Supporting Information

Flavan–Isoflavan Rearrangement: Bioinspired Synthetic Access to Isoflavonoids via 1,2-Shift–Alkylation Sequence

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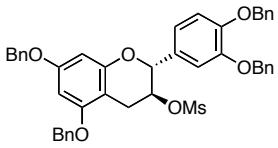
General Experimental Procedure

All reactions utilizing air- or moisture-sensitive reagents were performed in dried glassware under an atmosphere of dry argon. Ethereal solvents, CH_2Cl_2 and toluene (anhydrous; Kanto Chemical Co., Inc.) were used as received. DMF, Et_3N and *n*-Bu_3P were distilled prior to use according to the standard protocols. For thin-layer chromatography (TLC) analysis, Merck pre-coated plates (TLC silica gel 60 F_{254}, Art 5715, 0.25 mm) was used. Silica-gel preparative thin-layer chromatography (PTLC) was performed using plates prepared from Merck silica gel 60 PF_{254} (Art 7747). For flash column chromatography, silica gel 60N (Spherical, neutral, 63–210 μm) from Kanto Chemical was used. Melting point (m.p.) determinations were performed using a Yanaco MP-500 instrument or METTLER TOLEDO MP70 melting point system, and are uncorrected. ^{1}H- and ^{13}C-NMR were measured on a Bruker AV-600 (600 MHz) spectrometer. Chemical shifts (δ) 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 Spectrum 100 FTIR spectrometer or Thermo SCIENTIFIC NICOLET iS5 FTIR spectrometer. Attenuated total reflectance Fourier transform infrared (ATR-FTIR) spectra were recorded by using Perkin-Elmer Spectrum 100 FTIR spectrometer equipped with a universal ATR sampling accessory or Thermo SCIENTIFIC NICOLET iS5 FTIR spectrometer equipped iD5 ATR accessory. Elemental analyses were recorded on an Elementar vario MICRO CUBE analyzer. Optical rotations ($[\alpha]_D$) were measured on a JASCO P-3000 polarimeter. High performance liquid chromatography (HPLC) analyses were performed using a JASCO CO-2060 plus for column thermostat, UV-2077 plus for UV/VIS detector, PU-1580 for HPLC pump, and CD-2095 plus for CD detector. High-resolution mass spectra (HRMS) were obtained with Bruker Daltonics micrOTOF-Q II.

Preparation of 7 and 1,2-rearrangement

Preparation of 7



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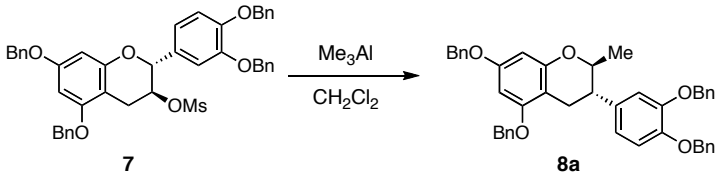
To a solution of tetrabenzyl catechin (5.01 g, 7.69 mmol) in CH_2Cl_2 (75 mL) was added Et_3N (5.4 mL, 39 mmol) and MsCl (1.20 mL, 15.5 mmol) at 0 °C. After stirring for 30 min, the reaction was quenched by the addition of saturated $NaHCO_3$ solution. The crude products were extracted with EtOAc (x3), and the combined organic extracts were washed with brine, dried (Na_2SO_4), filtered through SiO_2, and concentrated in vacuo. Recrystrallization from hexane/EtOAc/Et_2O to afford mesylate **7** (1st crop: 4.78 g, 85%, >99% e.e.; 2nd crop: 584 mg, 11%; total yield = 96%) as a white solid. Enantiomeric purity of **7** was assessed by HPLC analysis [CHIRALPAK® IE-3 (Daicel), ϕ 4.6 x 250 mm, hexane/*i*-PrOH = 80/20, 1.0 mL/min flow rate, 35 °C, 220 nm, t_R = 31.2 min for the (2*R*, 3*S*)-isomer and 38.3 min for the (2*S*, 3*R*)-isomer].

7: R_f 0.53 (hexane/toluene/EtOAc = 2/2/1); mp 93 ºC (decomp.); $[\alpha]_D^{20}$ +13.7 (*c* 1.02, $CHCl_3$); ^{1}H NMR (600 MHz, $CDCl_3$) δ 2.19 (s, 3H), 2.94 (dd, 1H, *J* = 16.8, 7.2 Hz), 3.14 (dd, 1H, *J* = 16.8, 5.4 Hz), 4.84–4.88 (m, 1H), 4.92 (d, 1H, *J* = 7.8 Hz), 4.97–5.04 (m, 4H), 5.14–5.20 (m, 4H), 6.21 (d, 1H, *J* = 2.4 Hz), 6.27 (d, 1H, *J* = 2.4 Hz), 6.90 (dd, 1H, *J* = 8.4, 1.8 Hz), 6.92 (d, 1H, *J* = 8.4 Hz), 7.01 (d, 1H, *J* = 1.8 Hz), 7.29–7.42 (m, 20H); ^{13}C NMR (150 MHz, $CDCl_3$) δ 26.6, 37.6, 70.1, 70.2, 71.17, 71.21, 77.7, 78.1, 94.2, 94.5, 100.8, 113.6, 115.1, 120.4, 127.2, 127.3, 127.5, 127.9, 128.00, 128.02, 128.1, 128.5, 128.60, 128.62, 130.4, 136.7, 136.8, 136.86, 136.92, 149.0, 149.3, 154.7, 157.6, 159.2 (several signals overlapped); IR (ATR) 3031, 2861, 1593, 1499, 1349, 1261, 1145, 1127, 920, 731, 694 cm^{-1}; HRMS (ESI) calcd for $C_{44}H_{41}O_8S$ ($[M+H]^+$) *m/z* 729.2517, found *m/z* 729.2483; Anal. calcd for $C_{44}H_{40}O_8S$: C, 72.51; H, 5.53; S, 4.40. found C, 72.34; H, 5.37; S, 4.10.

1,2-rearrangement by Me_3Al



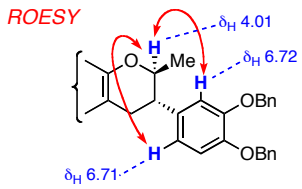
7 **8a**

To a solution of mesylate **7** (200 mg, 0.275 mmol), which was azeotropically dried with toluene (1 mL x 3), in CH_2Cl_2 (2.7 mL) was added Me_3Al (0.98 M in hexane, 0.56 mL, 0.55 mmol) at –78 °C. The reaction mixture was gradually warmed to 0 °C for 3 h, then the reaction was quenched by the addition

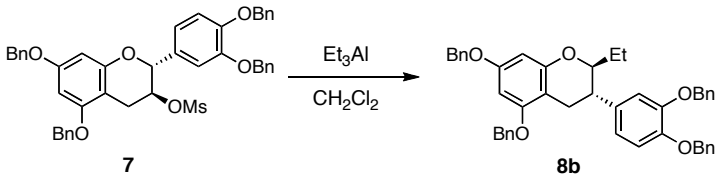
of phosphate buffer solution (pH 7) and 1 M HCl solution. The crude products were extracted with EtOAc (x3), and the combined organic extracts were washed with brine, dried (Na_2SO_4), and concentrated in vacuo. The residue was purified by flash column chromatography (hexane/EtOAc = 10/1) to afford 2-methylisoflavan **8a** (162 mg, 90%, >99% e.e.) as a white solid. Enantiomeric purity of **8a** was assessed by HPLC analysis [CHIRALPAK® IE-3 (Daicel), ϕ 4.6 x 250 mm, hexane/*i*-PrOH = 90/10, 1.0 mL/min flow rate, 35 °C, 220 nm, t_R = 10.4 min for the (*R*, *R*)-isomer and 11.6 min for the (*S*, *S*)-isomer].

8a: R_f 0.56 (hexane /EtOAc = 4/1); mp 140–141 ºC; $[\alpha]_D^{20}$ –13.6 (*c* 1.02, $CHCl_3$); ^{1}H NMR (600 MHz, $CDCl_3$) δ 1.06 (d, 3H, *J* = 6.6 Hz), 2.59–2.65 (m, 2H), 2.94–3.00 (m, 1H), 4.01 (dq, 1H, *J* = 9.0, 6.6 Hz), 4.97 (d, 1H, *J* = 11.4 Hz), 4.99 (d, 1H, *J* = 11.4 Hz), 5.01 (s, 2H), 5.13–5.17 (m, 4H), 6.17 (d, 1H, *J* = 1.8 Hz), 6.22 (d, 1H, *J* = 1.8 Hz), 6.71 (dd, 1H, *J* = 7.8, 1.8 Hz), 6.72 (d, 1H, *J* = 1.8 Hz), 6.89 (d, 1H, *J* = 7.8 Hz), 7.29–7.45 (m, 20 H); ^{13}C NMR (150 MHz, $CDCl_3$) δ 19.6, 28.2, 45.0, 69.9, 70.1, 71.4, 71.6, 76.3, 93.0, 94.3, 104.6, 115.2, 115.5, 121.0, 127.29, 127.33, 127.5, 127.6, 127.80, 127.82, 127.84, 128.0, 128.46, 128.49, 128.51, 128.6, 136.1, 137.0, 137.1, 137.2, 137.4, 148.1, 148.9, 155.9, 157.5, 158.5; IR (ATR) 2911, 1589, 1515, 1497, 1454, 1377, 1114, 1005, 810, 733, 694 cm^{-1}; HRMS (ESI) calcd for $C_{44}H_{41}O_5$ ($[M+H]^+$) *m/z* 649.2945, found *m/z* 649.2920; Anal. calcd for $C_{44}H_{40}O_5$: C, 81.46; H, 6.21. found C, 81.35; H, 6.31.

Diagnostic 2D NMR correlations for compound ***8a***



1,2-rearrangement by Et_3Al



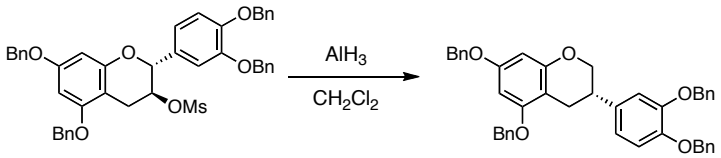
7 **8b**

To a solution of mesylate **7** (40 mg, 0.054 mmol), which was azeotropically dried with toluene (1 mL x 3), in CH_2Cl_2 (1.0 mL) was added Et_3Al (1.0 M in hexane, 0.16 mL, 0.16 mmol) at –78 °C. The reaction mixture was gradually warmed to –20 °C for 3.5 h, then the reaction was quenched by the addition of phosphate buffer solution (pH 7) and 1 M HCl solution. The crude 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 preparative TLC (hexane/EtOAc = 4/1) to afford 2-ethylisoflavan **8b** (31 mg, 86%) as a white solid.

8b: R_f 0.59 (hexane/ EtOAc = 4/1); mp 148–150 ºC; $[\alpha]_D^{20}$ –12.9 (*c* 0.995, $CHCl_3$); ^{1}H NMR (600 MHz, $CDCl_3$) δ 0.88 (t, 3H, *J* = 7.2 Hz), 1.27–1.43 (m, 2H), 2.61 (dd, 1H, *J* = 16.8, 11.4 Hz), 2.71 (ddd, 1H, *J* = 11.4, 9.6, 4.8 Hz), 2.97 (dd, 1H, *J* = 16.8, 4.8 Hz), 3.82–3.85 (m, 1H), 4.96–5.03 (m, 4H), 5.13–5.17 (m, 4H), 6.20 (d, 1H, *J* = 2.4 Hz), 6.22 (d, 1H, *J* = 2.4 Hz), 6.70 (dd, 1H, *J* = 7.8, 1.8 Hz), 6.72 (d, 1H, *J* = 1.8 Hz), 6.88 (d, 1H, *J* = 7.8 Hz), 7.26–7.46 (m, 20H); ^{13}C NMR (150 MHz, $CDCl_3$) δ 9.3, 25.9, 28.4, 42.7, 69.9, 70.2, 71.4, 71.5, 80.8, 93.0, 94.4, 104.5, 115.2, 115.5, 121.0, 127.3, 127.4, 127.5, 127.6, 127.8, 127.9, 128.0, 128.48, 128.53, 128.6, 136.2, 137.05, 137.10, 137.3, 137.5, 148.1, 148.8, 156.1, 157.5, 158.6 (several signals overlapped); IR (ATR) 2916, 1589, 1515, 1454, 1378, 1218, 1132, 1005, 809, 734, 695 cm^{-1}; HRMS (ESI) calcd for $C_{45}H_{43}O_5$ ($[M+H]^+$) *m/z* 663.3105, found *m/z* 663.3072; Anal. calcd for $C_{45}H_{42}O_5$: C, 81.54; H, 6.39. found C, 81.60; H, 6.64.

1,2-rearrangement by AlH_3



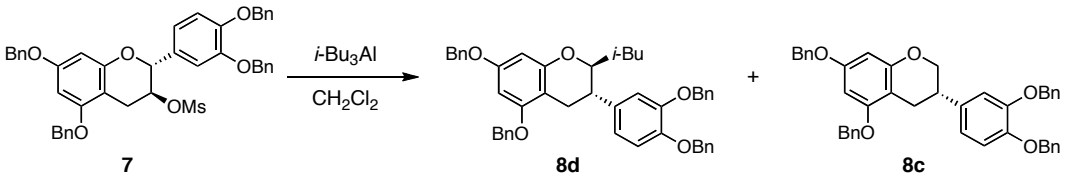
7 **8c**

To a solution of $AlCl_3$ (33 mg, 0.25 mmol) in Et_2O (1 mL) was added $LiAlH_4$ (6.5 mg, 0.17 mmol) at 0 °C. After stirring for 30 min, a solution of mesylate **7** (40 mg, 0.055 mmol), which was azeotropically dried with toluene (1 mL x 3), in CH_2Cl_2 (1 mL) was added to the reaction mixture. After stirring for 2 h at 0 °C, the reaction mixture was warmed to room temperature. After stirring for 45 min, the reaction was quenched by adding $Na_2SO_4 \cdot 10H_2O$ (225 mg, 0.698 mmol) and dried (Na_2SO_4). The mixture was filtered through a Celite® pad (washed with CH_2Cl_2) and concentrated in vacuo. The residue was purified by preparative TLC (hexane/toluene/EtOAc = 5/5/1) to afford isoflavan **8c** (25.7 mg, 73%) as a white solid.

8c: R_f 0.53 (hexane/ EtOAc = 4/1); mp 138–140 ºC; $[\alpha]_D^{20}$ +9.5 (*c* 1.0, $CHCl_3$); ^{1}H NMR (600 MHz, $CDCl_3$) δ 2.63 (dd, 1H, *J* = 16.2, 10.8 Hz), 2.99–3.07 (m, 2H), 3.87 (dd, 1H, *J* = 10.8, 10.8 Hz), 4.20–4.23 (m, 1H), 4.98–5.03 (m, 4H), 5.14 (s, 4H), 6.16 (d, 1H, *J* = 2.4 Hz), 6.24 (d, 1H, *J* = 2.4 Hz), 6.76 (dd, 1H, *J* = 8.4, 1.8 Hz), 6.82 (d, 1H, *J* = 1.8 Hz), 6.90 (d, 1H, *J* = 8.4 Hz), 7.27–7.45 (m, 20H); ^{13}C NMR (150 MHz, $CDCl_3$) δ 26.7, 37.9, 70.0, 70.2, 70.8, 71.4, 71.6, 93.2, 94.6, 104.2, 115.0, 115.3, 120.4, 127.28, 127.30, 127.5, 127.6, 127.8, 127.85, 127.88, 128.0, 128.49, 128.51, 128.54, 128.6,

135.1, 137.01, 137.02, 137.3, 137.4, 148.1, 149.0, 155.6, 157.7, 158.5; IR (ATR) 2917, 1587, 1516, 1454, 1377, 1218, 1146, 1111, 1051, 1004, 808, 734, 695 cm^{-1}; HRMS (ESI) calcd for $C_{43}H_{39}O_5$ ($[M+H]^+$) *m/z* 635.2792, found *m/z* 635.2761; Anal. calcd for $C_{43}H_{38}O_5$: C, 81.36; H, 6.03. found C, 81.43; H, 6.31.

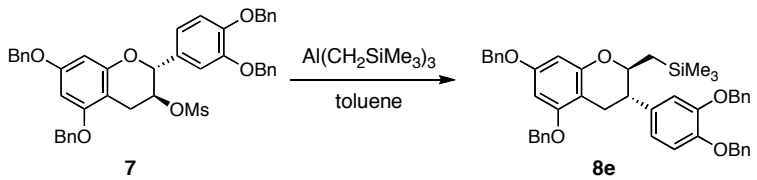
1,2-rearrangement by i-Bu_3Al



To a solution of mesylate **7** (39 mg, 0.054 mmol), which was azeotropically dried with toluene (1 mL x 3), in CH_2Cl_2 (1.0 mL) was added *i*-Bu_3Al (1.0 M in hexane, 0.16 mL, 0.16 mmol) at –78 °C. The reaction mixture was gradually warmed to 0 °C for 6 h, then the reaction was quenched by the addition of phosphate buffer solution (pH 7) and 1 M HCl solution. The crude 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 preparative TLC (hexane/EtOAc = 4/1) to afford 2-*i*-buthylisoflavan **8d** (27 mg, 74%) and isoflavan **8c** (3.7 mg, 11%) as white solids.

8d: R_f 0.62 (hexane/ EtOAc = 4/1); mp 144–145 ºC; $[\alpha]_D^{20}$ –22.6 (*c* 1.00, $CHCl_3$); ^{1}H NMR (600 MHz, $CDCl_3$) δ 0.77 (d, 3H, *J* = 6.6 Hz), 0.83 (d, 3H, *J* = 6.6 Hz), 1.00 (ddd, 1H, *J* = 14.4, 10.2, 2.4 Hz), 1.38 (ddd, 1H, *J* = 14.4, 10.2, 3.6 Hz), 1.86–1.93 (m, 1H), 2.61–2.69 (m, 2H), 2.97 (dd, 1H, *J* = 15.0, 4.2 Hz), 3.96–3.99 (m, 1H), 4.96–5.03 (m, 4H), 5.11–5.16 (m, 4H), 6.18 (d, 1H, *J* = 1.8 Hz), 6.22 (d, 1H, *J* = 1.8 Hz), 6.69 (dd, 1H, *J* = 8.4, 1.8 Hz), 6.72 (d, 1H, *J* = 1.8 Hz), 6.89 (d, 1H, *J* = 8.4 Hz), 7.27–7.45 (m, 20H); ^{13}C NMR (150 MHz, $CDCl_3$) δ 21.4, 23.8, 24.2, 28.4, 42.3, 43.8, 69.9, 70.2, 71.4, 71.5, 77.8, 93.0, 94.5, 104.5, 115.1, 115.3, 121.0, 127.3, 127.4, 127.6, 127.8, 127.85, 127.86, 128.0, 128.51, 128.54, 128.6, 136.5, 137.07, 137.10, 137.3, 137.5, 147.9, 149.0, 156.0, 157.5, 158.6 (several signals overlapped); IR (ATR) 2926, 1590, 1519, 1453, 1378, 1264, 1212, 1140, 1114, 1037, 809, 729, 692 cm^{-1}; HRMS (ESI) calcd for $C_{47}H_{47}O_5$ ($[M+H]^+$) *m/z* 691.3418, found *m/z* 691.3384.

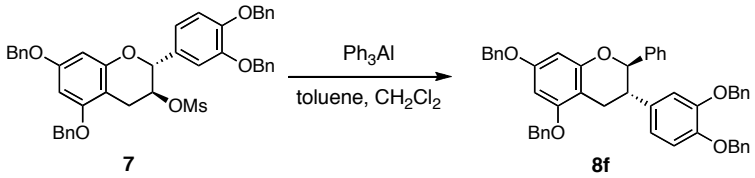
1,2-rearrangement by $Al(CH_2SiMe_3)_3$



To a solution of mesylate **7** (50 mg, 0.069 mmol), which was azeotropically dried with toluene (1 mL x 3), in toluene (1.0 mL) was added $Al(CH_2SiMe_3)_3$ 1,2-dichloroethene solution[1] at room temperature. [This reagent was in-situ prepared: To a solution of $AlCl_3$ (47 mg, 0.35 mmol) in 1,2-dichloroethene (1.0 mL) was added Me_3SiCH_2Li (1.0 M in pentane, 1.0 mL, 1.0 mmol) at room temperature. The reaction mixture was stirred for 30 min.] After stirring for 20 min, the reaction was quenched by the addition of phosphate buffer solution (pH 7) and 1 M HCl solution. The crude 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 preparative TLC (hexane/EtOAc = 3/1) to afford 2-(trimethylsilylmethyl)isoflavan **8e** (41.1 mg, 83%) as a white solid.

8e: R_f 0.56 (hexane/ EtOAc = 3/1); mp 131–133 ºC; $[\alpha]_D^{23}$ –14 (*c* 0.47, $CHCl_3$); ^{1}H NMR (600 MHz, $CDCl_3$) δ 0.02 (s, 9H), 0.54 (dd, 1H, *J* = 14.4, 3.6 Hz), 0.72 (dd, 1H, *J* = 14.4, 11.4 Hz), 2.61–2.68 (m, 2H), 2.93–3.00 (m, 1H), 4.05 (ddd, 1H, *J* = 11.4, 9.0, 3.6 Hz), 4.96–5.02 (m, 4H), 5.12–5.17 (m, 4H), 6.13 (d, 1H, *J* = 1.8 Hz), 6.21 (d, 1H, *J* = 1.8 Hz), 6.68 (dd, 1H, *J* = 8.4, 1.8 Hz), 6.72 (d, 1H, *J* = 1.8 Hz), 6.90 (d, 1H, *J* = 8.4 Hz), 7.25–7.46 (m, 20H); ^{13}C NMR (150 MHz, $CDCl_3$) δ –0.6, 21.7, 28.2, 46.2, 69.9, 70.2, 71.38, 71.44, 78.5, 92.7, 94.6, 104.6, 115.2, 115.3, 121.0, 127.25, 127.33, 127.4, 127.7, 127.77, 127.80, 128.0, 128.45, 128.46, 128.48, 128.6, 136.7, 137.0, 137.2, 137.4, 147.9, 148.8, 156.1, 157.5, 158.4 (several signals overlapped); IR (ATR) 2919, 1589, 1519, 1456, 1378, 1267, 1140, 1114, 1027, 847, 804, 727, 692 cm^{-1}; HRMS (ESI) calcd for $C_{47}H_{49}O_5Si$ ($[M+H]^+$) *m/z* 721.3344, found *m/z* 721.3310.

1,2-rearrangement by Ph_3Al



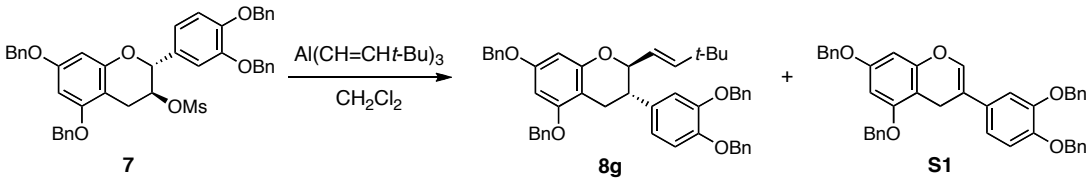
7 **8f**

To a solution of $AlCl_3$ (30 mg, 0.22 mmol) in Et_2O (1 mL) was added PhLi (1.13 M in cyclohexane/Et_2O, 0.54 mL, 0.61 mmol) at room temperature. After stirring for 35 min, a solution of mesylate **7** (50 mg, 0.069 mmol), which was azeotropically dried with toluene (1 mL x 3), in toluene/CH_2Cl_2 (1 mL / 0.4 mL) was added to the reaction mixture. After stirring for 2 h at 70 °C, the reaction was quenched by the addition of phosphate buffer solution (pH 7) and 1 M HCl solution. The crude 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 (hexane/EtOAc = 10/1) to afford 2-phenylisoflavan **8f** (46.7 mg, 95%) as a white

solid.

8f: R_f 0.59 (hexane/ EtOAc = 3/1); mp 126–128 ºC; $[\alpha]_D^{20}$ –40 (*c* 0.97, $CHCl_3$); ^{1}H NMR (600 MHz, $CDCl_3$) δ 2.87 (dd, 1H, *J* = 16.2, 10.8 Hz), 3.02–3.11 (m, 2H), 4.82 (d, 1H, *J* = 9.6 Hz), 4.95–5.05 (m, 8H), 6.26 (d, 1H, *J* = 2.4 Hz), 6.28 (d, 1H, *J* = 2.4 Hz), 6.50 (dd, 1H, *J* = 8.4, 1.8 Hz), 6.54 (d, 1H, *J* = 1.8 Hz), 6.70 (d, 1H, *J* = 8.4 Hz), 6.98–6.99 (m, 2H), 7.14–7.15 (m, 3H), 7.26–7.42 (m, 20H); ^{13}C NMR (150 MHz, $CDCl_3$) δ 27.6, 45.1, 70.0, 70.1, 71.28, 71.31, 82.9, 93.3, 94.5, 104.3, 114.9, 115.6, 121.2, 127.1, 127.28, 127.30, 127.32, 127.6, 127.68, 127.72, 127.8, 127.86, 127.94, 128.0, 128.4, 128.47, 128.52, 128.6, 134.7, 137.0, 137.30, 137.33, 139.6, 147.7, 148.6, 156.0, 157.5, 158.6 (several signals overlapped); IR (ATR) 2895, 1591, 1497, 1453, 1378, 1265, 1161, 1116, 1027, 809, 730, 693 cm^{-1}; HRMS (ESI) calcd for $C_{49}H_{43}O_5$ ($[M+H]^+$) *m/z* 711.3105, found *m/z* 711.3071; Anal. calcd for $C_{49}H_{42}O_5$: C, 82.79; H, 5.96. found C, 83.04; H, 6.08.

1,2-rearrangement by Al(CH=CH*t*-Bu)$_3$



7 **8g** **S1**

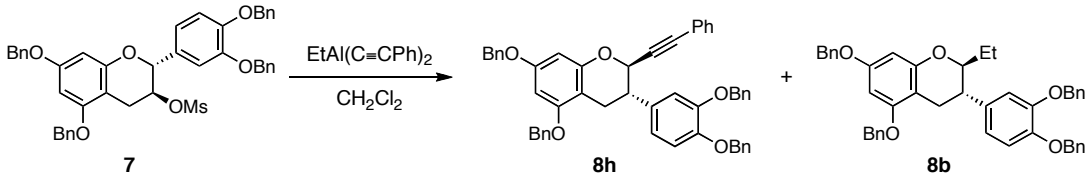
To a solution of IHC=CH(*t*-Bu)$_3$[2] (105 mg, 0.501 mmol) in Et_2O (2 mL) was added *n*-BuLi (1.64 M in hexane, 0.30 mL, 0.49 mmol) at –78 °C. After stirring for 15 min, a solution of $AlCl_3$ (22 mg, 0.17 mmol) in Et_2O (1.5 mL) was added to the reaction mixture. The reaction mixture was immediately warmed to room temperature. After stirring for 35 min, the reaction mixture was cooled at 0 °C, then a solution of mesylate **7** (40 mg, 0.055 mmol), which was azeotropically dried with toluene (1 mL x 3), in CH_2Cl_2 (1.5 mL) was added to the reaction mixture. The reaction mixture was gradually warmed to room temperature for 1 h, and to 80 °C for 3 h. After stirring for 1 h at 80 °C, the reaction was quenched by the addition of phosphate buffer solution (pH 7) and 1 M HCl solution. The crude 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 preparative TLC (hexane/EtOAc = 4/1) to afford 2-(*t*-buthylvinyl)isoflavan **8g** (21.5 mg, 54%) and 2,3-isoflavene **S1** (5.5 mg, 16%) as white solids.

8g: R_f 0.55 (hexane/ EtOAc = 4/1); mp 150–152 ºC; $[\alpha]_D^{20}$ –13.7 (*c* 1.19, $CHCl_3$); ^{1}H NMR (600 MHz, $CDCl_3$) δ 0.75 (s, 9H), 2.68–2.78 (m, 2H), 3.03 (dd, 1H, *J* = 15.6, 4.2 Hz), 4.24 (dd, 1H, *J* = 9.0, 9.0 Hz), 4.97–5.02 (m, 4H), 5.11–5.17 (m, 5H), 5.30 (d, 1H, *J* = 16.2 Hz), 6.23 (d, 1H, *J* = 2.4 Hz), 6.24 (d, 1H, *J* = 2.4 Hz), 6.63 (dd, 1H, *J* = 7.8, 1.8 Hz), 6.70 (d, 1H, *J* = 1.8 Hz), 6.84 (d, 1H, *J* = 7.8 Hz),

7.27–7.43 (m, 20H); ^{13}C NMR (150 MHz, $CDCl_3$) δ 27.6, 29.1, 32.6, 44.1, 69.9, 70.1, 71.4, 71.5, 81.7, 93.2, 94.5, 104.4, 115.2, 115.3, 121.5, 122.7, 127.2, 127.3, 127.4, 127.5, 127.7, 127.83, 127.84, 127.9, 128.46, 128.51, 128.52, 128.6, 135.7, 136.98, 137.03, 137.3, 137.4, 145.9, 147.8, 148.9, 155.6, 157.5, 158.5; IR (ATR) 2957, 1588, 1517, 1455, 1377, 1220, 1150, 1094, 1016, 976, 812, 743, 694 cm^{-1}; HRMS (ESI) calcd for $C_{49}H_{49}O_5$ ($[M+H]^+$) *m/z* 717.3575, found *m/z* 717.3539.

S1: R_f 0.50 (hexane/ EtOAc = 4/1); mp 83–85 ºC; ^{1}H NMR (600 MHz, $CDCl_3$) δ 3.51 (brd, 2H, *J* = 0.6 Hz), 5.00 (s, 2H), 5.04 (s, 2H), 5.16 (s, 2H), 5.17 (s, 2H), 6.18 (d, 1H, *J* = 2.4 Hz), 6.30 (d, 1H, *J* = 2.4 Hz), 6.79 (s, 1H), 6.91 (s, 2H), 6.98 (s,1H), 7.26–7.45 (m, 20H); ^{13}C NMR (150 MHz, $CDCl_3$) δ 21.4, 70.1, 70.2, 71.4, 71.7, 94.1, 95.5, 101.9, 112.1, 112.5, 115.1, 117.9, 127.25, 127.31, 127.5, 127.6, 127.8, 127.9, 128.0, 128.1, 128.5, 128.6, 131.6, 136.7, 136.8, 136.9, 137.32, 137.34, 148.3, 148.9, 151.7, 157.4, 158.6 (several signals overlapped); IR (ATR) 2920, 1659, 1587, 1499, 1453, 1380, 1268, 1168, 1138, 1027, 806, 731, 694 cm^{-1}; HRMS (ESI) calcd for $C_{43}H_{37}O_5$ ($[M+H]^+$) *m/z* 633.2636, found *m/z* 633.2604.

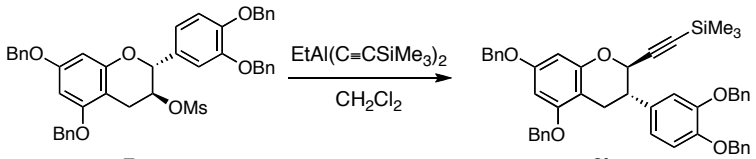
1,2-rearrangement by $EtAl(C{\equiv}CPh)_2$



To a solution of HC≡CPh (0.090 mL, 0.82 mmol) was added *n*-BuLi (1.63 M in hexane, 0.50 mL, 0.82 mmol) at 0 °C. After stirring for 50 min, $EtAlCl_2$ (1.04 M in hexane, 0.40 mL, 0.41 mmol) was added to the reaction mixture. After stirring for 30 min, a solution of mesylate **7** (100 mg, 0.138 mmol), which was azeotropically dried with toluene (1 mL x 3), in CH_2Cl_2 (1.5 mL) was added to the reaction mixture. After stirring for 20 min, the reaction was quenched by the addition of phosphate buffer solution (pH 7) and 1 M HCl solution. The crude 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 (hexane/EtOAc = 9/1 to 5/1) to afford 2-(phenylalkynyl)isoflavan **8h** (77.2 mg, 76%) and 2-ethylisoflavan **8b** (1.0 mg, 1.0%) as white solids.
8h: R_f 0.50 (hexane/ EtOAc = 3/1); mp 191–193 ºC; $[\alpha]_D^{20}$ –47.8 (*c* 1.03, $CHCl_3$); ^{1}H NMR (600 MHz, $CDCl_3$) δ 2.77–2.83 (m, 1H), 3.11–3.18 (m, 2H), 4.90 (d, 1H, *J* = 9.0 Hz), 5.01 (s, 4H), 5.09 (s, 2H), 5.14 (s, 2H), 6.27–6.28 (m, 2H), 6.82 (dd, 1H, *J* = 8.4, 1.8 Hz), 6.89 (d, 1H, *J* = 1.8 Hz), 6.91 (d, 1H, *J* = 8.4 Hz), 7.21–7.43 (m, 25H); ^{13}C NMR (150 MHz, $CDCl_3$) δ 26.4, 43.6, 70.0, 70.2, 71.3, 71.4, 71.6,

86.4, 86.9, 93.8, 94.8, 103.8, 115.2, 115.7, 121.1, 122.3, 127.3, 127.5, 127.6, 127.76, 127.78, 127.9, 128.0, 128.2, 128.4, 128.47, 128.54, 128.6, 131.8, 134.8, 136.90, 136.92, 137.2, 137.4, 148.2, 148.9, 154.6, 157.5, 158.6 (several signals overlapped); IR (ATR) 2870, 1615, 1586, 1516, 1435, 1378, 1243, 1145, 1092, 1010, 806, 745, 697 cm^{-1}; HRMS (ESI) calcd for $C_{51}H_{43}O_5$ ($[M+H]^+$) *m/z* 735.3105, found *m/z* 735.3072; Anal. calcd for $C_{51}H_{42}O_5$: C, 83.35; H, 5.76. found C, 83.22; H, 5.80.

1,2-rearrangement by $EtAl(C{\equiv}CSiMe_3)_2$



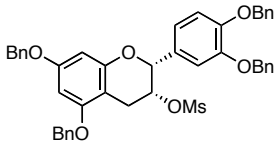
7 **8i**

To a solution of $HC{\equiv}CSiMe_3$ (0.12 mL, 0.87 mmol) was added *n*-BuLi (1.75 M in hexane, 0.48 mL, 0.84 mmol) at 0 °C. After stirring for 40 min, $EtAlCl_2$ (1.04 M in hexane, 0.40 mL, 0.41 mmol) was added to the reaction mixture. After stirring for 40 min, a solution of mesylate **7** (100 mg, 0.138 mmol), which was azeotropically dried with toluene (1 mL x 3), in CH_2Cl_2 (1.5 mL) was added to the reaction mixture. After stirring for 30 min, the reaction was quenched by the addition of phosphate buffer solution (pH 7) and 1 M HCl solution. The crude 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 (hexane/EtOAc = 9/1 to 5/1) to afford 2-(trimethylsilylalkynyl)isoflavan **8i** (96.4 mg, 96%) as a white solid.

8i: R_f 0.60 (hexane/ EtOAc = 3/1); mp 111–113 ºC; $[\alpha]_D^{20}$ –11.0 (*c* 1.03, $CHCl_3$); ^{1}H NMR (600 MHz, $CDCl_3$) δ 0.03 (s, 9H), 2.70–2.76 (m, 1H), 3.01–3.08 (m, 2H), 4.64 (d, 1H, *J* = 9.0 Hz), 4.99–5.00 (m, 4H), 5.12–5.16 (m, 4H), 6.24 (d, 1H, *J* = 1.8 Hz), 6.26 (d, 1H, *J* = 1.8 Hz), 6.76 (dd, 1H, *J* = 7.8, 1.8 Hz), 6.82 (d, 1H, *J* = 1.8 Hz), 6.89 (d, 1H, *J* = 7.8 Hz), 7.27–7.44 (m, 20H); ^{13}C NMR (150 MHz, $CDCl_3$) δ –0.2, 26.7, 43.8, 70.1, 70.3, 71.3, 71.6, 71.8, 92.4, 93.9, 94.9, 102.4, 104.0, 115.3, 115.6, 121.6, 127.38, 127.42, 127.6, 127.7, 127.9, 127.97, 128.04, 128.1, 128.60, 128.63, 128.67, 128.74, 134.8, 137.0, 137.1, 137.4, 137.6, 148.4, 149.0, 154.8, 157.6, 158.6; IR (ATR) 2912, 1587, 1515, 1454, 1379, 1241, 1147, 1091, 1051, 1008, 842, 743, 696 cm^{-1}; HRMS (ESI) calcd for $C_{48}H_{47}O_5Si$ ($[M+H]^+$) *m/z* 731.3187, found *m/z* 731.3155; Anal. calcd for $C_{48}H_{46}O_5Si$: C, 78.87; H, 6.34. found C, 79.09; H, 6.51.

*Preparayion of **9** and 1,2-rearrangement*

*Preparation of **9***

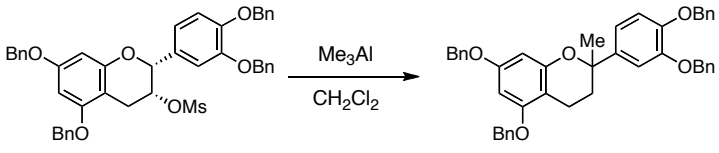


9

To a solution of tetra-benzyl-epicatechin (112 mg, 0.173 mmol) in CH_2Cl_2 (1.7 mL) was added Et_3N (0.12 mL, 0.86 mmol) and MsCl (27 μL, 0.35 mmol) at 0 °C. After stirring for 2 h, the reaction was quenched by the addition of saturated $NaHCO_3$ solution. The crude products were extracted with EtOAc (x3), and the combined organic extracts were washed with brine, dried (Na_2SO_4) and concentrated in vacuo. Recrystrallization from hexane/EtOAc to afford mesylate **9** (1st crop: 90.2 mg, 72%, >99% e.e.; 2nd crop: 19.9 mg, 16%; total yield = 88%) as a white solid. Enantiomeric purity of **9** was assessed by HPLC analysis [CHIRALPAK® IE-3 (Daicel), ϕ 4.6 x 250 mm, hexane/*i*-PrOH = 75/25, 1.0 mL/min flow rate, 35 °C, 220 nm, t_R = 31.8 min for the (*R*, *R*)-isomer and 51.6 min for the (*S*, *S*)-isomer].

9: R_f 0.29 (hexane/EtOAc = 3/1); mp 172 ºC (decomp.); $[\alpha]_D^{20}$ –28 (*c* 0.99, $CHCl_3$); ^{1}H NMR (600 MHz, $CDCl_3$) δ 2.08 (s, 3H), 3.07 (dd, 1H, *J* = 18.0, 4.2 Hz), 3.24 (d, 1H, *J* = 18.0 Hz), 4.98–5.03 (m, 6H), 5.18 (s, 2H), 5.21 (s, 2H), 6.26 (d, 1H, *J* = 1.8 Hz), 6.28 (d, 1H, *J* = 1.8 Hz), 6.95 (d, 1H, *J* = 7.8 Hz), 6.98 (dd, 1H, *J* = 7.8, 1.8 Hz), 7.14 (d, 1H, *J* = 1.8 Hz), 7.29–7.47 (m, 20H); ^{13}C NMR (150 MHz, $CDCl_3$) δ 27.5, 37.3, 70.1, 70.2, 71.2, 71.3, 76.6, 76.9, 94.3, 94.8, 99.7, 113.4, 115.1, 119.4, 127.29, 127.32, 127.51, 127.53, 127.9, 127.95, 128.00, 128.02, 128.5, 128.58, 128.59, 128.6, 130.6, 136.7, 136.8, 136.95, 136.99, 148.8, 149.0, 155.0, 157.9, 159.0; IR (ATR) 2932, 1499, 1591, 1363, 1329, 1170, 1134, 1025, 913, 761, 695 cm^{-1}; HRMS (ESI) calcd for $C_{44}H_{41}O_8S$ ($[M+H]^+$) *m/z* 729.2517, found *m/z* 729.2482; Anal. calcd for $C_{44}H_{40}O_8S$: C, 72.51; H, 5.53; S, 4.40. found C, 72.35; H, 5.76; S, 4.11.

1,2-rearrangement by Me_3Al



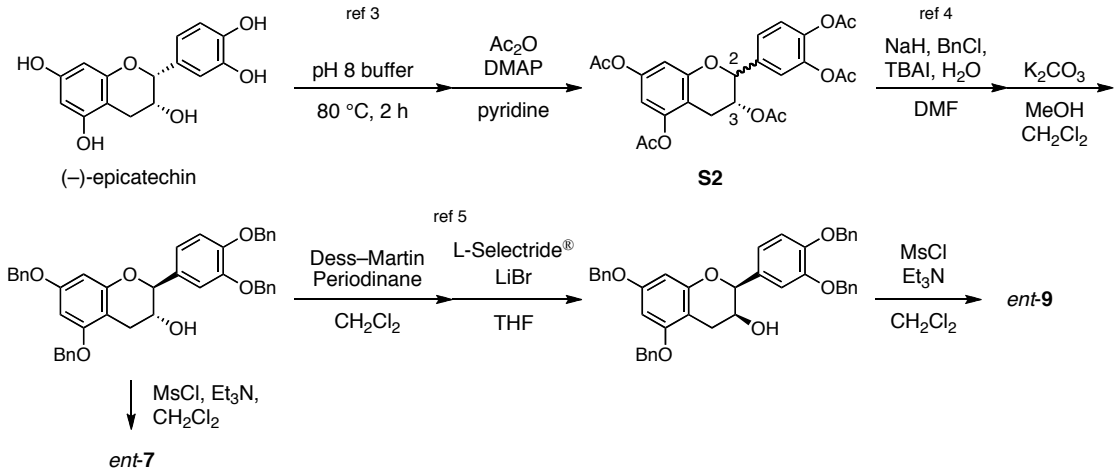
9 **10**

To a solution of mesylate **9** (20 mg, 0.028 mmol), which was azeotropically dried with toluene (1 mL x 3), in CH_2Cl_2 (0.5 mL) was added Me_3Al (0.98 M in hexane, 0.10 mL, 0.098 mmol) at –78 °C. The reaction mixture was gradually warmed to 0 °C for 4 h, and to room temperature for 1 h. After stirring

for 1 h at room temperature, the reaction was quenched by the addition of phosphate buffer solution (pH 7) and 1 M HCl solution. The crude 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 preparative TLC (hexane/EtOAc = 3/1) to afford 2-methylflavan **10** (3.7 mg, 21%, 0% e.e.) as a white amorphous solid and mesylate **9** (12.1 mg, 60%). Enantiomeric purity of **10** was assessed by HPLC analysis [CHIRALPAK® IE-3 (Daicel), ϕ 4.6 x 250 mm, hexane/*i*-PrOH = 90/10, 1.0 mL/min flow rate, 35 °C, 220 nm, t_R = 19.4 min and 26.4 min].

10: R_f 0.61 (hexane /EtOAc = 4/1); ^{1}H NMR (600 MHz, $CDCl_3$) δ 1.54 (s, 3H), 1.91–1.96 (m, 1H), 2.15–2.25 (m, 2H), 2.59–2.64 (m, 1H), 4.94 (s, 2H), 5.00 (d, 1H, *J* = 11.4 Hz), 5.03 (d, 1H, *J* = 11.4 Hz), 5.07 (s, 2H), 5.10 (s, 2H), 6.18 (d, 1H, *J* = 1.8 Hz), 6.26 (d, 1H, *J* = 1.8 Hz), 6.84 (d, 1H, *J* = 8.4 Hz), 6.86 (dd, 1H, *J* = 8.4, 1.8 Hz), 6.96 (d, 1H, *J* = 1.8 Hz), 7.26–7.44 (m, 20H); ^{13}C NMR (150 MHz, $CDCl_3$) δ 16.9, 29.9, 32.5, 69.8, 70.1, 71.3, 71.6, 78.1, 93.0, 94.9, 103.9, 113.1, 114.7, 118.1, 127.2, 127.3, 127.57, 127.59, 127.7, 127.76, 127.78, 128.0, 128.4, 128.5, 128.6, 137.1, 137.2, 137.3, 137.5, 138.9, 147.9, 148.5, 155.2, 157.5, 158.6 (several signals overlapped); IR (ATR) 2927, 1615, 1589, 1497, 1265, 1209, 1139, 1108, 1026, 808, 732, 694 cm^{-1}; HRMS (ESI) calcd for $C_{44}H_{41}O_5$ ($[M+H]^+$) *m/z* 649.2949, found *m/z* 649.2919.

*Preparation of ent-**7** and ent-**9***

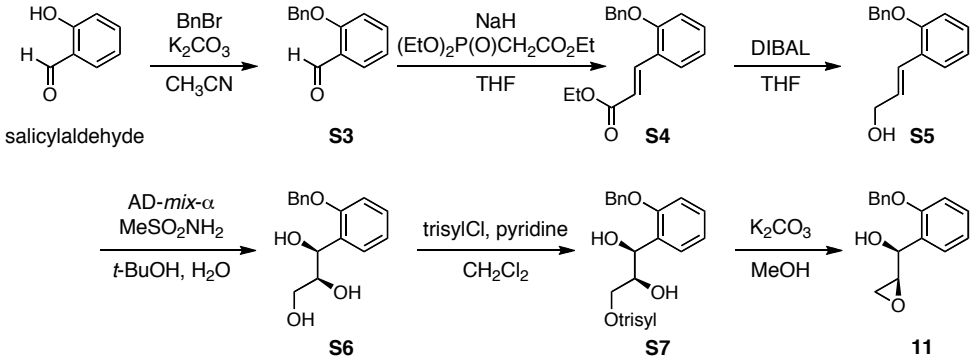


A solution of (–)-epicatechin (1.00 g, 3.45 mmol) in phosphate buffer solution (pH 8) was degassed three times and heated for 2 h at 80 °C. After cooling to room temperature, reaction mixture was extracted with EtOAc (x5), and the combined organic extracts were washed with brine, dried (Na_2SO_4), and concentrated in vacuo. The residue (1.22 g) was dissolved pyridine (15 mL), and added acetic anhydride (2.0 mL, 21 mmol) and 4-dimethylaminopyridine (18.2 mg, 0.149 mmol). After stirring for 21 h at room temperature, the reaction mixture was cooled at 0 °C, and quenched by the addition of 2M HCl solution. The crude 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 (hexane/EtOAc = 1/1) to afford acetate **S2** (427 mg, 25%, mixture of 2,3-*cis/trans*, ratio = 5/95) as a white solid.

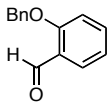
Subsequent conversion of **S2** to *ent*-**7** and *ent*-**9** were carried out according to the procedure described in the literatures (refs 4 and 5).

*Preparation of ortho-substituted catechin mesylate **17** and 1,2-rearrangement*

*Preparation of B-ring unit **11***[6]



*Preparation of **S3***

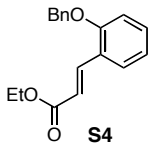


S3

To a suspension of K_2CO_3 (17.0 g, 123 mmol) and salicylaldehyde (4.3 mL, 41 mmol) in CH_3CN (206 mL) was added benzyl bromide (5.2 mL, 44 mmol) at room temperature, and the mixture was stirred at reflux for 1 h. The reaction was quenched by the addition of diethylamine (5.0 mL, 48 mmol), 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 flush column chromatography (hexane/EtOAc = 9/1) to afford 2-benzyloxybenzaldehyde (**S3**) (8.57 g, 98%) as a colorless oil.

S3: R_f 0.50 (hexane/EtOAc = 4/1); ^{1}H NMR (600 MHz, $CDCl_3$) δ 5.20 (s, 2H), 7.03–7.06 (m, 2H), 7.34–7.45 (m, 5H), 7.52–7.55 (m, 1H), 7.86 (dd, 1H, *J* = 7.8, 1.8 Hz), 10.56 (s, 1H); ^{13}C NMR (150 MHz, $CDCl_3$) δ 70.5, 113.0, 121.0, 125.2, 127.3, 128.3, 128.5, 128.8, 135.9, 136.1, 161.1, 189.8; IR (neat) 3034, 2863, 1686, 1597, 1482, 1456, 1285, 1238, 1161, 1006, 757, 696 cm^{-1}; HRMS (ESI) calcd for $C_{14}H_{12}NaO_2$ ($[M+Na]^+$) *m/z* 235.0730, found *m/z* 235.0726.

*Preparation of **S4***



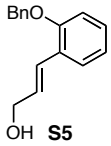
S4

To a suspension of NaH (2.18 g, 63% dispersion in mineral oil, 57.3 mmol, washed with hexane) in THF (222 mL) was dropped triethyl phosphonoacetate (10.4 mL, 52.0 mmol) at 0 °C. After stirring for 1 h at 0 °C, a solution of aldehyde **S3** (10.0 g, 47.4 mmol) in THF (15 mL) was added and the mixture

was stirred for 1 h. The reaction was quenched by the addition of water, 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 flush column chromatography (hexane/EtOAc = 9/1) to afford ether **S4** (13.1 g, 98%) as a white solid.

S4: R_f 0.47 (hexane/EtOAc = 4/1); mp 43–45 ºC; ^{1}H NMR (600 MHz, $CDCl_3$) δ 1.33 (t, 3H, J = 7.2 Hz), 4.25 (q, 2H, J = 7.2 Hz), 5.18 (s, 2H), 6.53 (d, 1H, J = 16.2 Hz), 6.94–6.98 (m, 2H), 7.29–7.44 (m, 6H), 7.54 (d, 1H, J = 7.8 Hz), 8.09 (d, 1H, J = 16.2 Hz); ^{13}C NMR (150 MHz, $CDCl_3$) δ 14.3, 60.3, 70.4, 112.8, 118.9, 121.0, 123.9, 127.1, 128.0, 128.6, 128.7, 131.3, 136.7, 139.8, 157.3, 167.4; IR (ATR) 3034, 2978, 1705, 1624, 1492, 1447, 1277, 1160, 1004, 867, 740, 695 cm^{-1}; HRMS (ESI) calcd for $C_{18}H_{18}NaO_3$ ([M+Na]$^+$) *m/z* 305.1148, found *m/z* 305.1144.

*Preparation of **S5***

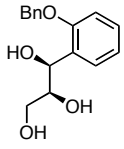


S5

To a solution of **S4** (2.50 g, 8.88 mmol) in THF (45 mL) was added (*i*-Bu)$_2$AlH (1.1 M in hexane, 20 mL, 22 mmol) at –78 °C. After stirring for 2 h, the reaction quenched by the careful addition of MeOH. After warming to 0 °C, saturated aqueous pottasium sodium tartrate (Rochell's salt) was added to the mixture, and the stirring was continued 1 day. 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 flush column chromatography (hexane/EtOAc = 9/1 to 3/1) to afford allyl alcohol **S5** (2.12 g, 99%) as a white solid.

S5: R_f 0.17 (hexane/EtOAc = 4/1); mp 49–50 ºC; ^{1}H NMR (600 MHz, $CDCl_3$) δ 1.46 (brs, 1H, OH), 4.30 (d, 2H, J = 6.0 Hz), 5.10 (s, 2H), 6.39 (dt, 1H, J = 15.6, 6.0 Hz), 6.91–6.95 (m, 2H), 6.99 (d, 1H, J = 15.6 Hz), 7.18–7.21 (m, 1H), 7.31–7.48 (m, 6H); ^{13}C NMR (150 MHz, $CDCl_3$) δ 64.3, 70.4, 112.5, 121.0, 126.1, 126.2, 127.0, 127.3, 127.9, 128.6, 128.8, 129.2, 137.1, 155.9; IR (ATR) 3000, 2866, 1598, 1490, 1449, 1382, 1295, 1243, 1112, 1014, 979, 742, 698 cm^{-1}; HRMS (ESI) calcd for $C_{16}H_{16}NaO_2$ ([M+Na]$^+$) *m/z* 263.1043, found *m/z* 263.1038.

*Preparation of **S6***

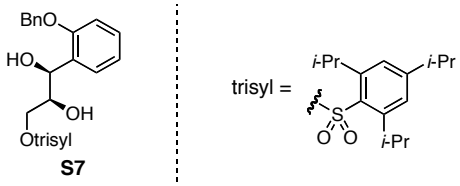


S6

To a suspension of potassium hexacyanoferrate (III) (41.1 g, 125 mmol) in the mixed solvent (1.08 L, *t*-BuOH/H_2O = 1/1), K_2CO_3 (17.2 g, 125 mmol), methanesulfonamide (4.75 g, 50.0 mmol), $(DHQ)_2$-PHAL (324 mg, 0.416 mmol), and $K_2OsO_2(OH)_4$ (76 mg, 0.21 mmol) were added at room temperature. After stirring for 35 min, allyl alcohol **S5** (10.0 g, 41.6 mmol) was added to the solution at 0 ºC. After stirring for 42 h at 0 ºC, the reaction was quenched by adding $Na_2S_2O_3$ (63.0 g, 500 mmol), then warm to room temperature and stirred for 1 day. The products were extracted with CH_2Cl_2 (x3) and the combined organic extracts were washed with 2 M KOH and brine, dried (Na_2SO_4), and concentrated in vacuo. The residue was purified by flash column chromatography (hexane/EtOAc = 1/1 to EtOAc only) to afford triol **S6** (11.5 g, quant.) as a white amorphous solid.

S6: R_f 0.26 (hexane/EtOAc = 1/3); $[\alpha]_D^{20}$ +53.9 (*c* 1.01, MeOH); ^{1}H NMR (600 MHz, CD_3OD) δ 3.49–3.54 (m, 2H), 3.79–3.83 (m, 1H), 5.08–5.14 (m, 3H), 6.97–7.02 (m, 2H), 7.21–7.24 (m, 1H), 7.29–7.32 (m, 1H), 7.36–7.39 (m, 2H), 7.47 (d, 2H, *J* = 7.2 Hz), 7.50 (d, 1H, *J* = 7.2 Hz); ^{13}C NMR (150 MHz, CD_3OD) δ 64.9, 69.4, 71.1, 76.8, 112.9, 121.9, 128.4, 128.87, 128.89, 129.4, 129.6, 131.9, 138.7, 156.7; IR (ATR) 3300, 2945, 1602, 1493, 1449, 1378, 1242, 1091, 1024, 979, 752, 692 cm^{-1}; HRMS (ESI) calcd for $C_{16}H_{18}NaO_4$ ([M+Na]$^+$) *m/z* 297.1097, found *m/z* 297.1094.

*Preparation of **S7***

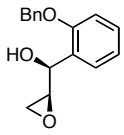


To a solution of triol **S6** (10.9 g, 39.7 mmol) in CH_2Cl_2 (50 mL), pyridine (32 mL, 0.40 mol) and 2,4,6-triisopropylbenzenesulfonyl chloride (30 g, 99 mmol) were added at 0 ºC and the reaction mixture was warmed to room temperature. After stirring for 19 h, the reaction was cooled to 0 °C and quenched by adding 2 M HCl solution. The crude 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 (hexane/EtOAc = 3/1) to afford sulfonyl ester **S7** (19.4 g, 90%) as a white amorphous solid.

S7: R_f 0.15 (hexane/EtOAc = 3/1); $[\alpha]_D^{20}$ +11.9 (*c* 1.29, $CHCl_3$); ^{1}H NMR (600 MHz, $CDCl_3$) δ 1.206 (s, 3H), 1.213 (s, 3H), 1.217 (s, 3H), 1.224 (s, 3H), 1.25 (s, 3H), 1.26 (s, 3H), 2.68–2.69 (m, 1H, OH), 2.87–2.94 (m, 1H), 3.00–3.01 (m, 1H, OH), 4.02 (dd, 1H, *J* = 10.2, 7.2 Hz), 4.07–4.12 (m, 3H), 4.14–4.17 (m, 1H), 4.99 (brt, 1H, *J* = 6.0 Hz), 5.06 (d, 1H, *J* = 11.4 Hz), 5.08 (d, 1H, *J* = 11.4 Hz), 6.94 (d, 1H, *J* = 7.8 Hz), 6.99 (dd, 1H, *J* = 7.8, 7.8 Hz), 7.16 (s, 2H), 7.25–7.28 (m, 1H), 7.31–7.38 (m,

6H); ^{13}C NMR (150 MHz, $CDCl_3$) δ 23.5, 24.7, 29.6, 34.3, 69.9, 70.0, 70.3, 72.4, 111.9, 121.4, 123.8, 127.3, 127.97, 128.01, 128.2, 128.8, 129.1, 129.3, 136.3, 150.9, 153.8, 155.5; IR (ATR) 3508, 2958, 1600, 1452, 1345, 1236, 1176, 966, 807, 752, 695, 664 cm^{-1}; HRMS (ESI) calcd for $C_{31}H_{40}NaO_6S$ ($[M+Na]^+$) *m/z* 563.2438, found *m/z* 563.2413.

*Preparation of **11***

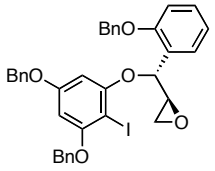


11

To a solution of sulfonyl ester **S7** (4.58 g, 8.48 mmol) in MeOH (42 mL) was added K_2CO_3 (2.34 g, 16.9 mmol) at 0 ºC. After stirring for 5 h, the mixture was filtered through a Celite® pad (washed with EtOAc). After concentrating in vacuo, adding water to the filtrate, and the products were 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 (hexane/EtOAc = 4/1 to 1/1) to afford epoxy alcohol **11** (2.12 g, 98%, 93% e.e.) as a colorless oil. Enantiomeric purity of **11** was assessed by HPLC analysis [CHIRALPAK® IE-3 (Daicel), ϕ 4.6 x 250 mm, hexane/*i*-PrOH = 90/10, 1.0 mL/min flow rate, 35 °C, 220 nm, t_R = 15.7 min for the (*S*, *S*)-isomer and 17.6 min for the (*R*, *R*)-isomer].[7]

11: R_f 0.48 (hexane/EtOAc = 3/2); $[\alpha]_D^{23}$ +26.3 (*c* 1.05, $CHCl_3$); ^{1}H NMR (600 MHz, $CDCl_3$) δ 2.69–2.72 (m, 1H, OH), 2.75–2.78 (m, 2H), 3.26 (dd, 1H, *J* = 6.0, 3.6, 3.0 Hz), 4.83 (dd, 1H, *J* = 6.0, 6.0 Hz), 5.10 (s, 2H), 6.97 (d, 1H, *J* = 8.4 Hz), 7.02 (dd, 1H, *J* = 7.2, 7.2 Hz), 7.27–7.30 (m, 1H), 7.33–7.41 (m, 5H), 7.48 (d, 1H, *J* = 7.2 Hz); ^{13}C NMR (150 MHz, $CDCl_3$) δ 45.6, 55.3, 70.2, 70.3, 111.8, 121.3, 127.4, 127.5, 128.2, 128.7, 128.8, 129.1, 136.5, 155.7; IR (neat) 3440, 3063, 2927, 1601, 1490, 1452, 1381, 1289, 1239, 1044, 919, 754, 698 cm^{-1}; HRMS (ESI) calcd for $C_{16}H_{16}NaO_3$ ($[M+H]^+$) *m/z* 279.0992, found *m/z* 279.0986.

*Preparation of **13***



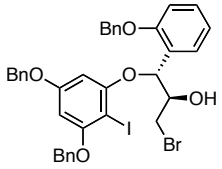
13

To a solution of epoxy alcohol **11** (26 mg, 0.10 mmol) in toluene (1.0 mL) was added iodophenol **12**

(30 mg, 0.069 mmol) and *N,N,N',N'*-tetramethylazodicarboxamide (36 mg, 0.21 mmol) at room temperature. After being cooled at 0 ºC, *n*-Bu_3P (43 μL, 0.17 mmol) was added to reaction mixture, and the resulting mixture was stirred for 2 h. The reaction was quenched by adding water. The crude 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 preparative TLC (hexane/toluene/EtOAc = 5/5/1) to afford ether **13** (39.0 mg, 83%, single diastereomer) as a white amorphous solid.

13: R_f 0.47 (hexane/toluene/EtOAc = 5/5/1); $[\alpha]_D^{25}$ +79.7 (*c* 1.05, $CHCl_3$); ^{1}H NMR (600 MHz, $CDCl_3$) δ 2.79 (dd, 1H, *J* = 5.4, 4.2 Hz), 3.28 (dd, 1H, *J* = 5.4, 2.4 Hz), 3.38–3.40 (m, 1H), 4.76 (d, 1H, *J* = 11.4 Hz), 4.79 (d, 1H, *J* = 11.4 Hz), 5.05 (s, 2H), 5.12 (d, 1H, *J* = 11.4 Hz), 5.17 (d, 1H, *J* = 11.4 Hz), 6.03 (d, 1H, *J* = 1.8 Hz), 6.15 (s, 2H), 6.96–6.99 (m, 2H), 7.22–7.47 (m, 17H); ^{13}C NMR (150 MHz, $CDCl_3$) δ 44.1, 53.6, 68.9, 70.1, 70.3, 70.9, 71.8, 94.3, 94.4, 111.8, 121.6, 125.2, 126.9, 127.2, 127.6, 127.8, 128.08, 128.13, 128.2, 128.5, 128.6, 128.7, 129.6, 136.4, 136.55, 136.56, 155.5, 157.7, 158.7, 160.8; IR (ATR) 3031, 2923, 1578, 1452, 1427, 1378, 1225, 1162, 1099, 1017, 733, 694 cm^{-1}; HRMS (ESI) calcd for $C_{36}H_{31}INaO_5$ ($[M+Na]^+$) *m/z* 693.1108, found *m/z* 693.1074.

*Preparation of **14***



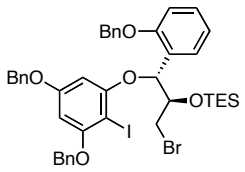
14

To a solution of ether **13** (38 mg, 0.056 mmol) in THF (1.0 mL) was added Li_2NiBr_4 (ca. 0.4 M in THF, 0.42 mL, 0.17 mmol) at 0 ºC. After being warmed at room temperature and stirring for 80 h, the reaction was quenched by the addition of phosphate buffer solution (pH 7). The crude 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 preparative TLC (hexane/EtOAc = 3/1) to afford bromohydrin **14** (38.7 mg, 91%) as a white amorphous solid.

14: R_f 0.35 (hexane/EtOAc = 3/1); $[\alpha]_D^{20}$ +89.8 (*c* 1.43, $CHCl_3$); ^{1}H NMR (600 MHz, $CDCl_3$) δ 2.56 (d, 1H, *J* = 7.2 Hz, OH), 3.71 (dd, 1H, *J* = 10.8, 3.0 Hz), 3.88 (dd, 1H, *J* = 10.8, 7.2 Hz), 4.26–4.29 (m, 1H), 4.73 (d, 1H, *J* = 11.4 Hz), 4.76 (d, 1H, *J* = 11.4 Hz), 5.06 (s, 2H), 5.13 (d, 1H, *J* = 11.4 Hz), 5.19 (d, 1H, *J* = 11.4 Hz), 5.86 (d, 1H, *J* = 5.4 Hz), 6.05 (d, 1H, *J* = 2.4 Hz), 6.17 (d, 1H, *J* = 2.4 Hz), 6.96–6.98 (m, 2H), 7.19–7.20 (m, 2H), 7.27–7.47 (m, 15H); ^{13}C NMR (150 MHz, $CDCl_3$) δ 36.5, 68.7, 70.1, 70.3, 70.9, 73.9, 76.3, 94.2, 94.5, 111.9, 121.7, 125.0, 126.9, 127.2, 127.6, 127.7, 127.8, 128.1,

128.2, 128.5, 128.6, 128.8, 129.6, 136.2, 136.4, 155.8, 157.3, 158.8, 160.9 (several signals overlapped); IR (ATR) 3544, 3031, 2870, 1579, 1452, 1427, 1377, 1223, 1162, 1101, 1016, 734, 694 cm^{-1}; HRMS (ESI) calcd for $C_{36}H_{32}BrINaO_5$ ($[M+Na]^+$) *m/z* 773.0370, found *m/z* 773.0335.

Preparation of ***15***

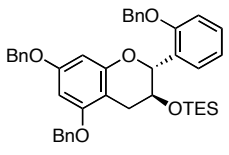


15

To a solution of bromohydrin **14** (185 mg, 0.246 mmol) in CH_2Cl_2 (2.0 mL) was added 2,6-lutidine (0.13 mL, 1.1 mmol) and triethylsilyl triflate (130 mg, 0.492 mmol) in CH_2Cl_2 (1.0 mL) at 0 ºC. After stirring for 20 min, the reaction was quenched by the addition of saturated $NaHCO_3$ solution. The crude products were extracted with EtOAc (x3), and the combined organic extracts were washed with 5% citric acid solution and brine, dried (Na_2SO_4), and concentrated in vacuo. The residue was purified by flash column chromatography (hexane/EtOAc = 9/1) to afford silyl ether **15** (204 mg, 95%) as a white amorphous solid.

15: R_f 0.32 (hexane/EtOAc = 9/1); $[\alpha]_D^{20}$ +106 (*c* 1.35, $CHCl_3$); ^{1}H NMR (600 MHz, $CDCl_3$) δ 0.34–0.47 (m, 6H), 0.80 (t, 9H, *J* = 7.8 Hz), 3.67 (dd, 1H, *J* = 10.8, 2.4 Hz), 4.06 (dd, 1H, *J* = 10.8, 4.8 Hz), 4.29–4.31 (m, 1H), 4.69 (s, 2H), 5.01–5.07 (m, 3H), 5.15 (d, 1H, *J* = 12.0 Hz), 5.86 (d, 1H, *J* = 6.0 Hz), 6.12 (d, 1H, *J* = 2.4 Hz), 6.18 (d, 1H, *J* = 2.4 Hz), 6.93–6.97 (m, 2H), 7.16–7.18 (m, 2H), 7.23–7.52 (m, 15H); ^{13}C NMR (150 MHz, $CDCl_3$) δ 4.7, 6.7, 37.4, 68.4, 70.0, 70.5, 70.8, 74.7, 75.6, 93.6, 94.4, 111.9, 121.6, 126.6, 126.9, 127.4, 127.7, 127.8, 128.0, 128.1, 128.5, 128.6, 129.4, 136.4, 136.6, 136.7, 156.6, 157.7, 158.7, 160.8 (several signals overlapped); IR (ATR) 2952, 2874, 1579, 1453, 1428, 1377, 1226, 1162, 1111, 1016, 731, 695 cm^{-1}; HRMS (ESI) calcd for $C_{42}H_{47}BrIO_5Si$ ($[M+H]^+$) *m/z* 865.1415, found *m/z* 865.1377.

Preparation of ***16***



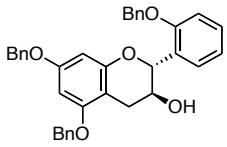
16

To a solution of PhMgBr (1.2 M in Et_2O, 0.38 mL, 0.46 mmol) and HMPA (0.10 mL, 0.57 mmol) in THF (1.0 mL) was added PhLi (1.1 M in cyclohexane/Et_2O, 0.85 mL, 0.93 mmol) at 0 °C. After stirring for 30 min, the reaction mixture was cooled to –78 °C, silyl ether **15** (202 mg, 0.234 mmol) in

THF (3.0 mL), which was azeotropically dried with toluene (1 mL x 3), was added and stirring for 10 min. The reaction mixture was warmed to 0 °C and stirred for 15 min, then the reaction was quenched by the addition of saturated NH_4Cl solution. The crude 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 (hexane/CH_2Cl_2 = 2/1) to afford flavan **16** (95.3 mg, 62%) as a colorless oil.

16: R_f 0.40 (hexane/CH_2Cl_2 = 2/1); $[\alpha]_D^{26}$ +0.93 (*c* 0.82, $CHCl_3$); ^{1}H NMR (600 MHz, $CDCl_3$) δ 0.31–0.43 (m, 6H), 0.76 (t, 9H, *J* = 7.8 Hz), 2.73 (dd, 1H, *J* = 16.2, 7.2 Hz), 2.87 (dd, 1H, *J* = 16.2, 4.8 Hz), 4.26–4.29 (m, 1H), 4.98 (s, 2H), 5.04 (s, 2H), 5.06 (d, 1H, *J* = 12.0 Hz), 5.10 (d, 1H, *J* = 12.0 Hz), 5.42 (d, 1H, *J* = 6.6 Hz), 6.23–6.24 (m, 2H), 6.93 (d, 1H, *J* = 8.4 Hz), 6.96 (dd, 1H, *J* = 7.8, 7.8 Hz), 7.23–7.24 (m, 1H), 7.28–7.43 (m, 16H); ^{13}C NMR (150 MHz, $CDCl_3$) δ 4.7, 6.6, 28.5, 67.7, 69.9, 70.1, 70.2, 76.5, 93.5, 94.3, 102.7, 111.9, 121.1, 126.9, 127.3, 127.5, 127.6, 127.7, 127.8, 127.9, 128.4, 128.45, 128.49, 128.6, 128.9, 137.0, 137.1, 137.3, 155.8, 156.4, 157.7, 158.6; IR (neat) 3032, 2952, 2874, 1618, 1592, 1498, 1453, 1377, 1238, 1147, 1099, 736, 696 cm^{-1}; HRMS (ESI) calcd for $C_{42}H_{47}O_5Si$ ($[M+H]^+$) *m/z* 659.3187, found *m/z* 659.3155.

*Preparation of **S8***



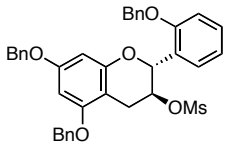
S8

To a solution of flavan **16** (90 mg, 0.14 mmol) in THF (1.5 mL) was added a solution of tetrabutylammonium fluoride (1.0 M in THF, 0.27 mL, 0.27 mmol) at 0 °C. After stirring for 20 min at room temperature, the reaction was quenched by the addition of phosphate buffer solution (pH 7). The crude 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 (hexane/EtOAc = 5/1 to 3/1) to afford flavan **S8** (74.6 mg, quant.) as a white solid.

S8: R_f 0.33 (hexane/EtOAc = 3/1); mp 43–45 ºC; $[\alpha]_D^{23}$ –14 (*c* 0.65, $CHCl_3$); ^{1}H NMR (600 MHz, $CDCl_3$) δ 1.95 (brs, 1H, OH), 2.73 (dd, 1H, *J* = 16.8, 7.2 Hz), 2.97 (dd, 1H, *J* = 16.8, 4.8 Hz), 4.27–4.31 (m, 1H), 4.99–5.03 (m, 4H), 5.11 (d, 1H, *J* = 12.0 Hz), 5.16 (d, 1H, *J* = 12.0 Hz), 5.44 (d, 1H, *J* = 6.6 Hz), 6.26–6.27 (m, 2H), 6.97–7.02 (m, 2H), 7.27–7.43 (m, 17H); ^{13}C NMR (150 MHz, $CDCl_3$) δ 27.3, 67.5, 70.0, 70.1, 70.3, 76.2, 93.7, 94.4, 101.9, 112.2, 121.5, 127.1, 127.2, 127.3, 127.6, 127.8, 128.0, 128.5, 128.6, 128.7, 129.4, 136.7, 136.9, 137.0, 155.5, 156.0, 158.0, 158.9; IR (ATR)

3444, 3032, 1616, 1588, 1492, 1451, 1375, 1220, 1142, 1098, 1042, 733, 694 cm^{-1}; HRMS (ESI) calcd for $C_{36}H_{33}O_5$ ($[M+H]^+$) *m/z* 545.2323, found *m/z* 545.2296.

*Preparation of **17***

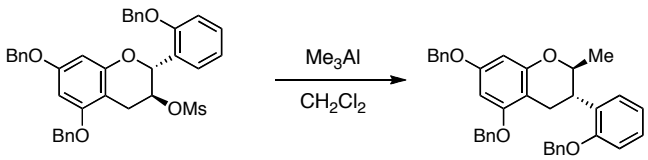


17

To a solution of flavan **S8** (77 mg, 0.14 mmol) in CH_2Cl_2 (1.5 mL) was added Et_3N (0.10 mL, 0.72 mmol) and MsCl (22 μL, 0.28 mmol) at 0 °C. After stirring for 40 min, the reaction was quenched by the addition of saturated $NaHCO_3$ solution. The crude 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 (hexane/toluene = 1/1 then hexane/EtOAc = 3/1) to afford mesylate **17** (83.2 mg, 94%) as a white solid.

17: R_f 0.47 (hexane/EtOAc = 2/1); mp 163 ºC (decomp.); $[\alpha]_D^{24}$ –37 (*c* 0.82, $CHCl_3$); ^{1}H NMR (600 MHz, $CDCl_3$) δ 2.42 (s, 3H), 2.76 (dd, 1H, *J* = 17.4, 4.2 Hz), 3.08 (dd, 1H, *J* = 17.4, 4.8 Hz), 4.99–5.08 (m, 4H), 5.08 (d, 1H, *J* =11.4 Hz), 5.13 (d, 1H, *J* = 11.4 Hz), 5.27–5.30 (m, 1H), 5.66 (d, 1H, *J* = 4.2 Hz), 6.27 (d, 1H, *J* = 1.8 Hz), 6.29 (d, 1H, *J* = 1.8 Hz), 6.94 (dd, 1H, *J* = 7.2, 7.2 Hz), 6.99 (d, 1H, *J* = 8.4 Hz), 7.27–7.47 (m, 17H); ^{13}C NMR (150 MHz, $CDCl_3$) δ 23.9, 37.5, 70.0, 70.2, 70.6, 73.7, 75.7, 93.9, 94.2, 99.8, 111.7, 121.3, 125.9, 126.9, 127.2, 127.6, 127.9, 128.0, 128.3, 128.45, 128.54, 128.6, 128.8, 129.7, 136.2, 136.7, 136.8, 154.6, 155.3, 157.8, 159.2; IR (ATR) 3031, 1587, 1499, 1453, 1344, 1242, 1142, 1102, 955, 922, 803, 729, 698 cm^{-1}; HRMS (ESI) calcd for $C_{37}H_{35}O_7S$ ($[M+H]^+$) *m/z* 623.2098, found *m/z* 623.2070.

*1,2-rearrangement of **17***



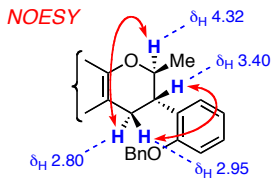
17 **18**

To a solution of mesylate **17** (40 mg, 0.064 mmol), which was azeotropically dried with toluene (1 mL x 3), in CH_2Cl_2 (1.0 mL) was added Me_3Al (ca. 1.4 M in hexane, 0.14 mL, 0.20 mmol) at –78 °C. The reaction mixture was gradually warmed to –10 °C for 1.5 h, the reaction was quenched by the addition of phosphate buffer solution (pH 7) and 1 M HCl solution. The crude 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 preparative TLC (hexane/toluene/EtOAc = 5/15/1) to afford 2-methyl-isoflavan **18** (29.4 mg, 84%) as a white solid.

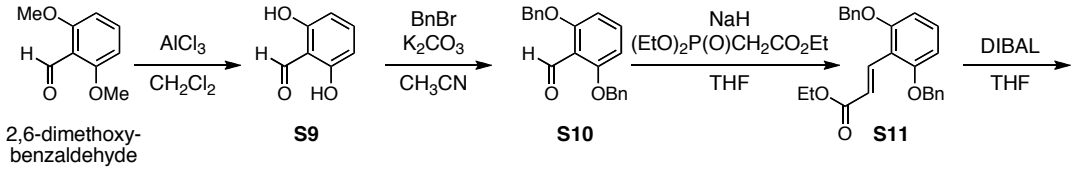
18: R_f 0.52 (hexane/toluene/EtOAc = 5/15/1); mp 41–44 ºC; $[\alpha]_D^{25}$ –28.2 (*c* 1.08, $CHCl_3$); ^{1}H NMR (600 MHz, $CDCl_3$) δ 1.21 (d, 3H, *J* = 6.0 Hz), 2.80 (brdd, 1H, *J* = 16.2, 6.0 Hz), 2.95 (dd, 1H, *J* = 16.2, 5.4 Hz), 3.40 (brm, 1H), 4.32 (brm, 1H), 4.96–5.02 (m, 4H), 5.07 (d, 1H, *J* = 12.0 Hz), 5.09 (d, 1H, *J* = 12.0 Hz), 6.19 (d, 1H, *J* = 1.8 Hz), 6.23 (d, 1H, *J* = 1.8 Hz), 6.94–6.97 (m, 2H), 7.13–7.21 (m, 2H), 7.27–7.43 (m, 15H); ^{13}C NMR (150 MHz, $CDCl_3$) δ 19.3, 26.8, 69.9, 70.1, 70.2, 75.9, 93.0, 94.4, 104.9, 112.1, 121.2, 127.2, 127.5, 127.6, 127.75, 127.83, 127.9, 128.5, 128.55, 128.58, 131.5, 137.05, 137.08, 137.09, 156.0, 156.4, 157.6, 158.4 (several signals overlapped); IR (ATR) 3031, 2930, 1615, 1589, 1492, 1451, 1377, 1218, 1119, 1070, 808, 733, 694 cm^{-1}; HRMS (ESI) calcd for $C_{37}H_{35}O_4$ ($[M+H]^+$) *m/z* 543.2530, found *m/z* 543.2505.

Diagnostic 2D NMR correlations for compound ***18***

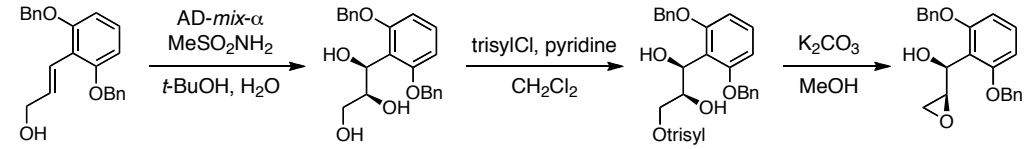


*Preparation of o,o'-disubstituted catechin mesylate **19** and 1,2-rearrangement*

*Preparation of B-ring unit **S15***[6]

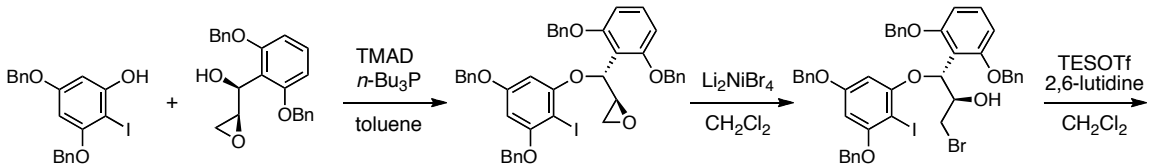


2,6-dimethoxy-benzaldehyde **S9** **S10** **S11**

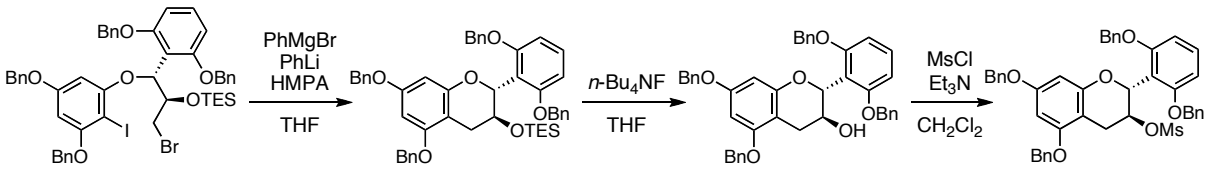


S12 **S13** **S14** **S15**

*Preparation of **19***

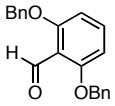


12 **S15** **S16** **S17**



S18 **S19** **S20** **19**

*Preparation of **S10***



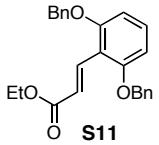
S10

To a suspension of K_2CO_3 (5.34 g, 38.6 mmol) in CH_3CN (20 mL) was added phenol **S9**[8] (1.07 g, 7.72 mmol) in CH_3CN (18 mL), and benzyl bromide (2.0 mL, 17 mmol) at room temperature, and the mixture was stirred at reflux for 2 h. The reaction was quenched by the addition of diethylamine (1.8 mL, 17 mmol), 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 flush column chromatography (hexane/EtOAc = 4/1 to 2/1) to afford 2,6-dibenzyloxybenzaldehyde (**S10**) (2.38 g, 97%) as a yellow oil.

S10: R_f 0.30 (hexane/EtOAc = 4/1); ^{1}H NMR (600 MHz, $CDCl_3$) δ 5.18 (s, 4H), 6.63 (d, 2H, J = 8.4 Hz), 7.30–7.33 (m, 2H), 7.36–7.40 (m, 5H), 7.45–7.47 (m, 4H), 10.65 (s, 1H); ^{13}C NMR (150 MHz,

$CDCl_3$) δ 70.6, 105.7, 115.3, 127.0, 128.0, 128.6, 135.6, 136.3, 161.1, 189.1; IR (neat) 3032, 2871, 1687, 1595, 1474, 1451, 1413, 1380, 1253, 1106, 777, 736, 696 cm^{-1}; HRMS (ESI) calcd for $C_{21}H_{18}NaO_3$ ($[M+Na]^+$) *m/z* 341.1148, found *m/z* 341.1146.

Preparation of ***S11***

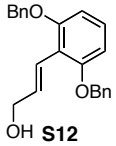


S11

To a suspension of NaH (284 mg, 63% dispersion in mineral oil, 7.46 mmol, washed with hexane) in THF (20 mL) was dropped triethyl phosphonoacetate (1.35 mL, 6.74 mmol) at 0 °C. After stirring for 1 h at 0 °C, a solution of aldehyde **S10** (1.99 g, 6.22 mmol) in THF (10 mL) was added and the mixture was stirred for 1 h. The reaction was quenched by the addition of water, 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 flush column chromatography (hexane/EtOAc = 4/1) to afford ether **S11** (2.21 g, 92%) as a white solid.

S11: R_f 0.52 (hexane/EtOAc = 3/1); mp 93–95 ºC; ^{1}H NMR (600 MHz, $CDCl_3$) δ 1.30 (t, 3H, *J* = 7.2 Hz), 4.22 (q, 2H, *J* = 7.2 Hz), 5.17 (s, 4H), 6.59 (d, 2H, *J* = 8.4 Hz), 6.96 (d, 1H, *J* = 16.2 Hz), 7.16 (dd, 1H, *J* = 8.4, 8.4 Hz), 7.30–7.44 (m, 10H), 8.27 (d, 1H, *J* = 16.2 Hz); ^{13}C NMR (150 MHz, $CDCl_3$) δ 14.3, 60.0, 70.6, 105.5, 113.3, 121.5, 127.0, 127.9, 128.6, 130.9, 135.3, 136.7, 159.0, 168.5; IR (ATR) 2987, 1690, 1573, 1469, 1446, 1285, 1268, 1193, 1104, 1073, 1048, 732, 696 cm^{-1}; HRMS (ESI) calcd for $C_{25}H_{25}O_4$ ($[M+H]^+$) *m/z* 389.1747, found *m/z* 389.1753.

Preparation of ***S12***

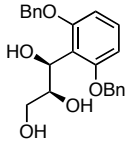


S12

To a solution of ether **S11** (2.09 g, 5.38 mmol) in THF (27 mL) was added (*i*-Bu)$_2$AlH (1.0 M in hexane, 13.6 mL, 13.6 mmol) at –78 °C. After stirring for 1.5 h, the reaction quenched by the careful addition of MeOH. After warming to 0 °C, saturated aqueous pottasium sodium tartrate (Rochell's salt) was added to the mixture, and the stirring was continued 1 day. 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 flush column chromatography (hexane/EtOAc = 4/1 to 2/1) to afford allyl alcohol **S12** (1.89 g, quant.) as a white solid.

S12: R_f 0.24 (hexane/EtOAc = 3/1); mp 70–71 ºC; ^{1}H NMR (600 MHz, $CDCl_3$) δ 1.32 (brs, 1H, OH), 4.25–4.27 (m, 2H), 5.12 (s, 4H), 6.61 (d, 2H, J = 8.4 Hz), 6.83 (dt, 1H, J = 16.2, 6.0 Hz), 6.97 (d, 1H, J = 16.2 Hz), 7.09 (dd, 1H, J = 8.4, 8.4 Hz), 7.31–7.44 (m, 10H); ^{13}C NMR (150 MHz, $CDCl_3$) δ 65.5, 70.7, 105.8, 115.0, 121.9, 127.3, 127.9, 128.1, 128.6, 133.1, 137.1, 157.7; IR (ATR) 3518, 2866, 1581, 1448, 1379, 1246, 1196, 1109, 1064, 984, 733, 698 cm^{-1}; HRMS (ESI) calcd for $C_{23}H_{22}NaO_3$ ([M+Na]$^+$) *m/z* 369.1461, found *m/z* 369.1460.

Preparation of ***S13***

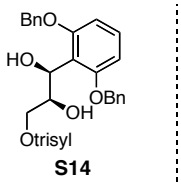


S13

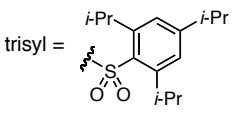
To a solution of potassium hexacyanoferrate (III) (4.32 g, 13.1 mmol) in the mixed solvent (95 mL, *t*-BuOH/H_2O = 40/55 mL), K_2CO_3 (1.82 g, 13.1 mmol), methanesulfonamide (503 mg, 5.29 mmol), $(DHQ)_2$-PHAL (34 mg, 0.044 mmol), and $K_2OsO_2(OH)_4$ (9.0 mg, 0.024 mmol) were added at room temperature. After stirring for 40 min, allyl alcohol **S12** (1.51 g, 4.37 mmol) in *t*-BuOH (15 mL) was added to the solution at 0 ºC. After stirring for 60 h at 0 ºC, the reaction was quenched by the addition of $Na_2S_2O_3$ (6.61 g, 52.4 mmol), then warm to room temperature and stirred for 1 day. The products were extracted with CH_2Cl_2 (x3) and the combined organic extracts were washed with 2 M KOH and brine, dried (Na_2SO_4), and concentrated in vacuo. The residue was purified by flash column chromatography (hexane/EtOAc = 3/1 to 1/3) to afford triol **S13** (810 mg, 49%) as a white solid.

S13: R_f 0.29 (hexane/EtOAc = 1/2); mp 127–128 ºC; $[\alpha]_D^{23}$ –0.87 (*c* 1.0, $CHCl_3$); ^{1}H NMR (600 MHz, CD_3OD) δ 3.33–3.38 (m, 2H), 4.19–4.22 (m, 1H), 5.10–5.15 (m, 5H), 6.74 (d, 2H, J = 8.4 Hz), 7.20 (dd, 1H, J = 8.4, 8.4 Hz), 7.30–7.39 (m, 6H), 7.47–7.49 (m, 4H); ^{13}C NMR (150 MHz, CD_3OD) δ 64.7, 70.1, 71.7, 76.3, 107.2, 118.3, 128.7, 129.0, 129.6, 130.5, 138.4, 158.9; IR (ATR) 3415, 2871, 1593, 1468, 1448, 1203, 1108, 1065, 953, 778, 740, 695 cm^{-1}; HRMS (ESI) calcd for $C_{23}H_{24}NaO_5$ ([M+Na]$^+$) *m/z* 403.1516, found *m/z* 403.1508.

Preparation of ***S14***



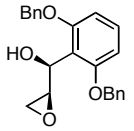
S14



To a solution of triol **S13** (764 mg, 2.01 mmol) in CH_2Cl_2 (10 mL), pyridine (1.6 mL, 20 mmol) and 2,4,6-triisopropylbenzenesulfonyl chloride (1.52 g, 5.02 mmol) were added at 0 ºC, and the reaction mixture was warmed to room temperature. After stirring for 41 h, the reaction was cooled to 0 °C and quenched by the addition of 2 M HCl solution. The crude 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 (hexane/EtOAc = 3/1) to afford sulfonyl ester **S14** (1.16 g, 89%) as a white solid.

S14: R_f 0.18 (hexane/EtOAc = 3/1); mp 121–122 ºC; $[\alpha]_D^{24}$ +0.19 (*c* 1.1, $CHCl_3$); ^{1}H NMR (600 MHz, $CDCl_3$) δ 1.16 (s, 3H), 1.17 (s, 3H), 1.19 (s, 3H), 1.20 (s, 3H), 1.23 (d, 3H, *J* = 1.8 Hz), 1.24 (d, 3H, *J* = 1.8 Hz), 2.85–2.92 (m, 1H, OH), 2.95 (brs, 1H, OH), 3.95 (dd, 1H, *J* = 10.2, 7.8 Hz), 3.99 (dd, 1H, *J* = 10.2, 3.0 Hz), 4.04–4.11 (m, 3H), 4.22–4.25 (m, 1H), 5.04–5.10 (m, 5H), 6.63 (d, 2H, *J* = 8.4 Hz), 7.13 (s, 2H), 7.19 (dd, 1H, *J* = 8.4, 8.4 Hz), 7.31–7.37 (m, 10H); ^{13}C NMR (150 MHz, $CDCl_3$) δ 23.5, 23.6, 24.67, 24.69, 29.5, 34.2, 68.7, 70.4, 70.8, 72.8, 105.8, 115.3, 123.7, 127.5, 128.3, 128.8, 129.3, 129.8, 136.0, 150.9, 153.5, 157.2; IR (ATR) 3545, 2957, 1594, 1456, 1343, 1232, 1175, 1085, 960, 785, 735, 697 cm^{-1}; HRMS (ESI) calcd for $C_{38}H_{46}NaO_7S$ ($[M+Na]^+$) *m/z* 669.2857, found *m/z* 669.2831.

*Preparation of **S15***



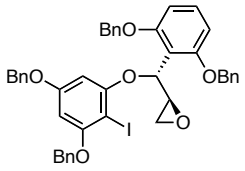
S15

To a solution of sulfonyl ester **S14** (1.06 g, 1.64 mmol) in MeOH (8.2 mL) was added K_2CO_3 (457 mg, 3.31 mmol) at 0 ºC. After stirring for 9 h, another K_2CO_3 (456 mg, 3.30 mmol) was added. After stirring for 1 h, the mixture was filtered through a Celite® pad (washed with EtOAc). After concentrating in vacuo, adding water to the filtrate, and the products were 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 (hexane/EtOAc = 3/1) to afford epoxy alcohol **S15** (539 mg, 91%, 8% e.e.) as a white solid. Enantiomeric purity of **S15** was assessed by HPLC analysis [CHIRALPAK® AS-H (Daicel), ϕ 4.6 x 250 mm, hexane/*i*-PrOH = 80/20, 1.0 mL/min flow rate, 35 °C, 220 nm, t_R = 14.3 min for the (*R*, *R*)-isomer and 15.8 min for the (*S*, *S*)-isomer].[7]

S15: R_f 0.25 (hexane/EtOAc = 3/1); mp 86–87 °C; $[\alpha]_D^{23}$ –0.34 (*c* 1.4, $CHCl_3$); ^{1}H NMR (600 MHz, $CDCl_3$) δ 2.68 (d, 2H, *J* = 3.0 Hz), 3.39 (dt, 1H, *J* = 6.0, 3.0 Hz), 3.99 (d, 1H, *J* = 11.4 Hz, OH), 5.02

(dd, 1H, J = 11.4, 6.0 Hz), 5.10 (s, 4H), 6.67 (d, 2H, J = 8.4 Hz), 7.20 (dd, 1H, J = 8.4, 8.4 Hz), 7.33–7.42 (m, 10H); ^{13}C NMR (150 MHz, $CDCl_3$) δ 44.9, 54.8, 69.2, 70.8, 105.8, 116.7, 127.5, 128.3, 128.8, 129.3, 136.3, 157.2; IR (ATR) 3544, 2932, 1593, 1453, 1378, 1265, 1230, 1188, 1068, 1020, 918, 735, 697 cm^{-1}; HRMS (ESI) calcd for $C_{23}H_{22}NaO_4$ ([M+Na]$^+$) *m/z* 385.1410, found *m/z* 385.1415.

Preparation of ***S16***

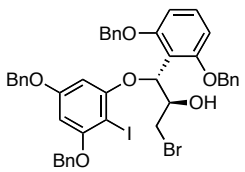


S16

To a solution of epoxy alcohol **S15** (143 mg, 0.390 mmol) in toluene (4.0 mL) was added iodophenol **12** (259 mg, 0.599 mmol) and *N,N,N',N'*-tetramethylazodicarboxamide (205 mg, 1.19 mmol) at room temperature. After being cooled at 0 ºC, *n*-Bu_3P (0.30 mL, 1.2 mmol) was added to reaction mixture, and the resulting mixture was stirred for 2 h. The reaction was quenched by adding water. The crude 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 (hexane/toluene = 1/1 to 1/9 then toluene/EtOAc =98/2) to afford ether **S16** (184 mg, 60%, single diastereomer) as a white amorphous solid.

S16: R_f 0.50 (hexane/toluene/EtOAc = 5/5/1); $[\alpha]_D^{26}$ –1.78 (*c* 1.41, $CHCl_3$); ^{1}H NMR (600 MHz, $CDCl_3$) δ 2.75–2.77 (m, 1H), 3.25–3.26 (m, 1H), 3.55–3.56 (m, 1H), 4.70 (s, 2H), 5.03 (s, 2H), 5.07 (d, 2H, J = 11.4 Hz), 5.15 (d, 2H, J = 11.4 Hz), 5.97 (d, 1H, J = 2.4 Hz), 6.14 (s, 1H), 6.49 (s, 1H), 6.64 (d, 2H, J = 8.4 Hz), 7.12–7.23 (m, 3H), 7.25–7.36 (m, 12H), 7.44–7.45 (m, 6H); ^{13}C NMR (150 MHz, $CDCl_3$) δ 47.0, 53.4, 69.0, 70.1, 70.8, 71.0, 72.2, 94.3, 94.4, 106.1, 114.1, 126.9, 127.6, 127.7, 127.8, 127.97, 128.04, 128.46, 128.49, 128.6, 130.6, 136.5, 136.6, 136.7, 158.4, 158.6, 158.8, 160.9; IR (ATR) 3031, 2925, 1579, 1452, 1427, 1248, 1229, 1163, 1095, 1017, 733, 694 cm^{-1}; HRMS (ESI) calcd for $C_{43}H_{37}INaO_6$ ([M+Na]$^+$) *m/z* 799.1527, found *m/z* 799.1488.

Preparation of ***S17***



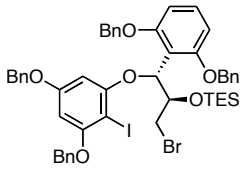
S17

To a solution of ether **S16** (77 mg, 99 μmol) in THF (1.0 mL) was added Li_2NiBr_4 (ca. 0.4 M in THF,

2.5 mL, 1.0 mmol) at room temperature. After stirring for 23 h, another Li_2NiBr_4 (ca. 0.4 M in THF, 2.5 mL, 1.0 mmol) was added. After stirring for 85 h, the reaction was quenched by the addition of phosphate buffer solution (pH 7). The crude 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 preparative TLC (hexane/EtOAc = 3/1) to afford bromohydrin **S17** (67.2 mg, 79%) as a white amorphous solid.

S17: R_f 0.30 (hexane/EtOAc = 3/1); $[\alpha]_D^{26}$ –5.9 (*c* 1.0, $CHCl_3$); ^{1}H NMR (600 MHz, $CDCl_3$) δ 2.30 (d, 1H, *J* = 7.2 Hz, OH), 3.93 (dd, 1H, *J* = 10.2, 3.0 Hz), 4.03 (dd, 1H, *J* = 10.2, 5.4 Hz), 4.66 (s, 2H), 4.82–4.86 (m, 1H), 5.02 (d, 1H, *J* = 12.0 Hz), 5.05 (d, 1H, *J* = 12.0 Hz), 5.09 (d, 2H, *J* = 12.0 Hz), 5.17 (d, 2H, *J* = 12.0 Hz), 6.00 (d, 1H, *J* = 7.8 Hz), 6.14 (d, 1H, *J* = 2.4 Hz), 6.44 (d, 1H, *J* = 2.4 Hz), 6.64 (d, 2H, *J* = 8.4 Hz), 7.15–7.17 (m, 2H), 7.22 (t, 1H, *J* = 8.4, 8.4 Hz), 7.27–7.37 (m, 12H), 7.45–7.47 (m, 6H); ^{13}C NMR (150 MHz, $CDCl_3$) δ 39.2, 68.2, 70.0, 70.8, 70.9, 74.6, 93.4, 94.4, 106.3, 113.4, 126.9, 127.2, 127.7, 127.8, 127.9, 128.1, 128.5, 128.6, 130.6, 136.4, 136.6, 158.4, 158.5, 158.7, 161.0 (several signals overlapped); IR (ATR) 3537, 3031, 2871, 1579, 1453, 1427, 1376, 1241, 1163, 1091, 1014, 732, 695 cm^{-1}; HRMS (ESI) calcd for $C_{43}H_{38}BrINaO_6$ ($[M+Na]^+$) *m/z* 879.0789, found *m/z* 879.0745.

*Preparation of **S18***



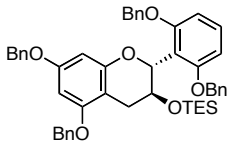
S18

To a solution of bromohydrin **S17** (45 mg, 52 μmol) in CH_2Cl_2 (0.5 mL) was added 2,6-lutidine (30 μL, 0.26 mmol) and triethylsilyl triflate (37 mg, 0.14 mmol) in CH_2Cl_2 (1.0 mL) at 0 ºC. After stirring for 20 min, the reaction was quenched by the addition of saturated $NaHCO_3$ solution. The crude products were extracted with EtOAc (x3), and the combined organic extracts were washed with 5% citric acid solution and brine, dried (Na_2SO_4), and concentrated in vacuo. The residue was purified by preparative TLC (hexane/EtOAc = 3/1) to afford silyl ether **S18** (48.0 mg, 95%) as a white amorphous solid.

S18: R_f 0.59 (hexane/EtOAc = 3/1); $[\alpha]_D^{23}$ –7.0 (*c* 0.93, $CHCl_3$); ^{1}H NMR (600 MHz, $CDCl_3$) δ 0.27–0.41 (m, 6H), 0.75 (t, 9H, *J* = 7.8 Hz), 3.75 (dd, 1H, *J* = 10.8, 2.4 Hz), 4.24 (dd, 1H, *J* = 10.8, 3.0 Hz), 4.53 (d, 1H, *J* = 10.8 Hz), 4.61 (d, 1H, *J* = 10.8 Hz), 4.99–5.05 (m, 5H), 5.16 (d, 2H, *J* = 11.4 Hz), 6.06 (d, 1H, *J* = 8.4 Hz), 6.10 (d, 1H, *J* = 1.8 Hz), 6.59 (d, 1H, *J* = 1.8 Hz), 6.65 (d, 2H, *J* = 8.4 Hz), 7.12–7.13 (m, 2H), 7.22 (dd, 1H, *J* = 8.4, 8.4 Hz), 7.28–7.36 (m, 12H), 7.44–7.46 (m, 2H), 7.55–7.56

(m, 4H); ^{13}C NMR (150 MHz, $CDCl_3$) δ 4.7, 6.6, 39.9, 67.6, 70.0, 70.4, 70.7, 71.2, 74.0, 92.8, 94.4, 106.6, 115.1, 126.9, 127.4, 127.7, 127.8, 127.99, 128.03, 128.38, 128.43, 128.5, 130.2, 136.5, 136.8, 136.9, 158.5, 158.7, 158.9, 161.1; IR (ATR) 2952, 2873, 1580, 1453, 1428, 1376, 1251, 1164, 1096, 1015, 731, 694 cm^{-1}; HRMS (ESI) calcd for $C_{49}H_{52}BrINaO_6Si$ ($[M+Na]^+$) *m/z* 993.1653, found *m/z* 993.1615.

Preparation of ***S19***

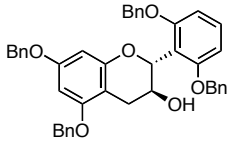


S19

To a solution of PhMgBr (1.2 M in Et_2O, 0.12 mL, 0.14 mmol) and HMPA (26 μL, 0.15 mmol) in THF (1.0 mL) was added PhLi (1.08 M in cyclohexane/Et_2O, 0.27 mL, 0.29 mmol) at 0 °C. After stirring for 30 min, the reaction mixture was cooled to –78 °C, silyl ether **S18** (46 mg, 47 μmol) in THF (1.0 mL) was added and stirring for 5 min. The reaction mixture was warmed to 0 °C and stirred for 30 min, then the reaction was quenched by the addition of saturated NH_4Cl solution. The crude 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 preparative TLC (hexane/CH_2Cl_2 = 1/1) to afford flavan **S19** (32.5 mg, 90%) as a colorless oil.

S19: R_f 0.50 (hexane/CH_2Cl_2 = 1/1); $[\alpha]_D^{23}$ –4.3 (*c* 1.4, $CHCl_3$); ^{1}H NMR (600 MHz, $CDCl_3$) δ 0.26–0.41 (m, 6H), 0.72 (t, 9H, *J* = 7.8 Hz), 2.60 (dd, 1H, *J* = 16.2, 9.6 Hz), 3.17 (dd, 1H, *J* = 16.2, 5.4 Hz), 4.78–4.82 (m, 1H), 4.93 (d, 1H, *J* = 11.4 Hz), 4.96 (d, 1H, *J* = 11.4 Hz), 5.03–5.08 (m, 4H), 5.10 (d, 2H, *J* = 12.0 Hz), 5.61 (d, 1H, *J* = 9.0 Hz), 6.18 (d, 1H, *J* = 1.8 Hz), 6.20 (d, 1H, *J* = 1.8 Hz), 6.62 (d, 2H, *J* = 8.4 Hz), 7.19 (dd, 1H, *J* = 8.4, 8.4 Hz), 7.23–7.43 (m, 20H); ^{13}C NMR (150 MHz, $CDCl_3$) δ 4.7, 6.5, 30.8, 65.2, 69.8, 70.1, 70.6, 74.9, 93.2, 94.4, 103.1, 106.3, 116.0, 126.8, 127.0, 127.48, 127.52, 127.6, 127.9, 128.3, 128.4, 128.5, 129.7, 137.1, 137.3, 137.4, 156.1, 157.4, 158.6, 159.0; IR (neat) 3031, 2951, 2874, 1617, 1593, 1453, 1376, 1250, 1147, 1099, 735, 696 cm^{-1}; HRMS (ESI) calcd for $C_{49}H_{53}O_6Si$ ($[M+H]^+$) *m/z* 765.3606, found *m/z* 765.3573.

Preparation of ***S20***

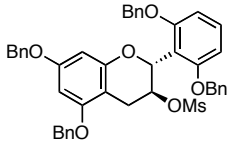


S20

To a solution of flavan **S19** (49 mg, 64 μmol) in THF (1.0 mL) was added a solution of tetrabutylammonium fluoride (1.0 M in THF, 0.13 mL, 0.13 mmol) at 0 °C. After stirring for 50 min at room temperature, the reaction was quenched by the addition of phosphate buffer solution (pH 7). The crude 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 preparative TLC (hexane/EtOAc = 3/1) to afford flavan **S20** (43.6 mg, quant.) as a white solid.

S20: R_f 0.24 (hexane/EtOAc = 3/1); mp 155–157 ºC; $[\alpha]_D^{23}$ –3.4 (*c* 0.71, $CHCl_3$); ^{1}H NMR (600 MHz, $CDCl_3$) δ 1.69 (d, 1H, *J* = 4.2 Hz, OH), 2.58 (dd, 1H, *J* = 15.6, 10.2 Hz), 3.27 (dd, 1H, *J* = 15.6, 5.4 Hz), 4.81–4.86 (m, 1H), 4.95 (d, 1H, *J* = 12.0 Hz), 4.98 (d, 1H, *J* = 12.0 Hz), 5.01 (d, 1H, *J* = 12.0 Hz), 5.04 (d, 1H, *J* = 12.0 Hz), 5.09 (d, 2H, *J* = 12.0 Hz), 5.13 (d, 2H, *J* = 12.0 Hz), 5.56 (d, 1H, *J* = 9.6 Hz), 6.21 (d, 1H, *J* = 1.8 Hz), 6.24 (d, 1H, *J* = 1.8 Hz), 6.67 (d, 2H, *J* = 8.4 Hz), 7.22–7.43 (m, 21H); ^{13}C NMR (150 MHz, $CDCl_3$) δ 29.4, 65.1, 69.9, 70.1, 70.7, 75.0, 93.3, 94.4, 102.9, 106.5, 113.9, 127.10, 127.11, 127.5, 127.8, 127.9, 128.48, 128.53, 128.6, 130.5, 136.9, 137.05, 137.13, 156.2, 157.7, 158.7, 159.1 (several signals overlapped); IR (ATR) 3510, 3030, 2932, 1590, 1471, 1374, 1211, 1151, 1091, 1040, 807, 738, 695 cm^{-1}; HRMS (ESI) calcd for $C_{43}H_{39}O_6$ ($[M+H]^+$) *m/z* 651.2741, found *m/z* 651.2711.

*Preparation of **19***



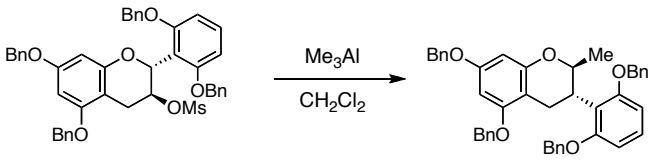
19

To a solution of flavan **S20** (44 mg, 70 μmol) in CH_2Cl_2 (1.0 mL) was added Et_3N (50 μL, 0.36 mmol) and MsCl (10 μL, 0.13 mmol) at 0 °C. After stirring for 15 min, the reaction was quenched by the addition of saturated $NaHCO_3$ solution. The crude 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 preparative TLC (hexane/toluene = 1/19) to afford mesylate **19** (46.3 mg, 94%) as a white solid.

19: R_f 0.41 (hexane/toluene = 1/19); mp 165 ºC (decomp.); $[\alpha]_D^{26}$ –6.9 (*c* 0.82, $CHCl_3$); ^{1}H NMR (600 MHz, $CDCl_3$) δ 2.31 (s, 3H), 2.92 (dd, 1H, *J* = 16.2, 9.6 Hz), 3.46 (dd, 1H, *J* = 16.2, 6.0 Hz), 4.96 (s, 2H), 5.01 (d, 1H, *J* = 12.0 Hz), 5.03 (d, 1H, *J* = 12.0 Hz), 5.10 (d, 2H, *J* = 12.0 Hz), 5.13 (d, 2H, *J* = 12.0 Hz), 5.71 (ddd, 1H, *J* = 9.6, 9.6, 6.0 Hz), 5.76 (d, 1H, *J* = 9.6 Hz), 6.18 (d, 1H, *J* = 1.8 Hz), 6.23 (d, 1H, *J* = 1.8 Hz), 6.64 (d, 2H, *J* = 8.4 Hz), 7.20–7.41 (m, 21H); ^{13}C NMR (150 MHz, $CDCl_3$) δ 28.4,

37.3, 70.0, 70.1, 70.8, 71.2, 75.6, 93.6, 94.3, 101.1, 106.3, 113.5, 127.15, 127.21, 127.5, 127.85, 127.89, 128.0, 128.57, 128.59, 130.8, 136.7, 136.8, 136.9, 155.4, 157.6, 158.8, 159.0 (several signals overlapped); IR (ATR) 3031, 2930, 1591, 1452, 1356, 1144, 1090, 957, 868, 782, 733, 694 cm^{-1}; HRMS (ESI) calcd for $C_{44}H_{41}O_8S$ ($[M+H]^+$) *m/z* 729.2517, found *m/z* 729.2489.

1,2-rearrangement of ***19***

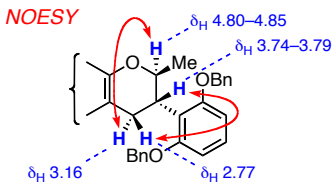


19 **20**

To a solution of mesylate **19** (46 mg, 0.063 mmol), which was azeotropically dried with toluene (1 mL x 3), in CH_2Cl_2 (1.0 mL) was added Me_3Al (ca. 1.4 M in hexane, 0.14 mL, 0.20 mmol) at –78 °C. The reaction mixture was gradually warmed to –30 °C for 1 h, the reaction was quenched by the addition of phosphate buffer solution (pH 7) and 1 M HCl solution. The crude 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 preparative TLC (hexane/toluene/EtOAc = 5/15/1) to afford 2-methyl-isoflavan **20** (32.8 mg, 79%) as a white solid.

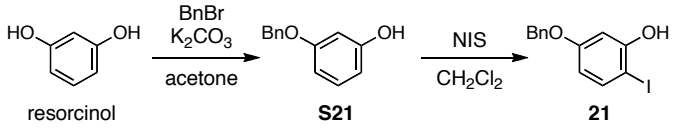
20: R_f 0.45 (hexane/toluene/EtOAc = 5/15/1); mp 142–144 ºC; $[\alpha]_D^{25}$ +3.8 (*c* 0.60, $CHCl_3$); ^{1}H NMR (600 MHz, $CDCl_3$) δ 1.22 (d, 3H, *J* = 6.0 Hz), 2.77 (dd, 1H, *J* = 16.2, 5.4 Hz), 3.16 (dd, 1H, *J* = 16.2, 12.0 Hz), 3.74–3.79 (m, 1H), 4.80–4.85 (m, 1H), 4.98 (s, 2H), 5.00 (s, 2H), 5.07 (s, 4H), 6.17 (s, 1H), 6.21 (s, 1H), 6.58 (d, 1H, *J* = 8.4 Hz), 6.62 (d, 1H, *J* = 8.4 Hz), 7.10 (dd, 1H, *J* = 8.4, 8.4 Hz), 7.26–7.43 (m, 20H); ^{13}C NMR (150 MHz, $CDCl_3$) δ 19.4, 24.7, 36.5, 69.8, 70.1, 70.2, 70.7, 74.3, 92.9, 94.5, 105.5, 105.7, 105.9, 119.2, 127.16, 127.21, 127.6, 127.66, 127.68, 127.77, 127.78, 127.9, 128.4, 128.5, 128.6, 137.0, 137.2, 137.3, 156.6, 157.68, 157.72, 158.0, 158.2 (several signals overlapped); IR (ATR) 3031, 2928, 1615, 1588, 1451, 1377, 1094, 1065, 900, 810, 733, 694 cm^{-1}; HRMS (ESI) calcd for $C_{44}H_{41}O_5$ ($[M+H]^+$) *m/z* 649.2949, found *m/z* 649.2923.

Diagnostic 2D NMR correlations for compound ***20***



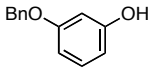
Total synthesis of (–)-equol

*Preparation of A-ring unit **21***[9]



resorcinol **S21** **21**

*Preparation of **S21***

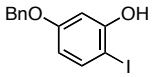


S21

To a solution of K_2CO_3 (629 mg, 4.55 mmol) and resorcinol (1.00 g, 9.09 mmol) in acetone (10 mL) was slowly added benzyl bromide (0.54 mL, 4.55 mmol) at room temperature, and the mixture was stirred at reflux for 2 h. The reaction was stopped by adding water, 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 flush column chromatography (hexane/EtOAc = 17/3 to 3/1) to afford phenol **S21** (532 mg, 58%, based on BnBr) as a colorless oil.

S21: R_f 0.38 (hexane/EtOAc = 3/1); ^{1}H NMR (600 MHz, $CDCl_3$) δ 4.76 (s, 1H), 5.04 (s, 2H), 6.43 (dd, 1H, *J* = 7.8, 1.8 Hz), 6.48 (t, 1H, *J* = 1.8 Hz), 6.57 (dd, 1H, *J* = 7.8, 1.8 Hz), 7.13 (t, 1H, *J* = 7.8 Hz), 7.32 (t, 1H, *J* = 7.8 Hz), 7.37–7.43 (m, 4H); ^{13}C NMR (150 MHz, $CDCl_3$) δ 70.1, 102.5, 107.4, 108.1, 127.5, 128.0, 128.6, 130.2, 136.9, 156.7, 160.2; IR (neat) 3298, 2917, 1592, 1496, 1452, 1278, 1171, 1142, 1026, 813, 761, 730 cm^{-1}; HRMS (ESI) calcd for $C_{13}H_{12}O_2Na$ ($[M+Na]^+$) *m/z* 223.0730, found *m/z* 223.0722.

*Preparation of **21***

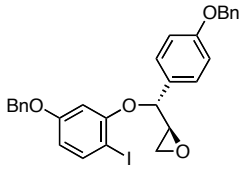


21

To a solution of phenol **S21** (502 mg, 2.51 mmol) in CH_2Cl_2 (5.0 mL) was added *N*-iodosuccinimide (562 mg, 2.50 mmol) at –18 °C. After stirring for 2 h, the reaction was quenched by the addition of saturated $NaHCO_3$ solution. The crude 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 (hexane/ EtOAc = 4/1) to afford iodophenol **21** (552 mg, 67%) as a white solid.

21: R_f 0.29 (hexane/EtOAc = 4/1); mp 64–66 ºC; ^{1}H NMR (600 MHz, $CDCl_3$) δ 5.03 (s, 2H), 5.22 (brs, 1H), 6.40 (d, 1H, *J* = 8.4 Hz) 7.33 (t, 1H, *J* = 7.2 Hz), 7.37–7.41 (m, 4H), 7.49 (d, 1H, *J* = 8.4 Hz); ^{13}C NMR (150 MHz, $CDCl_3$) δ 70.2, 70.4, 101.9, 110.2, 127.5, 128.1, 128.7, 136.5, 138.0, 155.7, 160.9; IR (ATR) 3480, 2917, 1583, 1496, 1413, 1336, 1298, 1256, 1187, 1002, 821, 799 cm^{-1}; HRMS (ESI) calcd for $C_{13}H_{12}O_2I$ ($[M+H]^+$) *m/z* 326.9877, found *m/z* 326.9879.

*Preparation of **23***

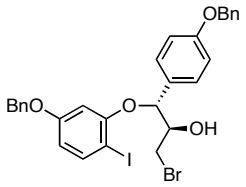


23

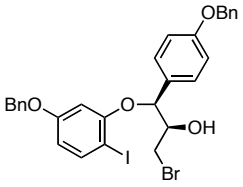
To a solution of epoxy alcohol **22**[6] (100 mg, 0.390 mmol) in toluene (4.0 mL) was added iodophenol **21** (190 mg, 0.583 mmol) and *N,N,N',N'*-tetramethylazodicarboxamide (201 mg, 1.17 mmol) at room temperature. After being cooled at 0 ºC, *n*-Bu_3P (0.24 mL, 0.96 mmol) was added to reaction mixture, and the resulting mixture was stirred for 1 h. The reaction was quenched by the addition of water. The crude 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 (hexane/toluene = 5/1 to 1/3 then toluene/EtOAc = 19/1 to 17/1) to afford ether **23** (173 mg, 78%, dr = 93/7) as white amorphous solids.

23: R_f 0.48 (hexane/EtOAc = 3/1); $[\alpha]_D^{20}$ –28.3 (*c* 1.12, $CHCl_3$); ^{1}H NMR (600 MHz, $CDCl_3$, diastereomer ratio = 93/7, minor isomer's peaks were marked with *) δ 2.75–2.76* (m, 0.07H) 2.82–2.84* (m, 0.07H), 2.83 (dd, 0.93H, *J* = 5.4, 4.2 Hz). 3.09 (dd, 0.93H, *J* = 5.4, 2.4 Hz), 3.28–3.30 (m, 0.93H), 3.41–3.43* (m, 0.07H), 4.85* (d, 0.07H, *J* = 6.0 Hz), 4.90 (s, 1.86H), 4.91* (s, 0.14H), 5.05 (s, 2H), 5.15 (d, 0.93H, *J* = 3.0 Hz), 6.33–6.35 (m, 1.93H), 6.41* (d, 0.07H, *J* = 3.0 Hz), 6.95–6.97 (m, 2H), 7.30–7.43 (m, 12H), 7.55–7.59 (m, 1H); ^{13}C NMR (150 MHz, $CDCl_3$, diastereomer ratio = 93/7, minor isomer's peaks were marked with *) δ 44.9*, 45.0, 54.5, 55.0*, 70.1, 70.2 76.5, 79.0, 82.2*, 102.9, 103.0*, 109.3, 115.1, 127.41, 127.44*, 127.5, 128.0*, 128.05*, 128.10, 128.2, 128.6, 128.8*, 129.0, 136.4, 136.5*, 136.8, 139.1, 156.7, 157.0*, 158.98*, 159.02, 160.0 (several signals overlapped); IR (neat) 3031, 2922, 1576, 1510, 1476, 1299, 1243, 1173, 1011, 832, 737 cm^{-1}; HRMS (ESI) calcd for $C_{29}H_{25}O_4INa$ ($[M+H]^+$) *m/z* 587.0690, found *m/z* 587.0667.

*Preparation of **24** and epimer **24'***



24



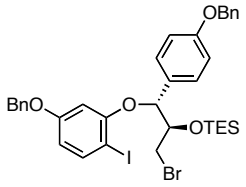
24'

To a solution of ether **23** (164 mg, 0.291 mmol) in THF (3.0 mL) was added Li_2NiBr_4 (ca. 0.4 M in THF, 2.1 mL, 0.84 mmol) at 0 ºC. After stirring for 24 h, the reaction was quenched by the addition of phosphate buffer solution (pH 7). The crude 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 (toluene/hexane = 1/1 to 9/1 then EtOAc/toluene = 1/24) to afford bromohydrin **24** (163 mg, 87%) and epimer **24'** (7.6 mg, 4.0%) as white amorphous solids.

24: R_f 0.30 (hexane/toluene/EtOAc = 5/5/1); $[\alpha]_D^{20}$ 14.6 (*c* 0.775, $CHCl_3$); ^{1}H NMR (600 MHz, $CDCl_3$) δ 2.33 (brd, 1H, *J* = 5.4 Hz, OH), 3.67 (dd, 1H, *J* = 10.8, 3.6 Hz), 3.79 (dd, 1H, *J* = 10.8, 6.6 Hz), 4.12–4.16 (m, 1H), 4.87 (s, 2H), 5.05 (s, 2H), 5.16 (d, 1H, *J* = 6.0 Hz), 6.29 (s, 1H), 6.35 (d, 1H, *J* = 8.4 Hz), 6.97 (d, 2H, *J* = 8.4 Hz), 7.29–7.43 (m, 12H), 7.57 (d, 1H, *J* = 8.4 Hz); ^{13}C NMR (150 MHz, $CDCl_3$) δ 35.5, 70.1, 70.3, 74.3, 81.6, 102.6, 109.3, 115.3, 127.46, 127.47, 127.53, 127.54, 128.1, 128.2, 128.3, 128.4, 128.7, 136.4, 136.7, 139.0, 156.3, 159.1, 160.2; IR (neat) 3567, 3031, 2869, 1577, 1509, 1476, 1419, 1299, 1245, 1173, 1011, 830, 738 cm^{-1}; HRMS (ESI) calcd for $C_{29}H_{26}BrINaO_4$ ($[M+Na]^+$) *m/z* 666.9951, found *m/z* 666.9934.

24': R_f 0.39 (hexane/toluene/EtOAc = 5/5/1); $[\alpha]_D^{20}$ –12 (*c* 0.52, $CHCl_3$); ^{1}H NMR (600 MHz, $CDCl_3$) δ 3.17 (brd, 1H, *J* = 4.2 Hz, OH), 3.25 (dd, 1H, *J* = 10.8, 4.8 Hz), 3.60 (dd, 1H, *J* = 10.8, 4.2 Hz), 4.09–4.12 (m, 1H), 4.87 (s, 2H), 5.05 (s, 2H), 5.21 (d, 1H, *J* = 6.0 Hz), 6.31 (d, 1H, *J* = 2.4 Hz), 6.36 (dd, 1H, *J* = 9.0, 2.4 Hz), 6.97 (d, 2H, *J* = 9.0 Hz), 7.29–7.43 (m, 12H), 7.57 (d, 1H, *J* = 9.0 Hz); ^{13}C NMR (150 MHz, $CDCl_3$) δ 33.9, 70.1, 70.2, 74.5, 82.6, 102.8, 109.6, 115.4, 127.45, 127.53, 128.11, 128.13, 128.2, 128.5, 128.65, 128.66, 136.3, 136.7, 138.9, 156.4. 159.2, 160.2 (several signals overlapped); IR (neat) 3548, 3031, 2927, 1578, 1511, 1453, 1245, 1173, 1011, 830, 736, 696 cm^{-1}; HRMS (ESI) calcd for $C_{29}H_{26}BrINaO_4$ ($[M+Na]^+$) *m/z* 666.9951, found *m/z* 666.9941.

Preparation of ***25***

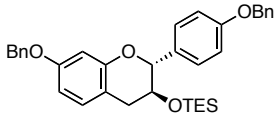


25

To a solution of bromohydrin **24** (144 mg, 0.222 mmol) in CH_2Cl_2 (3.0 mL) was added 2,6-lutidine (0.13 mL, 1.1 mmol) and triethylsilyl triflate (118 mg, 0.446 mmol) in CH_2Cl_2 (1.0 mL) at 0 ºC. After stirring for 20 min, the reaction was quenched by the addition of saturated $NaHCO_3$ solution. The crude products were extracted with EtOAc (x3), and the combined organic extracts were washed with 5% citric acid solution and brine, dried (Na_2SO_4), and concentrated in vacuo. The residue was purified by flash column chromatography (EtOAc/hexane = 1/19) to afford silyl ether **25** (165 mg, 97%) as a white amorphous solid.

25: R_f 0.54 (hexane/EtOAc = 5/1); $[\alpha]_D^{20}$ +29 (*c* 0.96, $CHCl_3$); ^{1}H NMR (600 MHz, $CDCl_3$) δ 0.35–0.47 (m, 6H), 0.81 (t, 9H, *J* = 7.8 Hz), 3.57 (dd, 1H, *J* = 10.8, 3.6 Hz), 4.01 (dd, 1H, *J* = 10.8, 3.0 Hz), 4.09–4.11 (m, 1H), 4.85 (d, 1H, *J* = 12.0 Hz), 4.88 (d, 1H, *J* = 12.0 Hz), 5.05 (s, 2H), 5.09 (d, 1H, *J* = 7.2 Hz), 6.30–6.32 (m, 2H), 6.91 (d, 2H, *J* = 8.4 Hz), 7.28–7.42 (m, 12H), 7.55 (d, 1H, *J* = 8.4 Hz); ^{13}C NMR (150 MHz, $CDCl_3$) δ 4.7, 6.7, 37.2, 70.0, 70.2, 74.4, 75.9, 81.1, 102.3, 109.1, 114.8, 127.4, 127.5, 128.0, 128.1, 128.57, 128.59, 128.9, 129.8, 136.4, 136.9, 138.9, 156.7, 158.8, 160.1; IR (neat) 2954, 2875, 1575, 1511, 1454, 1417, 1300, 1244, 1173, 1133, 1012, 828, 734 cm^{-1}; HRMS (ESI) calcd for $C_{35}H_{40}BrINaO_4Si$ ($[M+Na]^+$) *m/z* 781.0816, found *m/z* 781.0794.

Preparation of ***26***



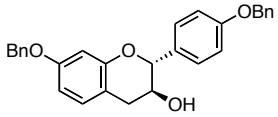
26

To a solution of PhMgBr (1.1 M in Et_2O, 0.42 mL, 0.46 mmol) and HMPA (0.10 mL, 0.57 mmol) in THF (2.0 mL) was added PhLi (0.80 M in cyclohexane/Et_2O, 1.2 mL, 0.96 mmol) at 0 °C. After stirring for 30 min, the reaction mixture was cooled to –78 °C, silyl ether **25** (181 mg, 0.238 mmol) in THF (3.0 mL) was added and stirring for 5 min. The reaction mixture was gradually warmed to 0 °C for 40 min, then the reaction was quenched by adding saturated NH_4Cl solution. The crude 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 (hexane/CH_2Cl_2 = 2/1) to afford flavan **26** (115 mg, 88%) as a colorless oil.

26: R_f 0.34 (hexane/CH_2Cl_2 = 2/1); $[\alpha]_D^{20}$ +15.7 (*c* 1.14, $CHCl_3$); ^{1}H NMR (600 MHz, $CDCl_3$) δ

0.26–0.40 (m, 6H), 0.76 (t, 9H, J = 7.8 Hz), 2.86 (dd, 1H, J = 15.6, 9.0 Hz), 2.95 (dd, 1H, J = 15.6, 5.4 Hz), 3.96–4.00 (m, 1H), 4.66 (d, 1H, J = 8.4 Hz), 5.01 (s, 2H), 5.10 (s, 2H), 6.53 (d, 1H, J = 2.4 Hz), 6.57 (dd, 1H, J = 9.0, 2.4 Hz), 6.96 (d, 3H, J = 9.0 Hz), 7.29–7.43 (m, 12H); ^{13}C NMR (150 MHz, $CDCl_3$) δ 4.6, 6.7, 35.2, 69.1, 70.05, 70.06, 82.1, 102.2, 108.6, 113.0, 114.7, 127.3, 127.4, 127.9, 128.6, 128.7, 130.1, 131.8, 137.08, 137.10, 155.1, 158.5, 158.7 (several signals overlapped); IR (neat) 2952, 2875, 1620, 1586, 1504, 1454, 1240, 1162, 1108, 1016, 829, 740, 696 cm^{-1}; HRMS (ESI) calcd for $C_{35}H_{40}NaO_4Si$ ([M+Na]$^+$) *m/z* 575.2588, found *m/z* 575.2569.

Preparation of ***S22***

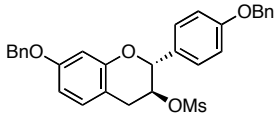


S22

To a solution of flavan **26** (32 mg, 58 μmol) in THF (1.0 mL) was added a solution of tetrabutylammonium fluoride (1.0 M in THF, 0.10 mL, 0.10 mmol) at 0 °C. After stirring for 15 min at room temperature, the reaction was quenched by the addition of phosphate buffer solution (pH 7). The crude 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 preparative TLC (hexane/EtOAc = 3/1) to afford flavan **S22** (24 mg, 95%) as a white solid.

S22: R_f 0.18 (hexane/EtOAc = 3/1); mp 105–107 ºC; $[\alpha]_D^{20}$ –18.5 (*c* 1.03, $CHCl_3$); ^{1}H NMR (600 MHz, $CDCl_3$) δ 1.67 (brs, 1H, OH), 2.84 (dd, 1H, J = 15.6, 9.0 Hz), 3.04 (dd, 1H, J = 15.6, 5.4 Hz), 4.07–4.10 (m, 1H), 4.73 (d, 1H, J = 8.4 Hz), 5.01 (s, 2H), 5.09 (s, 2H), 6.55 (d, 1H, J = 2.4 Hz), 6.59 (dd, 1H, J = 8.4, 2.4 Hz), 7.00 (d, 1H, J = 8.4 Hz), 7.02 (d, 2H, J = 9.0 Hz), 7.30–7.44 (m, 12H); ^{13}C NMR (150 MHz, $CDCl_3$) δ 32.4, 68.3, 70.06, 70.07, 81.7, 102.3, 108.9, 112.4, 115.2, 127.4, 127.9, 128.1, 128.5, 128.56, 128.63, 130.1, 130.4, 136.8, 137.0, 154.9, 158.6, 159.2 (several signals overlapped); IR (ATR) 3477, 2915, 1621, 1582, 1504, 1382, 1223, 1162, 1109, 1007, 826, 742, 695 cm^{-1}; HRMS (ESI) calcd for $C_{29}H_{26}NaO_4$ ([M+Na]$^+$) *m/z* 461.1723, found *m/z* 461.1705.

Preparation of ***27***



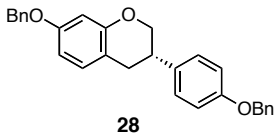
27

To a solution of flavan **S22** (81 mg, 0.18 mmol) in CH_2Cl_2 (2.0 mL) was added Et_3N (0.13 mL, 0.93 mmol) and MsCl (28 μL, 0.36 mmol) at 0 °C. After stirring for 10 min, the reaction was quenched by

the addition of saturated $NaHCO_3$ solution. The crude 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 preparative TLC (hexane/EtOAc = 3/2) to afford mesylate **27** (94.5 mg, 99%) as a white solid.

27: R_f 0.50 (hexane/EtOAc = 3/2); mp 114 ºC (decomp.); $[\alpha]_D^{20}$ –1.8 (*c* 1.1, $CHCl_3$); ^{1}H NMR (600 MHz, $CDCl_3$) δ 2.41 (s, 3H), 3.12 (dd, 1H, *J* = 16.2, 7.8 Hz), 3.21 (dd, 1H, *J* = 16.2, 5.4 Hz), 4.93–4.97 (m, 1H), 5.00–5.04 (m, 3H), 5.09 (s, 2H), 6.57 (d, 1H, *J* = 2.4 Hz), 6.61 (dd, 1H, *J* = 8.4, 2.4 Hz), 6.97 (d, 1H, *J* = 8.4 Hz), 7.00 (d, 1H, *J* = 8.4 Hz), 7.31–7.42 (m, 12H); ^{13}C NMR (150 MHz, $CDCl_3$) δ 31.3, 37.8, 70.0, 70.1, 77.6, 78.2, 102.4, 109.4, 110.7, 115.3, 127.4, 127.5, 128.0, 128.1, 128.3, 128.59, 128.63, 129.7, 130.2, 136.6, 136.8, 154.2, 158.9, 159.1; IR (ATR) 1615, 1583, 1506, 1456, 1354, 1249, 1167, 1036, 967, 870, 826, 742, 727 cm^{-1}; HRMS (ESI) calcd for $C_{30}H_{28}NaO_6S$ ($[M+Na]^+$) *m/z* 539.1499, found *m/z* 539.1524.

*Preparation of **28***

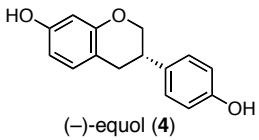


28

To a solution of $AlCl_3$ (30 mg, 0.23 mmol) in Et_2O (1 mL) was added $LiAlH_4$ (6.3 mg, 0.17 mmol) at 0 °C. After stirring for 30 min, the reaction mixture was cooled to –78 °C. A solution of mesylate **27** (26 mg, 50 μmol), which was azeotropically dried with toluene (1 mL x 3), in CH_2Cl_2 (1 mL) was added to the reaction mixture. After stirring for 2 h at 0 °C, the reaction mixture was warmed to room temperature. After stirring for 30 min, the reaction was quenched by the addition of $Na_2SO_4 \cdot 10H_2O$ (256 mg, 0.794 mmol) and dried (Na_2SO_4). The mixture was filtered through a Celite® pad (washed with CH_2Cl_2) and concentrated in vacuo. The residue was purified by PTLC (hexane/toluene/EtOAc = 24/72/4) to afford isoflavan **28** (18.0 mg, 85%) as a white solid.

28: R_f 0.36 (hexane/toluene = 1/3); mp 147–149 ºC; $[\alpha]_D^{20}$ –17 (*c* 0.89, $CHCl_3$); ^{1}H NMR (600 MHz, $CDCl_3$) δ 2.91–2.97 (m, 2H), 3.15–3.19 (m, 1H), 3.96 (dd, 1H *J* = 10.8, 10.8 Hz), 4.30 (dd, 1H, *J* = 10.8, 2.4 Hz), 5.03 (s, 2H), 5.06 (s, 2H), 6.50 (d, 1H, *J* = 2.4 Hz), 6.55 (dd, 1H, *J* = 8.4, 2.4 Hz), 6.96 (d, 2H, *J* = 9.0 Hz), 6.98 (d, 1H, *J* = 8.4 Hz), 7.16 (d, 2H, *J* = 9.0 Hz), 7.30–7.44 (m, 10 H); ^{13}C NMR (150 MHz, $CDCl_3$) δ 31.9, 37.9, 70.1, 71.1, 102.5, 108.1, 114.5, 115.1, 127.45, 127.47, 127.9, 128.0, 128.3, 128.56, 128.61, 130.2, 133.7, 137.0, 137.1, 155.0, 157.9, 158.3 (several signals overlapped); IR (ATR) 3059, 2914, 1612, 1581, 1506, 1453, 1381, 1246, 1164, 1113, 1021, 822, 736, 693 cm^{-1}; HRMS (ESI) calcd for $C_{29}H_{27}O_3$ ($[M+H]^+$) *m/z* 423.1955, found *m/z* 423.1940.

*Preparation of (–)-equol (**4**)*



(–)-equol (**4**)

A solution of isoflavan **28** (29 mg, 68 μmol) in mixed solvent (4.1 mL, THF/MeOH/H_2O = 20/20/1) was added ASCA-2® (5% Pd/$(OH)_2$/C, 81 mg,), and stirred under H_2 atmosphere at room temperature for 45 min. The reaction mixture was filtered through a glass fiber filter under Ar atmosphere (washed with MeOH), and roughly half volume of the filtrate was evaporated, and lyophilization gave (–)-equol (**4**) (20.2 mg, quant., 99% e.e.) as a white powder. Enantiomeric purity of **4** was assessed by HPLC analysis [CHIRALPAK® IE-3 (Daicel), ϕ 4.6 x 250 mm, hexane/*i*-PrOH = 90/10, 1.0 mL/min flow rate, 35 °C, 220 nm, t_R = 15.0 min for the (*R*)-isomer and 16.0 min for the (*S*)-isomer].

4: R_f 0.19 (hexane/EtOAc = 2/1); mp 186–188 ºC; $[\alpha]_D^{25}$ –13 (*c* 0.21, EtOH); ^{1}H NMR (600 MHz, DMSO-d_6) δ 2.77 (dd, 1H, *J* = 15.6, 4.8 Hz), 2.83 (dd, 1H, *J* = 15.6, 10.8 Hz), 2.99–3.03 (m, 1H), 3.90 (dd, 1H, *J* = 10.2, 10.2 Hz), 4.14 (brd, 1H, *J* = 10.2 Hz), 6.18 (s, 1H), 6.28 (d, 1H, *J* = 7.8 Hz), 6.72 (d, 2H, *J* = 7.8 Hz), 6.87 (d, 1H, *J* = 7.8 Hz), 7.10 (d, 2H, *J* = 7.8 Hz), 9.24 (brs, 2H, OH); ^{13}C NMR (150 MHz, DMSO-d_6) δ 31.2, 37.0, 70.1, 102.4, 107.9, 112.4, 115.2, 128.2, 130.0, 131.5, 154.4, 156.0, 156.4; IR (ATR) 3207, 2916, 1615, 1597, 1506, 1435, 1246, 1154, 1115, 1022, 828 cm^{-1}; HRMS (ESI) calcd for $C_{15}H_{14}NaO_3$ ($[M+Na]^+$) *m/z* 265.0841, found *m/z* 265.0828.

References

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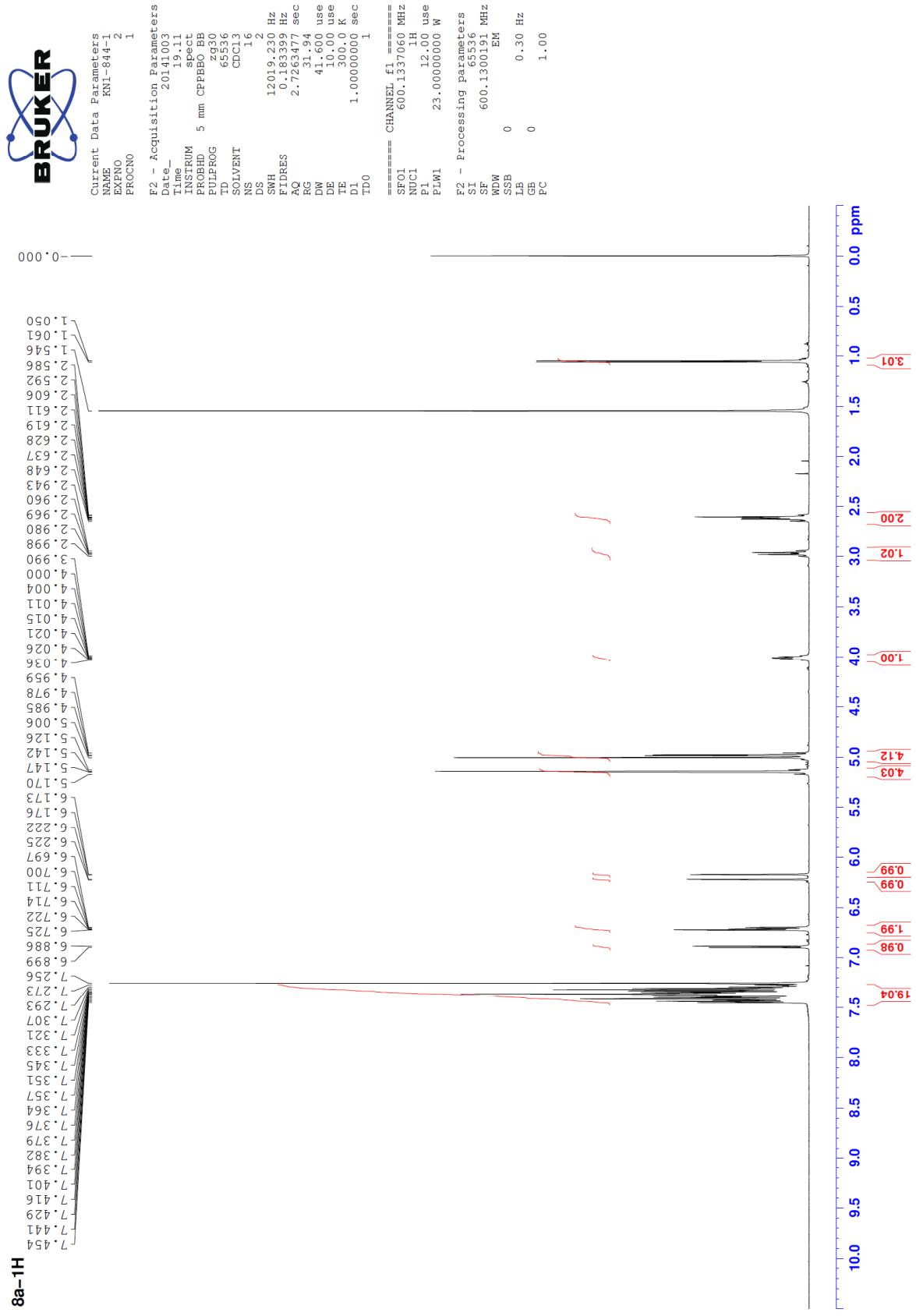
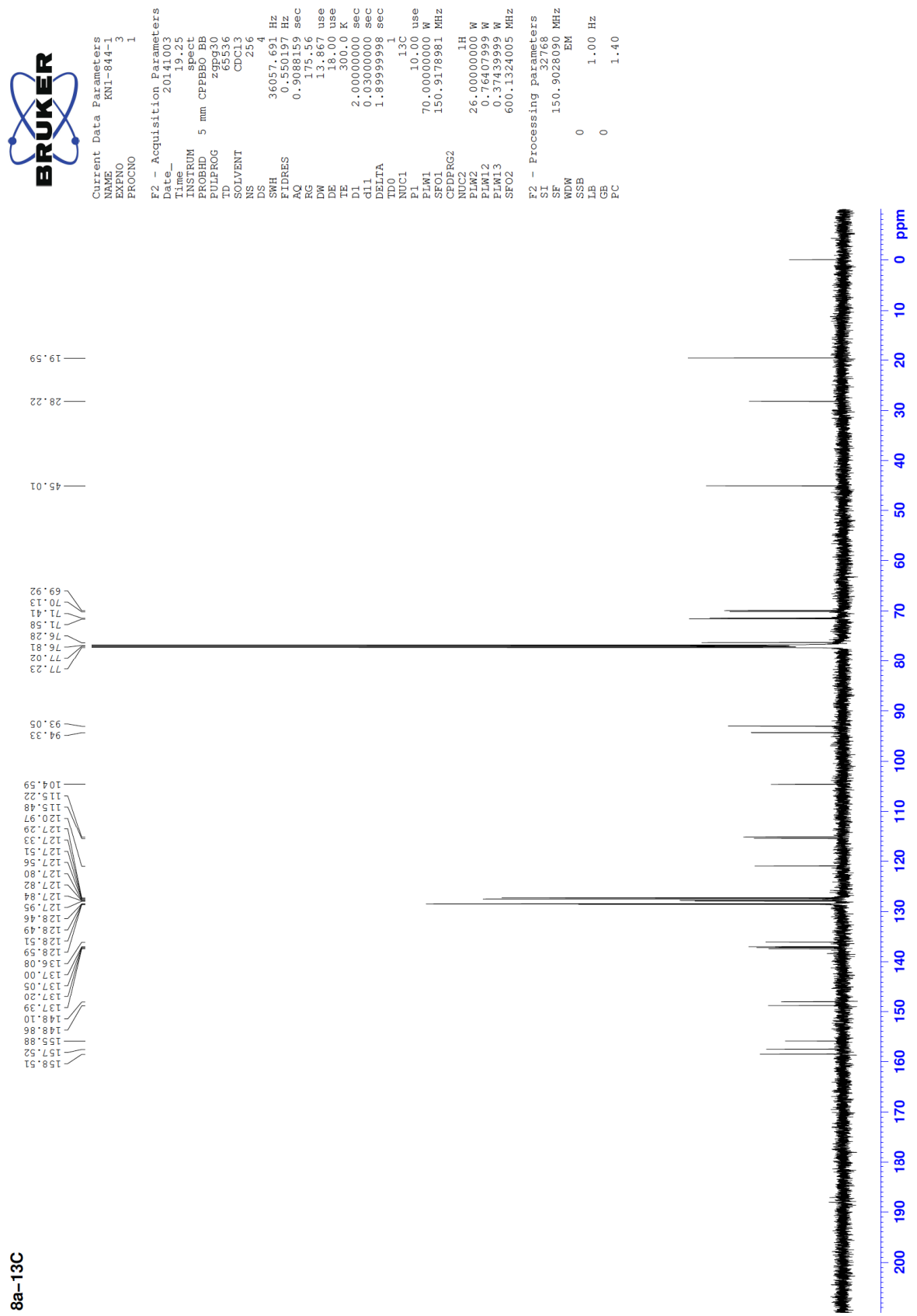
7. Authentic samples of (±)-**11** and (±)-**S15** was prepared from dihydroxylation without chiral ligands.
8. H. Gube, B. Kasumaj, C. Calle, B. Felber, M. Saito, G. Jeschke and F. Diederich, *Chem. Eur. J.* 2009, **15**, 125.
9. For spectrum data of iodophenol **21**, see T. Yamashita, T. Fujimoto, R. Mizojiri, K. Yonemori, H. Hirose, Z. Ikeda, I. Fujimori, K. Toyofuku, T. Yasuma and N. Matsunaga, US 20140243310, 2014.

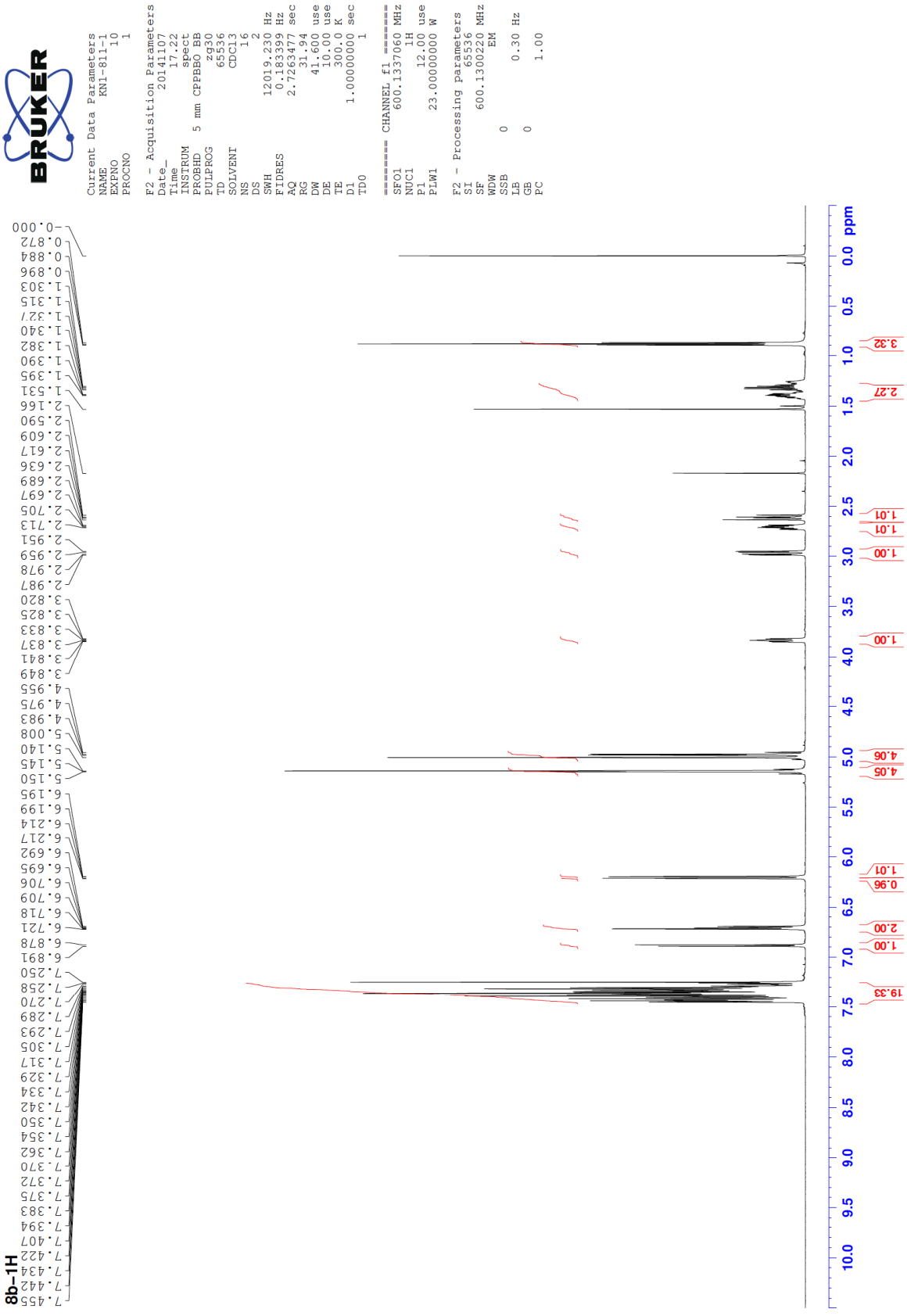
Compound **8a** (^{1}H NMR, 600 MHz, $CDCl_3$)



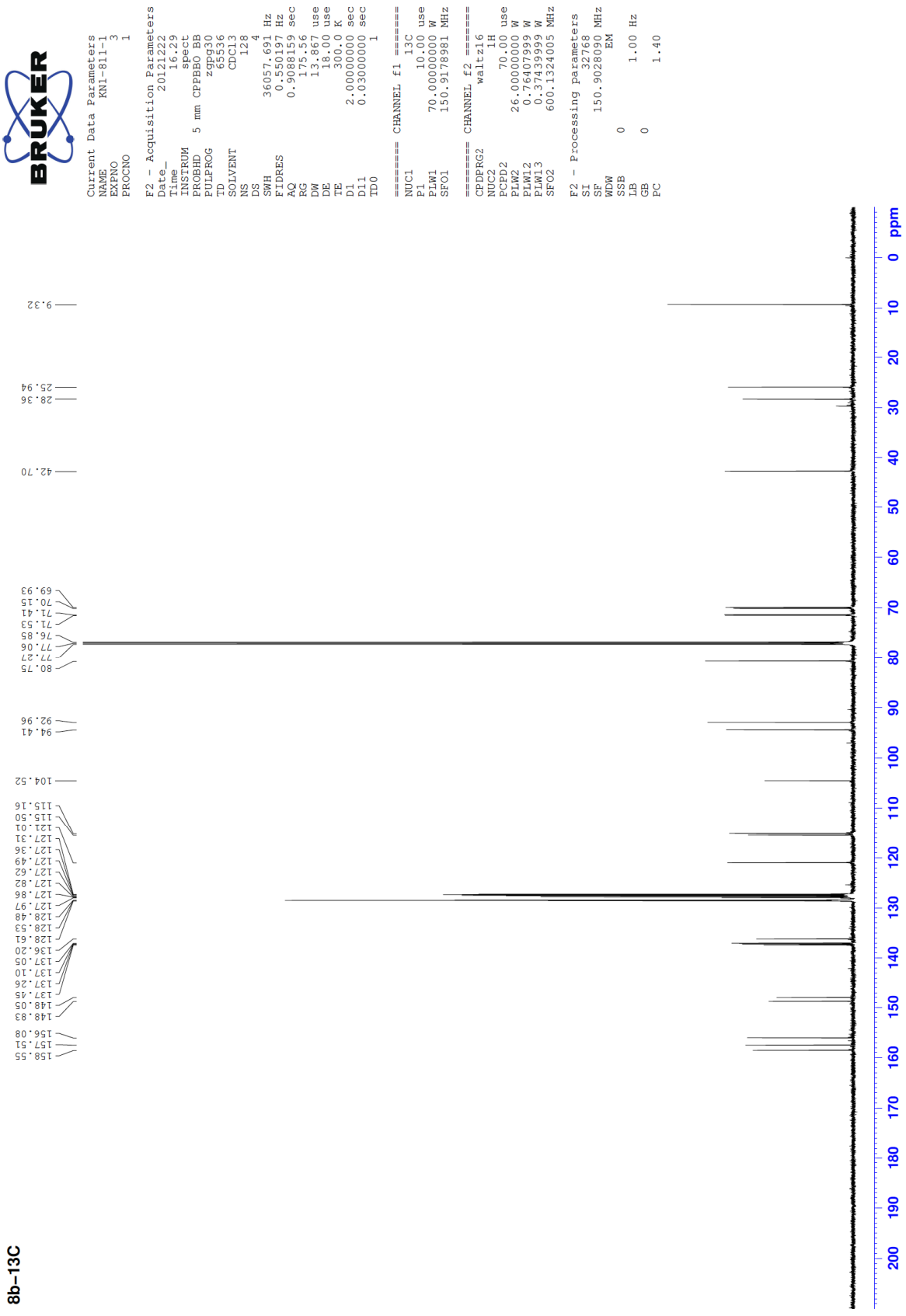
Compound **8a** (^{13}C NMR, 150 MHz, $CDCl_3$)



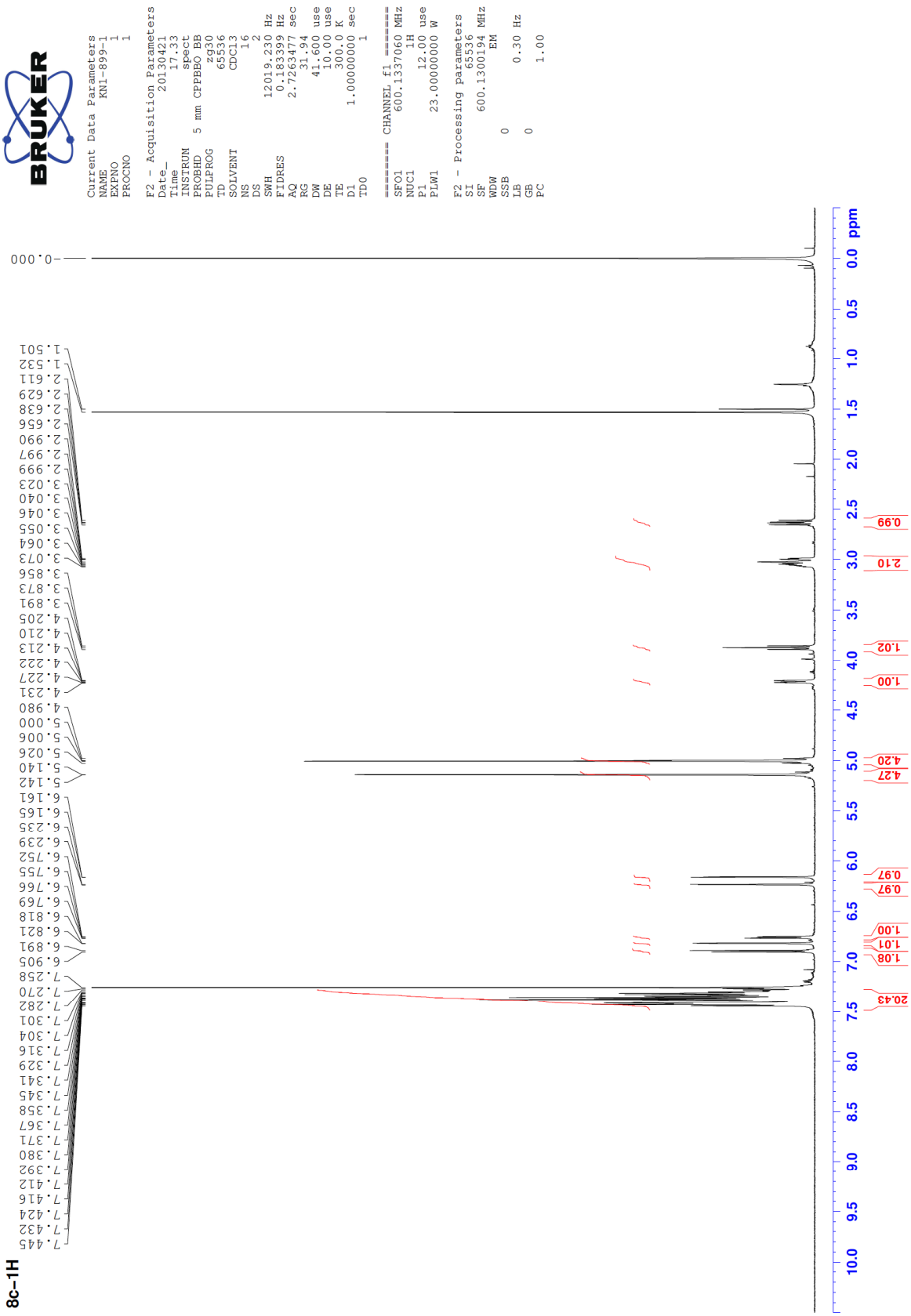
Compound **8b** (^{1}H NMR, 600 MHz, $CDCl_3$)



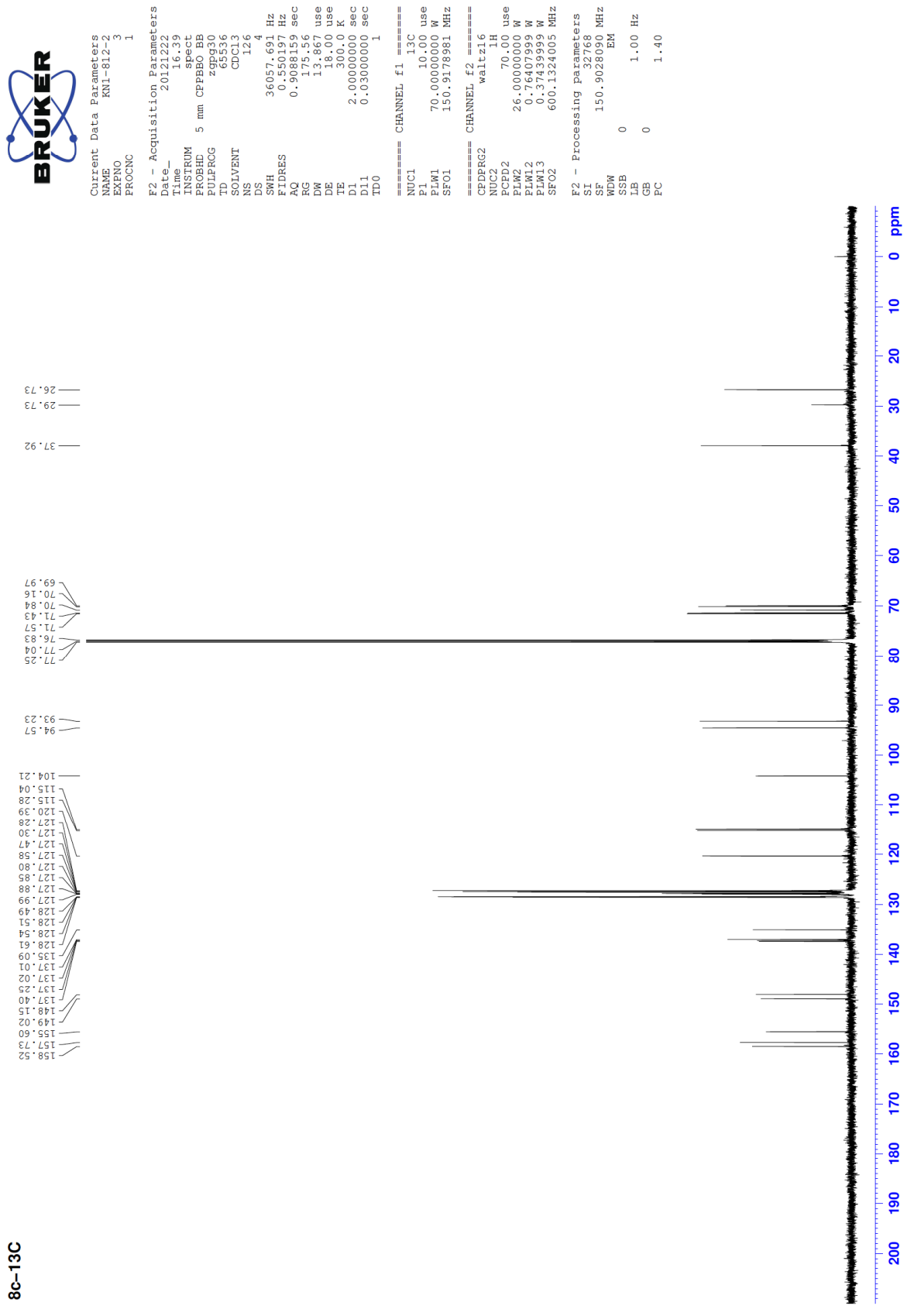
Compound **8b** (^{13}C NMR, 150 MHz, $CDCl_3$)



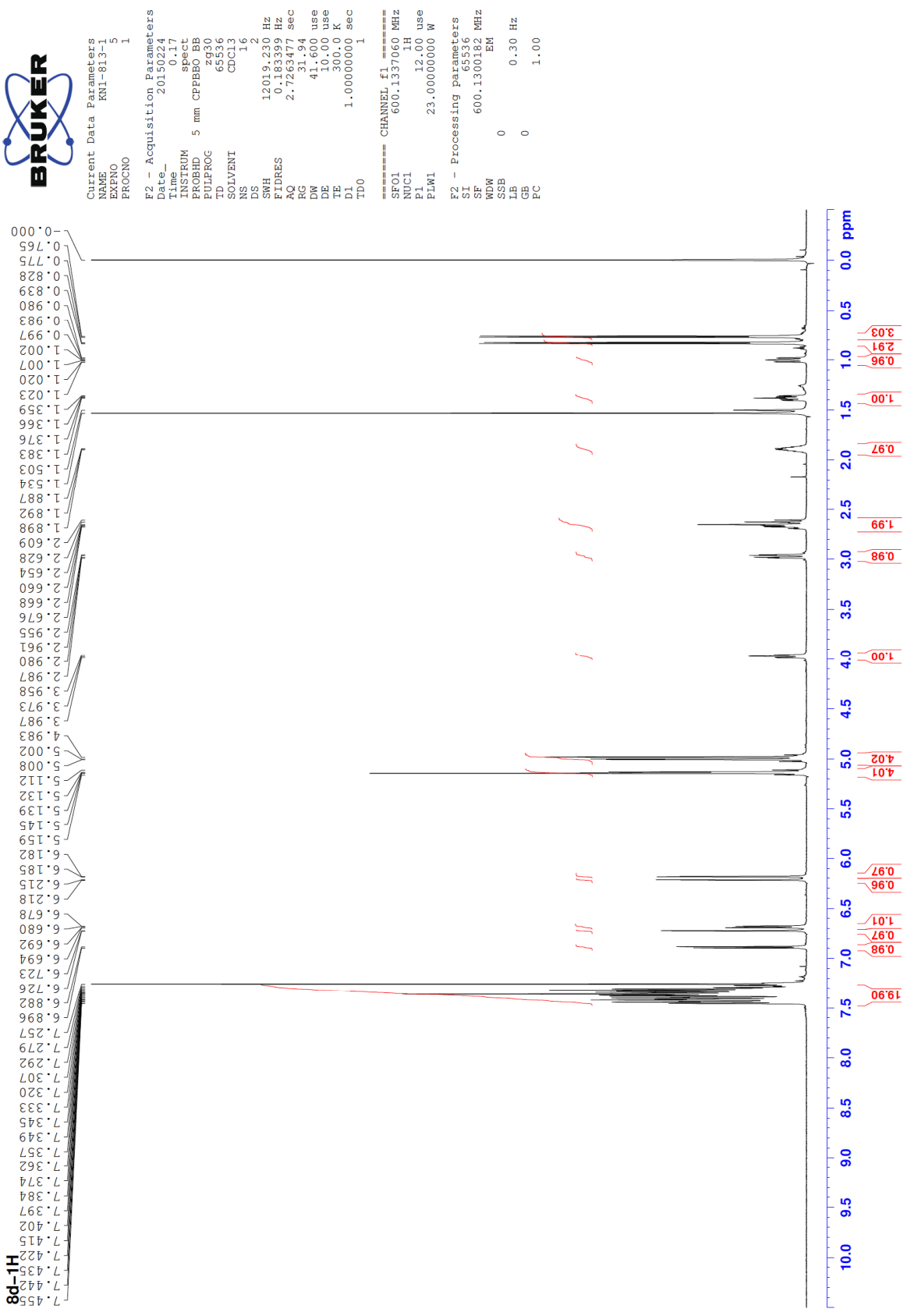
Compound **8c** (^{1}H NMR, 600 MHz, $CDCl_3$)



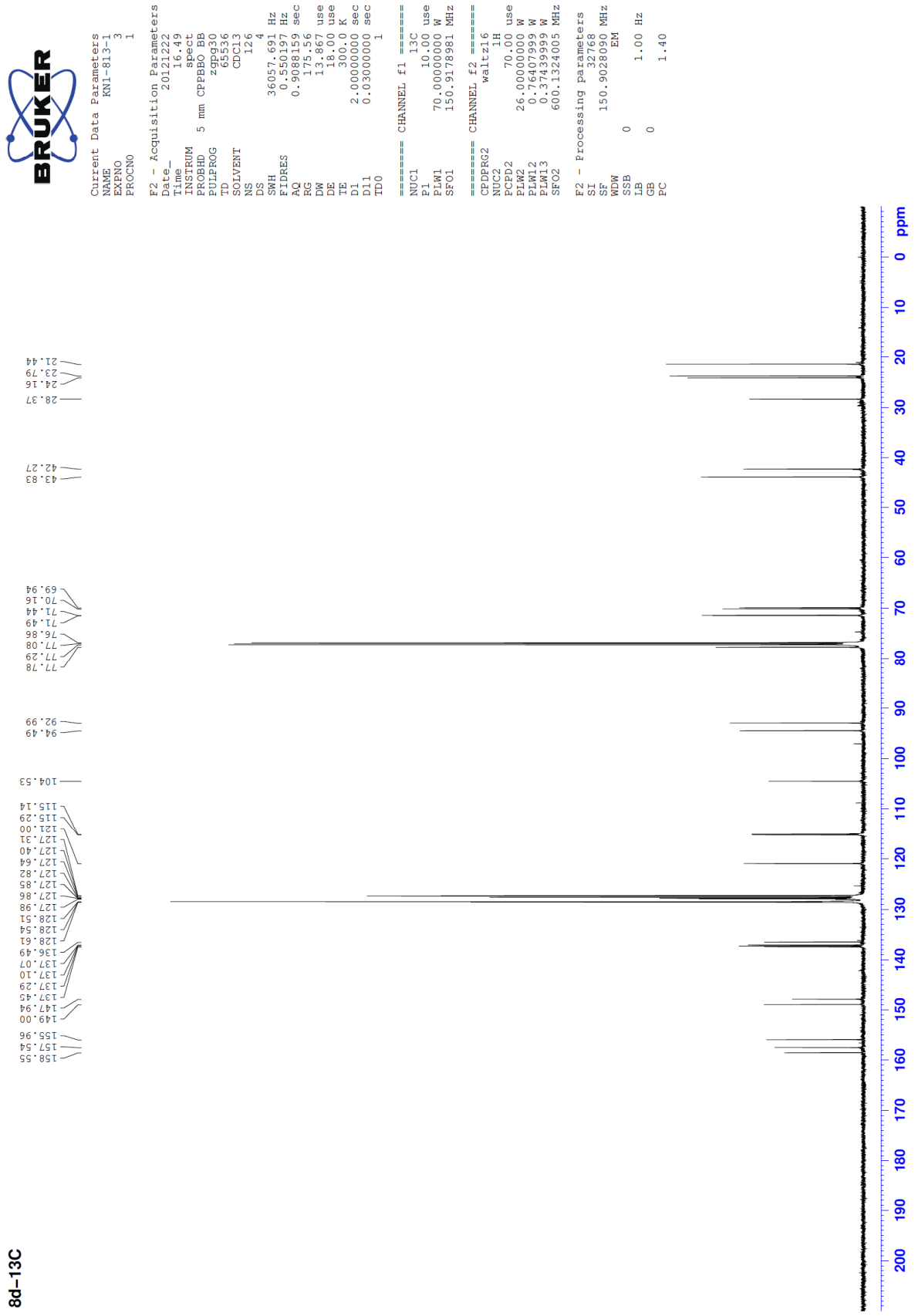
Compound **8c** (^{13}C NMR, 150 MHz, $CDCl_3$)



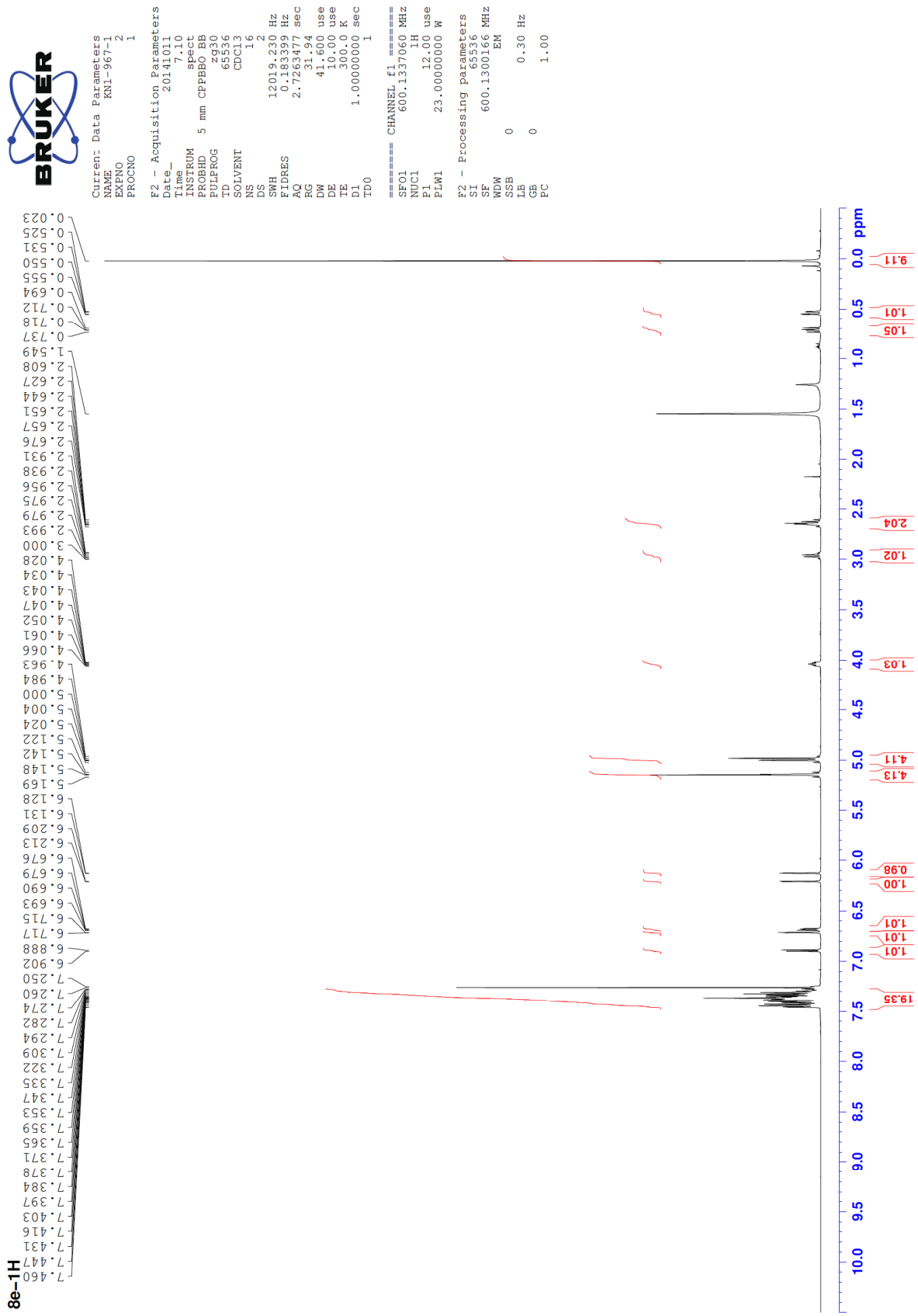
Compound **8d** (^{1}H NMR, 600 MHz, $CDCl_3$)



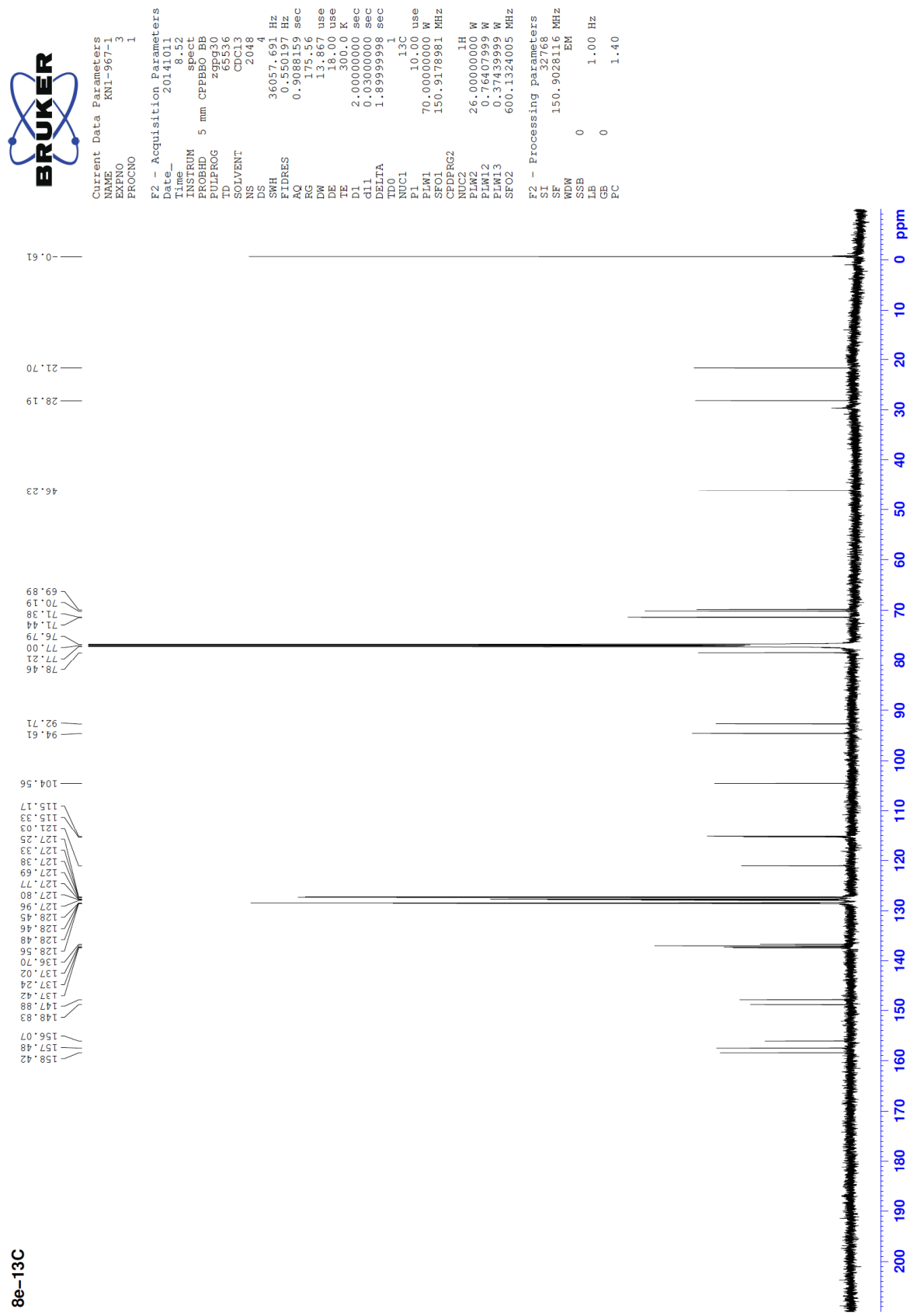
Compound **8d** (^{13}C NMR, 150 MHz, $CDCl_3$)



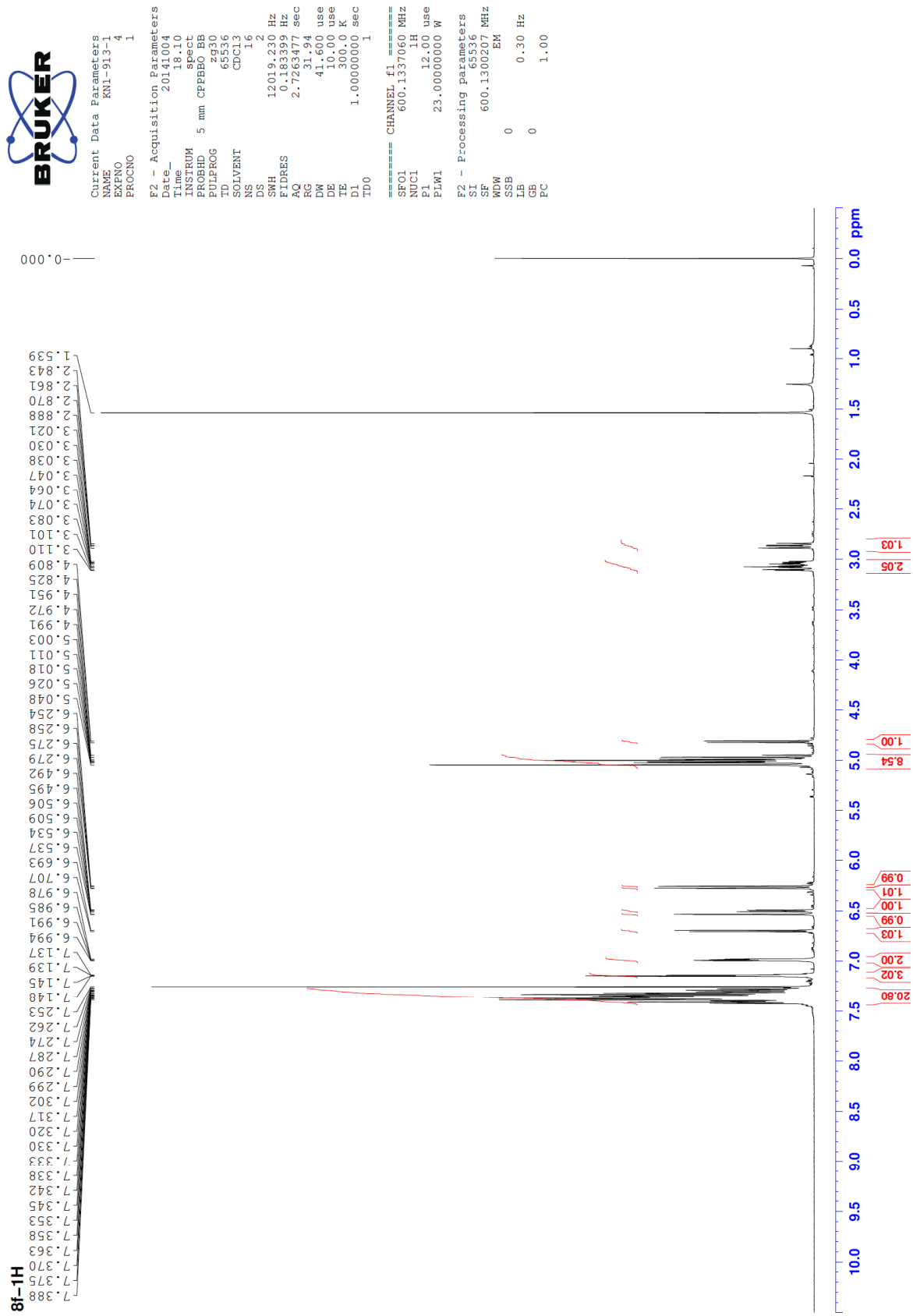
Compound **8e** (^{1}H NMR, 600 MHz, $CDCl_3$)



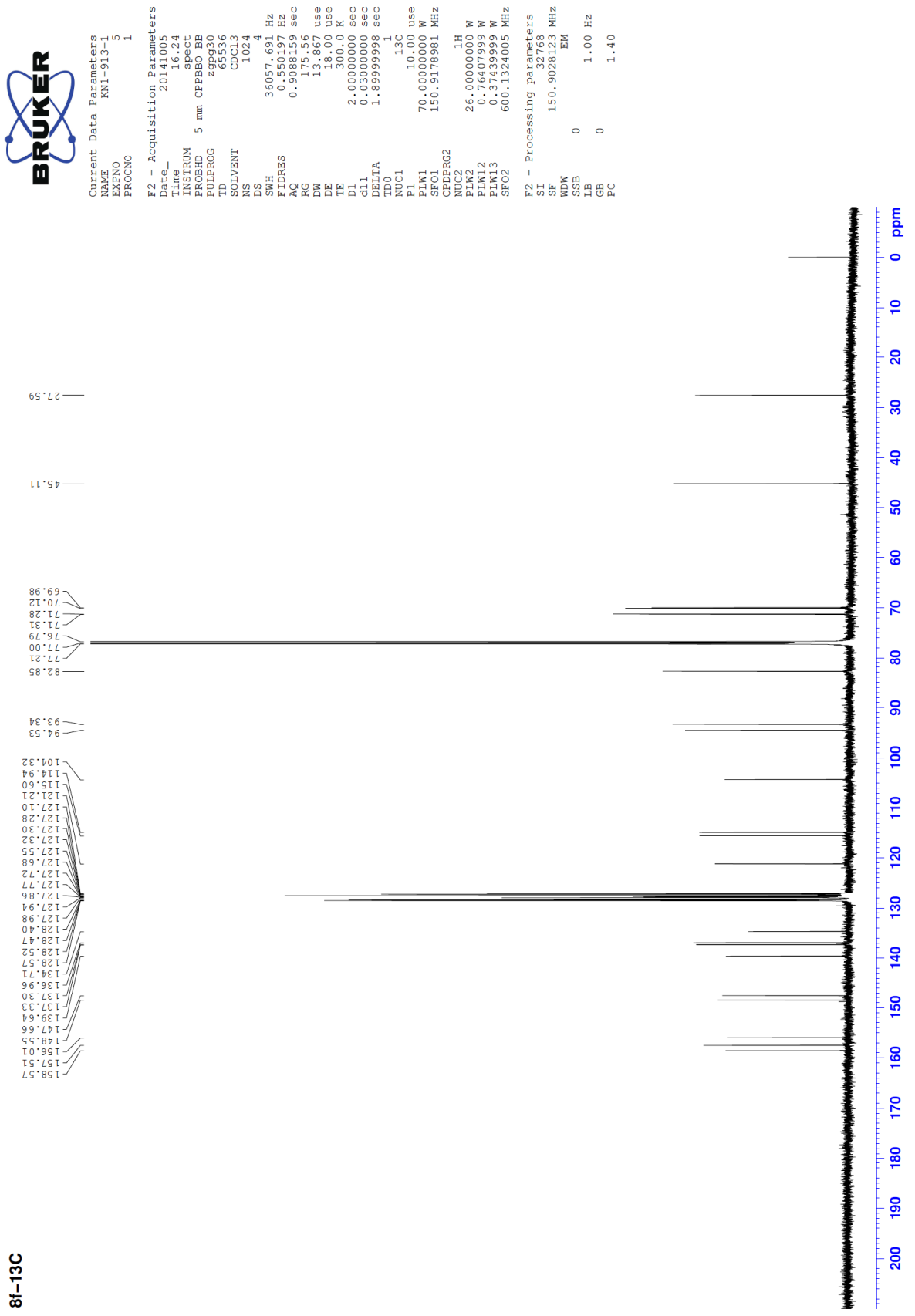
Compound **8e** (^{13}C NMR, 150 MHz, $CDCl_3$)



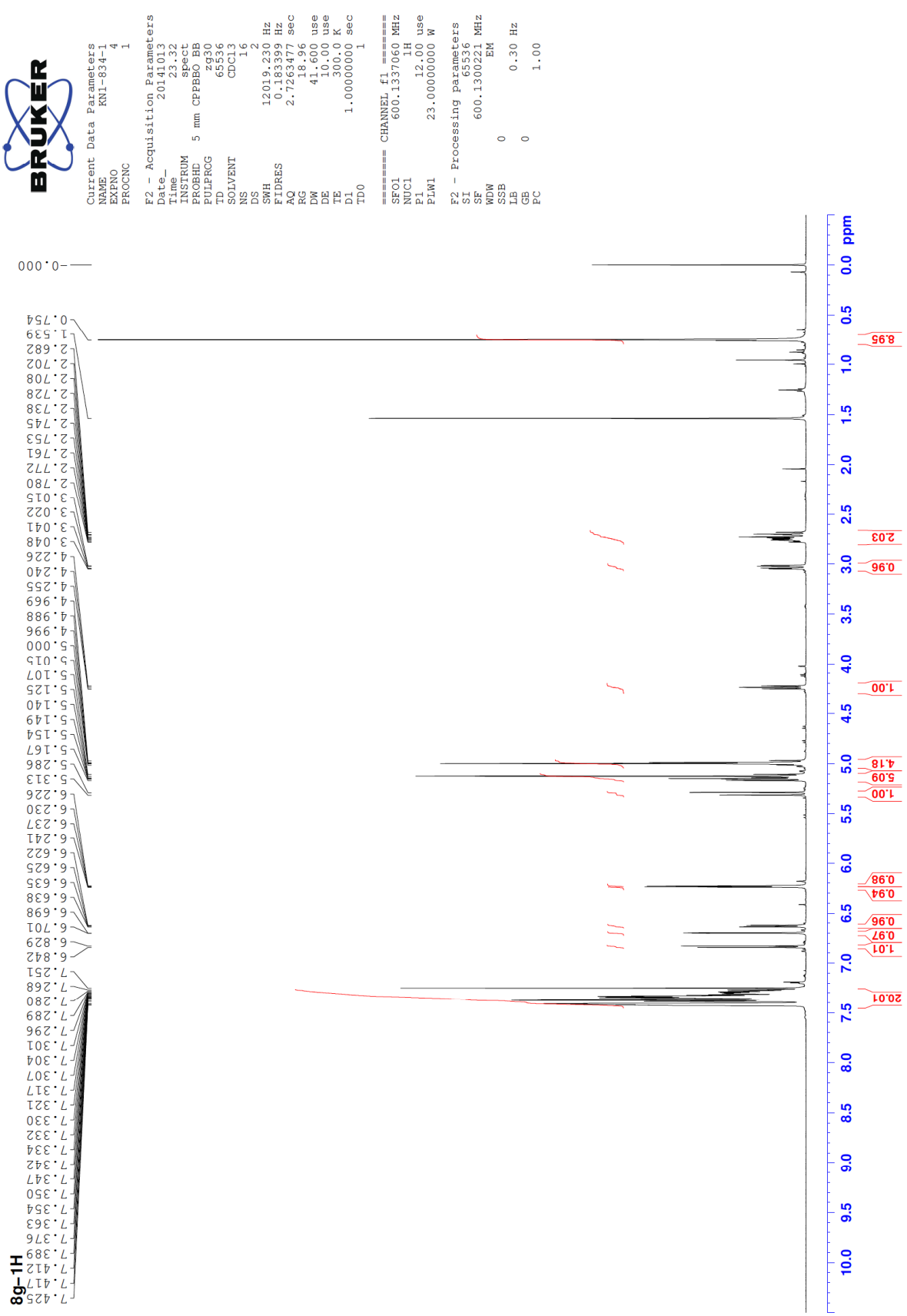
Compound **8f** (^{1}H NMR, 600 MHz, $CDCl_3$)



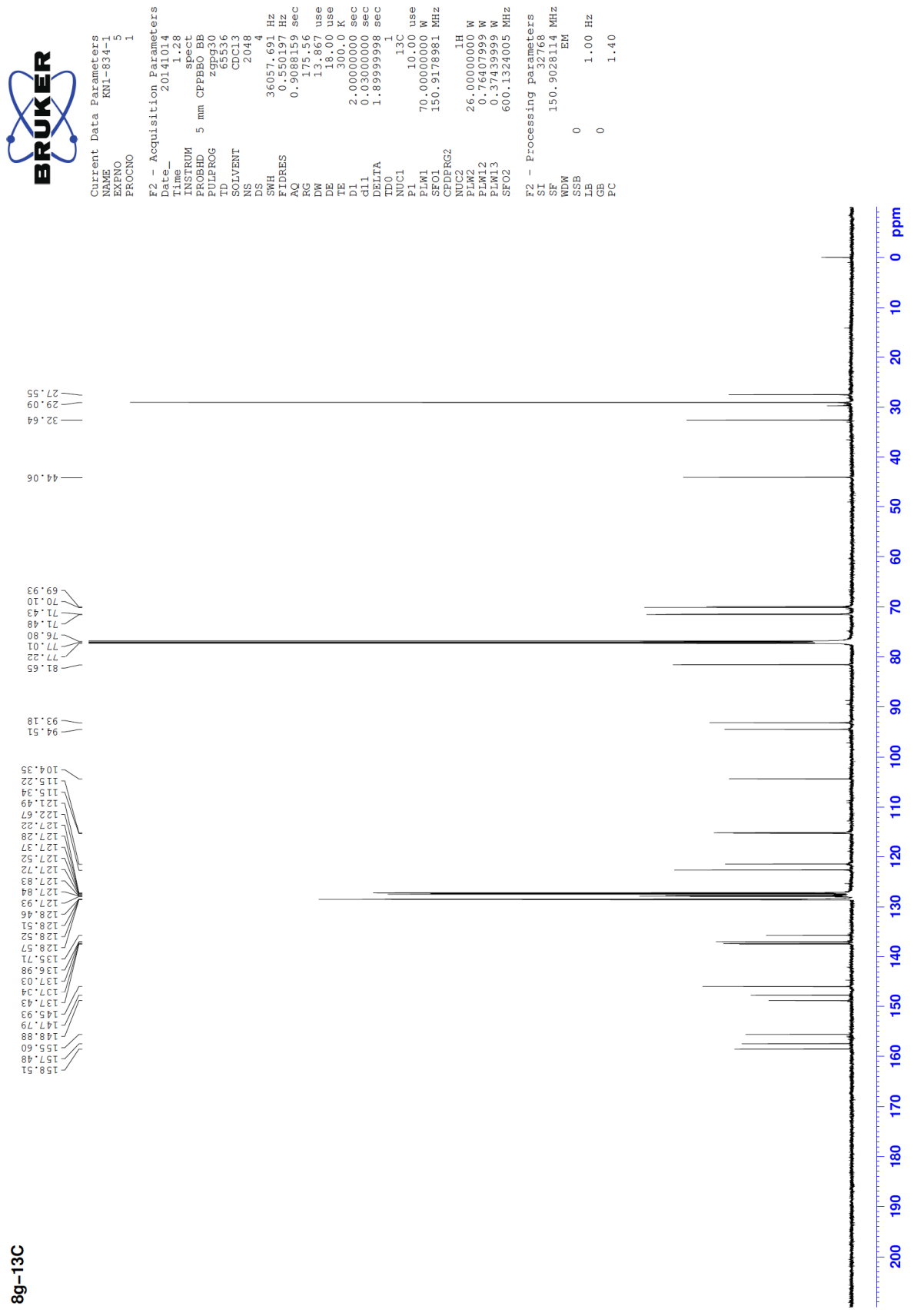
Compound **8f** (^{13}C NMR, 150 MHz, $CDCl_3$)



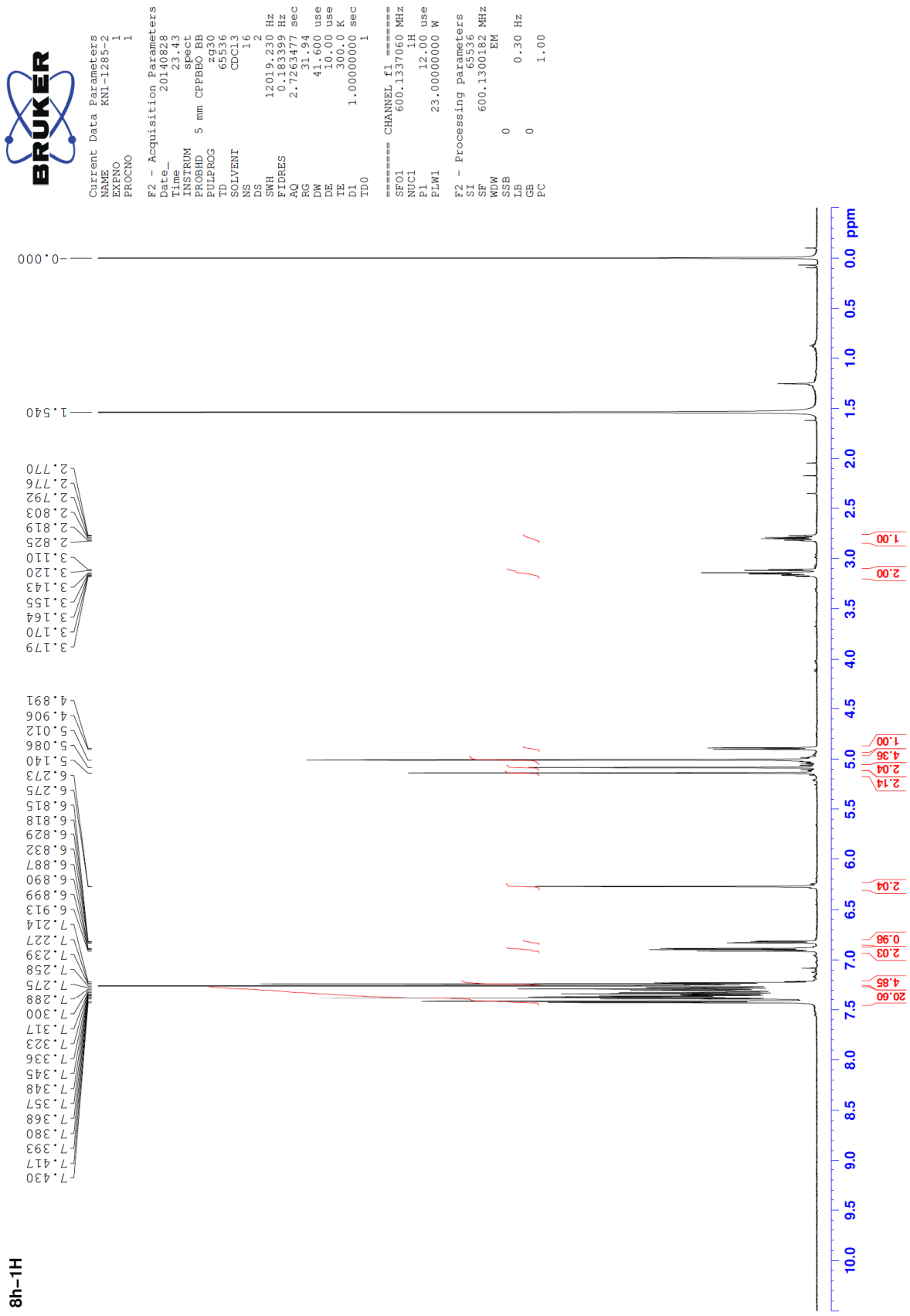
Compound **8g** (^{1}H NMR, 600 MHz, $CDCl_3$)



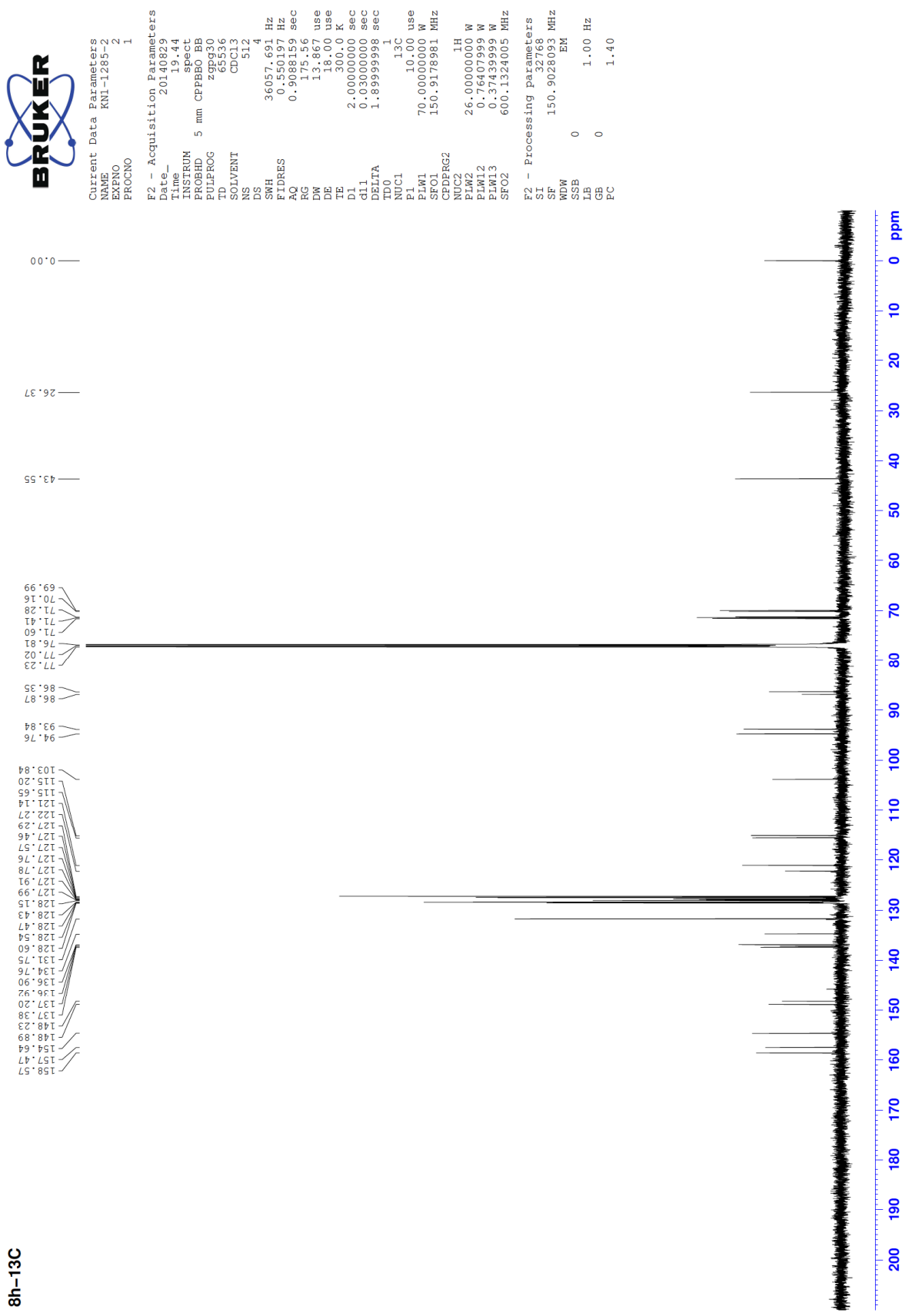
Compound **8g** (^{13}C NMR, 150 MHz, $CDCl_3$)



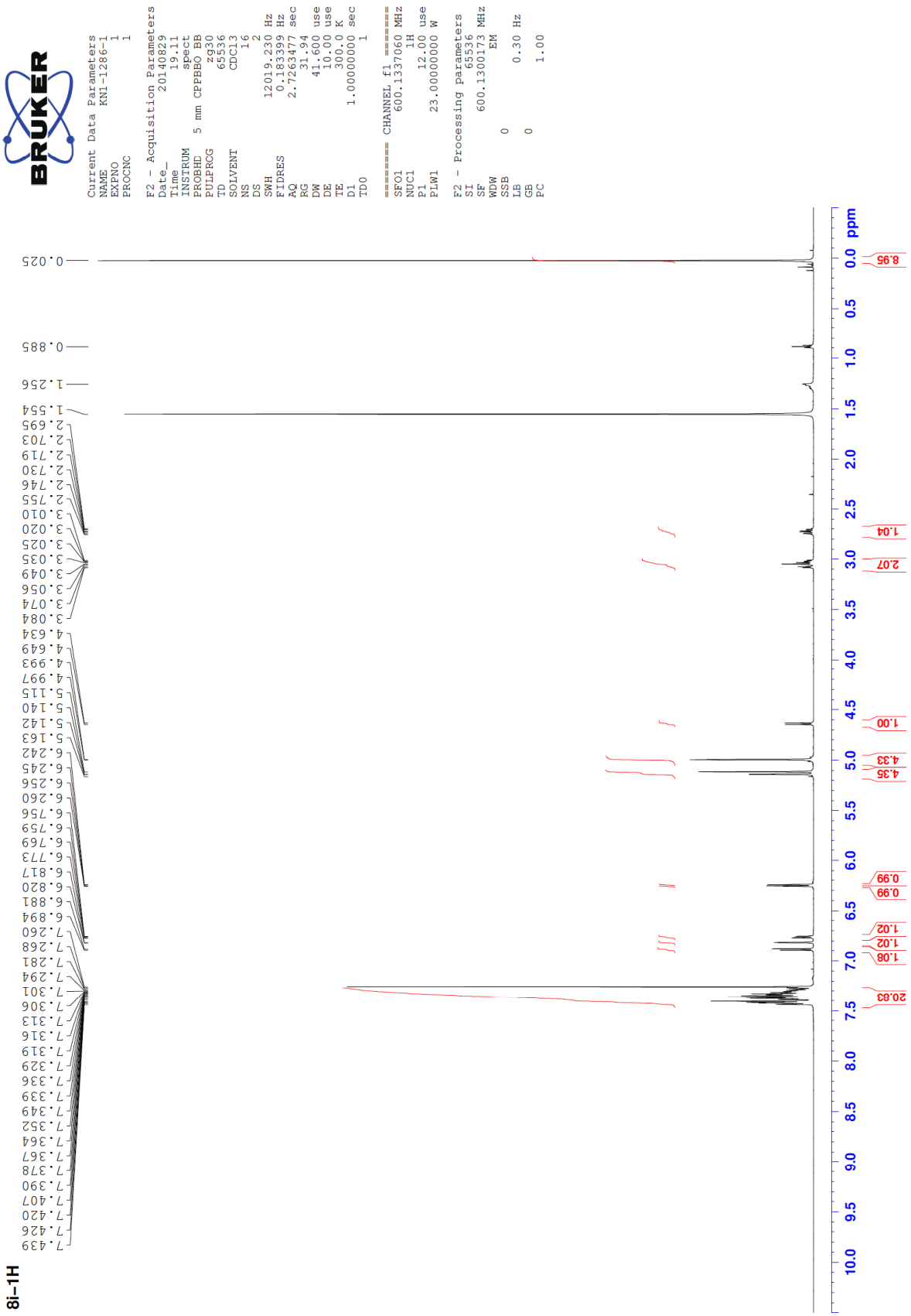
Compound **8h** (^{1}H NMR, 600 MHz, $CDCl_3$)



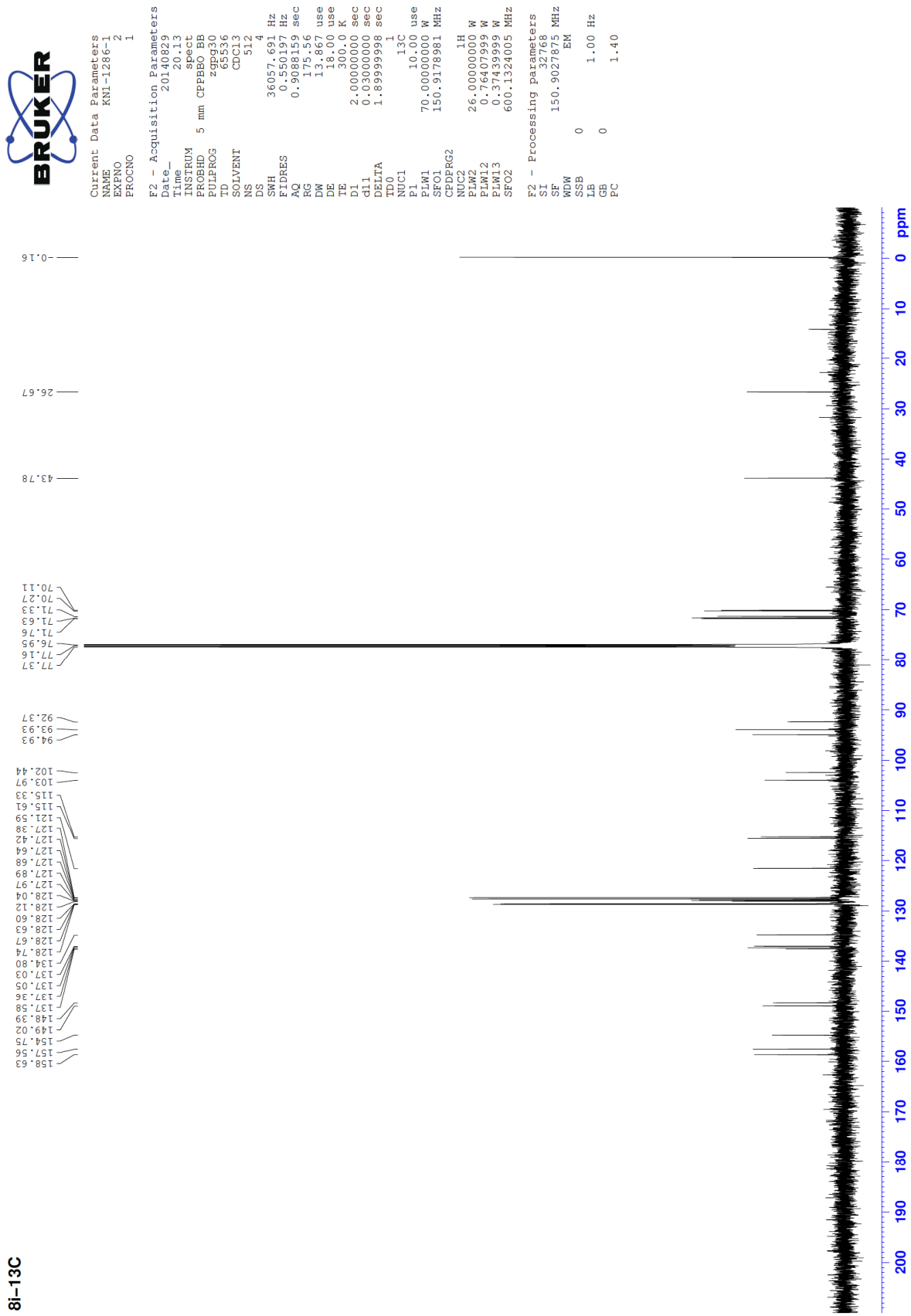
Compound **8h** (^{13}C NMR, 150 MHz, $CDCl_3$)



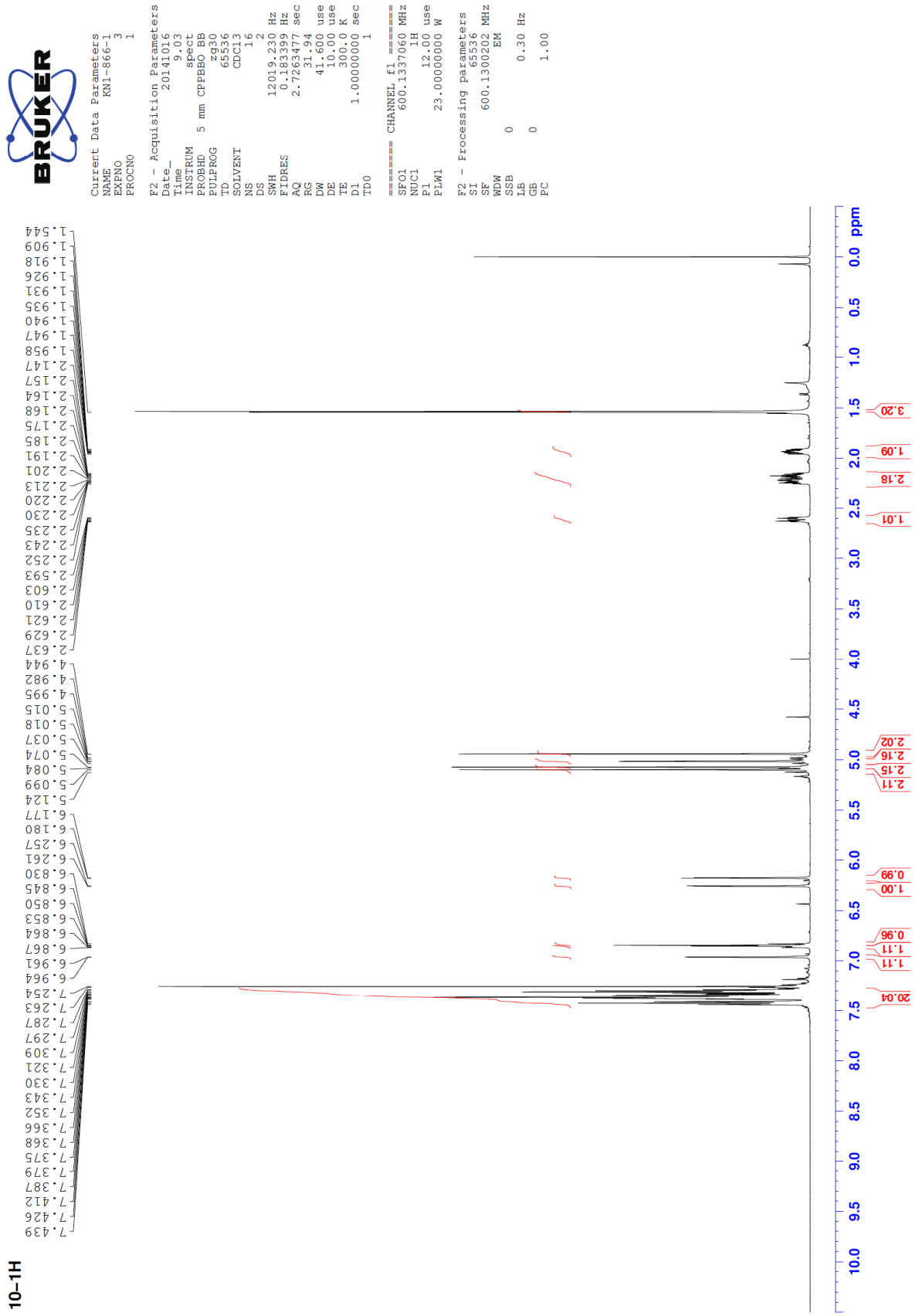
Compound **8i** (^{1}H NMR, 600 MHz, $CDCl_3$)



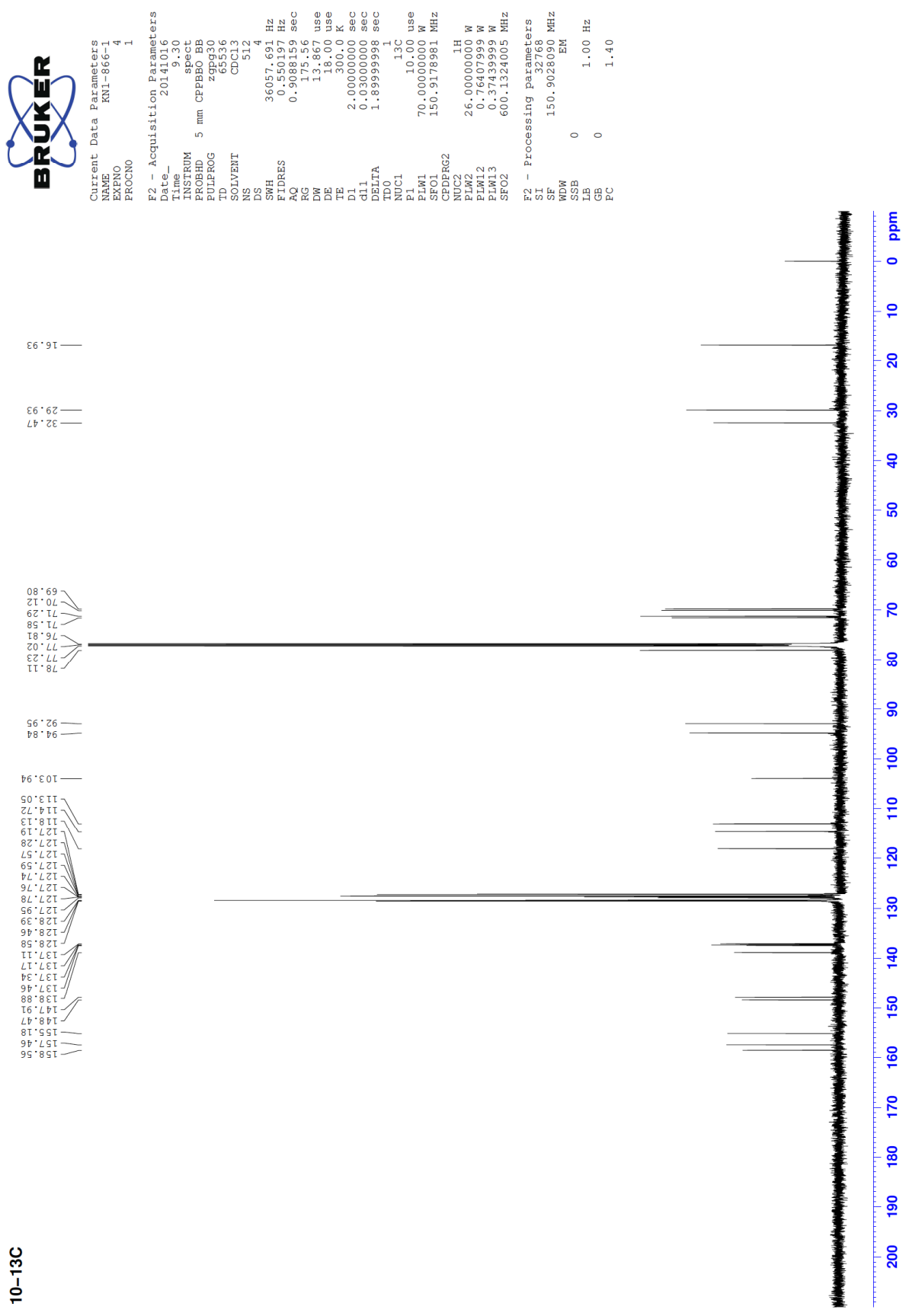
Compound **8i** (^{13}C NMR, 150 MHz, $CDCl_3$)



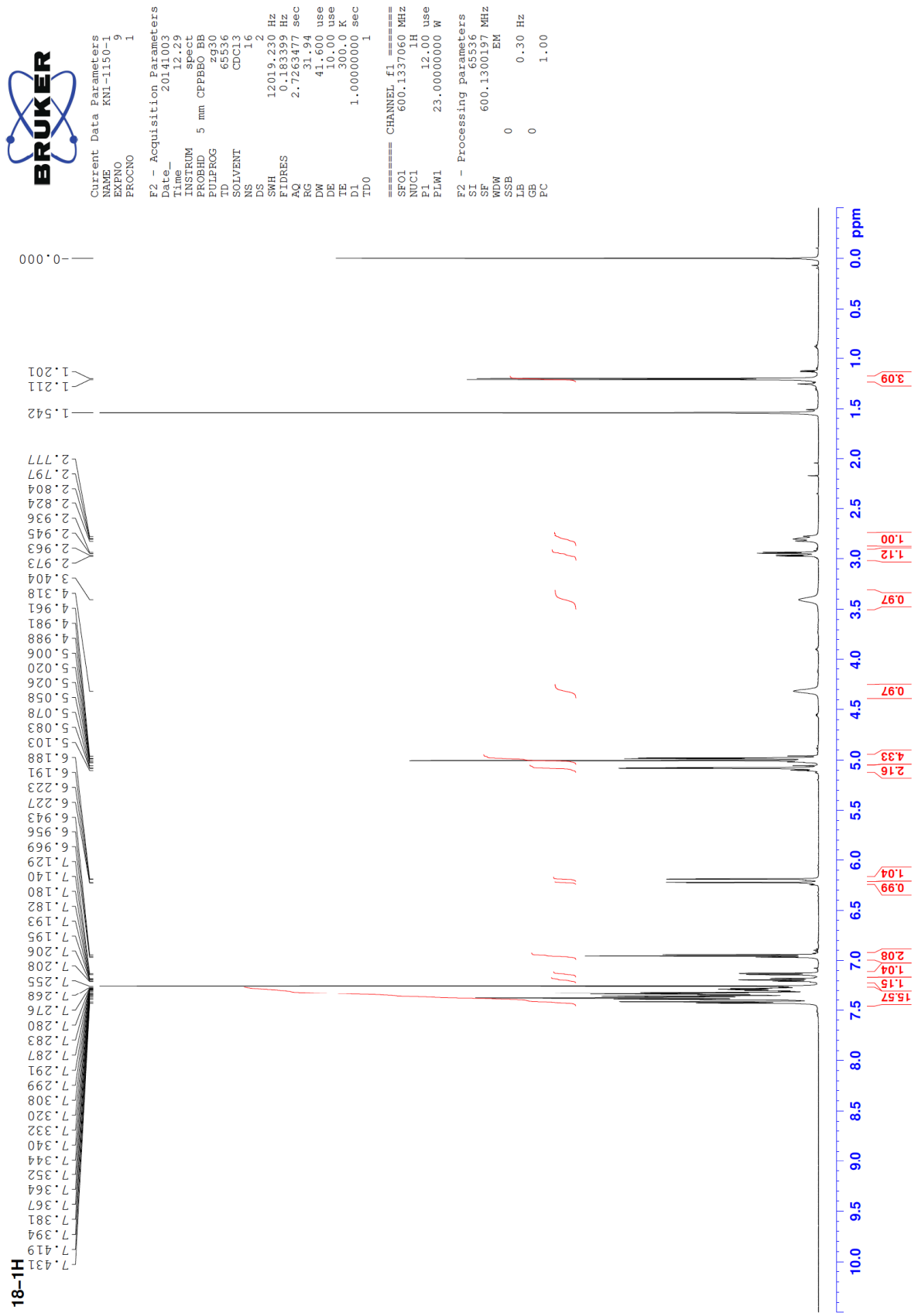
Compound **10** (^{1}H NMR, 600 MHz, $CDCl_3$)



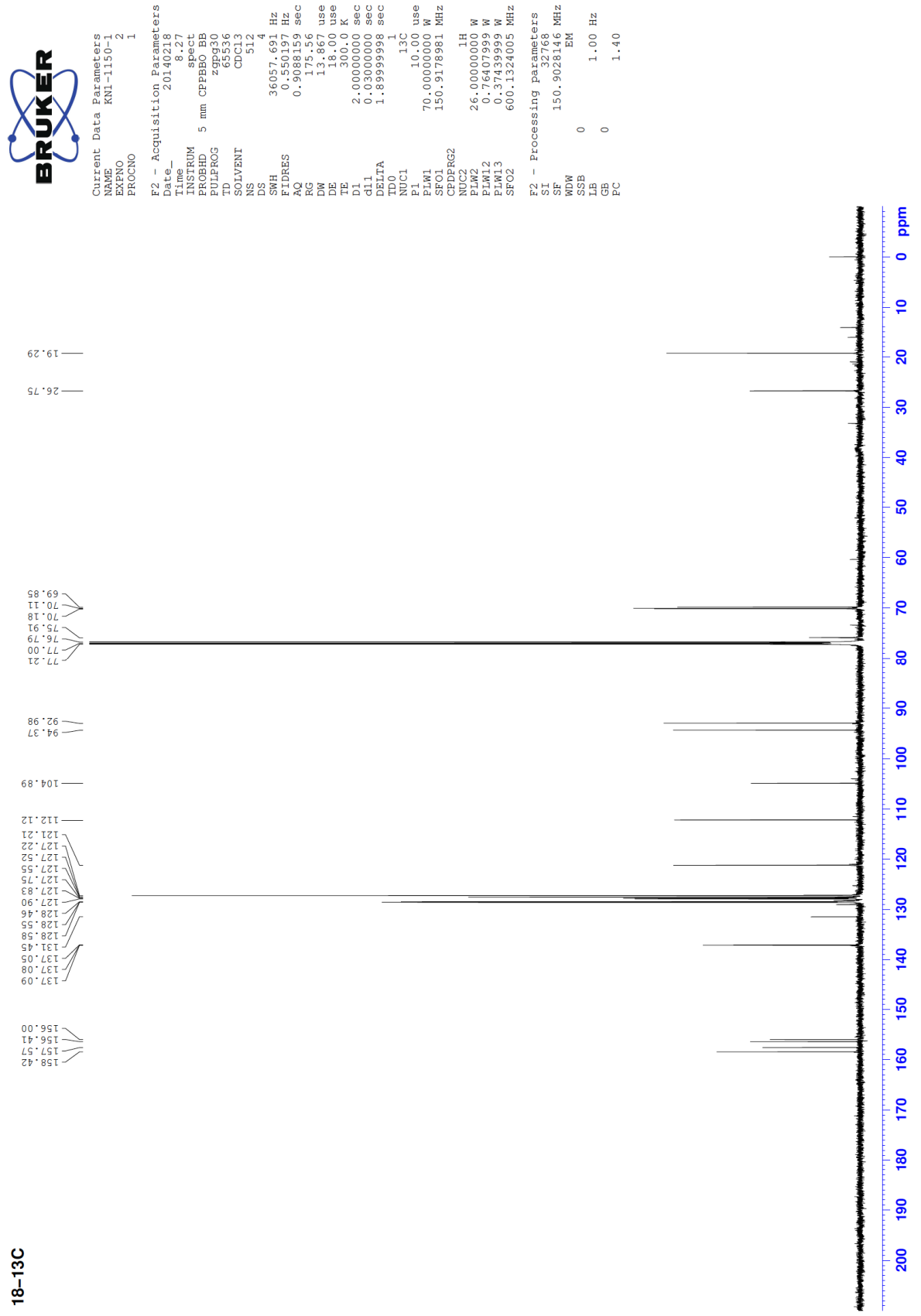
Compound **10** (^{13}C NMR, 150 MHz, $CDCl_3$)



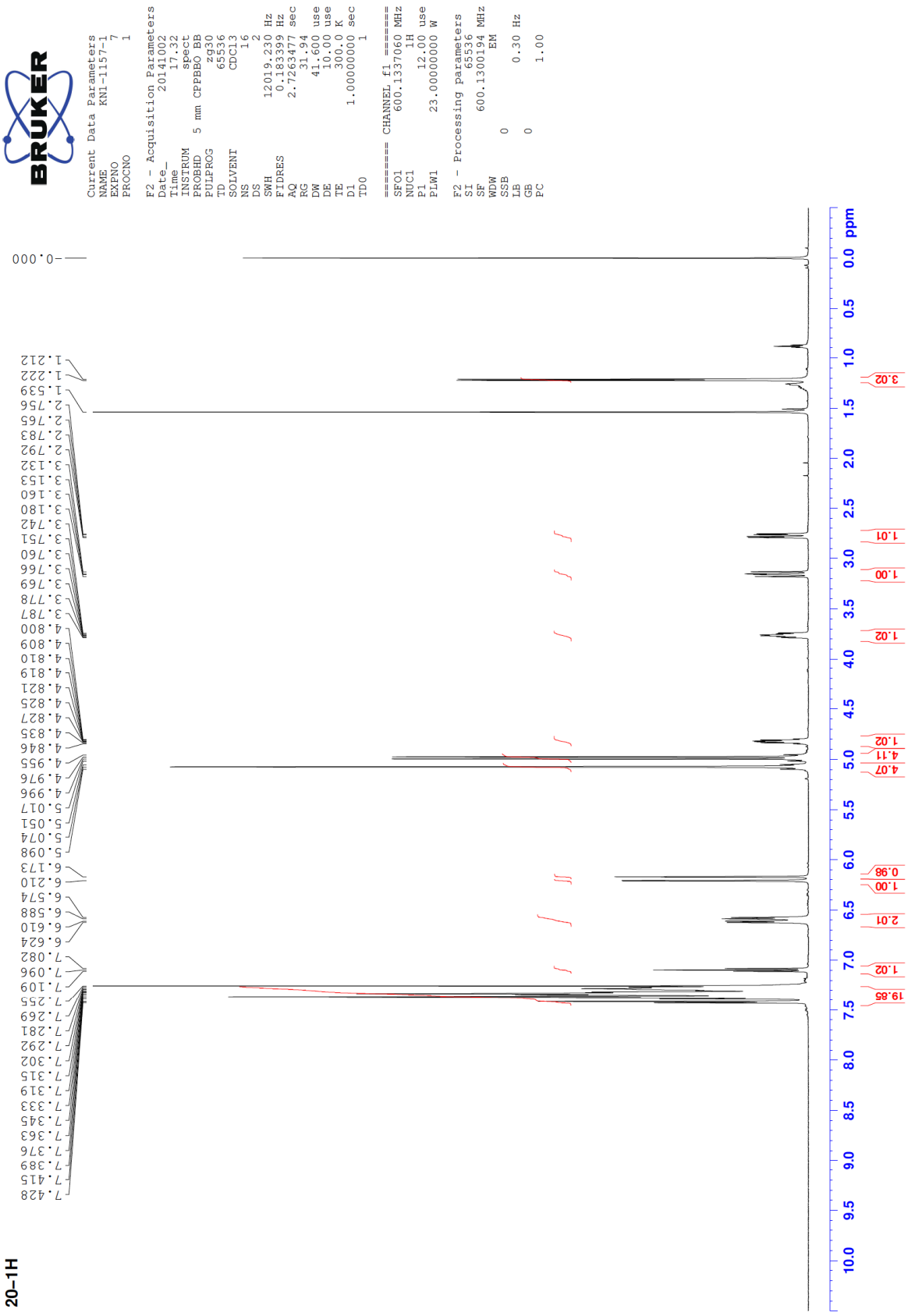
Compound **18** (^{1}H NMR, 600 MHz, $CDCl_3$)



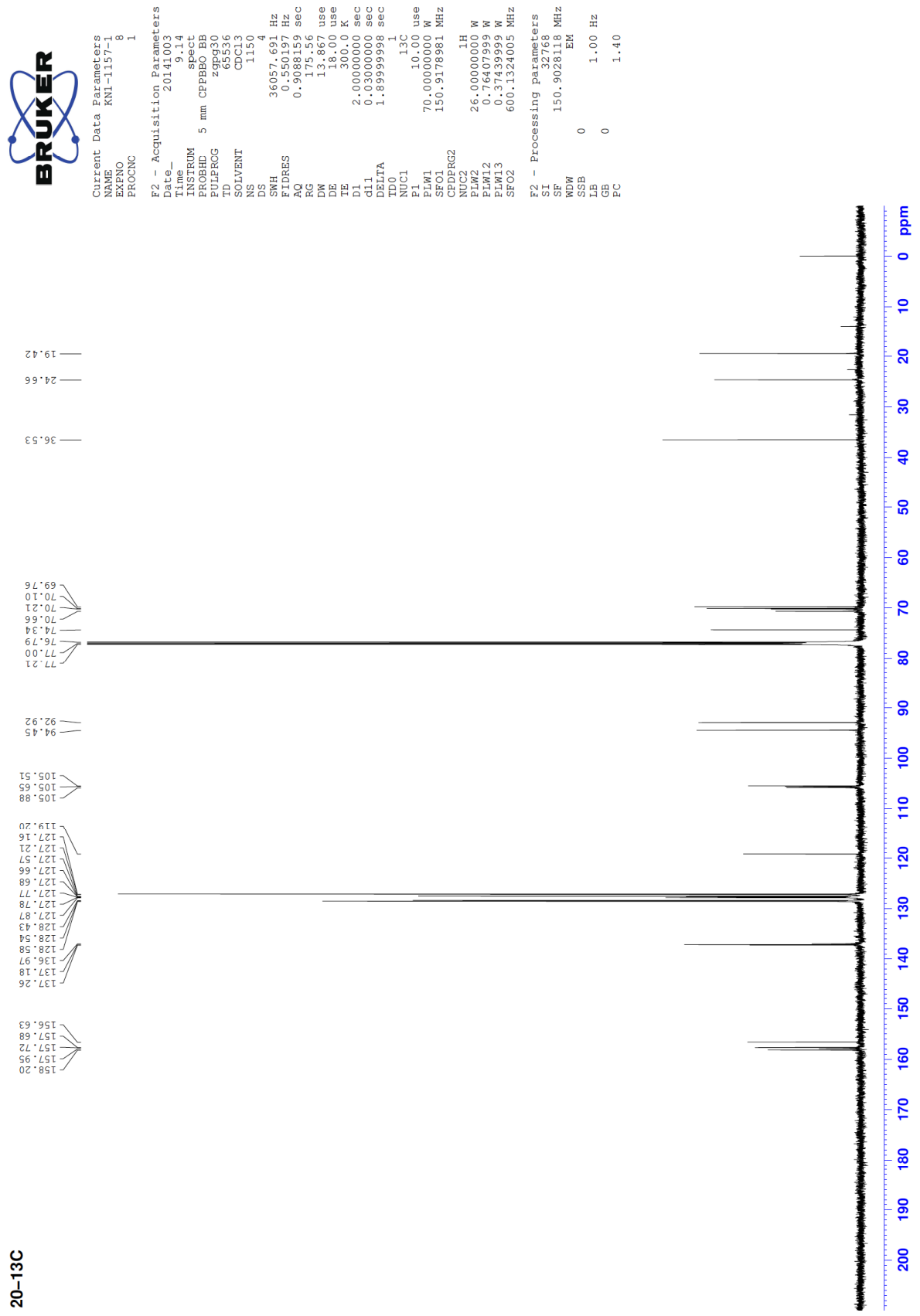
Compound **18** (^{13}C NMR, 150 MHz, $CDCl_3$)



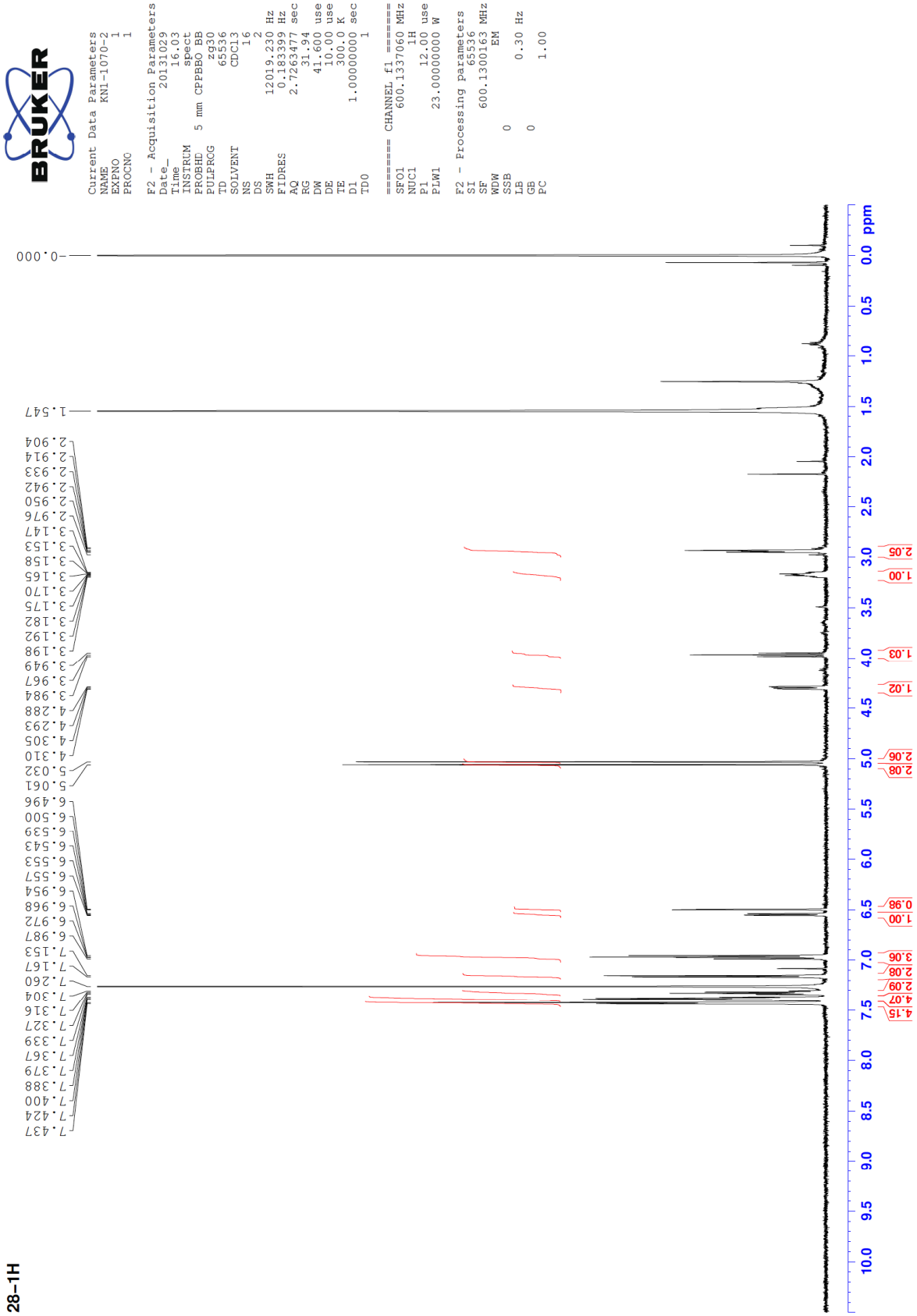
Compound **20** (^{1}H NMR, 600 MHz, $CDCl_3$)



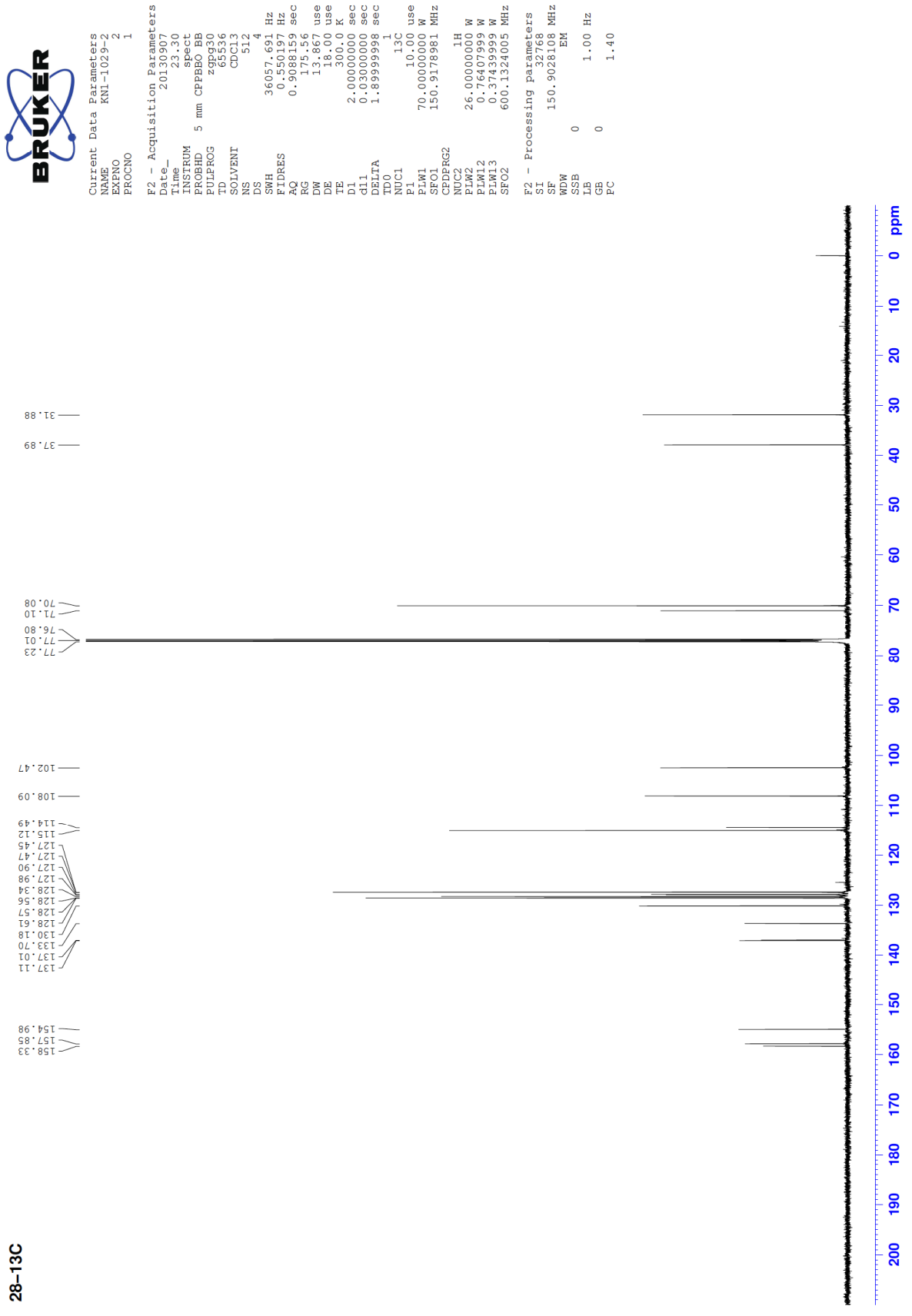
Compound **20** (^{13}C NMR, 150 MHz, $CDCl_3$)



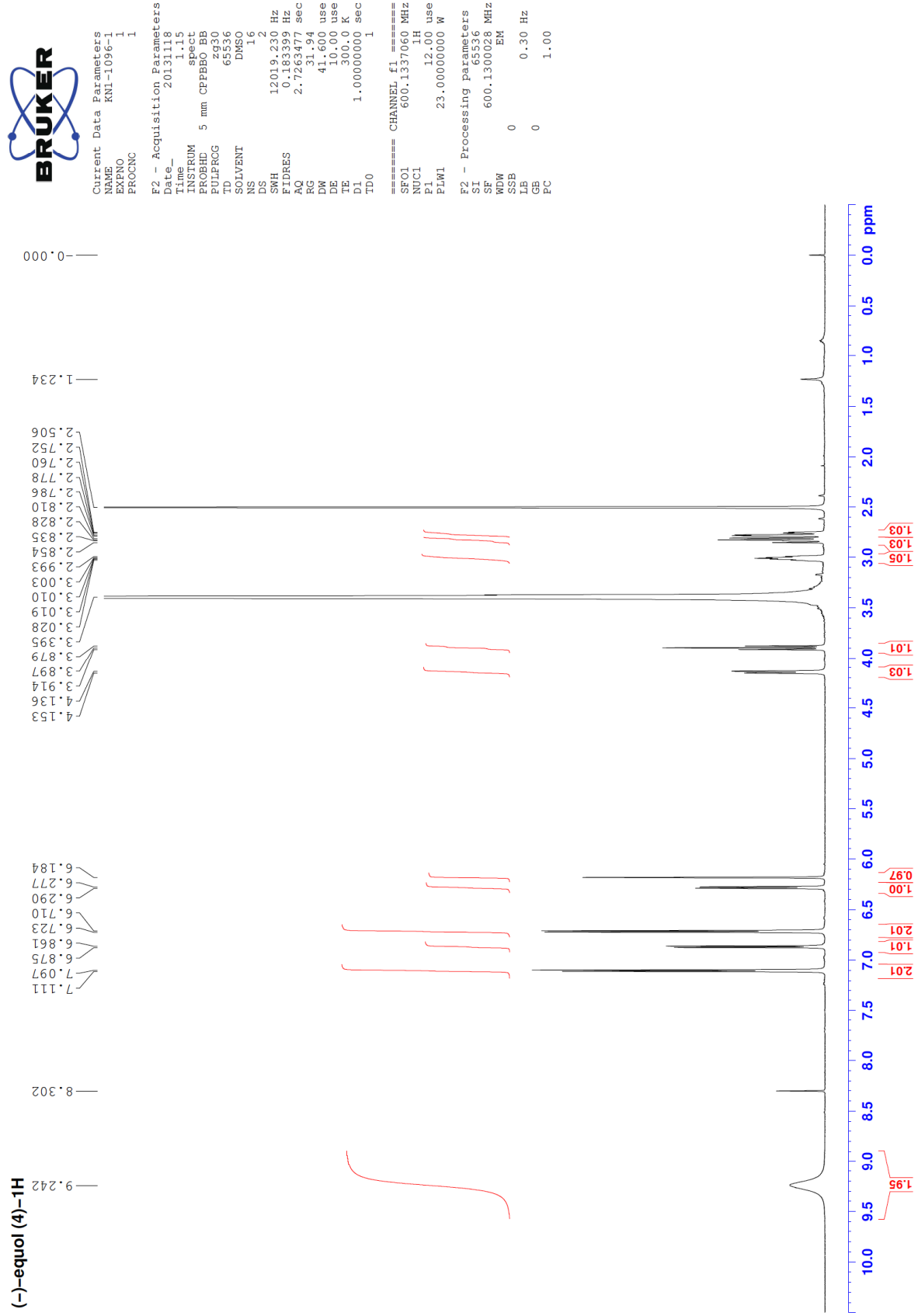
Compound **28** (^{1}H NMR, 600 MHz, $CDCl_3$)



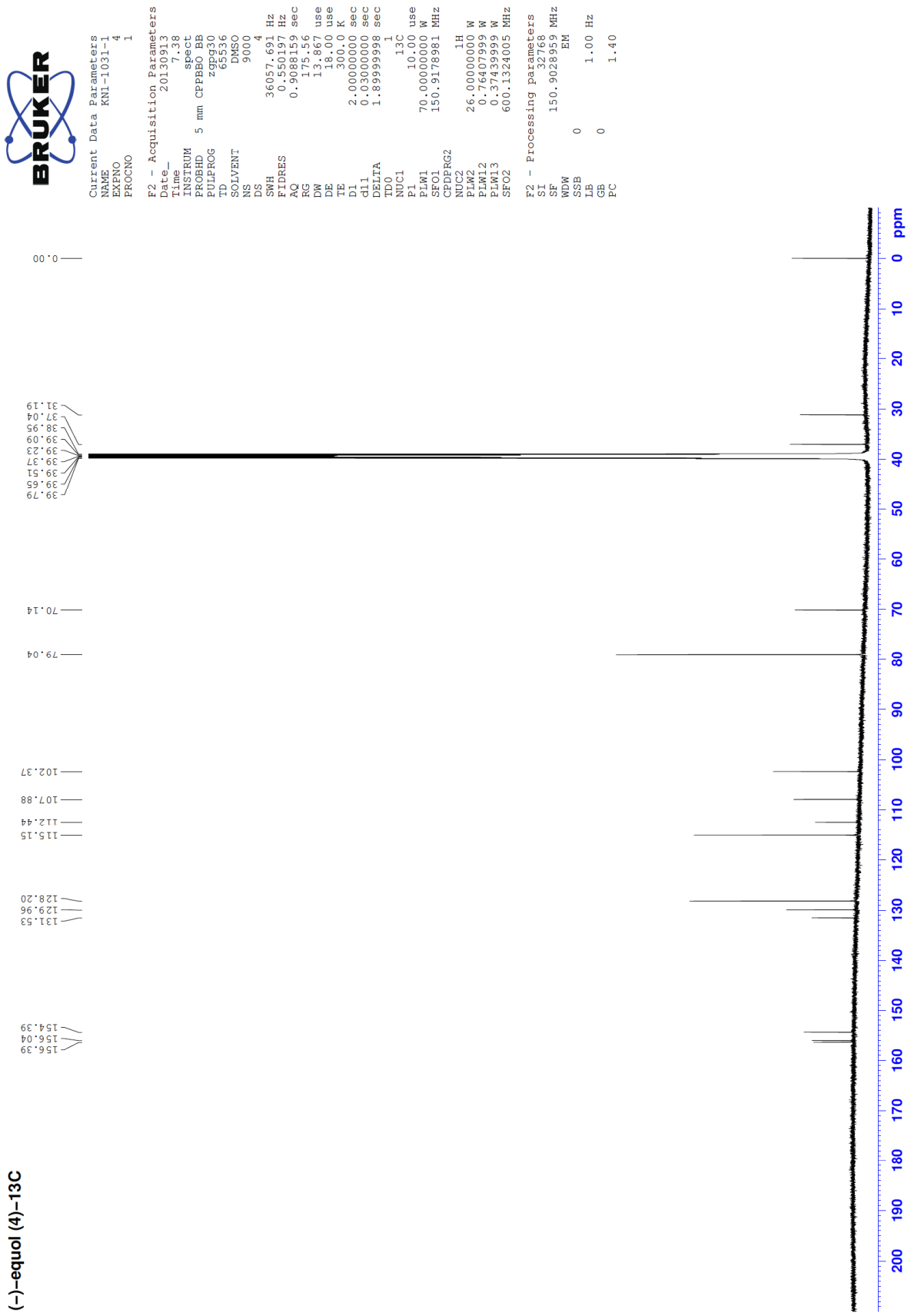
Compound **28** (^{13}C NMR, 150 MHz, $CDCl_3$)



(–)-equol (**4**) (^{1}H NMR, 600 MHz, DMSO-*d6*)



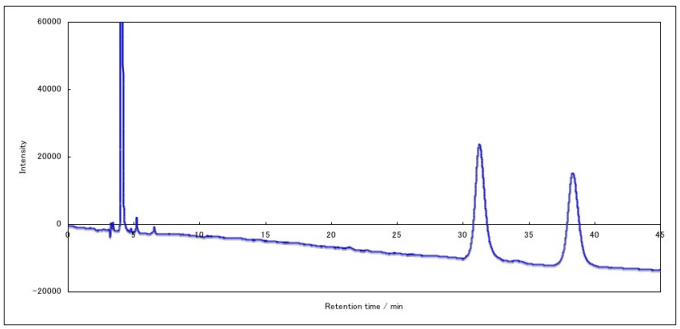
(–)-equol (**4**) (^{13}C NMR, 150 MHz, DMSO-*d6*)



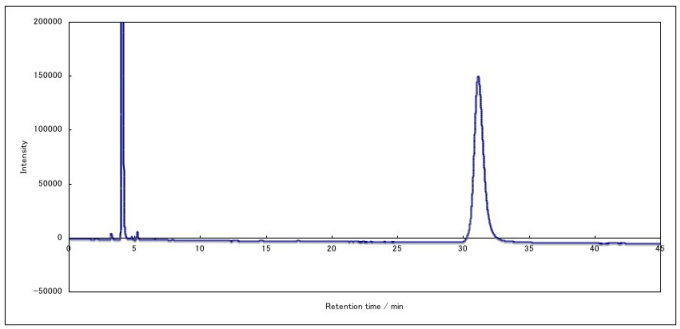
HPLC analyses for **7**

CHIRALPAK® IE-3 (Daicel), ϕ 4.6 x 250 mm, hexane/*i*-PrOH = 80/20, 1.0 mL/min flow rate, 35 °C, 220 nm, t_R = 31.2 min for **7** and 38.3 min for *ent*-**7**.

7 and *ent*-**7**
(co-injection)



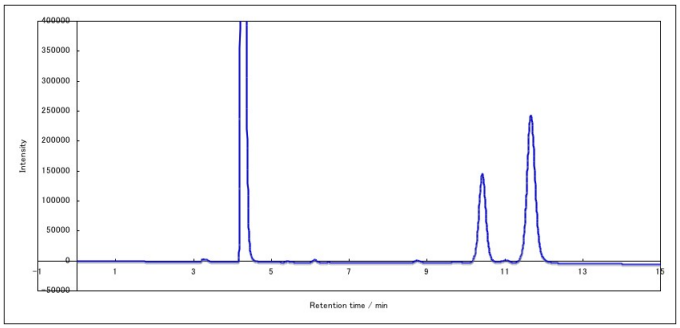
7



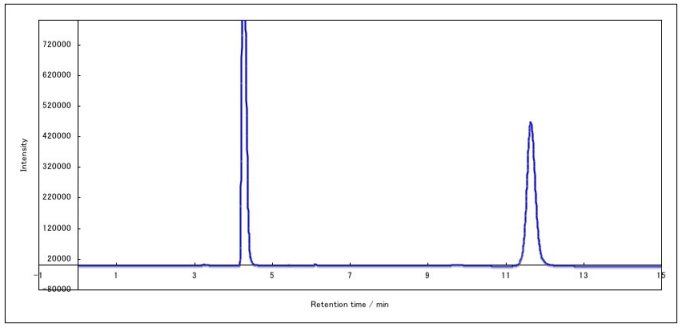
HPLC analyses for **8a**

CHIRALPAK® IE-3 (Daicel), ϕ 4.6 x 250 mm, hexane/*i*-PrOH = 90/10, 1.0 mL/min flow rate, 35 °C, 220 nm, t_R = 10.4 min for *ent*-**8a** and 11.6 min for **8a**.

8a and *ent*-**8a**
(co-injection)



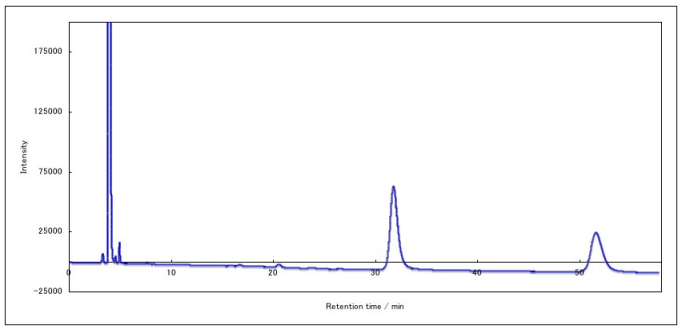
8a



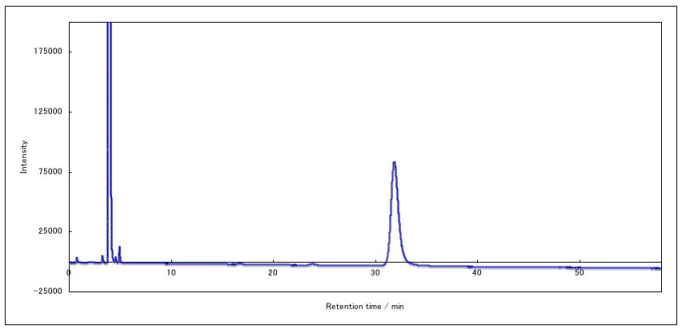
HPLC analyses for **9**

CHIRALPAK® IE-3 (Daicel), ϕ 4.6 x 250 mm, hexane/*i*-PrOH = 75/25, 1.0 mL/min flow rate, 35 °C, 220 nm, t_R = 31.8 min for **9** and 51.6 min for *ent*-**9**.

9 and *ent*-**9**
(co-injection)



9

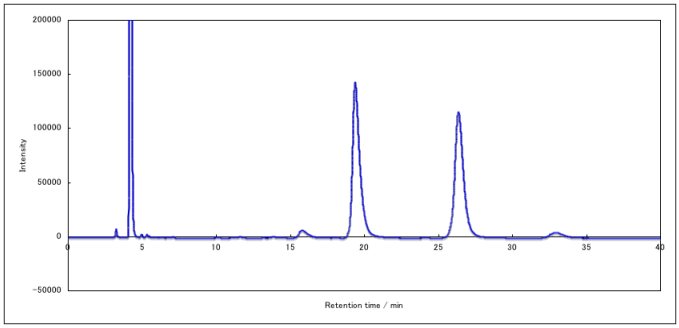


HPLC analyses for **10**

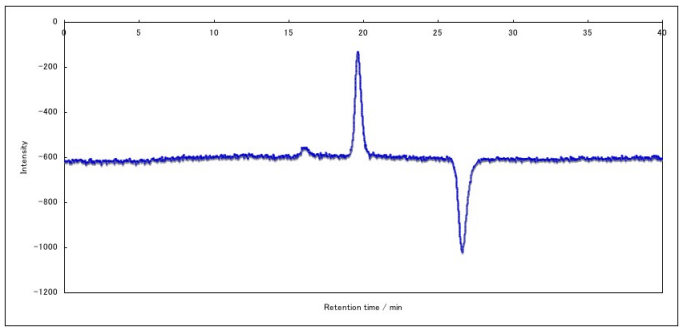
CHIRALPAK® IE-3 (Daicel), ϕ 4.6 x 250 mm, hexane/*i*-PrOH = 90/10, 1.0 mL/min flow rate, 35 °C, 220 nm, t_R = 19.4 min and 26.4 min.

10

UV (220 nm)



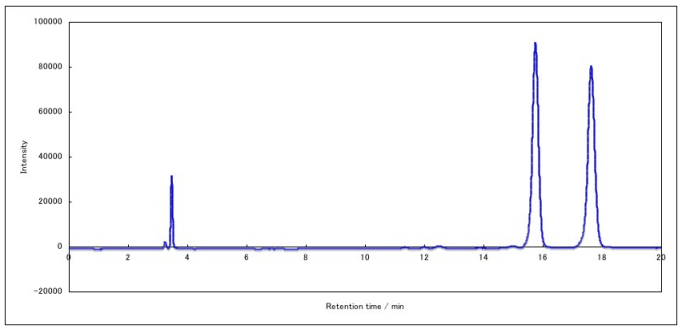
CD (280 nm)



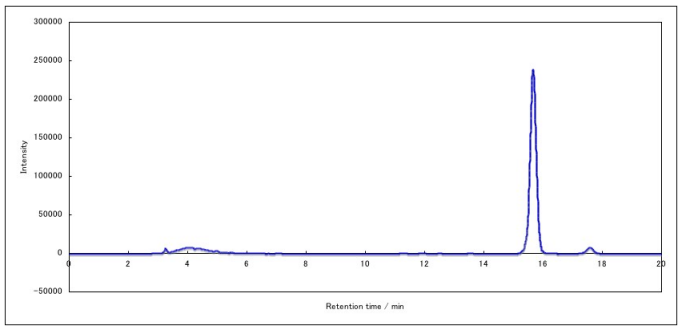
HPLC analyses for **11**

CHIRALPAK® IE-3 (Daicel), ϕ 4.6 x 250 mm, hexane/*i*-PrOH = 90/10, 1.0 mL/min flow rate, 35 °C, 220 nm, t_R = 15.7 min for **11** and 17.6 min for *ent*-**11**.

11 (racemate)



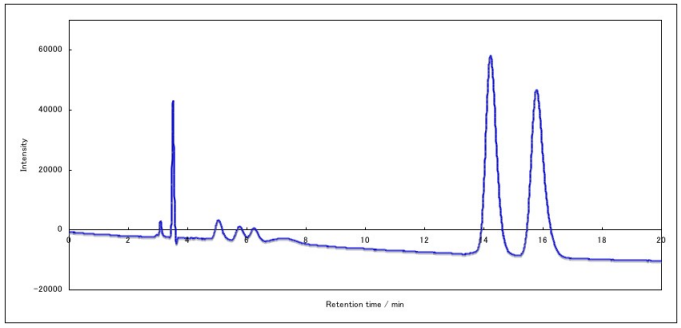
11



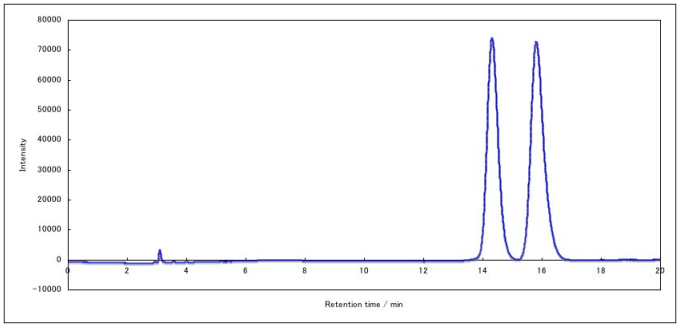
HPLC analyses for **S15**

CHIRALPAK® AS-H (Daicel), ϕ 4.6 x 250 mm, hexane/*i*-PrOH = 80/20, 1.0 mL/min flow rate, 35 °C, 220 nm, t_R = 14.3 min for *ent*-**S15** and 15.8 min for **S15**.

S15 (racemate)



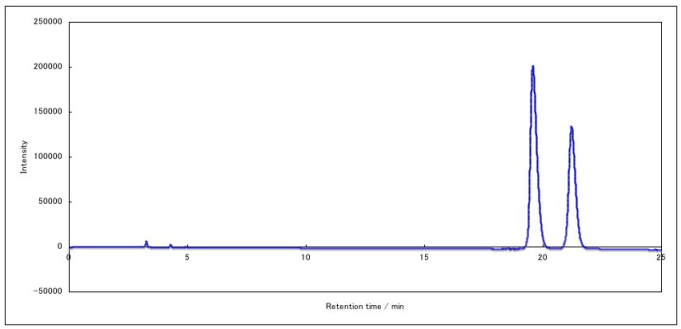
S15



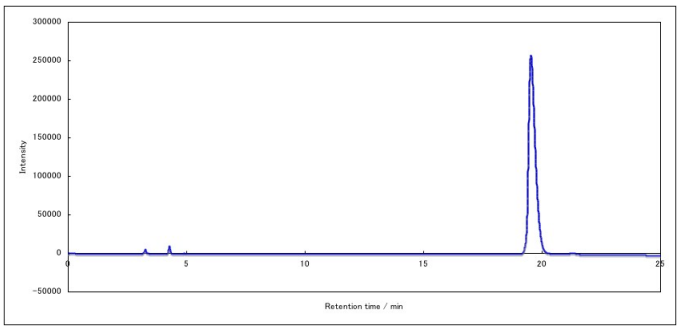
HPLC analyses for **22**

CHIRALPAK® IE-3 (Daicel), ϕ 4.6 x 250 mm, hexane/*i*-PrOH = 90/10, 1.0 mL/min flow rate, 35 °C, 220 nm, t_R = 19.5 min for **22** and 21.3 min for *ent*-**22**.

22 and *ent*-**22** (co-injection)



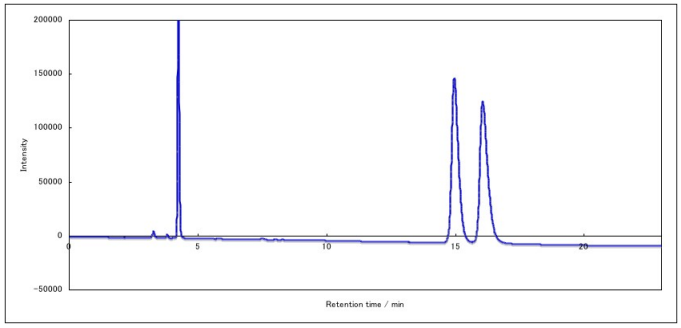
22



HPLC analyses for (–)-equol (**4**)

CHIRALPAK® IE-3 (Daicel), ϕ 4.6 x 250 mm, hexane/*i*-PrOH = 90/10, 1.0 mL/min flow rate, 35 °C, 220 nm, t_R = 15.0 min for the (+)-equol (*ent*-**4**) and 16.0 min for the (–)-equol (**4**).

(±)-equol (**4**) (authentic)



4 (synthetic)