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# Synthesis of γ-Acetoxy β-Keto Esters Through Regioselective Hydration of γ-Acetoxy-α,β-alkynoates

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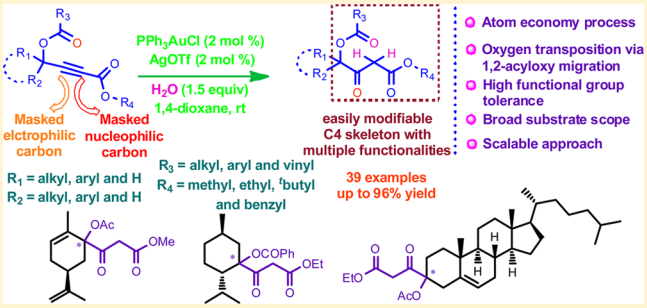
Supporting Information

**ABSTRACT:** The Au(I)-catalyzed regioselective hydration of γ-acetoxy-α,β-acetylinic ester by the assistance of a neighboring carbonyl group has been developed. Varieties of simple primary, secondary, and tertiary γ-acetoxy-α,β-acetylinic esters, even those bearing sensitive functional group in the remote reaction sites, are selectively hydrated to the corresponding β-keto esters. The reaction tolerates a wide variety of other carboxylates, such as benzoates, propionates, acrylates, and pivalates, including chiral carboxylates with retention of the configuration. The broad substrate scope, including the derivatization of complex natural products and neutral and open air conditions, makes this atom economical approach very practical. $^{18}O$ labeling experiments disclose that the oxygen transposition occurs from the carboxylate group to the triple bond, not from water.




## INTRODUCTION

β-Keto esters are a class of unique functionalized and highly valuable intermediates for not only the synthesis of various biologically active compounds, such as 3,4-dihydropyrimidines, 4-alkyl- or -arylcoumarins, and 1,4-dihydropyridines,[1] but also a variety of complex natural products.[2] Their popularity is based on several factors, one of which is facile bond formation with the two differentiable, electrophilic carbonyls and either of the nucleophilic α or γ $sp^3$ carbons. Most of the general methods for the synthesis of β-keto esters include traditional base-mediated[3] and Ti-Claisen[4] condensations. Aside from these, a plethora of other strategies have been developed for the synthesis of β-keto esters.[1] In particular, modifiable functional groups present in the β-keto esters make them more versatile for further organic transformations.[5]

Despite the tremendous successes of the meritorious methods described above, deficiencies exist in preparing modifiable functionalized β-keto esters. As β-keto esters are more prone to electrophilic substitution at either the α- or γ-carbons, further substitution of a modifiable nucleophilic functional group at the γ-carbon becomes difficult. A direct procedure for the synthesis of γ-hydroxy or γ-acetoxy β-keto esters involves the acylation of ester enolates by acid derivatives.[6] The disadvantage of this method is the use of a strong base for enolate generation, which potentially limits the preparation of a chiral γ-functionalized β-keto ester. On the other hand, Pd(II)-mediated oxidative cyclization−carbonylation of propargylic esters followed by acidic hydrolysis relies on the use of poisonous CO gas as well as acid catalysis,[7] rendering it unsuitable for large scale synthesis and also in terms of functional group tolerance. Thus, it was thought that propargylic alcohol (i.e., γ-hydroxy-α,β-alkynoate can become a surrogate for the synthesis of modifiable β-keto ester provided that the regioselective hydration of alkyne carbon α to the alcohol can be performed.

In the past few years, there has been significant progress in the development of gold-catalyzed regioselective hydration of both symmetrical and unsymmetrical internal alkynes.[8] During the course of a literature survey on gold-catalyzed trasformations,[9] Au(III)-catalyzed hydration has been reported by Hammond et al. for accessing both γ- or β-keto esters.[8e] This method of hydration has not been generalized to a broader scope, particularly for the synthesis of multifunctionalized β-keto ester. In 2010, Zhang and co-workers reported an intermolecular oxidation of γ-hydroxy-α,β-acetylinic ester in the presence of a gold catalyst and pyridine *N*-oxide for the synthesis of oxetan-3-ones through an α-oxo gold carbene intermediate (Scheme 1A, eq 1).[10] Alternatively, Nolan's group studied the Au(I)-catalyzed tandem alkoxylation/lactonization of γ-hydroxy-α,β-acetylinic ester to obtain 4-alkoxy-2(5*H*)-furanones (Scheme 1A, eq 2).[11] Although the direct hydration of γ-hydroxy-α,β-alkynoate is a potentially attractive solution, the difficulty of obtaining regioselectivity using gold-catalyzed conditions led us to another approach. We therefore hoped to harness the electronic bias, or perhaps catalytic chelation, of a neighboring carbonyl group in the form of a carboxylate to introduce regioselectivity in gold-catalyzed hydration. Herein, we report the successful implementation of neighboring carbonyl group-assisted regioselective hydration of γ-acetoxy-α,β-alkynoate to access easily modifiable multifunctionalized γ-acetoxy β-keto ester.

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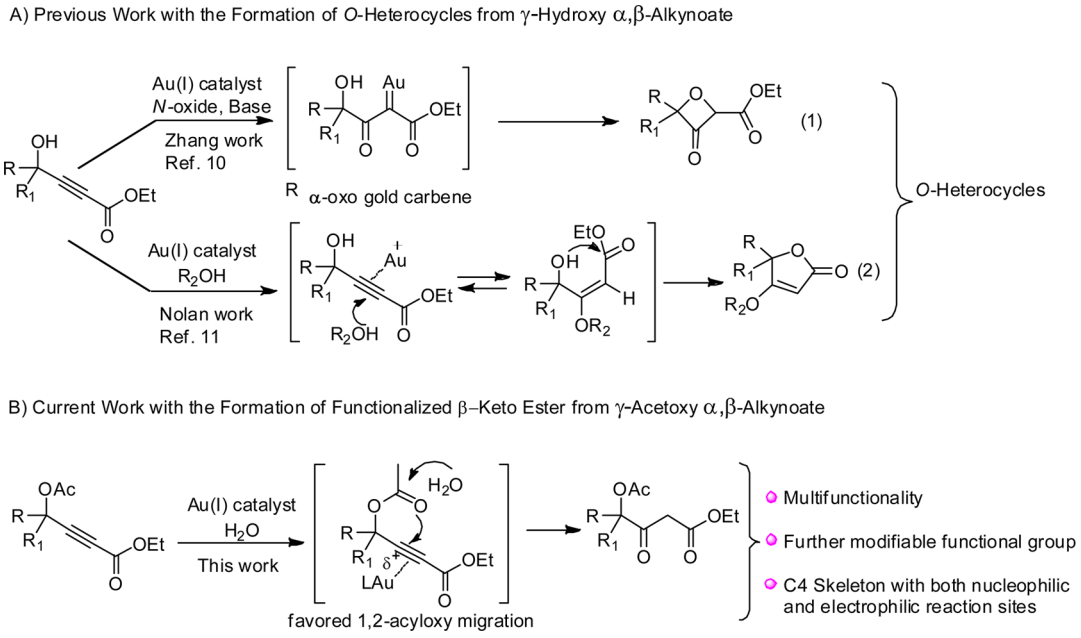
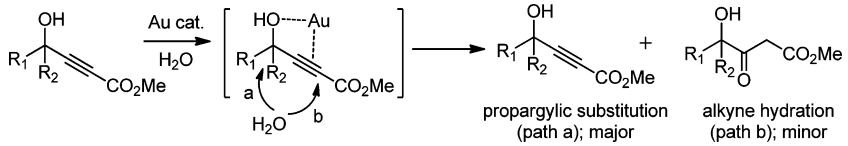
**Scheme 1. Gold(I)-Catalyzed Functionalization of γ-Hydroxy/Acetoxy-α,β-alkynoates**




**Scheme 2. Inhibition of the Hydration Process Due to Propargylic Nucleophilic Substitution**




## RESULTS AND DISCUSSION

Initially, it was envisioned that the electron withdrawing carboxylate function of γ-hydroxy-α,β-alkynoate would cause hydration to afford the corresponding β-keto ester. Thus, the reaction under the catalytic conditions ($NaAuCl_4 \cdot H_2O$, EtOH/$H_2O$) reported by Hammond's group was pursued.[8e] Testing the feasibility of this hydration process required subjecting ethyl 4-hydroxybut-2-ynoate to the same catalytic conditions. To our delight, the expected β-keto ester was formed but in a very low yield after 24 h at room temperature. Disappointingly, the same catalytic conditions for the secondaray and tertiary alcohols led to complete recovery of the starting material. Prolonged heating of the reaction led to decomposition of the starting material. Changing the catalyst or solvent had neither any improvement nor significant impact on the yield of the reaction. It was presumed that the propargylic substitution might be the cause of difficulty for alkyne hydration,[12] which was reasonable due to the formation of a five-membered transition state involved in the complexation of the gold catalyst with −OH and the alkyne bond (Scheme 2), thereby leading to low yield at room temprature and decomposition upon heating. To overcome this substrate scope limit, we contemplated that the exchange of the hydroxyl group with an acetoxy group might facilate regioselective hydration by the assistance of the carbonyl group[13a,b] via 1,2-acyloxy migration.[14] Accordingly, the hydration of primary γ-acetoxy-α,β-alkynoic ester **1a**, which can be easily accessed by the acetylation of ethyl 4-hydroxybut-2-ynoate, was attempted first.

Attempting the hydration of **1a** involved the use of various gold catalysts (4 mol %), 1.5 equiv of water (except entries 1−6) and different solvents (Table 1). Hammond's conditions of hydration led to only 21% of **2a** with the recovery of starting precursor **1a** (72%, entry 1). In the case of entries 1−6, the expected alkoxylation of the triple bond using alcohols as a cosolvent was not observed. In the presence of other Au(III) catalysts, more disappointing results were obtained (entries 2−6). Gratifyingly, the reaction proved to be efficient with various Au(I) catalysts. The combination of a Au(I) catalyst with a silver catalyst, such as $AgBF_4$, $AgSbF_6$, AgOTf, or $AgNTf_2$ (4 mol % of each), was helpful in improving the yield of **2a** (entries 7−12). Screening with different solvents (THF, acetonitrile, dichloroethane, 1,4-dioxane, and nitromethane) led to further improvement in the yield (entries 9−15). Hydration under Zhang's condition using water gave moderate yield (entry 13).[15] The best results were obtained with $PPh_3AuCl$ in combination with AgOTf in 1,4-dioxane as the solvent and also allowed us to reduce the amount of each of the catalysts to 2 mol % (entry 16). The reaction with only AgOTf afforded 32% of **2a**, even after a prolonged reaction time and more catalyst loading (entry 17). Furthermore, the Au(I) catalyst, $PPh_3AuCl$, alone did not afford any hydration product (entry 18). Finally, no reaction occurred in the presence of $PtCl_2$ or $PdCl_2(CH_3CN)_2$ (entries 19 and 20).

## SCOPE OF THE HYDRATION REACTION

Having established the optimized conditions ($PPh_3AuCl$, AgOTf, 1,4-dioxane, rt), we proceeded to investigate the scope of the reaction for different γ-acetoxy-α,β-alkynoates. In general, a wide variety of primary, secondary, and tertiary aliphatic or aromatic substrates were subjected to these conditions to obtain the corresponding hydration products in good to high yields after purification by column chromatography on


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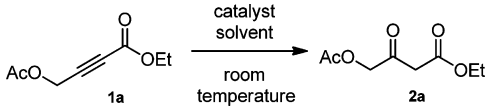
**Table 1. Optimization of the Gold-Catalyzed Hydration Reaction**

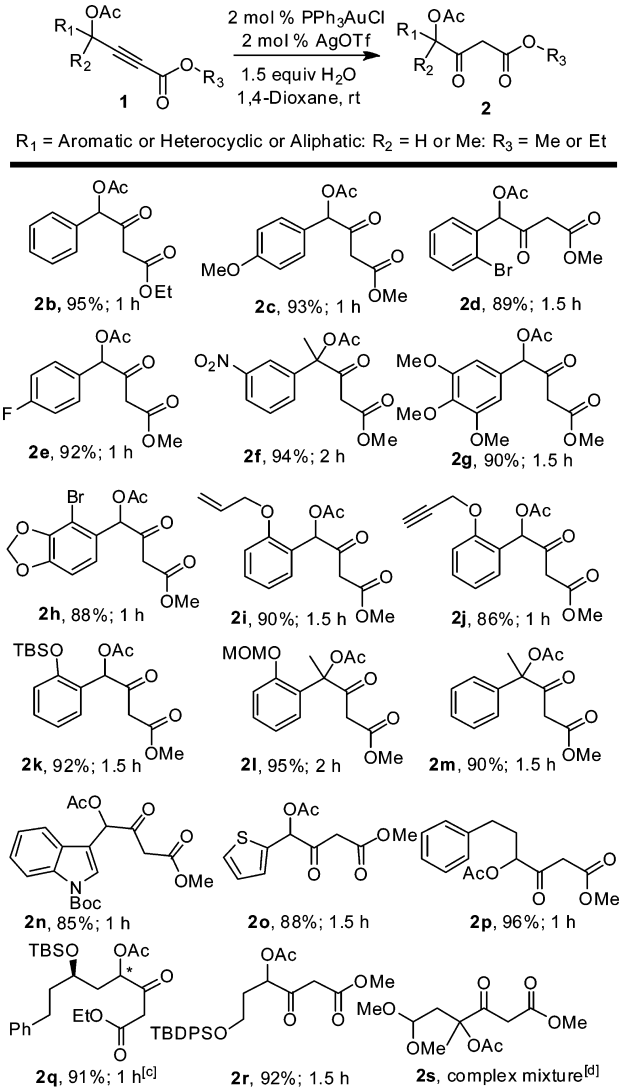



| entry[a] | catalyst/s | solvent/s | time (h) | yield (%)[b] |
|---|---|---|---|---|
| 1 | $NaAuCl_4{\cdot}2H_2O$ | EtOH/$H_2O$ (4:1) | 24 | 21 |
| 2 | $AuCl_3$ | EtOH/$H_2O$ (4:1) | 24 | 20 |
| 3 | $HAuCl_4{\cdot}4H_2O$ | EtOH/$H_2O$ (4:1) | 12 | NR |
| 4 | $AuCl_3$/AgOTf | MeOH/$H_2O$ (10:1) | 24 | 14 |
| 5 | $AuCl_3$/$AgSbF_6$ | MeOH/$H_2O$ (10:1) | 10 | 18 |
| 6 | $AuCl_3$/$AgNTf_2$ | MeOH/$H_2O$ (10:1) | 08 | 20 |
| 7 | AuCl/AgOTf | DCE | 06 | 38 |
| 8 | AuCl/$AgBF_4$ | DCE | 12 | 28 |
| 9 | Au($PPh_3$)Cl/$AgBF_4$ | THF | 06 | 48[c] |
| 10 | Au($PPh_3$)Cl/$AgNTf_2$ | THF | 06 | 46[c] |
| 11 | Au($PPh_3$)Cl/$AgSbF_6$ | THF | 06 | 46[c] |
| 12 | Au($PPh_3$)Cl/AgOTf | DCE | 06 | 62[c] |
| 13 | Au($PPh_3$)Cl/$AgNTf_2$ | DCE | 12 | 73[c] |
| 14 | Au($PPh_3$)Cl/AgOTf | $CH_3CN$ | 12 | 78[c] |
| 15 | Au($PPh_3$)Cl/AgOTf | $CH_3NO_2$ | 06 | 72[d,e] |
| **16** | **Au($PPh_3$)Cl/AgOTf** | **1,4-dioxane** | **01** | **96**[e] |
| 17 | AgOTf | 1,4-dioxane | 06 | 32[e] |
| 18 | Au($PPh_3$)Cl | 1,4-dioxane | 06 | NR[f] |
| 19 | $PtCl_2$ | toluene | 24 | NR[f] |
| 20 | $PdCl_2(CH_3CN)_2$ | toluene | 24 | NR[f] |

[a]The reactions were performed with **1a** (0.5 mmol) and water (1.5 equiv) in solvent (~1 mL) at room temperature under ambient atmosphere. [b]Yield of isolated product after column chromatography. [c]Used 4 mol % of each catalyst. [d]Used 4 mol % of silver catalyst. [e]Used 2 mol % of each catalyst. [f]The reaction was also continued for 48 h.

silica gel (Scheme 3). All of the reactions proceeded smoothly and were completed within 1−2 h. The process readily provided γ-acetoxy β-keto ester regardless of the electronic properties of the substituents on the arenes positioned α to the acetoxy group. The substitution of electron donating and withdrawing groups at any position (ortho, meta, para) of the aromatic ring had no impact on the rate or the yield of the reaction (**2b−f**). Multiple substituents (either donating or withdrawing or both) on the aromatic ring also had no adverse effect on the regioselective hydration (**2g** and **2h**). The presence of reactive functionalities, such as double and triple bonds on the aromatic ring, did not inhibit the hydration, and the desired products **2i** and **2j** were isolated in good yields (90% and 86%, respectively). Protecting groups like TBS and MOM ether of the phenolic hydroxyl were well tolerated under these catalytic conditions, affording the corresponding keto esters **2k** and **2l** in satisfactory yields. Only for tertiary substrates **1f**, **1l**, and **1m** were slightly extended times required, which might be due to steric effects. Heteroaryl substrates **1n** and **1o** were compatible with the optimized reaction conditions. Not only aryl but also alkyl substrates **1p−1r** gave β-keto ester products with satisfactory yields. Aliphatic substrates **1q**, **1r**, and **3b** containing the acid-sensitive protecting groups OTBS, OTBDPS, and OPMB, respectively, also underwent smooth hydration without any disturbance of the existing functionality. However, unidentified results were obtained for substrate **1s**, likely due to the acidity of the gold catalysis toward the acetal group.

**Scheme 3. Hydration of γ-Acetoxy-α,β-alkynoate**




[a]Reactions were carried out using **1** (0.5 mmol), $Ph_3PAuCl$/AgOTf (0.02 mmol), $H_2O$ (1.5 mmol), and 1,4-dioxane (2.0 mL) at ambient temperature. [b]Isolated yields. [c]Diastereomeric mixture of **1q** (dr = 7:3, determined from $^1H$ NMR and HPLC analysis) was taken for the hydration reaction. [d]Reaction of **1s** (0.5 mmol) was carried out under standard conditions at a low temperature (10 °C).

Encouraged by the results from the acetate-assisted hydration, we were subsequently interested in the hydration of other types of easily accessible alkynoates having less nucleophilic and higher sterically hindered carbonyl oxygens. The reaction proceeded equally well for both primary and secondary pivalates, benzoates, and propionates, providing the keto esters with excellent yields (Scheme 4). However, a longer reaction time was required for the tertiary substrates **3f** and **3g**, presumably due to steric hindrance. Hydration of both secondary and tertiary *o*-acrylates (**3e** and **3f**) also proceeded well when the reaction was carried out at low temperature (10 °C). Polyaryl substrates also delivered the corresponding hydration products **4c** and **4d** in high yields. Unfortunately, 2,4,6-trichlorobenzoate ester **3h** did not give the desired product under the reaction conditions, and unprecedented results were obtained. Groups such as Boc, Cbz, THP, MOM, Bn, Ts, and OMe were inert to direct the regioselective



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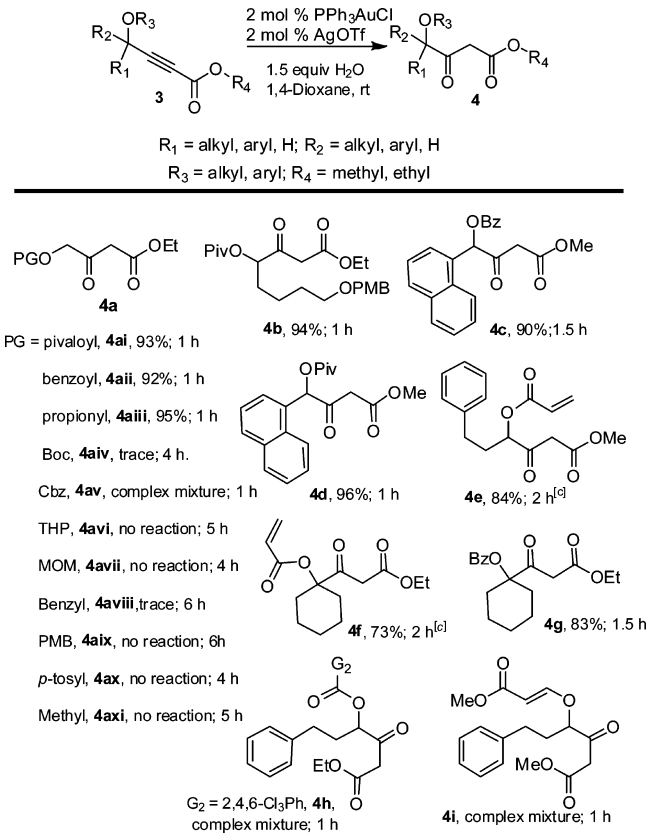
**Scheme 4. Effect of Hydroxyl Protecting Groups (Other than Acetate)**[a,b]



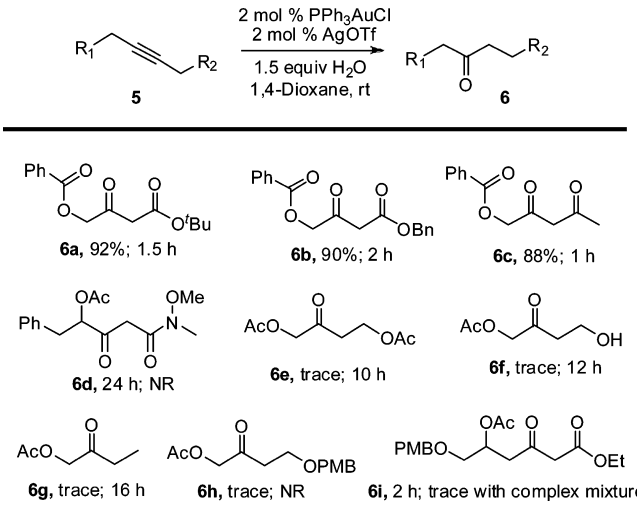

[a]Reactions were carried out using **3** (0.5 mmol), $Ph_3PAuCl/AgOTf$ (0.02 mmol), $H_2O$ (1.5 mmol), and 1,4-dioxane (2.0 mL) at ambient temperature. [b]Isolated yields. [c]Reaction of **3a** and **3f** (0.5 mmol each) was carried under the standard conditions but at a low temperature (10 °C).

hydration even after a longer incubation time (**3aiv**–**3axi**). Similarly, reactions of propargylic vinyl ether **3i** also did not afford any hydration product. The regiochemical outcomes of the successful substrates were similar to those of acetates, thus confirming the validity of the neighboring carbonyl-assisted hydration.

The hypothesis was tested by modifying the substituents on the alkyne terminus of propargylic carboxylate (Scheme 5). Methyl and ethyl propargylic esters readily participated in the hydration (Schemes 3 and 4). Likewise, *tert*-butyl (**5a**) and benzyl ester (**5b**) were also amenable to this reaction to afford the corresponding ketoesters **6a** and **6b**, respectively, in good yield. The transfomation of propargylic ketone **5c** formed **6c** in 88% yield, which left enough room for further transformation. No reaction was observed in the case of propargylic amide **5d** even after 24 h, presumably as a result of the decreasing electron withdrawing power of the amide (Scheme 5).

Substitution of other groups, such as alkyl or even functionalized aliphatic groups, did not lead to productive reactivity (for examples, see Scheme 5, **6e**–**6h**). An unpredictable result was also obtained for homopropargylic carboxylate **5i**. The inertness of substrates **5d**–**5i** toward hydration substantiated the necessity of an electron deficient group on the alkyne terminus as well as the presence of a carboxylate functionality at the other end for the directed hydration reaction.

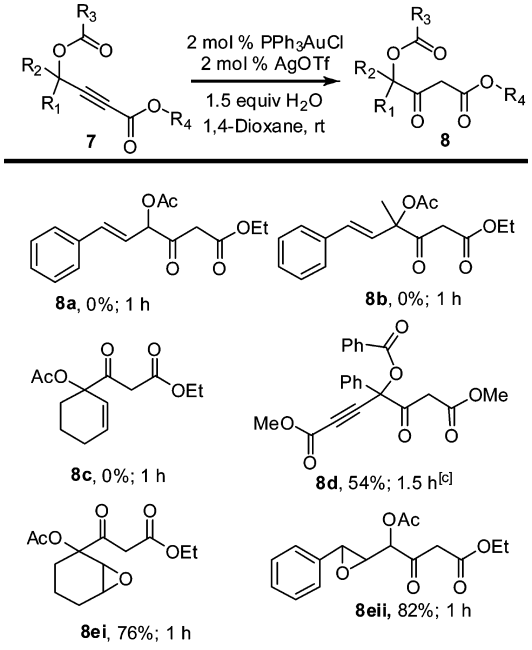
**Scheme 5. Effect of the Nature of the Substituent at the Alkyne Terminus of Propargylic Acetate**[a,b]




[a]Reactions were carried out using **5** (0.5 mmol), $Ph_3PAuCl/AgOTf$ (0.02 mmol each), $H_2O$ (1.5 mmol), and 1,4-dioxane (2.0 mL) at ambient temperature. [b]Isolated yields.

With this set of conditions for the hydration based on the use of a Au(I) catalyst [$PPh_3AuOTf$] and water (Table 1), we next evaluated the generality of our procedure in a series of substrates containing sensitive functionalities (Scheme 6). To

**Scheme 6. Effect of Substituents Directly Attached to the Acetate/Benzoate Bearing Carbon**[a,b]




[a]Reactions were carried out on a scale of 0.5 mmol of **7** in 2 mL of solvent under the standard conditions. [b]Yield of isolated product. [c]Reaction was carried out at 10 °C, and the starting diyne **7d** (30%) was recovered.

this end, a set of ethyl 4-acetoxyhex-5-en-2-ynoates **7a**–**c** possessing both secondary and tertiary acetates were subjected to the hydration conditions. Unfortunately, the corresponding hydration product was not obtained even in a traceable amount,



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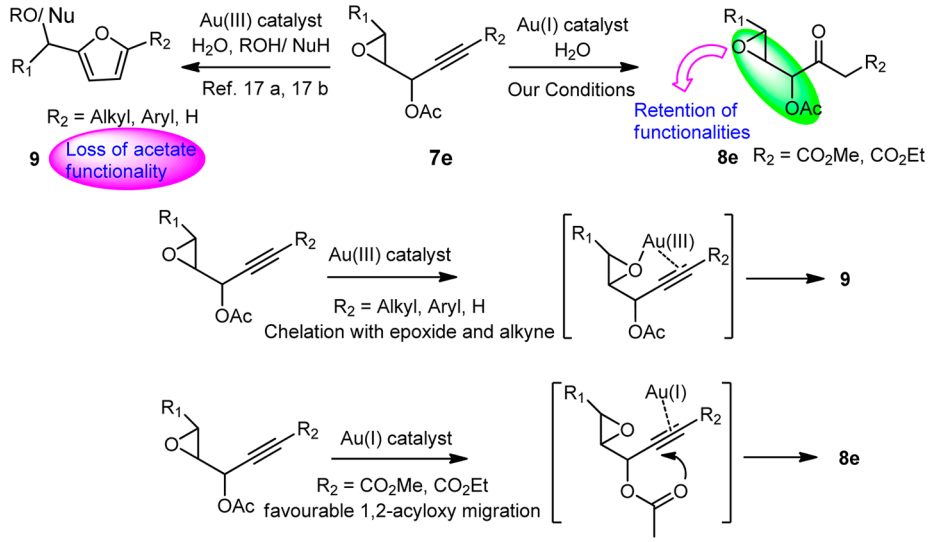
**Scheme 7. Mode of Reactivities of Au(I) and (III) Catalysts for Oxiranyl Carboxylate**

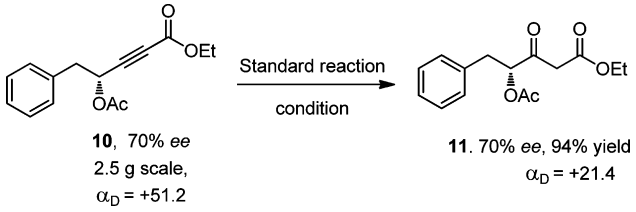



albeit some unidentified mixture was obtained. This result of hydration might be due to the competitive Rautenstrauch rearrangement in the presence of the Au(I) catalyst.[16] However, the tertiary skipped diyne **7d** underwent hydration to give the mono hydration product **8d**, albeit in 54% yield, by controlling the reaction temperature.

It is worth mentioning here that the hydration of ethyl 4-acetoxy-4-(oxiran-2-yl)-2-alkynoates proceeded smoothly in all cases, forming the corresponding *β*-keto esters **8ei** and **8eii** in good to excellent yield without affecting the epoxide functionality. Switching of the product selectivity from furan synthesis[17a,b] to *β*-keto esters might explain why the presence of an electron withdrawing group ($CO_2Me/CO_2Et$) makes 1,2-acyloxy migration more favorable than the reaction through epoxide chelation (Scheme 7).

Chirality retention in the hydration process was examined by preparing enantio-enriched propargyl acetate **10** according to the literature procedure.[18] Hydration of enantio-enriched acetate **10** (70% ee) under the standard conditions cleanly afforded **11** without any loss of the enantioselectivity (70% ee) (Scheme 8). Importantly, the hydration is not limited to the

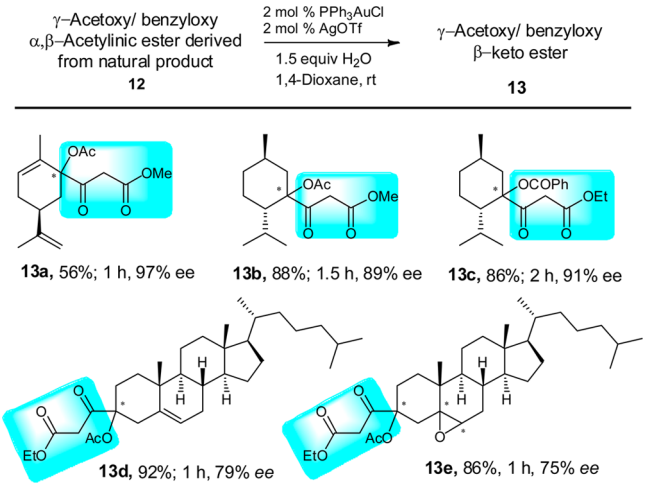
**Scheme 8. Scalable Hydration of Chiral Substrate 10**




small scale (e.g., 100 mg) used for the scope and limitation studies described above as it could be conveniently performed on a 2.5 g scale in excellent yield under the same standard conditions.

Late stage modifications of natural products are highly valuable in medicinal chemistry. We were delighted to determine that the current hydration reaction was also capable of tolerating a wide range of *γ*-acetoxy/benzoyloxy-*α*,*β*-alkynoates derived from natural products (Scheme 9).[19] For instance, the derivatized *γ*-acetoxy acetylinic ester of

**Scheme 9. Synthetic Utility of the Hydration Through Natural Product Derivatization**[a,b]




[a]Reactions were carried out on a scale of 0.4 mmol of **12** in 1.5 mL of solvent under the standard conditions. [b]Yield of isolated product. In substrates, asterisks (*) represent the undetected stereocenter.

(+)-carvone **13a** bearing an olefinic bond close to the reaction site proved to be competent (56%). Notably, both *γ*-acetoxy/benzoyloxy acetylinic ester derived from (+)-menthone (**13b** and **13c**) and cholesterol (**13d**) participated in the present transformation, highlighting the broad substrate scope and potential utility of this protocol. In addition, oxiranyl derivative **13e** underwent carbonyl-assisted hydration in acceptable yield without disturbance of the epoxide ring.

**Mechanistic Investigation.** Having demonstrated the efficiency of our carbonyl-assisted hydration reaction, we next focused our efforts on gaining more insights into the mechanism of this reaction. A plausible scenario for the regioselective formation of *β*-keto ester comprises two possible pathways, which are illustrated in Scheme 10. A traditional and more obvious pathway involves the nucleophilic attack of water on the *β*-carbon, which may be the result of a strong electron withdrawing effect of the ester group as assumed by Hammond's group (Scheme 10, path b).[8e]



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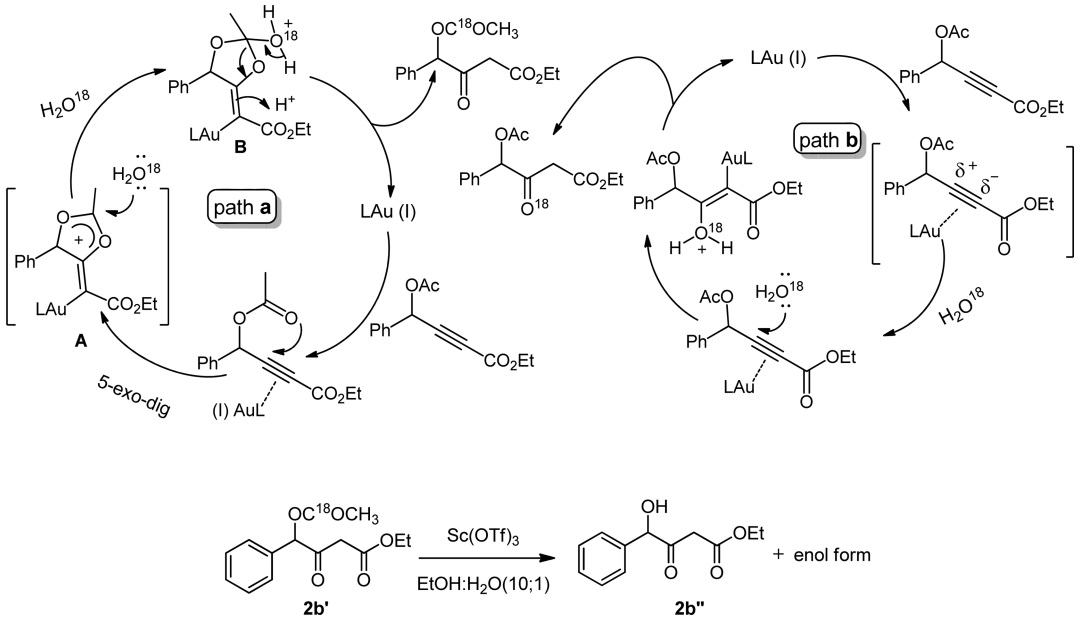
**Scheme 10. Plausible Mechanism for the Formation of the Hydration Product**




In contrast to the aforementioned pathway, an alternative plausible route is the 5-*exo* dig attack of the carbonyl oxygen of the $\gamma$-carbon to generate five-membered vinyl gold intermediate **A**. The formation of this intermediate could be attributed to the electron withdrawing nature of the ester group, which selectively renders such attack by developing a negative charge at the proximal end.[13b,15] The nucleophilic addition of water to this electrophilic gold intermediate results in **B**, which follows subsequent protodeauration to yield the keto ester.

To test the proposed mechanisms and to determine the source of carbonyl oxygen, the reaction was performed under the present reaction conditions using 5 mmol $H_2O^{18}$ under anhydrous conditions. Analysis of the isolated produt by HRMS(ESI) reveals a peak at 289.0931 $[M + Na]^+$, 2 mass units more than the regular hydration product **2b**. However, deacetylation[20] of the isotopic hydration product **2b′** gave **2b″** (245.0780 $[M + Na]^+$) with the loss of $^{18}O$, which favors the proposed mechanism (Scheme 10, path a).

## CONCLUSIONS

In summary, a remarkably mild, regioselective hydration and atom economical process has been developed for the synthesis of a series of $\gamma$-acetoxy $\beta$-keto esters that relies on simultaneous oxygen transposition from a neighboring carboxylate group to the C≡C bond and water to the carboxylate group in good to excellent yields. The mild catalytic conditions readily tolerate remote sensitive functional groups as well as protecting groups. This method provides efficient masking of easily modifiable electrophilic and nucleophilic carbons as acetylinic esters, offering a practical solution for constructing a C4 carbon skeleton. The utility of this method was demonstrated by further transformation of the natural product-derivatized alkynoates without loss of enantiomeric purity.

## EXPERIMENTAL SECTION

**General Information.** All reactions were carried out under ambient atmosphere unless otherwise stated. All starting materials and reagents were obtained from commercial producers and used without further purification. Solvents were generally used as supplied by the manufacturer except THF (THF was freshly distilled over sodium/benzophenone under inert atmosphere). Column chromatography was carried out using silica gel (60−120 mesh) unless otherwise mentioned. Reactions were monitored by TLC on silica gel GF254 (0.25 mm). Specific optical rotations $[\alpha]_D$ were given in $10^{-1}$ deg cm$^2$ g$^{-1}$. Infrared spectra were recorded in $CHCl_3$/neat (as mentioned) and reported in wavenumber (cm$^{-1}$). HRMS spectra were recorded using a Q-TOF mass spectrometer. HPLC was performed on HPLC systems consisting of the following: detector, 875-UV or UV-970 measured at 210 and 254 nm; column, ATLANTIS C18 (4.6 × 150 mm, 5 $\mu$) and LUX AMISOSE (4.6 × 250 mm, 5 $\mu$); mobile phase, acetonitrile, water, isopropanol, and hexane; and flow rate, 1 mL/min. $^1$H NMR spectra were recorded at 300, 400, and 500 and $^{13}$C NMR spectra at 75, 100, and 125 MHz in $CDCl_3$ solution unless otherwise mentioned. Chemical shifts are in ppm downfield from tetramethylsilane, and coupling constants ($J$) are reported in hertz (Hz). The following abbreviations are used to designate signal multiplicity: s = singlet, d = doublet, t = triplet, q = quartet, m = multiplet, and br = broad.

*Procedure for the Synthesis of* ***1a*** *and* ***3a*** *(P-1).*[21] To a solution of 2-(prop-2-yn-1-yloxy)tetrahydro-2*H*-pyran **1a‴** (5.0 g, 35.71 mmol) was added *n*-BuLi (4.28 mL, 2.5 M in hexane, 35.71 mmol) dropwise using a syringe at −78 °C under nitrogen atmosphere, and the mixture was stirred at this temperature for 20 min. Then, ethyl chloroformate (6.76 mL, 71.42 mmol) was added dropwise to this ylide solution. The reaction mixture was slowly (10 min) brought to room temperature and continued to stir until complete consumption of alkyne (monitored by TLC). The reaction was quenched with saturated aq $NH_4Cl$ solution (75 mL) and diluted with ethyl acetate (100 mL). The organic layer was separated, and the aq layer was extracted with ethyl acetate (3 × 75 mL). The combined organic layer was washed with brine (100 mL), dried over anhydrous $Na_2SO_4$, and concentrated under reduced pressure to get crude ethyl 4-((tetrahydro-2*H*-pyran-2-yl)oxy)but-2-ynoate (**1a″**) (6.8 g, 90%) as a thick yellow liquid.

The obtained crude THP ether **1a″** was treated with a catalytic amount of PTSA in ethanol (30 mL) and stirred for 5 h. EtOH was then removed, and the reaction was quenched with saturated aq $NaHCO_3$ solution (30 mL) and diluted with $CH_2Cl_2$ (50 mL). The organic layer was separated, and the aqueous layer extracted with $CH_2Cl_2$ (3 × 50 mL). The combined organic layer was washed with brine (2 × 75 mL), dried over anhydrous $Na_2SO_4$, and concentrated under reduced pressure to get the crude compound, which upon purification by column chromatography (1:4 ethyl acetate/hexane)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afforded ethyl 4-hydroxybut-2-ynoate (**1a′**) (3.36 g, 82%) as a colorless oil.

Hydration precursors **1a** and **3a** were synthesized from **1a′** following procedures (P-2b, -2c, -2d, and -2e) as described below.

*Representative Procedures for Synthesis of Hydration Precursors (P-2). (a). General Procedure for Synthesis of Secondary or Tertiary γ-Hydroxy-α,β-acetylinic Esters (P-2a).*[22] A flame-dried, round-bottom flask was charged with anhydrous THF (20 mL) and methyl/ethyl propiolate (7.50 mmol). The solution was cooled to −78 °C, and LHMDS (7.50 mmol, 1.0 M in THF) was added slowly over 10 min. The solution was allowed to stir for 30 min at −78 °C, and then aldehyde/ketone (5.0 mmol) was added slowly over 5 min. The mixture was stirred for an additional 45 min at the same temperature and was then warmed to 23 °C. After complete consumption of the starting material (monitored by TLC), saturated aq $NH_4Cl$ solution (25 mL) was added slowly and continued to stir for 15 min. The mixture was diluted with ethyl acetate (30 mL). The aqueous layer was extracted with ethyl acetate (2 × 30 mL), and the combined organic layer was washed with brine and dried over $Na_2SO_4$. The crude propargylic alcohol obtained after evaporation of the solvent under reduced pressure was directly used for the preparation of the hydration precursor by following the procedures as described below.

*(b). General Procedure for Acetylation of Primary, Secondary, or Tertiary γ-Hydroxy-α,β-acetylinic Esters (P-2b).*[23] To a solution of the crude propargyl alcohol (1.0 mmol) in anhydrous $CH_2Cl_2$ (15 mL) were added triethylamine (0.28 mL, 2.0 mmol), acetic anhydride (0.18 mL, 2.0 mmol), and DMAP (catalytic) under a nitrogen atmosphere at 0 °C. The resulting mixture was stirred at room temperature until complete consumption of the starting material (monitored by TLC). Then, the reaction mixture was washed with brine solution (2 × 15 mL) and dried over $MgSO_4$, and the solvent was removed under reduced pressure. The residue was purified by column chromatography to obtain the acetylated hydration precursor (up to 95% yield).

*(c). General Procedure for Benzoylation of Primary, Secondary, or Tertiary γ-Hydroxy-α,β-acetylinic Esters (P-2c).*[23] To a solution of the crude propargyl alcohol (1.0 mmol) in anhydrous $CH_2Cl_2$ (15 mL) were added triethylamine (0.28 mL, 2.0 mmol), benzoyl chloride (1.74 mL, 1.5 mmol), and DMAP (catalytic) under a nitrogen atmosphere at 0 °C. The resulting mixture was stirred for 5 h and then quenched with aqueous $NH_4Cl$ solution (15 mL). The aqueous layer was extracted with $CH_2Cl_2$ (2 × 20 mL), and the combined organic layer was washed with brine and dried over $MgSO_4$. The crude residue obtained after evaporation of the solvent under reduced pressure was purified by column chromatography to obtain the pure benzoate ester (up to 90% yield).

*(d). General Procedure for Acryloylation of Primary, Secondary, or Tertiary γ-Hydroxy-α,β-acetylinic Esters (P-2d).*[24] To a solution of the crude propargyl alcohol (1.0 mmol) in anhydrous $CH_2Cl_2$ (15 mL) were added triethylamine (0.28 mL, 2.0 mmol) followed by acryloyl chloride (0.16 mL, 2.0 mmol) and DMAP (catalytic) under a nitrogen atmosphere at 0 °C. The resulting mixture was stirred for 1 h and then quenched with aqueous $NH_4Cl$ solution (15 mL). The aqueous layer was extracted with $CH_2Cl_2$ (2 × 15 mL). The combined organic layer was washed with brine and dried over $Na_2SO_4$. The crude residue obtained after evaporation under reduced pressure was purified by flash column chromatography to obtain the pure acrylate ester (up to 85% yield).

*(e). General Procedure for Pivaloylation of Primary, Secondary, or Tertiary γ-Hydroxy-α,β-acetylinic Esters (P-2e).*[25] (This procedure is a minor modification of the literature procedure)

To a solution of the crude propargyl alcohol (1.0 mmol) in anhydrous $CH_2Cl_2$ (15 mL) were added triethylamine (0.28 mL, 2.0 mmol)) followed by pivaloyl chloride (0.24 mL, 2.0 mmol) and DMAP (catalytic) under a nitrogen atmosphere at 0 °C. The resulting mixture was stirred for 2 h and then quenched with aqueous $NH_4Cl$ solution (15 mL). The aqueous layer was extracted with $CH_2Cl_2$ (2 × 15 mL). The combined organic layer was washed with brine and dried over $Na_2SO_4$. The crude residue obtained after evaporation of solvent under reduced pressure was purified by column chromatography to obtain the pure pivaloate ester (up to 80% yield).

*Ethyl 4-Acetoxybut-2-ynoate (**1a**).* Following general procedure P-2b, **1a** was obtained from **1a′** (200 mg, 1.56 mmol) as a colorless liquid (249 mg, 94%). $R_f$ = 0.48 (9:1 hexane/EtOAc); IR (neat) $\nu_{max}$ 2954, 2852, 2249, 1763, 1740, 1376, 1244, 1056, 772 $cm^{-1}$; $^1H$ NMR (300 MHz, $CDCl_3$) $\delta$ 4.79 (s, 2H), 4.25 (q, $J$ = 7.2 Hz, 2H), 2.13 (s, 3H), 1.32 (t, $J$ = 7.2 Hz, 3H); $^{13}C$ NMR (75 MHz, $CDCl_3$) $\delta$ 169.7, 152.7, 80.7, 77.8, 62.2, 51.4, 20.4, 13.8; HRMS (ESI-TOF) $m/z$ $[M]^+$ calcd for $C_8H_{10}O_4$ 170.0574, found 170.0565.

*Ethyl 4-Acetoxy-4-phenylbut-2-ynoate (**1b**).* Following general procedures P-2a and 2b, **1b** (236 mg, 73%) was obtained from benzaldehyde as a light yellow liquid. $R_f$ = 0.52 (9:1 hexane/EtOAc); IR (neat) $\nu_{max}$ 2955, 2924, 2853, 2244, 1744, 1711, 1368, 1216, 1054, 771 $cm^{-1}$; $^1H$ NMR (300 MHz, $CDCl_3$) $\delta$ 7.54−7.46 (m, 2H), 7.44−7.37 (m, 3H), 6.53 (s, 1H), 4.25 (d, $J$ = 7.2 Hz, 2H), 2.1 (s, 3H), 1.31 (t, $J$ = 7.2 Hz, 3H); $^{13}C$ NMR (75 MHz, $CDCl_3$) $\delta$ 169.2, 152.8, 134.9, 129.3, 128.7, 127.6, 82.6, 78.1, 64.6, 62.2, 20.6, 13.8; HRMS (ESI-TOF) $m/z$ $[M + Na]^+$ calcd for $C_{14}H_{14}O_4Na$ 269.0784, found 269.0783.

*Methyl 4-Acetoxy-4-(4-methoxyphenyl)but-2-ynoate (**1c**).* Following general procedures P-2a and 2b, **1c** (210 mg, 79%) was obtained from 4-methoxybenzaldehyde as a yellow liquid. $R_f$ = 0.65 (9:1 hexane/EtOAc); IR (neat) $\nu_{max}$ 2926, 2949, 2376, 2246, 1747, 1720, 1515, 1217, 959, 837 $cm^{-1}$; $^1H$ NMR (500 MHz, $CDCl_3$) $\delta$ 7.43 (d, $J$ = 8.7 Hz, 2H), 6.91 (d, $J$ = 8.7 Hz, 2H), 6.48 (s, 1H), 3.82 (s, 3H), 3.79 (s, 3H), 2.10 (s, 3H); $^{13}C$ NMR (75 MHz, $CDCl_3$) $\delta$ 169.4, 160.5, 153.4, 129.4, 127.2. 114.2, 83.5, 77.7, 64.5, 55.3, 52.8, 20.8; HRMS (ESI-TOF) $m/z$ $[M + Na]^+$ calcd for $C_{14}H_{14}O_5Na$ 285.0742, found 285.0737.

*Methyl 4-Acetoxy-4-(2-bromophenyl)but-2-ynoate (**1d**).* Following general procedures P-2a and 2b, **1d** (220 mg, 72%) was obtained from 2-bromobenzaldehyde as a yellow liquid. $R_f$ = 0.55 (9:1 hexane/EtOAc); IR (neat) $\nu_{max}$ 2984, 2246, 1736, 1372, 1235, 1043, 772 $cm^{-1}$; $^1H$ NMR (500 MHz, $CDCl_3$) $\delta$ 7.70 (dd, $J$ = 1.7, 7.8 Hz, 1H), 7.60 (dd, $J$ = 1.2 Hz, 7.9 Hz, 1H), 7.39 (td, $J$ = 1.2, 7.6 Hz, 1H), 7.27 (td, $J$ = 1.7, 8.1 Hz, 1H), 6.80 (s, 1H), 3.79 (s, 3H), 2.15 (s, 3H); $^{13}C$ NMR (125 MHz, $CDCl_3$) $\delta$ 168.9, 153.1, 134.2, 133.1, 130.9, 129.5, 127.9, 123.0, 82.1, 77.9, 64.3, 52.8, 20.5; HRMS (ESI-TOF) $m/z$ $[M + Na]^+$ calcd for $C_{13}H_{11}O_4BrNa$ 332.9732, found 332.9729.

*Methyl 4-Acetoxy-4-(4-fluorophenyl)but-2-ynoate (**1e**).* Following general procedures P-2a and 2b, **1e** (150 mg, 76%) was obtained from 4-fluorobenzaldehyde as a yellow liquid. $R_f$ = 0.56 (9:1 hexane/EtOAc); IR (neat) $\nu_{max}$ 3009, 2957, 2246, 1748, 1722, 1511, 1436, 1259, 1219, 1016, 751 $cm^{-1}$; $^1H$ NMR (500 MHz, $CDCl_3$) $\delta$ 7.50−7.46 (m, 2H), 7.11−7.05 (m, 2H), 6.50 (s, 1H), 3.79 (s, 3H), 2.11 (s, 3H); $^{13}C$ NMR (75 MHz, $CDCl_3$) $\delta$ 169.2, 164.8, 161.5, 153.1, 129.8, 129.7, 115.9, 115.6, 82.8, 77.9, 63.9, 52.8, 20.6; HRMS (ESI-TOF) $m/z$ $[M + H]^+$ calcd for $C_{13}H_{12}O_4F$ 251.0714, found 251.0718.

*Methyl 4-Acetoxy-4-(3-nitrophenyl)pent-2-ynoate (**1f**).* Following general procedures P-2a and 2b, **1f** (180 mg, 69%) was obtained from 3-nitroacetophenone as a yellow liquid. $R_f$ = 0.35 (9:1 hexane/EtOAc); IR (neat) $\nu_{max}$ 3083, 2957, 2852, 2243, 1752, 1722, 1524, 1067, 857, 751 $cm^{-1}$; $^1H$ NMR (500 MHz, $CDCl_3$) $\delta$ 8.28−8.20 (m, 2H), 7.76−7.66 (m, 2H), 3.83 (s, 3H), 2.12 (s, 3H), 1.92 (s, 3H); $^{13}C$ NMR (75 MHz, $CDCl_3$) $\delta$ 168.3, 156.2, 147.8, 147.5, 125.7, 123.9, 84.1, 79.3, 73.7, 52.9, 31.0, 21.1; HRMS (ESI-TOF) $m/z$ $[M + Na]^+$ calcd for $C_{14}H_{13}O_6NNa$ 314.0635, found 314.0630.

*Methyl 4-Acetoxy-4-(3,4,5-trimethoxyphenyl)but-2-ynoate (**1g**).* Following general procedures P-2a and 2b, **1g** (185 mg, 74%) was obtained from 3,4,5-trimethoxybenzaldehyde as a colorless liquid. $R_f$ = 0.62 (9:1 hexane/EtOAc); IR (neat) $\nu_{max}$ 2929, 2851, 2377, 2313, 1749, 1729, 1510, 1225, 922 $cm^{-1}$; $^1H$ NMR (300 MHz, $CDCl_3$) $\delta$ 6.72 (s, 2H), 6.45 (s, 1H), 3.89 (s, 6H), 3.85 (s, 3H), 3.80 (s, 3H), 2.14 (s, 3H); $^{13}C$ NMR (75 MHz, $CDCl_3$) $\delta$ 169.2,153.3, 153.1, 138.7, 130.3, 104.8, 83.0, 77.7, 64.7, 60.6, 56.0, 52.7, 20.7; HRMS (ESI-TOF) $m/z$ $[M + H]^+$ calcd for $C_{16}H_{19}O_7$ 323.1125, found 323.1126.

*Methyl 4-Acetoxy-4-(4-bromobenzo[d][1,3]dioxol-5-yl)but-2-ynoate (**1h**).* Following general procedures P-2a and 2b, **1h** (160 mg, 70%) was obtained from 4-bromobenzo[*d*][1,3]dioxole-5-carbaldehyde



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as a colorless liquid. $R_f$ = 0.48 (9:1 hexane/EtOAc); IR (neat) $\nu_{max}$ 2925, 2851, 2376, 2315, 1752, 1719, 1480, 1254, 1212, 1036, 939 $cm^{-1}$; $^1H$ NMR (500 MHz, $CDCl_3$) $\delta$ 7.16 (s, 1H), 7.02 (s, 1H), 6.73 (s, 1H), 6.03 (s, 2H), 3.79 (s, 3H), 2.19 (s, 3H); $^{13}C$ NMR (125 MHz, $CDCl_3$) $\delta$ 169.0, 153.2, 149.3, 147.8, 127.3, 114.3, 112.8, 109.1, 102.3, 82.3, 77.7, 64.3, 52.9, 20.6; HRMS (ESI-TOF) $m/z$ $[M + Na]^+$ calcd for $C_{14}H_{11}O_6BrNa$ 376.9631, found 376.9641.

*Methyl 4-Acetoxy-4-(2-(allyloxy)phenyl)but-2-ynoate (**1i**).* Following general procedures P-2a and 2b, **1i** (160 mg, 74%) was obtained from 2-(allyloxy)benzaldehyde as a pale yellow liquid. $R_f$ = 0.50 (9:1 hexane/EtOAc); IR (neat) $\nu_{max}$ 2923, 2852, 2377, 1743, 1719, 1447, 1219, 952 $cm^{-1}$; $^1H$ NMR (500 MHz, $CDCl_3$) $\delta$ 7.59 (dd, $J$ = 1.5, 7.6 Hz, 1H), 7.34 (td, $J$ = 1.5, 7.6 Hz, 1H), 7.01 (brt, $J$ = 7.6 Hz, 1H), 6.93 (s, 1H), 6.89 (d, $J$ = 8.4 Hz, 1H), 6.08−5.95 (m, 1H), 5.45−5.37 (m, 1H), 5.31−5.24 (m, 1H), 4.62−4.55 (m, 2H), 3.77 (s, 3H), 2.10 (s, 3H); $^{13}C$ NMR (125 MHz, $CDCl_3$) $\delta$ 169.2, 155.5, 153.4, 132.5, 130.7, 128.8, 123.3, 120.8, 117.3, 112.0, 83.6, 77.1, 68.9, 59.7, 52.7, 20.7; HRMS (ESI-TOF) $m/z$ $[M + Na]^+$ calcd for $C_{16}H_{16}O_5Na$ 311.0889, found 311.0891.

*Methyl 4-Acetoxy-4-(2-(prop-2-ynyloxy)phenyl)but-2-ynoate (**1j**).* Following general procedures P-2a and 2b, **1j** (170 mg, 69%) was obtained from 2-(prop-2-ynyloxy)benzaldehyde as a colorless liquid. $R_f$ = 0.48 (9:1 hexane/EtOAc); IR (neat) $\nu_{max}$ 2923, 2246, 1732, 1492, 1220, 1043, 772, 685 $cm^{-1}$; $^1H$ NMR (300 MHz, $CDCl_3$) $\delta$ 7.61 (dd, $J$ = 1.5, 7.5 Hz, 1H), 7.38 (td, $J$ = 1.5, 7.5 Hz, 1H), 7.06 (t, $J$ = 7.5 Hz, 2H), 6.88 (s, 1H), 4.75 (d, $J$ = 2.3 Hz, 2H), 3.78 (s, 3H), 2.51 (t, $J$ = 2.3 Hz, 1H), 2.11 (s, 3H); $^{13}C$ NMR (75 MHz, $CDCl_3$) $\delta$ 169.3, 154.6, 153.4, 130.7, 129.0, 123.9, 121.7, 112.6, 83.5, 78.0, 77.2, 75.9, 59.6, 56.3, 52.8, 20.7; HRMS (ESI-TOF) $m/z$ $[M + Na]^+$ calcd for $C_{16}H_{14}O_5Na$ 309.0733, found 309.0734.

*Methyl 4-Acetoxy-4-(2-(tert-butyldimethylsilyloxy)phenyl)but-2-ynoate (**1k**).* Following general procedures P-2a and 2b, **1k** (220 mg, 72%) was obtained from 2-(*tert*-butyldimethyl- silyloxy)-benzaldehyde as a colorless liquid. $R_f$ = 0.65 (9:1 hexane/EtOAc); IR (neat) $\nu_{max}$ 2955, 2859, 2245, 1720, 1215, 1017, 747 $cm^{-1}$; $^1H$ NMR (300 MHz, $CDCl_3$) $\delta$ 7.30−7.21 (m, 1H), 7.11−7.05 (m, 1H), 6.98−6.94 (m, 1H), 6.89−6.52 (m, 1H), 6.46 (s, 1H), 3.79 (s, 3H), 2.12 (s, 3H), 0.99 (s, 9H), 0.21 (s, 6H); $^{13}C$ NMR (75 MHz, $CDCl_3$) $\delta$ 169.3, 155.9, 153.2, 136.2, 129.8, 121.0, 120.5, 119.3, 83.1, 77.7, 64.4, 52.8, 25.6, 20.7, 18.1, −4.5; HRMS (ESI-TOF) $m/z$ $[M + H]^+$ calcd for $C_{19}H_{27}O_5Si$ 363.1622, found 363.1625.

*Methyl 4-Acetoxy-4-(2-(methoxymethoxy)phenyl)pent-2-ynoate (**1l**).* Following general procedures P-2a and 2b, **1l** (180 mg, 68%) was obtained from 1-(2-(methoxymethoxy)phenyl)-ethanone as a yellow liquid. $R_f$ = 0.55 (9:1 hexane/EtOAc); IR (neat) $\nu_{max}$ 3021, 2956, 2243, 1731, 1374, 1256, 1045, 744 $cm^{-1}$; $^1H$ NMR (300 MHz, $CDCl_3$) $\delta$ 7.60−7.51 (m, 1H), 7.33−7.13 (m, 2H), 7.07−6.36 (m, 1H), 5.29−5.18 (m, 2H), 3.78 (s, 3H), 3.51 (s, 3H), 2.11 (s, 3H), 2.04 (s, 3H); $^{13}C$ NMR (75 MHz, $CDCl_3$) $\delta$ 168.4, 153.9, 140.0, 129.7, 127.9, 126.9, 121.5, 115.1, 94.5, 86.7, 77.1, 73.9, 56.1, 52.6, 27.7, 21.3; HRMS (ESI-TOF) $m/z$ $[M + Na]^+$ calcd for $C_{16}H_{18}O_6Na$ 329.0995, found 329.0994.

*Methyl 4-Acetoxy-4-phenylpent-2-ynoate (**1m**).* Following general procedures P-2a and 2b, **1m** (140 mg, 73%) was obtained from acetophenone as a pale yellow liquid. $R_f$ = 0.50 (9:1 hexane/EtOAc); IR (neat) $\nu_{max}$ 3033, 2938, 2247, 1752, 1716, 1373, 753, 702 $cm^{-1}$; $^1H$ NMR (300 MHz, $CDCl_3$) $\delta$ 7.55−7.52 (m, 2H), 7.39−7.35 (m, 2H), 7.33−7.29 (m, 1H), 3.81 (s, 3H), 2.09 (s, 3H), 1.92 (s, 3H); $^{13}C$ NMR (75 MHz, $CDCl_3$) $\delta$ 168.3, 153.6, 140.8, 128.5, 128.2, 124.6, 85.9, 78.7, 74.5, 52.7, 31.1, 21.4; HRMS (ESI-TOF) $m/z$ $[M + Na]^+$ calcd for $C_{14}H_{14}O_4Na$ 269.0784, found 269.0774.

*tert-Butyl 3-(1-Acetoxy-4-methoxy-4-oxobut-2-ynyl)-1H-indole-1-carboxylate (**1n**).* Following general procedures P-2a and 2b, **1n** (185 mg, 67%) was obtained from *tert*-butyl 3-formyl-1*H*-indole-1-carboxylate as a thick yellow gel. $R_f$ = 0.64 (9:1 hexane/EtOAc); IR (neat) $\nu_{max}$ 2924, 2243, 1734, 1728, 1453, 1370, 1219, 1096, 772 $cm^{-1}$; $^1H$ NMR (300 MHz, $CDCl_3$) $\delta$ 8.16 (d, $J$ = 8.3 Hz, 1H), 7.79 (s, 1H), 7.70 (d, $J$ = 7.6 Hz, 1H), 7.42−7.24 (m, 2H), 6.81 (s, 1H), 3.79 (s, 3H), 2.12 (s, 3H), 1.68 (s, 9H); $^{13}C$ NMR (75 MHz, $CDCl_3$) $\delta$ 169.4, 153.2, 149.1, 135.5, 132.5, 127.3, 125.8, 125.0, 123.0, 119.4, 115.4, 114.8, 84.3, 82.3, 76.9, 57.9, 52.8, 27.9, 20.6; HRMS (ESI-TOF) $m/z$ $[M + H]^+$ calcd for $C_{20}H_{22}O_6N$ 372.1442, found 372.1438.

*Methyl 4-Acetoxy-4-(thiophen-2-yl)but-2-ynoate (**1o**).* Following general procedures P-2a and 2b, **1o** (147 mg, 66%) was obtained from thiophene-2-carbaldehyde as a light yellow liquid. $R_f$ = 0.58 (9:1 hexane/EtOAc); IR (neat) $\nu_{max}$ 3119, 2926, 2247, 1751, 1725, 1514, 1268, 1215, 1016, 970 $cm^{-1}$; $^1H$ NMR (300 MHz, $CDCl_3$) $\delta$ 7.38 (dd, $J$ = 1.2, 5.2 Hz, 1H), 7.27−7.25 (m, 1H), 7.00 (dd, $J$ = 3.7, 5.2 Hz, 1H), 6.77 (s, 1H), 3.81 (s, 3H), 2.12 (s, 3H); $^{13}C$ NMR (75 MHz, $CDCl_3$) $\delta$ 169.2, 153.1, 137.1, 128.3, 126.8, 82.1, 77.2, 59.8, 52.9, 20.6; HRMS (ESI-TOF) $m/z$ $[M + Na]^+$ calcd for $C_{11}H_{10}O_4SNa$ 261.0201, found 261.0194.

*Methyl 4-Acetoxy-6-phenylhex-2-ynoate (**1p**).* Following general procedures P-2a and 2b, **1p** (146 mg, 76%) was obtained from 3-phenylpropanal as a colorless liquid. $R_f$ = 0.50 (9:1 hexane/EtOAc); IR (neat) $\nu_{max}$ 2924, 2856, 2245, 1742, 1731, 1492, 1220, 1033, 772, 685 $cm^{-1}$; $^1H$ NMR (300 MHz, $CDCl_3$) $\delta$ 7.32−7.27 (m, 2H), 7.23−7.17 (m, 3H), 6.42 (t, $J$ = 6.5 Hz, 1H), 3.8 (s, 3H), 2.78 (t, $J$ = 7.8 Hz, 2H), 2.20−2.12 (m, 2H), 2.09 (s, 3H); $^{13}C$ NMR (75 MHz, $CDCl_3$) $\delta$ 169.5, 153.3, 139.9, 128.5, 128.3, 126.3, 84.1, 76.8, 62.5, 52.8, 35.3, 31.0, 20.6; HRMS (ESI-TOF) $m/z$ $[M + Na]^+$ calcd for $C_{15}H_{16}O_4Na$ 283.0941, found 283.0934.

*(6R)-Ethyl 4-Acetoxy-6-(tert-butyldimethylsilyloxy)-8-phenyloct-2-ynoate (**1q**).*[26] Following general procedures P-2a and 2b, **1p** (222 mg, 71%) was obtained as an inseparable diastereomeric mixture (dr = 7:3, determined by $^1H$ NMR and HPLC analysis) from (*R*)-3-(*tert*-butyldimethylsilyloxy)-5-phenylpentanal. $R_f$ = 0.60 (9:1 hexane/EtOAc); $[\alpha]_D^{28}$ −8.5 (*c* 0.6); IR (neat) $\nu_{max}$ 2929, 2856, 2243, 1751, 1717, 1369, 1255, 1022, 836 $cm^{-1}$; $^1H$ NMR (300 MHz, $CDCl_3$) $\delta$ 7.33−7.29 (m, 2H), 7.23−7.18 (m, 3H), 5.62 (dd, $J$ = 6.0, 8.7 Hz, 1H), 4.27 (q, $J$ = 7.2 Hz, 2H), 4.00−3.95 (m, 1H), 2.72−2.62 (m, 2H), 2.11 (s, 3H), 2.09−2.02 (m, 2H), 1.89−1.82 (m, 2H), 1.34 (t, $J$ = 7.2 Hz, 3H), 0.94 (s, 9H), 0.12 (d, $J$ = 13.3 Hz, 6H); $^{13}C$ NMR (75 MHz, $CDCl_3$) $\delta$ 169.3, 152.9, 141.8, 128.3, 128.2, 125.8, 83.9, 68.0, 67.1, 62.1, 40.7, 39.1, 30.9, 25.8, 20.7, 17.9, 13.9, −4.4; HRMS (ESI-TOF) $m/z$ $[M + Na]^+$ calcd for $C_{24}H_{36}O_5SiNa$ 455.2234, found 455.2230.

*Methyl 4-Acetoxy-6-(tert-butyldiphenylsilyloxy)hex-2-ynoate (**1r**).* Following general procedures P-2a and 2b, **1r** (246 mg, 72%) was obtained from 3-(*tert*-butyldiphenylsilyloxy)propanal as a colorless liquid. $R_f$ = 0.70 (9:1 hexane/EtOAc); IR (neat) $\nu_{max}$ 2957, 2929, 2856, 2376, 1750, 1721, 1431, 1258, 1221, 1108, 741 $cm^{-1}$; $^1H$ NMR (300 MHz, $CDCl_3$) $\delta$ 7.70−7.59 (m, 4H), 7.48−7.34 (m, 6H), 5.72 (t, $J$ = 6.8 Hz, 1H), 3.83−3.69 (m, 5H), 2.13−2.03 (m, 5H), 1.04 (s, 9H); $^{13}C$ NMR (75 MHz, $CDCl_3$) $\delta$ 169.4, 153.3, 135.5, 133.2, 129.7, 127.7, 84.5, 60.3, 58.9, 52.7, 36.7, 26.7, 20.6, 19.1; HRMS (ESI-TOF) $m/z$ $[M + Na]^+$ calcd for $C_{25}H_{30}O_5SiNa$ 461.1754, found 461.1762.

*Ethyl 4-(Pivaloyloxy)but-2-ynoate (**3ai**).* Following general procedure P-2e, **3ai** (201 mg, 95%) was obtained from **1a′** as a colorless liquid. $R_f$ = 0.65 (9:1 hexane/EtOAc); IR (neat) $\nu_{max}$ 2977, 2931, 2249, 1741, 1719, 1462, 1252, 1137, 772 $cm^{-1}$; $^1H$ NMR (300 MHz, $CDCl_3$) $\delta$ 4.78 (s, 2H), 4.25 (q, $J$ = 6.8 Hz, 2H), 1.32 (t, $J$ = 6.8 Hz, 3H), 1.23 (s, 9H); $^{13}C$ NMR (75 MHz, $CDCl_3$) $\delta$ 177.2, 152.7, 80.9, 77.7, 62.0, 51.2, 38.6, 26.9, 26.4, 13.8; HRMS (ESI-TOF) $m/z$ $[M + Na]^+$ calcd for $C_{11}H_{16}O_4Na$ 235.0948, found 235.0941.

*4-Ethoxy-4-oxobut-2-ynyl Benzoate (**3aii**).* Following general procedure P-2c, **3aii** (297 mg, 96%) was obtained from **1a′** as colorless liquid. $R_f$ = 0.76 (9:1 hexane/EtOAc); IR (neat) $\nu_{max}$ 2926, 2854, 2244, 1636, 1385, 1286, 1025, 708 $cm^{-1}$; $^1H$ NMR (300 MHz, $CDCl_3$) $\delta$ 8.08 (d, $J$ = 7.5 Hz, 2H), 7.60 (t, $J$ = 7.5 Hz, 1H), 7.47 (t, $J$ = 7.5 Hz, 2H), 5.05 (s, 2H), 4.25 (q, $J$ = 6.8 Hz, 2H), 1.31 (t, $J$ = 6.8 Hz, 3H); $^{13}C$ NMR (75 MHz, $CDCl_3$) $\delta$ 165.3, 152.7, 133.4, 130.4, 129.7, 128.7, 128.4, 80.7, 78.0, 62.2, 51.7, 13.8; HRMS (ESI-TOF) $m/z$ $[M + Na]^+$ calcd for $C_{13}H_{12}O_4Na$ 255.0627, found 255.0626.

*Ethyl 4-(Propionyloxy)but-2-ynoate (**3aiii**).* To a solution of the crude propargyl alcohol **1a′** (200 mg, 1.56 mmol) in anhydrous $CH_2Cl_2$ (20 mL) were added triethylamine (0.48 mL, 3.12 mmol), propionic anhydride (0.39 mL, 3.12 mmol), and DMAP (catalytic) under a nitrogen atmosphere at 0 °C. The resultant mixture was stirred for 1 h and then quenched with aq $NH_4Cl$ solution (15 mL).



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The organic layer was separated, and the aq layer was extracted with $CH_2Cl_2$ (2 × 25 mL). The combined organic layer was washed with brine (50 mL) and dried over $Na_2SO_4$. The crude residue obtained after evaporation under reduced pressure was purified by silica gel column chromatography to obtain propionate ester **3aiii** as a colorless liquid (270 mg, 94%). $R_f$ = 0.55 (9:1 hexane/EtOAc); IR (neat) $\nu_{max}$ 2923, 2856, 2241, 1756, 1724, 1434, 1219, 1062, 772 $cm^{-1}$; $^1H$ NMR (500 MHz, $CDCl_3$) $\delta$ 4.80 (s, 2H), 4.25 (q, $J$ = 7.2 Hz, 2H), 2.40 (q, $J$ = 7.6 Hz, 2H), 1.32 (t, $J$ = 7.2 Hz, 3H), 1.16 (t, $J$ = 7.6 Hz, 3H); $^{13}C$ NMR (75 MHz, $CDCl_3$) $\delta$ 173.2, 152.8, 80.9, 77.8, 62.2, 51.1, 27.1, 13.9, 8.8; HRMS (ESI-TOF) $m/z$ $[M + Na]^+$ calcd for $C_9H_{12}O_4Na$ 207.0628, found 207.0622.

*Ethyl 8-(4-Methoxybenzyloxy)-4-(pivaloyloxy)oct-2-ynoate (**3b**).* Following general procedures P-2a and 2e, **3b** (245 mg, 72%) was obtained from 5-(4-methoxybenzyloxy)pentanal as a pale yellow liquid. $R_f$ = 0.60 (9:1 hexane/EtOAc); IR (neat) $\nu_{max}$ 2934, 2857, 2243, 1717, 1613, 1250, 1143, 751 $cm^{-1}$; $^1H$ NMR (300 MHz, $CDCl_3$) $\delta$ 7.25 (d, $J$ = 7.5 Hz, 2H), 6.88 (d, $J$ = 8.3 Hz, 2H), 5.43 (t, $J$ = 6.0 Hz, 1H), 4.43 (s, 2H), 4.23 (q, $J$ = 6.8 Hz, 2H), 3.81 (s, 3H), 3.45 (t, $J$ = 6.0 Hz, 2H), 1.90−1.79 (m, 2H), 1.69−1.48 (m, 4H), 1.31 (t, $J$ = 6.0 Hz, 3H), 1.22 (s, 9H); $^{13}C$ NMR (75 MHz, $CDCl_3$) $\delta$ 171.1, 159.1, 130.4, 129.2, 113.7, 84.1, 76.6, 72.5, 69.4, 62.8, 62.1, 55.1, 38.7, 33.6, 29.6, 29.0, 26.9, 21.6, 13.9; HRMS (ESI-TOF) $m/z$ $[M + Na]^+$ calcd for $C_{23}H_{32}O_6Na$ 427.2091, found 427.2095.

*4-Methoxy-1-(naphthalen-1-yl)-4-oxobut-2-ynyl Benzoate (**3c**).* Following general procedures P-2a and 2c, **3c** (198 mg, 73%) was obtained from 1-naphthaldehyde as a pale yellow liquid. $R_f$ = 0.68 (9:1 hexane/EtOAc); IR (neat) $\nu_{max}$ 2993, 2922, 2852, 2241, 1764, 1717, 1434, 1242, 1062, 772 $cm^{-1}$; $^1H$ NMR (300 MHz, $CDCl_3$) $\delta$ 8.27 (d, $J$ = 8.3 Hz, 2H), 8.06 (d, $J$ = 7.5 Hz, 2H), 7.92 (dd, $J$ = 3.8, 8.3 Hz, 2H), 7.85 (d, $J$ = 6.8 Hz, 1H), 7.65−7.45 (m, 3H), 7.42 (t, $J$ = 7.5 Hz, 2H), 7.37 (s, 1H), 3.77 (s, 3H); $^{13}C$ NMR (75 MHz, $CDCl_3$) $\delta$ 165.0, 153.3, 133.9, 133.5, 130.5, 130.4, 130.3, 129.9, 128.9, 128.4, 127.1, 127.0, 126.2, 125.1, 123.4, 83.1, 78.5, 63.9, 52.8; HRMS (ESI-TOF) $m/z$ $[M + H]^+$ calcd for $C_{22}H_{17}O_4$ 345.1121, found 345.1130.

*Methyl 4-(Naphthalen-1-yl)-4-(pivaloyloxy)but-2-ynoate (**3d**).* Following the general procedures 2a and 2e, **3d** (210 mg, 73%) was obtained from 1-naphthaldehyde as a yellow liquid. $R_f$ = 0.56 (9:1 hexane/EtOAc); IR (neat) $\nu_{max}$ 2924, 2856, 2239, 1756, 1721, 1434, 1256, 1220, 1130, 1062, 773 $cm^{-1}$; $^1H$ NMR (500 MHz, $CDCl_3$) $\delta$ 8.12 (br d, $J$ = 8.4 Hz, 1H), 7.90 (br d, $J$ = 8.4 Hz, 2H), 7.75 (br d, $J$ = 7.0 Hz, 1H), 7.61−7.51 (m, 2H), 7.51−7.46 (m, 1H), 7.10 (s, 1H), 3.76 (s, 3H), 1.21 (s, 9H); $^{13}C$ NMR (125 MHz, $CDCl_3$) $\delta$ 176.9, 153.4, 133.9, 130.6, 130.3, 128.8, 126.8, 126.7, 126.1, 125.1, 123.4, 83.3, 78.2, 63.3, 52.8, 38.9, 26.9; HRMS (ESI-TOF) $m/z$ $[M + Na]^+$ calcd for $C_{20}H_{20}O_4Na$ 347.1253, found 347.1253.

*Methyl 4-(Acryloyloxy)-6-phenylhex-2-ynoate (**3e**).* Following the general procedures 2a and 2d, **3e** (170 mg, 70%) was obtained from 3-phenylpropanal as a light yellow liquid. $R_f$ = 0.65 (9:1 hexane/EtOAc); IR (neat) $\nu_{max}$ 3117, 2937, 2377, 2314, 1786, 1693, 1550, 1514, 1216, 772 $cm^{-1}$; $^1H$ NMR (500 MHz, $CDCl_3$) $\delta$ 7.32−7.28 (m, 2H), 7.23−7.17 (m, 3H), 6.46 (dd, $J$ = 1.2, 17.2 Hz, 1H), 6.17−6.09 (m, 1H), 5.91 (dd, $J$ = 1.2, 10.5 Hz, 1H), 5.53−5.48 (m, 1H), 3.79 (s, 3H), 2.81 (t, $J$ = 7.9 Hz, 2H), 2.27−2.15 (m, 2H); $^{13}C$ NMR (75 MHz, $CDCl_3$) $\delta$ 164.6, 153.3, 139.9, 132.2, 128.5, 128.3,127.4, 126.3, 84.0, 62.6, 52.6, 35.3, 31.0; HRMS (ESI-TOF) $m/z$ $[M + Na]^+$ calcd for $C_{16}H_{16}O_4Na$ 295.0940, found 295.0945.

*1-(3-Ethoxy-3-oxoprop-1-ynyl)cyclohexyl Acrylate (**3f**).* Following the general procedures 2a and 2d, **3f** (130 mg, 68%) was obtained from cyclohexanone as a colorless liquid. $R_f$ = 0.68 (9:1 hexane/EtOAc); IR (neat) $\nu_{max}$ 3120, 2929, 2379, 1752, 1693, 1551, 1513, 772 $cm^{-1}$; $^1H$ NMR (500 MHz, $CDCl_3$) $\delta$ 6.41 (dd, $J$ = 1.2, 17.4 Hz, 1H), 6.09 (dd, $J$ = 10.5, 17.4 Hz, 1H), 6.85 (dd, $J$ = 1.2, 10.5 Hz, 1H), 4.23 (q, $J$ = 7.2 Hz, 2H), 2.22−2.11 (m, 2H), 2.04 (m, 2H), 1.68−1.62 (m, 4H), 1.58−1.49 (m, 1H), 1.46−1.37 (m, 1H), 1.31 (t, $J$ = 7.2 Hz, 3H); $^{13}C$ NMR (75 MHz, $CDCl_3$) $\delta$ 164.0, 153.4, 131.0, 128.7, 86.4, 78.2, 74.2, 62.0, 36.2, 24.9, 22.1, 14.0; HRMS (ESI-TOF) $m/z$ $[M + Na]^+$ calcd for $C_{14}H_{18}O_4Na$ 273.1097, found 273.1086.

*1-(3-Ethoxy-3-oxopropanoyl)cyclohexyl Benzoate (**3g**).* Following the general procedures 2a and 2c, **3g** (180 mg, 72%) was obtained from cyclohexanone as a colorless liquid. $R_f$ = 0.52 (9:1 hexane/EtOAc); IR (neat) $\nu_{max}$ 2981, 2938, 2863, 2236, 1789, 1720, 1451, 1245, 1102, 710 $cm^{-1}$; $^1H$ NMR (300 MHz, $CDCl_3$) $\delta$ 8.21−8.13 (m, 1H), 8.06−7.99 (m, 2H), 7.48−7.40 (m, 2H), 4.2 (q, $J$ = 7.2 Hz, 2H), 2.34−2.07 (m, 4H), 1.77−1.63 (m, 4H), 1.61−1.38 (m, 2H), 1.3 (t, $J$ = 7.2 Hz, 3H); $^{13}C$ NMR (75 MHz, $CDCl_3$) $\delta$ 164.1, 153.3, 134.4, 132.9, 129.4, 128.2, 86.4, 78.4, 74.2, 61.8, 36.1, 24.7, 22.0, 13.8; HRMS (ESI-TOF) $m/z$ $[M + Na]^+$ calcd for $C_{18}H_{20}O_4Na$ 323.1253, found 323.1251.

*4-tert-Butoxy-4-oxobut-2-ynyl Benzoate (**5a**).* Following a procedure similar to that for **1a″**, **5a** (172 mg, 78%) was synthesized from prop-2-ynyl benzoate and Boc-anhydride (instead of ethylchloroformate) as a light yellow liquid. $R_f$ = 0.63 (9:1 hexane/EtOAc); IR (neat) $\nu_{max}$ 2981, 2251, 1729, 1711, 1514, 1261, 1158, 712 $cm^{-1}$; $^1H$ NMR (500 MHz, $CDCl_3$) $\delta$ 8.09−8.01 (m, 2H), 7.60−7.55 (m, 1H), 7.47−7.42 (m, 2H), 5.01 (s, 2H), 1.49 (s, 9H); $^{13}C$ NMR (75 MHz, $CDCl_3$) $\delta$ 165.6, 151.9, 133.6, 130.0, 129.9, 129.0, 84.1, 79.36, 78.5, 51.9, 28.0; HRMS (ESI-TOF) $m/z$ $[M + Na]^+$ calcd for $C_{15}H_{16}O_4Na$ 283.0940, found 283.0935.

*4-(Benzyloxy)-4-oxobut-2-ynyl Benzoate (**5b**).* Following a procedure similar to that for **1a″**, **5b** (160 mg, 82%) was synthesized from prop-2-ynyl benzoate and benzylchloroformate (instead of ethylchloroformate) as a colorless liquid. $R_f$ = 0.61 (9:1 hexane/EtOAc); IR (neat) $\nu_{max}$ 3036, 2956, 2246, 1755, 1718, 1240, 1069 $cm^{-1}$; $^1H$ NMR (500 MHz, $CDCl_3$) $\delta$ 8.12−7.99 (m, 2H), 7.59 (tt, $J$ = 1.4, 7.5 Hz 1H), 7.49−7.42 (m, 2H), 7.40−7.32 (m, 5H), 5.21 (s, 2H), 5.03 (s, 2H); $^{13}C$ NMR (100 MHz, $CDCl_3$) $\delta$ 165.5, 134.4, 133.5, 129.8, 128.6, 128.4, 81.5, 77.0, 67.8, 51.7; HRMS (ESI-TOF) $m/z$ $[M + Na]^+$ calcd for $C_{18}H_{14}O_4Na$ 317.0784, found 317.0776.

*4-Oxopent-2-ynyl Benzoate (**5c**).* Following a procedure similar to that for **1a″**, **5c** (150 mg, 90%) was synthesized from prop-2-ynyl benzoate and acetic anhydride (instead of ethylchloroformate) as a colorless liquid. IR (neat) $\nu_{max}$ 2938, 2237, 1716, 1608, 1276, 1113, 712 $cm^{-1}$; $R_f$ = 0.56 (9:1 hexane/EtOAc); $^1H$ NMR (500 MHz, $CDCl_3$) $\delta$ 8.16−8.11 (m, 2H), 7.64−7.58 (m, 1H), 7.51−7.44 (m, 2H), 5.07 (s, 2H), 2.37 (s, 3H); $^{13}C$ NMR (100 MHz, $CDCl_3$) $\delta$ 183.6, 165.5, 133.5, 130.0, 129.8, 128.9, 128.4, 85.4, 84.9, 51.8, 32.4; HRMS (ESI-TOF) $m/z$ $[M + Na]^+$ calcd for $C_{12}H_{10}O_3Na$ 225.0524, found 225.0515.

*Dimethyl 4-(Benzoyloxy)-4-phenylhepta-2,5-diynedioate (**7d**).* Skipped diyne **7d** was prepared according to the literature procedure[27] from methyl propiolate (0.28 mL, 3.13 mol), $Et_3N$ (0.2 mL, 1.43 mmol), and benzoyl chloride (0.16 mL, 1.42 mmol) as a dark yellow gel (392 mg, 70%). $R_f$ = 0.50 (9:1 hexane/EtOAc); IR (neat) $\nu_{max}$ 3202, 2989, 2853, 2246, 1808, 1719, 1614, 1449, 1284, 1168, 711 $cm^{-1}$; $^1H$ NMR (300 MHz, $CDCl_3$) $\delta$ 8.07−8.01 (m, 2H), 7.87−7.80 (m, 2H), 7.65−7.56 (m, 1H), 7.52−7.43 (m, 5H), 3.80 (s, 6H); $^{13}C$ NMR (75 MHz, $CDCl_3$) $\delta$ 163.4, 152.9, 135.8, 133.8, 130.0, 129.9, 128.9, 128.7, 128.5, 126.4, 80.5, 78.9, 67.8, 53.0; HRMS (ESI-TOF) $m/z$ $[M + Na]^+$ calcd for $C_{22}H_{16}O_6Na$ 399.0839, found 399.0848.

*Ethyl 3-(2-Acetoxy-7-oxabicyclo[4.1.0]heptan-2-yl)propiolate (**7ei**).* Following the literature procedure[28] with minor modifications (see P-2a) and P-2b, **7ei** (173 mg, 64%) was obtained from 7-oxabicyclo[4.1.0]heptan-2-one as a colorless liquid. $R_f$ = 0.62 (9:1 hexane/EtOAc); IR (neat) $\nu_{max}$ 2945, 2237, 1748, 1717, 1441, 1369, 1229, 1021, 751 $cm^{-1}$; $^1H$ NMR (500 MHz, $CDCl_3$) $\delta$ 4.25 (q, $J$ = 7.2 Hz, 2H), 3.77 (d, $J$ = 3.8 Hz, 1H), 3.33 (td, $J$ = 1.1, 3.8 Hz, 1H), 2.11 (s, 3H), 2.01−1.94 (m, 1H), 1.93−1.90 (m, 2H), 1.90−1.84 (m, 1H), 1.61−1.54 (m, 2H), 1.32 (t, $J$ = 7.2 Hz, 3H); $^{13}C$ NMR (125 MHz, $CDCl_3$) $\delta$ 169.1, 153.0, 83.8, 78.6, 72.2, 62.2, 54.7, 54.6, 31.5, 22.4, 21.1, 16.6, 13.9; HRMS (ESI-TOF) $m/z$ $[M + Na]^+$ calcd for $C_{13}H_{16}O_5Na$ 275.0889, found 275.0894.

*Ethyl 4-Acetoxy-4-(3-phenyloxiran-2-yl)but-2-ynoate (**7eii**).* Following the literature procedure[28] with minor modifications (see P-2a) and P-2b, **7eii** (196 mg, 66%) was obtained from 3-phenyloxirane-2-carbaldehyde as a pale yellow liquid. $R_f$ = 0.58 (9:1 hexane/EtOAc); IR (neat) $\nu_{max}$ 2928, 2248, 1755, 1717, 1370, 1256, 1216, 1022, 751 $cm^{-1}$; $^1H$ NMR (300 MHz, $CDCl_3$) $\delta$ 7.39−7.33 (m, 3H), 7.31−7.27 (m, 2H), 5.71 (d, $J$ = 3.7 Hz, 1H), 4.26 (q, $J$ = 7.2 Hz, 2H),



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4.02 (d, $J$ = 1.8 Hz, 1H), 3.34 (dd, $J$ = 1.8, 3.7 Hz, 1H), 2.16 (s, 3H), 1.32 (t, $J$ = 7.2 Hz, 3H); $^{13}$C NMR (75 MHz, $CDCl_3$) $\delta$ 169.2, 152.5, 135.2, 128.7, 128.6, 125.8, 79.3, 78.4, 63.5, 62.3, 60.1, 56.3, 20.6, 13.9; HRMS (ESI-TOF) $m/z$ [M + Na]$^+$ calcd for $C_{16}H_{16}O_5Na$ 311.0891, found 311.0898.

*(R)-Ethyl 4-Acetoxy-5-phenylpent-2-ynoate (**10**).* Chiral acetate **10** was obtained by following the literature procedure[29] and P-2b as colorless oil from 2-phenylacetaldehyde (2.8 g, 56% yield) in 70% ee as determined by HPLC analysis. Retention time $t_{major}$ = 5.7 min, and $t_{minor}$ = 6.5 min; $[\alpha]_D^{28}$ +51.2 ($c$ 0.73, $CHCl_3$); $R_f$ = 0.46 (9:1 hexane/EtOAc); IR (neat) $\nu_{max}$ 2985, 2938, 2246, 1750, 1716, 1370, 1222, 1022, 702 cm$^{-1}$; $^1$H NMR (500 MHz, $CDCl_3$) $\delta$ 7.34−7.29 (m, 2H), 7.29−7.23 (m, 3H), 5.62 (t, $J$ = 6.9 Hz, 1H), 4.23 (q, $J$ = 7.2 Hz, 2H), 3.12 (d, $J$ = 6.9 Hz, 2H), 2.05 (s, 3H), 1.30 (t, $J$ = 7.2 Hz, 3H); $^{13}$C NMR (125 MHz, $CDCl_3$) $\delta$ 169.4, 152.9, 134.9, 129.5, 128.5, 127.2, 83.4, 77.4, 63.6, 62.2, 40.2, 20.7,13.9; HRMS (ESI-TOF) $m/z$ [M + Na]$^+$ calcd for $C_{15}H_{16}O_4Na$ 283.0944, found 283.0941.

*Methyl 3-((5R)-1-Acetoxy-2-methyl-5-(prop-1-en-2-yl)cyclohex-2-enyl)propiolate (**12a**).* Following the literature procedure with minor modifications to the use of ylide (see P-2a),[30] (*S*)-(+)-carvone gave two separable diastereomeric propargylic alcohols. Only the major isomer was subjected to acetylation following procedure P-2b to obtain **12a** (150 mg, 56%) as a colorless liquid. $R_f$ = 0.64 (9:1 hexane/EtOAc); $[\alpha]_D^{28}$ +72.6 ($c$ 1.2, $CHCl_3$); IR (neat) $\nu_{max}$ 2954, 2925, 2234, 1748, 1719, 1435, 1223, 1017, 772 cm$^{-1}$; $^1$H NMR (300 MHz, $CDCl_3$) $\delta$ 5.66 (brd, $J$ = 5.3 Hz, 1H), 4.73 (brd, $J$ = 9.8 Hz, 2H), 3.76 (s, 3H), 2.87 (dt, $J$ = 2.3, 12.1 Hz, 1H), 2.03−1.90 (m, 1H), 2.24−2.11 (m, 1H), 2.07 (s, 3H), 2.03−1.90 (m, 1H), 1.88−1.81 (m, 1H), 1.79 (s, 3H), 1.72 (s, 3H); $^{13}$C NMR (125 MHz, $CDCl_3$) $\delta$ 168.8, 153.6, 147.2, 131.7, 127.6, 109.7, 85.7, 77.4, 76.1, 52.6, 38.6, 38.1, 30.4, 21.5, 20.5, 17.5; HRMS (ESI-TOF) $m/z$ [M + Na]$^+$ calcd for $C_{16}H_{20}O_4Na$ 299.1253, found 299.1254.

*Methyl 3-((2S,5R)-1-Acetoxy-2-isopropyl-5-methylcyclohexyl)-propiolate (**12b**).* Following the literature procedure with minor modification to the use of the base (see P-2a),[31] (+)-menthone gave two separable diasetreomeric propargylic alcohols. Only the major isomer was subjected to acetylation following procedure P-2b to obtain **12b** (150 mg, 56%) as a colorless liquid. $R_f$ = 0.56 (9:1 hexane/EtOAc); $[\alpha]_D^{28}$ −11.3 ($c$ 1.7, $CHCl_3$); IR (neat) $\nu_{max}$ 2957, 2931, 2875, 2234, 1748, 1718, 1436, 1229, 1016, 751 cm$^{-1}$; $^1$H NMR (300 MHz, $CDCl_3$) $\delta$ 3.76 (s, 3H), 2.82−2.60 (m, 1H), 2.04 (s, 3H), 1.83−1.67 (m, 2H), 1.67−1.34 (m, 4H), 1.31−1.14 (m, 2H), 1.01−0.84 (m, 9H); $^{13}$C NMR (125 MHz, $CDCl_3$) $\delta$ 168.9, 153.7, 85.7, 80.4, 78.5, 52.6, 51.3, 45.1, 34.2, 29.9, 27.0, 24.1, 23.7, 21.9, 21.5, 18.6; HRMS (ESI-TOF) $m/z$ [M + Na]$^+$ calcd for $C_{16}H_{24}O_4Na$ 303.1566, found 303.1567.

*(2R,5S)-1-(3-Ethoxy-3-oxoprop-1-ynyl)-2-isopropyl-5-methylcyclohexyl Benzoate (**12c**).* The major isomer obtained by the reaction of (+)-menthone with Li-ylide (see the first step of the procedure described for **12b**) was subjected to benzoylation following P-2c to obtain **12c** (160 mg, 60%) as a thick yellow liquid. $R_f$ = 0.64 (9:1 hexane/EtOAc); $[\alpha]_D^{28}$ −16.3 ($c$ 1.0, $CHCl_3$); IR (neat) $\nu_{max}$ 2931, 2858, 2245, 1738, 1717, 1452, 1314, 1027, 705 cm$^{-1}$; $^1$H NMR (500 MHz, $CDCl_3$) $\delta$ 8.02−7.98 (m, 2H), 7.59−7.53 (m, 1H), 7.47−7.41 (m, 2H), 4.23 (q, $J$ = 7.2 Hz, 2H), 2.96−2.90 (m, 1H), 2.29 (qd, $J$ = 2.9, 7.2 Hz, 1H), 1.93−1.84 (m, 1H), 1.83−1.73 (m, 3H), 1.57−1.48 (m, 1H), 1.37−1.27 (m, 5H), 1.07 (d, $J$ = 7.0 Hz, 3H), 1.01 (d, $J$ = 6.9 Hz, 3H), 0.94 (d, $J$ = 6.6 Hz, 3H); $^{13}$C NMR (125 MHz, $CDCl_3$) $\delta$ 164.3, 153.3, 132.9, 130.7, 129.5, 128.3, 85.1, 80.9, 79.1, 62.0, 51.7, 45.2, 34.3, 30.0, 26.9, 23.9, 21.6, 18.5, 14.0; HRMS (ESI-TOF) $m/z$ [M + Na]$^+$ calcd for $C_{22}H_{28}O_4Na$ 379.1879, found 379.1887.

*Ethyl 3-((8S,9S,10R,13R,14S,17R)-3-Acetoxy-10,13-dimethyl-17-((R)-6-methylheptan-2-yl)-2,3,4,7,8,9,10,11,12,13,14,15,16,17-tetradecahydro-1H-cyclopenta[a]phenanthren-3-yl)propiolate (**12d**).* The major isomer obtained by the reaction of cholesterone[32] with Li-ylide (see the first step of the procedure described for **12a**) was subjected to acetylation by following P-2b to obtain **12d** (230 mg, 60%) as a pale yellow gel. $R_f$ = 0.68 (9:1 hexane/EtOAc); $[\alpha]_D^{28}$ −30.4 ($c$ 0.7, $CHCl_3$); IR (neat) $\nu_{max}$ 2934, 2869, 2237, 1748, 1716, 1466, 1368, 1228, 1021, 752 cm$^{-1}$; $^1$H NMR (500 MHz, $CDCl_3$) $\delta$ 5.50−5.46 (m, 1H), 4.21 (q, $J$ = 7.2 Hz, 2H), 2.77 (dd, $J$ = 2.7, 13.4 Hz, 1H), 2.61−2.55 (m, 1H), 2.38−2.31 (m, 1H), 2.05 (s, 3H), 2.04−1.95 (m, 3H), 1.90−1.79 (m, 4H), 1.64−1.57 (m, 3H), 1.55−1.40 (m, 4H), 1.39−1.33 (m, 1H), 1.30 (t, $J$ = 7.2 Hz, 3H), 1.21−1.03 (m, 10H), 1.02 (s, 3H), 0.92(d, $J$ = 6.6 Hz, 3H), 0.87 (dd, $J$ = 2.3, 6.6 Hz, 6H), 0.68 (s, 3H); $^{13}$C NMR (125 MHz, $CDCl_3$) $\delta$ 169.0, 153.4, 137.1, 125.0, 85.6, 78.8, 76.0, 62.0,56.5, 56.1, 49.7, 42.8, 42.3, 39.6, 39.5, 36.4, 36.1, 35.9, 35.8, 32.5, 31.9, 31.7, 28.2, 28.0, 24.2, 23.8, 22.8, 22.5, 21.7, 20.9, 19.1, 18.7, 14.0, 11.8; HRMS (ESI-TOF) $m/z$ [M + Na]$^+$ calcd for $C_{34}H_{52}O_4Na$ 547.3758, found 547.3739.

*Oxiranyl Derivative of Ethyl 3-((8S,9S,10R,13R,14S,17R)-3-Acetoxy-10,13-dimethyl-17-((R)-6-methylheptan-2-yl)-2,3,4,7,8,9,10,11,12,13,14,15,16,17-tetradecahydro-1H-cyclopenta[a]phenanthren-3-yl)propiolate (**12e**).* Following general procedure P-2a, cholesterone was converted to column separable diastereomeric $\gamma$-hydroxy-$\alpha,\beta$-alkynoates. The major isomer then followed an epoxidation reaction with *m*CPBA to give two easily separable diastereomeric oxiranyls. Finally, acetylation of the major oxiranyl was carried out following procedure P-2b to give hydration precursor **12e** (230 mg, 42%) as a colorless liquid. $R_f$ = 0.58 (9:1 hexane/EtOAc); $[\alpha]_D^{28}$ −20.3 ($c$ 1.7, $CHCl_3$); IR (neat) $\nu_{max}$ 2951, 2870, 2238, 1751, 1719, 1459, 1368, 1226, 1019, 750 cm$^{-1}$; $^1$H NMR (500 MHz, $CDCl_3$) $\delta$ 4.25 (q, $J$ = 7.2 Hz, 2H), 3.74 (s, 1H), 2.62 (dd, $J$ = 3.7, 15.3 Hz, 1H), 2.09 (s, 3H), 2.08−2.00 (m, 2H), 2.00−1.93 (m, 2H), 1.92−1.80 (m, 2H), 1.70−1.48 (m, 8H), 1.36−1.29 (m, 6H), 1.30−1.22 (m, 4H), 1.20−1.07 (m, 5H), 1.04 (s, 3H), 1.03−0.97 (m, 1H), 0.93 (d, $J$ = 6.4 Hz, 3H), 0.89−0.85 (m, 6H), 0.70 (s, 3H); $^{13}$C NMR (125 MHz, $CDCl_3$) $\delta$ 168.9, 152.8, 83.2, 78.9, 70.2, 68.7, 62.4, 62.0, 56.2, 55.9, 48.5, 46.4, 42.5, 39.4, 39.1, 38.0, 36.0, 35.6, 34.7, 29.0, 28.9, 27.9, 27.9, 24.0, 23.7, 22.7, 22.5, 21.4, 20.8, 18.6, 18.2, 14.1, 13.9, 11.8; HRMS (ESI-TOF) $m/z$ [M + Na]$^+$ calcd for $C_{34}H_{52}O_5Na$ 563.3708, found 563.3701.

*Representative Procedure for Gold-Catalyzed Hydration of Acetylinic Ester (P-3).* To a stirred solution of alkynoate (0.5 mmol) in dioxane (1.5 mL) were added $Ph_3PAuCl$ (5 mg, 0.01 mmol) and AgOTf (2.6 mg, 0.01 mmol) at ambient temperature. Distilled water (13.5 $\mu$L, 1.5 mmol) was then added to the above reaction mixture at the same temperature. The resulting reaction mixture was stirred for the times shown in the respective tables. After complete consumption of starting material (monitored by TLC), the solvent was evaporated under reduced pressure, and the crude product was purified over silica gel column chromatography on silica gel to obtain the hydration product along with a trace amount of the corresponding enolic compound.

*Ethyl 4-Acetoxy-3-oxobutanoate (**2a**).* General procedure P-3 was followed using **1a**, and the reaction mixture was stirred at room temperature for 1 h. Purification by column chromatography afforded **2a** (90 mg, 96%) as a colorless liquid. $R_f$ = 0.40 (9:1 hexane/EtOAc); IR (neat) $\nu_{max}$ 2959, 1747, 1651, 1375, 1232, 1034, 845 cm$^{-1}$; $^1$H NMR (300 MHz, $CDCl_3$) $\delta$ 4.79 (s, 2H), 4.21 (q, $J$ = 7.2 Hz, 2H), 3.50 (s, 2H), 2.17 (s, 3H), 1.29 (t, $J$ = 7.2 Hz, 3H); $^{13}$C NMR (75 MHz, $CDCl_3$) $\delta$ 196.5, 169.9, 166.2, 67.7, 61.6, 46.0. 20.2, 13.9; HRMS (EI-TOF) $m/z$ [M$^+$] calcd for $C_8H_{12}O_5$ 188.0680, found 188.0671.

*Ethyl 4-Acetoxy-3-oxo-4-phenylbutanoate (**2b**).* General procedure P-3 was followed using **1b**, and the reaction mixture was stirred at room temperature for 1 h. Purification by column chromatography afforded **2b** (127 mg, 95%) as a light yellow liquid. $R_f$ = 0.44 (9:1 hexane/EtOAc); IR (neat) $\nu_{max}$ 3020,2956, 2854, 1742, 1710, 1368, 1215, 929, 742 cm$^{-1}$; $^1$H NMR (500 MHz, $CDCl_3$) $\delta$ 7.41 (s, 5H), 6.17 (s, 1H), 4.12 (q, $J$ = 7.2 Hz, 2H), 3.48 (d, $J$ = 15.4 Hz, 1H), 3.42 (d, $J$ = 15.4 Hz, 1H), 2.18 (s, 3H), 1.20 (t, $J$ = 7.2 Hz, 3H); $^{13}$C NMR (125 MHz, $CDCl_3$) $\delta$ 196.4, 169.8, 166.0, 132.4, 129.6, 129.1, 128.3, 127.5, 80.0, 61.5, 45.9, 20.6, 13.9; HRMS (ESI-TOF) $m/z$ [M + Na]$^+$ calcd for $C_{14}H_{16}O_5Na$ 287.0889, found 287.0884.

*Methyl 4-Acetoxy-4-(4-methoxyphenyl)-3-oxobutanoate (**2c**).* General procedure P-3 was followed using **1c**, and the reaction mixture was stirred at room temperature for 1 h. Purification by column chromatography afforded **2c** (130 mg, 93%) as a yellow liquid.



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$R_f$ = 0.65 (9:1 hexane/EtOAc); IR (neat) $\nu_{max}$ 2956, 2851, 1746, 1721, 1514, 1229, 1030, 833 cm$^{-1}$; $^1$H NMR (300 MHz, $CDCl_3$) $\delta$ 7.32 (d, $J$ = 8.7 Hz, 2H), 6.93 (d, $J$ = 8.7 Hz, 2H), 6.10 (s, 1H), 3.82 (s, 3H), 3.67 (s, 3H), 3.49 (d, $J$ = 15.4 Hz, 1H), 3.42 (d, $J$ = 15.6 Hz, 1H), 2.17 (s, 3H); $^{13}$C NMR (75 MHz, $CDCl_3$) $\delta$ 196.4, 170.1, 166.5, 129.9, 129.1, 124.1, 114.5, 79.6, 55.3, 52.4, 45.6, 20.6; HRMS (ESI-TOF) $m/z$ [M + Na]$^+$ calcd for $C_{14}H_{16}O_6Na$ 303.0839, found 303.0843.

*Methyl 4-Acetoxy-4-(2-bromophenyl)-3-oxobutanoate (**2d**).* General procedure P-3 was followed using **1d**, and the reaction mixture was stirred at room temperature for 1.5 h. Purification by column chromatography afforded **2d** (146 mg, 89%) as a yellow liquid. $R_f$ = 0.42 (9:1 hexane/EtOAc); IR (neat) $\nu_{max}$ 3023, 2955, 2926, 1731, 1220, 1043, 751 cm$^{-1}$; $^1$H NMR (500 MHz, $CDCl_3$) $\delta$ 7.68−7.61 (m, 1H), 7.43−7.21 (m, 3H), 6.61 (s, 1H), 3.68 (s, 3H), 3.62 (d, $J$ = 15.9 Hz, 1H), 3.51 (d, $J$ = 15.9 Hz, 1H), 2.19 (s, 3H); $^{13}$C NMR (125 MHz, $CDCl_3$) $\delta$ 195.7, 169.5, 166.2, 133.3, 132.3, 131.0, 130.1, 128.0, 124.1, 78.6, 52.3, 45.9, 20.3; HRMS (ESI-TOF) $m/z$ [M + Na]$^+$ calcd for $C_{13}H_{13}O_5BrNa$ 350.9838, found 350.9840.

*Methyl 4-Acetoxy-4-(4-fluorophenyl)-3-oxobutanoate (**2e**).* General procedure P-3 was followed using **1e**, and the reaction mixture was stirred at room temperature for 1 h. Purification by column chromatography afforded **2e** (123 mg, 92%) as a pale yellow liquid. $R_f$ = 0.48 (9:1 hexane/EtOAc); IR (neat) $\nu_{max}$ 2957, 2853, 1739, 1607, 1327, 1225, 1039, 836 cm$^{-1}$; $^1$H NMR (500 MHz, $CDCl_3$) $\delta$ 7.43−7.37 (m, 2H), 7.13−7.06 (m, 2H), 6.12 (s, 1H), 3.67 (s, 3H), 3.54 (d, $J$ = 15.6 Hz, 1H), 3.50 (d, $J$ = 15.6 Hz, 1H), 2.17 (s, 3H); $^{13}$C NMR (75 MHz, $CDCl_3$) $\delta$ 196.3, 169.8, 164.9, 161.7, 130.2, 130.2, 130.1, 116.2, 115.9, 79.1, 52.3, 45.5, 20.4; HRMS (ESI-TOF) $m/z$ [M + Na]$^+$ calcd for $C_{13}H_{13}O_5FNa$ 291.0639, found 291.0641.

*Methyl 4-Acetoxy-4-(3-nitrophenyl)-3-oxopentanoate (**2f**).* General procedure P-3 was followed using **1f**, and the reaction mixture was stirred at room temperature for 2 h. Purification by column chromatography afforded **2f** (145 mg, 94%) as a pale yellow liquid. $R_f$ = 0.30 (9:1 hexane/EtOAc); IR (neat) $\nu_{max}$ 3114, 2956, 1732, 1716, 1435, 1267, 1014, 857 cm$^{-1}$; $^1$H NMR (300 MHz, $CDCl_3$) $\delta$ 8.29−8.21 (m, 2H), 7.76−7.66 (m, 2H), 3.58 (s, 3H), 3.40 (d, $J$ = 15.5 Hz, 1H), 3.32 (d, $J$ = 15.5 Hz, 1H), 2.29 (s, 3H), 1.89 (s, 3H); $^{13}$C NMR (75 MHz, $CDCl_3$) $\delta$ 197.0, 169.7, 166.4, 147.7, 144.3, 126.2, 123.8, 123.5, 86.9, 52.3, 43.0, 23.1, 21.1; HRMS (ESI-TOF) $m/z$ [M + Na]$^+$ calcd for $C_{14}H_{15}O_7NNa$ 332.0740, found 332.0736.

*Methyl 4-Acetoxy-3-oxo-4-(3,4,5-trimethoxyphenyl)butanoate (**2g**).* General procedure P-3 was followed using **1g**, and the reaction mixture was stirred at room temperature for 1.5 h. Purification by column chromatography afforded **2g** (153 mg, 90%) as a pale yellow liquid. $R_f$ = 0.54 (9:1 hexane/EtOAc); IR (neat) $\nu_{max}$ 2960, 2376, 2315, 1751, 1714, 1513, 1217, 1129, 772 cm$^{-1}$; $^1$H NMR (300 MHz, $CDCl_3$) $\delta$ 6.58 (s, 2H), 6.06 (s, 1H), 3.85 (s, 6H), 3.83 (s, 3H), 3.67 (s, 3H), 3.51 (d, $J$ = 15.5 Hz, 1H), 3.42 (d, $J$ = 15.5 Hz, 1H), 2.17 (s, 3H); $^{13}$C NMR (75 MHz, $CDCl_3$) $\delta$ 196.0, 169.8, 166.4, 153.5, 138.7, 105.3, 79.8, 60.6, 56.0, 52.3, 45.4, 20.4; HRMS (ESI-TOF) $m/z$ [M + Na]$^+$ calcd for $C_{16}H_{20}O_8Na$ 363.1050, found 363.1055.

*Methyl 4-Acetoxy-4-(4-bromobenzo[d][1,3]dioxol-5-yl)-3-oxobutanoate (**2h**).* General procedure P-3 was followed using **1h**, and the reaction mixture was stirred at room temperature for 1 h. Purification by column chromatography afforded **2h** as a thick yellow liquid (153 mg, 88% yield); $R_f$ = 0.40 (9:1 hexane/EtOAc); IR (neat) $\nu_{max}$ 2992, 2851, 2377, 2312, 1751, 1729, 1513, 1036, 772 cm$^{-1}$; $^1$H NMR (300 MHz, $CDCl_3$) $\delta$ 7.06 (s, 1H), 6.83 (s, 1H), 6.50 (s, 1H), 6.02 (s, 2H), 3.7 (s, 3H), 3.60 (d, $J$ = 16.6 Hz, 1H), 3.49 (d, $J$ = 15.9 Hz, 1H), 2.17 (s, 3H); $^{13}$C NMR (125 MHz, $CDCl_3$) $\delta$ 195.8, 169.7, 166.3, 149.5, 148.1, 125.1, 115.4, 113.0, 109.2, 102.3, 78.6, 52.4, 45.9, 20.5; HRMS (ESI-TOF) $m/z$ [M + Na]$^+$ calcd for $C_{14}H_{13}O_7BrNa$ 394.9736, found 394.9745.

*Methyl 4-Acetoxy-4-(2-(allyloxy)phenyl)-3-oxobutanoate (**2i**).* General procedure P-3 was followed using **1i**, and the reaction mixture was stirred at room temperature for 1.5 h. Purification by column chromatography afforded **2i** (137 mg, 90%) as a colorless liquid. $R_f$ = 0.43 (9:1 hexane/EtOAc); IR (neat) $\nu_{max}$ 2923, 2851, 1734, 1600, 1492, 1371, 1220, 927, 772 cm$^{-1}$; $^1$H NMR (300 MHz, $CDCl_3$) $\delta$ 7.35 (d, $J$ = 7.5 Hz, 2H), 7.03−6.89 (m, 2H), 6.55 (s, 1H), 6.14−5.96 (m, 1H), 5.48−5.25 (m, 2H), 4.68−4.52 (m, 2H), 3.65 (s, 3H), 3.57 (d, $J$ = 15.9 Hz, 1H), 3.50 (d, $J$ = 15.9 Hz, 1H), 2.16 (s, 3H); $^{13}$C NMR (125 MHz, $CDCl_3$) $\delta$ 196.7, 169.9, 166.8, 155.8, 132.5, 130.8, 130.1, 121.8, 121.2, 118.0, 112.3, 74.8, 69.3, 52.2, 45.6, 20.6; HRMS (ESI-TOF) $m/z$ [M + Na]$^+$ calcd for $C_{16}H_{18}O_6Na$ 329.0995, found 329.0999.

*Methyl 4-Acetoxy-3-oxo-4-(2-(prop-2-ynyloxy)phenyl)butanoate (**2j**).* General procedure P-3 was followed using **1j**, and the reaction mixture was stirred at room temperature for 1 h. Purification by column chromatography afforded **2j** (130 mg, 86%) as a colorless liquid. $R_f$ = 0.40 (9:1 hexane/EtOAc); IR (neat) $\nu_{max}$ 3276, 2923, 2853, 1738, 1731, 1492, 1373, 1221, 1020, 772 cm$^{-1}$; $^1$H NMR (300 MHz, $CDCl_3$) $\delta$ 7.34−7.27 (m, 2H), 7.11−7.00 (m, 2H), 6.51 (s, 1H), 4.77 (d, $J$ = 2.3 Hz, 2H), 3.66 (s, 3H), 3.60 (d, $J$ = 15.9 Hz, 1H), 3.53 (d, $J$ = 15.9 Hz, 1H), 2.53 (t, $J$ = 2.3 Hz, 1H), 2.16 (s, 3H); $^{13}$C NMR (75 MHz, $CDCl_3$) $\delta$ 196.7, 169.9, 166.8, 130.8, 130.2, 122.2, 122.0, 112.7, 77.8, 76.1, 74.7, 56.2, 52.2, 45.6, 20.6; HRMS (ESI-TOF) $m/z$ [M + Na]$^+$ calcd for $C_{16}H_{16}O_6Na$ 327.0839, found 327.0838.

*Methyl 4-Acetoxy-4-(2-(tert-butyldimethylsilyloxy)phenyl)-3-oxobutanoate (**2k**).* General procedure P-3 was followed using **1k**, and the reaction mixture was stirred at room temperature for 1.5 h. Purification by column chromatography afforded **2k** (174 mg, 92%) as a colorless liquid. $R_f$ = 0.60 (9:1 hexane/EtOAc); IR (neat) $\nu_{max}$ 2956, 2924, 1728, 1485, 1373, 1216, 1020, 751 cm$^{-1}$; $^1$H NMR (300 MHz, $CDCl_3$) $\delta$ 7.32−7.22 (m, 2H), 7.04−6.96 (m, 1H), 6.92−6.81 (m, 1H), 6.09 (s, 1H), 3.68 (s, 3H), 3.50 (d, $J$ = 15.5 Hz, 1H), 3.42 (d, $J$ = 15.5 Hz, 1H), 2.19 (s, 3H), 0.98 (s, 9H), 0.20 (s, 6H); $^{13}$C NMR (75 MHz, $CDCl_3$) $\delta$ 196.0, 169.8, 166.3, 156.1, 133.6, 130.1, 121.1, 121.0, 119.8, 79.7, 52.3, 45.4, 25.5, 20.4, −4.6; HRMS (ESI-TOF) $m/z$ [M + Na]$^+$ calcd for $C_{19}H_{28}O_6SiNa$ 403.1547, found 403.1543.

*Methyl 4-Acetoxy-4-(2-(methoxymethoxy)phenyl)-3-oxopentanoate (**2l**).* General procedure P-3 was followed using **1l**, and the reaction mixture was stirred at room temperature for 2 h. Purification by column chromatography afforded **2l** (153 mg, 95%) as a yellow liquid. $R_f$ = 0.60 (9:1 hexane/EtOAc); $R_f$ = 0.48 (9:1 hexane/EtOAc); IR (neat) $\nu_{max}$ 2954, 2854, 1744, 1602, 1236, 993, 757 cm$^{-1}$; $^1$H NMR (300 MHz, $CDCl_3$) $\delta$ 7.69−7.63 (m, 1H), 7.33−7.26 (m, 1H), 7.15−7.02 (m, 2H), 5.19−5.15 (m, 2H), 3.86 (d, $J$ = 16.6 Hz, 1H), 3.78 (d, $J$ = 16.6 Hz, 1H), 3.72 (s, 3H), 3.44 (s, 3H), 2.12 (s, 3H), 1.96 (s, 3H); $^{13}$C NMR (75 MHz, $CDCl_3$) $\delta$ 199.9, 169.1, 167.8, 153.1, 129.9, 128.3, 127.8, 121.6, 114.1, 94.1, 85.1, 56.1, 52.1, 44.9, 21.4, 21.3; HRMS (ESI-TOF) $m/z$ [M + Na]$^+$ calcd for $C_{16}H_{20}O_7Na$ 347.1101, found 347.1099.

*Methyl 4-Acetoxy-3-oxo-4-phenylpentanoate (**2m**).* General procedure P-3 was followed using **1m**, and the reaction mixture was stirred at room temperature for 1.5 h. Purification by column chromatography afforded **2m** (118 mg, 90%) as a pale yellow liquid. $R_f$ = 0.40 (9:1 hexane/EtOAc); IR (neat) $\nu_{max}$ 2927, 2856, 1742, 1639, 1373, 1034, 701 cm$^{-1}$; $^1$H NMR (300 MHz, $CDCl_3$) $\delta$ 7.45−7.52 (m, 2H), 7.41−7.36 (m, 2H), 7.35−7.31 (m, 1H), 3.57 (s, 3H), 3.37 (d, $J$ = 15.3 Hz, 1H), 3.30 (d, $J$ = 15.3 Hz, 1H), 2.26 (s, 3H), 1.87 (s, 3H); $^{13}$C NMR (75 MHz, $CDCl_3$) $\delta$ 197.6, 170.1, 166.8, 137.3, 128.8, 128.4, 124.9, 87.3, 52.2, 42.8, 22.9, 21.2; HRMS (ESI-TOF) $m/z$ [M + Na]$^+$ calcd for $C_{14}H_{16}O_5Na$ 287.0889, found 287.0881.

*tert-Butyl 3-(1-Acetoxy-4-methoxy-2,4-dioxobutyl)-1H-indole-1-carboxylate (**2n**).* General procedure P-3 was followed using **1n**, and the reaction mixture was stirred at room temperature for 1 h. Purification by column chromatography afforded **2n** (165 mg, 85%) as a yellow liquid. $R_f$ = 0.52 (9:1 hexane/EtOAc); IR (neat) $\nu_{max}$ 3118, 2924, 1748, 1676, 1728, 1516, 1091, 772 cm$^{-1}$; $^1$H NMR (300 MHz, $CDCl_3$) $\delta$ 8.19−8.13 (m, 1H), 7.74 (s, 1H), 7.59 (d, $J$ = 7.8 Hz, 1H), 7.40−7.34 (m, 1H), 7.31−7.27 (m, 1H), 6.47 (s, 1H), 3.64 (s, 3H), 3.57 (d, $J$ = 15.6 Hz, 1H), 3.49 (d, $J$ = 15.6 Hz, 1H), 2.19 (s, 3H), 1.68 (s, 9H); $^{13}$C NMR (75 MHz, $CDCl_3$) $\delta$ 202.7, 183.6, 177.3, 170.1, 128.0, 127.9, 126.7, 125.3, 123.4, 119.7, 115.5, 105.2, 84.6, 73.5, 52.5, 45.5, 28.2, 20.6; HRMS (ESI-TOF) $m/z$ [M + Na]$^+$ calcd for $C_{20}H_{23}NO_7Na$ 412.1368, found 412.1365.

*Methyl 4-Acetoxy-3-oxo-4-(thiophen-2-yl)butanoate (**2o**).* General procedure P-3 was followed using **1o**, and the reaction mixture was stirred at room temperature for 1.5 h. Purification by column



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chromatography afforded **2o** (112 mg, 88% yield) as a light yellow liquid. $R_f$ = 0.48 (9:1 hexane/EtOAc); IR (neat) $\nu_{max}$ 3119, 2925, 2377, 1749, 1695, 1549, 1516, 1221, 1020, 772 $cm^{-1}$; $^1H$ NMR (300 MHz, $CDCl_3$) $\delta$ 7.42 (dd, $J$ = 1.5, 5.3 Hz, 1H), 7.21−7.15 (m, 1H), 7.09−7.03 (m, 1H), 6.43 (s, 1H), 3.70 (s, 3H), 3.55 (d, $J$ = 2.3 Hz, 2H), 2.18 (s, 3H); $^{13}C$ NMR (75 MHz, $CDCl_3$) $\delta$ 195.2, 169.8, 166.4, 133.7, 128.9, 128.2, 127.4, 74.9, 52.5, 45.5, 20.5; HRMS (ESI-TOF) $m/z$ $[M + Na]^+$ calcd for $C_{11}H_{12}O_5SNa$ 279.0297, found 279.0302.

*Methyl 4-Acetoxy-3-oxo-6-phenylhexanoate (**2p**).* General procedure P-3 was followed using **1p**, and the reaction mixture was stirred at room temperature for 1 h. Purification by column chromatography afforded **2p** (133 mg, 96%) as a colorless liquid. $R_f$ = 0.50 (9:1 hexane/EtOAc); IR (neat) $\nu_{max}$ 2924, 2854, 1742, 1491, 1220, 773, 686 $cm^{-1}$; $^1H$ NMR (300 MHz, $CDCl_3$) $\delta$ 7.34−7.27 (m, 2H), 7.24−7.14 (m, 3H), 5.12 (dd, $J$ = 4.5, 8.3 Hz, 1H), 3.72 (s, 3H), 3.50 (s, 2H), 2.80−2.62 (m, 2H), 2.14 (s, 3H), 2.13−2.04 (m, 2H); $^{13}C$ NMR (75 MHz, $CDCl_3$) $\delta$ 169.5, 153.3, 139.9, 128.5, 128.3, 126.3, 84.1, 76.8, 62.5, 52.8, 35.3, 31.0, 20.6; HRMS (ESI-TOF) $m/z$ $[M + Na]^+$ calcd for $C_{15}H_{18}O_5Na$ 301.1051, found 301.1040.

*(6R)-Ethyl 4-Acetoxy-6-(tert-butyldimethylsilyloxy)-3-oxo-8-phenyl octanoate (**2q**).* General procedure P-3 was followed using **1q**, and the reaction mixture was stirred at room temperature for 1 h. Purification by column chromatography afforded **2q** (204 mg, 91%) as a colorless liquid. The diastereomeric ratio of **2q** was determined by $^1H$ NMR and HPLC analysis (dr = 7:3). $R_f$ = 0.52 (9:1 hexane/EtOAc); $[\alpha]_D^{28}$ −3.2 ($c$ 1.6); IR (neat) $\nu_{max}$ 2956, 2929, 2857, 1748, 1651, 1492, 1463, 1372, 1231, 1093, 775 $cm^{-1}$; $^1H$ NMR (300 MHz, $CDCl_3$) $\delta$ 7.36−7.30 (m, 2H), 7.24−7.17 (m, 3H), 5.33−5.25 (m, 1H), 4.23 (q, $J$ = 7.2 Hz, 2H), 3.97−3.87 (m, 1H), 3.52 (s, 2H), 2.76−2.60 (m, 2H), 2.14 (s, 3H), 2.08−1.95 (m, 2H), 1.94−1.77 (m, 2H), 1.30 (t, $J$ = 7.2 Hz, 3H), 0.94 (s, 9H), 0.10 (s, 6H); $^{13}C$ NMR (75 MHz, $CDCl_3$) $\delta$ 199.6, 170.1, 141.9, 128.4, 128.2, 125.8, 75.2, 68.3, 61.5, 45.8, 39.4, 31.3, 25.8, 20.5, 14.0, −4.6; HRMS (ESI-TOF) $m/z$ $[M + Na]^+$ calcd for $C_{24}H_{38}O_6SiNa$ 473.2329, found 473.2310.

*Methyl 4-Acetoxy-6-(tert-butyldiphenylsilyloxy)-3-oxohexanoate (**2r**).* General procedure P-3 was followed using **1r**, and the reaction mixture was stirred at room temperature for 1.5 h. Purification by column chromatography afforded **2r** (209 mg, 92% yield) as a colorless liquid. $R_f$ = 0.65 (9:1 hexane/EtOAc); IR (neat) $\nu_{max}$ 3138, 2928, 2377, 1751, 1729, 1550, 1514, 1109, 707 $cm^{-1}$; $^1H$ NMR (300 MHz, $CDCl_3$) $\delta$ 7.67−7.60 (m, 4H), 7.45−7.35 (m, 6H), 5.41−5.34 (m, 1H), 3.81−3.68 (m, 5H), 3.55 (s, 2H), 2.17−2.08 (m, 1H), 2.07 (s, 3H), 2.01−1.87 (m, 1H), 1.04 (s, 9H); $^{13}C$ NMR (75 MHz, $CDCl_3$) $\delta$ 199.9, 170.1, 166.8, 135.5, 133.1, 129.7, 127.7, 74.9, 58.9, 52.4, 45.7, 26.7, 20.4, 19.0; HRMS (ESI-TOF) $m/z$ $[M + Na]^+$ calcd for $C_{25}H_{32}O_6SiNa$ 479.1860, found 479.1860.

*Ethyl 3-Oxo-4-(pivaloyloxy)butanoate (**4ai**).* General procedure P-3 was followed using **3ai**, and the reaction mixture was stirred at room temperature for 1 h. Purification by column chromatography afforded **4ai** (107 mg, 93% yield) as a colorless liquid. $R_f$ = 0.58 (9:1 hexane/EtOAc); IR (neat) $\nu_{max}$ 2973, 2946, 2249, 1756, 1733, 1479, 1220, 772 $cm^{-1}$; $^1H$ NMR (300 MHz, $CDCl_3$) $\delta$ 4.76 (s, 2H), 4.21 (q, $J$ = 7.2 Hz, 2H), 3.50 (s, 2H), 1.29 (t, $J$ = 7.2 Hz, 3H), 1.26 (s, 9H); $^{13}C$ NMR (75 MHz, $CDCl_3$) $\delta$ 196.8, 177.4, 166.2, 67.6, 61.5, 45.8, 38.5, 26.9, 13.9; HRMS (ESI-TOF) $m/z$ $[M + Na]^+$ calcd for $C_{11}H_{18}O_5Na$ 253.1046, found 253.1045.

*4-Ethoxy-2,4-dioxobutyl benzoate (**4aii**).* General procedure P-3 was followed using **3aii**, and the reaction mixture was stirred at room temperature for 1 h. Purification by column chromatography afforded **4aii** (115 mg, 92%) as a colorless liquid. $R_f$ = 0.66 (9:1 hexane/EtOAc); IR (neat); $\nu_{max}$ 2927, 2856, 1634, 1385, 1271, 1026, 708 $cm^{-1}$; $^1H$ NMR (300 MHz, $CDCl_3$) $\delta$ 8.11−8.06 (m, 2H), 7.63−7.57 (m, 1H), 7.47 (t, $J$ = 7.8 Hz, 2H), 5.02 (s, 2H), 4.20 (q, $J$ = 7.2 Hz, 2H), 3.59 (s, 2H), 1.27 (t, $J$ = 7.2 Hz, 3H); $^{13}C$ NMR (75 MHz, $CDCl_3$) $\delta$ 196.8, 166.3, 165.5, 133.4, 129.7, 128.7, 128.3, 68.1, 61.5, 46.0, 13.8; HRMS (ESI-TOF) $m/z$ $[M + Na]^+$ calcd for $C_{13}H_{14}O_5Na$ 273.0733, found 273.0734.

*Ethyl 3-Oxo-4-(propionyloxy)butanoate (**4aiii**).* General procedure P-3 was followed using **3aiii**, and the reaction mixture was stirred at room temperature for 1 h. Purification by column chromatography afforded **4aiii** (95 mg, 95%) as a colorless liquid. $R_f$ = 0.48 (9:1 hexane/EtOAc); $R_f$ = 0.43 (9:1 hexane/EtOAc); IR (neat) $\nu_{max}$ 2923, 2852, 2244, 1742, 1431, 1220, 1064, 773 $cm^{-1}$; $^1H$ NMR (300 MHz, $CDCl_3$) $\delta$ 4.79 (s, 2H), 4.21 (q, $J$ = 7.2 Hz, 2H), 3.50 (s, 2H), 2.46 (q, $J$ = 7.5 Hz, 2H), 1.29 (t, $J$ = 7.2 Hz, 3H), 1.19 (t, $J$ = 7.5 Hz, 3H); $^{13}C$ NMR (75 MHz, $CDCl_3$) $\delta$ 196.8, 173.4, 166.3, 67.6, 61.6, 46.0, 26.9, 13.9, 8.8; HRMS (ESI-TOF) $m/z$ $[M + H]^+$ calcd for $C_9H_{15}O_5$ 203.0914, found 203.0903.

*Ethyl 8-(4-Methoxybenzyloxy)-3-oxo-4-(pivaloyloxy)octanoate (**4b**).* General procedure P-3 was followed using **3b**, and the reaction mixture was stirred at room temperature for 1 h. Purification by column chromatography afforded **4b** (198 mg, 94%) as a colorless liquid. $R_f$ = 0.48 (9:1 hexane/EtOAc); IR (neat) $\nu_{max}$ 2935, 2867, 1732, 1731, 1514, 1248, 1151, 820 $cm^{-1}$; $^1H$ NMR (300 MHz, $CDCl_3$) $\delta$ 7.25 (d, $J$ = 8.5 Hz, 2H), 6.87 (d, $J$ = 8.3 Hz, 2H), 5.14−5.06 (m, 1H), 4.42 (s, 2H), 4.18 (q, $J$ = 7.1 Hz, 2H), 3.80 (s, 3H), 3.50−3.39 (m, 4H), 1.90−1.74 (m, 2H), 1.67−1.38 (m, 4H), 1.31−1.22 (m, 12H); $^{13}C$ NMR (75 MHz, $CDCl_3$) $\delta$ 200.4, 177.6, 166.4, 159.0, 130.4, 129.1, 113.6, 88.1, 77.7, 72.4, 69.3, 61.4, 55.1, 45.6, 38.6, 30.0, 29.1, 26.9, 21.8, 13.9; HRMS (ESI-TOF) $m/z$ $[M + Na]^+$ calcd for $C_{23}H_{34}O_7Na$ 445.2196, found 445.2192.

*4-Methoxy-1-(naphthalen-1-yl)-2,4-dioxobutyl Benzoate (**4c**).* General procedure P-3 was followed using **3c**, and the reaction mixture was stirred at room temperature for 1.5 h. Purification by column chromatography afforded **4c** (198 mg, 90%) as a yellow liquid. $R_f$ = 0.60 (9:1 hexane/EtOAc); IR (neat) $\nu_{max}$ 2993, 2923, 2853, 2241, 1762, 1720, 1450, 1377, 1243, 1058, 709 $cm^{-1}$; $^1H$ NMR (300 MHz, $CDCl_3$) $\delta$ 8.24 (d, $J$ = 8.3 Hz, 1H), 8.10 (d, $J$ = 7.4 Hz, 2H), 7.93 (t, $J$ = 7.7 Hz, 2H), 7.71 (d, $J$ = 6.8 Hz, 1H), 7.66−7.39 (m, 6H), 7.09 (s, 1H), 3.58 (s, 3H), 3.56 (d, $J$ = 12.1 Hz, 1H), 3.43 (d, $J$ = 15.5 Hz, 1H); $^{13}C$ NMR (75 MHz, $CDCl_3$) $\delta$ 196.4, 166.4, 165.4, 134.1, 133.5, 131.3, 130.6, 129.9, 129.0, 128.6, 128.4, 127.3, 125.3, 123.8, 79.2, 52.4, 45.6; HRMS (ESI-TOF) $m/z$ $[M + Na]^+$ calcd for $C_{22}H_{18}O_5Na$ 385.1046, found 385.1059.

*Methyl 4-(Naphthalen-1-yl)-3-oxo-4-(pivaloyloxy)butanoate (**4d**).* General procedure P-3 was followed using **3d**, and the reaction mixture was stirred at room temperature for 1 h. Purification by column chromatography afforded **4d** (164 mg, 96% yield) as a light yellow liquid. $R_f$ = 0.45 (9:1 hexane/EtOAc); IR (neat) $\nu_{max}$ 2957, 2853, 1728, 1721, 1436, 1259, 1220, 1136, 1033, 773 $cm^{-1}$; $^1H$ NMR (500 MHz, $CDCl_3$) $\delta$ 8.11 (brd, $J$ = 8.1 Hz, 1H), 7.97−7.05 (m, 2H), 7.65−7.44 (m, 4H), 6.78 (s, 1H), 3.57 (s, 3H), 3.49 (d, $J$ = 15.7 Hz, 1H), 3.34 (d, $J$ = 15.5 Hz, 1H), 1.27 (s, 9H); $^{13}C$ NMR (75 MHz, $CDCl_3$) $\delta$ 196.5, 177.4, 166.4, 134.0, 131.1, 130.4, 128.8, 128.3, 127.1, 126.2, 125.2, 123.8, 78.7, 52.2, 45.4, 38.8, 30.0; HRMS (ESI-TOF) $m/z$ $[M + Na]^+$ calcd for $C_{20}H_{22}O_5Na$ 365.1359, found 365.1358.

*Methyl 4-(Acryloyloxy)-3-oxo-6-phenylhexanoate (**4e**).* General procedure P-3 was followed using **3e**, and the reaction mixture was stirred at 10 °C for 2 h. Purification by column chromatography afforded **4e** (121 mg, 84%) as a yellow liquid. $R_f$ = 0.55 (9:1 hexane/EtOAc); IR (neat) $\nu_{max}$ 3118, 2927, 1753, 1728, 1550, 1515, 1184, 772 $cm^{-1}$; $^1H$ NMR (500 MHz, $CDCl_3$) $\delta$ 7.32−7.25 (m, 2H), 7.23−7.13 (m, 3H), 6.49 (dd, $J$ = 1.2, 17.4 Hz, 1H), 6.25−6.16 (m, 1H), 5.96 (dd, $J$ = 1.2, 10.5 Hz, 1H), 5.21 (dd, $J$ = 4.4, 8.4 Hz, 1H), 3.72 (s, 3H), 3.53 (d, $J$ = 16.0 Hz, 1H), 3.49 (d, $J$ = 16.0 Hz, 1H), 2.79−2.67 (m, 2H), 2.28−2.10 (m, 2H); $^{13}C$ NMR (125 MHz, $CDCl_3$) $\delta$ 199.8, 166.8, 165.2, 140.1, 132.5, 128.5, 128.3, 127.1, 126.2, 77.4, 52.3, 45.5, 31.9, 31.1; HRMS (ESI-TOF) $m/z$ $[M + Na]^+$ calcd for $C_{16}H_{18}O_5Na$ 313.1046, found 313.1041.

*1-(3-Ethoxy-3-oxopropanoyl)cyclohexyl Acrylate (**4f**).* General procedure P-3 was followed using **3f**, and the reaction mixture was stirred at 10 °C for 2 h. Purification by column chromatography afforded **4f** (98 mg, 73%) as a pale yellow liquid. $R_f$ = 0.55 (9:1 hexane/EtOAc); IR (neat) $\nu_{max}$ 2924, 2377, 1752, 1693, 1412, 1219, 773 $cm^{-1}$; $^1H$ NMR (300 MHz, $CDCl_3$) $\delta$ 6.49 (dd, $J$ = 1.3, 17.2 Hz, 1H), 6.18 (dd, $J$ = 10.4, 17.4 Hz, 1H), 6.95 (dd, $J$ = 1.3, 10.4 Hz, 1H), 4.18 (q, $J$ = 7.2 Hz, 2H), 3.49 (s, 2H), 2.18−2.06 (m, 2H), 1.81−1.63 (m, 6H), 1.61−1.46 (m, 2H), 1.26 (t, $J$ = 7.2 Hz, 3H); $^{13}C$ NMR (75 MHz, $CDCl_3$) $\delta$ 201.3, 167.2, 165.1, 132.2, 127.8, 85.4, 61.3, 42.9,



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30.6, 24.9, 21.2, 14.1; HRMS (ESI-TOF) $m/z$ $[M + Na]^+$ calcd for $C_{14}H_{20}O_5Na$ 291.1202, found 291.1204.

*1-(3-Ethoxy-3-oxoprop-1-ynyl)cyclohexyl Benzoate (**4g**).* General procedure P-3 was followed using **3g**, and the reaction mixture was stirred at room temperature for 1.5 h. Purification by column chromatography afforded **4g** (150 mg, 83%) as a colorless liquid. $R_f$ = 0.60 (9:1 hexane/EtOAc); IR (neat) $\nu_{max}$ 2931, 2860, 1748, 1701, 1220, 771 $cm^{-1}$; $^1H$ NMR (300 MHz, $CDCl_3$) $\delta$ 8.11−8.07 (m, 2H), 7.64−7.59 (m, 1H), 7.51−7.46 (m, 2H), 4.16 (q, $J$ = 7.2 Hz, 2H), 3.54 (s, 2H), 2.2 (d, $J$ = 7.2 Hz, 2H), 1.87−1.71 (m, 5H), 1.69−1.57 (m, 2H), 1.38−1.28 (m, 1H), 1.24 (t, $J$ = 7.2 Hz, 3H); $^{13}C$ NMR (75 MHz, $CDCl_3$) $\delta$ 201.3, 167.2, 165.5, 133.6, 129.8, 129.4, 128.5, 85.6, 61.2, 42.9, 30.7, 24.9, 21.3, 14.0; HRMS (ESI-TOF) $m/z$ $[M + Na]^+$ calcd for $C_{18}H_{22}O_5Na$ 341.1359, found 341.1349.

*4-tert-Butoxy-2,4-dioxobutyl Benzoate (**6a**).* General procedure P-3 was followed using **5a**, and the reaction mixture was stirred at room temprature for 1.5 h. Purification by column chromatography afforded **6a** as a yellow liquid (127 mg, 92% yield). IR (neat) $\nu_{max}$ 2980, 2933, 1726, 1655, 1275, 712 $cm^{-1}$; $R_f$ = 0.63 (9:1 hexane/EtOAc); $^1H$ NMR (300 MHz, $CDCl_3$) $\delta$ 8.09 (d, $J$ = 7.4 Hz, 2H), 7.60 (t, $J$ = 7.4 Hz, 1H), 7.46 (t, $J$ = 7.6 Hz, 2H), 5.01 (s, 2H), 3.51(s, 2H), 1.46 (s, 9H); $^{13}C$ NMR (75 MHz, $CDCl_3$) $\delta$ 197.3, 165.6, 133.6, 129.9, 129.0, 128.5, 82.7, 68.3, 47.6, 27.9; HRMS (ESI-TOF) $m/z$ $[M + Na]^+$ calcd for $C_{15}H_{18}O_5Na$ 301.1046, found 301.1034.

*4-(Benzyloxy)-2,4-dioxobutyl Benzoate (**6b**).* General procedure P-3 was followed using **5b**, and the reaction mixture was stirred at room temprature for 2 h. Purification by column chromatography afforded **6b** as a colorless liquid (140 mg, 90% yield). IR (neat) $\nu_{max}$ 3067, 2958, 1729, 1453, 1246, 1070, 749 $cm^{-1}$; $R_f$ = 0.51 (9:1 hexane/EtOAc); $^1H$ NMR (400 MHz, $CDCl_3$) $\delta$ 8.08−8.04 (m, 2H), 7.61−7.56 (m, 1H), 7.48−7.42 (m, 2H), 7.38−7.29 (m, 5H), 5.17 (s, 2H), 4.98 (s, 2H) 3.63 (s, 2H); $^{13}C$ NMR (100 MHz, $CDCl_3$) $\delta$ 196.7, 166.2, 165.6, 134.9, 133.5, 129.8, 129.7, 128.8, 128.6, 128.5, 128.4, 128.3, 68.2, 67.4, 46.1; HRMS (ESI-TOF) $m/z$ $[M + Na]^+$ 335.0889 calcd for $C_{18}H_{16}O_5Na$, found 335.0876.

*(Z)-2-Hydroxy-4-oxopent-2-enyl Benzoate (**6c**).* General procedure P-3 was followed using **5c**, and the reaction mixture was stirred at room temperature for 1 h. Purification by column chromatography afforded **6c** (the enolic compound, major) as a colorless liquid (99 mg, 90% yield). $R_f$ = 0.56 (9:1 hexane/EtOAc); IR (neat) $\nu_{max}$ 3436, 2934, 1727, 1603, 1275, 712 $cm^{-1}$; $^1H$ NMR (300 MHz, $CDCl_3$) $\delta$ 15.1 (brs, 1H), 8.15−8.06 (m, 2H), 7.66−7.57 (m, 1H), 7.53−7.43 (m, 2H), 5.69 (s, 1H), 4.89 (s, 2H), 2.10(s, 3H); $^{13}C$ NMR (125 MHz, $CDCl_3$) $\delta$ 190.6, 188.97,165.7, 133.5, 129.8, 129.2, 128.2, 96.8, 65.0, 24.0; HRMS (ESI-TOF) $m/z$ $[M + Na]^+$ calcd for $C_{12}H_{12}O_4Na$ 243.0638, found 243.0648.

*Dimethyl 4-(Benzoyloxy)-5-oxo-4-phenylhept-2-ynedioate (**8d**).* General procedure P-3 was followed using **7d**, and the reaction mixture was stirred at 10 °C for 1.5 h. Purification by column chromatography afforded **8d** (106 mg, 54%) as a thick yellow liquid. $R_f$ = 0.40 (9:1 hexane/EtOAc); IR (neat) $\nu_{max}$ 2955, 2926, 2853, 2243, 1727, 1601, 1451, 1263, 1020, 758 $cm^{-1}$; $^1H$ NMR (300 MHz, $CDCl_3$) $\delta$ 8.16−8.05 (m, 2H), 7.81−7.73 (m, 1H), 7.68−7.57 (m, 2H), 7.53−7.42 (m, 5H), 3.98 (d, $J$ = 16.4 Hz, 1H), 3.83 (s, 3H), 3.74 (d, $J$ = 16.4 Hz, 1H), 3.64 (s, 3H); $^{13}C$ NMR (75 MHz, $CDCl_3$) $\delta$ 191.6, 166.2, 164.7, 134.1, 133.8, 130.0, 129.2, 128.6, 128.5, 126.8, 100.0, 81.6, 81.0, 53.2, 52.5, 44.1; HRMS (ESI-TOF) $m/z$ $[M + Na]^+$ calcd for $C_{22}H_{18}O_7Na$ 417.0944, found 417.0953.

*Ethyl 3-(2-Acetoxy-7-oxabicyclo[4.1.0]heptan-2-yl)-3-oxopropanoate (**8ei**).* General procedure P-3 was followed using **7ei**, and the reaction mixture was stirred at room temperature for 1 h. Purification by column chromatography afforded **8ei** (102 mg, 76% yield) as a colorless liquid. $R_f$ = 0.54 (9:1 hexane/EtOAc); IR (neat) $\nu_{max}$ 2941, 1742, 1371, 1246, 1029, 627 $cm^{-1}$; $^1H$ NMR (300 MHz, $CDCl_3$) $\delta$ 4.21 (q, $J$ = 7.2 Hz, 2H), 3.78 (d, $J$ = 4.0 Hz, 1H), 3.65 (d, $J$ = 15.5 Hz, 1H), 3.41−3.34 (m, 2H), 2.19 (s, 3H), 2.15−2.10 (m, 1H), 1.94−1.74 (m, 2H), 1.68−1.50 (m, 2H), 1.46−1.33 (m, 1H), 1.27 (t, $J$ = 7.2 Hz, 3H); $^{13}C$ NMR (75 MHz, $CDCl_3$) $\delta$ 200.7, 171.0, 166.6, 82.4, 61.5, 54.1, 52.4, 43.2, 29.6, 23.2, 20.4, 14.1, 14.0; HRMS (ESI-TOF) $m/z$ $[M + Na]^+$ calcd for $C_{13}H_{18}O_6Na$ 293.0995, found 293.0998.

*Ethyl 4-Acetoxy-3-oxo-4-(3-phenyloxiran-2-yl)butanoate (**8eii**).* General procedure P-3 was followed using **7eii**, and the reaction mixture was stirred at room temperature for 1 h. Purification by column chromatography afforded **8eii** (125 mg, 82%) as a colorless liquid. $R_f$ = 0.48 (9:1 hexane/EtOAc); IR (neat) $\nu_{max}$ 2924, 2853, 1736, 1718, 1373, 1217, 1024, 771 $cm^{-1}$; $^1H$ NMR (500 MHz, $CDCl_3$) $\delta$ 7.37−7.32 (m, 3H), 7.29−7.24 (m, 2H), 5.31 (d, $J$ = 5.0 Hz, 1H), 4.20 (q, $J$ = 7.2 Hz, 2H), 3.92 (d, $J$ = 1.8 Hz, 1H), 3.69 (d, $J$ = 16.0 Hz, 1H), 3.61 (d, $J$ = 7.3 Hz, 1H), 3.34 (dd, $J$ = 1.8, 4.9 Hz, 1H), 2.19 (s, 3H), 1.27 (t, $J$ = 7.2 Hz, 3H); $^{13}C$ NMR (125 MHz, $CDCl_3$) $\delta$ 197.4, 169.4, 166.1, 128.7, 128.7, 128.5, 125.7, 90.7, 61.6, 58.9, 56.4, 46.7, 20.4, 14.0; HRMS (ESI-TOF) $m/z$ $[M + Na]^+$ calcd for $C_{16}H_{18}O_6Na$ 329.0995, found 329.1001.

*(R)-Ethyl 4-Acetoxy-3-oxo-5-phenylpentanoate (**11**).* General procedure P-3 was followed using **10**, and the reaction mixture was stirred at room temperature for 1 h. Purification by column chromatography afforded **11** (2.57 g, 96%) as a colorless liquid. $R_f$ = 0.45 (9:1 hexane/EtOAc); 70% ee determined by HPLC analysis; retention time $t_{major}$ = 8.2 min, and $t_{minor}$ = 11.3 min; $[\alpha]_D^{28}$ +22.4 ($c$ 0.7, $CHCl_3$); IR (neat) $\nu_{max}$ 2926, 2853, 1739, 1637, 1370, 1227, 1029, 700 $cm^{-1}$; $^1H$ NMR (300 MHz, $CDCl_3$) $\delta$ 7.34−7.24 (m, 2H), 7.23−7.24 (m, 3H), 5.37 (dd, $J$ = 4.5, 8.3 Hz, 1H), 4.18 (q, $J$ = 7.2 Hz, 2H), 3.41 (s, 2H), 3.24−3.13 (m, 1H), 3.08−2.98 (m, 1H), 2.06 (s, 3H), 1.27 (t, $J$ = 7.2 Hz, 3H); $^{13}C$ NMR (125 MHz, $CDCl_3$) $\delta$ 200.1, 169.9, 166.3, 135.5, 129.3, 128.5, 128.3, 127.0, 78.3, 61.5, 46.6, 36.6, 20.4, 14.0; HRMS (ESI-TOF) $m/z$ $[M + Na]^+$ calcd for $C_{15}H_{18}O_5Na$ 301.1051, found 301.1046.

*Methyl 3-((5R)-1-Acetoxy-2-methyl-5-(prop-1-en-2-yl)cyclohex-2-enyl)-3-oxopropanoate (**13a**).* General procedure P-3 was followed using **12a**, and the reaction mixture was stirred at room temperature for 1 h. Purification by column chromatography afforded **13a** (66 mg, 56%) as a pale yellow liquid. $R_f$ = 0.58 (9:1 hexane/EtOAc); $[\alpha]_D^{28}$ +32.6 ($c$ 1.8, $CHCl_3$); IR (neat) $\nu_{max}$ 2958, 2924, 2236, 1735, 1721, 1438, 1220, 1020, 772 $cm^{-1}$; $^1H$ NMR (300 MHz, $CDCl_3$) $\delta$ 5.94−5.75 (m, 1H), 4.77−4.70 (m, 2H), 3.74 (s, 3H), 3.72 (d, $J$ = 15.7 Hz, 1H), 3.65 (d, $J$ = 15.7 Hz, 1H), 2.56−2.36 (m, 1H), 2.27−2.15 (m, 3H), 2.10 (s, 3H), 2.08−1.94 (m, 1H), 1.71 (s, 3H), 1.63−1.58 (m, 3H); $^{13}C$ NMR (75 MHz, $CDCl_3$) $\delta$ 199.8, 169.0, 167.3, 147.6, 130.5, 129.2, 109.7, 88.9, 52.3, 45.1, 38.1, 34.4, 30.2, 21.5, 20.4, 18.3; HRMS (ESI-TOF) $m/z$ $[M + Na]^+$ calcd for $C_{16}H_{22}O_5Na$ 317.1359, found 317.1356.

*Methyl 3-((2S,5R)-1-Acetoxy-2-isopropyl-5-methylcyclohexyl)-3-oxopropanoate (**13b**).* General procedure P-3 was followed using **12b**, and the reaction mixture was stirred at room temperature for 1.5 h. Purification by column chromatography afforded **13b** (105 mg, 88%) as a pale yellow liquid. $R_f$ = 0.48 (9:1 hexane/EtOAc); $[\alpha]_D^{28}$ +17.1 ($c$ 0.8, $CHCl_3$); IR (neat) $\nu_{max}$ 3117, 2926, 2855, 1750, 1728, 1693, 1551, 1514, 1025, 772 $cm^{-1}$; $^1H$ NMR (500 MHz, $CDCl_3$) $\delta$ 3.73 (s, 3H), 3.68 (d, $J$ = 16.2 Hz, 1H), 3.57 (d, $J$ = 16.2 Hz, 1H), 2.36−2.29 (m, 1H), 2.09 (s, 3H), 2.08−1.98 (m, 3H), 1.81−1.71 (m, 1H), 1.65−1.57 (m, 2H), 1.55−1.45 (m, 2H), 0.94 (d, $J$ = 6.7 Hz, 3H), 0.85 (d, $J$ = 6.7 Hz, 3H), 0.73 (d, $J$ = 6.7 Hz, 3H); $^{13}C$ NMR (125 MHz, $CDCl_3$) $\delta$ 203.0, 170.0, 167.5, 90.5, 52.1, 49.6, 47.7, 41.8, 34.1, 29.1, 25.6, 23.7, 22.2, 22.1, 18.3; HRMS (ESI-TOF) $m/z$ $[M + Na]^+$ calcd for $C_{16}H_{26}O_5Na$ 321.1672, found 321.1671.

*(2R,5S)-1-(3-Ethoxy-3-oxopropanoyl)-2-isopropyl-5-methylcyclohexyl Benzoate (**13c**).* General procedure P-3 was followed using **12c**, and the reaction mixture was stirred at room temperature for 2 h. Purification by column chromatography afforded **13c** (129 mg, 86%) as a pale yellow liquid. $R_f$ = 0.60 (9:1 hexane/EtOAc); $[\alpha]_D^{28}$ −8.0 ($c$ 0.6, $CHCl_3$); IR (neat) $\nu_{max}$ 2957, 2871, 1747, 1716, 1645, 1314, 1275, 1110, 713 $cm^{-1}$; $^1H$ NMR (500 MHz, $CDCl_3$) $\delta$ 8.04−8.00 (m, 2H), 7.63−7.58 (m, 1H), 7.51−7.44 (m, 2H), 4.20 (q, $J$ = 7.2 Hz, 2H), 3.81 (d, $J$ = 16.5 Hz, 1H), 3.68 (d, $J$ = 16.5 Hz, 1H), 2.64−2.58 (m, 1H), 2.25−2.12 (m, 3H), 1.86−1.78 (m, 1H), 1.72−1.64 (m, 1H), 1.63−1.48 (m, 2H), 1.29−1.24 (m, 4H), 1.02 (d, $J$ = 6.9 Hz, 3H), 0.88 (d, $J$ = 6.6 Hz, 3H), 0.79 (d, $J$ = 6.9 Hz, 3H); $^{13}C$ NMR (125 MHz, $CDCl_3$) $\delta$ 203.1, 167.1, 165.5, 133.3, 130.5, 129.6,128.5, 90.8, 61.2, 50.6, 47.9, 42.3, 34.2, 29.3, 25.7, 24.0, 22.3, 18.3, 14.1; HRMS



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(ESI-TOF) $m/z$ [M + Na]$^+$ calcd for $C_{22}H_{30}O_5Na$ 397.1985, found 397.1989.

*Ethyl 3-((8S,9S,10R,13R,14S,17R)-3-Acetoxy-10,13-dimethyl-17-((R)-6-methylheptan-2-yl)-2,3,4,7,8,9,10,11,12,13,14,15,16,17-tetradeca-hydro-1H-cyclopenta[a]phenanthren-3-yl)-3-oxopropanoate (**13d**).* General procedure P-3 was followed using **12d**, and the reaction mixture was stirred at room temperature for 1 h. Purification by column chromatography afforded **13d** (199 mg, 92%) as a pale yellow liquid. $R_f$ = 0.64 (9:1 hexane/EtOAc); $[\alpha]_D^{28}$ −45.6 ($c$ 1.1, $CHCl_3$); IR (neat) $\nu_{max}$ 2933, 2869, 2237, 1743, 1624, 1466, 1368, 1241, 1025, 769 cm$^{-1}$; $^1$H NMR (500 MHz, $CDCl_3$) $\delta$ 5.45−5.41 (m, 1H), 4.17 (q, $J$ = 7.2 Hz, 2H), 3.56 (d, $J$ = 15.4 Hz, 1H), 3.49 (d, $J$ = 15.4 Hz, 1H), 2.82 (dd, $J$ = 2.3, 14.4 Hz, 1H), 2.59−2.52 (m, 1H), 2.29−2.22 (m, 1H), 2.07 (s, 3H), 2.03−1.94 (m, 3H), 1.90−1.78 (m, 2H), 1.77−1.70 (m, 1H), 1.67−1.32 (m, 11H), 1.26 (t, $J$ = 7.2 Hz, 3H), 1.19−1.06 (m, 5H), 1.05 (s, 3H), 1.03−0.95 (m, 3H), 0.91 (d, $J$ = 6.6 Hz, 3H), 0.86 (dd, $J$ = 2.4, 6.6 Hz, 6H), 0.67 (s, 3H); $^{13}$C NMR (125 MHz, $CDCl_3$) $\delta$ 200.2, 170.4, 167.1, 137.6, 124.2, 85.2, 61.2, 56.5, 56.0, 49.2, 44.2, 42.3, 39.6, 39.5, 38.2, 36.4, 36.1, 35.8, 34.6, 31.8, 31.7, 29.0, 28.2, 28.0, 24.2, 23.8, 22.8, 22.5, 21.0, 20.9, 19.4, 18.7, 14.1, 11.8; HRMS (ESI-TOF) $m/z$ [M + Na]$^+$ calcd for $C_{34}H_{54}O_5Na$ 565.3862, found 565.3842.

*Oxiranyl Derivative of Ethyl 3-((8S,9S,10R,13R,14S,17R)-3-Acetoxy-10,13-dimethyl-17-((R)-6-methylheptan-2-yl)-2,3,4,7,8,9,10,11,12,13,14,15,16,17-tetradecahydro-1H-cyclopenta-[a] phenanthren-3-yl)-3-oxopropanoate (**13e**).* General procedure P-3 was followed using **12e**, and the reaction mixture was stirred at room temperature for 1 h. Purification by column chromatography afforded **13e** (195 mg, 86%) as a pale yellow liquid. $R_f$ = 0.50 (9:1 hexane/EtOAc); $[\alpha]_D^{28}$ −34.6 ($c$ 0.8, $CHCl_3$); IR (neat) $\nu_{max}$ 2930, 2869, 2238, 1744, 1728, 1464, 1369, 1237, 1047, 757 cm$^{-1}$; $^1$H NMR (500 MHz, $CDCl_3$) $\delta$ 4.20 (q, $J$ = 7.2 Hz, 2H), 3.66 (s, 1H), 3.63 (d, $J$ = 15.9 Hz, 1H), 3.37 (d, $J$ = 15.9 Hz, 1H), 2.58 (dd, $J$ = 3.9, 15.0 Hz, 1H), 2.17 (s, 3H), 2.15−2.09 (m, 2H), 2.06−2.01 (m, 2H), 1.92−1.79 (m, 4H), 1.66−1.43 (m, 10H), 1.41−1.32 (m, 3H), 1.29 (t, $J$ = 7.2 Hz, 3H), 1.19−1.06 (m, 6H), 1.02 (s, 3H), 0.91 (d, $J$ = 6.6 Hz, 3H), 0.87 (dd, $J$ = 2.6, 6.6 Hz, 6H), 0.69 (s, 3H); $^{13}$C NMR (125 MHz, $CDCl_3$) $\delta$ 200.8, 170.8, 166.5, 81.1, 69.0, 61.6, 60.0, 56.0, 55.9, 46.2, 46.0, 43.1, 42.6, 39.4, 39.0, 38.5, 36.0, 35.7, 35.2, 29.7, 28.0, 27.9, 25.9, 25.8, 24.0, 23.8, 22.8, 22.5, 21.4, 20.3, 18.6, 14.1, 11.8; HRMS (ESI-TOF) $m/z$ [M +Na]$^+$ calcd for $C_{34}H_{54}O_6Na$ 581.3813, found 581.3810.

*Ethyl 4-Acetoxy-3-oxo-4-phenylbutanoate (**2b′**).* General procedure P-3 was followed using **1b** (50 mg, 0.2 mmol), and the reaction mixture was stirred at room temperature for 1 h (3 equiv of $H_2O^{18}$ was used instead of distilled water). Purification by column chromatography afforded **2b′** (50 mg, 95%) as a light yellow liquid. $R_f$ = 0.44 (9:1 hexane/EtOAc); IR (neat) $\nu_{max}$ 2924, 2853, 1627, 1384, 1220, 771 cm$^{-1}$; $^1$H NMR (500 MHz, $CDCl_3$) $\delta$ 7.42 (s, 5H), 6.17 (s, 1H), 4.12 (q, $J$ = 7.0 Hz, 2H), 3.49 (d, $J$ = 15.5 Hz, 1H), 3.42 (d, $J$ = 15.5 Hz, 1H), 2.2 (s, 3H), 1.22 (t, $J$ = 7.0 Hz, 3H); $^{13}$C NMR (125 MHz, $CDCl_3$) $\delta$ 196.4, 169.9, 166.0, 132.5, 129.6, 129.1, 128.3, 127.6, 80.0, 61.6, 20.6, 14.0; HRMS (ESI-TOF) $m/z$ [M +Na]$^+$ calcd for $C_{14}H_{16}O_4{}^{18}ONa$ 289.0932, found 289.0931.

*Ethyl 4-Hydroxy-3-oxo-4-phenylbutanoate (**2b′′**).* To a stirred solution of **2b′** (45 mg, 0.17 mmol) in EtOH/$H_2O$ (2 mL, 10:1) was added $Sc(OTf)_3$ (catalytic) at 0 °C. The reaction mixture was continued to stir at room temperature until the complete consumption of starting material (indicated by TLC). Then, the solvent was evaporated under reduced pressure to obtain the crude material. The solid mass obtained was diluted with $CH_2Cl_2$ (10 mL). The organic layer was washed with brine (5 mL), dried over $Na_2SO_4$, and concentrated under reduced pressure. The crude residue was purified by column chromatography on silica gel to give **2b′′** (13 mg, 38%) along with it is enolic compound. $R_f$ = 0.5 (4:1 hexane/EtOAc); IR (neat) $\nu_{max}$ 3451, 2926, 2855, 1733, 1623, 1451, 1371, 1264, 1025, 701 cm$^{-1}$; $^1$H NMR (500 MHz, $CDCl_3$) $\delta$ 7.42−7.32 (m, 5H), 5.29 (s, 1H), 4.13 (q, $J$ = 7.2 Hz, 2H), 3.45 (d, $J$ = 15.9 Hz, 1H), 3.36 (d, $J$ = 15.9 Hz, 1H), 1.23 (t, $J$ = 7.2 Hz, 3H) (only for keto form); $^{13}$C NMR (125 MHz, $CDCl_3$) $\delta$ 202.1, 200.0, 170.4, 166.3, 136.8, 134.0, 129.1, 128.6, 127.5, 79.8, 70.2, 61.7, 61.1, 48.4, 44.5, 40.4, 14.0 (for both keto and enol form); HRMS (ESI-TOF) $m/z$ [M + Na]$^+$ calcd for $C_{12}H_{14}O_4Na$ 245.0784, found 245.0780.

## ■ ASSOCIATED CONTENT

### Supporting Information

Copies of $^1$H and $^{13}$C NMR spectra for all new compounds. The Supporting Information is available free of charge on the ACS Publications website at DOI: 10.1021/acs.joc.5b00400.

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### Notes

The authors declare no competing financial interest.

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