2H), 2.39 (s, 3H). \(^{13}\)C NMR (101MHz, CDCl\(_3\)) \( \delta \) 162.6 (d, \( J = 394.7 \) Hz), 144.9, 134.3, 133.6 (d, \( J = 32.0 \) Hz), 131.6, 129.6, 128.3 (d, \( J = 11.6 \) Hz), 128.0, 122.6, 118.1 (d, \( J = 13.2 \) Hz), 115.6, 115.4, 85.5, 82.0, 81.0, 71.2, 42.8, 21.6. \(^{19}\)F NMR (376 MHz, CDCl\(_3\)) \( \delta \) –110.1 (octet, \( J = 5.64 \) Hz). IR (KBr) \( \nu_{\text{max}} \) 3057, 2233, 1599, 1506, 1367, 1230, 1170, 1091, 1039 cm\(^{-1}\). HRMS (ESI) for C\(_{24}\)H\(_{18}\)FNO\(_2\)SNa (M+Na\(^+\))\(^+\): calcd 426.094, found 426.0936.

N-(3-(4-Chlorophenyl)prop-2-yn-1-yl)-4-methyl-N-(phenylethynyl)benzenesulfonamide (87e):

Pale yellow solid (688 mg, 69% yield). mp = 47–48 °C. \( R_f = 0.62 \) (4:1 hexane/EtOAc); [Silica, UV and I\(_2\)]. \(^1\)H NMR (400 MHz, CDCl\(_3\)) \( \delta \) 7.92 (d, \( J = 8.4 \) Hz, 2H), 7.44–7.36 (m, 2H), 7.35–7.21 (m, 7H), 7.11 (d, \( J = 8.4 \) Hz, 2H), 4.56 (s, 2H), 2.38 (s, 3H). \(^{13}\)C NMR (101 MHz, CDCl\(_3\)) \( \delta \) 145.0, 134.7, 134.3, 132.9, 131.6, 129.6, 128.5, 128.3, 128.2, 128.1, 122.6, 120.5, 85.4, 82.3, 82.0, 71.2, 42.8, 21.6. IR (KBr) \( \nu_{\text{max}} \) 2235, 1595, 1489, 1371, 1170, 1113 cm\(^{-1}\). MS (EI) \( m/z \) (%) 420 (M\(^{+}\) + 1, 100). Anal. calcd for C\(_{24}\)H\(_{18}\)ClNO\(_2\)S: C, 68.65; H, 4.32; N, 3.34. Found: C, 68.49; H, 4.38; N, 3.31.
N-(3-(4-Bromophenyl)prop-2-yn-1-yl)-4-methyl-N-(phenylethynyl)benzenesulfonamide (87f):
pale yellow solid (886 mg, 76% yield). mp = 77–78 °C. \( R_f = 0.60 \) (4:1 hexane/EtOAc); [Silica, UV and I\(_2\)]. \(^1\)H NMR (400 MHz, CDCl\(_3\)) \( \delta \) 7.92 (d, \( J = 8.4 \) Hz, 2H), 7.48–7.35 (m, 4H), 7.32–7.22 (m, 5H), 7.11–6.94 (m, 2H), 4.55 (s, 2H), 2.38 (s, 3H). \(^{13}\)C NMR (101 MHz, CDCl\(_3\)) \( \delta \) 144.9, 134.3, 133.1, 131.6, 129.6, 128.4, 128.3, 128.1, 123.0, 122.5, 121.0, 85.4, 82.5, 81.9, 71.2, 42.9, 21.6. IR (KBr) \( \nu_{\text{max}} \) 2233, 1593, 1371, 1170, 1114, 1033 cm\(^{-1}\). HRMS (ESI) for C\(_{24}\)H\(_{18}\)BrNO\(_2\)SNa (M+Na\(^+\)): calcd 486.014, found 486.014.

N-(3-(4-Iodophenyl)prop-2-yn-1-yl)-4-methyl-N-(phenylethynyl)benzenesulfonamide (87g):
pale yellow solid (751 mg, 62% yield). mp = 78–79 °C. \( R_f = 0.62 \) (4:1 hexane/EtOAc); [Silica, UV and I\(_2\)]. \(^1\)H NMR (400 MHz, CDCl\(_3\)) \( \delta \) 7.91 (d, \( J = 8.4 \) Hz, 2H), 7.64–7.58 (m, 2H), 7.42–7.35 (m, 2H), 7.34–7.28 (m, 5H), 6.92–6.86 (m, 2H), 4.54 (s, 2H), 2.38 (s, 3H). \(^{13}\)C NMR (101 MHz, CDCl\(_3\)) \( \delta \) 144.9, 137.4, 134.3, 133.1, 131.6, 129.6, 128.3, 128.2, 128.1, 122.5, 121.5, 94.7, 85.6, 82.7, 81.9, 71.2, 42.9, 21.6. IR (KBr) \( \nu_{\text{max}} \) 2233, 1595, 1485, 1483, 1371, 1170, 1114 cm\(^{-1}\). HRMS (ESI) for C\(_{24}\)H\(_{18}\)INO\(_2\)SNa (M+Na\(^+\)): calcd 534.0001, found 534.0001.

4-Methyl-N-(phenylethynyl)-N-(3-(\( m \)-tolyl)prop-2-yn-1-yl)benzenesulfonamide (87h):
thick brown liquid (622 mg, 65% yield). \( R_f = 0.60 \) (4:1 hexane/EtOAc); [Silica, UV and I\(_2\)]. \(^1\)H NMR (400 MHz, CDCl\(_3\)) \( \delta \) 7.92 (d, \( J = 8.4 \) Hz, 2H), 7.49–7.38 (m, 2H), 7.35–7.23 (m, 5H), 7.18–7.07 (m, 2H), 6.98 (d, \( J = 8.4 \) Hz, 2H), 4.57 (s, 2H), 2.38 (s, 3H), 2.30 (s, 3H). \(^{13}\)C NMR (101 MHz, CDCl\(_3\)) \( \delta \) 144.9, 137.8, 134.3, 132.3, 131.6, 129.6, 129.5, 128.7, 128.3, 128.1, 122.7, 121.9, 86.7, 82.1, 80.8, 71.2, 42.9, 21.6, 21.2. IR (Neat) \( \nu_{\text{max}} \) 2233, 1707, 1599, 1487, 1442, 1363, 1168 cm\(^{-1}\). MS (EI) \( m/\zeta \) (%): 401 (M\(^{+}\)+2, 72), 400 (M\(^{+}\)+1, 100), 171 (32). Anal. calcd for C\(_{25}\)H\(_{21}\)NO\(_2\)S: C, 75.16; H, 5.30; N, 3.51. Found: C, 75.21; H, 5.37; N, 3.46.

4-Methyl-N-(phenylethynyl)-N-(3-(\( o \)-tolyl)prop-2-yn-1-yl)benzenesulfonamide (87i):
pale yellow crystalline solid (696 mg, 73% yield). mp = 59–60 °C. \( R_f = 0.60 \) (4:1 hexane/EtOAc); [Silica, UV and I\(_2\)]. \(^1\)H NMR (400 MHz, CDCl\(_3\)) \( \delta \) 7.91 (d, \( J = 7.6 \) Hz, 2H), 7.40 (br s, 2H), 7.36–7.23 (m, 5H), 7.21–7.04 (m, 4H), 4.62 (s, 2H), 2.31 (s, 3H), 2.19 (s, 3H). \(^{13}\)C NMR (101 MHz, CDCl\(_3\)) \( \delta \) 145.0, 140.3, 134.2, 132.0, 131.6, 129.6, 129.3, 128.6, 128.3, 128.2, 128.1, 125.4, 122.6, 121.9, 85.6, 85.0, 82.1, 71.3, 43.0, 21.5, 20.4. IR (KBr) \( \nu_{\text{max}} \) 2227, 1595, 1485, 1440, 1365, 1168, 1103, 1026 cm\(^{-1}\). MS (EI) \( m/\zeta \) (%): 401 (M\(^{+}\)+2, 27), 400 (M\(^{+}\)+1, 100), 374 (27), 286 (20), 203 (24). Anal. calcd for C\(_{25}\)H\(_{21}\)NO\(_2\)S: C, 75.16; H, 5.30; N, 3.51. Found: C, 75.21; H, 5.38; N, 3.65.
N-(3-(2-Methoxyphenyl)prop-2-yn-1-yl)-4-methyl-N-(phenylethynyl)benzenesulfonamide (87j):

A thick brown liquid (630 mg, 64% yield). R<sub>f</sub> = 0.57 (4:1 hexane/EtOAc); [Silica, UV and I<sub>2</sub>]. 1H NMR (400 MHz, CDCl<sub>3</sub>) δ 7.93 (d, J = 8.4 Hz, 2H), 7.43–7.37 (m, 2H), 7.33–7.24 (m, 6H), 7.04 (dd, J = 7.6, 1.6 Hz, 1H), Rf = 0.57 (4:1 hexane/EtOAc); [Silica, UV and I<sub>2</sub>]. 1H NMR (400 MHz, CDCl<sub>3</sub>) δ 7.93 (d, J = 8.4 Hz, 2H), 7.43–7.37 (m, 2H), 7.33–7.24 (m, 6H), 7.04 (dd, J = 7.6, 1.6 Hz, 1H), 6.87–6.80 (m, 2H), 4.63 (s, 2H), 3.80 (s, 3H), 2.35 (s, 3H). 13C NMR (101 MHz, CDCl<sub>3</sub>) δ 160.0, 144.8, 134.2, 133.8, 131.6, 130.1, 129.5, 128.3, 128.2, 127.9, 122.8, 120.2, 111.2, 110.6, 85.1, 83.1, 82.1, 71.2, 55.7, 43.2, 21.6. IR (Neat) ν<sub>max</sub> 2235, 1597, 1493, 1367, 1265, 1170 cm<sup>-1</sup>. MS (EI) m/z (%) 417 (M<sup>+</sup>+2, 13), 416 (M<sup>+</sup>+1, 100). Anal. calcd for C<sub>25</sub>H<sub>21</sub>NO<sub>3</sub>S: C, 72.27; H, 5.09; N, 3.37. Found: C, 72.36; H, 5.13; N, 3.45.

N-(3-(2-Bromophenyl)prop-2-yn-1-yl)-4-methyl-N-(phenylethynyl)benzenesulfonamide (87k):

A pale yellow solid (650 mg, 56% yield). mp = 70–71 °C. R<sub>f</sub> = 0.59 (4:1 hexane/EtOAc); [Silica, UV and I<sub>2</sub>]. 1H NMR (400 MHz, CDCl<sub>3</sub>) δ 7.92 (d, J = 8.0 Hz, 2H), 7.52 (d, J = 8.0 Hz, 1H), 7.45–7.37 (m, 2H), 7.34–7.23 (m, 5H), 7.22–7.13 (m, 3H), 4.63 (s, 2H), 2.31 (s, 3H). 13C NMR (101 MHz, CDCl<sub>3</sub>) δ 145.0, 134.1, 133.6, 132.3, 131.6, 129.8, 129.6, 128.3, 128.0, 126.8, 125.3, HRMS (ESI) for C<sub>24</sub>H<sub>18</sub>BrNO<sub>2</sub>SNa (M<sup>+</sup>+Na)<sup>+</sup>: calcd 486.014, found 486.0121.

N-(3-(2-Iodophenyl)prop-2-yn-1-yl)-4-methyl-N-(phenylethynyl)benzenesulfonamide (87l):

A colorless solid (771 mg, 63% yield). mp = 83–84 °C. R<sub>f</sub> = 0.59 (4:1 hexane/EtOAc); [Silica, UV and I<sub>2</sub>]. 1H NMR (400 MHz, CDCl<sub>3</sub>) δ 7.92 (d, J = 8.4 Hz, 2H), 7.78 (d, J = 8.0 Hz, 1H), 7.47–7.38 (m, 2H), 7.34–7.21 (m, 6H), 7.15 (dd, J = 8.0, 1.6 Hz, 1H), 6.98 (td, J = 7.6, 1.6 Hz, 1H), 4.63 (s, 2H), 2.30 (s, 3H). 13C NMR (101 MHz, CDCl<sub>3</sub>) δ 145.0, 138.7, 134.2, 132.9, 131.6, 129.8, 129.6, 128.3, 128.0, 126.8, 125.3, 124.3, 122.6, 84.9, 71.3, 42.9, 21.6. IR (KBr) ν<sub>max</sub> 2235, 1593, 1462, 1363, 1166, 1117, 1084, 1023 cm<sup>-1</sup>. HRMS (ESI) for C<sub>24</sub>H<sub>18</sub>INO<sub>2</sub>SNa (M<sup>+</sup>+Na)<sup>+</sup>: calcd 534.0001, found 534.0001.

4-Methyl-N-(3-(naphthalen-1-yl)prop-2-yn-1-yl)-N-(phenylethynyl)benzenesulfonamide (87m):

A colorless solid (784 mg, 75% yield). mp = 84–85 °C. R<sub>f</sub> = 0.57 (4:1 hexane/EtOAc); [Silica, UV and I<sub>2</sub>]. 1H NMR (400 MHz, CDCl<sub>3</sub>) δ 7.98 (d, J = 6.8 Hz, 1H), 7.95 (d, J = 6.8 Hz, 2H), 7.82 (d, J = 6.4 Hz, 2H), 7.52–7.45 (m, 4H), 7.43–7.38 (m, 1H), 7.36–7.32 (m, 3H), 7.31–7.27 (m, 1H), 7.12 (d, J = 6.4 Hz, 2H), 4.76 (s, 2H), 2.07 (s, 3H). 13C NMR (101 MHz, CDCl<sub>3</sub>) δ 145.1, 134.0, 133.0, 132.9, 131.7, 130.4, 129.5, 129.1, 128.3, 128.2, 128.1, 128.0, 126.7, 126.4, 126.1, 125.0, 122.6.
Hydrative Cyclization…….

119.8, 86.0, 84.9, 82.3, 71.5, 43.3, 21.3. IR (KBr) \( \nu_{\text{max}} \) 2227, 1595, 1444, 1359, 1170, 1109 cm\(^{-1}\).

MS (EI) \( m/z (%) \) 437 (M\(^+\)+2, 82), 436 (M\(^+\)+1, 100). Anal. calcd for C\(_{28}\)H\(_{21}\)NO\(_2\)S: C, 77.21; H, 4.86; N, 3.22. Found: C, 77.36; H, 4.83; N, 3.31.

4-Methyl-N-(phenylethynyl)-N-(3-(thiophen-2-yl)prop-2-yn-1-yl)benzenesulfonamide (87n):

brown solid (539 mg, 58% yield). mp = 81–82 °C. \( R_f = 0.55 \) (4:1 hexane/EtOAc); [Silica, UV and I\(_2\)]. \(^1\)H NMR (400 MHz, CDCl\(_3\)) \( \delta \): 7.93 (d, \( J = 8.4 \) Hz, 2H), 7.47–7.37 (m, 2H), 7.36–7.27 (m, 5H), 7.24 (dd, \( J = 5.2, 0.8 \) Hz, 1H), 7.04 (d, \( J = 3.2 \) Hz, 1H), 6.93 (dd, \( J = 5.2, 4.0 \) Hz, 1H), 4.59 (s, 2H), 2.40 (s, 3H).

\(^{13}\)C NMR (101 MHz, CDCl\(_3\)) \( \delta \): 145.1, 134.1, 132.7, 131.7, 129.7, 128.3, 128.2, 128.1, 127.7, 126.9, 122.6, 121.9, 85.1, 82.0, 79.9, 71.3, 43.1, 21.7. IR (KBr) \( \nu_{\text{max}} \) 2230, 1364, 1167, 1084, 1035 cm\(^{-1}\). HRMS (ESI) for C\(_{22}\)H\(_{17}\)NO\(_2\)S\(_2\)Na (M+Na): calcd 414.0599, found 414.0594.

Ethyl 3-(3-(4-methyl-N-(phenylethynyl)phenylsulfonamido)prop-1-yn-1-yl)-1H-indole-1-carboxylate (87o):

thick brown liquid (630 mg, 53% yield). \( R_f = 0.55 \) (4:1 hexane/EtOAc); [Silica, UV and I\(_2\)]. \(^1\)H NMR (400 MHz, CDCl\(_3\)) \( \delta \): 8.13 (d, \( J = 8.4 \) Hz, 1H), 7.93 (d, \( J = 8.0 \) Hz, 2H), 7.61 (s, 1H), 7.47–7.12 (m, 10H), 4.65 (s, 2H), 4.51 (q, \( J = 6.8 \) Hz, 2H), 2.22 (s, 3H), 1.48 (t, \( J = 7.2 \) Hz, 3H).

\(^{13}\)C NMR (101 MHz, CDCl\(_3\)) \( \delta \): 150.3, 145.0, 144.9, 134.4, 134.2, 131.7, 130.1, 129.6, 128.6, 128.3, 128.1, 125.4, 123.4, 122.6, 120.1, 115.1, 103.0, 84.9, 82.1, 78.5, 71.3, 63.7, 43.1, 21.4, 14.4. IR (Neat) \( \nu_{\text{max}} \) 2229, 1758, 1725, 1456, 1402, 1380, 1341, 1308, 1232, 1166 cm\(^{-1}\). HRMS (ESI) for C\(_{29}\)H\(_{24}\)N\(_2\)O\(_4\)SNa (M+Na): calcd 519.1355, found 519.1354.

N-(3-(Benzo[d][1,3]dioxol-5-yl)prop-2-yn-1-yl)-4-methyl-N-(phenylethynyl)benzenesulfonamide (87p):

pale brown solid (723 mg, 71% yield). mp = 71–72 °C. \( R_f = 0.44 \) (4:1 hexane/EtOAc); [Silica, UV and I\(_2\)]. \(^1\)H NMR (400 MHz, CDCl\(_3\)) \( \delta \): 7.93 (d, \( J = 6.4 \) Hz, 2H), 7.44–7.38 (m, 2H), 7.34 (s, 1H), 7.32–7.28 (m, 5H), 6.79–6.67 (m, 2H), 5.98 (s, 2H), 4.55 (s, 2H), 2.42 (s, 3H). \(^{13}\)C NMR (101 MHz, CDCl\(_3\)) \( \delta \): 148.1, 147.2, 144.9, 134.4, 131.6, 129.7, 129.6, 129.3, 128.7, 128.3, 128.2, 127.9, 126.4, 122.7, 115.2, 111.6, 108.3, 101.3, 86.4, 82.1, 79.5, 71.2, 42.9, 21.6. IR (KBr) \( \nu_{\text{max}} \) 2231, 1597, 1491, 1442, 1367, 1248, 1213, 1168, 1113, 1035 cm\(^{-1}\). HRMS (ESI) for C\(_{23}\)H\(_{20}\)NO\(_2\)S (M+H): calcd 430.1035, found 430.1033.
N-(3-(3,5-Dimethylphenyl)prop-2-yn-1-yl)-4-methyl-N-(phenylethynyl)benzenesulfonamide (87q):

Pall yellow liquid (712 mg, 72% yield). Rf = 0.41 (4:1 hexane/EtOAc); [Silica, UV and I2]. 1H NMR (400 MHz, CDCl3) δ 7.94 (d, J = 8.0 Hz, 2H), 7.46–7.38 (m, 2H), 7.35–7.27 (m, 5H), 6.95 (s, 2H), 6.82 (s, 1H), 4.57 (s, 2H), 2.39 (s, 3H), 2.27 (s, 6H). 13C NMR (101 MHz, CDCl3) δ 144.7, 137.7, 134.4, 131.6, 130.5, 129.6, 129.3, 128.3, 128.2, 127.9, 122.7, 121.7, 86.9, 82.1, 80.4, 71.2, 43.0, 21.6, 21.1. IR (Neat) νmax 2230, 1598, 1365, 1169, 1086 cm−1. HRMS (ESI) for C26H23NO2SNa (M+Na)+: calcd 436.1347, found 436.1347.

N-(3-(3,4-Dimethylphenyl)prop-2-yn-1-yl)-4-methyl-N-(phenylethynyl)benzenesulfonamide (87r):

Pale brown solid (772 mg, 78% yield). mp = 53–54 °C. Rf = 0.58 (4:1 hexane/EtOAc); [Silica, UV and I2]. 1H NMR (400 MHz, CDCl3) δ 7.92 (d, J = 8.4 Hz, 2H), 7.43–7.37 (m, 2H), 7.34–7.25 (m, 5H), 7.02 (d, J = 7.6 Hz, 1H), 6.95 (s, 1H), 6.92 (d, J = 7.6 Hz, 1H), 4.56 (s, 2H), 2.38 (s, 3H), 2.25 (s, 3H). 13C NMR (101 MHz, CDCl3) δ 144.8, 137.6, 136.5, 134.3, 132.7, 131.6, 129.6, 129.5, 129.1, 128.3, 128.2, 127.9, 122.7, 119.3, 86.9, 82.1, 80.2, 71.2, 43.0, 21.6, 19.8, 19.6. IR (KBr) νmax 2229, 1597, 1442, 1363, 1170, 1107 cm−1. HRMS (ESI) for C26H23NO2SNa (M+Na)+: calcd 436.1347, found 436.1348.

N-(3-(2,4-Dimethoxyphenyl)prop-2-yn-1-yl)-4-methyl-N-(phenylethynyl)benzenesulfonamide (87s):

Thick yellow liquid (750 mg, 70% yield). Rf = 0.47 (7:3 hexane/EtOAc); [Silica, UV and I2]. 1H NMR (400 MHz, CDCl3) δ 7.92 (d, J = 7.6 Hz, 2H), 7.43–7.35 (m, 2H), 7.33–7.22 (m, 5H), 6.99 (d, J = 8.4 Hz, 1H), 6.38 (s, 1H), 6.36 (d, J = 7.6 Hz, 1H), 4.60 (s, 2H), 3.80 (s, 3H), 3.77 (s, 3H), 2.40 (s, 3H). 13C NMR (101 MHz, CDCl3) δ 161.4, 144.7, 134.6, 134.3, 131.5, 129.5, 128.3, 128.2, 127.8, 122.8, 104.7, 103.8, 98.2, 83.6, 83.1, 82.2, 71.2, 55.7, 55.5, 43.3, 21.6. IR (Neat) νmax 2937, 2230, 1711, 1606, 1504, 1464, 1365, 1304, 1211, 1168 cm−1. HRMS (ESI) for C26H23NO4SNa (M+Na)+: calcd 468.1246, found 468.1246.

N-(3-(2,6-Dimethoxyphenyl)prop-2-yn-1-yl)-4-methyl-N-(phenylethynyl)benzenesulfonamide (87t):

Brown solid (564 mg, 53% yield). mp = 103–104 °C. Rf = 0.25 (4:1 hexane/EtOAc); [Silica, UV and I2]. 1H NMR (400 MHz, CDCl3) δ 7.94 (d, J = 7.6 Hz, 2H), 7.40 (br s, 2H), 7.36–7.22 (m, 6H), 6.49 (d, J = 8.4 Hz, 2H), 4.69 (s, 2H), 3.76 (s, 6H), 2.34 (s, 3H). 13C NMR (101 MHz, CDCl3) δ 161.8, 144.5,
Hydrative Cyclization……..

134.2, 131.5, 130.1, 129.4, 128.3, 128.1, 127.7, 123.0, 103.4, 89.3, 82.2, 79.3, 71.4, 55.9, 43.5, 21.6. IR (KBr) $\nu_{\text{max}}$ 2930, 2233, 1593, 1475, 1365, 1253, 1170 cm$^{-1}$. HRMS (ESI) for C$_{26}$H$_{23}$NO$_3$SNa (M+Na)$^+$: calcd 468.1246, found 468.1246.

N-(Hept-2-yn-1-yl)-4-methyl-N-(phenylethynyl)benzenesulfonamide (87u):

N-(4-(Benzyloxy)but-2-yn-1-yl)-4-methyl-N-(phenylethynyl)benzenesulfonamide (87v):

N-(3-(Benzyloxy)prop-1-yn-1-yl)-N-(3-(4-iodophenyl)prop-2-yn-1-yl)-4-methyl-benzene-sulfonamide (87x):

4-Methyl-N-(6-methylhept-2-yn-1-yl)-N-(phenylethynyl)benzenesulfonamide (87w):
N-(3-(4-Iodophenyl)prop-2-ynyl)-4-methyl-N-(oct-1-ynyl)benzenesulfonamide (87y):

thick brown liquid (798 mg, 64% yield). \( R_f \) = 0.61 (4:1 hexane/EtOAc); [Silica, UV and I\( _2 \)]. \(^1\)H NMR (400 MHz, CDCl\( _3 \)) \( \delta \) 7.85 (d, \( J = 8.4 \) Hz, 2H), 7.59 (d, \( J = 8.4 \) Hz, 2H), 7.27 (d, \( J = 7.6 \) Hz, 2H), 6.86 (d, \( J = 8.4 \) Hz, 2H), 4.41 (s, 2H), 2.37 (s, 3H), 2.28 (t, \( J = 6.8 \) Hz, 2H), 1.53–1.42 (m, 2H), 1.36–1.28 (m, 2H), 1.26–1.16 (m, 4H), 0.85 (t, \( J = 6.4 \) Hz, 3H). \(^1\)C NMR (101 MHz, CDCl\( _3 \)) \( \delta \) 144.6, 137.2, 134.2, 131.0, 129.7, 129.4, 128.4, 128.2, 128.1, 127.9, 82.1, 79.1, 72.6, 71.2, 71.1, 57.0, 42.1, 31.3, 28.8, 28.4, 22.6, 21.6, 18.5, 14.1. IR (Neat) \( \nu_{\max} \) 2920, 2849, 2246, 1473, 1358, 1161 cm\(^{-1}\). HRMS (ESI) for C\(_{24}\)H\(_{27}\)INO\(_2\)S (M+H): calcd 520.0807, found 520.0807.

N-(4-(Benzyloxy)but-2-ynyl)-4-methyl-N-(oct-1-ynyl)benzenesulfonamide (87z):
pale yellow liquid (555 mg, 93% yield). \( R_f \) = 0.55 (4:1 hexane/EtOAc); [Silica, UV and I\( _2 \)]. \(^1\)H NMR (400 MHz, CDCl\( _3 \)) \( \delta \) 7.83 (d, \( J = 8.4 \) Hz, 2H), 7.42–7.22 (m, 7H), 4.42 (s, 2H), 4.29 (s, 2H), 4.01 (s, 2H), 2.38 (s, 3H), 2.25 (t, \( J = 7.2 \) Hz, 2H), 1.52–1.42 (m, 2H), 1.38–1.19 (m, 6H), 0.88 (t, \( J = 6.4 \) Hz, 3H). \(^1\)C NMR (101 MHz, CDCl\( _3 \)) \( \delta \) 144.6, 137.2, 134.2, 131.0, 129.7, 129.4, 128.4, 128.2, 128.1, 127.9, 82.1, 79.1, 72.6, 71.2, 71.1, 57.0, 42.1, 31.3, 28.8, 28.4, 22.6, 21.6, 18.5, 14.1. IR (Neat) \( \nu_{\max} \) 2930, 2852, 2253, 1457, 1346, 1173 cm\(^{-1}\). HRMS (ESI) for C\(_{24}\)H\(_{32}\)NO\(_3\)S (M+H): calcd 438.2103, found 438.2103.

N-((4-Chlorophenyl)ethynyl)-4-methyl-N-(3-phenylprop-2-yn-1-yl)benzenesulfonamide (92a):
yellow solid (742 mg, 74% yield). mp = 74–75 °C. \( R_f \) = 0.78 (4:1 hexane/EtOAc); [Silica, UV and I\( _2 \)]. \(^1\)H NMR (400 MHz, CDCl\( _3 \)) \( \delta \) 7.91 (d, \( J = 8.0 \) Hz, 2H), 7.37–7.24 (m, 9H), 7.17 (d, \( J = 8.0 \) Hz, 2H), 4.57 (s, 2H), 2.37 (s, 3H). \(^1\)C NMR (101 MHz, CDCl\( _3 \)) \( \delta \) 145.1, 134.2, 134.0, 132.8, 131.6, 129.7, 128.7, 128.6, 128.3, 128.2, 121.9, 121.1, 86.6, 82.9, 81.0, 70.2, 42.9, 21.6. IR (KBr) \( \nu_{\max} \) 2237, 1593, 1491, 1365, 1168, 1109 cm\(^{-1}\). MS (EI) \( m/z \) (%) 422 (M\(^+\)+2, 32), 421 (M\(^+\)+1, 22), 420 (M\(^+\), 100), 264 (24). Anal. calcd for C\(_{24}\)H\(_{14}\)ClNO\(_2\)S: C, 68.65; H, 4.32; N, 3.34. Found: C, 68.51; H, 4.28; N, 3.41.

Hydrative Cyclization......
Hydrative Cyclization……

4-Methyl-N-((4-nitrophenyl)ethyl)yl-N-(3-phenylprop-2-yn-1-yl)benzenesulfonamide (92b):
yellow solid (631 mg, 61% yield). mp = 95–96 °C. Rf = 0.37 (4:1 hexane/EtOAc); [Silica, UV and I2]. 1H NMR (400 MHz, CDCl3) δ8.16 (d, J = 8.8 Hz, 2H), 7.91 (d, J = 8.4 Hz, 2H), 7.49 (d, J = 9.2 Hz, 2H), 7.36–7.24 (m, 5H), 7.18 (d, J = 8.4 Hz, 2H), 4.60 (s, 2H), 2.38 (s, 3H). 

N-((4-Acetylphenyl)ethyl)yl-4-methyl-N-(3-phenylprop-2-yn-1-yl)benzenesulfonamide (92c):
pale brown solid (693 mg, 68% yield). mp = 86–87 °C. Rf = 0.52 (4:1 hexane/EtOAc); [Silica, UV and I2]. 1H NMR (400 MHz, CDCl3) δ7.91 (d, J = 8.0 Hz, 2H), 7.88 (d, J = 8.0 Hz, 2H), 7.45 (d, J = 8.0 Hz, 2H), 7.34–7.22 (m, 5H), 7.18 (br d, J = 6.8 Hz, 2H), 4.59 (s, 2H), 2.59 (s, 3H), 2.36 (s, 3H). 13C NMR (101 MHz, CDCl3) δ197.3, 145.2, 135.7, 134.2, 131.6, 131.0, 129.8, 128.7, 128.3, 128.2, 127.8, 121.9, 86.7, 85.6, 80.9, 71.2, 42.9, 26.6, 21.6. IR (KBr) νmax 2229, 1670, 1604, 1407, 1276, 1177, 1106 cm⁻¹. HRMS (ESI) for C26H21NO3SNa (M+Na)⁺: calcd 450.1140, found 450.1120.

Methyl 4-((methyl-N-(3-phenylprop-2-yn-1-yl)phenylsulfonamido)ethyl)benzoate (92d):
colorless solid (808 mg, 76% yield). mp = 120–121 °C. Rf = 0.63 (4:1 hexane/EtOAc); [Silica, UV and I2]. 1H NMR (400 MHz, CDCl3) δ7.96 (d, J = 8.0 Hz, 2H), 7.92 (d, J = 8.4 Hz, 2H), 7.43 (d, J = 8.4 Hz, 2H), 7.34–7.21 (m, 5H), 7.17 (br d, J = 6.8 Hz, 2H), 4.59 (s, 2H), 3.91 (s, 3H), 2.36 (s, 3H). 13C NMR (101 MHz, CDCl3) δ166.6, 145.2, 134.2, 131.7, 130.8, 129.7, 129.5, 128.9, 127.8, 128.2, 127.6, 121.9, 86.7, 85.2, 80.9, 71.2, 52.2, 42.9, 21.6. IR (KBr) νmax 2229, 1698, 1599, 1440, 1363, 1270, 1166, 1117 cm⁻¹. HRMS (ESI) for C26H21NO4SNa (M+Na)⁺: calcd 466.1089, found 466.1096.

4-Methyl-N-(3-phenylprop-2-yn-1-yl)-N-((4-(trifluoromethyl)phenyl)ethynyl)benzenesulfonamide (92e):
pale yellow solid (725 mg, 67% yield). mp = 45–46 °C. Rf = 0.50 (4:1 hexane/EtOAc); [Silica, UV and I2]. 1H NMR (400 MHz, CDCl3) δ7.94 (br d, J = 6.8 Hz, 2H), 7.69–7.45 (m, 4H), 7.42–7.15 (m, 7H), 4.61 (s, 2H), 2.40 (s, 3H). 13C NMR (101 MHz, CDCl3) δ145.2, 134.2, 131.6, 131.2, 129.7, 128.8, 128.2, 126.7, 125.2, 125.2, 121.9, 86.7, 84.6, 80.9, 70.5, 42.8, 21.6. 19F NMR (376 MHz, CDCl3) δ –62.7 (s). IR (KBr) νmax 2235, 1612, 1491, 1369, 1321, 1170, 1107 cm⁻¹. HRMS (ESI) for C26H18F3NO3SNa (M+Na)⁺: calcd 476.0908, found 476.0912.
N-((3,5-Dimethylphenyl)ethynyl)-4-methyl-N-(3-phenylprop-2-yn-1-yl)benzenesulfonamide (92f):
pale yellow solid (744 mg, 75% yield). mp = 136–137 °C. R_f = 0.58 (4:1 hexane/EtOAc); [Silica, UV and I_2]. \(^1\)H NMR (400 MHz, CDCl_3) δ 7.92 (d, \(J = 8.0\) Hz, 2H), 7.32–7.23 (m, 5H), 7.18 (d, \(J = 8.0\) Hz, 2H), 7.03 (s, 2H), 6.93 (s, 1H), 4.55 (s, 2H), 2.36 (s, 3H), 2.27 (s, 6H). \(^13\)C NMR (101 MHz, CDCl_3) δ 144.8, 137.8, 134.3, 131.7, 129.9, 129.6, 129.2, 128.6, 128.3, 128.1, 122.2, 122.1, 86.5, 81.3, 81.2, 71.4, 42.9, 21.6, 21.1. IR (KBr) ν max 2235, 1597, 1493, 1367, 1265, 1170 cm\(^{-1}\). MS (EI) m/z (%) 415 (M^+ + 2, 30), 414 (M^+ + 1, 100). Anal. calcd for C_{26}H_{23}NO_2S: C, 75.52; H, 5.61; N, 3.39. Found: C, 75.42; H, 5.68; N, 3.31.

N-((3-(4-Bromophenyl)prop-2-yn-1-yl)-N-((3-fluorophenyl)ethynyl)-4-methylbenzenesulfonamide (92g):
colorless solid (718 mg, 62% yield). mp = 72–73 °C. R_f = 0.62 (4:1 hexane/EtOAc); [Silica, UV and I_2]. \(^1\)H NMR (400 MHz, CDCl_3) δ 7.92 (d, \(J = 8.4\) Hz, 2H), 7.42 (d, \(J = 8.4\) Hz, 2H), 7.32 (d, \(J = 8.0\) Hz, 2H), 7.29–7.23 (m, 1H), 7.18 (dt, \(J = 7.6, 1.2\) Hz, 1H), 7.11–6.98 (m, 4H), 4.56 (s, 2H), 2.41 (s, 3H). \(^13\)C NMR (101 MHz, CDCl_3) δ 162.3 (d, \(J = 912.1\) Hz), 145.1, 134.2, 133.1, 131.5, 129.9 (d, \(J = 33.0\) Hz), 129.7, 128.2, 127.2 (d, \(J = 10.9\) Hz), 124.5 (d, \(J = 36.8\) Hz), 123.0, 120.9, 118.1 (d, \(J = 85.3\) Hz), 115.2 (d, \(J = 79.3\) Hz), 85.5, 82.9, 82.3, 70.3, 42.8, 21.6. \(^19\)F NMR (376 MHz, CDCl_3) δ −112.94 (sextet, \(J = 5.6\) Hz). IR (KBr) ν max 2241, 1579, 1485, 1437, 1361, 1165, 1091 cm\(^{-1}\). HRMS (ESI) for C_{24}H_{17}BrFNO_2SNa (M^+Na^+): calcd 504.0045, found 504.0045.

4-Methyl-N-(3-(p-tolyl)prop-2-yn-1-yl)-N-(p-tolylethynyl)benzenesulfonamide (92h):
pale brown solid (496 mg, 50% yield). mp = 50–51 °C. R_f = 0.62 (4:1 hexane/EtOAc); [Silica, UV and I_2]. \(^1\)H NMR (400 MHz, CDCl_3) δ 7.94 (d, \(J = 8.4\) Hz, 2H), 7.35–7.26 (m, 4H), 7.12 (d, \(J = 8.0\) Hz, 2H), 7.08 (s, 4H), 4.57 (s, 2H), 2.39 (s, 3H), 2.36 (s, 3H), 2.35 (s, 3H). \(^13\)C NMR (101 MHz, CDCl_3) δ 144.8, 138.7, 138.2, 134.3, 131.7, 129.6, 129.0, 128.9, 128.3, 119.5, 119.0, 86.6, 81.3, 80.5, 71.1, 43.0, 21.6, 21.5. IR (KBr) ν max 2235, 1510, 1365, 1168, 1107, 1035 cm\(^{-1}\). HRMS (ESI) for C_{26}H_{23}NO_2SNa (M^+Na^+): calcd 436.1347, found 436.1347.

N-((4-Chlorophenyl)ethynyl)-4-methyl-N-(3-(thiophen-2-yl)prop-2-yn-1-yl)benzenesulfonamide (92i):
colorless solid (577 mg, 56% yield). mp = 104–105 °C. R_f = 0.54 (4:1 hexane/EtOAc); [Silica, UV and I_2]. \(^1\)H NMR (400 MHz, CDCl_3) δ 7.90 (d, \(J = 8.4\) Hz, 2H), 7.36–7.26 (m, 4H), 7.12 (d, \(J = 8.0\) Hz, 2H), 7.08 (s, 4H), 4.57 (s, 2H), 2.39 (s, 3H), 2.36 (s, 3H), 2.35 (s, 3H). \(^13\)C NMR (101 MHz, CDCl_3) δ 144.8, 138.7, 138.2, 134.3, 131.7, 129.6, 129.0, 128.9, 128.3, 119.5, 119.0, 86.6, 81.3, 80.5, 71.1, 43.0, 21.6, 21.5. IR (KBr) ν max 2235, 1510, 1365, 1168, 1107, 1035 cm\(^{-1}\). HRMS (ESI) for C_{26}H_{23}NO_2SNa (M^+Na^+): calcd 436.1347, found 436.1347.
Hydrative Cyclization…

1H), 6.93 (dd, J = 5.2, 3.6 Hz, 1H), 4.58 (s, 2H), 2.40 (s, 3H). 13C NMR (101 MHz, CDCl3) δ 145.1, 134.1, 134.0, 132.8, 132.7, 129.8, 128.9, 128.6, 128.2, 127.7, 126.9, 121.8, 121.1, 85.0, 82.8, 79.9, 70.3, 43.0, 21.7. IR (KBr) νmax 2239, 1593, 1363, 1168, 1109, 1086 cm⁻¹. HRMS (ESI) for C22H16ClNO2S2Na (M+Na): calc 448.0202, found 448.0202.

Gold (I) Catalyzed 6-endo-dig Hydrative Cyclization of 5-yne-ynamides 87 and 92; General Procedure (GP-3):

A mixture of substrate 87/92 (0.25 mmol) and PTSA·H2O (119 mg, 0.625 mmol) were placed in a Schlenk flask under an argon atmosphere. The catalyst (2-biphenyl)di-tBu-phosphine(MeCN)Au)SbF6 (A; 5.8 mg, 0.0075 mmol) in 1,4-dioxane (3.0 mL) was introduced in to the Schlenk tube. The reaction mixture was stirred for the specified time shown in the respective Schemes at an ambient temperature. The progress of the reaction was periodically monitored by TLC. After satisfactory conversion of starting material, the reaction mixture was diluted with dichloromethane (10 mL), and filtered over a small pad of Celite. After evaporation of solvent under the reduced pressure, the residue was purified by column chromatography on silica gel.

3,4-Diphenyl-1-tosyl-1,6-dihydropyridin-2(3H)-one (89a):

3-Phenyl-4-(p-tolyl)-1-tosyl-1,6-dihydropyridin-2(3H)-one (89b):
136.6, 135.2, 134.9, 134.2, 129.4, 129.3, 129.1, 128.5, 127.9, 127.5, 125.5, 117.7, 53.4, 46.9, 21.7, 21.1. IR (KBr) \( \nu_{\text{max}} \) 2918, 1697, 1456, 1390, 1168 cm\(^{-1}\). HRMS (ESI) for C\(_{25}\)H\(_{23}\)NO\(_3\)SNa (M+Na)\(^+\): calcd 440.1297, found 440.1270.

**4-(4-Methoxyphenyl)-3-phenyl-1-tosyl-1,6-dihydropyridin-2(3H)-one (89c):**

[Image of the compound]

Colorless solid (92 mg, 85% yield). mp = 64–65 °C. \( R_f = 0.25 \) (4:1 hexane/EtOAc); [Silica, UV and I\(_2\)]. \(^1\)H NMR (400 MHz, CDCl\(_3\)) \( \delta \) 7.80 (d, \( J = 8.0 \) Hz, 2H), 7.29–7.18 (m, 9H), 6.79 (d, \( J = 8.8 \) Hz, 2H), 6.43 (dd, \( J = 5.6, 2.0 \) Hz, 1H), 4.78 (dd, \( J = 17.6, 1.0 \) Hz, 1H), 4.62 (s, 1H), 4.49 (d, \( J = 17.6 \) Hz, 1H), 3.75 (s, 3H), 2.40 (s, 3H). \(^{13}\)C NMR (101 MHz, CDCl\(_3\)) \( \delta \) 168.7, 159.7, 144.9, 136.2, 135.2, 134.9, 129.5, 129.2, 129.1, 128.4, 127.9, 127.4, 126.8, 116.8, 114.0, 55.3, 53.5, 46.9, 21.7. IR (Neat) \( \nu_{\text{max}} \) 2924, 1693, 1514, 1358, 1251, 1170 cm\(^{-1}\). HRMS (ESI) for C\(_{25}\)H\(_{23}\)NO\(_3\)SNa (M+Na)\(^+\): calcd 456.1246, found 456.1246.

**4-(4-Fluorophenyl)-3-phenyl-1-tosyl-1,6-dihydropyridin-2(3H)-one (89d):**

[Image of the compound]

Thick yellow liquid (80 mg, 76% yield). \( R_f = 0.38 \) (4:1 hexane/EtOAc); [Silica, UV and I\(_2\)]. \(^1\)H NMR (400 MHz, CDCl\(_3\)) \( \delta \) 7.82 (d, \( J = 8.0 \) Hz, 2H), 7.29–7.18 (m, 9H), 6.79 (t, \( J = 8.8 \) Hz, 2H), 6.47 (dd, \( J = 5.6, 2.0 \) Hz, 1H), 4.82 (ddd, \( J = 18, 5.6, 0.4 \) Hz, 1H), 4.60 (s, 1H), 4.55 (dd, \( J = 18, 2.0 \) Hz, 1H), 2.41 (s, 3H). \(^{13}\)C NMR (101 MHz, CDCl\(_3\)) \( \delta \) 168.4, 162.6 (d, \( J = 929.1 \) Hz), 145.0, 135.8, 135.1, 134.7, 133.3 (d, \( J = 12.0 \) Hz), 129.3, 129.2, 128.5 (d, \( J = 22.2 \) Hz), 128.1, 127.5 (d, \( J = 10.9 \) Hz), 127.4, 118.6, 115.7, 115.5, 53.6, 46.9, 21.7. \(^{19}\)F NMR (376 MHz, CDCl\(_3\)) \( \delta \) -113.1 (sextet, \( J = 5.6 \) Hz). IR (Neat) \( \nu_{\text{max}} \) 2924, 1693, 1599, 1510, 1358, 1232, 1170, 1087 cm\(^{-1}\). HRMS (ESI) for C\(_{24}\)H\(_{20}\)FNO\(_3\)SNa (M+Na)\(^+\): calcd 444.1046, found 444.1046.

**4-(4-Chlorophenyl)-3-phenyl-1-tosyl-1,6-dihydropyridin-2(3H)-one (89e):**

[Image of the compound]

Yellow solid (71 mg, 65% yield). mp = 95–96 °C. \( R_f = 0.28 \) (4:1 hexane/EtOAc); [Silica, UV and I\(_2\)]. \(^1\)H NMR (400 MHz, CDCl\(_3\)) \( \delta \) 7.80 (d, \( J = 8.4 \) Hz, 2H), 7.32–7.15 (m, 11H), 6.50 (dd, \( J = 5.6, 2.0 \) Hz, 1H), 4.80 (dd, \( J = 18, 5.6 \) Hz, 1H), 4.58 (s, 1H), 4.49 (dd, \( J = 18, 2.0 \) Hz, 1H), 2.40 (s, 3H). \(^{13}\)C NMR (101 MHz, CDCl\(_3\)) \( \delta \) 168.5, 145.0, 135.7, 135.5, 135.1, 134.6, 134.3, 129.3, 129.2, 128.9, 128.5, 128.1, 127.4, 127.0, 119.1, 53.3, 46.9, 21.7. IR (KBr) \( \nu_{\text{max}} \) 2924, 1689, 1593, 1454, 1361, 1178, 1089 cm\(^{-1}\). HRMS (ESI) for C\(_{24}\)H\(_{20}\)ClNO\(_3\)SNa (M+Na)\(^+\): calcd 460.075, found 460.075.

**4-(4-Bromophenyl)-3-phenyl-1-tosyl-1,6-dihydropyridin-2(3H)-one (89f):**

[Image of the compound]

Yellow solid (89 mg, 74% yield). mp = 169–170 °C. \( R_f = 0.33 \) (4:1 hexane/EtOAc); [Silica, UV and I\(_2\)]. \(^1\)H NMR (400 MHz, CDCl\(_3\)) \( \delta \) 7.80 (d, \( J = 8.0 \) Hz, 2H), 7.32–7.15 (m, 11H), 6.50 (dd, \( J = 5.6, 2.0 \) Hz, 1H), 4.80 (dd, \( J = 18, 5.6 \) Hz, 1H), 4.58 (s, 1H), 4.49 (dd, \( J = 18, 2.0 \) Hz, 1H), 2.40 (s, 3H). \(^{13}\)C NMR (101 MHz, CDCl\(_3\)) \( \delta \) 168.5, 145.0, 135.7, 135.5, 135.1, 134.6, 134.3, 129.3, 129.2, 128.9, 128.5, 128.1, 127.4, 127.0, 119.1, 53.3, 46.9, 21.7. IR (KBr) \( \nu_{\text{max}} \) 2924, 1689, 1593, 1454, 1361, 1178, 1089 cm\(^{-1}\). HRMS (ESI) for C\(_{24}\)H\(_{20}\)BrNO\(_3\)SNa (M+Na)\(^+\): calcd 460.075, found 460.075.
= 8.0 Hz, 2H), 7.38 (d, J = 8.4 Hz, 2H), 7.29–7.17 (m, 7H), 7.12 (d, J = 8.4 Hz, 2H), 6.51 (dd, J = 5.6, 2.4 Hz, 1H), 4.79 (dd, J = 18, 5.6 Hz, 1H), 4.58 (s, 1H), 4.52 (dd, J = 18, 2.4 Hz, 1H), 2.41 (s, 3H). \(^{13}\)C NMR (101 MHz, CDCl\(_3\)) \(\delta\) 168.3, 145.0, 136.0, 135.8, 135.1, 134.6, 131.8, 129.3, 129.2, 128.5, 128.1, 127.4, 127.2, 122.5, 119.2, 53.2, 46.9, 21.7. IR (KBr) \(\nu_{\text{max}}\) 2928, 1699, 1493, 1456, 1358, 1170 cm\(^{-1}\). HRMS (ESI) for C\(_{24}\)H\(_{20}\)BrNO\(_3\)SNa (M+Na): calcd 504.0245, found 504.0245.

4-(4-Iodophenyl)-3-phenyl-1-tosyl-1,6-dihydropyridin-2(3H)-one (89g):

\[
\begin{align*}
\text{89g} & \quad \text{colorless solid (96 mg, 73% yield). mp = 152–153 \degree C. R}_f = 0.30 (4:1 \text{ hexane/EtOAc); [Silica, UV and I}_2. \quad \text{H NMR (400 MHz, CDCl}_3\text{) } \delta 7.80 (d, J = 8.4 \text{ Hz, 2H), 7.58 (d, J = 8.4 \text{ Hz, 2H), 7.29–7.15 (m, 7H), 6.99 (d, J = 8.4 Hz, 2H), 6.51 (dd, J = 5.6, 2.4 Hz, 1H), 4.79 (dd, J = 18, 5.6 Hz, 1H), 4.57 (s, 1H), 4.54 (dd, J = 18, 2.0 Hz, 1H), 2.40 (s, 3H).} \\
\text{13C NMR (101 MHz, CDCl}_3\text{) } \delta 168.3, 145.0, 137.8, 136.6, 135.9, 135.1, 134.6, 129.3, 129.2, 128.5, 128.1, 127.4, 119.2, 94.2, 53.1, 46.9, 21.7. \text{IR (Neat) } \nu_{\text{max}} 2924, 1699, 1489, 1358, 1170, 1153, 1086 \text{ cm}^{-1}. \text{ HRMS (ESI) for C}_{24}\text{H}_{21}\text{INO}_3 \text{S} (M+H)}: \text{calcd 530.0287, found 530.0287.}
\end{align*}
\]

3-Phenyl-4-(m-tolyl)-1-tosyl-1,6-dihydropyridin-2(3H)-one (89h):

\[
\begin{align*}
\text{89h} & \quad \text{pale yellow liquid (86 mg, 83% yield). } R_f = 0.36 (4:1 \text{ hexane/EtOAc); [Silica, UV and I}_2. \quad \text{H NMR (400 MHz, CDCl}_3\text{) } \delta 7.80 (d, J = 8.4 \text{ Hz, 2H), 7.31–7.18 (m, 7H), 7.16–7.08 (m, 2H), 7.07 (br t, J = 6.8 Hz, 2H), 6.51 (dd, J = 5.6, 2.0 Hz, 1H), 4.66 (s, 1H), 4.50 (d, J = 18 Hz, 1H), 2.40 (s, 3H), 2.29 (s, 3H).} \\
\text{13C NMR (101 MHz, CDCl}_3\text{) } \delta 168.7, 144.9, 138.3, 137.1, 137.0, 135.2, 134.8, 129.3, 129.2, 128.6, 128.4, 127.9, 127.5, 126.3, 122.8, 118.5, 53.5, 46.9, 21.7, 21.5. \text{IR (Neat) } \nu_{\text{max}} 2924, 1695, 1597, 1462, 1358, 1170, 1086 \text{ cm}^{-1}. \text{ HRMS (ESI) for C}_{25}\text{H}_{23}\text{NO}_3 \text{SNa} (M+Na): \text{calcd 440.1297, found 440.1270.}
\end{align*}
\]

3-Phenyl-4-(o-tolyl)-1-tosyl-1,6-dihydropyridin-2(3H)-one (89i):

\[
\begin{align*}
\text{89i} & \quad \text{colorless solid (79 mg, 76% yield). mp = 130–131 \degree C. } R_f = 0.41 (4:1 \text{ hexane/EtOAc); [Silica, UV and I}_2. \quad \text{H NMR (400 MHz, CDCl}_3\text{) } \delta 7.88 (d, J = 8.0 \text{ Hz, 2H), 7.27 (d, J = 8.0 \text{ Hz, 2H), 7.25–6.95 (m, 8H), 6.87 (d, J = 7.6 Hz, 1H), 5.96 (dd, J = 5.2, 2.4 Hz, 1H), 4.81 (ddd, J = 17.6, 4.8, 2.0 Hz, 1H), 4.67 (dt, J = 17.6, 2.4 Hz, 1H), 4.34 (s, 1H), 2.42 (s, 3H), 2.16 (s, 3H).} \\
\text{13C NMR (101 MHz, CDCl}_3\text{) } \delta 168.8, 145.0, 138.2, 138.1, 136.0, 135.3, 135.1, 130.5, 129.3, 128.9, 128.6, 128.5, 127.9, 127.8, 125.7, 120.2, 55.4, 47.2, 21.7, 19.9. \text{IR (KBr) } \nu_{\text{max}} 2926, 1689, 1466, 1346, 1174, 1145, 1087 \text{ cm}^{-1}. \text{ HRMS (ESI) for C}_{25}\text{H}_{23}\text{NO}_3 \text{SNa} (M+Na): \text{calcd 440.1297, found 440.1299.}
\end{align*}
\]
4-(2-Methoxyphenyl)-3-phenyl-1-tosyl-1,6-dihydropyridin-2(3H)-one (89j):

```
colorless solid (83 mg, 77% yield). mp = 56−57 °C. Rf = 0.37 (4:1
hexane/EtOAc); [Silica, UV and I2]. ¹H NMR (400 MHz, CDCl₃) δ 7.86 (d, J =
8.4 Hz, 2H), 7.27 (d, J = 8.8 Hz, 2H), 7.23−7.06 (m, 6H), 7.01 (dd, J = 8.0, 2.0
Hz, 1H), 6.84−6.78 (m, 2H), 6.19 (dd, J = 4.8, 2.8 Hz, 1H), 4.83 (s, 1H), 4.77 (dd,
J = 17.2, 4.4 Hz, 1H), 6.0 (dd, J = 17.6, 5.2 Hz, 1H), 3.76 (s, 3H), 2.41 (s, 3H). ¹³C NMR
(101 MHz, CDCl₃) δ 169.3, 156.5, 144.9, 136.7, 136.2, 135.4, 130.1, 129.4, 129.2, 128.7, 128.6, 127.8, 127.4, 127.2, 120.7, 120.5, 110.7, 55.3, 53.4, 47.1, 21.7. IR (KBr) νmax 2924, 1695, 1491, 1458, 1358, 1170 cm⁻¹. HRMS (ESI) for C₂₅H₂₃NO₄SNa (M+Na)+: calcd 456.1246, found 456.1246.
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4-(2-Bromophenyl)-3-phenyl-1-tosyl-1,6-dihydropyridin-2(3H)-one (89k):

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pale brown solid (96 mg, 80% yield). mp = 88−89 °C. Rf = 0.69 (3:1
hexane/EtOAc); [Silica, UV and I2]. ¹H NMR (400 MHz, CDCl₃) δ 7.89 (d, J =
8.4 Hz, 2H), 7.50 (d, J = 7.6 Hz, 1H), 7.27 (d, J = 8.0 Hz, 3H), 7.23−7.06 (m,
6H), 6.90 (dd, J = 18, 4.8 Hz, 1H), 4.62 (s, 1H), 2.41 (s, 3H). ¹³C NMR (101 MHz, CDCl₃) δ 168.5,
145.0, 138.9, 138.0, 135.7, 135.3, 133.0, 130.7, 129.4, 129.3, 128.9, 128.6, 128.3, 128.0, 127.8,
127.3, 121.2, 121.8, 54.1, 47.0, 21.7. IR (KBr) νmax 2926, 1689, 1595, 1462, 1348, 1174, 1147,
1087 cm⁻¹. HRMS (ESI) for C₂₄H₂₀BrNO₃SNa (M+Na)+: calcd 504.0245, found 504.0245.
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4-(2-Iodophenyl)-3-phenyl-1-tosyl-1,6-dihydropyridin-2(3H)-one (89l):

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colorless solid (110 mg, 83% yield). mp = 54−55 °C. Rf = 0.34 (4:1
hexane/EtOAc); [Silica, UV and I2]. ¹H NMR (400 MHz, CDCl₃) δ 7.90 (d, J =
8.4 Hz, 2H), 7.80 (dd, J = 8.0, 1.2 Hz, 1H), 7.28 (d, J = 8.4 Hz, 2H), 7.25−7.18
(m, 3H), 7.16 (td, J = 7.2, 0.8 Hz, 1H), 7.12−7.05 (m, 2H), 6.92 (td, J = 8.0, 2.0 Hz, 1H), 6.85 (dd,
J = 7.6, 1.6 Hz, 1H), 6.04 (dd, J = 4.8, 2.4 Hz, 1H), 4.86 (ddd, J = 17.6, 4.8, 2.0 Hz, 1H), 4.69 (dt,
J = 17.6, 2.8 Hz, 1H), 4.52 (t, J = 2.4 Hz, 1H), 2.43 (s, 3H). ¹³C NMR (101 MHz, CDCl₃) δ 168.4,
145.0, 142.7, 140.6, 139.4, 135.6, 135.4, 129.7, 129.4, 129.3, 128.9, 128.6, 128.1, 128.0, 127.9,
121.8, 97.8, 54.6, 47.0, 21.7. IR (KBr) νmax 2922, 1695, 1595, 1462, 1348, 1174, 1147,
1087 cm⁻¹. HRMS (ESI) for C₂₄H₂₀INO₃SNa (M+Na)+: calcd 552.0107, found 552.0108.
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4-(Naphthalen-1-yl)-3-phenyl-1-tosyl-1,6-dihydropyridin-2(3H)-one (89m):

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colorless solid (86 mg, 76% yield). mp = 173−174 °C. Rf = 0.52 (4:1
hexane/EtOAc); [Silica, UV and I2]. ¹H NMR (400 MHz, CDCl₃) δ 7.92 (d, J =
8.4 Hz, 2H), 7.88−7.77 (m, 2H), 7.74 (d, J = 8.0 Hz, 1H), 7.51−7.43 (m, 2H),
7.33−7.24 (m, 3H), 7.21−7.13 (m, 3H), 7.11−7.02 (m, 3H), 6.20 (dd, J = 5.2, 2.4 Hz, 1H), 4.92
(ddd, J = 17.6, 5.2, 2.0 Hz, 1H), 4.76 (dt, J = 18, 2.4 Hz, 1H), 4.57 (s, 1H), 2.43 (s, 3H). ¹³C NMR
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180
Hydrative Cyclization........

(101 MHz, CDCl$_3$) $\delta$ 168.8, 145.1, 137.4, 136.1, 136.0, 135.2, 133.7, 130.7, 129.4, 128.9, 128.7, 128.6, 128.4, 127.8, 127.7, 126.5, 126.1, 126.0, 125.1, 124.8, 121.7, 55.8, 47.3, 21.7. IR (KBr) $\nu_{\text{max}}$ 2924, 1695, 1595, 1464, 1358, 1251, 1170 cm$^{-1}$. HRMS (ESI) for C$_{28}$H$_{24}$NO$_3$S (M+H)$^+$: calcd 454.1477, found 454.1476.

3-Phenyl-4-(thiophen-2-yl)-1-tosyl-1,6-dihydropyridin-2(3H)-one (89n):

pale yellow solid (79 mg, 77% yield). mp = 110–111 °C. $R_f$ = 0.47 (7:3 hexane/EtOAc); [Silica, UV and I$_2$]. $^1$H NMR (400 MHz, CDCl$_3$) $\delta$ 7.82 (d, $J$ = 8.4 Hz, 2H), 7.33–7.21 (m, 7H), 7.16 (d, $J$ = 4.8 Hz, 1H), 6.87 (t, $J$ = 3.6 Hz, 1H), 6.81 (d, $J$ = 3.2 Hz, 1H), 6.49 (dd, $J$ = 5.6, 2.4 Hz, 1H), 4.78 (dd, $J$ = 18.4, 5.6 Hz, 1H), 4.62 (s, 1H), 4.56 (dd, $J$ = 18.4, 2.4 Hz, 1H), 2.40 (s, 3H). $^{13}$C NMR (101 MHz, CDCl$_3$) $\delta$ 168.0, 145.0, 140.8, 135.2, 134.9, 131.1, 129.3, 129.1, 128.5, 128.1, 127.7, 127.5, 125.3, 124.7, 116.8, 53.5, 46.7, 21.7. IR (KBr) $\nu_{\text{max}}$ 2924, 1697, 1464, 1354, 1170, 1084, 1032 cm$^{-1}$. HRMS (ESI) for C$_{22}$H$_{19}$NO$_3$S$_2$Na (M+Na)$^+$: calcd 432.0704, found 432.0704.

Ethyl 3-(2-oxo-3-phenyl-1-tosyl-1,2,3,6-tetrahydropyridin-4-yl)-1H-indole-1-carboxylate (89o):

pale yellow solid (84 mg, 65% yield). mp = 82–83 °C. $R_f$ = 0.39 (4:1 hexane/EtOAc); [Silica, UV and I$_2$]. $^1$H NMR (400 MHz, CDCl$_3$) $\delta$ 8.20 (d, $J$ = 8.0 Hz, 1H), 7.85 (d, $J$ = 8.4 Hz, 2H), 7.81 (d, $J$ = 7.6 Hz, 1H), 7.42–7.22 (m, 10H), 6.71 (dd, $J$ = 6.0, 2.4 Hz, 1H), 4.89 (dd, $J$ = 16.8, 5.2 Hz, 1H), 4.62 (s, 1H), 4.56 (dt, $J$ = 18.4, 1.6 Hz, 1H), 4.48–4.38 (m, 2H), 2.42 (s, 3H), 1.42 (t, $J$ = 7.2 Hz, 3H). $^{13}$C NMR (101 MHz, CDCl$_3$) $\delta$ 168.4, 150.6, 145.0, 135.8, 135.2, 134.9, 130.6, 129.3, 129.1, 128.5, 128.1, 127.9, 127.4, 125.2, 123.6, 123.5, 120.1, 119.0, 118.6, 115.6, 63.5, 54.1, 46.8, 21.7, 14.3. IR (KBr) $\nu_{\text{max}}$ 2922, 1739, 1697, 1454, 1379, 1354, 1236, 1170, 1087, 1051 cm$^{-1}$. HRMS (ESI) for C$_{29}$H$_{26}$N$_2$O$_5$SNa (M+Na)$^+$: calcd 537.146, found 537.146.

4-(Benzo[d][1,3]dioxol-5-yl)-3-phenyl-1-tosyl-1,6-dihydropyridin-2(3H)-one (89p):

yellow solid (73 mg, 65% yield). mp = 175–176 °C. $R_f$ = 0.28 (7:3 hexane/EtOAc); [Silica, UV and I$_2$]. $^1$H NMR (400 MHz, CDCl$_3$) $\delta$ 7.80 (d, $J$ = 6.8 Hz, 2H), 7.32–7.23 (m, 7H), 6.79 (s, 1H), 6.74 (dd, $J$ = 6.4, 1.6 Hz, 1H), 6.69 (d, $J$ = 6.4 Hz, 1H), 6.41 (dd, $J$ = 4.8, 2.0 Hz, 1H), 5.94 (s, 2H), 4.79 (ddd, $J$ = 14.4, 4.4, 0.8 Hz, 1H), 4.58 (s, 1H), 4.56 (dt, $J$ = 14.4, 1.6 Hz, 1H), 2.42 (s, 3H). $^{13}$C NMR (101 MHz, CDCl$_3$) $\delta$ 168.6, 148.0, 147.8, 144.9, 136.4, 135.2, 134.7, 131.4, 129.3, 129.1, 128.4, 128.0, 127.4, 119.6, 117.5, 108.3, 106.0, 101.3, 53.7, 46.8, 21.7. IR (KBr) $\nu_{\text{max}}$ 2922, 1693, 1504, 1446, 1350, 1248, 1170, 1035 cm$^{-1}$. HRMS (ESI) for C$_{25}$H$_{21}$NO$_3$SNa (M+Na)$^+$: calcd 470.1038, found 470.1040.

181
4-(3,5-Dimethylphenyl)-3-phenyl-1-tosyl-1,6-dihydropyridin-2(3H)-one (89q):

pale yellow solid (82 mg, 76% yield). mp = 132–133 °C. Rf = 0.41 (4:1 hexane/EtOAc); [Silica, UV and I2]. 1H NMR (400 MHz, CDCl3) δ 7.79 (d, J = 8.4 Hz, 2H), 7.35–7.19 (m, 7H), 6.90 (s, 3H), 6.49 (dd, J = 5.6, 2.0 Hz, 1H), 4.79 (dd, J = 18, 6.0 Hz, 1H), 4.66 (s, 1H), 4.47 (d, J = 17.6 Hz, 1H), 2.41 (s, 3H), 2.24 (s, 6H). 13C NMR (101 MHz, CDCl3) δ 168.8, 144.9, 138.2, 137.2, 137.1, 135.2, 134.7, 130.1, 129.3, 129.1, 128.4, 127.9, 127.4, 123.5, 118.4, 53.5, 46.8, 21.7, 21.3. IR (KBr) νmax 2920, 1693, 1594, 1353, 1172, 1084 cm⁻¹. HRMS (ESI) for C26H25NO3SNa (M+Na)⁺: calcd 454.1453, found 454.1453.

4-(3,4-Dimethylphenyl)-3-phenyl-1-tosyl-1,6-dihydropyridin-2(3H)-one (89r):

pale yellow liquid (89 mg, 82% yield). Rf = 0.41 (4:1 hexane/EtOAc); [Silica, UV and I2]. 1H NMR (400 MHz, CDCl3) δ 7.80 (d, J = 8.0 Hz, 2H), 7.31–7.18 (m, 7H), 7.10 (s, 1H), 7.05–6.97 (m, 2H), 6.48 (dd, J = 5.6, 2.4 Hz, 1H), 4.79 (ddd, J = 18, 5.6, 0.8 Hz, 1H), 4.66 (s, 1H), 4.49 (dt, J = 17.6, 2.0 Hz, 1H), 2.41 (s, 3H), 2.20 (s, 6H). 13C NMR (101 MHz, CDCl3) δ 168.8, 144.8, 137.1, 136.9, 136.8, 135.3, 134.6, 129.9, 129.2, 129.0, 128.4, 127.9, 127.5, 126.8, 123.0, 117.6, 53.4, 46.8, 21.7, 19.9, 19.4. IR (Neat) νmax 2920, 1695, 1597, 1493, 1452, 1356, 1213, 1165 cm⁻¹. HRMS (ESI) for C26H25NO3SNa (M+Na)⁺: calcd 454.1453, found 454.1453.

4-(2,4-Dimethoxyphenyl)-3-phenyl-1-tosyl-1,6-dihydropyridin-2(3H)-one (89s):

colorless solid (87 mg, 75% yield). mp = 117–118 °C. Rf = 0.29 (7:3 hexane/EtOAc); [Silica, UV and I2]. 1H NMR (400 MHz, CDCl3) δ 7.84 (d, J = 8.4 Hz, 2H), 7.27 (d, J = 6.4 Hz, 2H), 7.21–7.16 (m, 3H), 7.15–7.08 (m, 2H), 6.91 (d, J = 8.4 Hz, 1H), 6.37 (s, 1H), 6.33 (dd, J = 8.4, 2.4 Hz, 1H), 6.18 (dd, J = 4.4, 2.4 Hz, 1H), 4.80 (s, 1H), 4.76 (dd, J = 14, 4.0 Hz, 1H), 4.57 (dd, J = 14, 4.0 Hz, 1H), 3.74 (s, 6H), 2.41 (s, 3H). 13C NMR (101 MHz, CDCl3) δ 169.4, 160.8, 157.7, 144.8, 136.2, 136.1, 135.4, 130.6, 129.2, 128.7, 128.6, 127.7, 127.4, 120.0, 119.8, 104.4, 98.6, 55.3, 53.6, 47.0, 21.7. IR (KBr) νmax 2922, 1695, 1608, 1504, 1466, 1358, 1213, 1165 cm⁻¹. HRMS (ESI) for C26H25NO5SNa (M+Na)⁺: calcd 486.1351, found 486.1351.

4-(2,6-Dimethoxyphenyl)-3-phenyl-1-tosyl-1,6-dihydropyridin-2(3H)-one (89t):

Following the general procedure (GP-3); A mixture of N-(3-(2,6-dimethoxyphenyl)prop-2-yn-1-yl)-4-methyl-N-(phenylethynyl)-benzenesulfonamide (87t; 111 mg, 0.25 mmol) and PTSA·H₂O (119 mg, 0.625 mmol) reacted with a solution of catalyst A (5.8 mg, 0.0075 mmol) in dioxane (3.0 mL) for 4 h. Upon filtration over Celite and evaporation, the crude mixture was purified by silica gel column chromatography eluting with hexane: ethyl acetate (4:1) to afford 89t (68 mg) in 59% yield.
yield as yellow solid and the corresponding mono-hydration product 90t (18 mg) in 17% yield as brown liquid.

mp = 148–149 °C. Rf = 0.31 (4:1 hexane/EtOAc); [Silica, UV and I2]. 1H NMR (400 MHz, CDCl3) δ 7.88 (d, J = 8.4 Hz, 2H), 7.27 (d, J = 8.4 Hz, 2H), 7.17–7.09 (m, 6H), 6.45 (d, J = 8.4 Hz, 2H), 6.01 (dd, J = 4.0, 3.2 Hz, 1H), 4.74–4.68 (m, 2H), 4.59 (t, J = 2.4 Hz, 1H), 3.65 (s, 6H), 2.43 (s, 3H). 13C NMR (101 MHz, CDCl3) δ 169.7, 157.5, 144.7, 136.7, 135.5, 130.8, 129.2, 128.7, 128.2, 128.1, 127.1, 121.9, 115.9, 103.9, 55.7, 53.7, 47.3, 21.7. IR (KBr) νmax 2926, 1697, 1593, 1469, 1356, 1246, 1165, 1109 cm⁻¹. HRMS (ESI) for C26H25NO5SNa (M+Na)⁺: calcd 486.1351, found 486.1351.

N-(3-(2,6-dimethoxyphenyl)prop-2-yn-1-yl)-2-phenyl-N-tosylacetamide (90t):

Rf = 0.29 (7:3 hexane/EtOAc); [Silica, UV and I2]. 1H NMR (400 MHz, CDCl3) δ 8.05 (d, J = 8.4 Hz, 2H), 7.38–7.08 (m, 8H), 6.54 (d, J = 8.4 Hz, 2H), 5.01 (s, 2H), 4.12 (s, 2H), 3.82 (s, 6H), 2.38 (s, 3H).

13C NMR (101 MHz, CDCl3) δ 170.8, 161.9, 144.5, 136.2, 133.0, 130.4, 129.5, 129.3, 129.2, 128.7, 128.6, 128.5, 127.3, 103.4, 91.7, 78.3, 56.0, 42.6, 37.0, 21.6. IR (Neat) νmax 3062, 2931, 1709, 1593, 1582, 1352, 1160 cm⁻¹. HRMS (ESI) for C26H26NO5S (M+H)⁺: calcd 464.1531, found 464.1532.

4-Butyl-3-phenyl-1-tosyl-1,6-dihydropyridin-2(3H)-one (89u):

thick yellow liquid (81 mg, 84% yield). Rf = 0.43 (4:1 hexane/EtOAc); [Silica, UV and I2]. 1H NMR (400 MHz, CDCl3) δ 7.82 (d, J = 8.0 Hz, 2H), 7.34–7.22 (m, 5H), 7.19–7.09 (m, 2H), 5.84–5.77 (m, 1H), 4.65–4.46 (m, 2H), 4.01 (s, 1H), 2.39 (s, 3H), 1.97–1.83 (m, 2H), 1.45–1.16 (m, 4H). 13C NMR (101 MHz, CDCl3) δ 169.0, 144.8, 137.8, 136.2, 135.4, 129.2, 129.0, 128.5, 127.8, 115.6, 54.0, 47.1, 33.6, 28.9, 22.2, 21.7, 13.8. IR (Neat) νmax 2957, 2930, 2872, 1695, 1597, 1466, 1359, 1170, 1087 cm⁻¹. HRMS (ESI) for C22H25NO3S Na (M+Na)⁺: calcd 406.1453, found 406.1452.

4-((Benzyloxy)methyl)-3-phenyl-1-tosyl-1,6-dihydropyridin-2(3H)-one (89v):

thick yellow liquid (96 mg, 86% yield). Rf = 0.28 (4:1 hexane/EtOAc); [Silica, UV and I2]. 1H NMR (400 MHz, CDCl3) δ 7.85 (d, J = 8.4 Hz, 2H), 7.38–7.22 (m, 10H), 7.19–7.09 (m, 2H), 6.11 (br s, 1H), 4.62 (s, 2H), 4.15 (q, J = 12 Hz, 2H), 4.15 (s, 1H), 3.80 (s, 2H), 2.40 (s, 3H). 13C NMR (101 MHz, CDCl3) δ 168.4, 145.0, 137.5, 136.2, 134.5, 129.3, 129.1, 128.7, 128.5, 127.9, 127.8, 117.8, 72.7, 70.0, 51.1, 47.2, 21.7. IR (Neat) νmax 3030, 2924, 2856, 1697, 1597, 1494, 1454, 1358, 1251, 1170, 1087 cm⁻¹. HRMS (ESI) for C26H26NO3SNa (M+Na)⁺: calcd 470.1402, found 470.1406.
4-Isopentyl-3-phenyl-1-tosyl-1,6-dihydropyridin-2(3H)-one (89w):

[Diagram]

thick yellow liquid (89 mg, 90% yield). \( R_f = 0.50 \) (4:1 hexane/EtOAc); [Silica, UV and \( R_f \)]. \( ^1H \) NMR (400 MHz, CDCl\(_3\)) \( \delta \) 7.82 (d, \( J = 8.4 \) Hz, 2H), 7.38–7.22 (m, 5H), 7.19–7.09 (m, 2H), 5.83–5.77 (m, 1H), 4.66–4.43 (m, 2H), 4.01 (s, 1H), 2.39 (s, 3H), 2.01–1.79 (m, 2H), 1.51–1.42 (m, 1H), 1.38–1.22 (m, 2H), 0.85–0.75 (m, 6H). \( ^1^C \) NMR (101 MHz, CDCl\(_3\)) \( \delta \) 168.9, 144.8, 138.1, 136.2, 129.2, 129.0, 128.5, 127.8, 115.5, 54.0, 47.1, 35.9, 31.7, 27.6, 22.6, 22.1, 21.7. IR (Neat) \( \nu_{\text{max}} \) 2961, 2930, 1695, 1597, 1466, 1359, 1170, 1087 cm\(^{-1}\). HRMS (ESI) for C\(_{23}\)H\(_{27}\)NO\(_3\)SNa (M+Na\(^+\)) : calcld 420.1610, found 420.1614.

3-(Benzoylomethyl)-4-(4-iodophenyl)-1-tosyl-1,6-dihydropyridin-2(3H)-one (89x):

[Diagram]

thick colorless liquid (106 mg, 74% yield). \( R_f = 0.31 \) (4:1 hexane/EtOAc); [Silica, UV and \( R_f \)]. \( ^1H \) NMR (400 MHz, CDCl\(_3\)) \( \delta \) 7.91 (d, \( J = 8.4 \) Hz, 2H), 7.66 (d, \( J = 8.4 \) Hz, 2H), 7.32–7.24 (m, 5H), 7.03 (d, \( J = 8.0 \) Hz, 4H), 6.21 (dd, \( J = 5.2, 2.4 \) Hz, 1H), 4.75 (ddd, \( J = 17.6, 5.2, 1.6 \) Hz, 1H), 4.50 (dt, \( J = 17.6, 2.4 \) Hz, 1H), 4.23 (q, \( J = 12 \) Hz, 2H), 3.79 (dd, \( J = 9.2, 3.6 \) Hz, 1H), 3.53 (t, \( J = 2.4 \) Hz, 1H), 3.44 (dd, \( J = 8.8, 2.8 \) Hz, 1H), 2.41 (s, 3H). \( ^1^C \) NMR (101 MHz, CDCl\(_3\)) \( \delta \) 169.5, 144.9, 137.9, 137.7, 136.9, 135.7, 134.3, 129.3, 128.7, 128.3, 127.7, 127.6, 127.1, 119.8, 93.9, 73.1, 70.3, 47.9, 47.2, 21.7. IR (Neat) \( \nu_{\text{max}} \) 2920, 1693, 1463, 1397, 1353, 1156 cm\(^{-1}\). HRMS (ESI) for C\(_{26}\)H\(_{25}\)INO\(_3\)S (M+H\(^+\)) : calcld 574.0549, found 574.0549.

3-Hexyl-4-(4-iodophenyl)-1-tosyl-1,6-dihydropyridin-2(3H)-one (89y):

[Diagram]

thick yellow liquid (109 mg, 81% yield). \( R_f = 0.35 \) (9:1 hexane/EtOAc); [Silica, UV and \( R_f \)]. \( ^1H \) NMR (400 MHz, CDCl\(_3\)) \( \delta \) 7.96 (d, \( J = 8.4 \) Hz, 2H), 7.67 (d, \( J = 8.4 \) Hz, 2H), 7.33 (d, \( J = 8.0 \) Hz, 2H), 7.04 (d, \( J = 8.4 \) Hz, 2H), 6.10 (dd, \( J = 5.2, 2.4 \) Hz, 1H), 4.72 (ddd, \( J = 17.6, 5.2, 1.2 \) Hz, 1H), 4.49 (dt, \( J = 18, 2.0 \) Hz, 1H), 3.43 (dd, \( J = 6.4, 4.4 \) Hz, 1H), 2.43 (s, 3H), 1.78–1.67 (m, 1H), 1.52–1.41 (m, 1H), 1.19–0.97 (m, 8H), 0.81 (t, \( J = 7.2 \) Hz, 3H). \( ^1^C \) NMR (101 MHz, CDCl\(_3\)) \( \delta \) 170.5, 145.1, 137.9, 137.3, 137.0, 135.6, 129.4, 128.8, 127.4, 117.7, 93.9, 46.9, 46.4, 32.0, 31.4, 28.9, 25.5, 22.4, 21.7, 14.0. IR (Neat) \( \nu_{\text{max}} \) 2923, 2856, 1702, 1593, 1464, 1350, 1164 cm\(^{-1}\). HRMS (ESI) for C\(_{23}\)H\(_{29}\)INO\(_3\)S (M+H\(^+\)) : calcld 538.0913, found 538.0912.

4-(Benzoylomethyl)-3-hexyl-1-tosyl-1,6-dihydropyridin-2(3H)-one (89z):

[Diagram]

thick yellow liquid (95 mg, 83% yield). \( R_f = 0.37 \) (4:1 hexane/EtOAc); [Silica, UV and \( R_f \)]. \( ^1H \) NMR (400 MHz, CDCl\(_3\)) \( \delta \) 7.91 (d, \( J = 8.4 \) Hz, 2H), 7.45–7.19 (m, 7H), 5.90 (s, 1H), 4.61–4.33 (m, 4H), 3.92 (q, \( J = 8.0 \) Hz, 2H), 2.99 (s, 1H), 1.79 (m, 2H), 1.51–1.42 (m, 1H), 1.38–1.22 (m, 2H), 0.85–0.75 (m, 6H).
2.42 (s, 3H), 1.83–1.69 (m, 1H), 1.57–1.43 (m, 1H), 1.32–1.02 (m, 8H), 0.85 (t, J = 6.8 Hz, 3H).

$^1$C NMR (101 MHz, CDCl$_3$) $\delta$ 170.6, 144.9, 137.6, 135.7, 135.1, 129.3, 128.8, 128.5, 127.9, 127.7, 117.7, 72.6, 70.2, 46.7, 45.0, 31.5, 31.4, 29.0, 25.3, 22.5, 21.6, 14.1. IR (Neat) $\nu_{\text{max}}$ 2931, 2860, 1698, 1474, 1358, 1178 cm$^{-1}$. HRMS (ESI) for C$_{26}$H$_{34}$NO$_4$S (M+H)$^+$: calcd 456.2208, found 456.2208.

3-(4-Chlorophenyl)-4-phenyl-1-tosyl-1,6-dihydropyridin-2(3H)-one (93a):

Colorless solid (91 mg, 83% yield). mp = 72–73 °C. $R_f$ = 0.38 (4:1 hexane/EtOAc); [Silica, UV and I$_2$]. $^1$H NMR (400 MHz, CDCl$_3$) $\delta$ 7.80 (d, J = 4.8 Hz, 2H), 7.32–7.21 (m, 8H), 7.19–7.16 (m, 3H), 6.52 (dd, J = 5.6, 2.4 Hz, 1H), 4.80 (ddd, J = 18, 5.6, 1.2 Hz, 1H), 4.61 (s, 1H), 4.54 (dt, J = 18, 2.0 Hz, 1H), 2.40 (s, 3H).

$^1$C NMR (101 MHz, CDCl$_3$) $\delta$ 168.1, 145.1, 136.8, 136.2, 134.9, 134.0, 133.4, 129.3, 129.2, 128.9, 128.8, 128.6, 128.5, 125.6, 118.8, 52.7, 47.0, 21.7. IR (KBr) $\nu_{\text{max}}$ 2924, 1695, 1491, 1359, 1170 cm$^{-1}$. HRMS (ESI) for C$_{24}$H$_{21}$ClNO$_4$S (M+Na)$^+$: calcd 471.0991, found 471.0992.

3-(4-Nitrophenyl)-4-phenyl-1-tosyl-1,6-dihydropyridin-2(3H)-one (93b):

Pale brown solid (81 mg, 72% yield). mp = 45–46 °C. $R_f$ = 0.45 (7:3 hexane/EtOAc); [Silica, UV and I$_2$]. $^1$H NMR (400 MHz, CDCl$_3$) $\delta$ 8.10 (d, J = 8.8 Hz, 2H), 7.85 (d, J = 8.4 Hz, 2H), 7.44 (d, J = 8.4 Hz, 2H), 7.35–7.18 (m, 7H), 6.57 (dd, J = 5.6, 2.8 Hz, 1H), 4.82 (ddd, J = 18, 5.2, 1.2 Hz, 1H), 4.78 (s, 1H), 4.59 (dt, J = 17.6, 2.4 Hz, 1H), 2.43 (s, 3H). $^1$C NMR (101 MHz, CDCl$_3$) $\delta$ 167.2, 147.6, 145.4, 142.5, 136.3, 135.6, 134.8, 129.3, 128.9, 128.8, 128.7, 125.5, 124.3, 119.3, 52.9, 47.0, 21.7. IR (KBr) $\nu_{\text{max}}$ 2924, 1695, 1521, 1458, 1346, 1170 cm$^{-1}$. HRMS (ESI) for C$_{24}$H$_{20}$N$_2$O$_5$S$^-$Na (M+Na)$^-$: calcd 471.0991, found 471.0992.

3-(4-Acetylphenyl)-4-phenyl-1-tosyl-1,6-dihydropyridin-2(3H)-one (93c):

Pale yellow solid (91 mg, 82% yield). mp = 42–43 °C. $R_f$ = 0.42 (3:1 hexane/EtOAc); [Silica, UV and I$_2$]. $^1$H NMR (400 MHz, CDCl$_3$) $\delta$ 7.83 (dd, J = 8.4, 2.0 Hz, 4H), 7.36 (d, J = 8.4 Hz, 2H), 7.31–7.20 (m, 7H), 6.54 (ddd, J = 5.2, 2.4 Hz, 1H), 4.83 (ddd, J = 18, 5.2, 1.2 Hz, 1H), 4.72 (s, 1H), 4.57 (dt, J = 18, 2.4 Hz, 1H), 2.56 (s, 3H), 2.41 (s, 3H). $^1$C NMR (101 MHz, CDCl$_3$) $\delta$ 197.6, 167.9, 145.2, 140.4, 136.7, 136.0, 134.9, 129.3, 129.1, 128.8, 128.6, 127.9, 125.6, 119.0, 53.3, 47.0, 26.6, 21.7. IR (KBr) $\nu_{\text{max}}$ 2926, 1725, 1682, 1358, 1265, 1172, 1084 cm$^{-1}$. HRMS (ESI) for C$_{26}$H$_{24}$NO$_5$S (M+H)$^+$: calcd 446.1426, found 446.1426.
Methyl-4-((2-oxo-4-phenyl-1-tosyl-1,2,3,6-tetrahydropyridin-3-yl)benzoate (93d):

pale yellow solid (77 mg, 67% yield). mp = 130–131 °C. R_f = 0.41 (3:1 hexane/EtOAc); [Silica, UV and I_2]. ^1H NMR (400 MHz, CDCl_3) δ 7.91 (d, J = 7.6 Hz, 2H), 7.81 (d, J = 7.6 Hz, 2H), 7.32 (d, J = 7.6 Hz, 2H), 7.31–7.20 (m, 7H), 6.55 (t, J = 2.4 Hz, 1H), 4.84 (dd, J = 18, 5.2 Hz, 1H), 4.71 (s, 1H), 4.54 (d, J = 18 Hz, 1H), 3.91 (s, 3H), 2.41 (s, 3H), 2.22 (s, 6H), 1.6 Hz, 1H), 4.83 (dd, J = 18, 5.6 Hz, 1H), 4.72 (s, 1H), 4.54 (d, J = 18 Hz, 1H), 2.43 (s, 3H). ^13C NMR (101 MHz, CDCl_3) δ 167.8, 166.6, 145.2, 140.0, 136.7, 136.2, 134.9, 130.3, 129.8, 129.3, 128.8, 128.6, 128.5, 127.6, 125.6, 118.9, 53.3, 52.2, 46.9, 21.6. IR (KBr) ν_max 2920, 1726, 1676, 1457, 1346, 1282, 1172, 1112 cm⁻¹. HRMS (ESI) for C_26H_24NO_3S (M+H)^+ : calc 462.1375, found 462.1375.

4-Phenyl-1-tosyl-3-(4-(trifluoromethyl)phenyl)-1,6-dihydropyridin-2(3H)-one (93e):

thick yellow liquid (98 mg, 83% yield). R_f = 0.31 (4:1 hexane/EtOAc); [Silica, UV and I_2]. ^1H NMR (400 MHz, CDCl_3) δ 7.78 (d, J = 8.0 Hz, 2H), 7.48 (d, J = 8.0 Hz, 2H), 7.36 (d, J = 8.4 Hz, 2H), 7.32–7.18 (m, 7H), 6.56 (dd, J = 5.2, 1.6 Hz, 1H), 4.83 (dd, J = 18, 5.6 Hz, 1H), 4.72 (s, 1H), 4.54 (d, J = 18 Hz, 1H), 2.43 (s, 3H). ^13C NMR (101 MHz, CDCl_3) δ 167.8, 145.2, 139.0, 136.6, 135.9, 134.7, 129.2, 128.8, 128.7, 128.5, 127.9, 126.0, 125.9, 125.5, 119.1, 53.3, 47.0, 21.6. ^19F NMR (376 MHz, CDCl_3) δ –62.65 (s). IR (Neat) ν_max 2926, 1698, 1594, 1320, 1172, 1095 cm⁻¹. HRMS (ESI) for C_26H_25F_3NO_3S (M+H)^+ : calc 472.1194, found 472.1194.

3-(3,5-Dimethylphenyl)-4-phenyl-1-tosyl-1,6-dihydropyridin-2(3H)-one (93f):

colorless solid (78 mg, 72% yield). mp = 65–66 °C. R_f = 0.45 (4:1 hexane/EtOAc); [Silica, UV and I_2]. ^1H NMR (400 MHz, CDCl_3) δ 7.80 (d, J = 8.4 Hz, 2H), 7.31–7.20 (m, 7H), 6.87 (s, 1H), 6.83 (s, 2H), 6.51 (dd, J = 5.6, 2.0 Hz, 1H), 4.80 (dd, J = 17.6, 6.0 Hz, 1H), 4.56 (s, 1H), 4.51 (dt, J = 17.6, 2.4 Hz, 1H), 2.41 (s, 3H), 2.22 (s, 6H). ^13C NMR (101 MHz, CDCl_3) δ 168.8, 144.8, 138.6, 137.3, 137.0, 135.2, 134.4, 129.7, 129.2, 128.7, 128.5, 128.3, 125.6, 125.1, 118.6, 53.5, 46.9, 21.7, 21.3. IR (KBr) ν_max 2920, 1695, 1597, 1462, 1358, 1170, 1087 cm⁻¹. HRMS (ESI) for C_26H_25NO_3SNa (M+Na)^+ : calc 454.1453, found 454.1452.

4-(4-Bromophenyl)-3-(3-fluorophenyl)-1-tosyl-1,6-dihydropyridin-2(3H)-one (93g):

colorless solid (86 mg, 69% yield). mp = 180–181 °C. R_f = 0.37 (4:1 hexane/EtOAc); [Silica, UV and I_2]. ^1H NMR (400 MHz, CDCl_3) δ 7.81 (d, J = 8.0 Hz, 2H), 7.40 (d, J = 8.4 Hz, 2H), 7.30–7.18 (m, 3H), 7.11 (d, J = 8.4 Hz, 2H), 7.02 (d, J = 8.0 Hz, 1H), 6.98–6.84 (m, 2H), 6.52 (dd, J = 5.6, 2.4 Hz, 1H), 4.80 (dd, J = 18, 5.2 Hz, 1H), 4.57 (s, 1H), 4.53 (dd, J = 18, 2.0 Hz, 1H), 2.41 (s, 3H). ^13C NMR (101 MHz, CDCl_3) δ 167.6, 163.1 (d, J = 741 Hz), 145.2, 137.1 (d, J = 21.8 Hz), 135.7, 135.3, 134.8, 131.9,
Hydrative Cyclization

130.7 (d, J = 24.1 Hz), 129.3, 128.5, 127.2, 123.2 (d, J = 9.4 Hz), 122.7, 119.5, 115.3, 115.1, 114.6, 114.4, 52.8, 46.8, 21.7. \textsuperscript{19}F NMR (376 MHz, CDCl\textsubscript{3}) \(\delta\)–111.54 (q, J = 9.0 Hz). IR (KBr) \(\nu_{\text{max}}\) 2924, 1697, 1591, 1487, 1458, 1390, 1356, 1249, 1168, 1078 cm\(^{-1}\). HRMS (ESI) for C\(_{24}\)H\(_{15}\)BrFNO\(_{3}\)SNa (M+Na\(^+\) : calcd 522.0151, found 522.0151.

3,4-Di-p-toly-1-tosyl-1,6-dihydropyridin-2(3H)-one (93h):

Colorless solid (87 mg, 81% yield). mp = 55–55 \(^{\circ}\)C. \(R_f = 0.33\) (4:1 hexane/EtOAc); [Silica, UV and I\(_2\)]. \(^1\)H NMR (400 MHz, CDCl\textsubscript{3}) \(\delta\) 7.82 (d, J = 8.4 Hz, 2H), 7.31–7.07 (m, 10H), 6.48 (dd, J = 5.6, 2.0 Hz, 1H), 4.79 (ddd, J = 18, 5.6, 1.2 Hz, 1H), 4.61 (s, 1H), 4.51 (dt, J = 17.6, 2.4 Hz, 1H), 2.42 (s, 3H), 2.30 (s, 6H). \(^{13}\)C NMR (101 MHz, CDCl\textsubscript{3}) \(\delta\) 168.9, 145.2, 145.2, 137.7, 136.7, 135.3, 134.3, 134.3, 131.8, 129.8, 129.3, 129.2, 128.5, 127.3, 125.5, 117.6, 53.1, 46.9, 21.7, 21.1, 21.0. IR (KBr) \(\nu_{\text{max}}\) 2922, 1695, 1512, 1462, 1170, 1087, 1041 cm\(^{-1}\). HRMS (ESI) for C\(_{26}\)H\(_{25}\)NO\(_3\)SNa (M+Na\(^+\) : calcd 454.1453, found 454.1453.

3-(4-Chlorophenyl)-4-(thiophen-2-yl)-1-tosyl-1,6-dihydropyridin-2(3H)-one (93i):

Brown solid (96 mg, 87% yield). mp = 73–74 \(^{\circ}\)C. \(R_f = 0.36\) (4:1 hexane/EtOAc); [Silica, UV and I\(_2\)]. \(^1\)H NMR (400 MHz, CDCl\textsubscript{3}) \(\delta\) 7.82 (d, J = 8.4 Hz, 2H), 7.31–7.20 (m, 6H), 7.18 (dd, J = 4.8, 0.8 Hz, 1H), 6.89 (t, J = 4.8 Hz, 1H), 6.79 (d, J = 3.2 Hz, 1H), 6.49 (dd, J = 5.6, 2.4 Hz, 1H), 4.81 (dd, J = 17.2, 5.6 Hz, 1H), 4.56 (dt, J = 20.4, 3.6 Hz, 2H), 2.43 (s, 3H). \(^{13}\)C NMR (101 MHz, CDCl\textsubscript{3}) \(\delta\) 167.5, 145.2, 140.5, 134.9, 134.2, 133.5, 130.6, 129.3, 129.2, 128.9, 128.6, 127.7, 125.5, 124.7, 117.0, 52.7, 46.7, 21.7. IR (KBr) \(\nu_{\text{max}}\) 2922, 1693, 1489, 1358, 1170, 1087 cm\(^{-1}\). HRMS (ESI) for C\(_{22}\)H\(_{18}\)ClNO\(_2\)S\(_2\)Na (M+Na\(^+\) : calcd 466.0315, found 466.0318.

General Procedure for Double Bond Isomerisation of 89 (GP-4):\(^{24}\)

![Diagram of the reaction](image)

Compound 89 (0.25 mmol) and Et\(_3\)N (1.0 mmol) in ethyl acetate (2.0 mL) was heated in a Schlenk tube at 110 \(^{\circ}\)C for 6 h. Reaction was monitored by TLC. After completion, the reaction mixture was evaporated under reduced pressure and the residue was purified by column chromatography.
3,4-Diphenyl-1-tosyl-5,6-dihydropyridin-2(1H)-one (94a):

[72x768]3,4-Diphenyl-1-tosyl-5,6-dihydropyridin-2(1H)-one (94a): colorless solid (92 mg, 92% yield). mp = 147–148 °C. Rf = 0.42 (3:1 hexane/EtOAc); [Silica, UV and I2]. 1H NMR (400 MHz, CDCl3) δ 7.97 (d, J = 8.0 Hz, 2H), 7.31 (d, J = 8.0 Hz, 2H), 7.23–7.07 (m, 6H), 7.05–6.92 (m, 4H), 4.29 (t, J = 6.4 Hz, 2H), 3.03 (t, J = 6.4 Hz, 2H), 2.42 (s, 3H). 13C NMR (101 MHz, CDCl3) δ 163.9, 152.1, 144.6, 138.8, 136.1, 134.3, 132.1, 131.1, 129.4, 128.7, 128.4, 128.2, 128.1, 127.7, 127.4, 43.6, 31.9, 21.7. IR (KBr) νmax 2934, 1693, 1442, 1352, 1321, 1165, 1082 cm⁻¹. HRMS (ESI) for C24H22NO3S (M+H)⁺: calcd 404.1320, found 404.1322.

4-(4-Iodophenyl)-3-phenyl-1-tosyl-5,6-dihydropyridin-2(1H)-one (94g):

[72x754]4-(4-Iodophenyl)-3-phenyl-1-tosyl-5,6-dihydropyridin-2(1H)-one (94g): pale yellow solid (124 mg, 94% yield). mp = 173–174 °C. Rf = 0.58 (3:1 hexane/EtOAc); [Silica, UV and I2]. 1H NMR (400 MHz, CDCl3) δ 7.97 (d, J = 8.0 Hz, 2H), 7.50 (d, J = 8.4 Hz, 2H), 7.42–7.27 (m, 2H), 7.22–7.12 (m, 3H), 7.50–6.94 (m, 2H), 6.73 (d, J = 8.4 Hz, 2H), 4.29 (t, J = 6.4 Hz, 2H), 3.01 (t, J = 6.8 Hz, 2H), 2.43 (s, 3H). 13C NMR (101 MHz, CDCl3) δ 150.7, 144.7, 138.2, 137.3, 135.9, 133.9, 132.5, 131.6, 131.3, 131.0, 130.0, 129.5, 128.7, 128.4, 127.9, 127.6, 94.6, 43.5, 31.5, 21.7. IR (KBr) νmax 2922, 1682, 1390, 1350, 1321 cm⁻¹. HRMS (ESI) for C24H20INO3Sn (M+Na)⁺: calcd 552.0107, found 552.0107.

4-(2-Iodophenyl)-3-phenyl-1-tosyl-5,6-dihydropyridin-2(1H)-one (94l):

[72x669]4-(2-Iodophenyl)-3-phenyl-1-tosyl-5,6-dihydropyridin-2(1H)-one (94l): brown solid (125 mg, 95% yield). mp = 143–144 °C. Rf = 0.29 (4:1 hexane/EtOAc); [Silica, UV and I2]. 1H NMR (400 MHz, CDCl3) δ 7.99 (d, J = 8.8 Hz, 2H), 7.75 (dd, J = 8.0, 0.8 Hz, 1H), 7.32 (d, J = 8.0 Hz, 2H), 7.16–7.06 (m, 6H), 6.85 (td, J = 8.0, 1.6 Hz, 1H), 6.77 (dd, J = 7.6, 1.6 Hz, 1H), 4.68–4.58 (m, 1H), 4.14 (td, J = 8.0, 4.4 Hz, 1H), 3.03 (dt, J = 14.0, 4.4 Hz, 1H), 2.96–2.83 (m, 1H), 2.43 (s, 3H). 13C NMR (101 MHz, CDCl3) δ 163.6, 154.7, 144.0, 139.0, 136.0, 133.4, 133.3, 130.0, 129.5, 129.3, 128.9, 128.7, 128.1, 127.6, 96.8, 44.2, 31.8, 21.7. IR (KBr) νmax 2924, 1685, 1348, 1323, 1170, 1087 cm⁻¹. HRMS (ESI) for C24H21INO3Sn (M+H)⁺: calcd 530.0287, found 530.0287.

Ethyl 3-(6-oxo-5-phenyl-1-tosyl-1,2,3,6-tetrahydropyridin-4-yl)-1H-indole-1-carboxylate (94o):

[72x189]Ethyl 3-(6-oxo-5-phenyl-1-tosyl-1,2,3,6-tetrahydropyridin-4-yl)-1H-indole-1-carboxylate (94o): colorless solid (114 mg, 89% yield). mp = 115–116 °C. Rf = 0.31 (3:1 hexane/EtOAc); [Silica, UV and I2]. 1H NMR (400 MHz, CDCl3) δ 8.11 (d, J = 8.4 Hz, 1H), 8.01 (d, J = 8.4 Hz, 2H), 7.32 (d, J = 8.0 Hz, 2H), 7.29–7.18 (m, 3H), 7.17–7.05 (m, 6H), 4.42 (q, J = 6.8 Hz, 2H), 4.33 (t, J = 6.4 Hz, 2H), 3.15 (t, J = 6.4 Hz, 2H), 2.44 (s, 3H). 13C NMR (101 MHz, CDCl3) δ 163.6, 150.1, 145.0, 144.6, 136.1, 135.3, 134.8, 132.4, 130.5, 129.4, 128.7, 127.9, 127.7, 127.6, 126.1, 124.9,
123.2, 120.4, 119.6, 115.2, 63.6, 43.7, 31.8, 21.7, 14.3. IR (KBr) \( \nu_{\text{max}} \) 2924, 1736, 1674, 1460, 1373, 1348, 1288, 1165, 1087 cm\(^{-1}\). HRMS (ESI) for C\(_{29}\)H\(_{27}\)N\(_2\)O\(_5\)S (M+H\(^+\)) : calcd 515.164, found 515.164.

5,6-Diphenyl-3-tosyl-7-oxa-3-azabicyclo[4.1.0]heptan-4-one (95):

![Diagram](image)

To a solution of \(89a\) (100 mg, 0.25 mmol) in CH\(_2\)Cl\(_2\) (2 mL) was added \(m\)-CPBA (64 mg, 0.38 mmol). The reaction mixture was stirred for 12 h at room temperature. The reaction mixture was then cooled to 0 °C and saturated aqueous Na\(_2\)S\(_2\)O\(_3\) and aqueous NaHCO\(_3\) were successively added. The organic layer was separated and dried over Na\(_2\)SO\(_4\). The organic layer was concentrated under reduced pressure. The crude residue was purified by silica gel column chromatography eluting with hexane: ethyl acetate (3:1) to afford 95 (96 mg) in 92% yield as colorless solid.

mp = 173–174 °C. \(R_f\) = 0.41 (3:1 hexane/EtOAc); [Silica, UV and I\(_2\)]. \(^1\)H NMR (400 MHz, CDCl\(_3\)) \(\delta\) 7.81 (d, \(J = 8.4\) Hz, 2H), 7.32–7.18 (m, 10H), 7.14 (dd, \(J = 17.6, 2.0\) Hz, 2H), 4.87 (dd, \(J = 15.2, 3.2\) Hz, 1H), 4.53 (s, 1H), 4.23 (d, \(J = 15.2\) Hz, 1H), 4.07 (dd, \(J = 2.4, 1.2\) Hz, 1H), 2.41 (s, 3H).

\(^{13}\)C NMR (101 MHz, CDCl\(_3\)) \(\delta\) 167.8, 144.9, 135.4, 135.0, 133.3, 129.3, 129.2, 128.8, 128.5, 128.4, 128.2, 126.9, 61.3, 56.8, 56.0, 44.2, 21.7. IR (KBr) \(\nu_{\text{max}}\) 1693, 1390, 1338, 1271, 1165 cm\(^{-1}\). HRMS (ESI) for C\(_{29}\)H\(_{21}\)NO\(_4\)SNa (M+Na\(^+\)) : calcd 442.1089, found 442.1089.

3,4-Diphenyl-1-tosylpiperidin-2-one (96):

![Diagram](image)

A mixture of \(89a\) (100 mg, 0.25 mmol) and 10 % Pd/C (30 mg) in EtOAc was stirred under H\(_2\) balloon pressure at room temperature for 12 h. Upon completion, the reaction mixture was diluted with CH\(_2\)Cl\(_2\) and filtered through a small pad of Celite and evaporated under reduced pressure. The crude reaction mixture was purified by silica gel column chromatography eluting with hexane: ethyl acetate (4:1) to afford 96 (97 mg) in 97% yield as colorless solid.
Hydrative Cyclization

mp = 170–171 °C. Rf = 0.30 (4:1 hexane/EtOAc); [Silica, UV and I₂]. ¹H NMR (400 MHz, CDCl₃) δ 8.02 (d, J = 8.4 Hz, 2H), 7.35 (d, J = 8.0 Hz, 2H), 7.21–7.08 (m, 4H), 7.01 (t, J = 7.6 Hz, 2H), 6.71 (dd, J = 7.2, 1.2 Hz, 2H), 6.54 (d, J = 7.6 Hz, 2H), 4.57–4.48 (m, 1H), 3.94 (d, J = 5.2 Hz, 1H), 3.85 (td, J = 12, 5.2 Hz, 1H), 3.48–3.39 (m, 1H), 2.45 (s, 3H), 2.42–2.36 (m, 1H), 2.16–2.07 (m, 1H). ¹³C NMR (101 MHz, CDCl₃) δ 170.8, 145.0, 139.7, 135.8, 135.4, 129.6, 129.3, 129.1, 128.2, 127.8, 127.7, 127.1, 127.0, 55.7, 46.1, 43.2, 23.9, 21.7. IR (KBr) νmax 1689, 1593, 1452, 1348, 1219, 1120, 1084 cm⁻¹. HRMS (ESI) for C₂₃H₂₃NO₅SNa (M+Na)⁺: calc 428.1297, found 428.1297.

Synthesis of 4-(biphenyl-4-yl)-3-phenyl-1-tosyl-5,6-dihydropyridin-2(1H)-one (97):²⁵

A mixture of compound 94g (70 mg, 0.13 mmol), PhB(OH)₂ (21 mg, 0.17 mmol), Pd(OAc)₂ (2.0 mg, 0.007 mmol) and Na₂CO₃ (16 mg, 0.16 mmol) in DMF/H₂O (2:1, 1.0 mL) was heated at 100 °C for 4 h. After complete consumption of starting material, reaction mixture was filtered through a small pad of Celite and evaporated under reduced pressure. The crude reaction mixture was purified by silica gel column chromatography eluting with hexane: ethyl acetate (4:1) to afford 97 (58 mg) in 91% yield as pale yellow solid.

mp = 205–206 °C. Rf = 0.32 (4:1 hexane/EtOAc); [Silica, UV and I₂]. ¹H NMR (400 MHz, CDCl₃) δ 7.98 (d, J = 8.4 Hz, 2H), 7.51 (d, J = 8.0 Hz, 2H), 7.43–7.28 (m, 7H), 7.19–6.98 (m, 7H), 4.31 (t, J = 6.4 Hz, 2H), 3.07 (t, J = 6.4 Hz, 2H), 2.43 (s, 3H). ¹³C NMR (101 MHz, CDCl₃) δ 163.9, 151.5, 144.6, 141.1, 139.9, 137.5, 136.1, 134.4, 132.1, 131.1, 129.5, 128.9, 128.8, 128.7, 127.8, 127.7, 127.4, 126.9, 126.7, 43.5, 31.7, 21.7. IR (KBr) νmax 2920, 1687, 1594, 1484, 1353, 1172 cm⁻¹. HRMS (ESI) for C₂₃H₂₃NO₅SNa (M+Na)⁺: calc 502.1453, found 502.1452.
Synthesis of 3-phenyl-4-(4-(phenylethynyl)phenyl)-1-tosyl-5,6-dihydropyridin-2(1H)-one (98):  

![Chemical structure of 98]

To a solution of compound 94g (80 mg, 0.15 mmol), PdCl₂(PPh₃)₂ (5.0 mg, 0.008 mmol) and CuI (3.0 mg, 0.016 mmol) in dry THF (1.0 mL) were added Et₃N (63 μL, 0.45 mmol) and phenylacetylene (25 μL, 0.23 mmol) successively under N₂ atmosphere. The reaction mixture was stirred for 4 h at an ambient temperature. After complete consumption of starting material, reaction mixture was filtered through a small pad of Celite and evaporated under reduced pressure. The crude reaction mixture was purified by silica gel column chromatography eluting with hexane: ethyl acetate (4:1) to afford 98 (72 mg) in 95% yield as pale yellow solid.

mp = 173–174 °C. Rₛ = 0.36 (4:1 hexane/EtOAc); [Silica, UV and I₂]. ¹H NMR (400 MHz, CDCl₃) δ 7.98 (d, J = 8.0 Hz, 2H), 7.53–7.43 (m, 2H), 7.38–7.21 (m, 7H), 7.18–7.05 (m, 3H), 7.01–6.88 (m, 4H), 4.30 (t, J = 6.4 Hz, 2H), 3.03 (t, J = 6.4 Hz, 2H), 2.42 (s, 3H). ¹³C NMR (101MHz, CDCl₃) δ 163.7, 151.0, 144.6, 138.5, 136.1, 134.1, 132.5, 131.6, 131.3, 131.1, 129.4, 128.7, 128.5, 128.4, 128.3, 127.8, 127.6, 123.4, 122.8, 90.8, 88.7, 43.5, 31.5, 21.7. IR (KBr) νmax 2926, 2854, 1698, 1358, 1161, 1035 cm⁻¹. HRMS (ESI) for C₁₂H₁₃NO₃SNa (M+Na)⁺ : calcd 526.1453, found 526.1453.

4-(2-Bromophenyl)-5-((4-bromophenyl)(hydroxy)methyl)-3-phenyl-1-tosyl-5,6-dihydropyridin-2(1H)-one (99):

![Chemical structure of 99]

To a stirred solution of (Pr)₂NH (36 μL, 0.26 mmol) in dry THF (2.0 mL) at −70 °C was added n-BuLi (0.2 mL, 0.20 mmol) dropwise over 20 minutes. After stirring the reaction...
mixture for 30 minutes at −70 °C, a solution of 89k (25 mg, 0.05 mmol) in THF (1.0 mL) was added dropwise. After being stirred for 2 h at −70 °C, a solution of 4–bromo benzaldehyde (10 mg, 0.05 mmol) in THF (0.5 mL) was introduced. The resulting reaction mixture was stirred for 2 h at −70 °C. Progress of the reaction was monitored by TLC. After consumption of the starting material 89k, the reaction mixture was brought to room temperature and quenched with HCl (1N, 1.0 mL). The solution was extracted with diethyl ether (3 × 4 mL) and the combine organic extract was dried over Na₂SO₄. Organic phase was concentrated under reduced pressure and purified by silica gel column chromatography eluting with hexane: ethyl acetate (3:1) to afford 99 (21 mg) in 62% yield as pale yellow solid.

mp = 155−156 °C. R f = 0.41 (7:3 hexane/EtOAc); [Silica, UV and I₂]. 1H NMR (400 MHz, CDCl₃) δ 7.59 (d, J = 8.0 Hz, 1H), 7.53 (d, J = 8.8 Hz, 2H), 7.36 (d, J = 8.0 Hz, 2H), 7.29 (d, J = 8.4 Hz, 2H), 7.25–7.16 (m, 7H), 7.14–7.08 (m, 2H), 6.91–6.83 (m, 1H), 6.06 (s, 1H), 4.09 (t, J = 7.2 Hz, 1H), 3.21–3.15 (m, 2H), 2.94–2.87 (m, 1H), 2.44 (s, 3H). 13C NMR (101 MHz, CDCl₃) δ 163.9, 153.5, 143.8, 138.1, 136.2, 135.0, 133.0, 132.7, 132.4, 132.3, 130.8, 130.1, 129.8, 129.7, 128.1, 127.8, 127.7, 126.9, 126.5, 122.6, 122.3, 78.9, 44.5, 39.8, 29.7, 21.6. IR (KBr) ν max 3243, 2914, 1715, 1419, 1331, 1205, 1161 cm⁻¹. HRMS (ESI) for C₃₁H₂₅Br₂NO₄SNa (M+Na)⁺: calcd 687.9769, found 687.9769.

Ethyl 3-(4-methyl-N-(3-phenylprop-2-yn-1-yl)phenylsulfonamido)propiolate (100): colorless solid (296 mg, 33% yield). mp = 70−71 °C. R f = 0.37 (4:1 hexane/EtOAc); [Silica, UV and I₂]. 1H NMR (400 MHz, CDCl₃) δ 7.90 (d, J = 8.0 Hz, 2H), 7.38–7.24 (m, 5H), 7.20 (d, J = 8.0 Hz, 2H), 4.55 (s, 2H), 4.24 (q, J = 7.2 Hz, 2H), 2.38 (s, 3H), 1.31 (t, J = 6.8 Hz, 3H). 13C NMR (101 MHz, CDCl₃) δ 154.0, 145.8, 134.0, 131.7, 129.9, 128.9, 128.3, 128.2, 121.6, 87.3, 81.7, 80.2, 67.8, 61.7, 42.6, 21.7, 14.2. IR (KBr) ν max 2218, 1709, 1484, 1369, 1254, 1171, 1151, 1018 cm⁻¹. HRMS (ESI) for C₂₁H₁₉NO₄SNa (M+Na)⁺: calcd 404.0933, found 404.0929.

Ethyl 2-oxo-4-phenyl-1-tosyl-1,2,5,6-tetrahydropyridine-3-carboxylate (101): Following the general procedure (GP-3); ethyl 3-(4-methyl-N-(3-phenylprop-2-ynyl)phenylsulfonamido)propiolate (100; 95 mg, 0.25 mmol) and PTSA·H₂O (119 mg, 0.625 mmol) reacted with a solution of catalyst A (5.8 mg, 0.0075 mmol) in acetonitrile (3.0 mL) for 4 h. Upon filtration over Celite and evaporation, the crude mixture was purified by silica gel column chromatography eluting with hexane: ethyl acetate (4:1) to afford 101 (58 mg) in 58% yield as colorless solid.
mp = 102–103 °C. \( R_f = 0.42 \) (3:1 hexane/EtOAc); [Silica, UV and I\(_2\)]. \(^1\)H NMR (400 MHz, CDCl\(_3\)) \( \delta \) 7.96 (d, \( J = 8.4 \) Hz, 2H), 7.42–7.35 (m, 3H), 7.34–7.28 (m, 4H), 4.19 (t, \( J = 6.4 \) Hz, 2H), 4.06 (q, \( J = 7.2 \) Hz, 2H), 2.96 (t, \( J = 6.4 \) Hz, 2H), 2.44 (s, 3H), 1.01 (t, \( J = 7.2 \) Hz, 3H). \(^{13}\)C NMR (101 MHz, CDCl\(_3\)) \( \delta \) 165.1, 160.8, 154.1, 145.0, 130.1, 129.5, 128.7, 127.4, 126.5, 61.7, 43.3, 30.6, 21.7, 13.6. IR (KBr) \( \nu_{\text{max}} \) 2926, 1742, 1687, 1353, 3062, 2920, 1742, 1687, 1353, 3062 cm\(^{-1}\). HRMS (ESI) for C\(_{21}\)H\(_{21}\)NO\(_5\)SNa (M+Na\(^+\)) : calcd 422.1038, found 422.1038.

**Ethyl 2-oxo-4-phenyl-1-tosylpiperidine-3-carboxylate (102):**

![Chemical Structure](image)

A mixture of 101 (80 mg, 0.20 mmol) and 10 % Pd/C (30 mg) in EtOAc was stirred under H\(_2\) balloon pressure at room temperature for 12 h. Upon completion, the reaction mixture was diluted with CH\(_2\)Cl\(_2\) and filtered through a small pad of Celite and evaporated under reduced pressure. The crude reaction mixture was purified by silica gel column chromatography eluting with hexane: ethyl acetate (4:1) to afford 102 (70 mg) in 88% yield as colorless solid.

mp = 112–113 °C. \( R_f = 0.23 \) (4:1 hexane/EtOAc); [Silica, UV and I\(_2\)]. \(^1\)H NMR (400 MHz, CDCl\(_3\)) \( \delta \) 7.93 (d, \( J = 7.6 \) Hz, 2H), 7.34 (d, \( J = 8.0 \) Hz, 2H), 7.31–7.22 (m, 3H), 7.12 (d, \( J = 7.6 \) Hz, 2H), 4.25 (dt, \( J = 12, 4.0 \) Hz, 1H), 4.07–3.94 (m, 2H), 3.81 (td, \( J = 11.2, 4.0 \) Hz, 1H), 3.58 (d, \( J = 10.8 \) Hz, 1H), 3.42 (td, \( J = 10.8, 2.8 \) Hz, 1H), 2.45 (s, 3H), 2.35–2.23 (m, 1H), 2.18–2.05 (m, 1H), 1.10 (t, \( J = 7.2 \) Hz, 3H). \(^{13}\)C NMR (101 MHz, CDCl\(_3\)) \( \delta \) 168.2, 166.4, 145.2, 140.4, 135.3, 129.5, 128.9, 128.8, 127.6, 126.8, 61.6, 57.9, 45.7, 42.1, 29.9, 21.7, 13.8. IR (KBr) \( \nu_{\text{max}} \) 2920, 1742, 1687, 1353, 1167, 1090 cm\(^{-1}\). HRMS (ESI) for C\(_{21}\)H\(_{21}\)NO\(_5\)SNa (M+Na\(^+\)) : calcd 424.1195, found 424.1195.

**Synthesis of 90a**

![Chemical Structure](image)

To solution of \( N^*-\) (3-dimethylaminopropyl)-N-ethylcarboximid, hydrochloride salt (EDC.HCl) (3.1 mmol), 4-N,N-dimethylaminopyridine (DMAP) (5.6 mmol) and phenylacetic acid (0.4 mL, 3.36 mmol) in CH\(_2\)Cl\(_2\) (5.0 mL, for 1.0 mmol of sulfoximine)
was added a solution of 87”a (0.8 g, 2.80 mmol) in DCM (5.0 mL) dropwise under an argon atmosphere at 0 °C. The resulting reaction mixture was stirred for about 1 h at 0 °C, and warmed to ambient temperature and stirred overnight. Upon complete consumption of 87”a, the reaction mixture was acidified with hydrochloric acid (HCl, 1N). The organic layer was separated; the aqueous layer was extracted with CH₂Cl₂ (3 times). The combined extracts were washed with 10% aqueous NaHCO₃ and brine. The organic layer was dried over Na₂SO₄. Solvent was filtered and evaporated under reduced pressure. The crude residue was purified using column chromatography on silica gel eluting with hexane: ethyl acetate (4:1) to afford 90a (650 mg) in 57% yield as colorless solid.

mp = 122−123 °C. Rf = 0.50 (4:1 hexane/EtOAc); [Silica, UV and I₂]. ¹H NMR (400 MHz, CDCl₃) δ 7.93 (d, J = 7.2 Hz, 2H), 7.34 (br s, 5H), 7.28 (d, J = 8.0 Hz, 5H), 7.15 (d, J = 7.2 Hz, 2H), 4.90 (s, 2H), 4.03 (s, 2H), 2.41 (s, 3H). ¹³C NMR (101 MHz, CDCl₃) δ 170.4, 145.1, 136.1, 132.9, 131.7, 129.6, 129.3, 128.8, 128.7, 128.3, 127.3, 122.0, 84.5, 83.5, 42.8, 36.4, 21.7. IR (KBr) νmax 2915, 1709, 1594, 1408, 1353, 1161, 1106 cm⁻¹. HRMS (ESI) for C₂₂H₂₂NO₂S (M+H)⁺: calcd 404.132, found 404.1317.

3.7.5. Alternate Plausible Mechanism:

![Mechanism Diagram]

3.7.6. X-Ray crystallography: Single crystal X-ray data for the compounds 89a, 89k, 96 and 102 were collected at on a Bruker SMART APEX CCD area detector system [λ(Mo-

**X-ray crystal structure and data for 89a, 89k, 96, and 102:**

![Crystal Structures]

**Figure 3.5.** Thermal ellipsoidal plot of compound 89a, 89k, 96, 102 with atom labeling scheme. Displacement ellipsoids are drawn at 30% probability level except for the H atoms, which are shown as circles of arbitrary radius.
### Table 3.8. Crystal data for 89a, 89k, 96 and 102:

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<th>Compound</th>
<th>Compound</th>
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<td>0.0446, 0.1131</td>
<td>0.0874, 0.2855</td>
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Kα = 0.71073 Å] at 298K respectively, graphite monochromator with a ω scan width of 0.3°, crystal-detector distance 60 mm, collimator 0.5 mm. The SMART software¹ was used for the intensity data acquisition and the SAINTPLUS Software² was used for the data extraction. In each case, absorption correction was performed with the help of SADABS program, an empirical absorption correction using equivalent reflections was performed with the program. The structure was solved using SHELXS-97,² and full-matrix least-squares refinement against F² was carried out using SHELXL-97.²⁷ All non-hydrogen atoms were refined anisotropically. Aromatic and methyl hydrogens were
introduced on calculated positions and included in the refinement riding on their respective parent atoms.

3.8. References


(15) Crystallographic data (see Supporting Information). CCDC 922157 (89a), 917427 (89k), 917428 (96) and 922158 (102) contain 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.
(16) Monohydrated product 90t was obtained in 17% yield.


3.9. Spectra
Hydative Cyclization....
Hydrative Cyclization…….
Hydrative Cyclization
Hydrative Cyclization...
Hydrative Cyclization
Hydrative Cyclization
Hydrative Cyclization........

[Chemical structures and NMR spectra are depicted, showing various compounds with labels like Ph, TsN=CH, COOH, and NO2.]
Hydrative Cyclization.......

$^{92g}$

$^{92h}$

$^{92i}$

$^{92j}$
Hydrative Cyclization
Hydrative Cyclization
Hydrative Cyclization
Hydrative Cyclization
Hydrative Cyclization......
Hydrative Cyclization...
Hydrative Cyclization......
Hydrative Cyclization....

[Chemical structures and plots are shown, depicting various aspects of chemical reactions and analysis.]
Hydrative Cyclization......
Hydrative Cyclization…….
Hydrative Cyclization......
Hydrative Cyclization......
Hydrative Cyclization......
Hydrative Cyclization.......

[Chemical structures and spectra images]

240
Hydrative Cyclization...
A practical and efficient method for the synthesis of iodo-substituted 1,2-dihydropyridines (DHP) involving 6-endo-dig cyclization and isomerization of stable ketene N,N-acetal by silver catalyst is developed.
Reference:

Nayan Ghosh, Sanatan Nayak, Prabagar B and Akhila K. Sahoo

(Manuscript under preparation)
4.1. Introduction

The ubiquitous heterocyclic building blocks are invariably found in natural products,\(^1\) pharmacologically active substances,\(^2\) and materials.\(^3\) Among various heterocycles, the six
membered nitrogen-bearing structural entities 1–4 are present in a wide variety of natural
products and pharmaceutically important molecules.\(^4\) Apart from pyridine (1) and
piperidine (2), the dihydropyridine (3 and 4) moiety is found in various biologically active
compounds (Figure 4.1).\(^5,6\)

![Figure 4.1: The six-membered N-bearing heterocycles](image)

The 1,4-dihydropyridine (1,4-DHP, 3) bearing pharmacophores showed better clinical
potential (Figure 4.2).\(^6\) For instance: nifedipine (5), felodipine (6), amlodipine (7), and
nicardipine (8) are some of the most notable 1,4-DHP-based calcium channel blocker
drugs; these compounds are used for the treatment of hypertension and related
cardiovascular diseases.\(^7\) The 1,4-DHP derivatives niguldipine (9), SNAP 5089 (10), and
SNAP 5540 (11) are potent antagonist to \(\alpha_{1a}\) receptor subtype and are useful for the
treatment of benign prostatic hyperplasia (BPH).\(^8\)

In contrast, the 1,2-DHP molecular entities are useful in the construction of nitrogen-
containing complex heterocycles.\(^9\) The most common method for the synthesis of 1,2-
dihydropyridines involves the addition of nucleophiles to \(N\)-acyl, \(N\)-alkyl or \(N\)-
heteroatompyridinium salts; however, these processes require harsh conditions and often
yielded regioisomeric products.\(^10\) The metal and metal-free synthesis of 1,2-DHP often
requires high temperature with the formation of mixture of non-regioselective products. A
detailed survey of the literature reports reveal that the strategies for the preparation of 1,4-
DHP is well studied, while the methods for 1,2-DHP synthesis is relatively poor.\(^9\) The
enormous importance of dihydropyridines thus encourages the development of an efficient
methods for the synthesis of 1,2-DHP derivatives from readily accessible materials.
4.2. Precedents to 1,2-DHP

The Sarpong group reported a novel strategy for the synthesis of highly-substituted 1,2-dihydropyridines 14 via Pt(II)-catalyzed cycloisomerization of aziridinyl propargyl esters 12 (Scheme 4.1). The 1,2-acetate migration of 12 generates metallocarbenoid species 13 in situ. The nucleophilic attack of nitrogen atom to the carbenoid center in 13 followed by aziridine ring opening delivers 14.\textsuperscript{11}

Scheme 4.1: Pt(II)-catalyzed synthesis of 1,2-dihydropyridine derivatives
The metal-free cyclization and N-iodosuccinimide-induced electrophilic iodo cyclization of 3-aza-1,5-enyne 15 produces 1,2-DHP derivatives 17. The reaction proceeds via aza-Claisen rearrangement of 15 followed by 1,3-H shift and 6π-electrocyclization of 16 to afford 17 (Scheme 4.2). Similarly, iodo-substituted 1,2-DHP derivative 19 is generated from 15 when heated with NIS in DMF at 80 °C. The activation of triple bond of 15 by iodonium ion forms 18 in situ, the cyclization of 18 furnishes 19 (Scheme 4.2).\(^\text{12}\)

**Scheme 4.2: Cyclization of 3-aza-1,5-enynes**

The reaction between propargyl alcohols 21 and enaminones 20 in the presence of BF\(_3\)OEt efficiently produces multi-substituted 1,2-dihydropyridines 22 (Scheme 4.3).\(^\text{13}\)

The reaction proceeds through the nucleophilic attack of enaminone 20 to the in situ generated allenyl cation 23, obtained from 21, followed by intramolecular cyclization.

**Scheme 4.3: Lewis acid-catalyzed cyclization of enaminones with propargyl alcohols**

The Tong group reported Ph\(_3\)P-catalyzed \([2 + 2 + 2]\) annulations between two units of activated terminal alkyne 24 and one unit of an aryl N-tosylimine (25) for the synthesis of highly substituted 1,2-dihydropyridines 28 (Scheme 4.4). Initial addition of Ph\(_3\)P to the
1,2-Dihydropyridine……

Scheme 4.4: PPh₃-Catalyzed [2 + 2 +2] and [4 + 2] annihilations

activated terminal alkyne generates zwitterionic compound 26. The reaction of imine 25 with 26 then generates 27. Finally, [4 + 2] annihilation between 24 and 27 furnishes 28.¹⁴

Microwave assisted synthesis of functionalized 1,2-dihydropyridines is demonstrated by Tejedor and Garcia-Tellado groups. Claisen rearrangement and isomerization of propargyl enol ether 29 gives 30. Condensation of 30 with amine followed by 6π-aza-electrocyclization provides 31 (Scheme 4.5).¹⁵

Scheme 4.5: Microwave assisted synthesis of functionalized 1,2-dihydropyridines

The reaction between vinylloxiranes 32 and imines 33 in the presence of Sc(OTf)₃ produces substituted 1,2-dihydropyridines 35 (Scheme 4.6). The reaction involves sequential opening of epoxide ring, 1,2-hydride shift, enolization followed by nucleophilic attack of enol moiety to imine 33 forming the intermediate 34. Finally, intramolecular condensation between amine and carbonyl moieties in 34 generates 35.¹⁶

Scheme 4.6: Synthesis of 1,2-dihydropyridines via imino-aldol reactions

The Ni-catalyzed reaction between two units of diphenyl acetylene (36) and one unit of imine (33) allows the highly substituted 1,2-dihydropyridine derivative 37 (Scheme 4.7). At first oxidative cyclization of an imine and alkyne with nickel(0) gives a nickela-
1,2-Dihydropyridine……

Scheme 4.7: Ni-Catalyzed synthesis of highly substituted 1,2-dihydropyridines

The gold-catalyzed rearrangement of readily accessible propargyl vinyl ethers 29 followed by condensation with amines lead to 1,2-dihydropyridines. The reaction involves gold-catalyzed propargyl-Claisen rearrangement of 29 to 40 followed by condensation of amine with 40 leading to 41. The Brønsted acid-catalyzed cyclization of 41 finally delivers 1,2-dihydropyridines 42 (Scheme 4.8).\(^\text{\textsuperscript{18}}\)

Scheme 4.8: Gold-catalyzed synthesis of 1,2-dihydropyridines

4.3. Motivation and Design Plan

Recently, we have reported a novel strategy for the synthesis of 1,6-dihydropyridine-2(3H)-ones from readily accessible 1,6-dynamides under gold(I) catalyst (eq 1, Scheme 4.9).\(^\text{\textsuperscript{19}}\) During the preparation of 1,6-dynamides, we could be able to synthesize stable ketene N,N-acetals via Cu-catalyzed C–N bond formation followed by Michael addition reaction between N-tosyl-protected propargyl amide and bromo propiolate. The structure of alkyne tethered ketene N,N-acetals 44 closely resemble to 3-aza-1,5-enyne 43 (Figure 4.3). The Wan and Saito groups have independently demonstrated the synthesis of various N-containing heterocycles from 3-aza-1,5-enynes. We therefore interested exploring new reactions on this novel ketene N,N-acetals moiety.
1,2-Dihydropyridine

**Figure 4.3**: 3-aza-1,5-enyne and ketene N,N-acetal

In our ongoing research interest on Au catalysis in our laboratory, first we have studied the reactivity of ketene N,N-acetals under gold catalysts. We have successfully demonstrated the synthesis of highly substituted 7,4-fused azabicyclo heterocycle 49 from ketene N,N-acetal 44 under the influence of Echavarren’s catalyst in 1,2-dichloroethane at room temperature (eq 2, Scheme 4.9). As the structure of 44 resemble to 3-aza-1,5-enyne, we therefore envisioned the one-step synthesis of 1,2-dihydropyridine system 50 from 44 (eq 3, Scheme 4.9).

**Scheme 4.9**: Gold-catalyzed 6-endo-dig cyclization of yne-ynamides and ketene N,N-acetals.

Herein an operationally simple strategy for the synthesis of iodo substituted highly functionalized 1,2-dihydropyridine derivatives involving Ag-catalyzed 6-endo-dig cyclization of ketene N,N-acetals is demonstrated.
4.4. Results and Discussion

4.4.1. Reaction Optimization

Following the literature procedures, the Cu-catalyzed C−N bond formation between N-tosyl-protected propargyl amide and bromo propiolate affords a wide range of precursors ketene N,N-acetals 44 in good yields (Table 4.1).\textsuperscript{20}

The iodonium ion efficiently activates the unsaturated C−C bonds. We therefore investigated the cyclization of ethyl 3,3-bis(4-methyl-N-(3-phenylprop-2-ynyl)-phenyl-sulfonamido)acrylate (44a) in the presence of iodonium ion containing reagents. Table 4.2 summarizes the results of optimization studies. The reaction of 44a with NIS (1.3 equiv) in CH\textsubscript{2}Cl\textsubscript{2} produced 1,2-dihydropyridine derivative 50a in 56% yield at room temperature.

Table 4.1: Synthesis of various substituted ketene N,N-acetals\textsuperscript{a,b}

\begin{center}
\begin{tabular}{|c|c|c|c|}
\hline
Compound & Reagent & Yield (\%) & \\
\hline
44a & CuSO\textsubscript{4}·5H\textsubscript{2}O (10 mol \%), 1,10-phenanthroline (20 mol \%), K\textsubscript{3}PO\textsubscript{4} (2.5 equiv), toluene, 60–65 °C, 6–8 h & 56 & \\
44b & CuSO\textsubscript{4}·5H\textsubscript{2}O (10 mol \%), 1,10-phenanthroline (20 mol \%), K\textsubscript{3}PO\textsubscript{4} (2.5 equiv), toluene, 60–65 °C, 6–8 h & 85 & \\
44c & CuSO\textsubscript{4}·5H\textsubscript{2}O (10 mol \%), 1,10-phenanthroline (20 mol \%), K\textsubscript{3}PO\textsubscript{4} (2.5 equiv), toluene, 60–65 °C, 6–8 h & 85 & \\
44d & CuSO\textsubscript{4}·5H\textsubscript{2}O (10 mol \%), 1,10-phenanthroline (20 mol \%), K\textsubscript{3}PO\textsubscript{4} (2.5 equiv), toluene, 60–65 °C, 6–8 h & 85 & \\
44e & CuSO\textsubscript{4}·5H\textsubscript{2}O (10 mol \%), 1,10-phenanthroline (20 mol \%), K\textsubscript{3}PO\textsubscript{4} (2.5 equiv), toluene, 60–65 °C, 6–8 h & 85 & \\
44f & CuSO\textsubscript{4}·5H\textsubscript{2}O (10 mol \%), 1,10-phenanthroline (20 mol \%), K\textsubscript{3}PO\textsubscript{4} (2.5 equiv), toluene, 60–65 °C, 6–8 h & 85 & \\
44g & CuSO\textsubscript{4}·5H\textsubscript{2}O (10 mol \%), 1,10-phenanthroline (20 mol \%), K\textsubscript{3}PO\textsubscript{4} (2.5 equiv), toluene, 60–65 °C, 6–8 h & 85 & \\
44h & CuSO\textsubscript{4}·5H\textsubscript{2}O (10 mol \%), 1,10-phenanthroline (20 mol \%), K\textsubscript{3}PO\textsubscript{4} (2.5 equiv), toluene, 60–65 °C, 6–8 h & 85 & \\
44i & CuSO\textsubscript{4}·5H\textsubscript{2}O (10 mol \%), 1,10-phenanthroline (20 mol \%), K\textsubscript{3}PO\textsubscript{4} (2.5 equiv), toluene, 60–65 °C, 6–8 h & 85 & \\
44j & CuSO\textsubscript{4}·5H\textsubscript{2}O (10 mol \%), 1,10-phenanthroline (20 mol \%), K\textsubscript{3}PO\textsubscript{4} (2.5 equiv), toluene, 60–65 °C, 6–8 h & 85 & \\
\hline
\end{tabular}
\end{center}

\textsuperscript{a}Reactions were carried out using 44" (1.0 mmol), 44' (0.5 mmol), CuSO\textsubscript{4}·5H\textsubscript{2}O (0.10 mmol), 1,10-phenanthroline (0.20 mmol) and K\textsubscript{3}PO\textsubscript{4} (2.0 mmol) in dry toluene (5.0 mL) at 60–65 °C. \textsuperscript{b}Isolated yields.
in 12 h (entry 1). Trace amount of the desired 50a was noticed when I₂ was used as an additive (entry 2). The use of AgNO₃ (15 mol %) along with NIS produced 45% of 50a (entry 3). Screening of other Ag-salts such as: AgOAc, AgSbF₆, AgBF₄, AgNTf₂ were found moderate (entries 4–7). Yield of 50a was increased to 87% when AgOCOCF₃ employed in this reaction (entry 8). The solvent DCE is equally efficient, furnishing 85% of 50a (entry 9). The other solvents CHCl₃, acetonitrile, 1,4-dioxane, acetone were found moderate (entries 10–13). The product 50a was isolated in 60% yield when the reaction mixture comprising of AgOCOCF₃ (15 mol %) and NIS was heated at 60 °C in CH₂Cl₂ for 12 h (entry 14).

Table 4.2: Optimization of reaction conditions

<table>
<thead>
<tr>
<th>Entry</th>
<th>Catalyst (mol %)</th>
<th>Additive (1.3 equiv)</th>
<th>Solvent</th>
<th>Yields 50a (%)</th>
</tr>
</thead>
<tbody>
<tr>
<td>1</td>
<td>none</td>
<td>NIS</td>
<td>CH₂Cl₂</td>
<td>56</td>
</tr>
<tr>
<td>2</td>
<td>none</td>
<td>I₂</td>
<td>CH₂Cl₂</td>
<td>trace</td>
</tr>
<tr>
<td>3</td>
<td>AgNO₃ (15)</td>
<td>NIS</td>
<td>CH₂Cl₂</td>
<td>45%</td>
</tr>
<tr>
<td>4</td>
<td>AgOAc (15)</td>
<td>NIS</td>
<td>CH₂Cl₂</td>
<td>58%</td>
</tr>
<tr>
<td>5</td>
<td>AgSbF₆ (15)</td>
<td>NIS</td>
<td>CH₂Cl₂</td>
<td>38 (42)⁶</td>
</tr>
<tr>
<td>6</td>
<td>AgBF₄ (15)</td>
<td>NIS</td>
<td>CH₂Cl₂</td>
<td>25 (54)⁶</td>
</tr>
<tr>
<td>7</td>
<td>AgNTf₂ (15)</td>
<td>NIS</td>
<td>CH₂Cl₂</td>
<td>50 (40)⁶</td>
</tr>
<tr>
<td>8</td>
<td>AgOCOCF₃ (15)</td>
<td>NIS</td>
<td>CH₂Cl₂</td>
<td>87</td>
</tr>
<tr>
<td>9</td>
<td>AgOCOCF₃ (15)</td>
<td>NIS</td>
<td>DCE</td>
<td>85</td>
</tr>
<tr>
<td>10</td>
<td>AgOCOCF₃ (15)</td>
<td>NIS</td>
<td>CHCl₃</td>
<td>43 (35)⁶</td>
</tr>
<tr>
<td>11</td>
<td>AgOCOCF₃ (15)</td>
<td>NIS</td>
<td>acetonitrile</td>
<td>53 (19)⁶</td>
</tr>
<tr>
<td>12</td>
<td>AgOCOCF₃ (15)</td>
<td>NIS</td>
<td>1,4-dioxane</td>
<td>62</td>
</tr>
<tr>
<td>13</td>
<td>AgOCOCF₃ (15)</td>
<td>NIS</td>
<td>acetone</td>
<td>60</td>
</tr>
<tr>
<td>14</td>
<td>AgOCOCF₃ (15)</td>
<td>NIS</td>
<td>CH₂Cl₂</td>
<td>60⁴</td>
</tr>
</tbody>
</table>

⁴Reactions were carried out using 44a (0.20 mmol), Ag(OCOCF₃) (15 mol %), NIS (0.26 mmol) in CH₂Cl₂ (2.0 mL) at room temperature. ⁵Isolated yields. ⁶Yield of the recovered starting material is given in parentheses. ⁷Reaction mixture was heated at 60 °C.
4.4.2. Reaction Scope

The substrate generality of this cyclization is investigated under the optimized reaction conditions [Ag(OCOCF₃) (15 mol %), NIS (1.3 equiv) in dichloromethane]. The results are detailed in Table 4.3. Electronically neutral phenyl ring bearing substrate ketene N,N-acetal 44a gave the desired iodo-substituted 1,2-dihydropyridine derivative 50a in 87% yield. Substrate 44b with electron donating p-Me group on the arene rings produced six membered heterocyclic product 50b in excellent yield. Poor yield of product 50c was obtained from substrate 44c. The desired 1,2-dihydropyridine derivatives 50d and 50e were isolated in 60% and 52% yield, respectively from the corresponding electron-withdrawing group containing substrates 44d and 44e. The precursors 44f and 44g having two-substituents on aryl ring gave products 50f and 50g in 49% and 74% yield.

Table 4.3: Cyclization reaction of differently aryl substituted ketene N,N-acetal

<table>
<thead>
<tr>
<th>R = COOEt, 87%, 50a</th>
<th>R = COOEt, 88%, 50b</th>
<th>R = COOEt, 44%, 50c</th>
<th>R = COOEt, 60%, 50d</th>
</tr>
</thead>
<tbody>
<tr>
<td>R = COOEt, 52%, 50e</td>
<td>R = COOEt, 49%, 50f</td>
<td>R = COOEt, 74%, 50g</td>
<td>R = COOBr, 67%, 50h</td>
</tr>
<tr>
<td>R = COOCMe, 69%, 50i</td>
<td>R = COOBn, 74%, 50j</td>
<td></td>
<td></td>
</tr>
</tbody>
</table>

*Reactions were carried out using 44a (0.20 mmol), Ag(OCOCF₃) (15 mol %), NIS (0.26 mmol) in CH₂Cl₂ (2.0 mL) at room temperature. Isolated yields.
respectively. The desired products $50h$ and $50i$ were isolated in moderate yields, when $\text{–COOEt}$ group at alkene terminus is replaced by $\text{COOBn}$ and $\text{COOMe}$ groups. The change of protecting group on nitrogen atom from Ts to Ms in $44j$ did not affect the product formation, producing $50j$ in 74% yield.

4.4.3. Plausible Reaction Mechanism

A plausible reaction mechanism for this cyclization reaction is outlined in Scheme 4.10. At first electrophilic silver cation coordinates to one of the triple bond of alkyne tethered ketene $N,N$-acetal $44$ to form a $\pi$-complex $51$. Next, the $6$-$\text{endo}$-dig attack of double bond, facilitated by the lone pair electron on nitrogen atom, to the activated triple bond of $51$ produces intermediate $52$. The intermediate $52$ is in resonance with intermediate $53$. Later vinylic C-Ag bond in intermediate $54$ is trapped by iodonium ion and generates six membered heterocyclic compound $55$. Finally, neutralization of positive charge by the removal of acidic proton attached to the carbon atom at $\alpha$-position to ester group furnishes 1,2-DHP derivative $50$.

**4.5. Conclusion**

In summary, we have developed an efficient method for the synthesis of iodo-substituted 1,2-dihydropyridines via 6-endo-dig cyclization and isomerization of ketene \( N, N \)-acetals under silver catalyst at room temperature. The current method delivers a wide range of 1,2-DHP derivatives in moderate to good yields. Replacement of iodo group on the periphery of heterocyclic ring for the synthesis of extended \( \pi \)-cojugated system is currently investigated in our laboratory.

**4.6. Future Work**

Pyran derivatives are the important class of heterocycles found in many natural products. Thus, synthesis of \( 2H \)-pyrans from readily available starting materials is always demanding. As \( 2H \)-pyrans undergo reversible electrocyclic ring-opening to 1-oxatrienes,\(^{21}\) the synthesis of stable \( 2H \)-pyrans is thus an ongoing challenge in organic synthesis. Few classical strategies have been developed for the synthesis of monocyclic \( 2H \)-pyrans.\(^{22}\) Kirsch group reported the silver catalyzed synthesis of stable \( 2H \)-pyrans.\(^{23}\) We have successfully accomplished the synthesis of 1,2-dihydropyridine derivatives from stable ketene \( N,N \)-acetal under the presence of silver catalyst. We thus envisioned the synthesis of highly substituted \( 2H \)-pyrans 57 from ketene \( O,O \)-acetals 56 (Scheme 4.11).

![Scheme 4.11: Transition-metal-catalyzed transformations of ketene \( O,O \)-acetals](image-url)
4.7. Experimental

4.7.1. General Experimental Information for all the Work in this Thesis

See pages 45 in chapter 2.

4.7.2. Materials

Purification procedure of the solvents is given in chapter 2, page no 46. Silver salts such as AgSbF$_6$, AgOOCCF$_3$, AgOAc, AgBF$_4$, AgNTf$_2$, and AgNO$_3$ are purchased from Aldrich Ltd. and used as received. The reagents CuSO$_4$·5H$_2$O, 1,10-phenanthroline, K$_3$PO$_4$, PdCl$_2$(PPh$_3$)$_2$, CuI and NIS (N-iodosuccinimide) are purchased from Sigma Aldrich Ltd. and used. Analytical and spectral data of all those known compounds are exactly matching with the reported values.

4.7.3. Experimental Procedures:

A detailed procedure for the preparation of compound 44'' is shown in chapter 3, page 166.

**General Procedure for the Synthesis of 44 (GP-1):**

A solution of 44'' (1.0 mmol), CuSO$_4$·5H$_2$O (0.10 mmol), 1,10-phenanthroline (0.20 mmol) and K$_3$PO$_4$ (2.0 mmol) in dry toluene (5.0 mL) was stirred in a Schlenck tube. The ethyl 3-bromopropiolate (44'''') (0.5 mmol) was subsequently introduced into the Schlenck tube. The reaction mixture was heated at 70 °C under the nitrogen atmosphere. The progress of the reaction was monitored periodically by TLC. Upon completion, the reaction mixture was cooled to room temperature and diluted with dichloromethane (10 mL). The crude mixture was filtered through a small pad of Celite and concentrated under reduced pressure. The crude residue was purified using column chromatography on silica gel to provide 44.
4.7.4. Spectra and Analytical data

Ethyl 3,3-bis(4-methyl-N-(3-phenylprop-2-ynyl)phenylsulfonamido)acrylate (44a):

Following the general procedure (GP-1), compound 44a (249 mg) was obtained in overall 78% yield as pale yellow gummy liquid. Rf = 0.57 (4:1 hexane/EtOAc); [Silica, UV and I2]. 1H NMR (400 MHz, CDCl3) δ 7.88 (t, J = 8.8 Hz, 4H), 7.36–7.23 (m, 10H), 7.17 (d, J = 7.6 Hz, 4H), 5.76 (s, 1H), 4.67 (s, 2H), 4.50 (s, 2H), 4.14 (q, J = 7.2 Hz, 2H), 2.39 (s, 3H), 2.33 (s, 3H), 1.28 (t, J = 6.8 Hz, 3H). 13C NMR (101 MHz, CDCl3) δ 163.9, 144.6, 144.3, 142.7, 136.3, 135.8, 131.8, 131.6, 129.6, 129.5, 128.6, 128.5, 128.3, 128.2, 122.3, 122.1, 113.1, 86.3, 83.1, 82.9, 60.8, 41.1, 39.8, 21.6, 21.5, 14.1. IR (Neat) νmax 2975, 2926, 1720, 1627, 1600, 1490, 1364, 1161 cm⁻¹. HRMS (ESI) for C37H34N2O6S2Na (M+Na)+: calcd 689.1756, found 689.1757.

Ethyl 3,3-bis(4-methyl-N-(3-p-tolyl-prop-2-ynyl)phenylsulfonamido)acrylate (44b):

Following the general procedure (GP-1), compound 44b (309 mg) was obtained in overall 89% yield as pale yellow gummy liquid. Rf = 0.39 (4:1 hexane/EtOAc); [Silica, UV and I2]. 1H NMR (400 MHz, CDCl3) δ 7.88 (t, J = 7.6 Hz, 4H), 7.26 (d, J = 7.6 Hz, 2H), 7.18 (t, J = 7.2 Hz, 4H), 7.07 (br s, 6H), 5.74 (s, 1H), 4.66 (s, 2H), 4.47 (s, 2H), 4.14 (q, J = 7.2 Hz, 2H), 2.39 (s, 3H), 2.34 (s, 9H), 1.28 (q, J = 7.2 Hz, 3H). 13C NMR (101 MHz, CDCl3) δ 164.0, 144.5, 144.2, 142.6, 138.7, 136.4, 135.9, 131.7, 131.5, 129.6, 129.5, 128.9, 128.5, 128.2, 119.2, 119.0, 113.2, 86.4, 82.4, 82.2, 60.8, 41.1, 39.8, 21.6, 21.6, 21.5, 14.1. IR (Neat) νmax 2975, 2920, 2241, 1715, 1621, 1512, 1358, 1156 cm⁻¹. HRMS (ESI) for C39H39N2O6S2 (M+H)+: calcd 695.2249, found 695.2250.

Ethyl 3,3-bis(N-(3-(4-methoxyphenyl)prop-2-ynyl)-4-methylphenylsulfonamido)-acrylate (44c):

Following the general procedure (GP-1), compound 44c (316 mg) was obtained in overall 87% yield as pale yellow gummy liquid. Rf = 0.44 (19:1 hexane/EtOAc); [Silica, UV and I2]. 1H NMR (400 MHz, CDCl3) δ 7.87 (dd, J = 11.6, 8.0 Hz, 4H), 7.24 (d, J = 8.4 Hz, 4H), 7.20 (d, J = 7.6 Hz, 2H), 7.12 (d, J = 8.8 Hz, 2H), 6.78 (dd, J = 8.8, 2.4 Hz, 4H), 5.72 (s, 1H), 4.64 (br s, 2H), 4.46 (br s, 2H), 4.13 (q, J = 7.2 Hz, 2H), 3.80 (s, 6H), 2.39 (s, 3H), 2.35 (s, 3H), 1.27 (br t, J = 7.2 Hz, 3H). 13C NMR (101 MHz, CDCl3) δ 164.0, 159.7, 144.4, 144.2, 142.6, 136.4, 135.9, 133.3, 133.1, 129.6, 129.5, 128.6, 128.2, 114.4, 114.2, 113.8, 113.8, 113.1, 86.2, 81.7, 81.6, 60.8, 55.3, 41.1, 39.8, 21.6, 14.1. IR (Neat) νmax 2980, 2931, 2832, 1715, 1610, 1512, 1364, 1287, 1249, 1156 cm⁻¹. HRMS (ESI) for C39H38N2O8S2Na (M+Na)+: calcd 749.2249, found 749.2250.

Ethyl 3,3-bis(N-(3-(4-fluorophenyl)prop-2-ynyl)-4-methylphenylsulfonamido)acrylate (44d):
Following the general procedure (GP-1), compound 44d (284 mg) was obtained in overall 81% yield as yellow oil. \( R_f = 0.58 \) (7:3 hexane/EtOAc); [Silica, UV and I2]. \( ^1\)H NMR (400 MHz, CDCl\(_3\)) \( \delta \) 7.88 (d, \( J = 8.4 \) Hz, 2H), 7.81 (d, \( J = 8.4 \) Hz, 2H), 7.32–7.24 (m, 4H), 7.20 (d, \( J = 8.0 \) Hz, 2H), 7.15 (dd, \( J = 8.8, 5.6 \) Hz, 2H), 6.95 (t, \( J = 8.4 \) Hz, 4H), 5.75 (s, 1H), 4.64 (br s, 2H), 4.51 (br s, 2H), 4.11 (q, \( J = 4.4 \) Hz, 2H). \( ^{13}\)C NMR (101 MHz, CDCl\(_3\)) \( \delta \) 163.8, 161.4, 144.5 (d, \( J = 32.3 \) Hz), 142.6, 136.0 (d, \( J = 52.5 \) Hz), 133.7 (d, \( J = 9.1 \) Hz), 133.5 (d, \( J = 9.1 \) Hz), 129.5 (d, \( J = 8.1 \) Hz), 128.6, 128.2, 118.2 (d, \( J = 19.2 \) Hz), 115.5 (d, \( J = 23.2 \) Hz), 113.0, 85.2, 82.9, 82.7, 60.8, 41.1, 39.6, 21.6, 14.1. \( ^{19}\)F NMR (376 MHz, CDCl\(_3\)) \( \delta \) −110.1 (heptate, \( J = 3.7 \) Hz), −110.2 (heptate, \( J = 3.7 \) Hz). IR (Neat) \( \nu_{max} \) 3068, 2975, 2926, 2849, 1715, 1621, 1600, 1512, 1458 cm\(^{-1}\). HRMS (ESI) for C\(_{37}\)H\(_{32}\)F\(_2\)N\(_2\)O\(_6\)S\(_2\)Na (M+Na): calcd 725.1568, found 725.1571.

**Ethyl 3,3-bis(4-methyl-N-(3-(4-(trifluoromethyl)phenyl)prop-2-ynyl)phenylsulfonamido)acrylate (44e):**

Following the general procedure (GP-1), compound 44e (350 mg) was obtained in overall 70% yield as thick pale yellow gummy liquid. \( R_f = 0.57 \) (4:1 hexane/EtOAc); [Silica, UV and I2]. \( ^1\)H NMR (400 MHz, CDCl\(_3\)) \( \delta \) 7.89 (d, \( J = 8.0 \) Hz, 2H), 7.78 (d, \( J = 8.4 \) Hz, 2H), 7.52–7.46 (m, 4H), 7.39 (d, \( J = 8.0 \) Hz, 2H), 7.29–7.19 (m, 6H), 5.81 (s, 1H), 4.68 (s, 2H), 4.59 (s, 2H), 4.09 (q, \( J = 7.2 \) Hz, 2H), 2.39 (s, 3H), 2.36 (s, 3H), 1.25 (t, \( J = 7.2 \) Hz, 3H). \( ^{13}\)C NMR (101 MHz, CDCl\(_3\)) \( \delta \) 163.6, 144.9, 144.5, 142.7, 136.1, 135.5, 132.0, 131.8, 130.4 (q, \( J = 30 \) Hz), 129.6, 129.5, 128.7, 128.1, 125.9 (d, \( J = 25.2 \) Hz), 125.2, 122.4, 112.8, 85.7, 85.6, 84.8, 60.8, 41.1, 39.4, 21.6, 21.5, 14.1. \( ^{19}\)F NMR (376 MHz, CDCl\(_3\)) \( \delta \) −63.0 (s), 62.9 (s). IR (Neat) \( \nu_{max} \) 2926, 2843, 1726, 1594, 1358, 1320, 1117 cm\(^{-1}\). HRMS (ESI) for C\(_{39}\)H\(_{33}\)F\(_6\)N\(_2\)O\(_6\)S\(_2\) (M+H): calcd 803.1684, found 803.1684.

**Ethyl 3,3-bis(N-(3-(benzo[d][1,3]dioxol-5-yl)prop-2-ynyl)-4-methylphenylsulfonamido)acrylate (44f):**

Following the general procedure (GP-1), compound 44f (264 mg) was obtained in overall 70% yield as yellow liquid. \( R_f = 0.44 \) (4:1 hexane/EtOAc); [Silica, UV and I2]. \( ^1\)H NMR (400 MHz, CDCl\(_3\)) \( \delta \) 7.88 (d, \( J = 8.0 \) Hz, 2H), 7.84 (d, \( J = 8.4 \) Hz, 2H), 7.27 (d, \( J = 8.0 \) Hz, 2H), 7.23 (d, \( J = 8.4 \) Hz, 2H), 6.82 (dd, \( J = 8.0, 1.6 \) Hz, 1H), 6.75–6.67 (m, 4H), 6.56 (br s, 1H), 5.96 (s, 4H), 5.72 (s, 1H), 4.62 (br s, 2H), 4.44 (br s, 2H), 4.13 (q, \( J = 7.2 \) Hz, 2H), 2.40 (s, 3H), 2.38 (s, 3H), 1.27 (br t, \( J = 7.2 \) Hz, 3H). \( ^{13}\)C NMR (101 MHz, CDCl\(_3\)) \( \delta \) 163.9, 148.1, 147.3, 144.6, 144.3, 142.6, 136.4, 135.9, 129.6, 129.5, 128.5, 126.5, 126.3, 115.5, 115.3, 113.0, 111.7, 111.5, 108.4, 108.3, 101.4, 86.2, 81.4, 81.3, 60.8, 41.0, 39.6, 21.6, 14.1. IR (Neat) \( \nu_{max} \)
1,2-Dihydropyridine......

2985, 2958, 2925, 2224, 1714, 1626, 1599, 1484, 1444, 1352, 1166 cm⁻¹. HRMS (ESI) for C₃₉H₃₅N₂O₁₀S₂Na (M+H)⁺: calcd 755.1733, found 755.1732.

*Ethyl 3,3-bis(N-(3-(3,4-dimethylphenyl)prop-2-ynyl)-4-methylphenylsulfonamido)-acrylate (44g):*

Following the general procedure (GP-1), compound 44g (206 mg) was obtained in overall 57% yield as brown liquid. Rᶠ = 0.62 (4:1 hexane/EtOAc); [Silica, UV and I₂]. ¹H NMR (400 MHz, CDCl₃) δ 7.88 (t, J = 8.4 Hz, 4H), 7.26 (d, J = 7.6 Hz, 2H), 7.20 (d, J = 8.0 Hz, 2H), 7.09–6.96 (m, 4H), 6.95–6.87 (m, 2H), 5.73 (s, 1H), 4.65 (br s, 2H), 4.46 (br s, 2H), 4.14 (q, J = 7.2 Hz, 2H), 2.40 (s, 3H), 2.36 (s, 3H), 2.24 (s, 6H), 2.20 (s, 3H), 1.28 (t, J = 7.2 Hz, 3H). ¹³C NMR (101 MHz, CDCl₃) δ 164.0, 144.4, 144.2, 142.7, 137.5, 136.5, 136.0, 132.8, 132.7, 129.6, 129.5, 129.4, 129.3, 129.1, 128.6, 128.2, 119.5, 119.4, 113.1, 86.5, 82.1, 82.0, 60.7, 41.1, 39.7, 21.63, 21.59, 19.8, 19.6, 14.1. IR (Neat) νmax 3024, 2975, 2920, 2860, 2224, 1720, 1632, 1501, 1452, 1358, 1112 cm⁻¹. HRMS (ESI) for C₄₁H₄₂N₂O₆S₂Na (M+Na)⁺: calcd 745.2382, found 745.2380.

*Benzyl 3,3-bis(4-methyl-N-(3-phenylprop-2-ynyl)phenylsulfonamido)acrylate (44h):*

Following the general procedure (GP-1), compound 44h (273 mg) was obtained in overall 75% yield as thick yellow liquid. Rᶠ = 0.56 (7:3 hexane/EtOAc); [Silica, UV and I₂]. ¹H NMR (400 MHz, CDCl₃) δ 7.88 (dd, J = 10.8, 2.8 Hz, 4H), 7.39–7.22 (m, 15H), 7.16 (t, J = 8.4 Hz, 4H), 5.87 (s, 1H), 5.14 (s, 2H), 4.66 (br s, 2H), 4.55 (br s, 2H), 2.39 (s, 3H), 2.32 (s, 3H). ¹³C NMR (101 MHz, CDCl₃) δ 163.5, 144.5, 144.2, 143.1, 136.1, 135.6, 135.5, 131.7, 131.5, 129.4, 129.3, 128.6, 128.5, 128.4, 128.3, 128.1, 122.1, 121.9, 112.0, 86.3, 86.2, 86.2, 66.2, 41.0, 39.6, 21.5, 21.4. IR (Neat) νmax 3086, 1720, 1621, 1490, 1364, 1172 cm⁻¹. HRMS (ESI) for C₄₂H₄₁N₂O₆S₂ (M+H)⁺: calcd 729.2093, found 729.2090.

*Methyl 3,3-bis(4-methyl-N-(3-phenylprop-2-ynyl)phenylsulfonamido)acrylate (44i):*

Following the general procedure (GP-1), compound 44i (229 mg) was obtained in overall 70% yield as pale brown liquid. Rᶠ = 0.58 (4:1 hexane/EtOAc); [Silica, UV and I₂]. ¹H NMR (400 MHz, CDCl₃) δ 7.88 (t, J = 7.2 Hz, 4H), 7.33–7.24 (m, 10H), 7.22–7.14 (m, 4H), 5.75 (s, 1H), 4.66 (s, 2H), 4.51 (s, 2H), 3.67 (s, 3H), 2.39 (s, 3H), 2.34 (s, 3H). ¹³C NMR (101 MHz, CDCl₃) δ 164.4, 144.6, 144.3, 142.9, 136.3, 135.8, 131.7, 131.6, 129.6, 129.5, 128.6, 128.5, 128.3, 128.2, 122.3, 122.1, 122.5, 86.3, 86.2, 83.0, 82.9, 51.7, 41.0, 39.7, 21.6, 21.5. IR (Neat) νmax 2947, 2843, 1726, 1638, 1495, 1358, 1221, 1178, 1112, 1041 cm⁻¹. HRMS (ESI) for C₃₆H₃₃N₂O₆S₂ (M+H)⁺: calcd 653.1780, found 653.1781.
1,2-Dihydropyridine……

Benzyl 3,3-bis(N-(3-(4-bromophenyl)prop-2-ynyl)methylsulfonamido)acrylate (44j):

Following the general procedure (GP-1), compound 44j (261 mg) was obtained in overall 71% yield as brown gummy liquid. \( R_f = 0.35 \) (7:3 hexane/EtOAc); [Silica, UV and I\(_2\)]. \(^1\)H NMR (400 MHz, CDCl\(_3\)) \( \delta \) 7.42–7.32 (m, 9H), 7.18 (d, \( J = 8.4 \) Hz, 2H), 7.14 (d, \( J = 8.4 \) Hz, 2H), 6.19 (s, 1H), 5.20 (s, 2H), 4.68 (s, 2H), 4.62 (s, 2H), 3.23 (s, 3H), 3.21 (s, 3H). \(^{13}\)C NMR (101 MHz, CDCl\(_3\)) \( \delta \) 163.7, 144.7, 135.3, 133.2, 133.1, 131.7, 131.6, 128.7, 128.6, 128.5, 123.4, 123.2, 120.8, 120.6, 110.6, 86.06, 85.3, 84.4, 83.4, 66.8, 41.48, 41.3, 41.0, 40.2, 30.9. IR (Neat) \( \nu \)\(_{\text{max}}\) 3029, 2931, 1709, 1632, 1489, 1358, 1155, 1117, 1067 cm\(^{-1}\). HRMS (ESI) for \( \text{C}_{36}\text{H}_{27}\text{Br}_2\text{N}_2\text{O}_8\text{S}_2 \) (M+H): calcd 732.9677, found 732.9677.

Silver–Catalyzed Cyclization of Ketene N,N-Acetal 44; General Procedure (GP-2):

A mixture of 44 (0.2 mmol), Ag(OOCF\(_3\)) (0.03 mmol, 6.0 mg) and NIS (0.26 mmol, 58 mg) in dichloromethane (2.0 mL) was stirred in a Schlenk flask under an argon atmosphere for 12 h at an ambient temperature. The progress of the reaction was monitored by TLC. Upon complete consumption of precursor 44, the reaction mixture was diluted with dichloromethane (10 mL), and filtered through a small pad of Celite. The solvent was evaporated under the reduced pressure and the crude reaction mixture was purified using column chromatography on silica gel.

Ethyl 5-iodo-2-(4-methyl-N-(3-phenylprop-2-ynyl)phenylsulfonamido)-4-phenyl-1-tosyl-1,6-dihydropyridine-3-carboxylate (50a):

Following the general procedure (GP-2), reaction of ethyl 3,3-bis(4-methyl-N-(3-phenylprop-2-ynyl)phenylsulfonamido)acrylate (44a; 130 mg, 0.2 mmol) under the optimized Au-catalyzed conditions gave 50a (138 mg) in 87% yield as pale yellow oil. \( R_f = 0.63 \) (7:3 hexane/EtOAc); [Silica, UV and I\(_2\)]. \(^1\)H NMR (400 MHz, CDCl\(_3\)) \( \delta \) 7.87 (d, \( J = 8.0 \) Hz, 4H), 7.29 (br s, 8H), 7.12 (d, \( J = 8.4 \) Hz, 4H), 6.58 (d, \( J = 8.4 \) Hz, 2H), 4.94 (s, 1H), 4.71 (s, 3H), 3.84 (br s, 2H), 2.40 (s, 3H), 2.34 (s, 3H), 0.83 (q, \( J = 6.8 \) Hz, 3H). \(^{13}\)C NMR (101 MHz, CDCl\(_3\)) \( \delta \) 163.3, 144.7, 144.2, 140.1, 137.4, 136.7, 136.6, 136.1, 134.7, 134.0, 133.2, 130.1, 129.9, 129.4, 128.6, 127.9, 127.8, 124.8, 121.1, 92.5, 85.1, 84.9, 61.6, 58.5, 43.2, 21.7, 21.6, 13.5. IR (Neat) \( \nu \)\(_{\text{max}}\) 2964, 1709, 1643, 1495 cm\(^{-1}\). HRMS (ESI) for \( \text{C}_{37}\text{H}_{33}\text{IN}_2\text{O}_8\text{S}_2\text{Na} \) (M+Na): calcd 815.0723, found 815.0725.
Following the general procedure (GP-2), reaction of ethyl 3,3-bis(4-methyl-N-(3-p-tolyl-prop-2-ynyl)phenylsulfonamido)acrylate (44b; 164 mg, 0.2 mmol) under the optimized Ag-catalyzed conditions gave 50b (144 mg) in 88% yield as pale yellow oil. \( R_f = 0.52 \) (4:1 hexane/EtOAc); [Silica, UV and I2]. \( ^1\)H NMR (400 MHz, CDCl3) \( \delta 7.90 \) (t, \( J = 6.4 \) Hz, 4H), 7.27 (d, \( J = 7.2 \) Hz, 4H), 7.12 (d, \( J = 7.6 \) Hz, 2H), 7.08 (d, \( J = 8.0 \) Hz, 2H), 6.94 (d, \( J = 7.6 \) Hz, 2H), 6.55 (d, \( J = 7.6 \) Hz, 2H), 4.91 (s, 1H), 4.75 (s, 3H), 3.81 (q, \( J = 6.8 \) Hz, 2H), 2.39 (s, 3H), 2.38 (s, 3H), 2.30 (s, 6H), 0.88 (t, \( J = 7.2 \) Hz, 3H). \( ^{13} \)C NMR (101 MHz, CDCl3) \( \delta 163.5, 144.4, 144.0, 141.1, 138.6, 137.8, 136.7, 136.3, 135.9, 135.8, 132.0, 129.8, 129.3, 128.9, 128.6, 128.5, 128.3, 127.9, 125.6, 119.7, 91.6, 86.3, 83.1, 61.4, 58.5, 43.3, 21.6, 21.5, 21.3, 13.4. IR (Neat) \( \nu_{max} 2920, 1726, 1605, 1506, 1161 \) cm\(^{-1}\). HRMS (ESI) for C\(_{39}\)H\(_{38}\)N\(_2\)O\(_8\)S\(_2\)(M+H): calcd 821.1216, found 821.1216.

Following the general procedure (GP-2), reaction of ethyl 3,3-bis(N-(3-(4-methoxyphenyl)prop-2-ynyl)-4-methylphenylsulfonamido)acrylate (44c; 145 mg, 0.2 mmol) under the optimized Ag-catalyzed conditions gave 50c (75 mg) in 44% yield as pale yellow oil. \( R_f = 0.50 \) (7:3 hexane/EtOAc); [Silica, UV and I2]. \( ^1\)H NMR (400 MHz, CDCl3) \( \delta 7.91 \) (t, \( J = 8.4 \) Hz, 4H), 7.34 (d, \( J = 7.6 \) Hz, 2H), 7.29 (d, \( J = 8.0 \) Hz, 2H), 7.10 (d, \( J = 8.0 \) Hz, 2H), 6.86 (d, \( J = 7.6 \) Hz, 2H), 6.65 (q, \( J = 8.4 \) Hz, 4H), 4.98 (s, 1H), 4.91 (s, 3H), 3.85 (br s, 5H), 3.79 (s, 3H), 2.41 (s, 3H), 2.31 (s, 3H), 0.92 (t, \( J = 7.2 \) Hz, 3H). \( ^{13} \)C NMR (101 MHz, CDCl3) \( \delta 163.5, 159.8, 159.1, 144.4, 144.0, 140.8, 136.7, 136.3, 136.0, 133.6, 131.2, 130.0, 129.8, 129.3, 128.6, 127.9, 125.5, 114.9, 113.8, 112.9, 91.6, 86.2, 82.5, 61.4, 58.5, 55.4, 55.1, 43.4, 21.7, 21.6, 13.5. IR (Neat) \( \nu_{max} 2920, 1726, 1610, 1506, 1161 \) cm\(^{-1}\). HRMS (ESI) for C\(_{39}\)H\(_{38}\)N\(_2\)O\(_8\)S\(_2\)(M+H): calcd 853.1114, found 853.1114.

Following the general procedure (GP-2), reaction of ethyl 3,3-bis(N-(3-(4-fluorophenyl)prop-2-ynyl)-4-methylphenylsulfonamido)acrylate (44d; 140 mg, 0.2 mmol) under the optimized Ag-catalyzed conditions gave 50d (99 mg) in 60% yield as brown liquid. \( R_f = 0.61 \) (4:1 hexane/EtOAc); [Silica, UV and I2]. \( ^1\)H NMR (400 MHz, CDCl3) \( \delta 7.88 \) (t, \( J = 7.2 \) Hz, 4H), 7.36 (t, \( J = 6.8 \) Hz, 2H), 7.28 (d, \( J = 8.0 \) Hz, 2H), 7.12 (d, \( J = 18.4 \) Hz, 2H), 7.02 (t, \( J = 8.4 \) Hz, 2H), 6.83 (t, \( J = 8.4 \) Hz, 2H), 6.63 (t, \( J = 8.0 \) Hz, 2H), 5.30 (s, 1H), 4.74 (s, 3H), 3.84 (q, \( J = 6.8 \) Hz, 2H), 2.40 (s, 3H), 2.32 (s, 3H), 0.92 (t, \( J = 7.2 \) Hz, 3H). \( ^{13} \)C NMR (125 MHz, CDCl3) \( \delta 163.4 \) (d, \( J = 48.0 \) Hz), 163 3, 161.5

258
1,2-Dihydropyridine......

(d, \( J = 46.0 \) Hz), 144.6, 144.2, 140.2, 136.7, 136.4, 136.2, 134.8 (d, \( J = 3.4 \) Hz), 133.9 (d, \( J = 8.3 \) Hz), 130.6 (d, \( J = 8.8 \) Hz), 129.8, 129.4, 128.6, 127.9, 125.1, 118.8 (d, \( J = 1.0 \) Hz), 115.5 (d, \( J = 22 \) Hz), 114.6 (d, \( J = 21.6 \) Hz), 92.5, 85.2, 83.6, 61.5, 58.5, 43.2, 21.6, 21.5, 13.5. \(^{19}\)F NMR (376 MHz, CDCl\(_3\)) \( \delta -110.2 \) (m), –112.8 (m). IR (Neat) \( \nu_{\text{max}} \) 2980, 1720, 1600, 1501, 1364, 1227 cm\(^{-1}\).

HRMS (ESI) for C\(_{37}\)H\(_{32}\)F\(_2\)IN\(_2\)O\(_6\)S\(_2\) (M+H): calcd 829.0714, found 829.0712.

Ethyl 5-iodo-2-(4-methyl-N-(3-(4-(trifluoromethyl)phenyl)prop-2-ynyl)phenylsulfonamido)-1-tosyl-4-(4-(trifluoromethyl)phenyl)-1,6-dihydropyridine-3-carboxylate (50e):

Following the general procedure (GP-2), reaction of ethyl 3,3-bis(4-methyl-N-(3-(4-(trifluoromethyl)phenyl)prop-2-ynyl)phenylsulfonamido)acrylate (44e; 186 mg, 0.2 mmol) under the optimized Ag-catalyzed conditions gave 50e (96 mg) in 52% yield as brown oil. \( R_f = 0.69 \) (4:1 hexane/EtOAc); [Silica, UV and I\(_2\)]. \(^1\)H NMR (400 MHz, CDCl\(_3\)) \( \delta 7.88 \) (d, \( J = 7.2 \) Hz, 4H), 7.57 (d, \( J = 8.0 \) Hz, 2H), 7.46 (d, \( J = 8.0 \) Hz, 2H), 7.39 (d, \( J = 8.0 \) Hz, 2H), 7.28 (d, \( J = 8.4 \) Hz, 2H), 7.17 (d, \( J = 8.0 \) Hz, 2H), 6.75 (d, \( J = 8.0 \) Hz, 2H), 4.95 (s, 1H), 4.77 (br s, 3H), 3.82 (q, \( J = 6.8 \) Hz, 2H), 2.39 (s, 3H), 2.35 (s, 3H), 0.88 (t, \( J = 6.8 \) Hz, 3H). \(^{13}\)C NMR (101 MHz, CDCl\(_3\)) \( \delta 163.1, 144.9, 144.4, 142.7, 140.0, 137.2, 136.5, 136.1, 132.2, 130.3 \) (q, \( J = 11.1 \) Hz), 129.9, 129.4, 128.6, 127.9, 126.3 (d, \( J = 14.1 \) Hz), 125.2, 124.7, 124.3, 122.5, 92.8, 86.4, 84.8, 61.7, 58.5, 43.2, 21.6, 21.5, 13.4. \(^{19}\)F NMR (376MHz, CDCl\(_3\)) \( \delta -62.7 \) (s), –62.9 (s). IR (Neat) \( \nu_{\text{max}} \) 2915, 1726, 1616, 1495, 1320 cm\(^{-1}\). HRMS (ESI) for C\(_{39}\)H\(_{32}\)F\(_6\)IN\(_2\)O\(_6\)S\(_2\)Na (M+Na): calcd 929.0651, found 929.0650.

Ethyl 4-(benzo[d][1,3]dioxol-5-yl)-2-(N-(3-(benzo[d][1,3]dioxol-5-yl)prop-2-ynyl)-4-methyl-phenylsulfonamido)-5-iodo-1-tosyl-1,6-dihydropyridine-3-carboxylate (50f):

Following the general procedure (GP-2), reaction of ethyl 3,3-bis(N-(3-(benzo[d][1,3]dioxol-5-yl)prop-2-ynyl)-4-methylphenylsulfonamido)acrylate (44f; 151 mg, 0.2 mmol) under the optimized Ag-catalyzed conditions gave 50f (86 mg) in 49% yield as pale yellow oil. \( R_f = 0.50 \) (7:3 hexane/EtOAc); [Silica, UV and I\(_2\)]. \(^1\)H NMR (400 MHz, CDCl\(_3\)) \( \delta 7.91 \) (dd, \( J = 8.4, 3.6 \) Hz, 4H), 7.30 (d, \( J = 8.0 \) Hz, 2H), 7.15 (d, \( J = 8.0 \) Hz, 2H), 6.93 (dd, \( J = 8.0, 1.2 \) Hz, 1H), 6.81 (s, 1H), 6.76 (d, \( J = 8.0 \) Hz, 1H), 6.60 (d, \( J = 8.0 \) Hz, 1H), 6.13 (dd, \( J = 8.0, 1.2 \) Hz, 1H), 6.04 (s, 1H), 6.01 (s, 2H), 5.95 (s, 2H), 4.93 (s, 1H), 4.72 (s, 3H), 3.90 (q, \( J = 6.8 \) Hz, 2H), 2.42 (s, 3H), 2.35 (s, 3H), 0.95 (t, \( J = 8.0 \) Hz, 3H). \(^{13}\)C NMR (101 MHz, CDCl\(_3\)) \( \delta 163.4, 148.0, 147.3, 147.2, 146.9, 144.6, 144.1, 140.7, 136.6, 136.2, 135.8, 132.5, 129.9, 129.3, 128.6, 127.9, 126.7, 125.6, 122.3, 115.9, 112.0, 109.4, 108.3, 107.6, 101.3, 101.1, 92.4, 86.1, 82.1, 61.5, 58.4, 43.3, 21.6, 21.5, 13.6. IR (Neat) \( \nu_{\text{max}} \) 2915, 1726, 1616, 1495, 1320 cm\(^{-1}\). HRMS (ESI) for C\(_{39}\)H\(_{33}\)IN\(_2\)O\(_{10}\)S\(_2\)Na (M+Na): calcd 903.0519, found 903.0520.
Ethyl 4-(3,4-dimethylphenyl)-2-(N-(3,4-dimethylphenyl)prop-2-ynyl)-4-methylphenylsulfonamido)-5-iodo-1-tosyl-1,6-dihydropyridine-3-carboxylate (50g):

Following the general procedure (GP-2), reaction of ethyl 3,3-bis(N-(3,4-dimethylphenyl)prop-2-ynyl)-4-methylphenylsulfonamido)acrylate (44g; 145 mg, 0.2 mmol) under the optimized Ag-catalyzed conditions gave 50g (125 mg) in 74% yield as pale yellow oil. \( R_f = 0.60 \) (4:1 hexane/EtOAc); [Silica, UV and I\(_2\)]. \(^1\)H NMR (400 MHz, CDCl\(_3\)) \( \delta \) 7.91 (t, \( J = 8.4 \) Hz, 4H), 7.28 (d, \( J = 8.0 \) Hz, 2H), 7.14 (d, \( J = 8.0 \) Hz, 4H), 7.05 (d, \( J = 7.6 \) Hz, 1H), 6.90 (d, \( J = 7.6 \) Hz, 1H), 6.40 (d, \( J = 8.0 \) Hz, 1H), 6.38 (s, 1H), 4.92 (s, 1H), 4.74 (s, 3H), 3.85 (br s, 2H), 2.40 (s, 3H), 2.33 (s, 3H), 2.28 (s, 3H), 2.22 (s, 3H), 2.19 (s, 3H), 2.10 (s, 3H), 0.88 (d, \( J = 8.0 \) Hz, 3H).

\(^{13}\)C NMR (101 MHz, CDCl\(_3\)) \( \delta \) 163.5, 144.3, 144.0, 141.2, 137.3, 136.7, 136.4, 136.3, 135.7, 135.5, 133.0, 129.9, 129.6, 129.5, 129.3, 128.9, 128.6, 128.0, 126.1, 126.0, 120.0, 91.7, 86.4, 82.8, 61.4, 58.5, 43.4, 21.6, 19.8, 19.6, 13.4. IR (Neat) \( \nu \) \( \text{max} \) 2920, 1726, 1600, 1495, 1364, 1167 cm\(^{-1}\). HRMS (ESI) for C\(_{41}\)H\(_{42}\)F\(_2\)IN\(_2\)O\(_6\)S\(_2\) (M+H): calcd 849.1529, found 849.1529.

Benzyl 5-iodo-2-(4-methyl-N-(3-phenylprop-2-ynyl)phenylsulfonamido)-4-phenyl-1-tosyl-1,6-dihydropyridine-3-carboxylate (50h):

Following the general procedure (GP-2), reaction of benzyl 3,3-bis(4-methyl-N-(3-phenylprop-2-ynyl)phenylsulfonamido)acrylate (44h; 146 mg, 0.2 mmol) under the optimized Ag-catalyzed conditions gave 50h (114 mg) in 67% yield as pale yellow liquid. \( R_f = 0.48 \) (4:1 hexane/EtOAc); [Silica, UV and I\(_2\)]. \(^1\)H NMR (400 MHz, CDCl\(_3\)) \( \delta \) 7.90 (d, \( J = 8.0 \) Hz, 4H), 7.44–7.15 (m, 11H), 7.05 (d, \( J = 6.4 \) Hz, 4H), 6.94 (d, \( J = 7.2 \) Hz, 2H), 6.60 (d, \( J = 7.6 \) Hz, 2H), 4.93 (s, 1H), 4.76 (d, \( J = 8.0 \) Hz, 5H), 2.40 (s, 3H), 2.22 (s, 3H). \(^{13}\)C NMR (101 MHz, CDCl\(_3\)) \( \delta \) 163.3, 144.5, 144.0, 141.2, 137.3, 136.7, 136.4, 136.3, 135.7, 135.5, 133.0, 129.9, 129.6, 129.5, 128.7, 128.6, 128.0, 126.1, 126.0, 120.0, 91.7, 86.4, 83.7, 63.8, 58.5, 43.4, 21.6, 19.8, 19.6, 13.4. IR (Neat) \( \nu \) \( \text{max} \) 3063, 2920, 1726, 1594, 1495, 1364 cm\(^{-1}\). HRMS (ESI) for C\(_{42}\)H\(_{36}\)IN\(_2\)O\(_6\)S\(_2\) (M+H): calcd 855.1059, found 855.1056.

Methyl 5-iodo-2-(4-methyl-N-(3-phenylprop-2-ynyl)phenylsulfonamido)-4-phenyl-1-tosyl-1,6-dihydropyridine-3-carboxylate (50i):

Following the general procedure (GP-2), reaction of methyl 3,3-bis(4-methyl-N-(3-phenylprop-2-ynyl)phenylsulfonamido)acrylate (44i; 130 mg, 0.2 mmol) under the optimized Ag-catalyzed conditions gave 50i (107 mg) in 69% yield as pale yellow oil. \( R_f = 0.55 \) (7:3 hexane/EtOAc); [Silica, UV and I\(_2\)]. \(^1\)H NMR (400 MHz, CDCl\(_3\)) \( \delta \) 7.91 (t, \( J = 8.0 \) Hz, 4H), 7.41–7.21 (m, 8H), 7.15 (t, \( J = 7.6 \) Hz, 2H), 7.09 (d, \( J = 8.4 \) Hz, 2H), 6.63 (d, \( J = 7.6 \) Hz, 2H), 4.92 (s, 1H), 4.75 (s, 3H), 3.34 (s, 3H), 2.39 (s, 3H), 2.31 (s, 3H). \(^{13}\)C NMR (101 MHz, CDCl\(_3\)) \( \delta \) 163.8, 144.6, 144.2, 141.1, 138.9, 136.7, 136.1, 136.0, 133.0, 129.9, 129.6, 129.5, 129.3, 128.9, 128.6, 128.0, 126.1, 126.0, 120.0, 91.7, 86.4, 83.7, 67.3, 58.5, 43.3, 21.7, 21.5. IR (Neat) \( \nu \) \( \text{max} \) 3063, 2920, 1726, 1594, 1495, 1364 cm\(^{-1}\). HRMS (ESI) for C\(_{43}\)H\(_{38}\)IN\(_2\)O\(_6\)S\(_2\) (M+H): calcd 855.1059, found 855.1056.
1,2-Dihydropyridine

132.0, 129.9, 129.4, 128.7, 128.1, 127.7, 125.2, 122.6, 92.1, 86.3, 83.7, 58.4, 52.1, 43.1, 21.6, 21.5. IR (Neat) \( \nu_{\text{max}} \) 2947, 1731, 1594, 1364, 1167 cm\(^{-1}\). HRMS (ESI) for C\(_{36}\)H\(_{32}\)IN\(_2\)O\(_6\)S\(_2\) (M+H): calcd 779.0746, found 779.0740.

Benzyl 4-(4-bromophenyl)-2-(N-(3-(4-bromophenyl)prop-2-ynyl)methylsulfon-amido)-5-iodo-1-(methylsulfonyl)-1,6-dihydropyridine-3-carboxylate (50j):

Following the general procedure (GP-2), reaction of benzyl 3,3-bis(N-(3-(4-bromophenyl)prop-2-ynyl)methylsulfonamido)acrylate (44j; 146 mg, 0.2 mmol) under the optimized Ag-catalyzed conditions gave 50j (127 mg) in 74% yield as pale yellow oil. \( R_f = 0.59 \) (7:3 hexane/EtOAc); [Silica, UV and I\(_2\)]. \(^1\)H NMR (400 MHz, CDCl\(_3\)) \( \delta \) 7.45 (d, \( J = 8.4 \) Hz, 2H), 7.35–7.25 (m, 5H), 7.22 (d, \( J = 8.4 \) Hz, 2H), 6.97 (d, \( J = 8.4 \) Hz, 2H), 6.92 (d, \( J = 7.2 \) Hz, 2H), 4.86 (s, 2H), 4.70 (s, 4H), 3.24 (s, 3H), 3.14 (s, 3H). \(^{13}\)C NMR (101 MHz, CDCl\(_3\)) \( \delta \) 163.3, 141.0, 137.9, 137.7, 134.2, 133.2, 131.8, 131.4, 130.2, 128.9, 128.5, 128.4, 123.4, 122.6, 121.9, 120.8, 88.4, 85.3, 84.1, 67.5, 58.5, 42.5, 42.4, 41.6. IR (Neat) \( \nu_{\text{max}} \) 2931, 1715, 1485, 1358, 1150 cm\(^{-1}\). HRMS (ESI) for C\(_{30}\)H\(_{26}\)Br\(_2\)IN\(_2\)O\(_6\)S\(_2\) (M+H): calcd 858.8644, found 858.8640.
4.8. References


1,2-Dihydropyridine......


4.9. Spectra
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