Asymmetric Synthesis of Di- and Trisubstituted Cyclopropanes through an Intramolecular Ring Closure

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SUPPORTING INFORMATION

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General Experimental

All reactions were performed in glassware under an atmosphere of dry nitrogen, unless noted. All chemicals and solvents purchased from commercial sources were used as received without further purification. “Brine” refers to a saturated solution of sodium chloride. All reaction temperatures correspond to internal temperatures measured with Teflon coated thermocouples. SiO₂ column chromatography was performed using commercially available pre-packed columns with an automated pump and fraction collector. ¹H and ¹³C NMR spectra were recorded on a Varian Mercury 400 NMR Spectrometer (400 MHz, ¹H; 100 MHz, ¹³C). Spectra were referenced to residual chloroform (7.26 ppm, ¹H; 77.0 ppm, ¹³C). Chemical shifts are reported in ppm, multiplicities are indicated by s (singlet), d (doublet), t (triplet), q (quartet), p (pentet), h (hextet), m (multiplet) and br (broad). Coupling constants, J, are reported in Hertz. Diastereomeric ratios of the cyclopropane products were determined by relative integration of diagnostic peaks in the ¹H NMR spectra. Mass spectra were obtained on a Kratos MS-50 instrument using +ESI or +DCI ionization as noted. Data are reported in the form of m/z (intensity relative to the base peak = 100). High Resolution Mass Spectrometry were performed on a Agilent G6220A TOF Ionization using ESI(+) Positive-ion Electrospray. Melting points were obtained in a capillary tube using a Thomas Hoover melting point apparatus and are uncorrected. HPLC analyses were conducted on a Hewlett Packard Series 1050 HPLC with 220 nm UV detection at 1.0 mL/min flow rate through a Chiralpak 4.6x250 mm column as noted. SFC analyses were conducted on a Thar Technologies SFC with 220 nm UV detection at 3.0 ml/min flow rate through a Chiralpak 4.6x250 mm column as noted.
Methyl 4-(4-bromophenyl)-4-oxobutanoate (1a): In a 100 ml rb flask the 4-(4′-bromophenyl)-4-oxobutanoic acid (5.14 g, 20 mmol), MeOH (40 ml) and H$_2$SO$_4$ (0.4 ml, 7.50 mmol) were combined. The reaction was heated to reflux under N$_2$. After 1h, the reaction was poured into 100 mL 0.25 M K$_2$CO$_3$, was stirred in ice bath for 30 min, and the product was collected by vacuum filtration. Drying in vacuum oven (45 °C, 26 inHg, 1 h) afforded 5.216 g (96%) of 1a as a white solid. The data matches those previously reported.

Data for 1a:
mp: 51-52 °C
HRMS: Calculated for C$_{11}$H$_{11}$O$_3$Br: 269.98916; Found: 269.9887

(S)-Methyl 4-(4-bromophenyl)-4-hydroxybutanoate (2a): In a 25 mL 3-necked round-bottomed flask were combined (R)-CBS-Me, 1.0 M in toluene (0.2 mL, 0.2 mmol) and THF (6 mL) and the solution was cooled in an ice bath. To this solution was simultaneously added by syringe pump a 1.0M solution of 1a in THF (2.0 mL, 2.0 mmol, 1.0 equiv) and 1.0 M BH$_3$ in THF (2.0 mL, 2.0 mmol, 1.0 equiv) over 1 hour. After stirring for 1 h in the ice bath, the reaction was quenched with 1M K$_2$CO$_3$ (6 mL) and warmed to rt. The aqueous layer was extracted with Et$_2$O (10 mL), and the combined organic layers were washed with brine (5 mL), dried over Na$_2$SO$_4$, filtered and concentrated. Purification by SiO$_2$ chromatography (1:2 Et$_2$O: hexanes) afforded 412 mg (75%) of 2a as a clear, colorless oil. The $^1$H NMR and IR match those previously reported.

Data for 2a:
$^{13}$C NMR: (100 MHz, CDCl$_3$)
δ 173.75, 142.64, 131.22, 127.16, 121.06, 72.80, 51.92, 33.93, 30.44.

MS: (DCI/NH$_3$)
292 (50, M+NH$_4$), 290 (55, M+NH$_4$), 257 (95), 255 (100)

HPLC: Chiralpak OJ, 4% IPA in heptane, t$_R$: 17.5 min, 96.6%, t$_R$: 21.3 min, 3.4%
(1S,2S)-methyl 2-(4-bromophenyl)cyclopropanecarboxylate (3a): In a 10 mL round-bottomed flask equipped with a N₂ inlet and magnetic stirbar were combined 2a (273 mg, 1.0 mmol), THF (4 mL), and triethylamine (0.279 mL, 2.0 mmol). This solution was cooled in an icebath and methanesulfonyl chloride (0.086 mL, 1.1 mmol) was added. After stirring the reaction mixture for 20 minutes, a 1.0 M KOTBu in THF (1.7 mL, 1.7 mmol) was added. After stirring for 20 minutes in the icebath, the reaction was quenched with 1M HCl (3 mL) and Et₂O (5 mL) and the aqueous layer was extracted with Et₂O (5 mL). The combined organic layers were washed with brine (3 mL), dried over MgSO₄, filtered and concentrated to give the crude product. Purification by SiO₂ chromatography (10:1 hexane/MTBE) afforded 174 mg (68%) of 3a as a clear, colorless oil.

Data for 3a:

^1H NMR: (400 MHz, CDCl₃)
δ 7.39 (d, J = 8.5, 2H), 6.97 (d, J = 8.4, 2H), 3.72 (s, 3H), 2.49 (ddd, J = 9.2, 6.5, 4.2, 1H), 1.88 (ddd, J = 8.5, 5.3, 4.2, 1H), 1.65 – 1.57 (m, 1H), 1.29 (ddd, J = 8.4, 6.5, 4.7, 1H).
Relative integration between the trans and cis isomers 3.00: 0.28 (3.72 ppm and 3.47 ppm)

^13C NMR: (100 MHz, CDCl₃)
δ 172.96, 138.64, 131.16, 127.62, 119.90, 52.10, 25.90, 24.20, 17.27.

IR: (ATR-Ge)
2951 (w), 1727 (s), 1492 (m), 1437 (m), 1198 (m), 1173 (s), 1074 (m), 1010 (m), 813 (m).

MS: (DCI/NH₃)
274 (90, M+NH₄³⁺), 272 (100, M+NH₄⁺), 210 (45).

HRMS: Calculated for C₁₁H₁₁O₂Br: 253.99424; Found: 253.99459

HPLC: Chiralpak AD-H, 1% IPA in heptane, t_R: 9.0 min, 96.0%, t_R: 12.5 min, 4.0%

Isopropyl 4-(4-bromophenyl)-4-oxobutanoate (1b): In a 100 mL rb flask the 4-(4-bromophenyl)-4-oxobutanoic acid (7.0 g, 27 mmol), i-PrOH (55 ml) and H₂SO₄ (1.0
ml) were combined and heated to reflux under N$_2$. After 1h, the reaction was poured into 100 mL 0.25 M K$_2$CO$_3$, was stirred in ice bath for 30 min, and the product was collected by vacuum filtration. Drying in vacuum oven (45 °C, 26 in Hg, 48 h) afforded 7.42g (92%) of 1b as a white solid.

Data for 1b:

mp: 65-66 °C

$^1$H NMR: (400 MHz, CDCl$_3$)
$\delta$ 7.84 (d, $J = 8.7$, 2H), 7.60 (d, $J = 8.7$, 2H), 5.02 (hept, $J = 6.3$, 1H), 3.25 (t, $J = 6.6$, 2H), 2.73 (t, $J = 6.6$, 2H), 1.24 (d, $J = 6.3$, 6H).

$^{13}$C NMR: (100 MHz, CDCl$_3$)
$\delta$ 196.47, 171.64, 134.99, 131.56, 129.20, 127.98, 68.08, 33.54, 28.76, 22.07.

MS: (DCI/NH$_3$) 318 (100, M+NH$_4$), 316 (100, M+NH$_4$), 301 (15, M+H), 299 (20, M+H).

HRMS: Calculated for C$_{13}$H$_{15}$O$_3$Br: 298.02046; Found: 298.20240

(S)-Isopropyl 4-(4-bromophenyl)-4-hydroxybutanoate (2b): In a 25 mL 3-necked round-bottomed flask were combined (R)-CBS-Me, 1.0 M in toluene (0.2 mL, 0.2 mmol) and THF (6 mL) and the solution was cooled in an icebath. To this solution was simultaneously added by syringe pump a 1.0 M solution of 1b in THF (2.0 mL, 2.0 mmol, 1.0 equiv) and 1.0 M BH$_3$ in THF (2.0 mL, 2.0 mmol, 1.0 equiv) over 1.5 hour. After stirring for 45 minutes in the icebath, the reaction was quenched with 1M K$_2$CO$_3$ (6 mL) and warmed to rt. The aqueous layer was extracted with MTBE (2 x 5 mL), and the combined organic layers were washed with brine (5 mL), dried over Na$_2$SO$_4$, filtered and concentrated. Purification by SiO$_2$ chromatography (2:1 MTBE: hexanes) afforded 504 mg (84%) of 2b as a clear, colorless oil.

Data for 2b:

$^1$H NMR: (400 MHz, CDCl$_3$)
$\delta$ 7.46 (d, $J = 8.4$, 2H), 7.22 (d, $J = 8.3$, 2H), 4.99 (hept, $J = 6.3$, 1H), 4.72 (td, $J = 6.2$, 3.6, 1H), 2.67 (s, 1H), 2.38 (t, $J = 7.5$, 2H), 2.02 (q, $J = 6.9$, 2H), 1.22 (s, 6H).

$^{13}$C NMR: (100 MHz, CDCl$_3$)
δ 172.91, 142.76, 131.19, 127.16, 120.99, 72.90, 68.08, 34.02, 31.09, 22.08.

IR: (ATR-Ge)
3438 (br, w), 2980 (w), 1726 (s), 1710 (s), 1487 (w), 1374 (m), 1108 (s), 1071 (m), 1010 (m), 821 (m).

MS: (DCI/NH$_3$)
320 (60, M+NH$_4^+$), 318 (60, M+NH$_4^+$), 303 (15, M+H), 301 (15, M+H), 285 (80), 283 (100).

HRMS: Calculated for C$_{13}$H$_{17}$O$_3$Br: 300.03611; Found: 300.0359

HPLC: Chiralpak OD, 4% IPA in heptane, $t_R$: 12.9 min, 95.7%, $t_R$: 15.1 min, 4.3%

(1S,2S)-Isopropyl 2-(4-bromophenyl)cyclopropanecarboxylate (3b): In a 10 mL round-bottomed flask equipped with a N$_2$ inlet and magnetic stirbar were combined 2b (301 mg, 1.0 mmol), THF (4 mL), and triethylamine (0.279 mL, 2.0 mmol). This solution was cooled in an icebath and methanesulfonyl chloride (0.086 mL, 1.1 mmol) was added. After stirring the reaction mixture for 20 minutes, a 1.0 M KOTBu in THF (2.0 mL, 2.0 mmol) was added. After stirring for 20 minutes in the icebath, the reaction was quenched with 1M HCl (3 mL) and Et$_2$O (5 mL) and the aqueous layer was extracted with Et$_2$O (5 mL). The combined organic layers were washed with brine (3 mL), dried over MgSO$_4$, filtered and concentrated to give the crude product. Purification by SiO$_2$ chromatography (14:1 hexane/MTBE) afforded 250 mg (88%) of 3b as a clear, colorless oil.

Data for 3b:

$^1$H NMR: (400 MHz, CDCl$_3$)
δ 7.39 (d, $J = 8.5$, 2H), 6.96 (d, $J = 8.3$, 2H), 5.03 (hept, $J = 6.3$, 1H), 2.46 (ddd, $J = 9.2$, 6.4, 4.2, 1H), 1.85 (ddd, $J = 8.5$, 5.3, 4.2, 1H), 1.59 (ddd, $J = 9.2$, 5.3, 4.6, 1H), 1.28 – 1.20 (m, 7H).
Relative integration between the trans: cis isomer 1.00: 0.11 (5.03 ppm and 4.74 ppm)

$^{13}$C NMR: (100 MHz, CDCl$_3$)
δ 172.00, 138.92, 131.12, 127.56, 119.78, 68.17, 25.67, 24.72, 22.15, 17.40.

IR: (ATR-Ge)
2985 (w), 1715 (s), 1396 (m), 1106 (s), 1009 (m), 823 (m).
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MS:  
(DCI/NH$_3$)
302 (100, M+NH$_4$), 300 (100, M+NH$_4$)

HRMS:  
Calculated for C$_{13}$H$_{15}$O$_2$Br:  282.02554; Found: 282.02509

HPLC:  
Chiralpak AD-H, 0.5% IPA in heptane, t$_R$: 11.3 min, 5.7%, t$_R$: 12.6 min, 94.3%

$t$-Butyl 4-(4'-bromophenyl)-4-oxobutanoate (1c):  
In a 100 mL round-bottomed flask was combined the 4-(4'-bromophenyl)-4-oxybutanonic acid (2.57g, 10 mmol, 1.0 equiv), CH$_2$Cl$_2$ (20 mL) and perchloric acid (0.060 mL, 0.1 equiv). The reaction mixture was sealed with a rubber septum and cooled in an ice bath. Isobutylene (6.1 g, 10.9 equiv) was bubbled into the sealed flask. The reaction solution was allowed to warm to rt, stirred for 30 min and quenched with 1M NaOH (13 mL). The organic layer was separated, dried oven MgSO$_4$ and concentrated to a solid. The product was purified by recrystallization from EtOH (15 mL) and H$_2$O (35 mL) to afford a white solid. Drying in a vacuum oven (45 °C, 16h, 26 in Hg) afforded 2.83g (90%) of 1c as a white solid.

Data for 1c:

\[
\text{mp: 77-78 °C}
\]

$^1$H NMR:  
(400 MH$_z$, CDCl$_3$)
\(\delta 7.84\ (d, J = 8.6, 2H), 7.59\ (d, J = 8.6, 2H), 3.21\ (t, J = 6.6, 2H), 2.68\ (t, J = 6.6, 2H), 1.45\ (s, 9H).

$^{13}$C NMR:  
(100 MH$_z$, CDCl$_3$)
\(\delta 196.6, 171.4, 135.1, 131.6, 129.2, 127.9, 80.7, 33.6, 29.6, 28.3.

IR:  
(ATR-Ge)
3025 (w), 2918 (w), 1724 (s), 1683 (s), 1583 (m), 1485 (w), 1413 (w), 1392 (w), 1366 (w), 1317 (s), 1151 (s), 1070 (m), 991 (m), 844 (m), 787 (s), 756 (w).

MS:  
(DCI/NH$_3$)
332 (60, M+NH$_4$), 330 (60, M+NH$_4$), 315 (20, M+H), 313 (20, M+H), 276 (100), 274 (100), 196 (80).

HRMS:  
Calculated for C$_{14}$H$_{17}$BrO$_3$:  312.03611; Found: 312.03651
(S)-tert-Butyl 4-(4-bromophenyl)-4-hydroxybutanoate (2c): In a 25 mL 3-necked round-bottomed flask were combined (R)-CBS-Me, 1.0 M in toluene (0.2 mL, 0.2 mmol) and THF (6 mL) and the solution was cooled in an icebath. To this solution was simultaneously added by syringe pump a 1.0 M solution of 1c in THF (2.0 mL, 2.0 mmol, 1.0 equiv) and 1.0 M BH$_3$ in THF (2.0 mL, 2.0 mmol, 1.0 equiv) over 1 hour. After stirring for 45 minutes in the icebath, the reaction was quenched with 1M K$_2$CO$_3$ (3 mL) and warmed to rt. The aqueous layer was extracted with MTBE (2 x 5 mL), and the combined organic layers were washed with brine (5 mL), dried over Na$_2$SO$_4$, filtered and concentrated. Purification by SiO$_2$ chromatography (3:1 MTBE: hexanes) afforded 556 mg (88%) of 2c as a white solid.

Data for 2c:

mp: 55-56 ºC

$^1$H NMR: (400 MHz, CDCl$_3$)
δ 7.47 (d, $J$ = 8.4, 2H), 7.23 (d, $J$ = 8.4, 2H), 4.74 (td, $J$ = 6.2, 4.0, 1H), 2.62 (d, $J$ = 3.8, 1H), 2.35 (t, $J$ = 7.3, 2H), 2.00 (q, $J$ = 7.0, 2H), 1.46 (s, 9H).

$^{13}$C NMR: (100 MHz, CDCl$_3$)
δ 172.86, 142.88, 131.17, 127.18, 120.93, 80.75, 72.96, 34.11, 31.99, 28.31

IR: (ATR-Ge)
3280 (br, m), 2978 (w), 2929 (w), 1724 (s), 1487 (w), 1386 (m), 1232 (m), 1152 (s), 1009 (s), 824 (s).

MS: (DCI/NH$_3$)
334 (70, M+NH$_4$), 332 (80, M+NH$_4$), 317 (20, M+H), 315 (20, M+H), 299 (15), 297 (15), 278 (80), 276 (100), 258 (50), 260 (50).

HRMS: Calculated for C$_{14}$H$_{19}$BrO$_3$: 314.05176; Found: 314.05225

HPLC: Chiralpak OD, 4% IPA in heptane, $t_R$: 10.7 min, 98.0%; $t_S$: 12.1 min: 2.0%
(1S,2S)-tert-Butyl 2-(4-bromophenyl)cyclopropanecarboxylate (3c): In a 10 mL round-bottomed flask equipped with a N₂ inlet and magnetic stirbar were combined 2c (315 mg, 1.0 mmol), THF (4 mL), and triethylamine (0.279 mL, 2.0 mmol). This solution was cooled in an icebath and methanesulfonyl chloride (0.086 mL, 1.1 mmol) was added. After stirring the reaction mixture for 20 minutes, a 1.0 M KOTBu in THF (2.0 mL, 2.0 mmol) was added. After stirring for 20 minutes in the icebath, the reaction was quenched with 1M HCl (3 mL) and Et₂O (5 mL) and the aqueous layer was extracted with Et₂O (5 mL). The combined organic layers were washed with brine (3 mL), dried over MgSO₄, filtered and concentrated to give the crude product. Purification by SiO₂ chromatography (14:1 hexane/MTBE) afforded 275mg (93%) of 3c as a white solid. ¹H and ¹³C NMR match those in the literature.³

Data for 3c:

mp: 76-77 ºC

¹H NMR: (400 MHz, CDCl₃)
Relative integration between the trans: cis isomer 1.00: 0.07 (1.80 ppm and 2.03 ppm)

IR: (ATR-Ge)
2978 (w), 1717 (s), 1491 (w), 1456 (w), 1392 (m), 1369 (m), 1110 (s), 1076 (w), 815 (m).

MS: (DCI/NH₃)
314 (100, M+NH₄), 316 (100, M+NH₄)

HRMS: Calculated for C₁₄H₁₇O₂Br: 296.04119, Found: 296.04136

HPLC: Chiralpak AD-H, heptane, tᵣ: 12.3 min, 97.5%, tᵣ: 14.5 min: 2.5%

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tert-Butyl 4-oxo-4-phenylbutanoate (1d): In a 250 mL round-bottomed flask equipped with a magnetic stirbar was combined 4-phenyl-4-oxybutanonic acid (2.67g, 15.0 mmol, 1.0 equiv), CH₂Cl₂ (10 mL) and sulfuric acid (0.31 mL, 6.0 mmol). The reaction mixture was sealed with a rubber septum and cooled in an ice bath. The isobutylene (21g, 375 mmol) was added. The reaction solution was stirred at 0 ºC for 3 h, and then allowed to warm to rt. After 24 h, the reaction was quenched with 8% sodium bicarbonate (20 mL). The organic layer was dried over MgSO₄ and concentrated to a clear, colorless oil. The product was dried in a vacuum oven (35 ºC, 26 inHg) to afford 2.19 g (62%) of 1d as a clear, colorless oil. ¹H and ¹³C match those previously reported.⁴
Data for 1d:

**IR:**  (KBr)  
2979 (w), 2362 (w), 1728 (m), 1450 (w), 1367 (w), 1229 (w), 1151 (s), 972 (w), 848 (w), 756 (m), 691 (m).

**MS:**  (ESI+)
257 (45, M+Na), 235 (30, M+H), 196 (40), 179 (100), 161 (40).

**HRMS:**  Calculated for C_{14}H_{20}O_3: 236.14124; Found: 236.14087

(S)-tert-Butyl 4-hydroxy-4-phenylbutanoate (2d): In a 50 mL 3-necked round-bottomed flask were combined (R)-CBS-Me, 1.0 M in toluene (0.20 mL, 0.20 mmol) and THF (6 mL) and the solution was cooled in an icebath. To this solution was simultaneously added by syringe pump a 1.0 M solution of 1d in THF (2.0 mL, 2.0 mmol, 1.0 equiv) and 1.0 M BH_3 in THF (2.0 mL, 2.0 mmol, 1.0 equiv) over 1 h. After stirring for 2 h in the icebath, the reaction was quenched with 1M K_2CO_3 (6 mL) and warmed to rt. The aqueous layer was extracted with MTBE (2 x 5 mL), and the combined organic layers were washed with brine (5 mL), dried over Na_2SO_4, filtered and concentrated. Purification by SiO_2 chromatography (gradient heptane to 50% EtOAc/heptane) afforded 362 mg (77%) of 2d as a thick colorless oil. Data matches those previously reported.}

Data for 2d:

**HRMS:**  Calculated for C_{14}H_{20}O_3: 236.14124; Found: 236.14087

**SFC:**  Chiralpak AD-H, 2% IPA, t_R: 12.3 min, 2.3%, t_R: 12.9 min: 97.7%

(1S,2S)-tert-Butyl 2-phenylcyclopropanecarboxylate (3d): In a 10 mL round-bottomed flask equipped with a N_2 inlet and magnetic stirbar were combined 2d (236 mg, 1.0 mmol), THF (4 mL), and triethylamine (0.278 mL, 2.0 mmol). This solution was cooled in an icebath and methanesulfonyl chloride (0.086 mL, 1.1 mmol) was added. After stirring the reaction mixture for 15 minutes, a 1.0 M KOtBu in THF (2.0 mL, 2.0 mmol) was added. After 15 min, 1 M HCl (3 mL) was added and the solution was allowed to warm to rt. The aqueous layer was extracted with MTBE (5 mL, 5 mL). The combined organic layers were washed with brine (3 mL), dried over MgSO_4, filtered and concentrated to give the crude product. Purification by SiO_2 chromatography (gradient...
heptane to 50% EtOAc/heptane) afforded 181 mg (83%) of 3d as a clear, colorless oil. Data matches those previously reported.5

Data for 3d:

HRMS: Calculated for C_{14}H_{18}O_2: 218.13068; Found: 218.13053

SFC: Chiralpak AD-H, 0% IPA, tR: 5.6 min, 97.6%, tR: 8.6 min: 2.4%

**tert-Butyl 4-oxo-4-p-tolylbutanoate (1e):** In a 250 mL round-bottomed flask equipped with a magnetic stirbar was combined 4-(4’-methylphenyl)-4-oxobutanonic acid (2.88g, 15.0 mmol, 1.0 equiv), CH_2Cl_2 (10 mL) and sulfuric acid (0.31 mL, 6.0 mmol). The reaction mixture was sealed with a rubber septum and cooled in an ice bath. The isobutylene (21g, 375 mmol) was added. The reaction solution was stirred at 0 °C for 3 h, and then allowed to warm to rt. After 24 h, the reaction was quenched with 8% sodium bicarbonate (20 mL). The organic layer was dried over MgSO_4 and concentrated to a clear, colorless oil. The product was dried in a vacuum oven (35 °C, 26 inHg) to afford 3.2 g (86%) of 1e as a white solid.

Data for 1e:

mp: 44-45 °C

^1^H NMR: (400 MHz, CDCl_3)
7.87 (s, 2H), 7.26 – 7.22 (m, 2H), 3.22 (t, J = 6.7, 2H), 2.66 (t, J = 6.7, 2H), 2.40 (s, 3H), 1.44 (s, 9H).

^13^C NMR: (100 MHz, CDCl_3)
δ 197.19, 171.62, 143.39, 133.86, 128.87, 127.77, 80.42, 33.53, 29.69, 28.28, 21.89.

IR: (ATR-Ge)
2953 (w), 1730 (m), 1682 (m), 1605 (w), 1480 (w), 1456 (w), 1415 (w), 1392 (w), 1365 (w), 1320 (w), 1305 (w), 1248 (w), 1149 (s), 997 (w), 948 (w), 856 (w), 786 (m), 754 (w).

MS: (DCI/NH_3)
249 (20, M+H), 210 (20), 193 (100), 174 (40).

HRMS: Calculated for C_{15}H_{20}O_3: 248.14124; Found: 248.14142
(S)-tert-Butyl 4-hydroxy-4-p-tolylbutanoate (2e): In a 25 mL 3-necked round-bottomed flask were combined (R)-CBS-Me, 1.0 M in toluene (0.2 mL, 0.2 mmol) and THF (6 mL) and the solution was cooled in an icebath. To this solution was simultaneously added by syringe pump a 1.0 M solution of 1e in THF (2.0 mL, 2.0 mmol, 1.0 equiv) and 1.0 M BH$_3$ in THF (2.0 mL, 2.0 mmol, 1.0 equiv). After stirring for 45 minutes in the icebath, the reaction was quenched with 1M K$_2$CO$_3$ (3 mL) and warmed to rt. The aqueous layer was extracted with MTBE (2 x 5 mL), and the combined organic layers were washed with brine (5 mL), dried over Na$_2$SO$_4$, filtered and concentrated. Purification by SiO$_2$ chromatography (3:1 MTBE: hexanes) afforded 400 mg (80%) of 2e as a clear, colorless oil.

Data for 2e:

$^1$H NMR: (400 MHz, CDCl$_3$)
$\delta$ 7.23 (d, $J = 8.1$, 2H), 7.15 (d, $J = 7.9$, 2H), 4.69 (ddd, $J = 7.2$, 5.7, 3.9, 1H), 2.52 (d, $J = 3.7$, 1H), 2.35 (s, 4H), 2.32 (d, $J = 7.1$, 2H), 2.10 – 1.95 (m, 2H), 1.45 (s, 9H).

$^{13}$C NMR: (100 MHz, CDCl$_3$)
$\delta$ 172.77, 140.84, 136.78, 128.77, 125.38, 80.39, 73.43, 34.16, 32.18, 28.30, 21.36.

MS: (DCI/NH$_3$)
268 (20, M + NH$_4$), 251 (10, M + H), 233 (75), 211 (20), 194 (100).

HRMS: Calculated for C$_{15}$H$_{22}$O$_3$: 250.1569; Found: 250.1574.

SFC: Chiralpak AD-H, 2% IPA, $t_R$: 15.7 min, 3.5%, $t_R$: 16.5 min, 96.5%.

(1S,2S)-tert-Butyl 2-p-tolylcyclopropanecarboxylate (3e): In a 10 mL round-bottomed flask equipped with a N$_2$ inlet and magnetic stirbar were combined 2e (280 mg, 1.1 mmol), THF (4 mL), and triethylamine (0.316 mL, 2.2 mmol). This solution was cooled in an icebath and methanesulfonyl chloride (0.096 mL, 1.2 mmol) was added. After stirring the reaction mixture for 20 minutes, a 1.0 M KOtBu in THF (2.2 mL, 2.2 mmol) was added. After stirring for 20 minutes in the icebath, the reaction was quenched with 1M HCl (5 mL) and Et$_2$O (5 mL) and the aqueous layer was extracted with MTBE
The combined organic layers were washed with brine (3 mL), dried over MgSO$_4$, filtered and concentrated to give the crude product. Purification by SiO$_2$ chromatography (14:1 hexane/MTBE) afforded 243mg (90%) of $3e$ as a clear, colorless oil. $^1$H and $^{13}$C data matches those previously reported.$^3$

Data for $3e$:

$^1$H NMR: (400 MH$_z$, CDCl$_3$)
Relative integration between the trans: cis isomer 1.00: 0.07 (1.48 ppm and 1.28 ppm)

MS: (DCI/NH$_3$)
250 (80, M+NH4), 134 (100).

HRMS: Calculated for C$_{15}$H$_{20}$O$_2$: 232.1463; Found: 232.1467

SFC: Chiralpak AD-H, 0% IPA, $t_R$: 7.0 min, 96.2%, $t_R$: 11.9 min, 3.8%.

**tert-Butyl 4-(4-cyanophenyl)-4-oxobutanoate (1f):** In a 100 mL round-bottomed flask was combined $1c$ (2.9g, 9.3 mmol), sodium carbonate (0.98g, 9.3 mmol), palladium acetate (21 mg, 0.093 mmol), $i$-PrOH (1.5 mL) and NMP (29 mL). This mixture was heated under N$_2$ to 140 ºC and K$_4$FeCN$_6$ 3H$_2$O (1.56g, 3.7 mmol) was added. After 3.5 h the reaction was cooled to rt, diluted with MTBE (50 mL) and filtered. The resulting solution was washed with H$_2$O (50 mL) and brine (20 mL). The organic layer was concentrated *in vacuo* to a yellow oil which was purified by SiO$_2$ chromatography (50% CH$_2$Cl$_2$ to 80% CH$_2$Cl$_2$ in hexanes) to afford 1.01 g (42%) of $1f$ as a white solid.

Data for $1f$:

$^1$H NMR: (400 MH$_z$, CDCl$_3$)
$\delta$ 8.06 (d, $J = 8.3$, 2H), 7.77 (d, $J = 8.3$, 2H), 3.25 (t, $J = 6.5$, 2H), 2.71 (t, $J = 6.5$, 2H), 1.45 (s, 9H).

$^{13}$C NMR: (100 MH$_z$, CDCl$_3$)
$\delta$ 196.42, 171.20, 139.27, 132.18, 128.13, 117.68, 116.15, 80.88, 33.95, 29.45, 28.31.

IR: (ATR-Ge)
2989 (w), 2230 (w), 1726 (s), 1688 (s), 1399 (m), 1366 (s), 1245 (m), 1233 (s), 1146 (s), 837 (s), 757 (w).
(S)-tert-Butyl 4-(4-cyanophenyl)-4-hydroxybutanoate (2f): In a 10 mL 1-necked round-bottomed flask were combined (R)-CBS-Me, 1.0 M in toluene (0.20 mL, 0.20 mmol) and THF (6 mL) and the solution was cooled in an ice bath. To this solution was simultaneously added by syringe pump a 1.0M solution of 1f in THF (2.0 mL, 2.0 mmol, 1.0 equiv) and 1.0 M BH$_3$ in THF (2.0 mL, 2.0 mmol) over 1 h. After the addition was complete, the reaction solution was stirred for 2 h in the ice bath, quenched with 1M K$_2$CO$_3$ (8 mL) and warmed to rt. The aqueous layer was extracted with MTBE (2 x 10 mL), and the combined organic layers were washed with brine (10 mL), dried over Na$_2$SO$_4$, filtered and concentrated. Purification by SiO$_2$ chromatography (1:1 MTBE: hexanes) afforded 305 mg (58%) of 2f as a clear, colorless oil.

Data for 2f:

$^1$H NMR: (400 MHz, CDCl$_3$)
δ 7.64 (d, $J = 8.4$, 2H), 7.48 (d, $J = 8.1$, 2H), 4.85 (dt, $J = 8.1$, 4.2, 1H), 2.97 (d, $J = 4.0$, 1H), 2.38 (td, $J = 6.8$, 2.4, 2H), 2.13 – 1.90 (m, 2H), 1.46 (s, 9H).

$^{13}$C NMR: (100 MHz, CDCl$_3$)
δ 182.60, 172.94, 149.29, 131.96, 126.11, 118.57, 81.09, 72.97, 34.06, 31.94, 28.33, 27.24.

IR: (ATR-Ge)
3479 (br, m), 2979 (m), 2932 (m), 2229 (m), 1726 (s), 1609 (w), 1368 (m), 1255 (m), 1151 (s), 1075 (m), 844 (m).

MS: (DCI/NH$_3$)
279 (100, M + NH$_4$), 262 (20, M+ H), 223 (10).

HRMS: Calculated for C$_{15}$H$_{19}$NO$_3$: 261.13649; Found: 261.13687

HPLC: Chirapak AD-H, 10% IPA in heptanes, $t_R$: 31.4 min, 87.4%, $t_R$: 34.8 min, 12.6%.
(1S,2S)-tert-Butyl 2-(4-cyanophenyl)cyclopropanecarboxylate (3f): In a 10 mL round-bottomed flask equipped with a N₂ inlet and magnetic stirbar were combined 2f (118 mg, 0.41 mmol), THF (1.7 mL), and triethylamine (0.117 mL, 0.83 mmol). This solution was cooled in an icebath and methanesulfonyl chloride (0.035 mL, 0.45 mmol) was added. After stirring the reaction mixture for 20 minutes, a 1.0 M KOTBu in THF (0.91 mL, 0.91 mmol) was added. After stirring for 20 minutes in the icebath, the reaction was quenched with 1M HCl (3 mL) and the aqueous layer was extracted with MTBE (6 mL then 1 mL). The combined organic layers were washed with brine (2 mL), dried over MgSO₄, filtered and concentrated to give the crude product. Purification by SiO₂ chromatography (5:1 hexane/MTBE) afforded 91mg (90%) of 3f as a clear, colorless oil.

Data for 3f:

^1^H NMR: (400 MHz, CDCl₃)
δ 7.56 (d, J = 8.4, 2H), 7.16 (d, J = 8.4, 2H), 2.47 (ddd, J = 9.2, 6.3, 4.2, 1H), 1.89 (ddd, J = 8.5, 5.5, 4.2, 1H), 1.62 (ddd, J = 9.1, 5.4, 4.8, 1H), 1.48 (s, 9H), 1.27 (ddd, J = 8.5, 6.3, 4.7, 1H).
Relative integration between the trans: cis isomer 9.00: 0.94 (1.48 ppm and 1.18 ppm)

^13^C NMR: (100 MHz, CDCl₃)
δ 171.12, 145.95, 131.89, 126.42, 118.60, 109.80, 81.10, 28.38, 26.21, 25.72, 17.92.

IR: (ATR-Ge)
2979 (w), 2228 (m), 1719 (s), 1609 (m), 1370 (m), 1339 (m), 1152 (s), 845 (m), 824 (m).

MS: (DCI/NH₃)
261 (100, M+NH₄⁺)

HRMS: Calculated for C₁₅H₁₇NO₂: 243.12593; Found: 243.12632

HPLC: Chirapak AD-H, 2% IPA in heptanes, tᵣ: 10.0 min, 85.8%, tᵣ: 10.6 min, 14.2%.
**tert-Butyl 4-(4-methoxyphenyl)-4-oxobutanoate (1g):** In a 250 mL round-bottomed flask equipped with a magnetic stirbar was combined 4-(4'-methoxyphenyl)-4-oxobutanoic acid (3.12 g, 15.0 mmol, 1.0 equiv), CH$_2$Cl$_2$ (10 mL) and sulfuric acid (0.31 mL, 6.0 mmol). The reaction mixture was sealed with a rubber septum and cooled in an ice bath. The isobutylene (21 g, 375 mmol) was added. The reaction solution was stirred at 0 °C for 3 h, and then allowed to warm to rt. After 24 h, the reaction was quenched with 8 % sodium bicarbonate (20 mL). The organic layer was dried over MgSO$_4$ and concentrated to a white solid. The product was dried in a vacuum oven (35 ºC, 26 inHg) to afford 2.91 g (73%) of 1g as a white solid.

Data for 1g:

- mp: 53-54 ºC
- $^1$H NMR: (400 MHz, CDCl$_3$) δ 7.98 – 7.92 (m, 2H), 6.95 – 6.89 (m, 2H), 3.86 (s, 3H), 3.20 (t, $J = 6.7$, 2H), 2.66 (t, $J = 6.7$, 2H), 1.45 (s, 9H).
- $^{13}$C NMR: (100 MHz, CDCl$_3$) δ 196.2, 171.7, 162.9, 129.9, 129.5, 113.5, 80.5, 55.5, 33.3, 29.8, 28.3.
- IR: (ATR-Ge) 2976 (w), 1728 (m), 1697 (w), 1673 (m), 1600 (s), 1573 (m), 1512 (w), 1421 (w), 1367 (w), 1317 (s), 1271 (m), 1249 (m), 1174 (s), 1150 (s), 1101 (m), 987 (w), 852 (m), 835 (w), 796 (m), 602 (m)
- MS: (DCI, NH$_3$) 265 (10, M+H), 231 (10), 209 (100), 191 (20)
- HRMS: Calculated for C$_{15}$H$_{20}$O$_4$: 264.13616; Found: 264.13591

[(S)-tert-Butyl 4-hydroxy-4-(4-methoxyphenyl)butanoate (2g):](#) In a 50 mL 3-necked round-bottomed flask were combined (R)-CBS-Me, 1.0 M in toluene (0.096 mL, 0.096 mmol) and THF (6 mL) and the solution was cooled in an icebath. To this solution was simultaneously added by syringe pump a 1.0 M solution of 1g in THF (0.96 mL, 0.96 mmol, 1.0 equiv) and 1.0 M BH$_3$ in THF (0.96 mL, 0.96 mmol, 1.0 equiv) over 1 h. After stirring for 2 h in the icebath, the reaction was quenched with 1M K$_2$CO$_3$ (6 mL) and warmed to rt. The aqueous layer was extracted with MTBE (2 x 5 mL), and the combined organic layers were washed with brine (5 mL), dried over Na$_2$SO$_4$, filtered and concentrated. Purification by SiO$_2$ chromatography (gradient heptane to 50% EtOAc/heptane) afforded 183 mg (72%) of 2g as a thick colorless oil.
Data for 2g:

$^1$H NMR: \((400 \text{ MHz, CDCl}_3)\)
\[\delta 7.29 - 7.24 \text{ (m, 3H)}, 6.92 - 6.83 \text{ (m, 2H)}, 4.71 - 4.64 \text{ (m, 1H)}, 3.80 \text{ (s, 3H)}, 2.36 - 2.23 \text{ (m, 3H)}, 2.08 - 1.92 \text{ (m, 2H)}, 1.45 \text{ (d, J = 6.1, 9H)}\]

$^{13}$C NMR: \((100 \text{ MHz, CDCl}_3)\)
\[\delta 172.74, 158.57, 136.02, 126.69, 113.62, 80.43, 73.33, 34.19, 32.26, 28.35.\]

IR: \((\text{ATR-Ge})\)
\[3433 \text{ (w)}, 2976 \text{ (w)}, 1727 \text{ (m)}, 1612 \text{ (w)}, 1513 \text{ (m)}, 1457 \text{ (w)}, 1367 \text{ (m)}, 1247 \text{ (s)}, 1149 \text{ (s)}, 1073 \text{ (m)}, 1036 \text{ (m)}, 833 \text{ (m)}, 554 \text{ (w)}\]

MS: \((\text{DCI, NH}_3)\)
\[284 \text{ (50, M+NH}_4\text{)}, 267 \text{ (40, M+H)}, 249 \text{ (60)}, 227 \text{ (10)}, 210 \text{ (100)}, 193 \text{ (40)}\]

HRMS: Calculated for C$_{15}$H$_{22}$O$_4$: 266.15181; Found: 266.15192

SFC: Chiralpak AD-H, 3% IPA in heptanes, $t_R$: 16.7 min, 3.7%, $t_R$: 18.4 min, 96.3%.

(1S,2S)-tert-Butyl 2-(4-methoxyphenyl)cyclopropanecarboxylate (3g): In a 10 mL round-bottomed flask equipped with a N$_2$ inlet and magnetic stirbar were combined 2g (133 mg, 0.5 mmol), THF (2 mL), and triethylamine (0.14 mL, 1.0 mmol). This solution was cooled in an icebath and methanesulfonyl chloride (0.043 mL, 0.55 mmol) was added. After stirring the reaction mixture for 15 minutes, a 1.0 M KOtBu in THF (1.0 mL, 1.0 mmol) was added. After 15 min, 1 M HCl (3 mL) was added and the solution was allowed to warm to rt. The aqueous layer was extracted with MTBE (5 mL, 5 mL). The combined organic layers were washed with brine (3 mL), dried over MgSO$_4$, filtered and concentrated to give the crude product. Purification by SiO$_2$ chromatography (gradient heptane to 50% EtOAc/heptane) afforded 94 mg (76%) of 3g as a clear, colorless oil. $^1$H and $^{13}$C NMR matches those previously reported.$^5$

Data for 3g:

$^1$H NMR: \((400 \text{ MHz, CDCl}_3)\)
Relative integration between the trans: cis isomer 1.00: 0.08 (2.39 ppm / 2.49 ppm and 1.75 ppm / 1.93 ppm)

IR: \((\text{KBr})\)
2975 (w), 1715 (m), 1613 (w), 1517 (m), 1456 (w), 1401 (w), 1368 (w), 1340 (w), 1293 (w), 1250 (m), 1211 (w), 1152 (s), 1035 (w), 845 (w), 762 (w), 748 (w), 553 (w), 539 (w).

MS: (DCI, NH₃)
266 (100, M+NH₄), 249 (20, M+H), 210 (20).

HRMS: Calculated for C₁₅H₂₀O₃: 248.14124; Found: 248.14118

HPLC: Chiralpak OJ, 0.2% IPA in heptanes, tᵣ: 18.3 min, 86.4%, tᵣ: 24.2 min, 13.6%.

**Ot-Bu**

**1h**

**tert-Butyl 4-oxo-4-(thiophen-2-yl)butanoate (1h):** In a 250 mL round-bottomed flask equipped with a magnetic stir bar was combined 4-(2'-thiophenyl)-4-oxobutanoic acid (2.76 g, 15.0 mmol, 1.0 equiv), CH₂Cl₂ (10 mL) and sulfuric acid (0.31 mL, 6.0 mmol). The reaction mixture was sealed with a rubber septum and cooled in an ice bath. The isobutylene (21 g, 375 mmol) was added. The reaction solution was stirred at 0 °C for 3 h, and then allowed to warm to rt. After 24 h, the reaction was quenched with 8% sodium bicarbonate (20 mL). The organic layer was dried over MgSO₄ and concentrated to a white solid. The product was dried in a vacuum oven (35 °C, 26 inHg) to afford 3.03 g (84%) of **1h** as a white solid.

**Data for 1h:**

- **mp:** 51-53 °C
- **¹H NMR:** (400 MHz, CDCl₃)
  δ 7.75 (dd, J = 3.8, 1.1, 1H), 7.62 (dd, J = 4.9, 1.1, 1H), 7.12 (dd, J = 4.9, 3.8, 1H), 3.19 (t, J = 6.7, 2H), 2.68 (t, J = 6.7, 2H), 1.44 (s, 9H)
- **¹³C NMR:** (100 MHz, CDCl₃)
  δ 190.57, 171.35, 143.44, 133.12, 131.52, 127.74, 80.67, 34.28, 29.69, 28.31.
- **IR:** (ATR-Ge)
  2978 (w), 1726 (m), 1665 (m), 1519 (w), 1417 (m), 1367 (m), 1233 (m), 1152 (s), 1067 (w), 846 (w), 725 (m)
- **MS:** (ESI+)
  263 (50, M+Na), 241 (15, M+H), 202 (25), 185 (100), 167 (25).
- **HRMS:** Calculated for C₁₂H₁₆O₃S: 240.08202; Found: 240.08233
(S)-tert-Butyl 4-hydroxy-4-(thiophen-2-yl)butanoate (2h): In a 50 mL 3-necked round-bottomed flask were combined (R)-CBS-Me, 1.0 M in toluene (0.2 mL, 0.2 mmol) and THF (6 mL) and the solution was cooled in an icebath. To this solution was simultaneously added by syringe pump a 1.0 M solution of 1h in THF (2.0 mL, 2.0 mmol, 1.0 equiv) and 1.0 M BH₃ in THF (2.0 mL, 2.0 mmol, 1.0 equiv) over 1 h. After stirring for 2 h in the icebath, the reaction was quenched with 1M K₂CO₃ (6 mL) and warmed to rt. The aqueous layer was extracted with MTBE (2 x 5 mL), and the combined organic layers were washed with brine (5 mL), dried over Na₂SO₄, filtered and concentrated. Purification by SiO₂ chromatography (gradient heptane to 50% EtOAc/heptane) afforded 333 mg (69%) of 2h as a thick colorless oil.

Data for 2h:

1H NMR: (400 MHz, CDCl₃)
δ 7.23 (dd, J = 3.7, 2.6, 1H), 6.97 – 6.94 (m, 2H), 4.99 (dd, J = 11.0, 6.4, 1H), 2.63 (s, 1H), 2.39 (dd, J = 10.7, 4.1, 2H), 2.13 (dd, J = 13.6, 6.9, 2H), 1.44 (s, 9H)

13C NMR: (100 MHz, CDCl₃)
δ 172.62, 147.90, 126.39, 124.21, 123.25, 80.64, 69.70, 34.39, 32.09, 28.34.

IR: (ATR-Ge)
2977 (w), 1727 (m), 1455 (w), 1367 (m), 1256 (w), 1152 (s), 1072 (w), 848 (w), 699 (m)

MS: (DCI, NH₃)
260 (80, M+NH₄), 243 (40, M+H), 225 (100), 186 (40), 169 (20)

HRMS: Calculated for C₁₂H₁₈O₃S: 242.09767; Found: 242.09787

SFC: Chiralpak OJ, 3% IPA, tᵣ: 8.1 min, 92.3%, tᵣ: 8.9 min, 7.7%.

(1S,2S)-tert-butyl 2-(thiophen-2-yl)cyclopropanecarboxylate (3h): In a 10 mL round-bottomed flask equipped with a N₂ inlet and magnetic stirbar were combined 2h (242 mg, 1.0 mmol), THF (4 mL), and triethylamine (0.278 mL, 2.0 mmol). This solution was cooled in an icebath and methanesulfonyl chloride (0.086 mL, 1.1 mmol) was added. After stirring the reaction mixture for 15 minutes, a 1.0 M KOtBu in THF (2.0 mL, 2.0 mmol) was added. After 15 min, 1 M HCl (3 mL) was added and the solution was
allowed to warm to rt. The aqueous layer was extracted with MTBE (5 mL, 5 mL). The combined organic layers were washed with brine (3 mL), dried over MgSO$_4$, filtered and concentrated to give the crude product. Purification by SiO$_2$ chromatography (gradient heptane to 50% EtOAc/heptane) afforded 189 mg (84%) of 3h as a clear, colorless oil.

Data for 3h:

$^1$H NMR: (400 MHz, CDCl$_3$)  
$\delta$ 7.07 (dd, $J = 5.1$, 1.2, 1H), 6.89 (dd, $J = 5.1$, 3.5, 1H), 6.81 – 6.79 (m, 1H), 2.68 – 2.59 (m, 1H), 1.85 (ddd, $J = 8.5$, 5.3, 4.1, 1H), 1.57 – 1.50 (m, 1H), 1.48 – 1.45 (m, 11H), 1.27 – 1.20 (m, 2H).  
Relative integration between the trans: cis isomer 1.00: 0.05 (2.62 ppm / 2.52 ppm and 1.85 ppm / 1.98 ppm)

$^{13}$C NMR: (100 MHz, CDCl$_3$)  
$\delta$ 171.47, 144.25, 126.53, 123.39, 122.57, 80.74, 28.39, 26.34, 21.40, 18.27.

IR: (KBr)  
2978 (w), 1719 (m), 1456 (w), 1395 (m), 1367 (w), 1214 (w), 1152 (s), 929 (w), 845 (w), 745 (w), 693 (m)

MS: (DCI)  
242 (100, M+NH$_4$), 225 (20, M+H), 184 (10)

HRMS: Calculated for C$_{12}$H$_{16}$O$_2$S: 224.0871; Found: 224.08701

SFC: Chiralpak AD-H, 0% IPA, $t_R$: 5.3 min, 65.6%, $t_R$: 6.3 min, 34.4%.

![Structure of 5a]

**tert-Butyl 2-methyl-4-oxo-4-phenylbutanoate (5a):** In a 100 mL round-bottomed flask equipped with a magnetic stirbar was combined 2-methyl-4-phenyl-4-oxobutanoic acid (1.92g, 10 mmol, 1.0 equiv), CH$_2$Cl$_2$ (20 mL) and perchloric acid (0.12 mL, 2.0 mmol). The reaction mixture was sealed with a rubber septum and cooled in an ice bath. The isobutylene (7.2g, 128 mmol) was added. The reaction solution was allowed to warm to rt, stirred for 30 min and quenched with 1 M NaOH (13 mL). The organic layer was separated, washed with 1 M K$_2$CO$_3$ (10 mL), brine (10 mL), dried over MgSO$_4$ filtered and concentrated to a solid. Purification by SiO$_2$ chromatography (10:1 hexane/MTBE) afforded 1.74g (74%) of 5a as a white solid.

Data for 5a:

mp: 59-60 °C


**H NMR:** (400 MHz, CDCl₃)  
δ 7.97 (d, J = 7.1, 2H), 7.55 (t, J = 7.4, 1H), 7.45 (t, J = 7.6, 2H), 3.43 (dd, J = 17.2, 7.6, 1H), 3.09 – 2.97 (m, 1H), 2.96 – 2.89 (m, 1H), 1.44 (s, 9H), 1.25 (d, J = 7.0, 3H).

**13C NMR:** (100 MHz, CDCl₃)  
δ 197.56, 174.63, 136.50, 132.70, 128.23, 127.70, 80.25, 42.11, 36.16, 28.23, 17.70.

**IR:** (ATR-Ge)  
2968 (w), 1729 (s), 1676 (s), 1448 (w), 1397 (w), 1234 (w), 1220 (m), 1149 (s), 765 (m).

**MS:** (DCI/NH₃)  
266 (100, M+NH₄⁺), 249 (50, M+H), 210 (95).

**HRMS:** Calculated for C₁₅H₂₀O₃: 248.14124; Found: 248.14217

![Image of chemical structure](image)

**(4S)-tert-Butyl 4-hydroxy-2-methyl-4-phenylbutanoate (6a):** In a 25 mL 3-necked round-bottomed flask were combined (R)-CBS-Me, 1.0 M in toluene (0.2 mL, 0.2 mmol) and THF (6 mL) and the solution was cooled in an icebath. To this solution was simultaneously added by syringe pump a 1.0 M solution of 5a in THF (2.0 mL, 2.0 mmol, 1.0 equiv) and 1.0 M BH₃ in THF (2.0 mL, 2.0 mmol, 1.0 equiv) over 1 hour. After stirring for 30 minutes in the icebath, the reaction was quenched with 1M K₂CO₃ (3 mL) and warmed to rt. The aqueous layer was extracted with MTBE (2 x 5 mL), and the combined organic layers were washed with brine (5 mL), dried over Na₂SO₄, filtered and concentrated. Purification by SiO₂ chromatography (3:7 MTBE/hexanes) afforded 444 mg (89%) of 6a as a clear, colorless oil.

Data for 6a:

**1H NMR:** (400 MHz, CDCl₃) Mixture of both isomers  
δ 7.38 – 7.33 (m, J = 6.6, 3.2, 8H), 7.33 – 7.26 (m, 2H), 4.79 (dt, J = 9.1, 3.7, 1H), 4.76 – 4.69 (m, 1H), 2.68 – 2.55 (m, 1H), 2.54 – 2.41 (m, 2H), 2.26 – 2.14 (m, 2H), 2.04 (dd, J = 13.6, 9.6, 3.7, 1H), 1.81 (dd, J = 13.9, 9.1, 4.4, 1H), 1.68 (dd, J = 16.1, 10.8, 5.3, 1H), 1.48 (s, 9H), 1.47 (s, 9H), 1.19 (d, J = 2.8, 3H), 1.17 (d, J = 2.8, 3H).

**13C NMR:** (100 MHz, CDCl₃) Mixture of both isomers
δ 175.79, 175.67, 144.17, 144.11, 128.18, 128.13, 127.32, 127.11, 125.53, 125.27, 80.28, 72.99, 72.20, 43.23, 43.11, 38.27, 37.52, 28.33, 28.30, 18.16, 18.00.

IR: (ATR-Ge)
3420 (br, w), 2976 (w), 1726 (s), 1454 (m), 1367 (m), 1152 (s), 847 (m), 700 (s).

MS: (DCI/NH₃)
268 (70, M+NH₄), 251 (40, M+H), 233 (25), 212 (80), 194 (100)

HRMS: Calculated for C₁₅H₂₂O₃: 250.15689; Found: 250.15638

HPLC: Chiralpak AD-H, 3% IPA in heptane
Isomer 1: tᵣ:12.9 min, 1.35%, tᵣ:13.4 min, 46.18%
Isomer 2: tᵣ:14.6 min, 48.59%, tᵣ:16.3 min, 3.88%

(1S,2R)-tert-Butyl 1-methyl-2-phenylcyclopropanecarboxylate (7a): In a 10 mL round-bottomed flask equipped with a N₂ inlet and magnetic stirbar were combined 6a (250 mg, 1.0 mmol), THF (4 mL), and triethylamine (0.279 mL, 2.0 mmol). This solution was cooled in an icebath and methanesulfonyl chloride (0.090 mL, 1.15 mmol) was added. After stirring the reaction mixture for 20 minutes, a 1.0 M KOTBu in THF (2.1 mL, 2.1 mmol) was added. After stirring for 20 minutes in the icebath, the reaction was quenched with 1M HCl (4 mL) and Et₂O (8 mL) and the aqueous layer was extracted with Et₂O (8 mL). The combined organic layers were washed with brine (4 mL), dried over MgSO₄, filtered and concentrated to give the crude product. Purification by SiO₂ chromatography (12:1 hexane/MTBE) afforded 161mg (69%) of 7a as a clear, colorless oil.

Data for 7a:

^1H NMR: (400 MHz, CDCl₃)
δ 7.36 – 7.30 (m, 2H), 7.28 – 7.18 (m, 3H), 2.77 (dd, J = 9.0, 7.0, 1H), 1.65 (dd, J = 9.1, 4.4, 1H), 1.52 (s, 9H), 1.14 (dd, J = 7.0, 4.4, 1H), 0.97 (s, 3H).

Relative integration between the trans: cis isomer 1.00: 0.042 (2.77 ppm and 1.93 ppm)

^13C NMR: (100 MHz, CDCl₃)
IR: (ATR-Ge)
2979 (w), 1712 (s), 1452 (w), 1367 (w), 1307 (w), 1149 (s), 852 (m), 766 (m).

MS: (DCI/NH₃)
250 (100, M+NH₄), 233 (10, M+H), 194 (20).

HRMS: Calculated for C₁₅H₂₀O₂: 232.14633; Found: 232.14642

HPLC: Chiralpak AD-H, heptane, tᵣ: 8.0 min, 5.0%, tᵣ: 8.7 min, 95.0%

**tert-Butyl 2-benzyl-4-oxo-4-phenylbutanoate (5b):** In a 100 mL round-bottomed flask equipped with a magnetic stirbar was combined 2-benzyl-4-phenyl-4-oxobutanoic acid (2.42g, 9.0 mmol, 1.0 equiv), CH₂Cl₂ (18 mL) and perchloric acid (0.054 mL, 0.9 mmol). The reaction mixture was sealed with a rubber septum and cooled in an ice bath. The isobutylene (6.9g, 109 mmol) was added. The reaction solution was allowed to warm to rt, stirred for 20 min and quenched with 0.5 M NaOH (23 mL). The organic layer was washed with 1M K₂CO₃ (20 mL), brine (10 ml), dried over MgSO₄ and concentrated to a yellow oil. Purification by SiO₂ chromatography (9:1 hexane : MTBE) afforded the crude product. The product was dried in a vacuum oven (45 °C, 26 inHg) to afford 2.59 g (89%) of 5b as a light yellow solid.

Data for 5b:

mp: 55-56 °C

**¹H NMR:** (400 MHz, CDCl₃)
δ 7.93 – 7.87 (m, 2H), 7.57 – 7.50 (m, 1H), 7.43 (t, J = 7.6, 2H), 7.32 – 7.26 (m, 2H), 7.25 – 7.18 (m, 3H), 3.38 (dd, J = 17.3, 9.0, 1H), 3.26 (tdd, J = 8.9, 6.7, 4.3, 1H), 3.07 (dd, J = 13.6, 6.7, 1H), 2.94 (dd, J = 17.3, 4.3, 1H), 2.84 (dd, J = 13.6, 8.2, 1H), 1.37 (s, 9H).

**¹³C NMR:** (100 MHz, CDCl₃)
δ 197.58, 173.39, 138.41, 136.46, 132.69, 128.82, 128.18, 128.09, 127.67, 126.17, 80.57, 43.23, 39.77, 38.21, 28.16.

IR: (ATR-Ge)
2979 (w), 1722 (s), 1680 (s), 1221 (m), 1149 (s), 849 (m0, 766 (m).

MS: (DCI/NH₃)
342 (90, M+NH₄), 325 (60, M+H), 286 (100).
(4S)-tert-butyl 2-benzyl-4-hydroxy-4-phenylbutanoate (6b): In a 25 mL 3-necked round-bottomed flask were combined (R)-CBS-Me, 1.0 M in toluene (0.25 mL, 0.25 mmol) and THF (8 mL) and the solution was cooled in an icebath. To this solution was simultaneously added by syringe pump a 1.0M solution of 5b in THF (2.5 mL, 2.5 mmol, 1.0 equiv) and 1.0 M BH₃ in THF (2.5 mL, 2.5 mmol, 1.0 equiv) over 1 h. After stirring for 2 h in the icebath, the reaction was quenched with 1M K₂CO₃ (8 mL) and warmed to rt. The aqueous layer was extracted with MTBE (2 x 10 mL), and the combined organic layers were washed with brine (5 mL), dried over Na₂SO₄, filtered and concentrated. Purification by SiO₂ chromatography (1:4 MTBE: hexanes) afforded 727 mg (89%) of 6b as a thick colorless oil as a 51:49 mixture of diastereomers.

Data for 6b:

\(^1\)H NMR: (400 MHz, CDCl₃) Mixture of Diastereomers
δ 7.37 – 7.10 (m, 21H), 4.77 (dt, J = 9.5, 3.5, 1H), 4.69 (ddd, J = 8.1, 5.8, 4.1, 1H), 3.01 – 2.84 (m, 3H), 2.83 – 2.71 (m, 2H), 2.64 (ddd, J = 8.5, 6.8, 4.5, 1H), 2.36 (d, J = 3.8, 1H), 2.21 (ddd, J = 13.9, 9.1, 8.1, 1H), 2.13 (d, J = 4.1, 1H), 2.11 – 1.98 (m, 1H), 1.95 – 1.77 (m, 2H), 1.38 (s, 9H), 1.37 (s, 9H).

\(^1\)C NMR: (100 MHz, CDCl₃) Mixture of Diastereomers
δ 174.40, 174.31, 143.97, 143.74, 138.63, 138.55, 128.76, 128.71, 128.18, 128.12, 127.94, 127.91, 127.39, 127.11, 125.98, 125.64, 125.21, 80.70, 80.53, 73.31, 72.05, 45.68, 44.97, 41.68, 41.24, 39.05, 39.01, 28.24, 28.20.

IR: (ATR-Ge)
3436 (br, w), 2977 (w), 1722 (m), 1455 (m), 1367 (m), 1149 (s), 846 (w), 741 (m).

MS: (DCI/NH₃)
344 (100, M+NH₄), 327 (60, M+H), 309 (20), 288 (30), 270 (25).

HRMS: Calculated for C₂₁H₂₄O₃: 324.17254; Found: 324.17352

HPLC: Chiracel AD-H, 3% IPA in heptane
Matched Isomer: tᵣ: 22.2 min, 1.57%, tᵣ: 26.3 min, 47.16%
Mismatched Isomer: tᵣ: 24.3 min, 47.21%, tᵣ: 29.7 min, 4.06%
(1R,2R)-tert-butyl 1-benzyl-2-phenylcyclopropanecarboxylate (7b): In a 10 mL round-bottomed flask equipped with a N₂ inlet and magnetic stirbar were combined 6b (326 mg, 1.0 mmol), THF (4 mL), and triethylamine (0.279 mL, 2.0 mmol). This solution was cooled in an icebath and methanesulfonyl chloride (0.086 mL, 1.1 mmol) was added. After stirring the reaction mixture for 10 minutes, a 1.0 M KOtBu in THF (2.5 mL, 2.5 mmol) was added. The reaction was warmed to rt. After 45 min, 1 M HCl (3 mL) was added and the aqueous layer was extracted with MTBE (10 mL, 5 mL). The combined organic layers were washed with brine (3 mL), dried over MgSO₄, filtered and concentrated to give the crude product. Purification by SiO₂ chromatography (92:8 hexane/MTBE) afforded 294 mg (95%) of 7b as a clear, colorless oil.

Data for 7b:

**¹H NMR:** (400 MHz, CDCl₃)
δ 7.37 – 7.10 (m, 10H), 3.11 (d, J = 15.7, 1H), 2.79 (dd, J = 9.0, 7.2, 1H), 2.04 (d, J = 15.7, 1H), 1.86 (ddd, J = 9.1, 4.8, 1.3, 1H), 1.37 (s, 9H).
Relative integration between the trans: cis isomer 1.00: 0.03 (3.11 ppm and 3.66 ppm)

**¹³C NMR:** (100 MHz, CDCl₃)
δ 173.10, 140.31, 136.64, 128.93, 128.11, 127.95, 127.63, 126.50, 125.39, 80.51, 34.09, 32.14, 31.66, 28.18, 18.09.

**IR:** (ATR-Ge)
2977 (w), 1711 (s), 1496 (w), 1367 (w), 1223 (m), 1147 (s), 850 (m).

**MS:** (DCI/NH₃)
326 (100, M+NH₄), 309 (20, M+H) 270 (20).

**HRMS:** Calculated for C₂₁H₂₄O₂: 308.17763; Found: 308.17845

**HPLC:** Chiracel AD-H, 0.5% IPA in heptane tᵣ: 6.0 min, 94.1%, tᵣ: 6.8 min, 5.9%

tert-Butyl 2-isopropyl-4-oxo-4-phenylbutanoate (5c): In a 100 mL round-bottomed flask equipped with a magnetic stirbar was combined 2-iso-propyl-4-phenyl-4-oxobutanoic acid (1.13 g, 5.13 mmol, 1.0 equiv), CH₂Cl₂ (25 mL) and pchloric acid (0.031 mL, 0.51 mol). The reaction mixture was sealed with a rubber septum and cooled
in an ice bath. The isobutylene (2.88g, 51 mmol) was added. The reaction solution was allowed to warm to rt, stirred for 20 min and quenched with 1 M NaOH (25 mL). MTBE (50 mL) was added and the organic layer was separated, washed with 1M K$_2$CO$_3$ (20 mL), brine (20 mL), dried over MgSO$_4$ and concentrated to a yellow oil. Purification by SiO$_2$ chromatography (10:1 hexanes/MTBE) afforded 1.32 g (93%) of 5c as a light yellow oil.

Data for 5c:

$^1$H NMR: (400 MHz, CDCl$_3$)
$\delta$ 8.00 – 7.94 (m, 2H), 7.58 – 7.51 (m, 1H), 7.50 – 7.42 (m, 2H), 3.54 – 3.36 (m, 1H), 2.97 – 2.81 (m, 2H), 2.14 – 1.96 (m, 1H), 1.44 (s, 9H), 1.01 (dd, $J$ = 6.8, 1.1, 6H).

$^{13}$C NMR: (100 MHz, CDCl$_3$)

IR: (ATR-Ge)
2966 (w), 1722 (s), 1688 (s), 1449 (w0, 1367 (m), 1258 (m), 1152 (s), 1003 (w), 849 (m), 756 (m).

MS: (DCI/NH$_3$)
294 (100, M+NH$_4$), 277 (40, M+H), 238 (20).

HRMS: Calculated for C$_{17}$H$_{24}$O$_3$: 276.17254; Found: 276.17267

(4S)-tert-Butyl 4-hydroxy-2-isopropyl-4-phenylbutanoate (6c): In a 25 mL 3-necked round-bottomed flask were combined (R)-CBS-Me, 1.0 M in toluene (0.25 mL, 0.25 mmol) and THF (8 mL) and the solution was cooled in an icebath. To this solution was simultaneously added by syringe pump a 1.0 M solution of 5c in THF (2.5 mL, 2.5 mmol, 1.0 equiv) and 1.0 M BH$_3$ in THF (2.5 mL, 2.5 mmol, 1.0 equiv) over 1 hour. After stirring for 2 h in the icebath, the reaction was quenched with 1M K$_2$CO$_3$ (8 mL) and warmed to rt. The aqueous layer was extracted with MTBE (2 x 10 mL), and the combined organic layers were washed with brine (5 mL), dried over Na$_2$SO$_4$, filtered and concentrated. Purification by SiO$_2$ chromatography (1:10 MTBE: hexanes) afforded 271 mg (38%) of the matched isomer 6c and 309 mg (44%) of the mismatched isomer 6c as clear, colorless oils.

Data for 6c, Major diastereomer:
$^1$H NMR: (400 MHz, CDCl$_3$)
$\delta$ 7.39 – 7.31 (m, 4H), 7.30 – 7.23 (m, 1H), 4.72 (dt, $J = 9.7$, 3.2, 1H), 2.41 (ddd, $J = 11.2$, 7.0, 3.2, 1H), 2.26 (dd, $J = 3.6$, 0.5, 1H), 2.00 (ddd, $J = 13.9$, 11.4, 2.7, 1H), 1.90 (oct, $J = 6.8$, 1H), 1.81 (ddd, $J = 14.0$, 9.7, 3.2, 1H), 1.50 (s, 9H), 0.94 (dd, $J = 8.9$, 6.8, 6H).

$^{13}$C NMR: (100 MHz, CDCl$_3$)
$\delta$ 174.57, 144.42, 128.10, 127.03, 125.14, 80.44, 72.32, 49.82, 39.34, 30.95, 28.44, 20.74, 20.19.

IR: (ATR-Ge)
3415 (br, w), 2964 (m), 1722 (s), 1367 (m), 1150 (s), 1052 (m).

MS: (DCI/NH$_3$)
296 (100, M+NH$_4$), 279 (80, M+H), 240 (30), 222 (15).

HRMS: Calculated for C$_{17}$H$_{26}$O$_3$: 278.18819; Found: 278.18888

HPLC: Chiralpak OJ, 0.5% IPA in heptane, $t_R$: 14.2 min, 10.7%, $t_R$: 21.8 min, 89.3%

Data for 6c, Minor diastereomer:

$^1$H NMR: (400 MHz, CDCl$_3$)
$\delta$ 7.38 – 7.32 (m, 4H), 7.31 – 7.25 (m, 1H), 4.63 (tt, $J = 12.3$, 6.2, 1H), 2.24 (br s, 1H), 2.18 (ddd, $J = 13.6$, 10.7, 7.4, 1H), 2.07 – 1.96 (m, 1H), 1.96 – 1.76 (m, 2H), 1.49 (s, 9H), 0.90 (dd, $J = 6.7$, 5.1, 6H)

$^{13}$C NMR: (100 MHz, CDCl$_3$)
$\delta$ 174.64, 143.94, 128.15, 127.34, 125.74, 80.35, 74.12, 50.55, 38.55, 31.06, 28.40, 20.27, 20.14.

IR: (ATR-Ge)
3413 (br, w), 2964 (m), 1724 (s), 1367 (m), 1148 (s).

MS: (DCI/NH$_3$)
296 (100, M+NH$_4$), 279 (75, M+H), 261 (15), 240 (25), 222 (20).

HPLC: Chiralpak OJ, 0.5% IPA in heptane, $t_R$: 14.2 min, 10.7%, $t_R$: 21.8 min, 89.3%
(1R,2R)-tert-Butyl 1-isopropyl-2-phenylcyclopropanecarboxylate (7c): In a 10 mL round-bottomed flask equipped with a N₂ inlet and magnetic stirbar were combined 6c, major diastereomer (185 mg, 0.67 mmol), THF (2.7 mL), and triethylamine (0.185 mL, 1.33 mmol). This solution was cooled in an ice bath and methanesulfonyl chloride (0.057 mL, 0.73 mmol) was added. After stirring the reaction mixture for 20 minutes, a 1.0 M KOtBu in THF (1.6 mL, 1.6 mmol) was added. The reaction was allowed to warm to rt. After stirring for 2.5 h at rt, the reaction was quenched with 1M HCl (3 mL) and extracted with MTBE (2 x 7 mL). The combined organic layers were washed with brine (3 mL), dried over MgSO₄, filtered and concentrated to give the crude product. Purification by SiO₂ chromatography (20:1 hexane/MTBE) afforded 133 mg (77%) of 7c as a clear, colorless oil.

Data for 7c:

\[ ^1H \text{NMR:} \quad (400 \text{ MHz, CDCl}_3) \\]
\[ \delta 7.31 - 7.18 \text{ (m, 6H), } 2.86 \text{ (dd, } J = 8.9, 7.3, 1H), 1.52 - 1.49 \text{ (m, 10H), } 1.16 - 1.10 \text{ (m, 4H), } 1.02 - 0.89 \text{ (m, 1H), } 0.81 \text{ (d, } J = 6.7, 3H). \]
Relative integration between the trans: cis isomer 1.00: 0.10 (2.86 ppm and 1.83 ppm)

\[ ^{13}C \text{NMR:} \quad (100 \text{ MHz, CDCl}_3) \\]
\[ \delta 172.84, 136.64, 129.12, 127.55, 126.13, 80.32, 35.98, 32.40, 29.41, 28.53, 20.40, 18.98, 18.67. \]

IR: (ATR-Ge)
2980 (w), 1712 (s), 1368 (m), 1146 (s), 1045 (m), 766 (m).

MS: (DCI/NH₃)
278 (90, M+NH₄), 225 (100), 184 (90).

HRMS: Calculated for C₁₇H₂₄O₂: 260.17763; Found: 260.17723

HPLC: Chiralpak OD, 0.1% IPA in heptane, \( t_R \): 3.9 min, 96.7%, \( t_R \): 4.6 min, 3.3%

In a 10 mL round-bottomed flask equipped with a N₂ inlet and magnetic stirbar were combined 6c, minor diastereomer (209 mg, 0.75 mmol), THF (3.0 mL), and triethylamine (0.209 mL, 1.5 mmol). This solution was cooled in an ice bath and methanesulfonyl chloride (0.061 mL, 0.79 mmol) was added. After stirring the reaction mixture for 15 minutes, a 1.0 M KOtBu in THF (1.6 mL, 1.6 mmol) was added. After stirring for 30 h in the ice bath, the reaction was quenched with 1M HCl (4 mL) and extracted with MTBE (2 x 5 mL). The combined organic layers were washed with brine (3 mL), dried over MgSO₄, filtered and concentrated to give the crude product. Purification by SiO₂ chromatography (20:1 hexane/MTBE) afforded 64 mg (33%) of 7c as a clear, colorless oil.

Data for 7c:
\[ \text{H NMR: (400 MHz, CDCl}_3\) } \]
\[ \delta 7.31 - 7.18 (m, 6H), 2.86 (dd, J = 8.9, 7.3, 1H), 1.52 - 1.49 (m, 10H), 1.16 - 1.10 (m, 4H), 1.02 - 0.89 (m, 1H), 0.81 (d, J = 6.7, 3H). \]
Relative integration between the trans: cis isomer 1.00: 0.09 (2.86 ppm and 1.83 ppm)

\[ \text{C NMR: (100 MHz, CDCl}_3\) } \]
\[ \delta 172.84, 136.64, 129.12, 127.55, 126.13, 80.32, 35.98, 32.40, 29.41, 28.53, 20.40, 18.98, 18.67. \]

IR: (ATR-Ge)
2980 (w), 1712 (s), 1368 (m), 1146 (s), 1045 (m), 766 (m).

MS: (DCI/NH\textsubscript{3})
278 (100, M+NH\textsubscript{4}), 261 (20, M+H), 222 (10).

HPLC: Chiralpak OD, 0.1% IPA in heptane, \( t_R \): 3.9 min, 89%, \( t_R \): 4.6 min, 11%

**tert-Butyl 4-oxo-2,4-diphenylbutanoate (5d):** In a 100 mL round-bottomed flask equipped with a magnetic stirbar was combined 2-phenyl-4-phenyl-4-oxobutanoic acid (0.55g, 2.2 mmol, 1.0 equiv), CH\textsubscript{2}Cl\textsubscript{2} (25 mL) and perchloric acid (0.013 mL, 0.2 mmol). The reaction mixture was sealed with a rubber septum and cooled in an ice bath. The isobutylene (1.5 g, 26 mmol) was added. The reaction solution was allowed to warm to rt, stirred for 20 min and quenched with 1 M NaOH (25 mL). The organic layer was washed with brine (10 ml), dried over MgSO\textsubscript{4} and concentrated to dryness. Purification by SiO\textsubscript{2} chromatography (9:1 hexane : MTBE) afforded the crude product. The product was dried in a vacuum oven (35 °C, 26 inHg) to afford 0.57 g (84%) of 5d as a white solid.

Data for 5d:

mp: 64-66 °C

\[ \text{H NMR: (400 MHz, CDCl}_3\) } \]
\[ \delta 7.96 (dd, J = 8.3, 1.2, 2H), 7.53 (d, J = 7.4, 1H), 7.43 (dd, J = 8.1, 7.0, 2H), 7.36 – 7.26 (m, 5H), 4.18 (dd, J = 10.3, 4.1, 1H), 3.87 (dd, J = 17.9, 10.3, 1H), 3.18 (dd, J = 17.9, 4.1, 1H), 1.38 (s, 9H) \]

\[ \text{C NMR: (100 MHz, CDCl}_3\) } \]
\[ \delta 197.12, 171.84, 138.70, 136.25, 132.82, 128.43, 128.25, 127.74, 127.39, 126.91, 80.87, 47.58, 42.92, 28.13. \]
(4S)-tert-Butyl 4-hydroxy-2,4-diphenylbutanoate (6d): In a 50 mL 3-necked round-bottomed flask were combined (R)-CBS-Me, 1.0 M in toluene (0.1 mL, 0.1 mmol) and THF (6 mL) and the solution was cooled in an icebath. To this solution was simultaneously added by syringe pump a 1.0 M solution of 5d in THF (1.0 mL, 1.0 mmol, 1.0 equiv) and 1.0 M BH$_3$ in THF (1.0 mL, 1.0 mmol, 1.0 equiv) over 1 h. After stirring for 2 h in the icebath, the reaction was quenched with 1M K$_2$CO$_3$ (6 mL) and warmed to rt. The aqueous layer was extracted with MTBE (2 x 5 mL), and the combined organic layers were washed with brine (5 mL), dried over Na$_2$SO$_4$, filtered and concentrated. Purification by SiO$_2$ chromatography (gradient heptane to 50% EtOAc/heptane) afforded 260 mg (83%) of 6d as a thick colorless oil as a mixture of diastereomers.

Data for 6d:

$^1$H NMR: (400 MHz, CDCl$_3$), Mixture of diastereomers.
δ 7.39 – 7.16 (m, 22H), 4.68 (dd, J = 8.0, 4.6, 1H), 4.49 (d, J = 9.0, 1H), 3.70 (ddd, J = 14.5, 8.4, 3.9, 2H), 2.56 – 2.40 (m, 2H), 2.21 (s, 1H), 2.17 – 1.98 (m, 3H), 1.41 – 1.35 (m, 18H).

$^{13}$C NMR: (100 MHz, CDCl$_3$), Mixture of diastereomers.
δ 172.80, 172.57, 144.01, 143.77, 139.07, 138.80, 128.25, 128.19, 128.17, 127.68, 127.49, 127.32, 126.77, 126.73, 125.48, 125.41, 80.89, 80.73, 72.39, 72.31, 49.81, 49.24, 42.83, 42.52, 28.18, 28.15.

IR: (KBr)
3453 (w), 2978 (w), 1724 (m), 1494 (w), 1454 (w), 1392 (w), 1368 (m), 1147 (s), 1060 (w), 1029 (w), 846 (w), 750 (m), 699 (s), 540 (w)

MS: (DCI, NH$_3$)
330 (100, M+NH$_4$), 313 (60, M+H), 295 (20), 274 (30), 256 (20)

HRMS: Calculated for C$_{20}$H$_{24}$O$_3$: 312.17254; Found: 312.17228
HPLC: Chiralpak OJ, 3% IPA in heptane
- major diastereomer: $t_R$: 11.8 min, 2.3%, $t_R$: 21.3 min, 49.0%
- Mismatched Isomer: $t_R$: 13.8 min, 4.9%, $t_R$: 48.7 min, 43.8%

**Ot-Bu**

**Ph**

(1S,2R)-**tert-Butyl 1,2-diphenylcyclopropanecarboxylate** (**7d**): In a 10 mL round-bottomed flask equipped with a N$_2$ inlet and magnetic stirbar were combined 6d (156 mg, 0.5 mmol), THF (4 mL), and triethylamine (0.14 mL, 1.0 mmol). This solution was cooled in an icebath and methanesulfonyl chloride (0.043 mL, 0.55 mmol) was added. After stirring the reaction mixture for 15 minutes, a 1.0 M KOtBu in THF (1.25 mL, 1.25 mmol) was added. After 15 min, 1 M HCl (3 mL) was added and the solution was allowed to warm to rt. The aqueous layer was extracted with MTBE (5 mL, 5 mL). The combined organic layers were washed with brine (3 mL), dried over MgSO$_4$, filtered and concentrated to give the crude product. Purification by SiO$_2$ chromatography (gradient heptane to 50% EtOAc/heptane) afforded 139 mg (95%) of **7d** as a white solid.

**Data for 7d:**

- mp: 63-64 °C

**$^1$H NMR:** (400 MHz, CDCl$_3$)
- $\delta$ 7.53 – 7.46 (m, 1H), 7.40 – 7.25 (m, 3H), 7.23 – 7.18 (m, 0H), 7.11 – 7.05 (m, 2H), 7.05 – 6.98 (m, 3H), 6.79 – 6.73 (m, 1H), 3.00 (dd, $J = 9.2$, 7.2, 1H), 2.05 (dd, $J = 9.2$, 4.9, 1H), 1.80 (dd, $J = 7.1$, 4.9, 1H), 1.39 (s, 6H), 1.00 (s, 3H).
- Relative integration between the trans: cis isomer 65: 35 (3.00 ppm / 2.78 ppm and 2.05 ppm / 2.27 ppm)

**$^{13}$C NMR:** (100 MHz, CDCl$_3$)
- $\delta$ 172.12, 136.47, 134.97, 131.51, 129.79, 129.08, 127.83, 127.72, 127.66, 127.30, 127.11, 126.71, 126.35, 126.31, 125.79, 80.78, 80.55, 38.76, 32.91, 32.49, 28.23, 27.73, 19.85, 17.43.

**IR:** (KBr)
- 2979 (w), 1709 (s), 1603 (w), 1497 (w), 1446 (w), 1390 (w), 1366 (w), 1330 (w), 1274 (m), 1255 (w), 1220 (w), 1155 (s), 1116 (w), 1096 (w), 1074 (w), 1029 (w), 979 (w), 847 (w), 766 (w), 754 (w), 717 (w), 697 (s), 663 (w), 590 (w), 550 (w)

**MS:** (DCI)
- 312 (100, M+NH4), 295 (20, M+H), 256 (20)
HRMS: Calculated for C$_{20}$H$_{22}$O$_2$: 294.16198; Found: 294.16202

HPLC: Chiralpak AD-H, 0.5% IPA in heptane
  major diastereomer: t$_R$: 14.5 min, 61.6%, t$_R$: 11.9 min, 5.9%
  Mismatched Isomer: t$_R$: 14.1 min, 3.2%, t$_R$: 16.0 min, 29.3%

General Experimental: Preparation of Racemic Reference Products.

NaBH$_4$ reduction of the ketones 1a-h and 5a-d according to the following general experimental afforded the racemic alcohol products. The ring closure to afford the racemic cyclopropane products was performed in the same manner as the chiral compounds. The racemic compounds matched the chiral compounds by $^1$H NMR and MS analysis and were used to develop the chiral HPLC or SFC analyses.

To a round bottomed flask equipped with a magnetic stir bar and N$_2$ inlet was added the 4-aryl-4-oxobutanoic ester (2.0 mmol, 1.0 equiv) and MeOH (4.0 mL). This solution was cooled to 2 ºC in an ice bath. Sodium borohydride (2.0 mmol, 1.0 equiv) was added and the reaction was stirred at 2 ºC for 45 min. The reaction was quenched by slow addition of 1M K$_2$CO$_3$ (5 mL). The aqueous layer was extracted with MTBE (2 x 10 mL). The combined organic layers were dried over Na$_2$SO$_4$, filtered and concentrated. Purification by SiO$_2$ chromatography afforded the racemic 4-aryl-4-hydroxybutanoic ester.

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