Syntheses of sialic acid derivatives based on chiral substrate-controlled selective aldol reactions using pyruvic acid oxabicyclo[2.2.2]octyl orthoester

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Supporting Information

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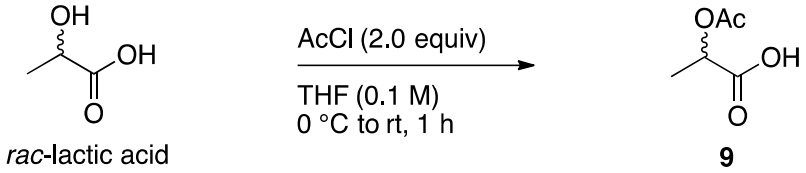
General information

IR spectra was obtained using a JASCO FT/IR 460-plus spectrophotometer. ^{1}H- and ^{13}C-NMR spectra were obtained on Agilent Technologies 400-MR DD2, 400-MR spectrometers. The chemical shifts are expressed in ppm downfield from internal solvent peaks $CDCl_3$ (7.26 ppm, ^{1}H NMR), $CDCl_3$ (77.0 ppm, ^{13}C-NMR), CD_3OD (3.31 ppm, ^{1}H NMR), CD_3OD (49.0, ^{13}C-NMR), D_2O (4.76 ppm, ^{1}H NMR) and coupling constant (*J* values) are given in Hertz. The coupling patterns are expressed by s (singlet), d (doublet), dd (doublet of doublet), ddd (doublet of doublet of doublet), dt (doublet of triplet), qd (quartet of doublet), quin (quintet), m (multiplet) and br (broad signal). MS spectra were measured with JEOL JMS-AX505HA, JMS-700V MStation, and JEOL JMS-T100LP spectrometers. Melting points were measured on a Yanaco Micro Melting System MP-500P. Commercial reagents and solvents were used without further purification unless otherwise indicated. Flash column chromatography was carried out with Kanto Chemical silica gel (Kanto Chemical Co., Inc., silica gel 60N, spherical neutral, particle size 63—210 μm). TLC was performed on 0.25 mm E Merck silica gel 60 F254 plates. HPLC analyses were performed on a JASCO PU-2089 plus and JASCO UV-2075 plus using 0.46 x 25 cm CHIRALPAK IA.

Preparation of pyruvic acid oxabicyclo[2.2.2]octyl orthoester 8

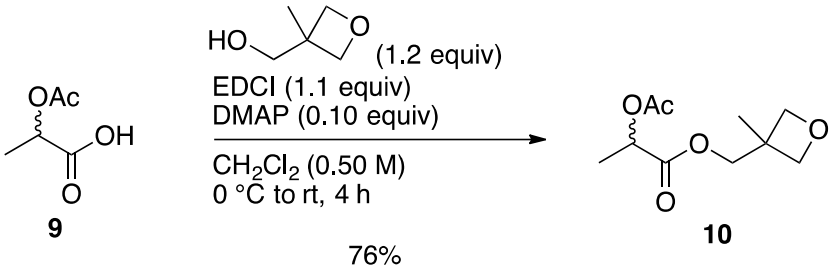
2-acetoxypropanoic acid 9[1]



2-Acetoxypropanoic acid **9** was prepared by the known procedure.[1]

To a stirred solution of *rac*-lactic acid (5.00 g, 55.5 mmol, 1.0 equiv) in THF (555 mL, 0.10 M) at 0 °C was added dropwise acetyl chloride (7.89 mL, 111 mmol) under N_2 atmosphere. After stirred for 1 h at room temperature, the reaction mixture was concentrated under reduced pressure. The obtained crude product was purified by silica gel column chromatography ($CHCl_3$: MeOH = 50 : 1) to give **9** (6.61 g, 50.0 mmol, 90% yield) as colorless oil.

(3-Methyloxetan-3-yl)methyl 2-acetoxypropanoate 10

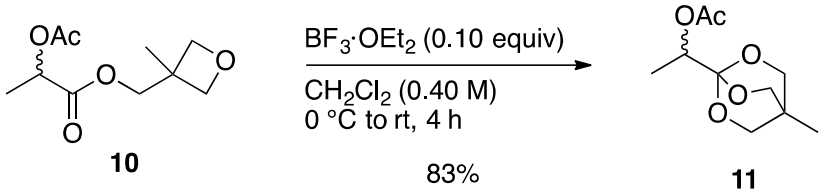


To a stirred solution of 3-methyl-3-oxetanemethanol (5.86 g, 57.4 mmol, 1.2 equiv), EDCI (10.1 g, 52.6 mmol, 1.1 equiv) and DMAP (584 mg, 4.78 mmol, 0.10 equiv) in CH_2Cl_2 (96 mL, 0.50 M) at 0 °C was added dropwise a solution of *rac*-2-acetoxypropanoic acid **9** (6.31g, 47.8 mmol) in CH_2Cl_2 (30 mL, 1.6 M) under N_2 atmosphere. After the mixture was stirred for 4 h at room temperature, the reaction was quenched with saturated aqueous NH_4Cl (100 mL). The resulting mixture was extracted with $CHCl_3$ (3 x 100 mL). The combined organic phases were washed with H_2O (2 x 100 mL) and brine (2 x 100 mL), dried over Na_2SO_4, filtered and concentrated under reduced pressure. The obtained crude product was purified by silica gel column chromatography (Hexane : AcOEt = 4 : 1) to give **10** (7.85 g, 36.3 mmol, 76% yield) as

colorless oil.

Colorless oil; Rf value on TLC 0.62 (Hexane : AcOEt = 1 : 1)
^{1}H-NMR (400 MHz, $CDCl_3$) δ 5.10 (q, *J* = 6.8 Hz, 1H), 4.52 (d, *J* = 11.6 Hz, 1H), 4.51 (d, *J* = 11.6 Hz, 1H), 4.38 (d, *J* = 6.0 Hz, 2H), 4.25 (d, *J* = 11.2 Hz, 1H), 4.21 (d, *J* = 11.2 Hz, 1H), 2.13 (s, 3H), 1.52 (d, *J* = 6.8 Hz, 3H), 1.33 (s, 3H)
^{13}C-NMR (100 MHz, $CDCl_3$) δ 170.9, 170.4, 79.3, 79.3, 69.1, 68.6, 39.1, 21.0, 20.6, 16.9
IR (neat) 2965, 2944, 2874, 1744, 1451, 1382, 1374, 1238, 1202, 1132, 1100, 1052, 984 cm^{-1}
HRMS (ESI) m/z calcd for $C_{10}H_{16}NaO_5$ $[M+Na]^+$ 239.0895, found 239.0886.

1-(4-Methyl-2,6,7-trioxabicyclo[2.2.2]octan-1-yl)ethyl acetate 11



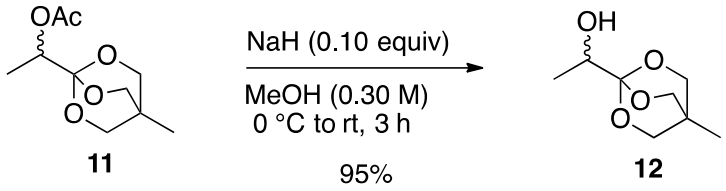
To a stirred solution of **10** (7.83 g, 36.2 mmol, 1.0 equiv) in CH_2Cl_2 (91 mL, 0.40 M) at 0 °C under N_2 atmosphere was added dropwise $BF_3{\cdot}OEt_2$ (0.447 mL, 3.62 mmol, 0.10 equiv). After 4 h at room temperature, the reaction was quenched with Et_3N (0.756 mL, 5.43 mmol, 0.15 equiv) at 0 °C and the mixture was stirred for 15 min. The resulting mixture was diluted with H_2O (100 mL) and extracted with $CHCl_3$ (3 x 200 mL). The combined organic phases were washed with H_2O (2 x 100 mL) and brine (2 x 100 mL), dried over Na_2SO_4, filtered and concentrated under reduced pressure. The obtained crude product was purified by silica gel column chromatography (Hexane : AcOEt = 6 : 1) to give **11** (6.49 g, 30.0 mmol, 83% yield) as white solid.

White solid; Mp 79–81 °C; Rf value on TLC 0.61 (Hexane : AcOEt = 1 : 1)
^{1}H-NMR (400 MHz, $CDCl_3$) δ 4.99 (q, *J* = 6.4 Hz, 1H), 3.92 (s, 6H), 2.09 (s, 3H), 1.24 (d, *J* = 6.4 Hz, 3H), 0.81 (s, 3H)
^{13}C-NMR (100 MHz, $CDCl_3$) δ 170.1, 107.6, 72.7, 69.9, 30.6, 21.3, 14.5, 14.3

IR (KBr) 2993, 2970, 2946, 2883, 1729, 1478, 1457, 1432, 1402, 1383, 1373, 1357, 1259, 1214, 1194, 1105, 1081, 1051, 1027, 1007, 982 cm^{-1}

HRMS (ESI) m/z calcd for $C_{10}H_{16}NaO_5$ $[M+Na]^+$ 239.0895, found 239.0888.

1-(4-Methyl-2,6,7-trioxabicyclo[2.2.2]octan-1-yl)ethan-1-ol 12



11 **12**

To a stirred solution of **11** (6.47 g, 29.9 mmol, 1.0 equiv) in MeOH (100 mL, 0.30 M) at 0 °C was added portionwise NaH (55% dispersion in oil, 131 mg, 2.99 mmol, 0.10 equiv), and the mixture was stirred for 3 h at room temperature. After the solvent was removed under reduced pressure, the obtained crude product was purified by silica gel column chromatography (Hexane : AcOEt = 4 : 1 contained 1% Et_3N) to give **12** (4.95 g, 28.4 mmol, 95%) as white solid.

White solid; Mp 63–66 °C; Rf value on TLC 0.28 (Hexane : AcOEt = 1 : 1)

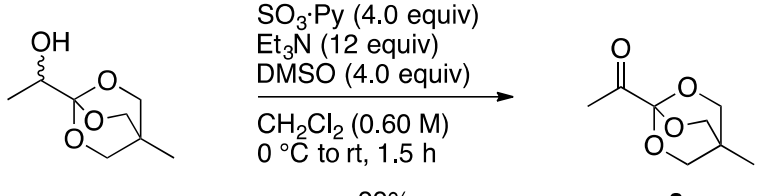
^{1}H-NMR (400 MHz, $CDCl_3$) δ 3.93 (s, 6H), 3.73 (q, *J* = 6.4 Hz, 1H), 2.13 (br s, 1H, -O<u>H</u>), 1.19 (d, *J* = 6.4 Hz, 3H), 0.81 (s, 3H)

^{13}C-NMR (100 MHz, $CDCl_3$) δ 108.3, 72.7, 69.4, 30.6, 16.2, 14.3

IR (KBr) 3529, 2992, 2969, 2943, 2884, 1475, 1458, 1399, 1363, 1281, 1195, 1132, 1077, 1048, 1023, 958 cm^{-1}

HRMS (ESI) m/z calcd for $C_8H_{14}NaO_4$ $[M+Na]^+$ 197.0790, found 197.0790.

1-(4-Methyl-2,6,7-trioxabicyclo[2.2.2]octan-1-yl)ethan-1-one 8



12 **8**

To a stirred solution of **12** (4.95 g, 28.4 mmol, 1.0 equiv), DMSO (8.10 mL, 114 mmol, 4.0 equiv) and Et_3N (47.5 mL, 341 mmol, 12 equiv) in CH_2Cl_2 (47 mL, 0.60 M) at 0 °C

was added portionwise SO_3·Py (18.1 g, 114 mmol, 4.0 equiv). After the mixture was stirred at room temperature for 1.5 h under N_2 atmosphere, the reaction was quenched with H_2O (100 mL). The resulting mixture was extracted with AcOEt (3 x 200 mL). The combined organic phases were washed with H_2O (2 x 200 mL) and brine (2 x 200 mL), dried over Na_2SO_4, filtered and concentrated under reduced pressure. The obtained crude product was purified by silica gel column chromatography (Hexane : AcOEt = 5 : 1) to give **8** (4.84 g, 28.1 mmol, 99% yield) as white solid.

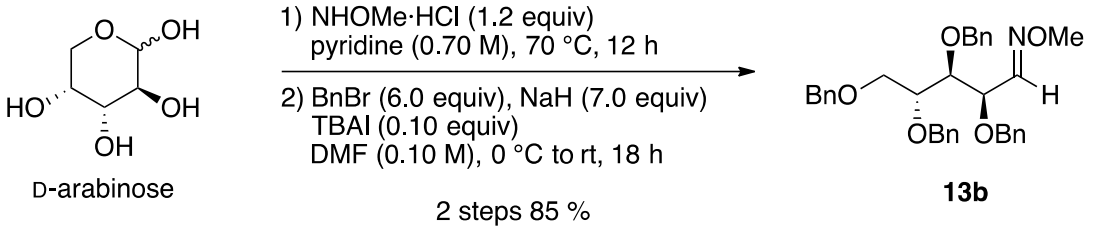
White solid; Mp 105–114 °C; Rf value on TLC 0.54 (Hexane : AcOEt = 1 : 1)
^{1}H-NMR (400 MHz, $CDCl_3$) δ 3.97 (s, 6H), 2.23 (s, 3H), 0.83 (s, 3H)
^{13}C-NMR (100 MHz, $CDCl_3$) δ 196.5, 103.2, 73.0, 30.8, 24.4, 14.1
IR (KBr) 2975, 2960, 2941, 2920, 2892, 1737, 1480, 1459, 1424, 1369, 1351, 1329, 1301, 1190, 1135, 1061, 1024, 982 cm^{-1}
HRMS (ESI) m/z calcd for $C_8H_{12}NaO_4$ $[M+Na]^+$ 195.0633, found 195.0639.

Orthoester **8** is non-hygroscopic solid and can be stored in the refrigerator over 6 months.

Preparation of the *O*-benzyl-protected aldehydes 14a–14f and 17b, 17d

D-Arabinose series

(2*R*,3*S*,4*R*,*Z*)-2,3,4,5-tetrakis(benzyloxy)pentanal *O*-methyl oxime 13b



A solution of D-arabinose (1.00 g, 6.66 mmol, 1.0 equiv) and *O*-methylhydroxylamine hydrochloride (667 mg, 7.99 mmol, 1.2 equiv) in pyridine (9.5 mL, 0.70 M) was stirred for 12 h at 70 °C under N_2 atmosphere. The reaction mixture was concentrated under reduced pressure to give colorless oil.

To a stirred solution of the above crude product in DMF (67 mL, 0.10 M) at 0 °C was added portionwise NaH (55% dispersion in oil, 2.04 g, 46.6 mmol, 7.0 equiv) and the mixture was stirred for 1 h under N_2 atmosphere. After the resulting mixture was cooled to 0 °C, BnBr (4.75 mL, 40.0 mmol, 6.0 equiv) and Bu_4NI (246 mg, 0.666 mmol, 0.10 equiv) was added. After stirred for 18 h at room temperature, the reaction mixture was concentrated under reduced pressure. The obtained residue was dissolved with AcOEt (100 mL), and the mixture was washed with H_2O (2 x 100 mL) and brine (2 x 100 mL), dried over Na_2SO_4, filtered and concentrated under reduced pressure. The crude product was purified by silica gel column chromatography (Hexane : AcOEt = 15 : 1) to give **13b** (3.04 g, 5.63 mmol, 85% yield in 2 steps) as pale yellow oil.

Pale yellow oil; Rf value on TLC 0.60 (Hexane : AcOEt = 4 : 1); $[\alpha]_D^{23}$ –17.5 (*c* 1.0, $CHCl_3$)

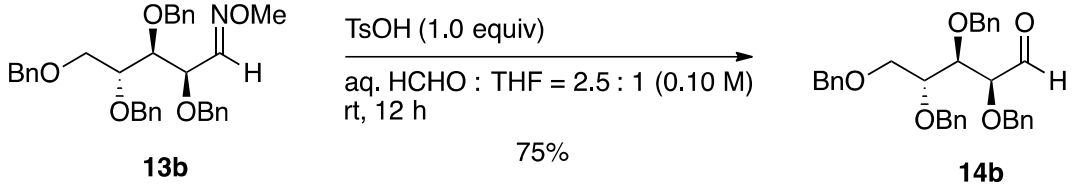
^{1}H-NMR (400 MHz, $CDCl_3$) δ 7.37 (d, *J* = 8.0 Hz, 1H), 7.34–7.23 (m, 20H), 4.65 (s, 2H), 4.62 (d, *J* = 11.6 Hz, 1H), 4.58 (d, *J* = 11.6 Hz, 1H), 4.54 (d, *J* = 12.0 Hz, 1H), 4.50 (d, *J* = 12.0 Hz, 1H), 4.38 (d, *J* = 11.6 Hz, 1H), 4.37 (d, *J* = 11.6 Hz, 1H), 4.29–4.26 (m, 1H), 3.85 (s, 3H), 3.85–3.79 (m, 3H), 3.72–3.69 (m, 1H)

^{13}C-NMR (100 MHz, $CDCl_3$) δ 148.8, 138.4, 138.3, 138.0, 137.8, 128.3, 128.3, 128.2, 128.2, 128.1, 127.7, 127.6, 127.5, 127.4, 80.1, 77.9, 77.0, 74.7, 73.3, 72.0, 71.1, 68.8, 61.6

IR (neat) 3086, 3064, 3030, 3002, 2936, 2897, 2866, 1496, 1454, 1324, 1207, 1092, 1073, 1041, 1028 cm^{-1}

HRMS (ESI) calcd for $C_{34}H_{37}NNaO_5$ $[M+Na]^+$ 562.2569, found 562.2566.

(2*S*,3*R*,4*R*)-2,3,4,5-tetrakis(benzyloxy)pentanal 14b



To a stirred solution of **13b** (200 mg, 0.371 mmol, 1.0 equiv) in THF and 36-38% aqueous HCHO (2.5 : 1, 3.7 mL, 0.10 M) at room temperature was added $TsOH \cdot H_2O$ (70.6 mg, 0.371 mmol, 1.0 equiv).[2] After the mixture was stirred for 12 h at room temperature, the reaction was quenched with saturated aqueous $NaHCO_3$. The resulting mixture was extracted with AcOEt (3 x 30 mL). The combined organic phases were washed with H_2O (2 x 50 mL) and brine (2 x 50 mL), dried over Na_2SO_4, filtered and concentrated under reduced pressure. The obtained crude product was purified by silica gel column chromatography (Hexane : AcOEt = 20 : 1) to give **14b** (142 mg, 0.278 mmol, 75% yield) as pale yellow oil.

Pale yellow oil; Rf value on TLC 0.49 (Hexane : AcOEt = 4 : 1); $[\alpha]_D^{27}$ –9.22 (*c* 1.0, $CHCl_3$)

^{1}H-NMR (400 MHz, $CDCl_3$) δ 9.61 (d, *J* = 1.6 Hz, 1H), 7.33-7.20 (m, 20H), 4.67 (d, *J* = 12.0 Hz, 1H), 4.62 (d, *J* = 11.6 Hz, 1H), 4.56–4.49 (m, 5H), 4.36 (d, *J* = 11.6 Hz, 1H), 4.14–4.09 (m, 2H), 3.85–3.78 (m, 2H), 3.68 (dd, *J* = 10.4, 4.0 Hz, 1H)

^{13}C-NMR (100 MHz, $CDCl_3$) δ 202.1, 138.1, 138.0, 137.6, 137.2, 128.4, 128.4, 128.3, 128.3, 128.2, 128.1, 128.0, 127.8, 127.8, 127.8, 127.6, 127.6, 84.1, 78.3, 77.4, 74.1, 73.3, 73.3, 71.9, 68.2

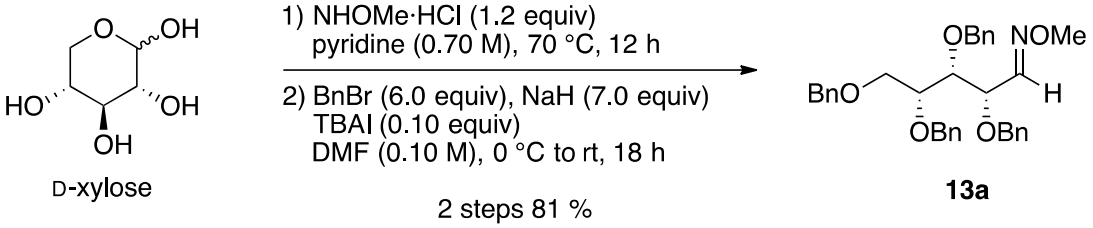
IR (neat) 3086, 3063, 3031, 2920, 2871, 1726, 1603, 1496, 1454, 1315, 1206, 1095,

1027, 914 cm^{-1}

HRMS (ESI) calcd for $C_{33}H_{34}NaO_5$ $[M+Na]^+$ 533.2304, found 533.2293.

D-Xylose series

(2*S*,3*R*,4*R*)-2,3,4,5-Tetrakis(benzyloxy)pentanal *O*-methyl oximes 13a



A solution of D-xylose (1.00 g, 6.66 mmol, 1.0 equiv) and *O*-methylhydroxylamine hydrochloride (667 mg, 7.99 mmol, 1.2 equiv) in pyridine (9.5 mL, 0.70 M) was stirred for 12 h at 70 °C under N_2 atmosphere. The reaction mixture was concentrated under reduced pressure to give colorless oil.

To a stirred solution of the above crude product in DMF (67 mL, 0.10 M) at 0 °C was added portionwise NaH (55% dispersion in oil, 2.04 g, 46.6 mmol, 7.0 equiv) and the mixture was stirred for 1 h under N_2 atmosphere. After the resulting mixture was cooled to 0 °C, BnBr (4.75 mL, 40.0 mmol, 6.0 equiv) and Bu_4NI (246 mg, 0.666 mmol, 0.10 equiv) was added. After stirred for 18 h at room temperature, the reaction mixture was concentrated under reduced pressure. The obtained residue was dissolved with AcOEt (100 mL), and the mixture was washed with H_2O (2 x 100 mL) and brine (2 x 100 mL), dried over Na_2SO_4, filtered and concentrated under reduced pressure. The crude product was purified by silica gel column chromatography (Hexane : AcOEt = 15 : 1) to give **13a** (2.90 g, 5.37 mmol, 81% yield in 2 steps) as pale yellow oil.

Pale yellow oil; Rf value on TLC 0.62 (Hexane : AcOEt = 4 : 1); $[\alpha]_D^{23}$ +12.6 (*c* 1.0, $CHCl_3$)

^{1}H-NMR (400 MHz, $CDCl_3$) δ 7.38 (d, *J* = 8.0 Hz, 1H), 7.35–7.24 (m, 20H), 4.71 (d, *J* = 11.6 Hz, 1H), 4.66 (d, *J* = 10.8 Hz, 2H), 4.61 (d, *J* = 11.6 Hz, 1H), 4.59 (d, *J* = 11.6 Hz, 1H), 4.38 (d, *J* = 11.6 Hz, 1H), 4.37 (s, 2H) 4.25 (dd, *J* = 8.0, 5.6 Hz, 1H), 3.86–

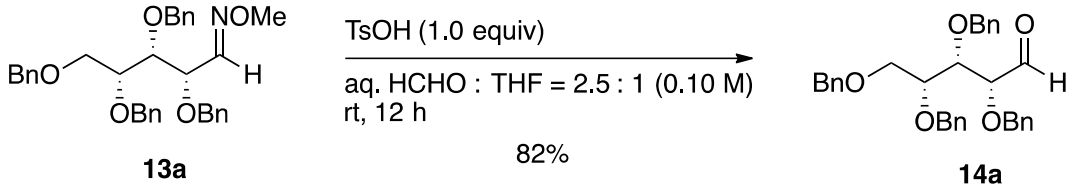
3.83 (m, 1H), 3.86 (s, 3H), 3.78 (dd, *J* = 5.6, 4.8 Hz, 1H), 3.58 (dd, *J* = 10.0, 4.4 Hz, 1H), 3.45 (dd, *J* = 10.0, 5.2 Hz, 1H),

^{13}C-NMR (100 MHz, $CDCl_3$) δ 148.4, 138.5, 138.1, 138.1, 137.6, 128.4, 128.3, 128.3, 128.2, 128.2, 128.0, 127.7, 127.7, 127.6, 127.5, 127.5, 79.8, 78.2, 76.5, 74.7, 73.2, 73.1, 71.1, 69.6, 61.7

IR (neat) 3088, 3063, 3030, 3006, 2936, 2897, 2866, 1496, 1454, 1363, 1350, 1207, 1089, 1078, 1046, 1030, 879 cm^{-1}

HRMS (ESI) calcd for $C_{34}H_{37}NNaO_5$ $[M+Na]^+$ 562.2569, found 562.2577.

(2*R*,3*S*,4*R*)-2,3,4,5-Tetrakis(benzyloxy)pentanal 14a



To a stirred solution of **13a** (400 mg, 0.741 mmol, 1.0 equiv) in THF and 36-38% aqueous HCHO (2.5 : 1, 7.4 mL, 0.10 M) at room temperature was added TsOH·H_2O (141 mg, 0.741 mmol, 1.0 equiv).[2] After the mixture was stirred for 12 h at room temperature, the reaction was quenched with saturated aqueous $NaHCO_3$. The resulting mixture was extracted with AcOEt (3 x 30 mL). The combined organic phases were washed with H_2O (2 x 50 mL) and brine (2 x 50 mL), dried over Na_2SO_4, filtered and concentrated under reduced pressure. The obtained crude product was purified by silica gel column chromatography (Hexane : AcOEt = 20 : 1) to give **14a** (309 mg, 0.605 mmol, 82% yield) as pale yellow oil.

Pale yellow oil; Rf value on TLC 0.43 (Hexane : AcOEt = 4 : 1); $[\alpha]_D^{27}$ +1.24 (*c* 0.5, $CHCl_3$)

^{1}H-NMR (400 MHz, $CDCl_3$) δ 9.65 (s, 1H), 7.35–7.17 (m, 20H), 4.71 (d, *J* = 11.6 Hz, 1H), 4.59–4.49 (m, 4H), 4.43 (d, *J* = 11.6 Hz, 1H), 4.39 (d, *J* = 12.4 Hz, 1H), 4.36 (d, *J* = 12.4 Hz, 1H), 3.95 (dd, *J* = 4.8, 4.0 Hz, 1H), 3.89–3.85 (m, 2H), 3.58 (dd, *J* = 10.0, 5.6 Hz, 1H), 3.46 (dd, *J* = 10.0, 5.2 Hz, 1H)

^{13}C-NMR (100 MHz, $CDCl_3$) δ 201.0, 138.0, 137.9, 137.5, 137.2, 128.4, 128.4, 128.4,

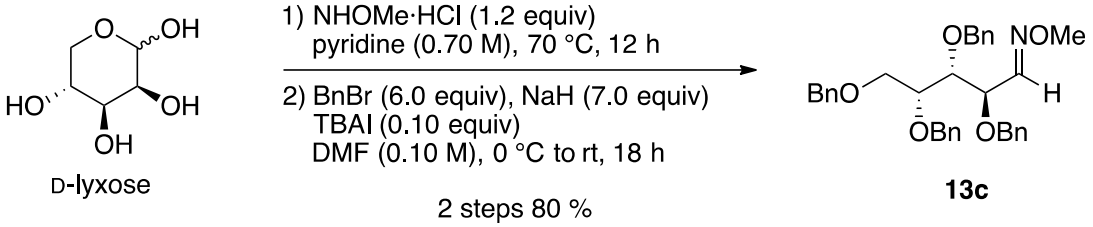
128.3, 128.3, 128.2, 128.1, 128.0, 128.0, 127.7, 127.7, 127.6, 81.4, 79.1, 76.8, 74.0, 73.3, 73.1, 73.0, 69.0

IR (neat) 3088, 3063, 3031, 2923, 2873, 1727, 1496, 1454, 1206, 1172, 1093, 1073, 1027 cm^{-1}

HRMS (ESI) calcd for $C_{33}H_{34}NaO_5$ $[M+Na]^+$ 533.2304, found 533.2305.

D-Lyxose series

(2*R*,3*R*,4*R*)-2,3,4,5-Tetrakis(benzyloxy)pentanal *O*-methyl oxime 13c



A solution of D-lyxose (1.00 g, 6.66 mmol, 1.0 equiv) and *O*-methylhydroxylamine hydrochloride (667 mg, 7.99 mmol, 1.2 equiv) in pyridine (9.5 mL, 0.70 M) was stirred for 12 h at 70 °C under N_2 atmosphere. The reaction mixture was concentrated under reduced pressure to give colorless oil.

To a stirred solution of the above crude product in DMF (67 mL, 0.10 M) at 0 °C was added portionwise NaH (55% dispersion in oil, 2.04 g, 46.6 mmol, 7.0 equiv) and the mixture was stirred for 1 h under N_2 atmosphere. After the resulting mixture was cooled to 0 °C, BnBr (4.75 mL, 40.0 mmol, 6.0 equiv) and Bu_4NI (246 mg, 0.666 mmol, 0.10 equiv) was added. After stirred for 18 h at room temperature, the reaction mixture was concentrated under reduced pressure. The obtained residue was dissolved with AcOEt (100 mL), and the mixture was washed with H_2O (2 x 100 mL) and brine (2 x 100 mL), dried over Na_2SO_4, filtered and concentrated under reduced pressure. The crude product was purified by silica gel column chromatography (Hexane : AcOEt = 15 : 1) to give **13c** (2.84 g, 5.26 mmol, 80% yield in 2 steps) as pale yellow oil.

Pale yellow oil; Rf value on TLC 0.67 (Hexane : AcOEt = 4 : 1); $[\alpha]_D^{24}$ –16.1 (*c* 1.0, $CHCl_3$)

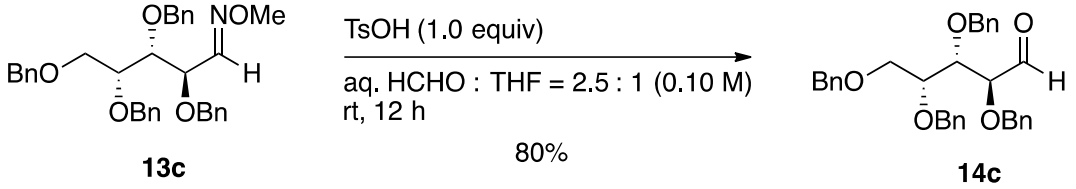
^{1}H-NMR (400 MHz, $CDCl_3$) δ 7.39 (d, *J* = 8.4 Hz, 1H), 7.35–7.23 (m, 20H), 4.70 (d, *J* = 11.6 Hz, 1H), 4.63 (d, *J* = 11.6 Hz, 1H), 4.61 (d, *J* = 11.6 Hz, 1H), 4.58 (d, *J* = 11.6 Hz, 1H), 4.53 (d, *J* = 11.6 Hz, 1H), 4.47 (d, *J* = 12.0 Hz, 1H), 4.43 (d, *J* = 12.0 Hz, 1H), 4.31 (d, *J* = 11.6 Hz, 1H), 4.24 (dd, *J* = 8.4, 5.6 Hz, 1H), 3.92 (dd, *J* = 5.6, 4.0 Hz, 1H), 3.87–3.83 (m, 1H), 3.86 (s, 3H), 3.64 (dd, *J* = 10.0, 5.2 Hz, 1H), 3.60 (dd, *J* = 10.0, 6.0 Hz, 1H)

^{13}C-NMR (100 MHz, $CDCl_3$) δ 148.5, 138.5, 138.2, 138.1, 137.9, 128.3, 128.3, 128.2, 127.8, 127.7, 127.7, 127.6, 127.6, 127.6, 127.4, 79.8, 77.9, 76.5, 74.3, 73.3, 73.2, 70.7, 69.7, 61.7

IR (neat) 3087, 3063, 3030, 3004, 2936, 2899, 2866, 1496, 1454, 1393, 1362, 1326, 1208, 1090, 1069, 1048, 1027 cm^{-1}

HRMS (ESI) calcd for $C_{34}H_{37}NNaO_5$ $[M+Na]^+$ 562.2569 found 562.2564.

(2*S*,3*S*,4*R*)-2,3,4,5-Tetrakis(benzyloxy)pentanal 14c



To a stirred solution of **13c** (400 mg, 0.741 mmol, 1.0 equiv) in THF and 36-38% aqueous HCHO (2.5 : 1, 7.4 mL, 0.10 M) at room temperature was added $TsOH \cdot H_2O$ (141 mg, 0.741 mmol, 1.0 equiv).[2] After the mixture was stirred for 12 h at room temperature, the reaction was quenched with saturated aqueous $NaHCO_3$. The resulting mixture was extracted with AcOEt (3 x 30 mL). The combined organic phases were washed with H_2O (2 x 50 mL) and brine (2 x 50 mL), dried over Na_2SO_4, filtered and concentrated under reduced pressure. The obtained crude product was purified by silica gel column chromatography (Hexane : AcOEt = 20 : 1) to give **14c** (303 mg, 0.593 mmol, 80% yield) as pale yellow oil.

Pale yellow oil; Rf value on TLC 0.46 (Hexane : AcOEt = 4 : 1); $[\alpha]_D^{27}$–14.3 (*c* 1.0, $CHCl_3$)

^{1}H-NMR (400 MHz, $CDCl_3$) δ 9.62 (d, *J* = 1.6 Hz, 1H), 7.32–7.20 (m, 20H), 4.62–4.38

(m, 8H), 4.02 (dd, *J* = 3.6, 1.6 Hz, 1H), 3.99 (dd, *J* = 4.8, 3.6 Hz, 1H), 3.84 (q, *J* = 4.8 Hz, 1H), 3.71 (dd, *J* = 10.0, 4.8 Hz, 1H), 3.69 (dd, *J* = 10.0, 4.8 Hz, 1H)

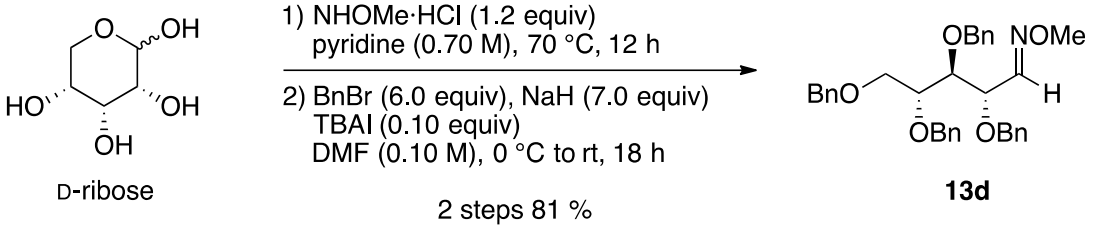
^{13}C-NMR (100 MHz, $CDCl_3$) δ 201.3, 138.0, 138.0, 137.7, 137.3, 128.4, 128.3, 128.3, 128.3, 128.0, 128.0, 127.9, 127.8, 127.8, 127.7, 127.7, 127.6, 83.7, 79.9, 78.3, 73.6, 73.2, 73.0, 72.7, 69.9

IR (neat) 3086, 3063, 3031, 2922, 2873, 1729, 1496, 1454, 1207, 1093, 1078, 1027 cm^{-1}

HRMS (ESI) calcd for $C_{33}H_{34}NaO_5$ $[M+Na]^+$ 533.2304, found 533.2299.

D-Ribose series

(2*S*,3*S*,4*R*)-2,3,4,5-Tetrakis(benzyloxy)pentanal *O*-methyl oxime 13d



A solution of D-ribose (1.00 g, 6.66 mmol, 1.0 equiv) and *O*-methylhydroxylamine hydrochloride (667 mg, 7.99 mmol, 1.2 equiv) in pyridine (9.5 mL, 0.70 M) was stirred for 12 h at 70 °C under N_2 atmosphere. The reaction mixture was concentrated under reduced pressure to give colorless oil.

To a stirred solution of the above crude product in DMF (67 mL, 0.10 M) at 0 °C was added portionwise NaH (55% dispersion in oil, 2.04 g, 46.6 mmol, 7.0 equiv) and the mixture was stirred for 1 h under N_2 atmosphere. After the resulting mixture was cooled to 0 °C, BnBr (4.75 mL, 40.0 mmol, 6.0 equiv) and Bu_4NI (246 mg, 0.666 mmol, 0.10 equiv) was added. After stirred for 18 h at room temperature, the reaction mixture was concentrated under reduced pressure. The obtained residue was dissolved with AcOEt (100 mL), and the mixture was washed with H_2O (2 x 100 mL) and brine (2 x 100 mL), dried over Na_2SO_4, filtered and concentrated under reduced pressure. The crude product was purified by silica gel column chromatography (Hexane : AcOEt = 15 : 1) to give **13d** (2.90 g, 5.37 mmol, 81% yield in 2 steps) as pale yellow oil.

Pale yellow oil; Rf value on TLC 0.60 (Hexane : AcOEt = 4 : 1); $[\alpha]_D^{24}$+21.4 (*c* 1.0, $CHCl_3$)

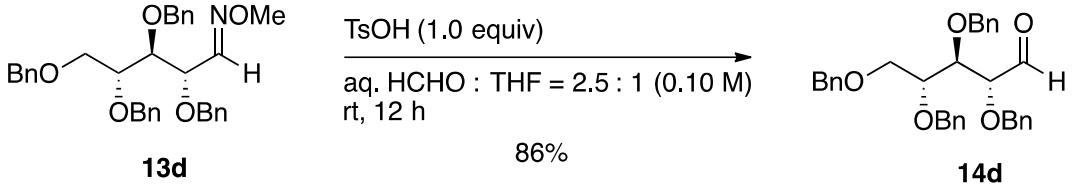
^{1}H-NMR (400 MHz, $CDCl_3$) δ 7.36 (d, *J* = 8.0 Hz 1H), 7.30–7.19 (m, 20H), 4.75 (d, *J* = 11.6 Hz, 1H), 4.64 (d, *J* = 11.6 Hz, 1H), 4.58 (d, *J* = 11.6 Hz, 2H), 4.54 (d, *J* = 11.6 Hz, 1H), 4.44 (s, 2H), 4.39 (d, *J* = 11.6 Hz, 1H), 4.30 (dd, *J* = 8.0, 4.0 Hz, 1H), 3.92 (dd, *J* = 6.8, 4.0 Hz, 1H), 3.84 (s, 3H), 3.70–3.65 (m, 2H), 3.60 (dd, *J* = 10.4, 5.6 Hz, 1H)

^{13}C-NMR (100 MHz, $CDCl_3$) δ 148.6, 138.4, 138.3, 138.3, 137.9, 128.3, 128.2, 128.2, 128.0, 128.0, 127.7, 127.7, 127.5, 127.5, 79.7, 78.0, 77.1, 74.0, 73.3, 72.6, 71.0, 69.4, 61.7

IR (neat) 3087, 3063, 3030, 3002, 2936, 2899, 2866, 2815, 1496, 1454, 1393, 1363, 1328, 1208, 1097, 1076, 1043, 1028, 940 cm^{-1}

HRMS (ESI) calcd for $C_{34}H_{37}NNaO_5$ $[M+Na]^+$ 562.2569 found 562.2549.

(2*R*,3*R*,4*R*)-2,3,4,5-Tetrakis(benzyloxy)pentanal 14d



To a stirred solution of **13d** (400 mg, 0.741 mmol, 1.0 equiv) in THF and 36-38% aqueous HCHO (2.5 : 1, 7.4 mL, 0.10 M) at room temperature was added $TsOH \cdot H_2O$ (141 mg, 0.741 mmol, 1.0 equiv).[2] After the mixture was stirred for 12 h at room temperature, the reaction was quenched with saturated aqueous $NaHCO_3$. The resulting mixture was extracted with AcOEt (3 x 30 mL). The combined organic phases were washed with H_2O (2 x 50 mL) and brine (2 x 50 mL), dried over Na_2SO_4, filtered and concentrated under reduced pressure. The obtained crude product was purified by silica gel column chromatography (Hexane : AcOEt = 20 : 1) to give **14d** (324 mg, 0.635 mmol, 86% yield) as pale yellow oil.

Pale yellow oil; Rf value on TLC 0.53 (Hexane : AcOEt = 4 : 1); $[\alpha]_D^{27}$+13.0 (*c* 1.0, $CHCl_3$)

^{1}H-NMR (400 MHz, $CDCl_3$) δ 9.45 (s, 1H), 7.31–7.17 (m, 20H), 4.72–4.64 (m, 3H),

4.55 (d, J = 11.6 Hz, 2H), 4.49 (d, J = 12.4 Hz, 1H), 4.44 (d, J = 11.6 Hz, 1H), 4.43 (d, J = 12.4 Hz, 1H), 4.07 (m, 1H), 3.98 (dd, J = 8.8, 2.4 Hz, 1H), 3.87 (ddd, J = 8.8, 4.4, 2.4 Hz, 1H), 3.67 (dd, J = 10.4, 2.4 Hz, 1H), 3.58 (dd, J = 10.4, 4.4 Hz, 1H)

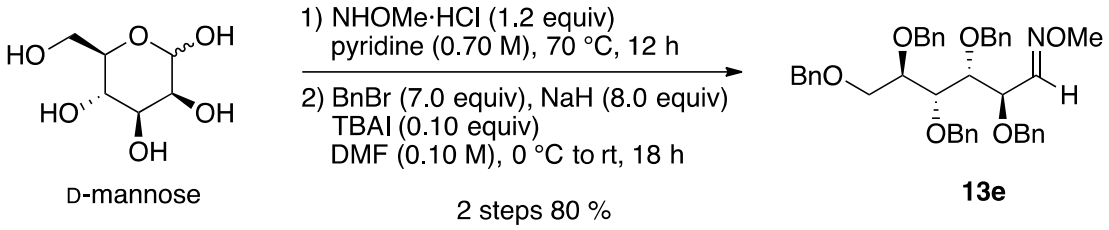
^{13}C-NMR (100 MHz, $CDCl_3$) δ 201.2, 138.2, 138.0, 137.6, 137.5, 128.4, 128.4, 128.3, 128.3, 127.9, 127.9, 127.8, 127.7, 127.6, 82.4, 80.5, 76.7, 73.4, 73.1, 72.8, 72.7, 69.1

IR (neat) 3088, 3063, 3031, 2925, 2870, 1726, 1496, 1454, 1326, 1207, 1098, 1073, 1027 cm^{-1}

HRMS (ESI) calcd for $C_{33}H_{34}NaO_5$ $[M+Na]^+$ 533.2304, found 533.2306.

D-Mannose series

(2*R*,3*R*,4*R*,5*R*)-2,3,4,5,6-Pentakis(benzyloxy)hexanal *O*-methyl oxime 13e



A solution of D-mannose (4.00 g, 22.2 mmol, 1.0 equiv) and *O*-methylhydroxylamine hydrochloride (2.22 g, 26.6 mmol, 1.2 equiv) in pyridine (32 mL, 0.70 M) was stirred for 12 h at 70 °C under N_2 atmosphere. The reaction mixture was concentrated under reduced pressure to give colorless oil.

To a stirred solution of the above crude product in DMF (222 mL, 0.10 M) at 0 °C was added portionwise NaH (55% dispersion in oil, 7.76 g, 178 mmol, 8.0 equiv) and the mixture was stirred for 1 h under N_2 atmosphere. After the resulting mixture was cooled to 0 °C, BnBr (18.4 mL, 155 mmol, 7.0 equiv) and Bu_4NI (820 mg, 2.22 mmol, 0.10 equiv) was added. After stirred for 18 h at room temperature, the reaction mixture was concentrated under reduced pressure. The obtained residue was dissolved with AcOEt (300 mL), and the mixture was washed with H_2O (2 x 200 mL) and brine (2 x 200 mL), dried over Na_2SO_4, filtered and concentrated under reduced pressure. The crude product was purified by silica gel column chromatography (Hexane : AcOEt = 15 : 1) to give **13e** (11.7 g, 17.7 mmol, 80% yield in 2 steps) as pale yellow oil.

Pale yellow oil; Rf value on TLC 0.61 (Hexane : AcOEt = 4 : 1); $[\alpha]_D^{24}$ –4.25 (*c* 1.0, $CHCl_3$)

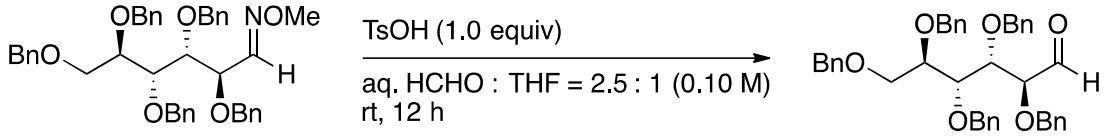
^{1}H-NMR (400 MHz, $CDCl_3$) δ 7.42 (d, *J* = 8.4 Hz 1H), 7.29–7.19 (m, 25H), 4.68 (d, *J* = 11.2 Hz, 1H), 4.62 (d, *J* = 11.6 Hz, 1H), 4.58–4.51 (m, 4H), 4.47 (d, *J* = 12.0 Hz, 1H), 4.43 (d, *J* = 12.0 Hz, 1H), 4.42 (d, *J* = 11.6 Hz, 1H), 4.27 (d, *J* = 11.6 Hz, 1H), 4.20 (dd, *J* = 8.4, 5.6 Hz, 1H), 4.02 (dd, *J* = 5.6, 4.0 Hz, 1H), 3.91 (dd, *J* = 6.4, 4.0 Hz, 1H), 3.87–3.76 (m, 2H), 3.79 (s, 3H), 3.65 (dd, *J* = 10.4, 4.4 Hz, 1H)

^{13}C-NMR (100 MHz, $CDCl_3$) δ 148.5, 138.6, 138.5, 138.3, 137.8, 128.3, 128.3, 128.3, 128.1, 127.9, 127.7, 127.7, 127.7, 127.6, 127.6, 127.5, 127.4, 127.4, 127.3, 80.1, 78.7, 78.3, 77.2, 74.3, 74.2, 73.3, 71.8, 70.5, 68.9, 61.7

IR (neat) 3087, 3063, 3030, 3002, 2934, 2899, 2866, 1496, 1454, 1392, 1361, 1208, 1092, 1073, 1046, 1032 cm^{-1}

HRMS (ESI) calcd for $C_{42}H_{45}NNaO_6$ $[M+Na]^+$ 682.3145, found 682.3161.

(2*S*,3*S*,4*R*,5*R*)-2,3,4,5,6-Pentakis(benzyloxy)hexanal 14e



13e 76% **14e**

To a stirred solution of **13e** (3.00 g, 4.55 mmol, 1.0 equiv) in THF and 36-38% aqueous HCHO (2.5 : 1, 46 mL, 0.10 M) at room temperature was added $TsOH \cdot H_2O$ (866 mg, 4.55 mmol, 1.0 equiv).[2] After the mixture was stirred for 12 h at room temperature, the reaction was quenched with saturated aqueous $NaHCO_3$. The resulting mixture was extracted with AcOEt (3 x 100 mL). The combined organic phases were washed with H_2O (2 x 100 mL) and brine (2 x 100 mL), dried over Na_2SO_4, filtered and concentrated under reduced pressure. The obtained crude product was purified by silica gel column chromatography (Hexane : AcOEt = 20 : 1) to give **14e** (2.18 g, 3.46 mmol, 76% yield) as pale yellow oil.

Pale yellow oil; Rf value on TLC 0.61 (Hexane : AcOEt = 4 : 1); $[\alpha]_D^{27}$ –4.68 (*c* 1.0, $CHCl_3$)

^{1}H-NMR (400 MHz, $CDCl_3$) δ 9.70 (d, *J* = 1.6 Hz, 1H), 7.34–7.22 (m, 25H), 4.68 (d, *J* = 11.2 Hz, 1H), 4.66 (d, *J* = 11.6 Hz, 1H), 4.65 (d, *J* = 11.2 Hz, 1H), 4.59–4.51 (m, 4H), 4.49 (d, *J* = 12.0 Hz, 1H), 4.45 (d, *J* = 11.6 Hz, 1H), 4.33 (d, *J* = 12.0 Hz, 1H), 4.12 (dd, *J* = 4.4, 4.0 Hz, 1H), 4.00–3.98 (m, 2H), 3.90–3.84 (m, 2H), 3.73–3.67 (m, 1H)

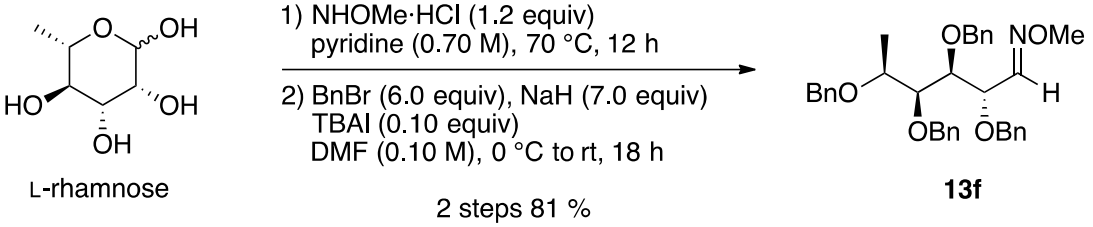
^{13}C-NMR (100 MHz, $CDCl_3$) δ 201.6, 138.4, 138.1, 138.1, 137.9, 137.3, 128.4, 128.3, 128.3, 128.3, 128.2, 128.1, 128.0, 127.9, 127.9, 127.8, 127.7, 127.7, 127.6, 127.5, 84.2, 80.4, 78.9, 78.3, 74.3, 74.0, 73.3, 72.4, 71.8, 68.8

IR (neat) 3090, 3067, 3030, 2918, 2869, 1728, 1496, 1454, 1206, 1093, 1076, 1028 cm^{-1}

HRMS (ESI) calcd for $C_{41}H_{42}NaO_6$ $[M+Na]^+$ 653.2879, found 653.2864.

L-Rhamnose series

(2*S*,3*S*,4*S*,5*S*)-2,3,4,5-Tetrakis(benzyloxy)hexanal *O*-methyl oxime 13f



A solution of L-rhamnose (1.00 g, 6.09 mmol, 1.0 equiv) and *O*-methylhydroxylamine hydrochloride (611 mg, 7.31 mmol, 1.2 equiv) in pyridine (8.7 mL, 0.70 M) was stirred for 12 h at 70 °C under N_2 atmosphere. The reaction mixture was concentrated under reduced pressure to give colorless oil.

To a stirred solution of the above crude product in DMF (61 mL, 0.10 M) at 0 °C was added portionwise NaH (55% dispersion in oil, 1.85 g, 42.6 mmol, 7.0 equiv) and the mixture was stirred for 1 h under N_2 atmosphere. After the resulting mixture was cooled to 0 °C, BnBr (4.33 mL, 36.5 mmol, 6.0 equiv) and Bu_4NI (225 mg, 0.609 mmol, 0.10 equiv) was added. After stirred for 18 h at room temperature, the reaction mixture was concentrated under reduced pressure. The obtained residue was dissolved with AcOEt (100 mL), and the mixture was washed with H_2O (2 x 100 mL) and brine (2 x 100 mL), dried over Na_2SO_4, filtered and concentrated under reduced pressure. The crude product

was purified by silica gel column chromatography (Hexane : AcOEt = 15 : 1) to give **13f** (2.74 g, 4.95 mmol, 81% yield in 2 steps) as pale yellow oil.

Pale yellow oil; Rf value on TLC 0.61 (Hexane : AcOEt = 4 : 1); $[\alpha]_D^{24}$ +10.5 (*c* 1.0, $CHCl_3$)

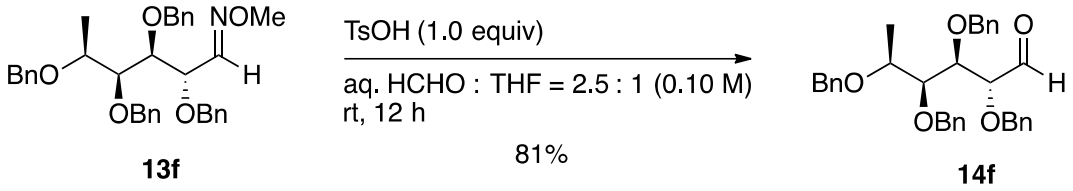
^{1}H-NMR (400 MHz, $CDCl_3$) δ 7.41 (d, *J* = 8.4 Hz 1H), 7.36–7.21 (m, 20H), 4.68 (d, *J* = 11.6 Hz, 1H), 4.65 (d, *J* = 11.6 Hz, 1H), 4.60 (d, *J* = 11.6 Hz, 1H), 4.58 (d, *J* = 11.6 Hz, 2H), 4.53 (d, *J* = 11.6 Hz, 1H), 4.34 (d, *J* = 11.6 Hz, 1H), 4.30 (d, *J* = 11.6 Hz, 1H), 4.15 (dd, *J* = 8.4, 5.6 Hz, 1H), 3.92 (dd, *J* = 6.0, 4.4 Hz, 1H), 3.82 (s, 3H), 3.76 (quin, *J* = 6.0 Hz, 1H), 3.68 (dd, *J* = 5.6, 4.4 Hz, 1H), 1.27 (d, *J* = 6.0 Hz, 3H)

^{13}C-NMR (100 MHz, $CDCl_3$) δ 148.4, 138.6, 138.6, 138.5, 137.7, 128.3, 128.3, 128.2, 128.1, 127.9, 127.8, 127.7, 127.7, 127.5, 127.4, 127.4, 127.3, 81.7, 80.3, 77.1, 75.2, 74.5, 74.3, 70.6, 70.4, 61.7, 15.7

IR (neat) 3088, 3063, 3030, 2967, 2935, 2895, 2871, 1496, 1454, 1390, 1208, 1088, 1070, 1026 cm^{-1}

HRMS (ESI) calcd for $C_{35}H_{39}NNaO_5$ $[M+Na]^+$ 576.2726, found 576.2711.

(2*R*,3*R*,4*S*,5*S*)-2,3,4,5-Tetrakis(benzyloxy)hexanal 14f



To a stirred solution of **13f** (400 mg, 0.722 mmol, 1.0 equiv) in THF and 36-38% aqueous HCHO (2.5 : 1, 7.2 mL, 0.10 M) at room temperature was added $TsOH \cdot H_2O$ (137 mg, 0.722 mmol, 1.0 equiv).[2] After the mixture was stirred for 12 h at room temperature, the reaction was quenched with saturated aqueous $NaHCO_3$. The resulting mixture was extracted with AcOEt (3 x 30 mL). The combined organic phases were washed with H_2O (2 x 50 mL) and brine (2 x 50 mL), dried over Na_2SO_4, filtered and concentrated under reduced pressure. The obtained crude product was purified by silica gel column chromatography (Hexane : AcOEt = 20 : 1) to give **14f** (307 mg, 0.585 mmol, 81% yield) as pale yellow oil.

Pale yellow oil; Rf value on TLC 0.54 (Hexane : AcOEt = 4 : 1); $[\alpha]_D^{27}$ +12.8 (*c* 1.0, $CHCl_3$)

^{1}H-NMR (400 MHz, $CDCl_3$) δ 9.65 (d, *J* = 2.0 Hz, 1H), 7.32–7.20 (m, 20H), 4.69 (d, *J* = 11.6 Hz, 1H), 4.63–4.51 (m, 5H), 4.34 (d, *J* = 11.6 Hz, 1H), 4.30 (d, *J* = 12.0 Hz, 1H), 3.99–3.96 (m, 2H), 3.75–3.68 (m, 2H), 1.28 (d, *J* = 6.0 H, 3H)

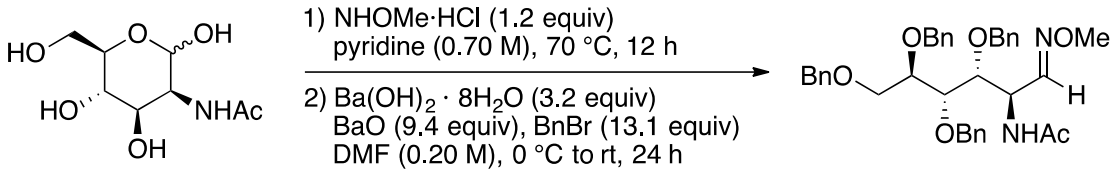
^{13}C-NMR (100 MHz, $CDCl_3$) δ 201.6, 138.4, 138.2, 137.9, 137.2, 128.4, 128.3, 128.3, 128.2, 128.0, 128.0, 127.9, 127.6, 127.6, 127.6, 127.5, 84.0, 81.7, 80.5, 75.3, 74.5, 74.1, 72.5, 70.4, 15.7

IR (neat) 3086, 3063, 3031, 2976, 2932, 2875, 1728, 1496, 1454, 1315, 1271, 1207, 1095, 1069, 1027, 915 cm^{-1}

HRMS (ESI) calcd for $C_{34}H_{36}NaO_5$ $[M+Na]^+$ 547.2460, found 547.2473.

N-Acetyl-D-mannosamine series

***N*-((2*R*,3*R*,4*S*,5*R*,*Z*)-3,4,5,6-tetrakis(benzyloxy)-1-(methoxyimino)hexan-2-yl)aceta mide 16d**



N-acetyl-D-mannosamine **15d**

2 steps 69 %

16d

A solution of *N*-acetyl-D-mannosamine **15d** (1.00 g, 4.52 mmol, 1.0 equiv) and *O*-methylhydroxylamine hydrochloride (453 mg, 5.42 mmol, 1.2 equiv) in pyridine (6.5 mL, 0.70 M) was stirred for 12 h at 70 °C under N_2 atmosphere. The reaction mixture was concentrated under reduced pressure to give colorless oil.

To a stirred solution of the above crude product in DMF (23 mL, 0.20 M) at 0 °C was successively added BnBr (7.01 mL, 59.2 mmol, 13.1 equiv), BaO (6.52 g, 42.5 mmol, 9.4 equiv) and $Ba(OH)_2 \cdot 8H_2O$ (4.57 g, 14.5 mmol, 3.2 equiv). After stirred at 0 °C for 6 h and then at room temperature for 18 h under N_2 atmosphere, the mixture was filtered through a Celite pad® by rinsing with $CHCl_3$. After the filtrate was concentrated under reduced pressure, the resulting residue was dissolved in AcOEt (100 mL) and washed

with H_2O (2 x 100 mL) and brine (2 x 100 mL), dried over Na_2SO_4, filtered and concentrated under reduced pressure. The obtained crude product was purified by silica gel column chromatography (Hexane : AcOEt = 6 : 1) to give **16d** (1.91 g, 3.13 mmol, 69% in 2 steps) as pale yellow oil.

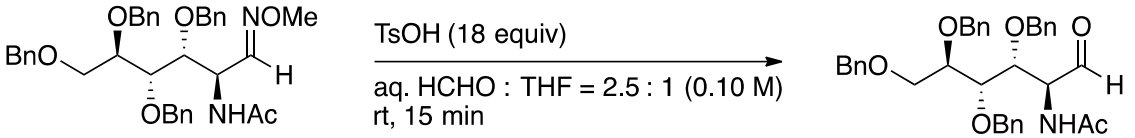
Pale yellow oil; Rf value on TLC 0.32 (Hexane : AcOEt = 2 : 1); $[\alpha]_D^{24}$ +3.23 (*c* 0.50, $CHCl_3$)

^{1}H-NMR (400 MHz, $CDCl_3$) δ 7.35–7.22 (m, 21H), 6.40 (d, *J* = 8.0 Hz, 1H, -NH), 5.02 (dt, *J* = 8.0, 4.8 Hz, 1H), 4.74 (d, *J* = 10.8 Hz, 1H), 4.69 (d, *J* = 11.6 Hz, 1H), 4.59 (d, *J* = 10.8 Hz, 1H), 4.56 (d, *J* = 11.6 Hz, 1H), 4.54 (s, 2H), 4.51 (d, *J* = 11.6 Hz, 1H), 4.49 (d, *J* = 11.6 Hz, 1H), 3.97 (dd, *J* = 9.2, 4.8 Hz, 1H), 3.94–3.90 (m, 3H), 3.85 (s, 3H), 3.75–3.70 (m, 1H), 1.66 (s, 3H)

^{13}C-NMR (100 MHz, $CDCl_3$) δ 169.7, 147.4, 138.4, 138.2, 137.9, 137.8, 128.5, 128.5, 128.4, 128.3, 128.3, 128.2, 128.0, 127.9, 127.7, 127.7, 127.6, 127.6, 80.1, 79.0, 74.3, 73.4, 72.9, 72.3, 69.1, 61.8, 49.5, 23.0

IR (neat) 3288, 3086, 3063, 3030, 3004, 2938, 2901, 2869, 2817, 1676, 1661, 1497, 1454, 1370, 1305, 1210, 1103, 1069, 1043, 1027, 907 cm^{-1}; HRMS (ESI) calcd for $C_{37}H_{42}N_2NaO_6$ $[M+Na]^+$ 633.2941, found 633.2934.

***N*-((2*S*,3*R*,4*S*,5*R*)-3,4,5,6-tetrakis(benzyloxy)-1-oxohexan-2-yl)acetamide 17d**



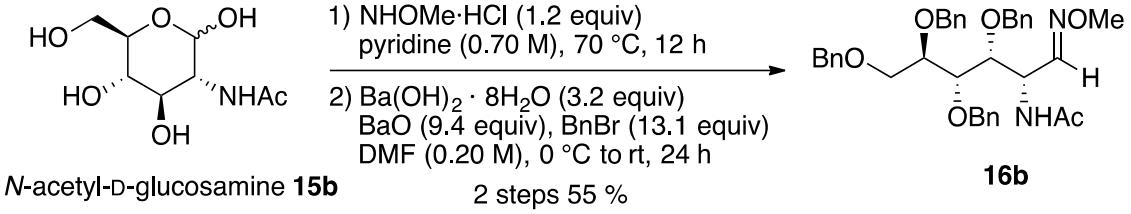
16d **17d**

To a stirred solution of **16d** (600 mg, 0.982 mmol, 1.0 equiv) in THF and 36-38% aqueous HCHO (2.5 : 1, 9.8 mL, 0.10 M) at room temperature was added $TsOH \cdot H_2O$ (3.37 g, 17.7 mmol, 18 equiv). The progress of the reaction was checked by TLC analysis ever 5 min.[a] After the mixture was stirred for 15 min at room temperature, the reaction was quenched with saturated aqueous $NaHCO_3$ and the resulting mixture was extracted with AcOEt (2 x 50 mL). The combined organic phases were washed with H_2O (2 x 50 mL) and brine (2 x 50 mL), dried over Na_2SO_4, filtered and concentrated

under reduced pressure. The obtained crude product was passed through a short column of silica gel using as an eluent (Hexane : AcOEt = 1 : 1). The obtained product **17d** (593 mg, pale yellow oil) was used for next reaction without further purification.[b]

N-Acetyl-D-glucosamine series

N-((2S,3R,4S,5R)-3,4,5,6-Tetrakis(benzyloxy)-1-(methoxyimino)hexan-2-yl)acetamide 16b



N-acetyl-D-glucosamine **15b**

16b

A solution of *N*-acetyl-D-glucosamine **15b** (1.00 g, 4.52 mmol, 1.0 equiv) and *O*-methylhydroxylamine hydrochloride (453 mg, 5.42 mmol, 1.2 equiv) in pyridine (6.5 mL, 0.70 M) was stirred for 12 h at 70 °C under N_2 atmosphere. The reaction mixture was concentrated under reduced pressure to give colorless oil.

To a stirred solution of the above crude product in DMF (23 mL, 0.20 M) at 0 °C was successively added BnBr (7.01 mL, 59.2 mmol, 13.1 equiv), BaO (6.52 g, 42.5 mmol, 9.4 equiv) and $Ba(OH)_2 \cdot 8H_2O$ (4.57 g, 14.5 mmol, 3.2 equiv). After stirred for 6 h at 0 °C and for 18 h at room temperature under N_2 atmosphere, the mixture was filtered through a Celite pad® by rinsing with $CHCl_3$. After the filtrate was concentrated under reduced pressure, the resulting residue was dissolved in AcOEt (100 mL) and washed with H_2O (2 x 100 mL) and brine (2 x 100 mL), dried over Na_2SO_4, filtered and concentrated under reduced pressure. The obtained crude product was purified by silica gel column chromatography (Hexane : AcOEt = 6 : 1) to give **16b** (1.51 g, 2.47 mmol, 55% in 2 steps) as pale yellow oil.

Pale yellow oil; Rf value on TLC 0.46 (Hexane : AcOEt = 2 : 1); $[\alpha]_D^{24}$ –10.5 (*c* 0.5, $CHCl_3$)

^{1}H-NMR (400 MHz, $CDCl_3$) δ 7.36–7.24 (m, 21H), 6.13 (d, *J* = 8.4 Hz, 1H, -NH), 4.91 (ddd, *J* = 8.4, 4.0, 2.8 Hz, 1H), 4.72 (d, *J* = 11.2 Hz, 1H), 4.68 (d, *J* = 11.2 Hz, 1H), 4.63

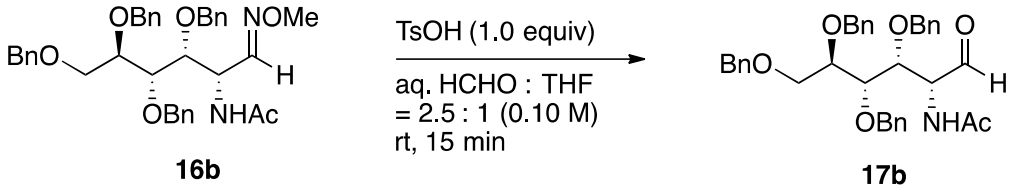
(d, J = 12.0 Hz, 1H), 4.60 (d, J = 11.2 Hz, 1H), 4.56 (d, J = 11.2 Hz, 1H), 4.54 (d, J = 12.0 Hz, 1H), 4.50 (d, J = 12.0 Hz, 1H), 4.46 (d, J = 12.0 Hz, 1H), 4.06 (dd, J = 6.0, 2.8 Hz, 1H), 3.91–3.84 (m, 2H), 3.82–3.79 (m, 1H), 3.79 (s, 3H), 3.71–3.66 (m, 1H), 1.92 (s, 3H)

^{13}C-NMR (100 MHz, $CDCl_3$) δ 169.8, 147.9, 138.5, 138.4, 138.1, 138.0, 128.4, 128.3, 128.3, 128.3, 128.2, 127.9, 127.8, 127.7, 127.6, 127.5, 127.5, 79.7, 78.7, 78.6, 74.5, 74.1, 73.4, 72.1, 68.9, 61.6, 49.9, 23.2

IR (neat) 3296, 3086, 3062, 3030, 3004, 2935, 2899, 2867, 1673, 1663, 1497, 1454, 1370, 1208, 1090, 1067, 1028 cm^{-1}

HRMS (ESI) calcd for $C_{37}H_{42}N_2NaO_6$ $[M+Na]^+$ 633.2941, found 633.2953.

_N_-((2_R_,3_R_,4_S_,5_R_)-3,4,5,6-Tetrakis(benzyloxy)-1-oxohexan-2-yl)acetamide 17b



To a stirred solution of **16b** (500 mg, 0.819 mmol, 1.0 equiv) in THF and 36-38% aqueous HCHO (2.5 : 1, 8.2 mL, 0.10 M) at room temperature was added $TsOH \cdot H_2O$ (156 mg, 0.819 mmol, 1.0 equiv).[2] The progress of the reaction was checked by TLC analysis ever 5 min.[a] After the mixture was stirred for 15 min at room temperature, the reaction was quenched with saturated aqueous $NaHCO_3$. The resulting mixture was extracted with AcOEt (2 x 50 mL). The combined organic phases were washed with H_2O (2 x 50 mL) and brine (2 x 50 mL), dried over Na_2SO_4, filtered and concentrated under reduced pressure. The obtained crude product was passed through a short column of silica gel using an eluent (Hexane : AcOEt = 1 : 1). The obtained product **17b** (493 mg, pale yellow oil) was used for the next reaction without further purification.[b]

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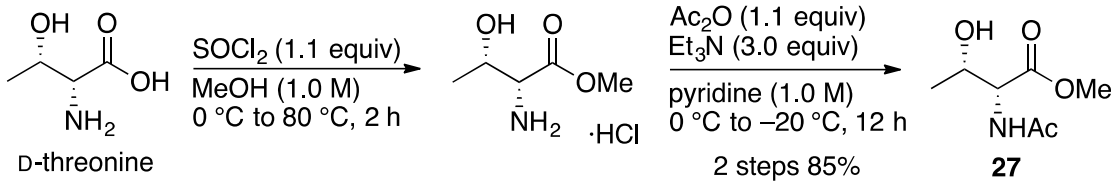
[a] Partial decompositions of *N*-acetylaldehydes **17b** and **17d** were observed at the prolonged reaction time.

[b] *N*-Acetylaldehydes **17b** and **17d** were slightly unstable on silica gel.

Preparation of the aldehydes 17a and 17c derived from D-threonine and L-*allo*-threonine

Preparation of the aldehyde 17a from D-threonine

Methyl *N*-acetyl-D-threoninate 27



$SOCl_2$ (6.67 mL, 92.3 mmol, 1.1 equiv) was added dropwise to anhydrous MeOH (84 mL, 1.0 M) at 0 °C under N_2 atmosphere. The solution was stirred at 0 °C for 30 min and then D-threonine (10.0 g, 83.9 mmol, 1.0 equiv) was added portionwise. The reaction mixture was warmed up to 80 °C and stirred for 2 h. The solvent was removed under reduced pressure to give colorless oil. The crude product was dissolved in pyridine (84 mL, 1.0 M), and Et_3N (35.1 mL, 252 mmol, 3.0 equiv) was added at 0 °C. After the mixture was stirred for 30 min at 0 °C, Ac_2O (8.72 mL, 92.3 mmol, 1.1 equiv) was added dropwise at –20 °C and the resulting mixture was furthermore stirred for 12 h. The reaction mixture was concentrated under reduced pressure, and the resulting residue was passed through a silica gel pad by rinsing with AcOEt. The filtrate was concentrated under reduced pressure. The obtained crude product was purified by silica gel column chromatography ($CHCl_3$: MeOH = 50 : 1) to give **27** (13.7 g, 78.2 mmol, 85% yield in 2 steps) as white solid.

White solid; Mp 98–102 °C; Rf value on TLC 0.65 ($CHCl_3$: MeOH = 10 : 1); $[\alpha]_D^{24}$ – 0.32 (*c* 1.0, $CHCl_3$)

^{1}H-NMR (400 MHz, $CDCl_3$) δ 6.39 (br d, *J* = 8.8 Hz, 1H, -NH), 4.59 (dd, *J* = 8.8, 2.8 Hz, 1H), 4.33 (qd, *J* = 6.4, 2.8 Hz, 1H), 3.76 (s, 3H), 2.08 (s, 3H), 1.22 (d, *J* = 6.4 Hz, 3H)

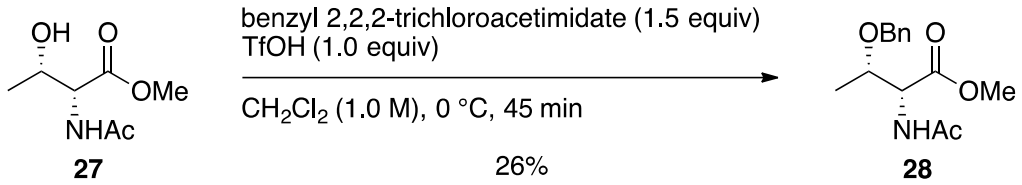
^{13}C-NMR (100 MHz, $CDCl_3$) δ 171.6, 171.0, 67.8, 57.4, 52.5, 22.9, 19.9

IR (KBr) 3290, 3191, 3077, 2980, 2959, 2934, 2847, 2749, 1750, 1647, 1543, 1457,

1433, 1377, 1309, 1252, 1213, 1155, 1115, 1079, 1035, 989 cm^{-1}

HRMS (ESI) calcd for $C_7H_{13}NNaO_4$ $[M+Na]^+$ 198.0742, found 198.0753.

Methyl *N*-acetyl-*O*-benzyl-D-threoninate 28



To stirred a solution of **27** (8.00 g, 45.7 mmol, 1.0 equiv) and benzyl 2,2, 2-trichloroacetimidate (12.7 mL, 68.6 mmol, 1.5 equiv) in CH_2Cl_2 (46 mL, 1.0 M) at 0 °C was added dropwise TfOH (4.04 mL, 45.7 mmol, 1.0 equiv) under N_2 atmosphere. After the reaction mixture was stirred for 45 min at 0 °C, the reaction was quenched with saturated aqueous $NaHCO_3$. The resulting mixture was extracted with $CHCl_3$ (3 x 100 mL). The combined organic phases were washed with H_2O (2 x 50 mL) and brine (2 x 50 mL), dried over Na_2SO_4, filtered and concentrated under reduced pressure. The obtained crude product was purified by silica gel column chromatography (Hexane : AcOEt = 1 : 2) to give **28** (3.10 g, 11.7 mmol, 26% yield) as colorless oil.

Colorless oil; Rf value on TLC 0.40 (Hexane : AcOEt = 1 : 2); $[\alpha]_D^{24}$ –6.56 (*c* 1.0, $CHCl_3$)

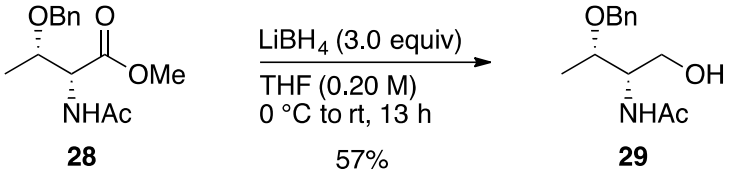
^{1}H-NMR (400 MHz, $CDCl_3$) δ 7.36–7.24 (m, 5H), 6.19 (d, *J* = 9.2 Hz, 1H, -NH), 4.67 (dd, *J* = 9.2, 2.4 Hz, 1H), 4.57 (d, *J* = 11.6 Hz, 1H), 4.37 (d, *J* = 11.6 Hz, 1H), 4.13 (qd, *J* = 6.4, 2.0 Hz, 1H), 3.67 (s, 3H), 2.07 (s, 3H), 1.23 (d, *J* = 6.4 Hz, 3H)

^{13}C-NMR (100 MHz, $CDCl_3$) δ 171.1, 170.5, 137.6, 128.3, 127.8, 127.7, 74.2, 70.8, 56.5, 52.2, 23.0, 16.1

IR (neat) 3297, 3064, 3030, 2979, 2951, 2934, 2871, 1750, 1656, 1528, 1437, 1376, 1344, 1317, 1286, 1211, 1163, 1089, 1053 cm^{-1}

HRMS (ESI) calcd for $C_{14}H_{19}NNaO_4$ $[M+Na]^+$ 288.1212, found 288.1207.

***N*-((2*S*,3*S*)-3-(Benzyloxy)-1-hydroxybutan-2-yl)acetamide 29**



28 57% **29**

To a stirred solution of **28** (3.19 g, 12.0 mmol, 1.0 equiv) in THF (60 mL, 0.20 M) at 0 °C was added $LiBH_4$ (784 mg, 36.0 mmol, 3.0 equiv). After the reaction mixture was stirred for 13 h at room temperature under N_2 atmosphere, the reaction was quenched with saturated aqueous NH_4Cl. The resulting mixture was extracted with AcOEt (3 x 100 mL). The combined organic phases were washed with H_2O (2 x 50 mL) and brine (2 x 50 mL), dried over Na_2SO_4, filtered and concentrated under reduced pressure. The obtained crude product was purified by silica gel column chromatography ($CHCl_3$: MeOH = 50 : 1) to give **29** (1.63 g, 6.87 mmol, 57% yield) as white solid.

White solid; Mp 97–99 °C; Rf value on TLC 0.45 ($CHCl_3$: MeOH = 10 : 1); $[\alpha]_D^{23}$ +30.3 (*c* 1.0, $CHCl_3$)

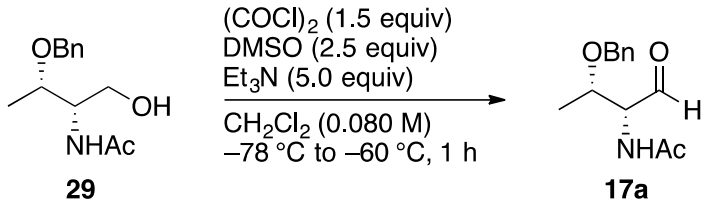
^{1}H-NMR (400 MHz, $CDCl_3$) δ 7.39–7.29 (m, 5H), 6.04 (d, *J* = 7.2 Hz, 1H, -NH), 4.64 (d, *J* = 11.2 Hz, 1H), 4.39 (d, *J* = 11.2 Hz, 1H), 3.98–3.93 (m, 1H), 3.87 (qd, *J* = 6.0, 2.4 Hz, 1H), 3.74 (dt, *J* = 11.2, 4.8 Hz, 1H), 3.64 (ddd, *J* = 11.2, 8.0, 5.6 Hz, 1H), 2.87–2.84 (m, 1H), 2.02 (s, 3H), 1.24 (d, *J* = 6.0 Hz, 3H)

^{13}C-NMR (100 MHz, $CDCl_3$) δ 171.0, 137.8, 128.5, 128.0, 127.9, 74.3, 70.9, 64.0, 55.2, 23.2, 16.3

IR (KBr) 3343, 3275, 3085, 3060, 3027, 3004, 2976, 2965, 2954, 2937, 2885, 2871, 2858, 1641, 1566, 1496, 1469, 1450, 1438, 1379, 1354, 1327, 1299, 1270, 1258, 1204, 1159, 1110, 1081, 1057, 1028, 1011, 980 cm^{-1}

HRMS (ESI) calcd for $C_{13}H_{19}NNaO_3$ $[M+Na]^+$ 260.1263, found 260.1256.

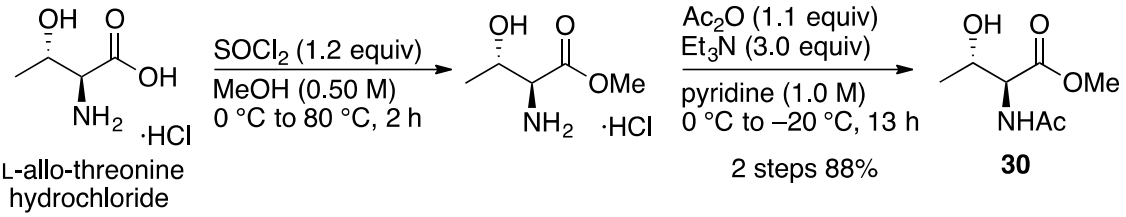
***N*-((2*R*,3*S*)-3-(Benzyloxy)-1-oxobutan-2-yl)acetamide 17a**



To a stirred solution of $(COCl)_2$ (0.216 mL, 2.52 mmol, 2.0 equiv) in CH_2Cl_2 (5.0 mL) at –78 °C was added dropwise a solution of DMSO (0.224 mL, 3.15 mmol, 2.5 equiv) in CH_2Cl_2 (3.6 mL) under N_2 atmosphere. After the mixture was stirred at –78 °C for 15 min, a solution of **29** (300 mg, 1.26 mmol, 1.0 equiv) in CH_2Cl_2 (3.6 mL) was added dropwise. After the resulting mixture was stirred for 30 min at –78 °C, a solution of Et_3N (0.877 mL, 6.30 mmol, 5.0 equiv) in CH_2Cl_2 (3.6 mL) was added dropwise at –78 °C, and then the mixture was warmed to –60 °C. After the reaction mixture was stirred for 1 h at –60 °C, the reaction was quenched with 20% aqueous $KHSO_4$ (10 mL). The resulting mixture was allowed to gently warm up to room temperature, and extracted with $CHCl_3$ (3 x 30 mL). The combined organic phases were washed with H_2O (2 x 20 mL) and brine (2 x 20 mL), dried over Na_2SO_4, filtered and concentrated under reduced pressure. The residue was passed through a short column of silica gel (Hexane : AcOEt = 1 : 1). The obtained product **17a** (297 mg, pale yellow oil) was used for the next reaction without further purification.[c]

Preparation of the aldehyde 17c from L-*allo*-threonine

Methyl acetyl-L-allothreoninate 30



$SOCl_2$ (9.15 mL, 127 mmol, 1.2 equiv) was added dropwise to anhydrous MeOH (212 mL, 0.50 M) at 0 °C under N_2 atmosphere. The solution was stirred at 0 °C for 30 min

and then L-allo-threonine hydrochloride[3] (17.9 g, 106 mmol, 1.0 equiv) was added portionwise. The reaction mixture was warmed up to 80 °C and stirred for 2 h. The solvent was removed under reduced pressure to give colorless oil. The crude product was dissolved in pyridine (106 mL, 1.0 M), and Et_3N (44.4 mL, 318 mmol, 3.0 equiv) was added at 0 °C. After the mixture was stirred for 30 min at 0 °C, Ac_2O (11.0 mL, 117 mmol, 1.1 equiv) was added dropwise at –20 °C and the resulting mixture was furthermore stirred for 13 h. The reaction mixture was concentrated under reduced pressure, and the resulting residue was passed through a silica gel pad by rinsing with AcOEt. The filtrate was concentrated under reduced pressure. The obtained crude product was purified by silica gel column chromatography ($CHCl_3$: MeOH = 50 : 1) to give **30** (16.3 g, 93.0 mmol, 88% yield) as colorless oil.

Colorless oil; Rf value on TLC 0.42 ($CHCl_3$: MeOH = 10 : 1); $[\alpha]_D^{24}$ +44.9 (*c* 1.0, $CHCl_3$)

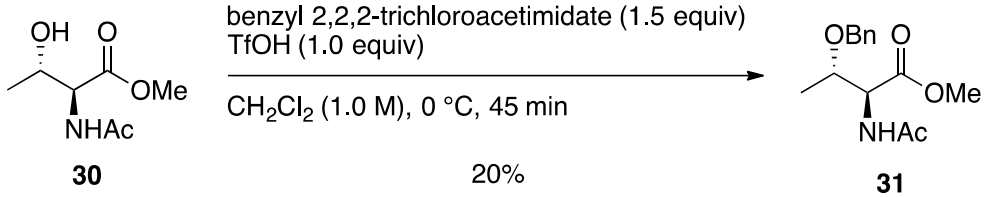
^{1}H-NMR (400 MHz, $CDCl_3$) δ 6.54 (br s, 1H, -NH), 4.69–4.66 (m, 1H), 4.19–4.13 (m, 1H), 3.78 (d, *J* = 0.8 Hz, 3H), 2.07 (d, *J* = 1.2 Hz, 3H), 1.17 (d, *J* = 6.4 Hz, 3H)

^{13}C-NMR (100 MHz, $CDCl_3$) δ 171.2, 170.7, 68.7, 58.1, 52.5, 22.9, 18.8

IR (neat) 3306, 3074, 2980, 2955, 2938, 1739, 1660, 1548, 1538, 1438, 1377, 1300, 1276, 1251, 1213, 1156, 1007, 939 cm^{-1}

HRMS (ESI) calcd for $C_7H_{13}NNaO_4$ $[M+Na]^+$ 198.0742, found 198.0748.

Methyl *N*-acetyl-*O*-benzyl-L-allothreoninate 31



To a stirred solution of **30** (8.00 g, 45.7 mmol, 1.0 equiv) and benzyl 2,2,2-trichloroacetimidate (12.7 mL, 68.6 mmol, 1.5 equiv) in CH_2Cl_2 (46 mL, 1.0 M) at 0 °C was added dropwise TfOH (4.04 mL, 45.7 mmol, 1.0 equiv) under N_2 atmosphere. After the reaction mixture was stirred for 45 min at 0 °C, the reaction was quenched with saturated aqueous $NaHCO_3$. The resulting mixture was extracted with

$CHCl_3$ (3 x 100 mL). The combined organic phases were washed with H_2O (2 x 50 mL) and brine (2 x 50 mL), dried (Na_2SO_4), filtered and concentrated under reduced pressure. The obtained crude product was purified by silica gel column chromatography (Hexane : AcOEt = 1 : 2) to give **31** (2.46 g, 9.27 mmol, 20% yield) as colorless oil.

Colorless oil; Rf value on TLC 0.45 (Hexane : AcOEt = 1 : 2); $[\alpha]_D^{24}$ +48.1 (*c* 1.0, $CHCl_3$)

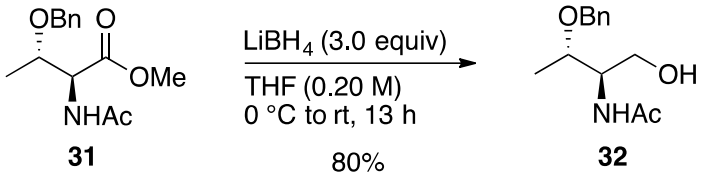
^{1}H-NMR (400 MHz, $CDCl_3$) δ 7.37–7.27 (m, 5H), 6.16 (br d, *J* = 8.4 Hz, 1H, -NH), 4.78 (dd, *J* = 8.4, 3.6 Hz, 1H), 4.59 (d, *J* = 12.0 Hz, 1H), 4.49 (d, *J* = 12.0 Hz, 1H), 3.84 (qd, *J* = 6.4, 3.6 Hz, 1H), 3.76 (s, 3H), 1.96 (s, 3H), 1.27 (d, *J* = 6.4 Hz, 3H)

^{13}C-NMR (100 MHz, $CDCl_3$) δ 170.6, 169.8, 137.9, 128.4, 127.7, 127.7, 74.9, 70.9, 55.5, 52.2, 23.0, 16.3

IR (neat) 3289, 3062, 3031, 2980, 2951, 2871, 1746, 1659, 1537, 1496, 1451, 1436, 1376, 1292, 1265, 1209, 1160, 1108, 1003 cm^{-1}

HRMS (ESI) calcd for $C_{14}H_{19}NNaO_4$ $[M+Na]^+$ 288.1212, found 288.1209.

***N*-((2*R*,3*S*)-3-(Benzyloxy)-1-hydroxybutan-2-yl)acetamide 32**



To a stirred solution of **31** (2.32 g, 8.74 mmol, 1.0 equiv) in THF (44 mL, 0.20 M) at 0 °C was added $LiBH_4$ (571 mg, 26.2 mmol, 3.0 equiv). After the reaction mixture was stirred for 13 h at room temperature under N_2 atmosphere, the reaction was quenched with saturated aqueous NH_4Cl. The resulting mixture was extracted with AcOEt (3 x 100 mL). The combined organic phases were washed with H_2O (2 x 50 mL) and brine (2 x 50 mL), dried over Na_2SO_4, filtered and concentrated under reduced pressure. The obtained crude product was purified by silica gel column chromatography ($CHCl_3$: MeOH = 50 : 1) to give **32** (1.65 g, 6.95 mmol, 80% yield) as white solid.

White solid; Mp 97–99 °C; Rf value on TLC 0.40 ($CHCl_3$: MeOH = 10 : 1); $[\alpha]_D^{24}$ +97.6 (*c* 1.0, $CHCl_3$)

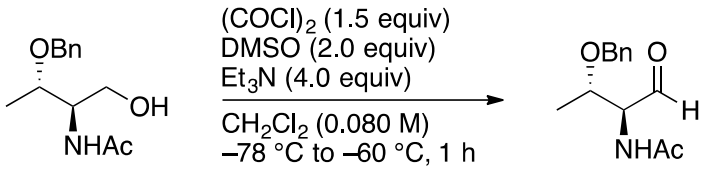
^{1}H-NMR (400 MHz, $CDCl_3$) δ 7.38–7.28 (m, 5H), 6.23 (m, 1H, -N<u>H</u>), 4.65 (d, *J* = 11.6 Hz, 1H), 4.34 (d, *J* = 11.6 Hz, 1H), 4.02 (dt, *J* = 11.6, 2.4 Hz, 1H), 3.87–3.80 (m, 2H), 3.62–3.56 (m, 1H), 3.09–3.06 (m, 1H), 1.92 (s, 3H), 1.29 (d, *J* = 6.4 Hz, 3H)

^{13}C-NMR (100 MHz, $CDCl_3$) δ 170.3, 137.8, 128.5, 127.9, 127.7, 76.7, 71.2, 61.5, 54.0, 23.2, 16.3

IR (KBr) 3285, 3208, 3092, 3033, 3972, 2951, 2930, 2888, 2863, 1638, 1569, 1457, 1430, 1376, 1333, 1298, 1231, 1152, 1101, 1075, 1046, 1009, 964 cm^{-1}

HRMS (ESI) calcd for $C_{13}H_{19}NNaO_3$ $[M+Na]^+$ 260,1263 found 260.1253.

_N_-((2_S_,3_S_)-3-(Benzyloxy)-1-oxobutan-2-yl)acetamide 17c



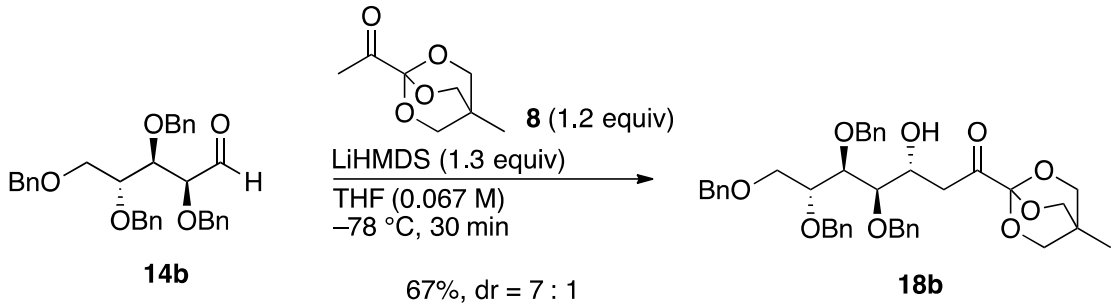
To a stirred solution of $(COCl)_2$ (0.162 mL, 1.89 mmol, 1.5 equiv) in CH_2Cl_2 (5.0 mL) at –78 °C was added dropwise a solution of DMSO (0.179 mL, 2.52 mmol, 2.0 equiv) in CH_2Cl_2 (3.6 mL) under N_2 atmosphere. After the mixture was stirred at –78 °C for 15 min, a solution of alcohol **32** (300 mg, 1.26 mmol, 1.0 equiv) in CH_2Cl_2 (3.6 mL) was added dropwise. After the resulting mixture was stirred for 30 min at –78 °C, a solution of Et_3N (0.702 mL, 5.04 mmol, 4.0 equiv) in CH_2Cl_2 (3.6 mL) was added dropwise at –78 °C, and then the mixture was warmed to –60 °C. After the reaction mixture was stirred for 1 h at –60 °C, the reaction was quenched with 20% aqueous $KHSO_4$ (10 mL). The resulting mixture was allowed to gently warm up to room temperature, and extracted with $CHCl_3$ (3 x 30 mL). The combined organic phases were washed with H_2O (2 x 20 mL) and brine (2 x 20 mL), dried over Na_2SO_4, filtered and concentrated under reduced pressure. The residue was passed through a short column of silica gel (Hexane : AcOEt = 1 : 1). The obtained product **17c** (295 mg, pale yellow oil) was used for the next reaction without further purification.[c]

[c] *N*-Acetylaldehydes **17a** and **17c** were slightly unstable on silica gel.

Synthesis of the aldol adducts 18a–18f and 19a–19d

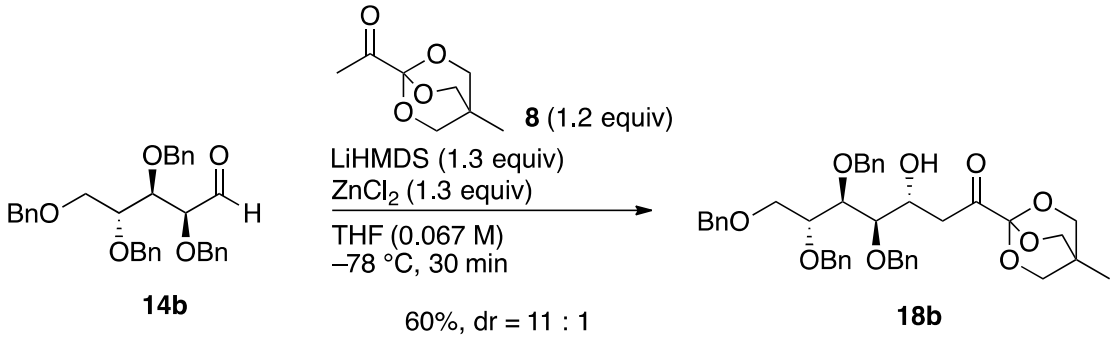
Representative procedure A using the Li enolate

(3*R*,4*R*,5*R*,6*R*)-4,5,6,7-tetrakis(benzyloxy)-3-hydroxy-1-(4-methyl-2,6,7-trioxabicyclo[2.2.2]octan-1-yl)heptan-1-one 18b



To a stirred solution of LiHMDS (1.0 M in THF solution, 0.255 mL, 0.255 mmol, 1.3 equiv) in THF (2.0 mL) at –78 °C was added dropwise a solution of pyruvic acid OBO orthoester **8** (40.5 mg, 0.235 mmol, 1.2 equiv) in THF (0.49 mL) under N_2 atmosphere. After 30 min at –78 °C, a solution of aldehyde **14b** (100 mg, 0.196 mmol, 1.0 equiv) in THF (0.49 mL) was added, and the resulting mixture was furthermore stirred for 30 min at –78 °C. The reaction was quenched with phosphate buffer (pH 6.86, 2.0 mL), and the mixture was allowed to gently warm up to room temperature. The resulting mixture was extracted with AcOEt (3 x 20 mL). The combined organic phases were washed with H_2O (2 x 50 mL) and brine (2 x 50 mL), dried over Na_2SO_4, filtered and concentrated under reduced pressure. The obtained crude product was purified by silica gel column chromatography (Hexane : AcOEt = 2 : 1) to give the aldol adduct **18b** (89.8 mg, 0.132 mmol, 67% yield, *anti* : *syn* = 7 : 1) as colorless oil.

Representative procedure B using the Zn enolate



To a stirred solution of LiHMDS (1.0 M in THF solution, 0.255 mL, 0.255 mmol, 1.3 equiv) in THF (2.0 mL) at –78 °C was added dropwise a solution of ketone **8** (40.5 mg, 0.235 mmol, 1.2 equiv) in THF (0.49 mL) under N_2 atmosphere. After 30 min at –78 °C, a solution of $ZnCl_2$ (1.0 M in Et_2O, 0.255 mL, 0.255 mmol, 1.3 equiv) was added. After 1 min at –78 °C, a solution of **14b** (100 mg, 0.196 mmol, 1.0 equiv) in THF (0.49 mL) was added, and the resulting mixture was furthermore stirred for 30 min at –78 °C. The reaction was quenched with phosphate buffer (pH 6.86, 2.0 mL), and the mixture was allowed to gently warm up to room temperature. The resulting mixture was extracted with AcOEt (3 x 20 mL). The combined organic phases were washed with H_2O (2 x 50 mL) and brine (2 x 50 mL), dried over Na_2SO_4, filtered and concentrated under reduced pressure. The obtained crude product was purified by silica gel column chromatography (Hexane : AcOEt = 2 : 1) to give the aldol adduct **18b** (80.4 mg, 0.118 mmol, 60% yield, *anti* : *syn* = 11 : 1) as colorless oil.

The following physical data were measured as an 11 : 1 mixture of diastereomers. Colorless oil; Rf value on TLC 0.48 (Hexane : AcOEt = 1 : 1); $[\alpha]_D^{26}$ +3.77 (*c* 1.0, $CHCl_3$)

For the major isomer : ^{1}H-NMR (400 MHz, $CDCl_3$) δ 7.33–7.26 (m, 20H), 4.69 (d, *J* = 11.6 Hz, 1H), 4.67 (s, 2H), 4.64 (d, *J* = 11.6 Hz, 1H), 4.57 (d, *J* = 11.6 Hz, 1H), 4.54 (d, *J* = 12.0 Hz, 1H), 4.50 (d, *J* = 12.0 Hz, 1H), 4.46 (d, *J* = 11.6 Hz, 1H) 4.34–4.28 (m, 1H), 3.99–3.83 (m, 3H), 3.94 (s, 6H), 3.77–3.71 (m, 2H), 3.09 (dd, *J* = 18.4, 2.8 Hz, 1H), 2.92–2.85 (m, 2H), 0.83 (s, 3H)

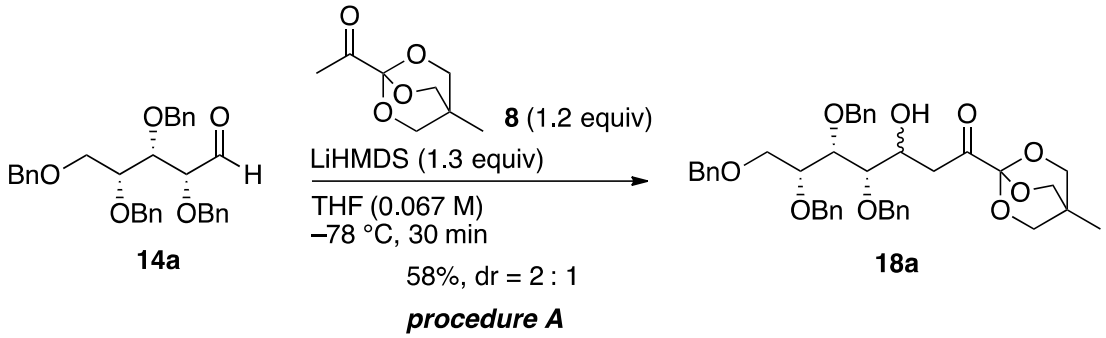
^{13}C-NMR (100 MHz, $CDCl_3$) δ 198.7, 138.5, 138.4, 138.2, 138.2, 128.3, 128.3, 128.3, 128.2, 128.2, 127.9, 127.7, 127.6, 127.6, 127.5, 127.4, 127.4, 103.2, 81.0, 78.7, 78.4,

74.1, 73.8, 73.3, 73.0, 71.8, 69.2, 67.7, 40.7, 30.8, 14.1

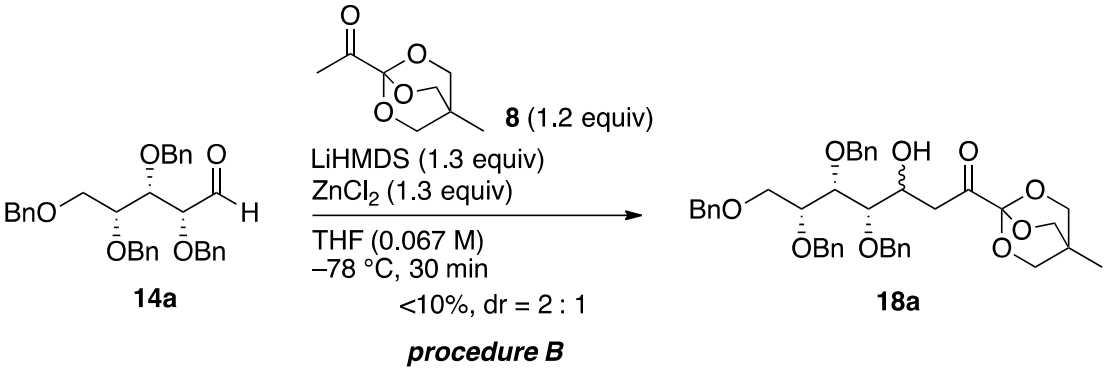
IR (neat) 3481, 3083, 3062, 3030, 2931, 2881, 1744, 1496, 1454, 1397, 1350, 1256, 1208, 1081, 995 cm^{-1}

HRMS (ESI) calcd for $C_{41}H_{46}NaO_9$ $[M+Na]^+$ 705.3040, found 705.3019.

(4*S*,5*S*,6*R*)-4,5,6,7-Tetrakis(benzyloxy)-3-hydroxy-1-(4-methyl-2,6,7-trioxabicyclo[2.2.2]octan-1-yl)heptan-1-one 18a



The aldol reaction between aldehyde **14a** (100 mg, 0.196 mmol) and ketone **8** was carried out according to the procedure A to give the aldol adduct **18a** (77.0 mg, 0.113 mmol, 58% yield, dr = 2 : 1).



The aldol reaction between aldehyde **14a** (100 mg, 0.196 mmol) and ketone **8** was carried out according to the procedure B to give the aldol adduct **18a** (<10% yield, dr = 2 : 1).

The following physical data were measured as a 1 : 1 mixture of diastereomers. Colorless oil; Rf value on TLC 0.47 (Hexane : AcOEt = 1 : 1); $[\alpha]_D^{27}$ –11.8 (*c* 0.5, $CHCl_3$)

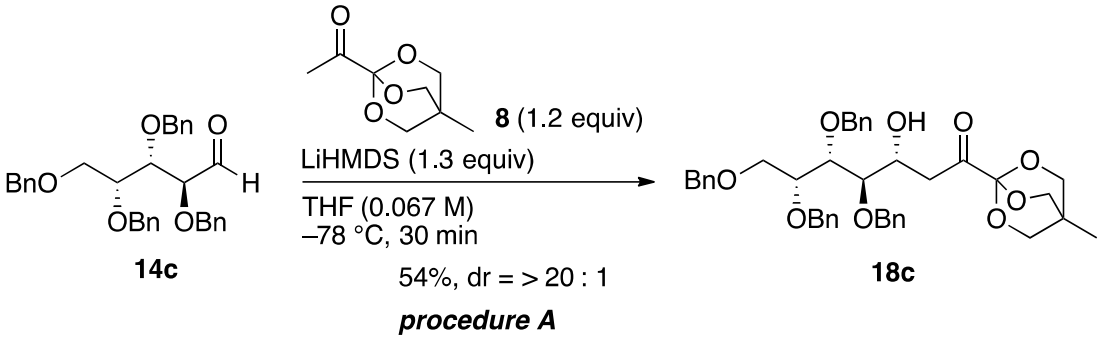
^{1}H-NMR (400 MHz, $CDCl_3$) δ 7.36–7.23 (m, 20H x 2), 4.79 (d, *J* = 11.2 Hz, 1H), 4.74 (d, *J* = 12.0 Hz, 1H), 4.73 (d, *J* = 11.2 Hz, 1H), 4.71 (d, *J* = 12.0 Hz, 1H), 4.65 (d, *J* = 12.0 Hz, 1H), 4.66 (s, 2H), 4.62 (d, *J* = 12.0 Hz, 1H), 4.61–4.54 (m, 4H), 4.45 (d, *J* = 12.0 Hz, 1H), 4.41 (d, *J* = 12.0 Hz, 1H), 4.41 (s, 2H), 4.34–4.26 (m, 1H), 4.09–4.02 (m, 1H), 3.96 (s, 6H x 2), 3.93 (dd, *J* = 7.6, 3.6 Hz, 1H), 3.88 (ddd, *J* = 5.2, 5.2, 4.0 Hz, 1H), 3.85–3.79 (m, 2H), 3.70–3.59 (m, 5H), 3.51 (dd, *J* = 10.0, 5.2 Hz, 1H), 3.04 (dd, *J* = 18.0, 3.2 Hz, 1H), 3.03 (br d, *J* = 4.4 Hz, 1 H, -O<u>H</u>), 2.94 (dd, *J* = 18.0, 8.0 Hz, 1H), 2.92 (dd, *J* = 18.0, 8.8 Hz, 1H), 2.71 (br s, 1H, -O<u>H</u>), 2.68 (dd, *J* = 18.0, 4.8 Hz, 1H), 0.84 (s, 3H), 0.84 (s, 3H)

^{13}C-NMR (100 MHz, $CDCl_3$) δ 198.2, 197.8, 138.4, 138.3, 138.3, 138.2, 138.2, 138.2, 138.2, 138.0, 128.5, 128.4, 128.3, 128.3, 128.3, 128.3, 128.2, 128.2, 128.2, 128.2, 128.1, 127.8, 127.7, 127.7, 127.6, 127.6, 127.6, 127.5, 127.5, 127.5, 103.3, 103.2, 80.3, 80.0, 79.0, 78.7, 78.2, 77.2, 77.1, 74.8, 74.6, 74.3, 73.4, 73.2, 73.2, 73.1, 73.0, 73.0, 72.9, 70.2, 69.8, 68.0, 66.5, 41.1, 40.6, 30.8, 14.2

IR (neat) 3480, 3086, 3062, 3030, 2931, 2881, 1746, 1496, 1454, 1398, 1350, 1207, 1080, 1058, 1028, 993 cm^{-1}

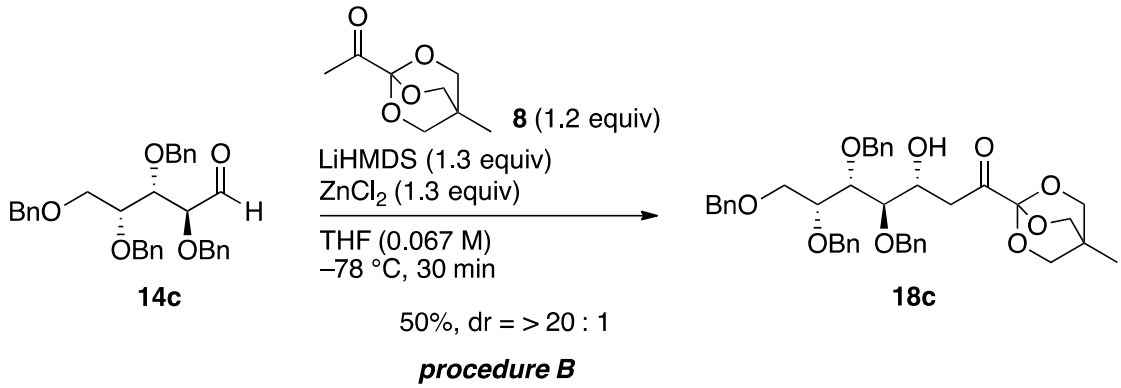
HRMS (ESI) calcd for $C_{41}H_{46}NaO_9$ $[M+Na]^+$ 705.3040, found 705.3067.

(3*R*,4*R*,5*S*,6*R*)-4,5,6,7-Tetrakis(benzyloxy)-3-hydroxy-1-(4-methyl-2,6,7-trioxabicyclo[2.2.2]octan-1-yl)heptan-1-one 18c



The aldol reaction between aldehyde **14c** (100 mg, 0.196 mmol) and ketone **8** was carried out according to procedure A to give the aldol adduct **18c** (71.5 mg, 0.105 mmol,

54% yield, *anti* : *syn* = > 20 : 1).



The aldol reaction between aldehyde **14c** (100 mg, 0.196 mmol) and ketone **8** was carried out according to the procedure B to give the aldol adduct **18c** (67.3 mg, 0.0986 mmol, 50% yield, *anti* : *syn* = > 20 : 1).

Colorless oil; Rf value on TLC 0.50 (Hexane : AcOEt = 1 : 1); $[\alpha]_D^{23}$ +4.30 (*c* 1.0, $CHCl_3$)

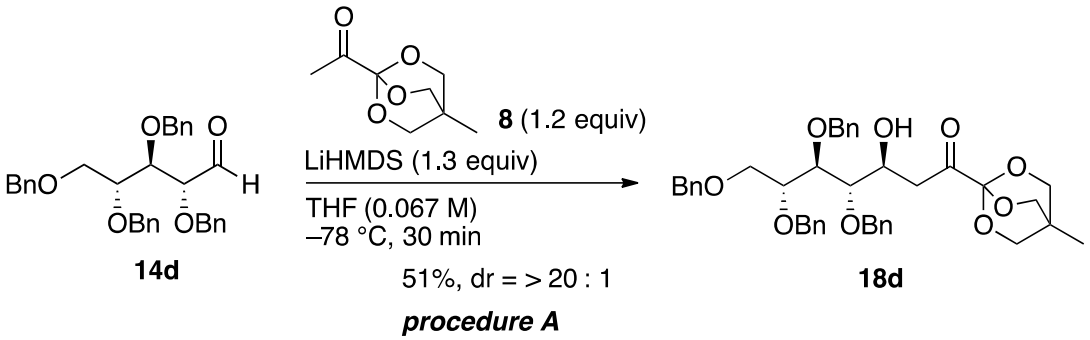
^{1}H-NMR (400 MHz, $CDCl_3$) δ 7.28–7.17 (m, 20H), 4.64 (d, *J* = 11.6 Hz, 1H), 4.62 (d, *J* = 11.6 Hz, 1H), 4.61–4.54 (m, 3H), 4.51 (d, *J* = 11.6 Hz, 1H), 4.45–4.39 (m, 1H), 4.44 (s, 2H), 3.91–3.87 (m, 2H), 3.90 (s, 6H), 3.69–3.60 (m, 3H), 3.01 (dd, *J* = 18.4, 2.8 Hz, 1H), 2.90 (dd, *J* = 18.4, 9.2 Hz, 1H), 2.89 (d, *J* = 4.4 Hz, 1H, -OH), 0.78 (s, 3H)

^{13}C-NMR (100 MHz, $CDCl_3$) δ 198.6, 138.6, 138.5, 138.4, 138.0, 128.3, 128.2, 128.2, 128.0, 127.9, 127.8, 127.6, 127.6, 127.4, 127.4, 103.3, 81.6, 79.4, 78.9, 74.2, 73.4, 73.1, 73.0, 73.0, 70.1, 67.4, 40.6, 30.8, 14.1

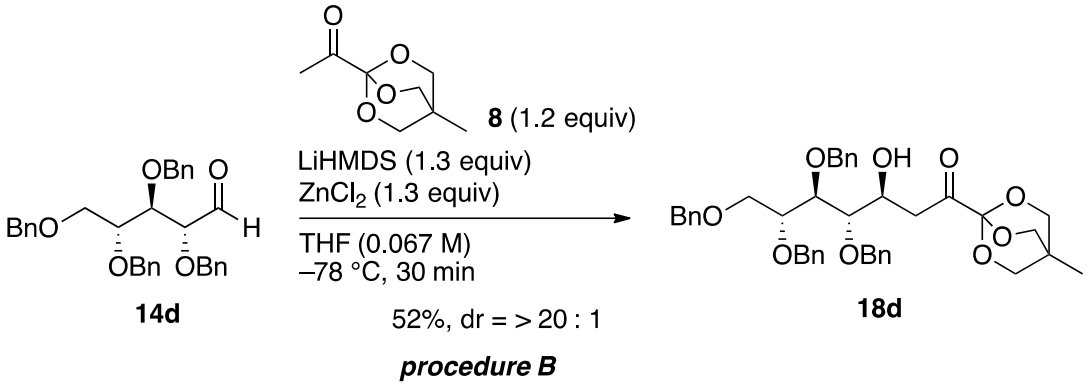
IR (neat) 3511, 3062, 3030, 2927, 2881, 1745, 1496, 1454, 1397, 1350, 1207, 1080, 1051, 1028, 993 cm^{-1}

HRMS (ESI) calcd for $C_{41}H_{46}NaO_9$ $[M+Na]^+$ 705.3040, found 705.3028.

(3*S*,4*S*,5*R*,6*R*)-4,5,6,7-Tetrakis(benzyloxy)-3-hydroxy-1-(4-methyl-2,6,7-trioxabicyclo[2.2.2]octan-1-yl)heptan-1-one 18d



The aldol reaction between **14d** (100 mg, 0.196 mmol) and ketone **8** was carried out according to the procedure A to give the aldol adduct **18d** (67.7 mg, 0.0991 mmol, 51% yield, *anti* : *syn* = > 20 : 1).



The aldol reaction between **14d** (100 mg, 0.196 mmol) and ketone **8** was carried out according to the procedure B to give the aldol adduct **18d** (69.8 mg, 0.102 mmol, 52% yield, *anti* : *syn* = > 20 : 1).

Colorless oil; Rf value on TLC 0.47 (Hexane : AcOEt = 1 : 1); $[\alpha]_D^{27}$ –9.12 (*c* 1.0, $CHCl_3$)

^{1}H-NMR (400 MHz, $CDCl_3$) δ 7.32–7.20 (m, 20H), 4.67 (d, *J* = 11.6 Hz, 1H), 4.64–4.57 (m, 5H), 4.48–4.38 (m, 3H), 3.96–3.89 (m, 1H), 3.91 (s, 6H), 3.87 (dd, *J* = 5.2, 4.8 Hz, 1H), 3.73–3.69 (m, 2H), 3.64 (dd, *J* = 10.4, 5.6 Hz, 1H), 2.97 (dd, *J* = 18.4, 3.6 Hz,

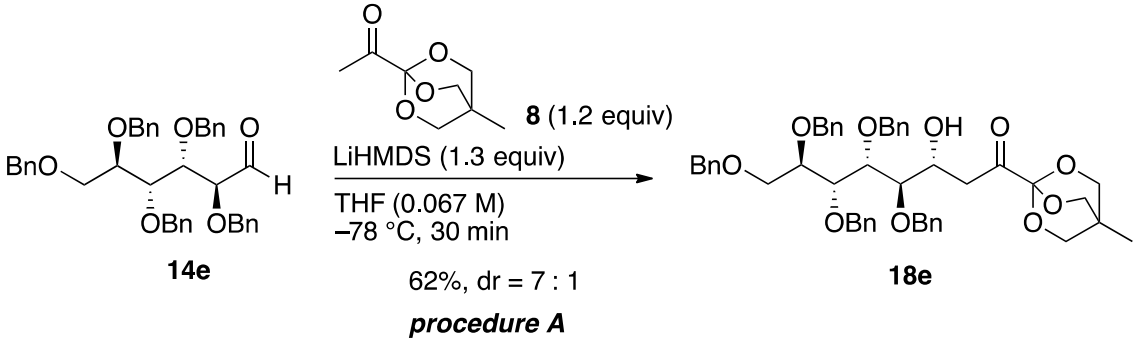
1H), 2.89 (dd, *J* = 18.4, 8.8 Hz, 1H), 2.87 (br d, *J* = 4.4 Hz, 1H, -OH), 0.79 (s, 3H)

^{13}C-NMR (100 MHz, $CDCl_3$) δ 198.6, 138.4, 138.4, 138.4, 138.2, 128.3, 128.2, 128.2, 128.0, 128.0, 127.8, 127.6, 127.5, 127.4, 127.4, 103.2, 81.3, 78.7, 78.5, 73.5, 73.3, 73.3, 73.0, 72.5, 70.0, 67.6, 40.4, 30.8, 14.1

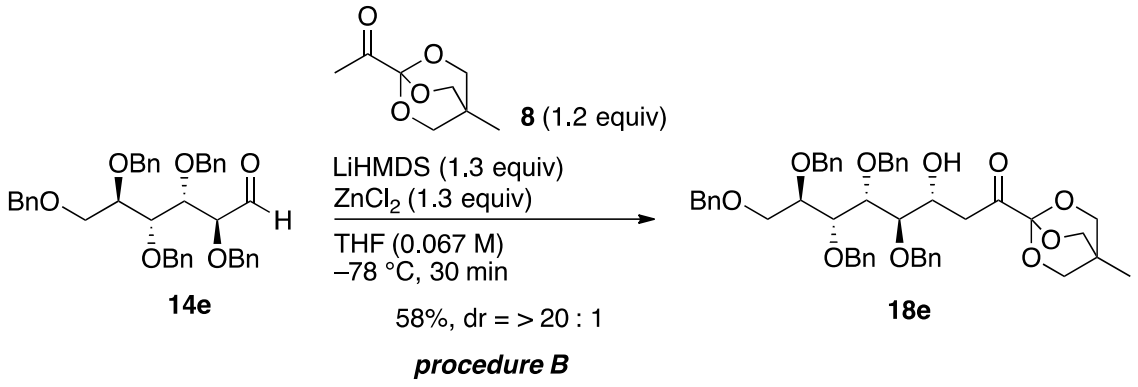
IR (neat) 3419, 3083, 3062, 3030, 2927, 2881, 1747, 1496, 1455, 1397, 1204, 1193, 1080, 1056, 1030, 993 cm^{-1}

HRMS (ESI) calcd for $C_{41}H_{46}NaO_9$ $[M+Na]^+$ 705.3040, found 705.3009.

(3*R*,4*R*,5*R*,6*R*,7*R*)-4,5,6,7,8-pentakis(benzyloxy)-3-hydroxy-1-(4-methyl-2,6,7-trioxabicyclo[2.2.2]octan-1-yl)octan-1-one 18e



The aldol reaction between **14e** (100 mg, 0.159 mmol) and ketone **8** was carried out according to the procedure A to give the aldol adduct **18e** (79.2 mg, 0.0986 mmol, 62% yield, *anti* : *syn* = 7 : 1).



The aldol reaction between **14e** (1.48 g, 2.35 mmol) and ketone **8** was carried out according to the procedure B to give the aldol adduct **18e** (1.09 g, 1.36 mmol, 58% yield, *anti* : *syn* = > 20 : 1).

Colorless oil; Rf value on TLC 0.54 (Hexane : AcOEt = 1 : 1); $[\alpha]_D^{27}$ +13.4 (*c* 1.0, $CHCl_3$)

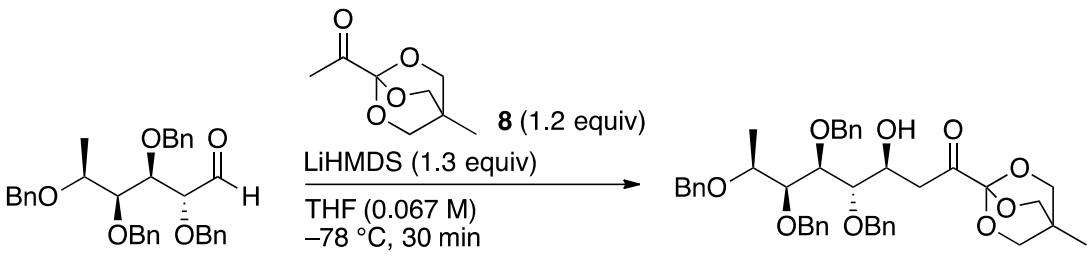
^{1}H-NMR (400 MHz, $CDCl_3$) δ 7.34–7.21 (m, 25H), 4.72–4.61 (m, 5H), 4.56 (d, *J* = 12.0 Hz, 1H), 4.54–4.49 (m, 3H), 4.49–4.43 (m, 1H), 4.47 (d, *J* = 12.0 Hz, 1H), 4.08 (dd, *J* = 5.2, 4.4 Hz, 1H), 3.98 (dd, *J* = 5.2, 3.6 Hz, 1H), 3.95 (s, 6H), 3.91–3.84 (m, 2H), 3.73–3.69 (m, 2H), 3.15 (dd, *J* = 18.4, 2.4 Hz, 1H), 2.94 (dd, *J* = 18.4, 9.6 Hz, 1H), 2.91 (d, *J* = 4.4 Hz, 1H, -O<u>H</u>), 0.83 (s, 3H)

^{13}C-NMR (100 MHz, $CDCl_3$) δ 198.9, 138.9, 138.7, 138.6, 138.5, 138.2, 128.3, 128.2, 128.2, 128.1, 128.1, 127.8, 127.8, 127.8, 127.7, 127.6, 127.5, 127.4, 127.3, 127.3, 127.3, 103.3, 82.0, 79.7, 79.6, 78.8, 74.4, 74.3, 73.3, 73.0, 72.8, 71.7, 69.5, 67.3, 40.7, 30.8, 14.1

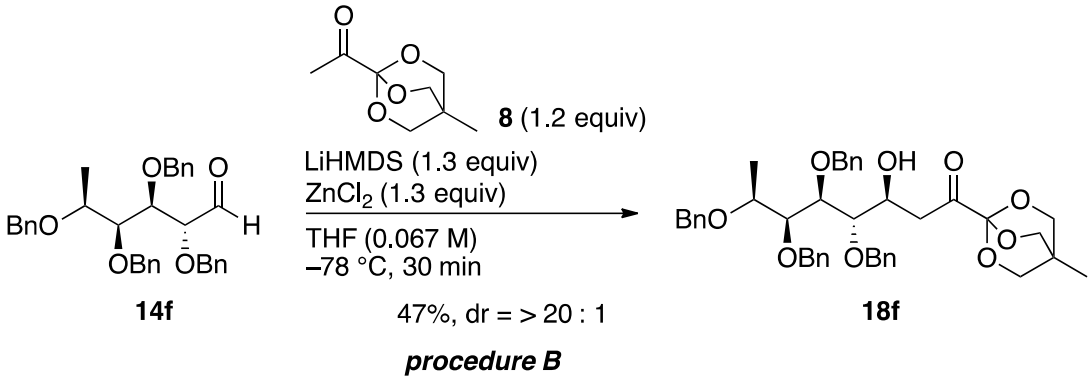
IR (neat) 3500, 3086, 3062, 3030, 2931, 2881, 1747, 1496, 1454, 1397, 1349, 1207, 1081, 1026, 992 cm^{-1}

HRMS (ESI) calcd for $C_{49}H_{54}NaO_{10}$ $[M+Na]^+$ 825.3615, found 825.3622.

(3*S*,4*S*,5*S*,6*S*,7*S*)-4,5,6,7-Tetrakis(benzyloxy)-3-hydroxy-1-(4-methyl-2,6,7-trioxabicyclo[2.2.2]octan-1-yl)octan-1-one 18f



The aldol reaction between **14f** (100 mg, 0.191 mmol) and ketone **8** was carried out according to the procedure A to give the **18f** (67.6 mg, 0.0970 mmol, 51% yield, *anti* : *syn* = 11 : 1).



The aldol reaction between **14f** (100 mg, 0.191 mmol) and ketone **8** was carried out according to the procedure B to give the aldol adduct **18f** (63.1 mg, 0.0906 mmol, 47% yield, *anti* : *syn* = > 20 : 1).

Colorless oil; Rf value on TLC 0.47 (Hexane : AcOEt = 1 : 1); $[\alpha]_D^{27}$ –21.0 (*c* 0.25, $CHCl_3$)

^{1}H-NMR (400 MHz, $CDCl_3$) δ 7.38–7.21 (m, 20H), 4.74 (d, *J* = 11.6 Hz, 1H), 4.69 (d, *J* = 11.6 Hz, 1H), 4.67 (s, 2H), 4.66 (d, *J* = 11.6 Hz, 1H), 4.57 (d, *J* = 11.6 Hz, 1H), 4.55 (d, *J* = 11.6 Hz, 1H), 4.48–4.43 (m, 1H), 4.40 (d, *J* = 11.6 Hz, 1H), 3.96 (s, 6H), 3.89 (dd, *J* = 5.6, 4.4 Hz, 1H), 3.85 (dd, *J* = 5.6, 4.0 Hz, 1H), 3.74 (qd, *J* = 6.4, 4.4 Hz, 1H), 3.65 (dd, *J* = 5.2, 4.0 Hz, 1H), 3.16 (dd, *J* = 18.4, 2.4 Hz, 1H), 2.96 (dd, *J* = 18.4, 9.2 Hz, 1H), 2.93 (d, *J* = 4.4 Hz, 1H, -O<u>H</u>), 1.28 (d, *J* = 6.4 Hz, 3H), 0.84 (s, 3H)

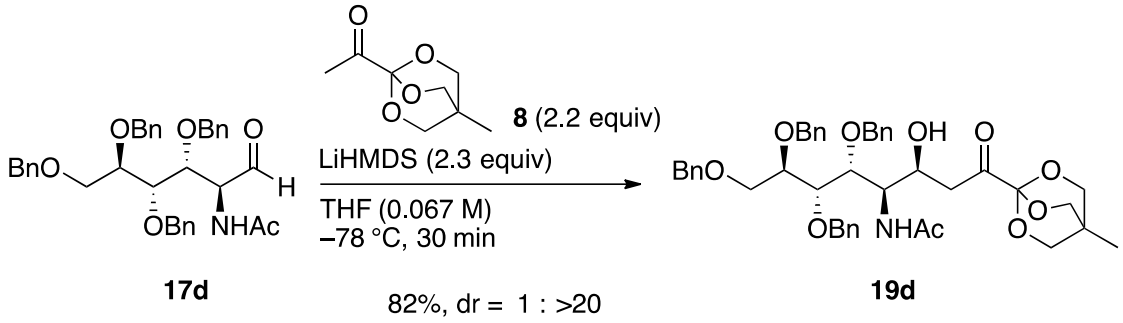
^{13}C-NMR (100 MHz, $CDCl_3$) δ 198.9, 139.0, 138.7, 138.6, 138.4, 128.3, 128.3, 128.2, 127.9, 127.8, 127.7, 127.6, 127.5, 127.4, 127.3, 127.3, 103.3, 82.0, 81.6, 79.8, 75.6, 74.3, 73.1, 73.0, 70.4, 67.5, 40.6, 30.8, 15.4, 14.1

IR (neat) 3511, 3086, 3063, 3030, 2964, 2933, 2881, 1746, 1496, 1454, 1397, 1349, 1208, 1198, 1081, 1026, 993 cm^{-1}

HRMS (ESI) calcd for $C_{42}H_{48}NaO_9$ $[M+Na]^+$ 719.3196, found 719.3176.

Representative procedure C using the Li enolate (for N-acetylaminoaldehydes)

N-((3S,4R,5R,6S,7R)-5,6,7,8-tetrakis(benzyloxy)-3-hydroxy-1-(4-methyl-2,6,7-trioxabicyclo[2.2.2]octan-1-yl)-1-oxooctan-4-yl)acetamide 19d



To a stirred solution of LiHMDS (1.0 M in THF solution, 1.69 mL, 1.69 mmol, 2.3 equiv) in THF (7.4 mL) at –78 °C was added dropwise a solution of ketone **8** (279 mg, 1.62 mmol, 2.2 equiv) in THF (1.8 mL) under N_2 atmosphere. After 30 min at –78 °C, a solution of **17d** (428 mg, 0.736 mmol, 1.0 equiv) in THF (1.8 mL) was added, and the resulting mixture was furthermore stirred for 30 min at –78 °C. The reaction was quenched with phosphate buffer (pH 6.86, 10 mL), and the mixture was allowed to gently warm up to room temperature. The resulting mixture was extracted with AcOEt (3 x 50 mL). The combined organic phases were washed with H_2O (2 x 100 mL) and brine (2 x 100 mL), dried over Na_2SO_4, filtered and concentrated under reduced pressure. The obtained crude product was purified by silica gel column chromatography (Hexane : AcOEt = 1 : 2) to give **19d** (452 mg, 0.600 mmol, 82% yield, *anti* : *syn* = 1 : > 20) as colorless oil.

Colorless oil; Rf value on TLC 0.30 (Hexane : AcOEt = 1 : 2); $[\alpha]_D^{27}$ +7.35 (*c* 0.25, $CHCl_3$)

^{1}H-NMR (400 MHz, $CDCl_3$) δ 7.34–7.22 (m, 20H), 5.99 (d, *J* = 9.2 Hz, 1H, -NH), 4.73 (d, *J* = 11.6 Hz, 1H), 4.73 (d, *J* = 10.4 Hz, 1H), 4.65 (d, *J* = 10.4 Hz, 1H), 4.63 (d, *J* = 11.6 Hz, 1H), 4.56 (d, *J* = 11.6 Hz, 1H), 4.54 (d, *J* = 12.0 Hz, 1H), 4.52 (d, *J* = 11.6 Hz, 1H), 4.51 (d, *J* = 12.0 Hz, 1H), 4.49–4.46 (m, 1H), 4.10 (ddd, *J* = 9.2, 6.0, 1.2 Hz, 1H), 3.96 (s, 6H), 3.91–3.82 (m, 4H), 3.72 (dd, *J* = 10.8, 4.8 Hz, 1H), 3.34 (br s, 1H, -OH),

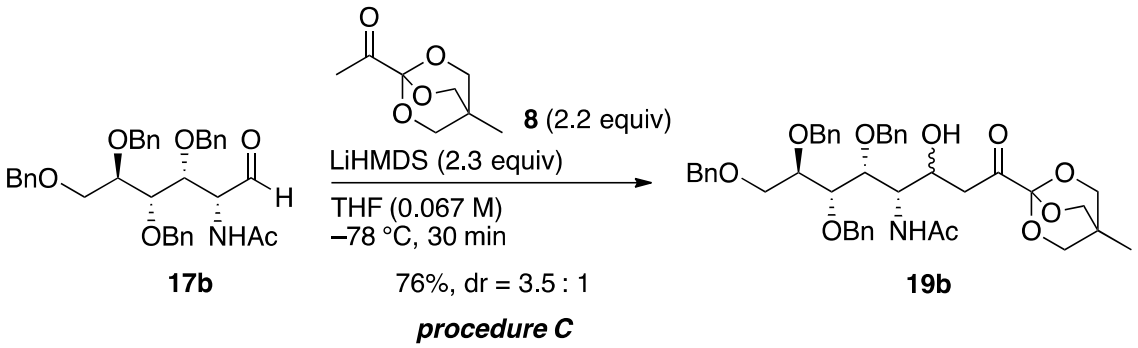
2.78 (dd, *J* = 18.4, 8.8 Hz, 1H), 2.70 (dd, *J* = 18.4, 3.6 Hz, 1H), 1.74 (s, 3H), 0.83 (s, 3H)

^{13}C-NMR (100 MHz, $CDCl_3$) δ 198.1, 170.3, 138.5, 138.3, 138.2, 138.0, 128.4, 128.3, 128.3, 128.3, 128.3, 128.1, 127.9, 127.8, 127.7, 127.6, 127.5, 127.5, 103.2, 79.1, 79.0, 79.0, 74.2, 73.3, 73.0, 72.2, 69.1, 65.7, 53.0, 41.6, 30.8, 23.2, 14.1

IR (neat) 3401, 3086, 3064, 3030, 2922, 2881, 1746, 1659, 1496, 1454, 1371, 1209, 1082, 1032, 998 cm^{-1}

HRMS (ESI) calcd for $C_{44}H_{51}NNaO_{10}$ $[M+Na]^+$ 776.3411, found 776.3394.

_N_-((4_S_,5_R_,6_S_,7_R_)-5,6,7,8-tetrakis(benzyloxy)-3-hydroxy-1-(4-methyl-2,6,7-trioxabicyclo[2.2.2]octan-1-yl)-1-oxooctan-4-yl)acetamide 19b



The aldol reaction between aldehyde **17b** (480 mg, 0.825 mmol) and ketone **8** was carried out according to the procedure C to give the aldol adduct **19b** (475 mg, 0.630 mmol, 76% yield, dr = 3.5 : 1).

The following physical data were measured for the isolated major isomer.

Colorless oil; Rf value on TLC 0.37 (Hexane : AcOEt = 1 : 2); $[\alpha]_D^{26}$ –15.6 (*c* 1.0, $CHCl_3$)

^{1}H-NMR (400 MHz, $CDCl_3$) δ 7.37–7.23 (m, 20H), 5.86 (d, *J* = 9.6 Hz, 1H, -NH), 4.81 (d, *J* = 11.2 Hz, 2H), 4.67 (d, *J* = 11.2 Hz, 1H), 4.66 (d, *J* = 12.0 Hz, 1H), 4.59 (d, *J* = 11.2 Hz, 1H), 4.57 (d, *J* = 12.0 Hz, 1H), 4.56 (d, *J* = 12.0 Hz, 1H), 4.52 (d, *J* = 12.0 Hz, 1H), 4.20 (dd, *J* = 8.0, 0.8 Hz, 1H), 4.09–3.96 (m, 2H), 3.96 (s, 6H), 3.91 (ddd, *J* = 5.6, 4.8, 2.8 Hz, 1H), 3.85 (dd, *J* = 10.0, 4.8 Hz, 1H), 3.79 (dd, *J* = 8.0, 2.8 Hz, 1H), 3.72 (dd, *J* = 10.0, 5.6 Hz, 1H), 2.85 (dd, *J* = 18.8, 7.2 Hz, 1H), 2.80 (dd, *J* = 18.8, 4.8 Hz,

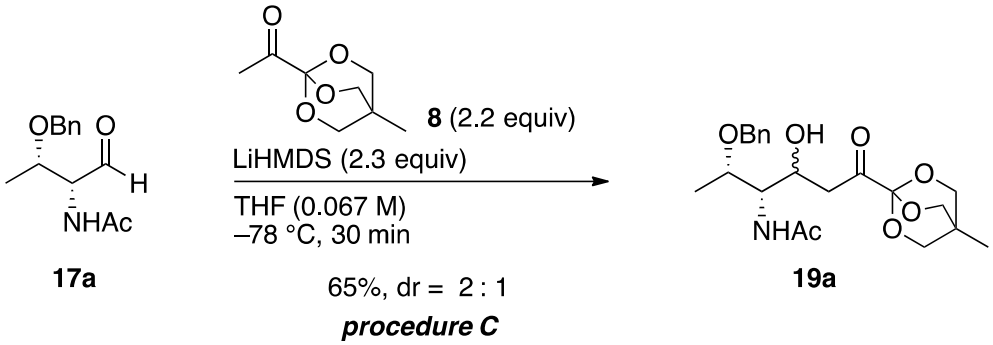
1H), 2.38 (d, *J* = 5.6 Hz, 1H, -OH), 1.88 (s, 3H), 0.84 (s, 3H)

^{13}C-NMR (100 MHz, $CDCl_3$) δ 198.5, 169.8, 138.8, 138.8, 138.3, 138.3, 128.5, 128.4, 128.3, 128.2, 128.2, 127.9, 127.7, 127.7, 127.6, 127.5, 127.3, 127.3, 103.2, 81.5, 79.1, 77.2, 76.2, 75.2, 74.6, 73.1, 73.0, 72.1, 69.4, 67.3, 53.7, 41.7, 30.8, 23.3, 14.1

IR (neat) 3420, 3351, 3086, 3062, 3030, 2936, 2881, 1745, 1672, 1497, 1454, 1370, 1083, 1053, 1030, 996 cm^{-1}

HRMS (ESI) calcd for $C_{44}H_{51}NNaO_{10}$ $[M+Na]^+$ 776.3411, found 776.3394.

_N_-((2_S_,3_S_,4_S_)-2-(benzyloxy)-4-hydroxy-6-(4-methyl-2,6,7-trioxabicyclo[2.2.2]octan-1-yl)-6-oxohexan-3-yl)acetamide 19a



The aldol reaction between aldehyde **17a** (70.0 mg, 0.298 mmol) and ketone **8** was carried out according to the procedure C to give the aldol adduct **19a** (79.1 mg, 0.194 mmol, 65% yield, dr = 2 : 1) except for the purification conditions (silica gel column chromatography, Hexane : AcOEt = 1 : 5).

The following physical data were measured as a 2 : 1 mixture of diastereomers.

Colorless oil; Rf value on TLC 0.36 (AcOEt); $[\alpha]_D^{24}$ +24.8 (*c* 1.0, $CHCl_3$)

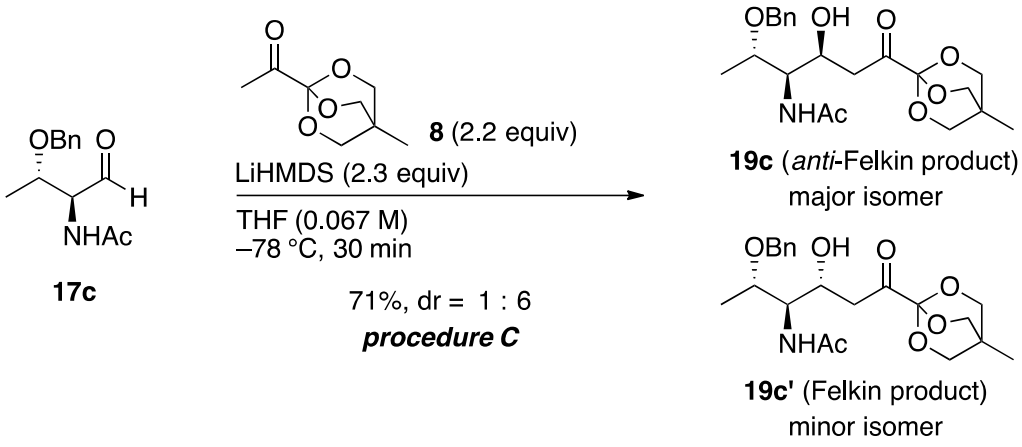
^{1}H-NMR (400 MHz, $CDCl_3$) δ 7.39–7.27 (m, 5H x 2), 6.03 (br d, *J* = 9.6 Hz, 1H, -NH), 5.82 (br d, *J* = 10.0 Hz, 1H, -NH), 4.63 (d, *J* = 11.2 Hz, 1H), 4.62 (d, *J* = 11.2 Hz, 1H), 4.46–4.41 (m, 1H), 4.43 (d, *J* = 11.2 Hz, 1H), 4.39 (d, *J* = 11.2 Hz, 1H), 4.16–4.08 (m, 1H), 3.98–3.83 (m, 3H), 3.97 (s, 9H), 3.44 (d, *J* = 1.6 Hz, 1H, -OH), 3.78–3.72 (m, 2H), 3.18 (br d, *J* = 1.6, 1H, -OH), 2.92 (dd, *J* = 18.4, 8.8 Hz, 1H), 2.88–2.81 (m, 2H), 2.69 (dd, *J* = 18.4, 3.6 Hz, 1H), 2.05 (s, 3H), 2.01 (s, 3H), 1.23 (d, *J* = 6.0 Hz, 3H), 1.16 (d, *J* = 6.4 Hz, 3H), 0.85 (s, 3H) , 0.84 (s, 3H)

^{13}C-NMR (100 MHz, $CDCl_3$) δ 198.6, 197.1, 170.6, 170.5, 138.0, 137.5, 128.6, 128.5, 128.1, 128.0, 127.9, 103.2, 103.2, 77.2, 77.1, 73.0, 73.0, 71.8, 71.1, 70.6, 68.4, 67.2, 56.8, 55.6, 41.7, 41.3, 30.8, 23.3. 23.3, 16.3, 16.1, 14.1, 14.1

IR (neat) 3352, 2969, 2937, 2883, 1747, 1658, 1530, 1472, 1455, 1398, 1375, 1349, 1305, 1263, 1194, 1158, 1082, 1050, 1033, 994 cm^{-1}

HRMS (ESI) calcd for $C_{21}H_{29}NNaO_7$ $[M+Na]^+$ 430.1842, found 430.1832.

_N_-((2_S_,3_R_,4_S_)-2-(Benzyloxy)-4-hydroxy-6-(4-methyl-2,6,7-trioxabicyclo[2.2.2]octan-1-yl)-6-oxohexan-3-yl)acetamide 19c



The aldol reaction between **17c** (210 mg, 0.893 mmol) and ketone **8** was carried out according to the procedure C to give the aldol adduct **19c** (260 mg, 0.638 mmol, 71% yield, *anti* : *syn* = 1 : 6) except for the purification conditions (silica gel column chromatography, hexane : AcOEt = 1 : 5).

The following physical data were measured for the isolated major isomer **19c**.

Colorless oil; Rf value on TLC 0.38 (AcOEt); $[\alpha]_D^{23}$ +23.4 (*c* 1.0, $CHCl_3$)

^{1}H-NMR (400 MHz, $CDCl_3$) δ 7.36–7.25 (m, 5H), 6.07 (br d, *J* = 8.8 Hz, 1H, -N<u>H</u>), 4.71–4.67 (m, 1H), 4.65 (d, *J* = 11.6 Hz, 1H), 4.35 (d, *J* = 11.6 Hz, 1H), 3.97 (s, 6H), 3.78–3.72 (m, 2H), 3.18 (br d, *J* = 1.6, 1H, -O<u>H</u>), 2.85 (dd, *J* = 18.4, 9.2 Hz, 1H), 2.69 (dd, *J* = 18.4, 3.6 Hz, 1H), 1.95 (s, 3H), 1.29 (d, *J* = 6.0 Hz, 3H), 0.84 (s, 3H)

^{13}C-NMR (100 MHz, $CDCl_3$) δ 197.5, 170.1, 137.9, 128.5, 127.9, 127.9, 103.2, 76.6, 73.0, 71.4, 64.4, 55.8, 41.2, 30.8, 23.3, 16.5, 14.1

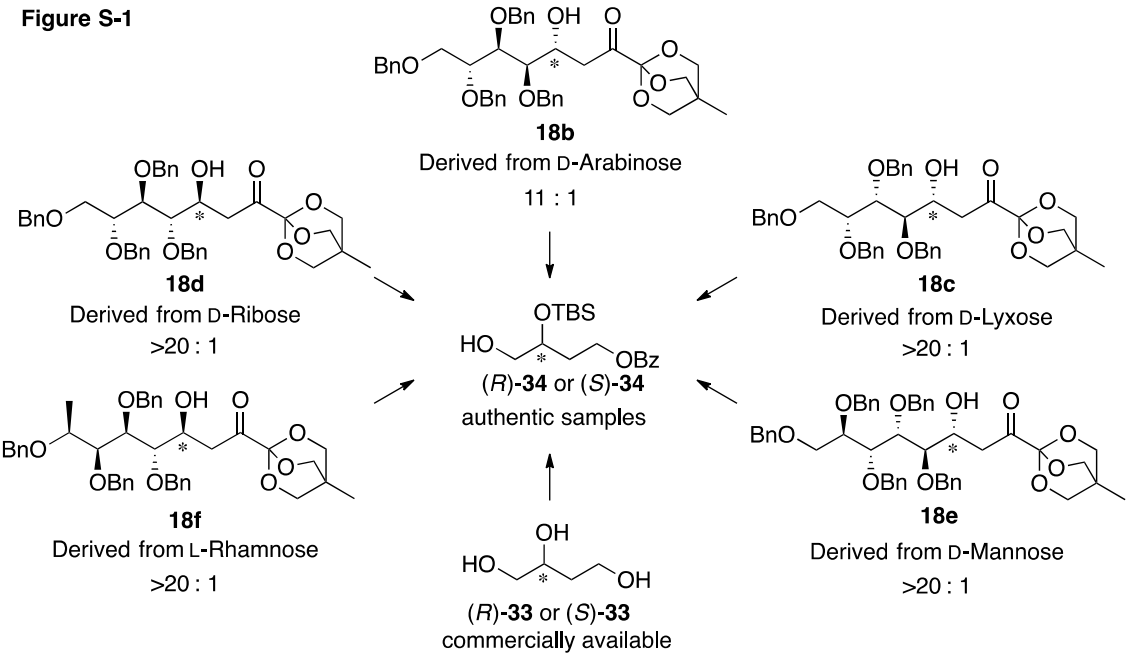
IR (neat) 3493, 3350, 2969, 2937, 2884, 1747, 1658, 1536, 1454, 1375, 1350, 1266, 1194, 1156, 1081, 1033, 995 cm^{-1}

HRMS (ESI) calcd for $C_{21}H_{29}NNaO_7$ $[M+Na]^+$ 430.1842, found 430.1824.

Determination of the newly formed stereogenic center of 18b–18f

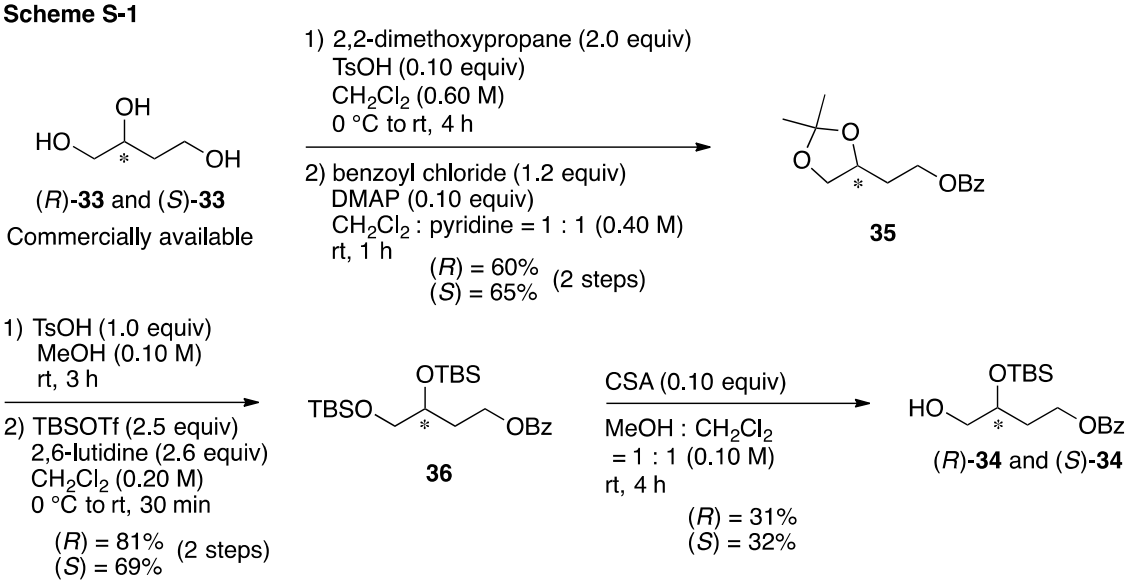
The newly formed stereogenic center in the aldol reactions was determined by the comparisons of the optical rotations and chiral HPLC data between the alcohol **34** derived from the aldol adducts and authentic samples (*R*)-**34** and (*S*)-**34** prepared from commercially available chiral (2*R*)- and (2*S*)-1,2,4-butanetriol ((*R*)-**33** and (*S*)-**33**) (Figure S-1).

Figure S-1



Authentic samples (*R*)-**34** and (*S*)-**34** can be prepared from triol (*R*)-**33** and (*S*)-**33** via 5 steps, respectively. Acetalizaion of the 1,2-diol, followed by bezoylation of the terminal alcohol to furnish the known compound **35**.[4, 5] Transformation of the isopropylidene acetal to the TBS ethers afforded **36**. Selective deprotection of the primary TBS group under acidic conditions afforded alcohol (*R*)-**34** and (*S*)-**34**, respectively. (Scheme S-1).

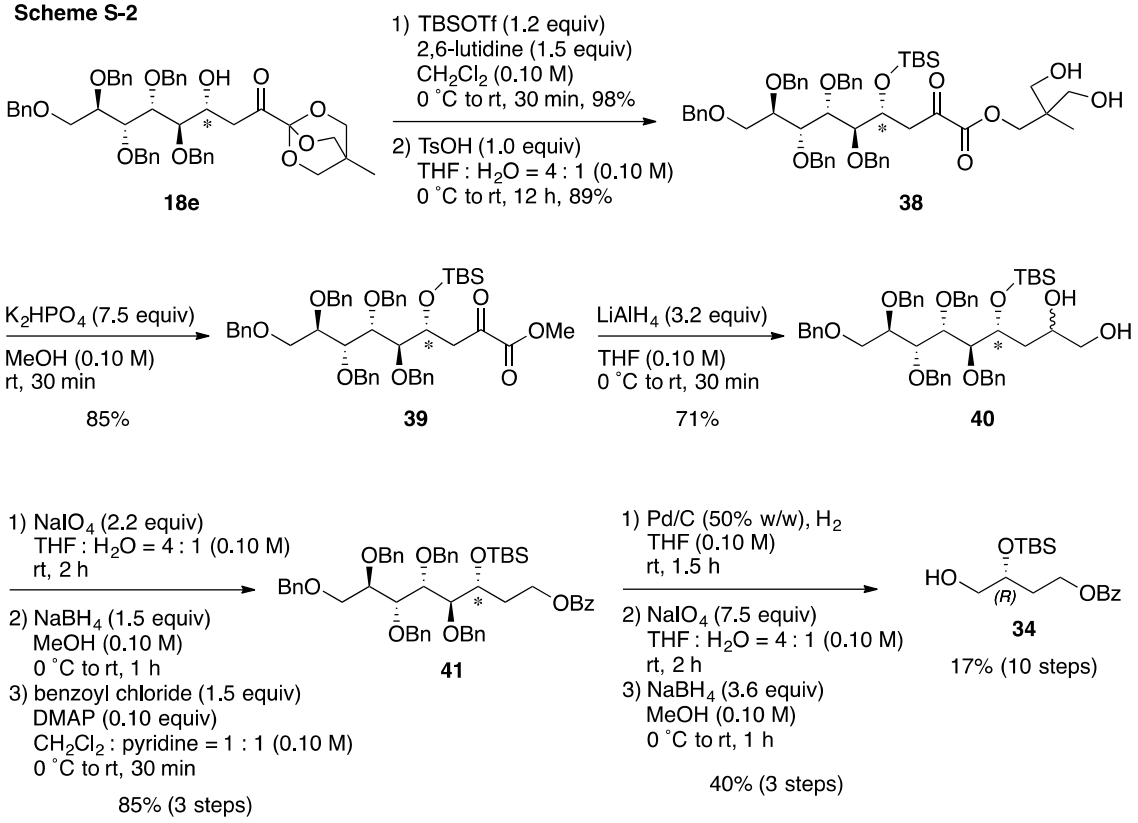
Scheme S-1



The synthesis of alcohol **34** from the aldol adduct **18e** required 10 steps including the carbon–carbon bond cleavage steps using sodium periodate. The representative synthetic route was shown in Scheme S-2.

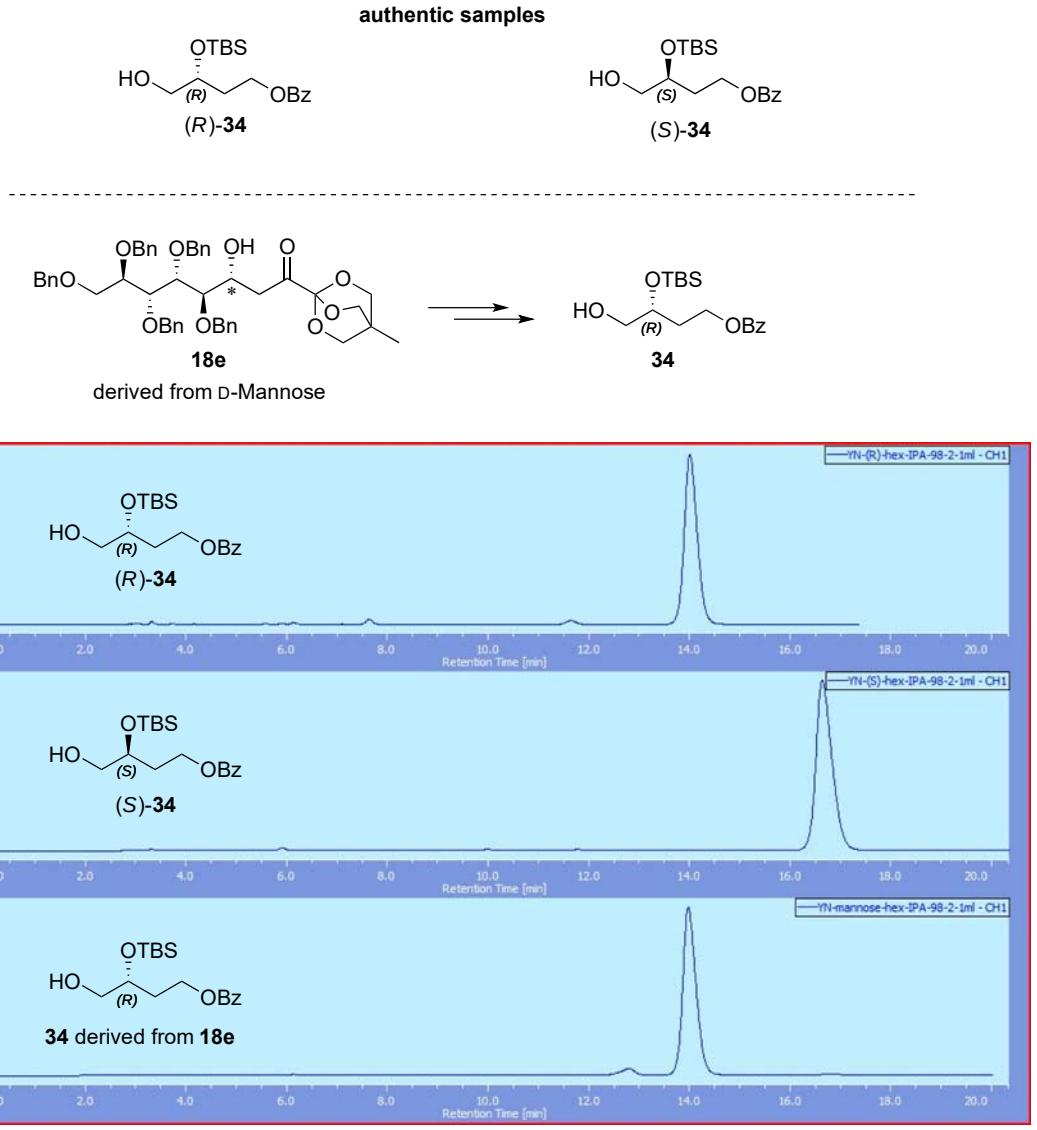
Protection of the hydroxy group of aldol adduct **18e** by TBS group, followed by partial hydrolysis of the α-keto-OBO orthoester moiety afforded α-keto ester **38**. After the transesterification to methyl ester **39** under basic conditions, the concomitant reduction of the ketone and the ester using $LiAlH_4$ gave the diol **40**. Oxidative cleavage of the 1,2-diol using sodium periodate, followed by reduction of the aldehyde to alcohol and the treatment of the benzoyl chloride and DMAP in pyridine-CH_2Cl_2 afforded the benzoate **41**. After hydrogenolysis of all benzyl ethers of benzoate **41**, the oxidative cleavage of the corresponding pentanol using sodium periodate, followed by reduction of the aldehyde provided alcohol **34**.

Scheme S-2



By the comparison of the optical rotation and chiral HPLC data between the alcohol **34** derived from the aldol adduct **18e** and authentic samples (*R*)-**34** and (*S*)-**34** from commercially available (*R*)-**33**, (*S*)-**33**, the stereochemistry of the alcohol **34** derived from the aldol adduct **18e** was determined as a (*R*) configuration (Figure S-2). Namely, the stereochemistry of the obtained aldol adduct **18e** as a major diastereomer was 4,5-*anti* configuration (Felkin product).

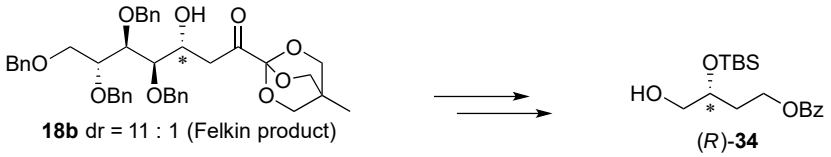
Figure S-2

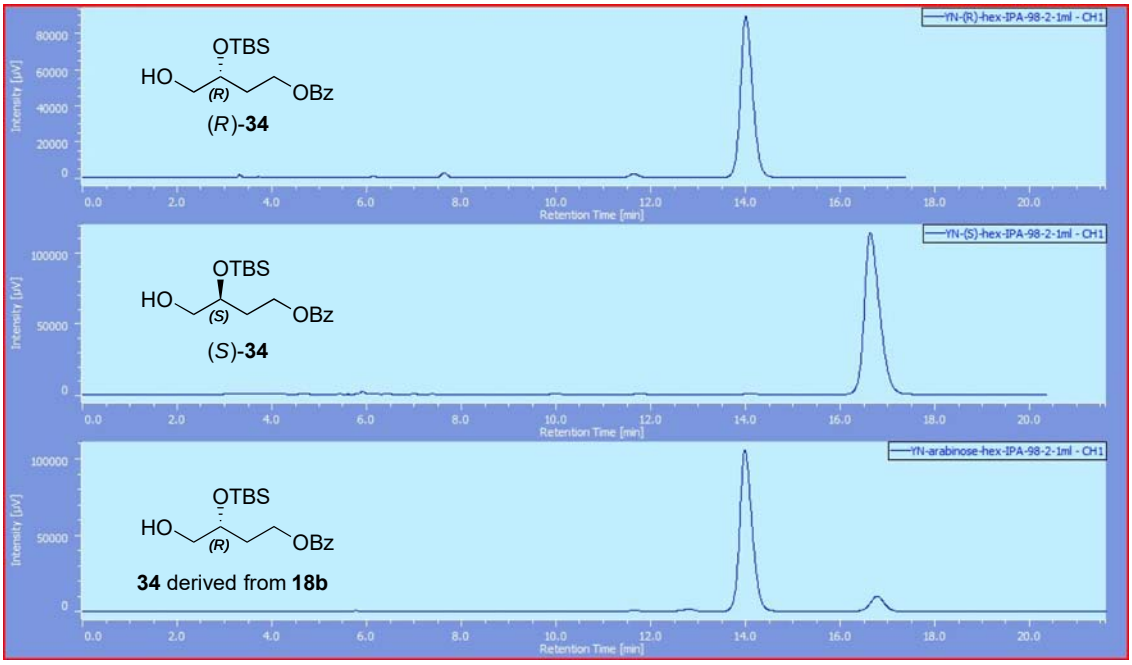


(*R*)-**34** : t_R = 14.0 min, (*S*)-**34** : t_R = 16.6 min, **34** derived from **18e** : t_R = 14.0 min (CHIRALPAK IA, hexane / ^{i}PrOH = 98 : 2, flow rate 1.0 mL / min, 254 nm)

Other aldol adducts **18b–18d** and **18f** were also converted to alcohol **34** and determined the stereochemistry according to the above method. As a results, the major diastereomers in the all aldol reactions had 4,5-*anti* configuration (Felkin product) (Figure S-3-1–4).

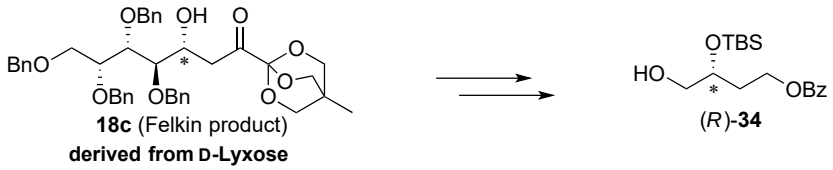
Figure S-3-1

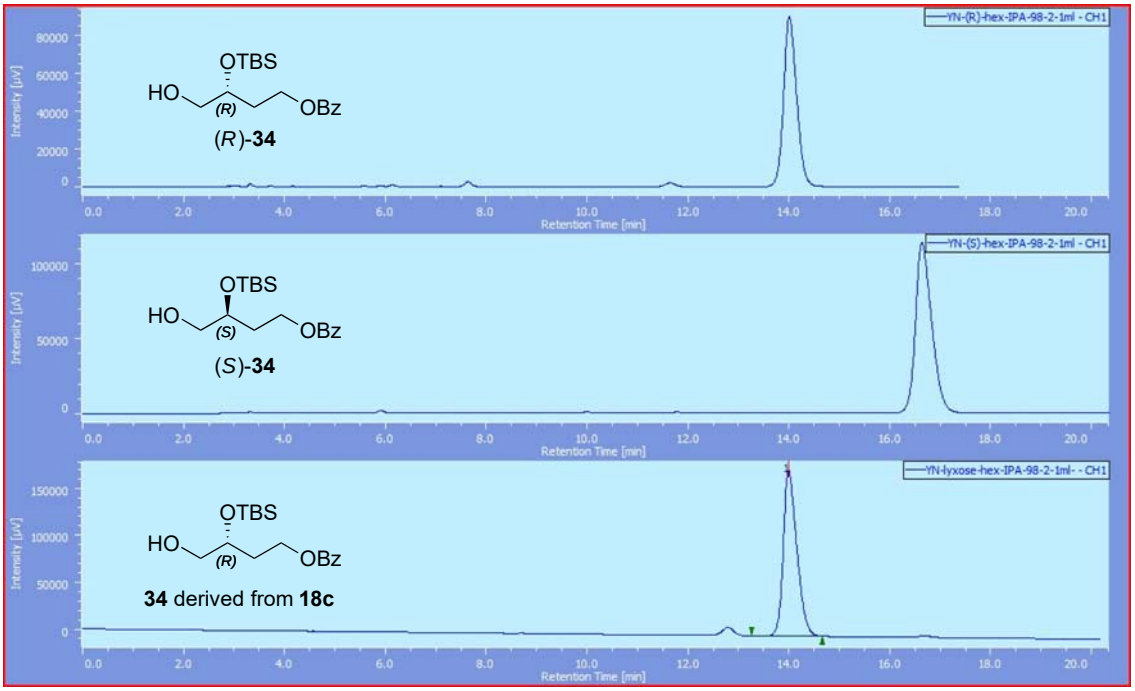




(*R*)-**34** : t_R = 14.0 min, (*S*)-**34** : t_R = 16.6 min, **34** derived from **18b** : t_R = 14.0 min (CHIRALPAK IA, hexane / ^{i}PrOH = 98 : 2, flow rate 1.0 mL / min, 254 nm)

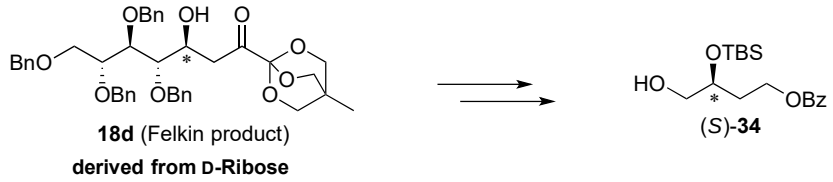
Figure S-3-2

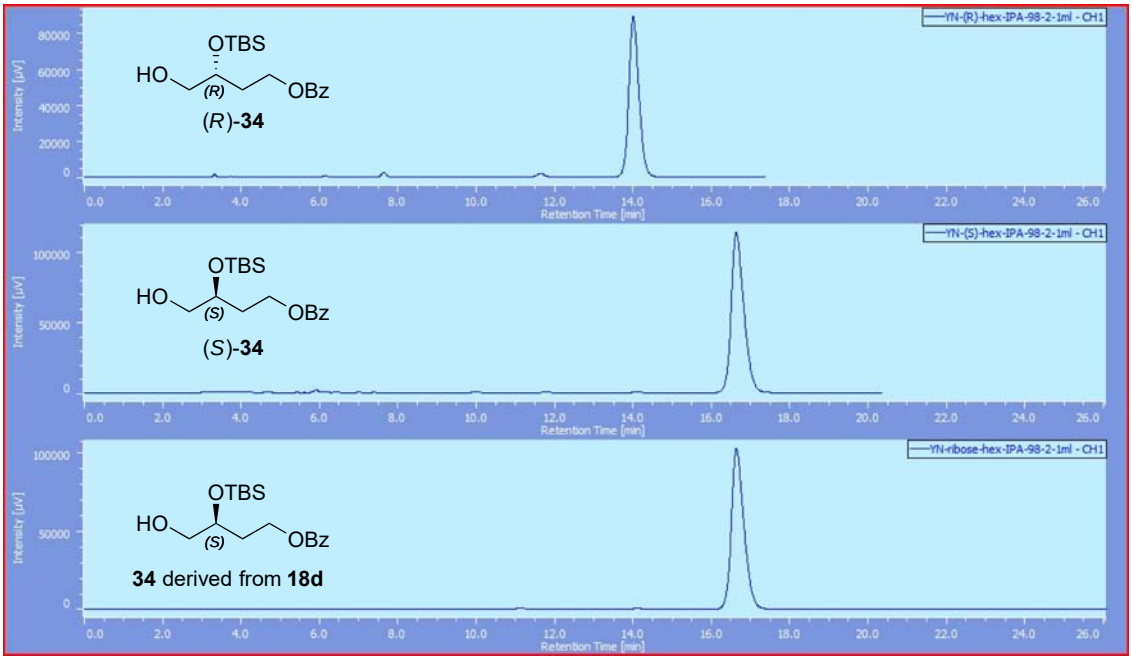




(*R*)-**34** : t_R = 14.0 min, (*S*)-**34** : t_R = 16.6 min, **34** derived from **18c** : t_R = 14.0 min (CHIRALPAK IA, hexane / ^{i}PrOH = 98 : 2, flow rate 1.0 mL / min, 254 nm)

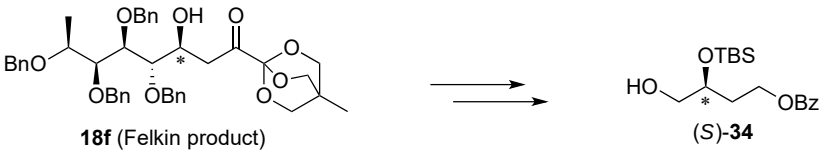
Figure S-3-3





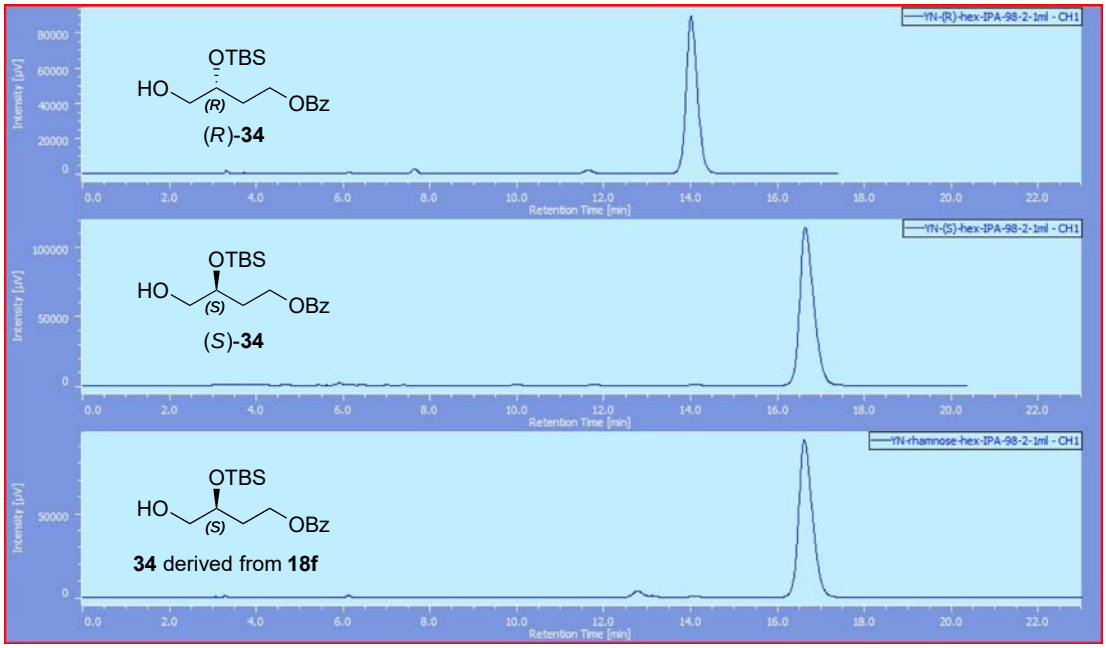
(*R*)-**34** : t_R = 14.0 min, (*S*)-**34** : t_R = 16.6 min, **34** derived from **18d** : t_R = 16.6 min (CHIRALPAK IA, hexane / ^{i}PrOH = 98 : 2, flow rate 1.0 mL / min, 254 nm)

Figure S-3-4



18f (Felkin product)
derived from L-Rhamnose

(*S*)-**34**

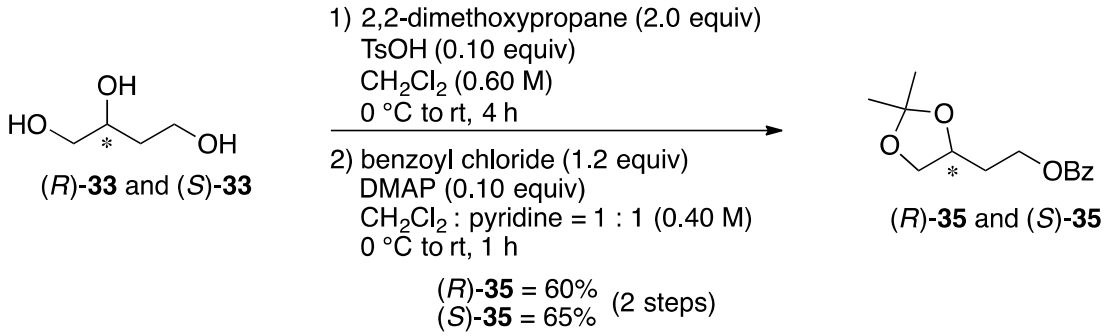


(*R*)-**34** : t_R = 14.0 min, (*S*)-**34** : t_R = 16.6 min, **34** derived from **18f** : t_R = 16.6 min (CHIRALPAK IA, hexane / ^{i}PrOH = 98 : 2, flow rate 1.0 mL / min, 254 nm)

Preparation of authentic samples (*R*)-34 and (*S*)-34

(*R*)-2-(2,2-Dimethyl-1,3-dioxolan-4-yl)ethyl benzoate (*R*)-35[4]

(*S*)-2-(2,2-Dimethyl-1,3-dioxolan-4-yl)ethyl benzoate (*S*)-35[5]



To a stirred solution of (*R*)-**33** (300 mg, 2.83 mmol, 1.0 equiv) and 2,2-dimethoxy propane (0.693 mL, 5.66 mmol, 2.0 equiv) in CH_2Cl_2 (4.7 mL, 0.60 M) at 0 °C was added $TsOH \cdot H_2O$ (53.8 mg, 0.283 mmol, 0.10 equiv). After the mixture was stirred for 4 h at room temperature under N_2 atmosphere, the reaction was quenched with saturated aqueous $NaHCO_3$ (5.0 mL). The resulting mixture was extracted with $CHCl_3$ (3 x 20 mL). The combined organic phases were washed with H_2O (2 x 20 mL) and brine (2 x 20 mL), dried over Na_2SO_4, filtered and concentrated under reduced pressure.

To a stirred solution of the above crude product in CH_2Cl_2 and pyridine (CH_2Cl_2 : pyridine = 1 : 1, 7.1 mL, 0.40 M) at 0 °C was added DMAP (34.6 mg, 0.283 mmol, 0.10 equiv) and benzoyl chloride (0.395 mL, 3.40 mmol, 1.2 equiv). After the mixture was stirred for 1 h at room temperature under N_2 atmosphere, the reaction was quenched with saturated aqueous NH_4Cl (5.0 mL). The resulting mixture was extracted with $CHCl_3$ (3 x 20 mL). The combined organic phases were washed with H_2O (2 x 30 mL) and brine (2 x 30 mL), dried over Na_2SO_4, filtered and concentrated under reduced pressure. The obtained crude product was purified by silica gel column chromatography (Hexane : AcOEt = 50 : 1) to give (*R*)-**35** (423 mg, 1.69 mmol, 60% yield) as colorless oil.

The (*S*)-**35** (458 mg, 1.83 mmol, 65% yield, colorless oil) was prepared according to the above procedure.

Colorless oil; Rf value on TLC 0.43 (Hexane : AcOEt = 5 : 1)

(*R*)-**35** : $[\alpha]_D^{23}$ +10.3 (*c* 1.0, $CHCl_3$)

(*S*)-**35** : $[\alpha]_D^{23}$ –13.5 (*c* 1.0, $CHCl_3$)

^{1}H-NMR (400 MHz, $CDCl_3$) δ 8.05–8.02 (m, 2H), 7.58–7.54 (m, 1H), 7.46–7.42 (m, 2H), 4.49 (dt, *J* = 11.2, 6.0 Hz, 1H), 4.39 (ddd, *J* = 11.2, 8.0, 5.6 Hz, 1H), 4.31–4.24 (m, 1H), 4.12 (dd, *J* = 8.0, 6.0 Hz, 1H), 3.64 (dd, *J* = 8.0, 7.2 Hz, 1H), 2.12–1.98 (m, 2H), 1.43 (s, 3H), 1.37 (s, 3H)

^{13}C-NMR (100 MHz, $CDCl_3$) δ 166.4, 133.0, 130.1, 129.5, 128.4, 108.9, 73.3, 69.4, 61.9, 33.0, 26.9, 25.7

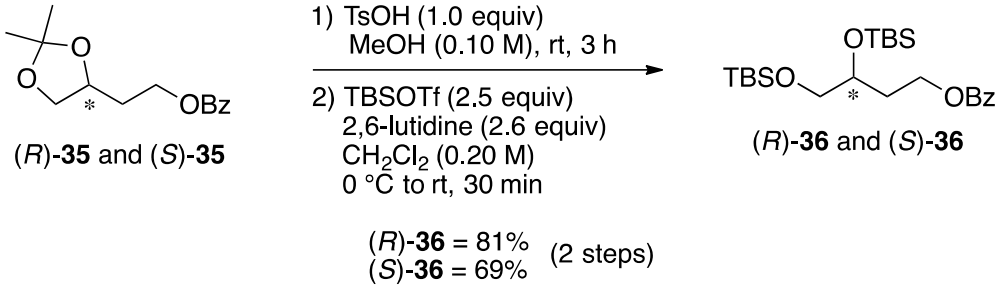
IR (neat) 2986, 2937, 2877, 1721, 1602, 1584, 1453, 1379, 1371, 1315, 1277, 1216, 1176, 1159, 1112, 1070, 1026, 990 cm^{-1}

(*R*)-**35**: HRMS (FAB, NBA) calcd for $C_{14}H_{19}O_4$ $[M+H]^+$ 251.1283, found 251.1288.

(*S*)-**35** : HRMS (FAB, NBA) calcd for $C_{14}H_{19}O_4$ $[M+H]^+$ 251.1283, found 251.1288.

(*R*)-3,4-Bis((*tert*-butyldimethylsilyl)oxy)butyl benzoate (*R*)-36

(*S*)-3,4-Bis((*tert*-butyldimethylsilyl)oxy)butyl benzoate (*S*)-36



To a stirred solution of (*R*)-**35** (100 mg, 0.40 mmol, 1.0 equiv) in MeOH (4.0 mL, 0.10 M) at room temperature was added $TsOH \cdot H_2O$ (76.1 mg, 0.40 mmol, 1.0 equiv). After the mixture was stirred for 3 h at room temperature, the reaction was quenched with saturated aqueous $NaHCO_3$ (5.0 mL). The resulting mixture was extracted with $CHCl_3$ (3 x 20 mL). The combined organic phases were washed with H_2O (2 x 20 mL) and brine (2 x 20 mL), dried over Na_2SO_4, filtered and concentrated under reduced pressure. To a stirred solution of the above crude product in CH_2Cl_2 (2.0 mL, 0.20 M) at 0 °C was added 2,6-lutidine (0.121 mL, 1.04 mmol, 2.6 equiv) and TBSOTf (0.230 mL, 1.00 mmol, 2.5 equiv) under N_2 atmosphere. After the mixture was stirred for 30 min at room

temperature, the reaction was quenched with saturated aqueous NH_4Cl (3.0 mL). The resulting mixture was extracted with $CHCl_3$ (3 x 10 mL). The combined organic phases were washed with H_2O (2 x 20 mL) and brine (2 x 20 mL), dried over Na_2SO_4, filtered and concentrated under reduced pressure. The obtained crude product was purified by silica gel column chromatography (Hexane : AcOEt = 50 : 1) to give (*R*)-**36** (142 mg, 0.324 mmol, 81% yield) as colorless oil.

The (*S*)-**36** (121 mg, 0.276 mmol, 69% yield, colorless oil) was prepared according to the above procedure.

Colorless oil; Rf value on TLC 0.53 (Hexane : AcOEt = 20 : 1)

(*R*)-**36**: $[\alpha]_D^{24}$ +22.4 (*c* 0.5, $CHCl_3$)

(*S*)-**36**: $[\alpha]_D^{24}$ –20.6 (*c* 0.5, $CHCl_3$)

^{1}H-NMR (400 MHz, $CDCl_3$) δ 8.06–8.03 (m, 2H), 7.58–7.53 (m, 1H), 7.46–7.41 (m, 2H), 4.47 (ddd, *J* = 11.2, 6.4, 5.6 Hz, 1H), 4.38 (ddd, *J* = 11.2, 8.0, 6.0 Hz, 1H), 3.92–3.86 (m, 1H), 3.62 (dd, *J* = 10.0, 5.2 Hz, 1H), 3.48 (dd, *J* = 10.0, 6.4 Hz, 1H), 2.14–2.05 (m, 1H), 1.86–1.77 (m, 1H), 0.89 (s, 9H), 0.89 (s, 9H), 0.07 (s, 3H), 0.06 (s, 3H), 0.06 (s, 3H), 0.05 (s, 3H)

^{13}C-NMR (100 MHz, $CDCl_3$) δ 166.5, 132.8, 130.5, 129.5, 128.3, 70.1, 67.5, 61.8, 33.5, 25.9, 25.8, 18.3, 18.1

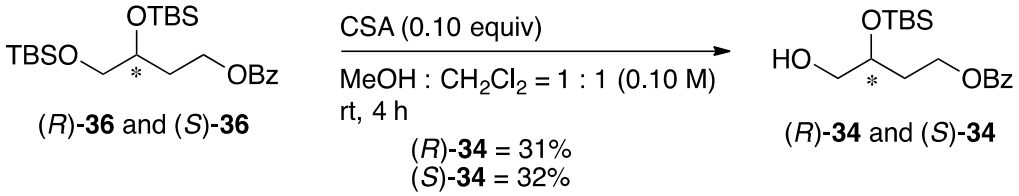
IR (neat) 2955, 2929, 2899, 2885, 2857, 1724, 1603, 1585, 1472, 1462, 1388, 1361, 1314, 1274, 1256, 1176, 1109, 1070, 1051, 1026, 1005, 939 cm^{-1}

(*R*)-**36** : HRMS (ESI) calcd for $C_{23}H_{42}NaO_4Si_2$ $[M+Na]^+$ 461.2519, found 461.2513.

(*S*)-**36** : HRMS (ESI) calcd for $C_{23}H_{42}NaO_4Si_2$ $[M+Na]^+$ 461.2519, found 461.2506.

(*R*)-3-((*tert*-Butyldimethylsilyl)oxy)-4-hydroxybutyl benzoate (*R*)-34

(*S*)-3-((*tert*-Butyldimethylsilyl)oxy)-4-hydroxybutyl benzoate (*S*)-34



To a stirred solution of (*R*)-**36** (50.0 mg, 0.114 mmol, 1.0 equiv) in MeOH and CH_2Cl_2

(1 : 1, 1.1 mL, 0.10 M) at room temperature was added 10-camphorsulfonic acid (2.65 mg, 0.0114 mmol, 0.10 equiv). After the mixture was stirred for 4 h at room temperature, the reaction was quenched with saturated aqueous $NaHCO_3$ (1.0 mL). The resulting mixture was extracted with $CHCl_3$ (3 x 5.0 mL). The combined organic phases were washed with H_2O (2 x 10 mL) and brine (2 x 10 mL), dried over Na_2SO_4, filtered and concentrated under reduced pressure. The obtained crude product was purified by silica gel column chromatography (Hexane : AcOEt = 8 : 1) to give (*R*)-**34** (11.5 mg, 0.0354 mmol, 31% yield) as colorless oil.

The (*S*)-**34** (11.8 mg, 0.0364 mmol, 32% yield, colorless oil) was prepared according to the above procedure.

Colorless oil; Rf value on TLC 0.30 (Hexane : AcOEt = 5 : 1)

(*R*)-**34** : $[\alpha]_D^{23}$ +15.0 (*c* 0.58, $CHCl_3$)

(*S*)-**34** : $[\alpha]_D^{23}$ –17.2 (*c* 0.59, $CHCl_3$)

^{1}H-NMR (400 MHz, $CDCl_3$) δ 8.05–8.02 (m, 2H), 7.59–7.54 (m, 1H), 7.47–7.42 (m, 2H), 4.45 (dt, *J* = 11.2 6.0 Hz, 1H), 4.35 (ddd, *J* = 11.2, 6.8, 6.4 Hz, 1H), 4.03–3.98 (m, 1H), 3.68–3.65 (m, 1H), 3.58–3.53 (m, 1H), 2.06–1.93 (m, 2H), 1.87 (br s, 1H, -O<u>H</u>), 0.91 (s, 9H), 0.10 (s, 3H), 0.10 (s, 3H)

^{13}C-NMR (100 MHz, $CDCl_3$) δ 166.5, 132.9, 130.2, 129.5, 128.4, 69.8, 66.4, 61.6, 32.9, 25.8, 18.0, –4.5, –4.8

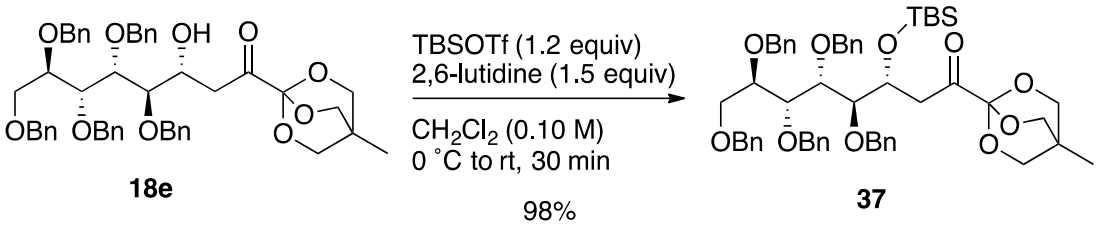
IR (neat) 3500, 2955, 2929, 2885, 2857, 1722, 1602, 1585, 1471, 1462, 1453, 1388, 1361, 1315, 1276, 1258, 1176, 1113, 1070, 1048, 1026, 1005, 937 cm^{-1}

(*R*)-**34** : HRMS (ESI) calcd for $C_{17}H_{28}NaO_4Si$ $[M+Na]^+$ 347.1655, found 347.1655.

(*S*)-**34** : HRMS (ESI) calcd for $C_{17}H_{28}NaO_4Si$ $[M+Na]^+$ 347.1655, found 347.1651.

The representative synthetic route of alcohol 34 from the aldol adduct

(3*R*,4*S*,5*S*,6*R*,7*R*)-4,5,6,7,8-Pentakis(benzyloxy)-3-((*tert*-butyldimethylsilyl)oxy)-1-(4-methyl-2,6,7-trioxabicyclo[2.2.2]octan-1-yl)octan-1-one 37



To a stirred solution of **18e** (800 mg, 0.996 mmol, 1.0 equiv) and 2,6-lutidine (0.160 mL, 1.49 mmol, 1.5 equiv) in CH_2Cl_2 (10 mL, 0.10 M) at 0 °C was added dropwise TBSOTf (0.275 mL, 1.20 mmol, 1.2 equiv) under N_2 atmosphere. After the mixture was stirred for 30 min at room temperature, the reaction was quenched with saturated aqueous NH_4Cl (10 mL). The resulting mixture was extracted with $CHCl_3$ (3 x 50 mL). The combined organic phases were washed with H_2O (2 x 100 mL) and brine (2 x 100 mL), dried over Na_2SO_4, filtered and concentrated under reduced pressure. The obtained crude product was purified by silica gel column chromatography (Hexane : AcOEt = 8 : 1) to give **37** (895 mg, 0.976 mmol, 98% yield) as colorless oil.

Colorless oil; Rf value on TLC 0.55 (Hexane : AcOEt = 2 : 1); $[\alpha]_D^{27}$ +3.20 (*c* 1.5, $CHCl_3$)

^{1}H-NMR (400 MHz, $CDCl_3$) δ 7.35–7.19 (m, 25H), 4.96 (d, *J* = 12.0 Hz, 1H), 4.80 (dd, *J* = 6.8, 4.4 Hz, 1H), 4.74 (d, *J* = 12.0 Hz, 1H), 4.64 (d, *J* = 11.6 Hz, 1H), 4.61 (d, *J* = 11.6 Hz, 1H), 4.55 (d, *J* = 11.6 Hz, 1H), 4.51 (d, *J* = 11.6 Hz, 1H), 4.50 (d, *J* = 12.0 Hz, 1H), 4.49 (d, *J* = 12.0 Hz, 1H), 4.46 (d, *J* = 12.0 Hz, 1H), 4.30 (d, *J* = 12.0 Hz, 1H), 4.13–4.09 (m, 1H), 3.96–3.88 (m, 2H), 3.91 (s, 6H), 3.80 (d, *J* = 10.8 Hz, 1H), 3.78 (d, *J* = 10.8 Hz, 1H), 3.71 (dd, *J* = 10.4, 4.8 Hz, 1H), 3.12 (dd, *J* = 18.8, 6.8 Hz, 1H), 3.06 (dd, *J* = 18.8, 4.4 Hz, 1H), 0.85 (s, 9H), 0.81 (s, 3H), 0.06 (s, 3H), 0.02 (s, 3H)

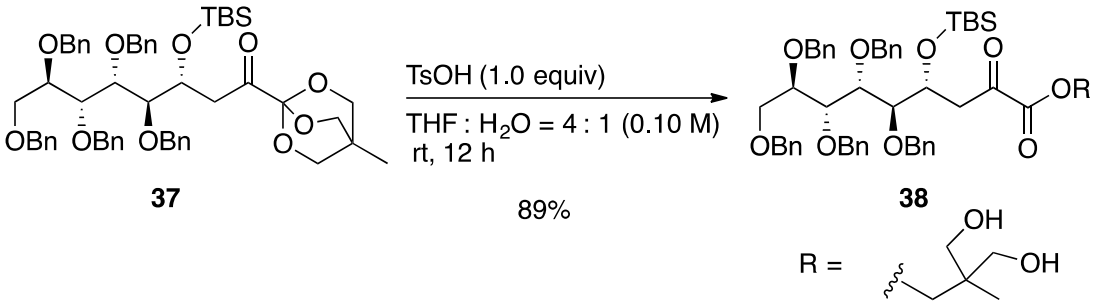
^{13}C-NMR (100 MHz, $CDCl_3$) δ 197.0, 138.9, 138.8, 138.7, 138.6, 138.4, 128.3, 128.2, 128.2, 128.1, 128.1, 128.1, 127.9, 127.7, 127.5, 127.5, 127.5, 127.3, 127.3, 127.2, 127.2, 103.4, 82.6, 78.9, 78.4, 78.4, 77.2, 73.9, 73.6, 73.2, 72.9, 72.7, 71.5, 69.7, 68.4, 40.8,

30.8, 25.9, 18.0, 14.2

IR (neat) 3083, 3062, 3030, 2950, 2928, 2881, 2854, 1750, 1496, 1454, 1395, 1348, 1333, 1305, 1254, 1097, 1073, 1027, 1001 cm^{-1}

HRMS (ESI) calcd for $C_{55}H_{68}NaO_{10}Si$ $[M+Na]^+$ 939.4479, found 939.4474.

3-Hydroxy-2-(hydroxymethyl)-2-methylpropyl(4*R*,5*S*,6*S*,7*R*,8*R*)-5,6,7,8,9-pentakis(benzyloxy)-4-((*tert*-butyldimethylsilyl)oxy)-2-oxononanoate 38



A solution of **37** (865 mg, 0.943 mmol, 1.0 equiv) and $TsOH \cdot H_2O$ (179 mg, 0.943 mmol, 1.0 equiv) in THF and H_2O (4 : 1, 9.4 mL, 0.10 M) was stirred for 12 h at room temperature. The reaction was quenched with saturated aqueous $NaHCO_3$ (10 mL). The resulting mixture was extracted with AcOEt (3 x 50 mL). The combined organic phases were washed with H_2O (2 x 100 mL) and brine (2 x 100 mL), dried over Na_2SO_4, filtered and concentrated under reduced pressure. The obtained crude product was purified by silica gel column chromatography (Hexane : AcOEt = 4 : 1) to give **38** (782 mg, 0.836 mmol, 89% yield) as colorless oil.

Colorless oil; Rf value on TLC 0.51 (Hexane : AcOEt = 1 : 1); $[\alpha]_D^{26}$ +5.54 (*c* 1.0, $CHCl_3$)

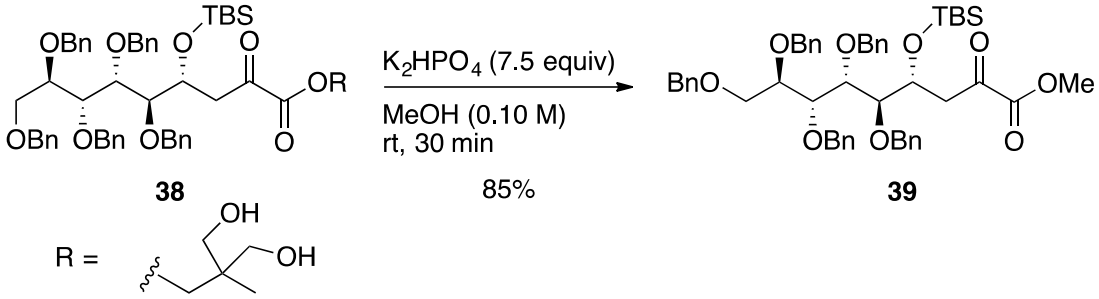
^{1}H-NMR (400 MHz, $CDCl_3$) δ 7.35–7.21 (m, 25H), 4.81 (d, *J* = 11.6 Hz, 1H), 4.77–4.74 (m, 1H), 4.74 (d, *J* = 11.6 Hz, 1H), 4.64 (s, 2H), 4.62 (d, *J* = 12.0 Hz, 1H), 4.52 (d, *J* = 12.0 Hz, 1H), 4.50 (d, *J* = 12.0 Hz, 1H), 4.50 (s, 2H), 4.33 (d, *J* = 12.0 Hz, 1H), 4.16 (d, *J* = 10.8 Hz, 1H), 4.11–4.08 (m, 1H), 4.09 (d, *J* = 10.8 Hz, 1H), 3.94–3.84 (m, 3H), 3.77 (dd, *J* = 8.0, 1.6 Hz, 1H), 3.72 (dd, *J* = 10.8. 4.8 Hz, 1H), 3.49–3.40 (m, 4H), 3.26 (dd, *J* = 16.4, 6.8 Hz, 1H), 2.99 (dd, *J* = 16.4. 5.2 Hz, 1H), 2.35 (br s, 2H, -O<u>H</u>), 0.86 (s, 9H), 0.74 (s, 3H), 0.07 (s, 3H), 0.03 (s, 3H)

^{13}C-NMR (100 MHz, $CDCl_3$) δ 191.8, 161.2, 138.7, 138.5, 138.4, 138.3, 138.2, 128.4, 128.3, 128.2, 128.2, 127.8, 127.7, 127.6, 127.6, 127.5, 127.5, 127.5, 127.4, 127.4, 82.5, 78.8, 78.7, 78.6, 74.2, 73.8, 73.3, 72.9, 71.6, 70.3, 69.2, 68.5, 67.5, 67.4, 42.7, 40.5, 29.7, 25.8, 17.9, 16.7

IR (neat) 3512, 3088, 3067, 3027, 2950, 2927, 2884, 2857, 1726, 1500, 1454, 1389, 1365, 1324, 1256, 1106, 1002 cm^{-1}

HRMS (ESI) calcd for $C_{55}H_{70}NaO_{11}Si$ $[M+Na]^+$ 957.4585, found 957.4572.

Methyl(5*R*,6*S*,7*S*,8*R*,9*R*)-6,7,8,9,10-pentakis(benzyloxy)-5-((*tert*-butyldimethylsilyl) oxy)-2,3-dioxodecanoate 39



To a stirred solution of **38** (753 mg, 0.805 mmol, 1.0 equiv) in MeOH (8.1 mL, 0.10 M) at room temperature was added K_2HPO_4 (1.05 g, 6.04 mmol, 7.5 equiv). After the mixture was stirred for 30 min, the reaction was quenched with H_2O (20 mL). The resulting mixture was extracted with $CHCl_3$ (3 x 50 mL). The combined organic phases were washed with H_2O (2 x 100 mL) and brine (2 x 100 mL), dried over Na_2SO_4, filtered and concentrated under reduced pressure. The obtained crude product was purified by silica gel column chromatography (Hexane : AcOEt = 20 : 1) to give **39** (577 mg, 0.681 mmol, 85% yield) as colorless oil.

Colorless oil; Rf value on TLC 0.82 (Hexane : AcOEt = 2 : 1); $[\alpha]_D^{26}$ +8.04 (*c* 1.0, $CHCl_3$)

^{1}H-NMR (400 MHz, $CDCl_3$) δ 7.35–7.22 (m, 25H), 4.83 (d, *J* = 12.0 Hz, 1H), 4.77–4.72 (m, 1H), 4.75 (d, *J* = 11.6 Hz, 1H), 4.68–4.61 (m, 3H), 4.57 (d, *J* = 11.6 Hz, 1H), 4.54 (d, *J* = 12.0 Hz, 1H), 4.52 (d, *J* = 12.0 Hz, 1H), 4.48 (d, *J* = 12.0 Hz, 1H), 4.33 (d, *J* = 12.0 Hz, 1H), 4.11 (dd, *J* = 6.0, 3.6 Hz, 1H), 3.96–3.89 (m, 2H), 3.84 (dd, *J* = 7.6,

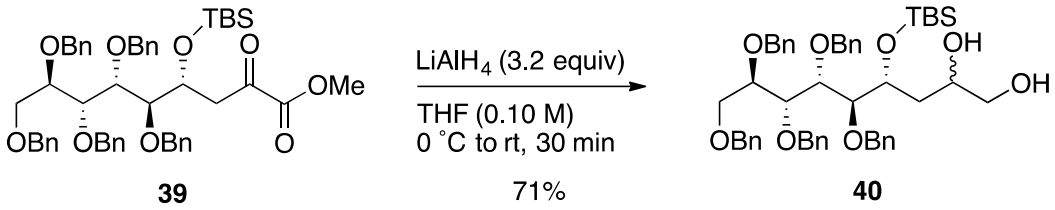
3.6 Hz, 1H), 3.78 (dd, *J* = 7.6, 2.0 Hz, 1H), 3.73 (dd, *J* = 10.4. 4.4 Hz, 1H), 3.68 (s, 3H), 3.29 (dd, *J* = 16.8, 7.6 Hz, 1H), 2.96 (dd, *J* = 16.8, 4.8 Hz, 1H), 0.86 (s, 9H), 0.07 (s, 3H), 0.02 (s, 3H)

^{13}C-NMR (100 MHz, $CDCl_3$) δ 192.0, 161.2, 138.9, 138.6, 138.4, 138.3, 138.3, 128.3, 128.3, 128.2, 128.2, 128.2, 127.8, 127.7, 127.6, 127.5, 127.5, 127.5, 127.4, 127.4, 127.3, 127.3, 82.7, 78.9, 78.8, 78.7, 74.2, 73.8, 73.3, 73.1, 71.6, 70.1, 69.5, 52.7, 42.8, 25.8, 17.9

IR (neat) 3092, 3067, 3030, 2955, 2927, 2856, 1730, 1496, 1454, 1253, 1206, 1092, 1076, 1028 cm^{-1}

HRMS (ESI) calcd for $C_{51}H_{62}NaO_9Si$ $[M+Na]^+$ 869.4061, found 869.4059.

(4*R*,5*S*,6*S*,7*R*,8*R*)-5,6,7,8,9-Pentakis(benzyloxy)-4-((*tert*-butyldimethylsilyl)oxy)nonane-1,2-diol 40



39 71% **40**

To a stirred solution of **39** (546 mg, 0.645 mmol, 1.0 equiv) in THF (6.5 mL, 0.10 M) at 0 °C was added portionwise $LiAlH_4$ (78.2 mg, 2.06 mmol, 3.2 equiv). After the mixture was stirred for 30 min under N_2 atmosphere, the reaction was quenched by the addition of H_2O (50 μL), 15% aqueous NaOH (50 μL) and H_2O (0.15 mL). The resulting mixture was diluted with Et_2O and filtered through a Celite pad® by rinsing with Et_2O. The obtained filtrate was washed with H_2O (2 x 100 mL) and brine (2 x 100 mL), dried over Na_2SO_4, filtered and concentrated under reduced pressure. The obtained crude product was purified by silica gel column chromatography (Hexane : AcOEt = 6 : 1) to give **40** (378 mg, 0.460 mmol, 71% yield, dr = 3 : 2) as colorless oil.

The following physical data were measured as a 3 : 2 mixture of diastereomers.

Colorless oil; Rf value on TLC 0.44 (Hexane : AcOEt = 2 : 1); $[\alpha]_D^{24}$ +10.2 (*c* 1.0, $CHCl_3$)

^{1}H-NMR (400 MHz, $CDCl_3$) δ 7.34–7.19 (m, 25H x 2), 5.00 (d, *J* = 11.6 Hz, 1H), 4.94

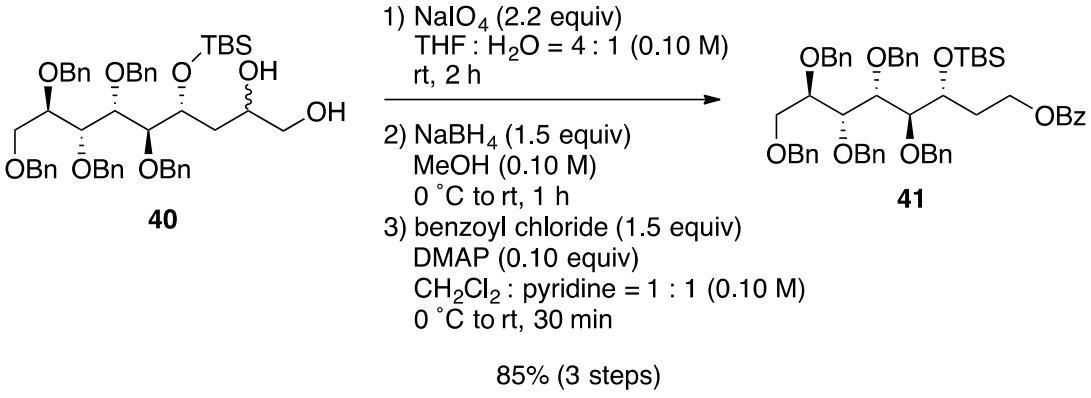
(d, *J* = 11.6 Hz, 1H), 4.77–4.40 (m, 18H), 4.33–4.26 (m, 3H), 4.13–4.09 (m, 2H), 3.96–3.69 (m, 12H), 3.63 (br s, 1H), 3.55 (dd, *J* = 11.2, 2.8 Hz, 1H), 3.45 (dd, *J* = 10.8, 2.4 Hz, 1H), 3.37–3.31 (m, 2H), 2.40 (br s, 1H, -O<u>H</u>), 2.01 (br s, 1H, -O<u>H</u>), 1.83–1.71 (m, 2H), 1.64–1.57 (m, 1H), 1.44 (ddd, *J* = 14.8, 4.4, 2.0 Hz, 1H), 0.90 (s, 9H x 2), 0.11 (s, 3H), 0.09 (s, 3H), 0.04 (s, 3H), 0.02 (s, 3H)

^{13}C-NMR (100 MHz, $CDCl_3$) δ 138.9, 138.7, 138.7, 138.6, 138.5, 138.4, 138.3, 138.3, 138.1, 128.3, 128.3, 128.3, 128.3, 128.2, 128.2, 128.2, 128.2, 127.8, 127.7, 127.7, 127.7, 127.6, 127.6, 127.6, 127.6, 127.5, 127.5, 127.5, 127.5, 127.4, 127.4, 127.4, 127.3, 127.3, 127.3, 82.9, 82.5, 78.9, 78.7, 78.6, 78.4, 78.2, 78.2, 77.2, 74.0, 74.0, 73.8, 73,7, 73.7, 73.3, 73.3, 73.2, 73.0, 71.5, 71.5, 70.5, 69.6, 69.4, 69.0, 68.9, 67.5, 66.9, 35.3, 34.6, 25.9, 25.9, 18.0, 17.8

IR (neat) 3457, 3088, 3063, 3030, 2950, 2927, 2882, 2856, 1496, 1454, 1390, 1360, 1335, 1255, 1210, 1098, 1071, 1027, 906 cm^{-1}

HRMS (ESI) calcd for $C_{50}H_{64}NaO_8Si$ $[M+Na]^+$ 843.4268, found 843.4273.

(3*R*,4*S*,5*S*,6*R*,7*R*)-4,5,6,7,8-Pentakis(benzyloxy)-3-((*tert*-butyldimethylsilyl)oxy)octyl benzoate 41

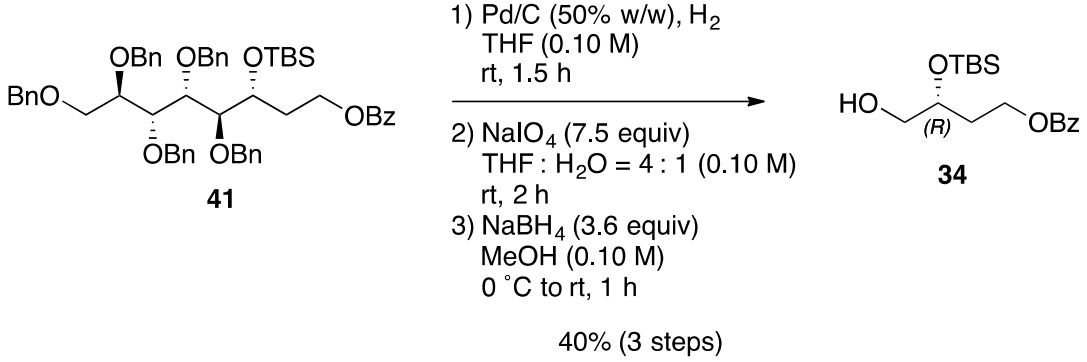


To a stirred solution of **40** (378 mg, 0.460 mmol, 1.0 equiv) in THF and H_2O (4 : 1, 4.6 mL, 0.10 M) at room temperature was added $NaIO_4$ (216 mg, 1.01 mmol, 2.2 equiv). After the mixture was stirred for 2 h, the reaction was quenched with H_2O (10 mL). The resulting mixture was extracted with AcOEt (3 x 20 mL). The combined organic phases were washed with H_2O (2 x 30 mL) and brine (2 x 30 mL), dried over Na_2SO_4, filtered and concentrated under reduced pressure.

To a stirred solution of the above crude product in MeOH (4.6 mL, 0.10 M) at 0 °C was added $NaBH_4$ (26.1 mg, 0.690 mmol, 1.5 equiv). After the mixture was stirred for 1 h at room temperature under N_2 atmosphere, the reaction was quenched with saturated aqueous NH_4Cl (5.0 mL). The resulting mixture was extracted with AcOEt (3 x 20 mL). The combined organic phases were washed with H_2O (2 x 30 mL) and brine (2 x 30 mL), dried over Na_2SO_4, filtered and concentrated under reduced pressure.
To a stirred solution of the obtained crude product in CH_2Cl_2 and pyridine (1 : 1, 4.6 mL, 0.10 M) at 0 °C was added DMAP (5.62 mg, 0.046 mmol, 0.10 equiv) and benzoyl chloride (80.1 μL, 0.690 mmol, 1.5 equiv) at 0 °C under N_2 atmosphere. After the mixture was stirred for 30 min at room temperature, the reaction was quenched with saturated aqueous NH_4Cl (5.0 mL). The resulting mixture was extracted with $CHCl_3$ (3 x 20 mL). The combined organic phases were washed with H_2O (2 x 30 mL) and brine (2 x 30 mL), dried over Na_2SO_4, filtered and concentrated under reduced pressure. The obtained crude product was purified by silica gel column chromatography (Hexane : AcOEt = 20 : 1) to give **41** (351 mg, 0.392 mmol, 85% yield) as colorless oil.

Colorless oil; Rf value on TLC 0.44 (Hexane : AcOEt = 5 : 1); $[\alpha]_D^{27}$ +8.81 (*c* 1.0, $CHCl_3$)
^{1}H-NMR (400 MHz, $CDCl_3$) δ 7.91–7.88 (m, 2H), 7.47–7.43 (m, 1H), 7.31–7.16 (m, 27H), 5.02 (d, *J* = 12.0 Hz, 1H), 4.72 (d, *J* = 12.0 Hz, 1H), 4.64 (d, *J* = 12.0 Hz, 1H), 4.59 (s, 2H), 4.54 (d, *J* = 12.0 Hz, 1H), 4.50–4.42 (m, 4H), 4.36 (dd, *J* = 10.0, 2.4 Hz, 1H), 4.30 (d, *J* = 12.0 Hz, 1H), 4.31–4.25 (m, 1H), 4.14 (d, *J* = 6.8, 2.4 Hz, 1H), 3.93–3.87 (m, 3H), 3.78 (dd, *J* = 9.6, 2.4 Hz, 1H), 3.69 (dd, *J* = 10.4, 4.4 Hz, 1H), 2.16–2.08 (m, 1H), 2.06–1.98 (m, 1H), 0.89 (s, 9H), 0.09 (s, 3H), –0.03 (s, 3H)
^{13}C-NMR (100 MHz, $CDCl_3$) δ 166.5, 138.9, 138.8, 138.7, 138.5, 138.4, 132.7, 130.2, 129.4, 128.3, 128.3, 128.3, 128.2, 128.2, 128.2, 127.7, 127.5, 127.5, 127.4, 127.3, 127.3, 127.1, 82.6, 78.8, 78.4, 73.7, 73.7, 73.4, 73.2, 71.5, 70.3, 69.5, 62.3, 30.7, 25.9, 18.0
IR (neat) 3088, 3067, 3030, 2953, 2931, 2886, 2857, 1719, 1599, 1584, 1496, 1453, 1389, 1363, 1314, 1274, 1111, 1028, 1002 cm^{-1}
HRMS (ESI) calcd for $C_{56}H_{66}NaO_8Si$ $[M+Na]^+$ 917.4425, found 917.4433.

(*R*)-3-((*tert*-Butyldimethylsilyl)oxy)-4-hydroxybutyl benzoate 34



A mixture of **41** (330 mg, 0.369 mmol, 1.0 equiv) and wet-type Pd-C (10% on carbon, 165 mg, 50% w/w) in THF (3.7 mL, 0.10 M) was strongly stirred for 1.5 h at room temperature under H_2 atmosphere. The reaction mixture was filtered through a filter paper by rinsing with MeOH. The combined filtrate was concentrated under reduced pressure.

To a stirred solution of the above crude product in THF and H_2O (4 : 1, 3.7 mL, 0.10 M) at room temperature was added $NaIO_4$ (592 mg, 2.77 mmol, 7.5 equiv). After the mixture was stirred for 2 h at room temperature, the reaction was quenched with H_2O (10 mL). The resulting mixture was extracted with AcOEt (3 x 20 mL). The combined organic phases were washed with H_2O (2 x 30 mL) and brine (2 x 30 mL), dried over Na_2SO_4, filtered and concentrated under reduced pressure.

To a stirred solution of the obtained crude product in MeOH (3.7 mL, 0.10 M) at 0 °C was added $NaBH_4$ (50.3 mg, 1.33 mmol, 3.6 equiv). After the mixture was stirred 1 h at room temperature, the reaction was quenched with saturated aqueous NH_4Cl (5.0 mL). The resulting mixture was extracted with $CHCl_3$ (3 x 20 mL). The combined organic phases were washed with H_2O (2 x 30 mL) and brine (2 x 30 mL), dried over Na_2SO_4, filtered and concentrated under reduced pressure. The obtained crude product was purified by silica gel column chromatography (Hexane : AcOEt = 8 : 1) to give **34** (48.3 mg, 0.149 mmol, 40% yield) as colorless oil.

Colorless oil; Rf value on TLC 0.30 (Hexane : AcOEt = 5 : 1); $[\alpha]_D^{23}$ +12.5 (*c* 1.0, $CHCl_3$)

^{1}H-NMR (400 MHz, $CDCl_3$) δ 8.05–8.02 (m, 2H), 7.59–7.54 (m, 1H), 7.47–7.42 (m,

2H), 4.45 (dt, *J* = 11.2, 6.0 Hz, 1H), 4.35 (ddd, *J* = 10.8, 6.8, 6.4 Hz, 1H), 4.03–3.98 (m, 1H), 3.68–3.65 (m, 1H), 3.58–3.53 (m, 1H), 2.06–1.93 (m, 2H), 1.87 (br s, 1H, -O<u>H</u>), 0.91 (s, 9H), 0.10 (s, 3H), 0.10 (s, 3H)

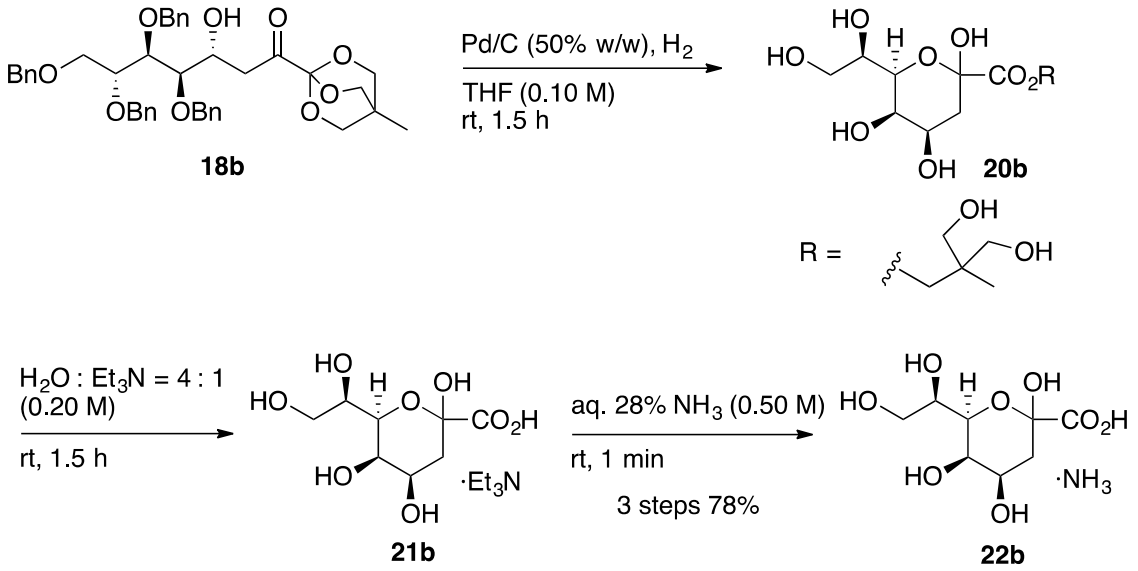
^{13}C-NMR (100 MHz, $CDCl_3$) δ 166.5, 132.9, 130.2, 129.5, 128.4, 69.8, 66.4, 61.6, 32.9, 25.8, 18.0, –4.5, –4.8

IR (neat) 3500, 3064, 3034, 2955, 2929, 2885, 2857, 1914, 1722, 1602, 1585, 1471, 1462, 1453, 1388, 1361, 1315, 1276, 1258, 1176, 1113, 1070, 1048, 1026, 1005, 937 cm^{-1}

HRMS (ESI) calcd for $C_{17}H_{28}NaO_4Si$ $[M+Na]^+$ 347.1655, found 347.1648.

Synthesis of Sialic acid and its analogues 22b, 24c and 26d

(4*R*,5*R*,6*R*)-6-((*R*)-1,2-Dihydroxyethyl)-2,4,5-trihydroxytetrahydro-2*H*-pyran-2-carboxylic acid, ammonia salt 22b[6]



A mixture of **18b** (340 mg, 0.498 mmol, 1.0 equiv) and wet-type Pd-C (10% on carbon, 170 mg, 50% w/w) in THF (4.8 mL, 0.10 M) was strongly stirred for 1.5 h at room temperature under H_2 atmosphere. The reaction mixture was filtered through a filter paper by rinsing with MeOH. The combined filtrate was concentrated under reduced pressure to give the crude product as colorless amorphous.

A solution of the crude product in H_2O and Et_3N (4 : 1, 2.5 mL, 0.20 M) was stirred for 1.5 h at room temperature. After the reaction mixture was concentrated under reduced pressure, the residue was passed through a column of silica gel ($CHCl_3$: MeOH = 30 : 1 then only MeOH) to remove 1,1,1-tris(hydroxymethyl)ethane. The obtained colorless amorphous was used for the next reaction without furthermore purification.

The obtained above product was treated with aqueous 28% NH_3 (0.96 mL, 0.50 M) for 1 min. After the mixture was evaporated under reduced pressure at room temperature to remove excess NH_3 as a gas, freeze drying of the aqueous solution afforded white solid. The obtained product was triturated with ethanol to give KDO·NH_3 **22b** (92.4 mg, 0.388 mmol, 78% yield) as white solid.

The physical data of the synthesized compound **22b** were good agreement with those reported in the references 6 (Mp, Rf value and ^{1}H-NMR), 7 (specific optical rotation), 8 (^{13}C-NMR), and 9 (IR and Mass). The ^{1}H and ^{13}C-NMR spectra of the synthesized compound **22b** was also good agreement with those of the commercially available KDO.[d]

White solid; Mp 122–123 °C; Rf value on TLC 0.56 (MeOH : $CHCl_3$: H_2O = 10 : 10 : 3); $[\alpha]_D^{25}$ +35.7 (*c* 1.0, H_2O)

Mixture of α-pyranose form, furanose form and lactone form[3]; ^{1}H-NMR (400 MHz, D_2O) δ 4.53–4.43 (m), 4.06–3.99 (m), 3.89–3.57 (m), 1.96[e] (dd, *J* = 12.8, 12.0 Hz, 1H), 1.86[e] (ddd, *J* = 12.8, 5.6, 1.2 Hz, 1H)

^{13}C-NMR (100 MHz, D_2O) δ 177.5, 176.9, 176.7, 175.4, 104.2, 103.0, 97.3, 96.4, 85.5, 85.0, 73.6, 72.5, 71.5, 71.5, 71.1, 70.9, 70.7, 69.8, 69.2, 69.0, 67.6, 66.6, 66.2, 65.3, 63.8, 63.0, 62.9, 62.9, 44.6, 43.5, 35.1, 33.6

IR (KBr) 3386, 2944, 1605, 1400, 1214, 1137, 1078, 1041, 1004 cm^{-1}

HRMS (FAB, thioglycerol and glycerol) calcd for $C_8H_{18}NO_8$ $[M+H]^+$ 256.1032, found 256.1021.

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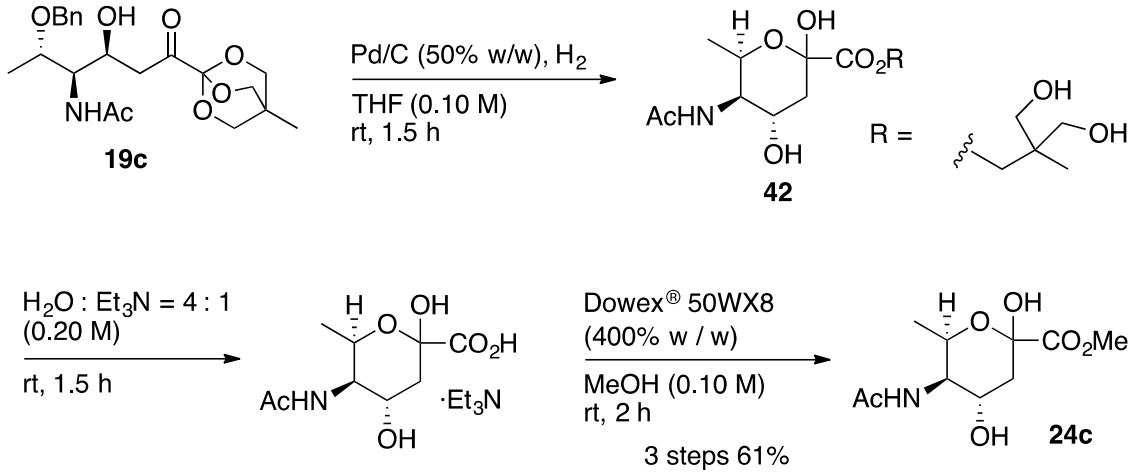
[d] Purchased from Sigma-Aldorich Co.

[e] C-3 protons for α-pyranose form.

Methyl (4*S*,5*R*,6*R*)-5-acetamido-2,4-dihydroxy-6-methyltetrahydro-2*H*-pyran-2-carboxylate 24c



A mixture of **19c** (112 mg, 0.275 mmol, 1.0 equiv) and wet-type Pd-C (10% on carbon, 56.0 mg, 50% w/w) in THF (2.8 mL, 0.10 M) was strongly stirred for 1.5 h under H_2 atmosphere. The reaction mixture was filtered through a filter paper by rinsing with MeOH. The combined filtrate was concentrated under reduced pressure to give the crude product as colorless amorphous.

A solution of the crude product in H_2O and Et_3N (4 : 1, 1.4 mL, 0.20 M) was stirred for 1.5 h at room temperature. After the reaction mixture was concentrated under reduced pressure, the residue was passed through a column of silica gel ($CHCl_3$: MeOH = 30 : 1 then only MeOH) to remove 1,1,1-tris(hydroxymethyl)ethane. The obtained product was used for the next reaction without furthermore purification.

A solution of the obtained above product in anhydrous MeOH (2.8 mL, 0.10 M) was treated with Dowex®50WX8 (400% w/w) at room temperature for 2 h. The mixture was filtered through a cotton filter, and concentrated under reduced pressure to give **24c** (41.7 mg, 0.169 mmol, 61% yield) as amorphous.

Amorphous; Rf value on TLC 0.30 ($CHCl_3$: MeOH = 5 : 1); $[\alpha]_D^{25}$ –30.1 (*c* 2.0, MeOH)

The NMR was observed as a mixture of anomers. For the major isomer: ^{1}H-NMR (400 MHz, CD_3OD) δ 3.95–3.85 (m, 2H), 3.77 (s, 3H), 3.51 (t, *J* = 10.0 Hz, 1H), 2.17 (dd, *J* = 12.8, 4.8 Hz, 1H), 1.99 (s, 3H), 1.87 (dd, *J* = 12.8, 11.6 Hz, 1H), 1.16 (d, *J* = 6.4 Hz,

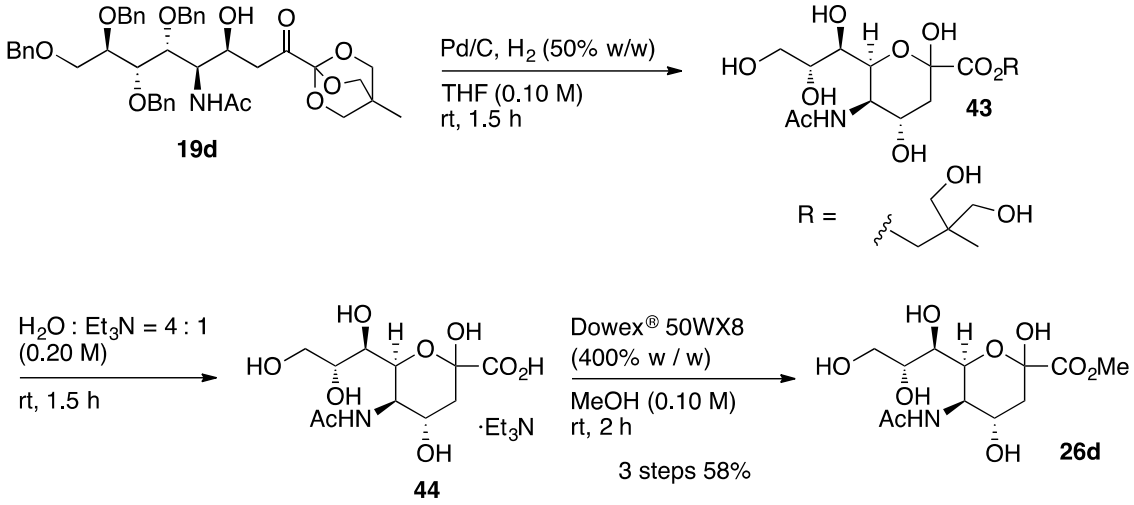
3H)

^{13}C-NMR (100 MHz, CD_3OD) δ 173.9, 171.9, 96.4, 70.0, 68.0, 59.5, 53.1, 41.0, 22.9, 18.4

IR (neat) 3358, 3289, 2983, 2953, 2941, 1745, 1659, 1642, 1634, 1556, 1443, 1379, 1307, 1279, 1221, 1155, 1126, 1089, 1029, 1000 cm^{-1}

HRMS (ESI) calcd for $C_{10}H_{17}NNaO_6$ $[M+Na]^+$ 270.0954, found 270.0944.

Methyl(4*S*,5*R*,6*S*)-5-acetamido-2,4-dihydroxy-6-((1*R*,2*R*)-1,2,3-trihydroxypropyl)tetrahydro-2*H*-pyran-2-carboxylate 26d



A mixture of **19d** (300 mg, 0.398 mmol, 1.0 equiv) and wet-type Pd-C (10% on carbon, 150 mg, 50% w/w) in THF (4.0 mL, 0.10 M) was strongly stirred for 1.5 h under H_2 atmosphere. The reaction mixture was filtered through a filter paper by rinsing with MeOH. The combined filtrate was concentrated under reduced pressure to give the crude product as colorless amorphous. A solution of the above crude product in H_2O and Et_3N (4 : 1, 2.0 mL, 0.20 M) was stirred for 1.5 h at room temperature. After the reaction mixture was concentrated under reduced pressure, the residue was passed through a column of silica gel ($CHCl_3$: MeOH = 30 : 1 then only MeOH) to remove 1,1,1-tris(hydroxymethyl)ethane. The obtained product was used for next reaction without purification. A solution of the above product in anhydrous MeOH (4.0 mL, 0.10 M) was treated with Dowex®50WX8 (400% w/w) at room temperature for 2 h. The

mixture was filtered through a cotton filter, and concentrated under reduced pressure to give **26d** (74.7 mg, 0.231 mmol, 58% yield) as white solid.

The physical data of the synthesized compound **26d** were good agreement with those reported in the references 10 (Mp) and 11 (^{1}H- and ^{13}C-NMR).

White solid; Mp 179–180 °C; Rf value on TLC 0.30 ($CHCl_3$: MeOH : AcOH : H_2O = 60 : 30 : 3 : 5); $[\alpha]_D^{25}$ –24.3 (*c* 0.5, MeOH)

^{1}H-NMR (400 MHz, CD_3OD) δ 4.07–3.96 (m, 2H), 3.85–3.78 (m, 2H), 3.78 (s, 3H), 3.72–3.68 (m, 1H), 3.62 (dd, *J* = 11.2, 5.6 Hz, 1H), 3.48 (dd, *J* = 8.8, 1.2 Hz, 1H), 2.22 (dd, *J* = 12.8, 5.2 Hz, 1H), 2.01 (s, 3H), 1.89 (dd, *J* = 12.8, 11.2 Hz, 1H)

^{13}C-NMR (100 MHz, CD_3OD) δ 175.1, 171.8, 96.7, 72.1, 71.7, 70.2, 67.9, 64.9, 54.3, 53.1, 40.7, 22.6

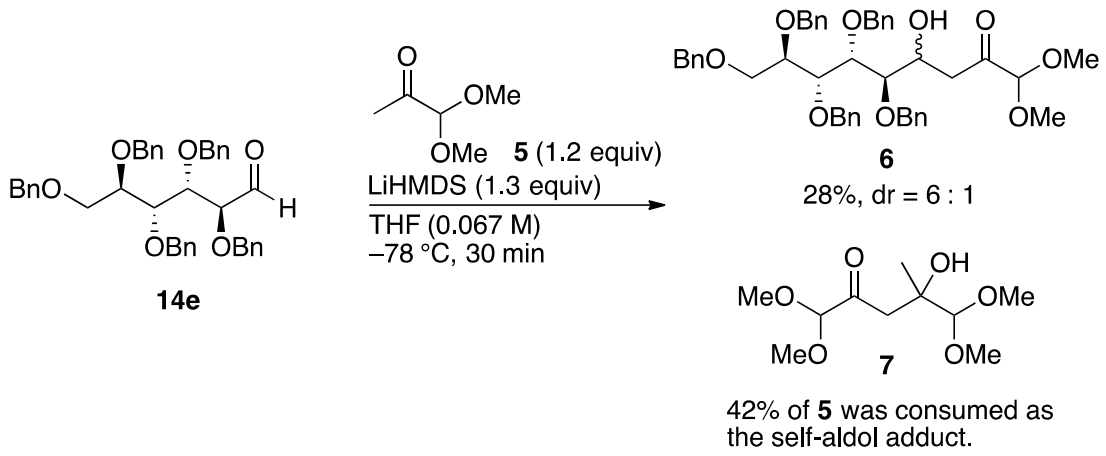
IR (KBr) 3386, 2959, 2936, 1749, 1742, 1701, 1686, 1654, 1638, 1627, 1560, 1542, 1509, 1490, 1475, 1458, 1438, 1375, 1311, 1279, 1127, 1069, 1035, 946 cm^{-1}

HRMS (ESI) calcd for $C_{12}H_{21}NNaO_9$ $[M+Na]^+$ 346.1114, found 346.1120.

Aldol reaction of aldehyde 14e and pyruvaldehyde dimethyl acetal 5

(5*R*,6*R*,7*R*,8*R*)-5,6,7,8,9-Pentakis(benzyloxy)-4-hydroxy-1,1-dimethoxynonan-2-one 6

4-Hydroxy-1,1,5,5-tetramethoxy-4-methylpentan-2-one 7



To a stirred solution of LiHMDS (1.0 M in THF solution, 0.207 mL, 0.207 mmol, 1.3 equiv) in THF (1.59 mL, 0.10 M) at –78 °C was added dropwise a solution of pyruvic aldehyde dimethyl acetal **5** (22.6 mg, 0.191 mmol, 1.2 equiv) in THF (0.40 mL, 0.40 M) under N_2 atmosphere. After 30 min at –78 °C, a solution of aldehyde **14e** (100 mg, 0.159 mmol, 1.0 equiv) in THF (0.40 mL, 0.40 M) was added, and the resulting mixture was furthermore stirred for 30 min at –78 °C. The reaction was quenched with phosphate buffer (pH 6.86, 2.0 mL), and the mixture was allowed to gently warm up to room temperature. The resulting mixture was extracted with AcOEt (3 x 20 mL), washed with H_2O (2 x 50 mL) and brine (2 x 50 mL), dried over Na_2SO_4, filtered and concentrated under reduced pressure. The obtained crude product was purified by silica gel column chromatography (Hexane : AcOEt = 2 : 1) to give the aldol adduct **6** (33.6 mg, 0.0449 mmol, 28% yield, dr = 6 : 1) as colorless oil and the self-aldol adduct **7** (7.89 mg, 0.0334 mmol, 42% of pyruvic aldehyde dimethyl acetal **5** was consumed as the self-aldol adduct) as colorless oil.

The following physical data of **6** were measured as a 6 : 1 mixture of diastereomers. Colorless oil; Rf value on TLC 0.54 (Hexane : AcOEt = 2 : 1); $[\alpha]_D^{23}$ +18.7 (*c* 1.5,

$CHCl_3$)

For the major isomer : ^{1}H-NMR (400 MHz, $CDCl_3$) δ 7.34–7.22 (m, 25H), 4.73–4.63 (m, 5H), 4.55–4.48 (m, 5H), 4.45–4.41 (m, 1H), 4.42 (s, 1H), 4.06–4.01 (m, 2H), 3.89–3.86 (m, 2H), 3.76–3.70 (m, 1H), 3.67 (dd, *J* = 6.0, 3.2 Hz, 1H), 3.34 (s, 3H), 3.34 (s, 3H), 2.96 (dd, *J* = 17.6, 3.2 Hz, 1H), 2.81 (dd, *J* = 17.6, 9.2 Hz, 1H)

^{13}C-NMR (100 MHz, $CDCl_3$) δ 206.0, 138.7, 138.6, 138.4, 138.3, 138.1, 128.3, 128.3, 128.2, 128.2, 128.2, 127.9, 127.9, 127.8, 127.7, 127.7, 127.6, 127.6, 127.5, 127.4, 127.4, 103.6, 82.4, 79.7, 79.6, 78.9, 74.4, 73.4, 72.8, 71.8, 69.4, 67.7, 54.4, 41.5 cm^{-1}

IR (neat) 3491, 3087, 3062, 3030, 3004, 2929, 2910, 2867, 1728, 1605, 1586, 1496, 1454, 1392, 1364, 1208, 1093, 1071, 1027 cm^{-1}

HRMS (ESI) calcd for $C_{46}H_{52}NaO_9$ $[M+Na]^+$ 771.3509, found 771.3510.

Self-aldol adduct **7**: Colorless oil; Rf value on TLC 0.16 (Hexane : AcOEt = 2 : 1)

^{1}H-NMR (400 MHz, $CDCl_3$) δ 4.55 (s, 1H), 4.11 (s, 1H), 3.51 (s, 3H), 3.51 (s, 3H), 3.41 (s, 3H), 3.40 (s, 3H), 2.96 (d, *J* = 16.4 Hz, 1H), 2.57 (d, *J* = 16.4 Hz, 1H), 1.23 (s, 3H)

^{13}C-NMR (100 MHz, $CDCl_3$) δ 206.1, 110.1, 103.7, 75.0, 58.0, 57.9, 54.6, 54.4, 42.6, 23.1

IR (neat) 3480, 2932, 2835, 1727, 1454, 1375, 1190, 1104, 1076, 993 cm^{-1}

HRMS (ESI) calcd for $C_{10}H_{20}NaO_6$ $[M+Na]^+$ 259.1158, found 259.1149.

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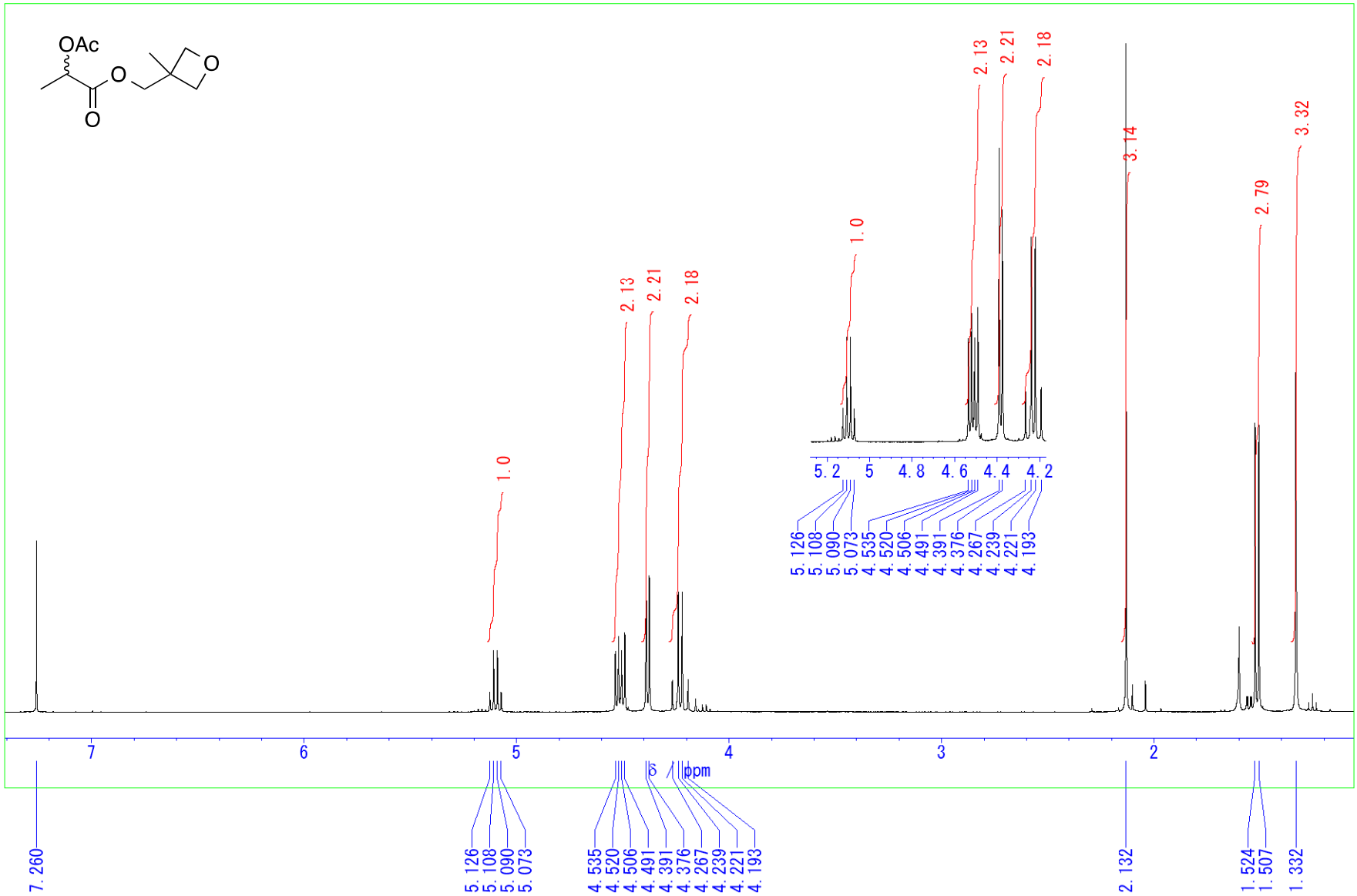
(3-methyloxetan-3-yl)methyl 2-acetoxypropanoate 10

YN-data-ortho-3



(3-methyloxetan-3-yl)methyl 2-acetoxypropanoate 10

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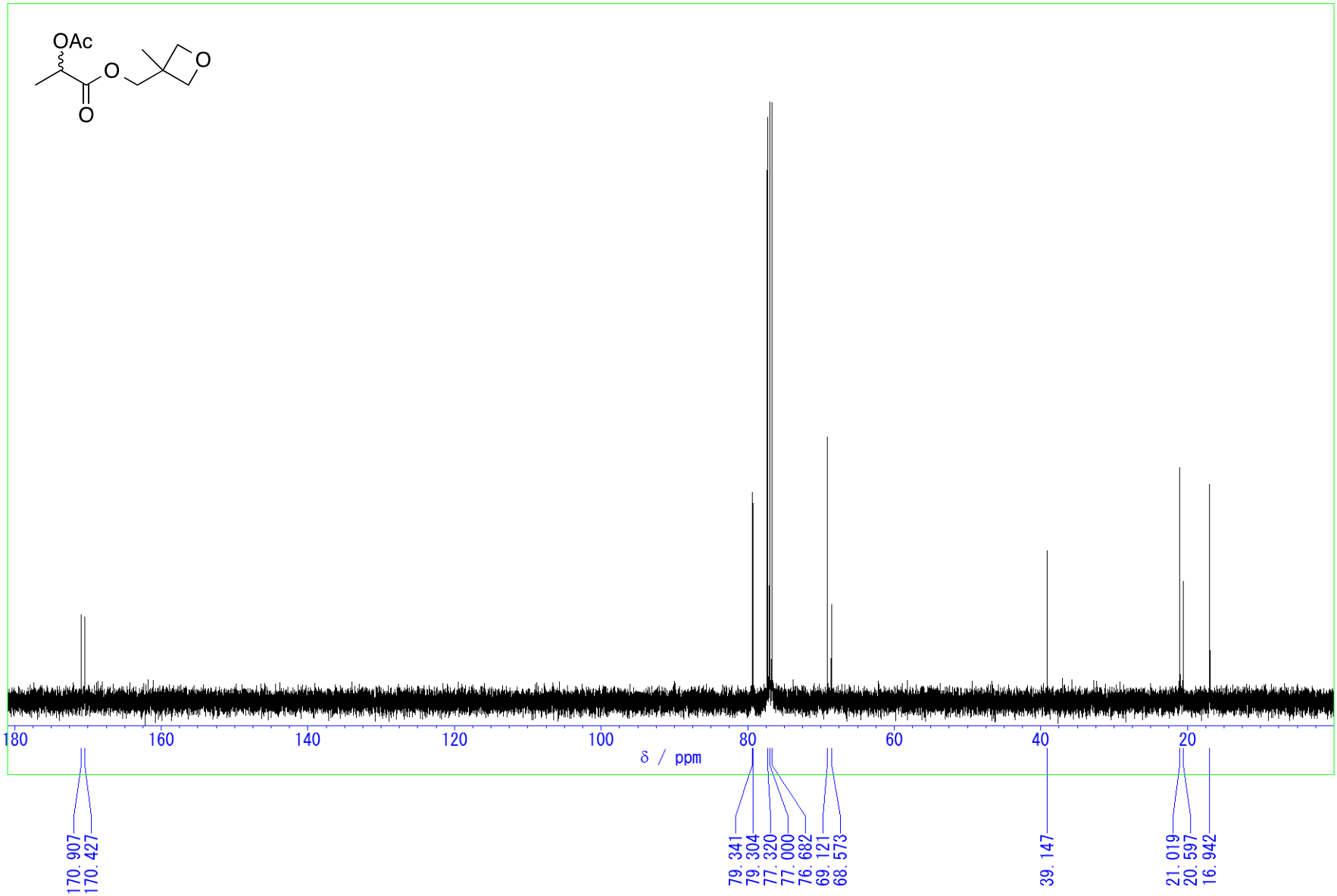

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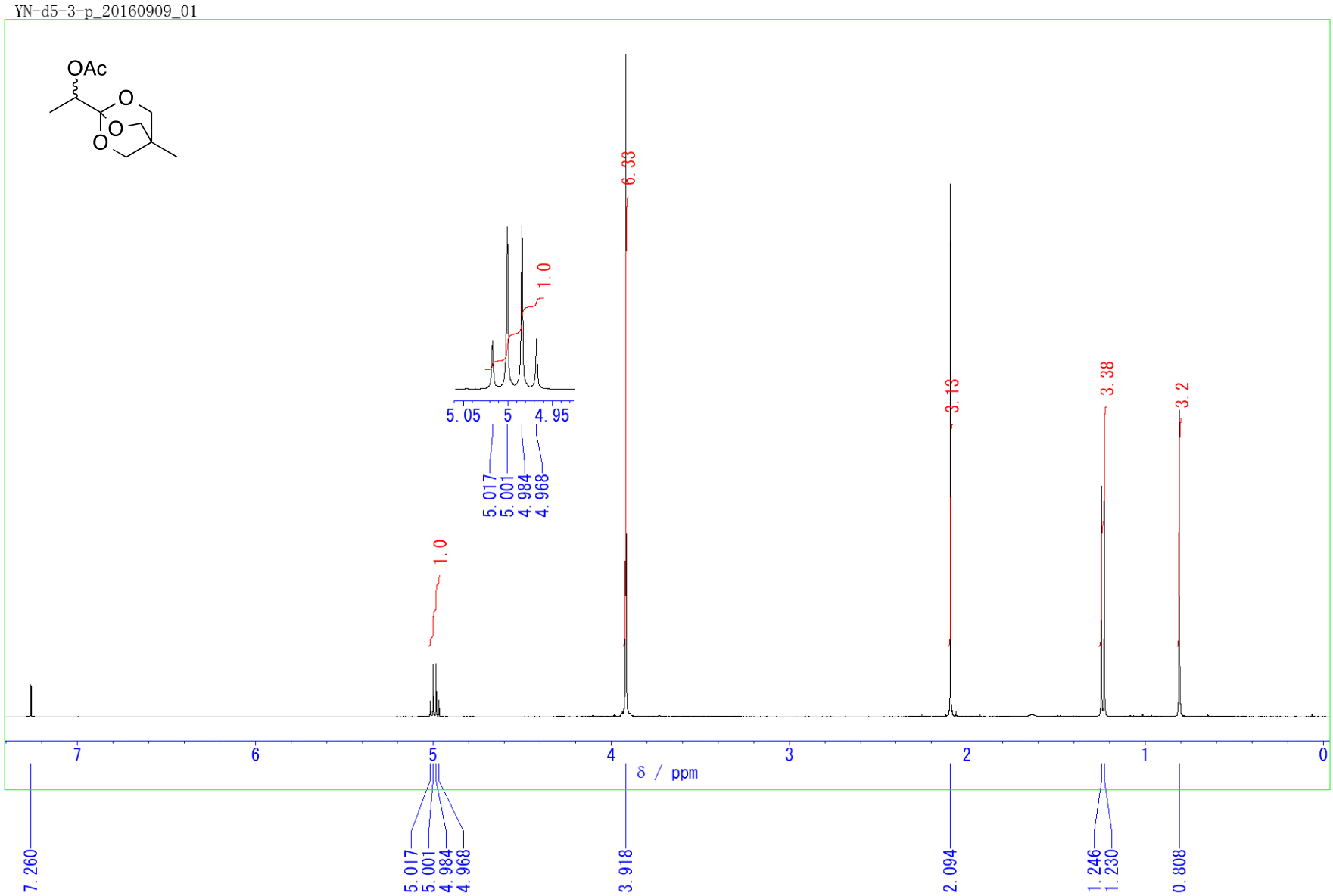

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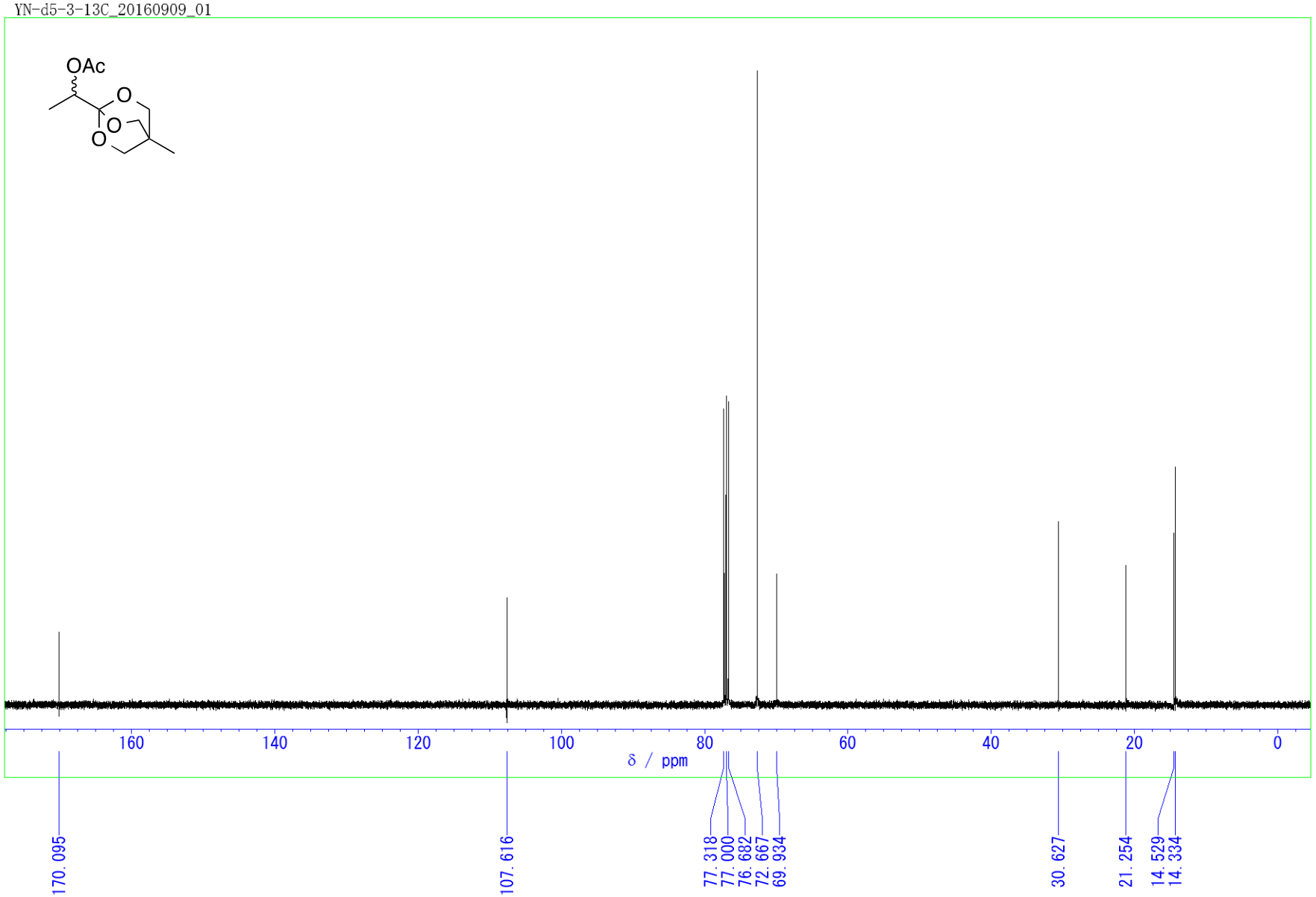

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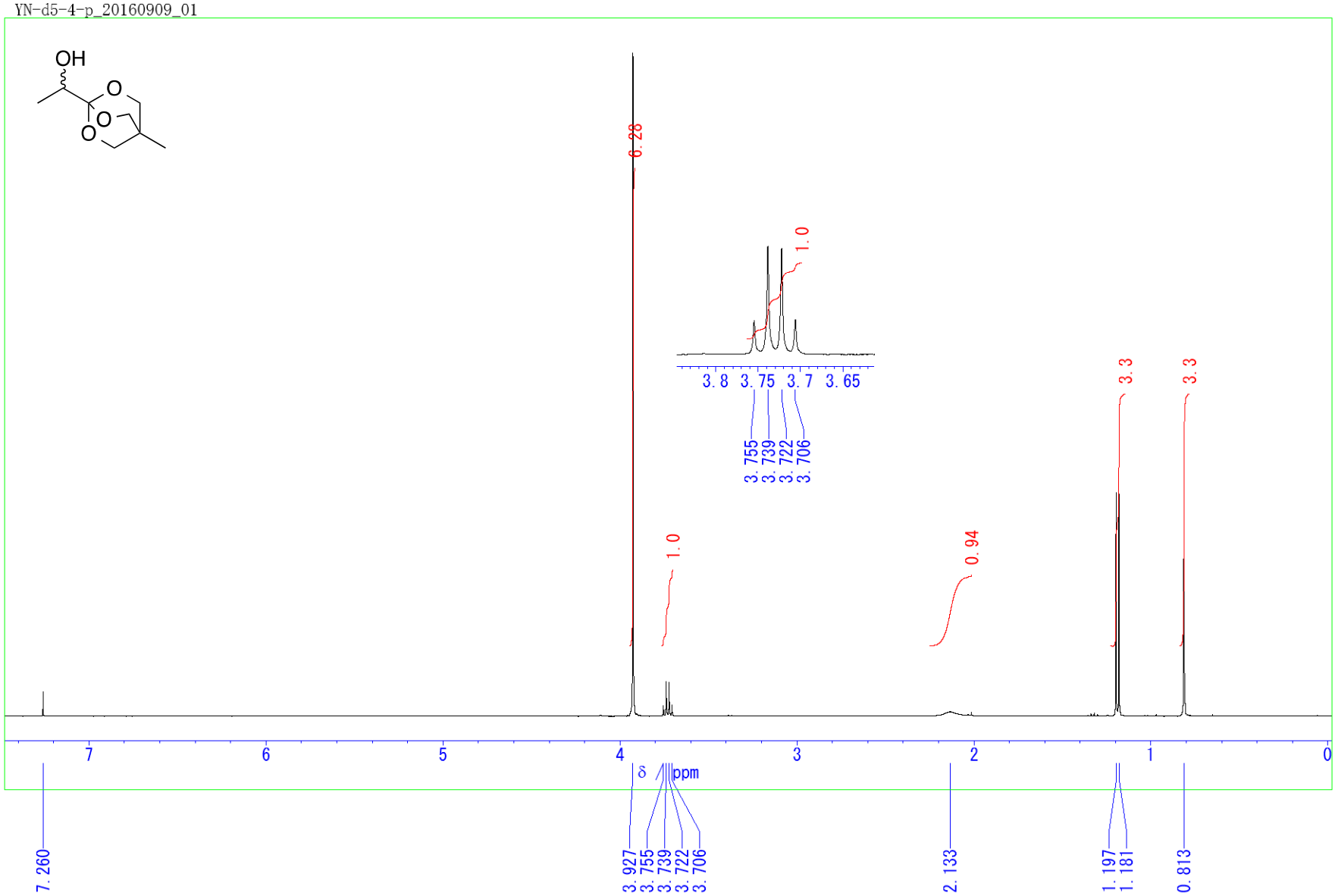

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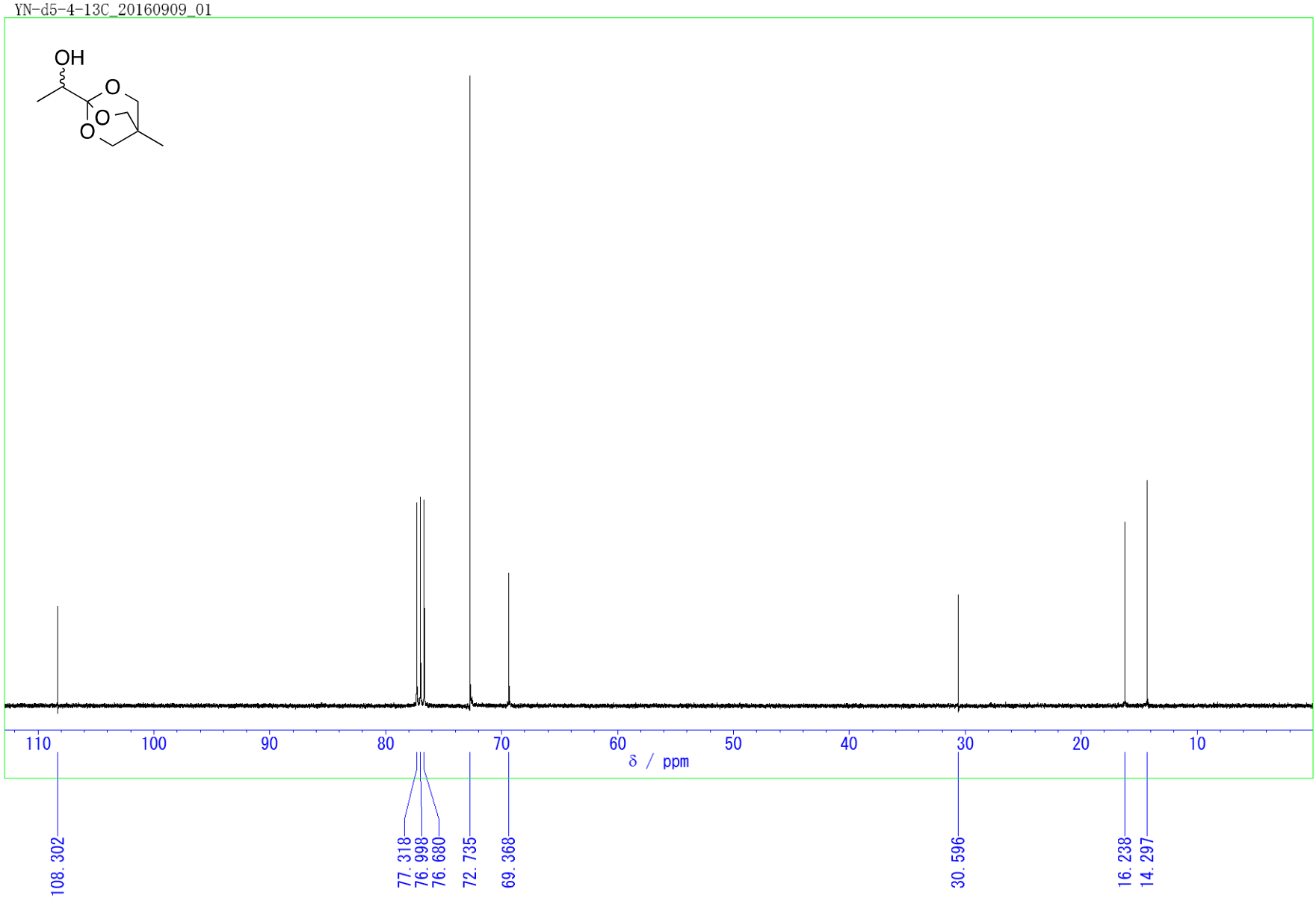
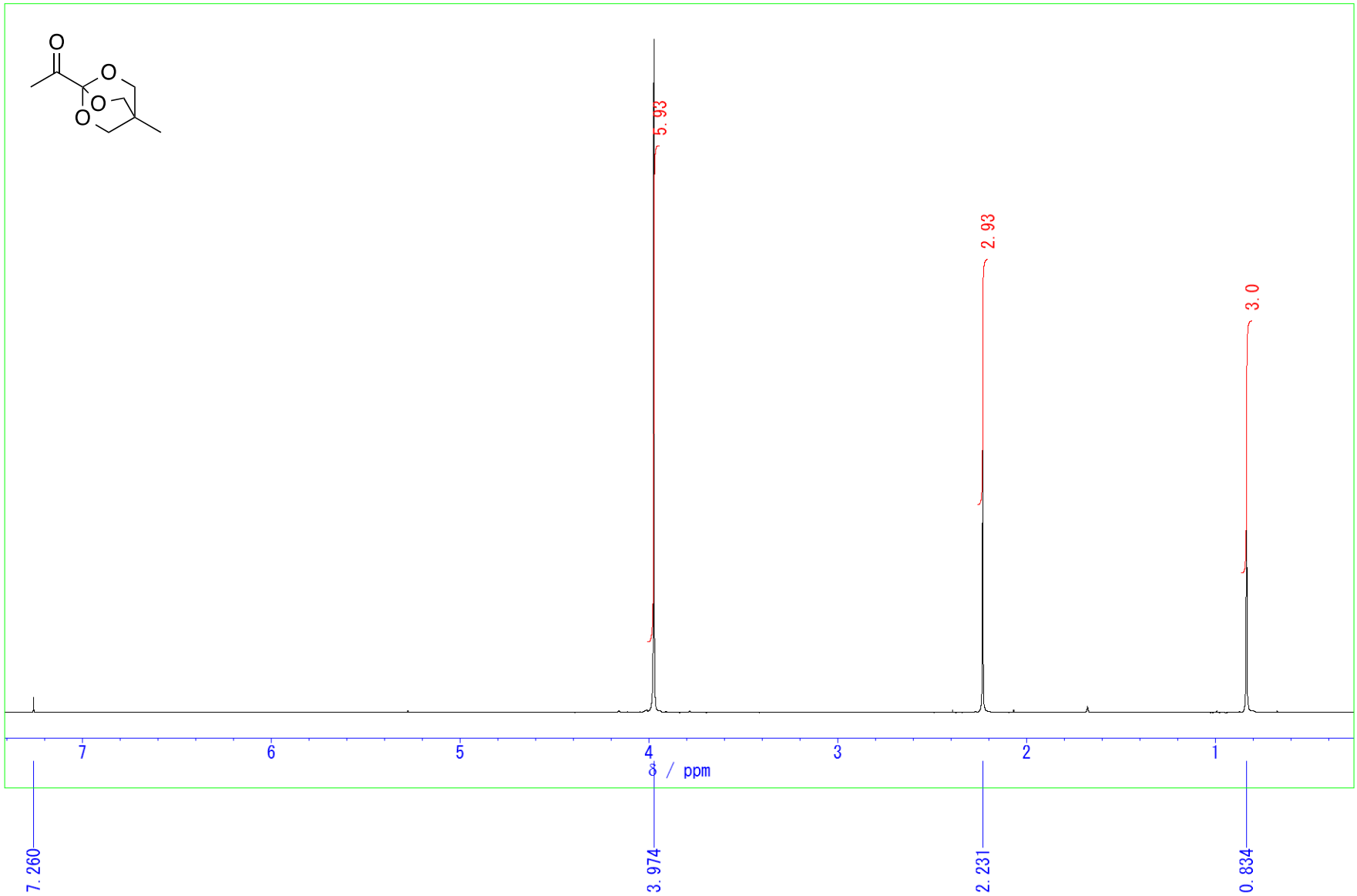
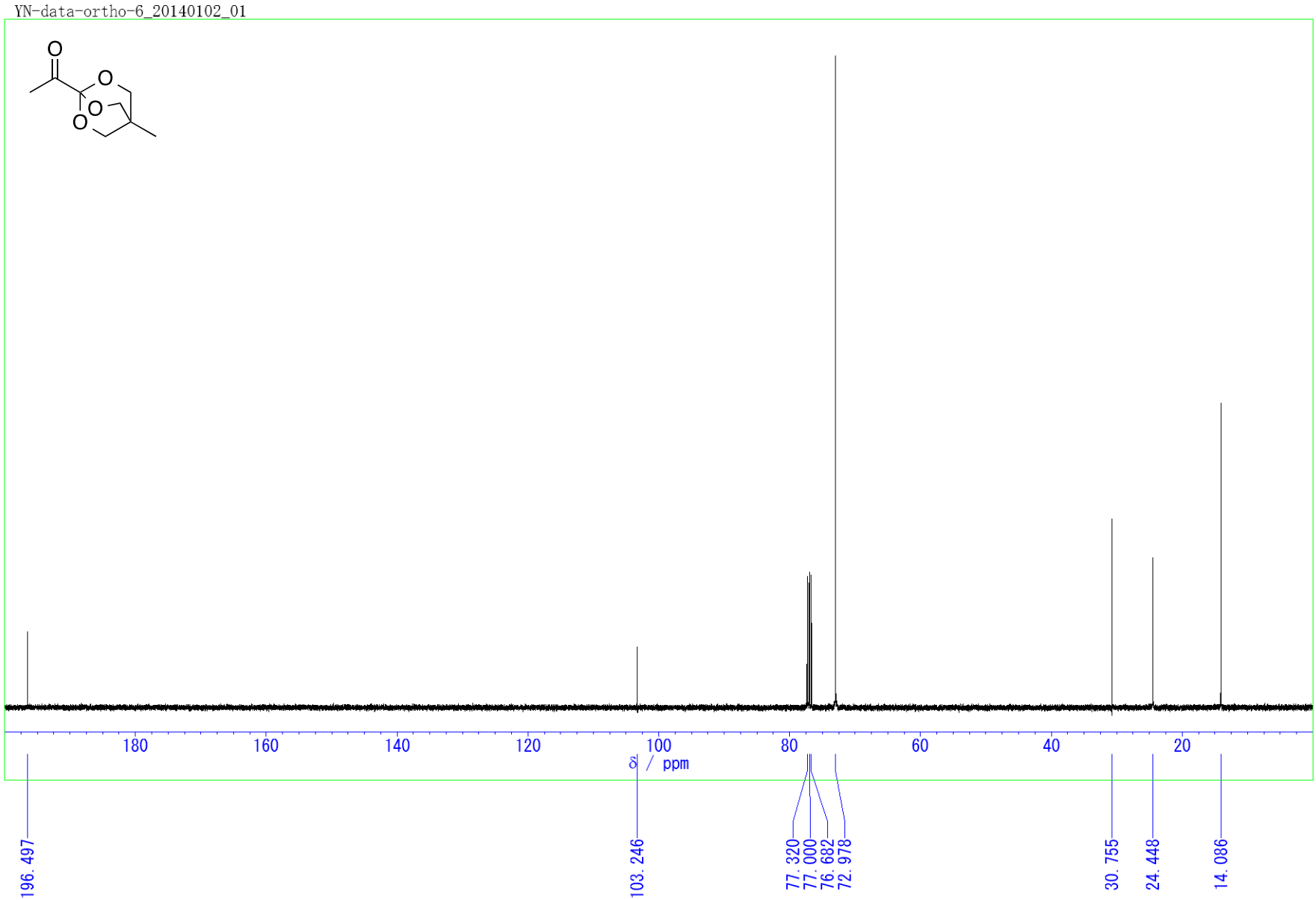


1-(4-methyl-2,6,7-trioxabicyclo[2.2.2]octan-1-yl)ethan-1-one 8

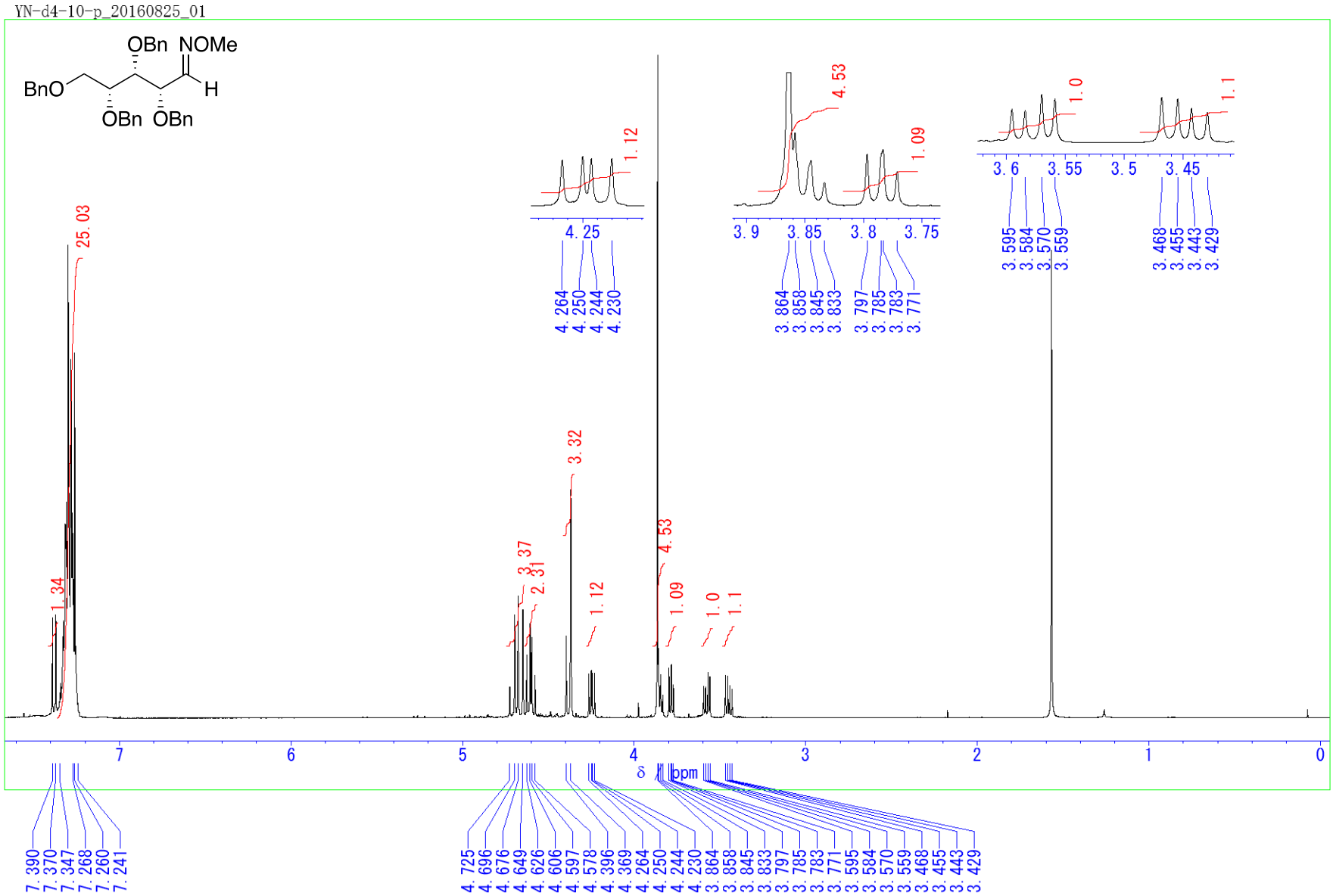
YN-data-ortho-6



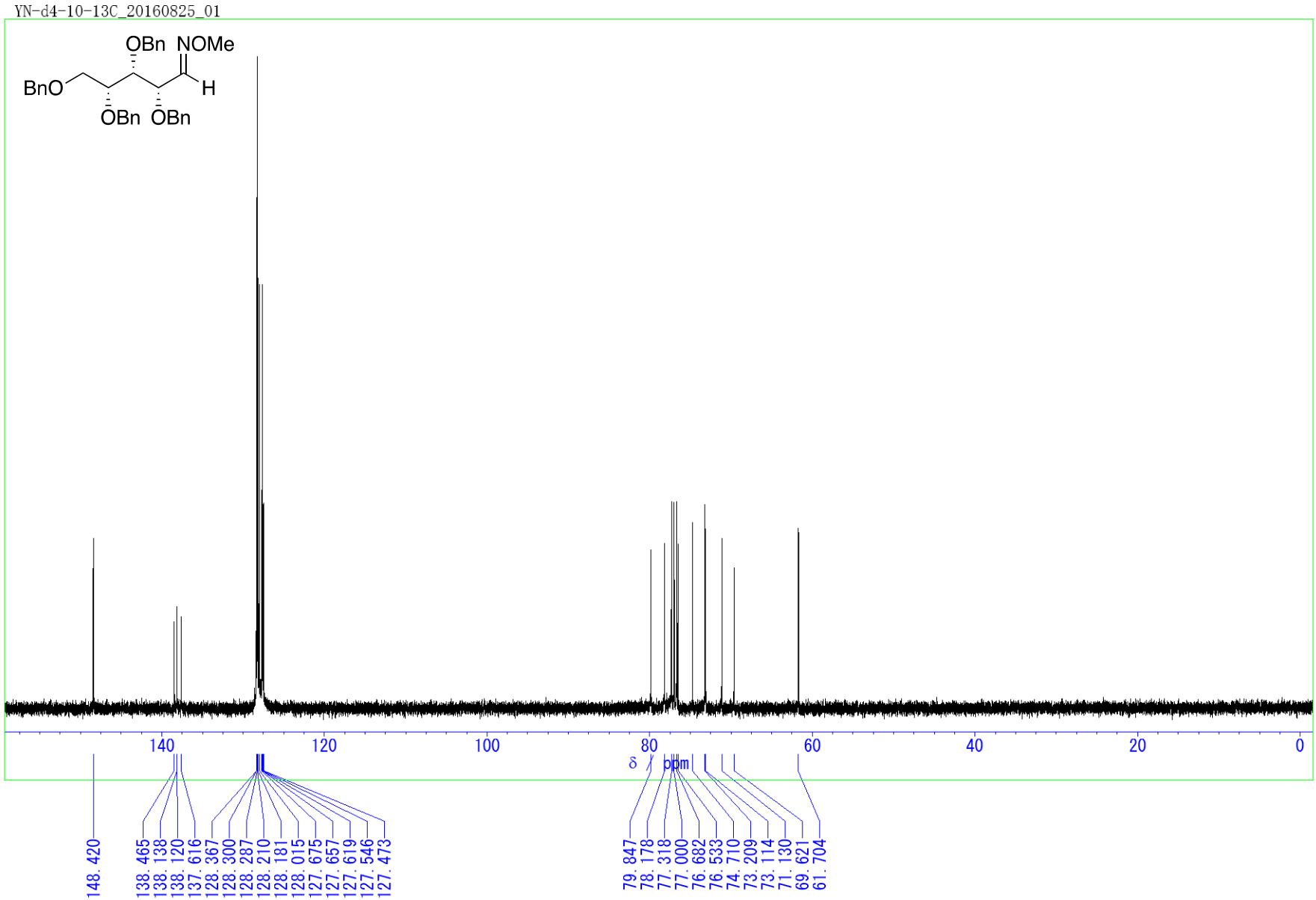
1-(4-methyl-2,6,7-trioxabicyclo[2.2.2]octan-1-yl)ethan-1-one 8



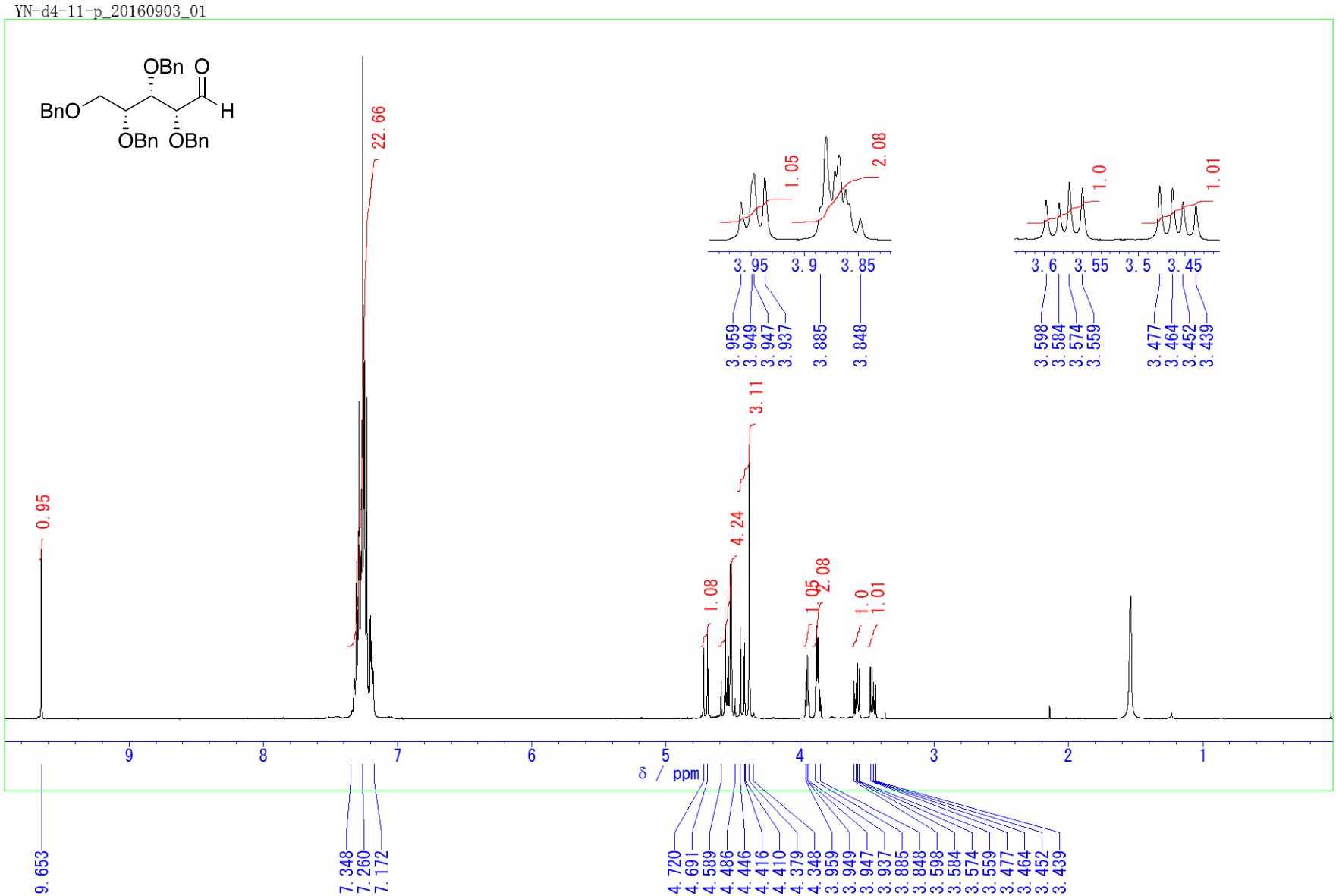
(2*S*,3*R*,4*R*)-2,3,4,5-tetrakis(benzyloxy)pentanal *O*-methyl oxime 13a



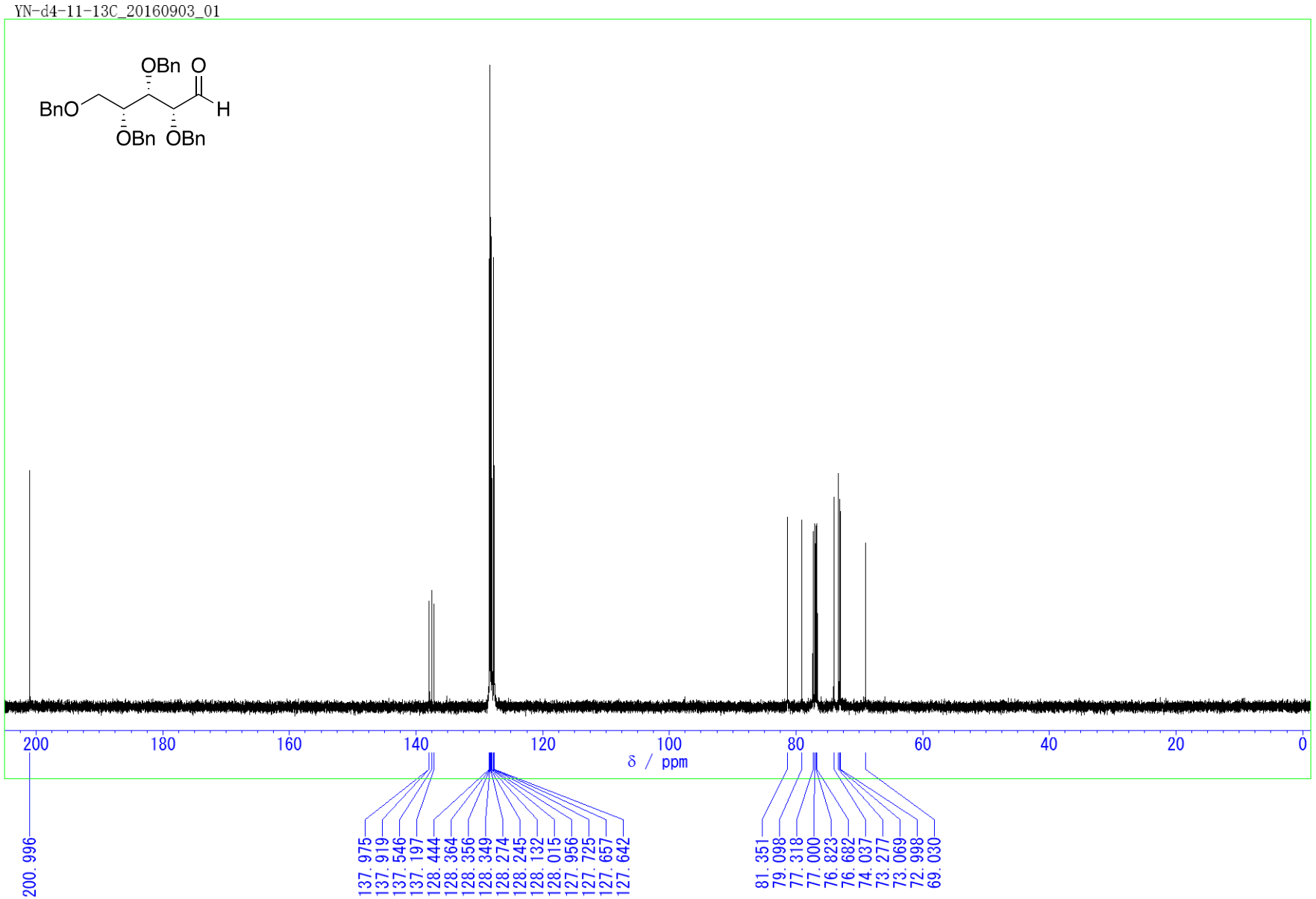
(2*S*,3*R*,4*R*)-2,3,4,5-tetrakis(benzyloxy)pentanal *O*-methyl oxime 13a



(2*R*,3*S*,4*R*)-2,3,4,5-tetrakis(benzyloxy)pentanal 14a



(2*R*,3*S*,4*R*)-2,3,4,5-tetrakis(benzyloxy)pentanal 14a



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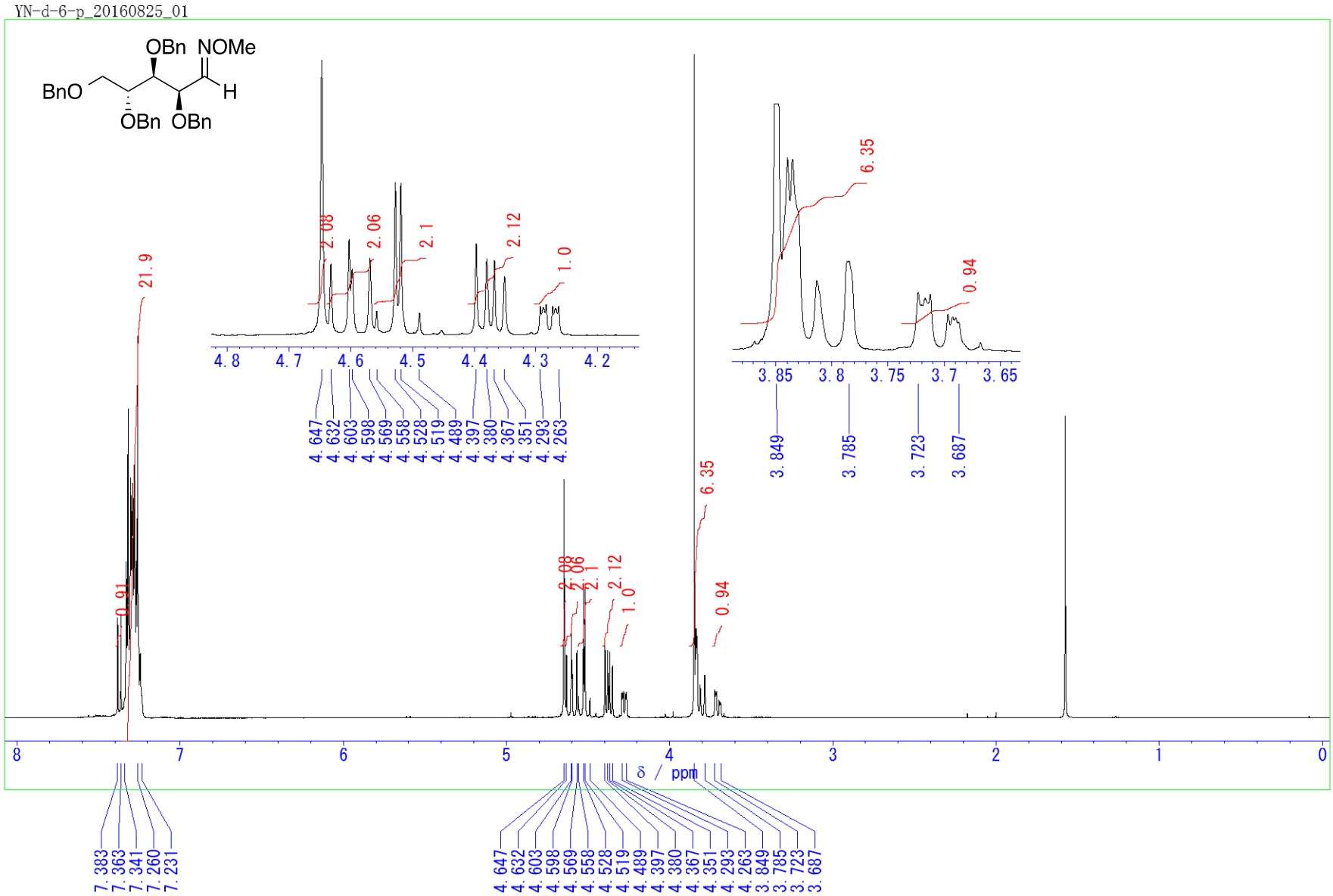
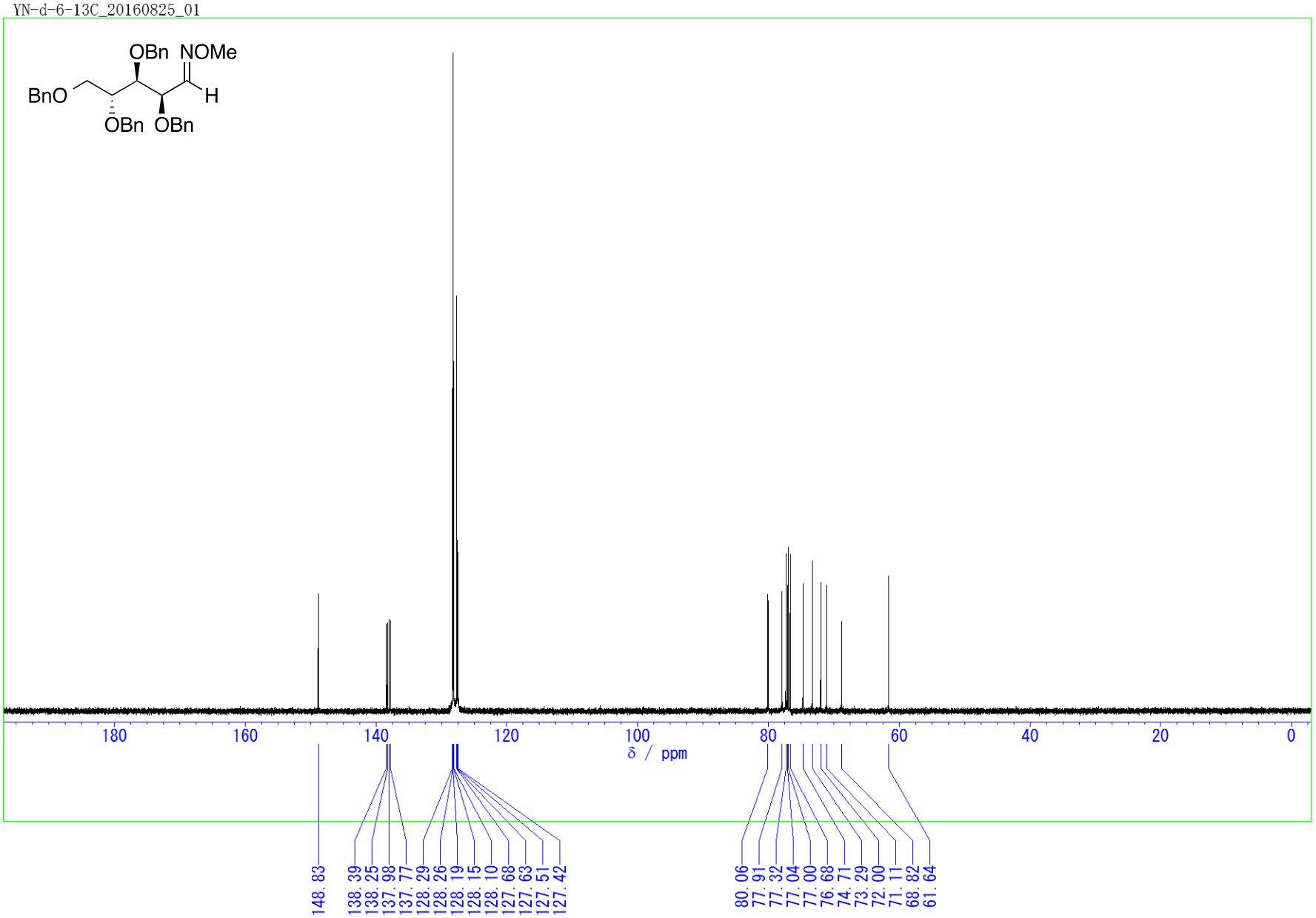
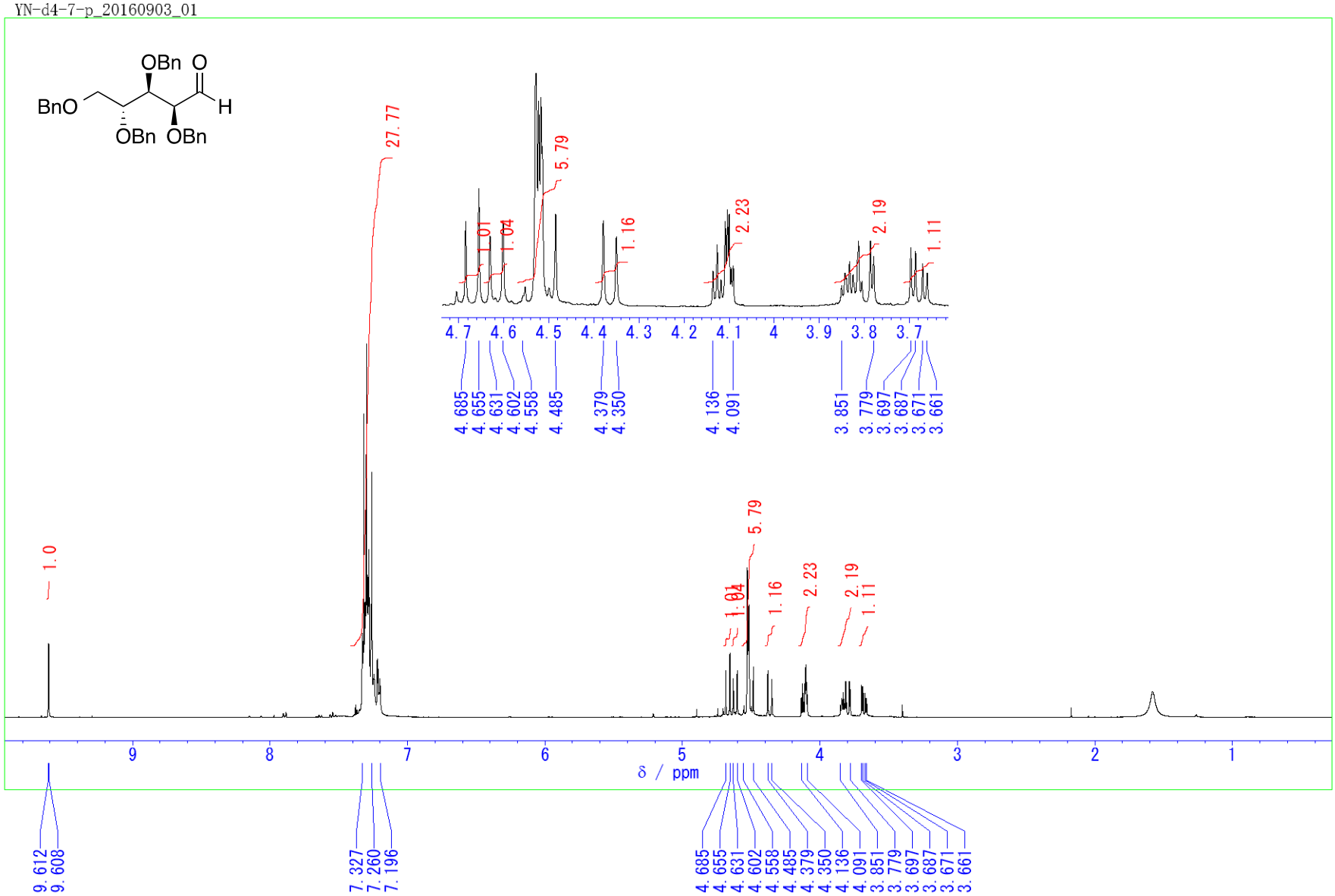


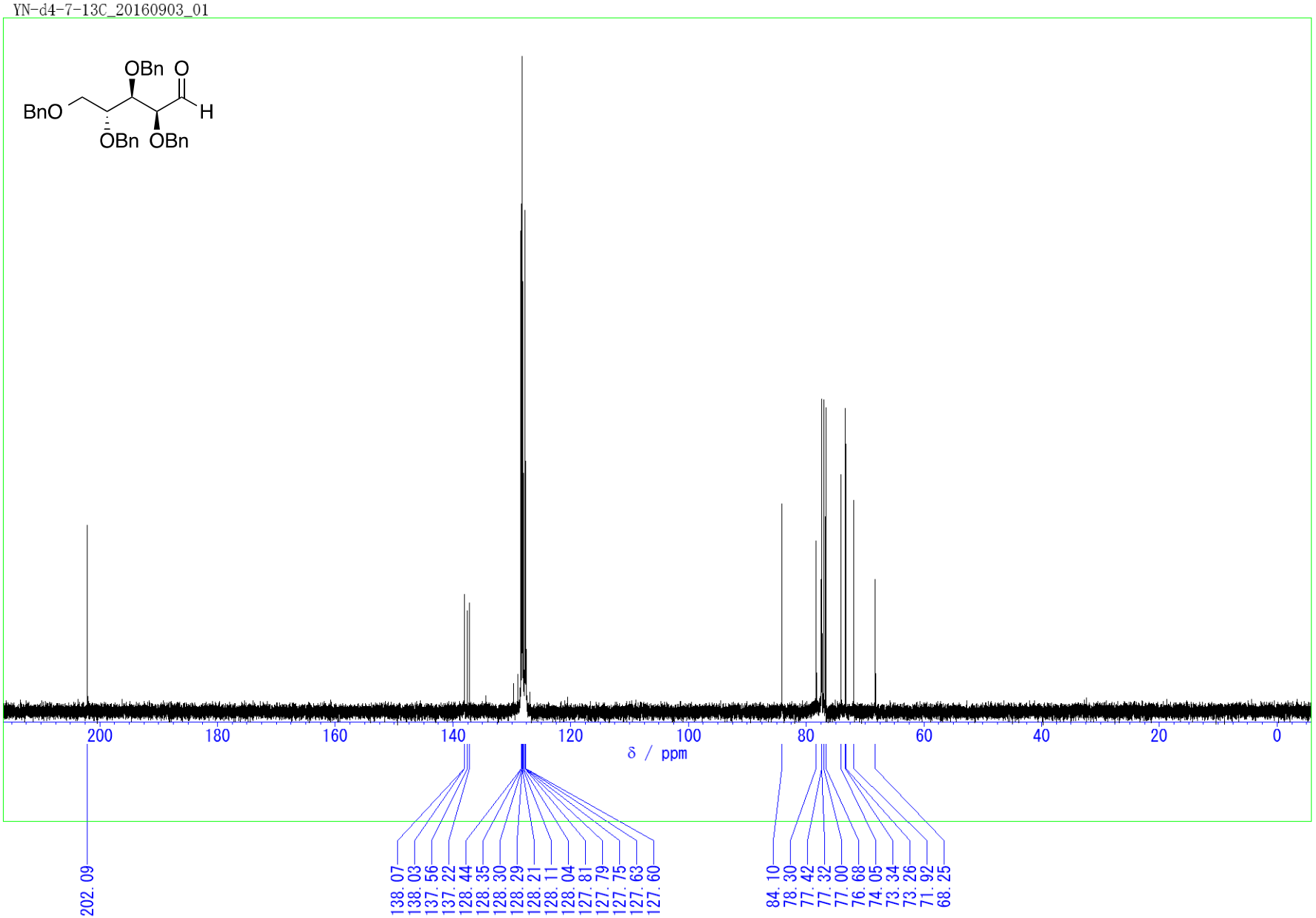
(2*R*,3*S*,4*R*)-2,3,4,5-tetrakis(benzyloxy)pentanal *O*-methyl oxime 13b



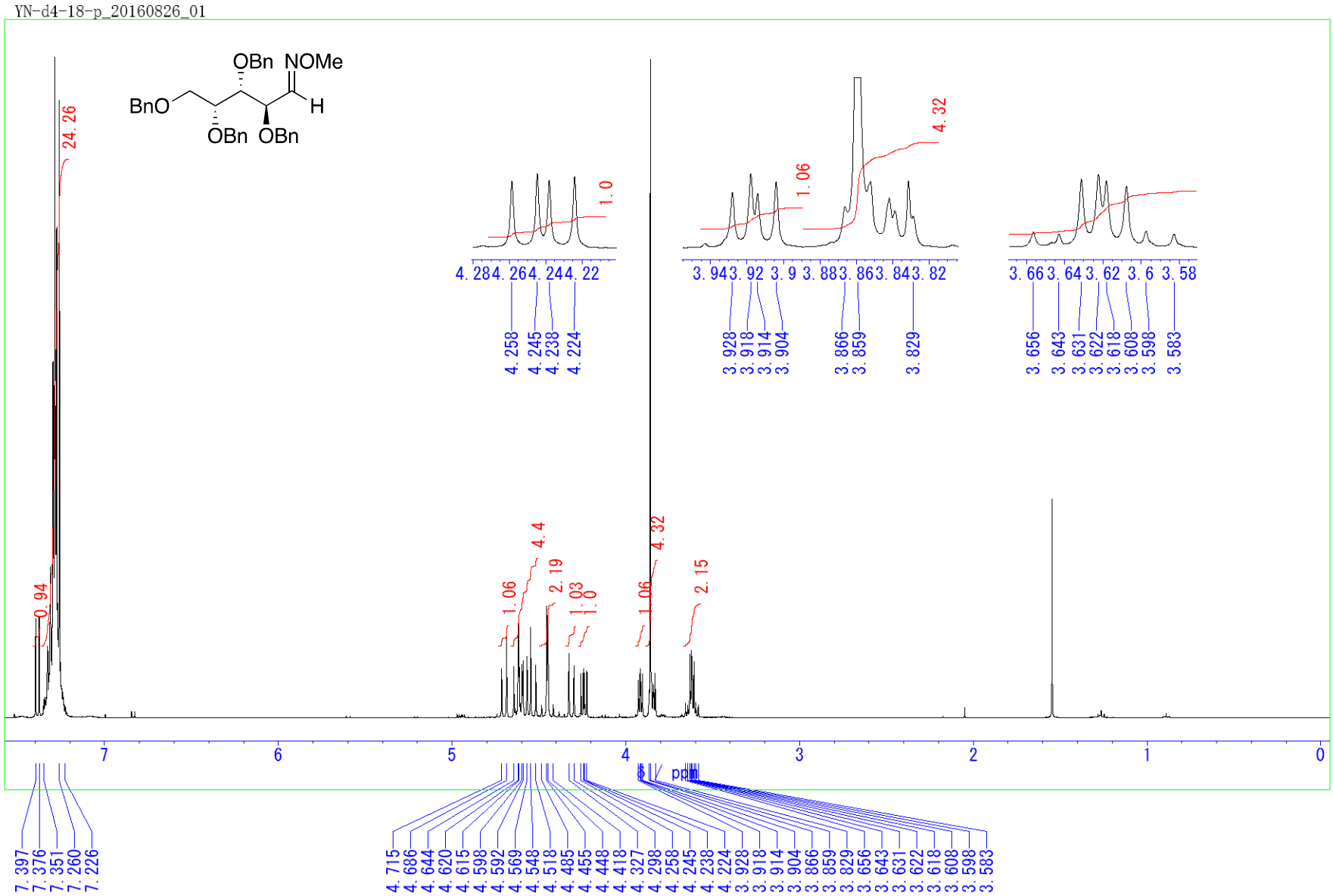
(2*S*,3*R*,4*R*)-2,3,4,5-tetrakis(benzyloxy)pentanal 14b



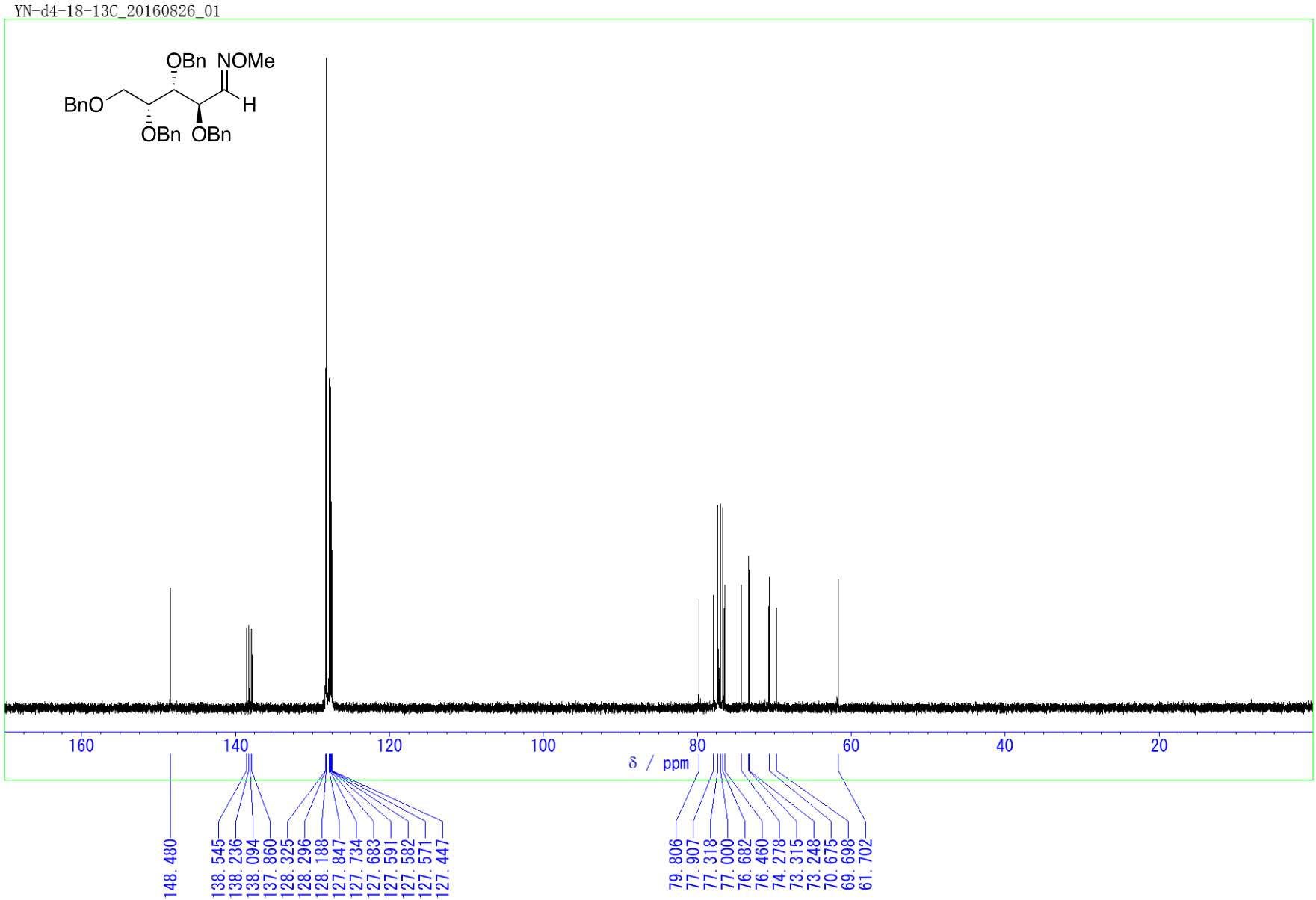
(2*S*,3*R*,4*R*)-2,3,4,5-tetrakis(benzyloxy)pentanal 14b



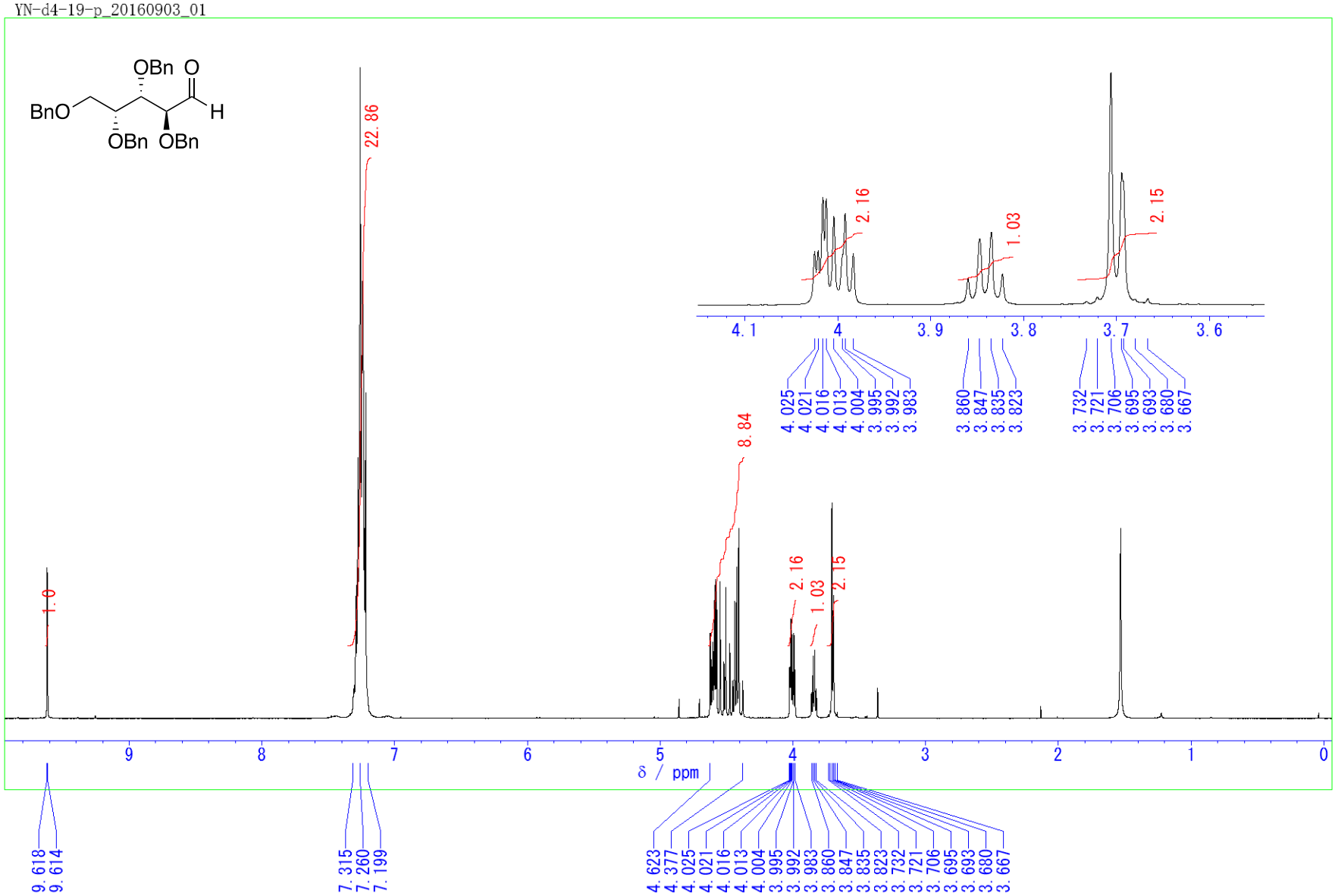
(2*R*,3*R*,4*R*)-2,3,4,5-tetrakis(benzyloxy)pentanal *O*-methyl oxime 13c



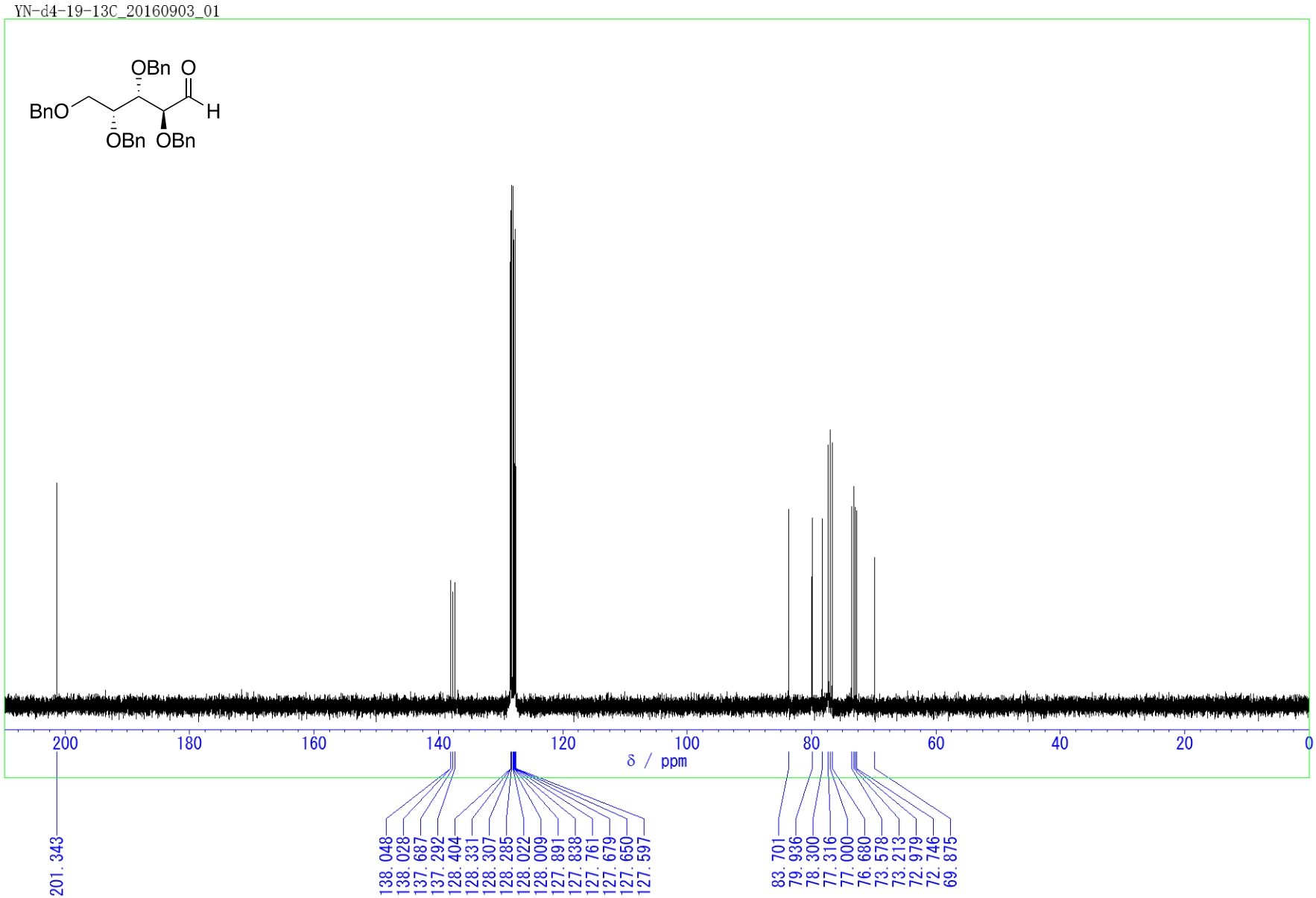
(2*R*,3*R*,4*R*)-2,3,4,5-tetrakis(benzyloxy)pentanal *O*-methyl oxime 13c



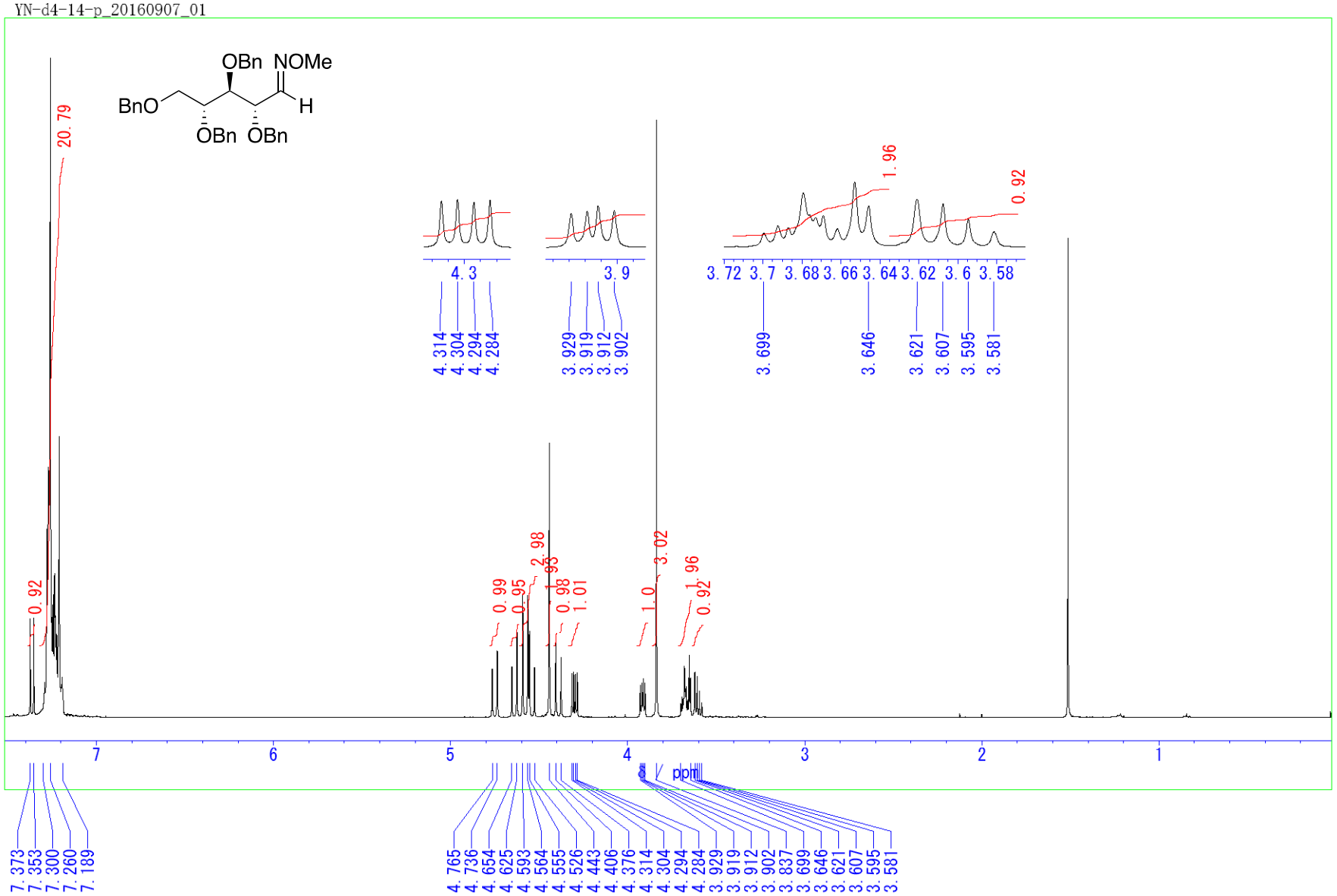
(2*S*,3*S*,4*R*)-2,3,4,5-tetrakis(benzyloxy)pentanal 14c



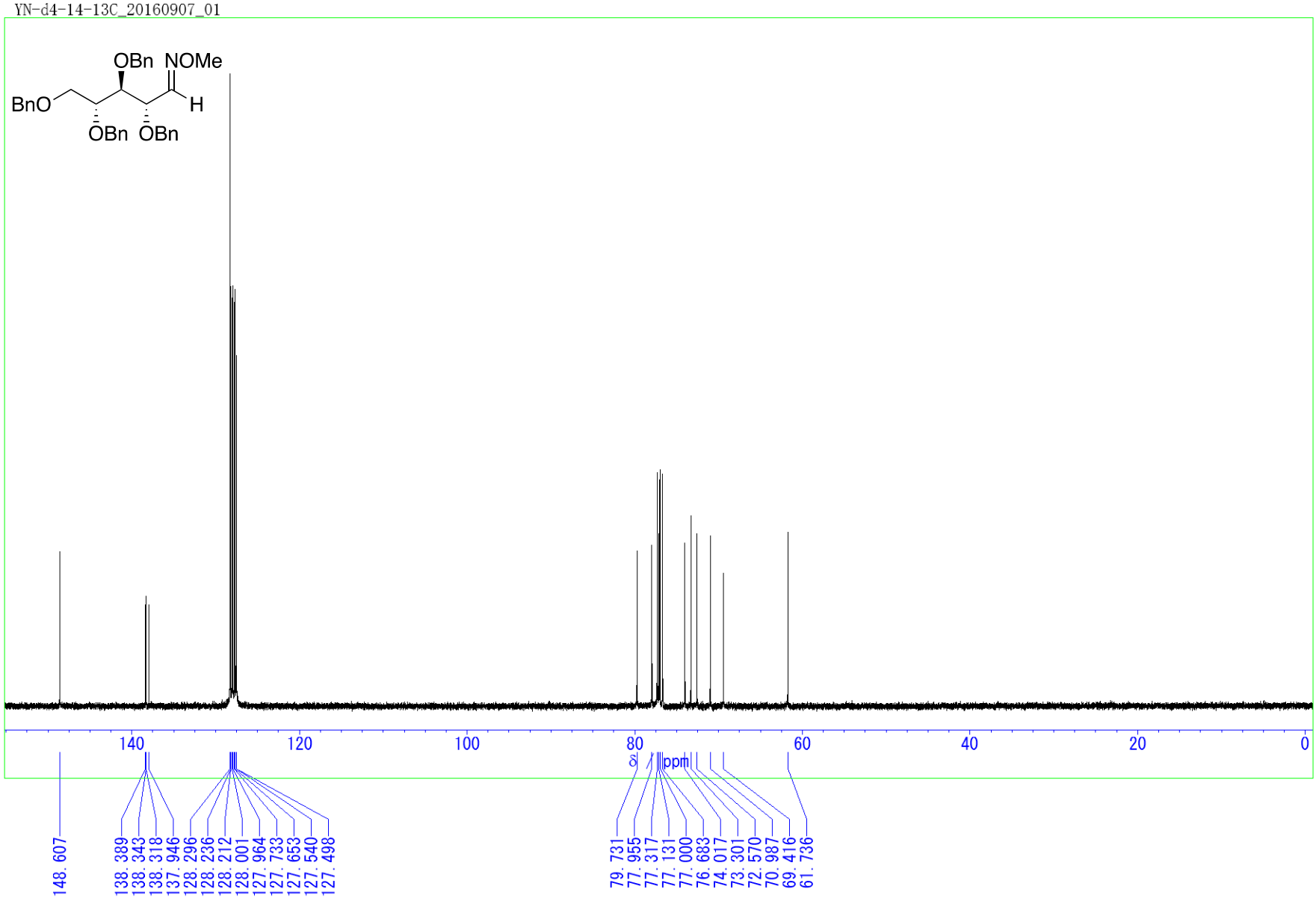
(2*S*,3*S*,4*R*)-2,3,4,5-tetrakis(benzyloxy)pentanal 14c



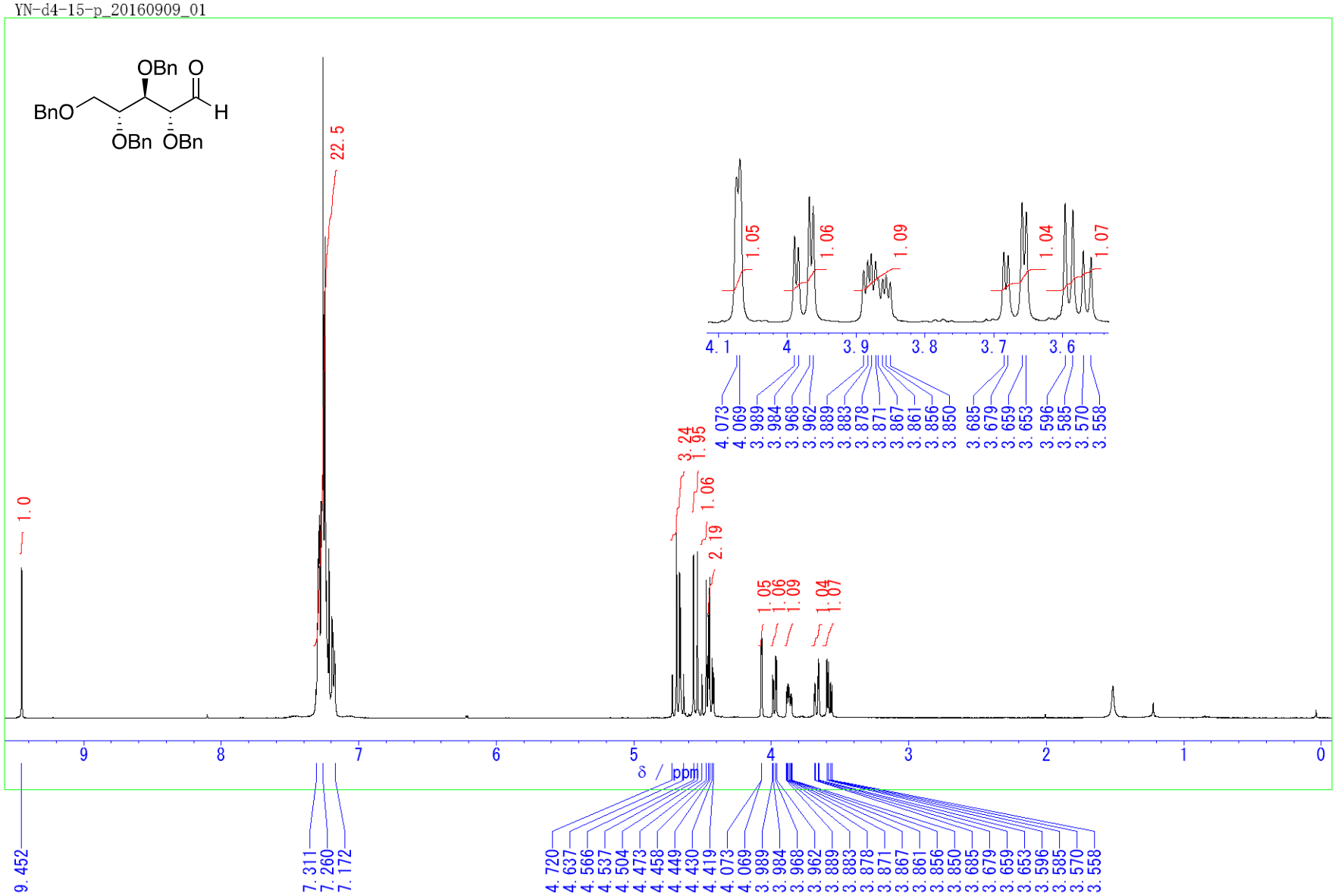
(2*S*,3*S*,4*R*)-2,3,4,5-tetrakis(benzyloxy)pentanal *O*-methyl oxime 13d



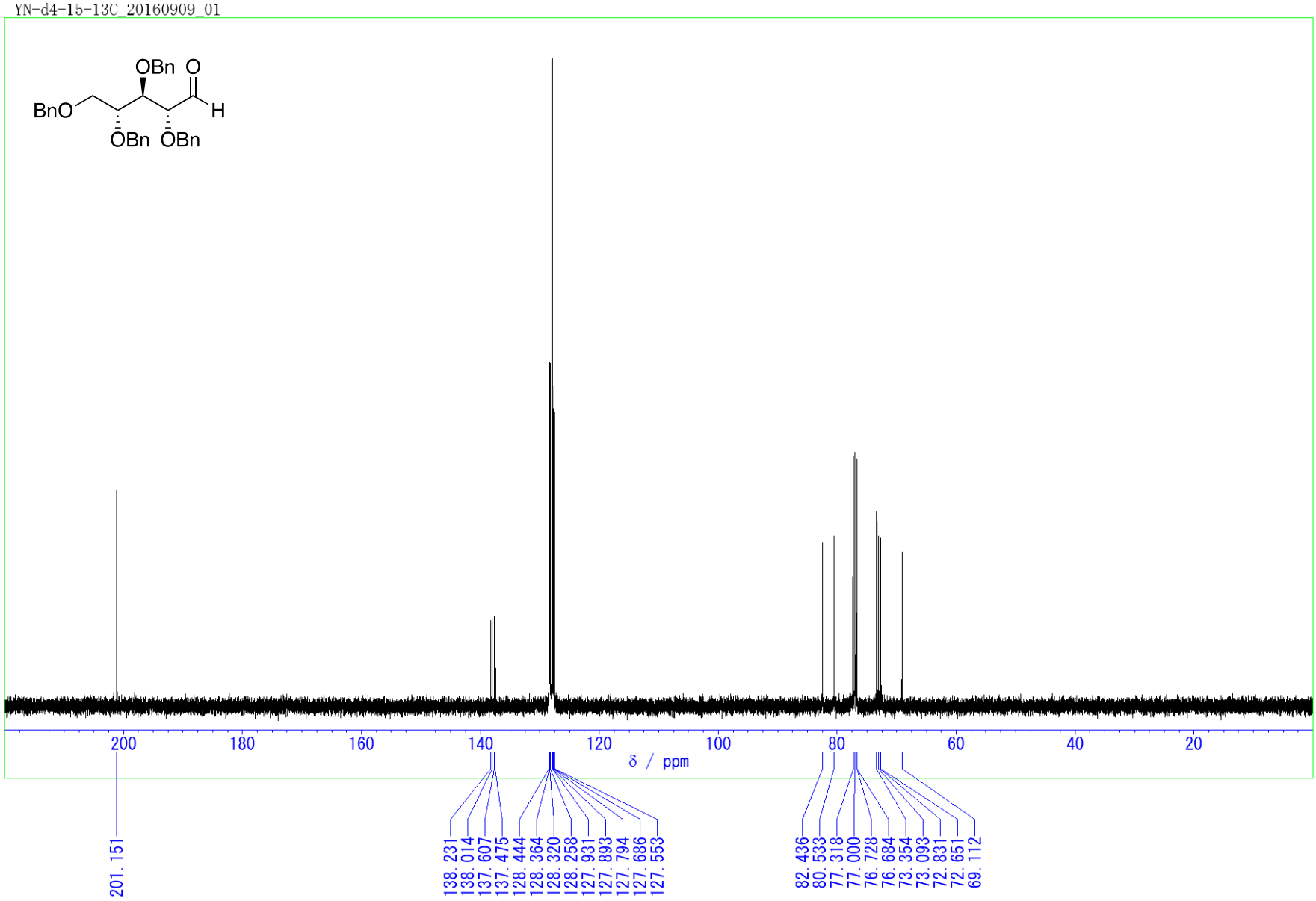
(2*S*,3*S*,4*R*)-2,3,4,5-tetrakis(benzyloxy)pentanal *O*-methyl oxime 13d



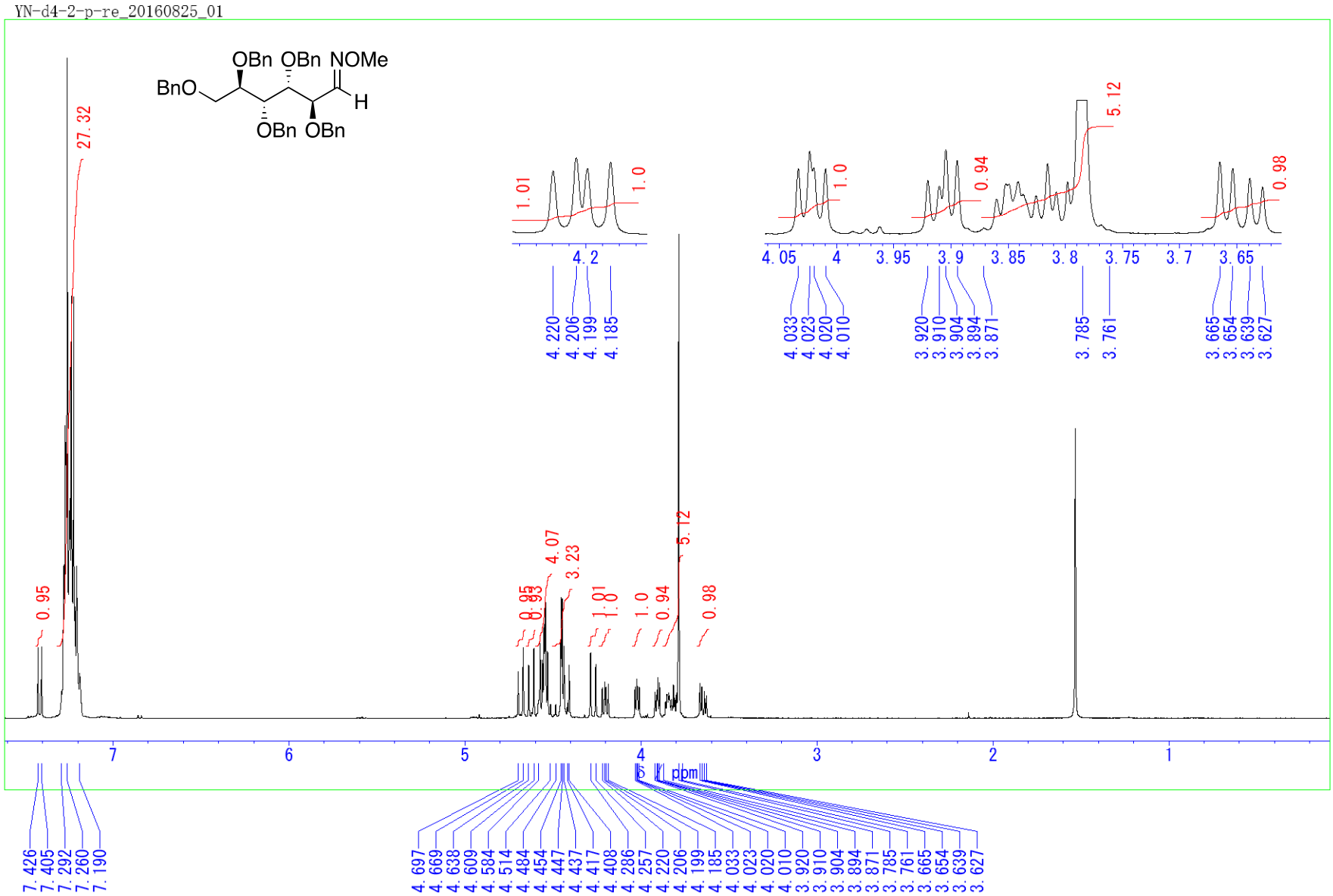
(2*R*,3*R*,4*R*)-2,3,4,5-tetrakis(benzyloxy)pentanal 14d



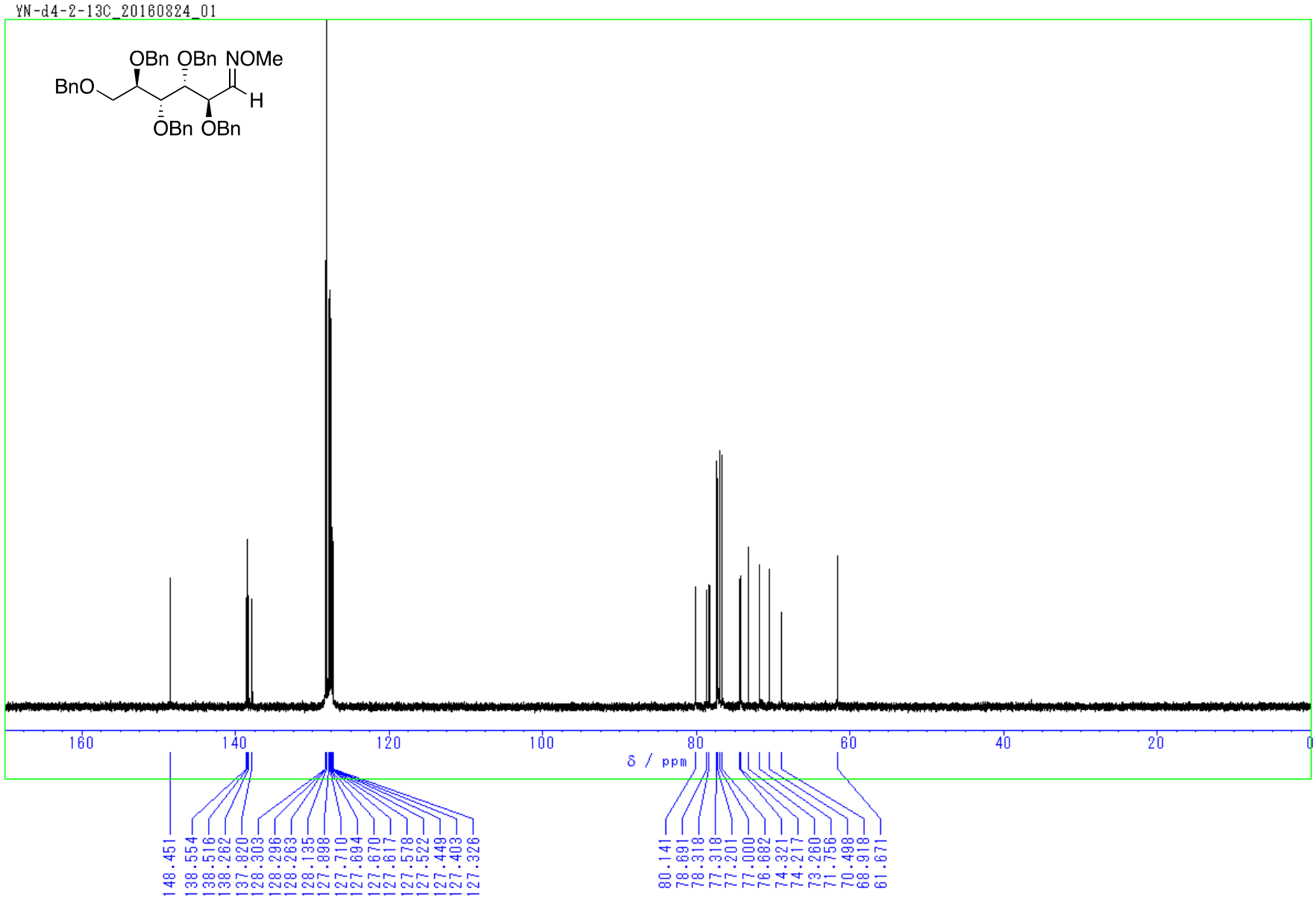
(2*R*,3*R*,4*R*)-2,3,4,5-tetrakis(benzyloxy)pentanal 14d



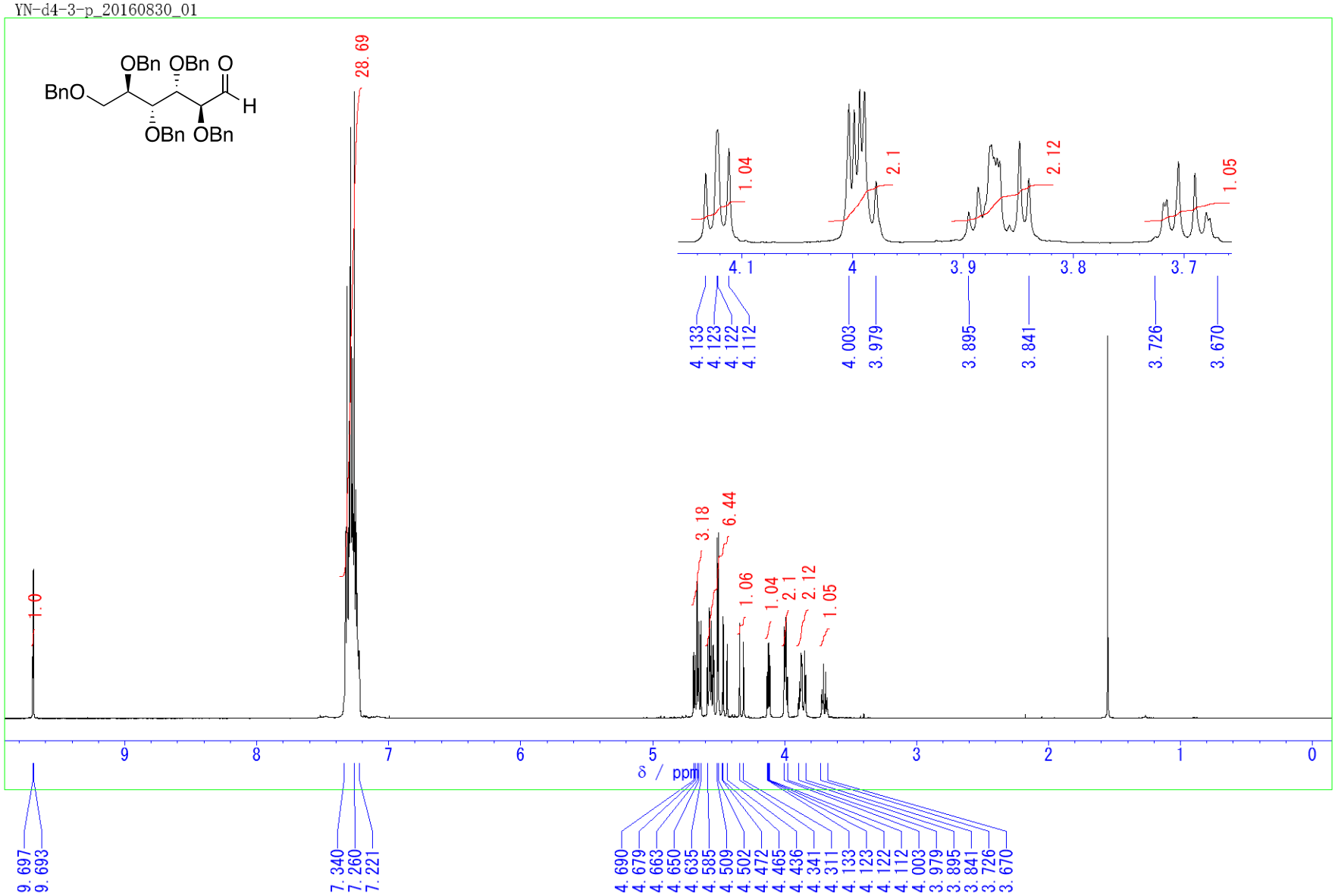
(2*R*,3*R*,4*R*,5*R*)-2,3,4,5,6-pentakis(benzyloxy)hexanal *O*-methyl oxime 13e



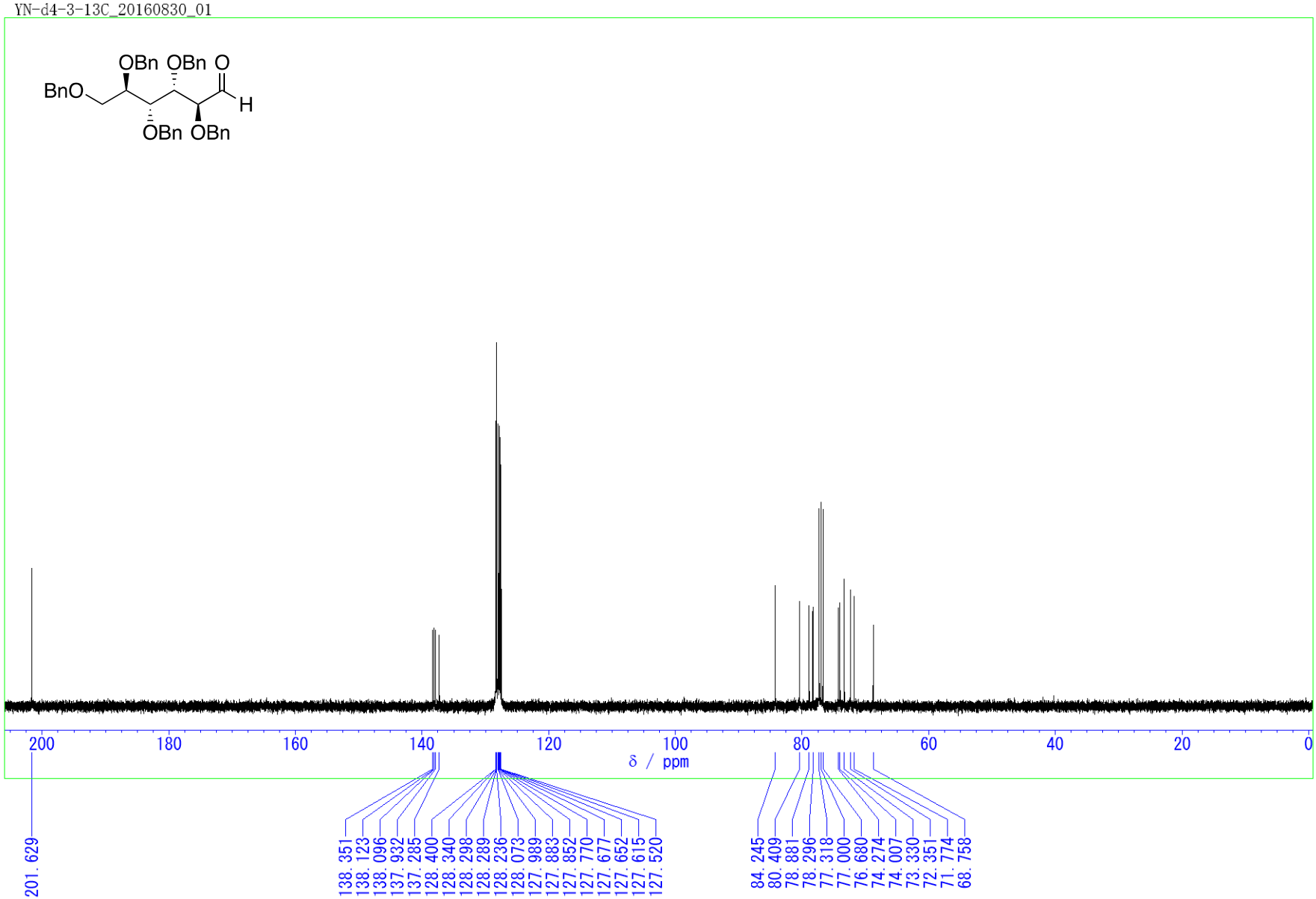
(2*R*,3*R*,4*R*,5*R*)-2,3,4,5,6-pentakis(benzyloxy)hexanal *O*-methyl oxime 13e



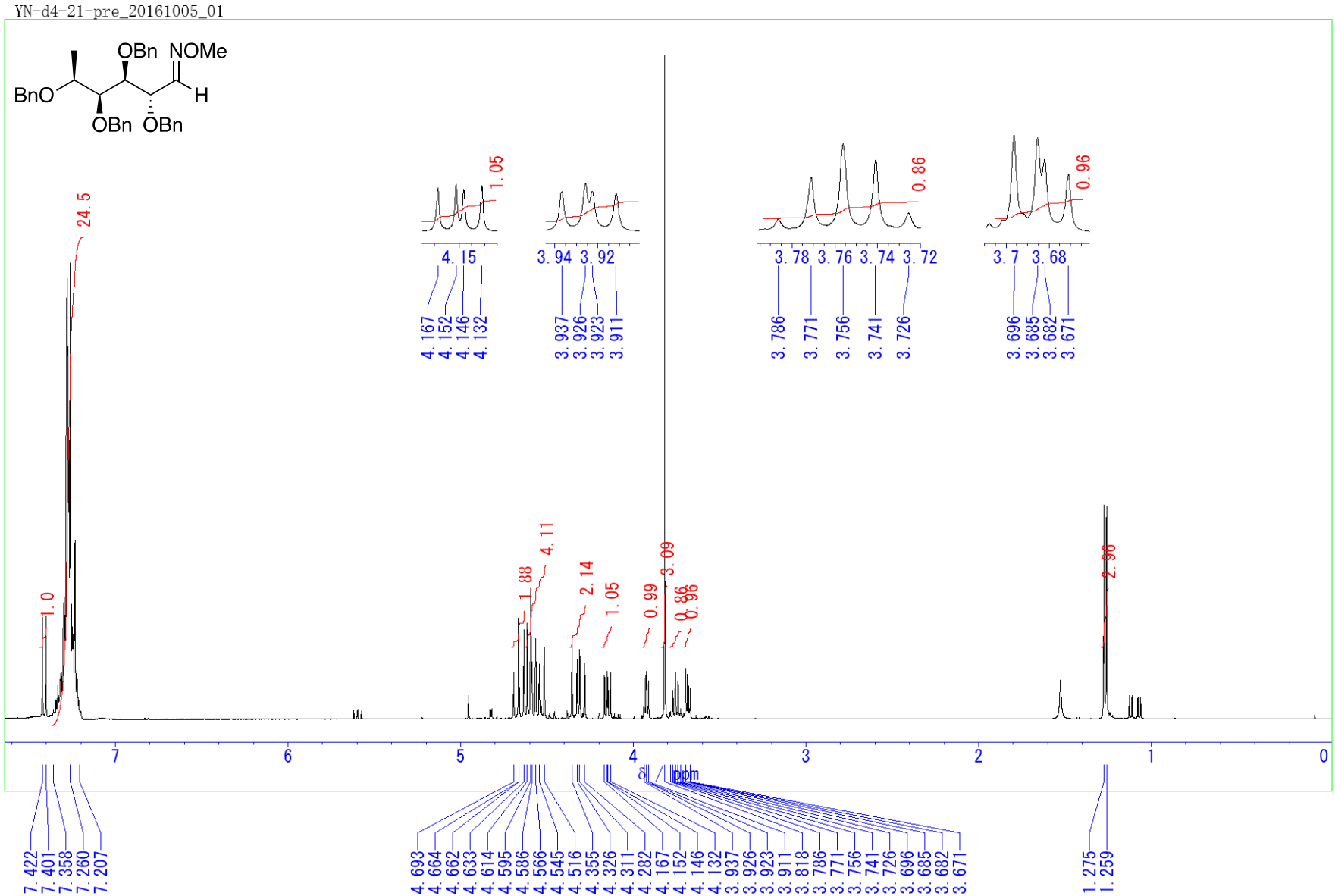
(2*S*,3*S*,4*R*,5*R*)-2,3,4,5,6-pentakis(benzyloxy)hexanal 14e



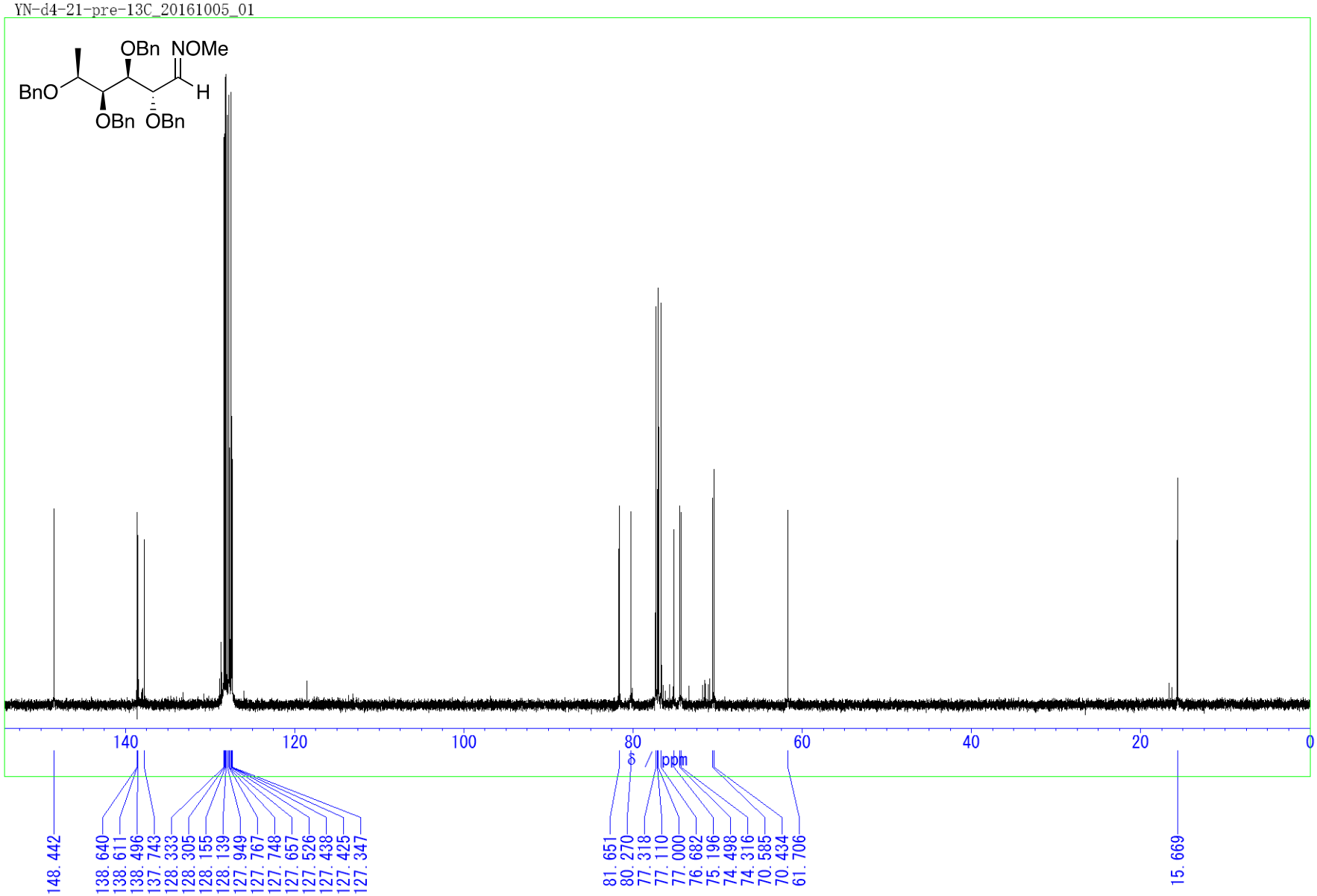
(2*S*,3*S*,4*R*,5*R*)-2,3,4,5,6-pentakis(benzyloxy)hexanal 14e



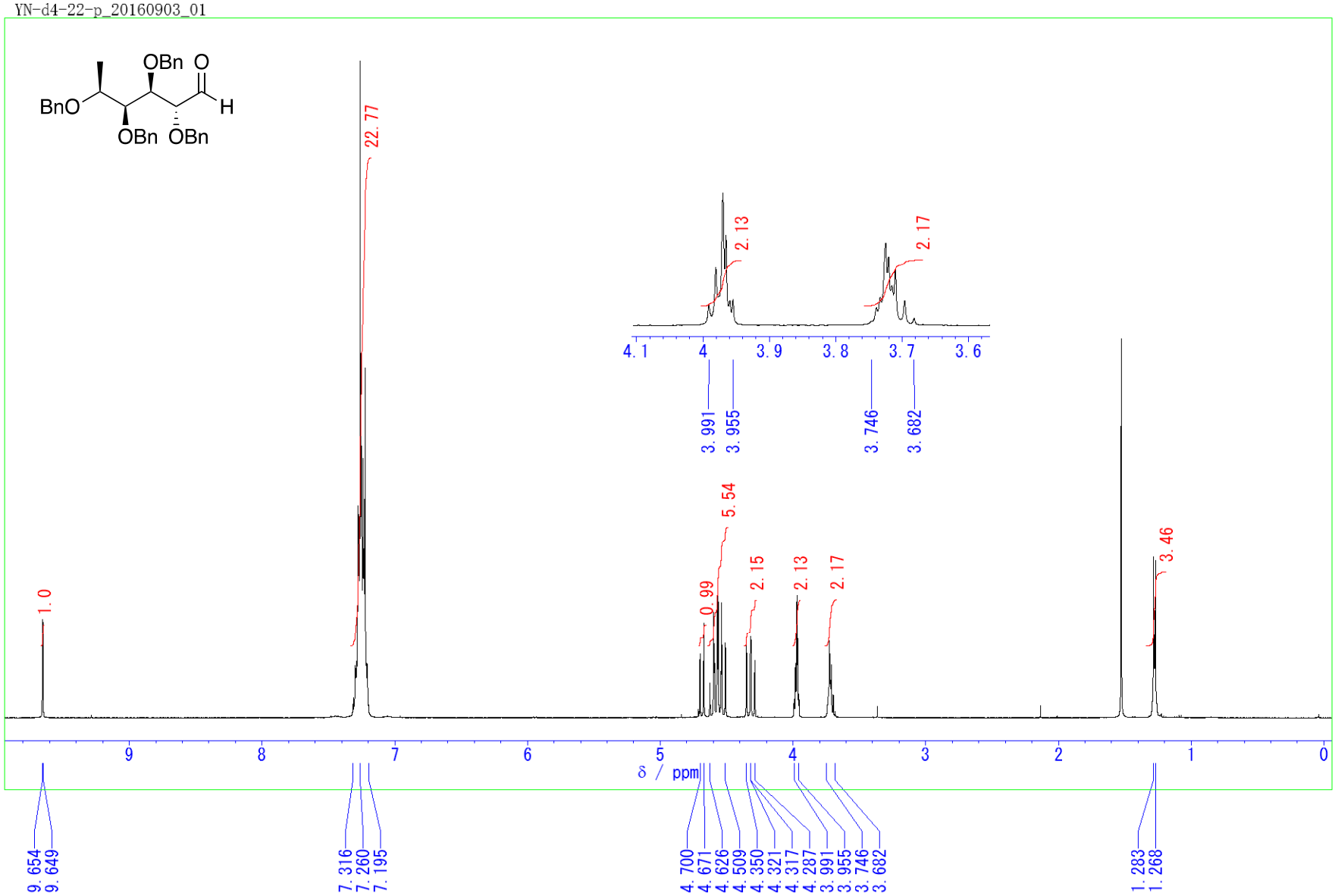
(2*S*,3*S*,4*S*,5*S*)-2,3,4,5-tetrakis(benzyloxy)hexanal *O*-methyl oxime 13f



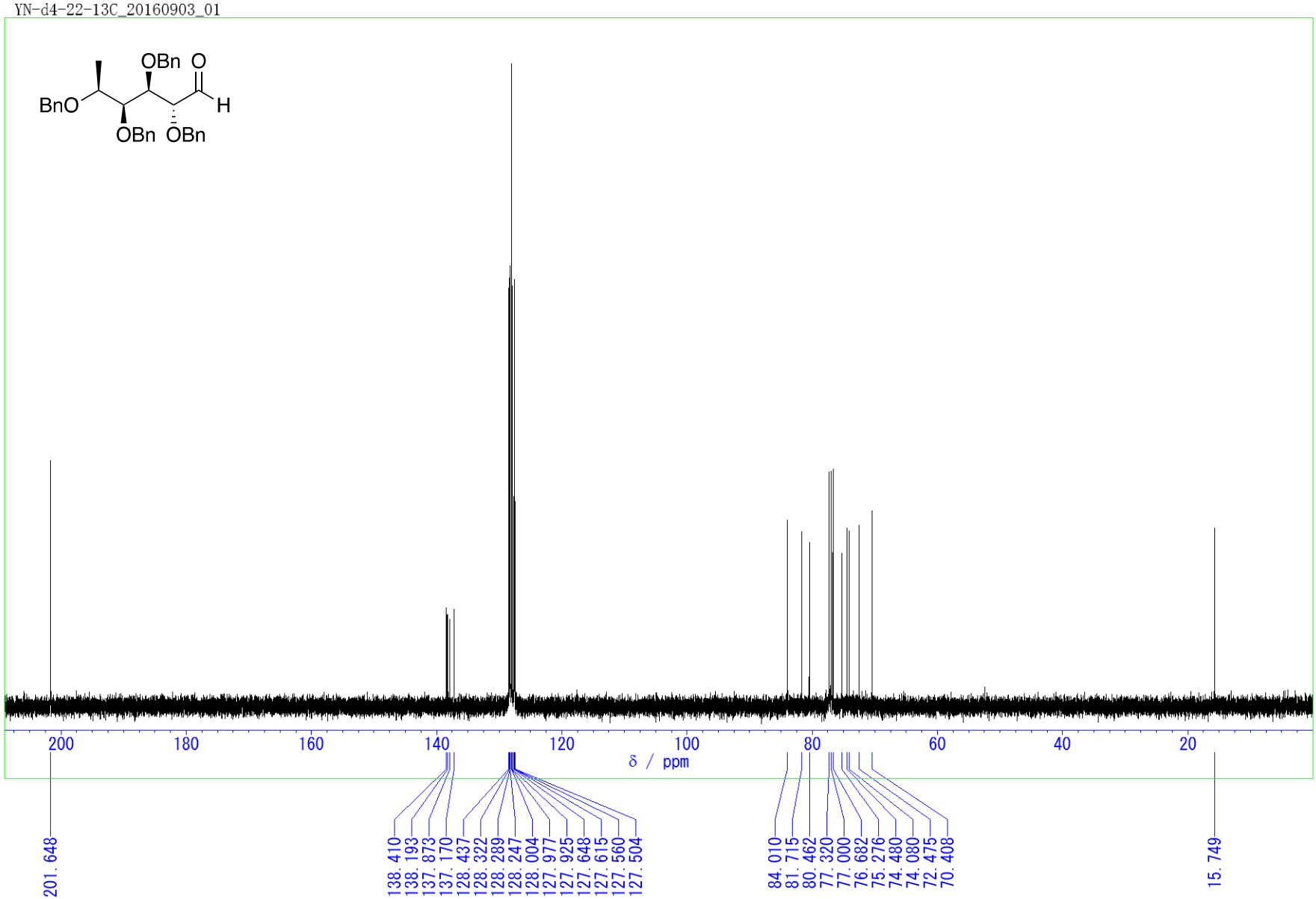
(2*S*,3*S*,4*S*,5*S*)-2,3,4,5-tetrakis(benzyloxy)hexanal *O*-methyl oxime 13f



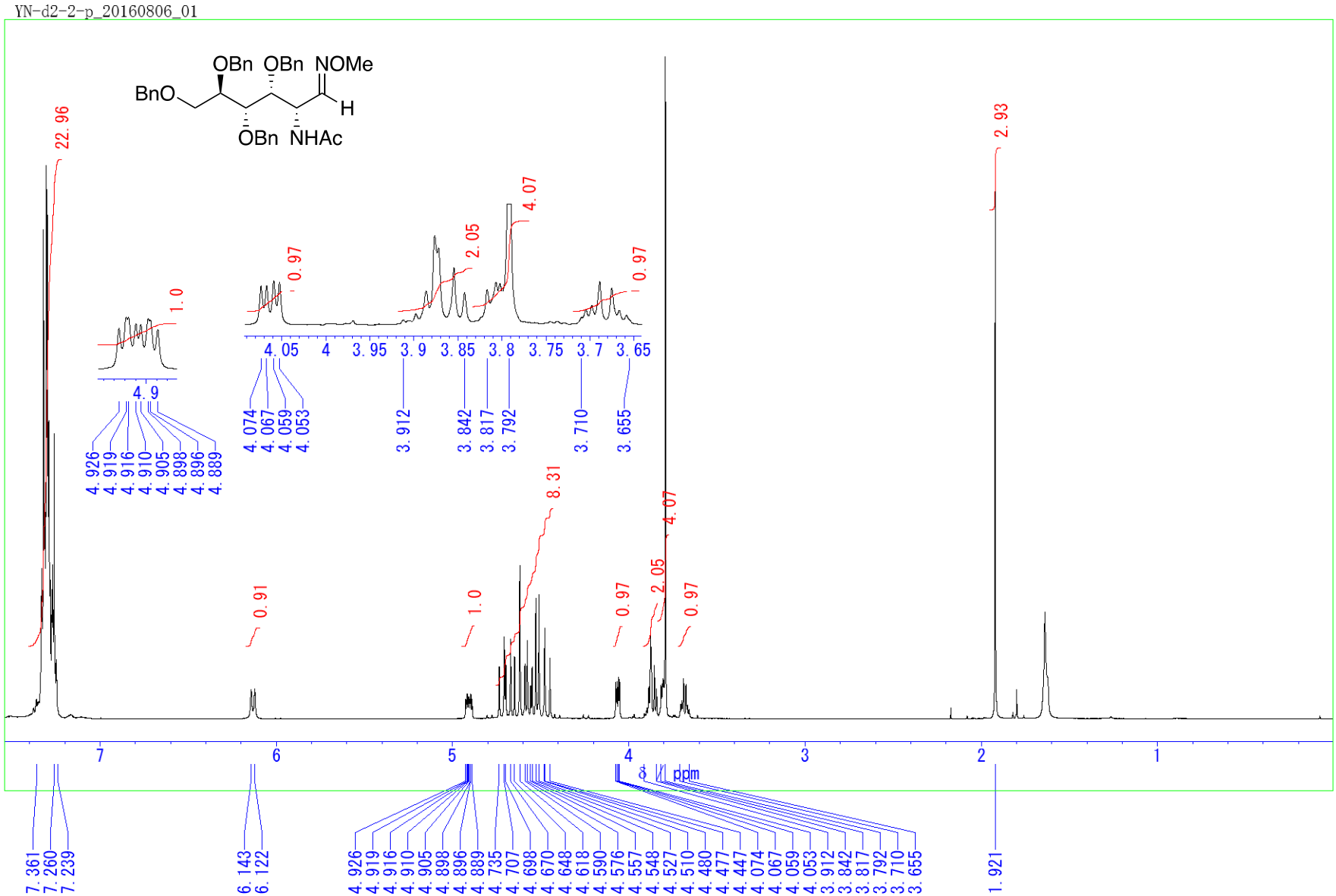
(2*R*,3*R*,4*S*,5*S*)-2,3,4,5-tetrakis(benzyloxy)hexanal 14f



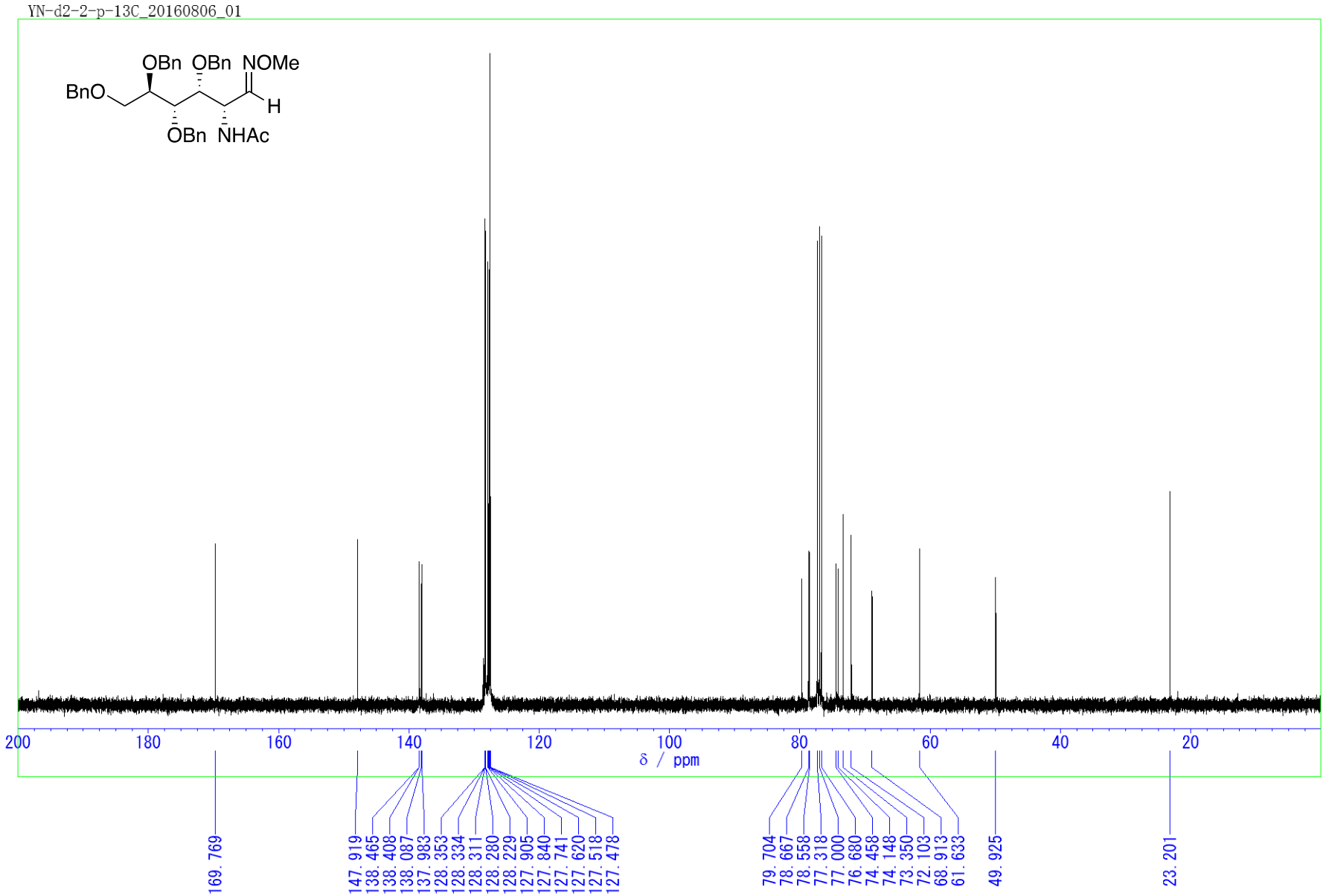
(2*R*,3*R*,4*S*,5*S*)-2,3,4,5-tetrakis(benzyloxy)hexanal 14f



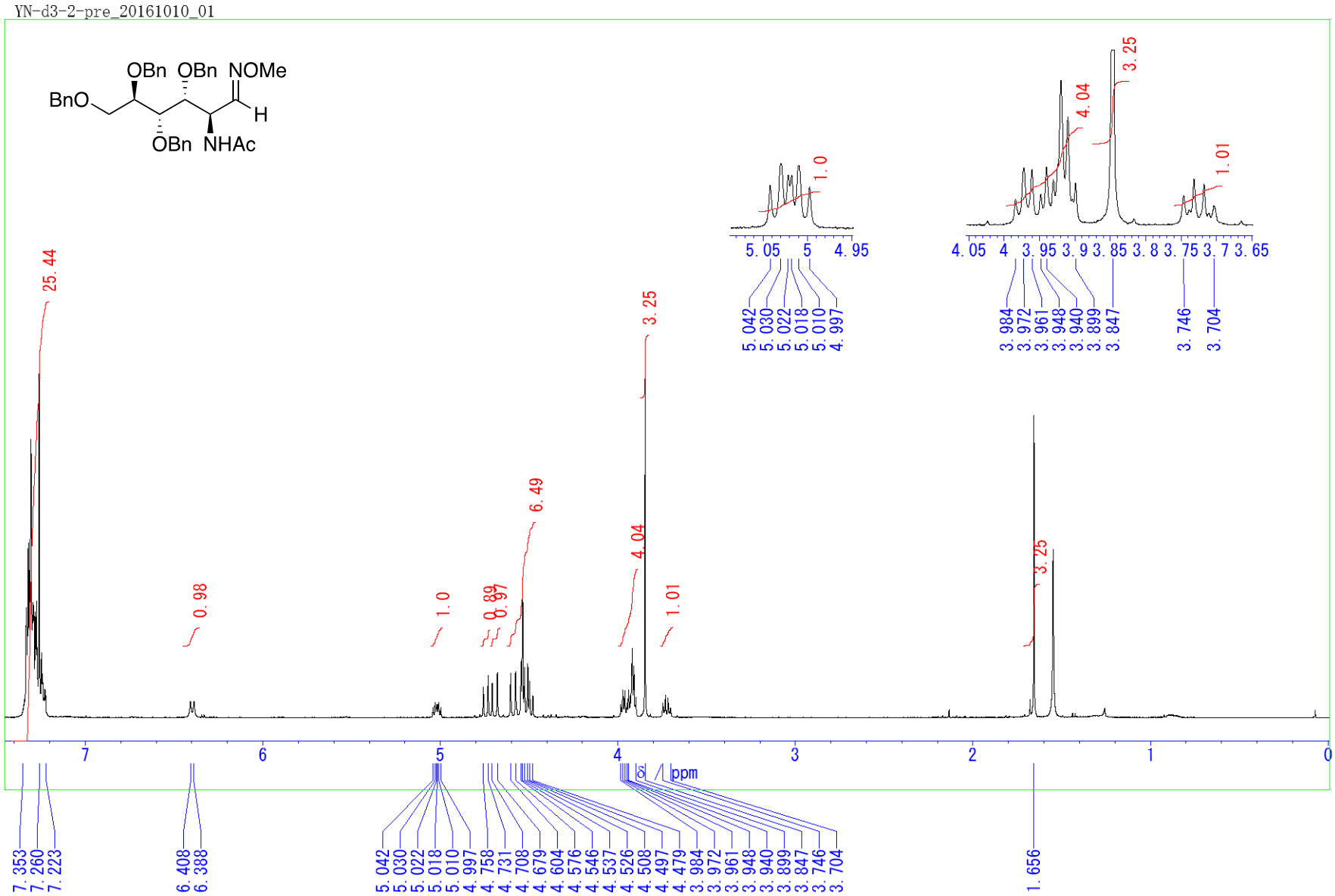
N-((2*S*,3*R*,4*S*,5*R*)-3,4,5,6-tetrakis(benzyloxy)-1-(methoxyimino)hexan-2-yl)acetamide 16b



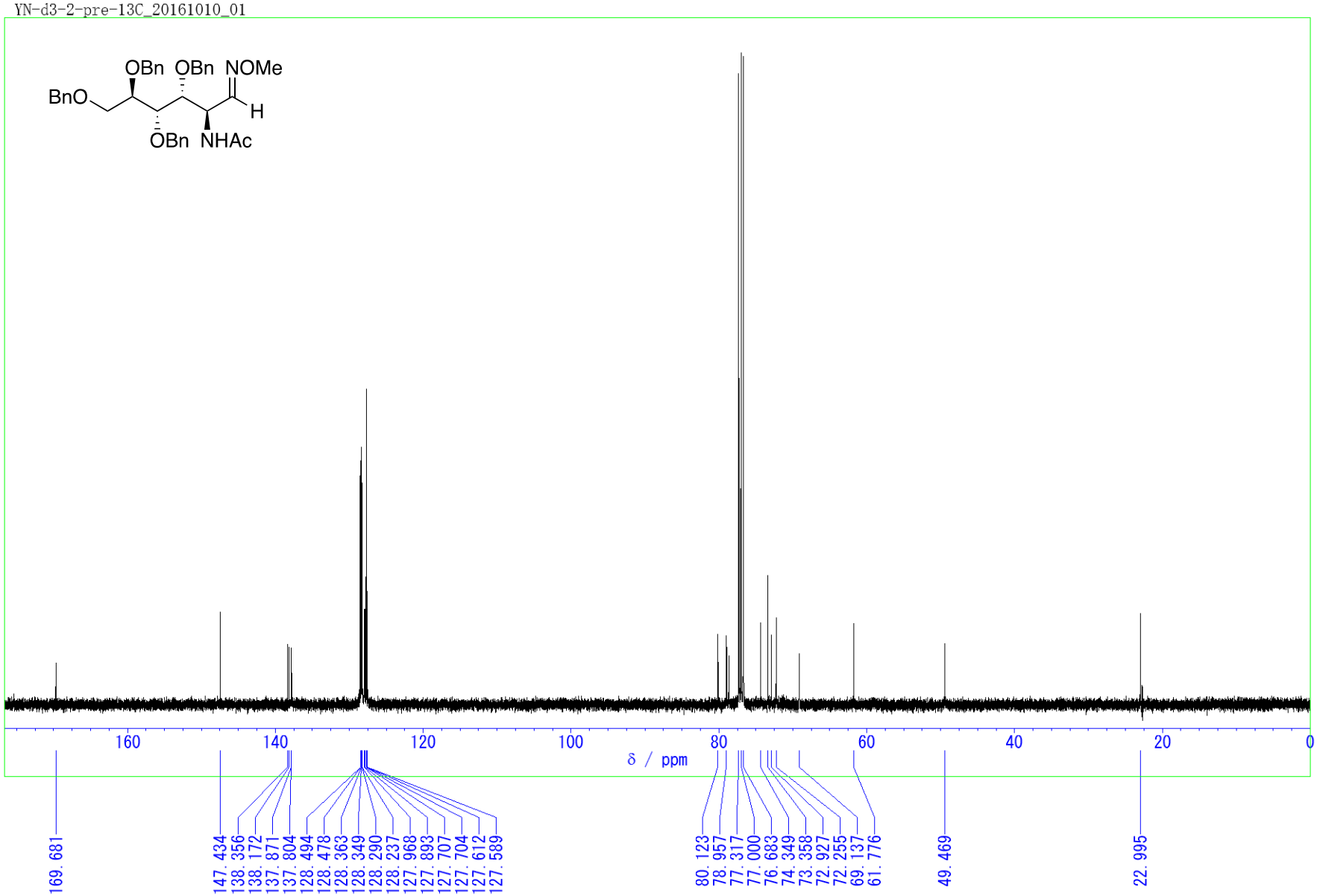
N-((2*S*,3*R*,4*S*,5*R*)-3,4,5,6-tetrakis(benzyloxy)-1-(methoxyimino)hexan-2-yl)acetamide 16b



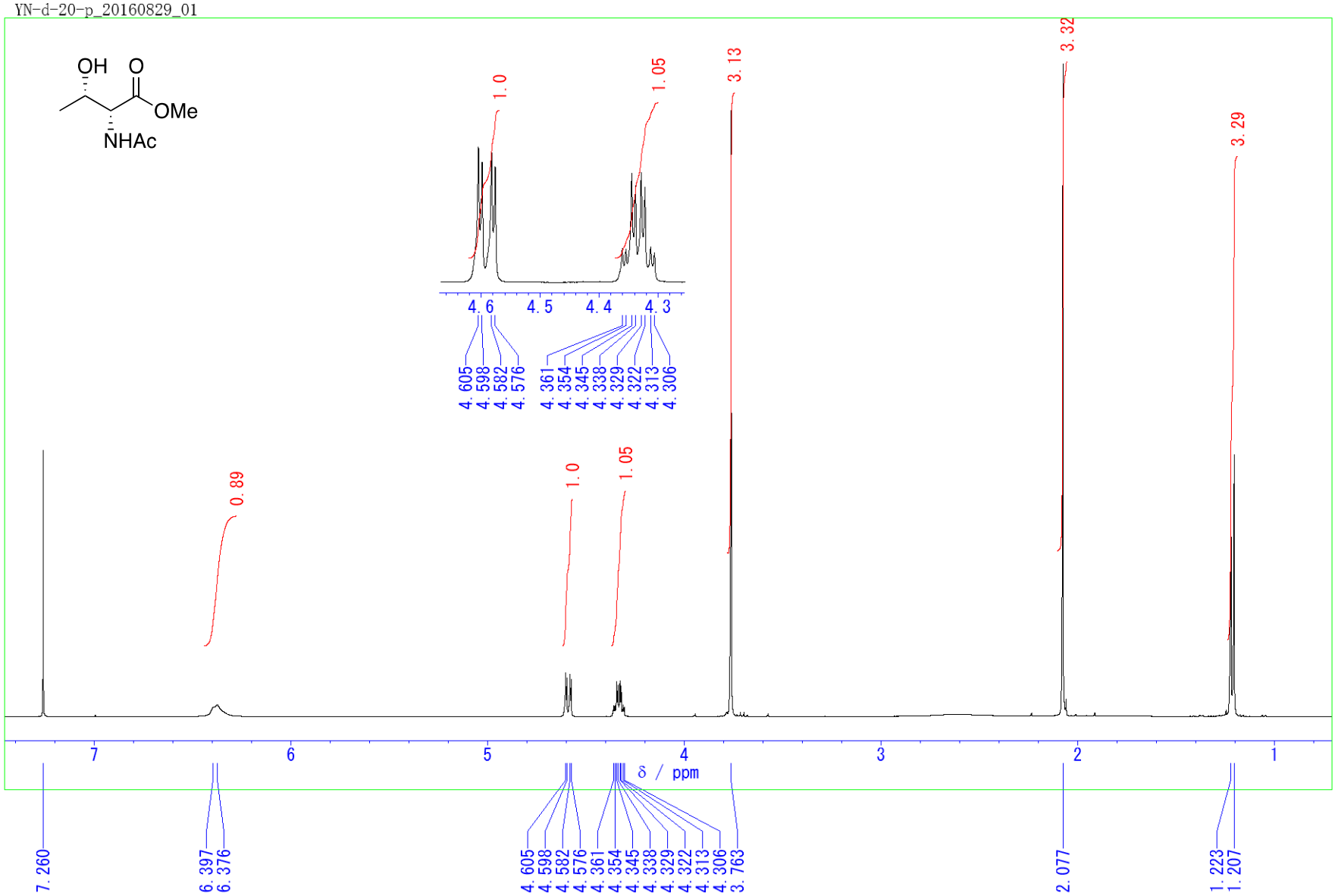
N-((2*R*,3*R*,4*S*,5*R*)-3,4,5,6-tetrakis(benzyloxy)-1-(methoxyimino)hexan-2-yl)acetamide 16d



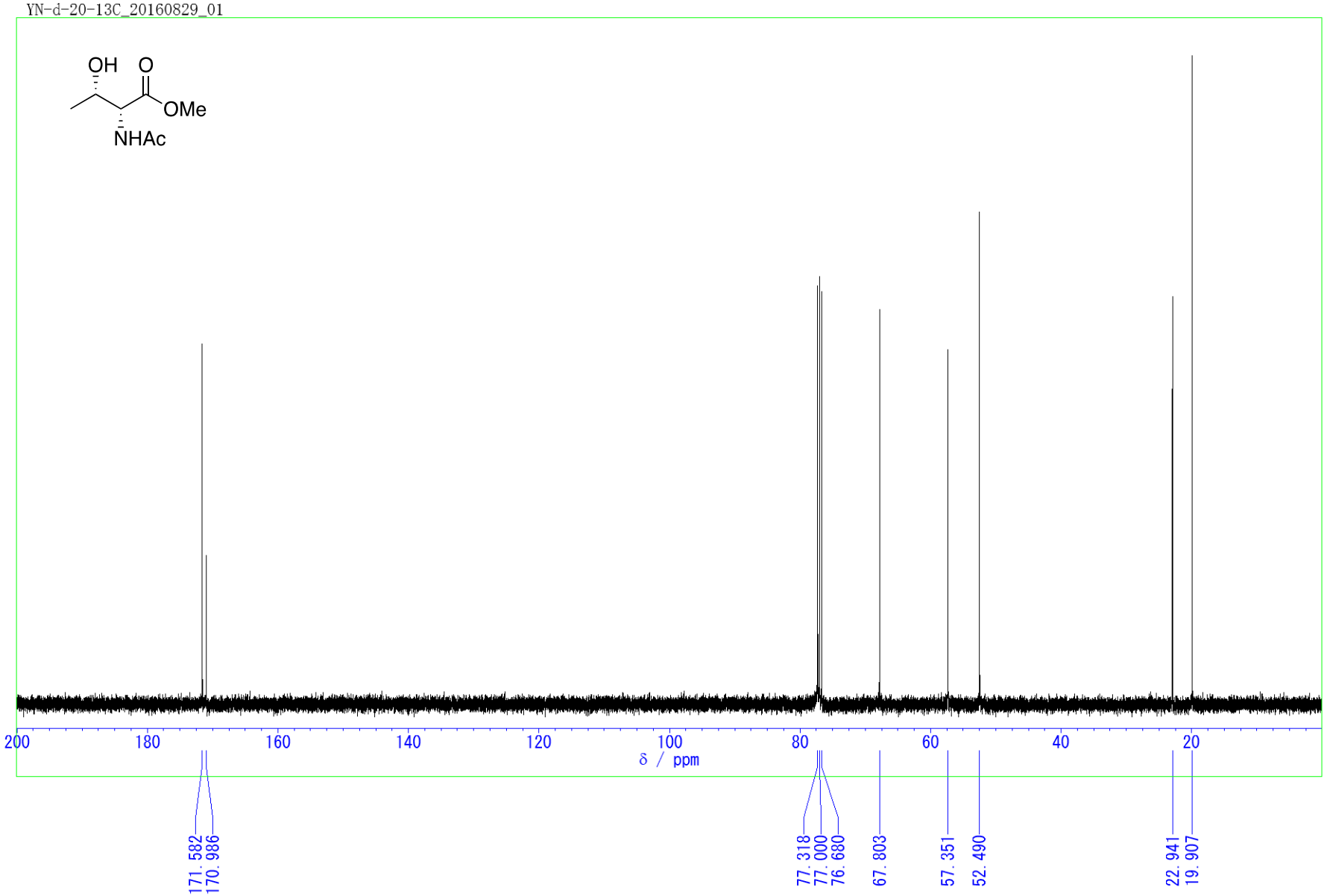
N-((2*R*,3*R*,4*S*,5*R*)-3,4,5,6-tetrakis(benzyloxy)-1-(methoxyimino)hexan-2-yl)acetamide 16d



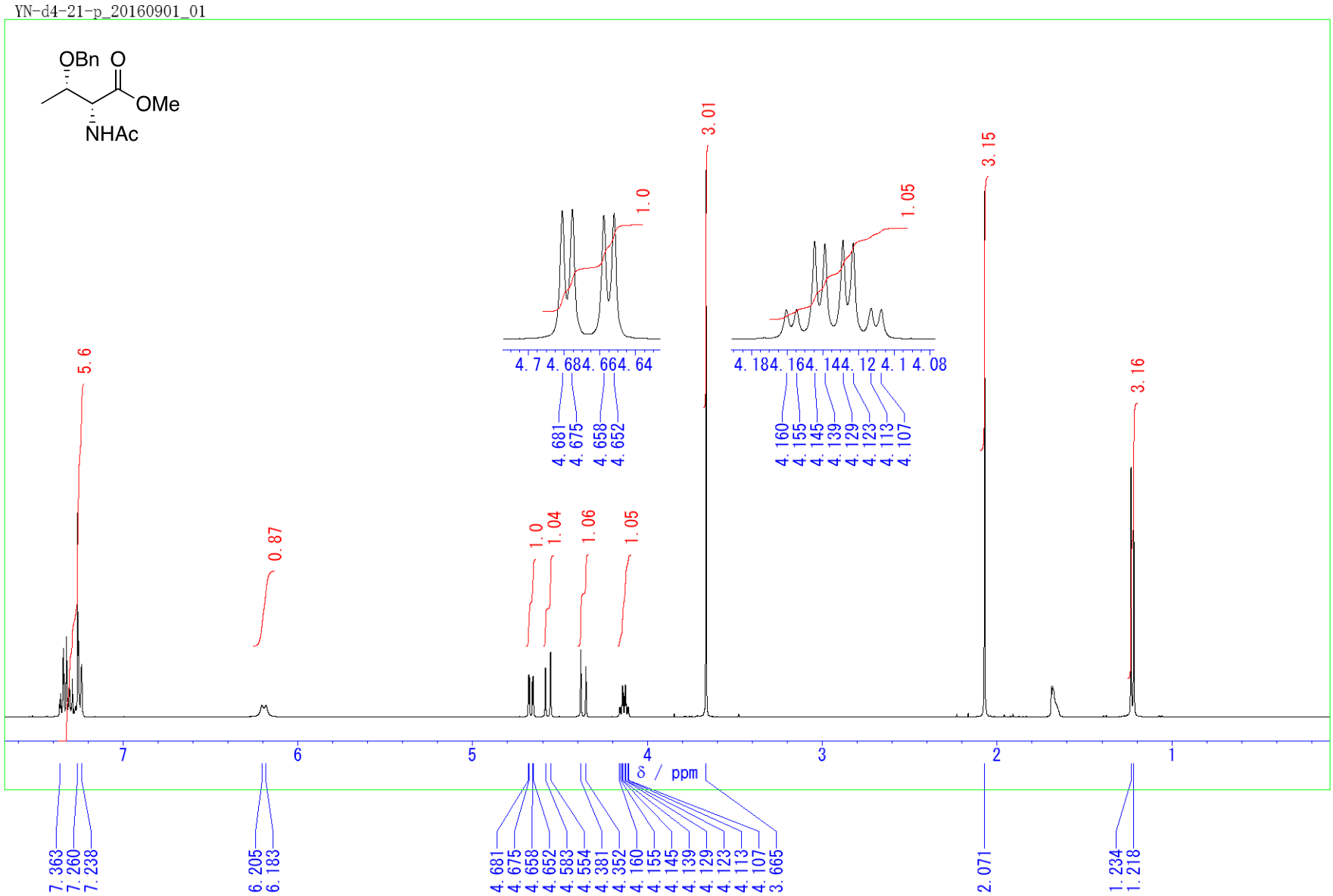
methyl acetyl-D-threoninate 27



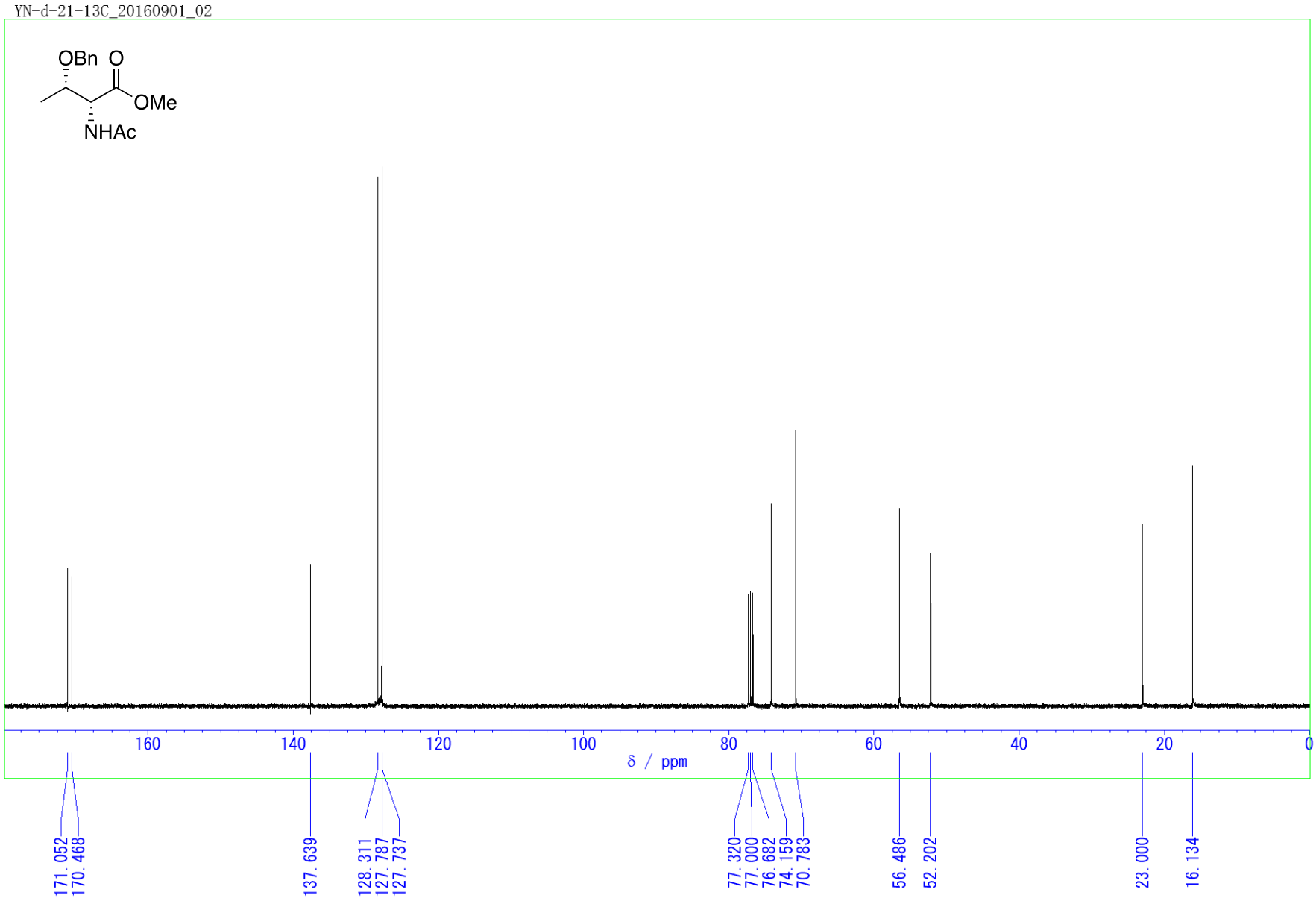
methyl acetyl-D-threoninate 27



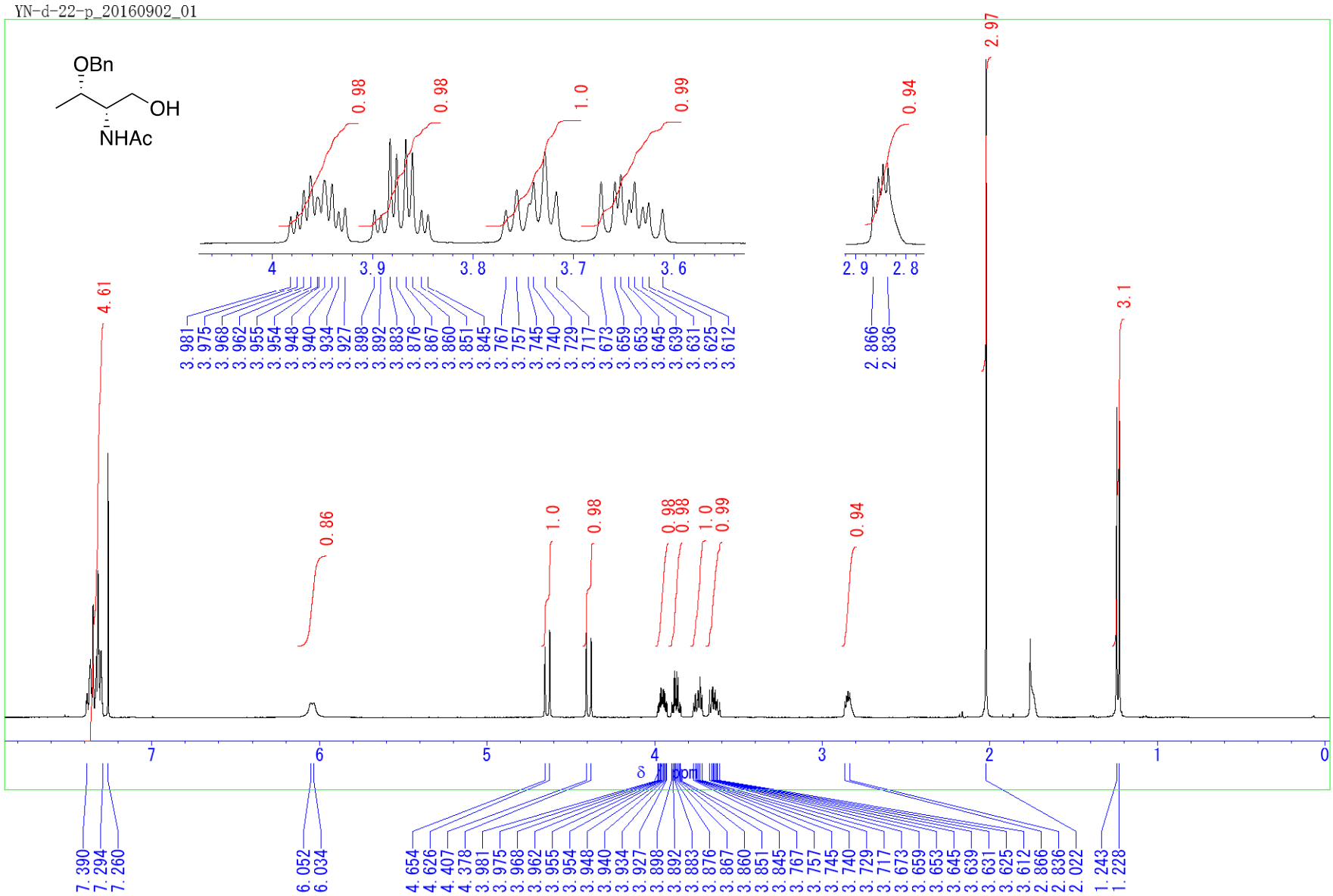
methyl *N*-acetyl-*O*-benzyl-D-threoninate 28



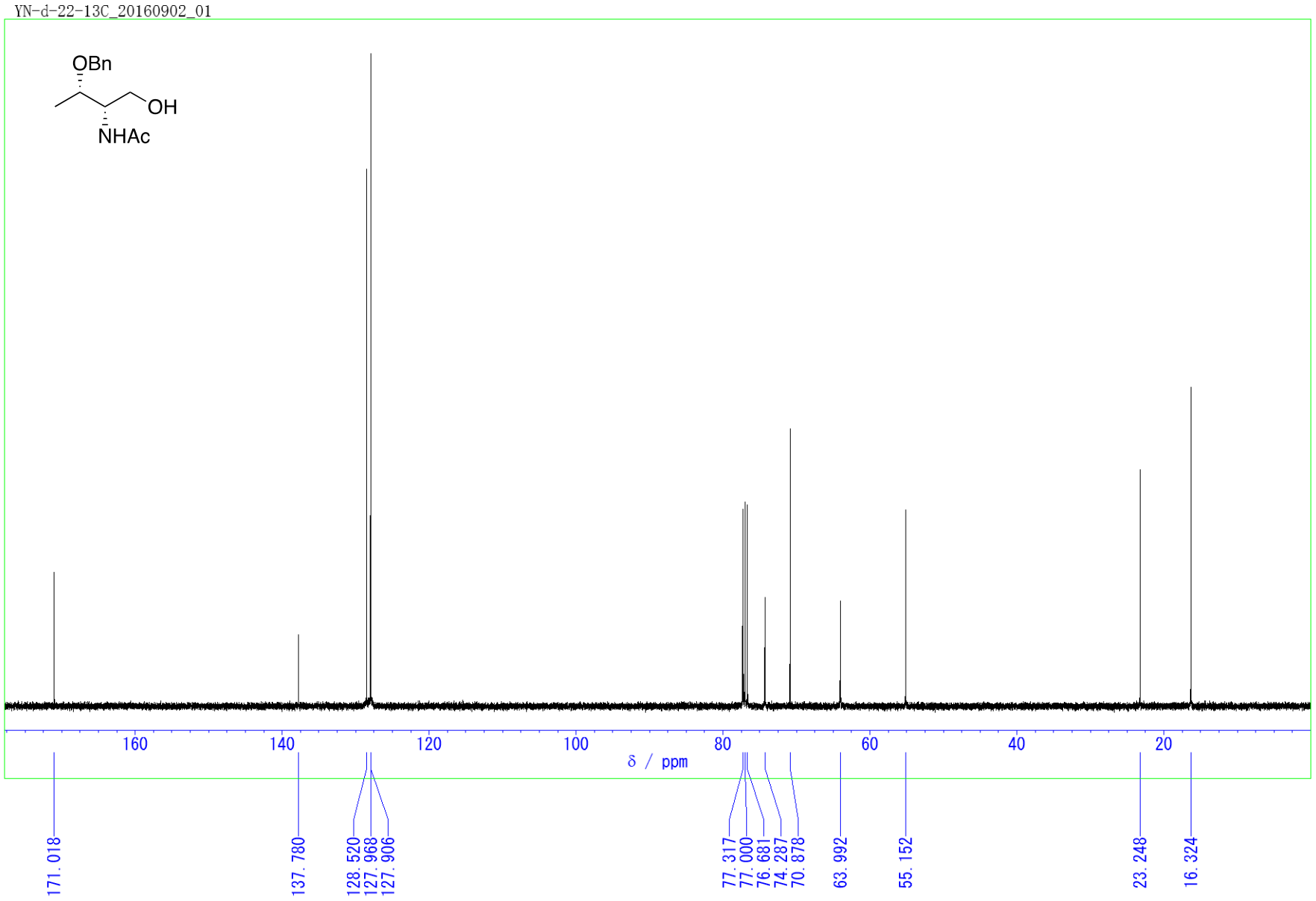
methyl *N*-acetyl-*O*-benzyl-D-threoninate 28



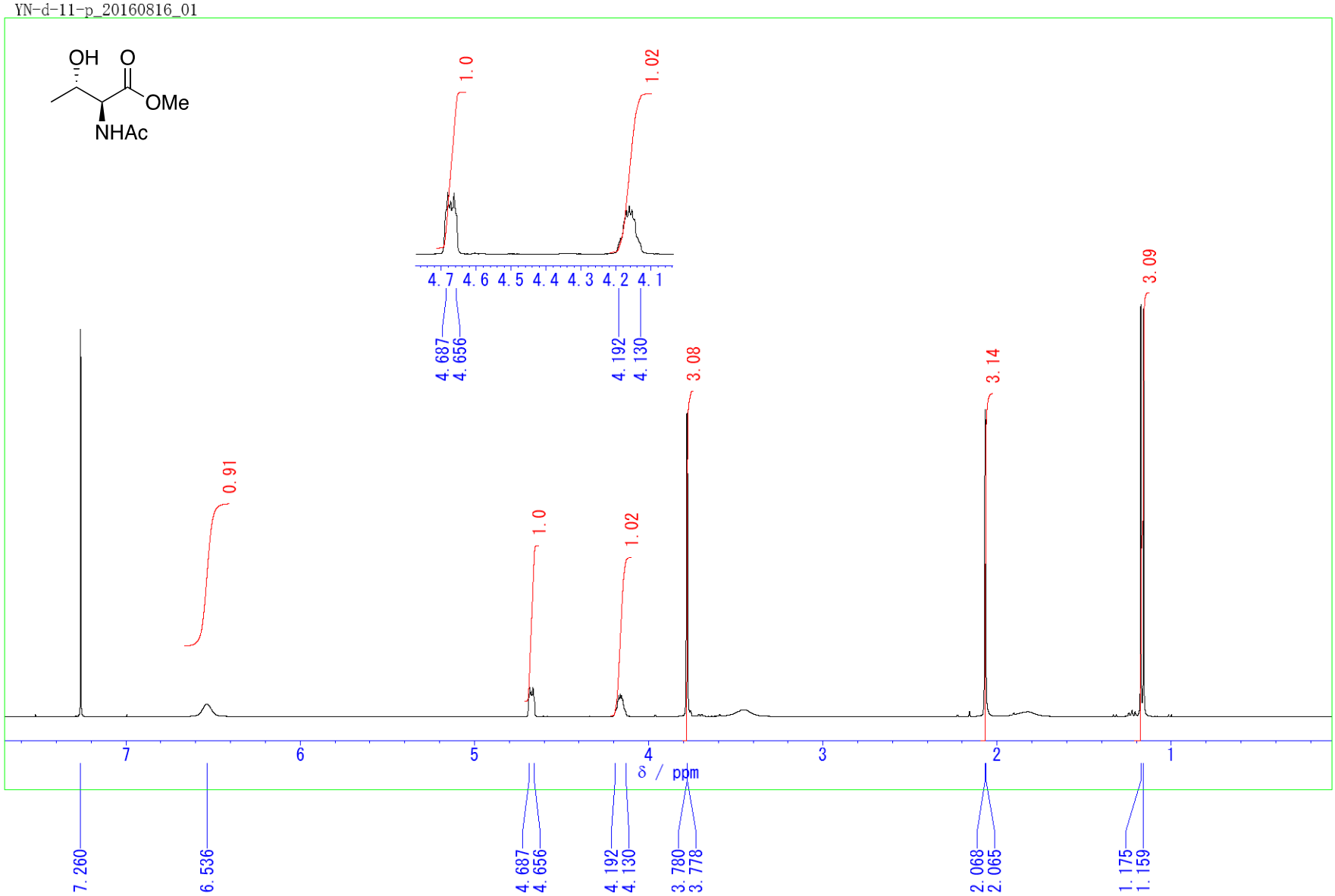
N-((2*S*,3*S*)-3-(benzyloxy)-1-hydroxybutan-2-yl)acetamide 29



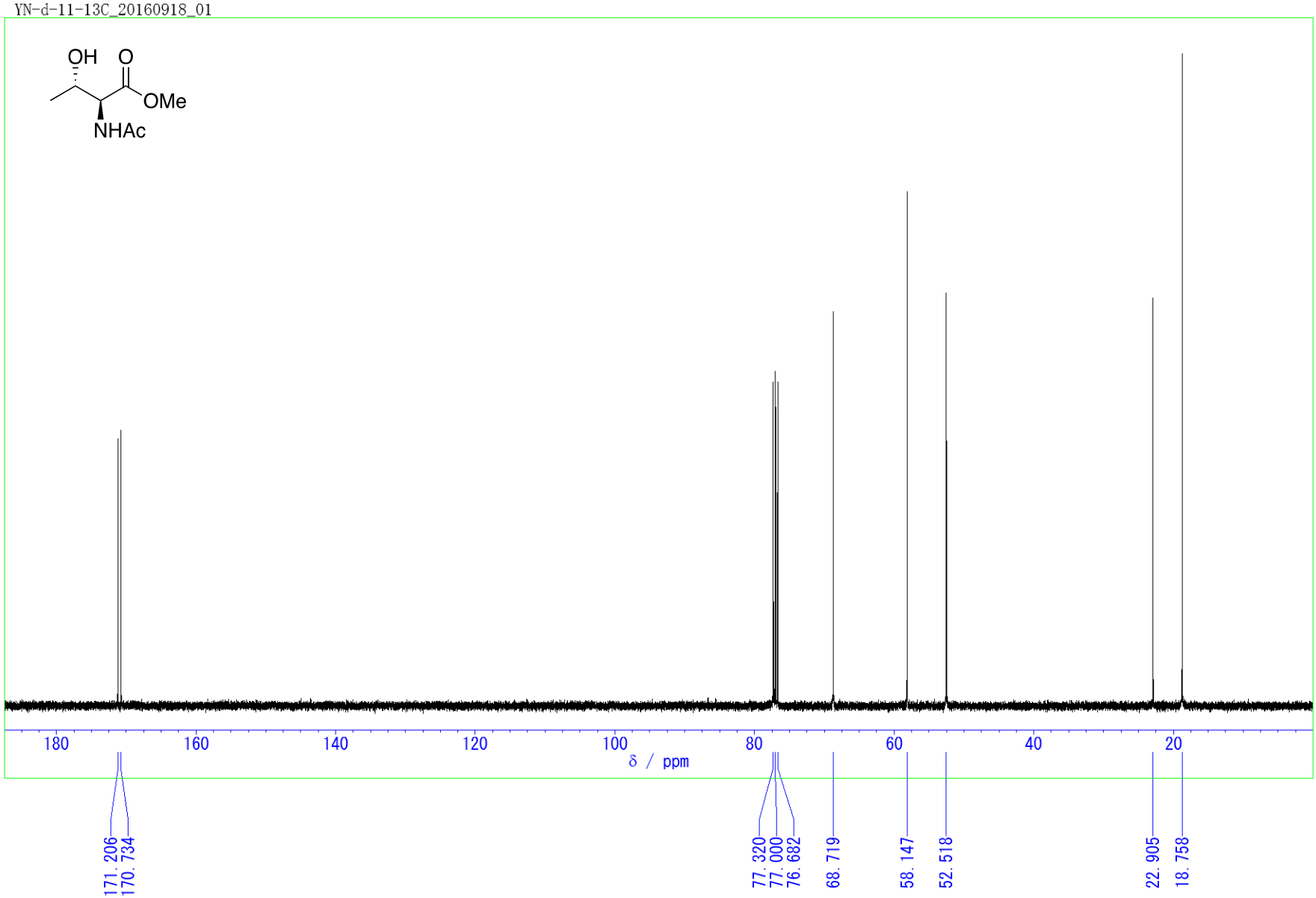
N-((2*S*,3*S*)-3-(benzyloxy)-1-hydroxybutan-2-yl)acetamide 29



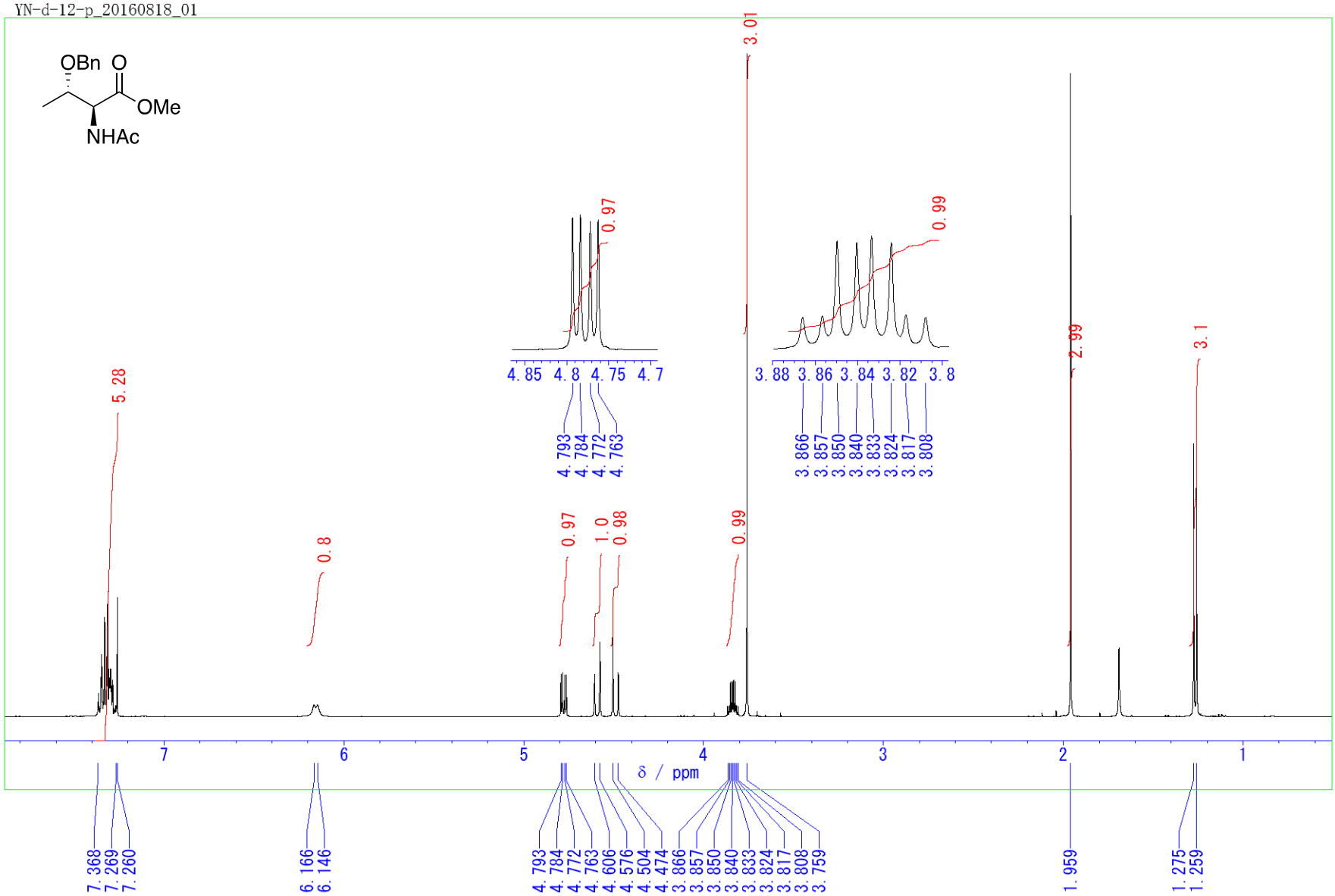
methyl acetyl-L-allothreoninate 30



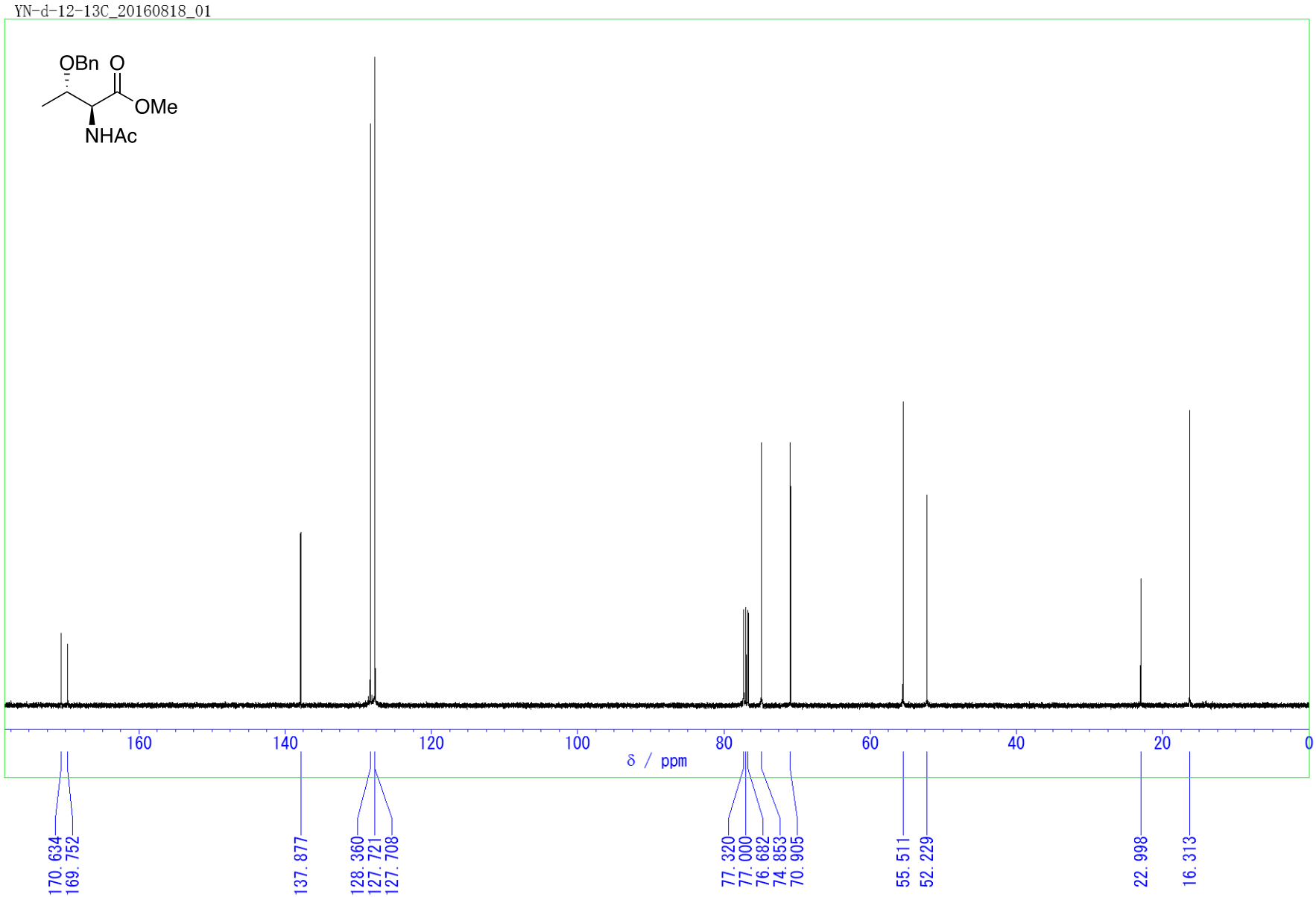
methyl acetyl-L-allothreoninate 30



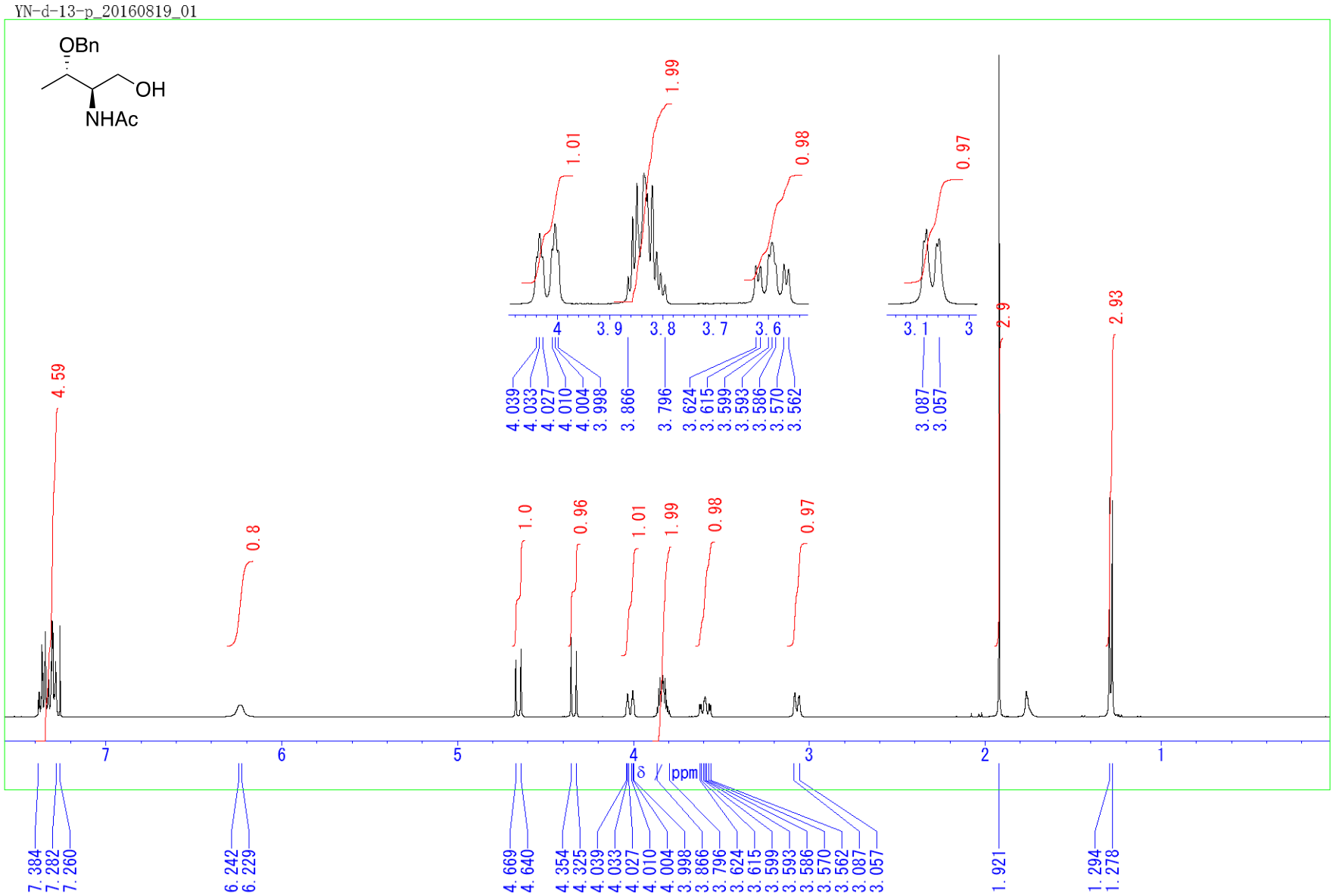
methyl *N*-acetyl-*O*-benzyl-L-allothreoninate 31



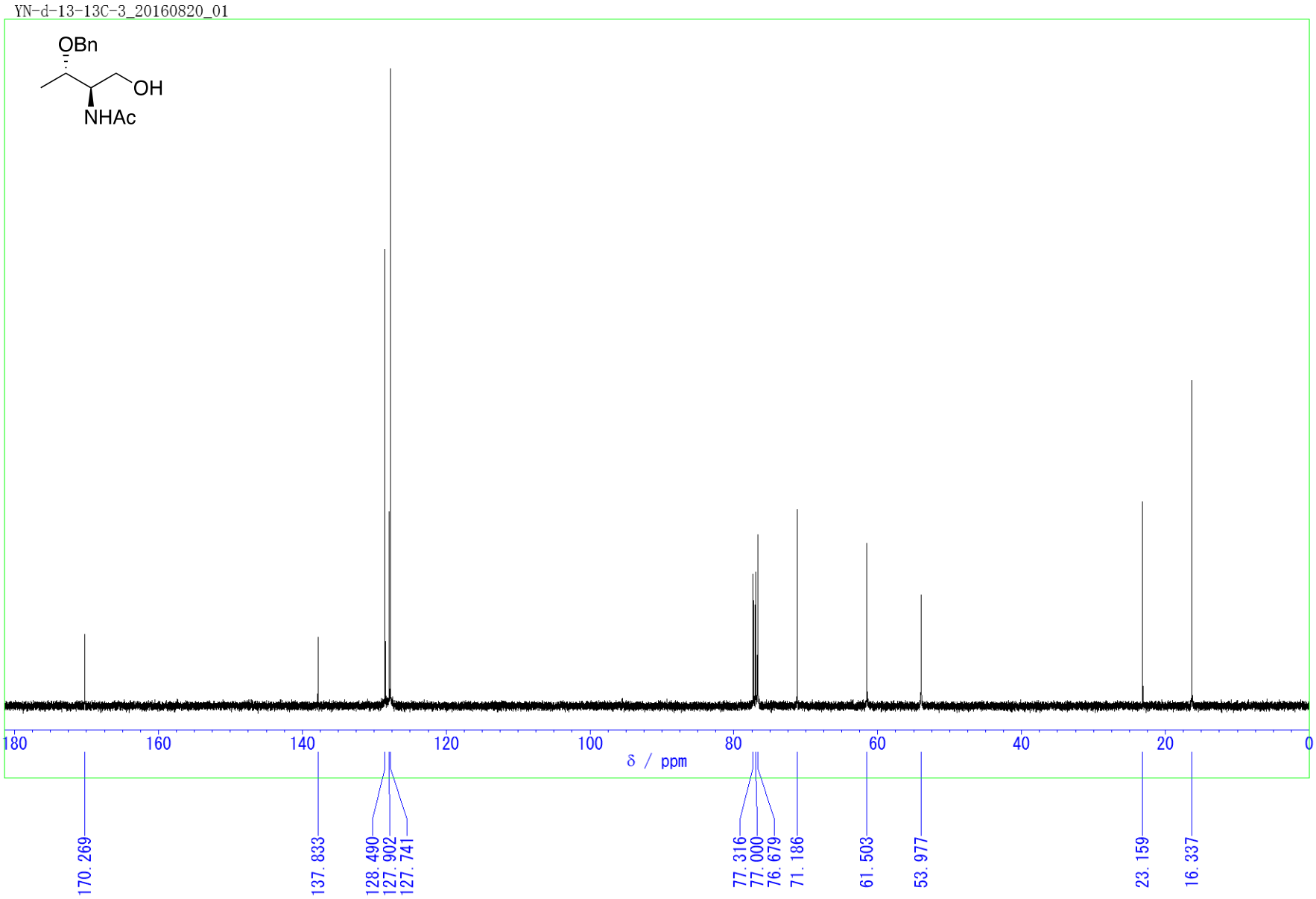
methyl *N*-acetyl-*O*-benzyl-L-allothreoninate 31



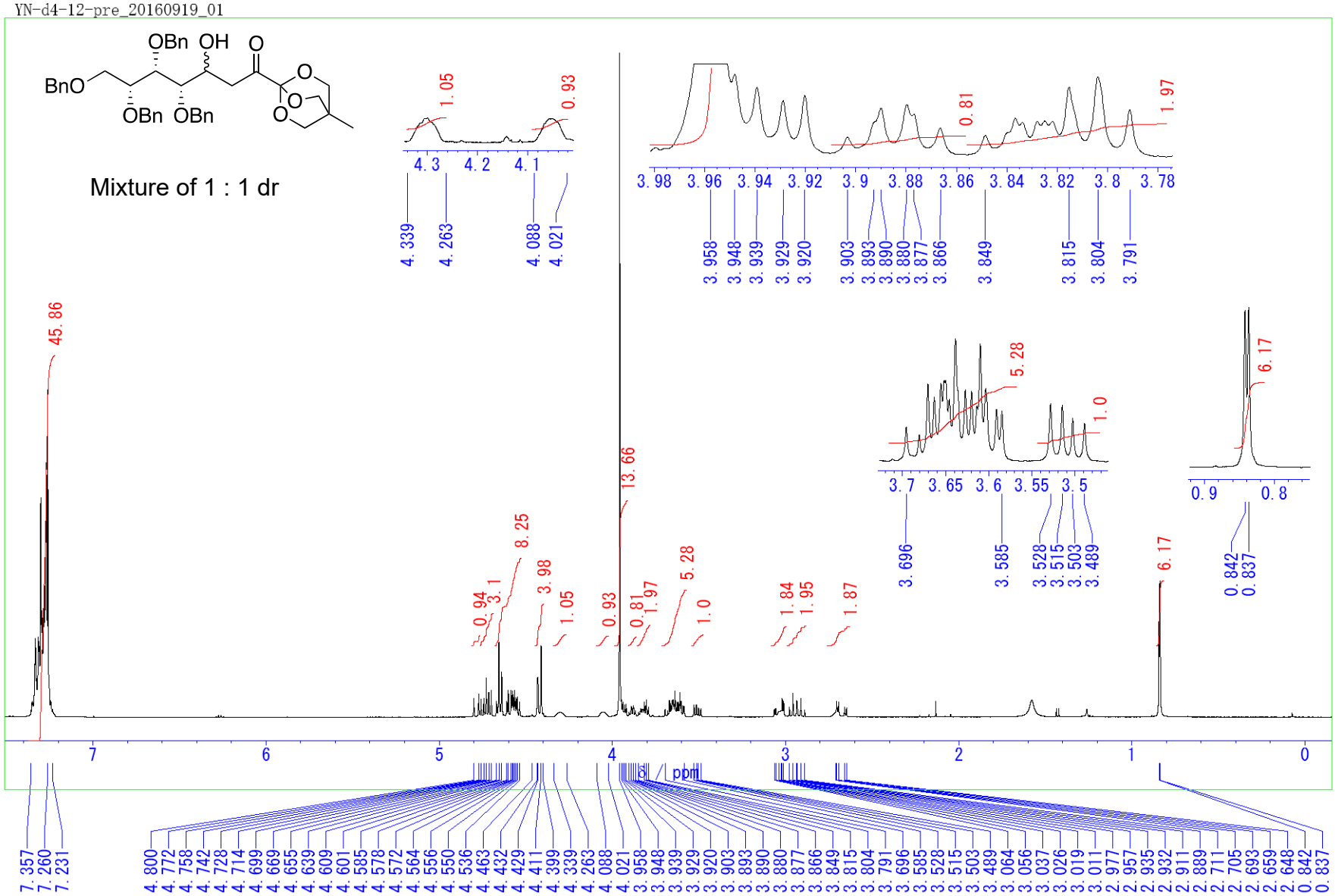
N-((2*R*,3*S*)-3-(benzyloxy)-1-hydroxybutan-2-yl)acetamide 32



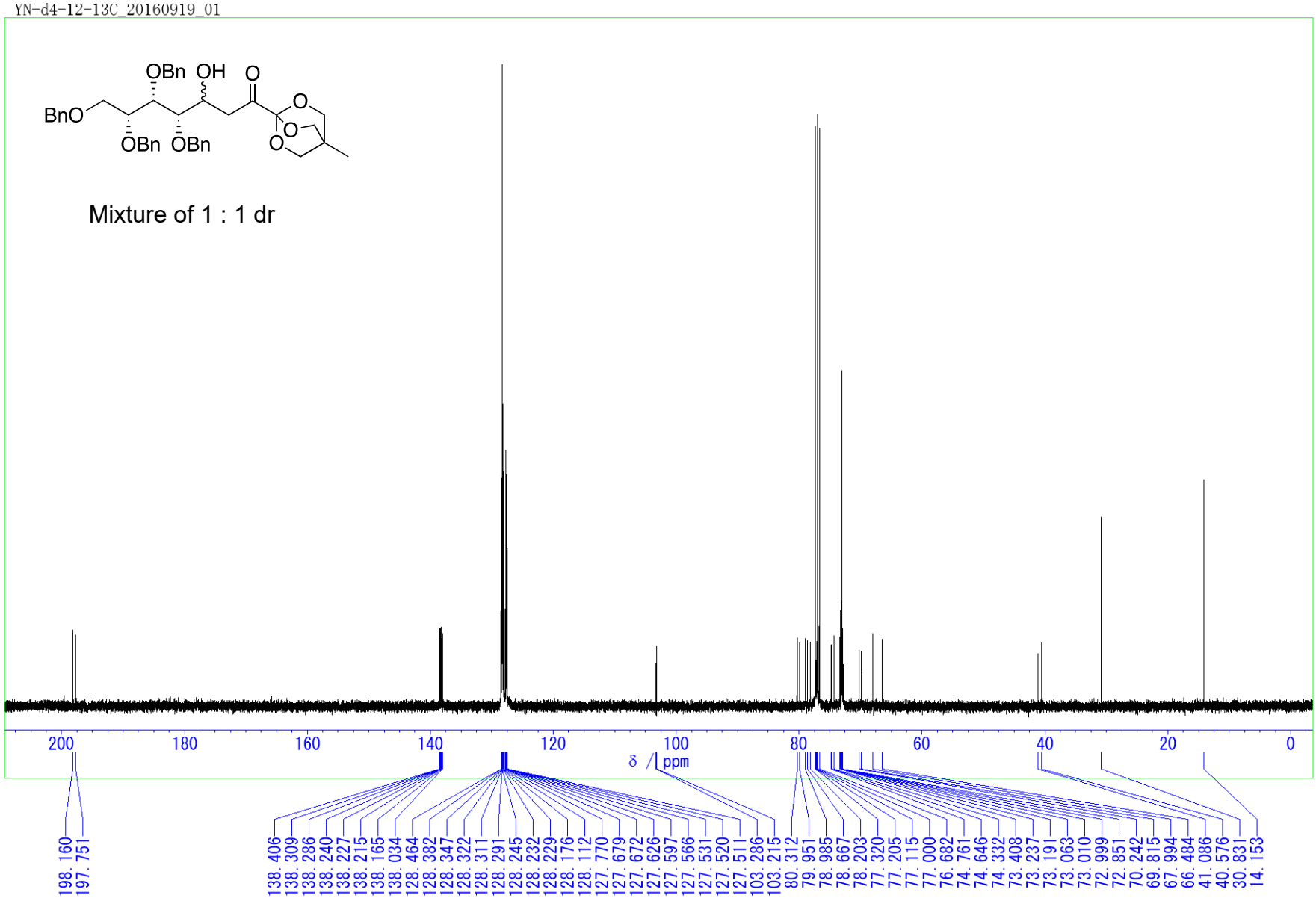
N-((2*R*,3*S*)-3-(benzyloxy)-1-hydroxybutan-2-yl)acetamide 32



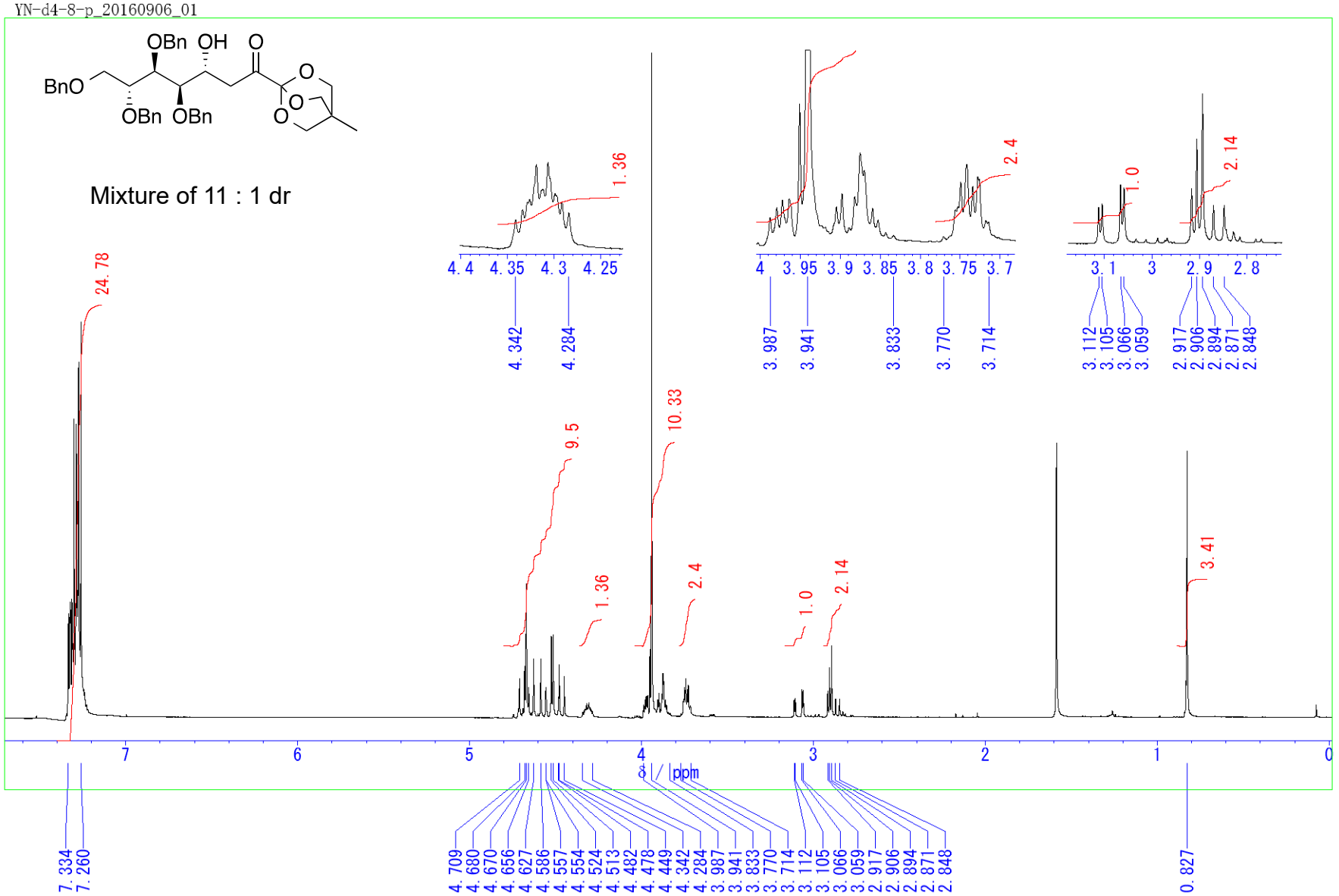
(4*S*,5*S*,6*R*)-4,5,6,7-tetrakis(benzyloxy)-3-hydroxy-1-(4-methyl-2,6,7-trioxabicyclo[2.2.2]octan-1-yl) heptan-1-one 18a



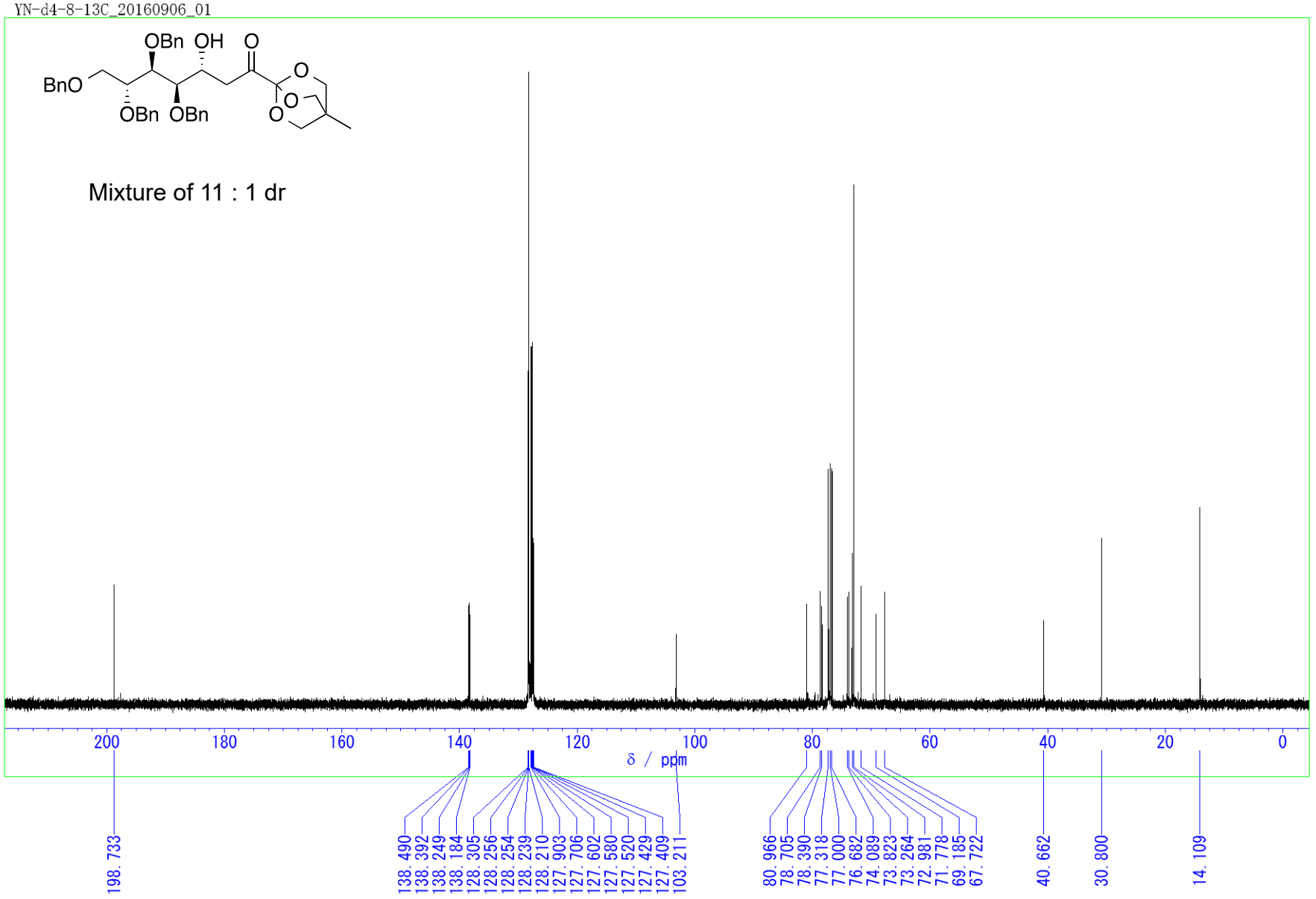
(4*S*,5*S*,6*R*)-4,5,6,7-tetrakis(benzyloxy)-3-hydroxy-1-(4-methyl-2,6,7-trioxabicyclo[2.2.2]octan-1-yl) heptan-1-one 18a



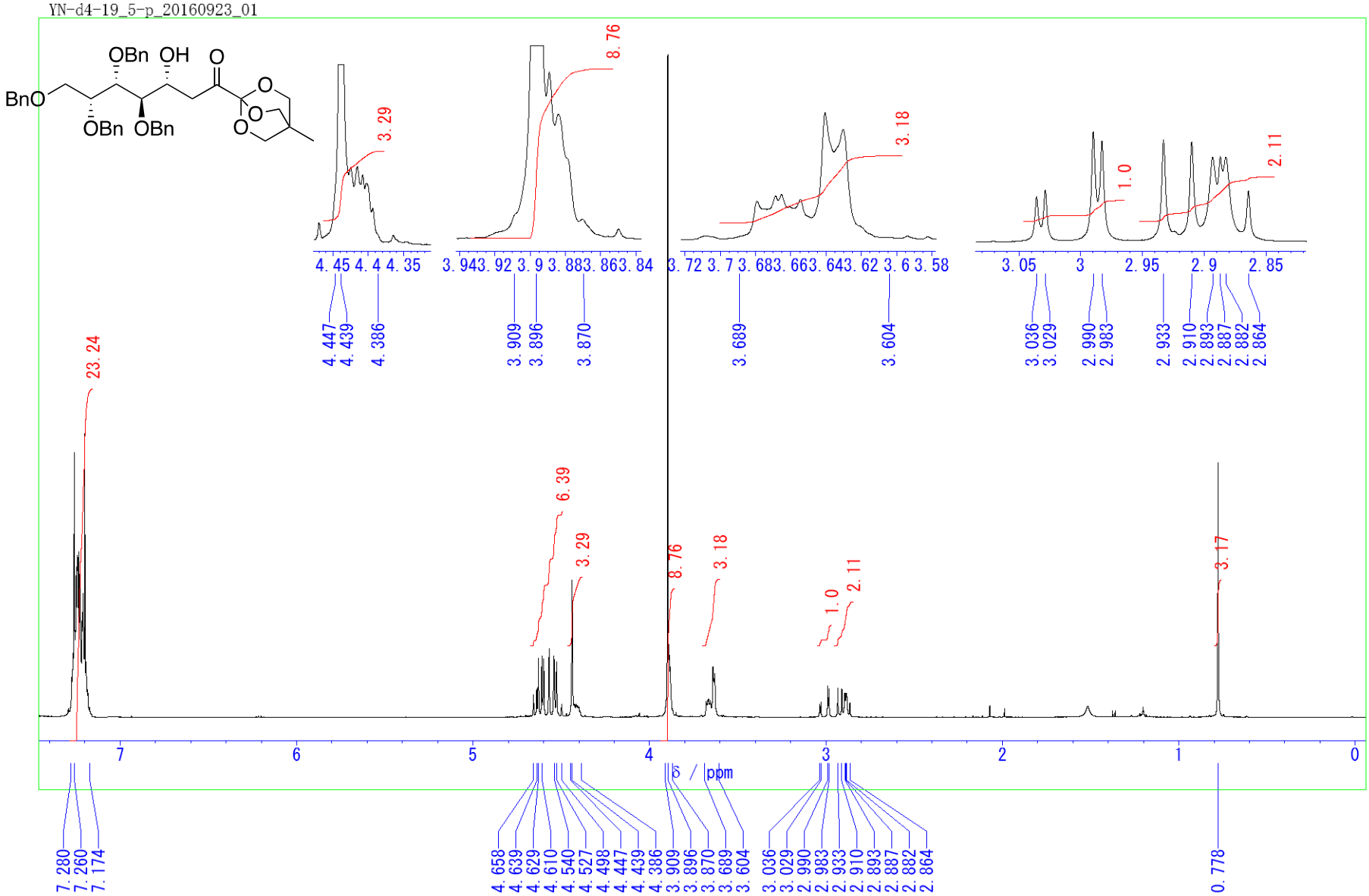
(3*R*,4*R*,5*R*,6*R*)-4,5,6,7-tetrakis(benzyloxy)-3-hydroxy-1-(4-methyl-2,6,7-trioxabicyclo[2.2.2]octan-1-yl) heptan-1-one 18b



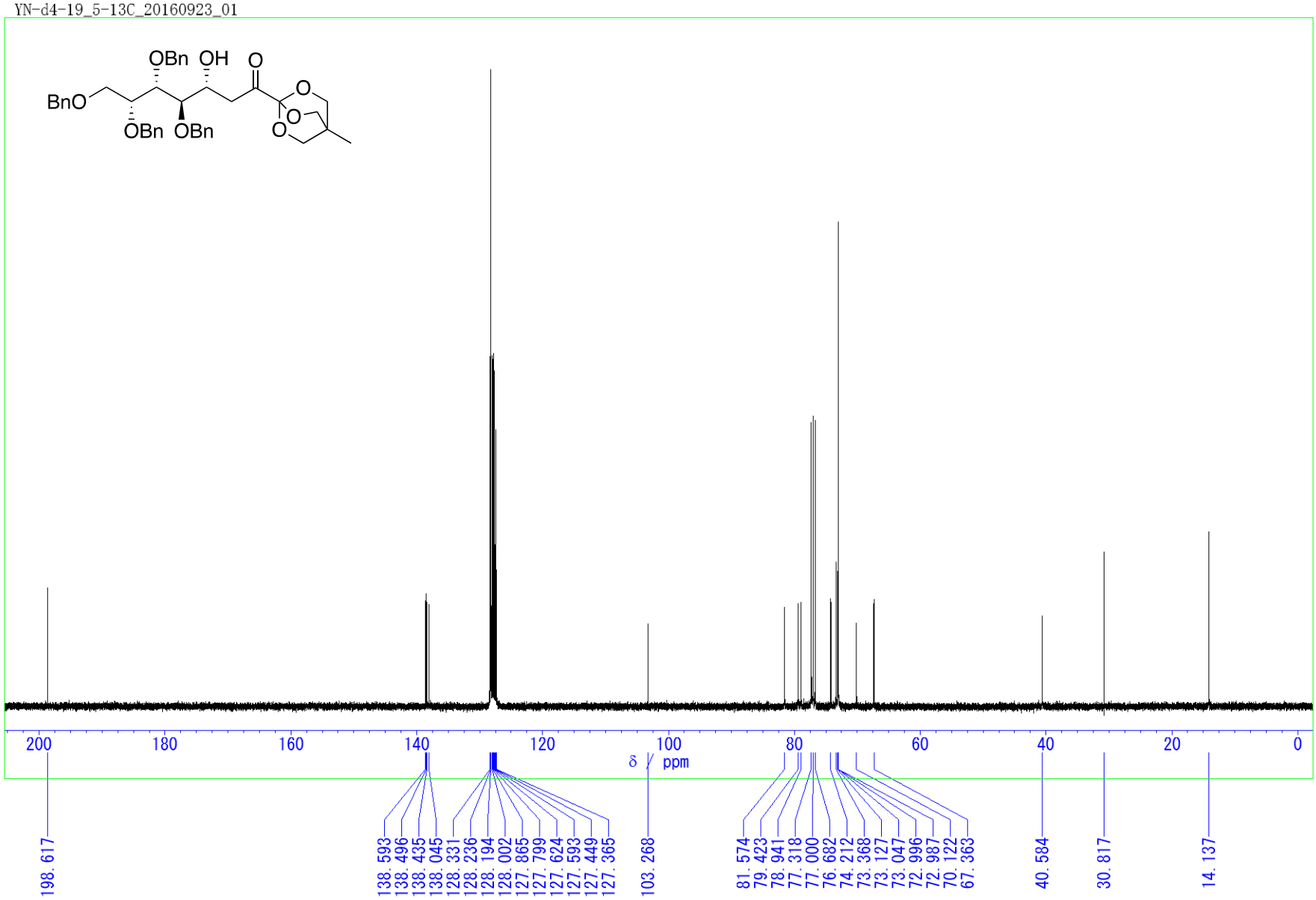
(3*R*,4*R*,5*R*,6*R*)-4,5,6,7-tetrakis(benzyloxy)-3-hydroxy-1-(4-methyl-2,6,7-trioxabicyclo[2.2.2]octan-1-yl) heptan-1-one 18b



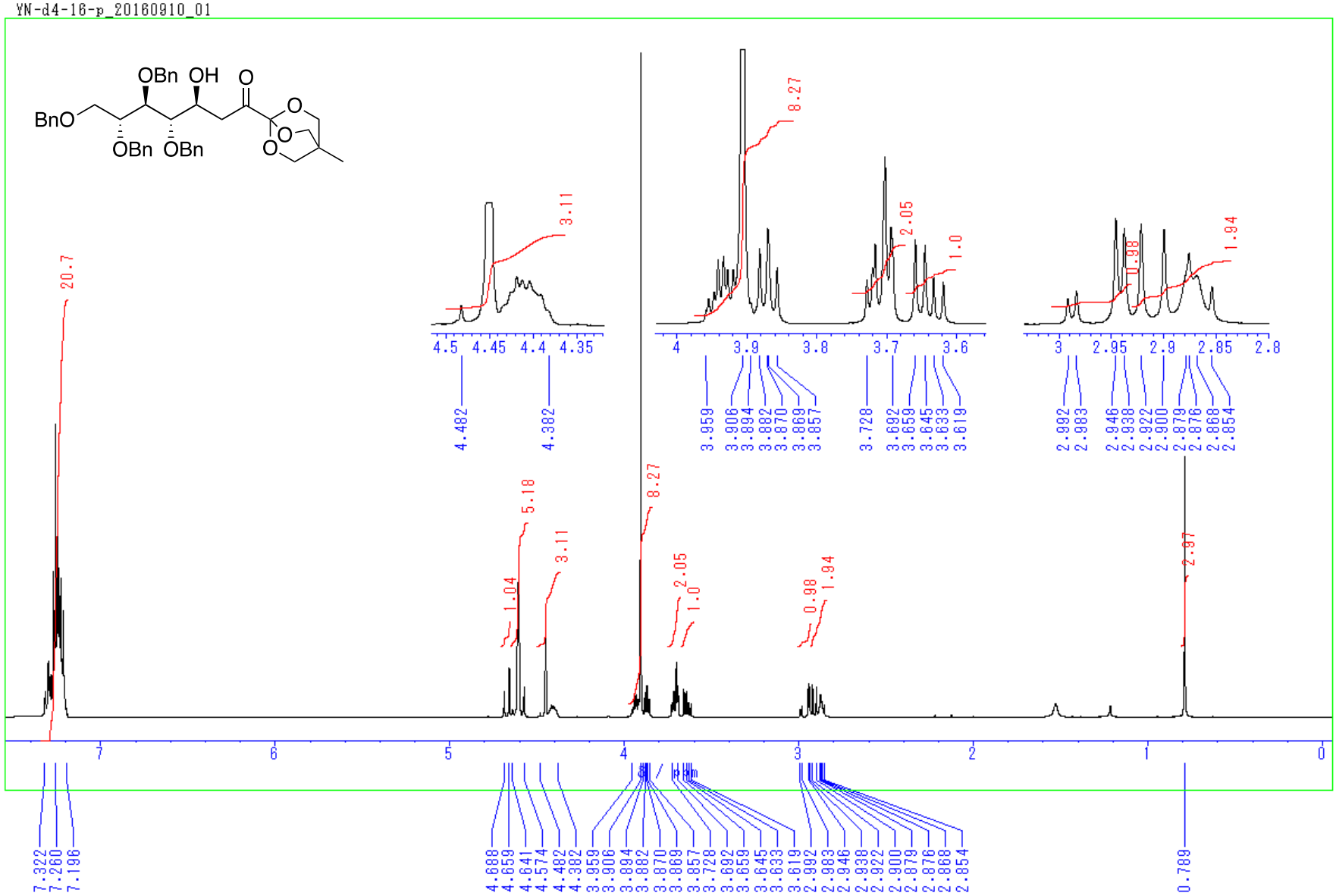
(3*R*,4*R*,5*S*,6*R*)-4,5,6,7-tetrakis(benzyloxy)-3-hydroxy-1-(4-methyl-2,6,7-trioxabicyclo[2.2.2]octan-1-yl) heptan-1-one 18c



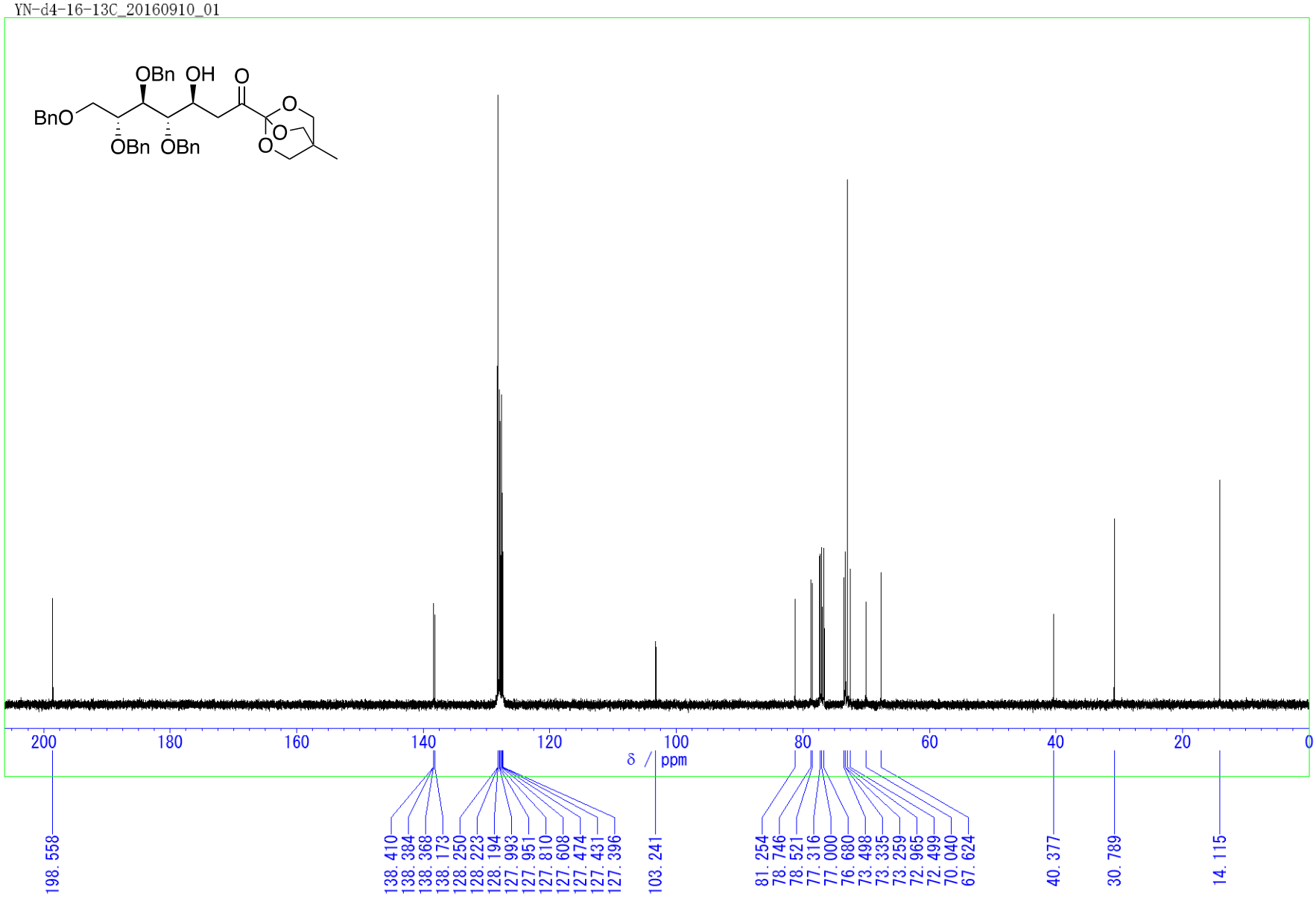
(3*R*,4*R*,5*S*,6*R*)-4,5,6,7-tetrakis(benzyloxy)-3-hydroxy-1-(4-methyl-2,6,7-trioxabicyclo[2.2.2]octan-1-yl) heptan-1-one 18c



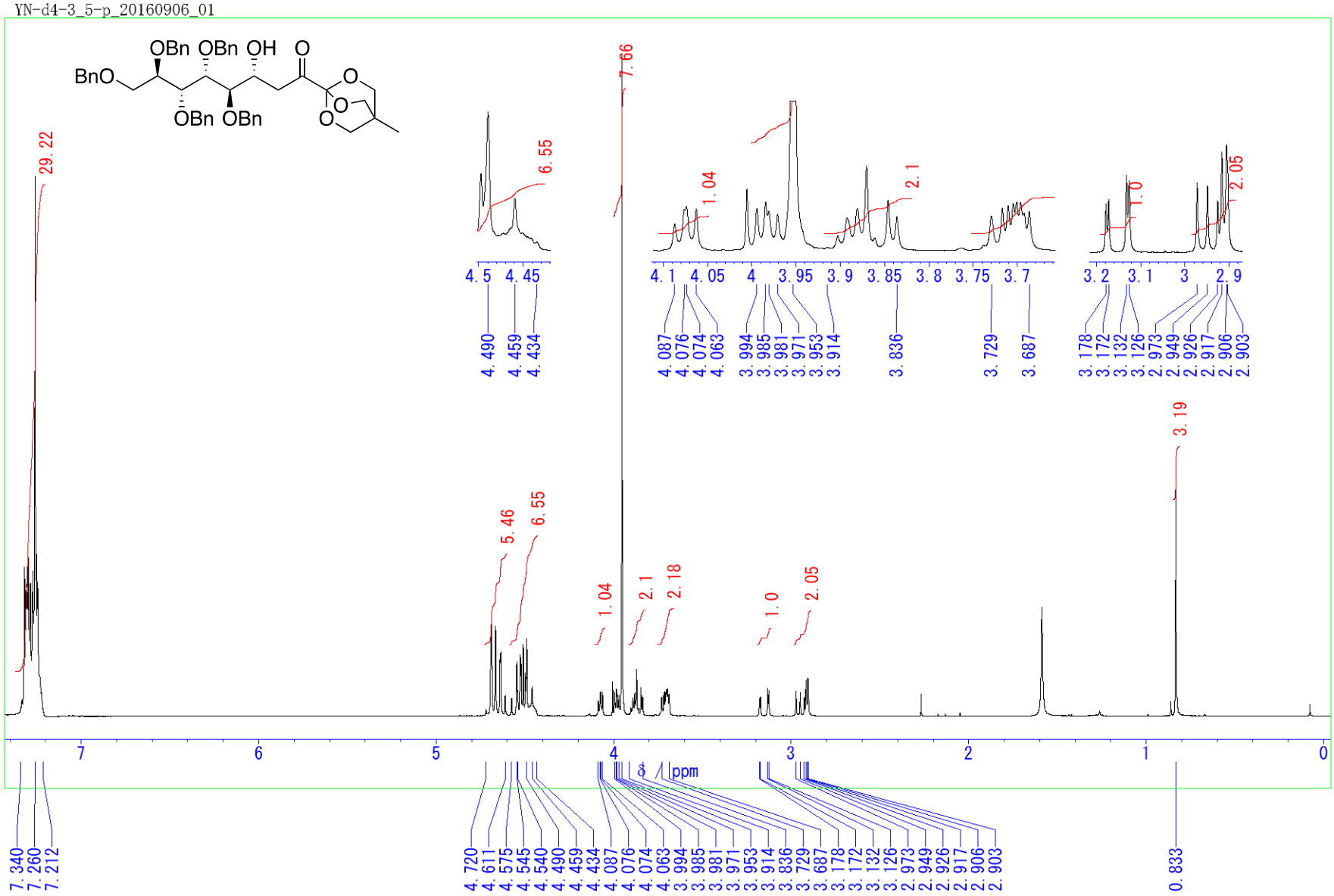
(3*S*,4*S*,5*R*,6*R*)-4,5,6,7-tetrakis(benzyloxy)-3-hydroxy-1-(4-methyl-2,6,7-trioxabicyclo[2.2.2]octan-1-yl) heptan-1-one 18d



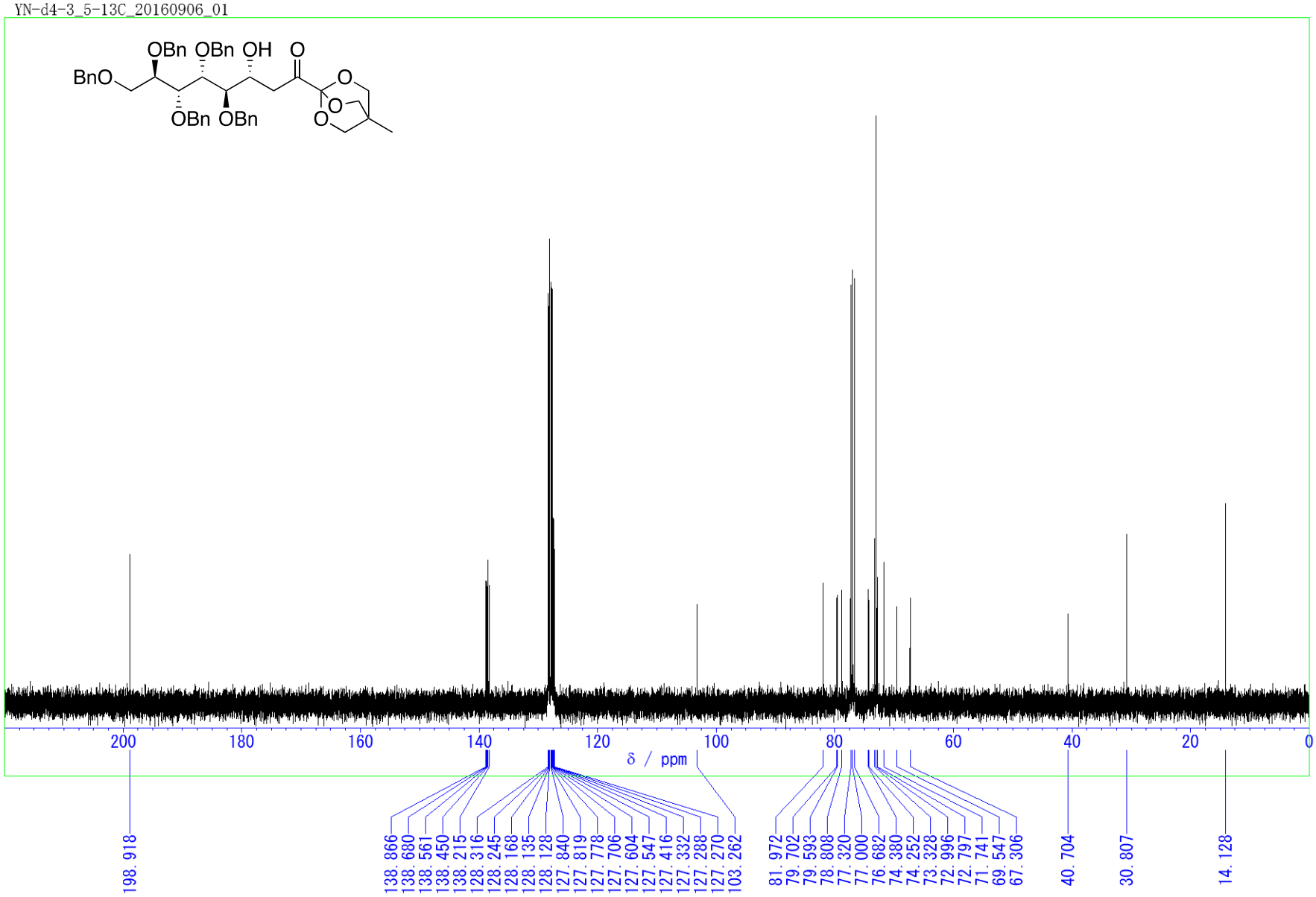
(3*S*,4*S*,5*R*,6*R*)-4,5,6,7-tetrakis(benzyloxy)-3-hydroxy-1-(4-methyl-2,6,7-trioxabicyclo[2.2.2]octan-1-yl) heptan-1-one 18d



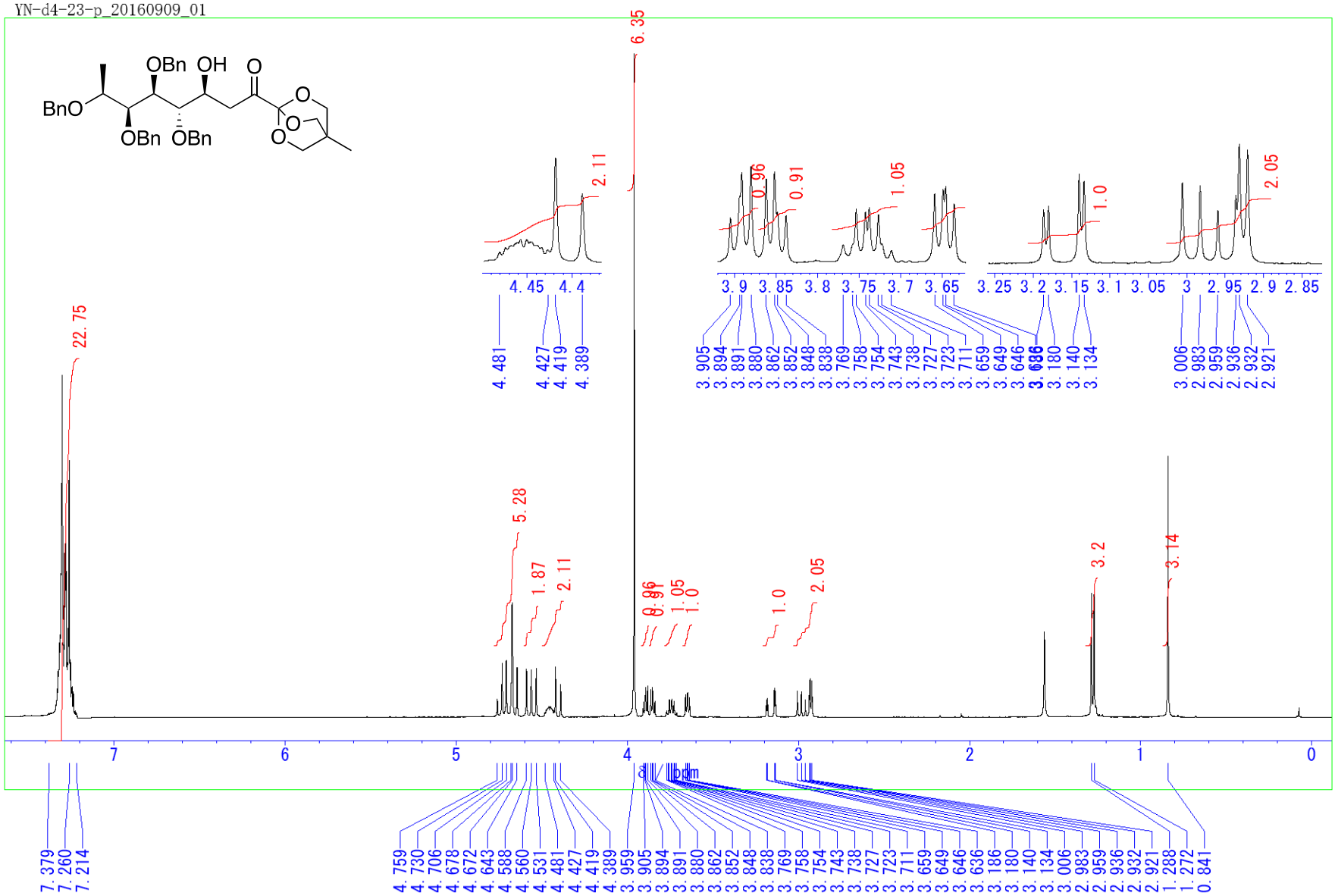
(3*R*,4*R*,5*R*,6*R*,7*R*)-4,5,6,7,8-pentakis(benzyloxy)-3-hydroxy-1-(4-methyl-2,6,7-trioxabicyclo [2.2.2]octan-1-yl)octan-1-one 18e



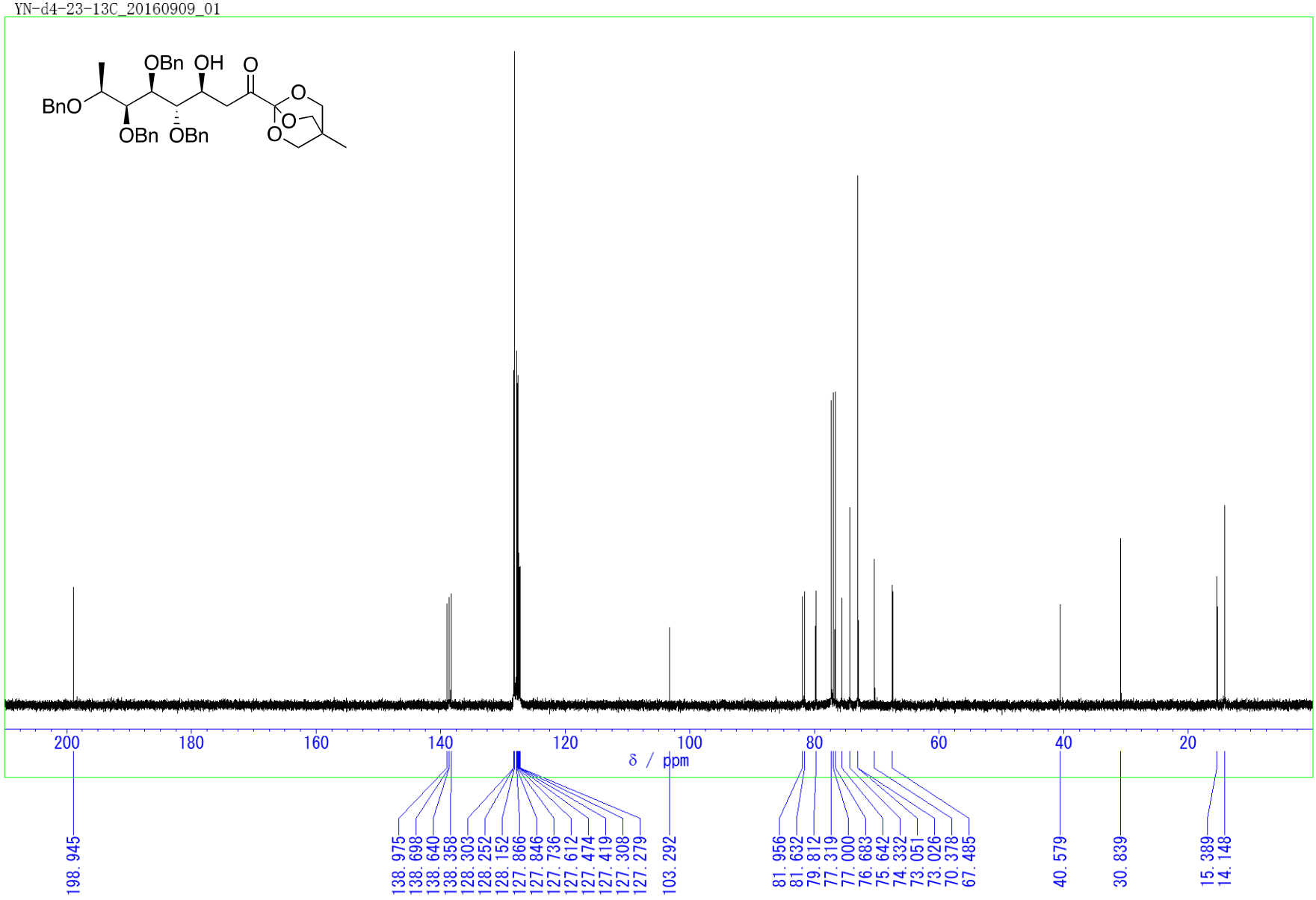
(3*R*,4*R*,5*R*,6*R*,7*R*)-4,5,6,7,8-pentakis(benzyloxy)-3-hydroxy-1-(4-methyl-2,6,7-trioxabicyclo [2.2.2]octan-1-yl)octan-1-one 18e



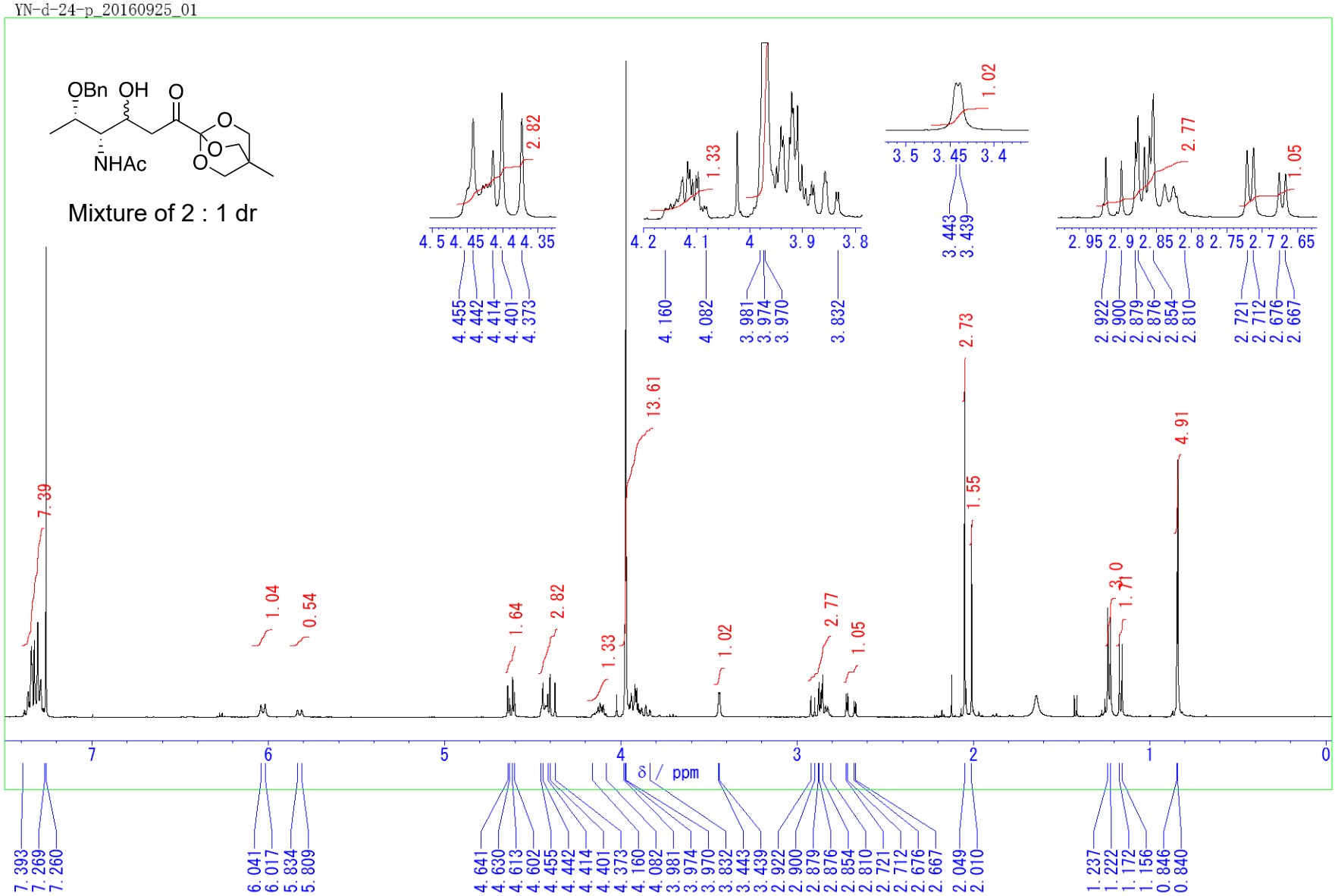
(3*S*,4*S*,5*S*,6*S*,7*S*)-4,5,6,7-tetrakis(benzyloxy)-3-hydroxy-1-(4-methyl-2,6,7-trioxabicyclo [2.2.2]octan-1-yl)octan-1-one 18f



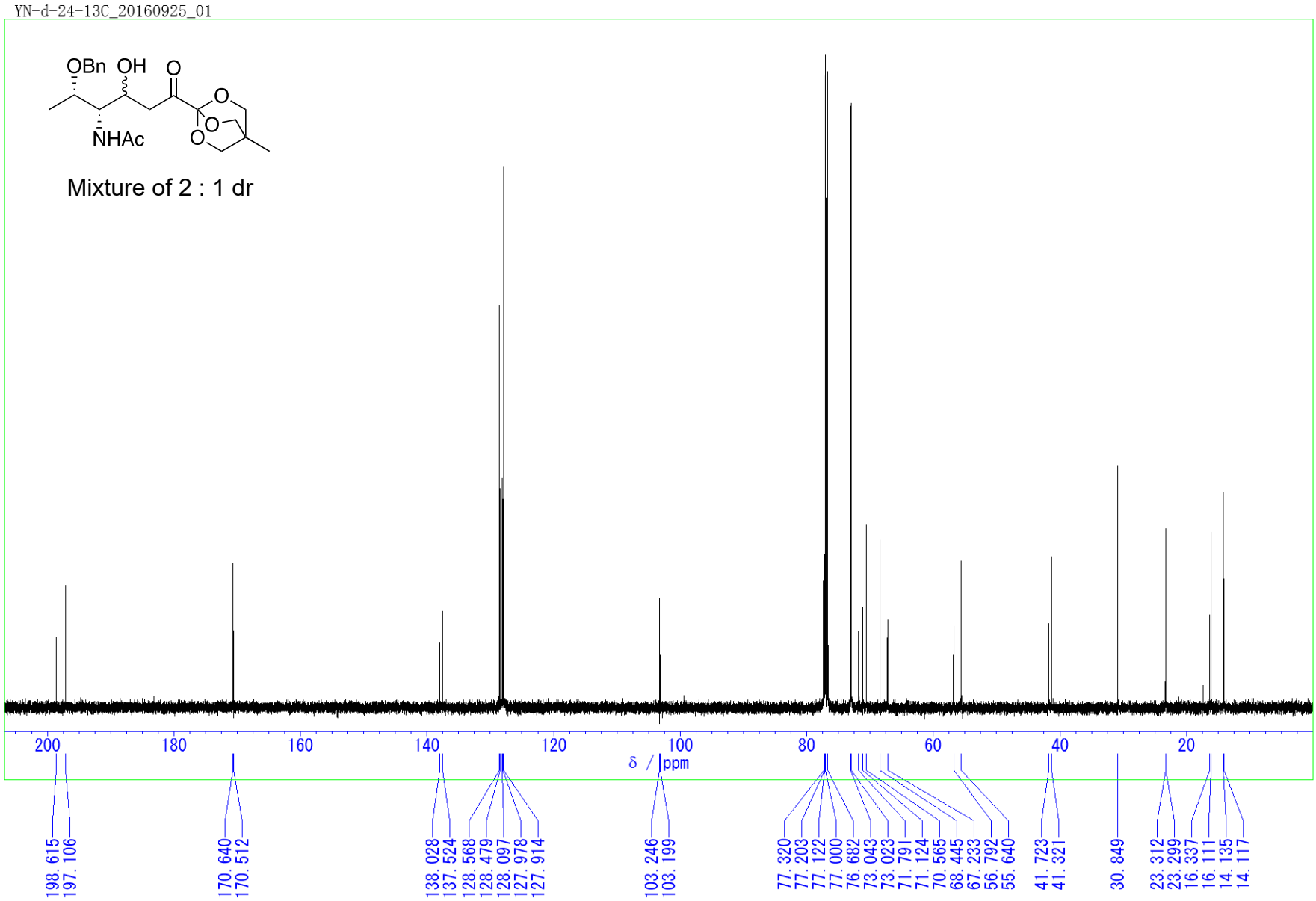
(3*S*,4*S*,5*S*,6*S*,7*S*)-4,5,6,7-tetrakis(benzyloxy)-3-hydroxy-1-(4-methyl-2,6,7-trioxabicyclo [2.2.2]octan-1-yl)octan-1-one 18f



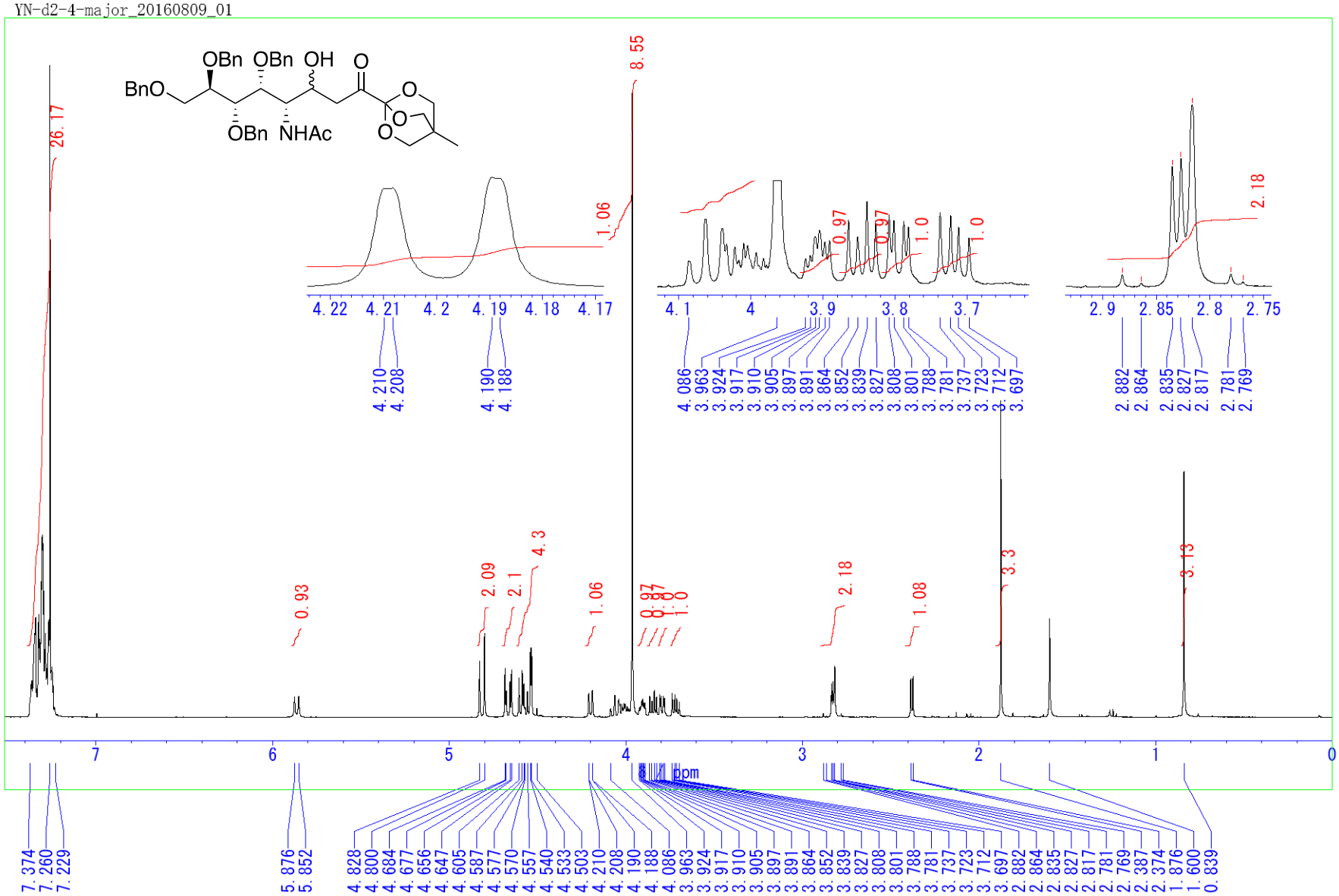
_N_-((2_S_,3_S_,4_S_)-2-(benzyloxy)-4-hydroxy-6-(4-methyl-2,6,7-trioxabicyclo[2.2.2]octan-1-yl)-6-oxohexan-3-yl)acetamide 19a



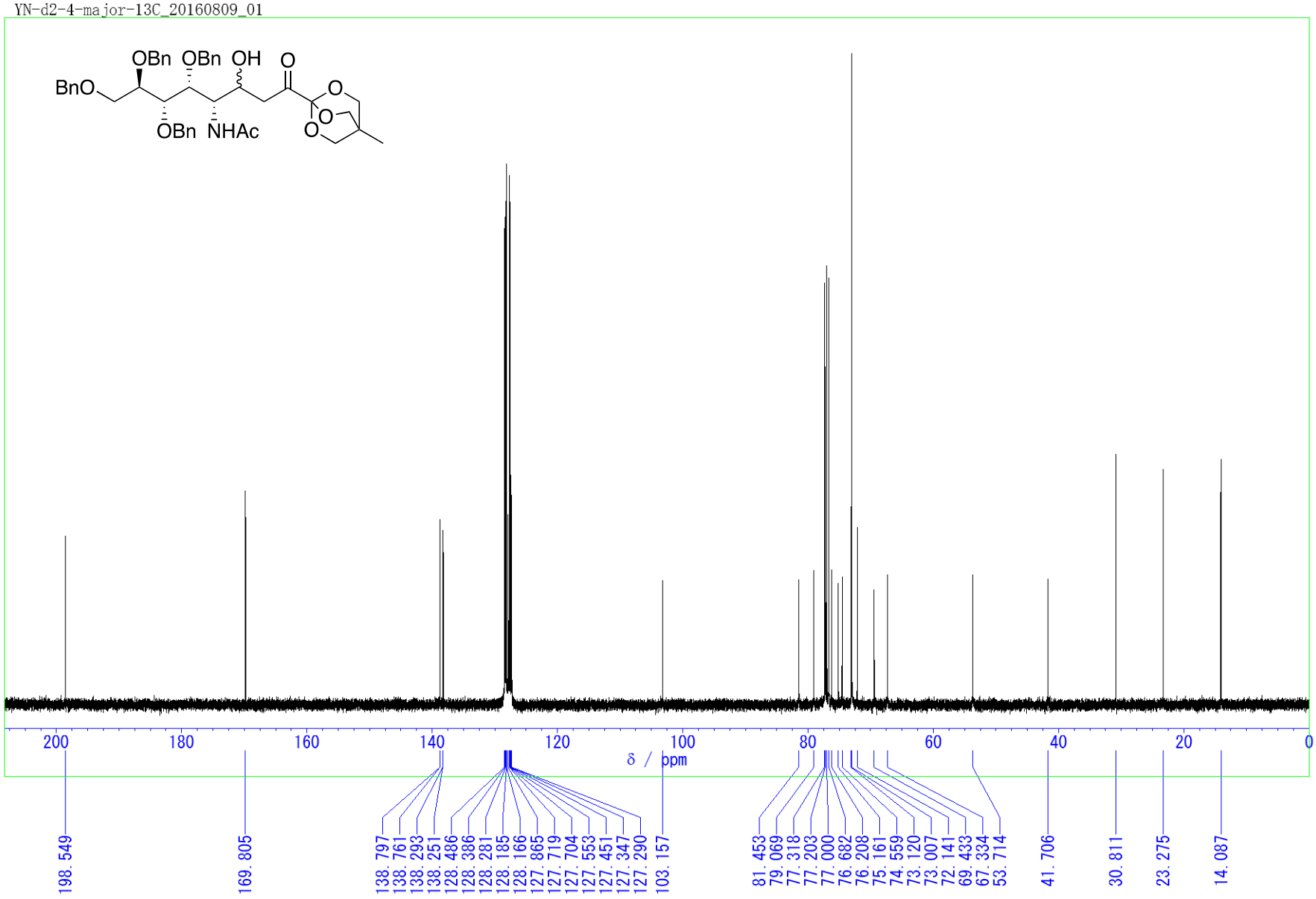
_N_-((2_S_,3_S_,4_S_)-2-(benzyloxy)-4-hydroxy-6-(4-methyl-2,6,7-trioxabicyclo[2.2.2]octan-1-yl)-6-oxohexan-3-yl)acetamide 19a



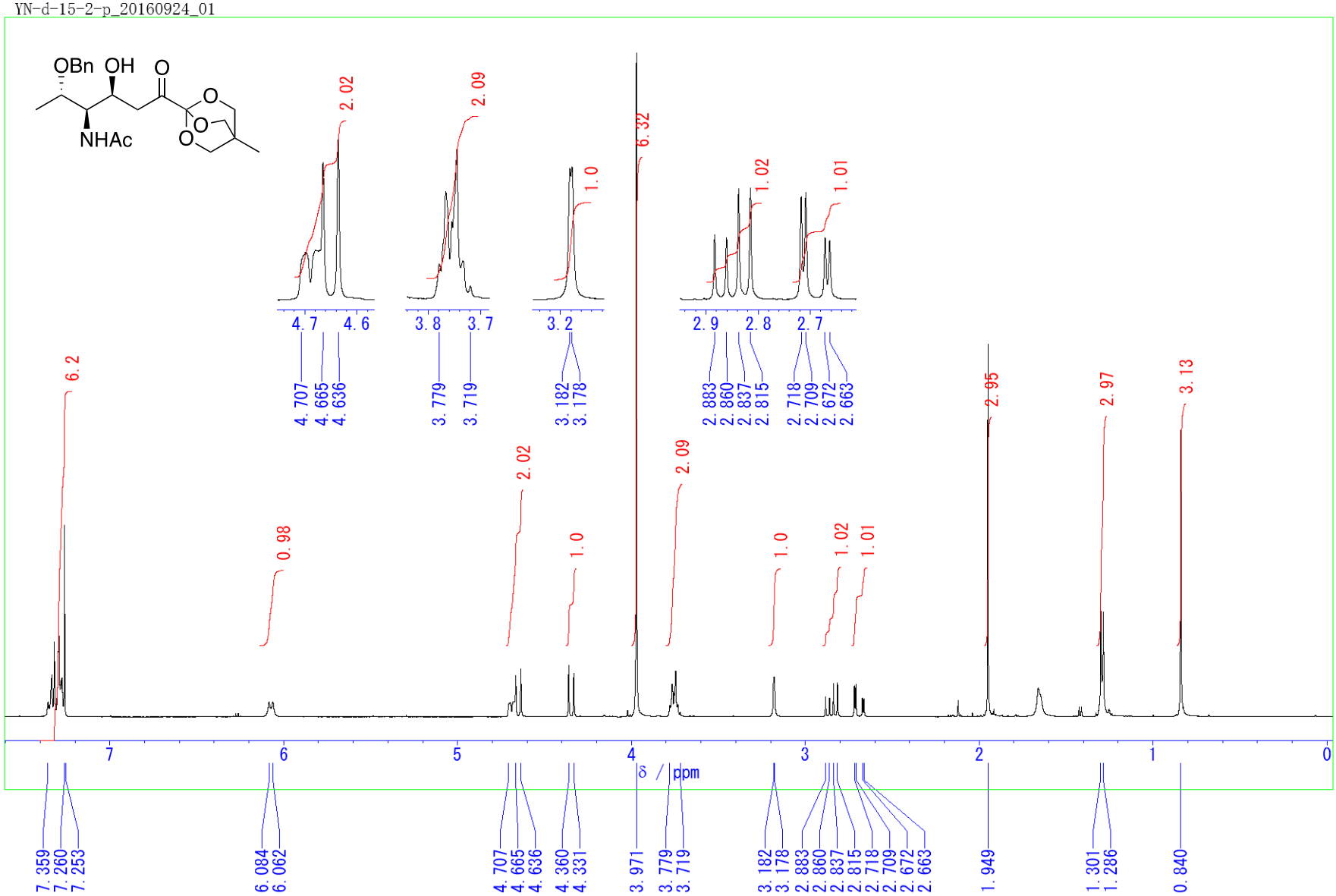
N-((4*S*,5*R*,6*S*,7*R*)-5,6,7,8-tetrakis(benzyloxy)-3-hydroxy-1-(4-methyl-2,6,7-trioxabicyclo[2.2.2]octan-1-yl)-1-oxooctan-4-yl)acetamide19b



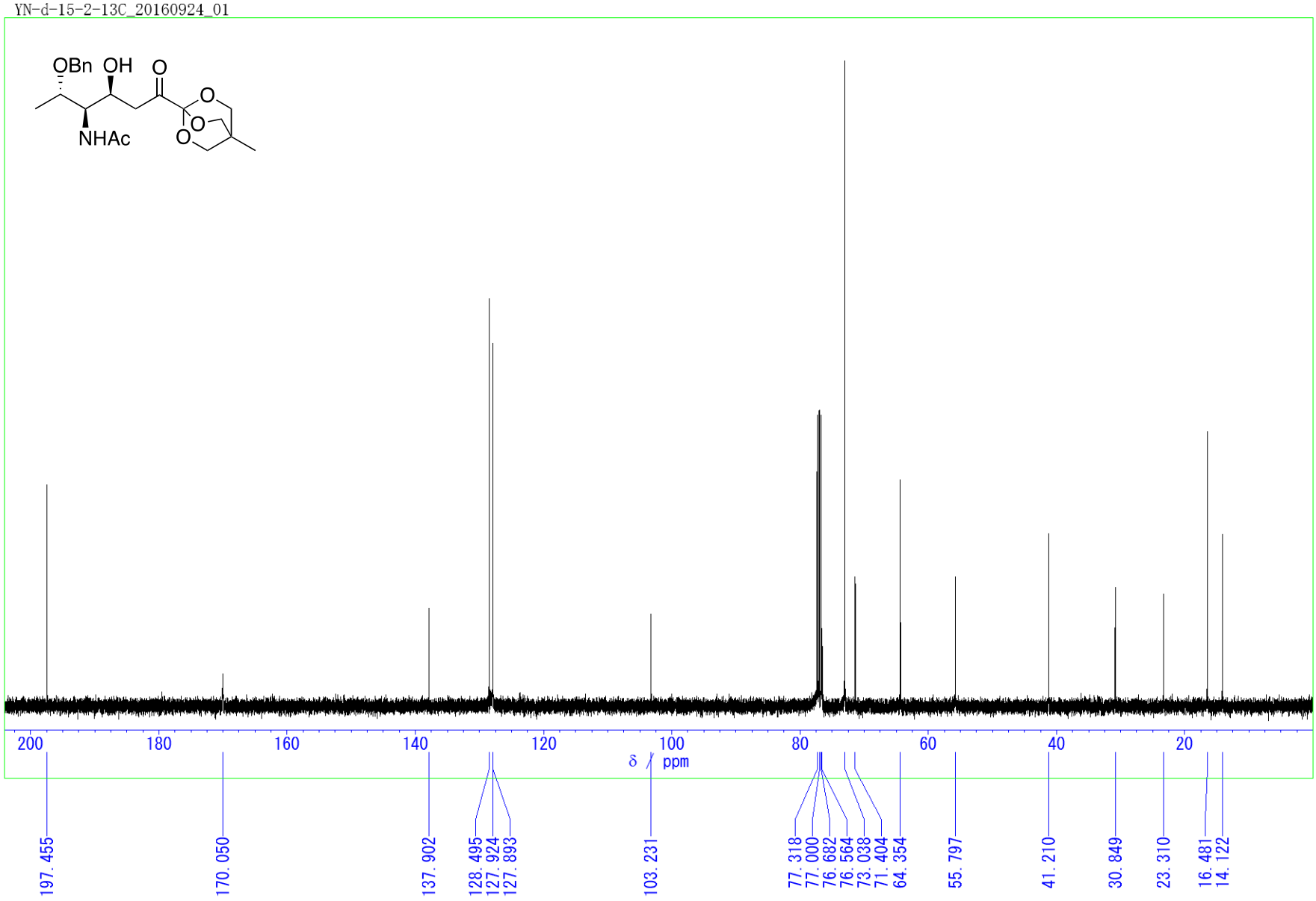
N-((3*S*,4*S*,5*R*,6*S*,7*R*)-5,6,7,8-tetrakis(benzyloxy)-3-hydroxy-1-(4-methyl-2,6,7-trioxabicyclo[2.2.2]octan-1-yl)-1-oxooctan-4-yl)acetamide 19b



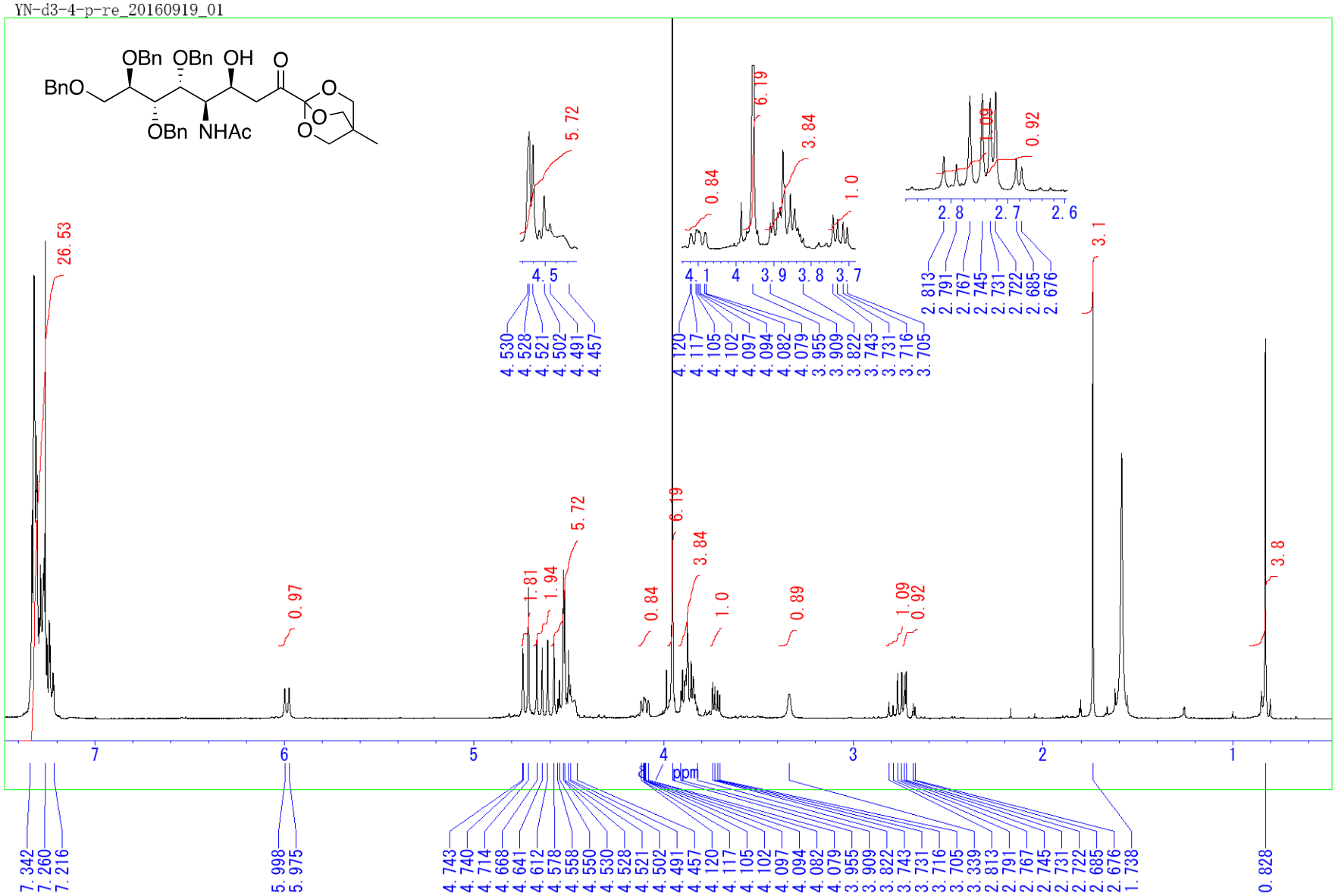
_N_-((2_S_,3_R_,4_S_)-2-(benzyloxy)-4-hydroxy-6-(4-methyl-2,6,7-trioxabicyclo[2.2.2]octan-1-yl)-6-oxohexan-3-yl)acetamide 19c



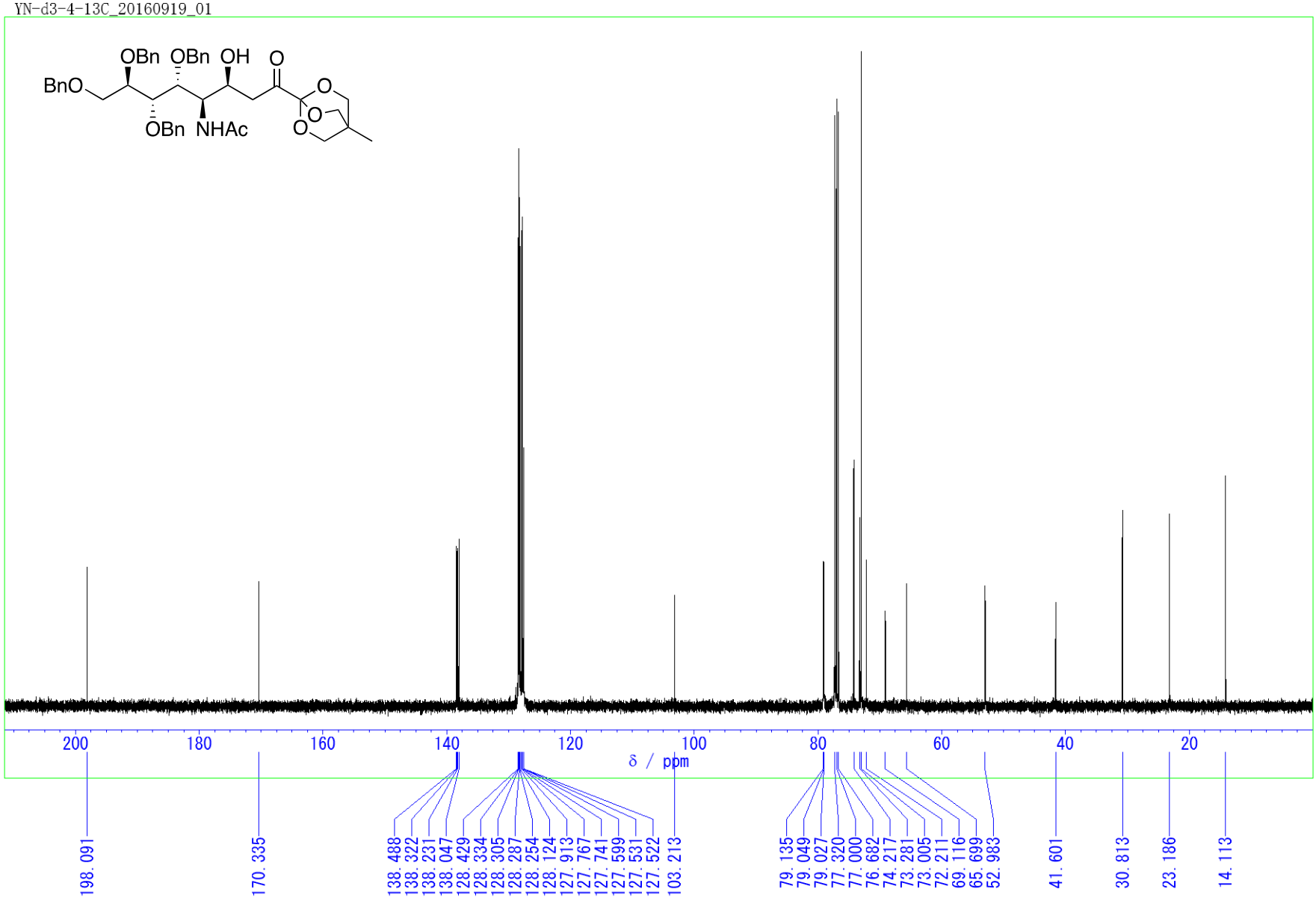
_N_-((2_S_,3_R_,4_S_)-2-(benzyloxy)-4-hydroxy-6-(4-methyl-2,6,7-trioxabicyclo[2.2.2]octan-1-yl)-6-oxohexan-3-yl)acetamide 19c



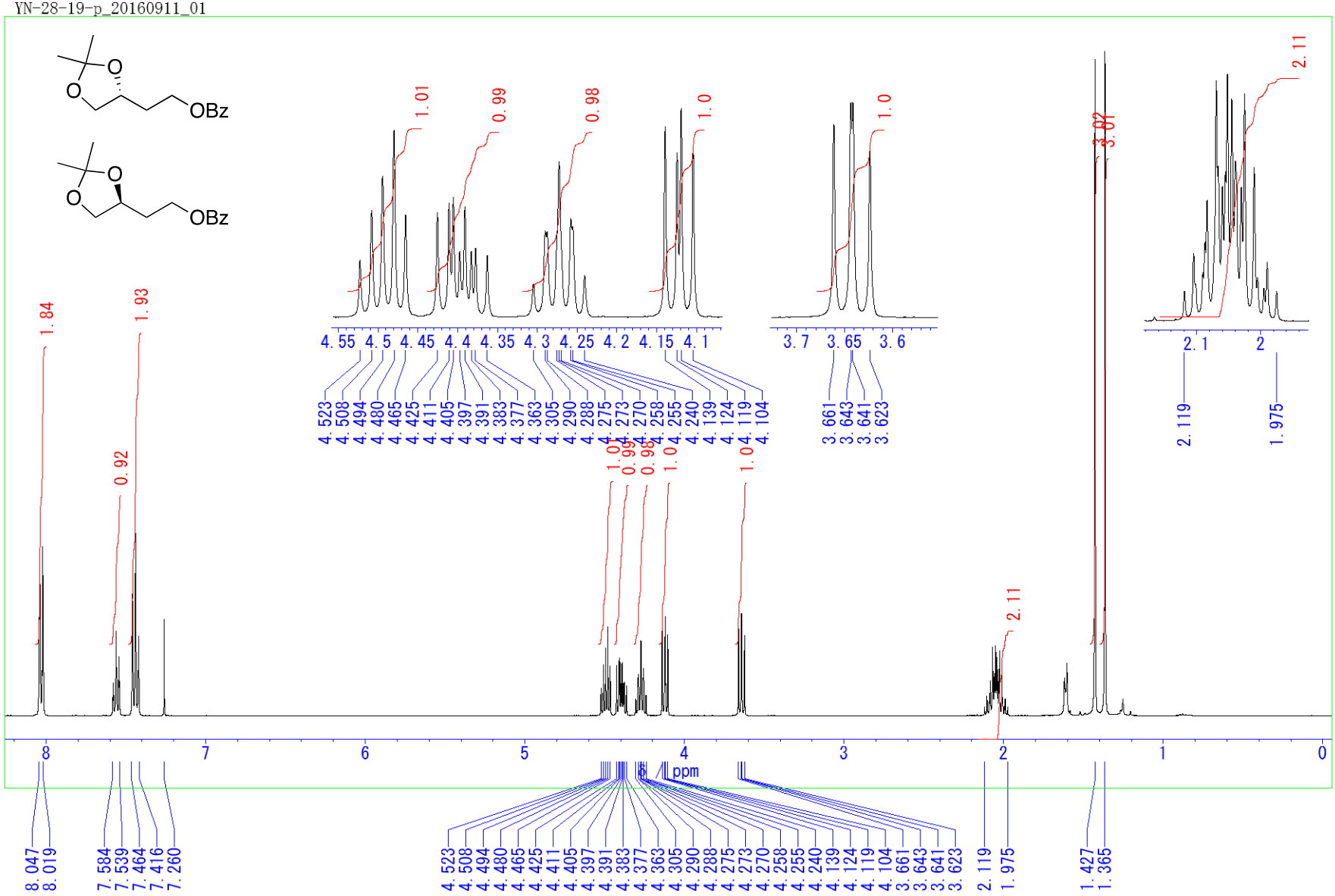
N-((3*S*,4*R*,5*R*,6*S*,7*R*)-5,6,7,8-tetrakis(benzyloxy)-3-hydroxy-1-(4-methyl-2,6,7-trioxabicyclo[2.2.2]octan-1-yl)-1-oxooctan-4-yl)acetamide 19d



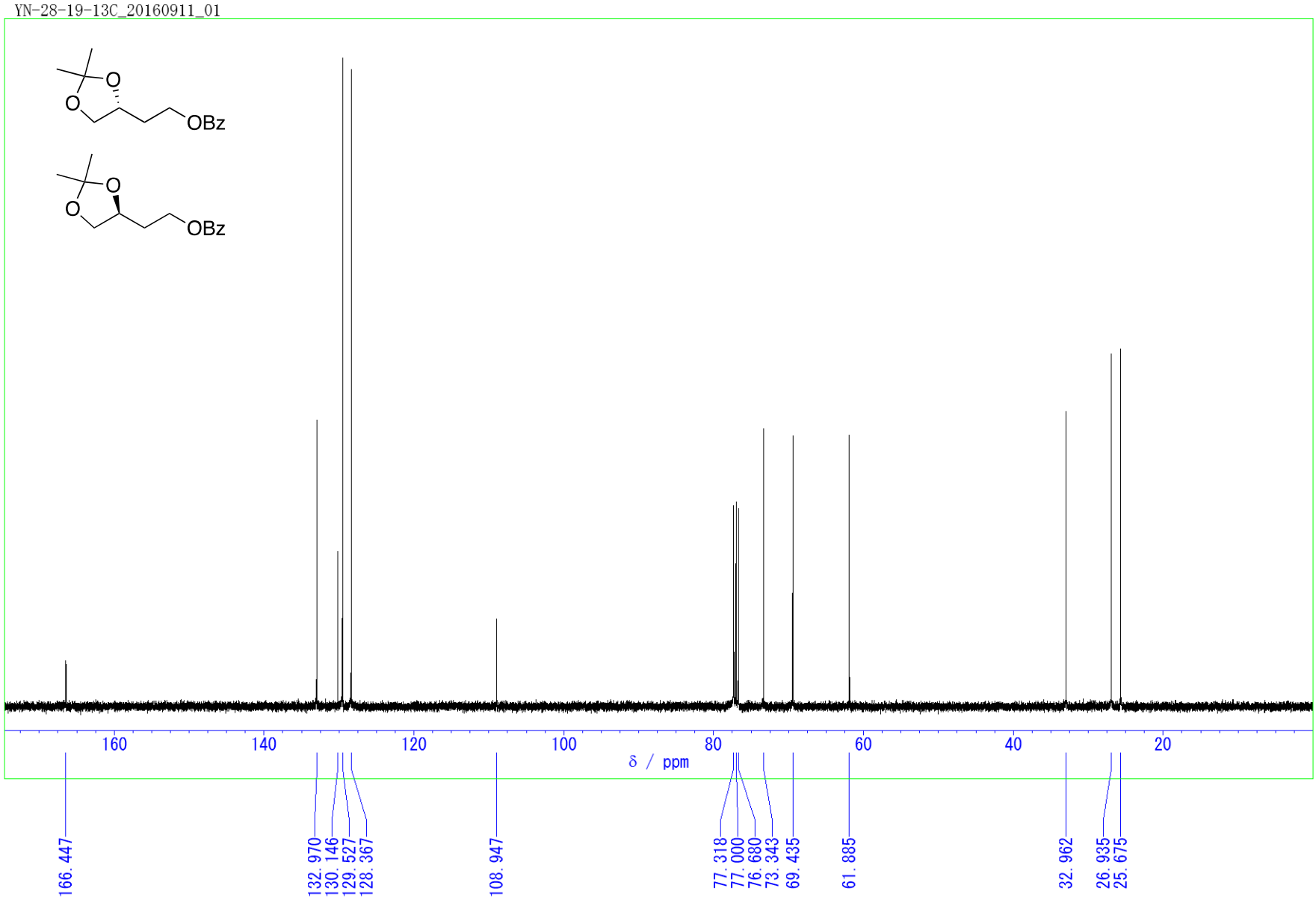
_N_-((3_S_,4_R_,5_R_,6_S_,7_R_)-5,6,7,8-tetrakis(benzyloxy)-3-hydroxy-1-(4-methyl-2,6,7-trioxabicyclo[2.2.2]octan-1-yl)-1-oxooctan-4-yl)acetamide 19d



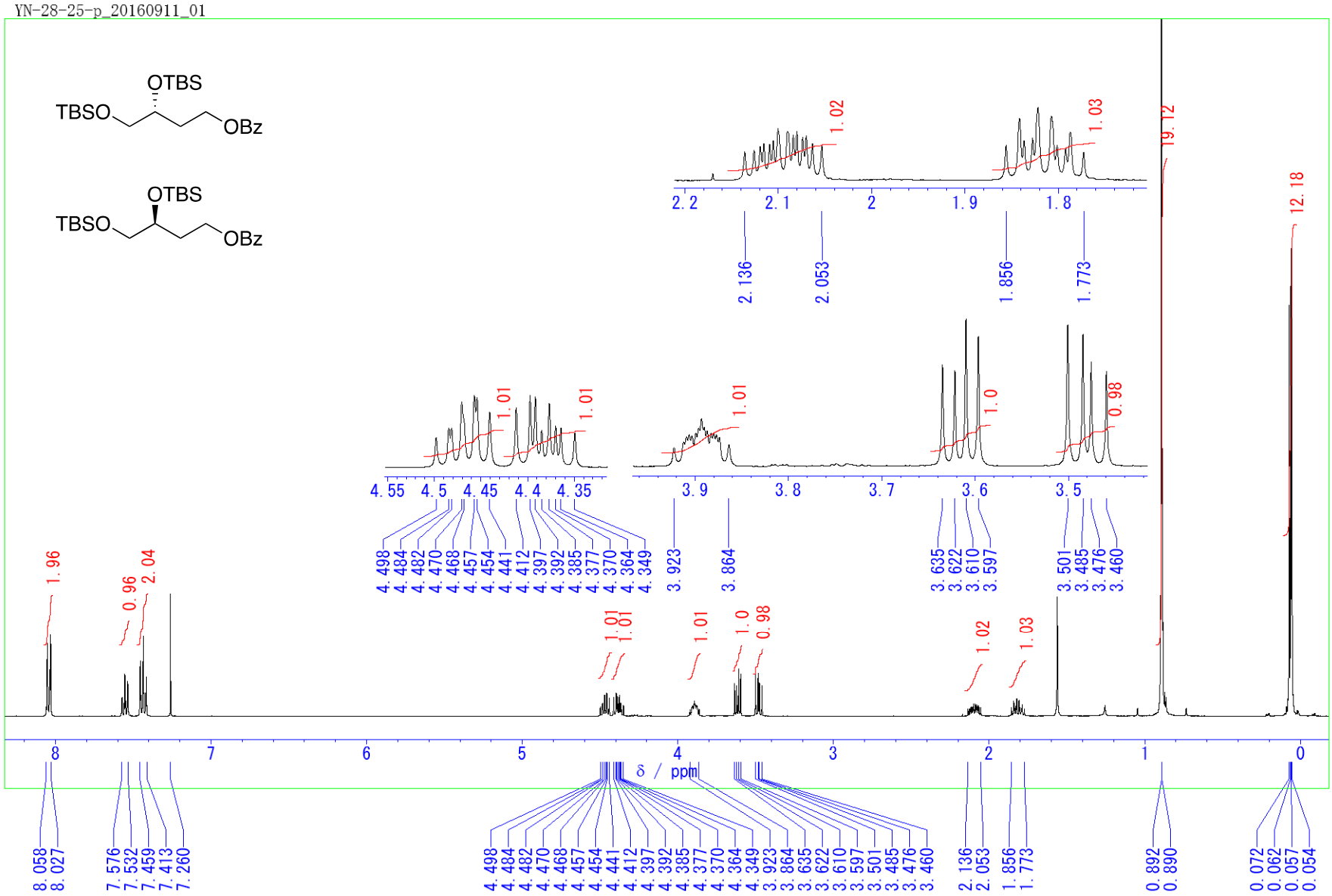
(*R*)-2-(2,2-dimethyl-1,3-dioxolan-4-yl)ethyl benzoate (*R*)-35
(*S*)-2-(2,2-dimethyl-1,3-dioxolan-4-yl)ethyl benzoate (*S*)-35



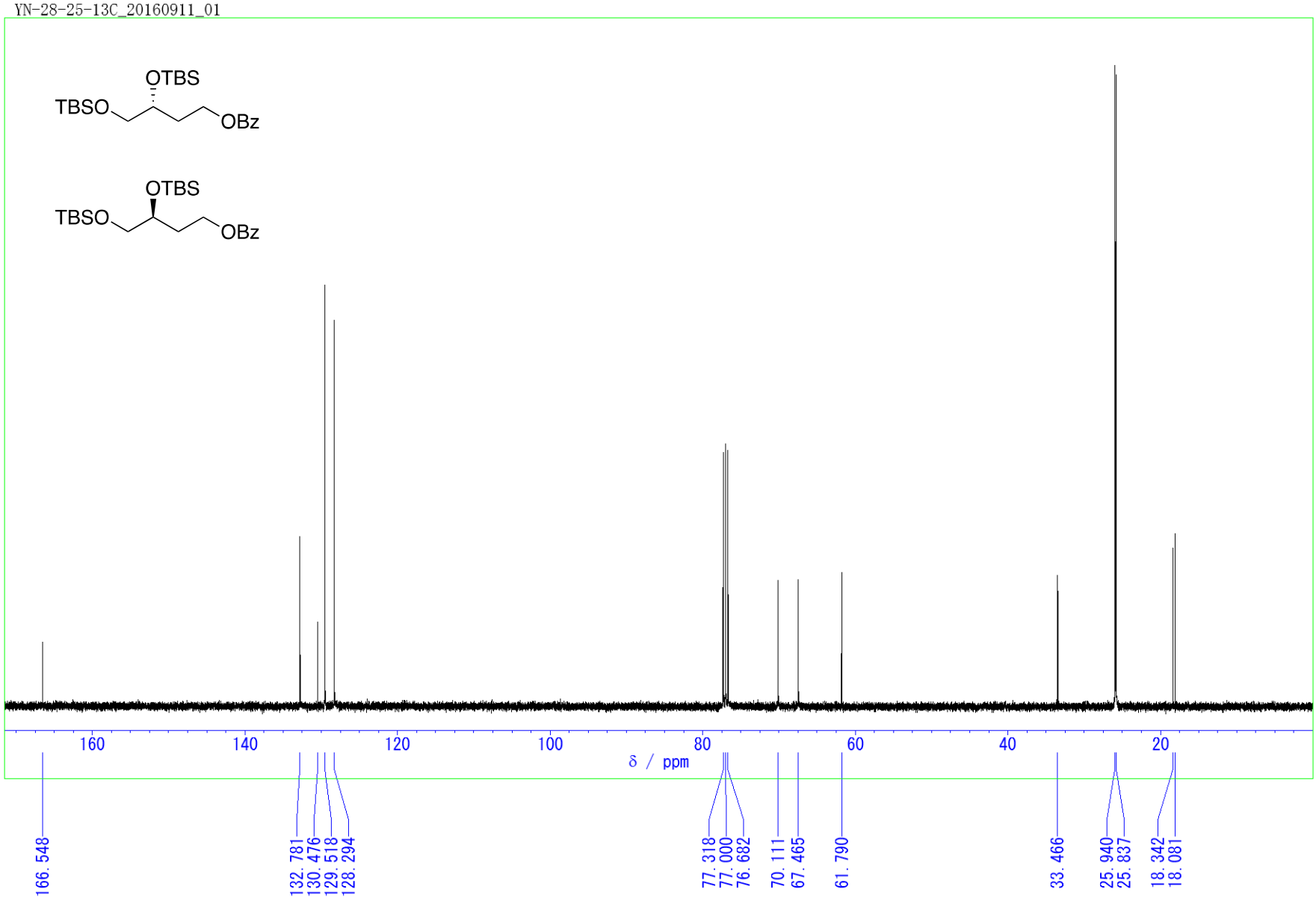
(*R*)-2-(2,2-dimethyl-1,3-dioxolan-4-yl)ethyl benzoate (*R*)-35
(*S*)-2-(2,2-dimethyl-1,3-dioxolan-4-yl)ethyl benzoate (*S*)-35



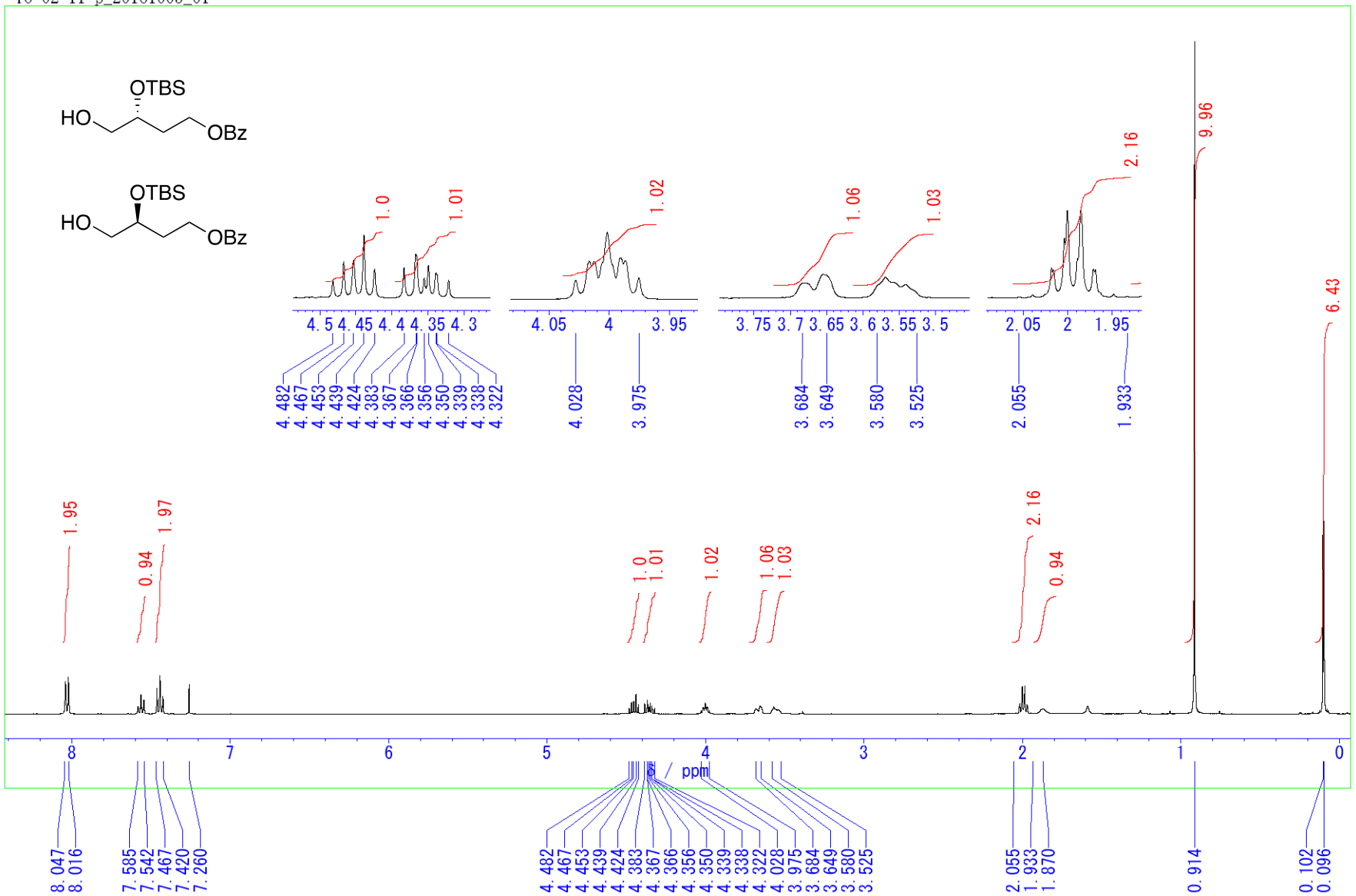
(*R*)-3,4-bis((*tert*-butyldimethylsilyl)oxy)butyl benzoate (*R*)-36
(*S*)-3,4-bis((*tert*-butyldimethylsilyl)oxy)butyl benzoate (*S*)-36



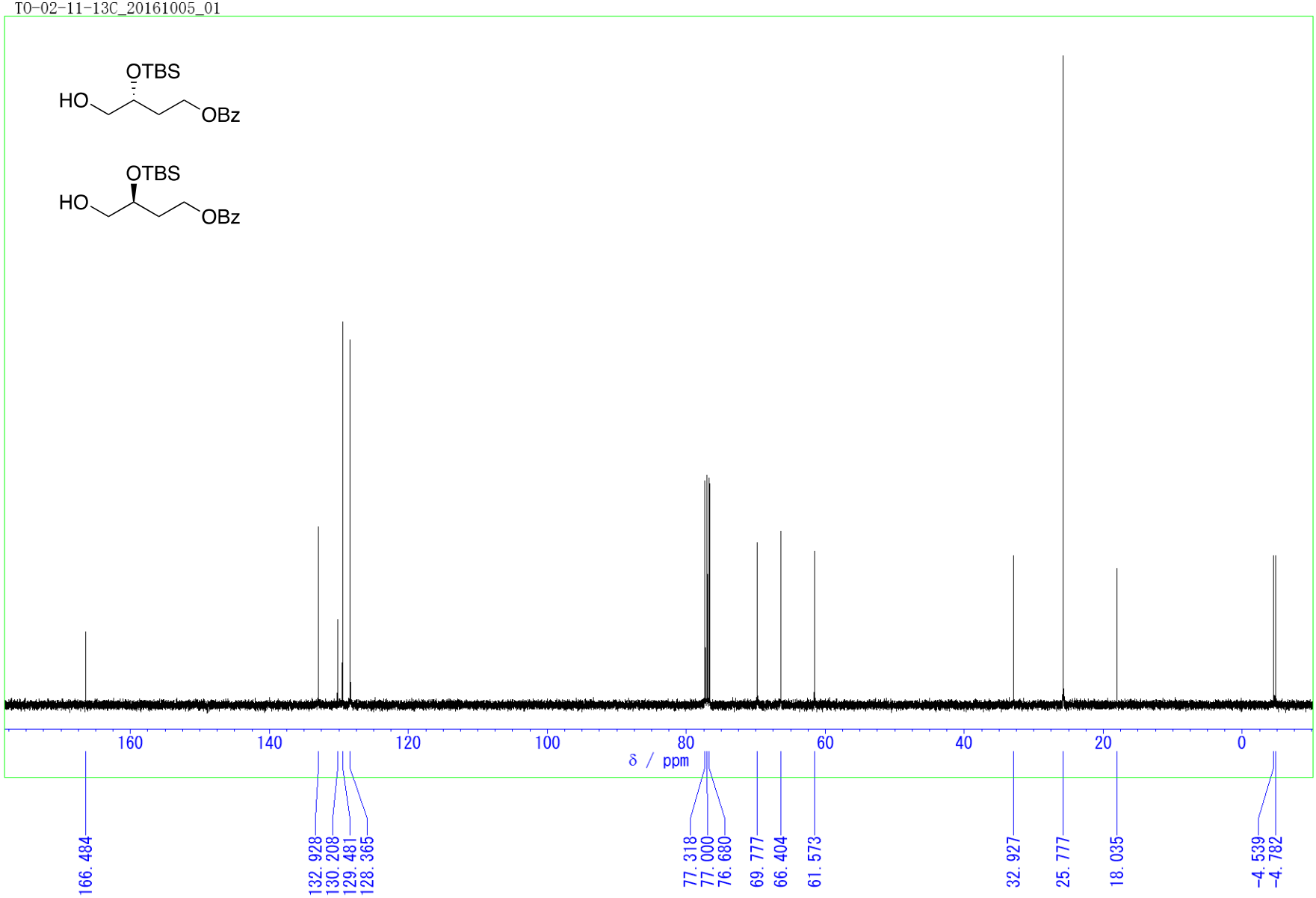
(*R*)-3,4-bis((*tert*-butyldimethylsilyl)oxy)butyl benzoate (*R*)-36
(*S*)-3,4-bis((*tert*-butyldimethylsilyl)oxy)butyl benzoate (*S*)-36



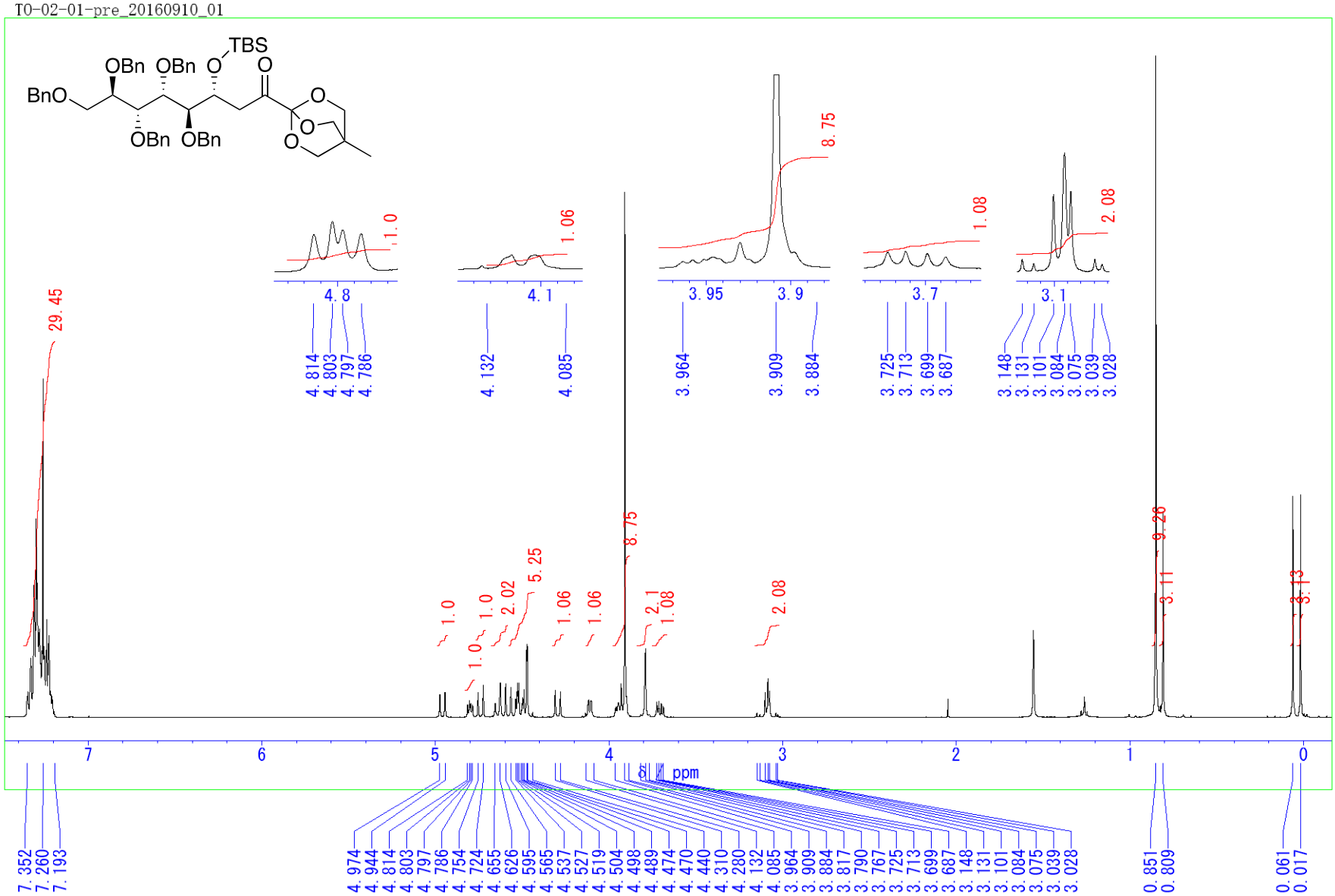
(*R*)-3-((*tert*-butyldimethylsilyl)oxy)-4-hydroxybutyl benzoate (*R*)-34
(*S*)-3-((*tert*-butyldimethylsilyl)oxy)-4-hydroxybutyl benzoate (*S*)-34



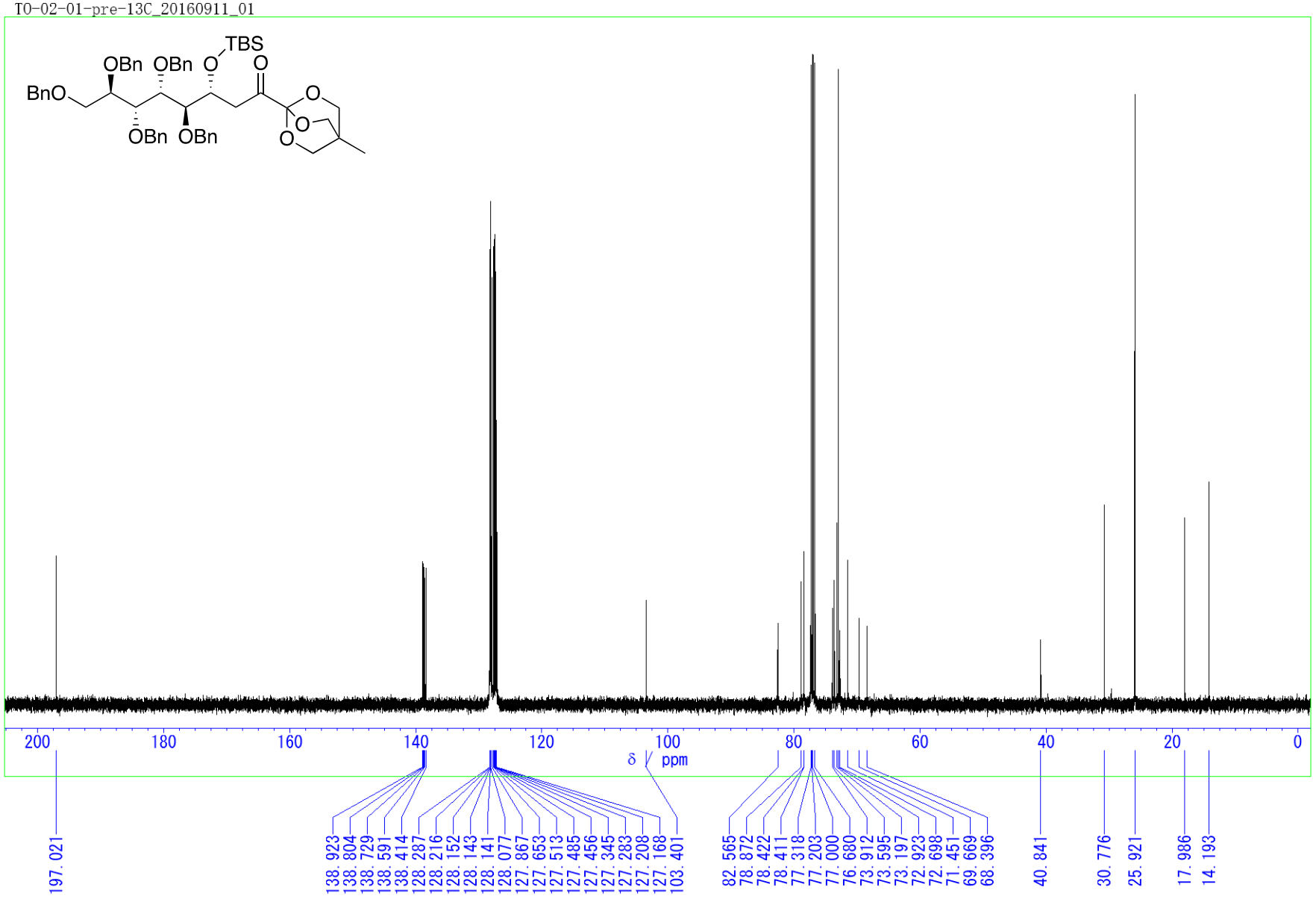
(*R*)-3-((*tert*-butyldimethylsilyl)oxy)-4-hydroxybutyl benzoate (*R*)-34
(*S*)-3-((*tert*-butyldimethylsilyl)oxy)-4-hydroxybutyl benzoate (*S*)-34



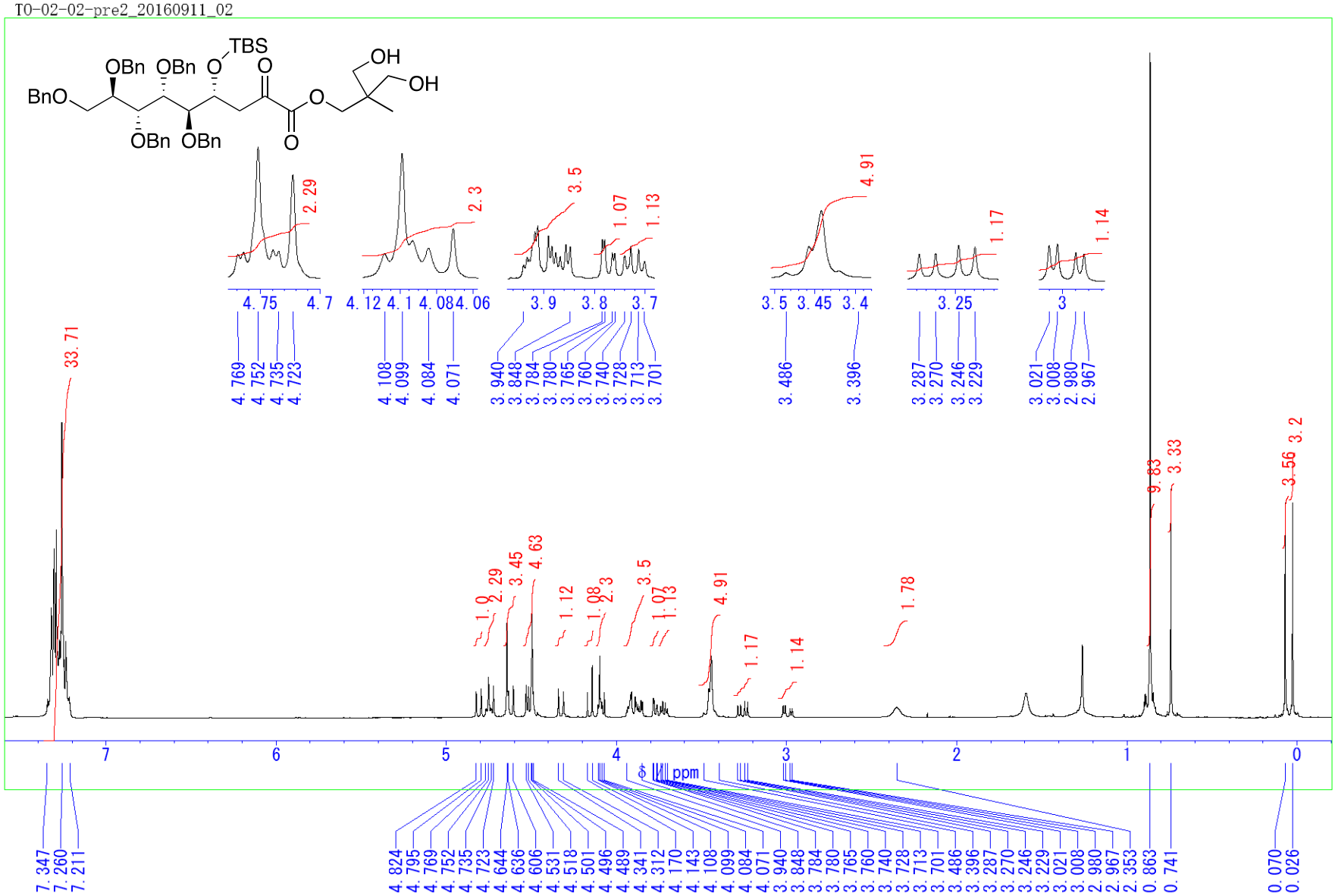
(3*R*,4*S*,5*S*,6*R*,7*R*)-4,5,6,7,8-pentakis(benzyloxy)-3-((*tert*-butyldimethylsilyl)oxy)-1-(4-methyl-2,6,7-trioxabicyclo[2.2.2]octan-1-yl)octan-1-one 37



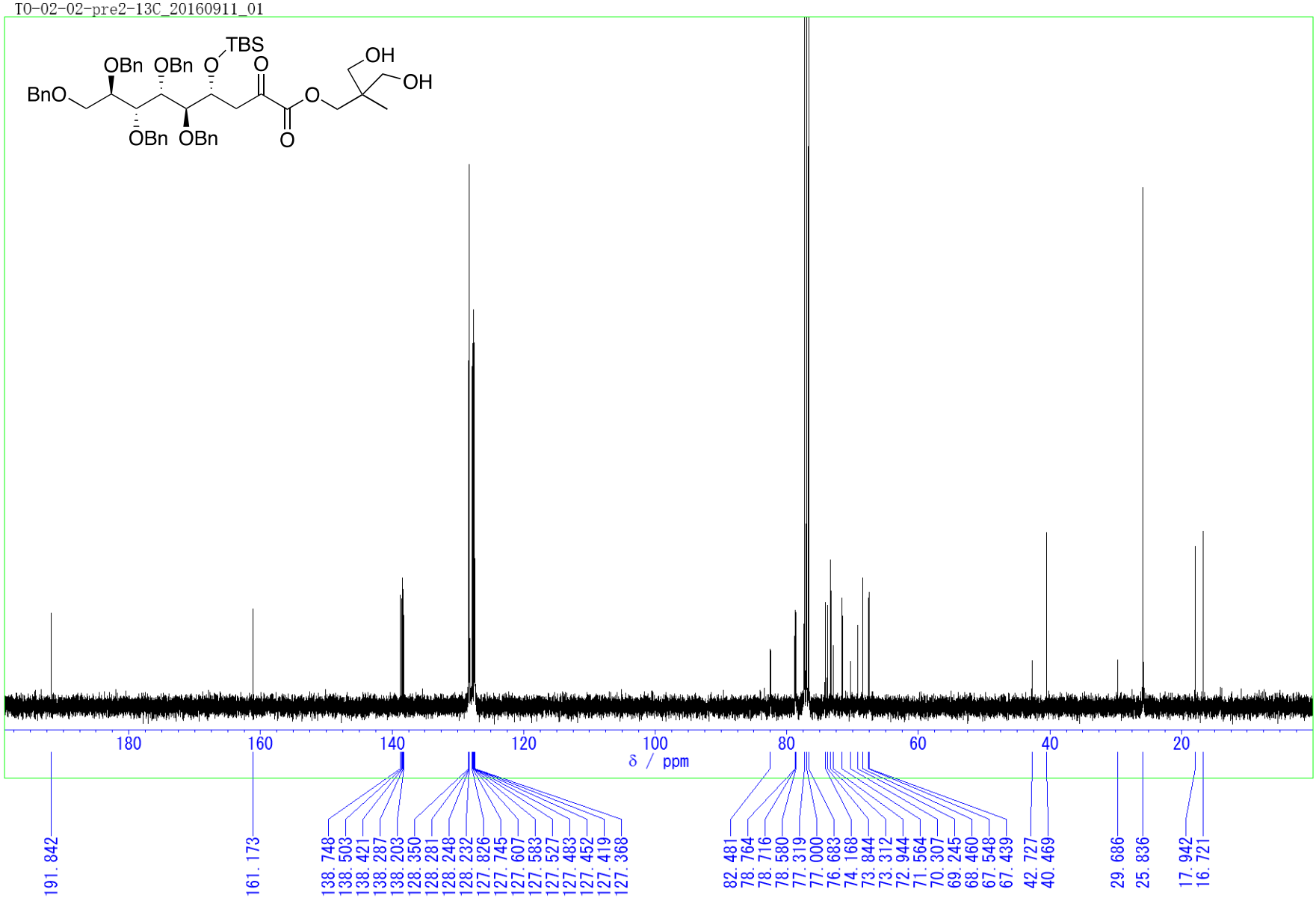
(3*R*,4*S*,5*S*,6*R*,7*R*)-4,5,6,7,8-pentakis(benzyloxy)-3-((*tert*-butyldimethylsilyl)oxy)-1-(4-methyl-2,6,7-trioxabicyclo[2.2.2]octan-1-yl)octan-1-one 37



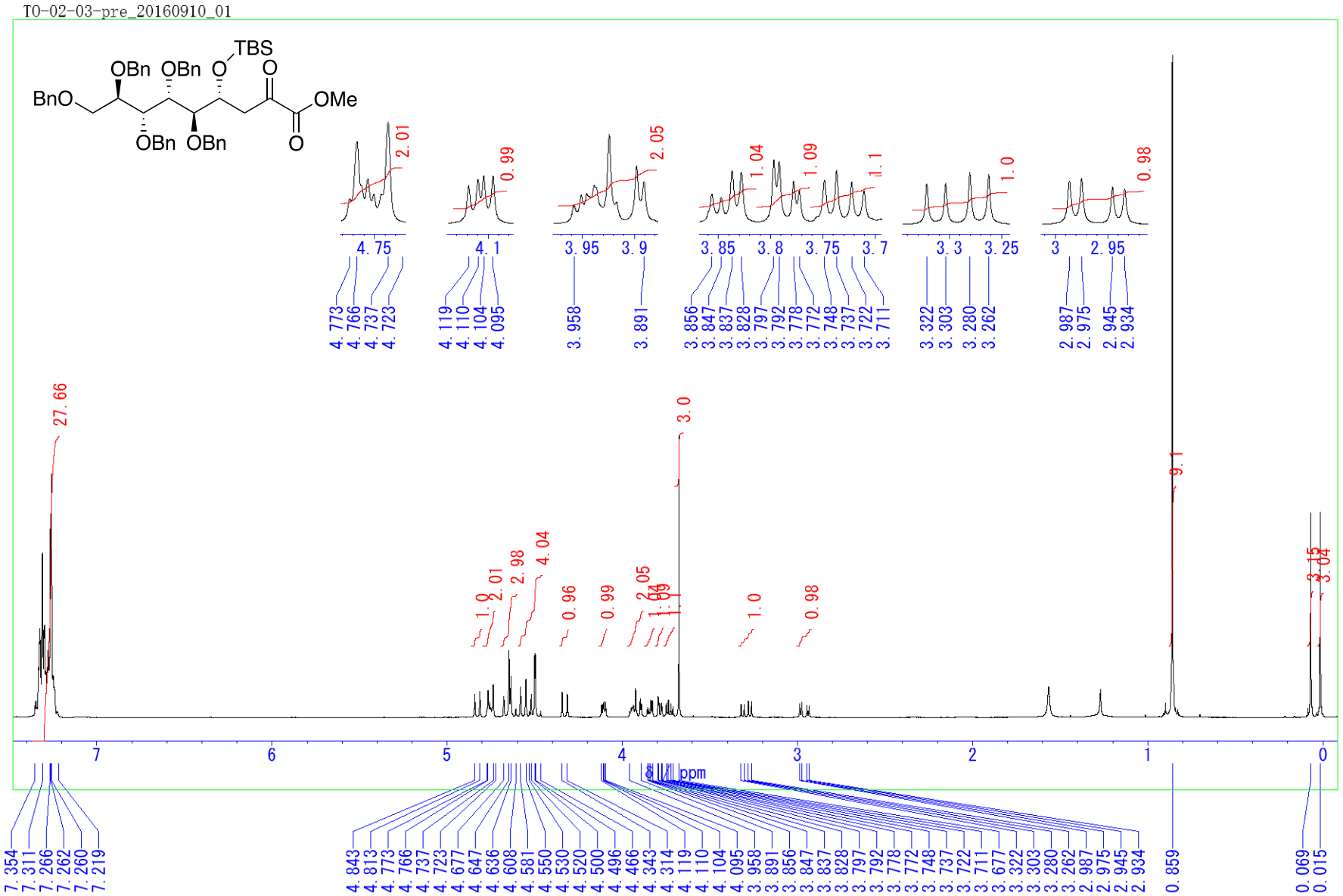
3-hydroxy-2-(hydroxymethyl)-2-methylpropyl (4*R*,5*S*,6*S*,7*R*,8*R*)-5,6,7,8,9-pentakis(benzyloxy)-4-((*tert*-butyldimethylsilyl)oxy)-2-oxononanoate 38



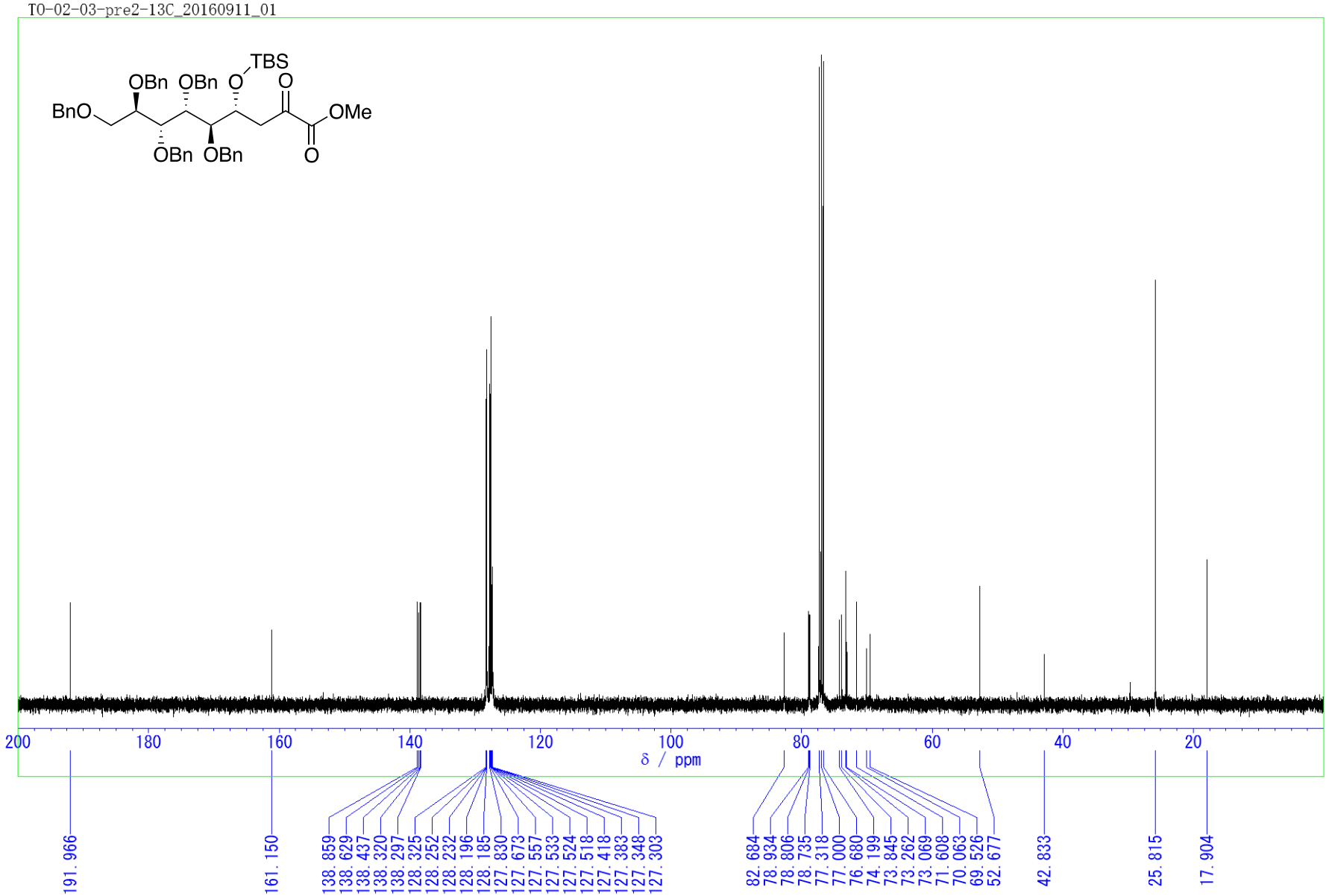
3-hydroxy-2-(hydroxymethyl)-2-methylpropyl (4*R*,5*S*,6*S*,7*R*,8*R*)-5,6,7,8,9-pentakis(benzyloxy)-4-((*tert*-butyldimethylsilyl)oxy)-2-oxononanoate 38



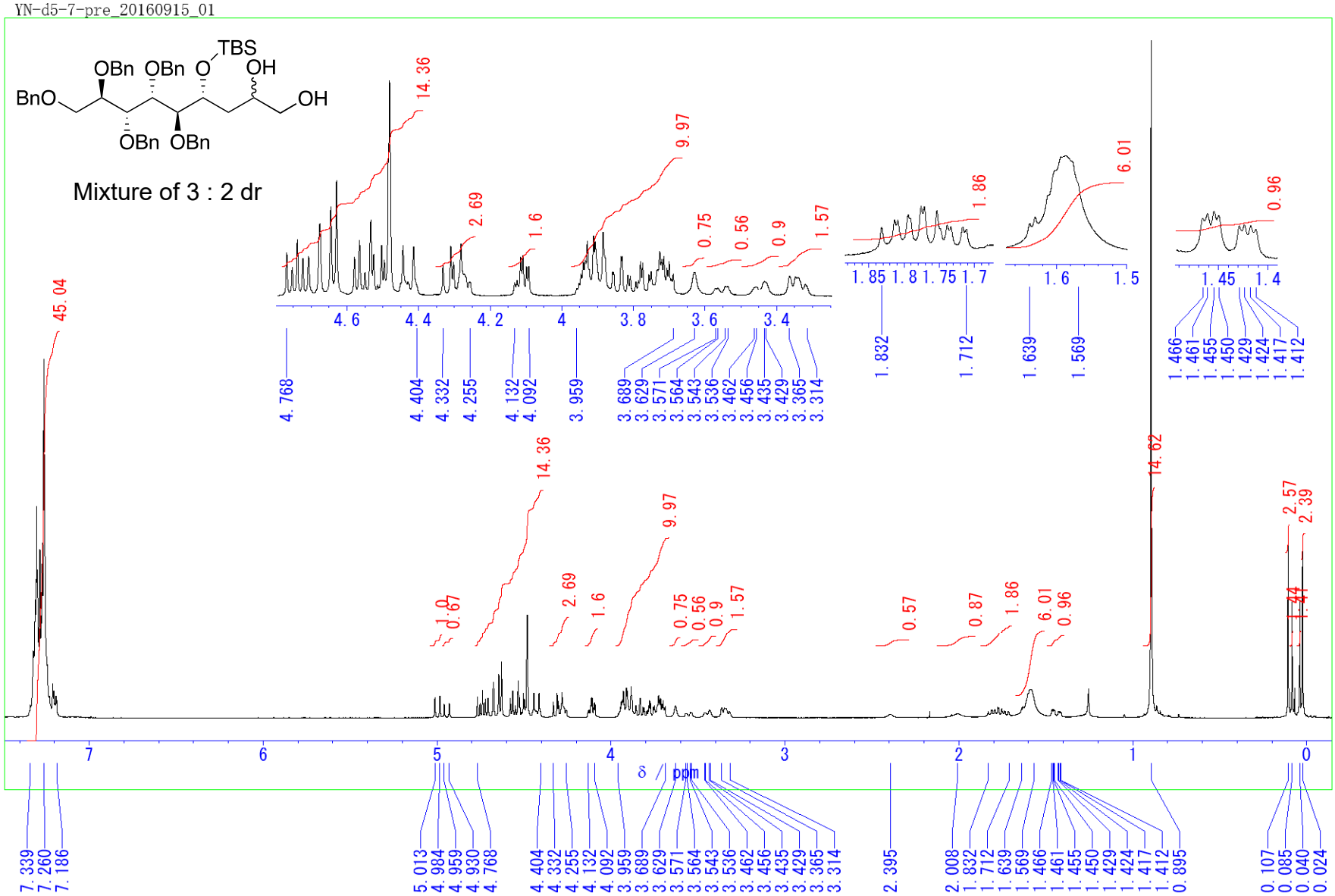
methyl (5*R*,6*S*,7*S*,8*R*,9*R*)-6,7,8,9,10-pentakis(benzyloxy)-5-((*tert*-butyldimethylsilyl)oxy)-2,3-dioxodecanoate 39



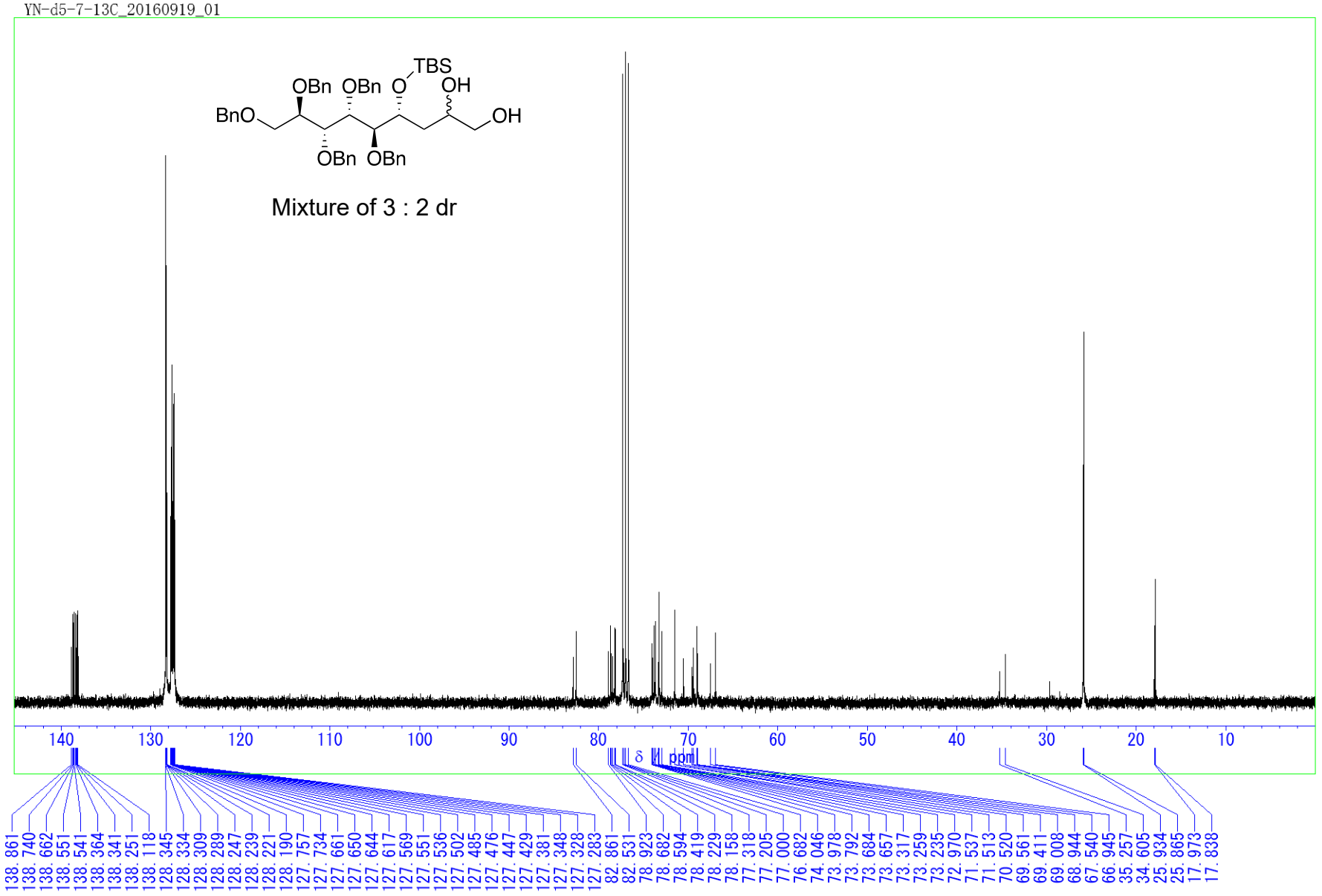
methyl (5*R*,6*S*,7*S*,8*R*,9*R*)-6,7,8,9,10-pentakis(benzyloxy)-5-((*tert*-butyldimethylsilyl)oxy)-2,3-dioxodecanoate 39



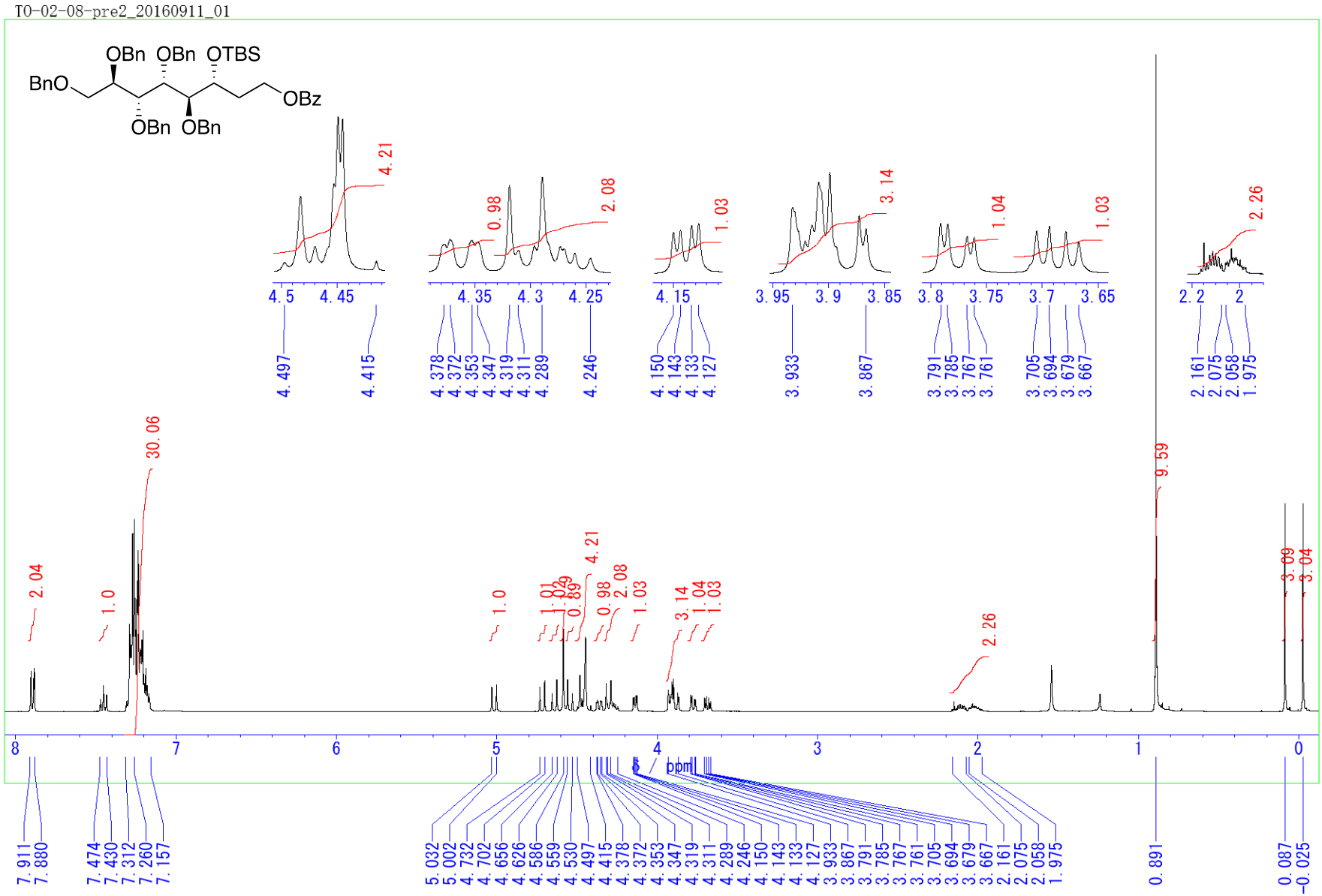
(4*R*,5*S*,6*S*,7*R*,8*R*)-5,6,7,8,9-pentakis(benzyloxy)-4-((*tert*-butyldimethylsilyl)oxy)nonane-1,2-diol 40



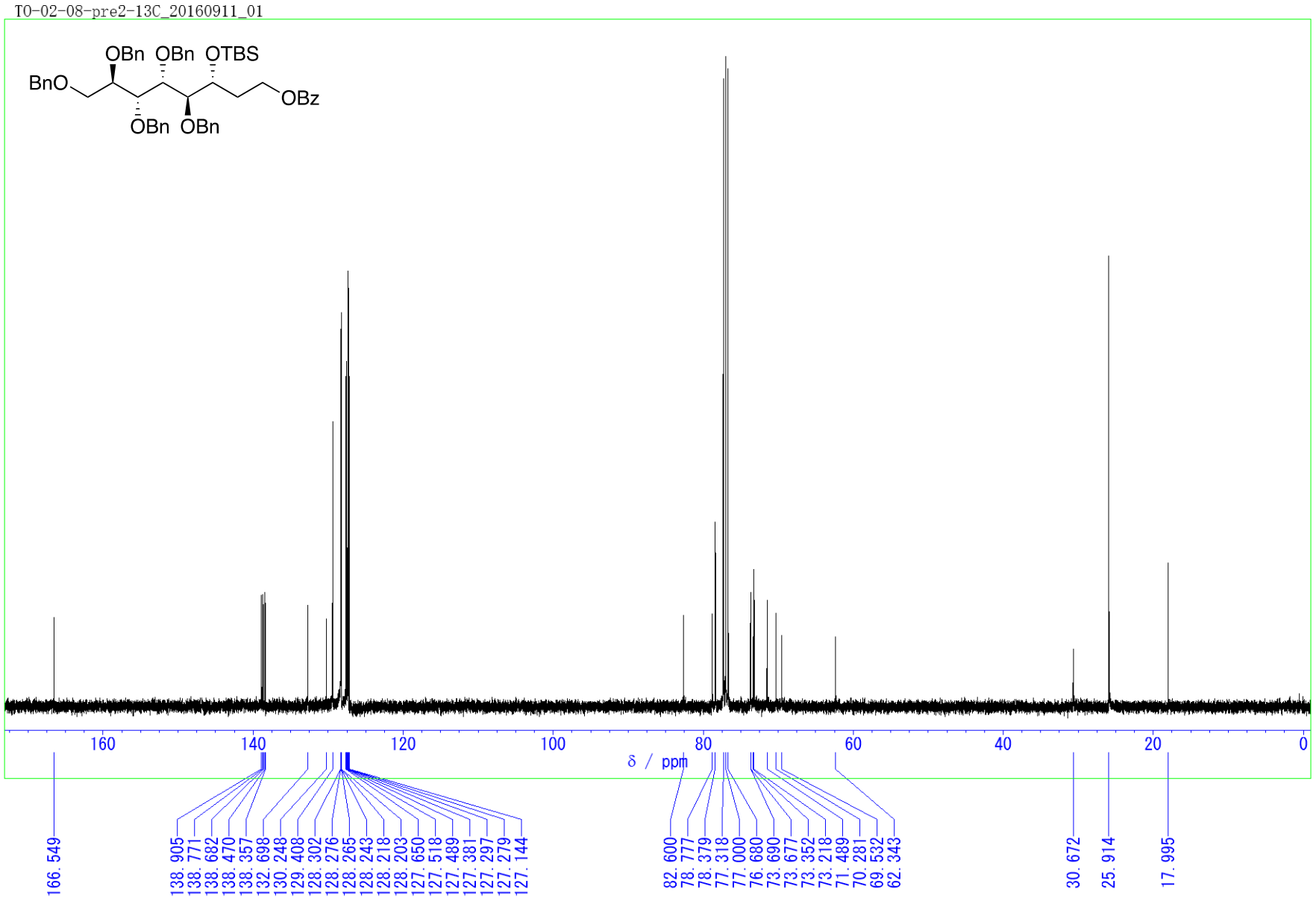
(4*R*,5*S*,6*S*,7*R*,8*R*)-5,6,7,8,9-pentakis(benzyloxy)-4-((*tert*-butyldimethylsilyl)oxy)nonane-1,2-diol 40



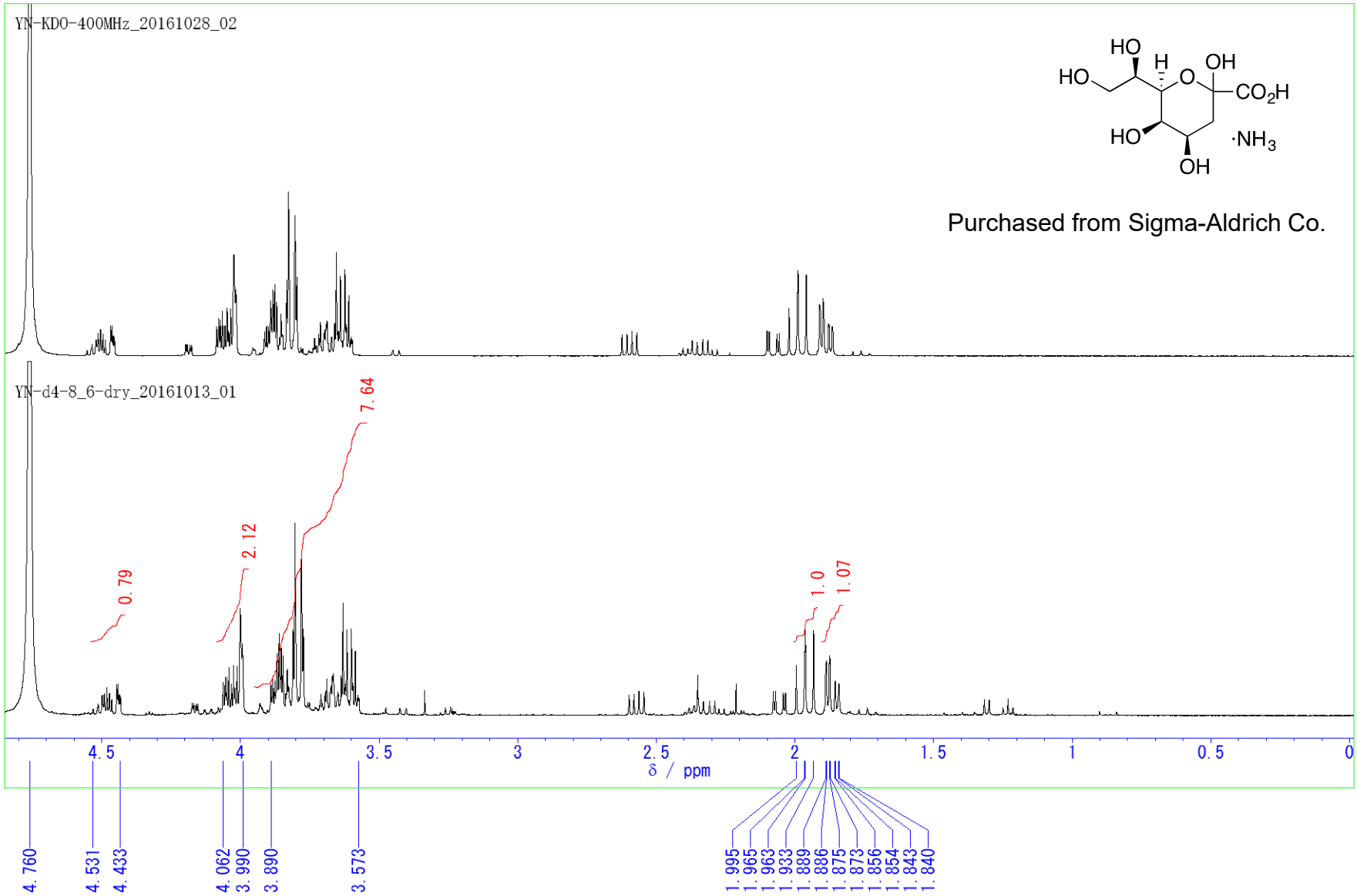
(3*R*,4*S*,5*S*,6*R*,7*R*)-4,5,6,7,8-pentakis(benzyloxy)-3-((*tert*-butyldimethylsilyl)oxy)octyl benzoate 41



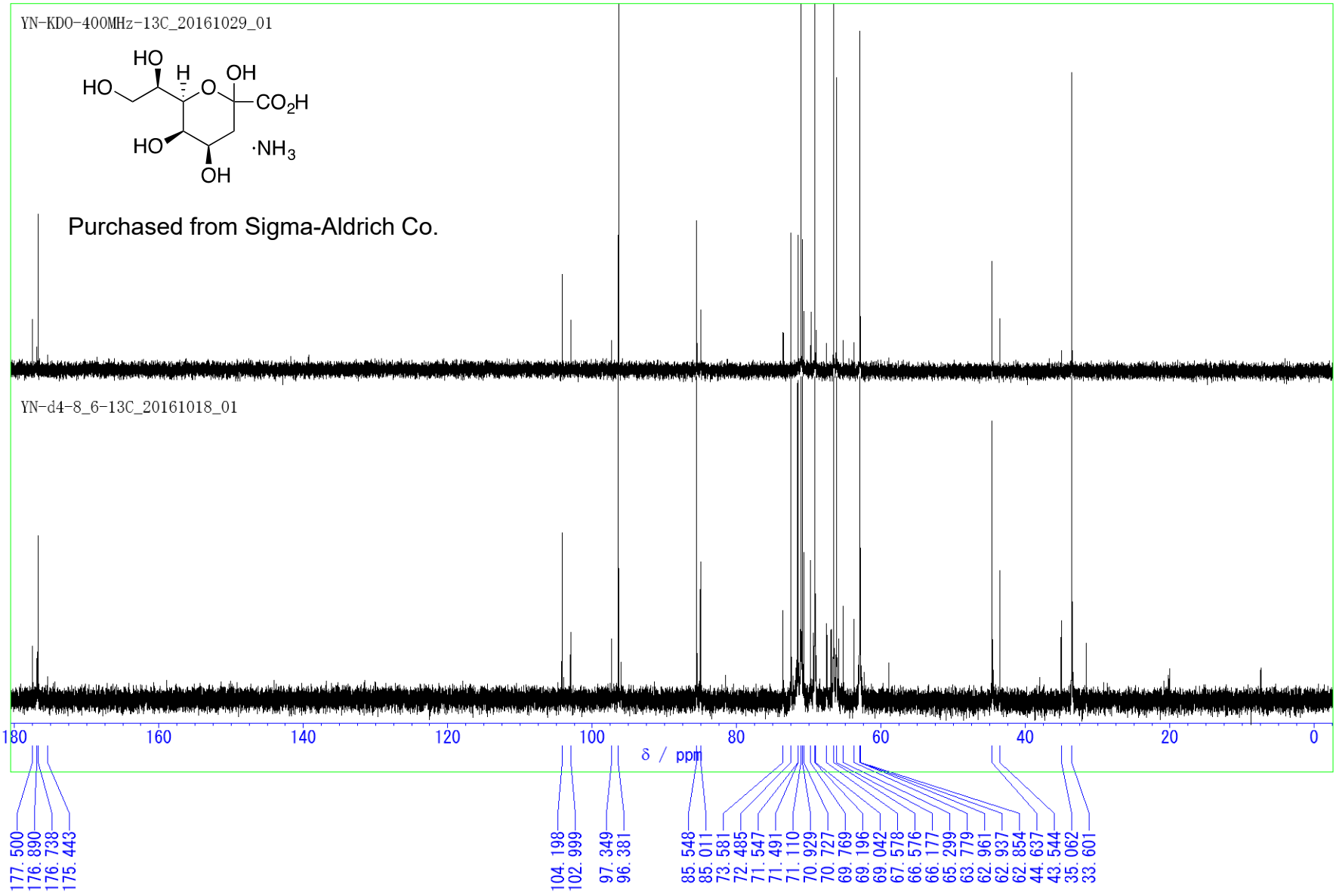
(3*R*,4*S*,5*S*,6*R*,7*R*)-4,5,6,7,8-pentakis(benzyloxy)-3-((*tert*-butyldimethylsilyl)oxy)octyl benzoate 41



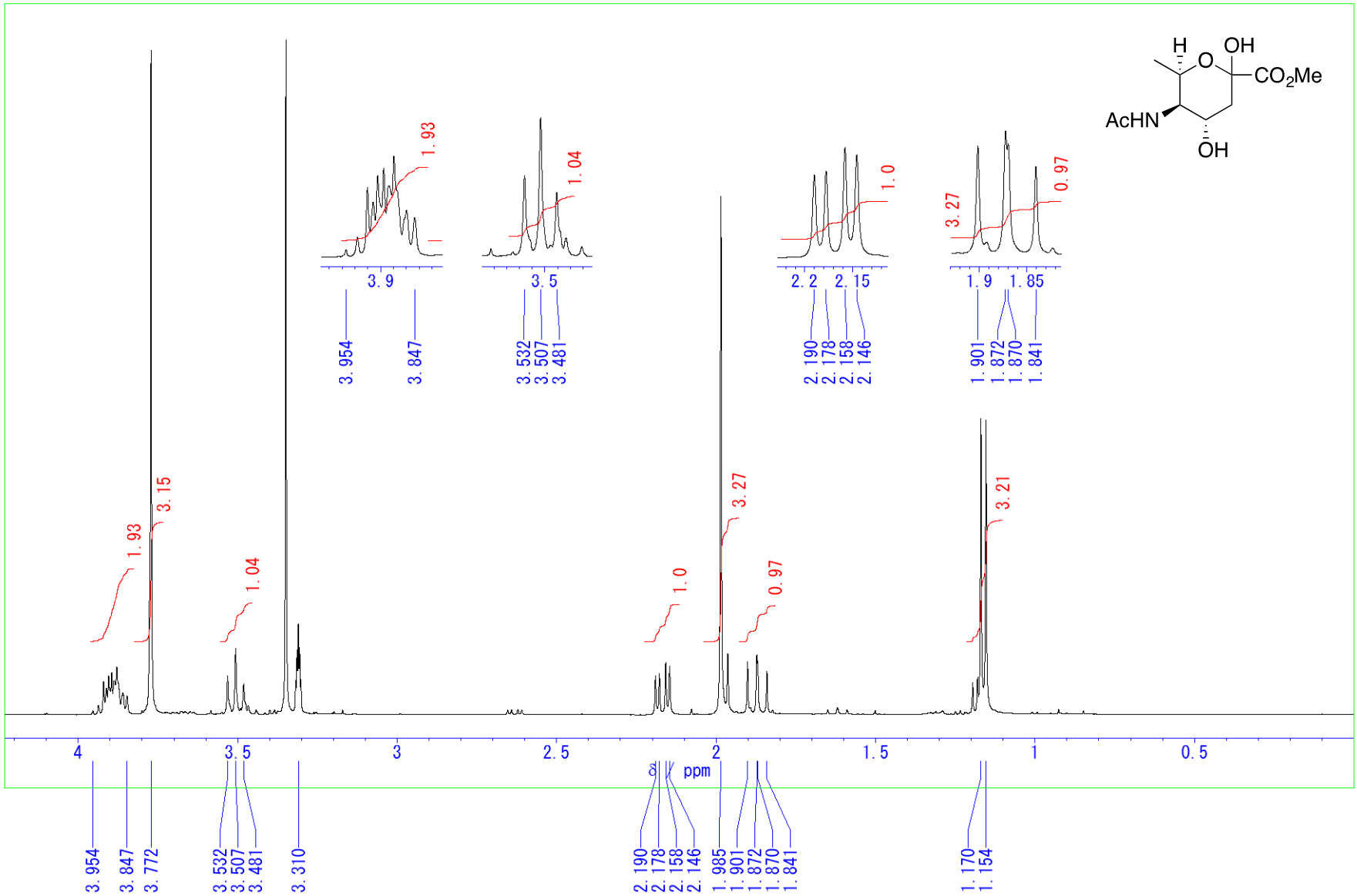
(4*R*,5*R*,6*R*)-6-((*R*)-1,2-dihydroxyethyl)-2,4,5-trihydroxytetrahydro-2*H*-pyran-2-carboxylic acid, ammonia salt 22b



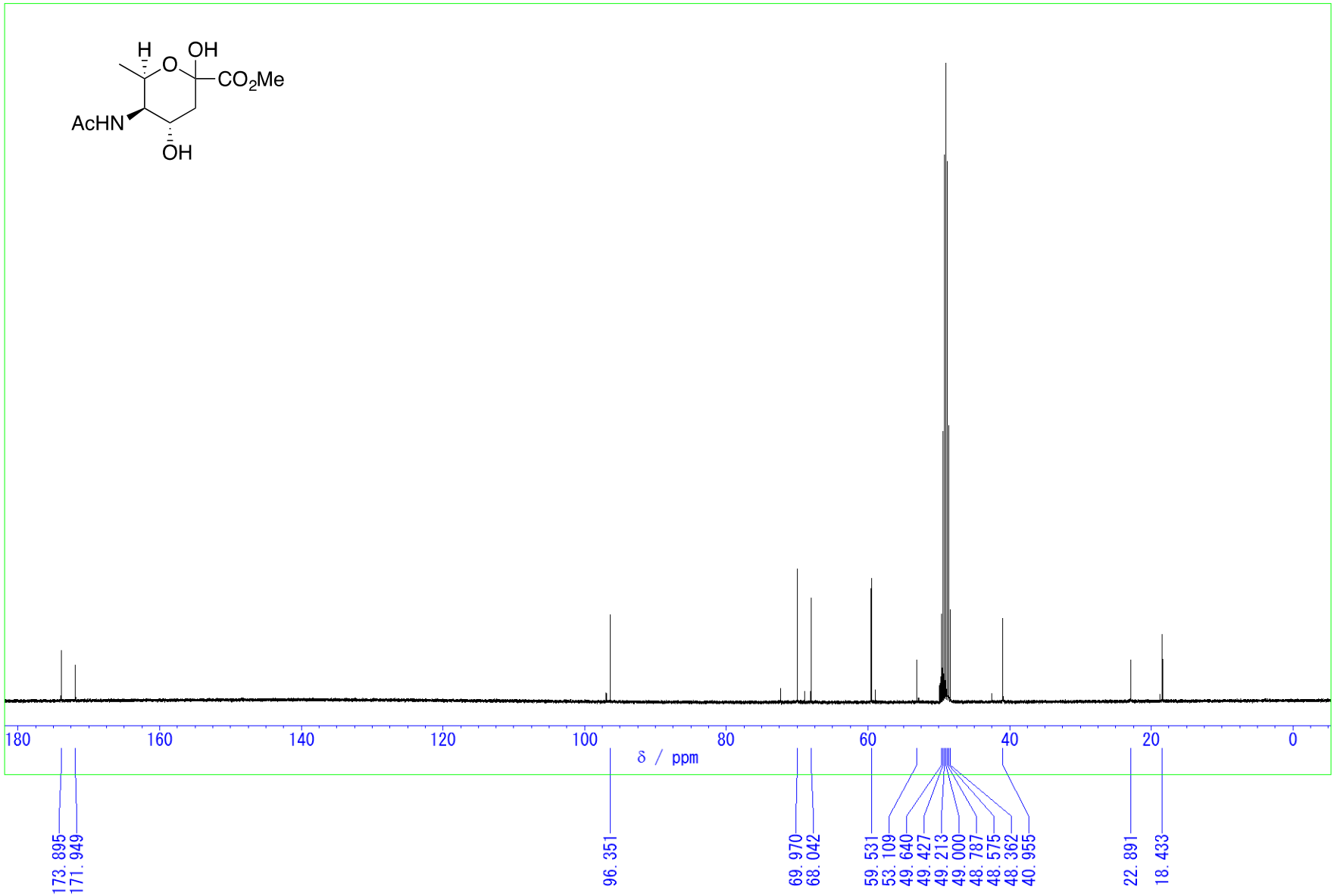
(4*R*,5*R*,6*R*)-6-((*R*)-1,2-dihydroxyethyl)-2,4,5-trihydroxytetrahydro-2*H*-pyran-2-carboxylic acid, ammonia salt 22b



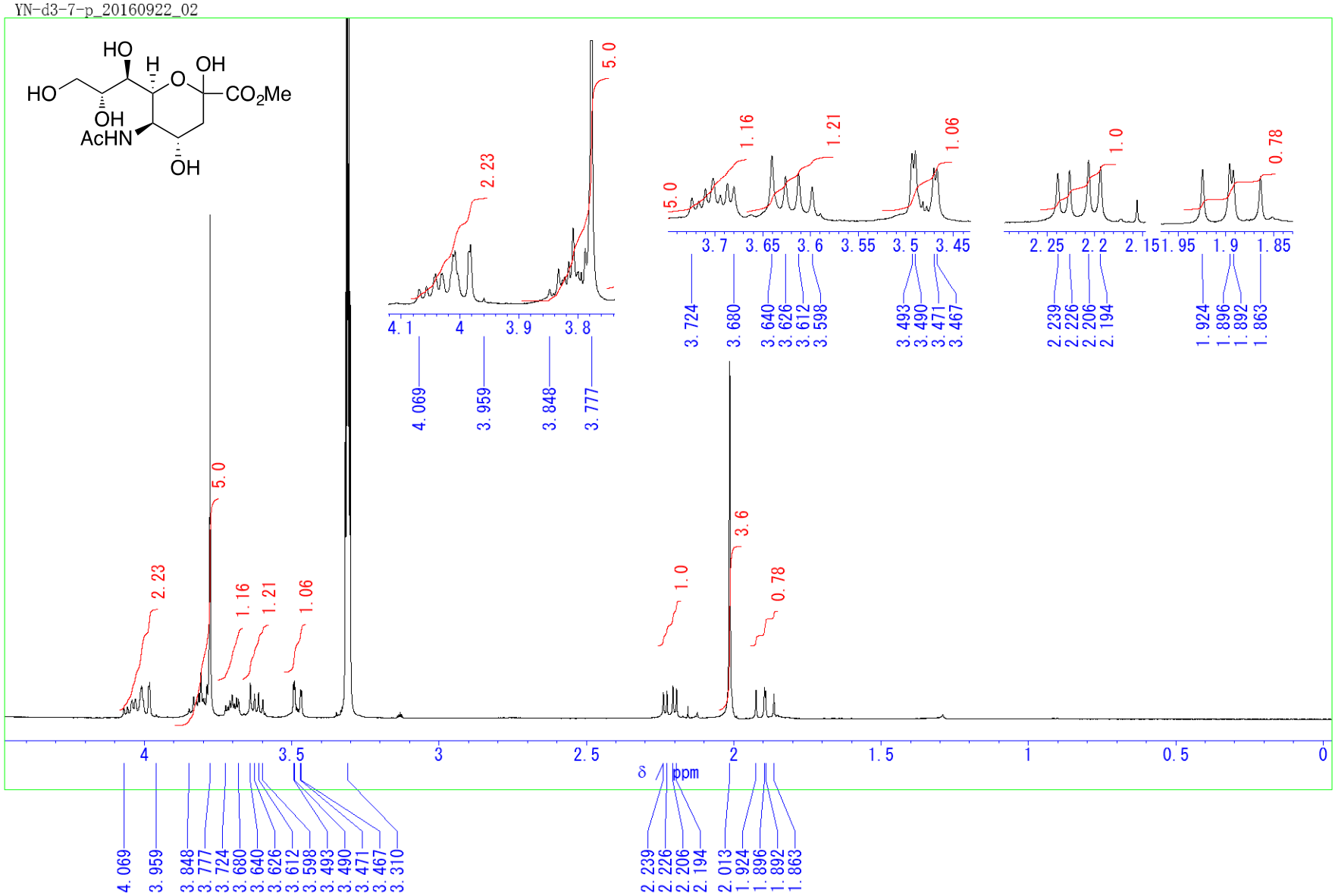
methyl (4*S*,5*R*,6*R*)-5-acetamido-2,4-dihydroxy-6-methyltetrahydro-2*H*-pyran-2-carboxylate 24c



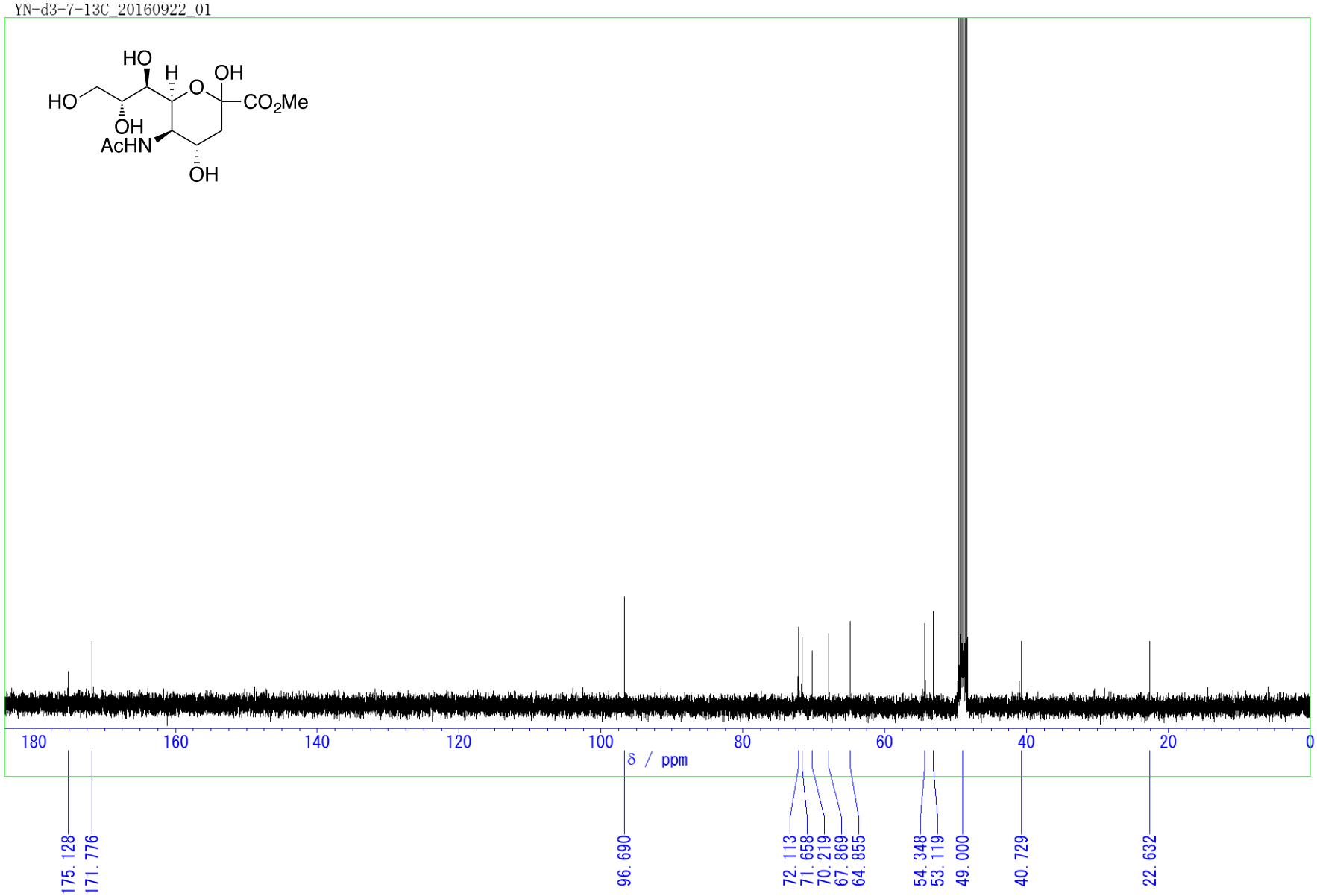
methyl (4*S*,5*R*,6*R*)-5-acetamido-2,4-dihydroxy-6-methyltetrahydro-2*H*-pyran-2-carboxylate 24c



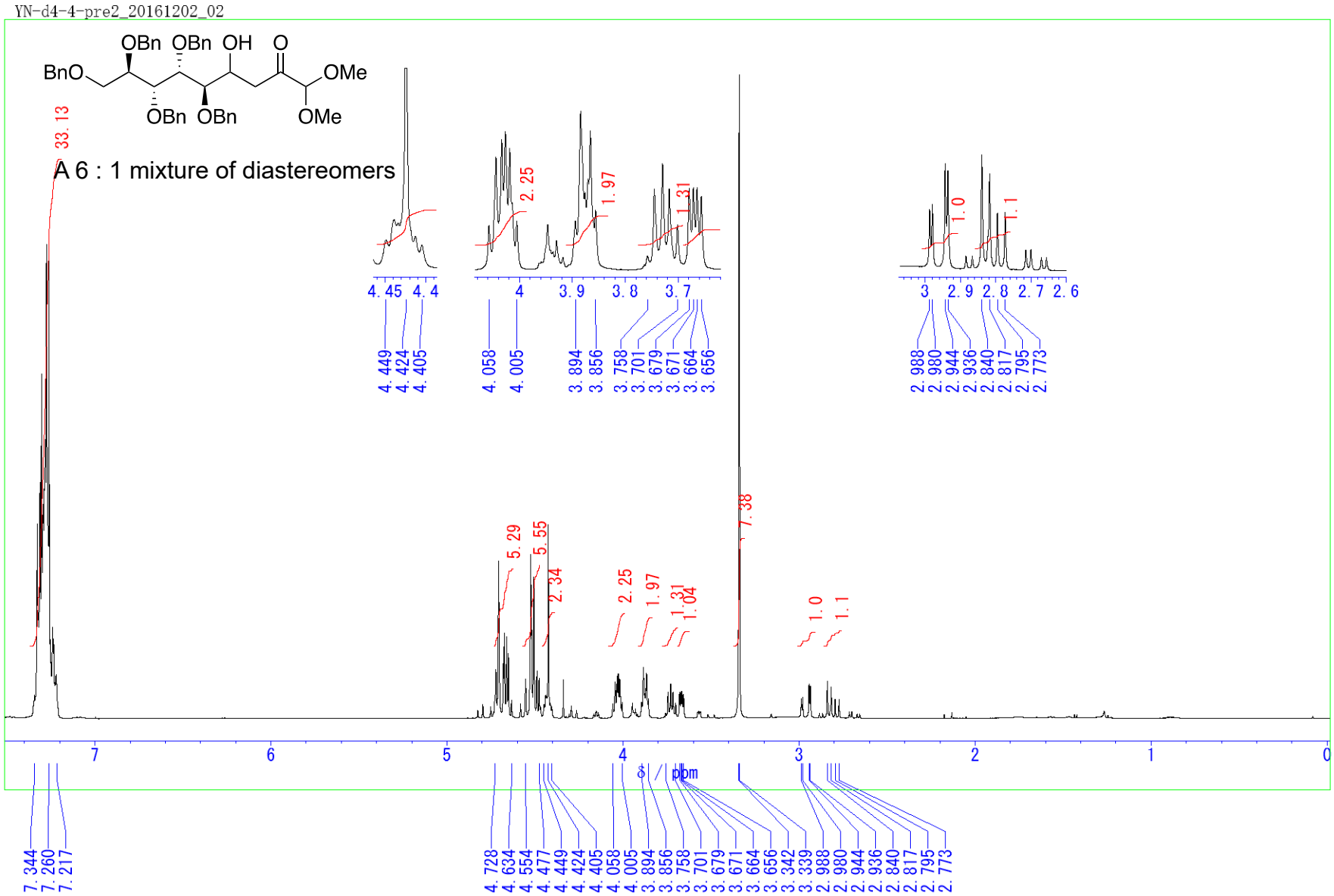
methyl (4*S*,5*R*,6*S*)-5-acetamido-2,4-dihydroxy-6-((1*R*,2*R*)-1,2,3-trihydroxypropyl) tetrahydro-2*H*-pyran-2-carboxylate 26d



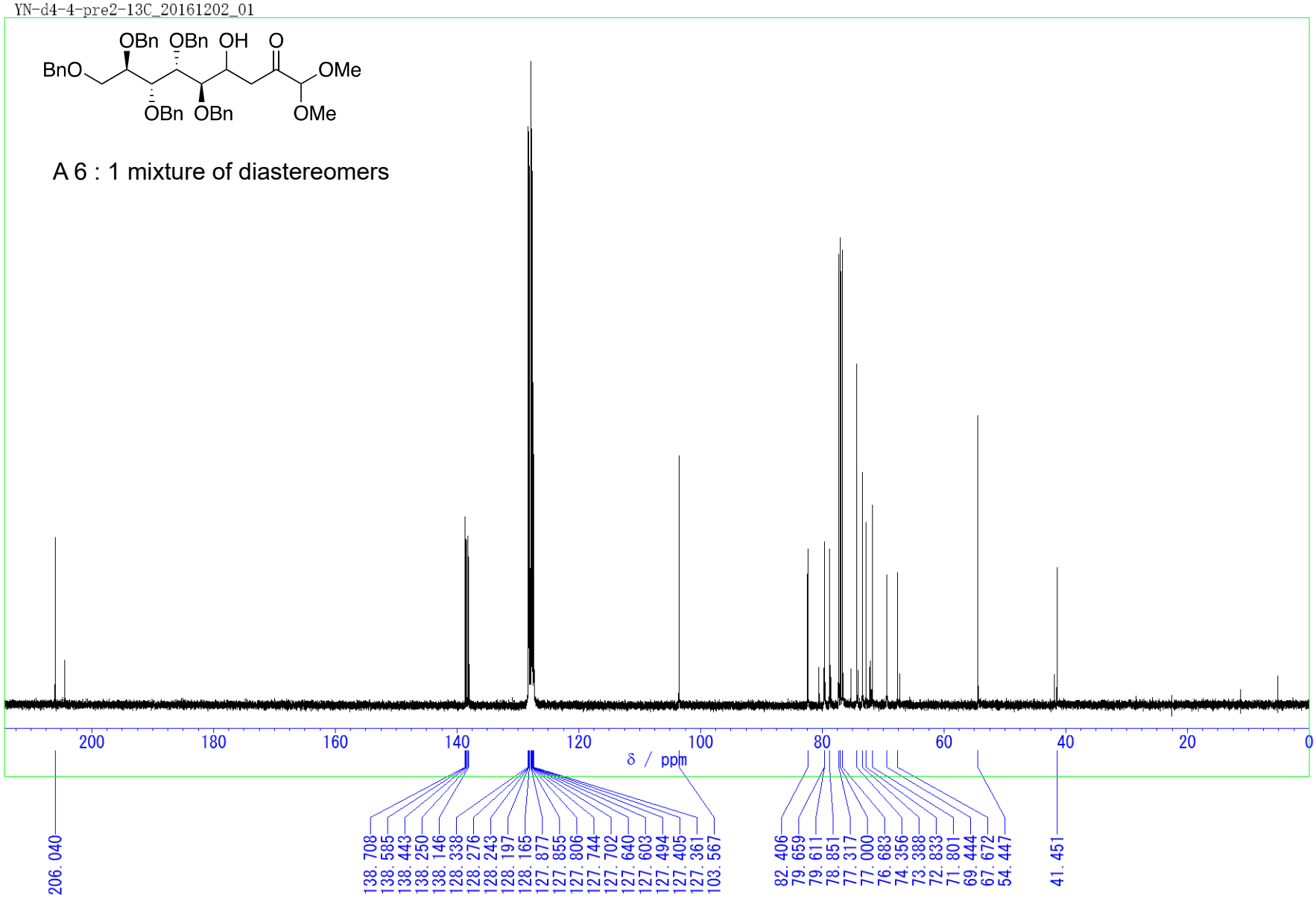
methyl (4*S*,5*R*,6*S*)-5-acetamido-2,4-dihydroxy-6-((1*R*,2*R*)-1,2,3-trihydroxypropyl) tetrahydro-2*H*-pyran-2-carboxylate 26d



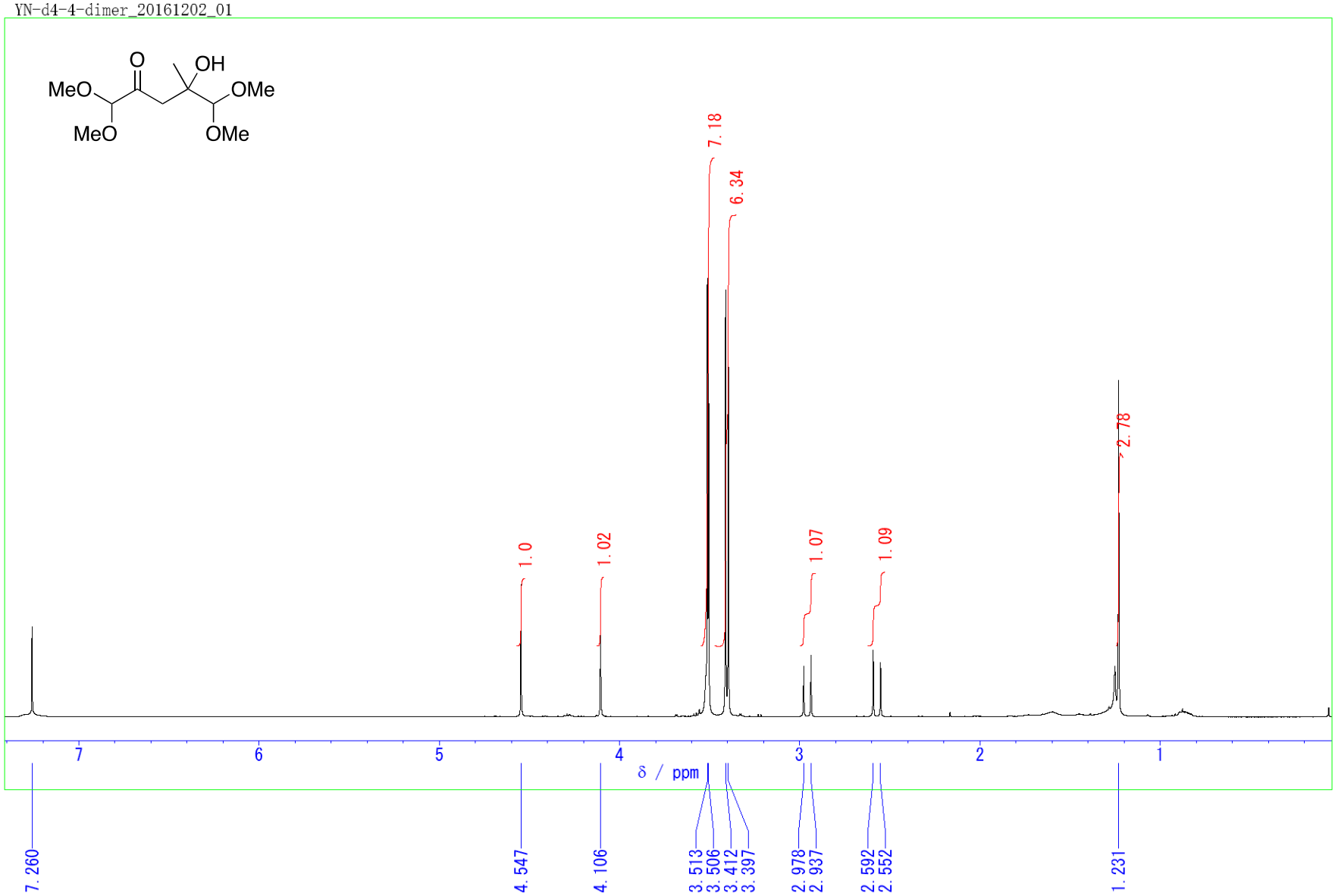
(5*R*,6*R*,7*R*,8*R*)-5,6,7,8,9-pentakis(benzyloxy)-4-hydroxy-1,1-dimethoxynonan-2-one 6



(5*R*,6*R*,7*R*,8*R*)-5,6,7,8,9-pentakis(benzyloxy)-4-hydroxy-1,1-dimethoxynonan-2-one 6



4-hydroxy-1,1,5,5-tetramethoxy-4-methylpentan-2-one 7



4-hydroxy-1,1,5,5-tetramethoxy-4-methylpentan-2-one 7