Supporting Information

for

Novel FR-900493 Analogs that Inhibit Outgrowth of Clostridium difficile Spores

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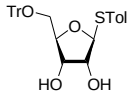
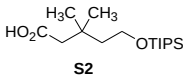
General

All chemicals were purchased from commercial sources and used without further purification unless otherwise noted. THF, CH_2Cl_2, and DMF were purified via Innovative Technology's Pure-Solve System. All reactions were performed under an Argon atmosphere. All stirring was performed with an internal magnetic stirrer. Reactions were monitored by TLC using 0.25 mm coated commercial silica gel plates (EMD, Silica Gel $60F_{254}$). TLC spots were visualized by UV light at 254 nm, or developed with ceric ammonium molybdate or anisaldehyde or copper sulfate or ninhydrin solutions by heating on a hot plate. Reactions were also monitored by using SHIMADZU LCMS-2020 with solvents: A: 0.1% formic acid in water, B: acetonitrile. Flash chromatography was performed with SiliCycle silica gel (Purasil 60 Å, 230-400 Mesh). Proton magnetic resonance (^{1}H-NMR) spectral data were recorded on 400, and 500 MHz instruments. Carbon magnetic resonance (^{13}C-NMR) spectral data were recorded on 100 and 125 MHz instruments. For all NMR spectra, chemical shifts (δH, δC) were quoted in parts per million (ppm), and *J* values were quoted in Hz. ^{1}H and ^{13}C NMR spectra were calibrated with residual undeuterated solvent ($CDCl_3$: δH = 7.26 ppm, δC = 77.16 ppm; CD_3CN: δH = 1.94 ppm, δC = 1.32ppm; CD_3OD: δH =3.31 ppm, δC =49.00 ppm; DMSO-d_6: δH = 2.50 ppm, δC = 39.52 ppm; D_2O: δH = 4.79 ppm) as an internal reference. The following abbreviations were used to designate the multiplicities: s = singlet, d = doublet, dd = double doublets, t = triplet, q = quartet, quin = quintet, hept = heptet, m = multiplet, br = broad. Infrared (IR) spectra were recorded on a Perkin-Elmer FT1600 spectrometer. HPLC analyses were performed with a Shimadzu LC-20AD HPLC system. HR-MS data were obtained from a Waters Synapt G2-Si (ion mobility mass spectrometer with nanoelectrospray ionization).



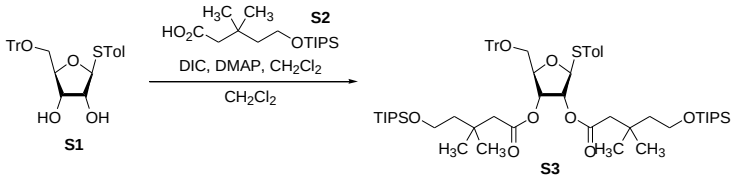
S1

(2*S*,5*R*)-2-(*p*-Tolylthio)-5-((trityloxy)methyl)tetrahydrofuran-3,4-diol (**S1**)**.** The title compound was synthesized according to the reported procedure [1]: TLC (hexanes/EtOAc 50:50) R_f = 0.50; $[\alpha]^{21}_D$ -1.029 (*c* = 1.42, $CHCl_3$); IR (thin film) ν_{max} = 3395 (br), 3058, 3021, 2921, 2870, 1491, 1448, 1216, 1075, 1012, 745, 698 cm^{-1}; ^1H NMR (400 MHz, $CDCl_3$) δ 7.46 (d, *J* = 7.3 Hz, 6H), 7.41 (d, *J* = 7.9 Hz, 2H), 7.32 – 7.21 (m, 9H), 7.07 (d, *J* = 7.8 Hz, 2H), 5.22 (d, *J* = 4.9 Hz, 1H), 4.16 (q, *J* = 4.7 Hz, 1H), 4.08 (dq, *J* = 12.9, 4.7 Hz, 2H), 3.26 (qd, *J* = 10.0, 4.4 Hz, 2H), 2.59 (d, *J* = 4.7 Hz, 1H), 2.41 (d, *J* = 4.0 Hz, 1H), 2.31 (s, 3H); ^{13}C NMR (101 MHz, $CDCl_3$) δ 143.7 (2C), 137.8, 132.8 (3C), 129.7 (2C), 129.4, 128.7 (6C), 127.9 (6C), 127.1 (3C), 90.5, 87.0, 83.4, 75.3, 72.5, 64.2, 21.1; HRMS (ESI+) *m*/*z* calcd for $C_{31}H_{30}O_4NaS$ [M + Na] 521.1762, found: 521.1741.



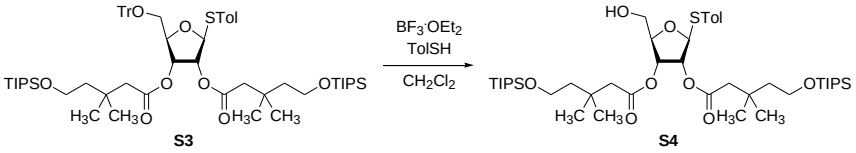
S2

3,3-Dimethyl-5-((triisopropylsilyl)oxy)pentanoic acid (**S2**)**.** The title compound was synthesized according to the reported procedure [1]: TLC (hexanes/EtOAc 50:50) R_f = 0.50; IR (thin film) ν_{max} = 2942, 2866, 1705, 1463, 1246, 1097, 996, 881, 738, 678 cm^{-1}; ^1H NMR (400 MHz, $CDCl_3$) δ 3.88 (t, *J* = 5.8 Hz, 2H), 2.38 (s, 2H), 1.71 (t, *J* = 5.8 Hz, 2H), 1.20 – 1.11 (m, 3H), 1.09 (s, 12H), 1.08 (s, 6H), 1.07 (s, 6H); ^{13}C NMR (101 MHz, $CDCl_3$) δ 173. 9, 60.7, 46.8, 42.6, 32.4, 28.5 (2C), 17.9 (6C), 11.8 (3C); HRMS (ESI+) *m*/*z* calcd for $C_{16}H_{34}O_3NaSi$ [M + Na] 325.2175, found 325.2171.

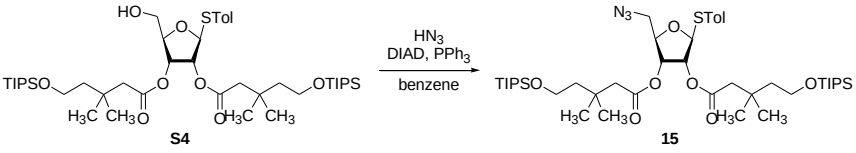


(2*S*,5*R*)-2-(*p*-Tolylthio)-5-((trityloxy)methyl)tetrahydrofuran-3,4-diyl bis(3,3-dimethyl-5-((triisopropylsilyl)oxy)pentanoate) (**S3**). To a stirred solution of **S1** (2.03 g, 4.07 mmol) and **S2** (2.71 g, 8.96 mmol) in CH_2Cl_2 (20 mL) were added DMAP (1.24 g, 10.18 mmol) and DIC (1.59 mL, 10.18 mmol) at 0 °C. The reaction mixture was stirred for 15 h at rt and concentrated in vacuo. The crude mixture was purified by silica gel column chromatography (hexanes/EtOAc 99:1 to 98:2) to afford **S3** (4.23 g, 3.96 mmol, 97%): TLC (hexanes/EtOAc 90:10) R_f = 0.60; $[\alpha]^{21}_D$ -0.693 (*c* = 2.70, $CHCl_3$); IR (thin film) ν_{max} = 2941, 2865, 1743, 1463, 1219, 1099, 1013, 999, 882, 745, 704, 681 cm^{-1}; ^1H NMR (400 MHz, $CDCl_3$) δ 7.47 (d, *J* = 7.2 Hz, 6H), 7.41 (d, *J* = 7.9 Hz, 2H), 7.29 (t, *J* = 7.5 Hz, 6H), 7.23 (q, *J* = 7.1 Hz, 3H), 7.06 (d, *J* = 7.8 Hz, 2H), 5.40 – 5.35 (m, 2H), 5.33 (d, *J* = 5.0 Hz, 1H), 4.18 (q, *J* = 4.1 Hz, 1H), 3.78 (t, *J* = 7.1 Hz, 2H), 3.73 (t, *J* = 6.9 Hz, 2H), 3.22 (dd, *J* = 10.3, 4.1 Hz, 1H), 3.13 (dd, *J* = 10.3, 4.6 Hz, 1H), 2.30 (s, 3H), 2.27 (d, *J* = 13.8 Hz, 2H), 2.22 (s, 2H), 1.65 (t, *J* = 6.9 Hz, 2H), 1.56 (t, *J* = 6.9 Hz, 2H), 1.12 – 1.01 (m, 48H), 0.97 (d, *J* = 5.5 Hz, 6H); ^{13}C NMR

(101 MHz, $CDCl_3$) δ 170.7, 170.5, 143.6 (2C), 138.0, 133.3 (2C), 129.7 (3C), 128.9, 128.8 (6C), 127.8 (6C), 127.0 (3C), 88.3, 86.9, 82.2, 73.6, 71.6, 63.6, 60.04, 59.98, 46.2, 46.1, 44.74, 44.71, 32.7, 32.5, 27.51, 27.48, 27.4, 22.7, 21.1, 18.07 (6C), 18.05 (6C), 11.94 (3C), 11.91 (3C); HRMS (ESI+) *m*/*z* calcd for $C_{63}H_{94}NaO_8SSi_2$ [M + Na] 1089.6106, found: 1089.6098.

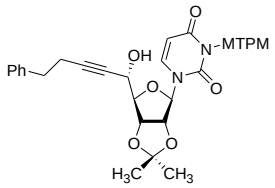


(2*R*,5*S*)-2-(Hydroxymethyl)-5-(p-tolylthio)tetrahydrofuran-3,4-diyl bis(3,3-dimethyl-5-((triisopropylsilyl)oxy)pentanoate) (S4). To a stirred solution of **S3** (4.23 g, 3.96 mmol) and thiocresol (0.98 g, 7.92 mmol) in CH_2Cl_2 (20 mL) was added $BF_3{\cdot}OEt_2$ (0.20 mL, 1.58 mmol) at 0 °C. After being stirred for 1.5 h, the reaction was quenched with aq. saturated $NaHCO_3$ and extracted with EtOAc. The combined organic solution was dried over Na_2SO_4 and concentrated in vacuo. The crude mixture was purified by silica gel column chromatography (hexanes/EtOAc 90:10 to 80:20) to afford **S4** (1.81 g, 2.19 mmol, 55%): TLC (hexanes/EtOAc 90:10) R_f = 0.20; $[\alpha]^{21}_D$ -1.733 (*c* = 3.98, $CHCl_3$); IR (thin film) ν_{max} = 3474 (br), 2941, 2891, 2866, 2724, 1743, 1493, 1464, 1389, 1367, 1326, 1250, 1219, 1190, 1099, 1070, 1054, 1013, 999, 882, 809, 772, 741, 681 cm^{-1}; ^1H NMR (400 MHz, $CDCl_3$) δ 7.42 (d, *J* = 7.8 Hz, 2H), 7.15 (d, *J* = 7.8 Hz, 2H), 5.26 (d, *J* = 5.4 Hz, 1H), 5.23 (t, *J* = 4.8 Hz, 1H), 5.19 (t, *J* = 5.3 Hz, 1H), 4.11 (q, *J* = 3.7 Hz, 1H), 3.81 – 3.73 (m, 4H), 3.72 (d, *J* = 3.2 Hz, 1H), 3.59 (dd, *J* = 12.4, 3.6 Hz, 1H), 2.34 (s, 3H), 2.31 (d, *J* = 8.7 Hz, 2H), 2.27 (d, *J* = 5.5 Hz, 2H), 1.63 (t, *J* = 7.5 Hz, 2H), 1.59 (t, *J* = 6.9 Hz, 2H), 1.05 (q, *J* = 4.8, 3.7 Hz, 54H); ^{13}C NMR (101 MHz, $CDCl_3$) δ 171.11, 170.51, 138.81, 133.89 (2C), 129.89 (2C), 127.66, 88.06, 83.80, 73.71, 71.26, 62.16, 60.02, 59.99, 46.18, 46.11, 44.65, 44.56, 32.67, 32.61, 27.52, 27.48, 27.42, 21.16, 18.05 (6C), 18.04 (6C), 11.92 (3C), 11.91 (3C); HRMS (ESI+) *m*/*z* calcd for $C_{44}H_{80}NaO_8SSi_2$ [M + Na] 847.5010, found: 847.5023.



(2*R*,5*S*)-2-(Azidomethyl)-5-(p-tolylthio)tetrahydrofuran-3,4-diyl bis(3,3-dimethyl-5-((triisopropylsilyl)oxy)pentanoate) (15). To a stirred solution of **S4** (1.81 g, 2.19 mmol) and PPh_3 (1.15 g, 4.38 mmol) in dry benzene (5 mL) were added HN_3 (0.6 M in benzene, 36.5 mL, 21.9 mmol) and DIAD (0.86 mL, 4.38 mmol). The reaction mixture was stirred for 24 h at rt and concentrated in vacuo. The crude mixture was purified by silica gel column chromatography (hexanes/EtOAc 95:5) to afford **15** (1.71 g, 2.01 mmol, 92%): TLC (hexanes/EtOAc 90:10) R_f = 0.60; $[\alpha]^{21}_D$ -0.293 (*c* = 1.39, $CHCl_3$); IR (thin film) ν_{max} = 2792, 2892, 2866, 2102, 1745, 1464, 1390, 1367, 1282, 1254, 1219, 1190, 1100, 1071, 1054, 1013, 998, 882, 809, 772, 742, 681 cm^{-1}; ^1H NMR (400 MHz, $CDCl_3$) δ 7.43 (d, *J* = 8.1 Hz, 2H), 7.14 (d, *J* = 7.9 Hz, 2H), 5.26 (d, *J* = 5.3 Hz, 1H), 5.18 (t, *J* = 5.3 Hz, 1H), 5.11 (t, *J* = 5.0 Hz, 1H), 4.13 (q, *J* = 4.7 Hz, 1H), 3.76 (dt, *J* = 10.6, 6.9 Hz, 4H), 3.42 (d, *J* = 4.7 Hz, 2H), 2.34 (s,

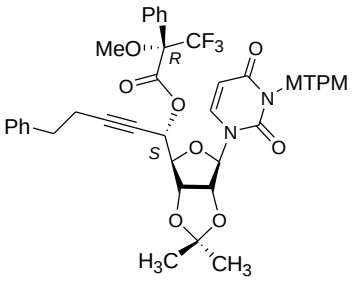
3H), 2.31 (d, *J* = 10.6 Hz, 2H), 2.26 (d, *J* = 4.9 Hz, 2H), 1.61 (dtd, *J* = 17.4, 6.9, 2.1 Hz, 4H), 1.08 – 1.00 (m, 54H); ^{13}C NMR (101 MHz, $CDCl_3$) δ 170.91, 170.54, 138.67, 133.89 (2C), 129.81 (2C), 127.88, 88.58, 81.48, 73.52, 71.70, 60.02, 59.97, 52.70, 46.15, 46.03, 44.64, 44.55, 32.68, 32.60, 27.51, 27.47, 27.38, 21.17, 18.06 (6C), 18.05 (6C), 11.93 (3C), 11.92 (3C); HRMS (ESI+) *m*/*z* calcd for $C_{44}H_{79}N_3NaO_7SSi_2$ [M + Na] 872.5075, found: 872.5088.



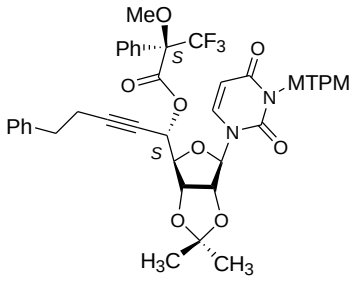
14

3-(((2,6-Dichloro-4-methoxyphenyl)(2,4-dichlorophenyl)methoxy)methyl)-1-((3a*R*,4*R*,6*R*,6a*R*)-6-((*S*)-1-hydroxy-5-phenylpent-2-yn-1-yl)-2,2-dimethyltetrahydrofuro[3,4-*d*][1,3]dioxol-4-yl)pyrimidine-2,4(1*H*,3*H*)-dione (14). Title compound was synthesized according to the reported procedure [1]: TLC (hexanes/EtOAc 50:50) R_f = 0.30; $[\alpha]^{22}_D$ -0.116 (*c* = 2.17, $CHCl_3$); IR (thin film) ν_{max} = 3387 (br), 2981, 2937, 1664, 1454, 1276, 1065, 1039, 856, 733, 698 cm^{-1}; ^{1}H NMR (400 MHz, $CDCl_3$) δ 7.53 (ddd, *J* = 20.4, 8.5, 0.7 Hz, 1H), 7.35 – 7.27 (m, 4H), 7.24 – 7.15 (m, 4H), 6.85 (d, *J* = 5.1 Hz, 2H), 6.51 (d, *J* = 5.4 Hz, 1H), 5.68 (dd, *J* = 8.1, 4.1 Hz, 1H), 5.60 – 5.50 (m, 3H), 4.89 – 4.78 (m, 2H), 4.57 (ddt, *J* = 12.0, 4.3, 2.0 Hz, 1H), 4.24 (dd, *J* = 4.4, 3.1 Hz, 1H), 3.78 (d, *J* = 3.3 Hz, 3H), 2.83 (t, *J* = 7.5 Hz, 2H), 2.53 (td, *J* = 7.4, 2.0 Hz, 2H), 1.57 (s, 3H), 1.36 (s, 3H); ^{13}C NMR (101 MHz, $CDCl_3$) δ 162.11, 162.08, 159.5, 150.87, 150.85, 141.1, 140.8, 140.30, 140.27, 136.9, 135.4, 135.3, 133.99, 133.95, 133.8, 133.6, 131.2, 129.4, 129.3, 128.41, 128.39, 126.4, 126.21, 126.18, 125.5, 125.4, 115.34, 115.32, 114.3, 114.2, 101.8, 101.7, 96.7, 96.4, 89.23, 89.19, 86.8, 86.7, 84.1, 84.0, 80.9, 69.5, 63.02, 62.99, 55.7, 34.72, 34.70, 27.2, 25.3, 20.87, 20.85; HRMS (ESI+) *m*/*z* calcd for $C_{37}H_{34}N_2O_8NaCl_4$ [M + Na] 797.0967, found: 797.0994.

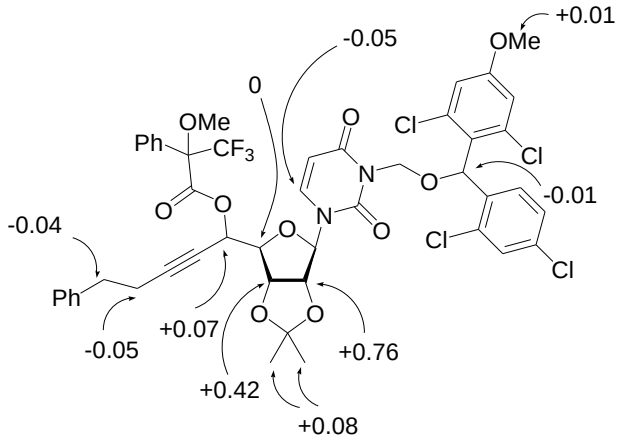
Figure S1. Determination of the stereochemistry of **14**[2] via the advanced Mosher method.[3]



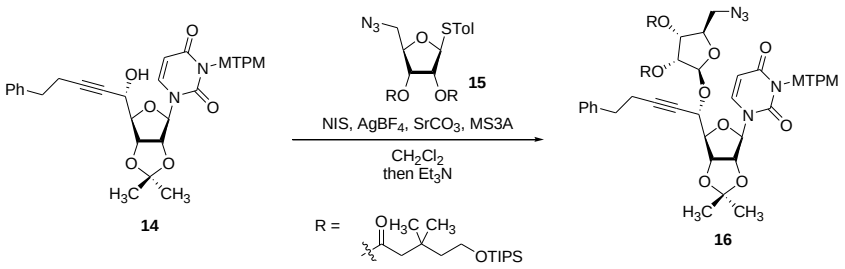
(*S*)-**14**-(*R*)-Mosher ester



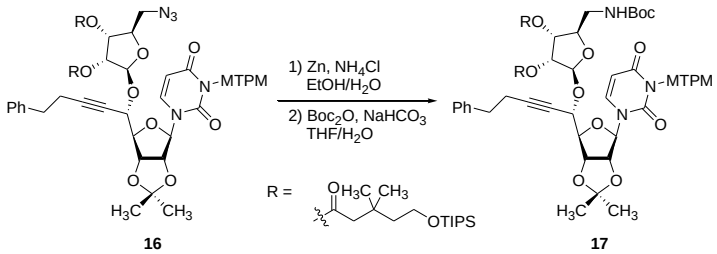
(*S*)-**14**-(*S*)-Mosher ester



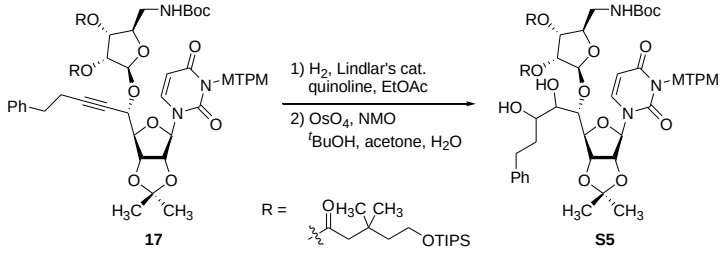
Δδ *S-R*



(2*R*,3*R*,4*R*,5*R*)-2-(Azidomethyl)-5-(((1*S*)-1-((3a*R*,4*R*,6*R*,6a*R*)-6-(3-(((2,6-dichloro-4-methoxyphenyl)(2,4-dichlorophenyl)methoxy)methyl)-2,4-dioxo-3,4-dihydropyrimidin-1(2*H*)-yl)-2,2-dimethyltetrahydrofuro[3,4-*d*][1,3]dioxol-4-yl)-5-phenylpent-2-yn-1-yl)oxy)tetrahydrofuran-3,4-diyl bis(3,3-dimethyl-5-((triisopropylsilyl)oxy)pentanoate) (16). To a stirred suspension of **14** (227 mg, 0.292 mmol), **15** (497 mg, 0.584 mmol), MS3A (900 mg) and $SrCO_3$ (431 mg, 2.920 mmol) in CH_2Cl_2 (12.0 mL) were added $AgBF_4$ (28.5 mg, 0.146 mmol) and NIS (131 mg, 0.584 mmol) at 0 ^oC. After 24 h, the reaction mixture was added Et_3N (2 mL) and passed through a silica gel pad (hexanes/EtOAc 1:1). The combined organic phase was concentrated in vacuo. The crude mixture was purified by silica gel column chromatography (hexanes/EtOAc 90:10 to 80:20 to 70:30) to afford **16** (416 mg, 0.277 mmol, 95%): TLC (hexanes/EtOAc 67:33) R_f = 0.70; $[\alpha]^{21}_D$ +0.100 (*c* = 2.09, $CHCl_3$); IR (thin film) ν_{max} = 2942, 2866, 2102, 1743, 1724, 1675, 1456, 1278, 1218, 1099, 1070, 882, 772 cm^{-1}; ^1H NMR (400 MHz, $CDCl_3$) δ 7.54 (dd, *J* = 23.1, 8.5 Hz, 1H), 7.32 – 7.27 (m, 4H), 7.24 – 7.16 (m, 4H), 6.84 (d, *J* = 7.3 Hz, 2H), 6.51 (d, *J* = 3.7 Hz, 1H), 5.71 – 5.64 (m, 2H), 5.60 – 5.49 (m, 2H), 5.20 – 5.16 (m, 3H), 4.79 (ddd, *J* = 7.5, 6.5, 3.1 Hz, 1H), 4.64 (td, *J* = 5.9, 2.6 Hz, 1H), 4.57 (ddt, *J* = 11.4, 6.3, 1.9 Hz, 1H), 4.28 (dt, *J* = 6.2, 2.8 Hz, 1H), 4.19 (tt, *J* = 6.1, 3.0 Hz, 1H), 3.79 – 3.72 (m, 7H), 3.50 (ddd, *J* = 13.0, 7.6, 3.3 Hz, 1H), 3.35 (dd, *J* = 13.0, 3.4 Hz, 1H), 2.83 (t, *J* = 7.4 Hz, 2H), 2.55 (td, *J* = 7.4, 1.8 Hz, 2H), 2.29 (t, *J* = 1.6 Hz, 2H), 2.24 (dd, *J* = 5.1, 2.1 Hz, 2H), 1.62 – 1.55 (m, 7H), 1.36 (d, *J* = 2.0 Hz, 3H), 1.08 – 1.00 (m, 54H); ^{13}C NMR (101 MHz, $CDCl_3$) δ 175.6, 171.0, 170.9, 170.71, 170.70, 170.6, 162.2, 162.1, 159.5, 150.8, 150.7, 140.4, 140.19, 140.15, 140.13, 136.92, 136.91, 135.4, 135.3, 133.9, 133.8, 133.7, 131.2, 129.4, 129.3, 128.5 (2C), 128.4 (2C), 126.5, 126.4, 126.2, 126.1, 125.6, 125.5, 115.29, 115.25, 114.23, 114.22, 104.61, 104.55, 101.83, 101.82, 88.8, 88.2, 84.44, 84.35, 83.9, 81.4, 81.3, 80.6, 79.9, 76.5, 75.9, 75.8, 74.1, 71.8, 71.7, 71.4, 70.7, 69.6, 69.5, 68.9, 68.8, 59.97, 59.96, 55.7, 46.2, 46.0, 44.7, 44.6, 34.7, 34.51, 34.49, 32.7, 32.61, 32.57, 28.0, 27.38, 27.35, 27.3, 27.1, 25.34, 25.27, 20.9, 18.1 (12C), 11.9 (6C); HRMS (ESI+) *m*/*z* calcd for $C_{74}H_{106}Cl_4N_5O_{15}Si_2$ [M + H] 1500.5978, found: 1500.5992.

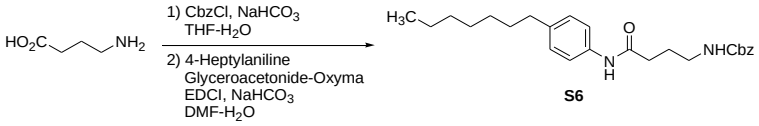


(2*R*,3*R*,4*R*,5*R*)-2-(((*tert*-Butoxycarbonyl)amino)methyl)-5-(((1*S*)-1-((3a*R*,4*R*,6*R*,6a*R*)-6-(3-(((2,6-dichloro-4-methoxyphenyl)(2,4-dichlorophenyl)methoxy)methyl)-2,4-dioxo-3,4-dihydropyrimidin-1(2*H*)-yl)-2,2-dimethyltetrahydrofuro[3,4-*d*][1,3]dioxol-4-yl)-5-phenylpent-2-yn-1-yl)oxy)tetrahydrofuran-3,4-diyl bis(3,3-dimethyl-5-((triisopropylsilyl)oxy)pentanoate) (17). A suspended solution of **16** (286 mg, 0.19 mmol), NH_4Cl (305 mg, 5.70 mmol) and Zn (373 mg, 5.70 mmol) in EtOH/H_2O (9:1, 9.5 mL) was stirred at 80 ^oC for 12 h and cooled to rt. The precipitates were filtered and the combined organic solution was concentrated in vacuo. The crude mixture was used for the next reaction without purification. To a stirred solution of crude mixture in THF (9.5 mL) were added saturated $NaHCO_3$ (aq., 9.5 mL) and Boc_2O (124 mg, 0.57 mmol). The reaction mixture was stirred for 6 h at rt, and the aqueous layer was extracted with EtOAc. The combined organic extracts were dried over Na_2SO_4 and concentrated in vacuo. The crude mixture was purified by silica gel column chromatography (hexanes/EtOAc 85:15 to 80:20 to 67:33) to afford **17** (258 mg, 0.16 mmol, 86% for 2 steps): TLC (hexanes/EtOAc 70:30) R_f = 0.30; $[\alpha]^{21}_D$ +0.012 (*c* = 0.90, $CHCl_3$); IR (thin film) ν_{max} = 2941, 2866, 1720, 1676, 1456, 1366, 1278, 1219, 1100, 1070, 882, 772 cm^{-1}; ^1H NMR (400 MHz, $CDCl_3$) δ 7.54 (dd, *J* = 19.9, 8.5 Hz, 1H), 7.33 – 7.27 (m, 4H), 7.24 – 7.16 (m, 4H), 6.85 (d, *J* = 7.3 Hz, 2H), 6.51 (d, *J* = 4.8 Hz, 1H), 5.72 – 5.64 (m, 2H), 5.60 – 5.48 (m, 2H), 5.26 (d, *J* = 6.0 Hz, 1H), 5.17 (d, *J* = 8.6 Hz, 2H), 5.13 – 5.08 (m, 1H), 4.82 – 4.76 (m, 1H), 4.65 (t, *J* = 7.0 Hz, 1H), 4.51 (dd, *J* = 13.8, 6.0 Hz, 1H), 4.31 – 4.26 (m, 1H), 4.23 – 4.17 (m, 1H), 3.78 (d, *J* = 2.7 Hz, 3H), 3.74 (d, *J* = 6.9 Hz, 4H), 3.48 – 3.40 (m, 1H), 3.36 – 3.26 (m, 1H), 2.83 (t, *J* = 7.4 Hz, 2H), 2.56 (t, *J* = 7.5 Hz, 2H), 2.27 (t, *J* = 2.6 Hz, 2H), 2.23 (t, *J* = 3.0 Hz, 2H), 1.62 – 1.55 (m, 7H), 1.42 (s, 9H), 1.37 (d, *J* = 2.6 Hz, 3H), 1.11 – 0.99 (m, 54H); ^{13}C NMR (101 MHz, $CDCl_3$) δ 159.5, 150.8, 136.9, 131.3, 129.3, 128.5 (2C), 128.4 (2C), 126.5, 126.1, 125.4, 115.30, 115.26, 80.0, 60.0, 55.7, 46.4, 46.2, 46.0, 44.83, 44.78, 42.5, 34.51, 34.49, 32.60, 32.55, 31.9, 29.7, 28.7, 28.4, 28.3, 27.4, 27.33, 27.29, 27.26, 27.09, 27.05, 25.4, 22.7, 22.6, 20.9, 18.1 (6C), 17.9 (6C), 14.1, 11.9 (3C), 11.8 (3C); HRMS (ESI+) *m*/*z* calcd for $C_{79}H_{116}Cl_4N_3O_{17}Si_2$ [M + H] 1574.6597, found: 1574.6609.

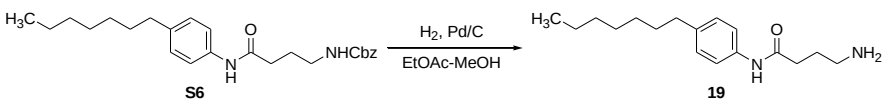


(2*R*,3*R*,4*R*,5*S*)-2-(((*tert*-Butoxycarbonyl)amino)methyl)-5-(((1*S*)-1-((3a*R*,4*R*,6*R*,6a*R*)-6-(3-(((2,6-dichloro-4-methoxyphenyl)(2,4-dichlorophenyl)methoxy)methyl)-2,4-dioxo-3,4-dihydropyrimidin-1(2*H*)-yl)-2,2-dimethyltetrahydrofuro[3,4-*d*][1,3]dioxol-4-yl)-2,3-dihydroxy-5-phenylpentyl)oxy)tetrahydrofuran-3,4-diyl bis(3,3-dimethyl-5-((triisopropylsilyl)oxy)pentanoate) (S5). To a stirred solution of **17** (258 mg, 0.16 mmol) and quinoline (38.7 μL, 0.33 mmol) in EtOAc (50 mL) and MeOH (50 mL) was added Lindlar catalyst (300 mg). H_2 gas was introduced and the reaction mixture was stirred under H_2 atmosphere (600 psi) at rt. After being stirred for 7 h, the reaction mixture was added Lindlar catalyst (150 mg). The reaction mixture was stirred for 11 h under H_2 atmosphere (600 psi) at rt. The solution was filtered through Celite and washed

with 1N HCl (aq.). The combined organic solution was dried over Na_2SO_4, concentrated in vacuo. The crude mixture was used for the next reaction without purification. To a stirred solution of the crude mixture and NMO (192 mg, 1.64 mmol) in t-BuOH/acetone (1:1, 2.1 mL) was added OsO_4 (4% in water, 1.04 mL, 0.16 mmol) at rt. After being stirred for 2 h at 40 ^oC, the reaction mixture was added NMO (192 mg, 1.64 mmol) and OsO_4 (4% in water, 1.04 mL, 0.16 mmol). After being stirred for 2 h at 40 ^oC, the reaction solution was diluted with EtOAc and quenched with saturated $NaHCO_3$ aq./ saturated Na_2SO_3 aq. (2:1). The heterogeneous mixture was stirred for 30 min, extracted with EtOAc. The combined organic extracts were dried over Na_2SO_4 and concentrated in vacuo. The crude mixture was passed through a silica gel pad (hexanes/EtOAc 33:67) to afford **S5** as diastereomeric mixture. This mixture was used for next reaction without further purification.

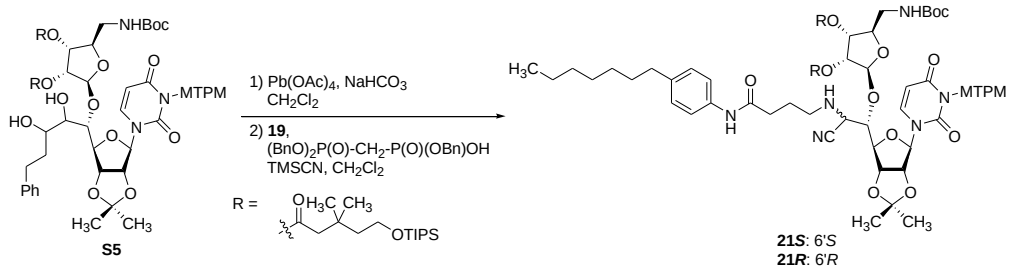


Benzyl (4-((4-heptylphenyl)amino)-4-oxobutyl)carbamate (S6). To a stirred solution of 4-aminobutyric acid (103 mg, 1 mmol) and $NaHCO_3$ (252 mg, 3 mmol) in THF-H_2O (1:1, 10 mL) was added CbzCl (214 μL, 1.5 mmol). After being stirred for 16 h at rt, the reaction mixture was quenched with 1N HCl (aq.) and extracted with $CHCl_3$. The combined organic solution was dried over Na_2SO_4 and concentrated in vacuo. To a stirred solution of the crude mixture, 4-heptylaniline (315 μL, 1.5 mmol), $NaHCO_3$ (840 mg, 10 mmol) and Glyceroacetonide-Oxyma (456 mg, 2 mmol) in DMF-H_2O (9:1, 5 mL), was added EDCI (959 mg, 5 mmol). After being stirred for 9 h at rt, the reaction mixture was quenched with H_2O and extracted with EtOAc. The combined organic solution was washed with 1N HCl (aq.), saturated $NaHCO_3$ (aq.), dried over Na_2SO_4 and concentrated in vacuo. The crude mixture was purified by silica gel column chromatography (hexanes/EtOAc 67:33 to 60:40) to afford **S6** (284 mg, 0.69 mmol, 69% for 2 steps) [4]: TLC (hexanes/EtOAc 50:50) R_f = 0.40; ^{1}H NMR (400 MHz, $CDCl_3$) δ 8.22 (d, *J* = 19.6 Hz, 1H), 7.46 (d, *J* = 8.0 Hz, 2H), 7.36 – 7.30 (m, 5H), 7.11 (d, *J* = 8.4 Hz, 2H), 5.15 – 5.04 (m, 1H), 5.09 (s, 2H), 3.30 (q, *J* = 6.1 Hz, 2H), 2.55 (t, *J* = 7.6 Hz, 2H), 2.36 (t, *J* = 7.3 Hz, 2H), 1.90 (q, *J* = 6.2, 5.7 Hz, 2H), 1.57 (quin, *J* = 7.1 Hz, 2H), 1.33 – 1.21 (m, 8H), 0.88 (t, *J* = 6.6 Hz, 3H); ^{13}C NMR (101 MHz, $CDCl_3$) δ 171.1, 157.4, 139.0, 136.3, 135.6, 128.8 (2C), 128.5 (2C), 128.2, 128.1, 119.9, 66.9, 63.2, 35.4, 34.6, 31.8, 31.5, 29.19, 29.16, 26.7, 22.7, 14.1, 14.0; HRMS (ESI+) *m*/*z* calcd for $C_{25}H_{34}N_2NaO_3$ [M + Na] 433.2467, found: 433.2481.



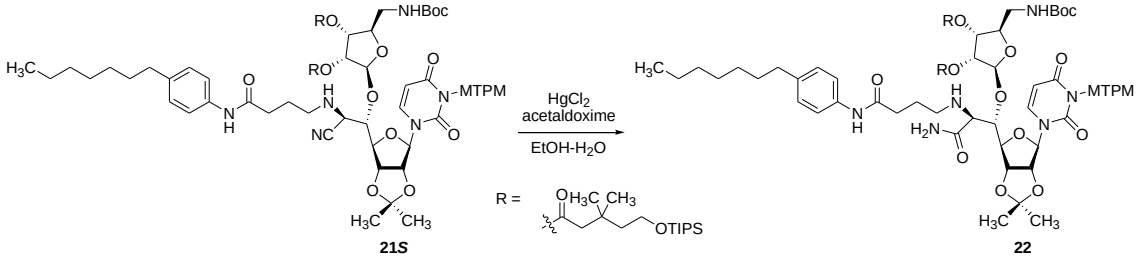
4-Amino-*N*-(4-heptylphenyl)butanamide (19). To a stirred solution of **S6** (28.1 mg, 0.069 mmol) in EtOAc-MeOH (1:1, 10 mL) was added Pd/C (10 wt % 6 mg). H_2 gas was introduced and the reaction mixture was stirred for 2 h under H_2. The solution was

filtered through Celite and concentrated in vacuo. The crude mixture of **19** was used for next reaction without purification.

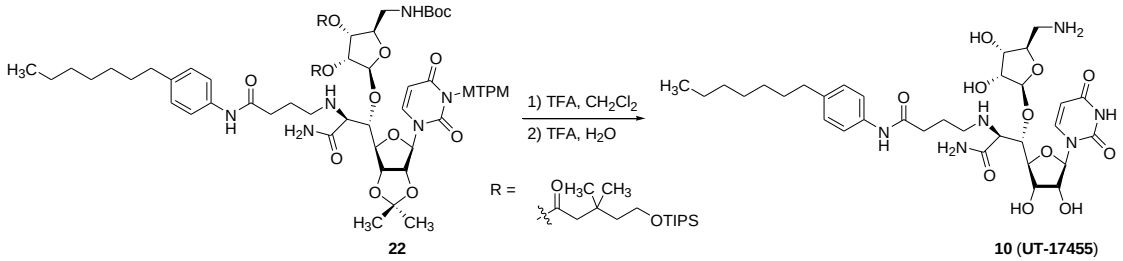


(2*R*,3*R*,4*R*,5*S*)-2-(((*tert*-Butoxycarbonyl)amino)methyl)-5-((1*S*,2*R*)-2-cyano-1-((3a*R*,4*R*,6*R*,6a*R*)-6-(3-(((2,6-dichloro-4-methoxyphenyl)(2,4-dichlorophenyl)methoxy)methyl)-2,4-dioxo-3,4-dihydropyrimidin-1(2*H*)-yl)-2,2-dimethyltetrahydrofuro[3,4-*d*][1,3]dioxol-4-yl)-2-((4-((4-heptylphenyl)amino)-4-oxobutyl)amino)ethoxy)tetrahydrofuran-3,4-diyl bis(3,3-dimethyl-5-((triisopropylsilyl)oxy)pentanoate) (21*S*). To a stirred solution of **S5** (22.1 mg, 0.014 mmol) and $NaHCO_3$ (11.5 mg, 0.14 mmol) in CH_2Cl_2 (0.7 mL) was added $Pb(OAc)_4$ (12.1 mg, 0.027 mmfol) at 0 ^oC. The reaction mixture was stirred for 2 h at 0 ^oC and quenched with saturated $NaHCO_3$ aq., extracted with EtOAc. The combined organic extracts were dried over Na_2SO_4 and concentrated in vacuo. The crude mixture of aldehyde **18** was used for the next reaction without purification. To a stirred solution of $(BnO)_2P(O)$-CH_2-P(O)(OBn)OH (30.6 mg, 0.069 mmol) in CH_2Cl_2 (0.4 mL) was added a CH_2Cl_2 (0.3 mL) solution of the mixture of **18**, **19** was added to the solution. After 9 h, the reaction was added TMSCN (17.1 μL, 0.14 mmol) and stirred for 9 h at rt. After completion, the reaction mixture was quenched with saturated $NaHCO_3$ aq., extracted with EtOAc. The combined organic extracts were dried over Na_2SO_4 and concentrated in vacuo. The crude product was purified by silica gel column chromatography (hexanes/EtOAc 80:20 to 60:40) to afford **21*S*** (16.7 mg, 9.49 μmol, 69% for 2 steps) and **21*R*** (4.1 mg, 2.34 μmol, 17% for 2 steps): TLC (hexanes/EtOAc 60:40) R_f = 0.40; $[\alpha]^{21}_D$ +0.075 (*c* = 0.73, $CHCl_3$); IR (thin film) ν_{max} = 3317 (br), 2930, 2865, 1719, 1675, 1600, 1462, 1102, 1071, 882, 772, 683 cm^{-1}; ^1H NMR (400 MHz, $CDCl_3$) δ 7.68 (s, 1H), 7.49 (dd, *J* = 11.4, 8.8 Hz, 1H), 7.39 (d, *J* = 7.9 Hz, 2H), 7.32 (s, 1H), 7.19 (d, *J* = 8.5 Hz, 2H), 7.11 (d, *J* = 8.0 Hz, 2H), 6.86 (d, *J* = 9.3 Hz, 2H), 6.50 (d, *J* = 15.4 Hz, 1H), 5.73 (dd, *J* = 23.0, 8.0 Hz, 1H), 5.59 (d, *J* = 5.9 Hz, 1H), 5.54 (d, *J* = 9.4 Hz, 2H), 5.42 (t, *J* = 10.1 Hz, 1H), 5.25 (s, 1H), 5.08 – 5.00 (m, 2H), 4.96 – 4.82 (m, 2H), 4.50 – 4.45 (m, 1H), 4.25 – 4.19 (m, 1H), 4.15 – 4.06 (m, 1H), 3.94 – 3.83 (m, 1H), 3.80 – 3.63 (m, 10H), 3.49 – 3.41 (m, 1H), 3.39 – 3.31 (m, 1H), 3.03 (dt, *J* = 12.0, 6.1 Hz, 1H), 2.71 – 2.61 (m, 1H), 2.54 (t, *J* = 7.3 Hz, 2H), 2.51 – 2.45 (m, 1H), 2.29 – 2.17 (m, 4H), 1.67 – 1.51 (m, 10H), 1.41 (s, 9H), 1.28 (dd, *J* = 15.7, 8.1 Hz, 10H), 1.05 (s, 42H), 1.01 (s, 6H), 0.95 (s, 6H), 0.87 (t, *J* = 6.4 Hz, 3H); ^{13}C NMR (101 MHz, $CDCl_3$) δ 170.9, 159.5, 136.9, 136.8, 131.3, 131.2, 129.42, 129.36, 128.84 (2C), 128.82 (2C), 128.80 (2C), 126.4, 126.2, 125.1, 120.09, 120.05, 115.4, 115.31, 115.30, 114.84, 114.81, 84.90, 84.87, 80.84, 80.78, 80.2, 79.8, 79.4, 78.2, 76.1, 74.3, 60.0, 59.9, 55.8, 55.7, 52.0, 46.2, 46.0, 44.83, 44.77, 35.4, 32.56, 32.55, 31.8, 31.5, 29.7, 29.19, 29.16, 28.4, 28.3, 27.3, 27.2, 22.7, 18.1 (12C), 14.1, 11.9 (6C); HRMS (ESI+) *m*/*z* calcd for $C_{88}H_{135}Cl_4N_6O_{18}Si_2$ [M + H] 1759.8126, found: 1759.8135. Data for **(2*R*,3*R*,4*R*,5*S*)-2-(((*tert*-butoxycarbonyl)amino)methyl)-5-((1*S*,2*S*)-2-cyano-1-((3a*R*,4*R*,6*R*,6a*R*)-6-(3-(((2,6-dichloro-4-methoxyphenyl)(2,4-dichlorophenyl)methoxy)methyl)-2,4-dioxo-3,4-dihydropyrimidin-1(2*H*)-yl)-2,2-dimethyltetrahydrofuro[3,4-*d*][1,3]dioxol-4-yl)-2-((4-((4-heptylphenyl)amino)-4-**

oxobutyl)amino)ethoxy)tetrahydrofuran-3,4-diyl bis(3,3-dimethyl-5-((triisopropylsilyl)oxy)pentanoate) (**21*R***): TLC (hexanes/EtOAc 60:40) R_f = 0.30; ^{1}H NMR (400 MHz, $CDCl_3$) δ 7.74 (dd, *J* = 16.8, 11.4 Hz, 1H), 7.51 (dd, *J* = 11.7, 8.5 Hz, 1H), 7.47 – 7.29 (m, 3H), 7.23 – 7.15 (m, 2H), 7.10 (t, *J* = 9.5 Hz, 2H), 6.85 (d, *J* = 8.8 Hz, 2H), 6.49 (d, *J* = 4.6 Hz, 1H), 5.76 (dd, *J* = 21.1, 8.1 Hz, 1H), 5.65 (d, *J* = 23.4 Hz, 1H), 5.56 (d, *J* = 9.2 Hz, 1H), 5.52 (d, *J* = 3.9 Hz, 1H), 5.46 (t, *J* = 10.8 Hz, 1H), 5.40 – 5.23 (m, 2H), 5.23 – 5.16 (m, 1H), 5.10 – 5.05 (m, 1H), 5.02 (s, 1H), 4.90 – 4.78 (m, 1H), 4.26 (t, *J* = 6.3 Hz, 1H), 4.21 (d, *J* = 8.9 Hz, 1H), 3.96 – 3.89 (m, 1H), 3.80 – 3.71 (m, 10H), 3.68 – 3.63 (m, 1H), 3.48 – 3.39 (m, 1H), 3.04 – 2.95 (m, 1H), 2.75 – 2.66 (m, 1H), 2.53 (t, *J* = 7.7 Hz, 2H), 2.44 (d, *J* = 12.1 Hz, 1H), 2.37 – 2.27 (m, 2H), 2.23 (d, *J* = 14.7 Hz, 2H), 1.65 – 1.51 (m, 10H), 1.42 (s, 9H), 1.36 – 1.23 (m, 10H), 1.08 – 1.01 (m, 42H), 0.97 (s, 6H), 0.90 – 0.85 (m, 9H); HRMS (ESI+) *m*/*z* calcd for $C_{88}H_{135}Cl_4N_6O_{18}Si_2$ [M + H] 1759.8126, found: 1759.8113.

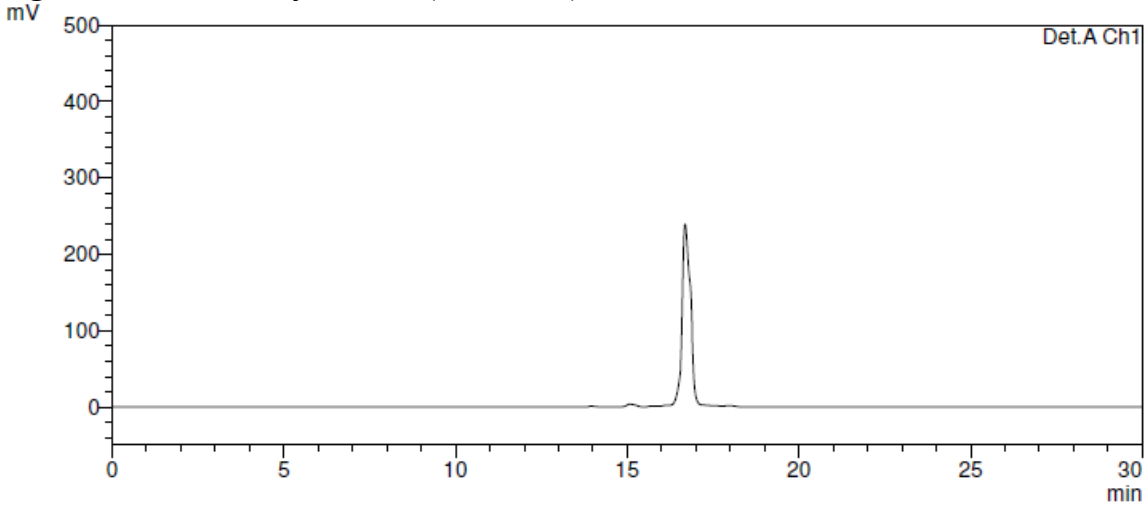


(2*S*,3*R*,4*R*,5*R*)-2-((1*S*,2*S*)-3-Amino-1-((3a*R*,4*R*,6*R*,6a*R*)-6-(3-(((2,6-dichloro-4-methoxyphenyl)(2,4-dichlorophenyl)methoxy)methyl)-2,4-dioxo-3,4-dihydropyrimidin-1(2*H*)-yl)-2,2-dimethyltetrahydrofuro[3,4-*d*][1,3]dioxol-4-yl)-2-((4-((4-heptylphenyl)amino)-4-oxobutyl)amino)-3-oxopropoxy)-5-(((*tert*-butoxycarbonyl)amino)methyl)tetrahydrofuran-3,4-diyl bis(3,3-dimethyl-5-((triisopropylsilyl)oxy)pentanoate) (22). To a stirred solution of **21*S*** (8.8 mg, 5.0 μmol) in EtOH/H_2O (9:1, 0.5 mL) were added $HgCl_2$ (2.7 mg, 0.010 mmol) and acetaldoxime (3.0 μL, 0.050 mmol) at rt. After being stirred for 6 h at rt, the reaction mixture was concentrated under reduced pressure. The residue was quenched with saturated $NaHCO_3$ aq., extracted with $CHCl_3$. The combined organic extracts were dried over Na_2SO_4 and concentrated in vacuo. The crude product was purified by silica gel column chromatography ($CHCl_3$/MeOH 99.5:0.5 to 99.2:0.8 to 98.8:1.2) to afford **22** (7.9 mg, 4.5 μmol, 89%): TLC ($CHCl_3$/MeOH 95:5) R_f = 0.40; IR (thin film) ν_{max} = 3335 (br), 2927, 2865, 1668, 1601, 1460, 1099, 1071, 882, 681 cm^{-1}; ^{1}H NMR (400 MHz, $CDCl_3$) δ 7.59 (dd, *J* = 19.5, 8.5 Hz, 1H), 7.40 (d, *J* = 8.0 Hz, 2H), 7.30 (t, *J* = 2.6 Hz, 1H), 7.24 – 7.18 (m, 1H), 7.11 (d, *J* = 8.0 Hz, 2H), 6.84 (d, *J* = 7.2 Hz, 2H), 6.50 (s, 1H), 5.84 (brs, 1H), 5.59 – 5.47 (m, 3H), 5.26 – 5.14 (m, 2H), 5.06 – 4.97 (m, 1H), 4.96 – 4.87 (m, 1H), 4.84 – 4.73 (m, 1H), 4.55 (t, *J* = 5.0 Hz, 1H), 4.28 – 4.14 (m, 2H), 3.80 – 3.70 (m, 7H), 3.59 – 3.46 (m, 1H), 3.41 (brs, 2H), 2.83 (brs, 2H), 2.54 (t, *J* = 7.7 Hz, 3H), 2.50 – 2.43 (m, 1H), 2.29 – 2.21 (m, 4H), 1.99 (brs, 2H), 1.65 – 1.53 (m, 10H), 1.43 (s, 9H), 1.35 (d, *J* = 5.2 Hz, 3H), 1.32 – 1.24 (m, 10H), 1.05 (d, *J* = 3.2 Hz, 48H), 1.00 – 0.97 (m, 6H), 0.87 (t, *J* = 6.8 Hz, 3H); ^{13}C NMR (101 MHz, $CDCl_3$) δ 159.6, 159.5, 136.87, 136.85, 136.4, 135.2, 134.0, 133.64, 133.59, 131.3, 129.42, 129.40, 128.9 (2C), 126.2, 125.3, 120.2, 120.1, 115.4 (2C), 74.5, 60.0, 59.9, 55.73, 55.72, 46.2, 46.1, 46.0, 44.8, 35.4, 32.7, 32.6, 31.8, 31.5, 29.69, 29.67, 29.6, 29.5, 29.4, 29.3, 29.24, 29.16, 29.09, 28.51, 28.49, 28.48, 28.45, 28.43, 28.42, 28.36, 28.33, 28.31, 28.28, 27.33, 27.30, 27.25, 27.2, 25.3, 22.7, 18.1 (12C), 14.1, 11.9 (6C); HRMS (ESI+) *m*/*z* calcd for $C_{88}H_{137}Cl_4N_6O_{19}Si_2$ [M + H] 1777.8231, found: 1777.8219.



4-(((2*S*,3*S*)-1-Amino-3-(((2*S*,3*R*,4*S*,5*R*)-5-(aminomethyl)-3,4-dihydroxytetrahydrofuran-2-yl)oxy)-3-((2*S*,5*R*)-5-(2,4-dioxo-3,4-dihydropyrimidin-1(2*H*)-yl)-3,4-dihydroxytetrahydrofuran-2-yl)-1-oxopropan-2-yl)amino)-*N*-(4-heptylphenyl)butanamide (10). To a stirred solution of **22** (7.9 mg, 4.5 μmol) in CH_2Cl_2 (0.70 mL) was added TFA (0.30 mL). The reaction mixture was stirred for 1 h at rt, and all volatile were evaporated in vacuo. To a stirred solution of the crude mixture in H_2O (0.2 mL) was added TFA (0.8 mL). The reaction mixture was stirred for 2 h at 40 ^oC, and all volatile were evaporated in vacuo. The crude mixture was purified by silica gel column chromatography ($CHCl_3$/MeOH 80:20 to $CHCl_3$/MeOH/H_2O/50% aqueous ammonia 56:42:7:3) to afford **10** (**UT-17455**) (2.4 mg, 3.4 μmol, 76%, 95.8% purity): TLC (n-butanol/ethanol/$CHCl_3$/28% aqueous ammonia 4:7:2:7) R_f = 0.50; $[\alpha]^{21}_D$ +0.538 (*c* = 0.24, methanol); IR (thin film) ν_{max} = 3302 (br), 2926, 1672, 1542, 1412, 1271, 1131, 1111, 1062, 819, 721 cm^{-1}; ^1H NMR (400 MHz, CD_3OD) δ 7.77 (d, *J* = 8.1 Hz, 1H), 7.43 (d, *J* = 8.1 Hz, 2H), 7.12 (d, *J* = 8.0 Hz, 2H), 5.74 (s, 1H), 5.73 (d, *J* = 12.6 Hz, 1H), 5.14 (s, 1H), 4.21 (dd, *J* = 4.7, 4.2 Hz, 1H), 4.19 – 4.13 (m, 2H), 4.11 (t, *J* = 4.7 Hz, 1H), 4.08 (s, 2H), 4.02 – 3.99 (m, 1H), 3.50 (d, *J* = 8.9 Hz, 1H), 3.24 (d, *J* = 13.0 Hz, 1H), 3.16 – 3.09 (m, 1H), 2.73 – 2.60 (m, 2H), 2.57 (t, *J* = 7.7 Hz, 2H), 2.43 (dd, *J* = 7.4, 4.0 Hz, 2H), 1.86 (quin, *J* = 7.2 Hz, 2H), 1.59 (quin, *J* = 6.4, 5.7 Hz, 2H), 1.35 – 1.26 (m, 8H), 0.92 – 0.87 (m, 3H); ^{13}C NMR (101 MHz, CD_3OD) δ 177.2, 174.2, 166.1, 152.1, 142.6, 140.1, 137.4, 129.7 (2C), 121.5 (2C), 110.6, 102.7, 92.5, 85.2, 80.5, 76.4, 75.0, 73.0, 71.2, 64.3, 43.2, 36.3, 35.5, 33.0, 32.8, 30.3, 26.6, 23.7, 14.4; HRMS (ESI+) *m*/*z* calcd for $C_{33}H_{51}N_6O_{11}$ [M + H] 707.3616, found: 707.3624.

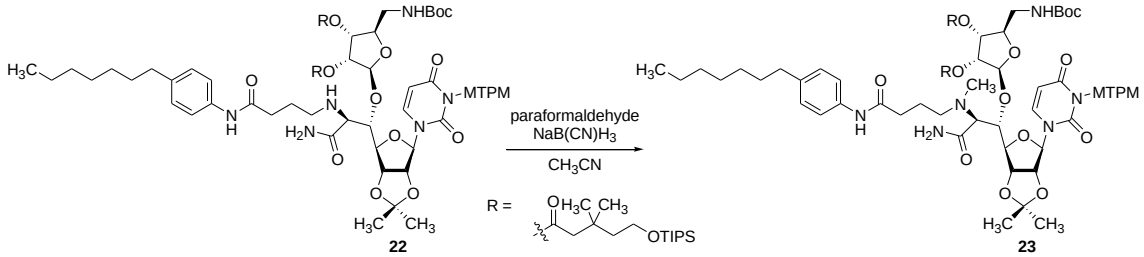
Figure S2. HPLC analysis of **10 (UT-17455)**.



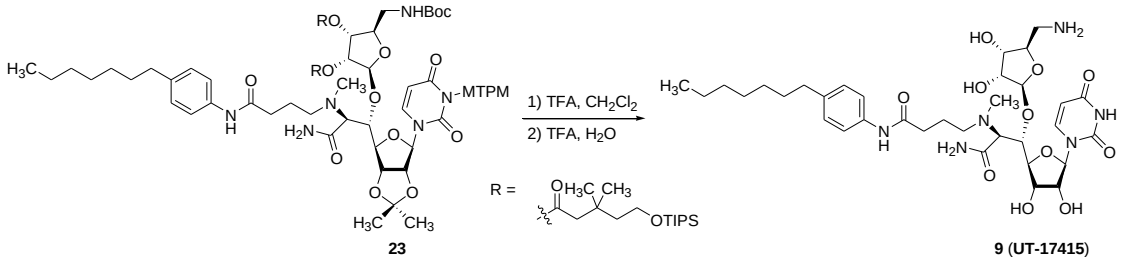
Area % purity: 95.8%

Conditions:

column: Phenomenex Kinetex 1.7 μ XB-C18 100 Å 150 x 2.10 mm column, solvents: 80 : 20 MeOH : 0.05M NH_4HCO_3 in water, UV: 254 nm

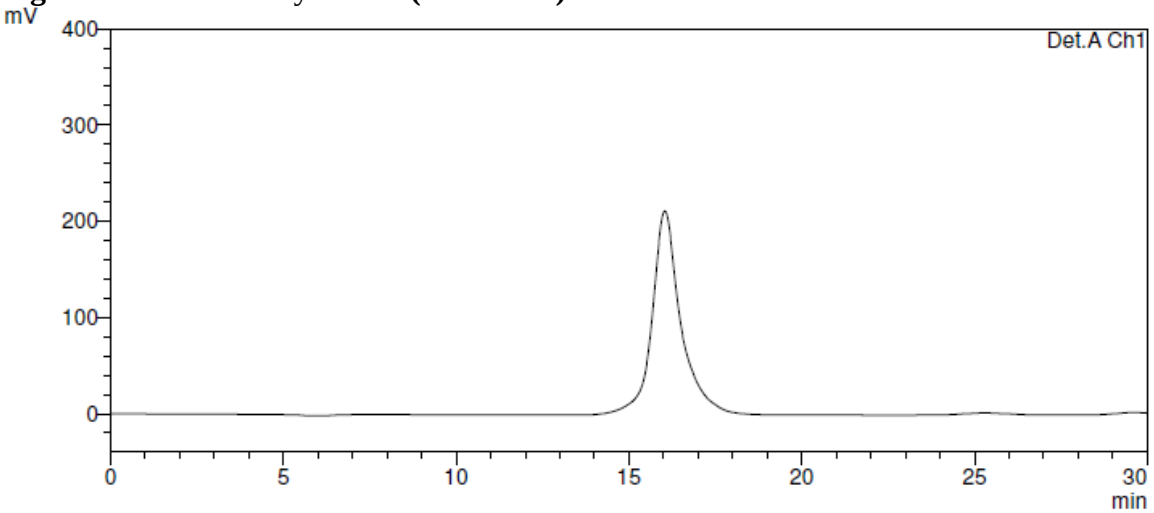


(2*S*,3*R*,4*R*,5*R*)-2-((1*S*,2*S*)-3-Amino-1-((3a*R*,4*R*,6*R*,6a*R*)-6-(3-(((2,6-dichloro-4-methoxyphenyl)(2,4-dichlorophenyl)methoxy)methyl)-2,4-dioxo-3,4-dihydropyrimidin-1(2*H*)-yl)-2,2-dimethyltetrahydrofuro[3,4-*d*][1,3]dioxol-4-yl)-2-((4-((4-heptylphenyl)amino)-4-oxobutyl)(methyl)amino)-3-oxopropoxy)-5-(((*tert*-butoxycarbonyl)amino)methyl)tetrahydrofuran-3,4-diyl bis(3,3-dimethyl-5-((triisopropylsilyl)oxy)pentanoate) (23). To a stirred solution of **22** (5.8 mg, 3.3 μmol) and paraformaldehyde (2.9 mg, 0.098 mmol) in CH_3CN (0.5 mL) were added $NaB(CN)H_3$ (6.2 mg, 0.098 mmol). After being stirred for 4 h at rt, the reaction mixture was quenched with saturated $NaHCO_3$ aq., extracted with $CHCl_3$. The combined organic extracts were dried over Na_2SO_4 and concentrated in vacuo. The crude product was purified by silica gel column chromatography (hexanes/EtOAc 40:60) to afford **23** (5.5 mg, 3.1 μmol, 95%): TLC (hexanes/EtOAc 33:67) R_f = 0.60; $[\alpha]^{21}_D$ +0.022 (*c* = 0.28, $CHCl_3$); IR (thin film) ν_{max} = 2932, 2866, 1718, 1672, 1601, 1463, 1101, 1071, 884 cm^{-1}; ^1H NMR (400 MHz, $CDCl_3$) δ 7.75 (d, *J* = 17.0 Hz, 1H), 7.56 (d, *J* = 8.6 Hz, 1H), 7.43 (d, *J* = 8.1 Hz, 2H), 7.34 (d, *J* = 8.1 Hz, 1H), 7.30 (s, 2H), 7.20 (dt, *J* = 8.5, 2.0 Hz, 1H), 7.10 (d, *J* = 8.1 Hz, 2H), 6.85 (s, 2H), 6.51 (d, *J* = 7.9 Hz, 1H), 6.28 (brs, 1H), 5.95 (d, *J* = 21.6 Hz, 1H), 5.84 – 5.78 (m, 1H), 5.74 (d, *J* = 23.3 Hz, 1H), 5.54 (s, 2H), 5.49 (d, *J* = 9.6 Hz, 1H), 5.18 (brs, 1H), 5.11 (s, 2H), 5.02 (brs, 1H), 4.88 – 4.83 (m, 1H), 4.80 – 4.74 (m, 1H), 4.39 – 4.31 (m, 2H), 4.24 – 4.18 (m, 1H), 3.92 (t, *J* = 5.8 Hz, 1H), 3.78 (s, 3H), 3.74 (q, *J* = 6.6 Hz, 4H), 3.68 – 3.63 (m, 1H), 3.50 – 3.40 (m, 2H), 3.37 – 3.30 (m, 1H), 2.83 – 2.74 (m, 1H), 2.68 – 2.59 (m, 1H), 2.54 (t, *J* = 7.8 Hz, 2H), 2.49 (s, 3H), 2.37 (q, *J* = 8.0, 7.6 Hz, 2H), 2.29 – 2.20 (m, 4H), 1.98 – 1.88 (m, 2H), 1.62 – 1.52 (m, 6H), 1.40 (s, 9H), 1.36 (brs, 3H), 1.33 – 1.23 (m, 6H), 1.09 – 1.01 (m, 48H), 0.98 (s, 6H), 0.87 (t, *J* = 6.4 Hz, 3H); ^{13}C NMR (101 MHz, $CDCl_3$) δ 171.0, 162.0, 159.5, 157.1, 136.9, 131.3, 129.4, 128.7 (2C), 119.9 (2C), 115.3, 115.1, 114.2, 70.6, 70.1, 69.9, 67.1, 60.4, 60.1, 59.96, 59.95, 58.9, 55.8, 55.7, 54.4, 54.1, 46.22, 46.16, 46.1, 45.3, 44.9, 44.8, 44.7, 42.3, 41.2, 39.93, 39.86, 39.6, 39.04, 38.97, 35.4, 32.7, 32.64, 32.63, 32.62, 32.58, 31.9, 31.8, 31.7, 31.6, 31.53, 31.48, 29.69, 29.67, 29.6, 29.4, 29.22, 29.17, 28.50, 28.49, 28.4, 27.29, 27.28, 27.21, 27.17, 25.23, 25.20, 22.68, 22.66, 18.1 (12C), 14.1, 11.9 (6C); HRMS (ESI+) *m/z* calcd for $C_{89}H_{139}Cl_4N_6O_{19}Si_2$ [M + H] 1791.8388, found: 1791.8404.



4-(((2*S*,3*S*)-1-Amino-3-(((2*S*,3*R*,4*S*,5*R*)-5-(aminomethyl)-3,4-dihydroxytetrahydrofuran-2-yl)oxy)-3-((2*S*,5*R*)-5-(2,4-dioxo-3,4-dihydropyrimidin-1(2*H*)-yl)-3,4-dihydroxytetrahydrofuran-2-yl)-1-oxopropan-2-yl)(methyl)amino)-*N*-(4-heptylphenyl)butanamide (9). To a stirred solution of **23** (2.9 mg, 1.6 μmol) in CH_2Cl_2 (0.70 mL) was added TFA (0.30 mL). The reaction mixture was stirred for 2 h at rt, and all volatile were evaporated in vacuo. To a stirred solution of the crude mixture in H_2O (0.2 mL) was added TFA (0.8 mL). The reaction mixture was stirred for 4 h at 40 ^oC, and all volatile were evaporated in vacuo. The crude mixture was purified by silica gel column chromatography ($CHCl_3$/MeOH 80:20 to $CHCl_3$/MeOH/H_2O/50% aqueous ammonia 56:42:7:3) to afford **9 (UT-17415)** (1.2 mg, 1.6 μmol, 100%): TLC (n-butanol/ethanol/$CHCl_3$/28% aqueous ammonia 4:7:2:7) R_f = 0.55; $[\alpha]^{20}_D$ +0.038 (*c* = 0.12, methanol); IR (thin film) ν_{max} = 3333 (br), 2926, 2855, 1676, 1204, 1135, 840, 801, 722 cm^{-1}; ^1H NMR (400 MHz, CD_3OD) δ 7.82 (d, *J* = 8.1 Hz, 1H), 7.44 (d, *J* = 8.0 Hz, 2H), 7.12 (d, *J* = 8.1 Hz, 2H), 5.76 (d, *J* = 8.0 Hz, 1H), 5.70 (s, 1H), 5.18 (s, 1H), 4.58 (s, 1H), 4.28 (d, *J* = 9.3 Hz, 1H), 4.21 – 4.16 (m, 3H), 4.14 – 4.07 (m, 3H), 3.61 (d, *J* = 9.4 Hz, 1H), 3.21 (dd, *J* = 13.6, 3.4 Hz, 1H), 2.83 (td, *J* = 12.1, 11.7, 5.0 Hz, 1H), 2.57 (t, *J* = 7.6 Hz, 2H), 2.46 (s, 3H), 2.46 – 2.40 (m, 2H), 2.00 – 1.89 (m, 1H), 1.79 (d, *J* = 12.4 Hz, 1H), 1.63 – 1.55 (m, 2H), 1.37 – 1.23 (m, 10H), 0.91 – 0.87 (m, 3H); ^{13}C NMR (101 MHz, CD_3OD) δ 173.9, 172.3, 142.4, 140.2, 137.3, 129.7 (2C), 121.5 (2C), 112.1, 102.4, 92.5, 84.2, 80.5, 78.4, 76.4, 75.4, 72.0, 70.8, 68.5, 54.5, 39.5, 36.3, 35.0, 33.0, 32.8, 30.29, 30.26, 24.3, 23.7, 14.4; HRMS (ESI+) *m/z* calcd for $C_{34}H_{53}N_6O_{11}$ [M + H] 721.3772, found: 721.3761.

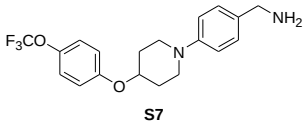
Figure S3. HPLC analysis of **9 (UT-17415)**.



Area % purity: 97.2%

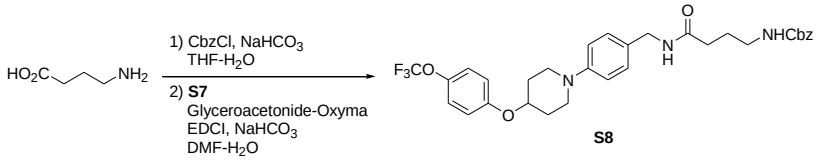
Conditions:

column: Phenomenex Kinetex 1.7 μ XB-C18 100 Å 150 x 2.10 mm column, solvents: 80 : 20 MeOH : 0.05M NH_4HCO_3 in water, UV: 254 nm



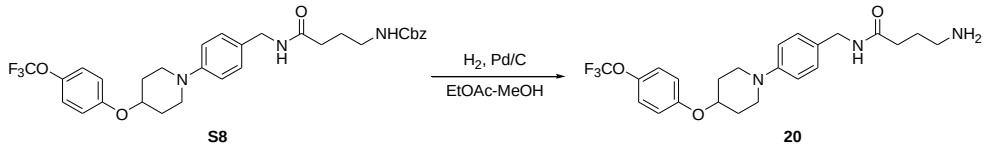
S7

(4-(4-(4-(Trifluoromethoxy)phenoxy)piperidin-1-yl)phenyl)methanamine (S7). The title compound was synthesized according to the reported procedure [5]: ^{1}H NMR (400 MHz, $CDCl_3$) δ 7.21 (d, *J* = 8.2 Hz, 2H), 7.14 (d, *J* = 8.6 Hz, 2H), 6.97 – 6.87 (m, 4H), 4.43 (tt, *J* = 7.7, 3.8 Hz, 1H), 3.79 (s, 2H), 3.49 (ddd, *J* = 11.7, 7.2, 3.7 Hz, 2H), 3.09 (ddd, *J* = 12.2, 8.2, 3.6 Hz, 2H), 2.15 – 2.06 (m, 2H), 1.98 – 1.88 (m, 2H); ^{13}C NMR (101 MHz, $CDCl_3$) δ 155.8, 150.2, 142.8, 134.6, 128.0 (2C), 122.5 (2C), 116.83 (2C), 116.76 (2C), 72.9, 46.9 (2C), 45.9, 30.4 (2C); HRMS (ESI+) *m*/*z* calcd for $C_{19}H_{22}F_3N_2O_2$ [M + H] 367.1633, found 367.1628.

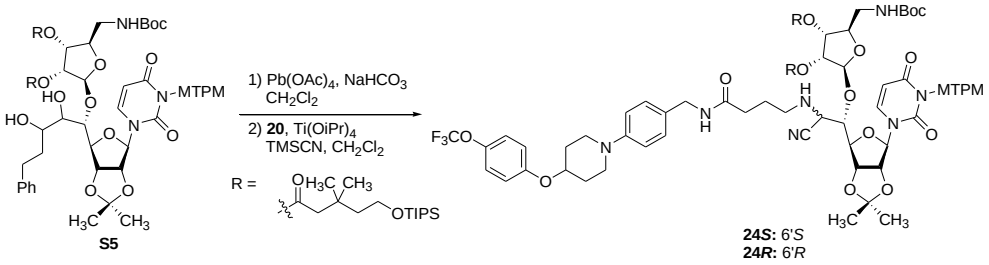


S8

Benzyl (4-oxo-4-((4-(4-(4-(trifluoromethoxy)phenoxy)piperidin-1-yl)benzyl)amino)butyl)carbamate (S8). To a stirred solution of 4-aminobutyric acid (61.9 mg, 0.60 mmol) and $NaHCO_3$ (151 mg, 1.80 mmol) in THF-H_2O (1:1, 6 mL) was added CbzCl (128 μL, 0.90 mmol). After being stirred for 8 h at rt, the reaction mixture was quenched with 1N HCl (aq.) and extracted with $CHCl_3$. The combined organic solution was dried over Na_2SO_4 and concentrated in vacuo. To a stirred solution of the crude mixture, **S7** (110 mg, 0.30 mmol), $NaHCO_3$ (126 mg, 1.50 mmol) and Glyceroacetonide-Oxyma (103 mg, 0.45 mmol) in DMF-H_2O (9:1, 1.5 mL), was added EDCI (115 mg, 2.0 mmol). After being stirred for 13 h at rt, the reaction mixture was quenched with H_2O and extracted with EtOAc. The combined organic solution was washed with 1N HCl (aq.), saturated $NaHCO_3$ (aq.), dried over Na_2SO_4 and concentrated in vacuo. The crude mixture was purified by silica gel column chromatography (hexanes/EtOAc 33:67 to 20:80) to afford **S8** (102 mg, 0.17 mmol, 58%) [4]: TLC (hexanes/EtOAc 20:80) R_f = 0.30; ^{1}H NMR (400 MHz, $CDCl_3$) δ 7.37 – 7.33 (m, 5H), 7.16 (dd, *J* = 14.6, 8.4 Hz, 4H), 6.91 (d, *J* = 9.1 Hz, 4H), 5.96 (brs, 1H), 5.09 (s, 2H), 5.04 (brs, 1H), 4.44 (tt, *J* = 7.4, 3.7 Hz, 1H), 4.34 (d, *J* = 5.5 Hz, 2H), 3.48 (ddd, *J* = 11.7, 7.3, 3.7 Hz, 2H), 3.25 (q, *J* = 6.4 Hz, 2H), 3.10 (ddd, *J* = 12.2, 8.2, 3.5 Hz, 2H), 2.23 (t, *J* = 7.0 Hz, 2H), 2.14 – 2.05 (m, 2H), 1.94 (tt, *J* = 8.6, 3.9 Hz, 2H), 1.86 (p, *J* = 6.6 Hz, 2H); ^{13}C NMR (101 MHz, $CDCl_3$) δ 172.1, 155.8, 136.5, 128.9 (2C), 128.5 (2C), 128.11, 128.08, 122.5 (2C), 116.8 (2C), 116.6 (2C), 72.8, 66.7, 46.6 (2C), 43.2, 40.4, 33.7, 30.3 (2C), 26.0; HRMS (ESI+) *m*/*z* calcd for $C_{31}H_{35}F_3N_3O_5$ [M + Na] 586.2529, found: 586.2521.

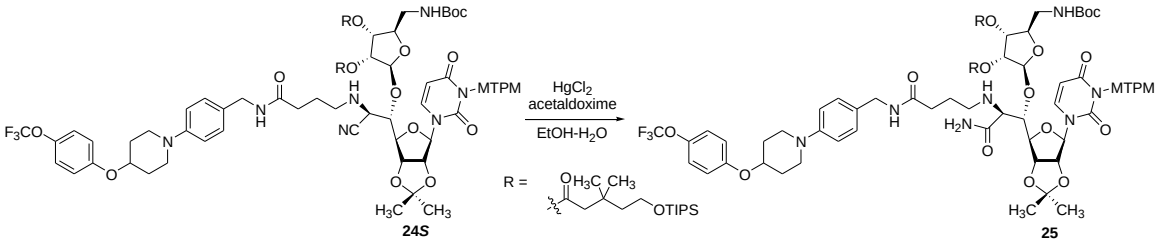


4-Amino-*N*-(4-(4-(4-(trifluoromethoxy)phenoxy)piperidin-1-yl)benzyl)butanamide (20). To a stirred solution of **S8** (59 mg, 0.10 mmol) in EtOAc-MeOH (1:1, 10 mL) was added Pd/C (10 wt % 12 mg). H_2 gas was introduced and the reaction mixture was stirred for 3 h under H_2. The solution was filtered through Celite and concentrated in vacuo. The crude mixture of **20** was used for next reaction without purification.



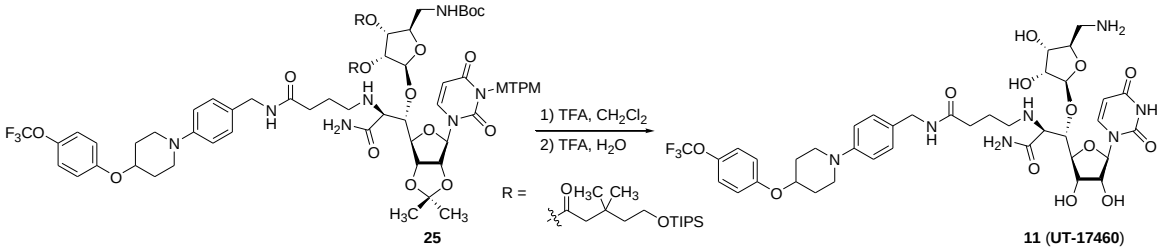
(2*R*,3*R*,4*R*,5*S*)-2-(((*tert*-Butoxycarbonyl)amino)methyl)-5-((1*S*,2*R*)-2-cyano-1-((3a*R*,4*R*,6*R*,6a*R*)-6-(3-(((2,6-dichloro-4-methoxyphenyl)(2,4-dichlorophenyl)methoxy)methyl)-2,4-dioxo-3,4-dihydropyrimidin-1(2*H*)-yl)-2,2-dimethyltetrahydrofuro[3,4-*d*][1,3]dioxol-4-yl)-2-((4-oxo-4-((4-(4-(4-(trifluoromethoxy)phenoxy)piperidin-1-yl)benzyl)amino)butyl)amino)ethoxy)tetrahydrofuran-3,4-diyl bis(3,3-dimethyl-5-((triisopropylsilyl)oxy)pentanoate) (24*S*). To a stirred solution of **S5** (32.5 mg, 0.020 mmol) and $NaHCO_3$ (16.9 mg, 0.20 mmol) in CH_2Cl_2 (1.0 mL) was added $Pb(OAc)_4$ (17.9 mg, 0.040 mmfol) at 0 ^oC. The reaction mixture was stirred for 2 h at 0 ^oC and quenched with saturated $NaHCO_3$ aq., extracted with EtOAc. The combined organic extracts were dried over Na_2SO_4 and concentrated in vacuo. The crude mixture of aldehyde **18** was used for the next reaction without purification. To a stirred solution of $(BnO)_2P(O)$-CH_2-P(O)(OBn)OH (45.0 mg, 0.10 mmol) in CH_2Cl_2 (0.5 mL) was added a CH_2Cl_2 (0.5 mL) solution of the mixture of **18**, **20** was added to the solution. After 6 h, the reaction was added TMSCN (25.2 μL, 0.20 mmol) and stirred for 12 h at rt. After completion, the reaction mixture was quenched with saturated $NaHCO_3$ aq., extracted with EtOAc. The combined organic extracts were dried over Na_2SO_4 and concentrated in vacuo. The crude product was purified by silica gel column chromatography (hexanes/EtOAc 80:20 to 60:40) to afford **24*S*** (23.9 mg, 0.012 mmol, 61% for 2 steps) and **24*R*** (5.1 mg, 2.56 μmol, 13% for 2 steps): TLC (hexanes/EtOAc 50:50) R_f = 0.40; $[\alpha]^{21}_D$ +0.102 (*c* = 0.75, $CHCl_3$); IR (thin film) ν_{max} = 3342 (br), 2941, 2866, 1718, 1675, 1505, 1464, 1243, 1164, 1101, 1071, 883, 772, 688 cm^{-1}; ^1H NMR (400 MHz, $CDCl_3$) δ 7.49 (dd, *J* = 8.5, 4.3 Hz, 1H), 7.32 (d, *J* = 2.0 Hz, 1H), 7.22 – 7.11 (m, 7H), 6.94 – 6.88 (m, 5H), 6.86 (d, *J* = 6.5 Hz, 2H), 6.50 (d, *J* = 8.6 Hz, 1H), 6.25 – 6.16 (m, 1H), 5.73 (dd, *J* = 22.2, 8.0 Hz, 1H), 5.60 (t, *J* = 8.8 Hz, 1H), 5.56 – 5.41 (m, 3H), 5.21 (d, *J* = 4.4 Hz, 1H), 5.05 – 4.98 (m, 2H), 4.94 – 4.77 (m, 2H), 4.53 – 4.37 (m, 3H), 4.25 – 4.16 (m, 2H), 4.05 – 3.98 (m, 1H), 3.80 – 3.69 (m, 6H), 3.68 – 3.63 (m, 1H), 3.56 (dd, *J* = 17.3, 3.4 Hz, 1H), 3.48 (ddt, *J* = 11.6, 7.2, 4.0 Hz, 2H), 3.44 – 3.29 (m, 1H),

3.08 (dq, *J* = 9.5, 5.3, 4.8 Hz, 2H), 2.95 (dt, *J* = 11.4, 5.5 Hz, 1H), 2.47 (td, *J* = 12.0, 11.4, 5.7 Hz, 1H), 2.36 – 2.14 (m, 5H), 2.13 – 2.05 (m, 2H), 1.97 – 1.85 (m, 3H), 1.84 – 1.75 (m, 1H), 1.58 (t, *J* = 6.9 Hz, 2H), 1.55 – 1.50 (m, 4H), 1.40 (s, 9H), 1.33 (d, *J* = 4.8 Hz, 3H), 1.28 – 1.23 (m, 3H), 1.08 – 1.02 (m, 42H), 1.01 (s, 6H), 0.94 (d, *J* = 2.1 Hz, 6H); ^{13}C NMR (101 MHz, $CDCl_3$) δ 172.4, 171.0, 170.9, 159.5, 155.8, 150.9, 150.7, 142.8, 136.9, 136.8, 135.3, 135.1, 134.13, 134.05, 133.86, 133.85, 133.78, 131.2, 131.1, 129.42, 129.37, 129.0, 126.4, 126.2, 125.5, 125.2, 122.5 (2C), 121.8, 119.3, 118.4, 116.8 (2C), 116.6 (2C), 115.4, 115.3, 114.71, 114.66, 106.4, 102.3, 102.2, 84.8, 80.7, 80.6, 79.9, 79.8, 79.3, 76.2, 74.32, 74.30, 72.9, 60.38, 60.35, 60.0, 59.9, 55.72, 55.71, 52.0, 46.6, 46.2, 45.9, 44.84, 44.77, 42.99, 42.96, 42.4, 41.2, 33.53, 33.49, 32.6, 32.5, 30.3, 28.4, 27.3 (2C), 27.17, 27.16, 27.1, 25.4, 18.1 (12C), 14.2, 14.1, 11.91 (3C), 11.90 (3C); HRMS (ESI+) *m*/*z* calcd for $C_{94}H_{135}Cl_4F_3N_7O_{20}Si_2$ [M + H] 1934.8007, found: 1934.8021. Data for **24*R***: TLC (hexanes/EtOAc 60:40) R_f = 0.30; ^{1}H NMR (400 MHz, Chloroform-*d*) δ 7.53 (d, *J* = 8.7 Hz, 1H), 7.33 – 7.29 (m, 1H), 7.21 – 7.07 (m, 7H), 6.94 – 6.88 (m, 5H), 6.85 (d, *J* = 6.8 Hz, 2H), 6.54 (s, 1H), 5.71 (d, *J* = 7.9 Hz, 1H), 5.58 – 5.49 (m, 3H), 5.46 (t, *J* = 8.9 Hz, 1H), 5.24 – 5.20 (m, 1H), 5.15 – 5.08 (m, 1H), 5.08 – 5.00 (m, 1H), 4.92 (dd, *J* = 11.5, 5.6 Hz, 1H), 4.85 – 4.78 (m, 1H), 4.49 – 4.39 (m, 2H), 4.39 – 4.18 (m, 3H), 3.98 (dd, *J* = 11.1, 5.4 Hz, 1H), 3.81 – 3.70 (m, 6H), 3.69 – 3.61 (m, 2H), 3.52 – 3.43 (m, 2H), 3.37 – 3.32 (m, 1H), 3.08 (ddd, *J* = 12.4, 8.5, 3.8 Hz, 2H), 2.99 – 2.91 (m, 1H), 2.65 (dd, *J* = 12.8, 6.5 Hz, 1H), 2.31 – 2.18 (m, 5H), 2.13 – 2.04 (m, 2H), 1.96 – 1.85 (m, 4H), 1.67 – 1.52 (m, 6H), 1.40 (s, 9H), 1.38 – 1.29 (m, 3H), 1.25 (s, 6H), 1.10 – 0.98 (m, 42H), 0.97 (s, 6H), 0.88 (t, *J* = 6.7 Hz, 3H) ; HRMS (ESI+) *m*/*z* calcd for $C_{94}H_{135}Cl_4F_3N_7O_{20}Si_2$ [M + H] 1934.8007, found: 1934.8000.



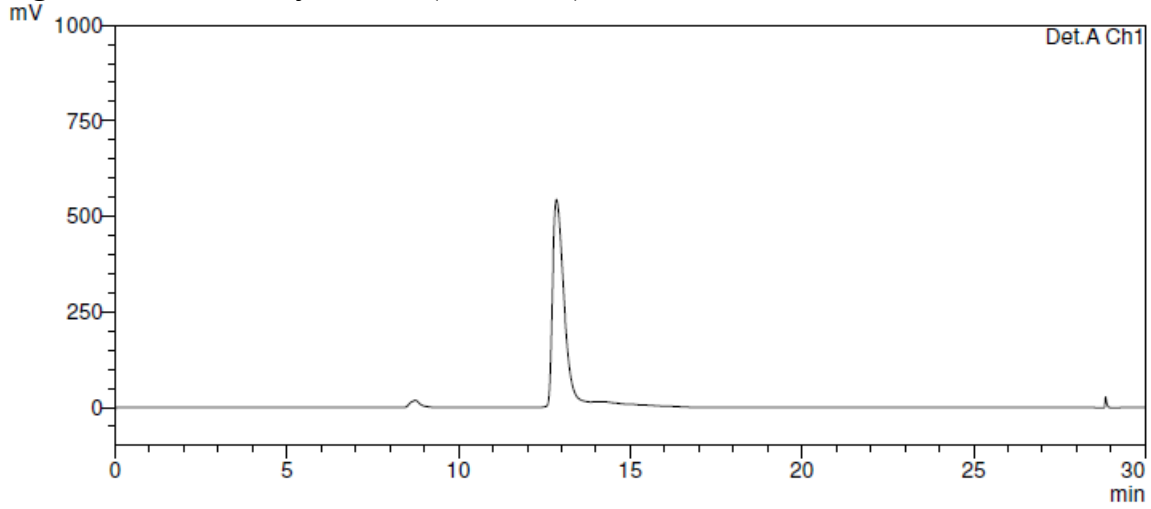
(2*S*,3*R*,4*R*,5*R*)-2-((1*S*,2*S*)-3-Amino-1-((3a*R*,4*R*,6*R*,6a*R*)-6-(3-(((2,6-dichloro-4-methoxyphenyl)(2,4-dichlorophenyl)methoxy)methyl)-2,4-dioxo-3,4-dihydropyrimidin-1(2*H*)-yl)-2,2-dimethyltetrahydrofuro[3,4-*d*][1,3]dioxol-4-yl)-3-oxo-2-((4-oxo-4-((4-(4-(4-(trifluoromethoxy)phenoxy)piperidin-1-yl)benzyl)amino)butyl)amino)propoxy)-5-(((*tert*-butoxycarbonyl)amino)methyl)tetrahydrofuran-3,4-diyl bis(3,3-dimethyl-5-((triisopropylsilyl)oxy)pentanoate) (25). To a stirred solution of **24*S*** (15.4 mg, 8.0 μmol) in EtOH/H_2O (9:1, 0.5 mL) were added $HgCl_2$ (4.3 mg, 0.016 mmol) and acetaldoxime (4.9 μL, 0.080 mmol) at rt. After being stirred for 6 h at rt, the reaction mixture was concentrated under reduced pressure. The residue was quenched with saturated $NaHCO_3$ aq., extracted with $CHCl_3$. The combined organic extracts were dried over Na_2SO_4 and concentrated in vacuo. The crude product was purified by silica gel column chromatography ($CHCl_3$/MeOH 99.5:0.5 to 99.2:0.8 to 98.8:1.2) to afford **25** (15.3 mg, 7.8 μmol, 98%): TLC ($CHCl_3$/MeOH 95:5) R_f = 0.30; $[\alpha]^{21}_D$ +0.144 (*c* = 0.53, $CHCl_3$); IR (thin film) ν_{max} = 3335 (br), 2940, 2866, 1719, 1676, 1505, 1464, 1367, 1242, 1162, 1101, 1070, 882, 681 cm^{-1}; ^{1}H NMR (400 MHz, $CDCl_3$) δ 7.53 (dd, *J* = 8.6, 5.1 Hz, 1H), 7.30 (s, 1H), 7.28 – 7.22 (m, 2H), 7.21 – 7.12 (m, 6H), 6.91 (d, *J* = 8.5 Hz, 4H), 6.86 (d, *J* = 2.6 Hz, 2H),

6.51 (d, *J* = 8.7 Hz, 1H), 5.94 (brs, 1H), 5.79 – 5.67 (m, 3H), 5.56 – 5.47 (m, 2H), 5.17 (brs, 1H), 5.06 (s, 1H), 4.96 (brs, 1H), 4.82 – 4.73 (m, 2H), 4.43 (tt, *J* = 7.8, 3.8 Hz, 1H), 4.39 – 4.28 (m, 3H), 4.21 (brs, 1H), 4.13 (brs, 1H), 3.78 (s, 3H), 3.73 (q, *J* = 7.4 Hz, 5H), 3.67 (brs, 1H), 3.48 (ddd, *J* = 11.7, 7.2, 3.7 Hz, 2H), 3.41 – 3.28 (m, 1H), 3.17 (s, 1H), 3.09 (ddd, *J* = 12.2, 8.2, 3.3 Hz, 2H), 2.80 – 2.60 (m, 2H), 2.38 – 2.15 (m, 7H), 2.13 – 2.05 (m, 2H), 1.93 (ddd, *J* = 12.8, 8.0, 3.7 Hz, 2H), 1.85 – 1.79 (m, 2H), 1.54 (s, 3H), 1.42 (s, 9H), 1.34 (s, 3H), 1.04 (d, *J* = 2.8 Hz, 42H), 1.01 (s, 6H), 0.96 (s, 6H); ^{13}C NMR (101 MHz, $CDCl_3$) δ 162.1, 162.0, 159.6, 159.5, 156.2, 155.8, 150.9, 150.4, 142.80, 142.78, 136.88, 136.86, 135.23, 135.21, 133.9, 133.6, 131.33, 131.30, 131.29, 129.40, 129.37, 129.2, 129.1, 129.02, 128.98, 126.24, 126.22, 126.21, 125.40, 125.36, 124.5, 124.4, 123.20, 123.19, 122.5 (2C), 121.8, 120.1, 119.3, 116.8 (2C), 115.4, 80.4, 80.02, 79.99, 79.96, 79.95, 79.92, 79.87, 79.85, 79.83, 74.51, 74.50, 72.7, 70.4, 70.3, 69.5, 60.0, 59.9, 55.73, 55.72, 46.7, 46.19, 46.15, 46.13, 46.11, 46.10, 46.07, 46.0, 44.8, 34.7, 34.5, 32.61, 32.58, 30.2, 29.7, 29.64, 29.60, 28.50, 28.45, 28.42, 28.38, 28.34, 27.25 (2C), 27.19, 27.16, 25.31, 25.29, 25.27, 18.1 (12C), 14.1, 12.2, 11.9 (6C); HRMS (ESI+) *m*/*z* calcd for $C_{94}H_{137}Cl_4F_3N_7O_{21}Si_2$ [M + H] 1952.8112, found: 1952.8098.

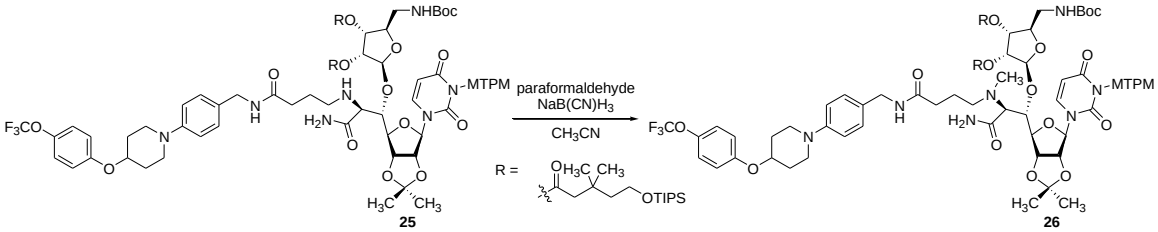


4-(((2*S*,3*S*)-1-Amino-3-(((2*S*,3*R*,4*S*,5*R*)-5-(aminomethyl)-3,4-dihydroxytetrahydrofuran-2-yl)oxy)-3-((2*S*,5*R*)-5-(2,4-dioxo-3,4-dihydropyrimidin-1(2*H*)-yl)-3,4-dihydroxytetrahydrofuran-2-yl)-1-oxopropan-2-yl)amino)-*N*-(4-(4-(4-(trifluoromethoxy)phenoxy)piperidin-1-yl)benzyl)butanamide (11). To a stirred solution of **25** (5.3 mg, 2.7 μmol) in CH_2Cl_2 (0.70 mL) was added TFA (0.30 mL). The reaction mixture was stirred for 1 h at rt, and all volatile were evaporated in vacuo. To a stirred solution of the crude mixture in H_2O (0.2 mL) was added TFA (0.8 mL). The reaction mixture was stirred for 2 h at 40 °C, and all volatile were evaporated in vacuo. The crude mixture was purified by silica gel column chromatography ($CHCl_3$/MeOH 80:20 to $CHCl_3$/MeOH/H_2O/50% aqueous ammonia 56:42:7:3) to afford **11 (UT-17460)** (2.2 mg, 2.5 μmol, 91%): TLC (n-butanol/ethanol/$CHCl_3$/28% aqueous ammonia 4:7:2:7) R_f = 0.50; $[\alpha]^{21}_D$ +0.375 (*c* = 0.30, methanol); IR (thin film) ν_{max} = 3352 (br), 2932, 1677, 1505, 1243, 1201, 1136, 801, 722 cm^{-1}; ^{1}H NMR (400 MHz, CD_3OD) δ 7.78 (d, *J* = 8.1 Hz, 1H), 7.18 (dd, *J* = 9.0, 3.5 Hz, 4H), 7.00 (dd, *J* = 16.0, 8.6 Hz, 4H), 5.77 (d, *J* = 2.9 Hz, 1H), 5.73 (d, *J* = 8.1 Hz, 1H), 5.14 (s, 1H), 4.57 – 4.50 (m, 1H), 4.28 (s, 2H), 4.22 – 4.13 (m, 3H), 4.10 (dd, *J* = 8.6, 4.4 Hz, 1H), 4.07 – 3.98 (m, 2H), 3.52 – 3.46 (m, 3H), 3.44 (d, *J* = 8.8 Hz, 1H), 3.17 (d, *J* = 13.0 Hz, 1H), 3.14 – 3.02 (m, 3H), 2.60 (ddq, *J* = 18.4, 11.8, 6.9 Hz, 2H), 2.29 (td, *J* = 7.3, 2.8 Hz, 2H), 2.12 (dd, *J* = 14.5, 5.6 Hz, 2H), 1.93 – 1.73 (m, 4H), 1.39 – 1.25 (m, 2H); ^{13}C NMR (101 MHz, CD_3OD) δ 175.6, 166.2, 157.6, 152.0, 142.6, 131.2, 129.6 (2C), 123.6 (2C), 118.11 (2C), 118.07 (2C), 110.5, 102.7, 92.3, 85.3, 81.4, 80.4, 76.5, 75.1, 74.1 (2C), 73.0, 71.3, 64.4, 43.7, 43.6, 34.7, 31.5, 26.9; HRMS (ESI+) *m*/*z* calcd for $C_{39}H_{51}F_3N_7O_{13}$ [M + H] 882.3497, found: 882.3512.

Figure S4. HPLC analysis of **11 (UT-17460)**.

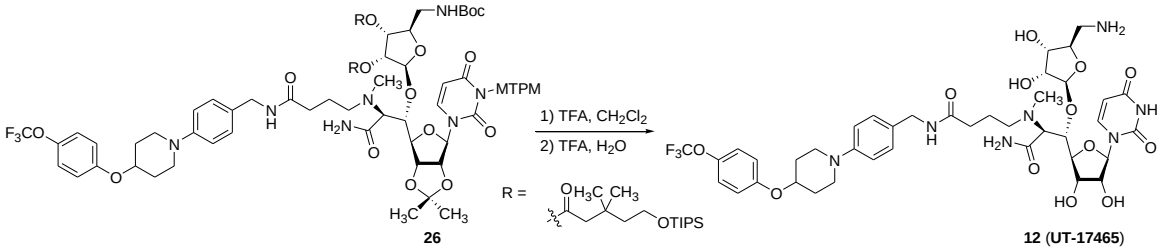


Area % purity: 95.6%
Conditions:
column: Phenomenex Kinetex 1.7 µ XB-C18 100 Å 150 x 2.10 mm column, solvents: 75 : 25 MeOH : 0.05M NH_4HCO_3 in water, UV: 254 nm



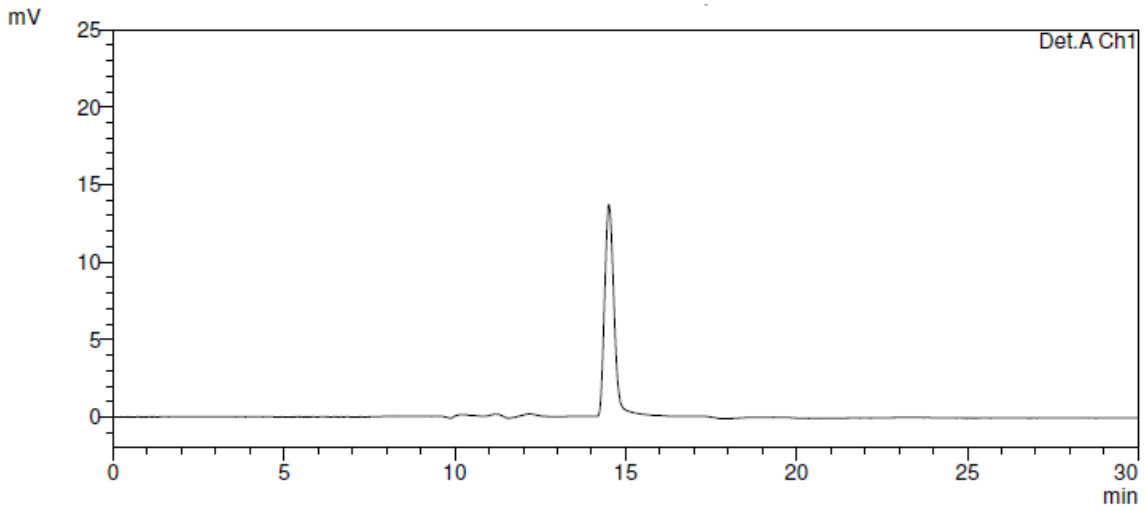
(2*S*,3*R*,4*R*,5*R*)-2-((1*S*,2*S*)-3-Amino-1-((3a*R*,4*R*,6*R*,6a*R*)-6-(3-(((2,6-dichloro-4-methoxyphenyl)(2,4-dichlorophenyl)methoxy)methyl)-2,4-dioxo-3,4-dihydropyrimidin-1(2*H*)-yl)-2,2-dimethyltetrahydrofuro[3,4-*d*][1,3]dioxol-4-yl)-2-(methyl(4-oxo-4-((4-(4-(4-(trifluoromethoxy)phenoxy)piperidin-1-yl)benzyl)amino)butyl)amino)-3-oxopropoxy)-5-(((*tert*-butoxycarbonyl)amino)methyl)tetrahydrofuran-3,4-diyl bis(3,3-dimethyl-5-((triisopropylsilyl)oxy)pentanoate) (26). To a stirred solution of **25** (7.8 mg, 4.0 µmol) and paraformaldehyde (3.6 mg, 0.12 mmol) in CH_3CN (0.5 mL) were added $NaB(CN)H_3$ (7.5 mg, 0.12 mmol). After being stirred for 17 h at rt, the reaction mixture was quenched with saturated $NaHCO_3$ aq., extracted with $CHCl_3$. The combined organic extracts were dried over Na_2SO_4 and concentrated in vacuo. The crude product was purified by silica gel column chromatography (hexanes/EtOAc 33:67) to afford **26** (4.7 mg, 2.4 µmol, 59%): TLC (hexanes/EtOAc 20:80) R_f = 0.50; ^{1}H NMR (400 MHz, Chloroform-*d*) δ 7.57 (d, *J* = 8.8 Hz, 1H), 7.38 (dd, *J* = 19.7, 7.9 Hz, 1H), 7.29 (s, 1H), 7.22 – 7.10 (m, 5H), 6.90 (d, *J* = 9.1 Hz, 4H), 6.85 (d, *J* = 3.6 Hz, 2H), 6.51 (d, *J* = 5.1 Hz, 1H), 6.25 (d, *J* = 27.7 Hz, 1H), 5.84 (dd, *J* = 13.4, 8.0 Hz, 1H), 5.55 (s, 1H), 5.48 (brs, 1H), 5.13 (brs, 1H), 5.09 (s, 1H), 4.99 (brs, 1H), 4.86 (d, *J* = 6.3 Hz, 1H), 4.74 (d, *J* = 7.0 Hz, 1H), 4.43 (tt, *J* = 7.5, 3.6 Hz, 1H), 4.36 – 4.28 (m, 4H), 4.20 (dd, *J* = 8.6, 3.5 Hz, 1H), 3.77 (s, 3H), 3.74 (t, *J* = 6.5 Hz, 4H), 3.69 – 3.63 (m, 2H), 3.51 – 3.42 (m, 4H), 3.29 (d, *J* = 14.5 Hz, 1H), 3.08 (ddd, *J* = 12.2, 8.4, 3.4 Hz, 2H), 2.76 – 2.68 (m, 1H),

2.61 – 2.51 (m, 1H), 2.45 (s, 3H), 2.29 – 2.14 (m, 5H), 2.12 – 2.05 (m, 2H), 1.96 – 1.83 (m, 4H), 1.55 (s, 3H), 1.39 (s, 9H), 1.37 (s, 3H), 1.26 (s, 3H), 1.04 (d, *J* = 4.6 Hz, 42H), 1.01 (s, 6H), 0.99 (s, 6H); ^{13}C NMR (101 MHz, $CDCl_3$) δ 173.0, 172.3, 171.22, 171.15, 162.0, 159.5, 157.5, 155.8, 150.6, 142.83, 142.81, 136.9, 135.4, 131.3, 129.36, 129.35, 129.31, 129.30, 129.03, 128.99, 128.95, 128.93, 126.1, 122.5 (2C), 116.8 (2C), 116.6, 115.33, 115.29, 107.3, 106.9, 84.1, 79.30, 79.28, 79.26, 79.24, 79.23, 74.88, 74.87, 73.6, 72.83, 72.80, 70.61, 70.56, 69.8, 67.3, 60.39, 60.36, 60.0, 59.9, 55.70 (2C), 54.2, 46.6 (2C), 46.1, 46.0, 45.0, 44.9, 44.7, 43.1, 41.2, 32.61, 32.59, 30.33 (2C), 30.27, 30.25, 29.69, 29.67, 29.65, 29.60, 28.52, 28.45, 27.31, 27.28, 27.24, 27.23, 27.22, 27.15, 25.14, 25.11, 22.7, 18.1 (12C), 14.2, 14.1, 11.9 (6C); HRMS (ESI+) *m*/*z* calcd for $C_{95}H_{139}Cl_4F_3N_7O_{21}Si_2$ [M + H] 1966.8269, found: 1966.8288.

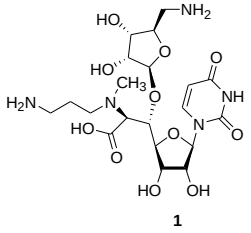


4-(((2*S*,3*S*)-1-Amino-3-(((2*S*,3*R*,4*S*,5*R*)-5-(aminomethyl)-3,4-dihydroxytetrahydrofuran-2-yl)oxy)-3-((2*S*,5*R*)-5-(2,4-dioxo-3,4-dihydropyrimidin-1(2*H*)-yl)-3,4-dihydroxytetrahydrofuran-2-yl)-1-oxopropan-2-yl)(methyl)amino)-*N*-(4-(4-(4-(trifluoromethoxy)phenoxy)piperidin-1-yl)benzyl)butanamide (12). To a stirred solution of **26** (4.7 mg, 2.4 μmol) in CH_2Cl_2 (0.70 mL) was added TFA (0.30 mL). The reaction mixture was stirred for 2 h at rt, and all volatile were evaporated in vacuo. To a stirred solution of the crude mixture in H_2O (0.2 mL) was added TFA (0.8 mL). The reaction mixture was stirred for 4 h at 40 °C, and all volatile were evaporated in vacuo. The crude mixture was purified by silica gel column chromatography ($CHCl_3$/MeOH 80:20 to $CHCl_3$/MeOH/H_2O/50% aqueous ammonia 56:42:7:3) to afford **12 (UT-17465)** (2.0 mg, 2.2 μmol, 92%): TLC (n-butanol/ethanol/$CHCl_3$/28% aqueous ammonia 4:7:2:7) R_f = 0.55; $[\alpha]^{20}_D$ +0.246 (*c* = 0.24, methanol); IR (thin film) ν_{max} = 3276 (br), 2933, 1675, 1505, 1465, 1271, 1243, 1199, 1111 cm^{-1}; ^{1}H NMR (400 MHz, CD_3OD) δ 7.84 (d, *J* = 7.7 Hz, 1H), 7.19 (dd, *J* = 8.5, 3.3 Hz, 4H), 7.01 (dd, *J* = 13.1, 8.6 Hz, 4H), 5.86 (d, *J* = 7.8 Hz, 1H), 5.73 (d, *J* = 2.4 Hz, 1H), 5.16 (s, 1H), 4.54 (tt, *J* = 7.3, 3.1 Hz, 1H), 4.30 – 4.25 (m, 3H), 4.26 (d, *J* = 9.2 Hz, 1H), 4.22 – 4.05 (m, 6H), 3.70 (d, *J* = 9.2 Hz, 1H), 3.52 – 3.44 (m, 2H), 3.09 (ddt, *J* = 12.3, 8.6, 4.3 Hz, 2H), 2.91 – 2.82 (m, 1H), 2.58 – 2.53 (m, 1H), 2.50 (s, 3H), 2.30 (q, *J* = 6.9 Hz, 2H), 2.15 – 2.08 (m, 2H), 1.96 – 1.82 (m, 3H), 1.81 – 1.71 (m, 1H), 1.39 – 1.25 (m, 2H); ^{13}C NMR (101 MHz, CD_3OD) δ 175.3, 172.2, 157.6, 152.0, 142.4, 131.3, 129.7 (2C), 123.6 (2C), 118.12 (2C), 118.08 (2C), 111.9, 92.1, 84.4, 80.3, 78.4, 76.4, 75.4, 74.1 (2C), 71.5, 70.8, 68.3, 43.7, 39.7, 34.5, 31.5 (2C), 24.5; HRMS (ESI+) *m*/*z* calcd for $C_{40}H_{53}F_3N_7O_{13}$ [M + H] 896.3653, found: 896.3640.

Figure S5. HPLC analysis of **12 (UT-17465)**.

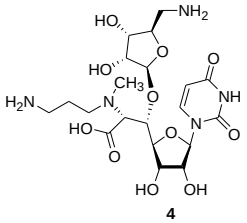


Area % purity: 94.3%
Conditions:
column: Phenomenex Kinetex 1.7 µ XB-C18 100 Å 150 x 2.10 mm column, solvents: 70 : 30 MeOH : 0.05M NH_4HCO_3 in water, UV: 254 nm



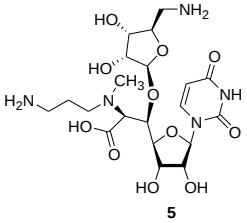
1

(2*S*,3*S*)-3-(((2*S*,3*R*,4*S*,5*R*)-5-(Aminomethyl)-3,4-dihydroxytetrahydrofuran-2-yl)oxy)-2-((3-aminopropyl)(methyl)amino)-3-((2*S*,5*R*)-5-(2,4-dioxo-3,4-dihydropyrimidin-1(2*H*)-yl)-3,4-dihydroxytetrahydrofuran-2-yl)propanoic acid (1).
^{1}H NMR (400 MHz, D_2O) δ 7.79 (d, *J* = 7.9 Hz, 1H), 5.83 (d, *J* = 7.8 Hz, 1H), 5.75 (d, *J* = 2.3 Hz, 1H), 5.20 (s, 1H), 4.33 (dd, *J* = 2.3, 5.1 Hz, 1H), 4.28 (dd, *J* = 2.3, 8.4 Hz, 1H), 4.23 – 4.19 (m, 2H), 4.16 (dd, *J* = 2.8, 6.1 Hz, 1H), 4.13 – 4.07 (m, 2H), 3.49 (d, *J* = 8.3 Hz, 1H), 3.18 (dd, *J* = 3.6, 13.7 Hz, 1H), 3.05 – 3.00 (m, 3H), 2.88 – 2.83 (m, 1H), 2.64 – 2.61 (m, 1H), 2.41 (s, 3H), 1.94 – 1.88 (m, 1H), 1.82 – 1.78 (m, 1H); ^{13}C NMR (101 MHz, D_2O) δ 175.7, 171.4, 155.2, 141.9, 110.1, 102.5, 91.4, 83.7, 80.8, 78.5, 75.4, 74.2, 71.4, 71.3, 70.0, 52.4, 41.8, 39.0, 38.7, 25.0; HRMS (ESI+) *m*/*z* calcd for $C_{20}H_{34}N_5O_{11}$ [M + H] 520.2255, found: 520.2262.



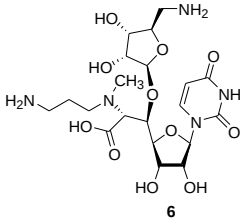
4

(2*R*,3*S*)-3-(((2*S*,3*R*,4*S*,5*R*)-5-(Aminomethyl)-3,4-dihydroxytetrahydrofuran-2-yl)oxy)-2-((3-aminopropyl)(methyl)amino)-3-((2*S*,5*R*)-5-(2,4-dioxo-3,4-dihydropyrimidin-1(2*H*)-yl)-3,4-dihydroxytetrahydrofuran-2-yl)propanoic acid (4).
^{1}H NMR (400 MHz, D_2O) δ 7.83 (d, *J* = 8.0 Hz, 1H), 5.90 (d, *J* = 8.3 Hz, 1H), 5.73 (d, *J* = 2.1 Hz, 1H), 5.25 (s, 1H), 4.36 (d, *J* = 7.7 Hz, 1H), 4.28 – 4.19 (m, 2H), 4.18 (d, *J* = 10.4 Hz, 1H), 4.12 – 4.06 (m, 2H), 3.45 (d, *J* = 10.4 Hz, 1H), 3.32 (dd, *J* = 14.1, 3.7 Hz, 1H), 3.15 (dd, *J* = 13.9, 5.6 Hz, 1H), 3.10 – 3.03 (m, 3H), 2.97 – 2.87 (m, 1H), 2.59 – 2.51 (m, 1H), 2.43 (s, 3H), 1.99 – 1.93 (m, 1H), 1.87 – 1.77 (m, 1H); HRMS (ESI+) *m*/*z* calcd for $C_{20}H_{34}N_5O_{11}$ [M + H] 520.2255, found: 520.2272.



5

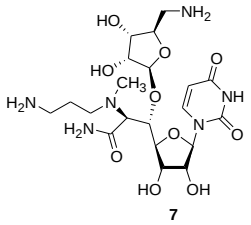
(2*S*,3*R*)-3-(((2*S*,3*R*,4*S*,5*R*)-5-(Aminomethyl)-3,4-dihydroxytetrahydrofuran-2-yl)oxy)-2-((3-aminopropyl)(methyl)amino)-3-((2*S*,5*R*)-5-(2,4-dioxo-3,4-dihydropyrimidin-1(2*H*)-yl)-3,4-dihydroxytetrahydrofuran-2-yl)propanoic acid (5).
^{1}H NMR (400 MHz, D_2O) δ 7.68 (d, *J* = 8.2 Hz, 1H), 5.93 (d, *J* = 8.1 Hz, 1H), 5.77 (d, *J* = 4.3 Hz, 1H), 5.33 (s, 1H), 4.50 – 4.44 (m, 3H), 4.20 – 4.11 (m, 3H), 4.06 (dd, *J* = 5.2, 4.7 Hz, 1H), 3.61 (d, *J* = 6.9 Hz, 1H), 3.37 (d, *J* = 13.2 Hz, 1H), 3.13 (dd, *J* = 13.2, 8.7 Hz, 1H), 3.06 (t, *J* = 7.3 Hz, 2H), 2.84 (dt, *J* = 13.5, 6.6 Hz, 1H), 2.74 (dt, *J* = 12.8, 6.7 Hz, 1H), 2.44 (s, 3H), 1.89 (dq, *J* = 13.8, 6.6 Hz, 2H); HRMS (ESI+) *m*/*z* calcd for $C_{20}H_{34}N_5O_{11}$ [M + H] 520.2255, found: 520.2251.



6

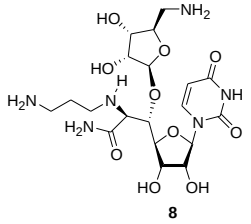
(2*R*,3*R*)-3-(((2*S*,3*R*,4*S*,5*R*)-5-(Aminomethyl)-3,4-dihydroxytetrahydrofuran-2-yl)oxy)-2-((3-aminopropyl)(methyl)amino)-3-((2*S*,5*R*)-5-(2,4-dioxo-3,4-dihydropyrimidin-1(2*H*)-yl)-3,4-dihydroxytetrahydrofuran-2-yl)propanoic acid (6).
^{1}H NMR (400 MHz, D_2O) δ 7.67 (d, *J* = 8.0 Hz, 1H), 5.91 (d, *J* = 8.0 Hz, 1H), 5.78 (d, *J* = 5.2 Hz, 1H), 5.31 (s, 1H), 4.49 – 4.44 (m, 1H), 4.43 (t, *J* = 5.3 Hz, 2H), 4.16 – 4.07 (m, 3H), 4.05 (t, *J* =

5.3 Hz, 1H), 3.54 (d, *J* = 7.3 Hz, 1H), 3.23 (dd, *J* = 13.3, 3.0 Hz, 1H), 3.10 – 2.98 (m, 3H), 2.80 (dt, *J* = 13.3, 6.7 Hz, 1H), 2.67 (dt, *J* = 13.3, 6.9 Hz, 1H), 2.38 (s, 3H), 1.86 (dq, *J* = 13.9, 7.1 Hz, 2H); HRMS (ESI+) *m*/*z* calcd for $C_{20}H_{34}N_5O_{11}$ [M + H] 520.2255, found: 520.2247.



7

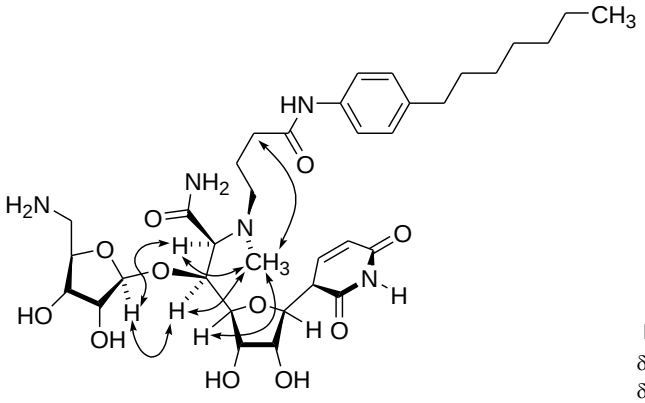
(2*S*,3*S*)-3-(((2*S*,3*R*,4*S*,5*R*)-5-(Aminomethyl)-3,4-dihydroxytetrahydrofuran-2-yl)oxy)-2-((3-aminopropyl)(methyl)amino)-3-((2*S*,5*R*)-5-(2,4-dioxo-3,4-dihydropyrimidin-1(2*H*)-yl)-3,4-dihydroxytetrahydrofuran-2-yl)propanamide (7). ^{1}H NMR (400 MHz, D_2O) δ 7.83 (d, *J* = 8.1 Hz, 1H), 5.91 (d, *J* = 8.0 Hz, 1H), 5.72 (s, 1H), 5.27 (s, 1H), 4.44 – 4.37 (m, 1H), 4.32 – 4.25 (m, 2H), 4.23 (t, *J* = 6.5 Hz, 1H), 4.20 – 4.14 (m, 1H), 4.11 (d, *J* = 8.2 Hz, 1H), 3.68 (dd, *J* = 16.3, 8.1 Hz, 1H), 3.43 (d, *J* = 14.0 Hz, 1H), 3.26 (dd, *J* = 13.6, 5.2 Hz, 2H), 3.07 (t, *J* = 7.3 Hz, 2H), 3.03 – 2.95 (m, 1H), 2.64 – 2.56 (m, 1H), 2.50 (s, 3H), 2.04 – 1.94 (m, 1H), 1.88 – 1.79 (m, 1H); HRMS (ESI+) *m*/*z* calcd for $C_{20}H_{35}N_6O_{10}$ [M + H] 519.2415, found: 519.2432.



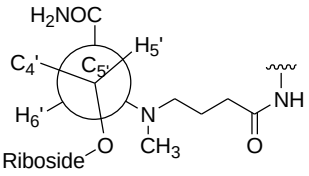
8

(2*S*,3*S*)-3-(((2*S*,3*R*,4*S*,5*R*)-5-(Aminomethyl)-3,4-dihydroxytetrahydrofuran-2-yl)oxy)-2-((3-aminopropyl)amino)-3-((2*S*,5*R*)-5-(2,4-dioxo-3,4-dihydropyrimidin-1(2*H*)-yl)-3,4-dihydroxytetrahydrofuran-2-yl)propanamide (8). ^{1}H NMR (400 MHz, D_2O) δ 7.78 (d, *J* = 8.1 Hz, 1H), 5.89 (d, *J* = 7.8 Hz, 1H), 5.78 (d, *J* = 3.1 Hz, 1H), 5.22 (s, 1H), 4.40 (dd, *J* = 5.5, 3.2 Hz, 1H), 4.29 (t, *J* = 6.3 Hz, 1H), 4.22 (dd, *J* = 6.8, 5.1 Hz, 1H), 4.18 (t, *J* = 4.5 Hz, 1H), 4.16 – 4.08 (m, 3H), 3.59 (d, *J* = 3.8 Hz, 1H), 3.28 (d, *J* = 12.6 Hz, 1H), 3.11 – 3.02 (m, 3H), 2.77 (dt, *J* = 12.8, 6.8 Hz, 1H), 2.64 (dt, *J* = 12.7, 7.0 Hz, 1H), 1.83 (quin, *J* = 7.1 Hz, 2H); HRMS (ESI+) *m*/*z* calcd for $C_{19}H_{33}N_6O_{10}$ [M + H] 505.2258, found: 505.2277.

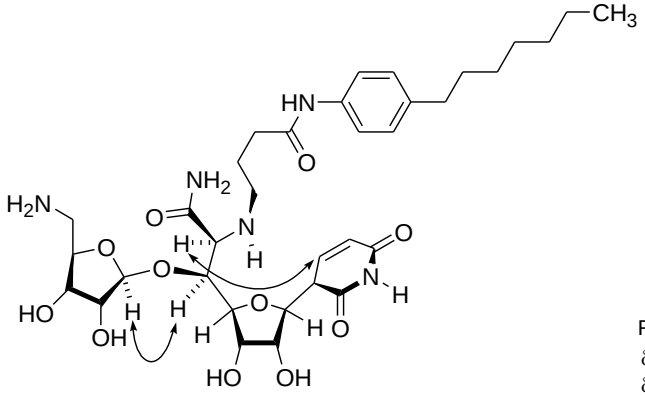
Figure S6. Conformational analyses of **9-12**.[6]



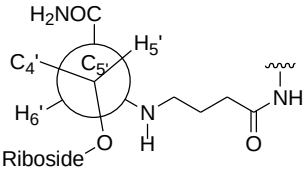
UT-17415 (9)



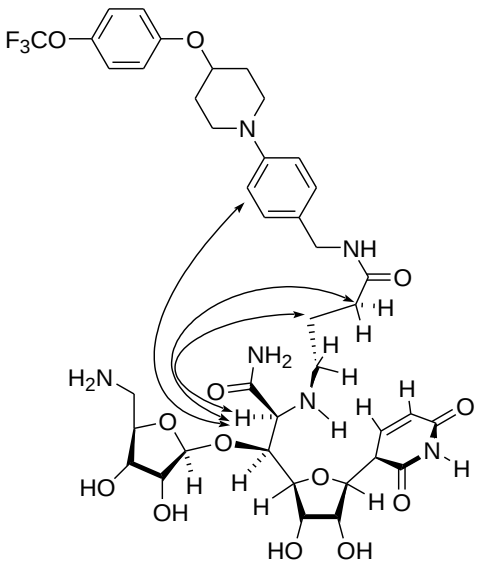
δ 4.28 (d, H-5', $J_{5'\text{-}6'}$ = 9.3 Hz, 1H)
δ 3.61 (d, H-6', $J_{6'\text{-}5'}$ = 9.4 Hz, 1H)
Calculated dihedral angle H5'-C-C-H6': ϕ192



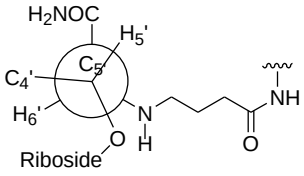
UT-17455 (10)



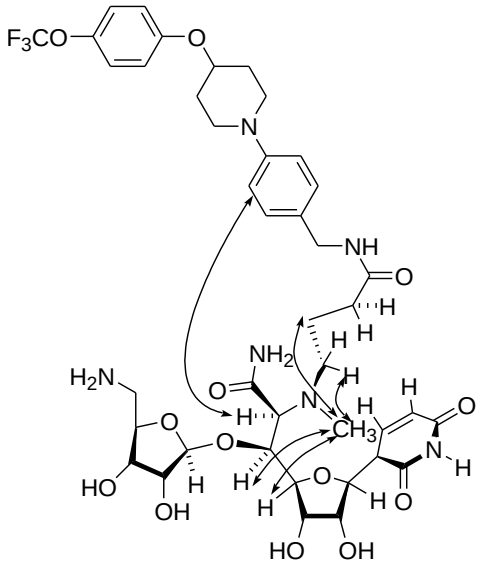
δ 4.21 (dd, H-5', $J_{5'\text{-}6'}$ = 9.3 Hz, $J_{5'\text{-}4'}$ = 4.7 Hz, 1H)
δ 3.50 (d, H-6', $J_{6'\text{-}5'}$ = 8.9 Hz, 1H)
Calculated dihedral angle H5'-C-C-H6': ϕ188



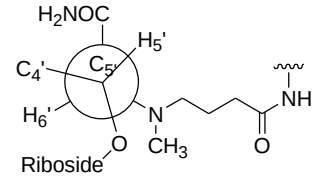
UT-17460 (11)



δ 4.10 (dd, H-5', $J_{5'\text{-}6'}$ = 8.6 Hz, $J_{5'\text{-}4'}$ = 4.4 Hz, 1H)
δ 3.44 (d, H-6', $J_{6'\text{-}5'}$ = 8.8 Hz, 1H)
Calculated dihedral angle H5'-C-C-H6': ϕ207



UT-17465 (12)

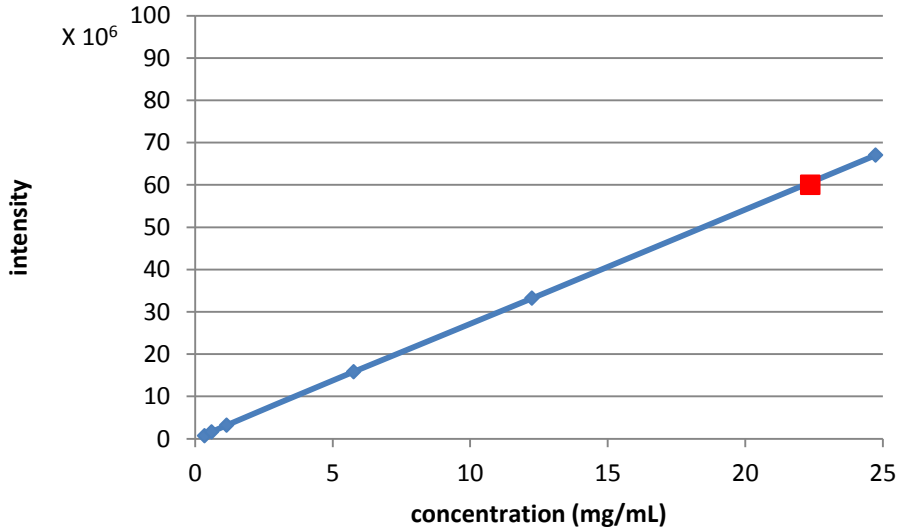


δ 4.26 (d, H-5', $J_{5'\text{-}6'}$ = 9.2 Hz, 1H)
δ 3.70 (d, H-6', $J_{6'\text{-}5'}$ = 9.2 Hz, 1H)
Calculated dihedral angle H5'-C-C-H6': ϕ196

Determination of water-solubility of 11 (UT-17460).

A suspension of **11** (3.0 mg) in H_2O (50 μL) was stirred for 24h, and the precipitate was separated by centrifugation at 10,000 x g for 5 min. The upper solution (1 μL) was analyzed via C18 reverse-phase HPLC [column: Kinetex (100 Å, 5 μm, 250 x 4.60 mm), solvents: 75:25 MeOH : 0.05M NH_4HCO_3 aq., flow rate: 0.5 mL/min, UV: 254 nm, retention time: 13.2 min]. The area of the peak for **11** was quantified. The concentrations were determined via the HPLC intensity-concentration curves.[7,8,9]

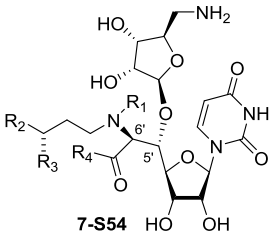
Figure S7. Concentration of **11**.



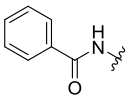
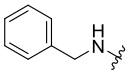
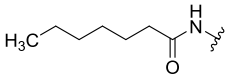
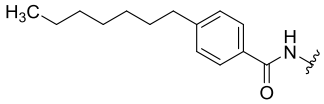
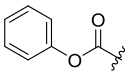
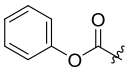
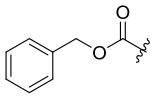
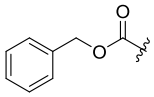
concentration (mg/mL)	0.35	0.6	1.15	5.77	12.25	22.36
intensity	662186	1559793	3197580	15843516	33184625	60023983

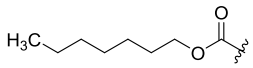
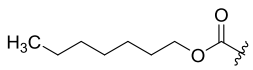
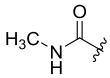
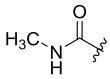
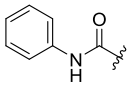
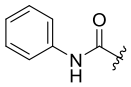
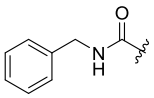
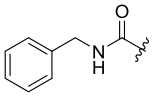
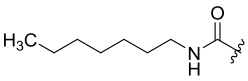
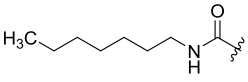
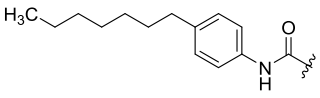
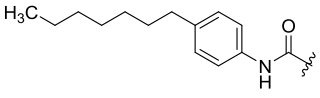
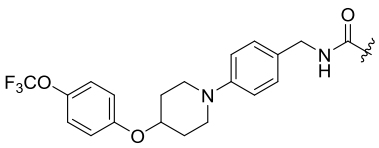
Table S1. Representative structures of a library of FR-900493 analogs.

1: FR-900493
4: 5'*S*, 6'*R*-diastereomer
5: 5'*R*, 6'*S*-diastereomer
6: 5'*R*, 6'*R*-diastereomer
(see Table 1 in text)



7-S54

Compound	R_1	R_2	R_3	R_4	WecA inhibition[a]	MraY inhibition[b]	anti *C. difficile* activity[c]
1	CH_3	NH_2	H	OH	+	+	–
4	CH_3	NH_2	H	OH	–	–	–
5	CH_3	NH_2	H	OH	–	–	–
6	CH_3	NH_2	H	OH	–	–	–
8	H	NH_2	H	NH_2	–	–	–
7	CH_3			NH_2	+	+	–
S9	H		H	NH_2	–	–	–
S10	CH_3			NH_2	–	–	–
S11	H		H	NH_2	–	–	–
S12	CH_3			NH_2	–	–	–
S13	H		H	NH_2	–	–	–
S14	CH_3			NH_2	–	–	–
S15	H		H	NH_2	–	–	–
S16	CH_3			NH_2	–	–	–
S17	H		H	NH_2	–	–	–
S18	CH_3			NH_2	–	–	–
S19	H		OH	NH_2	–	–	–
S20	CH_3			NH_2	–	–	–
S21	H		H	NH_2	–	–	–
S22	CH_3			NH_2	–	–	–
S23	H		OH	NH_2	–	–	–
S24	CH_3			NH_2	–	–	–
S25	H		H	NH_2	–	–	–
S26	CH_3			NH_2	–	–	–
S27	H		OH	NH_2	–	–	–
S28	CH_3			NH_2	–	–	–

Compound	R_1	R_2	R_3	R_4	WecA inhibition[a]	MraY inhibition[b]	anti *C. difficile* activity[c]
S29	H		H	NH_2	–	–	–
S30	CH_3			NH_2	–	–	–
S31	H		OH	NH_2	–	–	–
S32	CH_3			NH_2	–	–	–
S33	H		H	NH_2	–	–	–
S34	CH_3			NH_2	–	–	–
S35	H		OH	NH_2	–	–	–
S36	CH_3			NH_2	–	–	–
S37	H		H	NH_2	–	–	–
S38	CH_3			NH_2	–	–	–
S39	H		OH	NH_2	–	–	–
S40	CH_3			NH_2	–	–	–
S41	H		H	NH_2	–	–	–
S42	CH_3			NH_2	–	–	–
S43	H		OH	NH_2	–	–	–
S44	CH_3			NH_2	–	–	–
S45	H		H	NH_2	–	–	–
S46	CH_3			NH_2	–	–	–
S47	H		OH	NH_2	–	–	–
S48	CH_3			NH_2	–	–	–
S49	H		H	NH_2	–	–	–
S50	CH_3			NH_2	–	–	–
S51	H		OH	NH_2	–	–	–
S52	CH_3			NH_2	–	–	–
10	H		H	NH_2	+	+	+
9	CH_3			NH_2	+	+	+
S53	H		OH	NH_2	–	–	–
S54	CH_3			NH_2	–	–	–
11	H		H	NH_2	+	+	+
12	CH_3			NH_2	+	+	+

[a]WecA: at 25 μM.; [b]MraY assay: at 25 μM. [c]*C. difficile* ATCC43596: 50 μg/mL.

Bacterial strains and growth of bacteria

Mycobacterium smegmatis (ATCC 607), *Klebsiella pneumoniae* (ATCC 8047), *Pseudomonas aeruginosa* (ATCC 27853), *Acinetobacter baumannii* (ATCC 19606), *Staphylococcus aureus* (BAA-1683), *Clostridium difficile* (ATCC 43596), *Enterococcus faecium* (ATCC 349), *Fusobacterium periodontium* ATCC 33693), *Bacteroides fragilis* (ATCC 25285), *Streptococcus pneumoniae* (ATCC 6301), *Bacillus subtilis* (ATCC 6051), *Clostridium perfringens* (ATCC 13124), *Lactobacillus casei* (ATCC 393), *Lactobacillus acidophilus* (ATCC 4356), and *E. coli* (ATCC 10798) were obtained from American Type Culture Collection (ATCC). A single colony of *Mycobacterium smegmatis* was obtained on Difco Middlebrook 7H10 nutrient agar enriched with with albumin, dextrose, and catalase (ADC). Single colonies of *P. aeruginosa, K. pneumoniae, A. baumannii, S.aureus, E. faecium and E. coli* were grown on tryptic soy agar for 24 h at 37^{o}C in a static incubator and cultured in tryptic soy broth until log phase to be an optical density (OD) of 0.2-0.5. The OD was monitored at 600 and 570 nm using a 96-well microplate reader. A single colony of *C. difficile* was obtained on a BHI agar plate and incubated at 37 ^{o}C under anaerobic conditions for 48 h (Gas: 10% hydrogen, 5% carbon dioxide and 85% nitrogen mixture was used. Chambers: Plas Labs™ Model 855 Anaerobic Chambers was used.). The other bacteria were cultured in the recommended conditions by ATCC.

MIC assays

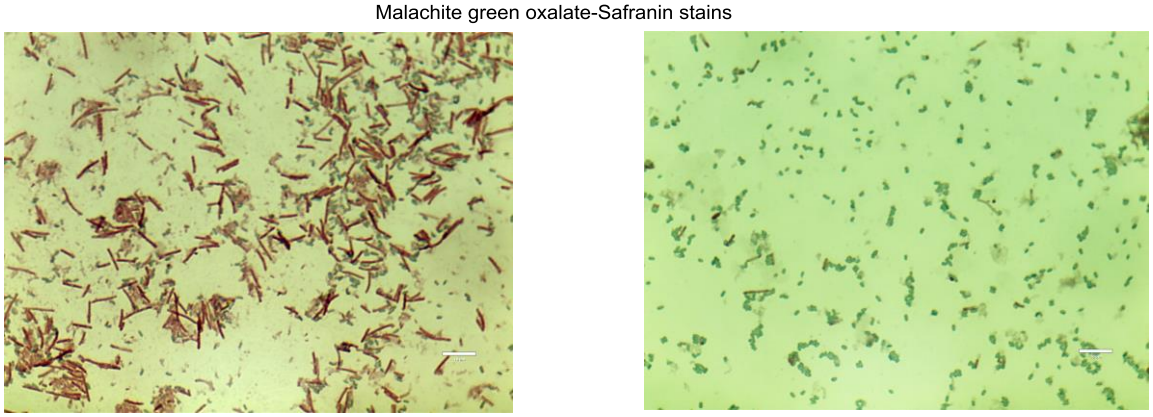
Minimum inhibitory concentrations were determined by broth dilution microplate alamar blue assay or by OD measurement. All compounds were stored in DMSO or PEG400-water (1/1) (1 mg/100 μL concentration). This concentration was used as the stock solution for all MIC studies. Each compound from stock solution was placed in the first well of a sterile 96 well plate and a serial dilution was conducted with the culturing broth (total volume of 10 μL). The bacterial suspension at log phase (190 μL) was added to each well (total volume of 200 μL). *M. smegmatis, P. aeruginosa, K. pneumoniae, A. baumannii, S. aureus, E. faecium, E. coli,* and the aerobic bacteria were incubated for 24 h at 37 ^{o}C. *Clostridium spp.* were incubated for 48 h at 37 ^{o}C under anaerobic condition. 20 μL of resazurin (0.02%) was added to each well and incubated for 4 h for *Mycobacterium spp.*, and 1 h for the other bacteria (National Committee for Clinical Laboratory Standards (NCCLS) method (pink = growth, blue = no visible growth)).The OD measurements were performed for all experiments prior to colorimetric The anaerobic bacteria were applied to a microplate reader. The MIC values were determined according to the colorimetric assays using resazurin. The absorbance of each well was also measured at 570 and 600 nm via UV-Vis. The MIC values of the anaerobic bacteria (*Clostridium spp*.) were determined via OD_{600} and OD_{570}. If necessary, CFU method was applied to confirm bactericidal activity.

***C. difficile* spore preparation.**

C. difficile (ATCC 43596) was inoculated on a BHI agar plate and incubated at 37 ^{o}C under anaerobic condition for 14 days. The spores were harvested by flooding plates with deionized water and gently scrapping the bacterial lawns. The harvested cells were

pelleted via centrifugation at 4,700 x g for 20 min. and washed with deionized water (x3). The obtained bacterial pellet was suspended sterile water and the vegetative forms of *C. difficile* were killed upon heating at 50 ^{0}C for 30 min.,[10,11] and the bacteria were washed with sterile water (x3). The washed pellet was resuspended in sterile water (10 mL) and layered on top of sterile 50% sucrose (in water). The gradient was centrifuged at 3,200 x g for 20 min. The 50% sucrose bed was separated and the spore pellet was washed with sterile water (x5). All cells appeared a bright greenish color upon staining with malachite green oxalate. The prepared spores were suspended (OD_{600} ~0.2) in sterile distilled water at 4 ^{o}C.

Figure S8. Microscopic analyses of *C. difficile* spores (x100).



Spore viability assays.

A solution of test compound was added to a suspension containing *C. difficile* spores (2 x 10^5 ml^{-1}), and the mixture was incubated at 37 ^{o}C for 24 h. The spore suspension treated with test compound was centrifuged (4,700 x g) and the pellet was washed with sterile distilled water, and plated on a BHI agar containing 0.1% sodium taurocholate (a germination agent) and incubated at 37 ^{o}C for 48h under anaerobic conations. The resulting colonies were counted. Separately, the *C. difficile* spore suspension treated with test molecules 24 h was cultured in a BHI medium containing 0.1% sodium taurocholate. After 48 h, variability of the *C. difficile* spores was quantitated by the OD_{600} value.

Table S2. MIC (μg/mL) against *C. difficile* (ATCC 43596)

Vancomycin:	2.50
Metronidazole:	0.39
Linezolid:	1.56
UT-17415 (**9**):	25.0
UT-17455 (**10**):	12.5
UT-17460 (**11**):	3.25
UT-17465 (**12**):	50.0

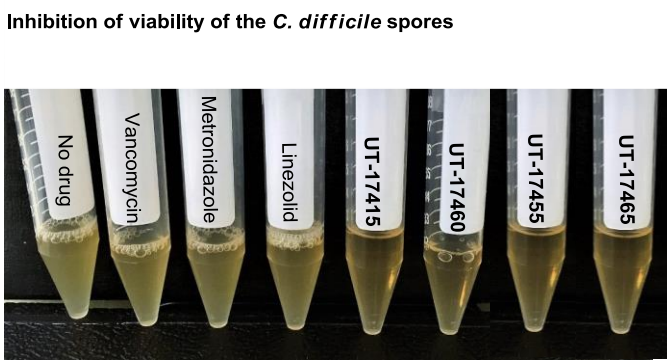
	No drug	Vancomycin[1]	Metronidazole[1]	Linezolid[1]
CFU (x10^6/mL)	1250	1150	1100	1200
OD_{600}	0.4-0.6	0.45	0.48	0.49

[1] X 5 MIC was used

	UT-17415 (**9**)[2]	UT-17455 (**10**)[2]	UT-17460 (**11**)[2]	UT-17465 (**12**)[2]
CFU	0	0	0	0
OD_{600}	0.02	0.02	0.02	0.02

[2] X 2 MIC was used

Figure S9. Growth of *C. difficile* spores treated with drugs.



The *C. difficile* spores (OD_{600} ~0.2) were treated with 2X MIC (9, 10, 11, and 12) or 5X MIC (vancomycin, metronidazole, and linezolid). After 24 h, portion (100 μL) of each spore suspension was cultured in a BHI medium containing 0.1% sodium taurocholate for 48 h.

Preparation of membrane fraction P-60 containing MraY and WecA

M. smegmatis cells were harvested by centrifugation (4700 rpm) at 4 ^oC followed by washing with 0.9% saline solution (thrice), and approximately 5 g of pellet (wet weight) was collected. The washed cell pellets were suspended in homogenization buffer (containing 50 mM MOPS [pH = 8.0], 10 mM $MgCl_2$, and 5 mM 2-mercaptoethanol) and disrupted by probe sonication on ice (10 cycles of 60 s on and 90 s off). The resulting suspension was centrifuged at 1,000 x g for 10 min at 4 ^oC to remove unbroken cells. The supernatant was centrifuged at 15,000 x g for 40 min at 4 ^oC (2 or 3 times). All pellets in each tube were pooled, and a second sonication was performed (10 cycles of 60 s on and 90 s off). The lysate was centrifuged once at 15,000 xg for 1 h, and the supernatant was subjected to ultracentrifugation at 60,000 x g for 1 h at 4 ^oC. The supernatant was discarded, and the membrane fraction containing MraY enzyme (P-60) was suspended in the Tris-HCl buffer (pH = 7.5) containing 2-mercaptoethanol. Total protein concentrations were approximately 8 to 10 mg/mL. Aliquots were stored in Eppendorf tubes at -80 ^oC. Similarly, the membrane fractions containing WecA enzyme (P-60) were prepared from *E. coli*.

Expression and purification of *Hy*MraY

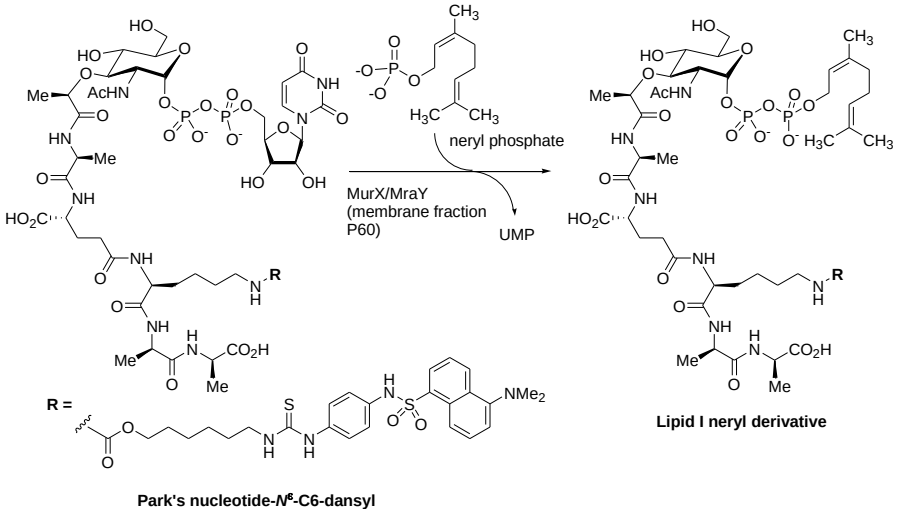
The gene *mraY* of *Hydrogenivirga spp.* 128-5-R1-1 was cloned with a *N*-terminal His_6 tag into a pET22b vector. The plasmid was transformed and expressed in *E. coli* NiCo21(DE3) pLEMO competent cells. The proteins were purified using a nickel, cation exchange, and size exclusion chromatography. The final storage buffer was 20 mM HEPES pH 7.5, 100 mM NaCl, 10% glycerol, 5 mM βME, 0.15% DM.

Expression and purification of *Mj*AglH

The gene *mj1113* of *Methanocaldococcus jannaschii* DSM 2661 was cloned with a *N*-terminal His_9 tag into a pET33b-derived vector. The plasmid was transformed and expressed in *E. coli* NiCo21(DE3) pLEMO competent cells. The proteins were purified using cobalt and size exclusion chromatography. The final storage buffer was 20 mM Tris-HCl, pH 7.5, 100 mM NaCl, 5% glycerol, 5 mM βME, 0.15% DM.

MraY assay.

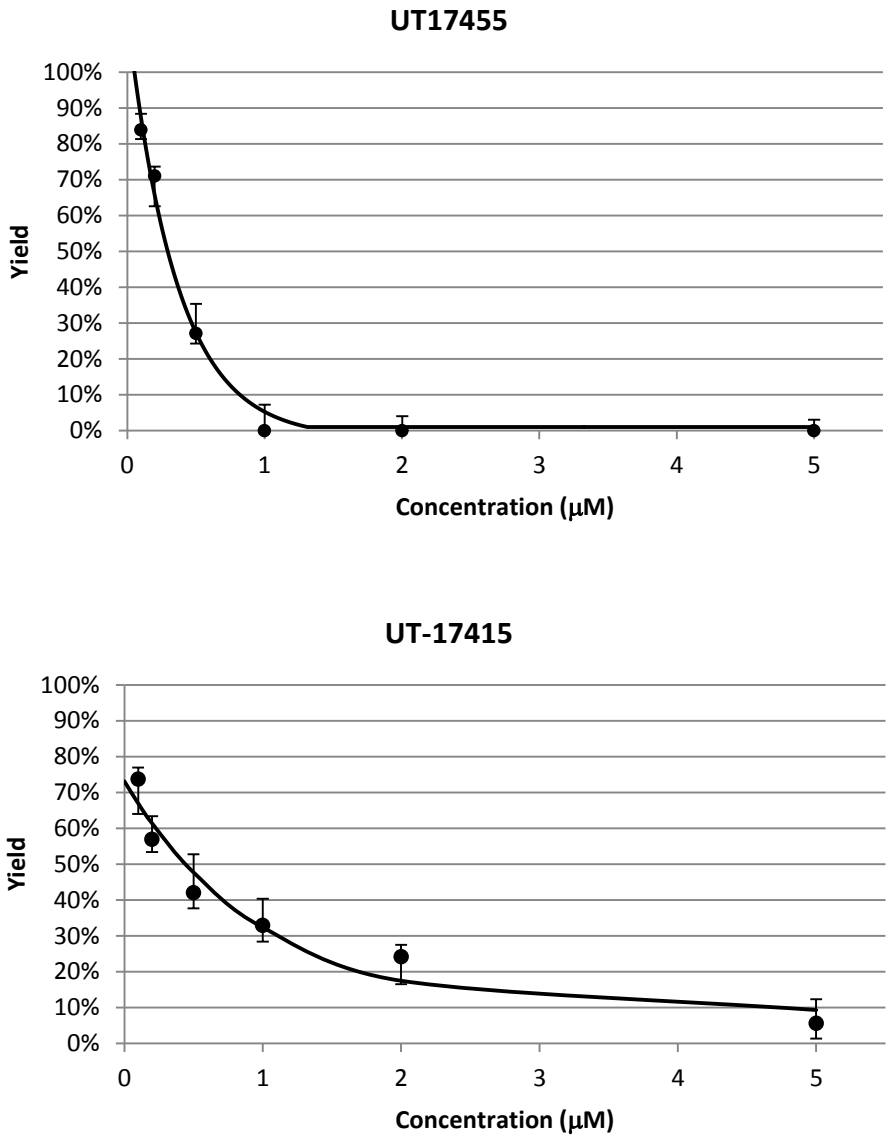
MraY assay substrates, Park's nucleotide-N^{ε}-C6-dansyl, neryl phosphate, were chemically synthesized according to the reported procedures. [12]

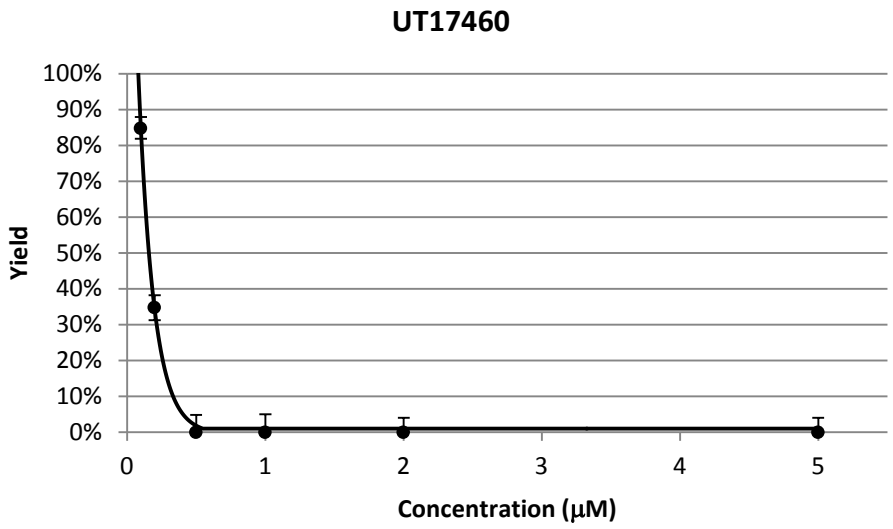


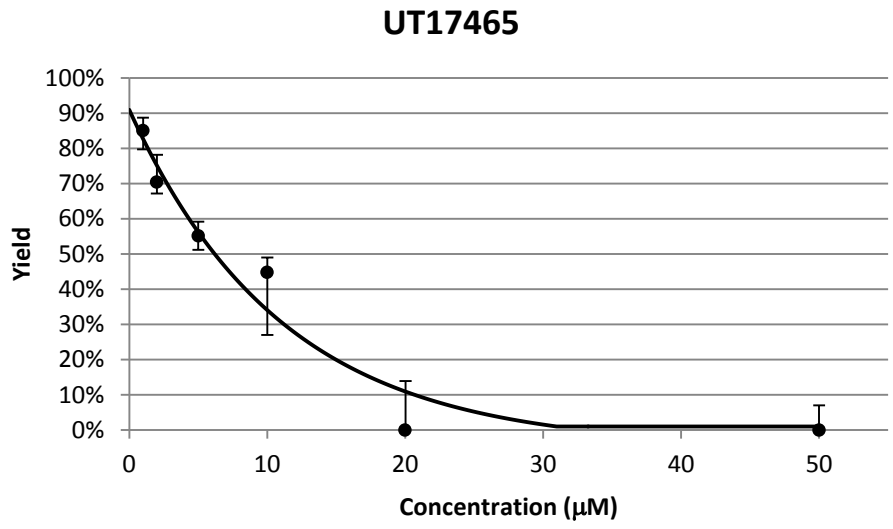
Park's nucleotide-N^{ε}-C6-dansyl (2 mM stock solution, 1.88 μL), $MgCl_2$ (0.5 M, 5 μL), KCl (2 M, 5 μL), Triton X-100 (0.5%, 5.63 μL), Tris buffer (pH 8.0, 50 mM), neryl phosphate (0.1 M, 2.25 μL), and inhibitor molecue (0 - 100 μg/mL in Tris buffer) were placed in a 500 μL Eppendorf tube. To a stirred reaction mixture, P-60 (10μL) was added (total volume of reaction mixture: 50 μL adjust with Tris buffer). The reaction mixture was incubated for 2 h at room temperature (26 ^{o}C) and quenched with $CHCl_3$ (100μL). Two phases were mixed via vortex and centrifuged at 25,000 xg for 10 min. The upper aqueous phase was assayed via reverse-phase HPLC. The water phase (10 μL) was injected into HPLC (solvent: CH_3CN/0.05 M aq. NH_4HCO_3 = 25:75; UV: 350 nm; flow rate: 0.5 mL/min; column: Kinetex 5μm C8, 100 A, 150 x 4.60 mm), and the area of the peak for lipid I-neryl derivative was quantified to obtain the IC_{50} value. The IC_{50} values were calculated from plots of the percentage product inhibition versus the inhibitor

concentration.

Figure S10.

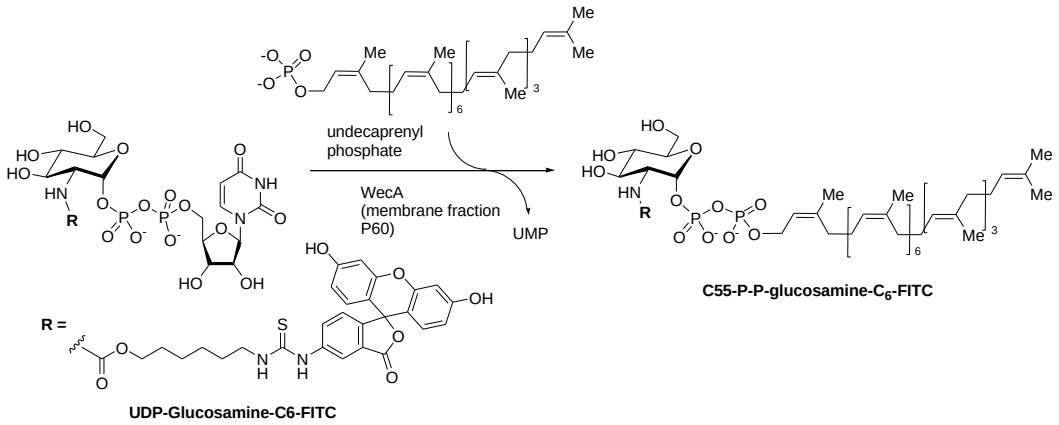



UT17460
100%
90%
80%
70%
60%
50%
40%
30%
20%
10%
0%
Yield
0
1
2
3
4
5
Concentration (μM)


UT17465
100%
90%
80%
70%
60%
50%
40%
30%
20%
10%
0%
Yield
0
10
20
30
40
50
Concentration (μM)

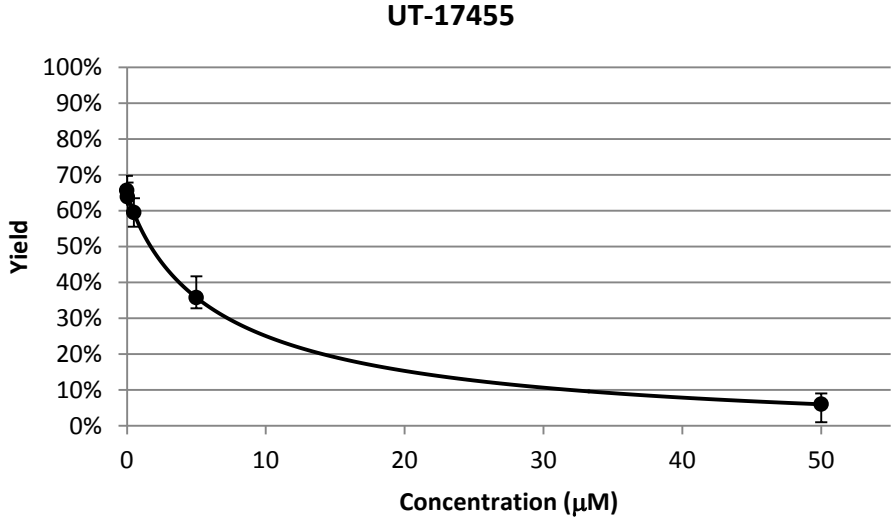
WecA assay.

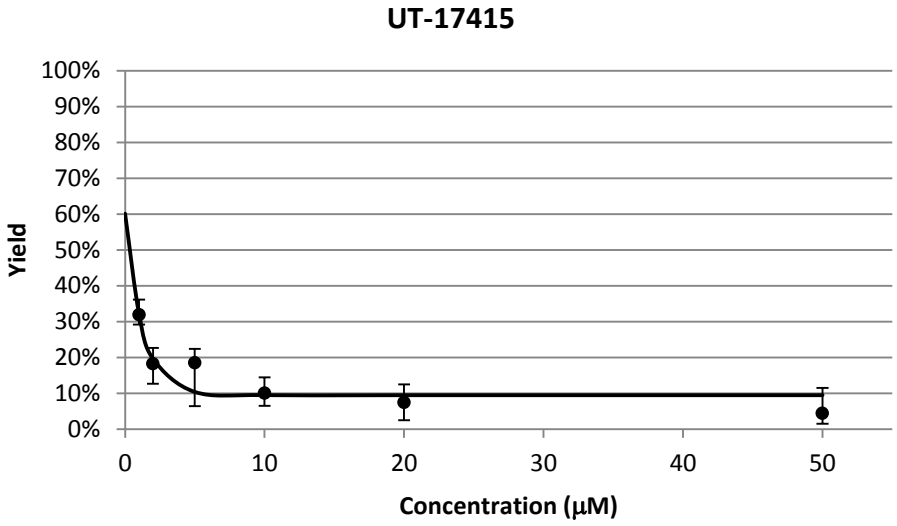
WecA assay substrate, UDP-Glucosamine-C6-FITC was chemically synthesized according to the reported procedures. [13]

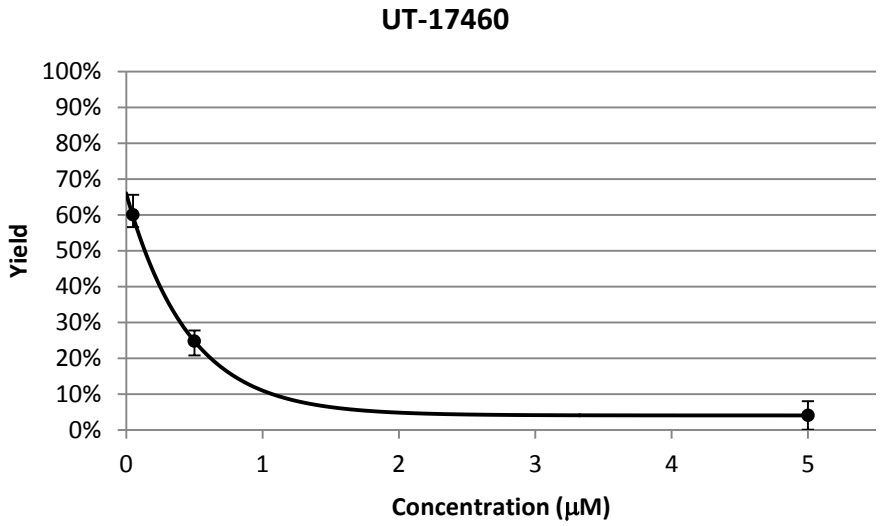


UDP-Glucosamine-C6-FITC (2 mM stock solution, 0.56 μL), $MgCl_2$ (0.5 M, 4 μL), β-mercaptoethanol (50 mM, 5 μL), CHAPS (5%, 11.25 μL), Tris buffer (pH 8.0, 50 mM), undecaprenyl phosphate (4 mM, 1.4 μL), and inhibitor molecue (0 - 100 μg/mL in Tris buffer) were place in a 500 μL Eppendorf tube. To a stirred reaction mixture, P-60 (10 μL) was added (total volume of reaction mixture: 50 μL adjust with Tris buffer). The reaction mixture was incubated for 4 h at 37 ^{o}C and quenched with n-butanol (150 μL). Two phases were mixed via vortex and centrifuged at 10,000 xg for 3 min. The upper organic phase was assayed via reverse-phase HPLC. The organic phase (30 μL) was injected into HPLC (solvent: gradient elution of 85:15 to 95:5 MeOH/0.05 M aq. NH_4HCO_3; UV: 485 nm; flow rate: 0.5 ml/ min; column: Kinetex 5 μm C8, 100 Å, 150 x 4.60 mm), and the area of the peak for C55-P-P-glucosamine-C_6-FITC was quantified to obtain the IC_{50} value. The IC_{50} values were calculated from plots of the percentage product inhibition versus the inhibitor concentration.

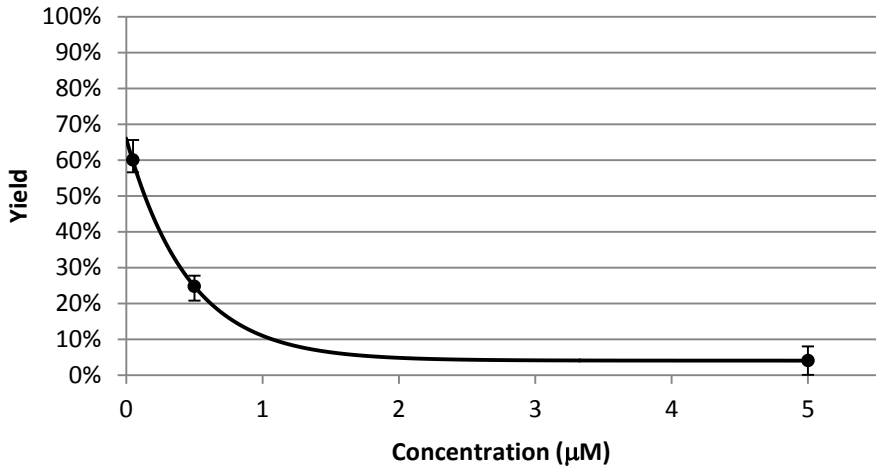
Figure S11.



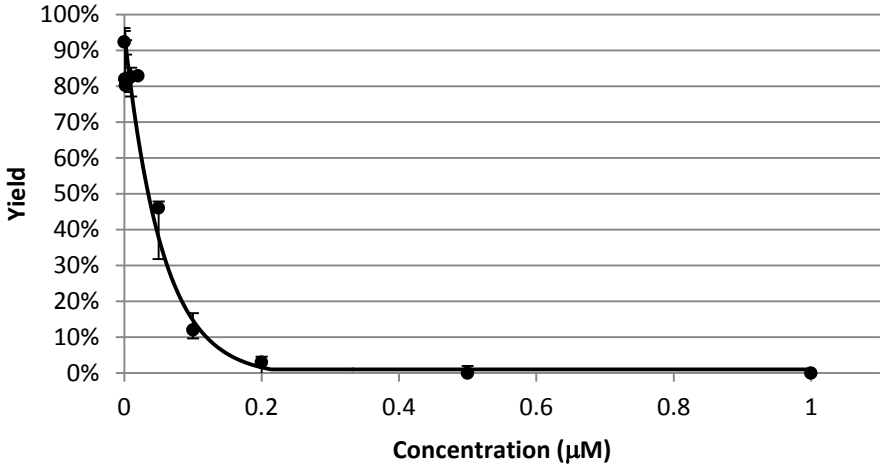

UT-17415
100%
90%
80%
70%
60%
50%
40%
30%
20%
10%
0%
Yield
0
10
20
30
40
50
Concentration (μM)

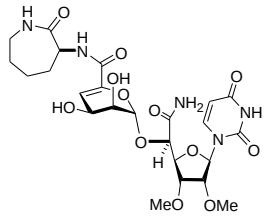

UT-17460
100%
90%
80%
70%
60%
50%
40%
30%
20%
10%
0%
Yield
0
1
2
3
4
5
Concentration (μM)

UT-17460



UT-01320



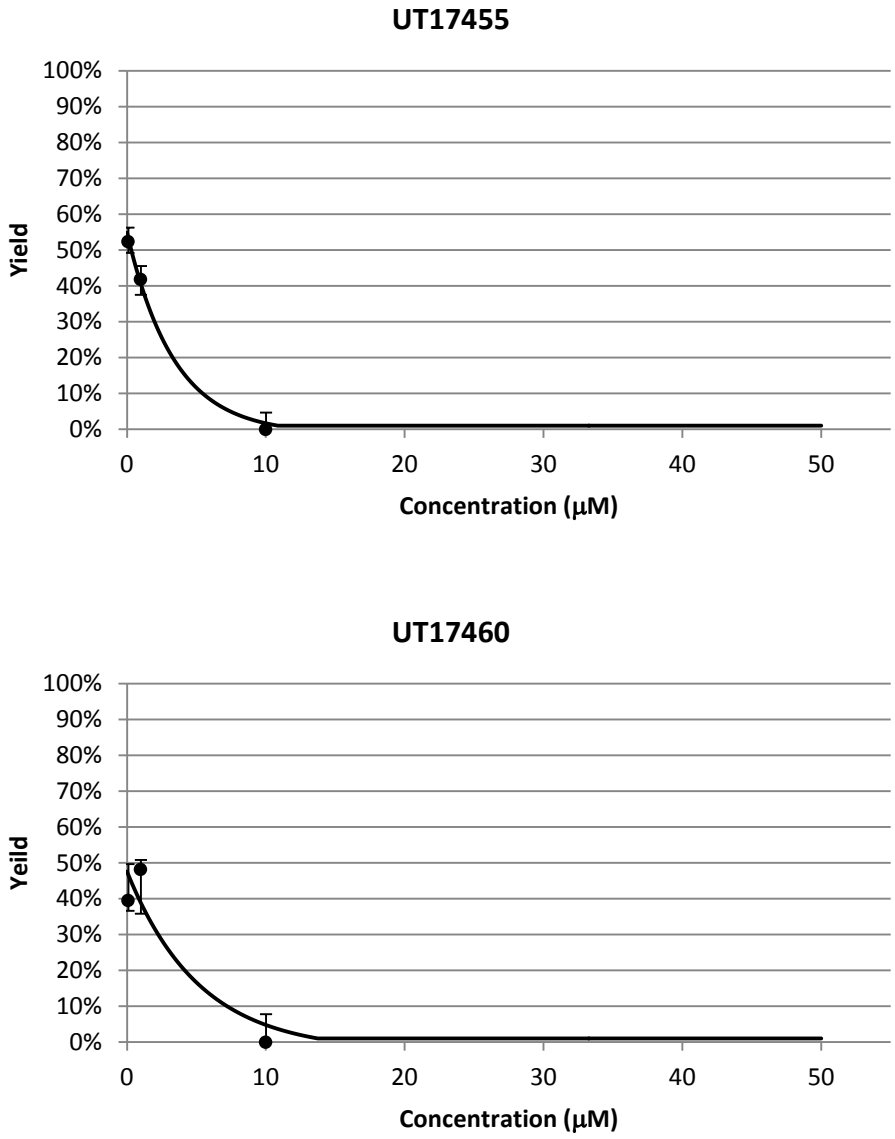


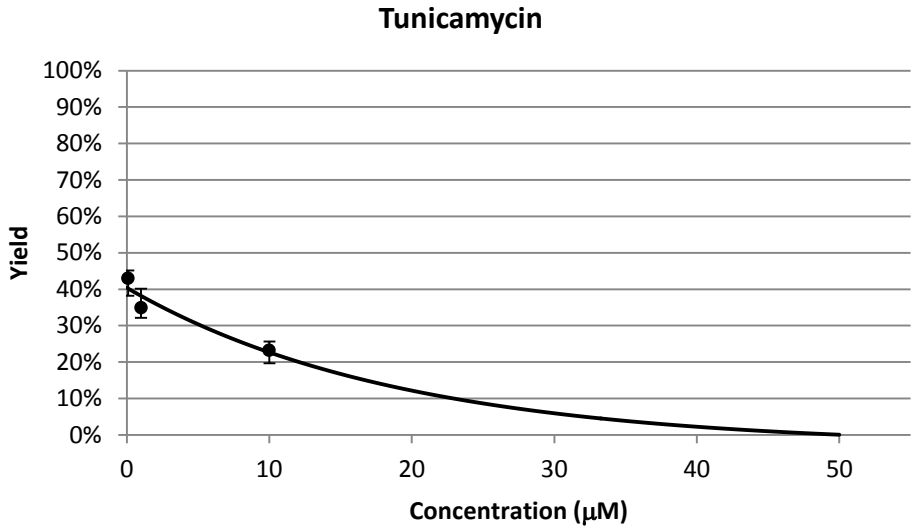
UT-01320

AglH assay.

AglH assays were performed as the procedure described for WecA assays, but used *Mj*AglH and α-dihydroundecaprenyl phosphate instead of WecA and undecaprenyl phosphate.

Figure S12.





Determination of cytotoxicity in Vero Cells

Selected molecules were tested for cytotoxicity (IC_{50}) in Vero cells via a MTT colorimetric assay. Vero cell line was cultured in Complete eagle`s minimum essential growth medium (EMEM) containing L-glutamine, sodium pyruvate, minimum essential amino acids, penicillin-streptomycin and 10% fetal bovine serum. Inoculating number of cells were 400,000 cells/mL and a final 40,000 cells/well. After 72h of exposure of molecules to this cell line at concentrations ranging from 0.78 to 200 μg/mL, the culture medium was changed to complete EMEM without phenol red before addition of yellow tetrazolium dye; MTT. Viability was assessed on the basis of cellular conversion of MTT into a purple formazan product. The absorbance of the colored formazan product was measured at 570 nm by BioTek Synergy HT Spectrophotometer. Linearity of the MTT response to the cell number was determined.

Figure S13. MTT response vs population of Vero cells.

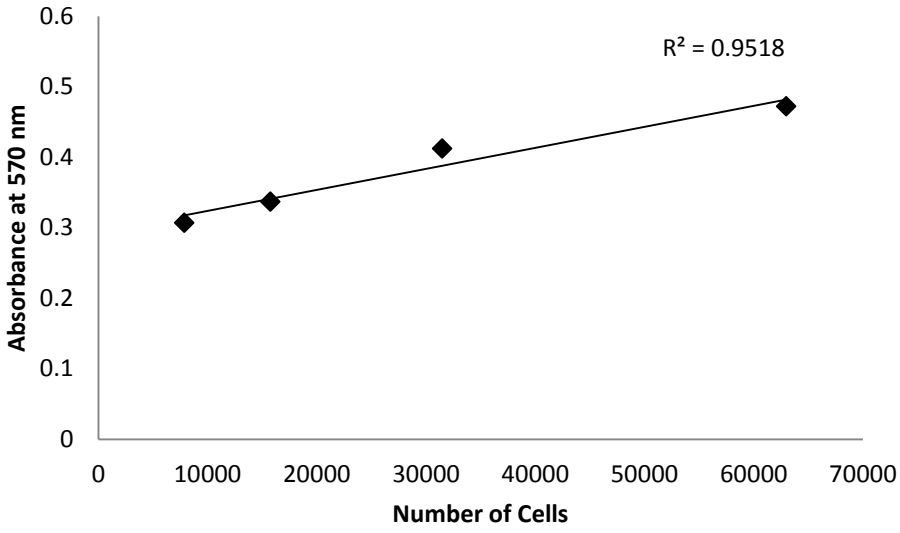


Figure S14. Cytotoxicity of UT-17455 against Vero cells.

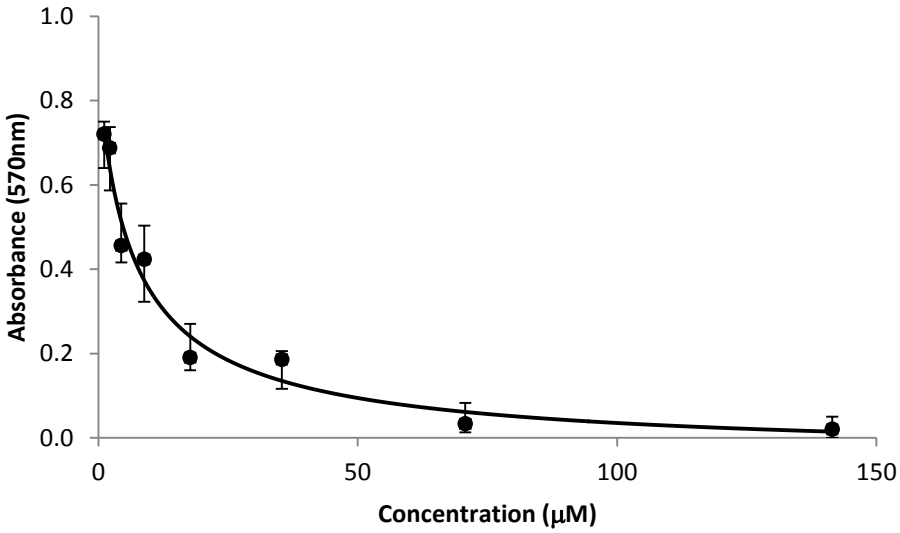


Figure S15. Cytotoxicity of UT-17460 against Vero cells.

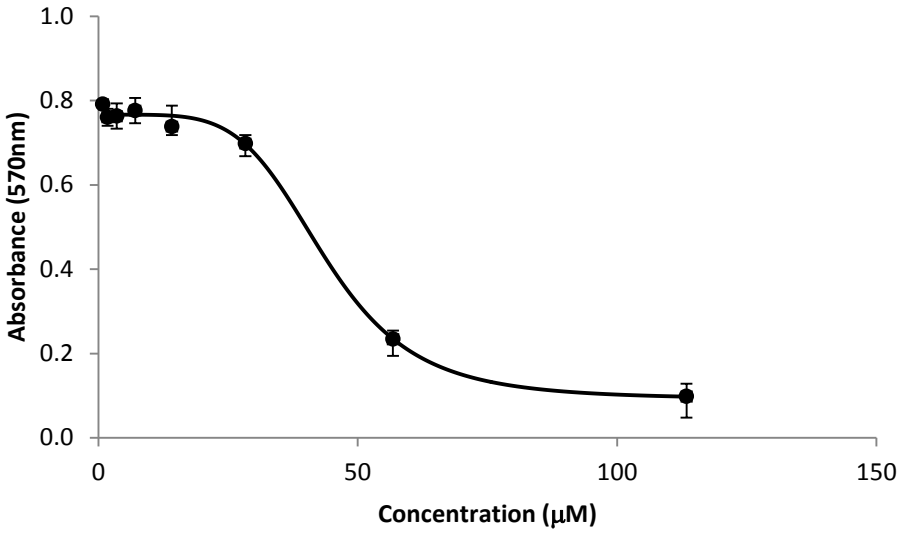


Figure S16. Cytotoxicity of tunicamycin against Vero cells.

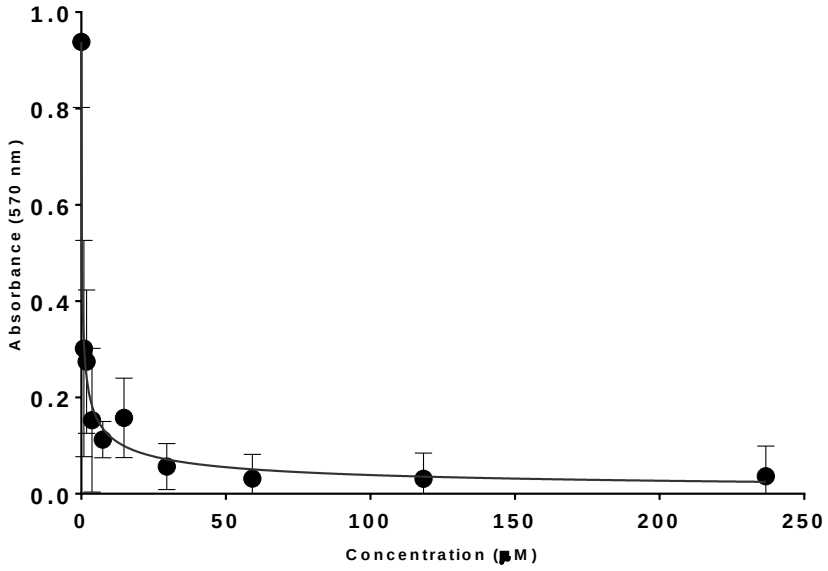


Table S3. Cytotoxicity of UT-17460 against Caco-2, HepG2 and Vero cells.

	HepG2 Human hepatocyte carcinoma	**Caco-2** Human colon adenocarcinoma	**Vero** Green monkey kidney epithelial cells
UT-17460	>60.0	>60.0	**65.0**
Tunicamycin	0.19	0.95	0.12
Taxol	2.33	5.50	4.67

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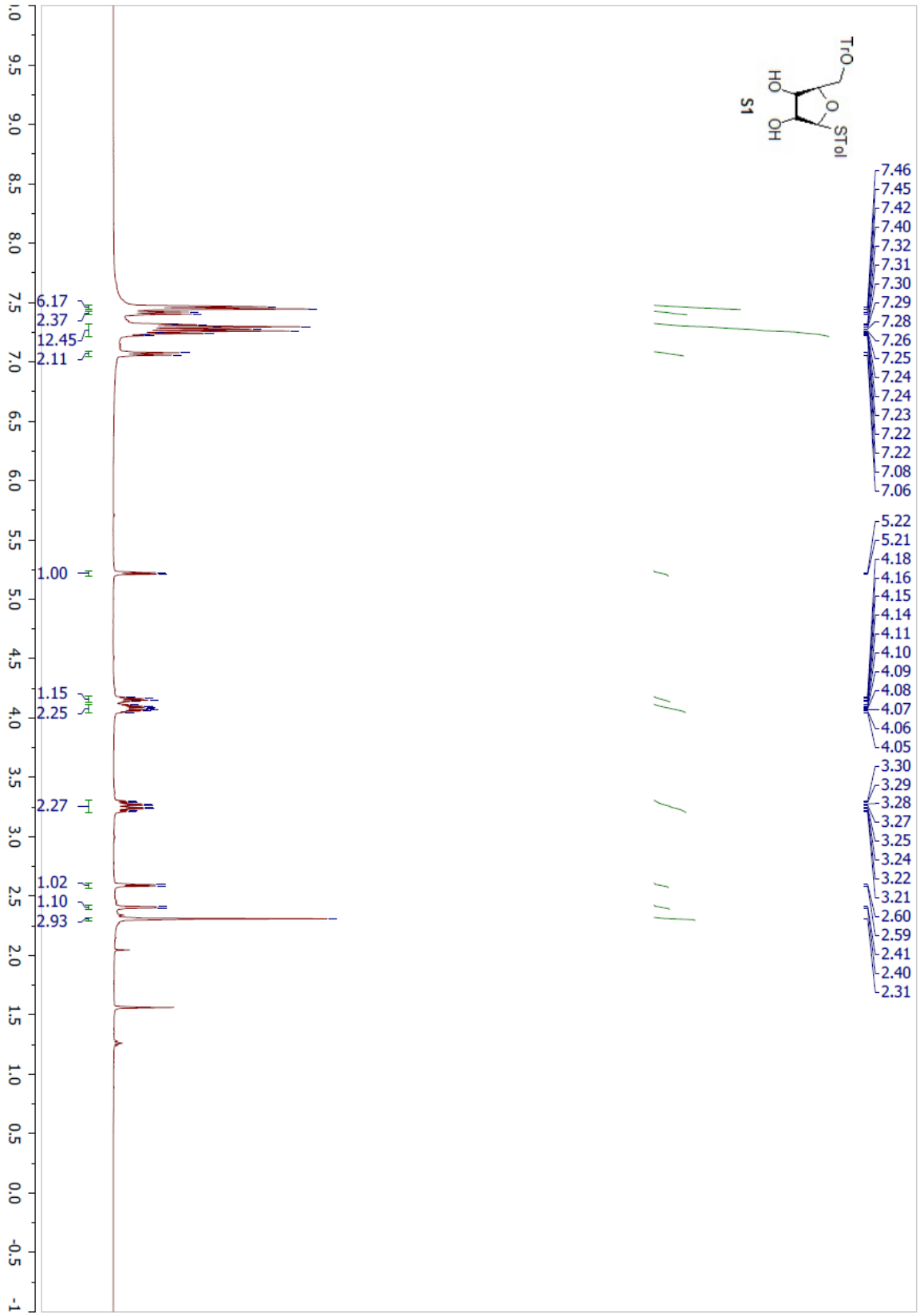
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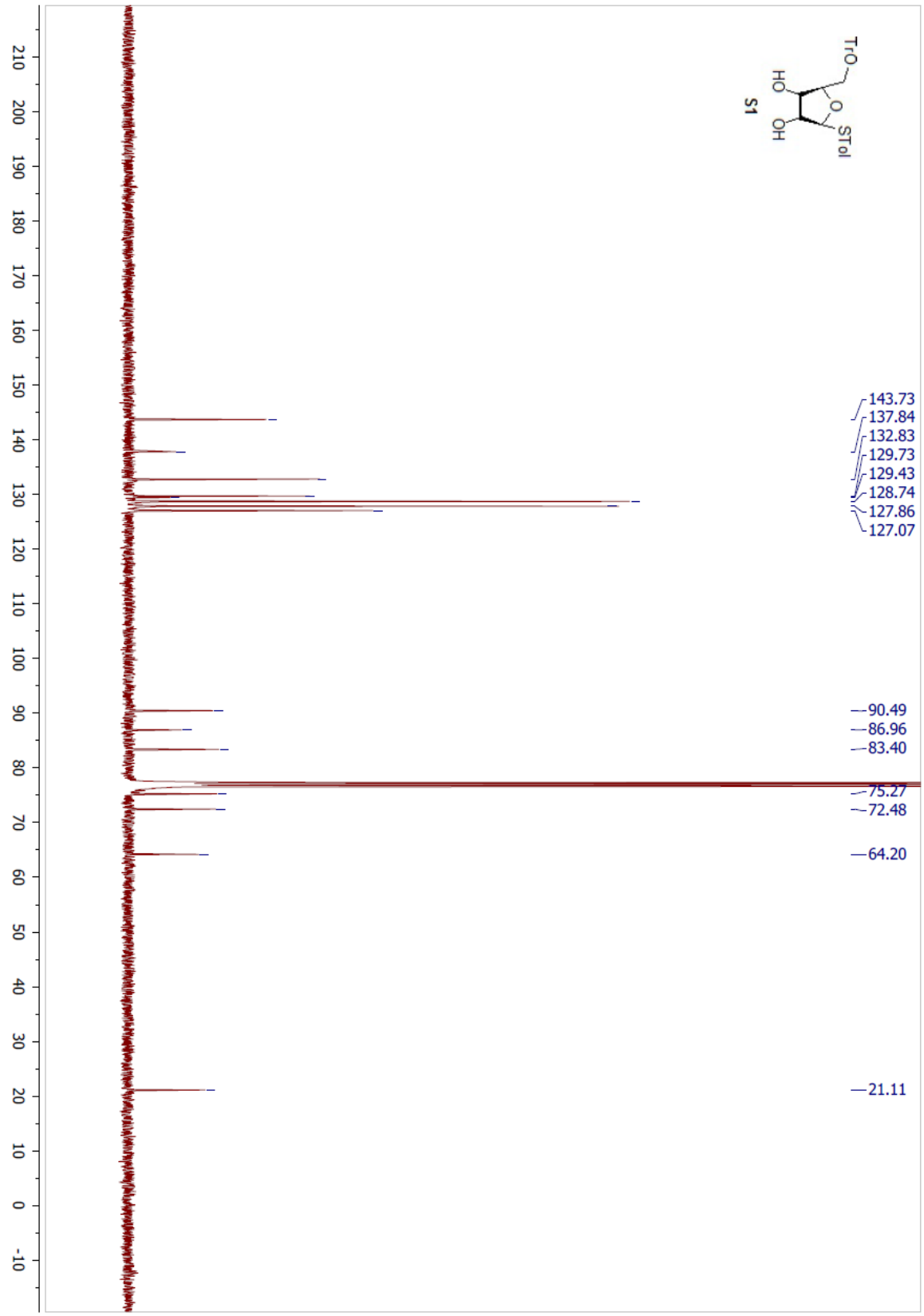
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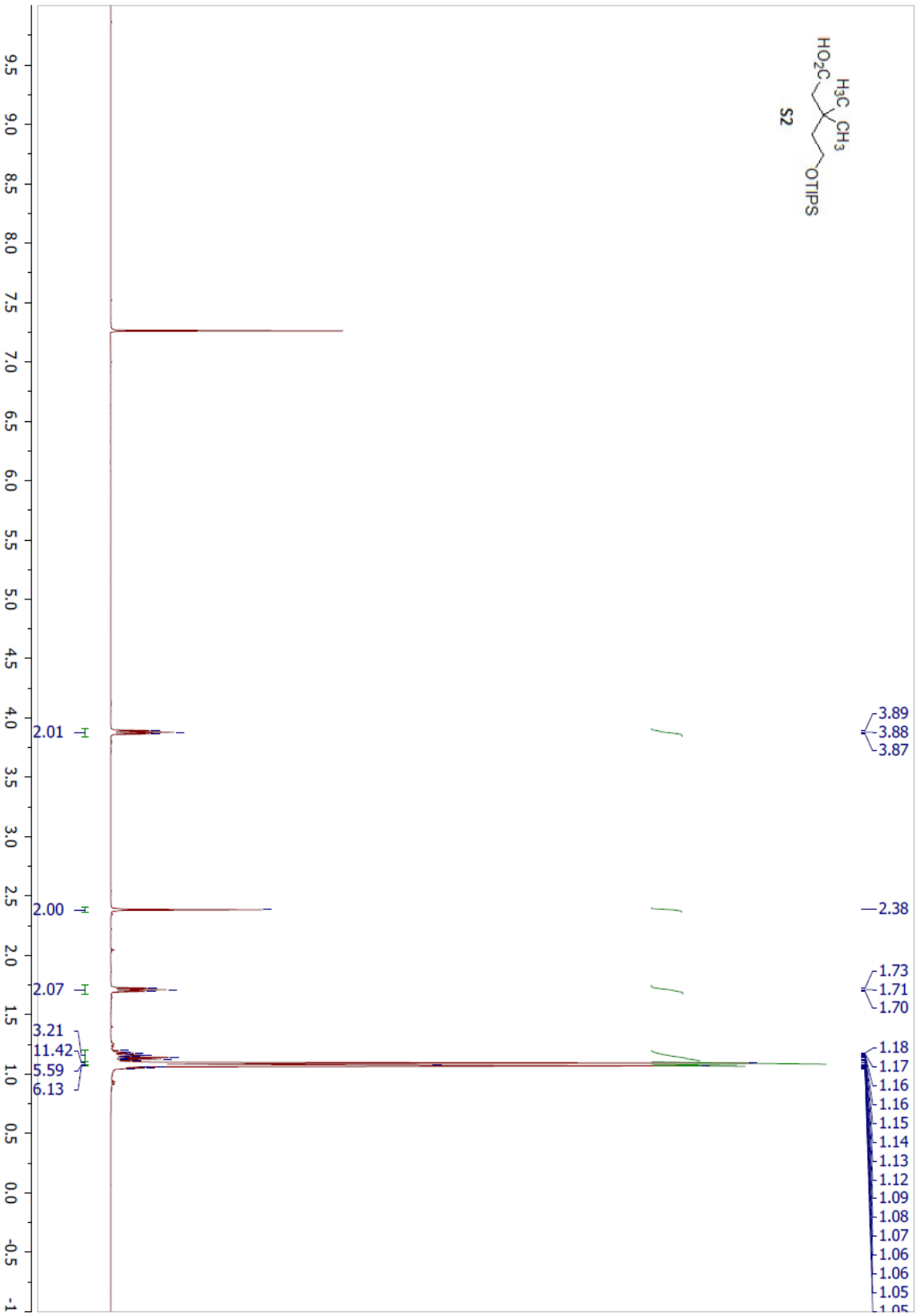
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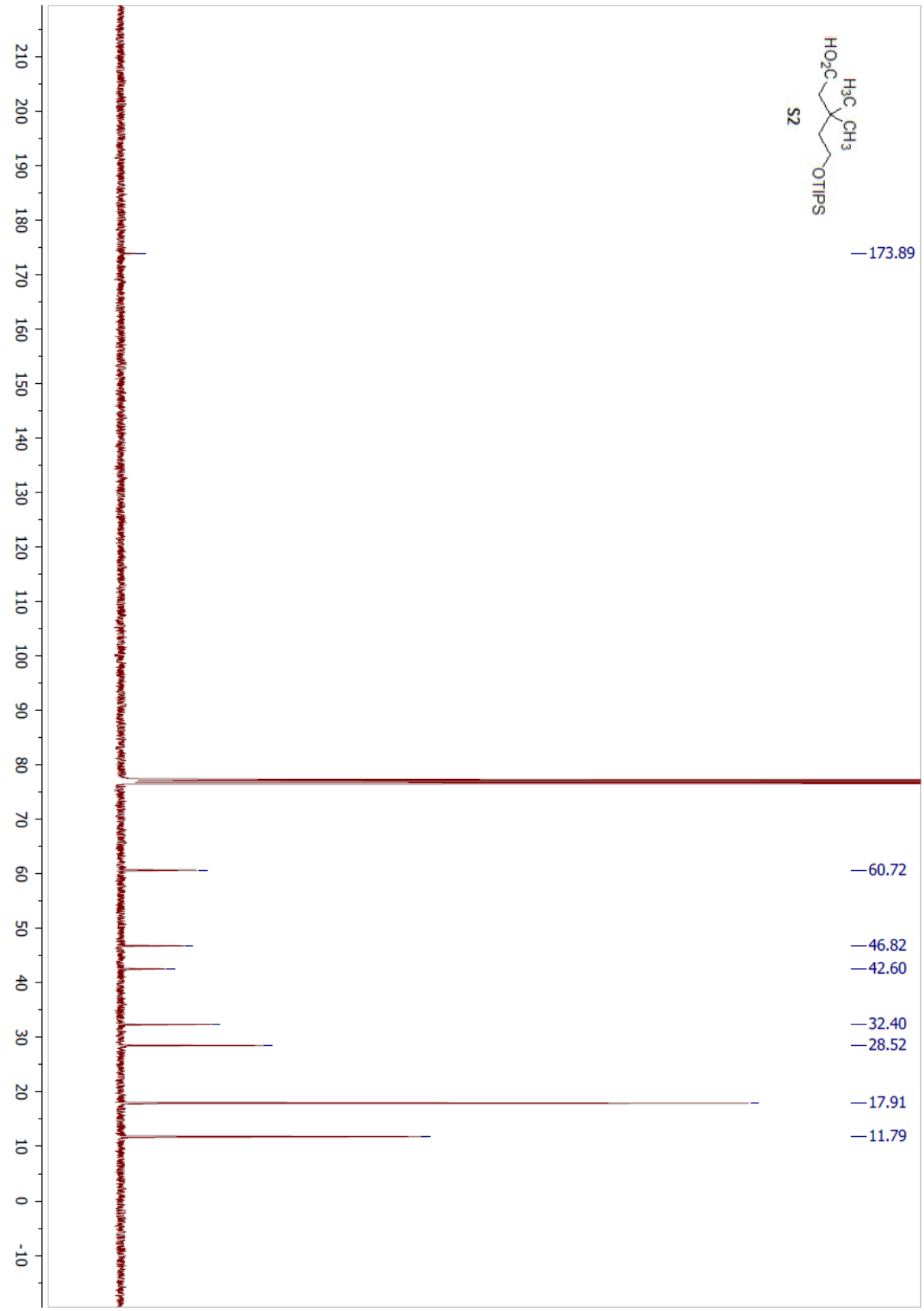
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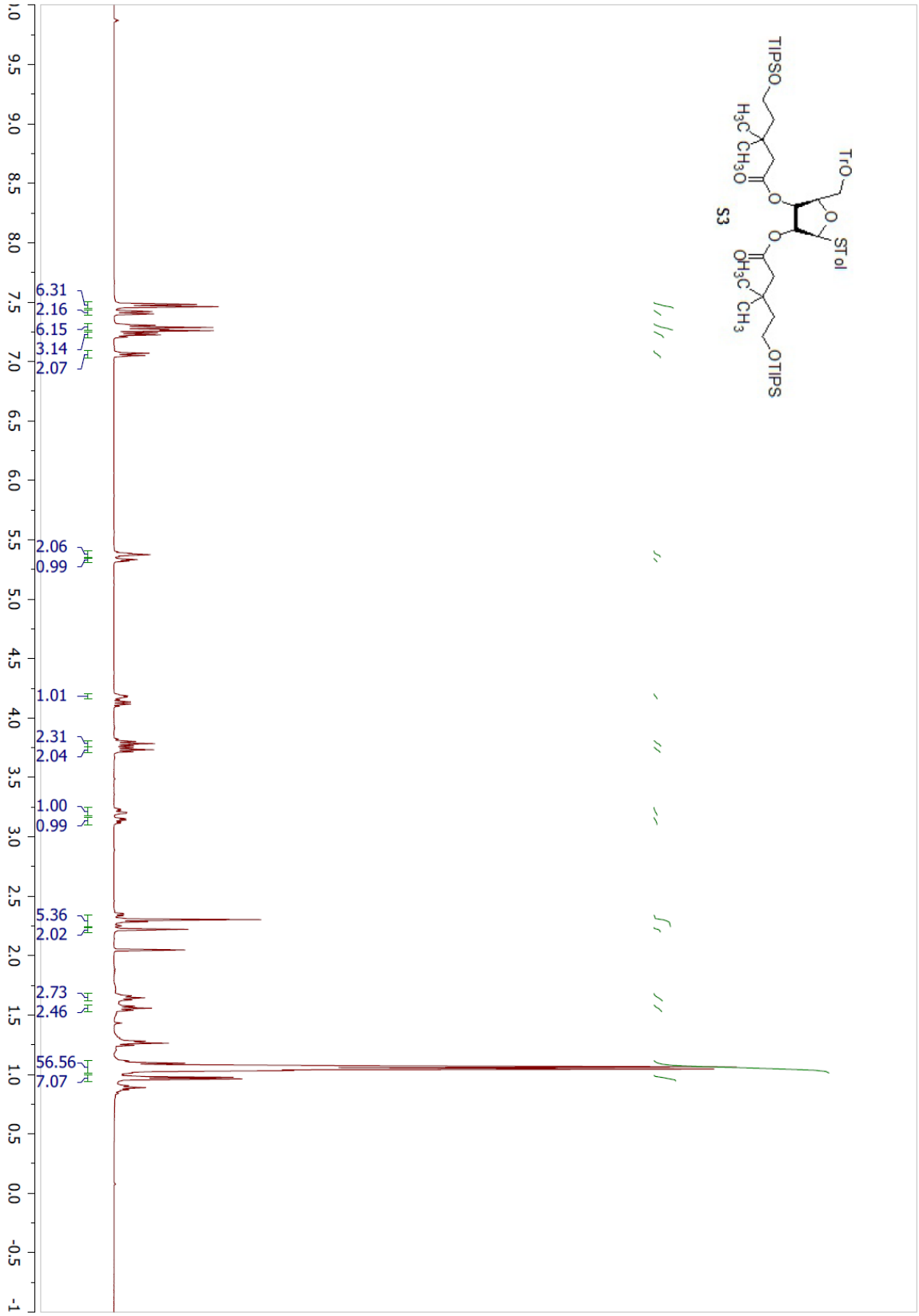
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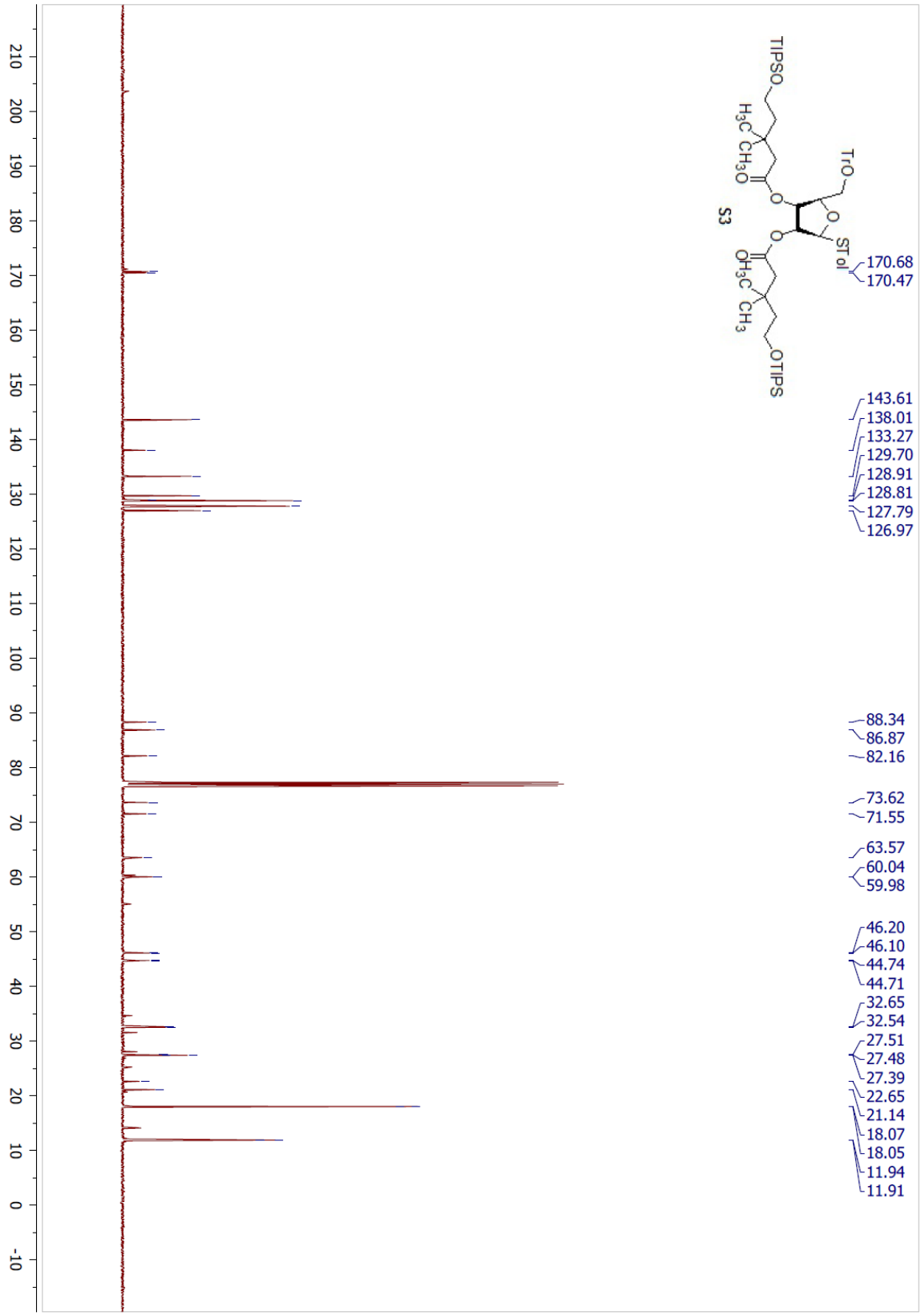
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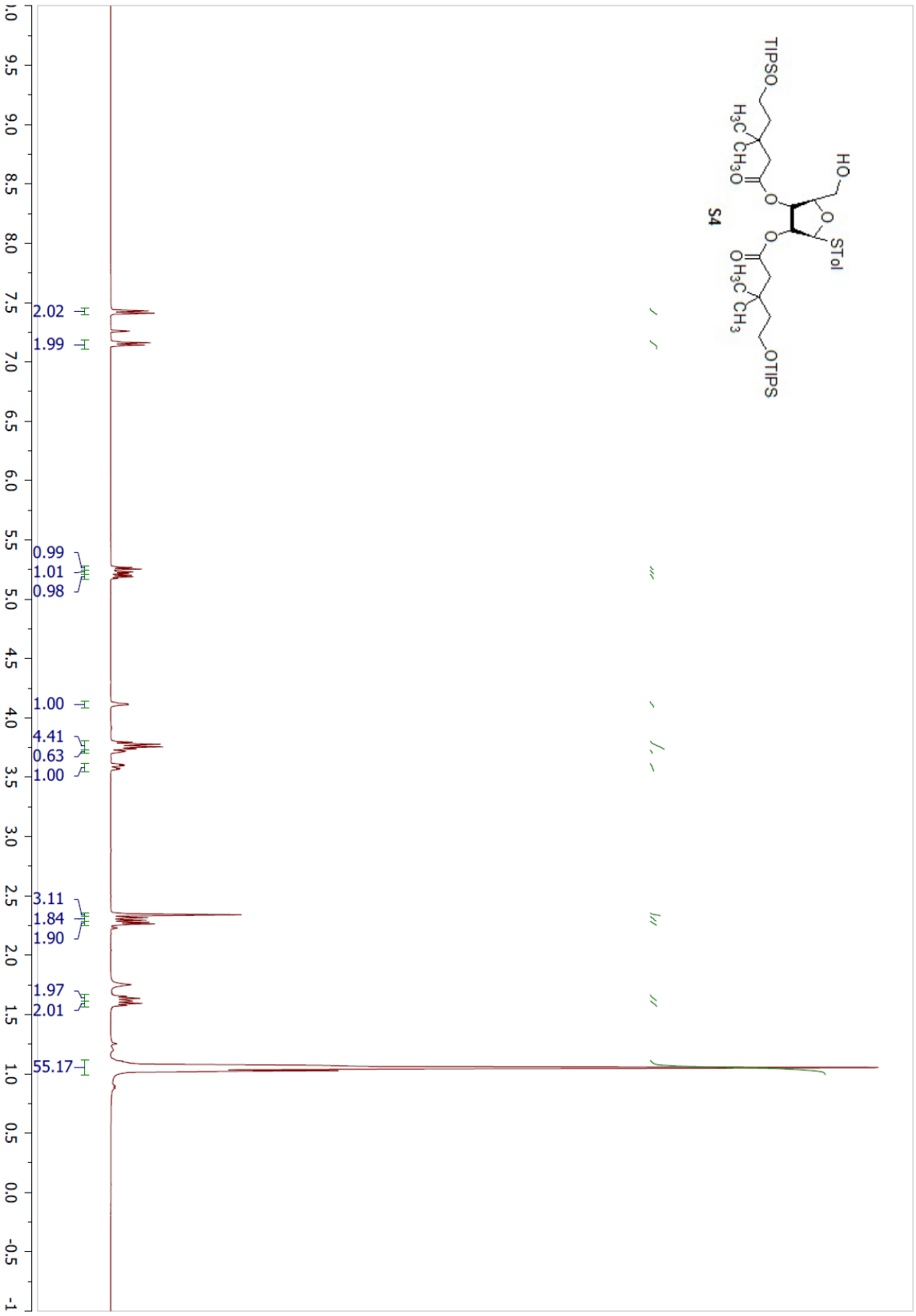
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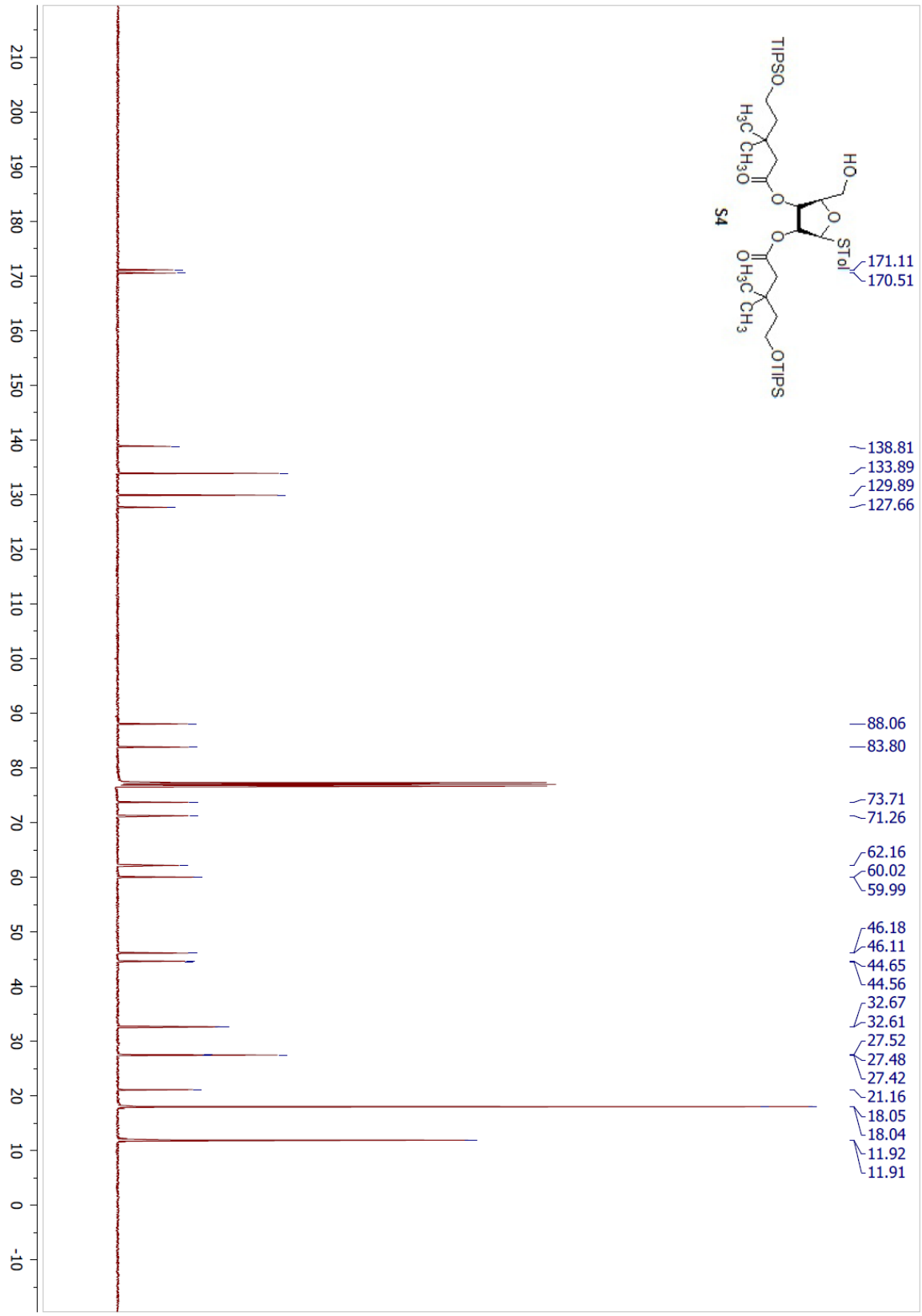
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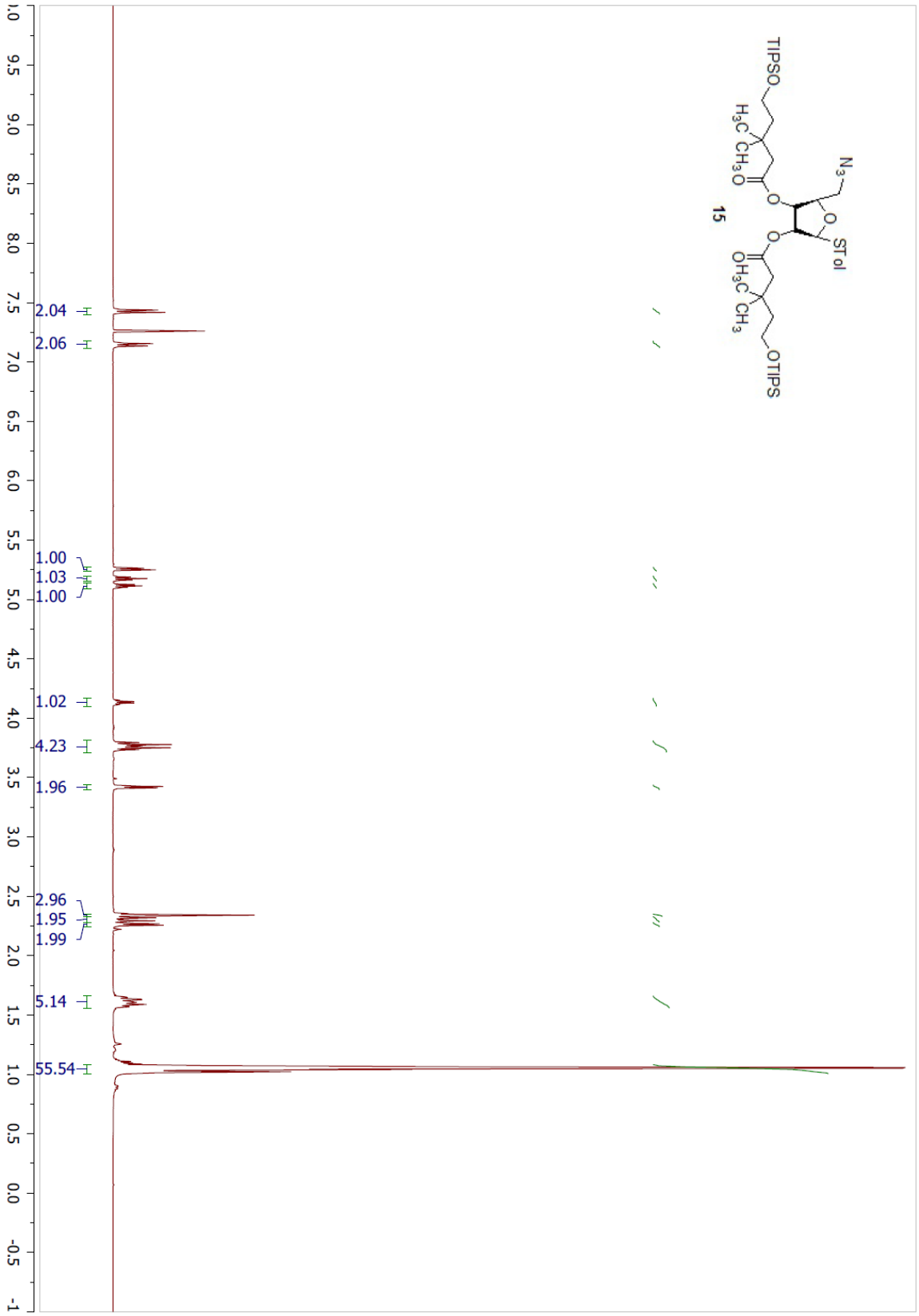
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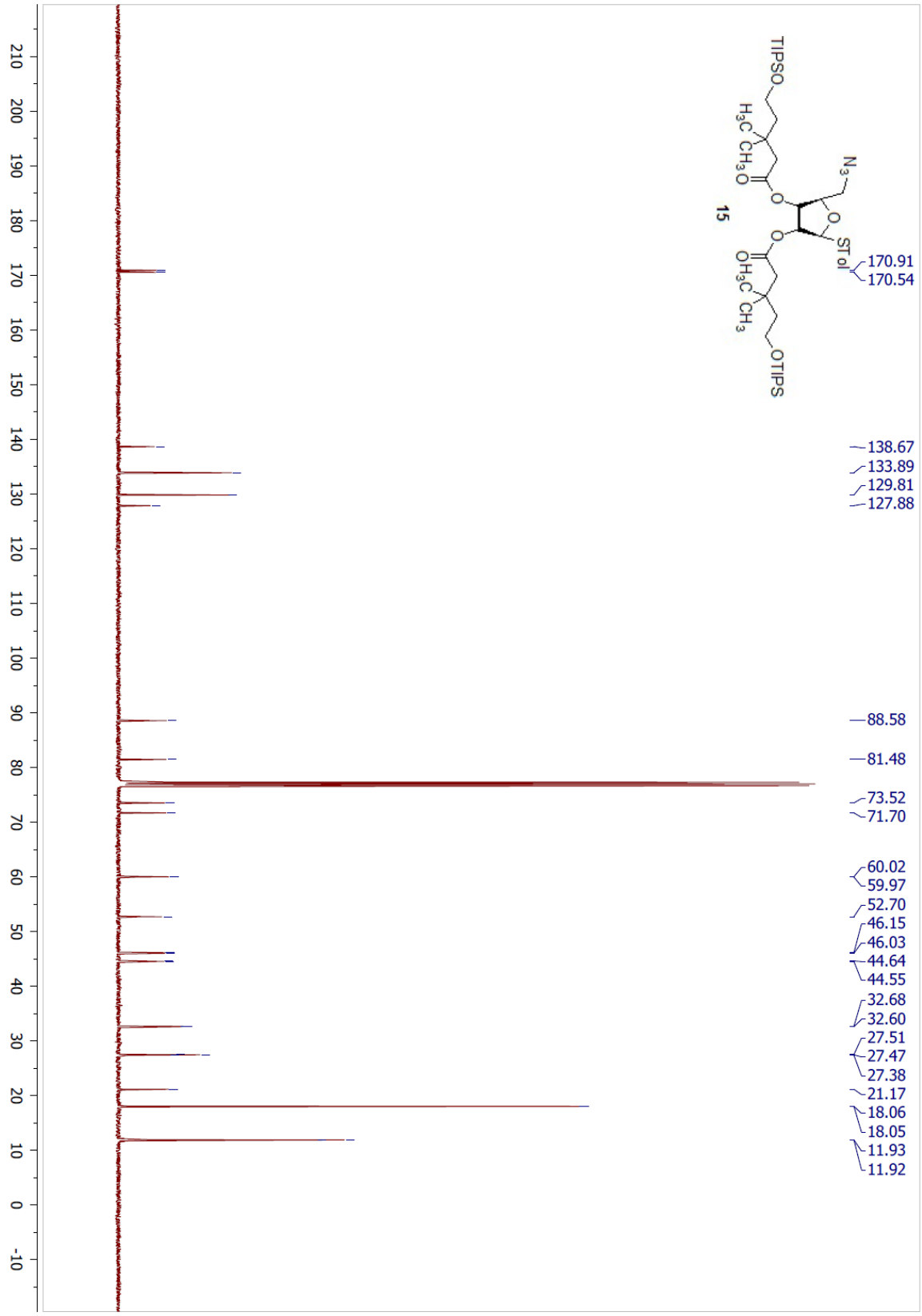
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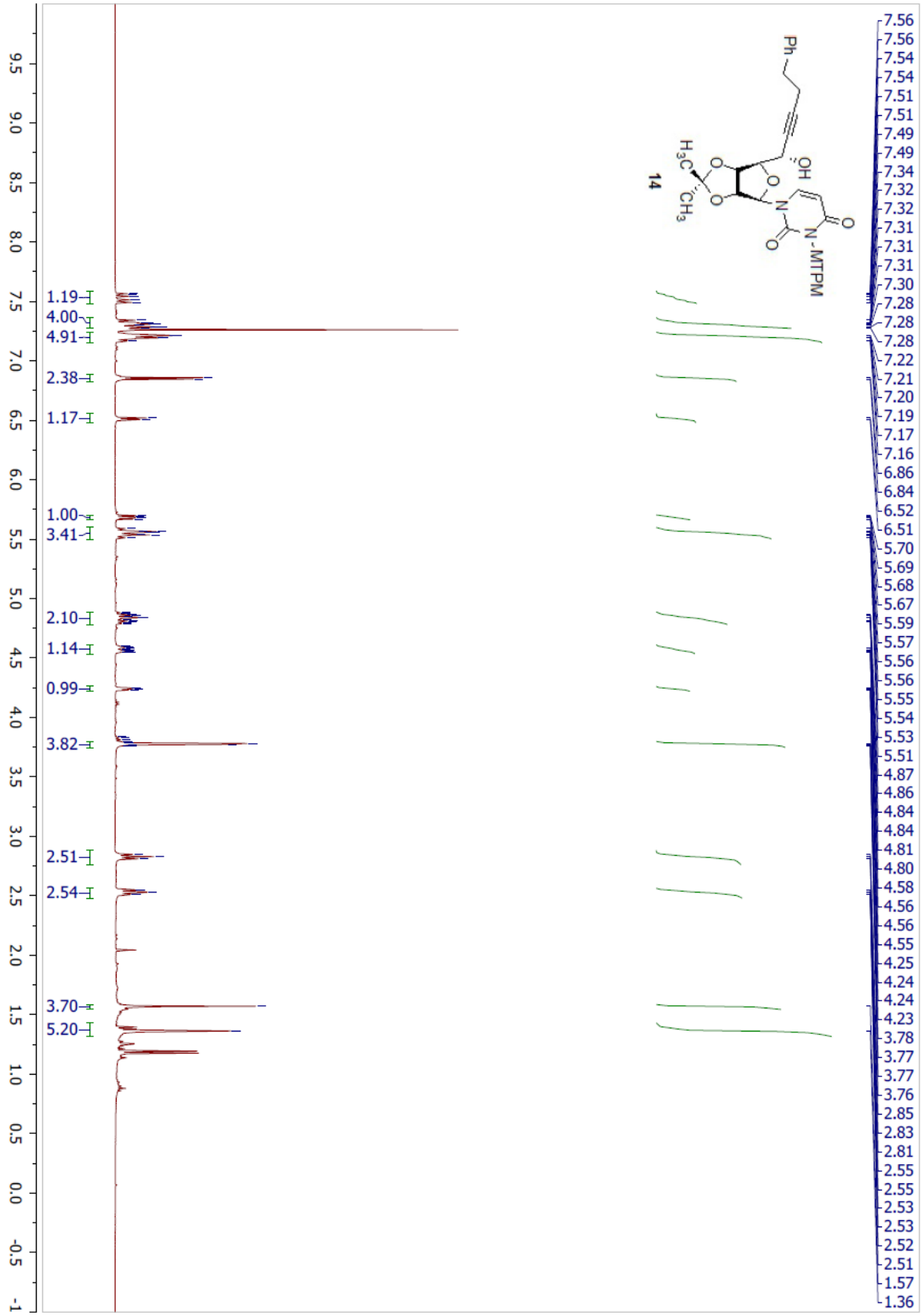
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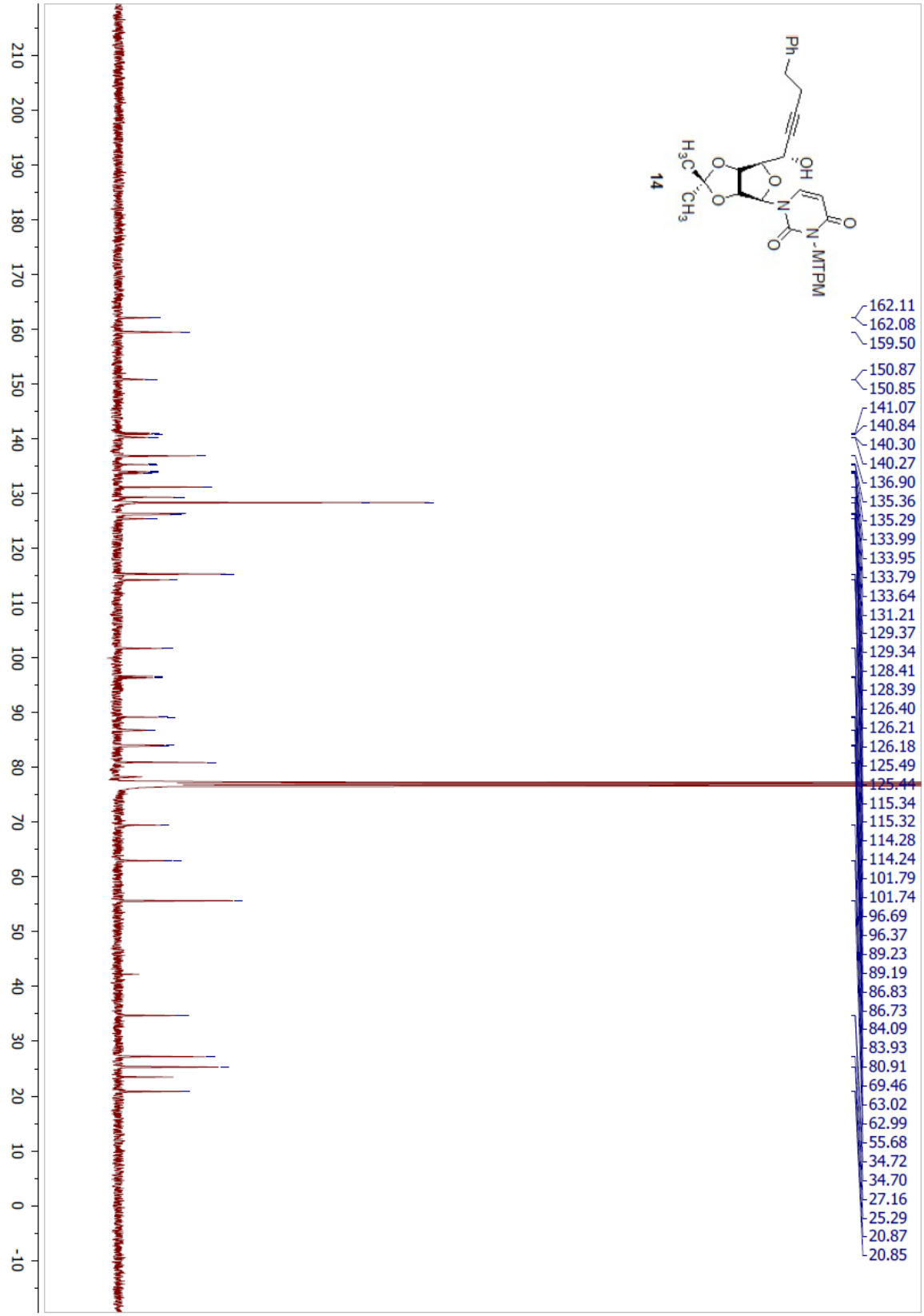
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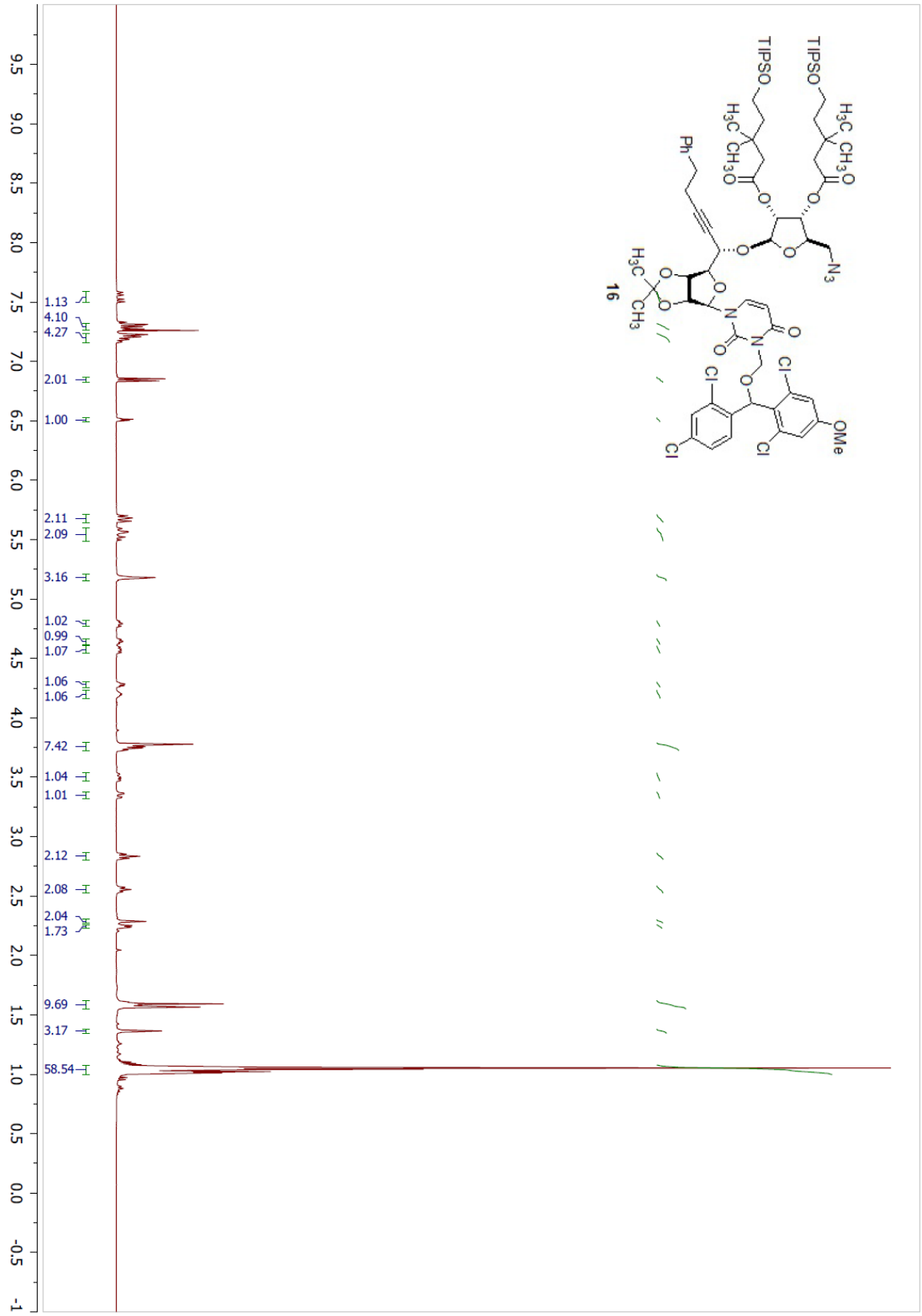
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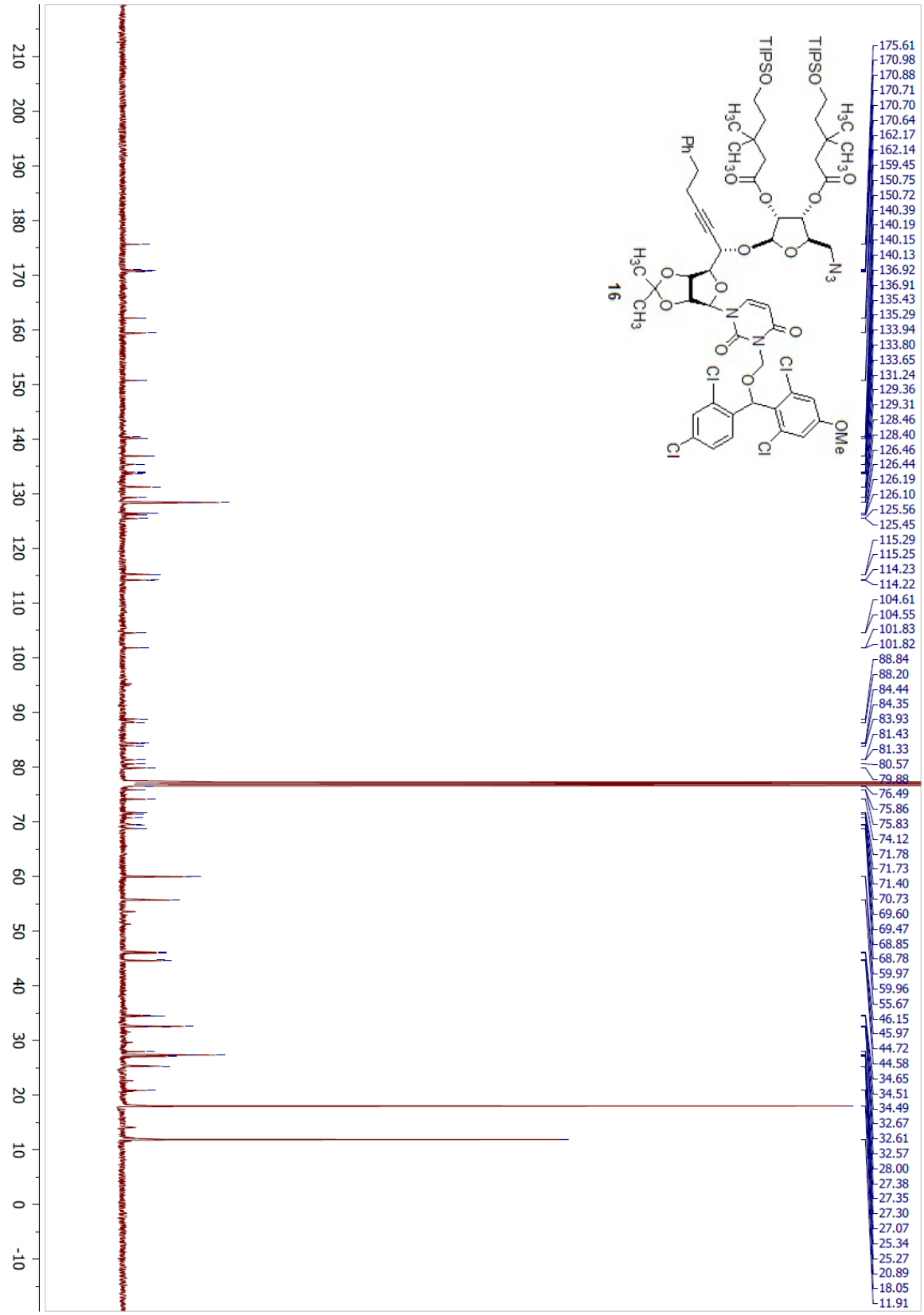
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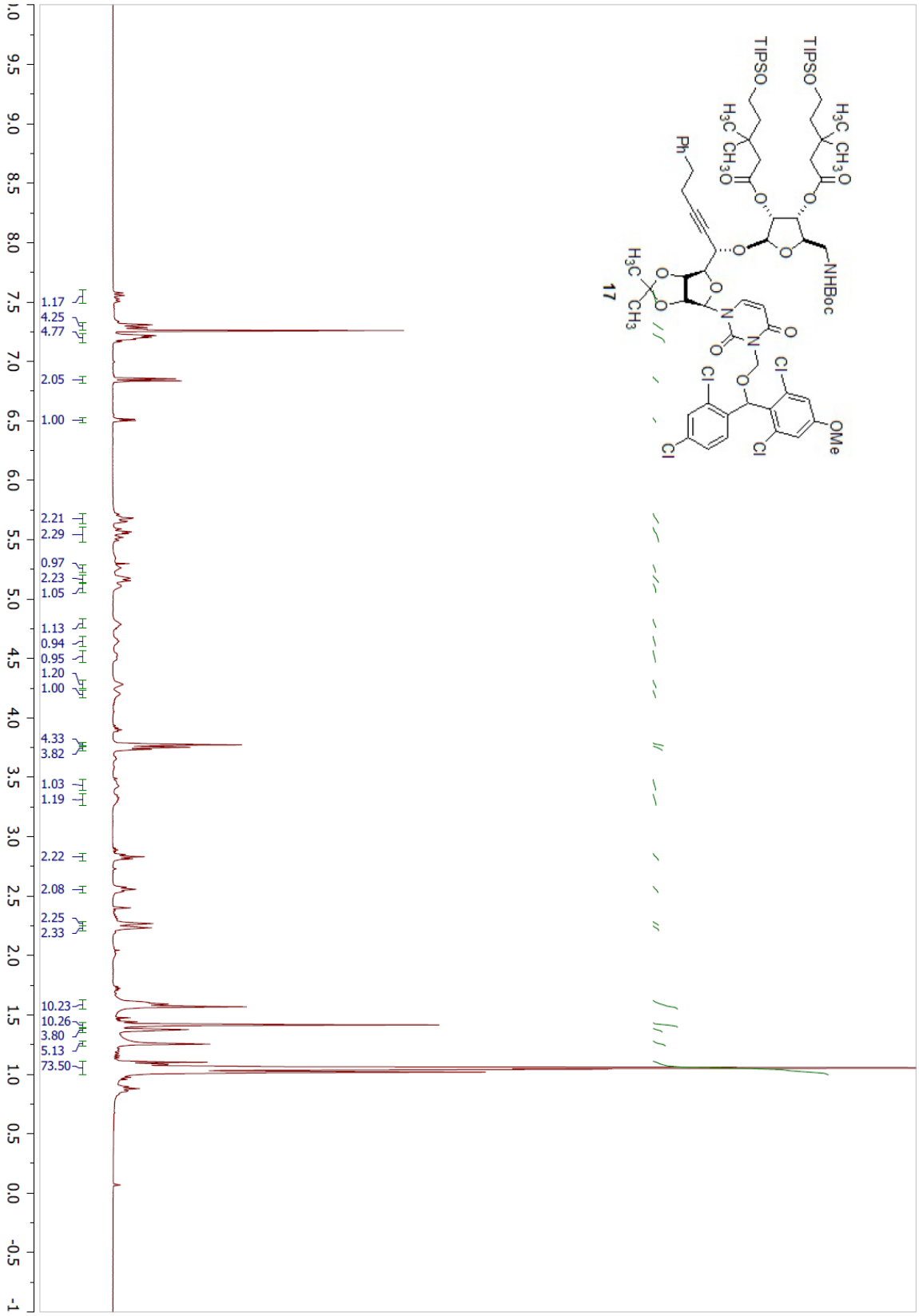
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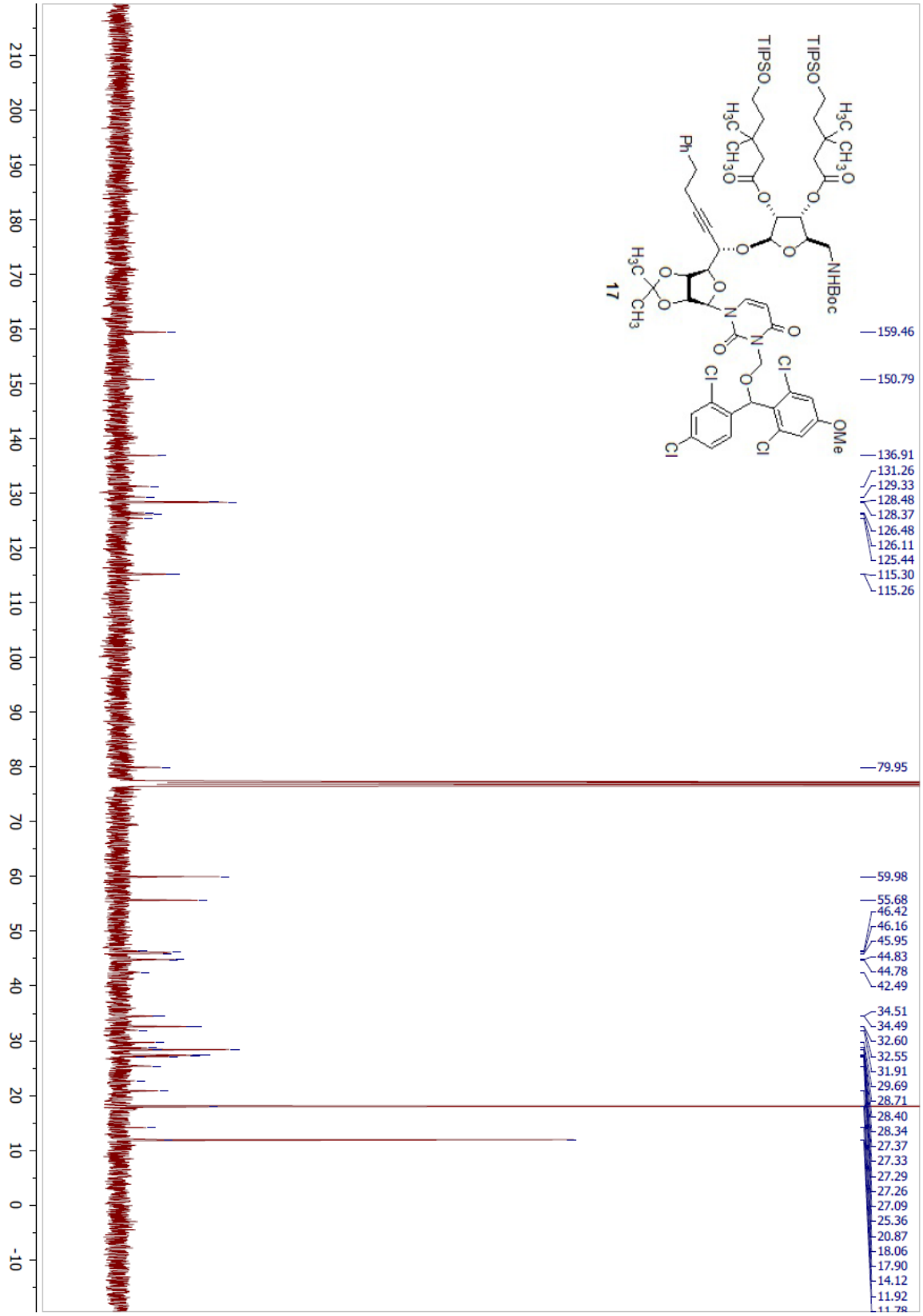
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34.49
32.60
32.55
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29.69
28.71
28.40
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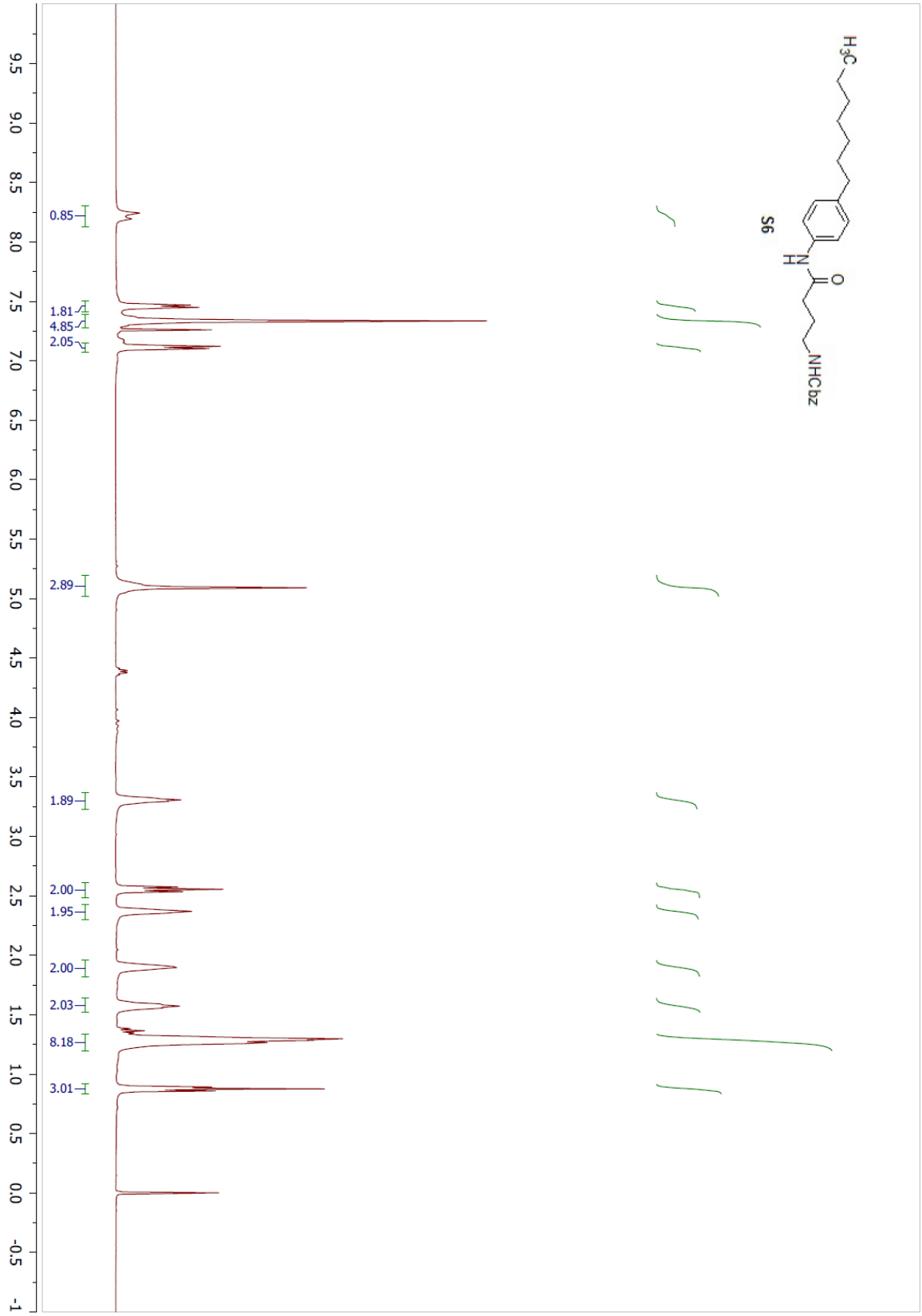
14.12
11.92


H3C
S6
N
H
O
NHCbz
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2.05
2.89
1.89
2.00
1.95
2.00
2.03
8.18
3.01
9.5
9.0
8.5
8.0
7.5
7.0
6.5
6.0
5.5
5.0
4.5
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3.5
3.0
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1.5
1.0
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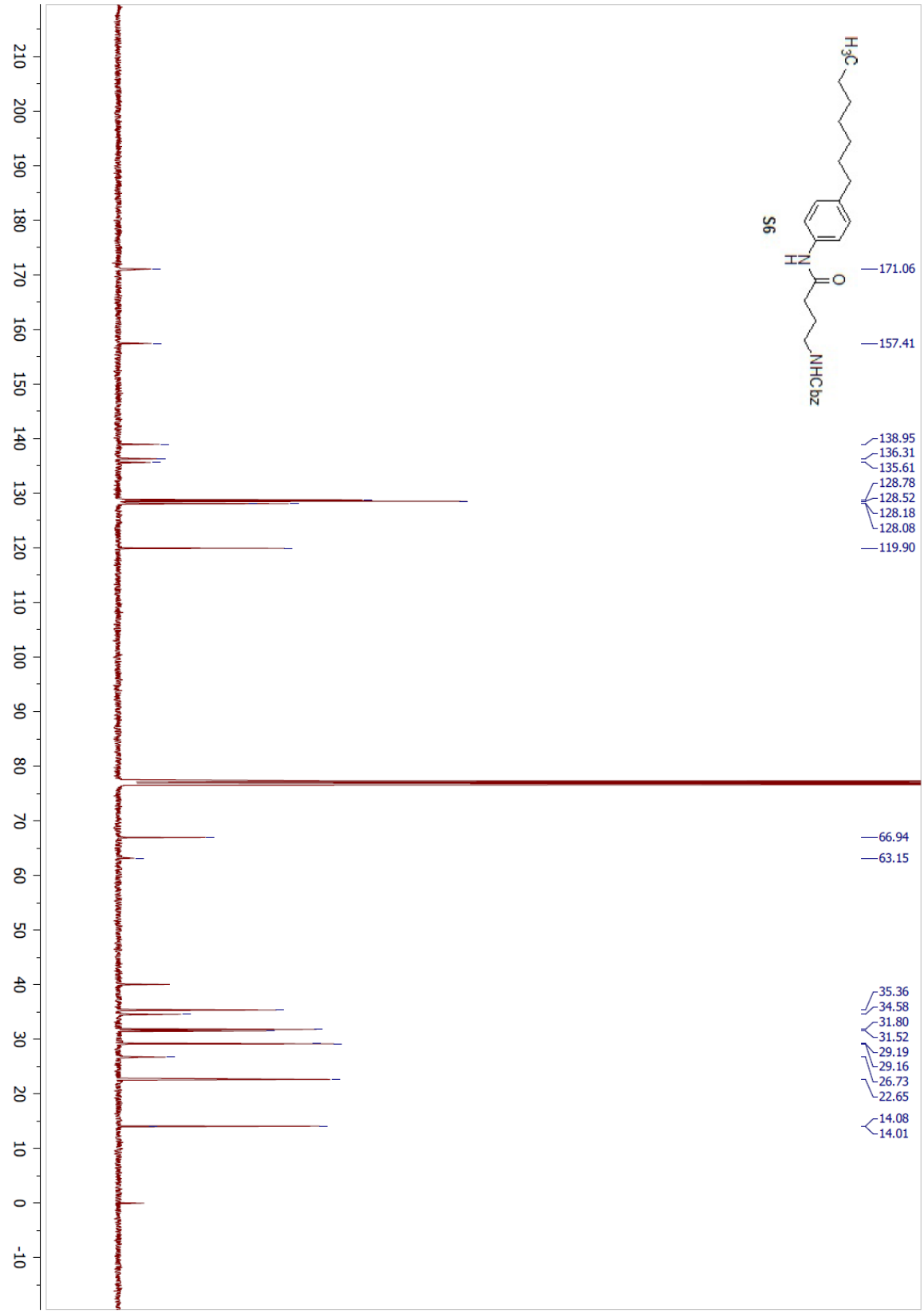
-1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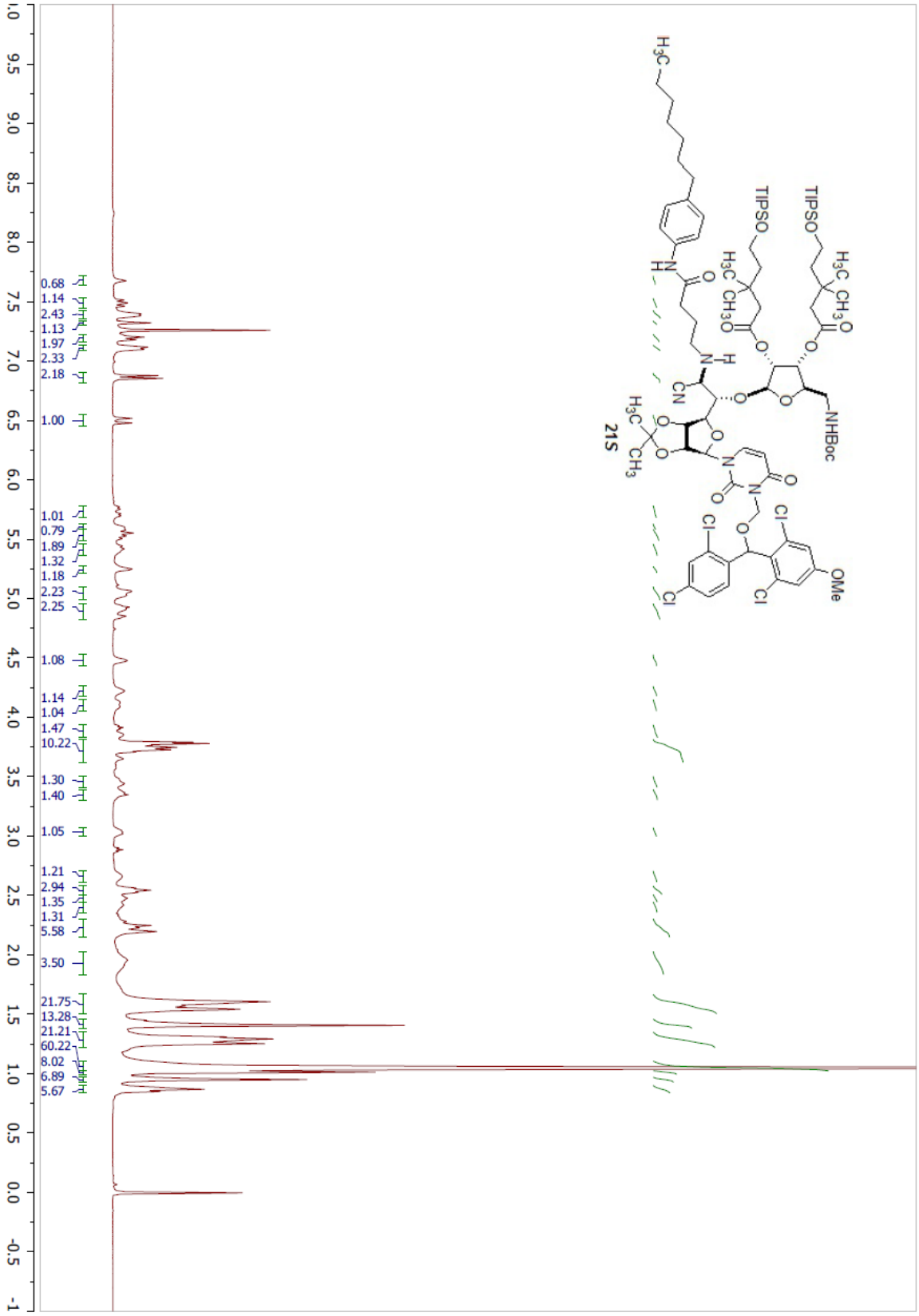
14.01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TIPSO
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OMe
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2.18
1.00
1.01
0.79
1.89
1.32
1.18
2.23
2.25
1.08
1.14
1.04
1.47
10.22
1.30
1.40
1.05
1.21
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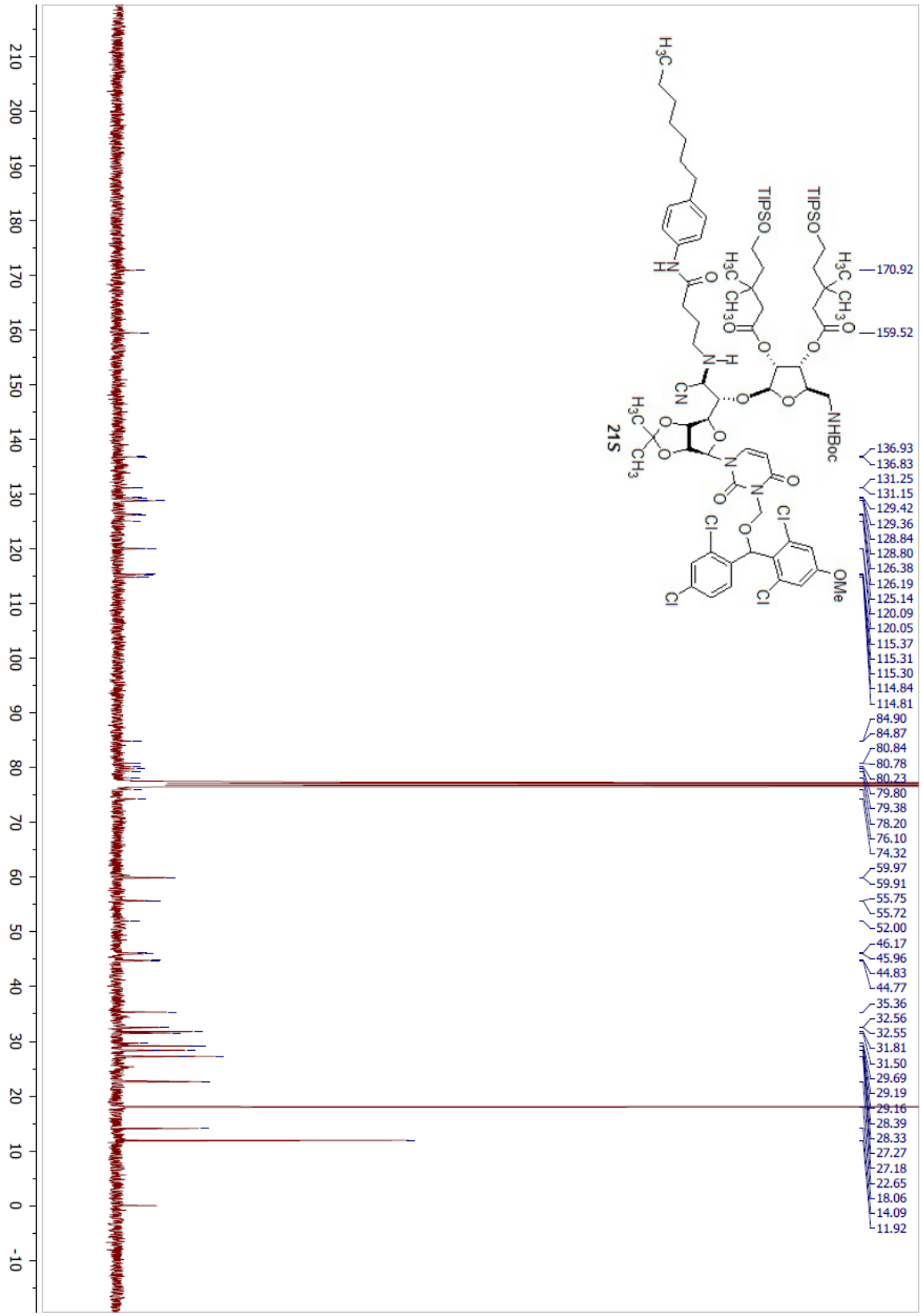
5.67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TIPSO
NHBoc
OMe
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129.36
128.84
128.80
126.38
126.19
125.14
120.09
120.05
115.37
115.31
115.30
114.84
114.81
84.90
84.87
80.84
80.78
80.23
79.80
79.38
78.20
76.10
74.32
59.97
59.91
55.75
55.72
52.00
46.17
45.96
44.83
44.77
35.36
32.56
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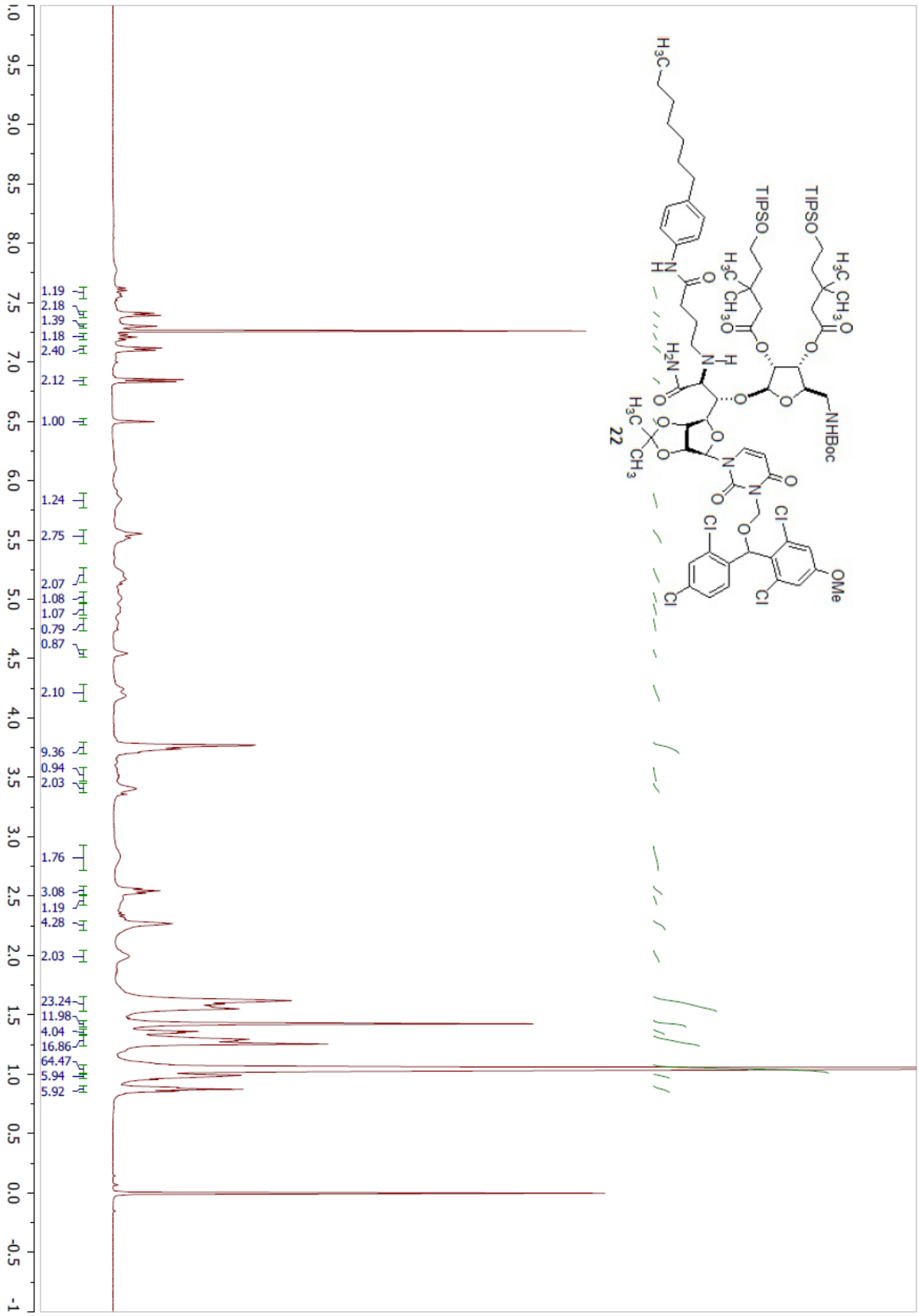
27.27
27.18
22.65
18.06
14.09
11.92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2.18
1.39
1.18
2.40
2.12
1.00
1.24
2.75
2.07
1.08
1.07
0.79
0.87
2.10
9.36
0.94
2.03
1.76
3.08
1.19
4.28
2.03
23.24
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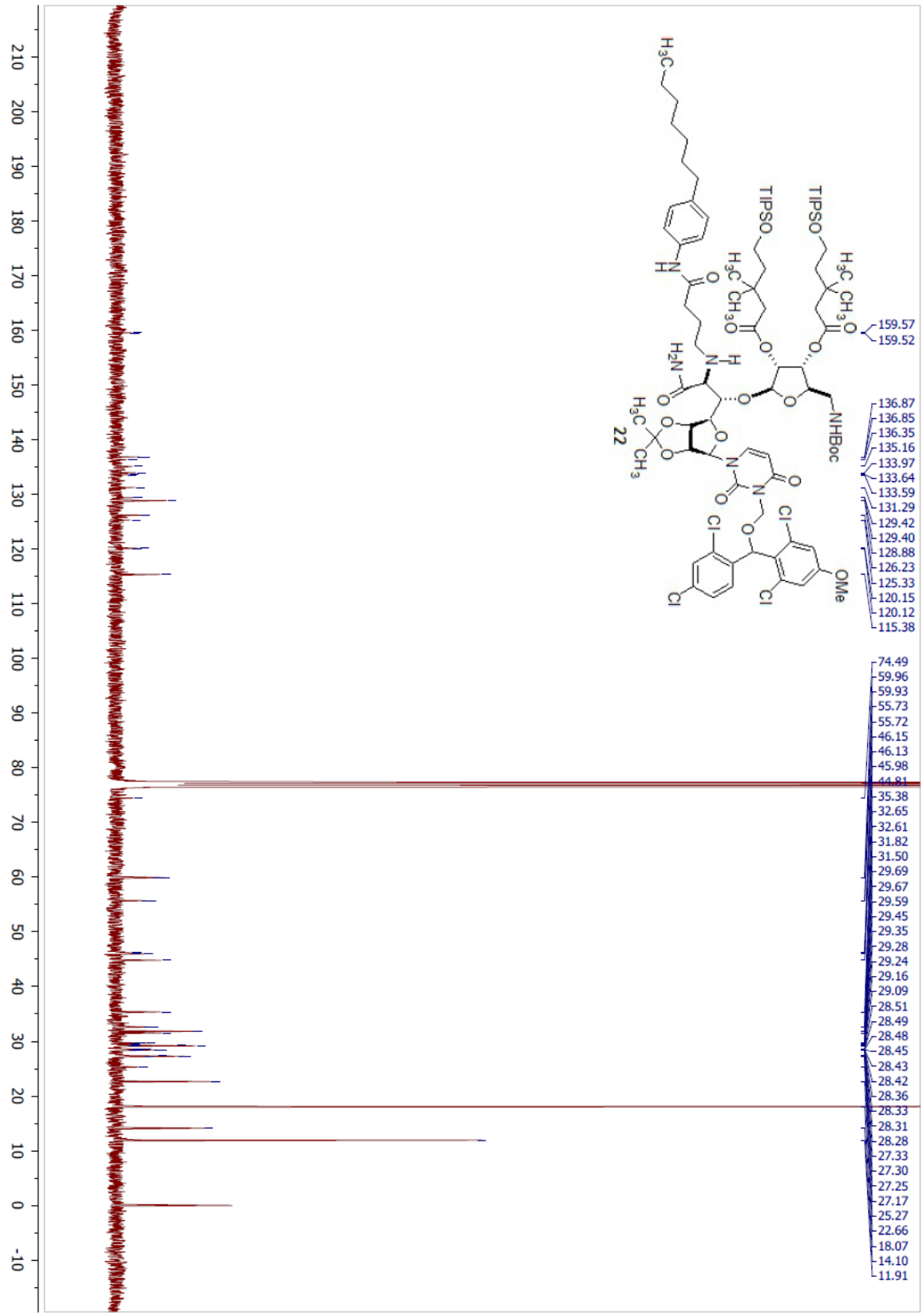
4.04
16.86
64.47
5.94
5.92
TIPSO
TIPSO
NHBoc
OMe
22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TIPSO
NHBoc
OMe
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159.52
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136.85
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133.59
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126.23
125.33
120.15
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59.93
55.73
55.72
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46.13
45.98
44.81
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29.69
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29.59
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29.35
29.28
29.24
29.16
29.09
28.51
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28.48
28.45
28.43
28.42
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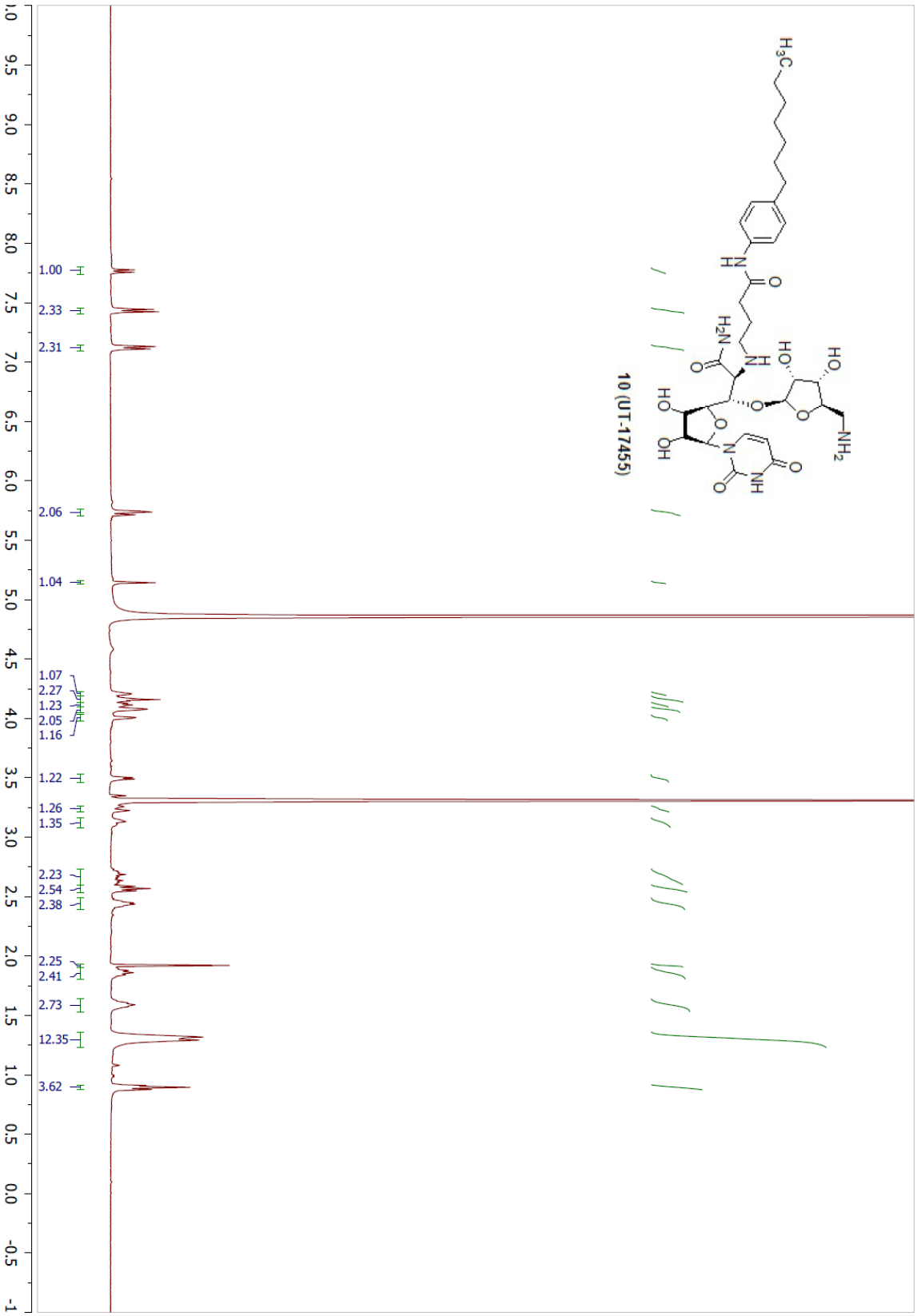
14.10
11.91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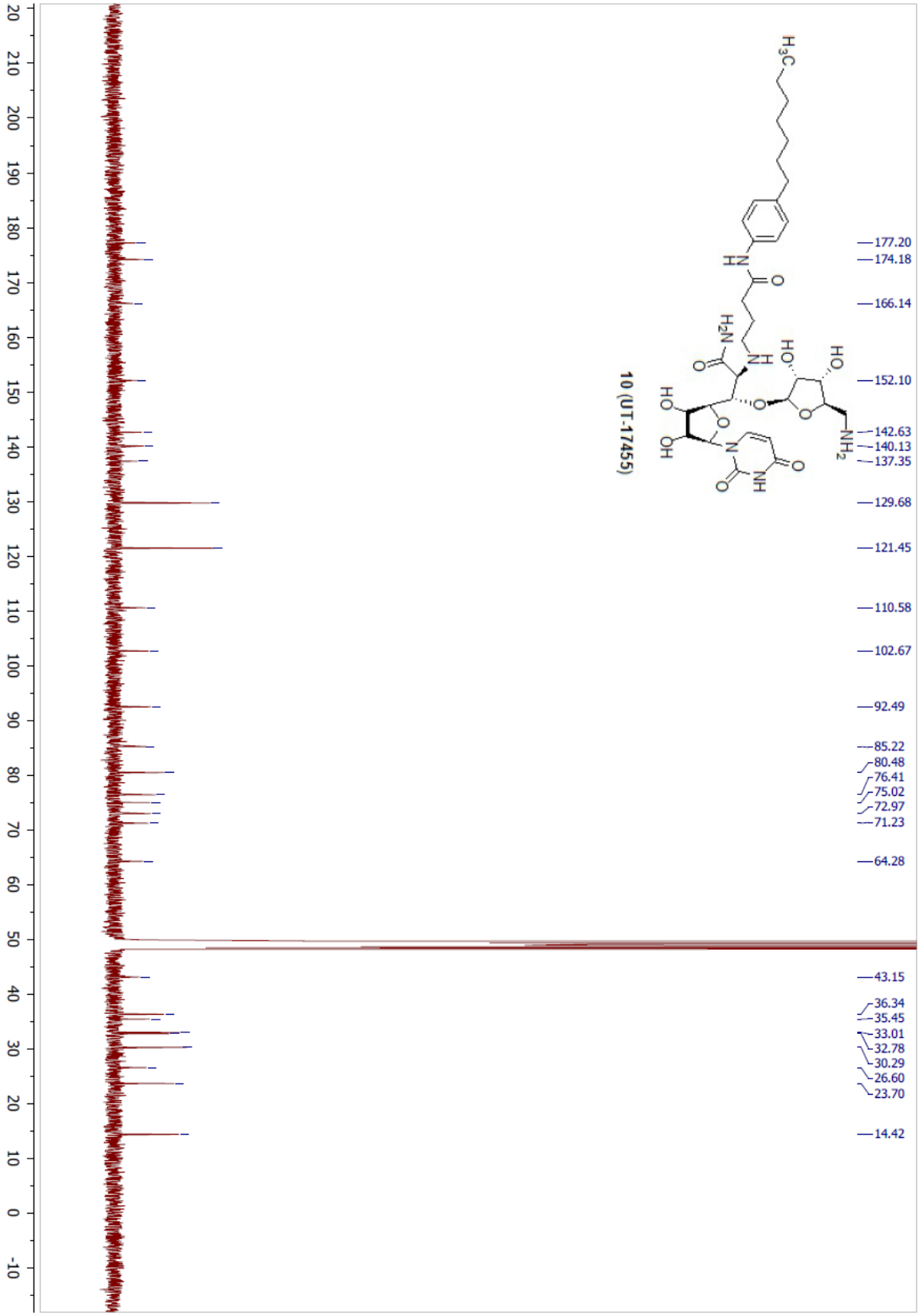
1.04
1.07
2.27
1.23
2.05
1.16
1.22
1.26
1.35
2.23
2.54
2.38
2.25
2.41
2.73
12.35
3.62


10 (UT-17455)
177.20
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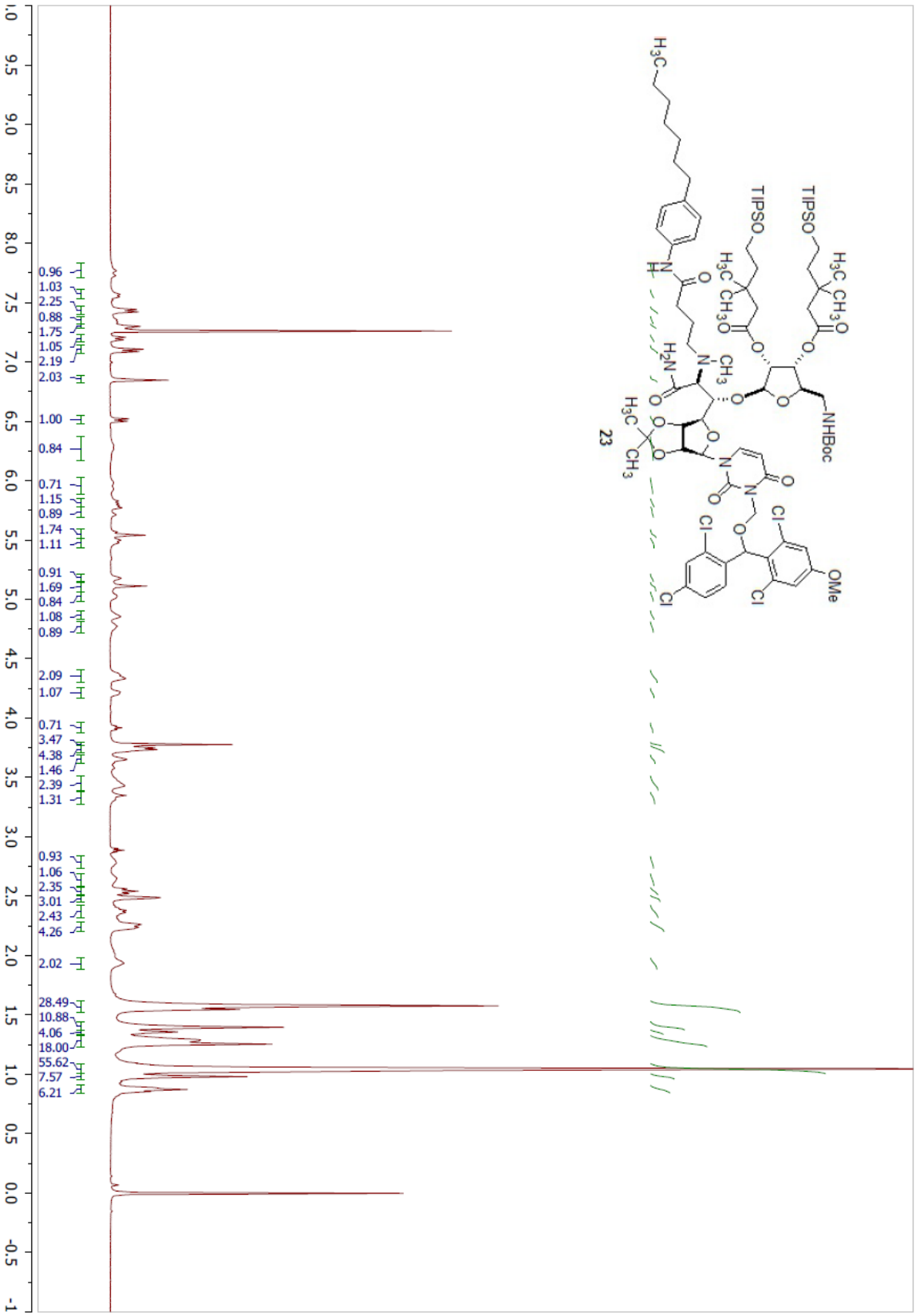
166.14
152.10
142.63
140.13
137.35
129.68
121.45
110.58
102.67
92.49
85.22
80.48
76.41
75.02
72.97
71.23
64.28
43.15
36.34
35.45
33.01
32.78
30.29
26.60
23.70
14.42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TIPSO
TIPSO
NHBoc
OMe
Cl
Cl
Cl
Cl
0.96
1.03
2.25
0.88
1.75
1.05
2.19
2.03
1.00
0.84
0.71
1.15
0.89
1.74
1.11
0.91
1.69
0.84
1.08
0.89
2.09
1.07
0.71
3.47
4.38
1.46
2.39
1.31
0.93
1.06
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3.01
2.43
4.26
2.02
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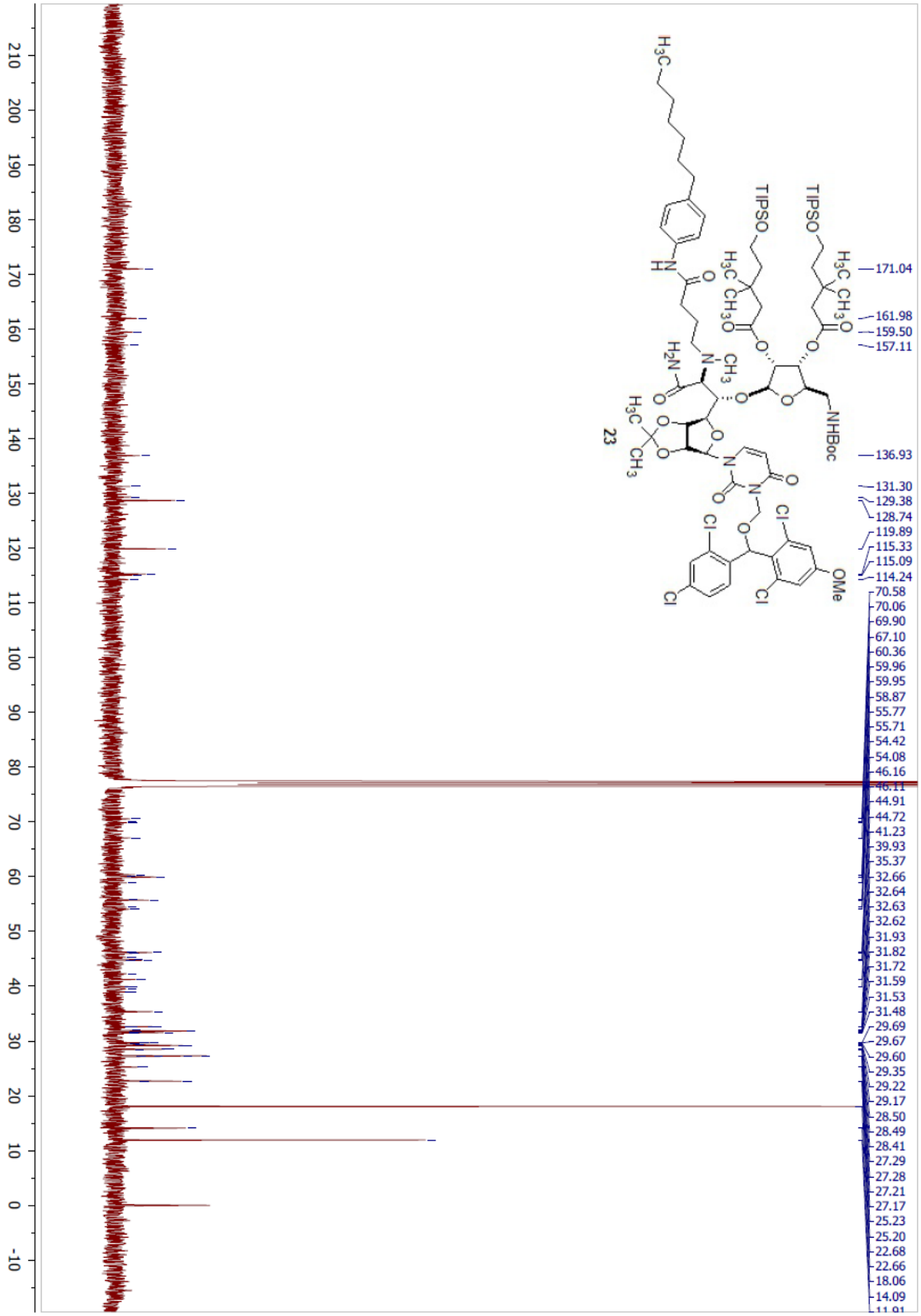
10.88
4.06
18.00
55.62
7.57
6.21


23
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157.11
136.93
131.30
129.38
128.74
119.89
115.33
115.09
114.24
70.58
70.06
69.90
67.10
60.36
59.96
59.95
58.87
55.77
55.71
54.42
54.08
46.16
44.91
44.72
41.23
39.93
35.37
32.66
32.64
32.63
32.62
31.93
31.82
31.72
31.59
31.53
31.48
29.69
29.67
29.60
29.35
29.22
29.17
28.50
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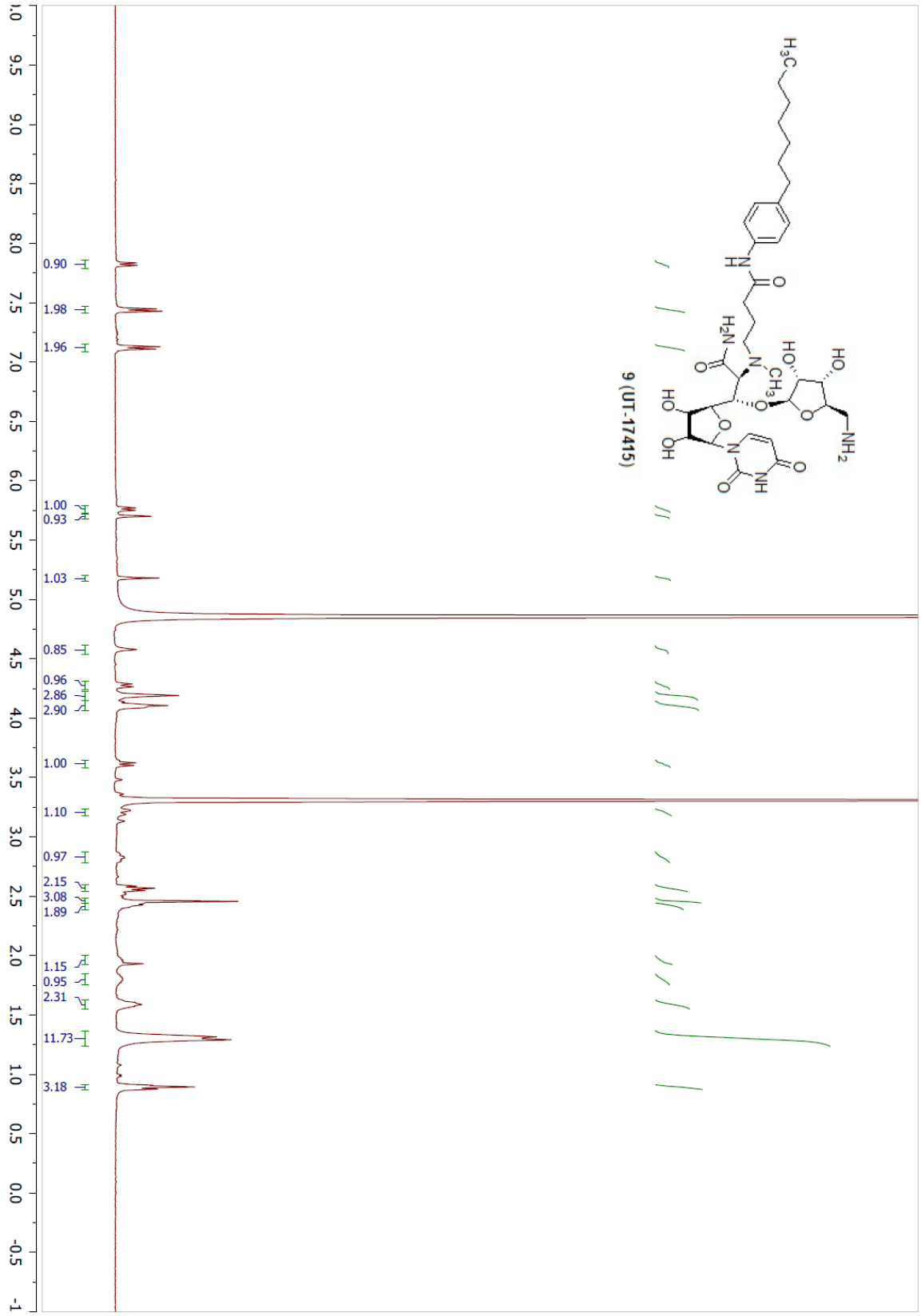
27.29
27.28
27.21
27.17
25.23
25.20
22.68
22.66
18.06
14.09


9 (UT-17415)
0.90
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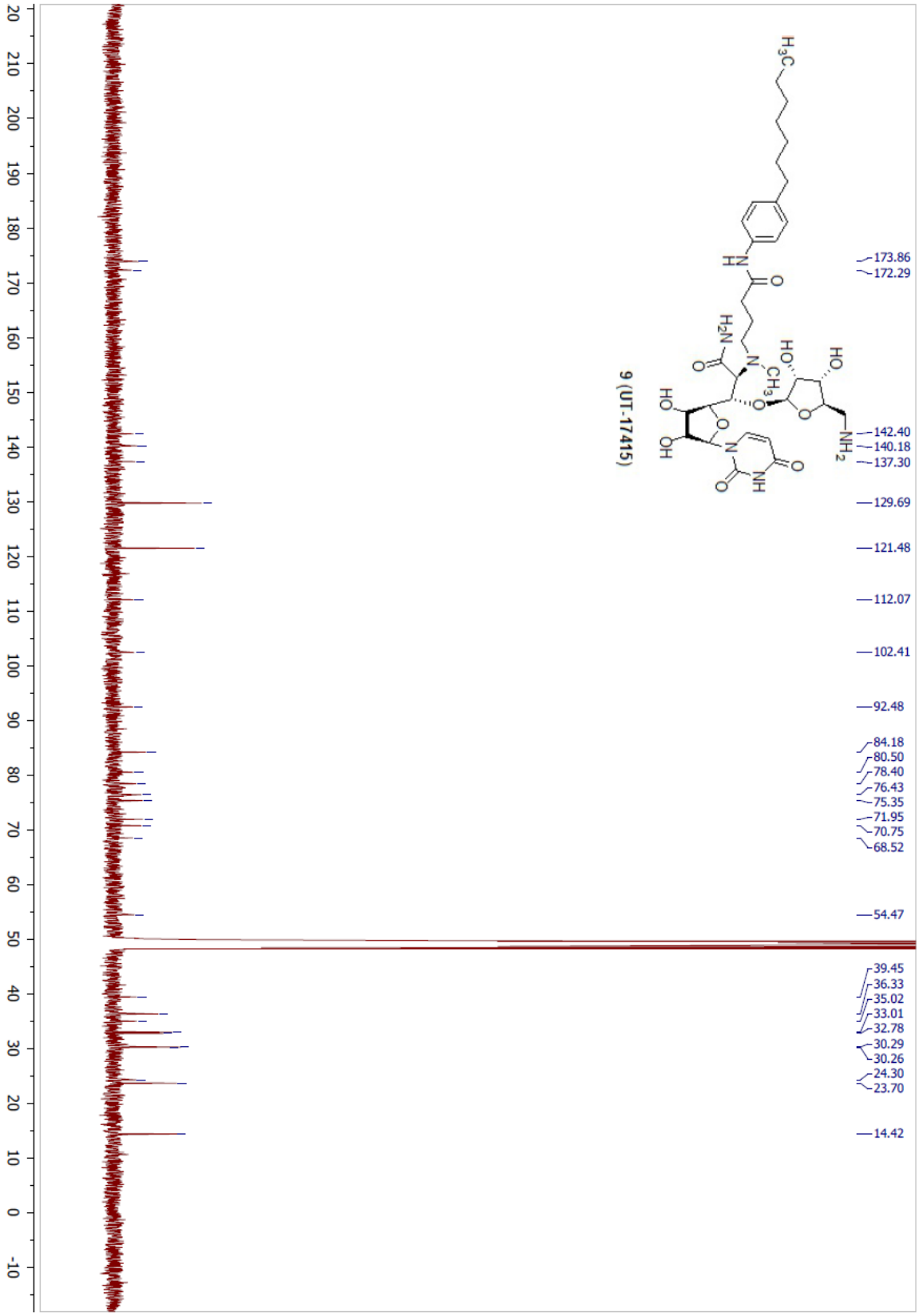
1.96
1.00
0.93
1.03
0.85
0.96
2.86
2.90
1.00
1.10
0.97
2.15
3.08
1.89
1.15
0.95
2.31
11.73
3.18


9 (UT-17415)
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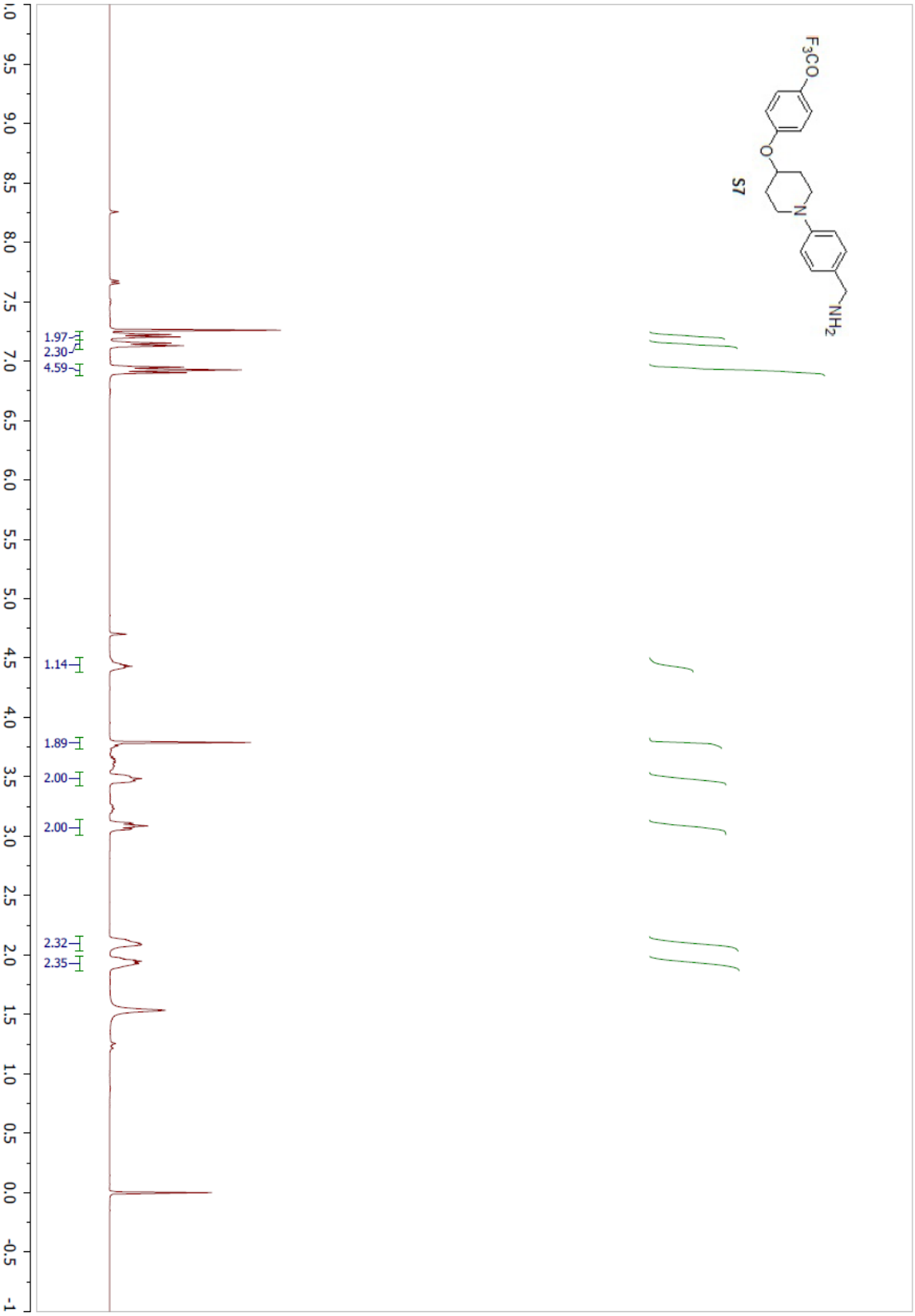
140.18
137.30
129.69
121.48
112.07
102.41
92.48
84.18
80.50
78.40
76.43
75.35
71.95
70.75
68.52
54.47
39.45
36.33
35.02
33.01
32.78
30.29
30.26
24.30
23.70
14.42


S7
F3CO
O
N
NH2
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2.30
4.59
1.14
1.89
2.00
2.00
2.32
2.35
10.0
9.5
9.0
8.5
8.0
7.5
7.0
6.5
6.0
5.5
5.0
4.5
4.0
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3.0
2.5
2.0
1.5
1.0
0.5
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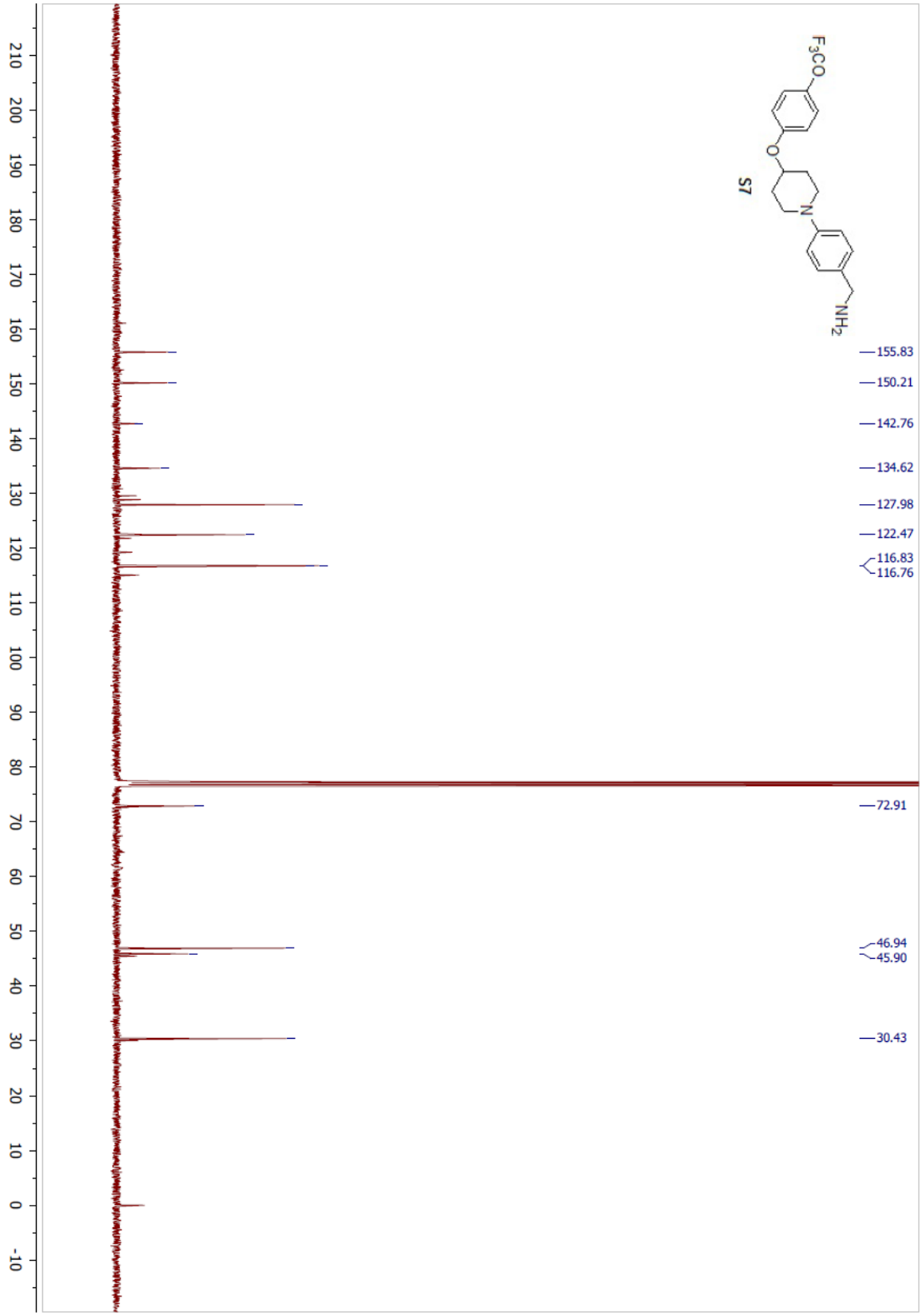
-0.5
-1.0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N
NH2
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134.62
127.98
122.47
116.83
116.76
72.91
46.94
45.90
30.43
210
200
190
180
170
160
150
140
130
120
110
100
90
80
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60
50
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30
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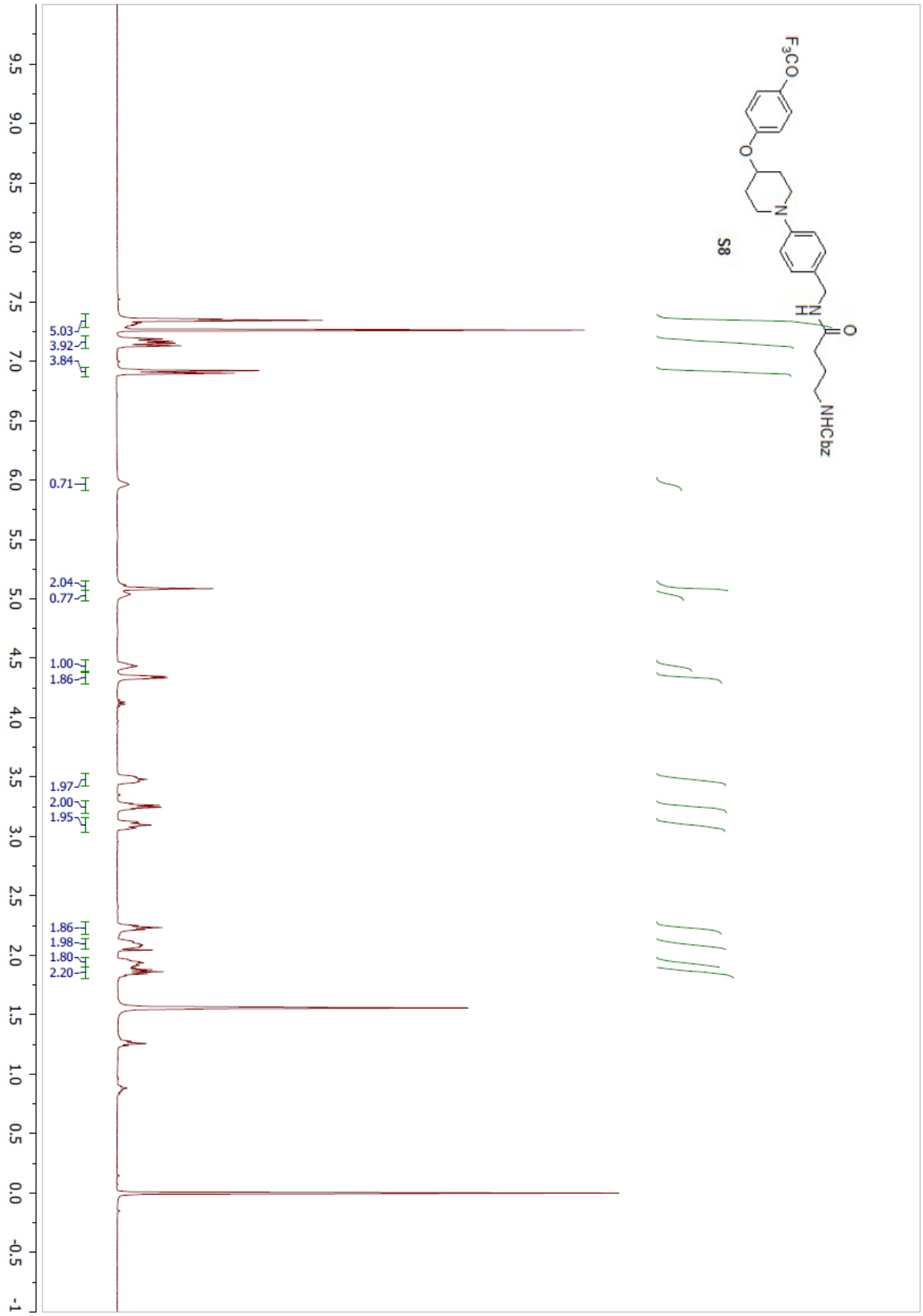
10
0
-10


S8
F3CO
O
N
H
O
NHCbz
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3.84
0.71
2.04
0.77
1.00
1.86
1.97
2.00
1.95
1.86
1.98
1.80
2.20
9.5
9.0
8.5
8.0
7.5
7.0
6.5
6.0
5.5
5.0
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4.0
3.5
3.0
2.5
2.0
1.5
1.0
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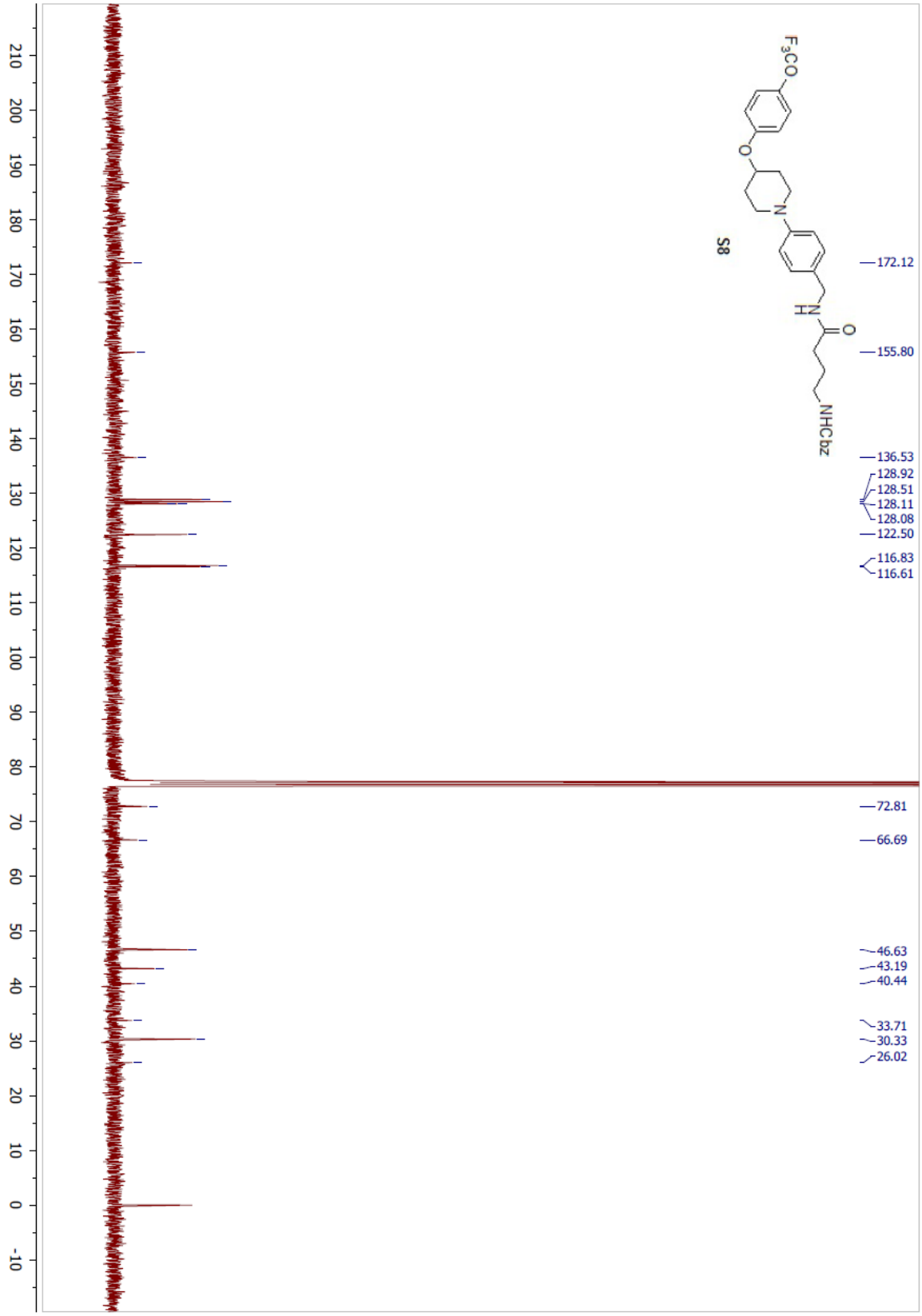
0.0
-0.5
-1


S8
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O
N
H
O
NHCbz
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128.11
128.08
122.50
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116.61
72.81
66.69
46.63
43.19
40.44
33.71
30.33
26.02
210
200
190
180
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120
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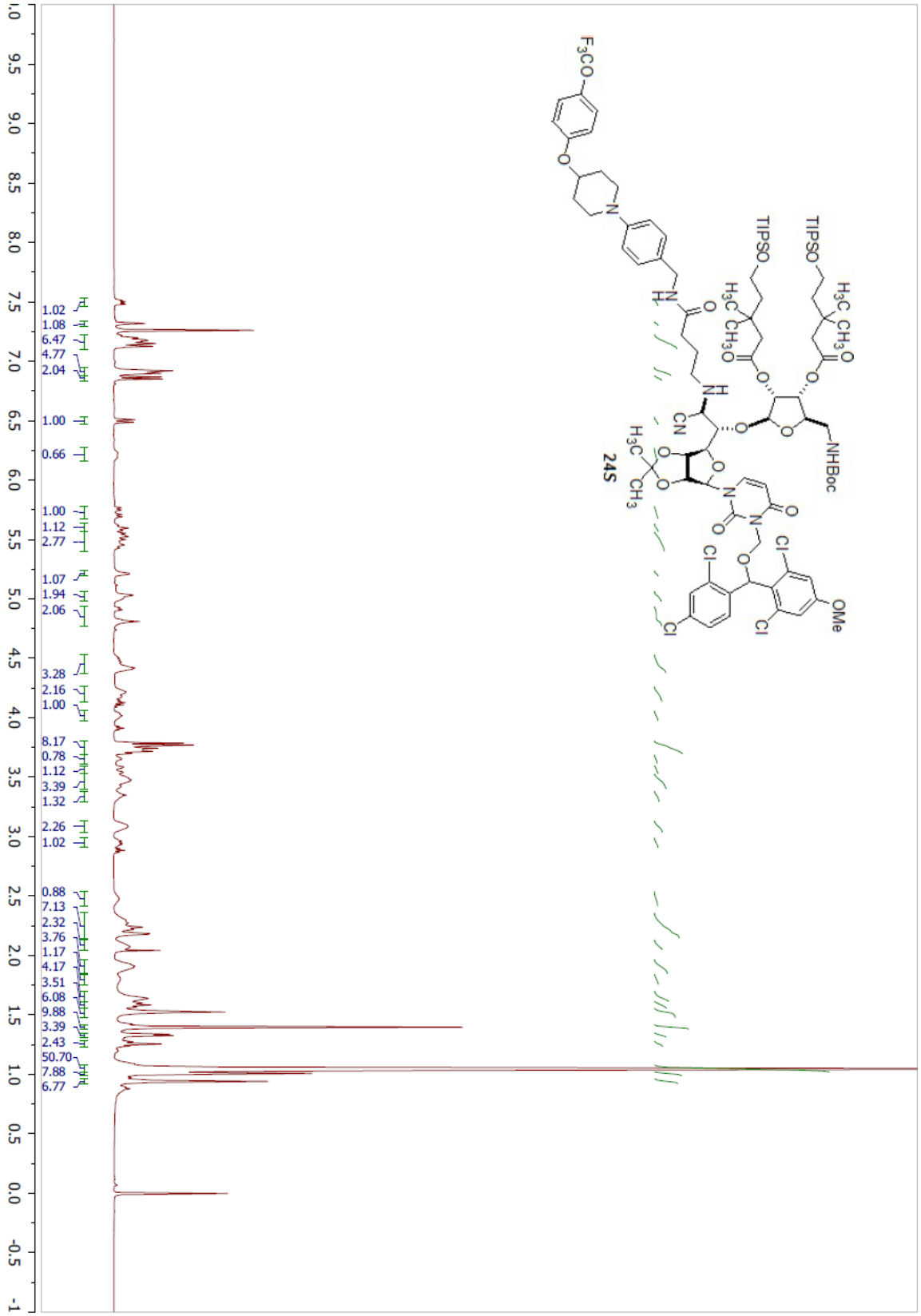
10
0
-10


24S
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TIPSO
NHBoc
OMe
F3CO
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2.04
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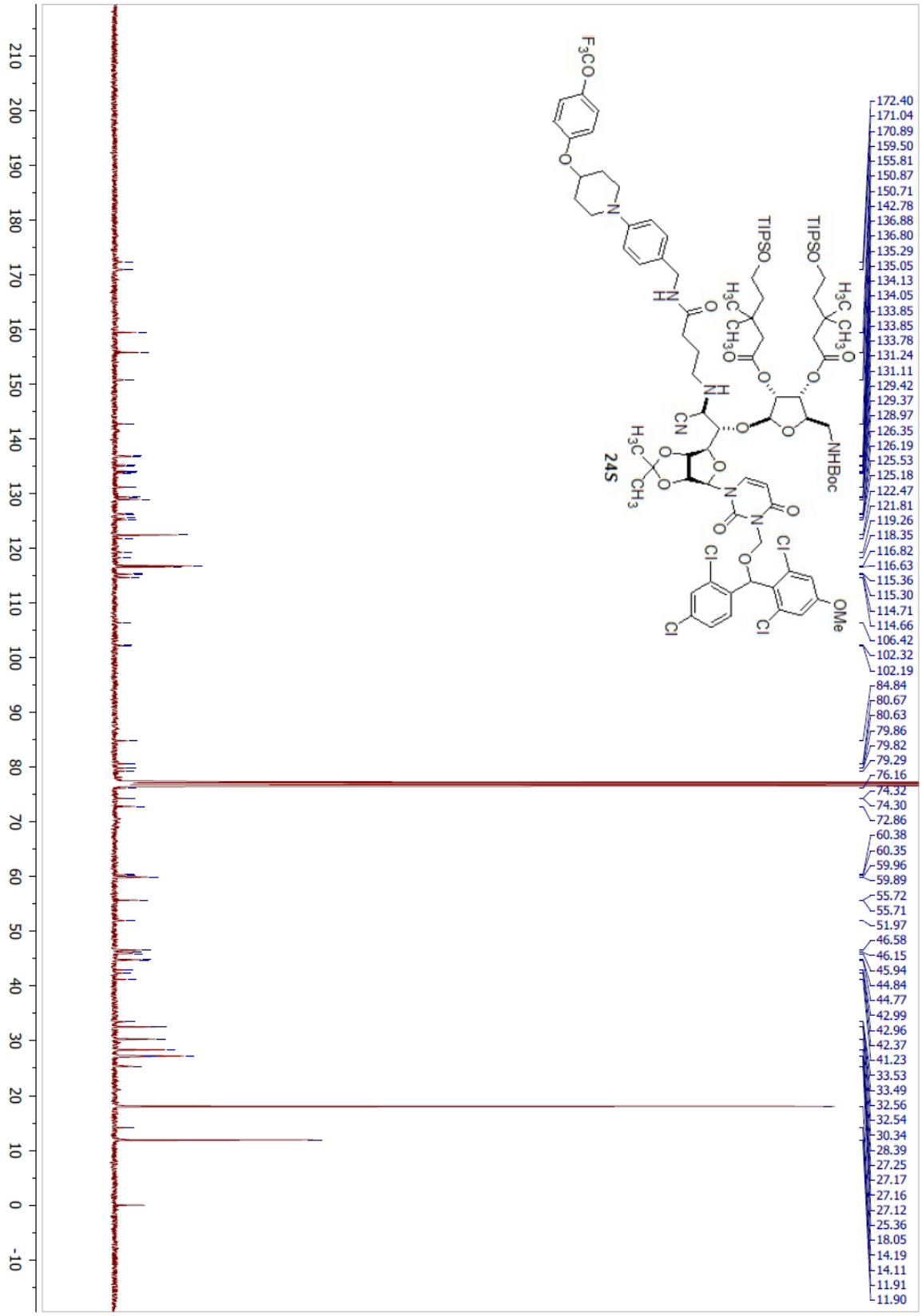
1.00
1.12
2.77
1.07
1.94
2.06
3.28
2.16
1.00
8.17
0.78
1.12
3.39
1.32
2.26
1.02
0.88
7.13
2.32
3.76
1.17
4.17
3.51
6.08
9.88
3.39
2.43
50.70
7.88
6.77


F3CO
TIPSO
TIPSO
NHBoc
OMe
24S
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170.89
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150.87
150.71
142.78
136.88
136.80
135.29
135.05
134.13
134.05
133.85
133.85
133.78
131.24
131.11
129.42
129.37
128.97
126.35
126.19
125.53
125.18
122.47
121.81
119.26
118.35
116.82
116.63
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115.30
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114.66
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79.86
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79.29
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59.89
55.72
55.71
51.97
46.58
46.15
45.94
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44.77
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42.96
42.37
41.23
33.53
33.49
32.56
32.54
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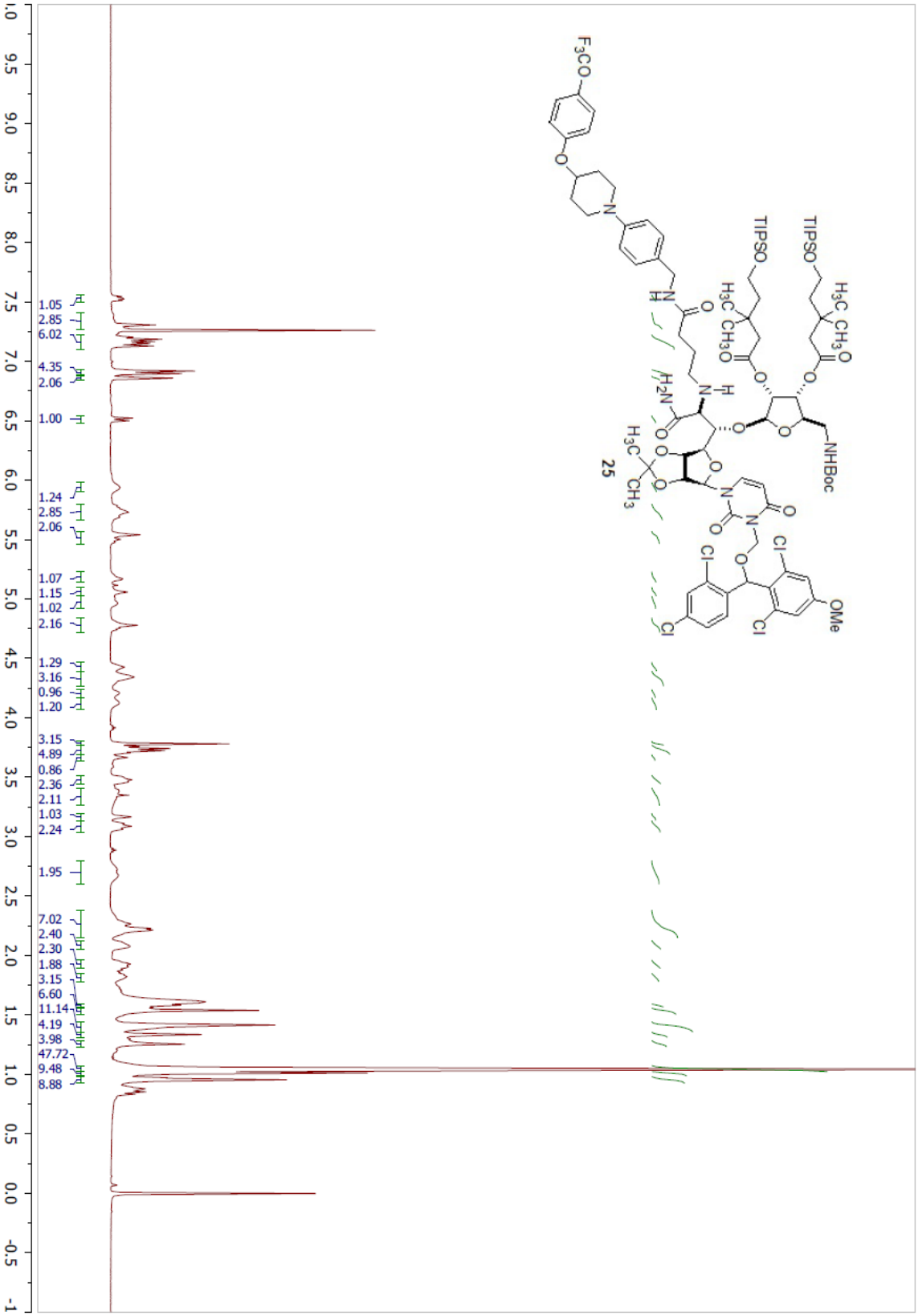
27.25
27.17
27.16
27.12
25.36
18.05
14.19
14.11
11.91
11.90


1.05
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4.35
2.06
1.00
1.24
2.85
2.06
1.07
1.15
1.02
2.16
1.29
3.16
0.96
1.20
3.15
4.89
0.86
2.36
2.11
1.03
2.24
1.95
7.02
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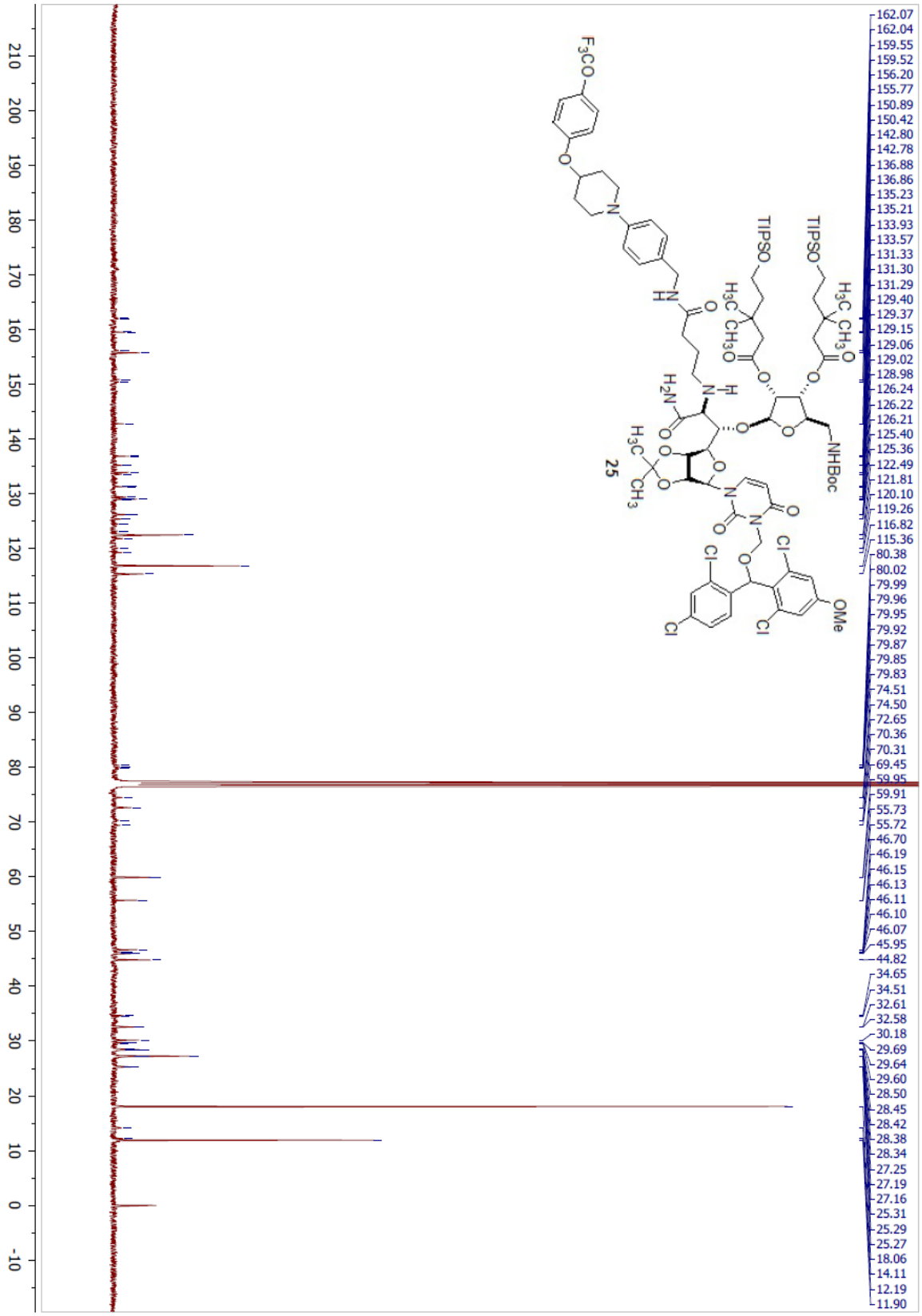
1.88
3.15
6.60
11.14
4.19
3.98
47.72
9.48
8.88
25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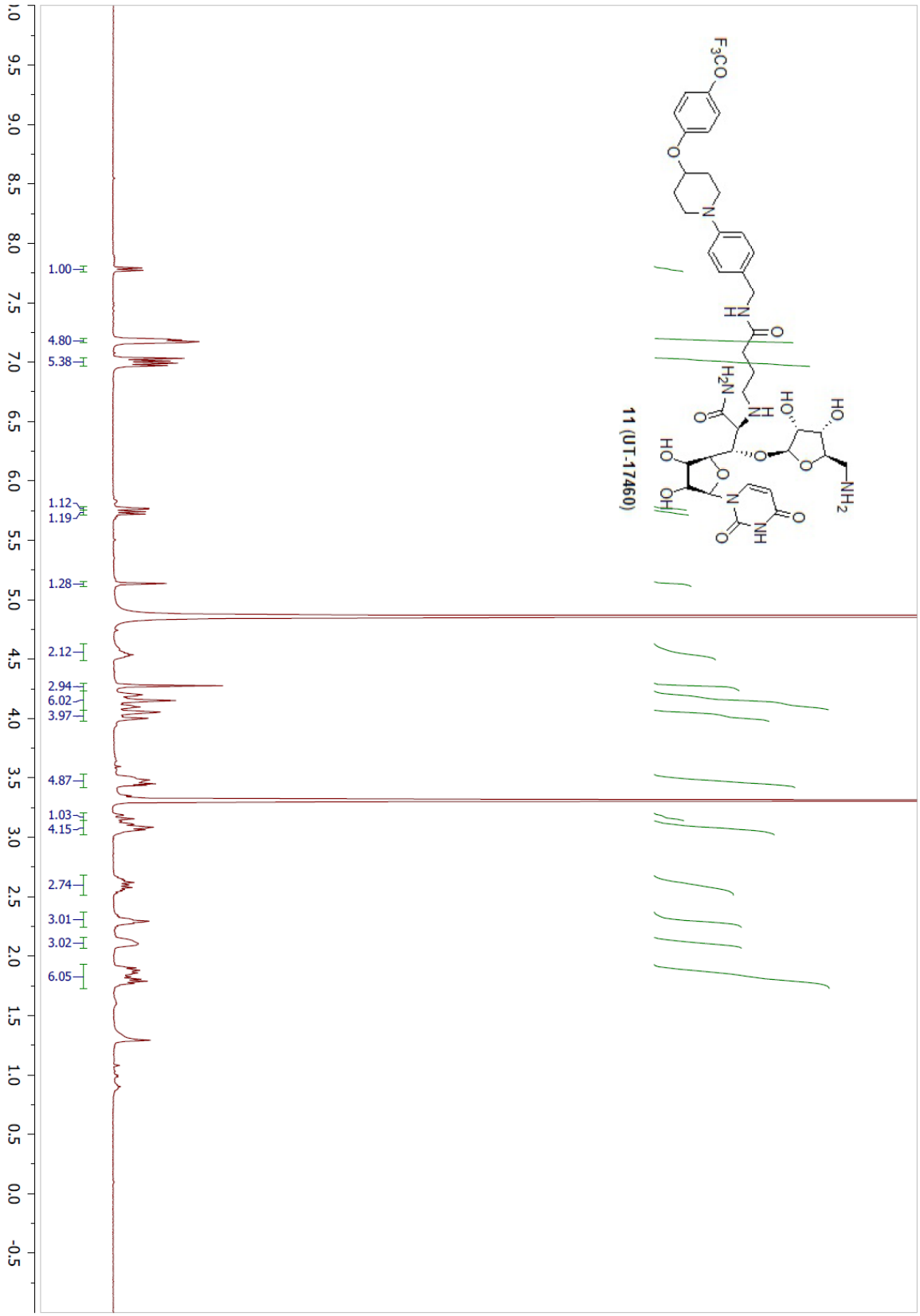
11 (UT-17460)
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1.19
1.28
2.12
2.94
6.02
3.97
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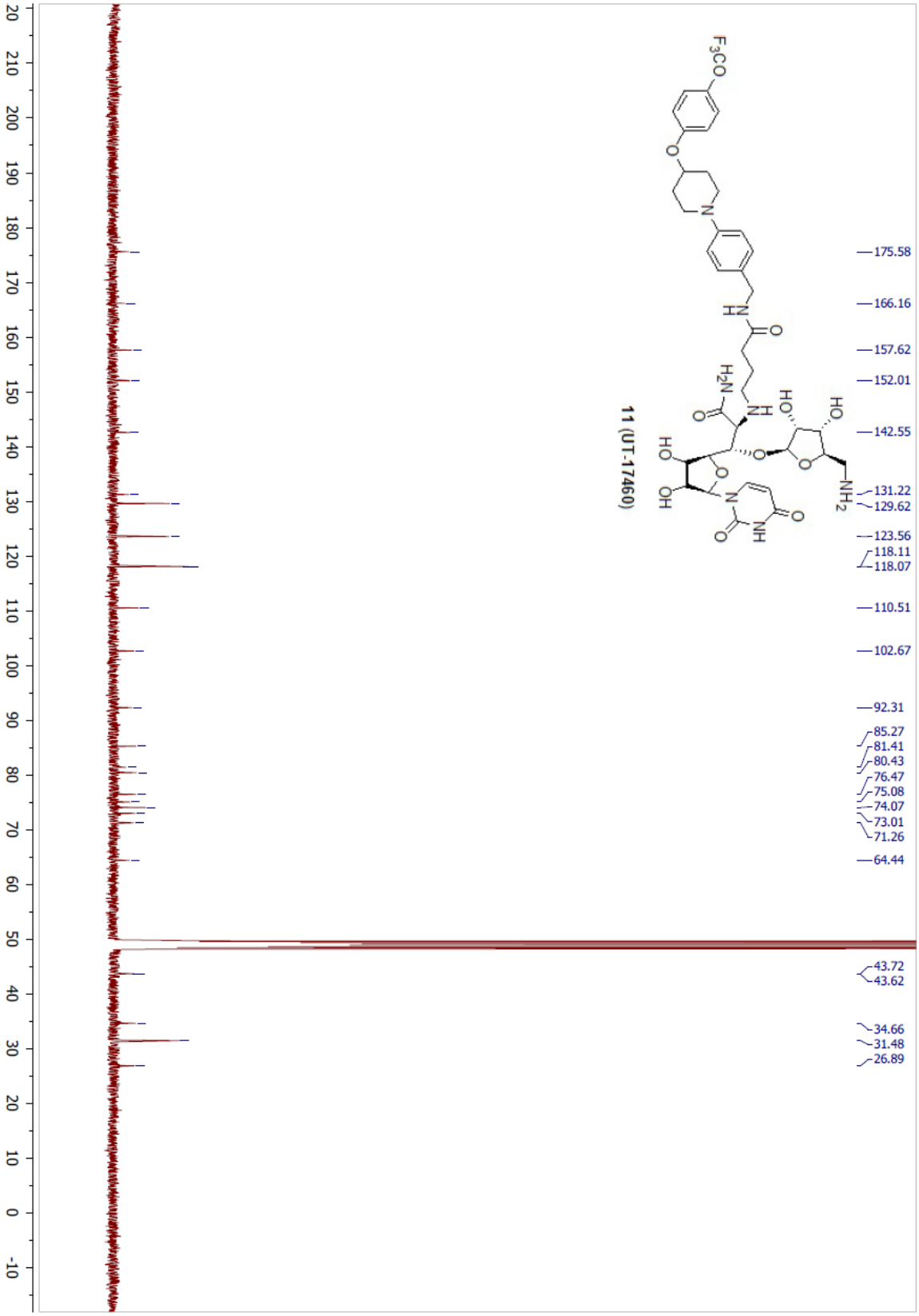
1.03
4.15
2.74
3.01
3.02
6.05


11 (UT-17460)
175.58
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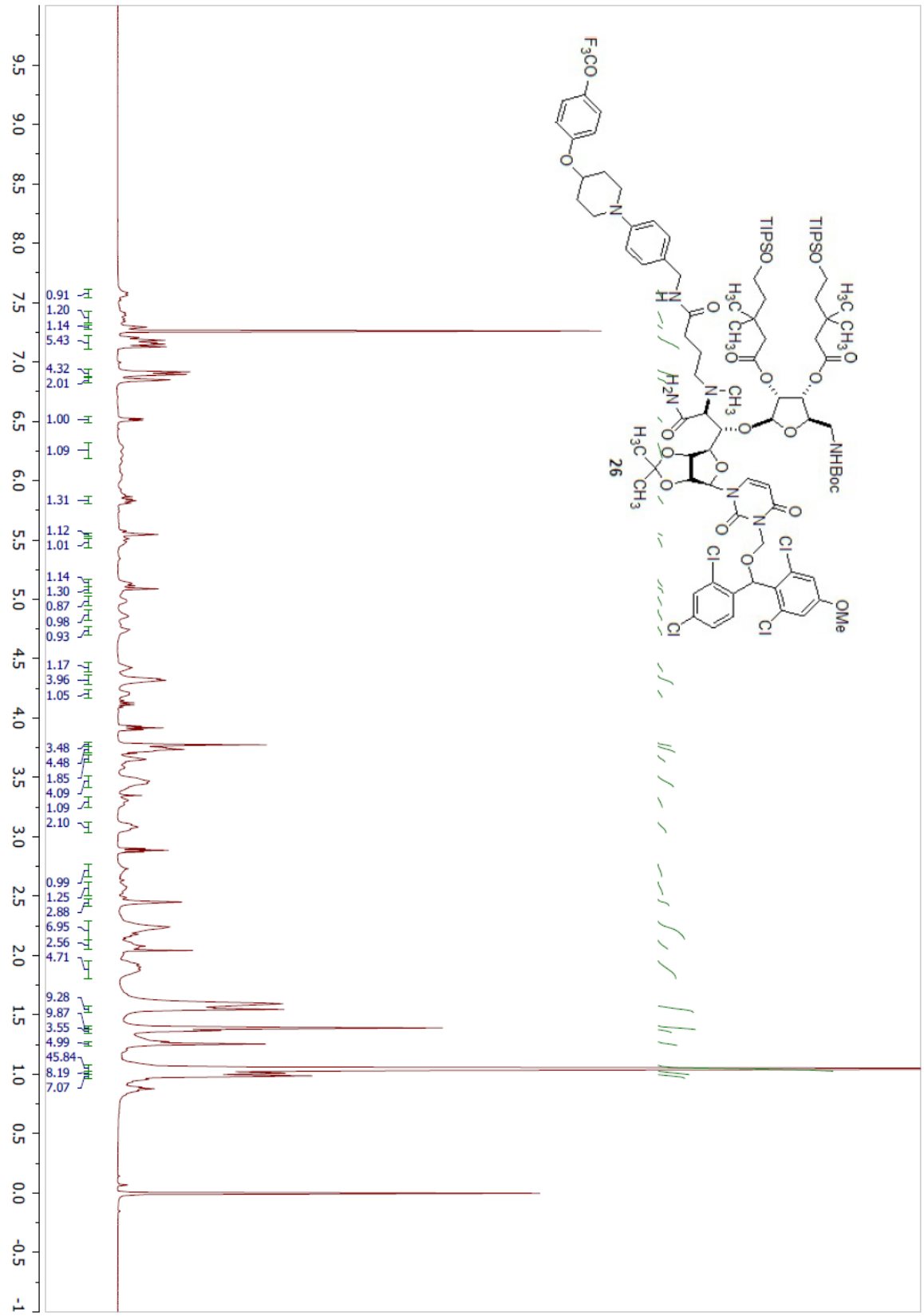
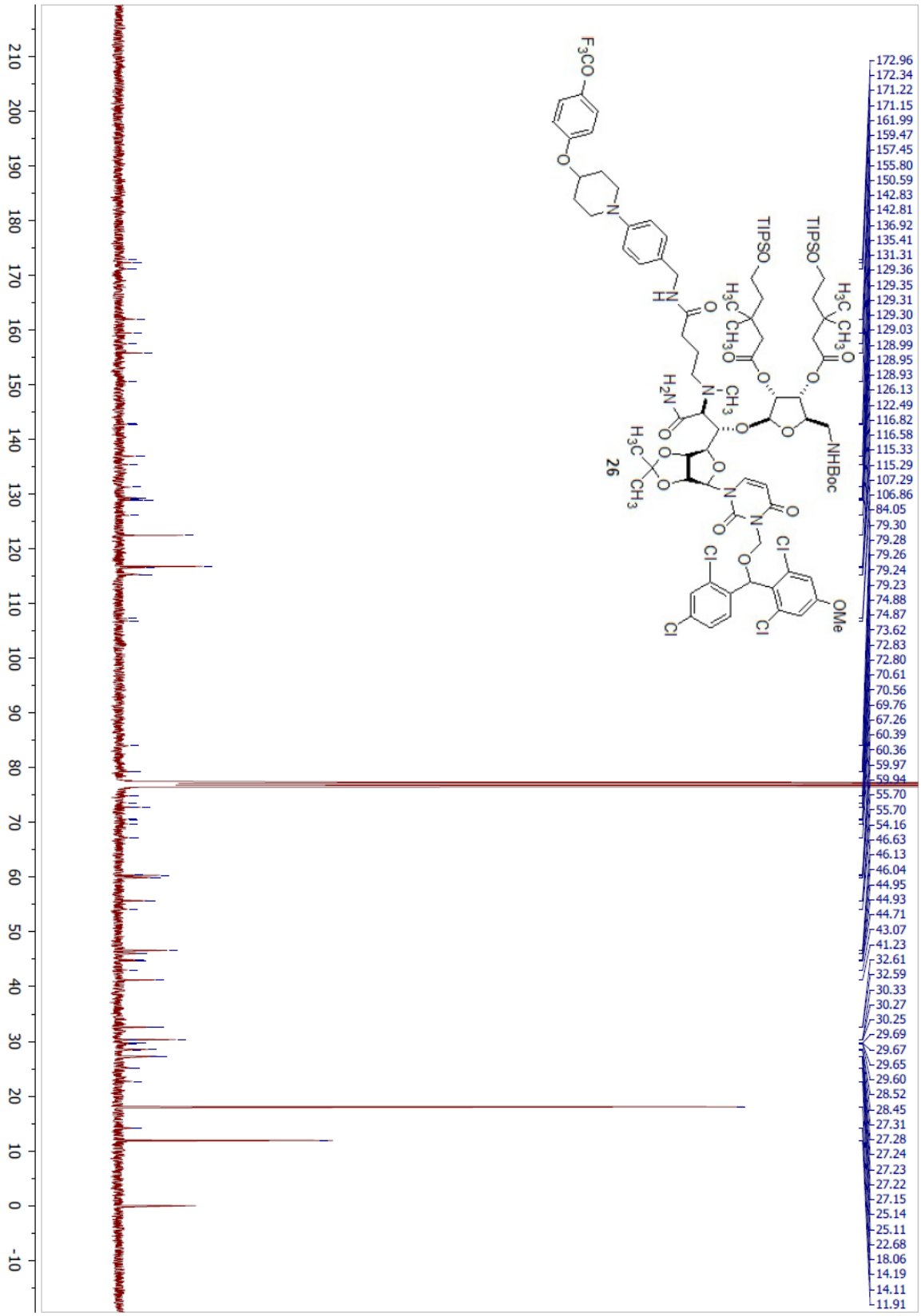
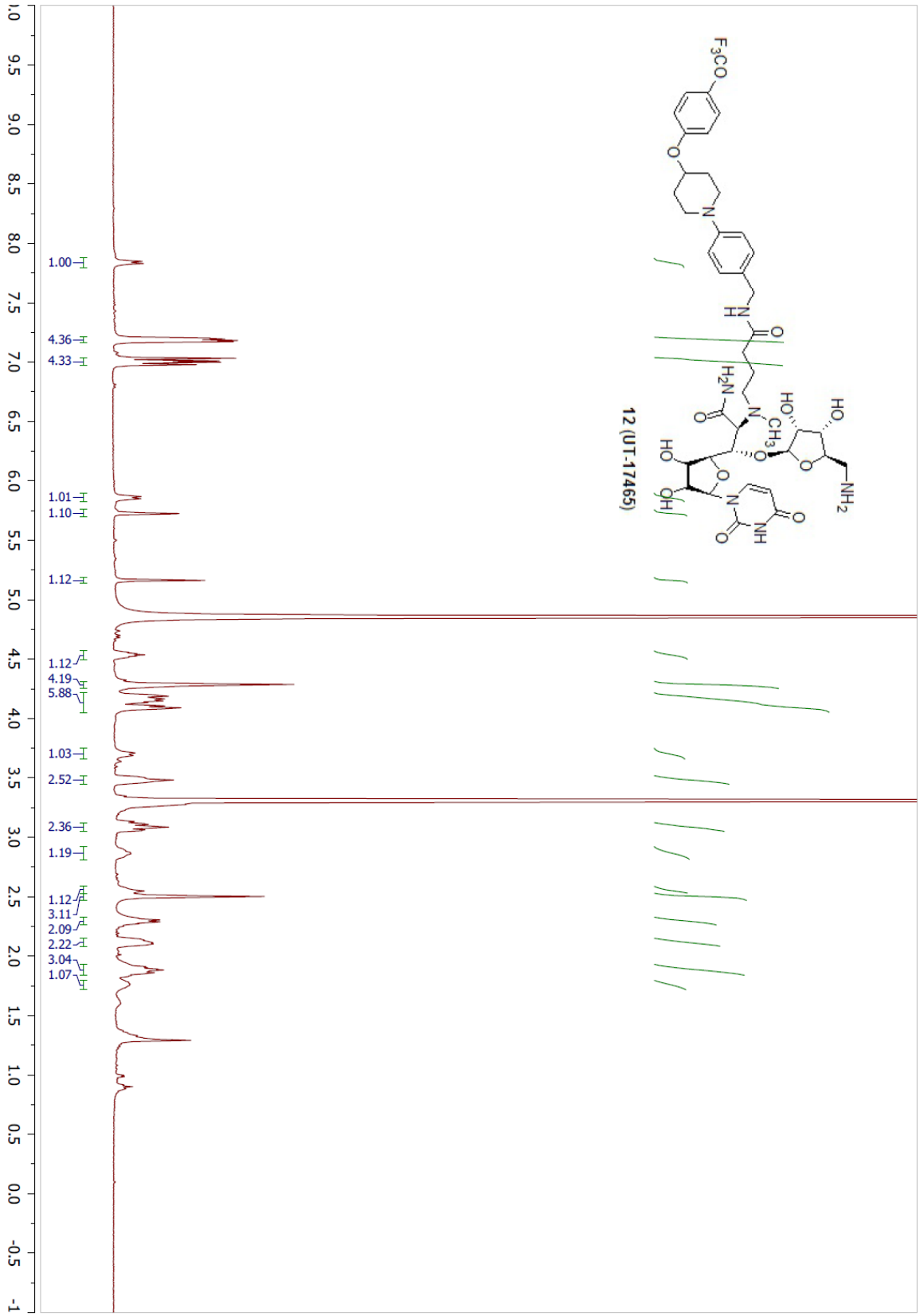
157.62
152.01
142.55
131.22
129.62
123.56
118.11
118.07
110.51
102.67
92.31
85.27
81.41
80.43
76.47
75.08
74.07
73.01
71.26
64.44
43.72
43.62
34.66
31.48
26.89


26


26


12 (UT-17465)
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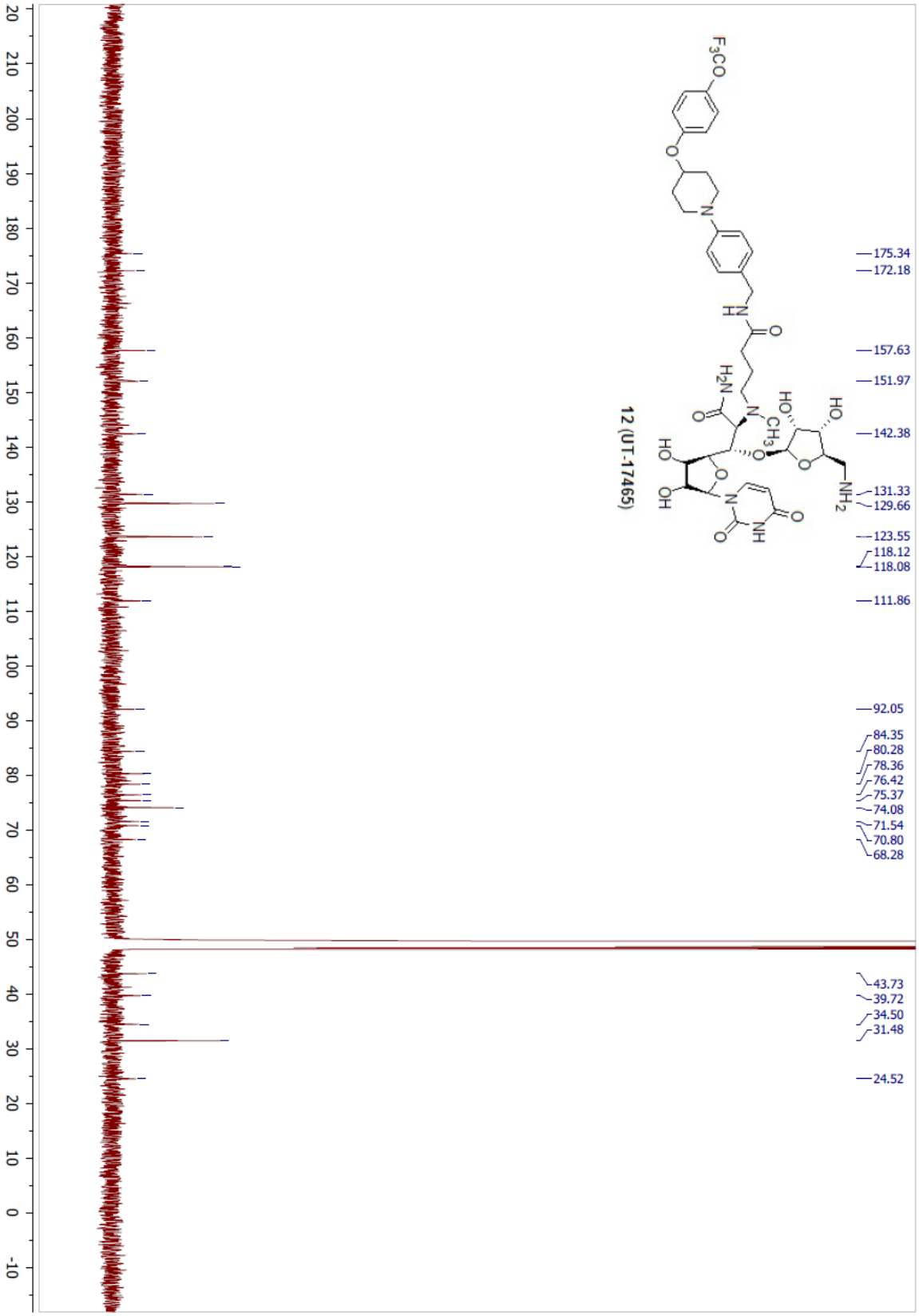
4.36
4.33
1.01
1.10
1.12
1.12
4.19
5.88
1.03
2.52
2.36
1.19
1.12
3.11
2.09
2.22
3.04
1.07


12 (UT-17465)
175.34
172.18
157.63
151.97
142.38
131.33
129.66
123.55
118.12
118.08
111.86
92.05
84.35
80.28
78.36
76.42
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70.80
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43.73
39.72
34.50
31.48
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