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Cascade Michael Addition/Cycloketalization of Cyclic 1,3-Dicarbonyl Compounds: Important Role of the Tethered Alcohol of α,β-Unsaturated Carbonyl Compounds on Reaction Rate and Regioselectivity

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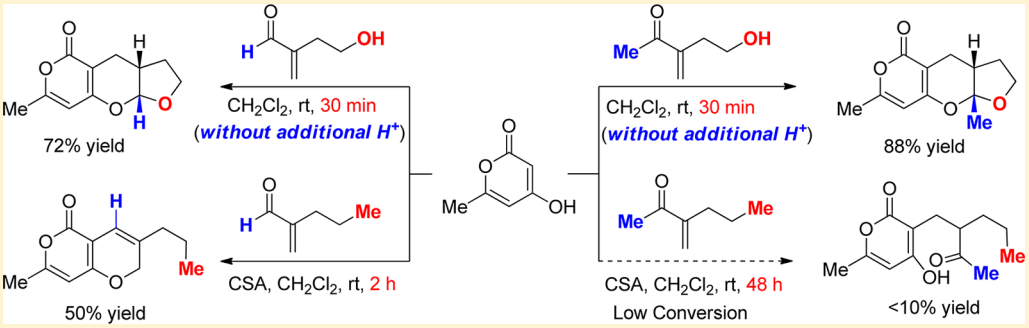
Supporting Information



ABSTRACT: Reactions of α,β-unsaturated aldehydes and cyclic 1,3-dicarbonyl compounds proceed primarily by cascade Knoevenagel condensation/six-π-electron electrocyclization (K6EC, formal [3 + 3] cycloaddition), while α,β-unsaturated ketones usually react with cyclic 1,3-dicarbonyl compounds in a 1,4-addition manner. This paper discloses our findings that under acidic conditions, α,β-unsaturated carbonyl compounds (ketones and aldehydes) with a tethered alcohol react with cyclic 1,3-dicarbonyl compounds in a highly regioselective 1,4-addition fashion via in situ generation of a hypothetical α-methylene cyclic oxonium ion as the reactive Michael acceptor. Our studies uncovered the important effect of the tethered alcohol on the reaction rate and/or efficiency and some new mechanistic aspects of the cascade Michael addition/cycloketalization. Finally, the substrate scope was examined, and 43 analogues of penicipyrone and tenuipyrone were prepared in good to excellent yields.

INTRODUCTION

4-Hydroxy-2-pyrone is an important scaffold that is present in numerous natural products with structural diversity and potent biological activities.[1] In fact, many 4-hydroxy-2-pyrone derivatives have been rigorously studied for potential medicinal applications as antimicrobial/fungal agents, anticancer agents, acetylcholinesterase (AChE) inhibitors (Alzheimer's diseases), and HIV protease inhibitors.[2] For example, natural product arisugacins[3] (e.g., arisugacin A) are potent anti-Alzheimer agents, and the 6-aryl-4-hydroxy-2-pyrone subunit of arisugacins have been found to be necessary for the biological activity (Figure 1). Therefore, 4-hydroxy-2-pyrone natural products with novel structural frameworks have attracted much attention from the synthetic community for their total synthesis and have served as a platform for the development of new synthetic strategies/methods.[4]

We recently were attracted by two newly isolated natural products, penicipyrone[5] and tenuipyrone,[6] whose structures are characterized by the presence of an unprecedented polycyclic acetal/ketal. Our previous synthetic work revealed that the reaction of 4-hydroxy-6-methyl-2-pyrone (also known as triacetic acid lactone) and α,β-unsaturated ketones proceeds smoothly in the presence of Amberlyst 15 (A-15) to give the corresponding penicipyrone and tenuipyrone through a cascade intermolecular Michael addition/cycloketalization (MACK)[7]

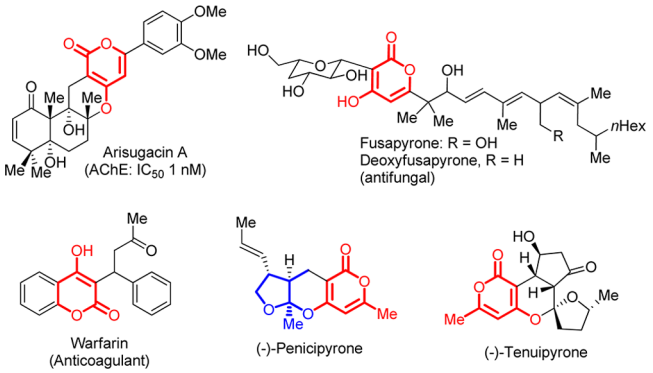


Figure 1. Representative examples of natural products containing a 4-hydroxy-2-pyrone subunit.

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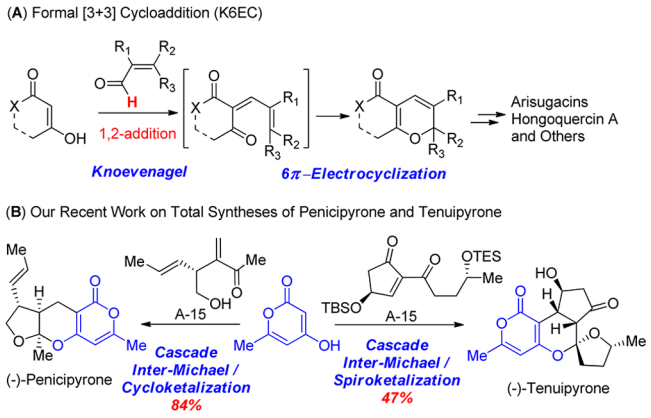
(Scheme 1B). This process, however, is mechanistically different from numerous examples in the literature in which

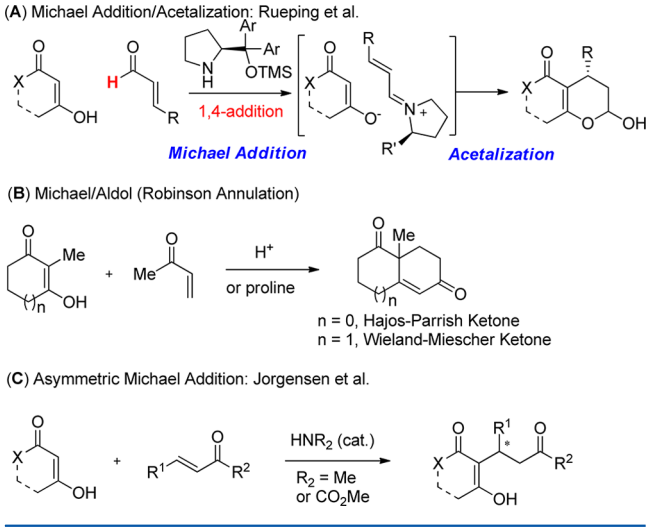
Scheme 1. Formal [3 + 3] Cycloaddition and Total Syntheses of Penicipyrone and Tenuipyrone



cyclic 1,3-dicarbonyl compounds (including 4-hydroxy-2-pyrones) tend to undergo Knoevenagel condensation with α,β-unsaturated aldehydes followed by six-π-electron electrocyclization, a well-established cascade process leading to formal [3 + 3] cycloadducts (Scheme 1A).[8]

In general, the reaction of cyclic 1,3-dicarbonyl compounds with α,β-unsaturated aldehydes preferably proceeds in a 1,2-addition fashion (aldol reaction or Knoevenagel condensation; Scheme 1A),[8,9] while the alternative 1,4-addition (i.e., Michael addition) is predominant when α,β-unsaturated ketones are employed as the electrophiles (Scheme 2B,C).[10] The only

Scheme 2. Michael Addition of Cyclic 1,3-Dicarbonyl Compounds to α,β-Unsaturated Ketones/Aldehydes

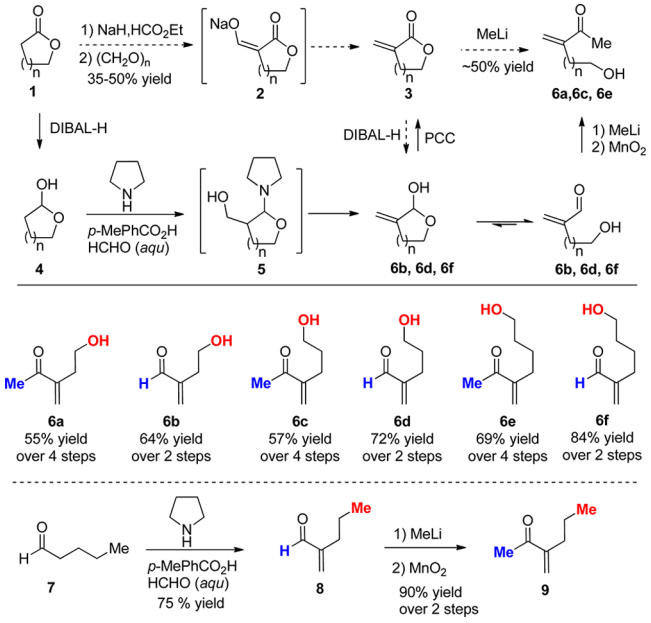


exception to this general regioselectivity is the diarylprolinol ether-catalyzed reaction of cyclic 1,3-dicarbonyl compounds with α,β-unsaturated aldehydes, which occurs via a highly regioselective and enantioselective 1,4-conjugate addition to afford bicyclic acetals as the major products (Scheme 2A).[11] In this case, the 1,2-addition pathway is probably suppressed significantly by the steric interaction of the bulky diarylprolinol ether with the nucleophile.[11c] Nevertheless, the reactions of cyclic 1,3-dicarbonyl compounds with α,β-unsaturated carbonyl compounds are generally slow (12 h to 6 days) at ambient temperature even with activation of the α,β-unsaturated compounds using primary or secondary amines through formation of iminium ions.[8−11] However, further studies of the MACK sequence led us to discover that the tethered alcohol of α,β-unsaturated carbonyl compounds plays a critical role in the reactivity and regioselectivity in the reaction with cyclic 1,3-dicarbonyl compounds. We herein disclose the results in full detail and the expansion of the substrate scope in the synthesis of analogues of penicipyrone and tenuipyrone.

RESULTS AND DISCUSSION

Synthesis of Alcohol-Tethered α,β-Unsaturated Carbonyl Compounds. To examine the role of the tethered alcohol of α,β-unsaturated carbonyl compounds in the reactivity and regioselectivity when they react with cyclic 1,3-dicarbonyl compounds, we prepared a small series of alcohol-tethered α,β-unsaturated carbonyl compounds as shown in Scheme 3. A method similar to that used in our previous

Scheme 3. Synthesis of Alcohol-Tethered α,β-Unsaturated Ketones/Aldehydes



synthesis[7] was first employed to prepare **6a**, **6c**, and **6e** in low yields (<25%) over three steps (cf. **1** → **2** → **3** → **6a**/**6c**/**6e**). Attempts to improve the yields were unsuccessful because the yield of α-methylenation[12] of lactone **1** was only moderate and the subsequent methyllithium addition to the resulting lactone produced a considerable amount of tertiary alcohols as side products. Inspired by the elegant work by Pihko and co-workers[13] on α-methylenation of aldehydes by organocatalysis, we set out to explore the α-methylenation of lactols **4**, which type of substrate has not been employed in the literature. We envisioned that the lactols would be in equilibrium with hydroxy aldehydes and might undergo a similar α-methylenation. To our delight, the organocatalytic α-methylenation of lactols **4** proceeded efficiently, and the alcohol-tethered α,β-unsaturated ketones/aldehydes **6a**−**f** could be prepared readily on a multigram scale in good to excellent yields in two or four steps using Pihko's protocol as the key step. Specifically, lactones **1** as starting materials were reduced by DIBAL-H, and

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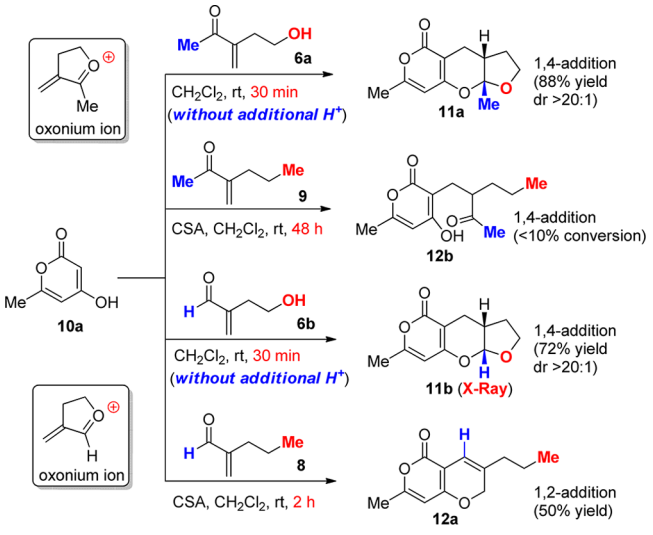
the resulting lactols **4** were subjected to the pyrrolidine-catalyzed α-methylenation to give the desired products **6b**, **6d**, and **6f** in excellent yields in only two steps. Methyl ketones **6a**, **6c**, and **6e** could be prepared in high yields by subsequent methyllithium addition to the corresponding lactols/aldehydes **6b**, **6d**, and **6f** followed by MnO_2 oxidation. One of the many obvious advantages of this new route is its operational simplicity on both large and small scales with higher overall yields compared with the protocol we used previously (dashed arrow, **1** → **2** → **3** → **6b**/**6d**/**6f**).[7] In addition, α,β-unsaturated aldehyde **8** and α,β-unsaturated ketone **9** were also prepared from aldehyde **7** using Pihko's method[13] for control experiments. It is noteworthy that PCC oxidation of lactols **6b**, **6d**, and **6f** quantitatively provided the corresponding α-methylene lactones, which constitutes a new approach for the synthesis of α-methylene lactones.[12]

Critical Role of the Tethered Alcohol of α,β-Unsaturated Carbonyl Compounds in the Regioselectivity and Reactivity. In the course of examining the substrate scope of the cascade MACK developed previously in our lab for the total syntheses of penicipyrone and tenuipyrone,[7] we were very delighted to observe that the reaction of γ'-hydroxy-α,β-unsaturated ketone **6a** with 4-hydroxy-6-methyl-2-pyrone (**10a**) proceeded rapidly at room temperature without additional acid as a promoter to provide tricyclic acetal **11a** in excellent yield within 30 min (Scheme 4). A-15 or

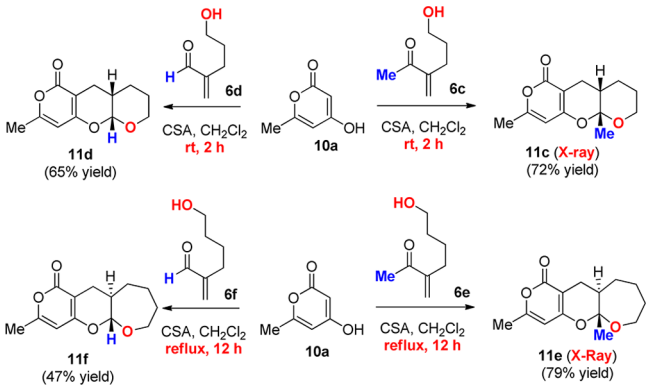
Scheme 4. Preliminary Discovery of the Effect of the Tethered Alcohol on the Reaction Rate and Regioselectivity



camphorsulfonic acid (CSA) used in our previous protocol[7] was found to be unnecessary for this substrate. In contrast, the reaction of **10a** with enone **9** lacking a tethered alcohol occurred sluggishly at room temperature even in the presence of CSA (0.5 equiv) as the promoter. These results suggested that the tethered alcohol of **6a** is involved mechanistically in the initial step of the cascade reaction, Michael addition of **10a** to enone **6a**. Given the fact that cyclic 1,3-dicarbonyl compounds are weak acids (pK_a = 4.0−5.0), we speculated that the in situ formation of a cyclic oxonium ion might be responsible for the reaction rate acceleration. Enal **6b** underwent a similar "catalyst-free" cascade MACK process with high efficiency to afford tricyclic acetal **11b** as the single isolable product. The molecular structure of **11b** was unambiguously substantiated by X-ray diffraction analysis (see the Supporting Information). Apparently, the competing Knoevenagel condensation/six-π-electron electrocyclization (K6EC), a cascade process initiated by 1,2-addition, did not occur. When the tethered alcohol of **6b** was replaced with a methyl group such as in compound **8**, the expected K6EC occurred smoothly in the presence of CSA at room temperature, leading to bicyclic pyrone **12a** in 50% yield (unoptimized). All of these findings clearly suggested that the tethered alcohol of the α,β-unsaturated carbonyl compounds can control the regioselectivity (1,4- vs 1,2-addition) and accelerate the cascade MACK reaction, which might be attributed to the in situ formation of a cyclic oxonium ion as the reactive Michael acceptor.

Interestingly, when δ-hydroxy enone **6c** or δ-hydroxy enal **6d** was employed (Scheme 5), the MACK reaction of **10a**

Scheme 5. Cascade MACK of ω/δ-Hydroxy Enones/Enals



occurred sluggishly. However, the cascade reaction could be efficiently promoted at room temperature by the addition of a catalytic amount of CSA (0.1 equiv) to provide the corresponding tricyclic ketal **11c** or acetal **11d**, respectively, in good yield. Notably, no K6EC adduct was isolated from the reaction mixture. In the case that ω-hydroxy enone **6e** or ω-hydroxy enal **6f** was used, the cascade MACK reaction required both reflux at 40 °C for 12 h and CSA as the promoter, under which conditions the desired product **11e** or **11f**, respectively, was obtained in good yield. These results revealed that the length of the alcohol tether has an influence on the rate of the MACK cascade reaction. As observed in Scheme 4, the tethered alcohol also controlled the regioselectivity (1,4-addition vs 1,2-addition) for enal substrates (**6d** and **6f**). It is noteworthy that the tricyclic ketal **11e** and acetal **11f** were surprisingly *trans*-fused, in contrast to the *cis*-fused ketals **11a**−**d**. The relative configurations and carbon skeletons of [6/6/5]-**11b**, [6/6/6]-**11c**,[7] and [6/6/7]-**11e** were confirmed by X-ray diffraction analysis (see the Supporting Information), which served as the basis for proposing the relative configuration of other MACK adducts.

Mechanism of Cascade Michael Addition/Cycloketalization. In light of the new findings from Schemes 4 and 5, we proposed that the cascade MACK process may begin with the formation of cyclic oxonium ion **16** as the Michael acceptor (**13** → **16**; Scheme 6b), which is mechanistically different from most conventional activation pathways of Michael acceptors via iminium formation or Lewis[14]/Brønsted acid coordination to the carbonyl oxygen (Scheme 6a).[10] In principle, a mild Brønsted acid would promote the intramolecular cyclization of the hydroxy-tethered enone or enal **13** to generate hemiacetal

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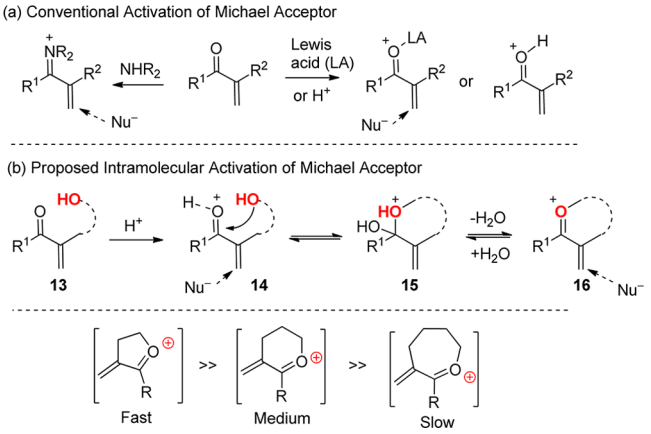
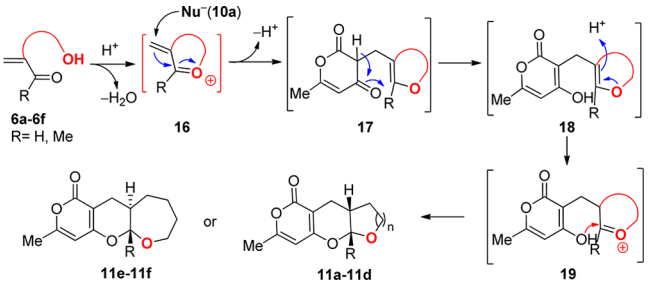
Scheme 6. Possible Intramolecular Activation of the Michael Acceptor



15, which would be in equilibrium with cyclic oxonium ion **16** as a highly reactive Michael acceptor. It is noted that a similar oxonium ion as the Michael acceptor generated in situ from treatment of 3-(hydroxymethyl)dihydrofuran with BF_3-Et_2O, was proposed in the literature.[15] The rate of formation of cyclic oxonium ion **16** is primarily governed by the length of the alcohol tether (five-membered to seven-membered rings), consistent with our experimental results in Schemes 4 and 5 and the well-established ring-closure kinetics.[16]

On the basis of this hypothetical intramolecular activation of the Michael acceptor, a full mechanistic picture of the cascade MACK can be proposed, as depicted as Scheme 7. Cyclic

Scheme 7. Proposed Mechanism for the Cascade Michael Addition/Cycloketalization



oxonium ion **16** generated in situ in the presence of the Brønsted acid (note: **10a** was the weak acid when CSA was not employed) would be attacked by **10a** (Michael addition) to produce intermediate enol **17**, which would undergo keto/enol tautomerization followed by protonation to form oxonium ion **19**. The subsequent intramolecular cycloketalization of **19** would proceed in a favorable *6-exo-trig* fashion[17] to provide the tricyclic ketal (or acetal) product. The *cis*-fused kinetic products **11a–d** (6/6/5 and 6/6/6 tricycles) were formed exclusively under mild acidic conditions, while the seven-membered *trans*-fused thermodynamic products **11e** and **11f** were dominant under harsher acidic conditions with extended reaction time.

Synthesis of Analogues of Penicipyrone. With a better understanding of the cascade MACK process, we hoped to expand the substrate scope and achieve the synthesis of natural product-like compounds (Table 1). Cascade MACK reactions of **6a–f** and three cyclic 1,3-dicarbonyl compounds [4-hydroxycoumarin (**10b**), 1,3-cyclohexanedione (**10c**), and 1,3-cyclopentanedione (**10d**)] were then performed in a parallel manner for the synthesis of penicipyrone-like compounds (Table 1). Most of the reactions proceeded smoothly to provide the desired MACK products (**11a–x**, except for **11w**) in good to excellent yields. Their relative stereochemistry was proposed on the basis of X-ray diffraction analysis of compounds **11b**, **11c**, **11e**, **11h**, **11l**, and **11p** (see the Supporting Information). In the case of **11w**, it remained unclear that the cascade MACK reaction of 1,3-cyclopentanedione and **6e** was unsuccessful. However, no K6EC adducts could be isolated from the reaction mixture. It is particularly noteworthy that the alcohol-tethered α,β-unsaturated aldehydes underwent the cascade MACK instead of K6EC to provide the polycyclic acetals with similar efficiency as with their counterpart ketones.

Synthesis of Analogues of Tenuipyrone. Next, we directed our attention to the synthetic application of the cascade MACK for preparation of the tenuipyrone-like spiroketals. A small series of alcohol-tethered enones were prepared readily in two or four steps as shown in Scheme 8. It should be noted that the butenolides **25a** and **25b** could not be synthesized efficiently from the corresponding commercially available 2(5*H*)-furanones through Morita–Baylis–Hillman and Dess–Martin periodinane (DMP) oxidation, which is a two-step sequence that could be employed for the syntheses of **23a** and **23b** from cyclopentenone (**22**) in high yields. Therefore, γ-lactones **24a** and **24b** were used as starting materials to prepare butenolides **25a** and **25b** through a four-step sequence: α-phenylselenation, aldol reaction, selenoxide elimination, and DMP oxidation.[18] Compounds **23a**, **23b**, **25a**, and **25b** prepared by DMP oxidation of the corresponding alcohols were unstable in the course of purification by column chromatography on silica gel and decomposed completely overnight even when stored in the refrigerator. The instability of these compounds prevented their purification, exact yield calculation, and characterization. Therefore, the crude products with triethylsilyl ether from DMP oxidation (presumably 100% yield for this step) were freshly prepared and used directly for the subsequent cascade MACK reaction.

Gratifyingly, the cascade MACK reactions of the crude enones **21**, **23a**, **23b**, **25a**, and **25b** with cyclic 1,3-dicarbonyl compounds proceeded efficiently with simultaneous desilylation to provide the polycyclic ketals **26a–t** in 60–90% yield, as shown in Table 2. The relative stereochemistry of the polycyclic spiroketals was proposed on the basis of X-ray diffraction analysis of **26b-1**, **26d**, and **26t** (see the Supporting Information). To our surprise, **25a** and **25b** (γ-lactones) gave the corresponding MACK products **26d**, **26e**, **26i**, **26j**, **26n**, **26o**, **26s**, and **26t** with high diastereoselectivity (dr >15:1), while the similar MACK reaction of **23a** and **23b** (cyclopentanones) produced a 5:1 to 1:1 mixture of spiroketals under identical conditions. It was intriguing that the subtle structural difference would lead to contrasting outcomes of diastereoselectivity (cf. **26b** vs **26d**). We suspected that different intermediates such as **27** and **28** might be responsible for the diastereoselectivity in the course of intramolecular oxa-Michael cyclization (i.e., spiroketalization). The hypothetical intermediate **27** could be produced from intermolecular Michael addition of **10a** to **23a** followed by dehydrative enol formation, while **28** might be generated from **10a** and **25a** via formation of an α-*exo*-methylene cyclic oxonium ion (similar to **16**) followed by intermolecular Michael addition (similar to the mechanism proposed in Scheme 7). Intermediate **27** would be

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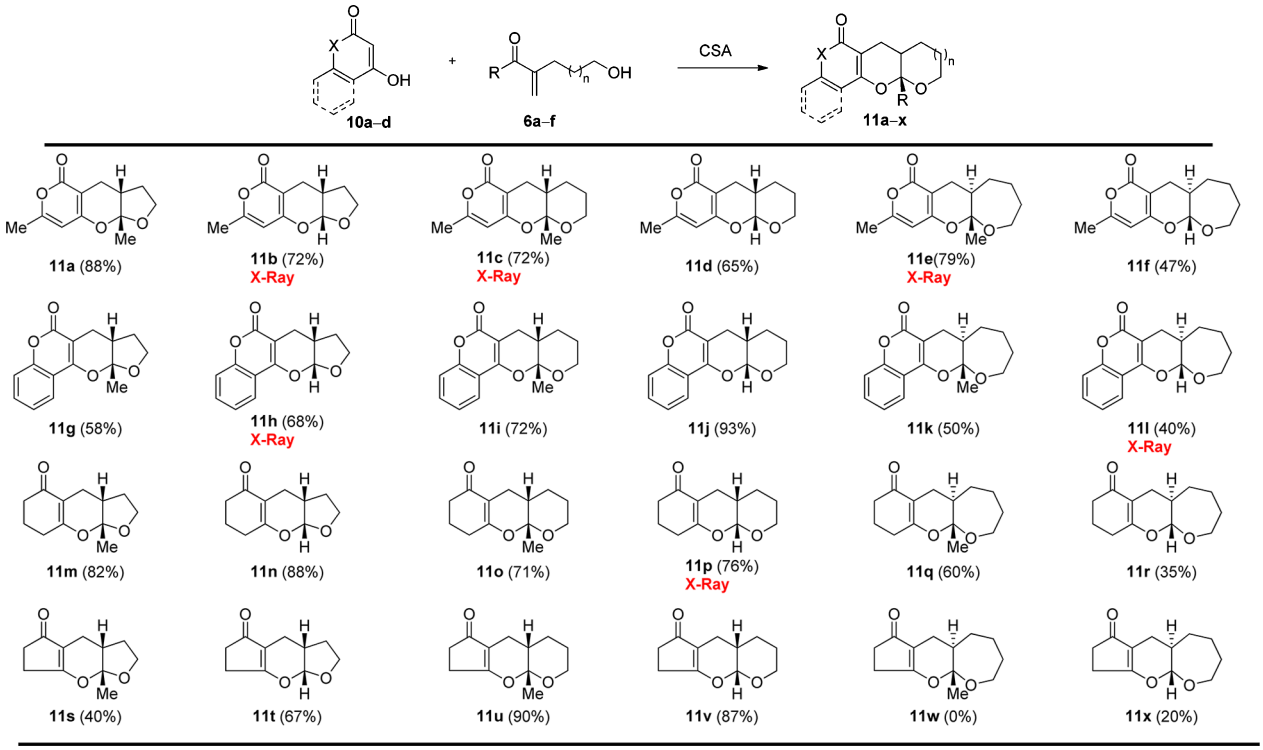
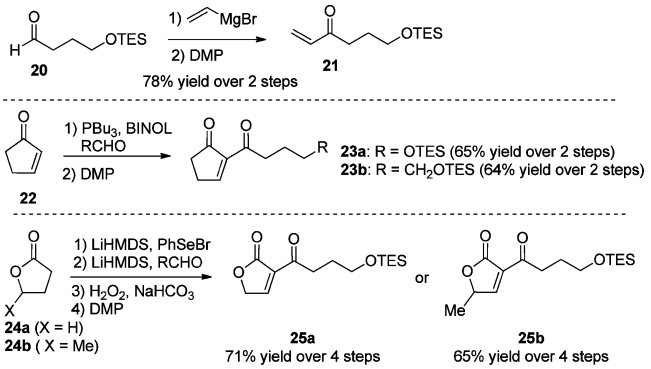
Table 1. Synthesis of Penicipyrone-like Polycyclic Ketals/Acetals via Cascade MACK



Scheme 8. Synthesis of Alcohol-Tethered Enones



pseudoplanar relative to the incoming oxygen nucleophile, while the oxygen nucleophile from pyrone of **28** might attack only one favorable side of the enone because of the presence of the chiral center. However, further studies on the cascade MACK reactions are needed to fully elucidate the unusual diastereoselectivity for different substrates.

CONCLUSION

We have studied the cascade Michael addition/cycloketalization (MACK) reaction of cyclic 1,3-dicarbonyl compounds and α,β-unsaturated carbonyl compounds and found that under acidic conditions the tethered alcohol of the α,β-unsaturated carbonyl compounds plays a critical role in the regioselectivity and reactivity. On the basis of our experimental results, we have proposed that an α-methylene cyclic oxonium ion might be generated in situ as the reactive electrophile, which would react rapidly with cyclic 1,3-dicarbonyl compounds in a highly regioselective 1,4-addition fashion. In addition, the reaction rate of the cascade MACK reaction decreased considerably when the length of the alcohol tether was increased from two carbons (**6a** and **6b**) to four carbons (**6e** and **6f**), which is consistent with the well-established ring-closure kinetics and supports our hypothesis that an α-methylene cyclic oxonium ion intermediate is generated in situ as the Michael acceptor. On the basis of these new findings, a detailed mechanism for the cascade MACK reaction has been proposed. Finally, 43 analogues of penicipyrone and tenuipyrone were prepared in good to excellent yields via the cascade MACK process. Biological studies of these analogues are underway and will be reported in due course.

EXPERIMENTAL SECTION

General Experimental Methods. Reactions were carried out in oven- or flame-dried glassware under a nitrogen atmosphere, unless otherwise noted. Tetrahydrofuran (THF) was freshly distilled before use from sodium using benzophenone as an indicator. Dichloromethane (CH_2Cl_2) was freshly distilled before use from calcium hydride (CaH_2). All of the other anhydrous solvents were dried over 3 or 4 Å molecular sieves. Solvents used in workup, extraction, and column chromatography were used as received from commercial suppliers without additional purification. ^{1}H and ^{13}C NMR spectra were recorded on a 400 MHz spectrometer (400 MHz for ^{1}H, 100 MHz for ^{13}C). Chemical shifts are reported in parts per million (ppm) as values relative to the internal chloroform-*d* (7.26 ppm for ^{1}H and 77.16 ppm for ^{13}C), benzene-d_6 (7.16 ppm for ^{1}H and 128.06 ppm for ^{13}C), or dichloromethane-d_2 (5.32 ppm for ^{1}H and 53.84 ppm for ^{13}C). Abbreviations for signal coupling are as follows: s, singlet; d, doublet; t, triplet; q, quartet; m, multiplet. Infrared (IR) spectra were recorded as neat samples (liquid films on KBr plates). HRMS spectra were recorded with a TOF detector. Melting points (mp) were recorded on a laboratory melting point apparatus.

Preparation of Compounds 6b, 6d, and 6f. To a solution of lactone **1** (90 mmol) in hexane/CH_2Cl_2 (95:5 v/v, 500 mL) at −78 °C was added diisobutylaluminum hydride (DIBAL-H) (90 mL, 1.0 M in hexane, 90 mmol) slowly, and the reaction mixture was stirred at −78 °C for 1 h. After complete consumption of the starting material as indicated by TLC, the reaction was quenched by the addition of ethyl

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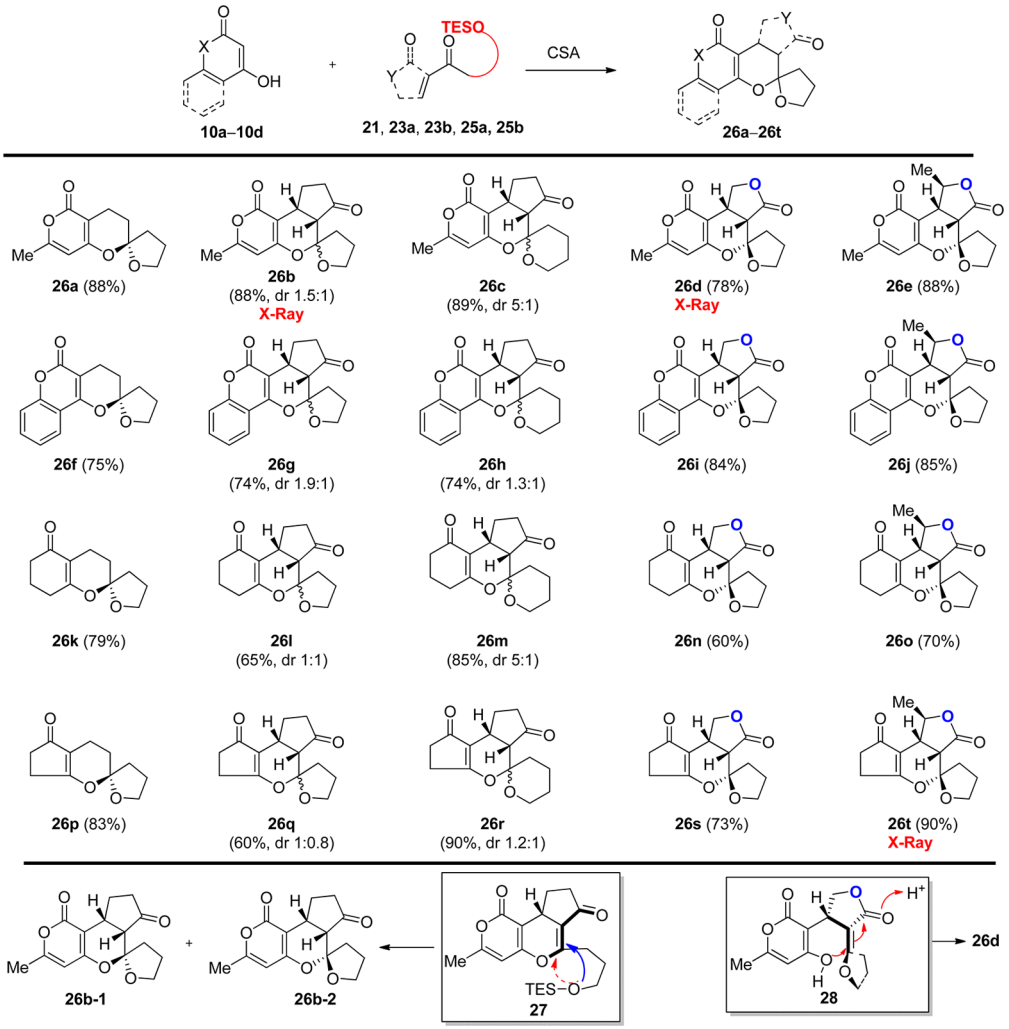
Table 2. Synthesis of Tenuipyrone-like Polycyclic Spiroketals via Cascade MACK



acetate (10 mL) at −78 °C followed by the addition of a saturated sodium potassium tartrate solution (500 mL). The resulting suspension was allowed to warm to room temperature with vigorous stirring for 2 h. The organic layer was collected, and the aqueous layer was extracted with CH_2Cl_2 (3 × 300 mL). The combined organic fractions were washed with brine, dried over Na_2SO_4, and concentrated under reduced pressure. The resulting crude product (lactol) was used directly for the next step without further purification. Following the similar procedure reported by Pihko,[13] to a solution of 4-methylbenzoic acid (1.2 g, 9.0 mmol) in CH_2Cl_2 (100 mL) were added pyrrolidine (1.5 mL, 18 mmol), the crude lactol obtained above, and aqueous formaldehyde (36.5 wt % in water, 8.0 mL). The mixture was rapidly heated to 45 °C and stirred for 12 h. After complete consumption of the starting material as indicated by TLC, the reaction was quenched by addition of a saturated $NaHCO_3$ solution. The organic layer was collected, and the aqueous layer was extracted with CH_2Cl_2 (3 × 40 mL). The combined organic fractions were washed with brine, dried over Na_2SO_4, and concentrated under reduced pressure. The resulting residue was purified by flash column chromatography on silica gel (hexane/EtOAc = 1:1) to afford the desired product.

Compound ***6b.***[19] 5.7 g, 64% yield over two steps; colorless oil. ^{1}H NMR (400 MHz, C_6D_6) δ: 9.14 (s, 1H), 5.66 (d, J = 1.2 Hz, 1H), 5.26 (s, 1H), 3.39−3.35 (m, 2H), 2.23−2.20 (m, 2H), 0.76 (br, 1H, OH). ^{13}C NMR (100 MHz, C_6D_6) δ: 194.7, 147.2, 135.8, 60.7, 31.7.

Compound ***6d.*** 7.4 g, 72% yield over two steps; colorless oil. IR (neat) cm^{-1}: 3442, 2920, 2851, 1647, 1633, 785. ^{1}H NMR (400 MHz, $CDCl_3$) δ: 9.18 (s, 1H), 5.55 (s, 1H), 5.21 (s, 1H), 3.21 (t, J = 6.4 Hz, 2H), 2.16−2.13 (m, 2H), 1.42−1.35 (m, 2H), 0.50 (br, 1H, OH). ^{13}C NMR (100 MHz, CD_2Cl_2) δ: 195.3, 150.2, 135.0, 61.9, 31.4, 24.3. HRMS (TOF, CI$^+$) m/z: calcd for $C_6H_{11}O_2$ $[M + H]^+$ 115.0759, found 115.0764.

Compound ***6f.*** 9.6 g, 84% yield over two steps; colorless oil. IR (neat) cm^{-1}: 3423, 2941, 2867, 1681, 1442, 1068, 958. ^{1}H NMR (400 MHz, C_6D_6) δ: 9.24 (s, 1H), 5.69 (s, 1H), 5.36 (s, 1H), 3.45 (t, J = 5.6 Hz, 2H), 2.66 (br, 1H, OH), 2.14−2.11 (m, 2H), 1.40−1.35 (m, 4H). ^{13}C NMR (100 MHz, C_6D_6) δ: 194.2, 150.4, 133.4, 62.2, 32.6, 27.8, 24.4. HRMS (TOF, CI$^+$) m/z: calcd for $C_7H_{13}O_2$ $[M + H]^+$ 129.0916, found 129.0915.

Preparation of Compounds 6a, 6c, and 6e. To a solution of α,β-unsaturated aldehyde **6b**, **6d**, or **6f** (12 mmol) in diethyl ether (120 mL) at −78 °C was added MeLi (18.7 mL, 1.6 M in diethyl ether, 30 mmol) dropwise. The resulting reaction mixture was stirred at −78 °C for 2 h, and then the reaction was quenched by addition of a saturated NH_4Cl solution (100 mL). The organic layer was collected, and the aqueous layer was extracted with diethyl ether (3 × 50 mL). The combined organic fractions were washed with brine, dried over Na_2SO_4, and concentrated under reduced pressure to afford the crude diol, which was used directly for oxidation without further purification. To a solution of the crude diol obtained above in CH_2Cl_2 (250 mL) was added activated MnO_2 (21 g) in several portions. After complete consumption of the starting material as indicated by TLC (about 3 h), the reaction mixture was filtered through a short pad of Celite, and the filtrate was concentrated under reduced pressure. The resulting residue was purified by flash column chromatography on silica gel (hexane/EtOAc = 1:1) to afford the desired product **6a**, **6c**, or **6e**, respectively.

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Compound ***6a***.[7] 1.18 g, 86% yield over two steps; colorless oil. ^{1}H NMR (400 MHz, C_6D_6) δ: 5.42 (s, 1H), 5.34 (s, 1H), 3.52 (t, J = 6.4 Hz, 2H), 2.36 (td, J = 6.4, 1.2 Hz, 2H), 1.85 (s, 3H), 1.50 (s, 1H, OH). ^{13}C NMR (100 MHz, C_6D_6) δ: 199.4, 146.6, 126.4, 61.9, 34.8, 25.3.

Compound ***6c***.[7] 1.20 g, 79% yield over two steps; colorless oil. ^{1}H NMR (400 MHz, C_6D_6) δ: 5.40 (s, 1H), 5.27 (s, 1H), 3.84 (s, 1H, OH), 3.33 (t, J = 6.4 Hz, 2H), 2.31−2.27 (m, 2H), 1.87 (s, 3H), 1.51−1.48 (m, 2H). ^{13}C NMR (100 MHz, C_6D_6) δ: 198.9, 149.1, 124.8, 61.7, 32.3, 27.1, 25.4.

Compound ***6e***. 1.40 g, 82% yield over two steps; colorless oil. IR (neat) cm^{-1}: 3421, 2935, 2867, 1670, 1457, 1370, 1259, 1061, 799. ^{1}H NMR (400 MHz, $CDCl_3$) δ: 6.00 (s, 1H), 5.77 (s, 1H), 3.62 (t, J = 6.0 Hz, 2H), 2.31 (s, 3H), 2.25 (t, J = 7.2 Hz, 2H), 2.04 (s, 1H, OH), 1.58−1.51 (m, 2H), 1.49−1.41 (m, 2H). ^{13}C NMR (100 MHz, $CDCl_3$) δ: 200.2, 149.0, 125.4, 62.5, 32.3, 30.2, 26.0, 24.7. HRMS (TOF, CI$^+$) m/z: calcd for $C_8H_{15}O_2$ [M + H]$^+$ 143.1072, found 143.1075.

Preparation of Compound 21. To a solution of aldehyde **20**[20] (101 mg, 0.50 mmol) in THF (5 mL) at 0 °C was added vinylmagnesium bromide solution (0.75 mL, 1.0 M in THF, 0.75 mmol) dropwise. After 30 min of stirring, the reaction was quenched by addition of a saturated NH_4Cl solution (2 mL). The organic layer was collected, and the aqueous layer was extracted with diethyl ether (3 × 2 mL). The combined organic fractions were washed with brine, dried over Na_2SO_4, and concentrated under reduced pressure to afford the crude allylic alcohol, which was used directly for oxidation without further purification. To a solution of the alcohol obtained above in dry CH_2Cl_2 (5 mL) at 0 °C were added $NaHCO_3$ (168 mg, 2.0 mmol) and Dess−Martin periodinane (DMP) (424 mg, 1.0 mmol). After vigorous stirring for 30 min at 0 °C, the reaction mixture was stirred at room temperature for 30 min until TLC indicated complete consumption of the starting material. The reaction mixture was diluted with Et_2O (3 mL) and poured into a saturated $NaHCO_3$ solution containing excess $Na_2S_2O_3$. The mixture was stirred until the solid was completely dissolved. The organic phase was collected; washed sequentially with a saturated $NaHCO_3$ solution, water, and brine; dried over Na_2SO_4; and concentrated under reduced pressure. The residue was purified by flash column chromatography on silica gel (hexane/EtOAc = 4:1) to afford conjugated ketone **21** (89 mg, 78% yield over two steps) as a colorless oil. IR (neat) cm^{-1}: 3095, 2956, 2912, 2878, 1702, 1684, 1461, 1412, 1239, 1102, 1012, 744. ^{1}H NMR (400 MHz, C_6D_6) δ: 6.09 (dd, J = 17.6, 10.4 Hz, 1H), 5.89 (dd, J = 17.6, 1.2 Hz, 1H), 5.25 (dd, J = 10.4, 1.2 Hz, 1H), 3.48 (t, J = 6.4 Hz, 2H), 2.37 (t, J = 7.2 Hz, 2H), 1.82−1.75 (m, 2H), 0.95 (t, J = 8.0 Hz, 9H), 0.54 (q, J = 8.0 Hz, 6H). ^{13}C NMR (100 MHz, C_6D_6) δ: 199.1, 136.9, 126.8, 62.0, 35.9, 27.3, 7.1 (3C), 4.8 (3C). HRMS (TOF, CI$^+$) m/z: calcd for $C_{12}H_{25}O_2Si$ [M + H]$^+$ 229.1624, found 229.1633.

Preparation of Compounds 23a and 23b. To a stirred solution of 2-cyclopenten-1-one (**22**) (98%, 213 μL, 2.5 mmol) and aldehyde **20** or its five-carbon homologue (3.0 mmol) in THF (3 mL) was added (*S*)-(−)-1,1′-bi-2-naphthol) (BINOL) (98%, 73 mg, 0.25 mmol). The reaction mixture was flushed with nitrogen for 20 min at room temperature. Tributylphosphine (123 μL, 0.50 mmol) was added to the reaction mixture. After complete consumption of the starting material as indicated by TLC (about 12 h), the reaction mixture was concentrated under reduced pressure. The residue was purified by flash column chromatography on silica gel (hexane/EtOAc = 2:1) to afford the Morita−Baylis−Hillman[21] adduct, which was subsequently oxidized using DMP to provide 1,3-diketone **23a** or **23b**, respectively, as a yellow oil.

Compound ***23a***. 458 mg, 65% overall yield over two steps; yellow oil. IR (neat) cm^{-1}: 3062, 2956, 2913, 2877, 1712, 1694, 1603, 1460, 1413, 1240, 1097, 970. ^{1}H NMR (400 MHz, C_6D_6) δ: 7.68 (t, J = 2.8 Hz, 1H), 3.62 (t, J = 6.4 Hz, 2H), 3.07 (t, J = 6.4 Hz, 2H), 2.02−1.96 (m, 2H), 1.82−1.79 (m, 2H), 1.56−1.53 (m, 2H), 1.01 (t, J = 8.0 Hz, 9H), 0.60 (q, J = 8.0 Hz, 6H). ^{13}C NMR (100 MHz, C_6D_6) δ: 203.7, 195.8, 170.1, 144.3, 62.2, 38.8, 35.9, 27.0, 26.1, 7.1 (3C), 4.9 (3C). HRMS (TOF, CI$^+$) m/z: calcd for $C_{15}H_{27}O_3Si$ [M + H]$^+$ 283.1729, found 283.1724.

Compound ***23b***. 474 mg, 64% overall yield over two steps; yellow oil. IR (neat) cm^{-1}: 2955, 2923, 2875, 2853, 1738, 1704, 1648, 1459, 1376, 1239, 1099, 973. ^{1}H NMR (400 MHz, C_6D_6) δ: 7.67 (t, J = 2.8 Hz, 1H), 3.57 (t, J = 6.4 Hz, 2H), 2.97 (t, J = 7.2 Hz, 2H), 1.87−1.79 (m, 4H), 1.63−1.59 (m, 2H), 1.53−1.50 (m, 2H), 1.02 (t, J = 8.0 Hz, 9H), 0.61 (q, J = 8.0 Hz, 6H). ^{13}C NMR (100 MHz, C_6D_6) δ: 203.8, 195.9, 170.3, 144.3, 62.8, 41.9, 35.9, 32.7, 26.2, 20.3, 7.1 (3C), 4.9 (3C). HRMS (TOF, CI$^+$) m/z: calcd for $C_{16}H_{29}O_3Si$ [M + H]$^+$ 297.1886, found 297.1883.

Preparation of Compounds 25a and 25b. To a solution of γ-butyrolactone **24a** or **24b** (0.78 mL, 10 mmol) in THF (10 mL) at −78 °C was added lithium bis(trimethylsilyl)amide (LiHMDS) solution (11 mL, 1.0 M in THF, 11 mmol) dropwise. After 15 min of stirring, trimethylsilyl chloride (TMSCl) (1.4 mL, 11 mmol) was added to the reaction mixture. After the reaction mixture was stirred for additional 30 min at −78 °C, phenylselenyl chloride (PhSeCl) (98%, 2.2 g, 11 mmol) in 17 mL of THF was added. The reaction mixture was allowed to warm to room temperature gradually over 2 h, and the reaction was quenched by addition of a saturated NH_4Cl solution (20 mL). The organic layer was collected, and the aqueous layer was extracted with Et_2O (3 × 20 mL). The combined organic fractions were washed with brine, dried over Na_2SO_4, and concentrated under reduced pressure. The residue was purified by flash column chromatography on silica gel (hexane/EtOAc = 3:1) to afford the desired product (1.84 g, 76% yield) as an orange oil. To a solution of the α-phenylselenated lactone (1.2 g, 5.0 mmol) in THF (17 mL) was added LiHMDS solution (5.5 mL, 1.0 M in THF, 5.5 mmol) dropwise at −78 °C. After the reaction mixture was stirred for 1 h, aldehyde **20** (1.3 g, 6.0 mmol) in THF (5 mL) was added. After 20 min of stirring at −78 °C, the reaction was quenched by addition of a saturated NH_4Cl solution (15 mL). The aqueous layer was extracted with diethyl ether (3 × 15 mL). The combined organic fractions were washed with brine, dried over Na_2SO_4, and concentrated under reduced pressure to afford the crude aldol product, which was used directly for oxidative selenium elimination without further purification. To a solution of crude aldol product obtained above in THF/EtOAc (1:1 v/v, 25 mL) were sequentially added $NaHCO_3$ (4.2 g, 49 mmol) and hydrogen peroxide (30 wt %, 1.5 mL). After 10 min of stirring at room temperature, the reaction was quenched by addition of a saturated $Na_2S_2O_3$ solution (25 mL). The organic layer was collected, and the aqueous layer was extracted with EtOAc (3 × 25 mL). The combined organic fractions were washed with brine, dried over Na_2SO_4, and concentrated under reduced pressure. The residue was purified by flash column chromatography on silica gel (hexane/EtOAc = 3:1) to afford the desired butenolide (precursor for **25a** or **25b**), which was subsequently oxidized using DMP to provide the desired product **25a** or **25b**, respectively. However, attempts to purify **25a** and **25b** for spectroscopic characterization were unsuccessful. Therefore, the crude products **25a** and **25b** were used directly after DMP oxidation.

Precursor of ***25a***. 1.0 g, 71% yield over three steps; colorless oil. IR (neat) cm^{-1}: 3416, 2956, 2914, 2878, 1744, 1648, 1451, 1239, 1065. ^{1}H NMR (400 MHz, C_6D_6) δ: 6.56−6.54 (m, 1H), 4.48−4.46 (m, 1H), 3.78 (t, J = 2.0 Hz, 2H), 3.63 (br, 1H, OH), 3.47−3.42 (m, 2H), 2.10−2.03 (m, 1H), 1.71−1.64 (m, 1H), 1.59−1.55 (m, 2H), 0.97 (t, J = 8.0 Hz, 9H), 0.56 (q, J = 8.0 Hz, 6H). ^{13}C NMR (100 MHz, C_6D_6) δ: 172.8, 144.6, 137.2, 69.6, 67.6, 63.1, 33.5, 29.4, 6.9 (3C), 4.6 (3C). HRMS (TOF, CI$^+$) m/z: calcd for $C_{14}H_{27}O_4Si$ [M + H]$^+$ 287.1679, found 287.1672.

Precursor of ***25b***. 0.97 g, 65% yield over three steps, dr 1:1; colorless oil. IR (neat) cm^{-1}: 3426, 3093, 2956, 2914, 2878, 1750, 1651, 1457, 1415, 1378, 1321, 1239, 1203, 1091, 978, 801, 745. ^{1}H NMR (400 MHz, C_6D_6) δ: 6.65−6.62 (m, 1H), 4.52−4.50 (m, 1H), 4.29−4.23 (m, 1H), 3.68 (br, 1H, OH), 3.48−3.44 (m, 2H), 2.12−2.06 (m, 1H), 1.74−1.68 (m, 1H), 1.62−1.58 (m, 2H), 0.99−0.95 (m, 9H), 0.79−0.78 (m, 3H), 0.59−0.53 (m, 6H). ^{13}C NMR (100 MHz, C_6D_6) δ: 172.1/172.0, 149.1/149.1, 137.3/137.3, 77.3/77.2, 67.4/67.3, 63.2/63.2, 33.6/33.6, 29.3/29.2, 18.8/18.7, 6.9 (3C)/6.9 (3C), 4.7 (3C)/4.7 (3C). HRMS (TOF, CI$^+$) m/z: calcd for $C_{15}H_{29}O_4Si$ [M + H]$^+$ 301.1835, found 301.1834.

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Cascade Michael Addition/Cycloketalization. *General Procedure A.* To a solution of α,β-unsaturated carbonyl compound **6a** or **6b** (0.2 mmol) in CH_2Cl_2 (2 mL) was added cyclic 1,3-dicarbonyl compound **10a−d** (0.3 mmol). After 30 min of stirring, the reaction was quenched by addition of a saturated $NaHCO_3$ solution (1 mL). The organic layer was collected, and the aqueous layer was extracted with EtOAc (3 × 1 mL). The combined organic fractions were washed with brine, dried over Na_2SO_4, and concentrated under reduced pressure. The residue was purified by flash column chromatography on silica gel (hexane/EtOAc = 1:2) to afford the desired product (Table 1).

General Procedure B. To a solution of α,β-unsaturated carbonyl compound **6c**, **6d**, **21**, **23a**, **23b**, **25a**, or **25b** (0.2 mmol) in CH_2Cl_2 (2 mL) were added cyclic 1,3-dicarbonyl compound **10a−d** (0.3 mmol) and (*R*)-(−)-10-camphorsulfonic acid (CSA) (0.1−0.5 equiv). After 2 h of stirring, the reaction was quenched by addition of a saturated $NaHCO_3$ solution (1 mL). Similar workup as described previously and purification of the reaction mixture afforded the desired product (Table 1 and Table 2).

General Procedure C. To a solution of α,β-unsaturated carbonyl compound **6e** or **6f** (0.2 mmol) in CH_2Cl_2 (2 mL) were added the cyclic 1,3-dicarbonyl compound **10a−d** (0.3 mmol) and CSA (0.1−0.5 equiv). The reaction mixture was heated to reflux for 12 h (overnight), and then the reaction was quenched by addition of a saturated $NaHCO_3$ solution (1 mL). Similar workup as described previously and purification of the reaction mixture afforded the desired product (Table 1).

*Compound **11a**.*[7] General procedure A; 39 mg, 88% yield; colorless solid, mp = 98−100 °C. ^{1}H NMR (400 MHz, $CDCl_3$) δ: 5.71 (s, 1H), 4.07−3.95 (m, 2H), 2.68 (d, *J* = 17.6 Hz, 1H), 2.58 (dd, *J* = 18.0, 6.4 Hz, 1H), 2.47−2.40 (m, 1H), 2.17 (s, 3H), 2.11−2.04 (m, 1H), 1.78−1.67 (m, 1H), 1.50 (s, 3H). ^{13}C NMR (100 MHz, $CDCl_3$) δ: 165.4, 163.2, 160.6, 108.8, 100.5, 93.9, 67.4, 40.0, 28.1, 22.1, 19.9, 19.8.

*Compound **11b**.* General procedure A; 30 mg, 72% yield; light-yellow solid, mp = 112 °C. IR (neat) cm^{-1}: 2956, 2903, 2858, 1702, 1654, 1588, 1142, 1067, 991. ^{1}H NMR (400 MHz, C_6D_6) δ: 5.28 (s, 1H), 4.98 (d, *J* = 3.6 Hz, 1H), 3.76 (td, *J* = 8.8, 2.8 Hz, 1H), 3.47 (q, *J* = 8.8 Hz, 1H), 2.49 (d, *J* = 17.2 Hz, 1H), 2.17 (dd, *J* = 17.2, 6.4 Hz, 1H), 1.78−1.70 (m, 1H), 1.52 (s, 3H), 1.24−1.14 (m, 2H). ^{13}C NMR (100 MHz, $CDCl_3$) δ: 165.1, 162.9, 160.6, 101.3, 100.2, 94.5, 69.0, 36.6, 27.2, 19.8, 19.3. HRMS (TOF, CI$^+$) *m*/*z*: calcd for $C_{11}H_{12}O_4$ [M]$^+$ 208.0736, found 208.0739. The structure of **11b** (CCDC 1013961) was confirmed by single-crystal X-ray diffraction analysis.

*Compound **11c**.*[7] General procedure B; 34 mg, 72% yield; colorless solid, mp = 118 °C. ^{1}H NMR (400 MHz, $CDCl_3$) δ: 5.76 (s, 1H), 3.83−3.74 (m, 2H), 2.63 (dd, *J* = 15.6, 6.4 Hz, 1H), 2.30 (d, *J* = 15.6 Hz, 1H), 2.18 (s, 3H), 1.99−1.93 (m, 1H), 1.76−1.70 (m, 1H), 1.58−1.54 (m, 2H), 1.38 (s, 3H), 1.36−1.29 (m, 1H). ^{13}C NMR (100 MHz, $CDCl_3$) δ: 165.2, 163.6, 160.5, 102.5, 100.3, 95.4, 62.5, 34.8, 25.4, 25.0, 24.9 (2C), 19.8. The structure of **11c** (CCDC 929150) was confirmed by single-crystal X-ray diffraction analysis.

*Compound **11d**.* General procedure B; 29 mg, 65% yield; colorless oil. IR (neat) cm^{-1}: 2929, 2861, 1708, 1655, 1588, 1449, 1189, 1136, 994. ^{1}H NMR (400 MHz, $CDCl_3$) δ: 5.80 (s, 1H), 5.35 (d, *J* = 2.4 Hz, 1H), 3.89 (td, *J* = 11.2, 3.2 Hz, 1H), 3.77−3.74 (m, 1H), 2.59 (dd, *J* = 17.2, 6.4 Hz, 1H), 2.39 (dd, *J* = 17.2, 3.2 Hz, 1H), 2.22−2.18 (m, 4H), 1.74−1.53 (m, 4H). ^{13}C NMR (100 MHz, $CDCl_3$) δ: 164.9, 163.2, 160.5, 99.9, 97.8, 96.2, 62.3, 31.0, 23.8, 23.6, 23.5, 19.8. HRMS (TOF, CI$^+$) *m*/*z*: calcd for $C_{12}H_{15}O_4$ [M + H]$^+$ 223.0970, found 223.0975.

*Compound **11e**.* General procedure C; 40 mg, 79% yield; light-yellow solid, mp = 133 °C. IR (neat) cm^{-1}: 2929, 2858, 1708, 1651, 1576, 1205, 1137, 1068. ^{1}H NMR (400 MHz, $CDCl_3$) δ: 5.71 (s, 1H), 3.95−3.88 (m, 1H), 3.78−3.74 (m, 1H), 2.56 (dd, *J* = 16.0, 4.0 Hz, 1H), 2.20−2.05 (m, 5H), 1.83−1.79 (m, 1H), 1.73−1.56 (m, 3H), 1.50−1.36 (m, 2H), 1.27 (s, 3H). ^{13}C NMR (100 MHz, $CDCl_3$) δ: 165.2, 164.7, 160.6, 109.0, 100.6, 98.0, 63.6, 39.7, 30.3, 29.0, 27.8, 27.5, 19.8 (2C). HRMS (TOF, CI$^+$) *m*/*z*: calcd for $C_{14}H_{18}O_4$ [M]$^+$ 250.1205, found 250.1206. The structure of **11e** (CCDC 1013962) was confirmed by single-crystal X-ray diffraction analysis.

*Compound **11f**.* General procedure C; 22 mg, 47% yield; white solid, mp = 111 °C. IR (neat) cm^{-1}: 2926, 2859, 1709, 1653, 1585, 1450, 1180, 1104, 992, 913. ^{1}H NMR (400 MHz, $CDCl_3$) δ: 5.76 (s, 1H), 5.02 (d, *J* = 8.8 Hz, 1H), 3.95−3.84 (m, 2H), 2.63 (dd, *J* = 16.0, 4.8 Hz, 1H), 2.23 (d, *J* = 16.0 Hz, 1H), 2.17 (s, 3H), 1.93−1.89 (m, 1H), 1.77−1.67 (m, 3H), 1.58−1.44 (m, 3H). ^{13}C NMR (100 MHz, $CDCl_3$) δ: 164.7, 164.6, 160.8, 106.4, 100.1, 98.6, 65.3, 38.0, 30.4, 29.6, 28.4, 27.8, 19.9. HRMS (TOF, CI$^+$) *m*/*z*: calcd for $C_{13}H_{16}O_4$ [M]$^+$ 236.1049, found 236.1055.

*Compound **11g**.* General procedure A; 30 mg, 58% yield; white solid, mp = 178 °C. IR (neat) cm^{-1}: 2929, 2853, 1709, 1632, 1171, 1003. ^{1}H NMR (400 MHz, $CDCl_3$) δ: 7.84−7.82 (m, 1H), 7.53−7.49 (m, 1H), 7.31−7.24 (m, 2H), 4.14−4.01 (m, 2H), 2.86 (d, *J* = 18.0 Hz, 1H), 2.74 (dd, *J* = 18.0, 6.4 Hz, 1H), 2.57−2.51 (m, 1H), 2.18−2.11 (m, 1H), 1.86−1.75 (m, 1H), 1.61 (s, 3H). ^{13}C NMR (100 MHz, $CDCl_3$) δ: 163.5, 158.4, 152.8, 131.7, 123.9, 122.9, 116.7, 115.7, 109.4, 96.8, 67.5, 40.1, 28.3, 22.2, 20.7. HRMS (TOF, CI$^+$) *m*/*z*: calcd for $C_{15}H_{14}O_4$ [M]$^+$ 258.0892, found 258.0898.

*Compound **11h**.*[22] General procedure A; 33 mg, 68% yield. ^{1}H NMR (400 MHz, $CDCl_3$) δ: 7.77 (dd, *J* = 8.0, 1.6 Hz, 1H), 7.49−7.44 (m, 1H), 7.26−7.20 (m, 2H), 5.67 (d, *J* = 3.6 Hz, 1H), 4.19 (td, *J* = 8.8, 2.8 Hz, 1H), 4.05 (q, *J* = 8.8 Hz, 1H), 2.80−2.78 (m, 2H), 2.76−2.69 (m, 1H), 2.17−2.09 (m, 1H), 1.78−1.67 (m, 1H). ^{13}C NMR (100 MHz, $CDCl_3$) δ: 163.2, 158.0, 152.6, 131.6, 123.9, 122.7, 116.5, 115.3, 101.7, 97.3, 69.0, 36.6, 27.3, 20.1. The structure of **11h** (CCDC 1013963) was confirmed by single-crystal X-ray diffraction analysis.

*Compound **11i**.* General procedure B; 39 mg, 72% yield; white solid, mp = 154 °C. IR (neat) cm^{-1}: 2999, 2940, 2882, 1702, 1631, 1608, 1397, 1111, 992. ^{1}H NMR (400 MHz, $CDCl_3$) δ: 7.83−7.81 (m, 1H), 7.50−7.45 (m, 1H), 7.28−7.22 (m, 2H), 3.94−3.87 (m, 1H), 3.82−3.78 (m, 1H), 2.76 (dd, *J* = 18.0, 6.4 Hz, 1H), 2.45 (dd, *J* = 18.0, 0.8 Hz, 1H), 2.06−2.01 (m, 1H), 1.79−1.71 (m, 1H), 1.59−1.57 (m, 2H), 1.45 (s, 3H), 1.37 (td, *J* = 12.8, 3.6 Hz, 1H). ^{13}C NMR (100 MHz, $CDCl_3$) δ: 163.4, 158.7, 152.8, 131.6, 124.0, 122.6, 116.7, 115.7, 103.2, 98.2, 62.7, 34.8, 26.2, 25.1, 25.0, 24.9. HRMS (TOF, CI$^+$) *m*/*z*: calcd for $C_{16}H_{17}O_4$ [M + H]$^+$ 273.1127, found 273.1136.

*Compound **11j**.*[22] General procedure B; 48 mg, 93% yield. ^{1}H NMR (400 MHz, $CDCl_3$) δ: 7.87−7.85 (m, 1H), 7.54−7.51 (m, 1H), 7.34−7.27 (m, 2H), 5.55 (d, *J* = 2.0 Hz, 1H), 4.03−3.97 (m, 1H), 3.85−3.82 (m, 1H), 2.75 (dd, *J* = 17.6, 6.0 Hz, 1H), 2.56 (dd, *J* = 17.2, 2.8 Hz, 1H), 2.33−2.29 (m, 1H), 1.83−1.77 (m, 1H), 1.73−1.70 (m, 2H), 1.63−1.60 (m, 1H). ^{13}C NMR (100 MHz, $CDCl_3$) δ: 163.0, 158.3, 152.6, 131.6, 123.9, 122.5, 116.6, 115.3, 99.1, 98.3, 62.4, 31.0, 24.5, 23.9, 23.6.

*Compound **11k**.* General procedure C; 29 mg, 50% yield; white solid, mp = 142 °C. IR (neat) cm^{-1}: 2931, 2859, 1708, 1623, 1493, 1452, 1208, 1143, 1060. ^{1}H NMR (400 MHz, $CDCl_3$) δ: 7.80−7.78 (m, 1H), 7.48−7.44 (m, 1H), 7.26−7.19 (m, 2H), 4.04−3.98 (m, 1H), 3.86−3.83 (m, 1H), 2.73 (dd, *J* = 16.8, 4.8 Hz, 1H), 2.36−2.20 (m, 2H), 1.88−1.84 (m, 1H), 1.77−1.63 (m, 3H), 1.54−1.40 (m, 2H), 1.36 (s, 3H). ^{13}C NMR (100 MHz, $CDCl_3$) δ: 163.0, 160.6, 152.8, 131.6, 123.8, 122.9, 116.6, 116.0, 109.7, 100.8, 63.8, 39.9, 30.4, 29.1, 28.3, 27.9, 20.0. HRMS (TOF, CI$^+$) *m*/*z*: calcd for $C_{17}H_{18}O_4$ [M]$^+$ 286.1205, found 286.1214.

*Compound **11l**.* General procedure C; 22 mg, 40% yield; yellow solid, mp = 126 °C. IR (neat) cm^{-1}: 2927, 2857, 1711, 1629, 1494, 1392, 1156, 1029. ^{1}H NMR (400 MHz, $CDCl_3$) δ: 7.79−7.77 (m, 1H), 7.48−7.44 (m, 1H), 7.25−7.20 (m, 2H), 5.16 (d, *J* = 9.2 Hz, 1H), 4.05−4.00 (m, 1H), 3.93−3.90 (m, 1H), 2.76 (dd, *J* = 16.8, 4.8 Hz, 1H), 2.34 (dd, *J* = 16.8, 12.8 Hz, 1H), 2.19−2.11 (m, 1H), 1.95−1.91 (m, 1H), 1.83−1.71 (m, 4H), 1.62−1.51 (m, 1H). ^{13}C NMR (100 MHz, $CDCl_3$) δ: 162.8, 160.0, 152.7, 131.6, 123.9, 122.8, 116.5, 115.5, 106.9, 101.3, 65.3, 38.0, 30.4, 29.6, 29.2, 27.9. HRMS (TOF, CI$^+$) *m*/*z*: calcd for $C_{16}H_{17}O_4$ [M + H]$^+$ 273.1127, found 273.1137. The structure of **11l** (CCDC 1013964) was confirmed by single-crystal X-ray diffraction analysis.

*Compound **11m**.*[23] General procedure A; 34 mg, 82% yield; yellow oil. ^{1}H NMR (400 MHz, $CDCl_3$) δ: 4.06−4.00 (m, 1H), 3.97−3.91 (m, 1H), 2.58 (d, *J* = 16.4 Hz, 1H), 2.38−2.31 (m, 6H), 2.04−1.92 (m, 3H), 1.75−1.64 (m, 1H), 1.46 (s, 3H). ^{13}C NMR (100 MHz,

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$CDCl_3$) δ: 198.8, 169.5, 108.3, 106.9, 67.3, 40.0, 36.8, 28.8, 28.2, 22.1, 21.1, 18.9.

Compound ***11n***.[24] General procedure A; 34 mg, 88% yield; light-yellow oil. ^{1}H NMR (400 MHz, $CDCl_3$) δ: 5.41 (d, J = 4.0 Hz, 1H), 4.14 (td, J = 8.8, 2.4 Hz, 1H), 3.97 (q, J = 8.8 Hz, 1H), 2.57−2.55 (m, 2H), 2.40−2.34 (m, 5H), 2.06−2.01 (m, 1H), 2.00−1.91 (m, 2H), 1.70−1.60 (m, 1H). ^{13}C NMR (100 MHz, $CDCl_3$) δ: 198.6, 169.2, 107.5, 101.1, 68.9, 36.8, 36.7, 28.6, 27.4, 21.0, 18.4.

Compound ***11o***. General procedure B; 32 mg, 71% yield; yellow oil. IR (neat) cm^{-1}: 2939, 2864, 1654, 1622, 1393, 1110, 1046, 985. ^{1}H NMR (400 MHz, $CDCl_3$) δ: 3.82−3.69 (m, 2H), 2.44−2.28 (m, 5H), 2.18 (d, J = 15.6 Hz, 1H), 2.00−1.94 (m, 2H), 1.86−1.83 (m, 1H), 1.71−1.66 (m, 1H), 1.56−1.47 (m, 2H), 1.32 (s, 3H), 1.29−1.21 (m, 1H). ^{13}C NMR (100 MHz, $CDCl_3$) δ: 198.7, 169.6, 108.4, 102.0, 62.4, 36.8, 34.8, 28.6, 25.0, 24.9, 24.8, 24.4, 21.1. HRMS (TOF, CI$^+$) m/z: calcd for $C_{13}H_{18}O_3$ $[M]^+$ 222.1256, found 222.1263.

Compound ***11p***. General procedure B; 32 mg, 76% yield; colorless solid, mp = 80 °C. IR (neat) cm^{-1}: 2938, 2868, 1624, 1388, 1147, 1089, 935. ^{1}H NMR (400 MHz, $CDCl_3$) δ: 5.24 (d, J = 2.8 Hz, 1H), 3.92−3.86 (m, 1H), 3.74−3.69 (m, 1H), 2.45−2.41 (m, 2H), 2.38−2.35 (m, 2H), 2.31−2.22 (m, 2H), 2.12−2.06 (m, 1H), 2.00−1.93 (m, 2H), 1.69−1.65 (m, 3H), 1.55−1.49 (m, 1H). ^{13}C NMR (100 MHz, $CDCl_3$) δ: 198.3, 169.1, 109.3, 97.6, 62.5, 36.7, 31.0, 28.1, 23.7, 23.6, 22.4, 20.9. HRMS (TOF, CI$^+$) m/z: calcd for $C_{12}H_{16}O_3$ $[M]^+$ 208.1099, found 208.1104. The structure of **11p** (CCDC 1013966) was confirmed by single-crystal X-ray diffraction analysis.

Compound ***11q***. General procedure C; 28 mg, 60% yield; light-yellow oil. IR (neat) cm^{-1}: 2930, 2858, 1650, 1614, 1386, 1137, 1097, 1056. ^{1}H NMR (400 MHz, $CDCl_3$) δ: 3.98−3.92 (m, 1H), 3.80−3.75 (m, 1H), 2.50−2.45 (m, 1H), 2.39−2.29 (m, 4H), 2.01−1.88 (m, 4H), 1.83−1.79 (m, 1H), 1.74−1.71 (m, 1H), 1.65−1.55 (m, 2H), 1.45−1.36 (m, 2H), 1.25 (s, 3H). ^{13}C NMR (100 MHz, $CDCl_3$) δ: 198.2, 171.5, 111.7, 108.6, 63.6, 39.9, 36.7, 30.6, 29.2, 28.8, 27.9, 26.8, 21.1, 19.8. HRMS (TOF, CI$^+$) m/z: calcd for $C_{14}H_{20}O_3$ $[M]^+$ 236.1412, found 236.1413.

Compound ***11r***. General procedure C; 16 mg, 35% yield; white solid, mp = 96 °C. IR (neat) cm^{-1}: 2928, 2859, 1731, 1650, 1617, 1388, 1177, 1152, 1086, 935. ^{1}H NMR (400 MHz, $CDCl_3$) δ: 4.90 (d, J = 8.4 Hz, 1H), 3.97−3.91 (m, 1H), 3.86−3.82 (m, 1H), 2.54−2.51 (m, 1H), 2.41−2.38 (m, 2H), 2.35−2.30 (m, 2H), 1.99−1.83 (m, 6H), 1.72−1.64 (m, 2H), 1.48−1.42 (m, 2H). ^{13}C NMR (100 MHz, $CDCl_3$) δ: 198.2, 170.8, 112.1, 106.3, 65.2, 38.2, 36.6, 30.6, 29.8, 28.3, 27.9, 27.8, 21.0. HRMS (TOF, CI$^+$) m/z: calcd for $C_{13}H_{19}O_3$ $[M + H]^+$ 223.1329, found 223.1326.

Compound ***11s***. General procedure A; 16 mg, 40% yield; white solid, mp = 116 °C. IR (neat) cm^{-1}: 2926, 2855, 1678, 1617, 1407, 1179, 1101, 1003. ^{1}H NMR (400 MHz, $CDCl_3$) δ: 4.09 (td, J = 8.8, 2.8 Hz, 1H), 4.00 (q, J = 8.8 Hz, 1H), 2.60−2.48 (m, 2H), 2.44−2.41 (m, 3H), 2.38−2.32 (m, 2H), 2.07−2.00 (m, 1H), 1.74−1.63 (m, 1H), 1.52 (s, 3H). ^{13}C NMR (100 MHz, $CDCl_3$) δ: 204.4, 182.6, 111.5, 110.2, 67.6, 39.9, 33.4, 28.1, 26.6, 22.2, 17.4. HRMS (TOF, CI$^+$) m/z: calcd for $C_{11}H_{15}O_3$ $[M + H]^+$ 195.1021, found 195.1028.

Compound ***11t***. General procedure A; 24 mg, 67% yield; light-yellow solid, mp = 98 °C. IR (neat) cm^{-1}: 2927, 1679, 1619, 1410, 1117, 1066. ^{1}H NMR (400 MHz, $CDCl_3$) δ: 5.57 (d, J = 7.2 Hz, 1H), 4.18 (td, J = 8.4, 1.2 Hz, 1H), 4.01 (q, J = 8.4 Hz, 1H), 2.59−2.51 (m, 3H), 2.42−2.39 (m, 4H), 2.08−2.01 (m, 1H), 1.68−1.57 (m, 1H). ^{13}C NMR (100 MHz, $CDCl_3$) δ: 204.2, 182.3, 110.8, 103.7, 69.1, 36.5, 33.3, 27.3, 26.4, 17.1. HRMS (TOF, CI$^+$) m/z: calcd for $C_{10}H_{12}O_3$ $[M]^+$ 180.0786, found 180.0789.

Compound ***11u***. General procedure B; 37 mg, 90% yield; yellow oil. IR (neat) cm^{-1}: 2929, 2861, 1629, 1404, 1118, 1076. ^{1}H NMR (400 MHz, C_6D_6) δ: 3.68−3.61 (m, 1H), 3.51−3.47 (m, 1H), 2.17−2.01 (m, 4H), 1.98−1.92 (m, 2H), 1.32−1.25 (m, 2H), 1.17 (s, 3H), 1.05−1.02 (m, 1H), 0.99−0.97 (m, 2H). ^{13}C NMR (100 MHz, C_6D_6) δ: 201.8, 181.1, 111.9, 104.9, 62.2, 34.8, 33.7, 26.1, 25.3, 25.0, 24.9, 23.2. HRMS (TOF, CI$^+$) m/z: calcd for $C_{12}H_{17}O_3$ $[M + H]^+$ 209.1188, found 209.1178.

Compound ***11v***.[25] General procedure B; 34 mg, 87% yield; yellow oil. ^{1}H NMR (400 MHz, $CDCl_3$) δ: 5.42 (d, J = 2.4 Hz, 1H), 3.91 (td, J = 11.2, 3.2 Hz, 1H), 3.79−3.75 (m, 1H), 2.62−2.57 (m, 2H), 2.46−2.43 (m, 2H), 2.37−2.31 (m, 1H), 2.17−2.09 (m, 2H), 1.79−1.64 (m, 3H), 1.53−1.46 (m, 1H). ^{13}C NMR (100 MHz, $CDCl_3$) δ: 203.9, 182.4, 112.9, 100.1, 62.4, 33.4, 30.8, 26.0, 23.9, 23.6, 21.3.

Compound ***11x***. General procedure C; 9 mg, 20% yield; white solid, mp = 96 °C. IR (neat) cm^{-1}: 2927, 2856, 1689, 1627, 1392, 1181, 1155. ^{1}H NMR (400 MHz, $CDCl_3$) δ: 5.10 (d, J = 8.4 Hz, 1H), 4.00−3.87 (m, 2H), 2.56−2.54 (m, 2H), 2.46−2.36 (m, 3H), 1.97−1.91 (m, 3H), 1.81−1.67 (m, 4H), 1.55−1.50 (m, 1H). ^{13}C NMR (100 MHz, $CDCl_3$) δ: 203.4, 184.4, 115.9, 108.4, 65.4, 38.0, 34.0, 30.4, 29.7, 28.0, 26.1, 25.5. HRMS (TOF, CI$^+$) m/z: calcd for $C_{12}H_{17}O_3$ $[M + H]^+$ 209.1178, found 209.1183.

Compound ***12a***. General procedure B; reaction of **8**[26] and 4-hydroxy-6-methyl-2-pyrone (**10a**) for 2 h afforded **12a** in 50% yield (20 mg) as an amorphous solid. IR (neat) cm^{-1}: 2960, 2924, 2873, 2852, 1641, 1587, 1571, 1465, 1262, 1144, 1007. ^{1}H NMR (400 MHz, $CDCl_3$) δ: 6.19 (s, 1H), 5.77 (s, 1H), 4.78 (s, 2H), 2.21 (s, 3H), 2.00 (t, J = 8.0 Hz, 2H), 1.53−1.47 (m, 2H), 0.94 (t, J = 7.2 Hz, 3H). ^{13}C NMR (100 MHz, $CDCl_3$) δ: 163.6, 162.7, 161.8, 129.5, 112.3, 99.8, 99.6, 69.8, 35.1, 20.2, 19.9, 13.9. HRMS (TOF, CI$^+$) m/z: calcd for $C_{12}H_{14}O_3$ $[M]^+$ 206.0943, found 206.0950.

Compound ***12b***. General procedure B; reaction of **9**[27] and **10a** for 48 h afforded **12b** in <10% yield (5 mg) as an amorphous solid. IR (neat) cm^{-1}: 3441, 2958, 2925, 2872, 2853, 1681, 1585, 1451, 1409, 1381, 1251, 1064, 995, 833. ^{1}H NMR (400 MHz, $CDCl_3$) δ: 9.22 (s, 1H, OH), 5.81 (s, 1H), 2.97−2.92 (m, 1H), 2.58 (dd, J = 14.0, 10.8 Hz, 1H), 2.46 (dd, J = 14.0, 2.0 Hz, 1H), 2.21−2.17 (m, 6H), 1.80−1.74 (m, 2H), 1.44−1.37 (m, 2H), 0.98 (t, J = 7.2 Hz, 3H). ^{13}C NMR (100 MHz, $CDCl_3$) δ: 217.9, 166.1, 166.0, 160.7, 101.4, 101.3, 52.2, 34.8, 28.9, 23.2, 19.9, 19.8, 14.2. HRMS (TOF, CI$^+$) m/z: calcd for $C_{13}H_{18}O_4$ $[M]^+$ 238.1205, found 238.1204.

Compound ***26a***. General procedure B; 39 mg, 88% yield; colorless oil. IR (neat) cm^{-1}: 2955, 2912, 2877, 1724, 1586, 1236, 1073, 1004. ^{1}H NMR (400 MHz, $CDCl_3$) δ: 5.69 (s, 1H), 4.11−4.06 (m, 1H), 4.04−3.98 (m, 1H), 2.63−2.49 (m, 2H), 2.24−2.17 (m, 5H), 2.06−2.00 (m, 2H), 1.98−1.84 (m, 2H). ^{13}C NMR (100 MHz, $CDCl_3$) δ: 164.8, 163.2, 160.1, 108.8, 100.6, 98.2, 69.0, 36.7, 29.1, 23.7, 19.7, 16.9. HRMS (TOF, CI$^+$) m/z: calcd for $C_{12}H_{15}O_4$ $[M + H]^+$ 223.0970, found 223.0979.

Compound ***26b*** *(Separable Diastereomers)*. General procedure B; 49 mg, 88% yield, dr 1.5:1. Major diastereomer (**26b-1**): light-yellow solid, mp = 149 °C. IR (neat) cm^{-1}: 2960, 2894, 1741, 1707, 1654, 1590, 1405, 1055. ^{1}H NMR (400 MHz, C_6D_6) δ: 5.23 (s, 1H), 3.63−3.58 (m, 1H), 3.47−3.42 (m, 1H), 3.00 (q, J = 9.6 Hz, 1H), 2.79−2.64 (m, 2H), 2.14 (d, J = 9.6 Hz, 1H), 2.06−2.01 (m, 2H), 1.92−1.78 (m, 2H), 1.75−1.66 (m, 1H), 1.55 (s, 3H), 1.47−1.43 (m, 1H). ^{13}C NMR (100 MHz, C_6D_6) δ: 214.2, 163.2, 160.8, 160.7, 107.2, 101.6, 99.7, 69.9, 47.4, 37.9, 35.0, 32.3, 27.2, 23.1, 19.3. HRMS (TOF, CI$^+$) m/z: calcd for $C_{15}H_{17}O_5$ $[M + H]^+$ 277.1076, found 277.1082. The structure of **26b-1** (major isomer, CCDC 1013972) was confirmed by single-crystal X-ray diffraction analysis. Minor diastereomer (**26b-2**): light-yellow solid, mp = 136 °C. IR (neat) cm^{-1}: 2956, 2922, 1742, 1706, 1652, 1581, 1073. ^{1}H NMR (400 MHz, C_6D_6) δ: 5.16 (s, 1H), 3.65−3.57 (m, 2H), 3.51−3.45 (m, 1H), 2.82 (dt, J = 12.8, 4.8 Hz, 1H), 2.67 (ddd, J = 14.0, 8.4, 3.2 Hz, 1H), 2.04 (d, J = 7.6 Hz, 1H), 1.94 (dt, J = 14.0, 9.6 Hz, 1H), 1.84−1.74 (m, 3H), 1.65−1.58 (m, 1H), 1.44 (s, 3H), 1.36−1.32 (m, 1H). ^{13}C NMR (100 MHz, C_6D_6) δ: 213.1, 163.9, 162.6, 161.1, 107.7, 100.5, 100.2, 67.6, 54.5, 35.6, 35.3, 32.9, 23.9, 23.8, 19.1. HRMS (TOF, CI$^+$) m/z: calcd for $C_{15}H_{16}O_5$ $[M]^+$ 276.0998, found 276.1001.

Compound ***26c*** *(Inseparable Diastereomers)*. General procedure B; 52 mg, 89% yield, dr 5:1. Major diastereomer: light-yellow solid, mp = 140−143 °C. IR (neat) cm^{-1}: 2949, 2881, 1743, 1711, 1654, 1592, 1446, 1405, 1125, 1105, 1071, 1045. ^{1}H NMR (400 MHz, $CDCl_3$) δ: 5.78 (s, 1H), 3.53−3.46 (m, 2H), 3.08−3.01 (m, 1H), 2.62−2.52 (m, 1H), 2.35−2.21 (m, 2H), 2.17−2.09 (m, 5H), 1.85−1.76 (m, 2H), 1.61−1.57 (m, 2H), 1.47−1.42 (m, 2H). ^{13}C NMR (100 MHz, $CDCl_3$) δ: 215.9, 164.1, 160.7, 160.4, 101.6, 99.9, 98.7, 62.1, 50.6, 37.9, 31.4, 30.6, 26.8, 23.9, 19.7, 17.7. Minor diastereomer: ^{1}H NMR (400 MHz, $CDCl_3$) δ: 5.71 (s, 1H), 3.53−3.46 (m, 2H), 2.62−2.52 (m,

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4H), 2.35−2.21 (m, 2H), 2.17−2.09 (m, 3H), 1.85−1.76 (m, 2H), 1.61−1.57 (m, 2H), 1.47−1.42 (m, 2H). ^{13}C NMR (100 MHz, $CDCl_3$) δ: 214.1, 163.4, 163.3, 161.2, 100.9, 100.4, 98.4, 62.2, 55.3, 36.6, 31.8, 31.1, 24.5, 22.8, 19.6, 17.5. HRMS (TOF, CI$^+$) m/z: calcd for $C_{16}H_{18}O_5$ $[M]^+$ 290.1154, found 290.1148.

Compound ***26d***. General procedure B; 43 mg, 78% yield; yellow solid, mp = 164 °C. IR (neat) cm^{-1}: 2958, 2922, 2855, 1774, 1703, 1651, 1588, 1210, 1150, 1021, 993. ^{1}H NMR (400 MHz, C_6D_6) δ: 5.04 (s, br, 1H), 4.66 (d, J = 9.6 Hz, 1H), 3.81 (dd, J = 9.6, 4.8 Hz, 1H), 3.59−3.53 (m, 1H), 3.46−3.38 (m, 2H), 2.76−2.69 (m, 1H), 2.13 (d, J = 8.4 Hz, 1H), 1.93 (dt, J = 14.0, 9.6 Hz, 1H), 1.79−1.72 (m, 1H), 1.48−1.42 (m, 1H), 1.36 (s, 3H). ^{13}C NMR (100 MHz, C_6D_6) δ: 172.7, 163.9, 162.8, 161.8, 106.7, 100.1, 98.4, 69.9, 68.3, 46.1, 35.3, 32.6, 23.8, 19.2. HRMS (TOF, CI$^+$) m/z: calcd for $C_{14}H_{14}O_6$ $[M]^+$ 278.0790, found 278.0787. The structure of **26d** (CCDC 1013967) was confirmed by single-crystal X-ray diffraction analysis.

Compound ***26e***. General procedure B; 51 mg, 88% yield; white solid, mp = 156 °C. IR (neat) cm^{-1}: 2978, 2943, 2929, 1773, 1706, 1651, 1588, 1447, 1403, 1081, 1036. ^{1}H NMR (400 MHz, C_6D_6) δ: 5.12 (s, 1H), 4.91 (q, J = 6.4 Hz, 1H), 3.63−3.57 (m, 1H), 3.54−3.48 (m, 1H), 3.27 (d, J = 8.8 Hz, 1H), 2.80−2.73 (m, 2H), 2.04 (dt, J = 14.0, 9.6 Hz, 1H), 1.85−1.76 (m, 1H), 1.55−1.51 (m, 1H), 1.44 (s, 3H), 1.11 (d, J = 6.4 Hz, 3H). ^{13}C NMR (100 MHz, C_6D_6) δ: 172.4, 163.4, 163.0, 161.8, 107.0, 100.2, 99.4, 79.2, 68.3, 45.0, 37.7, 35.4, 23.7, 20.2, 19.2. HRMS (TOF, CI$^+$) m/z: calcd for $C_{15}H_{17}O_6$ $[M + H]^+$ 293.1025, found 293.1021.

Compound ***26f***. General procedure B; 39 mg, 75% yield; colorless oil. IR (neat) cm^{-1}: 2954, 2927, 2855, 1712, 1632, 1611, 1576, 1398, 1175, 1047. ^{1}H NMR (400 MHz, $CDCl_3$) δ: 7.73 (d, J = 7.6 Hz, 1H), 7.49 (t, J = 8.0 Hz, 1H), 7.31−7.23 (m, 2H), 4.19−4.13 (m, 1H), 4.10−4.04 (m, 1H), 2.75−2.70 (m, 2H), 2.42−2.37 (m, 2H), 2.17−2.08 (m, 3H), 2.04−1.98 (m, 1H). ^{13}C NMR (100 MHz, $CDCl_3$) δ: 163.1, 158.3, 152.7, 131.4, 123.8, 122.3, 116.6, 116.0, 109.3, 101.3, 69.2, 36.9, 29.0, 23.9, 17.8. HRMS (TOF, CI$^+$) m/z: calcd for $C_{15}H_{15}O_4$ $[M + H]^+$ 259.0970, found 259.0977.

Compound ***26g*** *(Separable Diastereomers)*. General procedure B; 46 mg, 74% yield, dr 1.9:1. Major diastereomer: light-yellow solid, mp = 152 °C. IR (neat) cm^{-1}: 2959, 2923, 2897, 1743, 1710, 1634, 1393, 1053. ^{1}H NMR (400 MHz, C_6D_6) δ: 7.49 (d, J = 7.6 Hz, 1H), 7.00−6.93 (m, 2H), 6.84−6.81 (m, 1H), 3.52−3.47 (m, 1H), 3.43−3.38 (m, 1H), 3.03−2.96 (m, 1H), 2.81−2.68 (m, 2H), 2.14−1.92 (m, 4H), 1.83−1.68 (m, 2H), 1.47−1.44 (m, 1H). ^{13}C NMR (100 MHz, C_6D_6) δ: 213.9, 161.4, 155.8, 153.3, 131.4, 123.5, 122.4, 116.8, 116.2, 107.4, 105.0, 70.0, 47.2, 37.9, 35.1, 33.0, 27.2, 23.1. HRMS (TOF, CI$^+$) m/z: calcd for $C_{18}H_{16}O_5$ $[M]^+$ 312.0998, found 312.0994. Minor diastereomer: light-yellow solid, mp = 163 °C. IR (neat) cm^{-1}: 2956, 2921, 1743, 1709, 1626, 1390, 1075. ^{1}H NMR (400 MHz, C_6D_6) δ: 7.53 (d, J = 8.0 Hz, 1H), 6.95−6.89 (m, 2H), 6.80−6.76 (m, 1H), 3.72−3.69 (m, 1H), 3.48−3.42 (m, 2H), 2.76−2.64 (m, 2H), 2.08 (d, J = 8.0 Hz, 1H), 2.03−1.94 (m, 1H), 1.83−1.72 (m, 1H), 1.66−1.58 (m, 3H), 1.52−1.47 (m, 1H). ^{13}C NMR (100 MHz, C_6D_6) δ: 213.0, 160.9, 159.0, 153.4, 131.7, 123.6, 122.6, 116.6, 116.2, 108.2, 104.3, 67.8, 54.3, 35.7, 35.3, 33.6, 24.4, 23.8. HRMS (TOF, CI$^+$) m/z: calcd for $C_{18}H_{16}O_5$ $[M]^+$ 312.0998, found 312.1014.

Compound ***26h*** *(Inseparable Diastereomers)*. General procedure B; 48 mg, 74% yield, dr 1.3:1; light-yellow solid, mp = 146−148 °C. IR (neat) cm^{-1}: 2947, 2879, 1741, 1709, 1628, 1388, 1073, 1046, 1030. Diastereomer A: ^{1}H NMR (400 MHz, $CDCl_3$) δ: 7.81−7.76 (m, 1H), 7.51−7.46 (m, 1H), 7.30−7.22 (m, 2H), 3.70−3.67 (m, 1H), 3.58−3.48 (m, 2H), 2.84−2.80 (m, 1H), 2.76−2.68 (m, 2H), 2.53−2.46 (m, 1H), 2.27−2.18 (m, 1H), 2.11−1.94 (m, 2H), 1.82−1.55 (m, 4H). ^{13}C NMR (100 MHz, $CDCl_3$) δ: 214.0, 161.7, 158.4, 152.8, 131.8, 124.1, 122.4, 116.6, 115.5, 104.4, 99.1, 62.7, 55.4, 36.8, 32.8, 31.3, 24.6, 23.5, 18.1. Diastereomer B: ^{1}H NMR (400 MHz, $CDCl_3$) δ: 7.81−7.76 (m, 1H), 7.51−7.46 (m, 1H), 7.30−7.22 (m, 2H), 3.58−3.48 (m, 2H), 3.30−3.23 (m, 1H), 2.76−2.68 (m, 1H), 2.40−2.33 (m, 2H), 2.27−2.18 (m, 1H), 2.11−1.94 (m, 3H), 1.82−1.55 (m, 4H). ^{13}C NMR (100 MHz, $CDCl_3$) δ: 215.7, 162.3, 155.5, 152.7, 131.6, 124.1, 122.3, 116.7, 115.5, 104.9, 99.2, 62.7, 50.7, 38.1, 32.2, 31.0, 27.2, 24.1, 18.3. HRMS (TOF, CI$^+$) m/z: calcd for $C_{19}H_{18}O_5$ $[M]^+$ 326.1154, found 326.1157.

Compound ***26i***. General procedure B; 53 mg, 84% yield; white solid, mp = 214 °C. IR (neat) cm^{-1}: 2958, 2924, 2854, 1775, 1707, 1633, 1395, 1163, 1078, 1035, 1009. ^{1}H NMR (400 MHz, C_6D_6) δ: 7.44−7.42 (m, 1H), 6.91−6.83 (m, 2H), 6.76−6.72 (m, 1H), 4.54 (d, J = 9.2 Hz, 1H), 3.86 (dd, J = 9.6, 5.6 Hz, 1H), 3.48−3.38 (m, 3H), 2.81 (ddd, J = 16.0, 8.0, 3.6 Hz, 1H), 2.19 (d, J = 8.4 Hz, 1H), 1.97 (dt, J = 13.6, 10.0 Hz, 1H), 1.80−1.73 (m, 1H), 1.51−1.44 (m, 1H). ^{13}C NMR (100 MHz, C_6D_6) δ: 172.6, 161.1, 159.1, 153.4, 131.9, 123.7, 122.6, 116.8, 115.8, 107.2, 102.0, 70.1, 68.4, 45.9, 35.2, 33.1, 23.7. HRMS (TOF, CI$^+$) m/z: calcd for $C_{17}H_{14}O_6$ $[M]^+$ 314.0790, found 314.0796.

Compound ***26j***. General procedure B; 56 mg, 85% yield; white solid, mp = 181 °C. IR (neat) cm^{-1}: 2964, 2933, 2901, 1777, 1708, 1632, 1397, 1166, 1056, 1029. ^{1}H NMR (400 MHz, C_6D_6) δ: 7.46−7.44 (m, 1H), 6.95−6.87 (m, 2H), 6.79−6.76 (m, 1H), 4.80 (q, J = 6.4 Hz, 1H), 3.47−3.43 (m, 2H), 3.33 (d, J = 8.8 Hz, 1H), 2.87 (ddd, J = 14.0, 8.0, 3.2 Hz, 1H), 2.79 (d, J = 8.8 Hz, 1H), 2.07 (dt, J = 14.0, 10.0 Hz, 1H), 1.85−1.78 (m, 1H), 1.54−1.50 (m, 1H), 1.13 (d, J = 6.8 Hz, 3H). ^{13}C NMR (100 MHz, C_6D_6) δ: 172.2, 161.3, 158.6, 153.4, 132.0, 123.7, 122.7, 116.8, 115.9, 107.5, 102.9, 79.4, 68.4, 45.0, 38.3, 35.4, 23.7, 20.5. HRMS (TOF, CI$^+$) m/z: calcd for $C_{18}H_{17}O_6$ $[M + H]^+$ 329.1025, found 329.1033.

Compound ***26k***. General procedure B; 33 mg, 79% yield; colorless oil. IR (neat) cm^{-1}: 2945, 2893, 1651, 1623, 1393, 1112, 1009. ^{1}H NMR (400 MHz, $CDCl_3$) δ: 4.12−4.07 (m, 1H), 4.02−3.97 (m, 1H), 2.41−2.33 (m, 6H), 2.19−2.13 (m, 2H), 1.99−1.91 (m, 4H), 1.87−1.80 (m, 2H). ^{13}C NMR (100 MHz, $CDCl_3$) δ: 198.2, 169.4, 111.4, 108.5, 68.9, 36.7 (2C), 29.4, 28.8, 23.8, 20.9, 16.1. HRMS (TOF, CI$^+$) m/z: calcd for $C_{12}H_{16}O_3$ $[M]^+$ 208.1099, found 208.1098.

Compound ***26l*** *(Separable Diastereomers)*. General procedure B; 34 mg, 65% yield, dr 1:1. Diastereomer A: light-yellow solid, mp = 114 °C. IR (neat) cm^{-1}: 2955, 2893, 1742, 1630, 1389, 1055, 1010. ^{1}H NMR (400 MHz, C_6D_6) δ: 3.66−3.60 (m, 1H), 3.48−3.42 (m, 1H), 3.11−3.04 (m, 1H), 2.78−2.64 (m, 2H), 2.23−2.10 (m, 4H), 2.00−1.85 (m, 5H), 1.73−1.66 (m, 1H), 1.44−1.37 (m, 3H). ^{13}C NMR (100 MHz, C_6D_6) δ: 214.6, 195.9, 165.7, 114.0, 106.3, 69.5, 47.3, 37.8, 36.9, 34.9, 31.4, 28.2, 27.4, 22.9, 20.6. HRMS (TOF, CI$^+$) m/z: calcd for $C_{15}H_{19}O_4$ $[M + H]^+$ 263.1283, found 263.1289. Diastereomer B: light-yellow solid, mp = 118 °C. IR (neat) cm^{-1}: 2947, 2893, 1741, 1647, 1615, 1385, 1072. ^{1}H NMR (400 MHz, C_6D_6) δ: 3.64−3.60 (m, 2H), 3.50 (q, J = 8.0 Hz, 1H), 2.66−2.60 (m, 1H), 2.57−2.52 (m, 1H), 2.17 (dt, J = 16.8, 4.0 Hz, 1H), 2.08 (d, J = 8.0 Hz, 1H), 2.03−1.95 (m, 1H), 1.91−1.83 (m, 6H), 1.72−1.66 (m, 1H), 1.54−1.46 (m, 1H), 1.29−1.23 (m, 2H). ^{13}C NMR (100 MHz, C_6D_6) δ: 214.0, 196.0, 169.7, 113.7, 107.1, 67.5, 54.8, 37.3, 35.7, 35.3, 32.4, 29.0, 25.3, 23.9, 20.3. HRMS (TOF, CI$^+$) m/z: calcd for $C_{15}H_{19}O_4$ $[M + H]^+$ 263.1283, found 263.1292.

Compound ***26m*** *(Inseparable Diastereomers)*. General procedure B; 47 mg, 85% yield, dr 5:1; light-yellow solid, mp = 134−136 °C. IR (neat) cm^{-1}: 2946, 2878, 1741, 1656, 1631, 1387, 1073, 1045, 1008. Diastereomer A: ^{1}H NMR (400 MHz, C_6D_6) δ: 3.44−3.37 (m, 1H), 3.30−3.27 (m, 1H), 3.03−2.96 (m, 1H), 2.75−2.69 (m, 1H), 2.61−2.53 (m, 1H), 2.24−2.12 (m, 4H), 2.02−1.95 (m, 2H), 1.91−1.82 (m, 4H), 1.79−1.69 (m, 1H), 1.51−1.41 (m, 4H). ^{13}C NMR (100 MHz, C_6D_6) δ: 215.2, 196.3, 164.9, 115.0, 98.3, 62.1, 50.9, 38.2, 37.3, 31.5, 31.4, 28.0, 27.9, 24.4, 21.1, 18.3. Diastereomer B: ^{1}H NMR (400 MHz, C_6D_6) δ: 3.58−3.55 (m, 1H), 3.44−3.37 (m, 1H), 3.30−3.27 (m, 1H), 2.92−2.88 (m, 1H), 2.61−2.53 (m, 1H), 2.08−2.06 (m, 2H), 1.97−1.95 (m, 4H), 1.79−1.69 (m, 3H), 1.41−1.25 (m, 6H). ^{13}C NMR (100 MHz, C_6D_6) δ: 213.8, 196.0, 168.6, 114.6, 98.0, 62.1, 55.7, 37.4, 36.6, 32.0, 31.8, 28.6, 25.2, 24.5, 20.4, 18.2. HRMS (TOF, CI$^+$) m/z: calcd for $C_{16}H_{20}O_4$ $[M]^+$ 276.1362, found 276.1357.

Compound ***26n***. General procedure B; 32 mg, 60% yield; light-yellow solid, mp = 152 °C. IR (neat) cm^{-1}: 2925, 2854, 1776, 1623, 1389, 1191, 1072, 924. ^{1}H NMR (400 MHz, C_6D_6) δ: 4.45 (d, J = 9.6 Hz, 1H), 3.93 (dd, J = 9.2, 5.6 Hz, 1H), 3.62−3.56 (m, 1H), 3.48−3.39 (m, 2H), 2.71 (ddd, J = 14.0, 8.0, 3.6 Hz, 1H), 2.17 (d, J = 8.4 Hz, 1H), 2.09−1.93 (m, 2H), 1.84−1.72 (m, 4H), 1.46−1.40 (m, 1H), 1.18−1.13 (m, 2H). ^{13}C NMR (100 MHz, C_6D_6) δ: 196.2, 173.4,

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170.1, 111.9, 106.1, 71.4, 68.2, 46.3, 36.7, 35.3, 32.0, 28.7, 23.9, 19.9. HRMS (TOF, CI$^+$) m/z: calcd for $C_{14}H_{17}O_5$ $[M + H]^+$ 265.1076, found 265.1077.

Compound ***26o***. General procedure B; 39 mg, 70% yield; white solid, mp = 154 °C. IR (neat) cm^{-1}: 2947, 2895, 1774, 1627, 1390, 1163, 1032, 1002. ^{1}H NMR (400 MHz, C_6D_6) δ: 4.68 (q, J = 6.4 Hz, 1H), 3.64−3.59 (m, 1H), 3.49 (q, J = 7.6 Hz, 1H), 3.25 (d, J = 8.8 Hz, 1H), 2.79−2.72 (m, 2H), 2.11−2.02 (m, 2H), 1.89−1.74 (m, 4H), 1.52−1.46 (m, 1H), 1.20−1.16 (m, 5H). ^{13}C NMR (100 MHz, C_6D_6) δ: 196.4, 172.9, 169.4, 112.9, 106.4, 80.6, 68.2, 45.2, 37.2, 36.7, 35.4, 28.7, 23.8, 20.3, 20.0. HRMS (TOF, CI$^+$) m/z: calcd for $C_{15}H_{19}O_5$ $[M + H]^+$ 279.1232, found 279.1226.

Compound ***26p***. General procedure B; 32 mg, 83% yield; light-yellow oil. IR (neat) cm^{-1}: 2956, 2923, 2852, 1688, 1621, 1404, 1087. ^{1}H NMR (400 MHz, C_6D_6) δ: 3.83−3.78 (m, 1H), 3.60−3.54 (m, 1H), 2.48−2.40 (m, 1H), 2.29−2.25 (m, 1H), 2.05−2.03 (m, 2H), 1.96−1.95 (m, 2H), 1.81−1.73 (m, 2H), 1.55−1.49 (m, 1H), 1.38−1.34 (m, 3H). ^{13}C NMR (100 MHz, C_6D_6) δ: 201.5, 181.3, 115.0, 111.0, 68.8, 36.7, 33.4, 29.2, 26.5, 23.8, 15.3. HRMS (TOF, CI$^+$) m/z: calcd for $C_{11}H_{15}O_3$ $[M + H]^+$ 195.1021, found 195.1029.

Compound ***26q*** *(Separable Diastereomers)*. General procedure B; 30 mg, 60% yield, dr 1:0.8. Major diastereomer: white solid, mp = 178 °C. IR (neat) cm^{-1}: 2955, 2922, 2852, 1740, 1690, 1625, 1399, 1073, 1012. ^{1}H NMR (400 MHz, C_6D_6) δ: 3.67−3.61 (m, 1H), 3.50 (q, J = 7.6 Hz, 1H), 3.37−3.34 (m, 1H), 2.91−2.85 (m, 1H), 2.76−2.70 (m, 1H), 2.00−1.94 (m, 1H), 1.91−1.89 (m, 3H), 1.83−1.78 (m, 5H), 1.50−1.43 (m, 2H). ^{13}C NMR (100 MHz, C_6D_6) δ: 212.9, 201.6, 182.8, 114.7, 110.0, 67.7, 54.2, 35.3, 35.1, 33.5, 31.5, 26.3, 23.8, 22.2. HRMS (TOF, CI$^+$) m/z: calcd for $C_{14}H_{17}O_4$ $[M + H]^+$ 249.1127, found 249.1133. Minor diastereomer: white solid, mp = 130 °C. IR (neat) cm^{-1}: 2958, 2923, 1741, 1692, 1640, 1402, 1056, 1015. ^{1}H NMR (400 MHz, C_6D_6) δ: 3.64−3.58 (m, 1H), 3.43 (q, J = 7.6 Hz, 1H), 2.80−2.65 (m, 2H), 2.47−2.40 (m, 1H), 2.11−2.04 (m, 1H), 2.01−1.97 (m, 3H), 1.94−1.86 (m, 3H), 1.80−1.66 (m, 2H), 1.45−1.36 (m, 2H). ^{13}C NMR (100 MHz, C_6D_6) δ: 214.0, 201.9, 179.3, 117.6, 109.7, 70.1, 46.8, 38.3, 35.1, 33.2, 31.0, 26.9, 26.5, 22.9. HRMS (TOF, CI$^+$) m/z: calcd for $C_{14}H_{17}O_4$ $[M + H]^+$ 249.1127, found 249.1137.

Compound ***26r*** *(Inseparable Diastereomers)*. General procedure B; 47 mg, 90% yield, dr 1.2:1; yellow solid, mp = 156−158 °C. IR (neat) cm^{-1}: 2948, 2881, 1740, 1694, 1643, 1400, 1123, 1093, 1070, 1045. Diastereomer A: ^{1}H NMR (400 MHz, $CDCl_3$) δ: 3.71−3.64 (m, 1H), 3.59−3.55 (m, 1H), 3.02−2.95 (m, 1H), 2.61−2.59 (m, 2H), 2.49−2.39 (m, 4H), 2.35−2.30 (m, 1H), 2.21−2.05 (m, 4H), 1.84−1.79 (m, 2H), 1.59−1.52 (m, 2H). ^{13}C NMR (100 MHz, $CDCl_3$) δ: 216.1, 204.0, 180.1, 117.7, 102.0, 62.6, 50.5, 38.6, 33.4, 31.0, 30.7, 26.9, 26.5, 24.1, 17.9. Diastereomer B: ^{1}H NMR (400 MHz, $CDCl_3$) δ: 3.71−3.64 (m, 2H), 3.36 (t, J = 6.4 Hz, 1H), 2.79−2.75 (m, 1H), 2.72−2.67 (m, 1H), 2.53−2.49 (m, 2H), 2.47−2.39 (m, 4H), 2.21−2.05 (m, 1H), 1.94−1.89 (m, 2H), 1.72−1.68 (m, 4H). ^{13}C NMR (100 MHz, $CDCl_3$) δ: 214.3, 203.7, 183.5, 115.6, 101.4, 62.7, 55.3, 36.3, 33.7, 31.3, 30.8, 26.2, 24.8, 21.5, 17.6. HRMS (TOF, CI$^+$) m/z: calcd for $C_{15}H_{19}O_4$ $[M + H]^+$ 263.1283, found 263.1284.

Compound ***26s***. General procedure B; 37 mg, 73% yield; white solid, mp = 189 °C. IR (neat) cm^{-1}: 2956, 2924, 2854, 1775, 1691, 1630, 1401, 1198, 1152, 1024, 989. ^{1}H NMR (400 MHz, C_6D_6) δ: 4.74 (d, J = 8.8 Hz, 1H), 3.66 (dd, J = 9.2, 5.2 Hz, 1H), 3.62−3.56 (m, 1H), 3.44 (q, J = 8.0 Hz, 1H), 3.12−3.09 (m, 1H), 2.74 (ddd, J = 14.0, 8.0, 3.6 Hz, 1H), 2.01 (d, J = 8.0 Hz, 1H), 2.00−1.95 (m, 1H), 1.79−1.67 (m, 5H), 1.44−1.41 (m, 1H). ^{13}C NMR (100 MHz, C_6D_6) δ: 201.5, 183.1, 172.8, 112.8, 109.1, 68.6, 68.4, 45.6, 35.3, 33.3, 31.3, 26.3, 23.8. HRMS (TOF, CI$^+$) m/z: calcd for $C_{13}H_{15}O_5$ $[M + H]^+$ 251.0919, found 251.0925.

Compound ***26t***. General procedure B; 48 mg, 90% yield; light-yellow solid, mp = 154 °C. IR (neat) cm^{-1}: 2980, 2931, 1774, 1692, 1635, 1401, 1211, 1149, 1085. ^{1}H NMR (400 MHz, C_6D_6) δ: 5.06 (q, J = 6.4 Hz, 1H), 3.66−3.60 (m, 1H), 3.49 (q, J = 8.0 Hz, 1H), 3.03 (d, J = 7.2 Hz, 1H), 2.80−2.74 (m, 1H), 2.66 (d, J = 8.0 Hz, 1H), 2.08−2.00 (m, 1H), 1.83−1.74 (m, 5H), 1.49−1.47 (m, 1H), 0.98 (d, J = 6.4 Hz, 3H). ^{13}C NMR (100 MHz, C_6D_6) δ: 201.7, 182.6, 172.4, 113.6, 109.3, 77.3, 68.5, 44.4, 36.3, 35.4, 33.3, 26.4, 23.7, 19.7. HRMS (TOF, CI$^+$) m/z: calcd for $C_{14}H_{16}O_5$ $[M]^+$ 264.0998, found 264.1000. The structure of **26t** (CCDC 1013975) was confirmed by single-crystal X-ray diffraction analysis.

■ ASSOCIATED CONTENT

Ⓢ Supporting Information

Copies of ^{1}H and ^{13}C NMR spectra of new compounds and X-ray data (CIF) for compounds **11b**, **11e**, **11h**, **11l**, **11p**, **26b-1**, **26d**, and **26t**. This material is available free of charge via the Internet at http://pubs.acs.org. The supplementary crystallographic data have also been deposited at the Cambridge Crystallographic Data Centre (http://www.ccdc.cam.ac.uk) under the following entry numbers: **11b** (CCDC 1013961), **11e** (CCDC 1013962), **11h** (CCDC 1013963), **11l** (CCDC 1013964), **11p** (CCDC 1013966), **26b-1** (CCDC 1013972), **26d** (CCDC 1013967), and **26t** (CCDC 1013975).

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Notes

The authors declare no competing financial interest.

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