Supporting Information A (Experimental Section)

Catalytic Desymmetrization of Cyclohexadienes by Asymmetric Bromolactonization

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Analysis instruments

Nuclear magnetic resonance, [\(^1\text{H} \text{NMR} \text{(500 MHz)}, \text{\textsuperscript{13}C NMR} \text{(125 MHz)}\)] spectra were determined on JEOL ECA-500 and JEOL \(\alpha\)-500 instruments, and [\(^1\text{H} \text{NMR} \text{(400 MHz)}, \text{\textsuperscript{13}C NMR} \text{(100 MHz)}\)] spectra were determined on JEOL LA-400 instruments. Chemical shifts for \(^1\text{H} \text{NMR}\) were reported in parts per million downfields from tetramethylsilane (\(\delta\)) as the internal standard and coupling constants are in hertz (Hz). The following abbreviations are used for spin multiplicity: \(s\) = singlet, \(d\) = doublet, \(t\) = triplet, \(q\) = quartet, \(m\) = multiplet, \(br\) = broad. Chemical shifts for \(^{13}\text{C} \text{NMR}\) were reported in ppm relative to the centerline of a triplet at 77.0 ppm for deuteriochloroform.

High-resolution mass spectra (HRMS) were obtained on a JEOL MStation 700. Fast atom bombardment (FAB) mass spectra were obtained with 3-nitrobenzylalcohol as the matrix and ESI-MS was taken with a BRUKER DALTONICS micrTOF.

Analytical thin layer chromatography (TLC) was performed on Merck precoated analytical plates, 0.25 mm thick, silica gel 60 F\(_{254}\). Preparative TLC separations were made on 7 x 20 cm plates prepared with a 0.25 mm or 0.50 mm layer of Merck silica gel 60 F\(_{254}\). Compounds were eluted from the adsorbent with 10% methanol in chloroform.

Column chromatography separations were performed on KANTO CHEMICAL Silica Gel 60 (spherical) 40 - 50 \(\mu\)m, Silica Gel 60 (spherical) 63 - 210 \(\mu\)m or Silica Gel 60 N (spherical, neutral) 63 - 210 \(\mu\)m.

Reagents and solvents were commercial grades and were used as supplied with following exceptions:

dichloromethane, diethyl ether, \textit{n}-hexane, tetrahydrofuran toluene: dried over molecular sieves 4A.

Methanol, acetonitrile: dried over molecular sieves 3 A.

All reactions sensitive to oxygen or moisture were conducted under an argon atmosphere.
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General procedure

To a stirred solution of the resultant dienecarboxylic acid (1.87 mmol) in DMF (3 mL) were added imidazole (382 mg, 5.61 mmol) and TBDPSCI (0.73 mL, 2.80 mmol) at 0 °C. Then, the reaction mixture was stirred at room temperature for 20 min. The residue was poured into 3 M NaOH at 0 °C. The resulting mixture was stirred for 1 hr and extracted with EtO. The organic layer was washed with brine, dried over anhydrous Na₂SO₄ and concentrated under reduced pressure. The residue was purified by silica gel column chromatography to afford the desired dienecarboxylic acid.
1-(Hydroxymethyl)cyclohexa-2,5-dienecarboxylic acid (1a)

The title compound was prepared according to the general procedure using benzoic acid as the starting material. This compound was purified by recrystallization from CHCl₃ to afford 1a (51%) as a colorless solid.

IR (film, cm⁻¹): 3330, 2884, 1695, 1290, 1243, 1225, 1084, 1024

¹H NMR (500 MHz CDCl₃): δ 6.03 (dt, J = 10.2, 3.4 Hz, 2H), 5.80 (dt, J = 10.2, 2.0 Hz, 2H), 3.73 (s, 2H), 2.80-2.68 (m, 2H)

¹³C NMR (125 MHz, CDCl₃): δ 178.8, 128.2, 123.7, 68.5, 50.4, 26.4

HRMS (ESI) calcd for C₈H₁₀O₃Na 177.0522 [(M+Na)+], found 177.0526

1-(((Triisopropyldoxyl)methyl)cyclohexa-2,5-dienecarboxylic acid (1c)

The title compound was prepared in 68% as a white solid according to the general procedure using 1a as the starting material and TIPSCl as the reagent in the second reaction.

IR (film, cm⁻¹): 3339, 2945, 1712, 1463, 1116

¹H NMR (500 MHz CDCl₃): δ 5.93 (dt, J = 10.2, 3.4 Hz, 2H), 5.87 (dt, J = 10.2, 1.7 Hz, 2H), 3.81 (s, 2H), 2.70-2.64 (m, 2H), 1.13-1.10 (m, 21H).

¹³C NMR (125 MHz, CDCl₃): δ 178.8, 126.8, 124.6, 70.4, 50.5, 26.5, 17.9, 11.9

HRMS (ESI) calcd for C₁₇H₃₀O₆SiNa 333.1856 [(M+Na)+], found 333.1862
1-(((tert-Butyldiphenylsilyl)oxy)methyl)cyclohexa-2,5-dienecarboxylic acid (1d)

The title compound was prepared in 57% as a colorless oil according to the general procedure using 1a as the starting material in the second reaction.

IR (film, cm⁻¹): 3073, 3048, 2932, 2889, 1705, 1427, 1112

¹H NMR (500 MHz CDCl₃): δ 7.65-7.63 (m, 4H), 7.45-7.33 (m, 6H), 5.96-5.90 (m, 4H), 3.77 (s, 2H), 2.71 (d, J = 22.7 Hz, 1H), 2.64 (d, J = 22.7 Hz, 1H), 1.02 (s, 9H).

¹³C NMR (125 MHz, CDCl₃): δ 179.3, 135.6, 133.1, 129.7, 127.7, 127.0, 124.4, 70.3, 50.5, 26.8, 19.3

HRMS (ESI) calcld for C₂₄H₂₈O₃SiNa 415.1700 [(M+Na)⁺], found 415.1724

1-(((tert-Butyldiphenylsilyl)oxy)methyl)-4-methylcyclohexa-2,5-dienecarboxylic acid (S6)

The title compound was prepared according to the general procedure using 4-methylbenzoic acid as the starting material. S6 was obtained in 15% (2 steps) as a 1:1 mixture of the diastereoisomers as a colorless oil.

IR (film, cm⁻¹): 3073, 3048, 2932, 1705, 1112

¹H NMR (500 MHz CDCl₃): δ 7.73-7.69 (m, 4H), 7.47-7.39 (m, 6H), 5.99-5.94 (m, 2H), 5.92-5.87 (m, 2H), 3.83 (s, 2H), 2.86-2.79 (m, 0.5H), 2.79-2.73 (m, 0.5H), 1.14 (d, J = 7.4 Hz, 1.5 H), 1.10-1.06 (m, 10.5H).

¹³C NMR (125 MHz, CDCl₃): δ 180.2 (1/2C), 180.1 (1/2C), 135.7, 133.2 (1/2C), 133.1 (1/2C), 129.7, 127.7, 123.5 (1/2C), 123.4 (1/2C), 71.1 (1/2C), 70.4 (1/2C), 51.0 (1/2C), 50.9 (1/2C), 31.0, 26.7, 21.6 (1/2C), 21.4 (1/2C), 19.4

HRMS (ESI) calcld for C₂₅H₃₀O₃SiNa 429.1856 [(M+Na)⁺], found 429.1878
1-(((tert-Butyldiphenylsilyl)oxy)methyl)cyclohexa-2,5-dienecarboxylic acid (S11)

The title compound was prepared in 29% (2 steps) as a colorless solid according to the general procedure using 3,5-dimethylbenzoic acid as the starting material.

IR (film, cm⁻¹): 3071, 2932, 2859, 1705, 1427, 1269, 1246, 1113

¹H NMR (500 MHz CDCl₃): δ 7.65-7.61 (m, 4H), 7.42-7.34 (m, 6H), 5.60 (s, 2H), 3.72 (s, 2H), 2.51 (d, J = 22.3 Hz, 1H), 2.42 (d, J = 22.3 Hz, 1H), 1.75 (s, 6H), 1.02 (s, 9H).

¹³C NMR (125 MHz CDCl₃): δ 179.8, 135.7, 134.5, 133.3, 129.6, 127.6, 118.9, 70.5, 53.0, 36.2, 26.7, 23.0, 19.3

HRMS (ESI) calcd for C₂₆H₃₂O₃SiNa 443.2013 [(M+Na)⁺], found 443.2030
Synthesis of S7 and S8

1a

1) SOCl₂, MeOH
2) TBDPSCI, imidazole, DMF 80% (2 steps)

OH
CH₂

MeO₂C

OTBDPS

S1

Mn(OAc)₃·2H₂O, TBHP, MS4A

MeO₂C

OTBDPS

S2

1) MOMCl, i-Pr₂NEt, CH₂Cl₂
2) 3 M LiOH, THF/MeOH, 50 °C, 65% (2 steps)

OH
CH₂

MeO₂C

OTBDPS

S3

S7

1) MOMCl, i-Pr₂NEt, CH₂Cl₂
2) Me₃SnOH, 1,2-DCE, 80 °C, 27% (2 steps)

OH
CH₂

MeO₂C

OTBDPS

S4

S8

NaBH₄, CeCl₃·7H₂O

MeOH, 0 °C, 74% d.r. = 11:7
Methyl 1-(((tert-butylidiphenylsilyl)oxy)methyl)cyclohexa-2,5-dienecarboxylate (S'1)

To a stirred solution of **1a** (1.07 g, 6.94 mmol) in MeOH (5 mL) was added SOCl₂ (0.71 mL, 9.73 mmol) at 0 °C and the reaction mixture was stirred at room temperature for 2 hr. Then, the reaction mixture was concentrated. The residue was used for the next step without further purification.

To a stirred solution of the crude material in DMF (5 mL) were added imidazole (883 mg, 13.0 mmol) and TBDPSCI (2.0 mL, 8.45 mmol) at 0°C. Then, the reaction mixture was stirred at room temperature for 2 hr. The residue was poured into 3 M NaOH at 0°C and stirred for 1 hr and extracted with Et₂O. The organic layer was washed with brine, dried over anhydrous Na₂SO₄, and concentrated under reduced pressure. The residue was purified by silica gel column chromatography (n-hexane/EtOAc = 97/3 to 10/1) to afford **S'1** (2.27 g, 80%, 2 steps) as a colorless oil.

IR (film, cm⁻¹): 3045, 2951, 1734, 1430, 1220, 1112

¹H NMR (500 MHz CDCl₃): δ 7.64-7.62 (m, 4H), 7.40-7.32 (m, 6H), 5.92-5.89 (m, 4H), 3.75 (s, 2H), 3.72 (s, 3H), 2.72-2.60 (m, 2H), 1.02 (s, 9H).

¹³C NMR (125 MHz, CDCl₃): δ 173.8, 135.6, 133.3, 129.6, 127.6, 126.5, 125.1, 70.6, 52.1, 50.7, 26.6, 26.5, 19.3

HRMS (ESI) calcd for C₂₅H₃₆O₃SiNa 429.1856 [(M+Na)⁺], found 429.1866
Methyl-1-(((tert-butyldiphenylsilyl)oxy)methyl)-4-oxocyclohexa-2,5-dienecarboxylate (S’2)

S’2 was prepared using literature procedure \(^1\) with slight modification. To a stirred solution of S’1 (1.38 g, 3.41 mmol) in EtOAc (8 mL) were added TBHP (3.7 mL of 5.5 M in decane, 20.5 mmol) and MS4A (2.8 g) at room temperature. The reaction mixture was stirred at the same temperature for 30 min, followed by the addition of manganese (III) acetate dihydrate (183 mg, 0.682 mmol) at the same temperature. The reaction mixture was stirred for 48 h at the same temperature, then Et\(_3\)N (3.8 mL, 28.5 mmol) was added. The reaction mixture was stirred for 30 min, then the reaction mixture was filtered through a pad of silica gel. The resultant filtrate was concentrated under reduced pressure. The residue was purified by silica gel column chromatography (n-hexane/EtOAc = 1/0 to 6/1) to afford S’2 (1.14 g, 79%) as a colorless oil.

IR (film, cm\(^{-1}\)): 3073, 2954, 1745, 1670, 1230, 1120

\(^1\)H NMR (500 MHz, CDCl\(_3\)): \(\delta\) 7.62-7.58 (m, 4H), 7.45-7.35 (m, 6H), 7.13 (d, \(J = 10.9\) Hz, 2H), 6.37 (d, \(J = 10.9\) Hz, 1H), 3.90 (s, 2H), 3.77 (s, 3H), 1.02 (s, 9H).

\(^{13}\)C NMR (125 MHz, CDCl\(_3\)): \(\delta\) 185.0, 169.5, 145.6, 135.5, 132.3, 130.9, 127.9, 69.5, 55.1, 53.1, 26.6, 19.3

HRMS (ESI): Calculated for C\(_{25}\)H\(_{28}\)O\(_4\)SiNa 443.1649 ([M+Na\(^{+}\)], found 443.1650

Methyl 1-(((tert-butyl)diphenylsilyl)oxy)methyl)-4-hydroxycyclohexa-2,5-diene carboxylate (S'3, S'4)

To a stirred solution of S'2 (376 mg, 0.892 mmol) in MeOH (4 mL) were added CeCl$_3$•7H$_2$O (497 mg, 1.34 mmol) and NaBH$_4$ (50.6 mg, 1.34 mmol) at 0 °C. The reaction mixture was stirred at the same temperature for 20 min. Then, the reaction mixture was poured into saturated aqueous NH$_4$Cl at 0 °C and extracted with CH$_2$Cl$_2$. The organic layer was dried over anhydrous Na$_2$SO$_4$, filtered through silica gel pad, and concentrated under reduced pressure to afford S'3 and S'4 (280.4 mg, 74%, d.r.=11:7) as colorless oil. The diastereoisomers were separated by silica gel column chromatography (n-hexane/EtOAc = 5/1 to 3/1).

S'3 (β-isomer)
IR (film, cm$^{-1}$): 3333, 3073, 1730, 1233, 1113
$^1$H NMR (500 MHz, CDCl$_3$): δ 7.65-7.60 (m, 4H), 7.45-7.35 (m, 6H), 6.08 (dd, J = 10.3, 1.7 Hz, 2H), 6.02 (dd, J = 10.3, 3.4 Hz, 2H), 4.49 (brs, 1H), 3.80 (s, 2H), 3.71 (s, 3H), 1.02 (s, 9H).
$^{13}$C NMR (125 MHz, CDCl$_3$): δ 172.4, 135.6, 133.0, 130.0, 129.9, 129.7, 127.7, 127.6, 69.8, 62.4, 52.3, 51.3, 26.7, 19.3
HRMS (ESI): Calculated for C$_{25}$H$_{30}$O$_4$SiNa 445.1806 ([M+Na]$^+$), found 445.1787

S'4 (α-isomer)
IR (film, cm$^{-1}$): 3336, 3073, 1732, 1244, 1113
$^1$H NMR (500 MHz, CDCl$_3$): δ 7.62-7.60 (m, 4H), 7.45-7.35 (m, 6H), 6.12 (dd, J = 10.3, 1.7 Hz, 2H), 6.05 (dd, J = 10.3, 2.9 Hz, 1H), 4.45-4.41 (m, 1H), 3.72 (s, 2H), 3.72 (s, 3H), 1.04 (s, 9H).
$^{13}$C NMR (125 MHz, CDCl$_3$): δ 172.6, 135.6, 133.0, 130.0 (2C), 129.7, 127.7, 70.1, 62.1, 52.4, 51.3, 26.6, 19.3
HRMS (ESI): Calculated for C$_{25}$H$_{30}$O$_4$SiNa 445.1806 ([M+Na]$^+$), found 445.1793.
1,4-trans-1-(((tert-Butyldiphenylsilyl)oxy)methyl)-4-(methoxymethoxy)cyclohexa-2,5-dienecarboxylic acid (S7)

To a stirred solution of S3 (130 mg, 0.307 mmol) in CH2Cl2 (3 mL) were added DIPEA (0.48 mL, 2.76 mmol) and MOMCl (70 µL, 0.92 mmol) at 0 °C. The reaction mixture was stirred at room temperature for 3 hr. Then, the reaction mixture was poured into saturated aqueous NH4Cl at 0 °C and extracted with CH2Cl2. The organic layer was dried over anhydrous Na2SO4 and concentrated under reduced pressure. The residue was used for the next step without further purification.

To a stirred solution of the crude material in MeOH/THF=1/1 (3 mL) was added 3 M LiOH (1.0 mL) at room temperature. The reaction mixture was stirred at 50 °C for 12 h. After cooling, the reaction mixture was poured into saturated aqueous NH4Cl at 0 °C, and extracted with CH2Cl2. The organic layer was dried over anhydrous Na2SO4 and concentrated under reduced pressure. The residue was purified by silica gel column chromatography (n-hexane/EtOAc = 10/1 to 10/3) to afford S7 (81.1 mg, 65%, 2 steps) as a colorless oil.

IR (film, cm⁻¹): 2954, 1709, 1112, 1043, 702

¹H NMR (500 MHz, CDCl3): δ 7.65-7.60 (m, 4H), 7.42-7.35 (m, 6H), 6.14 (dd, J = 10.3, 1.7 Hz, 2H), 6.05 (dd, J = 10.3, 2.9 Hz, 2H), 4.71 (s, 2H), 4.55-4.52 (m, 1H), 3.82 (s, 2H), 3.38 (s, 3H), 1.02 (s, 9H).

¹³C NMR (125 MHz, CDCl3): δ 177.5, 135.6, 132.8, 129.8, 128.3, 127.7, 127.4, 95.5, 69.7, 68.1, 55.4, 51.0, 26.6, 19.3

HRMS (ESI): Calculated for C36H32O5SiNa 475.1911 ([M+Na⁺]), found 475.1916
To a stirred solution of S'4 (151 mg, 0.357 mmol) in CH₂Cl₂ (3 mL) were added DIPEA (0.56 mL, 3.21 mmol) and MOMCl (81 µL, 1.07 mmol) at 0 °C. The reaction mixture was stirred at room temperature for 3 hr. Then, the reaction mixture was poured into saturated aqueous NH₄Cl at 0 °C and extracted with CH₂Cl₂. The organic layer was dried over anhydrous Na₂SO₄ and concentrated under reduced pressure. The residue was used for the next step without further purification.

To a stirred solution of the crude material in 1,2-dichloroethane (3 mL) was added Me₃SnOH (258 mg, 1.43 mmol) at room temperature. The reaction mixture was stirred at 80 °C for 24 h. After cooling, the reaction mixture was evaporated. The residue was purified by silica gel column chromatography (n-hexane/EtOAc = 10/1 to 3/1) to afford S8 (43.6 mg, 27%, 2 steps) as a colorless oil and recovered S'4 (75.9 mg, 46%).

IR (film, cm⁻¹): 2954, 1708, 1112, 1029, 702
¹H NMR (500 MHz, CDCl₃): δ 7.64-7.60 (m, 4H), 7.42-7.35 (m, 6H), 6.14 (d, J = 10.3, 1.7 Hz, 2H), 6.06 (dd, J = 10.3, 2.9 Hz, 2H), 4.74 (s, 2H), 4.48 (brs, 1H), 3.74 (s, 2H), 3.39 (s, 3H), 1.03 (s, 9H).
¹³C NMR (125 MHz, CDCl₃): δ 176.8, 135.6, 132.9, 129.8, 128.3, 127.7, 127.4, 95.1, 69.9, 67.6, 55.4, 51.3, 26.7, 19.3
HRMS (ESI): Calculated for C₂₆H₃₂O₅SiNa 475.1911 ([M+Na⁺]), found 475.1915
The relative configuration of S7 and S8 was determined by $^1$H-NMR and NOESY of S7-a and S8-a, which were obtained by hydrogenolysis of their double bonds.
Synthesis of S9 and S10

General procedure

To a stirred solution of diisopropylamine (0.12 mL, 0.87 mmol) in THF (0.7 mL) was added n-BuLi (0.33 mL, 2.6 M in hexane, 0.87 mmol) at 0 °C and the solution was stirred at the same temperature for 15 min. Then, the solution was cooled to -78 °C and a solution of cyclohexadiene ester \(^2\) (293 mg, 0.72 mmol) in THF (0.7 mL) was added. After the reaction mixture was stirred at -78 °C for 30 min, alkyl bromide (0.87 mmol) was added, and the mixture was stirred at the same temperature for 1 hr. The reaction was quenched with saturated aqueous NH\(_4\)Cl and the aqueous layer was extracted with Et\(_2\)O. The combined organic layer was dried over Na\(_2\)SO\(_4\), filtered and evaporated. The residue was purified by short column chromatography to afford the crude material, which was used for the next step without further purification.

To a stirred solution of the crude material in THF/MeOH = 1/1 (0.7 mL) was added 3M LiOH (0.3 mL) at room temperature. The reaction mixture was stirred at the same temperature for 30 min. Then, the reaction mixture was poured into 1M HCl at 0 °C and extracted with CHCl\(_3\). The organic layer was dried over anhydrous Na\(_2\)SO\(_4\), and concentrated under reduced pressure. The residue was purified by silica gel column chromatography to afford carboxylic acid.

1-(2-(tert-Butoxy)-2-oxoethyl)cyclohexa-2,5-diene carboxylic acid (S9)

The title compound was prepared in 68% (2 steps) as a colorless oil according to the general procedure using t-butyl bromoacetate in the first step.

IR (film, cm$^{-1}$): 3041, 2983, 1732, 1691, 1419, 1367, 1254, 1163
$^1$H NMR (500 MHz CDCl$_3$): $\delta$ 5.92 (dt, $J = 12.2$, 2.8 Hz, 2H), 5.80 (dt, $J = 12.2$, 1.7 Hz, 2H), 2.75-2.60 (m, 2H), 2.65 (s, 2H), 1.29 (s, 9H)
$^{13}$C NMR (125 MHz, CDCl$_3$): $\delta$ 179.6, 169.2, 126.4, 125.7, 81.1, 45.5, 45.5, 27.7, 25.8
HRMS (ESI) calcd for C$_{13}$H$_{18}$O$_4$Na 261.1097 [(M+Na)$^+$], found 261.1035

1-(Naphthalen-2-ylmethyl)cyclohexa-2,5-diene carboxylic acid (S10)

The title compound was prepared in 77% (2 steps) as a colorless solid according to the general procedure using 2-(bromomethyl)-naphthalene in the first step.

IR (film, cm$^{-1}$): 3034, 2899, 2632, 1697, 1413, 1274, 947
$^1$H NMR (500 MHz CDCl$_3$): $\delta$ 7.83-7.79 (m, 2H), 7.73 (d, $J = 7.9$ Hz, 1H), 7.64 (brs, 1H), 7.55-7.42 (m, 2H), 7.33 (dd, $J = 8.5$, 1.7 Hz, 1H), 5.90-5.80 (m, 4H), 3.24 (s, 2H), 2.57 (d, $J = 24.4$ Hz, 1H), 2.36 (d, $J = 24.4$ Hz, 1H).
$^{13}$C NMR (125 MHz, CDCl$_3$): $\delta$ 180.5, 133.9, 133.2, 132.2, 129.2, 128.9, 127.7, 127.6, 127.2, 126.5, 126.4, 125.8, 125.5, 49.1, 46.1, 26.0
HRMS (ESI) calcd for C$_{18}$H$_{16}$O$_3$Na 287.1043 [(M+Na)$^+$], found 287.1037
Synthesis of 12a

![Chemical Reaction Diagram]

To a stirred solution of tert-butyl benzoate (1.6 g, 9.0 mmol) in liquid NH$_3$/THF = 3/1 (33 mL) was added Li (0.19 g, 27 mmol) at -78 °C. The reaction mixture was stirred at -78 °C for 30 min, followed by the addition of ethyl 2-bromoacetate (3.0 mL, 27 mmol) at the same temperature. The resulting mixture was stirred at -78 °C for 30 min. Then, the reaction mixture was stirred at room temperature to remove excess NH$_3$. The residue was poured into 6 M HCl at 0 °C and extracted with EtOAc. The organic layer was dried over anhydrous Na$_2$SO$_4$ and concentrated under reduced pressure.

The residue was purified by silica gel column chromatography (n-hexane/EtOAc = 9/1) to afford S'5 (1.8 g, 74%) as a colorless oil.

To a stirred solution of S'5 (279 mg, 1.05 mmol) in THF/MeOH = 1/1 (1 mL) was added 3 M LiOH (0.5 mL) at room temperature. The reaction mixture was stirred at the same temperature for 30 min. Then, the reaction mixture was poured into 1M HCl at 0 °C, and extracted with CHCl$_3$. The organic layer was dried over anhydrous Na$_2$SO$_4$, and concentrated under reduced pressure. The residue was purified by silica gel column chromatography (n-hexane/EtOAc = 9/1 to 4/1) to afford 12a (127 mg, 51%) as a colorless solid.

**tert-Butyl 1-(2-ethoxy-2-oxoethyl)cyclohexa-2,5-dienecarboxylate (S'5)**

IR (film, cm$^{-1}$): 2980, 1734, 1367, 1287, 1155

$^1$H NMR (500 MHz CDCl$_3$): $\delta$ 5.87 (dt, $J = 10.2, 3.4$ Hz, 2H), 5.78 (dt, $J = 10.2, 1.7$ Hz, 2H), 4.11 (q, $J = 6.8$ Hz, 2H), 2.67-2.64 (m, 4H), 1.41 (s, 9H), 1.21 (t, $J = 6.8$ Hz, 2H).

$^{13}$C NMR (125 MHz, CDCl$_3$): $\delta$ 174.2, 170.5, 126.8, 125.9, 81.0, 60.4, 46.3, 44.5, 27.8, 26.0, 14.2

HRMS (ESI) calcd for C$_{13}$H$_{18}$O$_4$Na 289.1410 [(M+Na)$^+$], found 289.1406

**2-(1-(tert-Butoxycarbonyl)cyclohexa-2,5-dien-1-yl)acetic acid (12a)**

IR (film, cm$^{-1}$): 2980, 1705, 1417, 1287, 1157

$^1$H NMR (500 MHz CDCl$_3$): $\delta$ 5.89 (dt, $J = 10.2, 3.4$ Hz, 2H), 5.78 (dt, $J = 10.2, 1.7$ Hz, 2H), 2.73 (s, 2H), 2.69-2.63 (m, 2H), 1.43 (s, 9H)

$^{13}$C NMR (125 MHz, CDCl$_3$): $\delta$ 177.3, 172.2, 130.1, 128.3, 81.2, 46.0, 44.1, 27.7, 25.9

HRMS (ESI) calcd for C$_{13}$H$_{18}$O$_5$Na 261.1097 [(M+Na)$^+$], found 261.1021
Synthesis of 2-1-((tert-butyldiphenylsilyl)oxy)methyl)cyclohexa-2,5-dien-1-yl)acetic acid (12b)

![Chemical Structure]

To a stirred solution of S'5 (1.07 g, 6.94 mmol) in CH₂Cl₂ (5 mL) was added TFA (710 μL, 9.73 mmol) at 0 °C and the reaction mixture was stirred at room temperature for 2 hr. Then, the reaction mixture was concentrated. The residue was used for the next step without further purification.

To a stirred solution of the crude material in THF (5 mL) were added chloromethylformate (0.11 mL, 1.36 mmol) and Et₃N (0.38 mL, 2.72 mmol) at 0°C. The reaction mixture was stirred at the same temperature for 30 min. The reaction mixture was filtered through Celite pad, then the filtrate was evaporated. The residue was used for the next step without further purification.

To a stirred solution of the crude material in MeOH (3 mL) was added NaBH₄ (60.0 mg, 1.59 mmol) at 0 °C. The reaction mixture was stirred at the same temperature for 40 min. Then, the reaction mixture was poured into saturated aqueous NH₄Cl at 0 °C and extracted with CH₂Cl₂. The organic layer was dried over anhydrous Na₂SO₄ and concentrated under reduced pressure. The residue was used for the next step without further purification.

To a stirred solution of the crude material containing S'6 in DMF (1.5 mL) were added imidazole (92.0 mg, 1.34 mmol) and TBDPSCI (0.16 mL, 0.679 mmol) at 0 °C. Then, the reaction mixture was stirred at room temperature for 30 min. The residue was poured into H₂O at 0°C and extracted with Et₂O. The organic layer was washed with brine, dried over anhydrous Na₂SO₄ and concentrated under reduced pressure. The residue was used for the next step without further purification.

To a stirred solution of the crude material in MeOH/THF=1/1 (3 mL) was added 3 M LiOH (1.5 mL) at room temperature. The reaction mixture was stirred at 50 °C for 12 h. After cooling, the reaction mixture was poured into 1M HCl at 0 °C and extracted with CH₂Cl₂. The organic layer was dried over anhydrous Na₂SO₄, and concentrated under reduced pressure. The residue was purified by silica gel column chromatography (n-hexane/EtOAc = 1/0 to 5/2) to afford 12b (147.2 mg, 52%, 5 steps) as a colorless oil.

IR (film, cm⁻¹): 2931, 1707, 1427, 1113

¹H NMR (500 MHz CDCl₃): δ 7.65-7.60 (m, 4H), 7.42-7.30 (m, 6H), 5.81 (dt, J = 10.2, 3.4 Hz, 2H), 5.69 (dt, J = 10.2, 2.3 Hz, 2H), 3.53 (s, 2H), 2.73-2.59 (m, 4 H), 1.05 (s, 9H).

¹³C NMR (125 MHz CDCl₃): δ 177.2, 135.7, 133.3, 129.6, 128.6, 127.2, 126.0, 70.7, 42.3, 41.1, 26.8, 26.6, 19.4

HRMS (ESI) calcd for C₂₅H₃₀O₃SiNa 429.1856 [(M+Na)^+], found 429.1867
II. Bromolactonization

General procedure

To a screw-top vial equipped with a stir bar were added the appropriate diene carboxylic acid (0.1 mmol) and (DHQD)\(_2\)PHAL (7.8 mg, 0.01 mmol). The mixture was dissolved in CHCl\(_3\)/\(n\)-Hex = 1/1 (2 mL) and cooled to -40 °C. To the stirred mixture was added NBS (21.4 mg, 0.12 mmol). The reaction mixture was stirred for 1 h. Then, the mixture was quenched by adding saturated aqueous Na\(_2\)S\(_2\)O\(_3\) at the same temperature and extracted with EtOAc. The organic layer was dried over anhydrous Na\(_2\)SO\(_4\) and concentrated under reduced pressure. The residue was purified by silica gel column chromatography (\(n\)-hexane/EtOAc = 1/0 to 20/1) to afford the desired lactone. The enantiomeric excess of the products so isolated were determined by chiral HPLC analysis.

\(\text{Br}-\text{OTIPS}\)

The title compound was prepared in 87% yield with 91% ee as a colorless solid according to the general procedure using 1c as the starting material. Recrystallization from hexane at -20 °C afforded the crystal, of which enantioselectivity was determined to be 97%.

m.p. 47-48 °C (97% ee)

\([\alpha]^{26}_D + 70.6 (c 0.95, \text{CHCl}_3, \text{91% ee})\)

IR (film, cm\(^{-1}\)): 2943, 2866, 1842, 1464, 1112

\(^1\mathrm{H}\) NMR (500 MHz CDCl\(_3\)): \(\delta\) 6.04-6.01 (m, 1H), 5.57 (dd, \(J = 9.6, 2.3\) Hz, 1H), 5.15 (brs, 1H), 4.61-4.58 (m, 1H), 4.15 (d, \(J = 10.3\) Hz, 1H), 3.82 (d, \(J = 10.3\) Hz, 1H), 2.80-2.72 (m, 2H), 1.13 (septet, \(J = 5.1\) Hz, 3H), 1.07 (d, \(J = 5.1\) Hz, 18H).

\(^{13}\)C NMR (125 MHz CDCl\(_3\)): \(\delta\) 168.1, 128.3, 119.7, 72.6, 62.3, 62.1, 41.3, 28.5, 17.9, 11.9

HRMS (ESI) calcd for C\(_{17}\)H\(_{29}\)O\(_3\)BrSiNa 411.0961 [(M+Na)+], found 411.0962

HPLC (DAICEL CHIRALPAK AD-H, \(n\)-Hexane/i-PrOH = 99.5/0.5, flow rate = 1.0 mL/min, 190 nm):

\(t_{\text{major}} = 7.01\) min, \(t_{\text{minor}} = 7.75\) min
The title compound was prepared in 93% yield with 88% ee as a colorless oil according to the general procedure using 1d as the starting material.

$\left[\alpha\right]_{D}^{26} = +37.2$ (c 1.26, CHCl$_3$, 88% ee)

IR (film, cm$^{-1}$): 3049, 2931, 2858, 1840, 1112

$^1$H NMR (500 MHz CDCl$_3$): $\delta$ 7.61 (t, $J = 6.8$ Hz, 4H), 7.45-7.39 (m, 6H), 6.03-5.99 (m, 1H), 5.51 (dd, $J = 9.6$, 2.3 Hz, 1H), 5.26 (brs, 1H), 4.63 (brd, 1H), 4.07 (d, $J = 10.8$ Hz, 1H), 3.76 (d, $J = 10.8$ Hz, 1H), 2.82-2.70 (m, 2H), 1.08 (s, 9H).

$^{13}$C NMR (125 MHz CDCl$_3$): $\delta$ 168.0, 135.6, 135.5, 132.3, 132.0, 130.0 (2C), 128.3, 127.9 (2C), 119.5, 72.5, 62.4, 62.0, 41.2, 28.4, 26.7, 19.3

HRMS (ESI) calcd for C$_{24}$H$_{27}$O$_3$BrSiNa $493.0805$ [(M+Na)$^+$], found 493.0825

HPLC (DAICEL CHIRALCEL OD-H, n-Hexane/i-PrOH = 99.5/0.5, flow rate = 1.0 mL/min, 254 nm): $t_{\text{major}} = 12.6$ min, $t_{\text{minor}} = 16.8$ min
Conversion of lactone 2c to epoxide 5

To a solution of 1c (1.01 g, 3.25 mmol) and (DHQD)_2PHAL (75.2 mg, 0.966 mmol) in CHCl_3/CH_2Cl_2 = 1:1 (30 mL) was added NBS (688 mg, 3.86 mmol) at -40 °C. The reaction mixture was stirred at the same temperature for 12 hr. Then, the reaction mixture was concentrated under reduced pressure. The residue was purified by silica gel column chromatography (n-Hexane/EOAc = 10:1) to afford 2c (1.26 g, 99%, 90% ee) as colorless oil.

To a stirred solution of 2c (6.25 g, 16.0 mmol) in THF (60 mL) was added 1.0 M solution of TBAF in THF (21 mL, 20.8 mmol) at -40 °C. The reaction mixture was stirred at the same temperature for 12 hr. Then, saturated aqueous NH_4Cl was added at the same temperature and the mixture was warmed to room temperature. The aqueous layer was extracted with EtOAc, dried over anhydrous Na_2SO_4 and concentrated under reduced pressure. The residue was used for the next step without further purification.

To a stirred solution of the crude material in MeOH (60 mL) was added K_2CO_3 (3.32 g, 24.0 mmol) at 0 °C. The reaction mixture was stirred at the same temperature for 1 hr. Then, the reaction mixture was poured into saturated aqueous NH_4Cl at 0 °C, and extracted with EtOAc. The organic layer was dried over anhydrous Na_2SO_4 and concentrated under reduced pressure. The residue was purified by silica gel column chromatography (n-Hexane/CH_2Cl_2 = 5:1) to afford S’7 (2.12 g, 72%, 2 steps) as a colorless oil.

To a stirred solution of S’7 (2.12 g, 11.5 mmol) in MeCN (15 mL) were added Boc_2O (3.01 g, 13.8 mmol) and DMAP (140 mg, 1.15 mmol) at 0 °C. The reaction mixture was stirred at room temperature for 10 hr. Then, the reaction mixture was poured into saturated aqueous NH_4Cl at 0 °C, and extracted with CH_2Cl_2. The organic layer was dried over anhydrous MgSO_4, and concentrated under reduced pressure. The residue was purified by silica gel column chromatography (n-Hexane/CH_2Cl_2 = 20:1 to 5:1) to afford 5 (3.17 g, 97%) as a pale yellow oil.

(1S,2R,6R)-Methyl 2-(hydroxymethyl)-7-oxabicyclo[4.1.0]hept-3-ene-2-carboxylate (S’7)

[α]_D^20 -40.4 (c 1.00, CHCl_3, 90% ee)

IR (film, cm⁻¹): 3466, 2953, 2895, 1732, 1435, 1253, 1084, 1064, 906

^1H NMR (500 MHz, CDCl_3): δ 5.75-5.55 (m, 2H), 3.90 (dd, J = 10.9, 6.9 Hz, 1H), 3.81 (s, 3H), 3.69 (dd, J = 10.9, 6.9 Hz, 1H), 3.65-3.45 (m, 1H), 3.40-3.25 (m, 1H), 2.63 (ddd, J = 18.9, 4.6, 1.2 Hz, 1H), 2.48 (dq, J = 18.9, 2.3 Hz, 1H)
$^{13}$C NMR (125 MHz, CDCl$_3$): δ 173.1, 124.9, 122.4, 66.2, 54.4, 52.5, 51.2, 50.7, 24.8

HRMS (FAB): Calculated for C$_9$H$_{13}$O$_4$ 185.0814 ([M+H]$^+$), found 185.0770

($JS,2R,6R$)-Methyl 2-((((tert-butoxycarbonyl)oxy)methyl)-7-oxabicyclo[4.1.0]hept-3-ene-2-carboxylate (5)

[α]$_{D}^{20}$ = -40.8 (c 1.04, CHCl$_3$, 90% ee)

IR (film, cm$^{-1}$): 2981, 2954, 1745, 1732, 1454, 1371, 1282, 1257, 1161

$^1$H NMR (500 MHz, CDCl$_3$): δ 5.65 (brs, 2H), 4.33 (d, $J$ = 10.9 Hz, 1H), 4.28 (d, $J$ = 10.9 Hz, 1H), 3.81 (s, 3H), 3.60 (brd, $J$ = 4.0 Hz, 1H), 3.36 (brs, 1H), 2.70-2.55 (m, 1H), , 2.55-2.45 (m, 1H), 1.47 (s, 9H)

$^{13}$C NMR (125 MHz, CDCl$_3$): δ 171.7, 153.0, 125.0, 122.1, 82.6, 68.4, 54.2, 52.7, 50.7, 49.5, 27.6, 24.8

HRMS (FAB): Calculated for C$_{14}$H$_{21}$O$_6$ 285.1338 ([M+H]$^+$), found 285.1327

Determination of the absolute configuration of 2c

The specific optical rotation of 5 was [α]$_{D}^{20}$ = -40.8 (c 1.04, CHCl$_3$). On the other hand, the same compound that we previously prepared by enzymatic kinetic resolution was [α]$_{D}^{20}$ = +34.7 (c 1.04 CHCl$_3$) . Therefore, the absolute configuration of 2c prepared by asymmetric bromolactonization using (DHQD)$_2$PHAL was determined to be ($IR,5S,6S$). The absolute configuration of 2d was determined by the same method.

5-Bromo-1-(((tert-butyldiphenyl)silyl)oxy)methyl)-4-methyl-7-oxabicyclo[4.2.0]oct-2-en-8-one (6)

The title compound was prepared in 89% yield with 81% ee as a colorless oil according to the general procedure using one of the epimer of S6* as the starting material. The relative configuration of 6 was tentatively determined by the comparison of chemical shifts and J values of the double bond with those of 7 and 8.

[α]D 26 32.2 (c 1.05, CHCl₃, 81% ee)
IR (film, cm⁻¹): 3072, 2932, 2858, 1836, 1589, 1472, 1381, 1112
¹H NMR (500 MHz CDCl₃): δ 7.70-7.65 (m, 4H), 7.48-7.35 (m, 6H), 5.99 (dd, J = 10.2, 5.1 Hz, 1H), 5.51 (d, J = 10.2 Hz, 1H), 5.32 (d, J = 3.4 Hz, 1H), 4.43 (t, J = 3.4 Hz, 1H), 4.03 (d, J = 10.8 Hz, 1H), 3.69 (d, J = 10.8 Hz, 1H), 2.86 (m, 1H), 1.27 (d, J = 7.4 Hz, 3H), 1.07 (s, 9H)
¹³C NMR (125 MHz CDCl₃): δ 169.0, 135.7, 135.5, 134.8, 134.6, 132.6, 132.2, 130.0, 127.9 (2C), 118.6, 75.5, 62.7, 62.5, 49.2, 37.2, 26.7, 19.4, 19.3
HRMS (ESI) calcd for C₂₅H₂₉O₃BrSiNa 507.0962 [(M+Na)^+] , found 507.0987
HPLC (DAICEL CHIRALCEL OD-H, n-Hexane/i-PrOH = 99.5/0.5, flow rate = 1.0 mL/min, 254 nm):
  t_major = 6.69 min, t_minor = 26.2 min

* It was difficult to separate the two diastereoisomers of S6 completely by silica gel column chromatography. However, since one of the epimer was eluted faster than the other, we could purify it partially, and separated pure epimer was subjected to bromolactonization.
5-Bromo-1-(((tert-butyldiphenylsilyl)oxy)methyl)-4-(methoxymethoxy)-7-oxabicyclo[4.2.0]oct-2-en-8-one (7)

The title compound was prepared in 34% yield with 74% ee as a colorless oil according to the general procedure using S7 as the starting material.

\[
\text{[\alpha]}^{26}_{D} +25.7 \text{ (c 0.41, CHCl}_3, 74\% \text{ ee)}
\]

IR (film, cm\(^{-1}\)): 2932, 2858, 1836, 1472, 1113, 1047

\(^1\)H NMR (500 MHz CDCl\(_3\)): \(\delta\) 7.68-7.64 (m, 4H), 7.45-7.35 (m, 6H), 5.97 (dd, \(J = 10.2, 1.7 \text{ Hz}, 1\)H), 5.48 (dd, \(J = 10.2, 2.3 \text{ Hz}, 1\)H), 5.30 (d, \(J = 2.8 \text{ Hz}, 1\)H), 4.81-4.78 (m, 3H), 4.40-4.37 (m, 1H), 4.06 (d, \(J = 10.9 \text{ Hz}, 1\)H), 3.74 (d, \(J = 10.9 \text{ Hz}, 1\)H), 3.50 (s, 3H), 1.07 (s, 9H)

\(^13\)C NMR (125 MHz CHCl\(_3\)): \(\delta\) 167.4, 135.6, 135.5, 133.1, 130.8, 130.6, 130.0 (2C), 127.9 (2C), 119.7, 96.4, 71.7, 70.6, 62.8, 62.3, 56.3, 47.0, 26.6, 19.3

HRMS (ESI) calcd for C\(_{26}\)H\(_{31}\)O\(_5\)BrSiNa 553.1016 [(M+Na)\(^+\)], found 553.1031

HPLC (DAICEC CHIRALCEL OD-H, n-Hexane/i-PrOH = 99.0/1.0, flow rate = 1.0 mL/min, 190 nm):
\(t_{\text{major}} = 15.6 \text{ min}, t_{\text{minor}} = 13.1 \text{ min}\)
5-Bromo-1-(((tert-butyldiphenylsilyl)oxy)methyl)-4-(methoxymethoxy)-7-oxabicyclo[4.2.0]oct-2-en-8-one (8)

The title compound was prepared in 46% with 87% ee as a colorless oil according to the general procedure using S8 as the starting material.

[α]D 26 -44.3 (c 1.17, CHCl3, 87% ee)
IR (film, cm⁻¹): 2932, 2858, 1836, 1472, 1113, 1031
1H NMR (500 MHz CDCl3): δ 7.68-7.64 (m, 4H), 7.45-7.35 (m, 6H), 6.19 (dd, J = 10.2, 5.1 Hz, 1H), 5.67 (d, J = 10.2 Hz, 1H), 5.27 (dd, J = 2.8, 1.1 Hz, 1H), 4.73 (s, 2H), 4.65 (dd, J = 3.4, 2.8 Hz, 1H), 4.47-4.45 (m, 1H), 4.05 (d, J = 10.8 Hz, 1H), 3.68 (d, J = 10.8 Hz, 1H), 3.50 (s, 3H), 1.07 (s, 9H)
13C NMR (125 MHz CDCl3): δ 168.6, 135.7, 135.5, 132.3, 132.1, 130.0 (2C), 129.6, 127.9 (2C), 123.0, 96.8, 76.8, 73.0, 62.7, 62.0, 56.0, 43.7, 26.7, 19.3
HRMS (ESI) calcd for C26H31O5BrSiNa 553.1016 [(M+Na)+], found 553.1043
HPLC (DAICEL CHIRALCEL OD-H, n-Hexane/i-PrOH = 99.5/0.5, flow rate = 1.0 mL/min, 254 nm):
tmajor = 8.90 min, tminor = 21.0 min
2-(-5-Bromo-8-oxo-7-oxabicyclo[4.2.0]oct-2-en-1-yl)acetate (9)

The title compound was prepared in 49% yield with 77% ee as a colorless oil according to the general procedure using S9 as the starting material.

\[ \alpha \] \text{D}^{25} +78.6 (c 0.69, CHCl₃, 77% ee)

IR (film, cm⁻¹): 2980, 1830, 1730, 1369, 1394, 1269, 1261, 1213, 1159, 1109

¹H NMR (500 MHz CDCl₃): δ 6.02-6.00 (m, 1H), 5.62 (dd, \( J = 10.2, 2.3 \) Hz, 1H), 5.01 (d, \( J = 2.8 \) Hz, 1H), 4.58-4.56 (m, 1H), 2.87 (d, \( J = 17.0 \) Hz, 1H), 2.74 (d, \( J = 17.0 \) Hz, 1H), 2.74-2.70 (m, 2H), 1.47 (s, 9H).

¹³C NMR (125 MHz, CDCl₃): δ 168.5, 168.0, 127.3, 122.5, 82.5, 74.3, 55.8, 41.2, 38.0, 27.9, 27.8

HRMS (ESI) calcd for C₁₃H₁₇O₄BrNa 339.0202 [(M+Na)⁺], found 339.0215

HPLC (DAICEL CHIRALPAK AD-H, n-Hexane/i-PrOH = 99.0/1.0, flow rate = 1.0 mL/min, 190 nm):

\( t_{\text{major}} = 15.1 \) min, \( t_{\text{minor}} = 18.0 \) min
5-Bromo-1-(naphthalen-2-ylmethyl)-7-oxabicyclo[4.2.0]oct-2-en-8-one (10)

The title compound was prepared in 71% yield with 47% ee as a colorless oil according to the general procedure using S10 as the starting material.

[α]$_D^{26}$ +26.4 (c 1.16, CHCl$_3$, 47% ee)
IR (film, cm$^{-1}$): 3049, 1829, 1601, 1508, 1421, 1366, 1273, 1211, 1111, 1010
$^1$H NMR (500 MHz CDCl$_3$): δ 7.85-7.78 (m, 3H), 7.75 (s, 1H), 7.51 (m, 3H), 6.07-5.99 (m, 1H), 5.90-5.79 (m, 1H), 4.67 (d, $J$ = 2.8 Hz, 1H), 4.50-4.43 (m, 1H), 4.46 (d, $J$ = 14.1 Hz, 1H), 3.15 (d, $J$ = 14.1 Hz, 1H), 2.69 (m, 2H).
$^{13}$C NMR (125 MHz, CDCl$_3$): δ 168.9, 133.4, 132.5, 132.3, 129.1, 128.6, 128.0, 127.8, 127.7, 126.8, 126.3, 126.0, 123.5, 73.2, 60.0, 41.2, 38.9, 27.9
HRMS (ESI) calcd for C$_{18}$H$_{15}$O$_2$BrNa 365.0148 [(M+Na)$^+$], found 365.0143
HPLC (DAICEL CHIRALCEL OD-H, n-Hexane/i-PrOH = 99.5/0.5, flow rate = 1.0 mL/min, 254 nm):
$^t_{major}$ = 42.2 min, $^t_{minor}$ = 36.9 min
5-Bromo-1-(((tert-butyldiphenylsilyloxy)methyl)-3,5-dimethyl-7-oxabicyclo[4.2.0]oct-2-en-8-one (11)

The title compound was prepared in 67% yield with 37% ee as a colorless oil according to the general procedure using S11 as the starting material.

[\alpha]^{26}_{D} +1.0 (c 0.93, CHCl\textsubscript{3}, 37% ee)

IR (film, cm\textsuperscript{-1}): 2958, 2932, 2858, 1793, 1429, 1382, 1112

\textsuperscript{1}H NMR (500 MHz CDCl\textsubscript{3}): \textit{\delta} 7.80-7.70 (m, 4H), 7.47-7.35 (m, 6H), 4.88 (s, 1H), 4.59 (s, 1H), 4.10 (d, J = 10.8 Hz, 1H), 3.63 (d, J = 10.8 Hz, 1H), 2.52 (d, J = 18.7 Hz, 1H), 2.32 (d, J = 18.7 Hz, 1H), 1.69 (s, 3H), 1.57 (s, 3H), 1.03 (s, 9H).

\textsuperscript{13}C NMR (125 MHz, CDCl\textsubscript{3}): \textit{\delta} 171.9, 137.7, 135.7, 135.6, 129.8, 127.8, 127.8, 117.1, 82.6, 59.9, 54.2, 51.6, 39.9, 26.7, 22.3, 21.7, 19.2

HRMS (ESI) calcd for C\textsubscript{26}H\textsubscript{31}O\textsubscript{3}BrSiNa 521.118 [(M+Na)	extsuperscript{+}], found 521.1107

HPLC (DAICEL CHIRALCEL OD-H, n-Hexane/i-PrOH = 99.5/0.5, flow rate = 1.0 mL/min, 254 nm):

\textit{t}_{\text{major}} = 9.09 \text{ min}, \textit{t}_{\text{minor}} = 10.9 \text{ min}
**tert-Butyl 7-bromo-2-oxo-2,3,3a,6,7,7a-hexahydrobenzofuran-3a-carboxylate (13a)**

![Chemical Structure](image)

The title compound was prepared in 70% yield with 92% ee as a colorless solid according to the general procedure using 12a as the starting material.

\([\alpha]^{26}_D +10.4(c 0.50, \text{CHCl}_3, 92\% \text{ ee})\)

IR (film, cm\(^{-1}\)): 3043, 2978, 2933, 2851, 1794, 1728, 1369, 1278, 1257, 1198, 1159, 1009

\(^1\)H NMR (500 MHz CDCl\(_3\)): \(\delta 5.89-5.79 (m, 2H), 5.22 (d, J = 5.1 \text{ Hz}, 1H), 4.45-4.42 (m, 1H), 3.08 (d, J = 17.0 \text{ Hz}, 1H), 2.82 (ddd, J = 19.3, 4.6, 2.3 \text{ Hz} 1H), 2.58 (d, J = 17.0 \text{ Hz}, 1H), 2.54 (ddd, J = 19.3, 4.0, 4.0 \text{ Hz}, 1H), 1.50 (s, 9H).

\(^13\)C NMR (125 MHz, CDCl\(_3\)): \(\delta 173.0, 170.0, 125.1, 124.5, 83.2, 80.8, 49.4, 42.4, 41.0, 28.7, 27.8\)

HRMS (ESI) calcd for \(\text{C}_{13}\text{H}_{17}\text{BrNaO}_3\) 339.0208 [(M+Na\(^+\)], found 339.0219

HPLC (DAICEL CHIRALCEL OD-H, \(n\)-Hexane/\(i\)-PrOH = 98.0/2.0, flow rate = 1.0 mL/min, 190 nm):
\(t_{\text{major}} = 12.4 \text{ min}, t_{\text{minor}} = 16.7 \text{ min}\)
7-Bromo-3a-((tert-butyldiphenylsilyl)oxy)methyl)-3,3a,7,7a-tetrahydrobenzofuran-2(6H)-one (13b)

The title compound was prepared in 90% yield with 92% ee as a colorless solid according to the general procedure using 12b as the starting material.

$\left[\alpha\right]_{D}^{25} = -32.9^\circ (c 0.74, \text{CHCl}_3, 92\% \text{ ee})$

IR (film, cm$^{-1}$): 2931, 2858, 1788, 1427, 1113

$^1$H NMR (500 MHz CDCl$_3$): $\delta$ 7.65-7.59 (m, 4H), 7.45-7.35 (m, 6H), 5.75 (dd, $J = 10.2, 4.5, 2.3$ Hz, 1H), 5.49 (dd, $J = 10.2, 1.7$ Hz, 1H), 4.82 (d, $J = 6.8$ Hz, 1H), 4.40 (dd, $J = 6.8, 4.5, 2.6$ Hz, 1H), 3.72 (d, $J = 10.2$ Hz, 1H), 3.59 (d, $J = 10.2$ Hz, 1H), 2.85 (d, $J = 17.6$ Hz, 1H), 2.82-2.75 (m, 1H), 2.55-2.49 (m, 1H), 2.37 (d, $J = 17.6$ Hz, 1H), 1.08 (s, 9H).

$^{13}$C NMR (125 MHz CDCl$_3$): $\delta$ 174.3, 135.7, 135.6, 131.9, 130.0, 127.9, 127.8, 126.0, 82.0, 67.3, 46.6, 44.9, 37.5, 31.3, 26.8, 19.3

HRMS (ESI) calcd for C$_{25}$H$_{29}$BrO$_3$SiNa $507.0962$ [(M+Na)$^+$], found 507.0955

HPLC (DAICEL CHIRALPAKAD-H, $n$-Hexane/i-PrOH = 99.0/1.0, flow rate = 1.0 mL/min, 190 nm):

$t_{\text{major}} = 7.45$ min, $t_{\text{minor}} = 9.58$ min
III. Kinetic resolution

1-(((tert-Butyldiphenylsilyl)oxy)methyl)-1,4-dihydronaphthalene-1-carboxylic acid (14)

![Chemical Structure](image)

The title compound was prepared in 22% (2 steps) as a colorless solid according to the general procedure for the synthesis of 1 (see page S3) using 1-naphthoic acid as the starting material.

IR (film, cm\(^{-1}\)): 3043, 2978, 1794, 1369, 1278, 1257, 1198, 1159

\(^1\)H NMR (CDCl\(_3\), 400 MHz): \(\delta\) 7.51-7.55 (m, 4H), 7.30-7.43 (m, 7H), 7.16-7.24 (m, 3H), 6.21 (ddd, \(J = 3.7, 3.7, 10.2\) Hz, 1H), 6.10 (ddd, \(J = 1.9, 1.9, 10.2\) Hz, 1H), 4.12 (d, \(J = 9.8\) Hz, 1H), 3.84 (d, \(J = 9.8\) Hz, 1H), 3.48 (ddd, \(J = 1.9, 3.7, 22.0\) Hz, 1H), 3.38 (ddd, \(J = 1.9, 3.7, 22.0\) Hz, 1H), 0.97 (s, 9H).

\(^1^3\)C NMR (125 MHz, CDCl\(_3\)): \(\delta\) 179.5, 135.6, 134.4, 133.0, 132.3, 130.0, 128.6, 127.6, 127.5, 127.3, 126.7, 126.2, 125.7, 69.7, 53.1, 29.8, 26.6, 19.2

HRMS (ESI) calcd for \(\text{C}_{28}\text{H}_{30}\text{O}_3\text{SiNa}\) 465.1856 [(M+Na)+], found 465.1865
To a screw-top vial equipped with a stir bar were added dienecarboxylic acid 14 (29.3 mg, 0.066 mmol, 1.0 equiv) and (DHQD)$_2$Pyr (6.2 mg, 0.007 mmol, 0.1 equiv). The mixture was dissolved in CHCl$_3$/n-Hex=1/1 (0.05 M) and cooled to -40 °C. To the stirred mixture was added NBS (5.9 mg, 0.033 mmol, 0.5 equiv). After the time given in Tables, the reaction mixture was quenched with saturated Na$_2$S$_2$O$_3$ and extracted with CH$_2$Cl$_2$. The organic layer was washed with H$_2$O, brine, dried over anhydrous Na$_2$SO$_4$, filtered and concentrated under reduced pressure. The residue was purified by silica gel column chromatography (n-hexane/EtOAc = 1/0 ~ 1/2) to afford 15 and 14 as a colorless solid. Enantiomeric excess of 15 and 14 was determined by chiral HPLC analysis.

<table>
<thead>
<tr>
<th>Entry</th>
<th>Time (h)</th>
<th>Product</th>
<th>recov. S.M.</th>
</tr>
</thead>
<tbody>
<tr>
<td></td>
<td></td>
<td>Yield (%)</td>
<td>Ee (%)</td>
</tr>
<tr>
<td>1</td>
<td>1</td>
<td>24</td>
<td>90</td>
</tr>
<tr>
<td>2</td>
<td>3</td>
<td>33</td>
<td>86</td>
</tr>
<tr>
<td>3</td>
<td>10</td>
<td>38</td>
<td>86</td>
</tr>
<tr>
<td>4$^b$</td>
<td>24</td>
<td>55</td>
<td>78</td>
</tr>
</tbody>
</table>

a) The ee was determined by chiral HPLC analysis after esterification with CH$_3$N$_2$.

b) 0.6 eq NBS was used.
3-Bromo-8b-(((tert-butyldiphenylsilyl)oxy)methyl)-2a,3,4,8b-tetrahydro-1H-naphtho[2,1-b]oxet-1-one (15)

\[
\begin{align*}
\text{OTBDPS} & \quad \text{Br} \\
\end{align*}
\]

\[\alpha^\circ_{D} = -30.8 (c 0.46, \text{CHCl}_3, \text{86\% ee})\]

IR (film, cm\(^{-1}\)) = 2930, 1836, 1102

\(^1\)H NMR (CDCl\(_3\), 400 MHz): \(\delta\) 7.69 (dd, \(J = 8.0, 1.6 \text{ Hz}, 2\text{H})\), 7.67 (dd, \(J = 8.0, 1.6 \text{ Hz}, 2\text{H})\), 7.37-7.47 (m, 6H), 7.12-7.30 (m, 4H), 5.45 (d, \(J = 3.6 \text{ Hz}, 1\text{H})\), 4.67 (ddd, \(J = 5.4, 3.8, 3.6 \text{ Hz}, 1\text{H})\), 4.57 (d, \(J = 10.6 \text{ Hz}, 1\text{H})\), 3.89 (d, \(J = 10.6 \text{ Hz}, 1\text{H})\), 3.42 (dd, \(J = 16.4, 3.8 \text{ Hz}, 1\text{H})\), 3.19 (dd, \(J = 16.4, 5.4 \text{ Hz}, 1\text{H})\), 1.10 (s, 9H).

\(^{13}\)C NMR (125 MHz, CDCl\(_3\)): \(\delta\) 168.5, 135.6, 135.5, 133.6, 132.4, 132.0, 130.1, 130.0, 129.4, 128.4, 128.1, 128.0 (2C), 127.5, 125.6, 76.7, 64.2, 62.8, 43.7, 33.9, 26.7, 19.3

HRMS (ESI) calcd for C\(_{28}\)H\(_{29}\)BrO\(_3\)SiNa 543.0962 [(M+Na)\(^{+}\)], found 543.0963

HPLC (DAICEL CHIRALCEL OD-H, \(n\)-Hexane/i-PrOH = 99.5/0.5, flow rate = 1.0 mL/min, 254 nm):
\(t_{\text{major}} = 7.90 \text{ min}, t_{\text{minor}} = 13.2 \text{ min}\)

Methyl 1-(((tert-butyldiphenylsilyl)oxy)methyl)-1,4-dihydronaphthalene-1-carboxylate (16)

\[
\begin{align*}
\text{MeO}_2\text{C} & \quad \text{OTBDPS} \\
\end{align*}
\]

\[\alpha^\circ_{D} = -19.1 (c 1.03, \text{CHCl}_3, \text{92\% ee})\]

IR (film, cm\(^{-1}\)) = 2953, 1732, 1429, 1224, 1111

\(^1\)H NMR (CDCl\(_3\), 400 MHz): \(\delta\) 7.61 (dd, \(J = 8.4, 1.6 \text{ Hz}, 2\text{H})\), 7.50 (dd, \(J = 8.4, 1.2 \text{ Hz}, 2\text{H})\), 7.35 (m, 7H), 7.19 (m, 3H), 6.19 (ddd, \(J = 10.2, 3.4, 3.4 \text{ Hz}, 1\text{H})\), 6.08 (ddd, \(J = 10.2, 2.2, 2.2 \text{Hz}, 1\text{H})\), 4.19 (d, \(J = 9.4 \text{ Hz}, 1\text{H})\), 3.85 (d, \(J = 9.4 \text{ Hz}, 1\text{H})\), 3.69 (s, 3H), 3.52-3.45 (m, 2H), 0.95 (s, 9H).

\(^{13}\)C NMR (125 MHz, CDCl\(_3\)): \(\delta\) 173.7, 135.6, 134.4, 133.2 (2C), 132.9, 129.5 (2C), 128.5, 127.6, 127.5, 127.2, 127.1, 126.2, 126.0, 70.1, 53.2, 52.4, 29.8, 26.5, 19.2

HRMS (ESI) calcd for C\(_{29}\)H\(_{32}\)O\(_3\)SiNa 479.2013 [(M+Na)\(^{+}\)], found 479.2001

HPLC (DAICEL CHIRALCEL OD-H, \(n\)-Hexane/i-PrOH = 99.5/0.5, flow rate = 1.0 mL/min, 254 nm):
\(t_{\text{major}} = 4.87 \text{ min}, t_{\text{minor}} = 6.15 \text{ min}\)
The image contains a chemical structure and a spectra chart. The chemical structure shows a molecule with labels such as Br, Me, and OTBDPS, indicating its components. The spectra chart likely represents the NMR or MS spectra of the compound, showing peaks at different chemical shifts (e.g., 7.465, 7.004, 5.999, 5.293, 5.133, etc.). The chart is labeled with parts per million (ppm) and the X-axis indicates the chemical shifts. The Y-axis likely represents the intensity of the peaks.
OTBDPS

MeO₂C"
The catalyst used
3mol % (DHQD)$_2$PHAL

The catalyst used
10mol % (DHQD)$_2$PHAL
The catalyst used 10mol % (DHQD)$_2$PHAL.

Reaction temperature was -60 °C.
二重クロマトグラム

10 racemic

ピークレポート

10 racemic

ピークレポート

11 optical active

ピークレポート

11 optical active
0.5 eq of NBS was used.

0.6 eq of NBS was used.
0.5 eq of NBS was used.

0.6 eq of NBS was used.

optical active

optical active