Advanced Synthesis & Catalysis

Supporting Information

Chemistry of Pyruvate Enolates: *anti*-Selective Direct Aldol Reactions of Pyruvate Ester with Sugar Aldehydes Promoted by Dinuclear Zinc Catalyst

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General Information. All starting materials and reagents were obtained from commercial sources and used as received unless otherwise noted. All solvents used were freshly distilled prior to use. Optical rotations were measured at room temperature with a digital polarimeter. High-resolution mass spectra were acquired using electrospray (ESI) ionization mode with a time-of-flight (TOF) detector. ^{1}H NMR spectra were recorded on spectrometers operating at 600 MHz in $CDCl_3$ or CD_3OD. Data were reported as follows: chemical shifts in parts per million (ppm) from tetramethylsilane as an internal standard, integration, multiplicity (s = singlet, d = doublet, t = triplet, q = quartet, dd = double-doublet, m = multiplet, br = broad), coupling constants (in Hz), and assignment. ^{13}C NMR spectra were measured at 150 MHz with complete proton decoupling. Chemical shifts were reported in ppm from the residual solvent as an internal standard. Reactions were controlled using TLC on silica [alu-plates (0.2 mm)]. Plates were visualized with UV light (254 nm) and by treatment with:, aqueous cerium(IV) sulfate solution with molybdic and sulfuric acid followed by heating. All organic solutions were dried over anhydrous sodium sulfate. Reaction products were purified by flash chromatography using silica gel 60 (240-400 mesh).

Synthesis and spectroscopic data for sugar aldehydes were described previously: (*R*)-2,3-*O*-isopropylidene-glyceraldehyde (**1**),[1] 2,3:4,5-di-*O*-isopropylidene-D-arabinose (**2**),[2] 2-*O*-benzyl-3,4-*O*-isopropylidene-D-erythrose (**9**),[3] 4-*O*-benzyl-2,3-*O*-isopropylidene-D-erythrose (**10**),[4] 2-*O*-benzyl-3,4:5,6-di-*O*-isopropylidene-D-mannose (**11**),[5] 4-*O*-benzyl-2,3:5,6-di-*O*-isopropylidene-D-mannose (**12**),[6] 4-*O*-benzyl-2,3:5,6-di-*O*-isopropylidene-D-glucose (**13**).[7] Commercial pyruvic acid esters **3** and **4** were used as received. Synthesis of 2,6-di-*t*-butyl-4-metoxyphenyl pyruvate (**5**) have been performed based on method presented by Morin.[8]

Representative Procedure for Direct Aldol Reaction of the Pyruvic Ester 5 with Protected Sugar Aldehydes. Commercial Trost ProPhenol ligand 12.8 mg (0.02 mmol) was dissolved in dry THF (0.5 mL) at room temperature under argon atmosphere and treated with a solution of diethylzinc (1M in hexane, 0.04 mL, 0.04 mmol). The reaction mixture was stirred for 30 min. to give 0.02 mmol of the catalyst **8**. Thus prepared catalyst was added to a solution od aldehyde (0.1 mmol) and aryl pyruvate **5** in 0.5 ml of THF at –25 ºC under argon atmosphere. Reaction mixture was stirred for 4 days at –25 ºC, next quenched by saturated ammonium chloride, extracted with ethyl acetate, dried with sodium sulphate and evaporated. The crude product was purified on silica gel by column chromatography using hexane-ethyl acetate (4:1 or 9:1) as eluent to afford desired *anti*-aldols. Isomeric *syn*-aldols have been isolated only in the case of more yielded and less selective reactions.

*3-Deoxy-5,6-O-isopropylidene-D-erythro-hex-2-ulosonic acid 2,6-di-t-butyl-4-metoxyphenyl ester (**6**, Table 1,2):* 24 mg (55%); pale yellow oil; ^{1}H NMR (600 MHz, $CDCl_3$) δ 6.88 (s, 2H), 4.18 (m, 1H), 4.11 (dd, J = 8.3, 6.3 Hz, 1H), 4.04 (dd, J = 11.9, 6.5 Hz, 1H), 3.97 (dd, J = 8.3, 5.3 Hz, 1H), 3.80 (s, 3H), 3.30 (dd, J = 18.3, 2.9 Hz, 1H), 3.12 (dd, J = 18.3, 8.9 Hz, 1H), 2.69 (s,1H), 1.42 (s, 3H), 1.35 (s, 3H), 1.31 (s, 9H), 1.30 (s, 9H); ^{13}C NMR {^{1}H} (150 MHz, $CDCl_3$) δ 193.3, 161.7, 156.9, 143.2, 140.9, 111.9, 109.7, 77.5, 68.5, 66.5, 55.3, 43.1, 35.7, 31.5, 31.4, 26.7, 25.1; HRMS (ESI-TOF) exact mass calcd for $C_{24}H_{36}O_7Na$ *m/z* 459.2359 ([M + Na]$^+$), found *m/z* 459.2345; IR (neat) 3441, 2961, 2931, 2873, 1739, 1590 cm^{-1}; $[\alpha]_D^{25}$ = –3.6 (*c* 1.0, $CHCl_3$).

*3-Deoxy-5,6:7,8-di-O-isopropylidene-D-manno-oct-2-ulosonic acid 2,6-di-t-butyl-4-metoxyphenyl ester (**7**, Table 1,3):* 46 mg (43%); pale yellow oil; ^{1}H NMR (600 MHz, $CDCl_3$) δ 6.88 (s, 2H), 4.34 (tdd, J = 8.2, 3.7, 1.7 Hz, 1H), 4.20 (dd, J = 8.7, 6.1 Hz, 1H), 4.07 (ddd, J

= 9.3, 7.8, 4.3 Hz, 1H), 4.02 (dd, *J* = 8.7, 5.2 Hz, 1H), 3.83 (t, *J* = 7.4 Hz, 1H), 3.80 (s, 3H), 3.77 (dd, *J* = 8.6, 7.4 Hz, 1H), 3.61 (s, 1H), 3.36 (dd, *J* = 17.5, 3.7 Hz, 1H), 3.17 (dd, *J* = 17.5, 8.2 Hz, 1H), 1.45 (s, 3H), 1.37 (s, 3H), 1.36 (s, 6H), 1.31 (s, 9H), 1.31 (s, 9H); $^{13}C\{^{1}H\}$ NMR (151 MHz, $CDCl_3$) δ 192.0, 161.9, 156.9, 143.4, 141.2, 112.0, 110.4, 109.8, 82.9, 81.1, 76.5, 68.5, 68.1, 55.4, 43.6, 35.8, 35.8, 31.6, 31.6, 27.0, 26.9, 26.6, 25.2; HRMS (ESI-TOF) exact mass calcd for calcd for $C_{29}H_{44}O_9Na$ *m/z* 559.2883, found *m/z* 559.2842; IR (neat) 3447, 2963, 2931, 2873, 1739, 1590 cm^{-1}; $[\alpha]_D^{25}$ = +10.2 (*c* 1.0, $CHCl_3$). The product was separated from its *syn*-isomer: *3-deoxy-5,6:7,8-di-O-isopropylidene-D-gluco-oct-2-ulosonic acid 2,6-di-t-butyl-4-metoxyphenyl ester*: 23 mg (21%); pale yellow oil; ^{1}H NMR (600 MHz, $CDCl_3$) δ 6.88 (s, 2H), 4.42 (tt, *J* = 9.0, 3.1 Hz, 1H), 4.16 (dd, *J* = 8.6, 6.1 Hz, 1H), 4.09 – 4.04 (m, 1H), 3.99 (dd, *J* = 8.7, 4.8 Hz, 1H), 3.98 – 3.93 (m, 2H), 3.80 (s, 3H), 3.33 (dd, *J* = 17.2, 9.2 Hz, 1H), 3.16 (dd, *J* = 17.2, 3.4 Hz, 1H), 2.74 (d, *J* = 8.3 Hz, 1H), 1.43 (s, 3H), 1.42 (s, 3H), 1.38 (s, 3H), 1.34 (s, 3H), 1.31 (s, 18H); $^{13}C\{^{1}H\}$ NMR (151 MHz, $CDCl_3$) δ 192.2, 161.9, 156.9, 143.4, 143.4, 141.2, 112.0, 110.1, 109.9, 82.6, 77.3, 68.1, 66.6, 55.4, 44.0, 35.8, 35.8, 31.6, 31.6, 27.3, 27.0, 26.8, 25.4; HRMS (ESI-TOF) exact mass calcd for $C_{29}H_{44}O_9Na$ *m/z* 559.2883, found *m/z* 559.2854. IR (neat) 3481, 2962, 2929, 2873, 1738, 1590 cm^{-1}; $[\alpha]_D^{25}$ = –2.8 (*c* 1.0, $CHCl_3$).

*5-O-Benzyl-3-deoxy-6,7-O-isopropylidene-D-ribo-hept-2-ulosonic acid 2,6-di-t-butyl-4-metoxyphenyl ester (**14**, Table 3):* 35 mg (62%); pale yellow oil; ^{1}H NMR (600 MHz, acetone-d_6) δ 7.41 – 7.25 (m, 5H), 6.89 (s, 2H), 4.82 (d, *J* = 11.5 Hz, 1H), 4.76 (d, *J* = 11.5 Hz, 1H), 4.53 – 4.48 (m, 1H), 4.31 (dd, *J* = 12.5, 6.5 Hz, 1H), 4.05 (dd, *J* = 8.2, 6.5 Hz, 1H), 3.90 (dd, *J* = 8.1, 6.8 Hz, 1H), 3.80 (s, 3H), 3.70 (dd, *J* = 5.8, 4.2 Hz, 1H), 3.40 (dd, *J* = 17.4, 9.2 Hz, 1H), 3.20 (dd, *J* = 17.4, 3.4 Hz, 1H), 1.35 (s, 3H), 1.33 (s, 3H), 1.29 (s, 9H), 1.29 (s, 9H); $^{13}C\{^{1}H\}$ NMR (151 MHz, acetone-d_6) δ 193.4, 162.8, 157.9, 144.2, 142.0, 139.7, 129.1, 128.7, 128.4, 112.6, 109.5, 83.1, 76.2, 74.5, 68.1, 67.0, 55.6, 43.3, 36.2, 31.8, 26.9, 25.6; HRMS (ESI-TOF) exact mass calcd for $C_{32}H_{44}O_8Na$ *m/z* 579.2934, found *m/z* 579.2920; IR (neat) 3463, 3059, 3023, 2956, 2923, 2854, 1734, 1589 cm^{-1}; $[\alpha]_D^{25}$ = +24.8 (*c* 0.07, $CHCl_3$).

*7-O-Benzyl-3-deoxy-5,6-O-isopropylidene-D-ribo-hept-2-ulosonic acid 2,6-di-t-butyl-4-metoxyphenyl ester (**15**, Table 3):* 23 mg (41%); pale yellow oil; ^{1}H NMR (600 MHz, $CDCl_3$) δ 7.41 – 7.28 (m, 5H), 6.88 (s, 2H), 4.62 (d, *J* = 11.7 Hz, 1H), 4.59 (d, *J* = 11.8 Hz, 1H), 4.49 – 4.42 (m, 1H), 4.41 (ddd, *J* = 9.5, 5.5, 4.1 Hz, 1H), 4.11 – 4.05 (m, 1H), 3.81 (s, 3H), 3.73 (t, *J* = 9.5 Hz, 1H), 3.54 (dd, *J* = 9.7, 4.0 Hz, 1H), 3.28 (dd, *J* = 17.2, 3.5 Hz, 1H), 3.22 (dd, *J* = 17.3, 8.6 Hz, 1H), 1.36 (s, 3H), 1.32 (s, 3H), 1.31 (s, 18H); $^{13}C\{^{1}H\}$ NMR (151 MHz, $CDCl_3$) δ 192.0, 161.9, 156.9, 143.5, 141.2, 136.8, 128.7, 128.4, 128.3, 112.0, 109.0, 79.9, 75.5, 74.2, 68.5, 65.7, 55.4, 43.9, 35.8, 35.7, 31.7, 31.6, 28.0, 25.5; HRMS (ESI-TOF) exact mass calcd for *m/z* $C_{32}H_{44}O_8Na$ 579.2934, found *m/z* 579.2894; IR (neat) 3454, 3059, 3029, 2960, 2935, 2911, 2868, 1758, 1739, 1588 cm^{-1}; $[\alpha]_D^{25}$ = –2.2 (*c* 0.5, $CHCl_3$). The product was separated from its *syn*-isomer: *7-O-benzyl-3-deoxy-5,6-O-isopropylidene-D-arabino-hept-2-ulosonic acid 2,6-di-t-butyl-4-metoxyphenyl ester:* 8 mg (14%); pale yellow oil; ^{1}H NMR (600 MHz, $CDCl_3$) δ 7.38 – 7.27 (m, 5H), 6.89 – 6.86 (s, 2H), 4.58 (d, *J* = 2.3 Hz, 2H), 4.56 – 4.52 (m, 1H), 4.47 – 4.41 (m, 1H), 3.80 (s, 3H), 3.57 (dd, *J* = 9.6, 4.3 Hz, 1H), 3.52 (dd, *J* = 9.6, 6.0 Hz, 1H), 3.22 (dd, *J* = 18.0, 8.0 Hz, 1H), 3.14 (dd, *J* = 18.0, 4.3 Hz, 1H), 2.69 (d, *J* = 4.6 Hz, 1H), 1.33 (s, 3H), 1.31 (s, 3H), 1.30 (s, 9H), 1.30 (s, 9H); $^{13}C\{^{1}H\}$ NMR (151 MHz, $CDCl_3$) δ 192.6, 161.8, 156.9, 143.4, 141.0, 137.8, 128.7, 128.6, 127.9, 112.0, 109.6, 73.9, 73.6, 73.1, 66.5, 65.5, 55.4, 43.2, 35.8, 35.8, 31.6, 31.6, 27.9, 25.5; HRMS (ESI-TOF) exact mass calcd for $C_{32}H_{44}O_8Na$ *m/z* 579.2934, found *m/z* 579.2915; IR (neat) 3448, 3087, 3063, 3029, 2960, 2935, 2914, 2868, 1758, 1743, 1588 cm^{-1}; $[\alpha]_D^{25}$ = +1.1 (*c* 0.9, $CHCl_3$).

*5-O-Benzyl-3-deoxy-6,7;8,9-di-O-isopropylidene-D-glycero-D-talo-non-2-ulosonic acid 2,6-di-t-butyl-4-metoxyphenyl ester (**16**, Table 3):* 39 mg (60%); pale yellow oil; ^{1}H NMR (600 MHz, $CDCl_3$) δ 7.38 – 7.27 (m, 5H), 6.87 (s, 2H), 4.93 (d, J = 11.4 Hz, 1H), 4.65 (d, J = 11.4 Hz, 1H), 4.48 (dd, J = 6.5, 3.1 Hz, 1H), 4.34 (td, J = 9.2, 2.8 Hz, 1H), 4.21 (dd, J = 8.6, 6.0 Hz, 1H), 4.17 – 4.09 (m, 2H), 3.99 (dd, J = 8.6, 6.0 Hz, 1H), 3.80 (s, 3H), 3.77 (dd, J = 8.2, 3.1 Hz, 1H), 3.46 (br. s, 1H), 3.25 (dd, J = 18.2, 9.2 Hz, 1H), 3.17 (dd, J = 18.1, 2.8 Hz, 1H), 2.38 (br. s, 1H), 1.50 (s, 3H), 1.44 (s, 3H), 1.38 (s, 3H), 1.37 (s, 3H), 1.29 (s, 9H), 1.28 (s, 9H); ^{13}C{^{1}H} NMR (151 MHz, $CDCl_3$) δ 192.6, 161.8, 156.8, 143.3, 141.0, 137.9, 128.5, 128.1, 127.9, 111.8, 110.3, 109.5, 80.7, 80.2, 77.7, 77.3, 74.9, 68.2, 66.9, 55.3 43.1, 35.6, 31.5, 31.5, 27.0, 26.9, 26.2, 25.4; HRMS (ESI-TOF) exact mass calcd for $C_{37}H_{52}O_{10}Na$ *m/z* 679.3458, found *m/z* 679.3450; IR (neat) 3478, 2953, 2922, 2850, 1738, 1589 cm^{-1}; $[\alpha]_D^{25}$ = +17.7 (*c* 0.5, $CHCl_3$).

*7-O-Benzyl-3-deoxy-5,6:8,9-di-O-isopropylidene-D-glycero-D-talo-non-2-ulosonic acid 2,6-di-t-butyl-4-metoxyphenyl ester (**17**, Table 3):* 52 mg (79%); pale yellow oil; ^{1}H NMR (600 MHz, $CDCl_3$) δ 7.38 – 7.24 (m, 5H), 6.87 (s, 2H), 4.95 (d, J = 11.6 Hz, 1H), 4.76 (d, J = 11.6 Hz, 1H), 4.48 – 4.43 (m, 1H), 4.32 – 4.30 (m, 1H), 4.29 (dd, J = 5.9, 4.1 Hz, 1H), 4.16 (t, J = 4.2 Hz, 1H), 4.11 (dd, J = 8.4, 6.4 Hz, 1H), 4.06 (dd, J = 9.4, 5.9 Hz, 1H), 4.03 (t, J = 8.1 Hz, 1H), 3.80 (s, 3H), 3.39 (dd, J = 18.4, 2.7 Hz, 1H), 3.19 (d, J = 4.7 Hz, 1H), 3.12 (dd, J = 18.4, 8.6 Hz, 1H), 1.45 (s, 3H), 1.44 (s, 3H), 1.37 (s, 3H), 1.34 (s, 3H), 1.29 (s, 18H); ^{13}C{^{1}H} NMR (151 MHz, $CDCl_3$) δ 193.7, 161.8, 157.0, 143.4, 141.1, 138.5, 128.5, 127.7, 112.0, 109.2, 108.8, 78.8, 78.1, 76.7, 73.9, 66.4, 66.3, 55.4, 44.5, 35.8, 31.6, 26.9, 26.5, 25.7, 25.3; HRMS (ESI-TOF) exact mass calcd for $C_{37}H_{52}O_{10}Na$ *m/z* 679.3458, found *m/z* 679.3438; IR (neat) 3451, 2961, 2932, 2868, 2362, 2343, 1745, 1730, 1588 cm^{-1}; $[\alpha]_D^{25}$ = +12.1 (*c* 1.2, $CHCl_3$).

*7-O-Benzyl-3-deoxy-5,6:8,9-di-O-isopropylidene-D-glycero-D-gulo-non-2-ulosonic acid 2,6-di-t-butyl-4-metoxyphenyl ester (**18**, Table 3):* 42 mg (64%); pale yellow oil; ^{1}H NMR (600 MHz, acetone-d_6) δ 7.44 – 7.25 (m, 5H), 6.91 (s, 2H), 4.90 (d, J = 11.3 Hz, 1H), 4.76 (d, J = 11.3 Hz, 1H), 4.32 (dd, J = 6.7, 3.8 Hz, 2H), 4.19 (dd, J = 7.3, 2.2 Hz, 1H), 4.11 (t, J = 7.6 Hz, 1H), 4.05 (dd, J = 8.3, 7.1 Hz, 1H), 4.00 (dd, J = 8.3, 6.6 Hz, 1H), 3.92 (dd, J = 3.8, 2.2 Hz, 1H), 3.81 (s, 3H), 3.30 (dd, J = 17.1, 3.5 Hz, 1H), 3.19 (dd, J = 17.1, 8.5 Hz, 1H), 1.37 (s, 3H), 1.33 (s, 3H), 1.32 (s, 3H), 1.31 (s, 12H), 1.31 (s, 9H); ^{13}C{^{1}H} NMR (151 MHz, acetone-d_6) δ 192.7, 162.7, 157.9, 144.1, 142.0, 139.9, 129.1, 128.5, 128.3, 112.6, 110.2, 108.7, 81.9, 79.7, 78.9, 78.6, 75.7, 70.1, 66.2, 55.6, 45.1, 36.2, 31.8, 27.7, 27.1, 26.9, 25.6; HRMS (ESI-TOF) exact mass calcd for $C_{37}H_{52}O_{10}Na$ *m/z* 679.3458, found *m/z* 679.3461; IR (neat) 3496, 2984, 2932, 1744, 1585 cm^{-1}; $[\alpha]_D^{25}$ = –3.4 (*c* 1.0, $CHCl_3$). The product was separated from its *syn*-isomer: *7-O-Benzyl-3-deoxy-5,6:8,9-di-O-isopropylidene-D-glycero-D-ido-non-2-ulosonic acid 2,6-di-t-butyl-4-metoxyphenyl ester:* 11 mg (16%); pale yellow oil; ^{1}H NMR (600 MHz, acetone-d_6) δ 7.44 – 7.25 (m, 5H), 6.91 (s, 2H), 4.89 (d, J = 11.4 Hz, 1H), 4.77 (d, J = 11.3 Hz, 1H), 4.37 – 4.31 (m, 1H), 4.29 (td, J = 6.9, 4.1 Hz, 1H), 4.24 (dd, J = 8.1, 2.9 Hz, 1H), 4.15 (dd, J = 8.1, 2.8 Hz, 1H), 4.03 (m, 2H), 3.83 (dd, J = 4.1, 2.9 Hz, 1H), 3.82 (s, 3H), 3.35 (dd, J = 17.5, 8.8 Hz, 1H), 3.12 (dd, J = 17.5, 4.0 Hz, 1H), 1.38 (s, 3H), 1.35 (s, 3H), 1.33 (s, 3H), 1.31 (s, 12H), 1.31 (s, 9H); ^{13}C{^{1}H} NMR (151 MHz, acetone-d_6) δ 192.7, 162.7, 157.9, 144.1, 144.1, 139.7, 129.1, 128.8, 128.4, 112.6, 109.9, 108.9, 79.5, 78.7, 78.5, 78.0, 75.6, 66.4, 65.9, 55.6, 44.4, 36.2, 31.8, 27.4, 27.2, 26.9, 25.6; HRMS (ESI-TOF) exact mass calcd for $C_{37}H_{52}O_{10}Na$ *m/z* 679.3458 found *m/z* 679.3448; IR (neat) 3466, 2956, 2923, 2868, 2853, 1734, 1589 cm^{-1}; $[\alpha]_D^{25}$ = –0.7 (*c* 1.1, $CHCl_3$).

Representative Procedure for Deprotection and Cyclization of Aldol Products. To a stirred solution of aldol (0.1 mmol) in 5 ml of methanol *DOWEX 50 WX 4* (one mass equivalent) and

palladium on carbon (0.2 mass eq.) were added. Reaction mixture was stirred for 24 hours under hydrogen atmosphere in room temperature. Ion exchange resin and palladium on carbon were removed by filtration and the solvent was evaporated. Products were purified on silica gel by column chromatography using as eluent mixture of ethyl acetate-methanol (15:2) for eight- and nine-carbon esters and dichloromethane-methanol (15:1) for six- and seven-carbon esters.

*3-Deoxy-D-erythro-hept-2-ulosonic acid 2,6-di-t-butyl-4-metoxyphenyl ester (**19**, KDG ester, Scheme 1):* 164 mg (88%); ^{1}H NMR (300 MHz, CD_3OD) δ 6.91 (s, 2H), 6.91 (s, 4H), 3.83 (s, 3H), 3.82 (s, 6H), 4.58 – 4.48 (m, 1.3H), 4.38 – 4.24 (m, 3H), 4.20 – 4.11 (m, 2H), 4.01 (ddd, *J* = 6.9, 5.0, 3.4 Hz, 1H), 2.98 (dd, *J* = 13.7, 7.2 Hz, 0.75H), 2.76 (dd, *J* = 12.7, 8.8 Hz, 1H), 2.51 (t, *J* = 12.5 Hz, 0.8H), 2.50 (dd, *J* = 12.7, 6.9 Hz, 1H), 2.38 (dd, *J* = 14.3, 3.1 Hz, 0.4H), 2.31 (dd, *J* = 14.2, 4.1 Hz, 0.4H), 2.21 (dd, *J* = 13.6, 3.9 Hz, 0.75H), 2.06 (dd, *J* = 12.5, 4.8 Hz, 0.8H), 1.39 (s, 7H), 1.38 (s, 9H), 1.38 (s, 22H), 1.37 (s, 8H), 1.36 (s, 6H); ^{13}C{^{1}H} NMR (75 MHz, CD_3OD) δ 180.5, 171.9, 158.1, 145.0, 143.3, 112.6, 106.4, 102.9, 98.5, 97.2, 88.7, 88.3, 75.2, 73.3, 73.1, 72.8, 71.4, 68.8, 66.5, 66.0, 63.7, 63.6, 63.5, 55.8, 55.1, 36.6, 35.3, 31.9, 31.8, 31.7; HRMS (ESI-TOF) exact mass calcd for $C_{21}H_{30}O_7Na$ *m/z* 419.2046, found *m/z* 419.2021; IR (neat) 3403, 2957, 2924, 2873, 1754 and 1590 cm^{-1}.

*3-Deoxy-D-ribo-hept-2-ulosonic acid 2,6-di-t-butyl-4-metoxyphenyl ester (**20**, DRH ester, Scheme 1):* 117 mg (86%); ^{1}H NMR (600 MHz, CD_3OD) δ 6.88 – 6.86 (m, 6H), 4.29 (dd, *J* = 9.5, 5.2 Hz, 1.2H), 4.21 (q, *J* = 3.2 Hz, 0.7H), 4.16 (dd, *J* = 7.5, 3.2 Hz, 1.3H), 4.00 (dd, *J* = 9.2, 5.6 Hz, 1.3H), 3.92 – 3.88 (m, 3H), 3.82 (dd, *J* = 6.2, 3.6 Hz, 1H), 3.79 – 3.78 (m, 10H), 3.74 (dd, *J* = 12.7, 3.7 Hz, 2.7H), 3.62 (dd, *J* = 10.7, 5.7 Hz, 1.3H), 3.60 – 3.57 (m, 1.6H), 3.56 – 3.52 (m, 1H), 2.87 (dd, *J* = 13.7, 7.1 Hz, 1.H), 2.72 (dd, *J* = 12.8, 8.6 Hz, 1H), 2.47 (dd, *J* = 12.8, 7.1 Hz, 1H), 2.37 (dd, *J* = 14.3, 3.0 Hz, 1H), 2.33 (dd, *J* = 14.3, 3.6 Hz, 1H), 2.18 (dd, *J* = 13.7, 2.7 Hz, 1H), 1.35 – 1.32 (m, 59H); ^{13}C{^{1}H} NMR (151 MHz, CD_3OD) δ 171.0, 170.7, 169.5, 157.6, 157.5, 144.7, 144.6, 144.5, 144.5, 143.2, 143.1, 112.3, 112.2, 110.2, 104.3, 102.8, 96.4, 76.5, 73.6, 73.3, 73.1, 72.8, 71.3, 70.9, 69.1, 68.5, 64.3, 64.2, 63.5, 55.5, 55.0, 49.8, 45.3, 44.7, 37.4, 36.3, 36.3, 31.8, 31.8, 31.6; HRMS (ESI-TOF) exact mass calcd for $C_{22}H_{34}O_8Na$ *m/z* 449.2151, found *m/z* 449.2129; IR (neat) 3372, 3002, 2959, 2908, 2871, 2832, 1758, 1589 cm^{-1}.

*3-Deoxy-D-manno-oct-2-ulosonic acid 2,6-di-t-butyl-4-metoxyphenyl ester (**21**, KDO ester, Scheme 1):* 38 mg (98%); ^{1}H NMR (600 MHz, CD_3OD) δ 6.90 (s, 0.15H), 6.89 (s, 2H), 4.12 (ddd, *J* = 11.9, 4.7, 3.0 Hz, 1H), 4.06 (dd, *J* = 13.4, 4.7 Hz, 1H), 3.97 (dd, *J* = 8.8, 1.1 Hz, 1H), 3.95 – 3.92 (m, 1H), 3.83 (dd, *J* = 11.6, 2.8 Hz, 1H), 3.81 (s, 0.45H), 3.81 (s, 3H), 3.74 (dd, *J* = 11.7, 4.6 Hz, 1H), 2.75 (dd, *J* = 12.5, 9.4 Hz, 0.15H), 2.56 (t, *J* = 12.2 Hz, 1H), 2.48 (dd, *J* = 12.5, 7.0 Hz, 0.15H), 1.97 (ddd, *J* = 12.5, 4.7, 0.7 Hz, 1H), 1.37 (s, 1.4H), 1.37 (s, 1.4H), 1.37 (s, 9H), 1.36 (s, 9H); ^{13}C{^{1}H} NMR (151 MHz, CD_3OD) δ 171.7, 170.3, 158.1, 145.1, 144.9, 143.4, 112.6, 112.6, 102.7, 97.4, 86.7, 73.5, 73.0, 71.3, 70.8, 67.8, 67.6, 65.7, 65.0, 64.5, 55.8, 49.8, 36.6, 36.6, 34.9, 31.9, 31.9, 31.8, 31.7; HRMS (ESI-TOF) exact mass calcd for $C_{23}H_{36}O_9Na$ *m/z* 479.2257, found *m/z* 479.2229; IR (neat) 3354, 2964, 2926, 2870, 1745 and 1591 cm^{-1}.

*3-Deoxy-D-glycero-D-talo-non-2-ulosonic acid 2,6-di-t-butyl-4-metoxyphenyl ester (**22**, 4-epi-KDN ester, Scheme 1):* 38 mg (99%); ^{1}H NMR (600 MHz, CD_3OD) δ 6.92 – 6.89 (m, 5H), 4.43 (dd, *J* = 10.3, 1.1 Hz, 0.9H), 4.34 (dd, *J* = 8.6, 3.4 Hz, 0.9H), 4.32 – 4.29 (m, 1.1H), 4.10 – 4.04 (m, 2H), 3.96 – 3.92 (m, 1.3H), 3.89 – 3.84 (m, 5H), 3.83 – 3.81 (m, 8H), 3.80 – 3.77 (m, 3H), 3.70 (ddd, *J* = 8.8, 5.3, 2.9 Hz, 1.7H), 3.67 – 3.63 (m, 1.3H), 2.94 (dd, *J* = 13.7, 7.1 Hz, 0.6H), 2.79 (dd, *J* = 12.8, 8.4 Hz, 0.9H), 2.56 (dd, *J* = 12.8, 7.1 Hz, 0.9H), 2.42 (dd, *J* = 14.3, 2.9 Hz, 1H), 2.34 (dd, *J* = 14.3, 3.7 Hz, 1H), 2.26 (dd, *J* = 13.7, 2.9 Hz, 0.6H), 1.39 – 1.37 (m, 45H);

$^{13}C\{^{1}H\}$ NMR (151 MHz, CD_3OD) δ 172.5, 171.8, 171.3, 158.1, 158.1, 145.0, 144.9, 144.9, 144.9, 144.8, 143.6, 143.3, 143.3, 143.2, 112.6, 104.2, 103.2, 97.2, 87.9, 87.5, 80.8, 74.5, 74.1, 73.0, 72.7, 72.2, 71.9, 71.8, 71.8, 71.4, 70.6, 70.4, 69.5, 69.3, 67.0, 66.9, 65.1, 65.0, 64.7, 61.6, 55.8, 49.8, 36.6, 36.6, 36.6, 36.5, 32.0, 31.9, 31.9, 31.8, 31.7; HRMS (ESI-TOF) exact mass calcd for $C_{24}H_{38}O_{10}Na$ *m/z* 509.2363, found *m/z* 509.2342; IR (neat) 3354, 2999, 2959, 2871, 2835, 1751, 1590 cm^{-1}.

*3-Deoxy-D-glycero-D-gulo-non-2-ulosonic acid 2,6-di-t-butyl-4-metoxyphenyl ester (**23**, 5-epi-KDN, Scheme 1):* 38 mg (98%); ^{1}H NMR (600 MHz, CD_3OD) δ 6.92 – 6.89 (m, 5H), 4.59 (dd, *J* = 6.7, 5.3 Hz, 2H), 4.42 (d, *J* = 3.6 Hz, 2H), 4.41 – 4.39 (m, 3H), 4.31 (d, *J* = 4.4 Hz, 1H), 4.15 (dd, *J* = 3.6, 2.3 Hz, 3H), 4.05 – 4.01 (m, 2H), 3.81 – 3.80 (m, 5H), 3.74 – 3.70 (m, 2H), 3.66 (dd, *J* = 11.2, 5.5 Hz, 2H), 3.60 (dd, *J* = 11.4, 6.1 Hz, 2H), 3.02 (dd, *J* = 13.6, 7.7 Hz, 0.2H), 2.75 (dd, *J* = 12.6, 9.0 Hz, 0.3H), 2.64 (t, *J* = 12.2 Hz, 1H), 2.51 (dd, *J* = 12.6, 7.1 Hz, 0.3H), 2.22 (dd, *J* = 13.6, 4.5 0.2H), 2.04 (dd, *J* = 12.3, 4.2 Hz, 1H), 1.39 – 1.36 (m, 27H); $^{13}C\{^{1}H\}$ NMR (151 MHz, CD_3OD) δ 177.3, 174.8, 159.5, 158.5, 145.0, 144.8, 142.6, 142.2, 112.6, 110.9, 110.5, 97.1, 82.2, 81.3, 75.0, 74.9, 74.8, 74.5, 74.5, 73.4, 72.9, 72.1, 72.1, 71.6, 71.5, 64.7, 64.3, 52.7, 52.6, 52.6, 36.6, 36.6, 3.9, 31.7; HRMS (ESI-TOF) exact mass calcd for $C_{24}H_{38}O_{10}Na$ *m/z* 509.2363, found *m/z* 509.2330; IR (neat) 3333, 2940, 2887, 2835, 1733, 1594 cm^{-1}.

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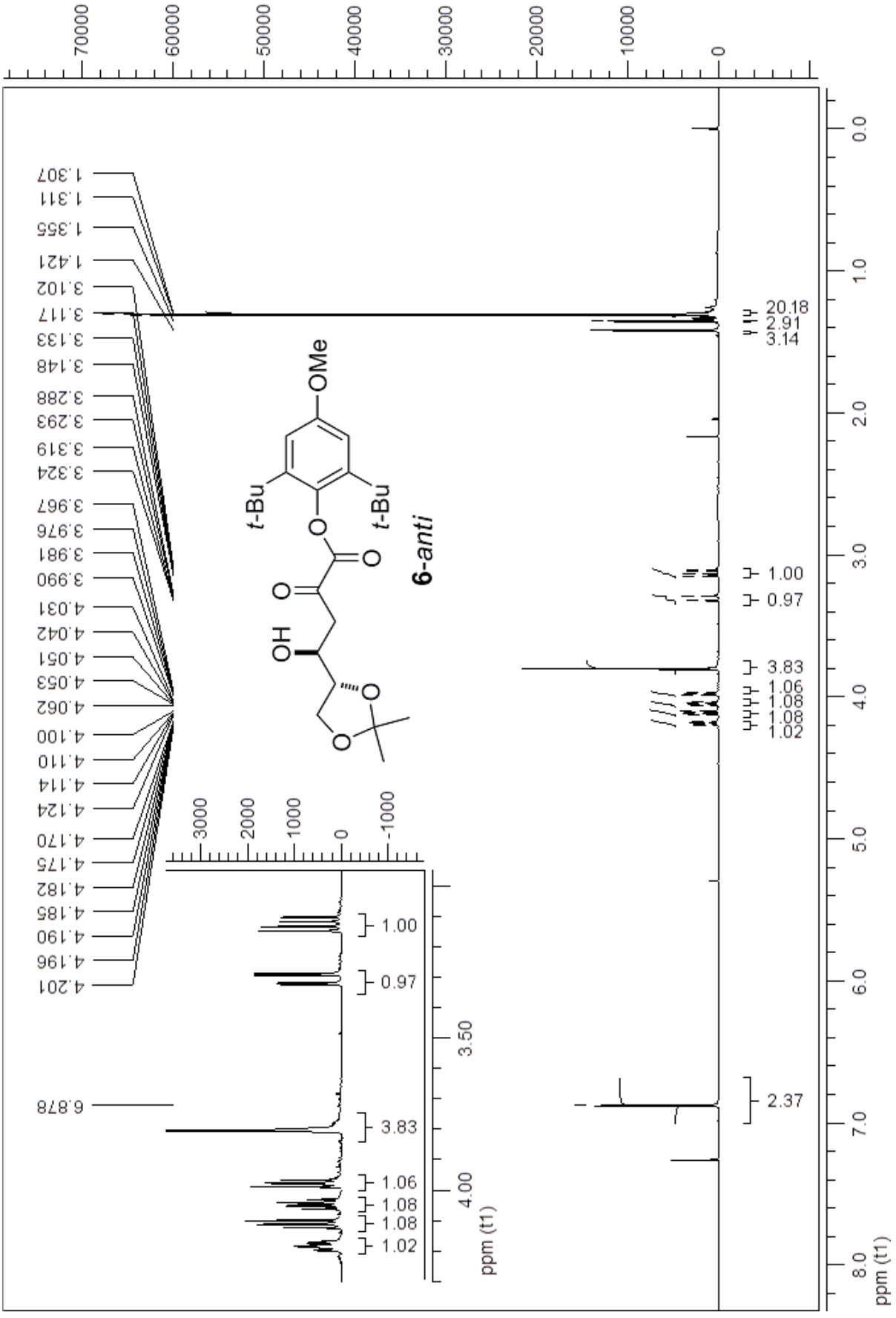
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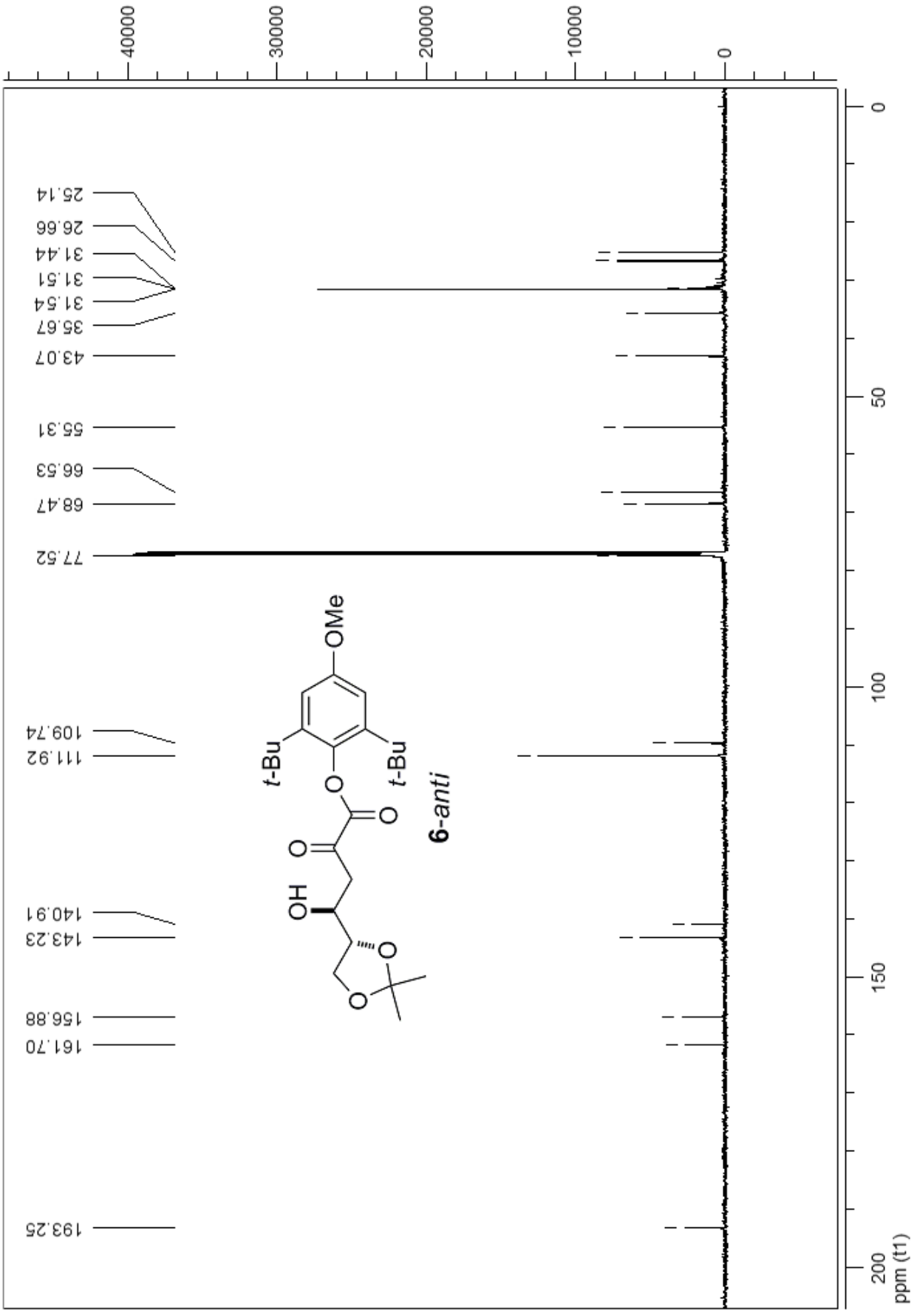
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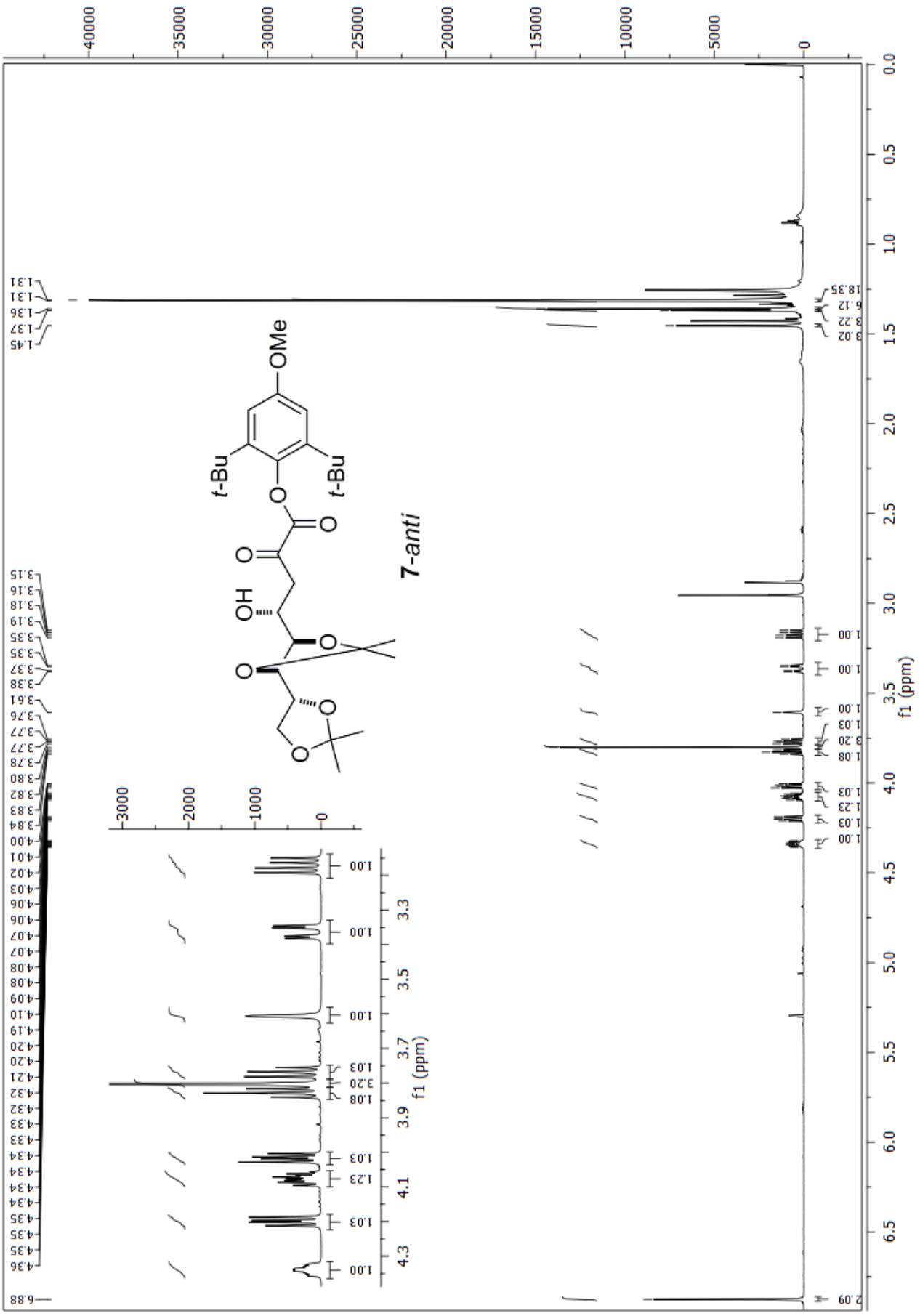
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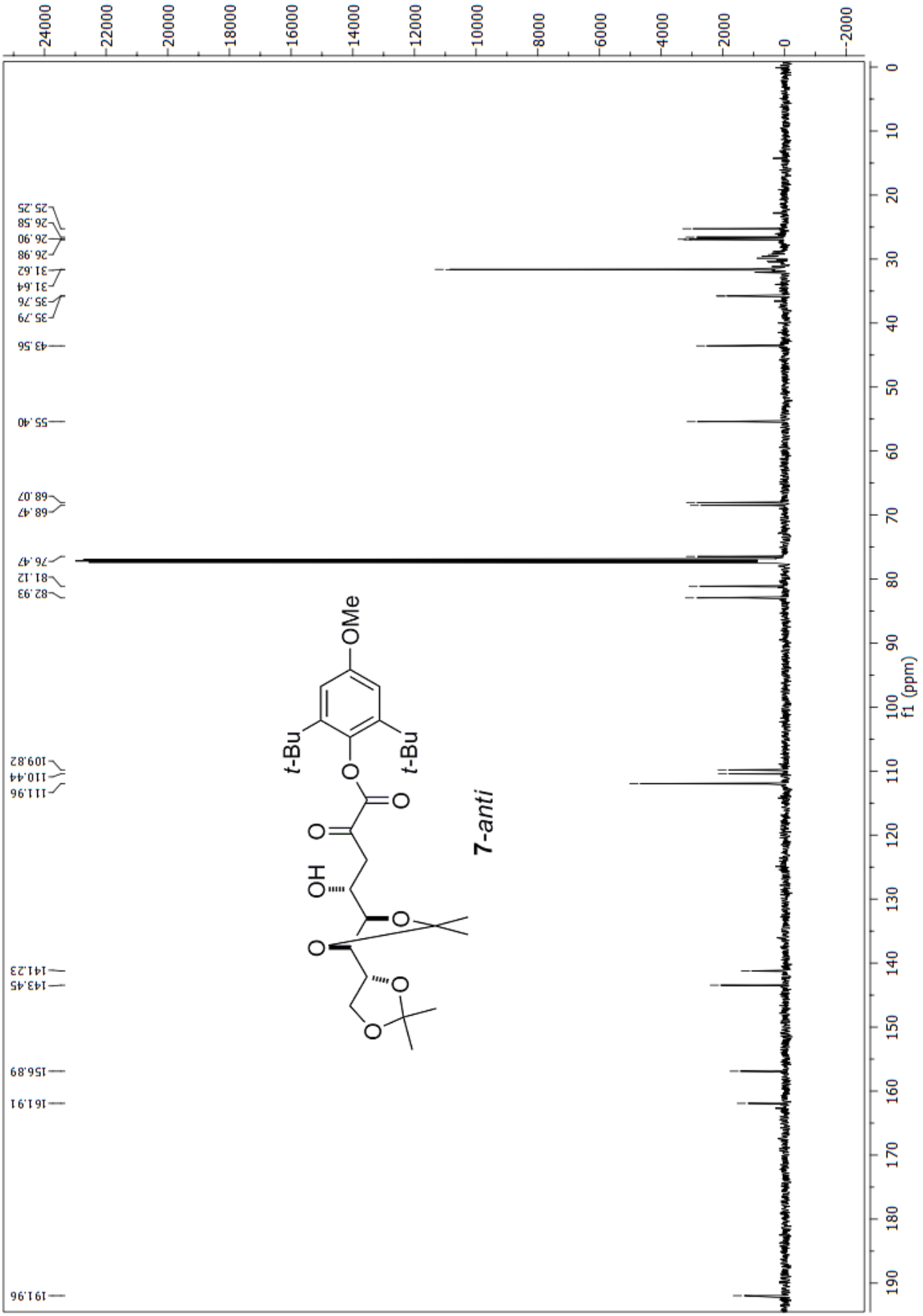
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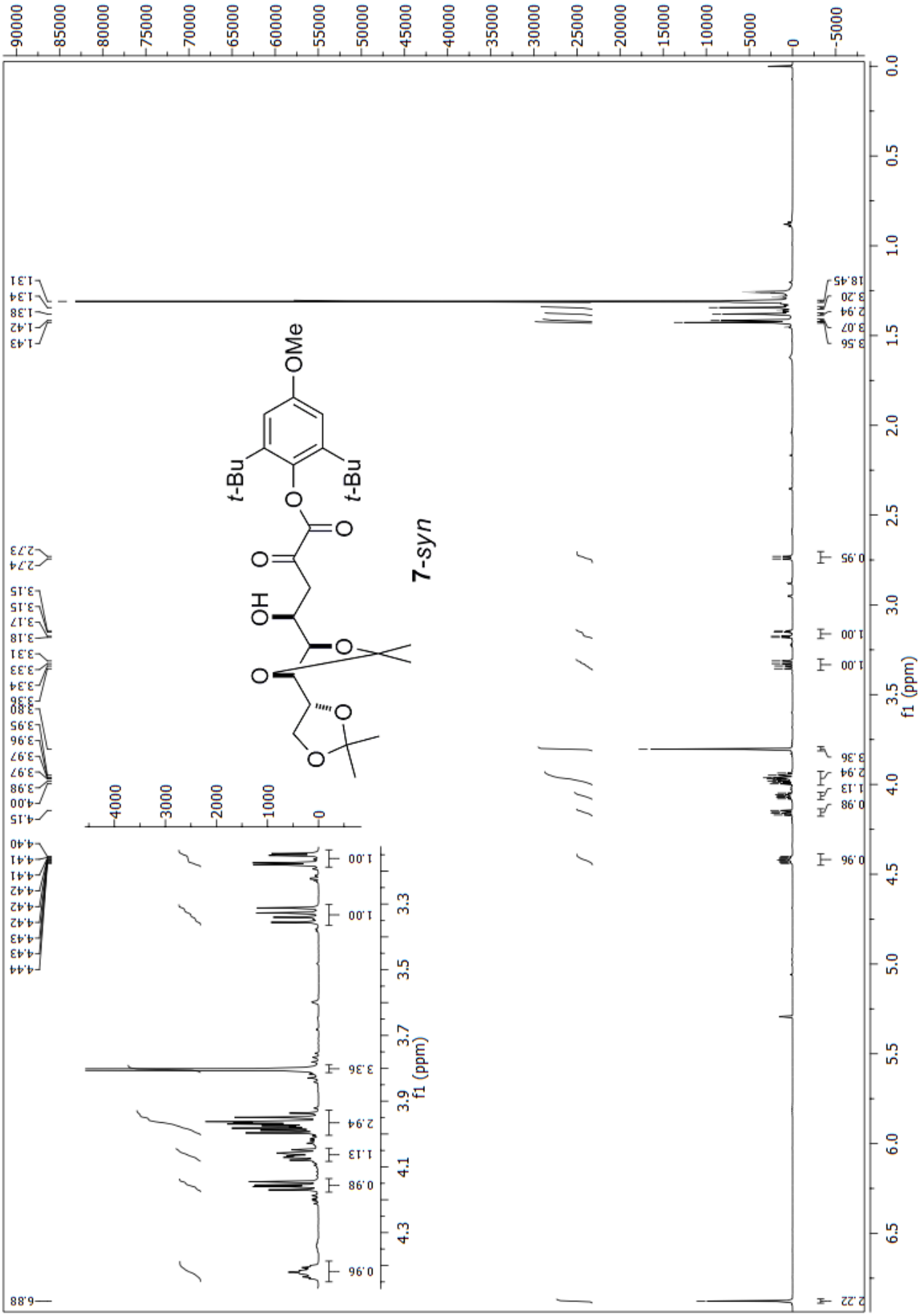
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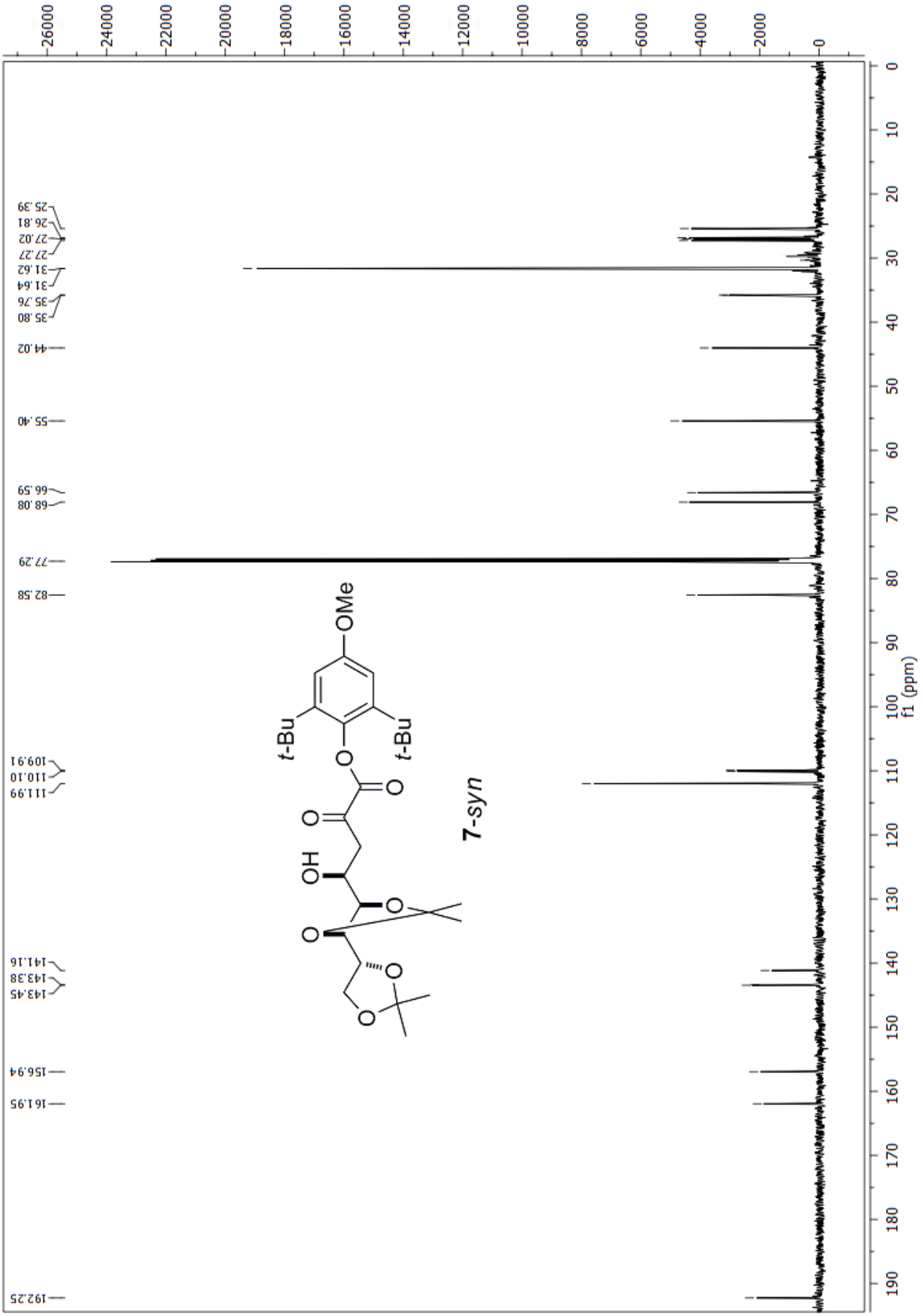
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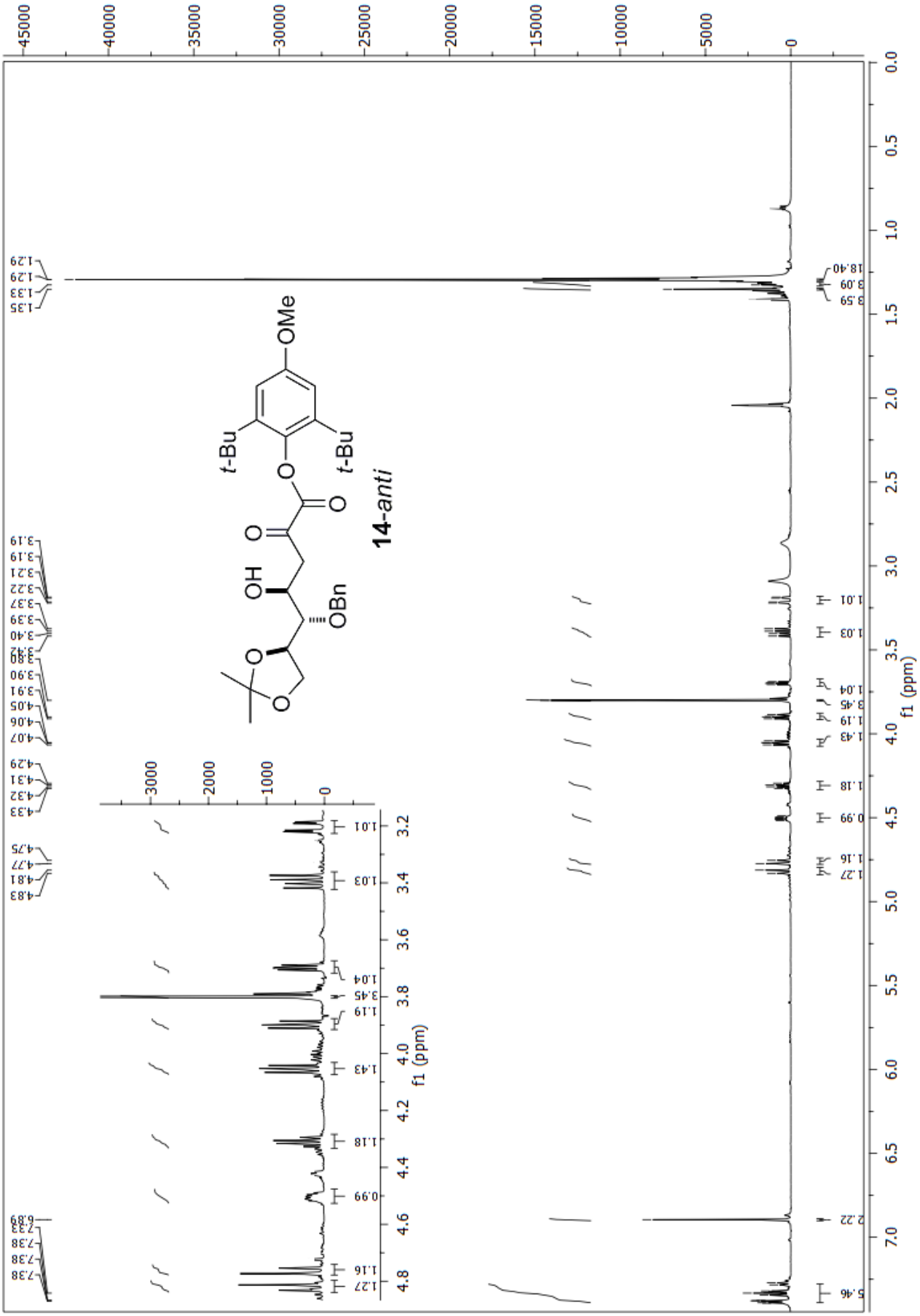
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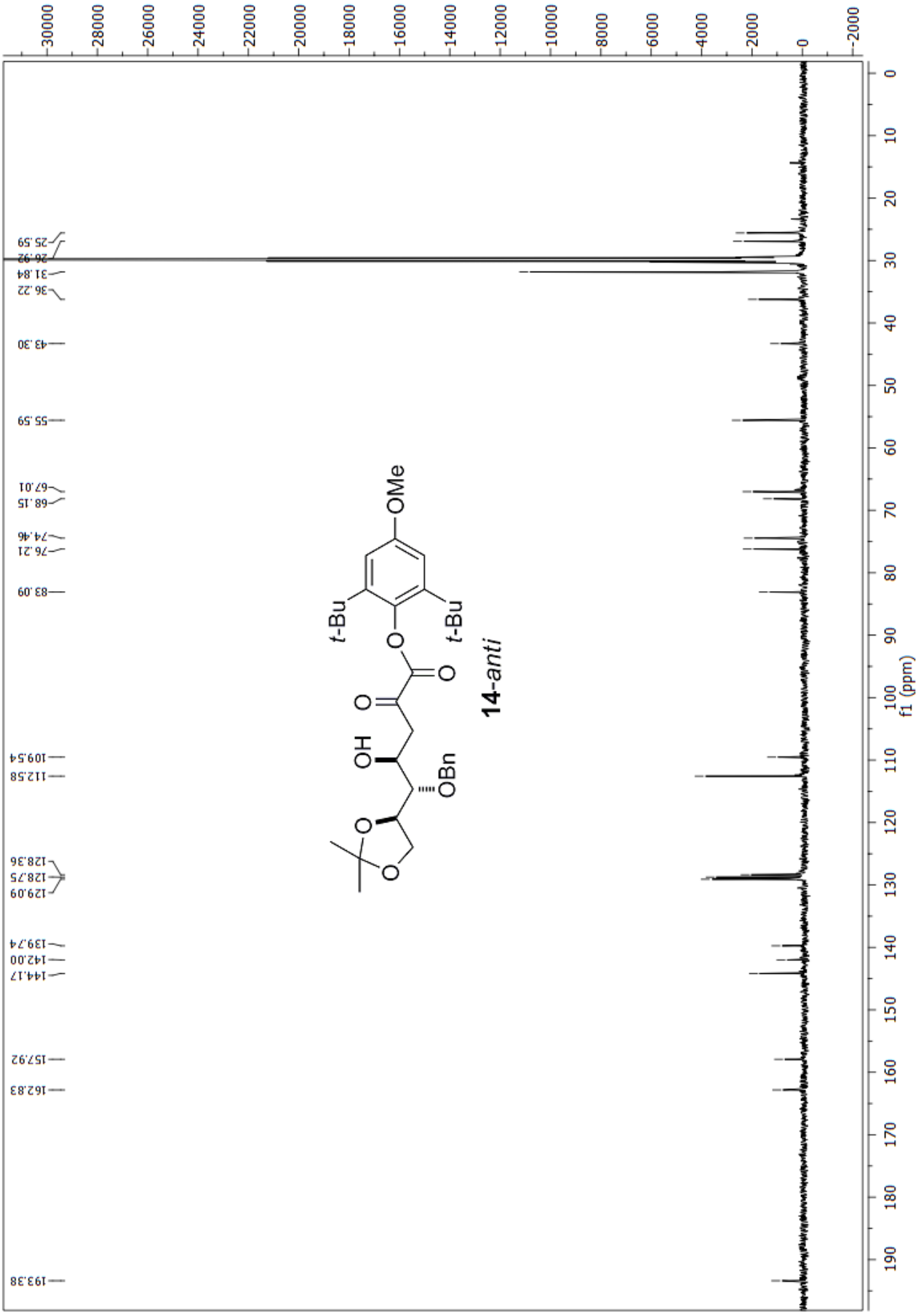
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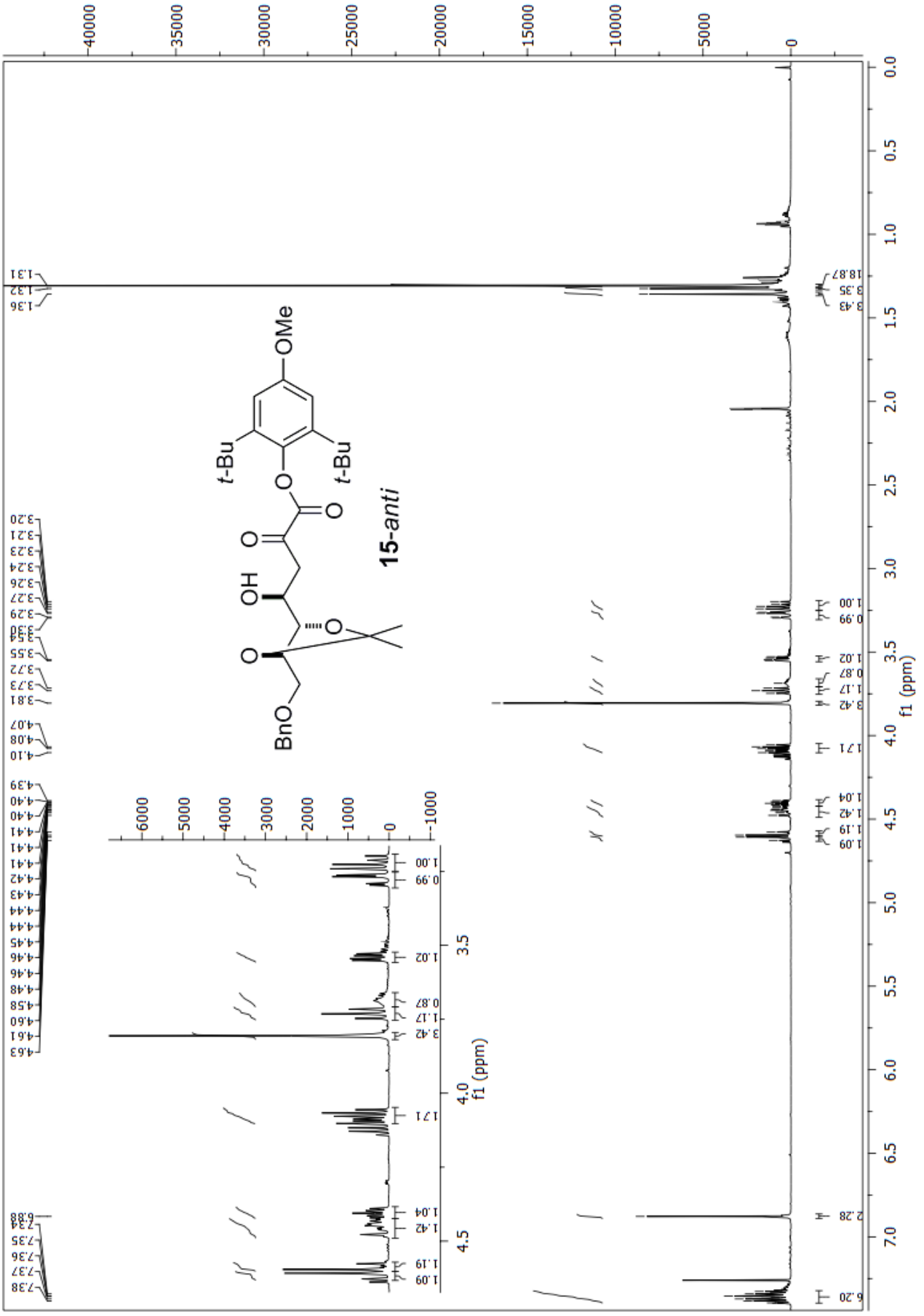
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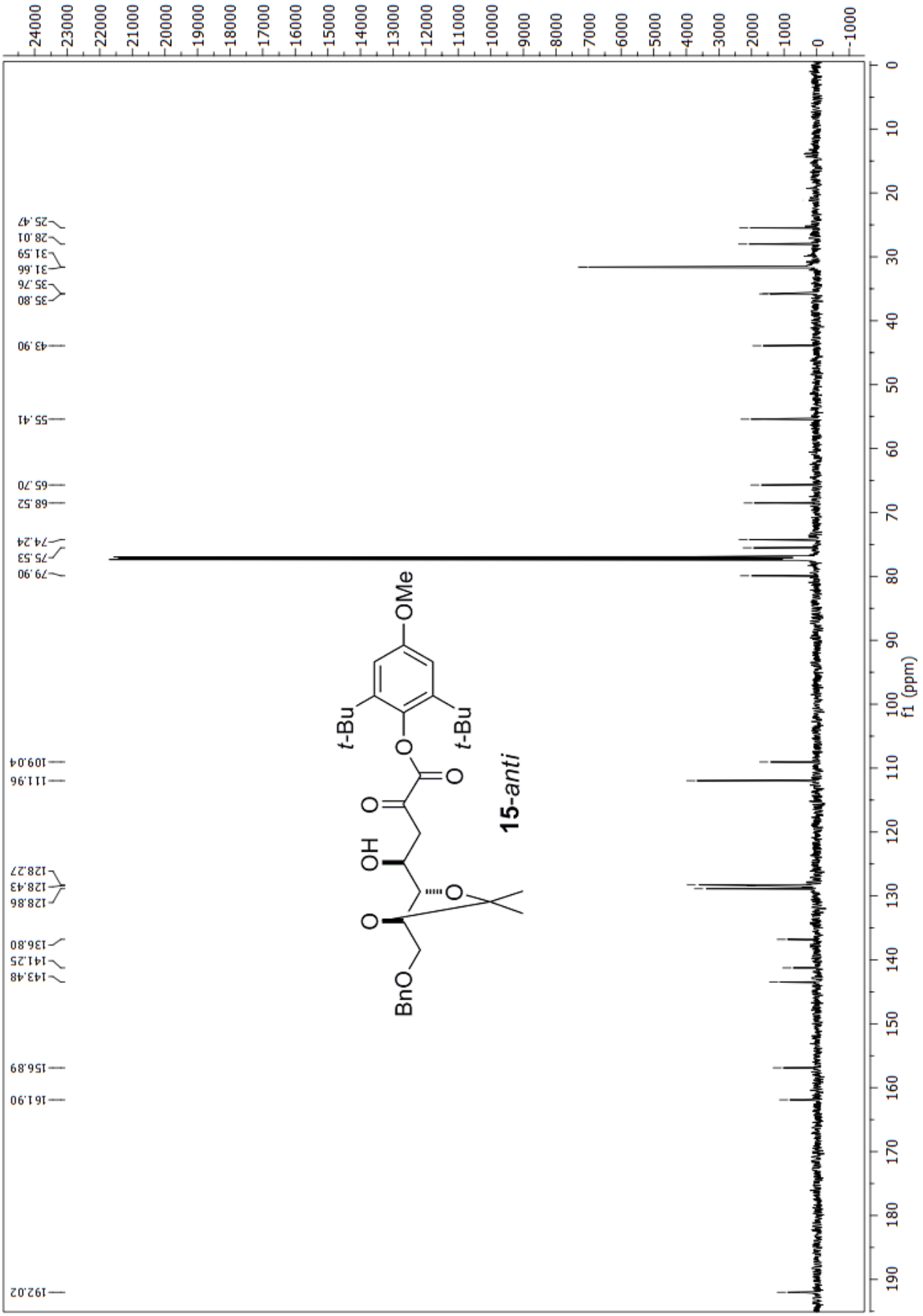
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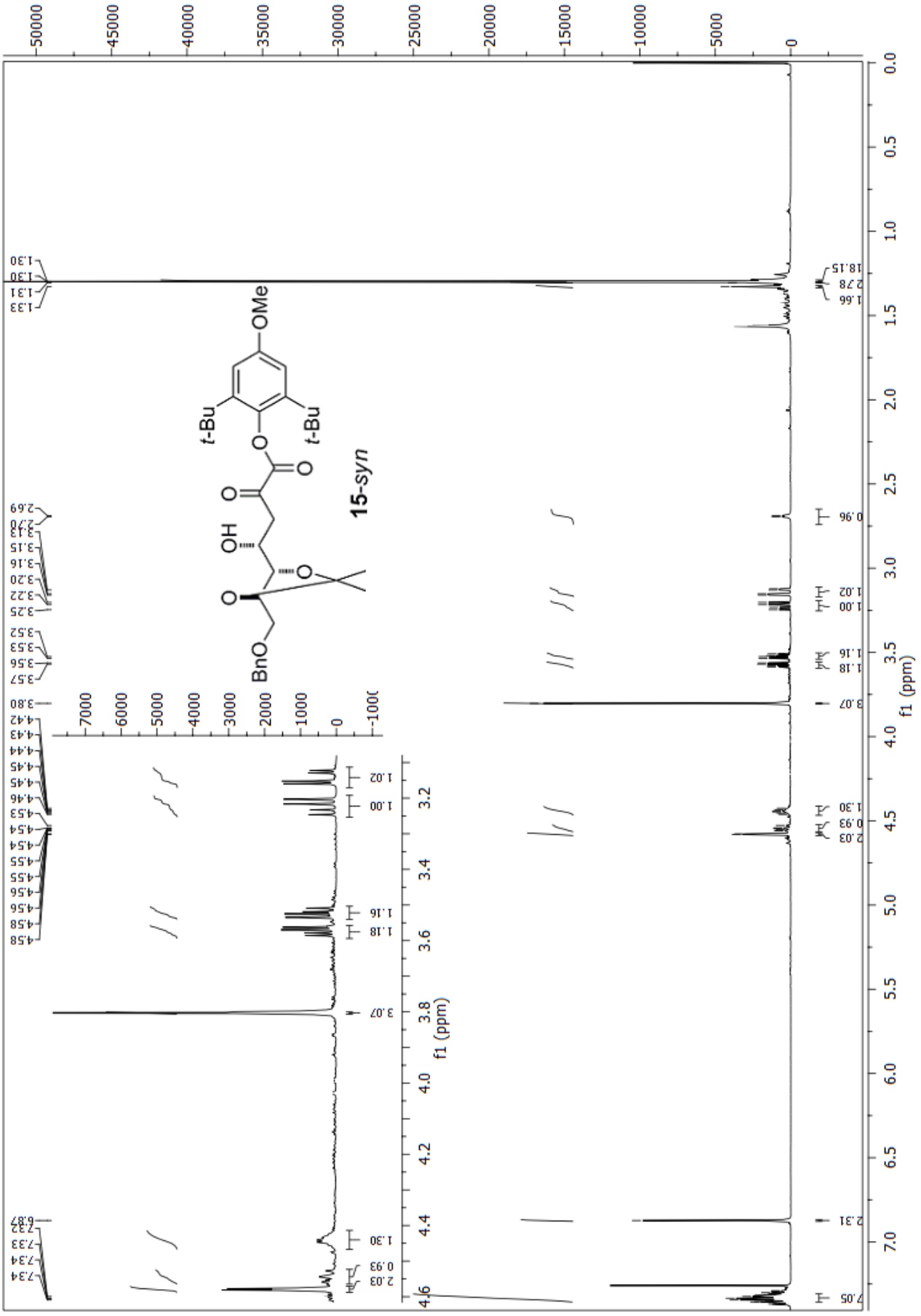
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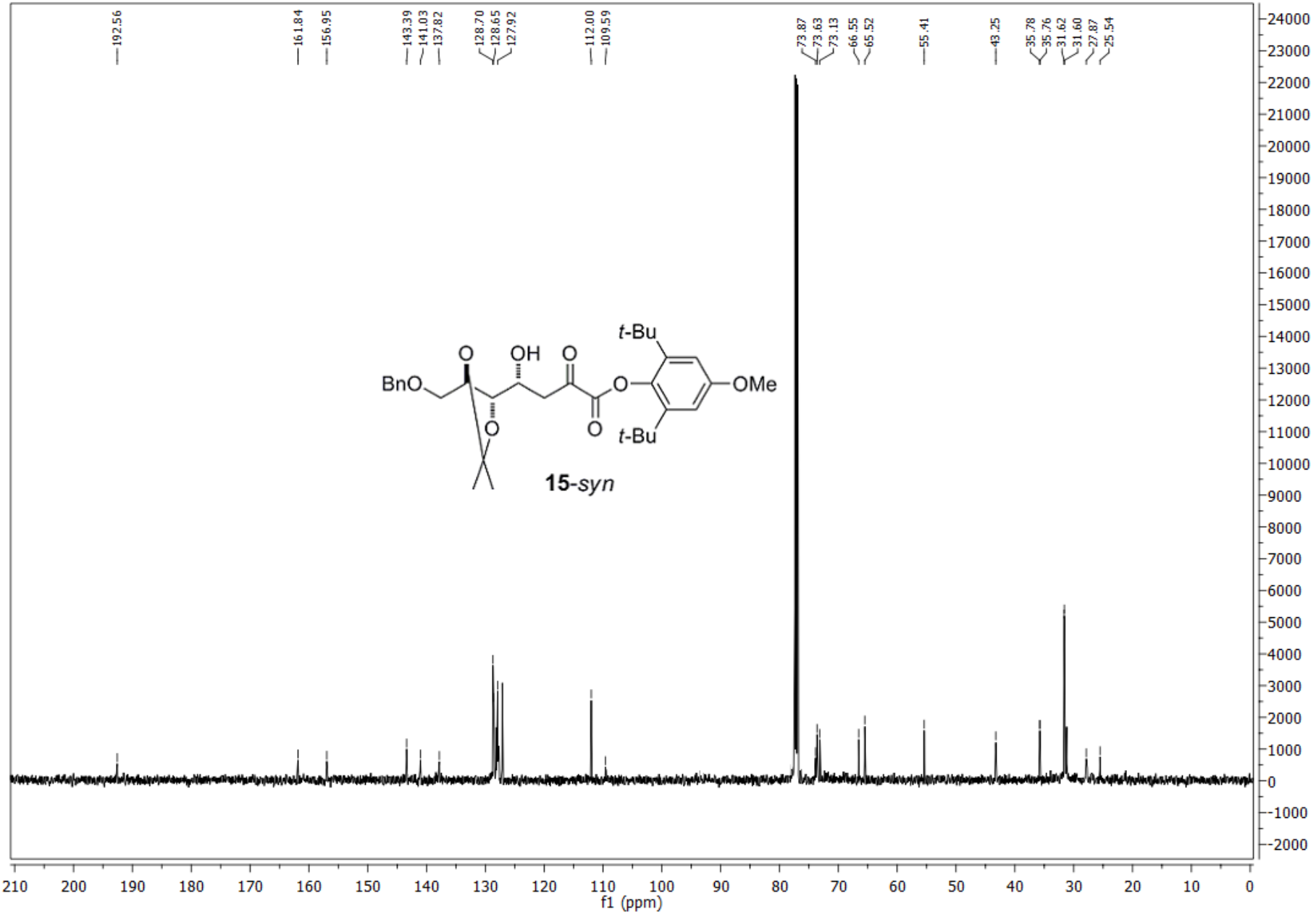
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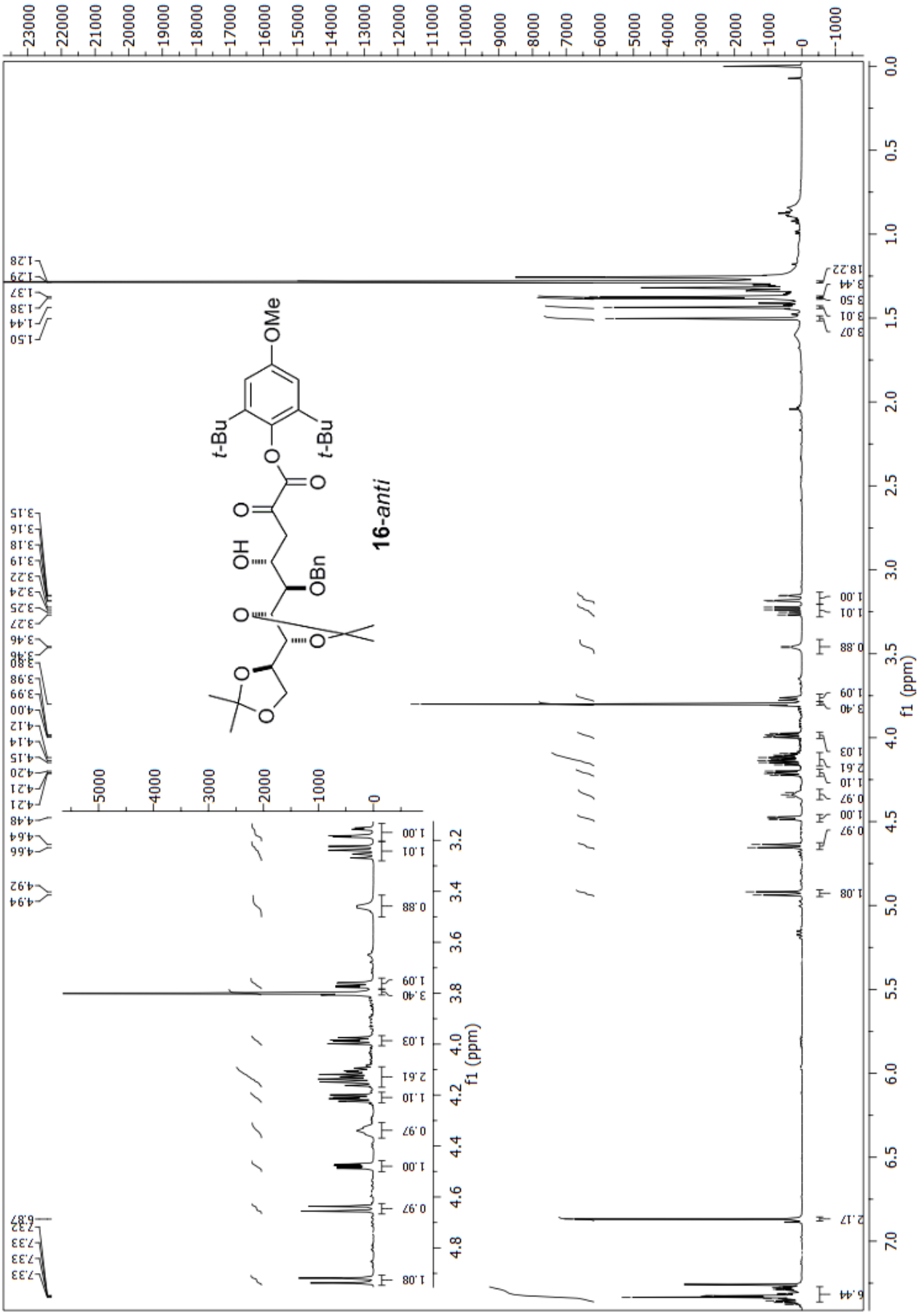
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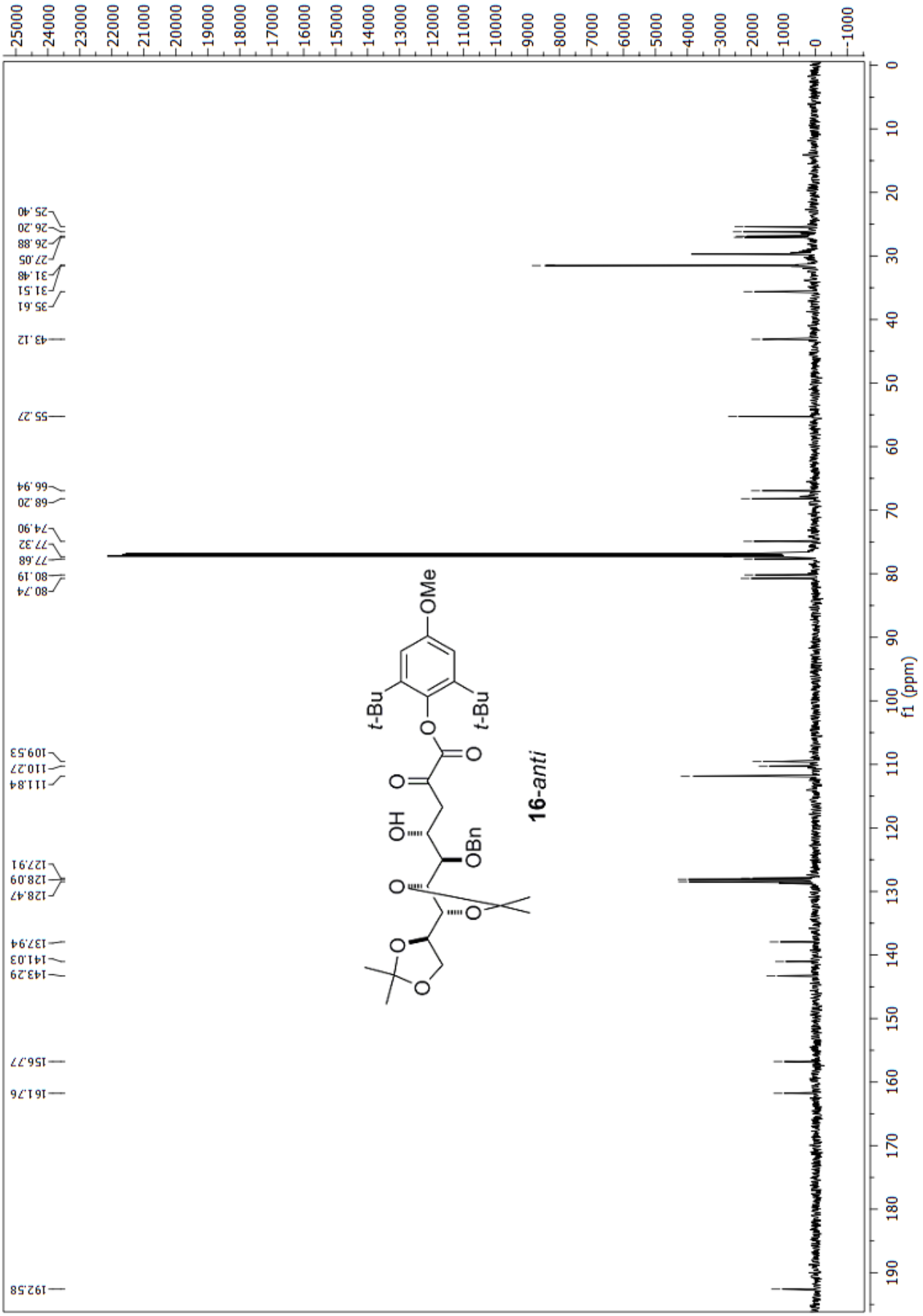
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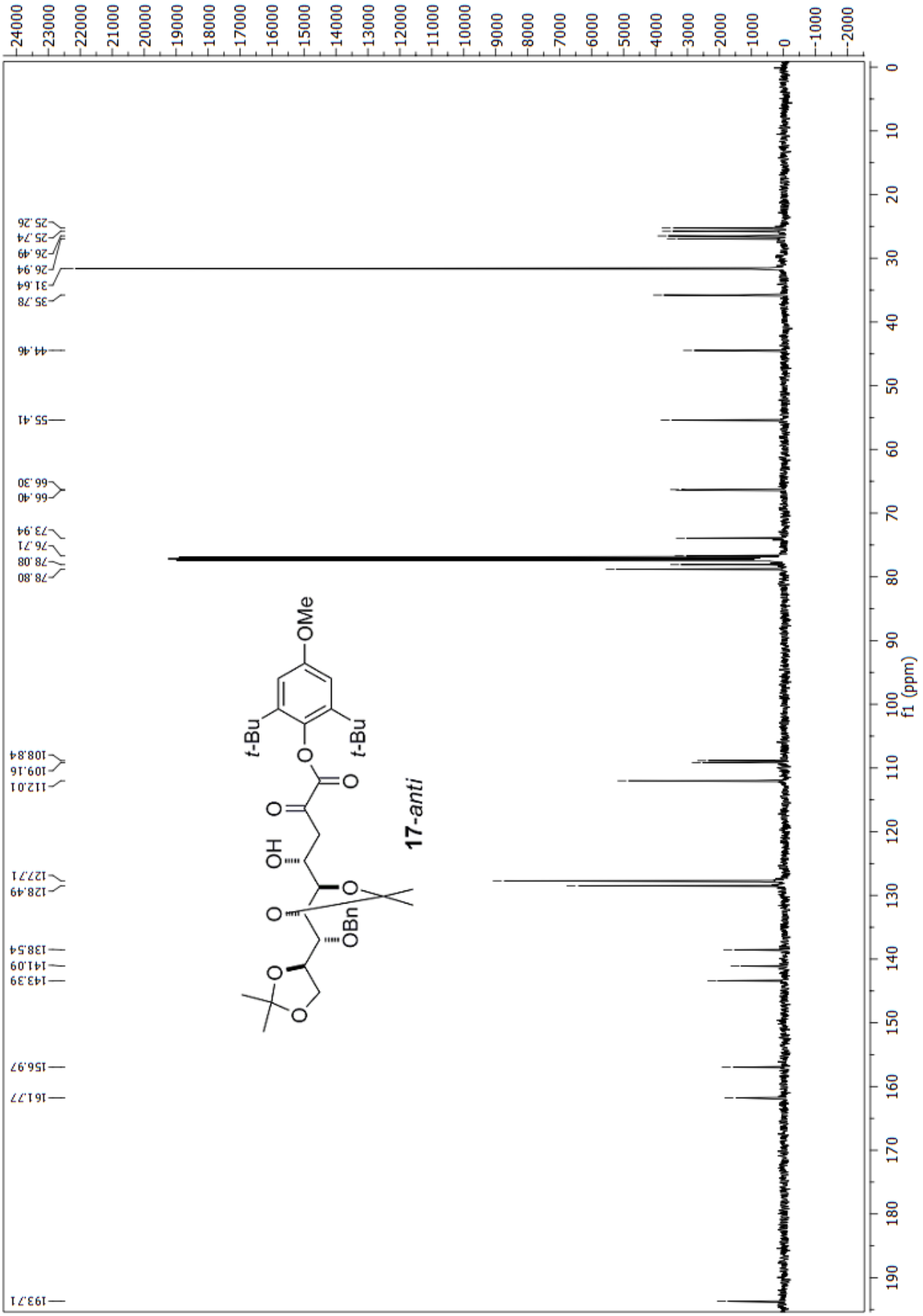
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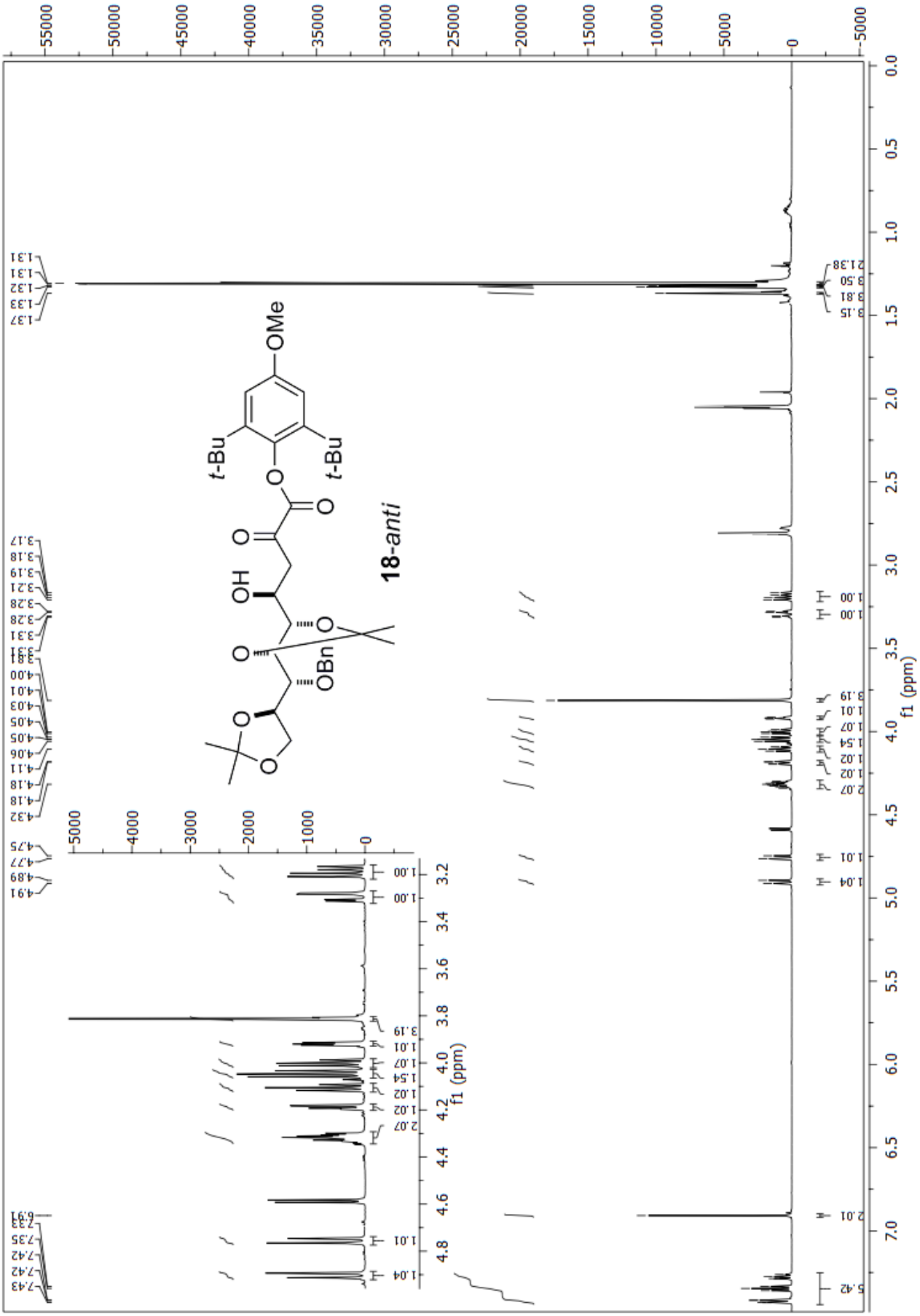
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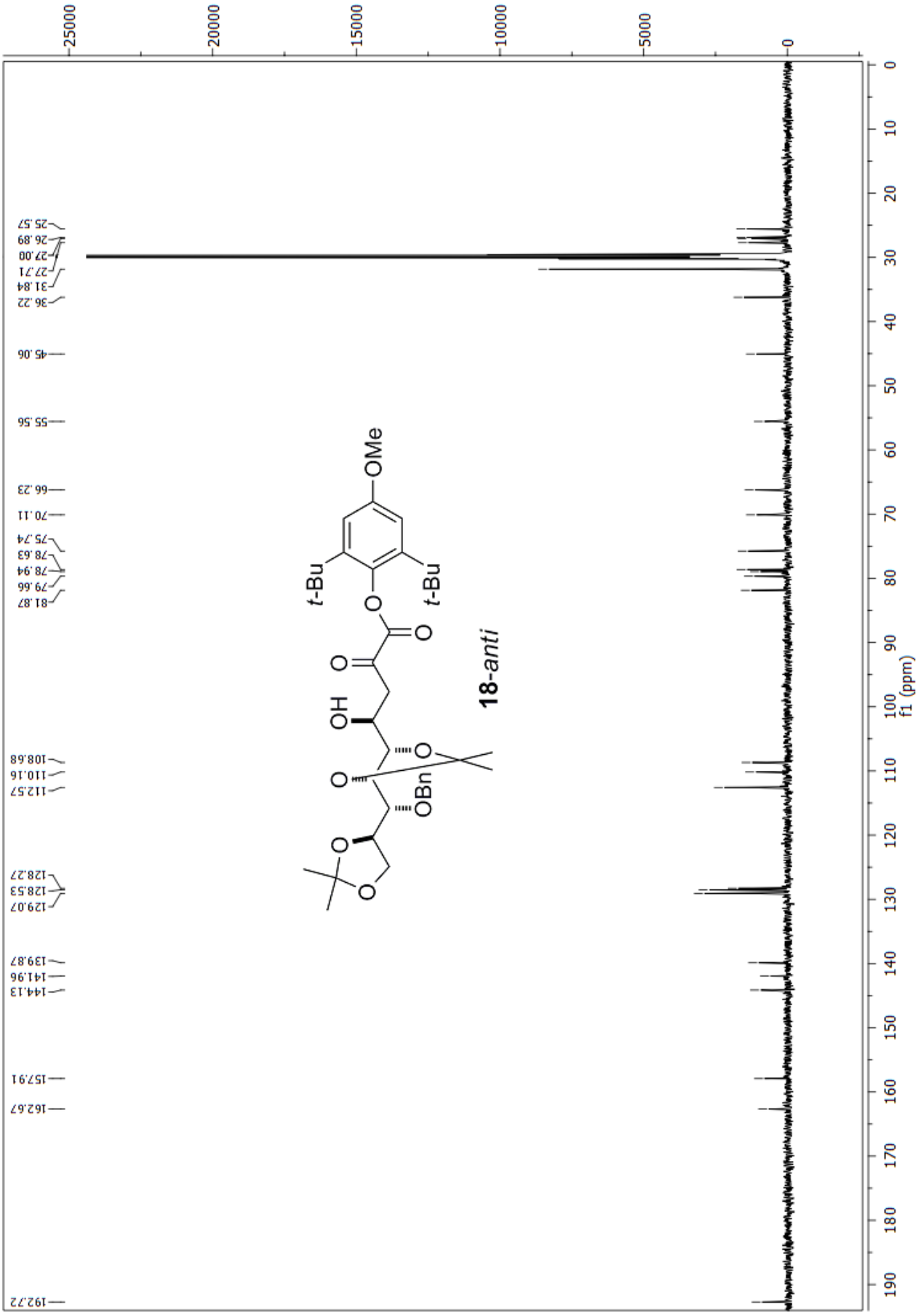
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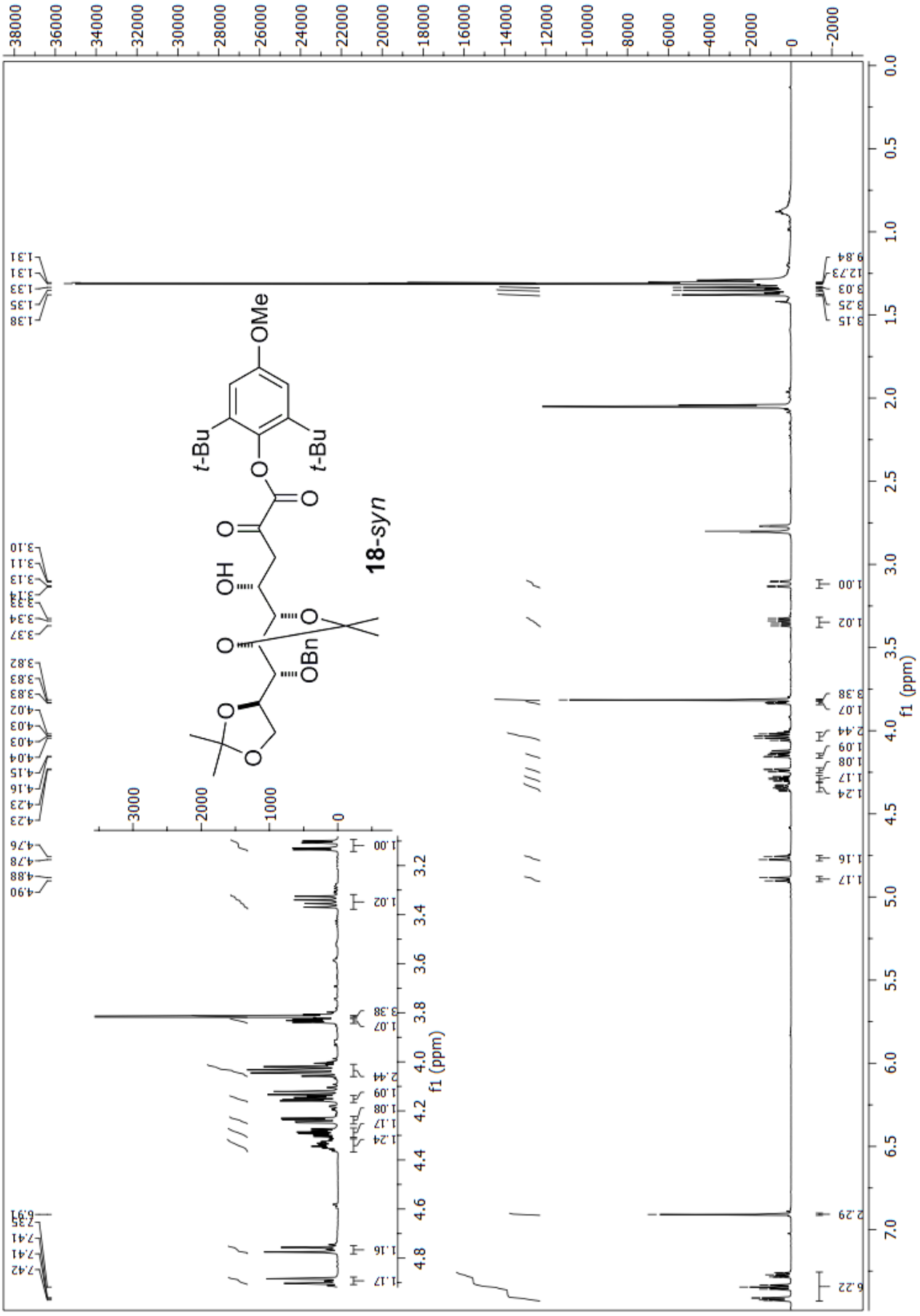
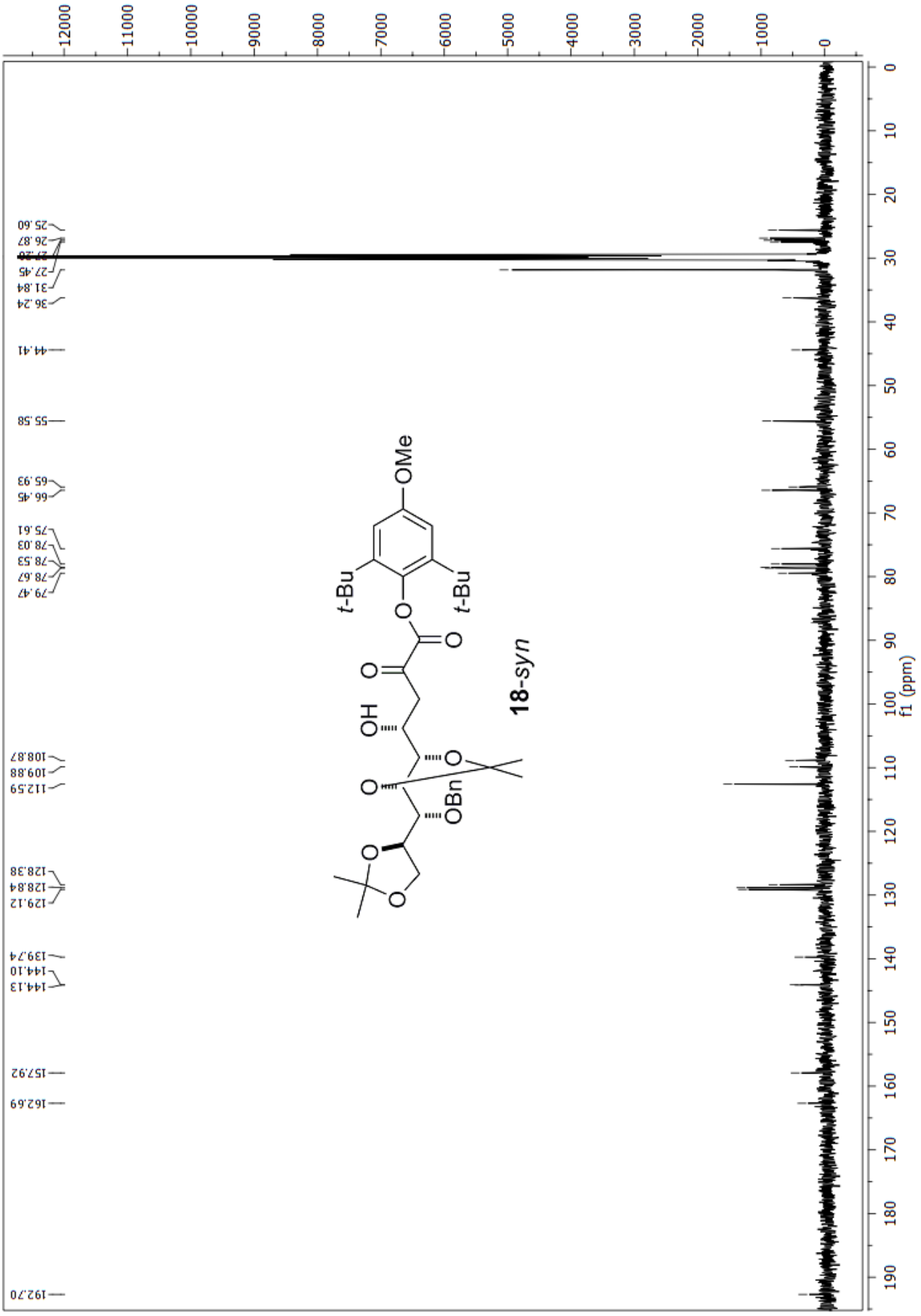
OBn
18-anti


18-syn
t-Bu
t-Bu
OMe
OH
OBn
f1 (ppm)

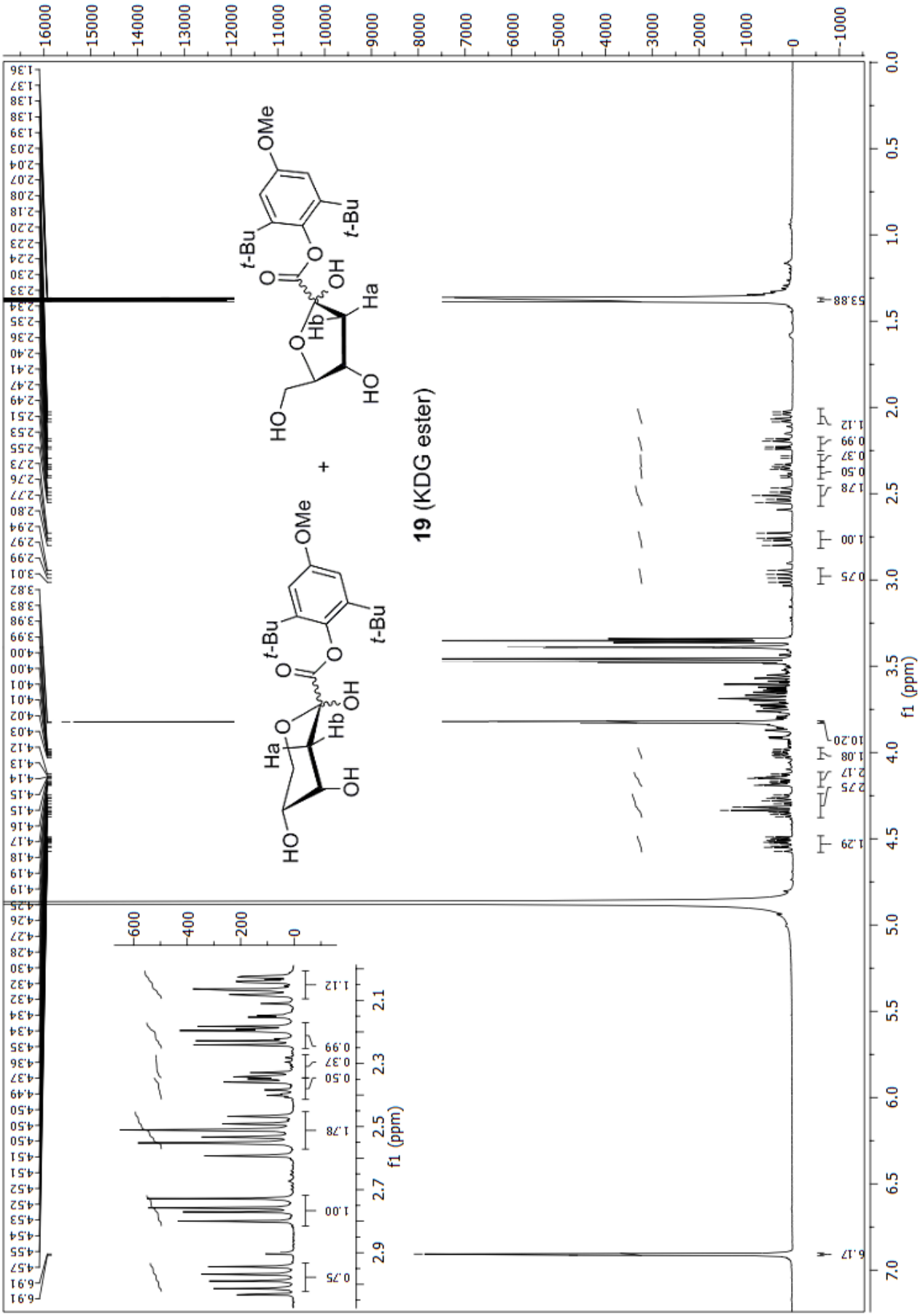

192.70
162.69
157.92
144.13
144.10
139.74
129.12
128.84
128.38
112.59
109.88
108.87
79.47
78.67
78.53
78.03
75.61
66.45
65.93
55.58
44.41
36.24
31.84
27.45
27.20
26.87
25.60
OMe
t-Bu
t-Bu
O
O
OH
O
O
O
OBn
O
O
18-syn
f1 (ppm)

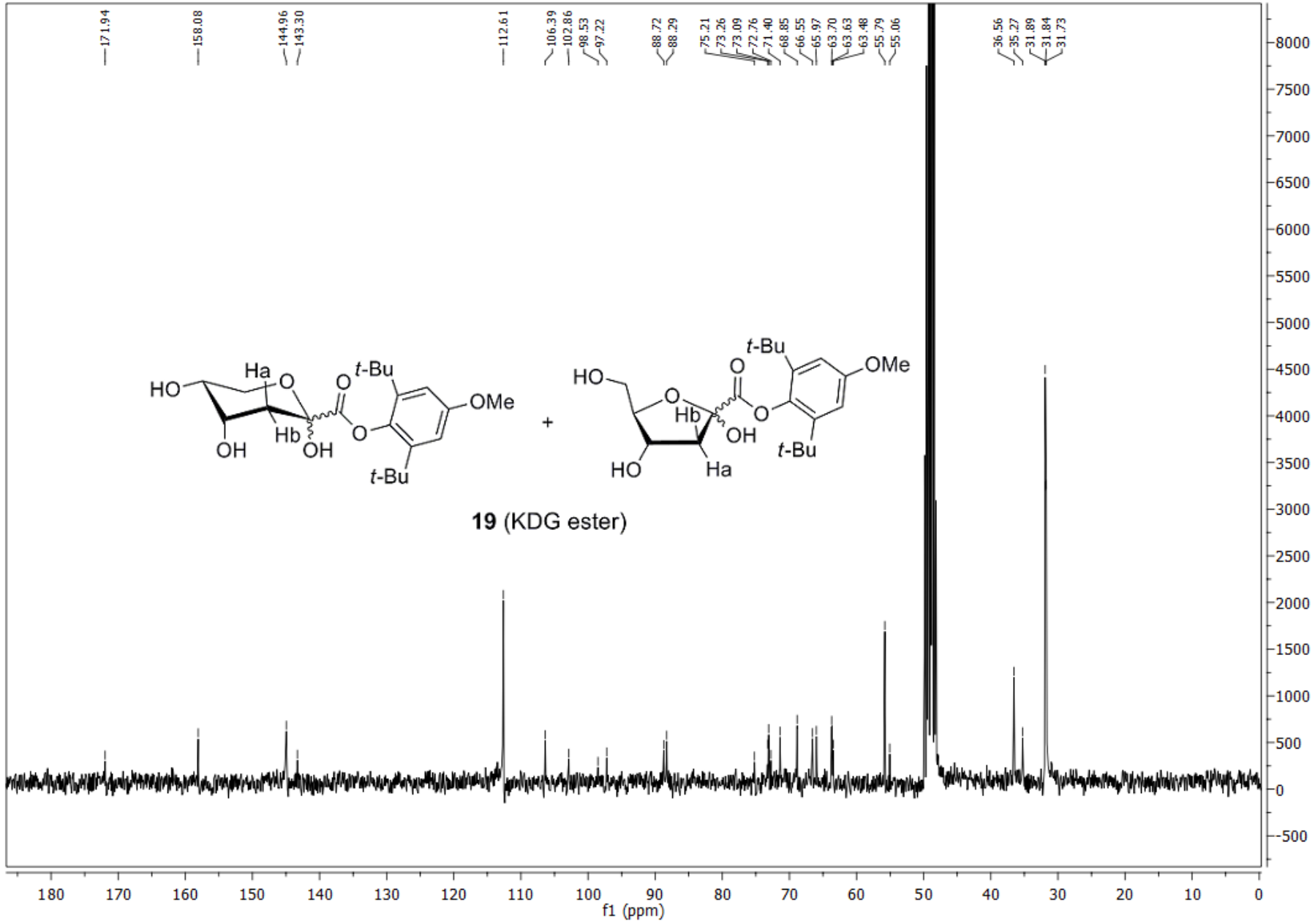
3-deoxy-D-*erythro*-hept-2-ulosonic acid 2,6-di-*t*-butyl-4-metoxyphenyl ester (19, KDG ester, Scheme 1)

Table 1. The assignment of the C-3 protons for the different cyclic forms, ^{1}H NMR (600 MHz, CD_3OD)

	δ_{3a}	δ_{3b}	$J_{3a,3b}$	$J_{3a,4}$	$J_{3b,4}$	%
***β*-pyranose**	2.06	2.51	12.5	4.8	12.5	27
***α*-pyranose**	2.38	2.31	14.3	3.1	4.1	13
***β*-furanose**	2.76	2.50	12.7	8.8	6.9	34
***α*-furanose**	2.98	2.21	13.7	7.2	3.9	26

The NMR of both pyranose and furanose forms are similar to those published for the corresponding methyl ester, see and R. Plantier-Royon, F. Cardona, D. Anker, *J. Carbohydr. Chem.* **1991**, *10*, 787-811.


19 (KDG ester)
f1 (ppm)

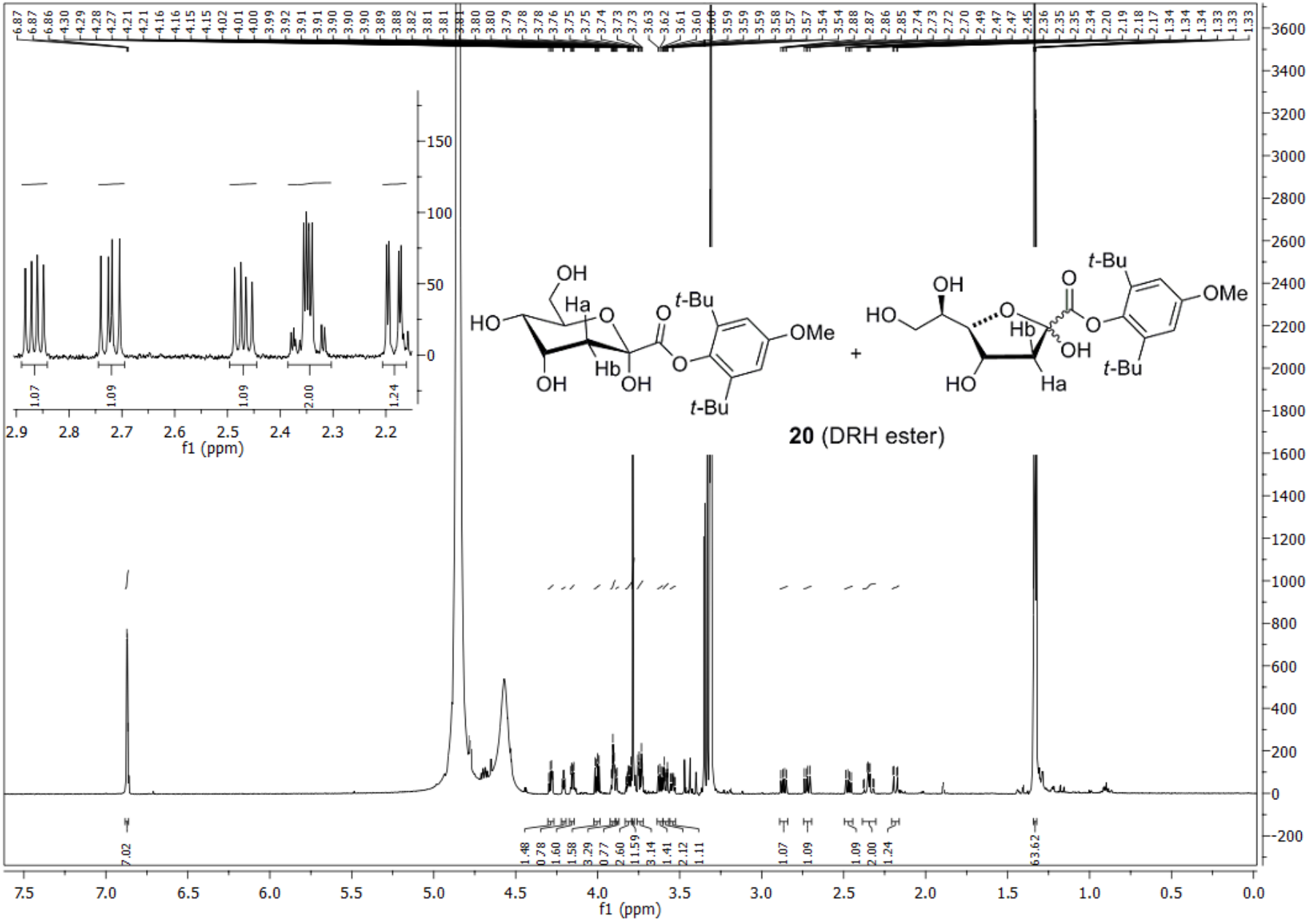

171.94
158.08
144.96
143.30
112.61
106.39
102.86
98.53
97.22
88.72
88.29
75.21
73.26
73.09
72.76
71.40
68.85
66.55
65.97
63.70
63.63
63.48
55.79
55.06
36.56
35.27
31.89
31.84
31.73
HO
Ha
O
O
t-Bu
OMe
OH
Hb
OH
O
t-Bu
+
HO
O
t-Bu
OMe
Hb
O
OH
HO
Ha
t-Bu
19 (KDG ester)
f1 (ppm)

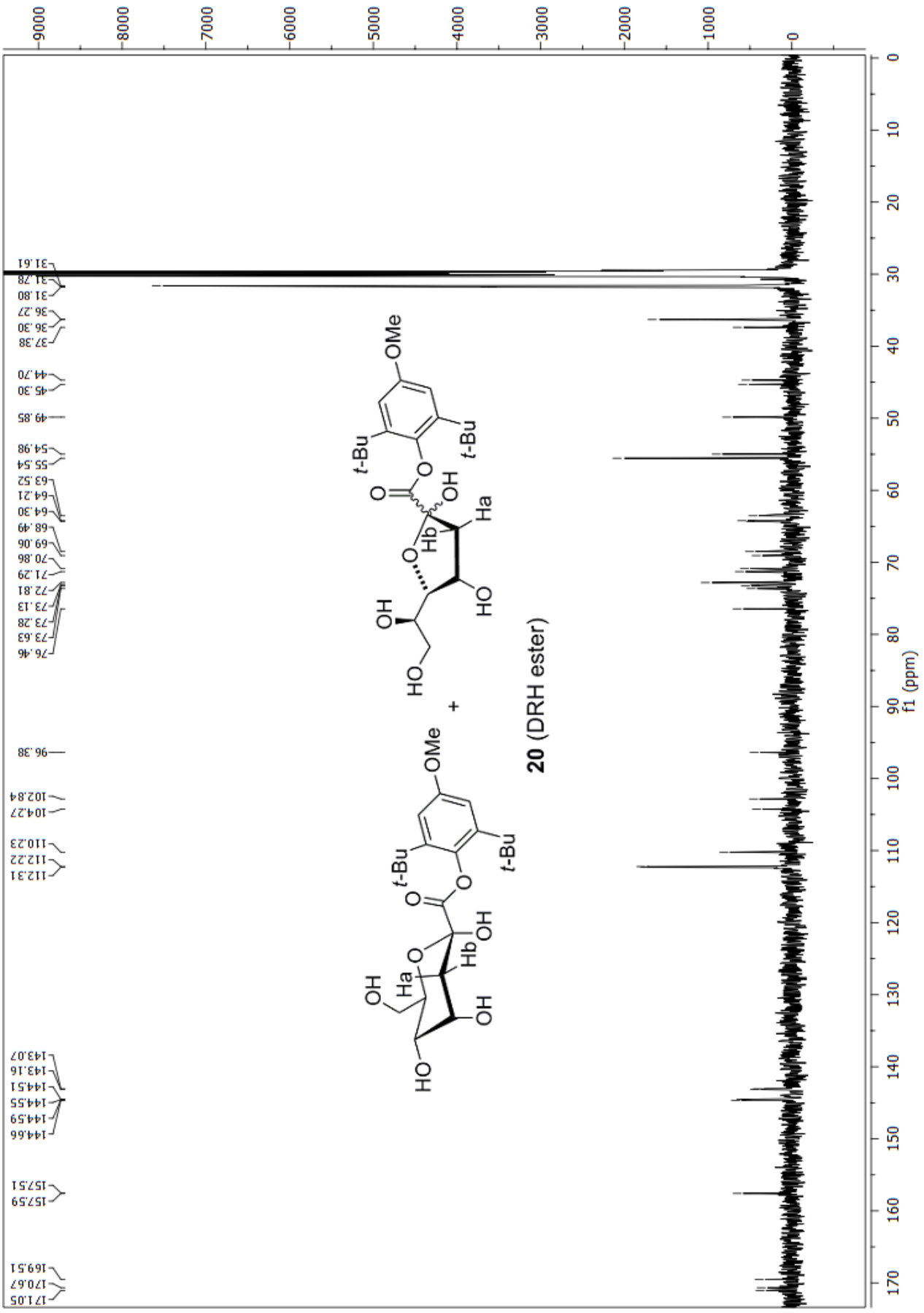
3-deoxy-D-*ribo*-hept-2-ulosonic acid 2,6-di-*t*-butyl-4-metoxyphenyl ester (20, DRH ester, Scheme 1)

Table 2. The assignment of the C-3 protons for the different cyclic forms, ^{1}H NMR (600 MHz, CD_3OD)

	δ_{3a}	δ_{3b}	$J_{3a,3b}$	$J_{3a,4}$	$J_{3b,4}$	%
***α*-pyranose**	2.37	2.33	14.3	3.0	3.6	32
***β*-furanose**	2.72	2.47	12.8	8.6	7.1	34
***α*-furanose**	2.87	2.18	13.7	7.1	2.7	34

The NMR of pyranose form is similar to this published for methyl ester of α-methyl-DRH-pyranoside, see J. Mlynarski and A. Banaszek, *Tetrahedron*, **1997**, *53*, 10643-10658.


OH
Ha
HO
O
t-Bu
OMe
Hb
OH
OH
t-Bu
+
HO
OH
O
t-Bu
OMe
Hb
OH
HO
Ha
t-Bu
20 (DRH ester)
f1 (ppm)
f1 (ppm)

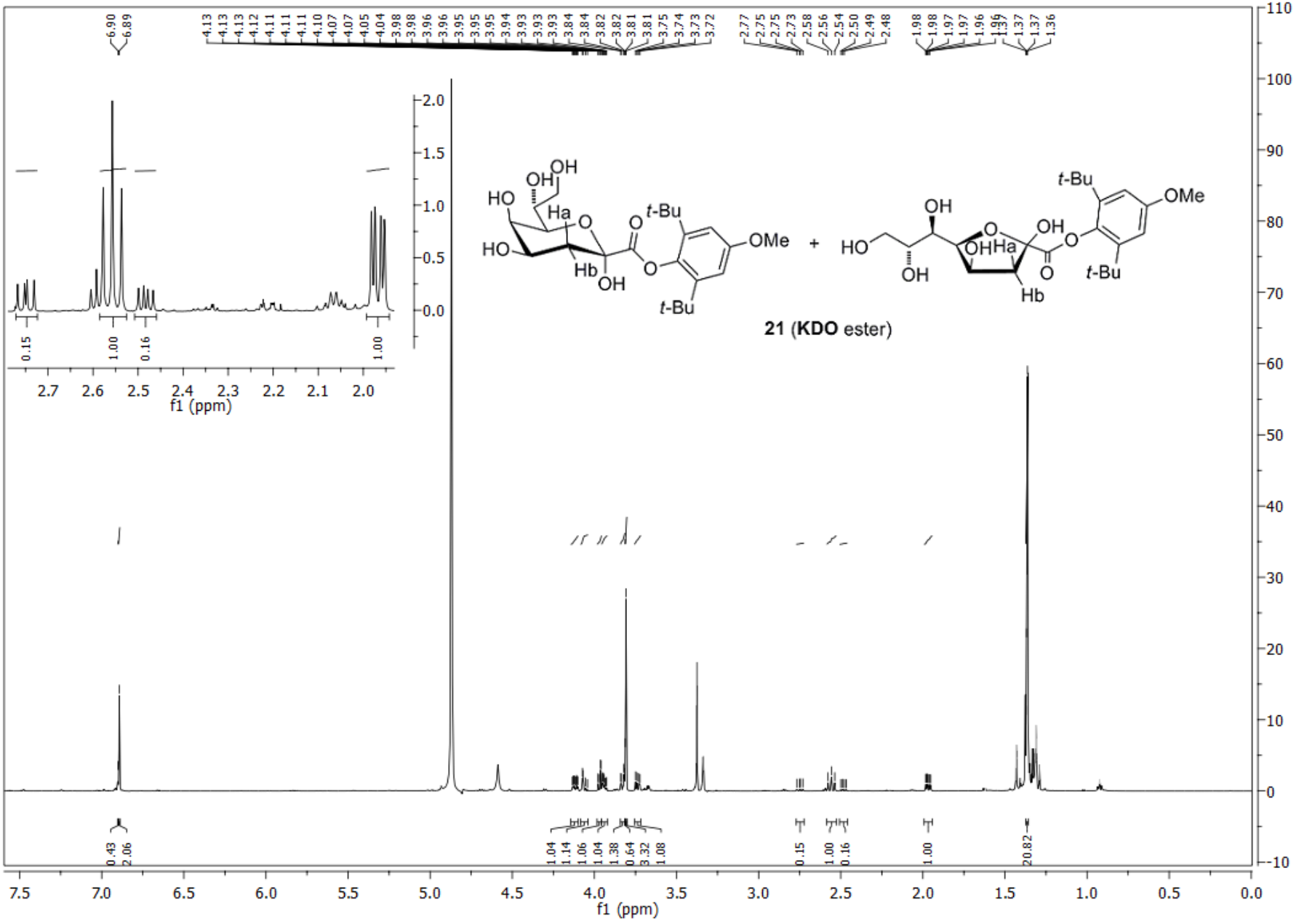

31.61
31.78
31.80
36.27
36.30
37.38
44.70
45.30
49.85
54.98
55.54
63.52
64.21
64.30
68.49
69.06
70.86
71.29
72.81
73.13
73.28
73.63
76.46
96.38
102.84
104.27
110.23
112.22
112.31
143.07
143.16
144.51
144.55
144.59
144.66
157.51
157.59
169.51
170.67
171.05
OMe
t-Bu
t-Bu
O
O
OH
Ha
Hb
O
HO
OH
HO
+
OMe
t-Bu
t-Bu
O
O
OH
Hb
O
Ha
OH
OH
HO
20 (DRH ester)
f1 (ppm)

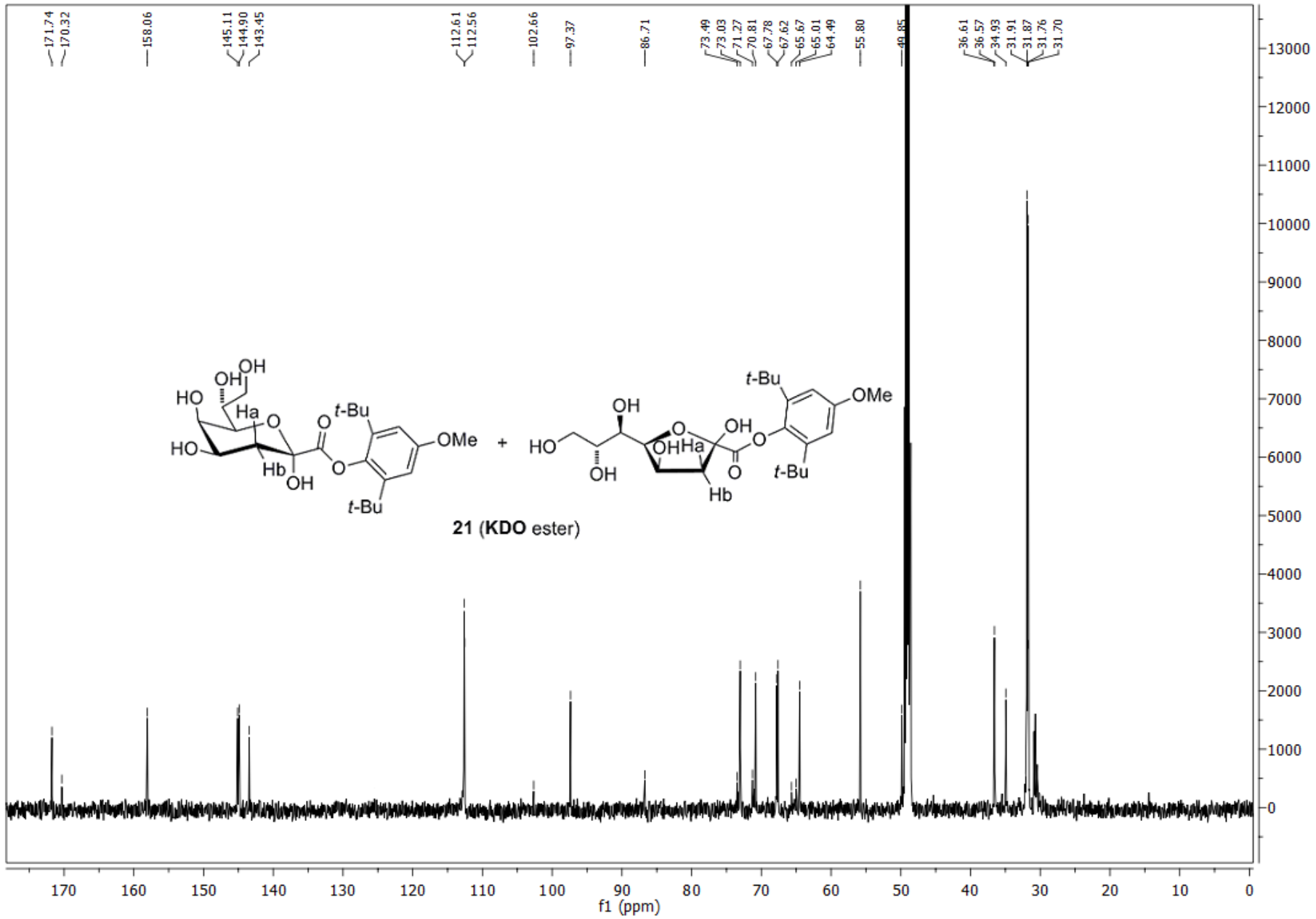
3-deoxy-D-*manno*-oct-2-ulosonic acid 2,6-di-*t*-butyl-4-metoxyphenyl ester (21, KDO ester, Scheme 1)

Table 3. The assignment of the C-3 protons for the different cyclic forms, ^{1}H NMR (600 MHz, CD_3OD)

	δ_{3a}	δ_{3b}	$J_{3a,3b}$	$J_{3a,4}$	$J_{3b,4}$	%
***α*-pyranose**	2.56	1.97	12.5	12.5	4.7	87
***β*-furanose**	2.75	2.48	12.5	9.4	7.00	13

The NMR of *α*-pyranose form is similar to this published for KDO, see Kragl U., Gödde A., Wandrey C., Lubin N., Augé C., *J. Chem. Soc. Perkin Trans. 1* **1994**, 119-124.

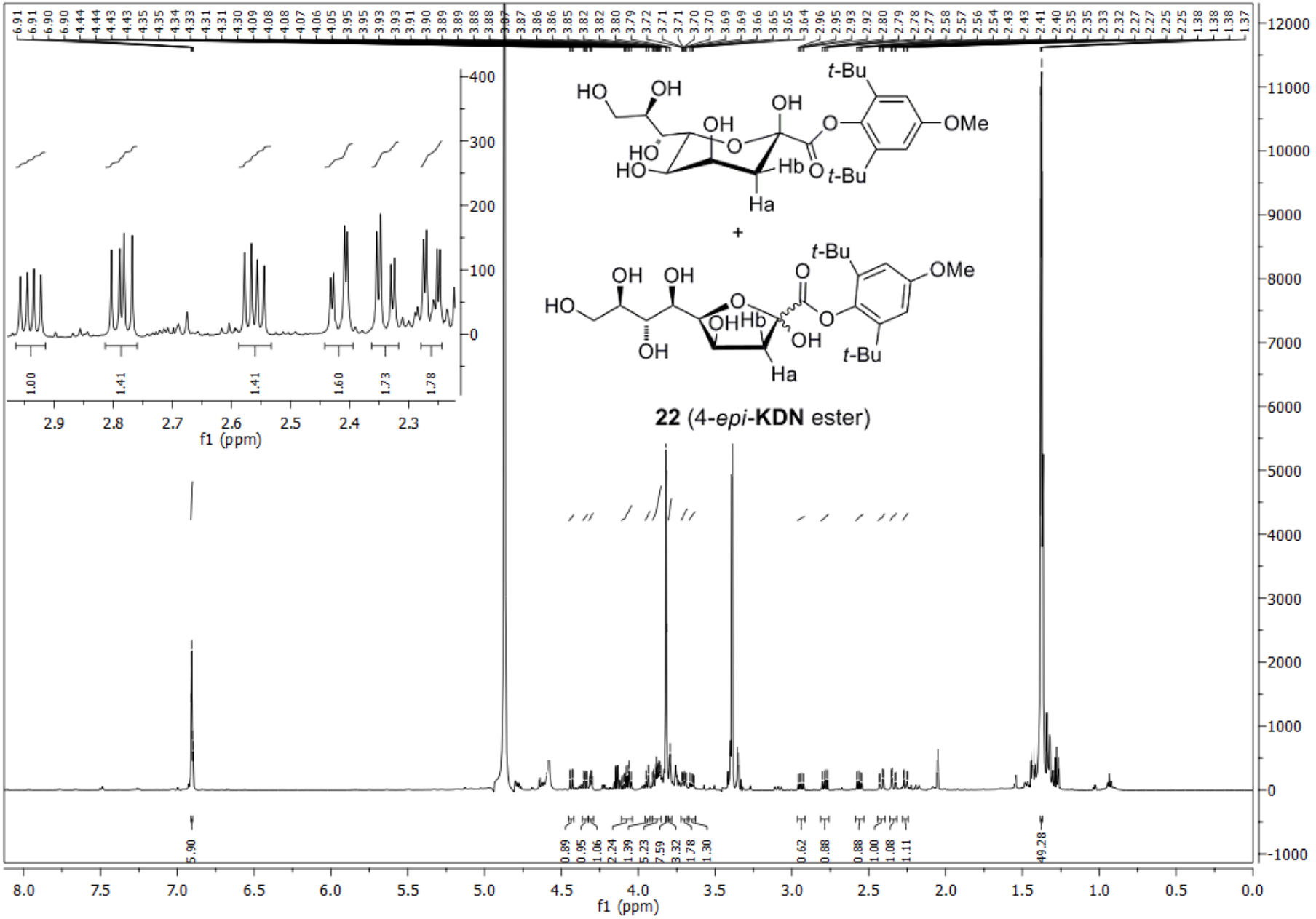

21 (KDO ester)
f1 (ppm)

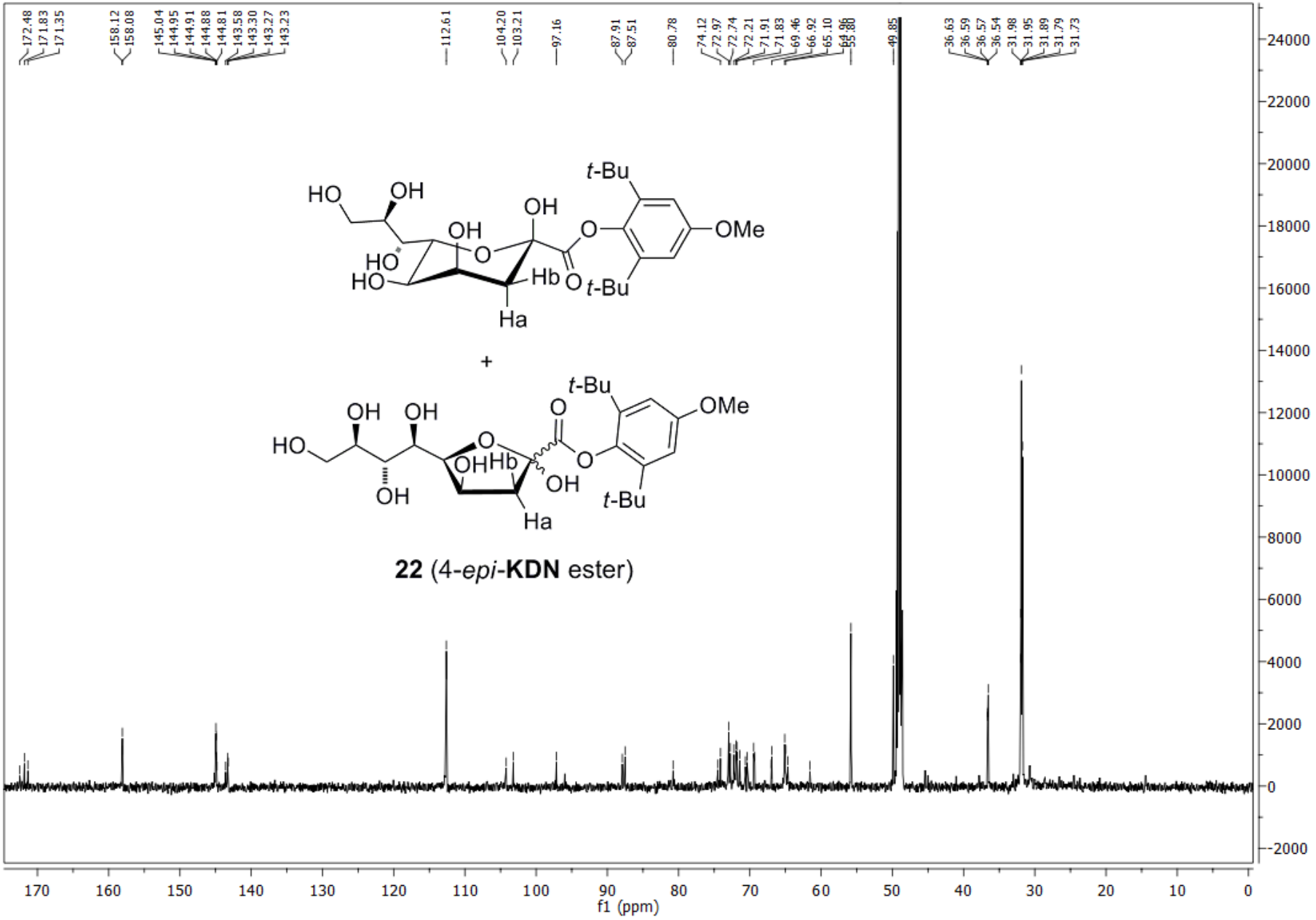

171.74
170.32
158.06
145.11
144.90
143.45
112.61
112.56
102.66
97.37
86.71
73.49
73.03
71.27
70.81
67.78
67.62
65.67
65.01
64.49
55.80
49.85
36.61
36.57
34.93
31.91
31.87
31.76
31.70
HO
OH
OH
Ha
Hb
OH
O
O
t-Bu
t-Bu
OMe
+
HO
OH
OH
OH
Ha
Hb
O
O
t-Bu
t-Bu
OMe
21 (KDO ester)
f1 (ppm)

3-deoxy-D-*glycero*-D-*talo*-non-2-ulosonic acid 2,6-di-*t*-butyl-4-metoxyphenyl ester (22, 4-*epi*-KDN ester, Scheme 1)

Table 4. The assignment of the C-3 protons for the different cyclic forms, ^{1}H NMR (600 MHz, CD_3OD)

	δ_{3a}	δ_{3b}	$J_{3a,3b}$	$J_{3a,4}$	$J_{3b,4}$	%
***α*-pyranose**	2.42	2.34	14.3	2.9	3.7	40
***β*-furanose**	2.79	2.56	12.8	7.1	8.4	35
***α*-furanose**	2.94	2.26	13.7	2.9	7.1	25


22 (4-epi-KDN ester)
f1 (ppm)

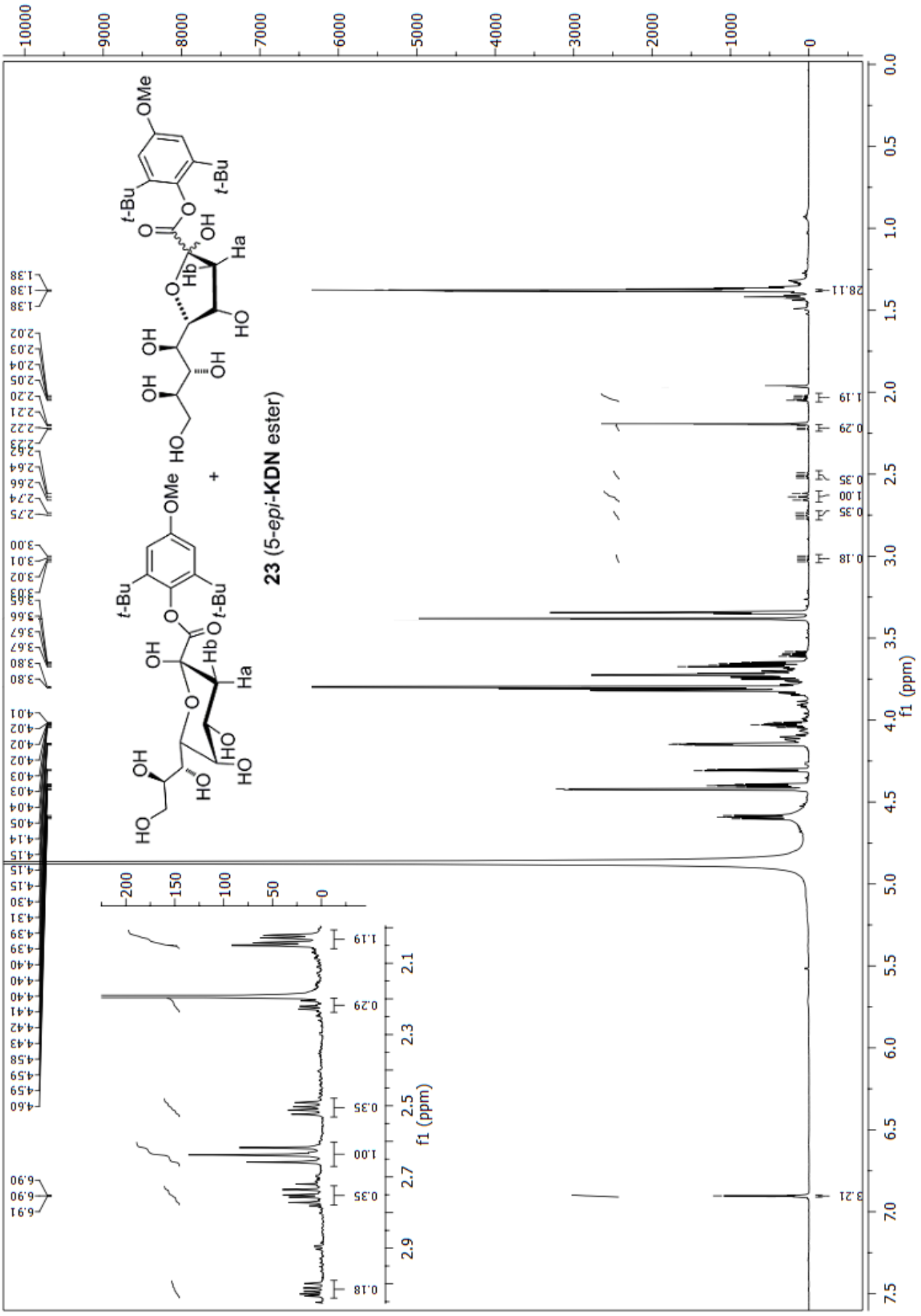

172.48
171.83
171.35
158.12
158.08
145.04
144.95
144.91
144.88
144.81
143.58
143.30
143.27
143.23
112.61
104.20
103.21
97.16
87.91
87.51
80.78
74.12
72.97
72.74
72.21
71.91
71.83
69.46
66.92
65.10
55.80
49.85
36.63
36.59
36.57
36.54
31.98
31.95
31.89
31.79
31.73
t-Bu
HO
OH
OH
OH
HO
HO
O
Hb
O
t-Bu
OMe
Ha
+
t-Bu
OMe
OH
OH
HO
O
OH
Hb
O
OH
OH
t-Bu
Ha
22 (4-epi-KDN ester)
24000
22000
20000
18000
16000
14000
12000
10000
8000
6000
4000
2000
0
-2000
170
160
150
140
130
120
110
100
90
80
70
60
50
40
30
20
10
0
f1 (ppm)

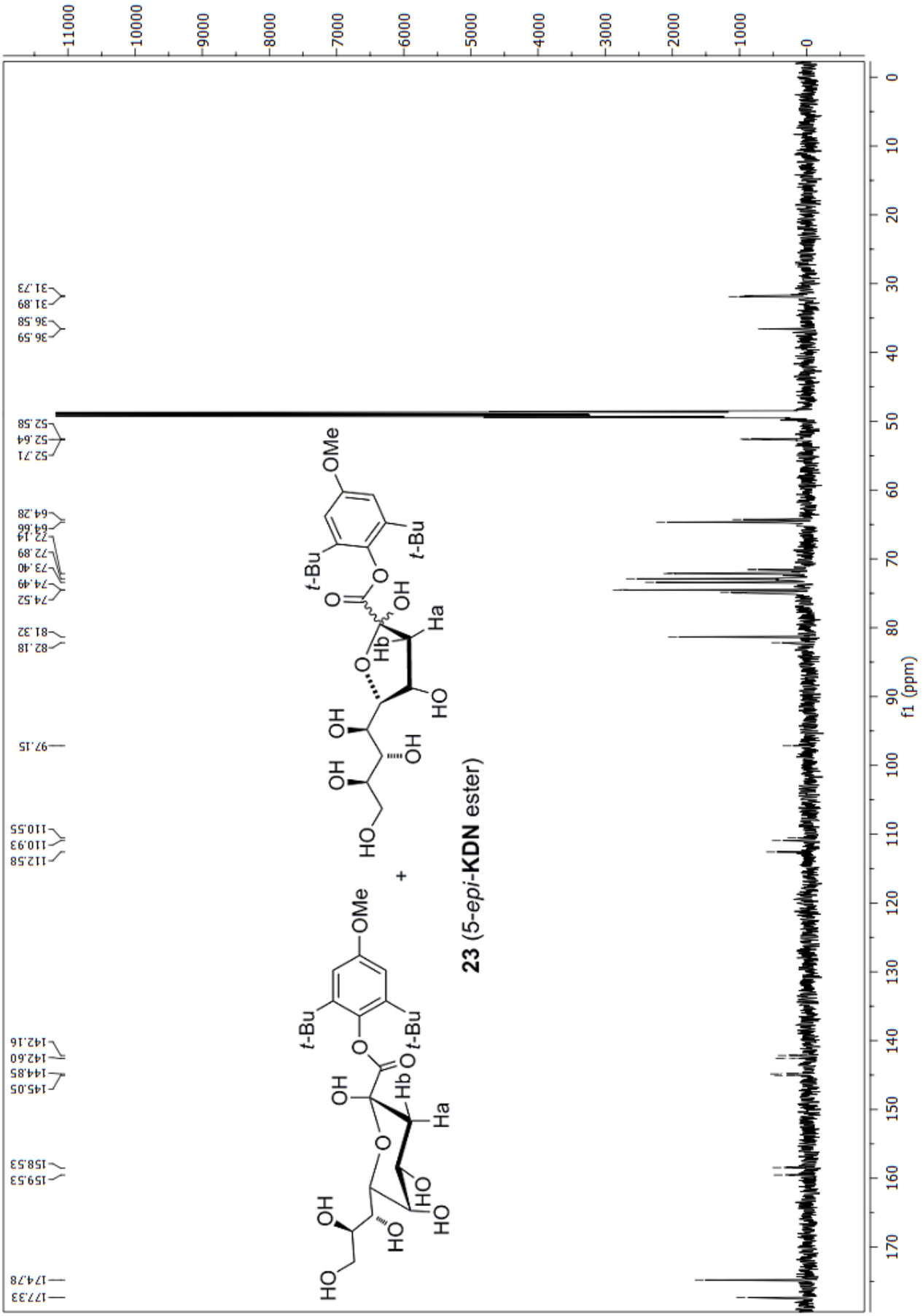
3-deoxy-D-*glycero*-D-*gulo*-non-2-ulosonic acid 2,6-di-*t*-butyl-4-metoxyphenyl ester (23, 5-*epi*-KDN, Scheme 1)

Table 5. The assignment of the C-3 protons for the different cyclic forms, ^{1}H NMR (600 MHz, CD_3OD)

	δ_{3a}	δ_{3b}	$J_{3a,3b}$	$J_{3a,4}$	$J_{3b,4}$	%
***α*-pyranose**	2.64	2.04	12.3	12.2	4.2	65
***β*-furanose**	2.75	2.51	12.6	9.0	7.1	23
***α*-furanose**	3.02	2.22	13.6	7.7	4.5	12

The NMR of *α*-pyranose form is similar to this published for peracetylated derivative of 5-*epi*-KDN, see Augé C., Bouxom B., Cavayé B., Gautheron C., *Tetrahedron Letters* **1989**, *30*, 2217-2220.


23 (5-epi-KDN ester)
f1 (ppm)


23 (5-epi-KDN ester)
f1 (ppm)