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Asymmetric Synthesis of Cyclopentanones through Dual Lewis Acid-Catalysed [3 + 2]-Cycloaddition of Donor-Acceptor Cyclopropanes with Ketenes

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Experimental Procedures & Characterization Data

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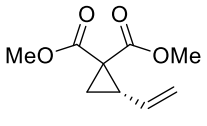
General Information:

THF was freshly distilled from benzophenone ketyl radical under nitrogen prior to use, while Hünig's base (diisopropylethylamine) was distilled from calcium hydride.[1] Most anhydrous solvents (dichloromethane and diethyl ether) were obtained by passing through activated alumina columns on a solvent purification system. All the chemicals were purchased from Sigma Aldrich and used as received from the supplier without further purification unless mentioned otherwise. All ketenes were synthesized according to reported literature procedures.[2]

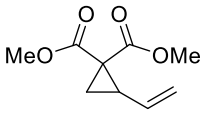
NMR spectra were recorded on a Bruker DPX Avance 200 spectrometer (200 MHz for ^{1}H and 50 MHz for ^{13}C) and on a Bruker Biospin AG 400 spectrometer (400 MHz for ^{1}H and 100 MHz for ^{13}C). NMR chemical shifts were reported relative to TMS (0 ppm) for ^{1}H and to $CDCl_3$ (77.23 ppm) for ^{13}C spectra. High resolution mass spectra were recorded on Agilent Technologies 6520 Accurate Mass Q-TOF LC-MS instrument at Oakland University. Low resolution mass spectra were recorded on a GC/MS Hewlett Packard HP 6890 GC instrument with a 5973 mass selective detector. IR spectra were recorded on a Bio Rad FTS-175C spectrometer. Optical rotations were measured on a Rudolph DigiPol 781 TDV automatic polarimeter.

Chiral high-performance liquid chromatography analysis (HPLC) was performed using Daicel Chiralpak AD, Chiralpak AD-H, Chiralpak AS, Chiralpak AS-H, Chiralpak OD and Chiralpak OD-H (25 × 0.46 cm) (Daicel chemical Ind., Ltd.) on a Perkin Elmer Flexar instrument attached with diode array detector (deuterium lamp, 190-600 nm) with HPLC-grade isopropanol and hexanes as the eluting solvents. Enantiomeric excesses were determined at λ = 254 or 225 nm (details given for each compound).

Donor-Acceptor Cyclopropanes:



(*S*)-**1a**
ee = 99%



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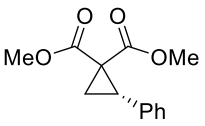

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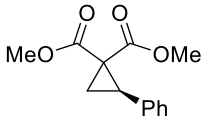

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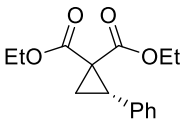
ee = 99%



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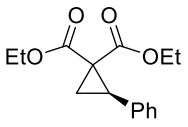

(*R*)-**1c** (*ent*-**1c**)
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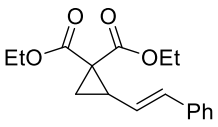
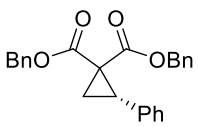
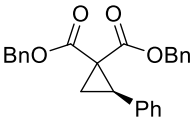


(±)-**1d**



(*S*)-**1e**
ee = 99%



(*R*)-**1e** (*ent*-**1e**)
ee = 99%

Cyclopropanes **1a-1e** were prepared according to procedures known in the literature.[3]

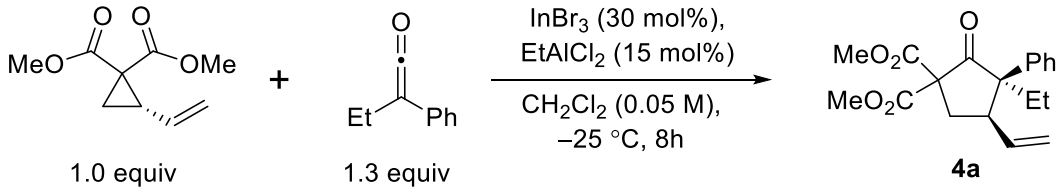
1) Armarego, W. L. F.; Perrin, D. D. *Purification of Laboratory Chemicals*, 4th Ed. Butterworth Heinemann, **2002**.
2) (a) Hodous, B. L.; Fu, G. C. *J. Am. Chem. Soc*. **2002**, *124*, 10006. (b) Wiskur, S. L.; Fu, G. C. *J. Am. Chem. Soc*. **2005**, *127*, 6176. (c) Allen, A. D.; Baigrie, L. M.; Gong, L.; Tidwell, T. T. *Can. J. Chem.* **1991**, *69*, 138. (d) Wilson, J. E.; Fu, G. C. *Angew. Chem. Int. Ed*. **2004**, *43*, 6358. (e) Ruden R. A. *J. Org. Chem*. **1974**, *39*, 3607. (f) Chen, S.; Ibrahim, A. A.; Peraino, N. J.; Nalla, D.; Mondal,

M.; Raaphorst, M. V.; Kerrigan, N. J. *J. Org. Chem.*, **2016**, *81*, 7824. (g) Douglas, J. J.; Churchill, G.; Slawin, A. M. Z.; Fox, D. J.; Smith, A. D. *Chem. Eur. J.* **2015**, *21*, 16354.

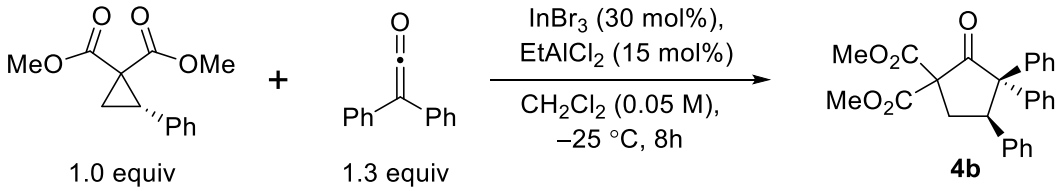
3) (a) Ieki, R.; Kani, Y.; Tsunoi, S.; Shibata, I. *Chem. Eur. J.* **2015**, *21*, 6295. (b) Vermaa, K.; Banerjee, P. *Adv. Synth. Catal*. **2017**, *359*, 3848. (c) Pohlhaus, P. D.; Sanders, S. D.; Parsons, A. T.; Li, W.; Johnson, J. S. *J. Am. Chem. Soc.*, **2008**, *130*, 8642. (d) Parsons, A. T.; Campbell, M. J.; Johnson, J. S. *Org. Lett.*, **2008,** *10*, 2541.

General procedure for cyclopentanone synthesis:

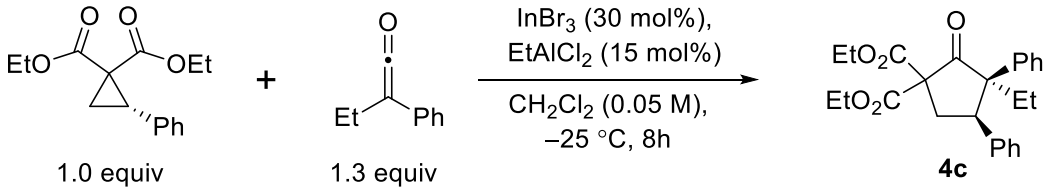
To a stirring suspension of indium bromide (0.09 mmol) in dichloromethane (3.0 mL) at –25 °C, a solution of cyclopropane (0.3 mmol) in dichloromethane (2.0 mL) and ethylaluminium dichloride solution (1.0 M in hexanes, 0.045 mmol) were added. To this stirring reaction mixture, a solution of ketene (0.39 mmol) in dichloromethane (1.0 mL) was added over a period of 4 h via syringe pump. The reaction was stirred at this temperature for another 4 h and then quenched by addition of a mixture of methanol-triethylamine (2:1, 1.0 mL). Then the reaction mixture was poured into cold 10% hydrochloric acid solution (20 mL) and extracted with dichloromethane (25 mL × 2). The combined organic layers were washed with water (30 mL), brine (30 mL), and dried over sodium sulfate. Diastereomeric ratio was determined by GC-MS analysis of the crude product after workup. Removal of the solvent under reduced pressure followed by regular silica gel column chromatographic purification using a mixture of ethyl acetate and hexanes (details mentioned below) afforded pure desired product.



Dimethyl (3*R*,4*R*)-3-ethyl-2-oxo-3-phenyl-4-vinylcyclopentane-1,1-dicarboxylate (4a): Following the general procedure, cyclopropane (*S*)-**1a** (60 mg, 0.33 mmol) solution in dichloromethane (2.0 mL) was added to a stirring suspension of $InBr_3$ (35 mg, 0.098 mmol) in dichloromethane (3.0 mL) at –25 °C. To this reaction mixture, $EtAlCl_2$ (1.0 M solution in hexanes) (0.049 mL, 0.049 mmol) was added dropwise. A solution of ethylphenylketene (62 mg, 0.42 mmol) in dichloromethane (1.0 ml) was added over 4 h to the reaction mixture at –25 °C. Elution with 5% EtOAc/hexanes through regular silica gel column afforded **4a** as a colorless gum (36 mg of major isomer and 71 mg as mixture of isomers, 99%). R_f = 0.5 (EtOAc/hexanes 1:7); dr = 2:1 (by crude GC-MS analysis); HPLC analysis: 90% ee [Daicel Chiralcel OD-H column; 1.0 mL/min; solvent system: 1% isopropanol in hexane; retention times: 10.2 min (minor), 10.8 min (major)]; $[\alpha]_D^{24}$ = –22 (c = 3.4, CH_2Cl_2); IR (thin film) 2955, 2881, 1764, 1730, 1434, 1255, 1214, 1152, 994, 921, 700 cm^{-1}; ^1H NMR (400 MHz, $CDCl_3$, TMS, Major isomer): δ 7.31-7.19 (m, 3H), 7.10-7.04 (m, 2H), 5.24-4.98 (m, 3H), 3.85 (s, 3H), 3.84 (s, 3H), 2.89-2.80 (m, 1H), 2.71 (dd, *J* = 13.4 & 5.9 Hz, 1H), 2.47 (dd, *J* = 13.3 & 12.4 Hz, 1H), 2.14-2.03 (m, 1H), 1.95-1.84 (m, 1H), 0.88 (t, *J* = 7.4 Hz, 3H); ^{13}C NMR (100 MHz, $CDCl_3$, Major isomer): δ 209.6, 167.5, 167.3, 138.5, 137.3, 128.8, 128.2, 127.1, 117.3, 69.4, 61.9, 53.7, 53.6, 49.1, 35.2, 30.1, 8.7; $(M + H)^+$ HRMS m/z calcd for $(C_{19}H_{23}O_5)^+$: 331.1545; found: 331.1538.

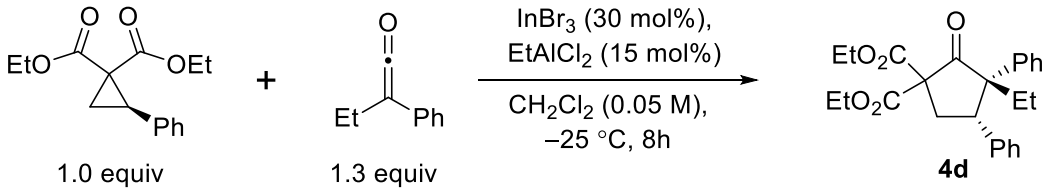


Dimethyl (*R*)-2-oxo-3,3,4-triphenylcyclopentane-1,1-dicarboxylate (4b): Following the general procedure, cyclopropane (*S*)-**1b** (76 mg, 0.32 mmol) solution in dichloromethane (2.0 mL) was added to a stirring suspension of $InBr_3$ (34 mg, 0.096 mmol) in dichloromethane (3.0 mL) at –25 °C. To this reaction mixture, $EtAlCl_2$ (1.0 M solution in hexanes) (0.048 mL, 0.048 mmol) was added dropwise. A solution of diphenylketene (82 mg, 0.42 mmol) in dichloromethane (1.0 ml) was added over 4 h to the reaction mixture at –25 °C. Elution with 9% EtOAc/hexanes through regular silica gel column afforded **4b** as a colorless gum (75 mg, 54%). R_f = 0.45 (EtOAc/hexanes 1:4); HPLC analysis: 58% ee [Daicel Chiralcel OD-H column; 1.0 mL/min; solvent system: 1% isopropanol in hexane; retention times: 15.4 min (major), 17.7 min (minor)]; $[\alpha]_D^{24}$ = 51.6 (c = 1.5, CH_2Cl_2); IR (thin film) 3080, 3060, 2955, 1767, 1729, 1497, 1434, 1262, 1215, 1104, 738, 697 cm^{-1}; ^1H NMR (400 MHz, $CDCl_3$, TMS, Major isomer): δ 7.44-7.39 (m, 2H), 7.36-7.24 (m, 3H), 7.16-7.00 (m, 6H), 6.79 (d, *J* = 7.3 Hz, 2H), 6.61 (d, *J* = 7.4 Hz, 2H), 4.52 (dd, *J* = 13.6 & 5.7 Hz, 1H), 3.87 (s, 3H), 3.72 (s, 3H), 3.06 (t, *J* = 13.5 Hz, 1H), 2.92 (dd, *J* = 13.3 & 5.7 Hz, 1H); ^{13}C NMR (100 MHz, $CDCl_3$, Major isomer): δ 207.2, 167.5, 167.3, 142.0, 139.9, 138.3, 130.5, 129.3, 128.9, 128.3, 128.1, 127.7, 127.5, 127.3, 127.2, 69.01, 69.0, 53.7, 53.6, 47.6, 34.4; $(M + Na)^+$ HRMS m/z calcd for $(C_{27}H_{24}NaO_5)^+$: 451.1521; found: 451.1521.

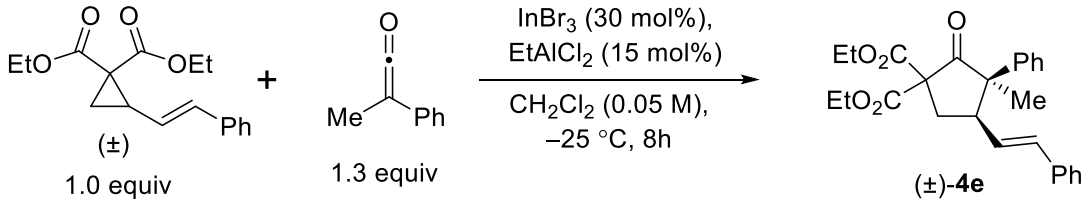


Diethyl (3*R*,4*R*)-3-ethyl-2-oxo-3,4-diphenylcyclopentane-1,1-dicarboxylate (4c): Following the general procedure, cyclopropane (*S*)-**1c** (85 mg, 0.33 mmol) solution in dichloromethane (2.0 mL) was added to a stirring suspension of $InBr_3$ (34 mg, 0.096 mmol) in dichloromethane (3.0 mL) at –25 °C. To this reaction mixture, $EtAlCl_2$ (1.0 M solution in hexanes) (0.048 mL, 0.048 mmol) was added dropwise. A solution of ethylphenylketene (62 mg, 0.42 mmol) in dichloromethane (1.0 ml) was added over 4 h to the reaction mixture at –25 °C. Elution with 3% EtOAc/hexanes through regular silica gel column afforded **4c** as a colorless gum (60 mg of major isomer and 72 mg as mixture of isomers, 99%). R_f = 0.5 (EtOAc/hexanes 1:9); dr = 2:1 (by crude GC-MS analysis); HPLC analysis: 98% ee [Daicel Chiralcel OD-H column; 1.0 mL/min; solvent system: 1% isopropanol in hexane; retention times: 9.4 min (major), 11.0 min (minor)]; $[\alpha]_D^{24}$ = –98 (c = 3.8, CH_2Cl_2); IR (thin film) 3030, 2980, 1765, 1721, 1497, 1448, 1251, 1198, 1011, 862, 775, 700 cm^{-1}; ^1H NMR (400 MHz, $CDCl_3$, TMS, Major isomer): δ 7.20-7.06 (m, 4H), 7.06-6.99 (m, 2H), 6.72 (d, *J* = 7.4 Hz, 2H), 6.56 (d, *J* = 7.4 Hz, 2H), 4.41-4.29 (m, 4H), 3.48 (dd, *J* = 13.9 & 5.5 Hz, 1H), 2.90 (t, *J* = 13.7 Hz, 1H), 2.76 (dd, *J* = 13.2 & 5.4 Hz, 1H) 2.20-2.09 (m, 1H), 2.04-1.93 (m, 1H), 1.38 (t, *J* = 7.2 Hz, 3H), 1.34 (t, *J* = 7.1 Hz, 3H), 0.97 (t, *J* = 7.4 Hz, 3H); ^{13}C NMR (100 MHz, $CDCl_3$, Major isomer): δ 210.1, 167.1, 166.8, 138.6, 138.0, 129.0, 128.7, 128.0, 127.7,

127.3, 126.9, 70.1, 63.3, 62.83, 62.8, 50.0, 34.2, 29.9, 14.3, 14.2, 9.0; $(M + H)^+$ HRMS m/z calcd for $(C_{25}H_{29}O_5)^+$: 409.2015; found: 409.2015.

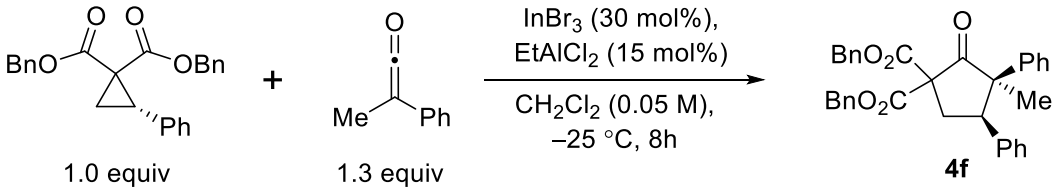


Diethyl (3*S*,4*S*)-3-ethyl-2-oxo-3,4-diphenylcyclopentane-1,1-dicarboxylate (4d): Following the general procedure, cyclopropane (*R*)-**1c**/*ent*-**1c** (85 mg, 0.33 mmol) solution in dichloromethane (2.0 mL) was added to a stirring suspension of $InBr_3$ (34 mg, 0.096 mmol) in dichloromethane (3.0 mL) at –25 °C. To this reaction mixture, $EtAlCl_2$ (1.0 M solution in hexanes) (0.048 mL, 0.048 mmol) was added dropwise. A solution of ethylphenylketene (62 mg, 0.42 mmol) in dichloromethane (1.0 ml) was added over 4 h to the reaction mixture at –25 °C. Elution with 3% EtOAc/hexanes through regular silica gel column afforded **4d** as a colorless gum (59 mg of major isomer and 72 mg as mixture of isomers, 99%). R_f = 0.5 (EtOAc/hexanes 1:9); dr = 2:1 (by crude GC-MS analysis); HPLC analysis: 99% ee [Daicel Chiralcel OD-H column; 1.0 mL/min; solvent system: 1% isopropanol in hexane; retention times: 9.8 min (minor), 10.5 min (major)]; $[\alpha]_D^{24}$ = 102 (c = 1.5, CH_2Cl_2); IR (thin film) 3030, 2979, 1765, 1718, 1497, 1449, 1250, 1197, 1008, 863, 775, 701 cm^{-1}; ^1H NMR (400 MHz, $CDCl_3$, TMS, Major isomer): δ 7.20-7.06 (m, 4H), 7.06-6.99 (m, 2H), 6.72 (d, *J* = 7.4 Hz, 2H), 6.56 (d, *J* = 7.4 Hz, 2H), 4.41-4.29 (m, 4H), 3.48 (dd, *J* = 13.9 & 5.5 Hz, 1H), 2.90 (t, *J* = 13.7 Hz, 1H), 2.76 (dd, *J* = 13.1 & 5.4 Hz, 1H) 2.20-2.09 (m, 1H), 2.04-1.93 (m, 1H), 1.38 (t, *J* = 7.1 Hz, 3H), 1.34 (t, *J* = 7.2 Hz, 3H), 0.97 (t, *J* = 7.4 Hz, 3H); ^{13}C NMR (100 MHz, $CDCl_3$, Major isomer): δ 210.1, 167.1, 166.8, 138.6, 138.0, 129.0, 128.7, 128.0, 127.7, 127.3, 126.9, 70.1, 63.3, 62.8, 62.7, 50.0, 34.2, 29.9, 14.3, 14.2, 9.0; $(M + H)^+$ HRMS m/z calcd for $(C_{25}H_{29}O_5)^+$: 409.2015; found: 409.2015.

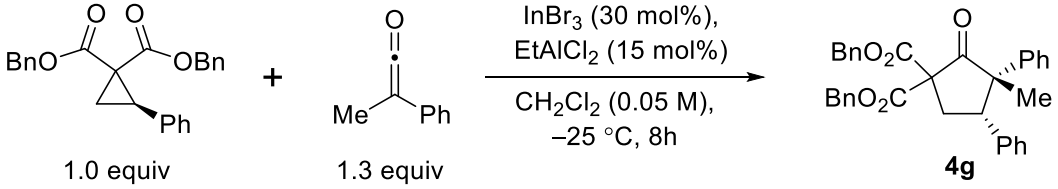


Diethyl 3-methyl-2-oxo-3-phenyl-4-((*E*)-styryl)cyclopentane-1,1-dicarboxylate (4e): Following the general procedure, cyclopropane (±)-**1d** (86 mg, 0.30 mmol) solution in dichloromethane (2.0 mL) was added to a stirring suspension of $InBr_3$ (32 mg, 0.09 mmol) in dichloromethane (3.0 mL) at –25 °C. To this reaction mixture, $EtAlCl_2$ (1.0 M solution in hexanes) (0.045 mL, 0.045 mmol) was added dropwise. A solution of methylphenylketene (51 mg, 0.39 mmol) in dichloromethane (1.0 ml) was added over 4 h to the reaction mixture at –25 °C. Elution with 4% EtOAc/hexanes through regular silica gel column afforded **4e** as a colorless gum (22 mg of major isomer and 86 mg as mixture of isomers, 86%). R_f = 0.45 (EtOAc/hexanes 1:9); dr = 1.5:1 (by crude GC-MS analysis); IR (thin film) 3059, 3027, 2980, 1765, 1725, 1496, 1446, 1367, 1251, 1186, 1011, 858, 748, 696 cm^{-1}; ^1H NMR (400 MHz, $CDCl_3$, TMS, Major isomer): δ 7.32-7.13 (m, 8H), 7.11-7.05 (m, 2H), 6.46 (d, *J* = 15.7 Hz, 1H), 5.42 (dd, *J* = 15.8 & 8.8 Hz, 1H), 4.41-4.27 (m, 4H), 2.92-2.82 (m, 1H), 2.75-2.61 (m, 2H), 1.57 (s, 3H), 1.34 (t, *J* = 7.2 Hz, 6H); ^{13}C NMR (100 MHz, $CDCl_3$, Major isomer): δ

211.0, 167.4, 166.8, 140.2, 137.1, 132.1, 128.8, 128.6, 128.3, 128.0, 127.7, 127.3, 126.5, 69.5, 62.9, 62.8, 58.4, 50.9, 35.9, 24.3, 14.2 (2-carbons); $(M + H)^+$ HRMS m/z calcd for $(C_{26}H_{29}O_5)^+$: 421.2015; found: 421.2019.

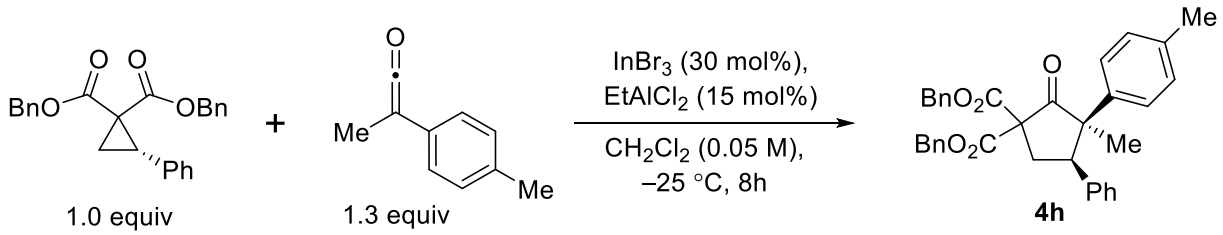


Dibenzyl (3*R*,4*R*)-3-methyl-2-oxo-3,4-diphenylcyclopentane-1,1-dicarboxylate (4f): Following the general procedure, cyclopropane (*S*)-**1e** (124 mg, 0.32 mmol) solution in dichloromethane (2.0 mL) was added to a stirring suspension of $InBr_3$ (34 mg, 0.096 mmol) in dichloromethane (3.0 mL) at –25 °C. To this reaction mixture, $EtAlCl_2$ (1.0 M solution in hexanes) (0.048 mL, 0.048 mmol) was added dropwise. A solution of methylphenylketene (55 mg, 0.42 mmol) in dichloromethane (1.0 ml) was added over 4 h to the reaction mixture at –25 °C. Elution with 3% EtOAc/hexanes through regular silica gel column afforded **4f** as a colorless gum (105 mg of major isomer and 48 mg as mixture of isomers, 92%). R_f = 0.55 (EtOAc/hexanes 1:9); dr = 3:1 (by crude GC-MS analysis); HPLC analysis: >99% ee [Daicel Chiralcel OD-H column; 1.0 mL/min; solvent system: 4% isopropanol in hexane; retention times: 15.8 min (major), 18.6 min (minor)]; $[\alpha]_D^{24}$ = –90 (c = 1.4, CH_2Cl_2); IR (thin film) 3089, 3063, 2960, 1765, 1728, 1497, 1454, 1373, 1262, 1232, 1192, 1174, 962, 735, 695 cm^{-1}; ^1H NMR (400 MHz, $CDCl_3$, TMS, Major isomer): δ 7.41-7.29 (m, 10H), 7.17-7.01 (m, 4H), 6.93 (t, *J* = 7.9 Hz, 2H), 6.65 (d, *J* = 7.2 Hz, 2H), 6.51 (d, *J* = 7.4 Hz, 2H), 5.38-5.17 (m, 4H), 3.25 (dd, *J* = 14.2 & 5.2 Hz, 1H), 3.03 (t, *J* = 14.0 Hz, 1H), 2.73 (dd, *J* = 13.3 & 5.2 Hz, 1H), 1.52 (s, 3H); ^{13}C NMR (100 MHz, $CDCl_3$, Major isomer): δ 210.6, 167.3, 166.5, 139.9, 137.5, 135.3, 135.1, 128.9 (2-carbons), 128.8, 128.7, 128.63, 128.6, 128.4, 128.0, 127.9, 127.8, 127.4, 127.0, 69.8, 68.5, 68.4, 59.2, 52.7, 34.7, 24.3; $(M + H)^+$ HRMS m/z calcd for $(C_{34}H_{31}O_5)^+$: 519.2171; found: 519.2170.

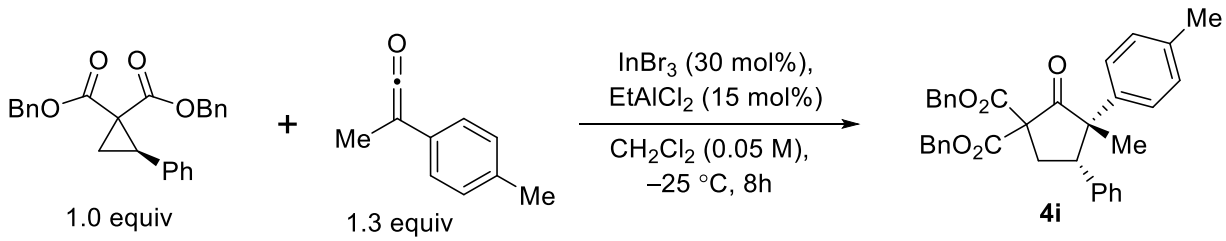


Dibenzyl (3*S*,4*S*)-3-methyl-2-oxo-3,4-diphenylcyclopentane-1,1-dicarboxylate (4g): Following the general procedure, cyclopropane (*R*)-**1e**/*ent*-**1e** (124 mg, 0.32 mmol) solution in dichloromethane (2.0 mL) was added to a stirring suspension of $InBr_3$ (34 mg, 0.096 mmol) in dichloromethane (3.0 mL) at –25 °C. To this reaction mixture, $EtAlCl_2$ (1.0 M solution in hexanes) (0.048 mL, 0.048 mmol) was added dropwise. A solution of methylphenylketene (55 mg, 0.42 mmol) in dichloromethane (1.0 ml) was added over 4 h to the reaction mixture at –25 °C. Elution with 3% EtOAc/hexanes through regular silica gel column afforded **4g** as a colorless gum (103 mg of major isomer and 53 mg as mixture of isomers, 94%). R_f = 0.55 (EtOAc/hexanes 1:9); dr = 3:1 (by crude GC-MS analysis); HPLC analysis: 99% ee [Daicel Chiralcel OD-H column; 1.0 mL/min; solvent system: 4% isopropanol in hexane; retention times: 16.1 min (minor), 18.1 min (minor)]; $[\alpha]_D^{24}$ = 88 (c =

1.0, CH_2Cl_2); IR (thin film) 3089, 3062, 2959, 1765, 1725, 1498, 1455, 1373, 1238, 1192, 1174, 961, 737, 695 cm^{-1}; ^1H NMR (400 MHz, $CDCl_3$, TMS, Major isomer): δ 7.42-7.29 (m, 10H), 7.18-7.02 (m, 4H), 6.93 (t, *J* = 8.0 Hz, 2H), 6.65 (d, *J* = 7.2 Hz, 2H), 6.51 (d, *J* = 7.4 Hz, 2H), 5.38-5.17 (m, 4H), 3.25 (dd, *J* = 14.3 & 5.3 Hz, 1H), 3.03 (t, *J* = 14.0 Hz, 1H), 2.73 (dd, *J* = 13.3 & 5.2 Hz, 1H), 1.52 (s, 3H); ^{13}C NMR (100 MHz, $CDCl_3$, Major isomer): δ 210.6, 167.3, 166.5, 139.9, 137.5, 135.3, 135.1, 128.9 (2-carbons), 128.8, 128.7, 128.64, 128.6, 128.4, 128.1, 127.9, 127.8, 127.4, 127.0, 69.8, 68.5, 68.4, 59.2, 52.7, 34.7, 24.3; $(M + Na)^+$ HRMS m/z calcd for $(C_{34}H_{30}NaO_5)^+$: 541.1991; found: 541.1992.

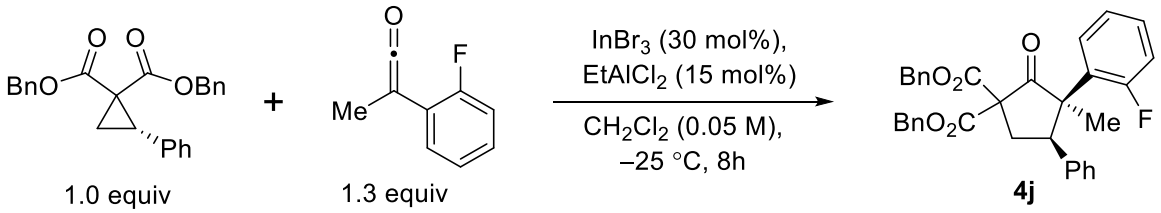


Dibenzyl (3*R*,4*R*)-3-methyl-2-oxo-4-phenyl-3-(*p*-tolyl)cyclopentane-1,1-dicarboxylate (4h): Following the general procedure, cyclopropane (*S*)-**1e** (77 mg, 0.20 mmol) solution in dichloromethane (1.5 mL) was added to a stirring suspension of $InBr_3$ (21 mg, 0.06 mmol) in dichloromethane (1.75 mL) at –25 °C. To this reaction mixture, $EtAlCl_2$ (1.0 M solution in hexanes) (0.03 mL, 0.03 mmol) was added dropwise. A solution of methyl-*p*-tolylketene (38 mg, 0.26 mmol) in dichloromethane (0.75 ml) was added over 4 h to the reaction mixture at –25 °C. Elution with 3% EtOAc/hexanes through regular silica gel column afforded **4h** as a colorless gum (44 mg of major isomer and 45 mg as mixture of isomers, 84%). R_f = 0.55 (EtOAc/hexanes 1:9); dr = 3:1 (by crude GC-MS analysis); HPLC analysis: >99% ee [Daicel Chiralcel AS-H column; 1.0 mL/min; solvent system: 1% isopropanol in hexane; retention times: 14.5 min (major), 19.4 min (minor)]; $[\alpha]_D^{24}$ = –83 (c = 2.0, CH_2Cl_2); IR (thin film) 3090, 3063, 2964, 2922, 1765, 1725, 1455, 1373, 1237, 1192, 1174, 961, 735, 696 cm^{-1}; ^1H NMR (400 MHz, $CDCl_3$, TMS, Major isomer): δ 7.42-7.27 (m, 10H), 7.18-7.06 (m, 3H), 6.75 (d, *J* = 8.0 Hz, 2H), 6.68 (d, *J* = 7.1 Hz, 2H), 6.38 (d, *J* = 8.2 Hz, 2H), 5.37-5.16 (m, 4H), 3.24 (dd, *J* = 14.3 & 5.2 Hz, 1H), 3.02 (t, *J* = 13.9 Hz, 1H), 2.71 (dd, *J* = 13.3 & 5.2 Hz, 1H), 2.18 (s, 3H), 1.50 (s, 3H); ^{13}C NMR (100 MHz, $CDCl_3$, Major isomer): δ 210.6, 167.3, 166.5, 137.7, 136.8, 136.6, 135.3, 135.1, 128.83 (2-carbons), 128.8 (2-carbons), 128.58, 128.56, 128.5, 128.3, 128.0, 127.8, 127.3, 69.7, 68.41, 68.35, 58.9, 52.5, 34.7, 24.4, 21.1; $(M + Na)^+$ HRMS m/z calcd for $(C_{35}H_{32}NaO_5)^+$: 555.2147; found: 555.2145.

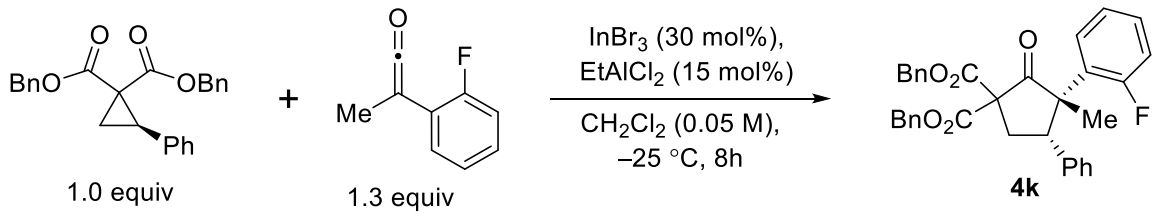


Dibenzyl (3*S*,4*S*)-3-methyl-2-oxo-4-phenyl-3-(*p*-tolyl)cyclopentane-1,1-dicarboxylate (4i): Following the general procedure, cyclopropane (*R*)-**1e**/*ent*-**1e** (77 mg, 0.20 mmol) solution in dichloromethane (1.5 mL) was added to a stirring suspension of $InBr_3$ (21 mg, 0.06 mmol) in dichloromethane (1.75 mL) at –25 °C. To this reaction mixture, $EtAlCl_2$ (1.0

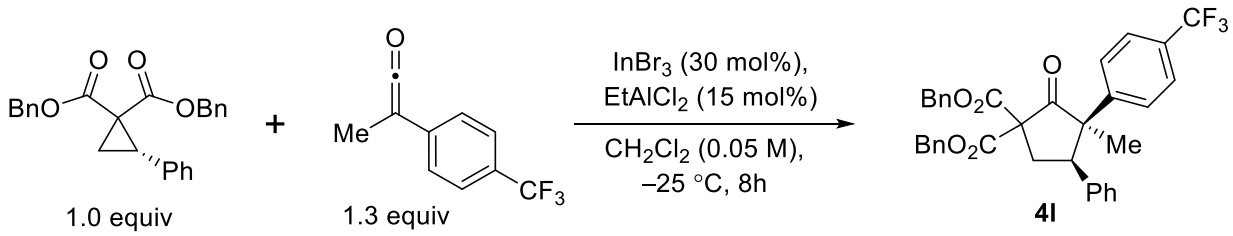
M solution in hexanes) (0.03 mL, 0.03 mmol) was added dropwise. A solution of methyl-*p*-tolylketene (38 mg, 0.26 mmol) in dichloromethane (0.75 ml) was added over 4 h to the reaction mixture at –25 °C. Elution with 3% EtOAc/hexanes through regular silica gel column afforded **4i** as a colorless gum (36 mg of major isomer and 56 mg as mixture of isomers, 87%). R_f = 0.55 (EtOAc/hexanes 1:9); dr = 3:1 (by crude GC-MS analysis); HPLC analysis: 99% ee [Daicel Chiralcel AS-H column; 1.0 mL/min; solvent system: 1% isopropanol in hexane; retention times: 14.2 min (minor), 17.8 min (major)]; $[\alpha]_D^{24}$ = 75 (c = 3.0, CH_2Cl_2); IR (thin film) 3090, 3032, 2970, 1765, 1726, 1454, 1372, 1237, 1193, 1174, 961, 734, 696 cm^{-1}; ^1H NMR (400 MHz, $CDCl_3$, TMS, Major isomer): δ 7.42-7.28 (m, 10H), 7.18-7.06 (m, 3H), 6.75 (d, *J* = 8.0 Hz, 2H), 6.68 (d, *J* = 7.1 Hz, 2H), 6.38 (d, *J* = 8.2 Hz, 2H), 5.37-5.16 (m, 4H), 3.24 (dd, *J* = 14.3 & 5.2 Hz, 1H), 3.02 (t, *J* = 14.0 Hz, 1H), 2.71 (dd, *J* = 13.3 & 5.2 Hz, 1H), 2.18 (s, 3H), 1.49 (s, 3H); ^{13}C NMR (100 MHz, $CDCl_3$, Major isomer): δ 210.6, 167.3, 166.5, 137.7, 136.8, 136.6, 135.3, 135.1, 128.83 (2-carbons), 128.8 (2-carbons), 128.58, 128.56, 128.5, 128.3, 128.0, 127.8, 127.3, 69.7, 68.41, 68.35, 58.9, 52.5, 34.7, 24.4, 21.1; $(M + Na)^+$ HRMS m/z calcd for $(C_{35}H_{32}NaO_5)^+$: 555.2147; found: 555.2147.



Dibenzyl (3*R*,4*R*)-3-(2-fluorophenyl)-3-methyl-2-oxo-4-phenylcyclopentane-1,1-dicarboxylate (4j): Following the general procedure, cyclopropane (*S*)-**1e** (77 mg, 0.20 mmol) solution in dichloromethane (1.5 mL) was added to a stirring suspension of $InBr_3$ (21 mg, 0.06 mmol) in dichloromethane (1.75 mL) at –25 °C. To this reaction mixture, $EtAlCl_2$ (1.0 M solution in hexanes) (0.03 mL, 0.03 mmol) was added dropwise. A solution of (2-fluorophenyl)methylketene (40 mg, 0.26 mmol) in dichloromethane (0.75 ml) was added over 4 h to the reaction mixture at –25 °C. Elution with 4% EtOAc/hexanes through regular silica gel column afforded **4j** as a colorless gum (40 mg of major isomer and 53 mg as mixture of isomers, 87%). R_f = 0.5 (EtOAc/hexanes 1:9); dr = 2.3:1 (by crude GC-MS analysis); HPLC analysis: >99% ee [Daicel Chiralcel OD-H column; 1.0 mL/min; solvent system: 2% isopropanol in hexane; retention times: 29.1 min (major)]; $[\alpha]_D^{24}$ = –70 (c = 2.0, CH_2Cl_2); IR (thin film) 2956, 2918, 2850, 1730, 1489, 1454, 1262, 1225, 961, 736, 695 cm^{-1}; ^1H NMR (400 MHz, $CDCl_3$, TMS, Major isomer): δ 7.43-7.23 (m, 10H), 7.14-6.99 (m, 4H), 6.85-6.75 (m, 3H), 6.70 (td, *J* = 7.8 & 1.1 Hz, 1H), 6.49 (td, *J* = 7.9 & 1.4 Hz, 1H), 5.37-5.15 (m, 4H), 3.36 (dd, *J* = 14.1 & 5.7 Hz, 1H), 3.23 (td, *J* = 13.7 & 2.0 Hz, 1H), 2.69 (ddd, *J* = 13.4, 5.7 & 2.2 Hz, 1H), 1.62 (s, 3H); ^{13}C NMR (100 MHz, $CDCl_3$, Major isomer): δ 207.9, 167.8, 165.9, 159.9 (d, *J* = 244.0 Hz, 1C), 137.8, 135.6, 135.0, 129.8 (d, *J* = 4.9 Hz, 1C), 129.0 (d, *J* = 8.9 Hz, 1C), 128.85, 128.8, 128.7, 128.5, 128.4, 128.3, 128.2, 128.1, 127.9 (d, *J* = 14.1 Hz, 1C), 127.4, 124.0 (d, *J* = 2.7 Hz, 1C), 115.6 (d, *J* = 24.4 Hz, 1C), 69.2 (d, *J* = 2.3 Hz, 1C), 68.4, 68.1, 56.0 (d, *J* = 2.3 Hz, 1C), 52.3, 35.0 (d, *J* = 3.5 Hz, 1C), 24.6; $(M + H)^+$ HRMS m/z calcd for $(C_{34}H_{30}FO_5)^+$: 537.2077; found: 537.2075.

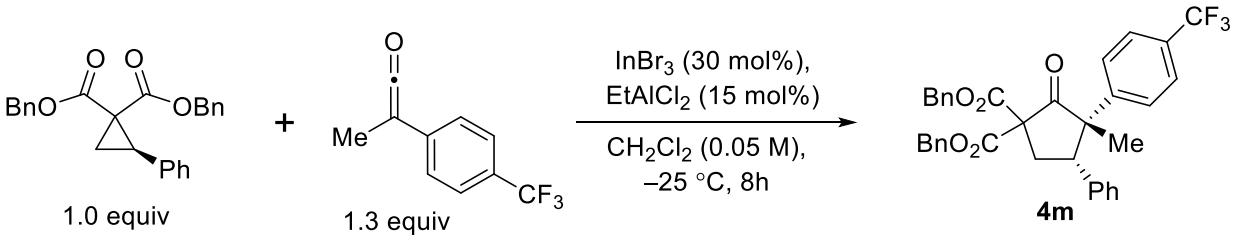


Dibenzyl (3*S*,4*S*)-3-(2-fluorophenyl)-3-methyl-2-oxo-4-phenylcyclopentane-1,1-dicarboxylate (4k): Following the general procedure, cyclopropane (*R*)-**1e**/*ent*-**1e** (77 mg, 0.20 mmol) solution in dichloromethane (1.5 mL) was added to a stirring suspension of $InBr_3$ (21 mg, 0.06 mmol) in dichloromethane (1.75 mL) at –25 °C. To this reaction mixture, $EtAlCl_2$ (1.0 M solution in hexanes) (0.03 mL, 0.03 mmol) was added dropwise. A solution of (2-fluorophenyl)methylketene (40 mg, 0.26 mmol) in dichloromethane (0.75 ml) was added over 4 h to the reaction mixture at –25 °C. Elution with 4% EtOAc/hexanes through regular silica gel column afforded **4k** as a colorless gum (44 mg of major isomer and 52 mg as mixture of isomers, 90%). R_f = 0.5 (EtOAc/hexanes 1:9); dr = 2.2:1 (by crude GC-MS analysis); HPLC analysis: >99% ee [Daicel Chiralcel OD-H column; 1.0 mL/min; solvent system: 2% isopropanol in hexane; retention times: 30.0 min (minor), 31.6 min (major)]; $[\alpha]_D^{24}$ = 74 (c = 1.8, CH_2Cl_2); IR (thin film) 2956, 2918, 2850, 1730, 1489, 1454, 1262, 1225, 961, 736, 695 cm^{-1}; ^1H NMR (400 MHz, $CDCl_3$, TMS, Major isomer): δ 7.43-7.25 (m, 10H), 7.14-7.00 (m, 4H), 6.85-6.75 (m, 3H), 6.70 (td, *J* = 7.6 & 1.0 Hz, 1H), 6.49 (td, *J* = 7.9 & 1.3 Hz, 1H), 5.37-5.15 (m, 4H), 3.36 (dd, *J* = 14.1 & 5.7 Hz, 1H), 3.23 (td, *J* = 13.9 & 2.0 Hz, 1H), 2.69 (ddd, *J* = 13.4, 5.7 & 2.2 Hz, 1H), 1.62 (s, 3H); ^{13}C NMR (100 MHz, $CDCl_3$, Major isomer): δ 207.9, 167.8, 165.9, 160.0 (d, *J* = 244.0 Hz, 1C), 137.9, 135.6, 135.0, 129.8 (d, *J* = 5.0 Hz, 1C), 129.0 (d, *J* = 9.0 Hz, 1C), 128.85, 128.8, 128.7, 128.5, 128.4, 128.3, 128.2, 128.1, 127.9 (d, *J* = 14.1 Hz, 1C), 127.4, 124.0 (d, *J* = 2.7 Hz, 1C), 115.6 (d, *J* = 24.5 Hz, 1C), 69.2 (d, *J* = 2.2 Hz, 1C), 68.4, 68.1, 56.0 (d, *J* = 2.1 Hz, 1C), 52.3, 35.0 (d, *J* = 3.5 Hz, 1C), 24.6; $(M + H)^+$ HRMS m/z calcd for $(C_{34}H_{30}FO_5)^+$: 537.2077; found: 537.2082.

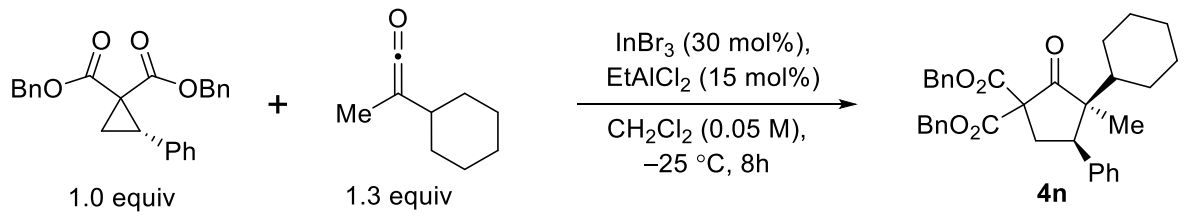


Dibenzyl (3*R*,4*R*)-3-methyl-2-oxo-4-phenyl-3-(4-(trifluoromethyl)phenyl)cyclopentane-1,1-dicarboxylate (4l): Following the general procedure, cyclopropane (*S*)-**1e** (77 mg, 0.20 mmol) solution in dichloromethane (1.5 mL) was added to a stirring suspension of $InBr_3$ (21 mg, 0.06 mmol) in dichloromethane (1.75 mL) at –25 °C. To this reaction mixture, $EtAlCl_2$ (1.0 M solution in hexanes) (0.03 mL, 0.03 mmol) was added dropwise. A solution of methyl(4-(trifluoromethyl)phenyl)ketene (52 mg, 0.26 mmol) in dichloromethane (0.75 ml) was added over 4 h to the reaction mixture at –25 °C. Elution with 4% EtOAc/hexanes through regular silica gel column afforded **4l** as a colorless gum (32 mg of major isomer and 66 mg as mixture of isomers, 84%). R_f = 0.5 (EtOAc/hexanes 1:9); dr = 3:1 (by crude GC-MS analysis); HPLC analysis: 92% ee [Daicel Chiralcel OD-H column; 1.0 mL/min; solvent system: 3% isopropanol in hexane; retention times: 17.4 min (major), 20.2 min (minor)];

$[\alpha]_D^{24}$ = –55 (c = 1.2, CH_2Cl_2); IR (thin film) 3034, 2965, 2928, 1766, 1727, 1325, 1262, 1199, 1166, 907, 736, 696 cm^{-1}; ^1H NMR (400 MHz, $CDCl_3$, TMS, Major isomer): δ 7.42-7.29 (m, 10H), 7.20-7.14 (m, 3H), 7.10 (t, *J* = 7.7 Hz, 2H), 6.65 (d, *J* = 7.3 Hz, 2H), 6.62 (d, *J* = 8.3 Hz, 2H), 5.38-5.18 (m, 4H), 3.28 (dd, *J* = 14.2 & 5.4 Hz, 1H), 2.97 (t, *J* = 13.9 Hz, 1H), 2.77 (dd, *J* = 13.4 & 5.4 Hz, 1H), 1.52 (s, 3H); ^{13}C NMR (100 MHz, $CDCl_3$, Major isomer): δ 210.0, 166.9, 166.5, 144.0, 136.9, 135.1, 135.0, 129.3 (q, *J* = 32.7 Hz, 1C), 129.1, 128.92, 128.9, 128.8 (2-carbons), 128.6, 128.5, 128.4, 128.3, 127.8, 124.7 (q, *J* = 3.8 Hz, 1C), 124.2 (q, *J* = 272.0 Hz, 1C), 69.8, 68.6 (2-carbons), 59.1, 52.6, 34.6, 24.3; $(M + Na)^+$ HRMS m/z calcd for $(C_{35}H_{29}NaF_3O_5)^+$: 609.1865; found: 609.1863.

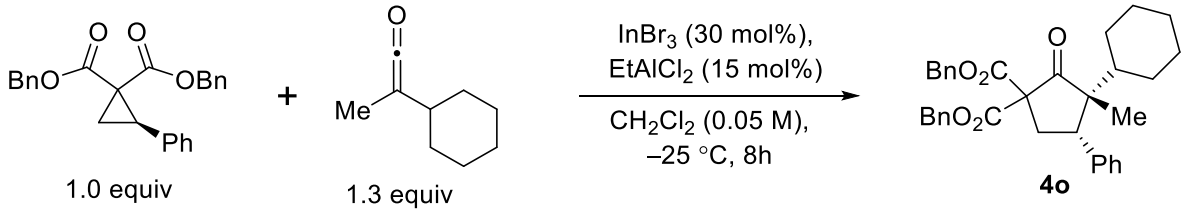


Dibenzyl (3*S*,4*S*)-3-methyl-2-oxo-4-phenyl-3-(4-(trifluoromethyl)phenyl)cyclopentane-1,1-dicarboxylate (4m): Following the general procedure, cyclopropane (*R*)-**1e**/*ent*-**1e** (77 mg, 0.20 mmol) solution in dichloromethane (1.5 mL) was added to a stirring suspension of $InBr_3$ (21 mg, 0.06 mmol) in dichloromethane (1.75 mL) at –25 °C. To this reaction mixture, $EtAlCl_2$ (1.0 M solution in hexanes) (0.03 mL, 0.03 mmol) was added dropwise. A solution of methyl(4-(trifluoromethyl)phenyl)ketene (52 mg, 0.26 mmol) in dichloromethane (0.75 ml) was added over 4 h to the reaction mixture at –25 °C. Elution with 4% EtOAc/hexanes through regular silica gel column afforded **4m** as a colorless gum (42 mg of major isomer and 61 mg as mixture of isomers, 88%). R_f = 0.5 (EtOAc/hexanes 1:9); dr = 3:1 (by crude GC-MS analysis); HPLC analysis: 92% ee [Daicel Chiralcel OD-H column; 1.0 mL/min; solvent system: 3% isopropanol in hexane; retention times: 18.5 min (minor), 19.9 min (major)]; $[\alpha]_D^{24}$ = 72 (c = 1.3, CH_2Cl_2); IR (thin film) 3034, 2965, 1766, 1729, 1325, 1263, 1199, 1166, 907, 736, 697 cm^{-1}; ^1H NMR (400 MHz, $CDCl_3$, TMS, Major isomer): δ 7.42-7.29 (m, 10H), 7.20-7.13 (m, 3H), 7.10 (t, *J* = 7.6 Hz, 2H), 6.65 (d, *J* = 7.3 Hz, 2H), 6.62 (d, *J* = 8.3 Hz, 2H), 5.38-5.18 (m, 4H), 3.28 (dd, *J* = 14.2 & 5.3 Hz, 1H), 2.97 (t, *J* = 13.8 Hz, 1H), 2.77 (dd, *J* = 13.4 & 5.4 Hz, 1H), 1.52 (s, 3H); ^{13}C NMR (100 MHz, $CDCl_3$, Major isomer): δ 210.0, 166.9, 166.5, 144.0, 136.9, 135.1, 135.0, 129.3 (q, *J* = 32.5 Hz, 1C), 129.1, 128.92, 128.9, 128.8 (2-carbons), 128.6, 128.5, 128.4, 128.3, 127.8, 124.7 (q, *J* = 3.8 Hz, 1C), 124.2 (q, *J* = 272.0 Hz, 1C), 69.8, 68.6 (2-carbons), 59.1, 52.6, 34.6, 24.3; $(M + Na)^+$ HRMS m/z calcd for $(C_{35}H_{29}NaF_3O_5)^+$: 609.1865; found: 609.1865.

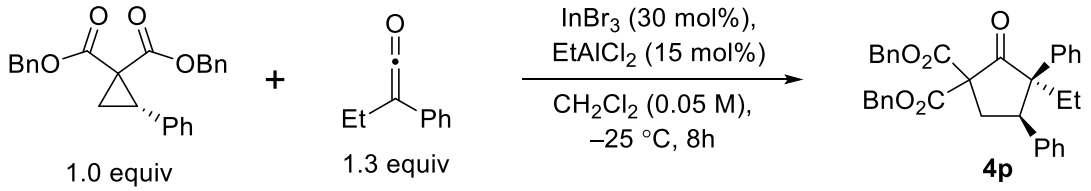


Dibenzyl (3*S*,4*R*)-3-cyclohexyl-3-methyl-2-oxo-4-phenylcyclopentane-1,1-dicarboxylate (4n): Following the general procedure, cyclopropane (*S*)-**1e** (77 mg, 0.20 mmol) solution in

dichloromethane (1.5 mL) was added to a stirring suspension of $InBr_3$ (21 mg, 0.06 mmol) in dichloromethane (1.75 mL) at –25 °C. To this reaction mixture, $EtAlCl_2$ (1.0 M solution in hexanes) (0.03 mL, 0.03 mmol) was added dropwise. A solution of cyclohexylphenylketene (36 mg, 0.26 mmol) in dichloromethane (0.75 ml) was added over 4 h to the reaction mixture at –25 °C. Elution with 3% EtOAc/hexanes through regular silica gel column afforded **4n** as a colorless gum (98 mg as inseparable mixture of isomers, 94%). R_f = 0.55 (EtOAc/hexanes 1:9); dr = 2.3:1 (by crude GC-MS analysis); $[\alpha]_D^{24}$ = –22 (c = 3.3, CH_2Cl_2); IR (thin film) 2925, 2852, 1730, 1498, 1452, 1374, 1260, 1189, 967, 735, 696 cm^{-1}; ^1H NMR (400 MHz, $CDCl_3$, TMS, Major isomer): δ 7.36-7.24 (m, 15H), 5.26-5.11 (m, 4H), 3.32-3.13 (m, 2H), 2.68 (dd, *J* = 12.9 & 5.4 Hz, 1H), 1.70-1.53 (m, 1H), 1.53-1.16 (m, 5H), 1.14 (s, 3H), 1.10-0.67 (m, 5H); ^{13}C NMR (100 MHz, $CDCl_3$, Major isomer): δ 209.2, 167.6, 166.5, 138.4, 135.3, 135.2, 129.7, 128.8, 128.73, 128.68, 128.6, 128.5, 128.4, 128.3, 127.5, 68.2, 68.1, 57.1, 50.8, 40.2, 33.7, 29.4, 28.6, 27.0, 26.2, 20.7; $(M + H)^+$ HRMS m/z calcd for $(C_{34}H_{37}O_5)^+$: 525.2641; found: 525.2641.

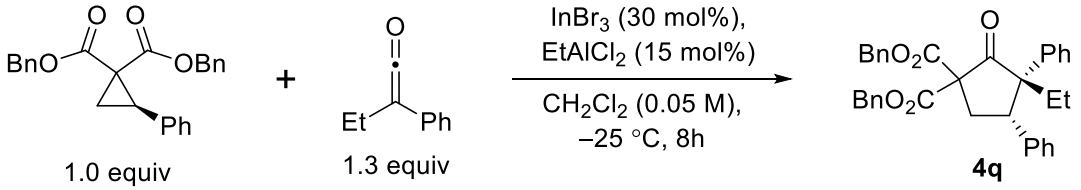


Dibenzyl (3*R*,4*S*)-3-cyclohexyl-3-methyl-2-oxo-4-phenylcyclopentane-1,1-dicarboxylate (4o): Following the general procedure, cyclopropane (*R*)-**1e**/*ent*-**1e** (77 mg, 0.20 mmol) solution in dichloromethane (1.5 mL) was added to a stirring suspension of $InBr_3$ (21 mg, 0.06 mmol) in dichloromethane (1.75 mL) at –25 °C. To this reaction mixture, $EtAlCl_2$ (1.0 M solution in hexanes) (0.03 mL, 0.03 mmol) was added dropwise. A solution of cyclohexylphenylketene (36 mg, 0.26 mmol) in dichloromethane (0.75 ml) was added over 4 h to the reaction mixture at –25 °C. Elution with 3% EtOAc/hexanes through regular silica gel column afforded **4o** as a colorless gum (96 mg as mixture of inseparable isomers, 92%). R_f = 0.55 (EtOAc/hexanes 1:9); dr = 2.2:1 (by crude GC-MS analysis); $[\alpha]_D^{24}$ = 21 (c = 4.3, CH_2Cl_2); IR (thin film) 2927, 2852, 1731, 1498, 1453, 1373, 1260, 1174, 967, 736, 696 cm^{-1}; ^1H NMR (400 MHz, $CDCl_3$, TMS, Major isomer): δ 7.36-7.23 (m, 15H), 5.26-5.11 (m, 4H), 3.32-3.13 (m, 2H), 2.67 (dd, *J* = 12.9 & 5.4 Hz, 1H), 1.73-1.53 (m, 1H), 1.53-1.16 (m, 5H), 1.14 (s, 3H), 1.10-0.67 (m, 5H); ^{13}C NMR (100 MHz, $CDCl_3$, Major isomer): δ 209.2, 167.6, 166.5, 138.4, 135.3, 135.2, 129.7, 128.8, 128.72, 128.67, 128.6, 128.5, 128.4, 128.3, 127.5, 68.2, 68.1, 57.1, 50.8, 40.2, 33.7, 29.4, 28.6, 27.0, 26.2, 20.7; $(M + H)^+$ HRMS m/z calcd for $(C_{34}H_{37}O_5)^+$: 525.2641; found: 525.2640.

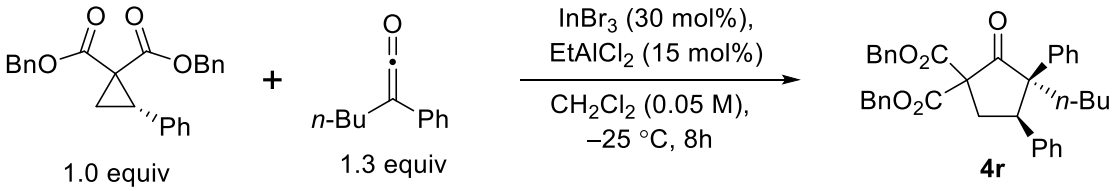


Dibenzyl (3*R*,4*R*)-3-ethyl-2-oxo-3,4-diphenylcyclopentane-1,1-dicarboxylate (4p): Following the general procedure, cyclopropane (*S*)-**1e** (125 mg, 0.32 mmol) solution in dichloromethane (2.0 mL) was added to a stirring suspension of $InBr_3$ (34 mg, 0.096 mmol)

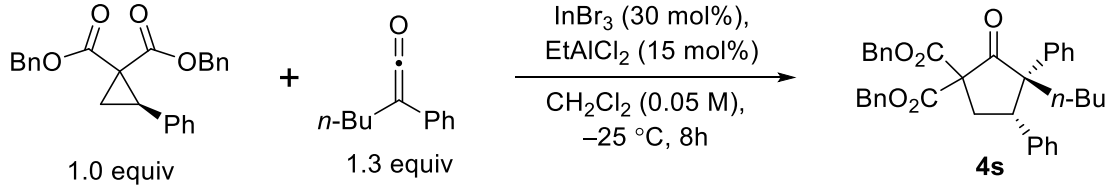
in dichloromethane (3.0 mL) at –25 °C. To this reaction mixture, $EtAlCl_2$ (1.0 M solution in hexanes) (0.048 mL, 0.048 mmol) was added dropwise. A solution of ethylphenylketene (62 mg, 0.42 mmol) in dichloromethane (1.0 ml) was added over 4 h to the reaction mixture at –25 °C. Elution with 4% EtOAc/hexanes through regular silica gel column afforded **4p** as a colorless gum (66 mg of major isomer and 85 mg as mixture of isomers, 88%). R_f = 0.5 (EtOAc/hexanes 1:9); dr = 3.2:1 (by crude GC-MS analysis); HPLC analysis: 98% ee [Daicel Chiralcel OD-H column; 1.0 mL/min; solvent system: 2% isopropanol in hexane; retention times: 18.5 min (minor), 19.9 min (major)]; $[\alpha]_D^{24}$ = –76 (c = 2.6, CH_2Cl_2); IR (thin film) 3033, 2969, 2933, 2881, 1763, 1729, 1498, 1455, 1374, 1257, 1239, 1173, 985, 773, 736 cm^{-1}; ^1H NMR (400 MHz, $CDCl_3$, TMS, Major isomer): δ 7.42-7.28 (m, 10H), 7.18-7.01 (m, 4H), 6.92 (t, *J* = 7.9 Hz, 2H), 6.64 (d, *J* = 7.4 Hz, 2H), 6.47 (d, *J* = 8.0 Hz, 2H), 5.36-5.19 (m, 4H), 3.40 (dd, *J* = 13.9 & 5.5 Hz, 1H), 2.89 (t, *J* = 13.6 Hz, 1H), 2.77 (dd, *J* = 13.2 & 5.5 Hz, 1H), 2.11-1.99 (m, 1H), 1.92-1.78 (m, 1H), 0.86 (t, *J* = 7.4 Hz, 3H); ^{13}C NMR (100 MHz, $CDCl_3$, Major isomer): δ 209.6, 166.8, 166.5, 138.4, 137.9, 135.3, 135.1, 129.0, 128.9, 128.81, 128.77, 128.69, 128.64, 128.63, 128.4, 128.0, 127.7, 127.3, 126.9, 70.1, 68.42, 68.36, 63.3, 50.1, 34.3, 29.9, 8.9; $(M + Na)^+$ HRMS m/z calcd for $(C_{35}H_{32}NaO_5)^+$: 555.2147; found: 555.2146.



Dibenzyl (3*S*,4*S*)-3-ethyl-2-oxo-3,4-diphenylcyclopentane-1,1-dicarboxylate (4q): Following the general procedure, cyclopropane (*R*)-**1e**/*ent*-**1e** (125 mg, 0.32 mmol) solution in dichloromethane (2.0 mL) was added to a stirring suspension of $InBr_3$ (34 mg, 0.096 mmol) in dichloromethane (3.0 mL) at –25 °C. To this reaction mixture, $EtAlCl_2$ (1.0 M solution in hexanes) (0.048 mL, 0.048 mmol) was added dropwise. A solution of ethylphenylketene (62 mg, 0.42 mmol) in dichloromethane (1.0 ml) was added over 4 h to the reaction mixture at –25 °C. Elution with 4% EtOAc/hexanes through regular silica gel column afforded **4q** as a colorless gum (62 mg of major isomer and 94 mg as mixture of isomers, 91%). R_f = 0.5 (EtOAc/hexanes 1:9); dr = 3:1 (by crude GC-MS analysis); HPLC analysis: 98% ee [Daicel Chiralcel OD-H column; 1.0 mL/min; solvent system: 2% isopropanol in hexane; retention times: 18.6 min (major), 21.8 min (minor)]; $[\alpha]_D^{24}$ = 73 (c = 2.6, CH_2Cl_2); IR (thin film) 3033, 2966, 2938, 2881, 1764, 1727, 1498, 1454, 1374, 1257, 1214, 1173, 985, 736, 697 cm^{-1}; ^1H NMR (400 MHz, $CDCl_3$, TMS, Major isomer): δ 7.41-7.29 (m, 10H), 7.18-7.01 (m, 4H), 6.92 (t, *J* = 7.8 Hz, 2H), 6.64 (d, *J* = 7.3 Hz, 2H), 6.47 (d, *J* = 7.6 Hz, 2H), 5.36-5.18 (m, 4H), 3.40 (dd, *J* = 13.9 & 5.4 Hz, 1H), 2.89 (t, *J* = 13.7 Hz, 1H), 2.77 (dd, *J* = 13.2 & 5.5 Hz, 1H), 2.11-1.99 (m, 1H), 1.92-1.79 (m, 1H), 0.86 (t, *J* = 7.3 Hz, 3H); ^{13}C NMR (100 MHz, $CDCl_3$, Major isomer): δ 209.7, 166.8, 166.5, 138.4, 137.9, 135.2, 135.1, 129.0, 128.9, 128.8, 128.77, 128.67, 128.64, 128.63, 128.4, 128.0, 127.7, 127.3, 126.9, 70.1, 68.42, 68.35, 63.2, 50.1, 34.3, 29.9, 8.9; $(M + Na)^+$ HRMS m/z calcd for $(C_{35}H_{32}NaO_5)^+$: 555.2147; found: 555.2148.

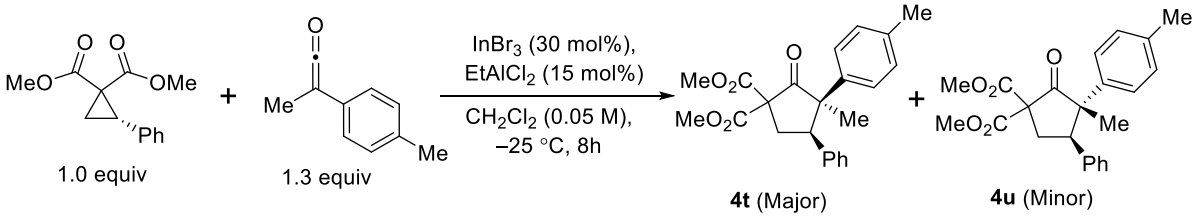


Dibenzyl (3*R*,4*R*)-3-butyl-2-oxo-3,4-diphenylcyclopentane-1,1-dicarboxylate (4r): Following the general procedure, cyclopropane (*S*)-**1e** (77 mg, 0.20 mmol) solution in dichloromethane (1.5 mL) was added to a stirring suspension of $InBr_3$ (21 mg, 0.06 mmol) in dichloromethane (1.75 mL) at –25 °C. To this reaction mixture, $EtAlCl_2$ (1.0 M solution in hexanes) (0.03 mL, 0.03 mmol) was added dropwise. A solution of *n*-butylphenylketene (45 mg, 0.26 mmol) in dichloromethane (0.75 ml) was added over 4 h to the reaction mixture at –25 °C. Elution with 3% EtOAc/hexanes through regular silica gel column afforded **4r** as a colorless gum (62 mg of major isomer and 41 mg as mixture of isomers, 92%). R_f = 0.55 (EtOAc/hexanes 1:9); dr = 3.2:1 (by crude GC-MS analysis); HPLC analysis: 99% ee [Daicel Chiralcel OD-H column; 1.0 mL/min; solvent system: 1% isopropanol in hexane; retention times: 14.9 min (minor), 16.1 min (major)]; $[\alpha]_D^{24}$ = –71 (c = 1.6, CH_2Cl_2); IR (thin film) 3032, 2955, 2931, 2871, 1762, 1731, 1498, 1455, 1375, 1239, 1171, 736, 696 cm^{-1}; ^1H NMR (400 MHz, $CDCl_3$, TMS, Major isomer): δ 7.41-7.29 (m, 10H), 7.17-7.01 (m, 4H), 6.91 (t, *J* = 8.0 Hz, 2H), 6.64 (d, *J* = 7.2 Hz, 2H), 6.47 (d, *J* = 8.0 Hz, 2H), 5.36-5.18 (m, 4H), 3.40 (dd, *J* = 13.9 & 5.4 Hz, 1H), 2.89 (t, *J* = 13.6 Hz, 1H), 2.76 (dd, *J* = 13.2 & 5.4 Hz, 1H), 2.03-1.92 (m, 1H), 1.83-1.71 (m, 1H), 1.57-1.43 (m, 1H), 1.27-1.13 (m, 2H), 1.10-0.94 (m, 1H), 0.80 (t, *J* = 7.4 Hz, 3H); ^{13}C NMR (100 MHz, $CDCl_3$, Major isomer): δ 209.7, 166.8, 166.6, 138.7, 137.9, 135.3, 135.1, 129.0, 128.9, 128.83, 128.77, 128.7, 128.6 (2-carbons), 128.4, 128.0, 127.7, 127.3, 126.8, 70.1, 68.43, 68.36, 62.9, 50.6, 37.1, 34.3, 26.2, 23.4, 14.0; $(M + Na)^+$ HRMS m/z calcd for $(C_{37}H_{36}NaO_5)^+$: 583.2460; found: 583.2462.



Dibenzyl (3*S*,4*S*)-3-butyl-2-oxo-3,4-diphenylcyclopentane-1,1-dicarboxylate (4s): Following the general procedure, cyclopropane (*R*)-**1e**/*ent*-**1e** (77 mg, 0.20 mmol) solution in dichloromethane (1.5 mL) was added to a stirring suspension of $InBr_3$ (21 mg, 0.06 mmol) in dichloromethane (1.75 mL) at –25 °C. To this reaction mixture, $EtAlCl_2$ (1.0 M solution in hexanes) (0.03 mL, 0.03 mmol) was added dropwise. A solution of *n*-butylphenylketene (45 mg, 0.26 mmol) in dichloromethane (0.75 ml) was added over 4 h to the reaction mixture at –25 °C. Elution with 3% EtOAc/hexanes through regular silica gel column afforded **4s** as a colorless gum (64 mg of major isomer and 41 mg as mixture of isomers, 94% yield). R_f = 0.55 (EtOAc/hexanes 1:9); dr = 3:1 (by crude GCMS); HPLC analysis: 98% ee [Daicel Chiralcel OD-H column; 1.0 mL/min; solvent system: 1% isopropanol in hexane; retention times: 14.2 min (major), 16.3 min (minor)]; $[\alpha]_D^{24}$ = 55 (c = 2.4, CH_2Cl_2); IR (thin film) 3032, 2956, 2872, 1762, 1730, 1498, 1455, 1375, 1240, 1172, 736, 696 cm^{-1}; ^1H NMR (400 MHz, $CDCl_3$, TMS, Major isomer): δ 7.41-7.30 (m, 10H), 7.17-7.01 (m, 4H), 6.91 (t, *J* = 8.0 Hz, 2H), 6.64 (d, *J* = 7.2 Hz, 2H), 6.47 (d, *J* = 7.6 Hz, 2H), 5.36-5.18 (m, 4H), 3.40 (dd, *J* = 13.9 & 5.4 Hz, 1H), 2.89 (t, *J* = 13.7 Hz, 1H), 2.76 (dd, *J* = 13.2 & 5.4 Hz, 1H), 2.03-1.92 (m, 1H), 1.83-1.71 (m, 1H), 1.57-1.43 (m, 1H), 1.27-1.13 (m, 2H), 1.10-0.94 (m, 1H), 0.80 (t,

J = 7.4 Hz, 3H); ^{13}C NMR (100 MHz, $CDCl_3$, Major isomer): δ 209.7, 166.8, 166.6, 138.7, 137.9, 135.3, 135.1, 129.0, 128.9, 128.83, 128.77, 128.7, 128.6 (2-carbons), 128.4, 128.0, 127.7, 127.3, 126.8, 70.1, 68.44, 68.37, 62.9, 50.6, 37.1, 34.3, 26.2, 23.4, 14.0; $(M + H)^+$ HRMS m/z calcd for $(C_{37}H_{37}O_5)^+$: 561.2641; found: 561.2642.

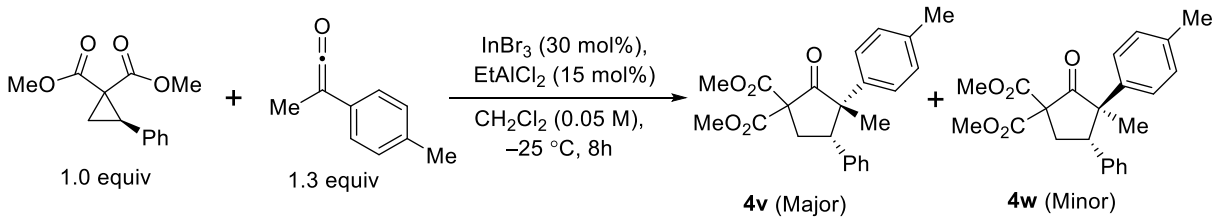


Following the general procedure, cyclopropane (*S*)-**1b** (200 mg, 0.85 mmol) solution in dichloromethane (5.0 mL) was added to a stirring suspension of $InBr_3$ (90 mg, 0.26 mmol) in dichloromethane (9.0 mL) at –25 °C. To this reaction mixture, $EtAlCl_2$ (1.0 M solution in hexanes) (0.128 mL, 0.128 mmol) was added dropwise. A solution of methyl-*p*-tolylketene (162 mg, 1.11 mmol) in dichloromethane (3.0 ml) was added over 4 h to the reaction mixture at –25 °C. Elution with 3% EtOAc/hexanes through regular silica gel column afforded 177 mg of **4t** (major isomer, 54%) and 145 mg of **4u** (minor isomer, 45%), both as a colorless gum (99%).

Dimethyl (3*R*,4*R*)-3-methyl-2-oxo-4-phenyl-3-(*p*-tolyl)cyclopentane-1,1-dicarboxylate (4t): R_f = 0.45 (EtOAc/hexanes 1:9); HPLC analysis: 89% ee [Daicel Chiralcel AD-H column; 1.0 mL/min; solvent system: 3% isopropanol in hexane; retention times: 8.8 min (major), 18.8 min (minor)]; $[\alpha]_D^{24}$ = –126 (c = 2.7, CH_2Cl_2); IR (thin film) 3030, 2953, 2925, 1760, 1732, 1433, 1247, 1198, 1177, 979, 700 cm^{-1}; ^{1}H NMR (400 MHz, $CDCl_3$, TMS): δ 7.21-7.09 (m, 3H), 6.85 (d, *J* = 8.0 Hz, 2H), 6.77 (d, *J* = 6.9 Hz, 2H), 6.45 (dt, *J* = 8.3 & 2.2 Hz, 2H), 3.92 (s, 3H), 3.87 (s, 3H), 3.31 (dd, *J* = 14.2 & 5.2 Hz, 1H), 3.03 (t, *J* = 14.1 Hz, 1H), 2.72 (dd, *J* = 13.3 & 5.3 Hz, 1H), 2.21 (s, 3H), 1.59 (s, 3H); ^{13}C NMR (100 MHz, $CDCl_3$): δ 210.9, 168.0, 167.2, 137.7, 136.7, 136.6, 128.8, 128.6, 128.1, 127.8, 127.4, 69.4, 59.0, 53.78, 53.75, 52.6, 34.7, 24.8, 21.1; $(M + Na)^+$ HRMS m/z calcd for $(C_{23}H_{24}NaO_5)^+$: 403.1521; found: 403.1521.

Dimethyl (3*S*,4*R*)-3-methyl-2-oxo-4-phenyl-3-(*p*-tolyl)cyclopentane-1,1-dicarboxylate (4u): R_f = 0.45 (EtOAc/hexanes 1:9); HPLC analysis: 94% ee [Daicel Chiralcel AD-H column; 1.0 mL/min; solvent system: 3% isopropanol in hexane; retention times: 9.8 min (minor), 25.4 min (minor)]; $[\alpha]_D^{24}$ = 80 (c = 0.5, CH_2Cl_2); IR (thin film) 3030, 2953, 2925, 1760, 1732, 1433, 1246, 1198, 1177, 979, 701 cm^{-1}; ^{1}H NMR (400 MHz, $CDCl_3$, TMS): δ 7.25-7.19 (m, 3H), 7.12 (d, *J* = 8.1 Hz, 2H), 6.96 (d, *J* = 8.3 Hz, 2H), 6.88-6.82 (m, 2H), 3.89 (s, 3H), 3.87 (s, 3H), 3.68 (dd, *J* = 13.8 & 6.1 Hz, 1H), 3.18 (t, *J* = 13.6 Hz, 1H), 2.91 (dd, *J* = 13.5 & 6.0 Hz, 1H), 2.34 (s, 3H), 1.15 (s, 3H); ^{13}C NMR (100 MHz, $CDCl_3$): δ 208.7, 167.9, 167.5, 139.3, 136.9, 136.7, 129.3, 128.7, 128.2, 127.6, 127.5, 68.7, 58.7, 53.80, 53.75, 52.0, 33.7, 21.2, 16.7; $(M + Na)^+$ HRMS m/z calcd for $(C_{23}H_{24}NaO_5)^+$: 403.1521; found: 403.1520.

Compound **4u** was recrystallized from a mixture of EtOAc/hexanes to provide a sample for X-ray crystallographic analysis.

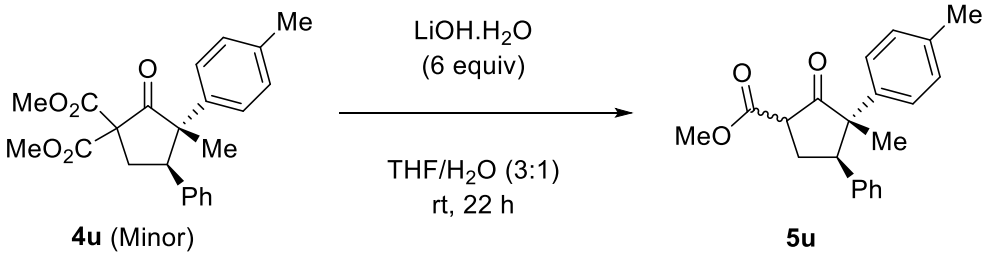


Following the general procedure, cyclopropane (*R*)-**1b**/*ent*-**1b** (200 mg, 0.85 mmol) solution in dichloromethane (5.0 mL) was added to a stirring suspension of $InBr_3$ (90 mg, 0.26 mmol) in dichloromethane (9.0 mL) at –25 °C. To this reaction mixture, $EtAlCl_2$ (1.0 M solution in hexanes) (0.128 mL, 0.128 mmol) was added dropwise. A solution of methyl-*p*-tolylketene (162 mg, 1.11 mmol) in dichloromethane (3.0 ml) was added over 4 h to the reaction mixture at –25 °C. Elution with 3% EtOAc/hexanes through regular silica gel column afforded 171 mg of **4v** (major isomer, 52%) and 152 mg of **4w** (minor isomer, 47%), both as a colorless gum (99%).

Dimethyl (3*S*,4*S*)-3-methyl-2-oxo-4-phenyl-3-(*p*-tolyl)cyclopentane-1,1-dicarboxylate (4v): R_f = 0.45 (EtOAc/hexanes 1:9); HPLC analysis: 95% ee [Daicel Chiralcel AD-H column; 1.0 mL/min; solvent system: 3% isopropanol in hexane; retention times: 8.8 min (minor), 17.2 min (major)]; $[\alpha]_D^{24}$ = 128 (c = 2.1, CH_2Cl_2); IR (thin film) 3030, 2953, 2923, 1760, 1731, 1433, 1248, 1208, 1176, 978, 680 cm^{-1}; ^1H NMR (400 MHz, $CDCl_3$, TMS): δ 7.21-7.09 (m, 3H), 6.85 (d, *J* = 8.0 Hz, 2H), 6.77 (d, *J* = 8.4 Hz, 2H), 6.45 (dt, *J* = 8.3 & 1.8 Hz, 2H), 3.92 (s, 3H), 3.87 (s, 3H), 3.31 (dd, *J* = 14.2 & 5.2 Hz, 1H), 3.03 (t, *J* = 14.1 Hz, 1H), 2.72 (dd, *J* = 13.3 & 5.3 Hz, 1H), 2.21 (s, 3H), 1.59 (s, 3H); ^{13}C NMR (100 MHz, $CDCl_3$): δ 210.9, 168.0, 167.2, 137.7, 136.7, 136.6, 128.8, 128.6, 128.1, 127.8, 127.4, 69.4, 59.0, 53.78, 53.75, 52.6, 34.7, 24.8, 21.1; $(M + Na)^+$ HRMS m/z calcd for $(C_{23}H_{24}NaO_5)^+$: 403.1521; found: 403.1520.

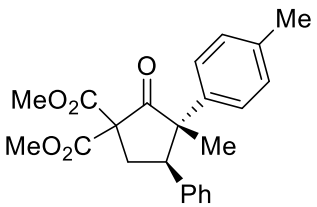
Dimethyl (3*R*,4*S*)-3-methyl-2-oxo-4-phenyl-3-(*p*-tolyl)cyclopentane-1,1-dicarboxylate (4w): R_f = 0.45 (EtOAc/hexanes 1:9); HPLC analysis: 96% ee [Daicel Chiralcel AD-H column; 1.0 mL/min; solvent system: 3% isopropanol in hexane; retention times: 9.8 min (major), 27.2 min (minor)]; $[\alpha]_D^{24}$ = –72 (c = 1.1, CH_2Cl_2); IR (thin film) 3030, 2953, 2926, 1760, 1731, 1433, 1248, 1199, 1176, 978, 680 cm^{-1}; ^1H NMR (400 MHz, $CDCl_3$, TMS): δ 7.25-7.19 (m, 3H), 7.12 (d, *J* = 8.1 Hz, 2H), 6.96 (d, *J* = 8.5 Hz, 2H), 6.88-6.82 (m, 2H), 3.89 (s, 3H), 3.87 (s, 3H), 3.68 (dd, *J* = 13.8 & 6.1 Hz, 1H), 3.18 (t, *J* = 13.6 Hz, 1H), 2.91 (dd, *J* = 13.5 & 6.0 Hz, 1H), 2.34 (s, 3H), 1.15 (s, 3H); ^{13}C NMR (100 MHz, $CDCl_3$): δ 208.7, 167.9, 167.5, 139.3, 136.9, 136.7, 129.3, 128.7, 128.2, 127.6, 127.5, 68.7, 58.7, 53.8, 53.7, 52.0, 33.7, 21.2, 16.7; $(M + Na)^+$ HRMS m/z calcd for $(C_{23}H_{24}NaO_5)^+$: 403.1521; found: 403.1521.

Compound **4w** was recrystallized from a mixture of EtOAc/hexanes to provide a sample for X-ray crystallographic analysis.

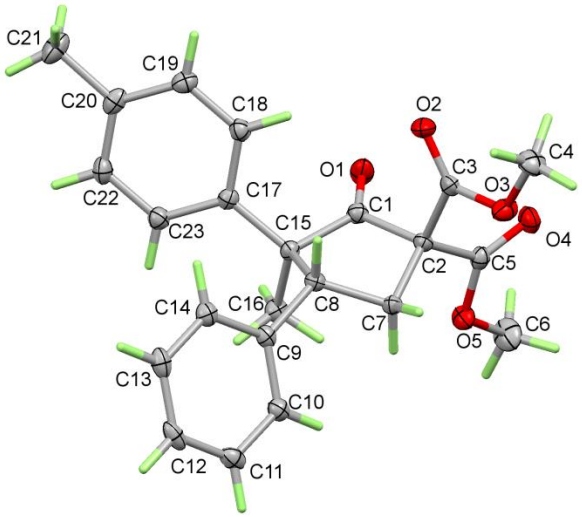


Methyl (3*R*,4*R*)-3-methyl-2-oxo-4-phenyl-3-(p-tolyl)cyclopentane-1-carboxylate [5u]: $LiOH.H_2O$ (30 mg, 0.71 mmol) was added to a solution of cyclopentanone **4u** (45 mg, 0.12 mmol) in THF/H_2O (3:1, 1.2 mL) at room temperature. The reaction was then stirred at room temperature overnight (total reaction time = 22 h). After this time THF was removed under reduced pressure. Cooled water (2 mL) was added to the residue and the pH of the mixture was adjusted to at least pH = 3 by addition of 1M HCl (*ca*. 2 mL). The aqueous solution was extracted with EtOAc (3 × 5 mL), and the combined organics were dried over sodium sulfate, before filtration, and evaporation of the organics afforded **5u** as an off-white oil (26.7 mg, 69%), with dr = 2.6:1 (by ^{1}H NMR analysis); IR (thin film) 2960, 2945, 1755, 1728 cm^{-1}; ^{1}H NMR for major diastereomer (400 MHz, $CDCl_3$, TMS): δ 7.17-6.77 (m, 9H), 3.77 (s, 3H), 3.58 (dd, *J* = 11.9, 8.5 Hz, 1H), 3.54 (dd, *J* = 13.3, 5.9 Hz, 1H), 2.85-2.77 (m, 1H), 2.49-2.44 (m, 1H), 2.27 (s, 3H), 1.03 (s, 3H); ^{13}C NMR for major diastereomer (100 MHz, $CDCl_3$): δ 213.4, 170.0, 140.0, 137.3, 136.8, 129.4, 128.6, 128.2, 127.5, 127.3, 57.9, 56.2, 53.2, 52.9, 28.0, 21.2, 15.6; $(M + Na)^+$ HRMS m/z calcd for $(C_{21}H_{22}NaO_3)^+$: 345.1467; found: 345.1468. Cyclopentanone **4t** was also exposed to the same conditions and **5t** was obtained with dr = 1.7:1.

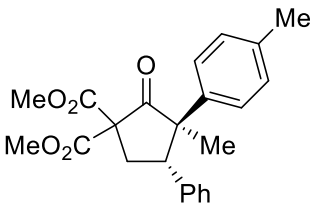
Determination of absolute and relative stereochemistry of cyclopentanones 4: The absolute stereochemistry of the major isomer of all cyclopentanones was deduced from X-ray crystal structure analysis of two crystalline minor isomers **4u** and **4w**, and comparing the chemical shift value of 3-Me group in major and minor isomer. Minor isomer **4u** was determined to have (3*S*,4*R*) absolute configuration and *trans* (*anti*)-relative stereochemistry. Major isomer **4t**, and all other major isomers by analogy, were deduced to possess (3*R*,4*R*) absolute stereochemistry and *cis (syn)*-relative stereochemistry. The assignment of *cis (syn)*-relative stereochemistry for the major isomer of cyclopentanones was further confirmed by NOESY experiments. Analogous results were obtained for **4v** and **4w**.



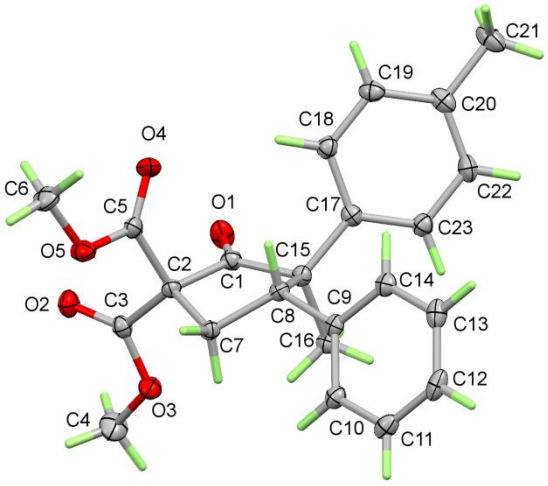
4u



4u at 50% ellipsoid plots



4w



4w at 50% ellipsoid plots

X-ray crystal structure data

Crystallographic data were collected at 100(1)K on a Synergy, Dualflex, AtlasS2 diffractometer using Cu*K*α radiation (λ = 1.54184 Å). The structures were solved by dual space methods (SHELXT[4]) and refined on F^2 using all the reflections (SHELXL-2018/3[5]). Crystal data, data collection and structure refinement details are summarised Table S1.

Refs:

4. G.M. Sheldrick, Acta Cryst., 2015, **A71**, 3-8.
5. G.M. Sheldrick, Acta Cryst., 2015, **C71**, 3-8.

Table S1 Crystal Data and Structure Refinement

Identification code	**4w**	**4u**
Empirical formula	$C_{23}H_{24}O_5$	$C_{23}H_{24}O_5$
Formula weight	380.42	380.42
Temperature /K	100.0(3)	100.01(10)
Crystal system	orthorhombic	orthorhombic
Space group	$P2_12_12_1$	$P2_12_12_1$
a/Å	6.80314(4)	6.80413(3)
b/Å	12.83574(7)	12.83725(7)
c/Å	22.67729(12)	22.67679(12)
β/°	90	90
Volume /Å^3	1980.257(18)	1980.736(18)
Z	4	4
ρ_{calc} g/cm^3	1.276	1.276
μ/mm^{-1}	0.728	0.728
F(000)	808.0	808.0
Crystal size/mm^3	0.222 × 0.203 × 0.061	0.273 × 0.163 × 0.049
2θ range for data collection /°	7.798 to 149.286	7.798 to 149.152
Reflections collected	47572	43150
Independent reflections, R_{int}, R_{sigma}	4043, 0.0278, 0.0111	4041, 0.0274, 0.0113
Data/restraints/parameters	4043/0/257	4041/0/257
Goodness-of-fit on F^2	1.029	1.044
Final R indexes [I>=2σ (I)]	R_1 = 0.0245, wR_2 = 0.0636	R_1 = 0.0246, wR_2 = 0.0641
Final R indexes [all data]	R_1 = 0.0251, wR_2 = 0.0640	R_1 = 0.0253, wR_2 = 0.0648
Largest diff. peak/hole / e Å^{-3}	0.15/-0.16	0.15/-0.16
Flack parameter	0.00(3)	0.04(3)
CCDC number	1895672	1895671

Experimental

The data were collected at 100(1)K on a Synergy, Dualflex, AtlasS2 diffractometer using CuK_α radiation (λ = 1.54184 Å) and the *CrysAlis PRO* 1.171.40.29a suite[6]. Using SHELXLE[7] and Olex2[8] the structure was solved by dual space methods (SHELXT[9]) and refined on F^2 using all the reflections (SHELXL-2018/3[10]). All the non-hydrogen atoms were refined using anisotropic atomic displacement parameters. Hydrogen atoms were inserted at calculated positions using a riding model. Absolute configurations were unambiguously determined for the enantiomeric pair **4w** and **4u**. Crystal data, data collection and structure refinement details are summarised in Table S1.

6. Rigaku Oxford Diffraction, (2018), CrysAlisPro Software system, version 1.171.39.27b, Rigaku Corporation, Oxford, UK.
7. C.B. Hübschle, G.M. Sheldrick and B. Dittrich. J. Appl. Cryst., 2011, **44**, 1281-1284.
8. O.V. Dolomanov, L.J. Bourhis, R.J. Gildea, J.A.K. Howard & H. Puschmann. J. Appl. Cryst., 2009, **42**, 339-341
9. G.M. Sheldrick, Acta Cryst., 2015, **A71**, 3-8.
10. G.M. Sheldrick, Acta Cryst., 2015, **C71**, 3-8.

4w and **4u** $C_{23}H_{24}O_5$

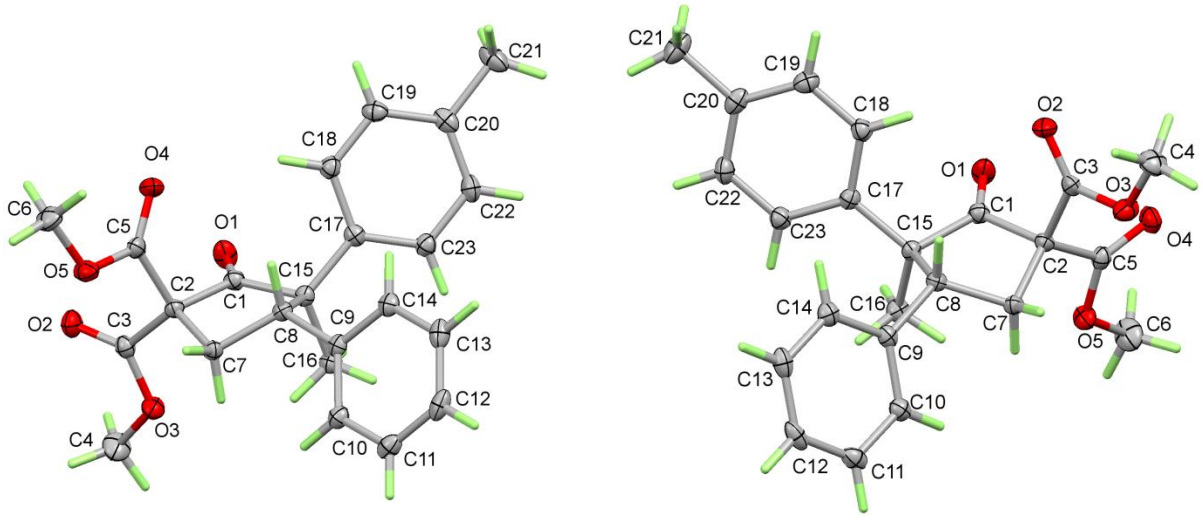


*Fig S5. 50% ellipsoid plots for **4w** (left) and **4u** (right).*

4w and **4u** constitute an enantiomeric pair, both refined in $P2_12_12_1$ and are chiral at C8 and C15.

There are no very striking intermolecular interactions in the structure.