Supporting Information
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Supporting Information
for

Enantiodivergent Synthesis of Tetra-ortho-Substituted Biphenyls by Enzymatic Desymmetrization

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**General Experimental Procedures**

All reactions dealing with air- and moisture-sensitive compounds were conducted under an atmosphere of argon. Dichloromethane was distilled successively from P$_2$O$_5$ and CaH$_2$ and stored over MS 4A. Commercially available dehydrated solvents, tetrahydrofuran (THF) and diethyl ether (Et$_2$O), were used. For thin-layer chromatography (TLC) analysis, Merck precoated plates (silica gel 60 F$_{254}$, Art 5715, 0.25 mm) were used. Merck Kieselgel 60 (70-230 mesh ASTM) was used for flash column chromatography. Silica gel preparative TLC (PTLC) was performed on Merck Kieselgel 60 F$_{254}$ (Art. 7747). Melting point (m.p.) determinations were performed by using Yanaco MP-S3 and MP-500V instruments and are uncorrected. $^1$H-NMR (300, 400 MHz) and $^{13}$C-NMR (75, 100 MHz) spectra were measured on JEOL JNM AL-300, JEOL JNM Lamda-300, JEOL JNM AL-400, and JEOL JNM Lamda-400 spectrometers. Chemical shifts are expressed in parts per million downfield from internal trimethylsilyl silane ($\delta = 0$). Infrared (IR) spectra were recorded on a Horiba FT-710 spectrometer. Attenuated total reflectance Fourier-transform infrared (ATR-FTIR) spectra were recorded by using a Perkin–Elmer 100 FTIR spectrometer. Optical rotations ($[\alpha]_D$) were measured on a Jasco DIP-1000 polarimeter. Elemental analyses were recorded on a Perkin–Elmer PE2400 Series II CHNS/O Analyzer.

All compounds given below bear the same formula numbers as used in the main text. Compounds unlabeled in the main text are labeled with letters [i-xii]. All reagents were used as obtained from commercial sources.
1. Synthesis of the \( \sigma \)-symmetric biphenyl diacetates 1a–1c, the substrates of the enzymatic hydrolysis (Scheme 2).

\[
\begin{align*}
\text{CH}_2\text{CHCH}_2\text{Br} & & \text{NaH, DMF} \\
1a: & & 99\%, 2 \text{ steps} \\
1b: & & \text{quant}, 2 \text{ steps} \\
1c: & & \text{quant}, 2 \text{ steps}
\end{align*}
\]

\[
\begin{align*}
\text{CHO} & & \text{MeO} \\
R_1 & & R_2 \quad R_3 \\
\text{Br} & & \text{MOMO} \\
\text{B(OH)}_2 & & \text{MOMO}
\end{align*}
\]

[\text{suffix; a: } R_1 = \text{OMe}, R_2 = R_3 = \text{H}; \ b: R_1 = R_3 = \text{H}, R_2 = \text{OMe}; \ c: R_1 = R_2 = \text{H}, R_3 = \text{OMe}]

\[
\begin{align*}
\text{1a: } & & \text{99\%, 2 steps} \\
\text{1b: } & & \text{quant, 2 steps} \\
\text{1c: } & & \text{quant, 2 steps}
\end{align*}
\]

\[
\begin{align*}
\text{MOMO} & & \text{OMOM} \\
\text{OMe} & & \text{OHC} \\
\text{MeO} & & \text{OAc}
\end{align*}
\]

1) 15 mol\% \text{Pd(PPh}_3)_4 \text{ base} \quad \text{DME, H}_2\text{O, reflux} \\
2) \text{NaBH}_4, \text{THF}

\[
\begin{align*}
\text{4a: } & & 53\%, 2 \text{ steps} \\
\text{4b: } & & 77\%, 2 \text{ steps} \\
\text{4c: } & & 89\%, 2 \text{ steps}
\end{align*}
\]

\[
\begin{align*}
\text{CH}_2\text{=CHCH}_2\text{Br} & & \text{NaH, DMF} \\
\text{5a: } & & \text{quant} \\
\text{5b: } & & \text{quant} \\
\text{5c: } & & \text{quant}
\end{align*}
\]

\[
\begin{align*}
\text{MeO} & & \text{OMOM} \\
\text{OAc} & & \text{OMOM} \\
\text{MeO} & & \text{OHC}
\end{align*}
\]

1) 2 M HCl \text{aq.} \quad \text{MeOH} \\
2) \text{Ac}_2\text{O, DMAP} \quad \text{pyridine}

\text{Scheme 1} \quad \text{"For 3a: Ba(OH)}_2\text{ (3 molar amounts), For 3b and 3c: K}_3\text{PO}_4\text{ (2 molar amounts).}"

A typical procedure of the Suzuki–Miyaura coupling reaction is described for the reaction of aryl bromide 3a with boronic acid 2 [in the reactions of bromides 3b, 3c, K$_3$PO$_4$ was used in place of Ba(OH)$_2$]: A mixture of 2 (11.1 g, 45.9 mmol), 3a (5.62 g, 23.0 mmol), Pd(PPh$_3$)$_4$ (3.99 g, 3.45 mmol), Ba(OH)$_2$$\cdot$8H$_2$O (21.8 g, 69.0 mmol) in DME (170 mL) and water (40 mL) was heated under reflux for 1 h. After cooling to room temperature, the mixture was filtered and extracted with EtOAc. The combined organic extracts were washed with brine, dried over Na$_2$SO$_4$, filtered and concentrated in vacuo. The residue was purified by silica-gel column chromatography (hexane/EtOAc = 6/1) to give aldehyde 1 (4.42 g, 53%) as pale yellow solids. Recrystallization from EtOAc gave 1 as colorless prisms.

\[
\begin{align*}
\text{MeO} & & \text{OMOM} \\
\text{OHC} & & \text{OMOM} \\
\text{OMe} & & \text{OMe}
\end{align*}
\]

\text{M.p. 130.5–132.0 °C;}

$^1$H NMR (400 MHz, CDCl$_3$, $\delta$)

3.29 (s, 6H), 3.68 (s, 3H), 3.91 (s, 3H), 5.02 (s, 4H), 6.88 (d, 2H, $J = 8.4$ Hz), 6.98 (d, 1H, $J = 9.0$ Hz), 7.15 (d, 1H, $J = 9.0$ Hz), 7.28 (t, 1H, $J = 8.4$ Hz), 10.0 (s, 1H);

$^{13}$C NMR (100 MHz, CDCl$_3$, $\delta$)
Aldehyde ii was obtained by silica-gel column chromatography (hexane/EtOAc = 1/1) as pale yellow solids (96%). Recrystallization from EtOAc gave ii as colorless prisms.

M.p. 148.0–148.5 °C;

$^1$H NMR (400 MHz, CDCl$_3$, δ)
3.28 (s, 6H), 3.73 (s, 3H), 3.90 (s, 3H), 5.01 (d, 2H, J = 6.8 Hz), 5.05 (d, 2H, J = 6.8 Hz), 6.78 (d, 1H, J = 2.4 Hz), 6.90 (d, 2H, J = 8.4 Hz), 7.13 (d, 1H, J = 2.4 Hz), 7.31 (t, 1H, J = 8.4 Hz), 9.69 (s, 1H);

$^{13}$C NMR (100 MHz, CDCl$_3$, δ)
55.6, 55.9, 55.9, 94.6, 100.2, 104.8, 108.4, 112.9, 121.6, 129.8, 135.6, 156.1, 156.6, 158.6, 160.1, 192.6;

IR (ATR)
2906, 2833, 2752, 1688, 1583, 1464, 1248, 1511, 1099, 1019, 1035, 991, 920 cm$^{-1}$;


Aldehyde iii was obtained by silica-gel column chromatography (hexane/EtOAc = 1/1) as pale yellow solids (99%). Recrystallization from EtOAc gave iii as colorless prisms.

M.p. 79.2–81.0 °C;

$^1$H NMR (400 MHz, CDCl$_3$, δ)
3.28 (s, 6H), 3.59 (s, 3H), 3.98 (s, 3H), 5.02 (d, 2H, J = 6.8 Hz), 5.08 (d, 2H, J = 6.8 Hz), 6.92 (d, 2H, J = 8.4 Hz), 7.05 (d, 1H, J = 8.8 Hz), 7.32 (t, 1H, J = 8.4 Hz), 7.84 (d, 1H, J = 8.8 Hz), 9.57 (s, 1H);

$^{13}$C NMR (100 MHz, CDCl$_3$, δ)
55.9, 56.0, 60.4, 94.6, 108.2, 111.2, 112.9, 123.9, 128.2, 130.0, 133.3, 146.8, 155.8, 157.5, 191.3;

IR (ATR)
2957, 2937, 2899, 2829, 1675, 1581, 1485, 1452, 1306, 1280, 1247, 1150, 1100, 1086, 1037 cm$^{-1}$;

Anal. calcd for C$_{19}$H$_{22}$O$_7$: C, 62.97; H, 6.12. Found: C, 63.26; H, 6.01.
A typical procedure of the reduction of the aldehydes is described for the reaction of \( i \). To a solution of aldehyde \( i \) (3.89 g, 10.7 mmol) in THF (130 mL) was added \( \text{NaBH}_4 \) (486 mg, 12.8 mmol) at 0 °C. The reaction mixture was stirred for 1.5 h at room temperature, and 2 M HCl was added dropwise until no further bubbling was observed. The mixture was extracted with EtOAc, and the combined organic extracts were washed with sat. aq. NaHCO\(_3\), brine, and dried over Na\(_2\)SO\(_4\), filtered and concentrated in vacuo. The obtained alcohol \( 4a \) (3.94 g, quant) was adequately pure for characterization and used directly in the next step. Recrystallization from Et\(_2\)O gave \( 4a \) as colorless prisms.

\[
\begin{align*}
  &\text{M.p. 109.0–111.0 °C;} \\
  &^1\text{H NMR (400 MHz, CDCl}_3, \delta) \\
  &2.81 (\text{br s, 1H}), 3.26 (\text{s, 6H}), 3.65 (\text{s, 3H}), 3.88 (\text{s, 3H}), 4.39 (\text{d, 2H, J = 6.6 Hz}), 4.99 (\text{s, 4H}), 6.86 (\text{d, 1H, J = 9.0 Hz}), 6.90 (\text{d, 1H, J = 9.0 Hz}), 6.91 (\text{d, 2H, J = 8.4 Hz}), 7.27 (\text{t, 1H, J = 8.4 Hz}); \\
  &^13\text{C NMR (100 MHz, CDCl}_3, \delta) \\
  &55.77, 55.84, 56.1, 58.8, 95.1, 109.8, 110.1, 110.4, 117.2, 124.5, 129.1, 129.1, 151.3, 152.1, 155.5; \\
  &\text{IR (KBr)} \\
  &3575, 2906, 2833, 1466, 1396, 1155, 1086, 1041, 1012, 806, 783 \text{ cm}^{-1}; \\
  &\text{Anal. calcd for C}_{19}\text{H}_{24}\text{O}_7: C, 62.63; H, 6.64. \text{ Found: C, 62.80; H, 6.43.}
\end{align*}
\]

Alcohol \( 4b \) was obtained by silica-gel column chromatography (hexane/EtOAc = 1/1) as white solids (80%). Recrystallization from EtOAc gave \( ii \) as colorless prisms.

\[
\begin{align*}
  &\text{M.p. 121.5–122.8 °C;} \\
  &^1\text{H NMR (300 MHz, CDCl}_3, \delta) \\
  &2.48 (\text{t, 1H, J = 5.4 Hz}), 3.26 (\text{s, 6H}), 3.68 (\text{s, 3H}), 3.87 (\text{s, 3H}), 4.29 (\text{d, 2H, J = 5.4 Hz}), 4.99 (\text{d, 2H, J = 6.8 Hz}), 5.01 (\text{d, 2H, J = 6.8 Hz}), 6.50 (\text{d, 1H, J = 2.4 Hz}), 6.74 (\text{d, 1H, J = 2.4 Hz}), 6.90 (\text{d, 2H, J = 8.4 Hz}), 7.27 (\text{t, 1H, J = 8.4 Hz}); \\
  &^13\text{C NMR (100 MHz, CDCl}_3, \delta) \\
  &55.3, 55.7, 55.9, 64.1, 95.3, 98.2, 104.5, 110.3, 114.9, 117.4, 129.1, 141.6, 155.9, 158.2, 160.2; \\
  &\text{IR (ATR)}
\end{align*}
\]
Alcohol 4e was obtained by silica-gel column chromatography (hexane/EtOAc = 1/1) as a colorless oil (90%).

\[ \text{H NMR (400 MHz, CDCl}_3, \delta) \]
\[ 2.35 \text{ (br s, 1H), 3.26 \text{ (s, 6H), 3.59 \text{ (s, 3H), 3.95 \text{ (s, 3H), 4.26 \text{ (s, 2H), 5.01 \text{ (d, 2H, J = 6.6 Hz), 5.06 \text{ (d, 2H, J = 6.6 Hz), 6.93 \text{ (d, 2H, J = 8.6 Hz), 6.97 \text{ (d, 1H, J = 8.3 Hz), 7.25 \text{ (d, 1H, J = 8.3 Hz), 7.30 \text{ (t, 1H, J = 8.6 Hz);}}}}}}\]

\[ \text{C NMR (100 MHz, CDCl}_3, \delta) \]
\[ 55.7, 56.0, 60.1, 63.6, 95.2, 109.5, 111.7, 116.7, 124.4, 128.2, 129.4, 132.9, 146.8, 152.1, 155.6; \]

\[ \text{IR (neat)} \]
\[ 3475, 2930, 2840, 1480, 1460, 1250, 1150, 1090, 1040, 810, 730 \text{ cm}^{-1}; \]
Anal. calcd for C_{10}H_{20}O_{10}: C, 62.63; H, 6.64. Found: C, 62.93; H, 6.71.

A typical procedure of the allyl ether formation is described for the reaction of 4a: A mixture of NaH (55% dispersion in mineral oil, 1.20 g, 27.4 mmol) and alcohol 4a (1.00 g, 2.74 mmol) in DMF (20 mL) was stirred at room temperature for 1 h, to which was added allyl bromide (0.71 mL, 8.2 mmol) and Bu₄NI (101 mg, 274 µmol) at 0 °C. After 2 h, the reaction was stopped by adding Et₂NH, and the mixture was diluted with water, and extracted with EtOAc. The combined organic extracts were washed with 2 M HCl, brine, sat.aq. NaHCO₃ and dried over Na₂SO₄, filtered and concentrated in vacuo. The residue was purified by silica-gel column chromatography (hexane/EtOAc = 5/1) to give 5a (1.11 g, quant) as white solids. Recrystallization from EtOAc gave 5a as colorless prisms.

\[ \text{M.p. 115.2–116.5 °C;} \]
\[ \text{H NMR (400 MHz, CDCl}_3, \delta) \]
\[ 3.30 \text{ (s, 6H), 3.65 \text{ (s, 3H), 3.72 \text{ (ddd, 2H, J₁ = 6.0, J₂ = 1.5, J₃ = 1.0 Hz), 3.85 \text{ (s, 3H), 4.29 \text{ (s, 2H), 4.96 \text{ (ddd, J₁ = 10.4, J₂ = 1.7, J₃ = 1.0 Hz), 4.98 \text{ (d, 2H, J = 6.6 Hz), 5.00 \text{ (d, 2H, J = 6.6 Hz), 5.01 \text{ (ddt, 1H, J = 1.0 Hz)}}}}}}\]

17.2, J₂ = 1.7, J₃ = 1.5 Hz), 5.64 (ddt, 1H, J₁ = 17.2, J₂ = 10.4, J₃ = 6.0 Hz), 6.88 (s, 2H), 6.89 (d, 2H, J = 8.4 Hz), 7.25 (t, 1H, J = 8.4 Hz);

¹³C NMR (100 MHz, CDCl₃, δ)
55.7, 56.1, 56.3, 64.2, 71.0, 94.7, 108.8, 110.3, 111.2, 116.2, 116.7, 126.4, 126.8, 128.9, 135.3, 151.4, 152.6, 155.7;

IR (ATR)
2097, 2831, 1590, 1463, 1248, 1150, 1070, 989, 917, 893 cm⁻¹;

Anal. calcd for C₂₂H₂₈O₇: C, 65.33; H, 6.98. Found: C, 65.05; H, 6.79.

Allyl ether ⁵b was obtained by silica-gel column chromatography (hexane/EtOAc = 4/1) as a colorless oil (quant).

¹H NMR (400 MHz, CDCl₃, δ)
3.30 (s, 6H), 3.68 (s, 3H), 3.866 (s, 3H), 3.867 (ddd, 2H, J₁ = 5.5, J₂ = 1.7, J₃ = 1.3 Hz), 4.24 (s, 2H), 4.99 (d, 2H, J = 6.8 Hz), 5.01 (d, 2H, J = 6.8 Hz), 5.09 (ddt, 1H, J₁ = 10.5, J₂ = 1.7, J₃ = 1.3 Hz), 5.19 (ddt, 1H, J₁ = 17.4, J₂ = J₃ = 1.7 Hz), 5.83 (ddt, 1H, J₁ = 17.4, J₂ = 10.5, J₃ = 5.5 Hz), 6.47 (d, 1H, J = 2.4 Hz), 6.79 (d, 1H, J = 2.4 Hz), 6.88 (d, 2H, J = 8.4 Hz), 7.25 (t, 1H, J = 8.4 Hz);

¹³C NMR (100 MHz, CDCl₃, δ)
55.2, 55.5, 55.7, 69.7, 71.0, 94.7, 97.6, 102.8, 109.1, 114.5, 116.2, 116.4, 128.9, 134.9, 139.7, 155.9, 158.1, 160.1;

IR (neat)
2940, 2925, 2890, 2825, 1590, 1460, 1320, 1240, 1200, 1150, 1040 cm⁻¹;


Allyl ether ⁵c was obtained by silica-gel column chromatography (hexane/EtOAc = 85/15) as a colorless oil (quant).

¹H NMR (400 MHz, CDCl₃, δ)
3.32 (s, 6H), 3.58 (s, 3H), 3.81 (ddd, 2H, J₁ = 5.6, J₂ = 2.0, J₃ = 1.2 Hz), 3.90 (s, 3H), 4.17 (s, 2H), 5.02 (d, 2H, J = 6.8 Hz), 5.05 (d, 2H, J = 6.8 Hz), 5.07 (ddt, 1H, J₁ = 10.4, J₂ = 1.6, J₃ = 1.2 Hz), 5.16 (ddt, 1H, J₁ = 17.2, J₂ = 1.6, J₃ = 2.0 Hz), 5.77 (ddt, 1H, J₁ = 17.2, J₂ = 10.4, J₃ = 5.6 Hz), 6.91 (d, 2H, J = 8.0 Hz),
6.96 (d, 1H, J = 8.4 Hz), 7.26 (d, 1H, J = 8.4 Hz), 7.27 (t, 1H, J = 8.0 Hz);

$^{13}$C NMR (100 MHz, CDCl$_3$, δ)
55.6, 55.8, 60.1, 69.6, 70.9, 94.6, 108.4, 111.2, 115.8, 116.4, 123.0, 128.3, 129.1, 130.5, 134.9, 146.8, 151.8, 155.7;

IR (neat)
3070, 2920, 2850, 1580, 1460, 1240, 1150, 1090, 1040, 920, 810, 780, 720 cm$^{-1}$;

Anal. calcd for C$_{22}$H$_{28}$O$_7$: C, 65.33; H, 6.98. Found: C, 65.28; H, 6.76.

A typical procedure of the removal of the MOM groups and the subsequent acetylation is described for the synthesis of $\mathbf{1a}$: To a solution of $\mathbf{5a}$ (4.10 g, 10.1 mmol) in MeOH (80 mL) was added 2 M HCl (51 mL) at 0 °C. After stirring for 24 h at room temperature, water was added and the mixture was extracted with EtOAc. The combined organic extracts were washed with sat. aq. NaHCO$_3$, brine, and dried over Na$_2$SO$_4$, filtered and concentrated in vacuo. The obtained crude material (3.19 g) was dissolved in pyridine (45 mL), to which was added acetic anhydride (7.6 mL, 81 mmol) at 0 °C. After stirring for 1.5 h at room temperature, the reaction was stopped by adding ice-water, and the mixture was extracted with EtOAc. The combined organic extracts were washed with 2 M HCl, brine, sat. aq. NaHCO$_3$, brine, and dried over Na$_2$SO$_4$, filtered and concentrated in vacuo. The residue was purified by silica-gel column chromatography (hexane/acetone = 3/2) to give $\mathbf{1a}$ (4.04 g, 99%) as white solids. Recrystallization from Et$_2$O gave $\mathbf{1a}$ as colorless prisms.

M.p. 79.5–81.0 °C;

$^1$H NMR (400 MHz, CDCl$_3$, δ)
1.92 (s, 6H), 3.64 (s, 3H), 3.80 (ddd, 2H, J$_1$ = 5.8, J$_2$ = 1.4, J$_3$ = 1.2 Hz), 3.84 (s, 3H), 4.19 (s, 2H), 5.05 (ddt, 1H, J$_1$ = 10.4, J$_2$ = 1.6, J$_3$ = 1.4 Hz), 5.15 (ddt, 1H, J$_1$ = 17.4, J$_2$ = 1.6, J$_3$ = 1.2 Hz), 5.78 (ddt, 1H J$_1$ = 17.4, J$_2$ = 10.4, J$_3$ = 5.8 Hz), 6.86 (d, 1H, J = 9.1 Hz), 6.90 (d, 1H, J = 9.1 Hz), 7.13 (d, 2H, J = 8.3 Hz), 7.40 (t, 1H, J =8.3 Hz);

$^{13}$C NMR (100 MHz, CDCl$_3$, δ)
20.8, 56.4, 56.5, 64.5, 71.6, 111.1, 111.5, 116.5, 119.7, 123.0, 123.4, 127.2, 128.1, 135.2, 149.4, 151.2, 152.7, 168.4;

IR (KBr)
3085, 3020, 2927, 2833, 1760, 1255, 1197, 1078, 1032, 912, 796 cm$^{-1}$;

Diacetate 1b was obtained by silica-gel column chromatography (hexane/acetone = 10/1) as white solids (quant). Recrystallization from Et2O gave 1b as colorless prisms.

M.p. 78.5–80.0 °C;

$^1$H NMR (400 MHz, CDCl$_3$, δ)
1.92 (s, 6H), 3.68 (s, 3H), 3.86 (s, 3H), 3.91 (ddd, 2H, $J_1 = 5.6, J_2 = 1.6, J_3 = 1.4$ Hz), 4.22 (s, 2H), 5.13 (ddt, 1H, $J_1 = 10.5, J_2 = 1.6, J_3 = 1.4$ Hz), 5.26 (ddt, 1H, $J_1 = 17.4, J_2 = 1.6$ Hz), 5.90 (ddt, 1H, $J_1 = 17.4, J_2 = 10.5, J_3 = 5.6$ Hz), 6.42 (d, 1H, $J = 2.4$ Hz), 6.78 (d, 1H, $J = 2.4$ Hz), 7.07 (d, 2H, $J = 8.4$ Hz), 7.39 (t, 1H, $J = 8.4$ Hz);

$^{13}$C NMR (100 MHz, CDCl$_3$, δ)
20.5, 55.3, 55.9, 69.2, 71.3, 97.5, 102.8, 111.7, 116.5, 119.5, 123.3, 128.5, 134.9, 140.3, 149.9, 158.1, 160.8, 168.8;

IR (KBr)
3008, 2969, 2938, 2844, 1765, 1602, 1456, 1188, 1070, 1027, 863, 825, 786, 764 cm$^{-1}$;

Anal. calcd for C$_{22}$H$_{24}$O$_7$: C, 65.99; H, 6.04. Found: C, 66.23; H, 6.27.

Diacetate 1c was obtained by silica-gel column chromatography (hexane/acetone = 3/2) as a colorless oil (quant).

$^1$H NMR (400 MHz, CDCl$_3$, δ)
1.94 (s, 6H), 3.60 (s, 3H), 3.85 (ddd, 2H, $J_1 = 5.6, J_2 = 1.4, J_3 = 1.2$ Hz), 3.88 (s, 3H), 4.15 (s, 2H), 5.11 (ddt, 2H, $J_1 = 10.4, J_2 = 1.4, J_3 = 1.2$ Hz), 5.22 (ddt, 1H, $J_1 = 17.4, J_2 = 1.4, J_3 = 1.6$ Hz), 5.86 (ddt, 1H, $J_1 = 17.4, J_2 = 10.4, J_3 = 5.6$ Hz), 6.97 (d, 1H, $J = 8.4$ Hz), 7.12 (d, 2H, $J = 8.2$ Hz), 7.25 (d, 1H, $J = 8.4$ Hz), 7.42 (t, 1H, $J = 8.2$ Hz);

$^{13}$C NMR (100 MHz, CDCl$_3$, δ)
20.7, 55.8, 60.4, 69.0, 71.2, 112.5, 116.4, 119.9, 122.8, 123.0, 125.0, 128.4, 130.7, 134.8, 146.5, 149.2, 151.4, 168.4;

IR (neat)
2925, 2825, 1770, 1480, 1450, 1410, 1360, 1270, 1250, 1190, 1120, 1130 cm$^{-1}$;

2. Enantioselective desymmetrization by enzymatic hydrolysis (Schemes 3 and Figure 1).

![Scheme 3]

**Scheme 3**

A typical procedure of the enzyme-catalyzed hydrolysis is described for the reaction of 1a with PPL: Diacetate 1a (1.00 g, 2.50 mmol) was dissolved in 40 mL of PhH, to which was added 60 mL of pH 7 phosphate buffer (0.1 M) and PPL (200 mg). The mixture was stirred at 35 °C for 9 h, and then 150 mg of the enzyme was again added. After 11 h, the reaction mixture was diluted with EtOAc and filtered through a Celite pad to remove the enzyme. The mixture was extracted with EtOAc, and the combined organic extracts were washed with brine, dried over Na$_2$SO$_4$, filtered and concentrated in vacuo. The
residue was purified by silica-gel column chromatography (hexane/acetone = 9/1) to give (+)-6a (895 mg, quant, >99% e.e.) as a colorless oil.

\[(S)-(+)\text{-}6a\]: \(\left[\alpha\right]_D^{19} +83\) (c 1.0, CHCl₃);

\[(R)-(–)\text{-}6a\]: \(\left[\alpha\right]_D^{20} -83\) (c 0.99, CHCl₃);

\(^1\)H NMR (400 MHz, CDCl₃, \(\delta\))

1.82 (s, 3H), 3.65 (s, 3H), 3.85 (s, 3H), 3.95 (d, 1H, \(J = 9.0\) Hz), 3.97 (dd, 2H, \(J_1 = 6.0, J_2 = 1.5, J_3 = 1.1\) Hz), 4.72 (d, 1H, \(J = 9.0\) Hz), 5.16 (ddt, 1H, \(J_1 = 10.5, J_2 = 1.6, J_3 = 1.1\) Hz), 5.24 (ddt, 1H, \(J_1 = 17.4, J_2 = 1.6, J_3 = 1.5\) Hz), 5.86 (ddt, 1H, \(J_1 = 17.4, J_2 = 10.5, J_3 = 6.0\) Hz), 6.77 (dd, 1H, \(J_1 = 8.1, J_2 = 1.2\) Hz), 6.81 (s, 1H), 6.94 (s, 2H), 6.99 (dd, 1H, \(J_1 = 1.2, J_2 = 8.4\) Hz), 7.30 (dd, 1H, \(J_1 = 8.1, J_2 = 8.4\) Hz);

\(^{13}\)C NMR (100 MHz, CDCl₃, \(\delta\))

20.5, 56.3, 56.7, 64.7, 72.2, 111.8, 112.5, 114.5, 116.1, 117.9, 119.1, 123.9, 126.9, 129.1, 133.8, 149.4, 151.6, 152.3, 155.2, 168.8;

IR (neat) 3300, 2970, 2820, 1750, 1580, 1460, 1250, 1190, 1080, 1050, 890, 860, 710 cm\(^{-1}\)


HPLC [CHIRALPAK® IA (Daicel), 0.46 x 25 cm, hexane/2-propanol = 9/1, 1.0 mL/min, 20 °C, 254 nm] \(t_R: 9.2\) min for (–)-6a, 14.5 min for (+)-6a.

\[(S)-(+)\text{-}6b\]: \(\left[\alpha\right]_D^{19} +56\) (c 1.9, CHCl₃);

\[(R)-(–)\text{-}6b\]: \(\left[\alpha\right]_D^{25} -58\) (c 1.2, CHCl₃);

\(^1\)H NMR (400 MHz, CDCl₃, \(\delta\))

1.85 (s, 3H), 3.69 (s, 3H), 3.86 (s, 3H), 3.93 (d, 2H, \(J_1 = 5.9, J_2 = 1.7, J_3 = 1.2\) Hz), 4.18 (d, 1H, \(J = 11.2\) Hz), 4.22 (d, 1H, \(J = 11.2\) Hz), 5.15 (ddt, 1H, \(J_1 = 10.3, J_2 = 1.5, J_3 = 1.2\) Hz), 5.23 (ddt, 1H, \(J_1 = 17.2, J_2 = 1.5, J_3 = 1.7\) Hz), 5.86 (ddt, 1H, \(J_1 = 17.2, J_2 = 10.3, J_3 = 5.9\) Hz), 5.91 (s, 1H), 6.52 (d, 1H, \(J = 2.4\) Hz), 6.71 (d, 1H, \(J = 2.4\) Hz), 6.74 (dd, 1H, \(J_1 = 1.0, J_2 = 8.0\) Hz), 6.93 (dd, 1H, \(J_1 = 1.0, J_2 = 8.2\) Hz), 7.28 (dd, 1H, \(J_1 = 8.0, J_2 = 8.2\) Hz);
$^{13}$C NMR (100 MHz, CDCl$_3$, $\delta$
20.5, 55.4, 56.0, 70.6, 71.9, 98.6, 105.4, 111.9, 114.3, 114.4, 117.4, 117.6, 129.1, 134.0, 140.0, 149.7, 155.0, 158.8, 161.1, 168.8;
IR (neat)
3261, 2954, 2931, 1760, 1457, 1207, 1122, 1035, 811, 730 cm$^{-1}$;
Anal. calcd for C$_{20}$H$_{22}$O$_6$: C, 67.03; H, 6.19. Found: C, 67.25; H, 6.27.
HPLC [CHIRALPAK$^\text{®}$ IA (Daicel), 0.46 x 25 cm, hexane/2-propanol = 9/1, 1.0 mL/min, 20 °C, 254 nm] $t_R$: 12.8 min for (–)$^6$b, 14.8 min for (+)$^6$b.

M.p. 121-122 °C (colorless needles from Et$_2$O);
(S)-(+)6c: $[\alpha]_D^{25} +67$ (c 1.1, CHCl$_3$);
(R)-(–)6c: $[\alpha]_D^{24} –67$ (c 0.88, CHCl$_3$);
$^1$H NMR (400 MHz, CDCl$_3$, $\delta$
1.84 (s, 3H), 3.56 (s, 3H), 3.90 (s, 3H), 3.92 (ddd, 2H, $J_1 = 5.6, J_2 = 1.5, J_3 = 1.2$ Hz), 4.16 (d, 1H, $J = 10.0$ Hz), 4.22 (d, 1H, $J = 10.0$ Hz), 5.16 (ddt, 1H, $J_1 = 10.4, J_2 = 1.7, J_3 = 1.2$ Hz), 5.23 (ddt, 1H, $J_1 = 17.2, J_2 = 1.7, J_3 = 1.2$ Hz), 5.84 (ddt, 1H, $J_1 = 17.5, J_2 = 10.4, J_3 = 5.6$ Hz), 6.53 (s, 1H), 6.79 (d, 1H, $J = 8.4$ Hz), 6.98 (d, 2H, $J = 8.0$ Hz), 7.19 (d, 1H, $J = 8.4$ Hz), 7.32 (t, 1H, $J = 8.0$ Hz);
$^{13}$C NMR (100 MHz, CDCl$_3$, $\delta$
20.5, 55.9, 60.6, 71.0, 71.7, 112.5, 114.7, 115.67 117.8, 118.7, 125.8, 126.8, 129.3, 130.0, 133.7, 147.4, 149.2, 152.8, 155.0, 168.9;
IR (KBr)
3261, 2954, 2931, 1760, 1457, 1207, 1122, 1035, 811, 730 cm$^{-1}$;
Anal. calcd for C$_{20}$H$_{22}$O$_6$: C, 67.03; H, 6.19. Found: C, 66.86; H, 6.27.
HPLC [CHIRALPAK$^\text{®}$ IA (Daicel), 0.46 x 25 cm, hexane/2-propanol = 9/1, 1.0 mL/min, 20 °C, 254 nm] $t_R$: 9.7 min for (–)$^6$c, 12.7 min for (+)$^6$c.
3. Determination of the absolute configurations of 6a–c.

**Determination of the absolute configurations of 6a and 6b.**

Mono-acetates (+)-6a and (–)-6b were derivatized with (–)-camphanic chloride [DMAP, pyridine, room temperature] to give crystalline esters 16a and 16b, respectively, whose stereostructures were determined by X-ray crystallography.

To a solution of (+)-6a (80.0 mg, 223 µmol) in pyridine (0.5 mL) was added (–)-camphanic chloride (96.7 mg, 446 µmol) and 4-dimethylaminopyridine (6.0 mg, 49.1 µmol) at 0 °C. After stirring for 1.0 h at room temperature, the reaction was stopped by adding ice-water, and the mixture was extracted with EtOAc. The combined organic extracts were washed with 2 M HCl, brine, and sat. aq. NaHCO₃, and dried over Na₂SO₄, filtered and concentrated in vacuo. The residue was purified by silica-gel column chromatography (hexane/acetone = 3/2) to give 16a (119 mg, 99%) as white solid. Recrystallization from EtOH gave 16a as colorless prisms.

Compound 16b was synthesized from 6b in the similar manner (88%).

**16b**

M.p. 113.0–114.5 °C; 
[α]D₁₂ = −6.0 (c 1.24, CHCl₃); 
¹H NMR (400 MHz, CDCl₃, δ)

0.73 (s, 3H), 0.77 (s, 3H), 1.03 (s, 3H), 1.54–1.80 (m, 3H), 1.95 (s, 3H), 2.05–2.11 (m, 1H), 3.64 (s, 3H), 3.76 (ddd, 2H, J₁ = 5.6, J₂ = 1.2, J₃ = 0.8 Hz), 3.82 (s, 3H), 4.12 (d, 1H, J = 10.2 Hz), 4.22 (d, 1H, J = 10.2 Hz).
Hz), 5.03 (ddt, 1H, J₁ = 10.3, J₂ = 1.5, J₃ = 0.8 Hz), 5.11 (ddt, 1H, J₁ = 17.1, J₂ = 1.5, J₃ = 1.2 Hz), 5.71 (ddt, 1H, J₁ = 17.1, J₂ = 10.3, J₃ = 5.6 Hz), 6.84 (d, 1H, J = 8.8 Hz), 6.89 (d, 1H, J = 8.8 Hz), 7.12 (d, 1H, J = 8.0 Hz), 7.20 (d, 1H, J = 8.4 Hz), 7.44 (dd, 1H, J₁ = 8.0, J₂ = 8.4 Hz);

13C NMR (100 MHz, CDCl₃, δ)
9.7, 16.2, 16.4, 20.9, 28.9, 30.4, 54.0, 54.7, 56.3, 56.8, 64.1, 71.7, 90.8, 100.1, 111.1, 112.1, 116.6, 119.1, 120.5, 123.1, 127.6, 128.4, 135.1, 148.8, 149.5, 151.3, 152.7, 164.7, 168.3, 177.6;

IR (ATR) 2970, 2940, 2830, 1790, 1770, 1450, 1260, 1200, 1100, 1050, 930, 870, 810, 790, 720 cm⁻¹;

Crystallographic data reported here have been deposited with Cambridge Crystallographic Data Centre as supplementary publication no. CCDC-711867 (16a) and no. CCDC-711955 (16b).
The absolute configuration of (+)-6c was determined by chemical correlation with (+)-6a as shown below.

\[
\begin{align*}
\text{(S)-(+)6a} & \quad (>99\% \text{ ee, by PPL}) \\
\text{(+)6c} & \quad (>99\% \text{ e.e.}, \text{by PLE}) \\
n & \quad f,g \quad 65\% \\
v & \quad 95\% \\
w & \quad 98\% \\
x & \quad h \quad 92\% \\
y & \quad i \quad 96\% \\
z & \quad j \quad 91\% \\
{19} & \quad (>99\% \text{ ee}) \\
\end{align*}
\]

\[
\begin{align*}
a & \quad \text{MOMCl, Pr}_2\text{NEt, CH}_2\text{Cl}_2, 0 \degree \text{C} \rightarrow 25 \degree \text{C}} \\
b & \quad 1 \text{ M NaOH aq., MeOH, 0 \degree \text{C}} \\
c & \quad (\text{MeO})_2\text{SO}_2, \text{NaH, DMF, 25 \degree \text{C}} \\
d & \quad 10 \text{ mol\% NiCl}_2(\text{dppp}), \text{DIBAL, Et}_2\text{O, } -20 \degree \text{C} \rightarrow 25 \degree \text{C}} \\
e & \quad \text{IBX, DMSO, 25 \degree \text{C}} \\
f & \quad \text{MMPP, MeOH, 0 \degree \text{C} \rightarrow 25 \degree \text{C}} \\
g & \quad 1 \text{ M NaOH aq., MeOH, 25 \degree \text{C}} \\
h & \quad (\text{MeO})_2\text{SO}_2, \text{NaH, DMF, 25 \degree \text{C}}. \quad \text{[MMPP: Magnesium monoperoxyphthalate hexahydrate]}
\end{align*}
\]
To a solution of aldehyde 11 (see scheme 4) (45.5 mg, 126 µmol) in MeOH (3.0 mL) was added MMPP (80%, 156 mg, 252 µmol) at −15 °C. After stirring for 4.5 h at room temperature, MMPP (80%, 78.0 mg, 126 µmol) was again added, and stirring was continued for 4 h. The reaction was stopped by adding 1 M NaOH, and the products were extracted with EtOAc. The combined organic extracts were washed with 2 M HCl, brine, sat. aq. NaHCO₃, brine, and dried over Na₂SO₄, filtered and concentrated in vacuo. The residue was purified by PTLC (hexane/acetone = 3/2) to give phenol iv (28.6 mg, 65%) as a colorless oil. [α]D²⁵ −2.2 (c 0.88, CHCl₃);

¹H NMR (300 MHz, CDCl₃, δ)
3.33 (s, 3H), 3.67 (s, 3H), 3.74 (s, 3H), 3.87 (s, 3H), 5.04 (s, 2H), 5.53 (s, 1H), 6.45 (d, 1H, J = 8.4 Hz), 6.71 (d, 1H, J = 8.4 Hz), 6.82 (d, 1H, J = 8.4 Hz), 6.87 (d, 1H, J = 8.4 Hz), 7.30 (dd, 1H, J₁ = J₂ = 8.4 Hz);
³C NMR (100 MHz, CDCl₃, δ)
55.7, 56.2, 56.3, 94.9, 101.5, 105.4, 108.4, 109.9, 111.0, 112.5, 129.3, 141.3, 144.0, 152.4, 156.0, 158.3;
IR (neat)
3475, 2925, 2825, 1590, 1470, 1460, 1240, 1070, 1010 cm⁻¹;
Anal. calcd for C₁₇H₂₀O₆: C, 63.74; H, 6.29. Found: C, 63.50; H, 6.41.

A mixture of phenol iv (38.1 mg, 119 µmol) and NaH (55% dispersion in mineral oil, 10 mg, 0.23 mmol) in DMF (0.5 mL) was stirred at room temperature for 1 h, to which was added (MeO)₂SO₂ (20 µL, 180 µmol). After 30 min, the reaction was quenched by adding Et₂NH, and the mixture was diluted with water, and extracted with EtOAc. The combined organic extracts were washed with 2 M HCl, brine, sat. aq. NaHCO₃, brine, and dried over Na₂SO₄, filtered and concentrated in vacuo. The residue was purified by PTLC (hexane/acetone = 3/2) to give methyl ether 19 (36.5 mg, 92%) as a colorless oil. [α]D²³ −17 (c 1.7, CHCl₃);

¹H NMR (400 MHz, CDCl₃, δ)
3.31 (s, 3H), 3.59 (s, 3H), 3.66 (s, 3H), 3.73 (s, 3H), 3.86 (s, 3H), 5.02 (d, 1H, J = 6.8 Hz), 5.05 (d, 1H, J = 6.8 Hz), 6.66 (d, 1H, J = 8.4 Hz), 6.69 (d, 1H, J = 8.4 Hz), 6.82 (d, 1H, J = 9.0 Hz), 6.89 (d, 1H, J = 9.0 Hz), 7.28 (dd, 1H, J₁ = J₂ = 8.4 Hz);
³C NMR (100 MHz, CDCl₃, δ)
55.7, 55.9, 56.2, 56.4, 60.3, 94.7, 105.0, 105.9, 108.0, 111.7, 113.6, 118.9, 128.8, 147.0, 148.0, 152.1,
155.8, 158.1;
IR (neat) 2975, 2925, 2880, 2820, 1590, 1470, 1460, 1430, 1410, 1260, 1240, 1090, 1065 cm⁻¹;
Anal. calcd for C₁₈H₂₂O₆: C, 64.66; H, 6.63. Found: C, 64.87; H, 6.47;
HPLC [CHIRALPAK® AD-H (Daicel), 0.46 x 25 cm, hexane:2-propanol = 90:10, 1.0 mL/min, 20 °C, 264 nm] tᵣ: 7.88 min ((+)-form: 7.27 min).

![Diagram](image1)

To a solution of (+)-6c (291 mg, 811 µmol) in CH₂Cl₂ (4.8 mL) was added MOMCl (0.12 mL, 1.6 mmol) and iPr₂NEt (0.29 mL, 1.6 mmol) at –20 °C. The reaction mixture was stirred at –20 °C for 5.4 h, to which was added MOMCl (0.24 mL, 3.2 mmol) and iPr₂NEt (0.44 mL, 2.4 mmol). After 8 h at room temperature, the reaction mixture was poured into sat. aq. NaHCO₃, and extracted with EtOAc. The combined organic extracts were washed with brine, and dried over Na₂SO₄, filtered and concentrated in vacuo. The residue was purified by silica-gel column chromatography (hexane/acetone = 9/1) to give MOM ether v (309 mg, 95%) as a colorless oil.

[α]₂⁰⁺⁺ +30.9 (c 1.00, CHCl₃);
¹H NMR (300 MHz, CDCl₃, δ)
1.91 (s, 3H), 3.33 (s, 3H), 3.59 (s, 3H), 3.84 (ddd, 2H, J₁ = 5.7, J₂ = J₃ = 1.5 Hz), 3.89 (s, 3H), 4.14 (d, 1H, J = 12.4 Hz), 4.20 (d, 1H, 12.4 Hz), 5.05 (s, 2H), 5.10 (ddt, 1H, J₁ = 10.6, J₂ = J₃ = 1.5 Hz), 5.09 (ddt, 1H, J₁ = 17.4, J₂ = J₃ = 1.5 Hz), 5.82 (ddt, 1H, J₁ = 17.4, J₂ = 10.6, J₃ = 5.7 Hz), 6.89 (dd, 1H, J₁ = 8.3, J₂ = 0.9 Hz), 6.96 (d, 1H, J = 8.6 Hz), 7.13 (dd, 1H, J₁ = 8.4, J₂ = 0.9 Hz), 7.26 (d, 1H, J = 8.6 Hz), 7.34 (dd, 1H, J₁ = 8.3, J₂ = 8.4 Hz);
¹³C NMR (75 MHz, CDCl₃, δ)
20.7, 55.8, 56.0, 60.4, 69.4, 71.9, 94.6, 112.1, 112.1, 116.1, 116.5, 119.5, 122.9, 129.5, 129.0, 130.9, 135.0, 146.8, 149.3, 151.7, 156.0, 168.8;
IR (neat)
2925, 2825, 1760, 1640, 1410, 1360, 1250, 1200, 1030, 910, 800 cm⁻¹;
HPLC [CHIRALPAK® IA (Daicel), 0.46 x 25 cm, hexane:2-propanol = 90:10, 1.0 mL/min, 20 °C, 264 nm] tᵣ: 11.6 min ((–)-form: 14.8 min).

![Diagram](image2)

To a solution of MOM ether v (278 mg, 691 µmol) in MeOH (8.0 mL) was added 1 M NaOH aq. (3.5 mL,
3.5 mmol) at 0 °C. After stirring at room temperature for 20 min, the reaction was quenched by adding ice-water, and the mixture was extracted with EtOAc. The combined organic extracts were washed with 2 M HCl, brine, and dried over Na₂SO₄, filtered and concentrated in vacuo. The residue was purified by silica-gel column chromatography (hexane/acetone = 9/1) to give phenol \( \text{vi} \) (243 mg, 98%) as a colorless oil.

\[
\alpha_{D}^{25} = -2.7 \ (c \ 1.09, \text{CHCl}_3)
\]

\(^1\)H NMR (400 MHz, CDCl₃, \( \delta \))

3.30 (s, 3H), 3.55 (s, 3H), 3.86 (ddd, 2H, \( J_1 = 4.5, J_2 = J_3 = 1.3 \) Hz), 3.91 (s, 3H), 4.10 (d, 1H, \( J = 10.8 \) Hz), 4.23 (d, 1H, \( J = 10.8 \) Hz), 4.99 (d, 1H, \( J = 6.4 \) Hz), 5.05 (d, 1H, \( J = 6.4 \) Hz), 5.12 (ddt, 1H, \( J_1 = 10.4, J_2 = J_3 = 1.3 \) Hz), 5.19 (ddt, 1H, \( J_1 = 17.2, J_2 = J_3 = 1.3 \) Hz), 5.68 (s, 1H), 5.80 (ddt, 1H, \( J_1 = 17.2, J_2 = 10.4, J_3 = 4.5 \) Hz), 6.74 (d, 1H, \( J = 8.4 \) Hz), 6.82 (d, 1H, \( J = 8.4 \) Hz), 6.99 (d, 1H, \( J = 8.4 \) Hz), 7.24 (dd, 1H, \( J_1 = J_2 = 8.4 \) Hz), 7.25 (d, 1H, \( J = 8.4 \) Hz);

\(^13\)C NMR (100 MHz, CDCl₃, \( \delta \))

55.8, 55.9, 60.5, 70.6, 71.6, 94.8, 107.2, 111.0, 112.1, 114.3, 117.4, 125.2, 127.5, 129.5, 130.4, 134.1, 147.5, 152.8, 154.5, 155.5;

IR (neat) 3350, 2925, 2825, 1600, 1570, 1480, 1450, 1300, 1270, 1250, 1150, 1080, 1130, 910 cm⁻¹;


A mixture of phenol \( \text{vi} \) (207 mg, 573 \( \mu \)mol) and NaH (55% dispersion in mineral oil, 31 mg, 0.71 mmol) in DMF (2.5 mL) was stirred at room temperature for 1 h, to which was added (MeO)₂SO₂ (108 \( \mu \)L, 1.15 mmol) at 0 °C. After stirring at room temperature for 1 h, the reaction was stopped by adding Et₂NH, and the mixture was diluted with water, and extracted with EtOAc. The combined organic extracts were washed with 2 M HCl, brine, sat. aq. NaHCO₃, brine, and dried over Na₂SO₄, filtered and concentrated in vacuo. The residue was purified by silica-gel column chromatography (hexane/Acetone = 9/1) to give methyl ether \( \text{vii} \) (206 mg, 96%) as a colorless oil.

\[
\alpha_{D}^{26} = +6.0 \ (c \ 0.98, \text{CHCl}_3)
\]

\(^1\)H NMR (300 MHz, CDCl₃, \( \delta \))

3.31 (s, 3H), 3.57 (s, 3H), 3.70 (s, 3H), 3.80 (ddd, 2H, \( J_1 = 5.5, J_2 = 1.6, J_3 = 1.3 \) Hz), 3.89 (s, 3H), 4.14 (s, 2H), 5.00 (d, 1H, \( J = 6.8 \) Hz), 5.04 (d, 1H, \( J = 6.8 \) Hz), 5.06 (ddt, 1H, \( J_1 = 10.4, J_2 = 1.6, J_3 = 1.3 \) Hz), 5.15 (ddt, 1H, \( J_1 = 17.6, J_2 = J_3 = 1.6 \) Hz), 5.77 (ddt, 1H, \( J_1 = 17.6, J_2 = 10.4, J_3 = 5.5 \) Hz), 6.66 (d, 1H, \( J = 8.4 \) Hz), 6.86 (d, 1H, \( J = 8.4 \) Hz), 6.95 (d, 1H, \( J = 8.5 \) Hz), 7.25 (d, 1H, \( J = 8.5 \) Hz), 7.29 (dd, 1H, \( J_1 = J_2 = 8.4 \) Hz);

\(^13\)C NMR (75 MHz, CDCl₃, \( \delta \))

56.4, 56.5, 56.6, 61.0, 70.4, 71.6, 95.5, 105.4, 108.4, 112.1, 115.7, 117.1, 123.9, 129.2, 129.9, 131.4,
To a solution of biphenyl vii (228 mg, 610 µmol) in Et₂O (2.3 mL) was added NiCl₂(dppp) (32.7 mg, 60.3 µmol) and DIBAL (0.63 M solution in CH₂Cl₂, 1.45 mL, 0.91 mmol) at –78 °C. After 1 h, the mixture was diluted with Et₂O, quenched by adding water, and dried directly with MgSO₄, filtered and concentrated in vacuo. The residue was purified by silica-gel column chromatography (hexane/EtOAc = 19/1) and PTLC (CHCl₃/EtOAc = 9/1) to give alcohol viii (197 mg, 97%) as a colorless oil.

\[ \left[ \alpha \right]_{D}^{26} +12 \ (c \ 1.1, \ \text{CHCl}_3) \]

\(^1\)H NMR (300MHz, CDCl₃, δ)
2.17 (t, 1H, J = 6.1 Hz), 3.26 (s, 3H), 3.57 (s, 3H), 3.73 (s, 3H), 3.90 (s, 3H), 4.23 (d, 2H, J = 6.1 Hz), 5.00 (d, 1H, J = 6.8 Hz), 5.06 (d, 1H, J = 6.8 Hz), 6.72 (d, 1H, J = 8.4 Hz), 6.88 (d, 1H, J = 8.4 Hz), 6.97 (d, 1H, J = 8.4 Hz), 7.25 (d, 1H, J = 8.4 Hz), 7.32 (dd, 1H, J₁ = J₂ = 8.4 Hz);

\(^{13}\)C NMR (100MHz, CDCl₃, δ)
55.7, 55.8, 56.0, 60.2, 63.8, 95.2, 105.1, 108.6, 111.7, 115.3, 124.5, 128.3, 129.4, 132.9, 146.8, 152.2, 155.6, 157.6;

IR (neat)
3450, 2925, 2825, 1580, 1475, 1460, 1265, 1240, 1095, 1060, 1020, 915 cm⁻¹;

Anal. calcd for C₁₈H₂₂O₆: C, 64.66; H, 6.63. Found: C, 64.45; H, 6.82.

To a solution of alcohol viii (14.7 mg, 44.0 µmol) in DMSO (0.2 mL) was added IBX (18.2 mg, 65.0 µmol) at 15 °C. After stirring for 3.5 h at room temperature, the reaction was stopped by adding 10% aq. Na₂S₂O₄, and extracted with EtOAc. The combined organic extracts were washed with sat. aq. NaHCO₃, brine, and dried over Na₂SO₄, filtered and concentrated in vacuo. The residue was purified by PTLC (hexane/Acetone = 3/2) to give aldehyde 17 (13.3 mg, 91%) as white solids.

M.p. 74.8–76.7°C;
\[ \left[ \alpha \right]_{D}^{26} +26 \ (c \ 0.98, \ \text{CHCl}_3) \]

\(^1\)H NMR (300 MHz, CDCl₃, δ)
3.28 (s, 3H), 3.58 (s, 3H), 3.71 (s, 3H), 3.97 (s, 3H), 5.01 (d, 1H, J = 7.0 Hz), 5.08 (d, 1H, J = 7.0 Hz),
6.69 (d, 1H, J = 8.4 Hz), 6.88 (dd, 1H, J₁ = 8.6, J₂ = 0.7 Hz), 7.04 (d, 1H, J = 8.8 Hz), 7.35 (dd, 1H, J₁ = 8.4, J₂ = 8.8 Hz), 7.83 (d, 1H, J = 8.6 Hz), 9.53 (d, 1H, J = 0.7 Hz);

13C NMR (100 MHz, CDCl₃, δ)
55.7, 55.7, 55.8, 60.2, 94.4, 104.3, 107.2, 111.1, 111.6, 123.8, 128.0, 129.9, 133.1, 146.6, 155.6, 157.4, 157.9, 191.2;

IR (KBr)
2954. 2844, 2754, 1682, 1598, 1585, 1473, 1282, 1261, 1247, 1103, 1074, 1003, 816, 793 cm⁻¹;


To a solution of aldehyde 17 (22.7 mg, 68.3 µmol) in MeOH (0.4 mL) was added MMPP (80%, 88.2 mg, 143 µmol) at –15 °C. After stirring for 1.8 h at room temperature, the reaction was stopped by adding 1 M NaOH, and extracted with EtOAc. The combined organic extracts were washed with 2 M HCl, brine, sat. aq. NaHCO₃, and dried over Na₂SO₄, filtered and concentrated in vacuo. The residue was purified by PTLC (CHCl₃/acetone = 9/1) to give phenol ix (19.1 mg, 87%) as white solids.

[α]D²⁶ +15 (c 1.1, CHCl₃);

1H NMR (300 MHz, CDCl₃, δ)
3.33 (s, 3H), 3.59 (s, 3H), 3.76 (s, 3H), 3.85 (s, 3H), 4.57 (s, 1H), 5.04 (d, 1H, J = 6.8 Hz), 5.12 (d, 1H, J = 6.8 Hz), 6.72 (d, 1H, J = 9.0 Hz), 6.72 (d, 1H, J = 8.4 Hz), 6.88 (d, 1H, J = 9.0 Hz), 6.90 (d, 1H, J = 8.4 Hz), 7.36 (dd, 1H, J₁ = J₂ = 8.4 Hz);

13C NMR (100 MHz, CDCl₃, δ)
56.0, 56.1, 56.4, 60.4, 94.8, 105.1, 108.2, 109.7, 110.9, 113.1, 116.3, 130.3, 146.5, 147.7, 147.7, 156.2, 158.4;

IR (KBr)
3354, 2944, 2839, 1581, 1468, 1265, 1236, 1147, 1100, 1053, 1012, 999, 733 cm⁻¹;

Anal. calcd for C₁₇H₂₀O₆: C, 63.74; H, 6.29. Found: C, 63.82; H, 6.59.

A mixture of phenol ix (7.1 mg, 22.0 µmol) and NaH (55% dispersion in mineral oil, 4 mg, 0.09 mmol) in DMF (0.1 mL) was stirred at room temperature for 2.4 h, to which was added (MeO)₂SO₂ (5.0 µL, 53 µmol). After 1 h, the reaction was stopped by adding Et₂NH, and the mixture was diluted with water and extracted with EtOAc. The combined organic extracts were washed with 2 M HCl, brine, sat. aq.
NaHCO₃, and dried over Na₂SO₄, filtered and concentrated in vacuo. The residue was purified by PTLC (hexane/EtOAc = 9/1) to give biphenyl 18 (6.3 mg, 85%) as a colorless oil. ^1H and ^13C NMR data were coincident with those of biphenyl 19.

\[ \alpha \] D₂₄ +16 (c 1.1, CHCl₃);

HPLC [CHIRALPAK® AD-H (Daicel), 0.46 x 25 cm, hexane:2-propanol = 90:10, 1.0 mL/min, 20 °C, 264 nm] \( t_R \): 7.27 min ((–)-form: 7.88 min).
3. Transformation of (S)-6 (Scheme 4).

(S)-(+)-6a (>99% e.e.)

RO

OR'

O

MeO

OMe

a or b

1 for 8

MeO

OMe

CHO

OAc

H

OTBS

OAc

MeO

OMe

X

g or h

i, j

MeO

OMe

CHO

OAc

H

OTBS

OAc

MeO

OMe

X

To a solution of (S)-6a (3.41 g, 9.51 mmol) in CH2Cl2 (5.0 mL) was added TBDMSCl (2.87 g, 19.0 mmol) and imidazole (1.94 g, 28.6 mmol) at 0 °C. The reaction was stirred at room temperature for 4.5 h, and quenched by adding sat. aq. NaHCO3. The products were extracted with CH2Cl2, and the combined organic extracts were washed with brine, dried over Na2SO4, filtered and concentrated in vacuo. The residue was purified by silica-gel column chromatography (hexane/EtOAc = 4/1) to give TBS ether 8 (4.26 g, 95%) as a colorless oil.

[α]D24 +18 (c 1.4, CHCl3);

ΔH NMR (300 MHz, CDCl3, δ)

δ 0.09 (s, 3H), 0.07 (s, 3H), 0.66 (s, 9H), 1.39 (s, 3H), 3.61 (s, 3H), 3.73 (s, 2H, J = 5.7, J1 = 5.7, J2 = 5.7 Hz), 3.82 (s, 3H), 4.30 (d, 1H, J = 10.4 Hz), 4.42 (d, 1H, J = 10.4 Hz), 4.98 (ddt, 1H, J1 = 10.4, J2 = 1.8, J3 = 1.7 Hz), 5.69 (ddt, 1H, J1 = 10.4, J2 = 10.4, J3 = 5.7 Hz), 6.74 (dd, 1H, J1 = 8.3, J2 = 0.9 Hz), 6.80 (d, 1H, J = 9.0 Hz), 6.86 (d, 1H, J = 9.0 Hz), 6.87 (dd, 1H, J1 =

Scheme 4

a) TBSCI, imidazole, CH2Cl2, 25 °C, 4.5 h, 95% (6a→8); b) MOMCl, iPr2NEt, CH2Cl2, 25 °C, 19 h, 91% (6a→9); c) (1) 1 M NaOH aq., MeOH, 0 °C, 5 min, (2) (MeO)2SO2, NaH, DMF, 25 °C, 25 min, 95%; d) 10 mol% NiCl2(dppp), DIBAL, Et2O, -78→20 °C, 3 h, 96%; e) IBX, DMSO, 25 °C, 4 h, 97%; f) 30 mol% Pd(PPh3)4, AcOH, 80 °C, 12 h, 91%; g) 1,4-dioxane–Br2, CH2Cl2, -78 °C, 2 h, 87%; h) BnMe2NiCl2, CuCO3, CH2Cl2, MeOH, 0→25 °C, 4 h, 88%; i) Mel, K2CO3, acetone, 25 °C, 3 h, 91%; j) (NH4)2Ce(NO3)6, MeCN, H2O, -15 °C, 10 min, 64%. [dppp = 1,3-bis(diphenylphosphino)propane]
8.3, J₂ = 0.9 Hz), 7.23 (dd, 1H, J₁ = J₂ = 8.3 Hz);

\(^{13}\)C NMR (100 MHz, CDCl₃, δ)
-5.1, -4.4, 17.7, 20.9, 25.2, 55.6, 56.6, 64.3, 71.0, 110.2, 111.1, 115.2, 115.9, 116.1, 121.3, 124.9, 127.4, 127.9, 135.3, 149.6, 151.2, 152.7, 153.9, 168.5;

IR (neat)
2930, 2850, 1770, 1450, 1250, 1200, 1040, 830, 770 cm\(^{-1}\);

Anal. calcd for C\(_{26}\)H\(_{36}\)O\(_6\)Si: C, 66.07; H, 7.68. Found: C, 66.27; H, 7.45.

HPLC [CHIRALPAK® AD-H (Daicel), 0.46 x 25 cm, hexane:2-propanol = 90:10, 1.0 mL/min, 20 °C, 264 nm] \(t_R\): 9.5 min ((–)-form: 10.8 min).

\[
\text{MeO} \quad \text{OMe} \\
\text{AcO} \quad \text{OMOM}
\]

To a solution of (+)-6\text{a} (885 mg, 2.47 mmol) in CH\(_2\)Cl\(_2\) (9.0 mL) was added MOMCl (0.28 mL, 3.7 mmol) and \(\text{iPr}_2\)NEt (0.88 mL, 4.9 mmol) at –15 °C. The reaction mixture was stirred at room temperature for 12.5 h, to which were added MOMCl (0.28 mL, 3.7 mmol) and \(\text{iPr}_2\)NEt (0.88 mL, 4.9 mmol). After 7 h, the reaction mixture was poured into sat. aq. NaHCO\(_3\), and extracted with EtOAc. The combined organic extracts were washed with brine, and dried over Na\(_2\)SO\(_4\), filtered and concentrated in vacuo. The residue was purified by silica-gel column chromatography (hexane/acetone = 9/1) to give MOM ether 9 (905 mg, 91%) as a colorless oil.

\([\alpha]_D^{27} +9.8 (c 1.2, \text{CHCl}_3)\);

\(^1\)H NMR (400 MHz, CDCl₃, δ)
1.87 (s, 3H), 3.30 (s, 3H), 3.62 (s, 3H), 3.73 (ddd, 2H, J₁ = 5.8, J₂ = 2.0, J₃ = 1.7 Hz), 3.83 (s, 3H), 4.23 (s, 2H), 4.98 (ddt, 1H, J₁ = 10.5, J₂ = 1.5, J₃ = 1.7 Hz), 5.00 (s, 2H), 5.05 (ddt, 1H, J₁ = 17.3, J₂ = 1.5, J₃ = 2.0 Hz), 5.68 (ddt, 1H, J₁ = 17.3, J₂ = 10.5, J₃ = 5.8 Hz), 6.84 (d, 1H, J = 9.0 Hz), 6.87 (d, 1H, J = 9.0 Hz), 6.88 (d, 1H, J = 8.3 Hz), 7.09 (d, 1H, J = 8.5 Hz), 7.31 (dd, 1H, J₁ = 8.3, J₂ = 8.5 Hz);

\(^{13}\)C NMR (100 MHz, CDCl₃, δ)
20.7, 55.7, 56.2 (2C), 64.2, 71.3, 94.9, 111.0, 111.1, 112.2, 115.9, 116.3, 119.8, 124.8, 126.9, 128.6, 130.5, 149.3, 151.4, 152.6, 156.1, 168.6;

IR (neat)
2930, 2820, 1760, 1450, 1250, 1200, 1040, 920, 790 cm\(^{-1}\);


HPLC [CHIRALPAK® IA (Daicel), 0.46 x 25 cm, hexane:2-propanol = 90:10, 1.0 mL/min, 20 °C, 264 nm] \(t_R\): 13.9 min ((–)-form: 12.8 min).
To a solution of MOM ether 9 (135 mg, 335 mmol) in MeOH (3.0 mL) was added 1 M NaOH aq. (1.7 mL, 1.7 mmol) at 0 °C. After stirring for 5 min at room temperature, the reaction was quenched by adding ice-water, and extracted with EtOAc. The combined organic extracts were washed with 2 M HCl aq., brine, and dried over Na₂SO₄, filtered and concentrated in vacuo. The residue was purified by PTLC (hexane/acetone = 2/2) to give phenol x (121 mg, quant) as a colorless oil.

\[ \alpha \] D\text{26} –13 (c 1.1, CHCl₃);

¹H NMR (400 MHz, CDCl₃, δ)
3.28 (s, 3H), 3.64 (s, 3H), 3.86 (s, 3H), 3.89 (ddd, 2H, J₁ = 5.6, J₂ = 1.4, J₃ = 1.2 Hz), 3.95 (d, 1H, J = 9.4 Hz), 4.67 (d, 1H, J = 9.4 Hz), 4.97 (d, 1H, J = 6.4 Hz), 5.01 (d, 1H, J = 6.4 Hz), 5.10 (ddt, 1H, J₁ = 10.4, J₂ = 1.6, J₃ = 1.4 Hz), 5.17 (ddt, 1H, J₁ = 17.2, J₂ = 1.6, J₃ = 1.2 Hz), 5.79 (ddt, 1H, J₁ = 17.2, J₂ = 10.4, J₃ = 5.6 Hz), 6.02 (s, 1H), 6.76 (d, 1H, J = 8.4 Hz), 6.79 (d, 1H, J = 8.0 Hz), 6.94 (s, 2H), 7.22 (dd, 1H, J₁ = 8.0, J₂ = 8.4 Hz);

¹³C NMR (100 MHz, CDCl₃, δ)
55.7, 56.2, 56.4, 64.7, 72.4, 94.8, 107.4, 111.3, 111.6, 112.3, 115.0, 117.5, 124.9, 126.9, 129.3, 134.2, 151.8, 152.4, 154.8, 155.6;

IR (neat)
3350, 2925, 2825, 1580, 1460, 1250, 1040 cm⁻¹;


A mixture of phenol x (105 mg, 290 µmol) and NaH (55% dispersion in mineral oil, 25 mg, 0.57 mmol) in DMF (1.0 mL) was stirred at room temperature for 15 min, to which was added (MeO)₂SO₂ (40 µL, 0.44 mmol) at 0 °C. After stirring at room temperature for 10 min, the reaction was quenched by adding Et₂NH, and the mixture was diluted with water, and extracted with EtOAc. The combined organic extracts were washed with 2 M HCl, brine, sat. aq. NaHCO₃, and dried over Na₂SO₄, filtered and concentrated in vacuo. The residue was purified by PTLC (hexane/acetone = 3/2) to give methyl ether 10 (103 mg, 95%) as a colorless oil.

\[ \alpha \] D\text{26} –6.3 (c 1.1, CHCl₃);

¹H NMR (400 MHz, CDCl₃, δ)
3.31 (s, 3H), 3.65 (s, 3H), 3.68 (s, 3H), 3.70 (ddd, 2H, J₁ = 5.8, J₂ = 1.4, J₃ = 1.2 Hz), 3.84 (s, 3H), 4.25 (d, 1H, J = 10.6 Hz), 4.29 (d, 1H, J = 10.6 Hz), 4.96 (ddt, 1H, J₁ = 10.5, J₂ = 1.7, J₃ = 1.2 Hz), 4.98 (d, 1H, J = 6.8 Hz), 5.00 (ddt, 1H, J₁ = 17.3, J₂ = 1.7, J₃ = 1.4 Hz), 5.01 (d, 1H, J = 6.8 Hz), 5.65 (ddt, 1H, J₁ = 17.3,
J₂ = 10.5, J₁ = 5.8 Hz), 6.67 (dd, 1H, J₁ = 8.6, J₂ = 1.0 Hz), 6.85 (dd, 1H, J₁ = 8.3, J₂ = 1.0 Hz), 6.87 (d, 1H, J = 9.0 Hz), 6.90 (d, 1H, J = 9.0 Hz), 7.28 (dd, 1H, J₁ = 8.3, J₂ = 8.6 Hz);

¹³C NMR (100 MHz, CDCl₃, δ)
55.7, 55.9, 56.1, 56.6, 64.2, 70.9, 94.7, 104.9, 107.8, 110.4, 111.6, 116.0, 125.5, 126.5, 126.9, 135.4, 151.5, 152.7, 155.7, 158.0;
IR (neat)
2925, 2825, 1585, 1460, 1430, 1250, 1150, 1100, 1060, 1010 cm⁻¹;

To a solution of allyl ether 10 (167 mg, 447 µmol) in Et₂O (2.0 mL) was added NiCl₂(dppp) (24.2 mg, 44.7 µmol) and DIBAL (0.95 M solution in CH₂Cl₂, 0.71 mL, 0.67 mmol) at –78 °C, and the mixture was gradually warmed up to –20 °C in 3.0 h. The reaction was stopped by adding water, and the products were extracted with EtOAc. The combined organic extracts were washed with 2 M HCl, brine, sat. aq. NaHCO₃, and dried over Na₂SO₄, filtered and concentrated in vacuo. The residue was purified by PTLC (hexane/acetone = 3/2) to give alcohol xi (143 mg, 96%) as a colorless oil.

[α]D²⁴ –9.6 (c 1.3, CHCl₃);
¹H NMR (400 MHz, CDCl₃, δ)
2.43 (br s, 1H), 3.26 (s, 3H), 3.65 (s, 3H), 3.71 (s, 3H), 3.88 (s, 3H), 4.35 (d, 1H, J = 11.6 Hz), 4.39 (d, 1H, J = 11.6 Hz), 5.00 (s, 2H), 6.71 (d, 1H, J = 8.4 Hz), 6.86 (d, 1H, J = 8.4 Hz), 6.88 (d, 1H, J = 9.2 Hz), 6.90 (d, 1H, J = 9.2 Hz), 7.29 (dd, 1H, J₁ = J₂ = 8.4 Hz);
¹³C NMR (100 MHz, CDCl₃, δ)
55.8, 55.9, 56.1, 56.5, 58.9, 95.2, 105.6, 108.9, 110.2, 111.0, 115.7, 124.7, 129.2, 129.3, 151.5, 152.1, 155.6, 157.8;
IR (neat)
3525, 2925, 2825, 1590, 1460, 1430, 1250, 1150, 1100, 1000 cm⁻¹;
Anal. calcd for C₁₈H₂₂O₆: C, 64.66; H, 6.63. Found: C, 64.42; H, 6.79.

To a solution of alcohol xi (94.5 mg, 283 µmol) in DMSO (1.0 mL) was added IBX (119 mg, 423 µmol) at 15 °C. After stirring at room temperature for 1.5 h, IBX (79.2 mg, 283 µmol) was again added, and stirring was continued for 2.5 h. The reaction was stopped by adding 10% aq. Na₂S₂O₅, and the products
were extracted with EtOAc. The combined organic extracts were washed with sat. aq. NaHCO₃, brine, and dried over Na₂SO₄, filtered and concentrated in vacuo. The residue was purified by PTLC (hexane/acetone = 3/2) to give aldehyde 11 (90.9 mg, 97%) as white solids. Recrystallization from EtOAc gave 11 as colorless prisms.

M.p. 86.0 – 88.0 °C; 
[α]₂⁰ -10 (c 1.0, CHCl₃);

¹H NMR (400 MHz, CDCl₃, δ)
3.29 (s, 3H), 3.68 (s, 3H), 3.69 (s, 3H), 3.90 (s, 2H), 6.66 (d, 1H, J = 8.4 Hz), 6.84 (d, 1H, J = 8.4 Hz), 6.97 (d, 1H, J = 9.2 Hz), 7.15 (d, 1H, J = 9.2 Hz), 7.30 (dd, 1H, J₁ = J₂ = 8.4 Hz), 9.96 (s, 1H);

¹³C NMR (100 MHz, CDCl₃, δ)
55.8, 55.9, 56.2, 56.8, 94.6, 104.8, 107.5, 111.4, 113.1, 117.4, 124.5, 128.2, 129.5, 151.3, 154.2, 155.5, 157.7, 191.6;

IR (KBr)
2954, 2940, 2829, 2360, 1687, 1585, 1469, 1405, 1245, 128.2, 129.5, 151.3, 154.2, 155.5, 157.7, 191.6;

To a solution of TBS ether 8 (418 mg, 884 µmol) in AcOH (4.0 mL) was added Pd(PPh₃)₄ (306 mg, 265 µmol, 30 mol%). After stirring at 80 °C for 12 h, the reaction was quenched by adding water, and extracted with CH₂Cl₂. The combined organic extracts were washed with sat. aq. NaHCO₃, brine, and dried over Na₂SO₄, filtered and concentrated in vacuo. The residue was purified by silica-gel column chromatography (hexane/ EtOAc = 4/1) to give phenol 12 (350 mg, 91%) as a colorless oil.

[α]₂⁰ +35 (c 2.3, CHCl₃);

¹H NMR (400 MHz, CDCl₃, δ)
-0.07 (s, 3H), 0.10 (s, 3H), 0.63 (s, 9H), 1.91 (s, 3H), 3.68 (s, 3H), 3.83 (s, 3H), 4.70 (d, 1H, J = 11.2 Hz), 4.77 (s, 1H), 5.15 (d, 1H, J = 11.2 Hz), 6.46 (dd, 1H, J₁ = 8.4, J₂ = 0.8 Hz), 6.62 (dd, 1H, J₁ = 8.0, J₂ = 0.8 Hz), 6.93 (d, 1H, J = 9.4 Hz), 6.95 (d, 1H, J = 9.4 Hz), 7.12 (dd, 1H, J₁ = 8.0, J₂ = 8.4 Hz);

¹³C NMR (100 MHz, CDCl₃, δ)
-4.9, -4.2, 17.7, 20.8, 25.2, 56.1, 56.5, 59.5, 108.4, 111.1, 112.0, 112.1, 114.6, 123.9, 126.1, 129.2, 151.8, 152.9, 153.3, 154.5, 170.6;

IR (neat)
3400, 2940, 2925, 2850, 1730, 1450, 1250, 1140, 1120 cm⁻¹;

Anal. calcd for C₁₈H₂₀O₆: C, 65.05; H, 6.07. Found: C, 64.95; H, 6.37.

HO
\begin{center}
\begin{tikzpicture}
\draw[thick] (0,0) circle (0.5 cm);
\draw[thick] (0.5,0) -- (1.5,1.5);
\draw[thick] (0.5,0) -- (1.5,-1.5);
\draw[thick] (0.5,0) circle (0.1 cm);
\draw[thick] (1.5,1.5) circle (0.1 cm);
\draw[thick] (1.5,-1.5) circle (0.1 cm);
\end{tikzpicture}
\end{center}

To a solution of TBS ether 8 (418 mg, 884 µmol) in AcOH (4.0 mL) was added Pd(PPh₃)₄ (306 mg, 265 µmol, 30 mol%). After stirring at 80 °C for 12 h, the reaction was quenched by adding water, and extracted with CH₂Cl₂. The combined organic extracts were washed with sat. aq. NaHCO₃, brine, and dried over Na₂SO₄, filtered and concentrated in vacuo. The residue was purified by silica-gel column chromatography (hexane/ EtOAc = 4/1) to give phenol 12 (350 mg, 91%) as a colorless oil.

[α]₂⁰ +35 (c 2.3, CHCl₃);

¹H NMR (400 MHz, CDCl₃, δ)
-0.07 (s, 3H), 0.10 (s, 3H), 0.63 (s, 9H), 1.91 (s, 3H), 3.68 (s, 3H), 3.83 (s, 3H), 4.70 (d, 1H, J = 11.2 Hz), 4.77 (s, 1H), 5.15 (d, 1H, J = 11.2 Hz), 6.46 (dd, 1H, J₁ = 8.4, J₂ = 0.8 Hz), 6.62 (dd, 1H, J₁ = 8.0, J₂ = 0.8 Hz), 6.93 (d, 1H, J = 9.4 Hz), 6.95 (d, 1H, J = 9.4 Hz), 7.12 (dd, 1H, J₁ = 8.0, J₂ = 8.4 Hz);

¹³C NMR (100 MHz, CDCl₃, δ)
-4.9, -4.2, 17.7, 20.8, 25.2, 56.1, 56.5, 59.5, 108.4, 111.1, 112.0, 112.1, 114.6, 123.9, 126.1, 129.2, 151.8, 152.9, 153.3, 154.5, 170.6;

IR (neat)
3400, 2940, 2925, 2850, 1730, 1450, 1250, 1140, 1120 cm⁻¹;

Anal. calcd for C₁₈H₂₀O₆: C, 65.05; H, 6.07. Found: C, 64.95; H, 6.37.
To a solution of phenol 12 (251 mg, 580 µmol) in CH₂Cl₂ (13 mL) was added 1,4-dioxane-Br₂ (160 mg, 580 µmol) in CH₂Cl₂ (5.0 mL) at −78 °C. After 2 h, the reaction was stopped by adding 10% aq. Na₂S₂O₄, and extracted with CH₂Cl₂. The combined organic extracts were washed with sat. aq. NaHCO₃, brine, and dried over Na₂SO₄, filtered and concentrated in vacuo. The residue was purified by PTLC (hexane/acetone = 3/2) to give bromide 13 (257 mg, 87%) as white solids. Recrystallization from Et₂O gave 13 as colorless prisms.

M.p. 103.4-104.0 °C; 
[α]D³¹ +17 (c 1.9, CHCl₃);

¹H NMR (400 MHz, CDCl₃, δ)
–0.07 (s, 3H), 0.10 (s, 3H), 0.64 (s, 9H), 1.90 (s, 3H), 3.67 (s, 3H), 3.82 (s, 3H), 4.75 (d, 1H, J = 11.5 Hz), 5.07 (d, 1H, J = 11.5 Hz), 5.28 (d, 1H, J = 8.8 Hz), 6.39 (d, 1H, J = 8.8 Hz), 6.91 (d, 1H, J = 9.1 Hz), 6.94 (d, 1H, J = 9.1 Hz), 7.32 (d, 1H, J = 8.8 Hz);

¹³C NMR (100 MHz, CDCl₃, δ)
–5.1 –4.3, 17.6, 20.7, 25.1, 55.9, 56.5, 59.2, 101.4, 111.9, 112.0, 112.5, 116.1, 124.3, 125.4, 131.5, 150.9, 151.6, 152.8, 153.2, 170.7;

IR (ATR) 3377, 2952, 2930, 1723, 1484, 1459, 1255, 1243, 1089 cm⁻¹;


To a solution of phenol 12 (47.1 mg, 109 µmol) in CH₂Cl₂ (1.0 mL) was added BnMe₃NICl₂ (37.9 mg, 109 µmol) and MeOH (0.1 mL) at 0 °C. After stirring at room temperature for 2 h, BnMe₃NICl₂ (3.8 mg, 11 µmol) and MeOH (0.2 mL) were again added at 0 °C. After stirring at room temperature for 2 h, the reaction was stopped by 10% Na₂S₂O₄ aq., and extracted with CH₂Cl₂. The combined organic extracts were washed with sat. aq. NaHCO₃, brine, and dried over Na₂SO₄, filtered and concentrated in vacuo.

5.28 (s) → HO

101.4

:: HMBC

To a solution of phenol 12 (47.1 mg, 109 µmol) in CH₂Cl₂ (1.0 mL) was added BnMe₃NICl₂ (37.9 mg, 109 µmol) and MeOH (0.1 mL) at 0 °C. After stirring at room temperature for 2 h, BnMe₃NICl₂ (3.8 mg, 11 µmol) and MeOH (0.2 mL) were again added at 0 °C. After stirring at room temperature for 2 h, the reaction was stopped by 10% Na₂S₂O₄ aq., and extracted with CH₂Cl₂. The combined organic extracts were washed with sat. aq. NaHCO₃, brine, and dried over Na₂SO₄, filtered and concentrated in vacuo.
The residue was purified by PTLC (hexane/acetone = 3/2) to give 14 (50.8 mg, 88%) as white solids. Recrystallization from hexane–EtOAc (1/1) gave iodide 14 as colorless prisms.

\[ \text{[aI}^{28}\text{]} +15 (c 1.8, \text{CHCl}_3); \]

M.p. 108–109 °C.

\[^1\text{H NMR (400 MHz, CDCl}_3, \delta)\]

\[ -0.06 (s, 3\text{H}), 0.10 (s, 3\text{H}), 0.63 (s, 9\text{H}), 1.91 (s, 3\text{H}), 3.67 (s, 3\text{H}), 3.83 (s, 3\text{H}), 4.71 (d, 1\text{H}, J = 11.5 \text{Hz}), 5.10 (d, 1\text{H}, J = 11.5 \text{Hz}), 5.22 (s, 1\text{H}), 6.30 (d, 1\text{H}, J = 8.6 \text{Hz}), 6.92 (d, 1\text{H}, J = 9.1 \text{Hz}), 6.94 (d, 1\text{H}, J = 9.1 \text{Hz}), 7.53 (d, 1\text{H}, J = 8.6 \text{Hz}); \]

\[^{13}\text{C NMR (100 MHz, CDCl}_3, \delta)\]

\[ -5.1, -4.3, 17.6, 20.8, 25.1, 55.9, 56.6, 59.1, 73.8, 112.0, 112.3, 113.4, 115.3, 124.2, 125.7, 137.8, 151.7, 152.8, 153.5, 154.1, 170.7; \]

IR (KBr)

3400, 2952, 2929, 2856, 1742, 1485, 1460, 1415, 1311, 1294, 1261, 1245, 1176, 1135, 1107, 1090, 1051, 1032 cm\(^{-1}\);


HPLC [CHIRALPAK® IA (Daicel), 0.46 x 25 cm, hexane:2-propanol = 90:10, 1.0 mL/min, 20 °C, 264 nm] t\(_R\): 9.6 min ((–)-form: 11.5 min).

To a solution of phenol 12 (140 mg, 324 µmol) in acetone (1.5 mL) was added MeI (50 µL, 0.81 mmol) and K\(_2\)CO\(_3\) (134 mg, 972 µmol) at 0 °C. After stirring at room temperature for 12 h, the reaction was quenched by adding Et\(_2\)NH, and the mixture was diluted with water. The products were extracted with EtOAc, and the combined organic extracts were washed with 2 M HCl, brine, sat. aq. NaHCO\(_3\), and dried over Na\(_2\)SO\(_4\), filtered and concentrated in vacuo. The residue was purified by PTLC (hexane/EtOAc = 4/1) to give xii (132 mg, 91%) as a colorless oil.

\[ [\alpha]^{26}_D +0.8 (c 1.7, \text{CHCl}_3) \]

\[^1\text{H NMR (400 MHz, CDCl}_3, \delta)\]

\[ -0.04 (s, 3\text{H}), 0.07 (s, 3\text{H}), 0.65 (s, 9\text{H}), 1.88 (s, 3\text{H}), 3.65 (s, 3\text{H}), 3.70 (s, 3\text{H}), 3.80 (s, 3\text{H}), 4.84 (d, 1\text{H}, \delta) \]
J = 11.5 Hz), 4.96 (d, 1H, J = 11.5 Hz), 6.51 (d, 1H, J = 8.3 Hz), 6.59 (d, 1H, J = 8.3 Hz), 6.85 (d, 1H, J = 9.2 Hz), 6.88 (d, 1H, J = 9.2 Hz), 7.18 (t, 1H, J = 8.3 Hz);

$^{13}$C NMR (100 MHz, CDCl$_3$, δ)

–4.9, –4.3, 17.7, 20.9, 25.2, 55.8, 56.1, 56.4, 59.8, 103.9, 110.7, 111.76, 111.78, 116.5, 124.8, 127.0, 128.8, 151.8, 152.8, 153.9, 158.5, 170.9;

IR (neat)

2950, 2930, 2850, 1730, 1580, 1465, 1435, 1250, 1100, 1025 cm$^{-1}$;

Anal. calcd for C$_{24}$H$_{34}$O$_6$Si: C, 64.54; H, 7.67. Found: C, 64.35; H, 7.95.

To a solution of xii (49.1 mg, 110 µmol) in CH$_3$CN (0.7 mL) was added CAN (0.47 M in H$_2$O, 0.7 mL, 0.33 mmol) at –15 °C. After stirring at room temperature for 10 min, the reaction was stopped by adding water, and the products were extracted with EtOAc. The combined organic extracts were washed with sat. aq. NaHCO$_3$ and brine, dried over Na$_2$SO$_4$, filtered and concentrated in vacuo. The residue was purified by PTLC (hexane/acetone = 3/2) to give 15 (29.4 mg, 64%) as a yellow oil.

$[\alpha]_D^{28.4} +8^\circ$ (c 0.3, CHCl$_3$);

$^1$H NMR (400 MHz, CDCl$_3$, δ)

0.09 (s, 3H), 0.18 (s, 3H), 0.82 (s, 9H), 1.88 (s, 3H), 3.72 (s, 3H), 4.76 (d, 1H, J = 12.2 Hz), 4.82 (d, 1H, J = 12.2 Hz), 6.52 (dd, 1H, J$_1$ = 8.3, J$_2$ = 0.7 Hz), 6.58 (dd, 1H, J$_1$ = 8.5, J$_2$ = 0.7 Hz), 6.84 (d, 1H, J = 10.2 Hz), 6.87 (d, 1H, J = 10.2 Hz), 7.25 (dd, 1H, J$_1$ = 8.5, J$_2$ = 8.3 Hz);

$^{13}$C NMR (100 MHz, CDCl$_3$, δ)

–4.6, –4.2, 17.8, 20.5, 25.4, 55.7, 58.8, 103.8, 111.4, 112.4, 130.7, 136.3, 136.9, 139.5, 142.6, 153.6, 157.7, 170.1, 185.4, 186.2;

IR (neat) 2940, 2920, 2840, 1720, 1655, 1580, 1460, 1250, 1220, 1095 cm$^{-1}$;

Anal. calcd for C$_{22}$H$_{30}$O$_6$Si: C, 63.13; H, 7.22. Found: C, 63.24; H, 7.32.

HPLC [CHIRALPAK® IB (Daicel), 0.46 x 25 cm, hexane:2-propanol = 90:10, 1.0 mL/min, 20 °C, 264 nm] $t_R$: 7.2 min ((–)-form: 6.1 min).