Enantioselective β-Alkylation of Aldehydes
Through an Organocatalyzed C-C Bond Scission Reaction
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Supporting Information

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General Information

Unless otherwise noted, all reactions were carried out in closed vial. $^1$H NMR spectra were recorded on a 500 MHz spectrometer (125 MHz for $^{13}$C). The following abbreviations were used to designate chemical shift multiplicities: s = singlet, d = doublet, t = triplet, q = quartet, h = heptet, m = multiplet, br = broad. All first-order splitting patterns were assigned on the basis of the appearance of the multiplet. Splitting patterns that could not be easily interpreted are designated as multiplet (m) or broad (br). TLC was performed with silica gel GF254 precoated on aluminum plates and spots were visualized with UV. Flash column chromatography was performed on silica gel. HPLC analysis was performed on an HPLC instrument equipped with a UV-Vis detector. Solvents were freshly distilled under nitrogen atmosphere before use using the standard protocols.

General Experimental Procedures

Synthesis of the Substrates (using substrate 3b as an example)$^{15}$

\[
\text{R} + 2 \text{HCOOH, Et}_3\text{N} \xrightarrow{\text{Pd(OAc)}_2(\text{Ph}_3\text{P})_2} 12
\]

Under argon protection, cinnamaldehyde (1.36 g, 10.0 mmol) was allowed to react with excessive amounts of the 4-iodophenol (4.40 g, 20.0 mmol), triethylamine (3.03 g, 30.0 mmol) and formic acid (1.15 g, 25.0 mmol), and a catalytic amount of bis(triphenylphosphine)palladium diacetate (37.5 mg, 0.05 mmol) in acetonitrile (4 mL) at 80 °C with stirring for 3 h. The mixture was then diluted with CH$_2$Cl$_2$ (20 mL), washed with water, and the CH$_2$Cl$_2$ layer was dried (MgSO$_4$), then concentrated under reduced pressure. The residue was subjected to column chromatography (CH$_2$Cl$_2$) to provide 12 (1.09 g, 48 %) as an orange oil.

A flame-dried round bottom flask (100 mL) was purged under vacuum for 5 min and then refilled with argon. It was then charged with 12 (904 mg, 4.0 mmol) and CH$_2$Cl$_2$ (2 mL) under argon. With stirring, methanol (4.8 mL, 120 mmol) and Phl(OAc)$_2$ (1.93 g, 6.0 mmol, dissolved in 15 mL of CH$_2$Cl$_2$) were then added dropwise over 2 h. The solution was then allowed to stir at ambient temperature for an additional 30 min. After
the solvent was removed under reduced pressure and the residue was subjected to column chromatography (CH$_2$Cl$_2$) to provide 3b (399 mg, 39%) as white solid.

**Synthesis of Compounds 10 and 11**

**Synthesis of compound 10:** The mixture of nitromethane (18.3 mg, 0.30 mmol, 3.0 equiv.) and NaOAc (8.2 mg, 0.10 mmol, 1.0 equiv.) in CH$_2$Cl$_2$ (0.4 mL) were stirred at rt for 5 min. Then catalyst 4a (3.2 mg, 0.01 mmol, 10 mol %) and aldehyde 3b (25.6 mg, 0.10 mmol, 1.0 equiv.) were added and the whole mixture was stirred at rt for 3 h. Then the reaction mixture was directly transferred to a silica gel column and purified by column chromatography (hexane/EtOAc) to give product 10 as a colorless oil (15.6 mg, 81% yield).

**Synthesis of compound 11:** The mixture of 1,2-cyclohexanedione (33.6 mg, 0.30 mmol, 3.0 equiv.) and LiOH·H$_2$O (4.2 mg, 0.10 mmol, 1.0 equiv.) in CH$_2$Cl$_2$ (0.4 mL) were stirred at rt for 5 min. Then catalyst 4a (3.2 mg, 0.010 mmol, 10 mol %) and aldehyde 3b (25.6 mg, 0.10 mmol, 1.0 equiv.) were added and the reaction mixture was stirred at rt for 3 h. Then the reaction mixture was directly transferred to a silica gel column and purified by column chromatography (hexane/EtOAc) to give the product 11 as a colorless oil (17.6 mg, 72% yield).

**Compound Characterization Data**

3-(1-Methoxy-4-oxocyclohexa-2,5-dien-1-yl)propanal (3a)$_{15b}$

Yellow oil. $^1$H NMR (500 MHz, CDCl$_3$) $\delta$ 9.72 (t, $J$ = 1.5 Hz, 1H), 6.74-6.72 (m, 2H), 6.39-6.37 (m, 2H), 3.21 (s, 3H), 2.50-2.47 (m, 2H), 2.09-2.06 (m, 2H); $^{13}$C NMR (125 MHz, CDCl$_3$) $\delta$ 200.4, 184.9, 150.1, 131.9, 74.8, 53.2, 38.2, 31.5.
3-(1-Methoxy-4-oxocyclohexa-2,5-dien-1-yl)-3-phenylpropanal (3b)

White solid. \(^1\)H NMR (500 MHz, CDCl\(_3\)) \(\delta 9.64\) (t, \(J = 1.5\) Hz, 1H), \(7.27\)–\(7.22\) (m, 3H), \(7.16\)–\(7.14\) (m, 2H), \(6.78\) (dd, \(J = 3.0, 10.5\) Hz, 1H), \(6.71\) (dd, \(J = 3.0, 10.5\) Hz, 1H), \(6.37\) (dd, \(J = 2.0, 10.0\) Hz, 1H), \(6.23\) (dd, \(J = 2.0, 10.0\) Hz, 1H), \(3.68\) (dd, \(J = 6.0, 8.5\) Hz, 1H), \(3.12\) (s, 3H), \(3.11\)–\(3.06\) (m, 1H), \(2.91\)–\(2.86\) (m, 1H); \(^1^3\)C NMR (125 MHz, CDCl\(_3\)) \(\delta 199.9, 184.7, 149.5, 148.2, 137.6, 132.9, 132.1, 128.2, 127.8, 77.1, 53.2, 48.9, 44.7; \(\nu_{\text{max}}\) (neat, cm\(^{-1}\)): 2825, 1704, 1665, 1662, 1493, 1450, 1369, 1177; HRMS (ESI): m/z calcd for C\(_{16}\)H\(_{16}\)O\(_3\)Na ([M+Na]\(^+\)) 279.0997, found 279.0991.

3-(4-Fluorophenyl)-3-(1-methoxy-4-oxocyclohexa-2,5-dien-1-yl)propanal (3c)

White solid. \(^1\)H NMR (500 MHz, CDCl\(_3\)) \(\delta 9.62\) (t, \(J = 1.5\) Hz, 1H), \(7.14\)–\(7.11\) (m, 2H), \(6.95\)–\(6.91\) (m, 2H), \(6.74\) (dd, \(J = 3.0, 10.5\) Hz, 1H), \(6.67\) (dd, \(J = 3.0, 10.5\) Hz, 1H), \(6.36\) (dd, \(J = 1.5, 10.5\) Hz, 1H), \(6.23\) (dd, \(J = 1.5, 10.0\) Hz, 1H), \(3.66\) (dd, \(J = 6.0, 8.5\) Hz, 1H), \(3.18\) (s, 3H), \(3.09\)–\(3.04\) (m, 1H), \(2.87\)–\(2.82\) (m, 1H); \(^1^3\)C NMR (125 MHz, CDCl\(_3\)) \(\delta 199.6, 184.5, 163.1, 161.1, 149.2, 148.1, 133.4, 133.0, 132.2, 130.9, 115.2, 115.0, 77.0, 53.3, 48.0, 44.7; \(\nu_{\text{max}}\) (neat, cm\(^{-1}\)): 2949, 2830, 1731, 1667, 1631, 1511, 1451, 1368, 1225; HRMS (ESI): m/z calcd for C\(_{16}\)H\(_{15}\)F\(_3\)O\(_3\)Na ([M+Na]\(^+\)) 297.0903, found 297.0901.

3-(4-Chlorophenyl)-3-(1-methoxy-4-oxocyclohexa-2,5-dien-1-yl)propanal (3d)

White solid. \(^1\)H NMR (500 MHz, CDCl\(_3\)) \(\delta 9.62\) (t, \(J = 1.5\) Hz, 1H), \(7.23\)–\(7.21\) (m, 2H), \(7.10\)–\(7.08\) (m, 2H), \(6.72\) (dd, \(J = 3.0, 10.5\) Hz, 1H), \(6.65\) (dd, \(J = 3.0, 10.0\) Hz, 1H), \(6.36\) (dd, \(J = 2.0, 10.0\) Hz, 1H), \(6.25\) (dd, \(J = 2.0, 10.0\) Hz, 1H), \(3.64\) (dd, \(J = 5.5, 9.0\) Hz, 1H), \(3.18\) (s, 3H), \(3.08\)–\(3.03\) (m, 1H), \(2.87\)–\(2.82\) (m, 1H); \(^1^3\)C NMR (125 MHz, CDCl\(_3\)) \(\delta 199.4, 184.4, 149.0, 148.1, 136.2, 133.0, 132.3, 130.6, 128.4, 76.9, 53.2, 48.0, 44.5; \(\nu_{\text{max}}\) (neat, cm\(^{-1}\)): 2971, 2828, 1739, 1668, 1628, 1609, 1570, 1433, 1367, 1276; HRMS (ESI): m/z calcd for C\(_{16}\)H\(_{15}\)Cl\(_3\)O\(_3\)Na ([M+Na]\(^+\)) 313.0607, found 313.0557.

3-(4-Bromophenyl)-3-(1-methoxy-4-oxocyclohexa-2,5-dien-1-yl)propanal (3e)

White solid. \(^1\)H NMR (500 MHz, CDCl\(_3\)) \(\delta 9.56\) (t, \(J = 1.5\) Hz, 1H), \(7.33\)–\(7.31\) (m, 2H), \(7.01\)–\(6.99\) (m, 2H), \(6.69\) (dd, \(J = 3.0, 10.5\) Hz, 1H), \(6.63\) (dd, \(J = 3.0, 10.0\) Hz, 1H), \(6.32\) (dd, \(J = 2.0, 10.0\) Hz, 1H), \(6.20\) (dd, \(J = 2.0, 10.5\) Hz, 1H), \(3.59\) (dd, \(J = 5.5, 9.0\) Hz, 1H), \(3.13\) (s, 3H), \(3.04\)–\(3.00\) (m, 1H), \(2.84\)–\(2.78\) (m, 1H); \(^1^3\)C NMR (125 MHz, CDCl\(_3\)) \(\delta 199.4, 184.4, 149.0, 148.2, 136.8, 133.0, 132.3, 131.2, 130.9, 121.6, 76.8, 53.2, 48.0, 44.4; \(\nu_{\text{max}}\) (neat, cm\(^{-1}\)): 2968, 2828, 1735, 1667, 1633, 1534, 1458, 1365, 1247; HRMS (ESI): m/z calcd for C\(_{16}\)H\(_{15}\)BrO\(_3\)Na ([M+Na]\(^+\)) 357.0102, found 357.0996.
3-(1-Methoxy-4-oxocyclohexa-2,5-dien-1-yl)-3-(4-(trifluoromethyl)phenyl)propanal (3f)

Yellow solid. $^1$H NMR (500 MHz, CDCl$_3$) $\delta$ 9.63 (t, $J = 1.5$ Hz, 1H), 7.52-7.51 (m, 2H), 7.30-7.26 (m, 2H), 6.70 (dd, $J = 3.0$, 10.5 Hz, 1H), 6.66 (dd, $J = 3.0$, 10.5 Hz, 1H), 6.38 (dd, $J = 2.0$, 10.0 Hz, 1H), 6.27 (dd, $J = 2.0$, 10.0 Hz, 1H), 3.73 (dd, $J = 5.5$, 9.0 Hz, 1H), 3.18 (s, 3H), 3.12-3.07 (m, 1H), 2.94-2.89 (m, 1H); $^{13}$C NMR (125 MHz, CDCl$_3$) $\delta$ 199.0, 184.4, 148.6, 148.2, 133.0, 132.4, 129.7, 125.1, 125.0, 76.7, 53.3, 48.2, 44.5. $\nu_{\text{max}}$ (neat, cm$^{-1}$): 2936, 2835, 1721, 1668, 1628, 1513, 1422, 1390, 1325, 1267; HRMS (ESI): m/z calcld for C$_{17}$H$_{13}$F$_3$O$_3$Na ([M+Na]$^+$) 347.0871, found 347.0865.

3-(1-Methoxy-4-oxocyclohexa-2,5-dien-1-yl)-3-(p-tolyl)propanal(3g)

White solid. $^1$H NMR (500 MHz, CDCl$_3$) $\delta$ 9.57 (t, $J = 1.5$ Hz, 1H), 7.02-6.98 (m, 5H), 6.75 (dd, $J = 3.0$, 10.5 Hz, 1H), 6.67 (dd, $J = 3.0$, 10.0 Hz, 1H), 6.33 (dd, $J = 2.0$, 10.0 Hz, 1H), 6.18 (dd, $J = 2.0$, 10.0 Hz, 1H), 3.61 (dd, $J = 6.0$, 9.0 Hz, 1H), 3.14 (s, 3H), 3.04-2.99 (m, 1H), 2.84-2.78 (m, 1H), 2.24 (s, 3H); $^{13}$C NMR (125 MHz, CDCl$_3$) $\delta$ 200.2, 184.8, 149.7, 148.3, 137.3, 134.4, 132.9, 131.9, 129.1, 128.8, 77.2, 53.2, 48.5, 44.6, 21.0. $\nu_{\text{max}}$ (neat, cm$^{-1}$): 2969, 2825, 2728, 1738, 1665, 1622, 1511, 1436, 1365, 1216; HRMS (ESI): m/z calcld for C$_{17}$H$_{15}$O$_3$Na ([M+Na]$^+$) 293.1154, found 293.1149.

3-(3-Chlorophenyl)-3-(1-methoxy-4-oxocyclohexa-2,5-dien-1-yl)propanal (3h)

White solid. $^1$H NMR (500 MHz, CDCl$_3$) $\delta$ 9.63 (t, $J = 1.5$ Hz, 1H), 7.23-7.14 (m, 3H), 7.06-7.01 (m, 1H), 6.69 (dd, $J = 22.5$, 10.5, 3.2, 0.6 Hz, 2H), 6.38 (ddd, $J = 10.3$, 2.0, 0.6 Hz, 1H), 6.30-6.23 (m, 1H), 3.63 (dd, $J = 8.8$, 5.6 Hz, 1H), 3.18 (s, 3H), 3.05 (ddd, $J = 17.3$, 5.7, 1.6, 0.6 Hz, 1H), 2.86 (ddd, $J = 17.4$, 8.8, 1.5, 0.6 Hz, 1H); $^{13}$C NMR (125 MHz, CDCl$_3$) $\delta$ 199.1, 184.4, 148.8, 147.9, 139.8, 134.0, 133.0, 132.3, 129.4, 127.9, 127.5, 53.2, 48.3, 44.4. $\nu_{\text{max}}$ (neat, cm$^{-1}$): 2998, 1712, 1666, 1626, 1479, 1394, 1173; HRMS (ESI): m/z calcld for C$_{16}$H$_{13}$ClO$_3$Na ([M+Na]$^+$) 313.0607, found 313.0601.

3-(1-Methoxy-4-oxocyclohexa-2,5-dien-1-yl)-3-(o-tolyl)propanal (3i)

White solid. $^1$H NMR (500 MHz, CDCl$_3$) $\delta$ 9.57 (t, $J = 1.5$ Hz, 1H), 7.12-7.08 (m, 4H), 6.78 (dd, $J = 3.0$, 10.5 Hz, 1H), 6.73 (dd, $J = 3.0$, 10.0 Hz, 1H), 6.37 (dd, $J = 2.0$, 10.0 Hz, 1H), 6.24 (dd, $J = 2.0$, 10.5 Hz, 1H), 3.98 (dd, $J = 5.5$, 9.0 Hz, 1H), 3.16 (s, 3H), 3.04-3.00 (m, 1H), 2.94-2.89 (m, 1H), 2.40 (s, 3H); $^{13}$C NMR (125 MHz, CDCl$_3$) $\delta$ 199.9, 184.6, 149.2, 149.0, 137.3, 136.6, 132.6, 131.9, 130.6, 127.6, 127.3, 125.8, 77.7, 53.2, 45.7, 42.9, 20.7. $\nu_{\text{max}}$ (neat, cm$^{-1}$):
2953, 1832, 1736, 1718, 1669, 1634, 1491, 1386; HRMS (ESI): m/z calcd for C$_{17}$H$_{18}$O$_3$Na ([M+Na]$^+$) 293.1154, found 293.1148.

3-(1-Methoxy-4-oxocyclohexa-2,5-dien-1-yl)hexanal (3j)

Yellow oil. $^1$H NMR (500 MHz, CDCl$_3$) $\delta$ 9.68 (t, $J = 1.5$ Hz, 1H), 6.69-6.63 (m, 2H), 6.42-6.37 (m, 2H), 3.13 (s, 3H), 2.56-2.51 (m, 1H), 2.44-2.41 (m, 1H), 2.32-2.28 (m, 1H), 1.38-1.29 (m, 1H), 1.19-1.14 (m, 1H), 0.98-0.91 (m, 1H), 0.83 (t, $J = 7.0$ Hz, 3H); $^{13}$C NMR (125 MHz, CDCl$_3$) $\delta$ 202.0, 185.2, 150.0, 147.8, 132.9, 132.6, 77.7, 52.8, 44.5, 41.6, 31.8, 20.9, 42.9, 20.7, 13.9. $\nu$ max (neat, cm$^{-1}$): 2969, 2828, 2728, 1737, 1668, 1632, 1512, 1454, 1365, 1228; HRMS (ESI): m/z calcd for C$_{17}$H$_{18}$O$_3$Na ([M+Na]$^+$) 245.1154, found 245.1150.

3-(1-Methoxy-4-oxocyclohexa-2,5-dien-1-yl)butanal (3k)

Yellow oil. $^1$H NMR (500 MHz, CDCl$_3$) $\delta$ 9.68 (t, $J = 1.5$ Hz, 1H), 6.65-6.63 (m, 2H), 6.40-6.37 (m, 2H), 3.14 (s, 3H), 2.75-2.70 (m, 1H), 2.52-2.48 (m, 1H), 2.20-2.14 (m, 1H), 0.84 (d, $J = 7.0$ Hz, 3H); $^{13}$C NMR (125 MHz, CDCl$_3$) $\delta$ 200.6, 185.1, 150.0, 147.7, 133.2, 132.5, 77.5, 52.9, 46.2, 36.3, 15.1. $\nu$ max (neat, cm$^{-1}$): 2969, 2828, 2728, 1737, 1667, 1631, 1511, 1455, 1365, 1228, 1216; HRMS (ESI): m/z calcd for C$_{17}$H$_{18}$O$_3$Na ([M+Na]$^+$) 217.0841, found 217.0837.

Diethyl (R)-2-(3-oxo-1-phenylpropyl)malonate (9a)$^{11,16}$

Colorless oil, 25.3 mg, 87% yield; $[\alpha]_D^{24} = -38.1$ ([c 1.0, CHCl$_3$, 96% ee]); lit. $[\alpha]_D^{23} = -25.8$ ([c 1.02, CHCl$_3$]$^2$); $^1$H NMR (500 MHz, CDCl$_3$) $\delta$ 9.60 (s, 1H), 7.30-7.20 (m, 5H), 4.21 (q, $J = 7.0$ Hz, 2H), 4.03-3.99 (m, 1H), 3.95 (q, $J = 7.0$ Hz, 2H), 3.72 (d, $J = 10$ Hz, 1H), 2.96-2.85 (m, 2H), 1.26 (t, $J = 7.0$ Hz, 3H), 1.00 (t, $J = 7.0$ Hz, 3H); $^{13}$C NMR (125 MHz, CDCl$_3$) $\delta$ 200.0, 168.0, 167.4, 139.8, 128.7, 128.1, 127.5, 61.8, 61.4, 57.5, 47.4, 39.5, 14.0, 13.7; Enantiomeric excess of 9a was determined by chiral stationary phase HPLC analysis using a ChiralPak AD-H column (80:20 hexanes/i-PrOH at 0.5 mL/min, $\lambda = 220$ nm), major enantiomer: $t_R = 17.9$ min, minor enantiomer: $t_R = 22.3$ min.

Dimethyl (R)-2-(3-oxo-1-phenylpropyl)malonate (9b)$^{11,16}$

Colorless oil, 21.3 mg, 81% yield; $[\alpha]_D^{24} = -69.3$ ([c 1.0, CHCl$_3$, 95% ee]); $^1$H NMR (500 MHz, CDCl$_3$) $\delta$ 9.59 (t, $J = 1.5$ Hz, 1H), 7.31-7.20 (m, 5H), 4.05-4.00 (m, 1H), 3.75 (d, $J = 10$ Hz, 1H), 3.73 (s, 3H), 3.50 (s, 3H), 2.96-2.87 (m, 2H); $^{13}$C NMR (125 MHz, CDCl$_3$) $\delta$ 199.9, 168.3, 167.8, 139.7, 128.7, 128.0, 127.5, 52.7, 52.4, 47.2, 39.5; Enantiomeric excess of 9b was determined by chiral stationary phase HPLC analysis using a ChiralPak IC column (80:20 hexanes/i-PrOH at 1.0 mL/min, $\lambda = 220$ nm), major enantiomer: $t_R = 27.4$ min, minor enantiomer: $t_R = 17.1$ min.
Dipropyl (R)-2-(3-oxo-1-phenylpropyl)malonate (9c)

Colorless oil, 24.9 mg, 78% yield; [α]D = -35.7 (c 1.0, CHCl3, 95% ee); 1H NMR (500 MHz, CDCl3) δ 9.59 (t, J = 1.5 Hz, 1H), 7.30-7.19 (m, 5H), 4.15-4.07 (m, 2H), 4.04-4.00 (m, 1H), 3.85 (t, J = 7.0 Hz, 2H), 3.75 (d, J = 10 Hz, 1H), 2.97-2.86 (m, 2H), 1.69-1.62 (m, 2H), 1.46-1.39 (m, 2H), 0.92 (t, J = 7.0 Hz, 3H); 13C NMR (125 MHz, CDCl3) δ 200.0, 167.6, 166.9, 139.9, 128.6, 128.2, 127.4, 68.9, 57.8, 47.7, 39.4, 21.6, 21.5, 21.3, 21.2; Enantiomeric excess of 9c was determined by chiral stationary phase HPLC analysis using a ChiralPak IC column (90:10 hexanes/i-PrOH at 1.0 mL/min, λ = 220 nm), major enantiomer: tR = 35.1 min, minor enantiomer: tR = 18.9 min.

Diisopropyl (R)-2-(3-oxo-1-phenylpropyl)malonate (9d)

Colorless oil, 22.3 mg, 70% yield; [α]D = -32.4 (c 1.0, CHCl3, 97% ee); 1H NMR (500 MHz, CDCl3) δ 9.60 (t, J = 1.5 Hz, 1H), 7.29-7.12 (m, 5H), 5.09-5.04 (m, 1H), 4.81-4.76 (m, 1H), 4.02-3.97 (m, 1H), 3.66 (d, J = 10 Hz, 1H), 2.95-2.82 (m, 2H), 1.25 (t, J = 5.0 Hz, 6H), 1.05 (d, J = 6.0 Hz, 3H), 0.95 (d, J = 6.0 Hz, 3H); 13C NMR (125 MHz, CDCl3) δ 200.2, 167.6, 166.9, 139.9, 128.6, 128.2, 127.4, 69.4, 68.9, 57.8, 47.7, 39.4, 21.6, 21.5, 21.3, 21.2; Enantiomeric excess of 9d was determined by chiral stationary phase HPLC analysis using a ChiralPak AD-H column (80:20 hexanes/i-PrOH at 0.5 mL/min, λ = 220 nm), major enantiomer: tR = 13.4 min, minor enantiomer: tR = 16.7 min.

Di-tert-butyl (R)-2-(3-oxo-1-phenylpropyl)malonate (9e)

Colorless oil, 20.1 mg, 58% yield; [α]D = -18.3 (c 1.0, CHCl3, 94% ee); 1H NMR (500 MHz, CDCl3) δ 9.60-9.59 (m, 1H), 7.29-7.20 (m, 5H), 3.92-3.88 (m, 1H), 3.53 (d, J = 10.5 Hz, 1H), 2.94-2.90 (m, 1H), 2.83-2.77 (m, 1H), 1.46 (s, 9H), 1.19 (s, 9H); 13C NMR (125 MHz, CDCl3) δ 200.5, 167.4, 166.7, 140.1, 128.5, 128.4, 127.3, 82.2, 81.6, 59.2, 48.0, 39.5, 27.9, 27.5; Enantiomeric excess of 9e was determined by chiral stationary phase HPLC analysis using a ChiralPak ID column (90:10 hexanes/i-PrOH at 0.5 mL/min, λ = 220 nm), major enantiomer: tR = 19.1 min, minor enantiomer: tR = 24.8 min.

Dibenzyl (R)-2-(3-oxo-1-phenylpropyl)malonate (9f)

White solid, 31.1 mg, 75% yield; [α]D = -23.6 ([c 1.0, CHCl3, 94% ee]; lit. [α]D = -15.7 (c 1.03, CHCl3)]; 1H NMR (500 MHz, CDCl3) δ 9.56 (t, J = 1.5 Hz, 1H), 7.36-7.21 (m, 13H), 7.08-7.006 (m, 2H), 5.17-5.14 (m, 2H), 4.92-4.88 (m, 2H), 4.09-4.04 (m, 1H), 3.85 (d, J = 10 Hz, 1H), 2.90-2.84 (m, 2H); 13C NMR (125 MHz, CDCl3) δ 199.8, 167.7, 167.2, 139.6, 135.0, 134.9, 128.8, 128.6, 128.5, 128.4, 128.3, 128.2, 128.1, 128.0, 127.5, 67.5, 67.2, 57.5, 47.2, 39.5; Enantiomeric excess of 9f was determined by chiral stationary phase HPLC analysis using a ChiralPak IC column (80:20 hexanes/i-PrOH at 1.0 mL/min, λ = 220 nm), major enantiomer: tR = 19.7 min, minor enantiomer: tR = 16.1 min.
Diethyl (R)-2-[1-(4-fluorophenyl)-3-oxopropyl]malonate (9g)\(^{16}\)

Colorless oil, 24.2 mg, 78% yield; \([\alpha]_D^{24} = -43.7\) (c 1.0, CHCl\(_3\), 95% ee); \(^1\)H NMR (500 MHz, CDCl\(_3\)) \(\delta 9.60\) (d, \(J = 1.0\) Hz, 1H), 7.26-7.21 (m, 2H), 7.01-6.96 (m, 2H), 4.24-4.18 (m, 2H), 4.05-3.95 (m, 3H), 3.70-3.66 (m, 1H), 2.98-2.83 (m, 2H), 1.26 (t, \(J = 7.0\) Hz, 3H), 1.04 (t, \(J = 7.0\) Hz, 3H). \(^1^3\)C NMR (125 MHz, CDCl\(_3\)) \(\delta 199.6, 167.8, 167.3, 162.9, 160.9, 135.6, 129.8, 115.61\) (s), 115.4, 61.8, 61.5, 57.5, 47.5, 38.7, 14.0, 13.8; Enantiomeric excess of 9g was determined by chiral stationary phase HPLC analysis using a ChiralPak IC column (95:5 hexanes/i-PrOH at 0.5 mL/min, \(\lambda = 220\) nm), major enantiomer: \(t_R = 29.6\) min, minor enantiomer: \(t_R = 28.4\) min.

Diethyl (R)-2-[1-(4-chlorophenyl)-3-oxopropyl]malonate (9h)\(^{16}\)

Colorless oil, 25.8 mg, 79% yield; \([\alpha]_D^{24} = -36.9\) (c 1.0, CHCl\(_3\), 98% ee); \(^1\)H NMR (500 MHz, CDCl\(_3\)) \(\delta 9.59\) (t, \(J = 7.0\) Hz, 1H), 7.26-7.24 (m, 2H), 7.20-7.18 (m, 2H), 4.22-4.16 (m, 2H), 4.02-3.95 (m, 3H), 3.66 (d, \(J = 10.0\) Hz, 1H), 2.97-2.83 (m, 2H), 1.25 (t, \(J = 7.0\) Hz, 3H), 1.04 (t, \(J = 7.0\) Hz, 3H). \(^1^3\)C NMR (125 MHz, CDCl\(_3\)) \(\delta 199.4, 167.8, 167.2, 138.4, 133.2, 129.5, 128.8, 61.8, 61.5, 57.2, 47.3, 38.7, 14.0, 13.7; Enantiomeric excess of 9h was determined by chiral stationary phase HPLC analysis using a ChiralPak IC column (95:5 hexanes/i-PrOH at 1.0 mL/min, \(\lambda = 220\) nm), major enantiomer: \(t_R = 25.3\) min, minor enantiomer: \(t_R = 27.5\) min.

Diethyl (R)-2-[1-(4-bromophenyl)-3-oxopropyl]malonate (9i)

Colorless oil, 28.1 mg, 76% yield; \([\alpha]_D^{24} = -27.5\) (c 1.0, CHCl\(_3\), 91% ee); \(^1\)H NMR (500 MHz, CDCl\(_3\)) \(\delta 9.59\) (t, \(J = 7.0\) Hz, 1H), 7.42-7.40 (m, 2H), 7.14-7.12 (m, 2H), 4.22-4.17 (m, 2H), 4.00-3.95 (m, 3H), 3.66 (d, \(J = 10.0\) Hz, 1H), 2.97-2.84 (m, 2H), 1.25 (t, \(J = 7.0\) Hz, 3H), 1.04 (t, \(J = 7.0\) Hz, 3H); \(^1^3\)C NMR (125 MHz, CDCl\(_3\)) \(\delta 199.4, 167.7, 167.2, 139.0, 131.8, 129.9, 121.4, 61.9, 61.6, 57.1, 47.3, 38.8, 14.0, 13.8; \(\nu_{\text{max}}\) (neat, cm\(^{-1}\)) = 2983, 1728, 1597, 1573, 1476, 1369, 1304, 1250; HRMS (ESI): \(m/z\) calcd for C\(_{19}\)H\(_{15}\)BrO\(_2\)Na ([M+Na\(^{+}\)]) 393.0314, found 393.0331; Enantiomeric excess of 9i was determined by chiral stationary phase HPLC analysis using a ChiralPak IC column (90:10 hexanes/i-PrOH at 1.0 mL/min, \(\lambda = 220\) nm), major enantiomer: \(t_R = 15.8\) min, minor enantiomer: \(t_R = 17.1\) min.

Diethyl (R)-2-[3-oxo-1-[4-(trifluoromethyl)phenyl]propyl]malonate (9j)\(^{17}\)

Colorless oil, 29.6 mg, 82% yield; \([\alpha]_D^{24} = -55.2\) (c 1.0, CHCl\(_3\), 95% ee); \(^1\)H NMR (500 MHz, CDCl\(_3\)) \(\delta 9.61\) (t, \(J = 7.0\) Hz, 1H), 7.55 (d, \(J = 8.0\) Hz, 2H), 7.39 (d, \(J = 8.0\) Hz, 2H), 4.23-4.18 (m, 2H), 4.11-4.06 (m, 1H), 3.96 (q, \(J = 7.0\) Hz, 2H), 3.72 (d, \(J = 10.0\) Hz, 1H), 3.03-2.90 (m, 2H), 1.26 (t, \(J = 7.0\) Hz, 3H), 1.01 (t, \(J = 7.0\) Hz, 3H); \(^1^3\)C NMR (125 MHz, CDCl\(_3\)) \(\delta 199.1, 167.7, 167.2, 144.2, 128.6, 125.6, 125.5, 61.9, 61.6, 56.9, 47.3, 38.9, 14.0, 13.7; Enantiomeric excess of 9j was determined by chiral stationary phase HPLC analysis using a ChiralPak IC column (95:5 hexanes/i-PrOH at 1.0 mL/min, \(\lambda = 220\) nm), major enantiomer: \(t_R = 16.0\) min, minor enantiomer: \(t_R = 17.7\) min.
Diethyl (R)-2-[3-oxo-1-(p-tolyl)propyl]malonate (9k)\textsuperscript{16}

Colorless oil, 23.9 mg, 78% yield; $[\alpha]_D^{24} = -66.8$ (c 1.0, CHCl\textsubscript{3}, 98% ee); $^1$H NMR (500 MHz, CDCl\textsubscript{3}) $\delta$ 9.58 (t, $J = 7.0$ Hz, 1H), 7.13-7.08 (m, 4H), 4.22-4.18 (m, 2H), 4.00-3.93 (m, 3H), 3.68 (d, $J = 10.0$ Hz, 1H), 2.92-2.81 (m, 2H), 2.28 (s, 3H), 1.26 (t, $J = 7.0$ Hz, 3H), 1.02 (t, $J = 7.0$ Hz, 3H); $^{13}$C NMR (125 MHz, CDCl\textsubscript{3}) $\delta$ 200.3, 168.0, 167.4, 137.1, 136.6, 129.4, 127.9, 61.8, 61.4, 57.6, 47.5, 39.2, 21.0, 14.0, 13.8; Enantiomeric excess of 9k was determined by chiral stationary phase HPLC analysis using a ChiralPak IC column (90:10 hexanes/i-PrOH at 1.0 mL/min, $\lambda = 220$ nm), major enantiomer: $t_R = 29.5$ min, minor enantiomer: $t_R = 24.2$ min.

Diethyl (R)-2-[1-(4-methoxyphenyl)-3-oxopropyl]malonate (9l)\textsuperscript{17}

Colorless oil, 26.3 mg, 82% yield; $[\alpha]_D^{24} = -45.2$ (c 1.0, CHCl\textsubscript{3}, 96% ee); $^1$H NMR (500 MHz, CDCl\textsubscript{3}) $\delta$ 9.57 (t, $J = 7.0$ Hz, 1H), 7.16-7.14 (m, 2H), 6.81-6.79 (m, 2H), 4.21-4.16 (m, 2H), 3.98-3.92 (m, 3H), 3.75 (s, 3H), 3.64 (d, $J = 10.0$ Hz, 1H), 2.91-2.97 (m, 2H), 1.24 (t, $J = 7.0$ Hz, 3H), 1.02 (t, $J = 7.0$ Hz, 3H); $^{13}$C NMR (125 MHz, CDCl\textsubscript{3}) $\delta$ 200.3, 168.0, 167.4, 158.8, 131.6, 129.1, 114.0, 61.7, 61.4, 57.7, 55.2, 47.5, 38.8, 14.0, 13.8; Enantiomeric excess of 9l was determined by chiral stationary phase HPLC analysis using a ChiralPak IC column (95:5 hexanes/i-PrOH at 1.0 mL/min, $\lambda = 220$ nm), major enantiomer: $t_R = 66.9$ min, minor enantiomer: $t_R = 65.0$ min.

Diethyl (R)-2-[1-(3-chlorophenyl)-3-oxopropyl]malonate (9m)\textsuperscript{16}

Colorless oil, 25.7 mg, 79% yield; $[\alpha]_D^{24} = -37.9$ (c 1.0, CHCl\textsubscript{3}, 94% ee); $^1$H NMR (500 MHz, CDCl\textsubscript{3}) $\delta$ 9.61 (s, 1H), 7.26-7.20 (m, 3H), 7.16-7.14 (m, 1H), 4.23-4.18 (m, 2H), 4.02-3.97 (m, 3H), 3.68 (d, $J = 10.0$ Hz, 1H), 2.98-2.86 (m, 2H), 1.26 (t, $J = 7.0$ Hz, 3H), 1.05 (t, $J = 7.0$ Hz, 3H); $^{13}$C NMR (125 MHz, CDCl\textsubscript{3}) $\delta$ 199.2, 167.7, 167.2, 142.1, 134.4, 129.9, 128.3, 127.7, 126.4, 61.8, 61.6, 57.1, 47.2, 38.9, 14.0, 13.7; Enantiomeric excess of 9m was determined by chiral stationary phase HPLC analysis using a ChiralPak IC column (90:10 hexanes/i-PrOH at 1.0 mL/min, $\lambda = 220$ nm), major enantiomer: $t_R = 18.4$ min, minor enantiomer: $t_R = 16.6$ min.

Diethyl (R)-2-[3-oxo-1-(o-tolyl)propyl]malonate (9n)\textsuperscript{17}

Colorless oil, 22.3 mg, 73% yield; $[\alpha]_D^{24} = -48.7$ (c 1.0, CHCl\textsubscript{3}, 97% ee); $^1$H NMR (500 MHz, CDCl\textsubscript{3}) $\delta$ 9.57 (t, $J = 7.0$ Hz, 1H), 7.14-7.09 (m, 4H), 4.31-4.26 (m, 1H), 4.23-4.19 (m, 2H), 3.95-3.90 (m, 2H), 3.72 (d, $J = 10.0$ Hz, 1H), 2.95-2.83 (m, 2H), 3.15 (s, 3H), 1.27 (t, $J = 7.0$ Hz, 3H), 0.97 (t, $J = 7.0$ Hz, 3H); $^{13}$C NMR (125 MHz, CDCl\textsubscript{3}) $\delta$ 200.0, 168.2, 167.5, 138.3, 136.6, 130.8, 127.1, 126.4, 126.3, 61.8, 61.4, 57.1, 48.1, 34.3, 19.9, 14.0, 13.7; Enantiomeric excess of 9n was determined by chiral stationary phase HPLC analysis using a ChiralPak IC column (95:5 hexanes/i-PrOH at 1.0 mL/min, $\lambda = 220$ nm), major enantiomer: $t_R = 20.1$ min, minor enantiomer: $t_R = 26.1$ min.
Dimethyl (R)-2-(1-oxohexan-3-yl)malonate (9o)

Colorless oil, 15.9 mg, 62% yield; [α]_D^{24} = -14.2 (c 0.7, CHCl₃, 94% ee); ¹H NMR (500 MHz, CDCl₃) δ 9.72 (t, J = 1.5 Hz, 1H), 3.72 (s, 3H), 3.71 (s, 3H), 3.54 (d, J = 6.0 Hz, 1H), 2.76-2.67 (m, 2H), 2.52-2.47 (m, 1H), 1.40-1.27 (m, 4H), 0.88 (t, J = 7.0 Hz, 3H); ¹³C NMR (125 MHz, CDCl₃) δ 201.1, 169.1, 168.8, 54.1, 52.5, 52.4, 52.3, 45.8, 34.6, 32.4, 20.0, 13.9; ν max (neat, cm⁻¹): 2956, 1730, 1436, 1196, 1159, 1038; HRMS (ESI): m/z calcd for C₁₃H₁₂O₄S₆Na ([M+Na]^+) 281.1365, found 281.1347; Enantiomeric excess of 9o was determined (after converted to corresponding α, β-unsaturated ester 9o' with Ph₃P=CHCO₂Et) by chiral stationary phase HPLC analysis using a ChiralPak OD-H column (97:3 hexanes/i-PrOH at 1.0 mL/min, λ = 220 nm), major enantiomer: t_R = 13.4 min, minor enantiomer: t_R = 12.6 min.

Dimethyl (R)-2-(4-oxobutan-2-yl)malonate (9p)

Colorless oil, 11.1 mg, 48% yield; [α]_D^{24} = -8.6 (c 0.55, CHCl₃, 84% ee); ¹H NMR (500 MHz, CDCl₃) δ 9.71 (t, J = 1.5 Hz, 1H), 3.72 (s, 3H), 3.71 (s, 3H), 3.39 (d, J = 7.0 Hz, 1H), 2.87-2.79 (m, 1H), 2.69-2.64 (m, 1H), 2.44-2.37 (m, 1H), 1.04 (d, J = 7.0 Hz, 3H); ¹³C NMR (125 MHz, CDCl₃) δ 200.7, 168.7, 168.6, 56.0, 52.4, 47.9, 27.9, 17.9; ν max (neat, cm⁻¹): 2958, 1728, 1440, 1191, 1155, 1036; HRMS (ESI): m/z calcd for C₁₁H₁₈O₂Na ([M+Na]^+) 253.1052, found 253.1038; Enantiomeric excess of 9p was determined (after being converted to the corresponding α, β-unsaturated ester 9p' with Ph₃P=CHCO₂Et) by chiral stationary phase HPLC analysis using a ChiralPak OD-H column (90:10 hexanes/i-PrOH at 1.0 mL/min, λ = 220 nm), major enantiomer: t_R = 11.2 min, minor enantiomer: t_R = 9.9 min.

(S)-4-Nitro-3-phenylbutanal (10)⁴b

Colorless oil, 13.7 mg, 72% yield; [α]_D^{24} = -28.5 [(c 0.68, CHCl₃, 98% ee); lit. [α]_D^{24} = -23.7 [(c 0.71, CHCl₃)]; ¹H NMR (500 MHz, CDCl₃) δ 9.70 (t, J = 1.0 Hz, 1H), 7.36-7.33 (m, 2H), 7.30-7.26 (m, 1H), 7.24-7.22 (m, 2H), 4.68 (dd, J = 7.0, 12.5 Hz, 1H), 4.62 (dd, J = 7.5, 12.5 Hz, 1H), 4.11-4.05 (m, 1H), 2.95 (dd, J = 1.5, 3.0 Hz, 1H), 2.94 (dd, J = 1.5, 3.0 Hz, 1H); ¹³C NMR (125 MHz, CDCl₃) δ 196.2, 135.6, 125.6, 124.8, 76.8, 43.9, 35.4; Enantiomeric excess of 10 (after being converted to the corresponding α, β-unsaturated ester 10' with Ph₃P=CHCO₂Et) was determined by chiral stationary phase HPLC analysis using a ChiralPak IC column (80:20 hexanes/i-PrOH at 1.0 mL/min, λ = 254 nm), major enantiomer: t_R = 20.3 min, minor enantiomer: t_R = 23.0 min.

(1S,5S,6R,7R)-5-Hydroxy-8-oxo-7-phenylbicyclo[3.2.1]octane-6-carbaldehyde (11)⁴²

Colorless oil, 17.6 mg, 72% yield; [α]_D^{24} = -39.1 [(c 0.88, CHCl₃, 97% ee); lit. [α]_D^{24} = -53.6 (c 1.0, CHCl₃)]; ¹H NMR (500 MHz, CDCl₃) δ 10.03 (s, 1H), 7.30-7.27 (m, 2H), 7.22-7.19 (m, 1H), 7.13-7.11 (m, 2H), 3.85 (d, J = 7.0 Hz, 1H), 3.32 (br s, 1H), 2.93 (dd, J = 1.5, 7.0 Hz, 1H), 2.71 (dd, J = 2.0, 4.0 Hz, 1H), 2.34-2.30 (m, 1H), 2.22-2.17 (m, 1H), 2.02-1.96 (m, 1H), 1.93-1.81 (m, 2H), 1.67-1.62 (m, 1H); ¹³C NMR (125 MHz, CDCl₃) δ 216.5, 199.3, 145.0, 129.1, 126.9, 126.6, 80.3, 63.1, 50.3, 39.6, 38.6, 35.1, 17.2; Enantiomeric excess of 11 (after
being converted to the corresponding $\alpha, \beta$-unsaturated ester 11' with Ph$_3$P=CHCO$_2$Et) was determined by chiral stationary phase HPLC analysis using a ChiralPak AD-H column (90:10 hexanes/i-PrOH at 1.0 mL/min, $\lambda = 254$ nm), major enantiomer: $t_R = 19.8$ min, minor enantiomer: $t_R = 23.0$ min.

**Additional References**

$^1$H NMR and $^{13}$C NMR Spectra of 3a

500 MHz $^1$H NMR and 125 MHz $^{13}$C NMR Spectra of 3a
500 MHz $^1$H NMR and 125 MHz $^{13}$C NMR Spectra of 3b
500 MHz $^1$H NMR and 125 MHz $^{13}$C NMR Spectra of 3c
500 MHz $^1$H NMR and 125 MHz $^{13}$C NMR Spectra of 3d
500 MHz $^1$H NMR and 125 MHz $^{13}$C NMR Spectra of 3e
500 MHz $^1$H NMR and 125 MHz $^{13}$C NMR Spectra of 3f
500 MHz $^1$H NMR and 125 MHz $^{13}$C NMR Spectra of 3g
500 MHz $^1$H NMR and 125 MHz $^{13}$C NMR Spectra of 3h
500 MHz $^1$H NMR and 125 MHz $^{13}$C NMR Spectra of 3i
500 MHz $^1$H NMR and 125 MHz $^{13}$C NMR Spectra of 3j
500 MHz $^1$H NMR and 125 MHz $^{13}$C NMR Spectra of 3k
500 MHz $^1$H NMR and 125 MHz $^{13}$C NMR Spectra of 9a
500 MHz $^1$H NMR and 125 MHz $^{13}$C NMR Spectra of 9b
500 MHz $^1$H NMR and 125 MHz $^{13}$C NMR Spectra of 9c
500 MHz $^1$H NMR and 125 MHz $^{13}$C NMR Spectra of 9d
500 MHz $^1$H NMR and 125 MHz $^{13}$C NMR Spectra of 9e
500 MHz $^1$H NMR and 125 MHz $^{13}$C NMR Spectra of 9f
500 MHz $^1$H NMR and 125 MHz $^{13}$C NMR Spectra of 9g
500 MHz $^1$H NMR and 125 MHz $^{13}$C NMR Spectra of 9h
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500 MHz $^1$H NMR and 125 MHz $^{13}$C NMR Spectra of 9j
500 MHz $^1$H NMR and 125 MHz $^{13}$C NMR Spectra of 9k
500 MHz $^1$H NMR and 125 MHz $^{13}$C NMR Spectra of 91
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500 MHz $^1$H NMR and 125 MHz $^{13}$C NMR Spectra of 9n
500 MHz $^1$H NMR and 125 MHz $^{13}$C NMR Spectra of 9o
500 MHz $^1$H NMR and 125 MHz $^{13}$C NMR Spectra of 9p
500 MHz $^1$H NMR and 125 MHz $^{13}$C NMR Spectra of 10
500 MHz $^1$H NMR and 125 MHz $^{13}$C NMR Spectra of 11
HPLC Chromatograms

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