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Copper-Catalyzed Asymmetric Synthesis of Bicyclo[3.*n*.1]alkenones

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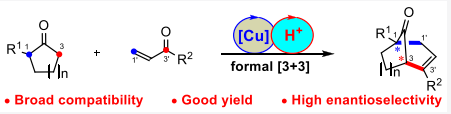
ABSTRACT: A series of highly strained bicyclo[3.*n*.1]alkenones have been successfully constructed in good-to-excellent enantioselectivities and moderate-to-good yields via copper-catalyzed formal [3+3] cycloaddition. The versatile chiral cycloadducts could be selectively converted into various valuable bridge systems, which hold considerable potential for the construction of natural and bioactive compounds containing a [3.*n*.1] moiety.



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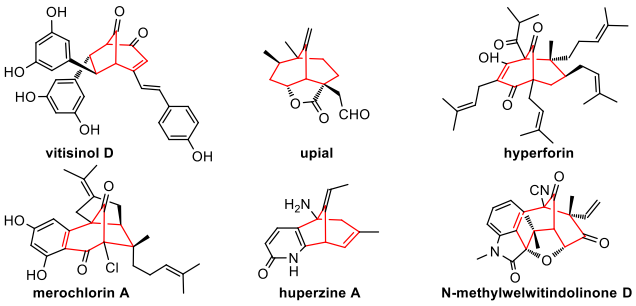
The highly strained bicyclo[3.*n*.1] system is an important structure that exists in a large number of bioactive natural products (Scheme 1).[1] For example, hyperforin has been proved versatile biological properties including antidepression and inhibition of tumor invasion.[1b] Huperzine A, a natural cholinesterase inhibitor from a Chinese herb, was recently unveiled that it might be used as a disease-modifying treatment for Alzheimer's disease (AD), and the phase II trial is under way.[1c,d] *N*-Methylwelwitindolinone D and its congeners display a wide variety of biological activities, ranging from antifungal effects to microtubule depolymerization and reversal of P-glycoprotein-mediated multidrug resistance in human carcinoma cells.[1e,f] Therefore, developing methods to construct such bicyclo [3.*n*.1] skeleton is highly desired, especially the asymmetric version by using simple materials.

Scheme 1. Natural Products Containing Bicyclo[3.*n*.1] Skeletons



During the past decades, diverse synthetic methods have been accumulated in the construction of this important skeleton. Typically, these methods were based on conia-ene-type cyclization,[2] pinacol rearrangement,[3] tandem Michael/aldol reaction,[4] biomimic dearomatization annulation,[5] trans-annulation,[6] double Tsuji−Trost cycloaddition,[7] and Effenberger cyclization.[8] Nevertheless, the methods for the enantioenriched bicyclo[3.*n*.1] system with a quaternary stereocenter are still limited, and most of them proceeded through aminocatalysis. For examples, Barluenga[9] and Hu[10] independently developed a transition-metal catalytic system to access such skeleton by desymmetrization of enamine. Similarly, Jia and their co-workers introduced an amine/copper dual catalytic protocol to synthesize a benezo-fused bicyclo compound via desymmetrization of cyclohexone.[11] In addition, a double activation strategy by combining amino-catalysis and N-heterocyclic carbene catalysis was adopted by Rodriguez and Coquerel, which enabled a direct enantioselective entry to such bridged bicyclic compound.[4c] Lately, several enantioselective versions by using other organo-catalysts, such as phosphoric acid,[12] dihydroquinine,[4b] bifunctional aminoquinine-thiourea,[5c] and transition metal,[13] were reported as well. Considering the limited ability of the organocatalyst in substrate activation and a relative high catalyst loading, we envisioned that transition-metal catalysis might be able to circumvent these challenges in a complementary way.

Structurally, the bicyclo[3.*n*.1]octene **4** could be regarded as a formal [3+3] cycloaddition adduct via a bridge-type Robinson annulation of **2** with **1** via intermediate **3**. The critical γ-quaternary chiral center,[14] which was less studied, comparing to the corresponding β-carbon stereocenter,[15] could be established by a regio- and enantioselective intermolecular Michael addition reaction (Scheme 2).

As part of our continuous effort in asymmetrical synthesis by using a chiral bisoxazoline (Box) ligand,[16] the combination of bisoxazoline and several triflate salts were tested first using methyl-β-ketoester **1a** and enone **2a** as model substrates (Table 1, entries 1−3). The results showed that the bisoxazoline L1/Cu(OTf)$_2$ catalytic system functioned better than others, which afforded intermediate **3a** in a promising

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Scheme 2. Access to the Bicyclo[3.*n*.1] System with a γ-Quaternary Chiral Stereocenter

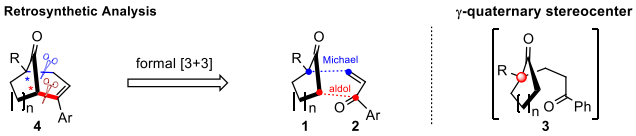
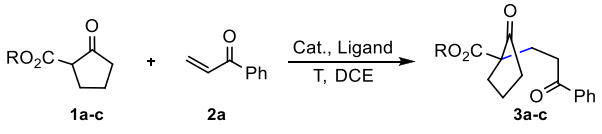
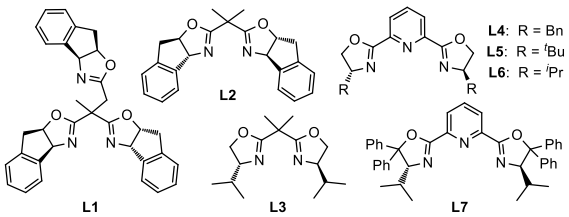


Table 1. Optimization of Reaction Conditions[a]



Entry	R	Cat.	Ligand	T [°C]	Yield [%]	ee [%]
1	Me (**1a**)	$Cu(OTf)_2$	**L1**	80	54	74
2	Me (**1a**)	$Fe(OTf)_2$	**L1**	80	69	4
3	Me (**1a**)	$Zn(OTf)_2$	**L1**	80	75	6
4[b]	Me (**1a**)	$Cu(OTf)_2$	**L1**	80	48	43
5[c]	Me (**1a**)	$Cu(OTf)_2$	**L1**	80	37	54
6	Me (**1a**)	$Cu(OTf)_2$	**L2**	rt	90	51
7	Me (**1a**)	$Cu(OTf)_2$	**L3**	rt	99	49
8	Me (**1a**)	$Cu(OTf)_2$	**L4**	rt	93	25
9	Me (**1a**)	$Cu(OTf)_2$	**L5**	rt	82	33
10	Me (**1a**)	$Cu(OTf)_2$	**L6**	rt	100	37
11	Me (**1a**)	$Cu(OTf)_2$	**L7**	rt	89	0
12	Me (**1a**)	$Cu(OTf)_2$	**L1**	rt	88	89
13[d]	Me (**1a**)	$Cu(OTf)_2$	**L1**	0	81	90
14[d]	Et (**1b**)	$Cu(OTf)_2$	**L1**	0	83	91
15[e]	iPr (1c)	$Cu(OTf)_2$	**L1**	0	84	92



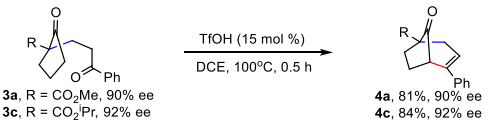
[a]Catalyst (20 mol %) and L1 (24 mol %) were stirred in DCE (0.1 M) for 5 min, and then **1** (0.2 mmol) and **2a** (0.24 mmol) were added; The mixture was tirred for 24 h, isolated yield. [b]20 mol % (R)-BNP acid was added. [c]20 mol % TfOH was added. [d]10 mol % $Cu(OTf)_2$, 12 mol %, 72 h. [e]10 mol % $Cu(OTf)_2$, 12 mol % L, 48 h.

yield and enantiomeric excess (entry 1). For the purpose of merging Michael addition, aldol cyclization, and dehydration in one operation, several acids as cocatalyst were also screened. However, instead of the desired bicyclic adduct **4a**, the intermediate **3a** was obtained in a compromised yield and enantioselectivity (entries 4 and 5).

Consequently, more attention was paid to developing a consequential stepwise process, which was initiated by evaluating the ligands effects in the construction of intermediate **3a**. The Box ligands (L2, L3) without side arm could promote the Michael addition process efficiently at ambient temperature to give **3a** in a slightly improved yield, but in moderate enantioselectivity (entries 6 and 7). When the coplanar tridentate Pyboxes (L4, L5, and L6) were used, dismal enantioselectivities were obtained (entries 8−10). However, the racemic product was obtained using bulky ligand L7 (entry 11). Based on the above feedbacks, the side arm-Box L1 was chosen as the chiral ligand for further optimization. It was found that decreasing the temperature had slightly beneficial effect on enantioselectivity (entries 12 and 13). Finally, the influence of steric effect was explored (entries 14 and 15). The enantioselectivity could be further enhanced to 92% ee with good yield when isopropyl ester **1c** was used as substrate (entry 15). Other ligands and solvents were screened as well, but no further improvements were obtained. It is noteworthy that the superiority of side arm-Box L1 in asymmetric induction might result from its ability to form a compact octahedral intermediate with the branch side arm posed in d_{Z^2} direction (see Supporting Information, page S5, for the proposed induction model).[14c,15b,c]

After the method for enantiomerically enriched 1,5-dicarbonyl product **3** was established, we set out to identify a suitable catalytic system that can achieve the intramolecular cyclization easily and economically. It is exciting to find that when the simple Brønsted acid (TfOH) was employed as catalyst, the desired product **4** was obtained in a high yield, and the ee value remained. (Table 2)

Table 2. Optimization of Reaction Conditions[a]



[a]The reaction was performed with **3** (0.1 mmol), TfOH (15 mol %), and DCE (0.1 M) under an air atmosphere for 0.5 h

Under the optimal conditions (Table 1, entry 15, and Table 2), the substrate scope of the reaction was then explored. As shown in Table 3, the catalytic system worked smoothly with a series of β-ketoesters **1** and enones **2** to afford **4a**−**u** in moderate to good yields and excellent enantioselectivities (87%−95%). The reaction was compatible with both electron-withdrawing and electron-donating groups on the aromatic rings (**4g** and **4l**). Furthermore, the substrates with heteroaromatic substituents (**4s**−**u**) generated the products in moderate yields and good enantioselectivies. Other β-ketoesters with different ring sizes could also be successfully employed to afford the expected structure; however, the enantioselectivity decreased when the ring size increased (**4v**−**w**).

Encouraged by the above success, we turned to exploit a new type of substrate with two different enone motifs owing to the potential application of the diene products. The cinnamaldehyde derivative **5a** was first tested. Surprisingly, the reaction displayed excellent regio- and enantioselectivity to give **7a** as a single product in 93% ee. As shown in Table 4, most substrates gave moderate-to-good yields and excellent enantioselectivities (**7a**−**e**). However, the enone bearing strong electron-donating group (−OCH_3) failed to provide the corresponding cyclization product in a good yield (**7f**) under the acid condition. We have investigated several Lewis acids and found that, when the TfOH was replaced by $Sc(OTf)_3$, the bicyclo[3.2.1] product (**7f**) was obtained in a higher yield with a slightly decreased enantioselectivity.

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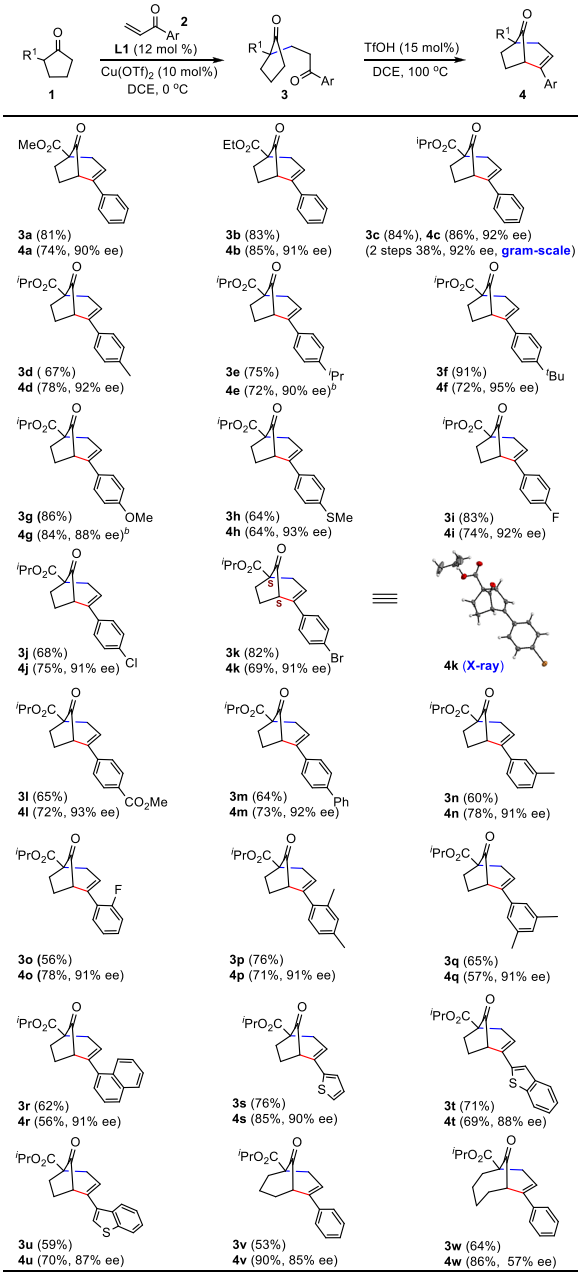
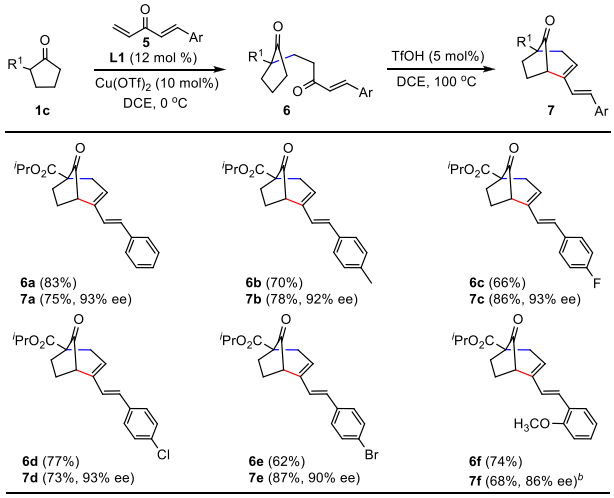
Table 3. Scope of the Substrates[a]



[a]The $Cu(OTf)_2$ (10 mol %) and L1 (12 mol %) in DCE (0.1 M) were stirred for 5 min. Then, **1** (0.2 mmol) and **2** (0.24 mmol) were added, and the mixture was stirred at 0 °C for 35−96 h. Purified **3** (0.1 mmol) was treated with TfOH (15 mol %) in DCE (0.1 M) at 100 °C for 10−120 min. [b]The reaction was conducted with **3** (0.1 mmol) and $Sc(OTf)_3$ (20 mol %) in 100 °C for 10−120 min.

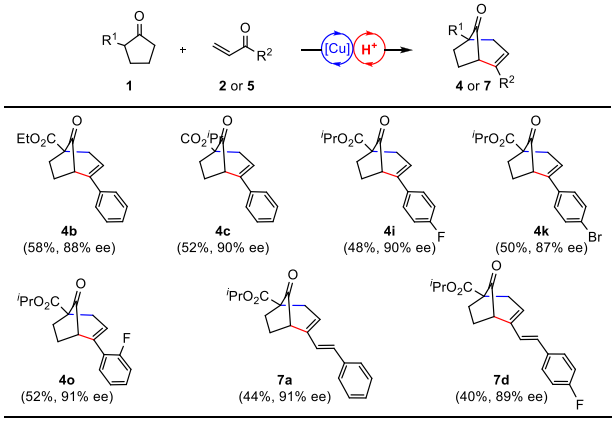
For the purpose of simplifying the processes, a sequential one-pot synthesis was tried. As shown in Table 1, directly introducing TfOH to the reaction system at the initial process not only failed to give the desired bicyclo[3.2.1] product but also was detrimental to the yield and enantioselectivity of the Michael addition reaction. So, a sequential addition procedure by adding TfOH when the first process had finished was applied. Gratifyingly, this one-pot catalytic relay annulation exhibited superior efficiency with the corresponding bicyclo[3.2.1]alkenones obtained in equally well enantioselectivities (Table 5).

Table 4. Scope of the Substrates[a]



[a]The $Cu(OTf)_2$ (10 mol %) and L1 (12 mol %) in DCE (0.1 M) were stirred for 5 min. Then, **1c** (0.2 mmol) and **5** (0.24 mmol) were added, and the mixture was stirred at 0 °C for 35−96 h. Purified **6** (0.1 mmol) was treated with TfOH (5 mol %) in DCE (0.1M) at 100 °C for 10−120 min. [b]The reaction was conducted with **6f** (0.1 mmol) and $Sc(OTf)_3$ (5 mol %) in 100 °C for 10 min.

Table 5. One-Pot Relay Catalytic Annulation



[a]The $Cu(OTf)_2$ (10 mol %) and L1 (12 mol %) in DCE (0.1 M) were stirred for 5 min; then, **1** (0.1 mmol) and **2**/**5** (0.12 mmol) were added, and then stirred at 0 °C until the reaction had finished. Finally, TfOH (50 mol %) was added, and the mixture was heated at 100 °C for 5−60 min.

With the chiral bicyclo[3.2.1] products **4** and **7** in hand, further transformations were carried out to demonstrate the potential applications of these products (Scheme 3). The C═O and carbon−carbon double bond of **4c** could be easily reduced to produce **8** and **9** independently, and the stereostructure was confirmed by the NOE spectrum. Considering the importance of the bridged C═C bond in a natural product (Scheme 1), the diene **10** was then synthesized via Wittig olefination from **4c**. Inspired by the architecture of the bioactivity-enriched huperzine A, further chemical transformation of **10** was performed. The ester group of **10** could be efficiently converted to a carboxyl group, which was used directly without purification for the following copper-catalyzed Curtius rearrangement the protocol disclsoed by Lu lately,[17] and the carbamate product **11** was eventually obtained in an

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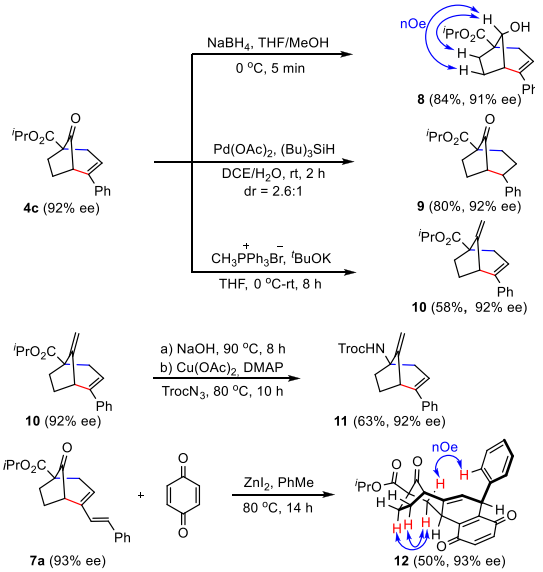
Scheme 3. Diversification of the Bicyclo[3.*n*.1]alkenones



overall yield of 63% for two steps. Furthermore, dienone **7a** could be used as a valid diene for the Diels–Alder reaction with *p*-benzoquinone, giving the unexpected oxidized adduct **12** in 50% yield. The stereochemistry was well retained in all of these transformations.

In summary, we have developed a copper-catalyzed formal [3+3] cycloaddition, which delivered a series of chiral bicyclo[3.*n*.1]alkenone frameworks with an all-carbon quaternary stereocenter in moderate yields and good-to-excellent enantioselectivities. In addition, a one-pot catalytic relay annulation was also established. The reaction was proposed to proceed through a tandem of Michael addition and intramolecular aldol cyclization. The functional group enriched chiral bicyclo[3.*n*.1] products could be selectively transformed into various value-added bridged systems via Curtius rearrangement, DA-reaction, olefination, and reduction, which hold considerable potential for the construction of natural or bioactive compounds containing the bicyclo[3.*n*.1] skeletons.

EXPERIMENTAL SECTION

General Information. All reactions were carried out under N_2 in a Schlenk tube under otherwise noted, ^{1}H, ^{13}C, ^{19}F NMR, and 2D NMR spectra were recorded on a Bruker AVANCE 400 and Bruker AVANCE 500. ^{1}H NMR and ^{13}C NMR chemical shifts were determined relative to an internal standard, TMS at δ 0.0. Chemical shifts (δ) are reported in ppm, and coupling constants (J) are in hertz (Hz). The following abbreviations were used to explain the multiplicities: s = singlet, d = doublet, t = triplet, q = quartet, m = multiplet. HRMS spectra were recorded on an Agilent UHD-Accurate Mass Q-TOF LC/MS. HPLC analysis was performed on WHELK-O1, OD-H, OJ-H, and IA columns. X-ray crystallographic analysis was performed on an Agilent SuperNova, Dual, Cu at zero, AtlasS2 diffractometer. Melting points were determined on a JH30 melting point apparatus bought from JIAHANG. Optical rotations were measured on ADP440+B+S. Infrared (IR) spectra were recorded on a Nicolet 210 spectrophotometer and were recorded in a potassium bromide (KBr) pellet.

Compounds **1a**, **1b**, and L1–**L26** and solvents were commercial and used without purification. Compound **1c**,[18] **1d**,[19] **2**,[20] and **5**[21] were synthesized according to the literature procedures. All of these compounds are known.

Procedure for the Preparation of 1e. LDA (10 mmol, 2.5 mmol/L in THF) was added dropwise to a solution of cycloheptanone (560 mg, 5 mmol) in dry THF (8 mL) at −78 °C, and then the solution was stirred for 1 h. Isobutyryl chloride (612 mg, 6 mmol) in 5 mL of dry THF was added via syringe. The mixture was warmed to room temperature over 4 h. The reaction was quenched with saturated NH_4Cl solution (10 mL). The organic phase was washed with NaCl solution (3 × 20 mL), dried with Na_2SO_4, and concentrated under a reduced vacuum. The residue was chromatography with EtOAc/petroleum ether (1:15) to give the desired product (380 mg, 40%) as a colorless oil. ^{1}H NMR (500 MHz, $CDCl_3$): δ 12.83 (s, 0.3 H), 5.29–4.91 (m, 0.9 H), 3.49 (dd, J = 10.2, 3.9 Hz, 0.6H), 2.84–2.51 (m, 1.3H), 2.51–2.34 (m, 1.3H), 2.07 (m, 0.7H), 1.98–1.80 (m, 2.7H), 1.77–1.65 (m, 0.7H), 1.56–1.62 (m,1.6H), 1.58–1.37 (m, 2H), 1.37–1.14 (m, 6H). ^{13}C{^{1}H} NMR (126 MHz, $CDCl_3$): δ 209.1, 179.3, 172.7, 170.1, 102.0, 69.0, 67.7, 59.1, 43.1, 35.4, 32.0, 29.7, 27.9, 27.6, 27.4, 24.6, 24.4, 24.3, 21.9, 21.7, 21.6. IR (KBr, cm^{-1}): 2950, 1737, 1706, 1453, 1306, 1242, 1106, 937, 909. HRMS (ESI-TOF): m/z [M + H]$^+$ calcd for $C_{11}H_{20}O_3$, 199.1329; found, 199.1324.

*General Procedure for the Preparation of **3/6**.* Copper(II) trifluoromethanesulfonate (7.0 mg) and L1 (12 mg) in 1 mL of dry DCE were stirred for 5 min in a 25 mL Schlenk tube. Ketene **2**/**5** (0.24 mmol) and β-Ketoesters (0.2 mmol) **1** were dissolved in 1 mL of dry DCE and added dropwise to the tube. The reaction was stirred at 0 °C until substrate **1** was completely consumed. The solvent was removed under a reduced vacuum, and the resulting mixture was purified by silica gel chromatography (EtOAc/petroleum ether = 1:10) to give the product **3**/**6**. Racemic samples were prepared by using the same procedure with copper(II) trifluoromethanesulfonate as a catalyst.

*Methyl 2-Oxo-1-(3-oxo-3-phenylpropyl)cyclopentane-1-carboxylate (**3a**).* Yield: 81% (44 mg), colorless oil, R_f = 0.6 (EtOAc/petroleum ether = 1:10). ^{1}H NMR (500 MHz, $CDCl_3$): δ 7.96 (d, J = 7.6 Hz, 2H), 7.55 (t, J = 7.5 Hz, 1H), 7.46 (t, J = 7.6 Hz, 2H), 3.73 (d, J = 2.1 Hz, 3H), 3.28–3.19 (m, 1H), 3.08–2.95 (m, 1H), 2.57–2.50 (m, 1H), 2.47–2.40 (m, 1H), 2.39–2.33 (m, 1H), 2.33–2.26 (m, 1H), 2.16–2.08 (m, 1H), 2.07–1.95 (m, 3H). ^{13}C{^{1}H} NMR (126 MHz, $CDCl_3$): δ 214.7, 199.3, 171.9, 136.7, 133.1, 128.6, 128.1, 59.2, 52.6, 38.0, 34.4, 34.1, 27.8, 19.6. IR (KBr, cm^{-1}): 3064, 1731, 1684, 1446, 1217, 1157, 992, 842, 765, 745, 692. HRMS (ESI-TOF): m/z [M + Na]$^+$ calcd for $C_{16}H_{18}O_4Na$, 297.1097; found, 297.1101. HPLC: OJH column, 90:10 hexanes/isopropanol, 0.80 mL/min, t_R = (major) 34.7 min, (minor) 38.1 min, 90% ee. $[\alpha]_D^{25}$ +13.1° (c 0.98, EtOAc)

*Ethyl 1-(3-(4-Methoxyphenyl)-3-oxopropyl)-2-oxocyclopentane-1-carboxylate (**3b**).* Yield: 83% (48 mg), colorless oil, R_f = 0.6 (EtOAc/petroleum ether = 1:10). ^{1}H NMR (500 MHz, $CDCl_3$): δ 7.96 (d, J = 7.6 Hz, 2H), 7.55 (t, J = 7.5 Hz, 1H), 7.45 (t, J = 7.6 Hz, 2H), 4.19 (q, J = 7.2 Hz, 2H), 3.30–3.19 (m, 1H), 3.05–2.95 (m, 1H), 2.57–2.48 (m, 1H), 2.48–2.39 (m, 1H), 2.39–2.23 (m, 2H), 2.16–1.92 (m, 4H), 1.26 (t, J = 7.2 Hz, 3H). ^{13}C{^{1}H} NMR (126 MHz, $CDCl_3$): δ 214.8, 199.4, 171.5, 136.7, 133.1, 128.6, 128.1, 61.5, 59.2, 38.0, 34.4, 34.1, 27.8, 19.6, 14.10. IR (KBr, cm^{-1}): 3064, 2960, 1731, 1684, 1463, 1217, 1157, 1217, 1157, 992, 745, 692. HRMS (ESI-TOF): m/z [M + Na]$^+$ calcd for $C_{17}H_{20}O_4Na$, 311.1254; found, 311.1257. HPLC: OJH column, 90:10 hexanes/isopropanol, 0.80 mL/min, t_R = (major) 21.7 min, (minor) 23.0 min, 91% ee. $[\alpha]_D^{26}$ +24.3° (c 0.64, DCM).

*Isopropyl 2-Oxo-1-(3-oxo-3-phenylpropyl)cyclopentane-1-carboxylate (**3c**).* Yield: 84% (48 mg), colorless oil, R_f = 0.6 (EtOAc/petroleum ether = 1:10). ^{1}H NMR (400 MHz, $CDCl_3$): δ 7.95 (d, J = 7.6 Hz, 2H), 7.53 (t, 1H), 7.44 (t, J = 7.6 Hz, 2H), 5.04 (hept, J = 6.3 Hz, 1H), 3.25 (ddd, J = 16.1, 10.2, 5.3 Hz, 1H), 2.98 (ddd, J = 17.5, 10.2, 5.1 Hz, 1H), 2.52–2.21 (m, 4H), 2.13–1.91 (m, 4H), 1.25–1.22 (m, 6H). ^{13}C{^{1}H} NMR (101 MHz, $CDCl_3$): δ 214.8, 199.5, 171.0, 136.7, 133.0, 128.6, 128.1, 69.0, 59.2, 38.0, 34.4, 34.0, 27.7, 21.7, 21.6, 19.6. IR (KBr, cm^{-1}): 3062, 2978, 1748, 1719, 1685, 1460, 1372, 1260, 1236, 1104, 745, 693. HRMS (ESI-TOF): m/z [M + Na]$^+$ calcd for $C_{18}H_{22}O_4Na$, 325.1410; found, 325.1415. HPLC:

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WHELK column, 95:5 hexanes/isopropanol, 0.80 mL/min, t_R = (major) 34.2 min, (minor) 31.6 min, 92% ee. $[\alpha]_D^{26}$ −4.3° (*c* 0.80, EtOAc)

*Isopropyl 2-Oxo-1-(3-oxo-3-(p-tolyl)propyl)cyclopentane-1-carboxylate (**3d**).* Yield: 67% (42 mg), colorless oil, R_f = 0.6 (EtOAc/petroleum ether = 1:10). ^{1}H NMR (400 MHz, $CDCl_3$): δ 7.86 (d, *J* = 7.9 Hz, 2H), 7.25 (d, *J* = 7.8 Hz, 2H), 5.05 (hept, 1H), 3.27−3.13 (m, 1H), 3.04−2.86 (m, 1H), 2.54−2.44 (m, 1H), 2.45−2.37 (m, 4H), 2.38−2.21 (m, 2H), 2.13−1.91 (m, 4H), 1.24 (d, *J* = 6.2 Hz, 6H). ^{13}C{^{1}H} NMR (101 MHz, $CDCl_3$): δ 214.9, 199.2, 171.0, 143.8, 134.3, 129.3, 128.2, 69.0, 59.3, 38.0, 34.3, 33.9, 27.8, 21.7, 21.6, 19.6. IR (KBr, cm^{-1}): 3032, 2978, 1748, 1718, 1607, 1374, 1233, 1104, 818, 568. HRMS (ESI-TOF): *m*/*z* [M + Na]$^+$ calcd for $C_{19}H_{24}O_4Na$, 339.1567; found, 339.1572.

*Isopropyl 1-(3-(4-Isopropylphenyl)-3-oxopropyl)-2-oxocyclopentane-1-carboxylate (**3e**).* Yield: 75% (47 mg), colorless oil, R_f = 0.6 (EtOAc/petroleum ether = 1:10). ^{1}H NMR (500 MHz, $CDCl_3$): δ 7.90 (d, *J* = 8.1 Hz, 2H), 7.30 (d, *J* = 8.0 Hz, 2H), 5.05 (hept, *J* = 6.3 Hz, 1H), 3.28−3.17 (m, 1H), 3.02−2.89 (m, 2H), 2.53−2.38 (m, 2H), 2.36−2.22 (m, 2H), 2.11−1.93 (m, 4H), 1.28−1.23 (m, 12H). ^{13}C{^{1}H} NMR (126 MHz, $CDCl_3$): δ 214.8, 199.1, 171.0, 154.5, 134.6, 128.4, 126.6, 69.0, 59.3, 38.0, 34.3, 34.2, 34.0, 27.8, 23.7, 21.7, 21.6, 19.6. IR (KBr, cm^{-1}): 2967, 1748, 1720, 1606, 1460, 1260, 1104, 831, 751. HRMS (ESI-TOF): *m*/*z* [M + Na]$^+$ calcd for $C_{21}H_{28}O_4Na$, 367.1880; found, 367.1882.

*Isopropyl 1-(3-(4-(tert-Butyl)phenyl)-3-oxopropyl)-2-oxocyclopentane-1-carboxylate (**3f**).* Yield: 91% (64 mg), colorless oil, R_f = 0.6 (EtOAc/petroleum ether = 1:10). ^{1}H NMR (500 MHz, $CDCl_3$): δ 7.91 (d, *J* = 8.4 Hz, 2H), 7.47 (d, *J* = 8.5 Hz, 2H), 5.11−4.97 (m, 1H), 3.33−3.12 (m, 1H), 3.04−2.81 (m, 1H), 2.58−2.19 (m, 4H), 2.17−1.88 (m, 4H), 1.34 (s, 9H), 1.27−1.15 (m, 6H). ^{13}C{^{1}H} NMR (126 MHz, $CDCl_3$): δ 214.9, 199.2, 171.0, 156.8, 134.1, 128.1, 125.5, 69.0, 59.3, 38.0, 35.1, 34.3, 34.0, 31.1, 27.8, 21.7, 21.6, 19.6. IR (KBr, cm^{-1}): 3066, 2971, 1752, 1604, 1463, 1408, 1265, 996, 837, 736. HRMS (ESI-TOF): *m*/*z* [M + Na]$^+$ calcd for $C_{22}H_{30}O_4Na$, 381.2036; found, 381.2033.

*Isopropyl 2-Oxo-1-(3-oxo-3-phenylpropyl)cyclopentane-1-carboxylate (**3g**).* Yield: 86% (57 mg), white solid, mp 75−80 °C, R_f = 0.6 (EtOAc/petroleum ether = 1:10). ^{1}H NMR (400 MHz, $CDCl_3$): δ 7.95 (d, *J* = 8.4 Hz, 2H), 6.92 (d, *J* = 8.4 Hz, 2H), 5.05 (p, *J* = 6.3 Hz, 1H), 3.86 (s, 3H), 3.19 (ddd, *J* = 16.1, 10.4, 5.3 Hz, 1H), 2.92 (ddd, *J* = 16.2, 10.4, 5.1 Hz, 1H), 2.56−2.44 (m, 1H), 2.44−2.38 (m, 1H), 2.37−2.31 (m, 1H), 2.31−2.19 (m, 1H), 2.14−1.92 (m, 4H), 1.20−1.27 (m, 6H). ^{13}C{^{1}H} NMR (101 MHz, $CDCl_3$): δ 214.9, 198.1, 171.0, 163.5, 130.4, 129.8, 113.7, 69.0, 59.3, 55.5, 38.0, 34.3, 33.7, 28.0, 21.7, 21.6, 19.6. IR (KBr, cm^{-1}): 3309, 2975, 2844, 1747, 1718, 1675, 1605, 1259, 1028, 990, 907, 766. HRMS (ESI-TOF): *m*/*z* [M + Na]$^+$ calcd for $C_{19}H_{24}O_5Na$, 355.1516; found, 355.1507.

*1-(3-(4-(Methylthio)phenyl)-3-oxopropyl)-2-oxocyclopentane-1-carboxylate (**3h**).* Yield: 64% (47 mg), colorless oil, R_f = 0.6 (EtOAc/petroleum ether = 1:10). ^{1}H NMR (500 MHz, $CDCl_3$): δ 7.88 (d, *J* = 8.6 Hz, 2H), 7.26 (d, *J* = 8.5 Hz, 2H), 5.04 (hept, *J* = 6.3 Hz, 1H), 3.26−3.15 (m, 1H), 2.99−2.88 (m, 1H), 2.52 (s, 4H), 2.47−2.38 (m, 1H), 2.38−2.19 (m, 2H), 2.13−1.90 (m, 4H), 1.27−1.21 (m, 6H). ^{13}C{^{1}H} NMR (126 MHz, $CDCl_3$): δ 214.9, 198.5, 171.0, 145.8, 133.0, 128.5, 125.0, 69.0, 59.2, 38.0, 34.4, 33.9, 3.8, 21.7, 21.6, 19.6, 14.8. IR (KBr, cm^{-1}): 2978, 2930, 1748, 1718, 1678, 1589, 1446, 1370, 1236, 1184, 1099, 994, 820. HRMS (ESI-TOF): *m*/*z* [M + Na]$^+$ calcd for $C_{19}H_{24}O_4SNa$, 371.1288; found, 371.1284.

*Isopropyl 1-(3-(4-Fluorophenyl)-3-oxopropyl)-2-oxocyclopentane-1-carboxylate (**3i**).* Yield: 83% (53 mg), colorless oil, R_f = 0.6 (EtOAc/petroleum ether = 1:10). ^{1}H NMR (400 MHz, $CDCl_3$): δ 7.92 (dd, *J* = 8.4, 5.5 Hz, 2H), 7.04 (t, *J* = 8.4 Hz, 2H), 4.97 (hept, *J* = 6.4 Hz, 1H), 3.17 (ddd, *J* = 16.1, 10.2, 5.3 Hz, 1H), 2.89 (ddd, *J* = 16.4, 10.2, 5.1 Hz, 1H), 2.52−2.31 (m, 2H), 2.30−2.11 (m, 2H), 2.09−1.78 (m, 4H), 1.19−1.14 (m, 6H). ^{13}C{^{1}H} NMR (101 MHz, $CDCl_3$): δ 214.9, 198.0, 171.0, 167.0 (C−F, $^1J_{C-F}$ = 255.5 Hz), 164.5 (C−F, $^1J_{C-F}$ = 255.5 Hz), 133.19 (C−F, $^4J_{C-F}$ = 3.0 Hz), 133.16 (C−F, $^4J_{C-F}$ = 3.0 Hz), 130.8 (C−F, $^3J_{C-F}$ = 9.1 Hz), 130.7 (C−F, $^3J_{C-F}$ = 9.1 Hz), 115.8 (C−F, $^2J_{C-F}$ = 19.1 Hz), 115.5 (C−F, $^2J_{C-F}$ = 19.1 Hz), 69.0, 59.1, 38.0, 34.5, 34.0, 27.7, 21.7, 21.6, 19.6. ^{19}F NMR (376 MHz, $CDCl_3$): δ −105.40. IR (KBr, cm^{-1}): 3075, 2979, 1749, 1720, 1478, 1267, 1104, 996, 826, 763 HRMS (ESI-TOF): *m*/*z* [M + Na]$^+$ calcd for $C_{18}H_{21}FO_4Na$, 343.1316; found, 343.1314.

*Isopropyl 1-(3-(4-Chlorophenyl)-3-oxopropyl)-2-oxocyclopentane-1-carboxylate (**3j**).* Yield: 68% (46 mg), colorless solid, m.p.=53−57 °C, R_f = 0.6 (EtOAc/petroleum ether = 1:10). ^{1}H NMR (400 MHz, $CDCl_3$): δ 7.91 (d, *J* = 8.4 Hz, 2H), 7.42 (d, *J* = 8.4 Hz, 2H), 5.04 (hept, *J* = 6.2 Hz, 1H), 3.31−3.18 (m, 1H), 3.03−2.90 (m, 1H), 2.54−2.38 (m, 2H), 2.38−2.19 (m, 2H), 2.15−1.89 (m, 4H), 1.28−1.20 (m, 6H). ^{13}C{^{1}H} NMR (101 MHz, $CDCl_3$): δ 214.9, 198.3, 171.0, 139.5, 135.1, 129.5, 128.9, 69.1, 59.0, 38.0, 34.6, 34.0, 27.6, 21.7, 21.6, 19.6. IR (KBr, cm^{-1}): 3042, 2968, 2777, 1717, 164, 150, 137, 1099, 829, 754, 526. HRMS (ESI-TOF): *m*/*z* [M + Na]$^+$ calcd for $C_{18}H_{21}ClO_4Na$ 359.1021; found, 359.1013.

*Isopropyl 1-(3-(4-Bromophenyl)-3-oxopropyl)-2-oxocyclopentane-1-carboxylate (**3k**).* Yield: 82% (62 mg), yellow solid, mp 56−60 °C, R_f = 0.6 (EtOAc/petroleum ether = 1:10). ^{1}H NMR (400 MHz, $CDCl_3$): δ 7.82 (d, *J* = 7.6 Hz, 2H), 7.59 (d, *J* = 7.9 Hz, 2H), 5.04 (hept, *J* = 12.5, 6.3, 5.7 Hz, 1H), 3.29−3.17 (m, 1H), 3.00−2.88 (m, 1H), 2.54−2.38 (m, 2H), 2.37−2.27 (m, 1H), 2.27−2.16 (m, 1H), 2.14−1.92 (m, 4H), 1.27−1.20 (m, 6H). ^{13}C{^{1}H} NMR (101 MHz, $CDCl_3$): δ 214.9, 198.5, 171.0, 135.4, 131.9, 129.6, 128.2, 69.1, 59.0, 38.0, 34.6, 34.0, 27.6, 21.7, 21.6, 19.6. IR (KBr, cm^{-1}): 3090, 2973, 1749, 1682, 1580, 1241, 1157, 822, 735, 566. HRMS (ESI-TOF): *m*/*z* [M + H]$^+$ calcd for $C_{18}H_{22}BrO_4$, 381.0696; found, 381.0698.

*Methyl 4-(3-(1-(Isopropoxycarbonyl)-2-oxocyclopentyl)-propanoyl)benzoate (**3l**).* Yield: 65% (46 mg), Yellow solid, m.p.=75−79 °C, R_f = 0.4 (EtOAc/petroleum ether = 1:10). ^{1}H NMR (500 MHz, $CDCl_3$): δ 8.11 (d, *J* = 8.2 Hz, 2H), 8.01 (d, *J* = 8.3 Hz, 2H), 5.05 (hept, *J* = 6.3 Hz, 1H), 3.95 (s, 3H), 3.36−3.26 (m, 1H), 3.08−2.98 (m, 1H), 2.54−2.39 (m, 2H), 2.38−2.21 (m, 2H), 2.15−1.95 (m, 4H), 1.27−1.22 (m, 6H). ^{13}C{^{1}H} NMR (126 MHz, $CDCl_3$): δ 214.9, 199.0, 171.0, 166.2, 139.9, 133.8, 129.8, 128.0, 69.1, 59.0, 52.4, 38.0, 34.6, 34.4, 27.5, 21.7, 21.6, 19.6. IR (KBr, cm^{-1}): 2978, 1723, 1690, 1441, 1406, 1280, 1107, 996, 756. HRMS (ESI-TOF): *m*/*z* [M + Na]$^+$ calcd for $C_{20}H_{24}O_5Na$, 383.1465; found, 383.1467.

*Isopropyl 2-Oxo-1-(3-oxo-3-phenylpropyl)cyclopentane-1-carboxylate (**3m**).* Yield: 64% (49 mg), white solid, m.p.=114−117 °C, R_f = 0.4 (EtOAc/petroleum ether = 1:10). ^{1}H NMR (400 MHz, $CDCl_3$): δ 8.06 (d, *J* = 8.0 Hz, 2H), 7.70 (d, *J* = 8.0 Hz, 2H), 7.65 (d, *J* = 7.6 Hz, 2H), 7.49 (t, *J* = 7.5 Hz, 2H), 7.42 (t, 1H), 5.15−5.00 (m, 1H), 3.38−3.25 (m, 1H), 3.11−2.98 (m, 1H), 2.59−2.24 (m, 4H), 2.21−1.95 (m, 4H), 1.30−1.25 (m, 6H). ^{13}C{^{1}H} NMR (101 MHz, $CDCl_3$): δ 215.0, 199.2, 171.1, 145.8, 139.9, 135.5, 128.9, 128.7, 128.2, 127.2, 127.3, 69.1, 59.3, 38.0, 34.5, 34.3, 27.8, 21.7, 21.6, 19.7. IR (KBr, cm^{-1}): 3052, 1979, 1746, 171, 1462, 1406, 1263, 1108, 997, 932, 763, 698. HRMS (ESI-TOF): *m*/*z* [M + Na]$^+$ calcd for $C_{24}H_{26}O_4Na$, 401.1723; found, 401.1722.

*Isopropyl 2-Oxo-1-(3-oxo-3-(m-tolyl)propyl)cyclopentane-1-carboxylate (**3n**).* Yield: 60% (38 mg), colorless oil, R_f = 0.6 (EtOAc/petroleum ether = 1:10). ^{1}H NMR (400 MHz, $CDCl_3$): δ 7.80−7.72 (m, 2H), 7.41−7.30 (m, 2H), 5.05 (hept, *J* = 6.3 Hz, 1H), 3.31−3.18 (m, 1H), 3.05−2.89 (m, 1H), 2.54−2.46 (m, 1H), 2.45−2.38 (m, 4H), 2.37−2.20 (m, 2H), 2.15−1.91 (m, 4H),, 1.25 (d, *J* = 6.1 Hz, 6H). ^{13}C{^{1}H} NMR (101 MHz, $CDCl_3$): δ 214.9, 199.7, 171.0, 138.3, 136.8, 133.8, 128.6, 128.5, 125.3, 69.0, 59.2, 38.0, 34.4, 34.1, 27.7, 21.7, 21.6, 21.4, 19.6. IR (KBr, cm^{-1}): 3044, 2975,2931, 1747, 1683, 1509, 1454, 1161, 1036, 982, 825. HRMS (ESI-TOF): *m*/*z* [M + Na]$^+$ calcd for $C_{19}H_{24}O_4Na$, 339.1567; found, 339.1569.

*Isopropyl 1-(3-(2-Fluorophenyl)-3-oxopropyl)-2-oxocyclopentane-1-carboxylate (**3o**).* Yield: 56% (34 mg), colorless oil, R_f = 0.6 (EtOAc/petroleum ether = 1:10). ^{1}H NMR (400 MHz, $CDCl_3$): δ 7.75 (d, *J* = 7.7 Hz, 1H), 7.64 (d, *J* = 9.5 Hz, 1H), 7.52−7.39 (m, 1H), 7.34−7.13 (m, 1H), 5.05 (hept, *J* = 6.3 Hz, 1H), 3.37−3.13 (m, 1H), 3.07−2.80 (m, 1H), 2.53−2.20 (m, 4H), 2.15−1.89 (m, 4H), 1.29−1.19 (m, 6H). ^{13}C{^{1}H} NMR (101 MHz, $CDCl_3$): δ 214.8,

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198.2, 171.0, 164.1 (C−F, $^{1}J_{C-F}$ = 249.5 Hz),161.6 (C−F, $^{1}J_{C-F}$ = 249.5 Hz), 138.9 (C−F, $^{3}J_{C-F}$ = 6.1 Hz), 138.8(C−F, $^{3}J_{C-F}$ = 6.1 Hz), 130.2(C−F, $^{3}J_{C-F}$ = 8.1 Hz), 130.3 (C−F, $^{3}J_{C-F}$ = 8.1 Hz), 123.9 (C−F, $^{4}J_{C-F}$ = 3.0 Hz), 123.8 (C−F, $^{4}J_{C-F}$ = 3.0 Hz), 120.1 (C−F, $^{2}J_{C-F}$ = 21.2 Hz)120.0 (C−F, $^{2}J_{C-F}$ = 21.2 Hz), 114.9 (C−F, $^{2}J_{C-F}$ = 17.1 Hz), 114.7 (C−F, $^{2}J_{C-F}$ = 17.1 Hz), 69.1, 59.0, 38.0, 34.5, 34.2, 27.6, 21.6, 21.6, 19.6. ^{19}F NMR (376 MHz, $CDCl_3$): δ −111.96, IR (KBr, cm^{-1}): 3075, 2979, 1749, 1720, 1478, 1267, 1104, 996, 826, 763. HRMS (ESI-TOF): m/z $[M + Na]^+$ calcd for $C_{18}H_{21}FO_4Na$, 343.1316; found, 343.1314.

*Isopropyl 1-(3-(2,4-Dimethylphenyl)-3-oxopropyl)-2-oxocyclopentane-1-carboxylate (**3p**).* Yield: 76% (51 mg), colorless oil, R_f = 0.6 (EtOAc/petroleum ether = 1:10). ^{1}H NMR (500 MHz, $CDCl_3$): δ 7.53 (d, J = 7.7 Hz, 1H), 7.03−6.91 (m, 2H), 4.96 (hept, J = 12.5, 6.2 Hz, 1H), 3.18−3.01 (m, 1H), 2.87−2.72 (m, 1H), 2.44−2.37 (m, 4H), 2.34−2.24 (m, 5H), 2.19−2.12 (m, 1H),, 2.01−1.90 (m, 3H), 1.90−1.81 (m, 1H), 1.18−1.12 (m, 6H). $^{13}C\{^{1}H\}$ NMR (126 MHz, $CDCl_3$): δ 214.9, 202.6, 171.0, 141.9, 138.6, 134.6, 132.8, 129.1, 126.3, 69.0, 59.3, 38.0, 36.5, 34.3, 27.9, 21.7, 21.6, 21.5, 21.3, 19.6. IR (KBr, cm^{-1}): 2973, 2930, 1748, 1719, 1681, 1450, 1259, 1234, 1145, 985, 935, 756. HRMS (ESI-TOF): m/z $[M + Na]^+$ calcd for $C_{20}H_{26}O_4Na$, 353.1723; found, 353.1718.

*Isopropyl 1-(3-(3,5-Dimethylphenyl)-3-oxopropyl)-2-oxocyclopentane-1-carboxylate (**3q**).* Yield: 65% (42 mg), colorless oil, R_f = 0.6 (EtOAc/petroleum ether = 1:10). ^{1}H NMR (400 MHz, $CDCl_3$): δ 7.57 (s, 2H), 7.19 (s, 1H), 5.06 (hept, J = 6.2 Hz, 1H), 3.33−3.13 (m, 1H), 3.06−2.89 (m, 1H), 2.55−2.47 (m, 1H), 2.44−2.30 (m, 8H), 2.29−2.20 (m, 1H), 2.13−1.91 (m, 4H), 1.27−1.20 (m, 6H). $^{13}C\{^{1}H\}$ NMR (101 MHz, $CDCl_3$): δ 214.9, 199.9, 171.0, 138.2, 136.9, 134.7, 125.9, 69.0, 59.3, 38.0, 34.4, 34.1, 27.7, 21.7, 21.6, 21.2, 19.6. IR (KBr, cm^{-1}): 3042, 2967, 1746, 1717, 1678, 1315, 1262, 854, 814, 752. HRMS (ESI-TOF): m/z $[M + Na]^+$ calcd for $C_{20}H_{26}FO_4Na$, 353.1723; found, 353.1725.

*Isopropyl 1-(3-(Naphthalen-1-yl)-3-oxopropyl)-2-oxocyclopentane-1-carboxylate (**3r**).* Yield: 62% (42 mg), yellow oil, R_f = 0.6 (EtOAc/petroleum ether = 1:10). ^{1}H NMR (400 MHz, $CDCl_3$): δ 8.56 (d, J = 8.5 Hz, 1H), 7.96 (d, J = 8.2 Hz, 1H), 7.89 (d, J = 7.1 Hz, 1H), 7.85 (d, J = 8.1 Hz, 1H), 7.57 (t, J = 7.6 Hz, 1H), 7.53−7.45 (m, 2H), 5.03 (hept, J = 6.4 Hz, 1H), 3.35 (ddd, J = 16.1, 9.9, 5.4 Hz, 1H), 3.06 (ddd, J = 16.3, 9.9, 5.1 Hz, 1H), 2.55−2.45 (m, 1H), 2.44−2.27 (m, 3H), 2.22−2.12 (m, 1H), 2.08−1.91 (m, 3H), 1.23 (t, J = 5.3 Hz, 6H). $^{13}C\{^{1}H\}$ NMR (101 MHz, $CDCl_3$): δ 214.9, 203.6, 171.0, 135.8, 133.9, 132.6, 130.1, 128.4, 127.9, 127.6, 126.4, 125.8, 124.4, 69.0, 59.2, 38.0, 37.5, 34.4, 28.0, 21.7, 21.6, 19.7. IR (KBr, cm^{-1}): 3051, 2978, 1748, 1717, 1591, 1508, 1459, 1369, 1234, 1102, 938, 802, 780, 598. HRMS (ESI-TOF): m/z $[M + Na]^+$ calcd for $C_{22}H_{24}O_4Na$, 375.1567; found, 375.1562.

*Isopropyl 2-Oxo-1-(3-oxo-3-(thiophen-2-yl)propyl)cyclopentane-1-carboxylate (**3s**).* Yield: 76% (43 mg), colorless oil, R_f = 0.6 (EtOAc/petroleum ether = 1:10). ^{1}H NMR (500 MHz, $CDCl_3$): δ 7.73−7.65 (m, 1H), 7.60−7.49 (m, 1H), 7.09−6.97 (m, 1H), 5.03−4.90 (m, 1H), 3.17−3.04 (m, 1H), 2.92−2.81 (m, 1H), 2.46−2.30 (m, 2H), 2.30−2.11 (m, 2H), 2.04−1.83 (m, 4H), 1.20−1.13 (m, 6H). $^{13}C\{^{1}H\}$ NMR (126 MHz, $CDCl_3$): δ 214.8, 192.4, 170.9, 143.9, 133.6, 132.1, 128.1, 69.0, 59.2, 37.9, 34.8, 34.2, 27.9, 21.7, 21.6, 19.6. IR (KBr, cm^{-1}): 3097, 2977, 1747, 1717, 1668, 1494, 1260, 1171, 1103, 765. HRMS (ESI-TOF): m/z $[M + Na]^+$ calcd for $C_{16}H_{20}O_4SNa$, 331.0975; found, 331.0977.

*Isopropyl 1-(3-(Benzo[b]thiophen-2-yl)-3-oxopropyl)-2-oxocyclopentane-1-carboxylate (**3t**).* Yield: 71% (45 mg), white solid, mp = 79−81 °C, R_f = 0.5 (EtOAc/petroleum ether = 1:10). ^{1}H NMR (500 MHz, $CDCl_3$): δ 8.01 (s, 1H), 7.89 (d, J = 7.9 Hz, 1H), 7.85 (d, J = 8.0 Hz, 1H), 7.45 (t, J = 7.5 Hz, 1H), 7.40 (t, J = 7.5 Hz, 1H), 5.06 (hept, J = 6.2 Hz, 1H), 3.41−3.20 (m, 1H), 3.14−2.98 (m, 1H), 2.56−2.23 (m, 4H), 2.21−1.93 (m, 4H), 1.31−1.18 (m, 6H). $^{13}C\{^{1}H\}$ NMR (126 MHz, $CDCl_3$): δ 214.9, 194.0, 171.0, 143.3, 142.5, 139.2, 129.3, 127.4, 126.0, 125.0, 123.0, 69.1, 59.2, 38.0, 34.7, 34.4, 27.9, 21.7, 21.6, 19.7. IR (KBr, cm^{-1}): 3061, 2978, 1747, 1718, 1666, 1558, 1258, 1233, 1166, 1103, 752. HRMS (ESI-TOF): m/z $[M + Na]^+$ calcd for $C_{20}H_{22}O_4SNa$, 381.1131; found, 381.1126.

*Isopropyl 1-(3-(Benzo[b]thiophen-3-yl)-3-oxopropyl)-2-oxocyclopentane-1-carboxylate (**3u**).* Yield: 59% (42 mg), colorless oil, R_f = 0.5 (EtOAc/petroleum ether = 1:10). ^{1}H NMR (500 MHz, $CDCl_3$): δ 8.73 (d, J = 8.2 Hz, 1H), 8.42 (s, 1H), 7.85 (d, J = 8.0 Hz, 1H), 7.47 (t, J = 7.6 Hz, 1H), 7.40 (t, J = 7.5 Hz, 1H), 5.06 (hept, J = 6.2 Hz, 1H), 3.40−3.16 (m, 1H), 3.10−2.90 (m, 1H), 2.58−2.24 (m, 4H), 2.22−1.91 (m, 4H), 1.31−1.17 (m, 6H). $^{13}C\{^{1}H\}$ NMR (126 MHz, $CDCl_3$): δ 214.9, 194.8, 171.1, 139.8, 137.3, 136.6, 134.7, 125.8, 125.6, 125.4, 122.2, 69.1, 59.3, 38.0, 35.8, 34.3, 28.2, 21.7, 21.6, 19.7. IR (KBr, cm^{-1}): 3097, 2977, 1747, 1717, 1668, 1494, 1260, 1171, 1103, 765. HRMS (ESI-TOF): m/z $[M + Na]^+$ calcd for $C_{20}H_{22}O_4SNa$, 381.1131; found, 381.1128.

*Isopropyl 2-Oxo-1-(3-oxo-3-phenylpropyl)cyclohexane-1-carboxylate (**3v**).* Yield: 53% (32 mg), colorless oil, R_f = 0.6 (EtOAc/petroleum ether = 1:10). ^{1}H NMR (400 MHz, $CDCl_3$): δ 7.97 (d, J = 7.7 Hz, 2H), 7.55 (t, J = 7.3 Hz, 1H), 7.45 (t, J = 7.6 Hz, 2H), 5.18−5.03 (m, 1H), 3.26−3.08 (m, 1H), 2.94−2.78 (m, 1H), 2.67−2.37 (m, 3H), 2.33−2.16 (m, 1H), 2.14−1.91 (m, 2H), 1.84−1.76 (m, 1H), 1.67 (t, J = 9.4 Hz, 2H), 1.57−1.42 (m, 1H), 1.27 (d, J = 6.2 Hz, 6H). $^{13}C\{^{1}H\}$ NMR (101 MHz, $CDCl_3$): δ 208.2, 199.5, 171.6, 136.8, 133.0, 128.6, 128.1, 69.1, 60.3, 41.1, 36.9, 34.0, 29.3, 27.6, 22.6, 21.7, 21.6. IR (KBr, cm^{-1}): 2939, 2866, 1711, 1597, 1448, 1370, 1300, 1214, 983, 693. HRMS (ESI-TOF): m/z $[M + Na]^+$ calcd for $C_{19}H_{24}O_4Na$, 339.1567; found, 339.1572.

*Isopropyl 2-Oxo-1-(3-oxo-3-phenylpropyl)cycloheptane-1-carboxylate (**3w**).* Yield: 64% (38 mg), colorless oil, R_f = 0.6 (EtOAc/petroleum ether = 1:10). ^{1}H NMR (500 MHz, $CDCl_3$): δ 7.97 (d, J = 7.7 Hz, 2H), 7.55 (t, J = 7.4 Hz, 1H), 7.45 (t, J = 7.7 Hz, 2H), 5.14−5.02 (m, 1H), 3.15 (ddd, J = 16.2, 10.8, 4.9 Hz, 1H), 2.91 (ddd, J = 16.4, 10.9, 4.8 Hz, 1H), 2.68 (td, J = 10.2, 7.9, 5.1 Hz, 1H), 2.52 (dd, J = 13.9, 7.3 Hz, 1H), 2.34 (ddd, J = 15.2, 10.8, 4.9 Hz, 1H), 2.21−2.13 (m, 1H), 2.07 (ddd, J = 14.6, 10.8, 4.7 Hz, 1H), 1.83−1.75 (m, 2H), 1.72−1.61 (m, 3H), 1.59−1.47 (m, 2H), 1.28−1.23 (m, 6H). $^{13}C\{^{1}H\}$ NMR (126 MHz, $CDCl_3$): δ 209.7, 199.5, 172.0, 136.8, 133.0, 128.5, 128.1, 68.9, 61.9, 42.3, 34.4, 34.3, 30.2, 29.8, 25.4, 25.0, 21.7, 21.6. IR (KBr, cm^{-1}): 3061, 1978, 2934,1689, 1597, 1450, 1373, 1231, 1179, 1105, 1004, 938, 752, 693. HRMS (ESI-TOF): m/z $[M + Na]^+$ calcd for $C_{20}H_{26}O_4Na$, 353.1723; found, 353.1720.

*Isopropyl (E)-2-Oxo-1-(3-oxo-5-phenylpent-4-en-1-yl)-cyclopentane-1-carboxylate (**6a**).* Yield: 83% (54 mg), colorless oil, R_f = 0.6 (EtOAc/petroleum ether = 1:10). ^{1}H NMR (500 MHz, $CDCl_3$): δ 7.61−7.52 (m, 3H), 7.42−7.37 (m, 3H), 6.72 (d, J = 16.2 Hz, 1H), 5.05 (hept, J = 6.2 Hz, 1H), 3.01−2.88 (m, 1H), 2.78−2.65 (m, 1H), 2.52−2.38 (m, 2H), 2.37−2.28 (m, 1H), 2.23−2.15 (m, 1H), 2.07−1.98 (m, 3H), 1.96−1.88 (m, 1H), 1.27−1.22 (m, 6H). $^{13}C\{^{1}H\}$ NMR (126 MHz, $CDCl_3$): δ 214.9, 199.4, 171.0, 142.8, 134.5, 130.5, 128.9, 128.3, 126.0, 69.0, 59.2, 38.0, 36.1, 34.3, 27.5, 21.7, 21.6, 19.6. IR (KBr, cm^{-1}): 3030, 2978, 1747, 1718, 1662, 1495, 1258, 1180, 1031, 753, 693. HRMS (ESI-TOF): m/z $[M + Na]^+$ calcd for $C_{20}H_{24}O_4Na$, 351.1567; found, 351.1568.

*Isopropyl (E)-2-Oxo-1-(3-oxo-5-(p-tolyl)pent-4-en-1-yl)-cyclopentane-1-carboxylate (**6b**).* Yield: 70% (47 mg), colorless oil, R_f = 0.5 (EtOAc/petroleum ether = 1:10). ^{1}H NMR (500 MHz, $CDCl_3$): δ 7.55 (d, J = 16.2 Hz, 1H), 7.44 (d, J = 7.9 Hz, 2H), 7.20 (d, J = 7.8 Hz, 2H), 6.68 (d, J = 16.2 Hz, 1H), 5.09−5.00 (m, 1H), 2.97−2.87 (m, 1H), 2.74−2.64 (m, 1H), 2.52−2.45 (m, 1H), 2.45−2.37 (m, 3H), 2.37−2.27 (m, 2H), 2.24−2.14 (m, 1H), 2.08−1.97 (m, 3H), 1.97−1.88 (m, 1H), 1.27−1.21 (m, 6H). $^{13}C\{^{1}H\}$ NMR (126 MHz, $CDCl_3$): δ 214.94, 199.48, 170.97, 142.86, 140.97, 131.72, 129.68, 128.32, 125.06, 68.99, 59.26, 38.00, 36.04, 34.26, 27.54, 21.68, 21.60, 21.50, 19.62. IR (KBr, cm^{-1}): 3051, 1978, 1749, 1665, 1612, 1490, 1450, 1403, 1373, 1319, 1177, 1013, 982, 817, 735. HRMS (ESI-TOF): m/z $[M + Na]^+$ calcd for $C_{21}H_{26}O_4Na$, 365.1723; found, 365.1725.

*Isopropyl (E)-1-(5-(4-Fluorophenyl)-3-oxopent-4-en-1-yl)-2-oxocyclopentane-1-carboxylate (**6c**).* Yield: 66% (45 mg), colorless oil, R_f = 0.5 (EtOAc/petroleum ether = 1:10). ^{1}H NMR (500 MHz, $CDCl_3$): δ 7.54−7.41 (m, 3H), 7.01 (t, J = 8.4 Hz, 2H), 6.57 (d, J = 16.2 Hz, 1H), 4.97 (hept, J = 6.1 Hz, 1H), 2.94−2.80 (m, 1H), 2.74−2.54 (m, 1H), 2.47−2.19 (m, 3H), 2.19−2.04 (m, 1H), 2.03−1.82

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(m, 4H), 1.24−1.10 (m, 6H). $^{13}C\{^1H\}$ NMR (126 MHz, $CDCl_3$): δ 215.0, 199.2, 171.0, 165.0 (C−F, $^1J_{C-F}$ = 256.0 Hz), 163.0 (C−F, $^1J_{C-F}$ = 256.0 Hz), 141.4, 130.73 (C−F, $^4J_{C-F}$ = 3.8 Hz), 130.70 (C−F, $^4J_{C-F}$ = 3.8 Hz), 130.2 (C−F, $^3J_{C-F}$ = 8.8 Hz), 130.1 (C−F, $^3J_{C-F}$ = 8.8 Hz), 125.70 (C−F, $^5J_{C-F}$ = 2.5 Hz), 125.68 (C−F, $^5J_{C-F}$ = 2.5 Hz), 116.2 (C−F, $^2J_{C-F}$ = 21.4 Hz), 116.0 (C−F, $^2J_{C-F}$ = 21.4 Hz), 69.0, 59.2, 38.0, 36.2, 34.4, 27.5, 21.7, 21.6, 19.6. ^{19}F NMR (471 MHz, $CDCl_3$): δ −109.28. IR (KBr, cm^{-1}): 3047, 2978, 1743, 1719, 1509, 1232, 1162, 1104, 826. HRMS (ESI-TOF): *m/z* $[M + H]^+$ calcd for $C_{20}H_{24}FO_4$, 347.1653; found, 347.1657.

*Isopropyl (E)-1-(5-(4-Chlorophenyl)-3-oxopent-4-en-1-yl)-2-oxocyclopentane-1-carboxylate (**6d**).* Yield: 77% (54 mg), colorless oil, R_f = 0.5 (EtOAc/petroleum ether = 1:10). ^1H NMR (500 MHz, $CDCl_3$): δ 7.56−7.43 (m, 3H), 7.36 (d, *J* = 8.5 Hz, 2H), 6.69 (d, *J* = 16.2 Hz, 1H), 5.15−4.97 (m, 1H), 3.05−2.89 (m, 1H), 2.76−2.62 (m, 1H), 2.55−2.29 (m, 3H), 2.27−2.11 (m, 1H), 2.07−1.86 (m, 4H), 1.32−1.19 (m, 6H). $^{13}C\{^1H\}$ NMR (126 MHz, $CDCl_3$): δ 214.9, 199.1, 171.0, 141.2, 136.3, 133.0, 129.4, 129.2, 126.4, 69.0, 59.1, 38.0, 36.3, 34.4, 27.4, 21.7, 21.6, 19.6. IR (KBr, cm^{-1}): 3051, 1978, 1749, 1665, 1612, 1490, 1450, 1403, 1373, 1319, 1177, 1013, 982, 817, 735. HRMS (ESI-TOF): *m/z* $[M + Na]^+$ calcd for $C_{20}H_{23}ClO_4Na$, 385.1177; found, 385.1180.

*Isopropyl (E)-1-(5-(4-Bromophenyl)-3-oxopent-4-en-1-yl)-2-oxocyclopentane-1-carboxylate (**6e**).* Yield: 62% (52 mg), colorless oil, R_f = 0.5 (EtOAc/petroleum ether = 1:10). ^1H NMR (500 MHz, $CDCl_3$): δ 7.55−7.47 (m, 3H), 7.41 (d, *J* = 8.4 Hz, 2H), 6.70 (d, *J* = 16.2 Hz, 1H), 5.04 (hept, *J* = 6.3 Hz, 1H), 3.00−2.89 (m, 1H), 2.75−2.64 (m, 1H), 2.52−2.28 (m, 3H), 2.21−1.98 (m, 4H), 1.97−1.88 (m, 1H), 1.26−1.21 (m, 6H). $^{13}C\{^1H\}$ NMR (126 MHz, $CDCl_3$): δ 215.0, 199.2, 171.0, 141.3, 133.4, 132.2, 129.6, 126.4, 124.7, 69.0, 59.1, 38.0, 36.3, 34.4, 27.4, 21.7, 21.6, 19.6. IR (KBr, cm^{-1}): 2976, 2842, 1747, 1781, 1601, 1249, 1170, 1104, 1024, 756. HRMS (ESI-TOF): *m/z* $[M + Na]^+$ calcd for $C_{20}H_{23}BrO_4Na$, 429.0672; found, 429.0667.

*Isopropyl (E)-1-(5-(2-Methoxyphenyl)-3-oxopent-4-en-1-yl)-2-oxocyclopentane-1-carboxylate (**6f**).* Yield: 74% (53 mg), colorless oil, R_f = 0.4 (EtOAc/petroleum ether = 1:10). ^1H NMR (500 MHz, $CDCl_3$): δ 7.83 (d, *J* = 16.4 Hz, 1H), 7.46 (d, *J* = 7.5 Hz, 1H), 7.28 (t, *J* = 7.8 Hz, 1H), 6.89 (t, *J* = 7.5 Hz, 1H), 6.84 (d, *J* = 8.3 Hz, 1H), 6.71 (d, *J* = 16.2 Hz, 1H), 4.97 (hept, *J* = 5.6 Hz, 1H), 3.82 (t, *J* = 1.6 Hz, 3H), 2.92−2.81 (m, 1H), 2.69−2.58 (m, 1H), 2.44−2.30 (m, 2H), 2.30−2.20 (m, 1H), 2.18−2.10 (m, 1H), 1.99−1.90 (m, 3H), 1.89−1.82 (m, 1H), 1.17 (d, *J* = 6.3 Hz, 6H). $^{13}C\{^1H\}$ NMR (126 MHz, $CDCl_3$): δ 214.9, 199.9, 170.9, 158.5, 138.1, 131.7, 128.7, 126.7, 123.4, 120.8, 111.1, 69.0, 59.4, 55.5, 38.0, 35.8, 34.1, 27.6, 21.7, 21.6, 19.6. IR (KBr, cm^{-1}): 2976, 1747, 1718, 1660, 1601, 1462, 1249, 1170, 1104, 1024, 756. HRMS (ESI-TOF): *m/z* $[M + Na]^+$ calcd for $C_{21}H_{26}O_5Na$, 381.1672; found, 381.1676.

Typical Procedure for the Synthesis of 4/7. *Condition A.* Compound **3** (0.1 mmol), TfOH (15 mol %), and 1 mL of DCE were added to a 25 mL Schlenk tube under air. The reaction was heated to 100 °C in an oil bath and then stirred for 5−60 min. When the reaction was finished, the solvent was removed under a reduced vacuum. The mixture was purified by silica gel chromatography (EtOAc/petroleum ether = 1:20) to afford product **4**. The racemic samples were prepared by using the same procedures with TfOH as a catalyst.

Condition B. Compound **6** (0.1 mmol), TfOH (5 mol %), and 1 mL of DCE were added to a 25 mL Schlenk tube under air. The reaction was heated to 100 °C in an oil bath and then stirred for 5−60 min. When the reaction was finished, the solvent was removed under a reduced vacuum. The mixture was purified by silica gel chromatography (EtOAc/petroleum ether = 1:20) to affor product **7**. Racemic samples were prepared by using the same procedures with TfOH as a catalyst.

*Methyl (1S,5S)-8-Oxo-4-phenylbicyclo[3.2.1]oct-3-ene-1-carboxylate (**4a**).* Yield: 74% (19 mg), white solid, mp = 90−92 °C, R_f = 0.6 (EtOAc/petroleum ether = 1:20). ^1H NMR (400 MHz, $CDCl_3$): δ 7.22 (dd, *J* = 21.8, 4.1 Hz, 5H), 5.91−5.80 (m, 1H), 3.71 (s, 3H), 3.31 (d, *J* = 18.0 Hz, 1H), 3.07 (s, 1H), 2.80−2.60 (m, 2H), 2.25−2.07 (m, 3H). $^{13}C\{^1H\}$ NMR (101 MHz, $CDCl_3$): δ 210.5, 171.6, 143.0, 138.7, 128.6, 127.8, 125.5, 120.9, 55.7, 52.6, 48.9, 43.2, 31.0, 29.0. IR (KBr, cm^{-1}): 3051, 1978, 1749, 1665, 1612, 1490, 1450, 1403, 1373, 1319, 1177, 1013, 982, 817, 735. HRMS (ESI-TOF): *m/z* $[M + Na]^+$ calcd for $C_{16}H_{16}O_3Na$, 279.0992; found, 279.0995. HPLC: OD-H column, 95:5 hexanes/isopropanol, 1.00 mL/min, t_R = (major) 12.3 min, (minor) 11.5 min. 90% ee. $[\alpha]_D^{31}$ −17.5° (*c* 0.55, EtOH).

*Ethyl (1S,5S)-8-Oxo-4-phenylbicyclo[3.2.1]oct-3-ene-1-carboxylate (**4b**).* Yield: 85% (23 mg), colorless oil, R_f = 0.6 (EtOAc/petroleum ether = 1:20). ^1H NMR (400 MHz, $CDCl_3$): δ 7.35−7.23 (m, 5H), 5.96−5.89 (m, 1H), 4.25 (q, *J* = 7.1 Hz, 2H), 3.40 (dd, *J* = 17.9, 3.1 Hz, 1H), 3.22−3.09 (m, 1H), 2.87−2.70 (m, 2H), 2.33−2.12 (m, 3H), 1.30 (t, *J* = 7.1 Hz, 3H). $^{13}C\{^1H\}$ NMR (101 MHz, $CDCl_3$): δ 210.3, 171.1, 143.1, 138.8, 128.6, 127.7, 125.5, 120.9, 61.4, 55.5, 49.0, 43.2, 31.0, 29.0, 14.2. IR (KBr, cm^{-1}): 2980, 1725, 1635, 1494, 1448, 1234, 1085, 1030, 760, 698, 529.HRMS (ESI-TOF): *m/z* $[M + Na]^+$ calcd for $C_{17}H_{18}O_3Na$, 293.1148; found, 293.1141. HPLC: WHELK-O1 column, 95:5 hexanes/isopropanol, 0.70 mL/min, t_R = (major) 17.9 min, (minor) 31.3 min, 91% ee. $[\alpha]_D^{29}$ −58.3° (*c* 0.60, DCM).

*Isopropyl (1S,5S)-8-Oxo-4-phenylbicyclo[3.2.1]oct-3-ene-1-carboxylate (**4c**).* Yield: 86% (24 mg), white solid, mp = 96−100 °C, R_f = 0.6 (EtOAc/petroleum ether = 1:20). ^1H NMR (500 MHz, $CDCl_3$): δ 7.35−7.30 (m, 4H), 7.30−7.26 (m, 1H), 5.93 (t, 1H), 5.16−5.07 (m, 1H), 3.38 (dt, *J* = 18.1, 2.6 Hz, 1H), 3.16−3.11 (m, 1H), 2.84−2.70 (m, 2H), 2.32−2.24 (m, 2H), 2.23−2.15 (m, 1H), 1.32−1.26 (m, 6H). $^{13}C\{^1H\}$ NMR (126 MHz, $CDCl_3$): δ 210.5, 170.7, 142.9, 138.8, 128.6, 127.7, 125.5, 121.0, 68.9, 55.5, 49.0, 43.2, 30.9, 29.0, 21.8, 21.8. IR (KBr, cm^{-1}): 3062, 2981, 1720, 1636, 1494, 1460, 1273, 1104, 831, 761, 700. HRMS (ESI-TOF): *m/z* $[M + Na]^+$ calcd for $C_{18}H_{20}O_3Na$, 307.1305; found, 307.1307. HPLC: WHELK-O1 column, 85:15 hexanes/isopropanol, 0.80 mL/min, t_R = (major) 8.6 min, (minor) 13.4 min, 92% ee. $[\alpha]_D^{22}$ −32.8° (*c* 0.13, DCM).

*Isopropyl (1S,5S)-8-Oxo-4-(p-tolyl)bicyclo[3.2.1]oct-3-ene-1-carboxylate (**4d**).* Yield: 78% (23 mg), colorless oil, R_f = 0.6 (EtOAc/petroleum ether = 1:20). ^1H NMR (400 MHz, $CDCl_3$): δ 7.27−7.20 (m, 1H), 7.19−7.08 (m, 3H), 5.93 (t, *J* = 3.5 Hz, 1H), 5.14 (hept, *J* = 6.0 Hz, 1H), 3.40 (d, *J* = 18.1 Hz, 1H), 3.15 (d, *J* = 3.7 Hz, 1H), 2.86−2.71 (m, 2H), 2.38 (s, 3H), 2.33−2.14 (m, 3H), 1.35−1.28 (m, 6H). $^{13}C\{^1H\}$ NMR (101 MHz, $CDCl_3$): δ 210.7, 170.7, 143.1, 138.8, 138.2, 128.5, 126.3, 122.6, 120.8, 68.9, 55.5, 49.1, 43.2, 30.9, 29.0, 21.8, 21.8, 21.5. IR (KBr, cm^{-1}): 2962, 1758, 1729, 1584, 1472, 1442, 1234, 1104, 1035, 499. HRMS (ESI-TOF): *m/z* $[M + Na]^+$ calcd for $C_{19}H_{22}O_3Na$, 321.1461; found, 321.1463. HPLC: WHELK-O1 column, 95:5 hexanes/isopropanol, 0.80 mL/min, t_R = (major) 11.5 min, (minor) 24.3 min, 92% ee. $[\alpha]_D^{28}$ +83.3° (*c* 0.24, EtOH).

*Isopropyl (1S,5S)-4-([1,1′-Biphenyl]-4-yl)-8-oxobicyclo[3.2.1]oct-3-ene-1-carboxylate (**4e**).* Yield: 72% (23 mg), colorless oil, R_f = 0.6 (EtOAc/petroleum ether = 1:20). ^1H NMR (500 MHz, $CDCl_3$): δ 7.27 (d, *J* = 8.0 Hz, 2H), 7.19 (d, *J* = 8.3 Hz, 2H), 5.89 (t, *J* = 4.4, 2.8 Hz, 1H), 5.11 (hept, *J* = 6.3 Hz, 1H), 3.37 (dt, *J* = 18.0, 2.6 Hz, 1H), 3.13 (d, *J* = 4.4 Hz, 1H), 2.90 (hept, *J* = 6.7 Hz, 1H), 2.84−2.68 (m, 2H), 2.33−2.21 (m, 2H), 2.21−2.10 (m, 1H), 1.32−1.27 (m, 6H), 1.24 (d, *J* = 6.9 Hz, 6H). $^{13}C\{^1H\}$ NMR (126 MHz, $CDCl_3$): δ 210.7, 170.7, 148.6, 142.8, 136.3, 126.6, 125.4, 120.2, 68.8, 55.5, 49.0, 43.1, 33.8, 30.9, 29.0, 23.9, 21.8, 21.8. IR (KBr, cm^{-1}): 2961, 1758, 1724, 1510, 1460, 1350, 1285, 1106, 959, 843. HRMS (ESI-TOF): *m/z* $[M + Na]^+$ calcd for $C_{21}H_{26}O_3Na$ 349.1774; found, 349.1771. HPLC: WHELK-O1 column, 85:15 hexanes/isopropanol, 0.80 mL/min, t_R = (major) 7.2 min, (minor) 11.6 min, 90% ee. $[\alpha]_D^{27}$ −28.8° (*c* 0.32, DCM).

*Isopropyl (1S,5S)-4-(4-(tert-Butyl)phenyl)-8-oxobicyclo[3.2.1]oct-3-ene-1-carboxylate (**4f**).* Yield: 72% (24 mg), colorless oil, R_f = 0.6 (EtOAc/petroleum ether = 1:20). ^1H NMR (400 MHz, $CDCl_3$): δ 7.35 (d, *J* = 7.5 Hz, 2H), 7.28 (d, *J* = 7.8 Hz, 2H), 5.91 (t, 1H), 5.11 (dt, *J* = 12.8, 6.1 Hz, 1H), 3.37 (d, *J* = 18.1 Hz, 1H), 3.13 (s, 1H), 2.84−2.68 (m, 2H), 2.33−2.22 (m, 2H), 2.23−2.12 (m, 1H), 1.35−1.25 (m, 15H). $^{13}C\{^1H\}$ NMR (101 MHz, $CDCl_3$): δ 210.7, 170.8, 150.8, 142.7, 135.8, 125.5, 125.1, 120.2, 68.8, 55.5, 49.0, 43.2, 34.6,

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31.3, 31.0, 29.0, 21.8. IR (KBr, cm^{-1}): 2959, 2870, 1758, 1724, 1462, 1882, 1235, 1181, 1106, 1082, 811, 561. HRMS (ESI-TOF): m/z [M + Na]$^+$ calcd for $C_{22}H_{28}O_3Na$, 363.1931; found, 363.1929. HPLC: WHELK-O1 column, 95:5 hexanes/isopropanol, 0.70 mL/min, t_R = (major) 11.8 min, (minor) 23.6 min, 95% ee. $[\alpha]_D^{29}$ −17.9° (c 0.28, EtOH).

*Isopropyl (1S,5S)-4-(4-Methoxyphenyl)-8-oxobicyclo[3.2.1]oct-3-ene-1-carboxylate (**4g**).* Yield: 84% (26 mg), colorless oil, R_f = 0.5 (EtOAc/petroleum ether = 1:20). ^{1}H NMR (500 MHz, $CDCl_3$): δ 7.19 (d, J = 8.7 Hz, 2H), 6.78 (d, J = 8.4 Hz, 2H), 5.75 (t, J = 3.5 Hz, 1H), 5.19−4.90 (m, 1H), 3.72 (s, 3H), 3.28 (d, J = 17.9 Hz, 1H), 3.02 (d, J = 5.2 Hz, 1H), 2.85−2.56 (m, 2H), 2.27−1.98 (m, 3H), 1.25−1.08 (m, 6H). ^{13}C{^{1}H} NMR (126 MHz, $CDCl_3$): δ 210.7, 170.7, 159.3, 142.4, 131.3, 126.6, 119.2, 113.9, 68.8, 55.5, 55.3, 49.1, 43.1, 30.9, 28.9, 21.81, 21.77. IR (KBr, cm^{-1}): 2973, 2840, 1888, 1835, 1512, 1282, 1223, 1181, 1106, 1103, 837. HRMS (ESI-TOF): m/z [M + Na]$^+$ calcd for $C_{19}H_{22}O_4Na$, 337.1410; found, 337.1412. HPLC: WHELK-O1 column, 85:15 hexanes/isopropanol, 0.80 mL/min, t_R = (major) 12.3 min, (minor) 22.3 min, 88% ee. $[\alpha]_D^{31}$ −12.1° (c 0.38, EtOH).

*Isopropyl (1S,5S)-4-(4-(Methylthio)phenyl)-8-oxobicyclo[3.2.1]-oct-3-ene-1-carboxylate (**4h**).* Yield: 64% (21 mg), white solid, mp = 92−96 °C, R_f = 0.5 (EtOAc/petroleum ether = 1:20). ^{1}H NMR (500 MHz, $CDCl_3$): δ 7.25 (d, J = 9.0 Hz, 2H), 7.20 (d, J = 8.2 Hz, 2H), 5.90 (t, J = 3.6 Hz, 1H), 5.11 (hept, J = 6.1 Hz, 1H), 3.37 (d, J = 18.1 Hz, 1H), 3.10 (d, J = 5.4 Hz, 1H), 2.83−2.69 (m, 2H), 2.48 (s, 3H), 2.33−2.24 (m, 2H), 2.22−2.14 (m, 1H), 1.29 (d, J = 6.0 Hz, 6H). ^{13}C{^{1}H} NMR (126 MHz, $CDCl_3$): δ 210.5, 170.6, 142.3, 138.1, 135.5, 126.6, 125.8, 120.5, 68.9, 55.5, 48.9, 43.1, 30.9, 29.0, 21.8, 21.8, 15.8. HRMS (ESI-TOF): m/z [M + Na]$^+$ calcd for $C_{19}H_{22}O_3SNa$, 353.1182; found, 353.1176. HPLC: WHELK-O1 column, 85:15 hexanes/isopropanol, 0.80 mL/min, t_R = (major) 13.5 min, (minor) 23.9 min, 93% ee. $[\alpha]_D^{31}$ −43.1° (c 0.23, EtOH).

*Isopropyl (1S,5S)-4-(4-Fluorophenyl)-8-oxobicyclo[3.2.1]oct-3-ene-1-carboxylate (**4i**).* Yield: 74% (22 mg), colorless oil, R_f = 0.6 (EtOAc/petroleum ether = 1:20). ^{1}H NMR (400 MHz, $CDCl_3$): δ 7.31−7.14 (m, 2H), 6.93 (t, J = 8.5 Hz, 2H), 5.79 (t, J = 3.4 Hz, 1H), 5.03 (hept, J = 8.1, 7.6 Hz, 1H), 3.29 (d, J = 18.0 Hz, 1H), 3.00 (d, J = 5.1 Hz, 1H), 2.79−2.58 (m, 2H), 2.28−2.04 (m, 3H), 1.21 (d, J = 6.3 Hz, 6H). ^{13}C{^{1}H} NMR (101 MHz, $CDCl_3$): δ 210.3, 170.6, 163.6 (C−F, $^1J_{C-F}$ = 248.5 Hz), 161.1 (C−F, $^1J_{C-F}$ = 248.5 Hz), 142.0, 134.94 (C−F, $^4J_{C-F}$ = 3.1 Hz), 134.91 (C−F, $^4J_{C-F}$ = 3.1 Hz) 127.2 (C−F, $^3J_{C-F}$ = 8.0 Hz), 127.1 (C−F, $^3J_{C-F}$ = 8.0 Hz), 121.0, 115.5 (C−F, $^2J_{C-F}$ = 21.2 Hz), 115.3 (C−F, $^2J_{C-F}$ = 21.2 Hz), 68.9, 55.4, 49.1, 43.1, 30.9, 28.9, 21.8. ^{19}F NMR (376 MHz, $CDCl_3$): δ −114.41. IR (KBr, cm^{-1}): 3073, 2980, 2908, 1757, 1723, 1601, 1510, 1285, 1232, 1104, 838. HRMS (ESI-TOF): m/z [M + Na]$^+$ calcd for $C_{18}H_{19}FO_3Na$, 325.1210; found, 325.1208. HPLC: WHELK-O1 column, 95:5 hexanes/isopropanol, 0.80 mL/min, t_R = (major) 11.0 min, (minor) 16.9 min, 92% ee. $[\alpha]_D^{22}$ −32.8° (c 0.13, DCM).

*Isopropyl (1S,5S)-4-(4-Chlorophenyl)-8-oxobicyclo[3.2.1]oct-3-ene-1-carboxylate (**4j**).* Yield: 75% (22 mg), yellow solid, mp = 79−83 °C, R_f = 0.6 (EtOAc/petroleum ether = 1:20). ^{1}H NMR (400 MHz, $CDCl_3$): δ 7.31−7.22 (m, 4H), 5.91 (t, J = 3.6 Hz, 1H), 5.15−5.05 (m, 1H), 3.37 (d, J = 18.1 Hz, 1H), 3.06 (d, J = 5.4 Hz, 1H), 2.85−2.69 (m, 2H), 2.36−2.10 (m, 3H), 1.29 (d, J = 6.3 Hz, 6H). ^{13}C{^{1}H} NMR (101 MHz, $CDCl_3$): δ 209.9, 170.4, 142.0, 137.2, 133.6, 128.7, 126.8, 121.6, 68.9, 55.4, 48.9, 43.1, 30.9, 28.9, 21.7. IR (KBr, cm^{-1}): 3073, 2980, 2908, 1757, 1723, 1601, 1510, 1285, 1232, 1104, 838. HRMS (ESI-TOF): m/z [M + Na]$^+$ calcd for $C_{18}H_{19}ClO_3Na$ 341.0915; found, 341.0911. HPLC: WHELK-O1 column, 95:5 hexanes/isopropanol, 0.80 mL/min, t_R = (major) 11.6 min, (minor) 18.0 min, 91% ee. $[\alpha]_D^{31}$ −32.0° (c 0.67, EtOH).

*Isopropyl (1S,5S)-4-(4-Bromophenyl)-8-oxobicyclo[3.2.1]oct-3-ene-1-carboxylate (**4k**).* Yield: 69% (25 mg), yellow solid, mp = 87−92 °C, R_f = 0.6 (EtOAc/petroleum ether = 1:20). ^{1}H NMR (400 MHz, $CDCl_3$): δ 7.45 (d, J = 8.1 Hz, 2H), 7.19 (d, J = 8.1 Hz, 2H), 5.94 (d, J = 3.6 Hz, 1H), 5.17−5.06 (m, 1H), 3.36 (d, J = 18.2 Hz, 1H), 3.07 (d, J = 5.4 Hz, 1H), 2.84−2.70 (m, 2H), 2.33−2.13 (m, 3H), 1.29 (d, J = 6.3 Hz, 6H). ^{13}C{^{1}H} NMR (101 MHz, $CDCl_3$): δ 210.2, 170.5, 141.9, 137.7, 131.7, 127.1, 121.7, 69.0, 55.4, 48.9, 43.1, 30.9, 28.9, 21.8. IR (KBr, cm^{-1}): 2960, 2937, 1759, 1723, 1488, 1287, 1235, 1182, 1148, 1105, 836. HRMS (ESI-TOF): m/z [M + Na]$^+$ calcd for $C_{18}H_{19}BrO_3Na$, 385.0409; found, 385.0410. HPLC: WHELK-O1 column, 95:5 hexanes/isopropanol, 0.80 mL/min, t_R = (major) 12.2 min, (minor) 19.2 min, 91% ee. $[\alpha]_D^{31}$ −25.7° (c 0.46, EtOH).

*Isopropyl (1S,5S)-4-(4-(Methoxycarbonyl)phenyl)-8-oxobicyclo-[3.2.1]oct-3-ene-1-carboxylate (**4l**).* Yield: 72% (25 mg), white solid, mp = 58−64 °C, R_f = 0.4 (EtOAc/petroleum ether = 1:20). ^{1}H NMR (500 MHz, $CDCl_3$): δ 7.99 (d, J = 8.2 Hz, 2H), 7.39 (d, J = 8.2 Hz, 2H), 6.06 (t, J = 3.6 Hz, 1H), 5.12 (hept, J = 6.5 Hz, 1H), 3.92 (s, 3H), 3.41 (d, J = 18.4 Hz, 1H), 3.14 (d, J = 5.6 Hz, 1H), 2.88−2.73 (m, 2H), 2.36−2.15 (m, 3H), 1.32−1.27 (m, 6H). ^{13}C{^{1}H} NMR (126 MHz, $CDCl_3$): δ 210.0, 170.4, 166.7, 143.0, 142.2, 129.9, 129.3, 125.3, 123.4, 69.0, 55.4, 52.1, 48.7, 43.2, 30.9, 29.0, 21.8, 21.8. IR (KBr, cm^{-1}): 2983, 2951, 1759, 1721, 1606, 1439, 1282, 1186, 1108, 919, 862, 739. HRMS (ESI-TOF): m/z [M + Na]$^+$ calcd for $C_{19}H_{22}O_5Na$, 365.1359; found, 365.1354. HPLC: WHELK-O1 column, 85:15 hexanes/isopropanol, 0.80 mL/min, t_R = (minor) 19.9 min, (major) 31.0 min, 93% ee. $[\alpha]_D^{23}$ −17.1° (c 0.03, DCM).

*Isopropyl (1S,5S)-4-([1,1′-Biphenyl]-4-yl)-8-oxobicyclo[3.2.1]oct-3-ene-1-carboxylate (**4m**).* Yield: 73% (28 mg), white solid, mp = 156−158 °C, R_f = 0.5 (EtOAc/petroleum ether = 1:20). ^{1}H NMR (400 MHz, $CDCl_3$): δ 7.57 (t, J = 8.6 Hz, 4H), 7.47−7.38 (m, 4H), 7.34 (t, J = 7.3 Hz, 1H), 5.99 (t, J = 3.6 Hz, 1H), 5.12 (hept, J = 6.0 Hz, 1H), 3.41 (d, J = 18.1 Hz, 1H), 3.18 (d, J = 3.8 Hz, 1H), 2.89−2.68 (m, 2H), 2.41−2.12 (m, 3H), 1.30 (d, J = 6.3 Hz, 6H). ^{13}C{^{1}H} NMR (101 MHz, $CDCl_3$): δ 210.5, 170.7, 142.5, 140.6, 140.4, 137.6, 128.8, 127.5, 127.3, 127.0, 125.8, 121.0, 68.9, 55.5, 48.9, 43.2, 31.0, 29.0, 21.8. IR (KBr, cm^{-1}): 3030, 2980, 1754, 1722, 1485, 1454, 1349, 1285, 1149, 812. HRMS (ESI-TOF): m/z [M + Na]$^+$ calcd for $C_{24}H_{24}O_3Na$, 383.1618; found, 383.1613. HPLC: OD-H column, 95:5 hexanes/isopropanol, 0.80 mL/min, t_R = (major) 17.0 min, (minor) 32.7 min, 92% ee. $[\alpha]_D^{22}$ −63.5° (c 0.40, DCM).

*Isopropyl (1S,5S)-8-Oxo-4-(m-tolyl)bicyclo[3.2.1]oct-3-ene-1-carboxylate (**4n**).* Yield: 78% (23 mg), colorless oil, R_f = 0.6 (EtOAc/petroleum ether = 1:20). ^{1}H NMR (500 MHz, chloroform-d): δ 7.22 (t, J = 7.5 Hz, 1H), 7.16−7.06 (m, 3H), 5.93−5.88 (m, 1H), 5.11 (hept, J = 6.3 Hz, 1H), 3.37 (d, J = 18.0 Hz, 1H), 3.13 (d, J = 4.1 Hz, 1H), 2.83−2.69 (m, 2H), 2.35 (s, 3H), 2.32−2.24 (m, 2H), 2.22−2.12 (m, 1H), 1.32−1.26 (m, 6H). ^{13}C{^{1}H} NMR (126 MHz, $CDCl_3$): δ 210.7, 170.7, 143.1, 138.8, 138.2, 128.5, 126.23, 122.6, 120.8, 68.9, 55.5, 49.1, 43.2, 30.9, 29.0, 21.8, 21.8, 21.5.IR (KBr, cm^{-1}): 3027, 2980, 2874, 1758, 1724, 1457, 1286, 1241, 1105, 784. HRMS (ESI-TOF): m/z [M + Na]$^+$ calcd for $C_{19}H_{22}O_3Na$, 321.1461; found, 321.1459. HPLC: WHELK-O1 column, 95:5 hexanes/isopropanol, 0.80 mL/min, t_R = (major) 12.0 min, (minor) 22.7 min, 91% ee. $[\alpha]_D^{28}$ −25.7° (c 0.42, EtOH).

*Isopropyl (1S,5S)-4-(2-Fluorophenyl)-8-oxobicyclo[3.2.1]oct-3-ene-1-carboxylate (**4o**).* Yield: 78% (24 mg), colorless oil, R_f = 0.6 (EtOAc/petroleum ether = 1:20). ^{1}H NMR (500 MHz, $CDCl_3$): δ 7.32−7.27 (m, 1H), 7.11 (d, J = 7.9 Hz, 1H), 7.02 (dt, J = 10.3, 2.1 Hz, 1H), 6.97 (td, J = 8.4, 2.6 Hz, 1H), 5.97 (t, J = 3.6 Hz, 1H), 5.12 (hept, J = 6.2 Hz, 1H), 3.38 (dt, J = 18.2, 2.7 Hz, 1H), 3.09 (d, J = 5.5 Hz, 1H), 2.85−2.71 (m, 2H), 2.33−2.14 (m, 3H), 1.31−1.27 (m, 6H). ^{13}C{^{1}H} NMR (126 MHz, $CDCl_3$): δ 210.0, 170.5, 163.9 (C−F, $^1J_{C-F}$ = 247.0 Hz), 162.0 (C−F, $^1J_{C-F}$ = 247.0 Hz), 141.88 (C−F, $^4J_{C-F}$ = 2.5 Hz), 141.86 (C−F, $^4J_{C-F}$ = 2.5 Hz), 141.03 (C−F, $^3J_{C-F}$ = 7.6 Hz), 140.91 (C−F, $^3J_{C-F}$ = 7.6 Hz), 130.08 (C−F, $^3J_{C-F}$ = 8.8 Hz), 130.01 (C−F, $^3J_{C-F}$ = 8.8 Hz), 122.2, 121.1 (C−F, $^4J_{C-F}$ = 3.8 Hz), 121.0 (C−F, $^4J_{C-F}$ = 3.8 Hz), 114.6 (C−F, $^2J_{C-F}$ = 21.4 Hz), 114.4 (C−F, $^2J_{C-F}$ = 21.4 Hz), 112.5 (C−F, $^2J_{C-F}$ = 22.7 Hz), 112.3 (C−F, $^2J_{C-F}$ = 22.7 Hz), 69.0, 55.4, 48.9, 43.0, 30.9, 29.0, 21.8, 21.8. ^{19}F NMR (376 MHz, $CDCl_3$): δ −112.87. IR (KBr, cm^{-1}): 2982, 2909, 2878, 1758, 1724, 1489, 1462, 1284, 1223, 1150, 814, 761. HRMS (ESI-TOF): m/z [M + Na]$^+$ calcd for $C_{18}H_{19}FO_3Na$, 325.1210; found, 325.1209. HPLC: WHELK-O1 column, 95:5 hexanes/isopropanol, 0.80 mL/min, t_R = (major) 11.2 min, (minor) 17.4 min, 91% ee. $[\alpha]_D^{28}$ −61.2° (c 0.32, DCM).

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*Isopropyl (1S,5S)-4-(2,4-Dimethylphenyl)-8-oxobicyclo[3.2.1]oct-3-ene-1-carboxylate (**4p**).* Yield: 71% (23 mg), colorless oil, R_f = 0.4 (EtOAc/petroleum ether = 1:20). ^{1}H NMR (500 MHz, $CDCl_3$): δ 7.04−7.00 (m, 2H), 6.97 (d, J = 8.0 Hz, 1H), 5.47 (t, 1H), 5.12 (hept, J = 6.3 Hz, 1H), 3.41 (d, J = 17.8 Hz, 1H), 2.79−2.70 (m, 3H), 2.31 (s, 3H), 2.26 (s, 3H), 2.24−2.17 (m, 2H), 2.16−2.10 (m, 1H), 1.29 (d, J = 6.3 Hz, 6H). ^{13}C{^{1}H} NMR (126 MHz, $CDCl_3$): δ 210.7, 170.8, 144.7, 137.4, 135.2, 131.2, 128.7, 126.3, 122.7, 68.8, 55.5, 51.2, 43.4, 30.9, 28.3, 21.8, 21.8, 21.0, 19.9.IR (KBr, cm^{-1}): 2975, 2929, 1755, 1726, 1603, 1447, 1406, 1238, 1104, 817. HRMS (ESI-TOF): m/z [M + Na]$^+$ calcd for $C_{20}H_{24}O_3Na$, 335.1618; found, 335.1617. HPLC: WHELK-O1 column, 95:5 hexanes/isopropanol, 0.80 mL/min, t_R = (major) 9.1 min, (minor) 7 min, 91% ee. $[\alpha]_D^{23}$ +12.4° (c 0.04, DCM).

*Isopropyl (1S,5S)-4-(3,5-Dimethylphenyl)-8-oxobicyclo[3.2.1]oct-3-ene-1-carboxylate (**4q**).* Yield: 57% (23 mg), colorless oil, R_f = 0.6 (EtOAc/petroleum ether = 1:20). ^{1}H NMR (500 MHz, $CDCl_3$): δ 6.96−6.90 (m, 3H), 5.88 (s, 1H), 5.16−5.08 (m, 1H), 3.36 (d, J = 18.0 Hz, 1H), 3.11 (s, 1H), 2.81−2.70 (m, 2H), 2.3 (s, 6H), 2.25 (s, 2H), 2.22−2.13 (m, 1H), 1.29 (d, J = 6.3 Hz, 6H). ^{13}C{^{1}H} NMR (126 MHz, $CDCl_3$): δ 210.7, 170.8, 143.2, 138.8, 138.1, 129.4, 123.4, 120.6, 68.8, 55.5, 49.1, 43.2, 30.9, 29.0, 21.8, 21.8, 21.3. IR (KBr, cm^{-1}): 2979, 2924, 1757, 1724, 1601, 1281, 1243, 1184, 1103, 850, 701. HRMS (ESI-TOF): m/z [M + Na]$^+$ calcd for $C_{20}H_{24}O_3Na$, 335.1618; found, 335.1614. HPLC: WHELK-O1 column, 95:5 hexanes/isopropanol, 0.80 mL/min, t_R = (major) 11.6 min, (minor) 23.7 min, 91% ee. $[\alpha]_D^{31}$ −11.2° (c 0.41, EtOH).

*Isopropyl (1S,5S)-4-(Naphthalen-1-yl)-8-oxobicyclo[3.2.1]oct-3-ene-1-carboxylate (**4r**).* Yield: 56% (17 mg), colorless oil, R_f = 0.6 (EtOAc/petroleum ether = 1:20). ^{1}H NMR (400 MHz, $CDCl_3$): δ 7.83 (d, J = 8.1 Hz, 1H), 7.76 (d, J = 8.0 Hz, 1H), 7.71 (d, J = 8.2 Hz, 1H), 7.47−7.37 (m, 2H), 7.33 (t, J = 7.6 Hz, 1H), 7.24 (d, J = 6.9 Hz, 1H), 5.62 (t, J = 3.4 Hz, 1H), 5.07 (hept, J = 6.2 Hz, 1H), 3.44 (d, J = 17.7 Hz, 1H), 2.90 (d, J = 5.8 Hz, 1H), 2.81−2.66 (m, 2H), 2.28−2.15 (m, 2H), 2.14−2.00 (m, 1H), 1.24 (d, J = 6.2 Hz, 6H). ^{13}C{^{1}H} NMR (101 MHz, $CDCl_3$): δ 210.9, 170.8, 144.2, 138.2, 133.7, 131.0, 128.4, 128.2, 126.5, 126.0, 125.8, 125.6, 125.2, 124.2, 68.9, 55.6, 51.5, 43.7, 30.9, 28.6, 21.8, 21.8. IR (KBr, cm^{-1}): 3055, 2979, 2874, 1756, 1723, 1468, 1348, 1186, 1106, 800. HRMS (ESI-TOF): m/z [M + Na]$^+$ calcd for $C_{22}H_{22}O_3Na$, 357.1461; found, 357.1462. HPLC: WHELK-O1 column, 95:5 hexanes/isopropanol, 0.80 mL/min, t_R = (major) 11.6 min, (minor) 13.5 min, 91% ee. $[\alpha]_D^{30}$ +11.6° (c 0.5, EtOH).

*Isopropyl (1S,5S)-8-Oxo-4-(thiophen-2-yl)bicyclo[3.2.1]oct-3-ene-1-carboxylate (**4s**).* Yield: 85% (23 mg), colorless oil, R_f = 0.6 (EtOAc/petroleum ether = 1:20). ^{1}H NMR (500 MHz, $CDCl_3$): δ 7.17 (d, J = 4.6 Hz, 1H), 6.99−6.92 (m, 2H), 5.98−5.92 (m, 1H), 5.14−5.06 (m, 1H), 3.36 (d, J = 18.3 Hz, 1H), 3.18−3.13 (m, 1H), 2.81−2.70 (m, 2H), 2.30−2.22 (m, 2H), 2.22−2.13 (m, 1H), 1.31−1.26 (m, 6H). ^{13}C{^{1}H} NMR (126 MHz, $CDCl_3$): δ 209.9, 170.5, 142.4, 136.8, 127.4, 124.5, 122.8, 119., 69.0, 55.2, 49.2, 42.9, 30.8, 28.5, 21.8, 21.8. IR (KBr, cm^{-1}): 2925, 1755, 1722, 1456, 1277, 1241, 1103, 1030, 754, 703. HRMS (ESI-TOF): m/z [M + Na]$^+$ calcd for $C_{16}H_{18}O_3SNa$, 313.0869; found, 313.0870. HPLC: WHELK-O1 column, 95:5 hexanes/isopropanol, 1.00 mL/min, t_R = (major) 10.2 min, (minor) 21.1 min, 90% ee. $[\alpha]_D^{30}$ +15.7° (c 0.23, EtOH).

*Isopropyl (1S,5S)-4-(Benzo[b]thiophen-2-yl)-8-oxobicyclo[3.2.1]-oct-3-ene-1-carboxylate (**4t**).* Yield: 69% (22 mg), colorless oil, R_f = 0.6 (EtOAc/petroleum ether = 1:20). ^{1}H NMR (500 MHz, $CDCl_3$): δ 7.87−7.82 (m, 2H), 7.42−7.32 (m, 2H), 7.27 (s, 1H), 5.92 (t, 1H), 5.20−5.07 (m, 1H), 3.48 (dt, J = 18.0, 2.6 Hz, 1H), 3.07 (d, J = 5.2 Hz, 1H), 2.86−2.74 (m, 2H), 2.31−2.20 (m, 3H), 1.31 (d, J = 6.2 Hz, 6H). ^{13}C{^{1}H} NMR (126 MHz, $CDCl_3$): δ 210.2, 170.6, 140.4, 138.8, 137.4, 135.8, 124.6, 124.5, 123.5, 123.1, 123.0, 122.9, 69.0, 55.6, 50.6, 43.3, 30.9, 29.0, 21.8, 21.8. IR (KBr, cm^{-1}): 3048, 2978, 2923, 1812, 1757, 1586, 1257, 1239, 757. HRMS (ESI-TOF): m/z [M + Na]$^+$ calcd for $C_{20}H_{20}O_3SNa$, 363.1025; found, 363.1020. HPLC: WHELK-O1 column, 90:10 hexanes/isopropanol, 0.80 mL/min, t_R = (major) 14.3 min, (minor) 31.1 min, 88% ee. $[\alpha]_D^{30}$ +11.6° (c 0.50, EtOH).

*Isopropyl (1S,5S)-4-(Benzo[b]thiophen-3-yl)-8-oxobicyclo[3.2.1]-oct-3-ene-1-carboxylate (**4u**).* Yield: 70% (21 mg), yellow solid, mp = 109−114 °C. R_f = 0.6 (EtOAc/petroleum ether = 1:20). ^{1}H NMR (500 MHz, $CDCl_3$): δ 7.73 (d, J = 6.8 Hz, 1H), 7.68 (d, J = 8.6 Hz, 1H), 7.38−7.28 (m, 2H), 7.13 (s, 1H), 6.11−5.97 (m, 1H), 5.18−5.08 (m, 1H), 3.41 (d, J = 18.5 Hz, 1H), 3.28 (d, J = 4.2 Hz, 1H), 2.92−2.67 (m, 2H), 2.35−2.14 (m, 3H), 1.34−1.26 (m, 6H). ^{13}C{^{1}H} NMR (126 MHz, $CDCl_3$): δ 209.7, 170.4, 142.1, 139.9, 138.8, 137.3, 124.9, 124.6, 123.6, 122.2, 122.0, 119.4, 69.0, 55.2, 48.6, 43.0, 30.8, 28.5, 21.8, 21.8. IR (KBr, cm^{-1}): 2980, 2937, 1758, 1723, 1456, 1283, 1240, 1150, 1106, 804. HRMS (ESI-TOF): m/z [M + Na]$^+$ calcd for $C_{20}H_{20}O_3SNa$, 363.1025; found, 363.1022. HPLC: WHELK-O1 column, 90:10 hexanes/isopropanol, 0.70 mL/min, t_R = (major) 13.9 min, (minor) 19.3 min, 87% ee. $[\alpha]_D^{31}$ −26.7° (c 0.33, EtOH).

*Isopropyl (1S,5S)-9-Oxo-4-phenylbicyclo[3.3.1]non-3-ene-1-carboxylate (**4v**).* Yield: 90% (26 mg), colorless oil, R_f = 0.6 (EtOAc/petroleum ether = 1:20). ^{1}H NMR (500 MHz, $CDCl_3$): δ 7.37−7.24 (m, 5H), 6.29 (t, J = 3.8 Hz, 1H), 5.12 (p, J = 6.3 Hz, 1H), 3.54 (d, J = 19.6 Hz, 1H), 3.46 (s, 1H), 2.66 (dd, J = 19.3, 4.0 Hz, 1H), 2.47−2.37 (m, 1H), 2.06−1.99 (m, 3H), 1.72−1.65 (m, 1H), 1.33−1.27 (m, 6H). ^{13}C{^{1}H} NMR (126 MHz, $CDCl_3$): δ 209.8, 171.5, 138.8, 136.2, 128.6, 127.6, 125.6, 124.6, 69.0, 57.4, 49.2, 39.0, 38.3, 32.4, 21.8, 17.5. IR (KBr, cm^{-1}): 2929, 2862, 1716, 1637, 1256, 1234, 1108, 1070, 755, 693. HRMS (ESI-TOF): m/z [M + Na]$^+$ calcd for $C_{19}H_{22}O_3Na$, 321.1461; found, 321.1460. HPLC: WHELK-O1 column, 95:5 hexanes/isopropanol, 0.80 mL/min, t_R = (major) 10.3 min, (minor) 14.8 min, 85% ee. $[\alpha]_D^{29}$ −61.0° (c 0.19, EtOH).

*Isopropyl (1S,6S)-10-Oxo-7-phenylbicyclo[4.3.1]dec-7-ene-1-carboxylate (**4w**).* Yield: 86% (23 mg), colorless oil, R_f = 0.6 (EtOAc/petroleum ether = 1:20). ^{1}H NMR (500 MHz, $CDCl_3$): δ 7.27 (dd, J = 15.5, 8.4 Hz, 5H), 5.93 (d, J = 6.1 Hz, 1H), 5.06 (dt, J = 12.2, 5.7 Hz, 1H), 3.57 (t, 1H), 3.10 (d, J = 18.0 Hz, 1H), 2.52−2.39 (m, 2H), 1.83−1.75 (m, 2H), 1.57−1.50 (m, 2H), 1.46−1.39 (m, 1H), 1.26−1.19 (m, 8H). ^{13}C{^{1}H} NMR (126 MHz, $CDCl_3$): δ 209.7, 172.9, 139.7, 139.3, 128.5, 127.6, 126.4, 124.3, 68.7, 59.4, 51.8, 36.7, 34.0, 29.7, 27.2, 26.3, 21.8, 21.7. IR (KBr, cm^{-1}): 3061, 2978, 2903, 1705, 1597, 1450, 1373, 1231, 1179, 1106, 1004, 903, 752, 693. HRMS (ESI-TOF): m/z [M + Na]$^+$ calcd for $C_{20}H_{24}O_3Na$, 335.1618; found, 335.1610. HPLC: WHELK-O1 column, 85:15 hexanes/isopropanol, 0.80 mL/min, t_R = (major) 10.3 min, (minor) 14.8 min, 57% ee. $[\alpha]_D^{22}$ +10.0° (c 0.40, DCM).

*Isopropyl (1S,5S)-8-Oxo-4-((E)-styryl)bicyclo[3.2.1]oct-3-ene-1-carboxylate (**7a**).* Yield: 75% (21 mg), colorless oil. R_f = 0.6 (EtOAc/petroleum ether = 1:20). ^{1}H NMR (500 MHz, $CDCl_3$): δ 7.39 (d, J = 7.2 Hz, 2H), 7.32 (t, J = 7.6 Hz, 2H), 7.23 (t, J = 7.3 Hz, 1H), 6.67 (d, J = 16.2 Hz, 1H), 6.47 (d, J = 16.1 Hz, 1H), 5.70 (t, J = 3.8 Hz, 1H), 5.17−5.04 (m, 1H), 3.36 (d, J = 18.7 Hz, 1H), 3.14 (d, J = 5.7 Hz, 1H), 2.85−2.67 (m, 2H), 2.31−2.08 (m, 3H), 1.32−1.25 (m, 6H). ^{13}C{^{1}H} NMR (126 MHz, $CDCl_3$): δ 210.9, 170.6, 142.0, 136.8, 128.7, 127.7, 127.1, 126.4, 124.9, 68.9, 55.5, 45.9, 43.1, 30.9, 28.3, 21.8, 21.78. IR (KBr, cm^{-1}): 3059, 3030, 2981, 2936, 1758, 1723, 1493, 1275, 1183, 1106, 740, 699. HRMS (ESI-TOF): m/z [M + Na]$^+$ calcd for $C_{20}H_{22}O_3Na$, 333.1461; found, 333.1464. HPLC: WHELK-O1 column, 95:5 hexanes/isopropanol, 0.60 mL/min, t_R = (major) 14.5 min, (minor) 18.3 min, 93% ee. $[\alpha]_D^{31}$ +23.8° (c 0.63, EtOH).

*Isopropyl (1S,5S)-4-((E)-4-Methylstyryl)-8-oxobicyclo[3.2.1]oct-3-ene-1-carboxylate (**7b**).* Yield: 78% (23 mg), colorless oil. R_f = 0.6 (EtOAc/petroleum ether = 1:20). ^{1}H NMR (500 MHz, $CDCl_3$): δ 7.28 (d, J = 8.0 Hz, 2H), 7.12 (d, J = 7.8 Hz, 2H), 6.62 (d, J = 16.1 Hz, 1H), 6.44 (d, J = 16.2 Hz, 1H), 5.66 (t, J = 3.7 Hz, 1H), 5.15−5.06 (m, 1H), 3.35 (d, J = 18.2 Hz, 1H), 3.13 (d, J = 5.7 Hz, 1H), 2.79−2.67 (m, 2H), 2.33 (s, 3H), 2.27−2.20 (m, 1H), 2.19−2.09 (m, 2H), 1.31−1.25 (m, 6H). ^{13}C{^{1}H} NMR (126 MHz, $CDCl_3$): δ 211.0, 170.7, 142.1, 137.6, 134.0, 129.4, 127.0, 126.7, 126.4, 124.3, 68.9, 55.5, 45.9, 43.1, 30.9, 28.3, 21.8, 21.8, 21.2. IR (KBr, cm^{-1}): 2981, 1758, 1721, 1511, 1440, 1277, 1182, 1105, 1206, 963, 819. HRMS (ESI-TOF): m/z [M + Na]$^+$ calcd for $C_{21}H_{24}O_3Na$, 347.1618; found, 347.1610. HPLC: WHELK-O1 column, 85:15 hexanes/

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isopropanol, 0.80 mL/min, t_R = (major) 9.3 min, (minor) 16.5 min, 92% ee. $[\alpha]_D^{30}$ −23.5° (*c* 0.34, EtOH).

*Isopropyl (1S,5S)-4-((E)-4-Fluorostyryl)-8-oxobicyclo[3.2.1]oct-3-ene-1-carboxylate (**7c**).* Yield: 86% (26 mg), colorless oil. R_f = 0.6 (EtOAc/petroleum ether = 1:20). ^{1}H NMR (500 MHz, $CDCl_3$): δ 7.35 (dd, *J* = 8.6, 5.5 Hz, 2H), 7.01 (t, *J* = 8.7 Hz, 2H), 6.58 (d, *J* = 16.1 Hz, 1H), 6.42 (d, *J* = 16.1 Hz, 1H), 5.69 (t, *J* = 3.7 Hz, 1H), 5.14−5.07 (m, 1H), 3.36 (d, *J* = 18.7 Hz, 1H), 3.12 (d, *J* = 5.8 Hz, 1H), 2.80−2.68 (m, 2H), 2.29−2.18 (m, 1H), 2.18−2.09 (m, 2H), 1.31−1.25 (m, 6H). ^{13}C NMR (126 MHz, $CDCl_3$) δ ^{13}C{^{1}H} NMR (126 MHz, $CDCl_3$): δ 210.8, 170.6, 163.3 (C−F, $^1J_{C-F}$ = 248.1 Hz), 161.1 (C−F, $^1J_{C-F}$ = 248.1 Hz), 141.9, 133.04 (C−F, $^5J_{C-F}$ = 2.7 Hz), 133.02 (C−F, $^5J_{C-F}$ = 2.7 Hz), 127.95 (C−F, $^3J_{C-F}$ = 7.6 Hz), 127.85 (C−F, $^3J_{C-F}$ = 7.6 Hz), 127.53 (C−F, $^4J_{C-F}$ = 2.7 Hz), 127.51 (C−F, $^4J_{C-F}$ = 2.7 Hz), 125.83, 125.01, 115.7 (C−F, $^2J_{C-F}$ = 21.4 Hz), 115.5 (C−F, $^2J_{C-F}$ = 21.4 Hz), 68.9, 55. 5, 45.9, 43.1, 30.9, 28.3, 21.8, 21.8. ^{19}F NMR (376 MHz, $CDCl_3$): δ −114.05. IR (KBr, cm^{-1}): 3039, 2981, 1759, 1722, 1507, 1282, 1231, 1105, 961, 831. HRMS (ESI-TOF): *m*/*z* [M + Na]$^+$ calcd for $C_{20}H_{21}FO_3Na$, 351.1367; found, 351.1360. HPLC: WHELK-O1 column, 85:15 hexanes/isopropanol, 0.80 mL/min, t_R = (major) 9.1 min, (minor) 14.8 min, 93% ee. $[\alpha]_D^{30}$ +54.2° (*c* 0.45, EtOH).

*Isopropyl (1S,5S)-4-((E)-4-Chlorostyryl)-8-oxobicyclo[3.2.1]oct-3-ene-1-carboxylate (**7d**).* Yield: 73% (33 mg, 0.13 mmol), yellow solid, mp = 104−109 °C. R_f = 0.6 (EtOAc/petroleum ether = 1:20). ^{1}H NMR (500 MHz, $CDCl_3$): δ 7.24−7.18 (m, 4H), 6.56 (d, *J* = 16.2 Hz, 1H), 6.33 (d, *J* = 16.1 Hz, 1H), 5.64 (t, *J* = 3.8 Hz, 1H), 5.06−5.00 (m, 1H), 3.29 (d, *J* = 18.8 Hz, 1H), 3.04 (d, *J* = 5.8 Hz, 1H), 2.71−2.63 (m, 2H), 2.20−2.13 (m, 1H), 2.09−2.02 (m, 2H), 1.21 (d, *J* = 6.3 Hz, 6H). ^{13}C{^{1}H} NMR (126 MHz, $CDCl_3$): δ 210.7, 170.6, 141.8, 135.4, 133.3, 128.9, 128.3, 127.6, 125.8, 125.6, 68.9, 55.5, 45.9, 43.1, 30.9, 28.3, 21.8, 21.8. IR (KBr, cm^{-1}): 3025, 2980, 2936, 1759, 1723, 1511, 1281, 1184, 961, 817. HRMS (ESI-TOF): *m*/*z* [M + Na]$^+$ calcd for $C_{19}H_{21}O_5Na$, 367.1071; found, 367.1076. HPLC: WHELK-O1 column, 85:15 hexanes/isopropanol, 0.80 mL/min, t_R = (major) 9.9 min, (minor) 15.8 min, 93% ee. $[\alpha]_D^{27}$ +142° (*c* 0.45, EtOH).

*Isopropyl (1S,5S)-4-((E)-4-Bromostyryl)-8-oxobicyclo[3.2.1]oct-3-ene-1-carboxylate (**7e**).* Yield: 87% (29 mg), yellow solid, mp = 96−98 °C. R_f = 0.6 (EtOAc/petroleum ether = 1:20). ^{1}H NMR (500 MHz, $CDCl_3$): δ 7.43 (d, *J* = 8.1 Hz, 2H), 7.25 (d, *J* = 8.2 Hz, 2H), 6.65 (d, *J* = 16.2 Hz, 1H), 6.39 (d, *J* = 16.1 Hz, 1H), 5.72 (t, *J* = 3.7 Hz, 1H), 5.15−5.06 (m, 1H), 3.35 (d, *J* = 18.8 Hz, 1H), 3.11 (d, *J* = 5.8 Hz, 1H), 2.80−2.68 (m, 2H), 2.28−2.19 (m, 1H), 2.18−2.09 (m, 2H), 1.31−1.25 (m, 6H). ^{13}C{^{1}H} NMR (126 MHz, $CDCl_3$): δ 210.7, 170.5, 141.8, 135.8, 131.8, 128.4, 127.9, 125.8, 125.7, 121.4, 68.9, 55.5, 45.8, 43.1, 30.9, 28.3, 21.8, 21.8. IR (KBr, cm^{-1}): 3034, 2979, 1758, 1721, 1485, 1279, 1184, 1147, 1009, 822, 755. HRMS (ESI-TOF): *m*/*z* [M + Na]$^+$ calcd for $C_{20}H_{21}BrO_3Na$, 411.0566; found, 411.0563. HPLC: WHELK-O1 column, 85:15 hexanes/isopropanol, 0.80 mL/min, t_R = (major) 9.7 min, (minor) 15.3 min, 90% ee. $[\alpha]_D^{31}$ +43.2° (*c* 0.35, EtOH).

*Isopropyl (1S,5S)-4-((E)-4-Methoxystyryl)-8-oxobicyclo[3.2.1]oct-3-ene-1-carboxylate (**7f**).* Yield: 68% (25 mg), yellow solid, mp = 55−58 °C R_f = 0.6 (EtOAc/petroleum ether = 1:20). ^{1}H NMR (400 MHz, $CDCl_3$): δ 7.47 (d, *J* = 6.7 Hz, 1H), 7.24 (t, *J* = 7.1 Hz, 1H), 6.95 (t, *J* = 7.5 Hz, 1H), 6.91−6.82 (m, 2H), 6.70 (d, *J* = 16.3 Hz, 1H), 5.70 (t, *J* = 3.7 Hz, 1H), 5.13 (hept, *J* = 6.2 Hz, 1H), 3.88 (s, 3H), 3.38 (d, *J* = 18.7 Hz, 1H), 3.23 (d, *J* = 5.5 Hz, 1H), 2.83−2.67 (m, 2H), 2.34−2.05 (m, 3H), 1.31 (d, *J* = 6.2 Hz, 6H). ^{13}C{^{1}H} NMR (101 MHz, $CDCl_3$): δ 211.2, 170.7, 156.8, 142.7, 128.8, 128.0, 126.3, 125.9, 124.3, 121.9, 120.7, 110.9, 68.9, 55.6, 46.0, 43.1, 31.0, 28.4, 21.81, 21.77. IR (KBr, cm^{-1}): 2977, 2934, 1755, 1721, 1599, 1490, 1247, 1103, 1025, 755. HRMS (ESI-TOF): *m*/*z* [M + Na]$^+$ calcd for $C_{21}H_{24}O_4Na$, 363.1567; found, 363.1565. HPLC: WHELK-O1 column, 85:15 hexanes/isopropanol, 0.80 mL/min, t_R = (major) 14.5 min, (minor) 18.3 min, 86% ee. $[\alpha]_D^{31}$ +17.7° (*c* 0.34, EtOH).

One-Pot Synthesis. Copper(II) trifluoromethanesulfonate (3.5 mg, 10 mol %) and L1 (6 mg, 12 mol %) were stirred for 5 min in 0.5 mL of dry DCE in a 25 mL Schlenk tube charged with a magnetic stirring bar. Ketone **2**/**5** (0.12 mmol) and β-ketoesters **1** (0.1 mmol) were added to the tube, and the reaction was stirred at 0 °C until substrate **1** was completely consumed (monitored by TLC). When the reaction was finished, 0.5 equiv of TfOH was added, and the reaction was stirred at 100 °C in an oil bath. When the reaction was finished (monitored by TLC), $NaHCO_3$ (2.0 equiv) was added to neutralize the acidic solution at room temperature. The mixture was filtered through a short pad of silica gel. The filtrate was removed under reduced pressure to give a residue, which was purified by silica gel chromatography (EtOAc/petroleum ether = 1:20) to afford the desired product.

*Gram Scale Synthesis of **4c**.* Copper(II) trifluoromethanesulfonate (5 mol %) and L1 (6 mol %) in 15 mL of dry DCE were stirred for 5 min in a 50 mL Schlenk tube. 1-Phenylprop-2-en-1-one (7.2 mmol, 953 mg) and β-ketoesters (6 mmol, 1.02 g) **1c** were dissolved in 5 mL of dry DCE and added dropwise to the mixture. The reaction was stirred at 0 °C for 4 days until **1c** was completely consumed. The solvent was removed under reduced a vacuum, and the mixture was purified by silica gel chromatography (EtOAc/petroleum ether = 1:10) to give product **3c** (1.08 g, 60%).

Compound **3c** (1.08 g), 5 mol % TfOH, and 15 mL of DCE were added to a Schlenk tube under air; the reaction was heated to 100 °C in an oil bath and then stirred for 30 min. When the reaction was finished, the solvent was removed under a reduced vacuum. The mixture was purified by silica gel chromatography (EtOAc/petroleum ether = 1:20) to afford the product in 651 mg (92% ee, 64%).

*Typical Procedure for the Synthesis of **8**.* To a solution of **4** (0.1 mmol, 1.0 equiv) in THF (1 mL) was added $NaBH_4$ (0.12 mmol, 1.2eq) in portion. Then MeOH (100 μL) was added dropwise at 0 °C. The mixture was stirred for 5 min and quenched by water. The organic phase was combined and concentrated *in vacuo* to give the desired product **8**. Yield: 84% (24 mg, 0.1 mmol), colorless liquid. R_f = 0.6 (EtOAc/petroleum ether = 1:10). ^{1}H NMR (400 MHz, $CDCl_3$): δ 7.38 (d, *J* = 7.2 Hz, 2H), 7.31 (t, *J* = 7.5 Hz, 2H), 7.23 (t, *J* = 7.2 Hz, 1H), 6.02 (t, *J* = 3.6 Hz, 1H), 5.07 (p, *J* = 6.2 Hz, 1H), 4.52 (d, *J* = 4.4 Hz, 1H), 3.03 (t, *J* = 5.0 Hz, 1H), 2.92−2.77 (m, 1H), 2.44−2.25 (m, 2H), 2.25−2.10 (m, 1H), 2.08−1.94 (m, 1H), 1.94−1.79 (m, 2H), 1.31−1.18 (m, 6H). ^{13}C{^{1}H} NMR (101 MHz, $CDCl_3$): δ 175.9, 140.7, 139.4, 128.4, 127.1, 125.4, 121.2, 75.1, 68.0, 49.2, 43.6, 34.5, 33.0, 29.9, 21.8, 21.8. IR (KBr, cm^{-1}): 3479, 2977, 1722, 1495, 1464, 1373, 1281, 1240, 1240, 763, 696. HRMS (ESI-TOF): *m*/*z* [M + H]$^+$ calcd for $C_{18}H_{23}O_3$, 287.1642; found, 287.1637. HPLC: OD-H column, 99:1 hexanes/isopropanol, 0.10 mL/min, t_R = (major) 7.9 min, (minor) 9.9 min, 91% ee $[\alpha]_D^{31}$ −35.7° (*c* 1.4, EtOAc).

*Typical Procedure for the Synthesis of **9**.* Tributylsilane (0.6 mmol, 3.0 equiv) was added to a solution of DCE/H_2O (10:1, 1 mL), **4c** (0.2 mmol, 1.0 equiv) and $Pd(OAc)_2$ (0.02 equiv) under air. The reaction was stirred at room temperature for 2 h. When the reaction was finished, the mixture was filtered through a short pad of Celite. The filtrate was concentrated and the resulting residue purified by column chromatography. Yield: 80% (38 mg, 2.6:1 dr), colorless liquid.

*Compound **9a** (Major).* R_f = 0.6 (EtOAc/petroleum ether = 1:20). ^{1}H NMR (400 MHz, $CDCl_3$): δ 7.38−7.32 (m, 2H), 7.27 (d, *J* = 6.7 Hz, 3H), 5.12 (hept, *J* = 6.2 Hz, 1H), 3.48−3.28 (m, 1H), 2.71−2.49 (m, 2H), 2.40−2.28 (m, 1H), 2.24−2.10 (m, 2H), 2.06−1.92 (m, 2H), 1.91−1.82 (m, 2H), 1.30 (d, *J* = 6.3 Hz, 6H). ^{13}C{^{1}H} NMR (101 MHz, $CDCl_3$): δ 213.9, 171.0, 141.6, 128.6, 127.2, 126.8, 68.6, 57.4, 52.5, 50.0, 36.1, 27.3, 22.6, 21.8, 21.8, 17.7. IR (KBr, cm^{-1}): 2928, 1750, 1719, 1652, 1400, 1384, 1267, 1175, 1106, 751, 698. HRMS (ESI-TOF): *m*/*z* [M + Na]$^+$ calcd for $C_{18}H_{22}O_3Na$, 287.1642; found, 287.1643. HPLC: OD-H column, 95:5 hexanes/isopropanol, 0.80 mL/min, t_R = (major) 13.4 min, (minor) 12.8 min, 92% $[\alpha]_D^{31}$ −109.8° (*c* 0.41, EtOAc).

*Compound **9b** (Minor).* R_f = 0.5 (EtOAc/petroleum ether = 1:20). ^{1}H NMR (400 MHz, $CDCl_3$): δ 7.34−7.26 (m, 4H), 7.23−7.17 (m, 1H), 5.06 (hept, *J* = 6.2 Hz, 1H), 3.50−3.34 (m, 1H), 2.75−2.53 (m, 3H), 2.44−2.19 (m, 2H), 2.18−2.00 (m, 3H), 1.98−1.88 (m, 1H), 1.26−1.22 (m, 6H). ^{13}C{^{1}H} NMR (101 MHz, $CDCl_3$): δ 212.4,

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171.0, 142.4, 128.5, 127.1, 126.5, 68.6, 56.8, 52.3, 50.6, 35.8, 26.4, 23.0, 22.7, 21.8, 21.8. IR (KBr, cm-1) 2926, 1749, 1719, 1452, 1384, 1274, 1237, 1207, 1179, 1101, 1042, 698, 635. HRMS (ESI-TOF): m/z $[M + Na]^+$ calcd for $C_{18}H_{22}O_3Na$, 287.1642; found, 287.1639. HPLC: OD-H column, 95:5 hexanes/isopropanol, 0.80 mL/min, t_R = (major) 11.5 min, (minor) 14.8 min, 92% $[\alpha]_D^{26}$ +30.73° (c 0.41, EtOAc).

Typical Procedure for the Synthesis of ***10****.* At 0 °C, potassium tert-butoxide (0.4 mmol, 2.0 equiv) was added in portion to the suspention of methyltriphenylphosphonium bromide (0.4 mmol, 2.0 equiv) in 2 mL dry THF in a 25 mL Schlenk tube and stirred for 1 h. **4c** (0.2 mmol, 1.0 equiv) was dissolved in 0.5 mL THF and added to the stirred mixture dropwise at −20 °C and then warmed to room temperature slowly. The reaction was quenched by H_2O after stirred for 12 h. The organic phase was collected and washed with brine (3 × 5 mL). The mixture was purified by silica gel chromatography (EtOAc/petroleum ether = 1:30) to afford **10** as a yellow solid (33 mg, 58%), mp = 48−49 °C. ^{1}H NMR (400 MHz, $CDCl_3$): δ 7.42 (d, J = 7.7 Hz, 2H), 7.36 (t, J = 7.5 Hz, 2H), 7.31−7.25 (m, 1H), 5.84 (t, J = 3.6 Hz, 1H), 5.27−5.11 (m, 1H), 4.93 (s, 1H), 4.76 (s, 1H), 3.41 (d, J = 4.7 Hz, 1H), 3.09 (d, J = 17.8 Hz, 1H), 2.66−2.44 (m, 2H), 2.21−2.07 (m, 2H), 2.03−1.88 (m, 1H), 1.40−1.28 (m, 6H). ^{13}C{^{1}H} NMR (101 MHz, $CDCl_3$): δ 174.1, 153.7, 144.0, 140.1, 128.4, 127.0, 125.2, 120.2, 100.7, 68.0, 52.4, 47.5, 42.7, 34.7, 33.8, 21.9, 21.8. IR (KBr, cm^{-1}): 3025, 2979, 1222, 1493, 1447, 1350, 1274, 1243, 118, 1108, 894, 759. HRMS (ESI-TOF): m/z $[M + H]^+$ calcd for $C_{20}H_{23}O_3$, 283.1693; found, 283.1702. HPLC: IA column, 99:1 hexanes/isopropanol, 0.60 mL/min, t_R = (major) 6.9 min, (minor) 8.4 min, 92% ee. $[\alpha]_D^{22}$ +36.1° (c 0.41, DCM).

Typical Procedure for the Synthesis of ***11****.* A mixture of **10** (0.1 mmol, 1.0eq) and 1 mL NaOH (2N)/THF/MeOH (2:1:2) was added to a 25 mL Schlenk tube, the tube was sealed and the reaction was heated to 90 °C in oil bath overnight. The solution was quenched by HCl (2M) and extracted with EtOAc (3 × 1 mL). The combined organic phases were washed with brine (2 mL), dried over Na_2SO_4, and concentrated under vacuum to give the white solid which was used without further purification. To a solution of the white solid in CH_3CN (0.5 mL), $Cu(OAc)_2$ (0.05 equiv) and DMAP (0.1 equiv) was added azidoformate (0.12 mmol, 1.2 equiv) which was dissolved in 0.5 mL CH_3CN. The tube was sealed and stirred under 80 °C in oil bath for 8 h. The reaction was monitored by TLC. When the reaction was finished, the solvent was removed and the residue was purified by silica gel chromatography. Yield: 63% (20 mg, 0.1 mmol), white solid, mp = 117−120 °C R_f = 0.7 (EtOAc/petroleum ether = 1:10). ^{1}H NMR (400 MHz, $CDCl_3$): δ 7.42 (d, J = 7.3 Hz, 2H), 7.36 (t, J = 7.5 Hz, 2H), 7.31−7.28 (m, 1H), 5.83 (t, J = 3.7 Hz, 1H), 5.30 (s, 1H), 4.96 (s, 1H), 4.84 (d, J = 11.7 Hz, 1H), 4.74 (s, 2H), 3.47 (d, J = 5.6 Hz, 1H), 3.01 (d, J = 14.1 Hz, 1H), 2.66 (d, J = 16.8 Hz, 1H), 2.39−2.32 (m, 1H), 2.32−2.24 (m, 1H), 2.24−2.10 (m, 1H), 2.10−2.01 (m, 1H). ^{13}C{^{1}H} NMR (101 MHz, $CDCl_3$): δ 153.3, 152.9, 144.4, 139.6, 128.5, 127.2, 125.2, 119.7, 98.2, 95.8, 74.2, 60.3, 46.1, 45.6, 35.1, 32.5. IR (KBr, cm-1) 3346, 2951, 1749, 1501, 1235, 1214, 1148, 1114, 1038, 817, 757, 730, 695. HRMS (ESI-TOF): m/z $[M + H]^+$ calcd for $C_{18}H_{19}C_{l3}NO_2$, 386.0476; found, 386.0473. HPLC: OD-H column, 99:1 hexanes/isopropanol, 1 mL/min, t_R = (major) 14.0 min, (minor) 16.0 min, 92% ee $[\alpha]_D^{31}$ +27.5° (c 0.56, EtOAc).

Typical Procedure for the Synthesis of ***12****.* To a 25 mL Schlenk tube charge with a magnetic stir bar was added **7a** (0.1 mmol, 1.0 equiv), benzoquinone (0.3 mmol, 3.0 equiv), zinc iodide (0.05 mmol, 0.5 equiv) and 1 mL toluene. The reaction was stirred at 80 °C in oil bath overnight. Then the mixture was filtered with a short pad of silica gel, the solvent was evaporated. The residue was purified by flash chromatography to afford the product as brown solid (50%, 21 mg). mp = 78−90 °C. ^{1}H NMR (500 MHz, $CDCl_3$): δ 7.26 (d, J = 7.2 Hz, 2H), 7.18 (t, J = 7.3 Hz, 1H), 7.11 (d, J = 7.5 Hz, 2H), 6.74 (d, J = 10.0 Hz, 1H), 6.62 (d, J = 10.1 Hz, 1H), 5.59 (d, J = 3.9 Hz, 1H), 5.15−5.02 (m, 1H), 4.62 (t, J = 4.9 Hz, 1H), 3.92−3.77 (m, 1H), 3.06 (d, J = 6.6 Hz, 1H), 2.89 (dd, J = 12.7, 5.6 Hz, 1H), 2.72 (td, J = 13.3, 4.5 Hz, 1H), 2.43−2.31 (m, 1H), 2.27−2.14 (m, 1H), 2.10−1.92 (m, 2H), 1.28 (d, J = 6.3 Hz, 6H). ^{13}C{^{1}H} NMR (126 MHz, $CDCl_3$): δ 208.2, 186.8, 185.7, 170.1, 142.0, 141.3, 139.9, 136.5, 136.4, 135.3, 128.8, 128.6, 127.1, 122.1, 69.1, 58.3, 54.9, 42.7, 41.7, 31.0, 27.1, 21.8, 21.8, 21.5. IR (KBr, cm^{-1}): 2979, 1758, 1722, 1656, 1451, 1295, 1270, 1106, 735, 701. HRMS (ESI-TOF): m/z $[M + H]^+$ calcd for $C_{26}H_{25}O_5Na$, 439.1516; found, 439.1514. HPLC: OD-H column, 90:10 hexanes/isopropanol, 0.80 mL/min, t_R = (major) 24.9 min, (minor) 56.9 min, 93% ee. $[\alpha]_D^{23}$ −28.6° (c 0.05, DCM).

■ ASSOCIATED CONTENT

Supporting Information

X-ray crystallographic data (ORTEP diagrams) of product **4k** (CCDC: 2042797) along with its important crystal data, table of experimental conditions for optimization studies, asymmetric induction model, HPLC traces for all products of this paper, ^{1}H NMR, ^{13}C{^{1}H} NMR spectra for all the new compounds and NOE spectra for **8**, **9**, **12** (PDF). The Supporting Information is available free of charge at https://pubs.acs.org/doi/10.1021/acs.joc.1c00146.

(PDF)

Accession Codes

CCDC 2042797 contains the supplementary crystallographic data for this paper. These data can be obtained free of charge via www.ccdc.cam.ac.uk/data_request/cif, or by emailing data_request@ccdc.cam.ac.uk, or by contacting The Cambridge Crystallographic Data Centre, 12 Union Road, Cambridge CB2 1EZ, UK; fax: +44 1223 336033.

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Notes

The authors declare no competing financial interest.

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