Gold-Catalyzed Neighboring Carbonyl Group Assisted Regioselective Hydration of Propargyl Acetates: Access to $\alpha$–Acyloxy Methyl Ketones, $\alpha$–Acyloxy-$\alpha'$–Halo Ketones and Synthesis of Actinopolymorphol B

Abstract

A general atom-economic approach for the synthesis of $\alpha$–acyloxy methyl ketone and $\alpha$-acyloxy-$\alpha'$-halo ketones is demonstrated through regioselective hydration of a wide range of terminal-H and -halo substituted propargyl acetates. The catalyst comprising of Ph$_3$PAuCl and AgSbF$_6$ efficiently hydrolyzes the respective alkyne-moiety of propargyl acetates in the absence of acid promoters at an ambient temperature. The chloro, bromo and iodo groups at the terminal position of propargyl acetates did not affect the hydration. Compatibility of functional moieties and tolerance of various acid-labile protecting groups to the catalytic conditions are observed. The catalytic condition is also suitable to perform hydration of TMS-substituted propargyl acetates, even though it requires prolonged reaction time for completion. Chirality of the propargylic acetate is retained during the hydration. The robustness of the system is successfully demonstrated through gram scale preparation of the product. The common $\alpha$–acyloxy methyl ketone is transformed to 1,2–diol and 1,2–amino alcohol derivatives. Synthesis of actinopolymorphol B is achieved for the first time involving hydration of the propargyl acetate as the key step. Synthetically useful 2-amino thiazole derivatives are successfully prepared from $\alpha$-acyloxy-$\alpha'$-bromo ketones and thiourea. The regioselective hydration is facilitated by the neighboring carbonyl group as demonstrated through $^{18}$O-labeling study.
Reference:


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Regioselective Hydration of Terminal Halo-Substituted Propargyl Carboxylate by Gold Catalyst: Synthesis of α-Acyloxy-α’-Halo Ketones

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2.1. Introduction

Addition of oxygen nucleophiles to alkynes 1 allows generating C–O bond as enol-ethers (3, Scheme 2.1); the tautomerization of enol-ethers finally lead to carbonyl derivatives 4 (Scheme 2.1). Therefore, alkynes are considered pro-carbonyls. The carbonyl group is one of the most important and versatile building blocks broadly useful in organic synthesis. As a consequence a single step synthesis of carbonyl functionality is always desirable. Among various methods known for the preparation of carbonyl-moiety, the metal-catalyzed addition of water to readily accessible alkyne is considered straightforward and environmentally-benign (Scheme 2.1).

Scheme 2.1: Metal assisted addition of oxygn-nucleophile to alkynes

2.2. Precedents

In principle, the electron-rich alkynes can be readily activated by various transition metals and Brønsted acids. Conventionally, the alkynes underwent hydration with toxic Hg(II) salts in the presence of Brønsted or Lewis acids. Other metal salts Pt, Ru, Au, Ir, Co, Os, Ag, Fe and Rh were successfully used for the hydration of alkynes. Under the harsh reaction conditions, hydration of alkynes were also possible in the absence of transition-metal catalysts.

2.2.1. Addition of Oxygen Containing Nucleophile to Alkynes

The addition of water to alkynes 5 successfully occurs with the aide of mercury salt in the presence of H$_2$SO$_4$ or BF$_3$-OEt$_2$ (Scheme 2.2). The use of toxic mercury-salt hinders the synthetic-utility of this process and is not environmentally-benign.

Scheme 2.2: Mercury-salt-catalyzed addition of water to terminal alkynes
Regioselective Hydration......

The Wakatsuki group reported the ruthenium-catalyzed anti-Markovnikov hydration of terminal alkyne 5 in 1998. Later Grotjahn and Hintermann groups showed the preparation of aldehyde 7 involving Ru-catalyzed hydration of terminal alkynes.\(^4\) The reaction proceeds with the formation of ruthenium-vinylidene intermediate 8 (Scheme 2.3).

\[
\begin{array}{c}
\text{R} \equiv \equiv \xrightarrow{[\text{Ru}](2.0 \text{ mol} \%) \quad \text{H}_2\text{O} (5.0 \text{ equiv})} \quad \text{acetone, 50-60 °C} \quad \text{R} \equiv \equiv \equiv \text{H}
\end{array}
\]

*Scheme 2.3: Anti-Markovnikov addition of water to terminal alkynes*

The Utimoto group described the palladium catalyzed regioselective hydration of alkynes 9 in neutral conditions; the reaction was performed under the ultrasonic irradiation (Scheme 2.4). The reaction begins with the intramolecular attack of the crobonyl-oxygen to the Pd-activated alkyne forming the cyclic intermediate 10.\(^5\) Finally, attack of H\(_2\)O to 10 delivers the 1,4-diketones 11 (Scheme 2.4).

\[
\begin{array}{c}
\text{R}^1\equiv\equiv\equiv\text{R}^2 \xrightarrow{\text{PdCl}_2(\text{MeCN})_2} \quad \text{CH}_3\text{CN/H}_2\text{O (10:1)} \quad \text{ultrasonic wave, rt} \quad \text{H}_2\text{O} \quad \text{R}^1\equiv\equiv\equiv\text{R}^2
\end{array}
\]

*Scheme 2.4: Palladium catalyzed regioselective hydration of alkynes*

The hydration of substituted alkynes 1 smoothly occurs under the influence of platinum catalyst. Zeise’s dimer [PtCl\(_2\)(C\(_2\)H\(_4\)\(_2\))] and PtCl\(_4\)-CO are generally used in these transformations (Scheme 2.5). The requirement of high catalyst loading, high temperature and the formation of non-regioselective mixture of products 4 and 12 are the major concerns.\(^6\)

\[
\begin{array}{c}
\text{R}^2\equiv\equiv\equiv\text{R}^1 \xrightarrow{\text{Zeise's dimer or PtCl}_4\text{-CO}} \quad \text{H}_2\text{O} \quad \text{THF, reflux} \quad \text{R}^2\equiv\equiv\equiv\text{R}^1 + \quad \text{R}^1\equiv\equiv\equiv\text{R}^2
\end{array}
\]

*Scheme 2.5: Platinum-catalyzed addition of water to alkyne*

The combination of iridium complex with phosphate ligand and Lewis acid in wet alcoholic solvent is successfully employed for the hydration of alkynes 5 (Scheme 2.6).\(^7\)

\[
\begin{array}{c}
\text{R} \equiv \equiv \ast \quad \text{nBuOH} \ast \quad \text{H}_2\text{O} \quad \xrightarrow{[\text{Ir(cod)}]_2\text{BF}_4^-\text{(0.01 mmol)} \quad \text{P(OPr)}_3} \quad \text{ZrCl}_4, 70 ^\circ \text{C} \quad \text{R} \equiv \equiv \equiv \text{CH}_3
\end{array}
\]

*Scheme 2.6: Iridium-complex catalyzed addition of water to alkyne*
Regioselective Hydration......

The reaction of alkyne, formic acid and methanesulfonic acid at 105 °C allows the attack of formic acid to unactivated alkynes 13, leading to carbonyl derivatives 15 in good yields (Scheme 2.7). The formic acid oxygen is useful for the formation of C–O double bond.8

![Scheme 2.7: Formic acid is useful as an oxygen source](image)

Interestingly, the alkyne 16 was readily hydrated in the presence of PTSA when the reaction conducted under the microwave irradiation at an elevated temperature (Scheme 2.8).9

![Scheme 2.8: PTSA-catalyzed synthesis of ketones from alkynes](image)

A large variety of interesting and complicated organic transformations have recently been accomplished with the aide of the gold-catalysts. Gold is soft and carbophilic Lewis acid, activates carbon-carbon π-bonds, and allows the formation of C–C, C–O, C–N, and C–S bonds by the attack of nucleophile to the activated multiple bonds (Scheme 2.9).10

![Scheme 2.9: Schematic representation of activation of alkyne by gold and addition of nucleophile to activated alkynes](image)

Hydration of unactivated alkyne by gold-catalyst has been reported by Utimoto group in 1991. Refluxing alkyne 1 with methanol in the presence of NaAuCl₄ produces the carbonyl derivatives 4 and 12 (eq 1, Scheme 2.10). The formation of poor-regioselective hydration products and the requirement of high temperature are the major drawbacks. Interestingly, the same group demonstrated an efficient method for the synthesis of α,β-unsaturated ketones 23 through regioselective hydration of methyl propargyl ether 21 under reflux conditions (eq 2, Scheme 2.10).11
Regioselective Hydration......

Scheme 2.10: Gold(III)-catalyzed addition of water to unactivated alkynes

The Teles group reported addition of alcohols to alkynes 24 by cationic gold(I) complex. The use of additives Lewis or Brønsted acid with cationic gold allows the effective addition of alcohol to alkyne, delivering the desired addition product 25 in good yields (Scheme 2.11).¹²

Scheme 2.11: Addition of alcohols to alkynes by cationic gold(I) complex

The Hayashi and Tanaka groups reported gold(I)-catalyzed hydration of alkynes 1 in the presence of catalytic amount of H₂SO₄ at 70 °C. The reaction conducted at an elevated temperature in the presence of Brønsted acid with the delivery of poor regioselective products 4 and 12; this in turn narrows down the broad synthetic utility of the method (Scheme 2.12).¹³

Scheme 2.12: Gold(I)/Brønsted acid-catalyzed hydration of alkyne

The Leyva and Corma group have independently shown the gold(I)-catalyzed hydration of wide range of alkynes 1 in the absence of acid promoter at room temperature. Unfortunately, the optimized conditions did not tolerate the acid labile oxygen-bearing functional groups and the products 4 and 12 are obtained with poor regioselectivity from the hydration of unsymmetrical alkynes. In addition, the reaction takes longer time for completion (Scheme 2.13).¹⁴
Regioselective Hydration......

\[
R^1\equiv R^2 \xrightarrow{\text{R}_3\text{PAuNTf}_2 (0.0-5 \text{ mol } \%)} \xrightarrow{\text{MeOH, H}_2\text{O, rt}} R^1\text{C}=\text{O} + R^2\text{C}=\text{O}
\]

\(1\) \(R^1\) and \(R^2\) = alkyl and aryl

\(4\) and \(12\) poor regioselectivity

Scheme 2.13: Room temperature hydration of alkyne by gold(I) catalyst

In 2009, Nolan group showed an acid free hydration of alkyne \(1\) by \([\text{IPr} \text{AuCl/AgSbF}_6]\) catalyst. It is noteworthy to mention that the reaction is highly efficient producing satisfactory yield of keto derivatives \(4\) and \(12\) under the loading of ppm level of catalyst. Moreover, full conversion of alkynes to ketone is possible when the reaction conducted at 120 °C (Scheme 2.14).\(^{15}\)

\[
\begin{align*}
R^1\equiv R^2 & \xrightarrow{[\text{IPrAuCl/AgSbF}_6]} \xrightarrow{\text{1,4-dioxane/H}_2\text{O (2:1)}} 120 ^\circ\text{C} \rightarrow R^1\text{C}=\text{O} + R^1\text{C}=\text{O} \\
\text{IPr} = \text{[1]} & \quad \text{[2]} \\
\end{align*}
\]

Scheme 2.14: \([\text{IPrAuCl/AgSbF}_6]\)-Catalyzed acid free hydration of alkyne

Various \(\alpha\)-acyloxy-\(\alpha\)-silyl ketones \(27\) and \(28\) have been synthesized from the hydration of \(\alpha\)-acyloxy-\(\alpha\)-alkynylsilanes \(26\) under Au(I) catalyst. Unfortunately, this reaction has limited substrate scope, posing concerns to broad synthetic applications (Scheme 2.15).\(^{16}\)

\[
\begin{align*}
\text{TBDMS} & \equiv \xrightarrow{\text{Ph}_3\text{PAuOTf (3.0 mol \%)}} \xrightarrow{\text{1,4-dioxane/H}_2\text{O (1 equiv)}} \text{TBDMS} \text{C}=\text{O} + \text{TBDMS} \text{C}=\text{O} \\
\text{When } R = \text{Me} & \quad \text{When } R = \text{H and EWG} \\
26 & \quad 27 \quad 28
\end{align*}
\]

Scheme 2.15: Synthesis of \(\alpha\)-acyloxy-\(\alpha\)-silyl ketones from \(\alpha\)-acyloxy-\(\alpha\)-alkynylsilanes.

The carbonyl group-assisted regioselective hydration of 3-alkynoates \(29\) under the Au catalyst efficiently delivered \(\gamma\)-keto ester \(32\) (Scheme 2.16). The nucleophilic attack of carbonyl group to the Au-activated triple bond in \(30\) forms the cyclic vinyl gold intermediate \(31\). The attack of water to \(31\) followed by ring opening produces \(32\).\(^{17}\)
Regioselective Hydration......

Scheme 2.16: Neighboring carbonyl group-assisted regioselective hydration of 3-alkynoates

Hammond group reported the synthesis of α-aryl-substituted α-fluoroketones 37 through hydrative cross-coupling of internal alkyne 13 under mild reaction conditions (Scheme 2.17). The reaction of unactivated internal alkynes 13 with aryl boronic acid and selectfluor 38 in the presence of Ph₃PAuCl in CH₃CN/H₂O gave 37. The reaction initiates with the attack of water to the activated gold-alkyne complex 33 forming the intermediate 34. The transmetallation between 34 and aryl boronic acid provides 35. The attack of enolate to selectfluor affords 36 in situ; finally reductive elimination of 36 delivers 37 (Scheme 2.17).

Scheme 2.17: Synthesis of α-aryl-substituted α-fluor ketones via hydrative cross-coupling of internal unactivated alkynes.

Recently, a novel method for the synthesis of cyclopentenones through Au-catalyzed rearrangement of 1,1-diethynylcarboxylate 39 is disclosed from Oh group (Scheme 2.18). The reaction proceeds with the 1,3-acetate migration in 39 to provide allene intermediate 40. The second acetate rearrangement of 40, water attack and cyclization of intermediate 41 finally delivers substituted cyclopentenone 42 (Scheme 2.18).
Regioselective Hydration......

Scheme 2.18: Gold(l)-catalyzed hydrative rearrangement of 1,1-diethylcarbinol acetates to cyclopentenones

2.3. Motivation and Design Plan

Survey of this hydration of alkynes reveals that the reactions invariably require mineral acid as promoters, higher temperature or both. As these harsh conditions are detrimental to the survival of acid-labile protecting groups, the utility of these catalytic systems in the synthesis of complex molecules would be limited. This scenario is therefore prompted us envisaging an alternate strategy for the efficient hydration of alkynes keeping in view of the following significant aspects: 1) use of commercially available and air stable gold catalysts, 2) elimination of acid-promoters, 3) ambient temperature reaction, 4) tolerance of acid-labile protecting units with broad functional group compatibility, 5) short reaction time leading to overall efficiency, 6) incorporation of multi-reactive functionalities in the products, and 7) development of precursors for the synthesis of complex molecules.

2.3.1 Reactivity of Propargyl Acetate via Neighboring Carbonyl Group Participation

The mode of rearrangement of neighboring carboxylate moiety directs the propargyl carboxylates to undergo various rearrangements under the influence of gold catalysts. On the basis of steric and electronic effects of substituents at either end of propargyl moiety, the activation of propargyl carboxylates 43 by gold complexes lead to 1,2- and/or 1,3-acyloxy migration of acetate moiety. For instance: the terminal propargyl carboxylates forms a five-membered cyclic intermediate 44 by 5-exo-dig mode of cyclization of carboxylate group to gold activated alkyne; further rearrangement of the cyclic intermediate 44 gives the gold-carbene species 45 involving 1,2-acyl shift (path a, Scheme 2.19).20 The highly reactive gold-carbene species is amenable to various transformations.20 While the internal propargylic carboxylates would form six-membered cyclic intermediate 46 via 6-endo-dig attack of carboxylate group to gold-activated alkyne species (path b, Scheme 2.19). The cyclic intermediate 46 would rearrange to reactive allenoate species 47. The electron-rich allenoates 47 participate to various transformations leading to complex molecule synthesis.21
Regioselective Hydration......

Scheme 2.19: The mode of rearrangements of propargyl acetates by gold catalyst

Taking the advantage of selective rearrangement of the propargyl carboxylate, we thought to carry out regioselective hydration of unactivated alkyne-moiety in the propargyl acetate. We envisioned that a neighboring carbonyl group such as acetate would assist in effective and regioselective alkyne hydration under the gold-catalysts. Activation of the terminal alkyne of the propargyl acetate by gold-catalyst would preferentially generate 5-membered electrophilic vinyl-gold species 44 involving 5-exo-dig\textsuperscript{20} attack of the carbonyl oxygen. The attack of water to 44 followed by rearrangement and proto-deauration of 48 would finally provide the regioselective hydration product α−acyloxy methyl ketone 49 (Scheme 2.20). This method would therefore create a carbonyl group adjacent to the acetate moiety; both functionalities would be available for further synthetic explorations.

Scheme 2.20: Synthetic plan for regioselective hydration of propargyl carboxylate

In this chapter an operationally simple strategies for the synthesis of a wide range of α-acyloxy methyl ketones and α-acyloxy-α'-halo ketones through regioselective hydration of propargyl acetates using commercially available Ph\textsubscript{3}PAuCl and AgSbF\textsubscript{6} at an ambient temperature is discussed in detail. Furthermore, this transformation is successfully employed accomplishing the first total synthesis of actinopolymorphol B.
2.4. Results and Discussion

2.4.1. Reaction Optimization

We first investigated the hydration of 1-phenylprop-2-ynyl acetate (50a). Precursor 50a was prepared in a straightforward three-step synthetic protocol, reacting trimethylsilyl acetylide with benzaldehyde followed by desilylation and acetylation of the –OH group, in

Table 2.1: Synthesis of compounds 50s

\[
\begin{array}{c}
\text{R} \to \text{OH} \to \text{OH} \to \text{Ac} \\
50^* \to \text{THF, } -70^\circ \text{C} \to \text{K}_2\text{CO}_3 \to \text{Ac}_2\text{O} \\
\text{rt, 30 min} \to \text{MeOH, rt, 12 h} \to \text{Et}_3\text{N, DMAP} \to \text{CH}_2\text{Cl}_2, \text{rt, 1 h}
\end{array}
\]
overall 52% yield; the isolation of respective intermediates is avoided. Following this procedure, other key synthetic precursors 50 are prepared in gram quantities with appreciable yields shown in Table 2.1.

The hydration of 50a under different catalytic conditions comprising of gold catalysts with silver salts, water amounts, and solvents was explored at first. Table 2.2 summarizes the results of optimization studies. Solvent dioxane and water (3.0 equivalents) are employed in this optimization studies.16 Trace amount of the desired hydration product α−acyloxy methyl ketone (51a) was noticed when a mixture of AuCl₃ and AgOAc was used (entry 1). Interestingly, AgSbF₆ salt in conjunction with AuCl₃ enhanced the product yield to 60% by NMR (entry 2). Other silver salts, such as AgOTf, AgBF₄ and AgNO₃ in combination with AuCl₃ found ineffective (entries 3–5). It appears that the weekly-coordinating SbF₆⁻ counteranion generates the active gold-cationic species with ease and activates the alkyne efficiently. Therefore, exploration of various combinations of gold catalysts with AgSbF₆ were surveyed; AuBr₃, AuCl were not effective (entries 6 and 7), whereas Ph₃PAuCl was found to be the best (entry 8). With selective catalysts [Ph₃PAuCl (5.0 mol %) and AgSbF₆ (5.0 mol %)] in hand, the amount of water required in this hydration reaction was then pursued. Use of more or less amount of water (5.0 and 2.0 equivalents) did not affect the product yield even though slightly longer reaction time was required for completion (entries 9 and 10); whereas, three equivalents of water appeared adequate and furnished the desired product in 97% isolated yield within 3 h (entry 8). We next evaluate the amount of catalyst needed to this reaction. Lower amount of the catalysts loading from 5.0 mol % to 1.0 mol % of Ph₃PAuCl and AgSbF₆ did not affect the reaction efficiency (entry 11) and the hydration product 51a was exclusively isolated in 97% yield. Extended reaction time (~3 days) was necessary to obtain satisfactory yield of 51a when Ph₃PAuCl (0.1 mol %) and AgSbF₆ (0.1 mol %) were used (entry 12). Even though the combination of Ph₃PAuCl with AgOTf or AgBF₄ provided the desired hydration product in good yield (by ¹H NMR), the reaction required ~24 h for completion (entries 13 and 14). Mixture of Ph₃PAuCl with AgOOCCF₃ appeared ineffective (entry 15); AgOAc and AgNO₃ were poor (entries 16 and 17). Absence of either Ph₃PAuCl or AgSbF₆ did not produce 51a (entries 18 and 19). Exploration of other solvents such as CH₂Cl₂ and MeOH resulted lower amounts of 51a (entries 20 and 21), whereas DMF and DMSO completely failed the reaction (entry 22). Dioxane appears effective among other solvents screened. The interesting disclosure from Nolan group describes the synthesis of α,β-unsaturated aldehyde through regioselective hydration of propargyl acetate 50a with [(NHC)AuCl],
Regioselective Hydration......

AgSbF₆ in THF–H₂O at 60 °C. In contrast, alkyne hydration of 50a under our optimized condition exclusively delivers α-acyloxy methyl ketone 51a. Not even a trace of α,β-unsaturated aldehyde product was detected by the ¹H NMR spectrum of the crude reaction mixture. These results show that hydration of 1-phenylprop-2-ynyl acetate (50a) under different reaction conditions provides two distinct products.

**Table 2.2: Optimization of reaction conditions**

<table>
<thead>
<tr>
<th>Entry</th>
<th>Catalyst (mol %)</th>
<th>Co-catalyst (mol %)</th>
<th>Solvent (0.5 mL)</th>
<th>Water (equiv)</th>
<th>Time (h)</th>
<th>Yields (%)</th>
</tr>
</thead>
<tbody>
<tr>
<td>1</td>
<td>5% AuCl₂</td>
<td>5% AgOAc</td>
<td>dioxane</td>
<td>3</td>
<td>36</td>
<td>&lt;5ᵇ</td>
</tr>
<tr>
<td>2</td>
<td>5% AuCl₂</td>
<td>5% AgSbF₆</td>
<td>dioxane</td>
<td>3</td>
<td>36</td>
<td>60ᵇ</td>
</tr>
<tr>
<td>3</td>
<td>5% AuCl₂</td>
<td>5% AgOTf</td>
<td>dioxane</td>
<td>3</td>
<td>36</td>
<td>35ᵇ</td>
</tr>
<tr>
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<td>5% AuCl₂</td>
<td>5% AgBF₄</td>
<td>dioxane</td>
<td>3</td>
<td>36</td>
<td>27ᵇ</td>
</tr>
<tr>
<td>5</td>
<td>5% AuCl₂</td>
<td>5% AgNO₃</td>
<td>dioxane</td>
<td>3</td>
<td>36</td>
<td>13ᵇ</td>
</tr>
<tr>
<td>6</td>
<td>5% AuBr₃</td>
<td>5% AgSbF₆</td>
<td>dioxane</td>
<td>3</td>
<td>36</td>
<td>30ᵇ</td>
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<tr>
<td>7</td>
<td>5% AuCl</td>
<td>5% AgSbF₆</td>
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<td>36</td>
<td>10ᵇ</td>
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<td>5% AgSbF₆</td>
<td>dioxane</td>
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<td>7</td>
<td>92ᶜ</td>
</tr>
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<td>1% Ph₃PAuCl</td>
<td>1% AgSbF₆</td>
<td>dioxane</td>
<td>3</td>
<td>8</td>
<td>97ᶜ</td>
</tr>
<tr>
<td>12</td>
<td>0.1% Ph₃PAuCl</td>
<td>0.1% AgSbF₆</td>
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<td>3</td>
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<td>13</td>
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<td>2% AgOTf</td>
<td>dioxane</td>
<td>3</td>
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<td>90ᵇ</td>
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<tr>
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<td>2% AgBF₄</td>
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</tr>
<tr>
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<td>2% Ph₃PAuCl</td>
<td>2% AgOOCCF₃</td>
<td>dioxane</td>
<td>3</td>
<td>36</td>
<td>15ᵇ</td>
</tr>
<tr>
<td>16</td>
<td>2% Ph₃PAuCl</td>
<td>2% AgOAc</td>
<td>dioxane</td>
<td>3</td>
<td>36</td>
<td>traceᵇ</td>
</tr>
<tr>
<td>17</td>
<td>2% Ph₃PAuCl</td>
<td>2% AgNO₃</td>
<td>dioxane</td>
<td>3</td>
<td>36</td>
<td>traceᵇ</td>
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<td>5% Ph₃PAuCl</td>
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<td>dioxane</td>
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<td>NR</td>
</tr>
<tr>
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<td>Nil</td>
<td>5% AgSbF₆</td>
<td>dioxane</td>
<td>3</td>
<td>36</td>
<td>NR</td>
</tr>
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<td>1% AgSbF₆</td>
<td>CH₂Cl₂</td>
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<td>24</td>
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<tr>
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<td>1% Ph₃PAuCl</td>
<td>1% AgSbF₆</td>
<td>MeOH</td>
<td>3</td>
<td>36</td>
<td>37ᵇ</td>
</tr>
<tr>
<td>22</td>
<td>1% Ph₃PAuCl</td>
<td>1% AgSbF₆</td>
<td>DMF or DMSO</td>
<td>3</td>
<td>36</td>
<td>NR</td>
</tr>
</tbody>
</table>

ᵃReactions were carried out using 50a (0.3 mmol) in solvent (0.5 mL) at rt.ᵇ¹H NMR yields.ᶜIsolated yields. NR = no reaction

2.4.2. Effect of Different Directing Groups

Optimization studies reveal that hydration of 50a effectively proceeds at ambient temperature. Presumably, the acetyl group in 50a plays crucial role in this hydration reaction. The effect of other directing group on the O-atom in propargyl alcohol was then
surveyed (Table 2.3). As shown in entry 1, terminal alkyne did not undergo hydration in the absence of directing group under the optimized catalytic condition [Ph₃PAuCl (1.0 mol %), AgSbF₆ (1.0 mol %), water (3.0 equiv) in 1,4-dioxane]. Pivoly and benzoyl protected propargylic esters (52b and 52c) furnished the corresponding products 53b and 53c, respectively in moderate yields (entries 2 and 3). We assume that the bulky group on the O-protecting moieties hinders the attack of H₂O to the reactive intermediate participated in the reaction. Protecting groups such as Boc, Cbz and Ts on the –OH failed to provide the corresponding hydration products (entries 5–7) even with prolonged reaction time. Fortunately, the catalytic conditions did not cleave these O-protecting moieties. Survival of O-Boc protecting group demonstrates the mild nature of the reaction condition. The

Table 2.3: Screening of different directing groups

<table>
<thead>
<tr>
<th>Entry</th>
<th>52/50a</th>
<th>R</th>
<th>Time (h)</th>
<th>53/51a</th>
<th>Yield (%)</th>
</tr>
</thead>
<tbody>
<tr>
<td>1</td>
<td>52a</td>
<td>H</td>
<td>24</td>
<td>53a</td>
<td>NR</td>
</tr>
<tr>
<td>2</td>
<td>52b</td>
<td>pivaloyl</td>
<td>10</td>
<td>53b</td>
<td>70ᵇ</td>
</tr>
<tr>
<td>3</td>
<td>52c</td>
<td>benzoyl</td>
<td>8</td>
<td>53c</td>
<td>78ᵇ</td>
</tr>
<tr>
<td>4</td>
<td>50a</td>
<td>acetyl</td>
<td>8</td>
<td>51a</td>
<td>97ᵇ</td>
</tr>
<tr>
<td>5</td>
<td>52d</td>
<td>Boc</td>
<td>24</td>
<td>53d</td>
<td>NR</td>
</tr>
<tr>
<td>6</td>
<td>52e</td>
<td>Cbz</td>
<td>24</td>
<td>53e</td>
<td>NR</td>
</tr>
<tr>
<td>7</td>
<td>52f</td>
<td>tosyl</td>
<td>10</td>
<td>53f</td>
<td>NR</td>
</tr>
<tr>
<td>8</td>
<td>52g</td>
<td>MOM</td>
<td>8</td>
<td>53g</td>
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</tr>
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<td>9</td>
<td>52h</td>
<td>Me</td>
<td>24</td>
<td>53h</td>
<td>NR</td>
</tr>
<tr>
<td>10</td>
<td>52i</td>
<td>SiMe₃</td>
<td>24</td>
<td>53i</td>
<td>NR</td>
</tr>
</tbody>
</table>

*Reactions were carried out using 52 (1.0 mmol), Ph₃PAuCl (1.0 mol %), AgSbF₆ (1.0 mol %), water (3.0 mmol) in 1,4-dioxane (1.5 mL) at room temperature. †Isolated yield. ‡Cleavage of O–TMS protecting group was observed. NR = no reaction.

MOM and methyl protected propargyl ethers are inert to the present catalytic system; formation of keto-compounds through alkyne hydration turned out futile (entries 8 and 9). However, this catalytic system cleaved the O–TMS protecting group of 52i and afforded 52a instead of the desired hydration product 53i (entry 10).

2.4.3. Reaction Scope

The optimal reaction condition [Ph₃PAuCl (1.0 mol %), AgSbF₆ (1.0 mol %), water (3.0
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equiv) in 1,4-dioxane] is surveyed to investigate the generality of the hydration of the terminal alkyne of propargyl acetates at an ambient temperature. The effect of electronic groups on the aryl moiety of 1-phenylprop-2-ynyl acetate (50a) to the hydration reaction explored at first (Table 2.4). As observed in the optimization reaction, the electronically neutral species reacted efficiently to provide the hydrated product 51a in 97% isolated yield. The electron-withdrawing groups on the aryl moiety did not affect the product yields (51b–d); halo groups are inert to the reaction conditions. Reaction proceeded effectively in the presence of two chloro groups on the aromatic ring (51e). These halo groups are the useful entities amenable to further manipulations by the transition-metal catalyzed cross-coupling strategies. Generally, formyl group actively participated in the gold–catalyzed transformations. Under this catalytic condition, formyl functionality was well-tolerated and the desired product 51f was obtained in 88% yield. Methyl, methoxy and phenoxy groups at the 4- and/or 3-positions on electron-rich aromatic ring gave the desired products in excellent yields (51g–i). Presence of free –OH group on aromatic ring did not affect the alkyne hydration (50j). Functional group manipulations are the tools used to the fabrication of complex molecular framework. It is therefore important to

### Table 2.4: Effect of electronic substitution on aryl derivatives at propargyl position \(^{a,b}\)

<table>
<thead>
<tr>
<th>R¹</th>
<th>Reaction Conditions</th>
<th>1,4-dioxane</th>
<th>Ph₃PAuCl (1.0 mol %)</th>
<th>AgSbF₆ (1.0 mol %)</th>
<th>H₂O, rt</th>
<th>Isolated Yield</th>
<th>Time</th>
</tr>
</thead>
<tbody>
<tr>
<td></td>
<td>50</td>
<td>51a, 97%, 5 h</td>
<td>51b, 92%, 5 h</td>
<td>51c, 94%, 5 h</td>
<td>51d, 89%, 4 h</td>
<td>51e, 96%, 3 h</td>
<td></td>
</tr>
<tr>
<td>F</td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Cl</td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Br</td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>HO</td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>MeO</td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>PhO</td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
</tbody>
</table>

\(^{a}\)Reactions were carried out using 50 (1.0 mmol), Ph₃PAuCl (1.0 mol %), AgSbF₆ (1.0 mol %), water (3.0 mmol) in 1,4-dioxane (1.5 mL) at room temperature. \(^{b}\)Isolated yields.
examine the relative stability of the protecting groups under this catalytic condition. Protecting groups of hydroxyl moiety are generally sensitive to the mild acidic and basic reagents. Thus, investigation of the acid labile silyl ethers to the optimized catalytic condition pursued. As observed previously, the reaction condition cleaved the mildest –OTMS group (Table 2.3, entry 10). Gratifyingly, the bulkier silyl protecting groups such as –OTPS (t-butyldiphenylsilyl) and –OTBS (t-butyldimethylsilyl) survived and the desired keto compounds 51k and 51l were isolated in 81% and 80% yields, respectively. In contrast, gold catalyst (AuSPhosNTf$_2$) used in the hydration of triple bond showed partial stability to the robust OTPS group, reported by Leyva and Corma (Scheme 2.13).

It appears that the present catalytic condition is relatively milder than the previously reported system. Furthermore, the electron-rich substrate 1-(benzo[d][1,3]dioxol-5-yl)prop-2-ynyl acetate 50m undergoes hydration efficiently within 2 h to afford 51m in 91% yield.

The effect of ortho-substitution on aryl moiety was next examined, and the results are shown in Table 2.5. Hydration of terminal triple bond proceeded smoothly in the presence of one or two electron−poor o-substituent, such as chloro and bromo groups, on aromatic ring of propargyl acetates (50n−q) producing the corresponding ketones (51n−q) in excellent yields. Similarly, 1-(naphthalen-1-yl)prop-2-ynyl acetate (50r) underwent hydration efficiently, affording 95% yield of 51r. The bulky methyl group at the 2-position did not inhibit hydration and delivered 51s in 92% yield. Gratifyingly, the ortho−O−allyl group did not participate in the hydration and the desired product 51t was isolated in 96% yield; the allyl functionality could be useful for further synthetic elaboration. The required ketone 51u was successfully obtained from the anthracene based propargyl acetate. More sterically demanding substrates having two ortho-substitutions on aryl moiety underwent efficient hydration under the optimized condition and the desired products 51v and 51w are obtained in excellent yields. X-Ray crystallographic analysis unambiguously elucidated the structure of 51w (Figure 2.1). Our experimental results reveal that electronic and steric effect on the aromatic ring did not impart pronounced effect to alkyne hydrations. Next, the effect of heteroaryls in the hydration of terminal alkynes of propargyl acetate was investigated. Intramolecular co-ordination of heteroatom to the gold-alkyne-activated species is a well known phenomenon. Therefore, we speculate that the heteroaryls in the propargyl acetate may hinder the hydration of triple bond. To probe our assumption, hydration of thienyl-2-substituted propargyl acetate 50x was performed under the optimized condition; interestingly the corresponding hydration
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Product 51x resulted in 75% yield in 2 h. Unfortunately, furyl-2-substituted propargyl acetate failed to provide the desired ketone; complex reaction profile was observed with the consumption of starting propargyl acetate. In case of N-methyl indole derivative, hydration reaction did not proceed; whereas, N-benzyol protected indole-2-substituted propargyl acetate (50y) provided the corresponding hydration product 51y in 78% yield. We believe that the lone pair electron on nitrogen in N-methyl indole inhibits the activity of the cationic gold species through coordination; in contrast, the stabilization of the lone pair electron on nitrogen in 51y led to the hydration product.

Table 2.5: Effect of ortho-substitued aryl groups and heteroaryls at propargyl position

<table>
<thead>
<tr>
<th>Ar</th>
<th>Product</th>
<th>Yield</th>
<th>Time</th>
</tr>
</thead>
<tbody>
<tr>
<td>ClOAcMe</td>
<td>51n, 93%, 4 h</td>
<td></td>
<td></td>
</tr>
<tr>
<td>BrOAcMe</td>
<td>51o, 87%, 6 h</td>
<td></td>
<td></td>
</tr>
<tr>
<td>ClOAcMe</td>
<td>51p, 94%, 3 h</td>
<td></td>
<td></td>
</tr>
<tr>
<td>ClOAcMe</td>
<td>51q, 94%, 3 h</td>
<td></td>
<td></td>
</tr>
<tr>
<td>AcOClOAcMe</td>
<td>51r, 95%, 3 h</td>
<td></td>
<td></td>
</tr>
<tr>
<td>MeOAcMe</td>
<td>51s, 92%, 2 h</td>
<td></td>
<td></td>
</tr>
<tr>
<td>OAcMe</td>
<td>51t, 96%, 2 h</td>
<td></td>
<td></td>
</tr>
<tr>
<td>ClOAcMe</td>
<td>51u, 85%, 4 h</td>
<td></td>
<td></td>
</tr>
<tr>
<td>ClOAcMe</td>
<td>51v, 91%, 3 h</td>
<td></td>
<td></td>
</tr>
<tr>
<td>ClOAcMe</td>
<td>51w, 93%, 2 h</td>
<td></td>
<td></td>
</tr>
<tr>
<td>ClOAcMe</td>
<td>51x, 75%, 2 h</td>
<td></td>
<td></td>
</tr>
<tr>
<td>ClOAcMe</td>
<td>51y, 78%, 3 h</td>
<td></td>
<td></td>
</tr>
</tbody>
</table>

*Reactions were carried out using 50 (1.0 mmol), Ph₃PAuCl (1.0 mol %), AgSbF₆ (1.0 mol %), water (3.0 mmol) in 1,4-dioxane (1.5 mL) at room temperature. b* Isolated yields.

Figure 2.1: ORTEP diagrams of 51w
Formation of α-acyloxy methyl ketones through regioselective hydration of terminal alkynes of the aryl and heteroaryl substituted propargyl acetates has successfully been demonstrated (Table 2.5). Next, we turned our attention to assess the steric effect in the alkyne hydration. The effects of substitution at the α-position to the propargyl acetates are examined and the results are detailed in Table 2.6. When n-hexyl and benzyl substituted propargyl acetates are subjected to the optimized condition, the corresponding hydration products 51z and 51aa are obtained in excellent yields. Although Nolan group observed the formation of α,β-unsaturated aldehyde through regioselective hydration of benzyl substituted propargyl acetate 50aa under [(NHC)AuCl], AgSbF₆ in THF-H₂O at 60 °C, our optimized condition exclusively delivered α-acyloxy methyl ketone 51aa from 50aa. The bromo (−Br) group on alkyl chain was survived under the catalytic system and the product 51ab resulted in 86% yield; further manipulation of the bromo group would deliver valuable building blocks. Deprotection of acid-labile−OTHP ethers generally occurs under aqueous Lewis acids at an ambient temperature. Surprisingly, the −OTHP protecting group was well-tolerated in this gold-catalyzed hydration protocol, and the product 51ac was isolated in 78% yield; this observation demonstrates the mild nature of the catalytic condition. The unactivated sterically hindered propargyl acetate such as 50ad

Table 2.6: Gold-catalyzed hydration of hindered 1-ethynyl-1′,1″-alkyl/aryl/H substituted acetates⁴,⁵

[Diagram showing chemical structures and yields]

⁴Reactions were carried out using 50 (1.0 mmol), Ph₃PAuCl (1.0 mol %), AgSbF₆ (1.0 mol %), water (3.0 mmol) in 1,4-dioxane (1.5 mL) at room temperature. ⁵Isolated yields.
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Similarly, both methyl and aryl substituted propargyl acetates 50ae and 50af effectively underwent hydration to furnish the desired α-acyloxy–α′,α″-disubstituted methyl ketones 51ae and 51af in good yields.

To further expand the scope of the reaction, exploration of hindered 1-ethynylcycloalkyl acetates to the alkyne hydrations pursued and the results are shown in Table 2.7. Excellent yields of the desired α-acyloxy methyl ketones (51ag–51ai) were obtained in the hydration of sterically demanding cyclic substituted propargyl acetates under the optimized condition; different rings (5-, 6- or 7-membered) did not interfere in the reaction efficiency. The 1,3-dioxolanes is a carbonyl protective moiety widely useful in organic synthesis. The acid-catalyzed hydrolysis and oxidation easily cleaves the 1,3-dioxolanes. The gold-catalyzed hydration of compound 50aj having both the propargyl acetate and the acid sensitive 1,3-dioxolane moieties, affords the product 51aj in 80% yield. Gratifyingly, the ketal protecting moiety survived under this catalytic condition; this observation once again proved the mildest nature of the catalysts.

Table 2.7. Gold-catalyzed hydration of 1-ethynylcycloalkyl acetates

\[
\begin{array}{cccc}
\text{Me} & \text{OAc} & \text{Ph}_3\text{PAuCl} (1.0 \text{ mol} \%) & \text{AgSbF}_6 (1.0 \text{ mol} \%) \\
50 & 1,4\text{-dioxane} & H_2O, rt & 51 \\
\end{array}
\]

\[
\begin{array}{cccc}
51ag, 96\%, 2 \text{ h} & \text{Me} & \text{OAc} & \text{Me} \\
51ah, 85\%, 4 \text{ h} & \text{Me} & \text{OAc} & \text{Me} \\
51ai, 91\%, 3 \text{ h} & \text{Me} & \text{OAc} & \text{Me} \\
51aj, 80\%, 2 \text{ h} & \text{Ac} & \text{Me} \\
\end{array}
\]

\(^a\)Reactions were carried out using 50 (1.0 mmol), Ph\(_3\)PAuCl (1.0 mol %), AgSbF\(_6\) (1.0 mol %), water (3.0 mmol) in 1,4-dioxane (1.5 mL) at room temperature. \(^b\)Isolated yields.

As observed previously, the O-trimethylsilyl ether protecting group did not survive under the optimized catalytic conditions (Table 2.3, entry 10). The Leyva and Corma groups have shown the cleavage of alkynyl C-TMS group by AuSPhosNTf\(_2\) (Scheme 2.13). Unfortunately, TMS-containing alkyne failed to react with the Nolan’s condition at an elevated temperature (Scheme 2.14). These observations motivated us to investigate the hydration of alkynyl-TMS protected propargyl acetates under the optimized catalytic conditions and the results are summarized in Table 2.8. Thus, the gold-catalyzed hydration of alkynyl-TMS protected phenyl propargyl acetates 54a provided α–acyloxy methyl
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ketone 51a in 82% yield, even though it requires prolonged reaction time (~ 20 h) for completion (entry 1). It appears that the catalytic condition cleaves the alkyne C-TMS bond at first followed by the hydration of the terminal alkyne of the propargyl acetate. Similar results are also obtained in case of 4-bromophenyl and benzyl substituted TMS-containing propargyl acetates 54d and 54aa (entries 2 and 6). Few other cases, mixture of desilylated as well as the hydration products are observed even though the reaction continued for 24 h (entries 3, 4, and 7). Reaction of thienyl-2-substituted TMS-containing propargyl acetates 54x under the catalytic condition resulted desilylated product 50x in 59% yield by 1H NMR without producing the required α-acyloxy methyl ketone 51x; incomplete conversion of 54x was noticed even with the extended reaction time. These observations reveal that TMS-containing propargyl acetates are not effective to this hydration reaction.

Table 2.8. Hydration of TMS-substituted propargyl acetate

<table>
<thead>
<tr>
<th>Entry</th>
<th>54</th>
<th>R¹</th>
<th>R²</th>
<th>Time (h)</th>
<th>Yield (%)</th>
<th>51</th>
<th>50</th>
</tr>
</thead>
<tbody>
<tr>
<td>1</td>
<td>54a</td>
<td>C₆H₅</td>
<td>H</td>
<td>20</td>
<td>82ᵇ</td>
<td>0ᵇ</td>
<td>0ᵇ</td>
</tr>
<tr>
<td>2</td>
<td>54d</td>
<td>4-Br-C₆H₄</td>
<td>H</td>
<td>24</td>
<td>91ᵇ</td>
<td>0ᵇ</td>
<td>0ᵇ</td>
</tr>
<tr>
<td>3</td>
<td>54h</td>
<td>3-MeO-C₆H₄</td>
<td>H</td>
<td>24</td>
<td>70ᶜ</td>
<td>30ᶜ</td>
<td>0ᶜ</td>
</tr>
<tr>
<td>4</td>
<td>54n</td>
<td>2-Cl-C₆H₄</td>
<td>H</td>
<td>24</td>
<td>28ᶜ</td>
<td>72ᶜ</td>
<td>0ᶜ</td>
</tr>
<tr>
<td>5</td>
<td>54x</td>
<td>2-Thiényl</td>
<td>H</td>
<td>24</td>
<td>0ᶜ</td>
<td>59ᶜ</td>
<td>0ᶜ</td>
</tr>
<tr>
<td>6</td>
<td>54aa</td>
<td>C₆H₅-CH₂</td>
<td>H</td>
<td>24</td>
<td>83ᵇ</td>
<td>0ᵇ</td>
<td>0ᵇ</td>
</tr>
<tr>
<td>7</td>
<td>54ah</td>
<td></td>
<td></td>
<td>24</td>
<td>79ᶜ</td>
<td>21ᶜ</td>
<td></td>
</tr>
</tbody>
</table>

ᵃReactions were carried out using 54 (1.0 mmol), Ph₃PAuCl (1.0 mol %), AgSbF₆ (1.0 mol %), water (5.0 mmol) in 1,4-dioxane (1.5 mL) at room temperature.ᵇIsolated yields.ᶜ1H NMR yields.

Next, we examined the effect of the catalytic condition to the hydration of the chiral propargylic acetate (Scheme 2.21). Following the reported procedure,²⁶ᵃ the optically active (R)-1-phenylprop-2-ynyl acetate 55 was prepared with 76% ee (determined by chiral HPLC). The optical rotation of (R)-55 agrees with the literature value.²⁶ᵇ Hydration
of \((R)\)-55 was carried out using the optimized catalytic condition, and the product \((S)\)-56 was obtained in 92% yield with 76% ee (determined by chiral HPLC). Optical rotation analysis confirms that the chiral centre of the acetate moiety did not racemize during the gold-catalyzed hydration of the triple bond (Scheme 2.21). Therefore, we believe that this protocol would allow the synthesis of optically active \(\alpha\)-acyloxy methyl ketones that would finally lead to enantio-enriched \(\alpha\)-hydroxy methyl ketones in simple synthetic operations.

**Scheme 2.21. Hydration of chiral propargyl acetate**

The robustness of the catalytic condition is demonstrated through gram scale synthesis of the hydration products. Screening of different amount of catalyst mixtures containing \(\text{Ph}_3\text{PAuCl}\) and \(\text{AgSbF}_6\) (0.1 mol % or 0.3 mol %) to the hydration of 50a (10 mmol) are independently performed. Sluggish reaction profile was observed, when 0.1 mol % of gold and silver catalysts are employed. Moreover, hydration of 50a successfully completed within appreciable time (~ 20 h) in the presence of 0.3 mol % of gold and silver catalysts. This modified catalytic condition allows furnishing 51a and 51c in 94% and 95% yields, respectively (Scheme 2.22). In addition, simple Celite filtration of the crude reaction mixture leads to pure products.

**Scheme 2.22. Gram scale synthesis of \(\alpha\)-acyloxy methyl ketones**

Reduction of both the keto and acetate moieties of \(\alpha\)-acyloxy methyl ketones would furnish 1,2-disubstituted glycol derivatives, which are useful building blocks.\(^{27}\) For an example, lithium aluminium hydride (\(\text{LiAlH}_4\)) reduces 51a to afford 57 in 82% yield at 0 °C (eq 1, Scheme 2.23). 1,2-Amino alcohols are the valuable precursors to the chiral auxiliaries.\(^{28}\) Imination of 2-oxo-1-phenylpropyl acetate (51a) followed by reduction with
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H₂ in 10% Pd/C resulted racemic 1,2-amino alcohol 58 in overall 36% yield (eq 2, Scheme 2.23).²⁹

Scheme 2.23. Synthesis of 1,2-glycol and 1,2-amino alcohol

The methodology presented here attests broad substrate scope in tolerating functionalities and acid-sensitive protecting groups. To prove the synthetic potential of this strategy, we embarked on the synthesis of a natural product involving hydration of the propargylic acetate as a key step. The α-hydroxy ketone moieties are found in many natural products of pharmacological significance,³⁰ and some representative molecules are shown in Figure 2.2.

Figure 2.2. Sesquiterpene, Cytochalasin, Sattazoline, Actinopolymorphol A & B and Kurasoin B are the classes of natural products having similar structural morphology

Sesquiterpene 59 was isolated from the methylene chloride solubles of the formosan soft coral clavularia inflate var. luzoniana.³⁰a It has significant cytotoxicity to HT-29 (human colon adenocarcinoma) and P-388 (mouse lymphocytic leukemia) cell cultures. Cytochalsin 60 was isolated from the marine-derived fungus Spicaria elegans.³⁰b Actinopolymorphol 62 and 63 were recently isolated from actinopolymorpha rutilus
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(YIM45725) originating from a soil sample. Bioluminescent resonance energy transfer (BRET) assay study reveals that actinopolymorphol A (Figure 2.2) induc...estrogen receptor Erα/β heterodimerization. Moreover, structural morphology of actinopolymorphol B (63) resembles closely with kurasoin B and sattazolin derivatives (Figure 2.2). Kurasoin B 64 and its derivatives are known protein farnesyl transferase (PFTase) inhibitors; and therefore these compounds have the potential showing anti-cancer properties. Moreover, sattazoline 61 and its derivatives expressed their antiviral activity against the Herpes simplex viruses type 1 and 2 (HSV1 & HSV2) and inhibit the protein synthesis in Herpesvirus-infected cells selectively. The central core α-hydroxy ketone unit is present in the natural products depicted in Figure 2.2. Potency of the compounds (Figure 2.2) is believed to rely primarily in the presence of α-hydroxy ketone core and the indole substitution, moreover, the stereochemistry of the hydroxyl functional group also plays critical role exhibiting PFTase inhibition. We anticipate that actinopolymorphol B would be a potentially important drug candidate as of kurasoin B and sattazoline. As our synthetic approach provides a simple route to access α-acyloxy methyl ketone moiety with broad substrate scope under milder reaction condition, we aimed for the synthesis of actinopolymorphol B involving the efficient gold-catalyzed intermolecular hydration of propargyl acetate at room temperature.

Campaign for the synthesis of actinopolymorphol B (Scheme 2.24) initiated from commercially available indole-3-acetic acid 65. Esterification followed by N-Boc protection of 65 provided 66 in 86% overall yield. Access to prepare large quantity of known aldehyde 68 was found to be critical since DIBAL-H reduction of ester 66 produced 68 in only 37% yield. Therefore, two step synthetic protocol involving reduction and oxidation sequences are considered. In order to reduce 66 effectively, various reducing agents were surveyed under different reaction conditions. Gratifyingly, reduction of ester with LiAlH₄ at −78 °C was found productive and resulted 67 in 92% isolated yield. Formation of unwanted side products are observed during the oxidation of 67 under Dess-Martin and Swern conditions. Oxidation of 67 with [bis(acetoxy)iodo]benzene (BAIB) in the presence of TEMPO led to aldehyde 68 in only 57% yield. Addition of TMS-acetylide to carbonyl moiety of 68 was effectively carried out at −78 °C and furnished 69 in 89% yield. Acetate formation (Ac₂O, DMAP, Et₃N) and subsequent desilylation (TBAF) delivered the desired propargyl acetate 70 in 83% overall yield. The precursor 70 was exposed to the optimized catalytic condition [Ph₃PAuCl (1.0 mol %) and AgSbF₆ (1.0 mol %)] in the presence of H₂O in 1,4-dioxane at room
Regioselective Hydration... temperature for 7 h, and the desired α-acyloxy methyl ketone 71 was isolated in 83% yield. Finally, cleavage of N-Boc and O-acetyl of 71 would result in actinopolymorphol B 63. At first, we investigated the deprotection of the N-Boc of 71 keeping the acetate moiety intact. Exploration of established conditions involving i) trifluoroacetic acid (TFA) in CH₂Cl₂, 2) TBAF refluxed in THF, 3) TMSCl in phenol to the deprotection of the N-Boc moiety of indole 71 failed; whereas, TMSOTf in the presence of DBU cleaved the Boc-group successfully. Subsequently, base induced deacetylation of the crude mixture of 71-NH led to complexity. Gratifyingly, Sc(OTf)₃ catalyzed saponification of the acetate moiety furnished 63 in 56% yield over the two-step sequence.

Scheme 2.24. Synthesis of Actinopolymorphol B

2.5. Regioselective Hydration of Halo Alkynes

The regioselective hydration of terminally unsubstituted propargyl carboxylates inspired us to investigate hydration of terminal-halo substituted propargyl carboxylate, which is poorly explored. Moreover, the presence of an electronegative halo group at the alkyne terminus enhances the polarization of alkynes and thus facilitates activating the alkyne-moiety by gold; this in turns would induce the regioselective nucleophilic attack of the neighboring acyloxy-group. Furthermore, halo groups in the rearranged product can be useful to various cross-couplings as well as routine transformations.
Recently, gold-catalyzed rearrangement of halo-substituted propargyl tert-butyl carbonates 72 to cyclic vinyl bromide or iodide derivatives 75 is reported by Gagosz group.\textsuperscript{37d} The vinyl bromides and iodides are synthetically useful building blocks.\textsuperscript{37c}

**Scheme 2.25:** Mode of reactivity of terminal halo-substituted propargyl carbonates

The Zhang group demonstrated the gold-catalyzed regioselective 1,2-acyloxy migration of terminally halogenated propargyl carboxylates 76 to the synthesis of 1-halo-2-carboxy-1,3-dienes 78 (Scheme 2.26).\textsuperscript{37c} The desired conjugated dienes 78 is formed via migration of 1,2-carboxylate group followed by hydride shift to adjacent positively-charged carbon center in 77. Later this multi-functionalized dienes 78 was used for the fabrication of complex molecular framework.

**Scheme 2.26:** Synthesis of dienes from terminally halo-substituted propargyl carboxylates

Apart from the formation of dienes, a trace amount of hydration product \(\alpha\)-acyloxy-\(\alpha\')-halo ketone 80 was also obtained during the reaction. The presence of easily modifiable multi-functional groups halo, keto and carboxylate makes the compound 80 an important building block useful to the synthesis of complex molecules.\textsuperscript{38} Inspired by the results of Zhang’s group,\textsuperscript{37c} and considering the broad synthetic utility of 80, we are interested in
establishing an efficient and gram scale synthetic procedures for 80 via the regioselective hydration of 76 by applying the previously developed gold-catalyzed conditions for the hydration of propargyl acetates (Scheme 2.27). Herein, we report an atom-economical hydration of readily accessible halo-substituted propargyl carboxylate 76 to the efficient synthesis of wide array of $\alpha$-acyloxy-$\alpha'$-halo ketones 80.

### 2.5.1. Reaction Optimization

At first, the regioselective hydration of 4-bromo-1-phenylbut-3-yn-2-yl acetate (76a) is examined under various Au-catalysts. The optimization studies are detailed in Table 2.8. The combination of Ph$_3$PAuCl (3.0 mol %), AgSbF$_6$ (3.0 mol %), and H$_2$O (3.0 equiv) in Table 2.8: Optimization of reaction conditions$^{a,b}$

<table>
<thead>
<tr>
<th>Entry</th>
<th>Catalyst (mol %)</th>
<th>Solvent</th>
<th>Time</th>
<th>Yields$^b$</th>
</tr>
</thead>
<tbody>
<tr>
<td>1</td>
<td>Ph$_3$PAuCl/AgSbF$_6$ (3)</td>
<td>1,4-dioxane</td>
<td>4 h</td>
<td>75</td>
</tr>
<tr>
<td>2</td>
<td>AuCl$_3$/AgSbF$_6$ (3)</td>
<td>1,4-dioxane</td>
<td>4 h</td>
<td>51 (21)$^c$</td>
</tr>
<tr>
<td>3</td>
<td>AuCl$_3$/AgSbF$_6$ (3)</td>
<td>1,4-dioxane</td>
<td>4 h</td>
<td>trace</td>
</tr>
<tr>
<td>4</td>
<td>Ph$_3$PAuCl/AgSbF$_6$ (3)</td>
<td>THF</td>
<td>4 h</td>
<td>67</td>
</tr>
<tr>
<td>5</td>
<td>Ph$_3$PAuCl/AgSbF$_6$ (3)</td>
<td>acetone</td>
<td>4 h</td>
<td>61</td>
</tr>
<tr>
<td>6</td>
<td>Ph$_3$PAuCl/AgSbF$_6$ (3)</td>
<td>CH$_2$Cl$_2$</td>
<td>4 h</td>
<td>32</td>
</tr>
<tr>
<td>7</td>
<td>Ph$_3$PAuCl/AgSbF$_6$ (3)</td>
<td>MeCN</td>
<td>4 h</td>
<td>42</td>
</tr>
<tr>
<td>8</td>
<td>Ph$_3$PAuCl/AgOTf (3)</td>
<td>1,4-dioxane</td>
<td>4 h</td>
<td>49 (36)$^c$</td>
</tr>
<tr>
<td>9</td>
<td>Ph$_3$PAuCl/AgBF$_4$ (3)</td>
<td>1,4-dioxane</td>
<td>4 h</td>
<td>39 (45)$^c$</td>
</tr>
<tr>
<td>10</td>
<td>Ph$_3$PAuN Tf$_2$ (3)</td>
<td>CH$_2$Cl$_2$</td>
<td>4 h</td>
<td>46 (52)$^c$</td>
</tr>
<tr>
<td>11$^d$</td>
<td>Ph$_3$PAuCl/AgSbF$_6$ (3)</td>
<td>1,4-dioxane/MeNO$_2$</td>
<td>4 h</td>
<td>93</td>
</tr>
<tr>
<td>12$^d$</td>
<td>Ph$_3$PAuCl/AgSbF$_6$ (3)</td>
<td>1,4-dioxane/DMSO</td>
<td>4 h</td>
<td>trace</td>
</tr>
<tr>
<td>13$^d$</td>
<td>Ph$_3$PAuCl/AgSbF$_6$ (3)</td>
<td>1,4-dioxane/DMF</td>
<td>4 h</td>
<td>trace</td>
</tr>
</tbody>
</table>

$^a$Reactions were carried out using 76a (0.5 mmol) and solvent (1.0 mL) at rt. $^b$Isolated yields. $^c$Yield of recovered 76a is given in the parenthesis. $^d$76a was added at 0 °C in a mixture of solvent (1.0 mL, 20:1) and then stirred at rt.

1,4-dioxane at room temperature furnished the desired $\alpha$-acyloxy-$\alpha'$-halo ketone 80a in 75% yield with the complete consumption of 76a within 4 h (entry 1). Screening of other
Regioselective Hydration......

Au-catalysts such as: AuCl₃ or AuCl along with AgSbF₆ yielded 80a up to 51% yield (entries 2 and 3). The yield of 80a was limited to 67%, when solvents THF, acetone, dichloromethane and acetonitrile were employed instead of dioxane (entries 4−7). The combinations of AgOTf or AgBF₄ with Ph₃PAuCl were found moderate; the reaction did not undergo completion even with prolonged time (entries 8 and 9). The reaction of 76a with water under the Zhang’s catalytic conditions produced 80a in only 46% yield, recovering the unreacted precursor 76a (52%) (entry 10); not even a trace of bromodiene/enones is observed from 76a. We next examined the effect of mixture of solvents on the reaction outcome. Gratifyingly, 80a was isolated in 93% yield, when a solvent mixture 1,4-dioxane and MeNO₂ (20:1) was employed (entry 11), while 1,4-dioxane with DMSO/DMF mixture were ineffective (entries 12 and 13). Interestingly, we did not observe either the bromodiene/enones from 76a under the optimized conditions shown in entry 11, Table 2.8. Thus, different catalytic conditions allows in accessing two distinct products from the precursor 76a (the hydration product over the dienes shown in Scheme 2.26).

2.5.2. Reaction Scope

The optimal reaction condition [Ph₃PAuCl, AgSbF₆, and H₂O in 1,4-dioxane:MeNO₂ Table 2.8] was surveyed to investigate the generality of the hydration of the terminal halo-substituted propargyl acetates (Tables 2.9−2.10). The stereo-electronic

| Table 2.9: Stereo-electronic effect of substituent’s on the aryl moiety

<table>
<thead>
<tr>
<th>Reaction</th>
<th>Product</th>
<th>Yield</th>
<th>Time</th>
</tr>
</thead>
<tbody>
<tr>
<td>76a → 80a</td>
<td>80b</td>
<td>86%</td>
<td>1.5 h</td>
</tr>
<tr>
<td>76a → 80c</td>
<td>80c</td>
<td>82%</td>
<td>1.5 h</td>
</tr>
<tr>
<td>76a → 80d</td>
<td>80d</td>
<td>83%</td>
<td>3 h</td>
</tr>
<tr>
<td>76a → 80e</td>
<td>80e</td>
<td>78%</td>
<td>2 h</td>
</tr>
<tr>
<td>76a → 80f</td>
<td>80f</td>
<td>86%</td>
<td>1 h</td>
</tr>
<tr>
<td>76a → 80g</td>
<td>80g</td>
<td>88%</td>
<td>1.5 h</td>
</tr>
<tr>
<td>76a → 80h</td>
<td>80h</td>
<td>81%</td>
<td>2 h</td>
</tr>
<tr>
<td>76a → 80i</td>
<td>80i</td>
<td>77%</td>
<td>1 h</td>
</tr>
<tr>
<td>76a → 80j</td>
<td>80j</td>
<td>90%</td>
<td>2.5 h</td>
</tr>
</tbody>
</table>

*Reactions were carried out using 76 (1.0 mmol), Ph₃PAuCl/AgSbF₆ (0.03 mmol), H₂O (3.0 mmol) and 1,4-dioxane:MeNO₂ (2.0 mL, 20:1) at 0 °C−rt. Isolated yields.*
effect of substituent’s on the aryl moiety at propargyl position was explored at first and the results are summarized in Table 2.9. The hydration of 3-bromo-1-phenylprop-2-ynyl acetate 76b gave 86% isolated yield of 80b. The electron-withdrawing and donating groups at 4/3/2 positions on the aryl moiety in Br-substituted propargyl acetates reacted efficiently and the desired keto-products were obtained in good to excellent yields (80c–g). The α-O-allyl moiety on aromatic ring in 76h did not affect the reaction outcome, producing 80h in 81% yield. The 1-naphthyl bearing hydration product 80i was cleanly obtained from 76i. Gratifyingly, the di-ortho-substituted sterically demanding substrate 76j efficiently hydrated, delivering 90% of 80j.

We next investigated the hydration of alkyl-moiety bearing Br-propargyl acetates (Table 2.10). As observed in the optimization reaction conditions (entry 11, Table 2.8), the α-benzyl-substituted α-acyloxy-α’-bromo ketone 80a was isolated in 92% yield from 76a. Similarly, hydration of N-Boc protected 3-indolyl-substituted bromo propargyl acetate 76k gave 79% of 80k within 1.5 h. The easily modifiable functional groups (Br and N3) as well as the -NHBoc, -OTHP, and -OBn protecting groups on alkyl chain are well-tolerated.

Table 2.10: Effect of alkyl substituents at propargyl position on hydration reaction

<table>
<thead>
<tr>
<th>Reaction</th>
<th>Product</th>
<th>Yield</th>
<th>Time</th>
</tr>
</thead>
<tbody>
<tr>
<td>76a, 92%, 2 h&lt;sup&gt;c&lt;/sup&gt;</td>
<td>80a, 92%, 2 h&lt;sup&gt;c&lt;/sup&gt;</td>
<td>80k, 79%, 1.5 h</td>
<td>80l, 89%, 2.5 h</td>
</tr>
<tr>
<td>80m, 89%, 3 h</td>
<td>80n, 87%, 1.5 h</td>
<td>80o, 72%, 2 h</td>
<td>80p, 94%, 1 h</td>
</tr>
<tr>
<td>80q, 92%, 2 h</td>
<td>80r, 87%, 3 h</td>
<td>80s, 78%, 2 h</td>
<td>80t, 85%, 1 h</td>
</tr>
</tbody>
</table>

<sup>a</sup>Reactions were carried out using 76 (1.0 mmol), Ph3PAuCl/AgSbF6 (0.03 mmol), H2O (3.0 mmol) and 1,4-dioxane:MeNO2 (20:1) at 0 °C–rt. <sup>b</sup>Isolated yields. <sup>c</sup>Reaction of 76a (1.0 g, 3.76 mmol) under the optimized conditions gave 80a (779 mg, 73%).

76k gave 79% of 80k within 1.5 h. The easily modifiable functional groups (Br and N3) as well as the -NHBoc, -OTHP, and -OBn protecting groups on alkyl chain are well-tolerated.
and the desired products 80l–p are obtained in lucrative yields, demonstrating the mild nature of the catalytic conditions. The Au-catalyzed hydration of O–Si protected 76q gave the desilylated 80q in 92% yield. The sterically demanding cyclic-substituted acetates 76r and 76s did not affect the hydration, affording 80r and 80s in good yields with the survival of acid-sensitive 1,3-dioxolane moiety. The O-pivolate group also directs the hydration of bromo alkyne 76t, generating the desired product 80t in 85% yield.

The chloro substituted propargyl acetate 81a underwent hydration efficiently and the desired product 83a was isolated in 81% yield (eq 1, Scheme 2.28). The pivolate group is equally effective, producing 81b from the hydration of 83b (Scheme 2.28). The sterically encumbered and 1,3-dioxolane protected cyclohexane bearing α-chloro-α'-acyloxy-ketone 83c was produced from 81c in 81% yield (eq 2, Scheme 2.28). Pleasingly, the substrate with iodo-substitution at the alkyne terminus in 82 underwent hydration easily, forming 4-iodo-3-oxo-1-phenylbutan-2-yl acetate 84 in 77% yield (eq 3, Scheme 2.28).

Scheme 2.28: Effect of chloro and iodo groups at alkyne terminus on propargyl acetates to the gold-catalyzed hydration reaction.

Finally, the acetate group was successfully saponified with Sc(OTf)₃ (20 mol %) in MeOH:H₂O (4:1) at rt (eq 1). The α-hydroxy-α'-bromo ketone 85 was obtained in 83% yield. The compound 85 is useful for the construction of various molecular fragments.
Thus, the Au-catalyzed hydration of terminal-halo substituted propargyl acetates provides an efficient access to a broad range of multi-functional groups halo, keto, and carboxylate bearing α-substituted-α-acyloxy-α’-halo ketones 80. We next envisaged exploring the utility of 80 towards the synthesis of heterocycles. The α-halo ketones are successfully used for the construction of large varieties of heterocycles.37a Gratifyingly, the condensation of 80b and 80e with thiourea in EtOH independently delivered 4-benzylsubstituted-2-amino thiazole 86a and 86b in good yields (eq 1, Scheme 2.29); the acetate group at the benzylic position is replaced with ethoxy-moiety during the reaction. However, the reaction between α-alkyl-α-acyloxy-α’-halo ketones 80a and thiourea did not affect the acetate moiety, affording 87 in 65% yield (eq 2, Scheme 2.29).

**Scheme 2.29:** Synthetic utility

### 2.5.3. Mechanistic Studies: Isotopic Labeling Experiment

Experimental results show that the hydration of propargyl acetate in dioxane and water proceeds efficiently under gold-catalyst at room temperature in the absence of acid promoters. The critical role of the acetate group located adjacent to the terminal alkyne in the regioselective hydration warrants careful investigation.16 In order to probe the reaction pathway and to validate the mode of water attack to the unsaturated bonds, oxygen-18 enriched water is employed.40 The affinity of alkyne to cationic gold(I) species such as [Me₃PAu]⁺ over methanol and water is well established.12,13 Thus, the reactive intermediate gold-alkyne-π complex 88, resulting from the activation of the alkyne 51ah by cationic gold(I)phosphine, is believed to take part in the first step of the transformation.
Experimental and theoretical studies reveal that enol ethers and ketals are the plausible intermediates involved in the hydration of alkynes in alcoholic solvents (Scheme 2.12).\textsuperscript{12} Therefore, participation of enol ether intermediates seems unlikely as the reactions are performed in dioxane. The Hayashi, Tanaka and the Laguna groups have independently demonstrated that the direct attack of water on the gold-alkyne-$\pi$ complex in non-alcoholic medium provides the desired hydration product. Pathway A is proposed based on the direct $S_N2'$ attack of $\text{H}_2\text{O}^{18}$ on $\text{88}$ followed by protodeauration of $\text{99}$ and isomerization of enol $\text{90}$ leading to the ketone $\text{91}$. Base induced deacetylation of $\text{91}$ would then generate $\text{92}$.

\textbf{Scheme 2.30: Proposed catalytic cycle}
the desired α−hydroxy methyl ketone \(92\) with \(18\)O insertion. However, the mass spectrum of the isolated product shows no sign of \(18\)O insertion. On the basis of this evidence, route A appears unlikely. The alternate route involves the stabilization of the electrophilic gold-alkyne−π complex intermediate \(88\) through neighboring nucleophilic carbonyl group participation (path B and C, Scheme 2.30). The 5-exo-dig attack of carbonyl oxygen on the γ-carbon would generate the 5-membered electrophilic vinyl-gold species \(93\) (path B),\(^{20}\) whereas the 6-endo-dig attack would provide the 6-membered intermediate \(98\) (path C).\(^{21}\) Even though as per the Baldwin’s rule,\(^{41}\) attack of the carbonyl oxygen on the activated alkyne is possible in both ways, the former is preferred in the case of gold-activated terminal alkynes. Involvement of such reactive intermediates in various gold-catalyzed organic transformations is well explored.\(^{20}\) The nucleophilic addition of \(\text{H}_2\text{O}^{18}\) to \(93\) produces the intermediate \(94\) as illustrated in path B. Protodemetalation of \(94\) followed by isomerization of \(95\) furnishes α−acyloxy methyl ketone \(96\) with \(18\)O in the ester carbonyl group. Molecular mass of \(96\) [187 (M+1)] confirms this. Base catalyzed deacetylation of \(96\) produces the corresponding α−hydroxy methyl ketone \(97\) [143 (M+1)] with the loss of \(18\)O. This observation clearly demonstrates that the rupture of the unsaturated bond leading to C–O bond formation is possible only through the intramolecular assistance of the carbonyl oxygen of the acetate moiety. The acetate moiety is regained through the subsequent attack of a water molecule. Attack of \(\text{H}_2\text{O}^{18}\) on \(98\) would generate aldehyde products (\(99\) or \(100\)) as depicted in path C; however, such products were never observed. This proves unambiguously that the regioselective hydration product resulted exclusively from the 5-exo-dig cyclized reactive intermediate \(93\) under the optimal conditions shown in path B, Scheme 2.30.

2.6. Conclusion

We have shown that the commercially available catalyst [Ph₃PAuCl and AgSbF₆] in \(\text{H}_2\text{O}\) efficiently hydrolyzes a wide range of readily accessible propargyl acetates at ambient temperature. This strategy allows the efficient synthesis of an array of α−acyloxy methyl ketones and α-acyloxy-α’-halo ketones in good to excellent yields. The highlights of this strategy are: (a) the mild reaction conditions, (b) operationally simple and easy to handle reagents, (c) absence of acidic promoters, (d) broad functional group compatibility and tolerance to acid-labile protecting groups, (e) short reaction time, (f) gram scale synthesis, (g) isolation of products through simple filtration and easy purification, and (h) retention of chirality of the acetate moiety. The method developed is useful for the synthesis of
Regioselective Hydration......

multi-functionalized molecule that finally leads to the generation of \( \alpha \)-hydroxy ketones, which are indeed synthetically versatile intermediates for various biologically active compounds.\(^{30}\) This protocol also allows the introduction of key \( \alpha \)-hydroxy methyl ketone group in actinopolymorphol B (63).\(^{30c}\) The first total synthesis of 63 is accomplished through 7-step route, in 16% overall yield, starting from commercially available indole-3-acetic acid. Based on an \(^{18}\)O-labeling study, the reaction is proposed to proceed through the addition of water to the favored 5-exo-dig cyclized intermediate. Ongoing research activities in our group are directed towards discovering the asymmetric variant of this reaction, finding efficient strategy to the regioselective hydration of internal alkynes (other than halo substituted), and exploring the total synthesis of natural products of pharmaceutical interest.

2.7. Future Work

Recently, Shi group showed the role of silver in the gold-catalyzed organic transformations.\(^{42}\) It has been observed that the silver-salt in the reaction medium plays vital role in carrying out hydration of propargyl acetates.\(^{42}\) For instance: the TA-Au complex is a highly efficient catalyst employed successfully in achieving the hydration of terminal alkynes (50), acetate rearrangement and so on (Scheme 2.32).

Scheme 2.32: TA-Au-catalyzed regioselective hydration of propargyl acetates

The silver,\(^{43a,b}\) iron\(^{43c}\) (eq 1, Scheme 2.33) and cobalt\(^{43d}\) (eq 2, Scheme 2.33) bearing

Scheme 2.33: Iron, silver and cobalt-catalyzed hydration of alkynes

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Regioselective Hydration......

catalysts are used for the hydration of terminal alkynes (5) at an elevated temperature.

After discovering highly efficient synthesis of α-acyloxy methyl ketones through regioselective hydration of propargyl carboxylate, we are interested to do regioselective hydration of internal alkynes (103) using metal or Lewis-acid catalyst (eq 1, Scheme 2.34). This strategy would allow in achieving the synthesis of wide range of natural products sattazolines (61) and qurasoin B (64) in a step-efficient manner. Furthermore, our interest is also directed to tackle the ever-lasting problem for the hydration of propargyl acetates (50 and 76) in an asymmetric fashion as shown in eq 2, Scheme 2.34; we believe the use of optically active metal catalyst would direct fixing the chirality of the acetate-center during hydration.

Scheme 2.34: Regioselective hydration of internal alkynes and synthesis of optically active α-acyloxy ketones
2.8. Experimental

2.8.1. General Experimental Information for the Work Presented in This Thesis

All the reactions were performed in an oven-dried Schlenk flask under an argon atmosphere. Commercial grade solvents were distilled prior to use. Column chromatography was performed using silica gel procured from Merck (100-200 Mesh) eluting with hexanes and ethyl acetate mixture. Flash column chromatography was performed using silica gel from Acme’s (230-400 Mesh) eluting with hexanes and ethyl acetate mixture. Thin layer chromatography (TLC) was performed on silica gel GF254 (Merck) plates. Visualization of spots on TLC plate was accomplished with UV light (254 nm) and staining over I$_2$ chamber or an aqueous alkaline KMnO$_4$ solution followed by heating.

Proton and carbon nuclear magnetic resonance spectra ($^1$H NMR, $^{13}$C NMR and $^{19}$F NMR) were recorded on a Bruker Avance 400 ($^1$H NMR, 400 MHz; $^{13}$C NMR, 101 MHz; $^{19}$F NMR, 376 MHz) spectrometer, Bruker Avance 500 ($^1$H NMR, 500 MHz; $^{13}$C NMR, 126 MHz; $^{19}$F NMR, 470 MHz) spectrometer having solvent resonance as internal standard ($^1$H NMR, CHCl$_3$ at 7.26 ppm; $^{13}$C NMR, CDCl$_3$ at 77.0 ppm). Few cases tetramethylsilane (TMS) at 0.00 ppm was used as reference standard. Data for $^1$H NMR are reported as follows: chemical shift (ppm), multiplicity (s = singlet; br s = broad singlet; d = doublet; br d = broad doublet, t = triplet; br t = broad triplet; q = quartet; m = multiplet), coupling constants, $J$, in (Hz), and integration. Data for $^{13}$C NMR, $^{19}$F NMR were reported in terms of chemical shift (ppm). GC analysis was performed on GCMS equipped with ZB-1 column (30 m x 0.25 mm, pressure = 20.0 kPa, detector = EI, 300 °C) with helium gas as carrier. IR spectra were recorded on FT/IR-5300 spectrometer and reported in cm$^{-1}$. LC-MS spectra were obtained with ionization voltage of 70ev; data was reported in the form of m/z (intensity relative to base peak = 100). HPLC analysis of the samples was performed Daicel Chiralpak AS-H column/Chiralcel OD-H column, hexanes--i-PrOH as eluent, flow rate = 0.3–1.0 mL/min at $\lambda$ = 254 nm. Elemental (C, H, N) analysis were carried out using FLASH EA 1112 analyzer. Melting points were determined on electro-thermal melting point apparatus and are uncorrected. The X-ray data was collected at 298K on a SMART APEX CCD single crystal diffractometer using graphite monochromated Mo-K$\alpha$ radiation (0.71073 Å).
**Regioselective Hydration...**

### 2.8.2. Materials

Unless otherwise noted, all the reagents and intermediates were obtained commercially and used without purification. Dichloromethane (DCM), dichloroethane (DCE), N,N-Dimethylformamide (DMF), Dimethyl sulfoxide (DMSO), acetonitrile and 1,4-dioxane were distilled over CaH₂. Tetrahydrofuran (THF) was freshly distilled over sodium/benzophenone ketyl under dry nitrogen. Methanol was dried over magnesium cake. Gold(III)chloride (AuCl₃, 99 %), AuBr₃ (99.9 %), AuCl (99.9 %) and Ph₃PAuCl (99.9 %) were purchased from Sigma Aldrich Ltd. and used as received. Silver salts such as AgSbF₆, AgOOCF₃, AgOAc, AgOTf and AgNO₃ are purchased from Aldrich Ltd. and used as received. Trimethylsilylacetylene, n-butyl lithium (1.6 M in THF), TBAF (1.0 M in THF), Ti(O’Pr)₄, Et₂Zn, TBDMSCl, TBDPSCl, DBU, TMS-OTf and Sc(OTf)₃ were purchased from Sigma Aldrich Ltd and used. Analytical and spectral data of all those known compounds are exactly matching with the reported values.

### 2.8.3. General Experimental Procedure

**General procedure for the preparation of estrating materials:**

![Diagram](image)

**Preparation of 50'' from 50'; General Procedure (GP-1):**

A solution of trimethylsilylacetylene (12 mmol) in THF (20 mL) was stirred in a 100 mL oven-dried two-necked round bottom flask under an argon atmosphere at -70 °C. n-Butyllithium (12 mmol, 1.60 M in THF) was introduced over 30 minutes at -70 °C. After an additional 1 h stirring, a solution of aldehyde (50’, 10 mmol) in THF (5.0 mL) was added at -70 °C. The resulting mixture was stirred for 1 h and warmed to room temperature slowly and continued for 30 minutes. The reaction mixture was quenched with saturated NH₄Cl aqueous solution (20 mL) at 0 °C. The organic layer was separated; the aqueous layer was extracted with Et₂O (2 × 20 mL). The combined extracts were washed with water (2 × 20 mL), brine (25 mL) and dried over Na₂SO₄. Solvent was filtered and evaporated under reduced pressure. The crude residue was subsequently used for the desilylation reaction (Scheme 1).
Regioselective Hydration......

Methanol (15 mL) and K₂CO₃ (2.5 equiv) was introduced to the crude residue obtained in the above reaction and the heterogeneous mixture was stirred under an argon atmosphere at ambient temperature overnight. The reaction mixture was diluted with ethyl acetate (50 mL) and washed with water (2 × 20 mL) and brine (10 mL). The organic layer was separated, dried over Na₂SO₄, filtered, and concentrated under vacuum. Most of the cases the crude residue was used for the acetylation reaction without purification, following the general procedure (GP 2).

Synthesis of 50 from 50''; General Procedure (GP-2):

To a solution of 50'' (1.0 mmol) and DMAP (0.1 mmol) in dichloromethane (5.0 mL) was added Et₃N (3.0 mmol), acetic anhydride (1.3 mmol) under an argon atmosphere at ambient temperature. The resulting reaction mixture was stirred for 1 h at ambient temperature. Water (20 mL) was added to the reaction mixture. The organic layer was separated; the aqueous layer was extracted with CH₂Cl₂ (2 × 20 mL). The combined extracts were washed with water (2 × 20 mL), brine (25 mL) and dried over Na₂SO₄. Solvent was filtered and evaporated under reduced pressure. The crude residue was purified using column chromatography on silica gel.

Preparation of 54 from 50'; General Procedure (GP-3):

A solution of trimethylsilylacetylene (12 mmol) in THF (50 mL) was stirred in a 100 mL oven-dried two-necked round bottom flask under an argon atmosphere at −70 °C. n-Butyllithium (12 mmol, 1.60 M in THF) was introduced over 30 minutes at −70 °C. After an additional 1 h stirring, a solution of aldehyde (50', 10 mmol) in THF (5.0 mL) was added at −70 °C. The resulting mixture was stirred for 1 h and warmed to room temperature slowly and continued for 30 minutes. The reaction mixture was quenched with saturated NH₄Cl aqueous solution (20 mL) at 0 °C. The organic layer was separated; the aqueous layer was extracted with Et₂O (2 × 20 mL). The combined extracts were washed with water (2 × 20 mL), brine (25 mL) and dried over Na₂SO₄. Solvent was filtered and evaporated under reduced pressure. The crude residue was subsequently used for the acetylation reaction.
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To a solution of the crude residue (10 mmol) obtained in the above reaction and DMAP (1.0 mmol) in dichloromethane (5.0 mL) was added Et$_3$N (30 mmol), acetic anhydride (13 mmol) under an inert atmosphere at ambient temperature. The resulting reaction mixture was stirred for 1−3 h at an ambient temperature. Water (20 mL) was added to the reaction mixture. The organic layer was separated; the aqueous layer was extracted with CH$_2$Cl$_2$ (2 × 20 mL). The combined extracts were washed with water (2 × 20 mL), brine (25 mL) and dried over Na$_2$SO$_4$. Solvent was filtered and evaporated under reduced pressure. The crude residue was purified using column chromatography on silica gel.

2.8.4. Spectra and Analytical Data

Physical characterization data is exactly matching with the reported values for the respective compounds 50a–e, 50g–h, 50m–s, 50x, 50z−50aa, 50ad–50ai, 50h, 54a, 54d, 54h, 54n, 54x, 54aa, 54ah, 54, 55, 57, 58, 59, 60, 61a, 62, 63, 64, 65, 66, 67, 68, whereas 50f, 50i–l, 50t–50w, 50y, 50ab–ac, 50aj, 69, 70, 71, 68 are new.

1-(4-Formylphenyl)prop-2-ynyl acetate (50f):

- **thick yellow oil (390 mg, 34% yield).**
- $R_f = 0.35$ (6:1 hexane/EtOAc); [Silica, UV and I$_2$].
- $^1$H NMR (400 MHz, CDCl$_3$) δ 10.04 (s, 1H), 7.91 (d, $J = 8.0$ Hz, 2H), 7.70 (d, $J = 8.0$ Hz, 2H), 6.50 (s, 1H), 2.70 (s, 1H), 2.15 (s, 3H).
- $^{13}$C NMR (101 MHz, CDCl$_3$) δ 191.6, 169.5, 142.6, 136.6, 130.0, 128.2, 128.1, 79.4, 76.2, 64.6, 20.9.
- IR (Neat) $\nu_{max}$ 3271, 1738, 1693, 1429, 1371, 1230, 1020 cm$^{-1}$. MS (EI) $m/z$ (%) 182 (14), 181 (100), 149 (28), 131 (14). Anal. calcd for C$_{12}$H$_{10}$O$_3$: C, 71.28; H, 4.98. Found: C, 71.15; H, 4.88.

1-(3-Phenoxyphenyl)prop-2-ynyl acetate (50i):

- **pale brown semi-solid (667 mg, 50% yield).**
- $R_f = 0.43$ (12:1 hexane/EtOAc); [Silica, UV and I$_2$].
- $^1$H NMR (400 MHz, CDCl$_3$) δ 7.42−7.33 (m, 3H), 7.26 (s, 1H), 7.23 (br s, 1H), 7.16 (t, $J = 8.0$ Hz, 1H), 6.70−6.97 (m, 3H), 6.43 (s, 1H), 2.66 (s, 1H), 2.14 (s, 3H).
- $^{13}$C NMR (101 MHz, CDCl$_3$) δ 169.6, 157.6, 156.7, 138.4, 130.1, 129.9, 123.7, 122.3, 119.1, 118.0, 80.0, 75.6, 64.9, 21.0. IR (Neat) $\nu_{max}$ 3290, 1745, 1587, 1371, 1224, 1081 cm$^{-1}$. MS (EI) $m/z$ (%) 240 (20), 239 (100), 225 (5), 207 (45). Anal. calcd for C$_{17}$H$_{14}$O$_3$: C, 76.68; H, 5.30. Found: C, 76.62; H, 5.33.

1-(3-Hydroxyphenyl)prop-2-ynyl acetate (50j):

- **pale yellow oil (315 mg, 39% yield).**
- $R_f = 0.32$ (4:1 hexane/EtOAc); [Silica, UV and I$_2$].
- $^1$H NMR (400 MHz, CDCl$_3$) δ 7.42−7.33 (m, 3H), 7.26 (s, 1H), 7.23 (br s, 1H), 7.16 (t, $J = 7.8$ Hz, 1H), 7.09−6.97 (m, 3H), 6.43 (s, 1H), 2.66 (s, 1H), 2.14 (s, 3H).
- $^{13}$C NMR (101 MHz, CDCl$_3$) δ 170.1, 156.0, 137.9, 130.1, 129.9, 123.7, 122.3, 119.1, 118.0, 80.0, 75.6, 64.9, 21.0. IR (Neat) $\nu_{max}$ 3290, 1745, 1587, 1371, 1224, 1081 cm$^{-1}$. MS (EI) $m/z$ (%) 240 (20), 239 (100), 225 (5), 207 (45). Anal. calcd for C$_{17}$H$_{14}$O$_3$: C, 76.68; H, 5.30. Found: C, 76.62; H, 5.33.
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119.9, 116.5, 114.6, 80.0, 75.5, 65.2, 21.1. IR (Neat) $\nu_{\text{max}}$ 3396, 3290, 2920, 1726, 1595, 1371, 1228, 1020 cm$^{-1}$. MS (EI) m/z (%) 192 (M$^+2$, 100), 190 (M$^+$, 26), 189 (M$^+1$, 21), 165 (8), 135 (5). Anal. calcd for C$_{11}$H$_{10}$O$_3$: C, 69.46; H, 5.30. Found: C, 69.55; H, 5.26.

1-(3-(tert-Butyldiphenylsilyloxy)phenyl)prop-2-ynyl acetate (50k):
thick yellow oil (513 mg, 41% yield). $R_f$ = 0.51 (12:1 hexane/EtOAc); [Silica, UV and I$_2$]. $^1$H NMR (400 MHz, CDCl$_3$) $\delta$ 7.73 (d, $J$ = 6.8 Hz, 4H), 7.52–7.35 (m, 6H), 7.14–7.01 (m, 2H), 6.98 (s, 1H), 6.73 (br d, $J$ = 8.0 Hz, 1H), 6.29 (s, 1H), 2.54 (s, 1H), 2.05 (s, 3H), 1.13 (s, 9H). $^{13}$C NMR (101 MHz, CDCl$_3$) $\delta$ 169.6, 155.8, 137.5, 135.5, 132.7, 129.9, 129.4, 127.8, 120.3, 120.2, 119.0, 80.0, 75.2, 64.9, 26.5, 21.0, 19.5. IR (Neat) $\nu_{\text{max}}$ 3290, 1747, 1602, 1487, 1442, 1369, 1286, 1111, 1020 cm$^{-1}$. MS (EI) m/z (%) 425 (2), 413 (54), 382 (22), 363 (4). Anal. calcd for C$_{27}$H$_{28}$O$_3$Si: C, 75.66; H, 6.58. Found: C, 75.48; H, 6.51.

1-(3-(tert-Butyldimethylsilyloxy)phenyl)prop-2-ynyl acetate (50l):
thick yellow oil (473 mg, 36% yield). $R_f$ = 0.47 (12:1 hexane/EtOAc); [Silica, UV and I$_2$]. $^1$H NMR (400 MHz, CDCl$_3$) $\delta$ 7.25 (t, $J$ = 8.0 Hz, 1H), 7.11 (d, $J$ = 4.0 Hz, 1H), 7.02 (s, 1H), 6.85 (d, $J$ = 8.0 Hz, 1H), 6.40 (s, 1H), 2.65 (s, 1H), 2.12 (s, 3H), 0.99 (s, 9H), 0.21 (s, 6H). $^{13}$C NMR (101 MHz, CDCl$_3$) $\delta$ 169.7, 155.9, 137.8, 129.7, 120.7, 120.5, 119.4, 80.2, 75.3, 65.1, 25.7, 21.0, –4.4. IR (Neat) $\nu_{\text{max}}$ 3294, 2932, 1745, 1604, 1487, 1369, 1224, 1016 cm$^{-1}$. MS (EI) m/z (%) 278 (30), 277 (100), 246 (25), 245 (96). Anal. calcd for C$_{17}$H$_{24}$O$_3$Si: C, 67.06; H, 7.95. Found: C, 67.21; H, 7.86.

1-(2-(Allyloxy)phenyl)prop-2-ynyl acetate (50t):
pale yellow oil (835 mg, 59% yield). $R_f$ = 0.43 (10:1 hexane/EtOAc); [Silica, UV and I$_2$]. $^1$H NMR (400 MHz, CDCl$_3$) $\delta$ 7.72 (dd, $J$ = 8.0, 1.6 Hz, 1H), 7.35 (ddd, $J$ = 8.0, 2.0, 0.4 Hz, 1H), 7.03 (ddd, $J$ = 8.0, 2.0, 0.4 Hz, 1H), 6.91 (dd, $J$ = 8.4, 0.4 Hz, 1H), 6.86 (d, $J$ = 2.4 Hz, 1H), 5.43 (dd, $J$ = 17.6, 1.6 Hz, 1H), 5.29 (dd, $J$ = 10.8, 1.6 Hz, 1H), 4.60 (d, $J$ = 4.8 Hz, 2H), 2.63 (s, 1H), 2.12 (s, 3H). $^{13}$C NMR (101 MHz, CDCl$_3$) $\delta$ 169.6, 155.7, 132.8, 130.4, 128.8, 124.8, 120.8, 117.3, 112.0, 80.3, 74.7, 68.9, 60.4, 20.9. IR (Neat) $\nu_{\text{max}}$ 3290, 1741, 1602, 1493, 1224, 1018 cm$^{-1}$. MS (EI) m/z (%) 232 (M$^+2$, 2), 217 (16), 216 (100), 203 (32), 171 (30), 131 (3). Anal. calcd for C$_{14}$H$_{14}$O$_3$: C, 73.03; H, 6.13. Found: C, 73.12; H, 6.05.

1-(Anthracen-9-yl)prop-2-ynyl acetate (50u):
brown color semi-solid (572 mg, 43% yield). mp = 135–136 °C. $R_f$ = 0.6 (10:1 hexane/EtOAc); [Silica, UV and I$_2$]. $^1$H NMR (400 MHz, CDCl$_3$) $\delta$ 8.71 (d, $J$ = 9.2 Hz, 2H), 8.52 (s, 1H), 8.05–8.02 (m, 3H), 7.61 (t, $J$ = 8.0 Hz, 2H), 7.51 (t, $J$ =
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7.6 Hz, 2H), 2.70 (s, 1H), 2.11 (s, 3H). $^{13}$C NMR (101 MHz, CDCl$_3$) $\delta$ 169.9, 131.6, 129.9, 129.6, 129.2, 127.0, 126.6, 125.1, 124.6, 81.1, 75.9, 60.0, 20.9. IR (Neat) $\nu_{max}$ 3271, 1739, 1446, 1371, 1236, 1012 cm$^{-1}$. MS (El) $m/z$ (%) 216 (40), 215 (100). Anal. calcd for C$_{19}$H$_{14}$O$_2$: C, 83.19; H, 5.14. Found: C, 83.31; H, 5.08.

1-(2,6-Dichlorophenyl)prop-2-ynyl acetate (50v): colorless solid (756 mg, 54% yield). mp = 63–64 °C. $R_f$ = 0.46 (10:1 hexane/EtOAc); [Silica, UV and I$_2$]. $^1$H NMR (400 MHz, CDCl$_3$) $\delta$ 7.24 (dd, $J$ = 7.6, 8.8 Hz, 1H), 7.18 (s, 1H), 2.64 (s, 1H), 2.14 (s, 3H). $^{13}$C NMR (101 MHz, CDCl$_3$) $\delta$ 169.3, 135.6, 131.8, 130.4, 129.2, 78.0, 75.2, 61.4, 20.7. IR (KBr) $\nu_{max}$ 3271, 1738, 1439, 1369, 1232, 1022 cm$^{-1}$. MS (EI) $m/z$ (%) 217 (92), 215 (100), 165 (8), 147 (3). Anal. calcd for C$_{11}$H$_8$Cl$_2$O$_2$: C, 54.35; H, 3.32. Found: C, 54.29; H, 3.41.

1-(2,6-Dimethoxyphenyl)prop-2-ynyl acetate (50w): 58%, 823 mg; pale yellow solid. mp = 101–102 °C. $R_f$ = 0.47 (10:1 hexane/EtOAc); [Silica, UV and I$_2$]. $^1$H NMR (400 MHz, CDCl$_3$) $\delta$ 7.32–7.25 (m, 1H), 7.09 (s, 1H), 6.59 (d, $J$ = 8.4 Hz, 2H), 3.88 (s, 6H), 2.47 (s, 1H), 2.09 (s, 3H). $^{13}$C NMR (101 MHz, CDCl$_3$) $\delta$ 170.0, 158.8, 130.8, 113.2, 104.7, 81.0, 71.9, 56.6, 56.2, 21.1. IR (KBr) $\nu_{max}$ 3260, 1741, 1597, 1479, 1253, 1224, 1109, 1012 cm$^{-1}$. MS (EI) $m/z$ (%) 233 (M$^+$−1, 28), 213 (66), 192 (28), 177 (5), 166 (47), 128 (19), 79 (14). Anal. calcd for C$_{13}$H$_{14}$O$_4$: C, 66.66; H, 6.02. Found: C, 66.71; H, 6.08.

1-(1-Benzoyl-1H-indol-3-yl)prop-2-ynyl acetate (50y): thick yellow oil (482 mg, 38% yield). $R_f$ = 0.37 (6:1 hexane/EtOAc); [Silica, UV and I$_2$]. $^1$H NMR (400 MHz, CDCl$_3$) $\delta$ 8.40 (d, $J$ = 8.0 Hz, 1H), 7.82–7.72 (m, 3H), 7.63 (br t, $J$ = 6.4 Hz, 1H), 7.56 (t, $J$ = 7.6 Hz, 1H), 7.52 (s, 1H), 7.42 (t, $J$ = 7.2 Hz, 2H), 7.38 (t, $J$ = 6.8 Hz, 1H), 6.69 (s, 1H), 2.63 (s, 1H), 2.12 (s, 3H). $^{13}$C NMR (101 MHz, CDCl$_3$) $\delta$ 169.8, 168.6, 136.7, 134.0, 132.3, 129.3, 128.8, 128.0, 127.2, 125.7, 124.2, 119.7, 117.6, 116.7, 79.2, 74.8, 58.4, 21.0. IR (Neat) $\nu_{max}$ 3285, 3059, 2932, 1741, 1697, 1454, 1367, 1219, 1018 cm$^{-1}$. MS (El) $m/z$ (%) 290 (14), 258 (100), 257 (14), 172 (12), 154 (70), 105 (16). Anal. calcd for C$_{20}$H$_{15}$NO$_3$: C, 75.70; H, 4.76; N, 4.41. Found: C, 75.62; H, 4.69; N, 4.48.

8-Bromoct-1-yn-3-yl acetate (50ab): colorless oil (603 mg, 44% yield). $R_f$ = 0.37 (6:1 hexane/EtOAc); [Silica and I$_2$]. $^1$H NMR (400 MHz, CDCl$_3$) $\delta$ 5.42–5.30 (m, 1H), 3.40 (t, $J$ = 6.8 Hz, 2H), 2.45 (s, 1H), 2.08 (s, 3H), 1.87 (t, $J$ = 6.4 Hz, 2H), 1.79 (d, $J$ = 6.4 Hz, 2H), 1.53–1.39 (br d, $J$ = 6.4 Hz, 4H). $^{13}$C NMR (101 MHz, CDCl$_3$) $\delta$ 169.9, 81.1, 73.6, 63.6, 34.3, 33.6, 32.5, 27.6,
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24.0, 21.0. IR (Neat) \( \nu_{\text{max}} \): 3292, 2937, 1741, 1371, 1232, 1020 cm\(^{-1}\). MS (EI) \( m/z \) (%): 248 (M\(^+\)+1, 5), 221 (94), 219 (100), 189 (15), 155 (13), 139 (10), 107 (18). Anal. calcd for C\(_{10}\)H\(_{15}\)BrO\(_2\): C, 48.60; H, 6.12. Found: C, 48.71; H, 6.05.

6-(Tetrahydro-2H-pyran-2-yloxy)hex-1-yn-3-yl acetate (50ac):

\[
\text{Colorless oil (614 mg, 44% yield). } R_f = 0.56 (10:1 hexane/EtOAc); \text{[Silica and I\(_2\)]. } ^1H \text{ NMR (400 MHz, CDCl}_3) \delta 5.39 \text{ (t, } J = 4.4 \text{ Hz, 1H), 4.58 (s, 1H), 3.87–3.73 (m, 2H), 3.54–3.42 (m, 2H), 2.45 (s, 1H), 2.08 (s, 3H), 1.93–1.65 (m, 6H), 1.62–1.47 (m, 4H). } ^{13}C \text{ NMR (101 MHz, CDCl}_3) \delta 169.8, 98.7, 81.1, 73.6, 66.6, 63.5, 62.2, 31.5, 31.6, 25.4, 25.2, 20.9, 19.5. IR (Neat) \nu_{\text{max}} \text{ 2943, 1743, 1373, 1234, 1022 cm\(^{-1}\). MS (EI) \( m/z \) (%): 239 (M\(^+\)+1, 33), 215 (41), 181 (50), 157 (58), 133 (100), 101 (33), 85 (16). Anal. calcd for C\(_{12}\)H\(_{16}\)O\(_4\): C, 64.98; H, 8.39. Found: C, 64.79; H, 8.41.

8-Ethynyl-1,4-dioxaspiro[4.5]decan-8-yl acetate (50aj):

\[
\text{Pale yellow oil (617 mg, 43% yield). } R_f = 0.43(10:1 hexane/EtOAc); \text{[Silica and I\(_2\)]. } ^1H \text{ NMR (400 MHz, CDCl}_3) \delta 3.95 \text{ (s, 1H), 2.23–2.13 (m, 4H), 2.05 (s, 3H), 1.89–1.68 (m, 4H). } ^{13}C \text{ NMR (101 MHz, CDCl}_3) \delta 169.3, 122.4, 107.4, 82.8, 74.2, 73.5, 64.3, 34.2, 30.9, 21.8. IR (Neat) \nu_{\text{max}} \text{ 2932, 1699, 1585, 1485, 1280, 1145, } 841, 785 \text{ cm\(^{-1}\). MS (EI) \( m/z \) (%): 224 (M\(^+\), 6), 188 (12), 169 (100), 128 (18), 96 (4). Anal. calcd for C\(_{12}\)H\(_{16}\)O\(_4\): C, 64.27; H, 7.19. Found: C, 64.12; H, 7.21.

Gold-Catalyzed Hydration of Propargyl Acetates (50); General Procedure (GP-4):

\[ \text{A mixture of Ph}_3\text{PAuCl (4.9 mg, 0.01 mmol) and AgSbF}_6 (3.4 mg, 0.01 mmol) in dioxane (1.5 mL) was stirred in a Schlenk flask under an argon atmosphere for 30 minutes at an ambient temperature. This freshly prepared light pink colored gold-silver complex mixture was introduced to the Schlenk flask having 50 (1.0 mmol) followed by the addition of de-ionized water (54 } \mu\text{L, 3.0 mmol) at an ambient temperature. The resulting reaction mixture was stirred at room temperature. Upon complete consumption of precursor, the reaction mixture was diluted with dichloromethane (10 mL), and filtered over a small pad of Celite. The solvent was evaporated under reduced pressure and the crude reaction mixture was purified using column chromatography on silica gel.} \]
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2-Oxo-1-phenylpropyl acetate (51a):

colorless oil (186 mg, 97% yield). \( R_f = 0.38 \) (10:1 hexane/EtOAc). \(^1\)H NMR (400 MHz, CDCl\(_3\)) \( \delta \) 7.42 (br s, 5H), 5.99 (s, 1H), 2.21 (s, 3H), 2.13 (s, 3H). \(^1\)C NMR (101 MHz, CDCl\(_3\)) \( \delta \) 201.7, 170.3, 133.2, 129.4, 129.1, 128.1, 80.9, 26.1, 20.7. IR (Neat) \( \nu_{max} \) 2601, 1745, 1730, 1372, 1232, 1049 cm\(^{-1}\). MS (EI) \( m/z \) (%) 193 (M\(^+\)+1, 70), 179 (16), 165 (12), 147 (10), 133 (100), 105 (10), 74 (6). Anal. calcd for C\(_{11}\)H\(_{12}\)O\(_3\): C, 68.74; H, 6.29. Found: C, 68.85; H, 6.19.

1-(4-Fluorophenyl)-2-oxopropyl acetate (51b):

colorless oil (193 mg, 92% yield). \( R_f = 0.31 \) (6:1 hexane/EtOAc). \(^1\)H NMR (400 MHz, CDCl\(_3\)) \( \delta \) 7.44−7.34 (m, 2H), 7.15−7.04 (m, 2H), 5.95 (s, 1H), 2.19 (s, 3H), 2.11 (s, 3H). \(^1\)C NMR (101 MHz, CDCl\(_3\)) \( \delta \) 201.6, 170.2, 164.5, 162.0, 129.97, 129.89, 129.0, 116.2, 116.0, 80.0, 26.1, 20.6. \(^1\)F NMR (376 MHz, CDCl\(_3\)) \( \delta \) −111.7 (heptate, \( J = 3.8 \)). IR (Neat) \( \nu_{max} \) 2937, 1743, 1732, 1606, 1510, 1373, 1228, 1051 cm\(^{-1}\). MS (EI) \( m/z \) (%) 211 (M\(^+\)+1, 100), 197 (5), 167 (10). Anal. calcd for C\(_{11}\)H\(_{11}\)FO\(_3\): C, 62.85; H, 5.27. Found: C, 62.78; H, 5.31.

1-(4-Chlorophenyl)-2-oxopropyl acetate (51c):

colorless oil (213 mg, 94% yield). \( R_f = 0.50 \) (10:1 hexane/EtOAc). \(^1\)H NMR (400 MHz, CDCl\(_3\)) \( \delta \) 7.59−7.52 (m, 2H), 7.35−7.27 (m, 2H), 5.94 (s, 1H), 2.21 (s, 3H), 2.14 (s, 3H). \(^1\)C NMR (101 MHz, CDCl\(_3\)) \( \delta \) 201.3, 170.1, 132.2, 129.6, 123.7, 80.2, 26.1, 20.7. IR (Neat) \( \nu_{max} \) 2930, 1736, 1731, 1371, 1232, 1053 cm\(^{-1}\). MS (EI) \( m/z \) (%) 229 (M\(^+\)+2, 100), 227 (M\(^+\), 100), 213 (18), 209 (45), 185 (11), 167 (66), 139 (18). Anal. calcd for C\(_{11}\)H\(_{11}\)ClO\(_3\): C, 58.29; H, 4.89. Found: C, 58.41; H, 4.85.

1-(4-Bromophenyl)-2-oxopropyl acetate (51d):

pale yellow oil (241 mg, 89% yield). \( R_f = 0.50 \) (10:1 hexane/EtOAc). \(^1\)H NMR (400 MHz, CDCl\(_3\)) \( \delta \) 7.54 (d, \( J = 8.0 \) Hz, 2H), 7.30 (d, \( J = 8.0 \) Hz, 2H), 5.94 (s, 1H), 2.21 (s, 3H), 2.14 (s, 3H). \(^1\)C NMR (101 MHz, CDCl\(_3\)) \( \delta \) 201.3, 170.1, 132.2, 129.6, 123.7, 80.2, 26.1, 20.7. IR (Neat) \( \nu_{max} \) 2930, 1749, 1732, 1487, 1371, 1232, 1053 cm\(^{-1}\). MS (EI) \( m/z \) (%) 273 (M\(^+\)+2, 100), 272 (M\(^+\)+1, 8), 271 (M\(^+\), 97), 253 (41), 231 (11), 211 (38), 183 (5), 146 (13), 132 (19). Anal. calcd for C\(_{11}\)H\(_{11}\)BrO\(_3\): C, 48.73; H, 4.09. Found: C, 48.65; H, 4.13.

1-(3,4-Dichlorophenyl)-2-oxopropyl acetate (51e):

pale yellow oil (250 mg, 96% yield). \( R_f = 0.31 \) (8:1 hexane/EtOAc). \(^1\)H NMR (400 MHz, CDCl\(_3\)) \( \delta \) 7.52 (s, 1H), 7.48 (d, \( J = 8.4 \) Hz, 1H), 7.25 (d, \( J = 8.0 \) Hz, 1H), 5.89 (s, 1H), 2.20 (s, 3H), 2.14 (s, 3H). \(^1\)C NMR (101 MHz, CDCl\(_3\))
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δ201.1, 169.9, 133.7, 133.4, 131.0, 129.8, 127.1, 79.4, 26.1, 20.6. IR (Neat) νmax 2930, 1749, 1732, 1487, 1371, 1236, 1062 cm⁻¹. MS (EI) m/z (%) 263 (M⁺+2, 60), 261 (M⁺, 100), 215 (39), 201 (37), 181 (79), 149 (21). Anal. calcd for C₁₁H₁₀Cl₂O₃: C, 50.60; H, 3.86. Found: C, 50.66; H, 3.90.

1-(4-Formylphenyl)-2-oxopropyl acetate (51f):

colorless oil (193 mg, 88% yield). Rf = 0.33 (4:1 hexane/EtOAc). ¹H NMR (400 MHz, CDCl₃) δ 10.03 (s, 1H), 7.92 (d, J = 8.0 Hz, 2H), 7.61 (d, J = 8.0 Hz, 2H), 6.03 (s, 1H), 2.22 (s, 3H), 2.15 (s, 3H).

13C NMR (101 MHz, CDCl₃) δ 201.1, 191.5, 169.9, 139.5, 136.8, 130.2, 128.3, 80.3, 26.1, 20.6. IR (Neat) νmax 3011, 1745, 1730, 1695, 1425, 1371, 1234, 1053 cm⁻¹. MS (EI) m/z (%) 223 (M⁺+2, 18), 193 (46), 161 (100), 105 (11). Anal. calcd for C₁₂H₁₂O₄: C, 65.45; H, 5.49. Found: C, 65.32; H, 5.41.

2-Oxo-1-(4-tolyl)propyl acetate (51g):

colorless oil (196 mg, 95% yield). Rf = 0.54 (10:1 hexane/EtOAc). ¹H NMR (400 MHz, CDCl₃) δ 7.29 (d, J = 8.0 Hz, 2H), 7.22 (d, J = 8.0 Hz, 2H), 5.95 (s, 1H), 2.37 (s, 3H), 2.18 (s, 3H), 2.10 (s, 3H).

13C NMR (101 MHz, CDCl₃) δ 201.8, 170.4, 139.5, 130.2, 129.8, 128.1, 80.8, 26.1, 20.7. IR (Neat) νmax 3028, 1745, 1732, 1429, 1371, 1235, 1049 cm⁻¹. MS (EI) m/z (%) 207 (M⁺+1, 32), 188 (14), 177 (22), 161 (14), 147 (100), 135 (12), 119 (14). Anal. calcd for C₁₂H₁₄O₃: C, 69.88; H, 6.84. Found: C, 69.75; H, 6.92.

1-(3-Methoxyphenyl)-2-oxopropyl acetate (51h):

pale yellow oil (202 mg, 91% yield). Rf = 0.29 (10:1 hexane/EtOAc). ¹H NMR (400 MHz, CDCl₃) δ 7.35–7.27 (m, 1H), 7.00 (d, J = 7.6 Hz, 1H), 6.96–6.88 (m, 2H), 5.94 (s, 1H), 3.81 (s, 3H), 2.19 (s, 3H), 2.11 (s, 3H).

13C NMR (101 MHz, CDCl₃) δ 201.5, 170.2, 159.9, 134.4, 130.1, 120.3, 114.9, 113.3, 80.8, 55.3, 26.0, 20.6. IR (Neat) νmax 2941, 1747, 1732, 1429, 1371, 1235, 1045 cm⁻¹. MS (EI) m/z (%) 223 (M⁺+1, 22), 209 (13), 195 (9), 177 (11), 163 (100), 135(13). Anal. calcd for C₁₂H₁₄O₃: C, 64.85; H, 6.35. Found: C, 64.91; H, 6.41.

2-Oxo-1-(3-phenoxyphenyl)propyl acetate (51i):

pale yellow oil (247 mg, 87% yield). Rf = 0.35 (6:1 hexane/EtOAc). ¹H NMR (400 MHz, CDCl₃) δ 7.36 (br t, J = 7.2 Hz, 3H), 7.15 (br t, J = 7.2 Hz, 2H), 7.09 (s, 1H), 7.05–6.97 (m, 3H), 5.93 (s, 1H), 2.19 (s, 3H), 2.13 (s, 3H).

13C NMR (101 MHz, CDCl₃) δ 201.4, 170.1, 157.9, 156.4, 134.9, 130.3, 129.9, 123.8, 122.4, 119.1, 118.1, 80.5, 26.1, 20.7. IR (Neat) νmax 3065, 1747, 1730, 1585, 1444, 1373, 1238, 1053 cm⁻¹. MS (EI) m/z (%) 285 (M⁺+1, 100), 243 (13). Anal. calcd for C₁₇H₁₆O₄: C, 71.82; H, 5.67. Found: C, 71.92; H, 5.59.
Regioselective Hydration……

1-(3-Hydroxyphenyl)-2-oxopropyl acetate (51j):

colorless oil (176 mg, 85% yield). $R_f = 0.40$ (3:1 hexane/EtOAc). $^1$H NMR (400 MHz, CDCl$_3$) $\delta$ 7.32–7.24 (m, 1H), 6.97 (d, $J = 7.6$ Hz, 1H), 6.89 (br s, 2H), 6.42–6.23 (br s, 1H, for –OH), 5.95 (s, 1H), 2.18 (s, 3H), 2.14 (s, 3H). $^{13}$C NMR (101 MHz, CDCl$_3$) $\delta$ 202.9, 170.7, 156.7, 134.3, 130.5, 120.2, 116.8, 114.7, 80.8, 26.2, 20.7. IR (Neat) $\nu_{\text{max}}$ 3412, 1749, 1728, 1456, 1373, 1240, 1051 cm$^{-1}$. MS (EI) $m/z$ (%) 209 (M$^+$+1, 78), 181 (11), 149 (100), 121 (9), 79 (9). Anal. calcd for C$_{11}$H$_{12}$O$_4$: C, 63.45; H, 5.81. Found: C, 63.32; H, 5.86.

1-(3-(tert-Butyldiphenylsilyloxy)phenyl)-2-oxopropyl acetate (51k):
pale brown oil (362 mg, 81% yield). $R_f = 0.56$ (10:1 hexane/EtOAc). $^1$H NMR (400 MHz, CDCl$_3$) $\delta$ 7.70 (br t, $J = 1.2$ Hz, 4H), 7.47–7.33 (m, 6H), 7.13 (t, $J = 7.6$ Hz, 1H), 6.91 (d, $J = 7.6$ Hz, 1H), 6.79 (d, $J = 7.6$ Hz, 1H), 6.77 (s, 1H), 5.74 (s, 1H), 2.12 (s, 3H), 1.88 (s, 3H), 1.13 (s, 9H). $^{13}$C NMR (101 MHz, CDCl$_3$) $\delta$ 201.4, 170.2, 156.0, 135.5, 134.2, 132.5, 130.1, 129.9, 127.9, 120.7, 120.6, 119.4, 80.7, 26.5, 25.8, 20.7, 19.5. IR (Neat) $\nu_{\text{max}}$ 3414, 2962, 1749, 1732, 1602, 1429, 1259, 1107, 1016 cm$^{-1}$. MS (EI) $m/z$ (%) 445 (M$^+$−1, 5) 432 (39), 431 (100), 347 (23), 323 (50), 203 (13). Anal. calcd for C$_{27}$H$_{30}$O$_4$Si: C, 72.61; H, 6.77. Found: C, 72.45; H, 6.81.

1-(3-(tert-Butyldimethylsilyloxy)phenyl)-2-oxopropyl acetate (51l):
pale brown oil (257 mg, 80% yield). $R_f = 0.47$ (10:1 hexane/EtOAc). $^1$H NMR (400 MHz, CDCl$_3$) $\delta$ 7.32–7.22 (m, 1H), 7.00 (d, $J = 8.0$ Hz, 1H), 6.87 (br s, 2H), 5.91 (s, 1H), 2.19 (s, 3H), 2.10 (s, 3H), 0.98 (s, 9H), 0.20 (s, 6H). $^{13}$C NMR (101 MHz, CDCl$_3$) $\delta$ 201.5, 170.2, 156.0, 134.5, 134.2, 132.5, 130.1, 129.9, 127.9, 120.7, 120.6, 119.4, 80.7, 26.1, 25.6, 20.7, 18.2, −4.4. IR (Neat) $\nu_{\text{max}}$ 2955, 2932, 1745, 1732, 1602, 1446, 1371, 1238, 1051 cm$^{-1}$. MS (EI) $m/z$ (%) 321 (M$^+$−1, 5) 320 (3), 297 (32), 291 (11), 230 (16), 207 (100), 165 (6). Anal. calcd for C$_{17}$H$_{26}$O$_4$Si: C, 63.32; H, 8.13. Found: C, 63.51; H, 8.22.

1-(Benzo[d][1,3]dioxol-5-yl)-2-oxopropyl acetate (51m):
pale yellow thick oil (214 mg, 91% yield). $R_f = 0.35$ (6:1 hexane/EtOAc). $^1$H NMR (400 MHz, CDCl$_3$) $\delta$ 6.89 (d, $J = 8.0$ Hz, 1H), 6.85–6.81 (m, 2H), 5.99 (s, 2H), 5.88 (s, 1H), 2.18 (s, 3H), 2.11 (s, 3H). $^{13}$C NMR (101 MHz, CDCl$_3$) $\delta$ 201.6, 170.3, 148.6, 148.2, 126.6, 122.4, 108.7, 108.2, 101.4, 80.5, 26.1, 20.7. IR (Neat) $\nu_{\text{max}}$ 2961, 2985, 1732, 1711, 1442, 1369, 1232, 1101, 1033 cm$^{-1}$. MS (EI) $m/z$ (%) 237 (M$^+$+1, 100), 229 (10), 217 (5), 151 (8). Anal. calcd for C$_{13}$H$_{12}$O$_4$: C, 61.01; H, 5.12. Found: C, 61.25; H, 5.08.
Regioselective Hydration……

1-(2-Chlorophenyl)-2-oxopropyl acetate (51n):

pale yellow oil (211 mg, 93% yield). \( R_f = 0.44 \) (10:1 hexane/EtOAc). \(^1\)H NMR (400 MHz, CDCl\(_3\)) \( \delta \) 7.46 (d, \( J = 7.6 \) Hz, 1H), 7.38 (d, \( J = 7.2 \) Hz, 1H), 7.36–7.28 (m, 2H), 6.52 (s, 1H), 2.18 (s, 3H), 2.16 (s, 3H). \(^1\)C NMR (101 MHz, CDCl\(_3\)) \( \delta \) 200.8, 169.9, 133.9, 131.5, 130.6, 130.1, 129.7, 127.5, 76.9, 26.6, 20.6. IR (Neat) \( \nu_{\text{max}} \) 2930, 1749, 1738, 1442, 1371, 1230, 1043 cm\(^{-1}\). MS (EI) \( m/z \) (%) 229 (M\(^+\) + 2, 27), 228 (M\(^+\) + 1, 10), 227 (M\(^+\) , 100), 191 (16), 151 (13), 135 (8), 91 (8). Anal. calcd for C\(_{11}\)H\(_{11}\)ClO\(_3\): C, 58.29; H, 4.89. Found: C, 58.41; H, 4.82.

1-(2-Bromophenyl)-2-oxopropyl acetate (51o):

colorless oil (236 mg, 87% yield). \( R_f = 0.47 \) (10:1 hexane/EtOAc). \(^1\)H NMR (400 MHz, CDCl\(_3\)) \( \delta \) 7.64 (d, \( J = 8.0 \) Hz, 1H), 7.39–7.31 (m, 2H), 7.29–7.22 (m, 1H), 6.51 (s, 1H), 2.18 (s, 3H), 2.16 (s, 3H). \(^1\)C NMR (101 MHz, CDCl\(_3\)) \( \delta \) 200.8, 169.9, 133.3, 133.1, 130.8, 129.8, 124.3, 79.2, 26.8, 20.6. IR (Neat) \( \nu_{\text{max}} \) 2926, 1749, 1732, 1568, 1471, 1371, 1228, 1028 cm\(^{-1}\). MS (EI) \( m/z \) (%) 294 (M\(^+\) + Na, 64), 273 (M\(^+\) + 2, 17), 271 (M\(^+\) , 19), 245 (13), 211 (21), 181 (10), 149 (100), 131 (23), 103 (3). Anal. calcd for C\(_{11}\)H\(_{11}\)BrO\(_3\): C, 48.73; H, 4.09. Found: C, 48.81; H, 4.13.

1-(2,4-Dichlorophenyl)-2-oxopropyl acetate (51p):

pale yellow oil (245 mg, 94% yield). \( R_f = 0.48 \) (10:1 hexane/EtOAc). \(^1\)H NMR (400 MHz, CDCl\(_3\)) \( \delta \) 7.48 (s, 1H), 7.37–7.25 (m, 2H), 6.44 (s, 1H), 2.18 (s, 3H), 2.17 (s, 3H). \(^1\)C NMR (101 MHz, CDCl\(_3\)) \( \delta \) 200.4, 169.8, 133.9, 133.8, 132.4, 131.3, 127.9, 77.2, 26.8, 20.5. IR (Neat) \( \nu_{\text{max}} \) 3080, 2924, 1757, 1738, 1566, 1475, 1371, 1228, 1043 cm\(^{-1}\). MS (EI) \( m/z \) (%) 263 (M\(^+\) + 2, 3), 262 (M\(^+\) + 1, 13), 261 (M\(^+\) , 100), 259 (16), 247(25). Anal. calcd for C\(_{11}\)H\(_{10}\)Cl\(_2\)O\(_3\): C, 50.60; H, 3.86. Found: C, 50.65; H, 3.82.

1-(2,3-Dichlorophenyl)-2-oxopropyl acetate (51q):

colorless oil (246 mg, 94% yield). \( R_f = 0.35 \) (10:1 hexane/EtOAc). \(^1\)H NMR (400 MHz, CDCl\(_3\)) \( \delta \) 7.53 (dd, \( J = 8.0, 2.0 \) Hz 1H), 7.33 (dd, \( J = 8.0, 2.0 \) Hz, 1H), 7.31–7.25 (m, 1H), 6.56 (s, 1H), 2.21 (s, 3H), 2.20 (s, 3H). \(^1\)C NMR (101 MHz, CDCl\(_3\)) \( \delta \) 200.4, 169.8, 133.9, 133.9, 132.4, 131.3, 127.9, 77.2, 26.8, 20.5. IR (Neat) \( \nu_{\text{max}} \) 2926, 1747, 1732, 1566, 1454, 1371, 1228, 1060 cm\(^{-1}\). MS (EI) \( m/z \) (%) 265 (M\(^+\) + 4, 38), 263 (M\(^+\) + 2, 40), 261 (M\(^+\) , 48), 235 (19), 201 (61), 183 (100), 181(21), 147 (19), 81 (6). Anal. calcd for C\(_{11}\)H\(_{10}\)Cl\(_2\)O\(_3\): C, 50.60; H, 3.86. Found: C, 50.51; H, 3.92.
Regioselective Hydration……

1-(Naphthalen-1-yl)-2-oxopropyl acetate (51r):

- pale yellow thick oil (230 mg, 95% yield). \( R_f = 0.34 \) (10:1 hexane/EtOAc). \(^1\)H NMR (400 MHz, CDCl\(_3\)) \( \delta 8.13 \) (d, \( J = 8.0 \) Hz, 1H), 7.91 (br t, \( J = 8.0 \) Hz, 2H), 7.59 (t, \( J = 8.0 \) Hz, 2H), 7.51 (dd, \( J = 8.0 \), 16.0 Hz, 2H), 6.68 (s, 1H), 2.22 (s, 3H), 2.07 (s, 3H). \(^1\)C NMR (101 MHz, CDCl\(_3\)) \( \delta 201.8, 170.2, 134.1, 131.2, 130.3, 129.4, 128.9, 128.3, 127.2, 126.3, 125.3, 123.8, 79.4, 26.3, 10.8. IR (Neat) \( \nu_{max} \) 3053, 2926, 1743, 1730, 1512, 1427, 1371, 1229, 1045 cm\(^{-1}\). MS (EI) \( m/z \) (%) 243 (M\(^+\) 1, 100), 217 (6), 185 (31). Anal. calcd for C\(_{15}\)H\(_{14}\)O\(_3\): C, 74.36; H, 5.82. Found: C, 74.46; H, 5.78.

2-Oxo-1-\(\alpha\)-tolylpropyl acetate (51s):

- colorless oil (189 mg, 92% yield). \( R_f = 0.33 \) (10:1 hexane/EtOAc). \(^1\)H NMR (400 MHz, CDCl\(_3\)) \( \delta 7.31 − 7.21 \) (m, 4H), 6.25 (s, 1H), 2.45 (s, 3H), 2.18 (s, 3H), 2.09 (s, 3H). \(^1\)C NMR (101 MHz, CDCl\(_3\)) \( \delta 201.7, 170.3, 137.2, 131.8, 131.3, 129.4, 128.7, 126.7, 78.3, 26.3, 10.8. IR (Neat) \( \nu_{max} \) 2930, 1747, 1732, 1566, 1429, 1373, 1234, 1045 cm\(^{-1}\). MS (EI) \( m/z \) (%) 205 (M\(^+\) 1, 100), 161 (76), 135 (36). Anal. calcd for C\(_{12}\)H\(_{14}\)O\(_3\): C, 69.88; H, 6.84. Found: C, 69.95; H, 6.78.

1-(2-(Allyloxy)phenyl)-2-oxopropyl acetate (51t):

- colorless oil (238 mg, 96% yield). \( R_f = 0.34 \) (10:1 hexane/EtOAc). \(^1\)H NMR (400 MHz, CDCl\(_3\)) \( \delta 7.38 − 7.29 \) (m, 2H), 6.99 (t, \( J = 8.0 \) Hz, 1H), 6.94 (d, \( J = 8.0 \) Hz, 1H), 6.51 (s, 1H), 6.12 − 5.98 (m, 1H), 5.43 (d, \( J = 16 \) Hz, 1H), 5.31 (d, \( J = 8.0 \) Hz, 1H), 4.66 − 4.53 (m, 2H), 2.17 (s, 3H), 2.12 (s, 3H). \(^1\)C NMR (101 MHz, CDCl\(_3\)) \( \delta 201.9, 170.3, 155.8, 132.6, 130.5, 129.4, 122.2, 121.2, 117.8, 112.3, 74.9, 69.1, 26.3, 20.7. IR (Neat) \( \nu_{max} \) 3447, 3080, 2928, 1728, 1732, 1601, 1493, 1454, 1371, 1230, 1047 cm\(^{-1}\). MS (EI) \( m/z \) (%) 247 (M\(^+\) 1, 100), 207 (52), 187 (31), 163 (65), 121 (13). Anal. calcd for C\(_{14}\)H\(_{16}\)O\(_4\): C, 67.73; H, 6.50. Found: C, 67.85; H, 6.44.

1-(Anthracen-9-yl)-2-oxopropyl acetate (51u):

- pale brown solid (248 mg, 85% yield). mp = 113−114 °C. \( R_f = 0.38 \) (6:1 hexane/EtOAc). \(^1\)H NMR (400 MHz, CDCl\(_3\)) \( \delta 8.58 \) (s, 1H), 8.39 (br d, \( J = 7.6 \) Hz, 2H), 7.66 (s, 1H), 7.61 (t, \( J = 8.0 \) Hz, 2H), 7.53 (t, \( J = 8.0 \) Hz, 2H), 7.22 (s, 1H), 6.88 (s, 1H). \(^1\)C NMR (101 MHz, CDCl\(_3\)) \( \delta 202.2, 170.3, 131.6, 130.9, 130.3, 129.4, 127.4, 125.3, 124.4, 124.0, 75.6, 26.3, 20.8. IR (KB) \( \nu_{max} \) 2935, 1738, 1722, 1523, 1371, 1240, 1074 cm\(^{-1}\). MS (EI) \( m/z \) (%) 292 (M\(^+\) 16), 291 (M\(^+\) − 1, 49), 279 (20), 263 (73), 249 (24), 223 (45), 208 (100). Anal. calcd for C\(_{19}\)H\(_{16}\)O\(_3\): C, 78.06; H, 5.52. Found: C, 78.12; H, 5.47.
Regioselective Hydration……

1-(2,6-Dichlorophenyl)-2-oxopropyl acetate (51v):

![Chemical structure](image)

colorless thick oil (237 mg, 91% yield). Rf = 0.41 (8:1 hexane/EtOAc). 1H NMR (400 MHz, CDCl3) δ 7.37 (d, J = 8.0 Hz, 2H), 7.28 (d, J = 8.0 Hz, 1H), 6.88 (s, 1H), 2.20 (s, 3H), 2.18 (s, 3H). 13C NMR (101 MHz, CDCl3) δ 200.7, 169.6, 136.6, 131.5, 130.9, 129.0, 76.2, 26.3, 20.6. IR (Neat) νmax 2930, 1768, 1730, 1562, 1435, 1373, 1229, 1047 cm⁻¹. MS (EI) m/z (%) 263 (M⁺+2, 24), 261 (M⁺, 25), 241 (32), 233 (67), 201 (45), 183 (100), 169 (40), 135 (32). Anal. calcd for C11H10Cl₂O₃: C, 50.60; H, 3.86. Found: C, 50.71; H, 3.90.

1-(2,6-Dimethoxyphenyl)-2-oxopropyl acetate (51w):

![Chemical structure](image)

colorless solid (235 mg, 93% yield). mp = 122–123 °C. Rf = 0.32 (10:1 hexane/EtOAc). 1H NMR (400 MHz, CDCl3) δ 7.32 (br t, J = 8.0 Hz, 1H), 6.67 (s, 1H), 6.58 (d, J = 8.0 Hz, 2H), 3.80 (s, 6H), 2.15 (s, 3H), 2.04 (s, 3H). 13C NMR (101 MHz, CDCl3) δ 202.6, 170.4, 158.9, 131.3, 111.7, 104.1, 71.6, 55.9, 25.4, 20.9. IR (KBr) νmax 2943, 1747, 1728, 1595, 1479, 1369, 1190, 1111, 1039 cm⁻¹. MS (EI) m/z (%) 275 (M⁺+Na, 38), 253 (M⁺+1, 6), 247 (10), 223 (4), 193 (100), 181 (2), 165 (100). Anal. calcd for C13H16O₅: C, 61.90; H, 6.39. Found: C, 61.85; H, 6.43.

2-Oxo-1-(thiophen-2-yl)propyl acetate (51x):

![Chemical structure](image)

thick pale brown oil (149 mg, 75% yield). Rf = 0.30 (6:1 hexane/EtOAc). 1H NMR (400 MHz, CDCl3) δ 7.40 (br d, J = 4.8 Hz, 1H), 7.15 (s, 1H), 7.05 (br d, J = 3.6 Hz, 1H), 6.24 (s, 1H), 2.19 (s, 6H). 13C NMR (101 MHz, CDCl3) δ 200.5, 170.1, 134.5, 128.4, 127.7, 127.3, 75.8, 26.0, 20.6. IR (Neat) νmax 3277, 3109, 2930, 1747, 1732, 1435, 1373, 1232, 1039 cm⁻¹. MS (EI) m/z (%) 198 (M⁺, 10), 197 (M⁺−1, 100), 185 (5), 155 (10), 153 (8). Anal. calcd for C9H10O₃S: C, 54.53; H, 5.08. Found: C, 54.68; H, 5.15.

1-(1-Benzoyl-1H-indol-3-yl)-2-oxopropyl acetate (51y):

![Chemical structure](image)

thick yellow oil (261 mg, 78% yield). Rf = 0.37 (5:1 hexane/EtOAc). 1H NMR (400 MHz, CDCl3) δ 8.37 (d, J = 8.0 Hz, 1H), 7.74 (d, J = 7.2 Hz, 2H), 7.66 (t, J = 8.0 Hz, 1H), 7.37 (t, J = 7.2 Hz, 1H), 6.25 (s, 1H), 2.19 (s, 3H), 2.17 (s, 3H). 13C NMR (101 MHz, CDCl3) δ 200.9, 170.3, 168.4, 136.5, 133.9, 132.4, 129.2, 128.9, 128.3, 127.6, 125.9, 124.5, 119.9, 116.6, 114.3, 74.1, 26.2, 20.7. IR (Neat) νmax 3449, 2926, 1743, 1730, 1695, 1454, 1359, 1222, 1053 cm⁻¹. MS (EI) m/z (%) 335 (M⁺, 28), 334 (M⁺−1, 100), 292 (8), 229 (5), 121 (5). Anal. calcd for C20H17NO₄: C, 71.63; H, 5.11; N, 4.18. Found: C, 71.48; H, 5.25; N, 4.22.
Regioselective Hydration……

2-Oxononan-3-yl acetate (51z):
- Colorless oil (188 mg, 94% yield). $R_f = 0.39$ (7:1 hexane/EtOAc).
- $^1$H NMR (400 MHz, CDCl$_3$) $\delta$ 4.96 (dd, $J = 8.0, 4.0$ Hz, 1H), 2.14 (s, 6H), 1.77–1.70 (m, 2H), 1.40–1.25 (m, 8H), 0.87 (br t, $J = 8.0$ Hz, 3H).
- $^{13}$C NMR (101 MHz, CDCl$_3$) $\delta$ 205.4, 170.6, 78.8, 31.5, 30.3, 28.9, 26.1, 25.1, 22.5, 20.7, 14.0. IR (Neat) $\nu_{max}$ 2926, 1745, 1728, 1564, 1429, 1373, 1238, 1043 cm$^{-1}$. MS (EI) $m/z$ (%) 201 (M$^+$+1, 100), 183 (13), 181 (10), 141 (29), 123 (8). Anal. calcd for C$_{11}$H$_{20}$O$_3$: C, 65.97; H, 10.07. Found: C, 65.85; H, 10.15.

3-Oxo-1-phenylbutan-2-yl acetate (51aa):
- Colorless oil (175 mg, 85% yield). $R_f = 0.36$ (10:1 hexane/EtOAc).
- $^1$H NMR (400 MHz, CDCl$_3$) $\delta$ 7.31 (br q, $J = 7.2$ Hz, 2H), 7.25 (d, $J = 6.0$ Hz, 1H), 7.21 (d, $J = 7.2$, 2H), 5.21 (dd, $J = 4.8, 8.0$ Hz, 1H), 3.11 (dd, $J = 4.8, 14.4$ Hz, 1H), 3.01 (dd, $J = 8.4, 14$ Hz, 1H), 2.08 (s, 3H), 2.07 (s, 3H).
- $^{13}$C NMR (101 MHz, CDCl$_3$) $\delta$ 205.3, 170.4, 135.9, 129.3, 128.6, 127.1, 79.1, 36.7, 26.9, 20.6. IR (Neat) $\nu_{max}$ 3460, 2928, 1745, 1730, 1496, 1433, 1373, 1238, 1070 cm$^{-1}$. MS (EI) $m/z$ (%) 207 (M$^+$+1, 86), 187 (43), 179 (41), 161 (13), 147 (100), 129 (25). Anal. calcd for C$_{12}$H$_{14}$O$_3$: C, 69.88; H, 6.84. Found: C, 69.75; H, 6.88.

8-Bromo-2-oxooctan-3-yl acetate (51ab):
- Colorless oil (228 mg, 86% yield). $R_f = 0.62$ (10:1 hexane/EtOAc).
- $^1$H NMR (400 MHz, CDCl$_3$) $\delta$ 4.97 (q, $J = 4.4$ Hz, 1H), 3.93 (t, $J = 6.4$ Hz, 2H), 2.14 (s, 6H), 1.92–1.81 (m, 2H), 1.80–1.65 (m, 2H), 1.53–1.45 (m, 4H).
- $^{13}$C NMR (101 MHz, CDCl$_3$) $\delta$ 205.3, 170.6, 98.9, 78.4, 66.6, 62.4, 30.6, 27.2, 26.0, 25.4, 20.6, 19.6. IR (Neat) $\nu_{max}$ 2946, 2941, 1741, 1726, 1491, 1372, 1253, 1097 cm$^{-1}$. MS (EI) $m/z$ (%) 267 (M$^+$+2, 66), 265 (M$^+$, 62), 245 (12), 199 (100), 167 (24), 107 (6). Anal. calcd for C$_{10}$H$_{17}$BrO$_3$: C, 45.30; H, 6.46. Found: C, 45.21; H, 6.52.

2-Oxo-6-(tetrahydro-2H-pyran-2-yloxy)hexan-3-yl acetate (51ac):
- Colorless oil (201 mg, 78% yield). $R_f = 0.47$ (10:1 hexane/EtOAc).
- $^1$H NMR (400 MHz, CDCl$_3$) $\delta$ 4.99 (br s, 1H), 4.52 (s, 1H), 3.83–3.66 (m, 2H), 3.48–3.33 (m, 2H), 2.12 (s, 3H), 2.11 (s, 3H), 1.92–1.84 (m, 1H), 1.84–1.72 (m, 2H), 1.72–1.58 (m, 3H), 1.58–1.42 (m, 4H).
- $^{13}$C NMR (101 MHz, CDCl$_3$) $\delta$ 205.1, 170.5, 98.9, 78.4, 66.6, 62.4, 30.6, 27.2, 26.0, 25.4, 20.6, 19.6. IR (Neat) $\nu_{max}$ 2941, 1741, 1726, 1491, 1372, 1253, 1097 cm$^{-1}$. MS (EI) $m/z$ (%) 242 (M$^+$+1, 16), 241 (M$^+$, 100), 140 (10), 108 (8). Anal. calcd for C$_{13}$H$_{22}$O$_5$: C, 60.45; H, 8.58. Found: C, 60.32; H, 8.49.

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Regioselective Hydration......

3,5-Dimethyl-2-oxohexan-3-yl acetate (51ad):

- Colorless oil (174 mg, 94% yield). 
- $R_f = 0.60$ (19:1 hexane/EtOAc).
- $^1$H NMR (400 MHz, CDCl$_3$) $\delta$ 2.11 (s, 3H), 2.07 (s, 3H), 1.81–1.59 (m, 3H), 1.50 (s, 3H), 0.93 (s, 6H).
- $^{13}$C NMR (101 MHz, CDCl$_3$) $\delta$ 206.2, 169.7, 86.2, 44.1, 24.2, 23.6, 23.4, 23.5, 20.8, 20.1. IR (Neat) $\nu_{\text{max}}$ 2959, 1738, 1718, 1469, 1371, 1253, 1130 cm$^{-1}$.
- MS (EI) $m/z$ (%) 187 (100), 159 (32), 127 (78), 109 (13). Anal. calcd for C$_{10}$H$_{18}$O$_3$: C, 64.49; H, 9.74. Found: C, 64.55; H, 9.69.

3-Oxo-2-phenylbutan-2-yl acetate (51ae):

- Pale yellow oil (156 mg, 76% yield). 
- $R_f = 0.41$ (10:1 hexane/EtOAc).
- $^1$H NMR (400 MHz, CDCl$_3$) $\delta$ 7.46 (d, $J = 8.0$ Hz, 2H), 7.38 (t, $J = 8.0$ Hz, 2H), 7.33 (d, $J = 8.0$ Hz, 1H), 2.26 (s, 3H), 1.95 (s, 3H), 1.85 (s, 3H).
- $^{13}$C NMR (101 MHz, CDCl$_3$) $\delta$ 203.6, 169.9, 138.5, 128.7, 128.1, 124.7, 87.4, 23.5, 22.8, 21.3. IR (Neat) $\nu_{\text{max}}$ 3007, 2941, 1739, 1724, 1494, 1448, 1255, 1105, 1018 cm$^{-1}$. MS (EI) $m/z$ (%) 205 (M$^+$−1, 100), 181 (5), 108 (10). Anal. calcd for C$_{12}$H$_{14}$O$_3$: C, 69.88; H, 6.84. Found: C, 69.95; H, 6.81.

2-(4-Chlorophenyl)-3-oxobutan-2-yl acetate (51af):

- Pale yellow oil (197 mg, 82% yield). 
- $R_f = 0.39$ (6:1 hexane/EtOAc).
- $^1$H NMR (400 MHz, CDCl$_3$) $\delta$ 7.36 (q, $J = 8.8$ Hz, 4H), 2.25 (s, 3H), 1.94 (s, 3H), 1.82 (s, 3H).
- $^{13}$C NMR (101 MHz, CDCl$_3$) $\delta$ 203.3, 169.9, 137.1, 134.2, 128.9, 126.3, 87.1, 23.6, 22.9, 21.3. IR (Neat) $\nu_{\text{max}}$ 2941, 1741, 1726, 1491, 1372, 1253, 1097 cm$^{-1}$. MS (EI) $m/z$ (%) 242 (M$^+$+1, 16), 241 (M$^+$, 100), 140 (10), 108 (8). Anal. calcd for C$_{12}$H$_{13}$ClO$_3$: C, 59.88; H, 5.44. Found: C, 59.76; H, 5.41.

1-Acetylcyclopentyl acetate (51ag):

- Colorless oil (163 mg, 96% yield). 
- $R_f = 0.45$ (10:1 hexane/EtOAc).
- $^1$H NMR (400 MHz, CDCl$_3$) $\delta$ 2.22−2.13 (m, 2H), 2.12 (s, 3H), 2.10 (s, 3H), 1.93−1.83 (m, 2H), 1.82−1.59 (m, 4H). $^1$C NMR (101 MHz, CDCl$_3$) $\delta$ 205.7, 170.8, 93.8, 35.5, 24.8, 24.3, 21.0. IR (Neat) $\nu_{\text{max}}$ 2962, 1738, 1716, 1435, 1371, 1257, 1176, 1020 cm$^{-1}$. MS (EI) $m/z$ (%) 185 (M$^+$+14, 100), 171 (M$^+$+1, 93), 167 (16), 153 (52), 135 (40), 111 (20), 91 (6). Anal. calcd for C$_9$H$_{14}$O$_3$: C, 63.51; H, 8.29. Found: C, 63.45; H, 8.32.

1-Acetylcyclohexyl acetate (51ah):

- Colorless oil (156 mg, 85% yield). 
- $R_f = 0.48$ (10:1 hexane/EtOAc).
- $^1$H NMR (400 MHz, CDCl$_3$) $\delta$ 2.11 (s, 3H), 2.07 (s, 3H), 2.02 (d, $J = 12.0$ Hz, 2H), 1.62 (br t, $J = 12.0$ Hz, 5H), 1.53 (q, $J = 12.0$ Hz, 2H), 1.25 (br q, $J = 12.0$ Hz, 1H). $^{13}$C NMR
Regioselective Hydration……

(101 MHz, CDCl$_3$) $\delta$ 207.3, 170.2, 85.2, 30.7, 25.0, 23.6, 21.1, 21.0. IR (Neat) $\nu_{max}$ 2941, 1738, 1716, 1452, 1371, 1240, 1140, 1018 cm$^{-1}$. MS (EI) $m/z$ (%) 185 (M$^+$+1, 68), 168 (4), 167 (47), 149 (4), 126 (8), 125 (100). Anal. calcd for C$_{10}$H$_{16}$O$_3$: C, 65.19; H, 8.75. Found: C, 65.35; H, 8.71.

1-Acetylcycloheptyl acetate (51ai):

A colorless oil (180 mg, 91% yield). $R_f$ = 0.42 (7:1 hexane/EtOAc). $^1$H NMR (400 MHz, CDCl$_3$) $\delta$ 2.10 (s, 3H), 2.07 (s, 3H), 2.03–1.87 (m, 4H), 1.56 (br s, 8H). $^1$C NMR (101 MHz, CDCl$_3$) $\delta$ 207.1, 170.4, 89.2, 34.4, 29.4, 23.6, 22.8, 21.1. IR (Neat) $\nu_{max}$ 2930, 1736, 1720, 1458, 1371, 1251, 1147, 1024 cm$^{-1}$. MS (EI) $m/z$ (%) 197 (M$^+$–1, 100), 185 (60), 181 (95), 141 (50), 125 (86), 93 (27). Anal. calcd for C$_{11}$H$_{18}$O$_3$: C, 66.64; H, 9.15. Found: C, 66.71; H, 9.22.

8-Acetyl-1,4-dioxaspiro[4.5]decan-8-yl acetate (51aj):

A pale yellow oil (194 mg, 80% yield). $R_f$ = 0.51 (6:1 hexane/EtOAc). $^1$H NMR (400 MHz, CDCl$_3$) $\delta$ 4.01–3.91 (m, 4H), 2.16 (s, 6H), 2.15–2.10 (m, 2H), 2.12–1.97 (m, 2H), 1.86–1.75 (m, 2H), 1.73–1.63 (m, 2H). $^1$C NMR (101 MHz, CDCl$_3$) $\delta$ 206.4, 170.3, 107.5, 83.9, 64.4, 64.3, 30.0, 28.8, 24.0, 21.0. IR (Neat) $\nu_{max}$ 2959, 1732, 1714, 1444, 1371, 1230, 1107, 1025 cm$^{-1}$. MS (EI) $m/z$ (%) 243 ((M$^+$+1, 38), 225 (20), 205 (2), 184 (22), 183 (100), 139 (6), 87 (16). Anal. calcd for C$_{12}$H$_{18}$O$_5$: C, 59.49; H, 7.49. Found: C, 59.71; H, 7.38.

Gold-Catalyzed Hydration of TMS-Substituted Propargyl Acetates (54); General Procedure (GP-5):

A mixture of Ph$_3$PAuCl (4.9 mg, 0.01 mmol) and AgSbF$_6$ (3.4 mg, 0.01 mmol) in dioxane (1.5 mL) was stirred in a Schlenk flask under an argon atmosphere for 30 minutes at an ambient temperature. This freshly prepared light pink colored gold-silver complex mixture was introduced to the Schlenk flask having 54 (1.0 mmol) followed by the addition of de-ionized water (54 µL, 3.0 mmol) at an ambient temperature. The resulting reaction mixture was stirred at room temperature. The reaction mixture was diluted with dichloromethane (10 mL), and filtered over a small pad of Celite. The solvent was evaporated under reduced pressure and the crude reaction mixture was purified using column chromatography on silica gel.
Regioselective Hydration......

2-Oxo-1-phenylpropyl acetate (51a):
Following the general procedure (GP-5) 51a was isolated in 82% (157 mg) yield as colorless oil. Analytical data concurrently matching with the values mentioned in this thesis (see: page 52).

1-(4-Bromophenyl)-2-oxopropyl acetate (51d):
Following the general procedure (GP-5) 51d was isolated in 91% (246 mg) yield as pale yellow oil. Analytical data concurrently matching with the values mentioned in this thesis (see: page 52).

1-(3-Methoxyphenyl)-2-oxopropyl acetate (51h) + 1-(3-Methoxyphenyl)prop-2-ynyl acetate (50h):
\(^1\)H NMR of the crude reaction mixture shows the formation of products 51h and 50h in 70% and 30% NMR yields, respectively.

1-(2-Chlorophenyl)-2-oxopropylacetate (51n) and 1-(2-Chlorophenyl)prop-2-ynyl acetate (50n):
\(^1\)H NMR of the crude reaction mixture shows the formation of products 51n and 50n in 28% and 72% NMR yields, respectively.

1-(Thiophen-2-yl)prop-2-ynyl acetate (50x) and 1-(Thiophen-2-yl)-3-(trimethylsilyl)prop-2-ynyl acetate (54x):
\(^1\)H NMR of the crude reaction mixture shows the formation of products 50x and 54x in 59% and 41% NMR yields, respectively.

3-Oxo-1-phenylbutan-2-yl acetate (51aa):
Following the general procedure (GP-5), the compound 51aa was isolated in 83% (171 mg) yield as yellow oil. Analytical data concurrently matching with the values mentioned in this thesis (see: page 58).

1-Acetylcyclohexyl acetate (51ag):
\(^1\)H NMR of the crude reaction mixture shows the formation of products 51ah and 50ah in 79% and 21% NMR yields, respectively.
Regioselective Hydration......

(S)-2-Oxo-1-phenylpropyl acetate (56):

Following the general procedure (GP-4), (R)-1-phenylprop-2-ynyl acetate (55; 174 mg, 1.0 mmol) reacted with the mixture of Ph3PAuCl (4.9 mg, 0.01 mmol) and AgSbF6 (3.4 mg, 0.01 mmol) in dioxane (1.5 mL) and H2O (54 µL, 3.0 mmol) for 5 h. Upon filtration over Celite and evaporation, the crude mixture was purified by silica gel column chromatography eluting with hexane: ethyl acetate (10:1) to afford 56 (176 mg) in 92% yield with 76% ee (determined by chiral HPLC) as colorless oil. Optical rotation of (S)-56 (c = 0.2 in CHCl3) was found; [α]D = + 9.0 at 25 °C.

Preparation of tert-butyl-3-(2-hydroxy-4-(trimethylsilyl)but-3-ynyl)-1H-indole-1-carboxylate (69):

thick yellow oil (1.46 g, 89% yield). Rf = 0.4 (12:1 hexane/EtOAc). 1H NMR (400 MHz, CDCl3) δ 8.15 (br s, 1H), 7.62 (d, J = 8.0 Hz, 1H), 7.54 (s, 1H), 7.35–7.31 (m, 1H), 7.27–7.23 (m, 1H), 4.67 (d, J = 4.0 Hz, 1H), 3.13 (t, J = 4.0 Hz, 2H), 2.10 (s, 1H), 1.67 (s, 9H), 0.15 (s, 9 H). 13C NMR (101 MHz, CDCl3) δ 149.6, 135.5, 130.7, 124.6, 124.4, 122.5, 119.3, 115.3, 115.2, 106.1, 90.2, 83.6, 62.5, 33.5, 28.2, −0.2. IR (Neat) νmax 2964, 2181, 1745, 1608, 1456, 1099 cm−1. MS (EI) m/z (%) 358 (M+ + 1, 100), 314 (13), 279 (13), 163 (11), 135 (11). Anal. calcd for C20H27NO3Si: C, 67.19; H, 7.61; N, 3.92. Found: C, 67.25; H, 7.58; N, 3.88.

tert-Butyl-3-(2-acetoxybut-3-ynyl)-1H-indole-1-carboxylate (70):

thick yellow oil (532 mg, 83% yield). Rf = 0.30 (19:1 hexane/EtOAc). 1H NMR (400 MHz, CDCl3) δ 8.21–8.11 (br s, 1H), 7.61 (d, J = 8.0 Hz, 1H), 7.54 (s, 1H), 7.32 (t, J = 8.0 Hz, 1H), 7.26 (d, J = 7.2 Hz, 1H), 5.64 (q, J = 6.8 Hz, 1H), 3.21 (q, J = 2.0 Hz, 2H), 2.48 (s, 1H), 2.07 (s, 3H), 1.68 (s, 9H). 13C NMR (101 MHz, CDCl3) δ 169.8, 149.7, 135.3, 130.5, 124.6, 122.5, 119.1, 115.3, 114.8, 83.7, 80.9, 74.3, 63.5, 30.6, 28.2, 21.0. IR (Neat) νmax 2978, 1730, 1612, 1452, 1371, 1226, 1151, 1022 cm−1. MS (EI) m/z (%) 328 (M+1, 100), 296 (43), 183 (14), 100 (8). Anal. calcd for C19H21NO4: C, 69.71; H, 6.47; N, 4.28. Found: C, 69.75; H, 6.41; N, 4.34.

tert-Butyl 3-(2-hydroxy-3-oxobutyl)-1H-indole-1-carboxylate(71):

thick yellow oil (350 mg, 83% yield). Rf = 0.32 (10:1 hexane/EtOAc). 1H NMR (400 MHz, CDCl3) δ 8.22–8.13 (br s, 1H), 7.57 (d, J = 8.0 Hz, 1H), 7.46 (s, 1H), 7.33 (t, J = 8.4 Hz, 1H), 7.27 (d, J = 6.0 Hz, 1H), 5.28 (q, J = 5.2 Hz, 1H), 3.21 (dd, J = 4.8, 15.2 Hz, 1H), 3.13 (dd, J = 7.6, 15.2 Hz, 1H), 2.14 (s, 3H), 2.10 (s, 3H), 1.68 (s, 9H). 13C NMR (101 MHz, CDCl3) δ 205.3, 170.4, 149.6, 135.3, 130.3, 124.6, 124.3, 122.6, 118.9, 115.3, 114.9, 83.8, 78.2, 28.2, 26.9, 26.2, 20.7. IR (Neat) νmax 2980, 1743, 1732, 1606, 1454, 1371, 1255, 1157, 1089 cm−1. MS (EI) m/z (%) 344 (M+−1, 15), 304 (34), 62
Regioselective Hydration……

277 (25), 244 (100), 200 (12), 184 (64). Anal. calcd for C_{19}H_{23}NO_{5}: C, 66.07; H, 6.71; N, 4.06. Found: C, 65.88; H, 6.78; N, 4.12.

3-Hydroxy-4-(1H-indol-3-yl)butan-2-one (actinopolymorphol B; 63):

A thick yellow oil (115 mg, 56% yield). R_f = 0.18 (5:1 hexane/EtOAc). 

^1^H NMR (400 MHz, CDCl_3) \( \delta \) 8.10 (br s, 1H), 7.64 (d, \( J = 8.0 \) Hz, 1H), 7.37 (d, \( J = 8.0 \) Hz, 1H), 7.27 (s, 1H), 7.22 (t, \( J = 7.2 \) Hz, 1H), 7.15 (t, \( J = 7.2 \) Hz, 1H), 4.53 (d, \( J = 4.8 \) Hz, 1H), 3.47 (d, \( J = 4.0 \) Hz, 1H), 3.32 (dd, \( J = 14.8, 4.4 \) Hz, 1H), 3.14 (dd, \( J = 15.2, 6.6 \) Hz, 1H), 2.21 (s, 3H). 

^13^C NMR (101 MHz, CDCl_3) \( \delta \) 209.8, 136.1, 127.5, 122.9, 122.2, 119.6, 118.7, 111.2, 110.4, 77.1, 29.6, 25.9. IR (Neat) \( \nu_{\text{max}} \) 3546, 2959, 1732, 1444, 1371, 1230, 1107, 1025 cm\(^{-1}\). MS (EI) \( m/z \) (%) 205 (M^+2, 38), 204 ((M^+1, 100). Anal. calcd for C_{12}H_{11}NO_{2}: C, 70.92; H, 6.45; N, 6.89. Found: C, 70.85; H, 6.39; N, 6.81.
Preparation of 76’’ from 50’; General Procedure (GP-6):39

A solution of trimethylsilylacetylene (0.69 mL, 6.0 mmol) in THF (50 mL) was stirred in a 100 mL oven-dried two-necked round bottom flask under an argon atmosphere at −70 °C. n-Butyllithium (4.0 mL, 6.0 mmol, 1.60 M in THF) was introduced over 30 minutes at −70 °C. After an additional 1 h stirring, a solution of aldehyde (50’, 5.0 mmol) in THF (10 mL) was added at −70 °C. The resulting mixture was stirred for 1 h and warmed to room temperature slowly and continued for 30 minutes. The reaction mixture was quenched with saturated NH₄Cl aqueous solution (20 mL) at 0 °C. The organic layer was separated; the aqueous layer was extracted with Et₂O (2 × 20 mL). The combined extracts were washed with water (2 × 20 mL), brine (25 mL) and dried over Na₂SO₄. Solvent was filtered and evaporated under reduced pressure. The crude residue was further used for the bromination reaction.

A solution of crude residue (3.0 mmol) and AgNO₃ (101 mg, 0.6 mmol) in acetone (10 mL) was stirred at room temperature for 25 min. NBS (796 mg, 4.5 mmol) was added to this reaction mixture. The reaction mixture was stirred at rt until the starting material completely consumed; the progress of the reaction was periodically monitored through TLC. The reaction mixture was diluted with ethyl acetate, washed with saturated Na₂S₂O₃ solution (2 × 20 mL) and brine (10 mL). The organic layer was separated, dried over Na₂SO₄, filtered, and concentrated under vacuum. The crude residue was purified using column chromatography on silica gel.

Synthesis of 76 from 76’’ through Acylation of –OH moiety; General Procedure (GP-7):39

To a solution of 76’’ (2.0 mmol) in dichloromethane (10 mL), DMAP (25 mg, 0.2 mmol), Et₃N (0.8 mL, 6.0 mmol) and acetic anhydride (2.5 mL, 2.6 mmol) were added successively under an argon atmosphere at ambient temperature. The resulting reaction mixture was stirred for 1 h at an ambient temperature. Water (20 mL) was added to the reaction mixture. The organic layer was extracted with CH₂Cl₂ (2 × 20 mL). The combined extracts were washed with brine solution (25 mL) and dried over Na₂SO₄. Solvent was filtered and evaporated under reduced pressure. The crude residue was purified using column chromatography on silica gel.
Preparation Chloro and Iodo Substituted Propargyl Acetate

\[
\begin{align*}
\text{O} & \quad \text{TMS} \\
R & \quad \text{H} \\
\text{THF}, -70^\circ \text{C} \\
n\text{BuLi} & \quad \text{rt}, 30 \text{ min} \\
\text{K}_2\text{CO}_3 & \quad \text{MeOH, rt, 12 h} \\
n\text{BuLi}, \text{NCS} & \quad \text{THF}, -78^\circ \text{C} \\
\text{Ac}_2\text{O} & \quad \text{DMAP} \\
& \quad \text{DCM, rt, 1 h} \\
\text{Cl} & \quad \text{Ac} \\
\end{align*}
\]

Preparation of 50"; General Procedures (GP-8):
A solution of trimethylsilylacetylene (0.69 mL, 6.0 mmol) in THF (50 mL) was stirred in a 100 mL oven-dried two-necked round bottom flask under an argon atmosphere at −70 °C. n-Butyllithium (4.0 mL, 6.0 mmol, 1.60 M in THF) was introduced over 30 minutes at −70 °C. After an additional 1 h stirring, a solution of aldehyde (50', 5.0 mmol) in THF (10 mL) was added at −70 °C. The resulting mixture was stirred for 1 h and warmed to room temperature slowly and continued for 30 minutes. The reaction mixture was quenched with saturated NH$_4$Cl aqueous solution (20 mL) at 0 °C. The organic layer was separated, the aqueous layer was extracted with Et$_2$O (2 × 20 mL). The combined extracts were washed with brine (25 mL) and dried over Na$_2$SO$_4$. Solvent was filtered and evaporated under reduced pressure. The crude residue was subsequently used for the desilylation reaction.

A solution of crude residue (5.0 mmol) in methanol (15 mL) was stirred with K$_2$CO$_3$ (1.7 g, 12.5 mmol) under an argon atmosphere at ambient temperature overnight. After the reaction was over methanol was evaporated under reduced pressure. The reaction mixture was diluted with ethyl acetate (50 mL) and washed with water (2 × 20 mL) and brine (10 mL). The organic layer was separated, dried over Na$_2$SO$_4$ filtered, and concentrated under vacuum. The crude residue was purified using column chromatography on silica gel.

Preparation of 81' from 50"; General Procedure (GP-9):\textsuperscript{37c}
A solution of a propargyl alcohol 50" (3.0 mmol) in THF (10 mL) was stirred at −78 °C for 10 min. After being stirred at this temperature, NCS (877 mg, 6.6 mmol) was added to the reaction mixture. The reaction mixture was stirred at −78 °C for 1 h and slowly warmed to room temperature. The reaction mixture was quenched with H$_2$O (15 mL) and extracted with ethyl acetate (2 × 20 mL). The organic layer was separated, dried over Na$_2$SO$_4$, filtered, and concentrated under vacuum. The crude residue was purified using column chromatography on silica gel.
Regioselective Hydration......

Preparation of 81 from 81′; General Procedure (GP-10):
To a solution of 81′ (2.0 mmol) in dichloromethane (15 mL), DMAP (25 mg, 0.2 mmol), Et₃N (0.8 mL, 6.0 mmol) and acetic anhydride (2.5 mL, 2.6 mmol) were added successively under an argon atmosphere at ambient temperature. The resulting reaction mixture was stirred for 1 h at an ambient temperature. Water (20 mL) was added to the reaction mixture. The organic layer was extracted with CH₂Cl₂ (2 × 20 mL). The combined extracts were washed with brine solution (25 mL) and dried over Na₂SO₄. Solvent was filtered and evaporated under the reduced pressure. The crude residue was purified using column chromatography on silica gel.

Preparation of 82′ from 50′′; General Procedure (GP-11):
A solution of 50′′ (3.0 mmol) and AgNO₃ (101 mg, 0.6 mmol) in DMF (5.0 mL) was stirred at room temperature for 25 min. NIS (1.0 g, 4.5 mmol) was added to this reaction mixture. The reaction mixture was stirred at rt until the starting material completely consumed; the progress of the reaction was periodically monitored through TLC. The reaction mixture was diluted with ethyl acetate, washed with saturated Na₂S₂O₃ solution (2 × 20 mL) and brine (10 mL). The organic layer was separated, dried over Na₂SO₄, filtered, and concentrated under vacuum. The crude residue was purified using column chromatography on silica gel.

Preparation of 82 from 82′; General Procedure (GP-12):
To a solution of 82′ (2.0 mmol) in dichloromethane (15 mL), DMAP (25 mg, 0.2 mmol), Et₃N (0.8 mL, 6.0 mmol) and acetic anhydride (2.5 mL, 2.6 mmol) were added successively under an argon atmosphere at ambient temperature. The resulting reaction mixture was stirred for 1 h at an ambient temperature. Water (20 mL) was added to the reaction mixture. The organic layer was extracted with CH₂Cl₂ (2 × 20 mL). The combined organic extracts were washed with brine (25 mL) and dried over Na₂SO₄. Solvent was filtered and evaporated under the reduced pressure. The crude residue was purified using column chromatography on silica gel.

4-Bromo-1-phenylbut-3-yn-2-yl acetate (76a):
yellow oil (957 mg, 43% yield). Rf = 0.55 (19:1 hexane/EtOAc); [UV and I₂]. ¹H NMR (400 MHz, CDCl₃) δ 7.36–7.21 (m, 5H), 5.54 (t, J = 4.0 Hz, 1H), 3.08 (d, J = 8.0 Hz, 2H), 2.05 (s, 3H). ¹³C NMR (101 MHz, CDCl₃) δ 169.7, 135.5, 129.6, 128.4, 127.1, 77.2, 65.1, 47.0, 41.0, 20.8. IR (Neat) νmax 3065, 3030, 2934, 2218, 1745, 1496, 1454, 1371, 1228, 1022, 702 cm⁻¹. MS (EI) m/z (%) 268 (M⁺+2, 100), 156 (15). Anal. calcd for C₁₁H₁₁BrO₂: C, 53.96; H, 4.15. Found: C, 53.86; H, 4.21.
Regioselective Hydration……

3-Bromo-1-phenylprop-2-ynyl acetate (76b):

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\text{pale yellow oil (1.10 g, 46% yield). } R_f = 0.26 \text{ (9:1 hexane/EtOAc). [Silica, UV and I₂]. } ^1H \text{ NMR (400 MHz, CDCl}_3) \delta 7.51 \text{ (d, } J = 6.8 \text{ Hz, 2H), 7.40 \text{ (d, } J = 5.6 \text{ Hz, 3H), 6.46 \text{ (s, 1H), 2.12 \text{ (s, 3H). } ^1C \text{ NMR (101 MHz, CDCl}_3) } \delta 169.7, 136.4, 129.1, 128.8, 127.7, 76.9, 66.1, 48.1, 21.0. IR (Neat) } \nu_{\text{max}} 2222, 1739, 1454, 1373, 1228, 1018 \text{ cm}^{-1}. MS (EI) m/z (\%) 254 (M}^+1, 253 \text{ (M}^+1, 100). \text{ Anal. calcd for C}_{11}H_{9}BrO_2: C, 52.20; H, 3.58. \text{ Found: C, 52.36; H, 3.51.}
\]

3-Bromo-1-(4-fluorophenyl)prop-2-ynyl acetate (76c):

\[
\text{colorless solid (857 mg, 39% yield). mp } = 49–50 \text{ °C. } R_f = 0.56 \text{ (30:1 hexane/EtOAc); [Silica, UV and I₂]. } ^1H \text{ NMR (400 MHz, CDCl}_3) \delta 7.49 \text{ (br t, } J = 5.6 \text{ Hz, 2H), 7.08 \text{ (t, } J = 8.8 \text{ Hz, 2H), 6.42 \text{ (s, 1H), 2.11 \text{ (s, 3H). } ^1C \text{ NMR (101 MHz, CDCl}_3) } \delta 169.6, 163.1 \text{ (d, } J = 249 \text{ Hz), 132.4, 129.7 \text{ (d, } J = 8.4 \text{ Hz), 115.7 \text{ (d, } J = 21.8 \text{ Hz), 76.5, 65.5, 48.4, 21.0. } ^19F \text{ NMR (470 MHz, CDCl}_3) \delta -110.72 \text{ (q, } J = 5.2 \text{ Hz). IR (KBr) } \nu_{\text{max}} 2220, 1732, 1604, 1512, 1369, 1226, 1059 \text{ cm}^{-1}. MS (EI) m/z (\%) 273 (M}^+2, 92), 271 (M}^+1, 100), 243 (34), 130 (18). \text{ Anal. calcd for C}_{11}H_{8}BrFO_2: C, 48.74; H, 2.97. \text{ Found: C, 48.85; H, 2.91.}
\]

3-Bromo-1-p-tolylprop-2-ynyl acetate (76d):

\[
\text{pale yellow oil (925 mg, 42% yield). } R_f = 0.62 \text{ (19:1 hexane/EtOAc); [Silica, UV and I₂]. } ^1H \text{ NMR (400 MHz, CDCl}_3) \delta 7.41 \text{ (d, } J = 8.0 \text{ Hz, 2H), 7.21 \text{ (d, } J = 7.6 \text{ Hz, 2H), 6.43 \text{ (s, 1H), 2.38 \text{ (s, 3H), 2.11 \text{ (s, 3H). } ^1C \text{ NMR (101 MHz, CDCl}_3) } \delta 169.7, 139.2, 133.5, 129.4, 127.7, 76.9, 66.1, 47.9, 21.2, 21.0. IR (Neat) } \nu_{\text{max}} 2928, 1745, 1516, 1373, 1230, 1022 \text{ cm}^{-1}. MS (EI) m/z (\%) 265 (M}^+1, 5), 235 (34), 192 (100), 151 (40). \text{ Anal. calcd for C}_{12}H_{11}BrO_2: C, 53.96; H, 4.15. \text{ Found: C, 53.91; H, 4.23.}
\]

3-Bromo-1-(3-methoxyphenyl)prop-2-ynyl acetate (76e):

\[
\text{pale yellow oil (1.1 g, 53% yield). } R_f = 0.34 \text{ (19:1 hexane/EtOAc); [Silica, UV and I₂]. } ^1H \text{ NMR (400 MHz, CDCl}_3) \delta 7.31 \text{ (t, } J = 8.0 \text{ Hz, 1H), 7.08 \text{ (d, } J = 7.6 \text{ Hz, 1H), 6.91 \text{ (d, } J = 8.0 \text{ Hz, 1H), 6.42 \text{ (s, 1H), 3.83 \text{ (s, 3H), 2.12 \text{ (s, 3H). } ^1C \text{ NMR (101 MHz, CDCl}_3) } \delta 169.6, 159.8, 137.8, 129.8, 119.9, 114.6, 113.2, 76.7, 66.0, 55.3, 48.1, 21.0. IR (Neat) } \nu_{\text{max}} 3472, 2942, 1743, 1602, 1228, 1037 \text{ cm}^{-1}. MS (EI) m/z (\%) 284 (M}^+2, 100), 270 (29), 183 (5). \text{ Anal. calcd for C}_{12}H_{11}BrO_3: C, 50.91; H, 3.92. \text{ Found: C, 51.06; H, 3.85.}
\]

3-Bromo-1-(2-chlorophenyl)prop-2-ynyl acetate (76f):

\[
\text{colorless solid (777 mg, 38% yield). mp } = 66–67 \text{ °C. } R_f = 0.49 \text{ (19:1 hexane/EtOAc); [Silica, UV and I₂]. } ^1H \text{ NMR (400 MHz, CDCl}_3) \delta 7.73 \text{ (br d, } J = 6.4 \text{ Hz, 1H), 7.41 \text{ (br d, } J = 6.8 \text{ Hz, 1H), 7.39–7.25 \text{ (m, 2H), 6.75 \text{ (s, 1H), 2.13 \text{ (s, 3H). } ^1C \text{ NMR (101 MHz, CDCl}_3) } \delta 169.3, 133.8, 133.3, 130.4, 129.8, 129.3, 127.2, 75.7, 63.3, 55.6, 48.1, 21.0. IR (Neat) } \nu_{\text{max}} 1735, 1509, 1373, 1228, 1037 \text{ cm}^{-1}. MS (EI) m/z (\%) 284 (M}^+2, 100), 270 (29), 183 (5). \text{ Anal. calcd for C}_{12}H_{11}BrClO: C, 51.06; H, 3.92. \text{ Found: C, 51.06; H, 3.85.}
\]
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48.5, 20.7. IR (KBr) \( \nu_{\text{max}} \) 2224, 1741, 1440, 1217, 1047 cm\(^{-1}\). MS (EI) \( m/z \) (\%) 288 (M\(^+\)+2, 100), 270 (11), 232 (8), 200 (10). Anal. calcd for C\(_{11}\)H\(_8\)BrClO\(_2\): C, 45.95; H, 2.80. Found: C, 46.08; H, 2.85.

3-Bromo-1-o-tolylprop-2-ynyl acetate (76g):

pale yellow oil (835 mg, 38% yield). \( R_f = 0.56 \) (30:1 hexane/EtOAc); [Silica, UV and I\(_2\)]. \(^1\)H NMR (400 MHz, CDCl\(_3\)) \( \delta \) 7.58 (d, \( J = 8.0 \) Hz, 1H), 7.33−7.25 (m, 2H), 7.20 (d, \( J = 8.0 \) Hz, 1H), 6.57 (s, 1H), 2.42 (s, 3H), 2.13 (s, 3H). \(^13\)C NMR (101 MHz, CDCl\(_3\)) \( \delta \) 169.6, 136.2, 134.4, 130.9, 129.1, 127.9, 126.4, 76.5, 64.2, 47.9, 20.9, 19.0. IR (Neat) \( \nu_{\text{max}} \) 2934, 2218, 1743, 1369, 1226, 1016 cm\(^{-1}\). MS (EI) \( m/z \) (\%) 288 (M\(^+\)+, 100), 270 (11), 232 (8), 200 (10). Anal. calcd for C\(_{11}\)H\(_8\)BrClO\(_2\): C, 45.95; H, 2.80. Found: C, 46.08; H, 2.85.

3-Bromo-1-(naphthalen-1-yl)prop-2-ynyl acetate (76i):

brown oil (884 mg, 45% yield). \( R_f = 0.51 \) (19:1 hexane/EtOAc); [UV and I\(_2\)]. \(^1\)H NMR (400 MHz, CDCl\(_3\)) \( \delta \) 8.15 (d, \( J = 7.6 \) Hz, 1H), 7.90 (br t, \( J = 4.0 \) Hz, 2H), 7.80 (d, \( J = 7.2 \) Hz, 1H), 7.63−7.45 (m, 3H), 7.08 (s, 1H), 2.13 (s, 3H). \(^13\)C NMR (101 MHz, CDCl\(_3\)) \( \delta \) 169.8, 134.0, 131.7, 130.4, 130.1, 128.9, 124.7, 120.8, 117.3, 112.0, 76.7, 68.9, 61.2, 47.2, 20.9. IR (Neat) \( \nu_{\text{max}} \) 2935, 2218, 1741, 1602, 1043 cm\(^{-1}\). MS (EI) \( m/z \) (\%) 309 (M\(^+\)+−1, 18), 307 (25), 251 (90), 249 (100), 141 (25), 100 (94), 83 (41). Anal. calcd for C\(_{15}\)H\(_{11}\)BrO\(_2\): C, 59.43; H, 3.66. Found: C, 59.23; H, 3.61.

3-Bromo-1-(2,6-dimethoxyphenyl)prop-2-ynyl acetate (76j):

colorless solid (820 mg, 43% yield). mp = 116−117 °C. \( R_f = 0.42 \) (9:1 hexane/EtOAc); [Silica, UV and I\(_2\)]. \(^1\)H NMR (400 MHz, CDCl\(_3\)) \( \delta \) 7.80 (d, \( J = 7.2 \) Hz, 1H), 7.58 (d, \( J = 8.4 \) Hz, 2H), 6.89 (d, \( J = 8.4 \) Hz, 1H), 6.85 (s, 1H), 6.10–5.95 (m, 1H), 5.41 (d, \( J = 17.2 \) Hz, 1H), 5.28 (d, \( J = 10.4 \) Hz, 1H), 4.58 (br d, \( J = 4.4 \) Hz, 2H), 2.10 (s, 3H). \(^13\)C NMR (101 MHz, CDCl\(_3\)) \( \delta \) 170.0, 158.7, 130.8, 112.9, 104.6, 77.2, 57.5, 56.3, 44.2, 21.1. IR (KBr) \( \nu_{\text{max}} \) 2214, 1743, 1597, 1479, 1255, 1224, 1109 cm\(^{-1}\). MS (EI) \( m/z \) (\%) 314
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(M′+2, 13), 313 (M′+1, 100). Anal. calcd for C_{13}H_{13}BrO_{4}; C, 49.86; H, 4.18. Found: C, 49.96; H, 4.12.

**tert-Butyl 3-(2-acetoxy-4-bromobut-3-ynyl)-1H-indole-1-carboxylate (76k):**

pale yellow oil (715 mg, 46% yield). \( R_f = 0.45 \) (12:1 hexane/EtOAc); [Silica, UV and I2]. \(^1\)H NMR (400 MHz, CDCl\(_3\)) \( \delta \) 8.15 (d, \( J = 7.2 \) Hz, 1H), 7.60 (d, \( J = 7.6 \) Hz, 1H), 7.53 (s, 1H), 7.34 (t, \( J = 7.6 \) Hz, 1H), 7.28 (t, \( J = 6.8 \) Hz, 1H), 5.62 (t, \( J = 6.8 \) Hz, 1H), 3.20 (d, \( J = 6.4 \) Hz, 2H), 2.06 (s, 3H), 1.69 (s, 9H). \(^{13}\)C NMR (101 MHz, CDCl\(_3\)) \( \delta \) 169.7, 149.6, 135.3, 130.5, 124.5, 124.4, 122.5, 119.0, 115.3, 114.6, 83.6, 77.4, 64.5, 47.0, 30.6, 28.2, 20.9. IR (Neat) \( \nu \) max 2980, 2220, 1734, 1454, 1373, 1018, 7463 cm\(^{-1}\). MS (EI) \( m/z \) (%) 407 (M\(^+\)+2, 100), 389 (06), 221 (10). Anal. calcd for C\(_{19}\)H\(_{20}\)BrNO\(_4\): C, 56.17; H, 4.96; N, 3.45. Found: C, 56.25; H, 4.92; N, 3.43.

**1,8-Dibromooct-1-yn-3-yl acetate (76l):**

Following the literature procedure, aldehyde 76l was prepared. Colorless oil (825 mg, 45% yield). \( R_f = 0.70 \) (10:1 hexane/EtOAc); [Silica and I\(_2\)]. \(^1\)H NMR (400 MHz, CDCl\(_3\)) \( \delta \) 5.35 (t, \( J = 6.8 \) Hz, 1H), 3.41 (t, \( J = 6.8 \) Hz, 2H), 2.08 (s, 3H), 1.93–1.84 (m, 2H), 1.81–1.73 (m, 2H), 1.53–1.40 (m, 4H). \(^{13}\)C NMR (101 MHz, CDCl\(_3\)) \( \delta \) 169.8, 77.5, 64.4, 46.0, 34.3, 33.5, 32.5, 27.6, 24.1, 20.9. IR (Neat) \( \nu \) max 2937, 2216, 1745, 1371, 1230, 1020 cm\(^{-1}\). MS (EI) \( m/z \) (%) 326 (M\(^+\)+2, 81), 324 (M\(^+\), 100), 246 (13), 234 (12).

**8-Azido-1-bromooct-1-yn-3-yl acetate (76m):**

Following the literature procedure, aldehyde 76m was prepared. Colorless oil (925 mg, 46% yield). \( R_f = 0.73 \) (4:1 hexane/EtOAc); [Silica and I\(_2\)]. \(^1\)H NMR (400 MHz, CDCl\(_3\)) \( \delta \) 5.36 (t, \( J = 6.8 \) Hz, 1H), 3.28 (t, \( J = 6.8 \) Hz, 2H), 2.08 (s, 3H), 1.83–1.74 (m, 2H), 1.69–1.58 (m, 2H), 1.52–1.35 (m, 4H). \(^{13}\)C NMR (101 MHz, CDCl\(_3\)) \( \delta \) 169.8, 77.5, 64.4, 51.3, 46.0, 34.4, 28.7, 26.2, 24.5, 20.9. IR (Neat) \( \nu \) max 3391, 2941, 2096, 1745, 1456, 1228, 1020 cm\(^{-1}\). MS (EI) \( m/z \) (%) 289 (M\(^+\)+2, 83), 288 (M\(^+\)+1, 100), 170 (13), 119 (10). Anal. calcd for C\(_{10}\)H\(_9\)BrN\(_3\)O\(_2\): C, 41.68; H, 4.90; N, 14.58. Found: C, 41.75; H, 4.86; N, 14.45.

**1-Bromo-8-(tert-butoxycarbonylamino)oct-1-yn-3-yl acetate (76n):**

Following the literature procedure, aldehyde 76n was prepared. Colorless oil (708 mg, 42% yield). \( R_f = 0.58 \) (4:1 hexane/EtOAc); [Silica and I\(_2\)]. \(^1\)H NMR (400 MHz, CDCl\(_3\)) \( \delta \) 5.33 (t, \( J = 6.4 \) Hz, 1H), 4.54 (br s, 1H), 3.10 (br d, \( J = 5.6 \) Hz, 2H), 2.07 (s, 3H), 1.82–1.79 (m, 2H), 1.55–1.40 (m, 13H), 1.39–1.27 (m, 2H). \(^{13}\)C NMR (101 MHz, CDCl\(_3\)) \( \delta \) 169.9, 156.0, 79.1, 77.5, 64.5, 45.9, 40.4, 34.5, 29.9, 28.4, 26.3, 24.6, 20.9. IR (Neat) \( \nu \) max 3373, 2934, 1743, 1699, 1521, 1234, 1020 cm\(^{-1}\).
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MS (EI) m/z (%) 363 (M+2, 24), 362 (M+1, 24), 361 (M+, 24), 339 (100), 306 (59), 164 (30). Anal. calcd for C₁₃H₁₉BrNO₂: C, 49.73; H, 6.68; N, 3.87. Found: C, 49.65; H, 6.73; N, 3.80.

1-Bromo-8-(tetrahydro-2H-pyran-2-yl oxy)oct-1-yn-3-yl acetate (76o):

Following the literature procedure, aldehyde 76o was prepared. Pale yellow liquid (750 mg, 43% yield). Rf = 0.26 (9:1 hexane/EtOAc); [Silica and I₂]. ¹H NMR (400 MHz, CDCl₃) δ 5.35 (t, J = 6.8 Hz, 1H), 4.57 (br t, J = 4.4 Hz, 1H), 3.92–3.79 (m, 1H), 3.77–3.69 (m, 1H), 3.56–3.44 (m, 1H), 3.42–3.31 (m, 1H), 2.08 (s, 3H), 1.89–1.69 (m, 3H), 1.68–1.48 (m, 7H), 1.47–1.34 (m, 4H). ¹³C NMR (101 MHz, CDCl₃) δ 169.9, 98.9, 77.6, 67.4, 64.6, 62.3, 45.8, 34.5, 30.8, 29.5, 25.8, 25.0, 24.8, 20.9, 19.7. IR (Neat) νmax 2941, 1745, 1371, 1230, 1024 cm⁻¹. MS (EI) m/z (%) 348 (M+2, 70), 347 (M+, 100), 276 (56), 219 (98). Anal. calcd for C₁₃H₁₉BrO₂: C, 51.88; H, 6.68. Found: C, 51.76; H, 6.75.

8-(Benzyloxy)-1-bromooct-1-yn-3-yl acetate (76p):

Following the literature procedure, aldehyde 76p was prepared. Yellow oil (757 mg, 44% yield). Rf = 0.33 (6:1 hexane/EtOAc); [Silica and I₂]. ¹H NMR (400 MHz, CDCl₃) δ 7.36–7.33 (m, 4H), 7.31–7.27 (m, 1H), 5.36 (t, J = 6.8 Hz, 1H) 4.51 (s, 2H), 3.48 (t, J = 6.4 Hz, 2H), 2.08 (s, 3H), 1.84–1.73 (m, 2H), 1.68–1.59 (m, 2H), 1.52–1.37 (m, 4H). ¹³C NMR (101 MHz, CDCl₃) δ 169.8, 138.6, 128.4, 127.6, 127.5, 77.7, 72.9, 70.2, 64.6, 45.8, 34.6, 29.6, 25.8, 24.8, 20.9. IR (Neat) νmax 3466, 2937, 2860, 2216, 1745, 1371, 1230, 1022 cm⁻¹. MS (EI) m/z (%) 354 (M+2, 92), 353 (M+1, 16), 352 (M+, 100), 197 (15). Anal. calcd for C₁₇H₂₁BrO₂: C, 57.80; H, 5.99. Found: C, 57.69; H, 5.92.

1-Bromo-8-(tert-butyldimethylsilyloxy)oct-1-yn-3-yl acetate (76q):

Following the literature procedure, aldehyde 76q was prepared. Colorless oil (635 mg, 39% yield). Rf = 0.70 (9:1 hexane/EtOAc); [Silica and I₂]. ¹H NMR (400 MHz, CDCl₃) δ 5.35 (br t, J = 6.4 Hz, 1H), 3.61 (br t, J = 4.4 Hz, 2H), 2.08 (s, 3H), 1.81–1.72 (m, 2H), 1.58–1.30 (m, 6H), 0.90 (s, 9H), 0.05 (s, 6H). ¹³C NMR (101 MHz, CDCl₃) δ 169.9, 77.6, 64.6, 62.9, 45.8, 34.6, 32.6, 26.0, 25.4, 24.7, 20.9, 18.4, –5.3. IR (Neat) νmax 2932, 2858, 1749, 1371, 1230, 1101, 1022 cm⁻¹. MS (EI) m/z (%) 378 (M+2, 100), 377 (M+1, 94), 317 (38), 187 (38), 105 (38). Anal. calcd for C₁₆H₂₆BrO₂Si: C, 50.92; H, 7.75. Found: C, 50.88; H, 7.69.

1-(Bromoethyl) cyclopentyl acetate (76r):

Pale yellow oil (1.25 g, 45% yield). Rf = 0.43 (19:1 hexane/EtOAc); [Silica and I₂]. ¹H NMR (400 MHz, CDCl₃) δ 2.25–2.11 (m, 4H), 2.04 (s, 3H), 1.81–1.68 (m, 4H). ¹³C NMR (101 MHz, CDCl₃) δ 169.5, 81.0, 80.3, 45.1, 40.2, 23.2, 21.6. IR (Neat) νmax
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3470, 2962, 2876, 2208, 1745, 1439, 1367, 1240, 1016 cm\(^{-1}\). MS (EI) \(m/z\) (%): 232 (M\(^+\)+2, 21), 231 (M\(^+\)+1, 100). Anal. calcd for C\(_9\)H\(_{11}\)BrO\(_2\): C, 46.78; H, 4.80. Found: C, 46.71; H, 4.87.

8-(Bromoethynyl)-1,4-dioxaspiro[4.5]decan-8-yl acetate (76s):

colorless oil (863 mg, 44% yield). \(R_f = 0.48\) (19:1 hexane/EtOAc); [silica and I\(_2\)]. \(^1\)H NMR (400 MHz, CDCl\(_3\)) \(\delta 3.95\) (s, 4H), \(2.26-2.11\) (m, 4H), \(2.05\) (s, 3H), \(1.83-1.67\) (m, 4H). \(^{13}\)C NMR (101 MHz, CDCl\(_3\)) \(\delta 169.3, 107.4, 79.1, 74.4, 64.4, 64.3, 46.5, 34.2, 30.9, 21.7\). IR (Neat) \(\nu_{\text{max}}\) 3470, 2959, 2883, 2206, 1743, 1444, 1371, 1226, 1168, 1103 cm\(^{-1}\). MS (EI) \(m/z\) (%): 303 (M\(^+\)+ 1, 100), 282 (12). Anal. calcd for C\(_{12}\)H\(_{15}\)BrO\(_4\): C, 47.54; H, 4.99. Found: C, 47.65; H, 5.06.

4-Bromo-1-phenylbut-3-yn-2-yl pivalate (76t):
pale yellow oil (1.2 g, 47% yield). \(R_f = 0.66\) (30:1 hexane/EtOAc); [Silica, UV and I\(_2\)]. \(^1\)H NMR (400 MHz, CDCl\(_3\)) \(\delta 7.31\) (br t, \(J = 8.0\) Hz, 2H), \(7.25\) (t, \(J = 8.0\) Hz, 3H), \(5.53\) (t, \(J = 6.8\) Hz, 1H), \(3.09\) (d, \(J = 6.8\) Hz, 2H), \(1.15\) (s, 9H). \(^{13}\)C NMR (101 MHz, CDCl\(_3\)) \(\delta 177.2, 135.7, 129.7, 128.3, 127.0, 64.9, 46.4, 41.1, 38.7, 27.0\). IR (Neat) \(\nu_{\text{max}}\) 2974, 2218, 1732, 1479, 1278, 1143, 1033 cm\(^{-1}\). MS (EI) \(m/z\) (%): 310 (M\(^+\)+ 2, 100). Anal. calcd for C\(_{15}\)H\(_{17}\)BrO\(_2\): C, 58.27; H, 5.54. Found: C, 58.15; H, 5.63.

4-Chloro-1-phenylbut-3-yn-2-yl acetate (81a):
pale yellow oil (785 mg, 42% yield). \(R_f = 0.58\) (19:1 hexane/EtOAc); [Silica, UV and I\(_2\)]. \(^1\)H NMR (400 MHz, CDCl\(_3\)) \(\delta 7.31\) (t, \(J = 7.6\) Hz, 2H), \(7.25\) (t, \(J = 7.6\) Hz, 3H), \(5.53\) (t, \(J = 6.8\) Hz, 1H), \(3.07\) (d, \(J = 6.8\) Hz, 2H), \(2.05\) (s, 3H). \(^{13}\)C NMR (101 MHz, CDCl\(_3\)) \(\delta 169.7, 135.5, 129.6, 128.4, 127.1, 66.4, 65.1, 64.6, 41.0, 20.9\). IR (Neat) \(\nu_{\text{max}}\) 2934, 2245, 1749, 1496, 1454, 1228, 1024 cm\(^{-1}\). MS (EI) \(m/z\) (%): 224 (M\(^+\)+ 2, 10), 223 (M\(^+\)+1, 100), 209 (09), 177 (22). Anal. calcd for C\(_{12}\)H\(_{11}\)ClO\(_2\): C, 64.73; H, 4.98. Found: C, 64.87; H, 4.92.

4-Chloro-1-phenylbut-3-yn-2-yl pivalate (81b):
pale yellow oil (815 mg, 36% yield). \(R_f = 0.81\) (19:1 hexane/EtOAc); [Silica, UV and I\(_2\)]. \(^1\)H NMR (400 MHz, CDCl\(_3\)) \(\delta 7.30\) (d, \(J = 7.2\) Hz, 2H), \(7.24\) (d, \(J = 8.0\) Hz, 3H), \(5.51\) (t, \(J = 6.8\) Hz, 1H), \(3.08\) (d, \(J = 6.8\) Hz, 2H), \(1.15\) (s, 9H). \(^{13}\)C NMR (101 MHz, CDCl\(_3\)) \(\delta 177.2, 135.7, 129.6, 128.3, 127.0, 66.7, 64.6, 64.4, 41.1, 38.7, 27.0\). IR (Neat) \(\nu_{\text{max}}\) 2974, 2245, 1736, 1479, 1280, 1143, 1032 cm\(^{-1}\). MS (EI) \(m/z\) (%): 265 (M\(^+\)+1, 23), 264 (M\(^+\), 100). Anal. calcd for C\(_{15}\)H\(_{17}\)ClO\(_2\): C, 68.05; H, 6.47. Found: C, 68.15; H, 6.38.
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8-(Chloroethynyl)-1,4-dioxaspiro[4.5]decan-8-yl acetate (81c):

Colorless oil (890 mg, 54% yield). Rf = 0.28 (30:1 hexane/EtOAc); [Silica and I2]. 1H NMR (400 MHz, CDCl3) δ 3.93 (s, 4H), 2.28–2.15 (m, 4H), 2.06 (s, 3H), 1.85–1.69 (m, 4H). 13C NMR (101 MHz, CDCl3) δ 169.2, 107.4, 73.8, 68.4, 64.7, 64.4, 34.2, 30.9, 21.7. IR (neat) νmax 2957, 2229, 1747, 1444, 1371, 1116, 1105, 1022 cm⁻¹. MS (EI) m/z (%): 256 (M⁺–2, 16), 225 (M⁺–3, 100), 229 (27), 169 (29). Anal. calcld for C12H13ClO2: C, 55.71; H, 5.84. Found: C, 55.61; H, 5.92.

4-Iodo-1-phenylbut-3-yn-2-yl acetate (82):

Colorless oil (1.31 g, 50% yield). Rf = 0.50 (9:1 hexane/EtOAc); [Silica, UV and I2]. 1H NMR (400 MHz, CDCl3) δ 7.48–7.22 (m, 5H), 5.64 (bt, J = 6.8 Hz, 1H), 3.07 (d, J = 7.4 Hz, 2H), 2.05 (s, 3H). 13C NMR (101 MHz, CDCl3) δ 169.7, 135.6, 129.7, 128.4, 127.1, 91.3, 77.2, 65.7, 41.2, 20.9. IR (Neat) νmax 2930, 1745, 1371, 1128, 1018, 750 cm⁻¹. MS (EI) m/z (%): 316 (M⁺+2, 29), 315 (M⁺+1, 100). Anal. calcld for C13H11IO2: C, 45.88; H, 3.53. Found: C, 45.76; H, 3.61.

Gold-Catalyzed Hydration of Propargyl Acetates 76; General Procedure (GP-13):

A mixture of PPh₃AuCl (14.7 mg, 0.03 mmol) and AgSbF₆ (10.2 mg, 0.03 mmol) in dioxane (2.0 mL) was stirred in a Schlenk flask under an argon atmosphere for 20 minutes at ambient temperature. This freshly prepared light pink colored gold-silver complex mixture was added to another Schlenk flask containing solution of 76 (1.0 mmol) in MeNO₂ (100 μL) followed by the addition of de-ionized water (54 μL, 3.0 mmol) at 0 °C. The resulting reaction mixture was slowly warmed to room temperature and stirred for the time shown in the respective Tables at an ambient temperature. Upon complete consumption of precursor, the reaction mixture was diluted with dichloromethane (10 mL), and filtered through a small pad of Celite. The solvent was evaporated under reduced pressure and the crude reaction mixture was purified using column chromatography on silica gel.

4-Bromo-3-oxo-1-phenylbutan-2-yl acetate (80a):

Pale yellow oil (262 mg, 92% yield). Rf = 0.56 (9:1 hexane/EtOAc); [Silica, UV and I2]. 1H NMR (400 MHz, CDCl3) δ 7.38–7.25 (m, 3H), 7.21 (d, J = 6.8 Hz, 2H), 3.00–2.83 (m, 2H), 2.08 (s, 3H).
Regioselective Hydration……

5.45 (dd, J = 6.4, 4.4 Hz, 1H), 3.93 (d, J = 11.2 Hz, 1H), 3.87 (d, J = 11.2 Hz, 1H), 3.21 (dd, J = 11.2, 4.4 Hz, 1H), 3.11 (dd, J = 11.6, 6.4 Hz, 1H), 2.11 (s, 3H). 13C NMR (101 MHz, CDCl3) δ198.7, 170.2, 135.2, 129.3, 128.7, 127.3, 77.0, 37.3, 32.4, 20.5. IR (Neat) νmax 2939, 1743, 1726, 1496, 1373, 1232, 1049, 702 cm⁻¹. MS (EI) m/z (%) 286 (M⁺+2, 65), 285 (M⁺+1, 100), 156 (33). Anal. calcd for C12H13BrO2: C, 50.55; H, 4.60. Found: C, 50.42; H, 4.71.

3-Bromo-2-oxo-1-phenylpropyl acetate (80b):

pale yellow oil (233 mg, 86% yield). Rf = 0.30 (9:1 hexane/EtOAc); [Silica, UV and I₂]. ¹H NMR (400 MHz, CDCl3) δ7.43 (br s, 5H), 6.30 (s, 1H), 4.02 (d, J = 13.6 Hz, 1H), 3.94 (d, J = 13.6 Hz, 1H), 2.20 (s, 3H). 13C NMR (101 MHz, CDCl3) δ195.6, 170.1, 132.4, 129.9, 129.3, 128.3, 78.3, 31.1, 20.6. IR (Neat) νmax 2937, 1747, 1720, 1375 cm⁻¹. MS (EI) m/z (%) 27 (M⁺+1, 100), 156 (62), 127 (28). Anal. calcd for C12H13BrO2: C, 48.37; H, 4.09. Found: C, 48.62; H, 4.15.

3-Bromo-1-(4-fluorophenyl)-2-oxopropyl acetate (80c):

colorless oil (237 mg, 82% yield). Rf = 0.24 (9:1 hexane/EtOAc); [Silica, UV and I₂]. ¹H NMR (400 MHz, CDCl3) δ7.46–7.38 (m, 2H), 7.12 (t, J = 8.4 Hz, 2H), 6.28 (s, 1H), 3.99 (d, J = 13.6 Hz, 1H), 3.97 (d, J = 13.6 Hz, 1H), 2.19 (s, 3H).

13C NMR (101 MHz, CDCl3) δ195.6, 170.0, 163.5 (d, J = 251 Hz), 130.2 (d, J = 8.5 Hz), 128.4, 116.4 (d, J = 21.9 Hz), 77.4, 30.8, 20.6. 19F NMR (376 MHz, CDCl3) δ–110.72 (q, J = 2.6 Hz). IR (Neat) νmax 2934, 1755, 1620, 1512, 1078 cm⁻¹. MS (EI) m/z (%) 289 (M⁺+1, 100), 287 (62), 269 (18), 201 (27), 81 (97). Anal. calcd for C11H9BrFO3: C, 45.70; H, 3.49. Found: C, 45.61; H, 3.55.

3-Bromo-2-oxo-1-p-tolylpropyl acetate (80d):

pale yellow oil (237 mg, 83% yield). Rf = 0.38 (9:1 hexane/EtOAc); [Silica, UV and I₂]. ¹H NMR (400 MHz, CDCl3) δ7.31 (br d, J = 8.0 Hz, 2H), 7.23 (br d, J = 8.0 Hz, 2H), 6.26 (s, 1H), 4.01 (d, J = 14.0 Hz, 1H), 3.92 (d, J = 13.6 Hz, 1H), 2.37 (s, 3H), 218 (s, 3H). 13C NMR (101 MHz, CDCl3) δ195.7, 170.2, 140.0, 130.0, 129.4, 128.3, 78.2, 31.2, 21.3, 20.6. IR (Neat) νmax 2934, 1738, 1725, 1514, 1371, 1230, 1024 cm⁻¹. MS (EI) m/z (%) 285 (M⁺+1, 64), 283 (M⁺–1, 55), 220 (33), 193 (55), 161 (100). Anal. calcd for C12H13BrO2: C, 50.55; H, 4.60. Found: C, 50.65; H, 4.53.

3-Bromo-1-(3-methoxyphenyl)-2-oxopropyl acetate (80e):

pale yellow oil (235 mg, 78% yield). Rf = 0.23 (9:1 hexane/EtOAc); [Silica, UV and I₂]. ¹H NMR (400 MHz, CDCl3) δ7.34 (t, J = 8.0 Hz, 1H), 7.01 (d, J = 7.6 Hz, 1H), 6.94 (br s, 2H), 6.26 (s, 1H), 4.02 (d, J = 13.6 Hz, 1H), 3.93 (d, J = 13.6 Hz, 1H), 3.83 (s, 3H), 2.20 (s, 3H). 13C NMR (101 MHz, CDCl3) δ195.4, 170.1, 160.2, 133.7, 130.4, 120.4, 115.5, 113.5, 78.2, 55.4, 31.0, 20.6. IR (Neat) νmax 2941, 1745, 1668, 1601, 1373, 1228,
Regioselective Hydration……

1039 cm⁻¹. MS (EI) m/z (%) 302 (M⁺+2, 54), 301 (M⁺+1, 100). Anal. calcd for C₁₂H₁₃BrO₄: C, 47.86; H, 4.35. Found: C, 47.92; H, 4.31.

3-Bromo-1-(2-chlorophenyl)-2-oxopropyl acetate (80f):

colorless oil (262 mg, 86% yield). R_f = 0.30 (9:1 hexane/EtOAc); [Silica, UV and I₂]. ¹H NMR (400 MHz, CDCl₃) δ7.52–7.28 (m, 4H), 6.70 (s, 1H), 4.13 (d, J = 14.0 Hz, 1H), 4.03 (d, J = 13.6 Hz, 1H), 2.19 (s, 3H). ¹³C NMR (101 MHz, CDCl₃) δ195.1, 169.9, 133.9, 131.1, 130.8, 130.2, 130.1, 127.7, 74.8, 31.6, 20.5. IR (Neat) ν_max 2941, 1745, 1637, 1477, 1371, 1224, 1032 cm⁻¹. MS (EI) m/z (%) 305 (M⁺+1, 100), 303 (M⁺−1, 70), 285 (21), 261 (32), 181 (86). Anal. calcd for C₁₁H₁₀BrClO₃: C, 43.24; H, 3.30. Found: C, 43.37; H, 3.26.

3-Bromo-2-oxo-1-o-tolylpropyl acetate (80g):
colorless oil (251 mg, 88% yield). R_f = 0.39 (9:1 hexane/EtOAc); [Silica, UV and I₂]. ¹H NMR (400 MHz, CDCl₃) δ7.36–7.22 (m, 4H), 6.57 (s, 1H), 3.96 (d, J = 13.6 Hz, 1H), 3.89 (d, J = 13.6 Hz, 1H), 2.46 (s, 3H), 2.19 (s, 3H). ¹³C NMR (101 MHz, CDCl₃) δ195.8, 170.0, 137.4, 131.5, 131.1, 129.9, 128.8, 126.8, 75.8, 30.9, 20.7, 19.5. IR (Neat) ν_max 2943, 1741, 1730, 1371, 1228, 1030 cm⁻¹. MS (EI) m/z (%) 286 (M⁺+2, 62), 285 (M⁺+1, 100), 156 (21). Anal. calcd for C₁₂H₁₃BrO₃: C, 50.55; H, 4.60. Found: C, 50.67; H, 4.54.

1-(2-(Allyloxy)phenyl)-3-bromo-2-oxopropyl acetate (80h):
colorless oil (265 mg, 81% yield). R_f = 0.47 (9:1 hexane/EtOAc); [Silica, UV and I₂]. ¹H NMR (400 MHz, CDCl₃) δ7.43–7.29 (m, 2H), 7.01 (br t, J = 7.6 Hz, 1H), 6.94 (d, J = 8.0 Hz, 1H), 6.64 (s, 1H), 5.43 (d, J = 16.8 Hz, 1H), 5.34 (d, J = 10.4 Hz, 1H), 4.69–4.52 (m, 2H), 4.14 (d, J = 14.0 Hz, 1H), 4.05 (d, J = 14.0 Hz, 1H), 2.18 (s, 3H). ¹³C NMR (101 MHz, CDCl₃) δ195.9, 170.1, 155.8, 132.4, 131.0, 121.8, 121.4, 118.5, 112.4, 77.4, 73.3, 69.4, 32.0, 20.7. IR (Neat) ν_max 3468, 2939, 1743, 1715, 1601, 1493, 1226, 1026, 756 cm⁻¹. MS (EI) m/z (%) 327 (M⁺+1, 16), 326 (M⁺, 100), 292 (24), 256 (32). Anal. calcd for C₁₄H₁₅BrO₄: C, 51.40; H, 4.62. Found: C, 51.36; H, 4.71.

3-Bromo-1-(naphthalen-1-yl)-2-oxopropyl acetate (80i):
thick brown color oil (247 mg, 77% yield). R_f = 0.56 (9:1 hexane/EtOAc); [Silica, UV and I₂]. ¹H NMR (400 MHz, CDCl₃) δ8.10 (d, J = 8.4 Hz, 1H), 7.94 (t, J = 8.8 Hz, 2H), 7.63–7.45 (m, 4H), 7.02 (s, 1H), 3.94 (d, J = 13.2 Hz, 1H), 3.80 (d, J = 12.8 Hz, 1H), 2.23 (s, 3H). ¹³C NMR (101 MHz, CDCl₃) δ195.9, 170.0, 134.2, 131.1, 130.9, 129.1, 128.5, 127.5, 126.5, 125.4, 123.5, 76.8, 30.8, 20.7. IR (Neat) ν_max 2937, 1743, 1725, 1510, 1369, 1230, 1020 cm⁻¹. MS (EI) m/z (%) 323 (M⁺+3, 100), 322 (M⁺+2, 70), 321 (M⁺+1, 21), 292 (19). Anal. calcd for C₁₅H₁₃BrO₃: C, 56.10; H, 4.08. Found: C, 56.18; H, 3.96.

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Regioselective Hydration……

3-Bromo-1-(2,6-dimethoxyphenyl)-2-oxopropyl acetate (80j):

[Chemical Structure]

colorless liquid (299 mg, 90% yield). \( R_f = 0.28 \) \((19:1 \text{ hexane/EtOAc})\); [Silica, UV and I2]. \(^1\)H NMR (400 MHz, CDCl\(_3\)) \( \delta \) 7.35 (t, \( J = 8.0 \text{ Hz}, 1\text{H} \)), 6.91 (s, 1\text{H}), 6.59 (d, \( J = 8.0 \text{ Hz}, 2\text{H} \)), 4.03 (d, \( J = 14.0 \text{ Hz}, 1\text{H} \)), 3.96 (d, \( J = 14.0 \text{ Hz}, 1\text{H} \)), 3.82 (s, 3\text{H}), 2.17 (s, 3\text{H}). \(^{13}\)C NMR (101 MHz, CDCl\(_3\)) \( \delta \) 196.6, 170.1, 158.9, 131.8, 111.3, 104.3, 69.6, 56.1, 31.8, 20.9. IR (Neat) \( \nu_{\text{max}} \) 2939, 1753, 1736, 1597, 1479, 1230, 1105, 1022, 783 cm\(^{-1}\). MS (EI) \( m/z \) (%) 332 (M\(^+\)+2, 100). Anal. calcd for C\(_{13}\)H\(_8\)BrO\(_2\): C, 47.15; H, 4.57. Found: C, 47.23; H, 4.51.

tert-Butyl 3-(2-acetoxyl-bromo-3-oxobutyl)-1H-indole-1-carboxylate (80k):

[Chemical Structure]

thick yellow oil (335 mg, 79% yield). \( R_f = 0.47 \) \((9:1 \text{ hexane/EtOAc})\); [Silica, UV and I2]. \(^1\)H NMR (400 MHz, CDCl\(_3\)) \( \delta \) 8.14 (br d, \( J = 7.2 \text{ Hz}, 1\text{H} \)), 7.57 (d, \( J = 7.6 \text{ Hz}, 1\text{H} \)), 7.46 (s, 1\text{H}), 7.34 (t, \( J = 7.2 \text{ Hz}, 1\text{H} \)), 7.27 (t, \( J = 7.6 \text{ Hz}, 1\text{H} \)), 5.51 (t, \( J = 5.2 \text{ Hz}, 1\text{H} \)), 3.95 (s, 2\text{H}), 3.30 (dd, \( J = 14.8, 5.2 \text{ Hz}, 1\text{H} \)), 3.22 (dd, \( J = 14.8, 5.2 \text{ Hz}, 1\text{H} \)), 2.10 (s, 3\text{H}), 1.68 (s, 9\text{H}). \(^{13}\)C NMR (101 MHz, CDCl\(_3\)) \( \delta \) 198.9, 170.3, 149.5, 135.3, 130.1, 124.7, 124.5, 122.7, 118.9, 115.4, 114.2, 83.9, 76.1, 32.4, 28.2, 26.9, 20.6. IR (Neat) \( \nu_{\text{max}} \) 3449, 2974, 1734, 1715, 1608, 1452, 1385, 1255, 937, 765 cm\(^{-1}\). MS (EI) \( m/z \) (%) 425 (M\(^+\)+2, 26), 424 (M\(^+\)+1, 100). Anal. calcd for C\(_{19}\)H\(_{22}\)BrNO\(_3\): C, 53.79; H, 5.23; N, 3.30. Found: C, 53.71; H, 5.28; N, 3.36.

1,8-Dibromo-2-oxo-2-octan-3-yl acetate (80l):

[Chemical Structure]

pale yellow oil (306 mg, 89% yield). \( R_f = 0.66 \) \((19:1 \text{ hexane/EtOAc})\); [Silica and I2]. \(^1\)H NMR (400 MHz, CDCl\(_3\)) \( \delta \) 5.24 (dd, \( J = 8.0, 4.4 \text{ Hz}, 1\text{H} \)), 4.06 (d, \( J = 13.6 \text{ Hz}, 1\text{H} \)), 4.01 (d, \( J = 13.6 \text{ Hz}, 1\text{H} \)), 3.40 (t, \( J = 6.8 \text{ Hz}, 2\text{H} \)), 2.16 (s, 3\text{H}), 1.94–1.77 (m, 4\text{H}), 1.55–1.38 (m, 4\text{H}). \(^{13}\)C NMR (101 MHz, CDCl\(_3\)) \( \delta \) 198.9, 170.5, 76.5, 33.5, 32.3, 31.4, 30.8, 27.6, 24.3, 20.6. IR (Neat) \( \nu_{\text{max}} \) 2939, 1739, 1713, 1373, 1028 cm\(^{-1}\). MS (EI) \( m/z \) (%) 344 (M\(^+\)+2, 16), 343 (M\(^+\)+1, 92), 342 (M\(^+\), 100), 282 (13). Anal. calcd for C\(_{19}\)H\(_{18}\)Br\(_2\)O\(_2\): C, 34.91; H, 4.69. Found: C, 34.85; H, 4.58.

8-Azido-1-bromo-2-oxo-2-octan-3-yl acetate (80m):

[Chemical Structure]

yellow liquid (272 mg, 89% yield). \( R_f = 0.44 \) \((6:1 \text{ hexane/EtOAc})\); [Silica and I2]. \(^1\)H NMR (400 MHz, CDCl\(_3\)) \( \delta \) 5.24 (dd, \( J = 8.4, 4.4 \text{ Hz}, 1\text{H} \)), 4.06 (d, \( J = 13.6 \text{ Hz}, 1\text{H} \)), 4.01 (d, \( J = 13.6 \text{ Hz}, 1\text{H} \)), 3.27 (t, \( J = 6.8 \text{ Hz}, 2\text{H} \)), 2.15 (s, 3\text{H}), 1.95–1.77 (m, 2\text{H}), 1.69–1.57 (m, 2\text{H}), 1.50–1.34 (m, 4\text{H}). \(^{13}\)C NMR (101 MHz, CDCl\(_3\)) \( \delta \) 198.9, 170.5, 76.5, 51.2, 31.4, 30.8, 28.6, 26.3, 24.7, 20.6. IR (Neat) \( \nu_{\text{max}} \) 2934, 2100, 1747, 1718, 1371, 1234, 1028 cm\(^{-1}\). MS (EI) \( m/z \) (%) 307 (M\(^+\)+2, 100). Anal. calcd for C\(_{19}\)H\(_{18}\)BrN\(_3\)O\(_2\): C, 39.23; H, 5.27; N, 13.73. Found: C, 39.36; H, 5.22; N, 13.65.
Regioselective Hydration……

1-Bromo-8-(tert-butoxycarbonylamo)-2-o xo octave 3-yl acetate (80n):

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<th>Chemical Structure</th>
<th>Spectral Data</th>
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<td>$^1$H NMR (400 MHz, CDCl$<em>3$) $\delta$5.23 (dd, $J$ = 8.0, 4.4 Hz, 1H), 4.53 (br s, 1H), 4.06 (d, $J$ = 13.6 Hz, 1H), 4.01 (d, $J$ = 13.6 Hz, 1H), 3.09 (br t, $J$ = 6.0 Hz, 2H), 2.15 (s, 3H), 1.92–1.77 (m, 2H), 1.55–1.29 (m, 15H). $^{13}$C NMR (101 MHz, CDCl$<em>3$) $\delta$198.9, 170.5, 156.0, 79.1, 76.5, 40.3, 31.4, 30.9, 29.8, 28.4, 26.3, 24.8, 20.6. IR (Neat) $\nu</em>{\text{max}}$ 3375, 2934, 1745, 1695, 1520, 1367, 1242, 1168 cm$^{-1}$. MS (EI) $m/z$ (%) 381 (M$^+$+2, 100). Anal. calcd for C$</em>{13}$H$_{19}$BrNO$_3$: C, 47.38; H, 6.89; N, 3.68. Found: C, 47.45; H, 6.82; N, 3.61.</td>
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1-Bromo-2-oxo-8-(tetrahydro-2H-pyranyloxy)octan-3-yl acetate (80o):

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<th>Spectral Data</th>
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<td>$^1$H NMR (400 MHz, CDCl$<em>3$) $\delta$5.22 (dd, $J$ = 8.0, 4.0 Hz, 1H), 4.54 (br t, $J$ = 4.0 Hz, 1H), 4.05 (d, $J$ = 13.6 Hz, 1H), 4.01 (d, $J$ = 13.6 Hz, 1H), 3.87–3.79 (m, 1H), 3.71 (dt, $J$ = 8.0, 4.0 Hz, 1H), 3.52–3.44 (m, 1H), 3.37 (dt, $J$ = 8.0, 4.0 Hz, 1H), 2.13 (s, 3H), 1.89–1.75 (m, 3H), 1.63–1.46 (m, 6H), 1.45–1.34 (m, 5H). $^{13}$C NMR (101 MHz, CDCl$<em>3$) $\delta$198.9, 170.5, 98.9, 76.6, 67.3, 62.4, 31.5, 30.9, 29.4, 25.9, 25.5, 25.0, 20.6, 19.7. IR (Neat) $\nu</em>{\text{max}}$ 2930, 1743, 1722, 1373, 1234, 1032 cm$^{-1}$. MS (EI) $m/z$ (%) 366 (M$^+$+2, 76), 365 (M$^+$+1, 76), 276 (31), 141 (21). Anal. calcd for C$</em>{13}$H$_{19}$BrO$_3$: C, 49.32; H, 6.90. Found: C, 49.38; H, 6.85.</td>
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8-(Benzzyloxy)-1-bromo-2-o xo octa 3-yl acetate (80p):

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<th>Spectral Data</th>
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<td>$^1$H NMR (400 MHz, CDCl$<em>3$) $\delta$7.39–7.27 (m, 5H), 5.23 (dd, $J$ = 8.4, 4.8 Hz, 1H), 4.50 (s, 2H), 4.05 (d, $J$ = 13.2 Hz, 1H), 4.02 (d, $J$ = 13.2 Hz, 1H), 3.47 (t, $J$ = 6.4 Hz, 2H), 2.14 (s, 3H), 1.92–1.77 (m, 2H), 1.71–1.58 (m, 2H), 1.47–1.38 (m, 4H). $^{13}$C NMR (101 MHz, CDCl$<em>3$) $\delta$198.9, 170.5, 138.6, 128.4, 127.6, 127.5, 76.6, 72.9, 70.1, 31.5, 30.9, 29.5, 25.9, 25.0, 20.6. IR (Neat) $\nu</em>{\text{max}}$ 2937, 1741, 1725, 1371, 1234, 1101, 738 cm$^{-1}$. MS (EI) $m/z$ (%) 372 (M$^+$+2, 79), 371 (M$^+$+1, 32), 370 (M$^+$, 100), 352 (30), 340 (98), 326 (13). Anal. calcd for C$</em>{17}$H$_{17}$BrO$_3$: C, 55.00; H, 6.24. Found: C, 55.16; H, 6.29.</td>
</tr>
</tbody>
</table>

1-Bromo-8-hydroxy-2-oxo octa 3-yl acetate (80q):

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<th>Spectral Data</th>
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<td>$^1$H NMR (400 MHz, CDCl$<em>3$) $\delta$5.23 (dd, $J$ = 8.0, 4.4 Hz, 1H), 4.06 (d, $J$ = 13.6 Hz, 1H), 4.02 (d, $J$ = 13.6 Hz, 1H), 3.09 (t, $J$ = 6.4 Hz, 2H), 2.13 (s, 3H), 2.05 (br s, 1H), 1.92–1.73 (m, 2H), 1.55 (t, $J$ = 6.4 Hz, 2H), 1.51–1.29 (m, 4H). $^{13}$C NMR (101 MHz, CDCl$<em>3$) $\delta$199.1, 170.6, 76.6, 62.5, 32.3, 31.6, 30.9, 25.3, 24.9, 20.6. IR (Neat) $\nu</em>{\text{max}}$ 3413, 2942, 1742, 1375, 1243 cm$^{-1}$. MS (EI) $m/z$ (%) 282 (M$^+$+2, 84), 281 (M$^+$+1, 16), 280 (M$^+$, 100). Anal. calcd for C$</em>{10}$H$_{17}$BrO$_3$: C, 42.72; H, 6.09. Found: C, 42.58; H, 6.15.</td>
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Regioselective Hydration……

1-(2-Bromoacetyl)cyclopentyl acetate (80r):

[Chemical structure image]
colorless solid (217 mg, 87% yield). mp = 42–43 °C. Rf = 0.52 (9:1 hexane/EtOAc); [Silica and I2]. ¹H NMR (400 MHz, CDCl₃) δ 4.05 (s, 2H), 2.32–2.21 (m, 2H), 2.11 (s, 3H), 2.02–1.97 (m, 2H), 1.86–1.69 (m, 4H). ¹³C NMR (101 MHz, CDCl₃) δ 199.5, 171.3, 93.1, 36.6, 30.6, 24.7, 21.0. IR (KBr) νmax 2964, 1728, 1715, 1431, 1373, 1024, 621 cm⁻¹. MS (EI) m/z (%) 251 (M⁺+3, 95), 250 (M⁺+2, 10), 249 (M⁺+1, 100), 221 (29), 189 (23), 171 (21), 143 (18), 109 (12). Anal. calcd for C₉H₁₃BrO₃: C, 43.39; H, 5.26. Found: C, 43.36; H, 5.21.

8-(2-Bromoacetyl)-1,4-dioxaspiro[4.5]decan-8-yl acetate (80s):

[Chemical structure image]
colorless solid (250 mg, 78% yield). mp = 43–44 °C. Rf = 0.31 (9:1 hexane/EtOAc); [Silica and I₂]. ¹H NMR (400 MHz, CDCl₃) δ 4.07 (s, 2H), 3.99–3.88 (m, 4H), 2.23–2.05 (m, 7H), 1.84–1.74 (m, 2H), 1.73–1.64 (m, 2H). ¹³C NMR (101 MHz, CDCl₃) δ 199.7, 170.7, 107.3, 83.3, 64.6, 64.4, 30.1, 29.7, 29.6, 20.8. IR (Neat) νmax 2957, 1732, 1722, 1446, 1373, 1230, 1097, 1033, 727 cm⁻¹. MS (EI) m/z (%) 321 (M⁺+1, 23), 263 (86), 261 (100). Anal. calcd for C₁₂H₁₇BrO₅: C, 44.88; H, 5.34. Found: C, 44.96; H, 5.31.

4-Bromo-3-oxo-1-phenylbutan-2-yl pivalate (80t):

[Chemical structure image]
colorless oil (278 mg, 85% yield). Rf = 0.59 (10:1 hexane/EtOAc); [Silica, UV and I₂]. ¹H NMR (400 MHz, CDCl₃) δ 7.35–7.24 (m, 3H), 7.21 (br d, J = 8.0 Hz, 2H), 5.41 (dd, J = 8.0, 4.0 Hz, 1H), 3.90 (s, 2H), 3.23 (dd, J = 12.0, 8.0 Hz, 1H), 3.11 (dd, J = 12.0, 8.0 Hz, 1H), 1.17 (s, 9H). ¹³C NMR (101 MHz, CDCl₃) δ 199.0, 177.8, 135.4, 129.4, 128.6, 127.3, 76.9, 38.6, 37.5, 32.4, 26.9. IR (Neat) νmax 2974, 1728, 1715, 1479, 1396, 1280, 1149, 700 cm⁻¹. MS (EI) m/z (%) 328 (M⁺+2, 19), 327 (M⁺+1, 73), 326 (M⁺, 100). Anal. calcd for C₁₅H₁₉BrO₃: C, 55.06; H, 5.85. Found: C, 55.16; H, 5.79.

4-Chloro-3-oxo-1-phenylbutan-2-yl acetate (83a):

[Chemical structure image]
colorless oil (195 mg, 81% yield). Rf = 0.59 (10:1 hexane/EtOAc); [Silica, UV and I₂]. ¹H NMR (400 MHz, CDCl₃) δ 7.34–7.25 (m, 3H), 7.20 (br d, J = 8.0 Hz, 2H), 5.41 (dd, J = 8.0, 4.0 Hz, 1H), 3.90 (s, 2H), 3.23 (dd, J = 12.0, 8.0 Hz, 1H), 3.11 (dd, J = 12.0, 8.0 Hz, 1H), 1.17 (s, 9H). ¹³C NMR (101 MHz, CDCl₃) δ 199.2, 170.3, 135.0, 129.3, 128.8, 127.4, 77.2, 47.1, 37.1, 20.5. IR (Neat) νmax 2974, 1728, 1715, 1479, 1396, 1280, 1149, 700 cm⁻¹. MS (EI) m/z (%) 328 (M⁺+2, 19), 327 (M⁺+1, 73), 326 (M⁺, 100). Anal. calcd for C₁₂H₁₉ClO₃: C, 59.88; H, 5.44. Found: C, 59.75; H, 5.51.
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4-Chloro-3-oxo-1-phenylbutan-2-yl pivalate (83b):

A colorless oil (238 mg, 73% yield). R_\text{f} = 0.26 (9:1 hexane/EtOAc); [Silica, UV and I_2].

^1\text{H} NMR (400 MHz, CDCl_3) \( \delta \) 7.37–7.28 (m, 3H), 7.22 (d, \( J = 6.4 \) Hz, 2H), 5.38 (dd, \( J = 7.6, 5.6 \) Hz, 1H), 4.13 (d, \( J = 16.4 \) Hz, 1H), 4.04 (d, \( J = 16.4 \) Hz, 1H), 3.15 (dd, \( J = 14.0, 4.8 \) Hz, 1H), 3.09 (dd, \( J = 14.0, 7.6 \) Hz, 1H), 1.17 (s, 9H).

13\text{C} NMR (101 MHz, CDCl_3) \( \delta \) 199.3, 177.8, 135.2, 129.4, 128.7, 127.3, 76.9, 47.0, 38.6, 37.1, 26.9. IR (Neat) \( \nu_{\text{max}} \): 2928, 1730, 1682, 1606, 1458, 1151, 1045, 750 cm\(^{-1}\). MS (EI) \( m/z \) (%) 284 (M^+ + 2, 26), 283 (M^+ + 1, 70), 245 (100). Anal. calcd for C_{15}H_{19}ClO_3: C, 63.71; H, 6.77. Found: C, 63.85; H, 6.71.

8-(2-Chloroacetyl)-1,4-dioxaspiro[4.5]decan-8-yl acetate (83c):

A colorless solid (224 mg, 81% yield). mp = 64–65 °C. R_\text{f} = 0.5 (4:1 hexane/EtOAc); [Silica and I_2].

^1\text{H} NMR (400 MHz, CDCl_3) \( \delta \) 4.27 (br s, 2H), 3.99–3.90 (m, 4H), 2.23–2.15 (m, 2H), 2.13 (s, 3H), 2.13–2.05 (m, 2H), 1.86–1.75 (m, 2H), 1.73–1.66 (m, 2H). 13\text{C} NMR (101 MHz, CDCl_3) \( \delta \) 199.7, 170.6, 107.2, 83.2, 64.6, 64.4, 44.3, 30.0, 29.3, 20.8. IR (Neat) \( \nu_{\text{max}} \) 2947, 1736, 1728, 1442, 1377, 1236, 1095, 746 cm\(^{-1}\). MS (EI) \( m/z \) (%) 278 (M^+ + 2, 31), 277 (M^+ + 1, 100), 247 (47), 219 (34). Anal. calcd for C_{12}H_{17}ClO_5: C, 52.09; H, 6.19. Found: C, 52.16; H, 6.23.

4-Iodo-3-oxo-1-phenylbutan-2-yl acetate (84):

A yellow oil (256 mg, 77% yield). R_\text{f} = 0.37 (9:1 hexane/EtOAc); [Silica, UV and I_2].

^1\text{H} NMR (400 MHz, CDCl_3) \( \delta \) 7.38–7.25 (m, 3H), 7.21 (d, \( J = 6.8 \) Hz, 2H), 5.49 (dd, \( J = 7.6, 4.8 \) Hz, 1H), 3.82 (d, \( J = 11.2 \) Hz, 1H), 3.76 (d, \( J = 11.2 \) Hz, 1H), 3.21 (dd, \( J = 14.0, 4.8 \) Hz, 1H), 3.11 (dd, \( J = 14.0, 8.0 \) Hz, 1H), 2.11 (s, 3H). 13\text{C} NMR (101 MHz, CDCl_3) \( \delta \) 200.0, 170.1, 135.5, 129.4, 128.7, 127.3, 76.7, 37.9, 20.6, 2.8. IR (Neat) \( \nu_{\text{max}} \) 2934, 1745, 1715, 1496, 1373, 1236, 1045, 750 cm\(^{-1}\). MS (ESI) \( m/z \) (%) 334 (M^+ + 2, 65), 333 (M^+ + 1, 100). Anal. calcd for C_{12}H_{13}IO_3: C, 43.39; H, 3.95. Found: C, 43.29; H, 4.05.

4-Bromo-3-oxo-1-phenylbutan-2-yl acetate (85):

To a stirred solution of 80a (70 mg, 0.25 mmol) in MeOH:H_2O (1 mL, 4:1), Sc(OTf)_3 (24 mg, 0.05 mmol) was added at room temperature. The reaction mixture was stirred overnight at an ambient temperature. Progress of the reaction was monitored by TLC. After complete consumption of starting material, the solvent was evaporated under reduced pressure. The crude material was diluted with diethyl ether (20 mL). The organic layer was washed with brine, dried over Na_2SO_4 and concentrated under reduced pressure. The crude reaction mixture was purified by column
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chromatography on silica gel eluting with hexane: ethyl acetate (10:1) to accomplish 85 (49 mg) in 83% yield as yellow oil.

\[ R_f = 0.37 \] (9:1 hexane/EtOAc); [Silica, UV and I\(_2\)]. \(^1\)H NMR (400 MHz, CDCl\(_3\)) \( \delta 7.44-7.16 \) (m, 5H), 4.70 (t, \( J = 6.0 \) Hz, 1H), 4.02 (s, 2H), 3.17 (dd, \( J = 14.4, 4.8 \) Hz, 1H) for 1H, 2.95 (dd, \( J = 14.0, 7.6 \) Hz, 2H). \(^{13}\)C NMR (101 MHz, CDCl\(_3\)) \( \delta 203.4, 135.8, 129.3, 128.9, 127.3 \) for 1H, 76.1, 40.4, 31.4. IR (Neat) \( \nu_{max} \) 3468, 1737, 1232, 1946 cm\(^{-1}\). HRMS (ESI) for C\(_{10}\)H\(_{12}\)BrO\(_2\) (M + H): calcd 243.002, found 243.0023.

Synthesis of 2-amino-thiazole (86 and 87); General Procedure (GP-14):

A mixture of \( \alpha \)-acyloxy-\( \alpha' \)-halo ketones 80 (0.25 mmol) and thiourea (0.37 mmol) was stirred in EtOH (1 mL) at 80 °C for overnight. Progress of the reaction was monitored by TLC. After complete consumption of 80, the reaction mixture was extracted with CH\(_2\)Cl\(_2\) (2 × 10 mL), and the organic layer was washed with brine, dried over Na\(_2\)SO\(_4\), and concentrated under reduced pressure. The residue was purified by column chromatography on silica gel.

4-(Ethoxy(phenyl)methyl)thiazol-2-amine (86a): brown oil (36 mg, 63% yield). \( R_f = 0.61 \) (3:2 hexane/EtOAc); [Silica, UV and I\(_2\)]. \(^1\)H NMR (400 MHz, CDCl\(_3\)) \( \delta 7.43 \) (dd, \( J = 7.2, 1.6 \) Hz, 2H), 7.37 (td, \( J = 7.2, 1.2 \) Hz, 2H), 7.31 (dt, \( J = 7.2, 1.6 \) Hz, 1H), 6.31 (s, 1H), 5.29 (s, 1H), 5.09 (br s, 2H), 3.62 - 3.46 (m, 2H), 1.27 (t, \( J = 7.2 \) Hz, 3H). \(^{13}\)C NMR (101 MHz, CDCl\(_3\)) \( \delta 167.9, 153.1, 140.5, 128.3, 127.8, 127.4, 105.1, 80.2, 64.7, 15.3. IR (Neat) \( \nu_{max} \) 3413, 2926, 1605, 1528 cm\(^{-1}\). HRMS (ESI) for C\(_{12}\)H\(_{14}\)N\(_2\)OSNa (M+Na): calcd 257.0725, found 257.0728.

4-(Ethoxy(3-methoxyphenyl)methyl)thiazol-2-amine (86b): yellow oil (44 mg, 67% yield). \( R_f = 0.54 \) (3:2 hexane/EtOAc); [Silica, UV and I\(_2\)]. \(^1\)H NMR (400 MHz, CDCl\(_3\)) \( \delta 7.25 \) (s, 1H), 7.00 (s, 2H), 6.84 (d, \( J = 8.0 \) Hz, 1H), 6.25 (s, 1H), 5.59 (br s, 2H), 5.25 (s, 1H), 3.81 (s, 3H), 3.62 - 3.46 (m, 2H), 1.26 (t, \( J = 6.0 \) Hz, 3H). \(^{13}\)C NMR (101 MHz, CDCl\(_3\)) \( \delta 168.5, 159.7, 151.4, 141.5, 129.4, 119.8, 113.6, 112.7, 104.8, 79.6, 64.9, 55.3, 15.3. IR (Neat) \( \nu_{max} \) 3287, 2926, 1600, 1517, 1260 cm\(^{-1}\). HRMS (ESI) for C\(_{13}\)H\(_{17}\)N\(_2\)O\(_2\)S (M+H): calcd 265.101, found 265.1013.

1-(2-Aminothiazol-4-yl)-2-phenylethyl acetate (87): yellow oil (42 mg, 65% yield). \( R_f = 0.61 \) (3:2 hexane/EtOAc); [Silica, UV and I\(_2\)]. \(^1\)H NMR (400 MHz, CDCl\(_3\)) \( \delta 7.30-7.24 \) (m, 2H), 7.22 (dt, \( J = 6.8, 1.2 \) Hz, 1H), 7.16 (dd, \( J = 6.8, 1.6 \) Hz, 2H), 6.31 (s, 1H), 5.87 (t, \( J = 6.8 \) Hz, 1H), 5.38 (br s, 2H), 3.22 (d, \( J = 7.2 \) Hz, 2H), 2.04 (s, 3H). \(^{13}\)C NMR (101 MHz, CDCl\(_3\)) \( \delta 170.2, 168.1, 149.5, 137.0, 129.4, 128.3, 126.6, 106.2, 72.6, 40.3, 21.2. IR (Neat) \( \nu_{max} \) 3386, 3156, 1709, 1638, 1523 cm\(^{-1}\). HRMS (ESI) for C\(_{13}\)H\(_{16}\)N\(_2\)O\(_2\)SNa (M+Na): calcd 285.0656, found 285.0675.

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O\textsuperscript{18}–Labeled 1-acetylcyclohexyl acetate (96):

Following the general procedure (GP-4); 1-ethynylcyclohexyl acetate (50ah; 166 mg, 1.0 mmol) reacted with the mixture of Ph\textsubscript{3}PAuCl (4.9 mg, 0.01 mmol) and AgSbF\textsubscript{6} (3.4 mg, 0.01 mmol) in dioxane (1.5 mL) and H\textsubscript{2}O\textsuperscript{18} (54 µL, 3.0 mmol) for 4 h. Upon filtration over Celite and evaporation, the crude mixture was purified by silica gel column chromatography eluting with hexane: ethyl acetate (10:1) to afford 96 (152 mg) in 82% yield as colorless oil. Analytical data pertaining to 96 is matching with the values of 51ah reported in this thesis (see: page 59).

152 mg, 82% yield; colorless oil. \(R_f = 0.44\) (10:1 hexane/EtOAc). \(\textsuperscript{1}H\) NMR (400 MHz, CDCl\textsubscript{3}) \(\delta\) 2.11 (s, 3H), 2.07 (s, 3H), 2.02 (d, \(J = 12.0\) Hz, 2H), 1.62 (br t, \(J = 12.0\) Hz, 5H), 1.53 (q, \(J = 12.0\) Hz, 2H), 1.25 (br q, \(J = 12.0\) Hz, 1H). \(\textsuperscript{13}C\) NMR (101 MHz, CDCl\textsubscript{3}) \(\delta\) 207.3, 170.2, 85.2, 30.7, 25.0, 23.6, 21.1, 21.0. MS (EI) \textit{m/z} (%) 187 (M++1, 100), 169 (27), 157 (13), 125 (30).

1-(1-Hydroxycyclohexyl)ethanone (97):

To a solution of 96 (80 mg, 0.43 mmol) in MeOH (2 mL) was added K\textsubscript{2}CO\textsubscript{3} (119 mg, 0.87 mmol) at ambient temperature. The reaction mixture was stirred at this temperature for 2 h. After completion of the reaction, the solvent was evaporated under reduced pressure. The residue was diluted with diethyl ether (50 mL), washed with saturated aqueous NH\textsubscript{4}Cl (5 mL) and brine. The organic layer was dried over Na\textsubscript{2}SO\textsubscript{4} and concentrated under reduced pressure. The crude residue was purified by flash chromatography on silica gel eluting with hexane: ethyl acetate (12:1) to give 97 (47 mg) in 78% yield as colorless oil.

47 mg, 78%, colorless oil. \(R_f = 0.33\) (8:1 hexane/EtOAc). \(\textsuperscript{1}H\) NMR (400 MHz, CDCl\textsubscript{3}) \(\delta\) 3.57 (s, 1H), 2.24 (s, 3H), 1.81–1.59 (m, 6H), 1.48 (d, \(J = 4.8\) Hz, 2H), 1.24 (br s, 2H). \(\textsuperscript{13}C\) NMR (101 MHz, CDCl\textsubscript{3}) \(\delta\) 212.8, 78.0, 33.8, 29.7, 25.3, 23.7, 21.1. IR (Neat) \(\nu\)\textsubscript{max} 3260, 1730, 1425, 1367, 1234, 1026 cm\textsuperscript{−1}. MS (EI) \textit{m/z} (%) 143 (M\textsuperscript{+}+1, 58), 129 (55), 125 (62), 99 (9), 81(11). Anal. calcd for C\textsubscript{8}H\textsubscript{14}O\textsubscript{2}: C, 67.57; H, 9.92. Found: C, 67.45; H, 9.86.

2.8.5. X-ray crystallography: Single crystal X-ray data for the compounds 51w was collected at on a Bruker SMART APEX CCD area detector system [\(\lambda(Mo-K\alpha) = 0.71073\) Å] at 298 K, graphite monochromator with a \(\omega\) scan width of 0.3\textdegree, crystal-detector distance 60 mm, collimator 0.5 mm. The SMART software\textsuperscript{1} was used for the intensity data acquisition and the SAINTPLUS Software 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, and full-matrix least-squares refinement against \(F^2\) was carried out using SHELXL-97. 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.
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Table 2.11. Crystal data for 51w.

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<th>Compound</th>
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<td>$\lambda$ (Å)</td>
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<td>$c$ (Å)</td>
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<tr>
<td>$\gamma$ (°)</td>
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<td>$Z$</td>
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<tr>
<td>$\rho_{\text{calcld}}$ (Mg m⁻³)</td>
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<td>$F(000)$</td>
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<td>Crystal Size (mm)</td>
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<td>Unique reflections</td>
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<td>$R1$, $wR2$ (all data)</td>
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<tr>
<td>Largest diff.Peak and hole (e·Å⁻³)</td>
<td>0.225 and -0.205</td>
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</table>
2.9. References


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(33) Hydration of TMS-substituted propargylic acetate of 69 was performed under the optimized catalytic condition [Ph3PAuCl (1mol %) and AgSbF6 (1 mol %)] in the presence of H2O in 1,4-dioxane at room temperature for 24 h. The reaction did not undergo completion; the 1H NMR spectrum of the crude reaction mixture showed the formation of 20% of hydration product 71, 24% of desilylated 70, and 51% of unreacted TMS-substituted propargylic acetate 69.


(41) (a) Smith, M. B.; March, J. March’s Advanced Organic Chemistry: Reaction,
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2.10. Spectra
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LCMS-2010A DATA REPORT
SCHOOL OF CHEMISTRY
UNIVERSITY OF HYDERABAD

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Inj. Volume: 5.0000
Data Name: C:\LCMISolution\User\Data\NG-018-CY-APCI-POS1.qld
Method Name: C:\LCMISolution\User\Method\esi.plm

LC Chromatogram

MS Spectrum

MS Peak Table

OPERATOR

115
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