Electronic Supplementary Material (ESI) for Organic Chemistry Frontiers.
This journal is © the Partner Organisations 2018

Supporting Information

Progress Towards the Synthesis of Aconitine: Construction of the AE Fragment and Attempts to Access the Pentacyclic Core

Rui-Jie Zhou, Gui-Ying Dai, Xiao-Han Zhou, Min-Jie Zhang, Ping-Zhou Wu, Dan Zhang*, Hao Song, Xiao-Yu Liu and Yong Qin*

Key Laboratory of Drug-Targeting and Drug Delivery System of the Education Ministry, Sichuan Engineering Laboratory for Plant-Sourced Drug and Sichuan Research Center for Drug Precision Industrial Technology, West China School of Pharmacy, Sichuan University, Sichuan University, Chengdu 610041, P. R. China.

Email: Yong Qin* yongqin@scu.edu.cn; Dan Zhang* danzhang@scu.edu.cn

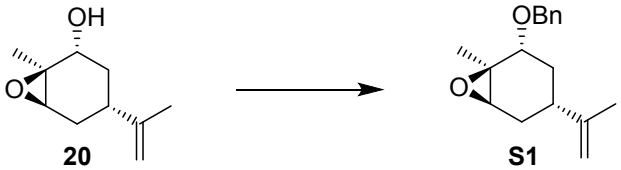
Table of contents:

General information:

All reactions that require anhydrous conditions were performed in flame-dried glassware under Ar atmosphere and all reagents were purchased from commercial suppliers ($Ir[dF(CF_3)ppy]_2(dtbbpy)PF_6$ was purchased from STREM) without further purification. Solvent purification was conducted according to Purification of Laboratory Chemicals 2nd edn.[1] The products were purified by flash column chromatography on silica gel (200 – 300 meshes) from the Anhui Liangchen Silicon Material Company (China). Reactions were monitored by thin layer chromatography (TLC, 0.2 mm, HSGF254) supplied by Yantai Chemicals (China). Visualization was accomplished with UV light, exposure to iodine, stained with ethanolic solution of phosphomolybdic acid or basic solution of $KMnO_4$. ^1H NMR and ^{13}C NMR spectra were recorded on Varian INOVA-400/54, Agilent DD2-600/54 and calibrated by using residual undeuterated chloroform (δ, ^1H NMR = 7.260, ^{13}C NMR = 77.00). The following abbreviations were used to explain the multiplicities: s = singlet, d = doublet, t = triplet, q = quartet, br = broad, td = triple doublet, dt = double triplet, m = multiplet, and coupling constants (J) are reported in Hertz (Hz). Infrared (IR) spectra were recorded on a Perkin Elmer Spectrum Two FT-IR spectrometer. High-resolution mass spectra (HRMS) were recorded on Bruker Apex IV FTMS or Agilent LC-MSD TOF ESI mass spectrometers. The specific optical rotation was obtained from *Rudolph Research Analytical Autopol VI automatic polarimeter*. LC-MS analysis was performed on HP Agilent 6420 Triple Quad LC/MS. The radical cascade substrate **14b** was provided by lyophilization via CHRIST Alpha 1-2 LDplus. Blue LEDs were purchased from Kessil (H150-Blue and A160WE).

Experimental Procedures and characterization:

(1*R*,2*R*,4*S*,6*R*)-2-(Benzyloxy)-1-methyl-4-(prop-1-en-2-yl)-7-oxabicyclo[4.1.0]heptane S1



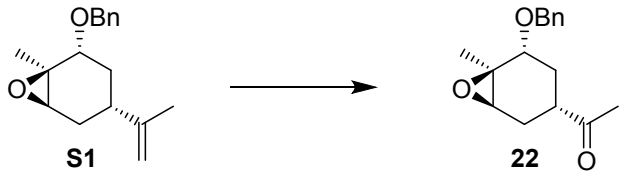
20 **S1**

Under argon, to a solution of alcohol **20** (350 g, 2.08 mol, 1.0 equiv.) in dry DMF (2200 mL) was added sodium hydride (60% dispersion in mineral oil, 166.4 g, 4.16 mol, 2.0 equiv.) in small portions at 0 °C. After 30 minutes, benzyl bromide (494.1 mL, 4.16 mol, 2.0 equiv.) was added to the solution dropwisely. After being stirred vigorously for 8 h at room temperature, the reaction was quenched by dropping sat. NH_4Cl aq. (1500 mL) and extracted with EtOAc (2×1000 mL). The combined organic phases were washed with brine, dried over anhydrous Na_2SO_4, and concentrated in vacuo. The crude product was purified by column chromatography (petroleum ether:EtOAc, 20:1 v/v) to give product **S1** (516 g, 96%) as a pale yellow oil.

TLC (petroleum ether:EtOAc, 10:1 v/v): R_f = 0.38; ^1H NMR (400 MHz, $CDCl_3$): δ 7.36 (d, J = 4.4 Hz, 4H), 7.33 – 7.27 (m, 1H), 4.76 – 4.64 (m, 3H), 4.58 (d, J = 11.6 Hz, 1H), 3.65 (dd, J = 10.4, 6.4 Hz, 1H), 3.12 (s, 1H), 2.21 – 2.00 (m, 3H), 1.75 – 1.57 (m, 1H), 1.70 (s, 3H) 1.44 (s, 3H), 1.24 – 1.11 (m, 1H); ^{13}C NMR (100 MHz, $CDCl_3$): δ 148.3, 138.3, 128.3, 128.3, 127.5, 127.4, 127.4, 109.4, 76.3, 72.3, 62.0, 60.2, 34.2, 33.8, 30.7, 20.5, 19.6; IR (neat): ν_{max} = 2930, 1645,

1497, 1453, 1375, 1096, 1075, 890, 736, 697 cm^{-1}; HRMS (*m/z*): $[M + Na]^+$ calcd. for $C_{17}H_{22}NaO_2$, 281.1512; found, 281.1516; $[\alpha]_D^{20} = -42.5$ (*c* 17.9, $CHCl_3$).

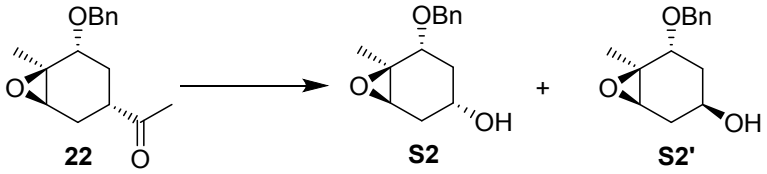
1-((1*R*,3*S*,5*R*,6*R*)-5-(Benzyloxy)-6-methyl-7-oxabicyclo[4.1.0]heptan-3-yl)ethan-1-one 22



Compound **S1** (180 g, 0.697 mol, 1.0 equiv.), NMO (163.4 g, 1.395 mol, 2.0 equiv.) and osmium tetroxide (531 mg, 2.09 mmol, 0.003 equiv.) were dissolved in acetone:H_2O (10:1) of 1600 mL. The reaction was stirred at room temperature for 6 h, and to the reaction solution was then added $PhI(OAc)_2$ (269.3 g, 0.836 mol, 1.2 equiv.). After being stirred for 18 h, the reaction was quenched by sat. Na_2SO_3 aq. (1100 mL), acetone was then removed in vacuo after the reaction mixture was stirred for 2 h. The concentrated mixture was extracted with EtOAc (3×650 mL), and the combined organic layer was washed with brine, dried over anhydrous Na_2SO_4, and concentrated in vacuo. The crude product was purified by column chromatography (petroleum ether:EtOAc, 8:1 v/v) to give product **22** (175.9 g, 97%) as a pale yellow oil.

TLC (petroleum ether:EtOAc, 7:1 v/v): $R_f = 0.28$; ^1H NMR (400 MHz, $CDCl_3$): δ 7.44 – 7.25 (m, 5H), 4.67 (d, J = 11.6 Hz, 1H), 4.53 (d, J = 11.6 Hz, 1H), 3.66 (dd, J = 8.0, 5.6 Hz, 1H), 3.16 (s, 1H), 2.52 – 2.41 (m, 1H), 2.21 – 2.07 (m, 2H), 2.13 (s, 3H), 2.02 (ddd, J = 15.2, 9.2, 2.4 Hz, 1H), 1.51 (ddd, J = 13.2, 10.0, 8.4 Hz, 1H), 1.39 (s, 3H); ^{13}C NMR (100 MHz, $CDCl_3$): δ 209.8, 137.9, 128.3, 128.3, 127.6, 127.5, 127.5, 75.4, 72.2, 60.5, 59.6, 41.2, 28.9, 27.8, 26.2, 19.5; IR (neat): ν_{max} = 2930, 1708, 1452, 1355, 1269, 1097, 1072, 1027, 737, 698 cm^{-1}; HRMS (*m/z*): $[M + H]^+$ calcd. for $C_{16}H_{21}O_3$, 261.1485; found, 261.1488; $[\alpha]_D^{20} = -43.7$ (*c* 0.94, $CHCl_3$).

(1*R*,3*S*,5*R*,6*R*)-5-(Benzyloxy)-6-methyl-7-oxabicyclo[4.1.0]heptan-3-ol S2 and (1*R*,3*R*,5*R*,6*R*)-5-(benzyloxy)-6-methyl-7-oxabicyclo[4.1.0]heptan-3-ol S2'



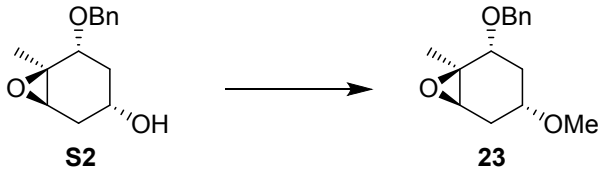
At room temperature, to a solution of ketone **22** (30.0 g, 0.115 mol, 1.0 equiv.) in hexane:EtOAc (3:1) of 500 mL was added 3-chloroperoxybenzoic acid (49.7 g, 0.288 mol, 2.5 equiv.). After being stirred vigorously and refluxed for 24 h, the reaction was quenched by sat. Na_2SO_3 aq. (400 mL) and extracted with EtOAc (3×300 mL). The combined organic layer was washed with brine, dried over anhydrous Na_2SO_4, and concentrated in vacuo. With crude ester product in hand, K_2CO_3 (47.7 g, 0.345 mol, 3.0 equiv.) was added to a solution of the ester above in 450 mL MeOH. The reaction was concentrated in vacuo after being stirred for 4 h, followed by addition of 500 mL sat. NH_4Cl aq. and 450 mL EtOAc. The aqueous layer was extracted with EtOAc (3×300 mL), and the combined organic layer was then washed with brine, dried over anhydrous Na_2SO_4, and concentrated in vacuo. Purification of the residue via column chromatography (petroleum ether:EtOAc, 6:1 v/v) furnished product **S2** (11.6 g, 43% for 2 steps) as a white solid and byproduct **S2'** (240 mg, 0.9%) as a pale yellow oil.

S2: TLC (petroleum ether:EtOAc, 4:1 v/v): $R_f = 0.33$; ^1H NMR (400 MHz, $CDCl_3$): δ 7.47 – 7.26 (m, 5H), 4.79 (d, J = 11.2 Hz, 1H), 4.53 (d, J = 11.2 Hz, 1H), 3.92 (t, J = 3.2 Hz, 1H), 3.85 (brs, 1H), 3.07 (d, J = 3.6 Hz, 1H), 2.22 – 2.08

(m, 2H), 2.04 (brd, J = 14.8 Hz, 1H), 1.78 – 1.68 (m, 1H), 1.42 (s, 3H); ^{13}C NMR (100 MHz, $CDCl_3$): δ 137.0, 128.4, 128.4, 128.0, 128.0, 128.0, 76.7, 72.6, 63.2, 58.2, 57.7, 33.5, 28.7, 19.7; IR (neat): ν_{max} = 3429, 2929, 1454, 1370, 1096, 1055, 1027, 738, 698 cm^{-1}; HRMS (*m/z*): [M + Na]$^+$ calcd. for $C_{14}H_{18}NaO_3$, 257.1148; found, 257.1151; $[\alpha]_D^{20}$= −8.0 (*c* 0.94, $CHCl_3$); m.p.: 70.4 – 73.2 °C.

S2': TLC (petroleum ether:EtOAc, 4:1 v/v): R_f = 0.36; ^{1}H NMR (600 MHz, $CDCl_3$): δ 7.39 – 7.27 (m, 5H), 4.69 (d, J = 11.4 Hz, 1H), 4.50 (d, J = 11.4 Hz, 1H), 4.04 – 3.95 (m, 1H), 3.91 (t, J = 4.2 Hz, 1H), 3.06 (d, J = 4.2 Hz, 1H), 2.29 (dt, J = 15.0, 4.8 Hz, 1H), 2.02 (brs, 1H), 1.88 (dd, J = 15.0, 8.4 Hz, 1H), 1.85 – 1.78 (m, 2H), 1.39 (s, 3H); ^{13}C NMR (100 MHz, $CDCl_3$): δ 137.9, 128.4, 128.4, 127.8, 127.8, 127.8, 76.4, 72.3, 62.4, 59.6, 58.9, 32.9, 32.9, 19.5; IR (neat): ν_{max} = 3394, 2930, 1454, 1330, 1100, 1056 cm^{-1}; HRMS (*m/z*): [M + Na]$^+$ calcd. for $C_{14}H_{18}NaO_3$, 257.1148; found, 257.1152; $[\alpha]_D^{20}$= +5.0 (*c* 0.32, $CHCl_3$).

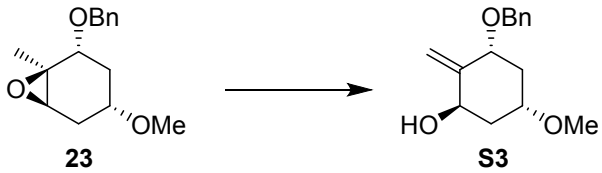
(1*R*,2*R*,4*S*,6*R*)-2-(Benzyloxy)-4-methoxy-1-methyl-7-oxabicyclo[4.1.0]heptane 23



To a solution of alcohol **S2** (106 g, 0.452 mol, 1.0 equiv.) in dry THF (1400 mL) was added sodium hydride (60% dispersion in mineral oil, 36.2 g, 0.905 mol, 2.0 equiv.) in portions at 0 °C under argon. After the reaction was stirred for 20 min, iodomethane (84.5 mL, 1.36 mol, 3.0 equiv.) was added dropwisely to the solution, and the reaction was allowed to be stirred at room temperature. The reaction was quenched by sat. NH_4Cl aq. (1000 mL) after being stirred for 3.5 h, and extracted with EtOAc (3×800 mL). The combined organic phases were washed with brine, dried over anhydrous Na_2SO_4, and concentrated in vacuo. Purification of the residue via column chromatography (petroleum ether:EtOAc, 10:1 v/v) furnished product **23** (106.7 g, 95%) as a colorless oil.

TLC (petroleum ether:EtOAc, 10:1 v/v): R_f = 0.23; ^{1}H NMR (400 MHz, $CDCl_3$): δ 7.36 (d, J = 4.0 Hz, 4H), 7.33 – 7.28 (m, 1H), 4.69 (d, J = 11.6 Hz, 1H), 4.55 (d, J = 11.6 Hz, 1H), 3.68 (dd, J = 8.4, 6.0 Hz, 1H), 3.36 – 3.27 (m, 1H), 3.32 (s, 3H), 3.12 (brs, 1H), 2.45 (dd, J = 14.4, 4.8 Hz, 1H), 2.26 – 2.17 (m, 1H), 1.73 (ddd, J = 14.4, 8.4, 2.0 Hz, 1H), 1.46 – 1.35 (m, 1H), 1.41 (s, 3H); ^{13}C NMR (100 MHz, $CDCl_3$): δ 138.1, 128.3, 128.3, 127.6, 127.6, 127.6, 75.3, 72.2, 71.8, 61.4, 59.9, 56.0, 32.8, 31.1, 19.4; IR (neat): ν_{max} = 2929, 1454, 1374, 1339, 1196, 1091, 1075, 1047, 1029 cm^{-1}; HRMS (*m/z*): [M + Na]$^+$ calcd. for $C_{15}H_{20}NaO_3$, 271.1305; found, 271.1309; $[\alpha]_D^{20}$= −36.6 (*c* 0.93, $CHCl_3$).

(1*R*,2*S*,3*R*,5*R*)-3-(Benzyloxy)-5-methoxy-2-methylcyclohexan-1-ol S3

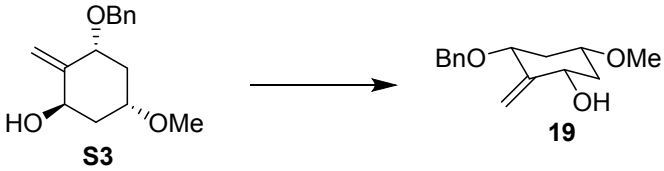


Under argon, compound **23** (73.0 g, 0.294 mol, 1.0 equiv.), activated zinc powder (96.1 g, 1.47 mol, 5.0 equiv.) and titanocene dichloride (175.7 g, 0.706 mol, 2.4 equiv.) were dispersed in dry and degassed THF (1100 mL). After being stirred for 2 h at room temperature, the reaction was quenched by sat. NaH_2PO_4 aq. (1200 mL) and stirred for 45 min. The mixture was then filtrated through celite and the filtrate was extracted with EtOAc (3×650 mL). The combined organic phases were washed with brine, dried over anhydrous Na_2SO_4, and concentrated in vacuo. Purification of the

residue via column chromatography (petroleum ether:EtOAc, 9:2 v/v) furnished product **S3** (63.5 g, 87%) as a pale yellow oil.

TLC (petroleum ether:EtOAc, 3:1 v/v): R_f = 0.27; ^{1}H NMR (400 MHz, $CDCl_3$): δ 7.40 – 7.26 (m, 5H), 5.18 (s, 1H), 5.09 (s, 1H), 4.70 – 4.53 (m, 3H), 4.20 (dd, J = 10.0, 4.4 Hz, 1H), 3.73 (m, 1H), 3.38 (s, 3H), 2.40 (ddt, J = 12.0, 4.0, 1.6 Hz, 1H), 2.15 (ddt, J = 13.2, 4.8, 1.6 Hz, 1H), 1.67 – 1.59 (m, 1H), 1.56 – 1.47 (m, 1H); ^{13}C NMR (100 MHz, $CDCl_3$): δ 149.0, 138.5, 128.3, 128.3, 127.4, 127.3, 127.3, 108.8, 74.6, 74.1, 70.9, 70.8, 56.1, 39.4, 38.4; IR (neat): ν_{max} = 3416, 2928, 1454, 1357, 1111, 1083, 1026, 736, 697 cm^{-1}; HRMS (*m/z*): $[M + Na]^+$ calcd. for $C_{15}H_{20}NaO_3$, 271.1305; found, 271.1306; $[\alpha]_D^{20}$= +0.9 (*c* 0.96, $CHCl_3$).

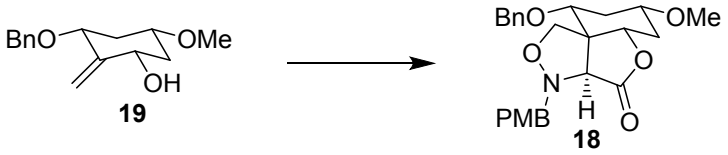
(1*S*,2*S*,3*R*,5*R*)-3-(Benzyloxy)-5-methoxy-2-methylcyclohexan-1-ol 19



Under argon, alcohol **S3** (41.0 g, 0.165 mol, 1.0 equiv.), triphenylphosphine (65.0 g, 0.248 mol, 1.5 equiv.) and p-nitrobenzoic acid (41.4 g, 0.248 mol, 1.5 equiv.) were dissolved in dry toluene (720 mL), followed by dropwise addition of DIAD (48.8 mL, 0.248 mol, 1.5 equiv.) at −10 °C. After being stirred for 1 h at −10 °C, the reaction was quenched by sat. $NaHCO_3$ aq. (550 mL) and extracted with EtOAc (2×450 mL). The combined organic phases were washed with brine, dried over anhydrous Na_2SO_4, and concentrated in vacuo. With crude product in hand, K_2CO_3 (45.6 g, 0.33 mol, 2.0 equiv.) was added to a solution of the crude product above in 650 mL MeOH. After being stirred for 10 h at room temperature, the reaction was concentrated in vacuo, followed by addition of 500 mL sat. NH_4Cl aq. and 500 mL EtOAc. The aqueous layer was extracted with EtOAc (2×450 mL), and the combined organic layer was then washed with brine, dried over anhydrous Na_2SO_4, and concentrated in vacuo. The crude product was purified by column chromatography (petroleum ether:EtOAc, 9:2 v/v) to give product **19** (34.9 g, 85% for 2 steps) as a white solid.

TLC (petroleum ether:EtOAc, 3:1 v/v): R_f = 0.27; ^{1}H NMR (600 MHz, $CDCl_3$): δ 7.37 – 7.26 (m, 5H), 5.18 (d, J = 8.4 Hz, 2H), 4.70 (d, J = 12.6 Hz, 1H), 4.50 (d, J = 12.6 Hz, 1H), 4.08 (dd, J = 8.4, 3.6 Hz, 1H), 3.82 (dd, J = 9.0, 4.8 Hz, 1H), 3.47 (tt, J = 8.4, 3.6 Hz, 1H), 3.37 (s, 3H), 2.76 (brs, 1H), 2.26 – 2.18 (m, 2H), 1.76 (dt, J = 12.6, 8.4 Hz, 1H), 1.68 (dt, J = 12.6, 8.4 Hz, 1H); ^{13}C NMR (150 MHz, $CDCl_3$): δ 148.7, 138.4, 128.3, 128.3, 127.5, 127.4, 127.4, 106.9, 75.4, 74.1, 70.7, 69.5, 56.2, 40.3, 37.8; IR (neat): ν_{max} = 3323, 2943, 2862, 1721, 1455, 1371, 1189, 1059, 1041 cm^{-1}; HRMS (*m/z*): $[M + Na]^+$ calcd. for $C_{15}H_{20}NaO_3$, 271.1305; found, 271.1309; $[\alpha]_D^{20}$= +39.0 (*c* 1.0, $CHCl_3$); m.p.: 73.3 – 77.4 °C.

(3a*S*,5a*S*,7*S*,9*R*,9a*S*)-9-(Benzyloxy)-7-methoxy-3-(4-methoxybenzyl)hexahydro-1*H*,4*H*,7*H*-benzofuro[3,3a-*c*]isoxazol-4-one 18

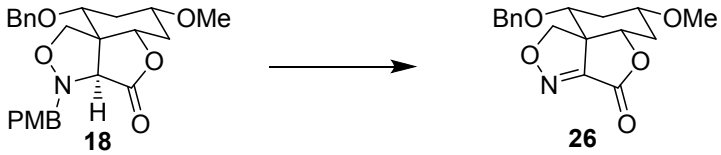


At 0 °C, to a solution of alcohol **19** (8.8 g, 35.4 mmol, 1.0 equiv.) and pyridine (8.6 mL, 0.106 mol, 3.0 equiv.) in dry CH_2Cl_2 (200 mL) was added bromoacetyl bromide (4.6 mL, 53.2 mmol, 1.5 equiv.) dropwisely under argon. After being stirred vigorously for 30 min at 0 °C, the reaction was quenched by sat. NH_4Cl aq. (200 mL) and extracted with CH_2Cl_2 (3×140 mL). The combined organic phases were washed with brine, dried over anhydrous Na_2SO_4, and concentrated in

vacuo to give crude ester. Sodium iodide dihydrate (10.5 g, 56.6 mmol, 1.6 equiv.) was added to the solution of the crude ester above in 100 mL acetone. After being stirred for 3 h at room temperature, the reaction mixture was filtrated and concentrated in vacuo. The residue was dissolved in mL CH_2Cl_2 and washed with sat. $NaHSO_3$ aq. (120 mL), and the aqueous layer was extracted by CH_2Cl_2 (2×90 mL). The combined organic phases were washed with brine, dried over anhydrous Na_2SO_4, and concentrated in vacuo. With crude iodide in hand, it was dissolved in 200 mL dry acetonitrile and stirred with silver nitrate (12.0 g, 70.8 mmol, 2.0 equiv.) at 40 °C for 2 h. The reaction mixture was filtrated and concentrated in vacuo, and the residue was dissolved in 80 mL CH_2Cl_2, then filtrated through a pad of silica gel. The filter cake was washed with EtOAc (3×100 mL), and the filtrate was concentrated in vacuo to give the nitrate as a pale yellow solid. At 10 °C, to a solution of the nitrate substrate in dry DMSO (160 mL) was added sodium acetate (2.61 g, 31.9 mmol, 0.9 equiv.) slowly in portions, and the reaction was allowed to be stirred at room temperature. After being stirred for 20 min, the reaction was quenched by dropping brine (700 mL) at 0 °C and extracted with EtOAc (3×210 mL). The combined organic phases were washed with brine, dried over anhydrous Na_2SO_4, and concentrated in vacuo to give the crude aldehyde. To a solution of the aldehyde in dry toluene (450 mL) was added N-(4-methoxybenzyl)hydroxylamine (4.88 g, 31.9 mmol, 0.9 equiv.) at room temperature. After being stirred for 30 min, the reaction solution was diluted with 450 mL dry acetonitrile, then allowed to be stirred vigorously at 80 °C. The reaction was concentrated in vacuo after 20 h, and the residue was purified by column chromatography (CH_2Cl_2:MeOH, 50:1 v/v) to give product **18** (7.94 g, 51% for 4 steps) as a white solid. A single crystal was obtained by crystallization in a mixture of petroleum ether:EtOAc (2:1).

TLC (petroleum ether:EtOAc, 1:1 v/v): R_f = 0.35; ^{1}H NMR (400 MHz, $CDCl_3$): δ 7.44 – 7.31 (m, 5H), 7.18 (d, J = 8.8 Hz, 2H), 6.81 (d, J = 8.8 Hz, 2H), 4.78 (d, J = 11.2 Hz, 1H), 4.61 (t, J = 5.2 Hz, 1H), 4.44 (d, J = 11.2 Hz, 1H), 4.22 (d, J = 8.8 Hz, 1H), 4.08 – 3.98 (m, 3H), 3.82 (d, J = 8.8 Hz, 1H), 3.78 (s, 3H), 3.65 (dd, J = 8.0, 5.6 Hz, 1H), 3.61 – 3.53 (m, 1H), 3.26 (s, 3H), 2.45 (dt, J = 14.4, 7.6 Hz, 1H), 2.23 – 2.11 (m, 1H), 1.95 (brd, J = 14.4 Hz, 1H), 1.77 – 1.66 (m, 1H); ^{13}C NMR (150 MHz, $CDCl_3$): δ 173.5, 158.9, 137.2, 130.3, 130.3, 128.6, 128.6, 128.6, 128.6, 128.2, 128.2, 113.8, 113.8, 82.3, 76.2, 72.5, 72.4, 71.2, 68.3, 59.7, 59.1, 55.7, 55.2, 32.5, 30.3; IR (neat): ν_{max} = 2920, 1770, 1512, 1458, 1246, 1073, 1025 cm^{-1}; HRMS (*m/z*): $[M + H]^+$ calcd. for $C_{25}H_{30}NO_6$, 440.2068; found, 440.2065; $[\alpha]_D^{20}$ = −44.2 (*c* 0.75, $CHCl_3$); m.p.: 134.9 – 136.0 °C.

(5a*S*,7*S*,9*R*,9a*S*)-9-(Benzyloxy)-7-methoxy-5a,6,8,9-tetrahydro-1*H*,4*H*,7*H*-benzofuro[3,3a-*c*]isoxazol-4-one 26

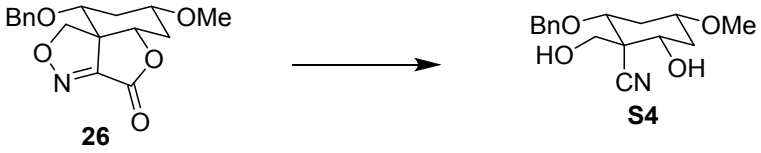


To a solution of compound **18** (21 g, 47.8 mmol, 1.0 equiv.) and Et_3N (7.3 mL, 52.6 mmol, 1.1 equiv.) in CH_2Cl_2:H_2O (10:1) of 650 mL was added DDQ (65.1 g, 0.287 mol, 6.0 equiv.) in portions at room temperature. After being stirred for 12 h, the reaction was then filtrated through celite and quenched by dropping sat. $NaHCO_3$ aq. (800 mL) and stirred for 20 min. The mixture was extracted with CH_2Cl_2 (3×250 mL), and the combined organic phases were washed with brine, dried over anhydrous Na_2SO_4, and concentrated in vacuo. Purification of the residue via column chromatography (petroleum ether:EtOAc, 3:1 v/v) furnished product **26** (10.2 g, 67%) as a pale yellow solid.

TLC (petroleum ether:EtOAc, 1:1 v/v): R_f = 0.44; ^{1}H NMR (600 MHz, $CDCl_3$): δ 7.33 (t, J = 7.2 Hz, 2H), 7.29 – 7.23 (m, 3H), 4.73 – 4.62 (m, 2H), 4.43 – 4.35 (m, 2H), 4.27 (d, J = 9.6 Hz, 1H), 3.94 (brs, 1H), 3.37 – 3.28 (m, 1H), 3.32 (s, 3H), 2.28 (t, J = 7.2 Hz, 2H), 2.18 (dt, J = 13.2, 5.4 Hz, 1H), 1.94 (ddd, J = 15.0, 7.8, 3.6 Hz, 1H); ^{13}C NMR (150 MHz, $CDCl_3$): δ 159.5, 158.2, 136.8, 128.4, 128.4, 127.8, 127.4, 127.4, 81.6, 81.0, 75.2, 71.8, 71.0, 60.1, 56.2, 30.0, 29.9; IR

(neat): ν_{max} = 2933, 1781, 1454, 1289, 1247, 1078, 1027 cm^{-1}; HRMS (*m/z*): [M + Na]$^+$ calcd. for $C_{17}H_{19}NNaO_5$, 340.1155; found, 340.1160; $[\alpha]_D^{20}$= −66.4 (*c* 0.9, $CHCl_3$); m.p.: 84.7 – 87.3 °C.

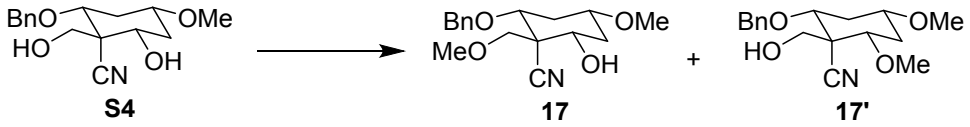
(1*R*,2*R*,4*R*,6*S*)-2-(Benzyloxy)-6-hydroxy-1-(hydroxymethyl)-4-methoxycyclohexane-1-carbonitrile S4



To a solution of compound **26** (1.0 g, 3.15 mmol, 1.0 equiv.) in MeOH:H_2O (3:1) of 50 mL was added LiOH·H_2O (145.4 mg, 3.47 mmol, 1.1 equiv.) at room temperature. After being stirred vigorously for 20 min, the reaction was heated by oil bath to 150 °C until all the solvent evaporated and kept being stirred for further 30 min. To the reaction mixture were added 50 mL H_2O and 50 mL EtOAc after the reaction was cooled down to the room temperature, and the aqueous layer was extracted with EtOAc (2×40 mL). The combined organic phases were washed with brine, dried over anhydrous Na_2SO_4, and concentrated in vacuo. Purification of the residue via column chromatography (petroleum ether:acetone, 1:1 v/v) furnished product **S4** (872 mg, 95%) as a white solid.

TLC (petroleum ether:acetone, 1:1 v/v): R_f = 0.45; ^{1}H NMR (400 MHz, $CDCl_3$): δ 7.42 – 7.27 (m, 5H), 4.71 (d, *J* = 12.0 Hz, 1H), 4.46 (d, *J* = 12.0 Hz, 1H), 4.11 (d, *J* = 10.8 Hz, 1H), 3.87 (d, *J* = 10.8 Hz, 1H), 3.76 – 3.60 (m, 2H), 3.38 – 3.27 (m, 1H), 3.34 (s, 3H), 3.19 – 3.01 (m, 2H), 2.47 (brd, *J* = 12.0 Hz, 1H), 2.35 (brd, *J* = 12.0 Hz, 1H), 1.71 – 1.55 (m, 2H); ^{13}C NMR (150 MHz, $CDCl_3$): δ 137.2, 128.6, 128.6, 128.1, 127.9, 127.9, 118.2, 72.6, 72.2, 71.3, 67.4, 62.3, 56.1, 53.7, 37.0, 33.4; IR (neat): ν_{max} = 3443, 2926, 1776, 1636, 1552, 1467, 1076, 1040 cm^{-1}; HRMS (*m/z*): [M + Na]$^+$ calcd. for $C_{16}H_{21}NNaO_4$, 314.1363; found, 314,1367; $[\alpha]_D^{20}$= −40.3 (*c* 0.75, $CHCl_3$); m.p.: 117.2 – 120.0 °C.

(1*R*,2*R*,4*R*,6*S*)-2-(Benzyloxy)-6-hydroxy-4-methoxy-1-(methoxymethyl)cyclohexane-1-carbonitrile 17 and (1*R*,2*R*,4*R*,6*S*)-2-(benzyloxy)-1-(hydroxymethyl)-4,6-dimethoxycyclohexane-1-carbonitrile 17'

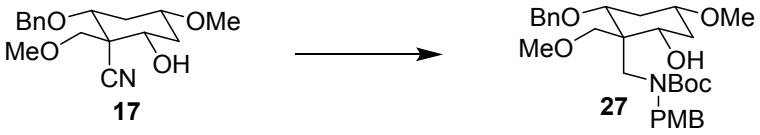


Under argon, compound **S4** (2.1 g, 7.21 mmol, 1.0 equiv.), proton sponge (2.32 g, 10.8 mmol, 1.5 equiv.) and 3Å molecular sieves (4.2 g) were dispersed in 200 mL dry CH_2Cl_2. To the reaction mixture was added trimethyloxonium tetrafluoroborate (1.1 g, 7.42 mmol, 1.03 equiv.) slowly in small portions at 0 °C, and the reaction was allowed to be stirred at 10 °C for 4.5 h. The reaction mixture was filtrated through celite and the filter cake was then washed with CH_2Cl_2. To the filtrate was added 300 mL H_2O, and the mixture was extracted with CH_2Cl_2 (2×100 mL). The combined organic layer was washed with brine, dried over anhydrous Na_2SO_4, and concentrated in vacuo. Purification of the residue via column chromatography (petroleum ether:EtOAc, 3:1 v/v) furnished product **17** (1.76 g, 80%, 93% brsm) and byproduct **17'** (44 mg, 2%) both as pale yellow oil, along with 302 mg of recovered **S4**.

17: TLC (petroleum ether:EtOAc, 2:1 v/v): R_f = 0.35; ^{1}H NMR (400 MHz, $CDCl_3$): δ 7.41 – 7.28 (m, 5H), 4.71 (d, *J* = 12.0 Hz, 1H), 4.46 (d, *J* = 12.0 Hz, 1H), 3.94 (d, *J* = 9.2 Hz, 1H), 3.72 (brd, *J* = 11.6 Hz, 1H), 3.64 (d, *J* = 9.2 Hz, 1H), 3.38 – 3.31 (m, 1H), 3.35 (s, 6H), 3.14 (tt, *J* = 11.6, 4.0 Hz, 1H), 2.99 (d, *J* = 3.2 Hz, 1H), 2.45 (d, *J* = 12.4 Hz, 1H), 2.37 (d, *J* = 12.4 Hz, 1H), 1.68 (dd, *J* = 12.0, 3.2 Hz, 1H), 1.62 (dd, *J* = 12.0, 3.2 Hz, 1H); ^{13}C NMR (150 MHz, $CDCl_3$): δ 137.4, 128.5, 128.5, 127.9, 127.8, 127.8, 117.7, 72.6, 72.2, 71.7, 71.3, 67.9, 59.4, 56.0, 52.6, 36.9, 33.4; IR (neat): ν_{max} = 2936, 1454, 1353, 1072, 1041, 736, 698 cm^{-1}; HRMS (*m/z*): [M + Na]$^+$ calcd. for $C_{17}H_{23}NNaO_4$, 328.1519; found, 328.1515; $[\alpha]_D^{20}$= −10.9 (*c* 0.35, $CHCl_3$).

17': TLC (petroleum ether:EtOAc, 2:1 v/v): R_f = 0.39; ^{1}H NMR (600 MHz, $CDCl_3$): δ 7.43 – 7.29 (m, 5H), 4.77 (d, J = 12.0 Hz, 1H), 4.45 (d, J = 12.0 Hz, 1H), 3.99 – 3.87 (m, 2H), 3.45 – 3.32(m, 1H), 3.39 (s, 3H), 3.37 (s, 3H), 3.19 (dd, J = 12.0, 3.0 Hz, 1H), 3.10 (t, J = 11.4 Hz, 1H), 2.51 (d, J = 12.0 Hz, 2H), 1.86 1.78 (m, 1H), 1.69 (dd, J = 24.0 ,12.0 Hz, 1H), 1.57 (dd, J = 24.0, 12.0 Hz, 1H); ^{13}C NMR (151 MHz, $CDCl_3$): δ 137.3, 128.7, 128.7, 128.3, 128.0, 128.0, 117.6, 74.5, 72.8, 71.3, 70.9, 60.7, 57.3, 56.1, 52.7, 33.2, 32.7; IR (neat): ν_{max} = 3424, 2931, 1455, 1353, 1083, 739 cm^{-1}; HRMS (*m/z*): $[M + Na]^+$ calcd. for $C_{17}H_{23}NNaO_4$, 328.1519; found, 328.1526; $[\alpha]_D^{20}$= −38.9 (*c* 0.22, $CHCl_3$).

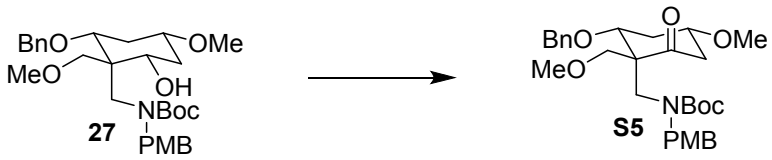
***tert*-Butyl (((1*R*,2*R*,4*R*,6*S*)-2-(benzyloxy)-6-hydroxy-4-methoxy-1-(methoxymethyl)cyclohexyl)methyl)(4-methoxybenzyl)carbamate 27**



Under argon, to a solution of compound **17** (6.5 g, 21.3 mmol, 1.0 equiv.) in dry THF (140 mL) was added $LiAlH_4$ (4.04 g, 0.106 mol, 5.0 equiv.) in portions at room temperature. After being stirred and refluxed for 45 min, the reaction was quenched by droping brine (50 mL), then filtrated through a pad of celite. After 180 mL H_2O was added, the mixture was extracted with EtOAc (3×120 mL). The combined organic layer was washed with brine, dried over anhydrous Na_2SO_4, and concentrated in vacuo to give the crude amine as a pale yellow oil. Under argon, the crude product and p-anisaldehyde (2.85 mL, 23.4 mmol, 1.1 equiv.) were dissolved in dry MeOH (150 mL), and the reaction was stirred for 36 h at room temperature. To the reaction solution was then added sodium borohydride (1.13 g, 29.8 mmol, 1.4 equiv.) in portions. After being stirred for 30 min at room temperature, the reaction was treated with sat. $NaHCO_3$ aq. (150 mL) and concentrated in vacuo to remove MeOH. The concentrated mixture was extracted with EtOAc (3×100 mL), and the combined organic layer was washed with brine, dried over anhydrous Na_2SO_4, and concentrated in vacuo to give the crude product as a pale yellow oil. To a solution of reductive amination product in CH_2Cl_2:H_2O (10:1) of 200 mL were added sodium carbonate (22.5 g, 0.212 mol, 10 equiv.) and Boc_2O (9.8 mL, 42.6 mmol, 2.0 equiv.). After being stirred for 12 h at room temperature, the reaction was treated with sat. NH_4Cl aq. (200 mL) and extracted with CH_2Cl_2 (3×120 mL). The combined organic layer was washed with brine, dried over anhydrous Na_2SO_4, and concentrated in vacuo. The crude product was purified by column chromatography (petroleum ether:EtOAc, 4:1 v/v) to give product **27** (9.2 g, 82% for 3 steps) as a colorless oil.

TLC (petroleum ether:EtOAc, 2:1 v/v): R_f = 0.50; ^{1}H NMR (400 MHz, $CDCl_3$, some signals exist as a pair due to the presence of amide rotamers): δ 7.42 – 7.28 (m, 5H), 6.93 (d, J = 8.4 Hz, 2H), 6.74 (d, J = 8.4 Hz, 2H), 5.03 (d, J = 8.4 Hz, 1H) 4.63 (d, J = 10.8 Hz, 1H), 4.59 (d, J = 14.0 Hz, 1H), 4.45 (d, J = 10.8 Hz, 1H), 4.01 (brs, 1H), 3.78 (s, 3H), 3.70 – 3.56 (m, 2H), 3.5 – 3.26 (m, 3H), 3.33 (s, 3H), 3.33 (s, 3H), 3.21 – 3.06 (m, 2H), 2.29 (brs, 2H), 1.51 – 1.33 (m, 2H), 1.46 (s, 9H); ^{13}C NMR (150 MHz, $CDCl_3$, some signals exist as a pair due to the presence of amide rotamers): δ 158.7, 157.8, 138.6, 129.9, 128.9, 128.9, 128.3, 128.3, 128.0, 128.0, 127.7, 113.7, 113.7, 81.1, 74.1, 73.8, 71.9, 69.4, 66.5, 59.1, 55.9, 55.2, 51.3, 49.1, 42.8, 36.2, 32.7, 28.4, 28.4, 28.4; IR (neat): ν_{max} = 3379, 2938, 1661, 1612, 1513, 1366, 1247, 1161, 1109, 1047 cm^{-1}; HRMS (*m/z*): $[M + Na]^+$ calcd. for $C_{30}H_{43}NNaO_7$, 552.2932; found, 552.2935; $[\alpha]_D^{20}$= −37.3 (*c* 0.38, $CHCl_3$).

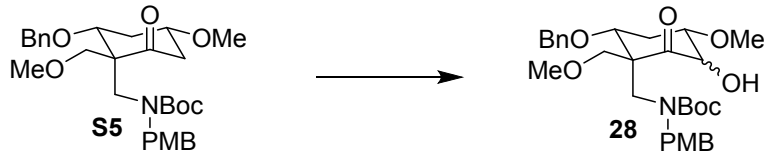
***tert*-Butyl (((1*S*,2*R*,4*S*)-2-(benzyloxy)-4-methoxy-1-(methoxymethyl)-6-oxocyclohexyl)methyl)(4-methoxybenzyl)carbamate S5**



Under argon, compound **27** (9.2 g, 17.4 mmol, 1.0 equiv.), NMO (6.1 g, 52.11 mmol, 3.0 equiv.) and 4Å molecular sieves (18.4 g) were dispersed in dry CH_2Cl_2 (280 mL). TPAP (610 mg, 1.74 mmol, 0.1 equiv.) was then added to the reaction mixture. After being stirred for 12 h at room temperature, the reaction was then filtrated through a pad of silica gel, and the filter cake was washed with EtOAc (3×170 mL), and the filtrate was concentrated in vacuo. The residue was dissolved in 250 mL CH_2Cl_2 and 200 mL sat. Na_2SO_3 aq., then extracted with CH_2Cl_2 (3×100 mL). The combined organic layer was washed with brine, dried over anhydrous Na_2SO_4, and concentrated in vacuo. Purification of the residue via column chromatography (petroleum ether:EtOAc, 5:1 v/v) furnished product **S5** (7.9 g, 86%) as a colorless oil.

TLC (petroleum ether:EtOAc, 2:1 v/v): R_f = 0.70; ^{1}H NMR (400 MHz, $CDCl_3$, some signals exist as a pair due to the presence of amide rotamers): δ 7.43 – 7.27 (m, 5H), 7.02 (d, J = 8.4 Hz, 2H), 6.87 – 6.74 (m, 2H), 4.65 (d, J = 11.2 Hz, 1H), 4.48 (d, J = 11.2 Hz, 1H), 4.42 (d, J = 15.6 Hz, 0.6H), 4.27 – 4.16 (m, 0.4H), 4.06 (d, J = 15.6 Hz, 0.6H), 3.99 – 3.83 (m, 3H), 3.78 (s, 3H), 3.67 (d, J = 14.8 Hz, 0.4H), 3.46 – 3.33 (m, 2.4H), 3.32 (s, 3H), 3.27 (brs, 3H), 2.95 – 2.74 (m, 1.6H), 2.56 – 2.40 (m, 1.4H), 1.90 (d, J = 11.6 Hz, 0.6H), 1.77 – 1.68 (m, 0.4H), 1.67 – 1.62 (m, 0.6H), 1.44 (s, 3H), 1.38 (s, 6H); ^{13}C NMR (150 MHz, $CDCl_3$, some signals exist as a pair due to the presence of amide rotamers): δ 207.0, 206.9, 158.7, 156.1, 138.3, 138.1, 130.1, 129.6, 129.0, 128.3, 128.3, 128.3, 127.9, 127.8, 127.7, 113.8, 113.8, 80.8, 80.1, 73.7, 73.4, 72.8, 72.3, 72.1, 70.7, 69.9, 59.6, 59.1, 59.0, 56.1, 55.9, 55.2, 51.7, 49.8, 46.4, 45.9, 45.7, 44.8, 32.1, 28.2, 28.2, 28.2; IR (neat): ν_{max} = 2932, 1693, 1612, 1513, 1456, 1366, 1247, 1165, 1106 cm^{-1}; HRMS (*m/z*): $[M + Na]^+$ calcd. for $C_{30}H_{41}NNaO_7$, 550.2775; found, 550.2783; $[\alpha]_D^{20}$ = −47.7 (*c* 0.50, $CHCl_3$).

***tert*-Butyl (((1*S*,4*S*,6*R*)-6-(benzyloxy)-3-hydroxy-4-methoxy-1-(methoxymethyl)-2-oxocyclohexyl)methyl)(4-methoxybenzyl)carbamate 28**

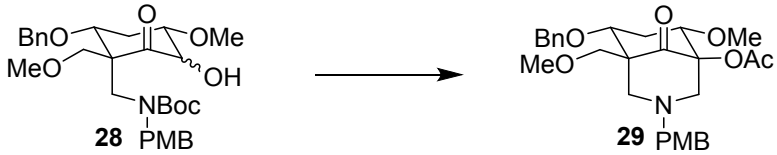


Under argon, to a solution of ketone **S5** (6.8 g, 12.9 mmol, 1.0 equiv.) in dry THF (220 mL) was added KHMDS (1M in THF, 19.3 mL, 19.3 mmol, 1.5 equiv.) dropwisely at −78 °C. After the reaction was stirred for 30 min, Davis' oxaziridine (5.05 g in 60 mL dry THF, 19.3 mmol, 1.5 equiv.) was then added dropwisely. After being stirred vigorously for 3 h at −78 °C, the reaction was quenched by sat. NH_4Cl aq. (280 mL) and extracted with EtOAc (3×130 mL). The combined organic phases were washed with brine, dried over anhydrous Na_2SO_4, and concentrated in vacuo. The crude product was purified by column chromatography (petroleum ether:EtOAc, 5:2 v/v) to give mixture product **28** (4.7 g, 67%) as a colorless oil.

TLC (petroleum ether:EtOAc, 2:1 v/v): R_f = 0.30; ^{1}H NMR (400 MHz, $CDCl_3$, some signals exist as a pair due to the presence of amide rotamers): δ 7.43 – 7.28 (m, 5H), 7.00 (d, J = 7.6 Hz, 2H), 6.80 (d, J = 7.6 Hz, 2H), 4.75 – 4.60 (m, 1.6H), 4.48 (d, J = 11.6 Hz, 1H), 4.36 (d, J = 16.4 Hz, 0.6H), 4.29 (brs, 1H), 4.06 (d, J = 15.6 Hz, 0.6H), 3.98 – 3.63 (m, 4.2H), 3.78 (s, 3H), 3.54 – 3.37 (m, 2H), 3.49 (s, 3H), 3.29 (brs, 3H), 3.09 (td, J = 10.0, 4.0 Hz, 1H), 2.45 (brs, 1H), 1.90 (dd, J = 24.4, 11.6 Hz, 0.6H), 1.76 (dd, J = 23.2, 11.2 Hz, 0.4H), 1.43 (s, 3H), 1.38 (s, 6H); ^{13}C NMR (101 MHz, $CDCl_3$, some signals exist as a pair due to the presence of amide rotamers): δ 207.6, 158.9, 156.0, 138.1, 132.8, 129.7, 129.1, 129.1, 129.0, 128.5, 128.4, 128.4, 128.4, 127.8, 127.7, 126.4, 113.9, 113.9, 81.3, 80.5, 79.0, 78.6, 78.5, 77.2, 72.9, 72.6,

72.4, 72.3, 70.4, 69.6, 59.1, 58.9, 58.5, 57.9, 57.7, 55.2, 51.8, 50.1, 46.9, 45.3, 29.9, 28.1, 28.1, 28.1; IR (neat): ν_{max} = 2930, 1692, 1513, 1408, 1366, 1245, 1160, 1112, 1029 cm^{-1}; HRMS (*m/z*): $[M + Na]^+$ calcd. for $C_{30}H_{41}NNaO_8$, 566.2724; found, 566.2726.

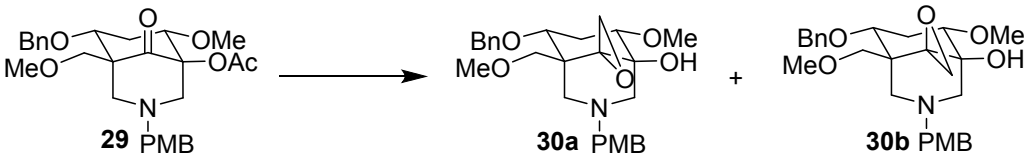
(1*R*,5*S*,6*R*,8*S*)-6-(Benzyloxy)-8-methoxy-3-(4-methoxybenzyl)-5-(methoxymethyl)-9-oxo-3-azabicyclo[3.3.1]nonan-1-yl acetate 29



To a solution of alchol **28** (4.7 g, 8.65 mmol, 1.0 equiv.) and pyridine (6.3 mL, 77.8 mmol, 9.0 equiv.) in dry CH_2Cl_2 (150 mL) was added acetyl chloride (1.23 mL, 17.3 mmol, 2.0 equiv.). After being stirred vigorously for 5 h at room teperature, the reaction was quenched by sat. NH_4Cl aq. (200 mL) and extracted with CH_2Cl_2 (2×120 mL). The combined organic layer was washed with brine, dried over anhydrous Na_2SO_4, and concentrated in vacuo. The crude product was purified by column chromatography (petroleum ether:EtOAc, 6:1 v/v) to give acetyl product. Under argon, the above acetyl product were dissolved in dry CH_2Cl_2 (520 mL), followed by addition of $Sc(OTf)_3$ (3.92 g, 7.96 mmol, 0.92 equiv.) at 0 °C. The reaction was then allowed to be stirred at 10 °C. After being stirred for 30 min, the reaction was quenched by sat. NH_4Cl aq. (450 mL) at 0 °C and extracted with CH_2Cl_2 (3×180 mL). The combined organic phases were washed with brine, dried over anhydrous Na_2SO_4, and concentrated in vacuo to give crude amine. To a solution of the crude amine in EtOH (400 mL) were added acetic acid (813 μL, 14.2 mmol, 1.6 equiv.) and formaldehyde (40% aq., 8.27 g, 0.11 mol, 12.7 equiv.), and the reaction was allowed to be stirred at 75 °C. After being stirred vigorously for 10 h, the reaction was cooled down, followed by addition of sat. $NaHCO_3$ aq. (50 mL) and concentration in vacuo. The mixture was treated with H_2O (350 mL) and EtOAc (200 mL), and extracted with EtOAc (2×180 mL). The combined organic phases were washed with brine, dried over anhydrous Na_2SO_4, and concentrated in vacuo. Purification of the residue via column chromatography (petroleum ether:EtOAc, 5:1 v/v) furnished product **29** (3.44 g, 80% for 3 steps) as a colorless oil.

TLC (petroleum ether:EtOAc, 3:1 v/v): R_f = 0.45; ^1H NMR (400 MHz, $CDCl_3$): δ 7.39 – 7.20 (m, 7H), 6.81 (d, J = 8.5 Hz, 2H), 4.65 (d, J = 11.6 Hz, 1H), 4.48 (d, J = 11.6 Hz, 1H), 4.08 (dd, J = 10.4, 7.2 Hz, 1H), 3.81 – 3.73 (m, 1H), 3.78 (s, 3H), 3.59 (d, J = 10.4 Hz, 1H), 3.55 (d, J = 13.6 Hz, 1H), 3.46 (d, J = 8.8 Hz, 1H), 3.45 – 3.38 (m, 1H), 3.43 (s, 3H), 3.36 – 3.25 (m, 2H), 3.30 (s, 3H), 3.18 (dd, J = 22.8, 11.6 Hz, 1H), 2.70 – 2.58 (m, 2H), 2.14 (d, J = 11.2 Hz, 1H), 2.10 (s, 3H); ^{13}C NMR (150 MHz, $CDCl_3$): δ 203.5, 169.1, 158.7, 138.5, 129.8, 129.8, 129.5, 128.2, 128.2, 127.5, 127.4, 127.4, 113.6, 113.6, 87.2, 77.2, 73.1, 71.8, 69.9, 60.4, 59.2, 58.6, 58.2, 57.3, 55.8, 55.2, 33.8, 21.7; IR (neat): ν_{max} = 2930, 2834, 1755, 1732, 1612, 1512, 1235, 1109, 1074, 1021 cm^{-1}; HRMS (*m/z*): $[M + H]^+$ calcd. for $C_{28}H_{36}NO_7$, 498.2486; found, 498.2487; $[\alpha]_D^{20}$ = −9.3 (*c* 0.72, $CHCl_3$).

(1*R*,5*S*,6*R*,8*S*,9*S*)-6-(Benzyloxy)-8-methoxy-3-(4-methoxybenzyl)-5-(methoxymethyl)-3-azaspiro[bicyclo[3.3.1]nonane-9,2'-oxiran]-1-ol 30a and (1*R*,5*S*,6*R*,8*S*,9*R*)-6-(benzyloxy)-8-methoxy-3-(4-methoxybenzyl)-5-(methoxymethyl)-3-azaspiro[bicyclo[3.3.1]nonane-9,2'-oxiran]-1-ol 30b

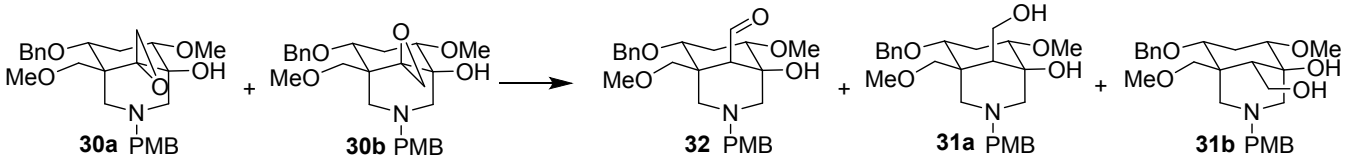


Under argon, trimethylsulfoxonium iodide (1.69 g, 7.66 mmol, 4.1 equiv.) and potassium tert-butoxide (818 mg, 7.29 mmol, 3.9 equiv.) were dissolved in dry THF:DMSO (1:1) of 70 mL. The reaction was allowed to be stirred at room temperature for 40 min, followed by dropwise addition of compound **29** (930 mg, 1.87 mmol, 1.0 equiv.) in dry THF (20 mL). After being stirred for 4 h at room temperature, the reaction was quenched by sat. NH_4Cl aq. (200 mL) and extracted with EtOAc (3×80 mL). The combined organic phases were washed with brine, dried over anhydrous Na_2SO_4, and concentrated in vacuo. Purification of the residue via column chromatography (petroleum ether:EtOAc, 2:1 v/v) furnished product **30a** (381 mg, 43%) as a white foam and product **30b** (356 mg, 41%) as a white solid.

30a: TLC (petroleum ether:EtOAc, 3:2 v/v): R_f = 0.43; ^{1}H NMR (400 MHz, $CDCl_3$): δ 7.36 – 7.19 (m, 7H), 6.79 (d, J = 8.4 Hz, 2H), 4.67 (d, J = 11.6 Hz, 1H), 4.47 (d, J = 11.6 Hz, 1H), 3.93 (dd, J = 11.2, 6.8 Hz, 1H), 3.77 (s, 3H), 3.56 (d, J = 13.2 Hz, 1H), 3.46 (s, 3H), 3.34 – 3.23 (m, 3H), 3.18 (s, 3H), 3.13 (d, J = 5.2 Hz, 1H), 3.07 – 2.95 (m, 3H), 2.95 – 2.88 (m, 2H), 2.60 (dt, J = 11.2, 6.8 Hz, 1H), 2.09 (d, J = 10.4 Hz, 1H), 2.00 (s, 1H), 1.71 (d, J = 10.8 Hz, 1H); ^{13}C NMR (150 MHz, $CDCl_3$): δ 158.4, 139.2, 130.2, 129.7, 129.7, 128.1, 128.1, 127.2, 127.2, 113.5, 113.5, 80.7, 73.4, 71.2, 70.5, 69.6, 61.6, 61.4, 58.3, 58.0, 57.4, 55.2, 55.1, 52.4, 47.6, 44.5, 32.3; IR (neat): ν_{max} = 3481, 2918, 1612, 1511, 1455, 1355, 1302, 1244, 1107, 1036 cm^{-1}; HRMS (*m/z*): $[M + H]^+$ calcd. for $C_{27}H_{36}NO_6$, 470.2537; found, 470.2542; $[\alpha]_D^{20}$= +36.2 (*c* 0.44, $CHCl_3$).

30b: TLC (petroleum ether:EtOAc, 3:2 v/v): R_f = 0.30; ^{1}H NMR (400 MHz, $CDCl_3$): δ 7.38 – 7.21 (m, 7H), 6.78 (d, J = 8.4 Hz, 2H), 4.70 (d, J = 11.6 Hz, 1H), 4.37 (d, J = 11.6 Hz, 1H), 3.77 (s, 3H), 3.59 (d, J = 13.6 Hz, 1H), 3.47 – 3.38 (m, 2H), 3.45 (s, 3H), 3.34 – 3.14 (m, 4H), 3.16 (s, 3H), 3.11 – 2.98 (m, 4H), 2.67 (dt, J = 11.2, 6.8 Hz, 1H), 2.23 (d, J = 11.6 Hz, 1H), 2.18 – 2.11 (m, 2H); ^{13}C NMR (150 MHz, $CDCl_3$): δ 158.4, 138.7, 130.5, 129.6, 129.6, 128.2, 128.2, 127.3, 127.2, 127.2, 113.5, 113.5, 81.0, 75.7, 71.1, 70.8, 69.8, 63.3, 61.6, 59.2, 58.7, 57.6, 55.2, 53.7, 46.5, 44.5, 31.6; IR (neat): ν_{max} = 3470, 2919, 1612, 1512, 1464, 1244, 1106, 1035 cm^{-1}; HRMS (*m/z*): $[M + H]^+$ calcd. for $C_{27}H_{36}NO_6$, 470.2537; found, 470.2542; $[\alpha]_D^{20}$= +8.5 (*c* 0.33, $CHCl_3$); m.p.: 153.2 – 157.4 °C.

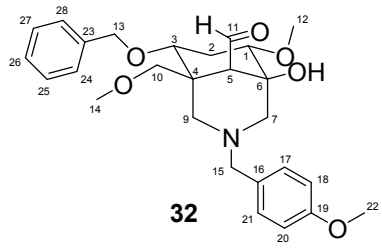
(1*R*,5*R*,6*R*,8*S*,9*S*)-6-(benzyloxy)-9-formyl-8-methoxy-3-(4-methoxybenzyl)-5-(methoxymethyl)-3-azabicyclo[3.3.1]nonan-1-yl acetate 32, (1*R*,5*R*,6*R*,8*S*,9*R*)-6-(Benzyloxy)-9-(hydroxymethyl)-8-methoxy-3-(4-methoxybenzyl)-5-(methoxymethyl)-3-azabicyclo[3.3.1]nonan-1-yl acetate 31a and (1*R*,5*R*,6*R*,8*S*,9*S*)-6-(benzyloxy)-9-(hydroxymethyl)-8-methoxy-3-(4-methoxybenzyl)-5-(methoxymethyl)-3-azabicyclo[3.3.1]nonan-1-yl acetate 31b



Under argon, activated zinc powder (719 mg, 11.0 mmol, 7.0 equiv.) and titanocene dichloride (1.95 g, 7.85 mmol, 5.0 equiv.) were dispersed in degassed and dry THF (60 mL), and the mixture was stirred for 45 min at room temperature. To the suspension above were added a mixture of compound **30a** and compound **30b** (737 mg, 1.57 mmol, 1.0 equiv, **30a**:**30b** 381:356) and cyclohexa-1,4-diene (1.3 mL, 14.1 mmol, 9.0 equiv.) dissolved in 25 mL THF. After being stirred for 6 h, the reaction was quenched by being stirred with sat. NaH_2PO_4 aq. (100 mL) for 30 min and then filtrated through a pad of celite. The filtrate was extracted with EtOAc (3×50 mL), and the combined organic layer was washed with brine, dried over anhydrous Na_2SO_4, and concentrated in vacuo. Purification of the residue via column chromatography (petroleum ether:EtOAc, 4:1 v/v then CH_2Cl_2:MeOH, 45:1 v/v) furnished product **31a** (352 mg, 48%) and product **31b** (65.1 mg, 9%) both as pale yellow oil, along with product **32** (212 mg, 29%) as a pale yellow foam.

32: TLC (petroleum ether:EtOAc, 4:1 v/v): R_f = 0.25; ^{1}H NMR (400 MHz, $CDCl_3$): δ 9.91 (d, J = 2.8 Hz, 1H), 7.36 – 7.29 (m, 2H), 7.28 (d, J = 6.8 Hz, 1H), 7.24 – 7.18 (m, 4H), 6.79 (d, J = 8.8 Hz, 2H), 4.68 (d, J = 11.6 Hz, 1H), 4.41 (d, J = 11.6 Hz, 1H), 4.08 (dd, J = 11.2, 6.8 Hz, 1H), 3.77 (s, 3H), 3.64 (dd, J = 11.2, 6.8 Hz, 1H), 3.52 (d, J = 13.2 Hz, 1H), 3.48 (d, J = 9.2 Hz, 1H), 3.42 (s, 3H), 3.29 (d, J = 10.4 Hz, 1H), 3.26 (d, J = 13.2 Hz, 1H), 3.19 (s, 3H), 3.13 (d, J = 11.2 Hz, 1H), 3.09 (d, J = 9.2 Hz, 1H), 2.89 (dd, J = 22.4, 11.2 Hz, 1H), 2.72 (d, J = 2.8 Hz, 1H), 2.69 (brs, 1H), 2.67 – 2.60 (m, 1H), 1.96 (d, J = 10.4 Hz, 1H), 1.77 (d, J = 11.2 Hz, 1H); ^{13}C NMR (150 MHz, $CDCl_3$): δ 203.2, 158.5, 138.9, 130.1, 129.7, 129.7, 128.2, 128.2, 127.3, 127.1, 127.1, 113.5, 113.5, 80.6, 75.3, 75.0, 73.0, 71.1, 61.5, 60.6, 60.6, 58.8, 57.4, 55.2, 55.2, 45.4, 32.0; IR (neat): ν_{max} = 2926, 1718, 1612, 1512, 1464, 1245, 1179, 1107, 1037 cm^{-1}; HRMS (m/z): [M + H]$^+$ calcd. for $C_{27}H_{36}NO_6$, 470.2537; found, 470.2538; $[\alpha]_D^{20}$ = +43.3 (c 0.25, $CHCl_3$).

Table S1. Results of 2D NMR experiments of 32



32

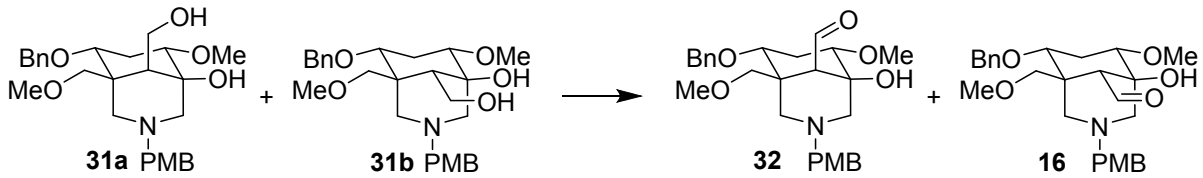
No.	δH mult. (J in Hz)	δC	COSY	HMBC
1	3.64 (dd, 11.2, 6.8)	80.6	H-2, H-2', H-7'	C-2, C-6, C-7, C-9, C-12, C-15
2	H-2: 2.89 (dd, 11.2, 11.2)	32.0	H-1, H-3, H-2'	C-1, C-3
	H-2': 2.67 – 2.60 (m)		H-2, H-1, H-3	C-1, C-3, C-4, C-6
3	4.08 (dd, 10.8, 6.8)	75.3	H-2, H-2', H-9'	C-2, C-4, C-9, C-10, C-13,
4	–	45.4	–	–
5	2.72 (d, 2.8)	60.6	H-11	C-1, C-3, C-4, C-6, C-11
6	–	73.0	–	–
7	H-7: 3.29 (d, 10.4)	60.6	H-7', H-9', H-15	C-1, C-5, C-6, C-9, C-11, C-12, C-15
	H-7': 1.96 (d, 10.4)		H-7, H-9', H-15	C-1, C-5, C-6, C-15
8 (N)	–	–	–	–
9	H-9: 3.13 (d, 11.2)	55.2	H-9', H-7, H-7', H-15	C-4, C-5, C-7, C-11, C-15
	H-9': 1.77 (d, 11.2)		H-2, H-9, H-7, H-3	C-3, C-4, C-5, C-7, C-15
10	H-10: 3.48 (d, 9.2)	75.0	H-10', H-2	C-3, C-4, C-5, C-9, C-14
	H-10': 3.09 (d, 9.2)		H-10, H-15'	C-3, C-4, C-5, C-9, C-14
11	9.91 (d, 2.8)	203.2	H-5	C-5
12 (OMe)	3.42 (s)	57.4	–	C-1, C-15
13	H-13: 4.68 (d, 11.6)	71.1	H-13'	C-3, C-23, C-24, C-28
	H-13': 4.41 (d, 11.6)		H-13	C-3, C-23, C-24, C-28
14 (OMe)	3.19 (s)	58.8	H-9'	C-10
15	H-15: 3.52 (d, 13.2)	61.5	H-9, H-15', H-7, H-10	C-7, C-9, C-12, C-16, C-17, C-18, C-20, C-21
	H-15': 3.26 (d, 13.2)		H-10, H-15	C-7, C-9, C-16, C-17, C-21
16	–	130.1	–	–
17	7.24 – 7.18 (m)	129.7	H-15, H-15', H-18	C-15, C-19, C-20, C-21
18	6.79 (d, 8.8)	113.5	H-17	C-16, C-19, C-20

19	–	158.5	–	–
20	6.79 (d, 8.8)	113.5	H-21	C-16, C-18, C-19
21	7.24 – 7.18 (m)	129.7	H-15, H-15', H-20	C-15, C-17, C-18, C-19
22 (OMe)	3.77 (s)	55.2	–	C-19
23	–	138.9	–	–
24	7.24 – 7.18 (m)	127.1	H-13, H-13', H-25	C-13, C-26, C-28
25	7.36 – 7.29 (m)	128.2	H-26, H-24	C-23, C-27, C-28
26	7.28 (d, 6.8)	127.3	H-25, H-27	C-24, C-28
27	7.36 – 7.29 (m)	128.2	H-26, H-28	C-23, C-24, C-25
28	7.24 – 7.18 (m)	127.1	H-13, H-13', H-27	C-13, C-24, C-26
OH	2.69 (s)	–	–	C-5

31a: TLC (CH_2Cl_2:MeOH, 30:1 v/v): R_f = 0.42; ^{1}H NMR (400 MHz, $CDCl_3$): δ 7.36 – 7.18 (m, 7H), 6.78 (d, J = 8.4 Hz, 2H), 4.67 (d, J = 11.6 Hz, 1H), 4.37 (d, J = 11.6 Hz, 1H), 3.95 (dt, J = 11.2, 5.6 Hz, 1H), 3.86 – 3.72 (m, 3H), 3.77 (s, 3H), 3.54 – 3.37 (m, 2H), 3.42 (s, 3H), 3.29 – 3.17 (m, 4H), 3.27 (s, 3H), 3.07 (d, J = 10.8 Hz, 1H), 2.84 (dd, J = 22.4, 11.2 Hz, 1H), 2.76 (s, 1H), 2.59 (dt, J = 11.6, 6.4 Hz, 1H), 1.99 – 1.90 (m, 2H), 1.73 (d, J = 10.8 Hz, 1H); ^{13}C NMR (150 MHz, $CDCl_3$): δ 158.4, 139.0, 130.4, 129.6, 129.6, 128.2, 128.2, 127.3, 127.1, 127.1, 113.4, 113.4, 80.1, 76.0, 75.2, 73.2, 71.0, 61.7, 61.2, 59.0, 58.4, 57.1, 56.0, 55.2, 51.4, 43.7, 31.5; IR (neat): ν_{max} = 3394, 2902, 1611, 1511, 1454, 1244, 1104, 1035 cm^{-1}; HRMS (*m/z*): [M + H]$^+$ calcd. for $C_{27}H_{38}NO_6$, 472.2694; found, 472.2697; $[\alpha]_D^{20}$= +38.6 (*c* 0.39, $CHCl_3$).

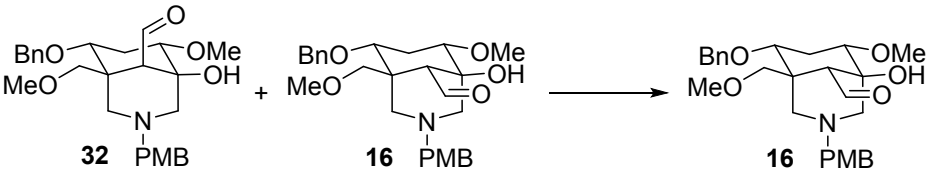
31b: TLC (CH_2Cl_2:MeOH, 30:1 v/v): R_f = 0.37; ^{1}H NMR (400 MHz, $CDCl_3$): δ 7.37 – 7.23 (m, 5H), 7.19 (d, J = 8.4 Hz, 2H), 6.78 (d, J = 8.4 Hz, 2H), 4.68 (d, J = 11.6 Hz, 1H), 4.43 (d, J = 11.6 Hz, 1H), 4.09 (dd, J = 10.8, 7.2 Hz, 1H), 3.86 – 3.71 (m, 2H), 3.77 (s, 3H), 3.67 (dd, J = 10.8, 6.8 Hz, 1H), 3.51 (d, J = 13.2 Hz, 1H), 3.41 (s, 3H), 3.34 (d, J = 9.2 Hz, 1H), 3.27 (d, J = 13.2 Hz, 1H), 3.23 (s, 3H), 3.19 (dd, J = 11.2, 6.4 Hz, 1H), 3.03 (d, J = 9.6 Hz, 1H), 2.98 (d, J = 11.2 Hz, 1H), 2.85 (s, 1H), 2.78 – 2.64 (m, 2H), 2.58 (dt, J = 11.6, 6.4 Hz, 1H), 2.32 (d, J = 10.8 Hz, 1H), 1.74 – 1.65 (m, 2H); ^{13}C NMR (150 MHz, $CDCl_3$): δ 158.5, 139.0, 129.7, 129.7, 129.7, 128.2, 128.2, 127.3, 127.3, 127.3, 113.5, 113.5, 84.2, 76.0, 73.6, 71.8, 71.4, 61.7, 58.9, 57.8, 57.1, 55.2, 54.9, 50.1, 44.3, 44.2, 31.1; IR (neat): ν_{max} = 2917, 1612, 1512, 1454, 1245, 1176, 1108, 1031 cm^{-1}; HRMS (*m/z*): [M + H]$^+$ calcd. for $C_{27}H_{38}NO_6$, 472.2694; found, 472.2697; $[\alpha]_D^{20}$= +6.5 (*c* 0.11, $CHCl_3$).

(1*R*,5*R*,6*R*,8*S*,9*S*)-6-(benzyloxy)-9-formyl-8-methoxy-3-(4-methoxybenzyl)-5-(methoxymethyl)-3-azabicyclo[3.3.1]nonan-1-yl acetate 32 and (1*R*,5*R*,6*R*,8*S*,9*R*)-6-(benzyloxy)-9-formyl-8-methoxy-3-(4-methoxybenzyl)-5-(methoxymethyl)-3-azabicyclo[3.3.1]nonan-1-yl acetate 16

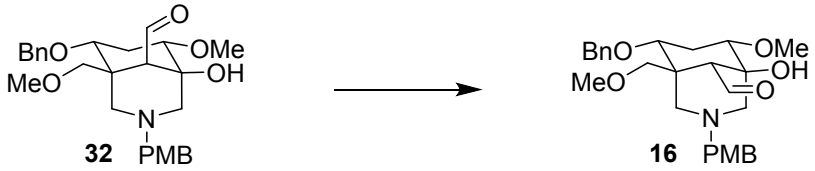


A mixture of compound **31a** and compound **31b** (417 mg, 0.884 mmol, 1.0 equiv., **31a**:**31b** 352:65) was dissolved in dry DMSO (17 mL) and IBX (495 mg, 1.77 mmol, 2.0 equiv.) was added. After being stirred for 2.5 h at room temperature, the reaction was quenched by sat. $NaHCO_3$ aq. (90 mL) and extracted with EtOAc (3×30 mL). The combined organic phases were washed with brine, dried over anhydrous Na_2SO_4, and concentrated in vacuo. Purification of the residue via column chromatography (petroleum ether:EtOAc, 4:1 v/v then CH_2Cl_2:MeOH, 23:1 v/v) furnished product **32** (312 mg, 75%) as a white solid and product **16** (57.4 mg, 14%) as a pale yellow oil.

16: TLC (CH_2Cl_2:MeOH, 15:1 v/v): R_f = 0.27; ^{1}H NMR (400 MHz, $CDCl_3$): δ 9.91 (s, 1H), 7.41 – 7.17 (m, 7H), 6.80 (d, J = 8.4 Hz, 2H), 4.68 (d, J = 11.6 Hz, 1H), 4.42 (d, J = 11.6 Hz, 1H), 3.78 (s, 3H), 3.63 – 3.53 (m, 2H), 3.44 (s, 3H), 3.36 (d, J = 13.2 Hz, 1H), 3.29 (brs, 2H), 3.25 – 3.08 (m, 2H), 3.19 (s, 3H), 2.87 (d, J = 11.6 Hz, 1H), 2.74 (dd, J = 22.4, 11.2 Hz, 1H), 2.56 (dt, J = 12.4, 6.4 Hz, 1H), 2.48 (d, J = 10.8 Hz, 1H), 2.33 (btr, 1H), 2.18 (d, J = 11.6 Hz, 1H); ^{13}C NMR (150 MHz, $CDCl_3$): δ 203.2, 158.5, 138.7, 130.0, 129.7, 129.7, 128.2, 128.2, 127.4, 127.3, 127.3, 113.5, 113.5, 83.3, 75.9, 73.2, 72.6, 71.2, 61.5, 58.7, 57.5, 56.2, 55.2, 54.2, 50.6, 45.4, 31.4; IR (neat): ν_{max} = 2913, 1719, 1612, 1512, 1454, 1244, 1172, 1109, 1034 cm^{-1}; HRMS (*m/z*): $[M + H]^+$ calcd. for $C_{27}H_{36}NO_6$, 470.2537; found, 470.2535; $[\alpha]_D^{20}$= +8.3 (*c* 0.58, $CHCl_3$).

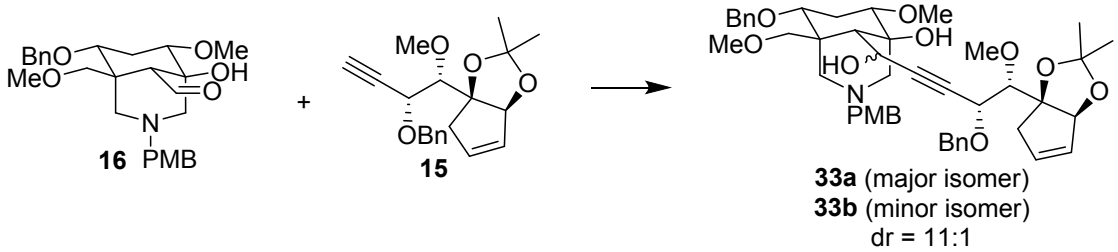


To a solution of aldehyde mixture (**32**:**16** = 5.4:1, 344 mg, 0.733 mmol, 1.0 equiv.) in 40 mL toluene was added *p*-toluenesulfonic acid monohydrate (279 mg, 1.467 mmol, 2.0 equiv.) at room temperature., and the reaction was allowed to be stirred at 85 °C for 40 min. After cooled down, the reaction was quenched by sat. $NaHCO_3$ aq. (50 mL) and extracted with EtOAc (3×30 mL). The combined organic phases were washed with brine, dried over anhydrous Na_2SO_4, and concentrated in vacuo. Purification of the residue via column chromatography (CH_2Cl_2:MeOH, 23:1 v/v) furnished product **16** (320 mg, 93%) as a pale yellow oil.



To a solution of aldehyde **32** (55.0 mg, 0.117 mmol, 1.0 equiv.) in 6 mL toluene was added *p*-toluenesulfonic acid monohydrate (44.6 mg, 0.234 mmol, 2.0 equiv.) at room temperature., and the reaction was allowed to be stirred at 85 °C for 30 min. After cooled down, the reaction was quenched by sat. $NaHCO_3$ aq. (6 mL) and extracted with EtOAc (3×4 mL). The combined organic phases were washed with brine, dried over anhydrous Na_2SO_4, and concentrated in vacuo. Purification of the residue via column chromatography (CH_2Cl_2:MeOH, 23:1 v/v) furnished product **16** (51.6 mg, 94%) as a pale yellow oil.

(1*R*,5*R*,6*R*,8*S*,9*S*)-6-(Benzyloxy)-9-((4*R*,5*S*)-4-(benzyloxy)-5-((3a*R*,6a*S*)-2,2-dimethyl-4,6a-dihydro-3a*H*-cyclopenta[*d*][1,3]dioxol-3a-yl)-1-hydroxy-5-methoxypent-2-yn-1-yl)-8-methoxy-3-(4-methoxybenzyl)-5-(methoxymethyl)-3-azabicyclo[3.3.1]nonan-1-ol 33a and 33b

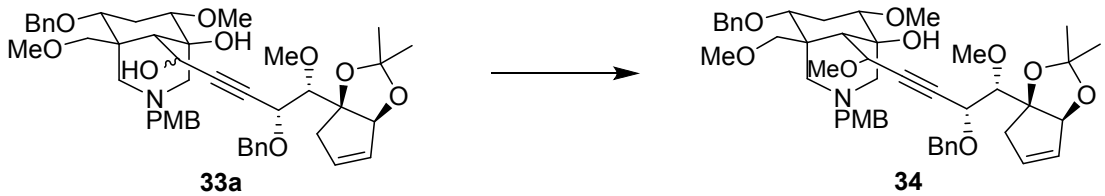


Under argon, to a solution of alkyne **15**[2] (400 mg, 1.22 mmol, 1.8 equiv.) in dry THF (25 mL) was added LiHMDS (1M in THF, 2.0 mL, 2.03 mmol, 3.0 equiv.) dropwisely at −78 °C. After the reaction was stirred for 30 min, aldehyde **16** (318 mg, 0.677 mmol, 1.0 equiv.) in dry THF (10 mL) was added dropwisely to the reaction, and the reaction was then allowed to be stirred at 0 °C. After being stirred for 4 h, the reaction was quenched by sat. NH_4Cl aq. (40 mL) and extracted with EtOAc (3×30 mL). The combined organic phases were washed with brine, dried over anhydrous Na_2SO_4, and concentrated in vacuo. Purification of the residue via column chromatography (petroleum ether:EtOAc, 5:2 v/v) furnished product **33a** (major isomer, 354 mg, 65%) and product **33b** (minor isomer, 30.4 mg, 6%) both as colorless oil, along with 297 mg alkyne **15** recovered.

33b: TLC (petroleum ether:EtOAc, 2:1 v/v): R_f = 0.31; ^{1}H NMR (400 MHz, $CDCl_3$): δ 7.40 (d, J = 6.8 Hz, 2H), 7.36 – 7.23 (m, 8H), 7.09 (d, J = 8.4 Hz, 2H), 6.73 (d, J = 8.4 Hz, 2H), 5.87 (d, J = 6.0 Hz, 1H), 5.78 – 5.72 (m, 1H), 5.15 (s, 1H), 4.94 (d, J = 12.0 Hz, 1H), 4.89 – 4.82 (m, 1H), 4.69 – 4.64 (m, 2H), 4.61 (d, J = 11.6 Hz, 1H), 4.43 (d, J = 12.0 Hz, 1H), 3.76 (s, 3H), 3.70 (s, 3H), 3.62 (dd, J = 10.8, 6.8 Hz, 1H), 3.56 (d, J = 2.4 Hz, 1H), 3.50 (d, J = 13.2 Hz, 1H), 3.40 (s, 3H), 3.35 (d, J = 8.8 Hz, 1H), 3.28 – 3.20 (m, 2H), 3.24 (s, 3H), 3.19 – 3.09 (m, 2H), 3.04 (brs, 1H), 3.01 – 2.90 (m, 2H), 2.77 (dd, J = 22.4, 11.2 Hz, 1H), 2.68 (d, J = 11.2 Hz, 1H), 2.57 (dt, J = 11.6, 6.4 Hz, 1H), 2.50 – 2.40 (m, 2H), 1.83 (d, J = 2.8 Hz, 1H), 1.39 (s, 3H), 1.34 (s, 3H); ^{13}C NMR (100 MHz, $CDCl_3$): δ 158.3, 138.9, 137.9, 134.5, 130.5, 130.5, 129.6, 129.6, 128.2, 128.2, 128.2, 127.9, 127.9, 127.4, 127.3, 127.3, 127.3, 113.4, 113.4, 110.9, 90.2, 90.1, 89.6, 86.3, 85.3, 84.5, 77.2, 76.3, 74.9, 71.9, 71.4, 71.4, 68.3, 61.4, 61.4, 60.2, 58.7, 57.0, 55.2, 54.4, 49.1, 46.3, 44.4, 40.4, 31.3, 29.5, 28.7; IR (neat): ν_{max} = 2918, 2850, 1512, 1454, 1243, 1175, 1147, 1102, 753 cm^{-1}; HRMS (*m/z*): $[M + H]^+$ calcd. for $C_{47}H_{60}NO_{10}$, 798.4212; found, 798.4216; $[\alpha]_D^{20}$ = +13.1 (*c* 0.31, $CHCl_3$).

33a: TLC (petroleum ether:EtOAc, 2:1 v/v): R_f = 0.28; ^{1}H NMR (600 MHz, $CDCl_3$): δ 7.38 (d, J = 7.2 Hz, 2H), 7.36 – 7.23 (m, 8H), 7.14 (d, J = 8.4 Hz, 2H), 6.80 (d, J = 8.4 Hz, 2H), 5.86 (d, J = 5.4 Hz, 1H), 5.76 – 5.71 (m, 1H), 5.12 (s, 1H), 4.93 (brs, 1H), 4.90 (d, J = 12.0 Hz, 1H), 4.64 – 4.60 (m, 2H), 4.57 (d, J = 11.4 Hz, 1H), 4.42 (d, J = 12.0 Hz, 1H), 3.78 (s, 3H), 3.69 (s, 3H), 3.55 (dd, J = 11.4, 6.0 Hz, 1H), 3.51 (d, J = 2.4 Hz, 1H), 3.47 – 3.37 (m, 3H), 3.44 (s, 3H), 3.21 (s, 3H), 3.17 (s, 1H), 3.13 (dd, J = 11.4, 6.0 Hz, 1H), 2.92 (d, J = 18.0 Hz, 1H), 2.81 (dd, J = 20.4, 12.0 Hz, 2H), 2.52 – 2.41 (m, 3H), 2.25 (d, J = 12.6 Hz, 1H), 2.12 (dd, J = 23.4, 11.4 Hz, 1H), 1.85 (brs, 1H), 1.35 (s, 3H), 1.32 (s, 3H); ^{13}C NMR (150 MHz, $CDCl_3$, some signals were hidden in the peaks of $CDCl_3$): δ 158.8, 138.5, 138.0, 134.5, 130.5, 130.1, 130.1, 129.0, 128.3, 128.3, 128.1, 128.1, 128.0, 128.0, 127.6, 127.6, 127.4, 113.8, 113.8, 110.9, 90.1, 90.1, 89.7, 85.2, 84.5, 84.1, 75.8, 74.2, 72.5, 71.6, 71.2, 68.1, 61.5, 61.1, 58.6, 58.2, 58.1, 57.0, 55.2, 49.9, 48.1, 45.0, 40.3, 30.9, 29.4, 28.7; IR (neat): ν_{max} = 3434, 2922, 1512, 1455, 1367, 1275, 1244, 1095 cm^{-1}; HRMS (*m/z*): $[M + H]^+$ calcd. for $C_{47}H_{60}NO_{10}$, 798.4212; found, 798.4214; $[\alpha]_D^{20}$ = −10.3 (*c* 0.18, $CHCl_3$).

(1*R*,5*R*,6*R*,8*S*,9*S*)-6-(Benzyloxy)-9-((4*R*,5*S*)-4-(benzyloxy)-5-((3a*R*,6a*S*)-2,2-dimethyl-4,6a-dihydro-3a*H*-cyclopenta[*d*][1,3]dioxol-3a-yl)-1,5-dimethoxypent-2-yn-1-yl)-8-methoxy-3-(4-methoxybenzyl)-5-(methoxymethyl)-3-azabicyclo[3.3.1]nonan-1-ol 34

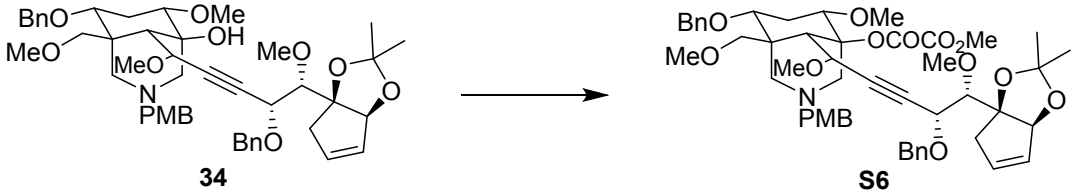


Under argon, to a solution of alcohol **33a** (282 mg, 0.353 mmol, 1.0 equiv.) in dry THF (20 mL) was added sodium hydride (60% dispersion in mineral oil, 32.5 mg, 0.813 mmol, 2.3 equiv.) in portions at 0 °C. After the reaction was stirred for 10 min, iodomethane (22.4 μL, 0.360 mmol, 1.02 equiv.) was added dropwisely to the solution, and the reaction was allowed to be stirred at 8 °C. The reaction was quenched by sat. NH_4Cl aq. (20 mL) at −5 °C after being

stirred for 1.7 h, and extracted with EtOAc (3×15 mL). The combined organic layer was washed with brine, dried over anhydrous Na_2SO_4, and concentrated in vacuo. Purification of the residue via column chromatography (petroleum ether:EtOAc, 4:1 v/v) furnished product **34** (255 mg, 89%) as a white foam.

TLC (petroleum ether:EtOAc, 3:1 v/v): R_f = 0.32; ^{1}H NMR (400 MHz, $CDCl_3$): δ 7.41 – 7.24 (m, 10H), 7.17 (d, J = 8.4 Hz, 2H), 6.76 (d, J = 8.4 Hz, 2H), 5.86 (d, J = 5.6 Hz, 1H), 5.75 (d, J = 5.6 Hz, 1H), 5.13 (s, 1H), 4.89 (d, J = 12.0 Hz, 1H), 4.70 – 4.51 (m, 4H), 4.45 (d, J = 12.0 Hz, 1H), 3.76 (s, 3H), 3.72 – 3.62 (m, 1H), 3.70 (s, 3H), 3.54 – 3.46 (m, 2H), 3.44 (s, 3H), 3.42 (s, 3H), 3.31 (d, J = 9.2 Hz, 1H), 3.27 – 3.11 (m, 3H), 3.20 (s, 3H), 3.06 (s, 1H), 3.02 (d, J = 10.4 Hz, 1H), 2.96 – 2.81 (m, 2H), 2.72 (d, J = 11.2 Hz, 1H), 2.65 (d, J = 10.4 Hz, 1H), 2.56 – 2.42 (m, 2H), 2.26 (d, J = 11.2 Hz, 1H), 1.80 (s, 1H), 1.36 (s, 3H), 1.33 (s, 3H); ^{13}C NMR (150 MHz, $CDCl_3$): δ 158.3, 139.3, 137.8, 134.4, 130.8, 130.5, 129.6, 129.6, 128.1, 128.1, 128.1, 128.1, 128.1, 127.5, 127.3, 127.3, 127.2, 113.3, 113.3, 110.9, 90.1, 90.0, 86.7, 86.6, 85.3, 84.4, 77.2, 75.9, 73.2, 72.1, 71.3, 71.2, 69.5, 68.1, 61.7, 61.3, 58.4, 57.8, 56.9, 55.3, 55.2, 49.6, 46.7, 45.0, 40.2, 32.0, 29.4, 28.7; IR (neat): ν_{max} = 2920, 1612, 1511, 1454, 1354, 1243, 1100 cm^{-1}; HRMS (*m/z*): [M + H]$^+$ calcd. for $C_{48}H_{62}NO_{10}$, 812.4368; found, 812.4374; $[\alpha]_D^{20}$ = −1.6 (*c* 0.32, $CHCl_3$).

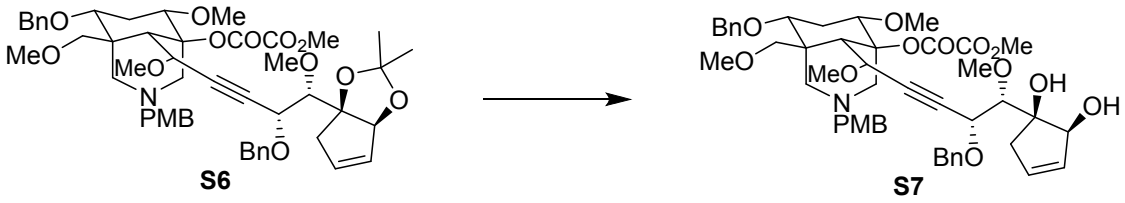
(1*R*,5*R*,6*R*,8*S*,9*S*)-6-(Benzyloxy)-9-((4*R*,5*S*)-4-(benzyloxy)-5-((3a*R*,6a*S*)-2,2-dimethyl-4,6a-dihydro-3a*H*-cyclopenta[*d*][1,3]dioxol-3a-yl)-1,5-dimethoxypent-2-yn-1-yl)-8-methoxy-3-(4-methoxybenzyl)-5-(methoxymethyl)-3-azabicyclo[3.3.1]nonan-1-yl methyl oxalate S6



At 0 °C, compound **34** (205 mg, 0.252 mmol, 1.0 equiv.), Et_3N (281 μL, 2.02 mmol, 8.0 equiv.) and DMAP (30.7 mg, 0.252 mmol, 1.0 equiv.) were dissolved in dry CH_2Cl_2 (20 mL) under argon, followed by dropwise addition of methyl oxalyl chloride (93 μL, 1.01mmol, 4.0 equiv.), and the reaction was then allowed to be stirred at 40 °C. After being stirred for 2.5 h, the reaction was quenched by sat. NH_4Cl aq. (25 mL) and extracted with CH_2Cl_2 (2×20 mL). The combined organic phases were washed with brine, dried over anhydrous Na_2SO_4, and concentrated in vacuo. Purification of the residue via column chromatography (petroleum ether:EtOAc, 15:2 v/v) furnished product **S6** (177 mg, 78%) as a colorless oil.

TLC (petroleum ether:EtOAc, 3:1 v/v): R_f = 0.60; ^{1}H NMR (600 MHz, $CDCl_3$): δ 7.39 (d, J = 7.2 Hz, 2H), 7.35 – 7.24 (m, 8H), 7.18 (d, J = 8.4 Hz, 2H), 6.77 (d, J = 8.4 Hz, 2H), 5.85 (d, J = 4.2 Hz, 1H), 5.74 (brs, 1H), 5.12 (s, 1H), 4.83 (d, J = 12.0 Hz, 1H), 4.67 (d, J = 11.4 Hz, 1H), 4.55 – 4.41 (m, 4H), 3.93 – 3.74 (m, 1H), 3.82 (s, 3H), 3.77 (s, 3H), 3.70 (dd, J = 10.8, 7.2 Hz,1H), 3.66 (s, 3H), 3.52 (d, J = 13.2 Hz, 1H), 3.47 (s, 1H), 3.38 (s, 3H), 3.36 – 3.29 (m, 2H), 3.33 (s, 3H), 3.24 (t, J = 9.0 Hz, 2H), 3.20 (s, 3H), 3.00 – 2.88 (m, 3H), 2.74 (d, J = 10.8 Hz, 1H), 2.64 – 2.56 (m, 2H), 2.47 – 2.39 (m, 2H), 1.39 (s, 3H), 1.33 (s, 3H); ^{13}C NMR (150 MHz, $CDCl_3$, some signals were hidden in the peaks of $CDCl_3$): δ 158.46, 158.39, 156.53, 139.11, 137.87, 134.47, 130.50, 130.35, 129.69, 129.69, 128.16, 128.16, 128.11, 128.11, 128.09, 127.41, 127.31, 127.31, 127.26, 113.43, 113.43, 110.93, 90.25, 89.97, 87.86, 86.89, 85.62, 85.16, 76.53, 75.36, 71.70, 71.49, 71.47, 69.39, 68.68, 61.50, 61.41, 58.52, 57.02, 56.85, 55.18, 53.24, 52.50, 49.48, 45.77, 42.25, 40.50, 32.31, 29.22, 28.66; IR (neat): ν_{max} = 2927, 1766, 1743, 1512, 1454, 1244, 1205, 1173, 1108 cm^{-1}; HRMS (*m/z*): [M + H]$^+$ calcd. for $C_{51}H_{64}NO_{13}$, 898.4372; found, 898.4373; $[\alpha]_D^{20}$ = −9.5 (*c* 0.17, $CHCl_3$).

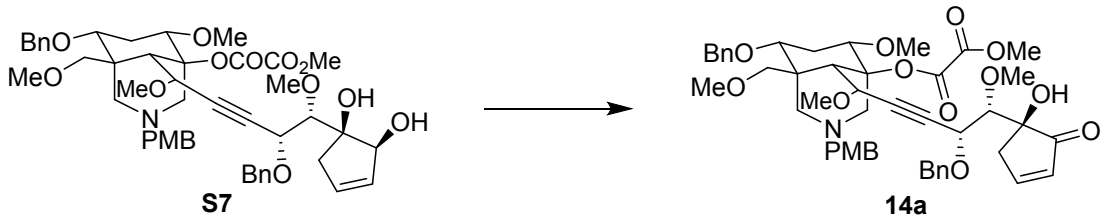
(1*R*,5*R*,6*R*,8*S*,9*S*)-6-(Benzyloxy)-9-((4*R*,5*S*)-4-(benzyloxy)-5-((1*R*,2*S*)-1,2-dihydroxycyclopent-3-en-1-yl)-1,5-dimethoxypent-2-yn-1-yl)-8-methoxy-3-(4-methoxybenzyl)-5-(methoxymethyl)-3-azabicyclo[3.3.1]nonan-1-yl methyl oxalate S7



To a solution of compound **S6** (120 mg, 0.134 mmol, 1.0 equiv.) in MeOH (9 mL) was added *p*-toluenesulfonic acid monohydrate (203 mg, 1.07 mmol, 8.0 equiv.). After being stirred for 16 h at room temperature, the reaction was treated with H_2O (45 mL) and extracted with EtOAc (3×20 mL). The combined organic phases were washed with brine, dried over anhydrous Na_2SO_4, and concentrated in vacuo. Purification of the residue via column chromatography (petroleum ether:EtOAc, 2:1 v/v) furnished product **S7** (63.1 mg, 55%, 85% brsm) as a colorless oil, along with 42 mg compound **S6** recovered.

TLC (petroleum ether:EtOAc, 2:1 v/v): R_f = 0.20; ^{1}H NMR (400 MHz, $CDCl_3$): δ 7.38 – 7.27 (m, 10H), 7.19 (d, J = 8.4 Hz, 2H), 6.78 (d, J = 8.4 Hz, 2H), 5.81 (d, J = 4.0 Hz, 1H), 5.63 (d, J = 5.6 Hz, 1H), 4.83 (d, J = 11.6 Hz, 1H), 4.73 – 4.64 (m, 2H), 4.58 (d, J = 1.6 Hz, 1H), 4.54 – 4.42 (m, 4H), 3.81 (s, 3H), 3.77 (s, 3H), 3.73 – 3.67 (m, 2H), 3.66 (s, 3H), 3.55 (d, J = 13.2 Hz, 1H), 3.42 – 3.36 (m, 2H), 3.39 (s, 3H), 3.35 – 3.29 (m, 1H), 3.33 (s, 3H), 3.25 (d, J = 10.4 Hz, 1H), 3.21 (s, 3H), 3.12 (d, J = 9.6 Hz, 1H), 3.03 – 2.92 (m, 2H), 2.74 (d, J = 10.8 Hz, 1H), 2.71 – 2.55 (m, 4H), 2.43 (d, J = 17.2 Hz, 1H), 2.33 (d, J = 10.8 Hz, 1H); ^{13}C NMR (150 MHz, $CDCl_3$): δ 158.6, 158.4, 156.7, 139.0, 137.2, 131.6, 130.8, 130.3, 129.7, 129.7, 128.4, 128.4, 128.4, 128.4, 128.2, 128.2, 127.9, 127.3, 127.3, 127.3, 113.4, 113.4, 87.9, 86.4, 85.3, 84.9, 81.8, 78.7, 76.4, 75.2, 71.7, 71.6, 71.4, 69.6, 69.3, 61.5, 61.4, 58.7, 57.0, 56.9, 55.2, 53.4, 52.8, 49.5, 45.8, 42.6, 42.1, 32.1; IR (neat): ν_{max} = 2920, 1764, 1742, 1512, 1454, 1332, 1206, 1173, 1110 cm^{-1}; HRMS (*m/z*): $[M + Na]^+$ calcd. for $C_{48}H_{59}NNaO_{13}$, 880.3879; found, 880.3884; $[\alpha]_D^{20}$ = −5.0 (*c* 0.56, $CHCl_3$).

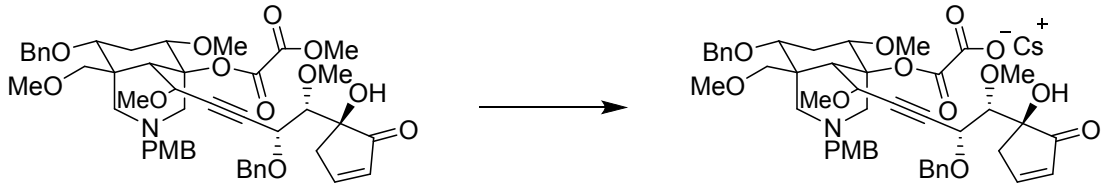
(1*R*,5*R*,6*R*,8*S*,9*S*)-6-(Benzyloxy)-9-((4*R*,5*S*)-4-(benzyloxy)-5-((*S*)-1-hydroxy-2-oxocyclopent-3-en-1-yl)-1,5-dimethoxypent-2-yn-1-yl)-8-methoxy-3-(4-methoxybenzyl)-5-(methoxymethyl)-3-azabicyclo[3.3.1]nonan-1-yl methyl oxalate 14a



Under argon, to a solution of DMSO (15.9 μL, 0.224 mmol, 6.0 equiv.) in dry CH_2Cl_2 (2 mL) was added oxalyl chloride (15.8 μL, 0.186 mmol, 5.0 equiv.) at −78 °C. The reaction was stirred for 45 min, followed by dropwise addition of compound **S8** (32 mg, 0.037 mmol, 1.0 equiv.) in dry CH_2Cl_2 (1.5 mL). After being stirred for 3 h at −78 °C, the reaction was treated with Et_3N (67.4 μL, 0.485 mmol, 13.0 equiv.) and allowed to be stirred at room temperature for 2 h. The reaction mixture was then quenched by sat. NH_4Cl aq. (5 mL) and extracted with CH_2Cl_2 (3×3 mL). The combined organic phases were washed with brine, dried over anhydrous Na_2SO_4, and concentrated in vacuo. Purification of the residue via column chromatography (petroleum ether:EtOAc, 5:2 v/v) furnished product **14a** (25.0 mg, 78%) as a colorless oil.

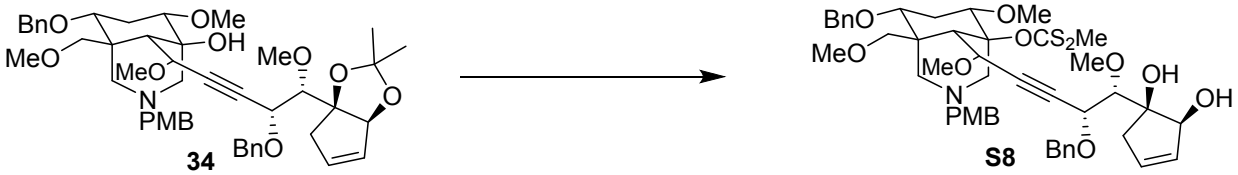
TLC (petroleum ether:EtOAc, 2:1 v/v): R_f = 0.30; ^{1}H NMR (400 MHz, $CDCl_3$): δ 7.77 (d, J = 6.0 Hz, 1H), 7.41 – 7.24 (m, 10H), 7.20 (d, J = 8.4 Hz, 2H), 6.78 (d, J = 8.4 Hz, 2H), 6.19 (d, J = 6.0 Hz, 1H), 4.80 (d, J = 11.6 Hz, 1H), 4.68 (d, J = 11.8 Hz, 1H), 4.60 (s, 1H), 4.57 – 4.40 (m, 4H), 3.89 (s, 3H), 3.77 (s, 3H), 3.69 (dd, J = 10.8, 6.4 Hz, 1H), 3.55 (d, J = 13.6 Hz, 1H), 3.50 (d, J = 2.4 Hz, 1H), 3.45 – 3.39 (m, 1H), 3.43 (s, 3H), 3.39 – 3.35 (m, 1H), 3.37 (s, 3H), 3.34 – 3.28 (m, 1H), 3.33 (s, 3H), 3.24 (d, J = 10.0 Hz, 1H), 3.21 (s, 3H), 3.09 (d, J = 9.6 Hz, 1H), 3.04 – 2.92 (m, 2H), 2.84 (s, 1H), 2.73 (d, J = 10.4 Hz, 1H), 2.61 (dt, J = 11.2, 6.4 Hz, 1H), 2.56 – 2.44 (m, 2H), 2.32 (d, J = 10.8 Hz, 1H); ^{13}C NMR (150 MHz, $CDCl_3$): δ 210.2, 166.1, 158.7, 158.4, 156.6, 139.0, 137.5, 130.8, 130.3, 129.7, 129.7, 128.3, 128.3, 128.3, 128.3, 128.3, 128.2, 128.2, 127.8, 127.3, 127.3, 113.4, 113.4, 87.9, 86.1, 85.3, 83.7, 76.4, 75.5, 75.2, 71.8, 71.6, 71.4, 69.5, 68.2, 61.4, 61.3, 58.7, 56.9, 56.8, 55.2, 53.7, 52.8, 49.5, 45.9, 42.1, 39.8, 32.1; IR (neat): ν_{max} = 2931, 1764, 1742, 1713, 1512, 1454, 1245, 1206, 1174, 1109, 1088 cm^{-1}; HRMS (*m/z*): $[M + Na]^+$ calcd. for $C_{48}H_{57}NNaO_{13}$, 878.3722; found, 878.3710; $[\alpha]_D^{20}$= +7.9 (*c* 0.14, $CHCl_3$).

Cesium 2-(((1*R*,5*R*,6*R*,8*S*,9*S*)-6-(benzyloxy)-9-((4*R*,5*S*)-4-(benzyloxy)-5-((*S*)-1-hydroxy-2-oxocyclopent-3-en-1-yl)-1,5-dimethoxypent-2-yn-1-yl)-8-methoxy-3-(4-methoxybenzyl)-5-(methoxymethyl)-3-azabicyclo[3.3.1]nonan-1-yl)oxy)-2-oxoacetate 14b



To a solution of compound **14a** (5.3 mg, 0.0062 mmol, 1.0 equiv.) in THF:H_2O (1:1) of 0.5 mL was added 50% CsOH aq. (1.86 mg, 0.0062mmol, 1.0 equiv.). After being stirred for 5 min at room temperature, the reaction mixture was concentrated in vacuo and dried by a lyophilizer to give compound **14b** as a white powder. *Note: compound **14b** was determined by LC-MS (See **LC-MS data**).*

***O*-((1*R*,5*R*,6*R*,8*S*,9*S*)-6-(Benzyloxy)-9-((4*R*,5*S*)-4-(benzyloxy)-5-((1*R*,2*S*)-1,2-dihydroxycyclopent-3-en-1-yl)-1,5-dimethoxypent-2-yn-1-yl)-8-methoxy-3-(4-methoxybenzyl)-5-(methoxymethyl)-3-azabicyclo[3.3.1]nonan-1-yl) *S*-methyl carbonodithioate S8**

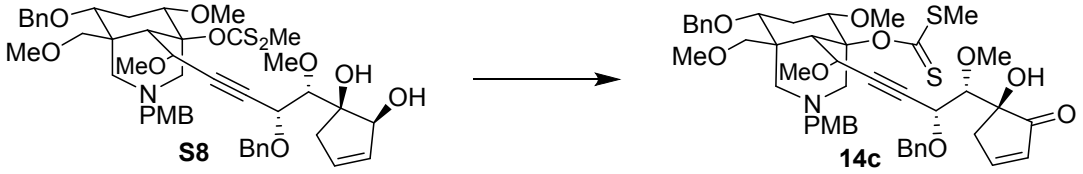


Under argon, to a solution of compound **34** (115 mg, 0.142 mmol, 1.0 equiv.) in dry THF (12 mL) was added sodium hydride (60% dispersion in mineral oil, 56.6 mg, 1.42 mmol, 10.0 equiv.) in portions at 0 °C. After the reaction was stirred for 10 min, carbon disulfide (85 μL, 1.42 mmol, 10.0 equiv.) was added dropwisely to the solution, and the reaction was stirred for 2 h at 0 °C. To the reaction mixture was added iodomethane (62 μL, 0.991 mmol, 7.0 equiv.) dropwisely, and after being stirred for 8 h at 0 °C, the reaction was quenched by sat. NH_4Cl aq. (20 mL) and extracted with EtOAc (3×15 mL). The combined organic phases were washed with brine, dried over anhydrous Na_2SO_4, and concentrated in vacuo to give crude product. To a solution of the crude product in MeOH (8 mL) was added *p*-toluenesulfonic acid monohydrate (215 mg, 1.13 mmol, 8.0 equiv.). After being stirred for 16 h at room temperature, the reaction was quenched by sat. $NaHCO_3$ aq. (10 mL) and concentrated in vacuo, and the mixture was then extracted with

EtOAc (3×8 mL). The combined organic phases were washed with brine, dried over anhydrous Na_2SO_4, and concentrated in vacuo. Purification of the residue via column chromatography (petroleum ether:EtOAc, 2:1 v/v) furnished product **S8** (29.8 mg, 24% for 2 steps) as a colorless oil.

TLC (petroleum ether:EtOAc, 3:2 v/v): R_f = 0.33; ^{1}H NMR (400 MHz, $CDCl_3$): δ 7.40 – 7.23 (m, 10H), 7.16 (d, J = 8.4 Hz, 2H), 6.77 (d, J = 8.4 Hz, 2H), 5.83 (d, J = 4.8 Hz, 1H), 5.65 (d, J = 4.8 Hz, 1H), 5.14 (dd, J = 10.0, 7.2 Hz, 1H), 4.89 (d, J = 11.6 Hz, 1H), 4.74 – 4.54 (m, 4H), 4.47 (d, J = 12.0 Hz, 1H), 4.38 (s, 1H), 3.83 – 3.74 (m, 1H), 3.77 (s, 3H), 3.74 – 3.65 (m, 1H), 3.68 (s, 3H), 3.56 (d, J = 13.2 Hz, 1H), 3.49 (d, J = 3.6 Hz, 1H), 3.39 – 3.30 (m, 1H), 3.39 (s, 3H), 3.36 (s, 3H), 3.31 – 3.24 (m, 4H), 3.21 (s, 3H), 3.07 – 2.88 (m, 2H), 2.82 – 2.68 (m, 3H), 2.67 – 2.49 (m, 3H), 2.46 (s, 3H); ^{13}C NMR (150 MHz, $CDCl_3$): δ 213.2, 158.4, 139.3, 136.9, 131.6, 130.9, 130.3, 129.6, 129.6, 128.5, 128.5, 128.3, 128.3, 128.1, 128.1, 128.1, 127.2, 127.2, 127.2, 113.4, 113.4, 93.4, 87.3, 87.1, 85.1, 81.9, 78.8, 75.4, 74.8, 71.9, 71.8, 71.5, 69.4, 68.9, 61.5, 61.3, 58.4, 57.5, 57.1, 55.2, 52.9, 49.1, 45.9, 42.7, 42.5, 33.0, 19.3; IR (neat): ν_{max} = 3446, 2919, 1511, 1454, 1240, 1110, 1033 cm^{-1}; HRMS (*m/z*): $[M + H]^+$ calcd. for $C_{47}H_{60}NO_{10}S_2$, 862.3653; found, 862.3662; $[\alpha]_D^{20}$ = −32.7 (*c* 0.21, $CHCl_3$).

_O_-((1_R_,5_R_,6_R_,8_S_,9_S_)-6-(Benzyloxy)-9-((4_R_,5_S_)-4-(benzyloxy)-5-((_S_)-1-hydroxy-2-oxocyclopent-3-en-1-yl)-1,5-dimethoxypent-2-yn-1-yl)-8-methoxy-3-(4-methoxybenzyl)-5-(methoxymethyl)-3-azabicyclo[3.3.1]nonan-1-yl) _S_-methyl carbonodithioate 14c



Under argon, to a solution of DMSO (8.7 μL, 0.122 mmol, 13.0 equiv.) in dry CH_2Cl_2 (0.8 mL) was added oxalyl chloride (4.8 μL, 0.056 mmol, 6.0 equiv.) at −78 °C. The reaction was stirred for 45 min, followed by dropwise addition of compound **S8** (8.1 mg, 9.40 μmol, 1.0 equiv.) in dry CH_2Cl_2 (0.5 mL). After being stirred for 3 h at −78 °C, the reaction was treated with Et_3N (23.5 μL, 0.169 mmol, 18.0 equiv.) and allowed to be stirred at room temperature for 2 h. The reaction mixture was then quenched by sat. NH_4Cl aq. (2 mL) and extracted with CH_2Cl_2 (3×1 mL). The combined organic phases were washed with brine, dried over anhydrous Na_2SO_4, and concentrated in vacuo. Purification of the residue via column chromatography (petroleum ether:acetone, 4:1 v/v) furnished product **14c** (6.1 mg, 75%) as a colorless oil.

TLC (petroleum ether:EtOAc, 3:2 v/v): R_f = 0.45; ^{1}H NMR (400 MHz, $CDCl_3$): δ 7.80 (d, J = 5.6 Hz, 1H), 7.42 – 7.25 (m, 10H), 7.15 (d, J = 8.4 Hz, 2H), 6.77 (d, J = 8.4 Hz, 2H), 6.23 (d, J = 5.6 Hz, 1H), 5.12 (dd, J = 9.2, 8.0 Hz, 1H), 4.87 (d, J = 11.6 Hz, 1H), 4.66 – 4.56 (m, 3H), 4.48 (d, J = 11.6 Hz, 1H), 4.37 (s, 1H), 3.77 (s, 3H), 3.73 – 3.68 (m, 1H), 3.62 (s, 1H), 3.56 (d, J = 13.2 Hz, 1H), 3.50 – 3.42 (m, 2H), 3.45 (s, 3H), 3.41 – 3.33 (m, 1H), 3.37 (s, 3H), 3.36 (s, 3H), 3.32 – 3.24 (m, 3H), 3.21 (s, 3H), 3.06 (d, J = 9.6 Hz, 1H), 2.99 – 2.91 (m, 1H), 2.85 (brs, 1H), 2.77 (d, J = 10.8 Hz, 1H), 2.69 – 2.63 (m, 1H), 2.60 – 2.53 (m, 2H), 2.47 (s, 3H); ^{13}C NMR (150 MHz, $CDCl_3$): δ 213.06, 210.10, 166.16, 158.32, 139.30, 137.16, 130.84, 130.27, 129.70, 129.70, 128.42, 128.42, 128.24, 128.24, 128.12, 128.12, 127.92, 127.25, 127.25, 127.18, 113.47, 113.47, 93.49, 87.42, 86.78, 83.88, 75.92, 75.48, 74.83, 71.95, 71.65, 71.48, 68.74, 68.51, 61.25, 58.34, 57.37, 57.14, 55.21, 52.75, 49.03, 45.85, 42.67, 40.12, 33.05, 29.70, 19.31; IR (neat): ν_{max} = 2924, 1713, 1511, 1455, 1244, 1091, 1032 cm^{-1}; HRMS (*m/z*): $[M + H]^+$ calcd. for $C_{47}H_{58}NO_{10}S_2$, 860.3497; found, 860.3505; $[\alpha]_D^{20}$ = −19.0 (*c* 0.17, $CHCl_3$).

References:

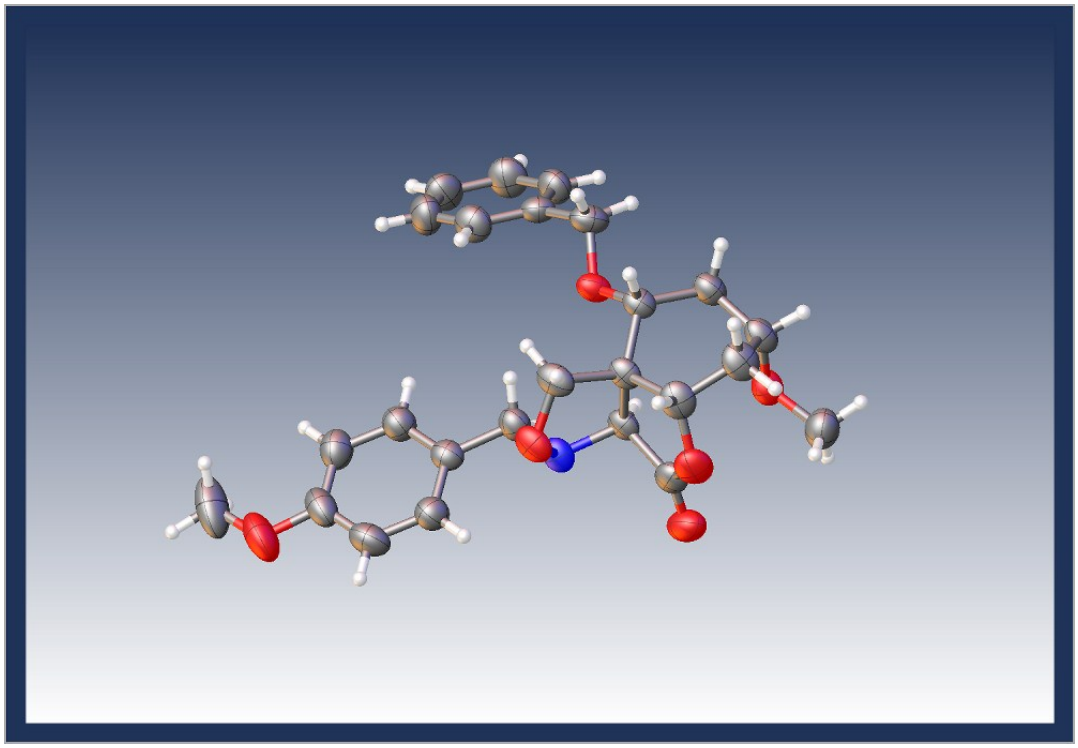
[1] Perrin, D. D., Armarego, W. L. F. and Perrin, D. R., Pergamon Press: Oxford, 1980.

[2] X.-H. Zhou, Y. Liu, R.-J. Zhou, H. Song, X.-Y. Liu and Y. Qin, *Chem. Commun.*, 2018, **54**, 12258.

X-ray crystallographic data

X-ray crystallographic data for 18.

A white single crystal of **18** was obtained by crystallization in a mixture of petroleum ether:EtOAc (2:1). Crystallographic data for x has been deposited in the Cambrige Crystallographic Data Centre (CCDC 1837272).



Crystal data and structure refinement for CCDC 1837272.

Identification code	141208_s1_wxp_m
Empirical formula	$C_{25}H_{29}NO_6$
Formula weight	439.49
Temperature/K	293.15
Crystal system	orthorhombic
Space group	$P2_12_12_1$
a/Å	8.4244(5)
b/Å	9.7309(4)
c/Å	27.0602(12)
α/°	90
β/°	90
γ/°	90
Volume/Å3	2218.3(2)
Z	4
ρ_{calc}mg/mm^3	1.316

m/mm^{-1}	0.094
F(000)	936.0
Crystal size/mm^3	0.3 × 0.2 × 0.2
Radiation	MoKα (λ = 0.71073)
2Θ range for data collection/°	6.022 to 52.742
Index ranges	−10 ≤ h ≤ 10, −12 ≤ k ≤ 11, −33 ≤ l ≤ 33
Reflections collected	9246
Independent reflections	4471 [R_{int} = 0.0236, R_{sigma} = 0.0462]
Data/restraints/parameters	4471/0/291
Goodness-of-fit on F^2	1.043
Final R indexes [I>=2σ (I)]	R_1 = 0.0502, wR_2 = 0.0899
Final R indexes [all data]	R_1 = 0.0756, wR_2 = 0.1002
Largest diff. peak/hole / e Å^{-3}	0.13/–0.15
Flack parameter	–0.5(6)

LC-MS data

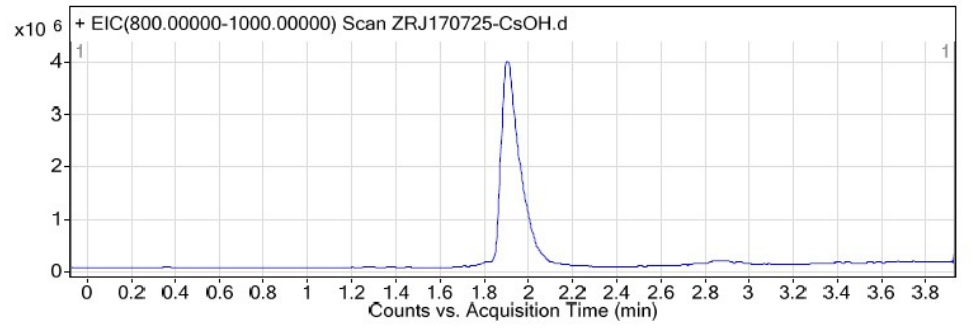
LC-MS data for 14b.

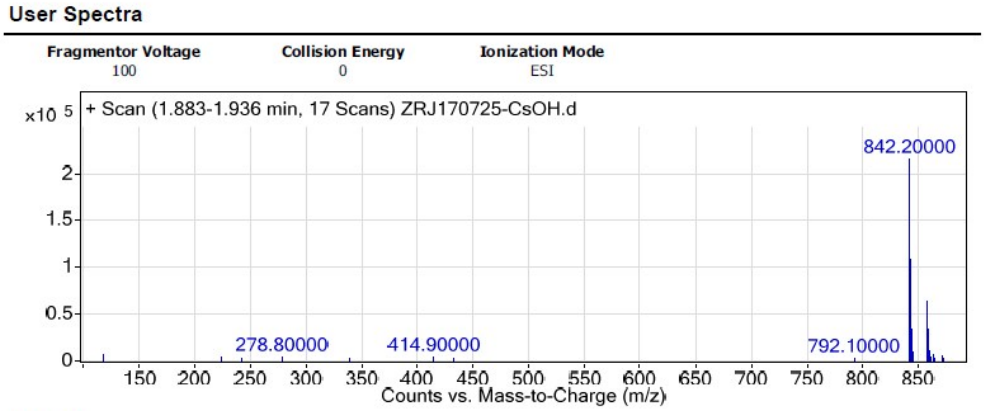
Qualitative Analysis Report

Data Filename	ZRJ170725-CsOH.d	**Sample Name**	
Sample Type	Sample	**Position**	P1-D1
Instrument Name	Instrument 1	**User Name**	
Acq Method	xin.m	**Acquired Time**	7/25/2017 20:57:21
IRM Calibration Status	Not Applicable	**DA Method**	3.m
Comment			
Sample Group		**Info.**	
Acquisition SW Version	6400 Series Triple Quadrupole B.07.00		

User Chromatograms

Fragmentor Voltage 100 **Collision Energy** 0 **Ionization Mode** ESI



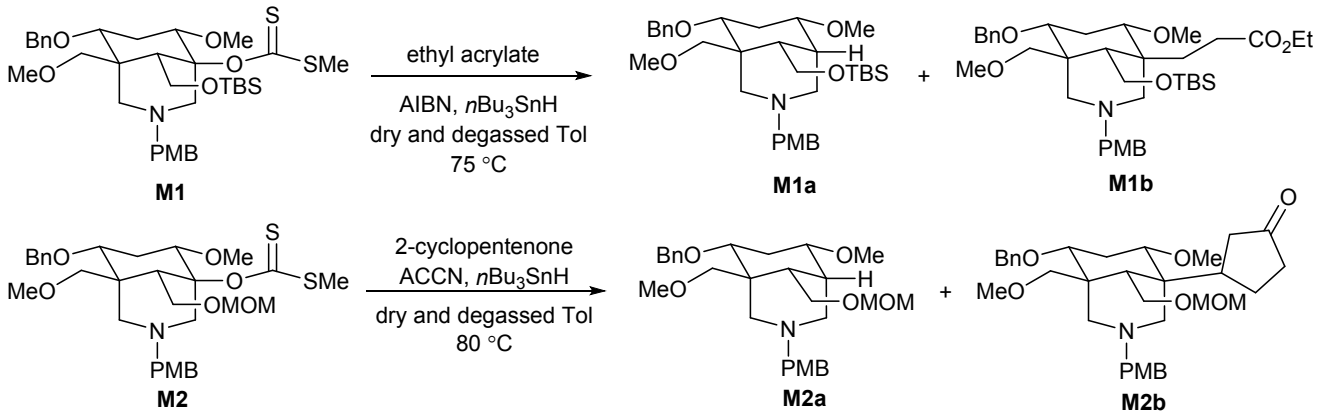


Peak List

m/z	Abund
118	6092.28
842.2	215332.67
843.2	108406.59
844.2	33317.47
845.2	8463.07
858.2	62693.21
859.2	33038.87
860.2	10519.87
864.2	6039.82
872.3	5034.96

--- End Of Report ---

Notes of model reaction on simplified substrates M1 and M2

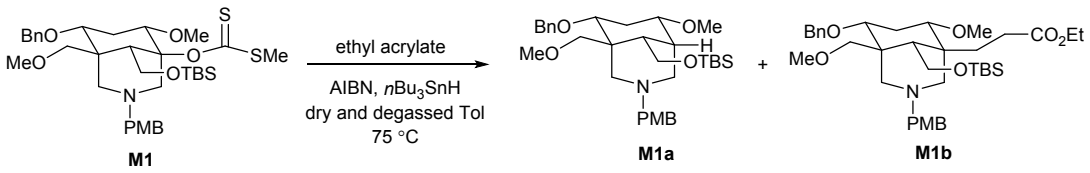


Scheme S1. Intermolecular radical model reaction

Notes: we had tested the model reaction using simplified substrates before the key radical cascade reactions were implemented on **14b** and **14c**. As shown in Scheme S1, intermolecular radical reaction on simplified AE bicyclic derivatives **M1** and **M2** with Michael acceptors were tested. The reactions proved complicated, but LC-MS did detected the signals of C11-deoxygenated products (**M1a** and **M2a**) and the desired coupling products (**M1b** and **M2b**). Although the amount of these products were not enough for NMR analysis, it did demonstrate that C11 radical activation strategy could be worked under such circumstances. So, we proceeded to investigate the intramolecular radical cascade reaction on **14b** and **14c**. Unfortunately, substrates decomposed quickly along with the progression of the reaction, without noticeable signals of valuable products. As there is no prior example of

similar radical cascade succeeded under such complex system, we hope our trial would benefit further exploration of the synthesis of C19-diterpernoid alkaloids.

LC-MS data of model experiment I



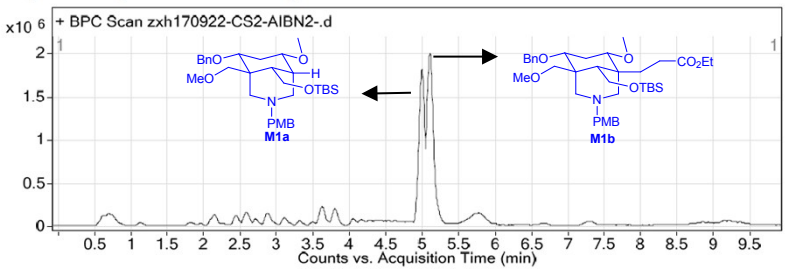
Qualitative Analysis Report

Data Filename	zxh170922-CS2-AIBN2-.d	**Sample Name**	
Sample Type	Sample	**Position**	P2-A3
Instrument Name	Instrument 1	**User Name**	
Acq Method	60-98%.m	**Acquired Time**	9/22/2017 17:21:35
IRM Calibration Status	Not Applicable	**DA Method**	42.m
Comment			

Sample Group	**Info.**
Acquisition SW Version	6400 Series Triple Quadrupole B.07.00

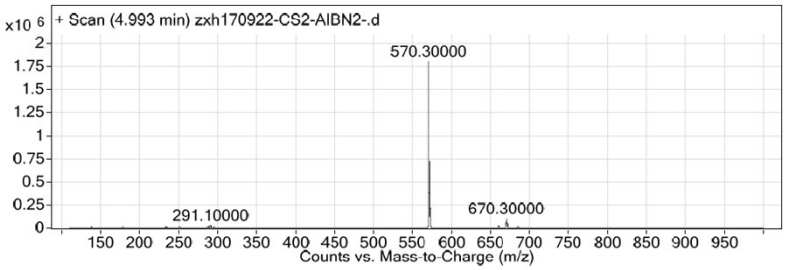
User Chromatograms

Fragmentor Voltage 120 **Collision Energy** 0 **Ionization Mode** ESI



User Spectra

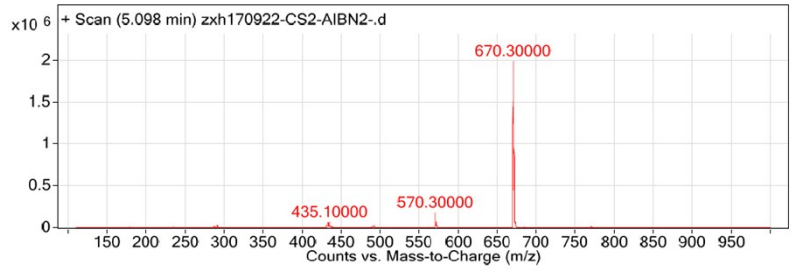
Fragmentor Voltage 120 **Collision Energy** 0 **Ionization Mode** ESI



Peak List

m/z	z	Abund
289.1		21079.34
291.1		25353.16
570.3	1	1807335.13
571.3	1	727016.63
572.3	1	218869.75
573.3	1	48839.3
660.2		20244.18
670.3	1	99564.33
671.4	1	49120.36

Fragmentor Voltage	Collision Energy	Ionization Mode
120	0	ESI



Peak List

m/z	z	Abund
431.1		33676
433.1	1	57531.66
434	1	29186.4
435.1	1	69506.91
570.3	1	181558
571.3	1	72896.8
670.3	1	1995220.5
671.4	1	965279.19
672.3	1	314267.91
673.3	1	72525.05

--- End Of Report ---

LC-MS data of compound M1

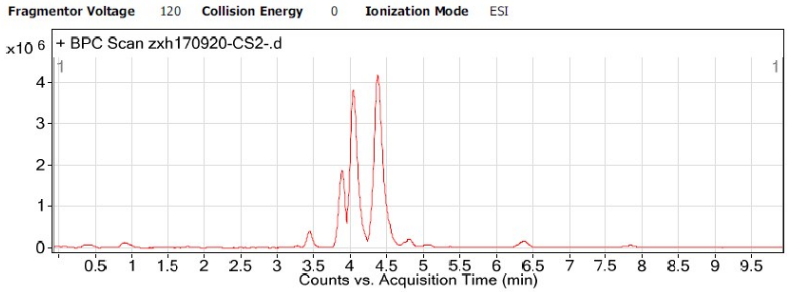
Qualitative Analysis Report

Data Filename	zxh170920-CS2-.d	**Sample Name**	
Sample Type	Sample	**Position**	P1-A9
Instrument Name	Instrument 1	**User Name**	
Acq Method	60-98%.m	**Acquired Time**	9/21/2017 11:10:32
IRM Calibration Status	Not Applicable	**DA Method**	42.m
Comment			

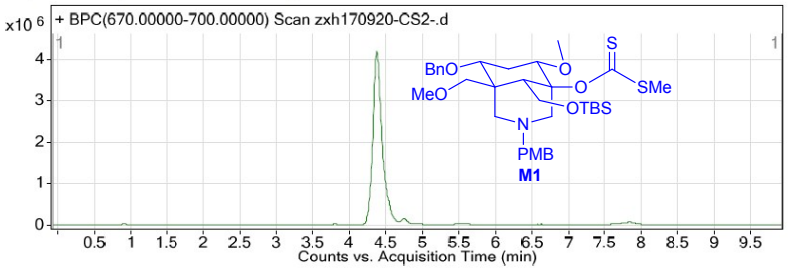
Sample Group		**Info.**
Acquisition SW Version	6400 Series Triple Quadrupole B.07.00	

User Chromatograms

Fragmentor Voltage	Collision Energy	Ionization Mode
120	0	ESI

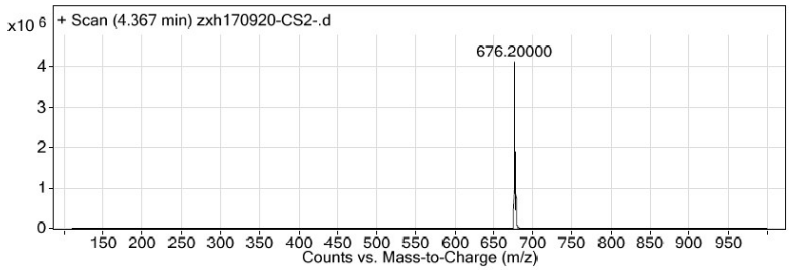


Fragmentor Voltage	Collision Energy	Ionization Mode
120	0	ESI



User Spectra

Fragmentor Voltage	Collision Energy	Ionization Mode
120	0	ESI

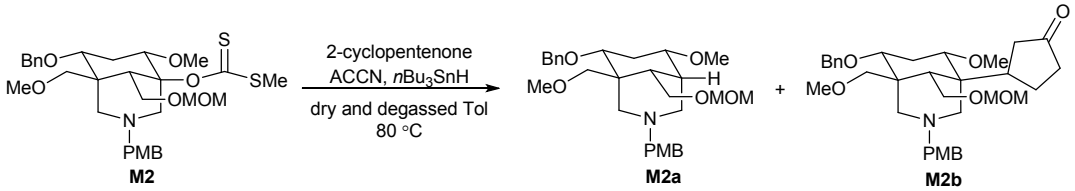


Peak List

m/z	z	Abund
676.2	1	4136917.5
677.2	1	1894596.88
678.2	1	879804.44
679.2	1	268317.69
680.3	1	81857.47

--- End Of Report ---

LC-MS data of model experiment II



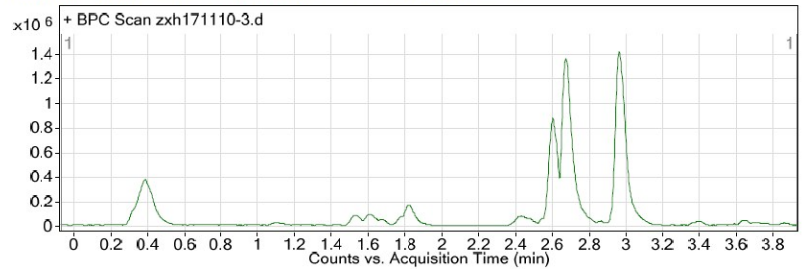
Qualitative Analysis Report

Data Filename	zxh171110-3.d	**Sample Name**	
Sample Type	Sample	**Position**	P2-C5
Instrument Name	Instrument 1	**User Name**	
Acq Method	xin.m	**Acquired Time**	11/10/2017 09:52:32
IRM Calibration Status	Not Applicable	**DA Method**	42.m
Comment			

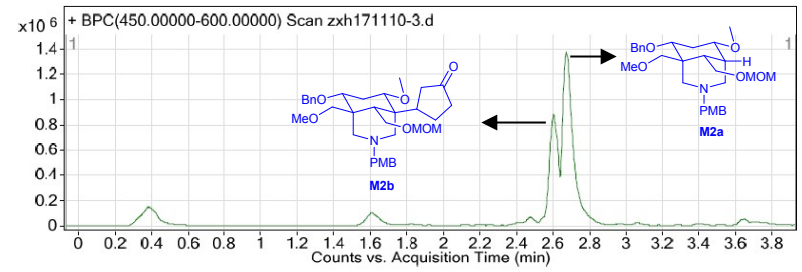
Sample Group		**Info.**
Acquisition SW Version	6400 Series Triple Quadrupole B.07.00	

User Chromatograms

Fragmentor Voltage 100 **Collision Energy** 0 **Ionization Mode** ESI

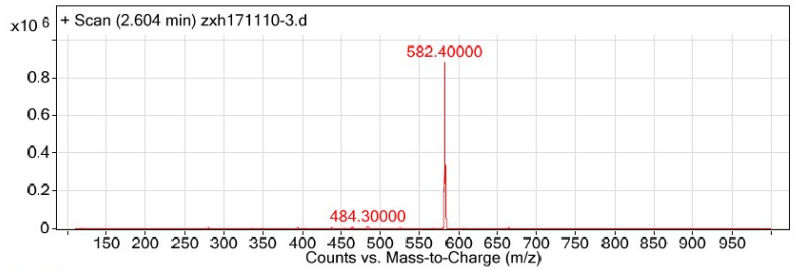


Fragmentor Voltage 100 **Collision Energy** 0 **Ionization Mode** ESI



User Spectra

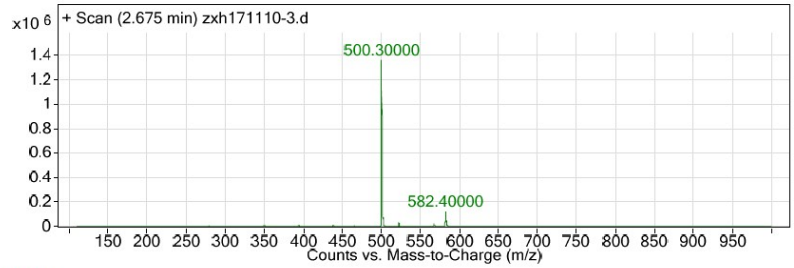
Fragmentor Voltage	Collision Energy	Ionization Mode
100	0	ESI



Peak List

m/z	z	Abund
465.3		9340.32
484.3		12719.54
582.4	1	882779
583.4	1	339234.72
584.4	1	68839.2
585.4	1	11727.92

Fragmentor Voltage 100 **Collision Energy** 0 **Ionization Mode** ESI



Peak List

m/z	z	Abund
500.3	1	1363875.75
501.3	1	409119
502.3	1	77236.47
522.4		35806.54
567.4		26039.02
582.4	1	121241.15
583.4	1	45834.86

--- End Of Report ---

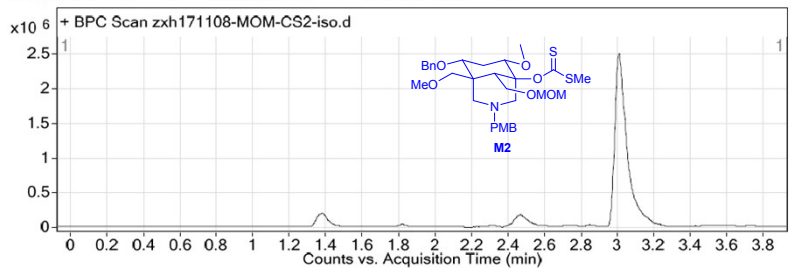
LC-MS data of compound M2

Qualitative Analysis Report

Data Filename	zxh171108-MOM-CS2-iso.d	**Sample Name**	
Sample Type	Sample	**Position**	P1-B8
Instrument Name	Instrument 1	**User Name**	
Acq Method	xin.m	**Acquired Time**	11/8/2017 13:58:24
IRM Calibration Status	Not Applicable	**DA Method**	42.m
Comment			
Sample Group		**Info.**	
Acquisition SW Version	6400 Series Triple Quadrupole B.07.00		

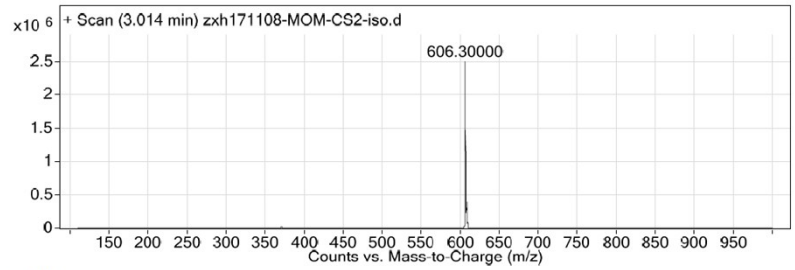
User Chromatograms

Fragmentor Voltage 100 **Collision Energy** 0 **Ionization Mode** ESI



User Spectra

Fragmentor Voltage	Collision Energy	Ionization Mode
100	0	ESI

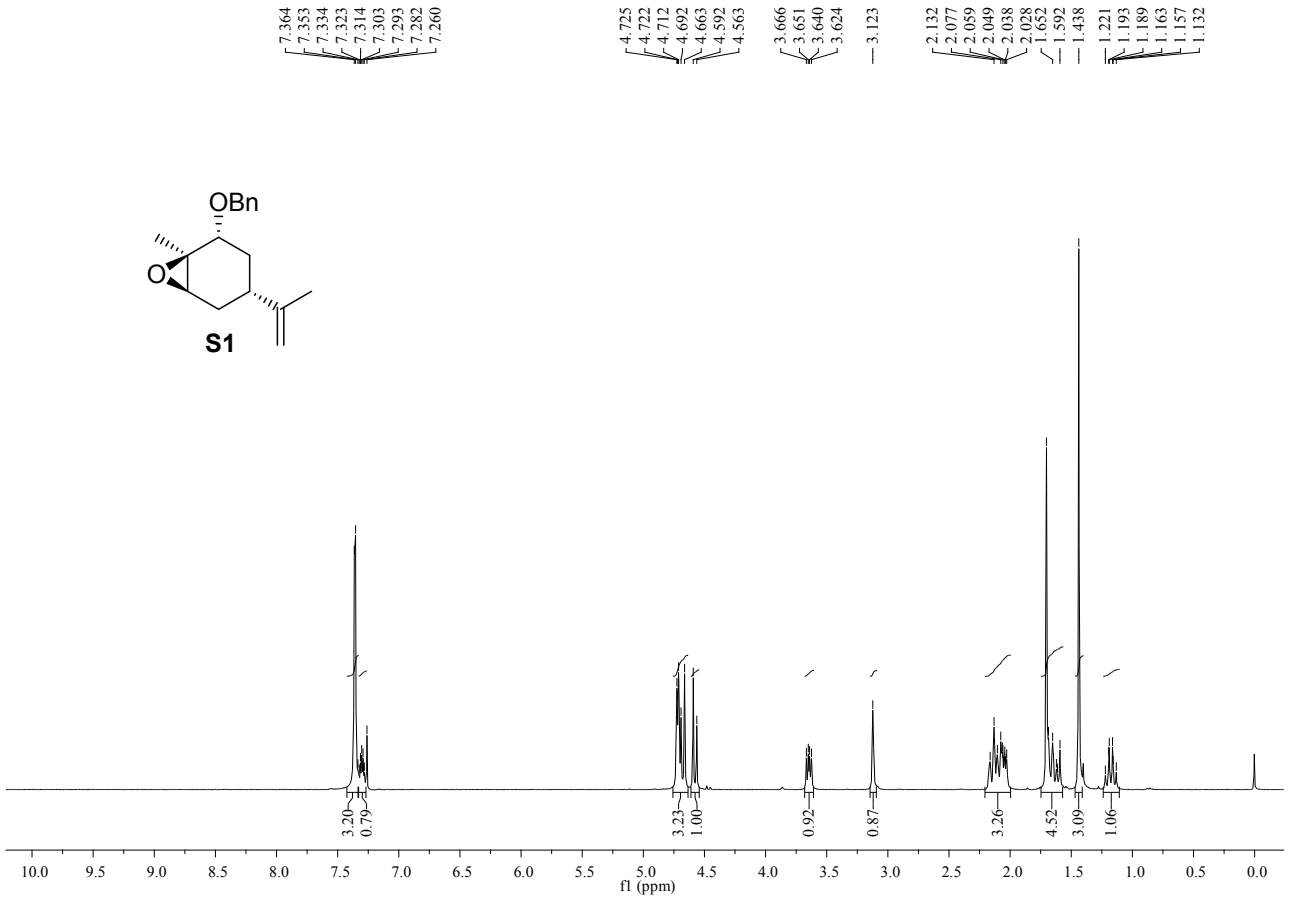


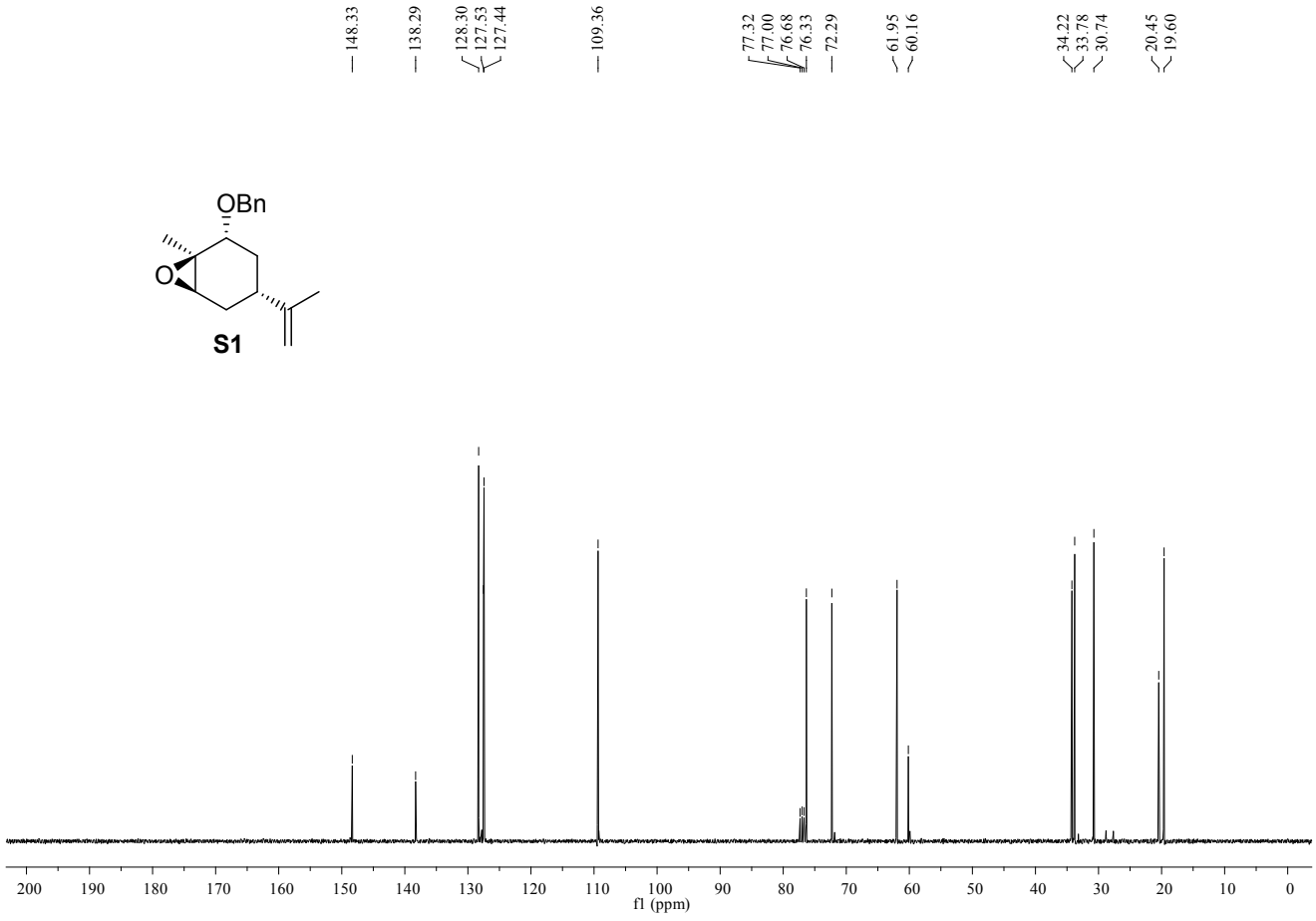
Peak List

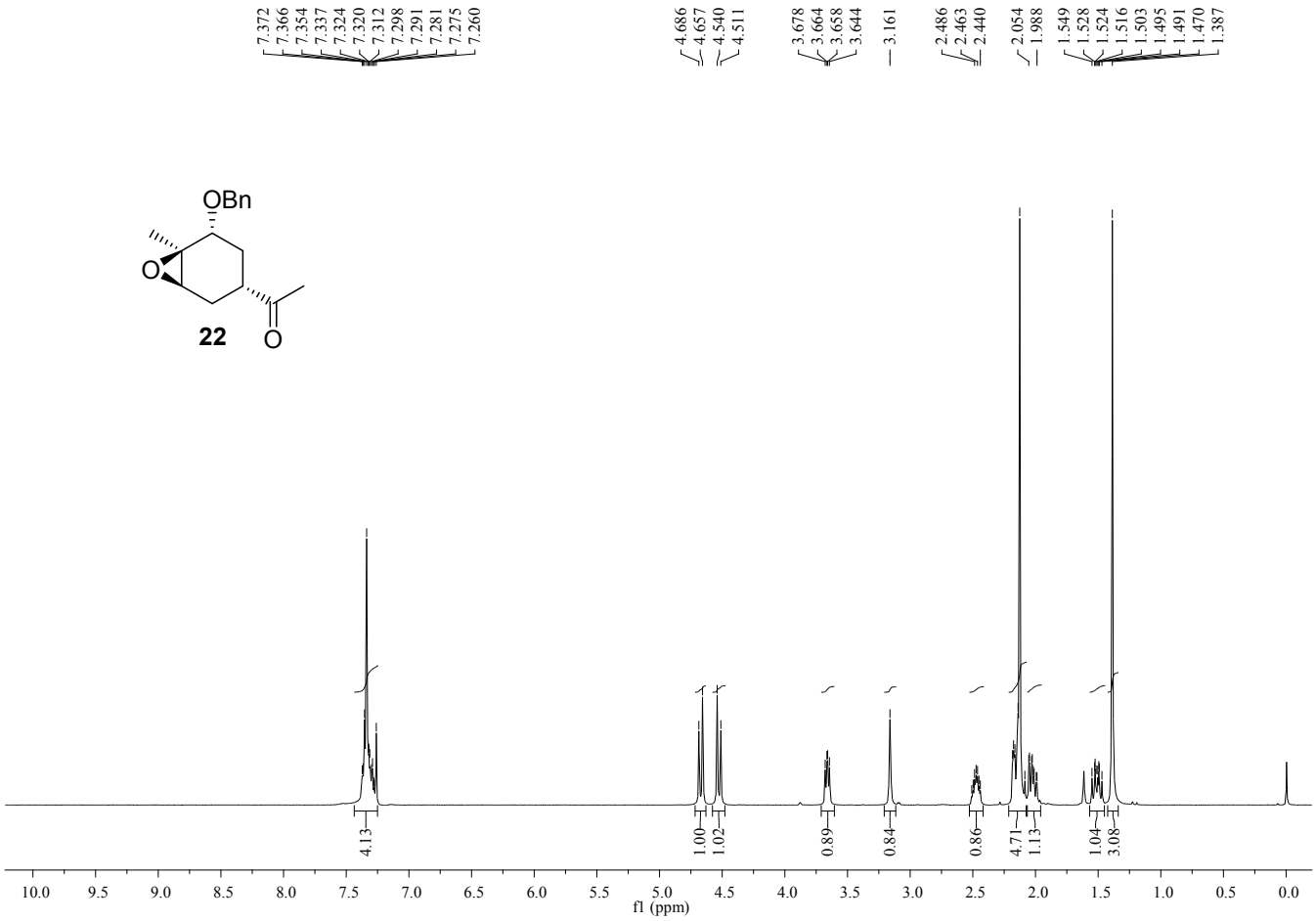
m/z	z	Abund
606.3	1	2501017.5
607.3	1	827187.81
608.3	1	389643.44
609.4	1	92418.43

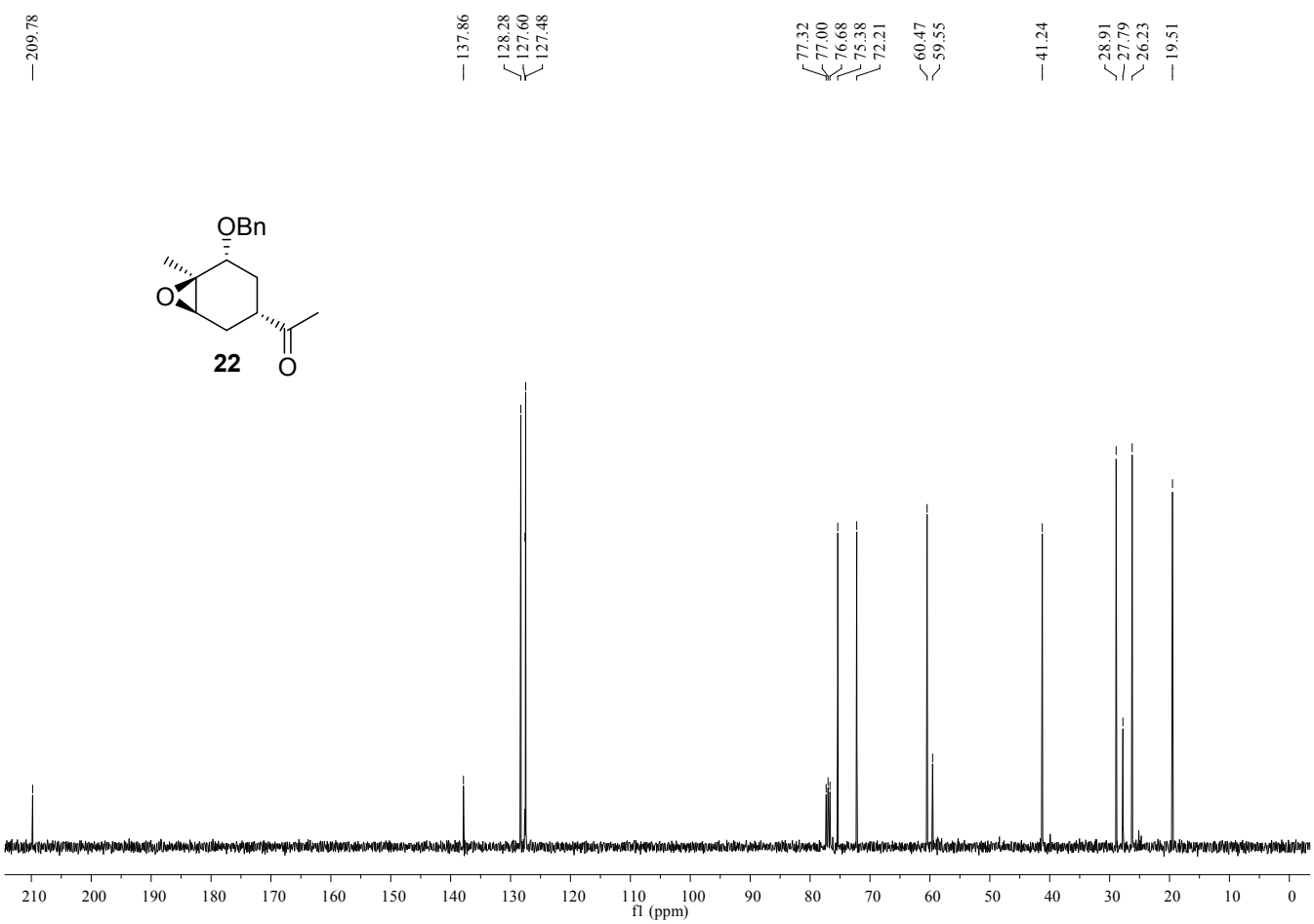
--- End Of Report ---

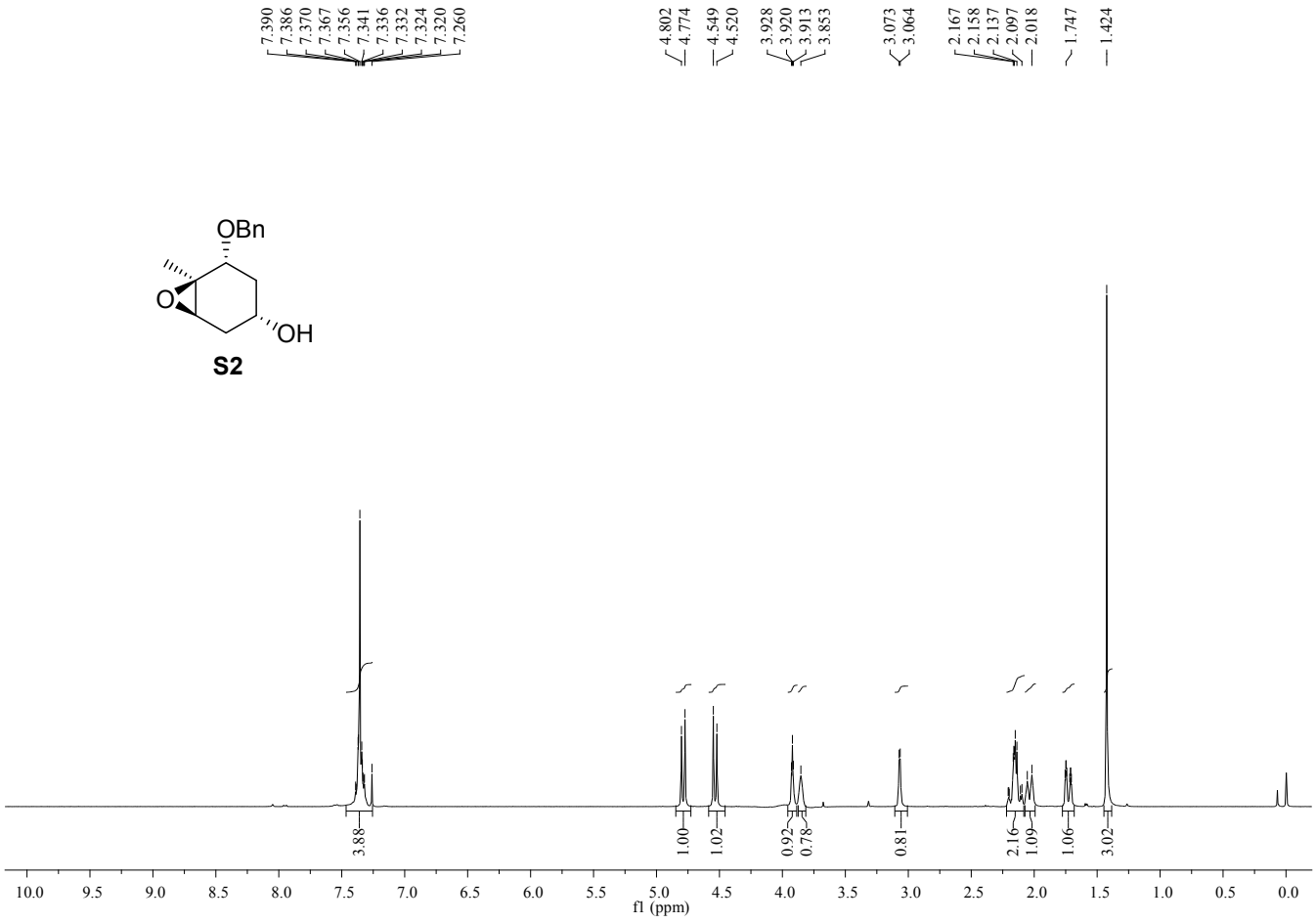
NMR spectra

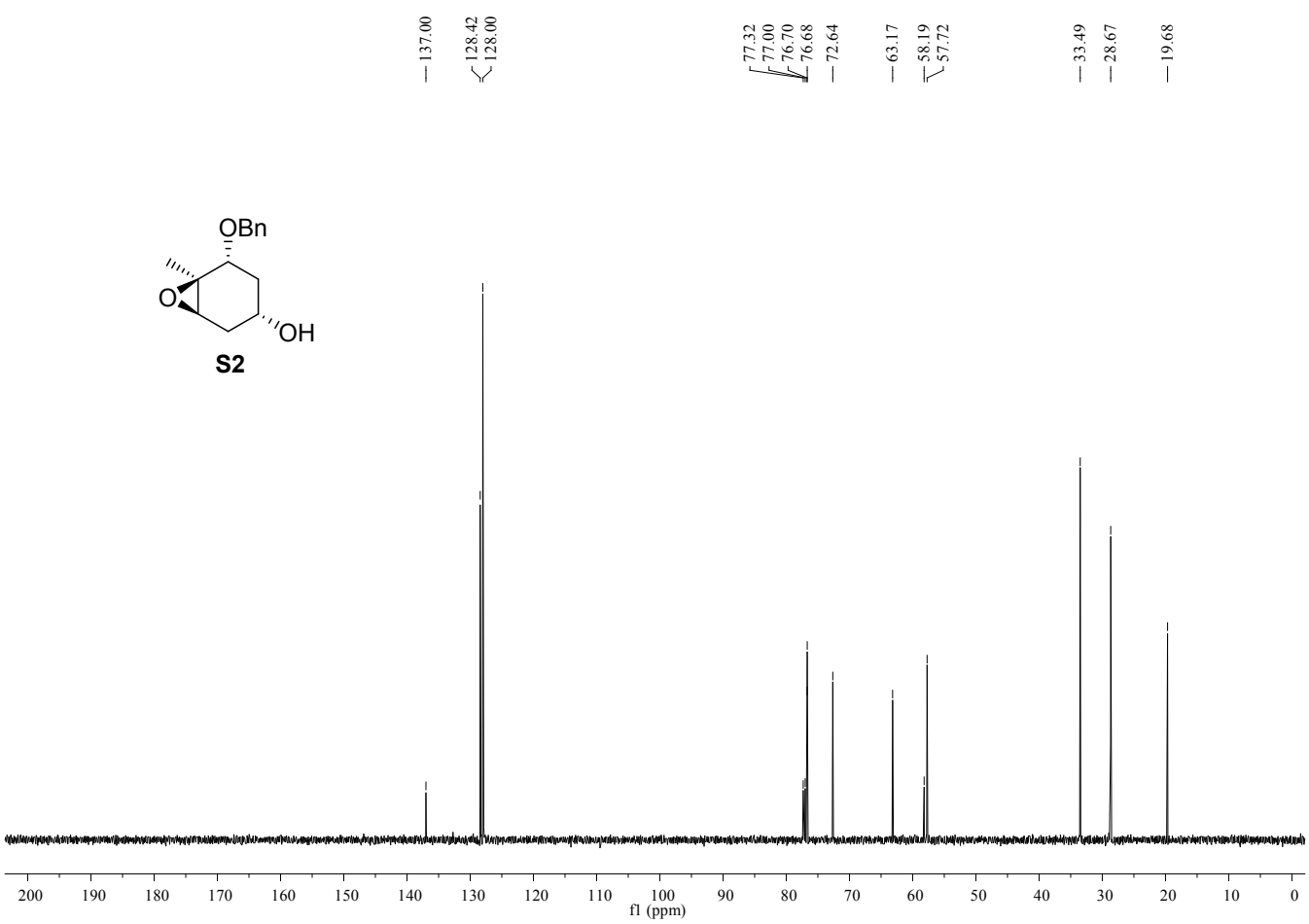

7.364
7.353
7.334
7.323
7.314
7.303
7.293
7.282
7.260
4.725
4.722
4.712
4.692
4.663
4.592
4.563
3.666
3.651
3.640
3.624
3.123
2.132
2.077
2.059
2.049
2.038
2.028
1.652
1.592
1.438
1.221
1.193
1.189
1.163
1.157
1.132
OBn
O
S1
3.20
0.79
3.23
1.00
0.92
0.87
3.26
4.52
3.09
1.06
10.0 9.5 9.0 8.5 8.0 7.5 7.0 6.5 6.0 5.5 5.0 4.5 4.0 3.5 3.0 2.5 2.0 1.5 1.0 0.5 0.0
f1 (ppm)

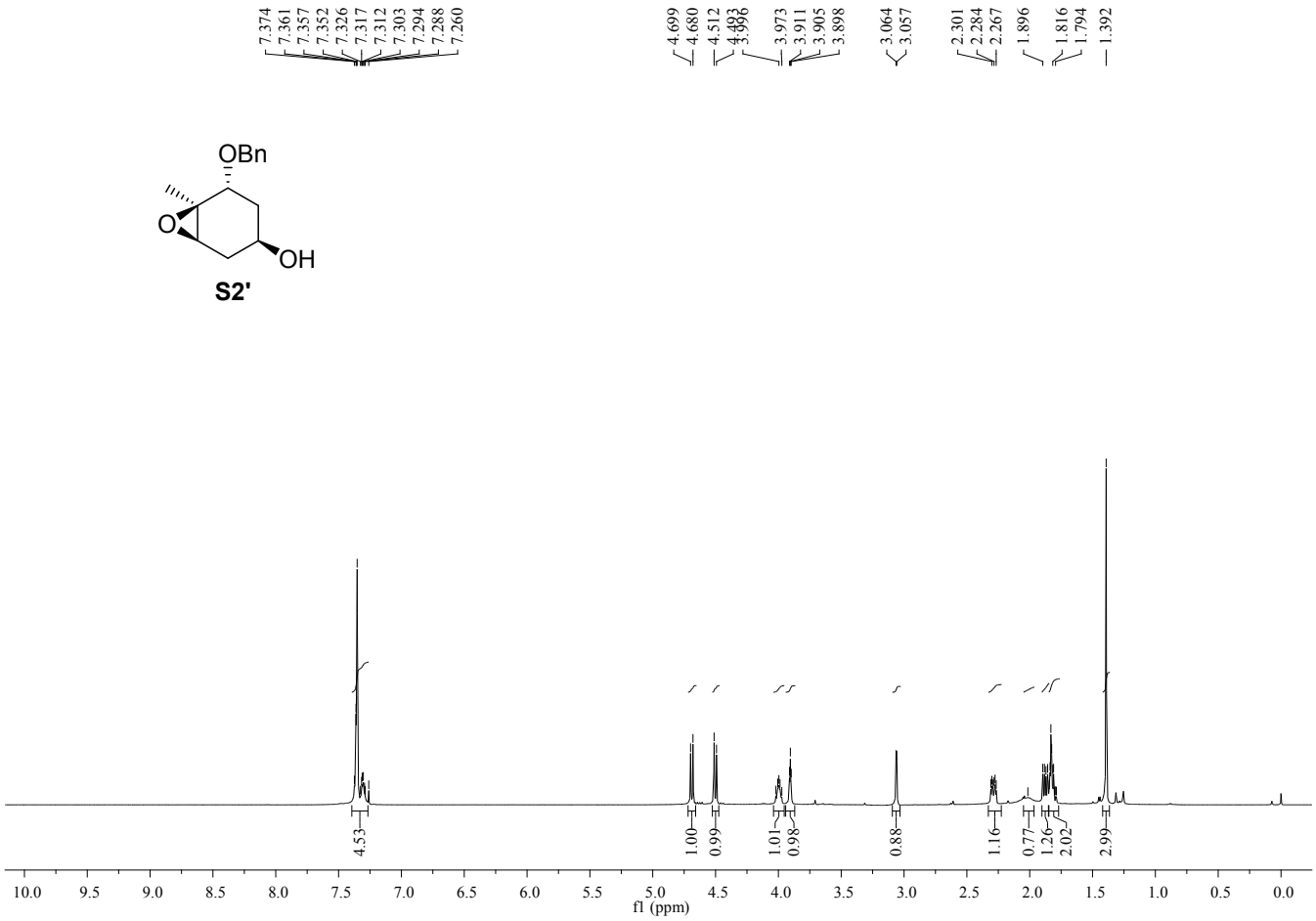

148.33
138.29
128.30
127.53
127.44
109.36
77.32
77.00
76.68
76.33
72.29
61.95
60.16
34.22
33.78
30.74
20.45
19.60
OBn
O
S1
200 190 180 170 160 150 140 130 120 110 100 90 80 70 60 50 40 30 20 10 0
f1 (ppm)

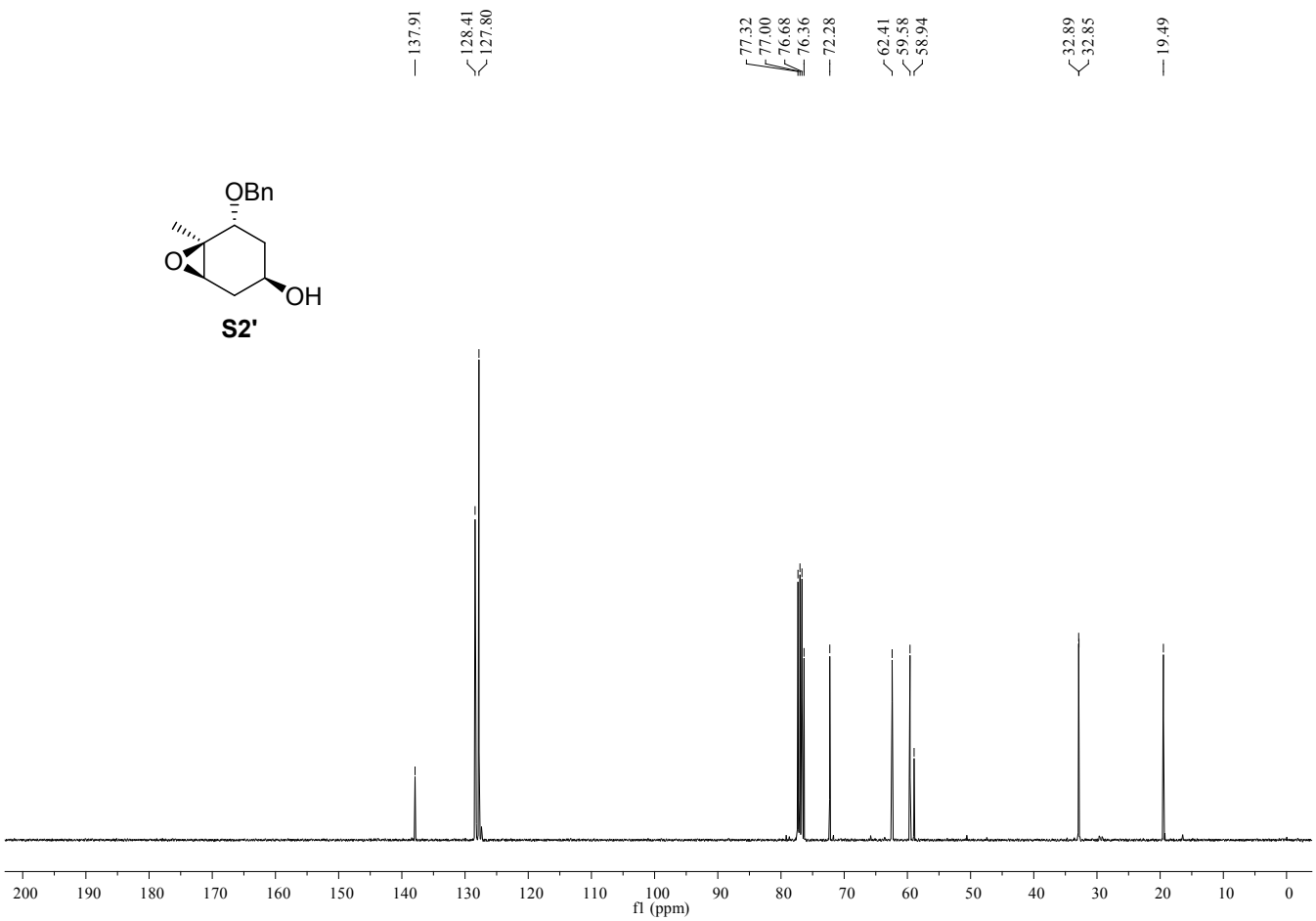

7.372
7.366
7.354
7.337
7.324
7.320
7.312
7.298
7.291
7.281
7.275
7.260
4.686
4.657
4.540
4.511
3.678
3.664
3.658
3.644
3.161
2.486
2.463
2.440
2.054
1.988
1.549
1.528
1.524
1.516
1.503
1.495
1.491
1.470
1.387
OBn
O
22
O
4.13
1.00
1.02
0.89
0.84
0.86
4.71
1.13
1.04
3.08
10.0
9.5
9.0
8.5
8.0
7.5
7.0
6.5
6.0
5.5
5.0
4.5
4.0
3.5
3.0
2.5
2.0
1.5
1.0
0.5
0.0
f1 (ppm)

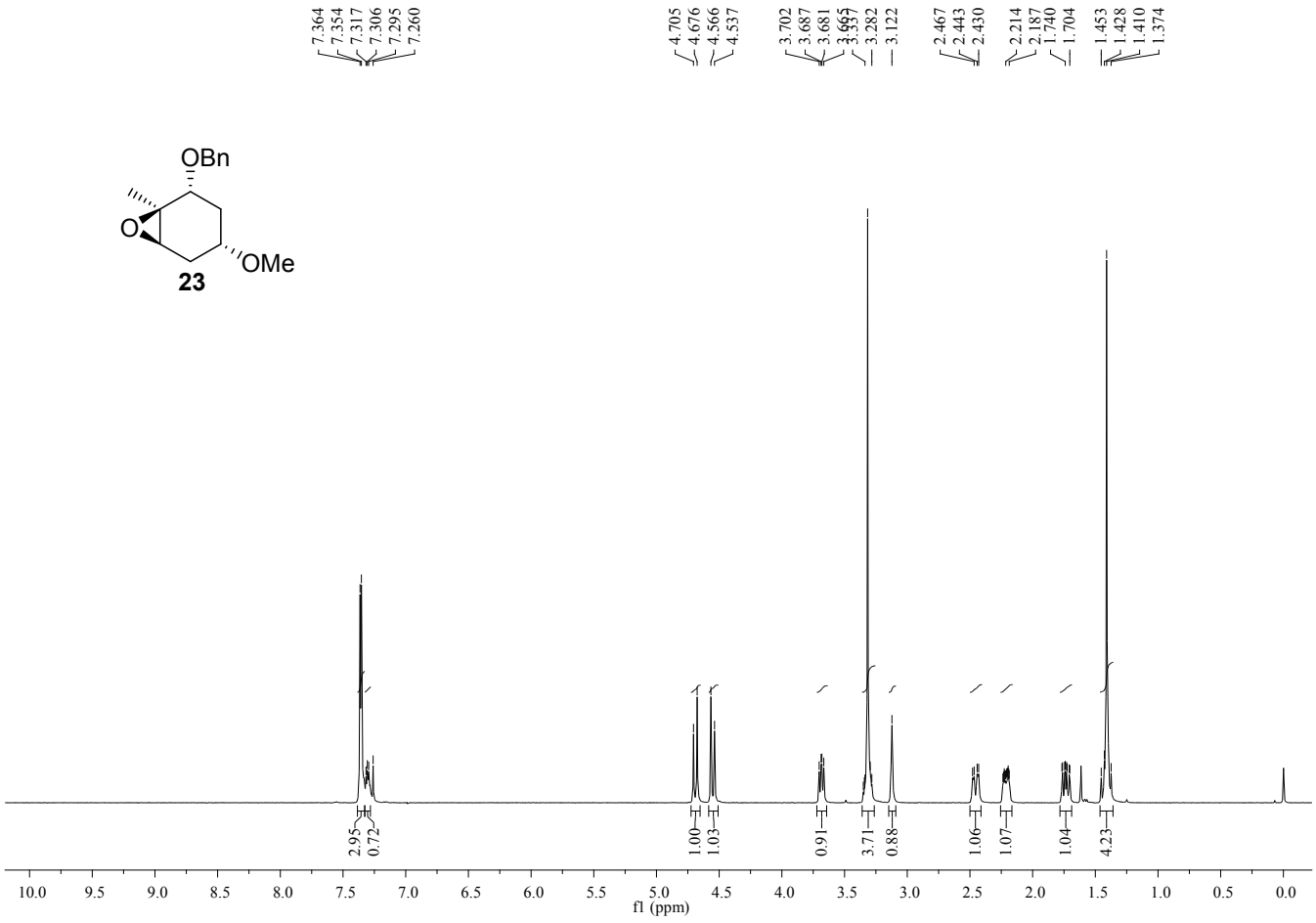

209.78
137.86
128.28
127.60
127.48
77.32
77.00
76.68
75.38
72.21
60.47
59.55
41.24
28.91
27.79
26.23
19.51
OBn
O
22
O
210
200
190
180
170
160
150
140
130
120
110
100
90
80
70
60
50
40
30
20
10
0
f1 (ppm)

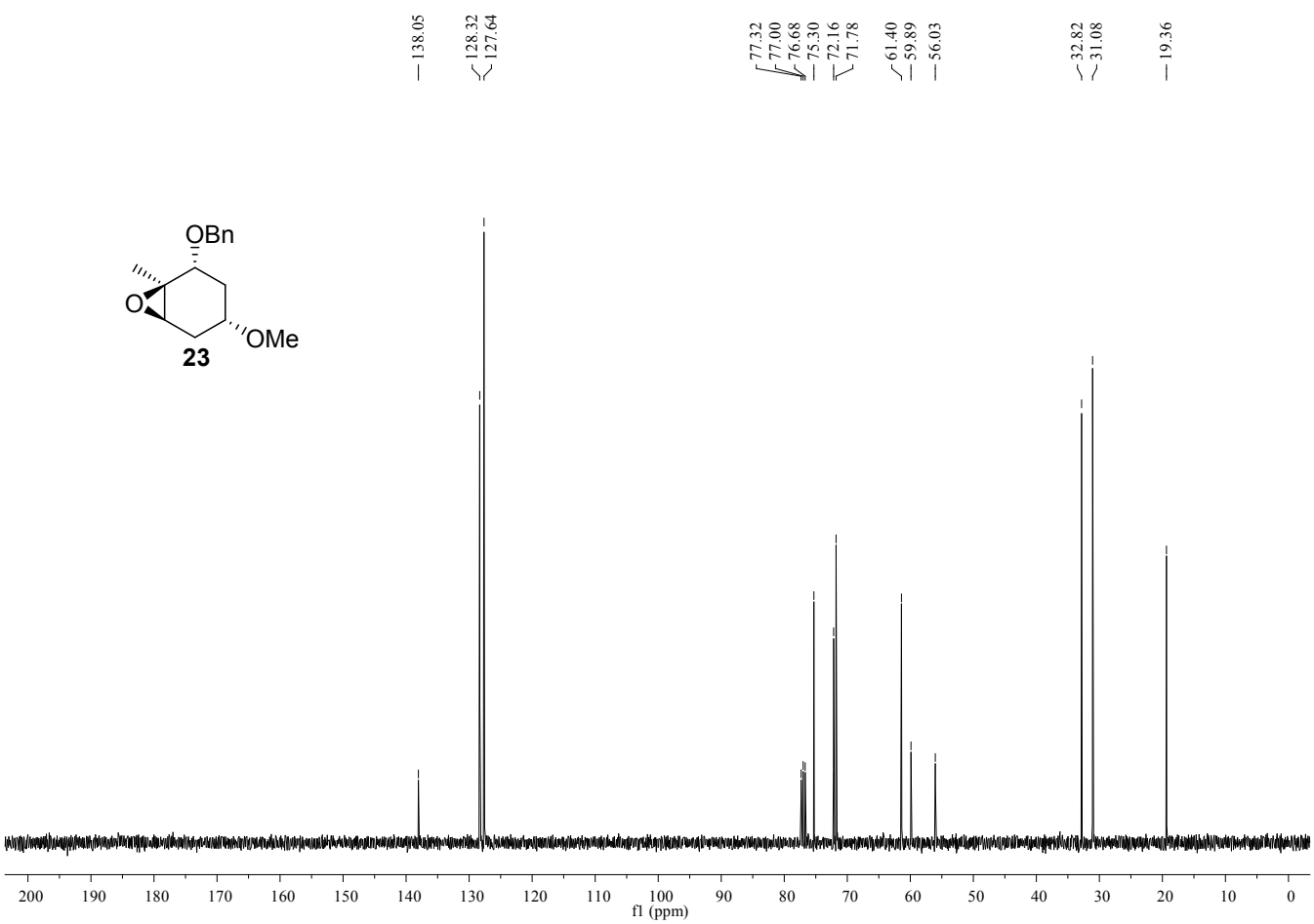

7.390
7.386
7.370
7.367
7.356
7.341
7.336
7.332
7.324
7.320
7.260
4.802
4.774
4.549
4.520
3.928
3.920
3.913
3.853
3.073
3.064
2.167
2.158
2.137
2.097
2.018
1.747
1.424
OBn
O
OH
S2
3.88
1.00
1.02
0.92
0.78
0.81
2.16
1.09
1.06
3.02
10.0
9.5
9.0
8.5
8.0
7.5
7.0
6.5
6.0
5.5
5.0
4.5
4.0
3.5
3.0
2.5
2.0
1.5
1.0
0.5
0.0
f1 (ppm)

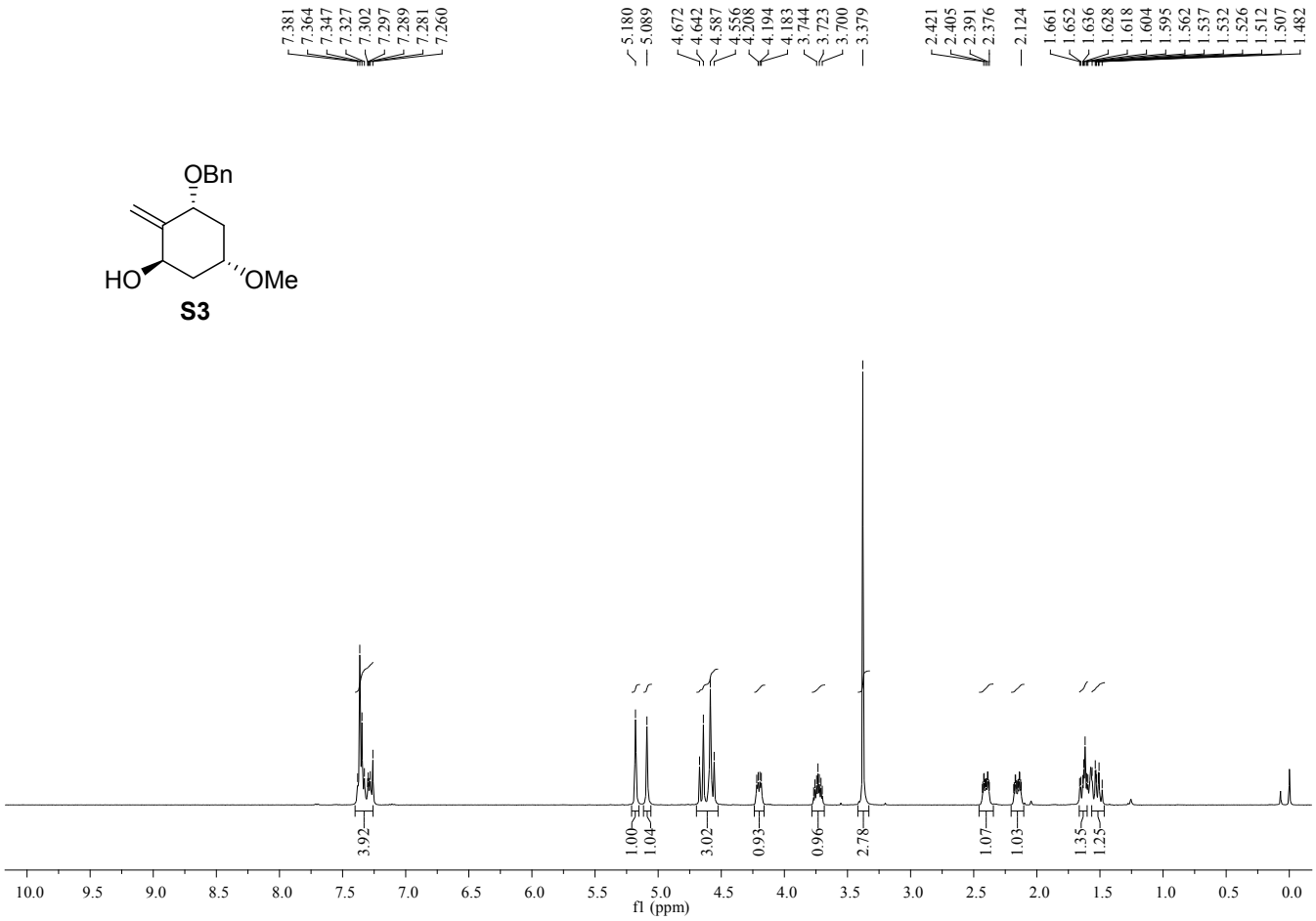

137.00
128.42
128.00
77.32
77.00
76.70
76.68
72.64
63.17
58.19
57.72
33.49
28.67
19.68
OBn
O
OH
S2
200
190
180
170
160
150
140
130
120
110
100
90
80
70
60
50
40
30
20
10
0
f1 (ppm)

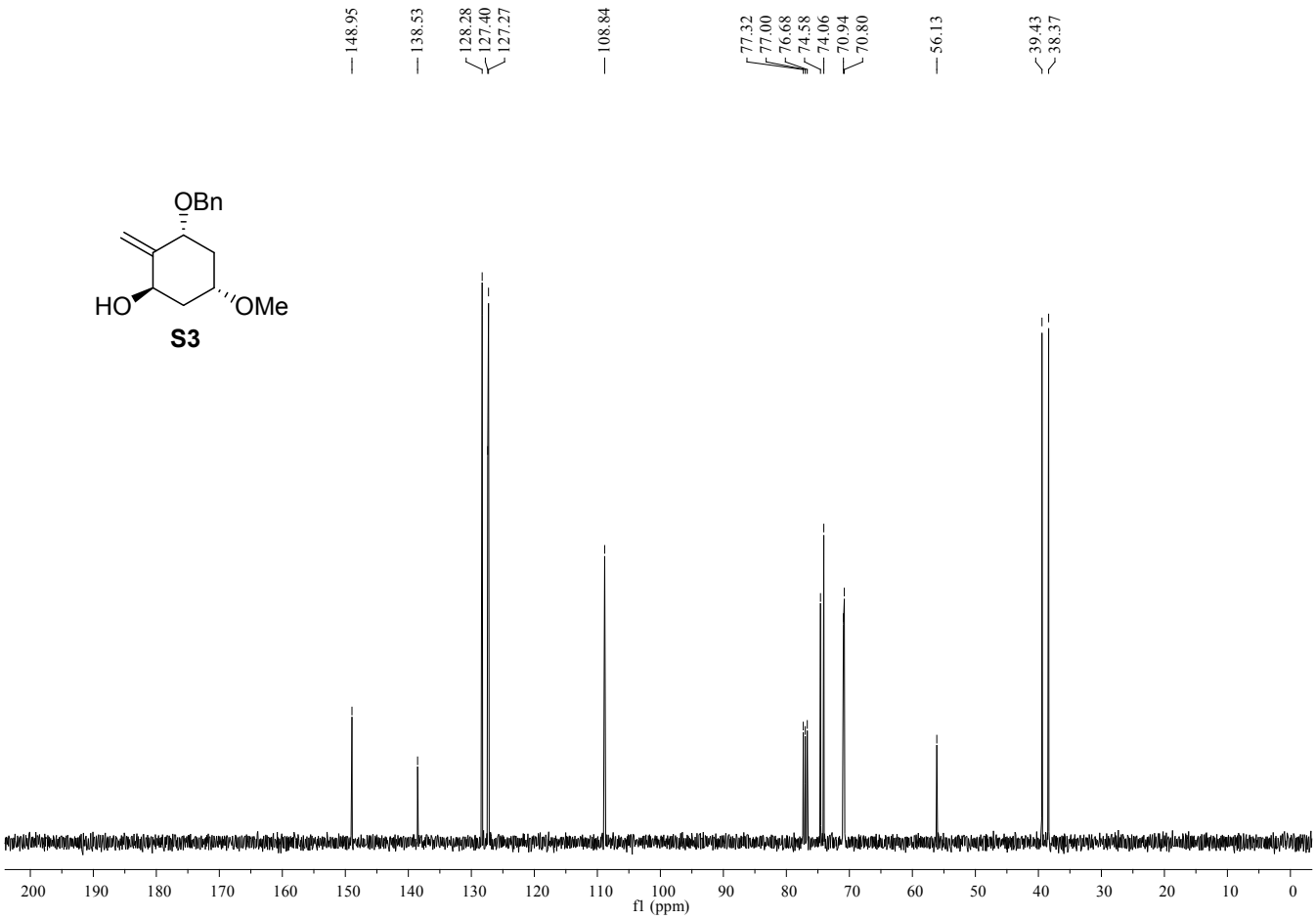

7.374
7.361
7.357
7.352
7.326
7.317
7.312
7.303
7.294
7.288
7.260
4.699
4.680
4.512
4.493
3.973
3.911
3.905
3.898
3.064
3.057
2.301
2.284
2.267
1.896
1.816
1.794
1.392
OBn
O
OH
S2'
4.53
1.00
0.99
1.01
0.98
0.88
1.16
0.77
1.26
2.02
2.99
10.0
9.5
9.0
8.5
8.0
7.5
7.0
6.5
6.0
5.5
5.0
4.5
4.0
3.5
3.0
2.5
2.0
1.5
1.0
0.5
0.0
f1 (ppm)

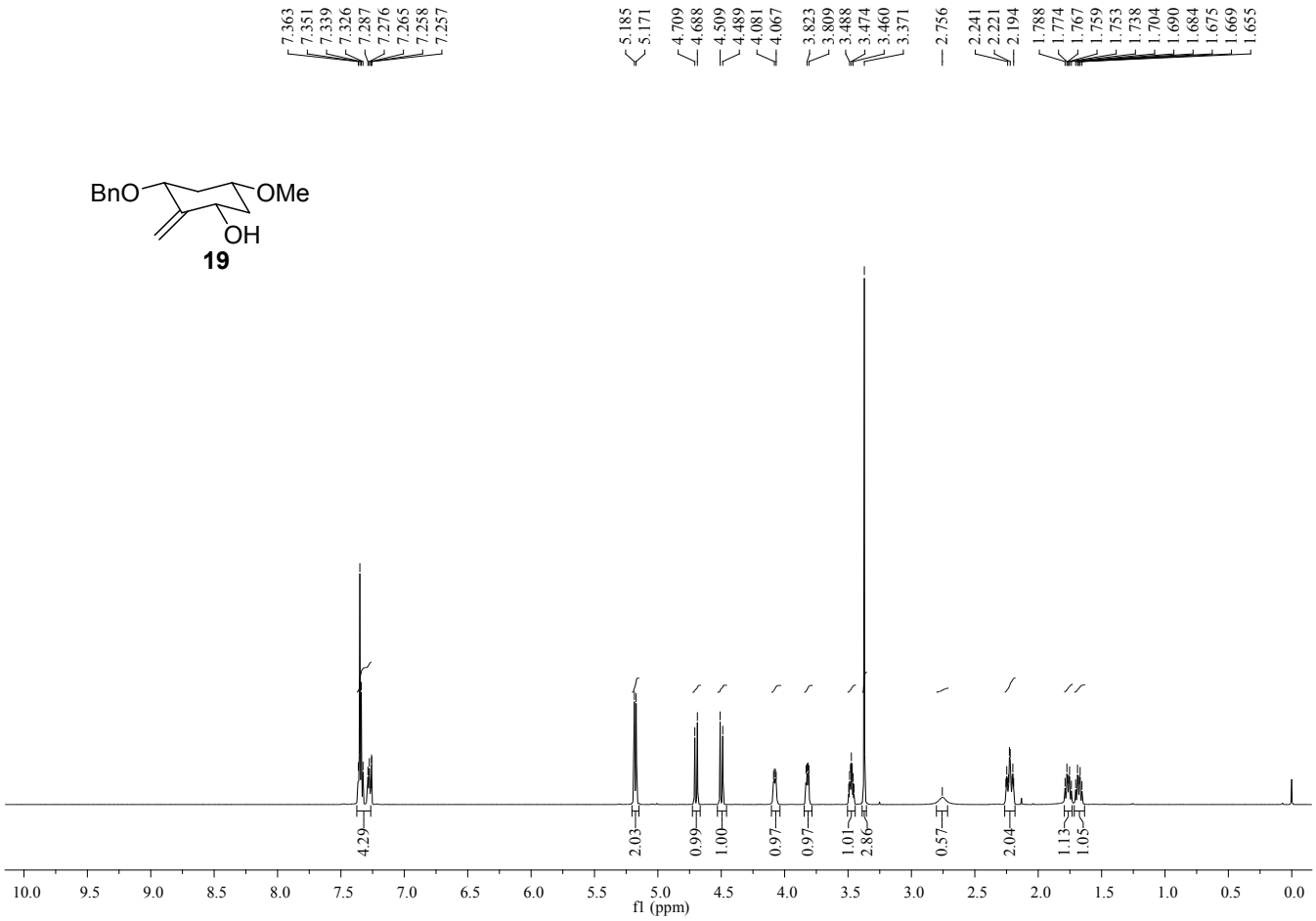

137.91
128.41
127.80
77.32
77.00
76.68
76.36
72.28
62.41
59.58
58.94
32.89
32.85
19.49
OBn
O
OH
S2'
200
190
180
170
160
150
140
130
120
110
100
90
80
70
60
50
40
30
20
10
0
f1 (ppm)

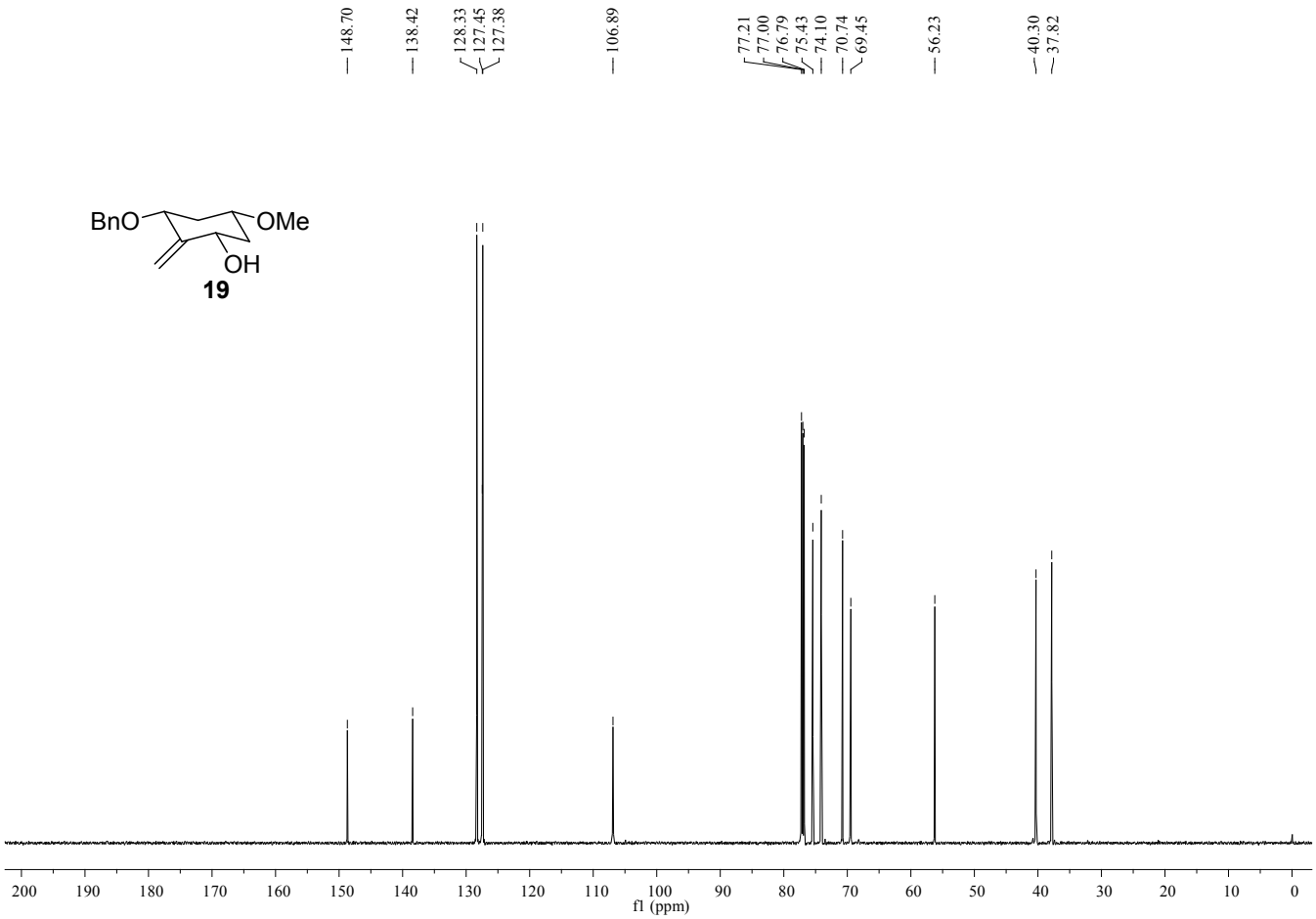

7.364
7.354
7.317
7.306
7.295
7.260
4.705
4.676
4.566
4.537
3.702
3.687
3.681
3.665
3.337
3.282
3.122
2.467
2.443
2.430
2.214
2.187
1.740
1.704
1.453
1.428
1.410
1.374
OBn
O
OMe
23
2.95
0.72
1.00
1.03
0.91
3.71
0.88
1.06
1.07
1.04
4.23
10.0 9.5 9.0 8.5 8.0 7.5 7.0 6.5 6.0 5.5 5.0 4.5 4.0 3.5 3.0 2.5 2.0 1.5 1.0 0.5 0.0
f1 (ppm)

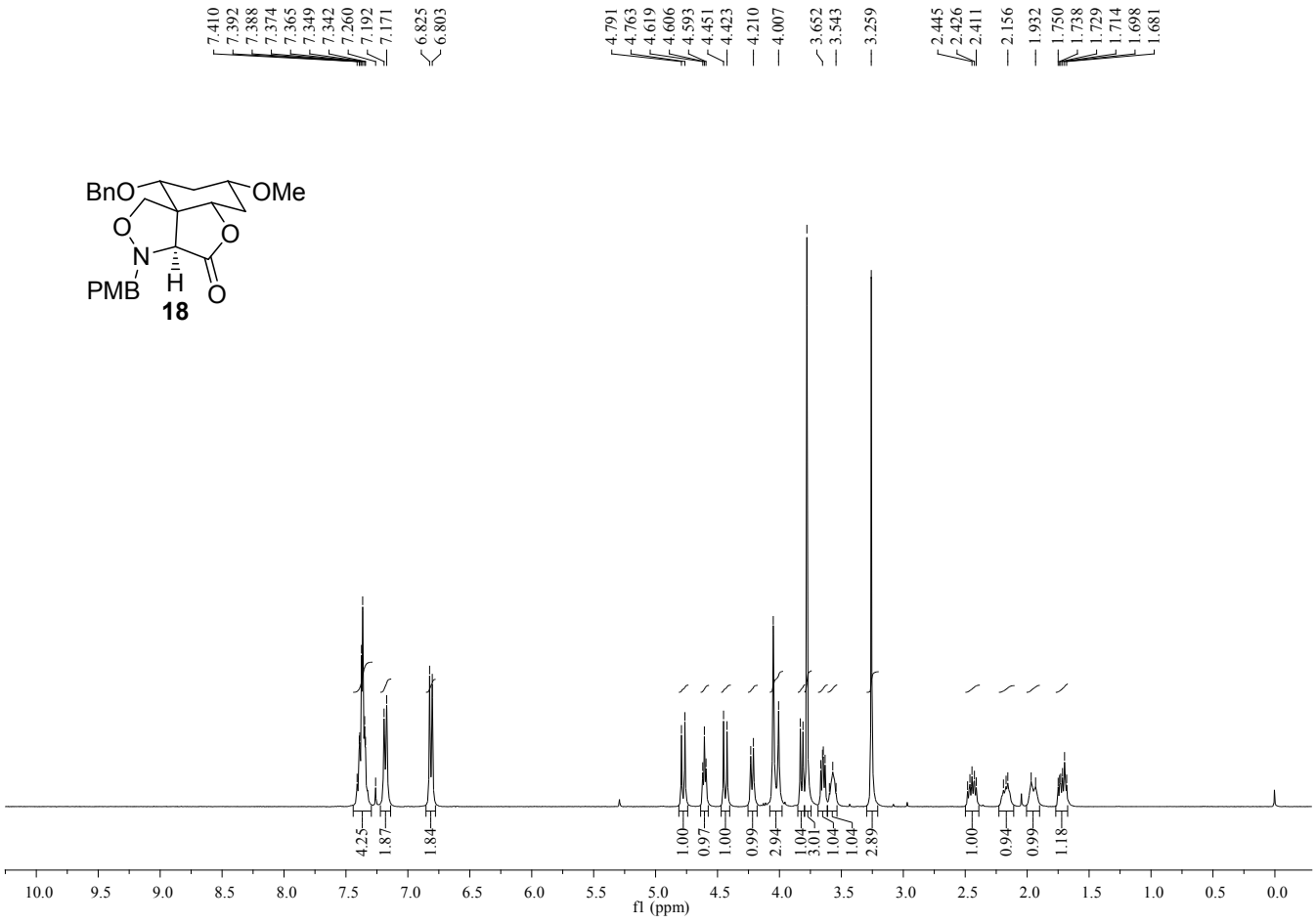

138.05
128.32
127.64
77.32
77.00
76.68
75.30
72.16
71.78
61.40
59.89
56.03
32.82
31.08
19.36
OBn
O
OMe
23
200 190 180 170 160 150 140 130 120 110 100 90 80 70 60 50 40 30 20 10 0
f1 (ppm)

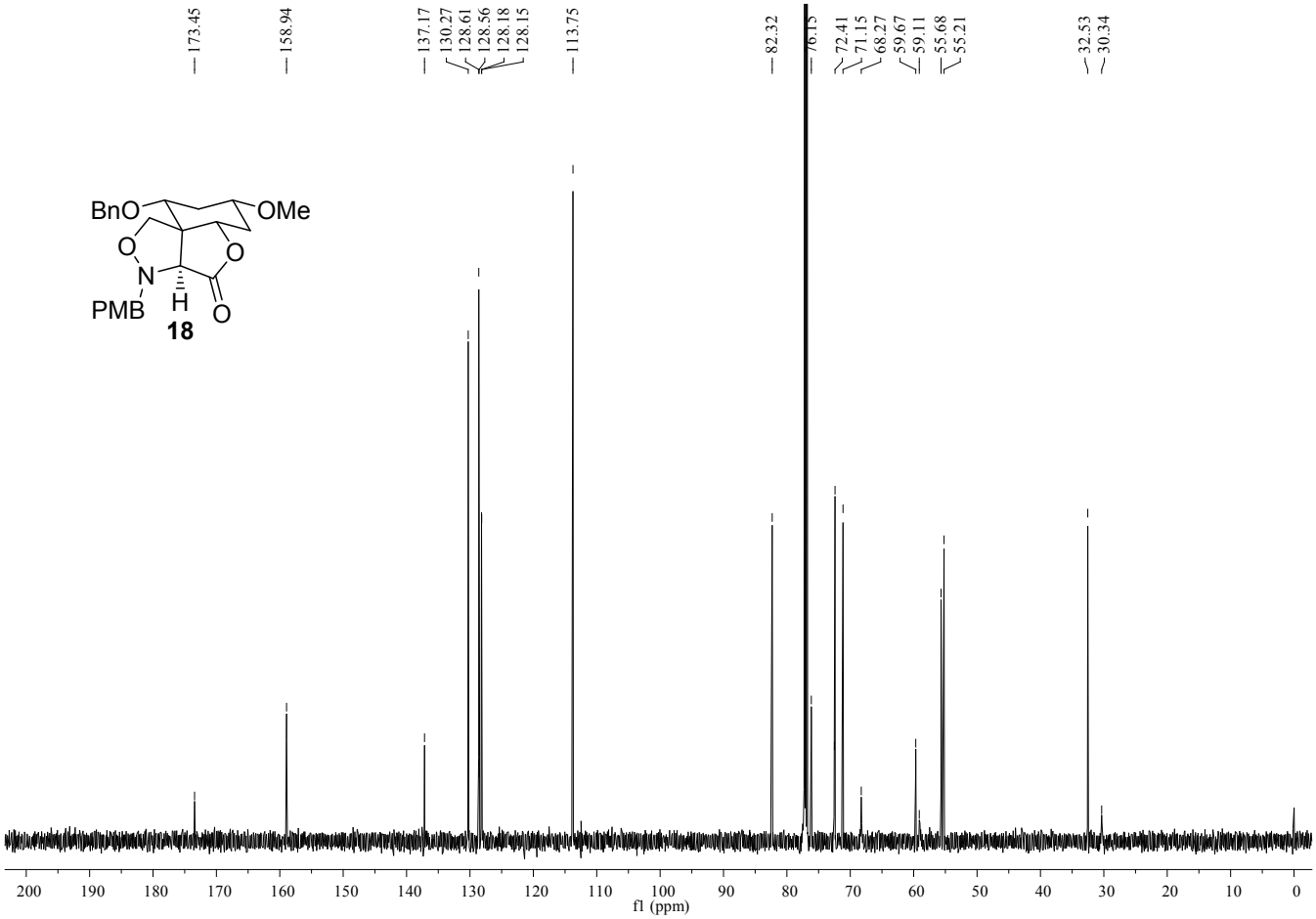

7.381
7.364
7.347
7.327
7.302
7.297
7.289
7.281
7.260
5.180
5.089
4.672
4.642
4.587
4.556
4.208
4.194
4.183
3.744
3.723
3.700
3.379
2.421
2.405
2.391
2.376
2.124
1.661
1.652
1.636
1.628
1.618
1.604
1.595
1.562
1.537
1.532
1.526
1.512
1.507
1.482
OBn
HO
OMe
S3
3.92
1.00
1.04
3.02
0.93
0.96
2.78
1.07
1.03
1.35
1.25
f1 (ppm)

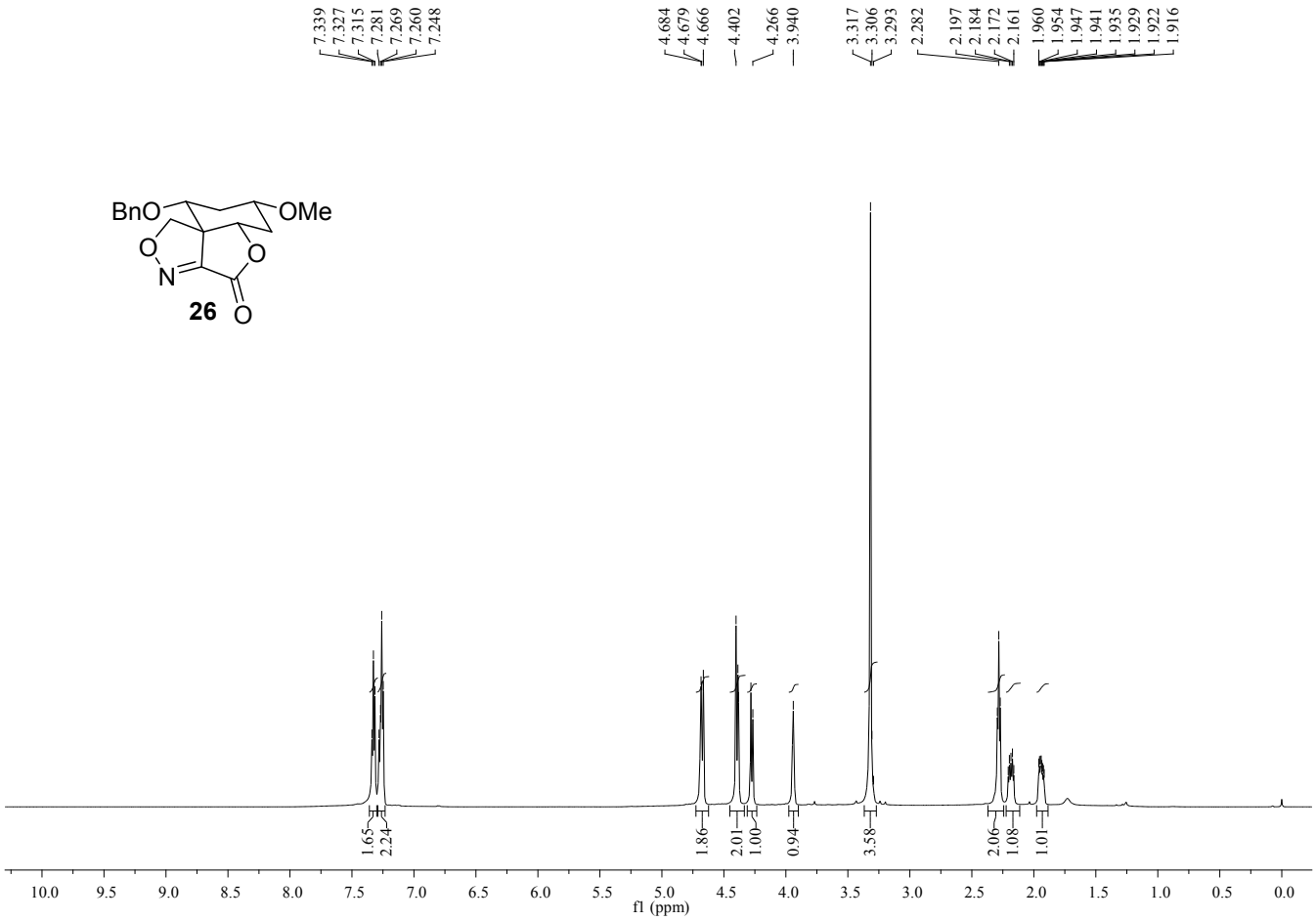

148.95
138.53
128.28
127.40
127.27
108.84
77.32
77.00
76.68
74.58
74.06
70.94
70.80
56.13
39.43
38.37
OBn
HO
OMe
S3
f1 (ppm)

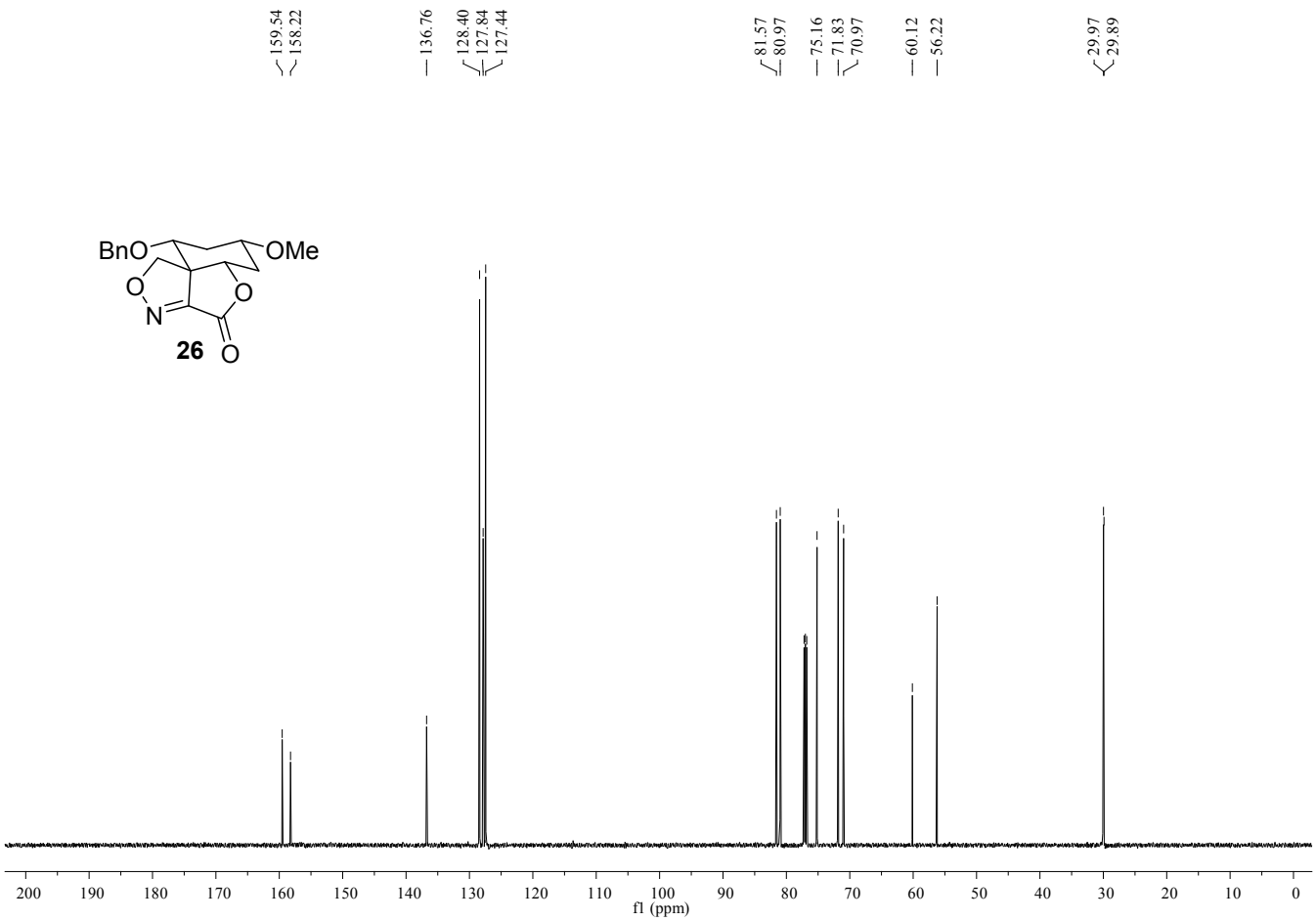

7.363
7.351
7.339
7.326
7.287
7.276
7.265
7.258
7.257
5.185
5.171
4.709
4.688
4.509
4.489
4.081
4.067
3.823
3.809
3.488
3.474
3.460
3.371
2.756
2.241
2.221
2.194
1.788
1.774
1.767
1.759
1.753
1.738
1.704
1.690
1.684
1.675
1.669
1.655
BnO
OMe
OH
19
4.29
2.03
0.99
1.00
0.97
0.97
1.01
2.86
0.57
2.04
1.13
1.05
10.0 9.5 9.0 8.5 8.0 7.5 7.0 6.5 6.0 5.5 5.0 4.5 4.0 3.5 3.0 2.5 2.0 1.5 1.0 0.5 0.0
f1 (ppm)

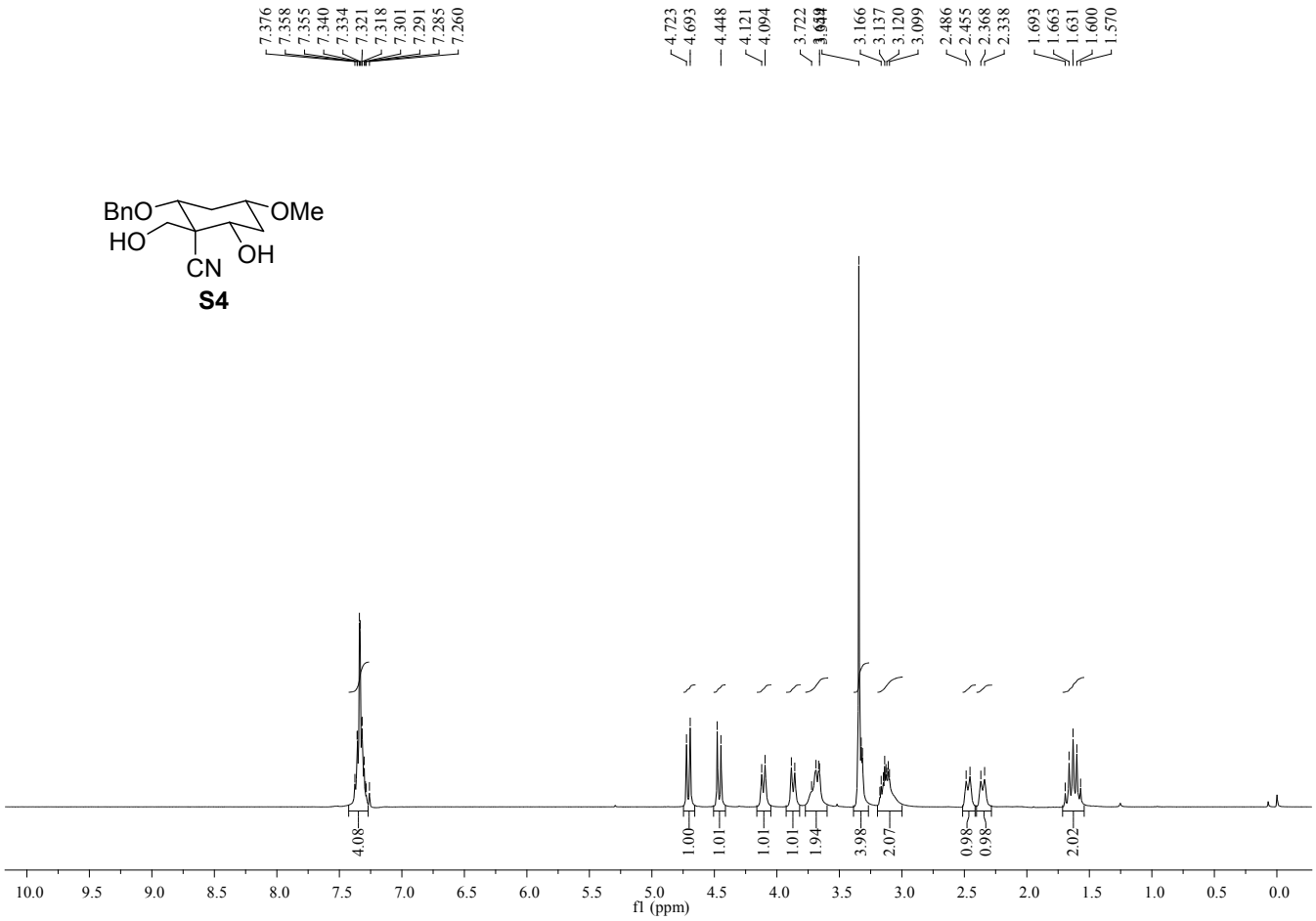

148.70
138.42
128.33
127.45
127.38
106.89
77.21
77.00
76.79
75.43
74.10
70.74
69.45
56.23
40.30
37.82
BnO
OMe
OH
19
200 190 180 170 160 150 140 130 120 110 100 90 80 70 60 50 40 30 20 10 0
f1 (ppm)

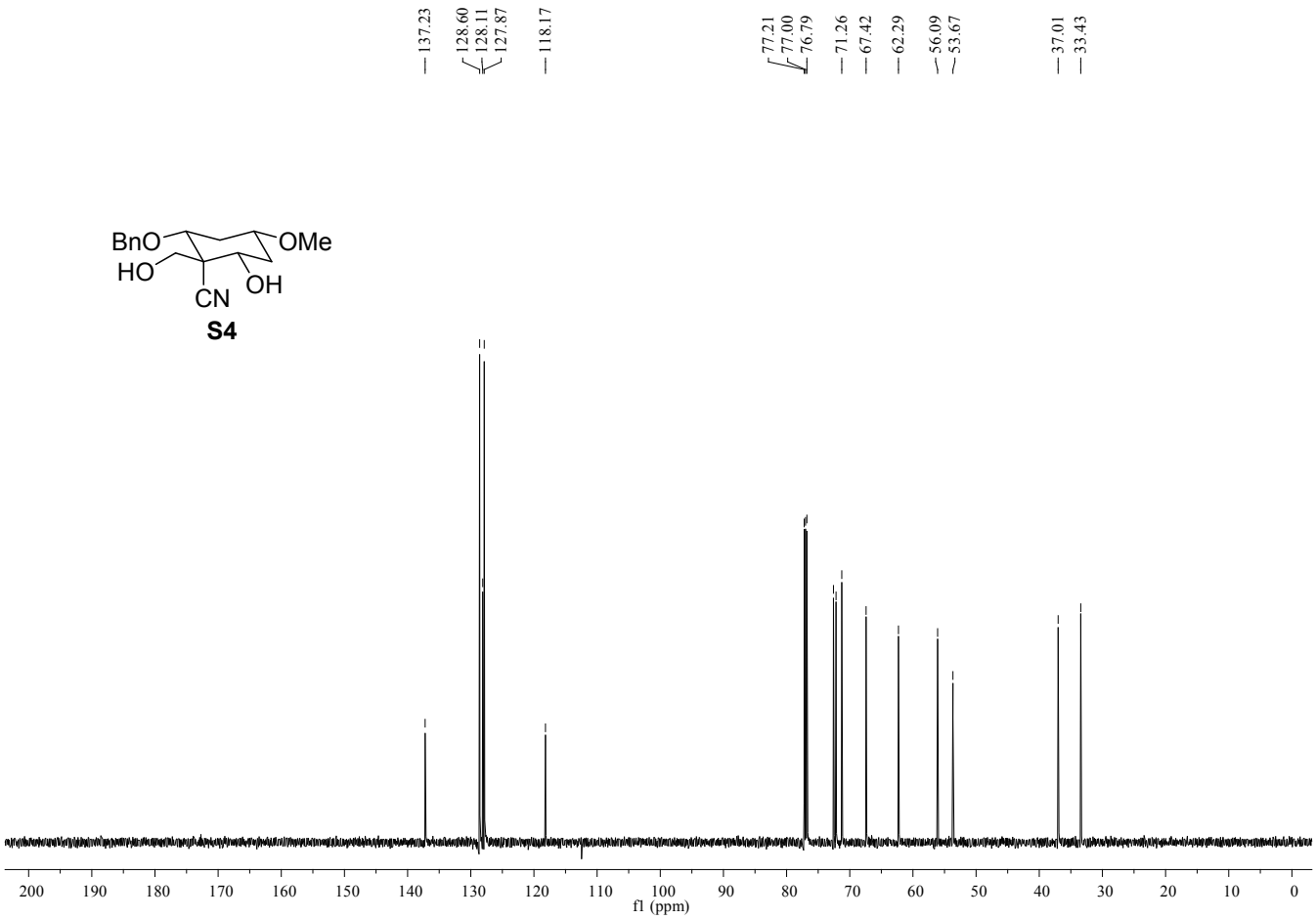

7.410
7.392
7.388
7.374
7.365
7.349
7.342
7.260
7.192
7.171
6.825
6.803
4.791
4.763
4.619
4.606
4.593
4.451
4.423
4.210
4.007
3.652
3.543
3.259
2.445
2.426
2.411
2.156
1.932
1.750
1.738
1.729
1.714
1.698
1.681
BnO
OMe
O
N
H
PMB
O
O
O
18
4.25
1.87
1.84
1.00
0.97
1.00
0.99
2.94
1.04
3.01
1.04
1.04
2.89
1.00
0.94
0.99
1.18
f1 (ppm)

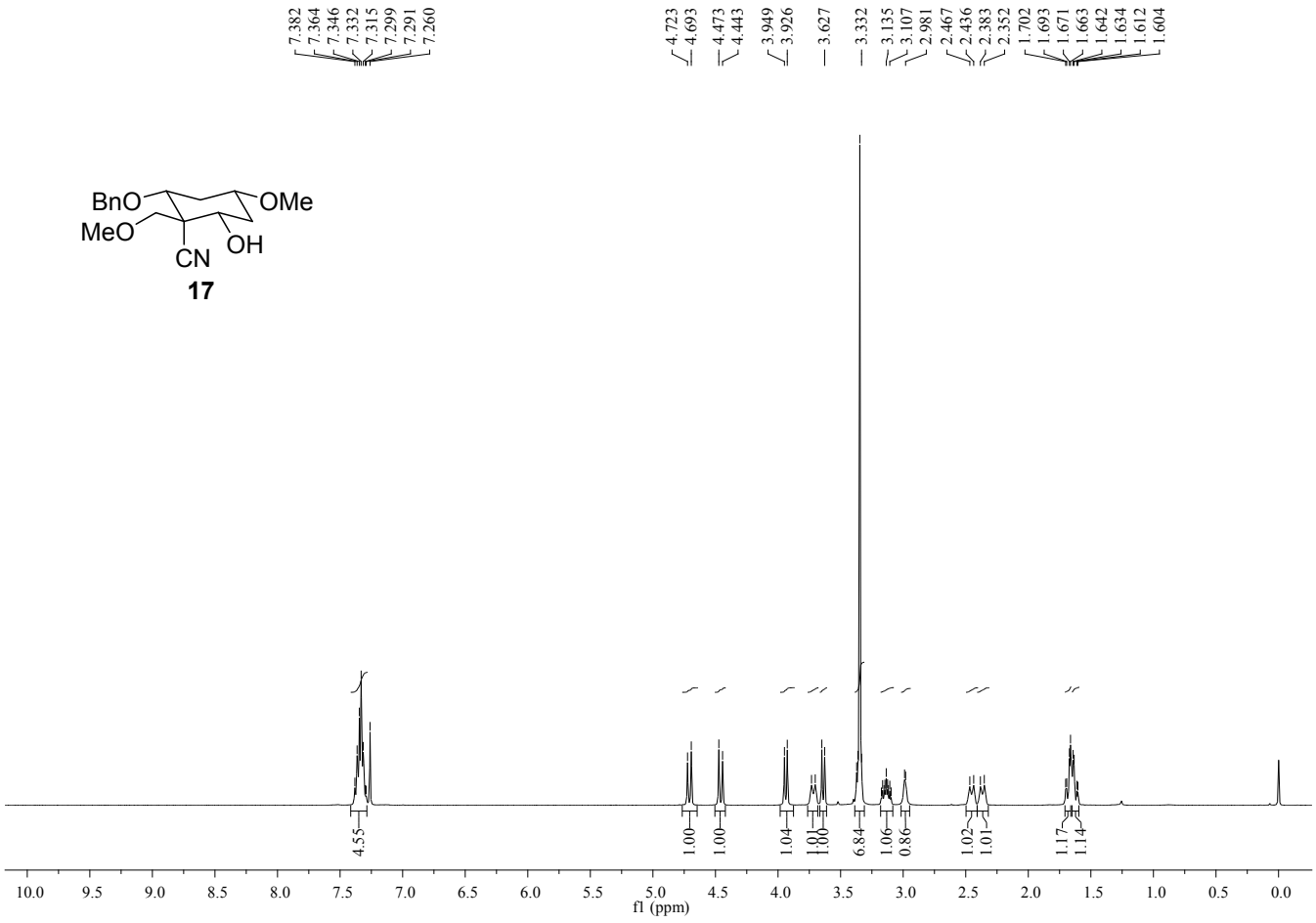

173.45
158.94
137.17
130.27
128.61
128.56
128.18
128.15
113.75
82.32
76.15
72.41
71.15
68.27
59.67
59.11
55.68
55.21
32.53
30.34
BnO
OMe
O
N
H
PMB
O
O
O
18
f1 (ppm)

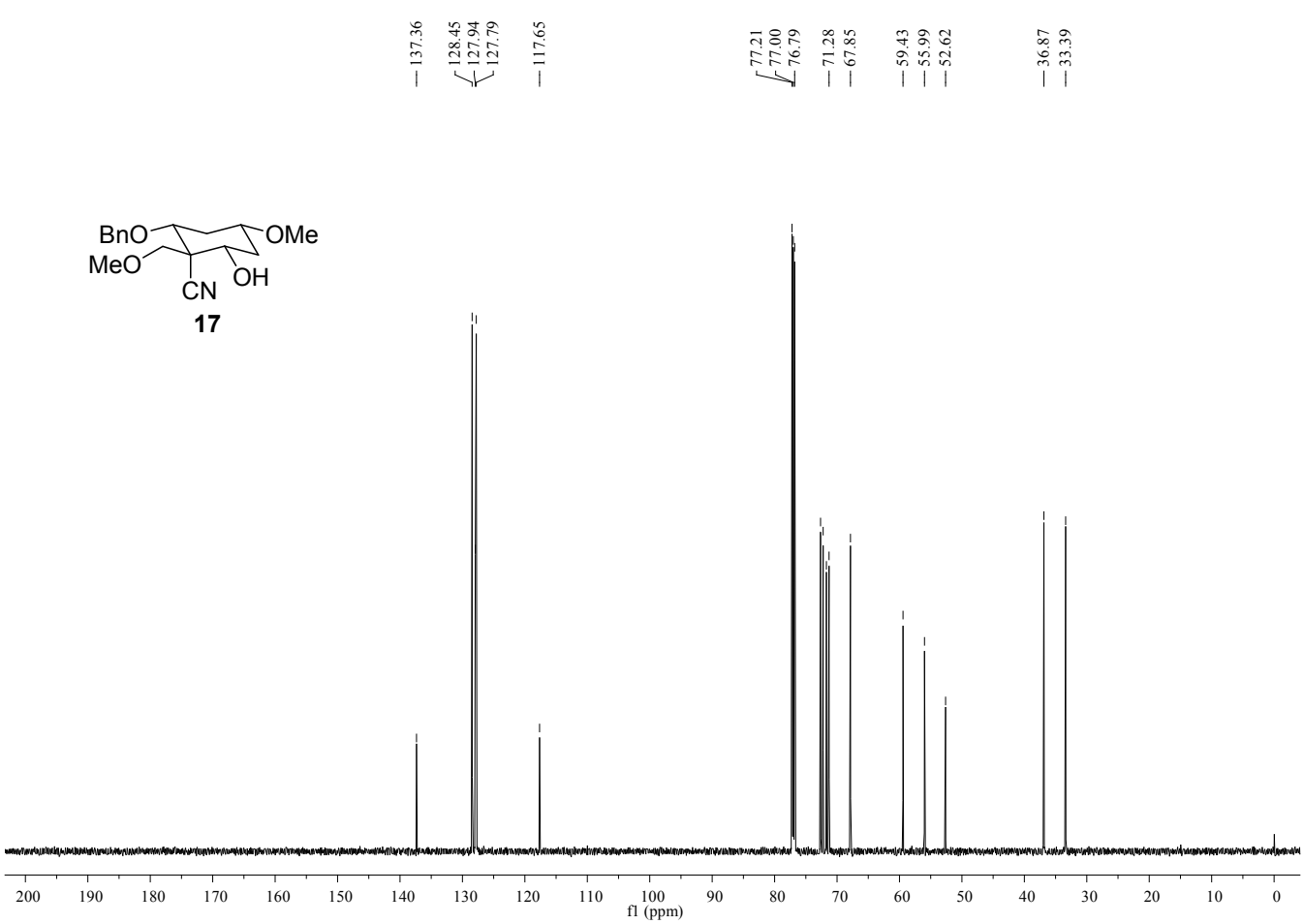

7.339
7.327
7.315
7.281
7.269
7.260
7.248
4.684
4.679
4.666
4.402
4.266
3.940
3.317
3.306
3.293
2.282
2.197
2.184
2.172
2.161
1.960
1.954
1.947
1.941
1.935
1.929
1.922
1.916
BnO
OMe
O
N
O
O
26
O
1.65
2.24
1.86
2.01
1.00
0.94
3.58
2.06
1.08
1.01
10.0
9.5
9.0
8.5
8.0
7.5
7.0
6.5
6.0
5.5
5.0
4.5
4.0
3.5
3.0
2.5
2.0
1.5
1.0
0.5
0.0
f1 (ppm)

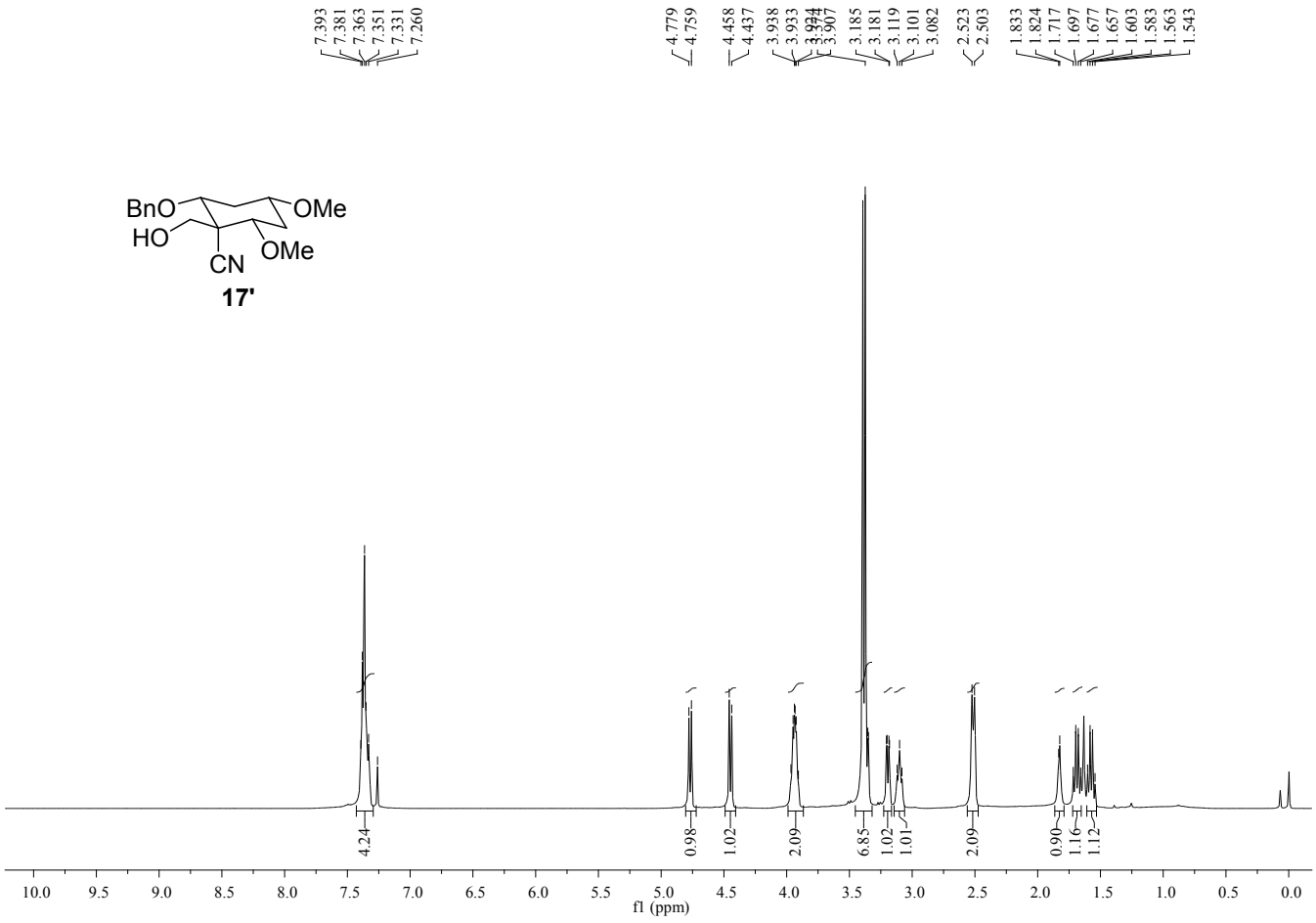

159.54
158.22
136.76
128.40
127.84
127.44
81.57
80.97
75.16
71.83
70.97
60.12
56.22
29.97
29.89
BnO
OMe
O
N
O
O
26
O
200
190
180
170
160
150
140
130
120
110
100
90
80
70
60
50
40
30
20
10
0
f1 (ppm)

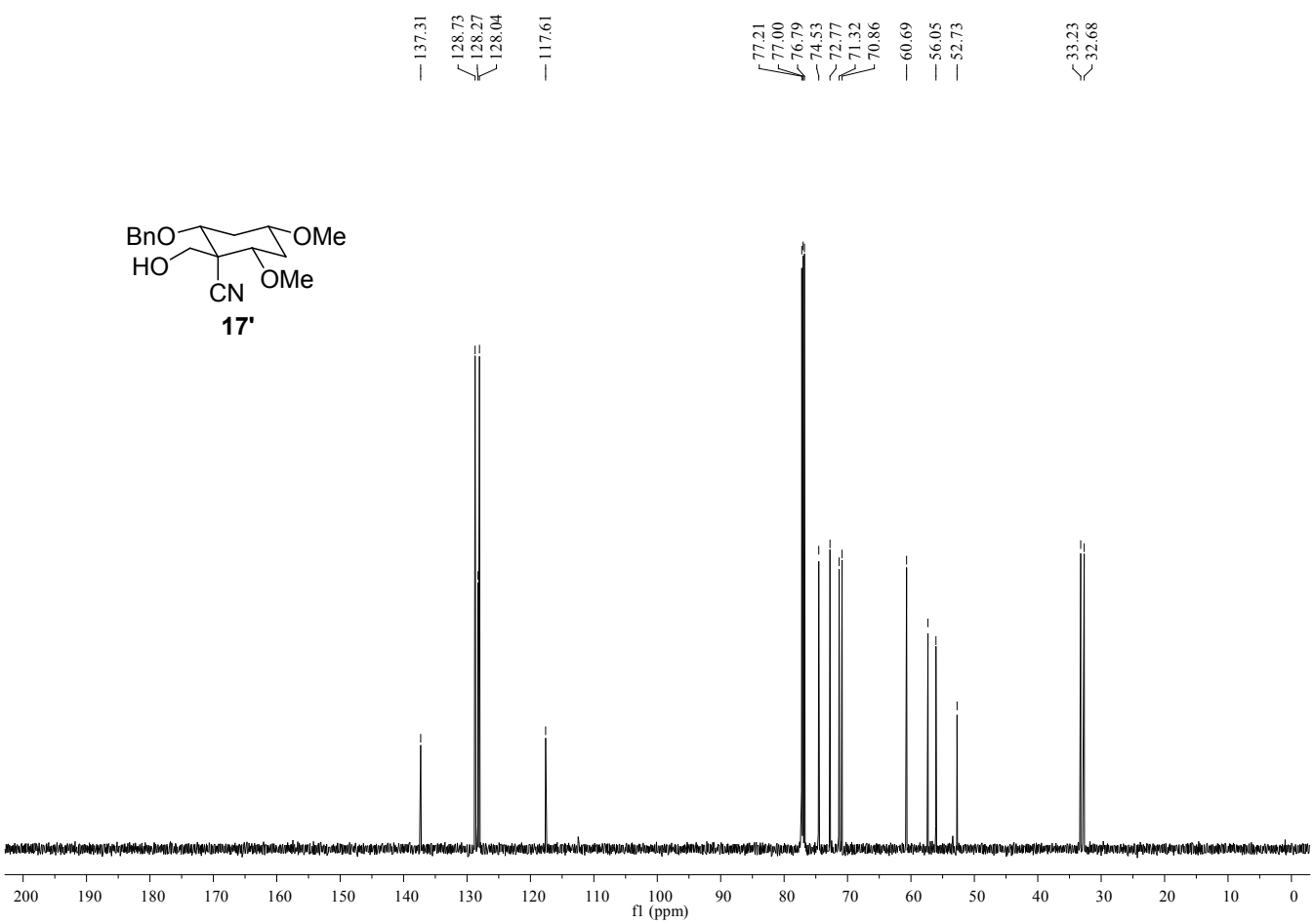

7.376
7.358
7.355
7.340
7.334
7.321
7.318
7.301
7.291
7.285
7.260
4.723
4.693
4.448
4.121
4.094
3.722
3.166
3.137
3.120
3.099
2.486
2.455
2.368
2.338
1.693
1.663
1.631
1.600
1.570
BnO
OMe
HO
OH
CN
S4
4.08
1.00
1.01
1.01
1.01
1.94
3.98
2.07
0.98
0.98
2.02
f1 (ppm)

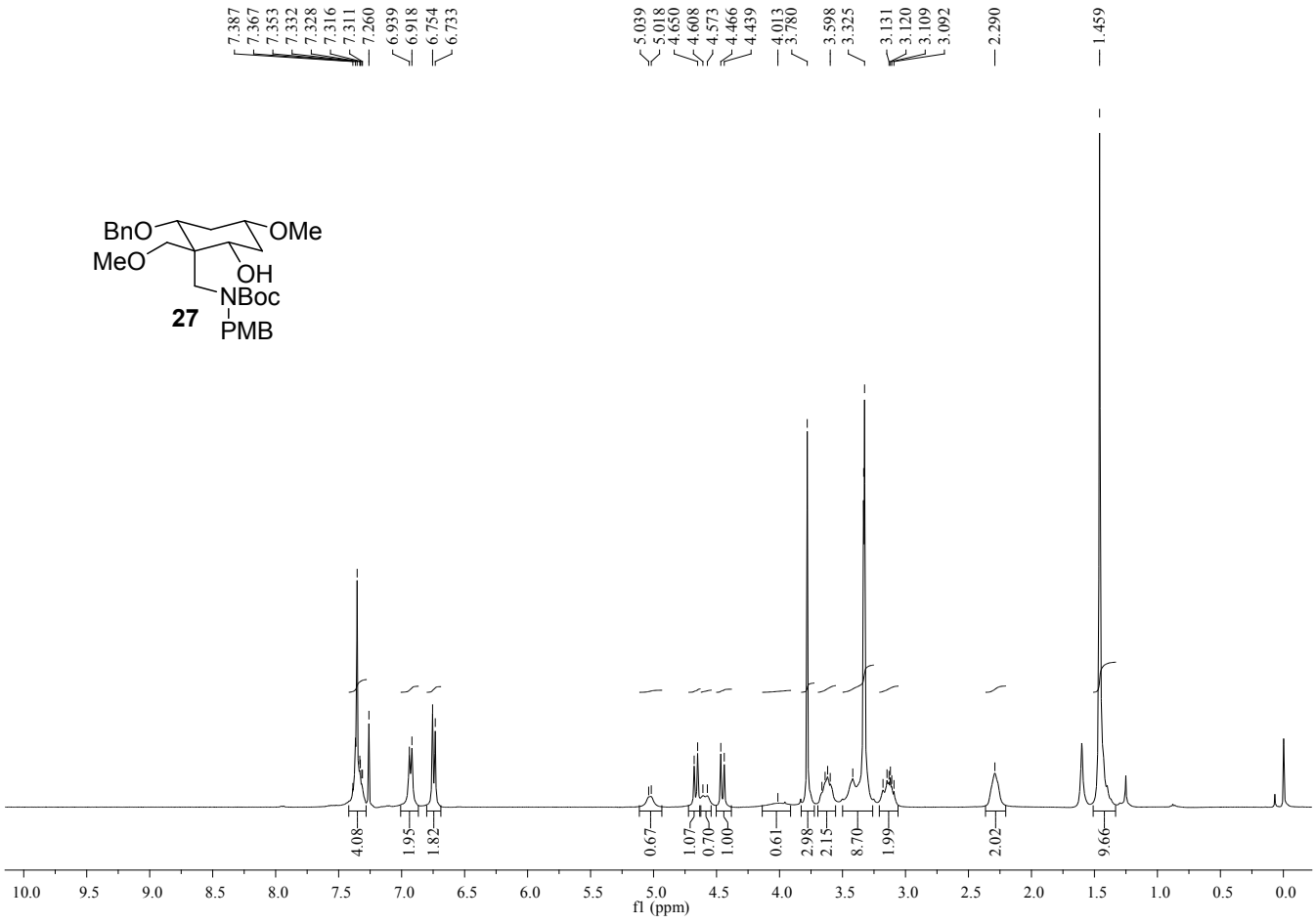

137.23
128.60
128.11
127.87
118.17
77.21
77.00
76.79
71.26
67.42
62.29
56.09
53.67
37.01
33.43
BnO
OMe
HO
OH
CN
S4
f1 (ppm)

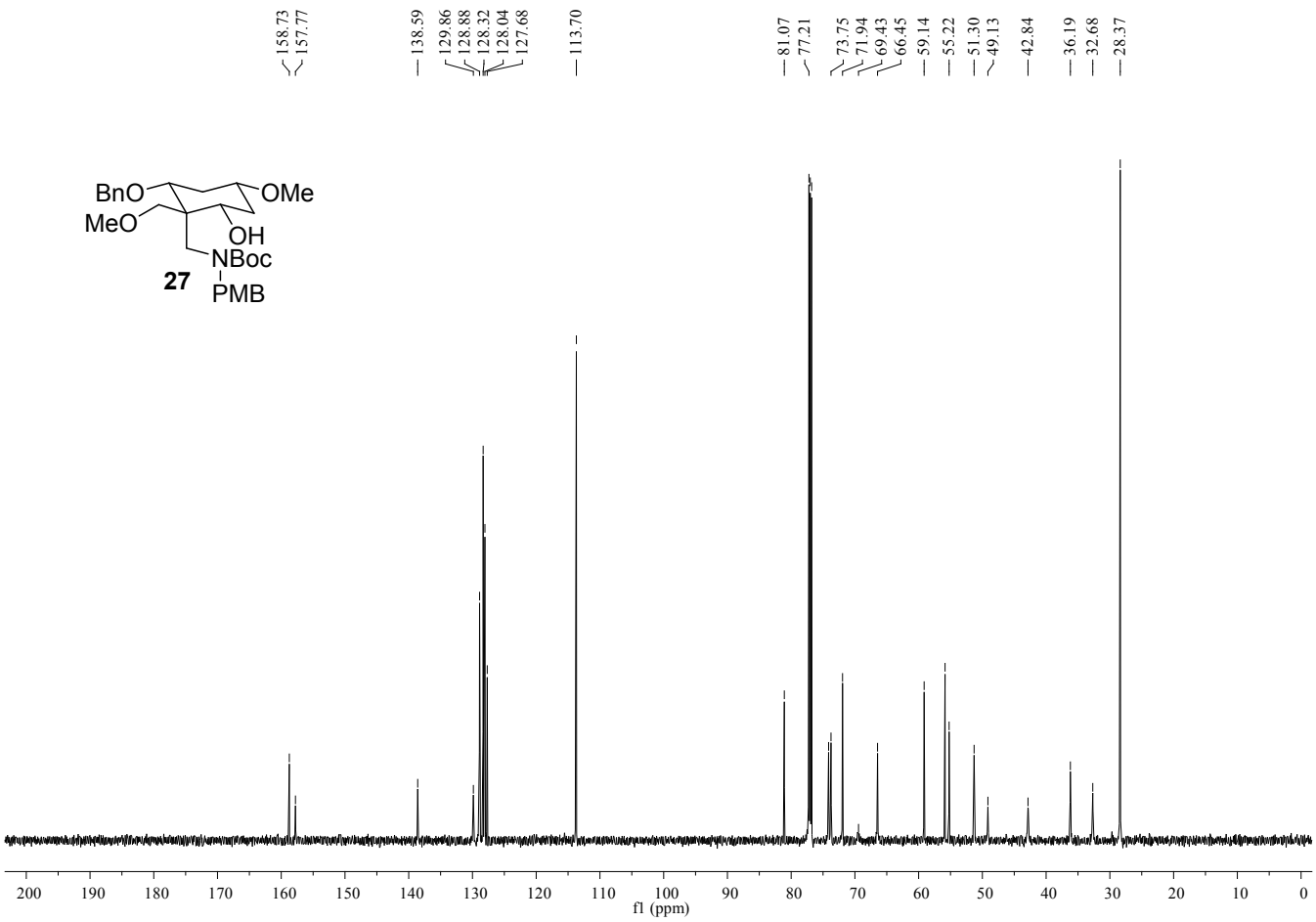

7.382
7.364
7.346
7.332
7.315
7.299
7.291
7.260
4.723
4.693
4.473
4.443
3.949
3.926
3.627
3.332
3.135
3.107
2.981
2.467
2.436
2.383
2.352
1.702
1.693
1.671
1.663
1.642
1.634
1.612
1.604
BnO
OMe
MeO
OH
CN
17
4.55
1.00
1.00
1.04
1.01
1.00
6.84
1.06
0.86
1.02
1.01
1.17
1.14
10.0 9.5 9.0 8.5 8.0 7.5 7.0 6.5 6.0 5.5 5.0 4.5 4.0 3.5 3.0 2.5 2.0 1.5 1.0 0.5 0.0
f1 (ppm)

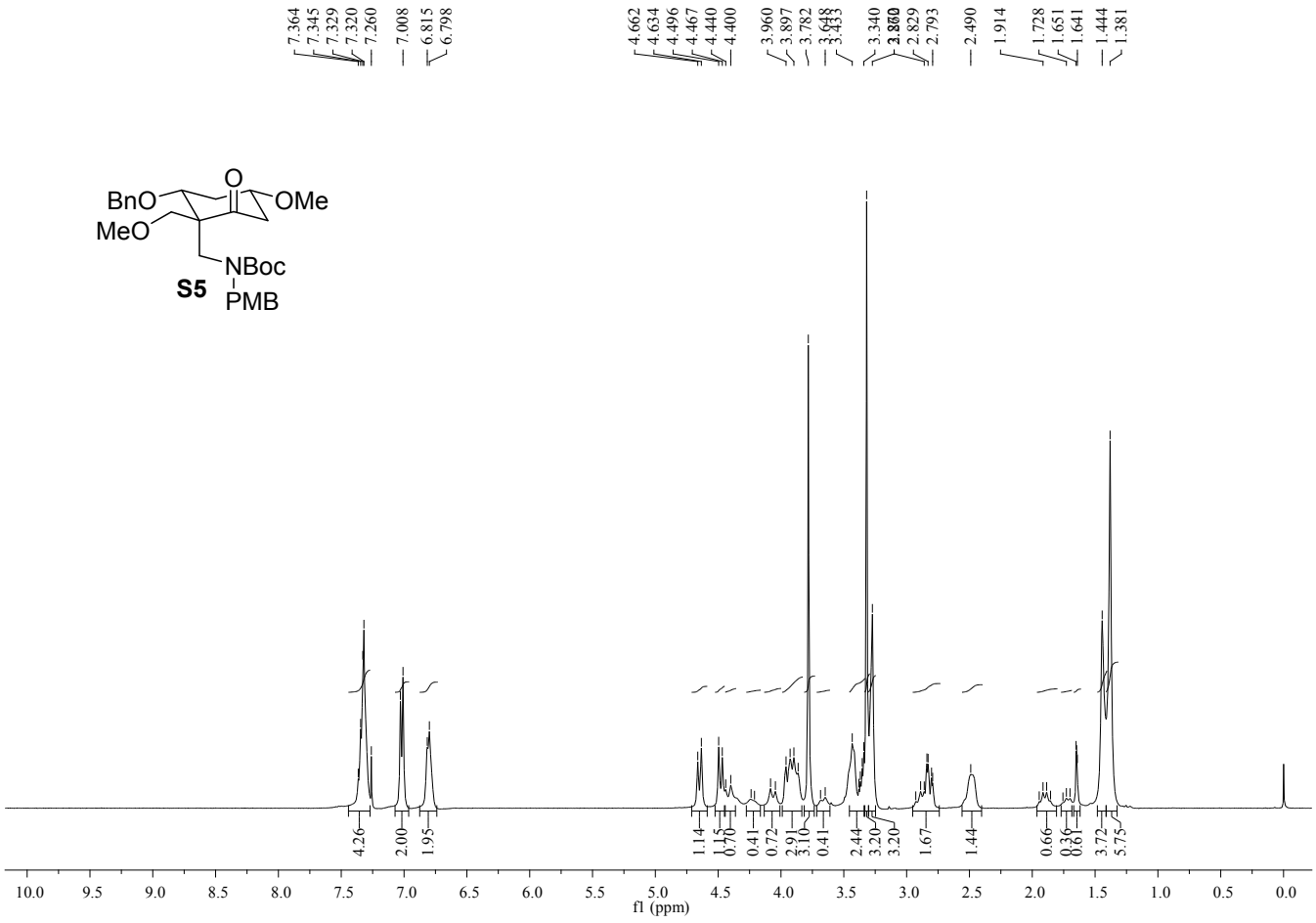

137.36
128.45
127.94
127.79
117.65
77.21
77.00
76.79
71.28
67.85
59.43
55.99
52.62
36.87
33.39
BnO
OMe
MeO
OH
CN
17
200 190 180 170 160 150 140 130 120 110 100 90 80 70 60 50 40 30 20 10 0
f1 (ppm)

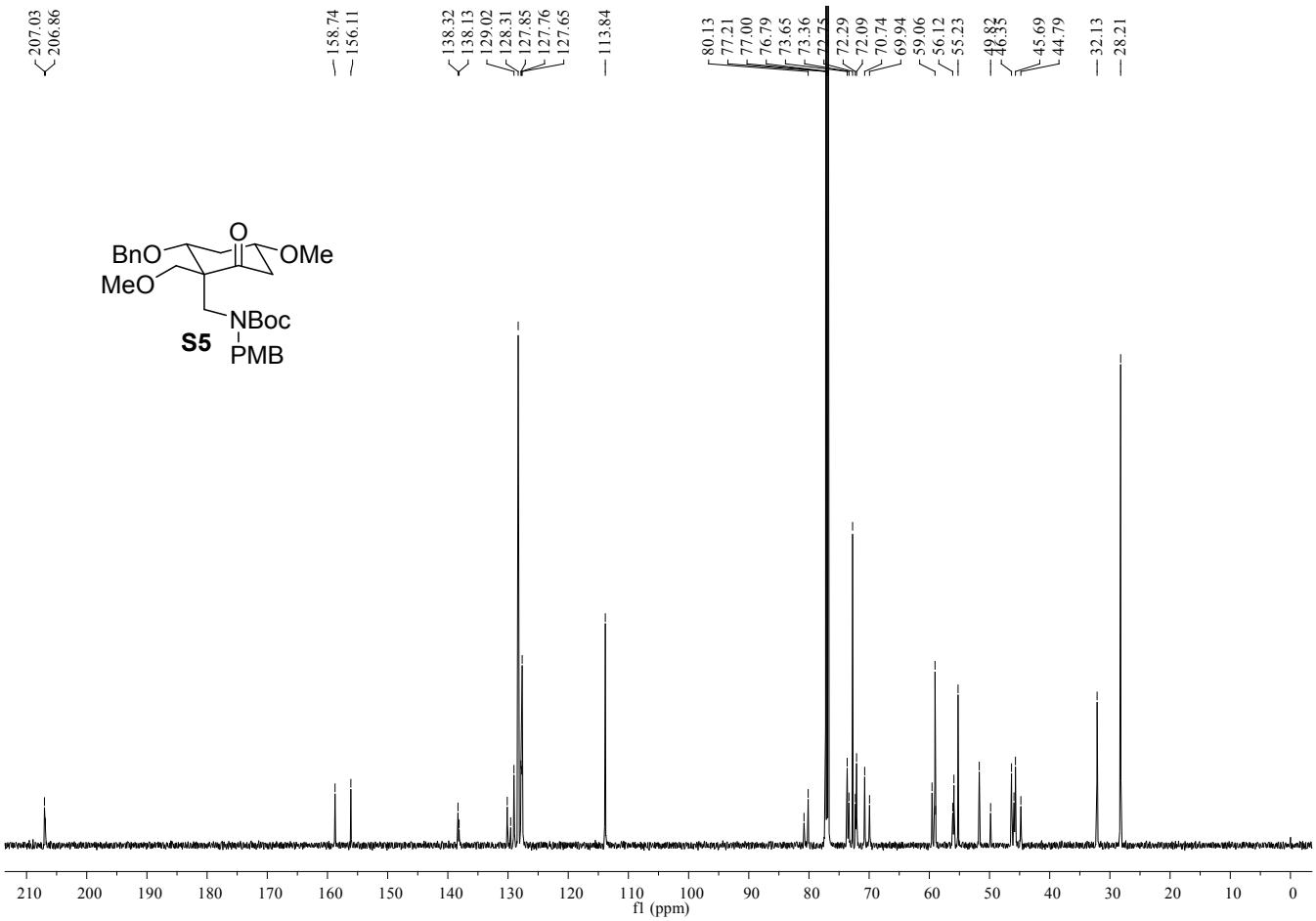

7.393
7.381
7.363
7.351
7.331
7.260
4.779
4.759
4.458
4.437
3.938
3.933
3.907
3.185
3.181
3.119
3.101
3.082
2.523
2.503
1.833
1.824
1.717
1.697
1.677
1.657
1.603
1.583
1.563
1.543
BnO
OMe
HO
OMe
CN
17'
4.24
0.98
1.02
2.09
6.85
1.02
1.01
2.09
0.90
1.16
1.12
f1 (ppm)

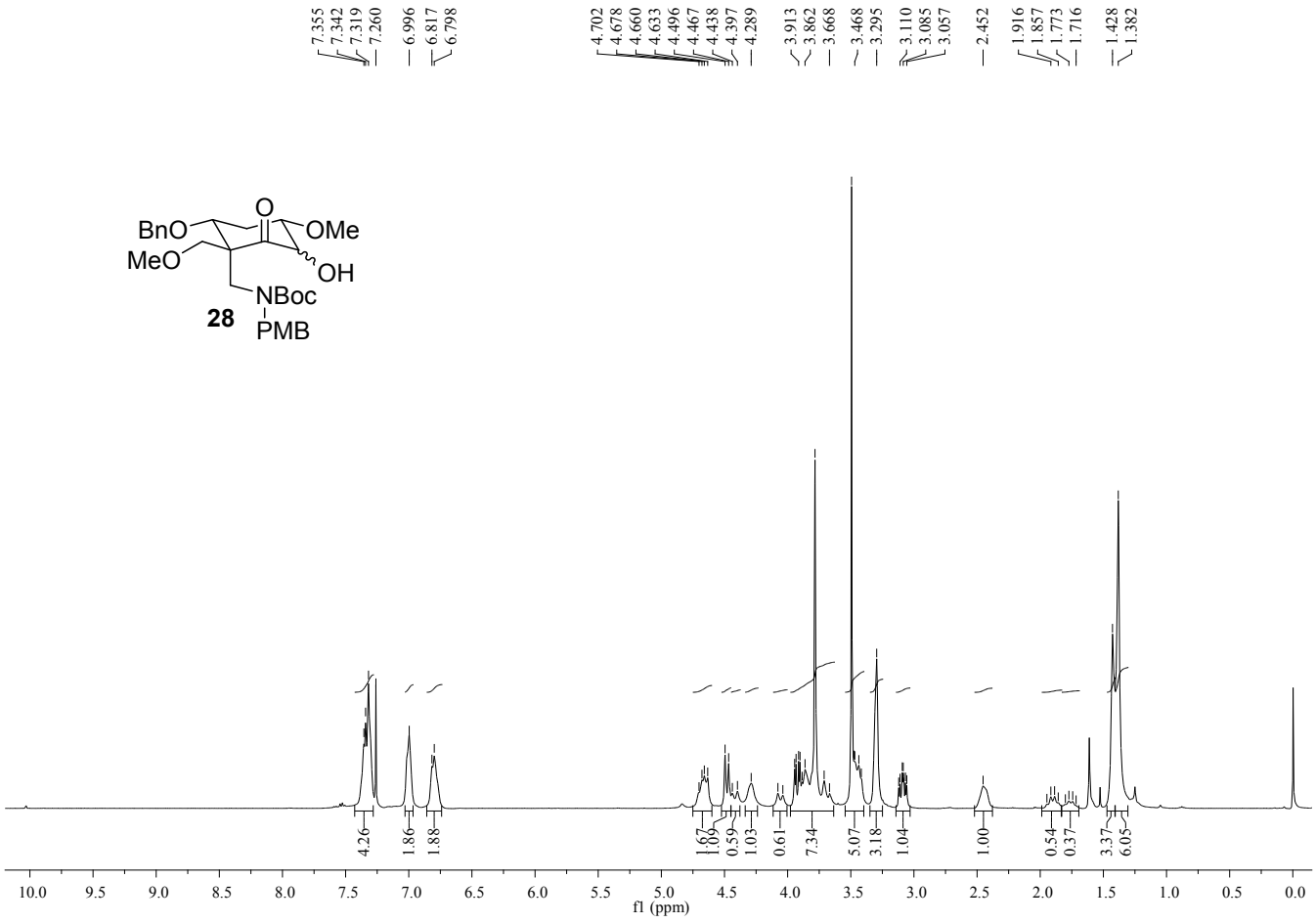

137.31
128.73
128.27
128.04
117.61
77.21
77.00
76.79
74.53
72.77
71.32
70.86
60.69
56.05
52.73
33.23
32.68
BnO
OMe
HO
OMe
CN
17'
f1 (ppm)

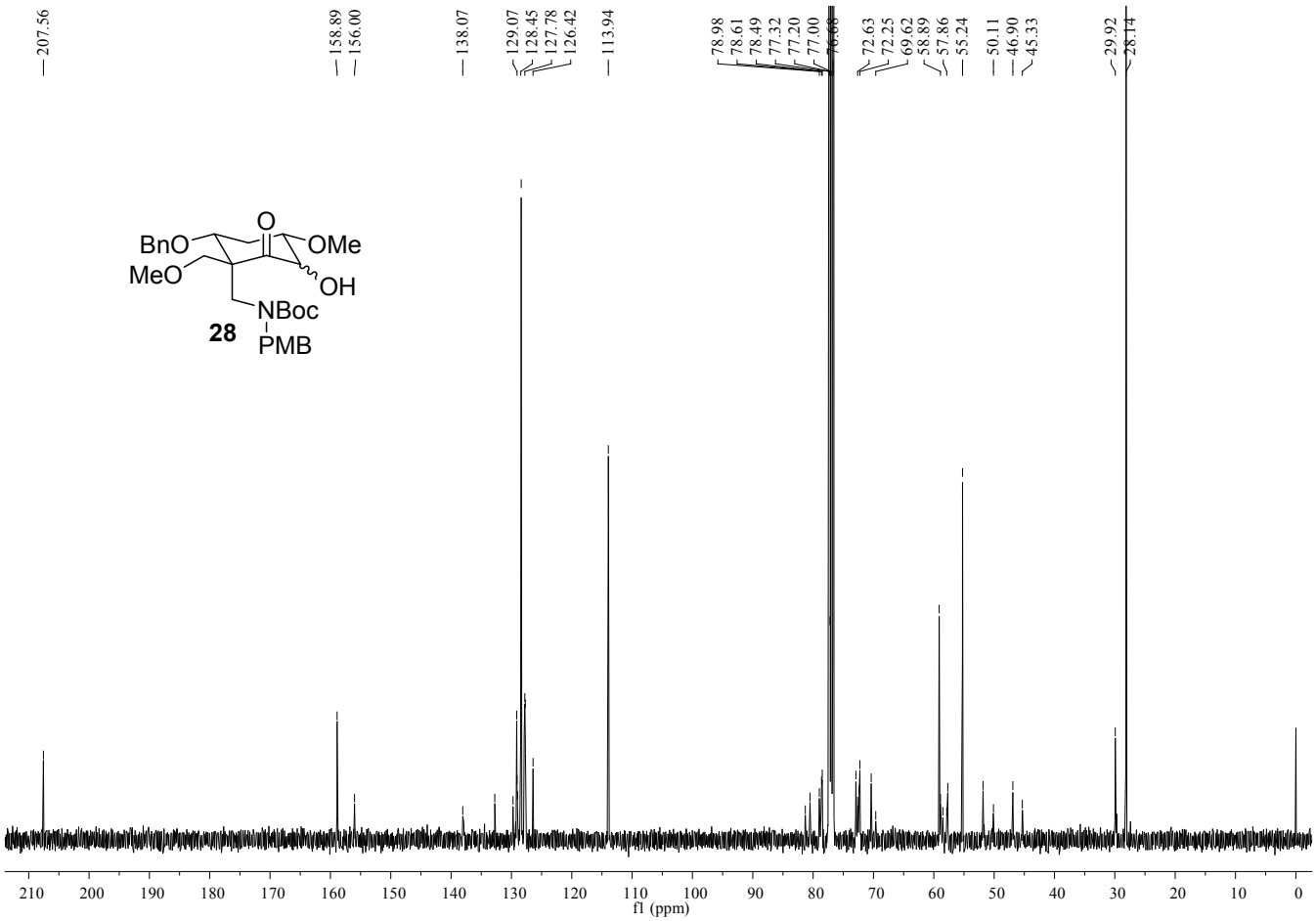

7.387
7.367
7.353
7.332
7.328
7.316
7.311
7.260
6.939
6.918
6.754
6.733
5.039
5.018
4.650
4.608
4.573
4.466
4.439
4.013
3.780
3.598
3.325
3.131
3.120
3.109
3.092
2.290
1.459
BnO
OMe
MeO
OH
NBoc
PMB
27
4.08
1.95
1.82
0.67
1.07
0.70
1.00
0.61
2.98
2.15
8.70
1.99
2.02
9.66
fl (ppm)

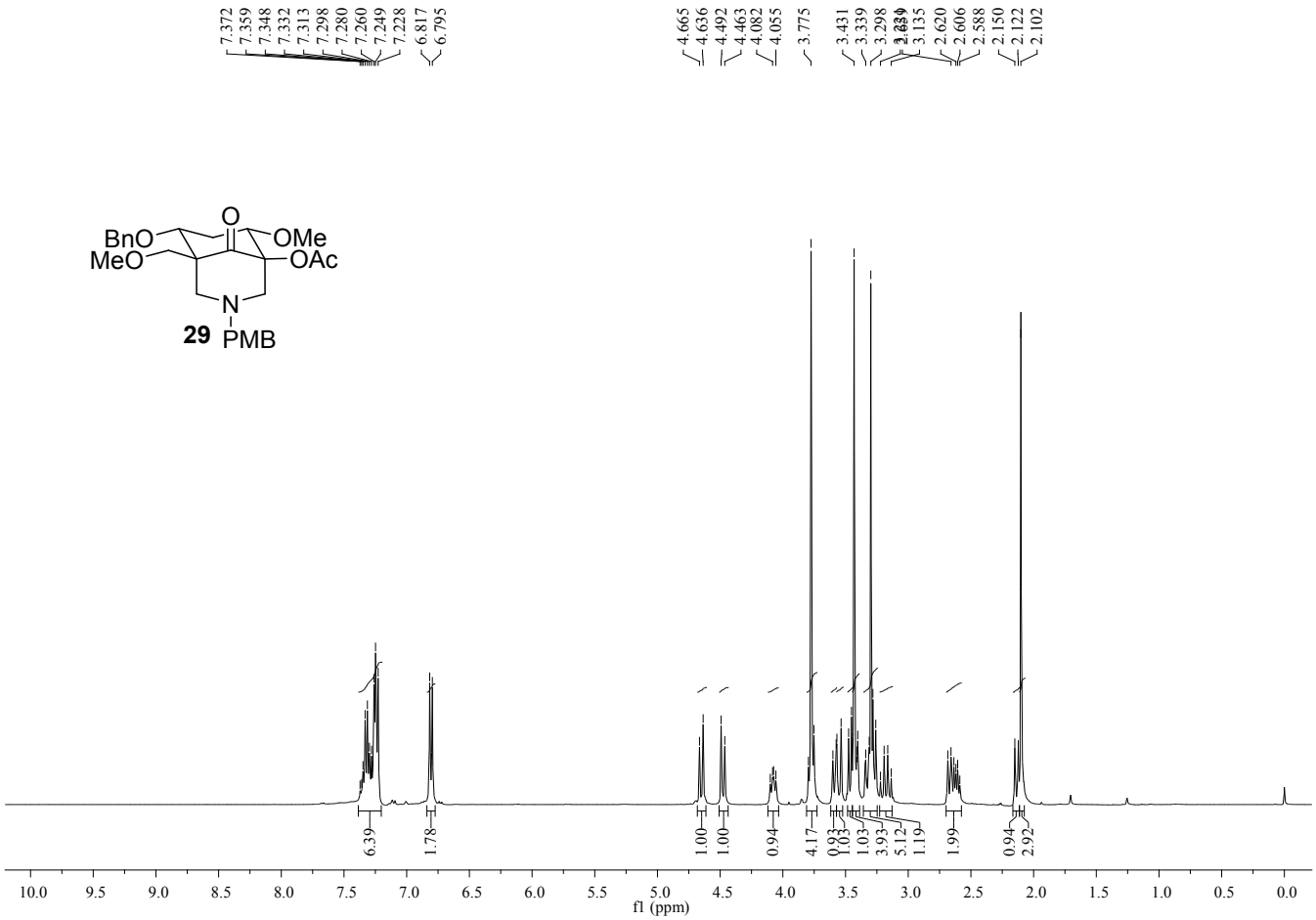

158.73
157.77
138.59
129.86
128.88
128.32
128.04
127.68
113.70
81.07
77.21
73.75
71.94
69.43
66.45
59.14
55.22
51.30
49.13
42.84
36.19
32.68
28.37
BnO
OMe
MeO
OH
NBoc
PMB
27
fl (ppm)

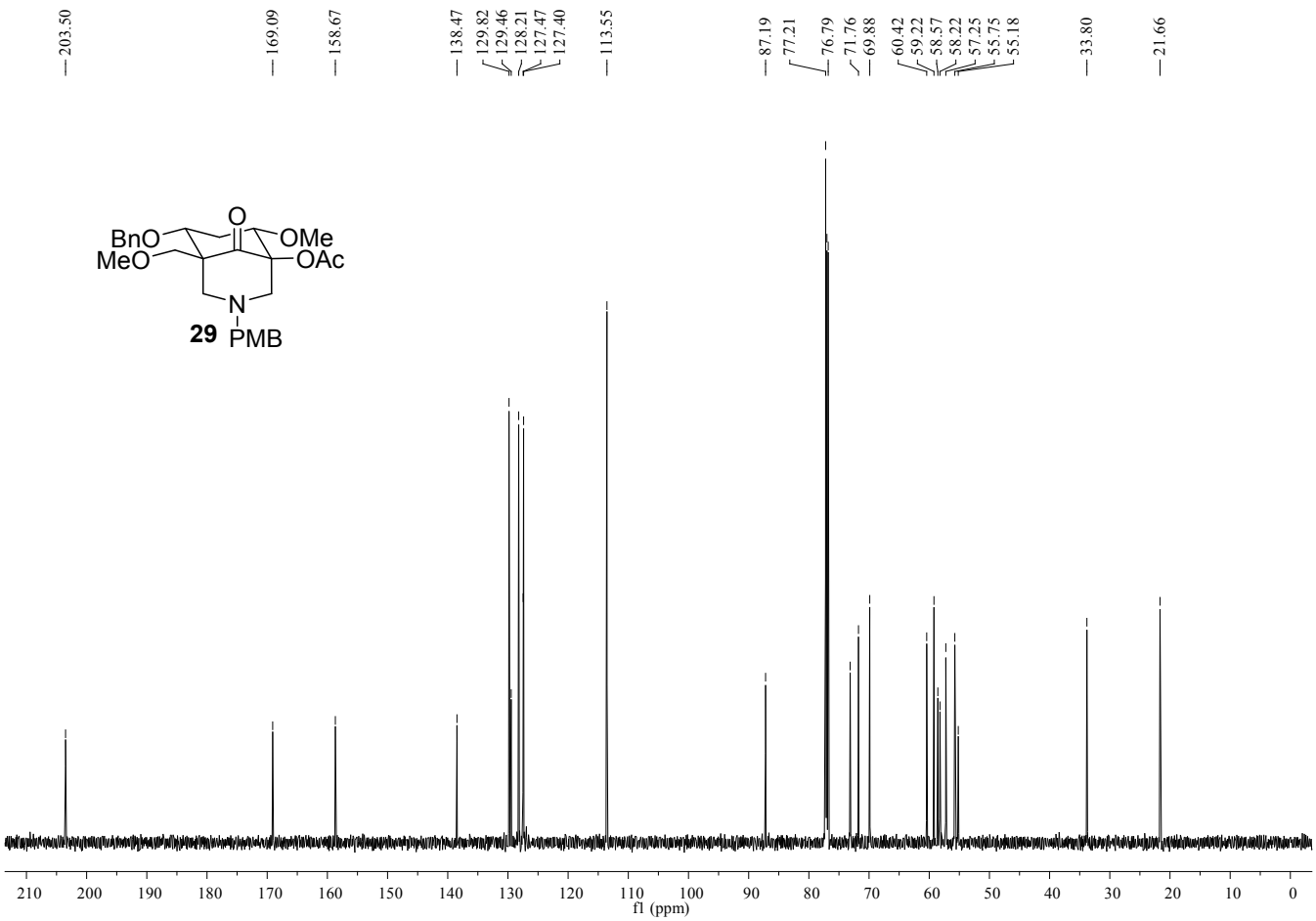

7.364
7.345
7.329
7.320
7.260
7.008
6.815
6.798
4.662
4.634
4.496
4.467
4.440
4.400
3.960
3.897
3.782
3.648
3.433
3.340
2.829
2.793
2.490
1.914
1.728
1.651
1.641
1.444
1.381
BnO
OMe
MeO
NBoc
PMB
S5
4.26
2.00
1.95
1.14
0.70
0.41
0.72
2.91
3.10
0.41
2.44
3.20
3.20
1.67
1.44
0.66
3.72
5.75
10.0
9.5
9.0
8.5
8.0
7.5
7.0
6.5
6.0
5.5
5.0
4.5
4.0
3.5
3.0
2.5
2.0
1.5
1.0
0.5
0.0
f1 (ppm)

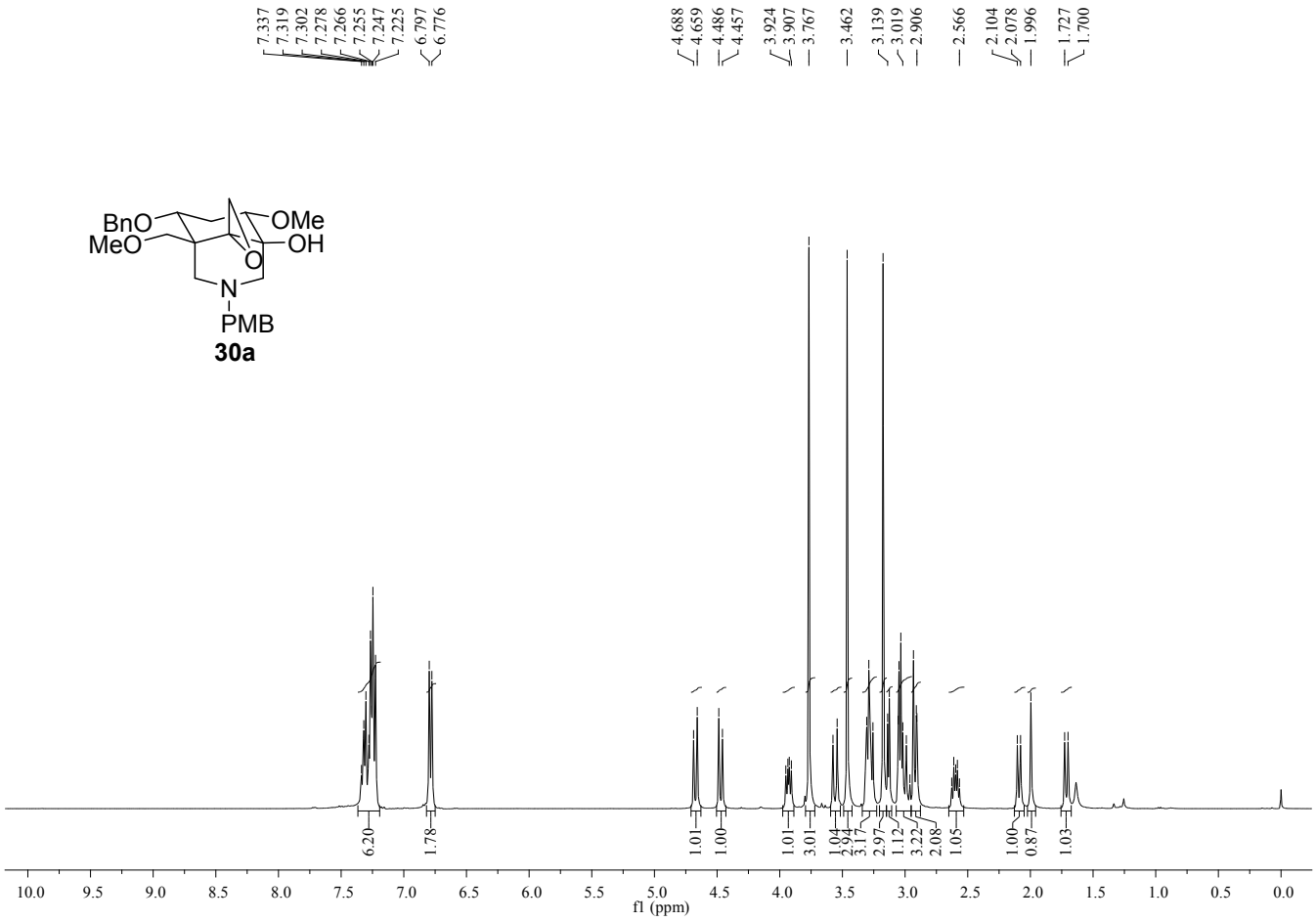

207.03
206.86
158.74
156.11
138.32
138.13
129.02
128.31
127.85
127.76
127.65
113.84
80.13
77.21
77.00
76.79
73.65
73.36
72.29
72.09
70.74
69.94
59.06
56.12
55.23
49.82
46.35
45.69
44.79
32.13
28.21
BnO
OMe
MeO
NBoc
PMB
S5
210
200
190
180
170
160
150
140
130
120
110
100
90
80
70
60
50
40
30
20
10
0
f1 (ppm)

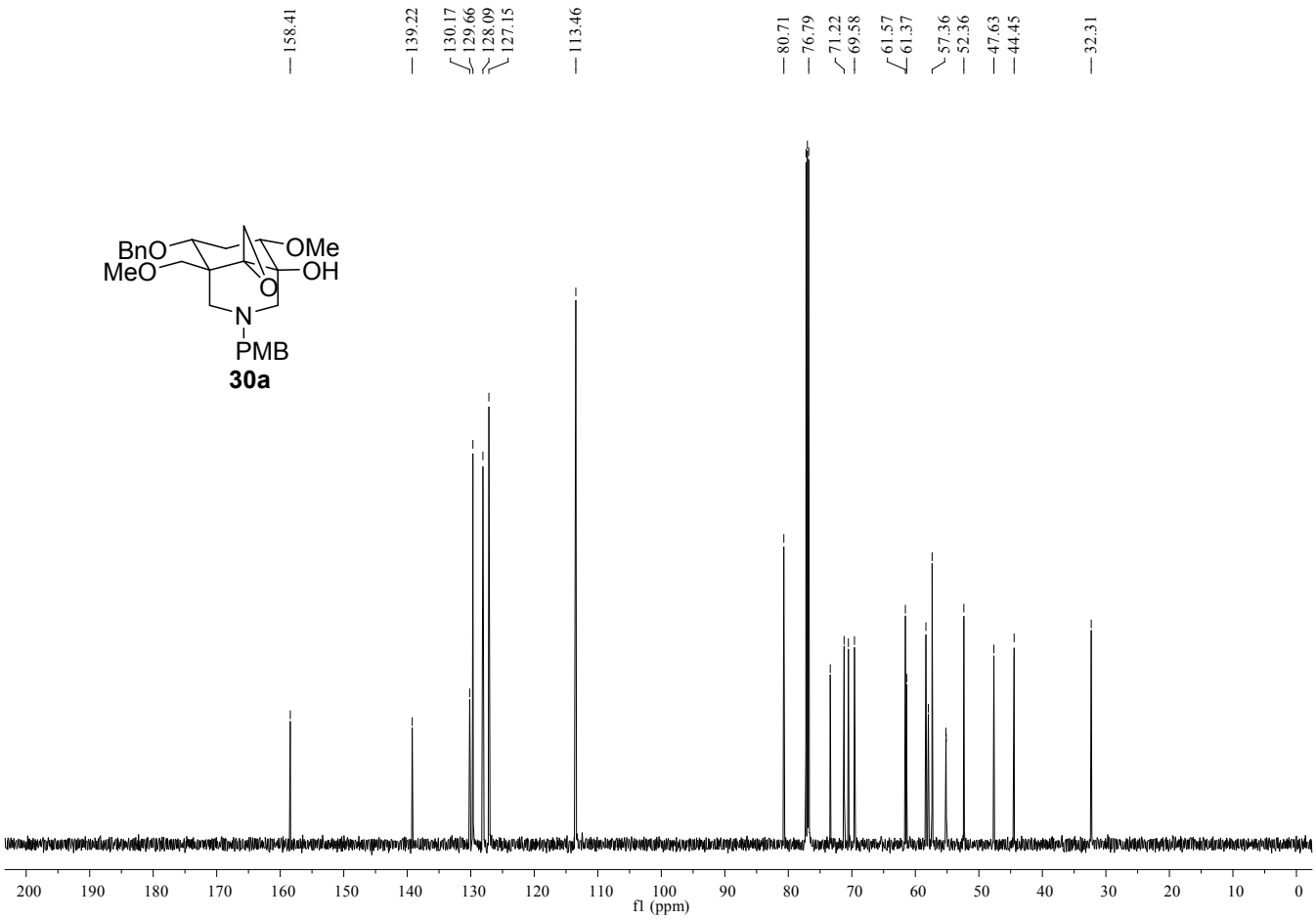

7.355
7.342
7.319
7.260
6.996
6.817
6.798
4.702
4.678
4.660
4.633
4.496
4.467
4.438
4.397
4.289
3.913
3.862
3.668
3.468
3.295
3.110
3.085
3.057
2.452
1.916
1.857
1.773
1.716
1.428
1.382
BnO
MeO
O
OMe
OH
NBoc
PMB
28
4.26
1.86
1.88
1.67
1.09
0.59
1.03
0.61
7.34
5.07
3.18
1.04
1.00
0.54
0.37
3.37
6.05
10.0 9.5 9.0 8.5 8.0 7.5 7.0 6.5 6.0 5.5 5.0 4.5 4.0 3.5 3.0 2.5 2.0 1.5 1.0 0.5 0.0
f1 (ppm)

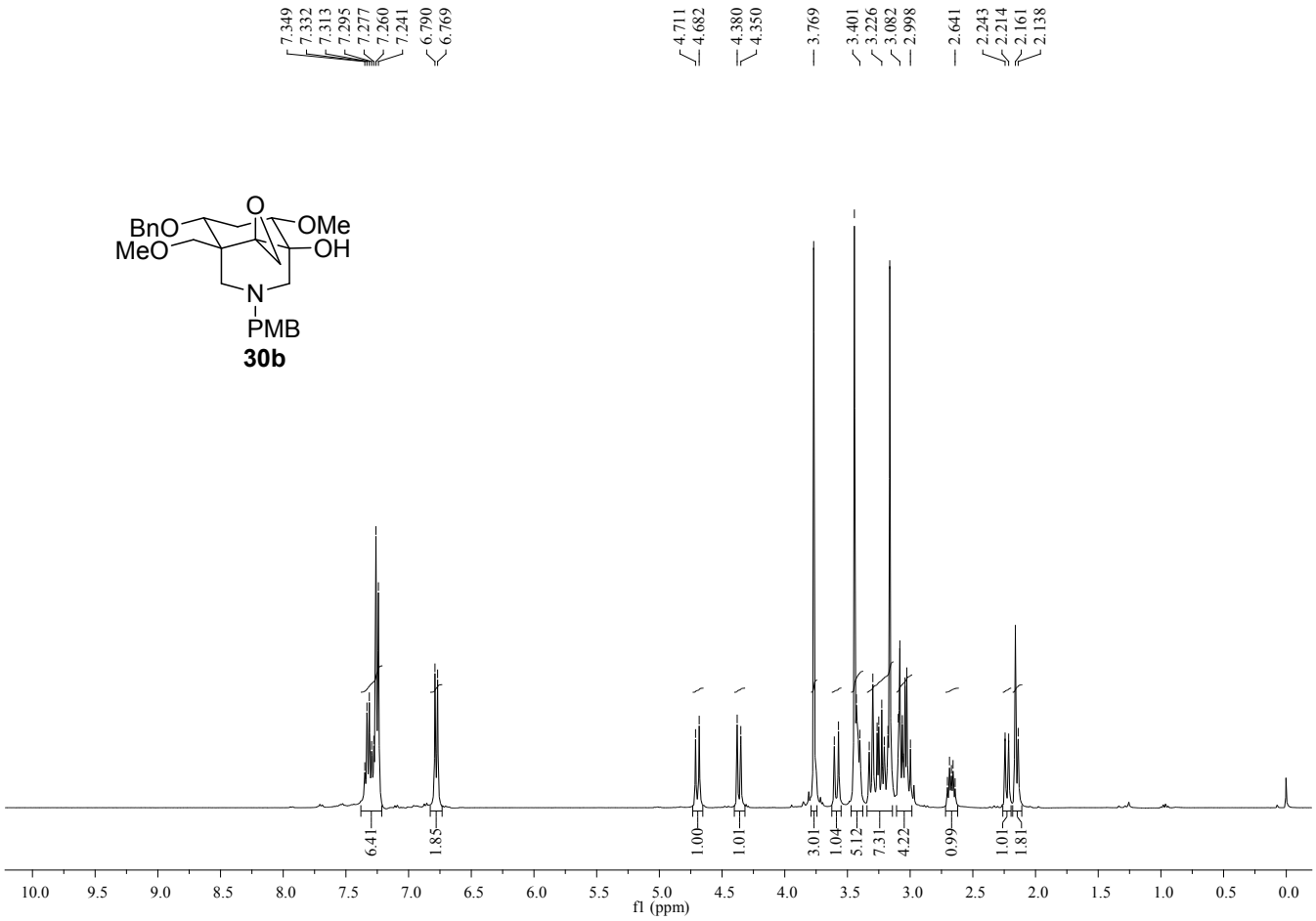

207.56
158.89
156.00
138.07
129.07
128.45
127.78
126.42
113.94
78.98
78.61
78.49
77.32
77.20
77.00
76.68
72.63
72.25
69.62
58.89
57.86
55.24
50.11
46.90
45.33
29.92
28.14
BnO
MeO
O
OMe
OH
NBoc
PMB
28
210 200 190 180 170 160 150 140 130 120 110 100 90 80 70 60 50 40 30 20 10 0
f1 (ppm)

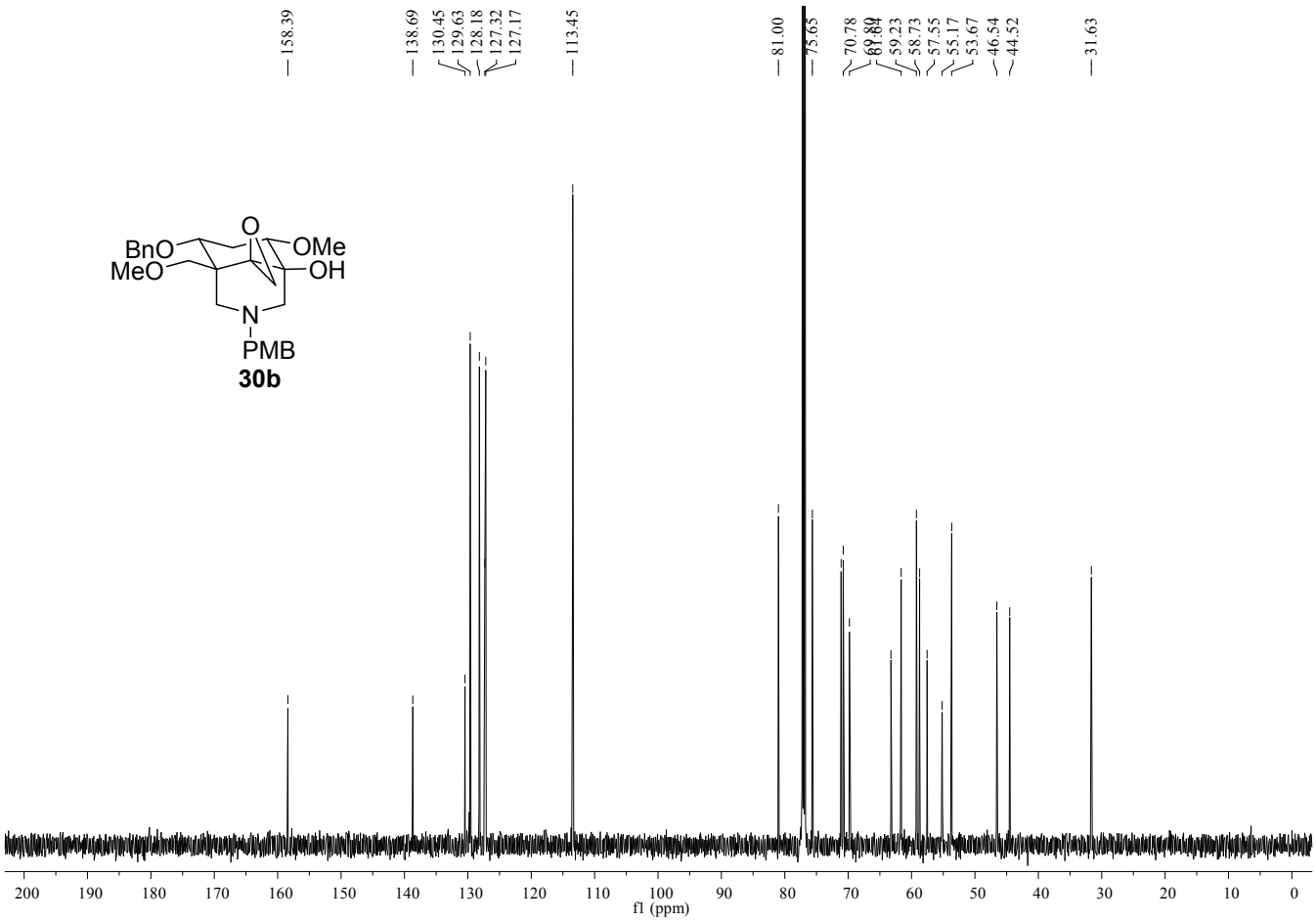

7.372
7.359
7.348
7.332
7.313
7.298
7.280
7.260
7.249
7.228
6.817
6.795
4.665
4.636
4.492
4.463
4.082
4.055
3.775
3.431
3.339
3.298
3.135
2.620
2.606
2.588
2.150
2.122
2.102
BnO
MeO
OMe
OAc
N
PMB
29
6.39
1.78
1.00
1.00
0.94
4.17
0.93
1.03
3.93
5.12
1.19
1.99
0.94
2.92
10.0
9.5
9.0
8.5
8.0
7.5
7.0
6.5
6.0
5.5
5.0
4.5
4.0
3.5
3.0
2.5
2.0
1.5
1.0
0.5
0.0
f1 (ppm)

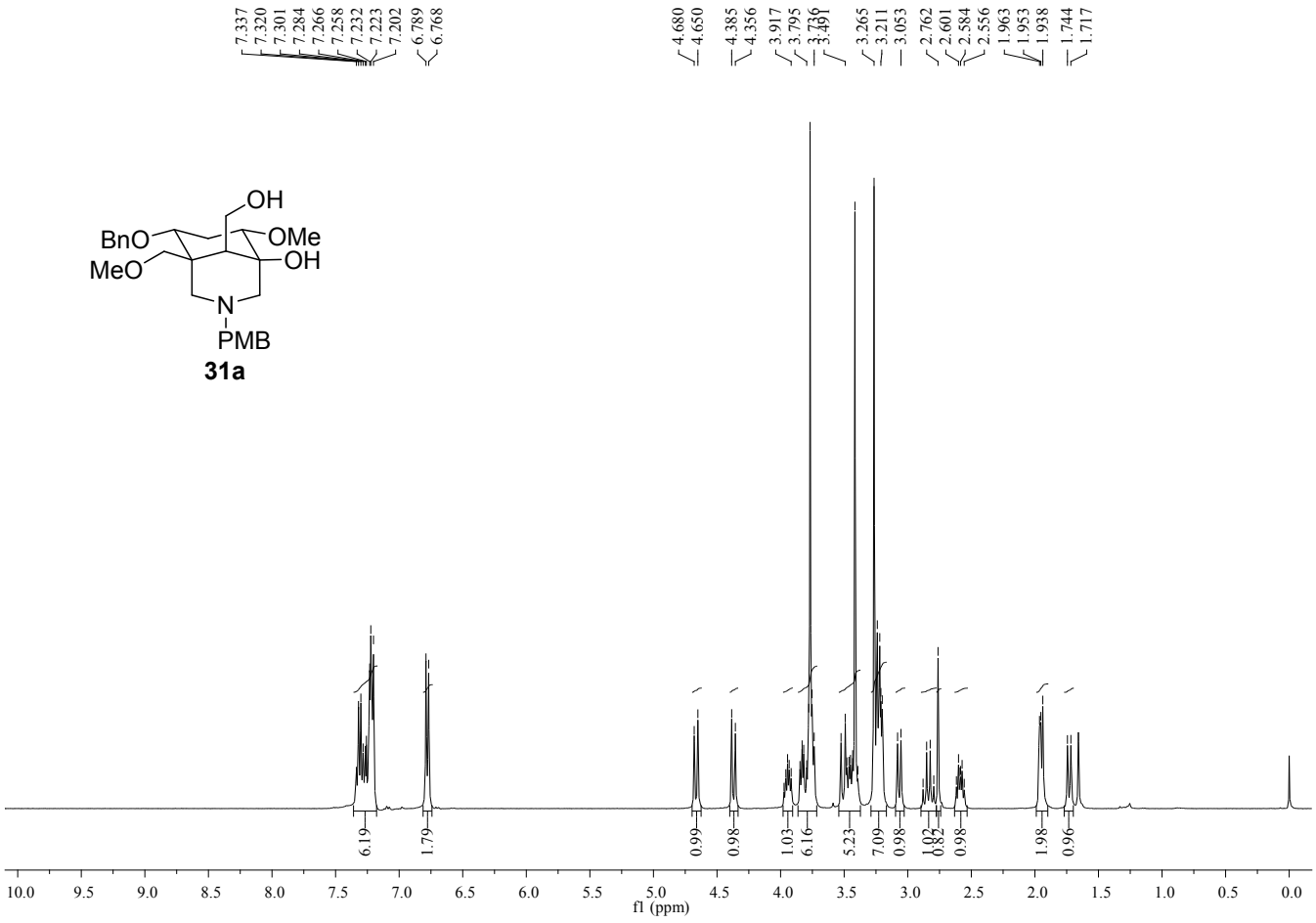

203.50
169.09
158.67
138.47
129.82
129.46
128.21
127.47
127.40
113.55
87.19
77.21
76.79
71.76
69.88
60.42
59.22
58.57
58.22
57.25
55.75
55.18
33.80
21.66
BnO
MeO
OMe
OAc
N
PMB
29
210
200
190
180
170
160
150
140
130
120
110
100
90
80
70
60
50
40
30
20
10
0
f1 (ppm)

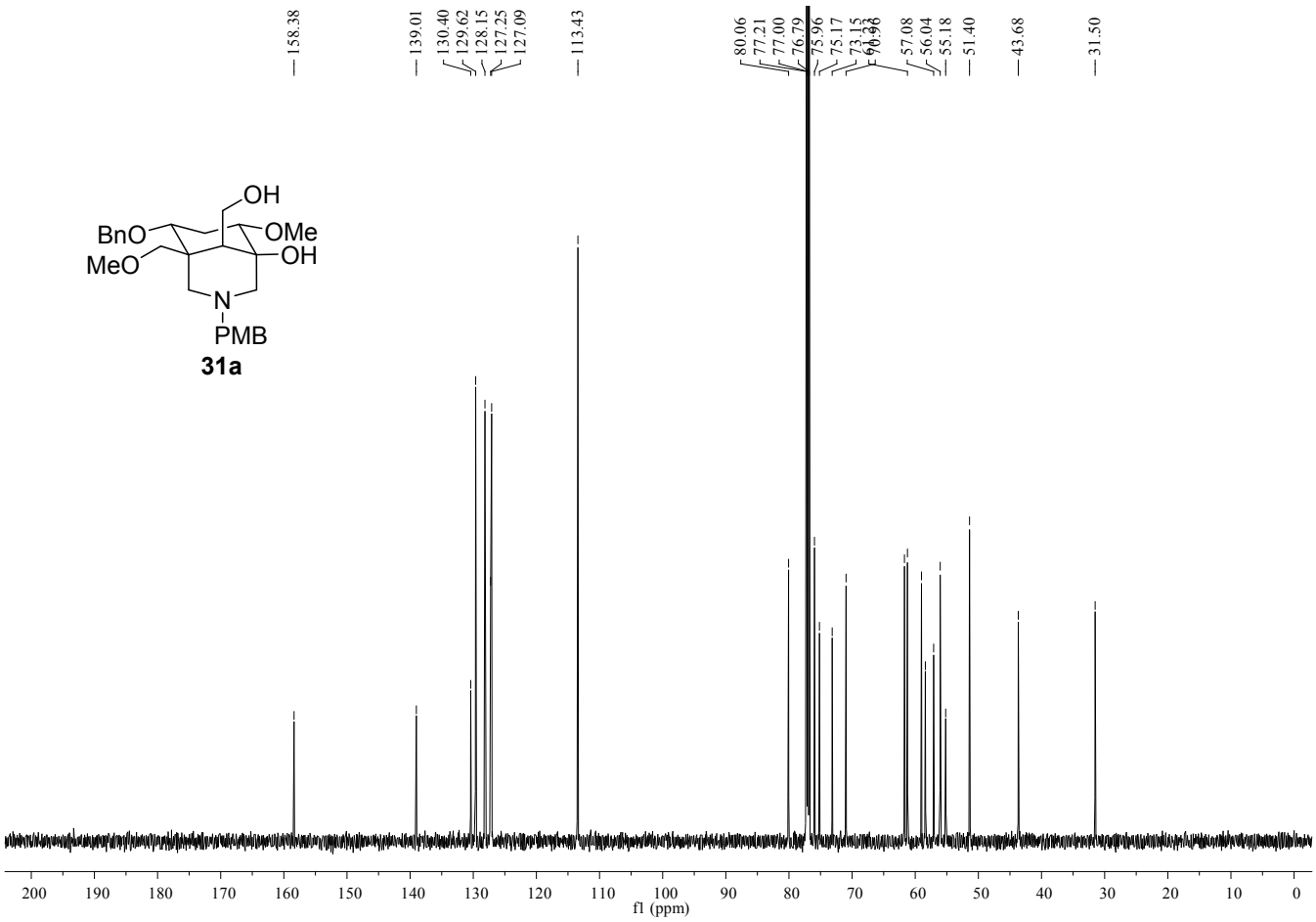

7.337
7.319
7.302
7.278
7.266
7.255
7.247
7.225
6.797
6.776
4.688
4.659
4.486
4.457
3.924
3.907
3.767
3.462
3.139
3.019
2.906
2.566
2.104
2.078
1.996
1.727
1.700
BnO
MeO
OMe
OH
O
N
PMB
30a
6.20
1.78
1.01
1.00
1.01
3.01
1.04
2.94
3.17
2.97
1.12
3.22
2.08
1.05
1.00
0.87
1.03
fl (ppm)

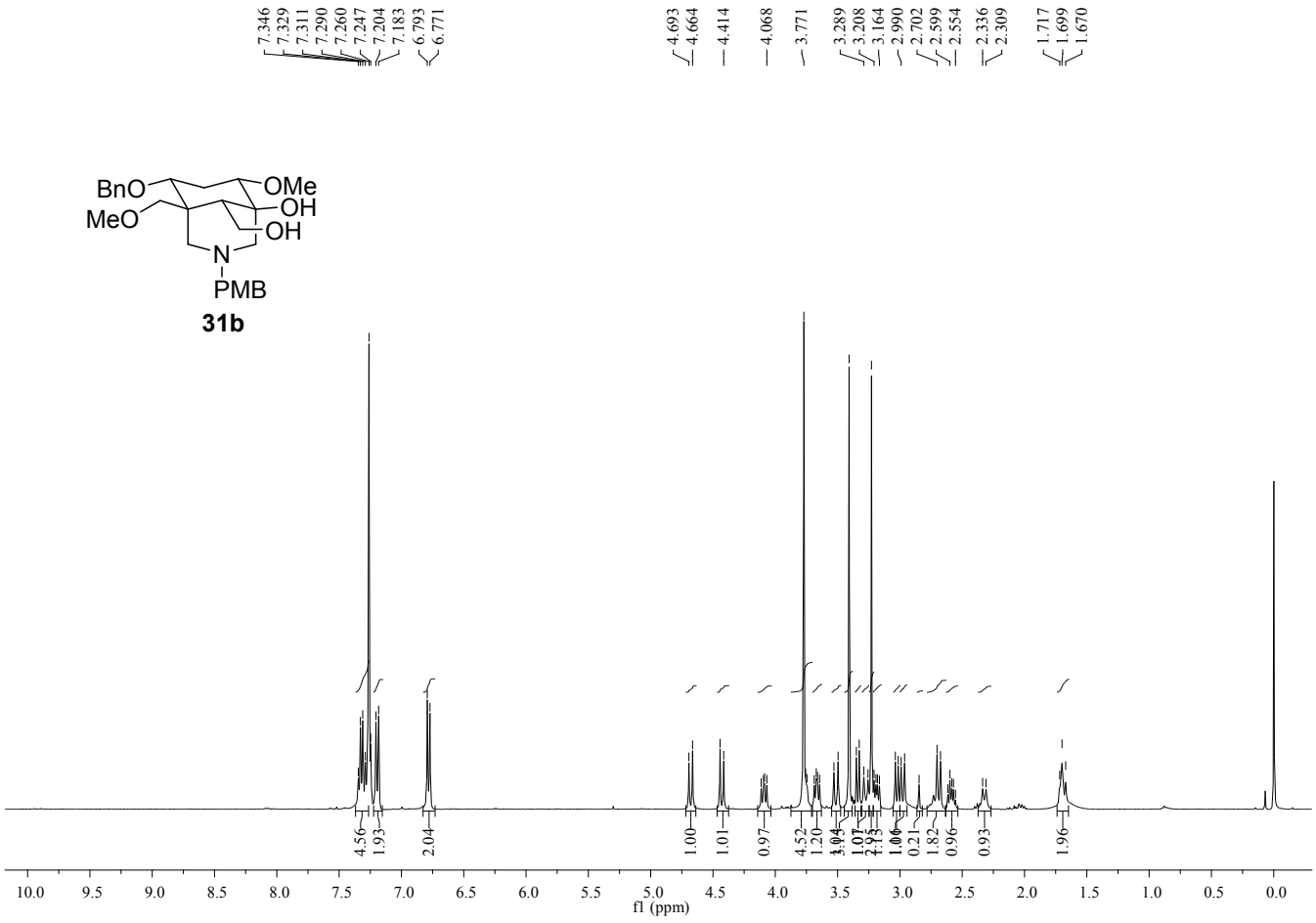

158.41
139.22
130.17
129.66
128.09
127.15
113.46
80.71
76.79
71.22
69.58
61.57
61.37
57.36
52.36
47.63
44.45
32.31
BnO
MeO
OMe
OH
O
N
PMB
30a
fl (ppm)

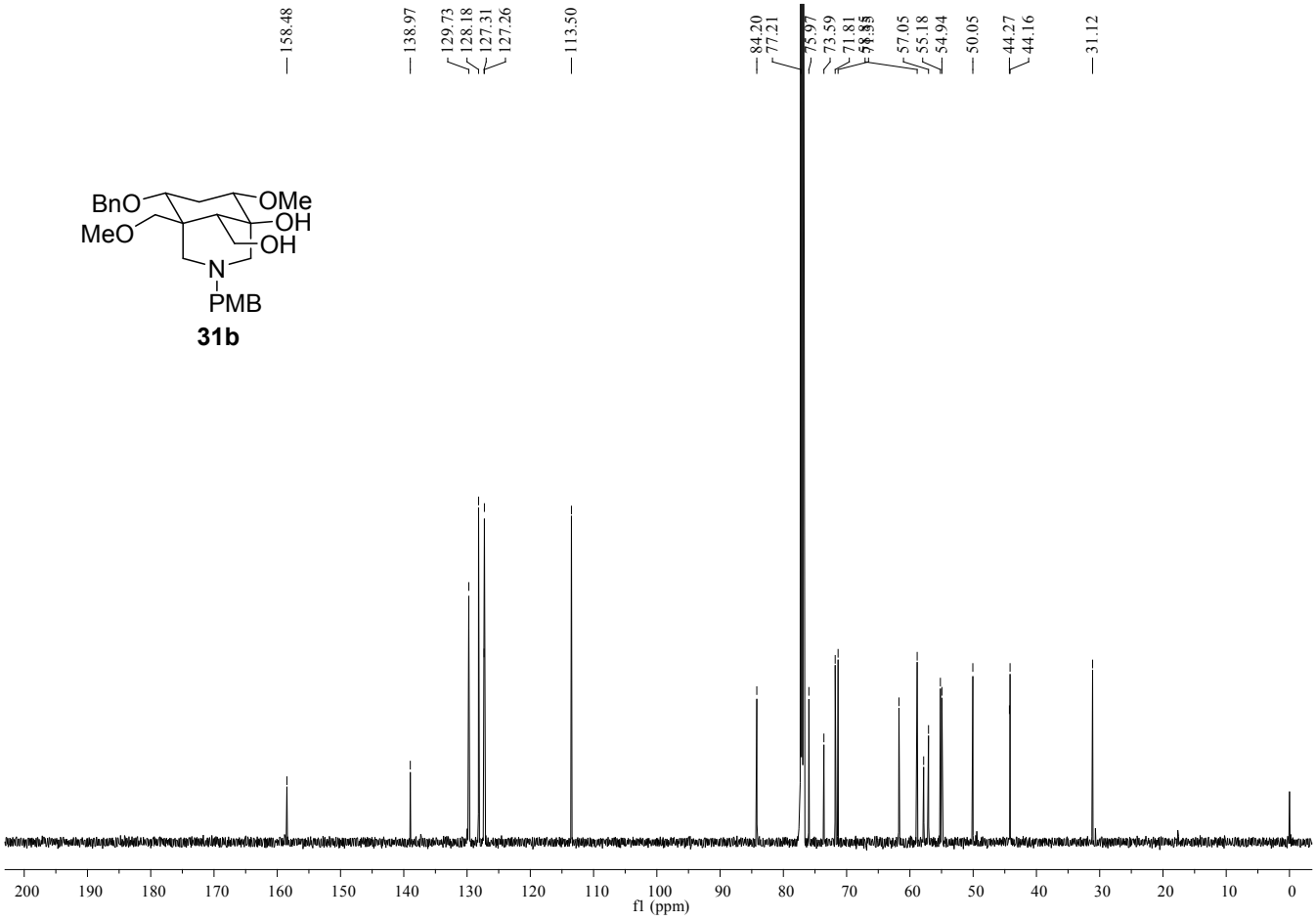

7.349
7.332
7.313
7.295
7.277
7.260
7.241
6.790
6.769
4.711
4.682
4.380
4.350
3.769
3.401
3.226
3.082
2.998
2.641
2.243
2.214
2.161
2.138
BnO
MeO
O
OMe
OH
N
PMB
30b
6.41
1.85
1.00
1.01
3.01
1.04
5.12
7.31
4.22
0.99
1.01
1.81
fl (ppm)

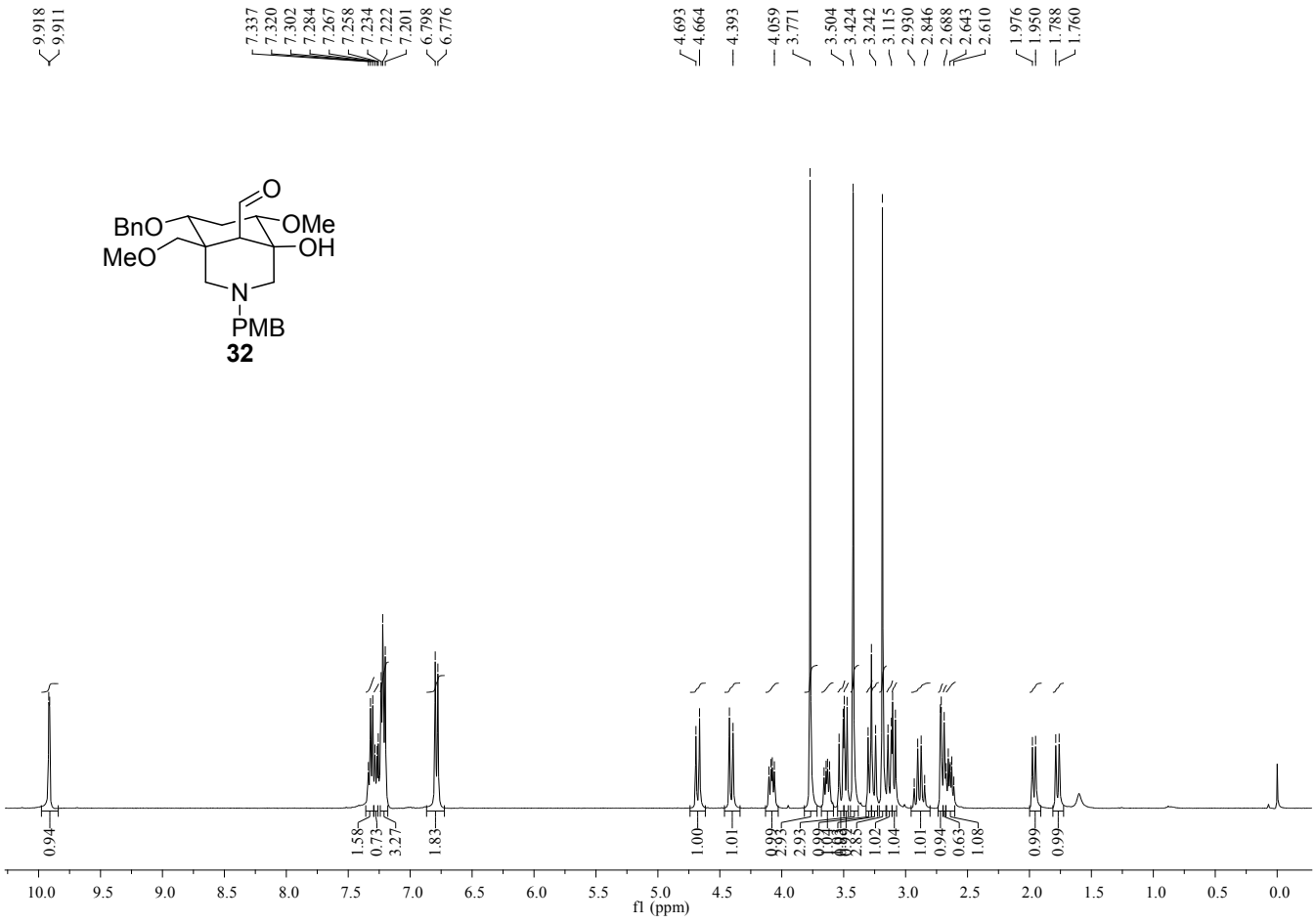

158.39
138.69
130.45
129.63
128.18
127.32
127.17
113.45
81.00
75.65
70.78
59.23
58.73
57.55
55.17
53.67
46.54
44.52
31.63
BnO
MeO
O
OMe
OH
N
PMB
30b
fl (ppm)

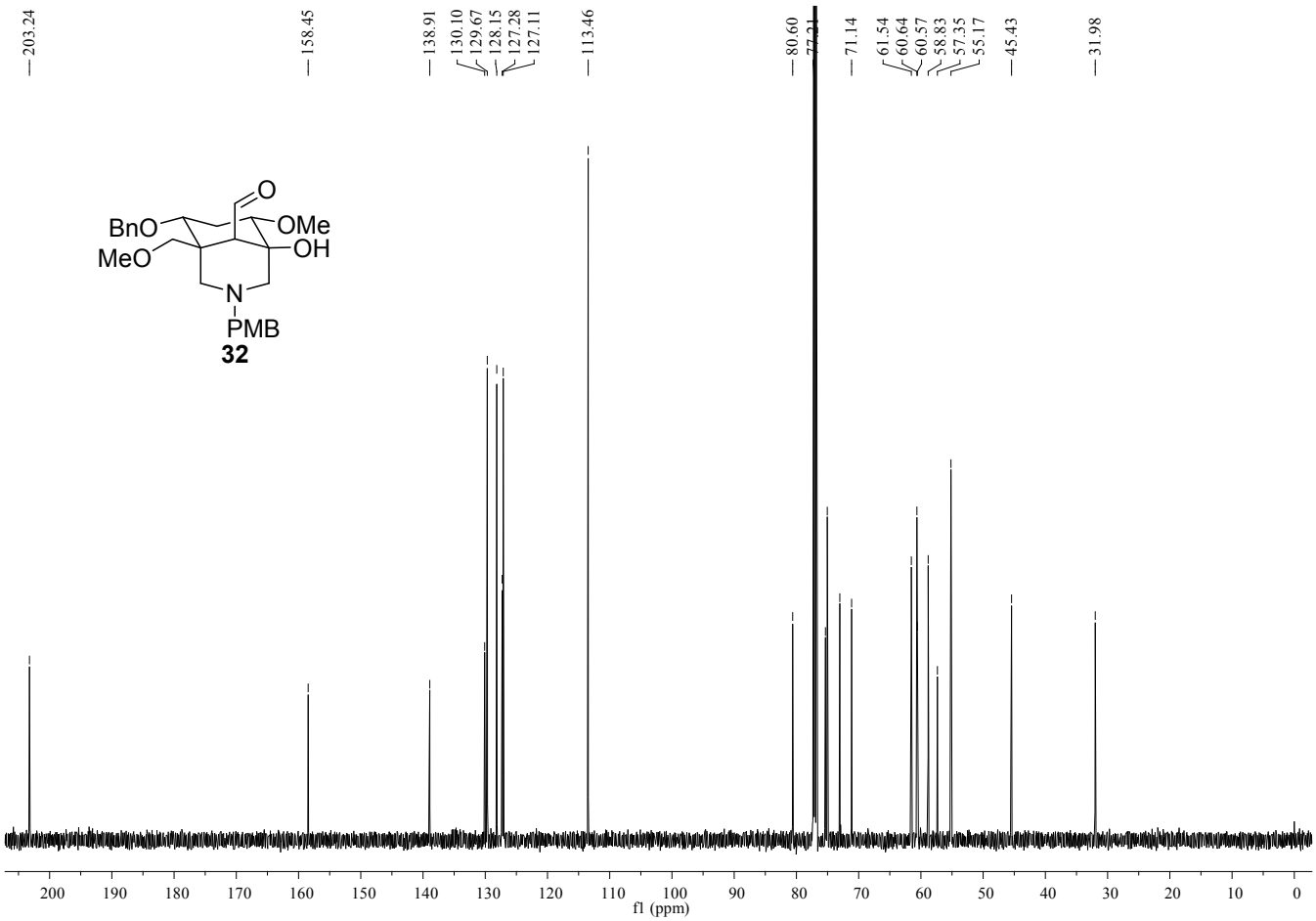

7.337
7.320
7.301
7.284
7.266
7.258
7.232
7.223
7.202
6.789
6.768
4.680
4.650
4.385
4.356
3.917
3.795
3.736
3.491
3.265
3.211
3.053
2.762
2.601
2.584
2.556
1.963
1.953
1.938
1.744
1.717
OH
BnO
OMe
MeO
OH
N
PMB
31a
6.19
1.79
0.99
0.98
1.03
6.16
5.23
7.09
0.98
1.02
0.82
0.98
1.98
0.96
10.0
9.5
9.0
8.5
8.0
7.5
7.0
6.5
6.0
5.5
5.0
4.5
4.0
3.5
3.0
2.5
2.0
1.5
1.0
0.5
0.0
f1 (ppm)

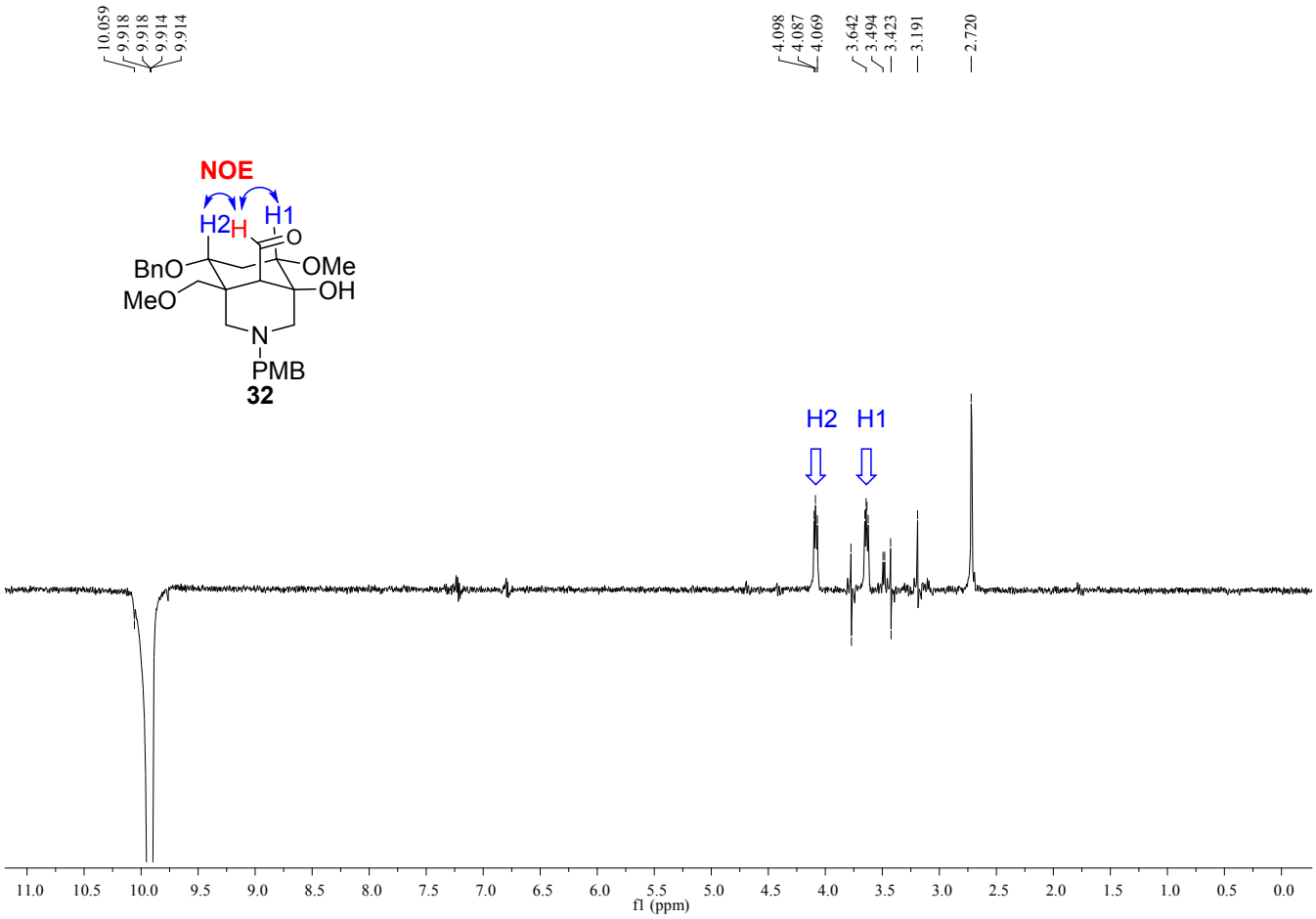

158.38
139.01
130.40
129.62
128.15
127.25
127.09
113.43
80.06
77.21
77.00
76.79
75.96
75.17
73.15
57.08
56.04
55.18
51.40
43.68
31.50
OH
BnO
OMe
MeO
OH
N
PMB
31a
200
190
180
170
160
150
140
130
120
110
100
90
80
70
60
50
40
30
20
10
0
f1 (ppm)

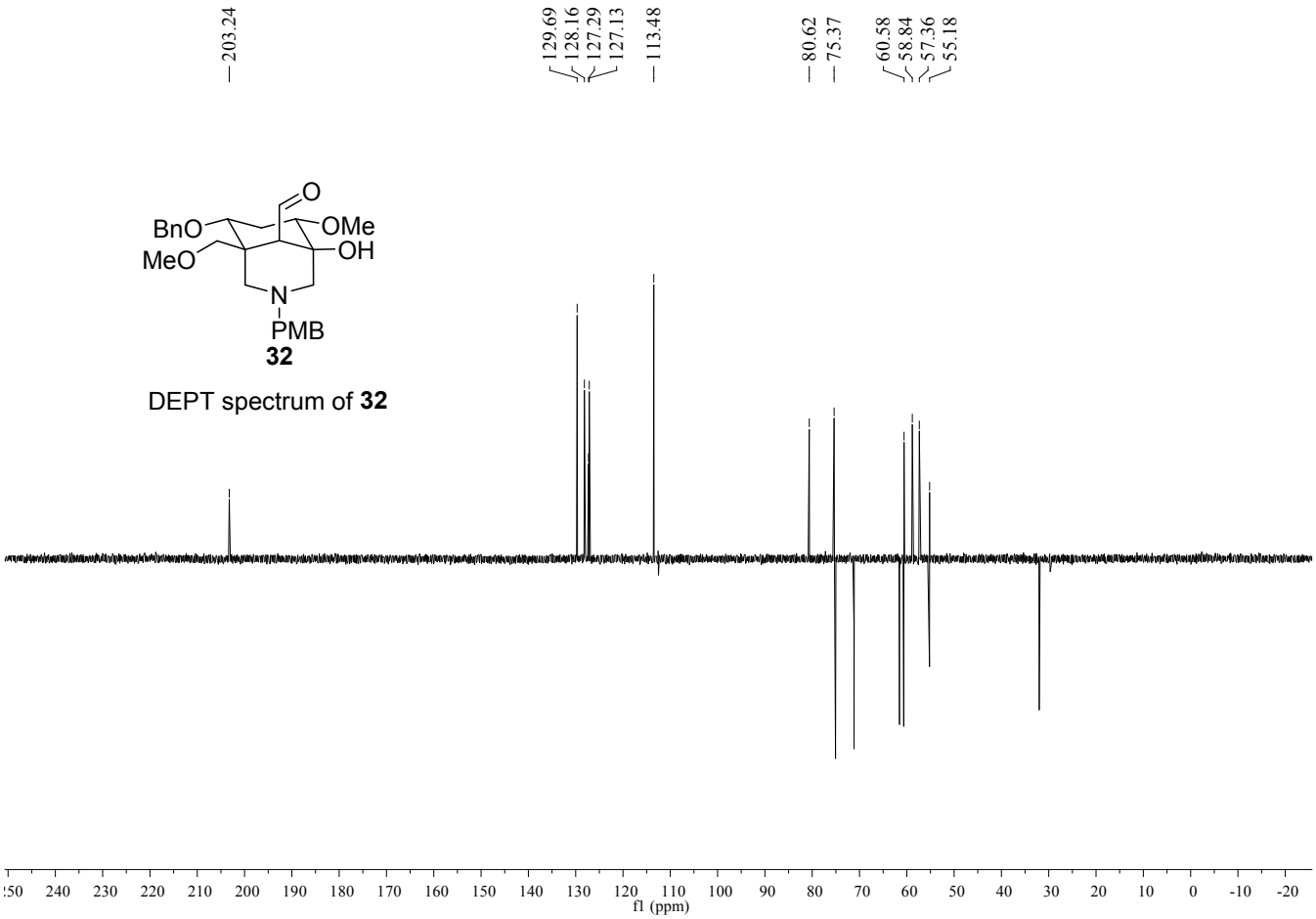

7.346
7.329
7.311
7.290
7.260
7.247
7.204
7.183
6.793
6.771
4.693
4.664
4.414
4.068
3.771
3.289
3.208
3.164
2.990
2.702
2.599
2.554
2.336
2.309
1.717
1.699
1.670
BnO
MeO
OMe
OH
OH
N
PMB
31b
4.56
1.93
2.04
1.00
1.01
0.97
4.52
1.20
0.21
1.82
0.96
0.93
1.96
10.0
9.5
9.0
8.5
8.0
7.5
7.0
6.5
6.0
5.5
5.0
4.5
4.0
3.5
3.0
2.5
2.0
1.5
1.0
0.5
0.0
f1 (ppm)


158.48
138.97
129.73
128.18
127.31
127.26
113.50
84.20
77.21
75.97
73.59
71.81
57.05
55.18
54.94
50.05
44.27
44.16
31.12
BnO
MeO
OMe
OH
OH
N
PMB
31b
200
190
180
170
160
150
140
130
120
110
100
90
80
70
60
50
40
30
20
10
0
f1 (ppm)

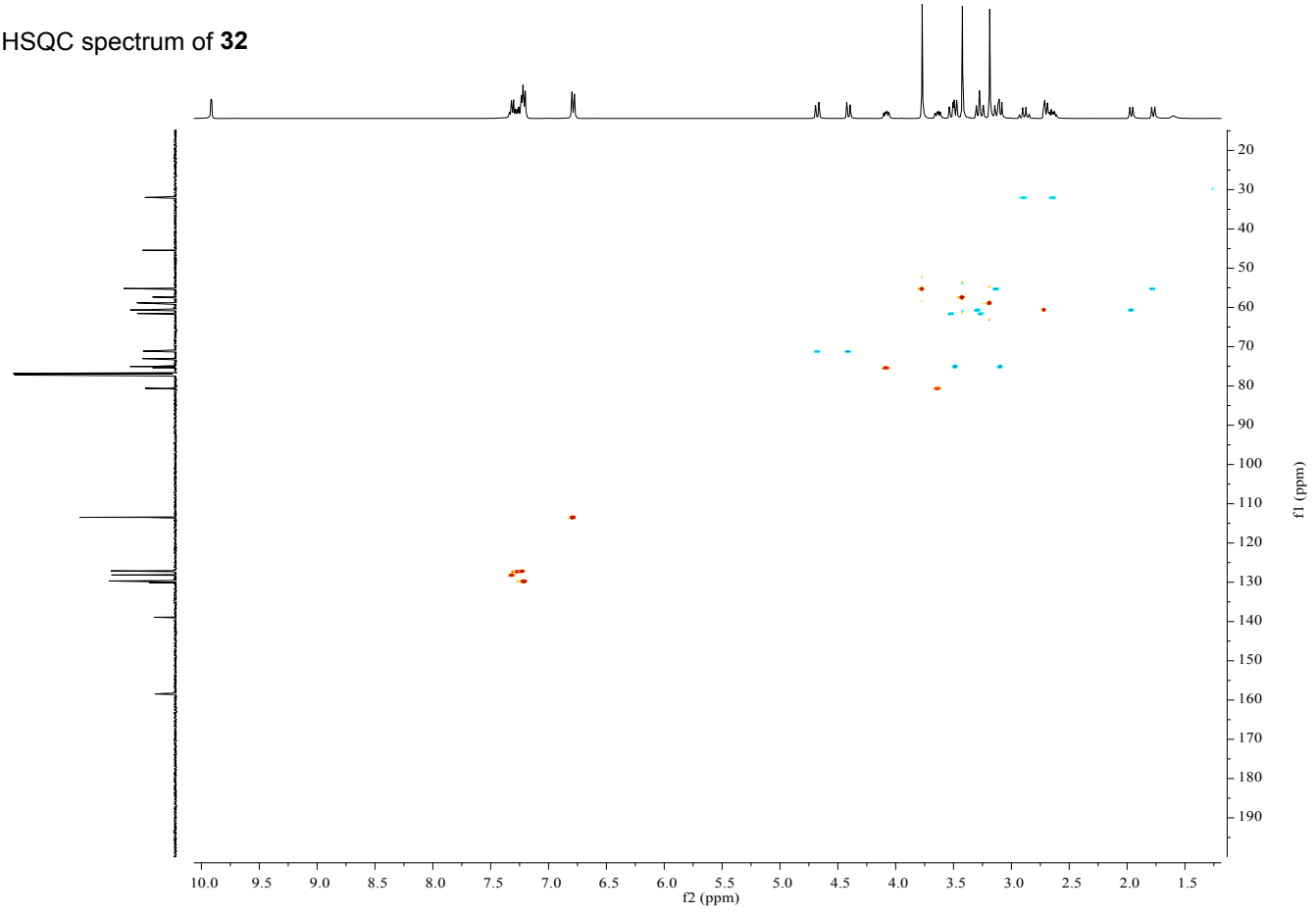

9.918
9.911
7.337
7.320
7.302
7.284
7.267
7.258
7.234
7.222
7.201
6.798
6.776
4.693
4.664
4.393
4.059
3.771
3.504
3.424
3.242
3.115
2.930
2.846
2.688
2.643
2.610
1.976
1.950
1.788
1.760
BnO
MeO
OMe
OH
N
PMB
32
0.94
1.58
0.73
3.27
1.83
1.00
1.01
2.93
1.02
1.04
1.01
0.94
0.63
1.08
0.99
0.99
10.0
9.5
9.0
8.5
8.0
7.5
7.0
6.5
6.0
5.5
5.0
4.5
4.0
3.5
3.0
2.5
2.0
1.5
1.0
0.5
0.0
f1 (ppm)


203.24
158.45
138.91
130.10
129.67
128.15
127.28
127.11
113.46
80.60
77.21
71.14
61.54
60.64
60.57
58.83
57.35
55.17
45.43
31.98
BnO
MeO
OMe
OH
N
PMB
32
200
190
180
170
160
150
140
130
120
110
100
90
80
70
60
50
40
30
20
10
0
f1 (ppm)

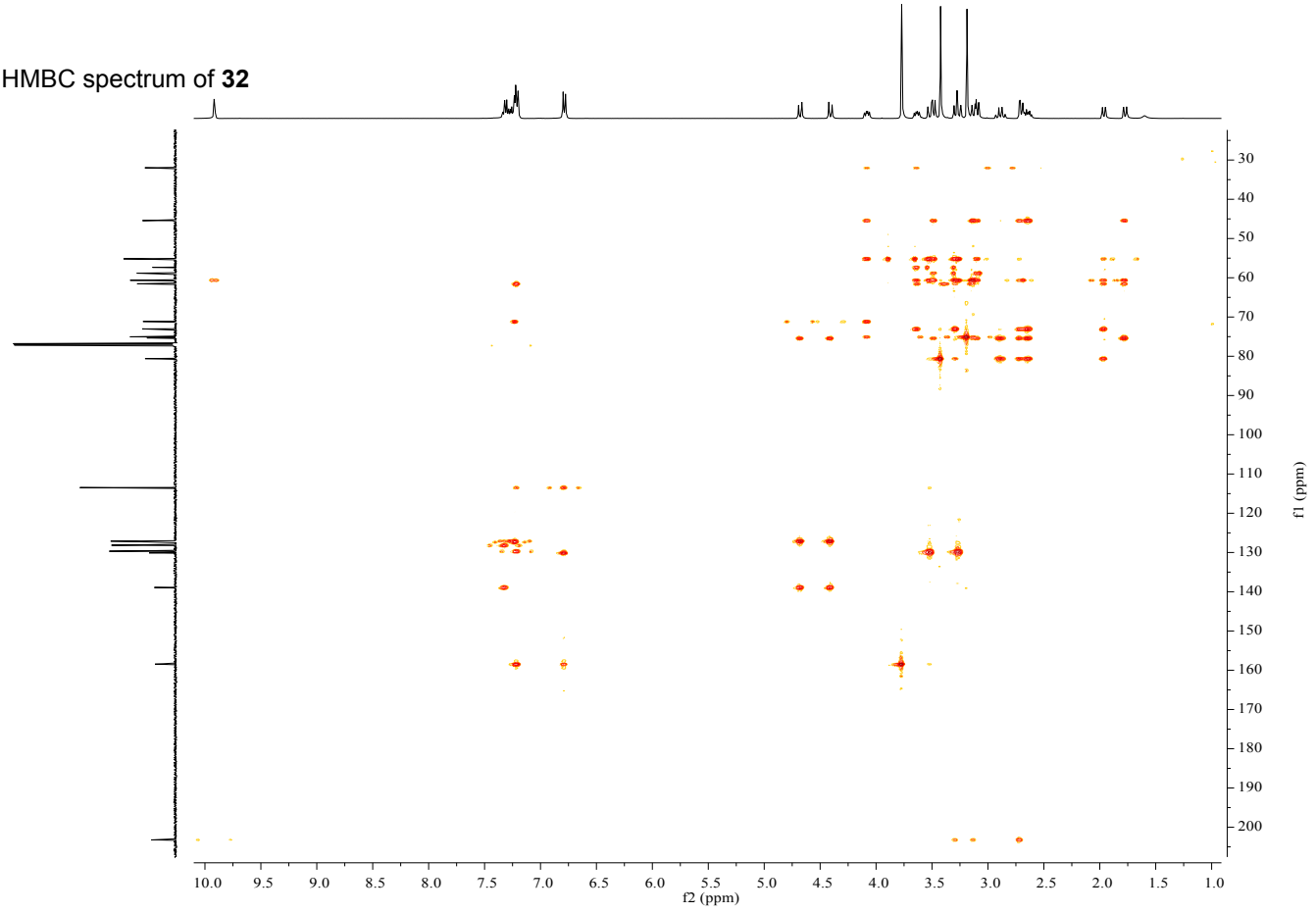

10.059
9.918
9.918
9.914
9.914
4.098
4.087
4.069
3.642
3.494
3.423
3.191
2.720
NOE
H2
H
H1
O
BnO
OMe
MeO
OH
N
PMB
32
H2
H1
11.0
10.5
10.0
9.5
9.0
8.5
8.0
7.5
7.0
6.5
6.0
5.5
5.0
4.5
4.0
3.5
3.0
2.5
2.0
1.5
1.0
0.5
0.0
f1 (ppm)


203.24
129.69
128.16
127.29
127.13
113.48
80.62
75.37
60.58
58.84
57.36
55.18
O
BnO
OMe
MeO
OH
N
PMB
32
DEPT spectrum of 32
250
240
230
220
210
200
190
180
170
160
150
140
130
120
110
100
90
80
70
60
50
40
30
20
10
0
-10
-20
f1 (ppm)

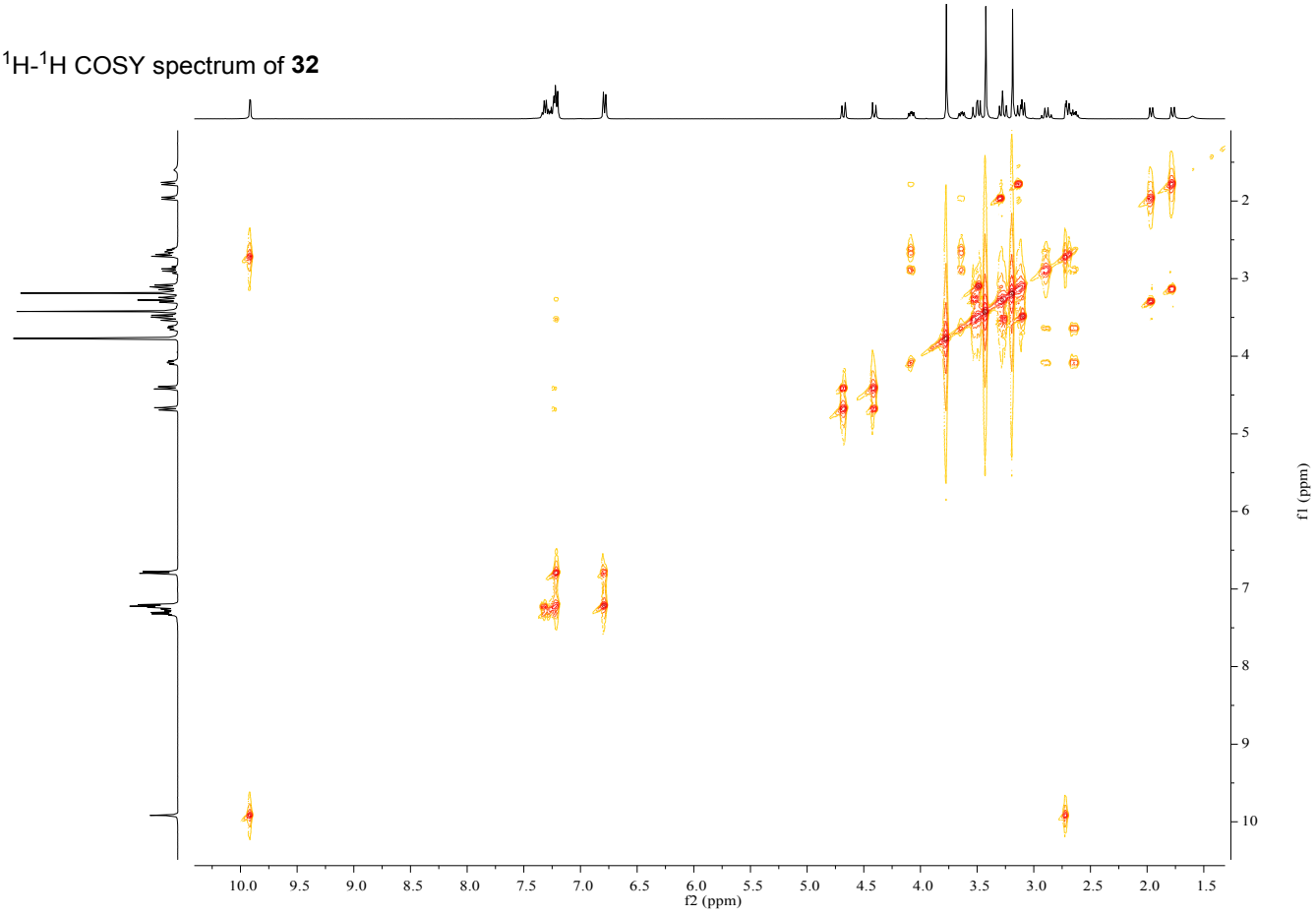
HSQC spectrum of **32**

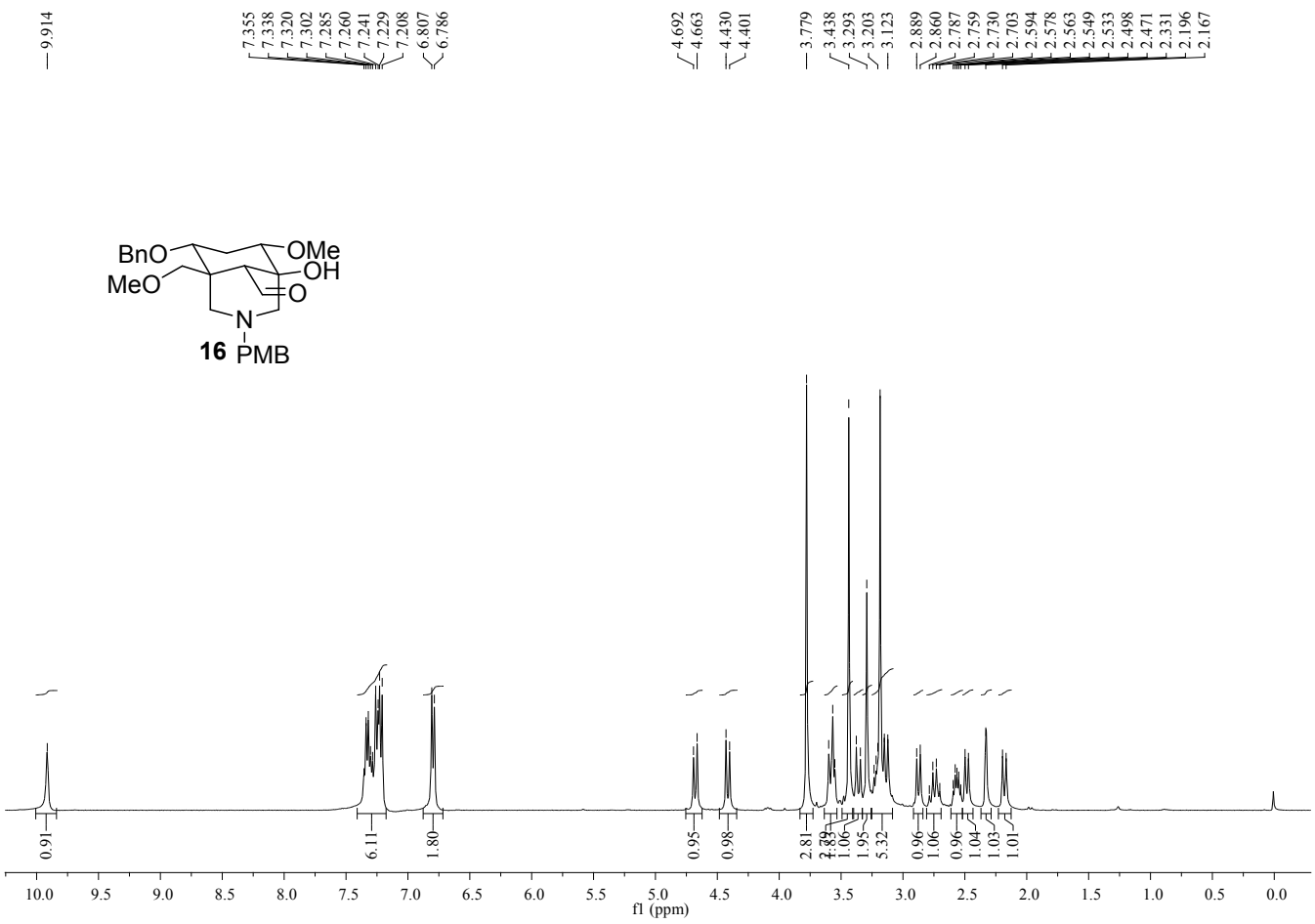


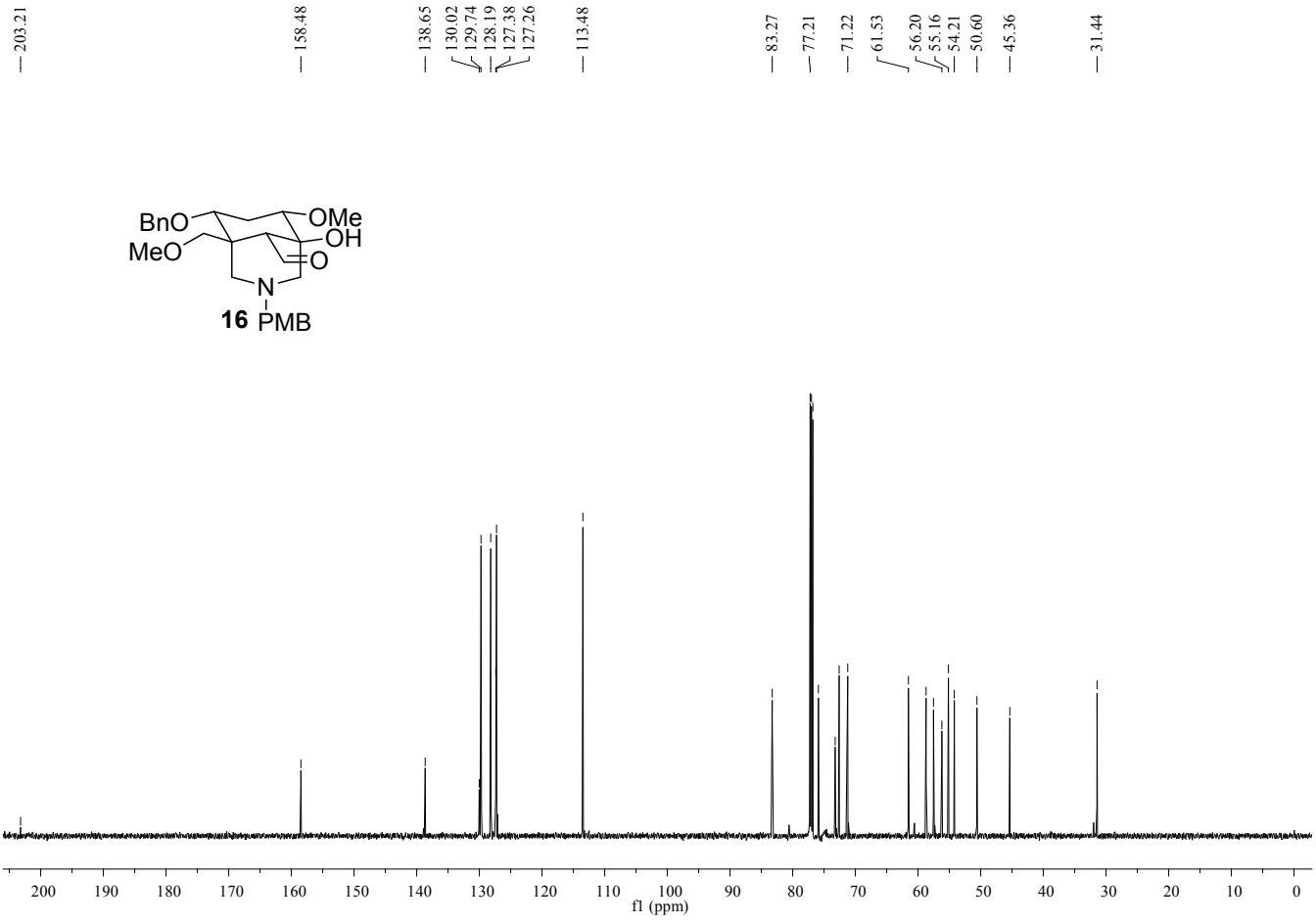
HMBC spectrum of **32**

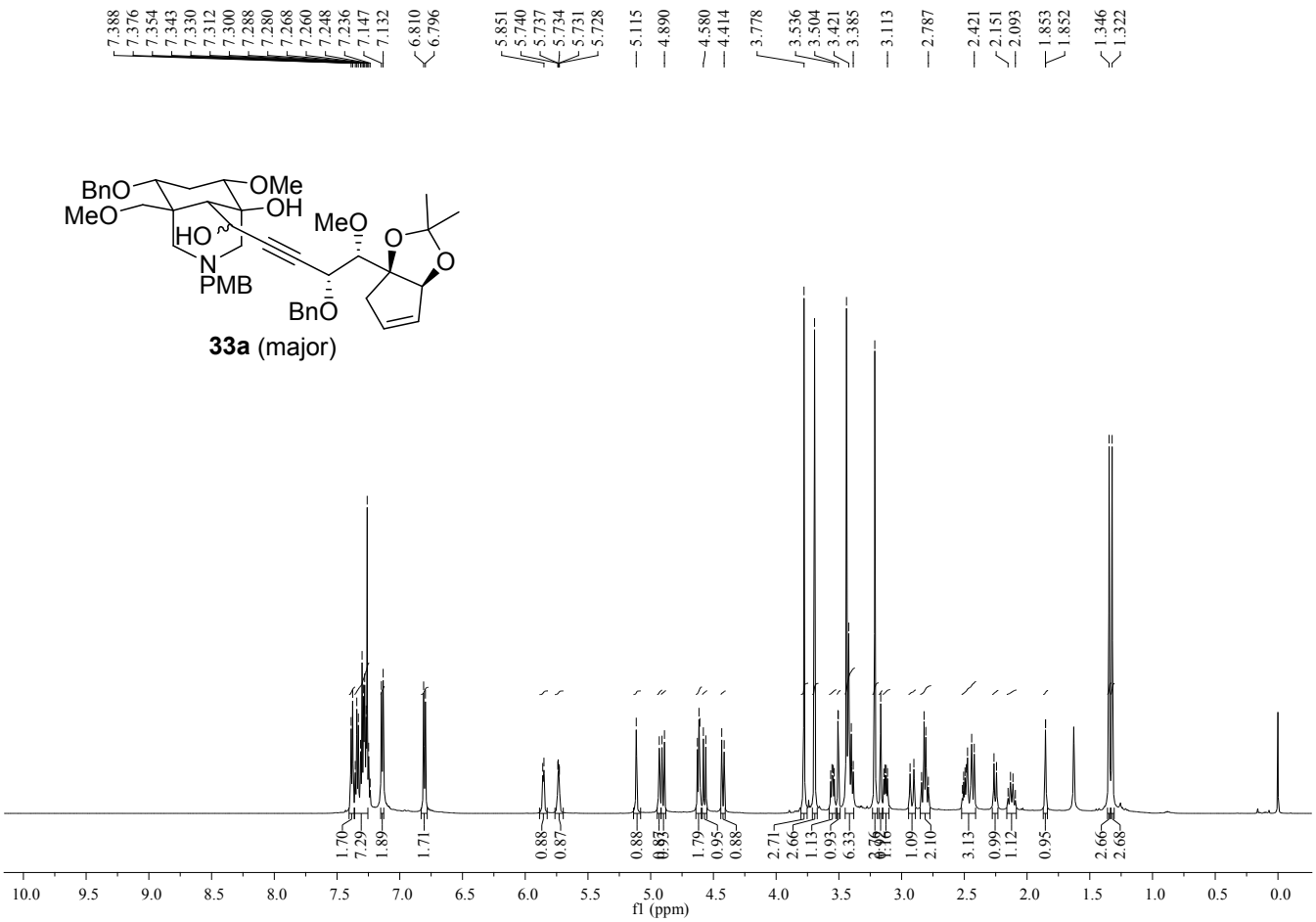


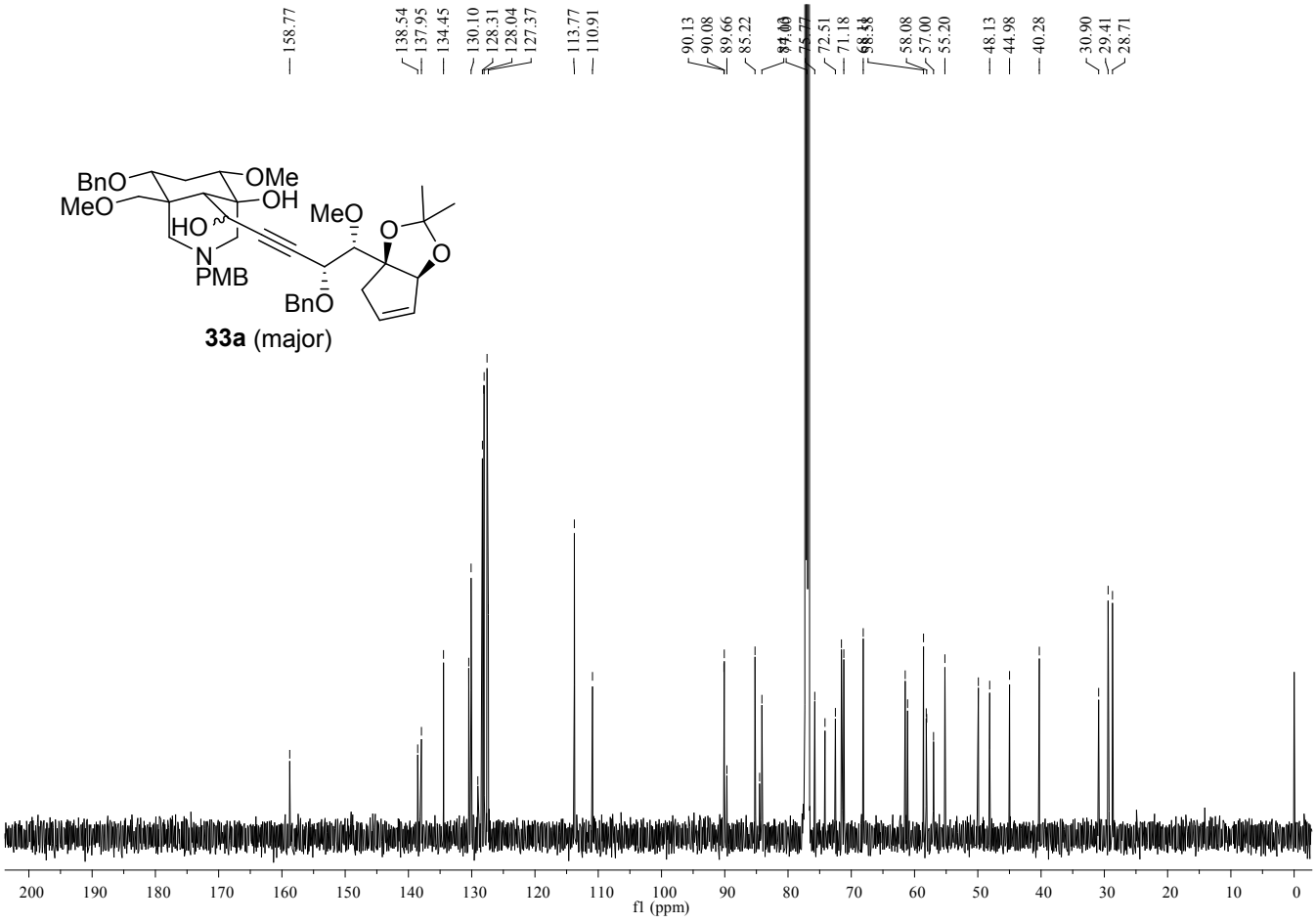
^{1}H-^{1}H COSY spectrum of **32**



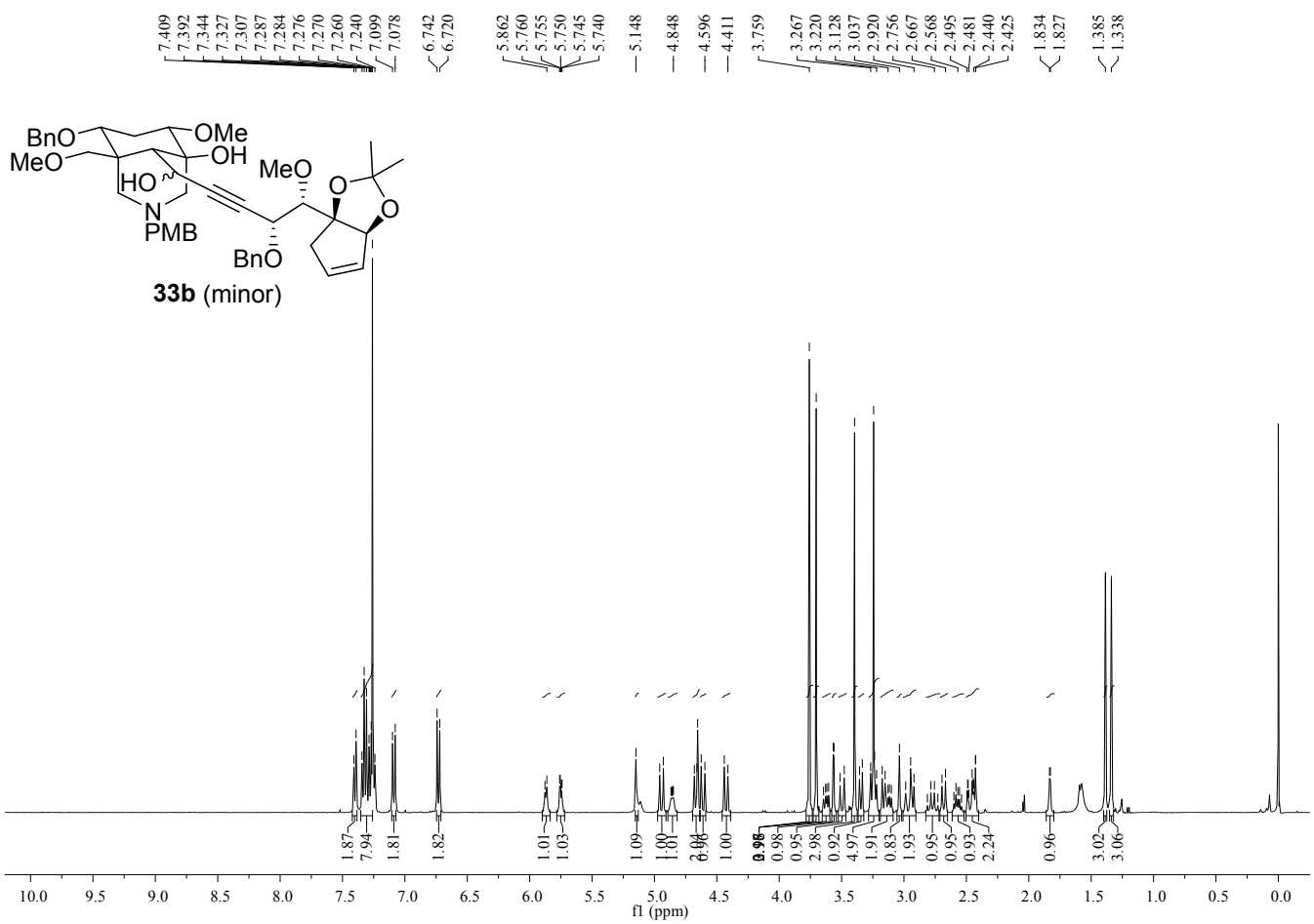

9.914
7.355
7.338
7.320
7.302
7.285
7.260
7.241
7.229
7.208
6.807
6.786
4.692
4.663
4.430
4.401
3.779
3.438
3.293
3.203
3.123
2.889
2.860
2.787
2.759
2.730
2.703
2.594
2.578
2.563
2.549
2.533
2.498
2.471
2.331
2.196
2.167
BnO
OMe
MeO
OH
O
N
PMB
16
0.91
6.11
1.80
0.95
0.98
2.81
1.06
1.95
5.32
0.96
1.06
0.96
1.04
1.03
1.01
10.0
9.5
9.0
8.5
8.0
7.5
7.0
6.5
6.0
5.5
5.0
4.5
4.0
3.5
3.0
2.5
2.0
1.5
1.0
0.5
0.0
f1 (ppm)


203.21
158.48
138.65
130.02
129.74
128.19
127.38
127.26
113.48
83.27
77.21
71.22
61.53
56.20
55.16
54.21
50.60
45.36
31.44
BnO
MeO
OMe
OH
O
N
PMB
16
fl (ppm)

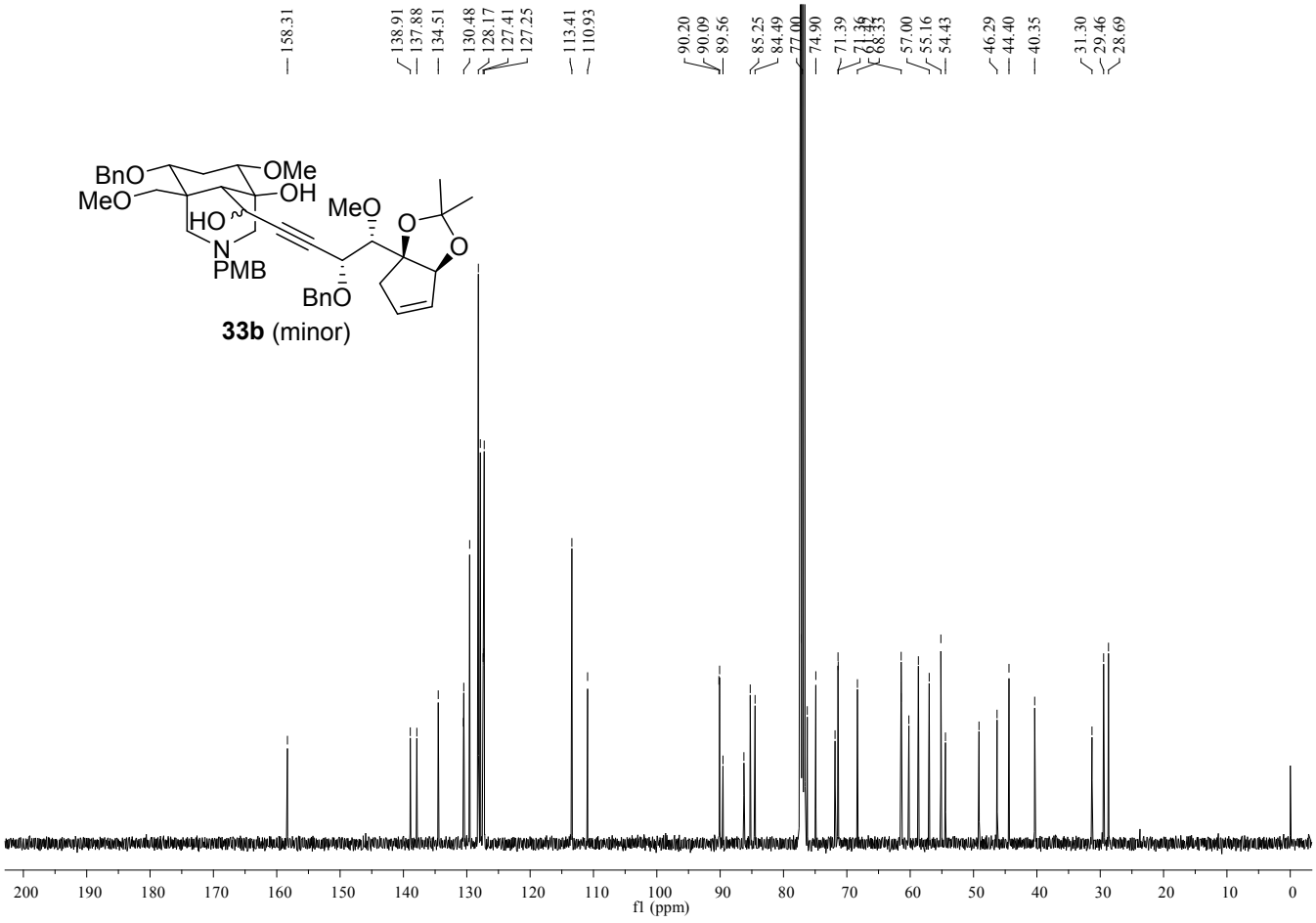

7.388
7.376
7.354
7.343
7.330
7.312
7.300
7.288
7.280
7.268
7.260
7.248
7.236
7.147
7.132
6.810
6.796
5.851
5.740
5.737
5.734
5.731
5.728
5.115
4.890
4.580
4.414
3.778
3.536
3.504
3.421
3.385
3.113
2.787
2.421
2.151
2.093
1.853
1.852
1.346
1.322
BnO
MeO
OMe
OH
HO
N
PMB
MeO
O
O
BnO
33a (major)
fl (ppm)

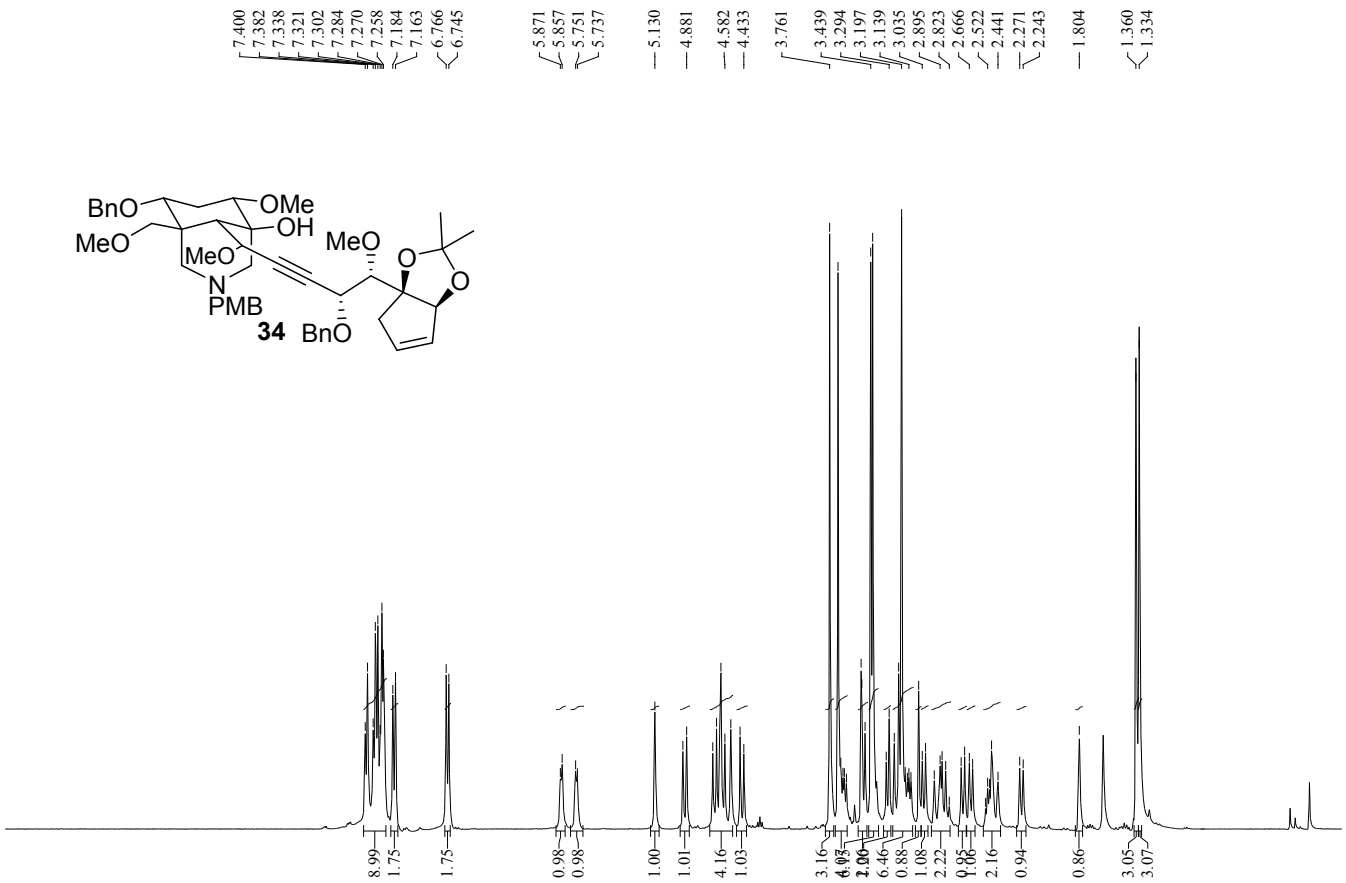


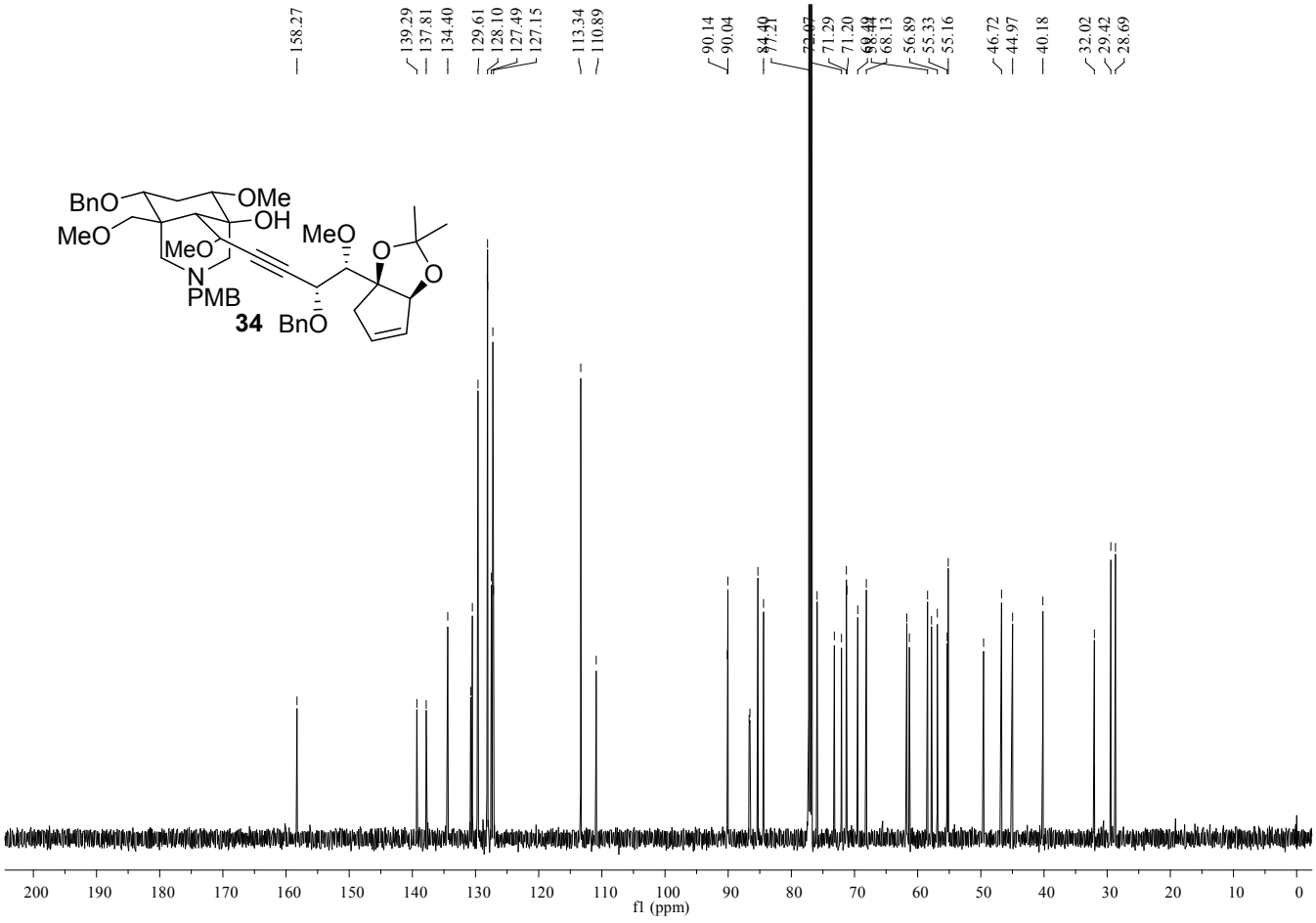
33a (major)

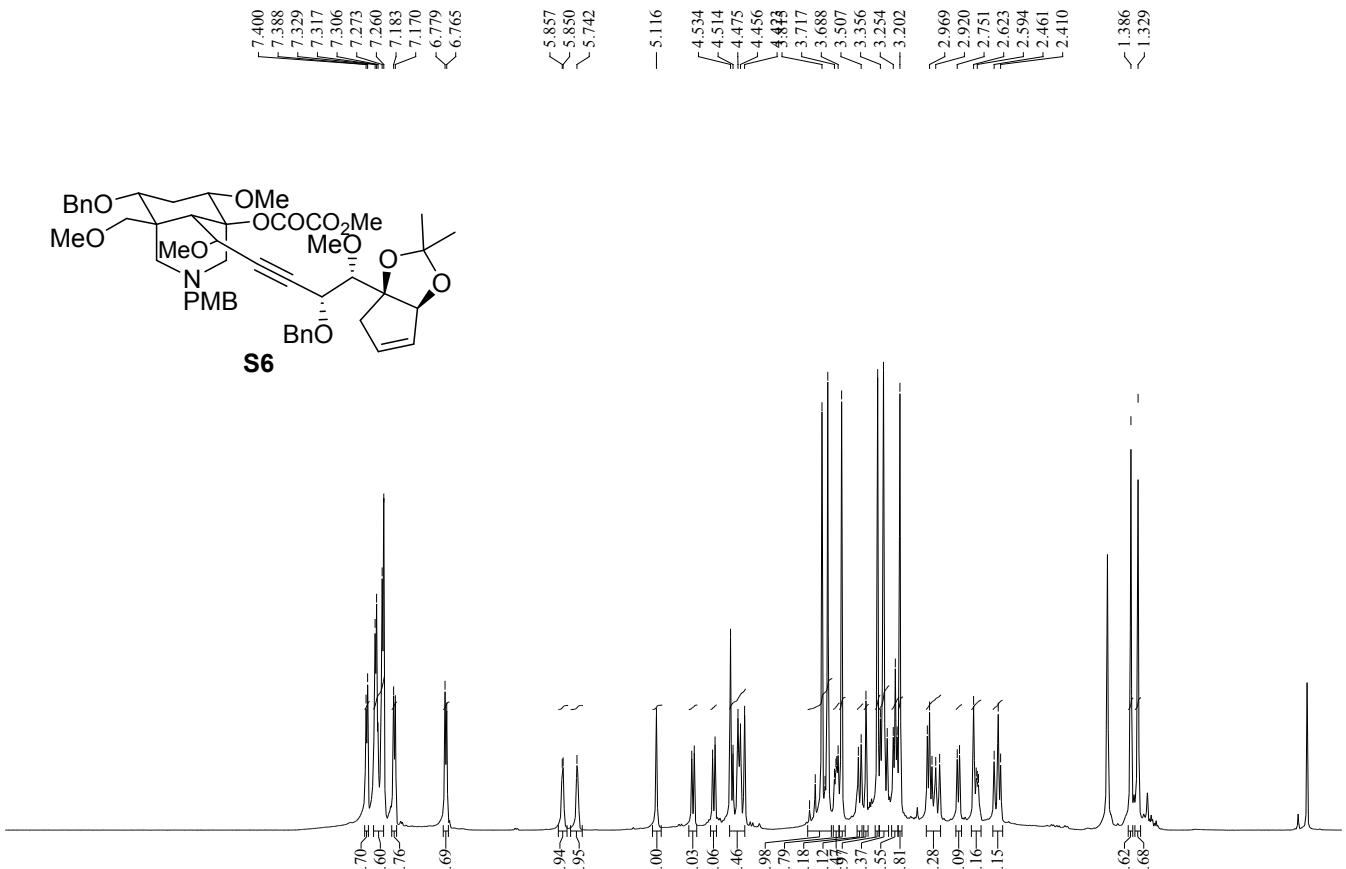


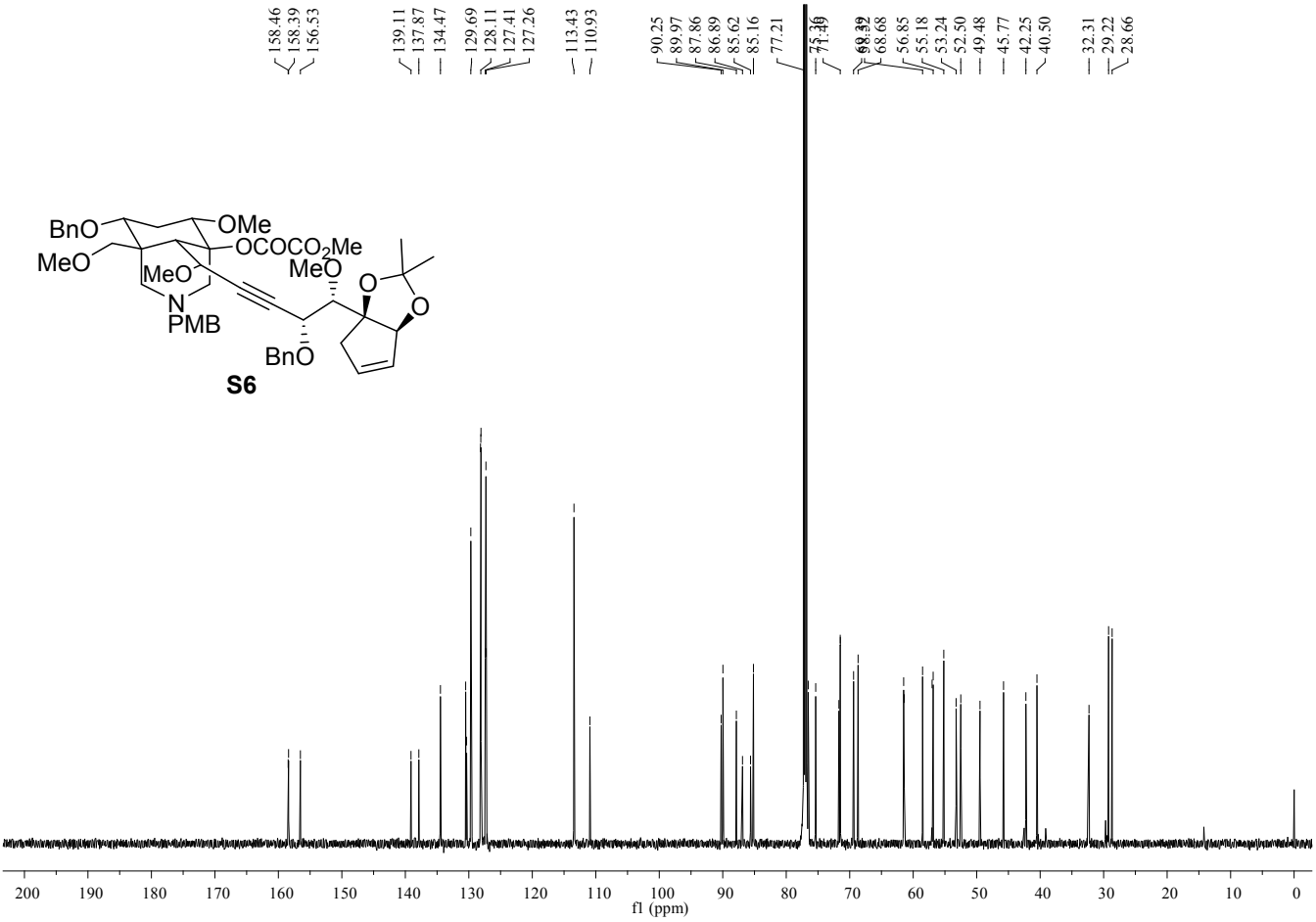
33b (minor)

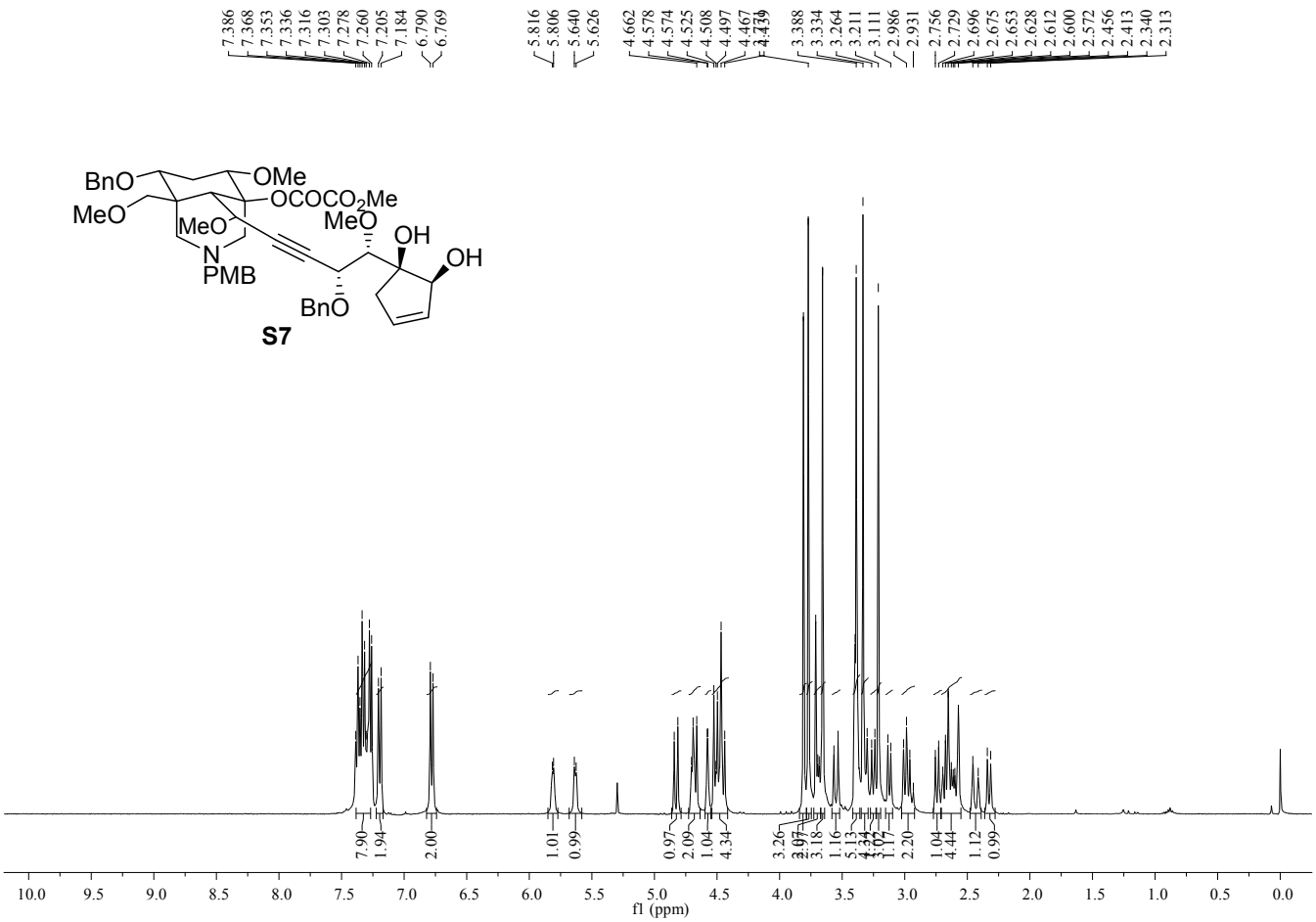

158.31
138.91
137.88
134.51
130.48
128.17
127.41
127.25
113.41
110.93
90.20
90.09
89.56
85.25
84.49
77.00
74.90
71.39
71.36
68.33
57.00
55.16
54.43
46.29
44.40
40.35
31.30
29.46
28.69
BnO
MeO
OMe
OH
HO
N
PMB
MeO
O
O
BnO
33b (minor)
200
190
180
170
160
150
140
130
120
110
100
90
80
70
60
50
40
30
20
10
0
f1 (ppm)

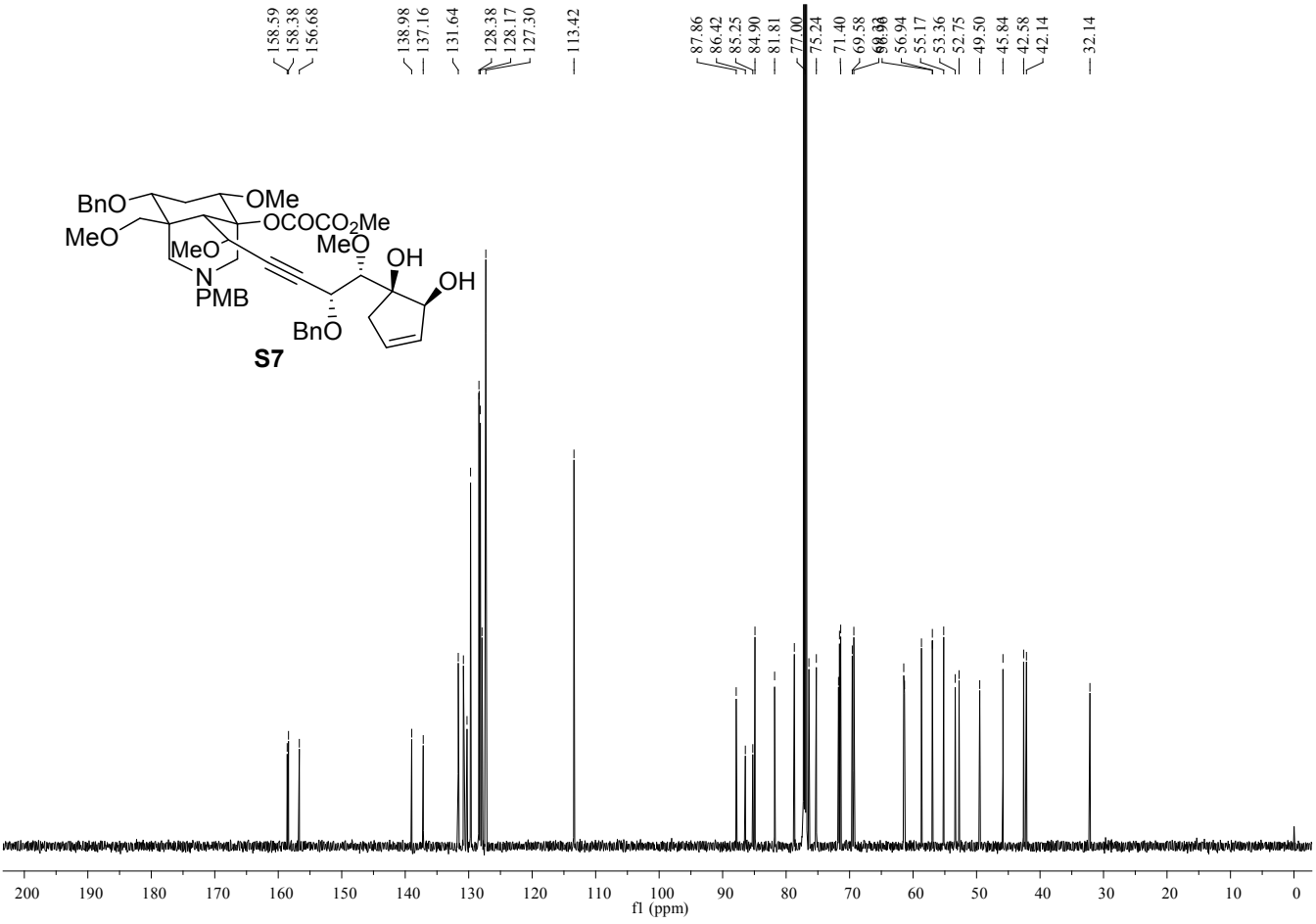

7.400
7.382
7.338
7.321
7.302
7.284
7.270
7.258
7.184
7.163
6.766
6.745
5.871
5.857
5.751
5.737
5.130
4.881
4.582
4.433
3.761
3.439
3.294
3.197
3.139
3.035
2.895
2.823
2.666
2.522
2.441
2.271
2.243
1.804
1.360
1.334
BnO
MeO
OMe
OH
MeO
MeO
N
PMB
34
BnO
O
O
8.99
1.75
1.75
0.98
0.98
1.00
1.01
4.16
1.03
3.16
6.46
0.88
1.08
2.22
2.16
0.94
0.86
3.05
3.07
10.0
9.5
9.0
8.5
8.0
7.5
7.0
6.5
6.0
5.5
5.0
4.5
4.0
3.5
3.0
2.5
2.0
1.5
1.0
0.5
0.0
f1 (ppm)

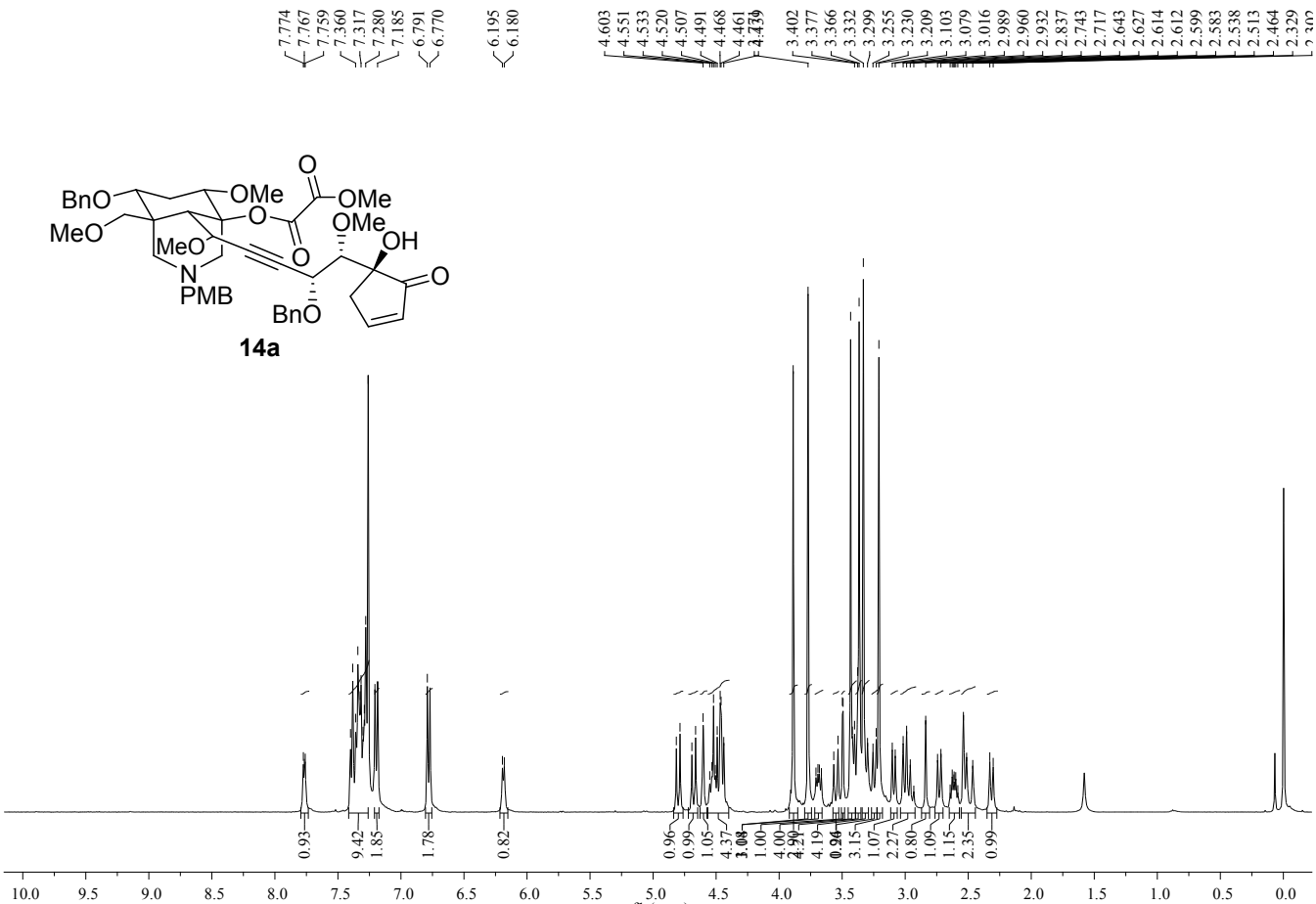

158.27
139.29
137.81
134.40
129.61
128.10
127.49
127.15
113.34
110.89
90.14
90.04
84.40
77.21
72.07
71.29
71.20
68.13
56.89
55.33
55.16
46.72
44.97
40.18
32.02
29.42
28.69
BnO
OMe
OH
MeO
MeO
MeO
N
PMB
MeO
O
O
BnO
34
200
190
180
170
160
150
140
130
120
110
100
90
80
70
60
50
40
30
20
10
0
f1 (ppm)

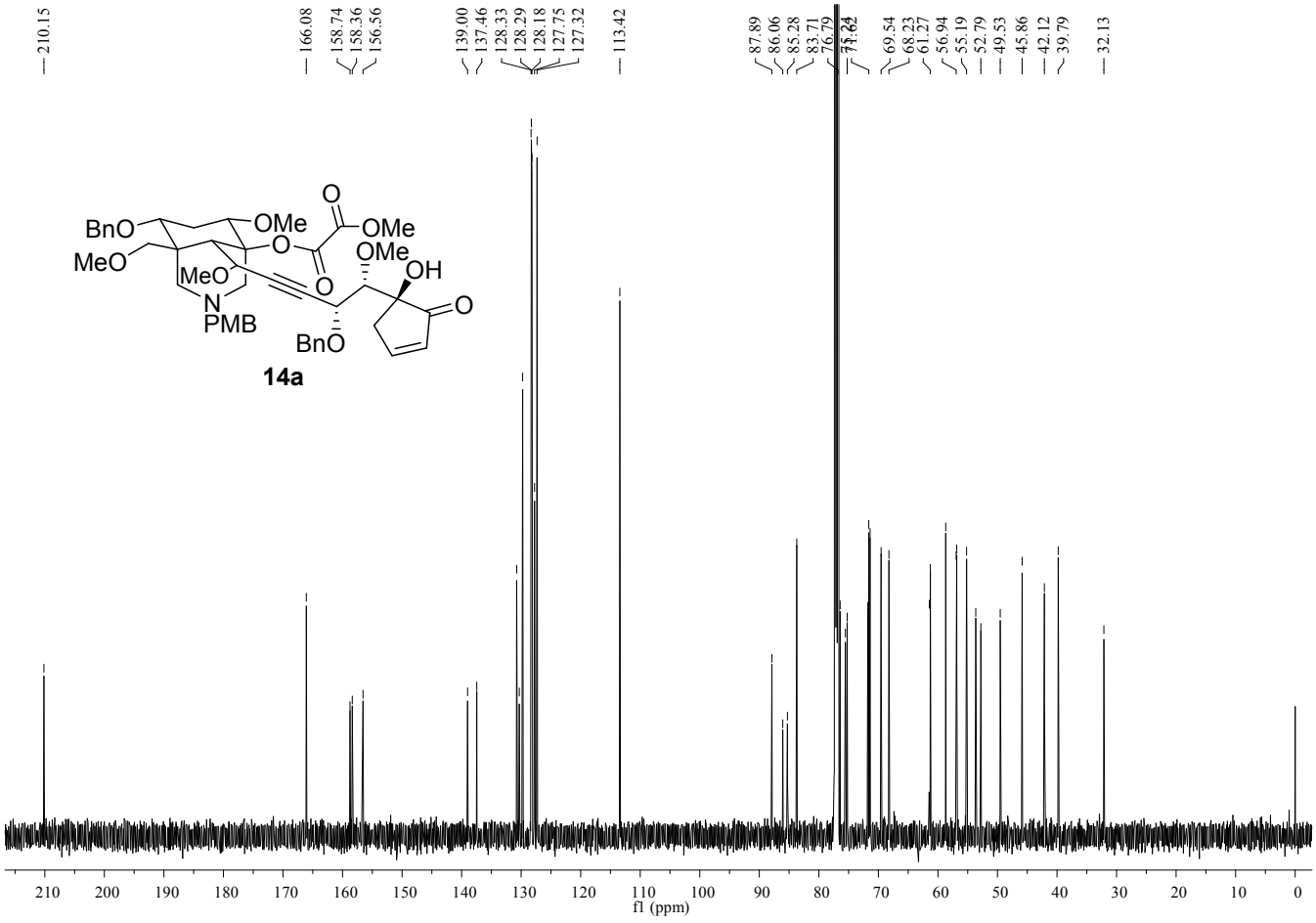

7.400
7.388
7.329
7.317
7.306
7.273
7.260
7.183
7.170
6.779
6.765
5.857
5.850
5.742
5.116
4.534
4.514
4.475
4.456
3.717
3.688
3.507
3.356
3.254
3.202
2.969
2.920
2.751
2.623
2.594
2.461
2.410
1.386
1.329
BnO
OMe
OCOCO2Me
MeO
MeO
MeO
N
PMB
MeO
O
O
BnO
S6
1.70
6.60
1.76
1.69
0.94
0.95
1.00
1.03
1.06
4.46
6.98
2.79
1.18
5.37
2.55
2.81
3.28
1.09
2.16
2.15
2.62
2.68
10.0
9.5
9.0
8.5
8.0
7.5
7.0
6.5
6.0
5.5
5.0
4.5
4.0
3.5
3.0
2.5
2.0
1.5
1.0
0.5
0.0
f1 (ppm)

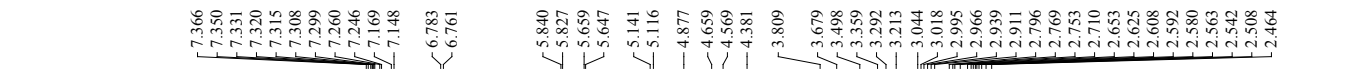

158.46
158.39
156.53
139.11
137.87
134.47
129.69
128.11
127.41
127.26
113.43
110.93
90.25
89.97
87.86
86.89
85.62
85.16
77.21
56.85
55.18
53.24
52.50
49.48
45.77
42.25
40.50
32.31
29.22
28.66
BnO
OMe
OCOCO2Me
MeO
MeO
MeO
N
PMB
BnO
O
O
S6
200
190
180
170
160
150
140
130
120
110
100
90
80
70
60
50
40
30
20
10
0
f1 (ppm)

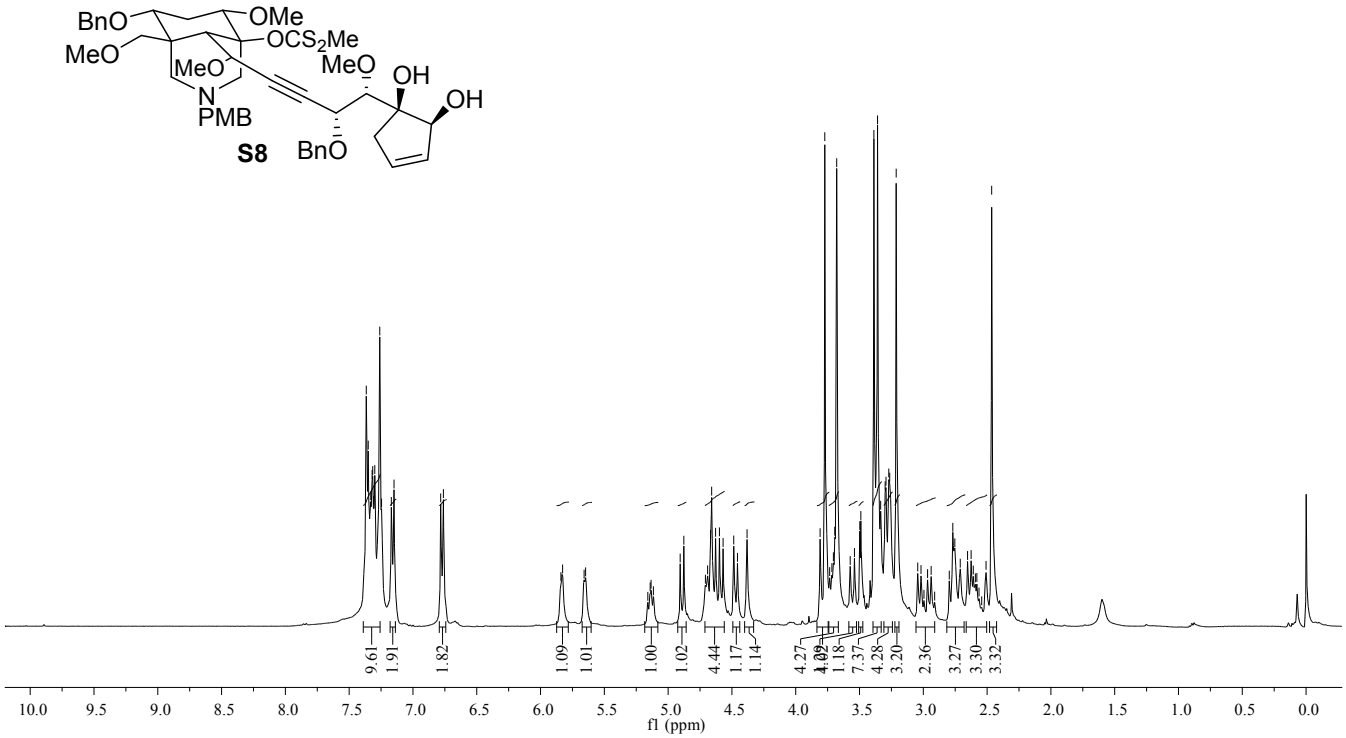

7.386
7.368
7.353
7.336
7.316
7.303
7.278
7.260
7.205
7.184
6.790
6.769
5.816
5.806
5.640
5.626
4.662
4.578
4.574
4.525
4.508
4.497
4.467
3.388
3.334
3.264
3.211
3.111
2.986
2.931
2.756
2.729
2.696
2.675
2.653
2.628
2.612
2.600
2.572
2.456
2.413
2.340
2.313
BnO
OMe
OCOCO2Me
MeO
MeO
MeO
N
PMB
BnO
OH
OH
S7
7.90
1.94
2.00
1.01
0.99
0.97
2.09
1.04
4.34
3.26
1.16
5.13
2.20
1.04
4.44
1.12
0.99
10.0
9.5
9.0
8.5
8.0
7.5
7.0
6.5
6.0
5.5
5.0
4.5
4.0
3.5
3.0
2.5
2.0
1.5
1.0
0.5
0.0
f1 (ppm)

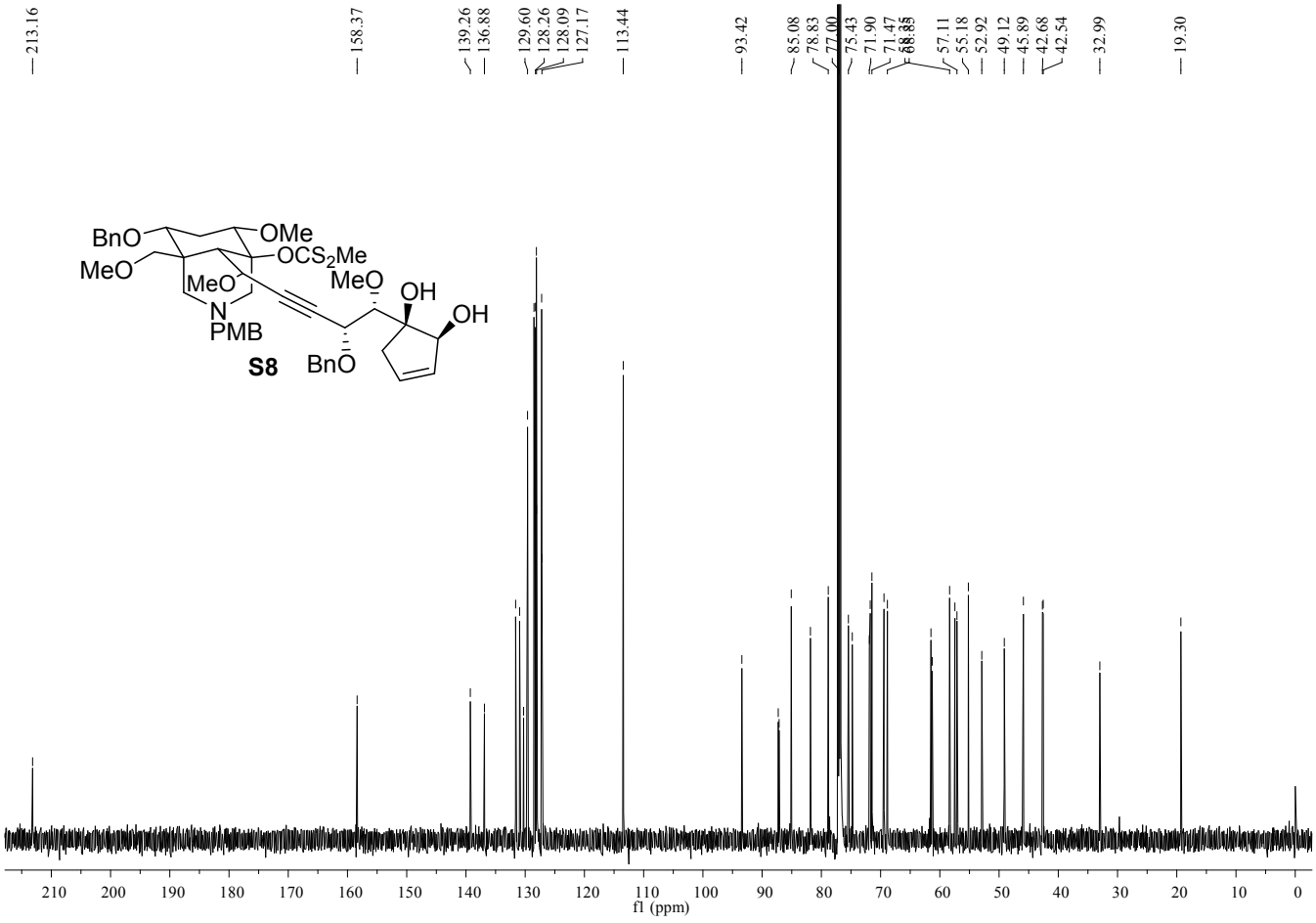

158.59
158.38
156.68
138.98
137.16
131.64
128.38
128.17
127.30
113.42
87.86
86.42
85.25
84.90
81.81
77.00
75.24
71.40
69.58
56.94
55.17
53.36
52.75
49.50
45.84
42.58
42.14
32.14
BnO
OMe
OCOCO2Me
MeO
MeO
MeO
OH
OH
N
PMB
BnO
S7
200
190
180
170
160
150
140
130
120
110
100
90
80
70
60
50
40
30
20
10
0
f1 (ppm)

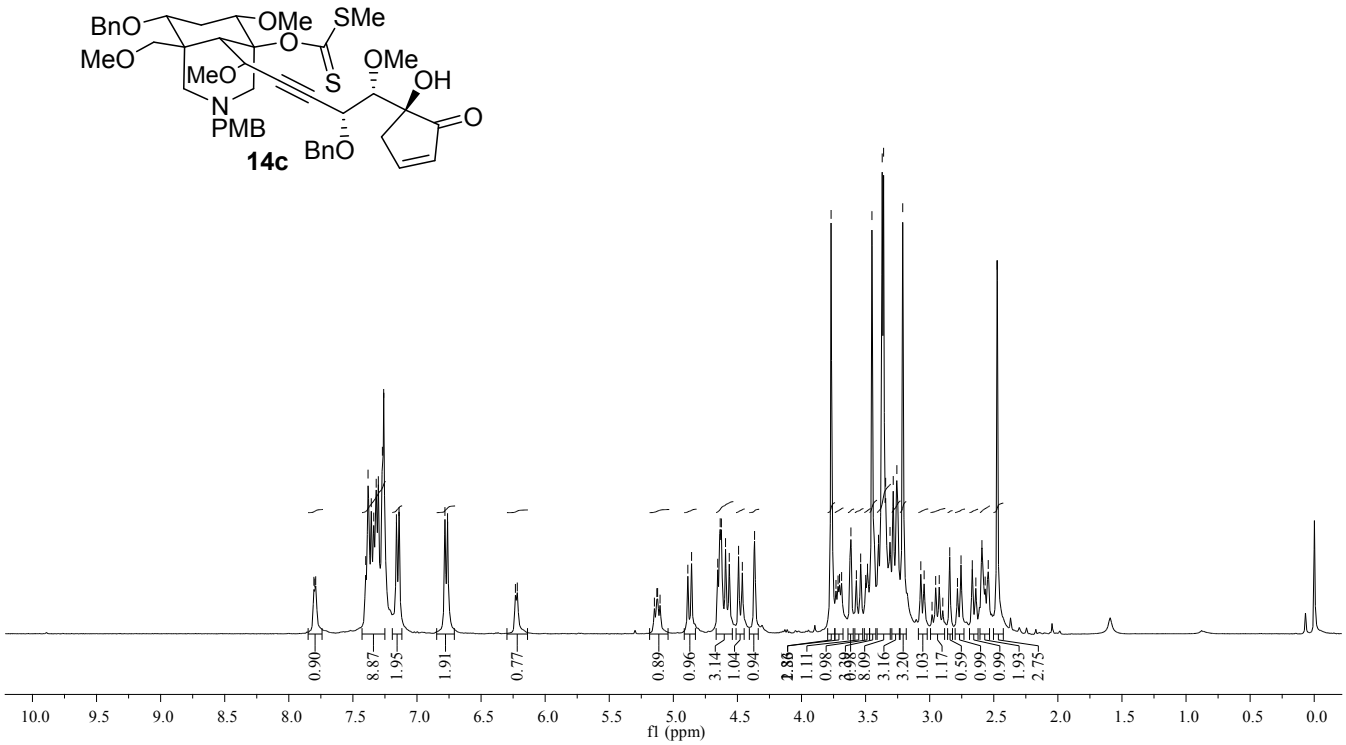

7.774
7.767
7.759
7.360
7.317
7.280
7.185
6.791
6.770
6.195
6.180
4.603
4.551
4.533
4.520
4.507
4.491
4.468
4.461
3.402
3.377
3.366
3.332
3.299
3.255
3.230
3.209
3.103
3.079
3.016
2.989
2.960
2.932
2.837
2.743
2.717
2.643
2.627
2.614
2.612
2.599
2.583
2.538
2.513
2.464
BnO
OMe
OMe
MeO
MeO
OMe
OH
N
PMB
BnO
14a
0.93
9.42
1.85
1.78
0.82
0.96
0.99
1.05
4.37
1.00
4.00
4.19
3.15
1.07
2.27
0.80
1.09
1.15
2.35
0.99
10.0
9.5
9.0
8.5
8.0
7.5
7.0
6.5
6.0
5.5
5.0
4.5
4.0
3.5
3.0
2.5
2.0
1.5
1.0
0.5
0.0
f1 (ppm)

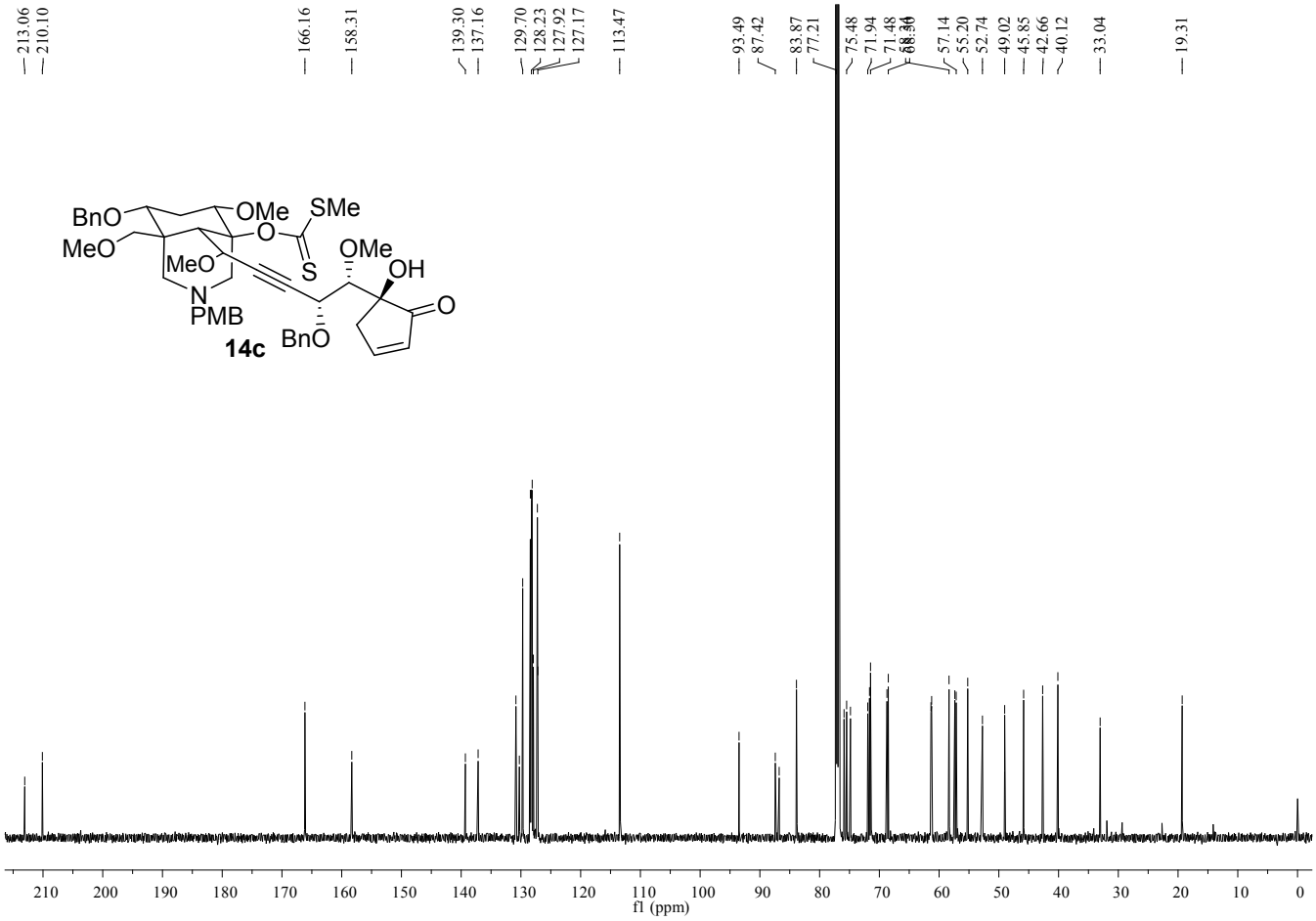

210.15
166.08
158.74
158.36
156.56
139.00
137.46
128.33
128.29
128.18
127.75
127.32
113.42
87.89
86.06
85.28
83.71
76.79
69.54
68.23
61.27
56.94
55.19
52.79
49.53
45.86
42.12
39.79
32.13
BnO
OMe
OMe
MeO
OMe
MeO
OH
O
O
N
PMB
BnO
O
14a
fl (ppm)


7.366
7.350
7.331
7.320
7.315
7.308
7.299
7.260
7.246
7.169
7.148
6.783
6.761
5.840
5.827
5.659
5.647
5.141
5.116
4.877
4.659
4.569
4.381
3.809
3.679
3.498
3.359
3.292
3.213
3.044
3.018
2.995
2.966
2.939
2.911
2.796
2.769
2.753
2.710
2.653
2.625
2.608
2.592
2.580
2.563
2.542
2.508
2.464


BnO
OMe
MeO
OCS2Me
MeO
MeO
OH
OH
N
PMB
S8
BnO
9.61
1.91
1.82
1.09
1.01
1.00
1.02
4.44
1.17
1.14
4.27
1.18
7.37
4.28
3.20
2.36
3.27
3.30
3.32
fl (ppm)


213.16
158.37
139.26
136.88
129.60
128.26
128.09
127.17
113.44
93.42
85.08
78.83
77.00
75.43
71.90
71.47
57.11
55.18
52.92
49.12
45.89
42.68
42.54
32.99
19.30
BnO
OMe
OCS2Me
MeO
MeO
MeO
N
PMB
OH
OH
BnO
S8
f1 (ppm)


BnO
OMe
SMe
MeO
O
MeO
OMe
S
OH
N
PMB
O
BnO
14c
f1 (ppm)


213.06
210.10
166.16
158.31
139.30
137.16
129.70
128.23
127.92
127.17
113.47
93.49
87.42
83.87
77.21
75.48
71.94
71.48
68.30
57.14
55.20
52.74
49.02
45.85
42.66
40.12
33.04
19.31
BnO
MeO
OMe
SMe
O
MeO
S
OMe
OH
N
PMB
BnO
O
14c
210
200
190
180
170
160
150
140
130
120
110
100
90
80
70
60
50
40
30
20
10
0
f1 (ppm)