Stereodivergency of Triazolium and Imidazolium-Derived N-Heterocyclic Carbenes for Catalytic, Enantioselective Cyclopentane Synthesis

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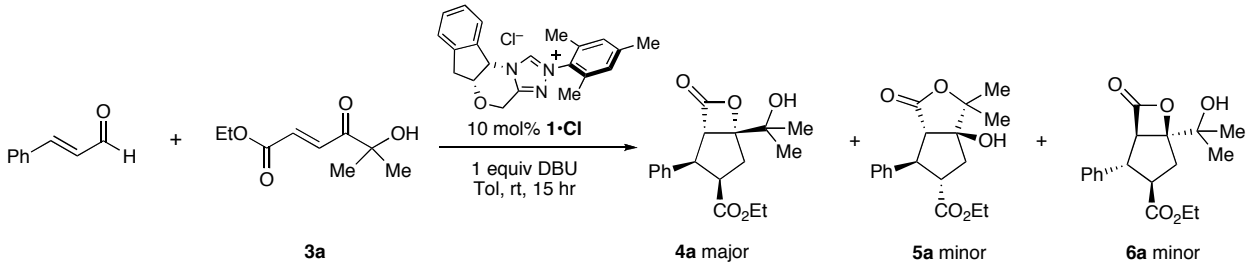
Supporting Information

General Methods. All reactions utilizing air- or moisture-sensitive reagents were performed in dried glassware under an atmosphere of dry Ar. Dichloromethane (CH_2Cl_2) was distilled over CaH_2; EtOH was distilled over Na. THF and toluene were dried by passage over activated alumina under an Ar atmosphere. Cinnamaldehyde, *trans*-2-hexene-1-al, and 1,8-diazabicyclo[5.4.0]undec-7-ene (DBU) were purified by vacuum distillation prior to use. *Trans*-3-(2-furyl)acrolein was purified by sublimation. Other reagents were used without further purification. Thin layer chromatography (TLC) was performed on Merck precoated plates (silica gel 60 F_{254}, Art 5715, 0.25 mm) and were visualized by fluorescence quenching under UV light or by staining with phosphomolybdic acid. Silica-gel preparative thin-layer chromatography (PTLC) was performed using plates prepared from Merck Kieselgel 60 PF_{254} (Art 7747). Flash column chromatography was performed on E. Merck Silica Gel 60 (230–400 Mesh) using a forced flow of 0.5–1.0 bar. ^{1}H NMR and ^{13}C NMR were measured on a Varian Unity 400 spectrometer 400 MHz, 100 MHz or on Bruker Avance II 500 MHz, 125 MHz respectively. Chemical shifts are expressed in parts per million (ppm) downfield from residual solvent peaks and coupling constants are reported as Hertz (Hz). Splitting patterns are indicated as follows: br, broad; s, singlet; d, doublet; ad, approximate doublet; t, triplet; q, quartet; m, multiplet; asterisks (*) indicate peaks arising from the minor diastereomers. Infrared (IR) spectra were recorded on a JASCO FT:IR-430 spectrophotometer and are reported as wavenumber (cm^{-1}). Optical rotations were measured on a JASCO DIP-1000 polarimeter or JASCO DIP-370 polarimeter operating at the sodium D line with a 100 mm path length cell, and were reported as follows: $[\alpha]_D^T$ (concentration (g:100 ml), solvent).

SFC Conditions. Column, Diacel Chiralpak AS-H (4.6 × 250 mm), Diacel Chiralpak AD-H (4.6 x 250 mm), Diacel Chiralpak OJ-H (4.6 x 250 mm); eluent: CO_2: *i*PrOH; oven temperature: 50 ^oC; pressure 100 bar; flow rate 2.0 mL/min; detection: 254 nm.

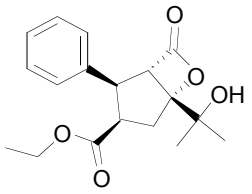
General procedure for using Chiral Triazolium as catalyst



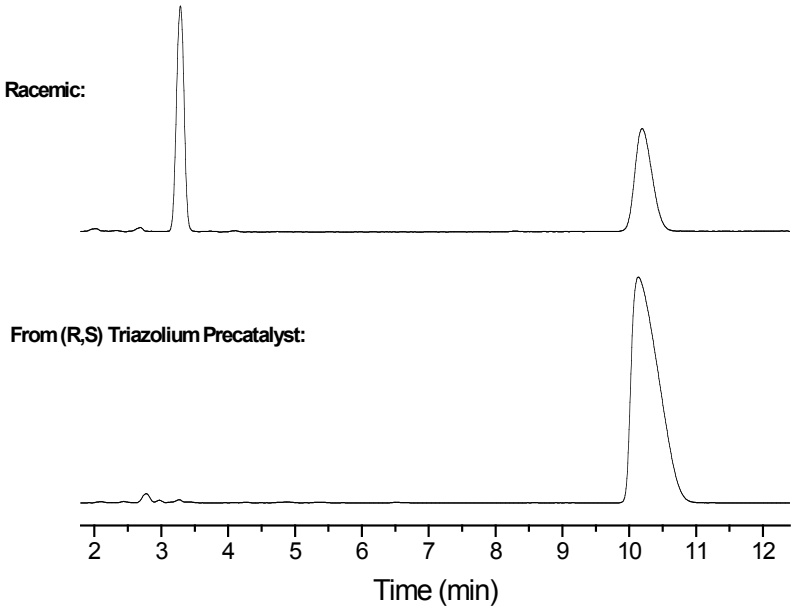
The reaction of *trans*-ethyl-4-oxo-5-hydroxy-5-methylhex-2-enoate and cinnamaldehyde is representative: Into an oven dried 10.0 mL round bottom flask was added **3a** (43 mg, 0.23 mmol, 1.0 equiv) and triazolium precatalyst **1•Cl** (8.2 mg, 0.020 mmol, 0.10 equiv). The flask was sealed with a septum and 2.3 mL toluene (0.1 M) and cinnamaldehyde (58 μL, 0.46 mmol, 2.0 equiv) were added via syringe. The solution was stirred at –10 ^oC for 15 min before DBU (23 μL, 0.23 mmol, 1.0 equiv) was added. The resulting solution was allowed to warm to rt and stirred 16 h before it was diluted with 2.0 mL EtOAc and poured into 4.0 mL H_2O. The mixture was extracted with 3 x 4.0 mL EtOAc. The combined organic extracts were washed with 10.0 mL brine and dried over Na_2SO_4. After filtration and concentration, the residue was purified by flash chromatography (4:1 hexane: EtOAc) to give **4a** as a colorless oil (47.6 mg, 65%) and a mixture of fractions containing **5a** and **6a**. These mixed fractions were further purified by preparative TLC (2:2:1 hexane: CH_2Cl_2: EtOAc) to give **5a** (15.3 mg, 21%) as a white solid and **6a** (6.5 mg, 9%) as a colorless oil.

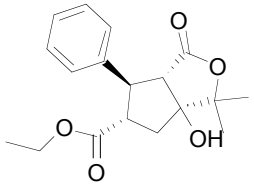
Racemic standards of the chiral *β*-lactone products were prepared by the use of 2-mesityl-6,7-dihydro-5H-pyrrolo[2,1-c][1,2,4]triazol-2-ium chloride[1] as the catalyst. In most of cases, this catalyst was less efficient in terms of chemical yield than the chiral triazolium salts. Racemic standards of **5a** and **6a** could be prepared by the mixture of products obtained from (*R,S*) triazolium (**1•Cl**) and (*S,R*) triazolium (***ent*-1•Cl**) precatalysts.

(1) Sohn. S. S.; Bode. J. W. *Org. Lett.* **2005**, *7*, 3873–3876.

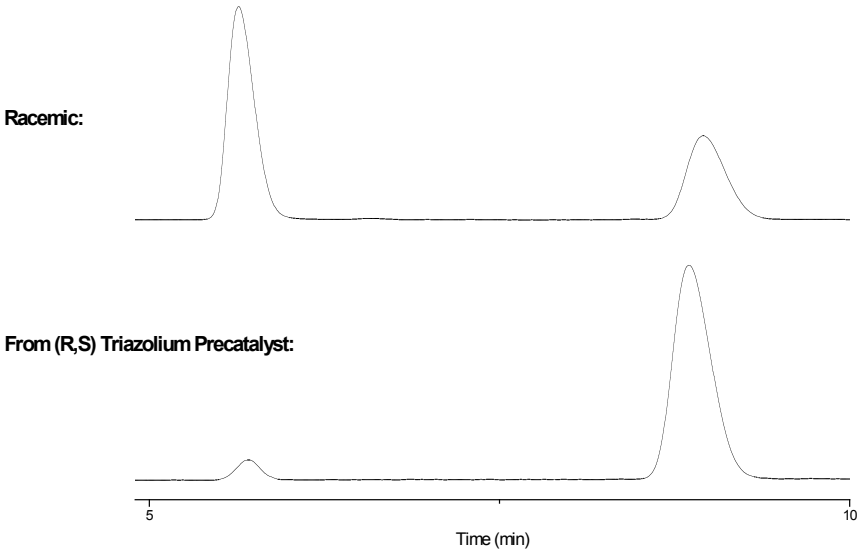


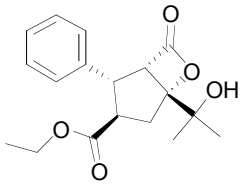
(*1S,2R,3R,5R*)-ethyl-5-(2-hydroxypropan-2-yl)-7-oxo-2-phenyl-6-oxabicyclo[3.2.0] heptane-3-carboxylate *(Table 1, entry 1,* **4a***)*. Prepared according to general procedure from cinnmaldehyde and *trans*-ethyl-4-oxo-5-hydroxy-5-methylhex-2-enoate using 10 mol % **1** as the catalyst in 65% yield as a colorless oil. $[\alpha]_D^{20}$ (c 0.85, $CHCl_3$): +20.1; ^1H NMR (400 MHz, $CDCl_3$) δ 7.25–7.23 (m, 2H), 7.22–7.19 (m, 2H), 3.85 (d, 1H, J = 8.0 Hz), 3.92–3.79 (m, 3H), 3.72–3.66 (m, 1H), 2.72 (dd, 1H, J = 15.2, 12.4 Hz), 2.34 (dd, 1H, J = 15.2, 7.2 Hz), 1.45 (s, 3H), 1.38 (s, 3H), 0.95 (t, 3H, J = 7.2 Hz); ^{13}C NMR (100 MHz, $CDCl_3$) δ 171.2, 169.9, 139.1, 128.7, 128.0, 127.6, 94.5, 71.4, 61.7, 60.9, 48.3, 47.5, 31.8, 25.5, 14.0; IR (thin film) ν 3500, 2981, 2359, 1824, 1732, 1375, 1207, 810, 702 cm^{-1}; HRMS (ESI) $[M+Na]^+$ calcd. for $C_{18}H_{22}O_5$ 341.1365, found, 341.1352; 99% *ee* as determined by SFC (AD-H, 15% *i*-PrOH in CO_2) t_r = 3.3 and 10.1 min.



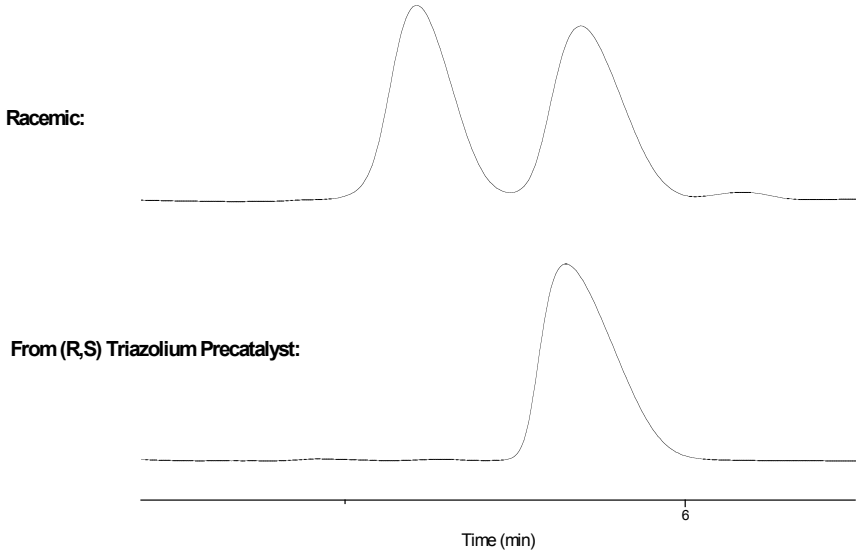


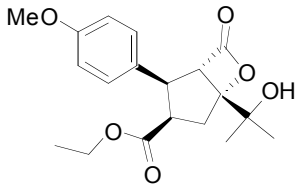
(*3aS,4R,5S,6aS*)-ethyl-6a-hydroxy-1,1-dimethyl-3-oxo-4-phenylhexahydro-1H-cyclopenta[c]furan-5-carboxylate *(Table 1, entry 1,* **5a***)*. 21% yield as a white solid. ^{1}H NMR (400 MHz, $CDCl_3$) δ 7.39–7.30 (m, 3H), 7.25–7.22 (m, 1H), 4.13–4.05 (m, 2H), 3.80 (dd, 1H, *J* = 10.0, 4.4 Hz), 3.49–3.41 (m, 1H), 3.07 (dd, 1H, *J* = 4.4, 2.4 Hz), 2.30–2.20 (m, 1H), 2.18–2.11 (m, 1H), 1.46 (s, 3H), 1.46 (s, 3H), 1.20 (t, *J* = 7.2 Hz); ^{13}C NMR (100 MHz, $CDCl_3$) δ 176.5, 173.5, 143.0, 128.9, 127.8, 127.1, 88.0, 85.4, 61.2, 59.0, 53.2, 51.1, 40.4, 24.7, 21.5, 14.3; IR (thin film) ν 3442, 2981, 1736, 1279, 1176, 702, 526 cm^{-1}; HRMS (ESI) $[M+Na]^+$ calcd. for $C_{18}H_{22}O_5$ 341.1365, found, 341.1358; 88% *ee* determined by SFC (OJ-H, 10% *i*-PrOH in CO_2) t_r = 5.7 and 8.8 min.



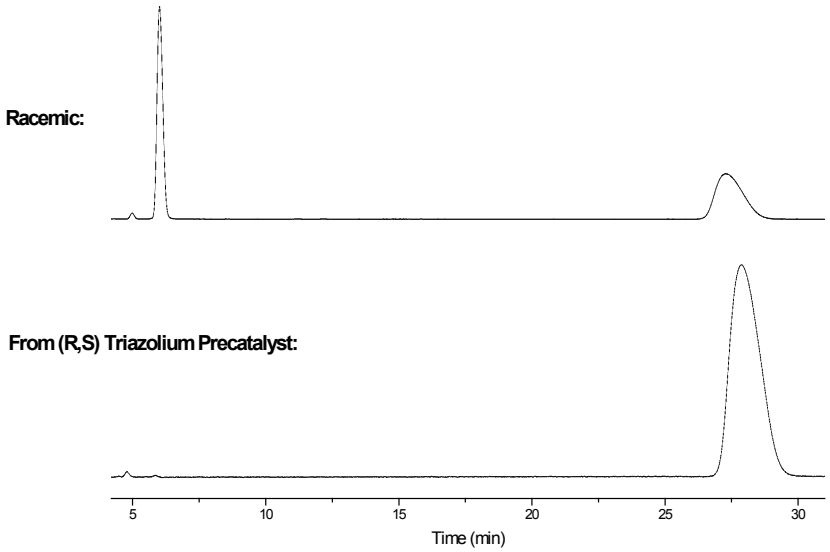


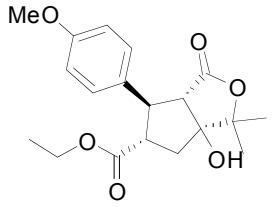
(*1S,2S,3R,5R*)-ethyl-5-(2-hydroxypropan-2-yl)-7-oxo-2-phenyl-6-oxabicyclo[3.2.0] heptane-3-carboxylate *(Table 1, entry 1,* **6a***)***.** 9% yield as a colorless oil. ^{1}H NMR (400 MHz, $CDCl_3$) δ 7.33–7.26 (m, 4H), 4.10–4.02 (m, 2H), 4.01 (d, 1H, *J* = 7.6 Hz), 3.56 (dd, 1H, *J* = 12.0, 7.6 Hz), 3.48–3.40 (m, 1H), 2.51 (dd, 1H, *J* = 14.4, 6.4 Hz), 2.20 (dd, 1H, *J* = 14.4, 11.2 Hz), 1.38 (s, 3H), 1.47 (s, 3H), 1.10 (t, *J* = 7.2 Hz); ^{13}C NMR (100 MHz, $CDCl_3$) δ 172.9, 168.1, 135.3, 128.8, 128.1, 128.0, 92.0, 71.2, 61.3, 59.8, 50.0, 46.8, 35.4, 25.1, 24.7, 14.2; IR (thin film) ν 3481, 2981, 1820, 1730, 1182, 1140, 820, 698 cm^{-1}; HRMS (ESI) $[M+Na]^+$ calcd. for $C_{18}H_{22}O_5$ 341.1365, found, 341.1370; 99% *ee* determined by SFC (OJ-H, 15% *i*-PrOH in CO_2) t_r = 5.3 and 5.6 min.



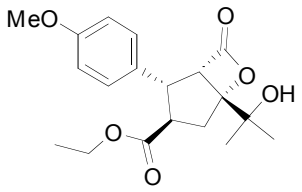


(*1S,2R,3R,5R*)-ethyl-5-(2-hydroxypropan-2-yl)-2-(4-methoxyphenyl)-7-oxo-6-oxabicyclo[3.2.0]heptane-3-carboxylate *(Table 1, entry 2,* **4b***)*. Prepared according to general procedure from 4-methoxycinnamaldehyde and *trans*-ethyl-4-oxo-5-hydroxy-5-methylhex-2-enoate (**3a**) using 10 mol % **1•Cl** as the catalyst in 60% yield as a colorless oil. $[\alpha]_D^{20}$ (c 0.75, $CHCl_3$): +22.4; ^{1}H NMR (400 MHz, $CDCl_3$) δ 7.13 (d, 1H, J = 9.2 Hz), 6.78 (d, 1H, J = 8.8 Hz), 3.93 (d, 1H, J = 8 Hz), 3.92–3.82 (m, 3H), 3.76 (s, 3H), 3.68–3.62 (m, 1H), 2.70 (dd, 1H, J = 14.8, 12.4 Hz), 2.30 (dd, 1H, J = 14.8, 7.2 Hz), 1.44 (s, 3H), 1.38 (s, 3H), 1.00 (t, 3H, J = 7.2 Hz); ^{13}C NMR (100 MHz, $CDCl_3$) δ 171.3, 170.0, 158.9, 131.1, 129.1, 114.0, 94.4, 71.5, 61.8, 60.9, 55.3, 48.3, 46.8, 31.6, 25.5, 14.1; IR (thin film) ν 3498, 2981, 2254, 1822, 1730, 1516, 1252, 910, 814, 735 cm^{-1}; HRMS (ESI) $[M+Na]^+$ calcd. for $C_{19}H_{24}O_6$ 371.1471, found, 371.1465; 99% *ee* as determined by SFC (AD-H, 10% *i*-PrOH in CO_2) t_r = 5.8 and 27.9 min.

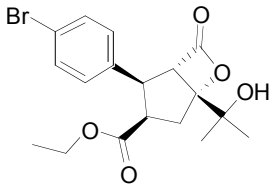




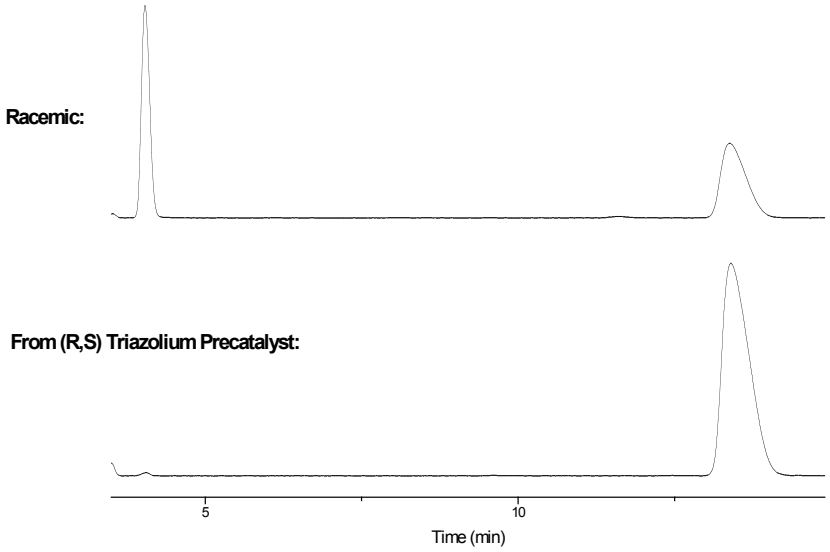
(*3aS,4R,5S,6aS*)-ethyl-6a-hydroxy-4-(4-methoxyphenyl)-1,1-dimethyl-3-oxohexahydro-1H-cyclopenta[c]furan-5-carboxylate *(Table 1, entry 2,* **5b***)*. 20% yield as a white solid. ^{1}H NMR (400 MHz, $CDCl_3$) δ 7.28 (d, 2H, *J* = 8.4 Hz), 6.85 (d, 2H, *J* = 8.8 Hz), 4.12–4.05 (m, 2H), 3.79 (s, 3H), 3.74 (dd, 1H, *J* = 10.4, 4.0 Hz), 3.43–3.36 (m, 1H), 3.02 (dd, 1H, *J* = 4.0, 2.4 Hz), 2.62–2.20 (m, 2H), 2.14 (ddd, 1H, *J* = 13.6, 6.0, 2.4 Hz), 1.45 (s, 3H), 1.44 (s, 3H), 1.18 (t, 3H, *J* = 7.2 Hz); ^{13}C NMR (100 MHz, $CDCl_3$) δ 176.0, 173.4, 158.7, 135.2, 128.9, 114.3, 88.1, 85.0, 61.1, 59.2, 55.5, 53.2, 50.5, 40.4, 24.7, 21.5, 14.3; IR (thin film) ν 3458, 2981, 1739, 1514, 1252, 1034, 831 cm^{-1}; HRMS (ESI) $[M+Na]^+$ calcd. for $C_{19}H_{24}O_6$ 371.1471, found, 371.1468.

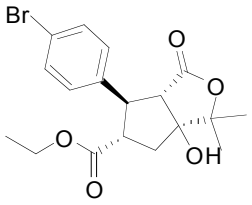


(*1S,2S,3R,5R*)-ethyl-5-(2-hydroxypropan-2-yl)-2-(4-methoxyphenyl)-7-oxo-6-oxabicyclo[3.2.0]heptane-3-carboxylate *(Table 1, entry 2,* **6b***)*. 10% yield as a colorless oil. ^{1}H NMR (400 MHz, $CDCl_3$) δ 7.22 Hz), 3.79 (s, 3H), 3.51 (dd, 1H, *J* = 12.4, 7.6 Hz), 3.42–3.34 (m, 1H), 2.49 (dd, 1H, *J* = 14.4, 11.6 Hz), 1.38 (s, 3H), 1.36 (s, 3H), 1.11 (t, 3H, *J* = 7.2 Hz); ^{13}C NMR (100 MHz, $CDCl_3$) δ 173.0, 168.3, 159.2, 129.2, 127.2, 114.1, 92.0, 71.2, 61.3, 59.8, 55.4, 49.4, 47.1, 35.4, 25.1, 24.7, 14.2; IR (thin film) ν 3502, 2979, 1819, 1730, 1516, 1250, 1182, 1034, 827 cm^{-1}; HRMS (ESI) $[M+Na]^+$ calcd. for $C_{19}H_{24}O_6$ 371.1471, found, 371.1465.

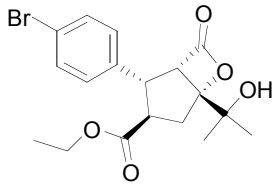


(*1S,2R,3R,5R*)-ethyl-2-(4-bromophenyl)-5-(2-hydroxypropan-2-yl)-7-oxo-6-oxabicyclo[3.2.0]heptane-3-carboxylate *(Table 1, entry 3,* **4c***)*. Prepared according to general procedure from 4-bromocinnamaldehyde and *trans*-ethyl-4-oxo-5-hydroxy-5-methylhex-2-enoate (**3a**) using 10 mol % **1** as the catalyst in 62% yield as a colorless oil. $[\alpha]_D^{20}$ (c 0.95, $CHCl_3$): +25.8; ^{1}H NMR (400 MHz, $CDCl_3$) δ 7.39 (d, 2H, *J* = 8.4 Hz), 7.12 (d, 2H, *J* = 8.4 Hz), 3.94–3.89 (m, 2H), 3.88–3.82 (m, 2H), 3.70–3.63 (m, 1H), 2.69 (dd, 1H, *J* = 14.8, 12.8 Hz), 2.32 (dd, 1H, *J* = 14.8, 7.2 Hz), 1.44 (s, 3H), 1.37 (s, 3H), 1.00 (t, 3H, *J* = 7.2 Hz); ^{13}C NMR (100 MHz, $CDCl_3$) δ 171.0, 169.6, 138.1, 131.8, 129.8, 121.7, 94.2, 71.4, 61.5, 61.1, 48.2, 46.9, 31.5, 25.6, 25.5, 14.1; IR (thin film) ν 3500, 2981, 1824, 1732, 1207, 816, 756 cm^{-1}; HRMS (ESI) $[M+Na]^+$ calcd. for $C_{18}H_{21}BrO_5$ 419.0470, found, 419.0462; 99% *ee* as determined by SFC (AD-H, 15% *i*-PrOH in CO_2) t_r = 4.0 and 13.4 min.

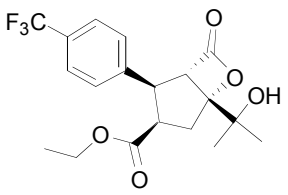




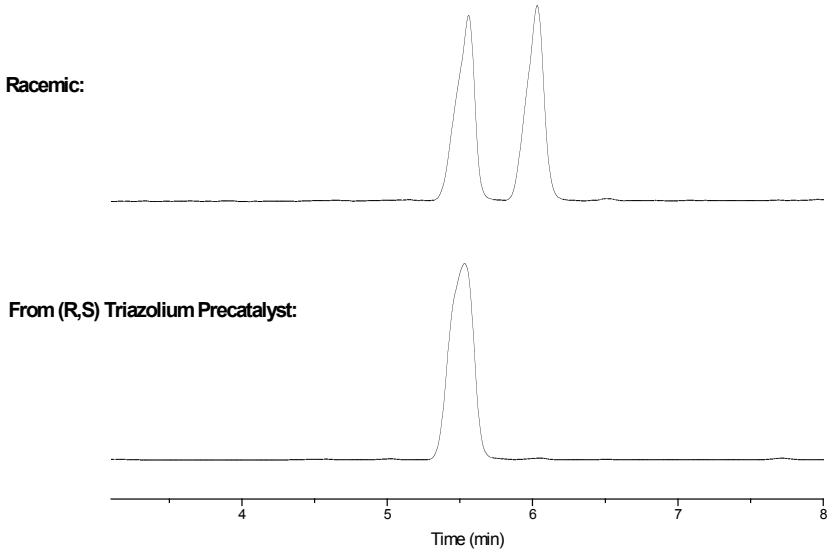
(*3aS,4R,5S,6aS*)-ethyl-4-(4-bromophenyl)-6a-hydroxy-1,1-dimethyl-3-oxohexahydro-1H-cyclopenta[c]furan-5-carboxylate *(Table 1, entry 3,* **5c***)*. 18% yield as a white solid. ^{1}H NMR (400 MHz, $CDCl_3$) δ 7.45 (d, 2H, *J* = 8.8 Hz), 7.26 (d, 2H, *J* = 8.8 Hz), 4.14–4.06 (m, 2H), 3.75 (dd, 1H, *J* = 10.0, 4.4 Hz), 3.43–3.36 (m, 1H), 3.02 (dd, 1H, *J* = 4.4, 2.4 Hz), 3.43–3.36 (m, 1H), 3.02 (dd, 1H, *J* = 4.4, 2.4 Hz), 2.29–2.14 (m, 2H), 1.48 (s, 3H), 1.46 (s, 3H), 1.19 (t, 3H, *J* = 7.2 Hz); ^{13}C NMR (100 MHz, $CDCl_3$) δ 175.7, 173.0, 142.2, 132.0, 129.7, 121.1, 88.1, 85.1, 61.3, 59.0, 53.1, 50.5, 40.4, 24.7, 21.6, 14.3; IR (thin film) ν 3446, 2981, 1738, 1280, 1252, 825, 732 cm^{-1}; HRMS (ESI) $[M+Na]^+$ calcd. for $C_{18}H_{21}BrO_5$ 419.0470, found, 419.0474.

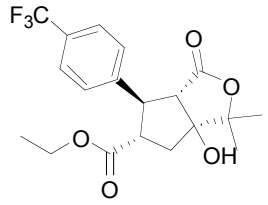


(*1S,2S,3R,5R*)-ethyl-2-(4-bromophenyl)-5-(2-hydroxypropan-2-yl)-7-oxo-6-oxabicyclo[3.2.0]heptane-3-carboxylate *(Table 1, entry 3,* **6c***)*. 11% yield as a colorless oil. ^{1}H NMR (400 MHz, $CDCl_3$) δ 7.45 (d, 2H, *J* = 8.4 Hz), 7.18 (d, 2H, *J* = 8.4 Hz), 4.06 (q, 2H, *J* = 7.2 HZ), 3.98 (d, 1H, *J* = 7.6 Hz), 3.50 (dd, 1H, *J* = 12.4 ,7.6 Hz), 3.42–3.35 (m, 1H), 2.51 (dd, 1H, *J* = 14.4, 6.0 Hz), 2.19 (dd, 1H, *J* = 14.4, 11.2 Hz), 1.38 (s, 3H), 1.36 (s, 3H), 1.12 (t, 3H, *J* = 7.2 Hz); ^{13}C NMR (100 MHz, $CDCl_3$) δ 172.7, 167.9, 134.4, 131.9, 129.9, 122.0, 92.0, 71.2, 61.4, 59.5, 49.3, 46.9, 35.4, 25.1, 24.7, 14.2; IR (thin film) ν 3494, 2981, 1819, 1730, 1184, 823, 737 cm^{-1}; HRMS (ESI) $[M+Na]^+$ calcd. for $C_{18}H_{21}BrO_5$ 419.0470, found, 419.0474.

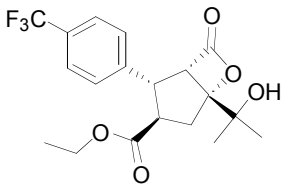


(*1S,2R,3R,5R*)-ethyl-5-(2-hydroxypropan-2-yl)-7-oxo-2-(4-(trifluoromethyl)phenyl)-6-oxabicyclo[3.2.0]heptane-3-carboxylate *(Table 1, entry 4,* **4d***)*. Prepared according to general procedure from (*E*)-3-(4-(trifluoromethyl)phenyl)acrylaldehyde and *trans*-ethyl-4-oxo-5-hydroxy-5-methylhex-2-enoate (**3a**) using 10 mol % **1•Cl** as the catalyst in 35% yield as a colorless oil. $[\alpha]_D^{20}$ (c 1.50, $CHCl_3$): +19.4; ^{1}H NMR (400 MHz, $CDCl_3$) δ 7.53 (d, 2H, *J* = 8.4 Hz), 7.38 (d, 2H, *J* = 8.0 Hz), 4.03 (d, 1H, *J* = 8.4 Hz), 3.92–3.81 (m, 3H), 3.75–3.68 (m, 1H), 2.73 (dd, 1H, *J* = 15.2, 12.4 Hz), 2.36 (dd, 1H, *J* = 15.2, 7.2 Hz), 1.46 (s, 3H), 1.39 (s, 3H), 0.96 (t, 3H, *J* = 7.2 Hz); ^{13}C NMR (100 MHz, $CDCl_3$) δ 170.8, 169.3, 128.5, 125.7, 125.6, 94.1, 71.6, 61.5, 61.2, 48.3, 47.2, 31.7, 25.7, 25.6, 14.0; IR (thin film) ν 3500, 2983, 1824, 1732, 1329, 1120, 825, 758 cm^{-1}; HRMS (ESI) $[M+Na]^+$ calcd. for $C_{19}H_{21}F_3O_5$ 409.1239, found, 409.1232; 99% *ee* as determined by SFC (AS-H, gradient 1%–25% *i*-PrOH in CO_2, rate 2%/min) t_r = 5.5 and 6.0 min.

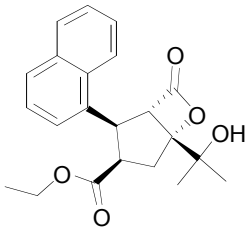




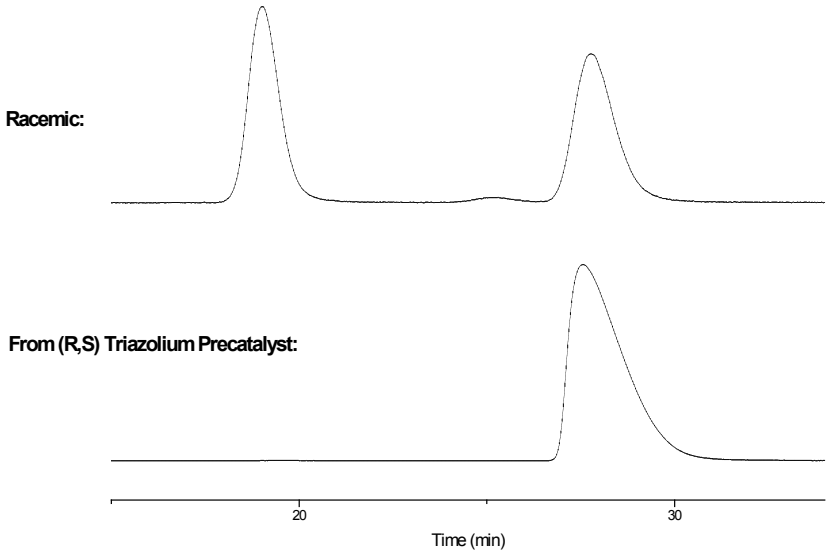
(*3aS,4R,5S,6aS*)-ethyl-6a-hydroxy-1,1-dimethyl-3-oxo-4-(4-(trifluoromethyl)phenyl) hexahydro-1H-cyclopenta[c]furan-5-carboxylate *(Table 1, entry 4,* **5d***)*. 23% yield as a white solid. ^{1}H NMR (400 MHz, $CDCl_3$) δ 7.59 (d, 2H, *J* = 8.4 Hz), 7.52 (d, 2H, *J* = 8.4 Hz), 4.15–4.07 (m, 2H), 3.86 (dd, 1H, *J* = 10.0, 4.4 Hz), 3.49–3.42 (m, 1H), 3.06 (dd, 1H, *J* = 4.4, 2.4 Hz), 2.32–2.22 (m, 1H), 2.20 (ddd, *J* = 13.2, 6.4, 2.4 Hz), 1.48 (s, 3H), 1.47 (s, 3H), 1.20 (t, 3H, *J* = 7.2 Hz); ^{13}C NMR (100 MHz, $CDCl_3$) δ 175.6, 172.9, 147.1, 129.3, 128.3, 126.0, 125.9, 88.2, 85.2, 61.4, 58.9, 53.1, 50.6, 40.5, 24.7, 21.6, 14.3; IR (thin film) ν 3452, 2985, 1739, 1620, 1327, 1119, 839, 735 cm^{-1}; HRMS (ESI) $[M+Na]^+$ calcd. for $C_{19}H_{21}F_3O_5$ 409.1239, found, 409.1243.

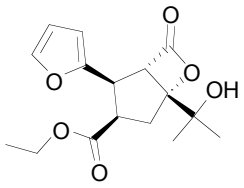


(*1S,2S,3R,5R*)-ethyl-5-(2-hydroxypropan-2-yl)-7-oxo-2-(4-(trifluoromethyl)phenyl)-6-oxabicyclo[3.2.0]heptane-3-carboxylate *(Table 1, entry 4,* **6d***)*. 31% yield as a colorless oil. ^{1}H NMR (400 MHz, $CDCl_3$) δ 7.59 (d, 2H, *J* = 8.4 Hz), 7.43 (d, 2H, *J* = 8.4 Hz), 4.09–4.02 (m, 3H), 3.61 (dd, 1H, *J* = 12.0, 7.6 Hz), 3.49–3.42 (m, 1H), 2.55 (dd, 1H, *J* = 14.4, 6.4 Hz), 2.35 (dd, 1H, *J* = 14.4, 11.2 Hz), 1.38 (s, 3H), 1.36 (s, 3H), 1.11 (t, 3H, *J* = 7.2 Hz); ^{13}C NMR (100 MHz, $CDCl_3$) δ 172.6, 167.9, 139.6, 128.6, 125.8, 125.7, 92.0, 71.1, 61.5, 59.5, 49.4, 46.8, 35.3, 25.0, 24.7, 14.2; IR (thin film) ν 3498, 2983, 1820, 1730, 1329, 1126, 833, 735 cm^{-1}; HRMS (ESI) $[M+Na]^+$ calcd. for $C_{19}H_{21}F_3O_5$ 409.1239, found, 409.1253.

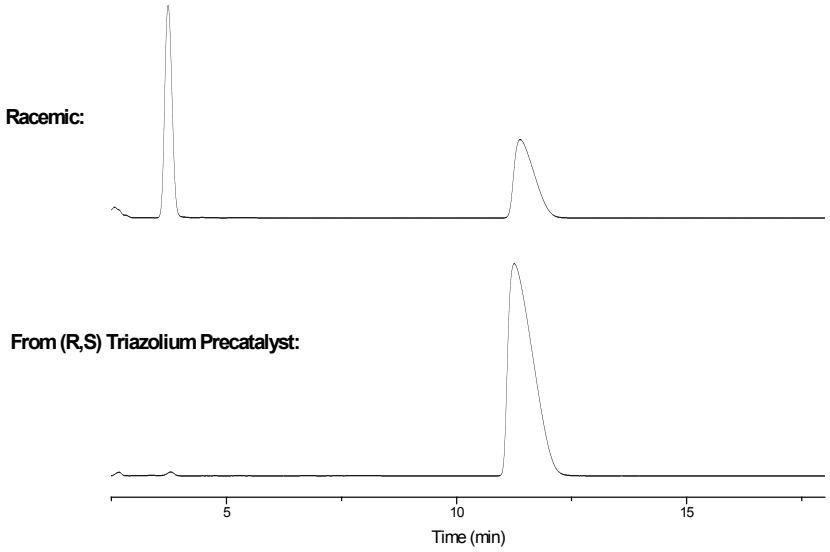


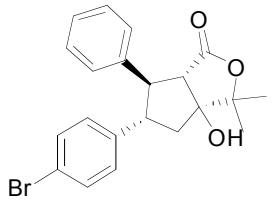
(*1S,2R,3R,5R*)-ethyl-5-(2-hydroxypropan-2-yl)-2-(naphthalen-1-yl)-7-oxo-6-oxabicyclo[3.2.0]heptane-3-carboxylate *(Table 1, entry 5,* **4e***)*. Prepared according to general procedure from 3-(1-napthyl)-propene-2-en-1-al and *trans*-ethyl-4-oxo-5-hydroxy-5-methylhex-2-enoate (**3a**) using 10 mol % **1•Cl** as the catalyst in 45% yield as a colorless oil. $[\alpha]_D^{20}$ (c 1.00, $CHCl_3$): -35.5; ^{1}H NMR (400 MHz, $CDCl_3$) δ 8.13 (d, 1H, *J* = 8.4 Hz), 7.86 (d, 1H, *J* = 8.0 Hz), 7.75–7.32 (m, 1H), 7.61–7.57 (m, 1H), 7.54–7.50 (m, 1H), 7.34–7.32 (m, 1H), 4.87 (d, 1H, *J* = 8.0 Hz), 3.93 (s, 1H), 3.91–3.84 (m, 2H), 3.74–3.70 (m, 1H), 2.83 (dd, 1H, *J* = 15.2, 12.8 Hz), 2.49 (dd, 1H, *J* = 15.2, 7.2 Hz), 1.39 (s, 3H), 1.11 (s, 3H), 0.80 (t, 3H, *J* = 7.2Hz); ^{13}C NMR (100 MHz, $CDCl_3$) δ 171.8, 170.0, 134.6, 134.3, 131.2, 129.3, 128.4, 126.8, 126.1, 125.0, 123.3, 123.1, 94.6, 71.2, 62.4, 61.1, 47.5, 41.8, 32.7, 25.4, 25.1, 13.9; IR (thin film) ν 3502, 2979, 1820, 1730, 1375, 1248, 1223, 800, 781, 733 cm^{-1}; HRMS (ESI) $[M+Na]^+$ calcd. for $C_{22}H_{24}O_5$ 391.1522, found, 391.1504; 99% *ee* as determined by SFC (AD-H, 5% *i*-PrOH in CO_2) t_r = 19.4 and 27.6 min.



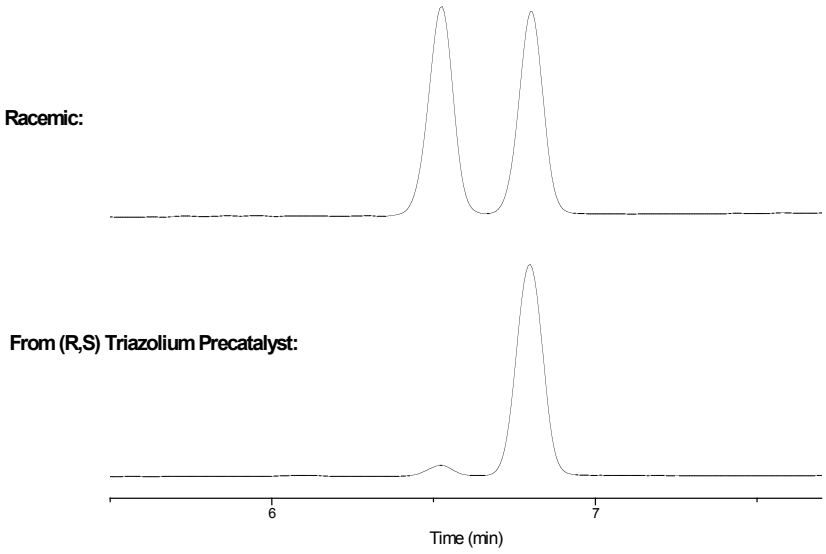


(*1S,2R,3R,5R*)-ethyl-2-(furan-2-yl)-5-(2-hydroxypropan-2-yl)-7-oxo-6-oxabicyclo [3.2.0]heptane-3-carboxylate *(Table 1, entry 6,* **4f***)*. Prepared according to general procedure from *trans*-3-(2-furyl)acrolein and *trans*-ethyl-4-oxo-5-hydroxy-5-methylhex-2-enoate (**3a**) using 10 mol % **1•Cl** as the catalyst in 40% yield as a colorless oil. $[\alpha]_D^{20}$ (c 1.25, $CHCl_3$): +39.6; ^{1}H NMR (400 MHz, $CDCl_3$) δ 7.28 (dd, 1H, *J* = 2.0, 0.8 Hz), 6.27 (dd, 1H, *J* = 3.2, 2.0 Hz), 6.10 (d, 1H, *J* = 3.2 Hz), 4.03 (q, 2H, *J* = 7.2 Hz), 3.96 (s, 1H), 3.54 (dt, 1H, *J* = 12.4, 6.8 Hz), 2.61 (dd, 1H, *J* = 14.8, 12.4 Hz), 2.30 (dd, 1H, *J* = 14.8, 6.8 Hz), 1.41 (s, 3H), 1.33 (s, 3H), 1.13 (t, 3H, *J* = 7.2 Hz); ^{13}C NMR (100 MHz, $CDCl_3$) δ 170.9, 169.1, 151.8, 142.2, 110.5, 107.5, 94.7, 71.5, 61.2, 59.6, 47.3, 40.9, 32.0, 25.5, 24.7, 14.2; IR (thin film) ν 3502, 2981, 1824, 1734, 1201, 1130, 1097, 742, 611 cm^{-1}; HRMS (ESI) $[M+Na]^+$ calcd. for $C_{16}H_{20}O_6$ 331.1158, found, 331.1162; 99% *ee* as determined by SFC (OJ-H, 10% *i*-PrOH in CO_2) t_r = 3.8 and 11.3 min.

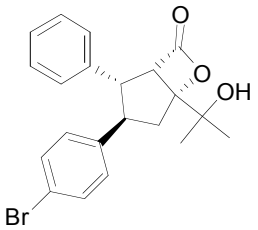




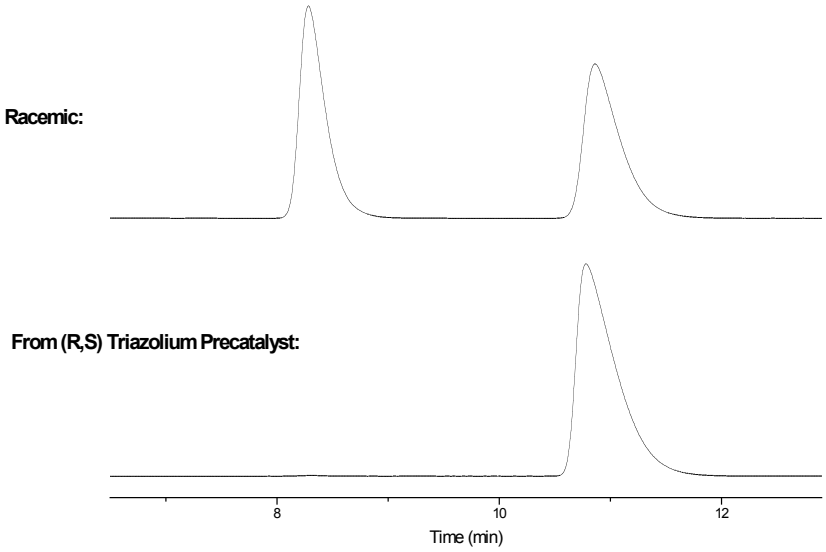
(3aS,5S,6R,6aS)*-5-(4-bromophenyl)-3a-hydroxy-3,3-dimethyl-6-phenylhexahydro-1H-cyclopenta[c]furan-1-one** *(Table 1, entry 7,* **5g)*. Prepared according to general procedure from cinnamaldehyde and 4-hydroxy-1-(4-bromophynyl)-4-methylpent-1-en-3-one[2] (**3b**) using 20 mol % **1•Cl** as the catalyst in 50% yield as a white solid. ^{1}H NMR (400 MHz, $CDCl_3$) δ 7.41–7.40 (m, 2H), 7.30–7.25 (m, 4H), 7.21–7.20 (m, 1H), 7.16–7.14 (m, 2H), 3.81–3.73 (m, 1H), 3.42 (dd, 1H, *J* = 10.0, 4.4 Hz), 3.22 (dd, 1H, *J* = 4.4, 2.4 Hz), 2.32–2.20 (m, 2H), 1.50 (s, 3H), 1.46 (s, 3H); ^{13}C NMR (100 MHz, $CDCl_3$) δ 176.9, 144.6, 142.0, 132.2, 130.4, 129.3, 128.8, 127.3, 120.8, 87.9, 85.8, 59.7, 57.2, 55.0, 44.9, 25.2, 21.9; IR (thin film) ν 3469, 2933, 1739, 1491, 1278, 1074, 752, 700 cm^{-1}; HRMS (ESI) $[M+Na]^+$ calcd. for $C_{21}H_{21}BrO_3$ 423.0572, found, 423.0583; 91% *ee* as determined by SFC (AS-H, 5%–20% *i*-PrOH in CO_2, rate 0.2%/min) *tr* = 6.5 and 6.8 min.

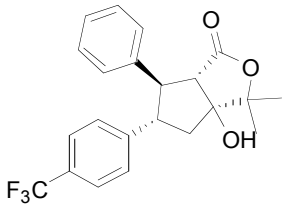


(2) Reiter, M.; Turner, H.; Mills-Webb, R.; Gouverneur, V. *J. Org. Chem.* **2005**, *70*, 8478–8485.

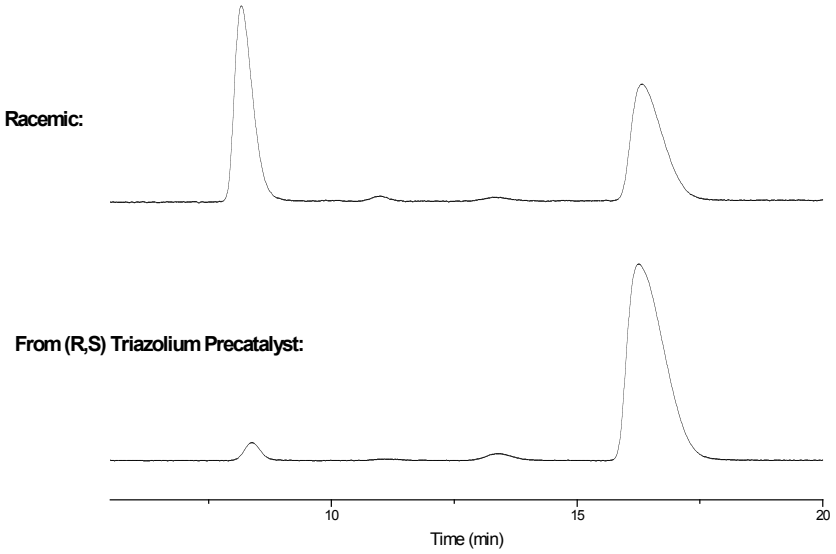


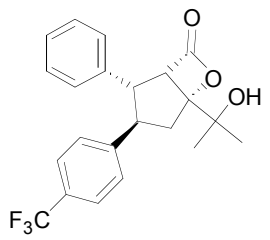
(*1S,2S,3R,5R*)-3-(4-bromophenyl)-5-(2-hydroxypropan-2-yl)-2-phenyl-6-oxabicyclo [3.2.0]heptan-7-one *(Table 1, entry 7,* **6g***)***.** 23% yield as a white solid. ^{1}H NMR (400 MHz, $CDCl_3$) δ 7.36 (d, 2H, *J* = 8.0 Hz), 7.26–7.22 (m, 2H), 7.21–7.18 (m, 3H), 7.06 (d, 2H, *J* = 8.4 Hz), 4.09 (d, 1H, *J* = 7.6 Hz), 3.78–3.70 (m, 1H), 3.42 (dd, 1H, *J* = 12.4, 7.6 Hz), 2.58 (dd, 1H, *J* = 14.4, 6.0 Hz), 2.06 (dd, 1H, *J* = 14.4, 11.6 Hz), 1.40 (s, 3H), 1.39 (s, 3H); ^{13}C NMR (100 MHz, $CDCl_3$) δ 168.6, 138.9, 135.5, 132.0, 129.3, 128.7, 128.3, 127.8, 121.0, 91.4, 71.3, 60.2, 52.2, 46.6, 39.8, 25.1, 24.8; IR (thin film) ν 3446, 2978, 1817, 1491, 1140, 823, 735 cm^{-1}; HRMS (ESI) $[M+Na]^+$ calcd. for $C_{21}H_{21}BrO_3$ 423.0572, found, 423.0567; 99% ee as determined by SFC (AS-H, 15% *i*-PrOH in CO_2) *tr* = 8.3 and 10.8 min.



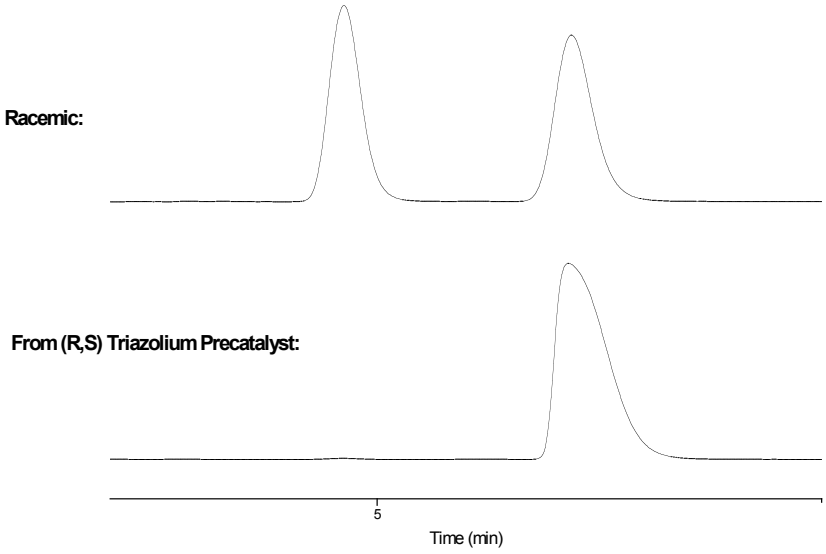


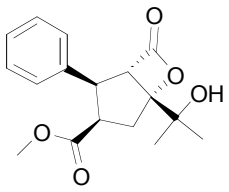
(*3aS,5S,6R,6aS*)-3a-hydroxy-3,3-dimethyl-6-phenyl-5-(4-(trifluoromethyl)phenyl) hexahydro-1H-cyclopenta[c]furan-1-one *(Table 1, entry 8,* **5h***)*. Prepared according to general procedure from cinnamaldehyde and 4-hydroxy-1-(4'-trifluoromethylphynyl)-4-methylpent-1-en-3-one (**3c**) using 20 mol % **1•Cl** as the catalyst in 71% yield as a white solid. $[\alpha]_D^{20}$ (c 1.23, $CHCl_3$): +97 ; ^{1}H NMR (400 MHz, $CDCl_3$) δ 7.51 (d, 1H, *J* = 8 Hz), 7.30–7.22 (m, 7H), 3.89–3.81 (m, 1H), 3.58 (dd, 1H, *J* = 10.0, 4.4 Hz), 3.18 (dd, 1H, *J* = 4.4, 2.4 Hz), 2.31–2.17 (m, 2H), 1.53 (s, 3H), 1.49 (s, 3H); ^{13}C NMR (100 MHz, $CDCl_3$) δ 176.4, 145.1, 142.8, 129.0, 127.9, 127.8, 127.2, 125.8, 125.7, 88.0, 85.1, 59.3, 55.8, 54.0, 44.4, 24.7, 21.6, 18.6; IR (thin film) ν 3479, 2933, 2360, 1738, 1327, 1126, 1068, 837, 739 cm^{-1}; HRMS (ESI) $[M+Na]^+$ calcd. for $C_{22}H_{21}F_3O_3$ 413.1341, found, 413.1353; 92% *ee* as determined by SFC (AD-H, 10% *i*-PrOH in CO_2) t_r = 8.4 and 16.3 min.



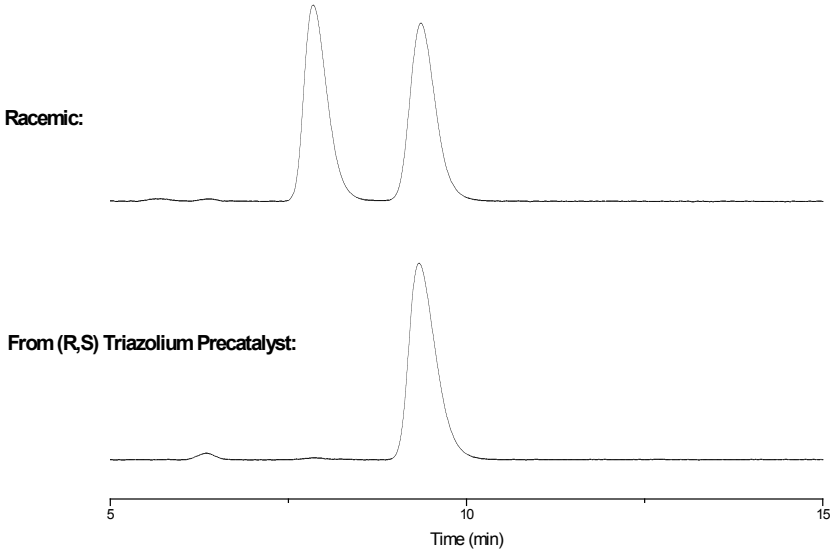


(*1S,2S,3R,5R*)-5-(2-hydroxypropan-2-yl)-2-phenyl-3-(4-(trifluoromethyl)phenyl)-6-oxabicyclo[3.2.0]heptan-7-one *(Table 1, entry 8,* **6h***)***.** 20% yield as a white solid. ^{1}H NMR (400 MHz, $CDCl_3$) δ 7.50 (d, 2H, *J* = 8.0 Hz), 7.32–7.20 (m, 7H), 4.12 (d, 1H, *J* = 7.6 Hz), 3.90–3.82 (m, 1H), 3.50 (dd, 1H, *J* = 12.0, 7.6 Hz), 2.62 (dd, 1H, *J* = 14.4, 6.4 Hz), 2.10 (dd, 1H, *J* = 14.4, 11.6 Hz), 1.41 (s, 3H), 1.40 (s, 3H); ^{13}C NMR (100 MHz, $CDCl_3$) δ 168.4, 144.1, 135.3, 128.8, 128.3, 128.0, 127.9, 125.9, 125.8, 91.4, 71.3, 60.3, 52.1, 46.8, 39.9, 25.2, 24.8; IR (thin film) ν 3444, 2977, 1819, 1327, 1120, 835, 698 cm^{-1}; HRMS (ESI) $[M+Na]^+$ calcd. for $C_{22}H_{21}F_3O_3$ 413.1341, found, 413.1351; 99% *ee* as determined by SFC (AS-H, 10% *i*-PrOH in CO_2) t_r = 4.8 and 6.1 min.

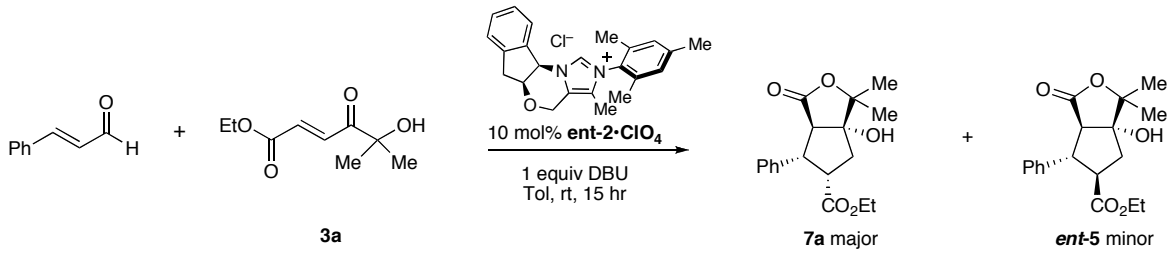




(*1S,2R,3R,5R*)-methyl-5-(2-hydroxypropan-2-yl)-7-oxo-2-phenyl-6-oxabicyclo [3.2.0]heptane-3-carboxylate. Prepared according to general procedure from cinnamaldehyde and (*E*)-methyl 5-hydroxy-5-methyl-4-oxohex-2-enoate using 10 mol % **1•Cl** as the catalyst in 60% yield as a white solid. $[\alpha]_D^{20}$ (c 0.56, $CHCl_3$): +9.5; ^{1}H NMR (400 MHz, $CDCl_3$) δ 7.27–7.23 (m, 2H), 7.22–7.18 (m, 2H), 3.98 (d, 1H, *J* = 8.0 Hz), 3.91 (s, 1H), 3.73–3.66 (m, 1H), 3.41 (s, 3H), 2.71 (dd, 1H, *J* = 14.8, 12.4 Hz), 2.32 (dd, 1H, *J* = 14.8, 7.2 Hz), 2.84 (s, 3H), 2.82 (s, 3H); ^{13}C NMR (100 MHz, $CDCl_3$) δ 171.7, 169.9, 139.0, 128.8, 127.8, 127.6, 94.4, 71.4, 61.6, 51.9, 48.2, 47.4, 31.6, 25.5; IR (thin film) ν 3442, 2981, 1822, 1736, 1211, 808, 704 cm^{-1}; HRMS (ESI) $[M+Na]^+$ calcd. for $C_{17}H_{20}O_5$ 327.1209, found, 327.1217; 99% *ee* as determined by SFC (AS-H, 5% *i*-PrOH in CO_2) *tr* = 7.9 and 9.3 min.

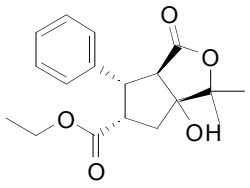


Procedure for with chiral imidazolium 2•ClO_4 as precatalyst.

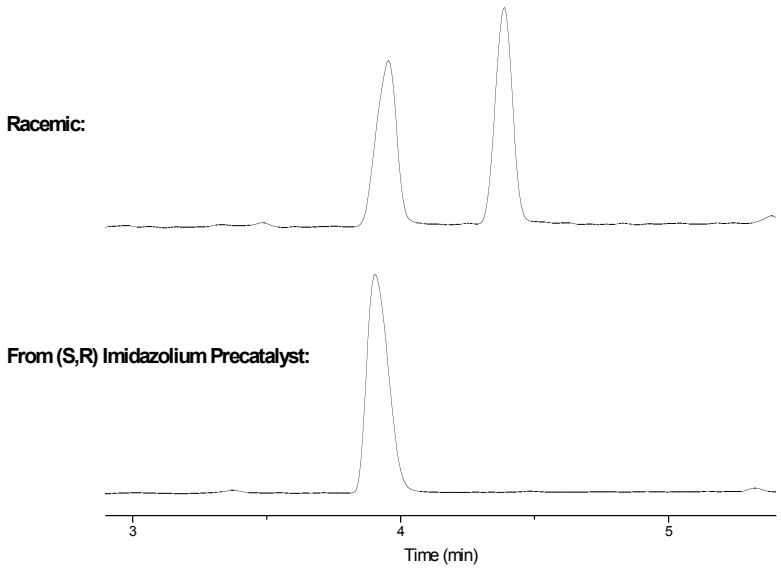


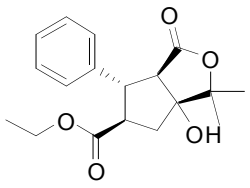
The reaction of *trans*-ethyl-4-oxo-5-hydroxy-5-methylhex-2-enoate (**3a**) and cinnamaldehyde is representative: Into an oven dried 10.0 mL round bottom flask was added **3a** (42 mg, 0.22 mmol, 1.0 equiv) and imidazolium precatalyst ***ent*-2•ClO_4** (9.8 mg, 0.020 mmol, 0.10 equiv). The flask was sealed with a septum and 2.2 mL toluene (0.1 M) and cinnamaldehyde (55 μL, 0.44 mmol, 2.0 equiv) were added via syringe. The solution was stirred at rt for 5 min before DBU (33 μL, 0.22 mmol, 1.0 equiv) was added. The resulting solution was stirred at rt for 18 h. The reaction mixture was diluted with 2.0 mL EtOAc and poured into 4.0 mL H_2O. The mixture was extracted with 3 x 4.0 mL EtOAc and the combined organic extracts were washed with 10.0 mL brine and dried over Na_2SO_4. After filtration and concentration, the residue was purified by silica chromatography (5:1 hexane: EtOAc) to give **7** as a white solid (48.9 mg, 70%) and a fraction containing impure ***ent*-5**. The mixture fraction was purified by preparative TLC (2:2:1 hexane: CH_2Cl_2: EtOAc) to give ***ent*-5** as a white solid (10.5 mg, 15%).

Racemic standard could be prepared from the mixture of the products from (*R,S*) imidazolium precatalyst (**2•ClO_4**)and (*S,R*) imidazolium precatalyst (***ent*-2•ClO_4**) in all cases.

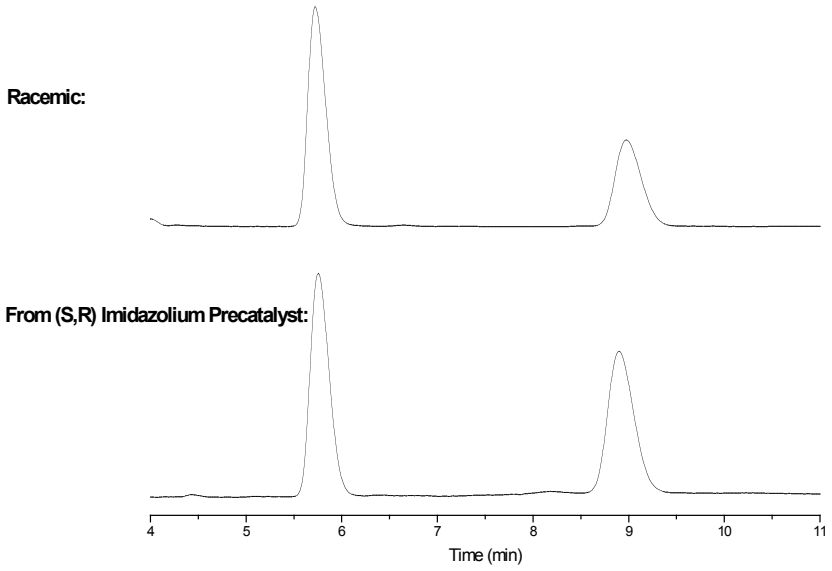


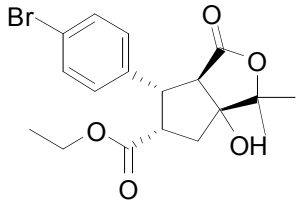
(*3aR,4S,5S,6aR*)-ethyl-6a-hydroxy-1,1-dimethyl-3-oxo-4-phenylhexahydro-1H-cyclopenta[c]furan-5-carboxylate *(Table 2, entry 1,* **7a***).* Prepared according to general procedure from cinnmaldehyde and (*E*)-ethyl 5-hydroxy-5-methyl-4-oxohex-2-enoate (**3a**) using 10 mol % chiral imidazolium ***ent*-2•ClO$_4$** as the precatalyst in 70% yield as a white solid. $[\alpha]_D^{20}$ (c 1.15, $CHCl_3$): +15.7; ^{1}H NMR (500 MHz, $CDCl_3$) δ 7.34–7.29 (m, 4H), 7.29–7.25 (m, 1H), 6.06 (s, 1H), 4.18 (dd, 1H, *J* = 3.5, 10.0 Hz), 3.74–3.67 (m, 1H), 3.60–3.56 (m, 1H), 3.42–3.35 (m, 2H), 2.24 (d, 2H, *J* = 4.5 Hz), 1.59 (s, 3H), 1.51 (s, 3H), 0.75 (t, 3H, *J* = 7.0 Hz); ^{13}C NMR (125 MHz, $CDCl_3$) δ 177.2, 176.7, 139.8, 128.5, 128.4, 127.3, 88.7, 85.2, 61.7, 58.4, 52.0, 51.4, 38.3, 24.7, 21.3, 13.3; IR (thin film) ν 3377, 2982, 1768, 1698, 1242, 1213, 1094, 1051 cm^{-1}; HRMS (ESI) $[M+Na]^+$ calcd. for $C_{18}H_{22}O_5$ 341.1365, found, 341.1346; 99% ee as determined by SFC (AD-H, gradient 5%–80% *i*-PrOH in CO_2, rate 10%/min) t_r = 3.9 and 4.5 min.



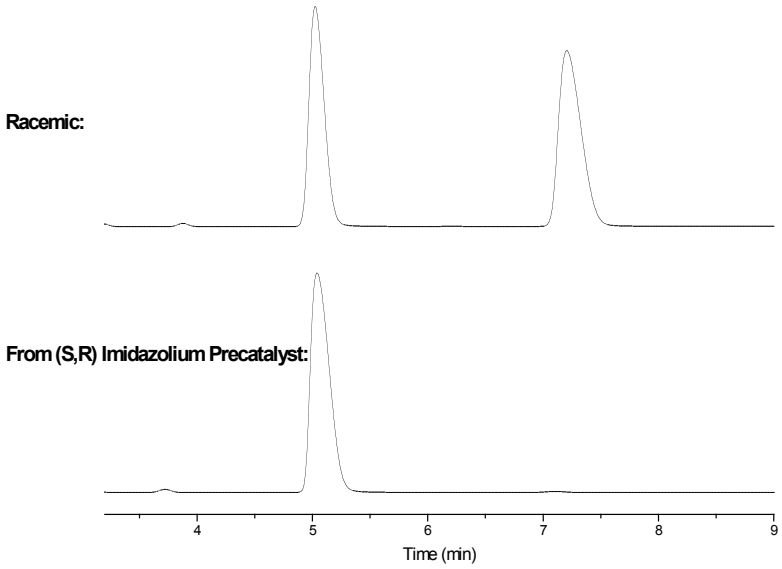


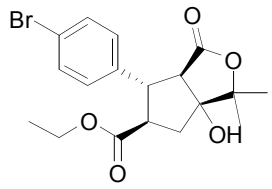
(*3aR,4S,5R,6aR*)-ethyl-6a-hydroxy-1,1-dimethyl-3-oxo-4-phenylhexahydro-1H-cyclopenta[c]furan-5-carboxylate *(Table 2, entry 1,* ***ent*****-5a*)*.** 15% as a white solid. ^{1}H NMR (500 MHz, $CDCl_3$) δ 7.38 (d, 2H, *J* = 7.5 Hz), 7.34–7.31 (m, 2H), 7.25–7.22 (m, 1H), 4.13–4.06 (m, 2H), 3.81 (dd, 1H, *J* = 4.5, 10.0 Hz), 3.48–3.42 (m, 1H), 3.06 (dd, 1H, *J* = 2.5, 4.5 Hz), 2.30–2.24 (m ,1H), 2.16 (ddd, 1H, *J* = 13.5, 6.0, 2.5 Hz), 1.88 (s, 1H), 1.47 (s, 3H), 1.46 (s, 3H), 1.18 (t, 3H, *J* = 7.0 Hz); ^{13}C NMR (125 MHz, $CDCl_3$) δ 175.3, 172.9, 128.8, 127.6, 127.0, 88.1, 84.5, 60.9, 59.0, 52.8, 50.9, 40.4, 24.5, 21.4, 14.1; 6% ee as determined by SFC (OJ-H, 15% *i*-PrOH in CO_2) *tr* = 5.7 and 8.9 min.



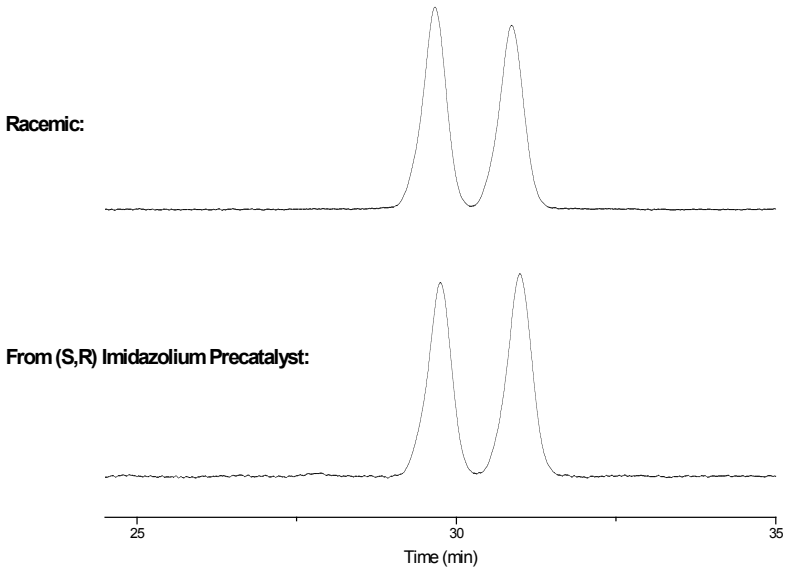


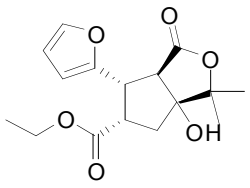
(*3aR,4S,5S,6aR*)-ethyl-4-(4-bromophenyl)-6a-hydroxy-1,1-dimethyl-3-oxohexahydro-1H-cyclopenta[c]furan-5-carboxylate *(Table 2, entry 2,* **7b***)*. Prepared according to general procedure from 4-bromocinnamaldehyde and (*E*)-ethyl 5-hydroxy-5-methyl-4-oxohex-2-enoate (**3a**) using 10 mol % chiral imidazolium ***ent*-2•ClO$_4$** as the precatalyst in 54% yield as white solid. $[\alpha]_D^{20}$ (c 2.45, $CHCl_3$): +58.6; ^{1}H NMR (500 MHz, $CDCl_3$) δ 7.42 (d, 2H, *J* = 8.5 Hz), 7.16 (d, 2H, *J* = 8.5 Hz), 5.94 (s, 1H), 4.09, (dd, 1H, *J* = 10.5, 3.5 Hz), 3.75–3.68 (m, 1H), 3.55–3.52 (m, 1H), 3.48–3.42 (m, 1H), 3.28 (d, 1H, *J* = 3.5 Hz), 2.20 (d, 2H, *J* = 5.0 Hz), 1.55 (s, 3H), 1.46 (s, 3H), 0.78 (t, 3H, *J* = 7.5 Hz); ^{13}C NMR (125 MHz, $CDCl_3$) δ 176.9, 176.4, 138.9, 131.5, 130.3, 121.3, 88.7, 85.3, 61.9, 58.4, 51.8, 50.7, 38.3, 24.7, 21.3, 13.4; IR (thin film) ν 3377, 2981, 1769, 1698, 1491, 1241, 1213, 1094, 980, 865 cm^{-1}; HRMS (ESI) $[M+Na]^+$ calcd. for $C_{18}H_{21}BrO_5$ 419.0470, found, 419.0463; 99% *ee* as determined by SFC (OJ-H, 10% *i*-PrOH in CO_2) *tr* = 5.0 and 7.1 min.



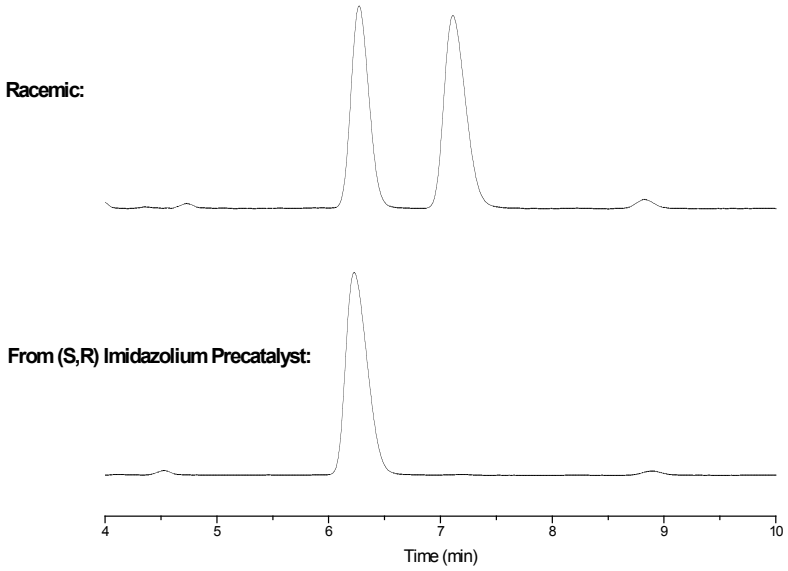


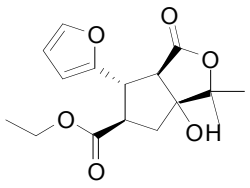
(*3aR,4S,5R,6aR*)-ethyl-4-(4-bromophenyl)-6a-hydroxy-1,1-dimethyl-3-oxohexahydro-1H-cyclopenta[c]furan-5-carboxylate *(Table 2, entry 2,* ***ent*****-5c***)*. 22% yield as a white solid. ^{1}H NMR (500 MHz, $CDCl_3$) δ 7.48–7.46 (m, 2H), 7.30–7.28 (m, 2H), 4.16–4.09 (m, 2H), 3.78 (dd, 1H, *J* = 9.5, 4.5 Hz), 3.45–3.39 (m, 1H), 3.04 (dd, 1H, *J* = 4.5, 2.5 Hz), 2.30–2.25 (m, 1H), 2.19 (ddd, 1H, *J* = 13.5, 6.5, 2.5 Hz), 1.50 (s, 3H), 1.48 (s, 3H), 1.22 (t, 3H, *J* = 7.0 Hz); ^{13}C NMR (125 MHz, $CDCl_3$) δ 175.4, 172.8, 141.9, 131.9, 129.5, 120.9, 88.0, 84.8, 61.1, 58.8, 52.9, 50.3, 40.3, 24.5, 21.4, 14.1; 4% *ee* as determined by SFC (AS-H, gradient 0.5%–50% *i*-PrOH in CO_2, rate 0.2%/min) *tr* = 29.8 and 31 min.



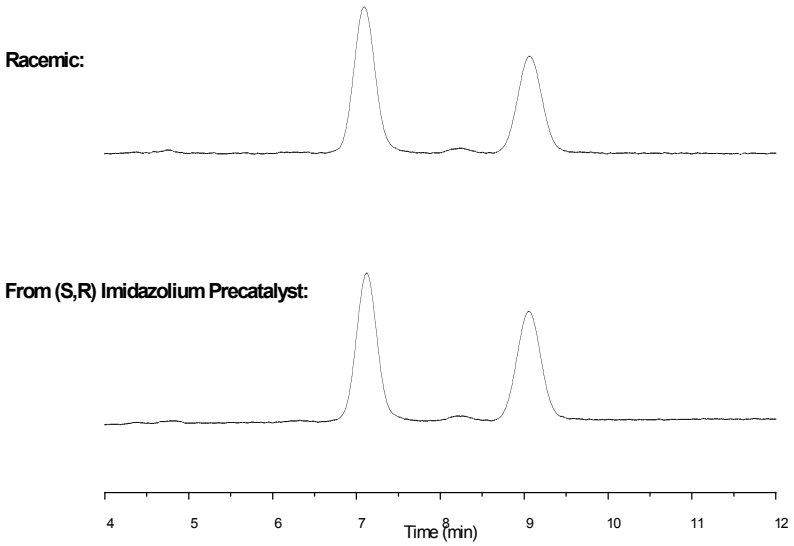


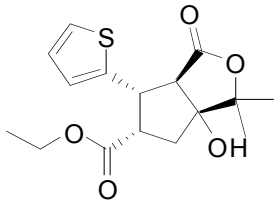
(*3aR,4S,5S,6aR*)-ethyl-4-(furan-2-yl)-6a-hydroxy-1,1-dimethyl-3-oxohexahydro-1H-cyclopenta[c]furan-5-carboxylate *(Table 2, entry 3,* **7c***)***.** Prepared according to general procedure from *trans*-3-(2-furyl)acrolein and (*E*)-ethyl 5-hydroxy-5-methyl-4-oxohex-2-enoate (**3a**) using 10 mol % chiral imidazolium ***ent*-2•ClO$_4$** as the precatalyst in 60% yield as pale yellow solid. $[\alpha]_D^{20}$ (c 0.61, $CHCl_3$): +36.2; ^{1}H NMR (500 MHz, $CDCl_3$) δ 7.35 (dd, 1H, *J* = 2.0, 1.0 Hz), 6.33 (dd, 1H, *J* = 3.5, 2.0 Hz), 6.24 (d, 1H, *J* = 3.5 Hz), 5.68 (s, 1H), 4.19 (dd, 1H, *J* = 10.0, 3.5 Hz), 4.00–3.98 (m, 1H), 3.81–3.75 (m, 1H), 3.51–3.47 (m, 1H), 3.36 (dd, 1H, *J* = 3.5, 1.0 Hz), 2.25 (dd, 2H, *J* = 4.0, 1.0 Hz), 1.56 (s, 3H), 1.49 (s, 3H), 1.06 (t, 3H, *J* = 7.0 Hz); ^{13}C NMR (125 MHz, $CDCl_3$) δ 176.3, 176.2, 153.0, 142.0, 110.6, 107.4, 88.1, 85.7, 62.1, 57.2, 49.9, 44.4, 38.1, 29.7, 24.9, 21.5, 13.7; IR (thin film) ν 3380, 2931, 1765, 1465, 1376, 1212, 1098, 864, 737 cm^{-1}; HRMS (ESI) $[M+H]^+$ calcd. for $C_{16}H_{20}O_6$ 309.1338, found, 309.1342; 99% *ee* as determined by SFC (OJ-H, 25% *i*-PrOH in CO_2) *tr* = 6.2 and 7.2 min.



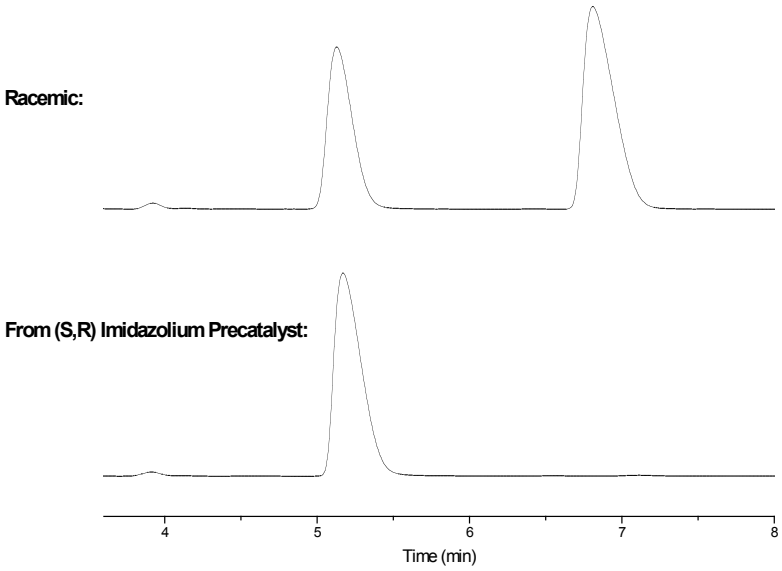


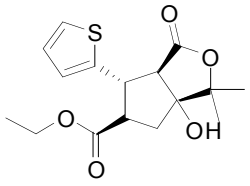
(*3aR,4S,5R,6aR*)-ethyl-4-(furan-2-yl)-6a-hydroxy-1,1-dimethyl-3-oxohexahydro-1H-cyclopenta[c]furan-5-carboxylate *(Table 2, entry 3,* ***ent*****-5f***)*. 20% yield as a yellow oil. ^{1}H NMR (500 MHz, $CDCl_3$) δ 7.35 (d,1H, *J* = 2.0 Hz), 6.34 (dd, 1H, *J* = 3.0, 2.0 Hz), 6.23 (d, 1H, *J* = 3.0 Hz), 4.21–4.14 (m, 2H), 3.99 (dd, 1H, *J* = 9.0, 4.0 Hz), 3.54–3.48 (m, 1H), 3.19 (dd, 1H, *J* = 5.5, 2.0 Hz), 2.26–2.21 (m, 2H), 1.52 (s, 3H), 1.48 (s, 3H), 1.26 (t, 3H, *J* = 7.5 Hz); ^{13}C NMR (125 MHz, $CDCl_3$) δ 174.7, 172.7, 154.3, 142.1, 110.6, 106.3, 87.8, 84.9, 61.1, 56.4, 49.8, 43.4, 39.6, 29.7, 24.5, 21.4, 14.1; IR (thin film) ν 3431, 2930, 1734, 1448, 1252, 1078, 1029 cm^{-1}; HRMS (ESI) $[M+H]^+$ calcd. for $C_{16}H_{20}O_6$ 309.1338, found, 309.1347; 8% *ee* as determined by SFC (OJ-H, 10% *i*-PrOH in CO_2) *tr* = 7.1 and 9.1 min.



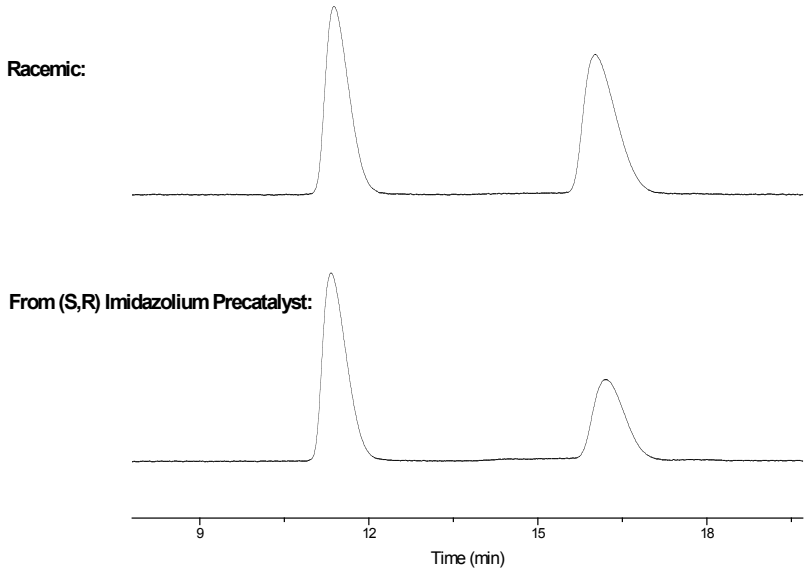


(*3aR,4S,5S,6aR*)-ethyl-6a-hydroxy-1,1-dimethyl-3-oxo-4-(thiophen-2-yl)hexahydro-1H-cyclopenta[c]furan-5-carboxylate *(Table 2, entry 4,* **7d***)* . Prepared according to general procedure from (*E*)-3-(thiophen-2-yl)acrylaldehyde and (*E*)-ethyl 5-hydroxy-5-methyl-4-oxohex-2-enoate (**3a**) using 10 mol % chiral imidazolium ***ent*-2•ClO$_4$** as the precatalyst in 51% yield as a pale yellow solid. $[\alpha]_D^{20}$ (c 0.97, $CHCl_3$): +88.04; ^{1}H NMR (500 MHz, $CDCl_3$) δ 7.19–7.18 (m, 1H), 6.96–6.95 (m, 1H), 4.38 (dd, 1H, *J* = 10.0, 4.0 Hz), 3.88–3.82 (m, 1H), 3.67–3.61 (m, 1H), 3.59–3.59 (m, 1H), 3.40 (dd, 1H, *J* = 4.0, 1.5 Hz), 3.24–3.23 (m, 2H), 1.58 (s, 3H), 1.49(s, 3H), 0.94 (t, 3H, *J* = 7.5 Hz); ^{13}C NMR (125 MHz, $CDCl_3$) δ 176.9, 176.2, 142.8, 127.2, 126.0, 124.4, 88.3, 85.5, 62.1, 60.3, 52.1, 45.9, 38.3, 24.9, 21.5, 13.6; IR (thin film) ν 3377, 2981, 1768, 1699, 1382, 1259, 1211, 1056, 978, 862, 705 cm^{-1}; HRMS (ESI) $[M+Na]^+$ calcd. for $C_{16}H_{20}O_5S$ 325.1109, found, 325.1100; 99% *ee* as determined by SFC (OJ-H, 10% *i*-PrOH in CO_2) *tr* = 5.2 and 7.1 min.

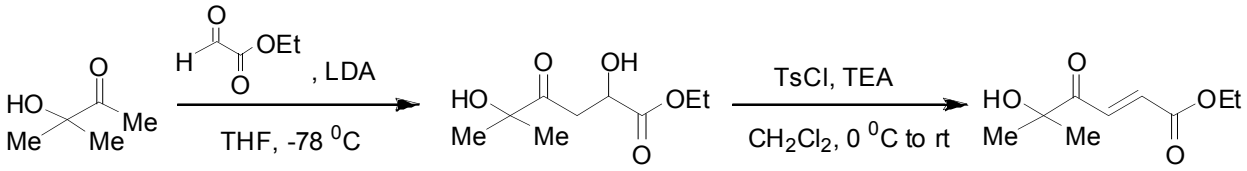




(*3aR,4S,5S,6aR*)-ethyl-6a-hydroxy-1,1-dimethyl-3-oxo-4-(thiophen-2-yl)hexahydro-1H-cyclopenta[c]furan-5-carboxylate *(Table 2, entry 4)***.** 17% yield as a pale yellow oil. ^{1}H NMR (500 MHz, $CDCl_3$) δ 7.18 (d, 1H, *J* = 5.0 Hz), 6.99 (d, 1H, *J* = 3.5 Hz), 6.93 (dd, 1H, *J* = 5.0, 3.5 Hz), 4.17–4.11 (m, 3H), 3.54–3.48 (m, 1H), 3.12 (dd, 1H, *J* = 4.5, 2.5 Hz), 2.24–2.16 (m, 3H), 1.47 (s, 3H), 1.44 (s, 3H), 1.23 (t, 3H, *J* = 7.0 Hz); ^{13}C NMR (125 MHz, $CDCl_3$) δ 175.0, 172.7, 146.4, 127.1, 124.8, 124.3, 87.9, 84.8, 61.2, 59.6, 53.4, 45.7, 40.1, 24.5, 21.3, 14.2; IR (thin film) ν 3464, 2982, 1732, 1444, 1280, 1094, 979, 866, 703 cm^{-1}; HRMS (ESI) $[2M+Na]^+$ calcd. for $C_{16}H_{20}O_5S$ 671.1960, found, 671.1972; 28% *ee* as determined by SFC (OJ-H, 10% *i*-PrOH in CO_2) *tr* = 11.3 and 16.2 min.



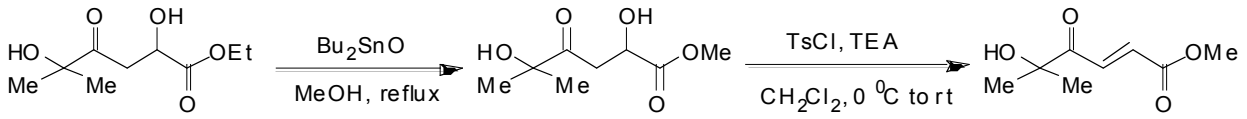
Preparation of *trans*-ethyl-4-oxo-5-hydroxy-5-methylhex-2-enoate (3a).



To an oven or flame-dried 2-neck round bottom flask fitted with a dropping funnel loaded with *n*-BuLi (2.57 M solution in hexane, 28.0 mL, 71.2 mmol) under Ar was added dry THF (70 mL) and *N,N*-diisopropylamine (10.0 mL, 71.2 mmol). The solution was cooled to –78 °C and *n*-BuLi was added dropwise such that the temperature remained below –70 ^{0}C. After the addition, the mixture was allowed to stir at –78 °C for 1 h before adding 3-hydroxy-3-methyl-butanone (3 mL, 28.5 mmol) dropwise. After complete addition, the mixture was allowed to stir at –78 °C for 1 h before transferring via cannula to a round bottom flask containing ethyl glyoxalate (50% in toluene, 18 mL, 85.5 mmol) in THF (60 mL) at –78 °C. The mixture was stirred at –78 °C and the reaction was monitored by TLC (1:1 EtOAc: hexane). After 1–2 h, the reaction was quenched with sat. NH_4Cl and extracted with EtOAc. The organic extracts were combined, dried over Na_2SO_4 and concentrated. The crude product was purified by flash chromatography (2:2:1 hexane:CH_2Cl_2:EtOAc) to give the *α,β′*-dihydroxy ketone as light yellow oil 65% yield. To this *α,β′*-dihydroxy ketone (3.18 g, 15.6 mmol) in CH_2Cl_2 (150 mL) at 0 ^{0}C were added *p*-toluenesulfonylchloride (5.95 g, 31.2 mmol) and NEt_3 (13.0 mL, 93.6 mmol). The reaction mixture was allowed to warm to rt and stirred overnight. The resulting mixture was washed with a solution of citic acid (1.25 g in 125.0 mL H_2O) and brine. The mixture was dried over Na_2SO_4 and concentrated. The crude product was purified by flash chromatography (8:1 hexane:EtOAc) to afford *trans*-ethyl-4-oxo-5-hydroxy-5-methylhex-2-enoate[3] **(3a)** in 85% yield as a light yellow oil. ^{1}H NMR (400 MHz, $CDCl_3$) δ 7.54 (d, 1H, *J* = 15.6 Hz), 6.94 (d, 1H, *J* = 15.6 Hz), 4.29 (q, 2H, *J* = 7.2 Hz), 3.56 (s, 1H), 1.44 (s, 6H), 1.35 (t, 3H, *J* = 7.2 Hz); ^{13}C NMR (100 MHz, $CDCl_3$) δ 202.4, 165.3, 133.6, 133.3, 76.2, 61.7, 26.1, 14.3; IR (thin film) ν 3481, 2983, 1726, 1699, 1302, 1184 cm^{-1}; HRMS (ESI) $[M+Na]^+$ calcd. for $C_9H_{14}O_4$ 209.0790, found, 207.0778.

(3) Baraldi, P. G.; Bazzanini, R.; Bigoni, A.; Manfredini, S.; Simoni, D.; Spalluto, G. *Synthesis* **1993**, 1206–1028.

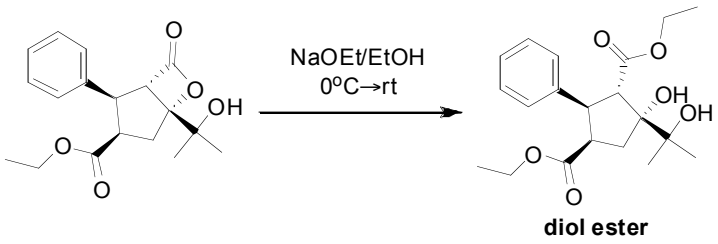
Preparation of (*E*)-methyl 5-hydroxy-5-methyl-4-oxohex-2-enoate



The *α,β′*-dihydroxy ketone ethyl ester (1.98 g, 9.7 mmol) was dissolved in MeOH (80.0 mL). After addition of dibutyltin oxide (10 mol %, 0.25 g, 0.97 mmol) the reaction mixture was heated at reflux for 16 h. The resulting mixture was poured into sat. aq $NaHCO_3$ (200.0 mL) and extracted with 3 x 100 mL EtOAc. The combined organic extracts, which contained the dibutyltin oxide as a fine white precipitate, were filtered through Celite, dried over Na_2SO_4 and concentrated. The crude product was purified by flash chromatography (2:2:1 hexane:CH_2Cl_2:EtOAc) to give the dihydroxy ketone methy lester in 90% yield as a yellow oil[4]. The corresponding enone was prepared by dehydration of the dihydroxy ketone methylester with *p*-toluenesulfonylchloride as described above in 80% yield as a yellow oil. ^{1}H NMR (400 MHz, $CDCl_3$) δ 7.46 (d, 1H, J = 15.6 Hz), 6.93 (d, 1H, J = 15.6 Hz), 3.84 (s, 3H), 3.54 (s, 1H), 1.44 (s, 6H); ^{13}C NMR (100 MHz, $CDCl_3$) δ 202.3, 165.8, 133.6, 133.1, 76.2, 52.7, 26.1; IR (thin film) ν 3483, 2981, 1730, 1701, 1308, 1176 cm^{-1}; HRMS (ESI) $[M+Na]^+$ calcd. for $C_8H_{12}O_4$ 195.0634, found, 195.0631.

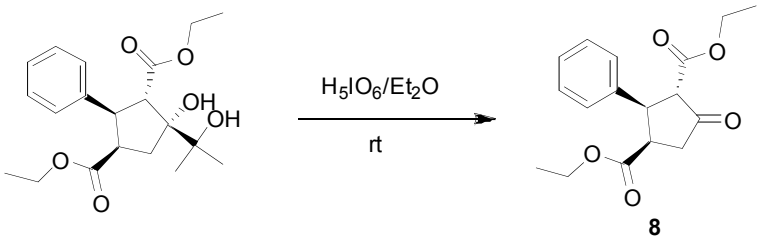
(4) Baumhof, P.; Mazitschek, R.; Giannis, A. *Angew. Chem. Int. Ed.* **2001**, *40*, 3672–3674.

Synthesis of (*1R,2R,3S,4R*)-diethyl-4-hydroxy-4-(2-hydroxypropan-2-yl)-2-phenylcyclopentane-1,3-dicarboxylate



To an oven-dried round bottom flask in an ice bath was added dry EtOH (1.0 mL) followed by sodium metal (25 mg) and the mixture was stirred until the sodium metal dissolved completely. The resulting solution was transfered to a flask containing **4a** (52 mg, 0.16 mmol) in EtOH (1.6 mL) at rt. The reaction was monitored by TLC (2:5 EtOAc:hexane). After 1 h, the reaction was quenched with sat. aq. NH_4Cl and extracted with EtOAc. The combined organic extracts were washed with brine, dried over Na_2SO_4 and concentrated. The residue was purified by flash chromatography to afford the diol ester in 96% yield as a colorless oil. ^{1}H NMR (400 MHz, $CDCl_3$) δ 7.28–7.19 (m, 4H), 4.13 (dd, 1H, *J* = 12.0, 10.4 Hz), 4.08–3.99 (m, 2H), 3.68–3.62 (m, 1H), 3.59 (d, 1H, *J* = 12.0 Hz), 3.55–3.47 (m, 1H), 3.46–3.40 (m, 1H), 2.37 (dd, 1 H, *J* = 14.0, 6.4 Hz), 2.04 (dd, 1H, *J* = 14.0, 8.8 Hz), 1.46 (s, 3H), 1.31 (s, 3H), 1.06, (t, 3H, *J* = 6.8 Hz), 0.74 (t, 3H, *J* = 7.2 Hz); ^{13}C NMR (100 MHz, $CDCl_3$) δ 175.6, 174.7, 138.1, 128.4, 128.3, 127.3, 87.2, 74.8, 61.4, 60.5, 51.2, 51.1, 47.1, 38.3, 25.5, 25.0, 14.0, 13.7; IR (thin film) ν 3471, 2981, 1720, 1454, 1377, 1186, 750, 700 cm^{-1}; HRMS (ESI) $[M+Na]^+$ calcd. for $C_{20}H_{28}O_6$ 387.1784, found 387.1771.

Synthesis of (*1R,2R,3S*)-diethyl 4-oxo-2-phenylcyclopentane-1,3-dicarboxylate (8)



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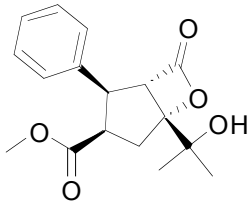
To a suspenion of the diol ester (45 mg, 0.12 mmol) in Et_2O (6.0 mL) was added periodic acid (34 mg, 0.15 mmol) in Et_2O (30.0 mL) was added under Ar at rt. After 3 h, the reaction mixture was filtered through Celite and concentrated. The residue was purified by flash chromatography to afford *β*-keto ester **8** in 85% yield (10:1 keto:enol) as a colorless oil.[5] ^{1}H NMR (500 MHz, $CDCl_3$) δ 7.37–7.36 (m, 2H), 7.31–7.30 (m, 1H), 7.26–7.23 (m, 2H), 4.25–4.18 (m, 3H), 4.09 (d, 1H, *J* = 12.5 Hz), 3.89–3.80 (m, 2H), 3.57 (dt, 1H, *J* = 8.0, 2.0 Hz), 2.83 (md, 1H, *J* = 18.5 Hz), 2.69 (dd, 1H, *J* = 18.5, 8.0 Hz), 1.28 (t, 1H, *J* = 7.5 Hz), 0.90 (t, 1H, *J* = 7.0 Hz); ^{13}C NMR (100 MHz, $CDCl_3$) δ 208.6, 173.4, 168.8, 137.1, 128.9, 127.9, 127.3, 62.0, 61.0, 56.7, 48.4, 45.5, 42.1, 14.3, 13.9; IR (thin film) ν 2983, 1761, 1726, 1194, 1115, 748, 700 cm^{-1}; HRMS (ESI) $[M+Na]^+$ calcd. for $C_{17}H_{20}O_5$ 327.1209, found 327.1189.

Determination of the relative and absolute stereochemistry of the *β*-lactone and *γ*-lactone products

The stereochemistry was determined by single crystal x-ray analysis of the products (see above for characterization data): A colorless crystal of approximate dimensions 0.4 × 0.05 × 0.04 mm was mounted on a glass fiber and transferred to a Bruker CCD platform diffractometer. The SMART program was used to determine the unit cell parameters and data collection (20 sec: frame, 0.3 deg.: frame for a sphere of diffraction data). The data were collected at room temperature. The raw frame data were processed using SAINT program. The empirical absorption correction was applied based on psi scan. The structure was solved by direct methods and refined on F2 by full-matrix least-squares techniques. Hydrogen atoms were theoretically added. At convergence, GOF = 1.207 for 206 variables refined to R1= 0.0632 for

(5) Seo, J.; Fain, H.; Blanc, J. B.; Montgomery, J. *J. Org. Chem.* **1999**, *64*, 6060–6065.

1415 reflections with I>2σ(I). The absolute structure was determined from the Flack parameters –0.02 (2). See the corresponding CIF file for further information.



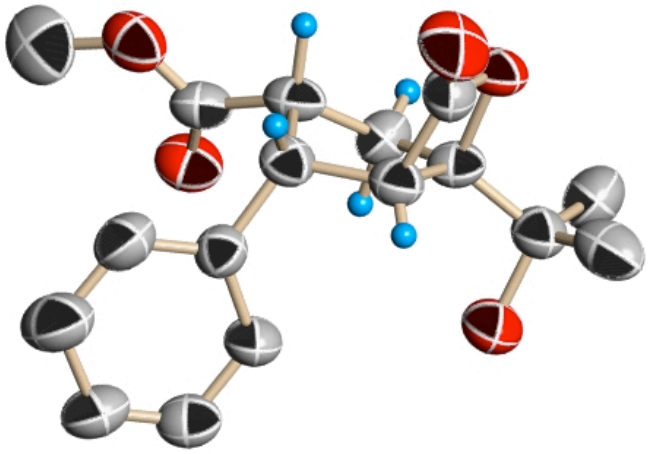
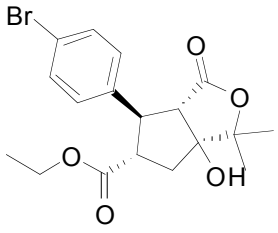


Figure 1. ORTEP presentation of (*1S,2R,3R,5R*)-methyl-5-(2-hydroxypropan-2-yl)-7-oxo-2-phenyl-6-oxabicyclo [3.2.0]heptane-3-carboxylate.



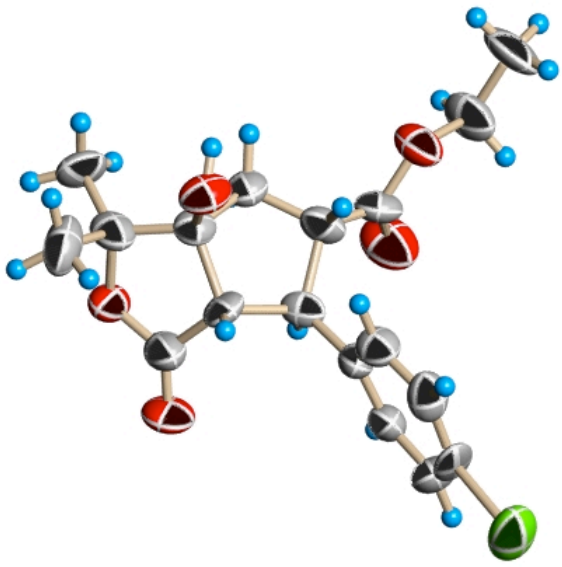
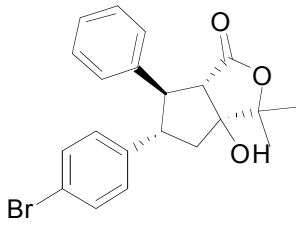


Figure 2. ORTEP presentation of (*3aS,4R,5S,6aS*)-ethyl-4-(4-bromophenyl)-6a-hydroxy-1,1-dimethyl-3-oxohexahydro -1H-cyclopenta[c]furan-5-carboxylate.



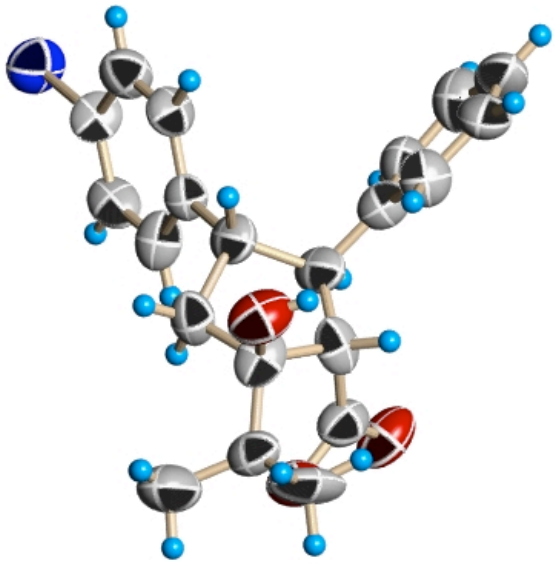


Figure 3. ORTEP presentation of *(3aS,5S,6R,6aS)*-5-(4-bromophenyl)-3a-hydroxy-3,3-dimethyl-6-phenylhexahydro-1H-cyclopenta[c]furan-1-one.

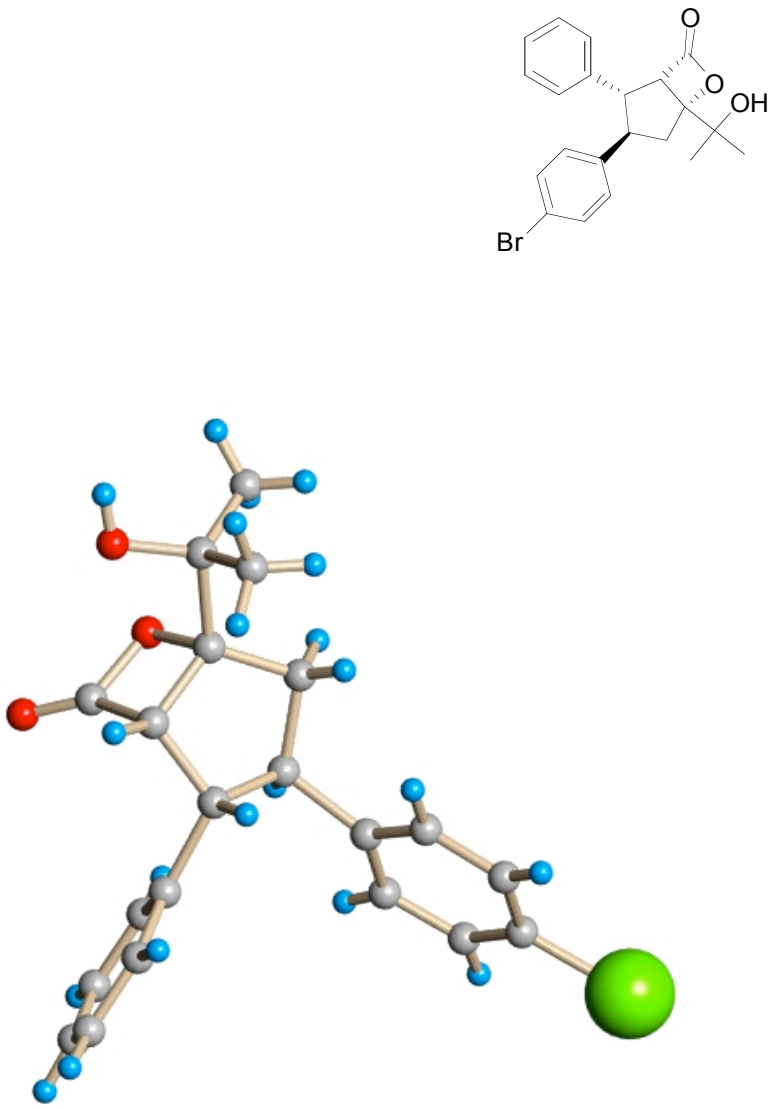


Figure 4. ORTEP presentation of (*1S,2S,3R,5R*)-3-(4-bromophenyl)-5-(2-hydroxypropan-2-yl)-2-phenyl-6-oxabicyclo [3.2.0]heptan-7-one.

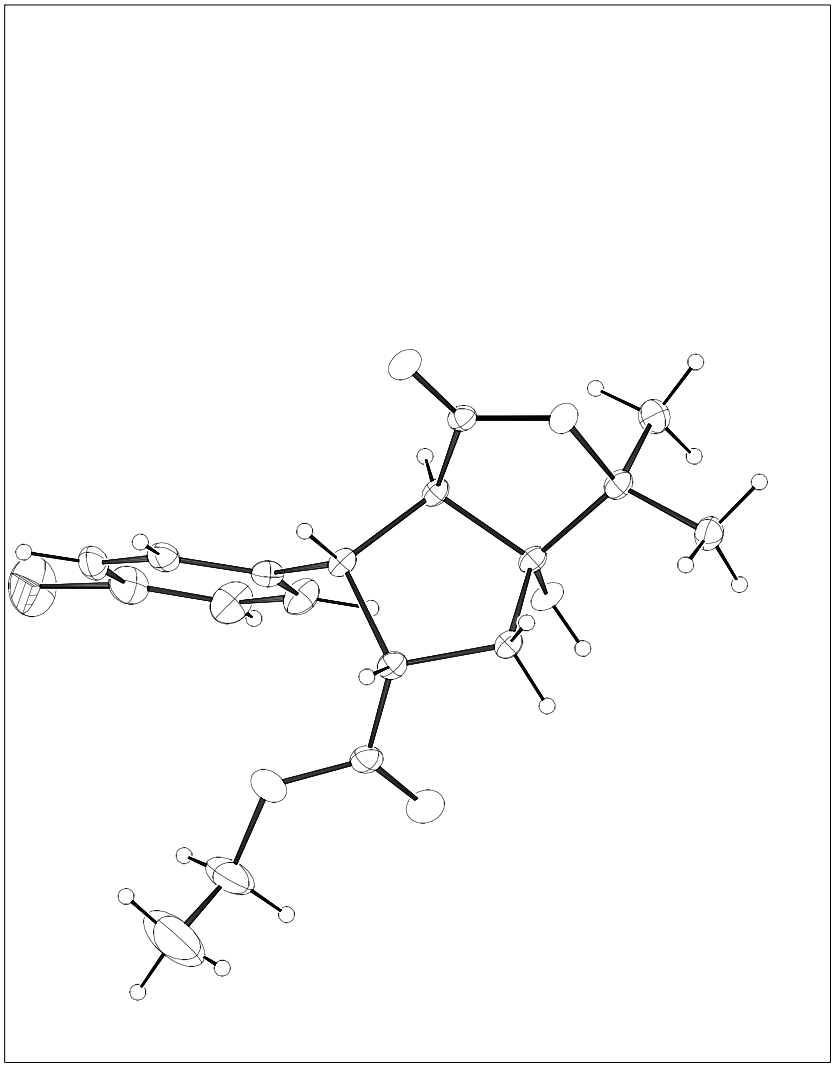


Figure 5. ORTEP presentation of (*3aR,4S,5R,6aR*)-ethyl-4-(4-bromophenyl)-6a-hydroxy-1,1-dimethyl-3-oxohexahydro-1H-cyclopenta[c]furan-5-carboxylate.