Supplementary Information

Design, Synthesis and Biological Evaluation of 5′-*C*-Piperidinyl-5′-*O*-Aminoribosyluridines as A Potential Antibacterial Agent

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Contents

1. Preparation of compounds

1-{(5*R*)-5-[(2*R*,4*R*)-1-Benzyloxycarbonyl-4-acetamido-hexahydro-2-pyridyl]-2,3-*O*-isopropylidene-β-D-*ribo*-pentofranosyl}uracil (**36**). Compound **32** (57.6 mg, 85.3 μmol) was added to a solution of AcCl (569 μL, 8.00 mmol) in MeOH (2 mL) at room temperature. The reaction mixture was stirred at room temperature for 2.5 h. The mixuture was concentrated *in vacuo*. A solution of the residue in acetone (2 mL) was treated with conc. H_2SO_4 (2.8 μL, 50 μmol) at room temperature for 2.5 h. Then conc. H_2SO_4 (2.8 μL, 50 μmol) and acetone (2 mL) was added to the reaction mixture,which was stirred for 1 h. After Et_3N (14 μL, 0.10 mol) was added, the mixuture was concentrated *in vacuo*. The residue was purified by preparative TLC (8% MeOH/$CHCl_3$) to afford **36** (39.8 mg, 84%) as a white solid. ^{1}H NMR (DMSO-d_6, D_2O, 400 MHz, a mixture of rotamers; selected data for the major rotamer) δ 7.76-7.72 (m, 2H, H-6, NH-4"), 7.38-7.31 (m, 5H, phenyl), 5.76 (br s, 1H, H-1'), 5.60 (d, 1H, H-5, $J_{5,6}$ = 8.2 Hz), 5.13-4.86 (m, 4H, H-2', H-3', CH_2Ph), 4.20-4.16 (m, 1H, H-2"), 4.01-3.83 (m, 4H, H-4', H-5', H-4", H-6"*eq.*), 2.85 (t, 1H, H-6"*ax.*, *J* = 13.1 Hz), 2.09 (d, 1H, H-3"*eq.*, *J* = 11.9 Hz), 1.77 (s, 4H, H-5"*ax.* or *eq.*, Ac), 1.41 (s, 3H, acetonide, major rotamer), 1.27-1.04 (m, 5H, H-3"ax, H-5"*ax.* or *eq.*, acetonide); ^{13}C NMR (DMSO-d_6, D_2O, 100 MHz, a mixture of rotamers) δ 168.4, 168.4, 163.2, 154.7, 154.5, 150.4, 142.5, 137.0, 128.5, 127.9, 127.8, 127.6, 127.4, 112.9, 101.9, 91.7, 91.6, 87.4, 87.3, 83.1, 82.9, 81.5, 81.0, 79.2, 69.1, 68.5, 66.4, 66.4, 53.2, 53.0, 42.0, 41.9, 32.0, 31.8, 30.7, 30.4, 29.1, 27.1, 25.2, 25.1, 22.8, 22.8; ESIMS-LR *m/z* 581 [(M + Na)$^+$]; ESIMS-HR calcd for $C_{27}H_{34}O_9N_4Na$ 581.2218, found 581.2211; $[\alpha]^{19}_D$ +15.6 (*c* 1.27, MeOH)

1-{5-[(2*R*,4*R*)-1-Benzyloxycarbonyl-4-acetamidohexahydro-2-pyridyl]-2,3-*O*-isopropylidene-5-oxo-β-D-*ribo*-pentofranosyl}uracil (**38**) **from 36**. A solution of **36** (10.7 mg, 19.2 μmol) in MeCN (1 mL) was treated with IBX (13.4 mg, 48.0 μmol) at 80 °C for 1 h. The reaction mixture was cooled in an ice bath, and the white precipitates were filtedered off through Celite pad. The filtrate was concentrated *in vacuo*. The residue was purified by flash silica gel column chromatography (3-7% MeOH-$CHCl_3$) to afford **38** (8.2 mg, 77%) as a white solid. ^{1}H NMR (acetone-d_6, 400 MHz, a mixture of rotamers; selected data for the major rotamer) δ 9.99 (br s, 1H, NH-3), 7.72 (d, 1H, H-6, $J_{6,5}$ = 8.2 Hz), 7.41-7.27 (m, 5H, phenyl), 7.11 (d, 1H, NH-4"', $J_{NH\text{-}4'',4''}$ = 7.3 Hz), 5.75 (s, 1H, H-1'), 5.65 (d, 1H, H-5, $J_{5,6}$ = 8.3 Hz), 5.39 (dd, 1H, H-3', $J_{3',2'}$ = 6.2, $J_{3',4'}$ = 2.1 Hz), 5.25 (d, 1H, H-2"*eq.*, $J_{2''eq,3''}$ = 6.4 Hz), 5.19 (d, 1H, H-2', $J_{2',3'}$ = 6.4 Hz), 5.31-5.11 (m, 2H, CH_2Ph), 4.78 (d, 1H, H-4', $J_{4',3'}$ = 2.1 Hz), 4.16-4.08 (m, 1H, H-6"*eq.*), 3.75-3.58 (m, 1H, H-4"*ax.*), 3.41 (td, 1H, H-6"ax, *J* = 13.7, *J* = 3.1 Hz), 2.52 (d, 1H, H-3"*eq.*, *J* = 13.8 Hz), 1.82 (s, 3H, Ac), 1.82-1.79 (m, 1H, H-5"*ax.* or *eq.*), 1.44-1.55 (m, 1H, H-3"*ax.*), 1.49 (s, 3H, acetonide), 1.39-1.28 (m, 1H, H-5"*ax.* or *eq.*), 1.34 (s, 3H, acetonide); ^{13}C NMR (DMSO-d_6, 100 MHz, a mixture of rotamers) δ 204.8, 204.1, 168.6, 168.5, 163.5, 163.4, 154.7, 154.6, 150.9, 150.8, 144.6, 144.5, 137.1, 136.7, 128.5, 128.4, 128.3, 127.9, 127.8, 127.7, 127.6, 127.5, 127.4, 127.3, 112.5, 112.3, 101.7, 101.6, 96.1, 95.8, 92.4, 92.3, 84.1, 84.0, 82.4, 82.3, 66.7, 66.4, 57.5, 56.7, 43.2, 42.9, 31.9, 31.1, 31.0, 30.6, 26.5, 24.8, 22.7, 22.6; ESIMS-LR *m/z* 579 [(M + Na)$^+$]; ESIMS-HR calcd for $C_{27}H_{32}O_9N_4Na$ 579.2062, found 579.2058; $[\alpha]^{20}_D$ +1.67 (*c* 0.82, MeOH).

1-{(5*S*)-5-[(2*R*,4*R*)-1-Benzyloxycarbonyl-4-acetamidohexahydro-2-pyridyl]-2,3-*O*-isopropylidene-β-D-*ribo*-pentofranosyl}uracil (**37**). Compound **34** (24.5 mg, 29.0 μmol) was added to a

solution of AcCl (285 μL, 4.00 mmol) in MeOH (1 mL) at room temperature. The reaction mixture was stirred at room temperature for 19.5 h and was concentrated *in vacuo*. A solution of the residue in acetone (1 mL) was treated with conc. H_2SO_4 (1.4 μL, 25 μmol) at room temperature for 3.5 h. After Et_3N (6.7 μL, 50 μmol) was added, the mixuture was concentrated *in vacuo*. The residue was purified by flash silica gel column chromatography (3-10% MeOH-$CHCl_3$) to afford **37** (8.5 mg, 52%) as a white solid. ^{1}H NMR (DMSO-d_6, D_2O, 400 MHz, a mixture of rotamers; selected data for the major rotamer) δ 7.99 (d, 1H, H-6, $J_{6,5}$ = 8.2 Hz), 7.80-7.77 (m, 1H, NH-4"), 7.37-7.24 (m, 5H, phenyl), 6.00-5.97 (m, 1H, H-1'), 5.21 (d, 1H, H-5, $J_{5,6}$ = 8.2 Hz), 5.08-5.05 (m, 2H, CH_2Ph), 4.88-4.85 (m, 1H, H-3'), 4.75-4.72 (m, 1H, H-2'), 4.39-4.31 (m, 2H, H-4', H-2"), 4.15-4.09 (m, 1H, H-5'), 4.05-3.94 (m, 1H, H-6"*ax.* or *eq.*), 3.83 (br s, 1H, H-4"), 3.08-2.96 (m, 1H, H-6"*ax.* or *eq.*), 1.89 (d, 1H, H-3"*eq.*, *J* = 12.8 Hz), 1.77 (s, 4H, H-5"*ax.* or *eq.*, Ac), 1.51 (s, 3H, acetonide), 1.29 (s, 3H, acetonide), 1.29-1.17 (m, 2H, H-3"*ax.*, H-5"*ax.* or *eq.*); ^{13}C NMR (DMSO-d_6, D_2O, 100 MHz, mixture of rotamers) δ 168.6, 163.1, 162.8, 155.2, 155.0, 150.5, 150.4, 141.4, 140.6, 137.4, 137.2, 128.5, 128.3, 127.8, 127.5, 127.4, 126.7, 113.0, 112.8, 102.1, 102.0, 90.2, 89.6, 84.9, 84.6, 83.5, 83.3, 81.4, 81.2, 66.9, 66.6, 66.1, 66.0, 53.1, 52.6, 42.2, 32.4, 32.1, 31.7, 31.4, 29.1, 27.3, 25.4, 22.8; ESIMS-LR *m/z* 581 [(M + Na)$^+$]; ESIMS-HR calcd for $C_{27}H_{34}O_9N_4Na$ 581.22180, found 581.22263; $[\alpha]^{20}_D$ +26.5 (*c* 0.66, MeOH).

1-{5-[(2*R*,4*R*)-1-Benzyloxycarbonyl-4-acetamidohexahydro-2-pyridyl]-2,3-*O*-isopropylidene-5-oxo-β-D-*ribo*-pentofranosyl}uracil (38) from 37. Compound **37** (6.6 mg, 12 μmol) in MeCN (1 mL) were treated with IBX (8.3 mg, 30 μmol) and, the mixture was heated at 80 °C for 2 h. The reaction mixture was cooled in an ice bath, then the white precipitates were filtedered off through Celite pad. The filtrate was concentrated *in vacuo*. The residue was purified by flash silica gel column chromatography (3-5% MeOH-$CHCl_3$) to afford **38** (3.5 mg, 53%) as a white solid. Characterization data were completely identical to those obtained from **36**.

1-{(5*R*)-5-[(2*S*,4*S*)-1-Benzyloxycarbonyl-4-acetamidohexahydro-2-pyridyl]-2,3-*O*-isopropylidene-β-D-*ribo*-pentofranosyl}uracil (40). Compound **30c** (35.1 mg, 41.6 μmol) was added to a solution of AcCl (285 μL, 4.00 mmol) in MeOH (1 mL) at room temperature. The reaction mixture was stirred at room temperature for 4.5 h was concentrated *in vacuo*. A solution of the residue in acetone (2 mL) was treated with conc. H_2SO_4 (2.8 μL, 50 μmol) at room temperature for 15.5 h. After Et_3N (14 μL, 0.10 mol) was added, the mixuture was concentrated *in vacuo*. The residue was purified by preparative TLC (8% MeOH/$CHCl_3$) to afford **40** (7.6 mg, 33%) as a white solid. ^{1}H NMR (DMSO-d_6, D_2O, 400 MHz) δ 7.78-7.70 (m, 2H, H-6, NH-4"), 7.38-7.29 (m, 5H, phenyl), 5.89 (s, 1H, H-1'), 5.66-5.61 (m, 1H, H-5), 5.10-4.99 (m, 2H, CH_2Ph), 4.93-4.79 (m, 2H, H-2', H-3'), 4.18 (t, 1H, H-2", *J* = 6.4 Hz), 4.08-3.90 (m, 4H, H-4', H-5', H-4", H-6"*eq.*), 2.97 (t, 1H, H-6"*ax.*, *J* = 6.4 Hz), 1.84-1.76 (m, 2H, H-3"*ax.* or *eq.*, H-5"*ax.* or *eq.*), 1.76 (s, 3H, Ac), 1.44 (s, 3H, acetonide), 1.41-1.33 (m, 1H, H-3"*ax.* or *eq.*), 1.23 (s, 3H, acetonide), 1.25-1.16 (m, 1H, H-5"ax or eq); ^{13}C NMR (DMSO-d_6, D_2O, 100 MHz, mixture of rotamers) δ 168.6, 168.5, 163.1, 155.7, 155.1, 150.4, 141.6, 137.1, 128.5, 128.4, 127.9, 127.8, 127.5, 113.5, 113.3, 102.1, 102.0, 89.6, 86.2, 86.1, 83.8, 83.6, 78.5, 68.0, 67.5, 66.3, 52.3, 42.3, 42.2, 32.5, 31.4, 29.1, 28.8, 27.1, 25.4, 25.2, 22.8, 22.7; ESIMS-LR *m/z* 581 [(M + Na)$^+$]; ESIMS-HR calcd for $C_{27}H_{34}O_9N_4Na$ 581.2218, found

581.2220; $[\alpha]^{20}_{D}$ −32.6 (*c* 0.76, MeOH).

1-{5-[(2*S*,4*S*)-1-Benzyloxycarbonyl-4-acetamidohexahydro-2-pyridyl]-2,3-*O*-isopropylidene-5-oxo-β-D-*ribo*-pentofranosyl}uracil (42). A mixture of **40** (7.6 mg, 14 μmol) and IBX (9.5 mg, 34.0 μmol) in MeCN (1 mL) was heated at 80 °C for 80 min. The reaction mixture was cooled in an ice bath, then the white precipitates were filtedered off through Celite pad. The filtrate was concentrated *in vacuo*. The residue was purified by flash silica gel column chromatography (3-6% MeOH-$CHCl_3$) to afford **42** (4.4 mg, 58%) as a white solid. ^{1}H NMR (DMSO-d_6, 400 MHz, a mixture of rotamers; selected data for the major rotamer) δ 11.4 (br s, 1H, NH-3), 7.78-7.69 (m, 2H, H-6, NH-4"), 7.41-7.26 (m, 5H, phenyl) 5.76 (s, 1H, H-1'), 5.62 (d, 1H, H-5, $J_{5.6}$ = 7.3 Hz), 5.22-5.02 (m, 4H, H-2', H-3', CH_2Ph), 4.98 (br s, 1H, H-2"), 4.71 (d, 1H, H-4', $J_{4',3'}$ =2.3 Hz), 3.98-3.95 (m, 1H, H-6"*eq*.), 3.79-3.71 (m, 1H, H-4"), 2.93 (t, 1H, H-6"*ax*., *J* = 12.9 Hz), 2.16-2.07 (m, 1H, H-3"*ax.* or *eq.*), 1.76 (s, 3H, Ac), 1.76-1.69 (m, 1H, H-5"*ax.* or *eq.*), 1.47 (s, 3H, acetonide), 1.30 (s, 3H, acetonide), 1.37-1.23 (m, 1H, H-3"ax or eq), 1.17-1.07 (m, 1H, H-5"*ax.* or *eq.*); ^{13}C NMR (DMSO-d_6, 100 MHz, a mixture of rotamers) δ 205.4, 204.5, 168.4, 163.5, 163.3, 154.7, 154.6, 151.1, 150.8, 144.3, 144.2, 136.8, 136.7, 128.5, 127.9, 127.5, 127.3, 112.7, 112.7, 101.6, 101.5, 95.8, 92.1, 91.4, 83.9, 83.3, 82.8, 66.6, 56.7, 56.2, 42.4, 42.2, 31.4, 31.0, 30.5, 30.2, 29.0, 26.5, 24.9, 22.8; ESIMS-LR *m/z* 579 [(M + Na)$^+$]; ESIMS-HR calcd for $C_{27}H_{32}O_9N_4Na$ 579.2062, found 579.2064; $[\alpha]^{18}_{D}$ −79.4 (*c* 0.42, MeOH).

1-{(5*S*)-5-[(2*S*,4*S*)-1-Benzyloxycarbonyl-4-acetamidohexahydro-2-pyridyl]-2,3-*O*-isopropylidene-β-D-*ribo*-pentofranosyl}uracil (41). Compound **35** (33.1 mg, 39.2 μmol) was added to a solution of AcCl (285 μL, 4.00 mmol) in MeOH (1 mL) at room temperature for 4.5 h. The mixuture was concentrated *in vacuo*. A solution of the residue in acetone (2 mL) was treated with conc. H_2SO_4 (2.8 μL, 50 μmol) at room temperature for 15.5 h. After Et_3N (14 μL, 0.10 mol) was added, the mixuture was concentrated *in vacuo*. The residue was purified by preparative TLC (8% MeOH/$CHCl_3$) to afford **41** (4.9 mg, 22%) as a white solid. ^{1}H NMR (DMSO-d_6, D_2O, 400 MHz, a mixture of rotamers; selected data for the major rotamer) δ 7.92-7.88 (m, 1H, H-6), 7.77-7.75 (m, 1H, NH-4"), 7.37-7.26 (m, 5H, phenyl), 5.92 (d, 1H, H-1', $J_{1',2'}$ = 3.2 Hz), 5.68 (d, 1H, H-5, $J_{5.6}$ = 8.2 Hz), 5.08-4.92 (m, 2H, CH$_2$Ph), 4.79-4.73 (m, 2H, H-2', H-3'), 4.24-4.22 (m, 1H, H-2"), 4.04-3.94 (m, 4H, H-4', H-5', H-4", H-6"*eq*.), 2.88 (t, 1H, H-6"*ax*., *J* = 13.3 Hz), 2.07 (d, 1H, H-3"*eq*., *J* = 11.4 Hz), 1.81-1.77 (m, 1H, H-5"a), 1.77 (s, 3H, Ac), 1.46 (s, 3H, acetonide), 1.27 (s, 3H, acetonide), 1.27-1.20 (m, 1H, H-3"*ax*.), 1.16-1.05 (m, 1H, H-5"*ax.* or *eq.*); ^{13}C NMR (DMSO-d_6, D_2O, 100 MHz, mixture of rotamers) δ 168.5, 168.4, 163.1, 154.7, 150.5, 141.5, 141.1, 137.1, 136.7, 128.5, 128.4, 128.2, 127.9, 127.8, 127.7, 127.5, 113.1, 113.0, 102.3, 102.1, 90.1, 89.7, 84.7, 84.1, 83.4, 83.2, 81.3, 81.1, 67.6, 66.8, 66.4, 51.9, 41.9, 41.8, 31.8, 30.7, 29.1, 27.3, 25.3, 22.8, 22.8; ESIMS-LR *m/z* 581 [(M + Na)$^+$]; ESIMS-HR calcd for $C_{27}H_{34}O_9N_4Na$ 581.2218, found 581.2221; $[\alpha]^{20}_{D}$ −50.1 (*c* 0.49, MeOH).

1-{5-[(2*S*,4*S*)-1-Benzyloxycarbonyl-4-acetamidohexahydro-2-pyridyl]-2,3-*O*-isopropylidene-5-oxo-β-D-*ribo*-pentofranosyl}uracil (42). A mixture of **41** (4.9 mg, 8.8 μmol) and IBX (6.1 mg, 22 μmol) in MeCN (1 mL) was treated with and, the mixture was heated at 80 °C for 80 min. Additional IBX (6.1 mg, 22 μmol) was added to the reaction mixture, and the mixture was stirred at

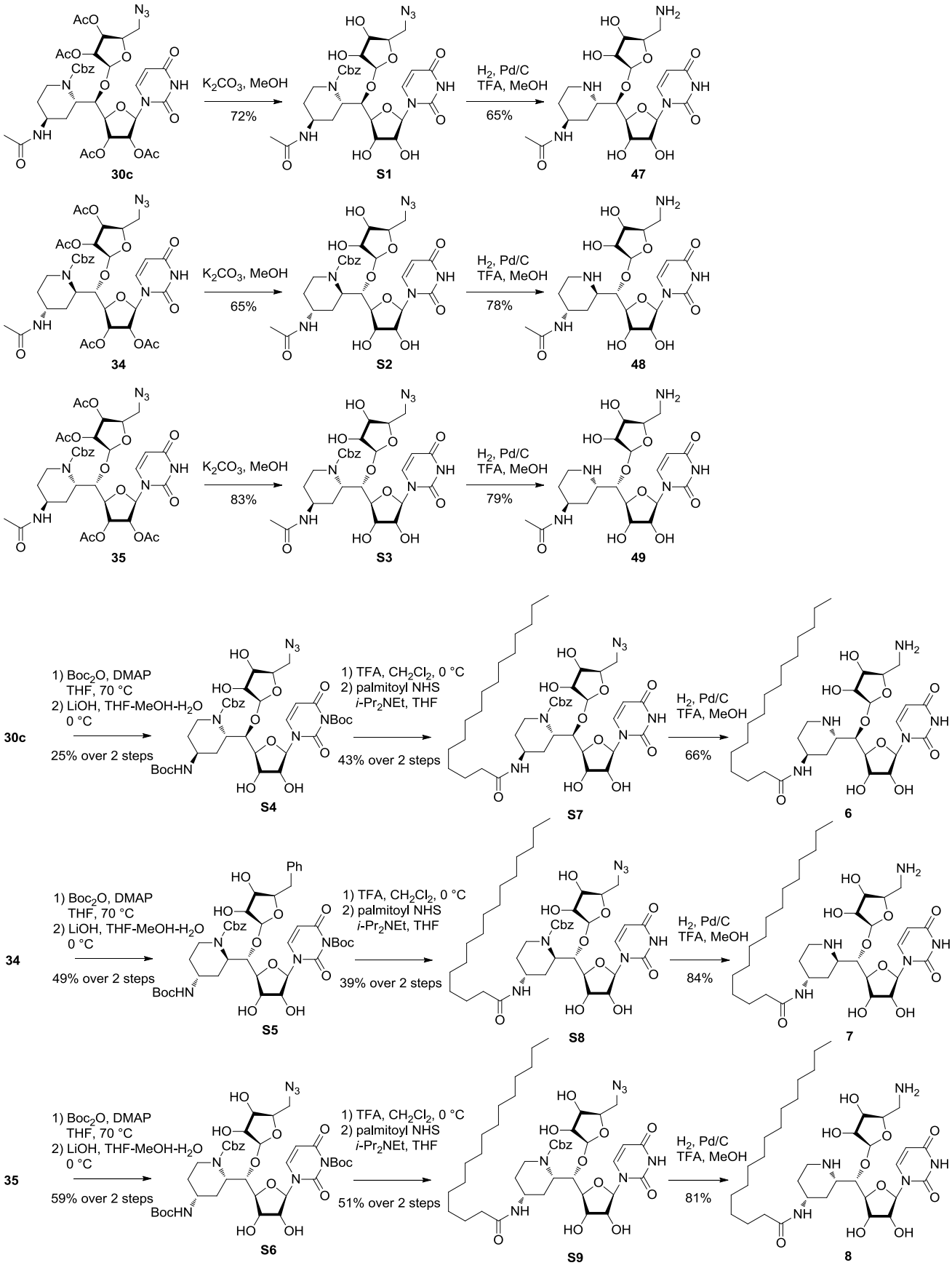
80 °C for further 70 min. The reaction mixture was cooled in an ice bath, then the white precipitates were filtedered off through Celite pad. The filtrate was concentrated *in vacuo*. The residue was purified by silica gel column chromatography (3-5% MeOH/$CHCl_3$) to afford **42** (4.2 mg, 86%) as a white solid.

Compound 39. A mixture of **36** (12.7 mg, 22.7 μmol) and Pd/C (2.5 mg) in MeOH (1 mL) was vigorously stirred under H_2 atmosphere at room temperature for 5 h. The catalyst was filtered off through Celite pad, and the filtrate was concentrated *in vacuo*. The residue and Pd/C (2.5 mg) in MeOH (1 mL) was vigorously stirred under H_2 atmosphere at room temperature for 5 h. The catalyst was filtered off through Celite pad, and the filtrate was concentrated *in vacuo*. A solution of the residue in THF (1 mL) was treated with 1,1'-carbonyl diimidazole (5.5 mg, 34 μmol) at room temperature for 22 h. The reaction mixuture was quenched with 1 M *aq*. HCl. The mixture was extracted with $CHCl_3$, which was dried (Na_2SO_4), filtered and concentrated *in vacuo*. The residue was purified by flash silica gel column chromatography (3-7% MeOH-$CHCl_3$) to afford **39** (2.6 mg, 25%) as a white solid. ^{1}H NMR ($CDCl_3$, 500 MHz) δ 9.77 (br s, 1H, N<u>H</u>-3), 7.26 (overlapped with solvent peak, 1H, H-6), 6.64 (br s, 1H, N<u>H</u>-4"), 5.74 (d, 1H, H-5, $J_{5,6}$ = 8.1 Hz), 5.48 (s, 1H, H-1'), 5.13 (dd, 1H, H-2', $J_{2',3'}$ = 6.9, $J_{2',1'}$ = 1.7 Hz), 5.04 (dd, 1H, H-3', $J_{3',2'}$ = 6.3, $J_{3',4'}$ = 3.4 Hz), 4.74 (t, 1H, H-5', $J_{5',4'}$ = $J_{5',2''}$ = 8.6 Hz), 4.38 (t, 1H, H-4", J = 3.5 Hz), 4.22 (dd, 1H, H-4', $J_{4',5'}$ = 9.2, $J_{4',3'}$ = 2.9 Hz), 3.97 (br s, 1H, H-2"), 3.76-3.74 (m, 1H, H-6"*eq*.), 3.13 (t, 1H, H-6"*ax*., J = 13.5 Hz), 2.00 (s, 3H, Ac), 2.00-1.95 (m, 1H, H-3"*ax.* or *eq*.), 1.65-1.78 (m, 3H, H-3"*ax.* or *eq.*, H-5"×2), 1.54 (s, 3H, acetonide), 1.33 (s, 3H, acetonide); ^{13}C NMR ($CDCl_3$, 100 MHz) δ 170.4, 163.5, 156.4, 150.2, 143.9, 114.8, 102.8, 97.4, 85.0, 84.1, 82.6, 75.0, 51.8, 42.6, 37.0, 29.2, 28.1, 27.1, 25.1, 23.5; ESIMS-LR m/z 473 [$(M + Na)^+$]; ESIMS-HR calcd for $C_{20}H_{26}O_8N_4Na$ 473.1643, found 473.1653; $[\alpha]^{19}_D$ +2.66 (*c* 1.61, $CHCl_3$).

Compound 43. A mixture of **40** (9.9 mg, 18 μmol) and Pd/C (3.3 mg) in MeOH (1 mL) was vigorously stirred under H_2 atmosphere at room temperature for 5 h. The catalyst was filtered off through Celite pad, and the filtrate was concentrated *in vacuo*. The residue and Pd/C (3.3 mg) in MeOH (1 mL) was vigorously stirred under H_2 atmosphere at room temperature for 2 h. The catalyst was filtered off through Celite pad, and the filtrate was concentrated *in vacuo*. A solution of the residue in CH_2Cl_2 (1 mL) was treated with 1,1'-carbonyl diimidazole (4.3 mg, 27 μmol) at room temperature for 24 h. DMAP (1.0 mg, 8.2 μmol) was added to the reaction mixuture at room temperature and the whole solution was stirred for 5 h. The reaction mixture was concentrated *in vacuo*. The residue was purified by preparative TLC (10% MeOH/$CHCl_3$) to afford **43** (2.4 mg, 30%) as a white solid. ^{1}H NMR (acetone-d_6, 400 MHz) δ 7.69 (d, 1H, H-6, $J_{6,5}$ = 7.8 Hz), 7.39 (br s, 1H, N<u>H</u>-4"), 5.80 (d, 1H, H-1', $J_{1',2'}$ = 2.3 Hz), 5.65 (d, 1H, H-5, $J_{5,6}$ = 8.2 Hz), 5.19 (dd, 1H, H-2', $J_{2',3'}$ = 6.4, $J_{2',1'}$ = 2.3 Hz), 4.96 (dd, 1H, H-3', $J_{3',2'}$ = 6.4, $J_{3',4'}$ = 3.7 Hz), 4.34 (dd, 1H, H-5', $J_{5',4'}$ = 7.3, $J_{5',2''}$ = 5.5 Hz), 4.24-4.19 (m, 1H, H-4"), 4.13 (dd, 1H, H-4', $J_{4',5'}$ = 7.8, $J_{4',3'}$ = 3.7 Hz), 3.90 (ddd, 1H, H-2", $J_{2",3"ax}$ = 11.8, $J_{2",5'}$ = 5.3 Hz, $J_{2",3"eq}$ = 3.9 Hz), 3.60 (ddd, 1H, H-6"*eq*, J_{gem} = 13.7, $J_{6"eq,5"eq}$ = 5.5, $J_{6"eq,5"ax}$ = 1.4 Hz), 3.16 (td, 1H, H-6"ax, J_{gem} = $J_{6"ax,5"ax}$ = 13.5 Hz, $J_{6"ax,5"eq}$ = 3.6 Hz), 1.94 (d, 1H, H-3"eq, J = 13.3 Hz), 1.87 (s, 3H, Ac), 1.77 (d, 1H, H-5"eq, J = 14.2 Hz), 1.71-1.58 (m, 2H, H-3"ax, H-5"ax), 1.51 (s, 3H, acetonide), 1.34 (s, 3H, acetonide); ^{13}C NMR (acetone-d_6, 100

MHz) δ 169.7, 163.4, 156.1, 151.3, 143.9, 114.7, 103.1, 95.5, 87.8, 84.9, 82.5, 79.1, 52.7, 43.2, 36.9, 34.8, 28.9, 27.4, 25.4, 23.0; ESIMS-LR *m/z* 473 [(M + Na)$^+$]; ESIMS-HR calcd for $C_{20}H_{26}O_8N_4Na$ 473.1643, found 473.1646; $[\alpha]^{20}_D$ +7.98 (*c* 0.24, MeOH).

Scheme S1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S1
47
34
S2
48
35
S3
49
K2CO3, MeOH
72%
65%
83%
H2, Pd/C
TFA, MeOH
65%
78%
79%
1) Boc2O, DMAP
THF, 70 °C
2) LiOH, THF-MeOH-H2O
0 °C
25% over 2 steps
49% over 2 steps
59% over 2 steps
1) TFA, CH2Cl2, 0 °C
2) palmitoyl NHS
i-Pr2NEt, THF
43% over 2 steps
39% over 2 steps
51% over 2 steps
66%
84%
81%
S4
S5
S6
S7
S8
S9
6
7
8

1-{(5*R*)-5-*O*-(5-Azido-5-deoxy-β-D-*ribo*-pentofuranosyl)-5-[(2*S*,4*S*)-1-benzyloxycarbonyl-4-acetamido-hexahydro-2-pyridyl]-β-D-*ribo*-pentofranosyl}uracil (S1). A mixture of **30c** (20.0 mg, 23.7 μmol) in MeOH (500 μL) was treated with K_2CO_3 (6.6 mg, 47 μmol) at 0 °C for 3 h, room temperature for 1 h. After AcOH (5.4 μL, 95 μmol) was added to the reaction mixture at 0 °C, then the mixture was concentrated *in vacuo*. The residue was purified by flash silica gel column chromatography (8%-13% MeOH/$CHCl_3$) to afford **S1** (11.5 mg, 17.0 μmol, 72%) as a white solid. ^{1}H NMR (CD_3OD, 400 MHz) δ 8.08 (d, 1H, H-6, $J_{6,5}$ = 8.2 Hz), 7.42-7.30 (m, 5H, phenyl), 5.88 (d, 1H, H-1', $J_{1',2'}$ = 7.4 Hz), 5.72 (d, 1H, H-5, $J_{5,6}$ = 7.8 Hz), 5.21-5.06 (m, 2H, C$\underline{H}_2$Ph), 4.98 (s, 1H, H-1"), 4.59 (t, 1H, H-2"', *J* = 7.6 Hz), 4.39-3.94 (m, 8H, H-2', H-3', H-4', H-5', H-2", H-4", H-4"', H-6"'ax or eq), 3.84-3.79 (m, 1H, H-3"), 3.62-3.51 (m, 1H, H-5"a), 3.17-3.05 (m, 2H, H-5"b, H-6"'ax or eq), 2.10 (d, 1H, H-3"'eq, *J* = 12.4 Hz), 1.95-1.88 (m, 1H, H-5"'ax or eq), 1.91 (s, 3H, Ac), 1.56-146 (m, 1H, H-3"'ax), 1.43-1.29 (m, 1H, H-5"'ax or eq); ^{13}C NMR (CD_3OD, 100 MHz, a mixture of rotamers; selected data for the major rotamer) δ 172.6, 166.1 152.7, 143.2, 138.0, 129.6, 129.2, 129.0, 112.1, 103.1, 87.9, 86.2, 81.8, 78.4, 76.5, 73.7, 72.7, 68.5, 54.8, 53.6, 44.1, 40.3, 33.5, 32.7, 32.4, 22.6; ESIMS-LR *m/z* 698 [(M + Na)$^+$]; ESIMS-HR calcd for $C_{29}H_{37}O_{12}N_7Na$ 698.2392, found 698.2394; $[\alpha]^{22}_D$ −38.0 (*c* 1.15, MeOH).

1-{(5*S*)-5-*O*-(5-Azido-5-deoxy-β-D-*ribo*-pentofuranosyl)-5-[(2*R*,4*R*)-1-benzyloxycarbonyl-4-acetamido-hexahydro-2-pyridyl]-β-D-*ribo*-pentofranosyl}uracil (S2). A mixture of **34** (21.8 mg, 25.8 μmol) in MeOH (500 μL) was treated with K_2CO_3 (7.1 mg, 52 μmol) at room temperature for 50 min. After AcOH (5.9 μL, 0.01 mmol) was added to the reaction mixture at 0 °C, the mixture was concentrated *in vacuo*. The residue was purified by C18 reverse phase column chromatography (34%-50% MeOH/H_2O) to afford **S2** (14.5 mg, 21.5 μmol, 83%) as a white solid. ^{1}H NMR (CD_3OD, 400 MHz, a mixture of rotamers; selected data for the major rotamer) δ 7.87 (d, 1H, H-6, $J_{6,5}$ = 8.2 Hz), 7.44-7.30 (m, 5H, phenyl), 5.81-5.74 (m, 1H, H-1'), 5.38 (d, 1H, H-5, $J_{5,6}$ = 8.2 Hz), 5.16-5.05 (m, 3H, H-1", C$\underline{H}_2$Ph), 4.79-4.75 (m, 1H, H-2"), 4.31-4.14 (m, 5H, H-2', H-3', H-4', H-5', H-6"'ax or eq), 3.94-3.87 (m, 2H, H-4", H-4"'), 3.79-3.73 (m, 1H, H-2"), 3.66 (t, 1H, H-3", *J* = 5.8 Hz), 3.47 (dd, 1H, H-5"a, J_{gem} = 13.1, $J_{5",4"}$ = 7.6 Hz), 3.27-3.17 (m, 2H, H-5"b, H-6"'ax or eq), 2.07 (d, 1H, H-3"'eq, *J* = 13.3 Hz), 1.95-1.92 (m, 4H, H-5"'ax or eq, Ac), 1.54-1.47 (m, 1H, H-3"'ax), 1.38-1.29 (m, 1H, H-5"'ax or eq); ^{13}C NMR (CD_3OD, 100 MHz, a mixture of rotamers) δ 172.5, 166.4, 166.1, 157.4, 152.2, 152.0, 142.2, 141.5, 138.1, 137.9, 129.7, 129.6, 129.4, 129.3, 128.8, 110.4, 110.3, 102.4, 102.2, 91.2, 84.1, 83.6, 82.5, 82.3, 76.3, 76.2, 76.1, 75.9, 75.5, 73.0, 70.9, 70.6, 68.6, 68.4, 54.5, 54.4, 53.9, 44.3, 40.3, 40.0, 33.2, 32.9, 32.6, 22.6; ESIMS-LR *m/z* 698 [(M + Na)$^+$]; ESIMS-HR calcd for $C_{29}H_{37}O_{12}N_7Na$ 698.2392, found 698.2393; $[\alpha]^{20}_D$ +35.3 (*c* 1.45, MeOH).

1-{(5*S*)-5-*O*-(5-Azido-5-deoxy-β-D-*ribo*-pentofuranosyl)-5-[(2*S*,4*S*)-1-benzyloxycarbonyl-4-acetamido-hexahydro-2-pyridyl]-β-D-*ribo*-pentofranosyl}uracil (S3). A mixture of **35** (15.6 mg, 18.5 μmol) in MeOH (500 μL) was treated with K_2CO_3 (5.1 mg, 37 μmol) at 0 °C for 1.5 h. After AcOH (4.2 μL, 74 μmol) was added to the reaction mixture at 0 °C, the mixture was concentrated *in vacuo*.

The residue was purified by C18 reverse phase column chromatography (33%-50% MeOH/H_2O) to afford **S3** (8.1 mg, 12 μmol, 65%) as a white solid. ^{1}H NMR (CD_3OD, 400 MHz, a mixture of rotamers; selected data for the major rotamer) δ 7.83 (d, 1H, H-6, $J_{6,5}$ = 7.7 Hz), 7.37-7.21 (m, 5H, phenyl), 5.69 (d, 1H, H-5, $J_{5,6}$ = 8.2 Hz), 5.64 (d, 1H, H-1', $J_{1',2'}$ = 3.2 Hz), 5.16-5.12 (m, 3H, H-1", C$\underline{H_2}$Ph), 4.62 (t, 1H, H-2'", J = 7.1 Hz), 4.30-3.92 (m, 9H, H-2', H-3', H-4', H-5', H-2", H-3", H-4", H-4'", H-6'"eq), 3.60-3.53 (m, 1H, H-5"a), 3.44-3.35 (m, 1H, H-5"b), 2.94 (t, 1H, H-6'"eq, J = 12.8 Hz), 2.51 (t, 1H, H-3'"eq, J = 14.6 Hz), 1.94 (br s, 4H, H-5'"ax or eq, Ac), 1.42 (td, 1H, H-3'"ax, J = 13.1, J = 5.7 Hz), 1.32-1.22 (m, 1H, H-5'"ax or eq); ^{13}C NMR (CD_3OD, 100 MHz, a mixture of rotamers) δ 172.3, 166.3, 157.1, 156.9, 152.1, 142.4, 141.9, 138.1, 137.7, 129.6, 129.4, 129.1, 129.0, 128.8, 128.7, 111.1, 102.4, 102.3, 91.2, 90.8, 83.7, 83.0, 78.4, 78.2, 76.4, 75.8, 72.2, 72.1, 71.0, 70.7, 68.8, 68.5, 54.0, 53.7, 53.2, 52.9, 43.9, 41.1, 40.7, 33.2, 33.0, 31.5, 31.2, 22.8; ESIMS-LR *m/z* 698 [(M + Na)$^+$]; ESIMS-HR calcd for $C_{29}H_{37}O_{12}N_7Na$ 698.2392, found 698.2399; $[\alpha]^{23}_D$ −14.7 (*c* 0.81, MeOH).

1-{(5*R*)-5-*O*-(5-Amino-5-deoxy-β-D-*ribo*-pentofuranosyl)-5-[(2*S*,4*S*)-4-acetamidohexahydro-2-pyridyl]-β-D-*ribo*-pentofranosyl}uracil (47). A mixture of **S1** (11.5 mg, 17.0 μmol) and Pd/C (3.5 mg), TFA (2.5 μL, 34 μmol) in MeOH (400 μL) was vigorously stirred under H_2 at room temperature for 3 h. The catalyst was filtered off through Celite pad, and the filtrate was concentrated *in vacuo*. The residue was purified by C18 reverse phase column chromatography (2% MeOH/H_2O), then coevaporated with 1M HCl/1,4-dioxane. The residue was washed with AcOEt to afforded **47** (6.7 mg, 11 μmol, 65 %) as a di-HCl salt. ^{1}H NMR (CD_3OD, 400 MHz) δ 7.73 (d, 1H, H-6, $J_{6,5}$ = 8.2 Hz), 5.75 (d, 1H, H-5, $J_{5,6}$ = 8.2 Hz), 5.54 (d, 1H, H-1', $J_{1',2'}$ = 4.6 Hz), 5.14 (s, 1H, H-1"), 4.53 (t, 1H, H-2', $J_{2',1'}$ = $J_{2',3'}$ = 5.5 Hz), 4.47 (t, 1H, H-3', $J_{3',2'}$ = $J_{3',4'}$ = 6.2 Hz), 4.22-4.10 (m, 5H, H-4', H-2", H-3", H-4", H-4'"), 4.00 (d, 1H, H-5', J = 4.6 Hz), 3.84 (d, 1H, H-2'", J = 10.1 Hz), 3.31 (overlapped with solvent peak, 3H, H-5"a, H-6'"×2), 3.12 (dd, 1H, H-5"b, J = 13.1, J = 9.4 Hz), 2.11-1.94 (m, 7H, H-3'"×2, H-5'"×2, Ac); ^{13}C NMR (CD_3OD, 100 MHz) δ 173.5, 166.0, 152.7, 145.7, 111.5, 103.3, 96.1, 85.5, 80.5, 80.1, 76.1, 73.5, 72.6, 71.5, 53.0, 44.3, 43.4, 42.0, 31.1, 26.9, 22.7; ESIMS-LR m/z 516 [(M + H)$^+$]; ESIMS-HR calcd for $C_{21}H_{34}O_{10}N_5$ 516.2300, found 516.2301; $[\alpha]^{22}_D$ –13.3 (*c* 0.50, MeOH).

1-{(5*S*)-5-*O*-(5-Amino-5-deoxy-β-D-*ribo*-pentofuranosyl)-5-[(2*R*,4*R*)-4-acetamidohexahydro-2-pyridyl]-β-D-*ribo*-pentofranosyl}uracil (48). A mixture of **S2** (14.5 mg, 21.5 μmol) and Pd/C (2.9 mg), TFA (3.2 μL, 43 μmol) in MeOH (500 μL) was vigorously stirred under H_2 at room temperature for 1.5 h. The catalyst was filtered off through Celite pad, and the filtrate was concentrated *in vacuo*. The residue was coevaporated with 1 M HCl/1,4-dioxane, then purified by C18 reverse phase column chromatography (100% H_2O) afforded **48** (10.0 mg, 17.0 μmol, 79 %) as a di-HCl salt. ^{1}H NMR (CD_3OD, 400 MHz) δ 7.83 (d, 1H, H-6, $J_{6,5}$ = 8.2 Hz), 5.81 (d, 1H, H-1', $J_{1',2'}$ = 1.8 Hz), 5.77 (d, 1H, H-5, $J_{5,6}$ = 8.2 Hz), 5.19 (d, 1H, H-1", $J_{1",2"}$ = 2.3 Hz), 4.33 (dd, 1H, H-3', J = 8.0, J = 5.3 Hz), 4.25-4.21 (m, 2H, H-2', H-4'"), 4.17-4.04 (m, 5H, H-4', H-5', H-2", H-3", H-4"), 3.81-3.77 (m, 1H, H-2'"), 3.42 (d, 1H, H-6'"eq, J = 12.8 Hz), 3.35-3.30 (m, 2H, H-5"a, H-6'"ax),

3.21 (dd, 1H, H-5"b, *J* = 13.3, *J* = 9.6 Hz), 2.23-2.04 (m, 2H, H-3'"ax or eq, H-5'"ax or eq), 2.00 (s, 3H, Ac), 2.00-1.90 (m, 2H, H-3'"ax or eq, H-5'"ax or eq); ^{13}C NMR (CD_3OD, 100 MHz) δ 173.4, 166.1, 152.0, 142.6, 110.8, 102.9, 92.6, 83.4, 80.5, 79.0, 75.6, 75.1, 72.4, 70.4, 54.5, 43.6, 42.9, 42.2, 30.8, 26.8, 22.7; ESIMS-LR *m/z* 516 [(M + H)$^+$]; ESIMS-HR calcd for $C_{21}H_{34}O_{10}N_5$ 516.2300, found 516.2299; $[\alpha]^{25}_D$ +3.49 (*c* 0.95, MeOH).

1-{(5*S*)-5-*O*-(5-Amino-5-deoxy-β-D-*ribo*-pentofuranosyl)-5-[(2*S*,4*S*)-4-acetamidohexahydro-2-pyridyl]-β-D-*ribo*-pentofranosyl}uracil (49). A mixture of **S3** (8.1 mg, 12 μmol) and Pd/C (2.4 mg), TFA (1.8 μL, 24 μmol) in MeOH (400 μL) was vigorously stirred under H_2 at room temperature for 4 h. The catalyst was filtered off through Celite pad, and the filtrate was concentrated *in vacuo*. A solution of the residue and Pd/C (2.4 mg), TFA (1.8 μL, 24 μmol) in MeOH (0.4 mL) was vigorously stirred under H_2 at room temperature for 1.5 h. The catalyst was filtered off through Celite pad, and the filtrate was concentrated *in vacuo*. The residue was coevaporated with 1 M HCl/1,4-dioxane, washed with MeOH and AcOEt, then purified by C18 reverse phase column chromatography (100% H_2O) to afforded **49** (5.5 mg, 9.3 μmol, 78 %) as a di-HCl salt. ^{1}H NMR (CD_3OD, 500 MHz) δ 7.76 (d, 1H, H-6, $J_{6,5}$ = 8.0 Hz), 5.82 (d, 1H, H-1', $J_{1',2'}$ = 1.7 Hz), 5.78 (d,1H, H-5, $J_{5,6}$ = 8.1 Hz), 5.26 (s, 1H, H-1"), 4.24-4.07 (m, 8H, H-2', H-3', H-4', H-5', H-2", H-3", H-4", H-4'"), 3.87 (d, 1H, H-2'", *J* = 10.3 Hz), 3.48-3.45 (m, 1H, H-6'"ax or eq), 3.37-3.22 (m, 3H, H-5"×2, H-6'"ax or eq), 2.21 (d, 1H, H-3'"eq, *J* = 13.8 Hz), 2.11 (t, 1H, H-5'"ax, *J* = 15.2 Hz), 2.03 (s, 3H, Ac), 1.95-1.87 (m, 2H, H-3'"ax, H-5'"eq); ^{13}C NMR (CD_3OD, 125 MHz) δ 173.5, 166.1, 152.1, 142.8, 110.5, 103.1, 93.0, 83.3, 80.6, 78.1, 75.8, 74.6, 72.4, 71.0, 55.7, 43.4, 43.2, 42.7, 29.6, 27.2, 22.8; ESIMS-LR *m/z* 516 [(M + H)$^+$]; ESIMS-HR calcd for $C_{21}H_{34}O_{10}N_5$ 516.2300, found 516.2297; $[\alpha]^{19}_D$ –7.69 (*c* 0.38, MeOH).

1-{(5*R*)-5-*O*-(5-Azido-5-deoxy-β-D-*ribo*-pentofuranosyl)-5-[(2*S*,4*S*)-1-benzyloxycarbonyl-4-*tert*-butoxycarbonylaminohexahydro-2-pyridyl]-β-D-*ribo*-pentofranosyl}-3-*tert*-butoxycarbonyl-uracil (S4). A mixture of **30c** (40.0 mg, 47.4 μmol) and DMAP (23.2 mg, 0.19 mmol) in THF (1 mL) was treated with di-*tert*-butyldicarbonate (44 μL, 0.19 mmol) at 70 °C and the mixture was stirred at 70 °C for 30 min. Di-*tert*-butyldicarbonate (44 μL, 190 μmol) was added to the reaction mixture, and the whole mixuture was stirred at 70 °C for 30 min. After the solution was cooled to room temperature, MeOH was added. The whole mixture poured onto AcOEt, and the organic phase was washed with *sat. aq*. NH_4Cl, and brine, dried (Na_2SO_4), filtered and concentrated *in vacuo*. The residue in THF-MeOH-H_2O (3:1:1, 1 mL) was treated with $LiOH\cdot H_2O$ (19.9 mg, 474 μmol) at 0 °C for 1 h. After AcOH (27.2 μL, 474 μmol) was added to the reaction mixture at 0 °C, the mixture was concentrated *in vacuo*. The residue was purified by flash silica gel column chromatography (1% MeOH/$CHCl_3$) to afford **S4** (10.0 mg, 12.0 μmol, 25 %) as a white solid. ^{1}H NMR (DMSO-d_6, D_2O, 400 MHz) δ 8.03 (d, 1H, H-6, $J_{6,5}$ = 8.0 Hz), 7.42-7.29 (m, 5H, phenyl), 6.79 (br s, 1H, N<u>H</u>-4'"), 5.87 (d, 1H, H-5, $J_{5,6}$ = 8.2 Hz), 5.72 (d, 1H, H-1', $J_{1',2'}$ = 7.3 Hz), 5.15-4.97 (m, 2H, C<u>H</u>$_2$Ph), 4.85 (s, 1H, H-1"), 4.37 (br s, 1H, H-2'"), 4.21-4.15 (m, 2H, H-4', H-5'), 4.03-3.70 (m, 6H,

H-2', H-3', H-2", H-3", H-4", H-6'"ax or eq), 3.63-3.53 (m, 2H, H-5"a, H-4'"), 3.17-3.15 (m, 1H, H-5"b), 2.96-2.90 (m, 1H, H-6'"ax or eq), 1.90-1.87 (m, 1H, H-3'"ax or eq), 1.77 (br s, 1H, H-5'"ax or eq), 1.51 (s, 9H, *tert*-butyl), 1.36 (s, 10H, H-3'"ax or eq, *tert*-butyl), 1.22 (s, 1H, H-5'"ax or eq); ^{13}C NMR (DMSO-d_6, D_2O, 100 MHz, a mixture of rotamers) δ 160.0, 155.5, 155.0, 148.8, 147.8, 141.8, 137.0, 128.6, 128.0, 127.8, 127.4, 110.6, 101.5, 86.7, 84.6, 79.9, 78.0, 74.6, 71.9, 71.1, 66.5, 53.2, 52.2, 43.5, 32.6, 29.2, 28.4, 27.2; ESIMS-LR *m/z* 856 [(M + Na)$^+$]; ESIMS-HR calcd for $C_{37}H_{51}O_{15}N_7Na$ 856.3335, found 856.3331; $[\alpha]^{22}_D$ –36.1 (*c* 1.00, MeOH).

1-{(5*S*)-5-*O*-(5-Azido-5-deoxy-β-D-*ribo*-pentofuranosyl)-5-[(2*R*,4*R*)-1-benzyloxycarbonyl-4-*tert*-butoxycarbonylaminohexahydro-2-pyridyl]-β-D-*ribo*-pentofranosyl}-3-*tert*-butoxycarbonyl-uracil (S5). A mixture of **34** (74.0 mg, 87.7 μmol) and DMAP (42.9 mg, 351 μmol) in THF (1 mL) was treated with di-*tert*-butyldicarbonate (81 μL, 0.35 mmol) at 70 °C for 10 min. Di-*tert*-butyldicarbonate (81 μL, 0.35 mmol) was added to the reaction mixture and the whole mixture was stirred at 70 °C for 10 min. Di-*tert*-butyldicarbonate (81 μL, 0.35 mmol) was added to the reaction mixture and the whole mixture was stirred at 70 °C for 30 min. Di-*tert*-butyldicarbonate (81 μL, 0.35 mmol) was added to the to the reaction mixture and the whole mixture was stirred at 70 °C for 10 min. After the solution was cooled to room temperature, MeOH was added. The whole mixture was poured onto AcOEt, and the organic phase was washed with *sat*. *aq*. NH_4Cl, and brine, dried (Na_2SO_4), filtered and concentrated *in vacuo*. The residue in THF-MeOH-H_2O (3:1:1, 1.5 mL) was treated with LiOH·H_2O (36.8 mg, 877 μmol) at 0 °C for 1 h. After AcOH (50 μL, 0.88 mmol) was added to the reaction mixture at 0 °C, the mixture was concentrated *in vacuo*. The residue was purified by flash silica gel column chromatography (1-3% MeOH-$CHCl_3$) to afford **S5** (43.0 mg, 51.6 μmol, 59%) as a yellow solid. ^{1}H NMR (DMSO-d_6, D_2O, 400 MHz, a mixture of rotamers; selected data for the major rotamer) δ 7.77 (d, 1H, H-6, $J_{6,5}$ = 7.5 Hz), 7.39-7.25 (m, 5H, phenyl), 6.85-6.80 (m, 1H, N<u>H</u>-4'"), 5.63 (d, 1H, H-1', $J_{1',2'}$ = 1.4 Hz), 5.45 (d, 1H, H-5, $J_{5,6}$ = 8.7 Hz), 5.13-4.95 (m, 3H, H-1", C<u>H</u>$_2$Ph), 4.55-4.51 (m, 1H, H-2'"), 4.15 (d, 1H, H-6'"eq, *J* = 10.6 Hz), 4.08-3.97 (m, 4H, H-2', H-3', H-4', H-5'), 3.84 (td, 1H, H-4", *J* = 8.0, *J* = 3.1 Hz), 3.73-3.70 (m, 1H, H-2"), 3.61-3.28 (m, 4H, H-3", H-4", H-5"×2), 3.11-3.04 (m, 1H, H-6'"ax), 1.85-1.78 (m, 2H, H-3'"ax or eq, H-5'"ax or eq), 1.51 (s, 9H, *tert*-butyl), 1.37 (s, 10H, H-3'"ax or eq, *tert*-butyl), 1.22-1.18 (m, 1H, H-5'"ax or eq); ^{13}C NMR (DMSO-d_6, D_2O, 100 MHz, a mixture of rotamers, selected data for the major rotamer) δ 159.9, 155.1, 154.9, 147.9, 147.8, 139.6, 136.9, 128.6, 128.4, 127.9, 127.4, 108.4, 100.3, 89.7, 86.4, 82.1, 80.3, 77.9, 74.3, 74.0, 72.8, 71.6, 68.9, 66.4, 53.0, 51.9, 43.6, 38.3, 31.9, 28.3, 27.1; ESIMS-LR *m/z* 832 [(M − H)$^-$]; ESIMS-HR calcd for $C_{37}H_{50}O_{15}N_7$ 832.3370, found 832.3380; $[\alpha]^{23}_D$ +36.4 (*c* 1.08, MeOH).

1-{(5*S*)-5-*O*-(5-Azido-5-deoxy-β-D-*ribo*-pentofuranosyl)-5-[(2*S*,4*S*)-1-benzyloxycarbonyl-4-*tert*-butoxycarbonylaminohexahydro-2-pyridyl]-β-D-*ribo*-pentofranosyl}-3-*tert*-butoxycarbonyl-uracil (S6). A mixture of **35** (80.7 mg, 95.6 μmol) and DMAP (46.7 mg, 382 μmol) in THF (2.0 mL) was treated with di-*tert*-butyldicarbonate (88 μL, 0.38 mmol) at 70 °C and the mixture was stirred at 70 °C for 30 min. Di-*tert*-Bu-dicarbonate (88 μL, 0.38 mmol) was added to the to the reaction

mixture and the mixture was stirred at 70 °C for 40 min. Di-*tert*-butyldicarbonate (88 μL, 0.38 mmol) was added to the reaction mixture, and the mixuture was stirred at 70 °C for 20 min. After the solution was cooled to room temperature, MeOH was added. The whole mixture was poured onto AcOEt, and the organic phase was washed with *sat. aq*. NH_4Cl, and brine, dried (Na_2SO_4), filtered and concentrated *in vacuo*. The residue in THF-MeOH-H_2O (3:1:1, 2 mL) was treated with $LiOH \cdot H_2O$ (40.1 mg, 956 μmol) at 0 °C for 1 h. After AcOH (54.7 μL, 956 μmol) was added to the reaction mixture at 0 °C, the mixture was concentrated *in vacuo*. The residue was purified by preparative TLC (5% MeOH/$CHCl_3$) to afford **S6** (39.4 mg, 47.3 μmol, 49%) as a yellow solid. ^{1}H NMR (DMSO-d_6, D_2O, 50 °C, 400 MHz) δ 7.91-7.80 (m, 1H, H-6), 7.38-7.25 (m, 5H, phenyl), 6.52 (br s, 1H, N<u>H</u>-4'''), 5.81 (d, 1H, H-5, $J_{5,6}$ = 8.2 Hz), 5.73-5.52 (m, 1H, H-1'), 5.18-4.90 (m, 3H, H-1'', C<u>H</u>$_2$Ph), 4.38 (m, 1H, H-2'''), 4.15-3.83 (m, 9H, H-2', H-3', H-4', H-5', H-2'', H-3'', H-4'', H-4''', H-6'''eq), 3.56-3.52 (m, 1H, H-5''a), 3.40-3.37 (m, 1H, H-5''b), 2.80 (t, 1H, H-6'''ax, J = 13.1 Hz), 2.29-2.25 (m, 1H, H-3'''ax or eq), 1.82 (d, 1H, H-5'''eq, J = 11.4 Hz), 1.54 (s, 9H, *tert*-butyl), 1.39 (s, 9H, *tert*-butyl), 1.35-1.28 (m, 1H, H-3'''ax or eq), 1.21-1.10 (m, 1H, H-5'''ax); ^{13}C NMR (DMSO-d_6, D_2O, 100 MHz, a mixture of rotamers) δ 160.1, 154.8, 154.6, 148.2, 148.0, 147.9, 140.7, 140.2, 137.0, 136.6, 128.5, 128.5, 128.1, 127.9, 127.7, 127.5, 127.3, 109.0, 100.9, 100.7, 89.5, 86.3, 81.9, 81.1, 77.5, 75.4, 74.6, 74.0, 73.6, 71.0, 70.8, 69.1, 66.8, 66.3, 52.3, 52.0, 51.4, 43.3, 32.3, 30.4, 29.4, 29.1, 28.8, 28.3, 27.8, 27.1; ESIMS-LR *m/z* 856 [$(M + Na)^+$]; ESIMS-HR calcd for $C_{37}H_{51}O_{15}N_7Na$ 856.3335, found 856.3340; $[\alpha]^{23}_D$ –6.17 (*c* 0.99, MeOH).

1-{(5*R*)-5-*O*-(5-Azido-5-deoxy-β-D-*ribo*-pentofuranosyl)-5-[(2*S*,4*S*)-1-benzyloxycarbonyl-4-palmitoylamino-hexahydro-2-pyridyl]-β-D-*ribo*-pentofranosyl}uracil (S7). A solution of **S4** (85.5 mg, 103 μmol) in CH_2Cl_2 (1 mL) was treated with TFA (200 μL) at 0 °C and the mixture was stirred for 2.5 h. Then TFA (200 μl) and CH_2Cl_2 (1 mL) were added to the reaction mixture at 0 °C and the mixture was stirred for 75 min. The mixture was concentrated *in vacuo*. A solution of the residue and DIPEA (36 μL, 0.21 mmol) in THF (1 mL) was treated with *N*-succinimidyl palmitate (43.8 mg, 124 μmol) at room temperature for 5 h. After H_2O was added, the mixture was extracted with AcOEt. The organic phase was washed with brine, dried (Na_2SO_4), filtered and concentrated *in vacuo*. The residue was purified by preparative TLC (10% MeOH-$CHCl_3$) to afford **S7** (38.9 mg, 44.6 μmol, 43%) as a white solid. ^{1}H NMR (DMSO-d_6, D_2O, 400 MHz) δ 7.92-7.86 (m, 1H, H-6), 7.73 (br s, 1H, N<u>H</u>-4'''), 7.38-7.29 (m, 5H, phenyl), 5.74 (d, 1H, H-1', $J_{1',2'}$ = 7.3 Hz), 5.65 (d, 1H, H-5, $J_{5,6}$ = 7.8 Hz), 5.16-4.98 (m, 2H, C<u>H</u>$_2$Ph), 4.87 (s, 1H, H-1''), 4.39 (br s, 1H, H-2'''), 4.22 (m, 1H, H-5'), 4.14 (t, 1H, H-3', J = 4.6 Hz), 4.03-3.75 (m, 5H, H-2', H-4', H-4'', H-4''', H-6'''eq), 3.64-3.61 (m, 1H, H-3''), 3.52-3.50 (m, 1H, H-5''a), 3.43 (overlapped with H_2O peak, 1H, H-2''), 3.13 (dd, 1H, H-5''b, J = 13.1, J = 6.2 Hz), 2.97 (t, 1H, H-6'''ax, J = 12.8 Hz), 2.00 (t, 2H, COC<u>H</u>$_2$, J = 7.3 Hz), 1.92 (d, 1H, H-3'''eq, J = 12.8 Hz), 1.77 (br s, 1H, H-5'''ax or eq), 1.45 (t, 2H, COCH$_2$C<u>H</u>$_2$, J = 6.4 Hz), 1.34-1.22 (m, 2H, H-3'''ax, H-5'''ax or eq), 1.22 (s, 24H, palmitoyl), 0.84 (t, 3H, palmitoyl terminal-Me, J = 6.8 Hz); ^{13}C NMR (DMSO-d_6, D_2O, 100 MHz, a mixture of rotamers) δ 171.6, 163.0, 155.5, 154.9, 151.0, 141.2, 137.0, 128.5, 127.9, 127.7, 127.3, 110.5, 109.8, 102.1, 85.7, 84.3, 84.1, 80.2, 79.9, 75.6, 75.2, 74.6, 71.8, 71.4, 71.1, 67.1, 67.0, 66.7, 66.4, 53.2,

52.3, 52.0, 41.9, 35.5, 32.5, 31.4, 29.2, 29.1, 29.1, 28.9, 28.8, 28.8, 25.4, 22.2, 14.1; ESIMS-LR *m/z* 894 [(M + Na)$^+$]; ESIMS-HR calcd for $C_{43}H_{65}O_{12}N_7Na$ 894.4583, found 894.4593; $[\alpha]^{24}_D$ -28.3 (*c* 0.97, $CHCl_3$).

1-{(5*S*)-5-*O*-(5-Azido-5-deoxy-β-D-*ribo*-pentofuranosyl)-5-[(2*R*,4*R*)-1-benzyloxycarbonyl-4-palmitoylamino-hexahydro-2-pyridyl]-β-D-*ribo*-pentofranosyl}uracil (**S8**)**.** A solution of **S5** (43.0 mg, 51.6 μmol) in CH_2Cl_2 (1 mL) was treated with TFA (200 μL) at 0 °C and the mixture was stirred for 3 h. The mixture was concentrated *in vacuo*. A solution of the residue and DIPEA (18 μL, 0.10 mmol) in THF (1 mL) was treated with *N*-succinimidyl palmitate (21.9 mg, 61.9 μmol) at room temperature for 2 h. Then DIPEA (18 μL, 0.10 mmol) was added to the reaction mixture and the mixture was stirred for 10 h. Then DIPEA (36 μL, 0.21 mmol) was added to the reaction mixture and the mixture was stirred for 13.5 h. After H_2O was added, the mixture was extracted with AcOEt. The organic phase was washed with brine, dried (Na_2SO_4), filtered and concentrated *in vacuo*. The residue was purified by preparative TLC (13% MeOH/$CHCl_3$) to afford **S8** (22.8 mg, 26.1 μmol, 51%) as a white solid. ^{1}H NMR (DMSO-d_6, D_2O, 400 MHz, a mixture of rotamers; selected data for the major rotamer) δ 7.81-7.69 (m, 2H, H-6, N<u>H</u>-4'''), 7.38-7.26 (m, 5H, phenyl), 5.63 (s, 1H, H-1'), 5.34 (d, 1H, H-5, $J_{5,6}$ = 8.2 Hz), 5.14-4.96 (m, 3H, H-1'', C<u>H</u>$_2$Ph), 4.55-4.53 (m, 1H, H-2'''), 4.18 (d, 1H, H-5', *J* = 10.5 Hz), 4.06-3.99 (m, 4H, H-2', H-3', H-4', H-6'''ax or eq), 3.84-3.71 (m, 3H, H-2'', H-4'', H-4'''), 3.54 (dd, 1H, H-3'', *J* = 7.8, *J* = 4.6 Hz), 3.38 (overlapped with H_2O peak, 1H, H-5''a), 3.28 (dd, 1H, H-5''b, *J* = 13.1, *J* = 3.0 Hz), 3.17-3.07 (m, 1H, H-6'''ax or eq), 2.01 (t, 2H, COC<u>H</u>$_2$, *J* = 7.4 Hz), 1.84-1.81 (m, 2H, H-3'''ax or eq, H-5'''ax or eq), 1.47-1.40 (m, 2H, COCH$_2$C<u>H</u>$_2$), 1.38-1.34 (m, 1H, H-3'''aq or eq), 1.25-1.17 (m, 25H, H-5'''aq or eq, palmitoyl), 0.84 (t, 3H, palmitoyl terminal-Me); ^{13}C NMR (DMSO-d_6, D_2O, 100 MHz, a mixture of rotamers) δ 171.6, 171.6, 163.2, 163.1, 155.0, 154.7, 150.4, 150.2, 139.9, 139.2, 137.0, 136.9, 128.5, 128.4, 128.0, 127.8, 127.8, 127.3, 108.5, 108.3, 101.4, 101.1, 89.0, 88.9, 82.5, 81.9, 80.2, 80.0, 74.3, 74.1, 73.9, 72.9, 71.7, 71.6, 69.3, 69.0, 66.4, 66.3, 53.2, 53.0, 52.1, 42.2, 42.1, 38.3, 35.5, 32.0, 31.6, 31.4, 29.1, 29.1, 29.0, 28.8, 28.7 25.3, 22.2, 14.0; ESIMS-LR *m/z* 894 [(M + Na)$^+$]; ESIMS-HR calcd for $C_{43}H_{65}O_{12}N_7Na$ 894.4583, found 894.4592; $[\alpha]^{24}_D$ +21.9 (*c* 1.14, MeOH)

1-{(5*S*)-5-*O*-(5-Azido-5-deoxy-β-D-*ribo*-pentofuranosyl)-5-[(2*S*,4*S*)-1-benzyloxycarbonyl-4-palmitoylamino-hexahydro-2-pyridyl]-β-D-*ribo*-pentofranosyl}uracil (**S9**). A solution of (5'*S*) **S6** (39.4 mg, 47.3 μmol) in CH_2Cl_2 (1 mL) was treated with TFA (200 μL) at 0 °C and the mixture was stirred for 3 h. Then TFA (100 μL) was added to the reaction mixture at 0 °C and the mixture was stirred at 0 °C for 2.5 h. The mixture was concentrated *in vacuo*. A solution of the residue and DIPEA (16 μL, 95 μmol) in THF (1 mL) was treated with *N*-succinimidyl palmitate (20.1 mg, 56.8 μmol) at room temperature for 40 min. Then DIPEA (49 μL, 49 μmol) was added to the reaction mixture and the mixture was stirred for 11.5 h. After H_2O was added, the mixture was extracted with AcOEt. The organic phase was washed with brine, dried (Na_2SO_4), filtered and concentrated *in vacuo*. The residue was purified by preparative TLC (13% MeOH-$CHCl_3$) to afford **S9** (16.2 mg, 18.6 μmol, 39%) as a white solid. ^{1}H NMR (DMSO-d_6, D_2O, 500 MHz, a mixture of rotamers;

selected data for the major rotamer) δ 7.76 (d, 1H, H-6, $J_{6,5}$ = 8.0 Hz), 7.61 (d, 1H, NH-4'", $J_{NH\text{-}4'",4'"}$ = 7.5 Hz), 7.38-7.21 (m, 5H, phenyl), 5.66 (d, 1H, H-5, $J_{5,6}$ = 8.0 Hz), 5.65 (br s, 1H, H-1'), 5.08-4.92 (m, 3H, H-1", CH_2Ph), 4.39 (br s, 1H, H-2'"), 4.20- 4.08 (m, 2H, H-5', H-4'"), 3.99-3.92 (m, 3H, H-2', H-3", H-6'"eq), 3.86-3.80 (m, 4H, H-3', H-4', H-2", H-4"), 3.54-3.50 (m, 1H, H-5"a), 3.32 (dd, 1H, H-5"b, *J* = 13.5, *J* = 4.3 Hz), 2.81 (t, 1H, H-6'"ax, *J* = 12.9 Hz), 2.30-2.15 (m, 1H, H-3'"ax or eq), 2.01 (t, 2H, COCH_2, *J* = 7.2 Hz), 1.82 (d, 1H, H-5'"eq, *J* = 9.8 Hz), 1.47 (t, 2H, $COCH_2CH_2$, *J* = 5.8 Hz), 1.33-1.22 (m, 25H, H-3'"ax or eq, palmitoyl), 1.12-1.04 (m, 1H, H-5'"ax), 0.84 (t, 3H, palmitoyl terminal-Me, *J* = 6.9 Hz); ^{13}C NMR (DMSO-d_6, D_2O, 100 MHz, a mixture of rotamers) δ 171.3, 171.2, 163.2, 154.6, 154.5, 150.5, 150.4, 140.2, 140.0, 137.0, 136.8, 128.5, 128.1, 127.9, 127.6, 127.3, 127.2, 109.3, 101.5, 88.6, 82.4, 81.7, 80.9, 77.0, 75.9, 74.6, 73.9, 73.7, 70.9, 70.7, 69.3, 66.6, 66.3, 52.4, 52.1, 51.5, 51.2, 41.7, 41.6, 35.6, 35.6, 32.2, 31.9, 31.4, 30.3, 30.0, 29.1, 29.1, 29.0, 28.9, 28.8, 28.7, 25.4, 22.2, 14.1; ESIMS-LR *m/z* 894 [$(M + Na)^+$]; ESIMS-HR calcd for $C_{43}H_{65}O_{12}N_7Na$ 894.4583, found 894.4588; $[\alpha]^{24}_D$ -6.37 (*c* 0.81, MeOH).

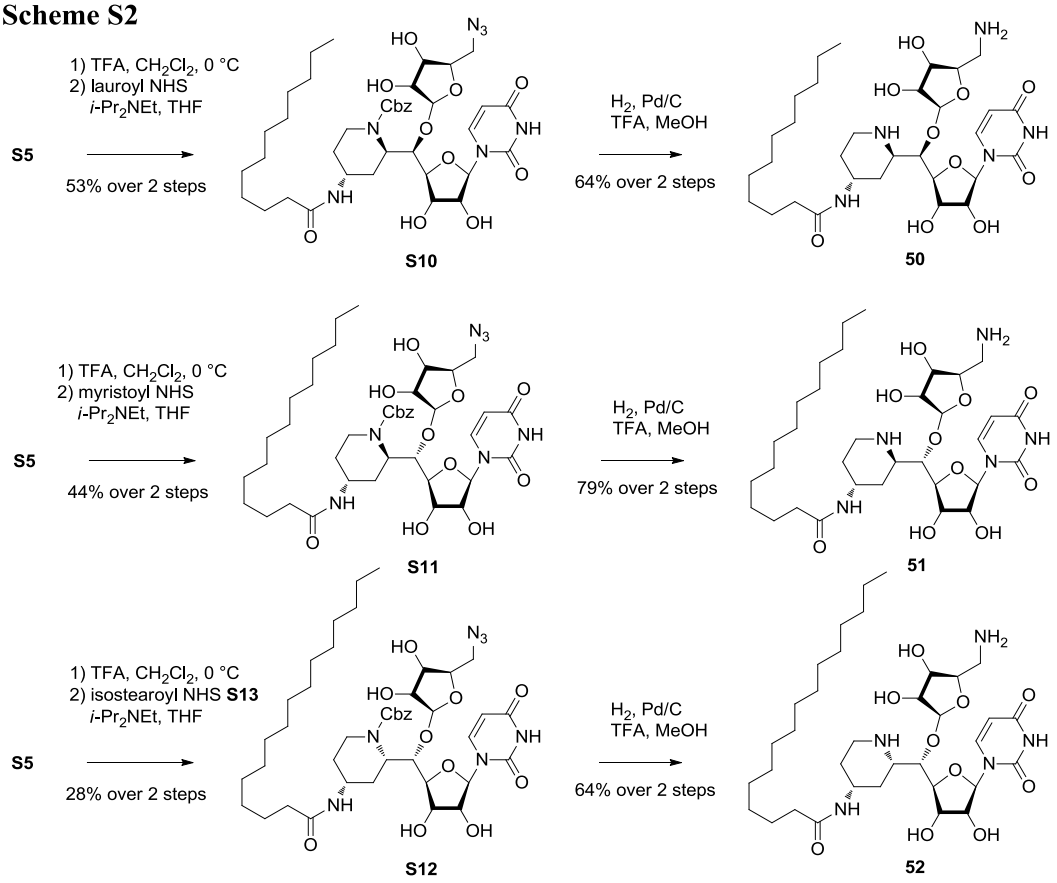
1-{(5*R*)-5-*O*-(5-Amino-5-deoxy-β-D-*ribo*-pentofuranosyl)-5-[(2*S*,4*S*)-4-palmitoylaminohexahydro-2-pyridyl]-β-D-*ribo*-pentofranosyl}uracil (6). A mixture of **S7** (21.9 mg, 25.1 μmol) and Pd/C (5.0 mg), TFA (3.7 μL, 50 μmol) in MeOH (1 mL) was vigorously stirred under H_2 at room temperature for 1.5 h. The catalyst was filtered off through Celite pad, and the filtrate was concentrated *in vacuo*. The residue was purified by C18 reverse phase column chromatography (70-90% MeOH/H_2O, 0.1% TFA) to afford **6** (15.5 mg, 16.5 μmol, 66%) as a di-TFA salt. ^{1}H NMR (CD_3OD, 400 MHz) δ 7.63 (d, 1H, H-6, $J_{6,5}$ = 8.0 Hz), 5.72 (d, 1H, H-5, $J_{5,6}$ = 8.0 Hz), 5.49 (d, 1H, H-1', $J_{1',2'}$ = 4.6 Hz), 5.12 (s, 1H, H-1"), 4.50 (t, 1H, H-2', $J_{1',2'}$ = $J_{2',3'}$ = 5.5 Hz), 4.44 (t, 1H, H-3', $J_{3',2'}$ = $J_{3',4'}$ = 6.3 Hz), 4.21 (br s, 1H, H-4'"), 4.16-4.12 (m, 4H, H-4', H-2", H-3", H-4"), 3.98 (d, 1H, H-5', *J* = 5.2 Hz), 3.79 (d, 1H, H-2'", *J* = 11.5 Hz), 3.31 (overlapped with solvent peak, 3H, H-5"a, H-6'"×2), 3.09 (dd, 1H, H-5"b, *J* = 13.2, *J* = 8.6 Hz), 2.24 (t, 2H, COCH_2, *J* = 7.5 Hz), 2.11-1.94 (m, 4H, H-3'"×2, H-5'"×2), 1.61 (t, 2H, $COCH_2CH_2$, *J* = 6.9 Hz), 1.32-1.28 (m, 24H, palmitoyl), 0.90 (t, 3H, palmitoyl terminal-Me, *J* = 6.9 Hz); ^{13}C NMR (CD_3OD, 100 MHz) δ 176.5, 165.9, 152.6, 145.5, 111.5, 103.2, 96.6, 85.4, 80.6, 80.0, 76.1, 73.6, 72.7, 71.6, 52.9, 44.3, 43.3, 41.9, 37.0, 33.1, 31.1, 30.8, 30.8, 30.6, 30.5, 30.4, 27.0, 26.9, 23.7, 14.4; ESIMS-LR *m/z* 712 [$(M + H)^+$]; ESIMS-HR calcd for $C_{35}H_{62}O_{10}N_5$ 712.4491, found 712.4512; $[\alpha]^{23}_D$ −11.2 (*c* 1.26, MeOH)

1-{(5*S*)-5-*O*-(5-Amino-5-deoxy-β-D-*ribo*-pentofuranosyl)-5-[(2*R*,4*R*)-4-palmitoylaminohexahydro-2-pyridyl]-β-D-*ribo*-pentofranosyl}uracil (7). A mixture of **S8** (22.8 mg, 26.1 μmol) and Pd/C (5.0 mg), TFA (3.9 μL, 0.052 mmol) in MeOH (1 mL) was vigorously stirred under H_2 at room temperature for 1.5 h. The catalyst was filtered off through Celite pad, and the filtrate was concentrated *in vacuo*. The residue was purified by C18 reverse phase column chromatography (70-90% MeOH/H_2O, 0.1% TFA) to afford **7** (19.8 mg, 21.1 μmol, 81 %) as a white solid. ^{1}H NMR (CD_3OD, 400 MHz) δ 7.79 (d, 1H, H-6, $J_{6,5}$ = 8.2 Hz), 5.79 (d, 1H, H-1', $J_{1',2'}$ = 1.8 Hz), 5.70 (d,1H, H-5, $J_{5,6}$ = 8.2 Hz), 5.17 (d, 1H, H-1", $J_{1",2"}$ = 3.2 Hz), 4.33 (dd, 1H, H-3', *J* = 8.0, *J* = 5.3 Hz), 4.20-4.14 (m, 3H, H-2', H-4', H-4'"), 4.08-4.03 (m, 3H, H-5', H-3", H-4"), 3.99 (t, 1H, H-2", $J_{2",1"}$ =

$J_{2'',3''}$ = 3.9 Hz), 3.77-3.73 (m, 1H, H-2'''), 3.43 (d, 1H, H-6'''eq, *J* = 12.8 Hz), 3.36-3.30 (overlapped with solvent peak, 2H, H-5''a, H-6'''ax), 3.19 (dd, 1H, H-5''b, *J* = 13.2, *J* = 7.8 Hz), 2.25-2.19 (m, 3H, H-3'''ax or eq, COC$\underline{H}_2$), 2.12-2.00 (m, 2H, H-3'''ax or eq, H-5'''ax), 1.92 (br d, 1H, H-5'''eq, *J* =14.7 Hz), 1.59 (t, 2H, $COCH_2C\underline{H}_2$, *J* = 6.9 Hz), 1.28 (s, 24 H, palmitoyl), 0.90 (t, 3H, palmitoyl-Me, *J* = 6.9 Hz); ^{13}C NMR (CD_3OD, 100 MHz) δ 176.5, 166.1, 152.0, 142.3, 110.9, 102.6, 92.7, 83.0, 80.7, 79.5, 75.5, 75.2, 72.3, 70.2, 54.2, 43.3, 42.8, 41.6, 36.9, 33.1, 30.8, 30.8, 30.6, 30.5, 30.4, 30.4, 30.3, 27.1, 26.9, 23.7, 14.4; ESIMS-LR *m/z* 712 [$(M + H)^+$]; ESIMS-HR calcd for $C_{35}H_{62}O_{10}N_5$ 712.4491, found 712.4505; $[\alpha]^{23}_D$ +4.31 (*c* 0.91, MeOH).

1-{(5*S*)-5-*O*-(5-Amino-5-deoxy-β-D-*ribo*-pentofuranosyl)-5-[(2*S*,4*S*)-4-palmitoylaminohexahydro-2-pyridyl]-β-D-*ribo*-pentofranosyl}uracil (8). A mixture of **S9** (16.2 mg, 18.6 μmol) and Pd/C (5.0 mg), TFA (2.8 μL, 37 μmol) in MeOH (1 mL) was vigorously stirred under H_2 at room temperature for 3.5 h. The catalyst was filtered off through Celite pad, and the filtrate was concentrated *in vacuo*. The residue was purified by C18 reverse phase column chromatography (70-90% MeOH/H_2O, 0.1% TFA) to afford **8** (14.7 mg, 15.6 μmol, 84 %) as a di-TFA salt. ^{1}H NMR (CD_3OD, 400 MHz) δ 7.66 (d, 1H, H-6, $J_{6,5}$ = 8.2 Hz), 5.79 (d, 1H, H-1', $J_{1',2'}$ = 1.8 Hz), 5.71 (d, 1H, H-5, $J_{5,6}$ = 8.2 Hz), 5.26 (d, 1H, H-1'', $J_{1'',2''}$ = 2.3 Hz), 4.23-4.01 (m, 8H, H-2', H-3', H-4', H-5', H-2'', H-3'', H-4'', H-4'''), 3.82 (d, 1H, H-2''', *J* = 13.3 Hz), 3.37 (m, 1H, H-6'''×2, *J* = 8.2 Hz), 3.31 (overlapped with solvent peak, 1H, H-5''a), 3.15 (dd, 1H, H-5''b, *J* = 13.3, *J* = 9.2 Hz), 2.24 (t, 2H, COC$\underline{H}_2$, *J* = 7.6 Hz), 2.29-2.22 (m, 1H, H-3'''), 2.09-2.06 (m, 1H, H-5'''), 1.99-1.89 (m, 2H, H-3''', H-5'''), 1.60 (t, 2H, $COCH_2C\underline{H}_2$, *J* = 6.9 Hz), 1.28 (s, 24H, palmitoyl), 0.90 (t, 3H, palmitoyl terminal-Me, *J* = 6.9 Hz); ^{13}C NMR (CD_3OD, 100 MHz) δ 176.6, 166.0, 152.0, 142.6, 110.4, 102.9, 93.4, 83.0, 80.3, 78.0, 75.7, 74.6, 72.8, 71.0, 55.4, 43.8, 43.1, 42.5, 37.0, 33.1, 30.8, 30.8, 30.6, 30.5, 30.4, 29.4, 27.0, 26.9, 23.7, 14.4; ESIMS-LR *m/z* 712 [$(M + H)^+$], ESIMS-HR calcd for $C_{35}H_{62}O_{10}N_5$ 712.4491, found 712.4496; $[\alpha]^{23}_D$ −5.70 (*c* 0.63, MeOH).

Scheme S2



1-{(5*S*)-5-*O*-(5-Azido-5-deoxy-β-D-*ribo*-pentofuranosyl)-5-[(2*R*,4*R*)-1-benzyloxycarbonyl-4-lua roylamino-hexahydro-2-pyridyl]-β-D-*ribo*-pentofranosyl}uracil (S10). A solution of **S5** (25.0 mg, 30.0 μmol) in CH_2Cl_2 (1 mL) was treated with TFA (200 μL) at 0 °C and the mixture was stirred for 2 h. The mixture was concentrated *in vacuo*. A solution of the residue and DIPEA (10.5 μL, 60.0 μmol) in THF (1 mL) was treated with *N*-succinimidyl laurate (13.4 mg, 45.0 μmol) at room temperature for 3.5 h. Then DIPEA (10.5 μl, 60.0 μmol) and *N*-succinimidyl laurate (13.4 mg, 45.0 μmol) were added to the reaction mixture, which was stirred for 20.5 h. After H_2O was added, the whole mixture was extracted with AcOEt. The organic phase was washed with brine, dried (Na_2SO_4), filtered and concentrated *in vacuo*. The residue was purified by preparative TLC (15% MeOH/$CHCl_3$) to afford **S10** (12.9 mg, 15.8 μmol, 53%) as a white solid. ^{1}H NMR (DMSO-d_6, D_2O, 400 MHz, a mixture of rotamers; selected data for the major rotamer) δ 11.3 (br s, 1H, NH-3), 7.72-7.68 (m, 2H, H-6, NH-4'''), 7.38-7.30 (m, 5H, phenyl), 5.64 (s, 1H, H-1'), 5.34 (d, 1H, H-5, $J_{5,6}$ = 8.2 Hz), 5.15-4.96 (m, 3H, H-1'', CH_2Ph), 4.55-4.52 (m, 1H, H-2'''), 4.18 (d, 1H, H-5', J = 10.5 Hz), 3.99 (m, 4H, H-2', H-3', H-4', H-6'''ax or eq), 3.85-3.71 (m, 3H, H-2'', H-4'', H-4'''), 3.61-3.50 (m, 1H, H-3''), 3.45-3.26 (m, 2H, H-5''×2), 3.19-3.07 (m, 1H, H-6'''ax or eq), 2.01 (t, 2H, $COCH_2$, J = 7.3 Hz), 1.84-1.81 (m, 2H, H-3'''ax or eq, H-5'''ax or eq), 1.47-1.44 (m, 2H, $COCH_2CH_2$), 1.38-1.34 (m, 1H, H-3'''ax or eq), 1.22 (br s, 17H, H-5'''ax or eq, lauroyl), 0.84 (t, 3H, lauryl terminal-Me, J = 6.8 Hz); ^{13}C NMR (DMSO-d_6, D_2O, 100 MHz, a mixture of rotamers) δ 171.6, 171.5, 163.0, 155.0, 150.2, 139.2, 136.9, 136.8, 128.5, 128.3, 128.0, 127.8, 127.8, 127.2, 108.3,

101.1, 90.0, 81.9, 80.2, 74.3, 74.0, 72.9, 71.6, 69.0, 66.3, 53.0, 52.0, 42.2, 42.1, 38.2, 35.4, 35.4, 32.0, 31.6, 31.3, 29.0, 29.0, 28.8, 28.7, 25.2, 22.2, 14.0; ESIMS-LR *m/z* 814 [(M − H)$^-$]; ESIMS-HR calcd for $C_{39}H_{56}O_{12}N_7$ 814.3992, found 814.4015; $[\alpha]^{20}_D$ +29.1 (*c* 1.29, MeOH).

1-{(5*S*)-5-*O*-(5-Azido-5-deoxy-β-D-*ribo*pentofuranosyl)-5-[(2*R*,4*R*)-1-benzyloxycarbonyl-4-myristoylamino-hexahydro-2-pyridyl]-β-D-*ribo*-pentofranosyl}uracil (S11). A solution of **S5** (25.0 mg, 30.0 μmol) in CH_2Cl_2 (1 mL) was treated with TFA (200 μL) at 0 °C and the mixture was stirred for 2.5 h. The mixture was concentrated *in vacuo*. A solution of the residue and DIPEA (10.5 μL, 60.3 μmol) in THF (1 mL) was treated with *N*-succinimidyl myristate (14.6 mg, 45.0 μmol) at room temperature for 24 h. After H_2O was added, the mixture was extracted with AcOEt. The organic phase was washed with brine, dried (Na_2SO_4), filtered and concentrated *in vacuo*. The residue was purified by preparative TLC (15% MeOH-$CHCl_3$) to afford **S11** (11.2 mg, 13.3 μmol, 44%) as a white solid. ^{1}H NMR (DMSO-d_6, D_2O, 500 MHz, a mixture of rotamers; selected data for the major rotamer) δ 7.72-7.68 (m, 2H, H-6, NH-4'''), 7.38-7.27 (m, 5H, phenyl), 5.64 (s, 1H, H-1'), 5.34 (d, 1H, H-5, $J_{5,6}$ = 8.6 Hz), 5.14-4.96 (m, 3H, H-1'', CH_2Ph), 4.54-4.53 (m, 1H, H-2'''), 4.18 (d, 1H, H-5', *J* = 9.8 Hz), 3.99 (m, 4H, H-2', H-3', H-4', H-6'''ax or eq), 3.84-3.71 (m, 3H, H-2'', H-4'', H-4'''), 3.61-3.50 (m, 1H, H-3''), 3.44-3.27 (m, 2H, H-5''×2), 3.21-3.07 (m, 1H, H-6'''), 2.01 (t, 2H, COCH_2, *J* = 7.2 Hz), 1.84-1.81 (m, 2H, H-3'''ax or eq, H-5'''ax or eq), 1.46 (br s, 2H, COCH$_2$CH_2), 1.41-1.35 (m, 1H, H-3'''ax or eq), 1.22 (br s, 21H, H-5'''ax or eq, myristoyl), 0.84 (t, 3H, myristoyl terminal-Me, *J* = 6.9 Hz); ^{13}C NMR (DMSO-d_6, D_2O, 125 MHz, a mixture of rotamers) δ 171.6, 163.2, 163.1, 155.0, 154.7, 150.4, 150.2, 139.9, 139.2, 137.0, 136.8, 128.5, 128.4, 128.0, 127.8, 127.8, 127.2, 108.5, 108.3, 101.3, 101.1, 89.0, 88.9, 82.5, 81.9, 80.2, 80.0, 74.3, 74.0, 73.9, 72.9, 71.7, 71.6, 69.0, 66.4, 66.3, 53.2, 53.0, 52.1, 42.2, 42.1, 38.3, 35.4, 32.0, 31.6, 31.4, 29.1, 29.1, 29.1, 29.0, 28.8, 28.7, 25.3, 22.2, 14.0; ESIMS-LR *m/z* 866 [(M + Na)$^+$]; ESIMS-HR calcd for $C_{41}H_{61}O_{12}N_7Na$ 866.4270, found 866.4291; $[\alpha]^{19}_D$ +28.4 (*c* 1.12, MeOH).

2,5-Dioxopyrrolidin-1-yl 2-octyldecanoate (S13). A solution of 2-octyldecanoic acid (100 mg, 352 μmol) and HOSu (52.7 mg, 458 μmol) in CH_2Cl_2 (4.0 mL) was treated with EDCI (176 mg, 918 μmol) at room temperature for 2.5 h. After sat. *aq.* $Na_2S_2O_3$ was added, the mixture was extracted with AcOEt. The organic phase was washed with brine, dried (Na_2SO_4), filtered and concentrated *in vacuo* to afford 2-octyldecanoic acid 2,5-dioxopyrrolidin-1-yl ester **S13** (119 mg, 312 μmol, 87%) as a colorless oil. ^{1}H NMR ($CDCl_3$, 400 MHz) δ 2.83-2.82 (m, 4H, COCH_2CH_2CO), 2.67-2.60 (m, 1H, COCH), 1.77-1.68 (m, 2H, COCHCH_2CH$_2$), 1.62-1.54 (m, 2H, COCHCH$_2$CH_2), 1.47-1.26 (m, 24H, (CH_2)$_6$CH$_3$×2), 0.89-0.85 (m, 6H, CH$_3$×2); ^{13}C NMR ($CDCl_3$, 100 MHz) δ 171.7, 169.3, 43.3, 32.4, 32.0, 32.0, 31.7, 29.7, 29.5, 29.4, 29.3, 29.2, 27.1, 27.1, 25.7, 22.8, 22.7, 14.2, 14.2; ESIMS-LR *m/z* 404 [(M + Na)$^+$]; ESIMS-HR calcd for $C_{22}H_{39}O_4NNa$ 404.2771, found 404.2774.

1-{(5*S*)-5-*O*-(5-Azido-5-deoxy-β-D-*ribo*-pentofuranosyl)-5-[(2*R*,4*R*)-1-benzyloxycarbonyl-4-2-octyldecanoyl -amino-hexahydro-2-pyridyl]-β-D-*ribo*-pentofranosyl}uracil (S12). A solution of

S5 (25.0 mg, 30.0 μmol) in CH_2Cl_2 (1 mL) was treated with TFA (200 μL) at 0 °C, and the mixture was stirred for 2.5 h. The mixture was concentrated *in vacuo*. A solution of the residue and and DIPEA (10.5 μL, 60.0 μmol) in THF (1 mL) was treated with *N*-succinimidyl 2-octyldecanoate (17.2 mg, 45.0 μmol) at room temperature for 24 h. Then DIPEA (10.5 μL, 60.0 μmol) and *N*-succinimidyl 2-octyldecanoate (17.2 mg, 45.0 μmol) were added to the reaction mixture and the mixture was stirred for 24 h. After H_2O was added, the mixture was extracted with AcOEt. The organic phase was washed with brine, dried (Na_2SO_4), filtered and concentrated *in vacuo*. The residue was purified by preparative TLC (15% MeOH-$CHCl_3$) to afford **S12** (7.5 mg, 8.3 μmol, 28%) as a white solid. ^{1}H NMR (DMSO-d_6, D_2O, 500 MHz, a mixture of rotamers; selected data for the major rotamer) δ 7.73-7.69 (m, 2H, H-6, NH-4'''), 7.38-7.27 (m, 5H, phenyl), 5.66 (s, 1H, H-1'), 5.32 (dd, 1H, H-5, $J_{5,6}$ = 8.0, $J_{5,NH-3}$ = 1.7 Hz), 5.14-4.96 (m, 3H, H-1'', CH_2Ph), 4.53-4.52 (m, 1H, H-2'''), 4.20 (d, 1H, H-5', J = 9.8 Hz), 4.07-3.99 (m, 4H, H-2', H-3', H-4', H-6'''ax or eq), 3.84-3.80 (m, 2H, H-4'', H-4'''), 3.72 (d, 1H, H-2'', $J_{2'',3''}$ = 4.6 Hz), 3.56-3.54 (m, 1H, H-3''), 3.39 (overlapped with H_2O peak, 1H, H-5''a), 3.27 (br d, 1H, H-5''b, J = 10.9 Hz), 3.22-3.08 (m, 1H, H-6'''ax or eq), 2.04-2.00 (m, 1H, COCH), 1.88-1.83 (m, 1H, H-3'''ax or eq), 1.79-1.77 (m, 1H, H-5'''ax or eq), 1.32-1.34 (m, 1H, H-3'''ax or eq), 1.22-1.15 (m, 1H, H-5'''ax or eq), 1.40-1.15 (m, 28H, $(CH_2)_7CH_3$×2), 0.85-0.80 (m, 6H, CH_3×2); ^{13}C NMR (DMSO-d_6, D_2O, 125 MHz, a mixture of rotamers) δ 174.5, 174.4, 163.1, 155.0, 150.3, 139.2, 137.0, 128.6, 128.4, 128.0, 127.8, 127.8, 127.2, 108.4, 101.2, 88.7, 80.2, 74.4, 74.0, 71.6, 66.4, 66.3, 53.0, 52.1, 45.6, 45.2, 42.2, 38.3, 32.6, 32.6, 31.3, 29.1, 29.0, 28.8, 28.8, 28.7, 27.0, 26.8, 22.2, 22.1,14.0; ESIMS-LR *m/z* 922 [$(M + Na)^+$]; ESIMS-HR calcd for $C_{45}H_{69}O_{12}N_7Na$ 922.4896, found 922.4910; $[\alpha]^{19}_D$ +21.9 (*c* 0.75, MeOH).

1-{(5*S*)-5-*O*-(5-Amino-5-deoxy-β-D-*ribo*-pentofuranosyl)-5-[(2*R*,4*R*)-4-luaroylaminohexahydro-2-pyridyl]-β-D-*ribo*-pentofranosyl}uracil (50). A mixture of **S10** (12.9 mg, 15.8 μmol), Pd/C (2.6 mg) and TFA (2.3 μL, 0.032 mmol) in MeOH (1 mL) was vigorously stirred under H_2 at room temperature for 3 h. The catalyst was filtered off through Celite pad, and the filtrate was concentrated *in vacuo*. A mixture of the residue, Pd/C (2.6 mg) and TFA (2.3 μL, 32 μmol) in MeOH (1 mL) was vigorously stirred under H_2 at room temperature for 1 h. The catalyst was filtered off through Celite pad, and the filtrate was concentrated *in vacuo*. The residue was purified by C18 reverse phase column chromatography (60-80% MeOH-H_2O, 0.1% TFA) to afford **50** (8.9 mg, 10 μmol, 64 %) as a di-TFA salt. ^{1}H NMR (CD_3OD, 500 MHz) δ 8.26 (d, 1H, NH-4'''), $J_{NH-4''',4'''}$ = 6.3 Hz), 7.77 (d, 1H, H-6, $J_{6,5}$ = 8.1 Hz), 5.78 (d, 1H, H-1', $J_{1',2'}$ = 1.7 Hz), 5.70 (d, 1H, H-5, $J_{5,6}$ = 8.0 Hz), 5.17 (d, 1H, H-1'', $J_{1'',2''}$ = 2.9 Hz), 4.33 (dd, 1H, H-3', $J_{3',4'}$ = 8.1, $J_{3',2'}$ = 5.2 Hz), 4.21-4.20 (m, 2H, H-2', H-4'''), 4.15 (dd, 1H, H-4', $J_{4',3'}$ = 8.0, $J_{4',5'}$ = 2.9 Hz), 4.08-4.03 (m, 3H, H-5', H-3'', H-4''), 4.00 (dd, 1H, H-2'', $J_{2'',3''}$ = 5.2, $J_{2'',1''}$ = 2.9 Hz), 3.74 (ddd, 1H, H-2''', J =11.8, J = 6.6, J = 2.9 Hz), 3.43 (dt, 1H, H-6'''eq, J = 13.2, 3.8 Hz), 3.35-3.32 (m, 1H, H-6'''ax), 3.31 (overlapped with solvent peak, 1H, H-5''a), 3.18 (dd, 1H, H-5''b, J = 13.5, J = 9.1 Hz), 2.28-2.18 (m, 3H, H-3'''ax or eq, $COCH_2$), 2.11-1.99 (m, 2H, H-3'''ax or eq, H-5'''ax), 1.92 (d, 1H, H-5'''eq, J = 14.3 Hz), 1.60 (quint, 2H, $COCH_2CH_2$, J = 7.3 Hz), 1.28 (s, 16H, lauryl), 0.90 (t, 3H, lauryl terminal-Me, J = 7.2 Hz); ^{13}C NMR (CD_3OD, 125 MHz) δ 176.5, 166.1, 151.9, 142.3, 110.9, 102.6, 92.9, 83.1, 80.7,

79.4, 75.6, 75.1, 72.3, 70.2, 54.3, 43.4, 42.8, 41.7, 36.9, 33.1, 30.8, 30.7, 30.6, 30.5, 30.5, 30.4, 30.3, 27.1, 26.9, 23.7, 14.4; ESIMS-LR *m/z* 656 [(M + H)$^+$]; ESIMS-HR calcd for $C_{31}H_{54}O_{10}N_5$ 656.3865, found 656.3872; $[\alpha]^{16}_D$ +4.01 (*c* 0.89, MeOH).

1-{(5*S*)-5-*O*-(5-Amino-5-deoxy-β-D-*ribo*-pentofuranosyl)-5-[(2*R*,4*R*)-4-myristoylaminohexahydro-2-pyridyl]-β-D-*ribo*-pentofranosyl}uracil (51). A mixture of **S11** (11.2 mg, 13.3 μmol), Pd/C (2.2 mg) and TFA (2.0 μL, 0.27 μmol) in MeOH (1 mL) was vigorously stirred under H_2 at room temperature for 2 h. The catalyst was filtered off through Celite pad, and the filtrate was concentrated *in vacuo*. The residue was purified by C18 reverse phase column chromatography (70-90% MeOH-H_2O, 0.1% TFA) to afford **51** (9.6 mg, 11 μmol, 79 %) as a di-TFA salt. ^{1}H NMR (CD_3OD, 400 MHz) δ 7.78 (d, 1H, H-6, $J_{6,5}$ = 8.2 Hz), 5.78 (d, 1H, H-1', $J_{1',2'}$ = 1.8 Hz), 5.70 (d, 1H, H-5, $J_{5,6}$ = 8.2 Hz), 5.17 (d, 1H, H-1", $J_{1",2"}$ = 3.2 Hz), 4.33 (dd, 1H, H-3', $J_{3',4'}$ = 8.2, $J_{3',2'}$ = 5.0 Hz), 4.22-4.19 (m, 2H, H-2', H-4'"), 4.15 (dd, 1H, H-4', $J_{4',3'}$ = 8.2, $J_{4',5'}$ = 2.7 Hz), 4.09-4.03 (m, 3H, H-5', H-3", H-4"), 4.00 (dd, 1H, H-2", $J_{2",3"}$ = 5.0, $J_{2",1"}$ = 3.2 Hz), 3.74 (ddd, 1H, H-2'", *J* =11.9, *J* = 6.8, *J* = 2.7 Hz), 3.43 (dt, 1H, H-6'"eq, *J* = 13.3, *J* = 4.1 Hz), 3.36-3.33 (m, 1H, H-6'"ax), 3.33-3.30 (overlapped with solvent peak, 1H, H-5"a), 3.18 (dd, 1H, H-5"b, *J* = 13.2, *J* = 8.7 Hz), 2.25-2.18 (m, 3H, H-3'"ax or eq, COC<u>H</u>$_2$), 2.13-1.99 (m, 2H, H-3'"ax or eq, H-5'"ax), 1.92 (br d, 1H, H-5'"eq, *J* = 13.3 Hz), 1.60 (quint, 2H, COCH$_2$C<u>H</u>$_2$, *J* = 7.2 Hz), 1.28 (s, 20H, myristoyl), 0.90 (t, 3H, myristoyl terminal-Me, *J* = 6.9 Hz); ^{13}C NMR (CD_3OD, 100 MHz) δ 176.5, 166.1, 152.0, 142.3, 110.9, 102.6, 92.9, 83.1, 80.7, 79.4, 75.6, 75.1, 72.3, 70.2, 54.3, 43.4, 42.8, 41.7, 36.9, 33.1, 30.8, 30.8, 30.6, 30.5, 30.4, 30.3, 27.1, 26.9, 23.7, 14.4; ESIMS-LR *m/z* 684 [(M + H)$^+$]; ESIMS-HR calcd for $C_{33}H_{58}O_{10}N_5$ 684.4178, found 684.4188; $[\alpha]^{17}_D$ +4.80 (*c* 0.96, MeOH).

1-{(5*S*)-5-*O*-(5-Amino-5-deoxy-β-D-*ribo*-pentofuranosyl)-5-[(2*R*,4*R*)-4-(2-octyldecanoylamino)-hexahydro-2-pyridyl]-β-D-*ribo*-pentofranosyl}uracil (**52).** A mixture of **S12** (7.5 mg, 8.3 μmol), Pd/C (3.0 mg) and TFA (1.2 μL, 0.17 μmol) in MeOH (1 mL) was vigorously stirred under H_2 at room temperature for 2 h. The catalyst was filtered off through Celite pad, and the filtrate was concentrated *in vacuo*. The residue was purified by C18 reverse phase column chromatography (80-95% MeOH-H_2O, 0.1% TFA) to afford **52** (5.2 mg, 5.4 μmol, 64%) as a di-TFA salt. ^{1}H NMR (CD_3OD, 400 MHz) δ 8.26 (d, 1H, N<u>H</u>-4'", $J_{N\underline{H}\text{-}4'",4'"}$ = 6.0 Hz), 7.81 (d,1H, H-6, $J_{6,5}$ = 8.2 Hz), 5.76 (d, 1H, H-1', $J_{1',2'}$ = 1.8 Hz), 5.69 (d, 1H, H-5, $J_{5,6}$ = 8.2 Hz), 5.16 (d, 1H, H-1", $J_{1",2"}$ = 3.2 Hz), 4.32 (dd, 1H, H-3', $J_{3',4'}$ = 8.2, $J_{3',2'}$ = 5.0 Hz), 4.21 (br s, 1H, H-4'"), 4.17 (dd, 1H, H-2', $J_{2',3'}$ = 6.0, $J_{2',1'}$ = 1.4 Hz), 4.15 (dd, 1H, H-4', $J_{4',3'}$ = 8.2, $J_{4',5'}$ = 2.8 Hz), 4.09-4.02 (m, 3H, H-5', H-3", H-4"), 3.98 (dd, 1H, H-2", $J_{2",3"}$ = 5.5, $J_{2",1"}$ = 3.2 Hz), 3.71 (t, 1H, H-2'", *J* =10.0 Hz), 3.46 (d, 1H, H-6'"eq, *J* = 12.8 Hz), 3.38-3.35 (m, 1H, H-6'"ax), 3.31 (overlapped with solvent peak, 1H, H-5"a), 3.19 (dd, 1H, H-5"b, *J* = 13.1, *J* = 8.5 Hz), 2.30-2.23 (m, 2H, H-3'"ax or eq, COC<u>H</u>), 2.11 (t, 1H, H-5'"ax, *J* = 13.5 Hz), 2.04-1.97 (m, 1H, H-3'"ax or eq), 1.93 (d, 1H, H-5'"eq, *J* = 16.0 Hz), 1.55 (br s, 2H, COCHC<u>H</u>$_2$CH$_2$), 1.39-1.23 (m, 26H, COCHCH$_2$C<u>H</u>$_2$, (C<u>H</u>$_2$)$_6$CH$_3$×2), 0.91-0.85 (m, 6H, CH$_3$×2); ^{13}C NMR (CD_3OD, 100 MHz) δ 179.4, 166.1, 151.9, 142.1, 111.0, 102.6, 92.8, 82.7, 80.8, 79.6, 75.5, 75.3, 72.2, 70.0, 54.3, 47.9, 43.2, 42.9, 41.6, 34.0, 33.1, 33.0, 32.9, 32.7, 30.8, 30.8, 30.7, 30.6,

30.6, 30.5, 30.5, 30.4, 30.3, 30.2, 28.7, 28.5, 26.9, 23.7, 23.7, 14.4; ESIMS-LR *m/z* 740 [$(M + H)^+$]; ESIMS-HR calcd for $C_{37}H_{66}O_{10}N_5$ 740.4804, found 740.4820; $[\alpha]^{18}_D$ +4.85 (*c* 0.52, MeOH).

2. Assay of cytotoxicity

Cytotoxicity of the compounds against HepG2 cell was measured using Cell Counting Kit-8 according to manufacturer's protocol. Briefly, HepG2cells (1×10^4 cells/well) in a 96 well plate were cultured in D-MEM (Low Glucose) medium containing 10% fetal bovine serum in the presence of test compounds at 37 °C for 24 h under 5% CO_2 atmosphere. The medium was aspirated, and a solution of Cell Counting Kit-8 reagent in medium (1:10) was added. The plates were incubate at 37 °C for 2 h under 5% CO_2 atmosphere, then 450 nm absorbance was measured. Experiments were conducted in 7 concentrations, n=4.

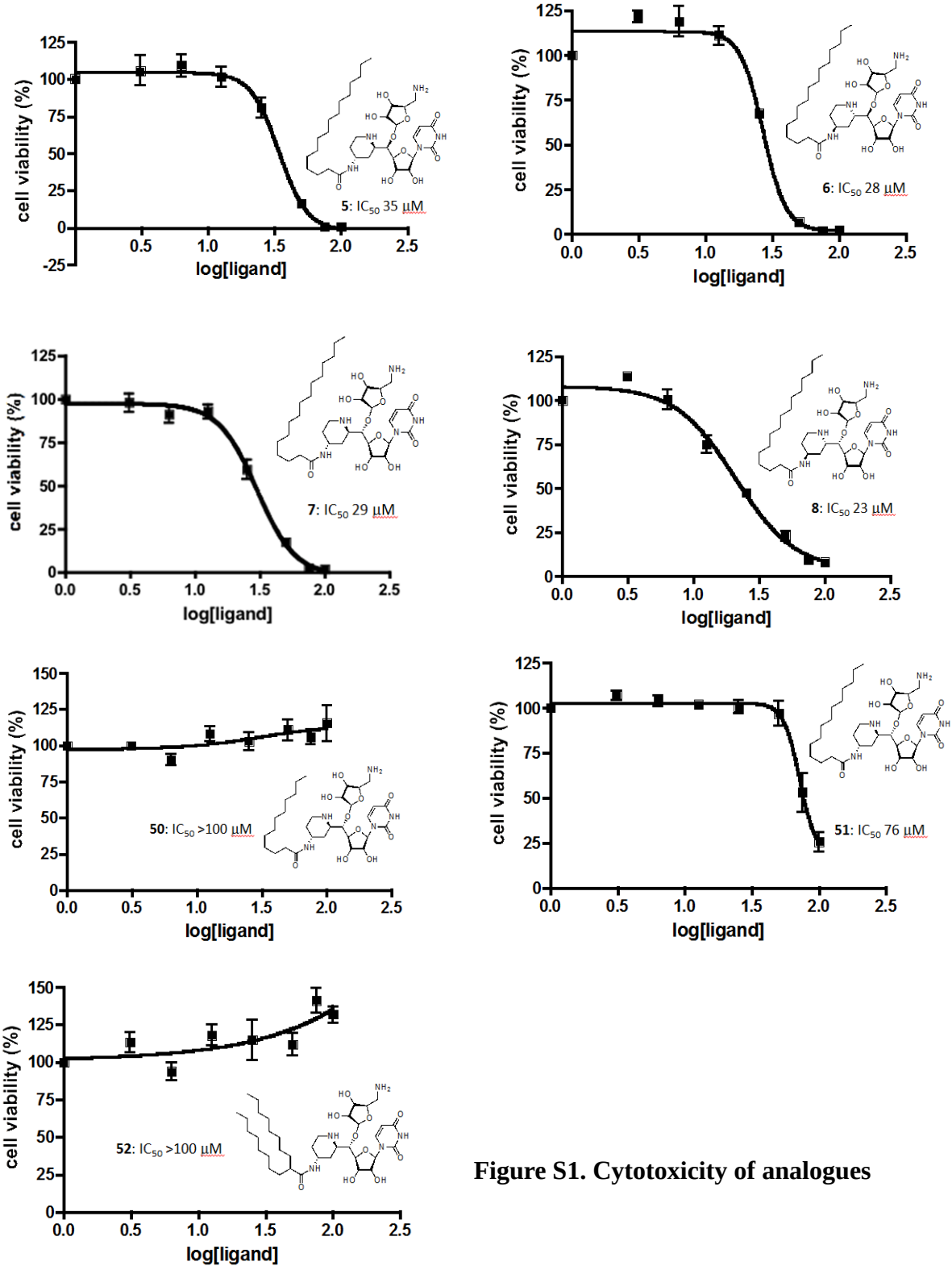


Figure S1. Cytotoxicity of analogues

3. In vitro CYP Inhibition assay

Pooled human liver microsomes were purchased from XenoTech LLC. Cytochrome P-450 (CYP) inhibition of human liver microsomes by **7** was conducted in 4 concentrations, n=1. To evaluate compounds as a direct inhibitor of CYP activity, human liver microsomes were pre-incubated at 37 °C for 30 min in 125 mM phosphate buffer containing compounds and cocktail solution of marker substrates (phenacetin for 1A2, bupropione for 2B6, amodiaquine for 2C8, diclofenac for 2C9, (*S*)-mephenitoin for 2C19, bufuralol for 2D6, and midazolam 3A4, respectively), before 1.3 mM NADPH was added to the reaction mixture. To evaluate time-dependent inhibition, human liver microsomes were pre-incubated at 37°C for 30 minutes in 125 mM phosphate buffer containing compounds and 1.3 mM NADPH, before a cocktail solution of marker substrates was

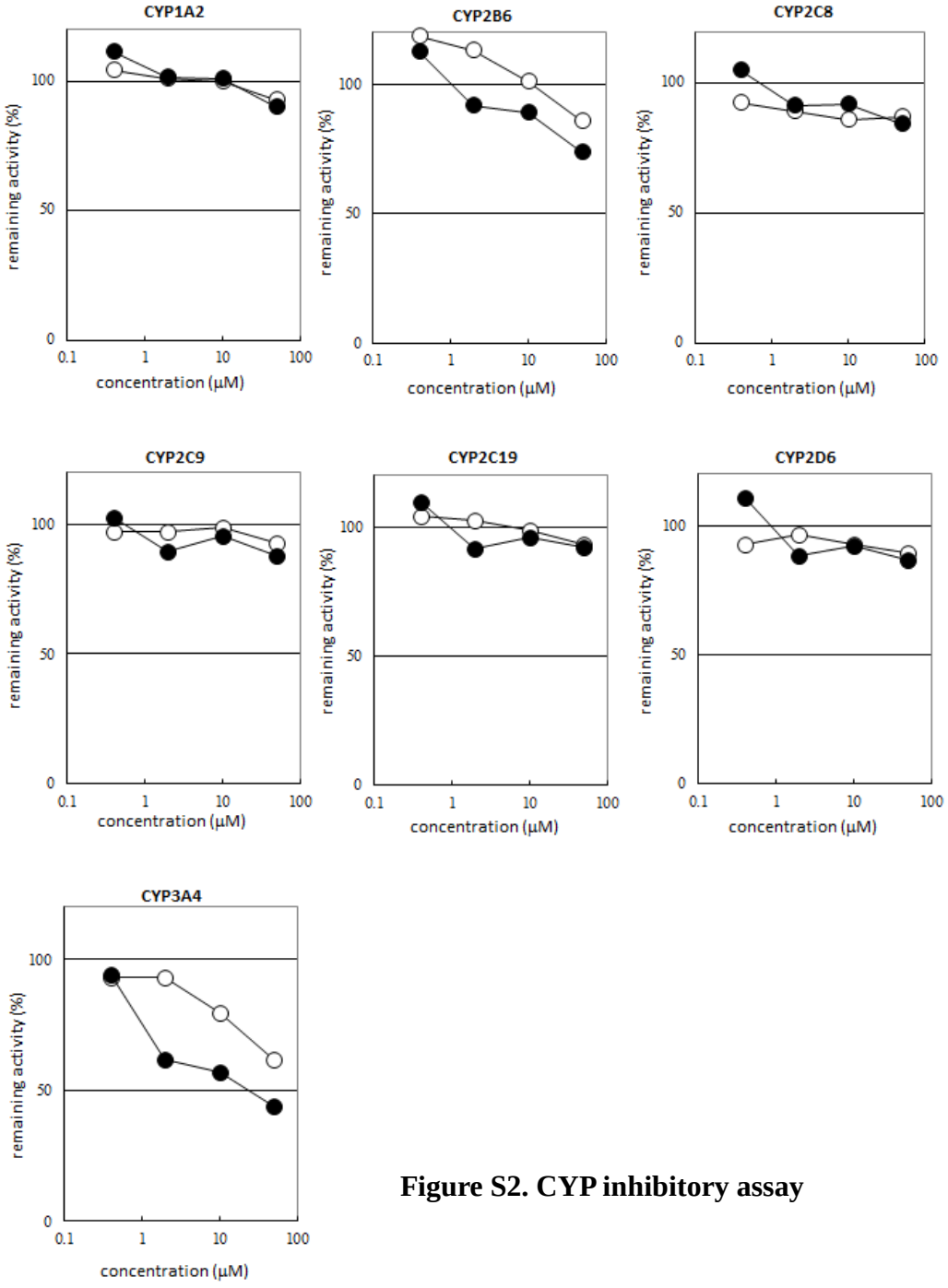
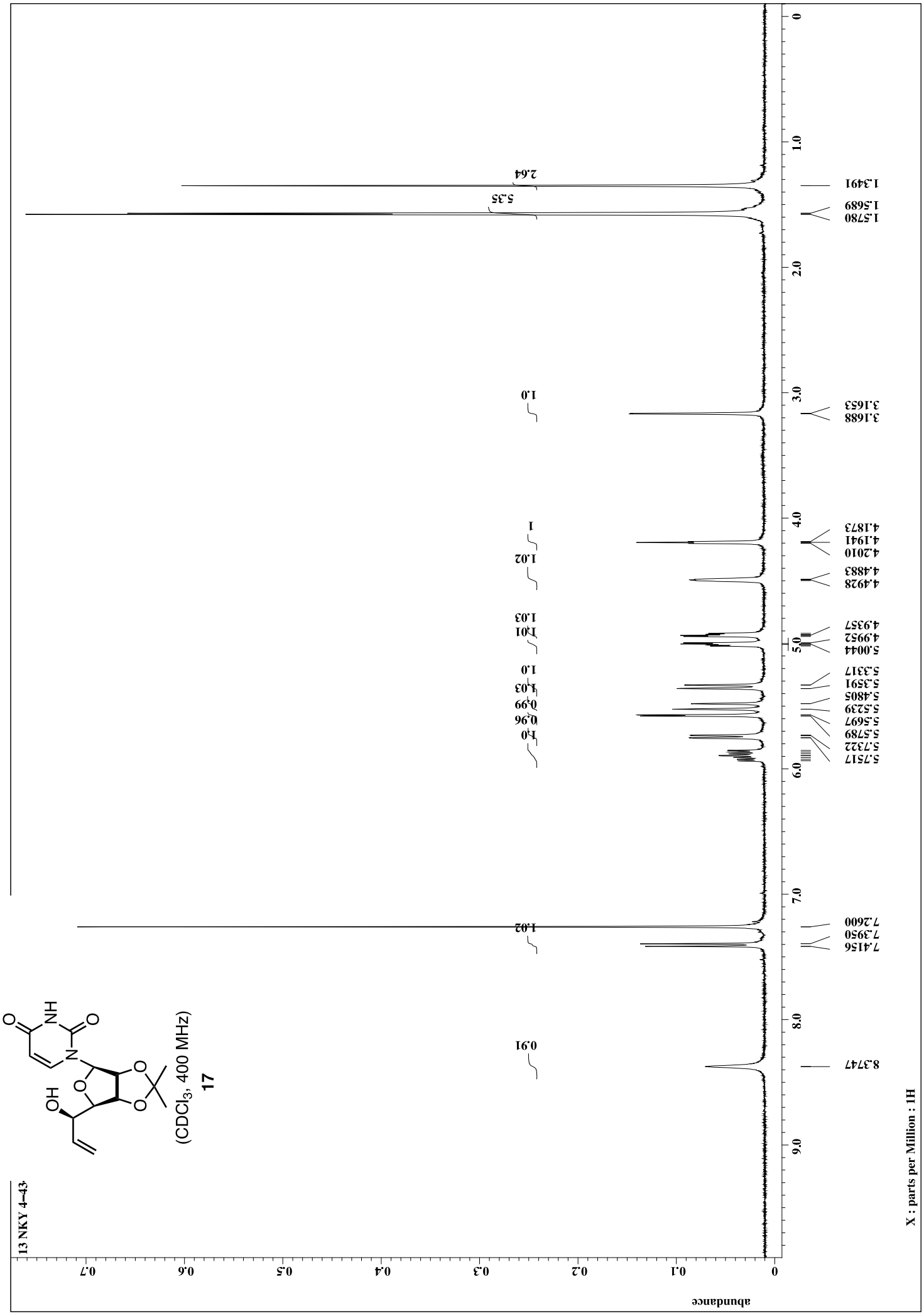
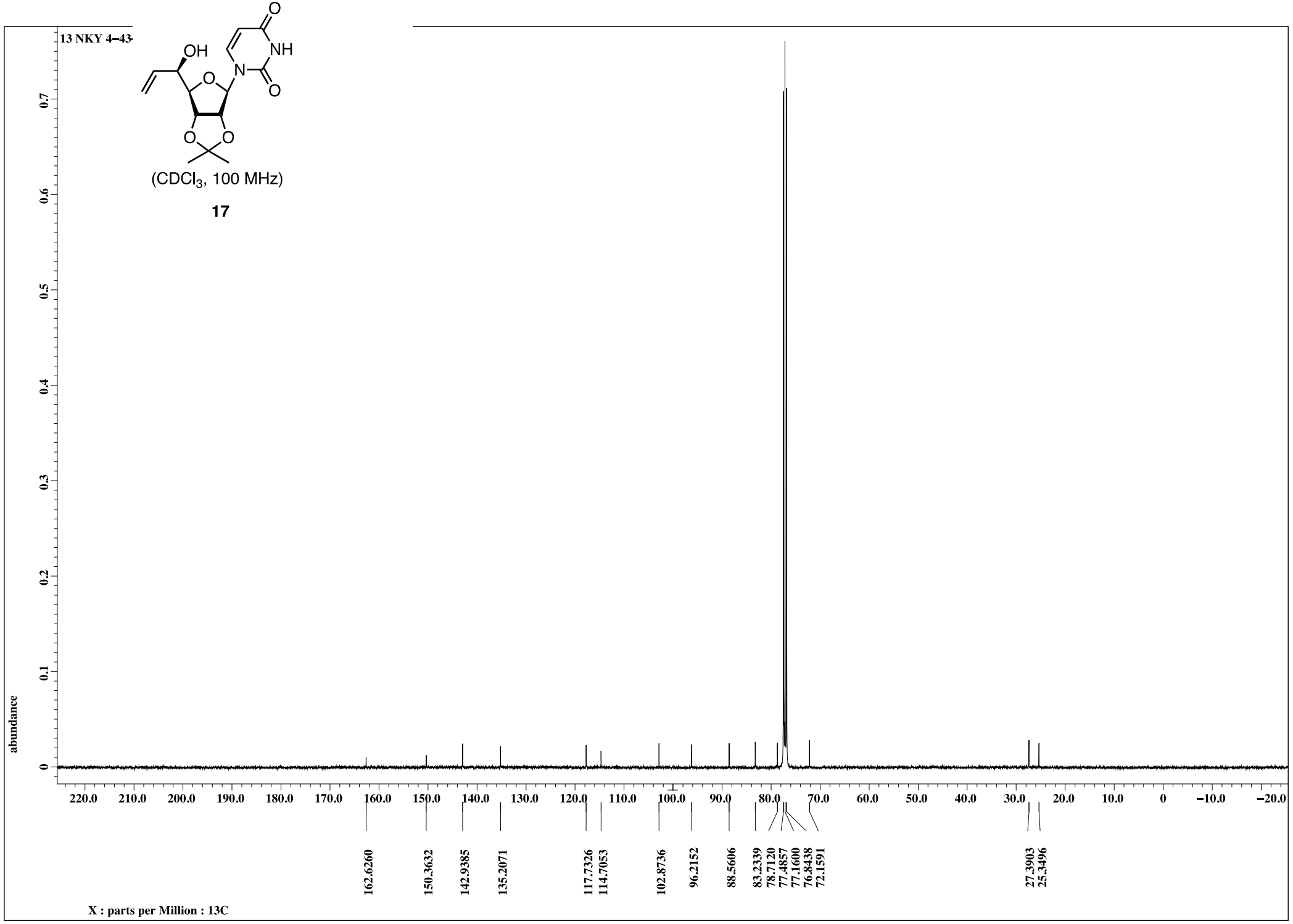


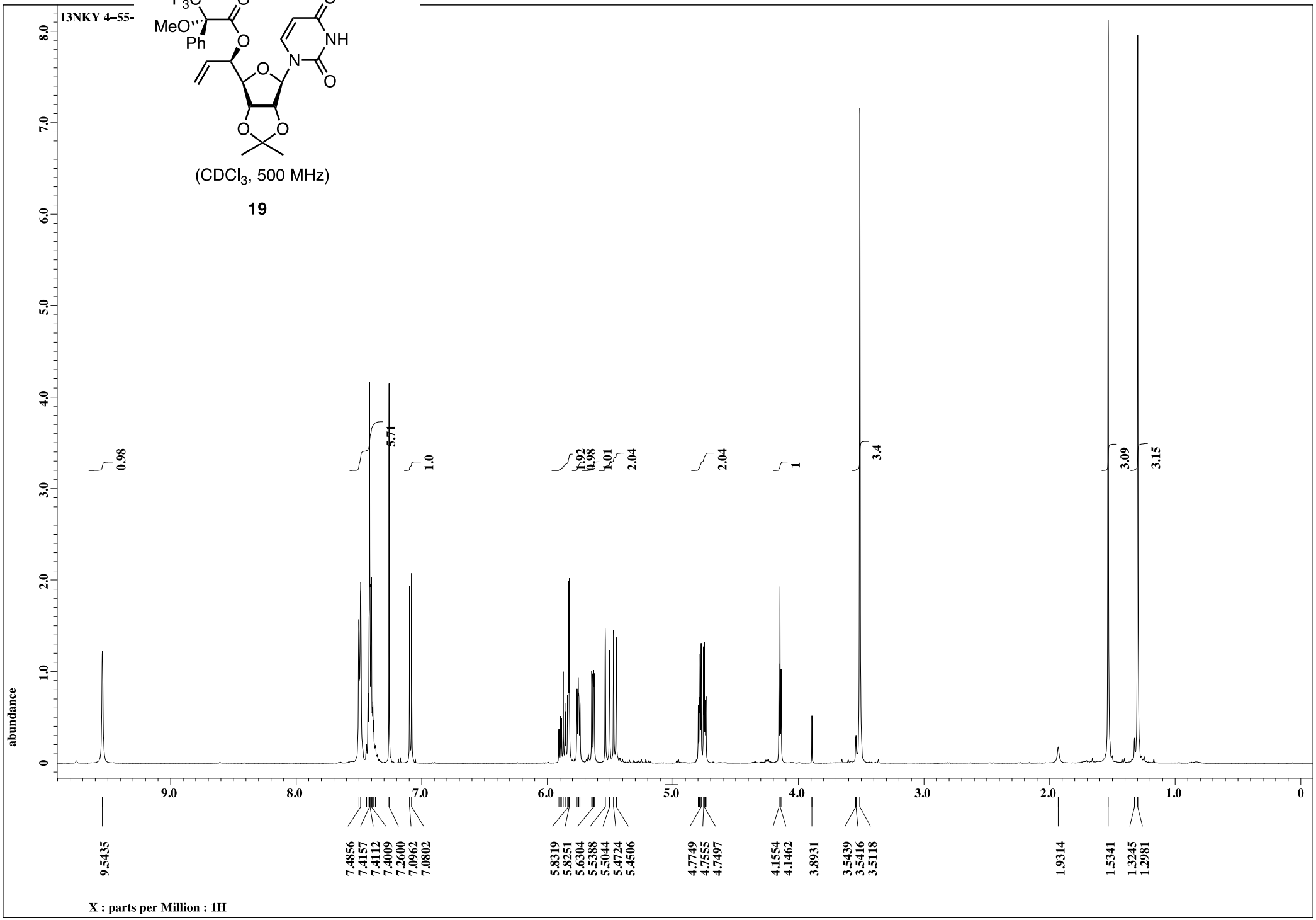
Figure S2. CYP inhibitory assay

added to the reaction mixture. The protein concentration was 0.05 mg protein/mL, and the final volume was 0.1 mL. Incubations were terminated by addition of methanol (300 μL) after 10 minutes of incubation. Samples were kept at −20°C for about 30 minutes and centrifuged (4°C, 3000 rpm, 10 min). Remaining activity was determined by LC/MS/MS analysis of the supernatants.

6. NMR charts of synthesizd compounds




13 NKY 4–43
OH
NH
O
N
O
O
O
O
(CDCl3, 100 MHz)
17
abundance
0
0.1
0.2
0.3
0.4
0.5
0.6
0.7
220.0
210.0
200.0
190.0
180.0
170.0
160.0
150.0
140.0
130.0
120.0
110.0
100.0
90.0
80.0
70.0
60.0
50.0
40.0
30.0
20.0
10.0
0
−10.0
−20.0
162.6260
150.3632
142.9385
135.2071
117.7326
114.7053
102.8736
96.2152
88.5606
83.2339
78.7120
77.4857
77.1600
76.8438
72.1591
27.3903
25.3496
X : parts per Million : 13C


13NKY 4–55-
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MeO
Ph
O
NH
N
(CDCl3, 500 MHz)
19
abundance
X : parts per Million : 1H
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5.71
1.0
1.92
0.98
1.01
2.04
2.04
1
3.4
3.09
3.15
9.5435
7.4856
7.4157
7.4112
7.4009
7.2600
7.0962
7.0802
5.8319
5.8251
5.6304
5.5388
5.5044
5.4724
5.4506
4.7749
4.7555
4.7497
4.1554
4.1462
3.8931
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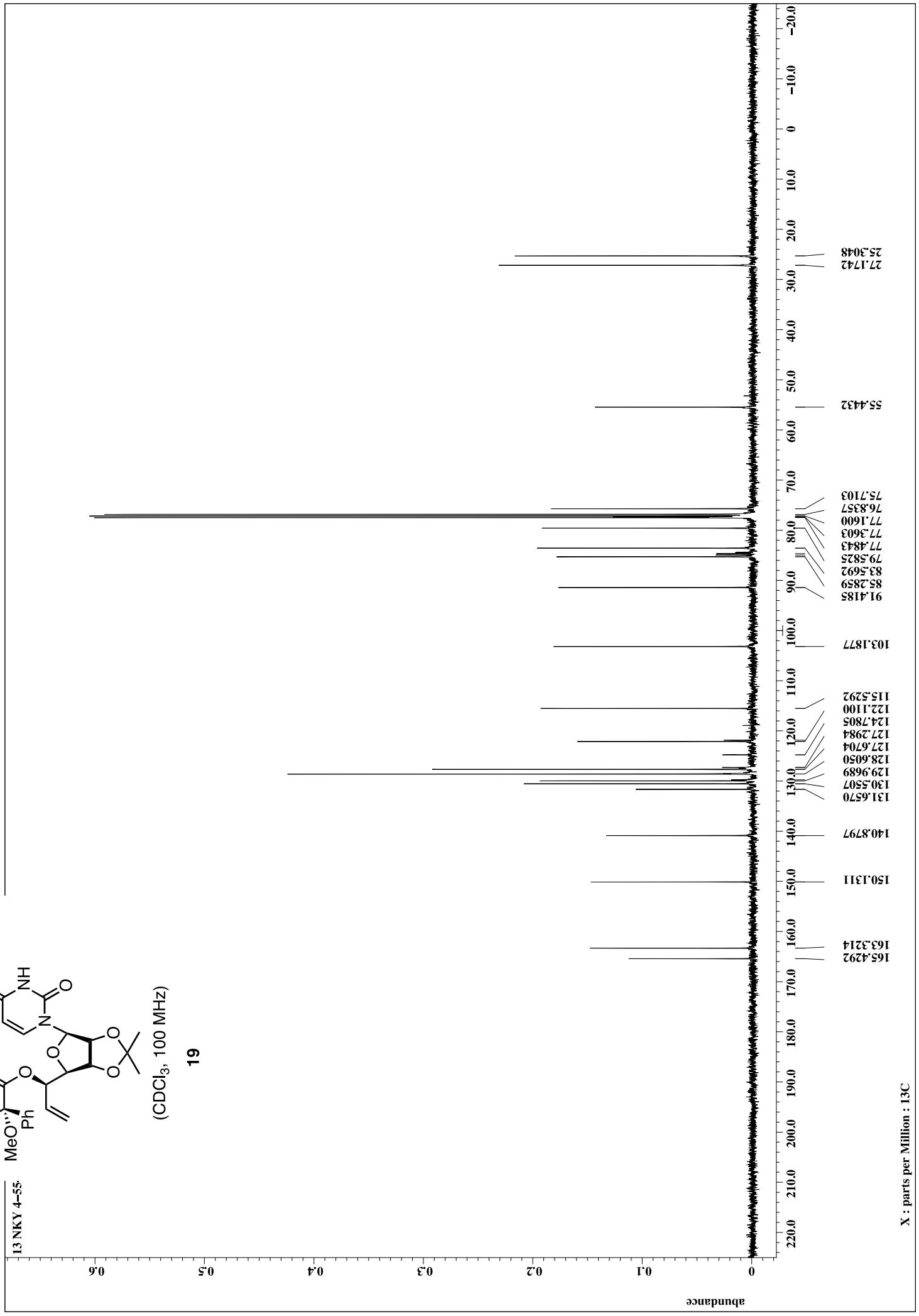
3.5118
1.9314
1.5341
1.3245
1.2981


13 NKY 4–55
19
(CDCl3, 100 MHz)
abundance
X : parts per Million : 13C
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150.1311
140.8797
131.6570
130.5507
129.9689
128.6050
127.6704
127.2984
124.7805
122.1100
115.5292
103.1877
91.4185
85.2859
83.5692
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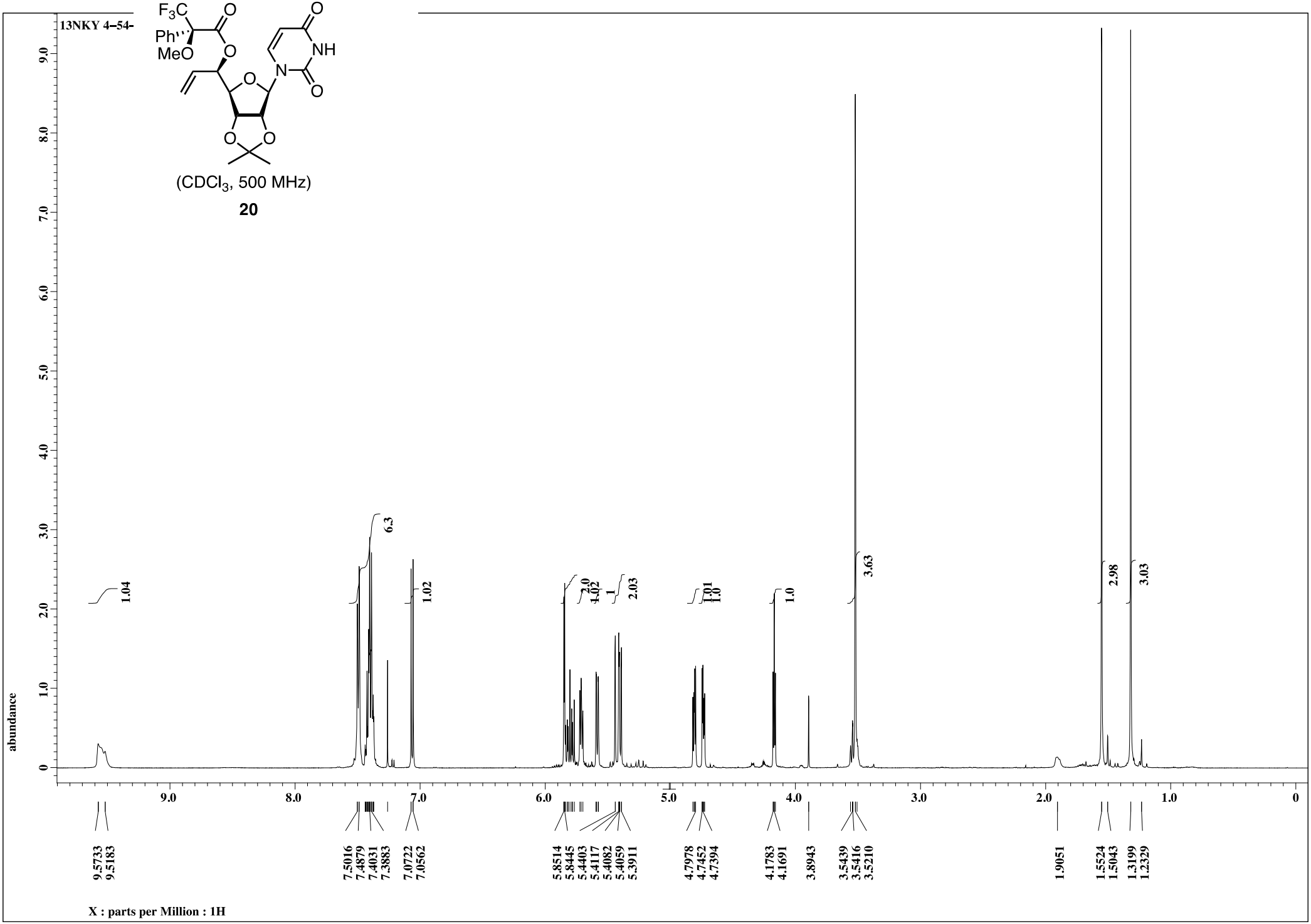
77.4843
77.3603
77.1600
76.8357
75.7103
55.4432
27.1742
25.3048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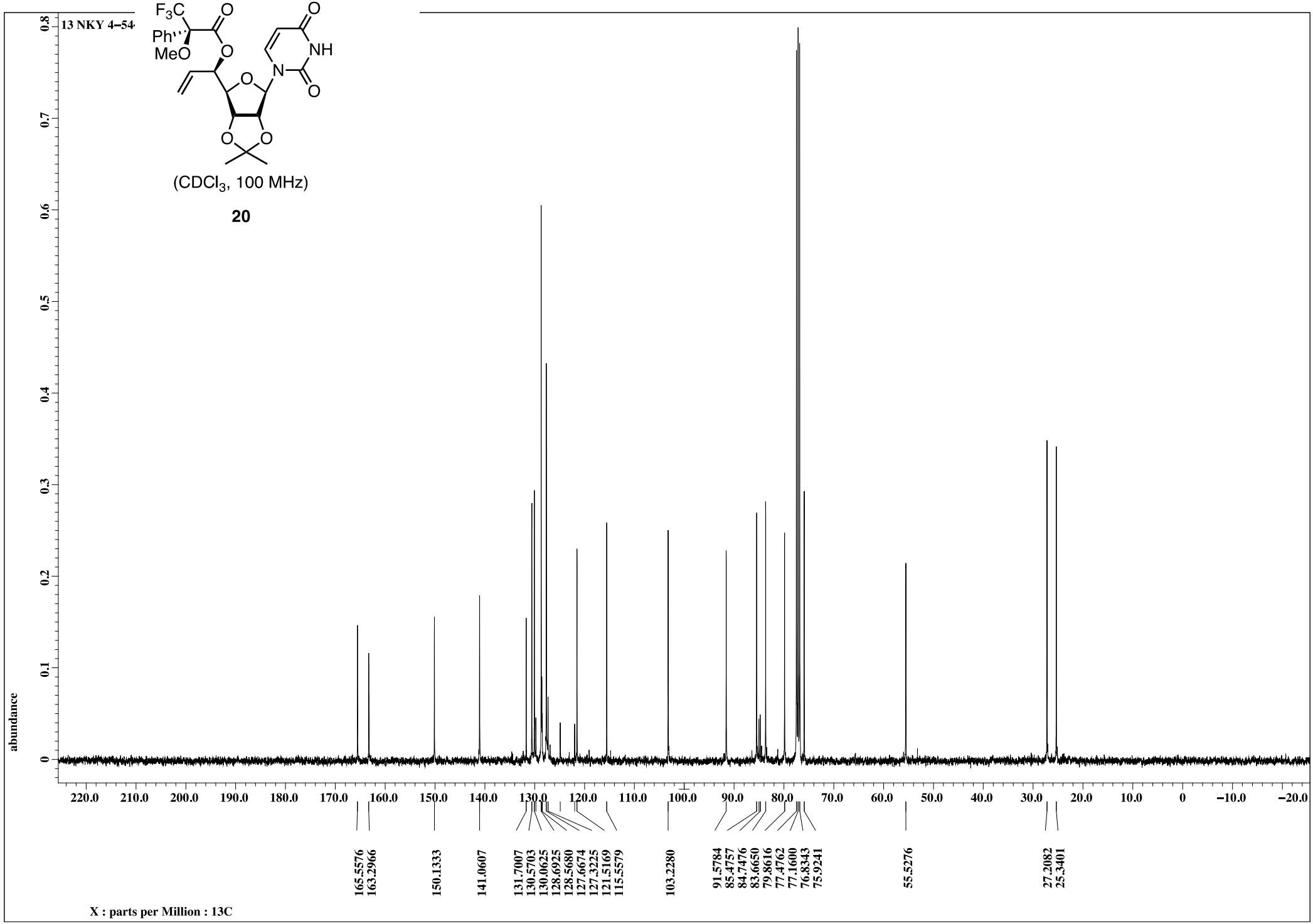
F3C
Ph
MeO
O
O
O
NH
N
O
O
O
O
(CDCl3, 500 MHz)
20
abundance
1.04
6.3
1.02
2.0
1.02
1
2.03
1.01
1.0
1.0
3.63
2.98
3.03
9.5733
9.5183
7.5016
7.4879
7.4031
7.3883
7.0722
7.0562
5.8514
5.8445
5.4403
5.4117
5.4082
5.4059
5.3911
4.7978
4.7452
4.7394
4.1783
4.1691
3.8943
3.5439
3.5416
3.5210
1.9051
1.5524
1.5043
1.3199
1.2329
X : parts per Million : 1H


13 NKY 4-54
F3C
Ph
MeO
O
NH
N
(CDCl3, 100 MHz)
20
abundance
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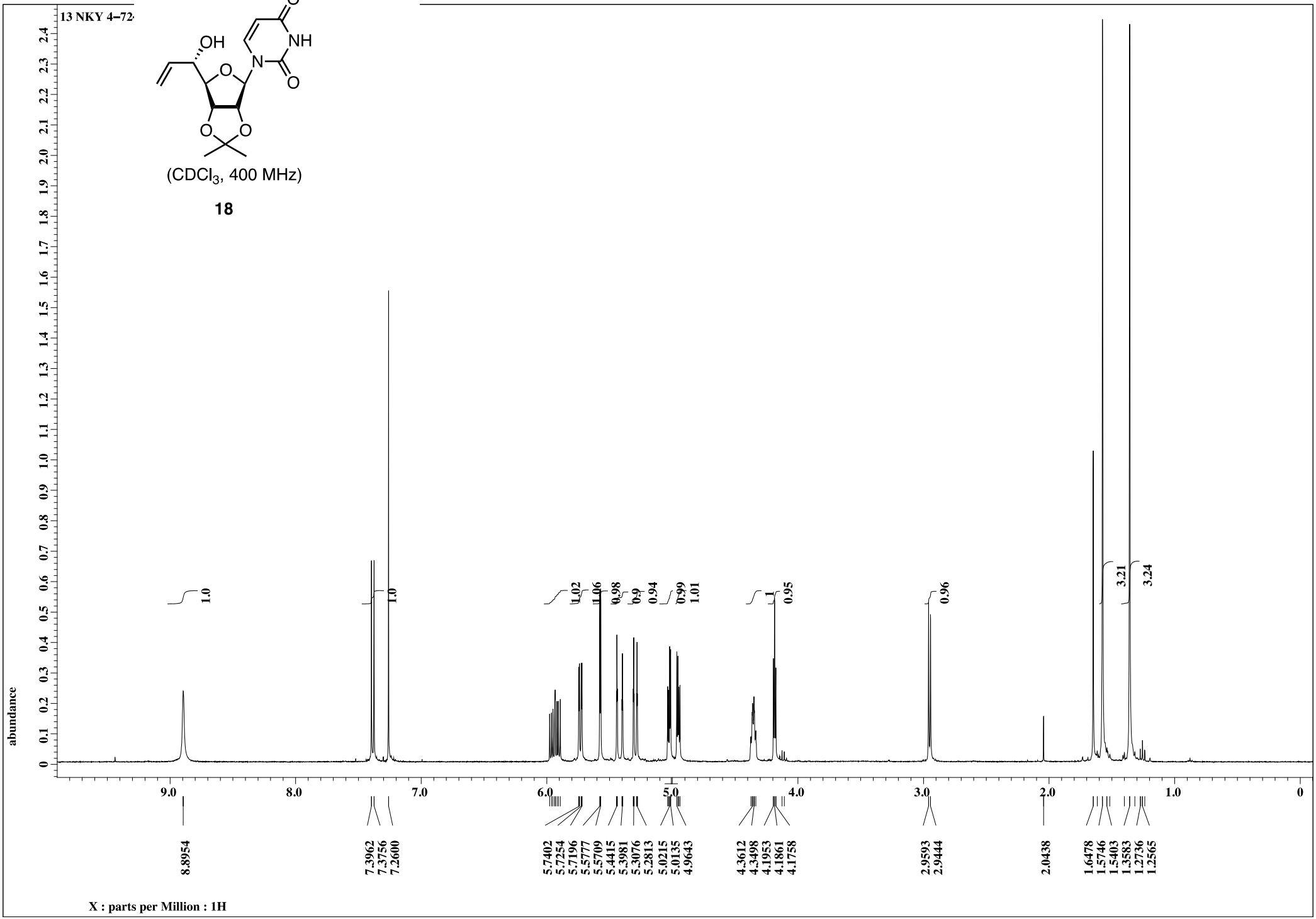
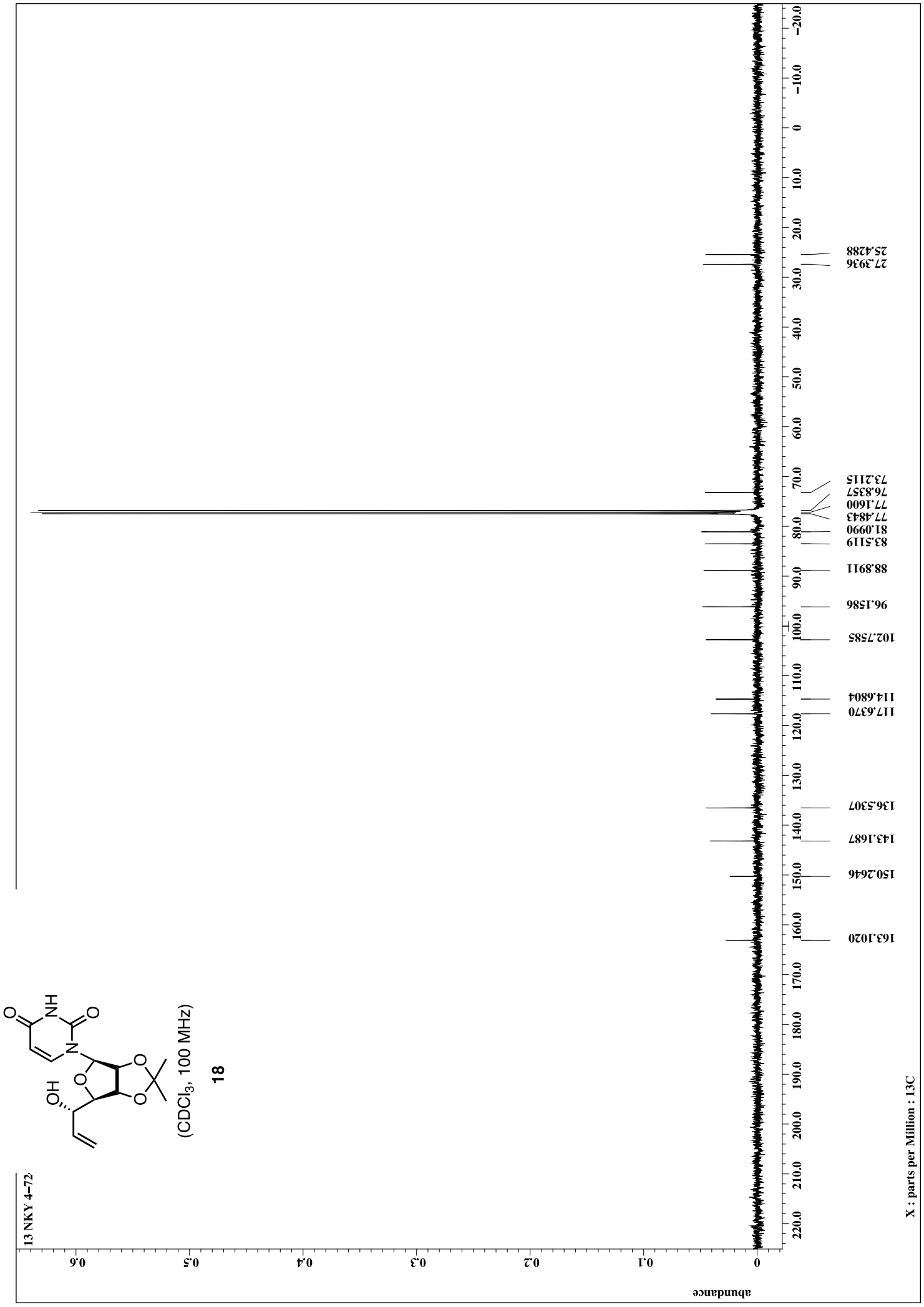
0.2
0.3
0.4
0.5
0.6
0.7
0.8
220.0
210.0
200.0
190.0
180.0
170.0
160.0
150.0
140.0
130.0
120.0
110.0
100.0
90.0
80.0
70.0
60.0
50.0
40.0
30.0
20.0
10.0
0
-10.0
-20.0
165.5576
163.2966
150.1333
141.0607
131.7007
130.5703
130.0625
128.6925
128.5680
127.6674
127.3225
121.5169
115.5579
103.2280
91.5784
85.4757
84.7476
83.6650
79.8616
77.4762
77.1600
76.8343
75.9241
55.5276
27.2082
25.3401
X : parts per Million : 13C


13 NKY 4–72
OH
NH
O
N
O
O
O
O
(CDCl3, 400 MHz)
18
abundance
X : parts per Million : 1H
8.8954
7.3962
7.3756
7.2600
5.7402
5.7254
5.7196
5.5777
5.5709
5.4415
5.3981
5.3076
5.2813
5.0215
5.0135
4.9643
4.3612
4.3498
4.1953
4.1861
4.1758
2.9593
2.9444
2.0438
1.6478
1.5746
1.5403
1.3583
1.2736
1.2565
1.0
1.0
1.02
1.06
0.98
0.9
0.94
0.99
1.01
1
0.95
0.96
3.21
3.24


13 NKY 4-72
(CDCl3, 100 MHz)
18
abundance
X : parts per Million : 13C
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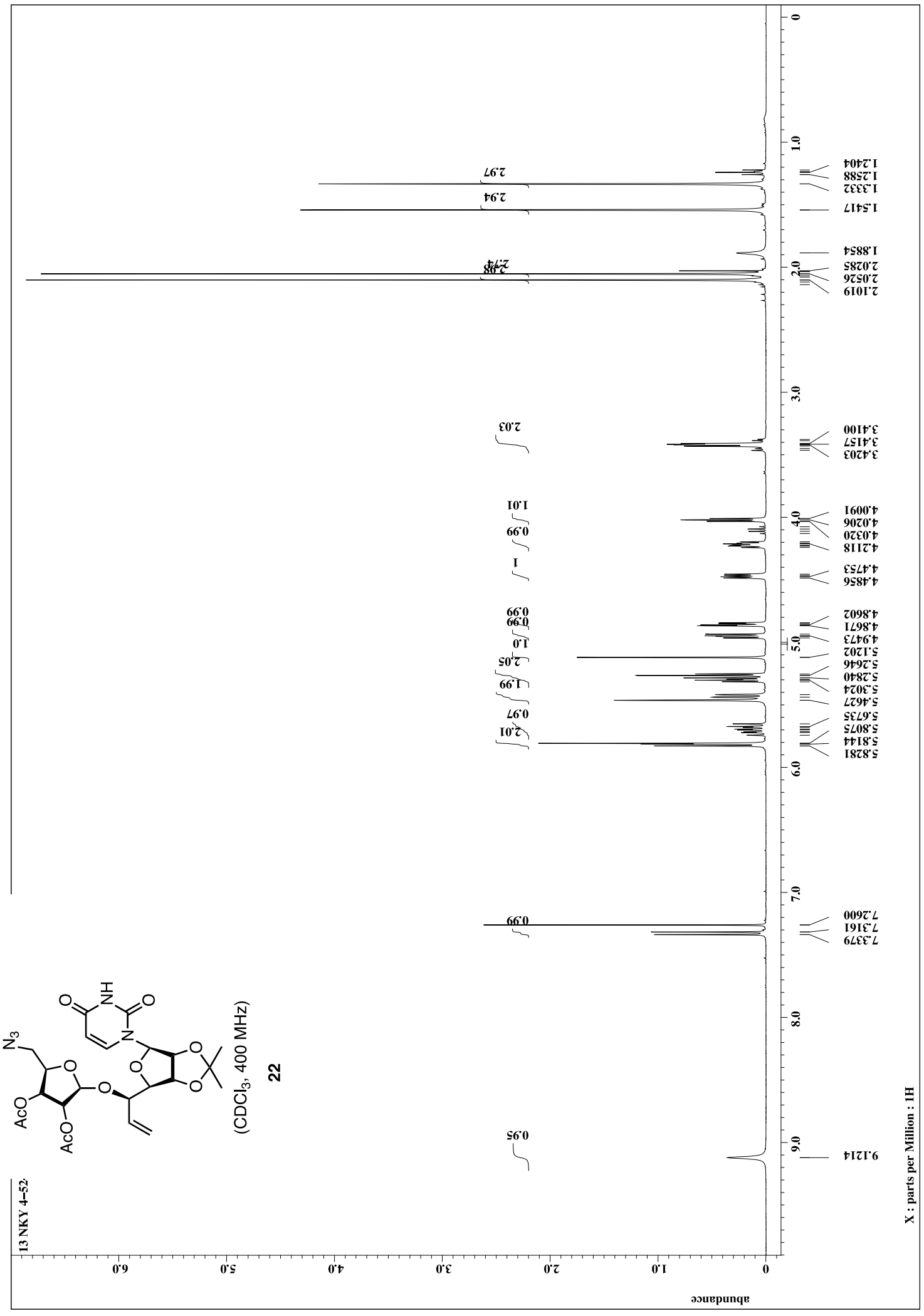
143.1687
136.5307
117.6370
114.6804
102.7585
96.1586
88.8911
83.5119
81.0990
77.4843
77.1600
76.8357
73.2115
27.3936
25.4288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abundance
X : parts per Million : 1H
(CDCl3, 400 MHz)
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AcO
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NH
O
N
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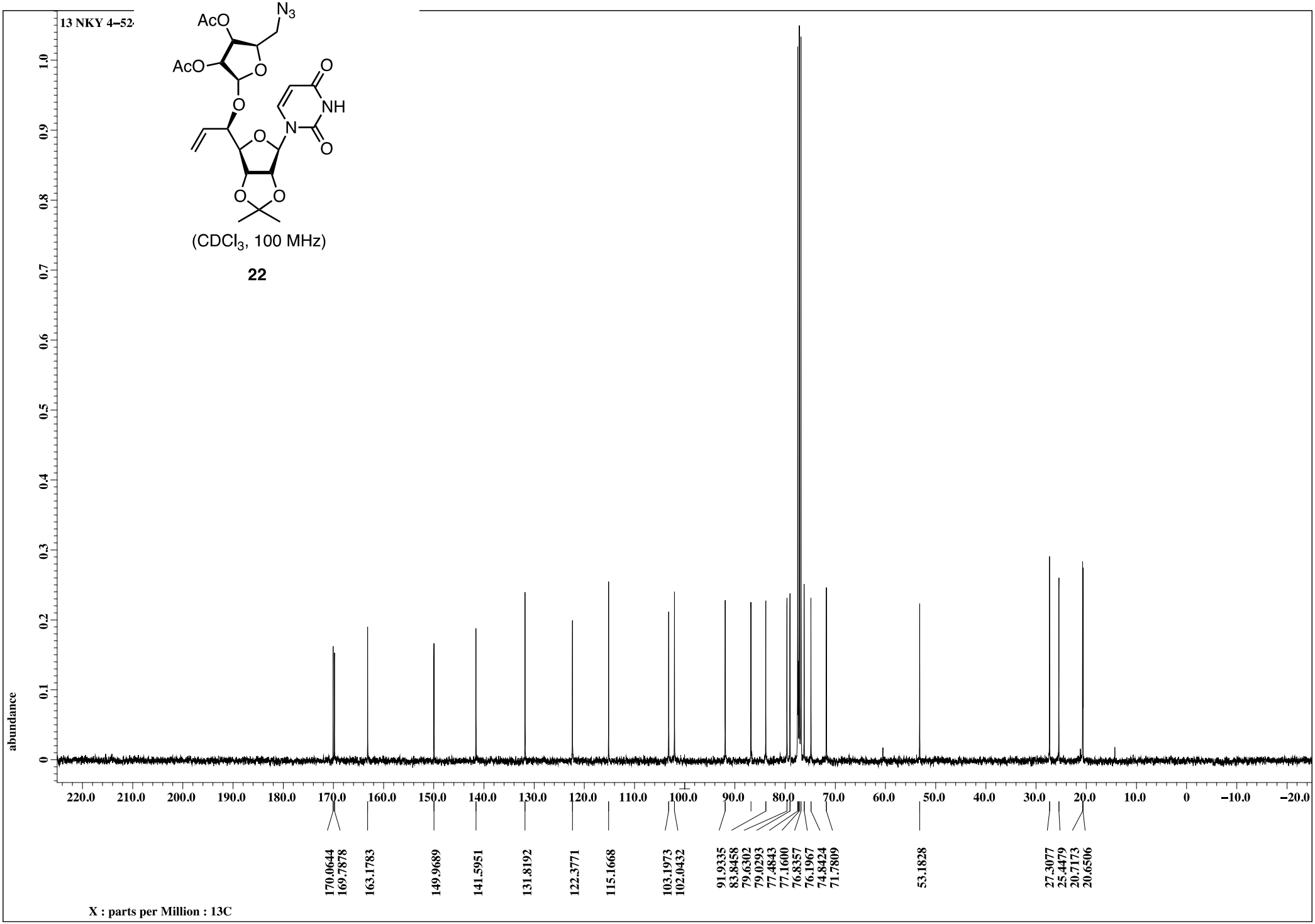
7.3379
7.3161
7.2600
5.8281
5.8144
5.8075
5.6735
5.4627
5.3024
5.2840
5.2646
5.1202
4.9473
4.8671
4.8602
4.4856
4.4753
4.2118
4.0320
4.0206
4.0091
3.4203
3.4157
3.4100
2.1019
2.0526
2.0285
1.8854
1.5417
1.3332
1.2588
1.2404
0.95
2.01
0.97
1.99
2.05
1.0
0.99
0.99
1
0.99
1.01
2.03
2.94
2.97
0.99


13 NKY 4-52
AcO
AcO
N3
O
O
O
NH
N
O
O
O
O
(CDCl3, 100 MHz)
22
abundance
X : parts per Million : 13C
170.0644
169.7878
163.1783
149.9689
141.5951
131.8192
122.3771
115.1668
103.1973
102.0432
91.9335
83.8458
79.6302
79.0293
77.4843
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27.3077
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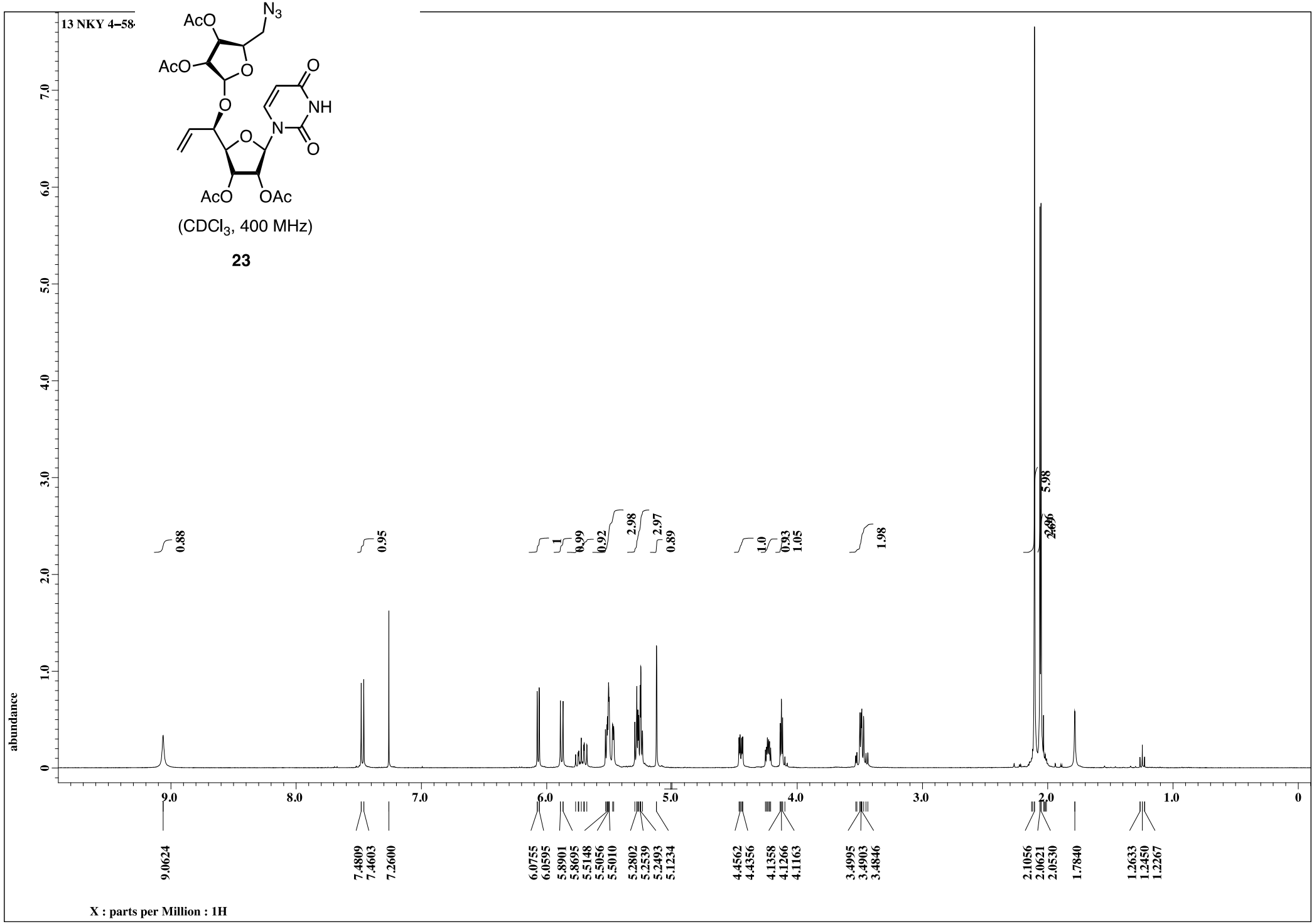
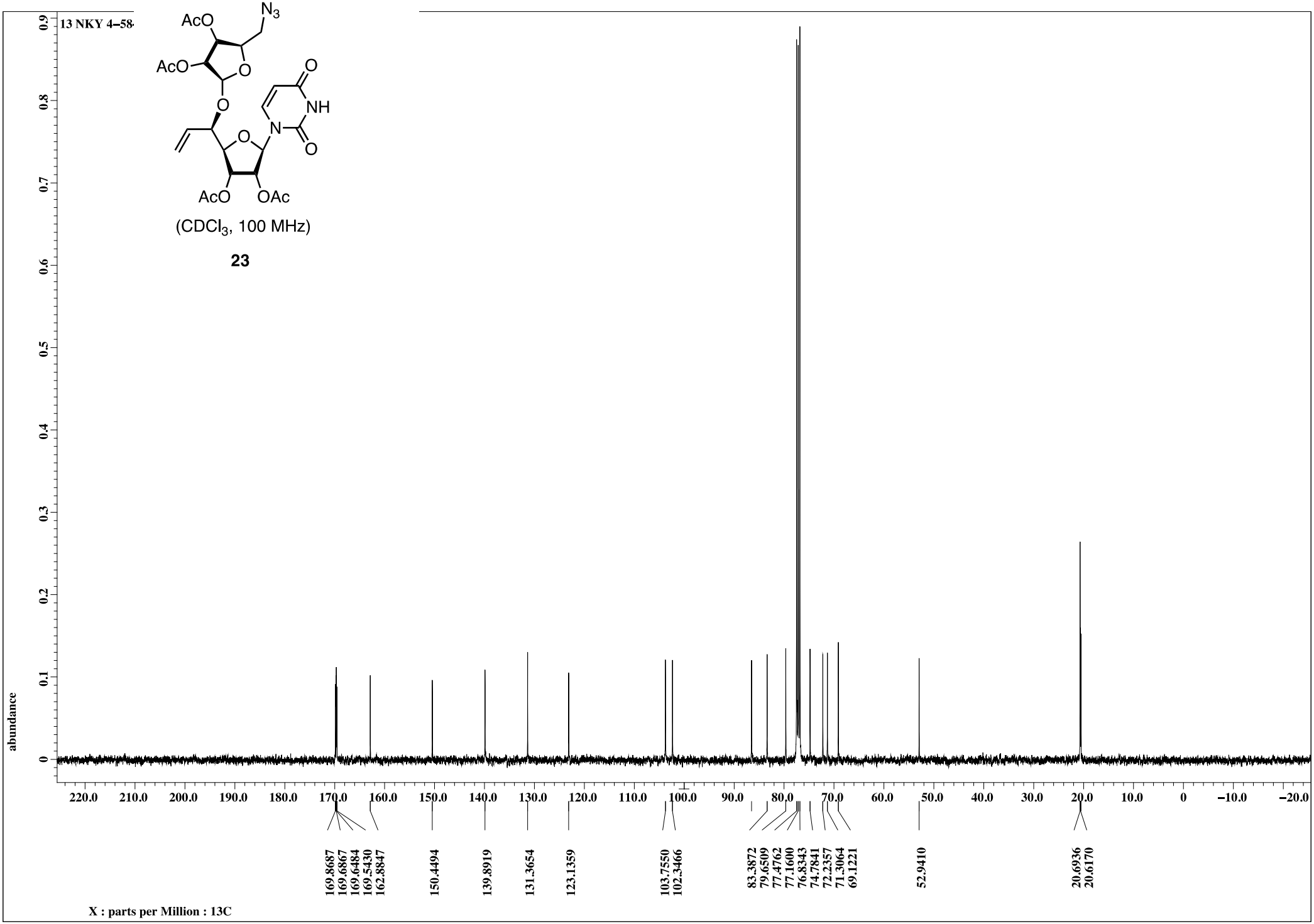
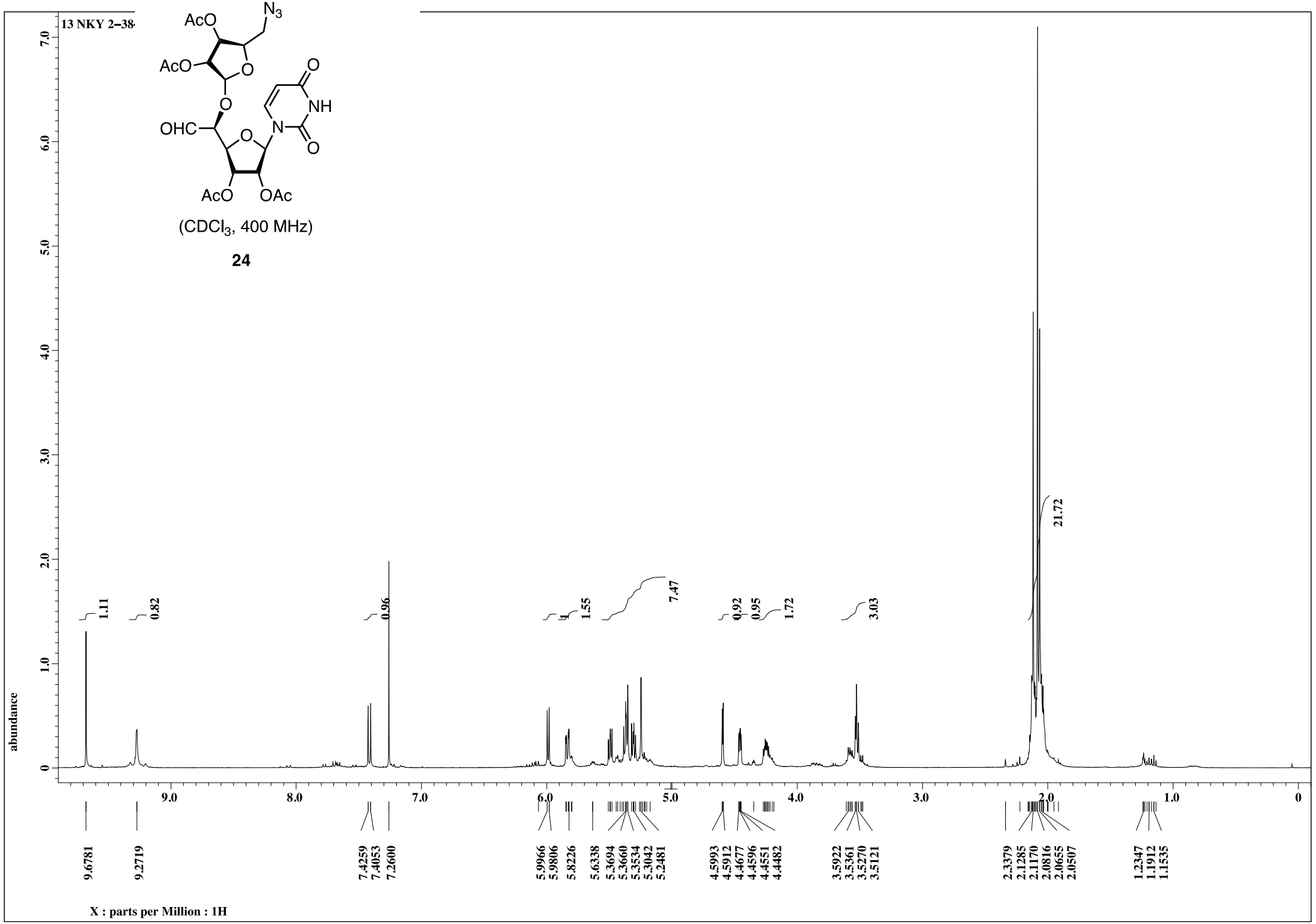
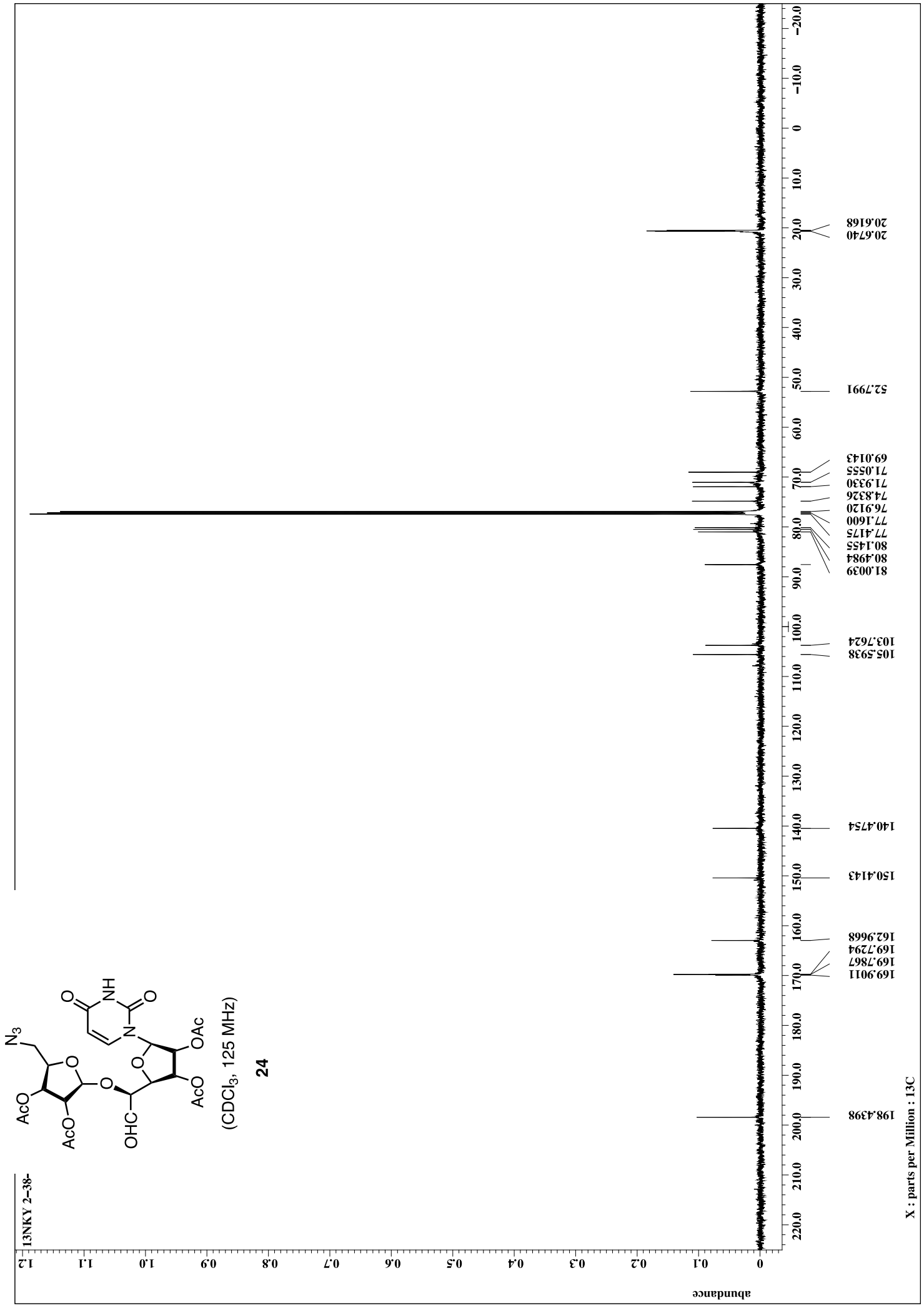
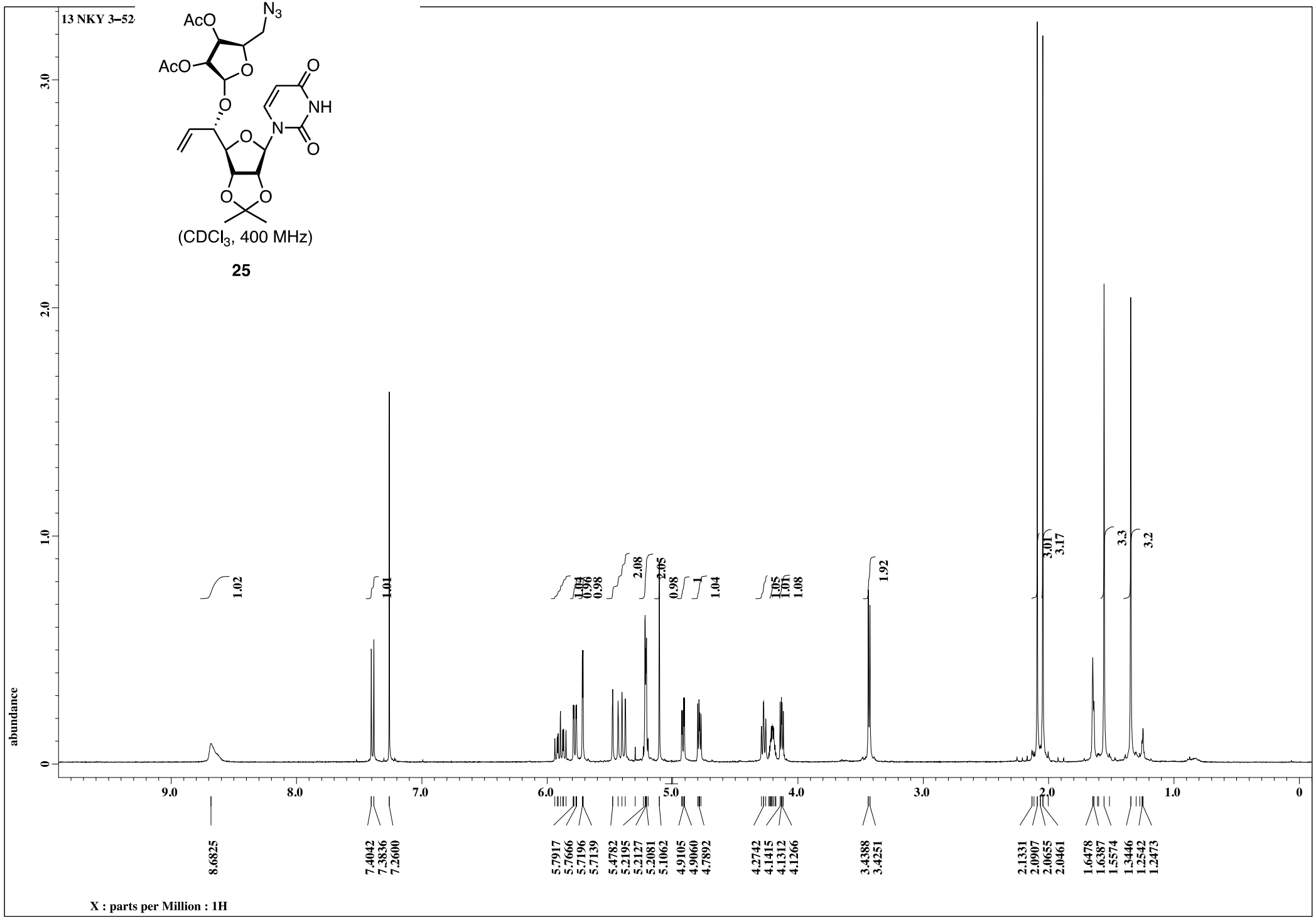
20.7173
20.6506

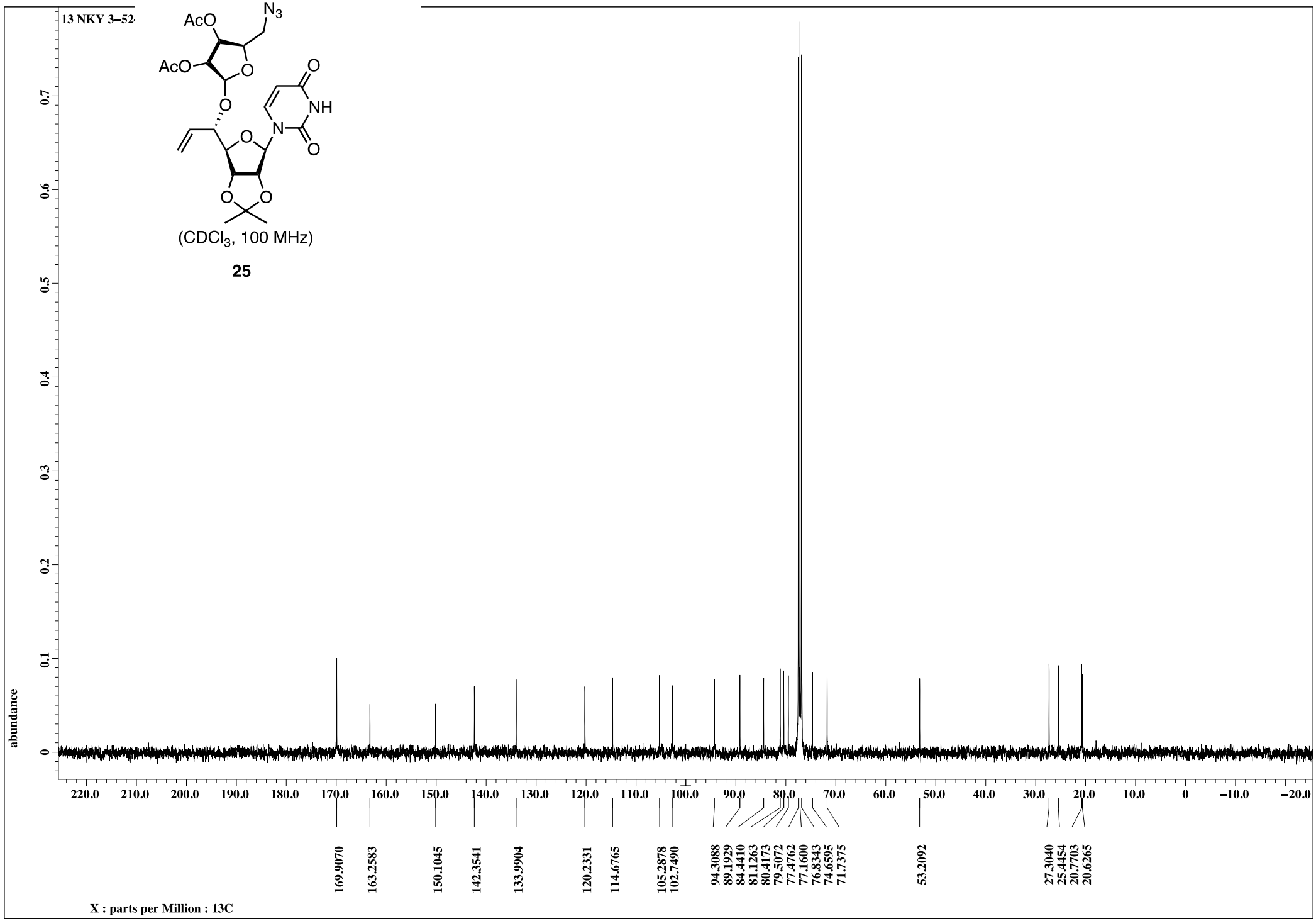

13 NKY 4-58
AcO
AcO
O
O
N3
O
NH
N
O
O
AcO
OAc
(CDCl3, 400 MHz)
23
abundance
X : parts per Million : 1H
9.0624
7.4809
7.4603
7.2600
6.0755
6.0595
5.8901
5.8695
5.5148
5.5056
5.5010
5.2802
5.2539
5.2493
5.1234
4.4562
4.4356
4.1358
4.1266
4.1163
3.4995
3.4903
3.4846
2.1056
2.0621
2.0530
1.7840
1.2633
1.2450
1.2267

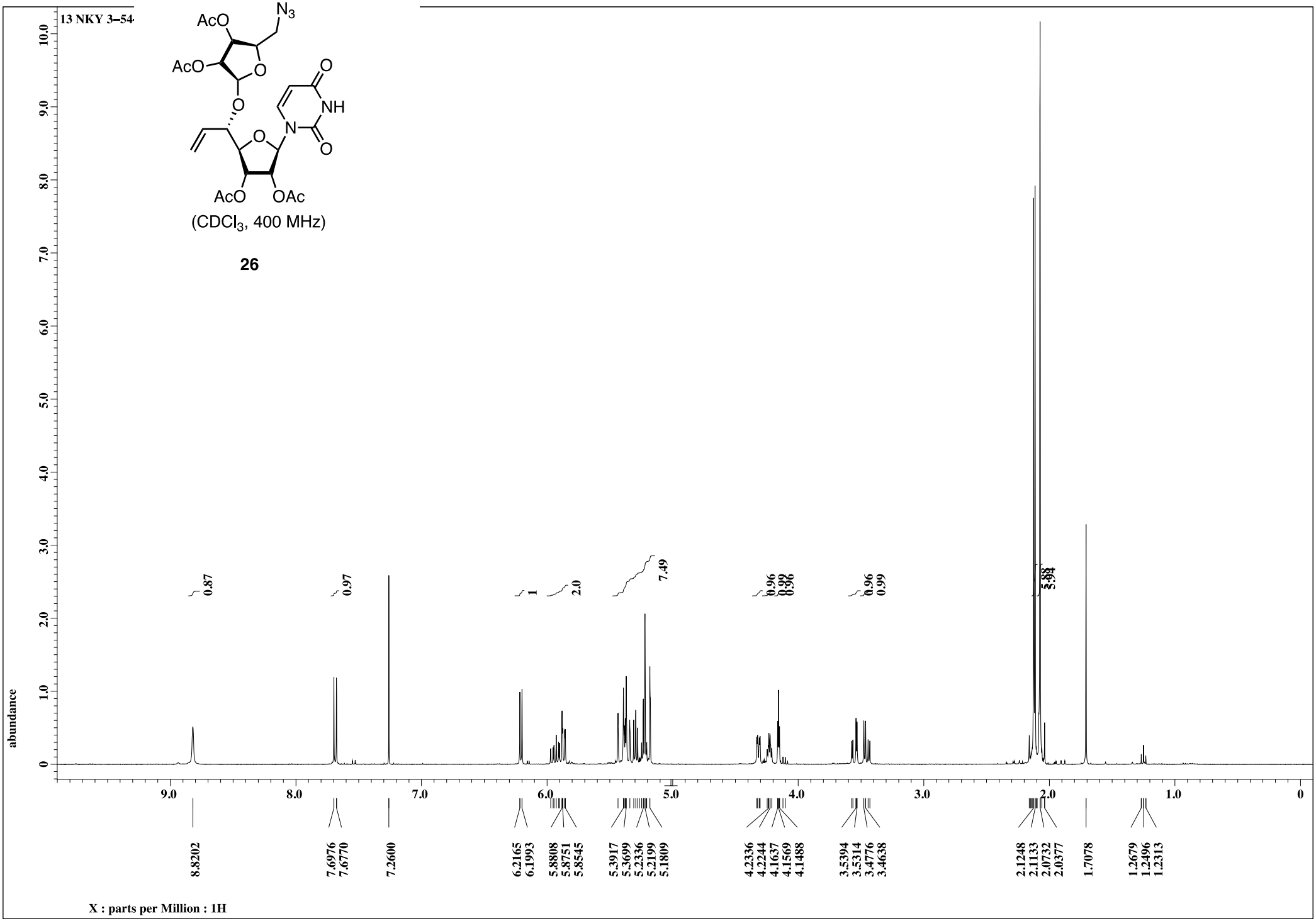

13 NKY 4–58
AcO
AcO
O
O
N3
O
NH
N
O
O
AcO
OAc
(CDCl3, 100 MHz)
23
abundance
0
0.1
0.2
0.3
0.4
0.5
0.6
0.7
0.8
0.9
220.0
210.0
200.0
190.0
180.0
170.0
160.0
150.0
140.0
130.0
120.0
110.0
100.0
90.0
80.0
70.0
60.0
50.0
40.0
30.0
20.0
10.0
0
−10.0
−20.0
169.8687
169.6867
169.6484
169.5430
162.8847
150.4494
139.8919
131.3654
123.1359
103.7550
102.3466
83.3872
79.6509
77.4762
77.1600
76.8343
74.7841
72.2357
71.3064
69.1221
52.9410
20.6936
20.6170
X : parts per Million : 13C

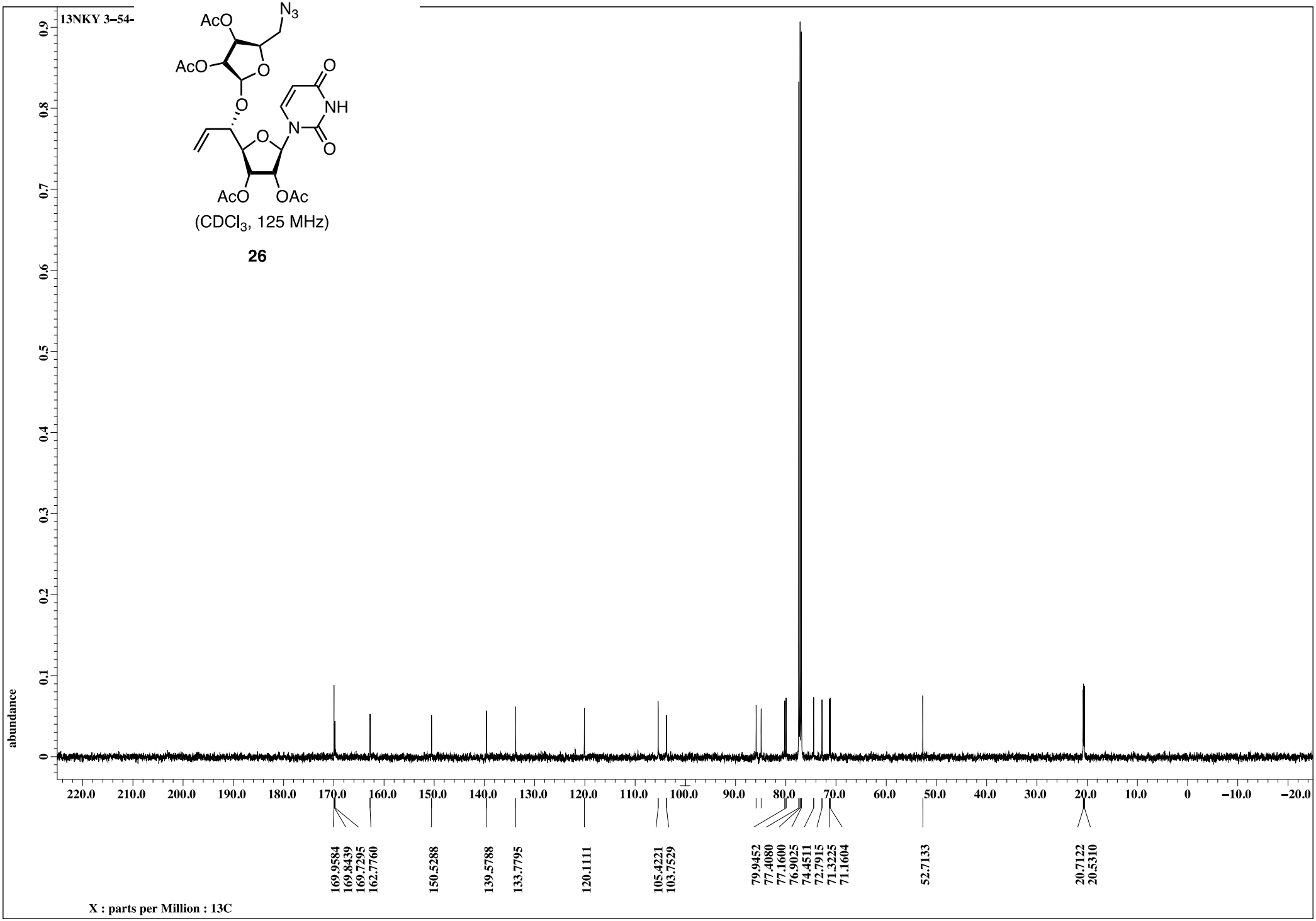

13 NKY 2-38
AcO
AcO
O
OHC
O
N3
O
NH
N
O
AcO
OAc
(CDCl3, 400 MHz)
24
abundance
1.11
0.82
0.96
1.55
7.47
0.92
0.95
1.72
3.03
21.72
9.6781
9.2719
7.4259
7.4053
7.2600
5.9966
5.9806
5.8226
5.6338
5.3694
5.3660
5.3534
5.3042
5.2481
4.5993
4.5912
4.4677
4.4596
4.4551
4.4482
3.5922
3.5361
3.5270
3.5121
2.3379
2.1285
2.1170
2.0816
2.0655
2.0507
1.2347
1.1912
1.1535
X : parts per Million : 1H

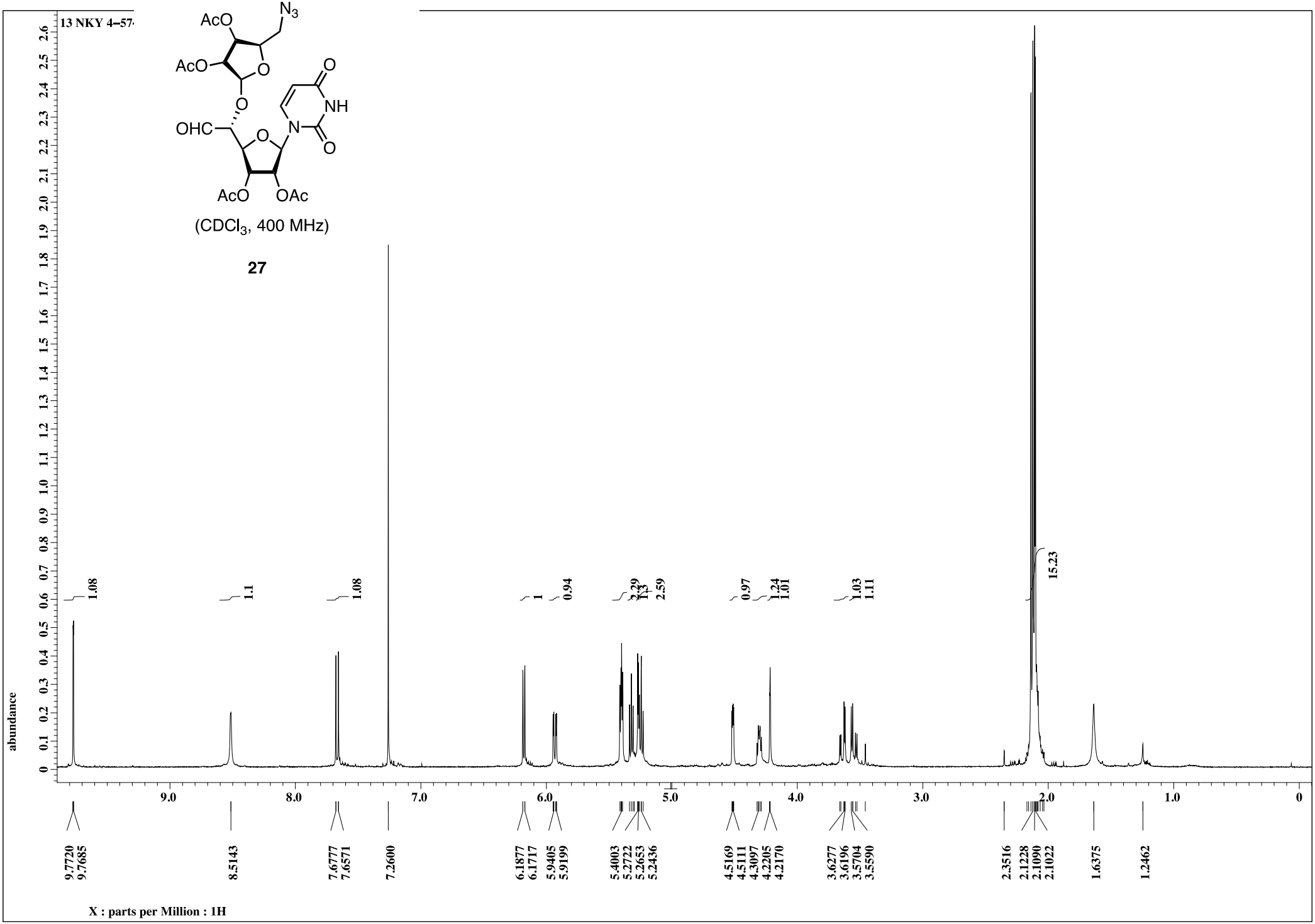

13NKY 2-38-
abundance
X : parts per Million : 13C
198.4398
169.9011
169.7867
169.7294
162.9668
150.4143
140.4754
105.5938
103.7624
81.0039
80.4984
80.1455
77.4175
77.1600
76.9120
74.8326
71.9330
71.0555
69.0143
52.7991
20.6740
20.6168
(CDCl3, 125 MHz)
24

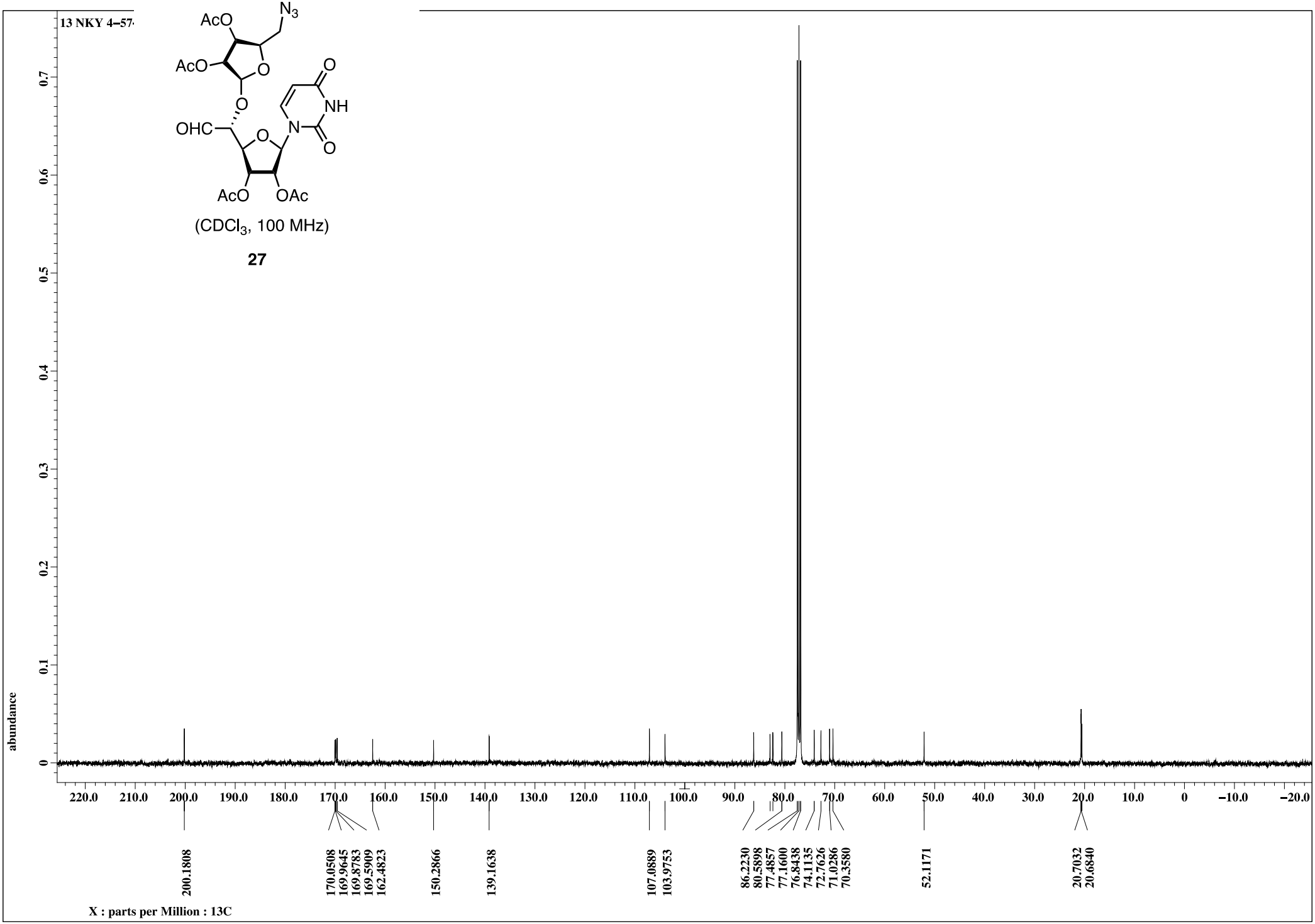

13 NKY 3–52
AcO
AcO
N3
O
NH
N
O
O
O
O
O
O
(CDCl3, 400 MHz)
25
abundance
1.02
1.01
0.96
0.98
2.08
2.05
0.98
1
1.04
1.05
1.01
1.08
1.92
3.01
3.17
3.3
3.2
9.0
8.0
7.0
6.0
5.0
4.0
3.0
2.0
1.0
0
8.6825
7.4042
7.3836
7.2600
5.7917
5.7666
5.7196
5.7139
5.4782
5.2195
5.2127
5.2081
5.1062
4.9105
4.9060
4.7892
4.2742
4.1415
4.1312
4.1266
3.4388
3.4251
2.1331
2.0907
2.0655
2.0461
1.6478
1.6387
1.5574
1.3446
1.2542
1.2473
X : parts per Million : 1H

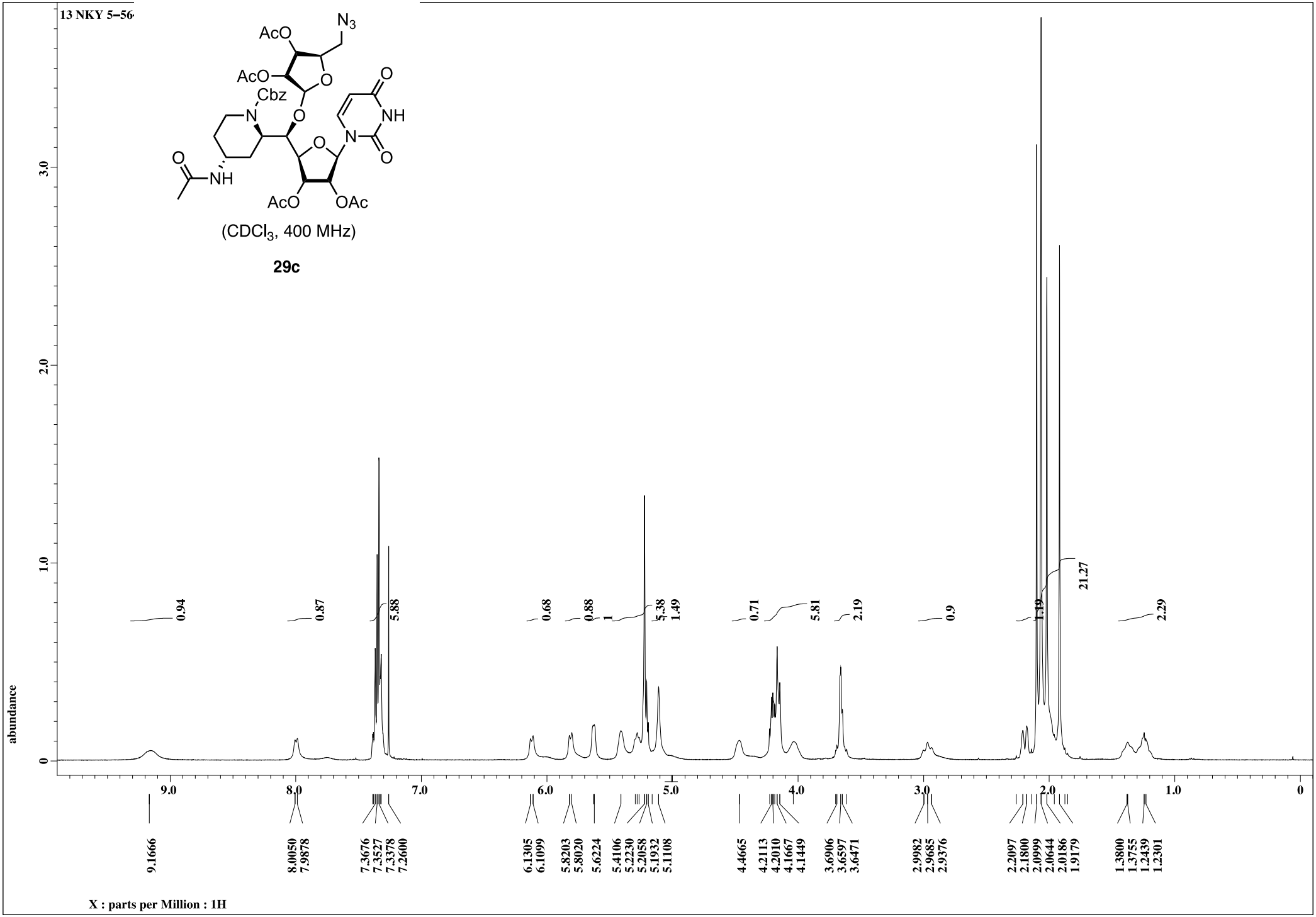

13 NKY 3–52
AcO
AcO
N3
O
O
O
O
NH
N
O
O
O
O
(CDCl3, 100 MHz)
25
abundance
0
0.1
0.2
0.3
0.4
0.5
0.6
0.7
220.0
210.0
200.0
190.0
180.0
170.0
160.0
150.0
140.0
130.0
120.0
110.0
100.0
90.0
80.0
70.0
60.0
50.0
40.0
30.0
20.0
10.0
0
−10.0
−20.0
169.9070
163.2583
150.1045
142.3541
133.9904
120.2331
114.6765
105.2878
102.7490
94.3088
89.1929
84.4410
81.1263
80.4173
79.5072
77.4762
77.1600
76.8343
74.6595
71.7375
53.2092
27.3040
25.4454
20.7703
20.6265
X : parts per Million : 13C

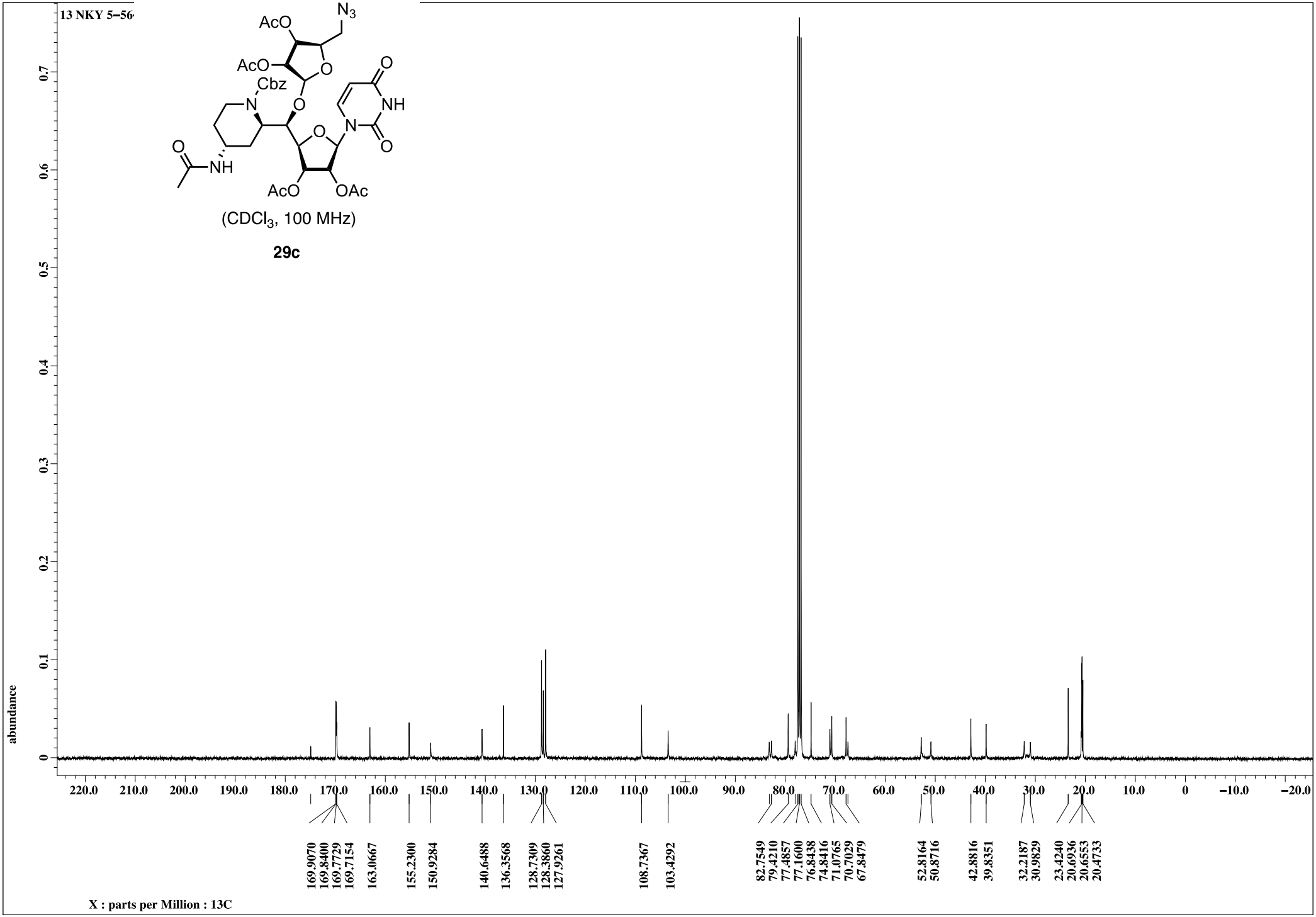

13 NKY 3–54
AcO
AcO
O
O
N3
O
NH
N
O
AcO
OAc
(CDCl3, 400 MHz)
26
abundance
X : parts per Million : 1H
8.8202
7.6976
7.6770
7.2600
6.2165
6.1993
5.8808
5.8751
5.8545
5.3917
5.3699
5.2336
5.2199
5.1809
4.2336
4.2244
4.1637
4.1569
4.1488
3.5394
3.5314
3.4776
3.4638
2.1248
2.1133
2.0732
2.0377
1.7078
1.2679
1.2496
1.2313

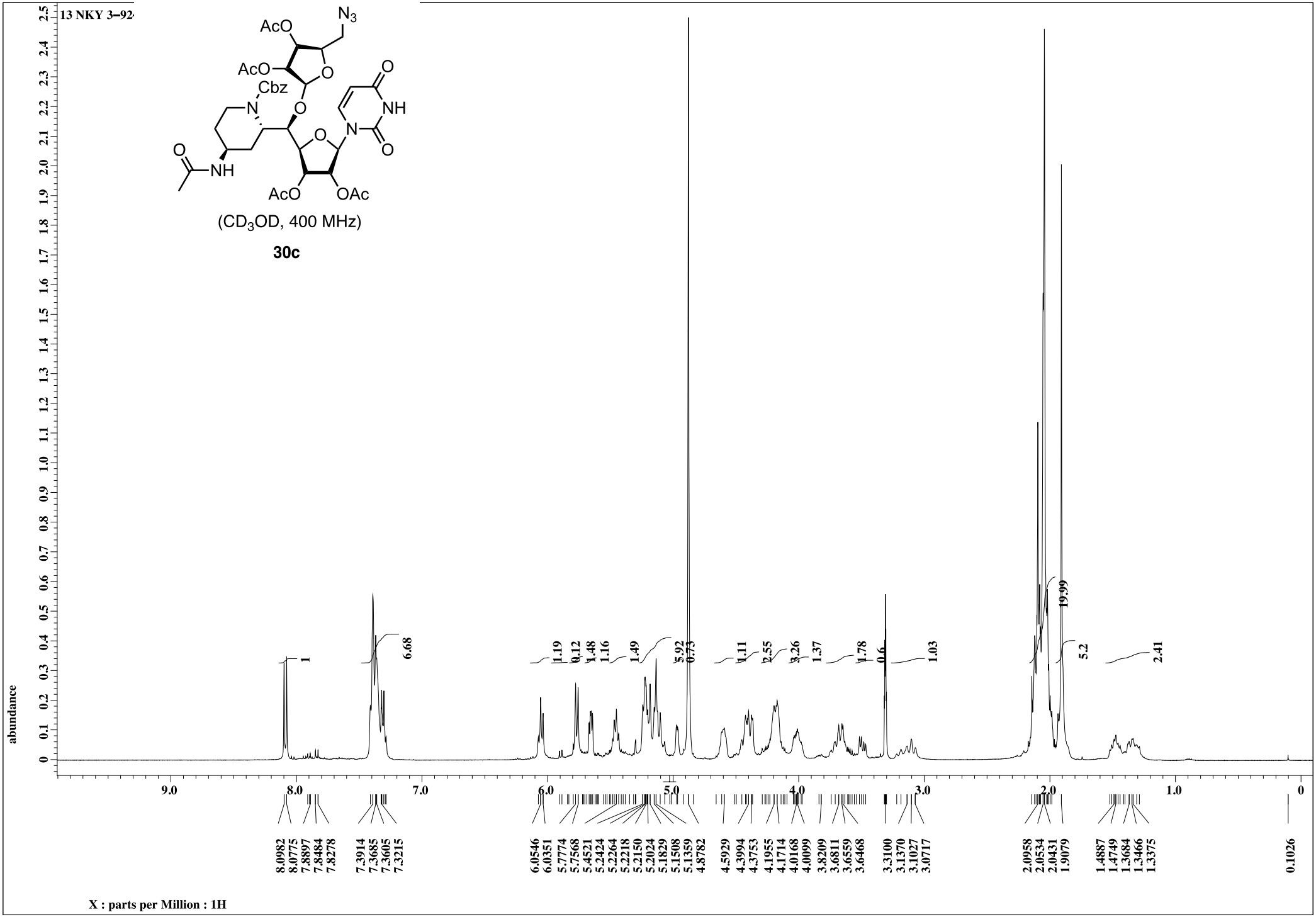

13NKY 3–54-
AcO
AcO
O
O
N3
O
NH
N
O
O
AcO
OAc
(CDCl3, 125 MHz)
26
abundance
0
0.1
0.2
0.3
0.4
0.5
0.6
0.7
0.8
0.9
220.0
210.0
200.0
190.0
180.0
170.0
160.0
150.0
140.0
130.0
120.0
110.0
100.0
90.0
80.0
70.0
60.0
50.0
40.0
30.0
20.0
10.0
0
−10.0
−20.0
169.9584
169.8439
169.7295
162.7760
150.5288
139.5788
133.7795
120.1111
105.4221
103.7529
79.9452
77.4080
77.1600
76.9025
74.4511
72.7915
71.3225
71.1604
52.7133
20.7122
20.5310
X : parts per Million : 13C

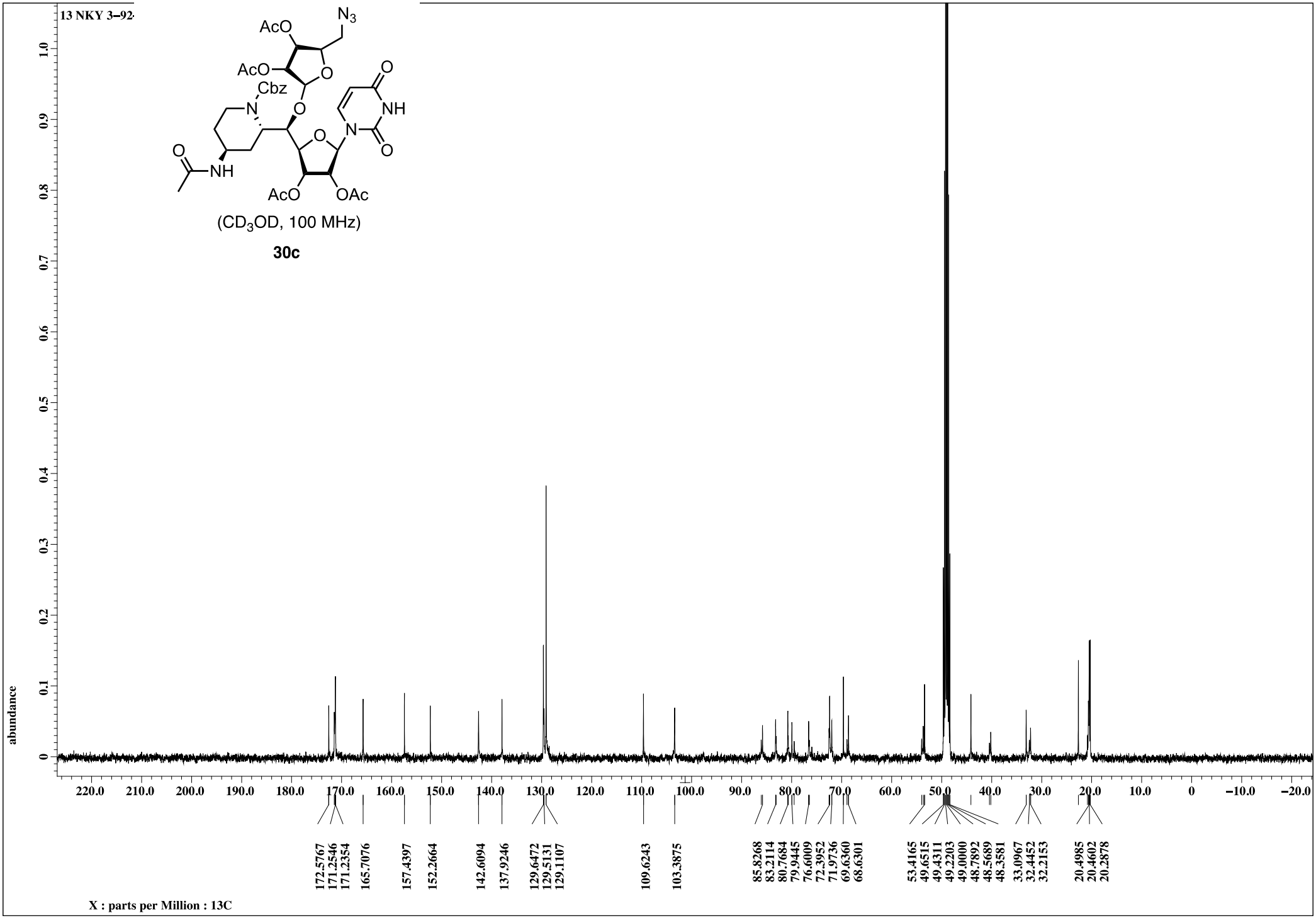

13 NKY 4–57
AcO
AcO
O
O
OHC
O
N3
NH
N
O
O
AcO
OAc
(CDCl3, 400 MHz)
27
abundance
1.08
1.1
1.08
1
0.94
2.29
1.3
2.59
0.97
1.24
1.01
1.03
1.11
15.23
9.7720
9.7685
8.5143
7.6777
7.6571
7.2600
6.1877
6.1717
5.9405
5.9199
5.4003
5.2722
5.2653
5.2436
4.5169
4.5111
4.3097
4.2205
4.2170
3.6277
3.6196
3.5704
3.5590
2.3516
2.1228
2.1090
2.1022
1.6375
1.2462
X : parts per Million : 1H

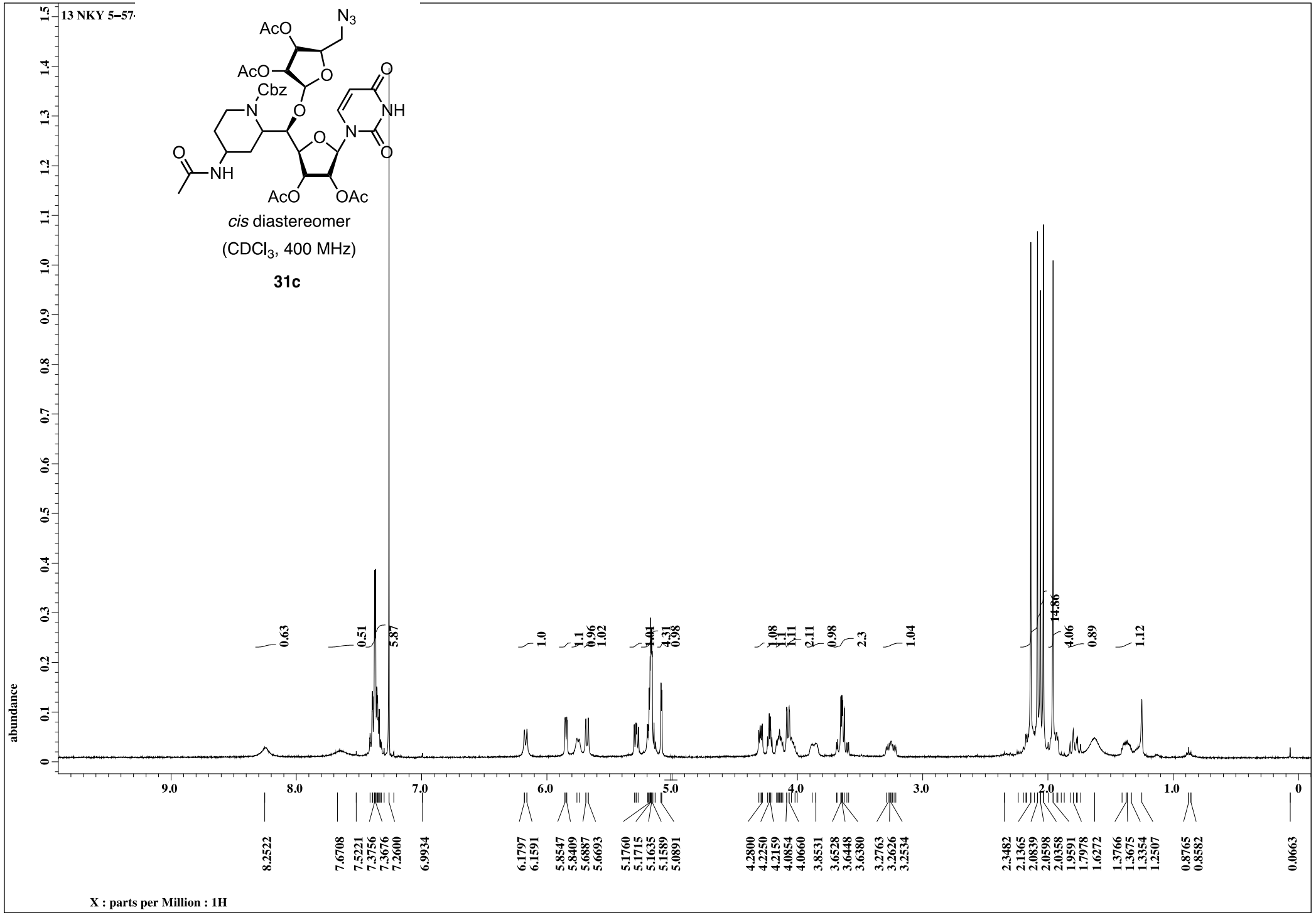

13 NKY 4–57
AcO
AcO
O
O
OHC
O
N3
O
NH
N
O
AcO
OAc
(CDCl3, 100 MHz)
27
abundance
0
0.1
0.2
0.3
0.4
0.5
0.6
0.7
220.0
210.0
200.0
190.0
180.0
170.0
160.0
150.0
140.0
130.0
120.0
110.0
100.0
90.0
80.0
70.0
60.0
50.0
40.0
30.0
20.0
10.0
0
−10.0
−20.0
200.1808
170.0508
169.9645
169.8783
169.5909
162.4823
150.2866
139.1638
107.0889
103.9753
86.2230
80.5898
77.4857
77.1600
76.8438
74.1135
72.7626
71.0286
70.3580
52.1171
20.7032
20.6840
X : parts per Million : 13C

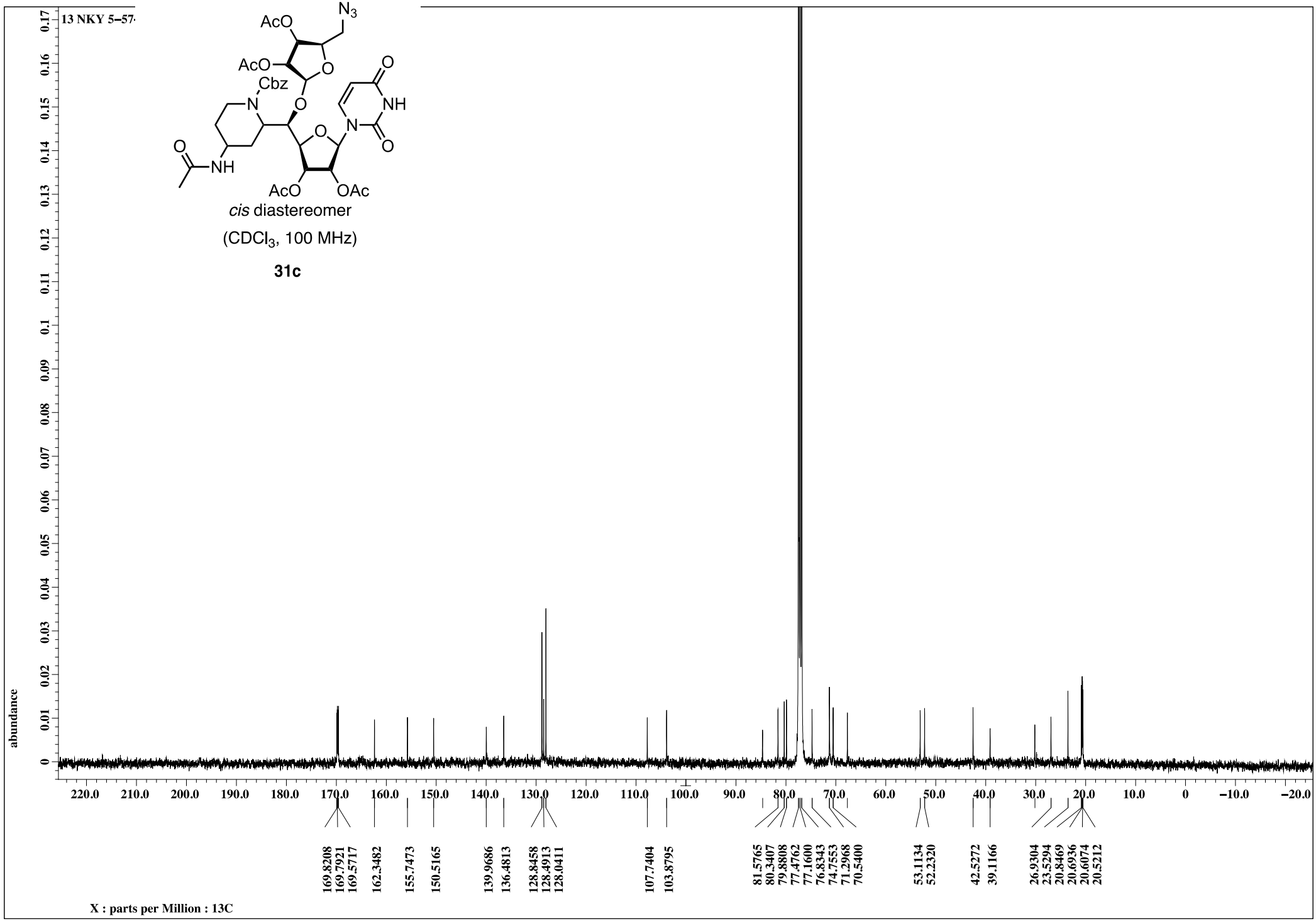

13 NKY 5–56
AcO
AcO
Cbz
N
O
N3
O
NH
N
O
O
NH
AcO
OAc
(CDCl3, 400 MHz)
29c
abundance
0
1.0
2.0
3.0
9.0
8.0
7.0
6.0
5.0
4.0
3.0
2.0
1.0
0
0.94
0.87
5.88
0.68
0.88
1
5.38
1.49
0.71
5.81
2.19
0.9
1.19
21.27
2.29
9.1666
8.0050
7.9878
7.3676
7.3527
7.3378
7.2600
6.1305
6.1099
5.8203
5.8020
5.6224
5.4106
5.2230
5.2058
5.1932
5.1108
4.4665
4.2113
4.2010
4.1667
4.1449
3.6906
3.6597
3.6471
2.9982
2.9685
2.9376
2.2097
2.1800
2.0999
2.0644
2.0186
1.9179
1.3800
1.3755
1.2439
1.2301
X : parts per Million : 1H


13 NKY 5–56
AcO
N3
AcO
O
Cbz
N
O
NH
O
N
O
O
NH
AcO
OAc
(CDCl3, 100 MHz)
29c
abundance
0
0.1
0.2
0.3
0.4
0.5
0.6
0.7
220.0
210.0
200.0
190.0
180.0
170.0
160.0
150.0
140.0
130.0
120.0
110.0
100.0
90.0
80.0
70.0
60.0
50.0
40.0
30.0
20.0
10.0
0
−10.0
−20.0
169.9070
169.8400
169.7729
169.7154
163.0667
155.2300
150.9284
140.6488
136.3568
128.7309
128.3860
127.9261
108.7367
103.4292
82.7549
79.4210
77.4857
77.1600
76.8438
74.8416
71.0765
70.7029
67.8479
52.8164
50.8716
42.8816
39.8351
32.2187
30.9829
23.4240
20.6936
20.6553
20.4733
X : parts per Million : 13C

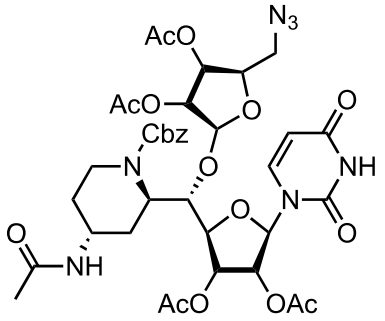

13 NKY 3-92
AcO
AcO
Cbz
N3
O
NH
O
O
O
NH
AcO
OAc
(CD3OD, 400 MHz)
30c
abundance
X : parts per Million : 1H


13 NKY 3–92
AcO
AcO
Cbz
N
O
N3
O
NH
N
O
O
NH
AcO
OAc
(CD3OD, 100 MHz)
30c
abundance
X : parts per Million : 13C
172.5767
171.2546
171.2354
165.7076
157.4397
152.2664
142.6094
137.9246
129.6472
129.5131
129.1107
109.6243
103.3875
85.8268
83.2114
80.7684
79.9445
76.6009
72.3952
71.9736
69.6360
68.6301
53.4165
49.6515
49.4311
49.2203
49.0000
48.7892
48.5689
48.3581
33.0967
32.4452
32.2153
20.4985
20.4602
20.2878


13 NKY 5–57
AcO
AcO
Cbz
N
O
O
N3
O
NH
N
O
O
O
NH
AcO
OAc
cis diastereomer
(CDCl3, 400 MHz)
31c
abundance
X : parts per Million : 1H


13 NKY 5–57
AcO
AcO
Cbz
N
O
O
O
N3
O
NH
N
O
O
NH
AcO
OAc
cis diastereomer
(CDCl3, 100 MHz)
31c
abundance
0 0.01 0.02 0.03 0.04 0.05 0.06 0.07 0.08 0.09 0.1 0.11 0.12 0.13 0.14 0.15 0.16 0.17
220.0 210.0 200.0 190.0 180.0 170.0 160.0 150.0 140.0 130.0 120.0 110.0 100.0 90.0 80.0 70.0 60.0 50.0 40.0 30.0 20.0 10.0 0 −10.0 −20.0
169.8208
169.7921
169.5717
162.3482
155.7473
150.5165
139.9686
136.4813
128.8458
128.4913
128.0411
107.7404
103.8795
81.5765
80.3407
79.8808
77.4762
77.1600
76.8343
74.7553
71.2968
70.5400
53.1134
52.2320
42.5272
39.1166
26.9304
23.5294
20.8469
20.6936
20.6074
20.5212
X : parts per Million : 13C

13NKY 3–74-

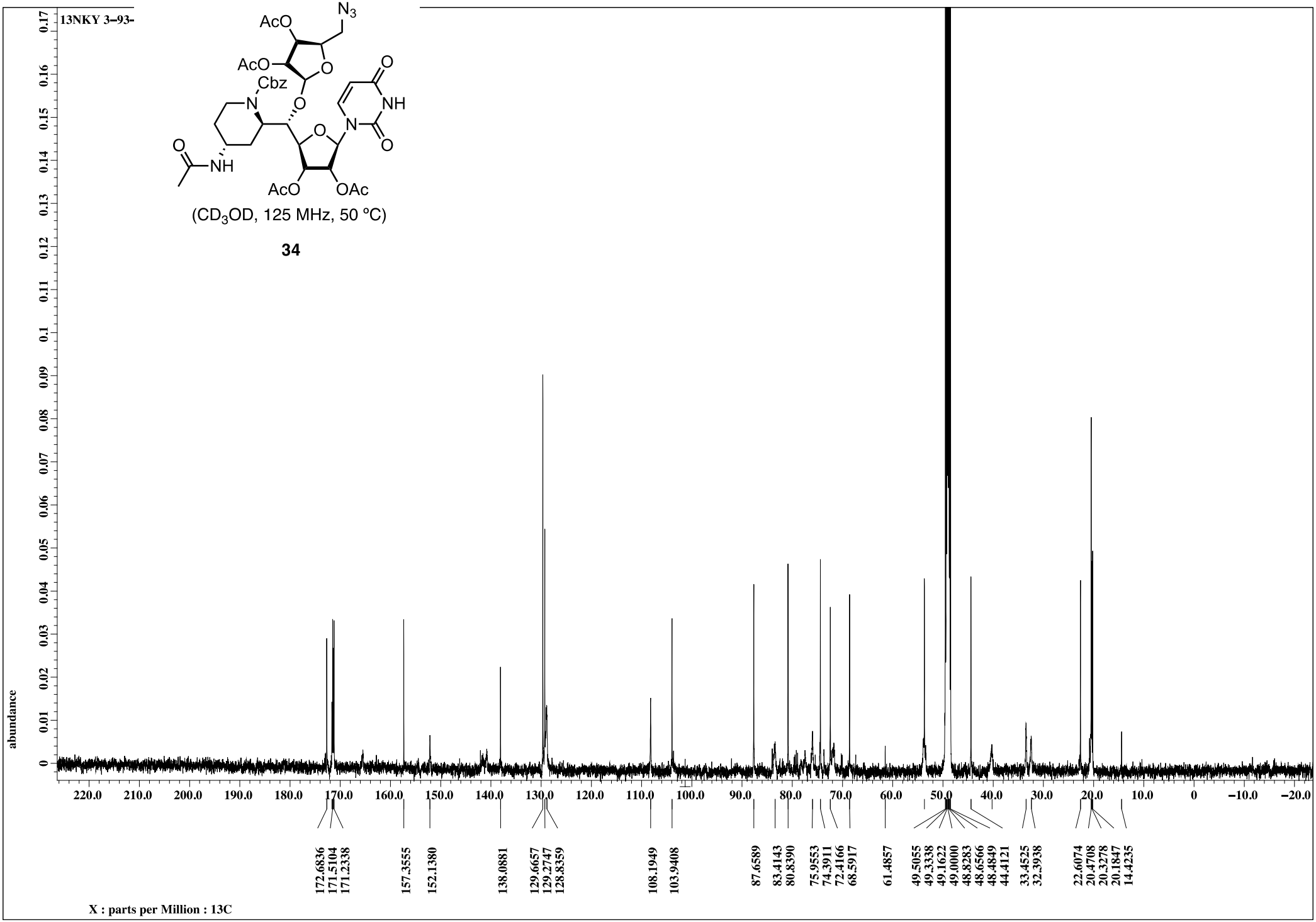


(CD_3OD, 500 MHz, 50 °C)

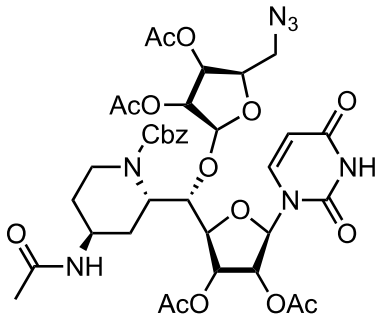
34

abundance

X : parts per Million : 1H


13NKY 3–93-
AcO
AcO
Cbz
N
O
O
N3
O
NH
N
O
O
NH
AcO
OAc
(CD3OD, 125 MHz, 50 °C)
34
abundance
0
0.01
0.02
0.03
0.04
0.05
0.06
0.07
0.08
0.09
0.1
0.11
0.12
0.13
0.14
0.15
0.16
0.17
220.0
210.0
200.0
190.0
180.0
170.0
160.0
150.0
140.0
130.0
120.0
110.0
100.0
90.0
80.0
70.0
60.0
50.0
40.0
30.0
20.0
10.0
0
−10.0
−20.0
172.6836
171.5104
171.2338
157.3555
152.1380
138.0881
129.6657
129.2747
128.8359
108.1949
103.9408
87.6589
83.4143
80.8390
75.9553
74.3911
72.4166
68.5917
61.4857
49.5055
49.3338
49.1622
49.0000
48.8283
48.6566
48.4849
44.4121
33.4525
32.3938
22.6074
20.4708
20.3278
20.1847
14.4235
X : parts per Million : 13C

13NKY 3–74-



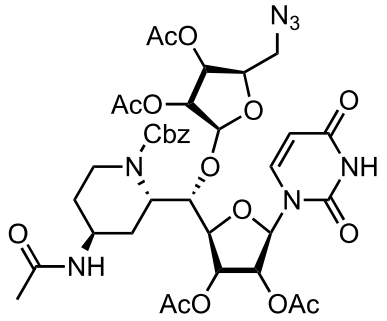
(CD_3OD, 500 MHz, 50 °C)

35

abundance

X : parts per Million : 1H

13 NKY 3–93



(CD_3OD, 100 MHz, 50 °C)

35

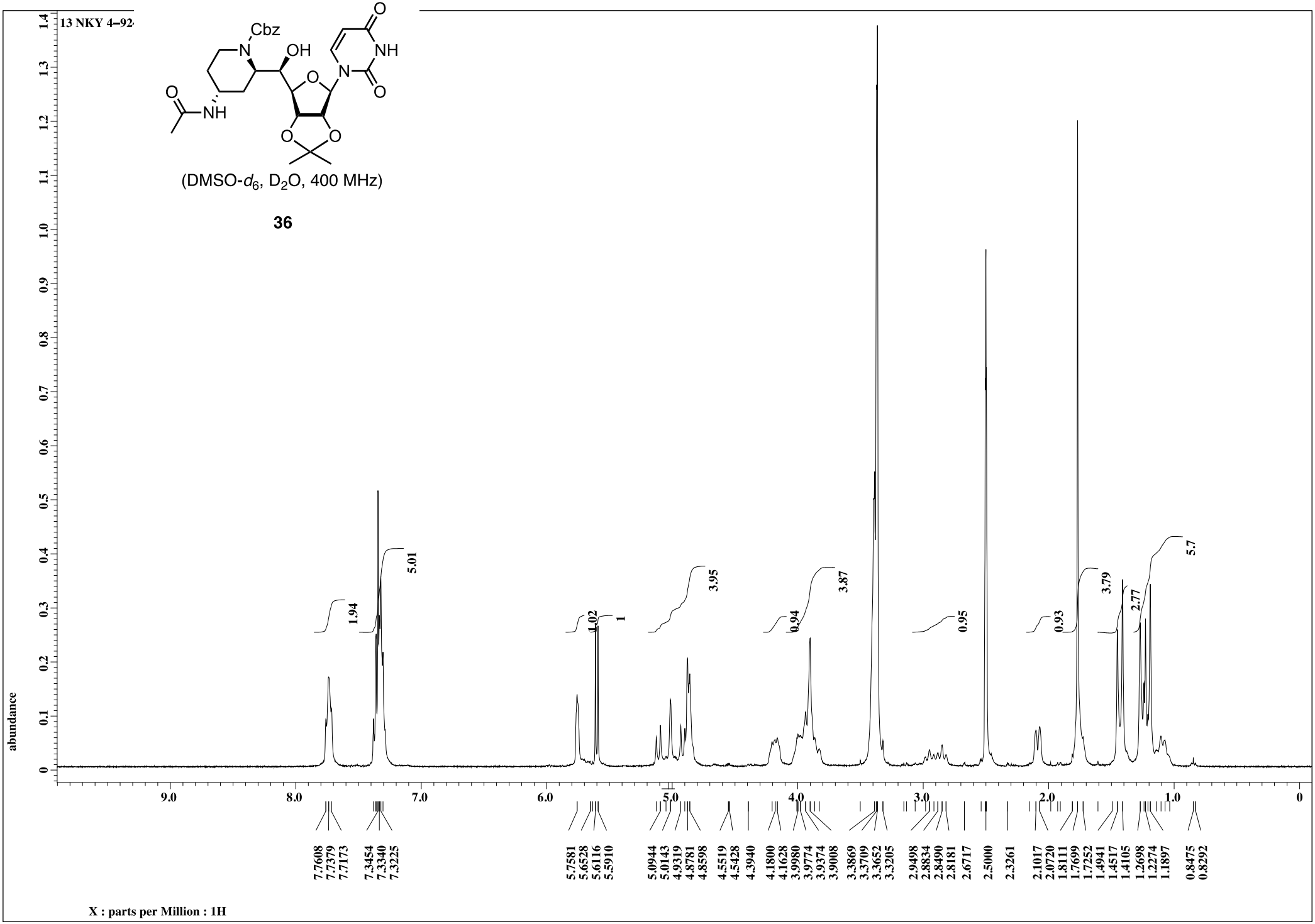
abundance

0.4
0.3
0.2
0.1
0

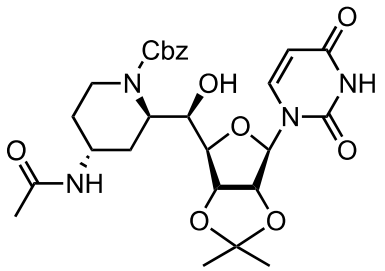
220.0 210.0 200.0 190.0 180.0 170.0 160.0 150.0 140.0 130.0 120.0 110.0 100.0 90.0 80.0 70.0 60.0 50.0 40.0 30.0 20.0 10.0 0 −10.0 −20.0

171.4749
171.2258
165.6980
157.0086
152.0077
129.4652
129.1874
128.9287
108.9537
103.7037
82.8665
81.1228
79.3792
76.2560
74.3975
72.1652
71.9449
68.8313
49.6419
49.4311
49.2203
49.0000
48.7892
48.5689
48.3581
32.7805
32.5314
31.4967
20.4602
20.3261
20.2015

X : parts per Million : 13C


13 NKY 4–92
Cbz
N
OH
O
NH
O
N
NH
O
O
O
O
O
(DMSO-d_6, D_2O, 400 MHz)
36
abundance
1.94
5.01
1.02
1
3.95
0.94
3.87
0.95
0.93
3.79
2.77
5.7
9.0
8.0
7.0
6.0
5.0
4.0
3.0
2.0
1.0
0
7.7608
7.7379
7.7173
7.3454
7.3340
7.3225
5.7581
5.6528
5.6116
5.5910
5.0944
5.0143
4.9319
4.8781
4.8598
4.5519
4.5428
4.3940
4.1800
4.1628
3.9980
3.9774
3.9374
3.9008
3.3869
3.3709
3.3652
3.3205
2.9498
2.8834
2.8490
2.8181
2.6717
2.5000
2.3261
2.1017
2.0720
1.8111
1.7699
1.7252
1.4941
1.4517
1.4105
1.2698
1.2274
1.1897
0.8475
0.8292
X : parts per Million : 1H

13 NKY 4–92



(DMSO-d_6, D_2O, 100 MHz)

36

abundance

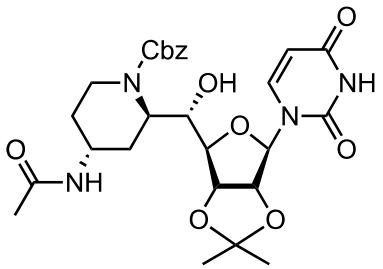
0 0.1 0.2 0.3 0.4 0.5 0.6 0.7 0.8 0.9

220.0 210.0 200.0 190.0 180.0 170.0 160.0 150.0 140.0 130.0 120.0 110.0 100.0 90.0 80.0 70.0 60.0 50.0 40.0 30.0 20.0 10.0 0 −10.0 −20.0

168.4423
168.3560
163.2018
154.6658
154.5029
150.3930
142.4892
137.0188
128.4732
127.6014
127.4194
112.9052
101.8878
91.7231
91.6177
87.4311
87.3162
83.1104
81.0219
79.2304
68.5100
66.4407
66.3640
53.1528
52.9612
39.9415
39.7308
39.5200
39.2997
31.7695
27.0943
25.1974
25.1304
22.8215
22.7736

X : parts per Million : 13C

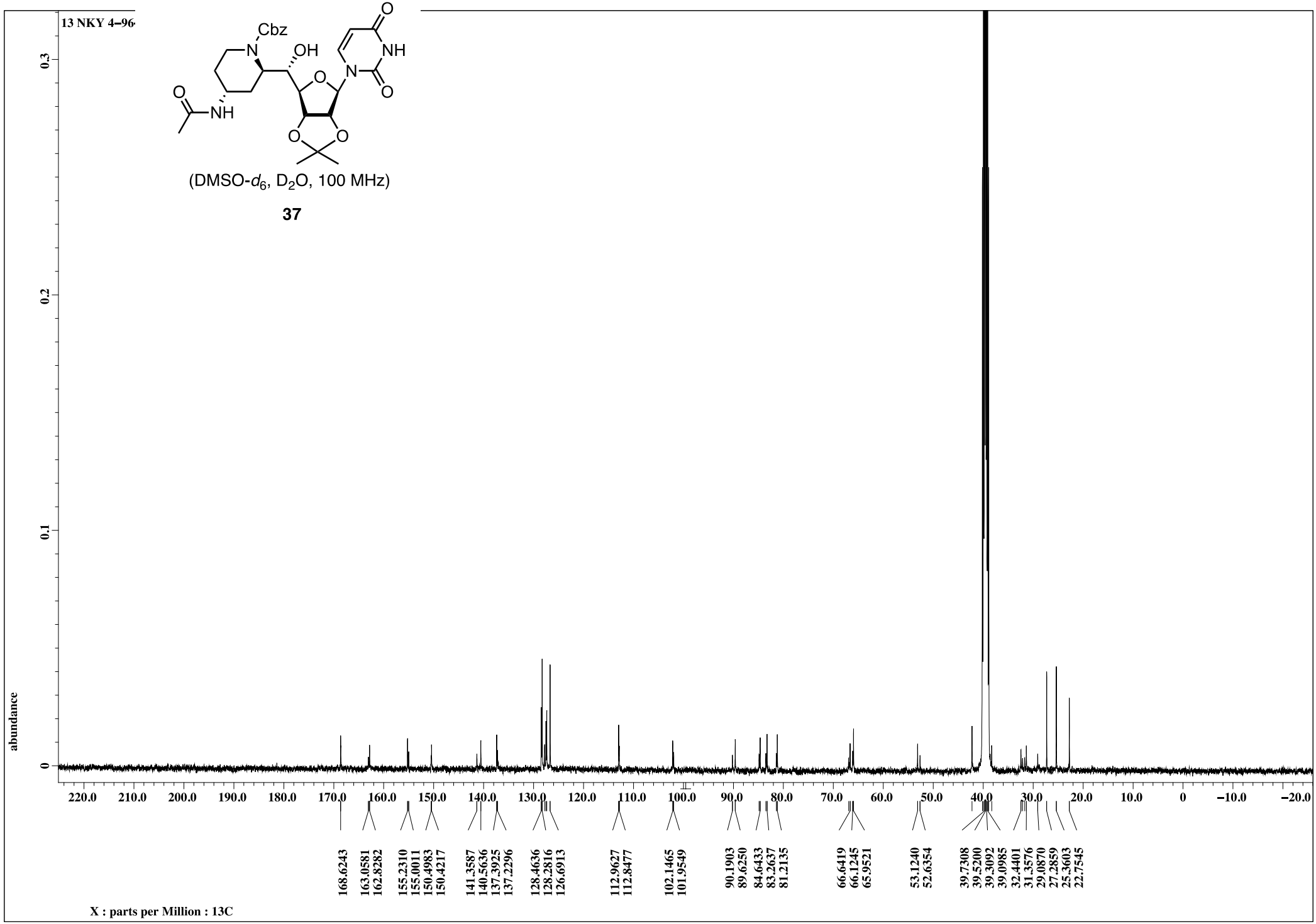
13 NKY 4–96

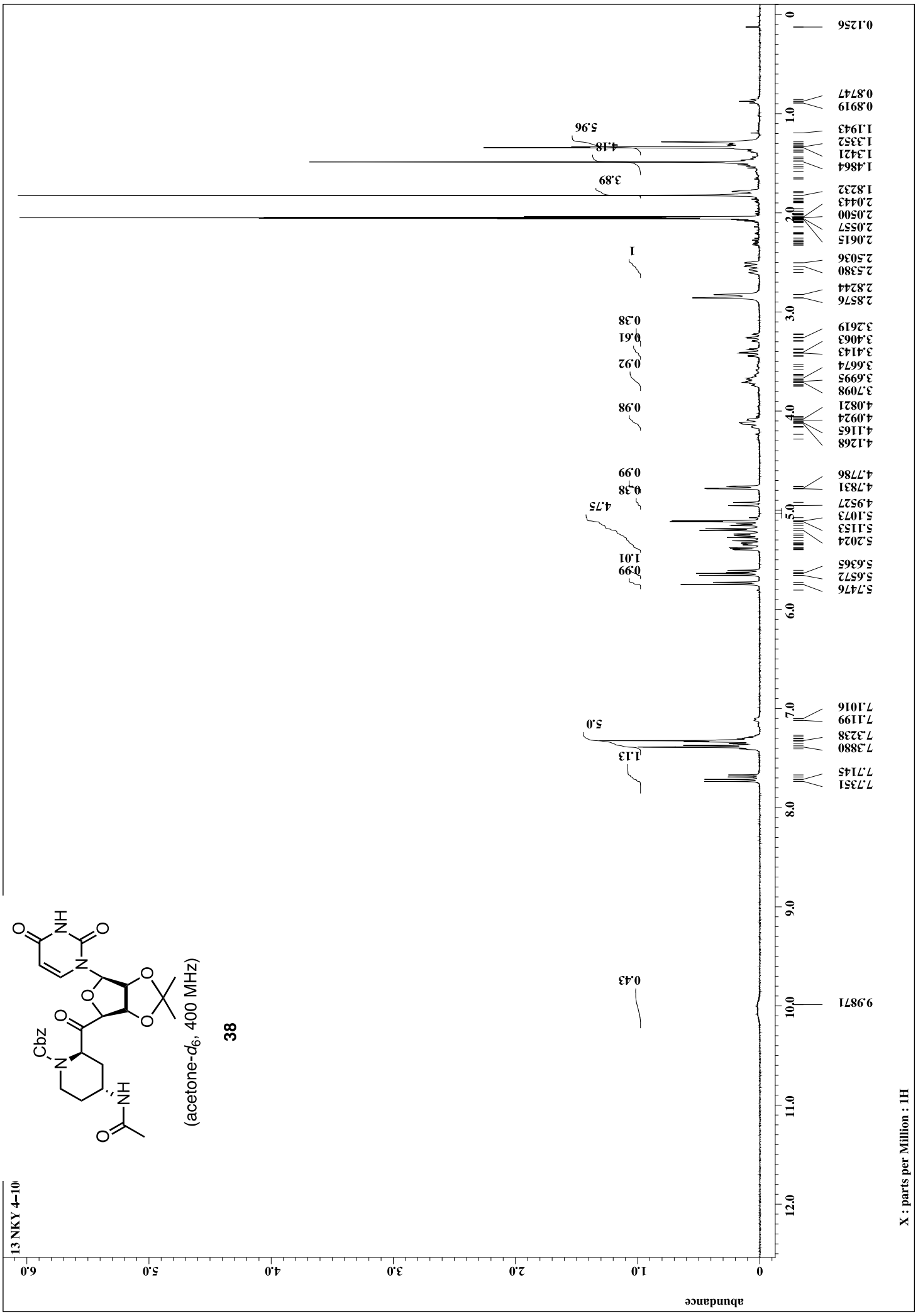


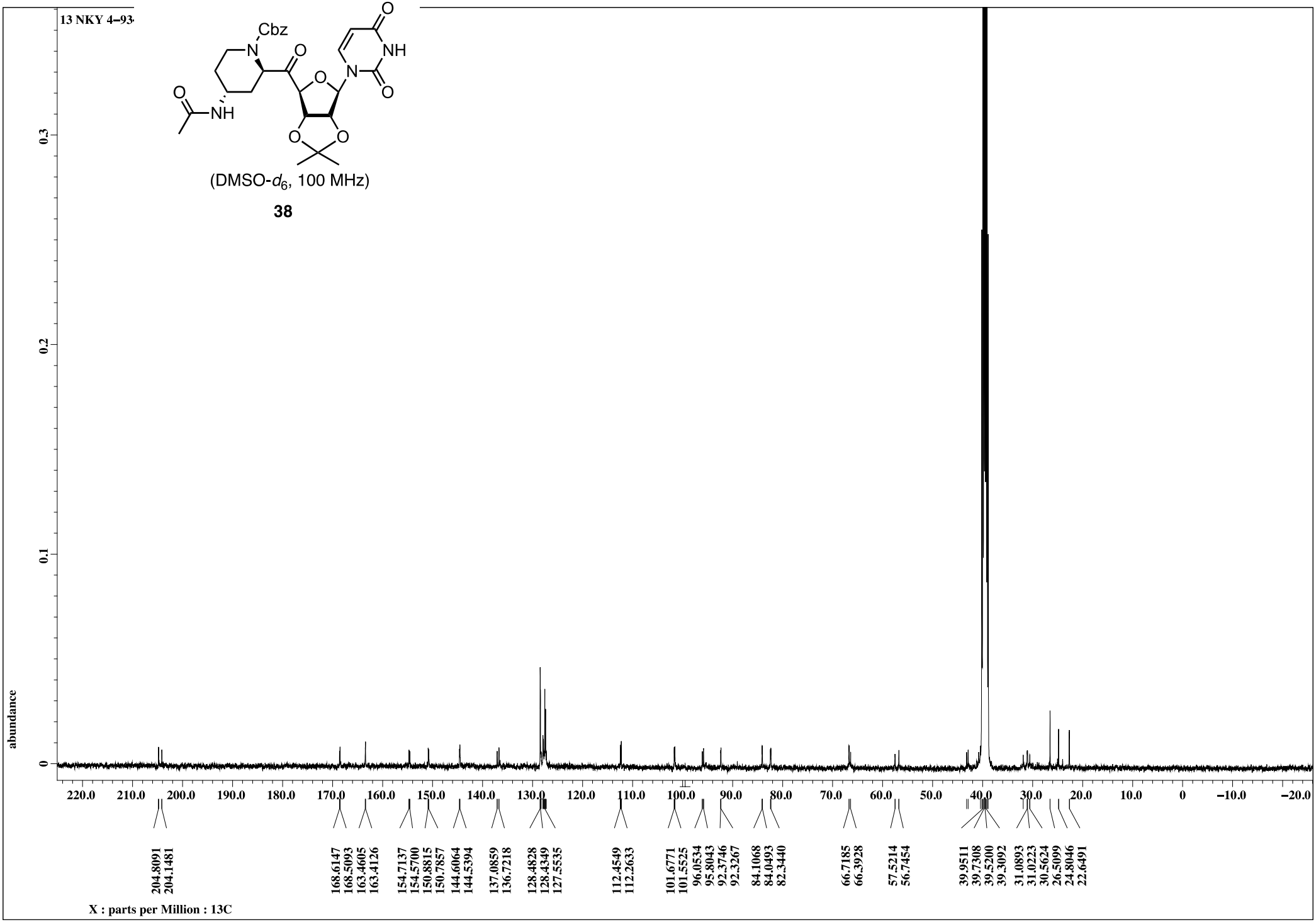
(DMSO-d_6, D_2O, 400 MHz)

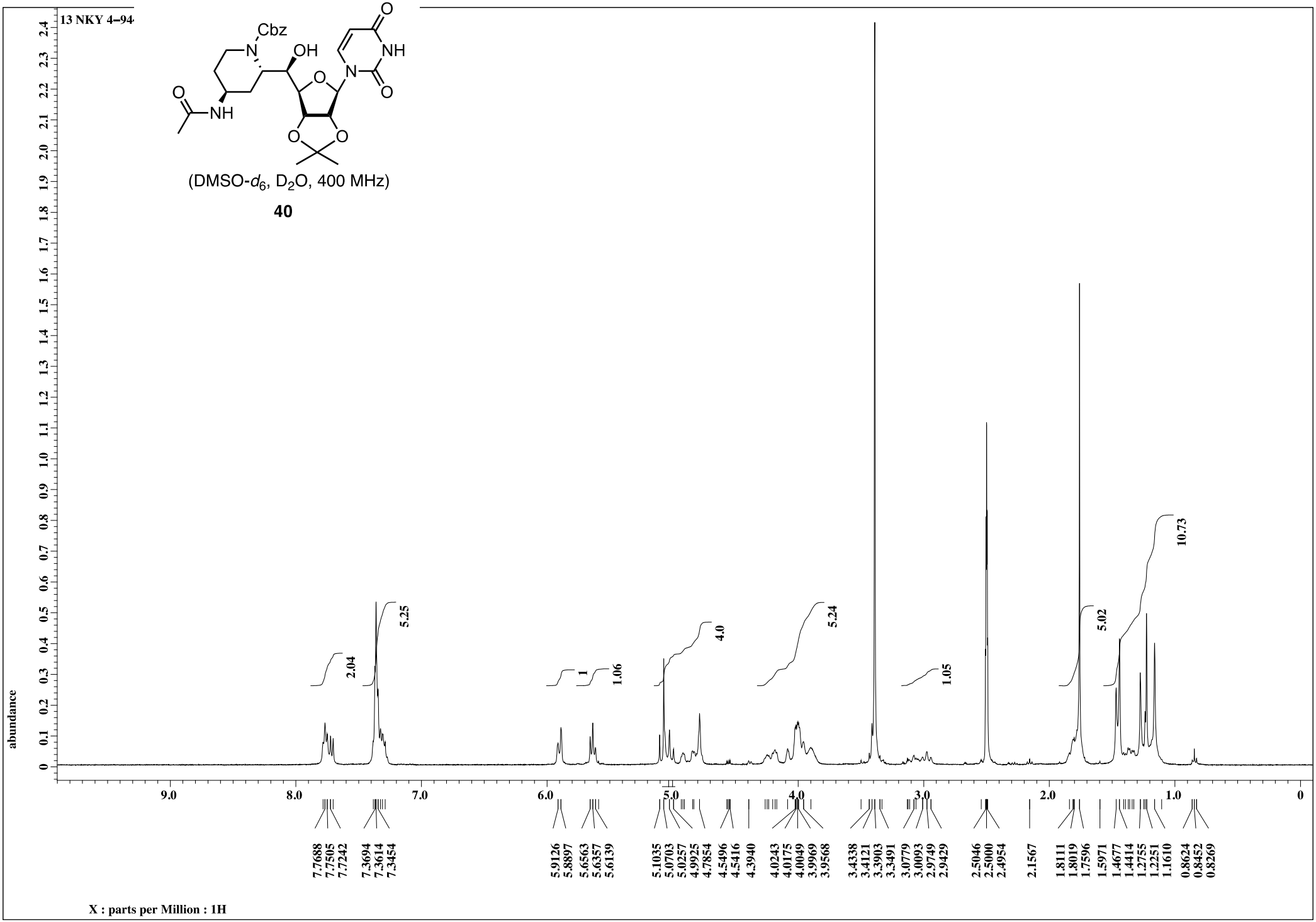
37

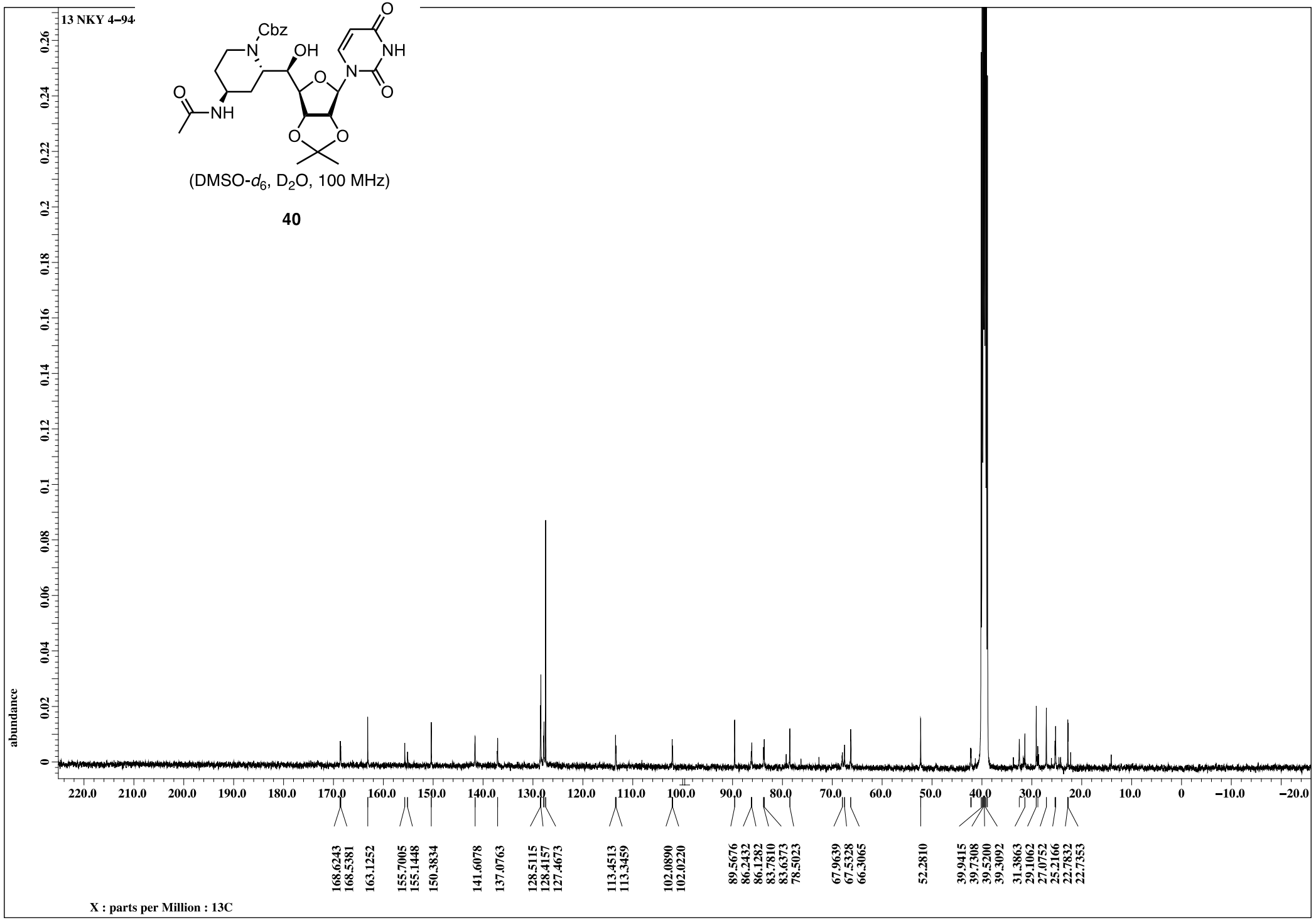
X : parts per Million : 1H

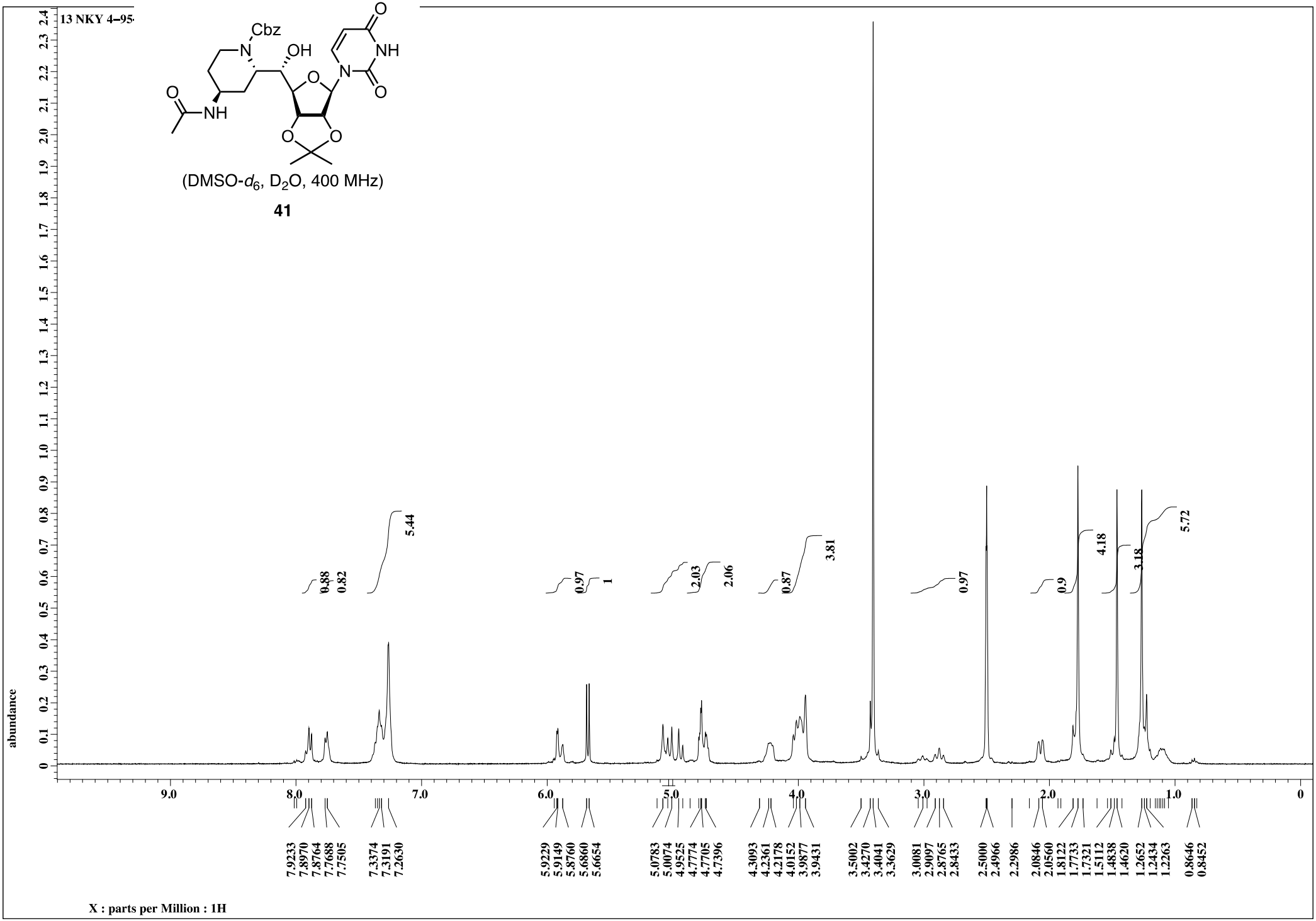

13 NKY 4-96
Cbz
N
OH
O
NH
N
O
O
NH
O
O
O
O
(DMSO-d_6, D_2O, 100 MHz)
37
abundance
0
0.1
0.2
0.3
220.0 210.0 200.0 190.0 180.0 170.0 160.0 150.0 140.0 130.0 120.0 110.0 100.0 90.0 80.0 70.0 60.0 50.0 40.0 30.0 20.0 10.0 0 −10.0 −20.0
168.6243
163.0581
162.8282
155.2310
155.0011
150.4983
150.4217
141.3587
140.5636
137.3925
137.2296
128.4636
128.2816
126.6913
112.9627
112.8477
102.1465
101.9549
90.1903
89.6250
84.6433
83.2637
81.2135
66.6419
66.1245
65.9521
53.1240
52.6354
39.7308
39.5200
39.3092
39.0985
32.4401
31.3576
29.0870
27.2859
25.3603
22.7545
X : parts per Million : 13C

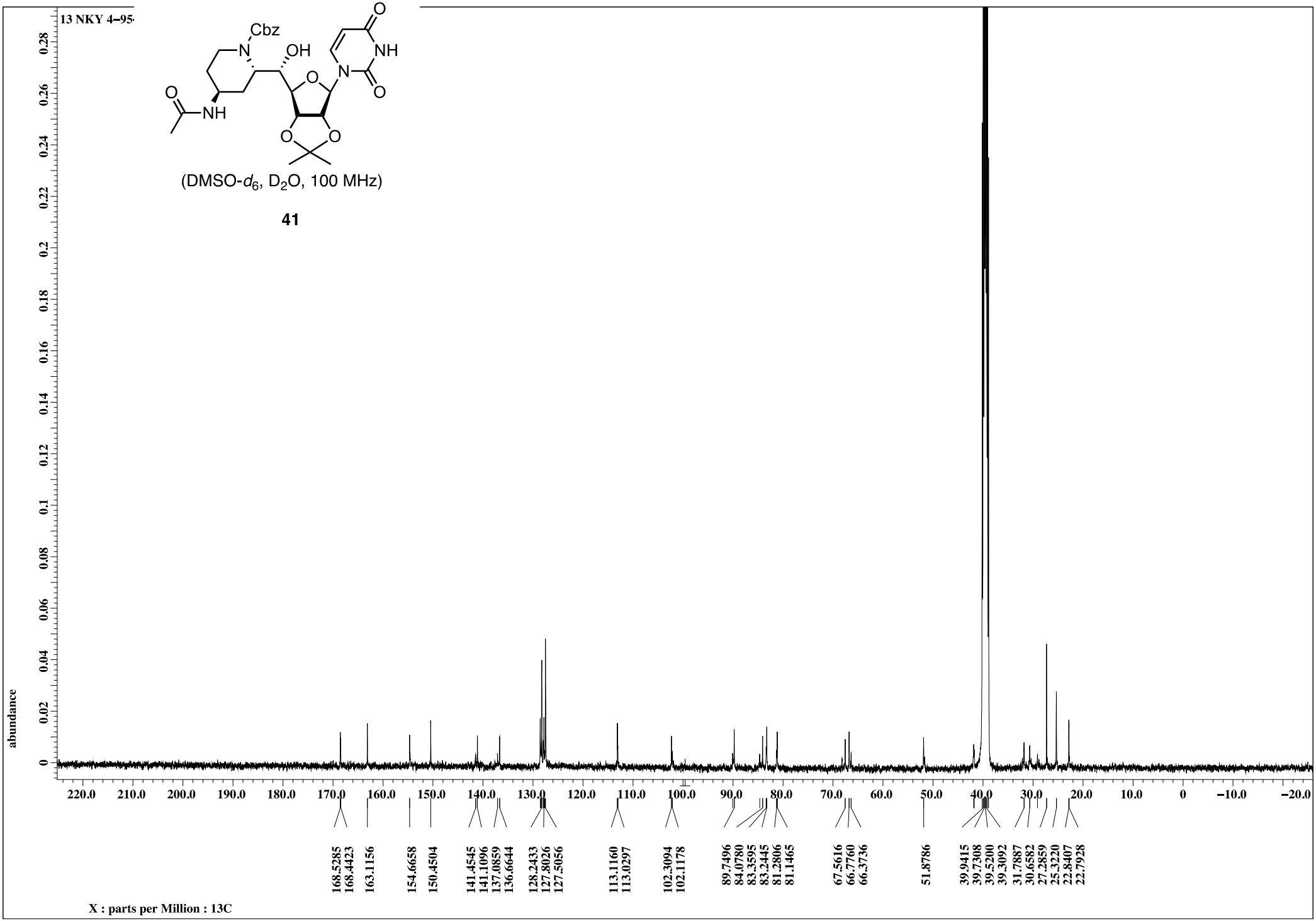

38
(acetone-d_6, 400 MHz)
Cbz
13 NKY 4-10
X : parts per Million : 1H
abundance

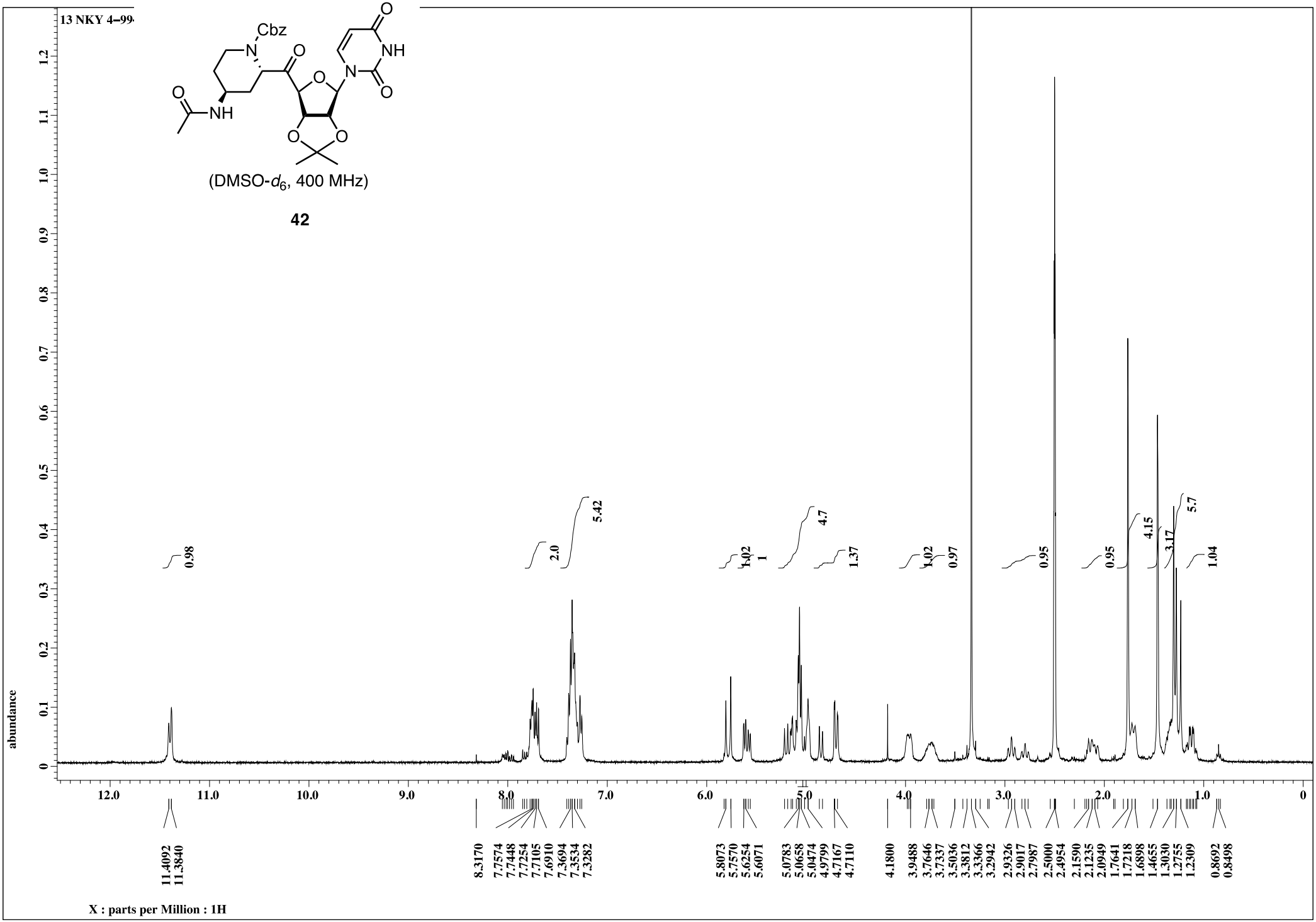

13 NKY 4–93
Cbz
N
O
O
NH
O
N
O
O
NH
O
O
O
(DMSO-d_6, 100 MHz)
38
abundance
0
0.1
0.2
0.3
220.0
210.0
200.0
190.0
180.0
170.0
160.0
150.0
140.0
130.0
120.0
110.0
100.0
90.0
80.0
70.0
60.0
50.0
40.0
30.0
20.0
10.0
0
−10.0
−20.0
204.8091
204.1481
168.6147
168.5093
163.4605
163.4126
154.7137
154.5700
150.8815
150.7857
144.6064
144.5394
137.0859
136.7218
128.4828
128.4349
127.5535
112.4549
112.2633
101.6771
101.5525
96.0534
95.8043
92.3746
92.3267
84.1068
84.0493
82.3440
66.7185
66.3928
57.5214
56.7454
39.9511
39.7308
39.5200
39.3092
31.0893
31.0223
30.5624
26.5099
24.8046
22.6491
X : parts per Million : 13C

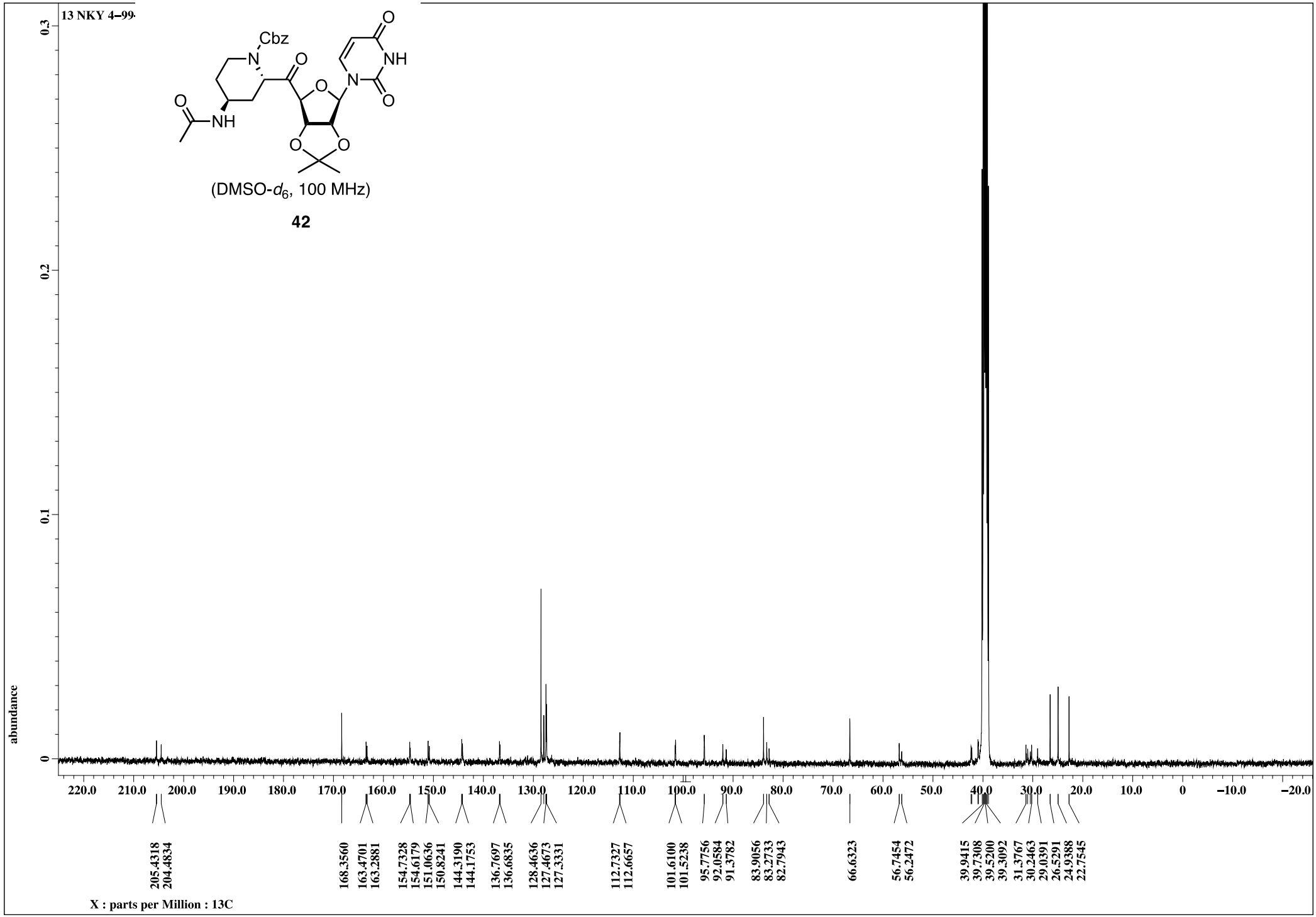

13 NKY 4–94
Cbz
N
OH
O
NH
N
O
O
NH
O
O
O
O
(DMSO-d_6, D_2O, 400 MHz)
40
abundance
2.04
5.25
1
1.06
4.0
5.24
1.05
5.02
10.73
9.0
8.0
7.0
6.0
5.0
4.0
3.0
2.0
1.0
0
7.7688
7.7505
7.7242
7.3694
7.3614
7.3454
5.9126
5.8897
5.6563
5.6357
5.6139
5.1035
5.0703
5.0257
4.9925
4.7854
4.5496
4.5416
4.3940
4.0243
4.0175
4.0049
3.9969
3.9568
3.4338
3.4121
3.3903
3.3491
3.0779
3.0093
2.9749
2.9429
2.5046
2.5000
2.4954
2.1567
1.8111
1.8019
1.7596
1.5971
1.4677
1.4414
1.2755
1.2251
1.1610
0.8624
0.8452
0.8269
X : parts per Million : 1H

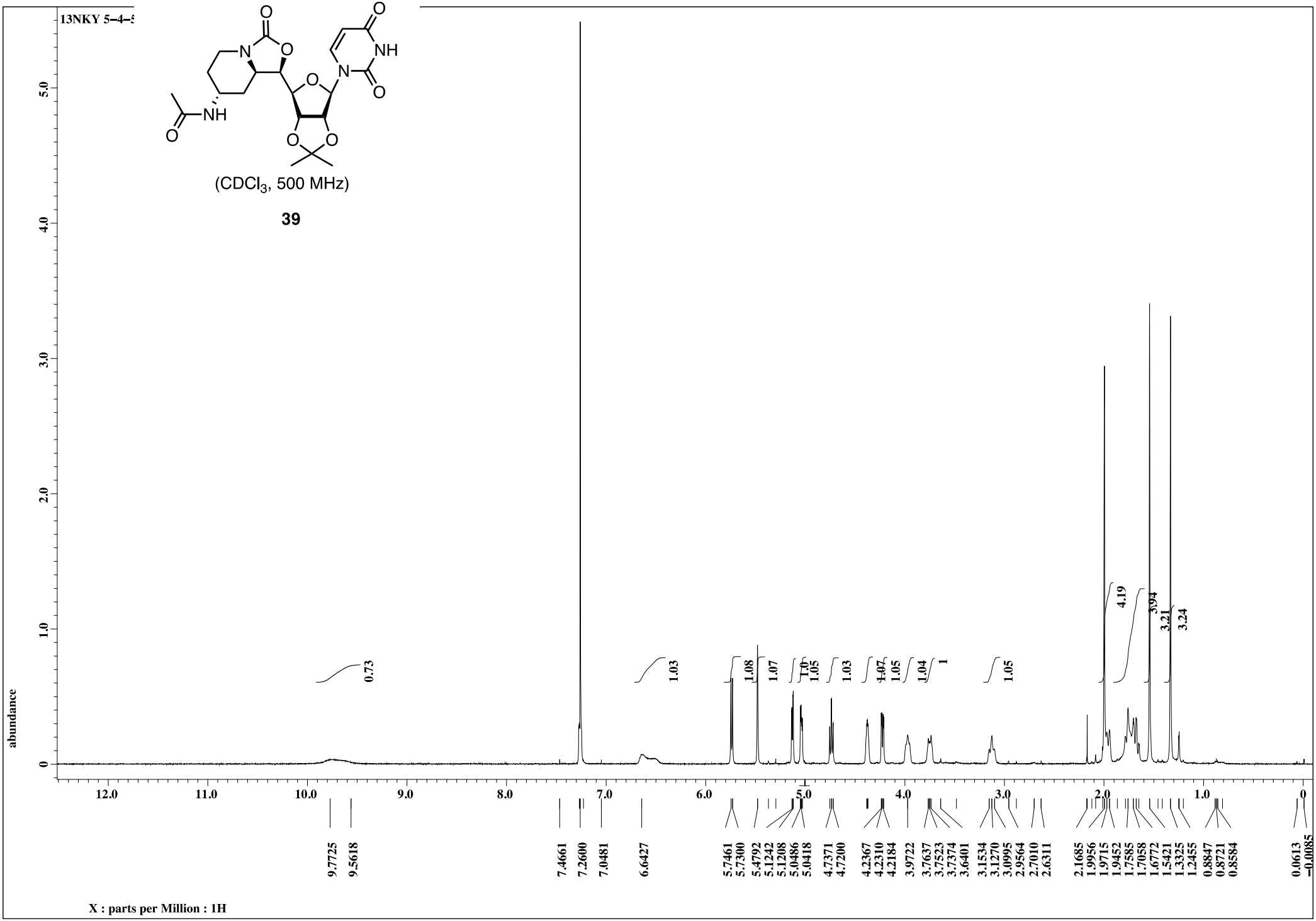

13 NKY 4–94
Cbz
N
OH
O
NH
N
O
O
NH
O
O
O
O
(DMSO-d_6, D_2O, 100 MHz)
40
abundance
0
0.02
0.04
0.06
0.08
0.1
0.12
0.14
0.16
0.18
0.2
0.22
0.24
0.26
220.0
210.0
200.0
190.0
180.0
170.0
160.0
150.0
140.0
130.0
120.0
110.0
100.0
90.0
80.0
70.0
60.0
50.0
40.0
30.0
20.0
10.0
0
−10.0
−20.0
168.6243
168.5381
163.1252
155.7005
155.1448
150.3834
141.6078
137.0763
128.5115
128.4157
127.4673
113.4513
113.3459
102.0890
102.0220
89.5676
86.2432
86.1282
83.7810
83.6373
78.5023
67.9639
67.5328
66.3065
52.2810
39.9415
39.7308
39.5200
39.3092
31.3863
29.1062
27.0752
25.2166
22.7832
22.7353
X : parts per Million : 13C

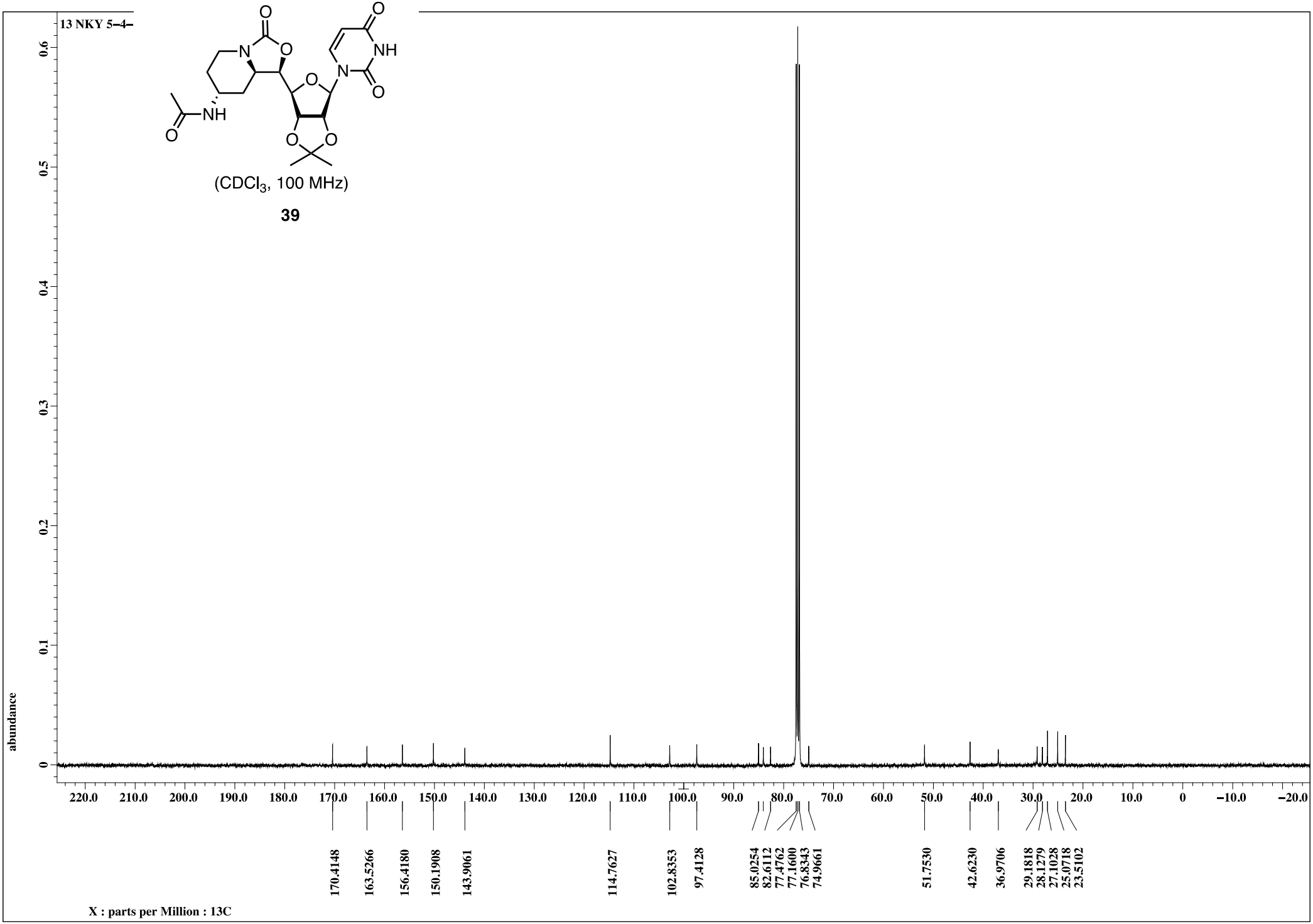

13 NKY 4–95
Cbz
N
OH
O
NH
O
N
NH
O
O
O
O
(DMSO-d_6, D_2O, 400 MHz)
41
abundance
X : parts per Million : 1H
0.88
0.82
5.44
0.97
1
2.03
2.06
0.87
3.81
0.97
0.9
4.18
3.18
5.72
7.9233
7.8970
7.8764
7.7688
7.7505
7.3374
7.3191
7.2630
5.9229
5.9149
5.8760
5.6860
5.6654
5.0783
5.0074
4.9525
4.7774
4.7705
4.7396
4.3093
4.2361
4.2178
4.0152
3.9877
3.9431
3.5002
3.4270
3.4041
3.3629
3.0081
2.9097
2.8765
2.8433
2.5000
2.4966
2.2986
2.0846
2.0560
1.8122
1.7733
1.7321
1.5112
1.4838
1.4620
1.2652
1.2434
1.2263
0.8646
0.8452


13 NKY 4–95
Cbz
N
OH
O
NH
O
N
O
O
NH
O
O
O
(DMSO-d_6, D_2O, 100 MHz)
41
abundance
0
0.02
0.04
0.06
0.08
0.1
0.12
0.14
0.16
0.18
0.2
0.22
0.24
0.26
0.28
220.0
210.0
200.0
190.0
180.0
170.0
160.0
150.0
140.0
130.0
120.0
110.0
100.0
90.0
80.0
70.0
60.0
50.0
40.0
30.0
20.0
10.0
0
−10.0
−20.0
168.5285
168.4423
163.1156
154.6658
150.4504
141.4545
141.1096
137.0859
136.6644
128.2433
127.8026
127.5056
113.1160
113.0297
102.3094
102.1178
89.7496
84.0780
83.3595
83.2445
81.2806
81.1465
67.5616
66.7760
66.3736
51.8786
39.9415
39.7308
39.5200
39.3092
31.7887
30.6582
27.2859
25.3220
22.8407
22.7928
X : parts per Million : 13C

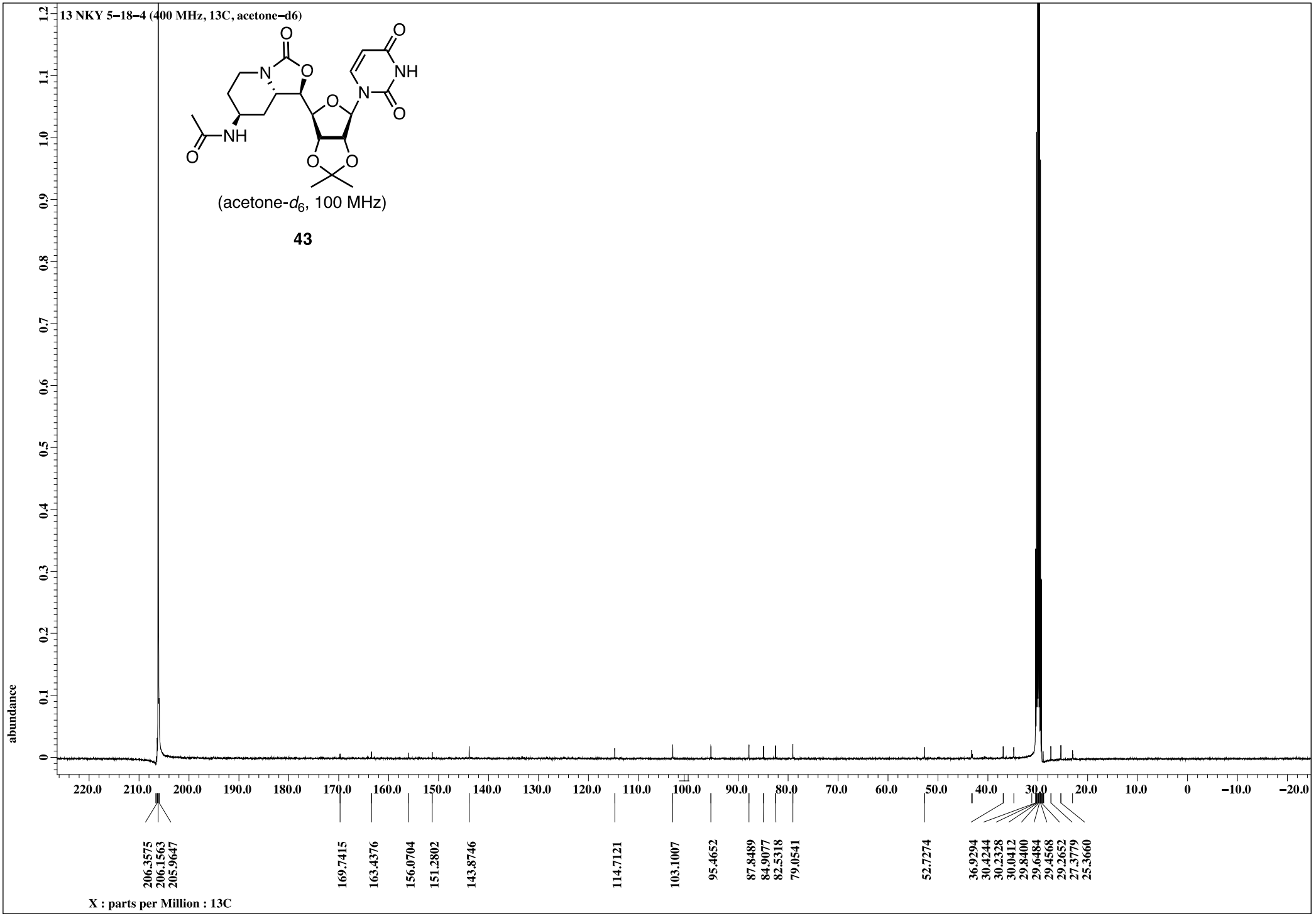

13 NKY 4–99
Cbz
N
O
O
NH
O
O
N
NH
O
O
O
O
(DMSO-d_6, 400 MHz)
42
abundance
0.98
2.0
5.42
1.02
1
4.7
1.37
1.02
0.97
0.95
0.95
4.15
3.17
5.7
1.04
12.0
11.0
10.0
9.0
8.0
7.0
6.0
5.0
4.0
3.0
2.0
1.0
0
11.4092
11.3840
8.3170
7.7574
7.7448
7.7254
7.7105
7.6910
7.3694
7.3534
7.3282
5.8073
5.7570
5.6254
5.6071
5.0783
5.0658
5.0474
4.9799
4.7167
4.7110
4.1800
3.9488
3.7646
3.7337
3.5036
3.3812
3.3366
3.2942
2.9326
2.9017
2.7987
2.5000
2.4954
2.1590
2.1235
2.0949
1.7641
1.7218
1.6898
1.4655
1.3030
1.2755
1.2309
0.8692
0.8498
X : parts per Million : 1H


13 NKY 4–99
Cbz
N
O
O
NH
O
N
O
NH
O
O
O
(DMSO-d_6, 100 MHz)
42
abundance
0.3
0.2
0.1
0
220.0 210.0 200.0 190.0 180.0 170.0 160.0 150.0 140.0 130.0 120.0 110.0 100.0 90.0 80.0 70.0 60.0 50.0 40.0 30.0 20.0 10.0 0 −10.0 −20.0
205.4318
204.4834
168.3560
163.4701
163.2881
154.7328
154.6179
151.0636
150.8241
144.3190
144.1753
136.7697
136.6835
128.4636
127.4673
127.3331
112.7327
112.6657
101.6100
101.5238
95.7756
92.0584
91.3782
83.9056
83.2733
82.7943
66.6323
56.7454
56.2472
39.9415
39.7308
39.5200
39.3092
31.3767
30.2463
29.0391
26.5291
24.9388
22.7545
X : parts per Million : 13C

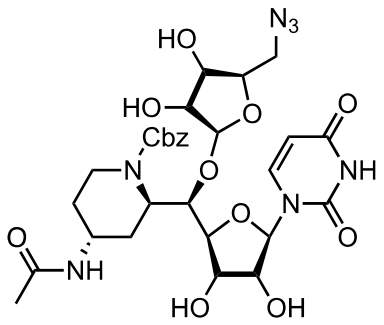

13NKY 5–4–5
(CDCl3, 500 MHz)
39
abundance
X : parts per Million : 1H
0.73
1.03
1.08
1.07
1.0
1.05
1.03
1.07
1.05
1.04
1
1.05
4.19
3.94
3.21
3.24
9.7725
9.5618
7.4661
7.2600
7.0481
6.6427
5.7461
5.7300
5.4792
5.1242
5.1208
5.0486
5.0418
4.7371
4.7200
4.2367
4.2310
4.2184
3.9722
3.7637
3.7523
3.7374
3.6401
3.1534
3.1270
3.0995
2.9564
2.7010
2.6311
2.1685
1.9956
1.9715
1.9452
1.7585
1.7058
1.6772
1.5421
1.3325
1.2455
0.8847
0.8721
0.8584
0.0613
−0.0085


13 NKY 5–4–
(CDCl3, 100 MHz)
39
abundance
X : parts per Million : 13C
170.4148
163.5266
156.4180
150.1908
143.9061
114.7627
102.8353
97.4128
85.0254
82.6112
77.4762
77.1600
76.8343
74.9661
51.7530
42.6230
36.9706
29.1818
28.1279
27.1028
25.0718
23.5102

13 NKY 5–18
(acetone-d_6, 400 MHz)
43
X : parts per Million : 1H
abundance


13 NKY 5-18-4 (400 MHz, 13C, acetone-d6)
(acetone-d_6, 100 MHz)
43
abundance
X : parts per Million : 13C
206.3575
206.1563
205.9647
169.7415
163.4376
156.0704
151.2802
143.8746
114.7121
103.1007
95.4652
87.8489
84.9077
82.5318
79.0541
52.7274
36.9294
30.4244
30.2328
30.0412
29.8400
29.6484
29.4568
29.2652
27.3779
25.3660

13 NKY 3–42–1 (400 MHz, 1H, CD3OD)



(CD_3OD, 400 MHz)

32

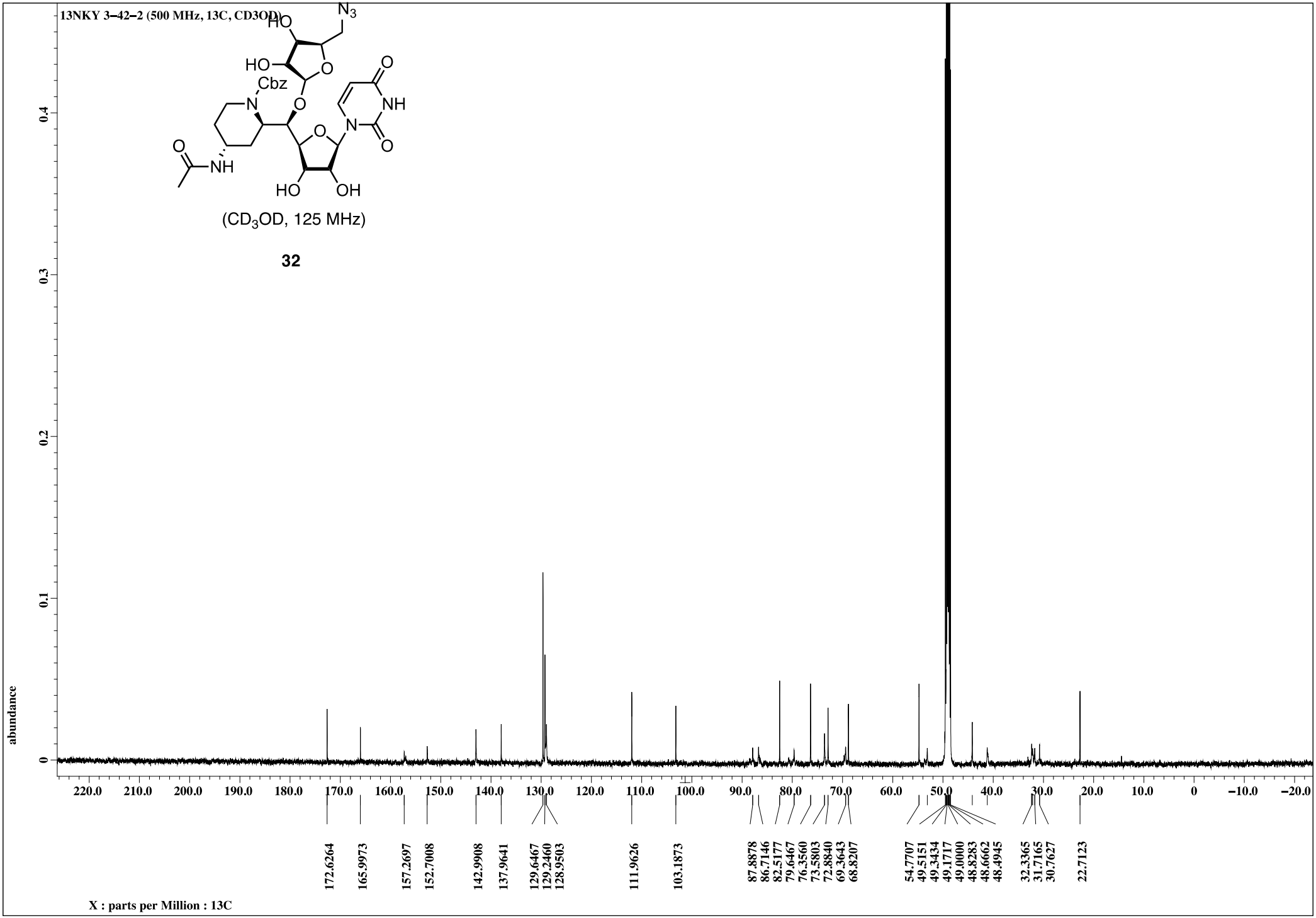
abundance

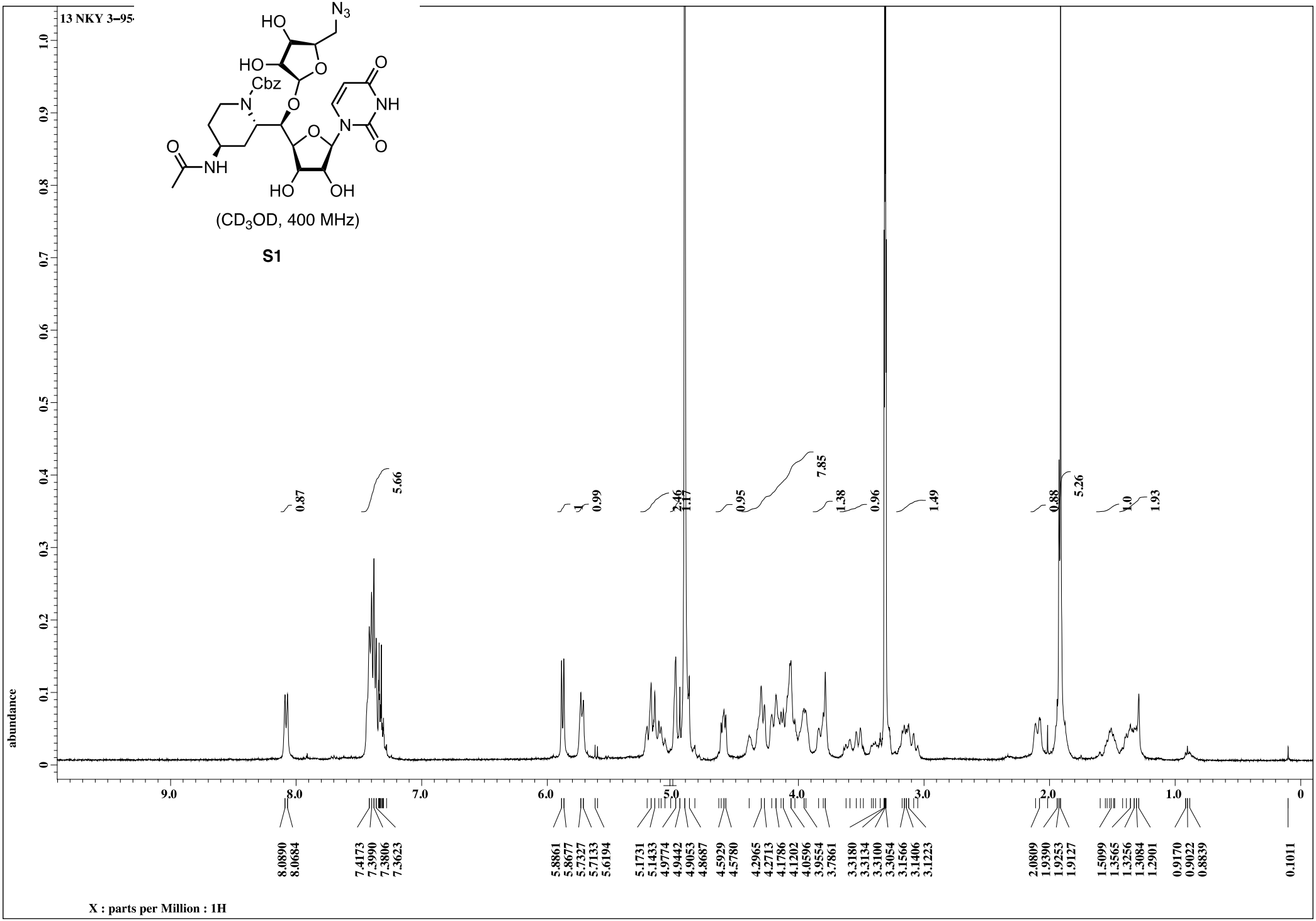
0.52 0.24 5.57 1.06 1.09 1.77 1.47 1.0 1.04 4.52 1.12 1.27 1.09 1.21 0.96 0.82 0.97 1.14 4.28

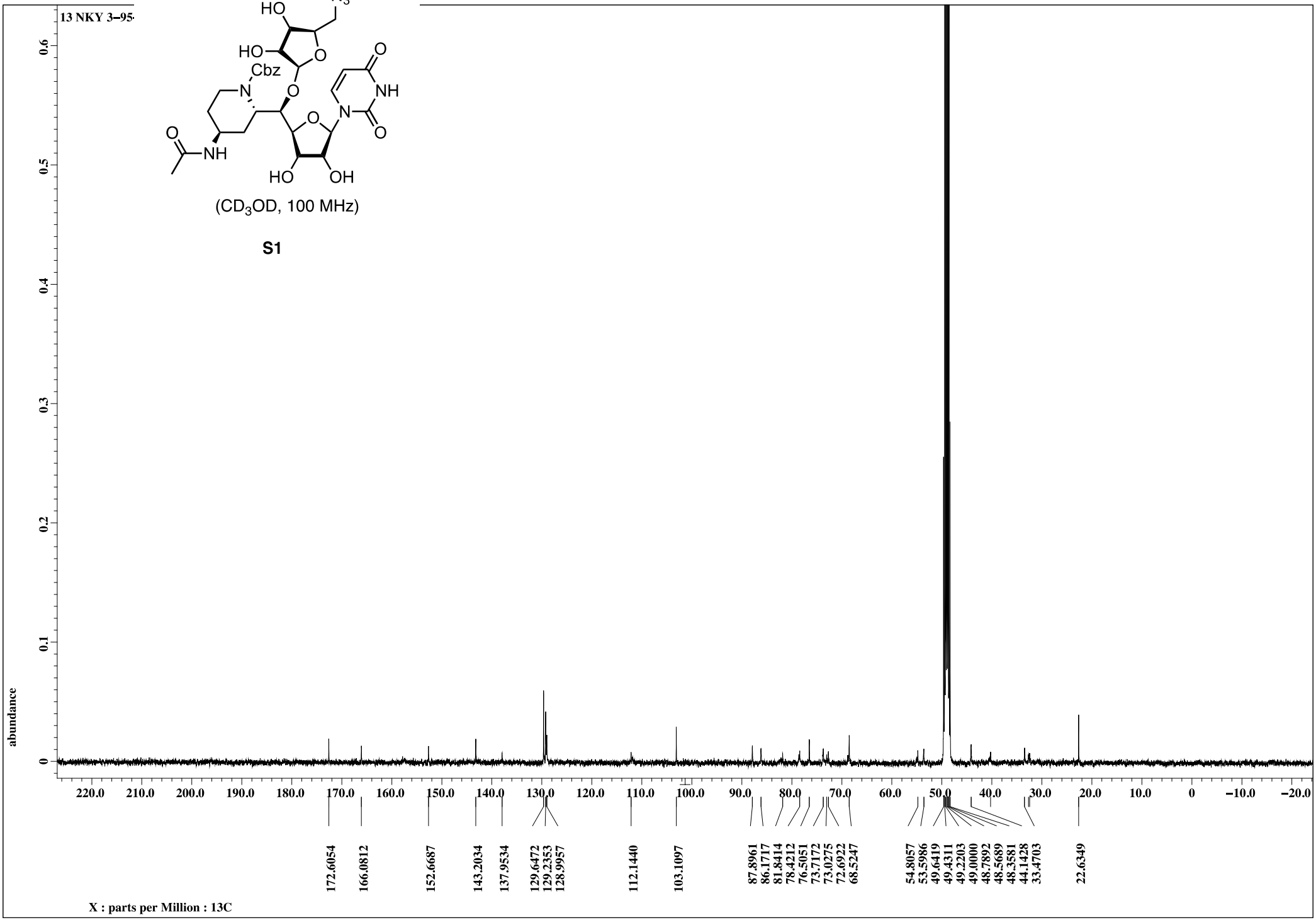
9.0 8.0 7.0 6.0 5.0 4.0 3.0 2.0 1.0 0

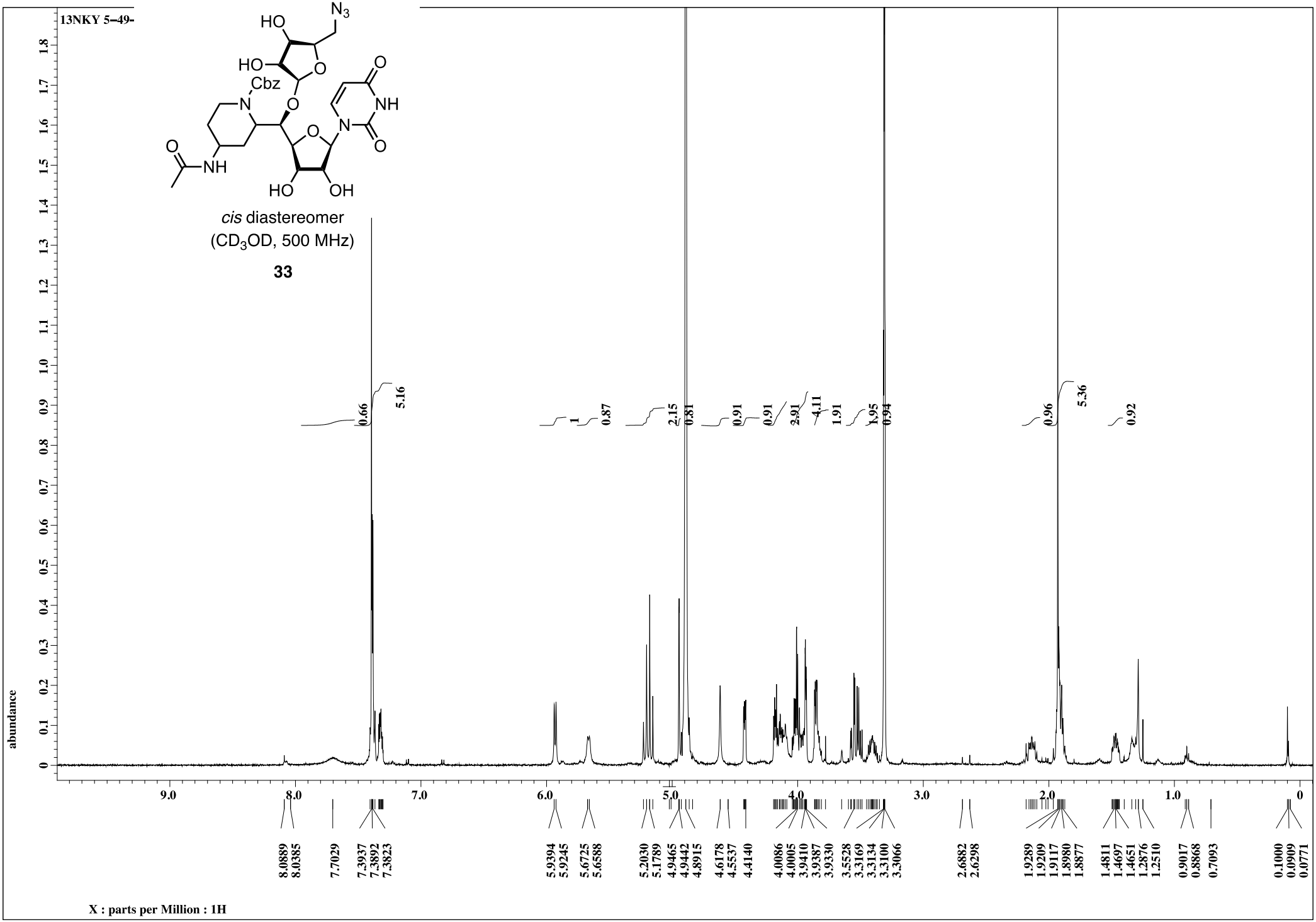
8.0536 8.0364 7.8476 7.3761 7.3635 7.3257 5.8780 5.8609 5.7544 5.7361 5.6183 5.1559 5.1079 4.9454 4.9316 4.8996 4.8561 4.3823 4.3754 4.3674 4.1958 4.1786 4.1626 4.0310 3.6064 3.6007 3.3180 3.3134 3.3100 3.3054 3.3020 2.3327 2.3041 1.9207 1.8864 1.8555 1.5968 1.3393 1.3279 1.2890 0.9022 0.8839 0.8713 0.1011

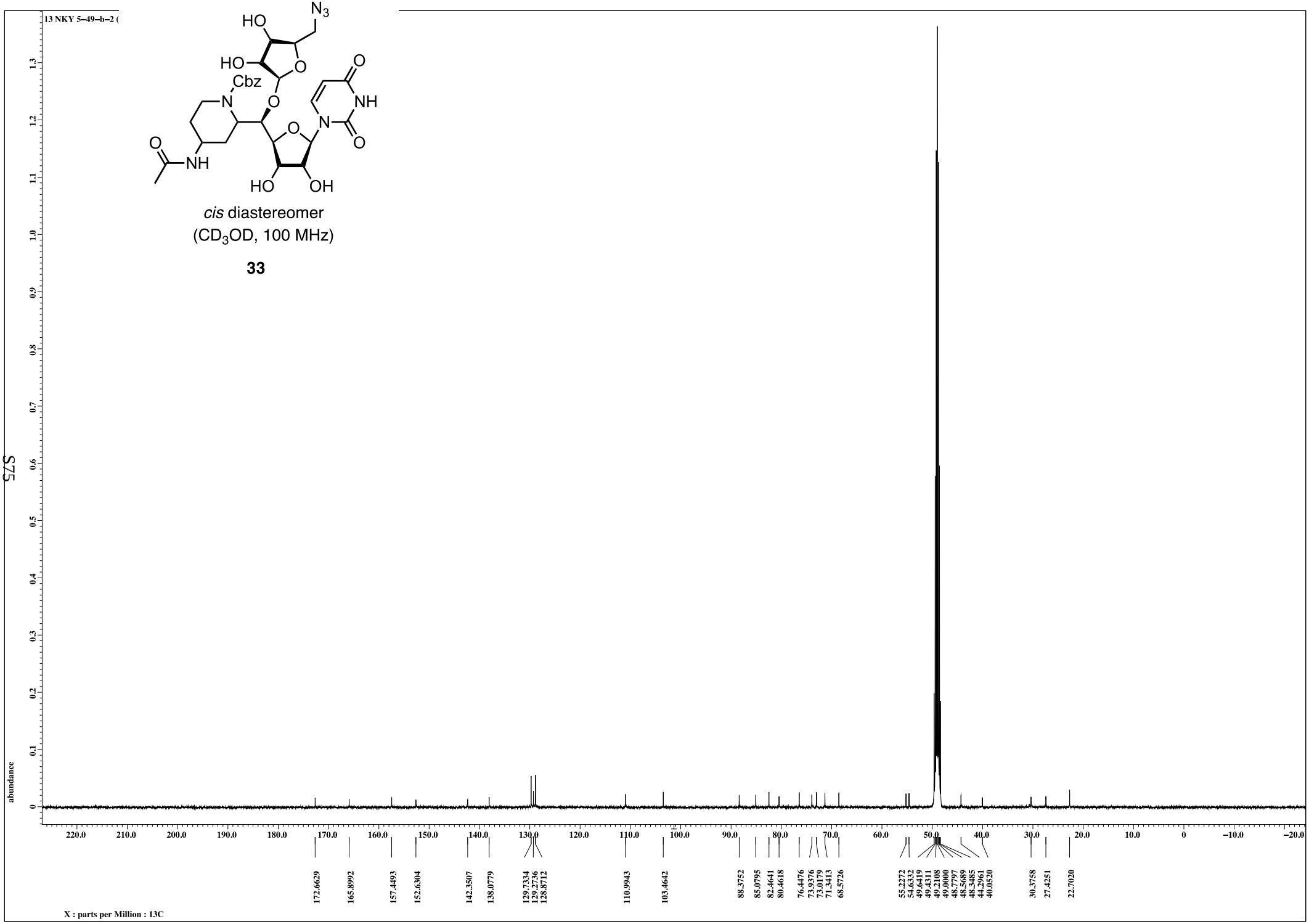
X : parts per Million : 1H


13NKY 3–42–2 (500 MHz, 13C, CD3OD)
HO
N3
HO
O
Cbz
N
O
O
NH
N
O
O
NH
HO
OH
(CD3OD, 125 MHz)
32
abundance
0
0.1
0.2
0.3
0.4
220.0
210.0
200.0
190.0
180.0
170.0
160.0
150.0
140.0
130.0
120.0
110.0
100.0
90.0
80.0
70.0
60.0
50.0
40.0
30.0
20.0
10.0
0
−10.0
−20.0
172.6264
165.9973
157.2697
152.7008
142.9908
137.9641
129.6467
129.2460
128.9503
111.9626
103.1873
87.8878
86.7146
82.5177
79.6467
76.3560
73.5803
72.8840
69.3643
68.8207
54.7707
49.5151
49.3434
49.1717
49.0000
48.8283
48.6662
48.4945
32.3365
31.7165
30.7627
22.7123
X : parts per Million : 13C

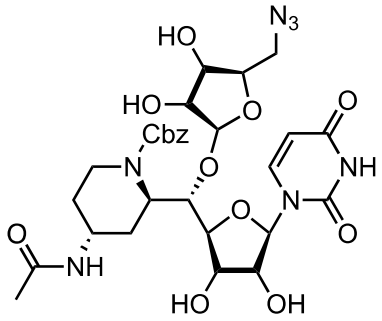

13 NKY 3-95
HO
HO
Cbz
N
O
O
N3
O
NH
O
N
O
O
NH
HO
OH
(CD3OD, 400 MHz)
S1
abundance
X : parts per Million : 1H
0.87
5.66
0.99
2.46
1.17
0.95
7.85
1.38
0.96
1.49
0.88
5.26
1.0
1.93
8.0890
8.0684
7.4173
7.3990
7.3806
7.3623
5.8861
5.8677
5.7327
5.7133
5.6194
5.1731
5.1433
4.9774
4.9442
4.9053
4.8687
4.5929
4.5780
4.2965
4.2713
4.1786
4.1202
4.0596
3.9554
3.7861
3.3180
3.3134
3.3100
3.3054
3.1566
3.1406
3.1223
2.0809
1.9390
1.9253
1.9127
1.5099
1.3565
1.3256
1.3084
1.2901
0.9170
0.9022
0.8839
0.1011


13 NKY 3–95
HO
N3
HO
O
Cbz
N
O
NH
O
N
O
O
NH
HO
OH
(CD3OD, 100 MHz)
S1
abundance
0
0.1
0.2
0.3
0.4
0.5
0.6
220.0
210.0
200.0
190.0
180.0
170.0
160.0
150.0
140.0
130.0
120.0
110.0
100.0
90.0
80.0
70.0
60.0
50.0
40.0
30.0
20.0
10.0
0
−10.0
−20.0
172.6054
166.0812
152.6687
143.2034
137.9534
129.6472
129.2353
128.9957
112.1440
103.1097
87.8961
86.1717
81.8414
78.4212
76.5051
73.7172
73.0275
72.6922
68.5247
54.8057
53.5986
49.6419
49.4311
49.2203
49.0000
48.7892
48.5689
48.3581
44.1428
33.4703
22.6349
X : parts per Million : 13C


13NKY 5--49-
HO
N3
HO
O
Cbz
N
O
O
NH
O
N
O
O
NH
HO
OH
cis diastereomer
(CD3OD, 500 MHz)
33
abundance
X : parts per Million : 1H


13 NKY 5–49–b–2 (
HO
N3
HO
O
Cbz
N
O
O
NH
O
N
O
O
NH
HO
OH
cis diastereomer
(CD3OD, 100 MHz)
33
abundance
X : parts per Million : 13C
172.6629
165.8992
157.4493
152.6304
142.3507
138.0779
129.7334
129.2736
128.8712
110.9943
103.4642
88.3752
85.0795
82.4641
80.4618
76.4476
73.9376
73.0179
71.3413
68.5726
55.2272
54.6332
49.6419
49.4311
49.2108
49.0000
48.7797
48.5689
48.3485
44.2961
40.0520
30.3758
27.4251
22.7020

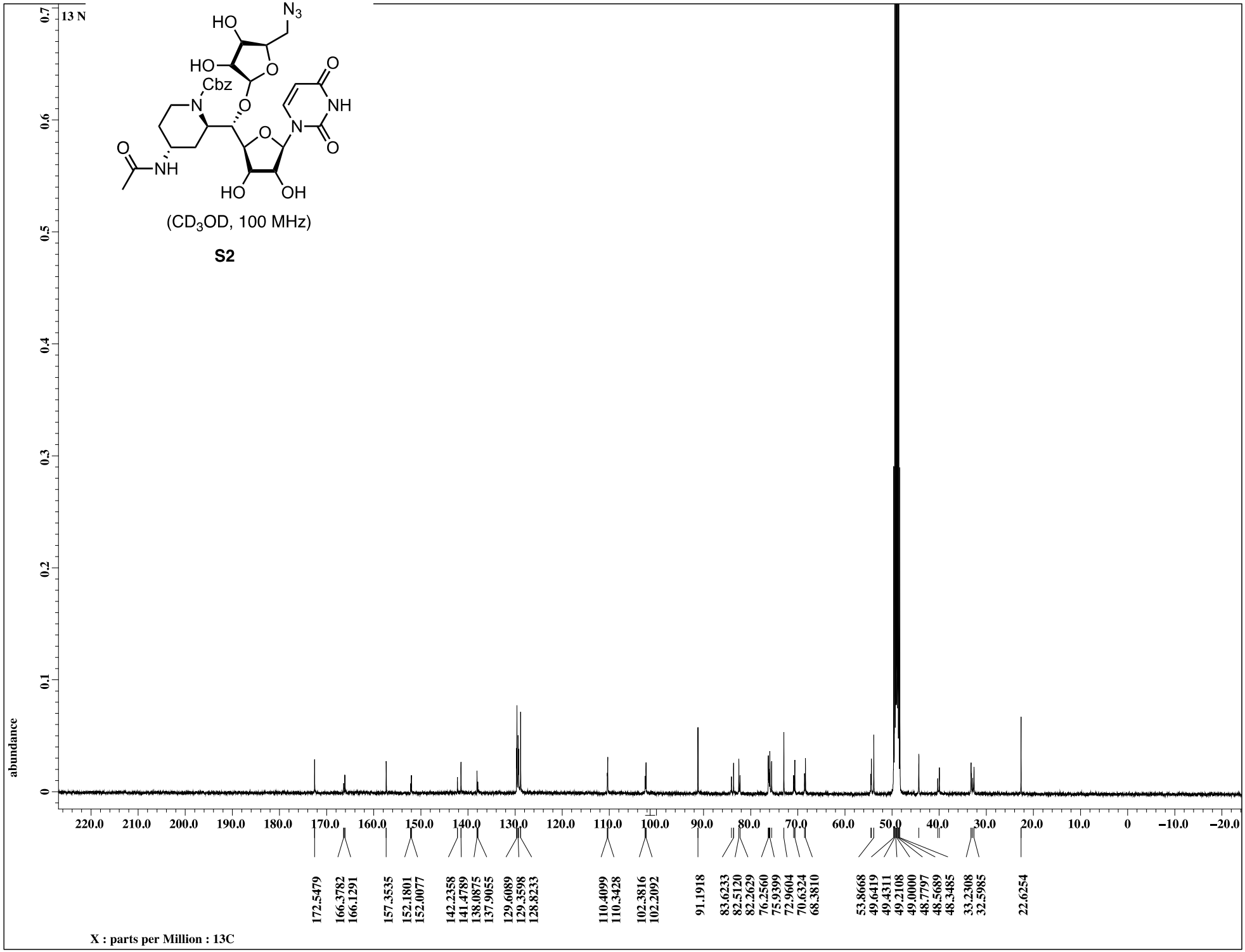
13 NKY 4-1-

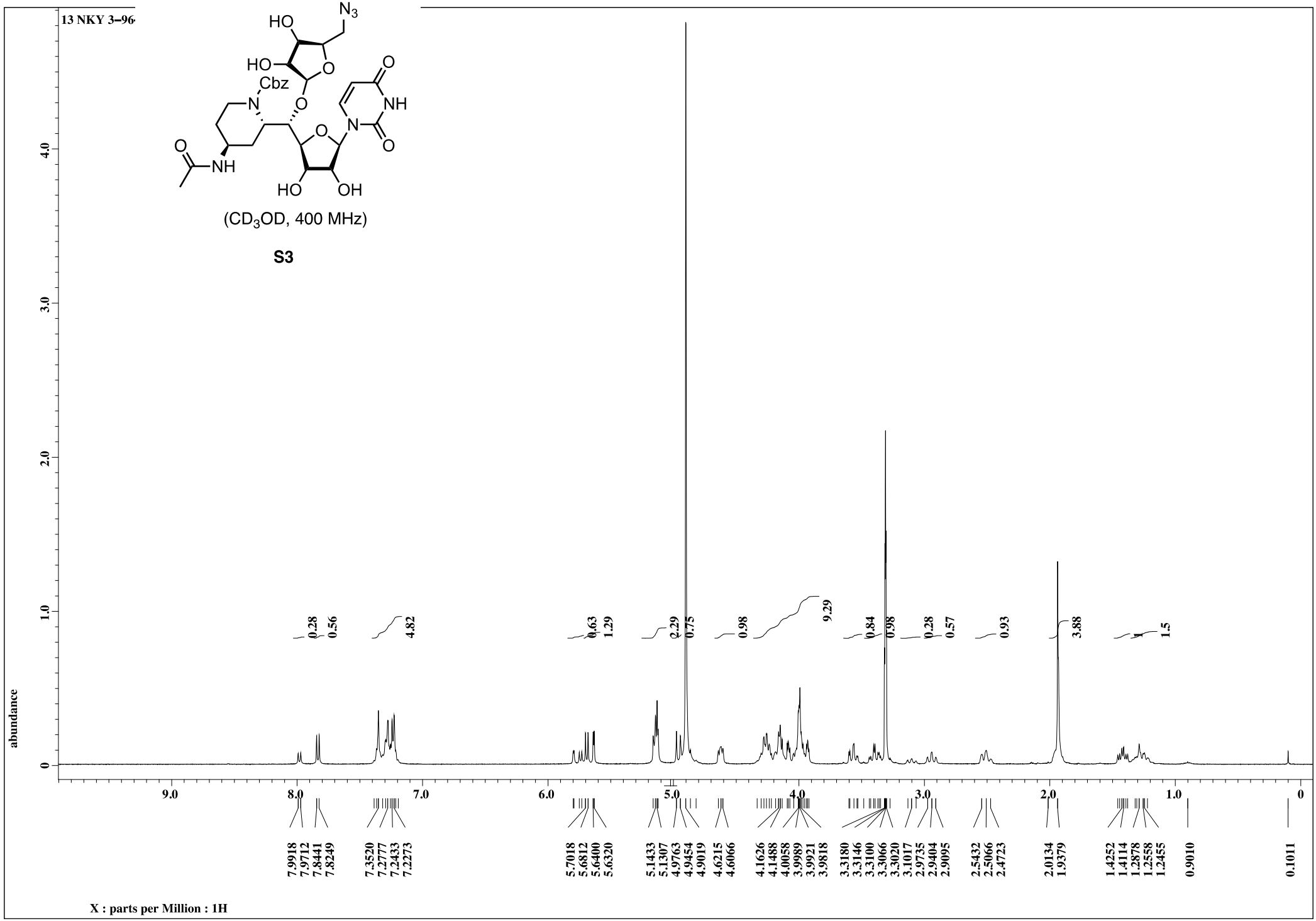


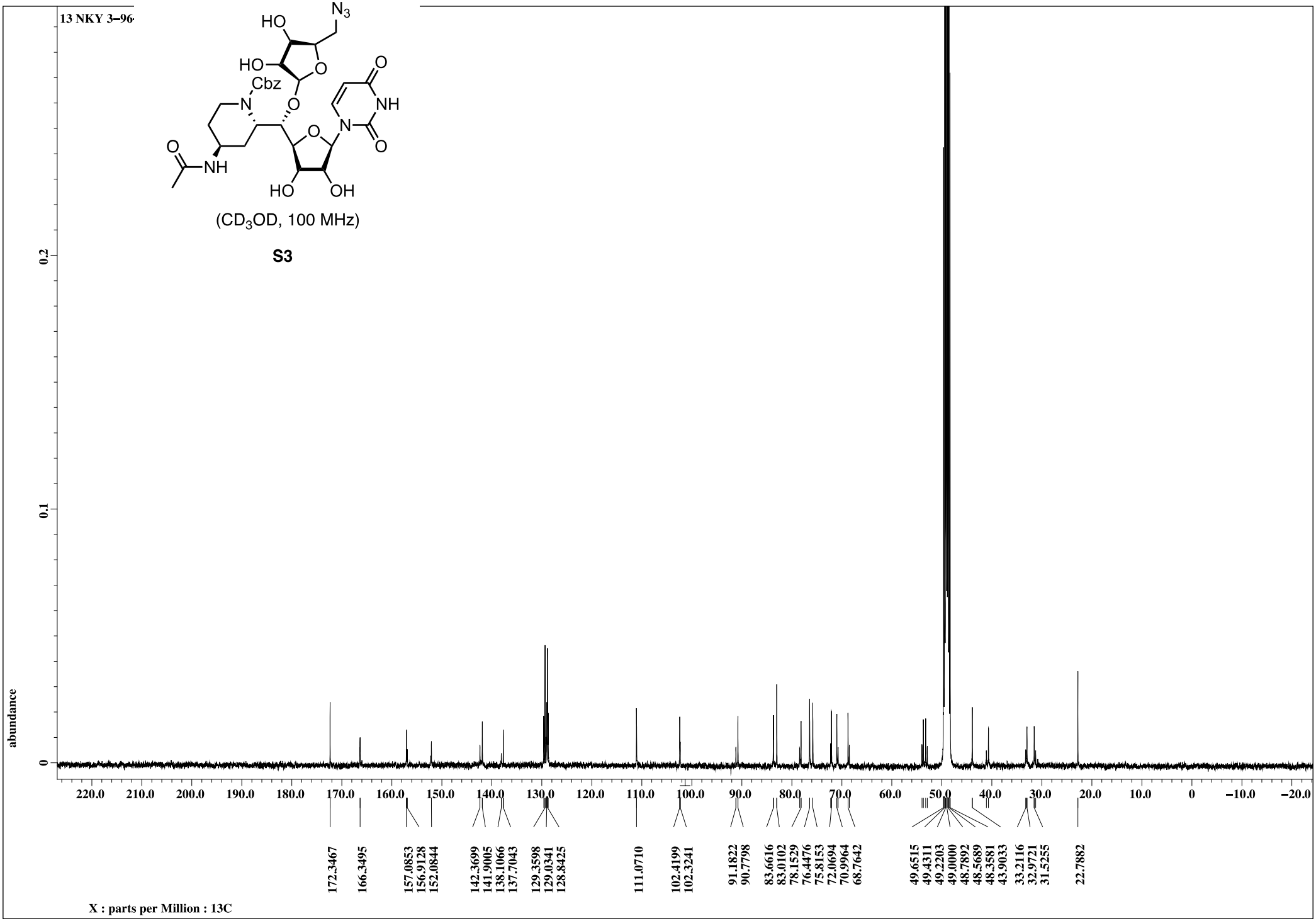
(CD_3OD, 400 MHz)

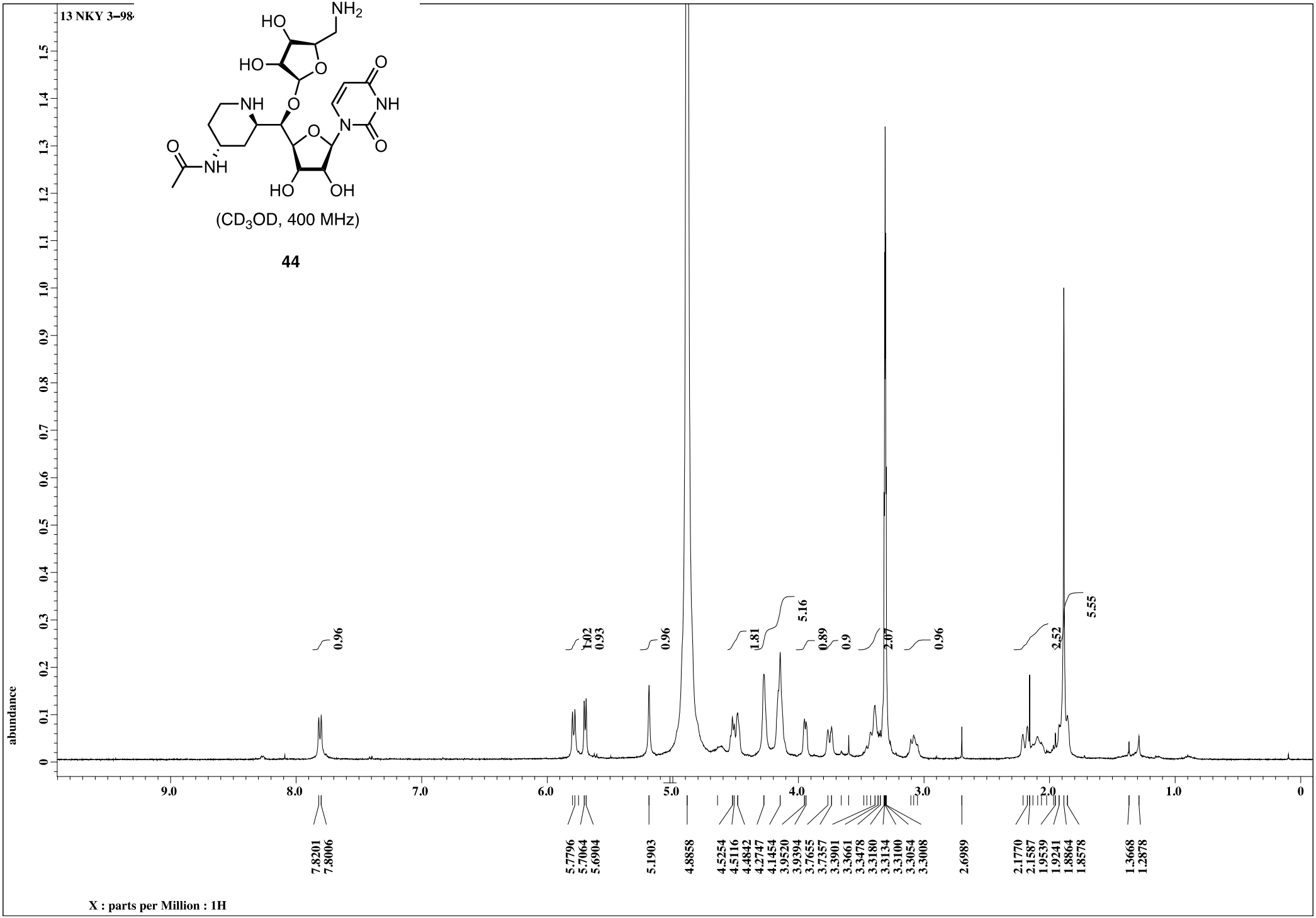
S2

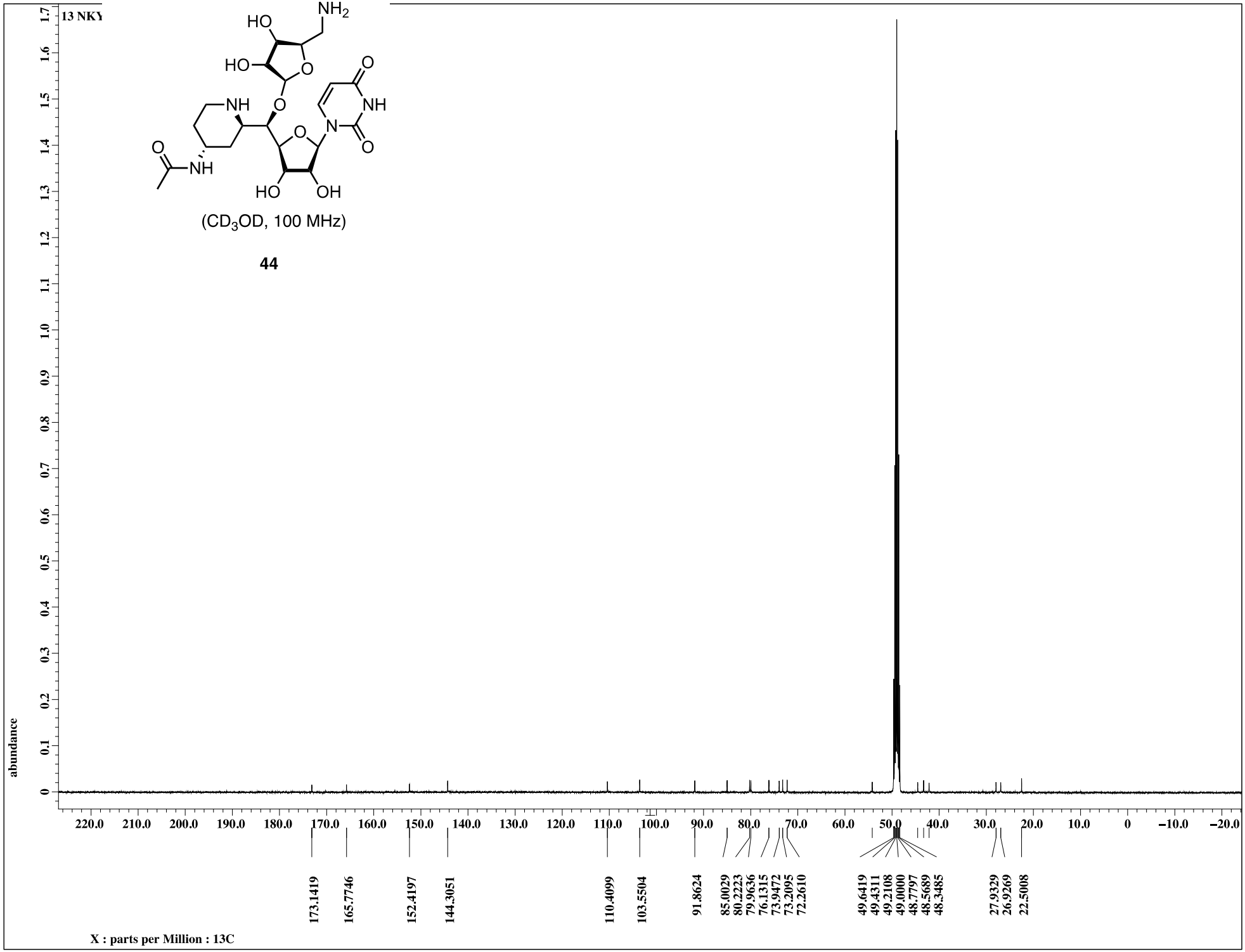
X : parts per Million : 1H


13 N
HO
N3
HO
O
Cbz
O
N
O
NH
O
N
O
NH
HO
OH
(CD3OD, 100 MHz)
S2
abundance
0.7
0.6
0.5
0.4
0.3
0.2
0.1
0
220.0 210.0 200.0 190.0 180.0 170.0 160.0 150.0 140.0 130.0 120.0 110.0 100.0 90.0 80.0 70.0 60.0 50.0 40.0 30.0 20.0 10.0 0 −10.0 −20.0
172.5479
166.3782
166.1291
157.3535
152.1801
152.0077
142.2358
141.4789
138.0875
137.9055
129.6089
129.3598
128.8233
110.4099
110.3428
102.3816
102.2092
91.1918
83.6233
82.5120
82.2629
76.2560
75.9399
72.9604
70.6324
68.3810
53.8668
49.6419
49.4311
49.2108
49.0000
48.7797
48.5689
48.3485
33.2308
32.5985
22.6254
X : parts per Million : 13C

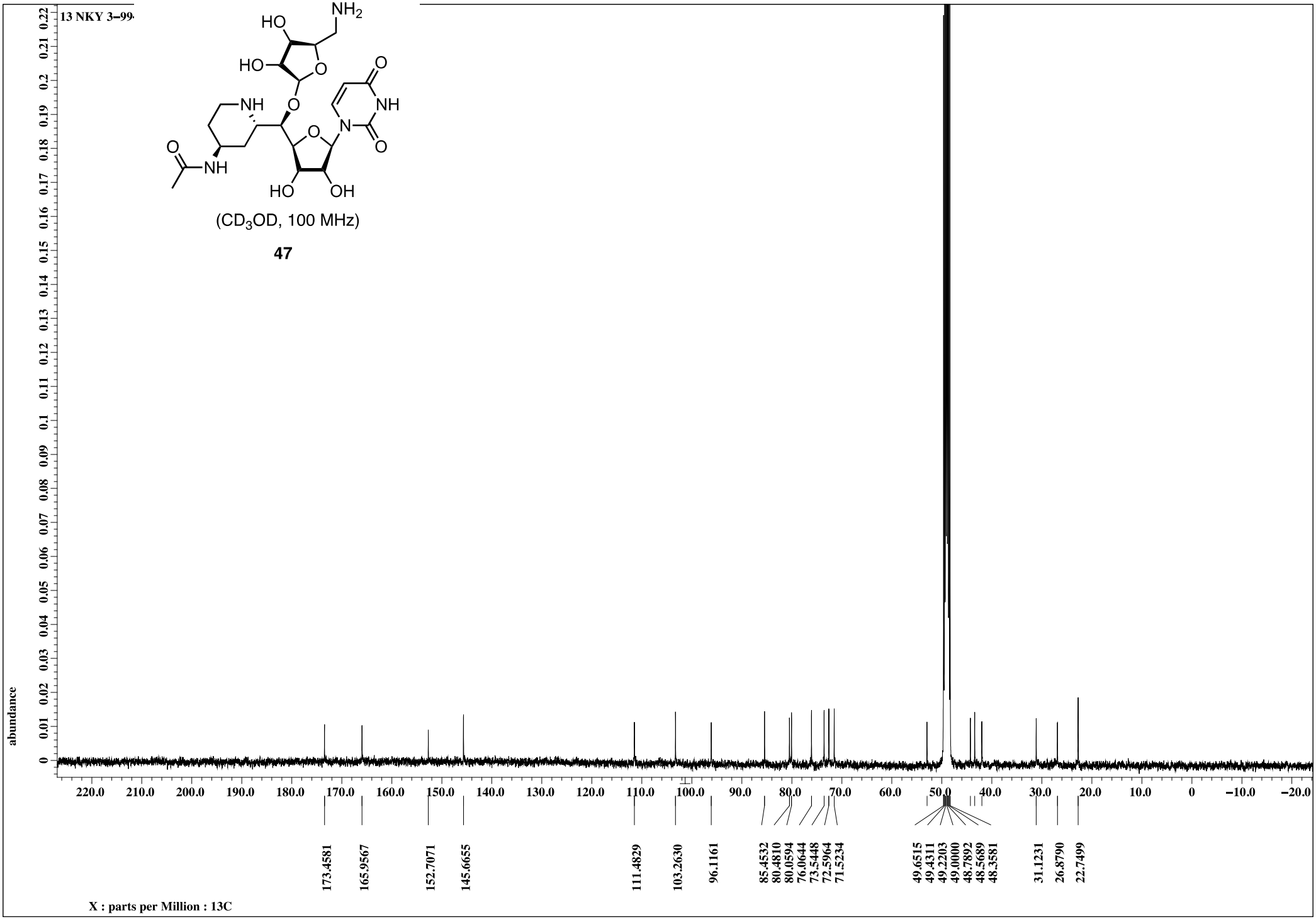

13 NKY 3–96
HO
HO
Cbz
N
O
O
N3
O
NH
N
O
O
NH
HO
OH
(CD3OD, 400 MHz)
S3
abundance
0
1.0
2.0
3.0
4.0
0.28
0.56
4.82
0.63
1.29
2.29
0.75
0.98
9.29
0.84
0.98
0.28
0.57
0.93
3.88
1.5
9.0
8.0
7.0
6.0
5.0
4.0
3.0
2.0
1.0
0
7.9918
7.9712
7.8441
7.8249
7.3520
7.2777
7.2433
7.2273
5.7018
5.6812
5.6400
5.6320
5.1433
5.1307
4.9763
4.9454
4.9019
4.6215
4.6066
4.1626
4.1488
4.0058
3.9989
3.9921
3.9818
3.3180
3.3146
3.3100
3.3066
3.3020
3.1017
2.9735
2.9404
2.9095
2.5432
2.5066
2.4723
2.0134
1.9379
1.4252
1.4114
1.2878
1.2558
1.2455
0.9010
0.1011
X : parts per Million : 1H

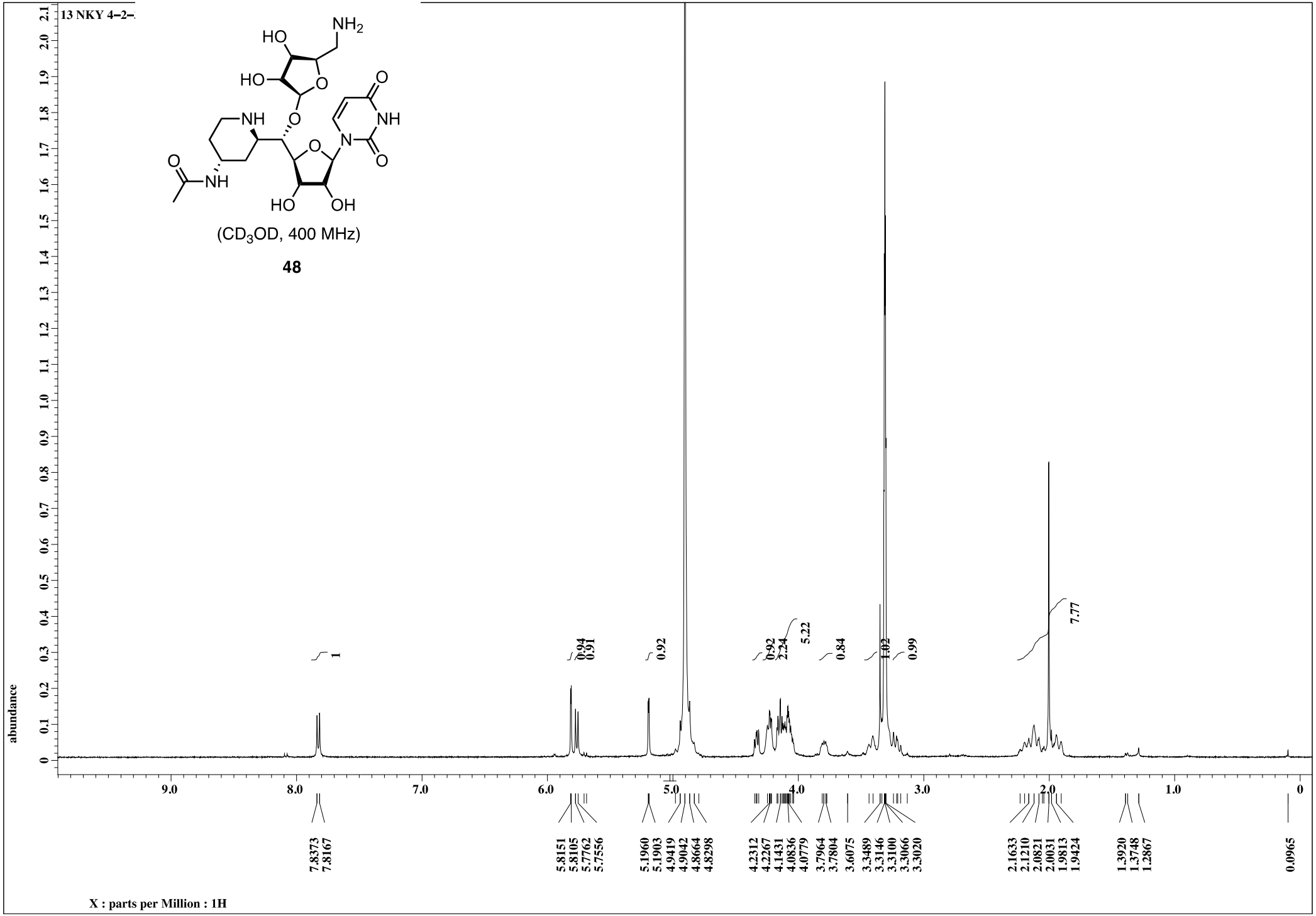

13 NKY 3–96
HO
N3
HO
O
O
Cbz
N
O
NH
O
N
O
O
NH
HO
OH
(CD3OD, 100 MHz)
S3
0.2
0.1
0
abundance
220.0 210.0 200.0 190.0 180.0 170.0 160.0 150.0 140.0 130.0 120.0 110.0 100.0 90.0 80.0 70.0 60.0 50.0 40.0 30.0 20.0 10.0 0 −10.0 −20.0
172.3467
166.3495
157.0853
156.9128
152.0844
142.3699
141.9005
138.1066
137.7043
129.3598
129.0341
128.8425
111.0710
102.4199
102.3241
91.1822
90.7798
83.6616
83.0102
78.1529
76.4476
75.8153
72.0694
70.9964
68.7642
49.6515
49.4311
49.2203
49.0000
48.7892
48.5689
48.3581
43.9033
33.2116
32.9721
31.5255
22.7882
X : parts per Million : 13C


13 NKY 3-98
(CD3OD, 400 MHz)
44
abundance
X : parts per Million : 1H
0.96
1.02
0.93
0.96
1.81
5.16
0.89
0.9
2.07
0.96
2.52
5.55
7.8201
7.8006
5.7796
5.7064
5.6904
5.1903
4.8858
4.5254
4.5116
4.4842
4.2747
4.1454
3.9520
3.9394
3.7655
3.7357
3.3901
3.3661
3.3478
3.3180
3.3134
3.3100
3.3054
3.3008
2.6989
2.1770
2.1587
1.9539
1.9241
1.8864
1.8578
1.3668
1.2878

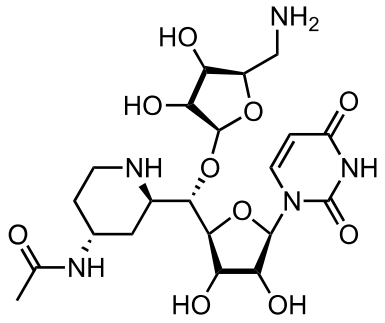

13 NKY
HO
NH2
HO
O
O
NH
O
NH
N
O
O
NH
HO
OH
(CD3OD, 100 MHz)
44
abundance
X : parts per Million : 13C
173.1419
165.7746
152.4197
144.3051
110.4099
103.5504
91.8624
85.0029
80.2223
79.9636
76.1315
73.9472
73.2095
72.2610
49.6419
49.4311
49.2108
49.0000
48.7797
48.5689
48.3485
27.9329
26.9269
22.5008

13 NKY 3--99.
abundance
X : parts per Million : 1H
(CD3OD, 400 MHz)
47
1.28
1.0
1.4
1
5.87
0.91
0.92
0.94
1.01
0.96
8.7
0.0988
1.2890
2.6977
2.0740
2.0168
1.9916
1.9779
1.9527
3.3180
3.3134
3.3100
3.3054
3.3020
3.9966
4.0081
4.1179
4.1557
4.1672
4.1820
4.2084
4.2187
4.4704
4.4853
4.5196
4.5311
4.9042
5.0312
5.1365
5.7625
5.7419
5.6927
5.5496
5.5382
7.7446
7.7240


13 NKY 3–99
(CD3OD, 100 MHz)
47
abundance
X : parts per Million : 13C
173.4581
165.9567
152.7071
145.6655
111.4829
103.2630
96.1161
85.4532
80.4810
80.0594
76.0644
73.5448
72.5964
71.5234
49.6515
49.4311
49.2203
49.0000
48.7892
48.5689
48.3581
31.1231
26.8790
22.7499


13 NKY 4-2-
(CD3OD, 400 MHz)
48
abundance
X : parts per Million : 1H
1
0.94
0.91
0.92
0.92
2.24
5.22
0.84
1.02
0.99
7.77
7.8373
7.8167
5.8151
5.8105
5.7762
5.7556
5.1960
5.1903
4.9419
4.9042
4.8664
4.8298
4.2312
4.2267
4.1431
4.0836
4.0779
3.7964
3.7804
3.6075
3.3489
3.3146
3.3100
3.3066
3.3020
2.1633
2.1210
2.0821
2.0031
1.9813
1.9424
1.3920
1.3748
1.2867
0.0965

13 NKY 4-2-



(CD_3OD, 100 MHz)

48

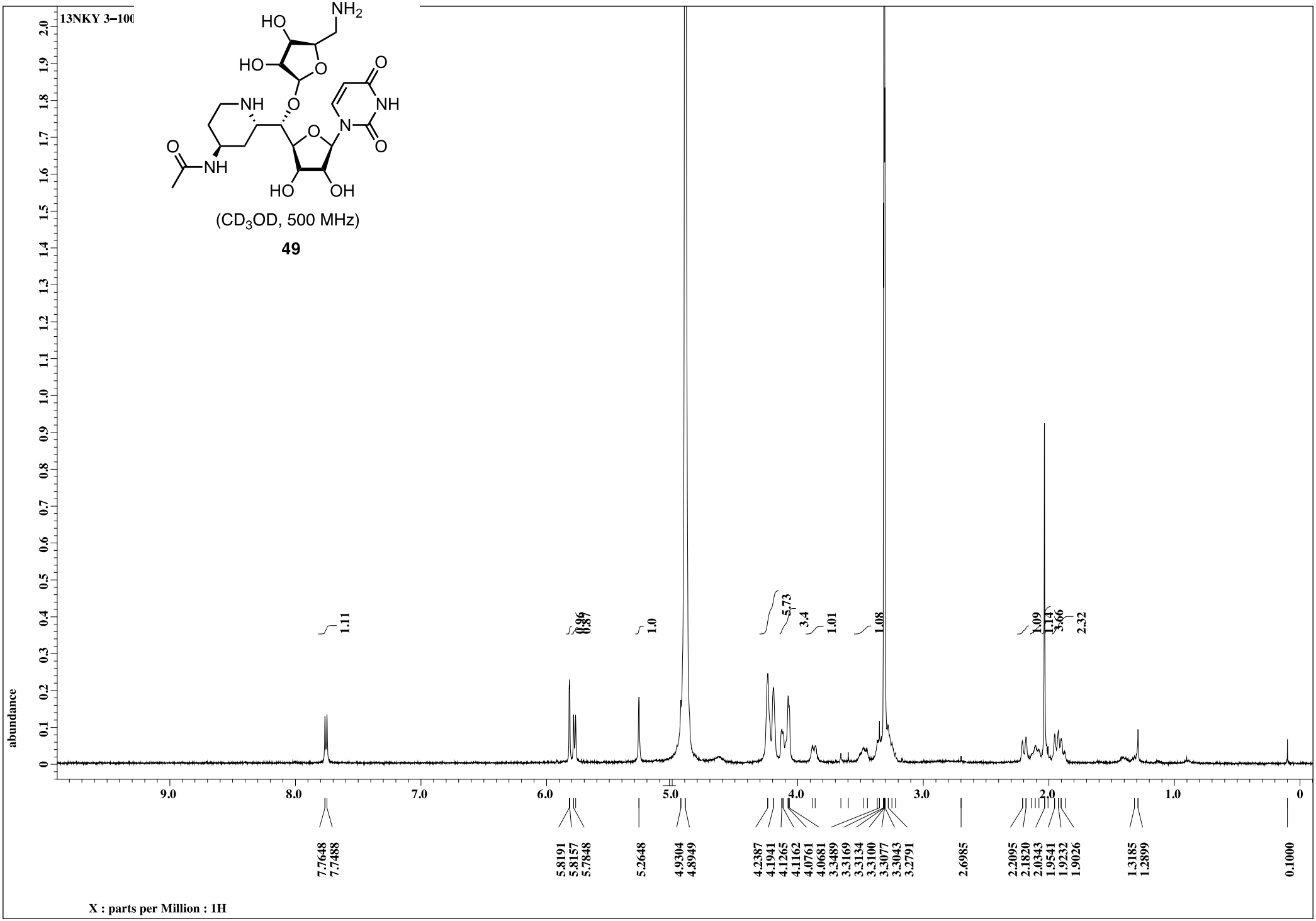
abundance

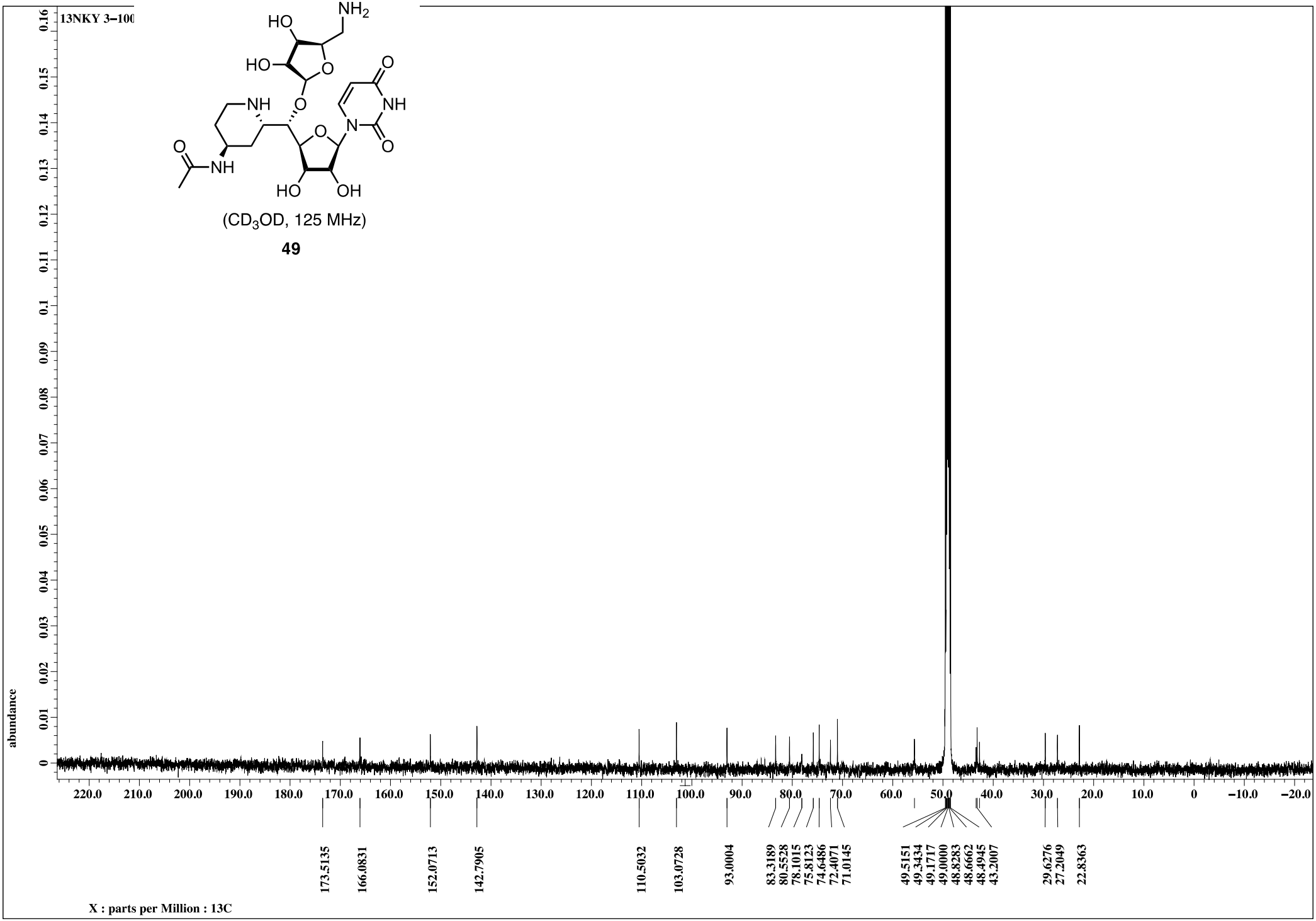
0 0.1 0.2 0.3

220.0 210.0 200.0 190.0 180.0 170.0 160.0 150.0 140.0 130.0 120.0 110.0 100.0 90.0 80.0 70.0 60.0 50.0 40.0 30.0 20.0 10.0 0 −10.0 −20.0

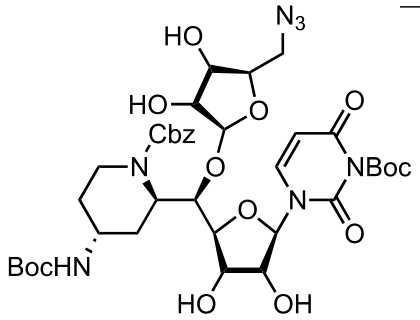
173.4197 166.1195 152.0460 142.6190 110.7548 102.9373 92.6001 83.4413 80.5001 79.0056 75.6142 75.0585 72.3952 70.4216 49.6419 49.4311 49.2108 49.0000 48.7797 48.5689 48.3485 30.8261 26.8407 22.7212

X : parts per Million : 13C


13NKY 3-100
(CD3OD, 500 MHz)
49
abundance
X : parts per Million : 1H
1.11
0.96
0.87
1.0
5.73
3.4
1.01
1.08
1.09
1.14
3.66
2.32
7.7648
7.7488
5.8191
5.8157
5.7848
5.2648
4.9304
4.8949
4.2387
4.1941
4.1265
4.1162
4.0761
4.0681
3.3489
3.3169
3.3134
3.3100
3.3077
3.3043
3.2791
2.6985
2.2095
2.1820
2.0343
1.9541
1.9232
1.9026
1.3185
1.2899
0.1000


13NKY 3-100
(CD3OD, 125 MHz)
49
abundance
X : parts per Million : 13C
173.5135
166.0831
152.0713
142.7905
110.5032
103.0728
93.0004
83.3189
80.5528
78.1015
75.8123
74.6486
72.4071
71.0145
49.5151
49.3434
49.1717
49.0000
48.8283
48.6662
48.4945
43.2007
29.6276
27.2049
22.8363

13 NKY 5–58



(DMSO-d_6, D_2O, 400 MHz)

45

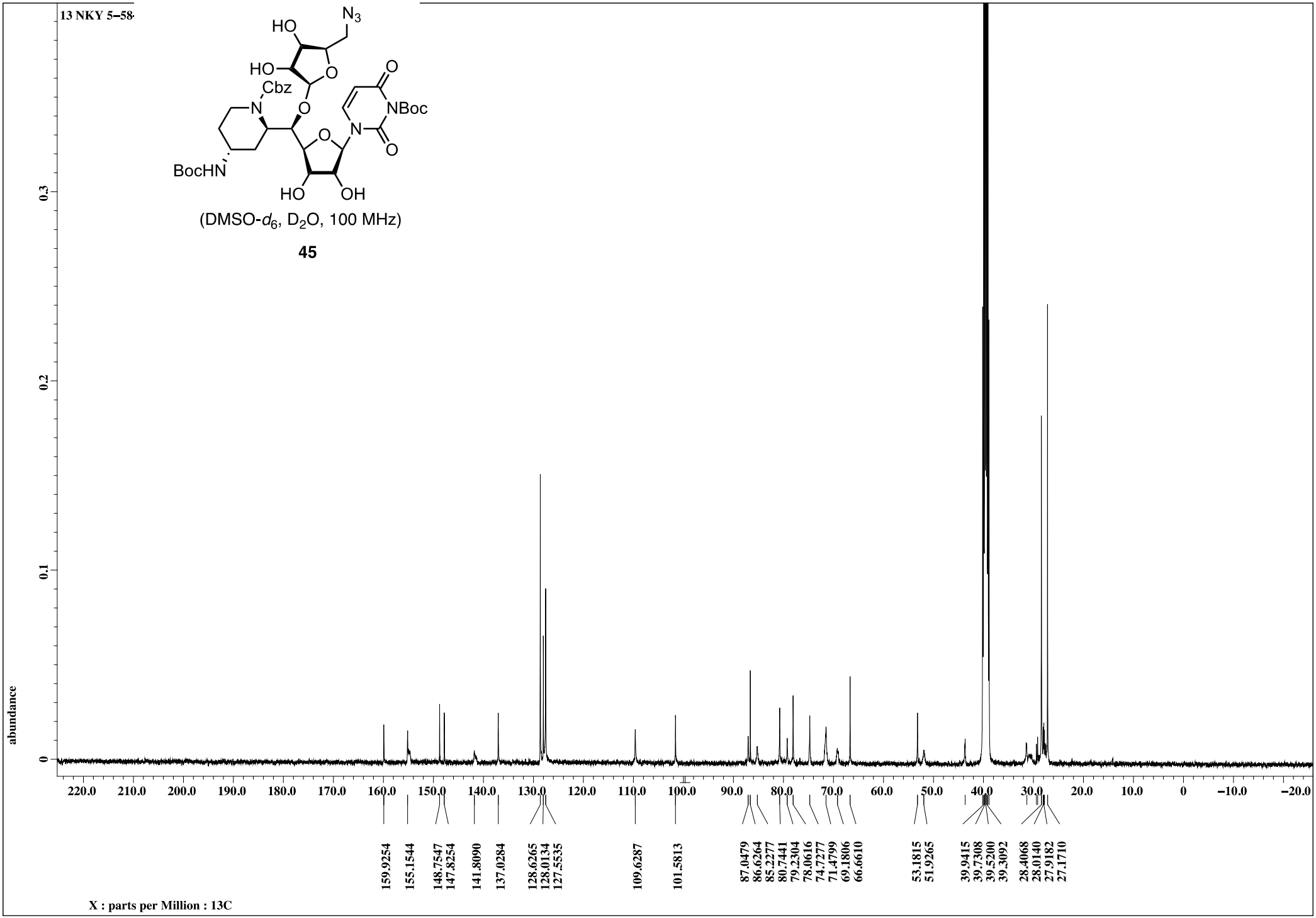
abundance

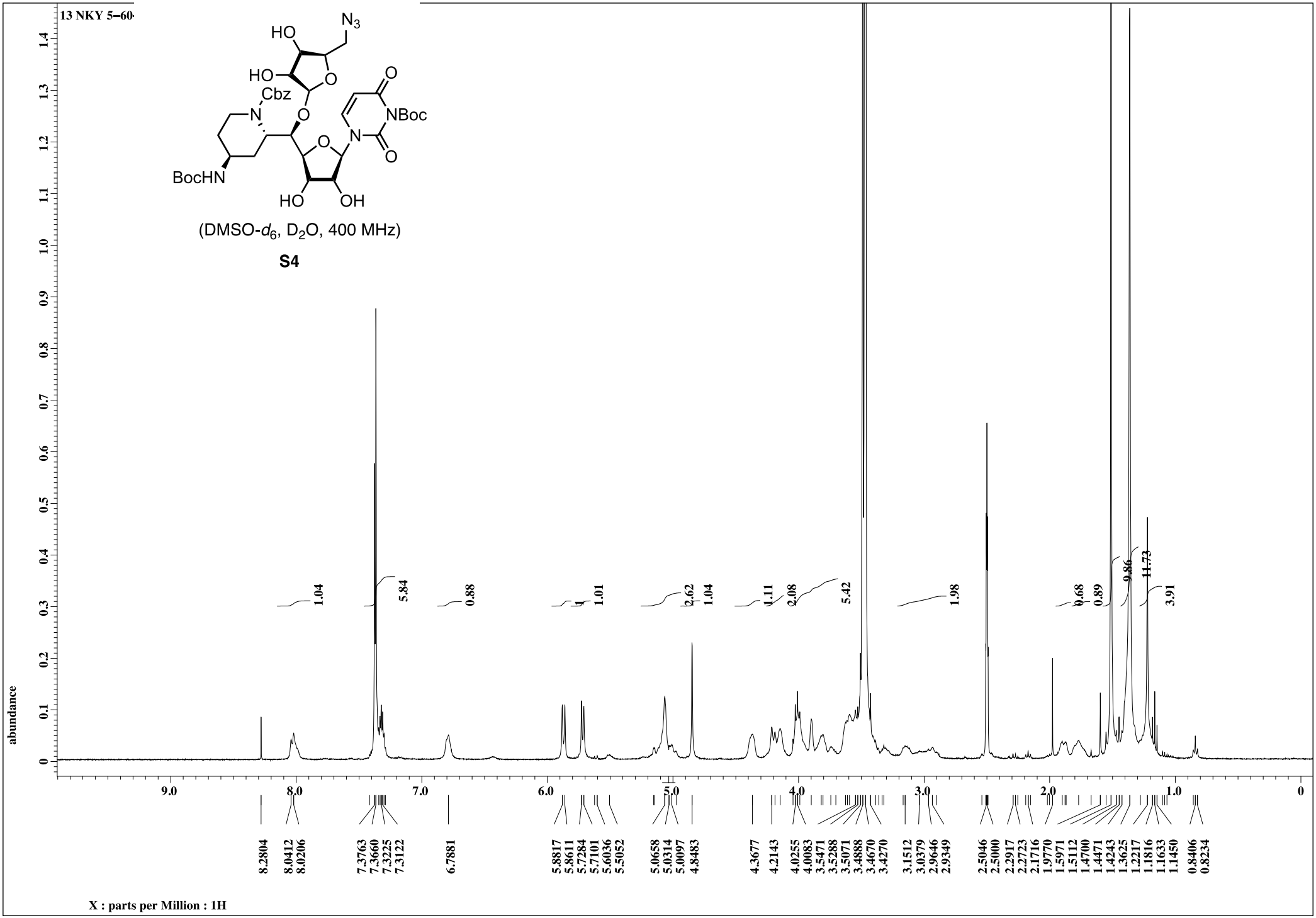
0.89 5.85 0.63 1.83 0.21 4.45 2.16 9.12 1.13 1 1.02 26.32

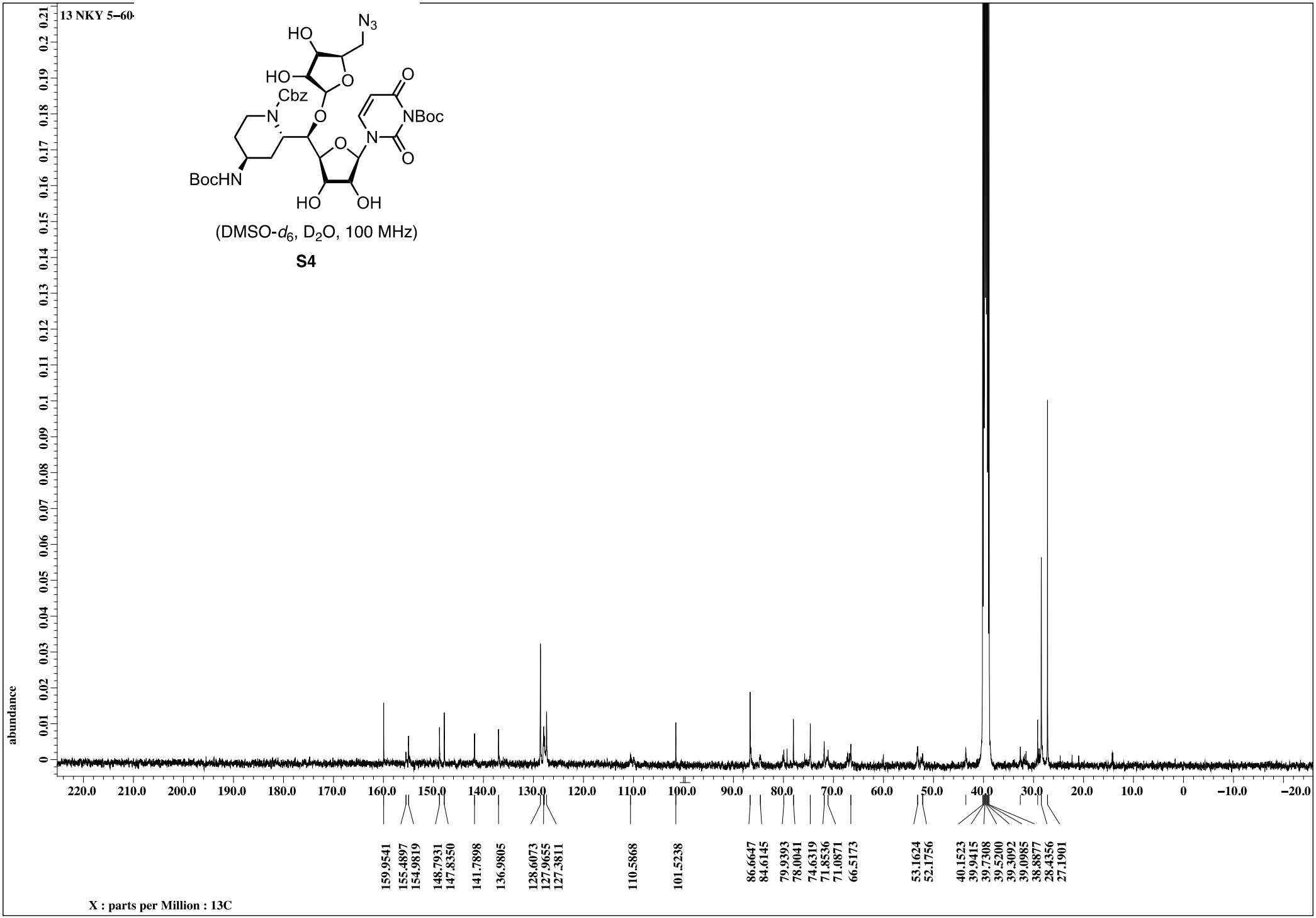
9.0 8.0 7.0 6.0 5.0 4.0 3.0 2.0 1.0 0

7.9371 7.7471 7.6121 7.3420 7.3363 7.3191 6.8213 6.8018 5.8382 5.7295 5.4777 5.1470 5.0875 5.0577 5.0463 4.9605 4.4489 4.4340 4.3150 4.2647 4.0392 3.9111 3.9019 3.8309 3.4922 3.4739 3.4441 3.4224 3.3789 3.0367 2.9337 2.9040 2.5046 2.5000 2.4954 2.4908 2.0491 2.0205 1.9038 1.5776 1.5032 1.4140 1.4082 1.4025 1.3899 1.3659 1.2228 0.8429 0.8246

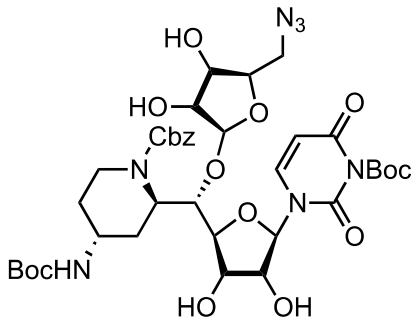
X : parts per Million : 1H


13 NKY 5–58
HO
N3
HO
O
Cbz
N
O
O
NBoc
N
O
BocHN
HO
OH
(DMSO-d6, D2O, 100 MHz)
45
abundance
0
0.1
0.2
0.3
220.0 210.0 200.0 190.0 180.0 170.0 160.0 150.0 140.0 130.0 120.0 110.0 100.0 90.0 80.0 70.0 60.0 50.0 40.0 30.0 20.0 10.0 0 −10.0 −20.0
159.9254
155.1544
148.7547
147.8254
141.8090
137.0284
128.6265
128.0134
127.5535
109.6287
101.5813
87.0479
86.6264
85.2277
80.7441
79.2304
78.0616
74.7277
71.4799
69.1806
66.6610
53.1815
51.9265
39.9415
39.7308
39.5200
39.3092
28.4068
28.0140
27.9182
27.1710
X : parts per Million : 13C


13 NKY 5-60
HO
N3
HO
O
O
Cbz
N
O
NBoc
O
N
O
BocHN
O
HO
OH
(DMSO-d6, D2O, 400 MHz)
S4
abundance
1.04
5.84
0.88
1.01
2.62
1.04
1.11
2.08
5.42
1.98
0.68
0.89
9.86
11.73
3.91
9.0
8.0
7.0
6.0
5.0
4.0
3.0
2.0
1.0
0
8.2804
8.0412
8.0206
7.3763
7.3660
7.3225
7.3122
6.7881
5.8817
5.8611
5.7284
5.7101
5.6036
5.5052
5.0658
5.0314
5.0097
4.8483
4.3677
4.2143
4.0255
4.0083
3.5471
3.5288
3.5071
3.4888
3.4670
3.4270
3.1512
3.0379
2.9646
2.9349
2.5046
2.5000
2.2917
2.2723
2.1716
1.9770
1.5971
1.5112
1.4700
1.4471
1.4243
1.3625
1.2217
1.1816
1.1633
1.1450
0.8406
0.8234
X : parts per Million : 1H

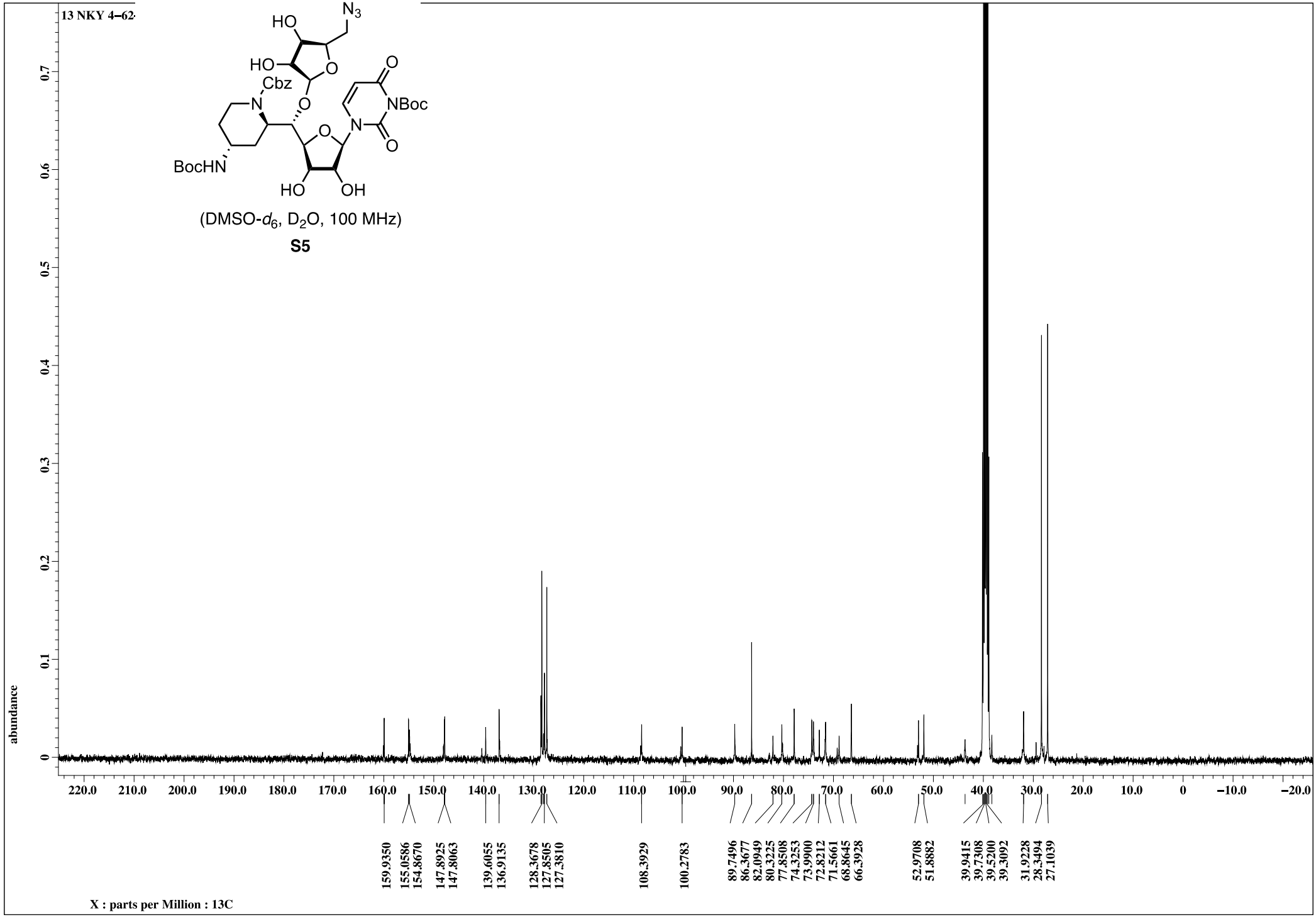

13 NKY 5-60
HO
N3
HO
O
Cbz
N
O
O
NBoc
N
O
BocHN
HO
OH
(DMSO-d6, D2O, 100 MHz)
S4
abundance
X : parts per Million : 13C
159.9541
155.4897
154.9819
148.7931
147.8350
141.7898
136.9805
128.6073
127.9655
127.3811
110.5868
101.5238
86.6647
84.6145
79.9393
78.0041
74.6319
71.8536
71.0871
66.5173
53.1624
52.1756
40.1523
39.9415
39.7308
39.5200
39.3092
39.0985
38.8877
28.4356
27.1901

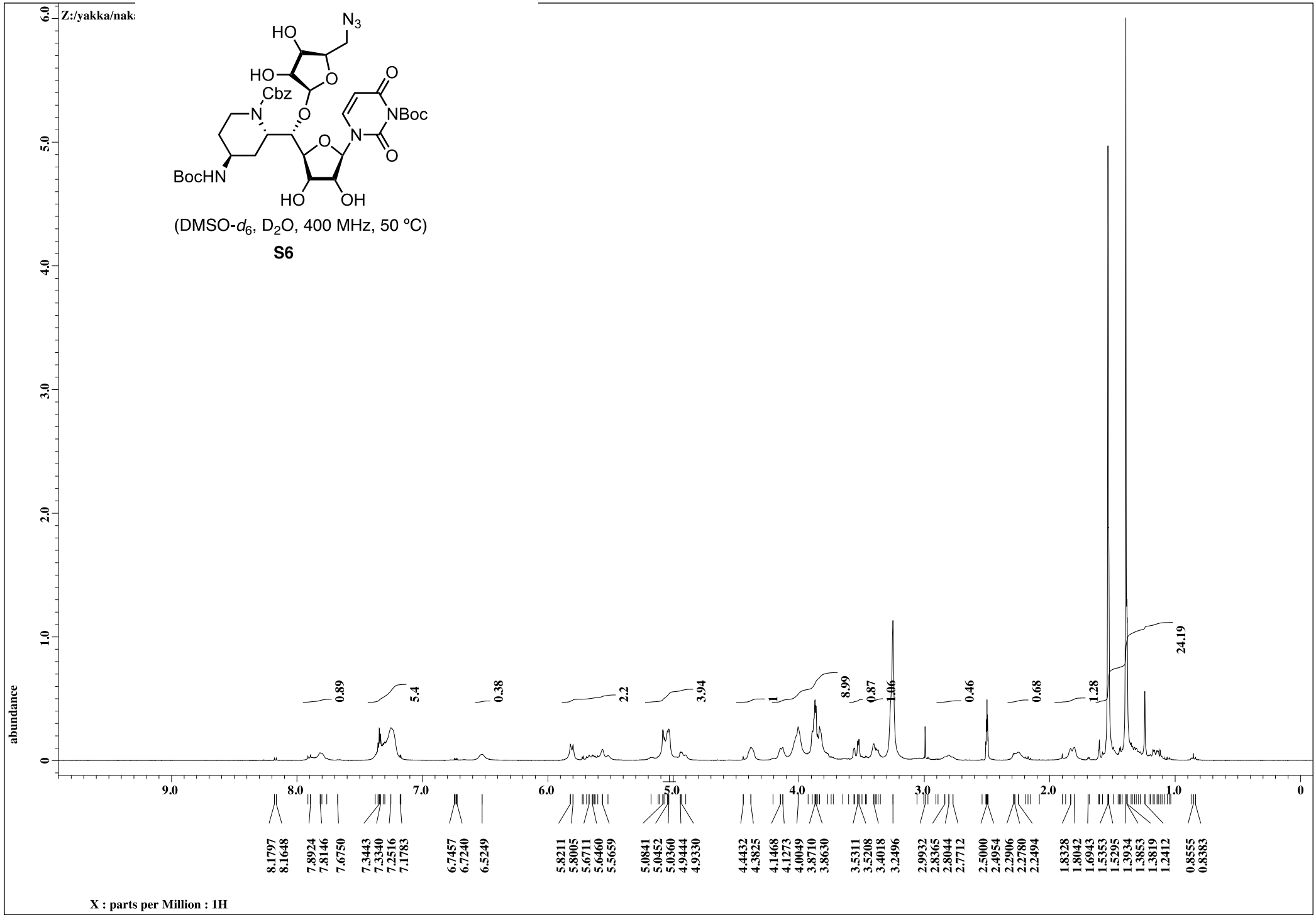
13 NKY 4–62

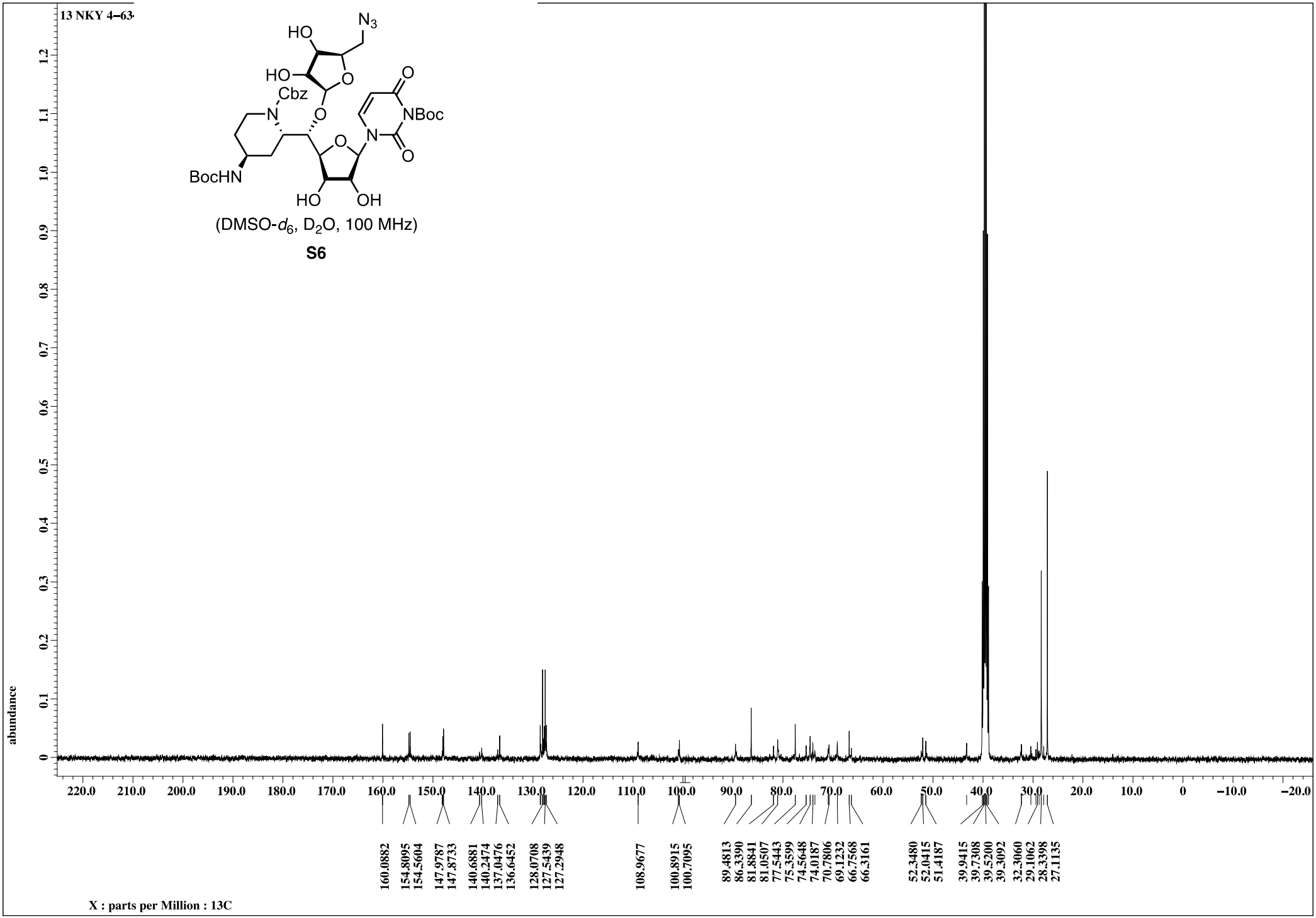


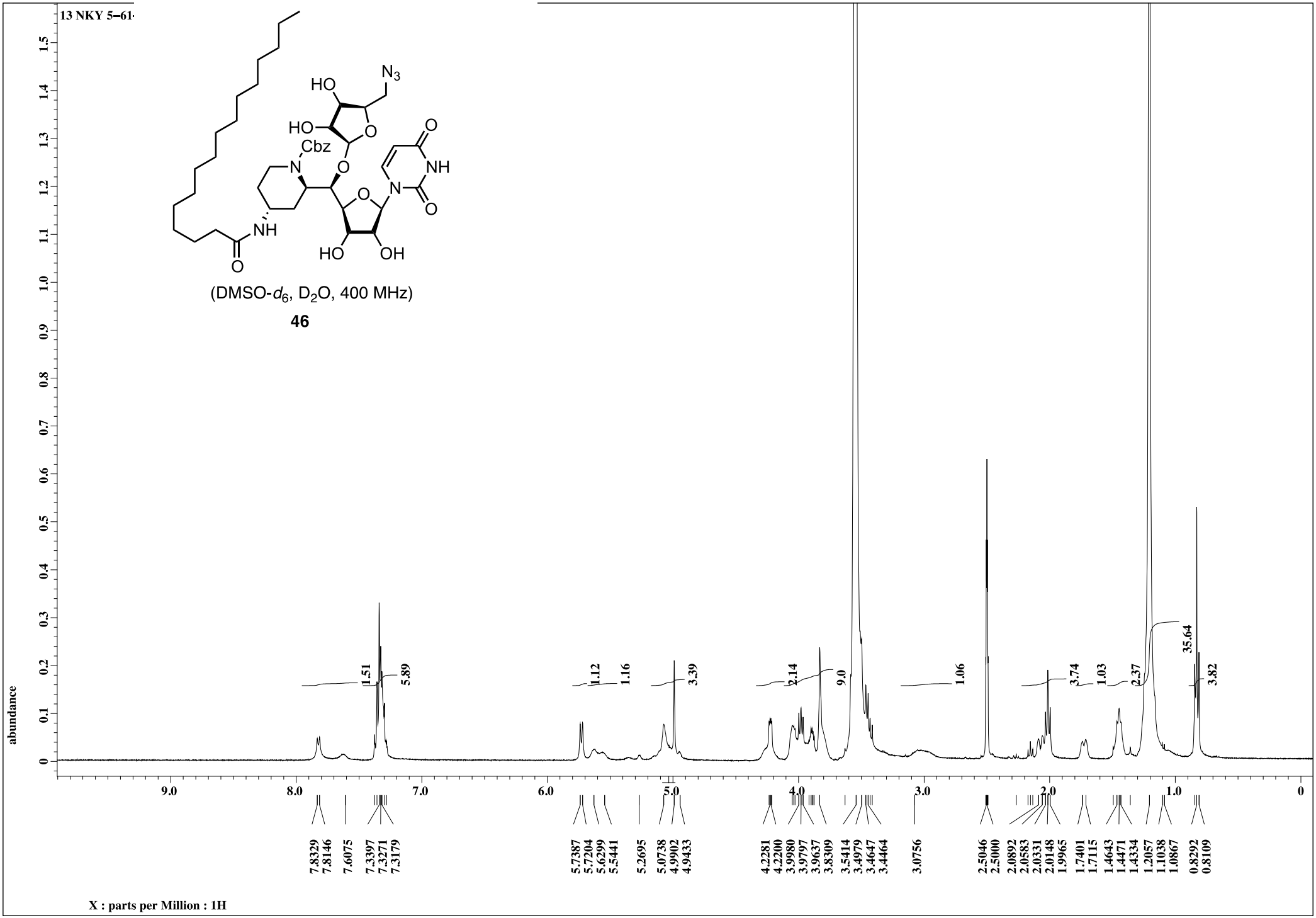
(DMSO-d_6, D_2O, 400 MHz)

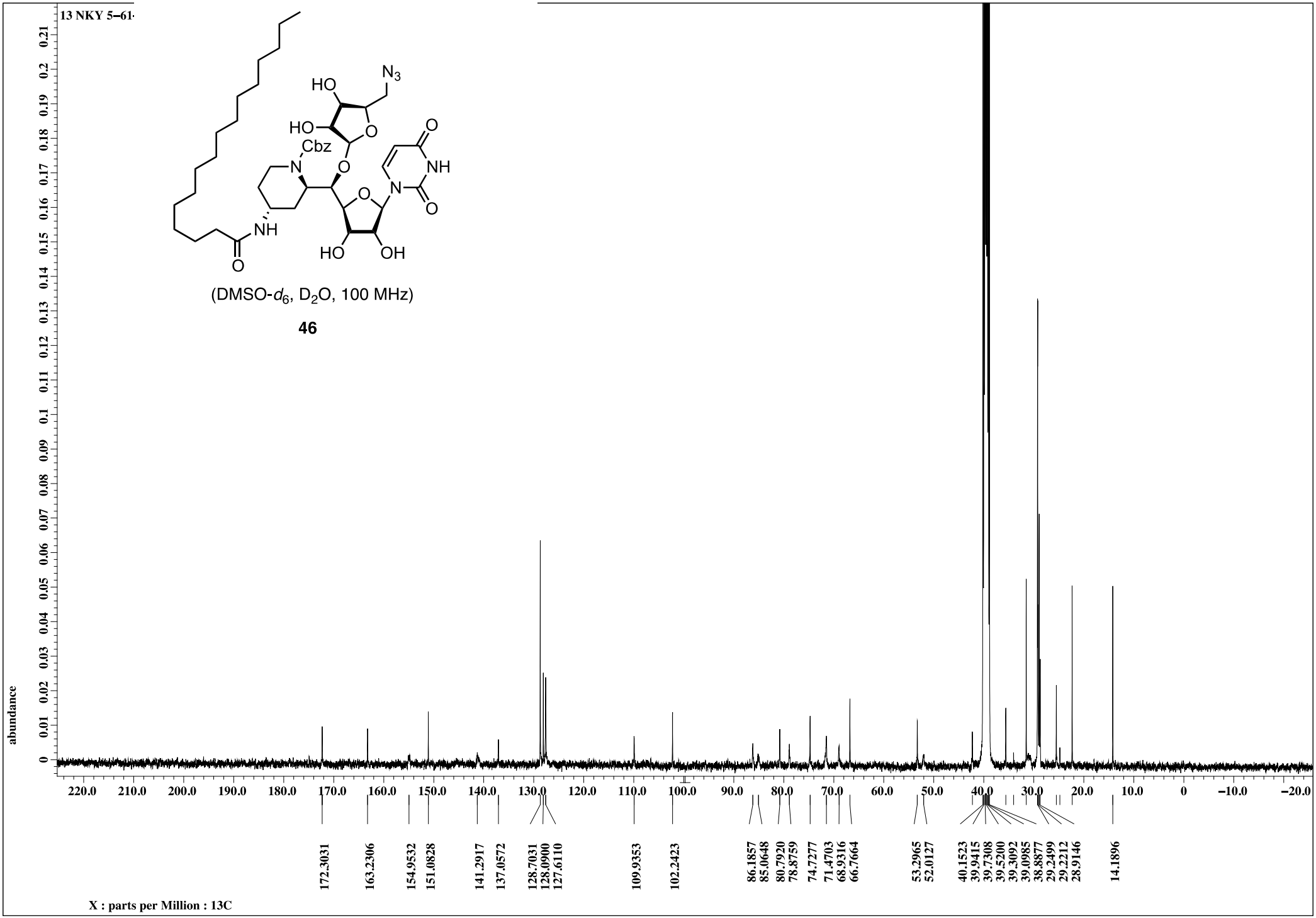
S5

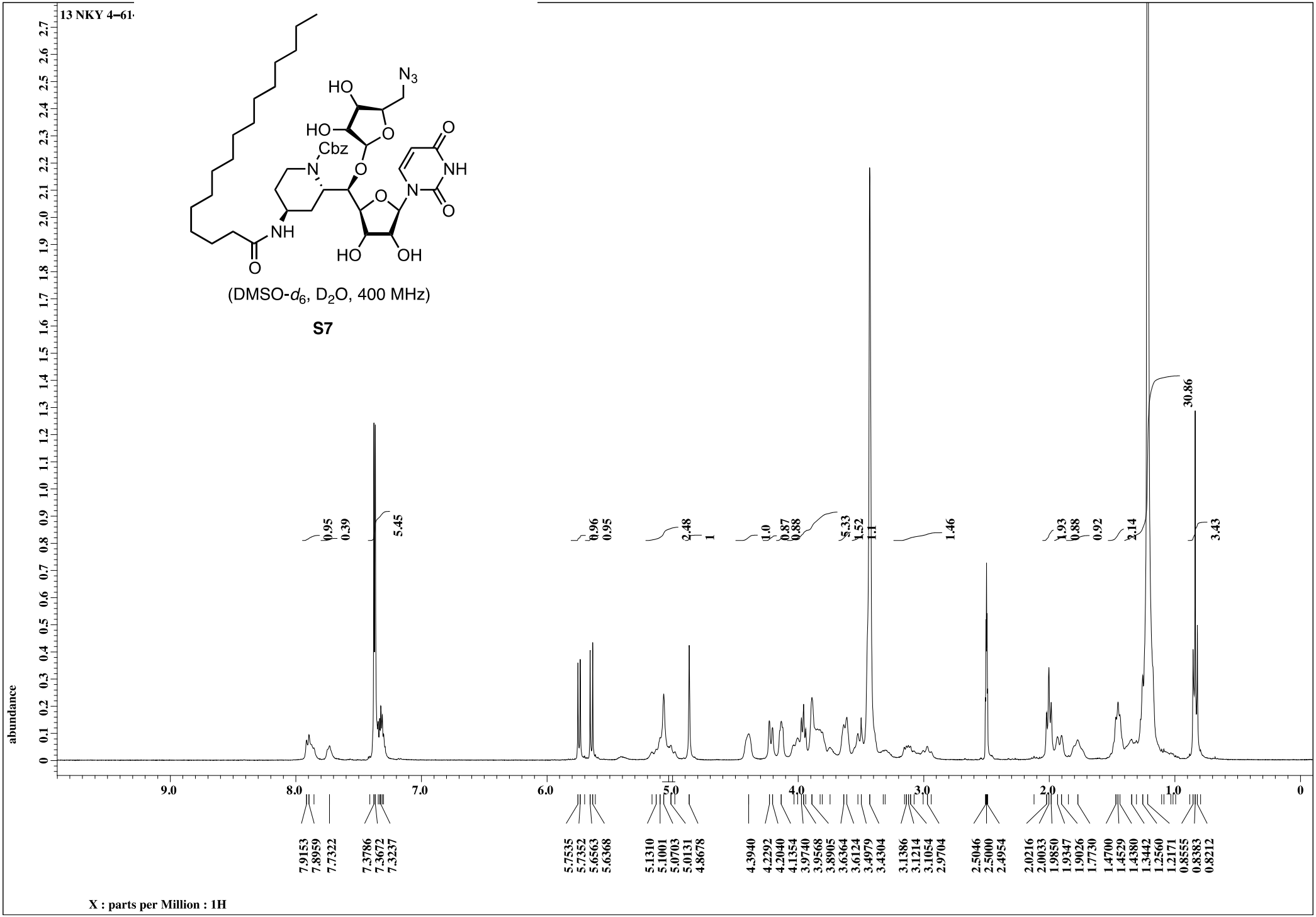

13 NKY 4–62
HO
N3
HO
O
Cbz
N
O
O
NBoc
N
O
BocHN
O
HO
OH
(DMSO-d6, D2O, 100 MHz)
S5
abundance
0
0.1
0.2
0.3
0.4
0.5
0.6
0.7
220.0
210.0
200.0
190.0
180.0
170.0
160.0
150.0
140.0
130.0
120.0
110.0
100.0
90.0
80.0
70.0
60.0
50.0
40.0
30.0
20.0
10.0
0
−10.0
−20.0
159.9350
155.0586
154.8670
147.8925
147.8063
139.6055
136.9135
128.3678
127.8505
127.3810
108.3929
100.2783
89.7496
86.3677
82.0949
80.3225
77.8508
74.3253
73.9900
72.8212
71.5661
68.8645
66.3928
52.9708
51.8882
39.9415
39.7308
39.5200
39.3092
31.9228
28.3494
27.1039
X : parts per Million : 13C


Z:/yakka/nak
HO
N3
HO
O
Cbz
N
O
O
NBoc
N
O
O
BocHN
HO
OH
(DMSO-d6, D2O, 400 MHz, 50 °C)
S6
abundance
0.89
5.4
0.38
2.2
3.94
1
8.99
0.87
1.06
0.46
0.68
1.28
24.19
X : parts per Million : 1H


13 NKY 4-63
HO
N3
HO
O
Cbz
N
O
O
NBoc
N
O
BocHN
HO
OH
(DMSO-d6, D2O, 100 MHz)
S6
abundance
160.0882
154.8095
154.5604
147.9787
147.8733
140.6881
140.2474
137.0476
136.6452
128.0708
127.5439
127.2948
108.9677
100.8915
100.7095
89.4813
86.3390
81.8841
81.0507
77.5443
75.3599
74.5648
74.0187
70.7806
69.1232
66.7568
66.3161
52.3480
52.0415
51.4187
39.9415
39.7308
39.5200
39.3092
32.3060
29.1062
28.3398
27.1135
X : parts per Million : 13C

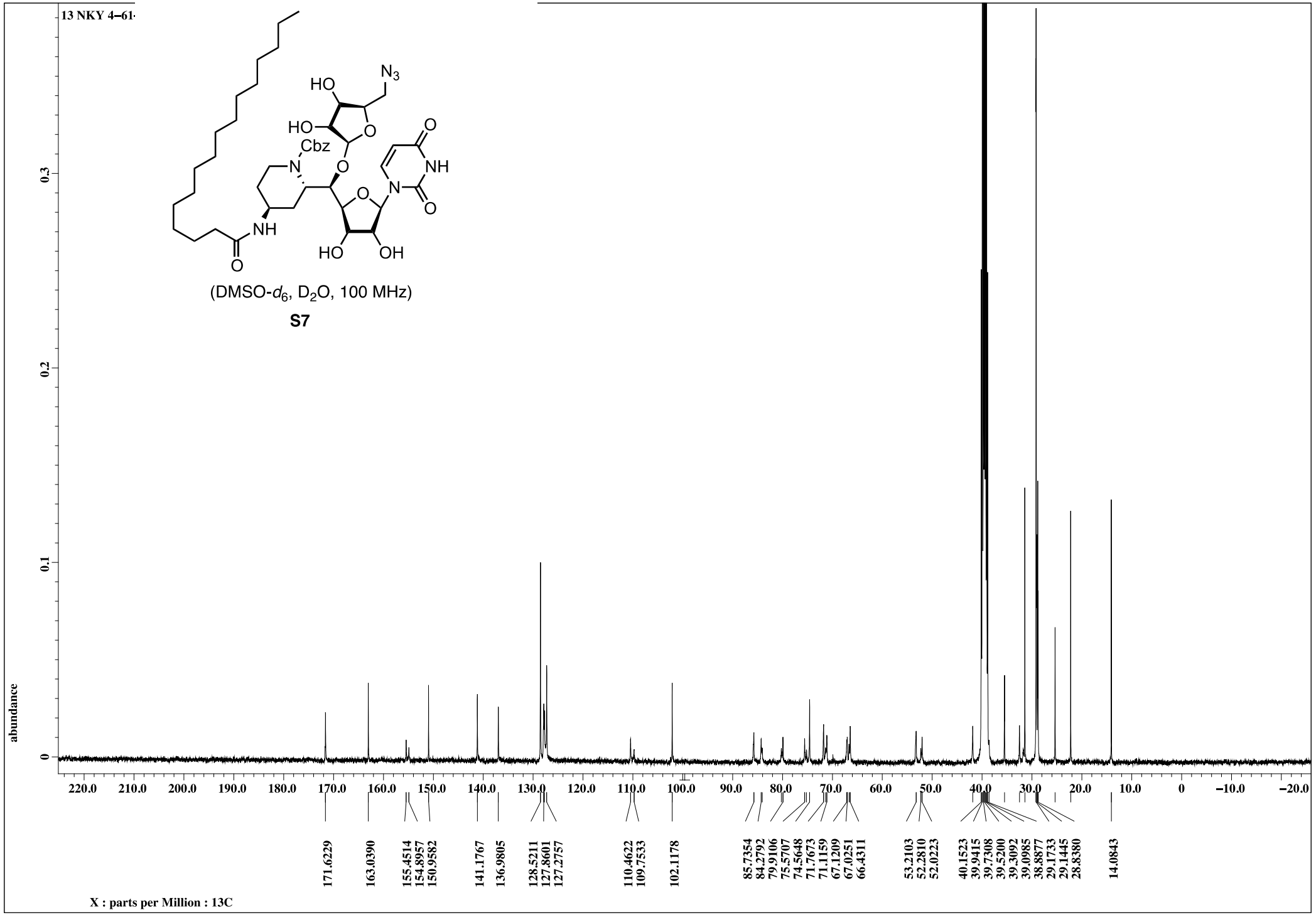

13 NKY 5–61
HO
N3
HO
O
O
Cbz
N
O
NH
N
O
O
NH
HO
OH
O
(DMSO-d6, D2O, 400 MHz)
46
abundance
1.51
5.89
1.12
1.16
3.39
2.14
9.0
1.06
3.74
1.03
2.37
35.64
3.82
9.0
8.0
7.0
6.0
5.0
4.0
3.0
2.0
1.0
0
7.8329
7.8146
7.6075
7.3397
7.3271
7.3179
5.7387
5.7204
5.6299
5.5441
5.2695
5.0738
4.9902
4.9433
4.2281
4.2200
3.9980
3.9797
3.9637
3.8309
3.5414
3.4979
3.4647
3.4464
3.0756
2.5046
2.5000
2.0892
2.0583
2.0331
2.0148
1.9965
1.7401
1.7115
1.4643
1.4471
1.4334
1.2057
1.1038
1.0867
0.8292
0.8109
X : parts per Million : 1H


13 NKY 5–61
HO
N3
HO
O
Cbz
N
O
O
NH
N
O
NH
HO
OH
O
(DMSO-d6, D2O, 100 MHz)
46
abundance
X : parts per Million : 13C
172.3031
163.2306
154.9532
151.0828
141.2917
137.0572
128.7031
128.0900
127.6110
109.9353
102.2423
86.1857
85.0648
80.7920
78.8759
74.7277
71.4703
68.9316
66.7664
53.2965
52.0127
40.1523
39.9415
39.7308
39.5200
39.3092
39.0985
38.8877
29.2499
29.2212
28.9146
14.1896

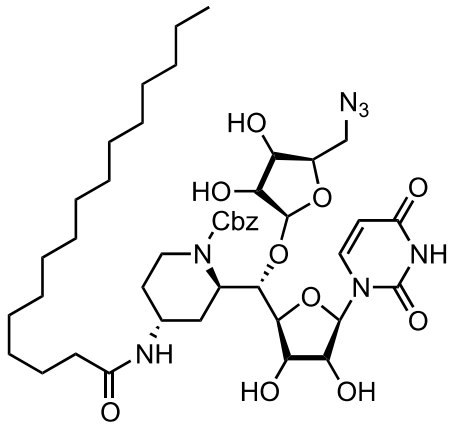


(DMSO-d_6, D_2O, 400 MHz)

S7


13 NKY 4–61
HO
N3
HO
O
Cbz
N
O
O
NH
N
O
NH
HO
OH
O
(DMSO-d6, D2O, 100 MHz)
S7
abundance
0
0.1
0.2
0.3
220.0 210.0 200.0 190.0 180.0 170.0 160.0 150.0 140.0 130.0 120.0 110.0 100.0 90.0 80.0 70.0 60.0 50.0 40.0 30.0 20.0 10.0 0 −10.0 −20.0
171.6229
163.0390
155.4514
154.8957
150.9582
141.1767
136.9805
128.5211
127.8601
127.2757
110.4622
109.7533
102.1178
85.7354
84.2792
79.9106
75.5707
74.5648
71.7673
71.1159
67.1209
67.0251
66.4311
53.2103
52.2810
52.0223
40.1523
39.9415
39.7308
39.5200
39.3092
39.0985
38.8877
29.1733
29.1445
28.8380
14.0843
X : parts per Million : 13C

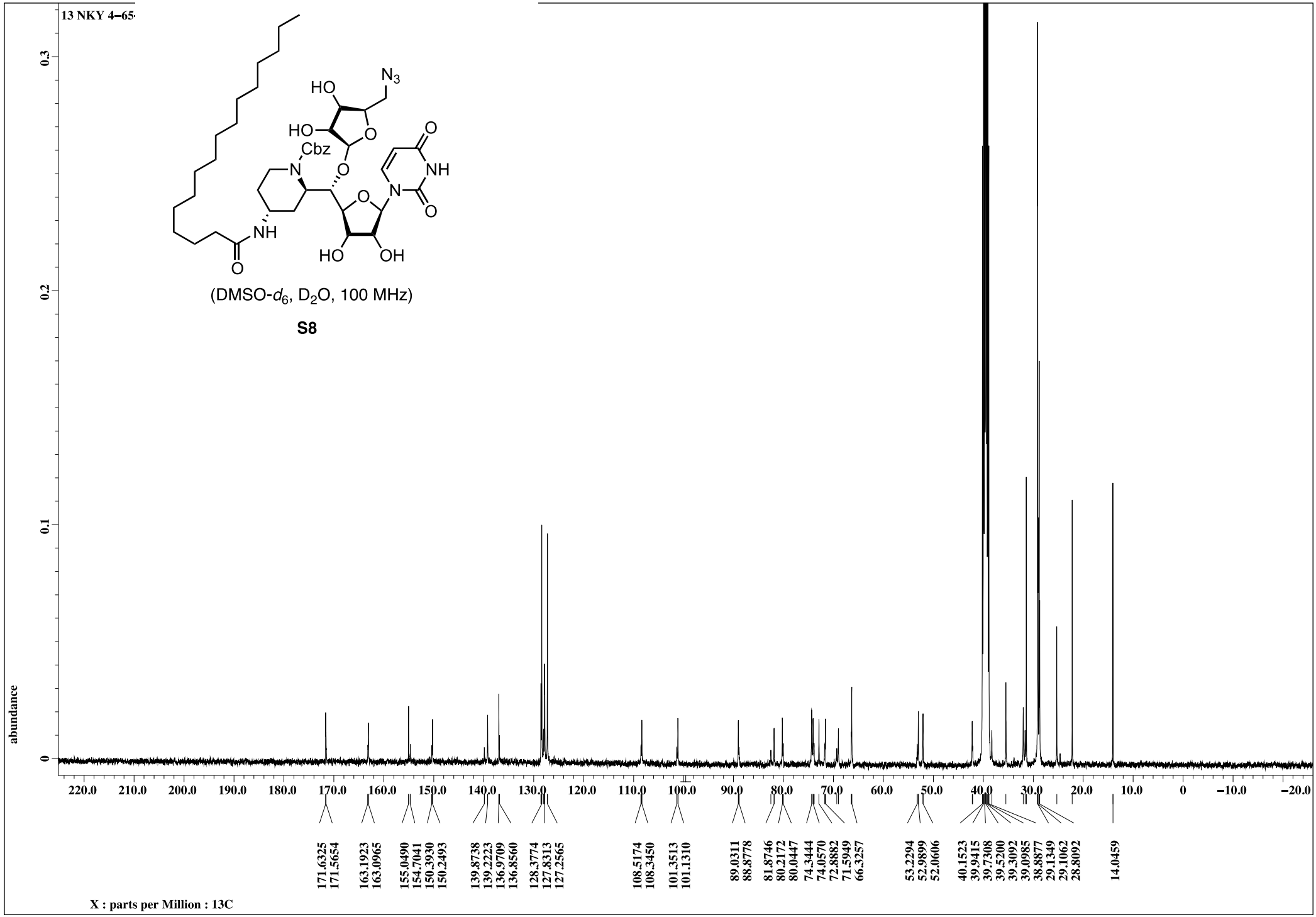
13 NKY 4–65



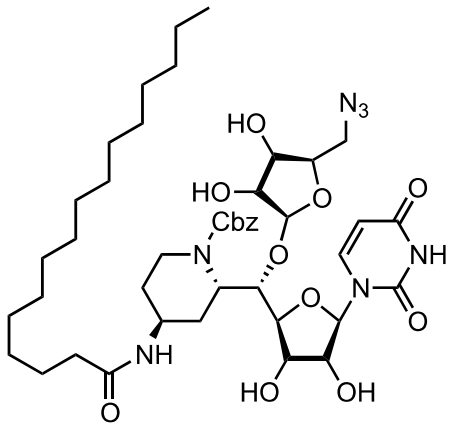
(DMSO-d_6, D_2O, 400 MHz)

S8

X : parts per Million : 1H


13 NKY 4-65
HO
N3
HO
O
Cbz
N
O
NH
O
N
O
NH
HO
OH
O
(DMSO-d6, D2O, 100 MHz)
S8
abundance
0
0.1
0.2
0.3
220.0 210.0 200.0 190.0 180.0 170.0 160.0 150.0 140.0 130.0 120.0 110.0 100.0 90.0 80.0 70.0 60.0 50.0 40.0 30.0 20.0 10.0 0 −10.0 −20.0
171.6325
171.5654
163.1923
163.0965
155.0490
154.7041
150.3930
150.2493
139.8738
139.2223
136.9709
136.8560
128.3774
127.8313
127.2565
108.5174
108.3450
101.3513
101.1310
89.0311
88.8778
81.8746
80.2172
80.0447
74.3444
74.0570
72.8882
71.5949
66.3257
53.2294
52.9899
52.0606
40.1523
39.9415
39.7308
39.5200
39.3092
39.0985
38.8877
29.1349
29.1062
28.8092
14.0459
X : parts per Million : 13C

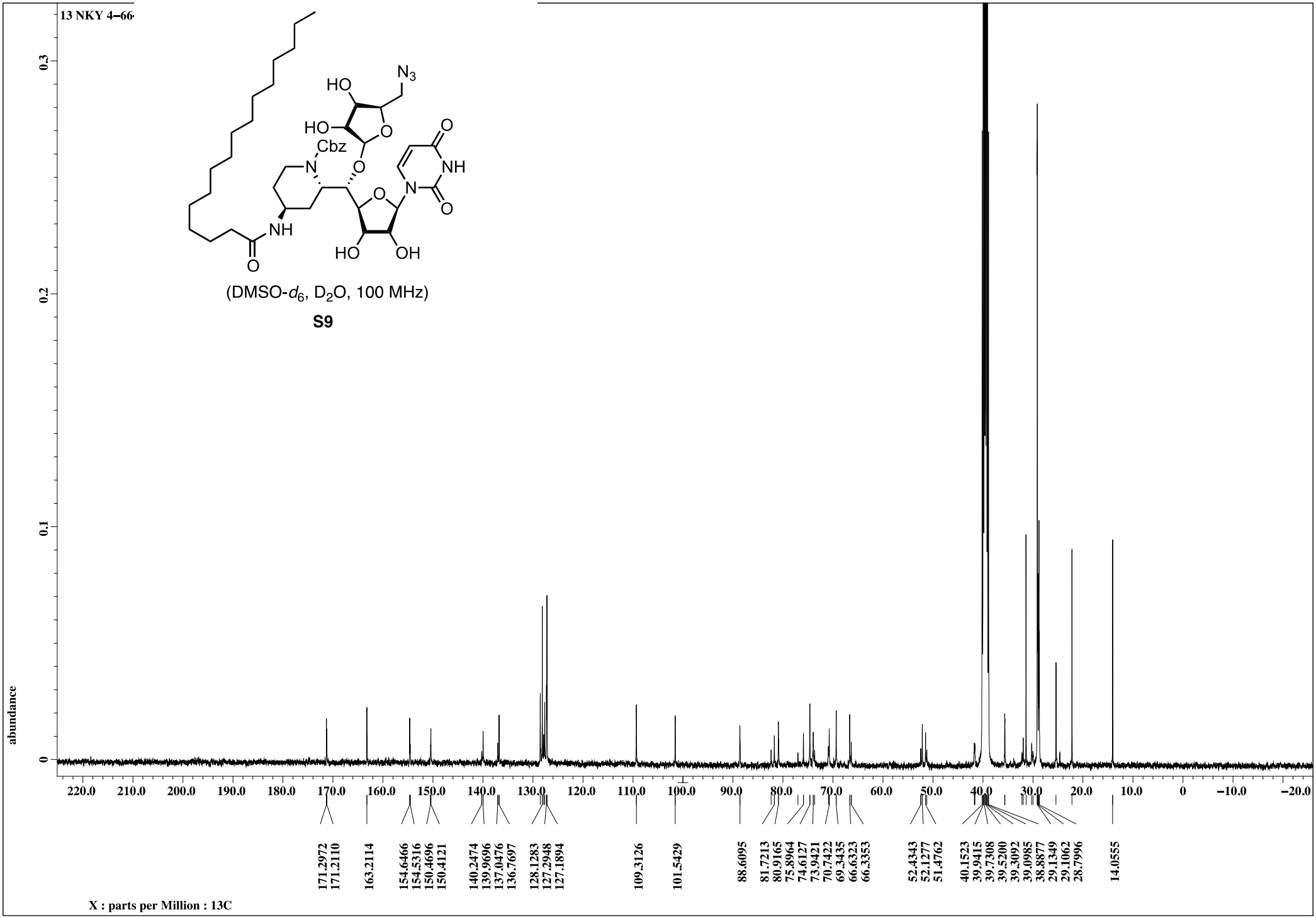
13NKY 4–66-



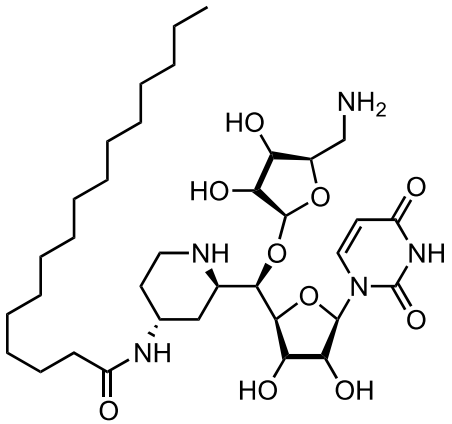
(DMSO-d_6, D_2O, 500 MHz)

S9

X : parts per Million : 1H


13 NKY 4-66
HO
N3
HO
O
Cbz
N
O
O
NH
N
O
O
NH
HO
OH
O
(DMSO-d6, D2O, 100 MHz)
S9
abundance
0
0.1
0.2
0.3
220.0 210.0 200.0 190.0 180.0 170.0 160.0 150.0 140.0 130.0 120.0 110.0 100.0 90.0 80.0 70.0 60.0 50.0 40.0 30.0 20.0 10.0 0 −10.0 −20.0
171.2972
171.2110
163.2114
154.6466
154.5316
150.4696
150.4121
140.2474
139.9696
137.0476
136.7697
128.1283
127.2948
127.1894
109.3126
101.5429
88.6095
81.7213
80.9165
75.8964
74.6127
73.9421
70.7422
69.3435
66.6323
66.3353
52.4343
52.1277
51.4762
40.1523
39.9415
39.7308
39.5200
39.3092
39.0985
38.8877
29.1349
29.1062
28.7996
14.0555
X : parts per Million : 13C

13 NKY 4-46



(CD_3OD, 400 MHz)

5

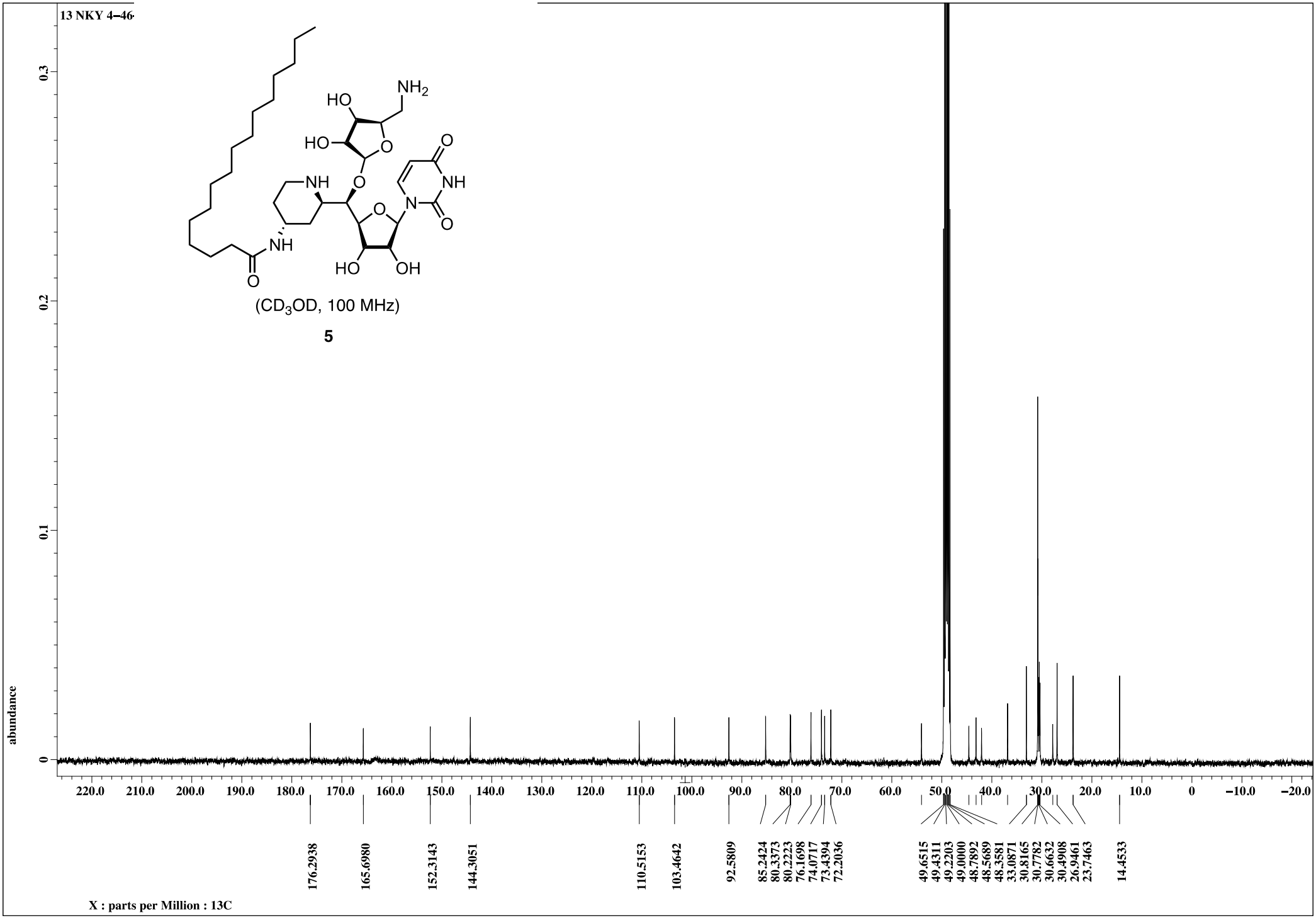
abundance

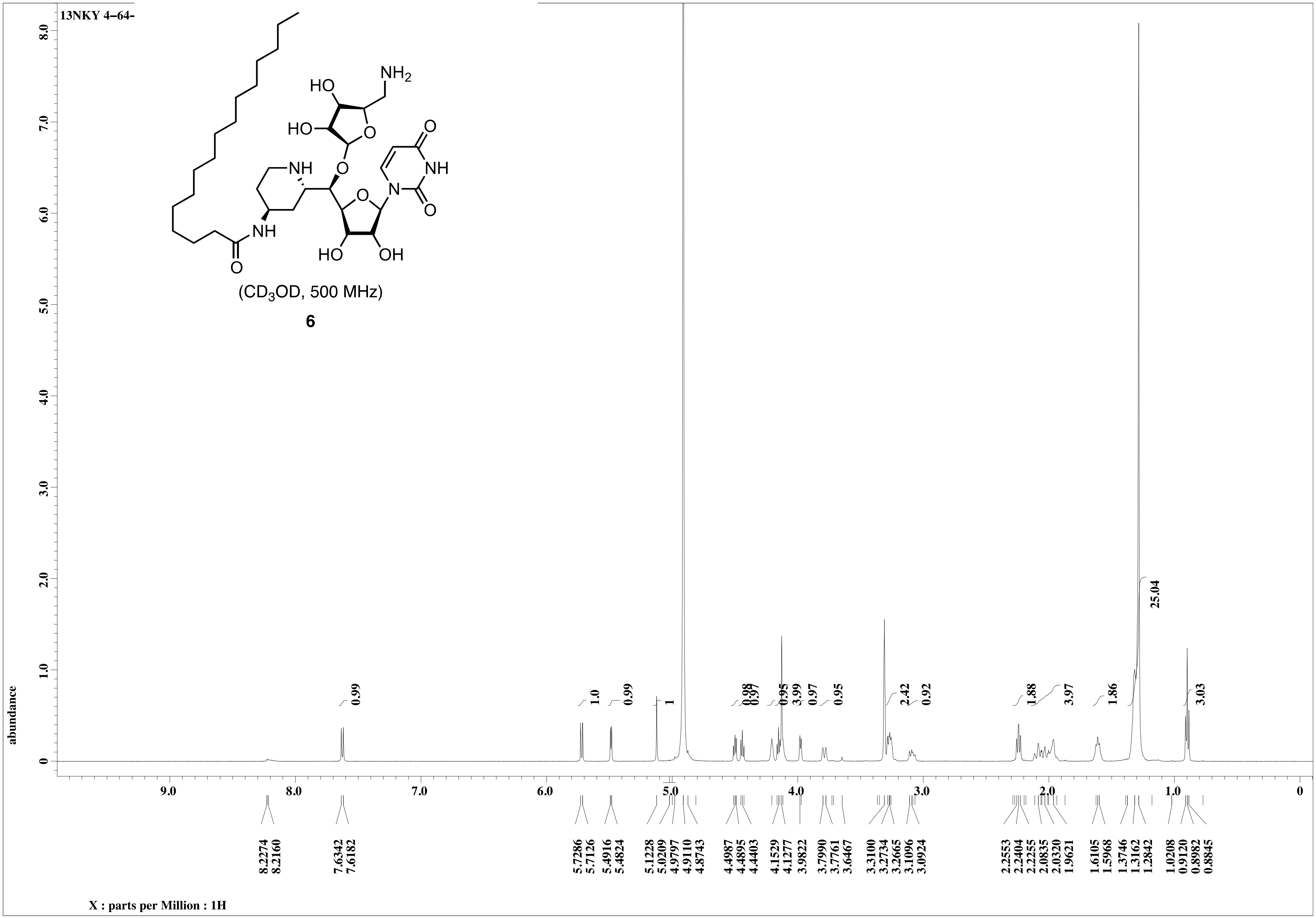
0.47 0.95 1.9 0.91 1.86 4.86 0.93 0.9 1.65 0.97 3.83 1.74 2.46 27.56 2.97

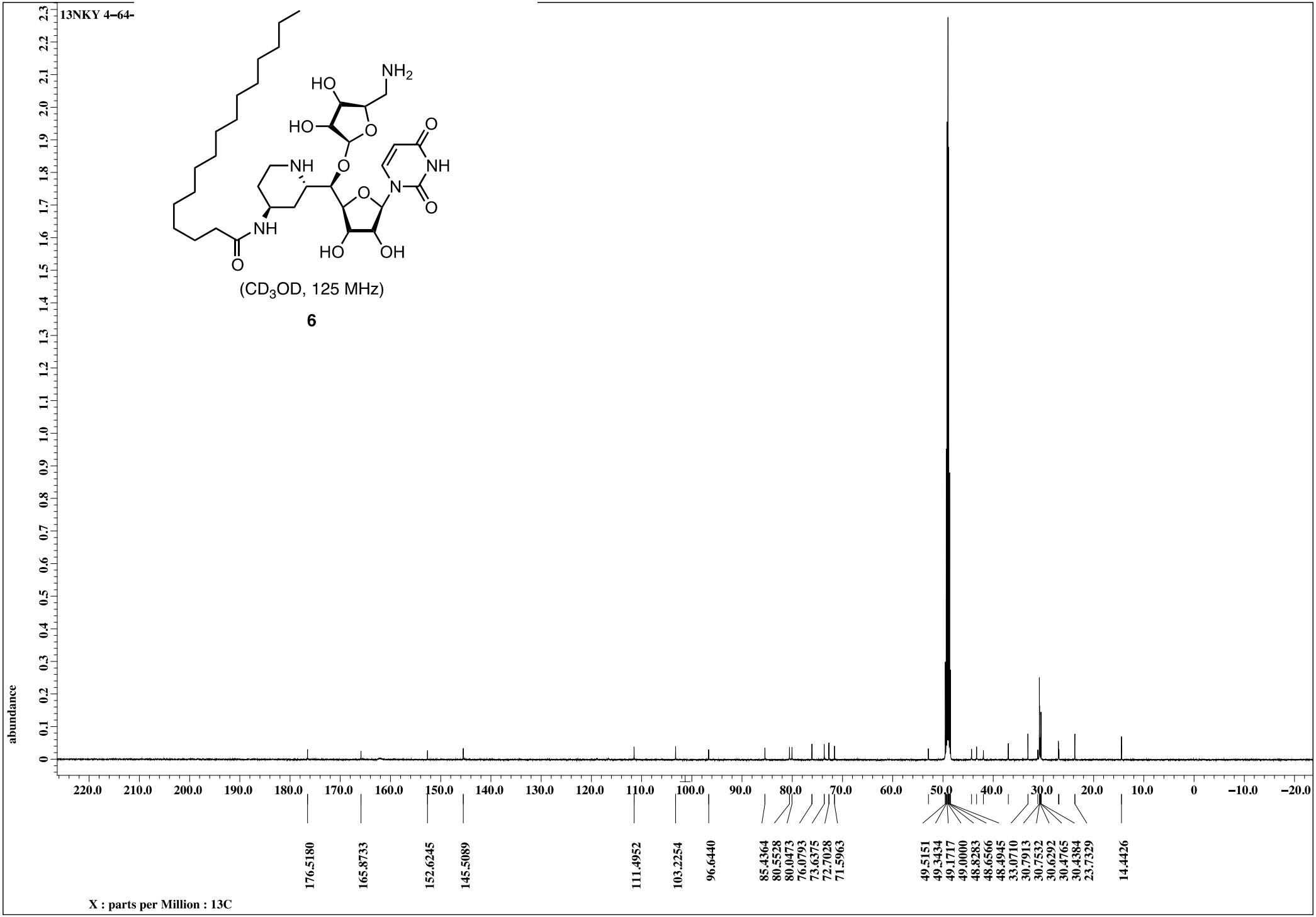
9.0 8.0 7.0 6.0 5.0 4.0 3.0 2.0 1.0 0

8.1474 8.1325 7.6656 7.6462 5.7453 5.7258 5.6400 5.6251 5.1296 4.9270 4.8893 4.8527 4.5151 4.5013 4.4773 4.2129 4.1260 4.1134 3.9348 3.9188 3.7266 3.6991 3.6522 3.3134 3.3100 3.3054 3.0937 3.0697 3.0617 2.0981 2.0809 2.0740 2.0592 1.8841 1.8509 1.5396 1.5121 1.4950 1.4732 1.3245 1.2867 1.2512 0.8999 0.8827

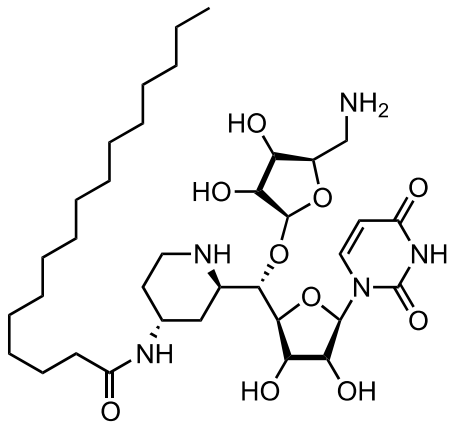
X : parts per Million : 1H


13 NKY 4–46
(CD3OD, 100 MHz)
5
abundance
X : parts per Million : 13C
176.2938
165.6980
152.3143
144.3051
110.5153
103.4642
92.5809
85.2424
80.3373
80.2223
76.1698
74.0717
73.4394
72.2036
49.6515
49.4311
49.2203
49.0000
48.7892
48.5689
48.3581
33.0871
30.8165
30.7782
30.6632
30.4908
26.9461
23.7463
14.4533


13NKY 4-64-
NH2
HO
HO
O
NH
O
N
NH
O
O
NH
O
HO
OH
(CD3OD, 500 MHz)
6
abundance
X : parts per Million : 1H
0.99
1.0
0.99
1
0.98
0.97
0.95
3.99
0.97
0.95
2.42
0.92
1.88
3.97
1.86
25.04
3.03
8.2274
8.2160
7.6342
7.6182
5.7286
5.7126
5.4916
5.4824
5.1228
5.0209
4.9797
4.9110
4.8743
4.4987
4.4895
4.4403
4.1529
4.1277
3.9822
3.7990
3.7761
3.6467
3.3100
3.2734
3.2665
3.1096
3.0924
2.2553
2.2404
2.2255
2.0835
2.0320
1.9621
1.6105
1.5968
1.3746
1.3162
1.2842
1.0208
0.9120
0.8982
0.8845


13NKY 4–64-
NH2
HO
HO
O
O
NH
NH
O
N
O
NH
O
HO
OH
(CD3OD, 125 MHz)
6
abundance
X : parts per Million : 13C
176.5180
165.8733
152.6245
145.5089
111.4952
103.2254
96.6440
85.4364
80.5528
80.0473
76.0793
73.6375
72.7028
71.5963
49.5151
49.3434
49.1717
49.0000
48.8283
48.6566
48.4945
33.0710
30.7913
30.7532
30.6292
30.4765
30.4384
23.7329
14.4426

13 NKY 4–69



(CD_3OD, 400 MHz)

7

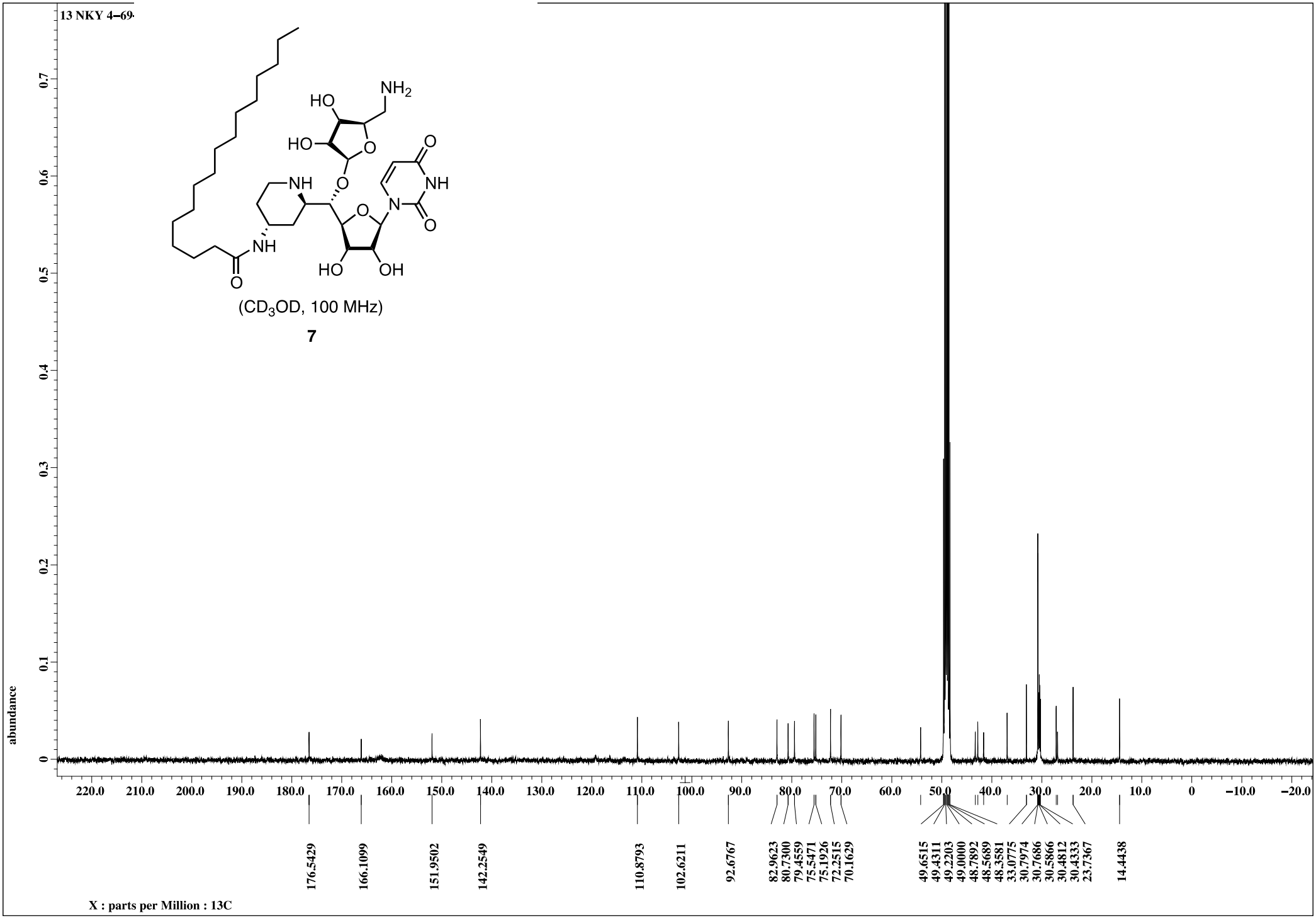
abundance

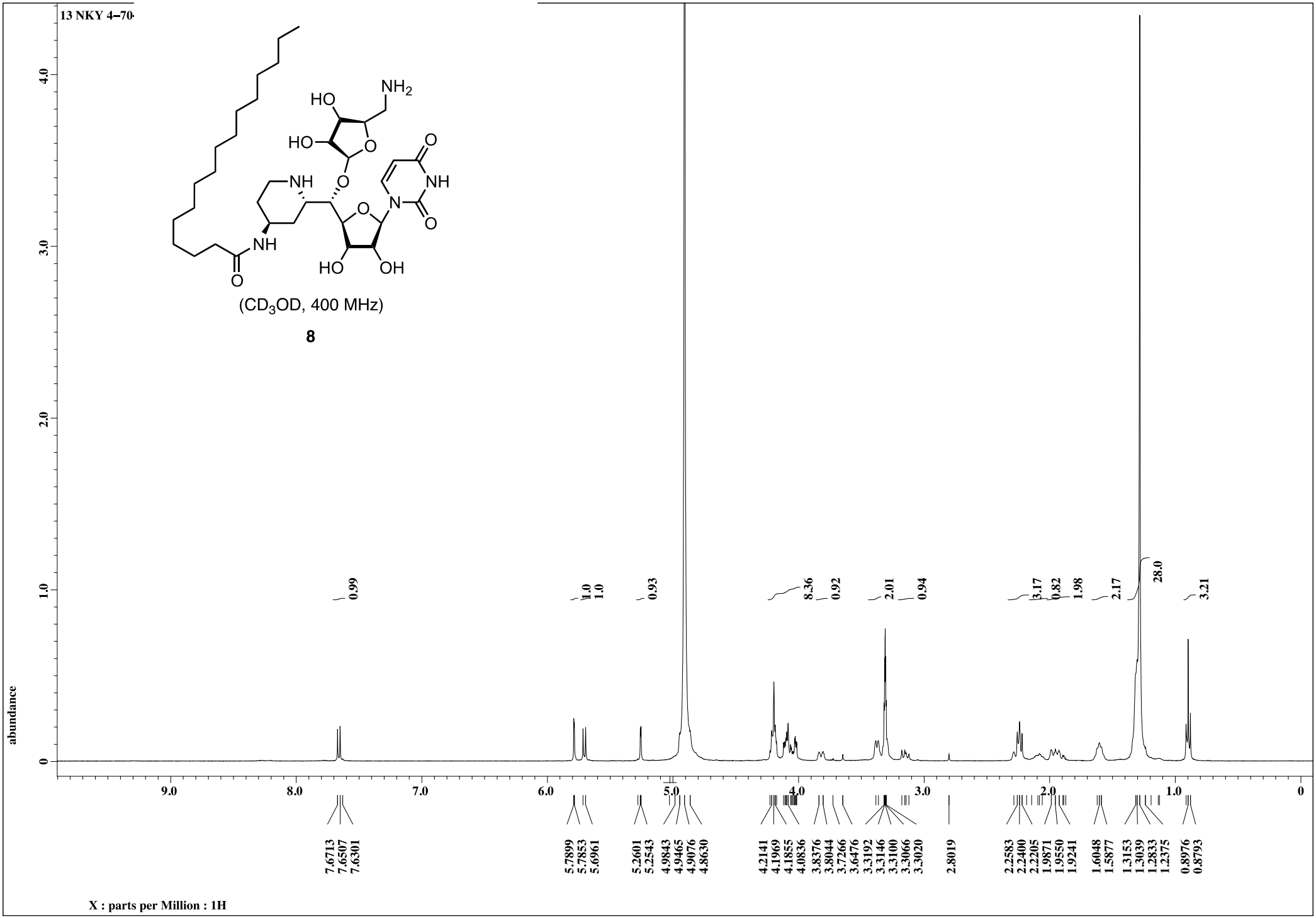
1.05 2.04 0.95 0.94 3.11 3.03 1.02 1 0.98 1.07 3.14 2.08 1.06 2.0 26.61 3.05

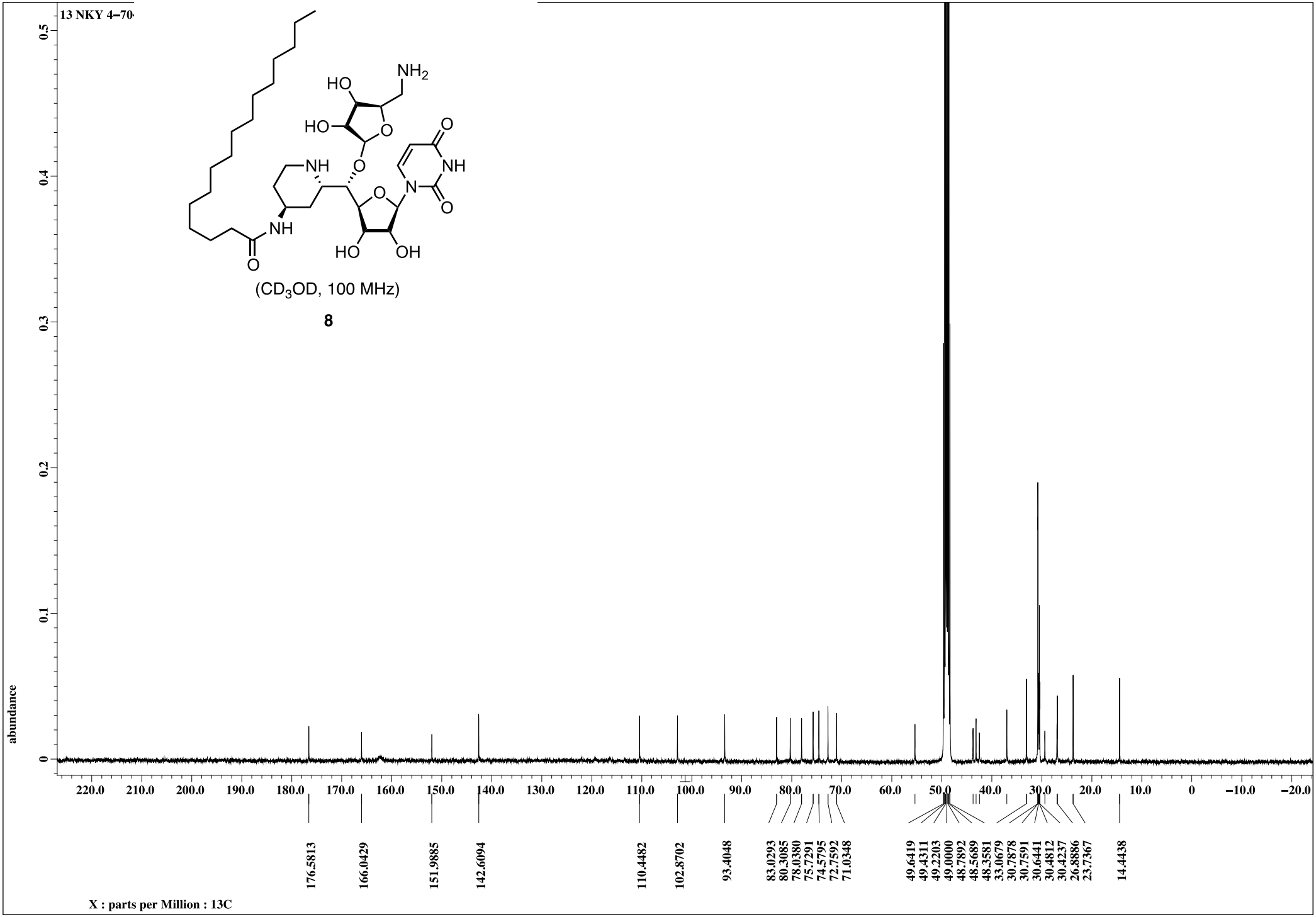
9.0 8.0 7.0 6.0 5.0 4.0 3.0 2.0 1.0 0

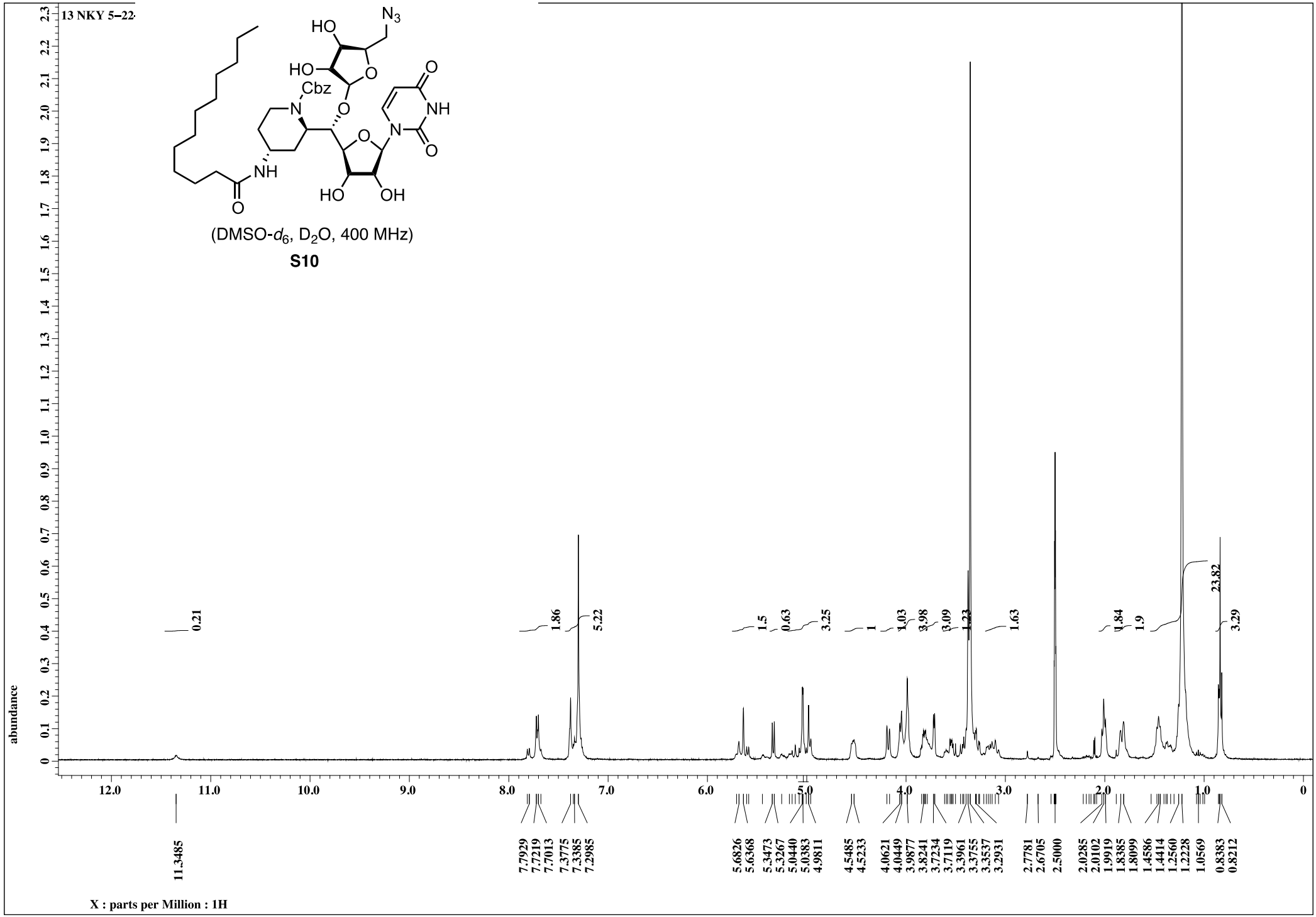
8.2790 8.2653 7.7961 7.7755 5.7876 5.7831 5.6904 5.1697 5.1616 4.9476 4.9087 4.8355 4.6512 4.2049 4.2003 4.1923 4.0733 4.0676 4.0481 3.7655 3.7437 3.7266 3.3283 3.3134 3.3100 3.3054 3.3008 2.8053 2.2400 2.2308 2.2217 2.2125 2.2034 2.1862 1.5934 1.5762 1.3920 1.3737 1.2775 1.1253 0.8976 0.8793

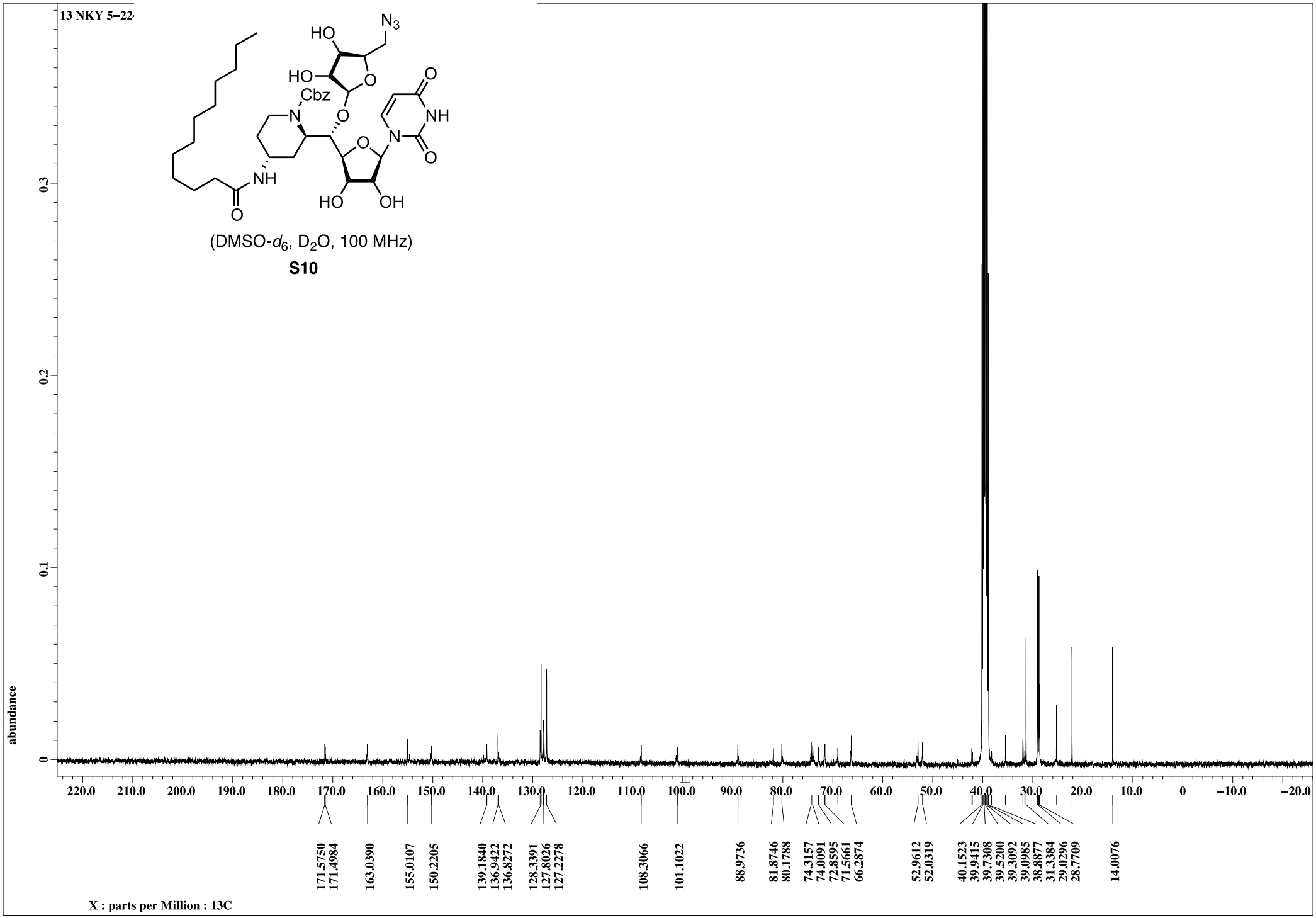
X : parts per Million : 1H

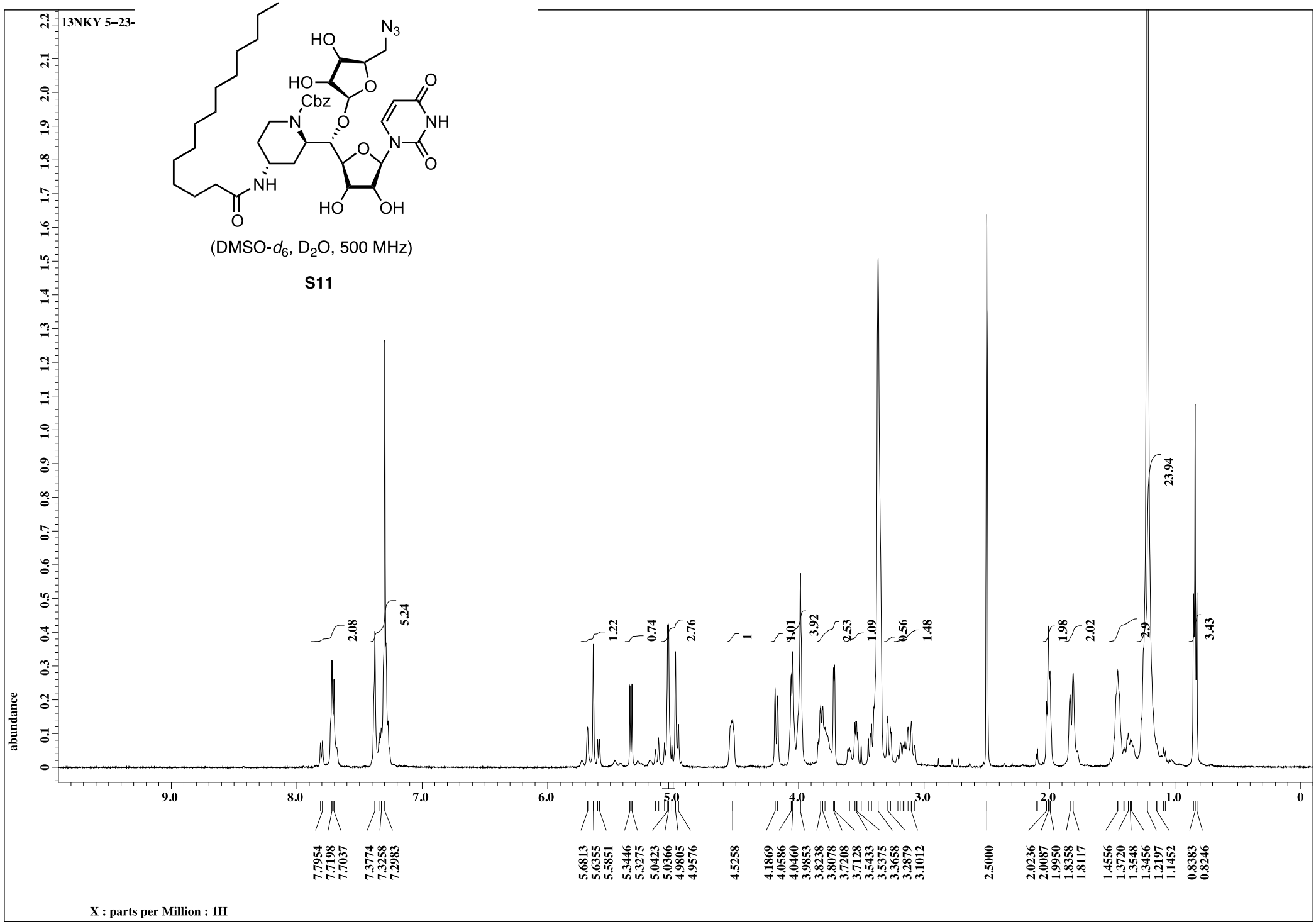

13 NKY 4–69
NH2
HO
HO
O
O
NH
NH
O
N
O
NH
HO
OH
O
(CD3OD, 100 MHz)
7
abundance
0
0.1
0.2
0.3
0.4
0.5
0.6
0.7
220.0
210.0
200.0
190.0
180.0
170.0
160.0
150.0
140.0
130.0
120.0
110.0
100.0
90.0
80.0
70.0
60.0
50.0
40.0
30.0
20.0
10.0
0
−10.0
−20.0
176.5429
166.1099
151.9502
142.2549
110.8793
102.6211
92.6767
82.9623
80.7300
79.4559
75.5471
75.1926
72.2515
70.1629
49.6515
49.4311
49.2203
49.0000
48.7892
48.5689
48.3581
33.0775
30.7974
30.7686
30.5866
30.4812
30.4333
23.7367
14.4438
X : parts per Million : 13C

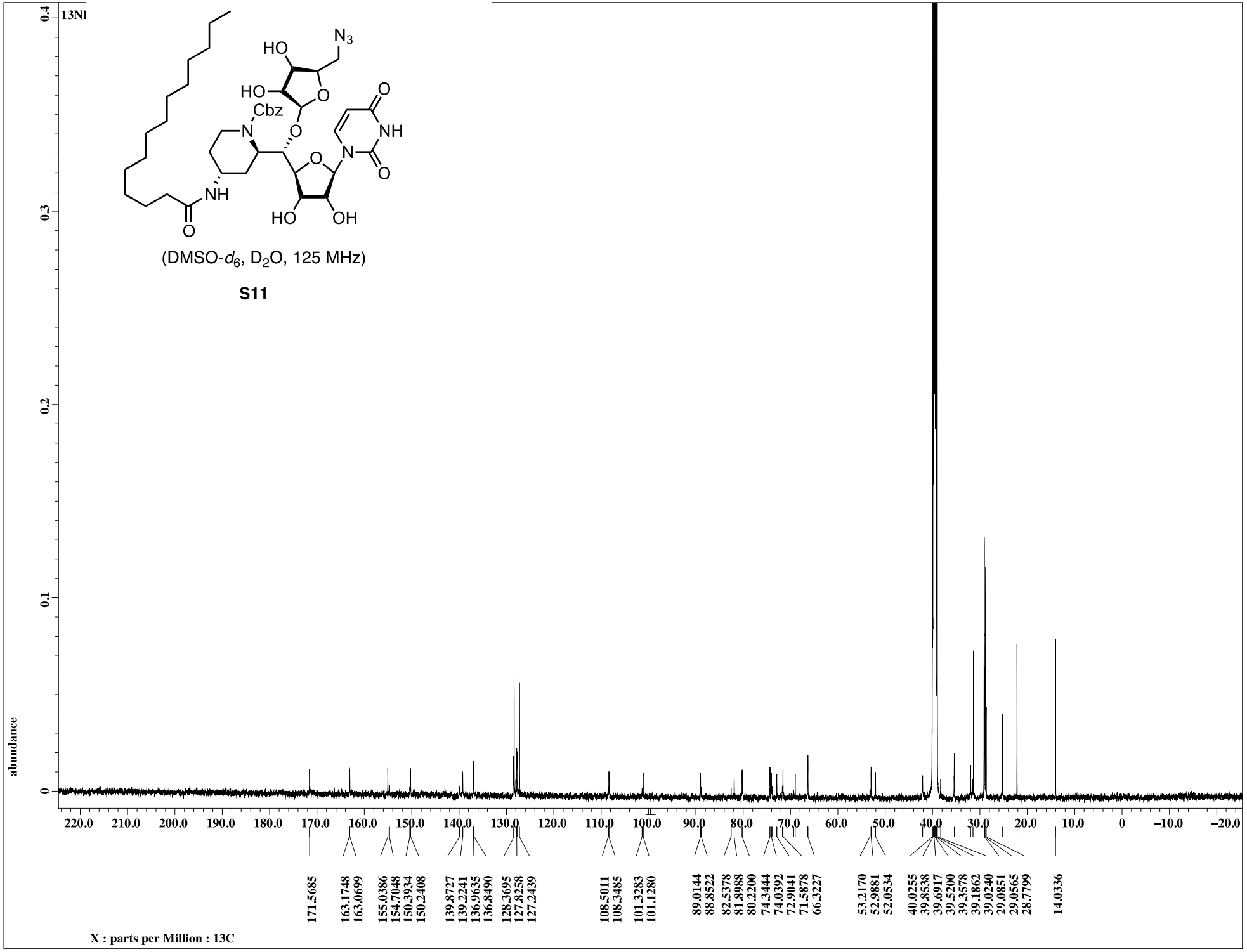

13 NKY 4-70
(CD3OD, 400 MHz)
8
abundance
X : parts per Million : 1H
0.99
1.0
1.0
0.93
8.36
0.92
2.01
0.94
3.17
0.82
1.98
2.17
28.0
3.21
7.6713
7.6507
7.6301
5.7899
5.7853
5.6961
5.2601
5.2543
4.9843
4.9465
4.9076
4.8630
4.2141
4.1969
4.1855
4.0836
3.8376
3.8044
3.7266
3.6476
3.3192
3.3146
3.3100
3.3066
3.3020
2.8019
2.2583
2.2400
2.2205
1.9871
1.9550
1.9241
1.6048
1.5877
1.3153
1.3039
1.2833
1.2375
0.8976
0.8793

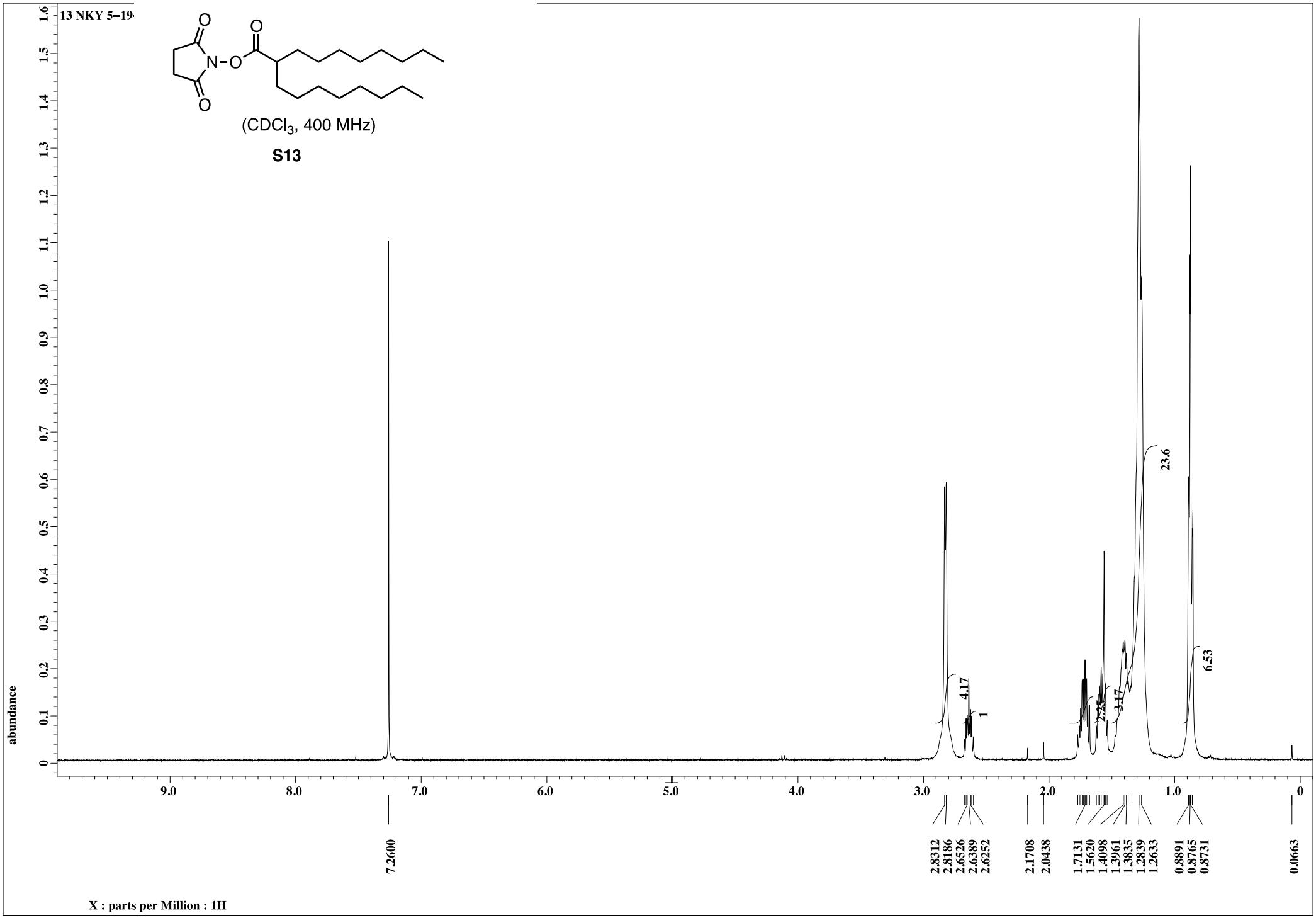

13 NKY 4-70
NH2
HO
HO
O
O
NH
NH
O
N
O
NH
HO
OH
O
(CD3OD, 100 MHz)
8
abundance
0.5
0.4
0.3
0.2
0.1
0
220.0
210.0
200.0
190.0
180.0
170.0
160.0
150.0
140.0
130.0
120.0
110.0
100.0
90.0
80.0
70.0
60.0
50.0
40.0
30.0
20.0
10.0
0
-10.0
-20.0
176.5813
166.0429
151.9885
142.6094
110.4482
102.8702
93.4048
83.0293
80.3085
78.0380
75.7291
74.5795
72.7592
71.0348
49.6419
49.4311
49.2203
49.0000
48.7892
48.5689
48.3581
33.0679
30.7878
30.7591
30.6441
30.4812
30.4237
26.8886
23.7367
14.4438
X : parts per Million : 13C

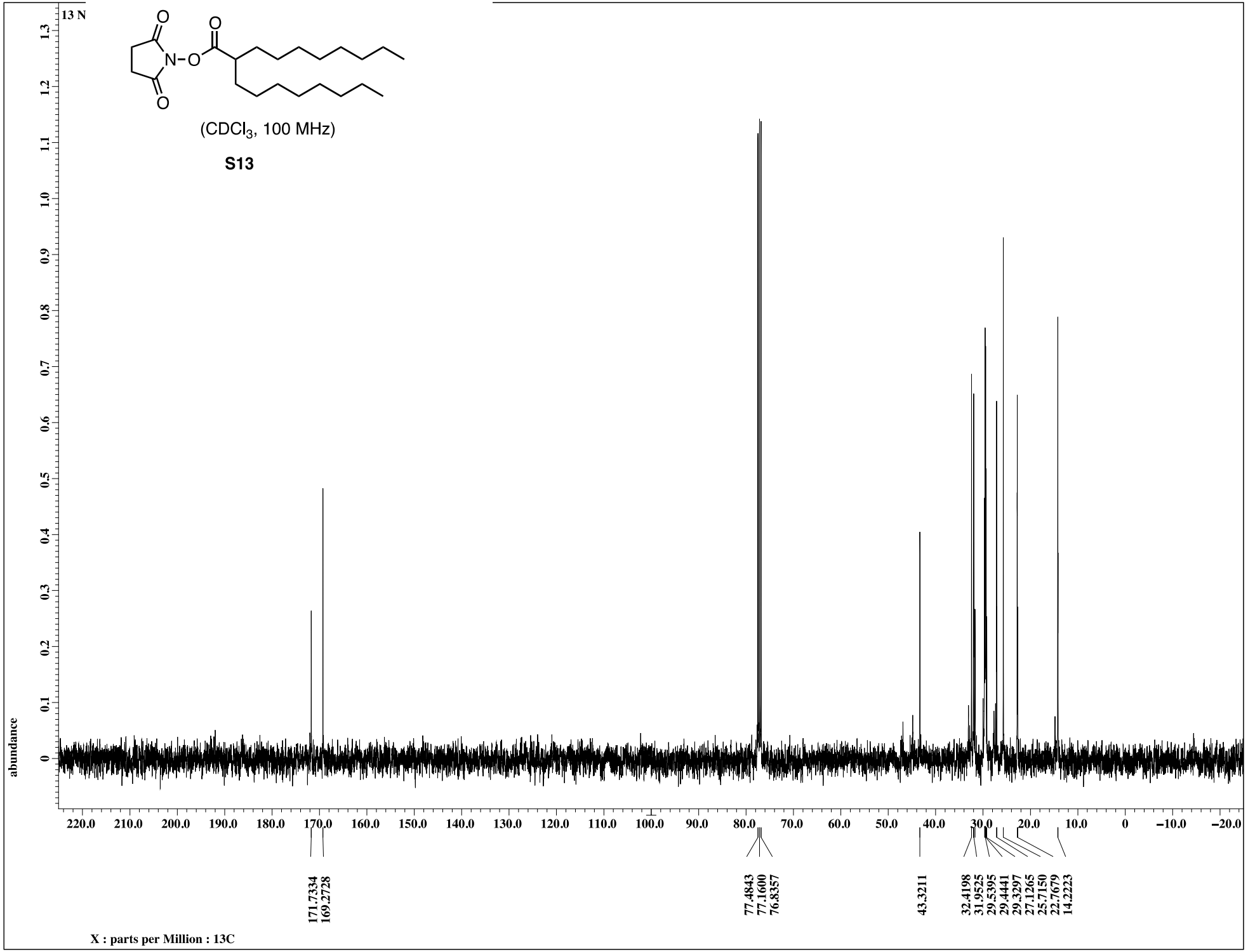

13 NKY 5–22
HO
N3
HO
O
Cbz
N
O
O
NH
N
O
O
NH
HO
OH
O
(DMSO-d6, D2O, 400 MHz)
S10
abundance
0.21
1.86
5.22
1.5
0.63
3.25
1
1.03
3.98
3.09
1.23
1.63
1.84
1.9
23.82
3.29
12.0
11.0
10.0
9.0
8.0
7.0
6.0
5.0
4.0
3.0
2.0
1.0
0
11.3485
7.7929
7.7219
7.7013
7.3775
7.3385
7.2985
5.6826
5.6368
5.3473
5.3267
5.0440
5.0383
4.9811
4.5485
4.5233
4.0621
4.0449
3.9877
3.8241
3.7234
3.7119
3.3961
3.3755
3.3537
3.2931
2.7781
2.6705
2.5000
2.0285
2.0102
1.9919
1.8385
1.8099
1.4586
1.4414
1.2560
1.2228
1.0569
0.8383
0.8212
X : parts per Million : 1H

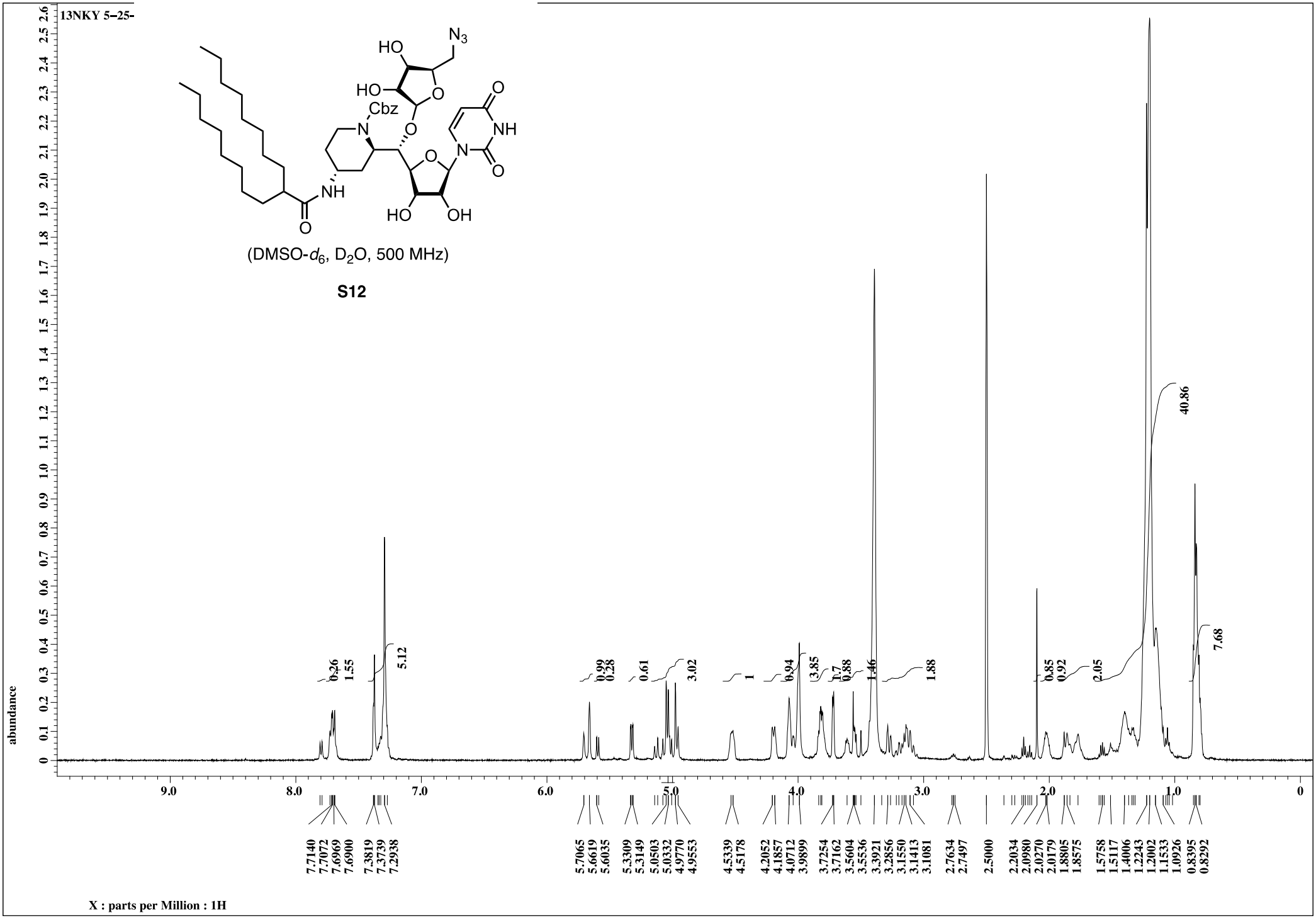

13 NKY 5–22
HO
N3
HO
O
O
Cbz
N
O
NH
N
O
O
NH
HO
OH
O
(DMSO-d6, D2O, 100 MHz)
S10
abundance
0
0.1
0.2
0.3
220.0 210.0 200.0 190.0 180.0 170.0 160.0 150.0 140.0 130.0 120.0 110.0 100.0 90.0 80.0 70.0 60.0 50.0 40.0 30.0 20.0 10.0 0 −10.0 −20.0
171.5750
171.4984
163.0390
155.0107
150.2205
139.1840
136.9422
136.8272
128.3391
127.8026
127.2278
108.3066
101.1022
88.9736
81.8746
80.1788
74.3157
74.0091
72.8595
71.5661
66.2874
52.9612
52.0319
40.1523
39.9415
39.7308
39.5200
39.3092
39.0985
38.8877
31.3384
29.0296
28.7709
14.0076
X : parts per Million : 13C

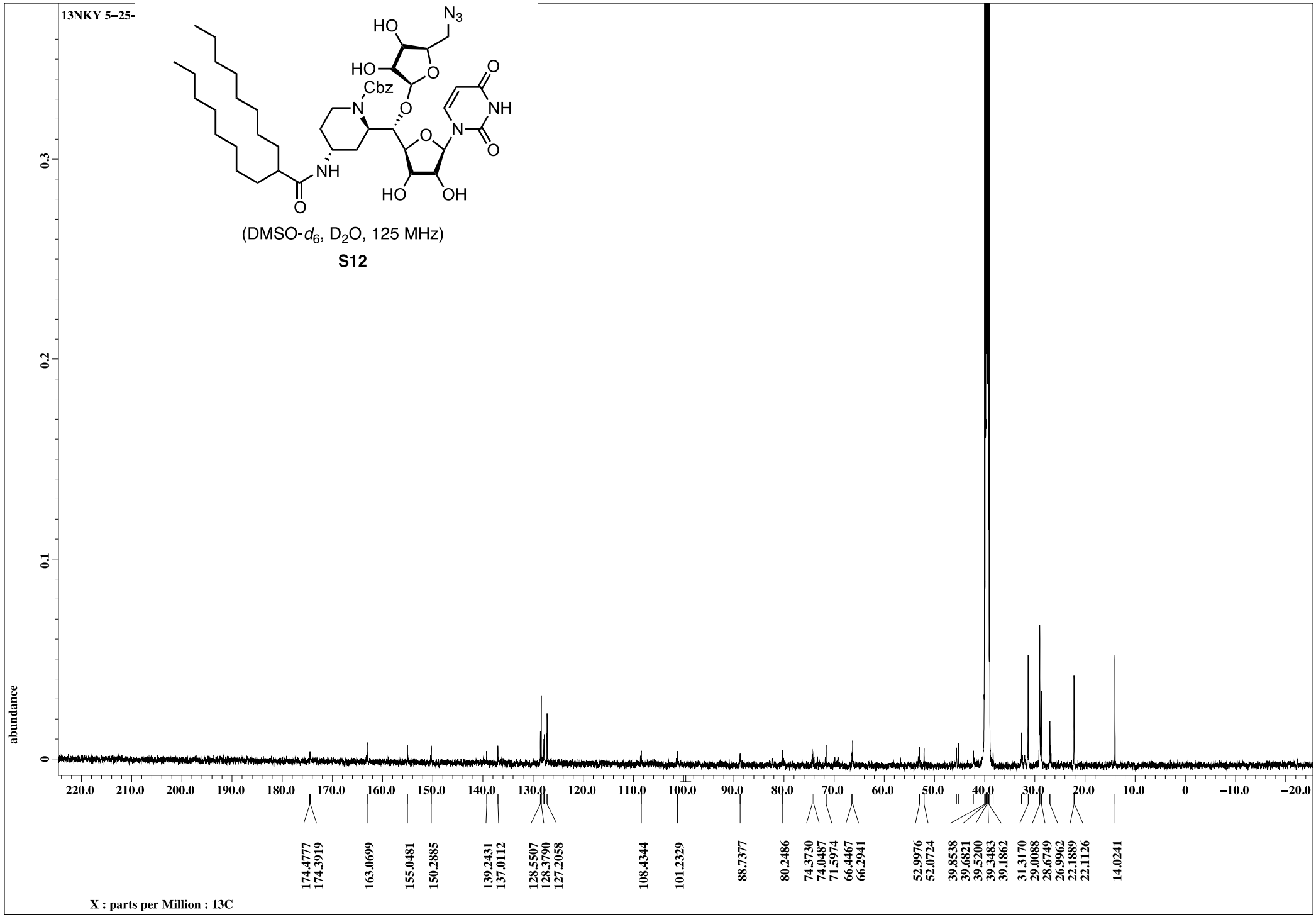

13NKY 5--23-
HO
N3
HO
O
Cbz
N
O
O
NH
N
O
O
NH
HO
OH
O
(DMSO-d6, D2O, 500 MHz)
S11
abundance
2.08
5.24
1.22
0.74
2.76
1
1.01
3.92
2.53
1.09
0.56
1.48
1.98
2.02
2.9
23.94
3.43
9.0
8.0
7.0
6.0
5.0
4.0
3.0
2.0
1.0
0
7.7954
7.7198
7.7037
7.3774
7.3258
7.2983
5.6813
5.6355
5.5851
5.3446
5.3275
5.0423
5.0366
4.9805
4.9576
4.5258
4.1869
4.0586
4.0460
3.9853
3.8238
3.8078
3.7208
3.7128
3.5433
3.5375
3.3658
3.2879
3.1012
2.5000
2.0236
2.0087
1.9950
1.8358
1.8117
1.4556
1.3720
1.3548
1.3456
1.2197
1.1452
0.8383
0.8246
X : parts per Million : 1H


13N
HO
N3
HO
O
Cbz
N
O
O
NH
N
O
O
NH
HO
OH
O
(DMSO-d6, D2O, 125 MHz)
S11
abundance
0.4
0.3
0.2
0.1
0
220.0 210.0 200.0 190.0 180.0 170.0 160.0 150.0 140.0 130.0 120.0 110.0 100.0 90.0 80.0 70.0 60.0 50.0 40.0 30.0 20.0 10.0 0 −10.0 −20.0
171.5685
163.1748
163.0699
155.0386
154.7048
150.3934
150.2408
139.8727
139.2241
136.9635
136.8490
128.3695
127.8258
127.2439
108.5011
108.3485
101.3283
101.1280
89.0144
88.8522
82.5378
81.8988
80.2200
74.3444
74.0392
72.9041
71.5878
66.3227
53.2170
52.9881
52.0534
40.0255
39.8538
39.6917
39.5200
39.3578
39.1862
39.0240
29.0851
29.0565
28.7799
14.0336
X : parts per Million : 13C

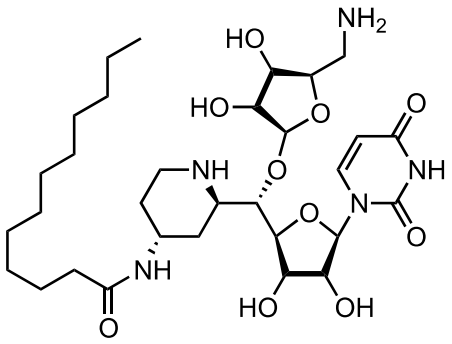

13 NKY 5–19
(CDCl3, 400 MHz)
S13
abundance
X : parts per Million : 1H
7.2600
2.8312
2.8186
2.6526
2.6389
2.6252
2.1708
2.0438
1.7131
1.5620
1.4098
1.3961
1.3835
1.2839
1.2633
0.8891
0.8765
0.8731
0.0663
4.17
1
3.17
23.6
6.53


13 N
(CDCl3, 100 MHz)
S13
abundance
X : parts per Million : 13C
171.7334
169.2728
77.4843
77.1600
76.8357
43.3211
32.4198
31.9525
29.5395
29.4441
29.3297
27.1265
25.7150
22.7679
14.2223


13NKY 5--25-
HO
N3
HO
O
Cbz
N
O
O
NH
N
O
NH
HO
OH
O
(DMSO-d6, D2O, 500 MHz)
S12
abundance
40.86
7.68
0.26
1.55
5.12
0.99
0.28
0.61
3.02
1
0.94
3.85
0.7
0.88
1.46
1.88
0.85
0.92
2.05
9.0
8.0
7.0
6.0
5.0
4.0
3.0
2.0
1.0
0
7.7140
7.7072
7.6969
7.6900
7.3819
7.3739
7.2938
5.7065
5.6619
5.6035
5.3309
5.3149
5.0503
5.0332
4.9770
4.9553
4.5339
4.5178
4.2052
4.1857
4.0712
3.9899
3.7254
3.7162
3.5604
3.5536
3.3921
3.2856
3.1550
3.1413
3.1081
2.7634
2.7497
2.5000
2.2034
2.0980
2.0270
2.0179
1.8805
1.8575
1.5758
1.5117
1.4006
1.2243
1.2002
1.1533
1.0926
0.8395
0.8292
X : parts per Million : 1H


13NKY 5–25-
HO
N3
HO
O
Cbz
N
O
NH
O
N
O
O
NH
O
HO
OH
(DMSO-d6, D2O, 125 MHz)
S12
abundance
0
0.1
0.2
0.3
220.0 210.0 200.0 190.0 180.0 170.0 160.0 150.0 140.0 130.0 120.0 110.0 100.0 90.0 80.0 70.0 60.0 50.0 40.0 30.0 20.0 10.0 0 −10.0 −20.0
174.4777
174.3919
163.0699
155.0481
150.2885
139.2431
137.0112
128.5507
128.3790
127.2058
108.4344
101.2329
88.7377
80.2486
74.3730
74.0487
71.5974
66.4467
66.2941
52.9976
52.0724
39.8538
39.6821
39.5200
39.3483
39.1862
31.3170
29.0088
28.6749
26.9962
22.1889
22.1126
14.0241
X : parts per Million : 13C

13NKY 5--43-

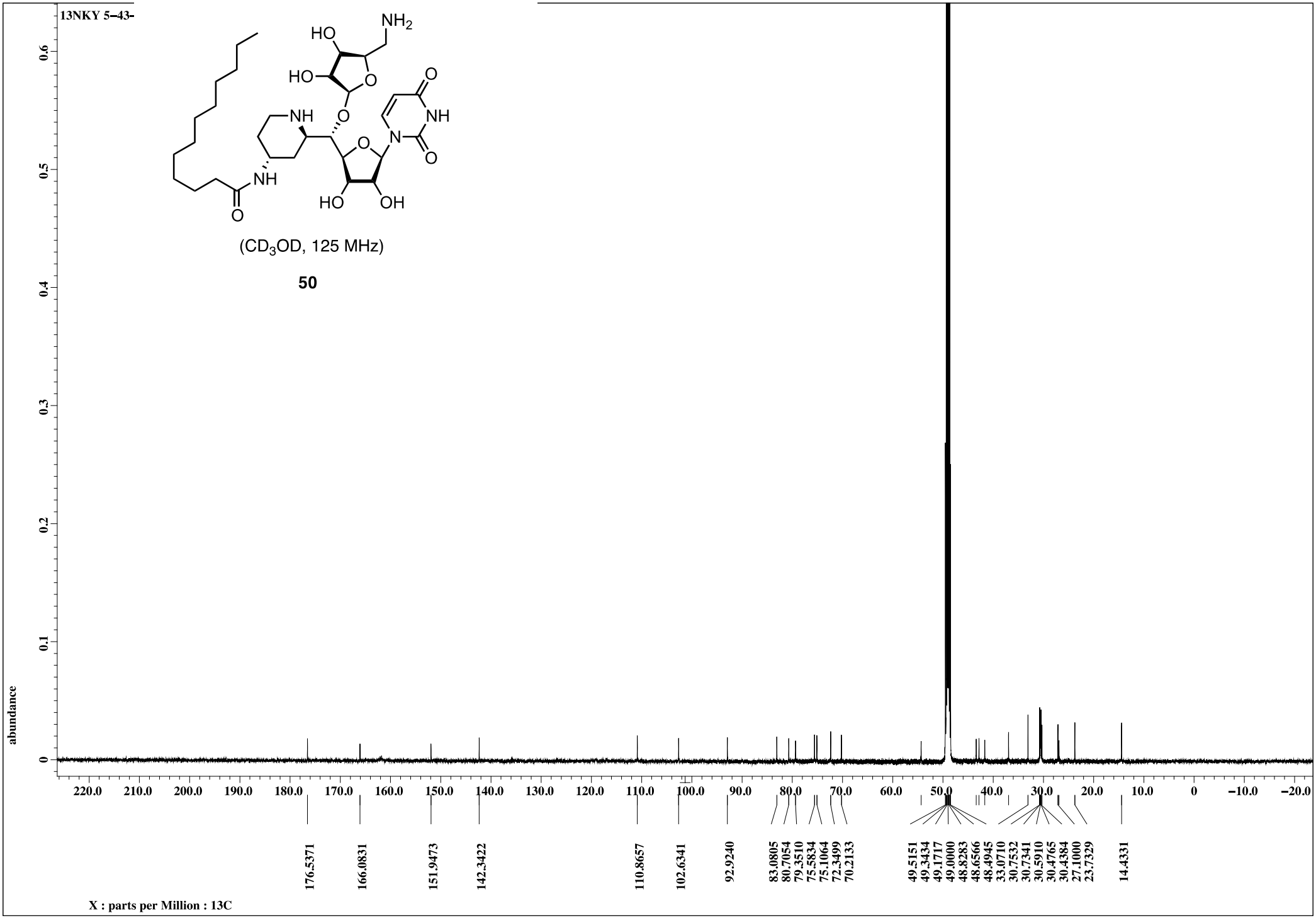


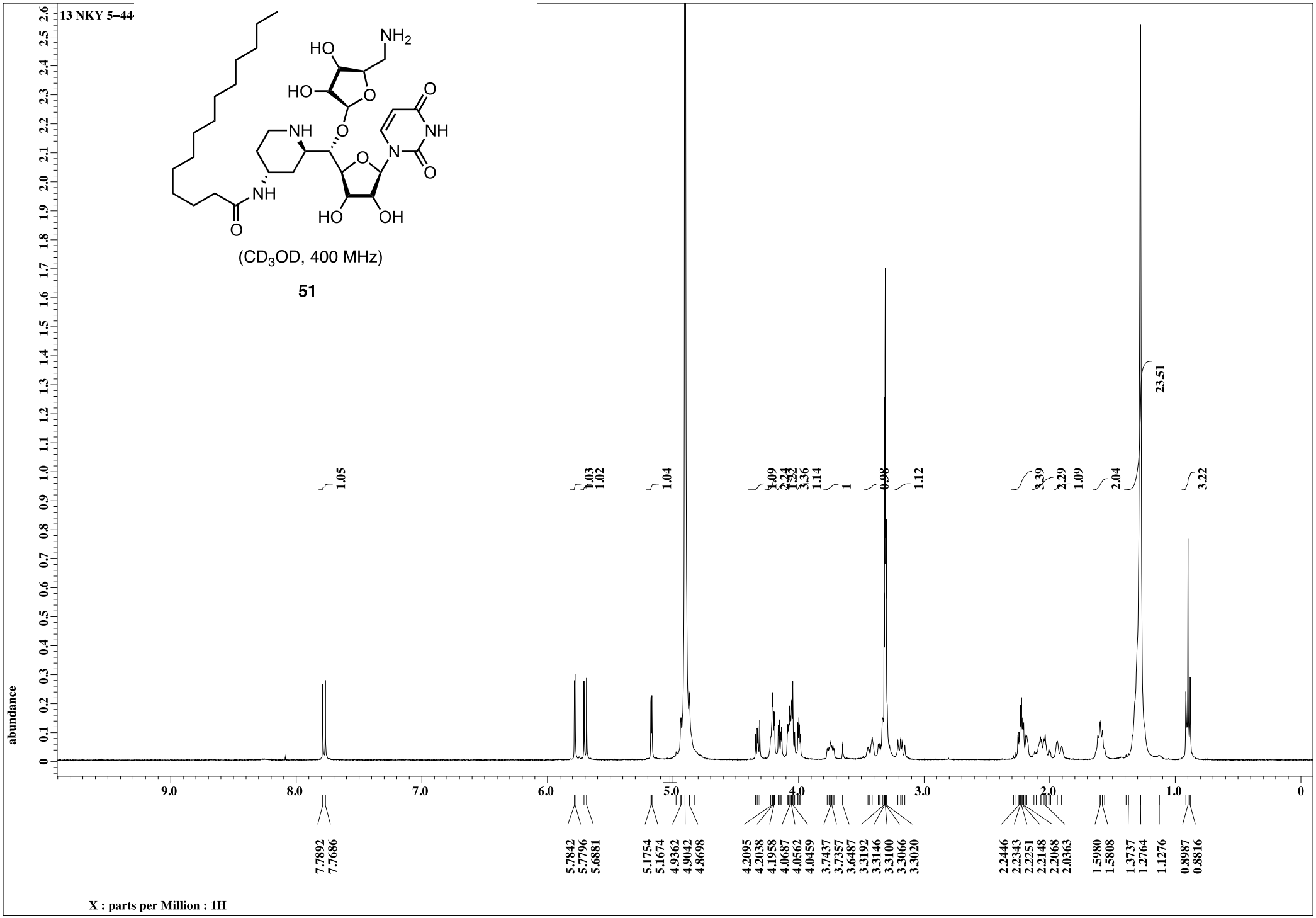
(CD_3OD, 500 MHz)

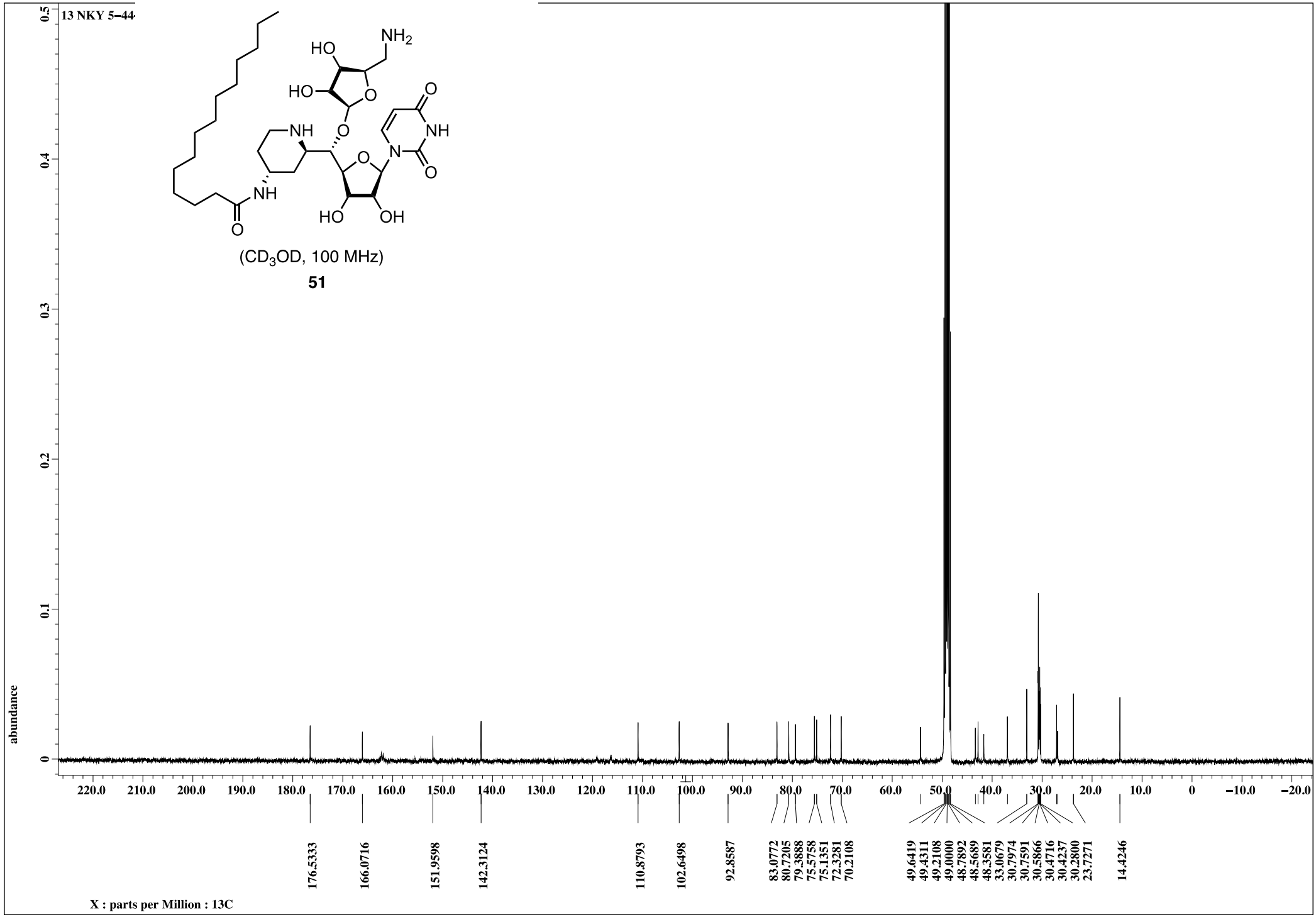
50

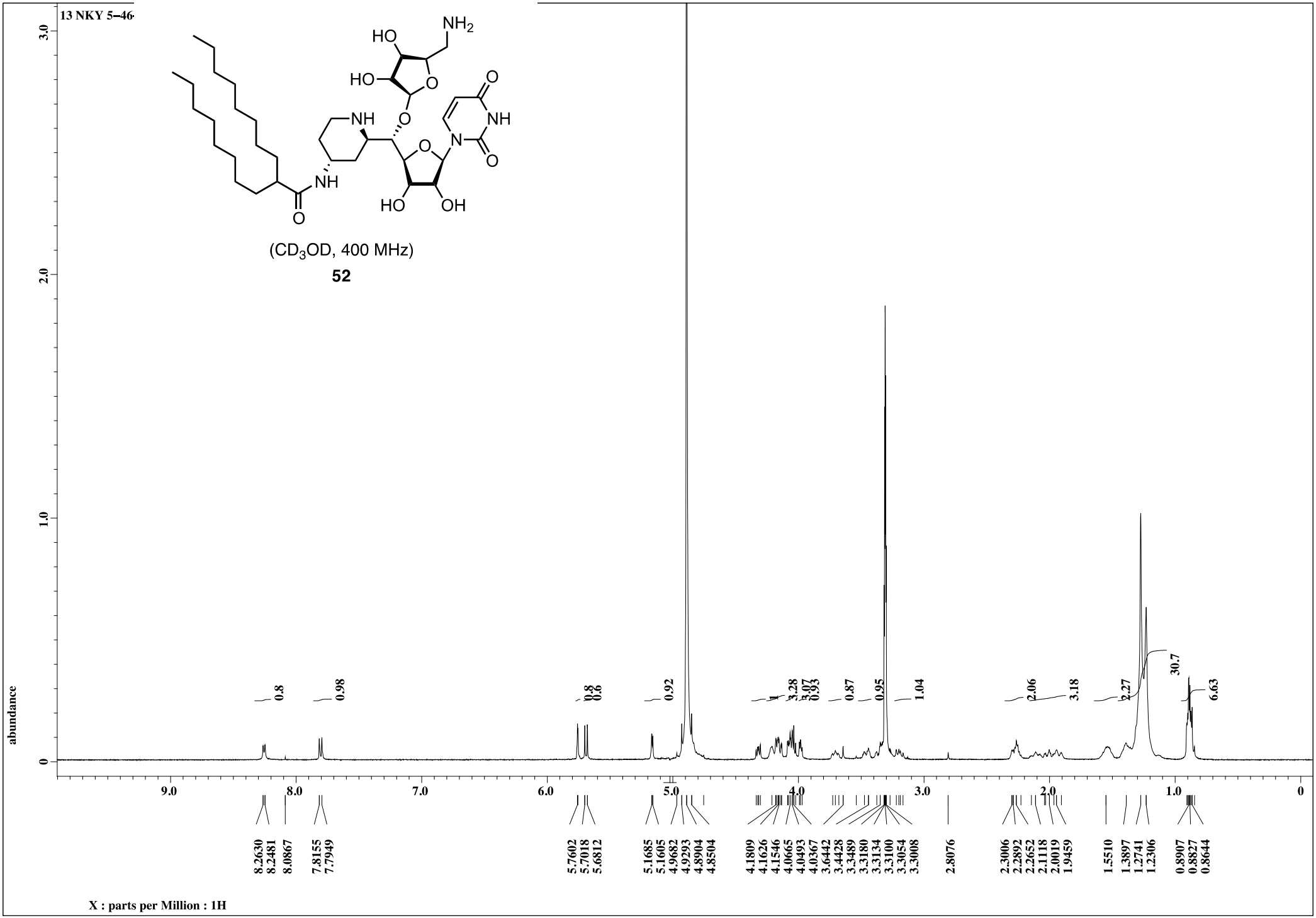
abundance

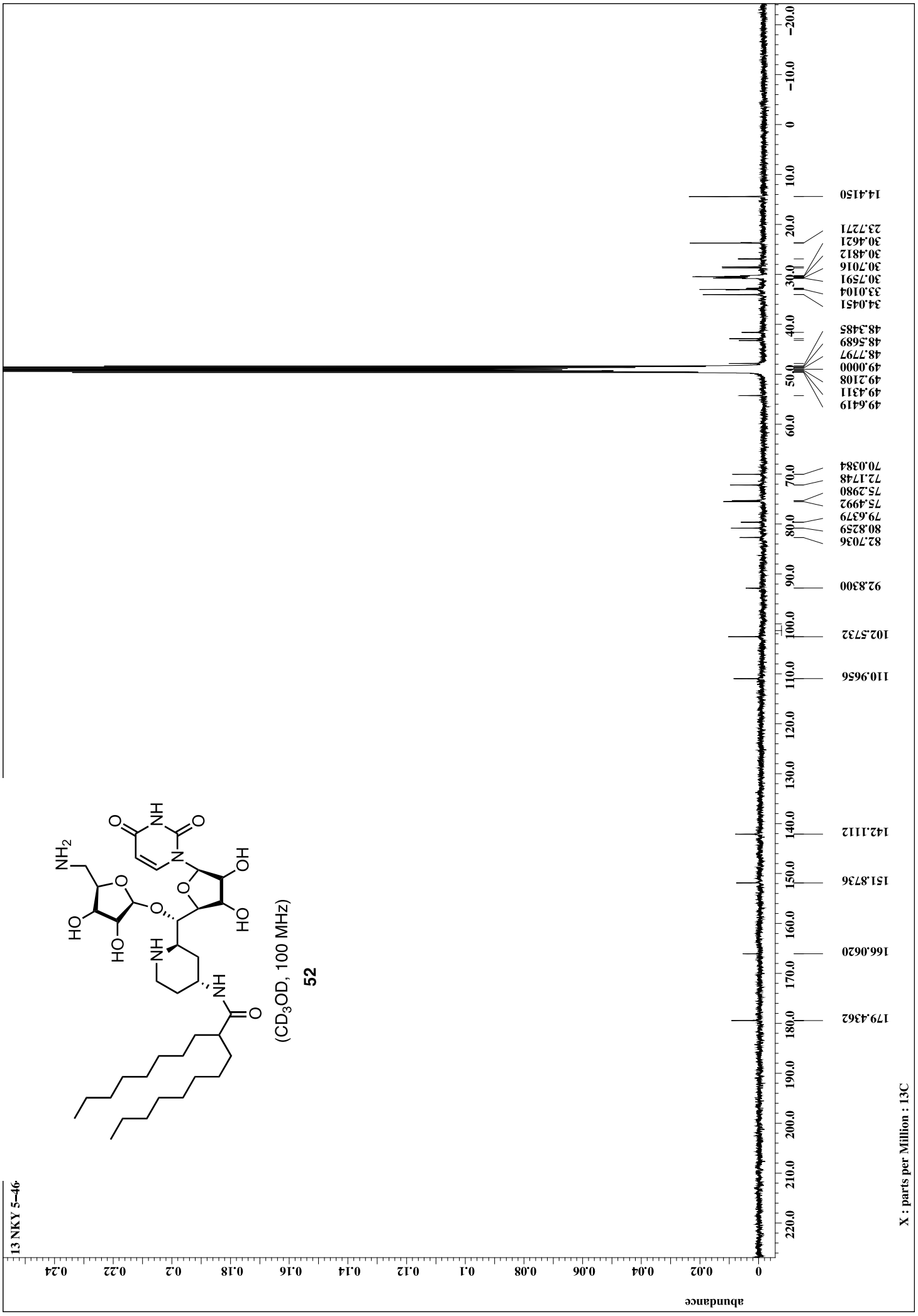
X : parts per Million : 1H

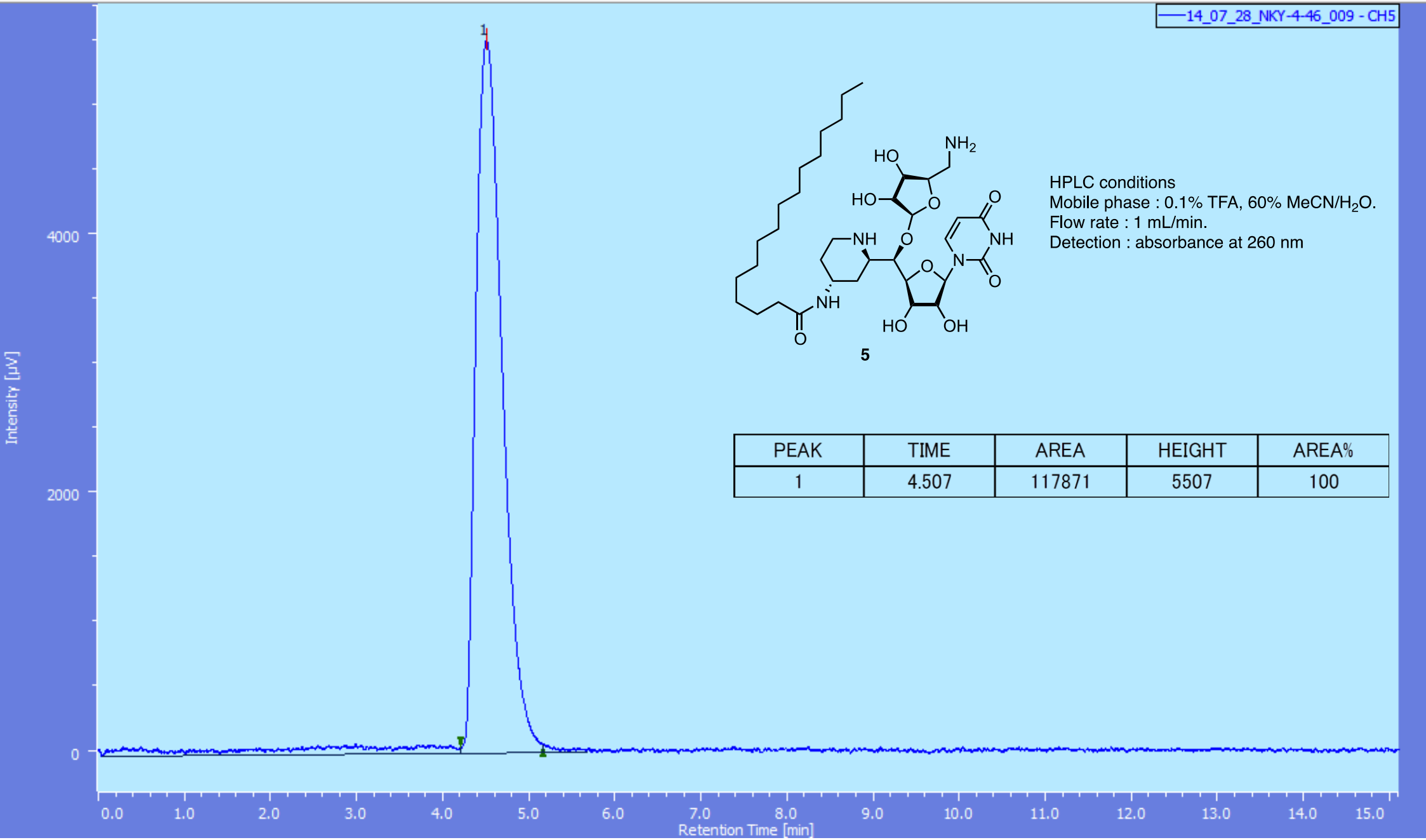

13NKY 5--43-
(CD3OD, 125 MHz)
50
abundance
X : parts per Million : 13C
176.5371
166.0831
151.9473
142.3422
110.8657
102.6341
92.9240
83.0805
80.7054
79.3510
75.5834
75.1064
72.3499
70.2133
49.5151
49.3434
49.1717
49.0000
48.8283
48.6566
48.4945
33.0710
30.7532
30.7341
30.5910
30.4765
30.4384
27.1000
23.7329
14.4331


13 NKY 5–44
(CD3OD, 400 MHz)
51
abundance
X : parts per Million : 1H
1.05
1.03
1.02
1.04
1.09
2.24
2.22
3.36
1.14
1
0.98
1.12
3.39
2.29
1.09
2.04
23.51
3.22
7.7892
7.7686
5.7842
5.7796
5.6881
5.1754
5.1674
4.9362
4.9042
4.8698
4.2095
4.2038
4.1958
4.0687
4.0562
4.0459
3.7437
3.7357
3.6487
3.3192
3.3146
3.3100
3.3066
3.3020
2.2446
2.2343
2.2251
2.2148
2.2068
2.0363
1.5980
1.5808
1.3737
1.2764
1.1276
0.8987
0.8816


13 NKY 5–44
(CD3OD, 100 MHz)
51
abundance
X : parts per Million : 13C
176.5333
166.0716
151.9598
142.3124
110.8793
102.6498
92.8587
83.0772
80.7205
79.3888
75.5758
75.1351
72.3281
70.2108
49.6419
49.4311
49.2108
49.0000
48.7892
48.5689
48.3581
33.0679
30.7974
30.7591
30.5866
30.4716
30.4237
30.2800
23.7271
14.4246


13 NKY 5–46
(CD3OD, 400 MHz)
52
abundance
X : parts per Million : 1H
8.2630
8.2481
8.0867
7.8155
7.7949
5.7602
5.7018
5.6812
5.1685
5.1605
4.9682
4.9293
4.8904
4.8504
4.1809
4.1626
4.1546
4.0665
4.0493
4.0367
3.6442
3.4428
3.3489
3.3180
3.3134
3.3100
3.3054
3.3008
2.8076
2.3006
2.2892
2.2652
2.1118
2.0019
1.9459
1.5510
1.3897
1.2741
1.2306
0.8907
0.8827
0.8644

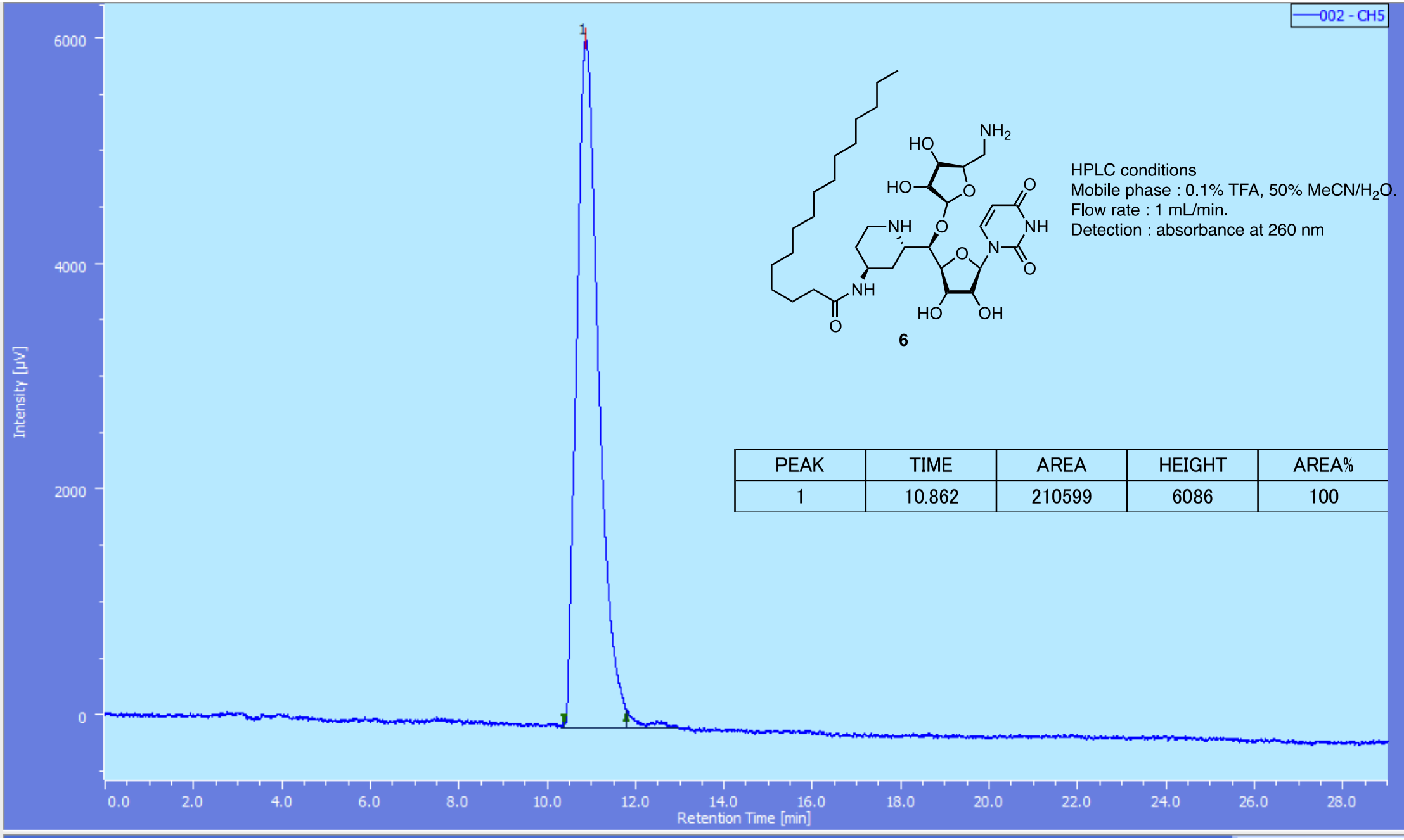

13 NKY 5–46
abundance
X : parts per Million : 13C
14.4150
23.7271
30.4621
30.4812
30.7016
30.7591
33.0104
34.0451
48.3485
48.5689
48.7797
49.0000
49.2108
49.4311
49.6419
70.0384
72.1748
75.2980
75.4992
79.6379
80.8259
82.7036
92.8300
102.5732
110.9656
142.1112
151.8736
166.0620
179.4362
52
(CD3OD, 100 MHz)



5

HPLC conditions
Mobile phase : 0.1% TFA, 60% MeCN/H_2O.
Flow rate : 1 mL/min.
Detection : absorbance at 260 nm

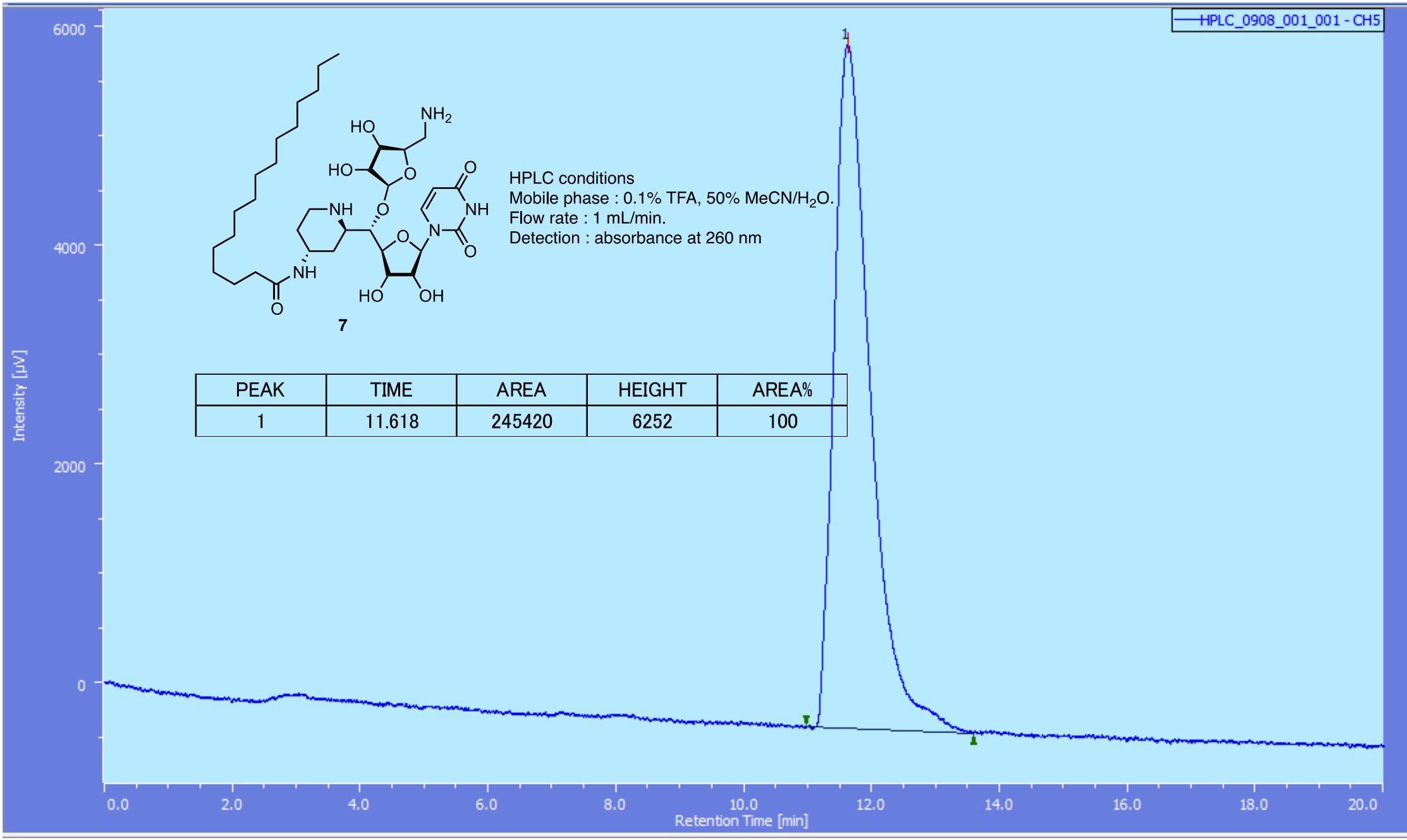
PEAK	TIME	AREA	HEIGHT	AREA%
1	4.507	117871	5507	100



6

HPLC conditions
Mobile phase : 0.1% TFA, 50% MeCN/H_2O.
Flow rate : 1 mL/min.
Detection : absorbance at 260 nm

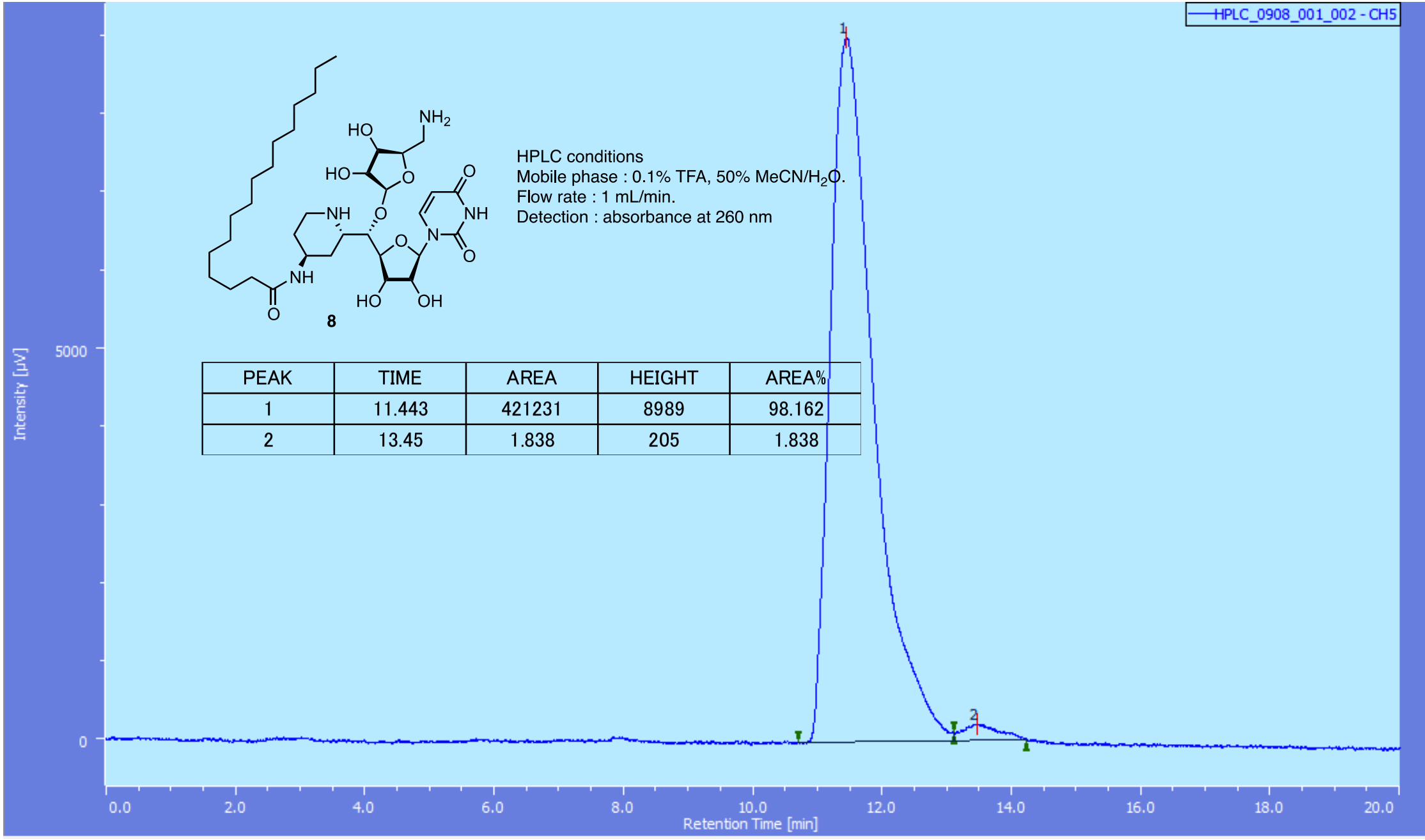
PEAK	TIME	AREA	HEIGHT	AREA%
1	10.862	210599	6086	100



7

HPLC conditions
Mobile phase : 0.1% TFA, 50% MeCN/H_2O.
Flow rate : 1 mL/min.
Detection : absorbance at 260 nm

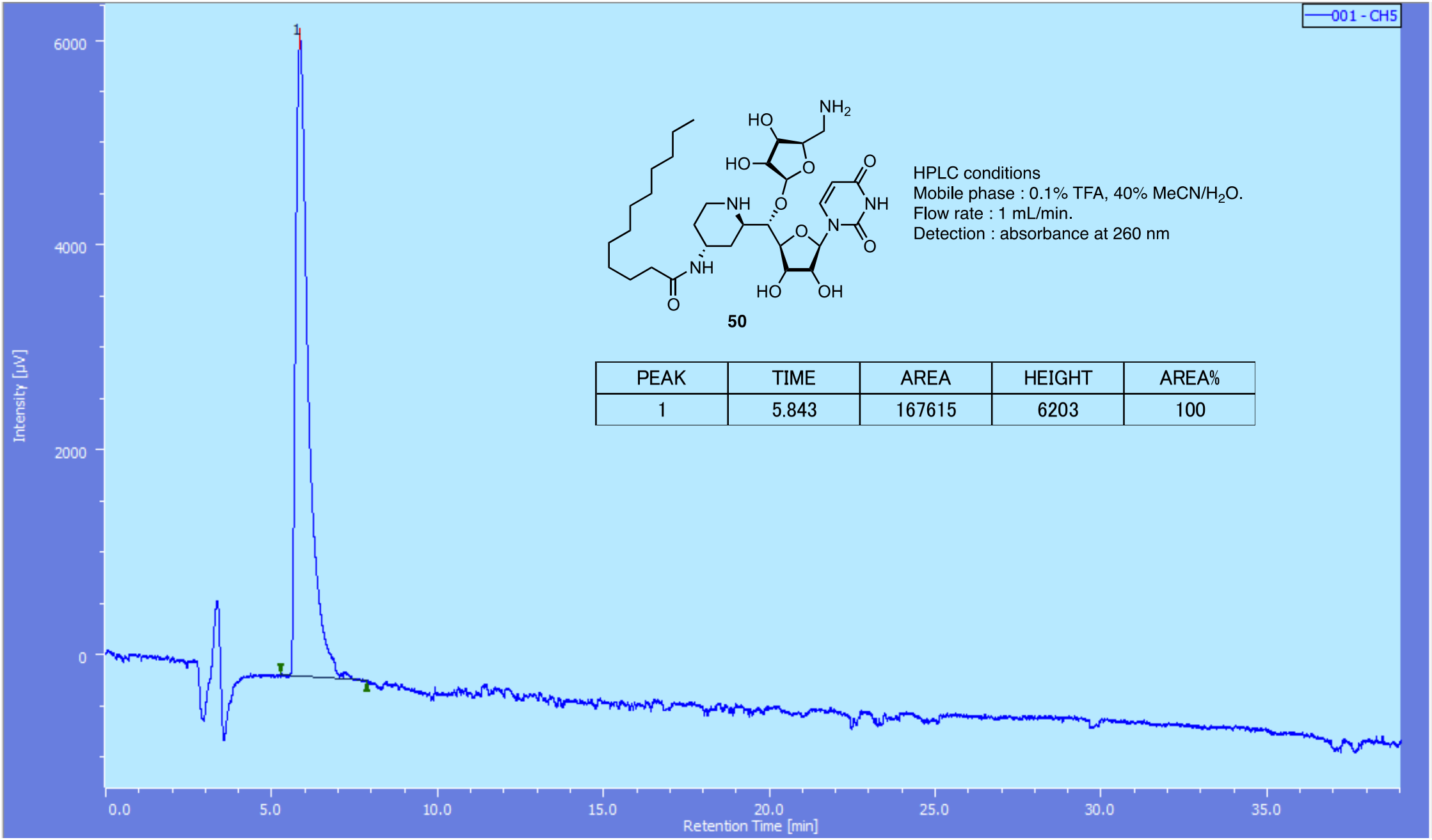
PEAK	TIME	AREA	HEIGHT	AREA%
1	11.618	245420	6252	100



8

HPLC conditions
Mobile phase : 0.1% TFA, 50% MeCN/H_2O.
Flow rate : 1 mL/min.
Detection : absorbance at 260 nm

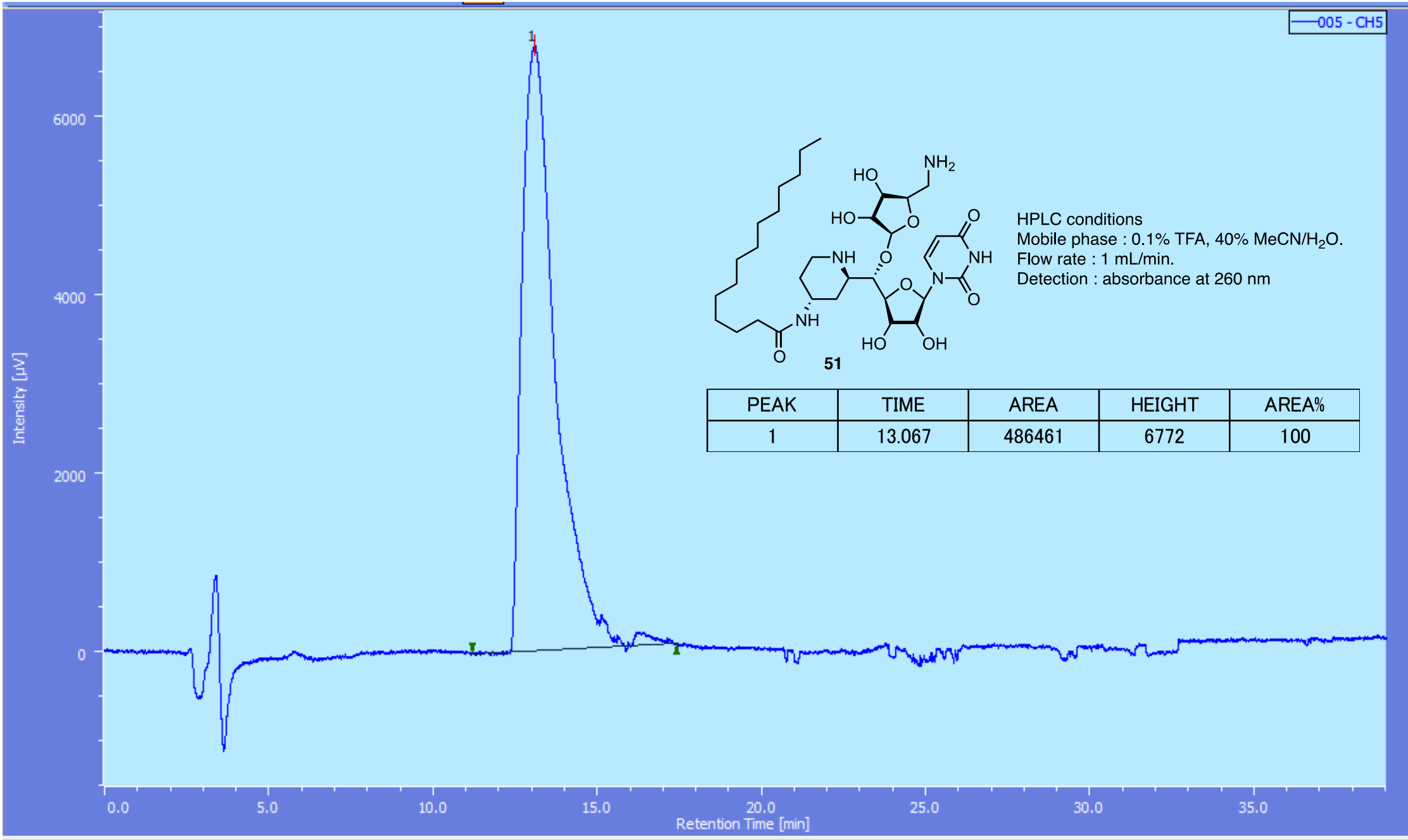
PEAK	TIME	AREA	HEIGHT	AREA%
1	11.443	421231	8989	98.162
2	13.45	1.838	205	1.838



50

HPLC conditions
Mobile phase : 0.1% TFA, 40% MeCN/H_2O.
Flow rate : 1 mL/min.
Detection : absorbance at 260 nm

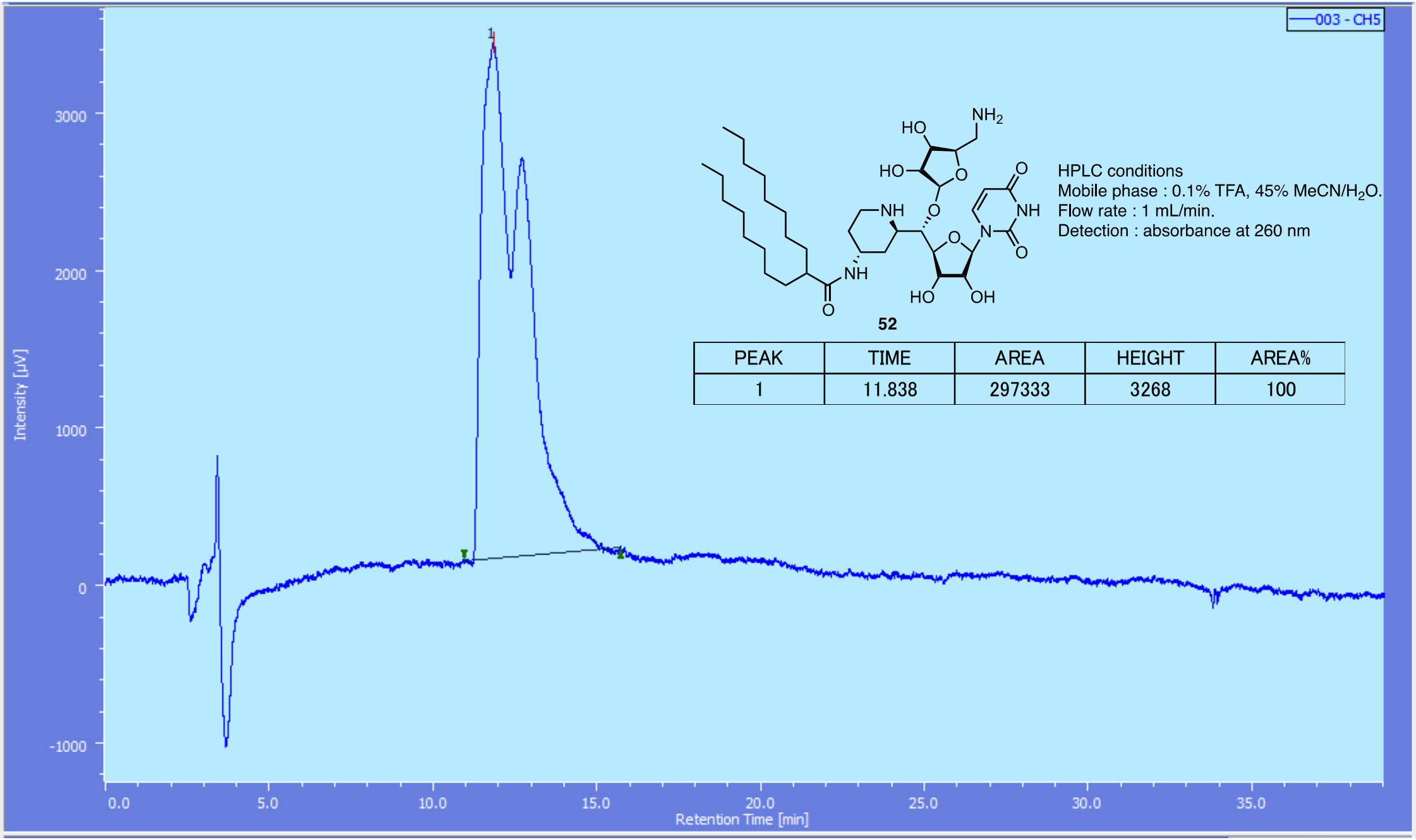
PEAK	TIME	AREA	HEIGHT	AREA%
1	5.843	167615	6203	100



51

HPLC conditions
Mobile phase : 0.1% TFA, 40% MeCN/H_2O.
Flow rate : 1 mL/min.
Detection : absorbance at 260 nm

PEAK	TIME	AREA	HEIGHT	AREA%
1	13.067	486461	6772	100



52

HPLC conditions
Mobile phase : 0.1% TFA, 45% MeCN/H_2O.
Flow rate : 1 mL/min.
Detection : absorbance at 260 nm

PEAK	TIME	AREA	HEIGHT	AREA%
1	11.838	297333	3268	100