Supplementary Material (ESI) for Organic & Biomolecular Chemistry

Supporting Information

Stereo-controlled Synthesis of Epi-series Catechins and their 3-Gallates: Reverse Polarity Strategy

Ken Ohmori, Takahisa Yano, and Keisuke Suzuki*

Department of Chemistry, Tokyo Institute of Technology, and SORST–JST Agency, O-okayama, Meguro-ku, Tokyo 152-8551, Japan

ksuzuki@chem.titech.ac.jp

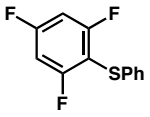
General Experimental Procedures

All reactions utilizing air- and moisture-sensitive reagents were performed in dried glassware under an atmosphere of dry argon or nitrogen. Ethereal solvents (anhydrous; *Kanto Chemical Co., Inc.*) were used as received. Dichloromethane was distilled successively from P_2O_5 and CaH_2, and stored over 4A molecular sieves.

For thin-layer chromatography (TLC) analysis, Merck pre-coated plates (silica gel 60 F_{254}, Art 5715, 0.25 mm) were used. Silica gel preparative TLC (PTLC) was performed on Merck Silica gel 60 PF_{254} (Art 7747).

Melting point (mp) determinations were performed by using a Yanako MP-S3 or MP-500 instrument and are uncorrected. ^{1}H NMR and ^{13}C NMR were measured on a JEOL JNM AL-400 (400 MHz), or a JEOL JNM Lambda-400 (400 MHz) spectrometer. Chemical shifts are expressed in parts per million (ppm) downfield from internal standard (tetramethylsilane, 0.00 ppm), and coupling constants are reported as hertz (Hz). Splitting patterns are indicated as follows: br, broad; s, singlet; d, doublet; t, triplet; q, quartet; m, multiplet. Infrared (IR) spectra were recorded on a Perkin Elmer 1600 FTIR, a Horiba FT-710, or a Perkin Elmer Spectrum 100 spectrometer. Attenuated Total Reflectance Fourier Transform Infrared (ATR-FTIR) spectra were recorded on a Perkin Elmer 1600 FTIR. Optical rotations ($[\alpha]_D$) were measured on a JASCO DIP-1000 polarimeter.

Preparation of sulfide 6

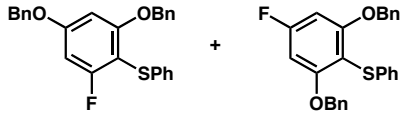


6

To a solution of 1,3,5-trifluorobenzene (5.03 g, 38.1 mmol) in Et_2O (135 mL) was added *n*-BuLi (1.65 M in hexane, 24.2 mL, 40.0 mmol) at –78 °C. After stirring for 2 h, benzenethiosulfonic acid *S*-phenylether (10.0 g, 40.0 mmol) in Et_2O (20 mL) was added, and the stirring was continued for 1 h. Then the reaction was quenched by addingf saturated aqueous $NaHCO_3$. The products were extracted with Et_2O (x3) and the combined organic extracts were washed with brine, dried ($MgSO_4$), and concentrated in vacuo. The residue was purified by distillation (96–97 °C, 0.3 mmHg) to afford sulfide **6** (7.62 g, 83%) as a colorless oil. The distilled residue was further purified by flash column chromatography (hexane to hexane/EtOAc = 20:1) to afford **6** (329 mg, 4%) as a colorless oil.

6: R_f 0.72 (hexane/acetone = 10/1); ^{1}H NMR (400 MHz, $CDCl_3$) δ 6.73–6.79 (m, 2H), 7.16–7.21 (m, 1H), 7.22–7.28 (m, 4H); ^{13}C NMR (100 MHz, $CDCl_3$) δ 100.5–101.1 (m, 2C), 106.1 (td, 1C, $J_{C–F}$ = 23.1, 4.9 Hz), 126.6, 128.6, 128.9, 134.7, 163.4 (dt, 1C, $J_{C–F}$ = 251, 14.9 Hz), 163.6 (ddd, 2C, $J_{C–F}$ = 250, 14.9, 6.6 Hz); ^{19}F NMR (376 MHz, $CDCl_3$) δ –107.7 (s, 1F), –103.5 (s, 2F); IR (neat) 3050, 1620, 1600, 1580, 1460, 1430, 1120, 1020 cm^{-1}; Anal. calcd for $C_{12}H_7F_3S$: C, 55.99; H, 2.94; S, 13.35. Found: C, 59.78; H, 3.13; S, 13.37.

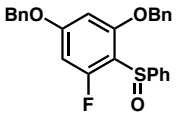
Preparation of sulfide 7 (as a mixture with 2,6-regioisomer 7')



7 **7'**

To a suspension of NaH (63% dispersion in mineral oil, washed with hexane, 1.7 g, 45 mmol) in DMF (41 mL) was added benzylalcohol (4.46 g, 41.2 mmol) at 0 °C. The mixture was stirred for 2 h, to which was added a trifluorophenylthio benzene **6** (4.00 g, 16.7 mmol) in DMF (31 mL) at 0 °C. After stirring for 2 h, the reaction mixture was poured into an ice water, and the products were extracted with Et_2O (x3). The combined organic extracts were washed with brine, dried ($MgSO_4$), and concentrated in vacuo. The residue was purified by flash column chromatography (hexane/EtOAc = 1/1) to afford a mixture of **7** and its 2,6-regioisomer **7'** (6.53 g, **7**/**7'** = ca.10:1). This mixture was used for the next reaction without further purification.

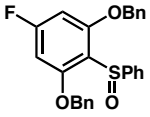
Preparation of sulfoxide 8



8

To a suspension of the mixture of **7** and **7'** (6.00 g) in CH_2Cl_2 (48 mL) was added *m*CPBA (65% chemical purity, 3.06 g, 11.5 mmol) at 0 °C. After stirring for 30 min, additional portions of *m*CPBA was added (38 mg, 0.14 mmol; 19 mg, 0.072 mmol; 19 mg, 0.072 mmol) with 20-min intervals. The reaction was quenched by adding 5% $Na_2S_2O_3$ solution and saturated aqueous $NaHCO_3$. The products were extracted with EtOAc (x3). The combined organic extracts were washed with brine, dried ($MgSO_4$), and concentrated in vacuo. The residue was purified by flash column chromatography (silica gel, hexane/EtOAc = 8/2 to 7/3, gradient elution) to afford the mixture of **8** (5.27 g, 2 steps 85%) and 2,6-regioisomer **8'** (501 mg, 2 steps 8 %) as white solids.

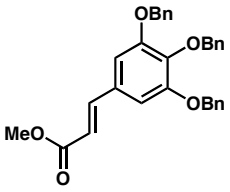
8: R_f 0.65 (hexane/EtOAc = 1/1); mp 88–89 °C (hexane/Et_2O); ^{1}H NMR (400 MHz, $CDCl_3$) δ 4.90 (d, 2H, J = 12.0 Hz), 4.99 (s, 2H), 5.09 (d, 1H, J = 12.0 Hz), 6.29–6.35 (m, 2H), 7.19–7.24 (m, 2H), 7.29–7.41 (m, 11H), 7.56–7.59 (m, 2H); ^{13}C NMR (100 MHz, $CDCl_3$) δ 70.6, 70.9, 95.5 (d, 1C, $J_{C–F}$ = 26.4 Hz), 97.1 (d, 1C, $J_{C–F}$ = 3.3 Hz), 113.7 (d, 1C, $J_{C–F}$ = 15.7 Hz), 124.2, 127.1, 127.4, 128.0 128.3, 128.4, 128.6, 129.5, 135.2, 135.3, 144.2, 159.0 (d, 1C, $J_{C–F}$ = 8.3 Hz), 163.2 (d, 1C, $J_{C–F}$ = 251 Hz), 163.5 (d, 1C, $J_{C–F}$ = 14 Hz); IR (neat) 3050, 3000, 2925, 2850, 2225, 1940, 1870, 1800, 1600, 1570, 1430, 1330, 1250, 1080 cm^{-1}; Anal. calcd for $C_{26}H_{21}FO_3S$: C, 72.20; H, 4.89; S, 7.41. Found: C, 72.42; H, 4.96; S, 7.25.



8'

8': R_f 0.53 (hexane/EtOAc = 1/1); mp 120–121 °C (hexane/Et_2O); ^{1}H NMR (400 MHz, $CDCl_3$) δ 4.90 (d, 2H, J = 12.0 Hz), 5.05 (d, 1H, J = 12.0 Hz), 6.27 (d, 2H, J = 10.4 Hz), 7.19–7.34 (m, 13Hz), 7.47–7.54 (m, 2H); ^{13}C NMR (100 MHz, $CDCl_3$) δ 70.7, 94.1 (d, 2C, $J_{C–F}$ = 26.5 Hz), 116.6 (d, 1C, $J_{C–F}$ = 4.1 Hz), 124.0, 126.9, 127.8, 128.0, 128.2, 128.8, 135.0, 144.1, 159.8 (d, 2C, $J_{C–F}$ = 14.1 Hz), 166.2, (d, 1C, $J_{C–F}$ = 250.1 Hz); IR (neat) 3050, 1600, 1580, 1430, 1190, 1150 cm^{-1}; Anal. calcd for $C_{26}H_{21}FO_3S$: C, 72.20; H, 4.89; S, 7.41. Found: C, 72.12; H, 5.07; S, 7.58.

Preparation of ester SUP-1

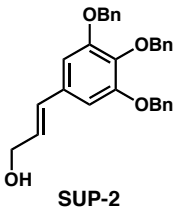


SUP-1

To a suspension of NaH (60% dispersion in mineral oil, washed with hexane, 4.79 g, 120 mmol) in THF (200 mL) was slowly added methyl diethylphosphonoacetate (25.0 g, 119 mmol) at 0 °C, and the mixture was vigorously stirred for 1 h. A solution of 3,4,5-tris(benzyloxy)benzaldehyde (48.5 g, 114 mmol) in THF (200 mL) was added over 30 min at 0 °C, and the stirring was continued for 11 h. The reaction was stopped by adding water, and the products were extracted with EtOAc (x3). The combined organic extracts were washed with brine, dried ($MgSO_4$) and concentrated in vacuo. Recrystallization (hexane/EtOAc = 5/1) gave **SUP-1** (53.5 g, 97%) as a white solid.

SUP-1: R_f 0.75 (hexane/acetone = 2/1); mp 108–109 °C (hexane/EtOAc); ^{1}H NMR (400 MHz, $CDCl_3$) δ 3.79 (s, 3H), 5.10 (s, 2H), 5.12 (s, 4H), 6.26 (d, 1H, J = 15.6 Hz), 6.81 (s, 2H), 7.24–7.43 (m, 15H), 7.54 (d, 1H, J = 15.6 Hz); ^{13}C NMR (100 MHz, $CDCl_3$) δ 51.6, 71.2, 75.2, 107.7, 116.9, 127.3, 127.8, 127.9, 128.0, 128.38, 128.40, 129.7, 126.6, 136.6, 137.4, 140.3, 144.6, 152.8, 167.1; IR (neat) 3050, 2940, 1700, 1630, 1580, 1500, 1450, 1430, 1130 cm^{-1}; Anal. calcd for $C_{31}H_{28}O_5$: C, 77.69; H, 5.87. Found: C, 77.69; H, 5.84.

Preparation of allyl alcohol SUP-2



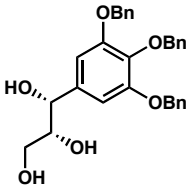
SUP-2

To a solution of **SUP-1** (20.0 g, 41.6 mmol) in THF (208 mL) was added diisopropylaluminium hydride (1.82 M in hexane, 52.6 mL, 95.7 mmol) at –78 °C over 30 min. After stirring for 6 h, the reaction was quenched by careful addition of MeOH at –78 °C. After warming to 0 °C, saturated aqueous potassium sodium tartrate (Rochell's salt) was added to the mixture, and the stirring was continued for 3 h. The products were extracted with EtOAc (x3), and the combined organic extracts were washed with brine, dried ($MgSO_4$), and concentrated in vacuo. Recrystallization (hexane/EtOAc =10/1) gave **SUP-2** (18.2 g, 96%) as colorless needles.

SUP-2: R_f 0.30 (hexane/acetone = 2/1); mp 94–95 °C (hexane/EtOAc); ^{1}H NMR (400 MHz, $CDCl_3$) δ 1.41 (t, 1H, J = 5.2 Hz), 4.29 (dd, 2H, J = 5.6, 5.2 Hz), 5.06 (s, 2H), 5.11 (s, 4H), 6.20 (dt, 1H, J = 16.0, 5.6 Hz), 6.48 (d, 1H, J = 16.0 Hz), 6.69, (s, 2H), 7.25–7.44 (m, 15H); ^{13}C NMR (100 MHz,

$CDCl_3$) δ 63.6, 71.3, 75.3, 106.3, 127.3, 127.7, 127.78, 127.9, 128.1, 128.4, 130.9, 132.3, 137.0, 137.7, 138.2, 152.8; IR (neat) 3250, 3050, 3020, 2850, 1580, 1500, 1450, 1420, 1370, 1330, 1240, 1120 cm^{-1}; Anal. calcd for $C_{30}H_{28}O_4$: C, 79.62; H, 6.24. Found: C, 79.82; H, 6.32.

Preparation of triol SUP-3

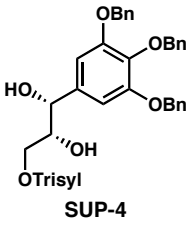


SUP-3

To a solution of potassium hexacyanoferrate(III) (21.8 g, 66.2 mmol) in the mixed solvent (540 mL, *t*-BuOH/H_2O = 1/1), were added K_2CO_3 (9.15 g, 66.2 mmol), methanesulfonamide (2.10 g, 22.1 mmol), $(DHQD)_2$-PHAL (0.172 g, 0.221 mmol), and $K_2OsO_2(OH)_4$ (40.5 mg, 0.110 mmol) at 0 °C. After the stirring for 30 min at the same temperature, **SUP-2** (10.0 g, 22.1 mmol) was added to the mixture at 0 °C. After the stirring for 40 h at 0 °C, the reaction was quenched by adding aqueous sodium sulfite. The products were extracted with EtOAc (x3) and the combined organic extracts were washed with aqueous 2 M KOH, dried (Na_2SO_4), and concentrated in vacuo. The residue was purified by flash column chromatography (silica gel, hexane/EtOAc = 1/4) to afford **SUP-3** (9.80 g, 91%, 99% *ee*) as a white solid. Enantiomeric purity of **SUP-3** was assessed by HPLC analysis [CHIRALPAK® IA (Daicel), ϕ 4.6 x 250 mm, hexane/*i*-PrOH = 85/15, 1.0 mL/min flow rate, 20 °C, 254 nm, t_R = 19.9 min for the (*R*,*R*)-isomer and 23.8 min for the (*S*,*S*)-isomer.]

SUP-3: R_f 0.30 (hexane/acetone = 1/1); mp 95–97 °C (hexane/EtOH); $[\alpha]_D^{27}$ –18 (*c* 0.36, $CHCl_3$); ^1H NMR (400 MHz, $CDCl_3$) δ 3.38 (dd, 1H, *J* = 11.6, 5.2 Hz), 3.52 (dd, 1H, *J* = 11.6, 3.2 Hz), 3.61–3.65 (m, 1H), 4.56 (d, 1H, *J* = 6.4 Hz), 5.04 (s, 2H), 5.10 (s, 4H), 6.65 (s, 2H), 7.22–7.43 (m, 15H); ^{13}C NMR (100 MHz, $CDCl_3$) δ 63.2, 71.1, 74.7, 75.2, 75.9, 106.1, 127.4, 127.7, 127.8, 128.0, 128.35, 128.44, 136.06, 136.07, 136.8, 137.5, 137.9, 152.6; IR (neat) 3375, 3050, 3025, 2950, 2850, 1940, 1870, 1800, 1590, 1500, 1440, 1380, 1320, 1240 cm^{-1}; Anal. calcd for $C_{30}H_{30}O_6$: C, 74.06; H, 6.21. Found: C, 74.28; H, 6.28.

Preparation of sulfonate SUP-4

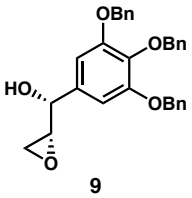


SUP-4

To a solution of **SUP-3** (2.00 g, 4.11 mmol) in pyridine (8.0 mL), 2,4,6-triisopropylbenzenesulfonyl chloride (3.11 g, 10.3 mmol) was added at 0 °C. After stirring for 18 h, the reaction mixture was diluted with EtOAc and quenched by adding 1 M HCl. The products were extracted with EtOAc (x3), and the combined organic extracts were washed with brine, dried ($MgSO_4$), and concentrated in vacuo. The residue was purified by flash column chromatography (silica gel, hexane/EtOAc = 4/1 to 1/1, gradient elution) to afford **SUP-4** (2.77 g, 90%) as a white solid.

SUP-4: R_f 0.55 (hexane/acetone = 1/1); mp 124–125 °C (hexane/EtOAc); $[\alpha]_{365}^{32}$ +4.1 (*c* 0.84, $CHCl_3$); ^{1}H NMR (400 MHz, $CDCl_3$) δ 1.25 (d, 12H, *J* = 6.8 Hz), 1.26 (d, 6H, *J* = 6.8 Hz), 2.61 (brs, 1H), 2.91 (sept, 1H, *J* = 6.8 Hz), 3.86–3.90 (m, 1H), 3.95 (dd, 1H, *J* = 10.4, 5.2 Hz), 4.02 (dd, 1H, *J* = 10.4, 6.4 Hz), 4.11 (sept, 2H, *J* = 6.8 Hz), 4.63 (d, 1H, *J* = 5.6 Hz), 5.03 (s, 2H), 5.08 (d, 2H, *J* = 11.6 Hz), 5.11 (d, 2H, *J* = 11.6 Hz), 6.68 (s, 2H), 7.19–7.42 (m, 17H); ^{13}C NMR (100 MHz, $CDCl_3$) δ 23.6, 24.76, 24.81, 29.7, 34.2, 69.3, 71.2, 73.4, 73.6, 75.1, 105.9, 123.8, 127.4, 127.7, 127.8, 128.0, 128.3, 128.5, 128.7, 128.7, 135.37, 135.42, 136.8, 137.5, 137.9, 150.8, 152.7, 153.9; IR (neat) 3250, 2950, 2850, 1950, 1870, 1800, 1660, 1590, 1500, 1440, 1380, 1325 cm^{-1}; Anal. calcd for $C_{45}H_{52}O_8S$: C, 71.78; H, 6.96. Found: C, 71.58; H, 7.15.

Preparation of epoxide 9



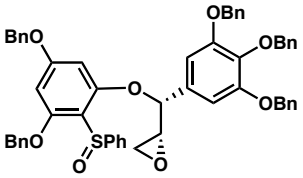
9

To a solution of **SUP-4** (1.00 g, 1.33 mmol) in a mixed solvent of MeOH (5.0 mL) and 1,4-dioxane (2.0 mL), powdered K_2CO_3 (368 mg, 2.66 mmol) was added at 0 °C in one portion. After stirring for 1.5 h, the reaction mixture was diluted with EtOAc, and the products were extracted with EtOAc (x3). The combined organic extracts were washed with brine, dried ($MgSO_4$), and concentrated in vacuo. The residue was purified by flash column chromatography (silica gel, hexane/EtOAc = 1/1) to afford epoxide **9** as a white solid.

9: R_f 0.45 (hexane/acetone = 1/1); mp 88–91 °C (hexane/EtOAc); $[\alpha]_{546}^{31}$ –3.3 (*c* 0.76, $CHCl_3$); ^{1}H

NMR (400 MHz, $CDCl_3$) δ 2.27 (d, 1H, *J* = 4.8 Hz), 2.74 (dd, 1H, *J* = 4.8, 2.8 Hz), 2.80 (t, 1H, *J* = 4.4 Hz), 3.14 (ddd, 1H, J = 4.8, 4.4, 2.8 Hz), 4.37 (t, 1H, *J* = 4.8 Hz), 5.05 (s, 2H), 5.12 (s, 4H), 6.72 (s, 2H), 7.24–7.43 (m, 15H); ^{13}C NMR (100 MHz, $CDCl_3$) δ 45.4, 55.8, 71.3, 74.3, 75.2, 106.0, 127.4, 127.7, 127.8, 128.1, 128.4, 128.5, 135.6, 136.9, 137.7, 138.19, 138.21, 138.3, 152.9; IR (neat) 3400, 3020, 2920, 2860, 1940, 1870, 1800, 1590, 1500, 1450, 1425, 1380, 1330 cm^{-1}; Anal. calcd for $C_{30}H_{28}O_5$: C, 76.90; H, 6.02. Found: C, 77.13; H, 6.29.

Preparation of oxirane 10



10

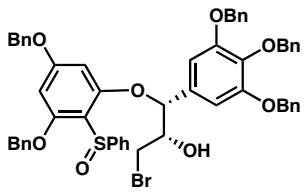
To a suspension of NaH (59.0 mg, 63% dispersion in mineral oil, washed with hexane, 1.55 mmol) in a mixed solvent of toluene (1.0 mL) and DMPU (0.25 mL) was added sulfoxide **8** (898 mg, 2.08 mmol) at room temperature. A solution of epoxy alcohol **9** (500 mg, 1.07 mmol) in a mixed solvent of toluene (0.60 mL) and DMPU (0.15 mL) was added at room temperature and the stirring was continued for 15 h. The reaction was stopped by adding saturated aqueous $NaHCO_3$, and the products were extracted with EtOAc (x3), and the combined organic extracts were washed with brine, dried (Na_2SO_4), and concentrated in vacuo. The residue was purified by flash column chromatography (silica gel, hexane/EtOAc =2/1 to 1/1, gradient elution) to afford less polar ether **10a** (356 mg, 38%) and more polar one **10b** (339 mg, 36%) as colorless oils respectively.

10a: R_f 0.60 (hexane/EtOAc = 1/1); $[\alpha]_D^{22}$ +11.7 (*c* 1.05, $CHCl_3$); ^{1}H NMR (400 MHz, $CDCl_3$) δ 2.38 (dd, 1H, *J* = 4.4, 2.4 Hz), 2.61 (t, 1H, *J* = 4.4 Hz), 3.02 (ddd, 1H, *J* = 5.6, 4.4, 2.4 Hz), 4.70 (d, 1H, *J* = 5.6 Hz), 4.82 (d, 1H, J = 12.0 Hz), 4.85 (d, 1H, J = 12.0 Hz), 4.96–5.16 (m, 8H), 5.98 (d, 1H, *J* = 2.0 Hz), 6.16 (d, 1H, *J* = 2.0 Hz), 6.79 (s, 2H), 7.20–7.44 (m, 28H), 7.56–7.59 (m, 2H); ^{13}C NMR (100 MHz, $CDCl_3$) δ 44.4, 54.2, 70.2, 70.6, 71.0, 74.9, 81.4, 93.7, 94.5, 106.2, 113.8, 124.2, 127.0, 127.37, 127.40, 127.55, 127.58, 127.8, 128.1, 128.2, 128.3, 128.5, 128.8, 131.3, 135.6, 135.7, 136.8, 137.7, 138.3, 145.5, 152.7, 158.5, 159.8, 163.4; IR (neat) 3050, 3000, 2900, 2850, 1940, 1860, 1800, 1580, 1490, 1420, 1330, 1220, 1150, 1100 cm^{-1}; Anal. calcd for $C_{56}H_{48}O_8S$: C, 76.34; H, 5.49; S, 3.64. Found: C, 76.64; H, 5.71; S, 3.39.

10b: R_f 0.45 (hexane/EtOAc = 1/1); $[\alpha]_D^{22}$ +117 (*c* 0.960, $CHCl_3$); ^{1}H NMR (400 MHz, $CDCl_3$) δ 2.75 (t, 1H, *J* = 4.4 Hz), 2.79 (dd, 1H, *J* = 4.8, 2.4 Hz), 3.32 (ddd, 1H, *J* = 5.6, 4.4, 2.4 Hz), 4.77 (d, 1H, *J* = 12.0 Hz), 4.79 (d, 1H, *J* = 5.6 Hz), 4.81 (d, 1H, *J* = 12.0 Hz), 4.88–5.15 (m, 8H), 5.96 (d,

1H, *J* = 2.0 Hz), 6.15 (d, 1H, *J* = 2.0 Hz), 6.40 (s, 2H), 7.21–7.41 (m, 28H), 7.64–7.66 (m, 2H); ^{13}C NMR (100 MHz, $CDCl_3$) δ 44.8, 54.66, 54.71, 70.2, 70.7, 71.3, 75.1, 81.9, 94.1, 94.8, 106.0, 114.0, 124.5, 127.1, 127.5, 127.66, 127.69, 127.8, 128.0, 128.1, 128.3, 128.4, 128.6, 128.9, 131.7, 135.7, 135.8, 136.7, 137.7, 138.5, 145.2, 152.9, 159.1, 159.8, 163.3; IR (neat) 3050, 3000, 2900, 2850, 1940, 1860, 1800, 1580, 1490, 1420, 1330, 1220, 1150, 1100, 1050 cm^{-1}; Anal. calcd for $C_{56}H_{48}O_8S$: C, 76.34; H, 5.49; S, 3.64. Found: C, 76.58; H, 5.76; S, 3.74.

Preparation of bromohydrin SUP-5a (more polar)

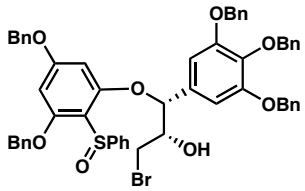


SUP-5a

To a solution of less polar ether **10a** (262 mg, 0.297 mmol) in THF (3.0 mL), a solution of Li_2NiBr_4 (1.11 mL, ca. 0.4 M THF solution, 0.444 mmol) was added at 0 °C. After stirring for 6 h, the reaction was quenched by adding pH 7 phosphate buffer, and the products were extracted with EtOAc (x3). The combined organic extracts were washed with brine, dried ($MgSO_4$), and concentrated in vacuo. The residue was purified by flash column chromatography (silica gel, hexane/EtOAc = 2/1) to afford more polar bromohydrin **SUP-5a** (288 mg, quant) as a colorless oil.

SUP-5a: R_f 0.50 (hexane/EtOAc = 2/1); $[\alpha]_D^{22}$ +17.8 (*c* 1.18, $CHCl_3$); ^{1}H NMR (400 MHz, $CDCl_3$) δ 2.87 (dd, 1H, *J* = 10.4, 6.4 Hz), 2.95 (dd, 1H, *J* = 10.4, 4.4 Hz), 3.55 (d, 1H, *J* = 6.8 Hz), 3.64–3.72 (m, 1H), 4.76 (d, 1H, *J* = 11.6 Hz), 4.82 (d, 1H, *J* = 11.6 Hz), 4.76 (d, 1H *J* = 11.6 Hz), 4.82 (d, 1H, *J* = 11.6 Hz), 4.98 (d, 1H, *J* = 11.2 Hz), 5.02 (d, 1H, *J* = 11.2 Hz), 5.06 (d, 2H, *J* = 12.0 Hz), 5.11 (d, 2H, *J* = 12.0 Hz), 5.16 (d, 2H, *J* = 4.0 Hz), 5.85 (d, 1H, *J* = 2.0 Hz), 6.22 (d, 1H, *J* = 2.0 Hz), 6.83 (s, 2H), 7.21–7.49 (m, 28H), 7.57–7.59 (m, 2H); ^{13}C NMR (100 MHz, $CDCl_3$) δ 33.6, 70.4, 70.8, 70.9, 74.5, 74.9, 106.5, 112.3, 124.0, 126.9, 127.4, 127.50, 127.55, 127.9, 128.0, 128.1, 128.2, 128.3, 128.5, 128.8, 129.4, 131.4, 135.4, 135.6, 136.8, 137.8, 138.1, 146.0, 152.7, 157.8, 159.7, 163.4; IR (neat) 3350, 3050, 3000, 2900, 1950, 1880, 1800, 1580, 1430, 1160, 1110 cm^{-1}; Anal. calcd for $C_{56}H_{49}BrO_8S$: C, 69.92; H, 5.13; S, 3.33. Found: C, 69.69; H, 5.25; S, 3.31.

Preparation of bromohydrin SUP-5b (less polar)

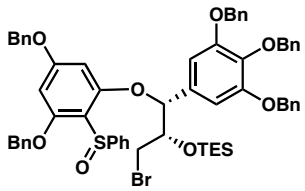


SUP-5b

To a solution of more polar ether **10b** (184 mg, 0.209 mmol) in THF (2.0 mL), a solution of Li_2NiBr_4 (0.679 mL, 0.4 M THF solution, 0.272 mmol) was added at 0 °C. After stirring for 6 h, the reaction was quenched by adding pH 7 phosphate buffer, and the products were extracted with EtOAc (x3). The combined organic extracts were washed with brine, dried ($MgSO_4$), and concentrated in vacuo. The residue was purified by flash column chromatography (silica gel, hexane/EtOAc = 2/1) to afford less polar bromohydrin **SUP-5b** (180 mg, 90%) as a colorless oil.

SUP-5b: R_f 0.60 (hexane/EtOAc = 2/1); $[\alpha]_D^{22}$ +143 (*c* 1.14, $CHCl_3$); ^{1}H NMR (400 MHz, $CDCl_3$) δ 2.90 (dd, 1H, *J* = 10.8, 2.8 Hz), 3.43 (dd, 1H, *J* = 10.8, 3.2 Hz), 3.75–3.78 (m, 1H), 4.75–4.88 (m, 7H), 4.95 (d, 1H, *J* = 10.8 Hz), 4.99 (d,1H, *J* = 10.8 Hz), 5.17 (s, 2H), 5.79 (d, 1H, *J* = 2.0 Hz), 6.21 (s, 2H), 6.25 (d, 1H, *J* = 2.0 Hz), 6.75 (s, 1H), 7.15–7.51 (m, 28H), 7.64–7.66 (m, 2H); ^{13}C NMR (100 MHz, $CDCl_3$) δ 34.4, 70.2, 71.0, 71.1, 73.6, 74.9, 85.7, 93.3, 95.2, 105.2, 112.7, 124.2, 126.95, 127.44, 127.5, 127.6, 127.88, 127.94, 128.1, 128.22, 128.30, 128.33, 128.4, 128.6, 129.0, 132.2, 135.4, 135.7, 136.3, 137.5, 138.4, 145.5, 152.8, 159,7, 160.0, 163.9; IR (neat) 3260, 3050, 3010, 2960, 2850, 1945, 1870, 1800, 1590, 1490, 1450, 1425, 1450, 1420, 1360, 1330, 1230, 1160, 1130, 1020 cm^{-1}; Anal. calcd for $C_{56}H_{49}BrO_8S$: C, 69.92; H, 5.13; S, 3.33. Found: C, 69.68; H, 5.14; S, 3.53.

Preparation of cyclization precursor 11a (less polar)



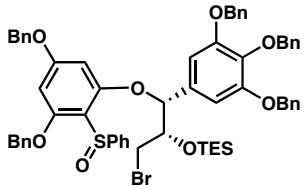
11a

To a solution of more polar bromohydrin **SUP-5a** (195 mg, 0.203 mmol) and 2,6-lutidine (66.4 mg, 0.620 mmol) in CH_2CL_2 (2.0 mL) was added TESOTf (80.5 mg, 0.305 mmol) at 0 °C. After stirring for 1 h, the reaction was quenched by adding diethylamine (0.5 mL), and the products were diluted by 5% citric acid solution and extracted with EtOAc (x3). The combined organic extracts were washed with saturated aqueous $NaHCO_3$ and brine, dried ($MgSO_4$), and concentrated in vacuo.

The residue was purified by flash column chromatography (hexane/EtOAc = 4/1) to afford less polar silyl ether **11a** (213 mg, 98%) as a colorless oil.

11a: R_f 0.70 (hexane/EtOAc = 3/1); $[\alpha]_D^{21}$ +43 (*c* 0.90, $CHCl_3$); ^{1}H NMR (400 MHz, $CDCl_3$) δ 0.46–0.61 (m, 6H), 0.90 (t, 9H, *J* = 8.0 Hz), 2.67 (dd, 1H, *J* = 10.4, 7.2 Hz), 3.42 (dd, 1H, *J* = 10.4, 4.0 Hz), 3.66–3.80 (m, 1H), 4.79 (s, 2H), 4.94–5.14 (m, 9H), 5.87 (d, 1H, *J* = 2.0 Hz), 6.16 (d, 1H, *J* = 2.0 Hz), 6.70 (s, 2H), 7.20–7.40 (m, 28H), 7.51–7.54 (m, 2H); ^{13}C NMR (100 MHz, $CDCl_3$) δ 5.0, 6.9, 35.0, 70.3, 70.7, 70.9, 74.8, 75.0, 81.2, 93.5, 94.4, 106.7, 113.6, 124.2, 127.0, 127.50, 127.57, 127.6, 127.85, 127.93, 128.23, 128.29, 128.4, 128.5, 128.7, 130.9, 135.6, 135.8, 136.8, 127.7, 138.1, 145.8, 152.4, 158.4, 160.0, 163.4; IR (neat) 3050, 3020, 2950, 2860, 1940, 1870, 1800, 1750, 1590, 1430, 1220, 1160, 1110, 1030 cm^{-1}; Anal. calcd for $C_{62}H_{63}BrO_8SSi$: C, 69.19; H, 5.90; S, 2.98. Found: C, 68.94; H, 6.06; S, 3.18.

Preparation of cyclization precursor 11b (more polar)



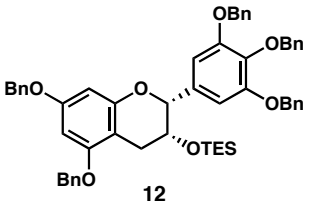
11b

To a solution of less polar bromohydrin **SUP-6b** (94.9 mg, 98.7μmol) and 2,6-lutidine (32.3 mg, 0.301 mmol) in CH_2Cl_2 (1.0 mL) was added TESOTf (39.1 mg, 0.148 mmol) at 0 °C. After stirring for 1 h, the reaction was quenched by adding diethylamine (0.5 mL), and the products were diluted by 5% citric acid solution and extracted with EtOAc (x3). The combined organic extracts were successively washed with saturated aqueous $NaHCO_3$ and brine, dried ($MgSO_4$), and concentrated in vacuo. The residue was purified by flash column chromatography (hexane/EtOAc = 4/1) to afford more polar silyl ether **11b** (106 mg, quant) as a colorless oil.

11b: R_f 0.60 (hexane/EtOAc = 3/1); $[\alpha]_D^{24}$ +128 (*c* 0.330, $CHCl_3$); ^{1}H NMR (400 MHz, $CDCl_3$) δ 0.39–0.54 (m, 6H), 0.87 (t, 9H, *J* = 8.0 Hz), 3.12 (dd, 1H, *J* = 9.2, 4.0 Hz), 4.01–4.12 (m, 2H), 4.72 (d, 1H, *J* = 11.6 Hz), 4.76 (d, 1H, *J* = 11.6 Hz), 4.84–5.12 (m, 8H), 5.22 (d, 1H, *J* = 2.8 Hz), 5.84 (d, 1H, *J* = 2.0 Hz), 6.15 (d, 1H, *J* = 2.0 Hz), 6.37 (s, 2H), 7.18–7.40 (m, 28H), 7.79 (m, 2H); ^{13}C NMR (100 MHz, $CDCl_3$) δ 4.8, 6.9, 34.1, 70.1, 70.7, 71.1, 75.0, 75.8, 81.4, 93.7, 94.6, 106.0, 113.8, 124.6, 127.0, 127.4, 127.6, 127.7, 127.8, 128.16, 128.26, 128.3, 128.4, 128.5, 128.8, 132.4, 135.6, 135.8, 136.8, 137.7, 138.0, 145.6, 152.6, 159.6, 159.7, 163.3; IR (neat) 3050, 3020, 2950, 2860, 1940, 1860, 1800, 1580, 1420, 1230, 1160, 1110 cm^{-1}; Anal. calcd for $C_{62}H_{63}BrO_8SSi$: C, 69.19; H, 5.90;

S, 2.98. Found: C, 69.39; H, 6.14; S, 3.17.

Preparation of 3-*O*-silyl flavan-3-ol 12



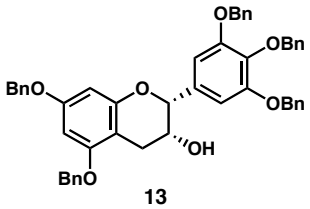
12

From **11a**: To a solution of less polar silylether **11a** (27.1 mg, 25.2 μmol) in THF (1.0 mL) was added PhLi (75 μL, 0.67 M cyclohexane–ether solution, 50 μmol) at room temperature. After stirring for 45 min, the reaction was quenched by adding saturated aqueous NH_4Cl, and the products were extracted with EtOAc (x3). The combined organic extracts were successively washed with saturated aqueous $NaHCO_3$ and brine, dried ($MgSO_4$), and concentrated in vacuo. The residue was purified by PTLC (hexane/acetone = 4/1) to afford flavan **12** (17.7 mg, 81%) as a colorless oil.

From **11b**: To a solution of more polar silylether **11b** (40.5 mg, 37.6 μmol) in THF (1.5 mL) was added PhLi (0.14 mL, 0.55 M cyclohexane–ether solution, 77 μmol) at room temperature. After stirring for 40 min, the reaction was quenched by adding saturated aqueous NH_4Cl, and the products were extracted with EtOAc (x3). The combined organic extracts were successively washed with saturated aqueous $NaHCO_3$ and brine, dried ($MgSO_4$), and concentrated in vacuo. The residue was purified by PTLC (hexane/acetone = 4/1) to afford flavan-3-ol **12** (20.2 mg, 62%) as a colorless oil.

12: R_f 0.55 (hexane/EtOAc = 2/1); $[\alpha]_D^{24}$ –18.7 (*c* 1.22, $CHCl_3$); ^{1}H NMR (400 MHz, $CDCl_3$) δ 0.34–0.49 (m, 6H), 0.78 (t, 9H, *J* = 7.6 Hz), 2.80 (dd, 1H, *J* = 16.8, 3.6 Hz), 2.87 (dd, 1H, *J* = 16.8, 4.0 Hz), 4.18–4.24 (m, 1H), 4.90 (s, 1H), 4.98–5.06 (m, 6H), 5.09 (s, 4H), 6.24 (d, 1H, *J* = 2.0 Hz), 6.26 (d, 1H, *J* = 2.0 Hz), 6.80 (s, 2H), 7.21–7.46 (m, 25H); ^{13}C NMR (100 MHz, $CDCl_3$) δ 4.8, 6.8, 28.6, 67.2, 69.9, 70.9, 71.3, 75.3, 79.1, 93.5, 94.6, 101.7, 106.9, 127.0, 127.4, 127.65, 127.69, 127.8, 128.0, 128.32, 128.39, 128.47, 128.50, 134.7, 136.9, 137.1, 137.2, 137.8, 138.0, 152.4, 155.3, 157.8, 158.5; IR (neat) 3350, 3050, 3000, 2950, 2860, 1940, 1870, 1800, 1615, 1590, 1150, 1120 cm^{-1}; Anal. calcd for $C_{56}H_{58}O_7Si$: C, 77.21; H, 6.71. Found: C, 76.98; H, 6.85.

Preparation of alcohol 13

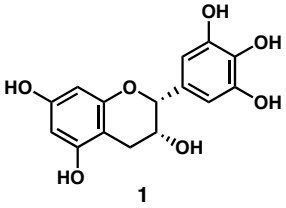


13

To a solution of silylether **12** (88.0 mg, 0.101 mmol) in THF (2.0 mL) was added TBAF (0.13 mL, 1.0 M THF solution, 0.13 mmol) at 0 °C. After stirring for 2 h, the reaction was quenched by adding pH 7 phosphate buffer, and the products were extracted with EtOAc (x3). The combined organic extracts were washed with brine, dried ($MgSO_4$), and concentrated in vacuo. The residue was purified by PTLC (hexane/EtOAc = 2/1) to afford alcohol **13** (75 mg, 99%) as an amorphous solid.

13: R_f 0.50 (hexane/EtOAc = 3/1); mp 40–42 °C; $[\alpha]_D^{24}$ –16.7 (*c* 1.20, $CHCl_3$); ^{1}H NMR (400 MHz, $CDCl_3$) δ 1.64 (d, 1H, *J* = 5.6 Hz), 2.93 (dd, 1H, *J* = 17.6, 4.4 Hz), 3.01 (dd, 1H, *J* = 17.6, 2.0 Hz), 4.21 (brs, 1H), 4.90 (s, 1H), 5.00–5.03 (m, 4H), 5.06 (s, 2H), 5.14 (s, 4H), 6.29 (s, 2H), 6.82 (s, 2H), 7.25–7.43 (m, 25H); ^{13}C NMR (100 MHz, $CDCl_3$) δ 28.2, 66.4, 69.9, 70.1, 71.3, 75.2, 78.5, 94.1, 94.7, 100.9, 106.1, 127.1, 127.4, 127.5, 127.7, 127.8, 127.9, 128.1, 128.42, 128.44, 128.5, 133.6, 136.8, 136.9, 137.7, 138.3, 152.9, 155.0, 158.2, 158.7; IR (neat) 3500, 3050, 3020, 2900, 1950, 1870, 1800, 1615, 1590, 1495, 1150, 1110 cm^{-1}; Anal. calcd for $C_{50}H_{44}O_7$: C, 79.35; H, 5.86. Found: C, 79.58; H, 6.05.

Preparation of (–)-EGC (1)



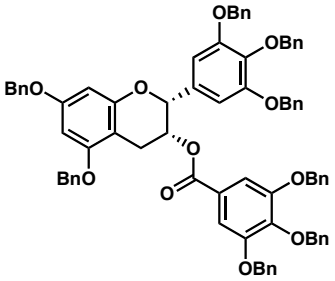
1

A mixture of **13** (41.0 mg, 54.2 μmol) and 20% $Pd(OH)_2$/C (8.0 mg, ASCA2^{TM}) in THF (4.0 mL), MeOH (4.0 mL), and H_2O (1.0 mL) was stirred under H_2 atmosphere for 5 h at room temperature. The mixture was carefully filtered through a Celite® pad under Ar atmosphere, and roughly half volume of the filtrate was evaporated. The residue was purified by Sephadex® LH-20 (eluent: MeOH) to afford a fraction including (–)-epigallocatechin (**1**) in a MeOH, to which H_2O (ca. 2 mL) was added, and concentration in vacuo until volatile materials were removed, lyophilization and vacuum-drying (P_2O_5) gave (–)-epigallocatechin (**1**) (11.8 mg, 72%) as a white powder.

1: R_f 0.40 ($CHCl_3$/MeOH = 2/1); mp 155–157 °C; $[\alpha]_D^{21}$ –56.0 (*c* 1.02, acetone/H_2O = 1/1); ^{1}H NMR (400 MHz, d_6-acetone) δ 2.73 (dd, 1H, *J* = 16.8, 3.4 Hz), 2.85 (dd, 1H, *J* = 16.8, 4.6 Hz),

4.15–4.21 (m, 1H), 4.82 (s, 1H), 5.91 (d, 1H, J = 2.0 Hz), 6.01 (d, 1H, J = 2.0 Hz), 6.56 (s, 2H); ^{13}C NMR (100 MHz, CD_3OD) δ 29.2, 67.5, 79.9, 95.8, 96.4, 100.0, 106.9, 131.3, 133.7, 146.7, 157.2, 157.6, 157.9; IR (neat) 3304, 3247, 1714, 1701, 1615, 1606, 1518, 1493, 1461, 1319, 1294, 1189, 1144, 1090, 1062, 1014 cm^{-1}; Anal. calcd for $C_{15}H_{14}O_7$: C, 58.82; H, 4.61. Found: C, 58.60; H, 4.72.

Preparation of ester SUP-6

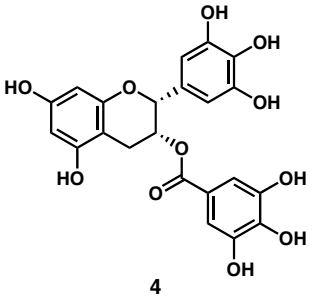


SUP-6

To a solution of **13** (69 mg, 91 μmol) and 3,4,5-tris(benzyloxy)benzoic acid (60.1 mg, 137 μmol) in CH_2Cl_2 (1.0 mL) were added DMAP (2.2 mg, 18 μmol), NEt_3 (51 μL, 0.36 mmol), and 1-ethyl-3-(3-dimethylaminopropyl)carbodiimide hydrochloride (EDC·HCl, 35 mg, 0.18 mmol) at 0 °C. After stirring for 17 h at room temperature, the reaction was quenched by adding water at 0 °C. The products were extracted with EtOAc (x3) and the combined organic extracts were washed with brine, dried (Na_2SO_4), and concentrated in vacuo. The residue was purified by PTLC (hexane/toluene/EtOAc = 3/3/1) to afford ester **SUP-6** (91 mg, 84%) as an amorphous solid.

SUP-6: R_f 0.65 (hexane/toluene/EtOAc = 3/3/1); mp 123–125 °C; $[\alpha]_D^{22}$ –70.0 (*c* 1.03, $CHCl_3$); ^{1}H NMR (400 MHz, $CDCl_3$) δ 3.05 (dd, 1H, J = 17.6, 2.4 Hz), 3.12 (dd, 1H, J = 17.6, 3.6 Hz), 4.67 (d, 2H, J = 12.0 Hz), 4.80 (d, 2H, J = 12.0 Hz), 4.91 (s, 1H), 4.91–5.08 (m, 12H), 5.64–5.69 (m, 1H), 6.34 (d, 1H, J = 2.0 Hz), 6.39 (d, 1H, J = 2.0 Hz), 6.73 (s, 2H), 7.15–7.42 (m, 42H); ^{13}C NMR (100 MHz, $CDCl_3$) δ 26.2, 68.2, 69.9, 70.1, 71.0, 71.1, 75.0, 75.1, 77.9, 93.9, 94.6, 100.9, 106.6, 109.1, 124.9, 127.1, 127.4, 127.6, 127.66, 127.69, 127.73, 127.8, 127.88, 127.91, 127.95, 128.04, 128.1, 128.2, 128.35, 128.41, 128.42, 128.46, 133.1, 136.3, 136.7, 137.3, 137.6, 138.3, 142.6, 152.2, 152.7, 155.5, 157.9, 158.7, 164.6; IR (neat) 3050, 3010, 2920, 2850, 1710, 1610, 1580, 1490, 1450, 1420, 1360, 1320, 1210, 1140, 1105, 1020, 905, 840, 805, 735, 695 cm^{-1}; Anal. calcd for $C_{78}H_{66}O_{11}$: C, 79.44; H, 5.64. Found: C, 79.73; H, 5.71.

Preparation of (–)-EGCg (4)

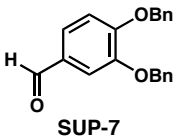


4

A mixture of **SUP-6** (58.2mg, 49.3 μmol) and 5% $Pd(OH)_2/C$ (12 mg, ASCA2^{TM}) in THF (4.0 mL), MeOH (4.0 mL) was hydrogenated under H_2 atmosphere at room temperature for 8 h. The mixture was filtered through a glass fiber filter under Ar atmosphere, and half volume of the filtrate was evaporated. The residue was purified by Sephadex® LH-20 (eluent: MeOH) to afford a fraction including (–)-epigallocatechin 3-gallate (**4**) in a MeOH, to which H_2O (ca. 2 mL) was added, and concentration in vacuo until volatile materials were removed, lyophilization and vacuum-drying (P_2O_5) gave (–)-epigallocatechin 3-gallate (**4**) (18.9 mg, 84%) as a white powder.

4: R_f 0.45 ($CHCl_3$/MeOH = 2/1); mp 219–221 °C (decomp.); $[\alpha]_D^{23}$ = –218 (*c* 0.660, acetone/H_2O = 1/1); ^{1}H NMR (400 MHz, CD_3OD) δ 2.83 (dd, 1H, *J* = 17.2, 2.4 Hz), 2.97 (dd, 1H, *J* = 17.2, 4.8 Hz), 4.96 (s, 1H), 5.50–5.55, (m, 1H), 5.95 (s, 2H), 6.49 (s, 2H), 6.94 (s, 2H); ^{13}C NMR (100 MHz, CD_3OD) δ 26.9, 69.9, 78.6, 95.8, 96.5, 99.4, 106.8, 110.2, 121.4, 130.7, 133.7, 139.7, 146.2, 146.6, 157.1, 157.69, 157.74, 167.5; IR (neat) 3312, 2519, 1686, 1605, 1533, 1517, 1448, 1308, 1226, 1188, 1137, 1092, 1012, 819, 743 cm^{-1}; Anal. calcd for $C_{22}H_{18}O_{11}$: C, 57.65; H, 3.96. Found: C, 57.42; H, 4.18.

Preparation of aldehyde SUP-7



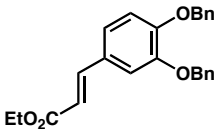
SUP-7

To a solution of 3,4-dihydroxybezaldehyde (10.0 g, 72.4 mmol) in acetone (100 mL) were added K_2CO_3 (40.0 g, 289 mmol) and benzylbromide (25.8 mL, 217 mmol) at 0 °C. After stirring for 15 h at room temperature, the reaction was quenched by adding ethylenediamine (10 mL) at 0 °C. The mixture was extrated with EtOAc (x3), and the combined organic extracts were washed with brine, dried (Na_2SO_4), and concentrated in vacuo. The residue was recrystallized from a mixed solvent (hexane/EtOAc = 5/1) to afford aldehyde **SUP-7** (17.9 g, 78%) as a pale yellow solid.

SUP-7: R_f 0.53 (hexane/EtOAc = 1/1); mp 84–86 °C (hexane/EtOAc); ^{1}H NMR (400 MHz, $CDCl_3$) δ 5.21 (s, 2H), 5.27 (s, 2H), 7.02 (d, 1H, *J* = 8.4 Hz), 7.30–7.49 (m, 12H), 9.81 (s, 1H); ^{13}C NMR

(100 MHz, $CDCl_3$) δ 70.8, 70.9, 112.3, 113.0, 126.5, 127.0, 127.2, 127.9, 128.0, 128.4, 128.5, 130.2, 136.1, 136.4, 149.1, 154.1, 190.6; IR (KBr) 3080, 3026, 2931, 2895, 2856, 2819, 2755, 2728, 1676, 1597, 1512, 1454, 1435, 1387, 1282, 1243, 1167, 1136, 1024, 821, 736, 698 cm^{-1}; Anal. calcd for $C_{21}H_{18}O_3$: C, 79.22; H, 5.70. Found: C, 79.19; H, 5.85.

Preparation of ester SUP-8

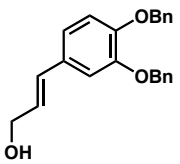


SUP-8

To a suspension of NaH (2.08 g, 63% dispersion in mineral oil, 54.6 mmol, washed with hexane) in THF (162 mL), was dropped phosphonoacetic acid triethyl ester (11.2 mL, 56.5 mmol) at 0 °C. After stirring for 1 h at the same temperature, a solution of aldehyde **SUP-7** (14.5 g, 45.5 mmol) in THF (20 mL) was added at 0 °C. The stirring was continued for 1 h at 0 °C. Adding water stopped the reaction, and the mixture was extracted with EtOAc (x3) and the combined organic extracts were washed with brine, dried (Na_2SO_4), and concentrated in vacuo. The residue was purified by flash column chromatography (hexane/EtOAc = 5/1) to afford unsaturated ester **SUP-8** (14.3 g, 81%) as a white solid.

SUP-8: R_f 0.59 (hexane/EtOAc = 1/2); mp 72–73 °C (hexane/EtOAc); ^1H NMR (300 MHz, $CDCl_3$) δ 1.28 (t, 3H, J = 7.1 Hz), 4.21 (q, 2H, J = 7.1 Hz), 5.13 (s, 2H), 5.14 (s, 2H), 6.20 (d, 1H, J = 16.0 Hz), 6.87 (d, 1 H, J = 8.2 Hz), 7.02 (dd, 1H, J = 8.2, 1.7 Hz), 7.20–7.50 (m, 11H), 7.53 (d, 1H, J = 16.0 Hz); ^{13}C NMR (75 MHz, $CDCl_3$) δ 14.2, 60.2, 70.8, 71.2, 113.6, 114.1, 116.0, 122.6, 127.0, 127.1, 127.4, 127.8, 136.6, 136.7, 144.1, 148.7, 148.8, 150.8, 167.0; IR (KBr) 3064, 3036, 2982, 2940, 2908, 2873, 1894, 1830, 1699, 1630, 1596, 1578, 1514, 1467, 1455, 1430, 1419, 1386, 1368, 1335, 1303, 1263, 1239, 1165, 1130, 1025, 1015, 998, 986, 975 cm^{-1}; Anal. calcd for $C_{25}H_{24}O_4$: C, 77.30; H, 6.23. Found: C, 77.46; H, 6.22.

Preparation of allyl alcohol SUP-9



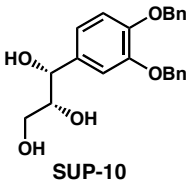
SUP-9

To a solution of unsaturated ester **SUP-8** (9.70 g, 25.0 mmol) in THF (125 mL) was slowly dropped DIBAL (1.01 M in hexane, 49.5 mL, 50.0 mmol) at –78 °C over 30 min. After stirring for 7 h at

–78 °C, the reaction was stopped by adding MeOH at –20 °C followed by warming to 0 °C. Saturated aqueous potassium sodium tartrate (Rochell's salt) was added, and the stirring was continued for 3 min. The products were extracted with EtOAc (x3), and the combined organic extracts were washed with brine, dried (Na_2SO_4), and concentrated in vacuo. Recrystallization (hexane/EtOAc =2/1) gave **SUP-2** (7.55 g, 87%) as a white solid.

SUP-9: R_f 0.17 (hexane/EtOAc = 2/1); mp 77–78 °C (hexane/EtOAc); ^{1}H NMR (300 MHz, $CDCl_3$) δ 1.39 (t, 1H, *J* = 5.0 Hz), 4.27 (dd, 2H, *J* = 6.0, 5.0 Hz), 5.15 (s, 2H), 5.16 (s, 2H), 6.17 (dt, 1H, *J* = 16.0, 6.0 Hz), 6.49 (d, 1H, *J* = 16.0 Hz), 6.82–6.85 (m, 2H), 7.01 (s, 1H), 7.25–7.47 (m, 10H); ^{13}C NMR (75 MHz, $CDCl_3$) δ 63.8, 71.3, 71.4, 113.0, 115.0, 120.3, 126.8, 127.3, 127.8, 128.4, 128.5, 130.5, 131.0, 137.2, 148.7, 148.9; IR (KBr) 3294, 3063, 3033, 2924, 2861, 1653, 1599, 1581, 1510, 1454, 1425, 1380, 1342, 1318, 1260, 1235, 1221, 1163, 1134, 1197, 1080, 1043, 1007, 963 cm^{-1}; Anal. calcd for $C_{23}H_{22}O_3$: C, 79.74; H, 6.40. Found: C, 79.98; H, 6.56.

Preparation of triol SUP-10



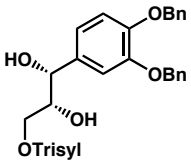
SUP-10

To a solution of potassium hexacyanoferrate(III) (11.7 g, 35.5 mmol) in a mixed solvent (118 mL, *t*-BuOH/H_2O = 1/1) were added K_2CO_3 (4.90 g, 35.5 mmol), methanesulfonamide (1.16 g, 11.8 mmol), $(DHQD)_2$-PHAL (462 mg, 0.592 mmol), and $K_2OsO_2(OH)_4$ (44.0 mg, 0.118 mmol) at room temperature. After stirring for 25 min at the same temperature, the mixture was cooled to 0 °C, to which allyl alcohol **SUP-9** (4.10 g, 11.8 mmol) was added at 0 °C. After stirring for 3.8 h, the reaction was quenched by adding aqueous sodium sulfite. The mixture was extracted with EtOAc (x3) and the combined organic extracts were washed with aqueous 2 M NaOH, dried (Na_2SO_4), and concentrated in vacuo. The residue was purified by flash column chromatography (silica gel, hexane/EtOAc = 5/1 to 0/1, gradient elution) to afford triol **SUP-10** (3.27g, 73%, 97% *ee*) as a white solid. Enantiomeric purity of **SUP-10** was assessed by HPLC analysis [CHIRALPAK® IB (Daicel), ϕ 4.6 x 250 mm, hexane/*i*-PrOH = 85/15, 1.0 mL/min flow rate, 45 °C, 239 nm, t_R = 17.8 min for the (*R*,*R*)-isomer and 18.7 min for the (*S*,*S*)-isomer.]

SUP-10: R_f 0.50 (EtOAc); mp 83–85 °C (hexane/EtOH); $[\alpha]_D^{27}$ –21 (*c* 1.0, $CHCl_3$); ^{1}H NMR (400 MHz, $CDCl_3$) δ 2.14 (brs, 1H), 2.85 (brs, 1H), 2.98 (brs, 1H), 3.39 (dd, 1H, *J* = 11.4, 4.9 Hz), 3.52 (dd, 1H, *J* = 11.4, 3.1 Hz), 3.61–3.70 (m, 1H), 4.57 (d, 1H, *J* = 6.7 Hz), 5.13 (s, 2H), 5.15 (s, 2H),

6.85 (dd, 1H, *J* = 8.2, 1.8 Hz), 6.90 (d, 1H, *J* = 8.2 Hz), 6.96 (d, 1H, *J* = 1.8 Hz), 7.24–7.50 (m, 10H); ^{13}C NMR (100 MHz, $CDCl_3$) δ 63.2, 71.2, 71.3, 74.5, 75.9, 113.6, 114.8, 119.7, 127.2, 127.4, 127.7, 128.3, 128.4, 133.6, 136.96, 137.00, 148.7, 148.8; IR (KBr) 3382, 3064, 3033, 2913, 2863, 1606, 1592, 1523, 1454, 1430, 1385, 1338, 1269, 1236, 1167, 1138, 1105, 1026, 1003, 731, 694 cm^{-1}; Anal. calcd for $C_{23}H_{24}O_5$: C, 72.61; H, 6.36. Found: C, 72.85; H, 6.26.

Preparation of sulfonate SUP-11

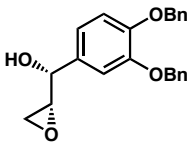


SUP-11

To a solution of 2,4,6-triisopropylbenzenesulfonyl chloride (2.98 g, 9.85 mmol) in pyridine (7.9 mL) was added triol **SUP-10** (1.50 g, 3.94 mmol) at 0 °C. After stirring for 23 h at 0 °C, the reaction mixture was poured into 1 M HCl at 0 °C. The mixture was extracted with EtOAc (x3), and the combined organic extracts were successively washed with water and brine, dried (Na_2SO_4), and concentrated in vacuo. The residue was purified by flash column chlomatography (silica gel, hexane/EtOAc = 2/1) to afford sulfonate **SUP-11** (2.30 g, 90%) as a white solid.

SUP-11: R_f 0.29 (hexane/EtOAc = 2/1); mp 75–78 °C (hexane/EtOAc); $[\alpha]_D^{27}$ +0.18 (*c* 0.53, $CHCl_3$); ^{1}H NMR (300 MHz, $CDCl_3$) δ 1.24 (d, 12H, *J* = 6.8 Hz), 1.25 (d, 6H, *J* = 7.0 Hz), 2.60 (d, 1H, *J* = 3.6 Hz), 2.64 (d, 1H, *J* = 4.8 Hz), 2.90 (sept, 1H, *J* = 7.0 Hz), 3.85–4.02 (m, 3H), 4.09 (sept, 2H, *J* = 6.8 Hz), 4.62 (dd, 1H, *J* = 5.8, 3.6 Hz), 5.12 (d, 2H, *J* = 8.7 Hz), 5.18 (d, 2H, *J* = 8.7 Hz), 6.83 (dd, 1H, *J* = 8.2, 1.9 Hz), 6.90 (d, 1H, *J* = 8.2 Hz), 6.99 (d, 1H, *J* = 1.9 Hz), 7.18 (s, 2H), 7.26–7.48 (m, 10H); ^{13}C NMR (75 MHz, $CDCl_3$) δ 23.8, 24.9, 25.0, 29.9, 34.4, 70.3, 72.1, 74.2, 74.7, 113.6, 115.2, 119.9, 124.1, 127.5, 127.7, 128.0, 128.7, 128.8, 129.1, 133.2, 137.3, 137.4, 149.2, 149.3, 151.2, 154.3; IR (neat) 3579, 3276, 3065, 3037, 2959, 2872, 1774, 1731, 1600, 1508, 1455, 1426, 1343, 1254, 1475, 1130, 1104 cm^{-1}; Anal. calcd for $C_{38}H_{46}O_7S$: C, 70.56; H, 7.17; S, 4.96. Found: C, 70.35; H, 7.38; S, 4.94.

Preparation of epoxide 14

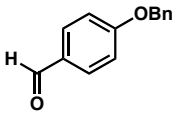


14

To a solution of sulfonyl ester **SUP-11** (685 mg, 1.06 mmol) in the mixed solvent (5.5 mL, methanol/1,4-dioxane = 2/1), K_2CO_3 (290 mg, 2.10 mmol) was added at 0 °C. After stirring for 2 h at 0 °C, the reaction mixture was diluted with EtOAc. The layers were separated, and the aqueous layer was extracted with EtOAc (x2). The combined organic extracts were washed with brine, dried (Na_2SO_4), and concentrated in vacuo. The residue was purified by flash column chromatography (silica gel, hexane/EtOAc = 2/1) to afford epoxide **14** (358 mg, 93%, 97% ee) as a colorless oil. Enantiomeric purity of **14** was assessed by the HPLC analysis [CHIRALPAK® AD-H (Daicel), ϕ 4.6 x 250 mm, hexane/*i*-PrOH = 85/15, 1.0 mL/min flow rate, 35 °C, 235 nm, t_R = 22.9 min for the (*R*,*R*)-isomer and 29.1 min for the (*S*,*S*)-isomer.]

14: R_f 0.31 (hexane/EtOAc = 2/1); $[\alpha]_D^{24}$ –0.60 (*c* 1.1, $CHCl_3$); ^{1}H NMR (400 MHz, $CDCl_3$) δ 2.36 (d, 1H, *J* = 5.1 Hz), 2.73 (dd, 1H, *J* = 4.9, 2.7 Hz), 2.79 (t, 1H, *J* = 4.9 Hz), 3.13 (ddd, 1H, *J* = 5.1, 4.9, 2.7 Hz), 4.35 (t, 1H, *J* = 5.1 Hz), 5.16 (s, 2H), 5.17 (s, 2H), 6.93 (d, 1H, *J* = 8.4 Hz), 6.89 (dd, 1H, *J* = 8.4, 1.3 Hz), 7.03 (d, 1H, *J* = 1.3 Hz), 7.23–7.50 (m, 10H); ^{13}C NMR (75 MHz, $CDCl_3$) δ 45.3, 55.9, 71.27, 71.32, 74.1, 113.3, 114.9, 119.3, 127.1, 127.3, 127.7, 127.73, 128.4, 133.4, 137.0, 137.1, 148.8, 149.0; IR (neat) 3420, 3050, 3024, 2923, 2872, 1600, 1582, 1510, 1450, 1421, 1378, 1260, 1217, 1015, 736, 696 cm^{-1}; Anal. calcd for $C_{23}H_{22}O_4$: C, 76.22; H, 6.12. Found: C, 76.06; H, 6.31.

Preparation of aldehyde SUP-12



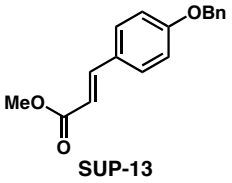
SUP-12

To a solution of *p*-hydroxybenzaldehyde (10.0 g, 81.9 mmol) in acetone (410 mL), potassium carbonate (31.7 g, 230 mmol) and benzyl bromide (10.7 mL, 90.2 mmol) were added at room temperature. After refluxing for 2 h, the reaction was stopped by adding diethylamine (10 mL) at room temperature. The products were extracted with EtOAc (x3), and the combined organic extracts were washed successively with water, saturated aqueous $NaHCO_3$, brine, and dried (Na_2SO_4), and concentrated in vacuo. The residue was purified by recrystallization (hexane/EtOAc = 3/1) to give **SUP-12** (14.05 g, 81%), and the filtrate was concentrated, and the residue was purified by flash column chromatography (hexane/EtOAc = 6/1) to give additional **SUP-12** (2.11 g, 12%) as a white solid.

SUP-12: R_f 0.46 (hexane/EtOAc = 4/1); mp 71–72 °C (hexane/EtOAc); ^{1}H NMR (300 MHz, $CDCl_3$) δ 5.16 (s, 2H), 7.08 (d, 2H, *J* = 8.9 Hz), 7.33–7.45 (m, 5H), 7.84 (d, 2H, *J* = 8.9 Hz), 9.89 (s,

1H); ^{13}C NMR (75 MHz, $CDCl_3$) δ 70.2, 115.1, 127.4, 128.2, 128.6, 130.0, 131.9, 135.9, 163.6, 190.7; IR (neat) 3050, 3036, 2830, 2804, 2745, 1685, 1598, 1574, 1509, 1462, 1452, 1425, 1394, 1321, 1301, 1259, 1210, 1163, 1110, 1077, 1018, 973, 944, 903, 866, 819, 788, 716, 695 cm^{-1}; Anal. calcd for $C_{14}H_{12}O_2$: C, 79.22; H, 5.70. Found: C, 79.05; H, 5.96.

Preparation of ester SUP-13

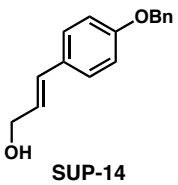


SUP-13

To a cooled suspension (0 °C) of NaH (1.9 g, 63% dispersion in mineral oil, 77 mmol, washed with hexane) in THF (300 mL), phosphonoacetic acid trimethyl ester (13.1 mL, 91.3 mmol) was slowly dropwised at 0 °C. After stirring for 1 h, a solution of aldehyde **SUP-12** (14.9 g, 70.2 mmol) in THF (50 mL) was slowly added at 0 °C over a 30-min period, and the stirring was continued for 16 h, and then the reaction was stopped by adding saturated aqueous $NaHCO_3$. The products were extracted with EtOAc (x3), and the combined organic extracts were washed with brine, dried (Na_2SO_4), and concentrated in vacuo. The residue was purified by precipitation (hexane/EtOAc = 3/1) to afford ester **SUP-13** (17.7 g, 94%) as a white solid.

SUP-13: R_f 0.45 (toluene/EtOAc = 8/1); mp 138–139 °C (hexane/EtOAc); ^{1}H NMR (300 MHz, $CDCl_3$) δ 3.78 (s, 3H), 5.08 (s, 2H), 6.30 (d, 1H, J = 16.0 Hz), 6.96 (d, 2H, J = 8.7 Hz), 7.26–7.43 (m, 5H), 7.45 (d, 2H, J = 8.7 Hz), 7.64 (d, 1H, J = 16.0 Hz); ^{13}C NMR (75 MHz, $CDCl_3$) δ 51.4, 69.9, 115.0, 115.2, 127.1, 127.2, 127.9, 128.5, 129.5, 136.2, 144.3, 160.3, 167.5; IR (neat) 3013, 2994, 2949, 2912, 2860, 1715, 1635, 1603, 1572, 1510, 1463, 1444, 1422, 1381, 1301, 1289, 1250, 1192, 1184, 1113, 1105, 1013, 986, 934, 818, 697 cm^{-1}; Anal. calcd for $C_{17}H_{16}O_3$: C, 76.10; H, 6.01. Found: C, 76.31; H, 6.17.

Preparation of allyl alcohol SUP-14



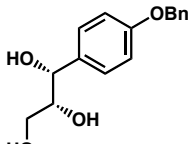
SUP-14

To a solution of ester **SUP-13** (5.00 g, 18.6 mmol) in THF (93 mL), a solution of DIBAL (17.2 mL,

2.39 M solution in THF, 41.0 mmol) was slowly dropped at –78 °C. After stirring for 2 h at the same temperature, the reaction was quenched by adding aqueous potassium sodium tartrate, and the stirring was continued over night at ambient temperature. The products were extracted with EtOAc (x3), and the combined organic extracts were washed with brine, dried (Na_2SO_4), and concentrated in vacuo. The residue was purified by precipitation (hexane/EtOAc = 3/1) to afford allyl alcohol **SUP-14** (4.16 g, 93%) as a white solid.

SUP-14: R_f 0.26 (hexane/EtOAc = 2/1); mp 114–115 °C (hexane/EtOAc); ^{1}H NMR (300 MHz, $CDCl_3$) δ 1.37 (t, 1H, *J* = 5.8 Hz), 4.30 (dd, 2H, *J* = 6.0, 5.8 Hz), 5.07 (s, 2H), 6.24 (dt, 1H, *J* = 15.9, 6.0 Hz), 6.56 (d, 1H, *J* = 15.9 Hz), 6.93 (d, 1H, *J* = 8.9 Hz), 7.26–7.45 (m, 7H); ^{13}C NMR (75 MHz, $CDCl_3$) δ 64.6, 70.8, 115.8, 127.2, 128.2, 128.5, 128.8, 129.4, 130.5, 131.6, 137.7, 159.3; IR (neat) 3327, 3061, 3036, 2866, 1604, 1576, 1509, 1470, 1382, 1304, 1244, 1175, 1084, 1022, 1004, 969, 911, 836, 808, 780 cm^{-1}; Anal. calcd for $C_{16}H_{16}O_2$: C, 79.97; H, 6.71. Found: C, 80.02; H, 6.87.

Preparation of triol SUP-15



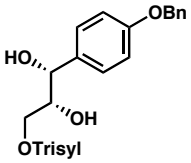
SUP-15

To a solution of potassium hexacyanoferrate(III) (14.5 g, 45.0 mmol) in the mixed solvent (375 mL, *t*-BuOH/H_2O = 1/1), were added K_2CO_3 (6.22 g, 45.0 mmol), methanesulfonamide (1.71 g, 18.0 mmol), $(DHQD)_2$-PHAL (0.12 g, 0.15 mmol), and $K_2OsO_2(OH)_4$ (28 mg, 0.075 mmol) at room temperature. After the stirring for 25 min at the same temperature, the resulting mixture was cooled to 0 °C, and allyl alcohol **SUP-14** (3.70 g, 15.4 mmol) was added to the mixture. After the stirring for 3.8 h at 0 °C, the reaction was quenched by adding aqueous sodium sulfite. The products was extracted with EtOAc (x3) and the combined organic extracts were washed with aqueous 2N KOH, dried (Na_2SO_4), and concentrated in vacuo. Recrystallization (hexane/EtOH = 6/1) gave triol **SUP-15** (3.85 g, 91%) as a white solid.

SUP-15: R_f 0.20 (hexane/EtOAc = 1/4); mp 90–92 °C (hexane/EtOH); $[\alpha]_D^{26}$ –24.9 (*c* 1.71, CD_3OD); ^{1}H NMR (300 MHz, CD_3OD) δ 3.35 (dd, 1H, *J* = 11.3, 6.5 Hz), 3.49 (dd, 1H, *J* = 11.3, 3.9 Hz), 3.68 (ddd, 1H, J = 6.5, 6.2, 3.9 Hz), 4.57 (d, 1H, *J* = 6.2 Hz), 5.04 (s, 2H), 6.98 (d, 2H, *J* = 8.9 Hz), 7.24–7.46 (m, 7H); ^{13}C NMR (75 MHz, CD_3OD) δ 64.6, 71.3, 75.5, 77.9, 116.1, 128.9, 129.2, 129.5, 129.9, 136.0, 139.1, 160.1; IR (neat) 3333, 2942, 2882, 2469, 1649, 1611, 1585, 1514, 1467, 1455, 1426, 1389, 1326, 1241, 1177, 1101, 1042, 1014, 991, 938, 919, 868, 828, 748, 699,

677 cm^{-1}; Anal. calcd for $C_{16}H_{18}O_4$: C, 70.02; H, 6.61. Found: C, 69.82; H, 6.53.

Preparation of sulfonate SUP-16

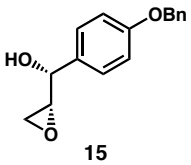


SUP-16

To a solution of triol **SUP-15** (1.00 g, 3.65 mmol) in CH_2Cl_2 (3.6 mL), pyridine (2.9 mL, 36 mmol) and 2,4,6-triisopropylbenzenesulfonyl chloride (2.76 g, 9.13 mmol) were added at 0 °C. After stirring for 27 h, the reaction was stopped by adding pH 7 phosphate buffer at 0 °C. The products were extracted with EtOAc (x3) and the combined organic extracts were washed with brine, dried (Na_2SO_4) and concentrated in vacuo. The residue was purified by flash column chromatography (silica gel, hexane/EtOAc = 2/1) to afford sulfonate **SUP-16** (1.54 g, 78%) as a white solid.

SUP-16: R_f 0.18 (hexane/EtOAc = 2/1); mp 104–106 °C (hexane/EtOAc); $[\alpha]_D^{26}$ –0.50 (*c* 1.0, $CHCl_3$); ^{1}H NMR (300 MHz, $CDCl_3$) δ 1.24 (d, 12H, *J* = 6.8 Hz), 1.26 (d, 6H, *J* = 6.8 Hz), 2.60 (d, 1H, *J* = 3.4 Hz), 2.68 (d, 1H, *J* = 4.5 Hz), 2.91 (sept, 1H, *J* = 6.8 Hz), 3.91–3.99 (m, 2H), 4.02–4.16 (m, 3H), 4.66 (dd, 1H, *J* = 5.5, 3.4 Hz), 5.06 (s, 2H), 6.95 (d, 2H, *J* = 8.8 Hz), 7.23–7.45 (m, 7H); ^{13}C NMR (75 MHz, $CDCl_3$) δ 23.5, 24.7, 29.7, 34.2, 69.5, 70.0, 73.2, 73.8, 115.0, 123.9, 127.5, 127.8, 128.0, 128.6, 128.9, 132.0, 136.8, 150.9, 154.0, 158.8; IR (neat) 3435, 2960, 2290, 2164, 2050, 1980, 1601, 1584, 1564, 1515, 1455, 1425, 1375, 1343, 1256, 1194, 1174, 1107, 1041, 972, 925, 880, 860, 847, 798, 780, 731, 695 cm^{-1}; Anal. calcd for $C_{31}H_{40}O_6S$: C, 68.86; H, 7.46; S, 5.93. Found: C, 69.03; H, 7.29; S, 5.66.

Preparation of epoxide 15



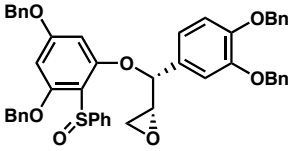
15

To a solution of **SUP-16** (1.42 g, 2.63 mmol) in MeOH (12.5 mL), powdered K_2CO_3 (686 mg, 2.68 mmol) was added at 0 °C in one portion. After stirring for 3 h at 0 °C, the mixture was filtered through a Celite® pad. After adding water to the filtrate, the products were extracted with EtOAc (x3) and the combined organic extracts were washed with brine, dried (Na_2SO_4), and concentrated in vacuo. The residue was purified by flash column chromatography (silica gel, hexane/EtOAc =

2/1) to afford epoxy alcohol **15** (616 mg, 92%, 99% *ee*) as a white solid. Enantiomeric purity of **15** was assessed by HPLC analysis [CHIRALPAK® AD-H (Daicel), ϕ 4.6 x 250 mm, hexane/*i*-PrOH = 95/5, 1.0 mL/min flow rate, 35 °C, 254 nm, t_R = 33.9 min for the (*S*,*S*)-isomer and 35.9 min for the (*R*,*R*)-isomer.]

15: R_f 0.45 (hexane/EtOAc = 1/1); mp 92–93 °C (hexane/EtOAc); $[\alpha]_D^{26}$ –4.56 (*c* 1.01, $CHCl_3$); ^{1}H NMR (300 MHz, $CDCl_3$) δ 2.57 (d, 1H, *J* = 4.6 Hz), 2.78 (dd, 1H, *J* = 4.8, 2.8 Hz), 2.82 (t, 1H, *J* = 4.8 Hz), 3.19 (ddd, 1H, *J* = 4.8, 4.6, 2.8 Hz), 4.39 (t, 1H, *J* = 4.6 Hz), 5.06 (s, 2H), 6.97 (d, 2H, *J* = 8.8 Hz), 7.26–7.50 (m, 7H); ^{13}C NMR (75 MHz, $CDCl_3$) δ 45.0, 55.6, 69.6, 73.7, 114.6, 127.0, 127.2, 127.6, 128.2, 132.2, 136.5, 158.3; IR (neat) 3450, 3008, 2896, 1613, 1584, 1513, 1498, 1455, 1384, 1316, 1241, 1198, 1179, 1138, 1100, 1077, 1040, 1025, 999, 921, 876, 696 cm^{-1}; Anal. calcd for $C_{16}H_{16}O_3$: C, 74.98; H, 6.29. Found: C, 74.80; H, 6.41.

Preparation of oixirane SUP-17



SUP-17

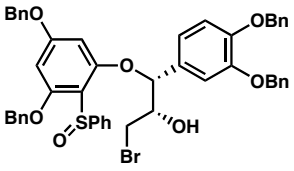
To a suspension of NaH (11 mg, 63% in mineral oil, 0.28 mmol, washed with hexane) in a mixed solvent of toluene (0.16 mL) and DMPU (0.04 mL) was added sulfoxide **8** (63.2 mg, 0.146 mmol) at room temperature. A solution of epoxide **14** (26.8 mg, 73.9 μmol) in a mixed solvent of toluene (0.21 mL) and DMPU (0.05 mL) was added at room temperature and stirring was continued for 80 min. The reaction was stopped by adding saturated aqueous $NaHCO_3$, and the mixture was extracted with EtOAc (x3). The combined organic extracts were washed with brine, dried (Na_2SO_4), and concentrated in vacuo. The residue was purified by PTLC (hexane/EtOAc = 1/1) to afford the less polar **SUP-17a** (19.0 mg, 33%) and the more polar **SUP-17b** (16.8 mg, 29%) as white a amorphous solid.

SUP-17a: R_f 0.75 (hexane/EtOAc = 1/1); mp 52–53 °C; $[\alpha]_D^{29}$ –7.05 (*c* 3.92, $CHCl_3$); ^{1}H NMR (300 MHz, $CDCl_3$) δ 2.41 (dd, 1H, *J* = 4.5, 2.6 Hz), 2.61(t, 1H, *J* = 4.5 Hz), 3.05 (ddd, 1H, *J* = 5.8, 4.5, 2.6 Hz), 4.71 (d, 1H, *J* = 5.8 Hz), 4.76–4.87 (m, 2H), 4.93 (d, 1H, *J* = 12.2 Hz), 5.06 (d, 1H, *J* = 12.2 Hz), 5.11 (s, 2H), 5.15 (d, 1H, *J* = 12.2 Hz), 5.20 (d, 1H, *J* = 12.2 Hz), 5.98 (d, 1H, *J* = 2.0 Hz), 6.13 (d, 1H, *J* = 2.0 Hz), 6.82 (dd, 1H, *J* = 8.2, 1.6 Hz), 6.85 (d, 1H, *J* = 8.2 Hz), 7.10–7.48 (m, 24H), 7.52–7.68 (m, 2H); ^{13}C NMR (75MHz, $CDCl_3$) δ 44.8, 54.6, 70.6, 71.0, 71.3, 71.5, 81.9, 94.2, 95.0, 113.7, 114.3, 115.0, 120.1, 124.7, 127.4, 127.5, 127.8, 127.9, 128.0, 128.1, 128.2, 128.5, 128.6,

128.8, 129.0, 129.2, 129.5, 136.1, 136.2, 137.4, 137.5, 145.8, 149.3, 149.4, 159.1, 160.3, 163.8; IR (neat) 3062, 3032, 2935, 2874, 1581, 1511, 1454, 1427, 1378, 1341, 1262, 1216, 1162, 1109, 1087, 1027, 911, 847, 809, 735, 695 cm^{-1}; Anal. calcd for $C_{49}H_{42}O_7S$: C, 75.95; H, 5.46; S, 4.14. Found: C, 75.74; H, 5.55; S, 4.03.

SUP-17b: R_f 0.53 (hexane/EtOAc = 1/1); mp 52–53 °C; $[\alpha]_D^{24}$ +106 (*c* 1.03, $CHCl_3$); ^1H NMR (300 MHz, $CDCl_3$) δ 2.70–2.79 (m, 2H), 3.26–3.34 (m, 1H), 4.74–4.84 (m, 3H), 4.93 (d, 1H, *J* = 12.2 Hz), 5.00 (d, 1H, *J* = 12.2 Hz), 5.06 (d, 1H, *J* = 12.2 Hz), 5.07 (d, 1H, *J* = 12.2 Hz), 5.11 (s, 2H), 5.97 (d, 1H, *J* = 2.1 Hz), 6.12 (d, 1H, *J* = 2.1 Hz), 6.51 (dd, 1H, *J* = 8.3, 1.9 Hz), 6.68 (d, 1H, *J* = 1.9 Hz), 6.79 (d, 1H, *J* = 8.3 Hz), 7.15–7.50 (m, 23H), 7.54–7.70 (m, 2H); ^{13}C NMR (75 MHz, $CDCl_3$) δ 44.4, 54.3, 69.8, 70.3, 70.8, 71.0, 81.2, 93.7, 94.3, 113.0, 113.7, 114.5, 119.2, 124.3, 126.8, 126.9, 127.1, 127.2, 127.4, 127.5, 127.6, 127.8, 127.9, 128.0, 128.1, 128.3, 128.5, 129.0, 135.5, 135.6, 136.6, 136.8, 145.0, 128.7, 148.8, 158.8, 159.6, 163.1; IR (neat) 3064, 3032, 2927, 2873, 1590, 1512, 1454, 1428, 1382, 1342, 1265, 1219, 1164, 1113, 1088, 1029, 912, 810, 748, 696 cm^{-1}; Anal. calcd for $C_{49}H_{42}O_7S$: C, 75.95; H, 5.55; S, 4.14. Found: C, 76.12; H, 5.68; S, 4.05.

Preparation of bromohydrin SUP-18



SUP-18

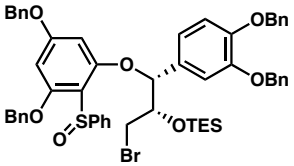
To a solution of **SUP-17** (81.7 mg, 0.105 mmol, **a**:**b** = 53:47 d.r.) in THF (1.5 mL), a solution of Li_2NiBr_4 (0.4 mL, ca. 0.4 M solution in THF, 0.16 μmol) was added at 0 °C. After stirring for 1 h, the reaction was quenched by adding pH 7 phosphate buffer, and the mixture was extracted with EtOAc (x3). The combined organic extracts were washed with brine, dried (Na_2SO_4), and concentrated in vacuo. The residue was purified by PTLC (hexane/EtOAc = 1.5/1) to afford the more polar **SUP-18a** (46.2 mg, 51%) and the less polar **SUP-18b** (38.0 mg, 42%) as a white amorphous solid, respectively.

SUP-18a: R_f 0.53 (hexane/EtOAc = 2/1); mp 56–58 °C; $[\alpha]_D^{21}$ –0.795 (*c* 3.70, $CHCl_3$); ^1H NMR (400 MHz, $CDCl_3$) δ 2.87 (dd, 1H, *J* = 10.0, 6.4 Hz), 2.97 (dd, 1H, *J* = 10.0, 3.2 Hz), 3.68 (brs, 2H), 4.74 (d, 1H, *J* = 11.6 Hz), 4.80 (d, 1H, *J* = 11.6 Hz), 5.05–5.25 (m, 7H), 5.85 (d, 1H, *J* = 2.0 Hz), 6.19 (d, 1H, *J* = 2.0 Hz), 6.82 (d, 1H, *J* = 8.0 Hz), 6.88 (dd, 1H, *J* = 8.0, 1.6 Hz), 7.15–7.50 (m, 24H), 7.51–7.60 (m, 2H); ^{13}C NMR (75 MHz, $CDCl_3$) δ 33.6, 70.4, 70.9, 71.1, 74.7, 79.4, 93.6, 95.7, 112.5, 113.6, 114.7, 120.1, 124.2, 127.1, 127.2, 127.5, 127.6, 127.8, 128.1, 128.2, 128.4, 128.5,

128.6, 128.7, 128.9, 129.3, 129.6, 135.7, 135.8, 137.1, 137.2, 146.1, 148.9, 149.0, 158.0, 159.9, 163.6; IR (neat) 3573, 3327, 3066, 3032, 2930, 2876, 1592, 1513, 1454, 1428, 1380, 1339, 1262, 1218, 1165, 1115, 087, 1021, 910, 812, 749, 696, 667 cm^{-1}; Anal. calcd for $C_{49}H_{43}BrO_7S$: C, 68.77; H, 5.06; S, 3.75. Found: C, 68.47; H, 5.28; S, 3.82.

SUP-18b: R_f 0.65 (hexane/EtOAc = 2/1); mp 53–55 °C; $[\alpha]_D^{23}$ +124 (*c* 1.94, $CHCl_3$); ^{1}H NMR (400 MHz, $CDCl_3$) δ 2.93 (dd, 1H, *J* = 8.3, 2.4 Hz), 3.43(dd, 1H, *J* = 8.3, 2.4 Hz), 3.76 (dt, 1H, *J* = 6.2, 2.4 Hz), 4.75–4.90 (m, 5H), 5.08 (s, 2H), 5.16 (s, 2H), 5.82 (d, 1H, *J* = 2.0 Hz), 6.23 (d, 1H, *J* = 2.0 Hz), 6.35 (d, 1H, *J* = 2.0 Hz), 6.48 (dd, 1H, *J* = 10.0, 2.0 Hz), 6.67 (brs, 1H), 6.76 (d, 1H, *J* = 10.0 Hz), 7.21–7.50 (m, 23H), 7.60–7.65 (m, 2H); ^{13}C NMR (75 MHz, $CDCl_3$) δ 34.5, 70.5, 71.3, 71.4, 73.9, 85.7, 93.7, 95.4, 112.6, 113.1, 115.1, 119.6, 124.6, 127.3, 127.4, 127.8, 127.9, 128.1, 128.2, 128.5, 128.6, 128.6, 128.7, 128.8, 129.0, 129.4, 130.1, 135.9, 136.1, 136.9, 137.2, 145.9, 149.3, 149.5, 160.2, 160.6, 164.3; IR (neat) 3279, 3046, 3032, 3012, 2933, 2872, 1591, 1583, 1513, 1454, 1426, 1383, 1342, 1266, 1232, 1165, 1119, 1088, 1017, 910, 814, 750, 696, 636, 500, 470, 457 cm^{-1}; Anal. calcd for $C_{49}H_{43}BrO_7S$: C, 68.77; H, 5.06; S, 3.75. Found: C, 68.53; H, 5.05; S, 3.66.

Preparation of cyclization precursor 16



16

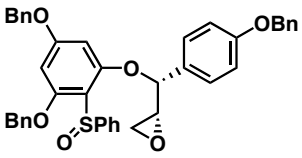
To a solution of **SUP-18** (79.6 mg, 93.0 μmol, **a**:**b** = 45:55 d.r.) in CH_2Cl_2 (1.5 mL), 2,6-lutidine (50.0 μL, 0.436 mmol) and TESOTf (42.4 mg, 0.161 mmol) were added at 0 °C. After stirring for 50 min, the reaction was quenched by saturated aqueous $NaHCO_3$ at 0 °C. The products were extracted with EtOAc (x3) and the combined organic extracts were washed with 5% citric acid solution, saturated aqueous $NaHCO_3$, and brine, dried (Na_2SO_4), and concentrated in vacuo. The residue was purified by PTLC (hexane/EtOAc = 1.5/1) to afford the less polar **16a** (44.1 mg, 49%) and the more polar **16b** (35.0 mg, 39%) as a colorless oil, respectively.

16a: R_f 0.65 (hexane/EtOAc = 1/1); $[\alpha]_D^{25}$ +27.0 (*c* 2.63, $CHCl_3$); ^{1}H NMR (300 MHz, $CDCl_3$) δ 0.40–0.60 (m, 6H), 0.90 (t, 9H, *J* = 8.0 Hz), 2.69 (dd, 1H, *J* = 10.4, 7.2 Hz), 3.48 (dd, 1H, *J* = 10.4, 4.0 Hz), 3.70 (ddd, 1H, *J* = 7.2, 5.2, 4.0 Hz), 4.78 (s, 2H), 4.96 (d, 1H, *J* = 12.0 Hz), 4.98 (d, 1H, *J* = 5.2 Hz), 5.05–5.12 (m, 5H), 5.88 (d, 1H, *J* = 2.0 Hz), 6.13 (d, 1H, *J* = 2.0 Hz), 6.79 (dd, 1H, *J* = 8.4, 1.6 Hz), 6.82 (d, 1H, *J* = 8.4 Hz), 7.05 (d, 1H, *J* = 1.6 Hz), 7.15–7.45 (m, 23H), 7.46–7.55 (m, 2H); ^{13}C NMR (75 MHz, $CDCl_3$) δ 4.94, 6.91, 35,2, 70.3, 70.7, 70.9, 71.2, 74.7, 81.4, 93.7, 94.5, 113.8,

114.0, 114.6, 120.3, 124.3, 127.1, 127.2, 127.6, 127.7, 127.8, 128.0, 128.3, 128.4, 128.5, 128.7, 128.8, 136.0, 137.1, 137.2, 145.9, 148.6, 148.9, 158.7, 160.1, 163.5; IR (neat) 3065, 3033, 2954, 2910, 2876, 1591, 1513, 1455, 1427, 1379, 1339, 1265, 1228, 1165, 1121, 1088, 1028, 904, 812, 737, 696, 634 cm^{-1}; Anal. calcd for $C_{55}H_{57}BrO_7SSi$: C, 68.10; H, 5.92; S, 3.31. Found: C, 68.40; H, 6.06; S, 3.46.

16b: R_f 0.54 (hexane/EtOAc = 1/1); $[\alpha]_D^{26}$ +118 (*c* 1.35, $CHCl_3$); ^1H NMR (300 MHz, $CDCl_3$) δ 0.43–0.51 (m, 6H), 0.85 (t, 9H, *J* = 8.0 Hz), 3.07 (dd, 1H, *J* = 10.0, 5.1 Hz), 3.95 (dd, 1H, *J* = 10.0, 6.7 Hz), 4.05 (ddd, 1H, *J* = 10.0, 5.1, 3.8 Hz), 4.72 (d, 1H, *J* = 11.8 Hz), 4.76 (d, 1H, *J* = 11.8 Hz), 4.85–5.15 (m, 6H), 5.23 (d, 1H, *J* = 3.8 Hz), 5.88 (d, 1H, *J* = 2.0 Hz), 6.11 (d, 1H, *J* = 2.0 Hz), 6.56 (dd,1H, *J* = 8.2, 1.6 Hz), 6.65 (d, 1H, *J* = 1.6 Hz), 6.79 (d, 1H, *J* = 8.2 Hz), 7.10–7.45 (m, 23H), 7.60–7.68 (m, 2H); ^{13}C NMR (75 MHz, $CDCl_3$) δ 4.77, 6.81, 34.4, 70.1, 70.7, 71.0, 71.3, 75.6, 81.4, 93.9, 94.5, 113.5, 113.9, 115.0, 119.6, 124.7, 127.1, 127.2, 127.5, 127.7, 127.9, 128.2, 128.3, 128.4, 128.5, 128.6, 128.9, 130.1, 135.8, 135.9, 137.0, 137.2, 145.7, 148.7, 148.9, 159.7, 159.8, 163.4; IR (neat) 3062, 3031, 2954, 2910, 2875, 1583, 1511, 1455, 1426, 1379, 1267, 1231, 1164, 1106, 1027, 811, 737, 696 cm^{-1}; Anal. calcd for $C_{55}H_{57}BrO_7SSi$: C, 68.10; H, 5.92; S, 3.31. Found: C, 68.17; H, 6.16; S, 3.48.

Preparation of oxirane SUP-19



SUP-19

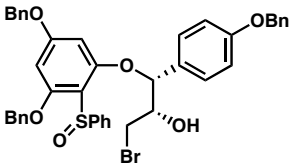
To a suspension of NaH (30 mg, 63% dispersion in mineral oil, 0.80 μmol, washed with hexane) in a mixed solvent of toluene (0.24 mL) and DMPU (0.06 mL) was added sulfoxide **8** (153 mg, 0.354 mmol) at room temperature. A solution of epoxide **15** (47.4 mg, 0.185 mmol) in a mixed solvent of toluene (0.32 mL) and DMPU (0.08 mL) was added at room temperature, and the stirring was continued for 50 min. The reaction was stopped by adding saturated aqueous $NaHCO_3$, and the mixture was extracted with EtOAc (x3). The combined organic extracts were washed with brine, dried (Na_2SO_4), and concentrated in vacuo. The residue was purified by flash column chromatography (silica gel, hexane/EtOAc=3:1 to 1:1, gradient elution) to afford the less polar **SUP-19a** (45 mg, 36%) and the more polar **SUP-19b** (45 mg, 36%) as white amorphous solids.

SUP-19a: R_f 0.5 (hexane/EtOAc = 1/1); mp 54–56 °C; $[\alpha]_D^{25}$ −22.9 (*c* 1.04, $CHCl_3$); ^1H NMR (400 MHz, $CDCl_3$) δ 2.55 (dd, 1H, *J* = 4.8, 2.8 Hz), 2.71 (t, 1H, *J* = 4.8 Hz), 3.15 (ddd, 1H, *J* = 6.0, 4.8,

2.8 Hz), 4.79 (d, 1H, *J* = 6.0 Hz), 4.83 (d, 1H, *J* = 12.0 Hz), 4.87 (d, 1H, *J* = 12.0 Hz), 4.92 (d, 1H, *J* = 12.0 Hz), 5.03 (s, 2H), 5.06 (d, 1H, *J* = 12.0 Hz), 6.03 (d, 1H, *J* = 2.0 Hz), 6.12 (d, 1H, *J* = 2.0 Hz), 6.95 (d, 2H, *J* = 8.4 Hz), 7.10–7.45 (m, 20H), 7.50–7.60 (m, 2H); ^{13}C NMR (75 MHz, $CDCl_3$) δ 45.3, 55.1, 70.8, 71.0, 71.4, 82.5, 94.7, 95.5, 114.7, 115.8, 125.1, 127.9, 128.1, 128.2, 128.6, 128.8, 128.9, 129.1, 129.2, 129.3, 129.4, 129.6, 136.6, 137.5, 161.4, 159.71, 159.74, 160.8, 164.3; IR (neat) 3063, 3033, 2924, 2872, 1579, 1510, 1454, 1432, 1380, 1340, 1227, 1162, 1106, 1086, 1028, 914, 808, 736, 695, 631 cm^{-1}; Anal. calcd for $C_{42}H_{36}O_6S$: C, 75.43; H, 5.43; S, 4.79. Found: C, 75.49; H, 5.73; S, 4.96.

SUP-19b: R_f 0.4 (hexane/EtOAc = 1/1); mp 60–62 °C; $[\alpha]_D^{25}$ +135 (*c* 1.04, $CHCl_3$); ^{1}H NMR (400 MHz, $CDCl_3$) δ 2.75–2.85 (m, 2H), 3.26–3.28 (m, 1H), 4.81 (d, 1H, *J* = 12.0 Hz), 4.84 (d, 1H, *J* = 12.0 Hz), 4.88 (d, 1H, *J* = 5.2 Hz), 4.95 (d, 1H, *J* = 12.4 Hz), 5.02 (s, 2H), 5.07 (d, 1H, *J* = 12.4 Hz), 5.99 (d, 1H, *J* = 2.0 Hz), 6.12 (d, 1H, *J* = 2.0 Hz), 6.83 (s, 4H), 7.15–7.45 (m, 18H), 7.55–7.65 (m, 2H); ^{13}C NMR (75 MHz, $CDCl_3$) δ 44.6, 54.6, 70.0, 70.1, 70.7, 81.0, 93.8, 94.6, 114.0, 115.0, 124.6, 127.1, 127.3, 127.4, 127.7, 127.9, 128.1, 128.2, 128.3, 128.4, 128.5, 128.6, 128.8, 135.8, 135.9, 136.7, 145.4, 158.8, 159.0, 160.1, 163.4; IR (neat) 3062, 3038, 2929, 2872, 1581, 1510, 1434, 1381, 1338, 1227, 1164, 1106, 1087, 1028, 914, 807, 737, 695 cm^{-1}; Anal. calcd for $C_{42}H_{36}O_6S$: C, 75.43; H, 5.43; S, 4.79. Found: C, 75.51; H, 5.53; S, 4.96.

Preparation of bromohydrin SUP-20



SUP-20

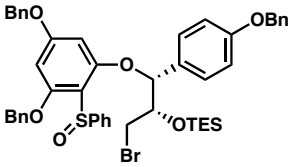
To a solution of **SUP-19** (1.16 g, 1.73 mmol, **a**:**b** = 50:50 d.r.) in THF (5.6 mL), a solution of Li_2NiBr_4 (6.2 mL, ca. 0.4 M solution in THF, 2.6 mmol) was added at 0 °C. After stirring for 2 h, the reaction was quenched by adding pH 7 phosphate buffer, and the mixture was extracted with EtOAc (x3). The combined organic extracts were washed with brine, dried (Na_2SO_4), and concentrated in vacuo. The residue was purified by flash column chromatography (silica gel, hexane/EtOAc = 2/1 to 1.5/1, gradient elution) to afford **SUP-20** (1.15 g, 88%, **a**:**b** = 50:50 d.r.) as a white amorphous solid. Analytical samples were further prepared from a mixture (50 mg) by PTLC (hexane/EtOAc = 1.5/1 x2) to afford the more polar **SUP-20a** (24 mg) and the less polar **SUP-20b** (24 mg) as a white amorphous solid, respectively.

SUP-20a: R_f 0.6 (hexane/EtOAc = 1.5/1); mp 131–132 °C; $[\alpha]_D^{27}$ –13.7 (*c* 1.03, $CHCl_3$); ^{1}H NMR

(300 MHz, $CDCl_3$) δ 2.89 (dd, 1H, *J* = 10.2, 7.3 Hz), 3.03 (dd, 1H, *J* = 10.2, 4.4 Hz), 3.76 (brs, 1H), 3.90 (brs, 1H), 4.76 (d, 1H, *J* = 11.7 Hz), 4.84 (d, 1H, *J* = 11.7 Hz), 4.98 (s, 2H), 5.04 (d, 1H, *J* = 12.0 Hz), 5.10 (d, 1H, *J* = 12.0 Hz), 5.29 (d, 1H, *J* = 3.2 Hz), 5.89 (d, 1H, *J* = 2.0 Hz), 6.20 (d, 1H, *J* = 2.0 Hz), 6.90 (d, 2H, *J* = 8.8 Hz), 7.05–7.50 (m, 20H), 7.54–7.60 (m, 2H); ^{13}C NMR (75 MHz, $CDCl_3$) δ 33.5, 69.9, 70.3, 70.9, 74.8, 79.3, 93.5, 95.8, 112.4, 115.0, 124.2, 127.1, 127.4, 127.9, 128.1, 128.3, 128.4, 128.4, 128.5, 128.6, 128.9, 129.5, 135.6, 135.7, 136.7, 145.9, 158.1, 158.8, 159.9, 163.5; IR (neat) 3314, 3066, 3026, 2937, 2893, 2860, 1580, 1513, 1499, 1436, 1377, 1358, 1332, 1312, 1251, 1224, 1173, 1138, 1090, 1023, 997, 908, 860, 808, 783, 765, 734, 692, 650, 634, 607 cm^{-1}; Anal. calcd for $C_{42}H_{37}BrO_6S$: C, 67.29; H, 4.97; S, 4.28. Found: C, 67.08; H, 5.05; S, 4.19.

SUP-20b: R_f 0.7 (hexane/EtOAc = 1.5/1); mp 63–65 °C; $[\alpha]_D^{23}$ +121 (*c* 1.04, $CHCl_3$); ^{1}H NMR (300 MHz, $CDCl_3$) δ 2.99 (dd, 1H, *J* = 10.9, 2.5 Hz), 3.47 (dd, 1H, *J* = 10.9, 3.1 Hz), 3.79 (ddd, 1H, *J* = 8.3, 3.1, 2.5 Hz), 4.85 (s, 2H), 4.88 (d, 1H, *J* = 8.3 Hz), 5.00 (s, 2H), 5.15 (s, 2H), 5.87 (d, 1H, *J* = 2.2 Hz), 6.22 (d, 1H, *J* = 2.2 Hz), 6.54 (s, 1H), 6.69 (d, 2H, *J* = 8.8 Hz), 6.79 (d, 2H, *J* = 8.8 Hz), 7.23–7.54 (m, 18H), 7.56–7.66 (m, 2H); ^{13}C NMR (75 MHz, $CDCl_3$) δ 34.2, 69.9, 70.3, 71.0, 73.8, 84.9, 93.3, 94.9, 112.9, 115.1, 124.3, 127.1, 127.3, 127.4, 127.5, 128.0, 128.2, 128.3, 128.6, 128.7, 129.1, 129.2, 135.6, 135.8, 136.6, 145.7, 159.0, 160.0, 160.2, 164.1; IR (neat) 3272, 3062, 3032, 2929, 2871, 1579, 1511, 1435, 1375, 1337, 1229, 1162, 1110, 1086, 1013, 909, 866, 827, 743, 694, 636 cm^{-1}; Anal. calcd for $C_{42}H_{37}BrO_6S$: C, 67.29; H, 4.97; S, 4.28. Found: C, 67.02; H, 5.09; S, 4.42.

Preparation of cyclization precursor 17



17

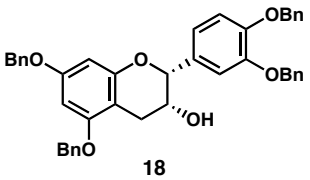
To a solution of **SUP-20** (1.13 g, 1.51 mmol, **a**:**b** = 50:50 d.r.) in CH_2Cl_2 (4.0 mL), 2,6-lutidine (0.54 mL, 4.6 mmol) and TESOTf (666 mg, 2.52 mmol) were added at 0 °C. After stirring for 2.6 h, the reaction was quenched by saturated aqueous $NaHCO_3$. The mixture was extracted with EtOAc (x3). The combined organic extracts were washed with 5% citric acid solution, saturated aqueous $NaHCO_3$, and brine, dried (Na_2SO_4), and concentrated in vacuo. The residue was purified by flash column chromatography (silica gel, hexane/EtOAc = 4/1 to 3/2, gradient elution) to afford silyl ether **17** (1.14 g, 87%, **a**:**b** = 57:43 d.r.) as a colorless oil. Analytical samples were

prepared form the mixture (50 mg) by PTLC (hexane/EtOAc = 3/1 x1, 2/1 x1) to afford the less polar **17a** (27 mg) and the more polar **17b** (21 mg) as a colorless oil, respectively.

17a: R_f 0.7 (hexane/EtOAc = 1/1); $[\alpha]_D^{27}$ +10.8 (*c* 1.01, $CHCl_3$); ^{1}H NMR (300 MHz, $CDCl_3$) δ 0.45–0.58 (m, 6H), 0.91 (t, 9H, *J* = 7.8 Hz), 2.86 (dd, 1H, *J* = 10.4, 7.1 Hz), 3.61 (dd, 1H, *J* = 10.4, 4.0 Hz), 3.79 (ddd, 1H, *J* = 7.1, 4.3, 4.0 Hz), 4.82 (s, 2H), 4.92 (d, 1H, *J* = 12.0 Hz), 5.02 (s, 2H), 5.06 (d, 1H, *J* = 12.0 Hz), 5.07 (d, 1H, *J* = 4.3 Hz), 5.94 (d, 1H, *J* = 2.0 Hz), 6.11 (d, 1H, *J* = 2.0 Hz), 6.90 (d, 2H, *J* = 8.7 Hz), 7.10–7.55 (m, 22H); ^{13}C NMR (75 MHz, $CDCl_3$) δ 4.93, 6.85, 35.2, 70.0, 70.2, 70.7, 74.7, 81.5, 93.7, 94.6, 113.2, 114.8, 124.3, 127.1, 127.4, 127.5, 127.9, 128.0, 128.3, 128.4, 128.5, 128.6, 128.7, 135.8, 135.9, 136.8, 145.8, 158.8, 158.9, 160.1, 163.5; IR (neat) 3067, 3034, 2953, 2875, 1580, 1511, 1454, 1432, 1375, 1339, 1225, 1161, 1108, 1087, 1021, 904, 811, 731, 694, 634 cm^{-1}; Anal. calcd for $C_{48}H_{51}BrO_6SSi$: C, 66.73; H, 5.95; S, 3.71. Found: C, 66.94; H, 5.99; S, 4.00.

17b: R_f 0.6 (hexane/EtOAc = 1/1); $[\alpha]_D^{27}$ +129 (*c* 0.805, $CHCl_3$); ^{1}H NMR (300 MHz, $CDCl_3$) δ 0.40–0.56 (m, 6H), 0.86 (m, 9H, *J* = 7.6 Hz), 3.13 (dd, 1H, *J* = 10.0, 5.1 Hz), 3.44 (dd, 1H, *J* = 10.0, 6.7 Hz), 3.62 (ddd, 1H, *J* = 6.7, 5.1, 4.0 Hz), 4.79 (d, 1H, *J* = 12.2 Hz), 4.83 (d, 1H, *J* = 12.2 Hz), 4.90 (d, 1H, *J* = 12.1 Hz), 5.01 (s, 2H), 5.03 (d, 1H, *J* = 12.1 Hz), 5.30 (d, 1H, *J* = 4.0 Hz), 5.96 (d, 1H, *J* = 2.0 Hz), 6.10 (d, 1H, *J* = 2.0 Hz), 6.82 (d, 2H, *J* = 8.9 Hz), 6.91 (d, 2H, *J* = 8.9 Hz), 7.15–7.45 (m, 18H), 7.15–7.43 (m, 2H); ^{13}C NMR (75 MHz, $CDCl_3$) δ 4.79, 6.83, 34.5, 70.0, 70.2, 70.7, 75.4, 81.2, 93.8, 94.4, 113.9, 114.8, 124.7, 127.2, 127.4, 127.5, 127.9, 128.0, 128.1, 128.2, 128.3, 128.5, 128.6, 128.7, 128.8, 128.9, 135.9, 136.0, 136.9, 145.7, 158.6, 159.8, 160.0, 163.5; IR (neat) 3064, 3032, 2954, 2875, 1580, 1510, 1454, 1433, 1374, 1334, 1225, 1161, 1105, 1088, 1021, 893, 811, 732, 694, 634 cm^{-1}; Anal. calcd for $C_{48}H_{51}BrO_6SSi$: C, 66.73; H, 5.95; S, 3.71. Found: C, 66.51; H, 6,06; S, 3.75.

Preparation of alcohol 18



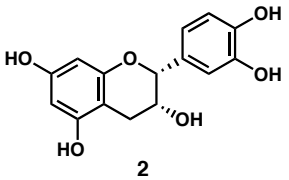
18

To a solution of **16** (83.3 mg, 85.9 μmol, **a**:**b** = 58:42) in THF (1.5 mL), PhLi (0.23 mL, 1.08 M cyclopropane-ether solution, 0.26 mmol) was added at room temperature. After stirring for 4 h, the reaction was quenched by adding water at 0 °C. The products were extracted with EtOAc (x3), and the combined organic extracts were washed with brine, dried (Na_2SO_4), and concentrated in

vacuo. The residue was purifed by PTLC (hexane/EtOAc = 3/1). To a solution of the mixture in THF (1.5 mL), TBAF (0.12 mL, 1.0 M solution in THF, 1.3 mmol) was added at 0 °C. After stirring for 1 h at 0 °C, the reaction was quenched by adding water at 0 °C. The products were extracted with EtOAc (x3) and the combined organic extracts were washed with brine, dried (Na_2SO_4), and concentrated in vacuo. The residue was purified by PTLC (toluene/EtOAc = 10/1) to afford flavan-3-ol **18** (42.4 mg, 76% 2 steps) as a white solid.

18: R_f 0.65 (toluene/EtOAc = 10/1); mp 130–131 °C (hexane/Et_2O/EtOAc); $[\alpha]_D^{25}$ –16.7 (*c* 3.33, $CHCl_3$); ^{1}H NMR (300 MHz, $CDCl_3$) δ 1.70 (d, 1H, *J* = 5.7 Hz), 2.88 (dd, 1H, *J* = 17.3, 4.5 Hz), 3.00 (dd, 1H, *J* = 17.3, 2.1 Hz), 4.17 (brs, 1H), 4.87 (s, 1H), 4.99 (s, 4H), 5.14 (s, 2H), 5.17 (s, 2H), 6.26 (s, 2H), 6.94 (d, 1H, *J* = 8.3 Hz), 6.98 (dd, 1H, *J* = 8.3, 1.2 Hz), 7.13 (d, 1H, *J* = 1.2 Hz), 7.20–7.50 (m, 20H); ^{13}C NMR (75 MHz, $CDCl_3$) δ 28.4, 66.5, 70.1, 70.3, 71.4, 71.5, 78.5, 94.2, 94.8, 101.2, 113.7, 115.2, 119.7, 127.3, 127.4, 127.6, 127.7, 127.9, 128.0, 128.2, 128.6, 128.7, 128.7, 128.8, 131.6, 137.1, 137.2, 137.3, 137.4, 149.0, 149.2, 155.4, 158.5, 158.9; IR (neat) 3564, 3089, 3064, 3032, 2932, 2906, 2871, 1618, 1592, 1512, 1499, 1454, 1442, 1425, 1377, 1265, 1218, 1144, 1112, 1078, 1027, 910, 812, 792, 737, 696, 623 cm^{-1}; Anal. calcd for $C_{43}H_{38}O_6$: C, 79.36; H, 5.89. Found: C, 79.63; H, 5.76.

Preparation of (–)-EC (2)



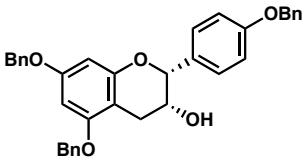
2

A mixture of **18** (42.7 mg, 65.6 μmol) and 5% $Pd(OH)_2$/C (173 mg, ASCA2^{TM}) in a mixed solvent of THF (2.0 mL), MeOH (2.0 mL), and H_2O (0.10 mL) was stirred under H_2 atmosphere at room temperature for 30 min. The mixture was carefully filtered through a glass fiber filter under Ar atmosphere, and half volume of the filtrate was evaporated. The residue was directly loaded on Sephadex® LH-20 (eluent: MeOH) to collect a fraction including (–)-epicatechin **2** in MeOH, to which H_2O (2 mL) was added, and all volatile solvents were removed in vacuo, and lyophilization gave (–)-epicatechin·monohydrate (**2**) (13.9 mg, 69%) as a white powder.

2: R_f 0.35 ($CHCl_3$/MeOH = 4/1); mp 139–142 °C; $[\alpha]_D^{24}$ –50 (*c* 0.69, MeOH); ^{1}H NMR (400 MHz, CD_3OD) δ 2.63 (dd, 1H, *J* = 16.8, 2.8 Hz), 2.76 (dd, 1H, *J* = 16.8, 4.8 Hz), 4.05–4.15 (m, 1H), 4.71 (s, 1H), 5.81 (d, 1H, *J* = 2.2 Hz), 5.84 (d, 1H, *J* = 2.2 Hz), 6.66 (d, 1H, *J* = 8.4 Hz), 6.70 (dd, 1H, *J* = 8.4, 2.0 Hz), 6.87 (d, 1H, *J* = 2.0 Hz); ^{13}C NMR (75 MHz, CD_3OD) δ 29.3, 67.5, 79.9, 95.9, 96.4,

100.0, 115.3, 115.9, 119.4, 132.3, 145.8, 145.9, 157.4, 157.7, 158.0; IR (neat) 3212, 1627, 1607, 1519, 1466, 1353, 1266, 1144, 1116, 1095, 1059, 1014, 981, 823, 785 cm^{-1}; Anal. calcd for $C_{15}H_{14}O_6 \bullet 1H_2O$: C, 58.44; H, 5.23. Found: C, 58.22; H, 5.23.

Preparation of alcohol 19

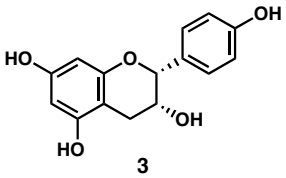


19

To a solution of silyl ether **17** (0.153 g, **a**:**b** = 57:43, 0.177 mmol) in THF (2.0 mL), PhLi (0.45 mL, 1.08 M cyclohexane-ether solution, 0.49 mmol) was added at room temperature. After stirring for 2 h, the reaction was quenched by adding water at 0 °C. The mixture was extracted with EtOAc (x3), and the combined organic extracts were washed with brine, dried (Na_2SO_4), and concentrated in vacuo. The residue was purified by flash column chromatography (silica gel, hexane/EtOAc = 8/1). To a solution of the products in THF (2.5 mL), was added TBAF (270 μL, 1.0 M solution in THF, 0.268 mmol) at 0 °C. After stirring for 1 h at room temperature, the reaction was quenched by adding water at 0 °C. The products were extracted with EtOAc (x3), and combined organic extracts were washed with brine, dried (Na_2SO_4), and concentrated in vacuo. The residue was purified by PTLC (toluene/EtOAc = 10/1) to afford the flavan-3-ol **19** (75 mg, 78% 2 steps) as an amorphous solid.

19: R_f 0.42 (toluene/EtOAc = 10/1); mp 43–45 °C; $[\alpha]_D^{23}$ –12.0 (*c* 1.70, $CHCl_3$); ^1H NMR (300 MHz, $CDCl_3$) δ 1.72 (d, 1H, *J* = 6.2 Hz), 2.95 (dd, 1H, *J* = 16.9, 4.3 Hz), 3.03 (dd, 1H, *J* = 16.9, 2.4 Hz), 4.22–4.34 (m, 1H), 4.98 (s, 1H), 5.01 (s, 2H), 5.02 (s, 2H), 5.09 (s, 2H), 6.28 (s, 2H), 7.03 (d, 2H, *J* = 8.5 Hz), 7.26–7.48 (m, 17H); ^{13}C NMR (75 MHz, $CDCl_3$) δ 28.4, 66.3, 69.9, 70.0, 70.1, 78.4, 94.1, 94.7, 101.0, 115.0, 127.2, 127.4, 127.5, 127.7, 127.8, 127.9, 128.4, 128.5, 128.6, 130.6, 136.9, 137.0, 155.4, 158.3, 158.6, 158.8; IR (neat) 3564, 3463, 3091, 3065, 3032, 2908, 2872, 1616, 1592, 1512, 1497, 1454, 1441, 1378, 1311, 1243, 1178, 1147, 1107, 1076, 1028, 910, 810, 736, 696 cm^{-1}; Anal. calcd for $C_{36}H_{32}O_5$: C, 79.39; H, 5.92. Found: C, 79.63; H, 6.13.

Preparation of (–)-EZ (3)

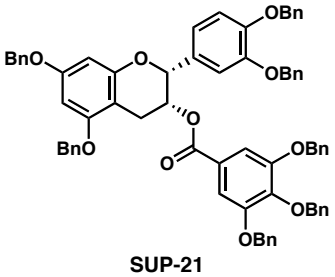


3

A mixture of **19** (20.1 mg, 38.7 μmol) and 5% $Pd(OH)_2$/C (69.2 mg, ASCA2^{TM}) in THF (2.0 mL), MeOH (2.0 mL), and H_2O (0.10 mL) was stirred under H_2 atmosphere at room temerature for 30 min. The mixture was filtered through a glass fiber filter under Ar atmosphere, and roughly half volume of the filtrate was evaporated. The residue was purified by Sephadex® LH-20 (eluent: MeOH) to collect a fraction including (–)-epiafzelechin (**3**) in MeOH, to which H_2O (ca. 2 mL) was added, and all volatile solvents were removed in vacuo, and lyophilization gave (–)-epiafzelechin·$(H_2O)_{1–2}$ (**3**) (7.3 mg, 65%) as a white powder.

3: R_f 0.17 ($CHCl_3$/MeOH = 9/1); mp 196–199 °C (decomp.); $[\alpha]_D^{23}$ –56 (*c* 0.50, MeOH); ^{1}H NMR (500 MHz, CD_3OD) δ 2.73 (dd, 1H, *J* = 16.8, 2.8 Hz), 2.87 (dd, 1H, *J* = 16.8, 4.6 Hz), 4.18 (ddd, 1H, *J* = 4.6, 2.8, 1.4 Hz), 4.80 (d, 1H, *J* = 1.4 Hz), 5.91 (d, 1H, *J* = 2.3 Hz), 5.94 (d, 1H, *J* = 2.3 Hz), 6.77 (d, 2H, *J* = 8.6 Hz), 7.31 (d, 2H, *J* = 8.6 Hz); ^{13}C NMR (75 MHz, $CDCl_3$) δ 27.9, 66.1, 78.5, 94.5, 95.1, 98.6, 114.4, 127.7, 130.1, 156.0, 156.4, 156.7; IR (neat) 3349, 2924, 1611, 1515, 1474, 1343, 1225, 1196, 1148, 1111, 1090, 1061, 1035, 1012, 977, 874, 819, 793, 666 cm^{-1}; Anal. calcd for $C_{15}H_{14}O_5 \cdot 1.7H_2O$: C, 59.09; H, 5.75. Found: C, 58.88; H, 5.33.

Preparation of ester SUP-21



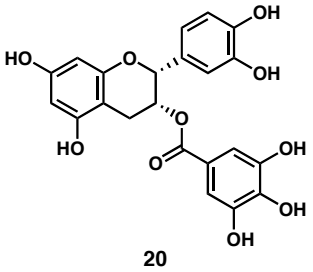
SUP-21

To a solution of **18** (66.6 mg, 0.102 mmol) in CH_2Cl_2 (3.0 mL), 3,4,5-tris(benzyloxy)benzoic acid (100 mg, 0.227 mmol), DMAP (9.0 mg), NEt_3 (75 μL, 0.53 mmol), and 1-ethyl-3-(3-dimethylaminopropyl)carbodiimide hydrochloride (EDC·HCl, 151 mg, 0.785 mmol) were added at 0 °C. After stirring for 12 h at room temperature, the reaction was quenched by adding water at 0 °C. The products were extracted with EtOAc (x3) and the combined organic extracts were washed with brine, dried (Na_2SO_4), and concentrated in vacuo. The residue was purified by flash column chromatography (silica gel, hexane/EtOAc = 6/1 to 3/1, gradient elution) to

afford ester **SUP-21** (101 mg, 92 %) as an amorphous solid.

SUP-21: R_f 0.30 (hexane/EtOAc = 4/1); mp 45–47 °C; $[\alpha]_D^{27}$ –86.9 (*c* 3.46, $CHCl_3$); ^{1}H NMR (400 MHz, $CDCl_3$) δ 3.05 (dd, 1H, *J* = 17.6, 3.2 Hz), 3.11 (dd, 1H, *J* = 17.6, 4.4 Hz), 4.63 (d, 1H, *J* = 11.6 Hz), 4.74 (d, 1H, *J* = 11.6 Hz), 4.90–5.10 (m, 13H), 5.56–5.64 (m, 1H), 6.32 (d, 1H, *J* = 2.4 Hz), 6.37 (d, 1H, *J* = 2.4 Hz), 6.82 (d, 1H, *J* = 8.0 Hz), 6.90 (dd, 1H, *J* = 8.0, 2.0 Hz), 7.03 (d, 1H, *J* = 2.0 Hz), 7.15–7.50 (m, 37H); ^{13}C NMR (75 MHz, $CDCl_3$) δ 26.1, 68.5, 69.9, 70.1, 70.9, 71.1, 75.0, 77.6, 93.8, 94.5, 100.9, 109.0, 113.5, 114.6, 120.0, 124.9, 127.2, 127.3, 127.5, 127.6, 127.7, 127.9, 128.0, 128.1, 128.2, 128.3, 128.4, 128.5, 128.6, 131.0, 136.4, 136.7, 136.9, 137.1, 137.4, 142.4, 148.8, 148.9, 152.3, 155.7, 158.0, 158.8, 164.9; IR (neat) 3090, 3064, 3032, 2930, 2872, 1715, 1619, 1592, 1499, 1454, 1429, 1373, 1327, 1266, 1215, 1145, 1112, 1028, 910, 860, 812, 735, 696 cm^{-1}; Anal. calcd for $C_{71}H_{60}O_{10}$: C, 79.46; H, 5.63. Found: C, 79.16; H, 5.74.

Preparation of (–)-ECg (20)

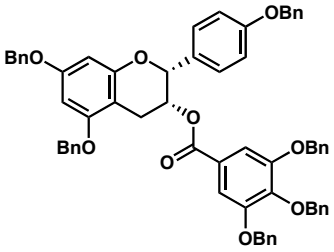


20

A mixture of **SUP-21** (67.0 mg, 62.4 μmol) and 5% $Pd(OH)_2$ (266 mg) in THF (5.0 mL), MeOH (3.0 mL), and H_2O (0.16 mL) was hydrogenated under H_2 atmosphere at room temperature for 30 min. The mixture was carefully filtered through a glass fiber filter under Ar atmosphere, and roughly half volume of the filtrate was evaporated. The residue was loaded on Sephadex® LH-20 (eluent: MeOH) to collect a fraction including (–)-epicatechin gallate (**20**) in MeOH, to which H_2O (ca. 2 mL) was added, and all volatile solvents were removed in vacuo, and lyophilization gave (–)-epicatechin gallate·$2H_2O$ (**20**) (29.4 mg, 98%) as a white powder.

20: R_f 0.16 ($CHCl_3$/MeOH = 4/1); mp 222–225 °C (decomp.); $[\alpha]_D^{25}$ –133 (*c* 1.29, acetone); ^{1}H NMR (400 MHz, CD_3OD) δ 2.75 (dd, 1H, *J* = 17.6, 2.0 Hz), 2.89 (dd, 1H, *J* = 17.6, 4.8 Hz), 4.91 (brs, 1H), 5.41, (brs, 1H), 5.86 (brs, 2H), 6.59 (d, 1H, *J* = 8.4 Hz), 6.70 (dd, 1H, *J* = 8.4, 2.0 Hz), 6.84 (d, 1H, *J* = 2.0 Hz), 6.87(s, 2H); ^{13}C NMR (75 MHz, CD_3OD) δ 26.9, 70.0, 78.7, 95.9, 96.6, 99.5, 110.2, 115.2, 116.1, 119.4, 120.9, 131.5, 140.7, 146.0, 146.5, 157.3, 157.9, 167.8; IR (neat) 3258, 1686, 1607, 1518, 1449, 1335, 1230, 1140, 1093, 1031, 972, 869, 816, 766 cm^{-1}; Anal. calcd for $C_{22}H_{18}O_{10}·2H_2O$: C, 55.23; H, 4.64. Found: C, 55.30; H, 4.50.

Preparation of ester SUP-22

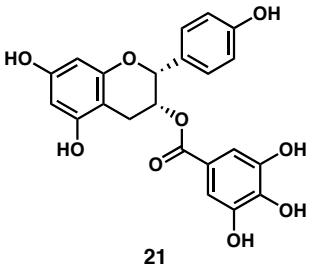


SUP-22

To a solution of alcohol **19** (27.6 mg, 50.7 μmol) and 3,4,5-tris(benzyloxy)benzoic acid (35.8 mg, 81.2 μmol) in CH_2Cl_2 (1.0 mL) was added DMAP (3 pieces, ca. 15 mg), NEt_3 (30 μL, 0.25 mmol), and 1-ethyl-3-(3-dimethylaminopropyl)carbodiimide hydrochloride (EDC·HCl, 74.6 mg, 0.389 mmol) at 0 °C. After stirring for 17 h at room temperature, the reaction was quenched by adding water at 0 °C. The products were extracted with EtOAc (x3), and the combined organic extracts were washed with brine, dried (Na_2SO_4), and concentrated in vacuo. The residue was purified by PTLC (hexane/EtOAc = 3/1 and toluene/EtOAc = 10/1) to afford **SUP-22** (47.1 mg, 96 %) as an amorphous solid.

SUP-22: R_f 0.55 (hexane/EtOAc = 3/1); mp 46–47 °C; $[\alpha]_D^{25}$ –84.9 (*c* 1.92, $CHCl_3$); ^{1}H NMR (400 MHz, $CDCl_3$) δ 3.06 (dd, 1H, *J* = 18.0, 3.2 Hz), 3.11 (dd, 1H, *J* = 18.0, 4.4 Hz), 4.95–5.10 (m, 12H), 5.12 (s, 1H), 5.57, (brs, 1H), 6.30 (d, 1H, *J* = 2.0 Hz), 6.37 (d, 1H, *J* = 2.0 Hz), 6.85 (d, 2H, *J* = 8.8 Hz); 7.13–7.57 (m, 34H); ^{13}C NMR (75 MHz, $CDCl_3$) δ 25.9, 68.8, 69.9, 70.1, 70.9, 75.1, 93.8, 94.6, 100.9, 109.0, 114.6, 125.0, 127.2, 127.4, 127.5, 127.8, 127.8, 127.9, 128.0, 128.2, 128.4, 128.5, 128.6, 130.1, 136.6, 136.8, 136.8, 137.4, 142.3, 152.2, 155.7, 158.0, 158.5, 158.8, 165.2; IR (neat) 3089, 3064, 3032, 2938, 2871, 1715, 1618, 1592, 1513, 1498, 1454, 1429, 1373, 1355, 1326, 1242, 1216, 1191, 1148, 1109, 1078, 1029, 966, 908, 863, 833, 812, 736, 696 cm^{-1}; Anal. calcd for $C_{64}H_{54}O_9$: C, 79.48; H, 5.63. Found: C, 79.21; H, 5.68.

Preparation of (–)-EZg (21)



21

A mixture of **SUP-22** (38.3 mg, 39.6 μmol) and 5% $Pd(OH)_2$ (155 mg) in THF (2.0 mL), MeOH (2.0 mL), and H_2O (0.10 mL) was stirred under H_2 atmosphere at room temperature for 30 min. The mixture was carefully filtered through a glass fiber filter under Ar atmosphere, and roughly half volume of the solution was evaporated. The residue was loaded on Sephadex® LH-20 (eluent: MeOH) to collect a fraction including (–)-epiafzelechin gallate (**21**) in MeOH, to which H_2O (ca. 2 mL) was added, and all volatile solvents were removed in vacuo, and lyophilization gave (–)-epiafzelechin gallate·$2H_2O$ (**21**) (15.0 mg, 82%) as a white powder.

21: R_f 0.30 ($CHCl_3$/MeOH = 4/1); mp 183–186 °C (decomp.); $[\alpha]_D^{28}$ –199 (*c* 0.613, MeOH); ^{1}H NMR (400 MHz, CD_3OD) δ 2.75 (dd, 1H, *J* = 17.6, 2.0 Hz), 2.91 (dd, 1H, *J* = 17.6, 4.4 Hz), 4.98 (brs, 1H), 5.38–5.44, (m, 1H), 5.85 (d, 1H, *J* = 2.0 Hz), 5.86 (d, 1H, *J* = 2.0 Hz), 6.61 (d, 2H, *J* = 8.4 Hz), 6.85 (s, 2H), 7.20 (d, 2H, *J* = 8.4 Hz); ^{13}C NMR (75 MHz, CD_3OD) δ 27.3, 70.4, 79.1, 96.3, 96.9, 99.7, 110.5, 116.2, 121.6, 129.4, 131.1, 140.4, 146.8, 157.7, 158.2, 158.5, 167.9; IR (neat) 3276, 1688, 1607, 1516, 1449, 1337, 1231, 1140, 1090, 1031, 1015, 969, 867, 816, 766, 717 cm^{-1}; Anal. calcd for $C_{22}H_{18}O_9 \cdot 2H_2O$: C, 57.14; H, 4.80. Found: C, 56.94; H, 4.50.