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Gold-Catalyzed Regioselective Hydration of Propargyl Acetates Assisted by a Neighboring Carbonyl Group: Access to α-Acyloxy Methyl Ketones and Synthesis of (±)-Actinopolymorphol B†

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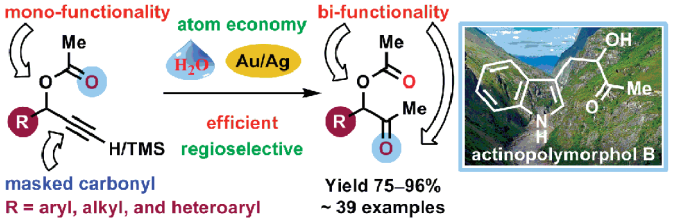

A general atom-economical approach for the synthesis of α-acyloxy methyl ketone is demonstrated through regioselective hydration of a wide range of propargyl acetates. Readily available catalyst comprising of 1% Ph_3PAuCl and 1% $AgSbF_6$ in dioxane−H_2O efficiently hydrolyzes the terminal alkynes of the propargyl acetate in the absence of acid promoters at ambient temperature within a short time. Effective regioselective hydration is facilitated by the neighboring carbonyl group as demonstrated through ^{18}O-labeling study. Compatibility of functional moieties and tolerance to various acid-labile protecting groups 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. Stereointegrity of the propargylic acetate is preserved during the hydration. The robustness of the system is successfully demonstrated through gram scale preparation of the product in nearly quantitative yield. The common α-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.

Introduction

A straightforward and atom-economical approach to the formation of carbonyl derivatives through alkyne hydration is not only environmentally benign, but also cost-effective.[1,2] Therefore, hydrocarbon alkynes can be considered as pro-ketones.[2] A functional group having a directing unit adjacent to terminal alkyne is expected to assist in the generation of either α- or β-substituted carbonyls through hydration.[3] A propargylic ester moiety would trigger regioselective Markovnikov's hydration of terminal alkynes with ease, and the hydration product would transform to α-hydroxy methyl ketones in a straightforward manner.[4] The α-hydroxy methyl ketone moieties are found in many natural products of pharmacological significance, and some representative molecules are shown in Figure 1.[5]

† Dedicated to Professor Tamejiro Hiyama on the occasion of his retirement from Kyoto University, Japan.

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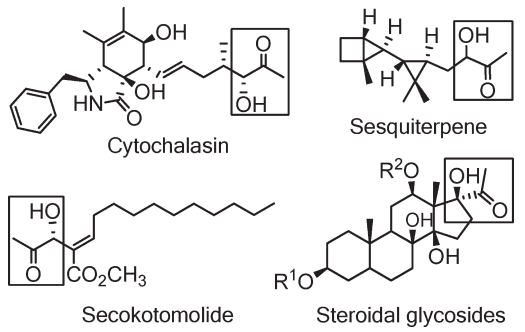

FIGURE 1. Examples of natural products containing α-hydroxy methyl ketones.

Combinations of toxic mercury salts (HgO) with Brønsted or Lewis acids (H_2SO_4 or $BF_3{-}OEt_2$ etc.) are the reagents commonly used to perform hydration of alkynes.[6] Addition of water and oxygen-bearing nucleophiles to activated as well as nonactivated alkynes has been carried out with use of transition metal catalysts and acid promoters.[7,8] Alkyne hydrations in the absence of metals generally require harsh conditions.[9] Addition of oxygen-bearing nucleophiles to alkynes through active alkynophilic gold complexes has been extensively investigated.[10,11] Utility of cationic gold complexes in alkyne hydrations has also been reported.[12] For example, terminal and internal alkynes undergo hydration in acid-free condition when refluxed in aqueous methanol with $NaAuCl_4$.[12o] Teles,[12n] Hayashi and Tanaka,[12m] Laguna,[12l] and others[12a,b,e,g−k,p,q] have reported the addition of methanol and water to alkynes in the presence of gold catalysts and acid promoters. Nonregioselective Au(I)-catalyzed hydration of propargylic alcohols resulted in mixtures of methyl ketones and α,β-unsaturated aldehydes.[12d,m] A highly efficient [(NHC)Au^I]-catalyzed hydration of nonactivated alkynes at 120 °C was demonstrated by Nolan and co-workers.[12c] Survey of the gold-catalyzed hydration of alkynes reveals that the reactions invariably require mineral acid as promoters, higher temperature, or both.[12] 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.[12] Recently, Leyva and Corma have demonstrated the hydration of terminal alkynes at room temperature in the presence of air-stable $AuSPhosNTf_2$; the reaction required 24 h for completion.[12f]

This scenario has prompted us to envisage an alternative strategy for the efficient hydration of alkynes keeping in view 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

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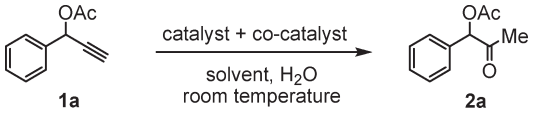
TABLE 1. Optimization of Reaction Conditions[a]



1a 2a

entry	catalyst (mol %)	cocatalyst (mol %)	solvent (0.5 mL)	water (equiv)	time (h)	yield (%)
1	5% $AuCl_3$	5% AgOAc	dioxane	3	36	$< 5^b$
2	5% $AuCl_3$	5% $AgSbF_6$	dioxane	3	36	60^b
3	5% $AuBr_3$	5% $AgSbF_6$	dioxane	3	36	30^b
4	5% AuCl	5% $AgSbF_6$	dioxane	3	36	10^b
5	5% Ph_3PAuCl	5% $AgSbF_6$	dioxane	3	3	97^c
6	5% Ph_3PAuCl	5% $AgSbF_6$	dioxane	5	4	93^c
7	5% Ph_3PAuCl	5% $AgSbF_6$	dioxane	2	7	92^c
8	**1% Ph_3PAuCl**	**1% $AgSbF_6$**	**dioxane**	**3**	**8**	**97^c**
9	0.1% Ph_3PAuCl	0.1% $AgSbF_6$	dioxane	3	70	89^c
10	2% Ph_3PAuCl	2% AgOTf	dioxane	3	28	90^b
11	2% Ph_3PAuCl	2% $AgBF_4$	dioxane	3	22	85^b
12	2% Ph_3PAuCl	2% $AgOOCCF_3$	dioxane	3	36	15^b
13	5% Ph_3PAuCl	Nil	dioxane	3	36	NR
14	Nil	5% $AgSbF_6$	dioxane	3	36	NR
15	1% Ph_3PAuCl	1% $AgSbF_6$	CH_2CI_2	3	24	63^b
16	1% Ph_3PAuCl	1% $AgSbF_6$	MeOH	3	36	37^b
17	1% Ph_3PAuCl	1% $AgSbF_6$	DMF/DMSO	3	36	NR

[a]Reactions were carried out with **1a** (0.3 mmol) in solvent (0.5 mL) at rt. [b]NMR yield. [c]Isolated yield.

of acid-labile protecting units with broad functional group compatibility,[13] (5) short reaction time leading to overall efficiency, (6) incorporation of multireactive functionalities in the products, and (7) development of precursor molecules for further complex synthesis. In the context of our wider interest in discovering new gold-catalyzed transformations of synthetic utility,[11a] we envisioned that a neighboring carbonyl group such as acetate would assist in effective and regioselective alkyne hydrations under gold-catalysis conditions. Activation of the terminal alkyne of the propargylic acetate by gold catalysts would preferentially generate 5-membered electrophilic vinyl-gold species involving 5-*exo*-*dig* attack of the carbonyl oxygen.[14] Finally, regioselective hydration would exclusively provide α-acyloxy methyl ketone, creating a carbonyl group adjacent to the acetate moiety; both functionalities would be available for further synthetic explorations. A recent report from Xu and Hammond describes the synthesis of γ-keto esters through regioselective hydration of 3-alkynoates involving neighboring carbonyl group participation.[12b] Moreover, gold-catalyzed transformation of propargylic acetates resulting in new and diverse molecular entities has been investigated extensively.[15] Herein we report an operationally simple strategy for the synthesis of a wide range of α-acyloxy methyl ketones through regioselective hydration of propargyl acetates using commercially available Ph_3PAuCl and $AgSbF_6$ in dioxane−H_2O at ambient temperature. Furthermore, this transformation is successfully employed to accomplish the first total synthesis of actinopolymorphol B.

Results and Discussion

We first investigated the hydration of 1-phenylprop-2-ynyl acetate (**1a**) (see Table 1). Precursor **1a** was prepared in a straightforward three-step synthetic protocol, reacting trimethylsilyl acetylide with benzaldehyde followed by desilylation and acetylation of the −OH group, in overall 52% yield; isolation of respective intermediates was avoided (see the Supporting Information). Following this procedure, other key synthetic precursors **1** are prepared in gram quantities with appreciable yields (see the Supporting Information).

Reaction Optimization. To start with, hydration of **1a** under different catalytic conditions comprised of gold catalysts with silver salts, water amounts, and solvents was explored. Table 1 summarizes the results of optimization studies. Solvents dioxane and water (3.0 equiv) are employed in this optimization study.[12g] A trace amount of the desired hydration product α-acyloxy methyl ketone (**2a**) was noticed when a mixture of $AuCl_3$ and AgOAc was used (entry 1). Interestingly, $AgSbF_6$ salt in conjunction with $AuCl_3$ enhanced the product yield to 60% by NMR (entry 2). Other silver salts, such as AgOTf, $AgBF_4$, and $AgNO_3$, in combination with $AuCl_3$ were ineffective. It appears that the weakly coordinating SbF_6^- counteranion generates the active gold-cationic species with ease and activates the alkyne efficiently.[10d,j] Therefore, exploration of various combinations of gold catalysts with $AgSbF_6$ were surveyed: $AuBr_3$ and AuCl were not effective (entries 3 and 4), whereas Ph_3PAuCl was found to be the best (entry 5). With selective catalysts [Ph_3PAuCl (5 mol %) and $AgSbF_6$ (5 mol %)] in hand, the amount of water required in this hydration reaction was then pursued. Whereas 3 equiv of water appeared adequate and furnished the desired product in 97% isolated yield within 3 h (entry 5), use of smaller or larger amounts

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TABLE 2. Effect of Directing Group[a]

3 **1a**; R = Ac — **4** **2a**; R = Ac

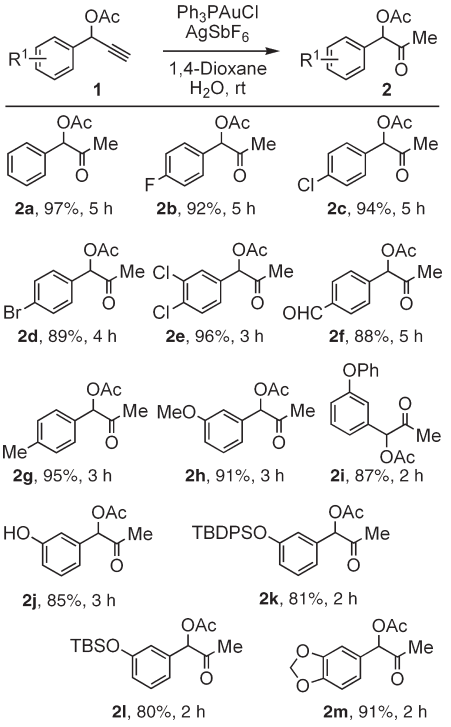
entry	3/1a	R	time (h)	4/2a	yield (%)
1	**3a**	H	24	**4a**	NR
2	**3b**	pivaloyl	10	**4b**	70[b]
3	**3c**	benzoyl	8	**4c**	78[b]
4	**1a**	acetyl	8	**2a**	97[b]
5	**3d**	Boc	24	**4d**	NR
6	**3e**	Cbz	24	**4e**	NR
7	**3f**	tosyl	10	**4f**	NR
8	**3g**	MOM	8	**4g**	NR
9	**3h**	Me	24	**4h**	NR
10	**3i**	$SiMe_3$	24	**4i**	NR[c]

[a]Reactions were carried out with **3** (1.0 mmol), Ph_3PAuCl (1 mol %), $AgSbF_6$ (1 mol %), and water (3.0 mmol) in 1,4-dioxane (1.5 mL) at room temperature. [b]Isolated yield. [c]Cleavage of O−TMS protecting group was observed.

of water (2 and 5 equiv) did not affect the product yield even though slightly longer reaction time was required for completion (entries 6 and 7). We next evaluate the amount of catalyst needed in this reaction. Lower amounts of the catalysts loading from 5 to 1 mol % of Ph_3PAuCl and $AgSbF_6$ did not affect the reaction efficiency (entry 8) and resulted in the hydration product **2a** exclusively in 97% isolated yield. Extended reaction time (~3 days) was necessary to obtain a satisfactory yield of **2a** when Ph_3PAuCl (0.1 mol %) and $AgSbF_6$ (0.1 mol %) were used (entry 9). Even though the combination of Ph_3PAuCl with AgOTf or $AgBF_4$ provided the desired hydration product in good yield (by NMR), the reaction required ~24 h for completion (entries 10 and 11). A mixture of Ph_3PAuCl with $AgOOCCF_3$ appeared ineffective (entry 12); AgOAc and $AgNO_3$ were poor. The absence of either Ph_3PAuCl or $AgSbF_6$ did not produce **2a** (entries 13 and 14). Exploration of other solvents such as CH_2Cl_2 and MeOH resulted in lower amounts of **2a** (entries 15 and 16), whereas DMF and DMSO completely failed the reaction (entry 17). Dioxane appears effective among other solvents screened. The interesting disclosure from Nolan's group describes the synthesis of α,β-unsaturated aldehyde through regioselective hydration of phenyl-substituted propargyl acetate **1a** with [(NHC)-AuCl], $AgSbF_6$ in THF−H_2O at 60 °C.[12j] In contrast, alkyne hydration of **1a** under our optimized condition exclusively delivers α-acyloxy methyl ketone **2a** (see the Supporting Information for the spectral data). 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 **1a** under different reaction conditions provides two distinct products.

Directing Group. Optimization studies reveal that hydration of **1a** effectively proceeds at ambient temperature. Presumably, the acetyl group in **1a** plays a crucial role in this hydration reaction. The effect of another directing group on the O−propargyl alcohol was then surveyed (Table 2). As shown in entry 1, terminal alkyne did not undergo hydration in the absence of directing group under the optimized catalytic condition [Ph_3PAuCl (1 mol %), $AgSbF_6$ (1 mol %), water (3.0 equiv) in 1,4-dioxane]. Pivaloyl- and benzoyl-protected propargylic esters (**3b** and **3c**) furnished the corresponding products **4b** and **4c**, respectively, in moderate yields (entries 2 and 3), whereas the O-protected propargyl acetate afforded the desired hydration product **2a** in 97% isolated yield (entry 4). We assume that the bulky group hinders the attack of H_2O to the reactive intermediate participating 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

TABLE 3. Effect of Electronic Substitution on Aryl Derivatives in Propargylic Position[a,b]



[a]Reactions were carried out with **1** (1.0 mmol), Ph_3PAuCl (1 mol %), $AgSbF_6$ (1 mol %), and water (3.0 mmol) in 1,4-dioxane (1.5 mL) at room temperature. [b]Isolated yields.

O-protecting moieties. MOM- and methyl-protected propargyl ethers are inert to the present catalytic system; formation of keto-compounds through alkyne hydration was ineffective (entries 8 and 9). Survival of Boc and MOM protecting groups testifies to the mildness of the reaction condition. However, this catalytic system cleaved the O−TMS protecting group of **3i** and afforded **3a** instead of the desired hydration product **4i** (entry 10).

Reaction Scope. The optimal reaction condition [Ph_3PAuCl (1 mol %), $AgSbF_6$ (1 mol %), water (3.0 equiv) in 1,4-dioxane] is surveyed to investigate the generality of the hydration of the terminal alkyne of the propargyl acetates at ambient temperature. The effect of the electronic groups on the aryl moiety of 1-phenylprop-2-ynyl acetate (**1a**) to the hydration reaction was explored at first (Table 3). As observed in the optimization reaction, the electronically neutral species reacted efficiently to provide the hydrated product **2a** in 97% isolated yield. Electron-withdrawing groups on the aryl moiety did not affect the product yields (**2b**−**d**); halo groups are inert to the reaction conditions. The reaction proceeded effectively in the presence of two chloro groups on the aromatic ring (**2e**). 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.[16] Under this catalytic condition, formyl functionality was well-tolerated and the desired product **2f** was obtained in 88% yield. Methyl, methoxy, and phenoxy groups at the 4- and/or 3-positions on the electron-rich aromatic ring gave the desired products in excellent yields (**2g**−**i**). The presence of the free −OH group on the aromatic ring did not affect the alkyne hydration (**2j**).

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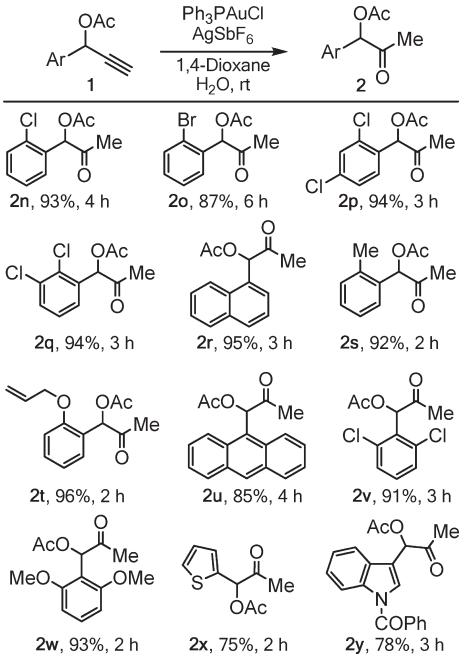
TABLE 4. Effect of Ortho-Substituted and Heteroaryls in the Propargylic Position[a,b]

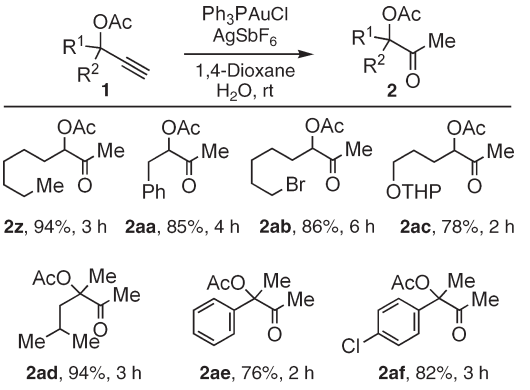


[a]Reactions were carried out with **1** (1.0 mmol), Ph_3PAuCl (1 mol %), $AgSbF_6$ (1 mol %), and water (3.0 mmol) in 1,4-dioxane (1.5 mL) at room temperature. [b]Isolated yields.

Functional group manipulations are the tools used in the fabrication of a complex molecular framework. It is therefore important to examine the relative stability of the protecting groups under this catalytic condition. Protecting groups of the 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, entry 9). Gratifyingly, the bulkier silyl protecting groups such as −TBDPS (*tert*-butyldiphenylsilyl) and −OTBS (*t*-butyldimethylsilyl) survived and the desired keto compounds **2k**, and **2*l*** were isolated in 81% and 80% yields, respectively. In contrast, gold catalyst ($AuSPhosNTf_2$) used in the hydration of the triple bond showed partial stability to the robust TBDPS group, reported by Leyva and Corma.[12f] It appears that the present catalytic condition is milder than the previously reported systems.[12] Furthermore, more electron-rich substrate **1m** undergoes hydration efficiently within 2 h to afford **2m** in 91% yield.

The effect of ortho-substitution on the aryl moiety was next examined, and the results are shown in Table 4. Hydration of the terminal triple bond proceeded smoothly in the presence of electron-poor ortho substituent, such as chloro and bromo groups, on the aromatic ring of propargyl acetates (**1n**−**q**) producing the corresponding ketones (**2n**−**q**) in excellent yields. Similarly, 1-(naphthalen-1-yl)prop-2-ynyl acetate (**1r**) underwent hydration efficiently, affording 95% yield of **2r**. The methyl group at the 2-position did not inhibit hydration and delivered **2s** in 92% yield. The *o*-O-allyl group did not participate in the hydration and the desired product **2t** was isolated in 96% yield; the allyl functionality could be useful for further synthetic elaboration. The required ketone **2u** was successfully obtained from the anthracene-based propargyl acetate. More sterically demanding substrates having two ortho-substitutions on the aryl moiety underwent efficient hydration under the optimized condition and the desired products **2v** and **2w** are obtained in excellent yields. X-ray crystallographic analysis

TABLE 5. Gold-Catalyzed Hydration of Hindered 1-Ethynyl-1′, 1′′-alkyl/aryl/H-Substituted Acetates[a,b]



[a]Reactions were carried out with **1** (1.0 mmol), Ph_3PAuCl (1 mol %), $AgSbF_6$ (1 mol %), and water (3.0 mmol) in 1,4-dioxane (1.5 mL) at room temperature. [b]Isolated yields.

unambiguously elucidated the structure of **2w** (see the Supporting Information). Our experimental results reveal that electronic and steric effect on the aromatic ring did not impart the pronounced effect to alkyne hydrations. Next, the effect of heteroaryls in the hydration of terminal alkynes of propargyl acetate was investigated. Intramolecular coordination of the heteroatom to the gold−alkyne-activated species is a well-known phenomenon.[17] Therefore, we speculate that the heteroaryls in the propargyl acetate may hinder the hydration of the triple bond. To probe our assumption, hydration of thienyl-2-substituted propargyl acetate (**1x**) was performed under the optimized condition and the corresponding hydration product **2x** resulted in 75% yield in 2 h. Unfortunately, furyl-2-substituted propargyl acetate failed to provide the desired ketone; a complex reaction profile was observed with the consumption of starting propargyl acetate. In the case of *N*-methyl indole derivative, the hydration reaction did not proceed, whereas *N*-benzoyl-protected indole-2-susbtituted propargyl acetate (**1y**) provided the corresponding hydration product **2y** 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 **2y** led to the hydration product.

Formation of α-acyloxy methyl ketones through regioselective hydration of the terminal alkynes of the aryl- and heteroaryl-substituted propargyl acetates has been successfully demonstrated. Next, we turned our attention to assess the effect of alkyl, dialkyl, and aryl-alkyl groups at the propargylic position to the alkyne hydration and the results are detailed in Table 5. When *n*-hexyl- and benzyl-substituted propargyl acetates are subjected to the optimized condition, the corresponding hydration products **2z** and **2aa** are obtained in excellent yields. Although Nolan observed the formation of α,β-unsaturated aldehyde through regioselective hydration of benzyl-substituted propargyl acetate **1aa** under [(NHC)AuCl], $AgSbF_6$ in THF−H_2O at 60 °C,[12j] our optimized condition exclusively delivered α-acyloxy methyl ketone **2aa** from **1aa**. The bromo group on the alkyl chain survived under the catalytic system and the product **2ab** 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 ambient temperature.[13]

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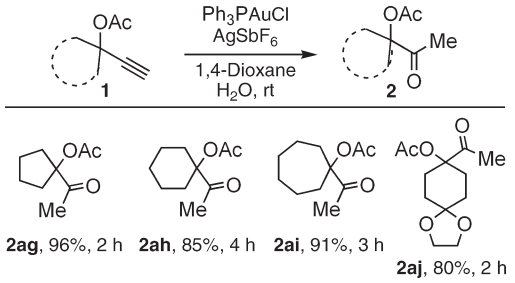
TABLE 6. Gold-Catalyzed Hydration of 1-Ethynylcycloalkyl Acetates[a,b]



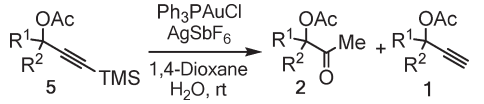
[a]Reactions were carried out with **1** (1.0 mmol), Ph_3PAuCl (1 mol %), $AgSbF_6$ (1 mol %), and water (3.0 mmol) in 1,4-dioxane (1.5 mL) at room temperature. [b]Isolated yields.

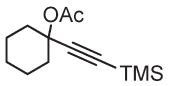
Surprisingly, the −OTHP protecting group was well-tolerated in this gold-catalyzed hydration protocol, and the product **2ac** was isolated in 78% yield; this observation demonstrates the mild nature of the catalytic conditions. Unactivated sterically hindered propargyl acetate such as **1ad** having a quaternary α-carbon center with two alkyl substituents did not affect the reaction efficiency and delivered the product **2ad** in 94% yield under the optimized condition. Similarly, both methyl- and aryl-substituted propargyl acetates **1ae** and **1af** effectively underwent hydration to furnish the desired α-acyloxy-α′,α″-disubstituted methyl ketones **2ae** and **2af** in good yields.

To further expand the scope of the reaction, exploration of hindered 1-ethynylcycloalkyl acetates to the alkyne hydrations was pursued and the results are shown in Table 6. Excellent yields of the desired α-acyloxy methyl ketones (**2ag**−**2ai**) were attained 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-dioxolane is the most widely carbonyl protective moiety used in organic synthesis.[13] Acid-catalyzed hydrolysis and oxidation easily cleaves the 1,3-dioxolanes.[13] Gold-catalyzed hydration of compound **1aj** having both the propargyl acetate and the acid-sensitive 1,3-dioxolane moieties affords the product **2aj** in 80% yield. Gratifyingly, the ketal protecting moiety survived under this catalytic condition; this observation once again proved the mildest nature of the catalysts.

Deprotection of trimethylsilyl ether under the optimized catalytic condition was previously observed (Table 2, entry 9). Leyva and Corma have shown the cleavage of the alkynyl C-TMS group by $AuSPhosNTf_2$.[12f] Unfortunately, TMS-containing alkyne failed to react with the Nolan's condition at an elevated temperature.[12j] These observations motivated us to investigate the hydration of alkynyl-TMS-protected propargyl acetates under the optimized catalytic condition and the results are summarized in Table 7. Thus, the gold-catalyzed hydration of alkynyl-TMS-protected phenyl propargyl acetates **5a** provided α-acyloxy methyl ketone **2a** in 82% yield, even though it requires prolonged reaction time (∼20 h) for completion (Table 7, entry 1). It appears that the catalytic conditions cleave 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 the case of 4-bromophenyl- and benzyl-substituted TMS-containing propargyl acetates **5d** and **5aa** (Table 7, entries 2 and 6). In a few other cases, a mixture of desilylated as well as the hydration products is observed even though the reaction continued for 24 h (entries 3, 4, and 7). Reaction of thienyl-2-substituted TMS-containing propargyl acetates **5x** under the catalytic conditions resulted in desilylated product **1x** in 59% yield by NMR without producing the required α-acyloxy methyl ketone **2x**; incomplete conversion of **5x** was noticed even with the extended reaction time. These

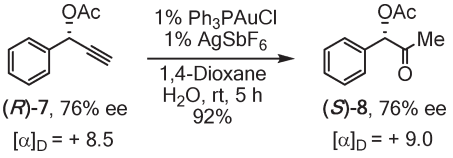
TABLE 7. Hydration of TMS-Substituted Propargyl Acetate[a]



entry	5	R^1	R^2	time (h)	yield (%) 2	1
1	**5a**	C_6H_5	H	20	82[b]	0[b]
2	**5d**	4-Br-C_6H_4	H	24	91[b]	0[b]
3	**5h**	3-MeO-C_6H_4	H	24	70[c]	30[c]
4	**5n**	2-Cl-C_6H_4	H	24	28[c]	72[c]
5	**5x**	2-Thienyl	H	24	0[c]	59[c]
6	**5aa**	C_6H_5-CH_2	H	24	83[b]	0[b]
7	**5ah**			24	79[c]	21[c]

[a]Reactions were carried out with **5** (1.0 mmol), Ph_3PAuCl (1 mol %), $AgSbF_6$ (1 mol %), and water (5.0 mmol) in 1,4-dioxane (1.5 mL) at room temperature. [b]Isolated yields. [c]^{1}H NMR yields.

SCHEME 1. Hydration of Chiral Propargyl Acetate



observations reveal that TMS-containing propargyl acetates are not effective in this hydration reaction.

Next, we examined the effect of the catalytic conditions on the hydration of the chiral propargylic acetate (Scheme 1). Following the reported procedure,[18a] the optically active (*R*)-1-phenylprop-2-ynyl acetate (**7**) was prepared with 76% ee (determined by chiral HPLC; see the SI). The optical rotation of (*R*)-**7** agrees with the literature value.[18b] Hydration of (*R*)-**7** was carried out by using the optimized catalytic condition, and the product (*S*)-**8** was obtained in 92% yield with 76% ee (determined by chiral HPLC, Scheme 1; see the SI). Optical rotation analysis confirms that the chiral center of the acetate moiety did not racemize during the gold-catalyzed hydration of the triple bond (Scheme 1; see the SI). Therefore, we believe that this protocol would allow the synthesis of optically active α-acyloxy methyl ketones that would finally lead to enantio-enriched α-hydroxy methyl ketones in simple synthetic operations.

The robustness of the catalytic conditions is demonstrated through gram scale synthesis of the hydration products. Screening of different amounts of catalyst mixtures containing Ph_3PAuCl and $AgSbF_6$ (0.1 or 0.3 mol %) to the hydration of **1a** (10 mmol) was performed. A sluggish reaction profile was observed when 0.1 mol % of gold and silver catalysts is employed. However, hydration of **1a** successfully completed within appreciable time (∼20 h) in the presence of 0.3 mol % of gold and silver catalysts. Under this modified catalytic condition, products **2a** and **2c** are obtained directly by filtering the crude reaction mixtures through a small pad of Celite, in 94% and 95% yields, respectively (Scheme 2).

Reduction of both the keto and acetate moieties of α-acyloxy methyl ketones would furnish 1,2-disubstituted glycol derivatives,

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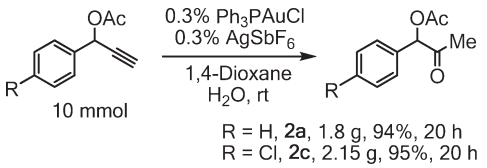
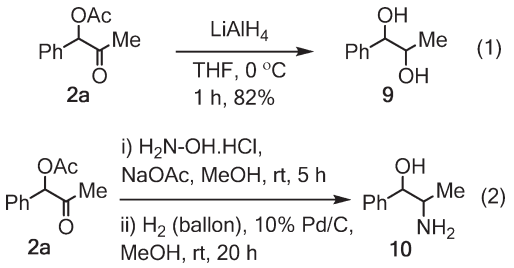
SCHEME 2. Gram Scale Synthesis of α-Acyloxy Methyl Ketones



SCHEME 3. Synthesis of 1,2-Glycol and 1,2-Amino Alcohol



which are useful building blocks.[19] For example, lithium aluminum hydride ($LiAlH_4$) reduces **2a** to afford **9** (dr 1.8:1) in 82% yield at 0 °C (Scheme 3, eq 1). 1,2-Amino alcohols are also valuable precursors to the chiral auxiliaries.[20] Imination of 2-oxo-1-phenylpropyl acetate (**2a**) followed by reduction with H_2 in 10% Pd/C resulted in racemic 1,2-amino alcohol **10** (dr 3:2) in overall 36% yield (Scheme 3, eq 2).[21]

This methodology attests to the 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. Recently, a series of a new class of natural products actinopolymorphol A, B, and C were isolated from *Actinopolymorpha rutilus* (YIM45725).[22a] Moreover, the structural morphology of actinopolymorphol B resembles closely that of kurasoin B and sattazolin derivatives (Figure 2).[22a] Kurasoin B and its derivatives are known protein farnesyltransferase (PFTase) inhibitors; and therefore these compounds have the potential to show anticancer properties.[22b,c] Moreover, sattazoline and its derivatives expressed their antiviral activity against the Herpes simplex viruses type 1 and 2 and inhibit the protein synthesis in Herpesvirus-infected cells selectively.[23] The central core α-hydroxy ketone unit is present in the natural products depicted in Figures 1 and 2. The potency of the compounds (Figure 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 a critical role in exhibiting PFTase inhibition.[24] We anticipate that actinopolymorphol B would be a potentially important drug candidate such as kurasoin B and sattazoline. As

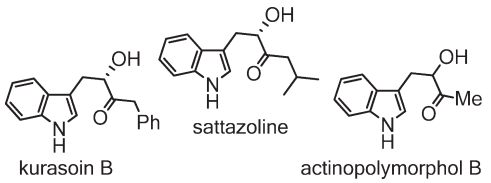


FIGURE 2. Kurasoin B, sattazoline, and actinopolymorphol B classes of natural products having similar structural morphology.

our synthetic approach provides a simple route to access α-acyloxy methyl ketone moiety with broad substrate scope under mild reaction conditions, we aimed for the synthesis of actinopolymorphol B involving the efficient gold-catalyzed intermolecular hydration of propargyl acetate at room temperature.

The campaign for the synthesis of actinopolymorphol B (Scheme 4) was initiated from commercially available indole-3-acetic acid (**11**). Esterification followed by *N*-Boc protection f **11** provided **12** in 86% overall yield. Access to preparing a large quantity of the known aldehyde **14** was found to be critical since DIBAL-H reduction of ester **12** produced **14** in only 37% yield.[25] Therefore, a two-step synthetic protocol involving reduction and oxidation sequences was considered. To reduce **12** effectively, various reducing agents were surveyed under different reaction conditions. Gratifyingly, reduction of ester with $LiAlH_4$ at −78 °C was found productive and resulted in **13** in 92% isolated yield. Formation of unwanted side products are observed during the oxidation of **13** under Dess−Martin and Swern conditions. Oxidation of **13** with [bis(acetoxy)iodo]benzene (BAIB) in the presence of TEMPO led to aldehyde **14** in only 57% yield. Addition of TMS-acetylide to the carbonyl moiety of **14** was effectively carried out at −78 °C and furnished **15** in 89% yield. Acetate formation (Ac_2O, DMAP, Et_3N) and subsequent desilylation (TBAF) delivered the desired propargyl acetate **16** in 83% overall yield. The starting precursor **16** was exposed to the optimized catalytic condition [Ph_3PAuCl (1 mol %) and $AgSbF_6$ (1 mol %)] in the presence of H_2O in 1,4-dioxane at room temperature for 7 h, and the desired α-acyloxy methyl ketone **17** was isolated in 83% yield.[26] Finally, cleavage of *N*-Boc and *O*-acetyl of **17** would give actinopolymorphol B (**18**). At first, we investigated the deprotection of the *N*-Boc of **17** while keeping the acetate moiety intact. Exploration of established conditions involving (i) trifluoro acetic acid (TFA) in CH_2Cl_2,[13a] (ii) TBAF refluxed in THF,[13a] and (iii) TMSCl in phenol to the deprotection of the *N*-Boc moiety of indole **17** failed,[13a] whereas TMSOTf in the presence of DBU cleaved the Boc-group successfully.[27] Subsequently, base-induced deacetylation of the crude mixture of **17**-NH led to complex mixtures. Gratifyingly, $Sc(OTf)_3$-catalyzed saponification of the acetate moiety furnished **18** in 56% yield over the two-step sequence.[13,28]

Mechanistic Studies

Experimental results show that the hydration of propargyl acetate in dioxane and water with gold catalyst proceeds efficiently at room temperature in the absence of acid promoters. The critical role of the acetate group located adjacent to the

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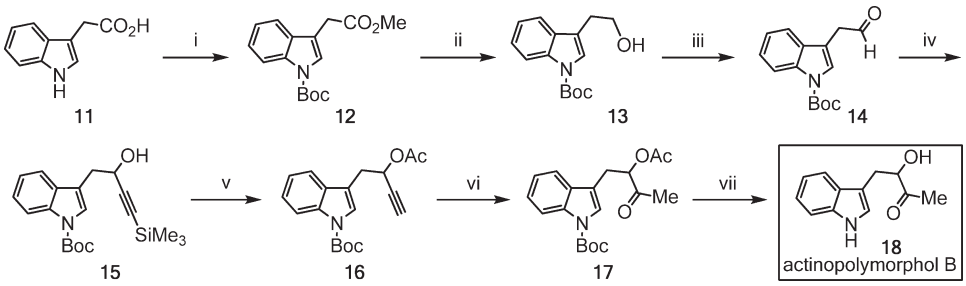
(26) Hydration of TMS-substituted propargylic acetate of **15** was performed under the optimized catalytic condition [Ph_3PAuCl (1 mol %) and $AgSbF_6$ (1 mol %)] in the presence of H_2O in 1,4-dioxane for 24 h. The reaction did not undergo completion; the ^1H NMR spectrum of the crude reaction mixture showed the formation of 20% of hydration product **17**, 24% of desilylated **16**, and 51% of unreacted TMS-substituted propargylic acetate of **15**.

(27) Bastiaans, H. M. M.; van derBaan, J. L.; Ottenheijm, H. C. J. *J. Org. Chem.* **1997**, *62*, 3880.

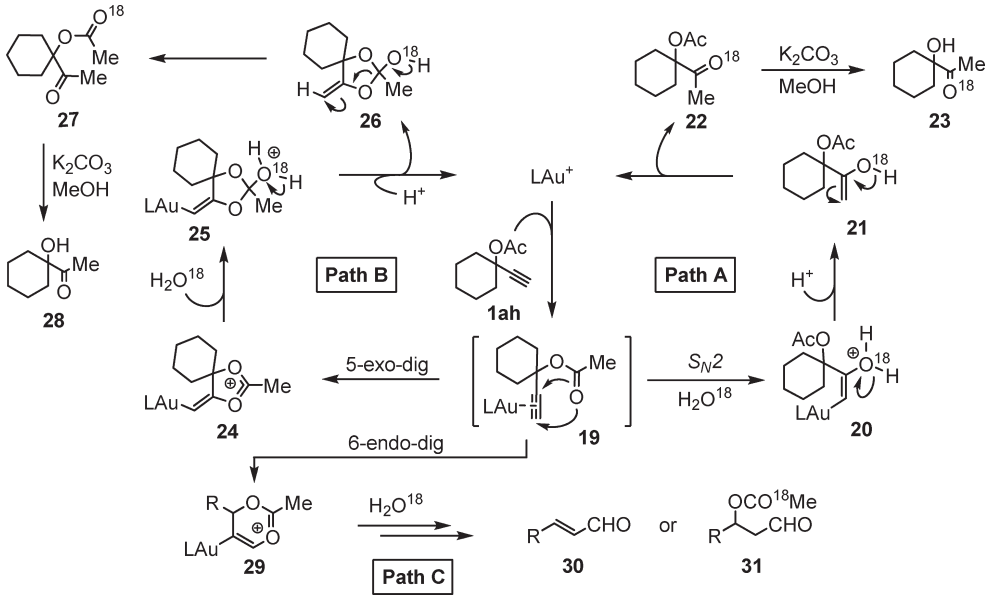
(28) Kajihiro, H.; Mitamura, S.; Mori, A.; Hiyama, T. *Tetrahedron Lett.* **1999**, *40*, 1689.

SCHEME 4. Synthesis of Actinopolymorphol B via Hydration of Propargyl Acetate[a]



[a]Reagents and conditions: (i) (a) $SOCl_2$, MeOH, 0 to 25 °C, 4 h, (b) Boc_2O, DMAP, CH_2Cl_2, rt, 8 h, 86% (over two steps); (ii) $LiAlH_4$, THF, −78 °C, 45 min, 92%; (iii) BAIB, TEMPO, 0 to 25 °C, 2 h, 57%; (iv) TMS-acetylene, *n*-BuLi (1.6 M solution in THF), THF, −78 °C, 3 h, 89%; (v) (a) Ac_2O, DMAP, Et_3N, CH_2Cl_2, rt, 1 h, (b) TBAF (1.0 M solution in THF), THF, 0 °C, 1 h, 83% (over two steps); (vi) Ph_3PAuCl (1 mol %), $AgSbF_6$ (1 mol %), H_2O (3.0 equiv), 1,4-dioxane, rt, 7 h, 83%; (vii) (a) TMSOTf, DBU, CH_2Cl_2, 0 °C to rt, 8 h, (b) $Sc(OTf)_3$ (20 mol %), MeOH/H_2O (4:1), rt, 12 h, 56% (over two steps).

SCHEME 5. Proposed Catalytic Cycle



terminal alkyne in the regioselective hydration warrants careful investigation.[12b] To probe the reaction pathway and to validate the mode of water attack to the unsaturated bonds, oxygen-18-enriched water is employed.[29] The affinity of alkyne to cationic gold(I) species such as $[Me_3PAu]^+$ over methanol and water is well established.[12] Thus, the reactive intermediate gold−alkyne−π complex **19**, resulting from the activation of the alkyne **1ah** by cationic gold(I)phosphine, is believed to take part in the first step of the transformation (Scheme 5). Experimental and theoretical studies reveal that enol ethers and ketals are the plausible intermediates involved in the hydration of alkynes in alcoholic solvents.[11b,12] Therefore, participation of enol ether intermediates seems unlikely as the reactions are performed in dioxane. Hayashi, Tanaka, and the Laguna group have independently demonstrated that the direct attack of water on the gold−alkyne−π complex in nonalcoholic medium provides the desired hydration product.[12l,m] Pathway A is proposed based on the direct S_N2' attack of H_2O^{18} on **19** followed by protodeauration of **20** and isomerization of enol **21** leading to the ketone **22**.[12j,l,m] Base-induced deacetylation of **22** would then generate the desired α-hydroxy methyl ketone **23** 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 **19** through neighboring nucleophilic carbonyl group participation (paths B and C, Scheme 5). The 5-*exo-dig* attack of carbonyl oxygen on the γ-carbon would generate the 5-membered electrophilic vinyl−gold species **24** (path B),[14] whereas the 6-*endo-dig* attack would provide the 6-membered intermediate **29** (path C).[14] Although as per the Baldwin's rule,[2] 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.[14] Involvement of such reactive intermediates in various gold-catalyzed organic transformations is well explored.[15] The nucleophilic addition of H_2O^{18} to **24** produces the intermediate **25** as illustrated in path B. Protodemetalation of **25** followed by isomerization of **26** furnishes α-acyloxy methyl ketone **27** with ^{18}O in the ester carbonyl group. Molecular mass of **27** [187 ($M^+ + 1$)] confirms this; see the Supporting Information. Base-catalyzed deacetylation of **27** produces the corresponding α-hydroxy methyl ketone **28** [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

(29) Li, Y.; Song, D.; Dong, V. *J. Am. Chem. Soc.* **2008**, *130*, 2962.

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 $H_2{}^{18}O$ on **29** would generate aldehyde products (**30** or **31**) 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 **24** under the optimal conditions shown in path B, Scheme 5.

Conclusion

We have shown that the commercially available catalyst [Ph_3PAuCl and $AgSbF_6$] in dioxane−H_2O efficiently hydrates a wide range of readily accessible propargyl acetates under ambient temperature. This strategy allows the efficient synthesis of an array of α-acyloxy methyl ketones in good to excellent yields. The highlights of this strategy are as follows: (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 times, (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 in the conversion of directed monofunctionality to reactive bifunctionality that finally leads to the generation of α-hydroxy ketones,[4] which are indeed synthetically versatile intermediates for various biologically active compounds.[5] This protocol also allows the introduction of the key α-hydroxy methyl ketone group in actinopolymorphol B (**18**).[22a] The first total synthesis of **18** is accomplished through a 7-step route, in 16% overall yield, starting from commercially available indole-3-acetic acid. On the basis of 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 toward discovering the asymmetric variant of this reaction, finding efficient strategy to the regioselective hydration of internal alkynes, and exploring the total synthesis of natural products of pharmaceutical interest.

Experimental Section

General Procedure for the Gold-Catalyzed Hydration of Propargyl Acetates (1). A mixture of Ph_3PAuCl (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 min at ambient temperature. This freshly prepared light pink gold−silver complex mixture was introduced to the Schlenk flask having **1** (1.0 mmol) followed by the addition of deionized water (54 μL, 3.0 mmol) at ambient temperature. The resulting reaction mixture was stirred for the time shown in the respective tables at ambient temperature. Upon complete consumption of starting 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 by using column chromatography on silica gel.

2-Oxo-1-phenylpropyl acetate (2a): 186 mg, 97% yield; colorless oil; R_f 0.38 (10:1 hexane/EtOAc); ^1H NMR (400 MHz, $CDCl_3$) δ 7.42 (br s, 5H), 5.99 (s, 1H), 2.21 (s, 3H), 2.13 (s, 3H); ^{13}C NMR (101 MHz, $CDCl_3$) δ 201.7, 170.3, 133.2, 129.4, 129.1, 128.1, 80.9, 26.1, 20.7; IR (neat) ν_{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 (2b): 193 mg, 92% yield; colorless oil; R_f 0.31 (6:1 hexane/EtOAc); ^1H NMR (400 MHz, $CDCl_3$) δ 7.44−7.34 (m, 2H), 7.15−7.04 (m, 2H), 5.95 (s, 1H), 2.19 (s, 3H), 2.11 (s, 3H); ^{13}C NMR (101 MHz, $CDCl_3$) δ 201.6, 170.2, 164.5, 162.0, 129.97, 129.89, 129.0, 116.2, 116.0, 80.0, 26.1, 20.6; ^{19}F NMR (376 MHz, $CDCl_3$) δ −111.70; IR (neat) ν_{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 (2c): 213 mg, 94% yield; colorless oil; R_f 0.50 (10:1 hexane/EtOAc); ^1H NMR (400 MHz, $CDCl_3$) δ 7.59−7.52 (m, 2H), 7.35−7.27 (m, 2H), 5.94 (s, 1H), 2.21 (s, 3H), 2.14 (s, 3H); ^{13}C NMR (101 MHz, $CDCl_3$) δ 201.3, 170.1, 132.29, 132.25, 129.6, 123.7, 80.2, 26.1, 20.7; IR (neat) ν_{max} 2930, 1736, 1731, 1371, 1232, 1053 cm^{-1}; MS (EI) *m*/*z* (%) 229 ($M^+ + 2$, 37), 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 (2d): 241 mg, 89% yield; pale yellow oil; R_f 0.55 (10:1 hexane/EtOAc); ^1H NMR (400 MHz, $CDCl_3$) δ 7.54 (d, J = 8.0 Hz, 2H), 7.30 (d, J = 8.0 Hz, 2H), 5.92 (s, 1H), 2.19 (s, 3H), 2.11 (s, 3H); ^{13}C NMR (101 MHz, $CDCl_3$) δ 201.3, 170.1, 132.3, 129.6, 123.7, 80.2, 26.1, 20.7; IR (neat) ν_{max} 2930, 1749, 1732, 1371, 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 (2e): 250 mg, 96% yield; pale yellow oil; R_f 0.31 (8:1 hexane/EtOAc); ^1H NMR (400 MHz, $CDCl_3$) δ 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); ^{13}C NMR (101 MHz, $CDCl_3$) δ 201.1, 169.9, 133.7, 133.4, 131.0, 129.8, 127.1, 79.4, 26.1, 20.6; IR (neat) ν_{max} 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 $C_{11}H_{10}Cl_2O_3$: C, 50.60; H, 3.86. Found: C, 50.66; H, 3.90.

1-(4-Formylphenyl)-2-oxopropyl acetate (2f): 193 mg, 88% yield; colorless oil; R_f 0.33 (4:1 hexane/EtOAc); ^1H NMR (400 MHz, $CDCl_3$) 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); ^{13}C NMR (101 MHz, $CDCl_3$) δ 201.1, 191.5, 169.9, 139.5, 136.8, 130.2, 128.3, 80.3, 26.1, 20.6; IR (neat) ν_{max} 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 $C_{12}H_{12}O_4$: C, 65.45; H, 5.49. Found: C, 65.32; H, 5.41.

2-Oxo-1-*p*-tolylpropyl acetate (2g): 196 mg, 95% yield; colorless oil; R_f 0.54 (10:1 hexane/EtOAc); ^1H NMR (400 MHz, $CDCl_3$) 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); ^{13}C NMR (101 MHz, $CDCl_3$) δ 201.8, 170.4, 139.5, 130.2, 129.8, 128.1, 80.8, 26.1, 21.2, 20.7; IR (neat) ν_{max} 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 $C_{12}H_{14}O_3$: C, 69.88; H, 6.84. Found: C, 69.75; H, 6.92.

1-(3-Methoxyphenyl)-2-oxopropyl acetate (2h): 202 mg, 91% yield; pale yellow oil; R_f 0.29 (10:1 hexane/EtOAc); ^1H NMR (400 MHz, $CDCl_3$) 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); ^{13}C NMR (101 MHz, $CDCl_3$) 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) ν_{max} 2941, 1747, 1732, 1602, 1489, 1373, 1236, 1045 cm^{-1}; MS (EI) *m*/*z* (%) 223 ($M^+ + 1$, 22), 209 (13), 195 (9), 177 (11), 163 (100), 135 (13). Anal. Calcd for $C_{12}H_{14}O_4$: C, 64.85; H, 6.35. Found: C, 64.91; H, 6.41.

2-Oxo-1-(3-phenoxyphenyl)propyl acetate (2i): 247 mg, 87% yield; pale yellow oil; R_f 0.35 (6:1 hexane/EtOAc); ^{1}H NMR (400 MHz, $CDCl_3$) 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); ^{13}C NMR (101 MHz, $CDCl_3$) 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) ν_{max} 3065, 1747, 1730, 1585, 1444, 1373, 1238, 1053 cm^{-1}; MS (EI) m/z (%) 285 (M^+ + 1, 100), 243 (13). Anal. Calcd for $C_{17}H_{16}O_4$: C, 71.82; H, 5.67. Found: C, 71.92; H, 5.59.

1-(3-Hydroxyphenyl)-2-oxopropyl acetate (2j): 176 mg, 85% yield; colorless oil; R_f 0.40 (3:1 hexane/EtOAc); ^{1}H NMR (400 MHz, $CDCl_3$) δ 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, $CDCl_3$) δ 202.9, 170.7, 156.7, 134.3, 130.5, 120.2, 116.8, 114.7, 80.8, 26.2, 20.7; IR (neat) ν_{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 (2k): 362 mg, 81% yield; pale brown oil; R_f 0.56 (10:1 hexane/EtOAc); ^{1}H NMR (400 MHz, $CDCl_3$) δ 7.70 (br t, J = 7.2 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, $CDCl_3$) δ 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) ν_{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 $C_{27}H_{30}O_4Si$: C, 72.61; H, 6.77. Found: C, 72.45; H, 6.81.

1-(3-(*tert*-Butyldimethylsilyloxy)phenyl)-2-oxopropyl acetate (2l): 257 mg, 80% yield; pale brown oil; R_f 0.47 (10:1 hexane/EtOAc); ^{1}H NMR (400 MHz, $CDCl_3$) δ 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, $CDCl_3$) δ 201.5, 170.2, 156.2, 134.5, 130.1, 121.0, 120.9, 119.7, 80.7, 26.1, 25.6, 20.7, 18.2, −4.4; IR (neat) ν_{max} 2955, 2932, 1745, 1732, 1602, 1446, 1371, 1238, 1051 cm^{-1}; MS (EI) m/z (%) 321 (M^+ − 1, 17), 303 (8), 289 (52), 279 (11), 230 (16), 207 (100), 165 (6). Anal. Calcd for $C_{17}H_{26}O_4Si$: C, 63.32; H, 8.13. Found: C, 63.51; H, 8.22.

1-(Benzo[*d*][1,3]dioxol-5-yl)-2-oxopropyl acetate (2m): 214 mg, 91% yield; pale yellow thick oil; R_f 0.35 (6:1 hexane/EtOAc); ^{1}H NMR (400 MHz, $CDCl_3$) δ 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, $CDCl_3$) δ 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) ν_{max} 2961, 2885, 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 $C_{12}H_{12}O_5$: C, 61.01; H, 5.12. Found: C, 61.25; H, 5.08.

1-(2-Chlorophenyl)-2-oxopropyl acetate (2n): 211 mg, 93% yield; pale yellow oil; R_f 0.44 (10:1 hexane/EtOAc); ^{1}H NMR (400 MHz, $CDCl_3$) δ 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); ^{13}C NMR (101 MHz, $CDCl_3$) δ 200.8, 169.9, 133.9, 131.5, 130.6. 130.1, 129.7, 127.5, 76.9, 26.6, 20.6; IR (neat) ν_{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 (2o): 236 mg, 87% yield; colorless oil; R_f 0.47 (10:1 hexane/EtOAc); ^{1}H NMR (400 MHz, $CDCl_3$) δ 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); ^{13}C NMR (101 MHz, $CDCl_3$) δ 200.8, 169.9, 133.3, 133.1, 130.8, 129.8, 128.1, 124.3, 79.2, 26.8, 20.6; IR (neat) ν_{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 (2p): 245 mg, 94% yield; pale yellow oil; R_f 0.48 (8:1 hexane/EtOAc); ^{1}H NMR (400 MHz, $CDCl_3$) δ 7.48 (s, 1H), 7.37−7.25 (m, 2H), 6.44 (s, 1H), 2.18 (s, 3H), 2.17 (s, 3H); ^{13}C NMR (101 MHz, $CDCl_3$) δ 200.4, 169.8, 133.9, 133.8, 132.4, 131.3, 127.9, 77.2, 26.8, 20.5; IR (neat) ν_{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 $C_{11}H_{10}Cl_2O_3$: C, 50.60; H, 3.86. Found: C, 50.65; H, 3.82.

1-(2,3-Dichlorophenyl)-2-oxopropyl acetate (2q): 246 mg, 94% yield; colorless oil; R_f 0.35 (10:1 hexane/EtOAc); ^{1}H NMR (400 MHz, $CDCl_3$) δ 7.53 (dd, J = 2.0, 8.0 Hz, 1H), 7.33 (dd, J = 2.0, 8.0 Hz, 1H), 7.31−7.25 (m, 1H), 6.56 (s, 1H), 2.21 (s, 3H), 2.20 (s, 3H); ^{13}C NMR (101 MHz, $CDCl_3$) δ 200.4, 169.8, 133.9, 133.9, 132.4, 131.3, 127.9, 127.8, 77.2, 26.8, 20.5; IR (neat) ν_{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 $C_{11}H_{10}Cl_2O_3$: C, 50.60; H, 3.86. Found: C, 50.51; H, 3.92.

1-(Naphthalen-1-yl)-2-oxopropyl acetate (2r): 230 mg, 95% yield; pale yellow thick oil; R_f 0.34 (10:1 hexane/EtOAc); ^{1}H NMR (400 MHz, $CDCl_3$) δ 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 Hz, 2H), 6.68 (s, 1H), 2.22 (s, 3H), 2.07 (s, 3H); ^{13}C NMR (101 MHz, $CDCl_3$) δ 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, 20.8; IR (neat) ν_{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-*o*-tolylpropyl acetate (2s): 189 mg, 92% yield; colorless oil; R_f 0.33 (10:1 hexane/EtOAc); ^{1}H NMR (400 MHz, $CDCl_3$) δ 7.31−7.21 (m, 4H), 6.25 (s, 1H), 2.45 (s, 3H), 2.18 (s, 3H), 2.09 (s, 3H); ^{13}C NMR (101 MHz, $CDCl_3$) δ 201.7, 170.3, 137.2, 131.8, 131.3, 129.4, 128.7, 126.7, 78.3, 26.3, 20.8, 19.5; IR (neat) ν_{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 (2t): 238 mg, 96% yield; colorless oil; R_f 0.34 (10:1 hexane/EtOAc); ^{1}H NMR (400 MHz, $CDCl_3$) δ 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); ^{13}C NMR (101 MHz, $CDCl_3$) δ 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) ν_{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 (2u): 248 mg, 85% yield; pale brown solid; mp 113−114 °C; R_f 0.38 (6:1 hexane/EtOAc); ^{1}H NMR (400 MHz, $CDCl_3$) δ 8.58 (s, 1H), 8.39 (br d, J = 7.6 Hz, 2H), 8.07 (d, J = 8.4 Hz, 2H), 7.66 (s, 1H), 7.61 (t, J = 8.0 Hz, 2H), 7.53 (t, J = 8.0 Hz, 2H), 2.24 (s, 3H), 1.88 (s, 3H); ^{13}C NMR (101 MHz, $CDCl_3$) δ 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 (KBr) ν_{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.

1-(2,6-Dichlorophenyl)-2-oxopropyl acetate (2v): 237 mg, 91% yield; colorless thick oil; R_f 0.41 (8:1 hexane/EtOAc); ^{1}H NMR (400 MHz, $CDCl_3$) 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); ^{13}C NMR (101 MHz, $CDCl_3$) δ 200.7, 169.6, 136.6, 131.5, 130.9, 129.0, 76.2, 26.3, 20.6; IR (neat) ν_{max} 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 $C_{11}H_{10}Cl_2O_3$: C, 50.60; H, 3.86. Found: C, 50.71; H, 3.90.

1-(2,6-Dimethoxyphenyl)-2-oxopropyl acetate (2w): 235 mg, 93% yield; colorless solid; mp 122−123 °C; R_f 0.32 (10:1 hexane/EtOAc); ^{1}H NMR (400 MHz, $CDCl_3$) 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); ^{13}C NMR (101 MHz, $CDCl_3$) δ 202.6, 170.4, 158.9, 131.3, 111.7, 104.1, 71.6, 55.9, 25.4, 20.9; IR (KBr) ν_{max} 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 (60). Anal. Calcd for $C_{13}H_{16}O_5$: C, 61.90; H, 6.39. Found: C, 61.85; H, 6.43.

2-Oxo-1-(thiophen-2-yl)propyl acetate (2x): 149 mg, 75% yield; thick pale brown oil; R_f 0.30 (6:1 hexane/EtOAc); ^{1}H NMR (400 MHz, $CDCl_3$) 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); ^{13}C NMR (101 MHz, $CDCl_3$) δ 200.5, 170.1, 134.5, 128.4, 127.7, 127.3, 75.8, 26.0, 20.6; IR (neat) ν_{max} 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 $C_9H_{10}O_3S$: C, 54.53; H, 5.08. Found: C, 54.68; H, 5.15.

1-(1-Benzoyl-1*H*-indol-3-yl)-2-oxopropyl acetate (2y): 261 mg, 78% yield; thick yellow oil; R_f 0.37 (5:1 hexane/EtOAc); ^{1}H NMR (400 MHz, $CDCl_3$) δ 8.37 (d, *J* = 8.0 Hz, 1H), 7.74 (d, *J* = 7.2 Hz, 2H), 7.66 (t, *J* = 8.4 Hz, 2H), 7.56 (t, *J* = 7.6 Hz, 2H), 7.46 (s, 1H), 7.43 (d, *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); ^{13}C NMR (101 MHz, $CDCl_3$) 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) ν_{max} 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 $C_{20}H_{17}NO_4$: C, 71.63; H, 5.11; N, 4.18. Found: C, 71.48; H, 5.25; N, 4.22.

2-Oxononan-3-yl acetate (2z): 188 mg, 94% yield; colorless oil; R_f 0.39 (7:1 hexane/EtOAc); ^{1}H NMR (400 MHz, $CDCl_3$) δ 4.96 (dd, *J* = 4.0, 8.0 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, $CDCl_3$) δ 205.4, 170.6, 78.8, 31.5, 30.3, 28.9, 26.1, 25.1, 22.5, 20.7, 14.0; IR (neat) ν_{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 (2aa): 175 mg, 85% yield; colorless oil; R_f 0.36 (10:1 hexane/EtOAc); ^{1}H NMR (400 MHz, $CDCl_3$) δ 7.31 (br q, *J* = 7.2 Hz, 2H), 7.25 (d, *J* = 6.0 Hz, 1H), 7.21 (d, *J* = 7.2 Hz, 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, $CDCl_3$) δ 205.3, 170.4, 135.9, 129.3, 128.6, 127.1, 79.1, 36.7, 26.9, 20.6; IR (neat) ν_{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 (2ab): 228 mg, 86% yield; colorless oil; R_f 0.62 (10:1 hexane/EtOAc); ^{1}H NMR (400 MHz, $CDCl_3$) δ 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, $CDCl_3$) δ 205.3, 170.6, 78.5, 33.5, 32.4, 30.1, 27.7, 26.1, 24.3, 20.7; IR (neat) ν_{max} 3456, 2947, 1743, 1730, 1433, 1373, 1240, 1047 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-2*H*-pyran-2-yloxy)hexan-3-yl acetate (2ac): 201 mg, 78% yield; colorless oil; R_f 0.47 (10:1 hexane/EtOAc); ^{1}H NMR (400 MHz, $CDCl_3$) δ 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, $CDCl_3$) δ 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) ν_{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.

3,5-Dimethyl-2-oxohexan-3-yl acetate (2ad): 174 mg, 94% yield; colorless oil; R_f 0.60 (19:1 hexane/EtOAc); ^{1}H NMR (400 MHz, $CDCl_3$) δ 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, $CDCl_3$) δ 206.2, 169.7, 86.2, 44.1, 24.2, 23.6, 23.4, 23.5, 20.8, 20.1; IR (neat) ν_{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 (2ae): 156 mg, 76% yield; pale yellow oil; R_f 0.41 (10:1 hexane/EtOAc); ^{1}H NMR (400 MHz, $CDCl_3$) δ 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, $CDCl_3$) δ 203.6, 169.9, 138.5, 128.7, 128.1, 124.7, 87.4, 23.5, 22.8, 21.3; IR (neat) ν_{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 (2af): 197 mg, 82% yield; pale yellow oil; R_f 0.39 (6:1 hexane/EtOAc); ^{1}H NMR (400 MHz, $CDCl_3$) δ 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, $CDCl_3$) δ 203.3, 169.9, 137.1, 134.2, 128.9, 126.3, 87.1, 23.6, 22.9, 21.3; IR (neat) ν_{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 (2ag): 163 mg, 96% yield; colorless oil; R_f 0.45 (10:1 hexane/EtOAc); ^{1}H NMR (400 MHz, $CDCl_3$) δ 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); ^{13}C NMR (101 MHz, $CDCl_3$) δ 205.7, 170.8, 93.8, 35.5, 24.8, 24.3, 21.0; IR (neat) ν_{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 $C_9H_{14}O_3$: C, 63.51; H, 8.29. Found: C, 63.45; H, 8.32.

1-Acetylcyclohexyl acetate (2ah): 156 mg, 85% yield; colorless oil; R_f 0.48 (10:1 hexane/EtOAc); ^{1}H NMR (400 MHz, $CDCl_3$) δ 2.11 (s, 3H), 2.07 (s, 3H), 2.02 (d, *J* = 12.0 Hz, 2H), 1.62 (bt, *J* = 12.0 Hz, 5H), 1.53 (q, *J* = 12 Hz, 2H), 1.25 (br q, *J* = 12.0 Hz, 1H); ^{13}C NMR (101 MHz, $CDCl_3$) δ 207.3, 170.2, 85.2, 30.7, 25.0, 23.6, 21.1, 21.0; IR (neat) ν_{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 (2ai): 180 mg, 91% yield; colorless oil; R_f 0.42 (7:1 hexane/EtOAc); ^{1}H NMR (400 MHz, $CDCl_3$) δ 2.10 (s, 3H), 2.07 (s, 3H), 2.03−1.87 (m, 4H), 1.56 (br s, 8H); ^{13}C NMR (101 MHz, $CDCl_3$) δ 207.1, 170.4, 89.2, 34.4, 29.4, 23.6, 22.8, 21.1; IR (neat) ν_{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 (2aj): 194 mg, 80% yield; pale yellow oil; R_f 0.51 (6:1 hexane/EtOAc); ^{1}H NMR (400 MHz, $CDCl_3$) δ 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); ^{13}C NMR (101 MHz, $CDCl_3$) δ 206.4, 170.3, 107.5, 83.9, 64.4, 64.3, 30.0, 28.8, 24.0, 21.0 ; IR (neat) ν_{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.

Preparation of *tert*-butyl-3-(2-hydroxy-4-(trimethylsilyl)but-3-ynyl)-1*H*-indole-1-carboxylate (15): 1.46 g, 89% yield; thick yellow oil; R_f 0.4 (12:1 hexane/EtOAc); ^{1}H NMR (400 MHz, $CDCl_3$) 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, 9H); ^{13}C NMR (101 MHz, $CDCl_3$) 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) ν_{max} 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 $C_{20}H_{27}NO_3Si$: 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)-1*H*-indole-1-carboxylate (16):** 532 mg, 83% yield; thick yellow oil; R_f 0.30 (19:1 hexane/EtOAc); ^{1}H NMR (400 MHz, $CDCl_3$) 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); ^{13}C NMR (101 MHz, $CDCl_3$) δ 169.8, 149.7, 135.3, 130.5, 124.4, 122.5, 119.1, 115.3, 114.8, 83.7, 80.9, 74.3, 63.5, 30.6, 28.2, 21.0; IR (neat) ν_{max} 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 $C_{19}H_{21}NO_4$: 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)-1*H*-indole-1-carboxylate (17):** 350 mg, 83% yield; thick yellow oil; R_f 0.32 (10:1 hexane/EtOAc); ^{1}H NMR (400 MHz, $CDCl_3$) 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); ^{13}C NMR (101 MHz, $CDCl_3$) 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) ν_{max} 2980, 1743,1732, 1606, 1454, 1371, 1255, 1157,1089 cm^{-1}; MS (EI) m/z (%) 344 ($M^+ - 1$, 15), 304 (34), 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-(1*H*-indol-3-yl)butan-2-one (actinopolymorphol B; 18): 115 mg, 56% yield; thick yellow oil; R_f 0.18 (5:1 hexane/EtOAc); ^{1}H NMR (400 MHz, $CDCl_3$) δ 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 = 4.4, 14.8 Hz, 1H), 3.14 (dd, J = 6.6, 15.2 Hz, 1H), 2.21 (s, 3H); ^{13}C NMR (101 MHz, $CDCl_3$) δ 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) ν_{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 $C_{12}H_{13}NO_2$: C, 70.92; H, 6.45; N, 6.89. Found: C, 70.85; H, 6.39; N, 6.81.

O^{18}-Labeled 1-acetylcyclohexyl acetate (27): 152 mg, 82% yield; colorless oil; R_f 0.44 (10:1 hexane/EtOAc); ^{1}H NMR (400 MHz, $CDCl_3$) δ 2.11 (s, 3H), 2.07 (s, 3H), 2.02 (d, J = 12 Hz, 2H), 1.62 (br t, J = 12 Hz, 5H), 1.53 (q, J = 12 Hz, 2H), 1.25 (br q, J = 12 Hz, 1H); ^{13}C NMR (101 MHz, $CDCl_3$) δ 207.3, 170.2, 85.2, 30.7, 25.0, 23.6, 21.1, 21.0; MS (EI) m/z (%) 187 ($M^+ + 1$, 100), 169 (27), 157 (13), 125 (30).

1-(1-Hydroxycyclohexyl)ethanone (28): 47 mg, 78%, colorless oil; R_f 0.33 (8:1 hexane/EtOAc); ^{1}H NMR (400 MHz, $CDCl_3$) δ 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); ^{13}C NMR (101 MHz, $CDCl_3$) δ 212.8, 78.0, 33.8, 29.7, 25.3, 23.7, 21.1; IR (neat) ν_{max} 3260, 1730, 1425, 1367, 1234, 1026 cm^{-1}; MS (EI) m/z (%) 143 ($M^+ + 1$, 58), 129 (55), 125 (62), 99 (9), 81(11). Anal. Calcd for $C_8H_{14}O_2$: C, 67.57; H, 9.92. Found: C, 67.45; H, 9.86.

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Supporting Information Available: Detailed experimental procedures, spectra, and X-ray data. This material is available free of charge via the Internet at http://pubs.acs.org.