JOC The Journal of Organic Chemistry

Article

Synthesis of gamma-Acetoxy beta-Keto Esters Through Regioselective Hydration of gamma-Acetoxy alpha,beta-Alkynoates

Tapas Ranajn Pradhan, Kishore L. Mendhekar, and Debendra Kumar Mohapatra

J. Org. Chem., **Just Accepted Manuscript** • Publication Date (Web): 05 May 2015

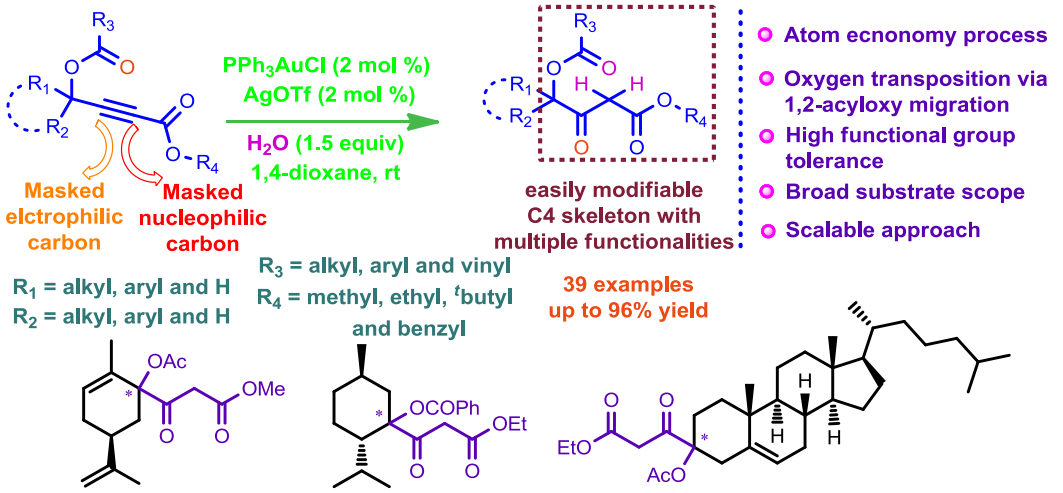
Just Accepted

The Journal of Organic Chemistry is published by the American Chemical Society.
1155 Sixteenth Street N.W., Washington, DC 20036

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

Tapas R. Pradhan, Kishor L. Mendhekar and Debendra K. Mohapatra*

Natural Products Chemistry Division, CSIR-Indian Institute of Chemical Technology, Hyderabad 500 007, INDIA; mohapatra@iict.res.in



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 bearing sensitive functional group in the remote reaction sites, are selectively hydrated in to the corresponding *β*-keto esters. The reaction tolerates a wide variety of other carboxylates such as benzoates, propionates, acrylates, pivalates including chiral carboxylates with retention of the configuration. The broad substrate scope including the derivatization of complex natural products, neutral and open air conditions make 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.

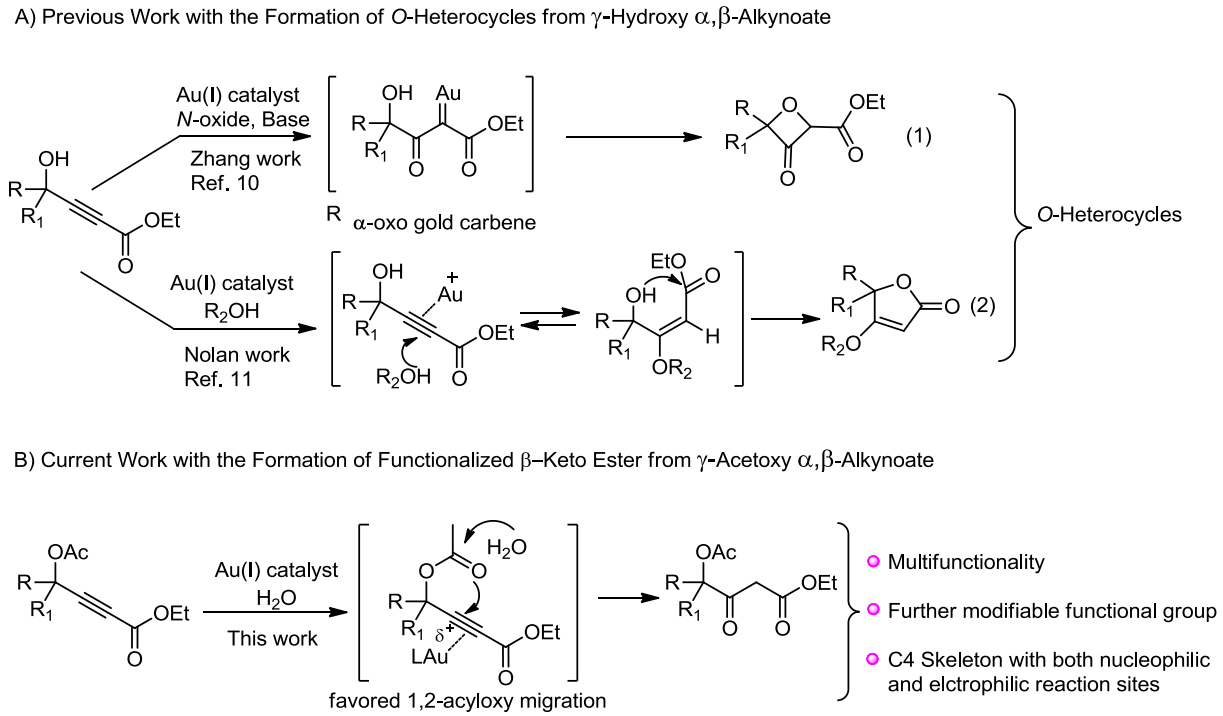
INTRODUCTION

β-keto esters are a class of unique functionalized and highly valuable intermediates, not only for the synthesis of various biologically active compounds such as 3,4-dihydropyrimidines, 4-alkyl or arylcoumarins, 1,4-dihydropyridines[1] but also for 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 condensation[3] and the Ti-Claisen condensation.[4] Besides these, a plethora of other strategies have been developed for the synthesis of β-keto esters.[1] In particular, modifiable functional group present in the β-keto esters make them more versatile for further organic transformations.[5]

Despite the tremendous successes of above meritorious methods deficiency exists to prepare modifiable functionalized β-keto esters. As β-keto esters are more prone to electrophilic substitution either at 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 the acid derivatives.[6] The disadvantage of this method is the use of strong base for the enolate generation which possibly 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 on acid catalysis,[7] rendering it unsuitable for the large scale synthesis and also in terms of functional groups tolerance. Thus, it was thought that propargylic alcohol i.e. γ-hydroxy-α,β-alkynoate can become surrogates 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 devlopement of gold catalyzed regioselective hydration of both symmetrical and unsymmetrical internal alkynes.[8] During the course of literature survey on gold catalyzed trasformation,[9] Au(III)-catalyzed hydration has been reported by Hammond et al. for accessing both γ- or β-keto ester.[8e] This method of hydration has not been generalized in a broader scope, particularly for the synthesis of multi-functionalized β-keto ester. In 2010, Zhang and co-workers reported an intermolecular oxidation

Scheme 1. Gold(I)-Catalyzed Functinalization of γ-Hydroxy/Acetoxy-α,β- Alkynoates



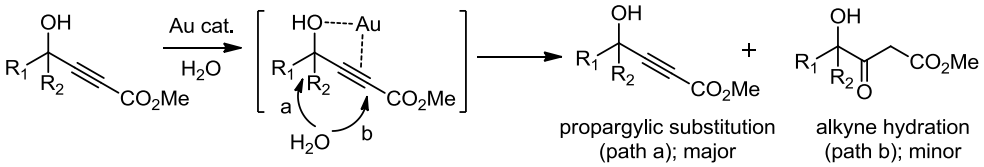
of γ-hydroxy-α,β-acetylinic ester in presence of gold catalyst and pyridine *N*-oxide for the synthesis of oxetan-3-ones through α-oxo gold carbene intermediate (Scheme 1A, eq. 1).[10] Alternatively, Nolan's group studied the Au(I)-catalyzed tandem alkoxylation/lactonization of γ-hydroxy-α,β-acetylinic 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 potential attractive solution, the difficulty of

obtaining regioselectivity using gold catalyzed condition 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 the gold catalyzed hydration. Herein, we report a 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.

RESULTS AND DISCUSSION

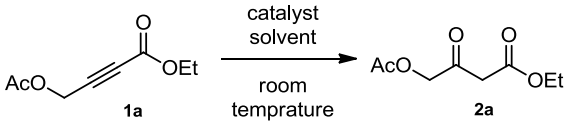
Initially, it was envisioned that the electron withdrawing carboxylate function of γ-hydroxy α,β-alkynoate would cause a hydration to afford the corresponding β-keto ester. So, the reaction under the catalytic conditions ($NaAuCl_4.H_2O$, EtOH/ H_2O) reported by Hammond's group was pursued.[8e] To test the feasibility of this hydration process, ethyl 4-hydroxybut-2-ynoate was subjected 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 the decomposition of the starting material. Changing the catalyst or solvent had neither any improvement nor significant impact in the yield of the reaction. It was presumed that the propargylic substitution might be the cause of difficulty for alkyne hydration,[12] reasonably due to the formation of five-membered transition state involved in the complexation of gold catalyst with –OH and the alkyne bond (Scheme 2), thereby leading to low yield (at room temprature) and decomposition (on heating). To overcome

Scheme 2: The Inhibition of Hydration Process Due to The Propargylic Nucleophilic Substitution



this substrate scope limit, it was contemplated that the exchange of hydroxyl group with an acetoxy group might facilate the 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.

Table 1. Optimization of the Gold Catalyzed Hydration Reaction



entry[a]	catalyst/s	solvent/s	time (h)	yield (%)[b]
1	$NaAuCl_4$. $2H_2O$	EtOH/ H_2O (4:1)	24	21
2	$AuCl_3$	EtOH/ H_2O (4:1)	24	20
3	$HAuCl_4$. $4H_2O$	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

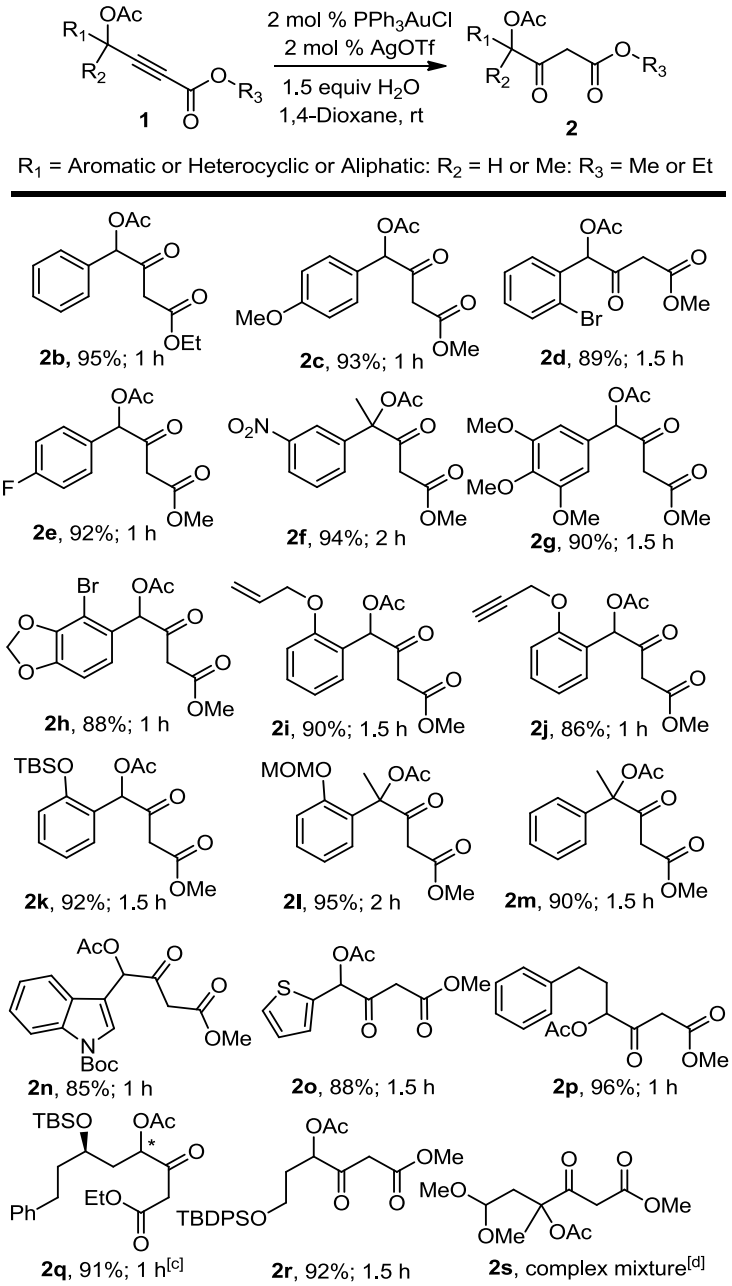
[a]The reactions were performed with **1a** (0.5 mmol) and water (1.5 equiv.) in solvent (approx. 1 mL) at room temperature under ambient atmosphere. [b]Yield of isolated product after column chromatography. [c]4 mol% of each of the catalyst was used. [d]4 mol % of silver catalyst was used. [e]2 mol%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

The attempt towards hydration of **1a** involved the use of various gold catalysts (4 mol%), 1.5 equivalents 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 case of entries 1-6, the expected alkoxylation of triple bond by the use of alcohols as co-solvent 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. Combination of Au(I) catalyst with silver catalysts such as $AgBF_4$, $AgSbF_6$, AgOTf , $AgNTf_2$ (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, nitromethane) led to further improvement in the yield (entries 9-15). Hydration under Zhang's condition using water gave moderate yield (entry 13).[15] Best results were obtained with PPh_3AuCl in combination with AgOTf in 1,4-dioxane as solvent and also allowed to reduce the amount of each of the catalyst to 2 mol% (entry 16). The reaction with only AgOTf afforded 32% of **2a,** even after prolonged reaction time and more catalyst loading (entry 17). Furthermore, the only Au(I) catalyst, PPh_3AuCl did not afford any hydration product (entry 18). Finally, no reaction occurred in the presence of $PtCl_2$, $PdCl_2(CH_3CN)_2$ (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 this conditions to obtain the corresponding hydration products in good to high yields after purification by column chromatography on 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 as well as the yield of the reaction (**2b-f**). Multiple substituents (either

Scheme 3. Hydration of γ-Acetoxy α,β-Alkynoate

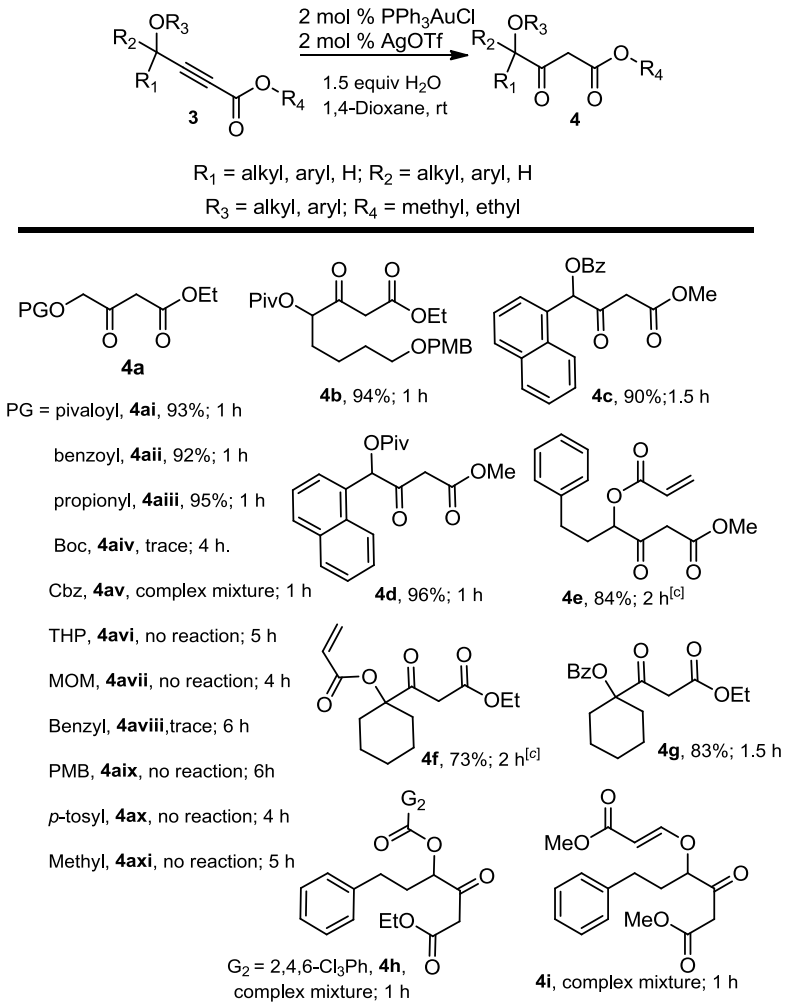


[a]Reactions were carried out using **1** (0.5 mmol), $Ph_3PAuCl/AgOTf$ (0.02 mmol), H_2O (1.5 mmol), and 1,4-dioxane (2.0 mL) at ambient temperature. [b]Isolated yields. [c]diastereomeric mixture of **1q** (*dr* = 7:3, determined from ^1H NMR and HPLC analysis) was taken for the hydration reaction.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

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 bond and triple bond 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, MOM ether of the phenolic hydroxyl were well tolerated to this catalytic conditions affording the corresponding keto esters, **2k** and **2l** in a satisfactory yield. Only for tertiary substrates **2f**, **2l** and **2m**, slightly extended time was required which might be due to the steric effects. Heteroaryl substrates **2n** and **2o** were well compatible with the optimized reaction conditions. Not only aryl but also alkyl substrates **2p**-**2r** gave β-ketoester products with satisfactory yield. Aliphatic substrates **2q**, **2r** and **4b** containing 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 **2s**, likely due to the acidity of the gold catalysis towards the acetal group.

Encouraged by the results from the acetate assisted hydration, we were subsequently interested in the hydration of other type of easily accessible alkynoates, having less nucleophilic and higher steric hindered carbonyl oxygen. 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 the steric hindrance. Hydration of both secondary and tertiary *o*-acrylates (**3e** and **3f**) also proceeded well when the reaction was carried out at lower temperature (i.e. at 10 ^{o}C). Polyaryl substrates also delivered the corresponding hydration products **4c** and **4d** in high yields. Unfortunately, 2,4,6-trichlorobenzoate ester **3h** did not

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



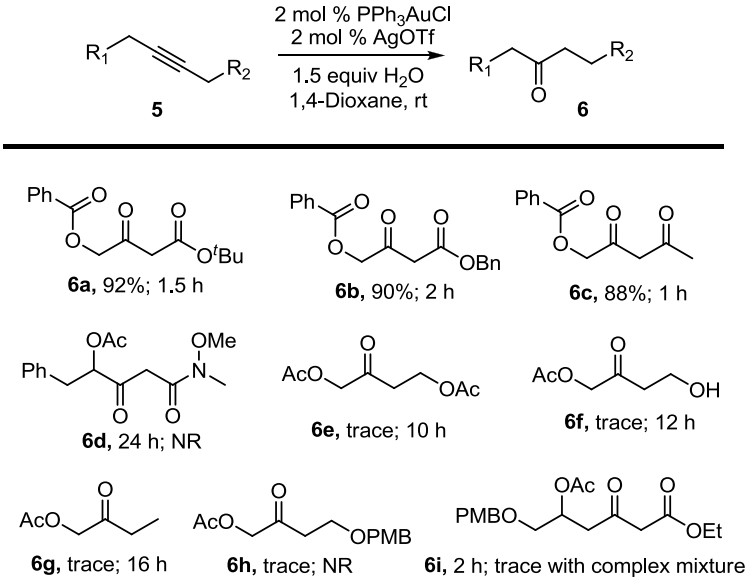
[a]Reactions were carried out using **3** (0.5 mmol), $Ph_3PAuCl/AgOTf$ (0.02 mmol), H_2O (1.5 mmol), and 1,4-dioxane 2.0 mL at ambient temperature. [b]Isolated yields. [c]Reaction of **3a** and **3f** (0.5 mmol each) was carried under the standard conditions but at a low temperature (10 ^oC).

give the desired product under the reaction conditions and unprecedented results were obtained. Groups such as Boc, Cbz, THP, MOM, Bn, Ts, OMe were inert to direct the regioselective hydration even after a longer 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.

To test the hypothesis, studies were initiated by modifying the substituents on the alkyne terminus of propargylic carboxylate (Scheme 5). Methyl and ethyl prpoargylic esters readily participated in the hydration (Scheme 3 and 4). Likewise, *tert*-butyl (**5a**) and benzyl ester (**5b**) were also well amenable to this reaction to afford the corresponding ketoesters **6a** and **6b** 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 decreasing electron withdrawing power of amide (Scheme 5).

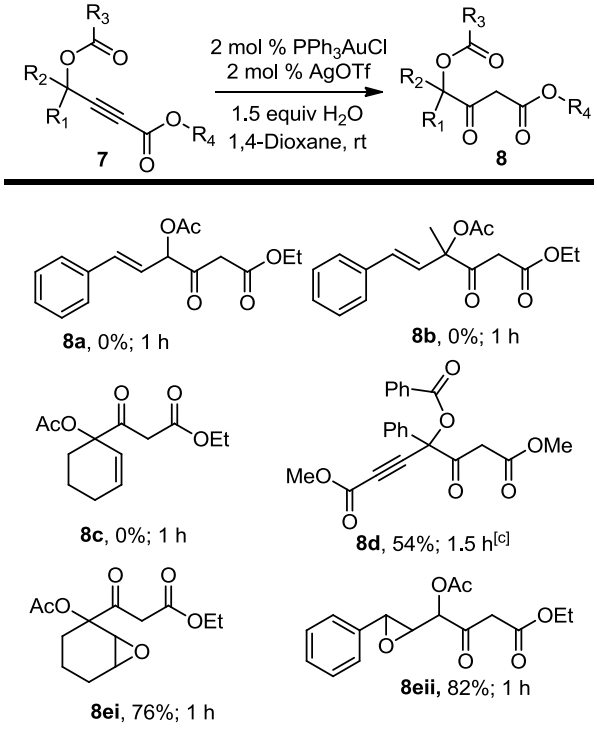
Scheme 5. Effect of the Nature of the Substituent at the Alkyne Terminus of Propargylic Acetate[a,b]



[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.

Substitution of other groups such as alkyl or even functionalized aliphatic groups did not lead to productive reactivity (for examples see Scheme 5, **5e-5h**). Unpredictable result was also obtained for homopropargylic carboxylate **5i**. The inertness of the substrates **5d-5i** towards 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 6. Effect of Sustituents Directly Attached to Acetate/Benzoate Bearing Carbon[a,b]

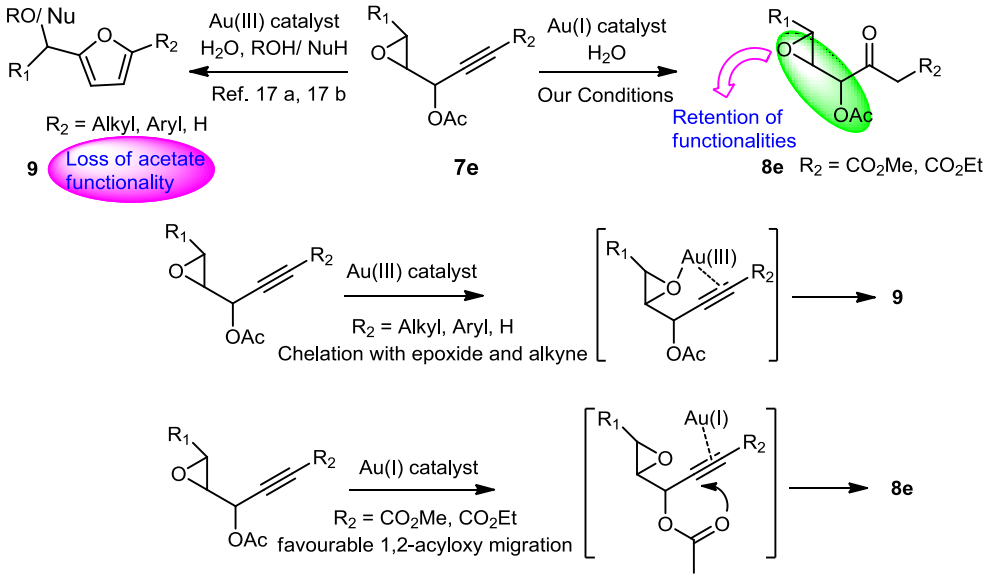


[a]Reactions were carried out on a scale of 0.5 mmol of **7** in 2 mL of solvent under standard condition. [b]Yield of isolated product. [c]Reaction was carried out at 10 ^{o}C and the starting diyne **7d** (30%) was recovered.

With this set of conditions for the hydration based on the use of Au(I) catalyst [PPh_3AuOTf] and water (Table 1). The generality of our procedure in a series of substrates containing sensitive functionalities was evaluated next (Scheme 6). To 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 traceable amount, albeit some unidentified mixture was obtained. This result of hydration might be due to the competitive Rautenstrauch rearrangement in presence of 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.

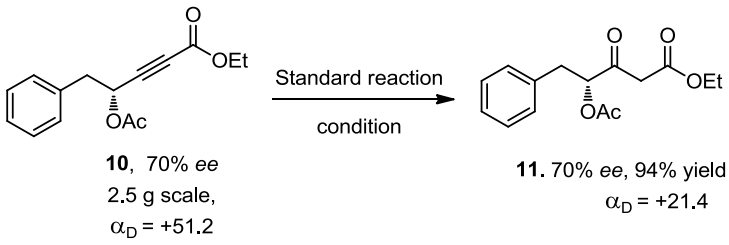
Scheme 7. Mode of Reactivities of Au(I) and (III) Catalysts for Oxiranyl Carboxylate



It is noteworthy to mention 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 in **8ei** and **ii** in good to excellent yield without affecting the epoxide functionality. The switching of the product selectivity from furan synthesis[17a,17b] to β-keto esters might be attributed to the reason that the presence of electron withdrawing (CO_2Me/ CO_2Et) group makes 1,2-acyloxy migration more favorable in contrast to the reaction through epoxide chelation (Scheme 7).

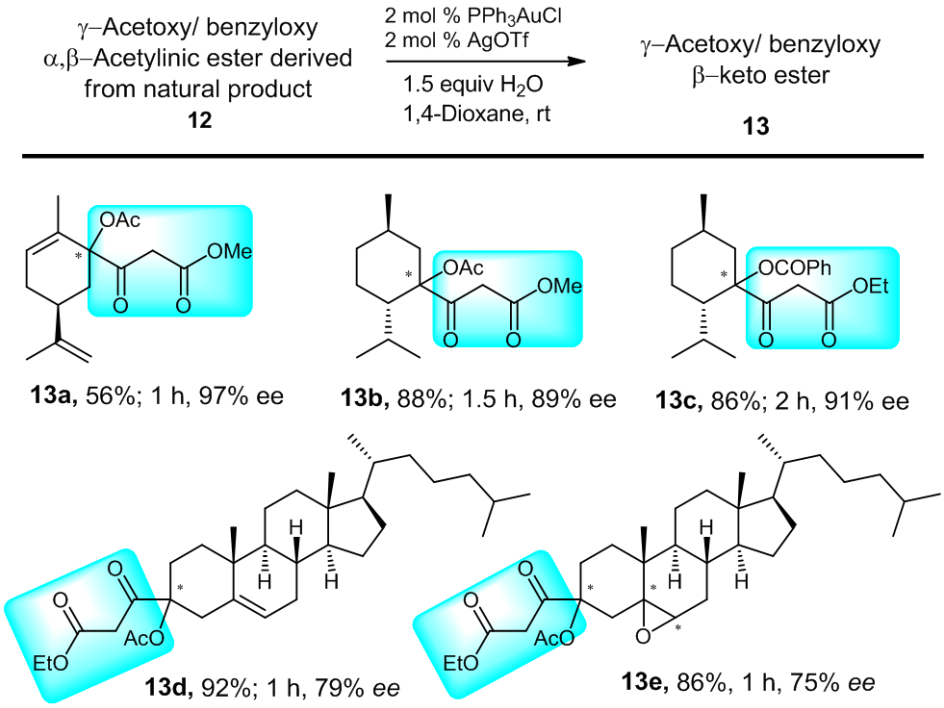
In order to examine the chirality retention in the hydration process, enantio-enriched propargyl acetate **10** was prepared according to the literature procedure.[18] Hydration of enantio-enriched acetate **10** (70% *ee*) under the standard conditions cleanly afforded **11** without any loss of the enantioselectivity (70% *ee*). Importantly, the hydration is not limited to the small scale (ca 100 mg) used for the scope and limitation studies described above as it could be conveniently performed on a 2.5 gram scale in excellent yield, under the same standard conditions.

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



The late stage modifications of natural products is highly valuable in medicinal chemistry. We were delighted to figure out that the current hydration reaction was also capable of tolerating a wide range of γ-acetoxy/benzoyloxy α,β-alkynoate derived from the natural products (Scheme 8).[19] For instance, the derivatized γ-acetoxy acetylinic ester of (+)-carvone **12a** bearing an olefinic bond closer to the reaction site, was proved to be competent (56%). Notably, both γ-acetoxy/benzoyloxy acetylinic ester derived from (+)-menthone (**12b and 12c**) and cholesterol (**12d**) participated in the present transformation, highlighting the broad substrate scope and potential utility of this protocol. In addition, the oxiranyl derivative **12e** underwent the carbonyl assisted hydration in acceptable yield without the disturbance of epoxide ring.

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



13a, 56%; 1 h, 97% ee **13b,** 88%; 1.5 h, 89% ee **13c,** 86%; 2 h, 91% ee

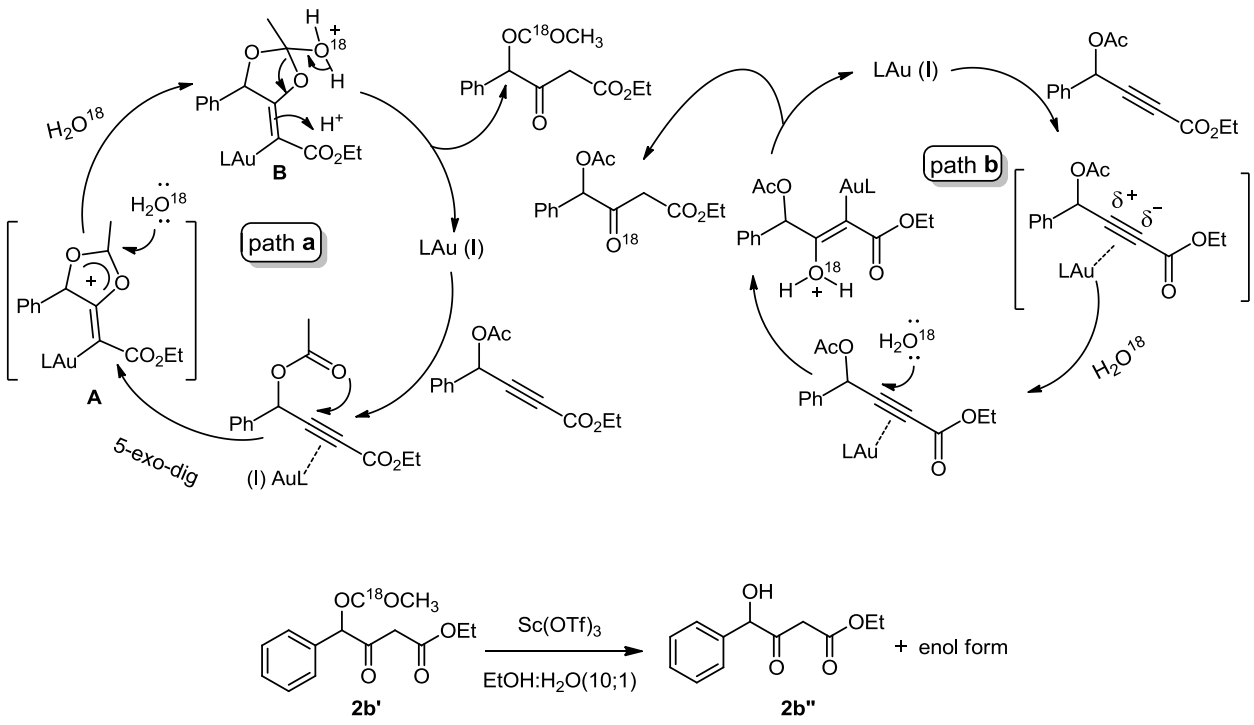
13d, 92%; 1 h, 79% *ee* **13e,** 86%, 1 h, 75% *ee*

[a]Reactions were carried out on a scale of 0.4 mmol of **12** in 1.5 mL of solvent under standard condition. [b]Yield of isolated product. [c]*mark in substrates represents the undetected stereocenter.

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 to the β-carbon which may be the result of strong electron withdrawing effect of the ester group as assumed by Hammond's group (Scheme 10**,** path b).[8e]

Scheme 10. Plausible Mechanisim for the Formation of Hydration Product



In contrast to the aforementioned pathway, an alternative plausible route is the 5-*exo* dig attack of carbonyl oxygen of the γ-carbon to generate a 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, 20] 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 also to determine the source of carbonyl oxygen, the reaction was performed under the present reaction condition using 5 mmol of H_2O^{18} under anhydrous condition. Analysis of the isolated produt by HRMS(ESI) reveals a peak at 289.0931 $[M + Na]^+$, 2 mass unit more than the regular hydration product **2b**. However, deacetylation[21] 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 γ-acetoxy β-keto esters that relies on simultaneous oxygen transposition from a neighboring carboxylate group to the C≡C bond and water to carboxylate group in good to excellent yields. The mild catalytic conditions readily tolerate remote sensitive functional groups and protecting groups as well. This method provides an efficient masking of easily modifiable electrophilic and nucleophilic carbons as acetylinic ester, offering a practical solution to construct 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 are 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 by 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} degcm^{2}g^{-1}. Infrared spectra were recorded in $CHCl_3$/neat (as mentioned) and reported in wave number (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 nm and 254 nm; column, ATLANTIS C18 (4.6 × 150 mm, 5μ) and LUX AMISOSE (4.6 × 250 mm, 5μ); mobile phase, acetonitrile,

water, isopropanol and hexane; flow rate, 1 mL/min. ^{1}H NMR spectra were recorded at 300, 400, 500 and ^{13}C NMR spectra 75, 100, 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, br = broad.

Procedure for Synthesis of 1a and 3a (P-1)[22]

To a solution of 2-(prop-2-yn-1-yloxy)tetrahydro-2*H*-pyran **1a'"** (5.0 g, 35.71 mmol), *n*-BuLi (4.28 mL, 2.5 M in hexane, 35.71 mmol) was added dropwise using a syringe at −78 °C under nitrogen atmosphere and stirred at this temperature for 20 min. Then ethyl chloroformate (6.76 mL, 71.42 mmol) was added dropwise to this ylide solution. Reaction mixture was slowly (10 min) brought to room temperature and continued to stir until the complete consumption of alkyne (monitored by TLC). The reaction was quenched with saturated aqueous NH_4Cl solution (75 mL) and diluted with ethyl acetate (100 mL). The organic layer was separated and the aqueous layer 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 the crude ethyl 4-((tetrahydro-2*H*-pyran-2-yl)oxy)but-2-ynoate (**1a″**) (6.8 g, 90%) as a thick yellow liquid.

The crude THP-ether **1a″** obtained was treated with catalytic amount of PTSA in ethanol (30 mL) and stirred for 5 h. EtOH was then removed and the reaction was quenched with saturated aqueous $NaHCO_3$ 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 on purification by column chromatography (ethyl acetate/hexane = 1:4) afforded the ethyl 4-hydroxybut-2-ynoate (**1a′**) (3.36 g, 82%) as colorless oil.

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

Representative Procedure for Synthesis of Hydration precursors (P-2)

(a) General procedure for synthesis of secondary or tertiary γ-hydroxy α,β-acetylinic ester (P-2a)[23]

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 same temperature and was allowed to warm to 23 °C. After complete consumption of the starting material (monitored by TLC), saturated aqueous 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 hydration precursor by following the procedures as described below.

(b) General procedure for acetylation of primary, secondary or tertiary γ-hydroxy α,β-acetylinic ester (P-2b)[24]

To a solution of the crude propargyl alcohol (1.0 mmol) in anhydrous CH_2Cl_2 (15 mL) was 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 resultant mixture was stirred at room temperature until the complete consumption of starting material (monitored by TLC). Then the reaction mixture was washed with brine solution (2 × 15 mL), 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 ester (P-2c)[24]

To a solution of the crude propargyl alcohol (1.0 mmol) in anhydrous CH_2Cl_2 (15 mL) was added triethylamine (0.28 mL, 2.0 mmol), benzoyl chloride (1.74 mL, 1.5 mmol), and DMAP (catalytic) under nitrogen atmosphere at 0 °C. The resultant 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 ester (P-2d)[25]

To a solution of the crude propargyl alcohol (1.0 mmol) in anhydrous CH_2Cl_2 (15 mL) was added triethylamine (0.28 mL, 2.0 mmol), followed by acryloyl chloride (0.16 mL, 2.0 mmol), and DMAP (cat.) under a nitrogen atmosphere at 0 °C. The resultant 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 ester (P-2e)[26]

(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), was 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 resultant 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 the 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) ν_{max} 2954, 2852, 2249, 1763, 1740, 1376, 1244, 1056, 772 cm^{-1}; ^1H NMR (300 MHz, $CDCl_3$) δ 4.79 (s, 2H), 4.25 (q, J = 7.2 Hz, 2H), 2.13 (s, 3H), 1.32 (t, J = 7.2 Hz, 3H) ppm; ^{13}C NMR (75 MHz, $CDCl_3$) δ 169.7, 152.7, 80.7, 77.8, 62.2, 51.4, 20.4, 13.8 ppm; HRMS (EI-TOF) $[M]^+$ calcd. for $C_8H_{10}O_4$ 170.0574; found: 170.0565.

Ethyl 4-acetoxy-4-phenylbut-2-ynoate (1b): Following the general procedure P-2a and 2b, **1b** (236 mg, 73%) was obtained from benzaldehyde as light yellow liquid. R_f 0.52 (9:1 hexane/EtOAc); IR (neat) ν_{max} 2955, 2924, 2853, 2244, 1744, 1711, 1368, 1216, 1054, 771 cm^{-1};

^{1}H NMR (300 MHz, $CDCl_3$) δ 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) ppm; ^{13}C NMR (75 MHz, $CDCl_3$) δ 169.2, 152.8, 134.9, 129.3, 128.7, 127.6, 82.6, 78.1, 64.6, 62.2, 20.6, 13.8 ppm; 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 the general procedure P-2a and 2b, **1c** (210 mg, 79%) was obtained from 4-methoxybenzaldehyde as yellow liquid. R_f 0.65 (9:1 hexane/EtOAc); IR (neat) ν_{max} 2926, 2949, 2376, 2246, 1747, 1720, 1515, 1217, 959, 837 cm^{-1}; ^{1}H NMR (500 MHz, $CDCl_3$) δ 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) ppm; ^{13}C NMR (75 MHz, $CDCl_3$) δ 169.4, 160.5, 153.4, 129.4, 127.2. 114.2, 83.5, 77.7, 64.5, 55.3, 52.8, 20.8 ppm; 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 the general procedure P-2a and 2b, **1d** (220 mg, 72%) was obtained from 2-bromobenzaldehyde as yellow liquid. R_f 0.55 (9:1 hexane/EtOAc); IR (neat) ν_{max} 2984, 2246, 1736, 1372, 1235, 1043, 772 cm^{-1}; ^{1}H NMR (500 MHz, $CDCl_3$) δ 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) ppm; ^{13}C NMR (125 MHz, $CDCl_3$) δ 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 ppm; 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 the general procedure P-2a and 2b, **1e** (150 mg, 76%) was obtained from 4-fluorobenzaldehyde as yellow liquid. R_f 0.56 (9:1 hexane/EtOAc); IR (neat) ν_{max} 3009, 2957, 2246, 1748, 1722, 1511, 1436, 1259, 1219, 1016, 751 cm^{-1}; ^{1}H NMR (500 MHz, $CDCl_3$) δ 7.50-7.46 (m, 2H), 7.11-7.05 (m, 2H), 6.50 (s, 1H), 3.79 (s,

3H), 2.11 (s, 3H) ppm; ^{13}C NMR (75 MHz, $CDCl_3$) δ 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 ppm; 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 the general procedure P-2a and 2b, **1f** (180 mg, 69%) was obtained from 3-nitroacetphenone as yellow liquid. R_f 0.35 (9:1 hexane/EtOAc); IR (neat) ν_{max} 3083, 2957, 2852, 2243, 1752, 1722, 1524, 1067, 857, 751 cm^{-1}; ^{1}H NMR (500 MHz, $CDCl_3$) δ 8.28-8.20 (m, 2H), 7.76-7.66 (m, 2H), 3.83 (s, 3H), 2.12 (s, 3H), 1.92 (s, 3H) ppm; ^{13}C NMR (75 MHz, $CDCl_3$) δ 168.3, 156.2, 147.8, 147.5, 125.7, 123.9, 84.1, 79.3, 73.7, 52.9, 31.0, 21.1 ppm; 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 the general procedure P-2a and 2b, **1g** (185 mg, 74%) was obtained from 3,4,5-trimethoxybenzaldehyde as colorless liquid. R_f 0.62 (9:1 hexane/EtOAc); IR (neat) ν_{max} 2929, 2851, 2377, 2313, 1749, 1729, 1510, 1225, 922 cm^{-1}; ^{1}H NMR (300 MHz, $CDCl_3$) δ 6.72 (s, 2H), 6.45 (s, 1H), 3.89 (s, 6H), 3.85 (s, 3H), 3.80 (s, 3H), 2.14 (s, 3H) ppm; ^{13}C NMR (75 MHz, $CDCl_3$) δ 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 ppm; 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 the general procedure P-2a and 2b, **1h** (160 mg, 70%) was obtained from 4-bromobenzo[d][1,3]dioxole-5-carbaldehyde as colorless liquid. R_f 0.48 (9:1 hexane/EtOAc); IR (neat) ν_{max} 2925, 2851, 2376, 2315, 1752, 1719, 1480, 1254, 1212, 1036, 939 cm^{-1}; ^{1}H NMR (500 MHz, $CDCl_3$) δ 7.16 (s, 1H), 7.02 (s, 1H), 6.73 (s, 1H), 6.03 (s, 2H), 3.79 (s, 3H), 2.19 (s, 3H) ppm; ^{13}C NMR (125 MHz, $CDCl_3$) δ 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 ppm; 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 the general procedure 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) ν_{max} 2923, 2852, 2377, 1743, 1719, 1447, 1219, 952 cm^{-1}; ^1H NMR (500 MHz, $CDCl_3$) δ 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) ppm; ^{13}C NMR (125 MHz, $CDCl_3$) δ 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 ppm; 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 the general procedure 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) ν_{max} 2923, 2246, 1732, 1492, 1220, 1043, 772, 685 cm^{-1}; ^1H NMR (300 MHz, $CDCl_3$) δ 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) ppm; ^{13}C NMR (75 MHz, $CDCl_3$) δ 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 ppm; 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 the general procedure P-2a and 2b, **1k** (220 mg, 72%) was obtained from 2-(*tert*-butyldimethylsilyloxy)benzaldehyde as a colorless liquid. R_f 0.65 (9:1 hexane/EtOAc); IR (neat) ν_{max} 2955, 2859, 2245, 1720, 1215, 1017, 747 cm^{-1}; ^1H NMR (300 MHz, $CDCl_3$) δ 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) ppm; ^{13}C NMR (75 MHz, $CDCl_3$) δ 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 ppm; 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 the general procedure 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) ν_{max} 3021, 2956, 2243, 1731, 1374, 1256, 1045, 744 cm^{-1}; ^{1}H NMR (300 MHz, $CDCl_3$) δ 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) ppm; ^{13}C NMR (75 MHz, $CDCl_3$) δ 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 ppm; 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 the general procedure 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) ν_{max} 3033, 2938, 2247, 1752, 1716, 1373, 753, 702 cm^{-1}; ^{1}H NMR (300 MHz, $CDCl_3$) δ 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) ppm; ^{13}C NMR (75 MHz, $CDCl_3$) δ 168.3, 153.6, 140.8, 128.5, 128.2, 124.6, 85.9, 78.7, 74.5, 52.7, 31.1, 21.4 ppm; 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 the general procedure 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) ν_{max} 2924, 2243, 1734, 1728, 1453, 1370, 1219, 1096, 772 cm^{-1}; ^{1}H NMR (300 MHz, $CDCl_3$) δ

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) ppm; ^{13}C NMR (75 MHz, $CDCl_3$) δ 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 ppm; 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 the general procedure 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) ν_{max} 3119, 2926, 2247, 1751, 1725, 1514, 1268, 1215, 1016, 970 cm^{-1}; ^{1}H NMR (300 MHz, $CDCl_3$) δ 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) ppm; ^{13}C NMR (75 MHz, $CDCl_3$) δ 169.2, 153.1, 137.1, 128.3, 126.8, 82.1, 77.2, 59.8, 52.9, 20.6 ppm; 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 the general procedure 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) ν_{max} 2924, 2856, 2245, 1742, 1731, 1492, 1220, 1033, 772, 685 cm^{-1}; ^{1}H NMR (300 MHz, $CDCl_3$) δ 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) ppm; ^{13}C NMR (75 MHz, $CDCl_3$) δ 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 ppm; HRMS (ESI-TOF) m/z: $[M + Na]^+$ calcd for $C_{15}H_{16}O_4Na$ 283.0941; found: 283.0934.

(6*R*)-Ethyl 4-acetoxy-6-(*tert*-butyldimethylsilyloxy)-8-phenyloct-2-ynoate (1q)[27]: Following the general procedure P-2a and 2b, **1p** (222 mg, 71%) was obtained as an inseparable diastereomeric mixture (*dr* = 7:3, determined by ^{1}H 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) ν_{max} 2929, 2856, 2243, 1751, 1717, 1369, 1255, 1022, 836 cm^{-1}; ^{1}H NMR (300 MHz,

$CDCl_3$) δ 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) ppm; ^{13}C NMR (75 MHz, $CDCl_3$) δ 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 ppm; 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 the general procedure 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) ν_{max} 2957, 2929, 2856, 2376, 1750, 1721, 1431, 1258, 1221, 1108, 741 cm^{-1}; ^{1}H NMR (300 MHz, $CDCl_3$) δ 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) ppm; ^{13}C NMR (75 MHz, $CDCl_3$) δ 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 ppm; 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 the 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) ν_{max} 2977, 2931, 2249, 1741, 1719, 1462, 1252, 1137, 772 cm^{-1}; ^{1}H NMR (300 MHz, $CDCl_3$) δ 4.78 (s, 2H), 4.25 (q, *J* = 6.8 Hz, 2H), 1.32 (t, *J* = 6.8 Hz, 3H), 1.23 (s, 9H) ppm; ^{13}C NMR (75 MHz, $CDCl_3$) δ 177.2, 152.7, 80.9, 77.7, 62.0, 51.2, 38.6, 26.9, 26.4, 13.8 ppm; 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 the 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) ν_{max} 2926, 2854, 2244, 1636, 1385, 1286, 1025, 708 cm^{-1}; ^{1}H NMR (300 MHz, $CDCl_3$) δ 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) ppm; ^{13}C NMR (75 MHz, $CDCl_3$) δ 165.3, 152.7, 133.4, 130.4, 129.7, 128.7, 128.4, 80.7, 78.0, 62.2, 51.7, 13.8 ppm; 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), was added triethylamine (0.48 mL, 3.12 mmol), propionic anhydride (0.39 mL, 3.12 mmol), and DMAP (catalytic) under nitrogen atmosphere at 0 °C. The resultant mixture was stirred for 1 h and then quenched with aqueous NH_4Cl solution (15 mL). The organic layer was separated and the aqueous layer 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 the propionate ester **3aiii** as colorless liquid (270 mg, 94%). R_f 0.55 (9:1 hexane/EtOAc); IR (neat) ν_{max} 2923, 2856, 2241, 1756, 1724, 1434, 1219, 1062, 772 cm^{-1}; ^{1}H NMR (500 MHz, $CDCl_3$) δ 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) ppm; ^{13}C NMR (75 MHz, $CDCl_3$) δ 173.2, 152.8, 80.9, 77.8, 62.2, 51.1, 27.1, 13.9, 8.8 ppm; 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 the general procedure P-2a and 2e, **3b** (245 mg, 72%)was obtained from 5-(4-methoxybenzyloxy)pentanal as pale yellow liquid. R_f 0.60 (9:1 hexane/EtOAc); IR (neat) ν_{max} 2934, 2857, 2243, 1717, 1613, 1250, 1143, 751 cm^{-1}; ^{1}H NMR (300 MHz, $CDCl_3$) δ 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) ppm;

^{13}C NMR (75 MHz, $CDCl_3$) δ 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 ppm; 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 the general procedure 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) ν_{max} 2993, 2922, 2852, 2241, 1764, 1717, 1434, 1242, 1062, 772 cm^{-1}; ^{1}H NMR (300 MHz, $CDCl_3$) δ 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) ppm; ^{13}C NMR (75 MHz, $CDCl_3$) δ 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 ppm; 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 procedure 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) ν_{max} 2924, 2856, 2239, 1756, 1721, 1434, 1256, 1220, 1130, 1062, 773 cm^{-1}; ^{1}H NMR (500 MHz, $CDCl_3$) δ 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) ppm; ^{13}C NMR (125 MHz, $CDCl_3$) δ 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 ppm; 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 procedure 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) ν_{max} 3117, 2937, 2377, 2314, 1786, 1693, 1550, 1514, 1216, 772 cm^{-1};

^{1}H NMR (500 MHz, $CDCl_3$) δ 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) ppm; ^{13}C NMR (75 MHz, $CDCl_3$) δ 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 ppm; 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 procedure 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) ν_{max} 3120, 2929, 2379, 1752, 1693, 1551, 1513, 772 cm^{-1}; ^{1}H NMR (500 MHz, $CDCl_3$) δ 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) ppm; ^{13}C NMR (75 MHz, $CDCl_3$) δ 164.0, 153.4, 131.0, 128.7, 86.4, 78.2, 74.2, 62.0, 36.2, 24.9, 22.1, 14.0 ppm; 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 procedure 2a and 2c, **3g** (180 mg, 72%) was obtained from cyclohexanone as colorless liquid. R_f 0.52 (9:1 hexane/EtOAc); IR (neat) ν_{max} 2981, 2938, 2863, 2236, 1789, 1720, 1451, 1245, 1102, 710 cm^{-1}; ^{1}H NMR (300 MHz, $CDCl_3$) δ 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) ppm; ^{13}C NMR (75 MHz, $CDCl_3$) δ 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 ppm; 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 the similar procedure as that followed for **1a"**, **5a** (172 mg, 78%) was synthesized from prop-2-ynyl benzoate and Boc-anhydride

(instead of ethylchloroforamte) as a light yellow liquid. R_f 0.63 (9: 1 hexane/EtOAc); IR (neat) ν_{max} 2981, 2251, 1729, 1711, 1514, 1261, 1158, 712 cm^{-1}; ^1H NMR (500 MHz, $CDCl_3$) δ 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) ppm; ^{13}C NMR (75 MHz, $CDCl_3$) δ 165.6, 151.9, 133.6, 130.0, 129.9, 129.0, 84.1, 79.36, 78.5, 51.9, 28.0 ppm; 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 the similar procedure as that followed for **1a"**, **5b** (160 mg, 82%) was synthesized from prop-2-ynyl benzoate and benzylchloroformate (instead of ethylchloroforamte) as a colorless liquid. R_f 0.61 (9: 1 hexane/EtOAc); IR (neat) ν_{max} 3036, 2956, 2246, 1755, 1718, 1240, 1069 cm^{-1}; ^1H NMR (500 MHz, $CDCl_3$) δ 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) ppm; ^{13}C NMR (100 MHz, $CDCl_3$) δ 165.5, 134.4, 133.5, 129.8, 128.6, 128.4, 81.5, 77.0, 67.8, 51.7 ppm; 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 the similar procedure as that followed for **1a"**, **5c** (150 mg, 90%) was synthesized from prop-2-ynyl benzoate and acetic anhydride (instead of ethylchloroforamte) as a colorless liquid. IR (neat) ν_{max} 2938, 2237, 1716, 1608, 1276, 1113, 712 cm^{-1}; R_f 0.56 (9: 1 hexane/EtOAc); ^1H NMR (500 MHz, $CDCl_3$) δ 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) ppm; ^{13}C NMR (100 MHz, $CDCl_3$) δ 183.6, 165.5, 133.5, 130.0, 129.8, 128.9, 128.4, 85.4, 84.9, 51.8, 32.4 ppm; 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): The skipped diyne **7d** was prepared according to the literature procedure[28] 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 dark yellow gel (392

mg, 70%). R_f 0.50 (9:1 hexane/EtOAc); IR (neat) ν_{max} 3202, 2989, 2853, 2246, 1808, 1719, 1614, 1449, 1284, 1168, 711 cm^{-1}; ^1H NMR (300 MHz, $CDCl_3$) δ 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) ppm; ^{13}C NMR (75 MHz, $CDCl_3$) δ 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 ppm; 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[29] (with minor modification; 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) ν_{max} 2945, 2237, 1748, 1717, 1441, 1369, 1229, 1021, 751 cm^{-1}; ^1H NMR (500 MHz, $CDCl_3$) δ 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) ppm; ^{13}C NMR (125 MHz, $CDCl_3$) δ 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 ppm; 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[29] (with minor modification; 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) ν_{max} 2928, 2248, 1755, 1717, 1370, 1256, 1216, 1022, 751 cm^{-1}; ^1H NMR (300 MHz, $CDCl_3$) δ 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), 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) ppm; ^{13}C NMR (75 MHz, $CDCl_3$) δ 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 ppm; 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) The chiral acetae **10** was obtained by following literature procedure[30] 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) ν_{max} 2985, 2938, 2246, 1750, 1716, 1370, 1222, 1022, 702 cm^{-1}; ^1H NMR (500 MHz, $CDCl_3$) δ 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) ppm; ^{13}C NMR (125 MHz, $CDCl_3$) δ 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 ppm; HRMS (ESI-TOF) m/z: $[M + Na]^+$ calcd for $C_{15}H_{16}O_4Na$ 283.0944; found: 283.0941.

Methyl 3-((5*R*)-1-acetoxy-2-methyl-5-(prop-1-en-2-yl)cyclohex-2-enyl)propiolate (12a): Following the literature procedure (with minor modification on the use of ylide; see P-2a)[31], (*S*)-(+)-carvone gave two separable diastereomeric propargylic alcohols. Only the major isomer was subjected to acetylation by 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) ν_{max} 2954, 2925, 2234, 1748, 1719, 1435, 1223, 1017, 772 cm^{-1}; ^1H NMR (300 MHz, $CDCl_3$) δ 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) ppm; ^{13}C NMR (125 MHz, $CDCl_3$) δ 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 ppm; HRMS (ESI-TOF) m/z: $[M + Na]^+$ calcd for $C_{16}H_{20}O_4Na$ 299.1253; found: 299.1254.

Methyl 3-((2*S*,5*R*)-1-acetoxy-2-isopropyl-5-methylcyclohexyl)propiolate (12b) Following the literature procedure (with minor modification on the use of base; see P-2a)[32] (+)-menthone gave two separable diasetreomeric propargylic alcohols. Only the major isomer was subjected to

acetylation by 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) ν_{max} 2957, 2931, 2875, 2234, 1748, 1718, 1436, 1229, 1016, 751 cm^{-1}; ^1H NMR (300 MHz, $CDCl_3$) δ 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) ppm; ^{13}C NMR (125 MHz, $CDCl_3$) δ 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 ppm; HRMS (ESI-TOF) m/z: $[M + Na]^+$ calcd for $C_{16}H_{24}O_4Na$ 303.1566; found: 303.1567.

(2*R*,5*S*)-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 by following P-2c to obtain **12c** (160 mg, 60%)as thick yellow liquid. R_f 0.64 (9:1 hexane/EtOAc); $[\alpha]_D^{28}$ = –16.3 (*c* 1.0, $CHCl_3$); IR (neat) ν_{max} 2931, 2858, 2245, 1738, 1717, 1452, 1314, 1027, 705 cm^{-1}; ^1H NMR (500 MHz, $CDCl_3$) δ 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) ppm; ^{13}C NMR (125 MHz, $CDCl_3$) δ 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 ppm; HRMS (ESI-TOF) m/z: $[M + Na]^+$ calcd for $C_{22}H_{28}O_4Na$ 379.1879; found: 379.1887.

Ethyl 3-((8*S*,9*S*,10*R*,13*R*,14*S*,17*R*)-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-1*H*-cyclopenta[a]phenanthren-3-yl) propiolate (12d): The major isomer obtained by the reaction of cholesterone[33] 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) ν_{max} 2934, 2869, 2237, 1748, 1716, 1466, 1368, 1228, 1021, 752 cm^{-1}; ^1H NMR (500 MHz, $CDCl_3$) δ 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) ppm; ^{13}C NMR (125 MHz, $CDCl_3$) δ 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 ppm; 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-((8*S*,9*S*,10*R*,13*R*,14*S*,17*R*)-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-1*H*-cyclopenta[a] phenanthren-3-yl)propiolate (12e): Following the general procedure P-2a, cholesterone was converted to column separable diastereomeric γ-hydroxy α,β-alkynoates. The major isomer was then followed an epoxidation reaction with *m*CPBA to give two easily separable diastereomeric oxiranyls. Finally, the acetylation of the major oxiranyl was carried out by following procedure P-2b to give the 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) ν_{max} 2951, 2870, 2238, 1751, 1719, 1459, 1368, 1226, 1019, 750 cm^{-1}; ^1H NMR (500 MHz, $CDCl_3$) δ 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) ppm; ^{13}C NMR (125 MHz, $CDCl_3$) δ 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 ppm; 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), Ph_3PAuCl (5 mg, 0.01 mmol) and AgOTf (2.6 mg, 0.01 mmol) were added at ambient temperature. Distilled water (13.5 μL, 1.5 mmol) was then added to the above reaction mixture at the same temperature. The resulting reaction mixture was stirred for the time 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 get the hydration product along with trace amount of the corresponding enolic compound.

Ethyl 4-acetoxy-3-oxobutanoate (**2a**)**:** The general procedure (P-3) was followed by 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) ν_{max} 2959, 1747, 1651, 1375, 1232, 1034, 845 cm^{-1}; ^1H NMR (300 MHz, $CDCl_3$) δ 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) ppm; ^{13}C NMR (75 MHz, $CDCl_3$) δ 196.5, 169.9, 166.2, 67.7, 61.6, 46.0. 20.2, 13.9 ppm; 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**)**:** The general procedure (P-3) was followed by 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) ν_{max} 3020,2956, 2854, 1742, 1710, 1368, 1215, 929, 742 cm^{-1}; ^1H NMR (500 MHz, $CDCl_3$) δ 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) ppm; ^{13}C NMR (125 MHz, $CDCl_3$) δ 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 ppm; 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): The general procedure (P-3) was followed by 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. R_f 0.65 (9:1 hexane/EtOAc); IR (neat) ν_{max} 2956, 2851, 1746, 1721, 1514, 1229, 1030, 833 cm^{-1}; ^{1}H NMR (300 MHz, $CDCl_3$) δ 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) ppm; ^{13}C NMR (75 MHz, $CDCl_3$) δ 196.4, 170.1, 166.5, 129.9, 129.1, 124.1, 114.5, 79.6, 55.3, 52.4, 45.6, 20.6 ppm; 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): The general procedure (P-3) was followed by 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) ν_{max} 3023, 2955, 2926, 1731, 1220, 1043, 751 cm^{-1}; ^{1}H NMR (500 MHz, $CDCl_3$) δ 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) ppm; ^{13}C NMR (125 MHz, $CDCl_3$) δ 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 ppm; 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): The general procedure (P-3) was followed by 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) ν_{max} 2957, 2853, 1739, 1607, 1327, 1225, 1039, 836 cm^{-1};

^{1}H NMR (500 MHz, $CDCl_3$) δ 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) ppm; ^{13}C NMR (75 MHz, $CDCl_3$) δ 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 ppm; 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): The general procedure (P-3) was followed by 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) ν_{max} 3114, 2956, 1732, 1716, 1435, 1267, 1014, 857 cm^{-1}; ^{1}H NMR (300 MHz, $CDCl_3$) δ 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) ppm; ^{13}C NMR (75 MHz, $CDCl_3$) δ 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 ppm; 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): The general procedure (P-3) was followed by 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) ν_{max} 2960, 2376, 2315, 1751, 1714, 1513, 1217, 1129, 772 cm^{-1}; ^{1}H NMR (300 MHz, $CDCl_3$) δ 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) ppm; ^{13}C NMR (75 MHz, $CDCl_3$) δ 196.0, 169.8, 166.4, 153.5, 138.7, 105.3, 79.8, 60.6, 56.0, 52.3, 45.4, 20.4 ppm; 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): The general procedure (P-3) was followed by 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) ν_{max} 2992, 2851, 2377, 2312, 1751, 1729, 1513, 1036, 772 cm^{-1}; ^1H NMR (300 MHz, $CDCl_3$) δ 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) ppm; ^{13}C NMR (125 MHz, $CDCl_3$) δ 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 ppm; 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): The general procedure (P-3) was followed by 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) ν_{max} 2923, 2851, 1734, 1600, 1492, 1371, 1220, 927, 772 cm^{-1}; ^1H NMR (300 MHz, $CDCl_3$) δ 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) ppm; ^{13}C NMR (125 MHz, $CDCl_3$) δ 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 ppm; 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): The general procedure (P-3) was followed by 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) ν_{max} 3276, 2923, 2853, 1738, 1731, 1492, 1373, 1221, 1020, 772 cm^{-1}; ^1H NMR (300 MHz, $CDCl_3$) δ 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) ppm; ^{13}C NMR (75 MHz, $CDCl_3$) δ 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 ppm; 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): The general procedure (P-3) was followed by 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) ν_{max} 2956, 2924, 1728, 1485, 1373, 1216, 1020, 751 cm^{-1}; ^1H NMR (300 MHz, $CDCl_3$) δ 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) ppm; ^{13}C NMR (75 MHz, $CDCl_3$) δ 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 ppm; 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): The general procedure (P-3) was followed by 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) ν_{max} 2954, 2854, 1744, 1602, 1236, 993, 757 cm^{-1}; ^1H NMR (300 MHz, $CDCl_3$) δ 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) ppm; ^{13}C NMR (75 MHz, $CDCl_3$) δ 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 ppm; 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): The general procedure (P-3) was followed by 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) ν_{max} 2927, 2856, 1742, 1639, 1373, 1034, 701 cm^{-1}; ^1H NMR (300 MHz, $CDCl_3$) δ 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) ppm; ^{13}C NMR (75 MHz, $CDCl_3$) δ 197.6, 170.1, 166.8, 137.3, 128.8, 128.4, 124.9, 87.3, 52.2, 42.8, 22.9, 21.2 ppm; 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):** The general procedure (P-3) was followed by 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) ν_{max} 3118, 2924, 1748, 1676, 1728, 1516, 1091, 772 cm^{-1}; ^1H NMR (300 MHz, $CDCl_3$) δ 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) ppm; ^{13}C NMR (75 MHz, $CDCl_3$) δ 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 ppm; 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): The general procedure (P-3) was followed by using **1o** and the reaction mixture was stirred at room temperature for 1.5 h. Purification by column chromatography afforded **2o** (112 mg, 88% yield) as a light yellow liquid. R_f 0.48 (9:1 hexane/EtOAc); IR (neat) ν_{max} 3119, 2925, 2377, 1749, 1695, 1549, 1516, 1221, 1020, 772 cm^{-1}; ^1H NMR (300 MHz, $CDCl_3$) δ 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) ppm; ^{13}C NMR (75 MHz, $CDCl_3$) δ 195.2, 169.8, 166.4, 133.7, 128.9, 128.2, 127.4, 74.9, 52.5,

45.5, 20.5 ppm; 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): The general procedure (P-3) was followed by 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) ν_{max} 2924, 2854, 1742, 1491, 1220, 773, 686 cm^{-1}; ^1H NMR (300 MHz, $CDCl_3$) δ 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) ppm; ^{13}C NMR (75 MHz, $CDCl_3$) δ 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 ppm; HRMS (ESI-TOF) m/z: $[M + Na]^+$ calcd for $C_{15}H_{18}O_5Na$ 301.1051; found: 301.1040.

(6*R*)-Ethyl 4-acetoxy-6-(*tert*-butyldimethylsilyloxy)-3-oxo-8-phenyl octanoate (2q): The general procedure (P-3) was followed by 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) ν_{max} 2956, 2929, 2857, 1748, 1651, 1492, 1463, 1372, 1231, 1093, 775 cm^{-1}; ^1H NMR (300 MHz, $CDCl_3$) δ 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) ppm; ^{13}C NMR (75 MHz, $CDCl_3$) δ 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 ppm; 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): The general procedure (P-3) was followed by 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) ν_{max} 3138, 2928, 2377, 1751, 1729, 1550, 1514, 1109, 707 cm^{-1}; ^1H NMR (300 MHz, $CDCl_3$) δ 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) ppm; ^{13}C NMR (75 MHz, $CDCl_3$) δ 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 ppm; 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): The general procedure (P-3) was followed by 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) ν_{max} 2973, 2946, 2249, 1756, 1733, 1479, 1220, 772 cm^{-1}; ^1H NMR (300 MHz, $CDCl_3$) δ 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) ppm; ^{13}C NMR (75 MHz, $CDCl_3$) δ 196.8, 177.4, 166.2, 67.6, 61.5, 45.8, 38.5, 26.9, 13.9 ppm; 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): The general procedure (P-3) was followed by 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); ν_{max} 2927, 2856, 1634, 1385, 1271, 1026, 708 cm^{-1}; ^1H NMR (300 MHz, $CDCl_3$) δ 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) ppm; ^{13}C NMR (75 MHz, $CDCl_3$) δ 196.8, 166.3, 165.5, 133.4, 129.7, 128.7, 128.3, 68.1, 61.5, 46.0, 13.8 ppm; 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): The general procedure (P-3) was followed by 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) ν_{max} 2923, 2852, 2244, 1742, 1431, 1220, 1064, 773 cm^{-1}; ^1H NMR (300 MHz, $CDCl_3$) δ 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) ppm; ^{13}C NMR (75 MHz, $CDCl_3$) δ 196.8, 173.4, 166.3, 67.6, 61.6, 46.0, 26.9, 13.9, 8.8 ppm; 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): The general procedure (P-3) was followed by 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) ν_{max} 2935, 2867, 1732, 1731, 1514, 1248, 1151, 820 cm^{-1}; ^1H NMR (300 MHz, $CDCl_3$) δ 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) ppm; ^{13}C NMR (75 MHz, $CDCl_3$) δ 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 ppm; 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): The general procedure (P-3) was followed by 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) ν_{max} 2993, 2923, 2853, 2241, 1762, 1720, 1450, 1377, 1243, 1058, 709 cm^{-1}; ^1H NMR (300 MHz, $CDCl_3$) δ 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) ppm; ^{13}C NMR (75 MHz, $CDCl_3$) δ 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 ppm; 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): The general procedure (P-3) was followed by 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) ν_{max} 2957, 2853, 1728, 1721, 1436, 1259, 1220, 1136, 1033, 773 cm^{-1}; ^{1}H NMR (500 MHz, $CDCl_3$) δ 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) ppm; ^{13}C NMR (75 MHz, $CDCl_3$) δ 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 ppm; 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): The general procedure (P-3) was followed by using **3e** and the reaction mixture was stirred at 10 ^{o}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) ν_{max} 3118, 2927, 1753, 1728, 1550, 1515, 1184, 772 cm^{-1}; ^{1}H NMR (500 MHz, $CDCl_3$) δ 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) ppm; ^{13}C NMR (125 MHz, $CDCl_3$) δ 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 ppm; 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): The general procedure (P-3) was followed by using **3f** and the reaction mixture was stirred at 10 ^{o}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) ν_{max} 2924, 2377, 1752, 1693, 1412, 1219, 773 cm^{-1}; ^{1}H NMR (300 MHz, $CDCl_3$) δ 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) ppm; ^{13}C NMR (75 MHz, $CDCl_3$) δ 201.3, 167.2, 165.1, 132.2, 127.8, 85.4, 61.3, 42.9, 30.6, 24.9, 21.2, 14.1 ppm; 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): The general procedure (P-3) was followed by 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) ν_{max} 2931, 2860, 1748, 1701, 1220, 771 cm^{-1}; ^{1}H NMR (300 MHz, $CDCl_3$) δ 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) ppm; ^{13}C NMR (75 MHz, $CDCl_3$) δ 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 ppm; 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): The general procedure (P-3) was followed by 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) ν_{max} 2980, 2933, 1726, 1655, 1275, 712 cm^{-1}**;** R_f 0.63 (9: 1 hexane/EtOAc); ^{1}H NMR (300 MHz, $CDCl_3$) δ 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) ppm; ^{13}C NMR (75 MHz, $CDCl_3$) δ 197.3, 165.6, 133.6, 129.9, 129.0, 128.5, 82.7, 68.3, 47.6, 27.9 ppm; 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): The general procedure (P-3) was followed by 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) ν_{max} 3067, 2958, 1729, 1453, 1246, 1070, 749 cm^{-1}**;** R_f 0.51 (9: 1 hexane/EtOAc); ^{1}H NMR (400 MHz, $CDCl_3$) δ 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) ppm; ^{13}C NMR (100 MHz, $CDCl_3$) δ 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 ppm; 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): The general procedure (P-3) was followed by using **5c** and the reaction mixture was stirred at room temprature 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) ν_{max} 3436, 2934, 1727, 1603, 1275, 712 cm^{-1}; ^{1}H NMR (300 MHz, $CDCl_3$) δ 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) ppm; ^{13}C NMR (125 MHz, $CDCl_3$) δ 190.6, 188.97,165.7, 133.5, 129.8, 129.2, 128.2, 96.8, 65.0, 24.0 ppm; 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): The general procedure (P-3) was followed by using **7d** and the reaction mixture was stirred at 10 ^oC 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) ν_{max} 2955, 2926, 2853, 2243, 1727, 1601, 1451, 1263, 1020, 758 cm^{-1};

^{1}H NMR (300 MHz, $CDCl_3$) δ 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) ppm; ^{13}C NMR (75 MHz, $CDCl_3$) δ 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 ppm; 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): The general procedure (P-3) was followed by 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) ν_{max} 2941, 1742, 1371, 1246, 1029, 627 cm^{-1}; ^{1}H NMR (300 MHz, $CDCl_3$) δ 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) ppm; ^{13}C NMR (75 MHz, $CDCl_3$) δ 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 ppm; 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): The general procedure (P-3) was followed by 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) ν_{max} 2924, 2853, 1736, 1718, 1373, 1217, 1024, 771 cm^{-1}; ^{1}H NMR (500 MHz, $CDCl_3$) δ 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) ppm; ^{13}C NMR (125 MHz, $CDCl_3$) δ 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 ppm; 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): The general procedure (P-3) was followed by 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) ν_{max} 2926, 2853, 1739, 1637, 1370, 1227, 1029, 700 cm^{-1}; ^1H NMR (300 MHz, $CDCl_3$) δ 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) ppm; ^{13}C NMR (125 MHz, $CDCl_3$) δ 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 ppm; HRMS (ESI-TOF) m/z: $[M + Na]^+$ calcd for $C_{15}H_{18}O_5Na$ 301.1051; found: 301.1046.

Methyl 3-((5*R*)-1-acetoxy-2-methyl-5-(prop-1-en-2-yl)cyclohex-2-enyl)-3-oxopropanoate (13a): The general procedure (P-3) was followed by 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) ν_{max} 2958, 2924, 2236, 1735, 1721, 1438, 1220, 1020, 772 cm^{-1}; ^1H NMR (300 MHz, $CDCl_3$) δ 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) ppm; ^{13}C NMR (75 MHz, $CDCl_3$) δ 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 ppm; HRMS (ESI-TOF) m/z: $[M + Na]^+$ calcd for $C_{16}H_{22}O_5Na$ 317.1359; found: 317.1356.

Methyl 3-((2*S*,5*R*)-1-acetoxy-2-isopropyl-5-methylcyclohexyl)-3-oxop ropanoate (13b): The general procedure (P-3) was followed by 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 yelllow liquid. R_f 0.48 (9:1 hexane/EtOAc); $[\alpha]_D^{28}$ = +17.1 (*c* 0.8, $CHCl_3$); IR (neat) ν_{max} 3117, 2926, 2855, 1750, 1728, 1693, 1551, 1514, 1025, 772 cm^{-1}; ^1H NMR (500 MHz, $CDCl_3$) δ 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) ppm; ^{13}C NMR (125 MHz, $CDCl_3$) δ 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 ppm; HRMS (ESI-TOF) m/z: $[M + Na]^+$ calcd for $C_{16}H_{26}O_5Na$ 321.1672; found: 321.1671.

(2*R*,5*S*)-1-(3-Ethoxy-3-oxopropanoyl)-2-isopropyl-5-methylcyclohexyl benzoate (13c): The general procedure (P-3) was followed by 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 yelllow liquid. R_f 0.60 (9:1 hexane/EtOAc); $[\alpha]_D^{28}$ = −8.0 (*c* 0.6, $CHCl_3$); IR (neat) ν_{max} 2957, 2871, 1747, 1716, 1645, 1314, 1275, 1110, 713 cm^{-1}; ^1H NMR (500 MHz, $CDCl_3$) δ 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) ppm; ^{13}C NMR (125 MHz, $CDCl_3$) δ 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 ppm; HRMS (ESI-TOF) m/z: $[M + Na]^+$ calcd for $C_{22}H_{30}O_5Na$ 397.1985; found: 397.1989.

Ethyl 3-((8*S*,9*S*,10*R*,13*R*,14*S*,17*R*)-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-1*H*-cyclopenta[a]phenanthren-3-yl)-3-oxopropanoate (13d): The general procedure (P-3) was followed by 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 yelllow liquid. R_f 0.64 (9:1 hexane/EtOAc); $[\alpha]_D^{28}$ =

−45.6 (*c* 1.1, $CHCl_3$); IR (neat) ν_{max} 2933, 2869, 2237, 1743, 1624, 1466, 1368, 1241, 1025, 769 cm^{-1}; ^1H NMR (500 MHz, $CDCl_3$) δ 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) ppm.ppm; ^{13}C NMR (125 MHz, $CDCl_3$) δ 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 ppm; 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-((8*S*,9*S*,10*R*,13*R*,14*S*,17*R*)-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-1*H*-cyclopenta[*a*] phenanthren-3-yl)-3-oxopropanoate (13e): The general procedure (P-3) was followed by 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 yelllow liquid. R_f 0.50 (9:1 hexane/EtOAc); $[\alpha]_D^{28}$ = −34.6 (*c* 0.8, $CHCl_3$); IR (neat) ν_{max} 2930, 2869, 2238, 1744, 1728, 1464, 1369, 1237, 1047, 757 cm^{-1}; ^1H NMR (500 MHz, $CDCl_3$) δ 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) ppm; ^{13}C NMR (125 MHz, $CDCl_3$) δ 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 ppm; 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'): The general procedure (P-3) was followed by using **1b** (50 mg, 0.2 mmol) and the reaction mixture was stirred at room temperature for 1 h (3 equivalent 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) ν_{max} 2924, 2853, 1627, 1384, 1220, 771 cm^{-1}; ^1H NMR (500 MHz, $CDCl_3$) δ 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) ppm; ^{13}C NMR (125 MHz, $CDCl_3$) δ 196.4, 169.9, 166.0, 132.5,129.6, 129.1, 128.3, 127.6, 80.0, 61.6, 20.6, 14.0 ppm; 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 $Sc(OTf)_3$ (cat.) at 0 ^oC. 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's enolic compound. R_f 0.5 (4:1 hexane/EtOAc); IR (neat) ν_{max} 3451, 2926, 2855, 1733, 1623, 1451, 1371, 1264, 1025, 701 cm^{-1}; ^1H NMR (500 MHz, $CDCl_3$) δ 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) ppm (only for keto form); ^{13}C NMR (125 MHz, $CDCl_3$) δ 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

ppm (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.

Acknowledgements

This work is dedicated to Dr. J. S. Yadav, Former Director, CSIR-IICT, Hyderabad, on the occasion of his 65th birthday. The authors thank CSIR, New Delhi for financial support as part of XII Five Year plan program under title ORIGIN (CSC-0108). D.K.M. thanks the CSIR for a research grant (INSA Young Scientist Award Scheme). T.R.P. and K.L.M. thank the Council of Scientific and Industrial Research (CSIR), and University Grants Commission (UGC), New Delhi, India, for financial assistance in the form of fellowship.

Supporting Information Available: Copies of ^1H and ^{13}C NMR spectra for all new compounds. This material is available free of charge via the Internet at http://pubs.acs.org.

References

(1) (a) Hauser, C. R.; Hudson, B. E. *Org. React*. **1942**, *1*, 266. (b) Pollet, P. L. *J. Chem. Educ.* **1983**, *60*, 244. (c) Benetti, S.; Romagnoli, R. De Risi, C.; Spalluto, G.; Zanirato, V. *Chem. Rev.* **1995**, *95*, 1065. (d) For reviews on the synthesis of heterocyclyes from β-keto esters, see: Simon, C.; Constantieux, T.; Rodriguez, J. *Eur. J. Org. Chem*. **2004**, 4957 and see the references therein.

(2) (a) Ishida, T.; Wada, K. *Chem. Commun*. **1975**, 209. (b) Hoffmann, R. W.; Helbig, W.; Ladner, W. *Tetrahedron Lett*. **1982**, *23*, 3479. (c) Wang, C. L. J.; Salvino, J. M. *Tetrahedron Lett*. **1984**, *25*, 5243. (d) Magriotis, P. A.; Johnson, F. *J. Org. Chem*. **1984**,

49, 1460. (e) Gilbert, J. C.; Kelly, T. A. *Tetrahedron Lett*. **1989**, *30*, 4193. (f) Emmer, G. *Tetrahedron*. **1992**, *48,* 7165. (g) Ward, R. S. *Synthesis*. **1992**, 719. (h) Urban, E.; Knuehl, G.; Helmchen, G. *Tetrahedron* **1995**, *51*, 13031. (i) Bellina, F.; Ciucci, D.; Rossi, R.; Vergamini, P. *Tetrahedron* **1999**, *55*, 2103. (j) Benbakkar, M.; Baltas, M.; Gorrichon, L.; Gorrichon, J. P. *Synth. Commun.* **1989**, *19*, 3241.

(3) (a) Fisher, N.; McElvain, S. M. *J. Am. Chem. Soc.* **1934**, *56*, 1766. (b) Brown, C. A. *Synthesis* **1975**, 326. (c) McMurry, J. E.; Fleming, M. P.; Kees, K. L.; Krepski, L. R. *J. Org. Chem*. **1978**, *43*, 3255. (d) Cooke, M. P., Jr. *J. Org. Chem*. **1993**, *58*, 2910. (e) Lombart, H.-G.; Lubell, W. D. *J. Org. Chem*. **1994**, *59*, 6147.(f) Loubinoux, B.; Sinnes, J.-L.; O'Sullivan, A. C. *J. Chem. Soc., Perkin Trans. 1* **1995**, 521. (g) Yoshizawa, K.; Toyota, S.; Toda, F. *Tetrahedron Lett.* **2001**, *42*, 7983. (h) Austad, B. C.; Hart, A. C.; Burke, S. D. *Tetrahedron* **2002**, *58*, 2011.

(4) (a) Tanabe, Y. *Bull. Chem. Soc. Jpn.* **1989**, *62*, 1917. (b) Crane, S. N.; Corey, E. J. *Org. Lett.* **2001**, *3*, 1395. (c) Tanabe, Y.; Makita, A.; Funakoshi, S.; Hamasaki, R.; Kawakusu, T. *Adv. Synth. Catal.* **2002**, *344*, 507. (d) Tanabe, Y.; Manta, N.; Nagase, R.; Misaki, T.; Nishii, Y.; Sunagawa, M.; Sasaki, A. *Adv. Synth. Catal.* **2003**, *345*, 967. (e) Hashimoto, Y.; Konishi, H.; Kikuchi, S. *Synlett* **2004**, 1264. (f) Misaki, T.; Nagase, R.; Matsumoto, K. Tanabe, Y. *J. Am. Chem. Soc.* **2005**, *127*, 2854.

(5) (a) Pandit, R. P.; Lee, Y. R. *Org. Biomol. Chem*. **2014**, *12*, 4407. (b) Kato, K.; Nishimura, A.; Yamamoto, Y.; Akita, H. *Tetrahedron Lett*. **2002**, *43*, 643. (c) Kato, K.; Sasaki, T.; Takayama, H.; Akita, H. *Tetrahedron* **2003**, *59*, 2679. (d) Sasaki, T.; Kato, K.; Akita, H. *Chem. Pharm. Bull.* **2004**, *52*, 770. (e) Akita, H.; Sasaki, T.; Kato, K.; Suzuki, Y.; Kondo, K.; Sakagami, Y.; Ojika, M.; Fudou, R.; Yamanaka, S. *Tetrahedron* **2004**, *60*, 4735.

(6) (a) For the synthesis of γ-hydroxy *β*-keto esters, see: (a) Damon, R. E.; Luo, T.; Schlessinger, R. H. *Tetrahedron Lett*. **1976**, *17*, 2749. (b) For the synthesis of γ-acetoxy *β*-keto esters, see: Pollet, P.; Gelin, S. *Tetrahedron***, 1978**, *34*, 1453.

(7) (a) Kato, K.; Yamamoto, Y.; Akita, H. *Tetrahedron Lett*. **2002**, *43*, 6587. (b) Kato, K.; Nouchi, H.; Keisuke Ishikura, K.; Takaishi, S.; Motodate, S.; Tanaka, H.; Okudaira, K.; Mochida, T.; Nishigaki, R.; Shigenobua, K.; Akita, H. *Tetrahedron.* **2006**, *62*, 2545.

(8) For selected gold-catalyzed hydration of alkynes, see: (a) Cordon, J.; Jiménez-Oses, G.; Lopez-de-Luzuriaga, J. M.; Miguel Monge, M.; Olmos, M. E.; Pascual, D. *Organometallics* **2014**, *33*, 3823. (b) Xie, L.; Wu, Y.; Yi, W.; Zhu, L.; Xiang, J.; He W. *J. Org. Chem.*, **2013**, *78*, 9190. (c) Wang, D.; Shi, X. *J. Am. Chem. Soc.* **2012**, *134*, 9012. (d) Wang, W.; Jasinski, J.; Hammond, G. B.; Xu, B. *Angew. Chem., Int. Ed*. **2010**, *49*, 7247. (e) Wang, W.; Xu, B.; Hammond, B. *J. Org. Chem*. **2009**, *74*, 1640. (f) Marion, N.; Ramón, R. S.; Nolan, S. P. *J. Am. Chem. Soc*. **2009**, *131*, 448. (g) Ramón, R. S.; Marion, N.; Nolan, S. P. *Tetrahedron*. **2009**, *65*, 1767. (h) Yang, C.-Y.; Lin, G.-Y.; Liao, H.-Y.; Datta, S.; Liu, R.-S. *J. Org. Chem.* **2008**, *73*, 4907. (i) Fukuda, Y.; Utimoto, K. *J. Org. Chem*. **1991**, *56*, 3729.

(9) For recent reviews of homogeneous Au catalysis, see: (a) Rudolph, M.; Hashmi, A. S. K. *Chem. Soc. Rev*. **2012**, *41*, 2448. (b) Garayalde, D.; Nevado, C. *ACS Catal*. **2012**, *2*, 1462. (c) Corma, A.; Leyva-Pérez, A.; Sabater, M. J. *Chem. Rev*. **2011**, *111*, 1657 (d) Rudolph, M.; Hashmi, A. S. K. *Chem. Commun*. **2011**, *47*, 6536. (e) Nolan, S. P. *Acc. Chem. Res*. **2011**, *44*, 91. (f) Hashmi, A. S. K. *Angew. Chem., Int. Ed*. **2010**, *49*, 5232. (g) Hashmi, A. S. K.; Buhrle, M. *Aldrichimica Acta* **2010**, *43*, 27. (h) Sohel, S. M. A.; Liu, R.-S. *Chem. Soc. Rev*. **2009**, *38*, 2269. (i) Díez- González, S.; Marion, N.; Nolan, S. P.

Chem. Rev. **2009**, *109*, 3612. (j) Li, Z.; Brower, C.; He, C. *Chem. Rev*. **2008**, *108*, 3239. (k) Jiménez-Núñez, E.; Echavarren, A. M. *Chem. Rev.* **2008**, *108*, 3326. (l) Gorin, D. J.; Sherry, B. D.; Toste, F. D. *Chem. Rev.* **2008**, *108*, 3351. (m) Widenhoefer, R. A. *Chem. Eur. J.* **2008**, *14*, 5382. (n) Arcadi, A. *Chem. Rev*. **2008**, *108*, 3266. (o) Furstner, A.; Davies, P. W. *Angew. Chem., Int. Ed*. **2007**, *46*, 3410. (p) Gorin, D. J.; Toste, F. D. *Nature* **2007**, *446*, 395. (q) Hashmi, A. S. K. *Chem. Rev.* **2007**, *107*, 3180. (r) Hashmi, A. S. K.; Hutchings, G. J. *Angew. Chem., Int. Ed.* **2006**, *45*, 7896.

(10) Ye, L.; He, W.; Zhang, L. *J. Am. Chem. Soc*. **2010**, *132*, 8550.

(11) Ramon, R. S.; Pottier,C.; Suarez, A. G.; Nolan. S. P. *Adv. Synth. Catal*. **2011**, *353*, 1575.

(12) (a) Georgy, M.; Boucard, V.; Campagne, J.-M. *J. Am. Chem. Soc.* **2005,** *127*, 14180. (b) Debleds, O.; Gayon, E.; Vrancken, E.; Campagne. J. M. *Beilstein J.Org. Chem.* **2011,** *7*, 866.

(13) For selected examples of directed hydration of alkyne by a neighbouring functionality, see: (a) Ghosh, N.; Nayak, S.; Sahoo, A. K. *J. Org. Chem*. **2011**, *76*, 500. (b) Ghosh, N.; Nayak, S.; Prabagar B.; Sahoo, A. K. *J. Org. Chem*. **2014**, *79*, 2453. (c) Francisco, L. W.; Moreno, D. A.; Atwood, J. D. *Organometallics* **2001**, *20*, 4237. (d) Arcadi, A.; Cerichelli, G.; Chiarini, M.; Di Giuseppe, S.; Marinelli, F. *Tetrahedron Lett.* **2000**, *41*, 9195. (e) Jennings, P. W.; Hartman, J. W.; Hiscox, W. C. *Inorg. Chim. Acta* **1994**, *222*, 317. (f) Imi, K.; Imai, K.; Utimoto, K. *Tetrahedron Lett.* **1987**, *28*, 3127. (g) Detert, H.; Meier, H. *Liebigs Ann. Recl.* **1997**, 1565. (h) Utimoto, K. *Pure Appl. Chem.* **1983**, *55*, 1845. (i) Stork, G.; Borch, R. *J. Am. Chem. Soc.* **1964**, *86*, 935.

(14) For selected examples of gold-catalyzed 1, 2-shifts, see: (a) Jimenez-Nu ń ez, E.; Echavarren, A. M. *Chem. Commun*. **2007**, 333. (b) Barluenga, J.; Riesgo, L.; Vicente, R.;

Lopez, L.; Tomas, M. *J. Am. Chem. Soc.* **2007**, *129*, 7772. (c) Hashmi, A. S. K.; Hutchings, G. J. *Angew. Chem., Int. Ed*. **2006**, *45*, 7896. (d) Wang, S.; Zhang, L. *J. Am. Chem. Soc*. **2006**, *128*, 14274. (e) Zhang, L.; Wang, S. *J. Am. Chem. Soc.* **2006,** *128*, 1442. (f) Gorin, D. J.; Dube, P.; Toste, F. D. *J. Am. Chem. Soc.* **2006,** *128*, 14480. (g) Johansson, M. J.; Gorin, D. J.; Staben, S. T.; Toste, F. D. *J. Am. Chem. Soc.* **2005**, *127*, 18002. (h) Mamane, V.; Gress, T.; Krause, H.; Fürstner, A. *J. Am. Chem. Soc*. **2004**, *126*, 8654.

(15) Wang, Y.; Lu, B.; Zhang, L. *Chem. Commun.,* **2010**, *46*, 9179.

(16) Shi, X.; Gorin, D. J.; and Toste, F. D. *J. Am. Chem. Soc*. **2005**, *127*, 5802

(17) (a) Shu, X. Z.; Liu, X. Y.; Xiao, H. Q.; Ji, K. G.; Guo, L. N.; Qi, C. Z.; Liang, Y. M. *Adv. Synth. Catal.*, **2007**, *349*, 2493.(b) Ji, K. G.; Shu, X.Z.; Chen, J.; Zhao, S. C.; Zheng, Z. J.; Liu, X. Y.; Liang, Y. M. *Org. Biomol. Chem.*, **2009**, *7*, 2501–2505.

(18) Rajaram, A. R.; Pu, L. *Org. Lett*. **2006**, *8*, 2019.

(19) The major isomer obtained from Li-acetylide reaction of the corresponding ketone of natural products was taken for the acetylation/ benzoylation reaction without any confirmation of the resulting stereogenic centre. See Supporting Information for a detailed description for the synthesis of the substrates.

(20) Wang, Y.; Lu, B.; Zhang, L. *Chem. Commun.,* **2010**, *46*, 9179.

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

(22) (a) Leonard, M. S.; Carroll, P. J.; Joullié, M. M. *J. Org. Chem.,* **2003**, *69*, 2526; (b) Cai, G.; Wei Zhu, W.; Ma, D. *Tetrahedron* **2006**, *62*, 5697.

(23) (a) Midland, M. M.; Tramontano, A.; Cable, J. R. *J. Org. Chem*, **1980**, *45*, 28; (b) Halim, M.; Tremblay, M. S.; Jockusch, S.; Turro, N. J.; Sames, D. *J. Am. Chem. Soc.* **2007**, *129*, 7704.

(24) Bhanu Prasad, B. A.; Yoshimoto, F. K.; Sarpong, R. *J. Am. Chem. Soc.* **2005,** *127*, 12468.

(25) Desrat, S.; Weghe, P. *J. Org. Chem.*, **2009**, *74*, 6728.

(26) Jiang, L.; Chan, Tak-H. *J. Org. Chem*. **1998**, *63*, 6035.

(27) The chiral aldehyde was synthesized as per the literature procedure. See: a) Kumar, D. N.; Reddy, C. R.; Das, B. *Synthesis* **2011**, *19*, 3190; (b) Daumas, M.; Vo-Quang. L. Y.; Le Goffie, F. *Synthesis* **1989**, *1*, 64.

(28) Tejedor, D.; Lo´pez-Tosco, S.; Gonza´lez-Platas, J.; Garcı´a-Tellado, F. *J. Org. Chem*. **2007**, *72*, 5454.

(29) Crimmins, M. T.; Nantermet, P. G.; Trotter, B. W.; Vallin, I. M.; Watson, P. S. *J. Org. Chem*. **1993** , *58*, 1038.

(30) For enantioselective Synthesis of γ-Hydroxy-α,β-acetylenic esters by asymmetric alkyne Addition to Aldehydes, see : Rajaram, A. R.; Pu, L. *Org. Lett*. **2006**, *8*, 2019.

(31) Srikrishna, A.; Sharma, G. V. M.; Danieldoss, S.; Hemamalini, P. J. *Chem. Soc., Perkin Trans. I* , **1996**, 1305.

(32) Spino, C.; Beaulieu, C.; Lafrenie`re, J. *J. Org. Chem.* **2000,** *65*, 7091.

(33) The corresponding ketone for the synthesis of compound **12d** was synthesized by the oxidation of cholesterol using PCC. For PCC oxidation see: Corey, E. J.; Suggs, W. *Tetrahedron Lett.* **1975**, *16*, 2647.