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

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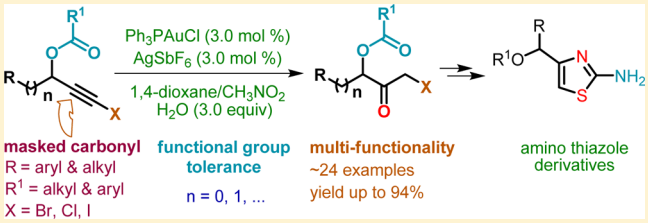
Supporting Information

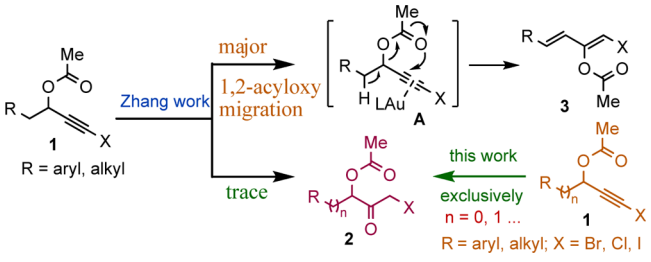
ABSTRACT: Regioselective hydration of the terminal halo-substituted propargyl carboxylate by gold(I) catalyst is reported. The mild catalytic conditions tolerate common acid-labile protecting groups, and a wide variety of α-acyloxy α′-halo ketones are efficiently synthesized within a short reaction time. The α-acyloxy α′-halo ketones are used for the synthesis of 2-aminothiazoles.



INTRODUCTION

The hydration of alkynes results in the incorporation of an easily modifiable carbonyl functional moiety in the molecules.[1] Despite the numerous findings available on the acid-mediated attack of water on unactivated alkynes,[2] the use of gold catalyst for the regioselective hydration of alkynes is noteworthy.[3,4] Moreover, the presence of a neighboring ester moiety in alkynes, e.g., propargyl carboxylates, would induce the regioselective incorporation of the carbonyl functional group.[5] In general, the structure of the propargyl carboxylates determines the 1,2- and 1,3-migration of the carboxylate group in the gold-catalyzed transformations.[6,7] Recently, the Zhang group demonstrated the gold-catalyzed regioselective 1,2-acyloxy migration of terminally halogenated propargyl carboxylates to the synthesis of 1-halo-2-carboxy-1,3-dienes (**3** in Scheme 1).[8] Interestingly, the presence of an electronegative

Scheme 1. Mode of Rearrangements of Terminal Halo-Substituted Propargyl Carboxylate



halo group at the alkyne terminus enhances the polarization of the alkynes and facilitates activating the alkyne moiety by gold;[9] this in turn induces the regioselective nucleophilic attack of the neighboring acyloxy group (**A** in Scheme 1). Surprisingly, the Zhang group observed the formation of a trace amount of hydration product α-acyloxy α′-halo ketone (**2**) along with **3** in the optimization studies (Scheme 1).[8]

The presence of easily modifiable multifunctional groups such as halo, keto, and carboxylate makes the compound **2** an important building block in the fabrication of complex molecules.[10] Inspired by the results of Zhang's group,[8] and considering the broad synthetic utility of **2**, we are interested in establishing an efficient and gram scale synthetic procedures for **2** via the regioselective hydration of **1** by applying our previously developed gold-catalyzed conditions.[11a] Herein, we report an atom-economical hydration of readily accessible halo-substituted propargyl carboxylate **1** under the catalytic conditions comprising of $Ph_3PAuCl/AgSbF_6$ (3.0 mol %) and H_2O (3.0 equiv) in 1,4-dioxane/CH_3NO_2 (20:1) at room temperature to the efficient synthesis of wide array of α-acyloxy α′-halo ketones.

RESULTS AND DISCUSSION

We first examined the regioselective hydration of 4-bromo-1-phenylbut-3-yn-2-yl acetate (**1a**) under various gold catalysts.[11a,12,13] The optimization studies are detailed in Table 1. The combination of Ph_3PAuCl (3.0 mol %), $AgSbF_6$ (3.0 mol %), and H_2O (3.0 equiv) in 1,4-dioxane at room temperature furnished the desired 4-bromo-3-oxo-1-phenylbutan-2-yl acetate (**2a**) in 75% yield with the complete consumption of **1a** within 4 h (entry 1). Screening of other Au catalysts such as $AuCl_3$ or AuCl along with $AgSbF_6$ yielded **2a** in up to 51% yield (entries 2 and 3). The yield of **2a** was improved to 67% when solvents THF, acetone, dichloromethane, and acetonitrile were employed instead of dioxane (entries 4−7). The combinations of AgOTf or $AgBF_4$ with Ph_3PAuCl were found to be moderate; the reaction did not undergo completion even with prolonged time (entries 8 and 9). The reaction of **1a** with water under Zhang's catalytic conditions produced **2a** in only 46% yield,[8] recovering the unreacted precursor **1a** (52%) (entry

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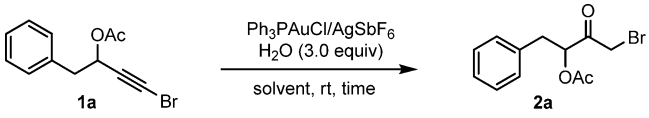
Table 1. Optimization of Reaction Conditions[a]



entry	catalyst (3.0 mol %)	cocatalyst (3.0 mol %)	solvent	time (h)	yield (%)[b]
1	Ph_3PAuCl	$AgSbF_6$	1,4-dioxane	4	75
2	$AuCl_3$	$AgSbF_6$	1,4-dioxane	4	51 (21)[c]
3	AuCl	$AgSbF_6$	1,4-dioxane	4	trace
4	Ph_3PAuCl	$AgSbF_6$	THF	4	67
5	Ph_3PAuCl	$AgSbF_6$	acetone	4	61
6	Ph_3PAuCl	$AgSbF_6$	CH_2Cl_2	4	32
7	Ph_3PAuCl	$AgSbF_6$	CH_3CN	4	42
8	Ph_3PAuCl	AgOTf	1,4-dioxane	4	49 (36)[c]
9	Ph_3PAuCl	$AgBF_4$	1,4-dioxane	4	39 (45)[c]
10	$Ph_3PAuNTf_2$		CH_2Cl_2	4	46 (52)[c]
11[d]	**Ph_3PAuCl**	**$AgSbF_6$**	**1,4-dioxane/ CH_3NO_2**	**4**	**93**
12	Ph_3PAuCl	$AgSbF_6$	1,4-dioxane/ DMSO	4	trace
13	Ph_3PAuCl	$AgSbF_6$	1,4-dioxane/ DMF	4	trace
14	Ph_3PAuCl	$AgSbF_6$	CH_3NO_2	4	67

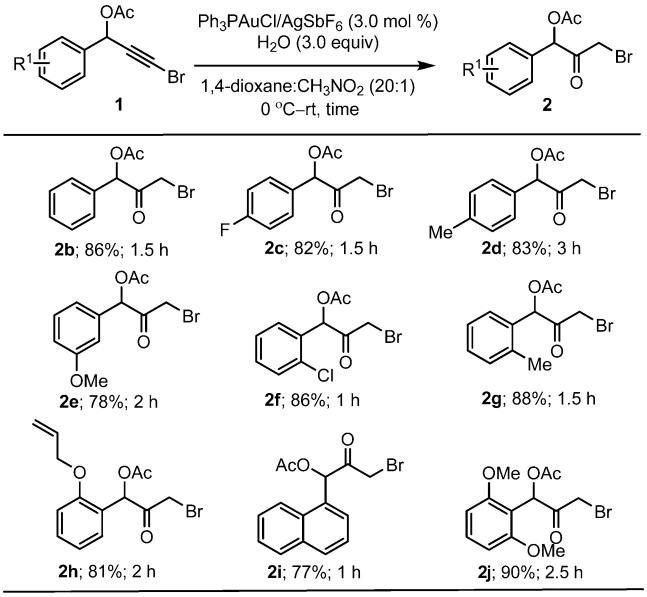
[a]Reactions were carried out using **1a** (0.5 mmol) and solvent (1.0 mL) at rt. [b]Isolated yields. [c]Yield of recovered **1a** is given in the parentheses. [d]**1a** was added at 0 °C in a mixture of solvent (1.0 mL, 20:1) and then stirred at rt.

10). We next examined the effect of mixture of solvents on the reaction outcome. Gratifyingly, **2a** was isolated in 93% yield, when a solvent mixture 1,4-dioxane and CH_3NO_2 (20:1) was employed (entry 11), while 1,4-dioxane with DMSO/DMF mixture were ineffective (entries 12 and 13). The reaction in wet nitromethane produced **2a** in 67% yield (entry 14). *Thus, different catalytic conditions allow in accessing two distinct products from the precursor* ***1a***.[8]

Reaction Scope. The optimal reaction conditions [Ph_3PAuCl, $AgSbF_6$, and H_2O in 1,4-dioxane/CH_3NO_2 (20:1); entry 11, Table 1] were surveyed to investigate the generality of the hydration of the terminal halo-substituted propargyl acetates (Tables 2 and 3). The stereoelectronic effect of substituents on the aryl moiety at the propargyl position was explored at first, and the results are summarized in Table 2. The hydration of 3-bromo-1-phenylprop-2-ynyl acetate **1b** gave 86% isolated yield of **2b**. The electron-withdrawing and -donating groups at the 4/3/2 positions on the aryl moiety reacted efficiently, and the desired keto products were obtained in good to excellent yields (**2c**–**g**). The *o*-*O*-allyl moiety on aromatic ring in **1h** did not affect the reaction outcome, producing **2h** in 81% yield. The 1-naphthyl-bearing hydration product **2i** was cleanly obtained from **1i**. Gratifyingly, the di-*ortho*-substituted sterically demanding substrate **1j** efficiently hydrated, delivering 90% of **2j**.

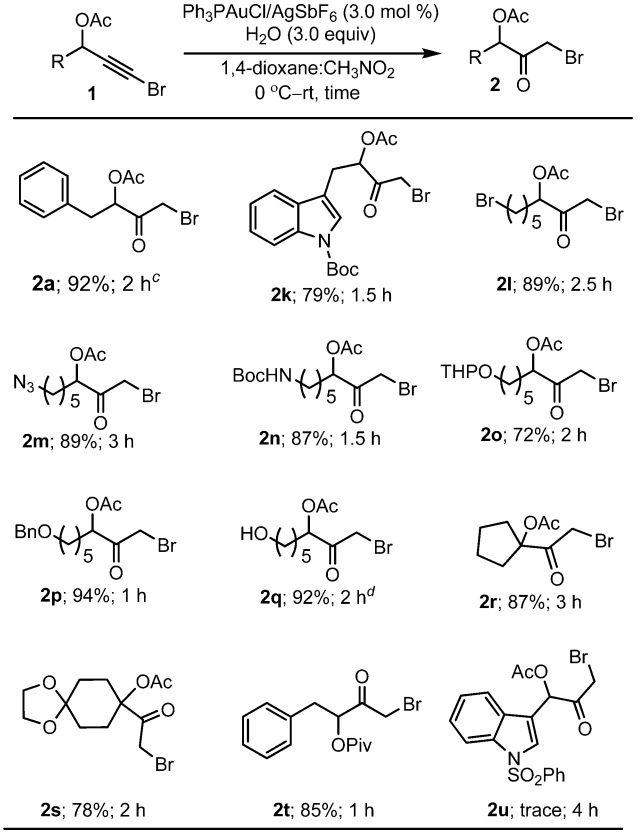
We next investigated the hydration of alkyl moieties bearing Br-propargyl acetates (Table 3). As observed in the optimization reaction conditions (entry 11, Table 1), the α-benzyl-substituted α-acyloxy-α'-bromo ketone **2a** was isolated in 92% yield from **1a**. Similarly, hydration of *N*-Boc-protected 3-indolyl-substituted bromo propargyl acetate **1k** gave 79% of **2k** within 1.5 h. The easily modifiable functional groups (Br and N_3) as well as the -NHBoc, -OTHP, and -OBn protecting groups on alkyl chain are well-tolerated and the desired

Table 2. Effect of Aryl Substituents at the Propargyl Position toward Hydration of 1[a,b]



[a]Reactions were carried out using **1** (1.0 mmol), $Ph_3PAuCl/AgSbF_6$ (0.03 mmol), H_2O (3.0 mmol), and 1,4-dioxane/CH_3NO_2 (2.0 mL, 20:1) at 0 °C to rt. [b]Isolated yields.

Table 3. Effect of Alkyl Group at the Propargyl Position toward Hydration of 1[a,b]



[a]Reactions were carried out using **1** (1.0 mmol), $Ph_3PAuCl/AgSbF_6$ (0.03 mmol), H_2O (3.0 mmol), and 1,4-dioxane/CH_3NO_2 (2.0 mL, 20:1) at 0 °C–rt. [b]Isolated yields. [c]Reaction of **1a** (1.0 g, 3.76 mmol) under the optimized conditions gave **2a** (779 mg, 73%). [d]*O*-TBDMS bond of **1q** cleaved under optimized conditions and produced **2q**.

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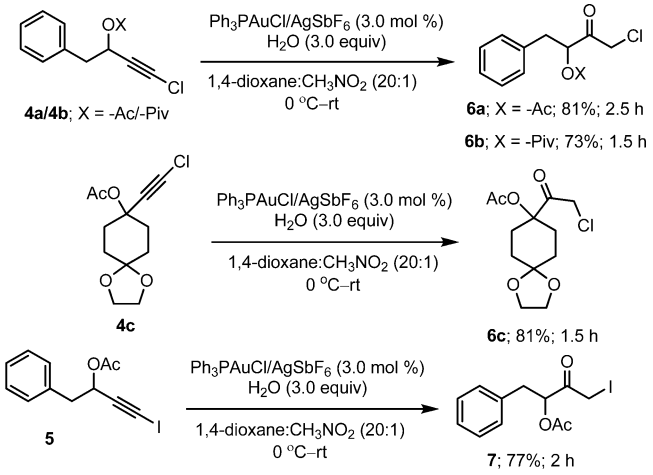
products **2l–p** are obtained in lucrative yields, demonstrating the mild nature of the catalytic conditions. The Au-catalyzed hydration of *O*-TBDMS-protected **1q** gave the desilylated **2q** in 92% yield. The sterically demanding cyclic-substituted acetates **1r** and **1s** did not affect the hydration, affording **2r** and **2s** in good yields with the survival of the acid-sensitive 1,3-dioxolane moiety in **2s**. The *O*-pivolate group also directs the hydration of bromoalkyne **1t**, generating the desired product **2t** in 85% yield. The reaction of N-SO_2Ph-protected indole-3-susbtituted bromopropargyl acetate **1u** under the optimized conditions was found to be complex, although a trace amount of the desired hydration product was detected in crude ^{1}H NMR; however, our effort in obtaining the pure product **2u** failed.

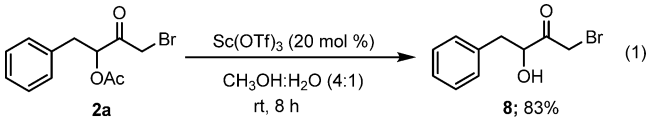
Next, the hydration of terminal chloro- and iodo-substituted propargyl acetates were examined (Scheme 2). The chloro-

Scheme 2. Effect of Chloro and Iodo Groups at Alkyne Terminus on Propargyl Acetates to the Gold-Catalyzed Hydration Reaction



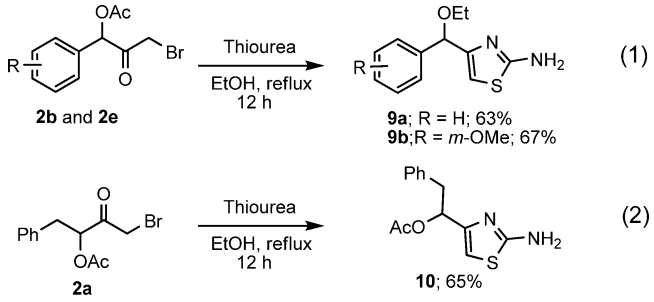
substituted propargyl acetate **4a** underwent hydration efficiently, and the desired product **6a** was isolated in 81% yield (Scheme 2). The pivolate group is equally effective, producing **6b** from the hydration of **4b** (Scheme 2). The sterically encumbered and 1,3-dioxolane-protected cyclohexane bearing α-acyloxy-α'-chloro ketone **6c** was produced from **4c** in 81% yield (Scheme 2). Pleasingly, the substrate with iodo substitution at the alkyne terminus in **5** underwent hydration easily, forming 4-iodo-3-oxo-1-phenylbutan-2-yl acetate (**7**) in 77% yield (Scheme 2).

Finally, the acetate group in the hydration product **2a** was successfully deacetylated with $Sc(OTf)_3$ (20 mol %) in CH_3OH/H_2O (4:1) at rt (eq 1). The α-hydroxy α'-bromo ketone **8** was obtained in 83% yield.[11a,14] The compound **8** is useful for the construction of various molecular fragments.[10]



Thus, the Au-catalyzed hydration of terminal-halo-substituted propargyl acetates provides an efficient access to a broad range of multifunctional groups such as halo, keto, and carboxylate bearing α-substituted α-acyloxy α'-halo ketones (**2**). We next envisaged exploring the utility of **2** toward the synthesis of heterocycles. The α-halo ketones are successfully used for the construction of large varieties of heterocycles.[9a] Gratifyingly, the condensation of **2b** and **2e** with thiourea in EtOH independently delivered 4-benzyl-substituted 2-amino-thiazole **9a** and **9b** in good yields (eq 1, Scheme 3); the acetate

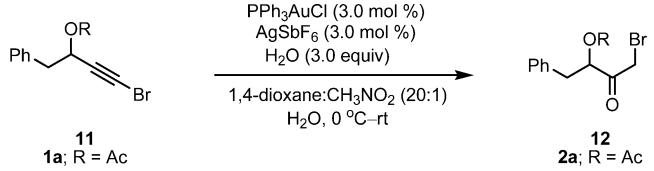
Scheme 3. Synthetic Utility of α-Acyloxy α'-Halo Ketones



group at the benzylic position is replaced with an ethoxy moiety during the reaction. However, the reaction between α-alkyl α-acyloxy α'-halo ketones **2a** and thiourea did not affect the acetate moiety, affording **10** in 65% yield (eq 2, Scheme 3).

We then investigated the effect of different protecting groups on the *O*-propargyl alcohol for the hydration reaction (Table 4). A trace amount of hydration product **12a** was noticed when

Table 4. Effect of Directing Group[a,b]



entry	11/1a/1t	R	time (h)	12/2a/2t	yield[b] (%)
1	**11a**	H	4	**12a**	trace
2	**11b**	Me	4	**12b**	NR
3	**11c**	benzoyl	4	**12c**	83
4	**1a**	acetyl	4	**2a**	92
5	**1t**	pivaloyl	4	**2t**	85

[a]Reactions were carried out using **1**/**11** (1.0 mmol), $Ph_3PAuCl/AgSbF_6$ (0.03 mmol), H_2O (3.0 mmol), and 1,4-dioxane/CH_3NO_2 (2.0 mL, 20:1) at 0 °C to rt. [b]Isolated yields. NR = no reaction.

propargyl alcohol **11a** reacted under the optimization catalytic conditions (entry 1). The methyl-protected propargyl ethers **11b** did not undergo hydration (entry 2). The benzoyl-protected propargyl ester **11c** furnished the hydration product **12c** in 83% yield (entry 3). As shown previously, the substrates **1a** and **1t** having acetyl and pivaloyl protecting groups on propargyl alcohol produced the desired hydration products **2a** and **2t** in 92% and 85% yields, respectively (entries 4 and 5). These results reveal that the O-directing group is mandatory in assisting the regioselective hydration of the alkyne moiety at an ambient temperature.

On the basis of our previous studies and the effect of O-directing group to the hydration of alkyne moiety shown in Table 4,[11a] the plausible reaction mechanism[11b] is sketched in Scheme 4. The reaction initiates with the activation of alkyne triple bond by carbophilic Au catalyst, forming the transient coordination complex **I**. The intramolecular 5-*exo*-*dig* attack of acetate carbonyl group to activated alkyne would lead to the 5-

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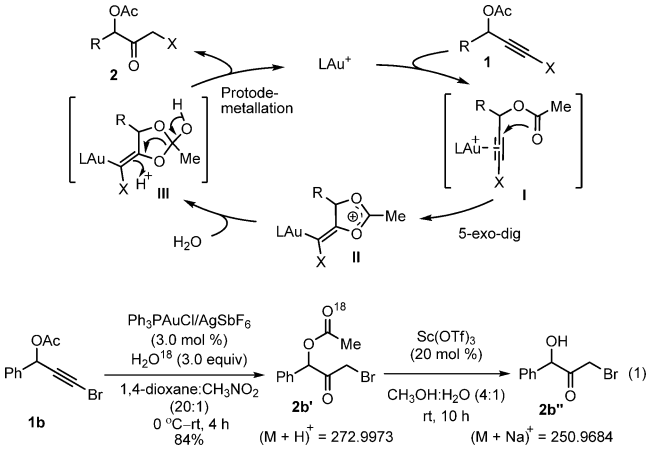
Scheme 4. Plausible Mechanism



membered electrophilic vinyl-Au species **II**.[11c] The nucleophilic attack of H_2O to **II** then generates the species **III**. Protodemetalation[11d] and isomerization of **III** finally delivers the desired α-acyloxy α'-halo ketone **2**. To validate the mode of water attack to alkyne,[15] hydration of **1b** with oxygen-18-enriched water was performed under the optimized conditions. As anticipated, the ^{18}O-incorporated product **2b′** was obtained from **1b**; molecular mass [272.9973 $(M + H)^+$] confirms the formation of **2b′**.[16] Finally, $Sc(OTf)_3$-catalyzed deacetylation of **2b′** gave **2b″** [250.9684 $(M + Na)^+$] with the loss of ^{18}O.[14,16] This observation supports the intramolecular assistance of carbonyl oxygen of the −OAc moiety to the hydration of alkyne (eq 1, Scheme 4).

■ CONCLUSION

In summary, the combination of commercially available catalyst [Ph_3PAuCl and $AgSbF_6$] in dioxane/CH_3NO_2 hydrates a wide range of readily accessible terminal halo-substituted propargyl carboxylates (Br, Cl, and I), delivering a series of α-acyloxy α'-halo ketones in good to excellent yields. Various acid-sensitive protecting groups survived, and the reaction conditions did not affect the common functional groups. The hydration products α-acyloxy α'-bromo ketones have been used for the synthesis of substituted 2-aminothiazole derivatives. Current efforts are directed toward unraveling the synthetic potential of this strategy.

■ EXPERIMENTAL SECTION

General Information. Unless otherwise noted, all of the reagents and intermediates were obtained commercially and used without purification. Dichloromethane (CH_2Cl_2), acetonitrile (CH_3CN), acetone, nitromethane (CH_3NO_2), dimethyl sulfoxide (DMSO), and dimethylformamide (DMF) were distilled over CaH_2. THF was freshly distilled over sodium/benzophenone ketyl under dry nitrogen. Methanol was dried over a magnesium cake. Analytical and spectral data of all of the known compounds matched the reported values.

Proton and carbon nuclear magnetic resonance spectra (^1H NMR, ^{13}C NMR, and ^{19}F NMR) were recorded on 400 MHz (^1H NMR, 400 MHz; ^{13}C NMR, 101 MHz; ^{19}F NMR, 376 MHz) and 500 MHz spectrometers (^1H NMR, 500 MHz; ^{13}C NMR, 126 MHz; ^{19}F NMR, 470 MHz) with the solvent resonance as internal standard (^1H NMR, $CHCl_3$ at 7.26 ppm; ^{13}C NMR, $CDCl_3$ at 77.0 ppm). In a few cases, tetramethylsilane (TMS) at 0.00 ppm was used as the reference standard. IR spectra were recorded and reported in cm^{-1}. LC−MS spectra were obtained (EI positive/negative mode) with an ionization voltage of 70 eV; data are reported in the form of m/z (intensity relative to base peak 100). Elemental (C, H, N) analysis was carried out using an EA 1112 analyzer. HRMS were obtained in ESI mode. TOF and quadrupole mass analyzers were used for the HRMS measurements. Melting points were determined on an electrothermal melting point apparatus and are uncorrected.

Preparation of 1 and 5: General Procedure (GP-1). Following the known synthetic methods,[11a] the O-acetylation of **1″** and **5′** gave **1** and **5**, respectively, in excellent yields. The first step involves the addition of TMS-acetylide to aldehydes (**1′**) followed by K_2CO_3-assisted desilylation to provide **3**.[8,11a] Next, the Ag-catalyzed Br/I insertion to the alkyne terminus in **3** delivered the desired **1″** and **5′** (Scheme 5).[8] The spectral data of compounds **1″** and **5′** match the reported values.[8] The aldehydes **1′l−q** were prepared following the literature procedures.[13]

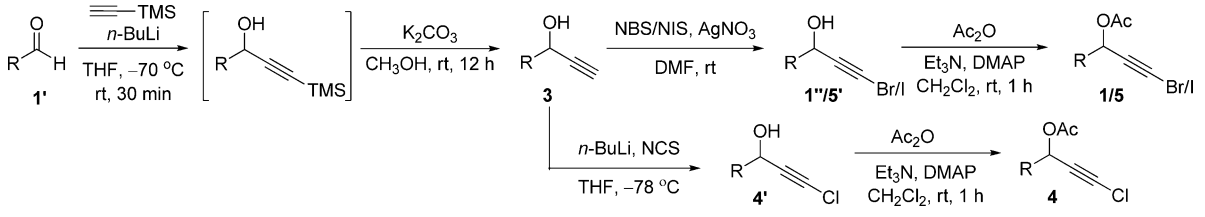
*4-Bromo-1-phenylbut-3-yn-2-yl acetate (**1a**):* yellow oil (957 mg, 43% yield); R_f = 0.55 (19:1 hexane/EtOAc) (silica, UV, and I_2); ^1H NMR (400 MHz, $CDCl_3$) δ 7.36−7.21 (m, 5H), 5.54 (t, J = 4.0 Hz, 1H), 3.08 (d, J = 8.0 Hz, 2H), 2.05 (s, 3H); ^{13}C NMR (101 MHz, $CDCl_3$) δ 169.7, 135.5, 129.6, 128.4, 127.1, 77.2, 65.1, 47.0, 41.0, 20.8; IR (neat) ν_{max} 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 $C_{12}H_{11}BrO_2$: C, 53.96; H, 4.15. Found: C, 53.86; H, 4.21.

*3-Bromo-1-phenylprop-2-ynyl acetate (**1b**):* pale yellow oil (1.11 g, 46% yield); R_f = 0.26 (9:1 hexane/EtOAc) (silica, UV, and I_2); ^1H NMR (400 MHz, $CDCl_3$) δ 7.51 (d, J = 6.8 Hz, 2H), 7.40 (d, J = 5.6 Hz, 3H), 6.46 (s, 1H), 2.12 (s, 3H); ^{13}C NMR (101 MHz, $CDCl_3$) δ 169.7, 136.4, 129.1, 128.8, 127.7, 76.9, 66.1, 48.1, 21.0; IR (neat) ν_{max} 2222, 1739, 1454, 1373, 1228, 1018 cm^{-1}; MS (EI) m/z 254 (M^+ + 2, 19), 253 (M^+ + 1, 100). Anal. Calcd for $C_{11}H_9BrO_2$: C, 52.20; H, 3.58. Found: C, 52.36; H, 3.51.

*3-Bromo-1-(4-fluorophenyl)prop-2-ynyl acetate (**1c**):* colorless solid (857 mg, 39% yield); mp = 49−50 °C; R_f = 0.56 (30:1 hexane/EtOAc) (silica, UV, and I_2); ^1H NMR (400 MHz, $CDCl_3$) δ 7.49 (br t, J = 5.6 Hz, 2H), 7.08 (t, J = 8.8 Hz, 2H), 6.42 (s, 1H), 2.11 (s, 3H). ^{13}C NMR (101 MHz, $CDCl_3$) δ 169.6, 163.1 (d, J = 249 Hz), 132.4, 129.7 (d, J = 8.4 Hz), 115.7 (d, J = 21.8 Hz), 76.5, 65.5, 48.4, 21.0. ^{19}F NMR (470 MHz, $CDCl_3$) δ −110.72 (q, J = 5.2 Hz). IR (KBr) ν_{max} 2220, 1732, 1604, 1512, 1369, 1226, 1059 cm^{-1}. MS (EI) m/z 273 (M^+ + 3, 92), 271 (M^+ + 1, 100), 243 (34), 130 (18). Anal. Calcd for $C_{11}H_8BrFO_2$: C, 48.74; H, 2.97. Found: C, 48.85; H, 2.91.

*3-Bromo-1-p-tolylprop-2-ynyl acetate (**1d**).* pale yellow oil (925 mg, 42% yield). R_f = 0.62 (19:1 hexane/EtOAc) (silica, UV, and I_2); ^1H NMR (400 MHz, $CDCl_3$) δ 7.41 (d, J = 8.0 Hz, 2H), 7.21 (d, J = 7.6 Hz, 2H), 6.43 (s, 1H), 2.38 (s, 3H), 2.11 (s, 3H); ^{13}C NMR (101 MHz, $CDCl_3$) δ 169.7, 139.2, 133.5, 129.4, 127.7, 76.9, 66.1, 47.9, 21.2, 21.0; IR (neat) ν_{max} 2928, 1745, 1516, 1373, 1230, 1022 cm^{-1};

Scheme 5. General Procedure for the Synthesis of Precursors 1, 4, and 5



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MS (EI) m/z 265 ($M^+ - 1$, 5), 235 (34), 192 (100), 151 (40). Anal. Calcd for $C_{12}H_{11}BrO_2$: C, 53.96; H, 4.15. Found: C, 53.91; H, 4.23.

*3-Bromo-1-(3-methoxyphenyl)prop-2-ynyl acetate (**1e**):* pale yellow oil (1.10 g, 53% yield); R_f = 0.34 (19:1 hexane/EtOAc) (silica, UV, and I_2); ^{1}H NMR (400 MHz, $CDCl_3$) δ 7.31 (t, J = 8.0 Hz, 1H), 7.08 (d, J = 7.6 Hz, 1H), 7.04 (s, 1H), 6.91 (d, J = 8.0 Hz, 1H), 6.42 (s, 1H), 3.83 (s, 3H), 2.12 (s, 3H); ^{13}C NMR (101 MHz, $CDCl_3$) δ 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) ν_{max} 3472, 2942, 1743, 1602, 1228, 1037 cm^{-1}; MS (EI) m/z 284 (M^+ + 2, 100), 270 (29), 183 (5). Anal. Calcd for $C_{12}H_{11}BrO_3$: C, 50.91; H, 3.92. Found: C, 51.06; H, 3.85.

*3-Bromo-1-(2-chlorophenyl)prop-2-ynyl acetate (**1f**):* colorless solid (777 mg, 38% yield); mp = 66−67 °C; R_f = 0.49 (19:1 hexane/EtOAc) (silica, UV, and I_2); ^{1}H NMR (400 MHz, $CDCl_3$) δ 7.73 (br d, J = 6.4 Hz, 1H), 7.41 (br d, J = 6.8 Hz, 1H), 7.39−7.25 (m, 2H), 6.75 (s, 1H), 2.13 (s, 3H); ^{13}C NMR (101 MHz, $CDCl_3$) δ 169.3, 133.8, 133.3, 130.4, 129.8, 129.3, 127.2, 75.7, 63.3, 48.5, 20.7; IR (KBr) ν_{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 $C_{11}H_8BrClO_2$: C, 45.95; H, 2.80. Found: C, 46.08; H, 2.85.

*3-Bromo-1-o-tolylprop-2-ynyl acetate (**1g**):* 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, $CDCl_3$) δ 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, $CDCl_3$) δ 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) ν_{max} 2934, 2218, 1743, 1369, 1226, 1016 cm^{-1}; MS (EI) m/z 266 (M^+, 23), 265 ($M^+ - 1$, 100), 205 (38), 175 (46), 143 (69), 79(15). Anal. Calcd for $C_{12}H_{11}BrO_2$: C, 53.96; H, 4.15. Found: C, 54.10; H, 4.08.

*1-(2-(Allyloxy)phenyl)-3-bromoprop-2-ynyl acetate (**1h**):* pale yellow oil (695 mg, 37% yield); R_f = 0.73 (9:1 hexane/EtOAc) (silica, UV, and I_2); ^{1}H NMR (400 MHz, $CDCl_3$) δ 7.65 (d, J = 7.6 Hz, 1H), 7.34 (t, J = 8.0 Hz, 1H), 7.02 (t, J = 7.6 Hz, 1H), 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, $CDCl_3$) δ 169.6, 155.6, 132.8, 130.5, 128.9, 124.7, 120.8, 117.3, 112.0, 76.7, 68.9, 61.2, 47.2, 20.9; IR (neat) ν_{max} 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 $C_{14}H_{13}BrO_3$: C, 54.39; H, 4.24. Found: C, 54.28; H, 4.35.

*3-Bromo-1-(naphthalen-1-yl)prop-2-ynyl acetate (**1i**):* brown oil (884 mg, 45% yield); R_f = 0.51 (19:1 hexane/EtOAc) (silica, UV, and I_2); ^{1}H NMR (400 MHz, $CDCl_3$) δ 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, $CDCl_3$) δ 169.8, 134.0, 131.7, 130.4, 130.1, 128.9, 126.8, 126.6, 126.1, 125.2, 123.5, 77.1, 64.5, 48.6, 21.0; IR (neat) ν_{max} 3055, 2935, 2220, 1938, 1747, 1597, 1512, 1371, 1217, 777 cm^{-1}; MS (EI) m/z 301 ($M^+ - 1$, 16), 229 (59), 212 (38), 197 (100). 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 (**1j**):* 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, $CDCl_3$) δ 7.28 (d, J = 8.0 Hz, 1H), 7.10 (s, 1H), 6.58 (d, J = 8.4 Hz, 2H) 3.88 (s, 6H), 2.08 (s, 3H); ^{13}C NMR (101 MHz, $CDCl_3$) δ 170.0, 158.7, 130.8, 112.9, 104.6, 77.2, 57.5, 56.3, 44.2, 21.1; IR (KBr) ν_{max} 2214, 1743, 1597, 1479, 1255, 1224, 1109 cm^{-1}; MS (EI) m/z 314 (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 (**1k**):* pale yellow oil (715 mg, 46% yield); R_f = 0.45 (12:1 hexane/EtOAc) (silica, UV, and I_2); ^{1}H NMR (400 MHz, $CDCl_3$) δ 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, $CDCl_3$) δ 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) ν_{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 (**1l**):* colorless oil (825 mg, 45% yield); R_f = 0.70 (10:1 hexane/EtOAc) (silica, UV, and I_2); ^{1}H NMR (400 MHz, $CDCl_3$) δ 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, $CDCl_3$) δ 169.8, 77.5, 64.4, 46.0, 34.3, 33.5, 32.5, 27.6, 24.1, 20.9; IR (neat) ν_{max} 2937, 2216, 1745, 1371, 1230, 1020 cm^{-1}; MS (EI) m/z 326 (M^+ + 2, 81), 324 (M^+, 100), 246 (13), 234 (12). Anal. Calcd for $C_{10}H_{14}Br_2O_2$: C, 36.84; H, 4.33. Found: C, 36.85; H, 4.39.

*8-Azido-1-bromooct-1-yn-3-yl acetate (**1m**):* colorless oil (925 mg, 46% yield); R_f = 0.73 (4:1 hexane/EtOAc) (silica, UV, and I_2); ^{1}H NMR (400 MHz, $CDCl_3$) δ 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, $CDCl_3$) δ 169.8, 77.5, 64.4, 51.3, 46.0, 34.4, 28.7, 26.2, 24.5, 20.9; IR (neat) ν_{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 $C_{10}H_{14}BrN_3O_2$: 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 (**1n**):* colorless oil (708 mg, 42% yield); R_f = 0.58 (4:1 hexane/EtOAc) (silica, UV, and I_2); ^{1}H NMR (400 MHz, $CDCl_3$) δ 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, $CDCl_3$) δ 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) ν_{max} 3373, 2934, 1743, 1699, 1521, 1234, 1020 cm^{-1}; MS (EI) m/z 363 (M^+ + 2, 24), 362 (M^+ + 1, 24), 361 (M^+, 24), 339 (100), 306 (59), 164 (30). Anal. Calcd for $C_{15}H_{24}BrNO_4$: 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-yloxy)oct-1-yn-3-yl acetate (**1o**):* pale yellow oil (750 mg, 43% yield); R_f = 0.26 (9:1 hexane/EtOAc) (silica, UV, and I_2); ^{1}H NMR (400 MHz, $CDCl_3$) 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); ^{13}C NMR (101 MHz, $CDCl_3$) δ 169.9, 98.9, 77.6, 67.4, 64.6, 62.3, 45.8, 34.5, 30.8, 29.5, 25.8, 25.5, 24.8, 20.9, 19.7; IR (neat) ν_{max} 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 $C_{15}H_{23}BrO_4$: C, 51.88; H, 6.68. Found: C, 51.76; H, 6.75.

*8-(Benzyloxy)-1-bromooct-1-yn-3-yl acetate (**1p**):* yellow oil (757 mg, 44% yield); R_f = 0.33 (6:1 hexane/EtOAc) (silica, UV, and I_2); ^{1}H NMR (400 MHz, $CDCl_3$) 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); ^{13}C NMR (101 MHz, $CDCl_3$) 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) ν_{max} 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 $C_{17}H_{21}BrO_3$: C, 57.80; H, 5.99. Found: C, 57.69; H, 5.92.

*1-Bromo-8-(tert-butyldimethylsilyloxy)oct-1-yn-3-yl acetate (**1q**):* colorless oil (635 mg, 39% yield); R_f = 0.70 (9:1 hexane/EtOAc) (silica, UV, and I_2); ^{1}H NMR (400 MHz, $CDCl_3$) δ 5.35 (br t, J = 6.4 Hz, 1H), 3.61 (br t, J = 6.4 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); ^{13}C NMR (101 MHz, $CDCl_3$) 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) ν_{max} 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 $C_{16}H_{29}BrO_3Si$: C, 50.92; H, 7.75. Found: C, 50.88; H, 7.69.

*1-(Bromoethynyl)cyclopentyl acetate (**1r**):* pale yellow oil (1.25 g, 45% yield); R_f = 0.43 (19:1 hexane/EtOAc) (silica, UV, and I_2); ^{1}H NMR (400 MHz, $CDCl_3$) δ 2.25−2.11 (m, 4H), 2.04 (s, 3H), 1.81−1.68 (m, 4H); ^{13}C NMR (101 MHz, $CDCl_3$) δ 169.5, 81.0, 80.3, 45.1, 40.2, 23.2, 21.6; IR (neat) ν_{max} 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 $C_9H_{11}BrO_2$: C, 46.78; H, 4.80. Found: C, 46.71; H, 4.87.

*8-(Bromoethynyl)-1,4-dioxaspiro[4.5]decan-8-yl acetate (**1s**):* colorless oil (863 mg, 44% yield); R_f = 0.48 (19:1 hexane/EtOAc)

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(silica, UV, and I_2); ^{1}H NMR (400 MHz, $CDCl_3$) δ 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, $CDCl_3$) δ 169.3, 107.4, 79.1, 74.4, 64.4, 64.3, 46.5, 34.2, 30.9, 21.7; IR (neat) ν_{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 (**1t**):* pale yellow oil (1.21 g, 47% yield); R_f = 0.66 (30:1 hexane/EtOAc) (silica, UV, and I_2); ^{1}H NMR (400 MHz, $CDCl_3$) δ 7.31 (br t, J = 8.0 Hz, 2H), 7.25 (t, J = 8.0 Hz, 3H), 5.53 (t, J = 8.0 Hz, 1H), 3.09 (d, J = 8.0 Hz, 2H), 1.15 (s, 9H); ^{13}C NMR (101 MHz, $CDCl_3$) δ 177.2, 135.7, 129.7, 128.3, 127.0, 64.9, 46.4, 41.1, 38.7, 27.0; IR (neat) ν_{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.

*3-Bromo-1-(1-(phenylsulfonyl)-1H-indol-3-yl)prop-2-yn-1-yl acetate (**1u**):* pale yellow oil (55 mg, 20% yield); R_f = 0.12 (9:1 hexane/EtOAc) (silica, UV, and I_2; ^{1}H NMR (400 MHz, $CDCl_3$) δ 7.98 (d, J = 8.4 Hz, 1H), 7.93 (d, J = 7.6 Hz, 2H), 7.76 (s, 1H), 7.65 (d, J = 8.0 Hz, 1H), 7.58 (t, J = 7.6 Hz, 1H), 7.48 (t, J = 8.0 Hz, 2H), 7.37 (t, J = 7.6 Hz, 1H), 7.30 (d, J = 8.0 Hz, 1H), 6.94 (s, 1H), 2.10 (s, 3H); ^{13}C NMR (101 MHz, $CDCl_3$) δ 169.7, 138.0, 135.2, 134.1, 129.4, 128.0, 127.0, 125.7, 125.3, 123.7, 120.1, 118.1, 113.7, 75.5, 59.1, 47.9, 20.9; IR (neat) ν_{max} 2931, 2224, 1747, 1451, 1369, 1232, 1177, 1128 cm^{-1}; HRMS (ESI) for $C_{19}H_{14}BrNO_4SNa$ $(M + Na)^+$ calcd 453.9725, found 453.9727.

*4-Iodo-1-phenylbut-3-yn-2-yl acetate (**5**):* colorless oil (1.31 g, 50% yield); R_f = 0.50 (9:1 hexane/EtOAc) (silica, UV, and I_2); ^{1}H NMR (400 MHz, $CDCl_3$) δ 7.48−7.22 (m, 5H), 5.64 (br t, J = 6.8 Hz, 1H), 3.07 (d, J = 7.4 Hz, 2H), 2.05 (s, 3H); ^{13}C NMR (101 MHz, $CDCl_3$) δ 169.7, 135.6, 129.7, 128.4, 127.1, 91.3, 77.2, 65.7, 41.2, 20.9; IR (neat) ν_{max} 2930, 1745, 1371, 1128, 1018, 750 cm^{-1}; MS (EI) m/z 316 (M^+ + 2, 29), 315 (M^+ + 1, 100). Anal. Calcd for $C_{12}H_{11}IO_2$: C, 45.88; H, 3.53. Found: C, 45.76; H, 3.61.

Preparation of 4 from 3: General procedure (GP-2). Following the known synthetic procedures,[8] compounds **4** were prepared from **4′** through O-acetylation in excellent yields. The reaction of **3** with *n*-BuLi (2.0 equiv) followed by quenching with NCS allowed access to **4′** in good yields. Spectral data of compound **4′** match reported values.[8]

*4-Chloro-1-phenylbut-3-yn-2-yl acetate (**4a**):* 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, $CDCl_3$) δ 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, $CDCl_3$) δ 169.7, 135.5, 129.6, 128.4, 127.1, 66.4, 65.1, 64.6, 41.0, 20.9; IR (neat) ν_{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 (**4b**):* 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, $CDCl_3$) δ 7.30 (d, J = 7.2 Hz, 2H), 7.24 (d, J = 8.0 Hz, 3H), 5.51 (t, J = 7.2 Hz, 1H), 3.08 (d, J = 6.8 Hz, 2H), 1.15 (s, 9H); ^{13}C NMR (101 MHz, $CDCl_3$) δ 177.2, 135.7, 129.6, 128.3, 127.0, 66.7, 64.6, 64.4, 41.1, 38.7, 27.0; IR (neat) ν_{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.

*8-(Chloroethynyl)-1,4-dioxaspiro[4.5]decan-8-yl acetate (**4c**):* colorless oil (890 mg, 54% yield); R_f = 0.28 (30:1 hexane/EtOAc) (silica, UV, and I_2); ^{1}H NMR (400 MHz, $CDCl_3$) δ 3.93 (s, 4H), 2.28−2.15 (m, 4H), 2.06 (s, 3H), 1.85−1.69 (m, 4H); ^{13}C NMR (101 MHz, $CDCl_3$) δ 169.2, 107.4, 73.8, 68.4, 64.7, 64.4, 34.2, 30.9, 21.7; IR (neat) ν_{max} 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. Calcd for $C_{12}H_{15}ClO_4$: C, 55.71; H, 5.84. Found: C, 55.61; H, 5.92.

Gold-Catalyzed Hydration of 1, 4, 5, and 11 for the Preparation of 2, 6, 7, and 12, Respectively: General Procedure (GP-3). A mixture of PPh_3AuCl (14.7 mg, 0.03 mmol) and $AgSbF_6$ (10.2 mg, 0.03 mmol) in dioxane (2.0 mL) was stirred in a Schlenk flask under an argon atmosphere for 20 min an ambient temperature. This freshly prepared light pink colored gold−silver complex mixture was added to another Schlenk flask containing a solution of **1** (1.0 mmol) in CH_3NO_2 (100 μL) followed by the addition of deionized 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 (**2a**):* pale yellow oil (262 mg, 92% yield); R_f = 0.56 (9:1 hexane/EtOAc) (silica, UV, and I_2); ^{1}H NMR (400 MHz, $CDCl_3$) δ 7.38−7.25 (m, 3H), 7.21 (d, J = 6.8 Hz, 2H), 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); ^{13}C NMR (101 MHz, $CDCl_3$) δ 198.7, 170.2, 135.2, 129.3, 128.7, 127.3, 77.0, 37.3, 32.4, 20.5; IR (neat) ν_{max} 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 $C_{12}H_{13}BrO_3$: C, 50.55; H, 4.60. Found: C, 50.42; H, 4.71.

*3-Bromo-2-oxo-1-phenylpropyl acetate (**2b**):* pale yellow oil (233 mg, 86% yield); R_f = 0.30 (9:1 hexane/EtOAc) (silica, UV, and I_2); ^{1}H NMR (400 MHz, $CDCl_3$) δ 7.43 (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); ^{13}C NMR (101 MHz, $CDCl_3$) δ 195.6, 170.1, 132.4, 129.9, 129.3, 128.3, 78.3, 31.1, 20.6; IR (neat) ν_{max} 2937, 1747, 1720, 1375 cm^{-1}; MS (EI) m/z 27 (M^+ + 1, 100), 156 (62), 127 (28). Anal. Calcd for $C_{11}H_{11}BrO_3$: C, 48.37; H, 4.09. Found: C, 48.62; H, 4.15.

*3-Bromo-1-(4-fluorophenyl)-2-oxopropyl acetate (**2c**):* colorless oil (237 mg, 82% yield); R_f = 0.24 (9:1 hexane/EtOAc) (silica, UV, and I_2); ^{1}H NMR (400 MHz, $CDCl_3$) δ 7.46−7.38 (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); ^{13}C NMR (101 MHz, $CDCl_3$) δ 195.6, 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. ^{19}F NMR (376 MHz, $CDCl_3$) δ −110.72 (q, J = 2.6 Hz); IR (neat) ν_{max} 2934, 1755, 1620, 1512, 1221, 1078 cm^{-1}; MS (EI) m/z 289 (M^+ + 1, 100), 287 (62), 269 (18), 201 (27), 81 (97). Anal. Calcd for $C_{11}H_{10}BrFO_3$: C, 45.70; H, 3.49. Found: C, 45.61; H, 3.55.

*3-Bromo-2-oxo-1-p-tolylpropyl acetate (**2d**):* pale yellow oil (237 mg, 83% yield); R_f = 0.38 (9:1 hexane/EtOAc) (silica, UV, and I_2); ^{1}H NMR (400 MHz, $CDCl_3$) δ 7.31(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); ^{13}C NMR (101 MHz, $CDCl_3$) δ 195.7, 170.2, 140.0, 130.0, 129.4, 128.3, 78.2, 31.2, 21.3, 20.6; IR (neat) ν_{max} 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 $C_{12}H_{13}BrO_3$: C, 50.55; H, 4.60. Found: C, 50.65; H, 4.53.

*3-Bromo-1-(3-methoxyphenyl)-2-oxopropyl acetate (**2e**):* pale yellow oil (235 mg, 78% yield); R_f = 0.23 (9:1 hexane/EtOAc) (silica, UV, and I_2); ^{1}H NMR (400 MHz, $CDCl_3$) δ 7.34 (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); ^{13}C NMR (101 MHz, $CDCl_3$) δ 195.4, 170.1, 160.2, 133.7, 130.4, 120.4, 115.5, 113.5, 78.2, 55.4, 31.0, 20.6; IR (neat) ν_{max} 2941, 1745, 1668, 1601, 1373, 1228, 1039 cm^{-1}; MS (EI) m/z 302 (M^+ + 2, 54), 301 (M^+ + 1, 100). Anal. Calcd for $C_{12}H_{13}BrO_4$: C, 47.86; H, 4.35. Found: C, 47.92; H, 4.31.

*3-Bromo-1-(2-chlorophenyl)-2-oxopropyl acetate (**2f**):* colorless oil (262 mg, 86% yield); R_f = 0.30 (9:1 hexane/EtOAc) (silica, UV, and I_2); ^{1}H NMR (400 MHz, $CDCl_3$) δ 7.52−7.28 (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); ^{13}C NMR (101 MHz, $CDCl_3$) δ 195.1, 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 $C_{11}H_{10}BrClO_3$: C, 43.24; H, 3.30. Found: C, 43.37; H, 3.26.

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*3-Bromo-2-oxo-1-o-tolylpropyl acetate (**2g**):* colorless oil (251 mg, 88% yield); R_f = 0.39 (9:1 hexane/EtOAc) (silica, UV, and I_2); ^{1}H NMR (400 MHz, $CDCl_3$) δ 7.36−7.22 (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); ^{13}C NMR (101 MHz, $CDCl_3$) δ 195.8, 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 $C_{12}H_{13}BrO_3$: C, 50.55; H, 4.60. Found: C, 50.67; H, 4.54.

*1-(2-(Allyloxy)phenyl)-3-bromo-2-oxopropyl acetate (**2h**):* colorless oil (265 mg, 81% yield); R_f = 0.47 (9:1 hexane/EtOAc) (silica, UV, and I_2); ^{1}H NMR (400 MHz, $CDCl_3$) δ 7.43−7.29 (m, 2H), 7.01 (br t, J = 7.6 Hz, 1H), 6.94 (d, J = 8.0 Hz, 1H), 6.64 (s, 1H), 6.12−5.97 (m, 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); ^{13}C NMR (101 MHz, $CDCl_3$) δ 195.9, 170.1, 155.8, 132.4, 131.0, 130.1, 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 $C_{14}H_{15}BrO_4$: C, 51.40; H, 4.62. Found: C, 51.36; H, 4.71.

*3-Bromo-1-(naphthalen-1-yl)-2-oxopropyl acetate (**2i**):* thick brown oil (247 mg, 77% yield); R_f = 0.56 (9:1 hexane/EtOAc) (silica, UV, and I_2); ^{1}H NMR (400 MHz, $CDCl_3$) δ 8.10 (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); ^{13}C NMR (101 MHz, $CDCl_3$) δ 195.9, 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 $C_{15}H_{13}BrO_3$: C, 56.10; H, 4.08. Found: C, 56.18; H, 3.96.

*3-Bromo-1-(2,6-dimethoxyphenyl)-2-oxopropyl acetate (**2j**):* colorless liquid (299 mg, 90% yield); R_f = 0.28 (19:1 hexane/EtOAc) (silica, UV, and I_2); ^{1}H NMR (400 MHz, $CDCl_3$) δ 7.35 (t, J = 8.0 Hz, 1H), 6.91 (s, 1H), 6.59 (d, J = 8.0 Hz, 2H), 4.03 (d, J = 14.0 Hz, 1H), 3.96 (d, J = 14.0 Hz, 1H), 3.82 (s, 6H), 2.17 (s, 3H); ^{13}C NMR (101 MHz, $CDCl_3$) δ 196.6, 170.1, 158.9, 131.8, 111.3, 104.3, 69.6, 56.1, 31.8, 20.9. IR (neat) ν_{max} 2939, 1753, 1736, 1597, 1479, 1230, 1105, 1022, 783 cm^{-1}; MS (EI) m/z 332 (M^+ + 2, 100). Anal. Calcd for $C_{13}H_{15}BrO_5$: C, 47.15; H, 4.57. Found: C, 47.23; H, 4.51.

*tert-Butyl 3-(2-acetoxy-4-bromo-3-oxobutyl)-1H-indole-1-carboxylate (**2k**):* thick yellow oil (335 mg, 79% yield); R_f = 0.47 (9:1 hexane/EtOAc) (silica, UV, and I_2); ^{1}H NMR (400 MHz, $CDCl_3$) δ 8.14 (br d, J = 7.2 Hz, 1H), 7.57 (d, J = 7.6 Hz, 1H), 7.46 (s, 1H), 7.34 (t, J = 7.2 Hz, 1H), 7.27 (t, J = 7.6 Hz, 1H), 5.51 (t, J = 5.2 Hz, 1H), 3.95 (s, 2H), 3.30 (dd, J = 14.8, 5.2 Hz, 1H), 3.22 (dd, J = 14.8, 7.2 Hz, 1H), 2.10 (s, 3H), 1.68 (s, 9H); ^{13}C NMR (101 MHz, $CDCl_3$) δ 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) ν_{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 $C_{19}H_{22}BrNO_5$: C, 53.79; H, 5.23; N, 3.30. Found: C, 53.71; H, 5.28; N, 3.36.

*1,8-Dibromo-2-oxooctan-3-yl acetate (**2l**):* pale yellow oil (306 mg, 89% yield); R_f = 0.66 (19:1 hexane/EtOAc) (silica and I_2); ^{1}H NMR (400 MHz, $CDCl_3$) δ 5.24 (dd, J = 8.0, 4.4 Hz, 1H), 4.06 (d, J = 13.6 Hz, 1H), 4.01 (d, J = 13.6 Hz, 1H), 3.40 (t, J = 6.8 Hz, 2H), 2.16 (s, 3H), 1.94−1.77 (m, 4H), 1.55−1.38 (m, 4H); ^{13}C NMR (101 MHz, $CDCl_3$) δ 198.9, 170.5, 76.5, 33.5, 32.3, 31.4, 30.8, 27.6, 24.3, 20.6; IR (neat) ν_{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 $C_{10}H_{16}Br_2O_3$: C, 34.91; H, 4.69. Found: C, 34.85; H, 4.58.

*8-Azido-1-bromo-2-oxooctan-3-yl acetate (**2m**):* yellow liquid (272 mg, 89% yield); R_f = 0.44 (6:1 hexane/EtOAc) (silica and I_2); ^{1}H NMR (400 MHz, $CDCl_3$) δ 5.24 (dd, J = 8.4, 4.4 Hz, 1H), 4.06 (d, J = 13.6 Hz, 1H), 4.01 (d, J = 13.6 Hz, 1H), 3.27 (t, J = 6.8 Hz, 2H), 2.15 (s, 3H), 1.95−1.77 (m, 2H), 1.69−1.57 (m, 2H) 1.50−1.34 (m, 4H); ^{13}C NMR (101 MHz, $CDCl_3$) δ 198.9, 170.5, 76.5, 51.2, 31.4, 30.8, 28.6, 26.3, 24.7, 20.6; IR (neat) ν_{max} 2934, 2100, 1747, 1718, 1371, 1234, 1028 cm^{-1}; MS (EI) m/z 307 (M^+ + 2, 100). Anal. Calcd for $C_{10}H_{16}BrN_3O_3$: C, 39.23; H, 5.27; N, 13.73. Found: C, 39.36; H, 5.22; N, 13.65.

*1-Bromo-8-(tert-butoxycarbonylamino)-2-oxooctan-3-yl acetate (**2n**):* colorless oil (331 mg, 87% yield); R_f = 0.39 (4:1 hexane/EtOAc) (silica and I_2); ^{1}H NMR (400 MHz, $CDCl_3$) δ 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, $CDCl_3$) δ 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) ν_{max} 3375, 2934, 1745, 1695, 1520, 1367, 1242, 1168 cm^{-1}; MS (EI) m/z 381 (M^+ + 2, 100). Anal. Calcd for $C_{15}H_{26}BrNO_5$: C, 47.38; H, 6.89; N, 3.68. Found: C, 47.45; H, 6.82; N, 3.61.

*1-Bromo-2-oxo-8-(tetrahydro-2H-pyran-2-yloxy)octan-3-yl acetate (**2o**):* colorless oil (263 mg, 72% yield); R_f = 0.37 (9:1 hexane/EtOAc) (silica and I_2); ^{1}H NMR (400 MHz, $CDCl_3$) δ 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, $CDCl_3$) δ 198.9, 170.5, 98.9, 76.6, 67.3, 62.4, 31.5, 30.9, 30.7, 29.4, 25.9, 25.5, 25.0, 20.6, 19.7; IR (neat) ν_{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 $C_{15}H_{25}BrO_5$: C, 49.32; H, 6.90. Found: C, 49.38; H, 6.85.

*8-(Benzyloxy)-1-bromo-2-oxooctan-3-yl acetate (**2p**):* colorless oil (349 mg, 94% yield); R_f = 0.35 (4:1 hexane/EtOAc) (silica, UV, and I_2); ^{1}H NMR (400 MHz, $CDCl_3$) δ 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, $CDCl_3$) δ 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) ν_{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 $C_{17}H_{23}BrO_4$: C, 55.00; H, 6.24. Found: C, 55.16; H, 6.29.

*1-Bromo-8-hydroxy-2-oxooctan-3-yl acetate (**2q**):* colorless oil (258 mg, 92% yield); R_f = 0.73 (4:1 hexane/EtOAc) (silica and I_2); ^{1}H NMR (400 MHz, $CDCl_3$) δ 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, $CDCl_3$) δ 199.1, 170.6, 76.6, 62.5, 32.3, 31.6, 30.9, 25.3, 24.9, 20.6; IR (neat) ν_{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 $C_{10}H_{17}BrO_4$: C, 42.72; H, 6.09. Found: C, 42.58; H, 6.15.

*1-(2-Bromoacetyl)cyclopentyl acetate (**2r**):* colorless solid (217 mg, 87% yield); mp = 42−43 °C; R_f = 0.52 (9:1 hexane/EtOAc) (silica and I_2); ^{1}H NMR (400 MHz, $CDCl_3$) 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); ^{13}C NMR (101 MHz, $CDCl_3$) δ 199.5, 171.3, 93.1, 36.6, 30.6, 24.7, 21.0; IR (KBr) ν_{max} 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 $C_9H_{13}BrO_3$: 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 (**2s**):* colorless solid (250 mg, 78% yield); mp = 43−44 °C; R_f = 0.31 (9:1 hexane/EtOAc) (silica and I_2); ^{1}H NMR (400 MHz, $CDCl_3$) 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); ^{13}C NMR (101 MHz, $CDCl_3$) δ 199.7, 170.7, 107.3, 83.3, 64.6, 64.4, 30.1, 29.7, 29.6, 20.8; IR (neat) ν_{max} 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 $C_{12}H_{17}BrO_5$: C, 44.88; H, 5.34. Found: C, 44.96; H, 5.31.

*4-Bromo-3-oxo-1-phenylbutan-2-yl pivalate (**2t**):* colorless oil (278 mg, 85% yield); R_f = 0.59 (10:1 hexane/EtOAc) (silica, UV, and I_2); ^{1}H NMR (400 MHz, $CDCl_3$) 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); ^{13}C NMR (101 MHz, $CDCl_3$) 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) ν_{max} 2974, 1728,

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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 $C_{15}H_{19}BrO_3$: C, 55.06; H, 5.85. Found: C, 55.16; H, 5.79.

*4-Chloro-3-oxo-1-phenylbutan-2-yl acetate (**6a**):* colorless oil (195 mg, 81% yield); R_f = 0.52 (9:1 hexane/EtOAc) (silica, UV, and I_2); ^1H NMR (400 MHz, $CDCl_3$) δ 7.34−7.25 (m, 3H), 7.20 (d, J = 6.8 Hz, 2H), 5.39 (dd, J = 7.6, 5.6 Hz, 1H), 4.12 (d, J = 16.4 Hz, 1H), 3.99 (d, J = 16.4 Hz, 1H), 3.15 (dd, J = 14.0, 5.2 Hz, 1H), 3.11 (dd, J = 14.0, 8.0 Hz, 1H), 2.10 (s, 3H); ^{13}C NMR (101 MHz, $CDCl_3$) δ 199.2, 170.3, 135.0, 129.3, 128.8, 127.4, 77.2, 47.1, 37.1, 20.5; IR (neat) ν_{max} 2935, 1741, 1732, 1496, 1373, 1051, 702 cm^{-1}; MS (EI) m/z 241 (M^+ + 1, 23), 240 (M^+, 21), 239 (M^+ − 1, 68), 219 (51), 161 (100), 143 (18). Anal. Calcd for $C_{12}H_{13}ClO_3$: C, 59.88; H, 5.44. Found: C, 59.75; H, 5.51.

*4-Chloro-3-oxo-1-phenylbutan-2-yl pivalate (**6b**):* colorless oil (238 mg, 73% yield); R_f = 0.26 (9:1 hexane/EtOAc) (silica, UV, and I_2); ^1H NMR (400 MHz, $CDCl_3$) δ 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}C NMR (101 MHz, $CDCl_3$) δ 199.3, 177.8, 135.2, 129.4, 128.7, 127.3, 76.9, 47.0, 38.6, 37.1, 26.9; IR (neat) ν_{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 (**6c**):* colorless solid (224 mg, 81% yield); mp = 64−65 °C; R_f = 0.5 (4:1 hexane/EtOAc) (silica and I_2); ^1H NMR (400 MHz, $CDCl_3$) δ 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}C NMR (101 MHz, $CDCl_3$) δ 199.7, 170.6, 107.2, 83.2, 64.6, 64.4, 44.3, 30.0, 29.3, 20.8; IR (neat) ν_{max} 2947, 1736, 1728, 1442, 1377, 1236, 1095, 1033, 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 (**7**):* yellow oil (256 mg, 77% yield); R_f = 0.37 (9:1 hexane/EtOAc) (silica, UV and I_2); ^1H NMR (400 MHz, $CDCl_3$) δ 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}C NMR (101 MHz, $CDCl_3$) δ 200.0, 170.1, 135.5, 129.4, 128.7, 127.3, 76.7, 37.9, 20.6, 2.8; IR (neat) ν_{max} 2934, 1745, 1715, 1496, 1373, 1236, 1045, 750 cm^{-1}; MS (EI) 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-Iodo-3-oxo-1-phenylbutan-2-yl Acetate (**8**).* To a stirred solution of **2a** (70 mg, 0.25 mmol) in CH_3OH/H_2O (1 mL, 4:1) was added $Sc(OTf)_3$ (24 mg, 0.05 mmol) 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 chromatography on silica gel eluting with hexane/ethyl acetate (10:1) to accomplish **8**:[11] yellow oil (49 mg, 83% yield); R_f = 0.37 (9:1 hexane/EtOAc) (silica, UV, and I_2); ^1H NMR (400 MHz, $CDCl_3$) δ 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), 2.95 (dd, J = 14.0, 7.6 Hz, 2H); ^{13}C NMR (101 MHz, $CDCl_3$) δ 203.4, 135.8, 129.3, 128.9, 127.3, 76.1, 40.4, 31.4; IR (neat) ν_{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-Aminothiazole 9 and 10: General Procedure (GP-4). A mixture of α-acyloxy α'-halo ketones **2** (0.25 mmol) and thiourea (0.37 mmol) was stirred in EtOH (1.0 mL) at 80 °C overnight. Progress of the reaction was monitored by TLC. After complete consumption of **2**, the reaction mixture was extracted with CH_2Cl_2 (2 × 10 mL), and the organic layers were washed with brine, dried over Na_2SO_4, and concentrated under reduced pressure. The residue was purified by column chromatography on silica gel.[9a]

*4-(Ethoxy(phenyl)methyl)thiazol-2-amine (**9a**):* brown oil (36 mg, 63% yield); R_f = 0.61 (3:2 hexane/EtOAc) (silica, UV, and I_2); ^1H NMR (400 MHz, $CDCl_3$) δ 7.45−7.41 (m, 2H), 7.39−7.34 (m, 2H), 7.31 (dt, J = 7.2, 1.6 Hz, 1H), 6.31 (s, 1H), 5.29 (s, 1H), 5.09 (brs, 2H), 3.62−3.46 (m, 2H), 1.27 (t, J = 7.2 Hz, 3H); ^{13}C NMR (101 MHz, $CDCl_3$) δ 167.9, 153.1, 140.5, 128.3, 127.8, 127.4, 105.1, 80.2, 64.7, 15.3; IR (neat) ν_{max} 3413, 2926, 1605, 1528 cm^{-1}; HRMS (ESI) for $C_{12}H_{14}N_2OSNa$ (M + Na)$^+$ calcd 257.0725, found 257.0728.

*4-(Ethoxy(3-methoxyphenyl)methyl)thiazol-2-amine (**9b**):* yellow oil (44 mg, 67% yield); R_f = 0.54 (3:2 hexane/EtOAc) (silica, UV, and I_2); ^1H NMR (400 MHz, $CDCl_3$) δ 7.25 (br s, 1H), 6.99 (br 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, $CDCl_3$) δ 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) ν_{max} 3287, 2926, 1600, 1517, 1260 cm^{-1}; HRMS (ESI) for $C_{13}H_{17}N_2O_2S$ (M + H)$^+$: calcd 265.101, found 265.1013.

*1-(2-Aminothiazol-4-yl)-2-phenylethyl acetate (**10**):* yellow oil (42 mg, 65% yield); R_f = 0.61 (3:2 hexane/EtOAc) (silica, UV, and I_2); ^1H NMR (400 MHz, $CDCl_3$) δ 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, $CDCl_3$) δ 170.2, 168.1, 149.5, 137.0, 129.4, 128.3, 126.6, 106.2, 72.6, 40.3, 21.2; IR (neat) ν_{max} 3386, 3156, 1709, 1638, 1523 cm^{-1}; HRMS (ESI) for $C_{13}H_{14}N_2O_2SNa$ (M + Na)$^+$ calcd 285.0656, found 285.0675.

*(4-Bromo-2-methoxybut-3-yn-1-yl)benzene (**11b**):* pale yellow oil (130 mg, 83% yield); R_f = 0.66 (9:1 hexane/EtOAc) (silica, UV, and I_2); ^1H NMR (400 MHz, $CDCl_3$) δ 7.31 (t, J = 6.8 Hz, 2H), 7.26 (d, J = 7.2 Hz, 3H), 4.17 (t, J = 6.8 Hz, 1H), 3.41 (s, 3H). 3.03 (dd, J = 8.8, 4.0 Hz, 2H); ^{13}C NMR (101 MHz, $CDCl_3$) δ 136.9, 129.6, 128.3, 126.7, 78.7, 73.1, 56.8, 46.3, 42.0, 29.7; IR (neat) ν_{max} 2931, 2213, 1500, 1456, 1330 cm^{-1}; HRMS (ESI) for $C_{11}H_{11}BrONa$ (M + Na)$^+$ calcd 260.9891, found 260.9890.

*4-Bromo-1-phenylbut-3-yn-2-yl benzoate (**11c**):* pale yellow oil (170 mg, 58% yield); R_f = 0.54 (9:1 hexane/EtOAc) (silica, UV, and I_2); ^1H NMR (400 MHz, $CDCl_3$) δ 8.04 (d, J = 7.6 Hz, 2H), 7.58 (t, J = 7.2 Hz, 1H), 7.45 (t, J = 7.6 Hz, 2H), 7.36−7.30 (m, 4H), 7.28−7.25 (m, 1H), 5.80 (t, J = 6.8 Hz, 1H), 5.38 (dd, J = 6.8, 3.6 Hz, 2H); ^{13}C NMR (101 MHz, $CDCl_3$) δ 165.3, 135.6, 133.3, 129.8, 129.7, 129.6, 128.5, 127.1, 77.2, 65.7, 47.3, 41.1; IR (neat) ν_{max} 2920, 2219, 1725, 1451, 1254, 1111 cm^{-1}; HRMS (ESI) for $C_{17}H_{13}BrO_2Na$ (M + Na)$^+$ calcd 350.9997, found 350.9999.

*4-Bromo-3-oxo-1-phenylbutan-2-yl benzoate (**12c**):* yellow oil (287 mg, 83% yield); R_f = 0.34 (9:1 hexane/EtOAc) (silica, UV, and I_2); ^1H NMR (400 MHz, $CDCl_3$) δ 8.02 (d, J = 7.6 Hz, 2H), 7.61 (t, J = 7.2 Hz, 1H), 7.47 (t, J = 7.6 Hz, 2H), 7.36−7.24 (m, 5H), 5.67 (dd, J = 7.2, 5.2 Hz, 1H), 3.97 (s, 2H), 3.38−3.24 (m, 2H); ^{13}C NMR (101 MHz, $CDCl_3$) δ 198.8, 165.9, 135.3, 133.8, 129.9, 129.5, 128.8, 128.6, 127.4, 77.7, 37.7, 32.8; IR (neat) ν_{max} 2925, 1714, 1445, 1265 cm^{-1}; HRMS (ESI) for $C_{17}H_{16}BrO_3$ (M + H)$^+$ calcd 347.0283, found 347.0283.

3-Bromo-2-oxo-1-phenylpropyl Acetate (^{18}*O-Labeled, **2b′**).* Following the general procedure GP-3, hydration of **1b** (200 mg, 0.80 mmol) under the optimized conditions in the presence of $H_2{}^{18}O$ (48 μL, 2.40 mmol) gave **2b′** (180 mg, 84% yield) as a pale yellow oil: R_f = 0.33 (9:1 hexane/EtOAc) (silica, UV, and I_2); ^1H NMR (400 MHz, $CDCl_3$) δ 7.43 (br s, 5H), 6.30 (s, 1H), 3.97 (q, J = 13.6 Hz, 2H), 2.20 (s, 3H); ^{13}C NMR (101 MHz, $CDCl_3$) δ 195.6, 170.1, 132.4, 129.9, 129.3, 128.3, 78.3, 31.1, 20.6; IR (neat) ν_{max} 2936, 1736, 1720, 1500, 1347, 1221 cm^{-1}; HRMS (ESI) for $C_{11}H_{12}BrO_2O^{18}$ (M + H)$^+$ calcd 272.997, found 272.9973.

*3-Bromo-1-hydroxy-1-phenylpropan-2-one (**2b″**).* To a stirred solution of **2b′** (100 mg, 0.37 mmol) in CH_3OH/H_2O (1.0 mL, 4:1) was added $Sc(OTf)_3$ (36 mg, 0.07 mmol) at room temperature. The reaction mixture was stirred overnight an ambient temperature. The solvent was evaporated under reduced pressure. The crude material was diluted with diethyl ether (20 mL). The organic layer was washed with brine (5.0 mL), dried over Na_2SO_4, and concentrated under reduced pressure. The crude mixture was purified by column

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chromatography on silica gel eluting with hexane/ethyl acetate (10:1) to obtain **2b″**:[11] pale yellow oil (27 mg, 33% yield); R_f = 0.43 (4:1 hexane/EtOAc) (silica, UV, and I_2); ^{1}H NMR (400 MHz, $CDCl_3$) δ 7.45−7.32 (m, 5H), 5.52 (s, 1H), 3.81 (d, J = 13.2 Hz, 1H), 3.94 (d, J = 13.2 Hz, 1H); ^{13}C NMR (101 MHz, $CDCl_3$) δ 200.6, 134.6, 131.7, 130.3, 129.3, 128.9, 127.3, 26.4; IR (neat) ν_{max} 3479, 2920, 1714, 1599, 1445 cm^{-1}; HRMS (ESI) for $C_9H_9BrO_2Na$ $(M + Na)^+$ calcd 250.9684, found 250.9684.

■ ASSOCIATED CONTENT

Supporting Information

Figures giving the ^{1}H and ^{13}C spectra of new compounds. This material is available free of charge via the Internet at http://pubs.acs.org

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Notes

The authors declare no competing financial interest.

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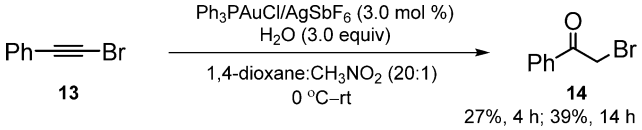
(15) The reaction of bromoalkyne **13**, having no α-acyloxy group, under the optimized conditions produced the hydration product **14** in 27% and 39% yields in 4 and 14 h, respectively.



(16) See the Supporting Information for details.

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