Supporting Information

Tricyclanos: conformationally constrained nucleoside analogues with a new heterotricycle obtained from the D-ribofuranose unit

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Relevant numbering of nucleosides and tricyclanos

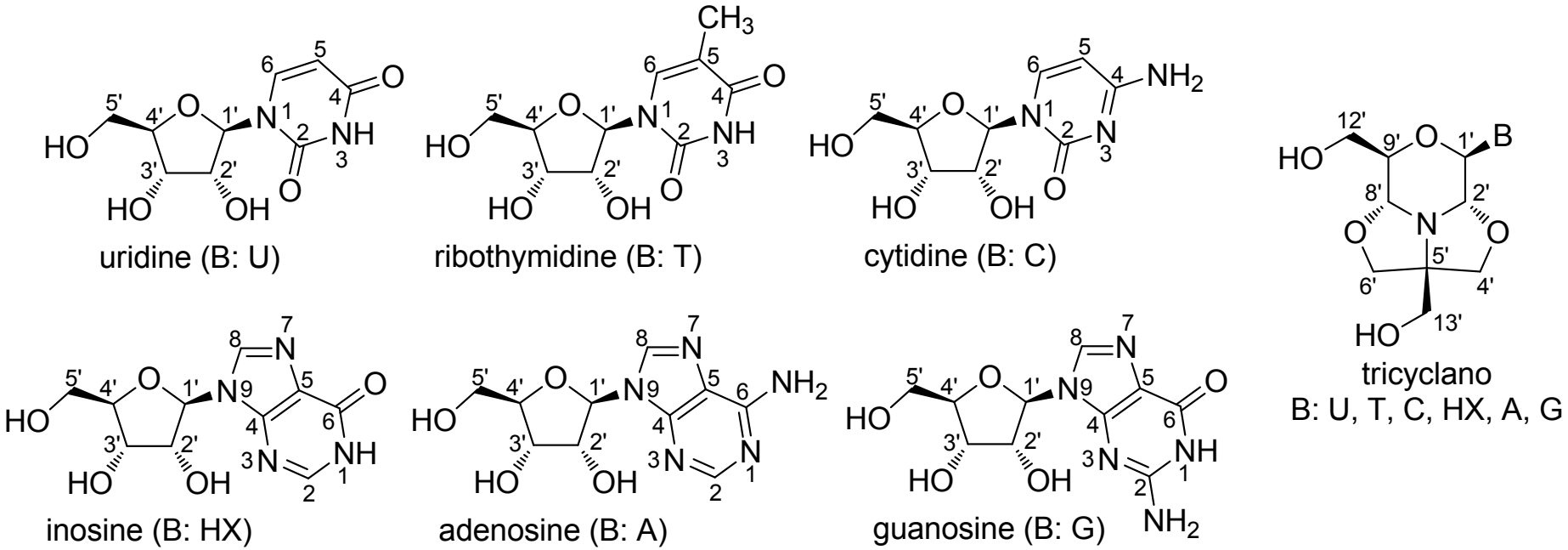


Figure S1. Relevant numbering of nucleosides and tricyclanos

Experimental

Synthetic procedures

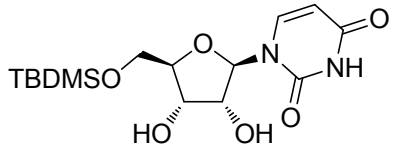
General Information

TLC was performed on Kieselgel 60 F_{254} (Merck) with detection by UV-light (254 nm) and immersing into sulfuric acidic ammonium-molibdenate solution followed by heating. Column chromatography was performed on Silica gel 60 (Merck 0.040-0.063 mm). Organic solutions were dried over anhydrous Na_2SO_4, and concentrated in vacuum. The ^1H NMR (360, 400 and 500 MHz) and ^{13}C NMR (90, 100 and 125 MHz) spectra were recorded with DRX-360, DRX-400, and Bruker Avance II 500 spectrometers at 25 °C. Chemical shifts are referenced to Me_4Si (0.00 ppm for ^1H), to the residual solvent signals (C_5D_5N: 7.22 or 8.74, D_2O: 4.79, DMSO-d_6: 2.50 ppm for ^1H) and to the residual solvent signals ($CDCl_3$: 77.16, DMSO-d_6: 39.52, C_5D_5N: 135.91 or 153.35, CD_3OD: 49.00 ppm for ^{13}C). MALDI-TOF MS analyses of the compounds were carried out in the positive reflectron mode using a BIFLEX III mass spectrometer (Bruker, Germany) equipped with delayed-ion extraction. 2,5-Dihydroxybenzoic acid (DHB) was used as matrix and $F_3CCOONa$ as cationising agent in DMF. ESI-TOF MS spectra were recorded by a microTOF-Q type QqTOFMS mass spectrometer (Bruker) in the positive ion mode using MeOH as the solvent. X-ray data collection was performed using a Synergy, Dualflex diffractometer equipped with microfocus sealed X-ray tube and Pilatus 200K detector (Rigaku Oxford Diffraction) at 293 K using Cu-Kα radiation (λ=1.5418 Å). Numerical multi-scan absorption collection using spherical harmonics was performed using CrysAlisPro software The structure was solved with direct methods and refined by full-matrix least squares on F^2 SHELXL-2016/4[1] under WinGX.[2] Crystallographic calculations were done using PLATON[3] and Mercury,[4] the cif file was edited using publCIF[5] and manually. Elemental analysis (C, H, N) was performed on an Elementar Vario MicroCube instrument.

Preparation of periodate resin[6]

To a solution of NaOH (40 g) in water (3 L) Amberlite IRA-400 (200 g, 20-50 mesh anion Cl-Form) resin was added and stirred for 2 hours. The resin was neutralized by washing with water and added to a suspension of $NaIO_4$ (233 g) in water (4-5 L). After stirring overnight the resin was filtered, washed with water and dried in vacuum over P_2O_5 and KOH for a night. After drying the resin is required to store in dark.

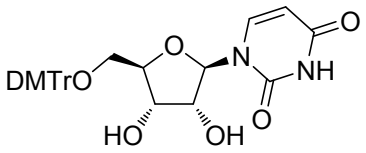
5'-*O-tert*-butyldimethylsilyl-uridine (2a)[Ref. 21 in the main text]



Uridine **1** (6.0 g, 25.57 mmol) was dissolved in dry DMF (60 mL). Imidazole (3.35 g, 49.14 mmol, 2.0 equiv.) and *tert*-butyldimethylsilyl chloride (3.88 g, 25.74 mmol, 1.05 equiv) were added to the reaction mixture and stirred overnight. The solution was poured into ice-water, the solid phase was filtered off and dried in vacuum over P_2O_5 and KOH overnight. The crude

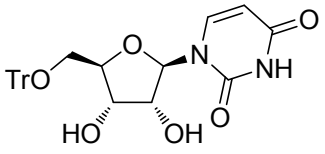
white solid was purified by flash column chromatography (CH_2Cl_2/MeOH 98:2 → 95:5 → 9:1) to yield **2a** (5.64 g, 64%) as a white foam. R_f= 0.45 (CH_2Cl_2/MeOH 9:1); ^{1}H NMR 360 MHz (CD_3OD) δ = 8.01 (d, J = 8.1 Hz, 1H, uracil C*H*-6), 5.91 (d, J = 3.8 Hz, 1H, H-1'), 5.63 (d, J = 8.1 Hz, 1H, uracil C*H*-5), 4.16 – 4.10 (m, 2H, H-2', H-3'), 4.04 (dd, J = 4.6, 2.3 Hz, 1H, H-4'), 3.99 (dd, J = 11.7 Hz, J = 2.3 Hz, 1H, H-5'a), 3.85 (dd, J = 11.7 Hz, J = 2.3 Hz, 1H, H-5'b), 0.96 (s, 9H, TBDMS *t*-Bu 3 x CH_3), 0.15 (2 x s, 6H, TBDMS 2 x Si-CH_3); ^{13}C NMR 90 MHz (CD_3OD) δ = 175.2, 166.1 (2C, uracil *C*O-2, *C*O-4), 142.2 (1C, uracil *C*H-6), 102.2 (1C, uracil *C*H-5), 90.5, 86.0, 76.3, 71.0 (4C, C-1', C-2', C-3', C-4'), 63.7 (1C, C-5'), 26.4 (3C, TBDMS *t*-Bu 3 x *C*H$_3$), 19.3 (1C, TBDMS *t*-Bu C_q), -5.4. (2C, TBDMS 2 x Si-*C*H$_3$); ESI-TOF-MS: *m/z* calcd for $C_{15}H_{26}N_2NaO_6Si$ $[M+Na]^+$ 381.146, found 381.145.

5'-*O*-(4,4'-dimethoxytrityl)-uridine (2b)[Ref. 10 in the main text]



To the solution of uridine **1** (2.44 g, 10.00 mmol) in dry pyridine (30 mL) dry triethylamine (1.40 ml, 1.01 g, 10.00 mmol, 1.0 equiv.) and 4,4'-dimethoxytrityl chloride (3.38 g, 10.00 mmol, 1.0 equiv.) were added. After stirring for one hour the reaction was quenched with 5% aqueous $NaHCO_3$ solution (100 mL) and extracted with CH_2Cl_2. The organic phase was dried over Na_2SO_4, filtered and the solvent was evaporated under reduced pressure. The crude product was purified by flash column chromatography (CH_2Cl_2/MeOH 150:5 → 15:1) to afford **2b** (4.43 g, 81%) as a white foam. R_f= 0.21 (CH_2Cl_2/MeOH 15:1); ^{1}H NMR 360 MHz ($CDCl_3$) δ = 10.43 (s, 1H, N*H*), 8.02 (d, J = 8.1 Hz, 1H, uracil C*H*-6), 7.47 – 7.14 (m, 9H, 9 x DMTr Ar-H), 6.83 (d, J = 8.9 Hz, 4H, 4 x DMTr Ar-H), 5.90 (d, J = 2.2 Hz, 1H, H-1'), 5.54 (s, 1H), 5.34 (d, J = 8.1 Hz, 1H, uracil C*H*-5), 4.43 (s, 1H), 4.35 (s, 1H), 4.17 (d, J = 6.3 Hz, 1H), 3.76 (s, 6H, 2 x DMTr-OCH_3), 3.49 (d, J = 16.6 Hz, 3H); ^{13}C NMR 125 MHz ($CDCl_3$+DMSO-d_6) δ = 162.9, 157.3, 150.1, 147.4, 139.4 (7C, uracil *C*O-2, *C*O-4, 5 x DMTr Ar-C), 140.0 (1C, uracil *C*H-6), 128.3, 127.1, 126.5, 125.6 111.9 (13C, 13 x DMTr Ar-*C*H), 101.1 (1C, uracil *C*H-5), 88.3, 84.3, 73.7, 69.2 (4C, C-1', C-2', C-3', C-4'), 79.6 (1C, DMTr C_q), 60.3 (1C, C-5'), 54.2 (2C, 2 x DMTr-O*C*H$_3$); ESI-TOF-MS: *m/z* calcd for $C_{30}H_{30}N_2NaO_8$ $[M+Na]^+$ 569.190, found 569.189.

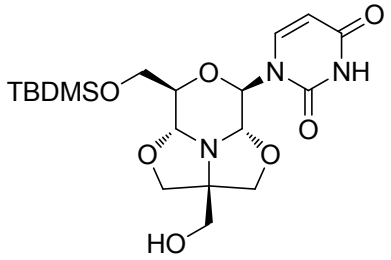
5'-*O*-trityl-uridine (2c)[7]



To the solution of uridine **1** (2.50 g, 10.24 mmol) in dry pyridine (30 mL), triphenylmethyl chloride (4.28 g, 15.36 mmol, 1.5 equiv.) was added. The reaction mixture was stirred at overnight. The solvent was evaporated under reduced pressure and the crude product was dissolved in EtOAc and extracted with water. The organic phase was dried over anhydrous Na_2SO_4, filtered and the solvent was evaporated in *vacuo*. The residue was purified by flash column chromatography (CH_2Cl_2/MeOH 98:2 → 95:5 → 9:1 to yield **2c** (4.13 g, 83%) as a

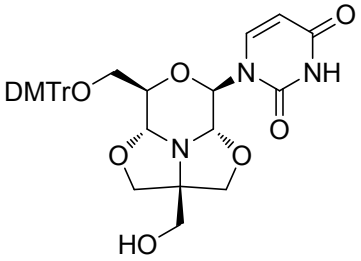
white foam. R_f= 0.33 (CH_2Cl_2/MeOH 95:5); ^{1}H NMR 360 MHz ($CDCl_3$) δ = 10.48 (s, 1H, N*H*), 7.98 (d, *J* = 8.1 Hz, 1H, uracil C*H*-6), 7.40 – 7.20 (m, 15H, 15 x Tr Ar-H), 5.89 (d, *J* = 2.4 Hz, 1H, H-1'), 5.56 (s, 1H, O*H*), 5.31 (d, *J* = 8.1 Hz, 1H, uracil C*H*-5), 4.45 – 4.42 (m, 1H), 4.35 (s, 1H, O*H*), 4.16 – 4.14 (m, 1H), 3.61 (d, *J* = 6.8 Hz, 1H), 3.50 (d, *J* = 1.5 Hz, 2H, H-5'a,b); ^{13}C NMR 90 MHz ($CDCl_3$) δ = 164.1, 151.4 (2C, uracil *C*O-2, *C*O-4), 143.4 (3C, 3 x Tr Ar-C), 140.5 (1C, uracil *C*H-6), 128.8, 128.2, 127.5 (15C, 15 x Tr Ar-*C*H), 102.4 (1C, uracil *C*H-5), 90.5 (1C, C-1'), 87.7 (1C, Tr C_q), 83.6, 75.5, 69.7 (3C, C-2', C-3', C-4'), 62.2 (1C, C-5'); ESI-TOF-MS: *m/z* calcd for $C_{28}H_{26}N_2NaO_6$ $[M+Na]^+$ 509.169, found 509.167.

12'-*O-tert*-butyldimethylsilyl-uracil-tricyclano (3a)



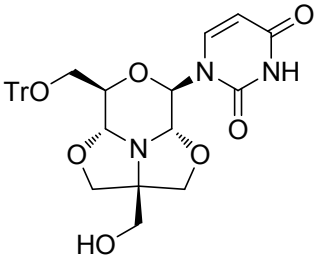
To a solution of **2a** (3.00 g, 8.37 mmol) in MeOH (100 mL) IO_4^--form of anion exchange resin (12.0 g) was added and stirred overnight in dark. Next day the resin was filtered off through a short pad of Celite® and washed successively with MeOH and CH_2Cl_2. The solvents were evaporated in vacuum. The residue was dissolved in dry MeOH (200 mL) and 3 Å molecular sieves (3 g) were added to the reaction. After stirring for half an hour Tris (1.52 g, 12.56 mmol, 1.5 equiv.) was added to the mixture and stirred overnight. After stirring overnight the molecular sieves were filtered off through a short pad of Celite® and washed successively with MeOH and CH_2Cl_2. The solvents were evaporated in vacuum and the crude product was purified by flash column chromatography (CH_2Cl_2/MeOH 95:5) to give compound **3a** (2.64 g, 72%, over two steps) as a white foam. R_f= 0.31 (CH_2Cl_2/MeOH 95:5); ^{1}H NMR 400 MHz ($CDCl_3$) δ = 9.72 (s, 1H, N*H*), 7.56 (d, *J* = 8.1 Hz, 1H, uracil C*H*-6), 6.15 (d, *J* = 4.1 Hz, 1H, H-1'), 5.73 (d, *J* = 8.2 Hz, 1H, uracil C*H*-5), 4.78 (d, *J* = 5.2 Hz, 1H, H-8'), 4.68 (d, *J* = 4.2 Hz, 1H, H-2'), 4.08 – 4.05 (m, 1H, H-9'), 3.95 – 3.79 (m, 6H, H-4'a,b, H-6'a,b, H-12'a,b), 3.67 (s, 2H, H-13'a,b), 2.92 (s, 1H, O*H*), 0.90 (s, 9H, TBDMS *t*-Bu 3 x CH_3), 0.07 (2 x s, 6H, TBDMS 2 x Si-CH_3); ^{13}C NMR 100 MHz ($CDCl_3$) δ = 163.5 (1C, uracil *C*O-4), 150.5 (1C, uracil *C*O-2), 140.0 (1C, uracil *C*H-6), 102.9 (1C, uracil *C*H-5), 90.5 (1C, C-2'), 87.6 (1C, C-8'), 77.8 (1C, C-1'), 75.3 (1C, C-5'), 74.7 (1C, C-9'), 72.0 (1C, C-6'), 71.4 (1C, C-4'), 63.7 (1C, C-13'), 62.8 (1C, C-12'), 25.9 (3C, TBDMS *t*-Bu 3 x *C*H_3), 18.4 (1C, TBDMS *t*-Bu C_q), -5.3 (2C, TBDMS 2 x Si-*C*H_3); MALDI-TOF-MS: *m/z* calcd for $C_{19}H_{31}N_3NaO_7Si$ $[M+Na]^+$ 464.183, found 464.27; Elemental analysis: calcd (%) for $C_{19}H_{31}N_3O_7Si$: C 51.68, H 7.08, N 9.52, found C 51.71, H 7.10, N 9.51.

12'-*O*-(4,4'-dimethoxytrityl)-uracil-tricyclano (3b)



To a solution of **2b** (2.50 g, 4.57 mmol) in MeOH (100 mL) IO_4^--form of anion exchange resin (10.0 g) was added and stirred overnight in dark. Next day the resin was filtered off through a short pad of Celite® and washed successively with MeOH and CH_2Cl_2. The solvent was evaporated in vacuum. The residue was dissolved in dry MeOH (50 mL) and 3 Å molecular sieves (2.5 g) were added to the reaction. After stirring for half an hour Tris (831 mg, 6.86 mmol, 1.5 equiv.) was added to the mixture. After stirring overnight the molecular sieves were filtered off through a short pad of Celite® and washed successively with MeOH and CH_2Cl_2. The solvent was evaporated in vacuum and the crude product was purified by flash chromatography (CH_2Cl_2/MeOH 100:0 → 95:5) to yield compound **11** (2.19 g, 76%, over two steps) as a white foam. R_f= 0.33 (EtOAc/MeOH 9:1); ^{1}H NMR 400 MHz ($CDCl_3$) δ = 9.21 (s, 1H, N*H*), 7.46 – 6.82 (m, 14H, 1 x uracil C*H*-6, 13 x DMTr Ar-H), 6.13 (d, *J* = 5.0 Hz, 1H, H-1'), 5.69 (d, *J* = 8.1 Hz, 1H, uracil C*H*-5), 4.78 – 4.76 (m, 1H, H-8'), 4.65 (d, *J* = 4.9 Hz, 1H, H-2'), 4.23 – 4.20 (m, 1H, H-9'), 3.89 – 3.80 (m, 4H, H-4'a,b, H-6'a,b), 3.79 (s, 6H, 2 x DMTr-OCH_3), 3.64 (d, *J* = 4.9 Hz, 2H, H-13'a,b), 3.38 (d, *J* = 4.2 Hz, 2H, H-12'a,b), 2.48 (s, 1H, O*H*); ^{13}C NMR 100 MHz ($CDCl_3$) δ = 163.0, 158.7, 150.4, 144.6, 135.7 (7C, 2 x uracil *C*O uracil, 5 x DMTr Ar-C), 139.7 (1C, uracil *C*H-6), 130.2, 128.2, 128.0, 127.1, 113.3 (13C, 13 x DMTr Ar-*C*H), 103.1 (1C, uracil *C*H-5), 90.4 (1C, C-2'), 88.6 (1C, C-8'), 86.6 (1C, DMTr C_q), 77.6 (1C, C-1'), 75.3 (1C, C-5'), 74.0 (1C, C-9'), 72.1 (1C, C-4'), 71.2 (1C, C-6'), 63.7, 63.5 (2C, C-13', C-12'), 55.4 (2C, 2 x DMTr-O*C*H_3); ESI-TOF-MS: *m/z* calcd for $C_{34}H_{35}N_3NaO_9$ $[M+Na]^+$ 652.227, found 652.225.

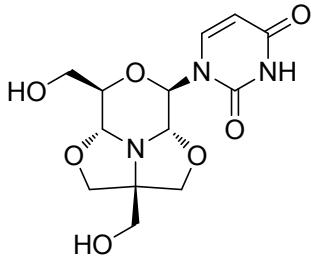
12'-*O*-trityl-uracil-tricyclano (3c)



To a solution of **2c** (2.00 g, 4.13 mmol) in MeOH (100 mL) IO_4^--form of anion exchange resin (8.0 g) was added and stirred overnight in dark. Next day the resin was filtered off through a short pad of Celite® and washed successively with MeOH and CH_2Cl_2. The solvent was evaporated in vacuum. The residue was dissolved in dry MeOH (100 mL) and 3 Å molecular sieves (2 g) were added to the reaction. After stirring for half an hour Tris (747 mg, 6.17 mmol, 1.5 equiv.) was added to the mixture. Next day another portion of Tris (249 mg, 2.06 mmol, 0.5 equiv.) was added to the reaction mixture. After stirring overnight the molecular sieves were filtered off through a short pad of Celite® and washed successively

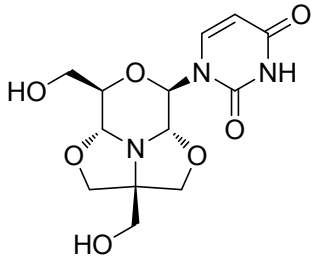
with MeOH and CH_2Cl_2. The solvent was evaporated in vacuum and the crude product was purified by flash column chromatography (CH_2Cl_2/MeOH 98:2 → 98:3 → 97:3) to yield compound **3c** (1.78 g, 76%, over two steps) as a white foam. R_f= 0.42 (CH_2Cl_2/MeOH 95:5); ^{1}H NMR (400 MHz, $CDCl_3$) δ = 9.77 (s, 1H, N*H*), 7.48 (d, *J* = 8.2 Hz, 1H, uracil C*H*-6), 7.43 (d, *J* = 7.3 Hz, 6H, 6 x Tr Ar-H), 7.29 (t, *J* = 7.4 Hz, 6H, 6 x Tr Ar-H), 7.23 (t, *J* = 7.2 Hz, 3H, 3 x Tr Ar-H), 6.14 (d, *J* = 4.7 Hz, 1H, H-1'), 5.67 (d, *J* = 8.2 Hz, 1H, uracil C*H*-5), 4.80 (d, *J* = 4.6 Hz, 1H, H-8'), 4.68 (d, *J* = 4.7 Hz, 1H, H-2'), 4.21 (q, *J* = 4.4 Hz, 1H, H-9'), 3.87 (d, *J* = 9.0 Hz, 2H, H-6'a, H-4'a), 3.78 (d, *J* = 8.9 Hz, 1H, H-6'b), 3.77 (d, *J* = 8.8 Hz, 1H, H-4'b), 3.64 (d, *J* = 5.5 Hz, 2H, H-13'a,b), 3.38 (d, *J* = 4.3 Hz, 2H, H-12'a,b), 2.90 (t, *J* = 5.8 Hz, 1H, O*H*); ^{13}C NMR (100 MHz, $CDCl_3$) δ = 163.4 (1C, uracil *C*O-4), 150.5 (1C, uracil *C*O-2), 143.5 (3C, 3 x Tr Ar-C), 139.9 (1C, uracil *C*H-6), 128.7, 128.0, 127.3 (15C, 15 x Tr Ar-*C*H), 103.0 (1C, uracil *C*H-5), 90.3 (1C, C-2'), 88.4 (1C, C-8'), 87.1 (1C, Tr C_q), 77.7 (1C, C-1'), 75.3 (1C, C-5'), 73.9 (1C, C-9'), 72.0 (1C, C-4'), 71.3 (1C, C-6'), 63.7 (1C, C-13'), 63.6 (1C, C-12'); ESI-TOF-MS: *m/z* calcd for $C_{32}H_{31}N_3NaO_7$ $[M+Na]^+$ 592.206, found 592.205.

Uracil-tricyclano (4) - Synthesis without protecting group



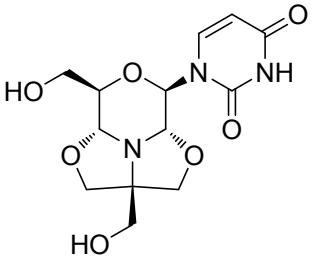
To a solution of **1** (244 mg, 1.00 mmol) in MeOH (20 mL) IO_4^--form of anion exchange resin (1.0 g) was added and stirred overnight in dark. Next day the resin was filtered off through a short pad of Celite® and washed with MeOH. The solvent was evaporated in vacuum. The residue was dissolved in dry MeOH (100 mL) and 3 Å molecular sieves (250 mg) were added to the reaction. After stirring for half an hour Tris (182 mg, 1.5 mmol, 1.5 equiv.) was added to the mixture. After stirring overnight the molecular sieves were filtered off through a short pad of Celite® and washed with MeOH. The solvent was evaporated in vacuum and the crude product was purified by flash column chromatography (EtOAc/MeOH 95:5) to yield **4** (190 mg, 58%, over two steps) as a white foam.

Uracil-tricyclano (4) - Deprotection of 3a



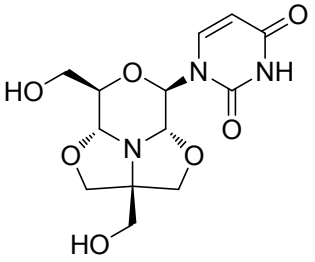
3a (167 mg, 0.38 mmol) was dissolved in dry THF (3 mL). Tetrabutylammonium fluoride solution (570 mL, 1.5 equiv., 1.0 M in THF) was added to the reaction mixture. After stirring for two hours the solvent was evaporated and the crude product was purified by flash column chromatography (EtOAc/MeOH 95:5) to afford **4** (59 mg, 48%) as a white foam.

Uracil-tricyclano (4) - Deprotection of 3b



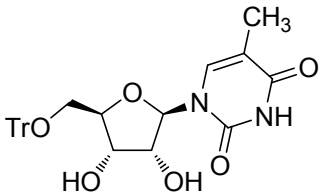
3b (157 mg, 0.25 mmol) was dissolved in a mixture of hexafluoroisopropanol (2.5 mL), $MeNO_2$ (1.25 mL) and Et_3SiH (600 μL, 1.88 mmol, 7.5 equiv.). Then $ZnCl_2$ (157 mg, 1.15 mmol, 4.6 equiv.) was added to the reaction mixture. After stirring for half an hour saturated $NaHCO_3$-solution was added and the solvents were evaporated. The crude product was purified by flash column chromatography (CH_2Cl_2/MeOH 95:5 → 9:1 → 8:2) to yield **4** (58 mg, 71%) as a white foam.

Uracil-tricyclano (4) - Deprotection of 3c



3c (342 mg, 0.60 mmol) was added to the mixture of $ZnCl_2$ (342 mg, 2.51 mmol, 4.2 equiv.), hexafluoroisopropanol (6 mL), $MeNO_2$ (3 mL) and Et_3SiH (600 μL, 3.76 mmol, 6.3 equiv.). After 2 hours saturated $NaHCO_3$-solution was added and the solvents were evaporated. The crude product was purified by flash column chromatography (CH_2Cl_2/MeOH 9:1 → 8:1 → 85:15 → 8:2) to yield **4** (129 mg, 66%) as a white foam. R_f= 0.45 (CH_2Cl_2/MeOH 85:15); ^{1}H NMR (400 MHz, D_2O + CD_3OD) δ = 7.78 (d, J = 8.1 Hz, 1H, uracil C*H*-6), 6.04 (d, J = 5.0 Hz, 1H, H-1'), 5.88 (d, J = 8.1 Hz, 1H, uracil C*H*-5), 4.77 (d, J = 5.1 Hz, 1H, H-2'), 4.70 (d, J = 4.1 Hz, 1H, H-8'), 4.15 (dd, J = 3.9, 1.3 Hz, 1H, H-9'), 4.00 (d, J = 9.1 Hz, 1H, H-6'a), 3.93 – 3.86 (m, 2H, H-4'a,b), 3.85 – 3.71 (m, 3H, H-6'b, H-12'a,b), 3.69 (s, 2H, H-13'a,b); ^{13}C NMR (100 MHz, D_2O + CD_3OD) δ = 166.6 (1C, uracil *C*O-4), 152.3 (1C, uracil *C*O-2), 142.6 (1C, uracil *C*H-6), 103.8 (1C, uracil *C*H-5), 90.8 (1C, C-2'), 89.1 (1C, C-8'), 79.1 (1C, C-1'), 75.9 (1C, C-9'), 75.6 (1C, C-5'), 73.0 (1C, C-4'), 72.2 (1C, C-6'), 63.6 (1C, C-13'), 62.7 (1C, C-12'); ESI-TOF-MS: *m/z* calcd for $C_{13}H_{17}N_3NaO_7$ $[M+Na]^+$ 350.096, found 350.093.

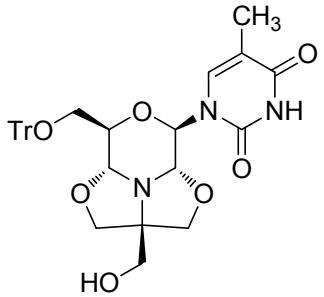
5'-*O*-trityl-ribothymidine (6)[Ref. 25 in the main text]



To a solution of ribothymidine **5** (2.50 g, 9.68 mmol) in dry pyridine (20 mL) was added triphenylchloromethane (3.24 g, 11.62 mmol, 1.2 equiv.) and stirred overnight. The solvent

was evaporated in *vacuo*, the residue was dissolved in EtOAc (400 mL) and extracted with distilled water (2 x 50 mL) and brine (50 mL). The organic layer was dried over anhydrous Na_2SO_4. The solid phase was filtered and the solvent was evaporated under reduced pressure. The crude product was purified by flash column chromatography (CH_2Cl_2/MeOH 96:4 → 9:1) to yield compound **6** (3.64 g, 75%) as a white solid. R_f= 0.27 (CH_2Cl_2/MeOH 95:5); ^{1}H NMR (400 MHz, DMSO-d_6) δ = 11.38 (s, 1H, N*H*), 7.51 (s, 1H, thymine C*H*-6), 7.41 (d, *J* = 7.5 Hz, 6H, 6 x Tr Ar-H), 7.35 (t, *J* = 7.5 Hz, 6H, 6 x Tr Ar-H), 7.28 (t, *J* = 7.1 Hz, 3H, 3 x Tr Ar-H), 5.83 (d, *J* = 5.1 Hz, 1H, H-1'), 5.48 (s, 1H, O*H*), 5.18 (s, 1H, O*H*), 4.21 (s, 1H), 4.14 (s, 1H), 3.99 (dd, *J* = 7.0, 4.2 Hz, 1H, H-4'), 3.28 (dd, *J* = 10.6, 4.3 Hz, 1H, H-5'a), 3.20 (dd, *J* = 10.5, 2.4 Hz, 1H, H-5'b), 1.45 (s, 3H, timin C*H*$_3$); ^{13}C NMR (100 MHz, DMSO-d_6) δ = 163.7, 150.7 (2C, thymine *C*O-2, *C*O-4), 143.5 (3C, 3 x Tr Ar-C), 135.9 (1C, thymine *C*H-6), 128.3, 128.0, 127.2 (15C, 15 x Tr Ar-*C*H), 109.6 (1C, thymine C-5), 88.1, 82.8, 73.2, 70.1 (4C, C-1', C-2', C-3', C-4'), 86.5 (1C, Tr C_q), 63.8 (1C, C-5'), 11.7 (thymine *C*H$_3$); MALDI-TOF-MS: *m/z* calcd for $C_{29}H_{28}N_2NaO_6$ $[M+Na]^+$ 523.185, found 523.23; Elemental analysis: calcd (%) for $C_{29}H_{28}N_2O_6$: C 69.59, H 5.64, N 5.60, found C 69.57, H 5.66, N 5.61.

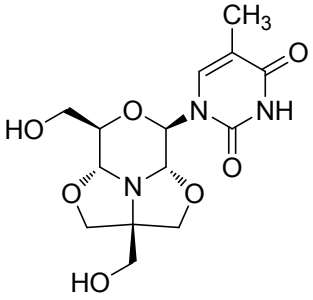
12'-*O*-trityl-thymine-tricyclano (7)



To a solution of **6** (1.30 g, 2.60 mmol) in MeOH (100 mL) IO_4^--form of anion exchange resin (5.2 g) was added and stirred overnight in dark. Next day the resin was filtered off through a short pad of Celite® and washed with MeOH. The solvent was evaporated in vacuum. The residue was dissolved in dry MeOH (70 mL) and 3 Å molecular sieves (1.3 g) were added to the reaction. After stirring for half an hour Tris (474 mg, 3.91 mmol, 1.5 equiv.) was added to the mixture. After stirring overnight the molecular sieves were filtered off through a short pad of Celite® and washed successively with MeOH and CH_2Cl_2. The solvent was evaporated in vacuum and the crude product was purified byflash column chromatography (CH_2Cl_2/MeOH 98:2 → 97:3) to yield **7** (976 mg, 64%, over two steps) as a white foam. R_f= 0.35 (CH_2Cl_2/MeOH 95:5); ^{1}H NMR 400 MHz ($CDCl_3$) δ = 9.64 (s, 1H, N*H*), 7.45 (d, *J* = 7.4 Hz, 6H, 6 x Tr Ar-H), 7.26 (dt, *J* = 24.4, 7.1 Hz, 10H, 9 x Tr Ar-H, 1 x thymine C*H*-6), 6.14 (d, *J* = 5.2 Hz, 1H, H-1'), 4.76 (d, *J* = 4.0 Hz, 1H, H-8'), 4.71 (d, *J* = 5.2 Hz, 1H, H-2'), 4.24 (q, *J* = 4.4 Hz, 1H, H-9'), 3.88 (d, *J* = 8.9 Hz, 2H, H-4'a, H-6'a), 3.80 (d, *J* = 8.9 Hz, 1H, H-4'b), 3.76 (d, *J* = 8.9 Hz, 1H, H-6'b), 3.64 (d, *J* = 5.7 Hz, 2H, H-13'a,b), 3.36 (d, *J* = 4.6 Hz, 2H, H-12'a,b), 2.86 (t, *J* = 5.9 Hz, 1H, O*H*), 1.87 (s, 3H, thymine C*H*$_3$); ^{13}C NMR 100 MHz ($CDCl_3$) δ = 163.8 (1C, thymine *C*O-4), 150.7 (1C, thymine *C*O-2), 143.6 (3C, 3 x Tr Ar-C) 135.4 (1C, thymine *C*H-6), 128.7, 128.0, 127.3 (15C, 15 x Tr Ar-*C*H), 111.5 (1C, thymine C-5), 90.3 (1C, C-2'), 88.7 (1C, C-8'), 87.0 (1C, Tr C_q), 77.7 (1C, C-1'), 75.3 (1C, C-5'), 74.0 (1C, C-9'), 72.0 (1C, C-4'), 71.3 (1C, C-6'), 63.8 (1C, C-12'), 63.6 (1C, C-13'), 12.6 (1C, thymine *C*H$_3$); MALDI-TOF-MS: *m/z* calcd for $C_{33}H_{33}N_3NaO_7$ $[M+Na]^+$ 606.222, found

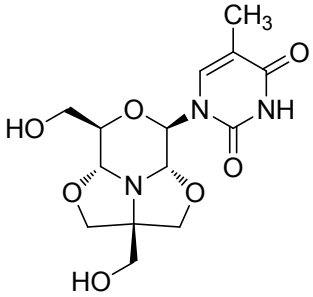
606.41; Elemental analysis: calcd (%) for $C_{33}H_{33}N_3O_7$: C 67.91, H 5.70, N 7.20, found C 67.88, H 5.72, N 7.23.

Thymine-tricyclano (8) - Synthesis without protecting group



To a solution of ribothymidine **5** (516 mg, 2.00 mmol) in MeOH (50 mL) IO_4^--form of anion exchange resin (2.0 g) was added and stirred overnight in dark. Next day the resin was filtered off through a short pad of Celite® and washed with MeOH. The solvent was evaporated in vacuum. The residue was dissolved in dry MeOH (50 mL) and 3 Å molecular sieves (600 mg) were added to the reaction. After stirring for half an hour Tris (363 mg, 3.00 mmol, 1.5 equiv.) was added to the mixture. After stirring overnight the molecular sieves were filtered off through a short pad of Celite® and washed with MeOH. The solvent was evaporated in vacuum and the crude product was purified by flash column chromatography ($CHCl_3$/MeOH 95:5) to yield compound **8** (362 mg, 53%, 2 steps) as a white foam.

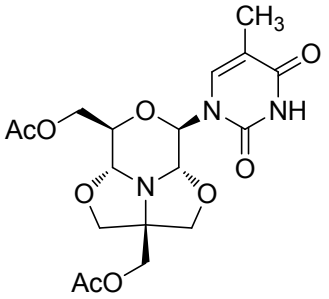
Thymine-tricyclano (8) - Deprotection of 7



7 (350 mg, 0.60 mmol) was added to the mixture of $ZnCl_2$ (350 mg, 2.57 mmol, 4.3 equiv.), hexafluoroisopropanol (6 mL), $MeNO_2$ (3 mL) and Et_3SiH (600 µL, 3.76 mmol, 6.3 equiv.). After 1 hour saturated $NaHCO_3$-solution was added and the solvents were evaporated. The crude product was purified by flash column chromatography (CH_2Cl_2/MeOH 95:5 → 9:1 → 85:15) to yield **8** (112 mg, 55%) as a white foam. R_f= 0.50 (CH_2Cl_2/MeOH 85:15); ^{1}H NMR 400 MHz (D_2O + CD_3OD) δ = 7.59 (d, J = 1.0 Hz, 1H, thymine C*H*-6), 6.02 (d, J = 5.4 Hz, 1H, H-1'), 4.78 (d, J = 4.5 Hz, 1H, H-2'), 4.71 (d, J = 4.3 Hz, 1H, H-8'), 4.17 (dt, J = 5.2, 3.9 Hz, 1H, H-9'), 4.00 (d, J = 9.1 Hz, 1H, H-6'a), 3.90 (s, 2H, H-4'a,b), 3.81 (d, J = 9.2 Hz, 1H, H-6'b), 3.86 – 3.73 (m, 2H, H-12'a,b), 3.71 (s, 2H, H-13'a,b), 1.88 (d, J = 0.7 Hz, 3H, thymine C*H*$_3$); ^{13}C NMR 100 MHz (D_2O + CD_3OD) δ = 167.0 (1C, thymine *C*O-4), 152.5 (1C, thymine *C*O-2), 138.0 (1C, thymine *C*H-6), 113.0 (1C, thymine C-5), 90.7 (1C, C-2'), 89.1 (1C, C-8'), 79.0 (1C, C-1'), 75.8 (1C, C-9'), 75.5 (1C, C-5'), 73.0 (1C, C-4'), 72.2 (1C, C-6'), 63.5 (1C, C-13'), 62.7 (1C, C-12'), 12.4 (1C, thymine *C*H$_3$); MALDI-TOF-MS: *m/z*

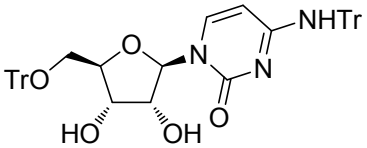
calcd for $C_{13}H_{17}N_3NaO_7$ $[M+Na]^+$ 364.112, found 364.21; Elemental analysis: calcd (%) for $C_{13}H_{17}N_3O_7$: C 49.27, H 5.61, N 12.31, found C 49.29, H 5.58, N 12.30.

12',13'-di-*O*-acetyl-thymine-tricyclano (9)



8 (110 mg, 0.32 mmol) was dissolved in dry pyridine (1 mL). Then acetic anhydride (122 μL, 1.28 mmol, 4.0 equiv.) was added to the reaction mixture and it was stirred overnight. After that saturated $NaHCO_3$ solution (100 mL) was added and stirred for half an hour. The solvent was evaporated and the residue was dissolved in CH_2Cl_2 (30 mL) and it was extracted with 10% $NaHSO_4$ solution (2 x 5 mL) then saturated $NaHCO_3$ solution (2 x 5 mL). The organic layer was dried over anhydrous Na_2SO_4. The solid phase was filtered off and solvent was evaporated in vacuum. The crude product was purified by flash chromatography (*i*-hexane/acetone 7:3 → 6:4) to yield compound **9** (100 mg, 73%) as a white foam. R_f= 0.51 (*i*-hexane/acetone 1:1); ^{1}H NMR (400 MHz, $CDCl_3$) δ = 9.70 (s, 1H, N*H*), 7.17 (d, *J* = 1.0 Hz, 1H, thymine C*H*-6), 6.19 (d, *J* = 4.0 Hz, 1H, H-1'), 4.63 – 4.57 (m, 2H, H-2', H-8'), 4.32 – 4.17 (m, 4H, H-12'a,b, H-13'a, H-9'), 4.10 (d, *J* = 11.5 Hz, 1H, H-13'b), 3.98 (d, *J* = 9.0 Hz, 1H, H-6'a), 3.80 – 3.75 (m, 3H, H-4'a,b, H-6'b), 2.07 (2 x s, 6H, 2 x COC*H*$_3$), 1.91 (s, 3H, thymine C*H*$_3$); ^{13}C NMR (100 MHz, $CDCl_3$) δ = 170.6 (1C, 12'-O*C*OCH$_3$), 170.5 (1C, 13'-O*C*OCH$_3$), 163.7 (1C, thymine *C*O-4), 150.5 (1C, thymin *C*O-2), 135.2 (1C, thymine *C*H-6), 112.0 (1C, thymine C-5), 90.7 (1C, C-2'), 87.7 (1C, C-8'), 77.4 (1C, C-1'), 72.8 (1C, C-5'), 72.3 (1C, C-9'), 72.3 (1C, C-4'), 72.1 (1C, C-6'), 65.1 (1C, C-13'), 63.5 (1C, C-12'), 20.8, 20.7 (2C, 2 x CO*C*H$_3$), 12.5 (1C, thymine *C*H$_3$); MALDI-TOF-MS: *m/z* calcd for $C_{18}H_{23}N_3NaO_9$ $[M+Na]^+$ 448.133, found 448.307; Elemental analysis: calcd (%) for $C_{18}H_{23}N_3O_9$: C 50.82, H 5.45, N 9.88, found C 50.81, H 5.48, N 9.87.

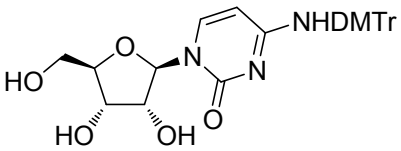
4-*N*,5'-*O*-*bis*trityl-cytidine (11a)



To a suspension of cytidine **10** (2.00 g, 8.22 mmol) in dry DMF (20 mL) trityl chloride (4.65 g, 16.68 mmol, 2.03 equiv.), 4-dimethylaminopyridine (0.02 g, 0.02 equiv.), Et_3N (2.8 mL, 19.98 mmol, 2.43 equiv.) were added and stirred at 50 °C. Et_3N (1.88 ml, 13.47 mmol, 1.64 equiv.) and triphenylchloromethane (1.81 g, 6.50 mmol, 0.79 equiv.) were added after two days, four days and seven days. After ten days the mixture was evaporated in *vacuo*, and the residue was dissolved in CH_2Cl_2. The organic layer was washed with 10%-os $NaHSO_4$ solution, saturated $NaHCO_3$-solution and dried over anhydrous Na_2SO_4. The solid phase was filtered off and the solvent was evaporated under reduce pressure. The crude product was

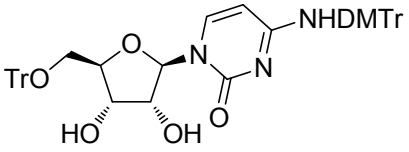
purified by flash chromatography (CH_2Cl_2/MeOH 98:2 → 97:3 → 95:5) to afford **11a** (1.81g, 30%) as a tan solid. R_f= 0.36 (CH_2Cl_2/MeOH 95:5); ^{1}H NMR (400 MHz, DMSO-d_6) δ = 8.51 (s, 1H, N*H*), 7.62 (d, *J* = 7.3 Hz, 1H, cytosine C*H*-6), 7.48 – 7.09 (m, 30H, 30 x Tr Ar-H), 6.16 (d, *J* = 7.3 Hz, 1H, cytosine C*H*-5), 5.70 (d, *J* = 3.1 Hz, 1H, H-1'), 5.36 (d, *J* = 4.0 Hz, 1H), 5.04 (s, 1H), 4.03 (d, *J* = 2.4 Hz, 1H), 3.95 – 3.86 (m, 2H), 3.24 (s, 2H); ^{13}C NMR (100 MHz, DMSO-d_6) δ = 163.3, 154.0 (2C, cytosine *C*O-2, C-4), 144.6, 143.5 (6C, 6 x Tr Ar-C), 128.8, 128.3, 128.0, 127.5, 127.1, 126.3 (30C, 30 x Tr Ar-*C*H), 96.2, 89.5, 81.8, 73.8, 70.2, (5C, cytosine *C*H-5, C-1', C-2', C-3', C-4') 86.3 (1C, OTr C_q), 70.4 (1C, NTr C_q), 63.3 (1C, C-5'); MALDI-TOF-MS: *m/z* calcd for $C_{47}H_{41}N_3NaO_5$ $[M+Na]^+$ 750.294, found 750.208; Elemental analysis: calcd (%) for $C_{47}H_{41}N_3O_5$: C 77.56, H 5.68, N 5.77, found C 77.58, H 5.67, N 5.79.

4-*N*-(4,4'-dimethoxytrityl)-cytidine (11b)[Ref. 26 in the main text]



To a suspension of cytidine **10** (243 mg, 1.00 mmol) in dry C_5H_5N (5 mL) chlorotrimethylsilane (952 mL, 7.50 mmol, 7.5 equiv.) was added and stirred under argon atmosphere. After 1 hour dimethoxytrityl chloride (406 mg, 1.20 mmol, 1.2 equiv.) was added and the mixture was stirred overnight. Next day dry DMF (2 mL) and dimethoxytrityl chloride (102 mg, 0.30 mmol, 0.3 equiv.) were added and the mixture was stirred for 4 days. After that the reaction mixture was quenched by saturated $NaHCO_3$-solution and the volatiles were evaporated in *vacuo*. The crude product was purified by flash column chromatography (CH_2Cl_2/MeOH 95:5 → 93:7 → 9:1 → 8:2) to afford **11b** (447 mg, 82%) as an off-white foam. R_f= 0.18 (CH_2Cl_2/MeOH 95:5); ^{1}H NMR (360 MHz, DMSO-d_6) δ = 8.39 (s, 1H, N*H*), 7.74 (d, *J* = 7.5 Hz, 1H, cytosine C*H*-6), 7.24 (t, *J* = 8.3 Hz, 5H, 5 x DMTr Ar-H), 7.14 (d, *J* = 8.7 Hz, 4H, 4 x DMTr Ar-H), 6.83 (d, *J* = 8.5 Hz, 4H, 4 x DMTr Ar-H), 6.25 (d, *J* = 7.3 Hz, 1H, cytosine C*H*-5), 5.67 (s, 1H), 5.25 (s, 1H), 5.08 (s, 2H), 3.91 (s, 2H), 3.77 (s, 1H), 3.72 (s, 6H, 2 x DMTr OC*H*$_3$), 3.54 (d, *J* = 20.1 Hz, 2H, H-5'a,b); ^{13}C NMR (90 MHz, DMSO-d_6) δ = 163.3, 157.4, 154.3, 145.1, 137.0 (7C, cytosine *C*O-2, C-4, 5 x DMTR Ar-C), 140.1 (1C, cytosine *C*H-6), 129.9, 128.5, 127.4, 126.0, 112.7 (13C, 13 x DMTr Ar-*C*H), 96.3, 88.8, 84.3, 73.6, 69.7, (5C, cytosine *C*H-5, C-1', C-2', C-3', C-4'), 69.4 (1C, NDMTr C_q), 60.8 (1C, C-5'), 55.0 (2C, 2 x DMTr O*C*H$_3$); MALDI-TOF-MS: *m/z* calcd for $C_{30}H_{31}N_3NaO_7$ $[M+Na]^+$ 568.206, found 568.492; Elemental analysis: calcd (%) for $C_{30}H_{31}N_3O_7$: C 66.04, H 5.73, N 7.70, found C 66.02, H 5.69, N 7.73.

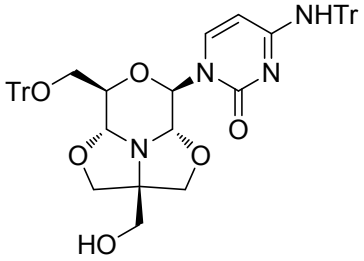
4-*N*-(4,4'-dimethoxytrityl)-5'-*O*-trityl-cytidine (12b)



To a solution of **11b** (370 mg, 0.68 mmol) in dry C_5H_5N (4 mL) trityl chloride (246 mg, 0.88 mmol, 1.3 equiv.) was added and the mixture was stirred overnight. Next day trityl chloride

(132 mg, 0.48 mmol, 0.7 equiv.) and dry C_5H_5N (1 mL) were added and the mixture was stirred overnight. After that trityl chloride (189 mg, 0.68 mmol, 1.0 equiv.) and dry C_5H_5N (1 mL) were added and the mixture was stirred for 2 days. Then trityl chloride (189 mg, 0.68 mmol, 1.0 equiv.) and dry C_5H_5N (2 mL) were added and the mixture was stirred overnight. Next day trityl chloride (189 mg, 0.68 mmol, 1.0 equiv.) was added and the mixture was stirred overnight. The reaction mixture was quenched by saturated $NaHCO_3$-solution and the volatiles were evaporated in *vacuo*. The residue was dissolved in EtOAc and washed with water, extracted with 10% aqueous $NaHSO_4$ solution, aqueous saturated $NaHCO_3$ solution, brine and dried over anhydrous Na_2SO_4. The solid phase was filtered off and the crude product was purified by flash column chromatography (CH_2Cl_2/MeOH 97:3 → 96:4 → 95:5) to afford **12b** (365 mg, 68%) as a white foam. R_f= 0.24 (CH_2Cl_2/MeOH 95:5); ^{1}H NMR (360 MHz, $CDCl_3$ + CD_3OD) δ = 7.83 (d, *J* = 7.7 Hz, 1H, cytosine C*H*-6), 7.32 – 7.02 (m, 24H, 9 x DMTr, 15x Tr Ar-H), 6.77 (d, *J* = 8.9 Hz, 4H, 4 x DMTr Ar-H), 5.73 (d, *J* = 1.6 Hz, 1H, H-1'), 4.75 (d, *J* = 7.7 Hz, 1H cytosine C*H*-5), 4.34 (dd, *J* = 7.0, 5.2 Hz, 1H, H-3'), 4.17 (dd, *J* = 5.0, 1.4 Hz, 1H, H-2'), 4.09 (d, *J* = 7.2 Hz, 1H, H-4'), 3.73 (s, 6H, 2 x DMTr OC*H*$_3$), 3.45 (ddd, *J* = 33.0, 11.1, 2.3 Hz, 1H, H-5'a,b); ^{13}C NMR (90 MHz, $CDCl_3$ + CD_3OD) δ = 165.6, 158.7, 156.3, 144.2, 143.2, 136.2, 135.7 (5C, cytosine *C*O-2, C-4, 5 x DMTr Ar-C), 140.9 (1C, cytosine *C*H-6), 130.0, 129.9, 128.6, 128.5, 128.3, 127.9, 127.4, 127.2, 113.6, 113.5 (28C, 13 x DMTr Ar-*C*H, 15 x Tr Ar-*C*H), 95.2, 91.7, 83.5, 75.5, 69.3, (5C, cytosine *C*H-5, C-1', C-2', C-3', C-4') 87.4 (1C, OTr C_q), 70.1 (1C, NDMTr C_q), 61.6 (1C, C-5'), 55.2 (2C, 2 x DMTr O*C*H$_3$); MALDI-TOF-MS: *m/z* calcd for $C_{49}H_{45}N_3NaO_7$ $[M+Na]^+$ 810.316, found 810.15; Elemental analysis: calcd (%) for $C_{49}H_{45}N_3O_7$: C 74.70, H 5.76, N 5.33, found C 74.72, H 5.75, N 5.31.

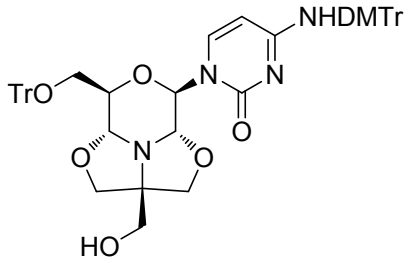
4-*N*,5'-*O*-*bis*trityl-cytosine-tricyclano (13a)



11a (1.00 g, 1.37 mmol) was dissolved in a mixture of MeOH (75 mL) and CH_2Cl_2 (25 mL). Then IO_4^--form of anion exchange resin (4 g) was added and stirred overnight in dark. Next day the resin was filtered off through a short pad of Celite® and washed successively with MeOH and CH_2Cl_2. The solvent was evaporated in vacuum. The residue was dissolved in dry MeOH (50 mL) and 3 Å molecular sieves (1 g) were added to the reaction. After stirring for half an hour Tris (249 mg, 2.06 mmol, 1.5 equiv.) was added to the mixture and stirred overnight. Next day Tris (166 mg, 1.37 mmol, 1.0 equiv.) was also added. After stirring overnight the molecular sieves were filtered off through a short pad of Celite® and washed successively with MeOH and CH_2Cl_2. The solvent was evaporated in vacuum and the crude product was purified by flash column chromatography (CH_2Cl_2/MeOH 98:2 → 97:3) to afford **13a** (726 mg, 65%, over two steps) as a jonquil foam. R_f= 0.46 (CH_2Cl_2/MeOH 95:5); ^{1}H NMR (400 MHz, $CDCl_3$) δ = 7.35 (dd, *J* = 7.8, 1.4 Hz, 7H, 1 x cytosine C*H*-6, 6 x Tr Ar-H), 7.33 – 7.13 (m, 24H, 24 x Tr Ar-H), 6.18 (d, *J* = 3.7 Hz, 1H, H-1'), 5.00 (d, *J* = 7.7 Hz, 1H,

cytosine C*H*-5), 4.77 (d, *J* = 5.9 Hz, 1H, H-8'), 4.64 (d, *J* = 3.8 Hz, 1H, H-2'), 4.11 (dt, *J* = 5.8, 3.8 Hz, 1H, H-9'), 3.90 – 3.81 (m, 3H, H-6'a,b, H-4'a), 3.77 (d, *J* = 8.9 Hz, 1H, H-4'b), 3.66 – 3.57 (m, 2H, H-13'a,b), 3.37 – 3.27 (m, 2H, H-12'a,b), 3.24 – 3.05 (m, 1H), 2.17 – 1.95 (m, 1H); ^{13}C NMR (100 MHz, $CDCl_3$) δ = 165.6 (1C, cytosine C-4), 155.3 (1C, cytosine *C*O-2), 143.9, 143.6 (6C, 6 x Tr Ar-C), 140.7 (1C, cytosine *C*H-6), 128.8, 128.7, 128.5, 127.9, 127.7, 127.2 (30C, 30 x Tr Ar-*C*H), 95.2 (1C, cytosine *C*H-5), 90.5 (1C, C-2'), 87.8 (1C, C-8'), 87.0 (1C, OTr C_q), 78.6 (1C, C-1'), 75.3 (1C, C-5'), 73.7 (1C, C-9'), 72.1 (1C, C-4'), 71.7 (1C, C-6'), 71.1 (1C, NTr C_q), 64.0 (1C, C-13'), 63.5 (1C, C-12'); MALDI-TOF-MS: *m/z* calcd for $C_{52}H_{46}N_6NaO_6$ $[M+Na]^+$ 833.332, found 833.4; Elemental analysis: calcd (%) for $C_{52}H_{46}N_6O_6$: C 75.54, H 5.72, N 6.91, found C 75.57, H 5.71, N 6.92.

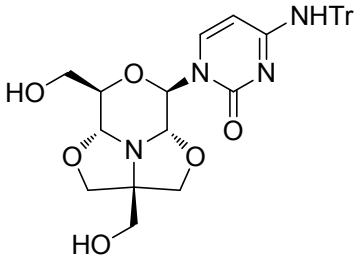
4-*N*-(4,4'-dimethoxytrityl)-5'-*O*-trityl-cytosine-tricyclano (13b)



12b (330 mg, 0.42 mmol) was dissolved in a mixture of MeOH (15 mL) and CH_2Cl_2 (15 mL). Then IO_4^--form of anion exchange resin (1.3 g) was added and stirred overnight in dark. Next two days IO_4^--form of anion exchange resin (1.3 g) were also added daily and stirred overnight in dark. On the third day the resin was filtered off through a short pad of Celite® and washed successively with MeOH and CH_2Cl_2. The solvent was evaporated in vacuum. The residue was dissolved in dry MeOH (25 mL) and 3 Å molecular sieves (330 mg) were added to the reaction. After stirring for half an hour Tris (102 mg, 0.84 mmol, 2.0 equiv.) was added to the mixture and stirred overnight. After stirring overnight the molecular sieves were filtered off through a short pad of Celite® and washed successively with MeOH and CH_2Cl_2. The solvent was evaporated in vacuum and the crude product was purified by flash column chromatography (CH_2Cl_2/MeOH 98:2 → 97:3 → 96:4) to afford **13b** (258 mg, 71%, over two steps) as a white foam. R_f= 0.44 (CH_2Cl_2/MeOH 95:5); ^{1}H NMR (400 MHz, $CDCl_3$) δ = 7.36 (dd, *J* = 7.6, 2.1 Hz, 7H, cytosine C*H*-6, 6 x Tr Ar-H), 7.32 – 7.16 (m, 14H, 9 x Tr Ar-H, 5 x DMTr Ph Ar-H), 7.12 (dd, *J* = 8.9, 2.1 Hz, 4H, DMTr $H_3COC_6H_4$- Ar-H), 6.80 (dd, *J* = 8.8, 0.8 Hz, 4H, DMTr $H_3COC_6H_4$- Ar-H), 6.20 (d, *J* = 3.8 Hz, 1H), 5.04 (d, *J* = 7.7 Hz, 1H, cytosine C*H*-5), 4.77 (d, *J* = 5.8 Hz, 1H, H-8'), 4.65 (d, *J* = 3.8 Hz, 1H, H-2'), 4.12 (dt, *J* = 5.6, 3.9 Hz, 1H, H-9'), 3.89 – 3.82 (m, 3H, H-6'a,b, H-4'a), 3.77 (dd, *J* = 8.4, 3.9 Hz, 1H, H-4'b), 3.73 (s, 6H, 2 x DMTr OC*H*$_3$), 3.66 – 3.58 (m, 2H, H-13'a,b), 3.34 – 3.29 (m, 2H, H-12'a,b); ^{13}C NMR (100 MHz, $CDCl_3$) δ = 165.5 (1C, cytosine C-4), 158.8 (2C, 2 x DMTr $H_3COC_6H_4$- Ar-C), 155.4 (1C, cytosine *C*O-2), 144.6 (1C, DMTr Ph Ar-C), 143.6 (3C, 3 x Tr Ar-C), 140.6 (1C, cytosine *C*H-6), 136.3, 136.1 (2C, 2 x DMTr $H_3COC_6H_4$- Ar-C), 130.0, 129.9 (4C, 4 x DMTr $H_3COC_6H_4$- Ar-*C*H), 128.7, 127.9, 127.2 (15C, 15 x Tr Ar-*C*H), 128.6, 128.4, 127.5 (5C, 5 x DMTr Ph Ar-*C*H), 113.7 (4C, 4 x DMTr $H_3COC_6H_4$- Ar-*C*H), 95.3 (1C, cytosine *C*H-5), 90.5 (1C, C-2'), 87.8 (1C, C-8'), 86.9 (1C, OTr C_q), 78.6 (1C, C-1'), 75.3 (1C, C-5'), 73.7 (1C, C-9'), 72.1 (1C, C-4'), 71.7 (1C, C-6'), 70.3 (1C, NDMTr C_q), 63.9 (1C,

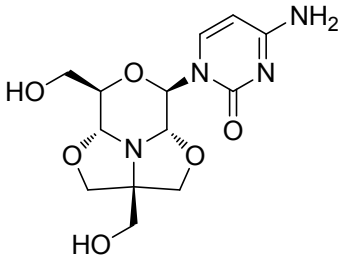
C-13'), 63.5 (1C, C-12'), 55.3 (2C, 2 x DMTr O*C*H_3); ESI-TOF-MS: *m/z* calcd for $C_{53}H_{50}N_4NaO_8$ $[M+Na]^+$ 893.353, found 893.347; Elemental analysis: calcd (%) for $C_{53}H_{50}N_4O_8$: C 73.09, H 5.79, N 6.43, found C 73.11, H 5.78, N 6.41.

4-*N*-trityl-cytosine-tricyclano (14a) - Deprotection of 13a



13a (247 mg, 0.30 mmol) was dissolved in a mixture of hexafluoroisopropanol (3 mL), $MeNO_2$ (1.5 mL) and Et_3SiH (364 µL, 2.28 mmol, 7.6 equiv.) then $ZnCl_2$ (333 mg, 2.44 mmol, 8.0 equiv.) was added to the mixture. After 5 hours saturated $NaHCO_3$-solution was added and the solvents were evaporated. The crude product was purified by flash column chromatography (CH_2Cl_2/MeOH 95:5 → 93:7) to yield **14a** (97 mg, 56%) as an off-white foam. R_f= 0.40 (CH_2Cl_2/MeOH 9:1); ^{1}H NMR (400 MHz, $CDCl_3$ + CD_3OD) δ = 7.29 (dt, *J* = 23.5, 6.9 Hz, 16H, cytosine C*H*-6, 15 x Tr Ar-H), 6.09 (d, *J* = 3.9 Hz, 1H, H-1'), 5.16 (d, *J* = 7.7 Hz, 1H, cytosine H-5), 4.62 (dd, *J* = 5.3, 2.4 Hz, 1H, H-2'), 4.57 (d, *J* = 4.6 Hz, 1H, H-8'), 4.04 (d, *J* = 3.8 Hz, 1H, H-9'), 3.88 (d, *J* = 8.8 Hz, 1H, H-6'a), 3.78 (ddd, *J* = 15.6, 13.5, 6.0 Hz, 4H, H-4'a,b, H-6'b, H-12'a), 3.65 (dd, *J* = 12.3, 4.5 Hz, 1H, H-12'b), 3.59 (s, 2H, H-13'a,b); ^{13}C NMR (100 MHz, $CDCl_3$ + CD_3OD) δ = 165.5 (1C, cytosine C-4), 155.7 (1C, cytosine *C*O-2), 143.5 (3C, 3 x Tr Ar-C), 141.3 (1C, cytosine *C*H-6), 128.6, 128.3, 127.5 (15C, 15 x Tr Ar-*C*H), 95.9 (1C, cytosine *C*H-5), 90.5 (1C, C-2'), 88.1 (1C, C-8'), 79.3 (1C, C-1'), 74.8 (1C, C-9'), 74.7 (1C, C-5'), 71.9 (1C, C-4'), 71.3 (1C, C-6'), 70.9, 63.4 (1C, C-13'), 62.1 (1C, C-12'); ESI-TOF-MS: *m/z* calcd for $C_{32}H_{32}N_4NaO_6$ $[M+Na]^+$ 591.222, found 591.224.

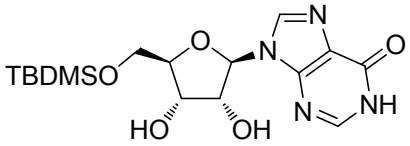
Cytosine-tricyclano (14b) - Deprotection of 13b



13b (244 mg, 0.28 mmol) was dissolved in a mixture of hexafluoroisopropanol (2.8 mL), $MeNO_2$ (1.4 mL) and Et_3SiH (340 µL, 2.13 mmol, 7.6 equiv.) then $ZnCl_2$ (305 mg, 2.24 mmol, 8.0 equiv.) was added to the mixture. After 7 hours the reaction mixture was diluted with Et_2O and the solid was filtrated off. The crude product was purified by flash column chromatography (MeCN/MeOH/H_2O 90:5:5 → 85:7.5:7.5 → 8:1:1 + 0.1% of cc. NH_3-solution) to yield **14b** (24 mg, 26%) as an off-white solid. R_f= 0.25 (MeCN/MeOH/H_2O 8:1:1 + 0.1% of cc. NH_3-solution); ^{1}H NMR (400 MHz, DMSO-d_6) δ = 7.50 (d, *J* = 7.5 Hz, 1H, cytosine C*H*-6), 7.42 – 7.18 (m, 2H, N*H*$_2$), 5.93 (d, *J* = 1.7 Hz, 1H, H-1'), 5.75 (d, *J* = 7.5 Hz,

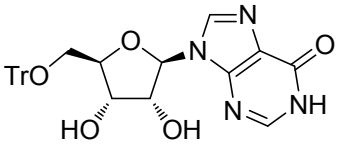
1H, cytosine C*H*-5), 5.01 (s, 1H, H-13'-O*H*), 4.92 (s, 1H, H-12'-O*H*), 4.27 (d, *J* = 1.7 Hz, 1H, H-2'), 4.15 (d, *J* = 1.5 Hz, 1H, H-8'), 4.08 (td, *J* = 5.9, 1.6 Hz, 1H, H-9'), 3.99 (dd, *J* = 12.5, 8.7 Hz, 2H, H-4'a,b or H-6'a,b), 3.62 (d, *J* = 5.8 Hz, 2H, H-12'a,b), 3.57 (d, *J* = 8.6 Hz, 2H, H-4'a,b or H-6'a,b), 3.54 (s, 2H, H-13'a,b); ^{13}C NMR (100 MHz, DMSO-d_6) δ = 165.5 (1C, cytosine C-4), 154.3 (1C, cytosine *C*O-2), 142.6 (1C, cytosine *C*H-6), 93.5 (1C, cytosine *C*H-5), 85.7 (2C, C-2', C-8'), 79.0 (1C, C-1'), 77.0 (1C, C-9'), 74.3 (2C, C-4', C-6'), 73.6 (1C, C-5'), 63.8 (1C, C-13'), 60.6 (1C, C-12'); ESI-TOF-MS: *m/z* calcd for $C_{13}H_{18}N_4NaO_6$ $[M+Na]^+$ 349.112, found 349.112.

5'-*O-tert*-butyldimethylsilyl-inosine (16a)[Ref. 27 in the main text]



Inosine **15** (5.30 g, 19.76 mmol) was dissolved in dry DMF (60 mL). Imidazole (2.92 g, 42.89 mmol, 2.2 equiv.) and *tert*-butyldimethylsilyl chloride (3.16 g, 20.97 mmol, 1.06 equiv.) were added to the reaction mixture and stirred overnight. The solution was poured into ice-water, the solid phase was filtered and dried in vacuum over P_2O_5 and KOH overnight. The crude white solid was purified by flash column chromatography (CH_2Cl_2/MeOH 9:1) to yield **16a** (4.08 g, 54%) as a white foam. R_f= 0.63 (CH_2Cl_2/MeOH 9:1); ^{1}H NMR 360 MHz (CD_3OD) δ = 8.31 (s, 1H, hypoxanthine C*H*), 8.07 (s, 1H, hypoxanthine C*H*), 6.06 (d, *J* = 4.5 Hz, 1H, H-1'), 4.55 (t, *J* = 4.7 Hz, 1H), 4.35 (t, *J* = 4.8 Hz, 1H), 4.20 – 4.08 (m, 1H), 3.99 (dd, *J* = 11.5 Hz, *J* = 3.0 Hz, 1H, H-5'a), 3.87 (dd, *J* = 11.6 Hz, *J* = 3.0 Hz, 1H, H-5'b), 0.92 (s, 9H, TBDMS *t*-Bu 3 x CH_3), 0.11 (2 x s, 6H, TBDMS 2 x Si-CH_3); ^{13}C NMR 90 MHz (CD_3OD) δ = 158.8, 149.9, 125.6 (3C, hypoxanthine *C*O-6, C-4, C-5), 146.9, (1C, hypoxanthine *C*H), 90.0, 86.6, 76.6, 71.5 (4C, C-1', C-2', C-3', C-4'), 63.9 (1C, C-5'), 26.5 (3C, TBDMS *t*-Bu 3 x *C*H_3), 19.3 (1C, TBDMS *t*-Bu C_q), -5.3 (2C, TBDMS 2 x Si-*C*H_3); ESI-TOF-MS: *m/z* calcd for $C_{16}H_{26}N_4NaO_5Si$ $[M+Na]^+$ 405.157, found 405.154.

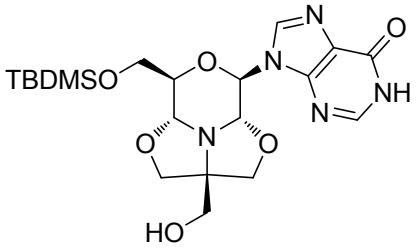
5'-*O*-trityl-inosine (16b)[Ref. 28 in the main text]



Inosine **15** (2.15 g, 8.00 mmol) was suspended in a mixture of dry pyridine (25 mL) and dry DMF (25 mL) then trityl chloride (2.68 g, 9.60 mmol, 1.2 equiv.) was added to the reaction mixture. Next day dry DMSO (15 mL) and trityl chloride (0.67 g, 2.40 mmol, 0.3 equiv.) was added. After that trityl chloride (2.24 g, 8.00 mmol, 1.0 equiv.) was added in two portions and the mixture was warmed at 60 °C. The solvent was evaporated in *vacuo*, the residue was diluted with CH_2Cl_2. The organic layer was extracted with distilled water, brine and dried over anhydrous Na_2SO_4. The solid phase was filtered and the solvent was evaporated under reduced pressure. The crude product was purified by flash column chromatography (CH_2Cl_2/MeOH 15:1 → 11:1 → 9:1) to yield compound **16b** (1.58 g, 39%) as a jonquil foam. R_f= 0.32 (CH_2Cl_2/MeOH 9:1); ^{1}H NMR 360 MHz (DMSO-d_6) δ = 12.40 (s, 1H, N*H*), 8.23 (s, 1H, hypoxanthine C*H*), 8.02 (s, 1H, hypoxanthine C*H*), 7.47 – 7.19 (m, 15H, 15 x Tr Ar-H),

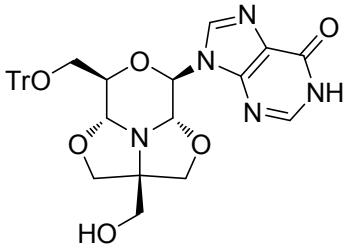
5.95 (d, *J* = 4.5 Hz, 1H, H-1'), 5.61 (s, 1H, O*H*), 5.26 (s, 1H, O*H*), 4.62 (s, 1H), 4.28 (s, 1H), 4.11 (dd, *J* = 8.9, 4.7 Hz, 1H), 3.31 – 3.20 (m, 2H); ^{13}C NMR 90 MHz (DMSO-d_6) δ = 156.6, 148.2, 124.6 (3C, hypoxanthine *C*O-6, C-4, C-5), 145.8 (1C, hypoxanthine *C*H), 143.6 (3C, 3 x Tr Ar-C), 128.3, 127.9, 127.0 (15C, 15 x Tr Ar-*C*H), 88.0, 83.1, 73.4, 70.2 (4C, C-1', C-2', C-3', C-4'), 86.1 (1C, Tr C_q) 64.0 (1C, C-5'); MALDI-TOF-MS: *m/z* calcd for $C_{29}H_{26}N_4NaO_5$ $[M+Na]^+$ 533.180, found 533.4; Elemental analysis: calcd (%) for $C_{29}H_{26}N_4O_5$: C 68.22, H 5.13, N 10.97, found C 68.24, H 5.12, N 10.99.

12'-*O-tert*-butyldimethylsilyl-hypoxanthine-tricyclano (17a)



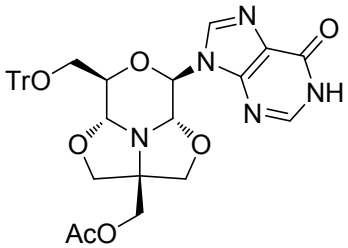
To a solution of **16a** (1.90 g, 4.97 mmol) in MeOH (150 mL) IO_4^--form of anion exchange resin (7.6 g) was added and stirred overnight in dark. Next day the resin was filtered off through a short pad of Celite® and washed with MeOH. The solvent was evaporated in vacuum. The residue was dissolved in dry MeOH (80 mL) and 3 Å molecular sieves (2 g) were added to the reaction. After stirring for half an hour Tris (903 mg, 7.46 mmol, 1.5 equiv.) was added to the mixture. After stirring overnight the molecular sieves were filtered off through a short pad of Celite® and washed with MeOH. The solvent was evaporated in vacuum and the crude product was purified by flash column chromatography (CH_2Cl_2/MeOH 95:5) to yield compound **17a** (1.20 g, 52%, over two steps) as a white powder. R_f= 0.31 (CH_2Cl_2/MeOH 9:1); ^{1}H NMR 500 MHz (DMSO-d_6) δ = 8.33 (s, 1H, hypoxanthine C*H*), 8.09 (s, 1H, hypoxanthine C*H*), 6.01 (d, *J* = 6.3 Hz, 1H, H-1'), 5.20 (d, *J* = 6.3 Hz, 1H, H-2'), 5.10 (s, 1H, O*H*), 4.72 (d, *J* = 3.1 Hz, 1H, H-8'), 4.11 – 4.09 (m, 1H, H-9'), 3.88 – 3.74 (m, 6H, H-4'a,b, H-6'a,b, H-12'a,b), 3.53 (s, 2H, H-13'a,b), 0.84 (s, 9H, TBDMS *t*-Bu 3 x CH_3), 0.03 (2 x s, 6H, TBDMS 2 x Si-CH_3); ^{13}C NMR 125 MHz (DMSO-d_6) δ = 156.5 (1C, hypoxanthine *C*O-6), 148.2 (1C, hypoxanthine C-4), 146.3 (1C, hypoxanthine *C*H-2), 138.3 (1C, hypoxanthine *C*H-8), 124.0 (1C, hypoxanthine C-5), 88.8 (1C, C-2'), 88.0 (1C, C-8'), 77.1 (1C, C-1'), 74.5 (1C, C-5'), 74.4 (1C, C-9'), 72.3 (1C, C-4'), 71.6 (1C, C-6'), 63.9 (1C, C-13'), 63.1 (1C, C-12'), 25.7 (3C, TBDMS *t*-Bu 3 x *C*H_3), 18.0 (1C, TBDMS *t*-Bu C_q), -5.4 (2C, TBDMS 2 x Si-*C*H_3); ESI-TOF-MS: *m/z* calcd for $C_{20}H_{31}N_5NaO_6Si$ $[M+Na]^+$ 488.194, found 488.192.

12'-*O*-trityl-hypoxanthine-tricyclano (17b)



To a solution of **16b** (1.00 g, 1.96 mmol) in MeOH (50 mL) IO_4^--form of anion exchange resin (4.0 g) was added and stirred overnight in dark. Next day the resin was filtered off through a short pad of Celite® and washed with MeOH. The solvent was evaporated in vacuum. The residue was dissolved in dry MeOH (50 mL) and 3 Å molecular sieves (1 g) were added to the reaction. After stirring for half an hour Tris (357 mg, 2.95 mmol, 1.5 equiv.) was added to the mixture. After stirring overnight the molecular sieves were filtered off through a short pad of Celite® and washed successively with MeOH and CH_2Cl_2. The solvent was evaporated in vacuum and the crude product was purified by flash chromatography (CH_2Cl_2/MeOH 98:2 → 95:5) to afford compound **17b** (492 mg, 42%, over two steps) as a white solid. R_f= 0.33 (CH_2Cl_2/*i*-PrOH 8:2); ^{1}H NMR (500 MHz, C_5D_5N) δ = 8.67 (s, 1H, hypoxanthine C*H*-8), 8.42 (s, 1H, hypoxanthine C*H*-2), 7.67 (d, *J* = 7.5 Hz, 6H, 6 x Tr Ar-H), 7.34 (t, *J* = 7.7 Hz, 6H, 6 x Tr Ar-H), 7.25 (t, *J* = 7.3 Hz, 3H, 3 x Tr Ar-H), 6.93 (s, 1H), 6.71 (d, *J* = 5.2 Hz, 1H, H-1'), 5.56 (d, *J* = 5.2 Hz, 1H, H-2'), 5.24 (d, *J* = 4.2 Hz, 1H, H-8'), 4.98 (s, 1H), 4.67 (q, *J* = 4.6 Hz, 1H, H-9'), 4.27 (d, *J* = 8.6 Hz, 1H, H-4'a), 4.17 – 4.08 (m, 3H, H-4'b, H-6'a,b), 4.03 (q, *J* = 11.0 Hz, 2H, H-13'a,b), 3.68 – 3.61 (m, 2H, H-12'a,b); ^{13}C NMR (125 MHz, C_5D_5N) δ = 158.4 (1C, hypoxanthine *C*O-6), 149.8 (1C, hypoxanthine C-4), 147.0 (1C, hypoxanthine *C*H-2), 144.9 (3C, 3 x Tr Ar-C), 129.7, 128.8, 128.0 (15C, 15 x Tr Ar-*C*H), 126.4 (1C, hypoxanthine C-5), 91.5 (1C, C-2'), 89.9 (1C, C-8'), 87.7 (1C, Tr C_q), 79.0 (1C, C-1'), 76.3 (1C, C-5'), 75.1 (1C, C-9'), 73.6 (1C, C-4'), 73.2 (1C, C-6'), 65.4 (1C, C-13'), 65.3 (1C, C-12'); MALDI-TOF-MS: *m/z* calcd for $C_{33}H_{31}N_5NaO_6$ $[M+Na]^+$ 616.207, found 616.38; Elemental analysis: calcd (%) for $C_{33}H_{31}N_5O_6$: C 66.77, H 5.26, N 11.80, found C 66.75, H 5.27, N 11.79.

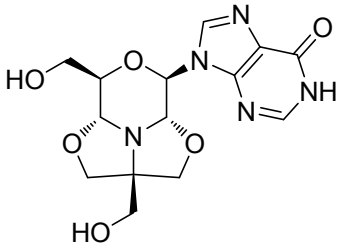
13'-*O*-acetyl-12'-*O*-trityl-hypoxanthine-tricyclano (18b)



17b (100 mg, 0.17 mmol) was dissolved in dry pyridine (2 mL). Acetic anhydride (31.8 µL, 0.34 mmol, 2.0 equiv.) was added to the reaction mixture and it was stirred overnight. Next day the mixture was quenched with saturated $NaHCO_3$ solution and stirred one hour. The solvent was evaporated under reduced pressure and the crude product was purified by flash chromatography (CH_2Cl_2/MeOH 100:0 → 98:2 → 95:5) to yield compound **18b** (91 mg, 86%) as a white powder. R_f= 0.36 (CH_2Cl_2/MeOH 95:5); ^{1}H NMR (400 MHz, $CDCl_3$) δ = 8.21 (s, 1H, hypoxanthine C*H*-8), 8.01 (s, 1H, hypoxanthine C*H*-2), 7.49 – 7.43 (m, 6H, 6 x Tr Ar-H), 7.34 – 7.22 (m, 9H, 9 x Tr Ar-H), 6.16 (d, *J* = 6.2 Hz, 1H, H-1'), 5.01 (d, *J* = 6.1 Hz, 1H, H-2'), 4.83 (d, *J* = 2.9 Hz, 1H, H-8'), 4.37 (dd, *J* = 7.8, 4.8 Hz, 1H, H-9'), 4.21 (dd, *J* = 24.2, 11.4 Hz, 2H, H-13'a,b), 3.95 (d, *J* = 9.1 Hz, 1H, H-6'a) 3.93 (q, *J* = 9.1 , 2H, H-4'a,b), 3.76 (d, *J* = 9.1 Hz, 1H, H-6'b), 3.44 – 3.34 (m, 2H, H-12'a,b), 2.05 (s, 3H, COC*H*$_3$); ^{13}C NMR (100 MHz, $CDCl_3$) δ = 170.7 (1C, *C*OCH$_3$), 159.3 (1C, hypoxanthine *C*O-6), 149.1 (1C, hypoxanthine C-4), 143.6, (3C, 3 x Tr Ar-C) 128.7, 128.0, 127.3 (15C, 15 x Tr Ar-*C*H), 124.5 (1C, hypoxanthine C-5), 90.8 (1C, C-2'), 89.5, (1C, C-8') 87.1 (1C, Tr C_q), 78.0 (1C,

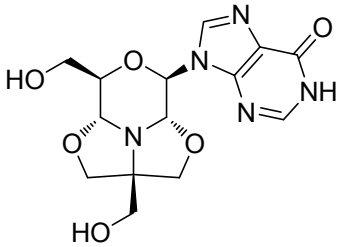
C-1'), 74.1 (1C, C-9'), 72.9 (1C, C-5'), 72.7 (1C, C-4'), 71.9 (1C, C-6'), 66.0 (1C, C-13'), 63.9 (1C, C-12'), 20.8 (1C, CO*C*H$_3$); MALDI-TOF-MS: *m/z* calcd for $C_{35}H_{33}N_5NaO_7$ $[M+Na]^+$ 658.228, found 658.164; Elemental analysis: calcd (%) for $C_{35}H_{33}N_5O_7$: C 66.13, H 5.23, N 11.02, found C 66.15, H 5.26, N 11.01.

Hypoxanthine-tricyclano (19) - Synthesis without protecting group



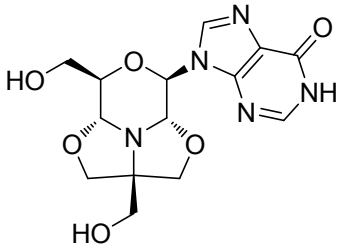
To a solution of inosine **15** (268 mg, 1.00 mmol) in MeOH (50 mL) IO_4^--form of anion exchange resin (1.0 g) was added and stirred overnight in dark. Next day the resin was filtered off through a short pad of Celite® and washed with MeOH. The solvent was evaporated in vacuum. The residue was dissolved in dry MeOH (20 mL) and 3 Å molecular sieves (270 mg) were added to the reaction. After stirring for half an hour Tris (182 mg, 1.50 mmol, 1.5 equiv.) was added to the mixture. After stirring overnight the molecular sieves were filtered off through a short pad of Celite® and washed with MeOH. The solvent was evaporated in vacuum and the crude product was purified by flash column chromatography (CH_2Cl_2/*n*-PrOH 8:2 → 7:3) to give **19** (132 mg, 38%, over two steps) as a white powder.

Hypoxanthine-tricyclano (19) - Deprotection of 17a



17a (153 mg, 0.33 mmol) was dissolved in dry THF (4 mL). Tetrabutylammonium fluoride solution (657 mL, 2.0 equiv., 1.0 M in THF) was added to the reaction mixture. After stirring overnight the solvent was evaporated and the crude product was purified by flash chromatography (EtOAc/MeOH 85:15) to afford **19** (65 mg, 56%) as a white powder.

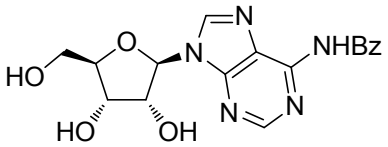
Hypoxanthine-tricyclano (19) - Deprotection of 17b



17b (297 mg, 0.50 mmol) was added to the mixture of $ZnCl_2$ (297 mg, 2.18 mmol, 4.4 equiv.), hexafluoroisopropanol (10 mL), $MeNO_2$ (5 mL) and Et_3SiH (503 μL, 3.15 mmol, 6.3 equiv.). After 2 hours saturated $NaHCO_3$-solution was added and the solvents were

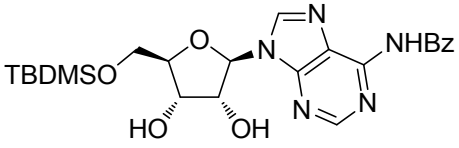
evaporated. The crude product was purified by flash column chromatography (CH_2Cl_2/MeOH 85:15 → 8:2) to yield **19** (101 mg, 58%) as a white solid. R_f= 0.47 (CH_2Cl_2/MeOH 8:2); ^{1}H NMR (400 MHz, D_2O + CD_3OD) δ = 8.37 (s, 1H, hypoxanthine C*H*-8), 8.20 (s, 1H, hypoxanthine C*H*-2), 6.10 (d, *J* = 6.3 Hz, 1H, H-1'), 5.17 (d, *J* = 6.3 Hz, 1H, H-2'), 4.83 (d, *J* = 2.8 Hz, 1H, H-8'), 4.37 (dd, *J* = 7.4, 4.4 Hz, 1H, H-9'), 4.03 (dd, *J* = 15.7, 9.2 Hz, 3H, H-6'a, H-4'a,b), 3.93 – 3.80 (m, 3H, H-12'a,b, H-6'b), 3.81 – 3.72 (m, 2H, H-13'a,b); ^{13}C NMR (100 MHz, D_2O + CD_3OD) δ = 159.2 (1C, hypoxanthine *C*O-6), 149.3 (1C, hypoxanthine C-4), 147.3 (1C, hypoxanthine *C*H-2), 124.7 (1C, hypoxanthine C-5), 90.5 (1C, C-2'), 89.6 (1C, C-8'), 79.6 (1C, C-1'), 76.0 (1C, C-9'), 75.6 (1C, C-5'), 73.1 (1C, C-4'), 72.1 (1C, C-5'), 63.7 (1C, C-13'), 62.9 (1C, C-12'); MALDI-TOF-MS: *m/z* calcd for $C_{14}H_{17}N_5NaO_6$ $[M+Na]^+$ 374.108, found 374.12; Elemental analysis: calcd (%) for $C_{14}H_{17}N_5O_6$: C 47.86, H 4.88, N 19.93, found C 47.89, H 4.85, N 19.91.

6-*N*-benzoyl-adenosine (21)[Ref. 29 in the main text]



Adenosine **20** (10.00 g, 37.42 mmol) was coevaporated with dry pyridine then it was suspended in pyridine (200 mL) and stirred under argon atmosphere. Chlorotrimethylsilane (47.50 mL, 374.2 mmol, 10 equiv.) was added dropwise and after 1 hour benzoic anhydride (16.93 g, 74.84 mmol, 2.0 equiv.) was added and the mixture was stirred overnight. The reaction was cooled to 0 ºC and quenched with water (100 mL). Then concentrated aqueous ammonia solution (80 mL) was added and the mixture was stirred at room temperature. The solvent was evaporated in *vacuo* and the residue was stirred with cold water and the precipitated product was filtered off. The crude product was washed with cold water then with ether and dried in vacuum over P_2O_5 and KOH overnight to afford compound **21** (13.39 g, 96%) as a white solid. R_f= 0.28 (CH_2Cl_2/MeOH 9:1); ^{1}H NMR 400 MHz (DMSO-d_6) δ = 11.22 (s, 1H, N*H*), 8.77 (s, 1H, adenine C*H*), 8.74 (s, 1H, adenine C*H*), 8.07 – 7.54 (m, 5H, 5 x Bz Ar-H), 6.06 (d, *J* = 5.8 Hz, 1H, H-1'), 5.58 (d, *J* = 6.0 Hz, 1H), 5.26 (d, *J* = 4.9 Hz, 1H), 5.15 (t, *J* = 5.5 Hz, 1H), 4.67 (dd, *J* = 11.1 Hz, *J* = 5.6 Hz, 1H), 4.21 (dd, *J* = 8.5 Hz, *J* = 4.6 Hz, 1H), 4.01 (q, *J* = 3.6 Hz, 1H), 3.74 – 3.57 (m, 2H, H-5'a,b); ^{13}C NMR 100 MHz (DMSO-d_6) δ = 165.7 (1C, Bz *C*O), 152.3, 150.4, 133.4, 125.9 (4C, adenine C-4, C-5, C-6, Bz Ar-C), 132.5, 128.5 (5C, 5 x Bz Ar-*C*H), 151.7 (1C, adenin *C*H), 87.6, 85.7, 73.7, 70.4 (4C, C-1', C-2', C-3', C-4'), 61.4 (1C, C-5'); ESI-TOF-MS: *m/z* calcd for $C_{17}H_{17}N_5NaO_5$ $[M+Na]^+$ 394.113, found 394.109.

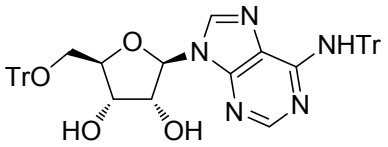
6-*N*-benzoyl-5'-*O*-*tert*-butyldimethylsilyl-adenosine (22a)[Ref. 30 in the main text]



To a solution of **21** (5.00 g, 13.46 mmol) in dry pyridine (50 mL) 4 Å molecular sieves (5 g) and 4-(dimethylamino)pyridine (catalytic amount) were added. After one hour stirring at room temperature *tert*-butyldimethylchlorosilane (3.65 g, 24.22 mmol, 1.8 equiv.) was added

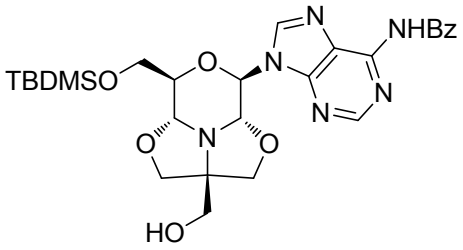
and the mixture was stirred overnight. The reaction mixture was filtered through a pad of Celite® and the filter cake was washed with $CHCl_3$. The solvent was evaporated under reduced pressure and the residue was dissolved in $CHCl_3$. The organic phase was extracted with 10% aqueous $NaHSO_4$ solution, aqueous saturated $NaHCO_3$ solution and dried over anhydrous Na_2SO_4 and filtered. The filtrate was evaporated in *vacuo* and the crude product was purified by flash column chromatography (CH_2Cl_2/EtOAc 6:4 → 1:1, then CH_2Cl_2/MeOH 9:1) to give **22a** (5.45 g, 83%) as a white foam. R_f= 0.52 (CH_2Cl_2/MeOH 9:1); ^{1}H NMR 400 MHz ($CDCl_3$) δ = 9.53 (s, 1H, CON*H*), 8.52 (s, 1H, adenine C*H*), 8.37 (s, 1H, adenine C*H*), 7.94 (d, *J* = 7.5 Hz, 2H, 2 x Bz Ar-H), 7.50 (t, *J* = 7.4 Hz, 1H, Bz Ar-H), 7.41 (t, *J* = 7.5 Hz, 2H, 2 x Bz Ar-H), 6.16 (d, *J* = 5.1 Hz, 2H, H-1', O*H*), 4.75 (s, 1H), 4.67 (s, 1H), 4.45 (s, 1H), 4.22 (d, *J* = 3.0 Hz, 1H), 3.93 – 3.76 (m, 2H, H-5'a,b), 3.54 (s, 1H, O*H*), 0.82 (s, 9H, TBDMS *t*-Bu 3 x CH_3), 0.02, 0.01 (2 x s, 6H, TBDMS 2 x Si-CH_3); ^{13}C NMR 100 MHz ($CDCl_3$) δ = 165.1 (1C, Bz *C*O), 151.2, 149.1, 133.4, 122.5 (4C, adenine C-4, C-5, C-6, Bz Ar-C), 132.9, 128.7, 128.0 (5C, 5 x Bz Ar-*C*H), 89.0, 86.0, 75.9, 71.2 (4C, C-1', C-2', C-3', C-4'), 63.1 (1C, C-5'), 26.0 (3C, TBDMS *t*-Bu 3 x *C*H_3), 18.4 (1C, TBDMS *t*-Bu C_q), -5.3, -5.4 (2C, TBDMS 2 x Si-*C*H_3); ESI-TOF-MS: *m/z* calcd for $C_{23}H_{32}N_5NaO_5Si$ $[M+Na]^+$ 508.199, found 508.191; Elemental analysis: calcd (%) for $C_{23}H_{32}N_5O_5Si$: C 56.89, H 6.43, N 14.42, found C 56.88, H 6.45, N 14.44.

6-*N*,5'-*O*-*bis*trityl-adenosine (22b)[Ref. 31 in the main text]



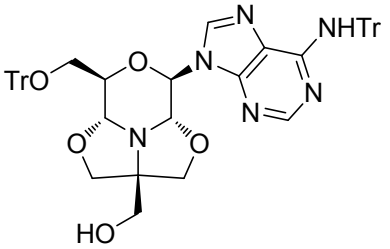
To a suspension of adenosine **20** (1.34 g, 5.00 mmol) in dry pyridine (30 mL) triphenylmethyl chloride (4.18 g, 15.00 mmol, 3 equiv.) was added and the reaction mixture was heated to 60 ºC and stirred overnight. The reaction mixture was concentrated in *vacuo* and coevaporated with toluene. The residue was dissolved in CH_2Cl_2 (300 mL) and extracted with 10% aqueous $NaHSO_4$ solution, aqueous saturated $NaHCO_3$ solution and dried over anhydrous Na_2SO_4. The solid phase was filtered and the solvent was evaporated under reduced pressure. The crude product was purified by flash column chromatography (CH_2Cl_2/acetone 9:1 → 85:15) to yield compound **22b** (2.38 g, 63%) as a white solid. R_f= 0.39 (CH_2Cl_2/acetone 85:15); ^{1}H NMR 500 MHz (DMSO-d_6) δ = 8.37 (s, 1H, adenine C*H*), 7.85 (s, 1H, adenine C*H*), 7.47 (s, 1H, N*H*), 7.36 – 7.20 (m, 30H, 30 x Tr Ar-H), 5.95 (d, *J* = 4.6 Hz, 1H, H-1'), 5.51 (s, 1H, O*H*), 5.24 (s, 1H, O*H*), 4.77 (t, *J* = 4.8 Hz, 1H), 4.33 (d, *J* = 4.9 Hz, 1H), 4.09 (q, *J* = 4.2 Hz, 1H), 3.24 (d, *J* = 4.3 Hz, 2H, H-5'a,b); ^{13}C NMR 125 MHz (DMSO-d_6) δ = 153.6, 148.4, 144.9, 143.6, 121.0 (9C, adenine C-4, C-5, C-6, 6 x Tr Ar-C), 151.2, 140.6 (2C, adenine *C*H-2, *C*H-8), 128.6-126.6 (30C, 30 x Tr Ar-*C*H), 88.3 (1C, C-1'), 86.0 (1C, OTr C_q), 83.1, 72.7, 70.3 (3C, C-2', C-3', C-4'), 70.4 (1C, NTr C_q), 63.9 (1C, C-5'); ESI-TOF-MS: *m/z* calcd for $C_{48}H_{41}N_5NaO_4$ $[M+Na]^+$ 774.306, found 774.302.

6-*N*-benzoyl-12'-*O*-*tert*-butyldimethylsilyl-adenine-tricyclano (23a)



To a solution of **22a** (1.20 g, 2.47 mmol) in MeOH (15 mL) IO_4^--form of anion exchange resin (4.8 g) was added and stirred overnight in dark. Next day the resin was filtered off through a short pad of Celite® and washed with MeOH. The solvent was evaporated in vacuum. The residue was dissolved in dry MeOH (30 mL) and 3 Å molecular sieves (270 mg) were added to the reaction. After stirring for half an hour Tris (449 mg, 3.71 mmol, 1.5 equiv.) was added to the mixture. After stirring overnight the molecular sieves were filtered off through a short pad of Celite® and washed with MeOH. The solvent was evaporated in vacuum and the crude product was purified by flash column chromatography (*i*-hexane/acetone 7:3 → 6:4) to yield compound **23a** (337 mg, 24%, over two steps) as a white foam. R_f= 0.50 (CH_2Cl_2/MeOH 9:1); ^{1}H NMR 400 MHz ($CDCl_3$) δ = 9.46 (s, 1H, N*H*), 8.78 (s, 1H, adenine C*H*), 8.26 (s, 1H, adenine C*H*), 8.02 (d, J = 7.4 Hz, 2H, 2 x Bz Ar-H), 7.58 (t, J = 7.4 Hz, 1H, Bz Ar-H), 7.50 (t, J = 7.6 Hz, 1H, Bz Ar-H), 6.30 (d, *J* = 5.1 Hz, 1H, H-1'), 5.05 (d, *J* = 5.1 Hz, 1H, H-2'), 4.84 (d, *J* = 4.2 Hz, 1H, H-8'), 4.20 (q, *J* = 4.6 Hz, 1H, H-9'), 3.93 – 3.82 (m, 6H, H-4'a,b, H-6a,b, H-12'a,b), 3.66 (q, *J* = 11.4 Hz, 2H, H-13'a,b), 3.37 (s, 1H, O*H*), 0.89 (s, 9H, TBDMS *t*-Bu 3 x CH_3), 0.07, 0.06 (2 x s, 6H, TBDMS 2 x Si-CH_3); ^{13}C NMR 100 MHz ($CDCl_3$) δ = 165.0 (1C, Bz *C*O), 153.0 (1C, adenine *C*H), 151.7, 149.7, 133.7, 122.8 (4C, adenine C-4, C-5, C-6, Bz Ar-C), 132.8, 128.8, 128.0 (5C, 5 x Bz Ar-*C*H), 90.7, 88.3, 78.2, 75.1 (4C, C-1', C-2', C-8', C-9'), 75.2 (1C, C-5'), 72.2, 71.6 (2C, C-4', C-6'), 63.4, 63.1 (2C, C-12', C-13'), 25.9 (3C, TBDMS *t*-Bu 3 x *C*H_3), 18.4 (1C, TBDMS *t*-Bu C_q), -5.3 (2C, TBDMS 2 x Si-*C*H_3); ESI-TOF-MS: *m/z* calcd for $C_{27}H_{36}N_6NaO_6Si$ $[M+Na]^+$ 591.236, found 591.234.

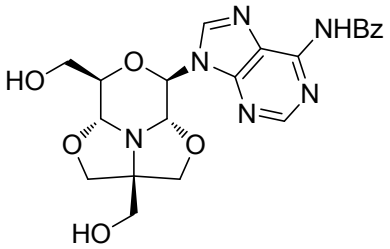
6-*N*,12'-*O*-*bis*trityl-adenine-tricyclano (23b)



To a solution of **22b** (2.00 g, 2.66 mmol) in a mixture of MeOH (30 mL) and CH_2Cl_2 (20 mL) IO_4^--form of anion exchange resin (4.0 g) was added and stirred overnight in dark. Next day the resin was filtered off through a short pad of Celite® and washed with MeOH. The solvent was evaporated in vacuum. The residue was dissolved in dry MeOH (50 mL) and 3 Å molecular sieves (2 g) were added to the reaction. After stirring for half an hour Tris (483 mg, 3.99 mmol, 1.5 equiv.) was added to the mixture. After stirring overnight the molecular sieves were filtered off through a short pad of Celite® and washed successively with MeOH and CH_2Cl_2. The solvent was evaporated in vacuum and the crude product was purified by flash

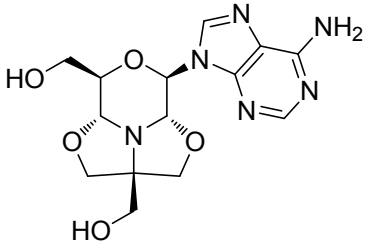
column chromatography (*i*-hexane/acetone 8:2 → 7:3) to yield compound **23b** (1.55 g, 70%, over two steps) as a white foam. R_f= 0.33 (*i*-hexane/acetone 6:4); ^{1}H NMR (400 MHz, $CDCl_3$) δ = 8.06 (s, 1H, adenine C*H*-2), 7.97 (s, 1H, adenine C*H*-8), 7.48 – 7.41 (m, 6H, 6 x OTr Ar-H), 7.34 (dd, *J* = 8.1, 1.3 Hz, 6H, 6 x NTr Ar-H), 7.30 – 7.17 (m, 18H, 18 x Tr Art-H), 7.10 (s, 1H, N*H*), 6.12 (d, *J* = 6.0 Hz, 1H, H-1'), 5.11 (d, *J* = 6.0 Hz, 1H, H-2'), 4.75 (d, *J* = 3.1 Hz, 1H, H-8'), 4.33 (q, *J* = 4.7 Hz, 1H, H-9'), 3.87 (q, *J* = 8.9 Hz, 2H, H-4'a,b) 3.84 (d, *J* = 8.8 Hz, 1H, H-6'a), 3.69 (d, *J* = 8.9 Hz, 1H, H-6'b), 3.57 (qd, *J* = 11.5, 5.9 Hz, 2H, H-13'a,b), 3.41 – 3.31 (m, 2H, H-12'a,b), 2.81 (t, *J* = 5.9 Hz, 1H, O*H*); ^{13}C NMR (100 MHz, $CDCl_3$) δ = 154.2 (1C, adenine C-6), 152.8 (1C, adenine *C*H-2), 148.9 (1C, adenine C-4), 145.0 (3C, 3 x NTr Ar-C), 143.7 (3C, 3 x OTr Ar-C), 129.1, 128.7, 128.0, 128.0, 127.3, 127.0 (30C, 30 x Tr Ar-*C*H), 120.8 (1C, adenine C-5), 90.4 (1C, C-2'), 89.2 (1C, C-8'), 87.0 (1C, OTr C_q), 78.2 (1C, C-1'), 75.1 (1C, C-5'), 74.2 (1C, C-9'), 72.1 (1C, C-4'), 71.5 (1C, C-6', NTr C_q), 64.1 (1C, C-12'), 63.4 (1C, C-13'); MALDI-TOF-MS: *m/z* calcd for $C_{52}H_{46}N_6NaO_5$ $[M+Na]^+$ 857.343, found 857.33; Elemental analysis: calcd (%) for $C_{52}H_{46}N_6O_5$: C 74.80, H 5.55, N 10.07, found C 74.77, H 5.56, N 10.10.

6-*N*-benzoyl-adenine-tricyclano (24a)



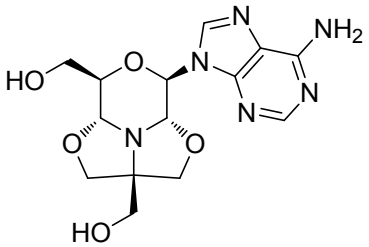
23a (350 mg, 0.33 mmol) was dissolved in dry THF (3 mL). Tetrabutylammonium fluoride solution (495 mL, 1.5 equiv., 1.0 M in THF) was added to the reaction mixture. After stirring for two hours the solvent was evaporated and the crude product was purified by flash column chromatography (CH_2Cl_2/MeOH 98:2 → 9:1) to afford **24a** (257 mg, 92%) as a white foam. R_f= 0.32 (CH_2Cl_2/MeOH 9:1); ^{1}H NMR 400 MHz (C_5D_5N) δ = 12.37 (s, 1H, CON*H*), 9.01 (s, 1H, adenine C*H*), 8.98 (s, 1H, adenine C*H*), 8.35 (d, *J* = 7.0 Hz, 2H, 2 x Bz Ar-H), 7.53 (t, *J* = 7.3 Hz, 1H, 1 x Bz Ar-H), 7.47 (t, *J* = 7.3 Hz, 2H, 2 x Bz Ar-H), 6.77 (d, *J* = 5.6 Hz, 1H, H-1'), 5.69 (d, *J* = 5.6 Hz, 1H, H-2'), 5.34 (d, *J* = 3.7 Hz, 1H, H-8'), 5.12 (s, 1H, O*H*), 4.68 (dd, *J* = 8.9, 5.0 Hz, 1H), 4.30 (d, *J* = 8.6 Hz, 1H), 4.22 – 4.12 (m, 5H), 4.03 (q, *J* = 11.1 Hz, 2H, H-13'a,b), 3.56 – 3.48 (m, 1H, O*H*); ^{13}C NMR 100 MHz (C_5D_5N) δ = 167.9 (1C, Bz *C*O), 153.5, 152.3, 135.9, 126.2 (4C, adenine C-4, C-5, C-6, Bz Ar-C), 133.0, 129.7, 129.3 (5C, 5 x Bz Ar-*C*H), 91.3, 90.0, 79.4, 77.1 (4C, C-1', C-2', C-8', C-9'), 76.3 (1C, C-5'), 73.8, 73.2 (2C, C-4', C-6'), 65.3, 63.2 (2C, C-12', C-13'); ESI-TOF-MS: *m/z* calcd for $C_{21}H_{22}N_6NaO_6$ $[M+Na]^+$ 477.150, found 477.146.

Adenine-tricyclano (25) - Deprotection of 24a



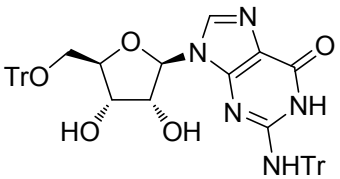
To a solution of **24a** (150 mg, 0.33 mmol) in MeOH (30 mL) cc. NH_3 solution (3 mL) was added and stirred overnight. The solvent was evaporated in *vacuo*. The crude product was purified by trituration with CH_2Cl_2 to yield **25** (109 mg, 95%) as a white solid.

Adenine-tricyclano (25) - Deprotection of 23b



23b (83 mg, 0.10 mmol) was dissolved in the mixture of $MeNO_2$ (1.5 mL), hexafluoroisopropanol (0.5 ml) and Et_3SiH (120 μL, 0.76 mmol, 7.6 equiv.) then $ZnCl_2$ (109 mg, 0.80 mmol, 8.0 equiv.) was added to the mixture. After 24 hours saturated $NaHCO_3$-solution was added and the solvents were evaporated. The crude product was purified by flash column chromatography (CH_2Cl_2/MeOH 95:5 → 9:1 → 85:15) to yield **25** (22 mg, 63%) as a white solid. R_f= 0.34 (CH_2Cl_2/MeOH 85:15); ^{1}H NMR 500 MHz (DMSO-d_6) δ = 8.40 (s, 1H, adenine C*H*-8), 8.15 (s, 1H, adenine C*H*-2), 7.35 (s, 2H, NH_2), 5.97 (d, *J* = 6.9 Hz, 1H, H-1'), 5.24 (d, *J* = 6.9 Hz, 1H, H-2'), 4.69 (d, *J* = 2.4 Hz, 1H, H-8'), 4.09 (td, *J* = 5.8, 2.3 Hz, 1H, H-9'), 3.88 – 3.83 (m, 3H, H-6'a, H-4'a,b,), 3.70 (d, *J* = 8.8 Hz, 1H, H-6'b), 3.56 (d, *J* = 5.8 Hz, 2H, H-12'a,b), 3.54 (d, *J* = 3.6 Hz, 2H, H-13'a,b); ^{13}C NMR 125 MHz (DMSO-d_6) δ = 156.1 (1C, adenine C-6), 152.9, (1C, adenine *C*H-2), 149.3 (1C, adenine C-4), 139.0 (1C, adenine *C*H-8), 118.6 (1C, adenine C-5), 88.8 (2C, C-2', C-8'), 77.2 (1C, C-1'), 75.0 (1C, C-9'), 74.5 (1C, C-5'), 72.4 (1C, C-4'), 71.4 (1C, C-6'), 63.9 (1C, C-13'), 61.7 (1C, C-12'); ESI-TOF-MS: *m/z* calcd for $C_{14}H_{18}N_6NaO_5$ $[M+Na]^+$ 373.124, found 373.121.

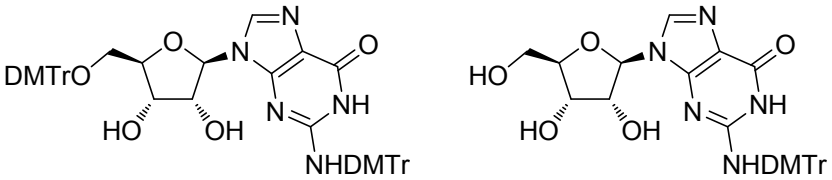
2-*N*,5'-*O*-*bis*trityl-guanosine (27)[Ref. 32 in the main text]



To a suspension of guanosine **26** (5.00 g, 17.65 mmol) in dry DMF (50 mL) triphenylmethyl chloride (10.00 g, 35.87 mmol, 2.0 equiv.), 4-dimethylaminopyridine (0.05 g, 0.41 mmol, 0.02 equiv.), Et_3N (6.00 mL, 43.05 mmol, 2.4 equiv.) were added and stirred at 50 °C. After two days Et_3N (4.00 mL, 29.00 mmol, 1.64 equiv.) was added to the mixture. After four days trityl chloride (10.00 g, 35.87 mmol, 2.0 equiv.) and Et_3N (6.00 mL, 43.05 mmol, 2.4 equiv.)

was also added. After one week Et_3N (10 mL) and MeOH (10 mL) was added to the mixture and stirred for 30-30 minutes. The solvent was evaporated under reduced pressure and the residue was coevaporated with dry toluene. The crude product was purified by flash column chromatography (CH_2Cl_2/MeOH 98:2 → 95:5) to yield compound **27** (6.70 g, 49%) as a tan foam. R_f= 0.24 (CH_2Cl_2/MeOH 95:5); ^{1}H NMR (400 MHz, $CDCl_3$) δ = 11.13 (s, 1H, N*H*), 7.70 (s, 1H, guanine C*H*), 7.43 – 7.04 (m, 30H, 30 x Tr Ar-H), 5.32 (d, 1H, H-1'), 4.20 – 4.09 (m, 1H), 4.00 (s, 2H), 3.58 (s, 1H, O*H*), 3.25 (ddd, *J* = 15.3, 10.4, 4.4 Hz, 2H, H-5'a,b), 3.03 (s, 1H, O*H*), 2.01 (s, 1H, Tr N*H*); ^{13}C NMR (100 MHz, $CDCl_3$) δ = 158.4, 151.6, 149.5, 117.9 (4C, guanine C-2, C-4, C-5, *C*O-6), 144.2, 143.7 (6C, 6 x Tr Ar-C), 128.9, 128.7, 128.0, 127.3, 127.1 (30C, 30 x Tr Ar-*C*H), 89.6 (1C, C-1'), 87.1 (1C, OTr C_q), 84.0, 74.4, 71.4 (3C, C-2', C-3', C-4'), 71.2 (1C, NTr C_q), 64.1 (1C, C-5'); ESI-TOF-MS: *m/z* calcd for $C_{48}H_{41}N_5NaO_5$ $[M+Na]^+$ 790.301, found 790.290; Elemental analysis: calcd (%) for $C_{48}H_{41}N_5O_5$: C 75.08, H 5.38, N 9.12, found C 75.10, H 5.39, N 9.11.

2-*N*,5'-*O*-*bis*(4,4'-dimethoxytrityl)-gunaosine (27b)[Ref. 33 in the main text] and 2-*N*-(4,4'-dimethoxytrityl)-gunaosine (27c)



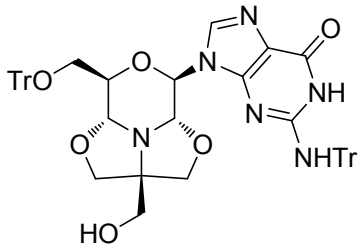
To a suspension of guanosine **26** (2.12 g, 7.50 mmol) in dry C_5H_5N (40 mL) the reaction flask was flushed by argon gas. After that TMSCl (7.14 mL, 56.25 mmol, 7.5 equiv.) was added to the mixture. After stirring one hour DMTrCl (3.65 g, 9.00 mmol, 1.2 equiv.) was added and the reaction mixture was stirred overnight. Next day dry DMF (10 mL), TMSCl (7.14 mL, 56.25 mmol, 7.5 equiv.) and after one hour DMTrCl (762 mg 2.25 mmol, 0.3 equiv.) were added and strirred two days. Next day DMTrCl (1.27 g, 3.75 mmol, 0.5 equiv.) and abs. DMF (40 mL) were added. After stirring overnight saturated $NaHCO_3$-solution was added and stirred for two hours. Then the solvent was evaporated and the residue was dissolved in EtOAc. The organic layer was extracted with H_2O, 10% aqueous $NaHSO_4$-solution, saturated $NaHCO_3$-solution and brine. Then it was dried over anhydrous Na_2SO_4-the solid was filtered off and the solvent was evaporated. The crude product was purified by flash chromatography (CH_2Cl_2/MeOH 98:2 → 97:3 → 95:5 → 93:7 → 9:1 → 8:2 → 7:3) to yield compound **27b** (3.11 g, 47%) as a jonquil foam and compound **27b** (1.32 g, 30%) as an off-white foam.

27b: R_f= 0.35 (CH_2Cl_2/MeOH 95:5); ^{1}H NMR (400 MHz, $CDCl_3$ + CD_3OD) δ = 7.60 (s, 1H, guanine C*H*-8), 7.36 (d, *J* = 7.4 Hz, 2H, 2 x DMTr Ar-H), 7.26 (d, *J* = 8.8 Hz, 6H, 6 x DMTr Ar-H), 7.23 – 7.13 (m, 10H, 10 x DMTr Ar-H), 6.77 (t, *J* = 8.6 Hz, 8H, 8 x DMTr Ar-H), 5.36 (d, *J* = 4.4 Hz, 1H, H-1'), 4.11 (dd, *J* = 8.0, 4.2 Hz, 1H, H-4'), 4.09 – 4.04 (m, 1H, H-2'), 4.00 (t, *J* = 4.4 Hz, 1H, H-3'), 3.74 (s, 6H, 2 x DMTr OC*H*$_3$), 3.71 (2 x s, 6H, 2 x DMTr OC*H*$_3$) 3.31 (dd, *J* = 10.5, 3.3 Hz, 1H, H-5'a), 3.25 – 3.18 (m, 1H, H-5'b), 3.12 (s, 2H); ^{13}C NMR (100 MHz, $CDCl_3$ + CD_3OD) δ = 158.5, 158.4, 157.7, 151.2, 149.9, 144.6, 144.4, 136.6, 136.3, 135.8, 117.7, (14C, guanine C-2, C-4, C-5, *C*O-6, 10 x DMTr Ar-C), 130.0, 129.9, 129.9, 128.5, 128.1, 128.0, 127.9, 127.1, 126.9, 113.3, 113.3, 113.2 (26C, 26 x DMTr Ar-*C*H), 89.1 (1C, C-1'), 86.5 (1C, ODMTr C_q), 84.0 (1C, C-4'), 74.4 (1C, C-2'), 71.2 (1C, C-

3'), 70.3 (1C, NDMTr C_q), 63.7 (1C, C-5'), 55.2 (4C, 4 x DMTr O*C*H_3); MALDI-TOF-MS: *m/z* calcd for $C_{52}H_{49}N_5NaO_9$ $[M+Na]^+$ 910.343, found 910.653; Elemental analysis: calcd (%) for $C_{52}H_{49}N_5O_9$: C 70.34, H 5.56, N 7.89, found C 70.37, H 5.55, N 7.86.

27c: R_f= 0.36 (CH_2Cl_2/MeOH 10:1); ^{1}H NMR (400 MHz, CD_3OD) δ = 7.88 (s, 1H, guanine C*H*-8), 7.35 – 7.18 (m, 9H, 9 x DMTr Ar-H), 6.84 (d, *J* = 8.9 Hz, 4H, 4 x DMTr Ar-H), 5.34 (d, *J* = 4.7 Hz, 1H, H-1'), 4.00 (t, *J* = 4.9 Hz, 1H, H-2'), 3.90 (t, *J* = 5.2 Hz, 1H, H-3'), 3.86 (dd, *J* = 8.6, 4.8 Hz, 1H, H-4'), 3.75 (s, 6H, 2 x DMTr OCH_3), 3.59 (dd, *J* = 12.1, 3.4 Hz, 1H, H-5'a), 3.52 (dd, *J* = 12.1, 4.7 Hz, 1H, H-5'b); ^{13}C NMR (100 MHz, CD_3OD) δ = 159.9, 159.3, 152.5, 151.6, 146.5, 138.2, 118.3, (9C, guanine C-2, C-4, C-5, *C*O-6, 5 x DMTr Ar-C), 138.8 (1C, guanine *C*H-8), 131.2, 131.2, 129.8, 128.8, 127.9, 114.1 (13C, 13 x DMTr Ar-*C*H), 89.8 (1C, C-1'), 86.0 (1C, C-4'), 74.5 (1C, C-2'), 71.3 (1C, C-3'), 62.9 1C, C-5'), 55.7 (2C, 2 x DMTr O*C*H_3); MALDI-TOF-MS: *m/z* calcd for $C_{31}H_{31}N_5NaO_7$ $[M+Na]^+$ 608.212, found 608.35; Elemental analysis: calcd (%) for $C_{31}H_{31}N_5O_7$: C 63.58, H 5.34, N 11.96, found C 63.61, H 5.33, N 11.94.

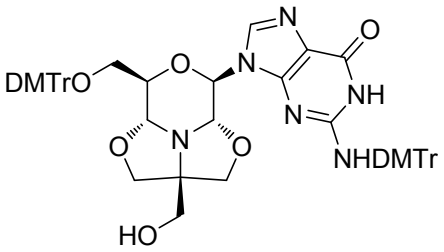
2-*N*,12'-*O*-*bis*trityl-guanine-tricyclano (28a)



27a (1.00 g, 1.30 mmol) and $NaIO_4$ (298 mg, 1.39 mmol, 1.07 equiv.) were dissolved in a mixture of MeOH (75 mL) and H_2O (25 mL). After stirring overnight in dark the MeOH was evaporated in vacuum and CH_2Cl_2 (250 mL) was added to the mixture. The organic layer was extracted with H_2O (2 x 100 mL) and brine (100 mL) then it was dried over anhydrous Na_2SO_4. After that the solid phase was filtered off and the solvent was evaporated. The residue was dissolved in dry MeOH (20 mL) and 3 Å molecular sieves (1 g) were added to the reaction. After stirring for half an hour Tris (236 mg, 1.95 mmol, 1.5 equiv.) was added to the mixture and stirred overnight. Next day Tris (79 mg, 0.65 mmol, 0.5 equiv.) was also added. After stirring overnight the molecular sieves were filtered off through a short pad of Celite® and washed successively with MeOH and CH_2Cl_2. The solvent was evaporated in vacuum and the crude product was purified by flash chromatography (CH_2Cl_2/MeOH 97:3 → 96:4 → 95:5) to yield **28** (806 mg, 73%, over two steps) as an off-white foam. R_f= 0.46 (CH_2Cl_2/MeOH 9:1); ^{1}H NMR (400 MHz, $CDCl_3$) δ = 11.73 (s, 1H, N*H*), 8.06 (s, 1H, N*H*), 7.48 – 7.40 (m, 6H, 6 x Tr Ar-H), 7.36 (d, *J* = 7.6 Hz, 6H, 6 x Tr Ar-H), 7.33 – 7.18 (m, 9H, 9 x Tr Ar-H), 7.04 (dt, *J* = 34.3, 7.3 Hz, 10H, 9 x Tr Ar-H, 1 x guanine C*H*-8), 5.36 (d, *J* = 6.9 Hz, 1H, H-1'), 4.61 (d, *J* = 2.0 Hz, 1H, H-8'), 4.54 (d, *J* = 6.9 Hz, 1H, H-2'), 4.19 (dd, *J* = 6.8, 4.6 Hz, 1H, H-9'), 3.63 – 3.42 (m, 5H, H-6'a,b, H-4'a, H-13'a,b), 3.33 – 3.14 (m, 3H, H-12'a,b, H-4'b), 2.44 (s, 1H, O*H*); ^{13}C NMR (100 MHz, $CDCl_3$) δ = 159.3 (1C, guanine *C*O-6), 151.3 (1C, guanine C-2), 150.5 (1C, guanine C-4), 144.8, 143.7 (6C, 6 x Tr Ar-C), 129.3, 128.7, 128.1, 127.7, 127.4, 126.5 (30C, 30 x Tr Ar-*C*H), 117.0 (1C, guanine C-5), 90.1 (1C, C-2'), 89.8 (1C, C-8'), 86.9 (1C, OTr C_q), 76.3 (1C, C-1'), 75.0 (1C, C-5'), 73.8 (1C, C-9'), 71.9 (1C, C-4'), 71.0 (1C, NTr C_q), 70.7 (1C, C-6'), 64.0 (1C-12'), 63.7 (1C, C-13');

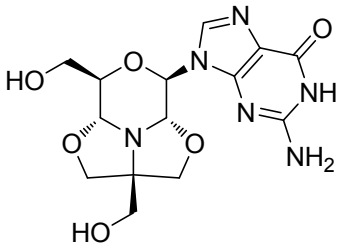
MALDI-TOF-MS: *m/z* calcd for $C_{52}H_{46}N_6NaO_6$ $[M+Na]^+$ 873.338, found 873.3; Elemental analysis: calcd (%) for $C_{52}H_{46}N_6O_6$: C 73.39, H 5.45, N 9.88, found C 73.41, H 5.42, N 9.91.

2-*N*,12'-*O*-*bis*(4,4'-dimethoxytrityl)-guanine-tricyclano (28b)



To a solution of **27b** (1.80 g, 2.03 mmol) in a mixture of CH_2Cl_2 (30 mL) and MeOH (20 mL) IO_4^--form of anion exchange resin (7.2 g) was added and stirred overnight in dark. Next day the resin was filtered off through a short pad of Celite® and washed successively with MeOH and CH_2Cl_2. The solvent was evaporated in vacuum. The residue was dissolved in dry MeOH (75 mL) and 3 Å molecular sieves (1.8 g) were added to the reaction. After stirring for half an hour Tris (491 mg, 4.05 mmol, 2.0 equiv.) was added to the mixture and stirred overnight. After stirring overnight the molecular sieves were filtered off through a short pad of Celite® and washed successively with MeOH and CH_2Cl_2. The solvent was evaporated in vacuum and the crude product was purified by flash chromatography (CH_2Cl_2/MeOH 98:2 → 97:3 → 95:5 → 9:1) to yield **28b** (1,59 g, 80%, over two steps) as a white foam. R_f= 0.21 (CH_2Cl_2/MeOH 95:5); ^{1}H NMR (400 MHz, $CDCl_3$) δ = 7.45 (d, *J* = 7.5 Hz, 2H, 2 x DMTr Ar-H), 7.35 – 7.15 (m, 18H, 18 x DMTr Ar-H), 7.07 (t, *J* = 7.1 Hz, 2H, 2 x DMTr Ar-H), 6.81 (d, *J* = 8.9 Hz, 4H, 4 x DMTr Ar-H), 5.48 (d, *J* = 6.3 Hz, 1H, H-1'), 4.64 (d, *J* = 2.1 Hz, 1H, H-8'), 4.60 (d, *J* = 5.7 Hz, 1H, H-2'), 4.22 (d, *J* = 2.7 Hz, 1H, H-9'), 3.73 (s, 6H, 2 x DMTr OC*H*$_3$), 3.66 – 3.38 (m, 11H, 2 x DMTr OC*H*$_3$, H-13'a,b, H-6'a,b, H-4'a), 3.35 – 3.19 (m, 3H, H-12'a,b,H-4'b); ^{13}C NMR (100 MHz, $CDCl_3$) δ = 158.7, 144.7, 135.8, 135.8 (10C, 10 x DMTr Ar-C), 158.0 (1C, guanine *C*O-6), 151.4 (1C, guanine C-2), 150.5 (1C, guanine C-4), 130.5, 130.1, 128.7, 128.2, 128.0, 127.8, 127.1, 113.3, 113.0 (26C, 26 x DMTr Ar-*C*H), 117.0 (1C, guanine C-5), 90.3 (1C, C-2'), 89.6 (1C, C-8'), 86.4 (1C, ODMTr C_q), 76.5 (1C, C-1'), 75.0 (1C, C-5'), 73.9 (1C, C-9'), 71.8 (1C, C-4'), 70.9 (1C, C-6'), 70.2 (1C, NDMTr C_q), 63.9 (1C, C-12'), 63.8 (1C, C-13'), 55.3, 55.1, 55.0 (4C, 4 x DMTr O*C*H$_3$); MALDI-TOF-MS: *m/z* calcd for $C_{56}H_{54}N_6NaO_{10}$ $[M+Na]^+$ 993.379, found 993.38; Elemental analysis: calcd (%) for $C_{56}H_{54}N_6O_{10}$: C 69.26, H 5.61, N 8.65, found C 69.28, H 5.60, N 8.67.

Guanine-tricyclano (29) - Deprotection of 28b



28b (486 mg, 0.50 mmol) was dissolved in the mixture of hexafluoroisopropanol (5 mL), $MeNO_2$ (2.5 ml) and Et_3SiH (607 μL, 3.8 mmol, 7.6 equiv.) then $ZnCl_2$ (545 mg, 4.0 mmol, 8.0 equiv.) was added to the mixture. After 5 hours the mixture was diluted with Et_2O and the

solid was filtered off. The crude product was purified by flash column chromatography (CH_2Cl_2/MeOH 9:1 → 8:2 → 7:3, then MeCN/H_2O 9:1 → 85:15 → 8:2) to yield **29** (37 mg, 20%) as an off-white solid. R_f= 0.38 (MeCN/H_2O 8:2); ^{1}H NMR 400 MHz (DMSO-d_6) δ = 10.77 (s, 1H, guanine CON*H*), 7.95 (s, 1H, guanine C*H*-8), 6.64 (s, 2H, NH_2), 5.75 (d, *J* = 6.7 Hz, 1H, H-1'), 5.11 (d, *J* = 6.7 Hz, 1H, H-2'), 5.04 (s, 2H, 2 x O*H*), 4.64 (d, *J* = 2.0 Hz, 1H, H-8'), 4.01 (td, *J* = 5.6, 2.3 Hz, 1H, H-9'), 3.88 (s, 2H, H-4'a,b,), 3.79 (d, *J* = 8.7 Hz, 1H, H-6'a), 3.68 (d, *J* = 8.7 Hz, 1H, H-6'b), 3.53 (s, 4H, H-13'a,b, H-12'a,b); ^{13}C NMR 100 MHz (DMSO-d_6) δ = 156.8 (1C, guanine *C*O-6), 154.1, (1C, guanine C-2), 151.2 (1C, guanine C-4), 116.3 (1C, guanine C-5), 88.8 (1C, C-2'), 88.7 (1C, C-8'), 76.6 (1C, C-1'), 75.1 (1C, C-9'), 74.4 (1C, C-5'), 72.4 (1C, C-4'), 71.5 (1C, C-6'), 63.7 (1C, C-13'), 61.7 (1C, C-12'); ESI-TOF-MS: *m/z* calcd for $C_{14}H_{18}N_6NaO_6$ $[M+Na]^+$ 389.119, found 389.121.

Computational section

Mixed torsional/low-frequency mode conformational searches were carried out by means of the Macromodel 10.8.011 software using the OPLS[Ref. 38 in the main text] (Optimized Potentials for Liquid Simulations) force field with an implicit solvent model for $CHCl_3$.[8] Geometry reoptimizations were carried out at the B3LYP/6-31+G(d,p) level in vacuo and NMR calculations were performed at the mPW1PW91/6-311+G(2d,p) level[Ref. 39 in the main text] as implemented in the Gaussian 09 package.[9] For compound **13a** an additional AM1 level optimization and declastering of the trityl phenyls was included before the DFT level reoptimization in order to decrease the number of the initial OPLS conformers (846). Boltzmann distributions were estimated from the B3LYP/6-31+G(d,p) energies. Computed C-NMR data were corrected with I = 185.4855 and S = -1.0306 and H-NMR data with I = 31.8996 and S = -1.0734.[Ref. 40 in the main text] The VMD software package was used for visualization of the results.[10]

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Figures for DFT calculations

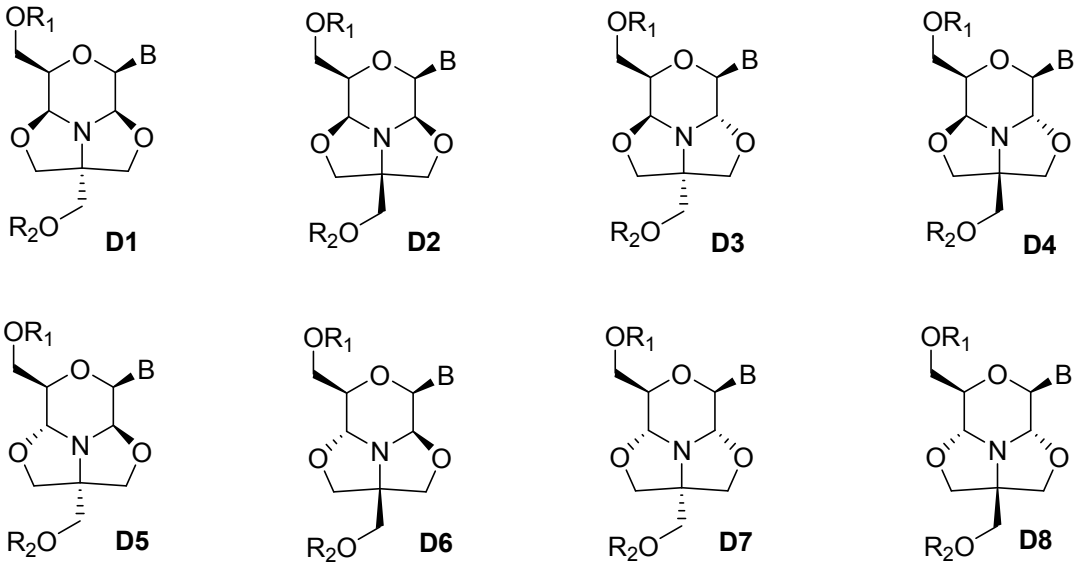


Figure S2. Notations of the possible stereoisomers of the tricyclanos.

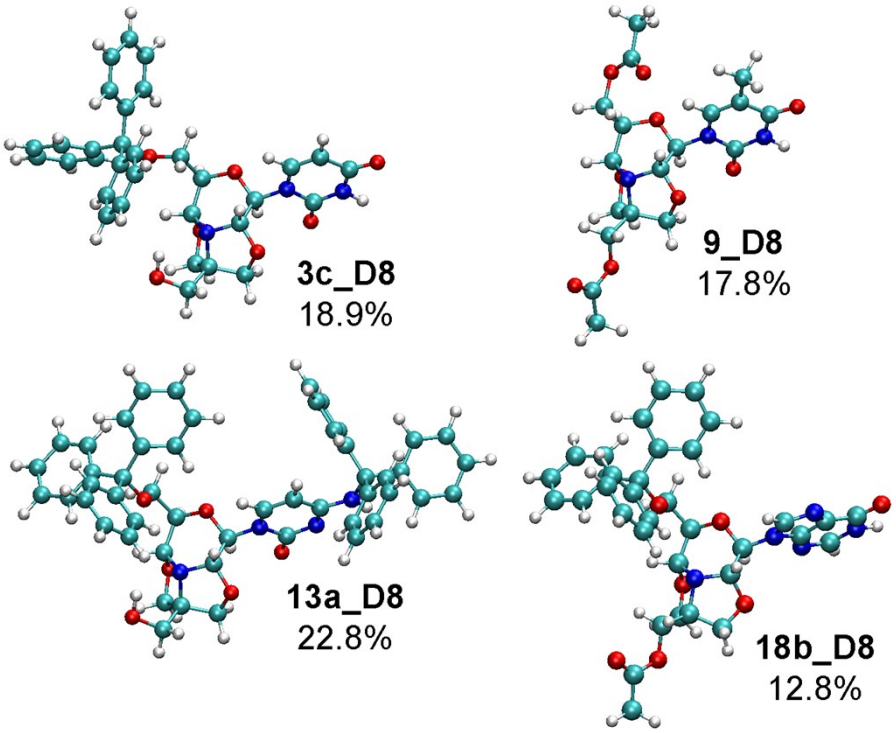


Figure S3. B3LYP/6-31+G(d,p) level global minima of **3c_D8**, **9_D8**, **13a_D8** and **18b_D8** along with their Boltzmann-populations.

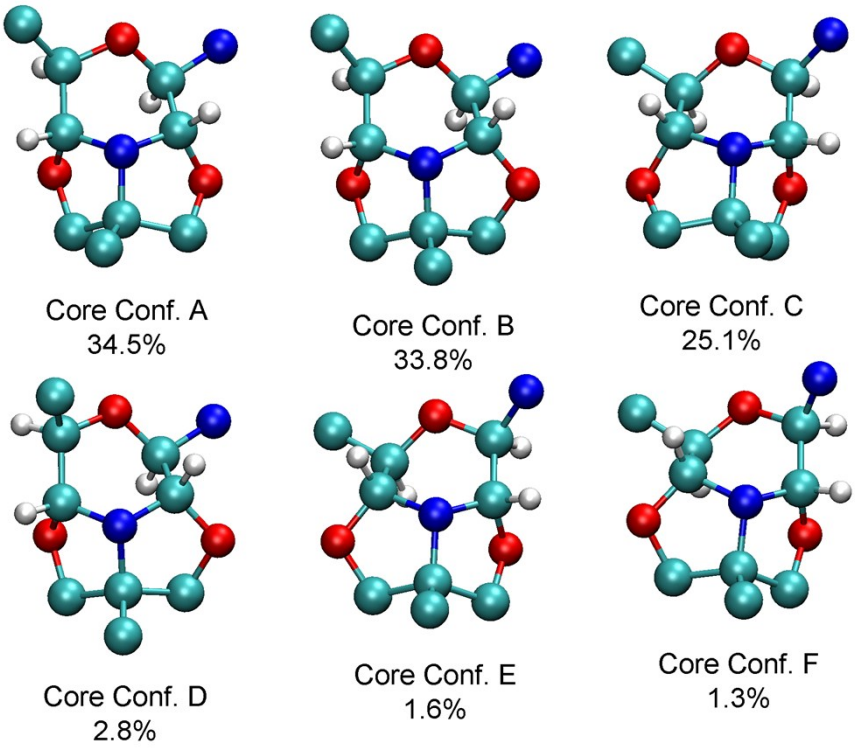


Figure S4. Prevalent conformers of the core part of **18b_D8** obtained by Boltzmann weighting and clustering of the B3LYP/6-31+G(d,p) reoptimized 686 OPLS conformers for the heavy atoms of the tricycle and the connecting first non-hydrogen atoms. For better comparison only these atoms and the four key hydrogens connecting to C-1', C-2', C-8' and C-9' are shown.

^{1}H and ^{13}C NMR spectra of the compounds

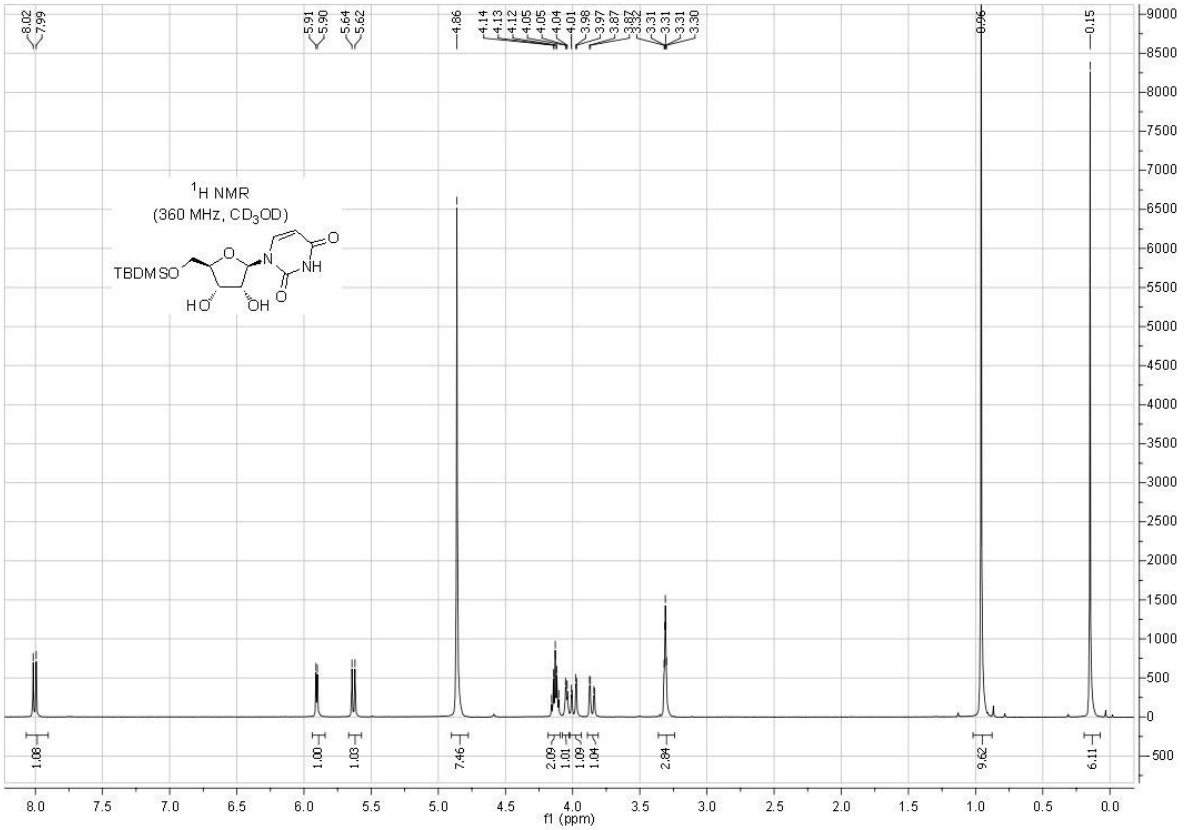


Figure S5. ^{1}H spectrum of compound 2a

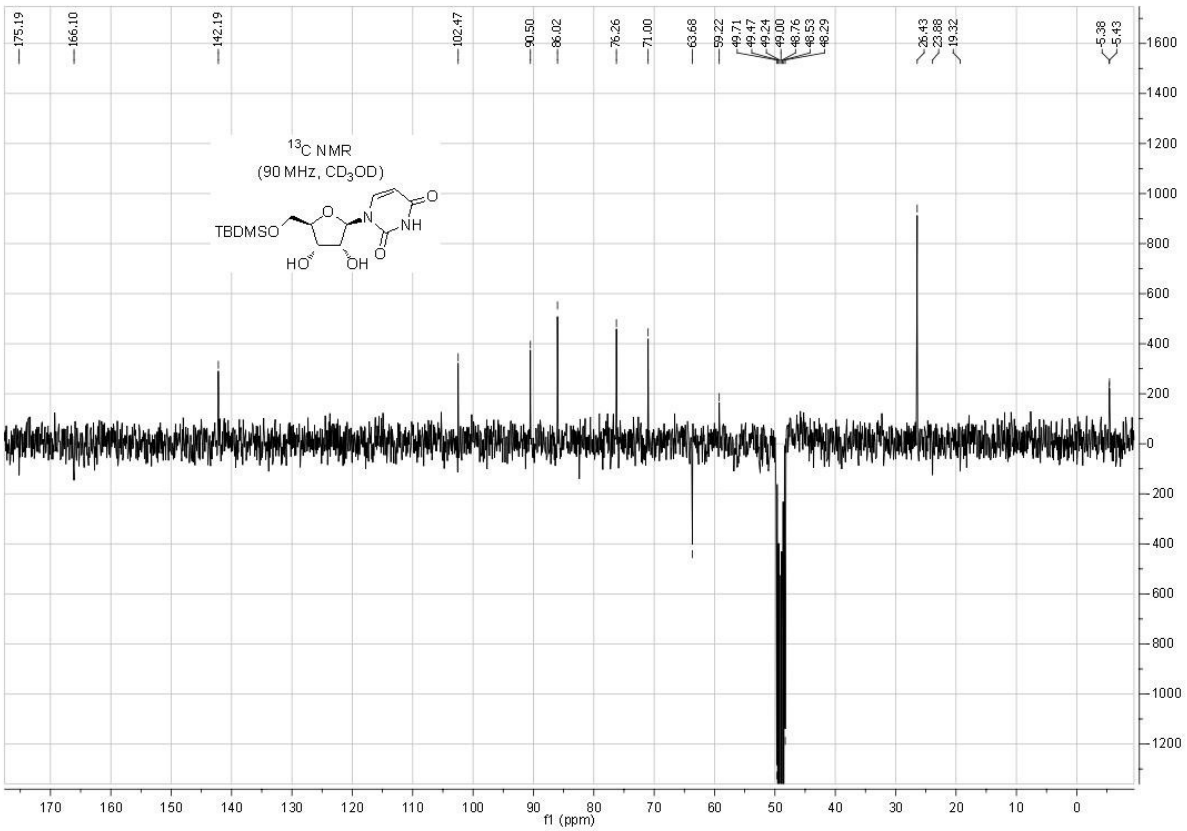


Figure S6. ^{13}C spectrum of compound 2a

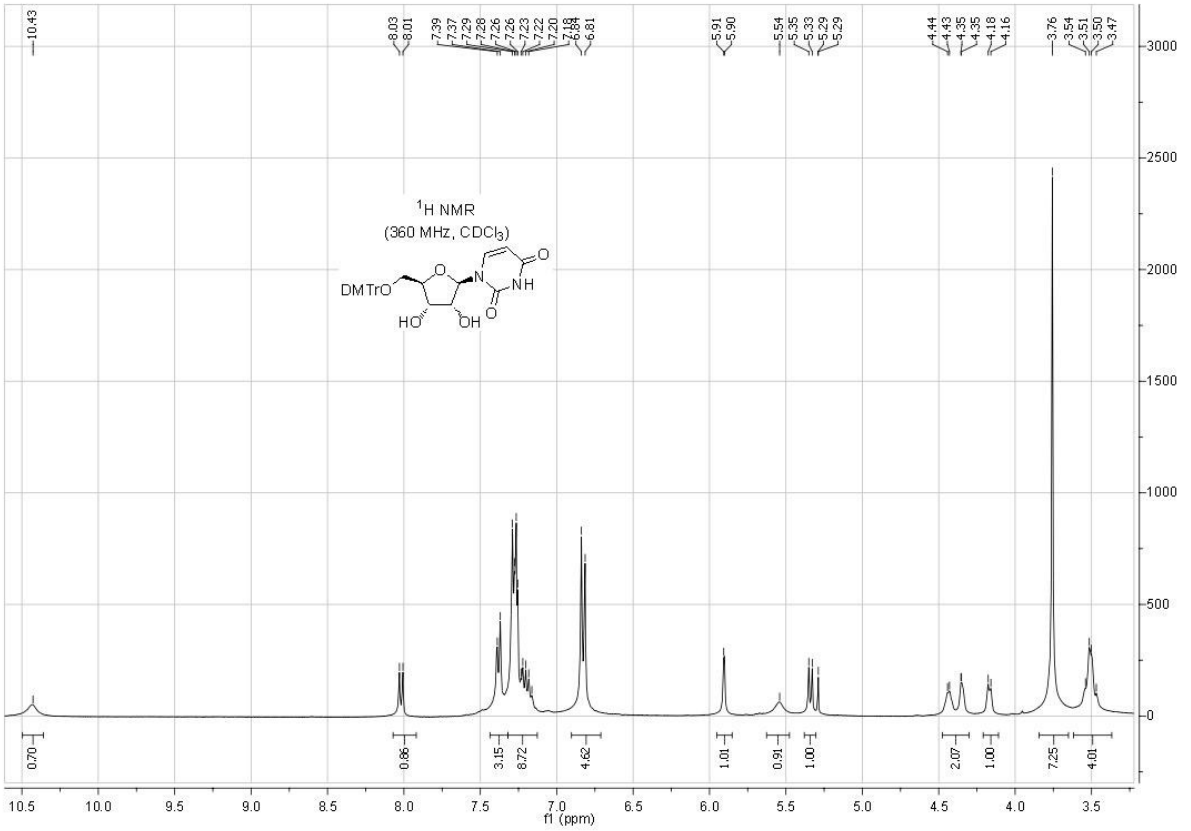


Figure S7. ^{1}H spectrum of compound 2b

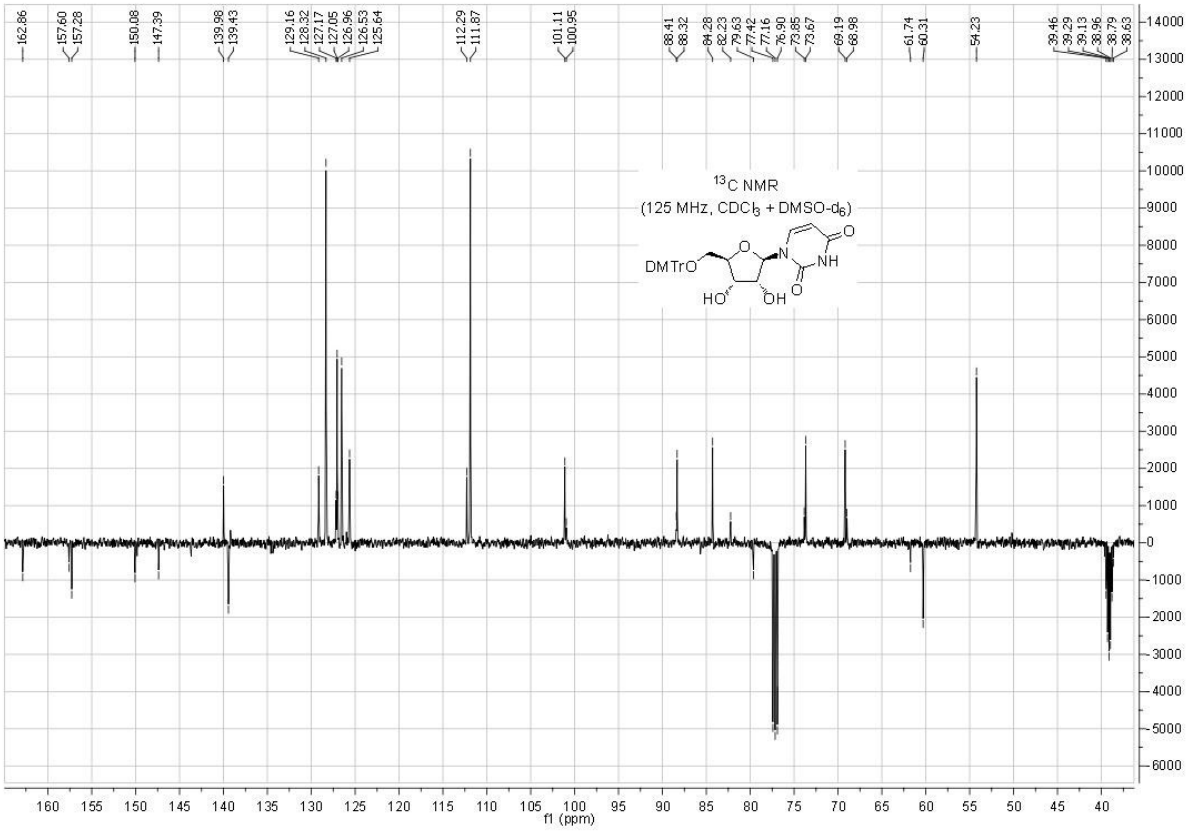


Figure S8. ^{13}C spectrum of compound 2b

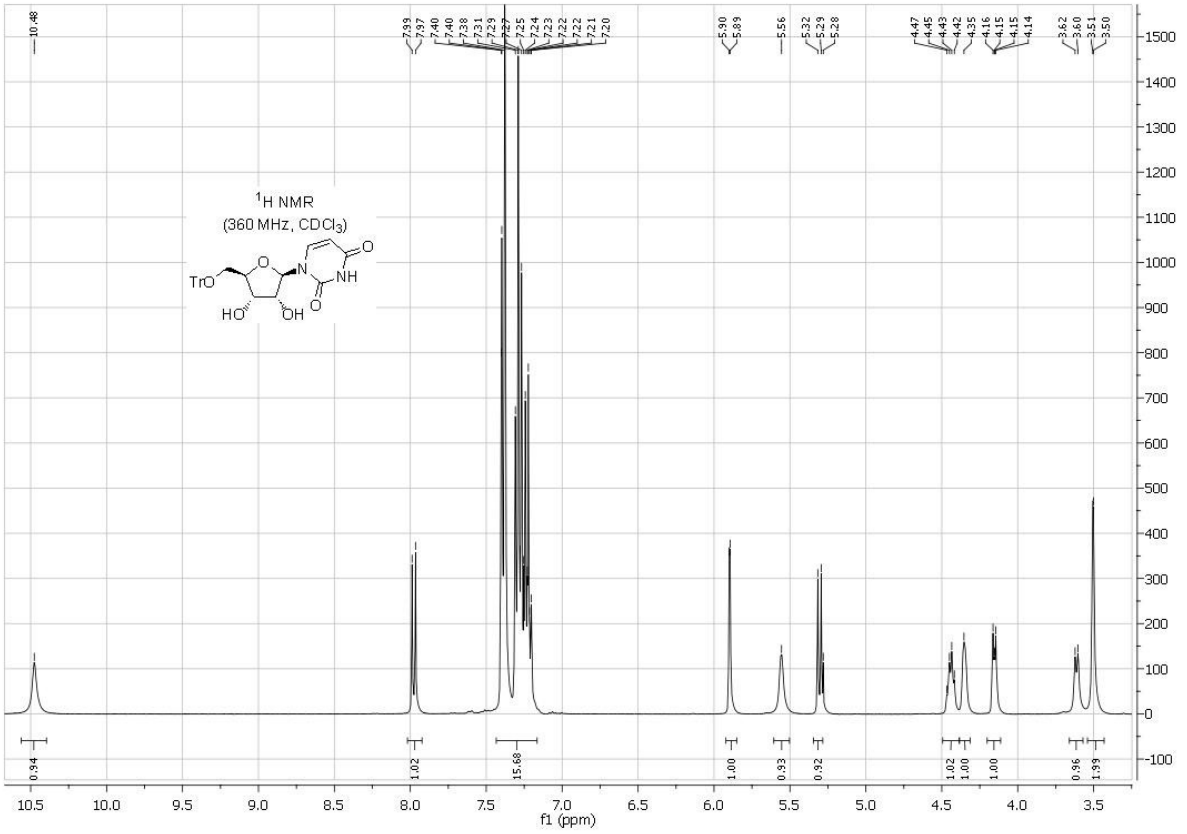


Figure S9. ^{1}H spectrum of compound 2c

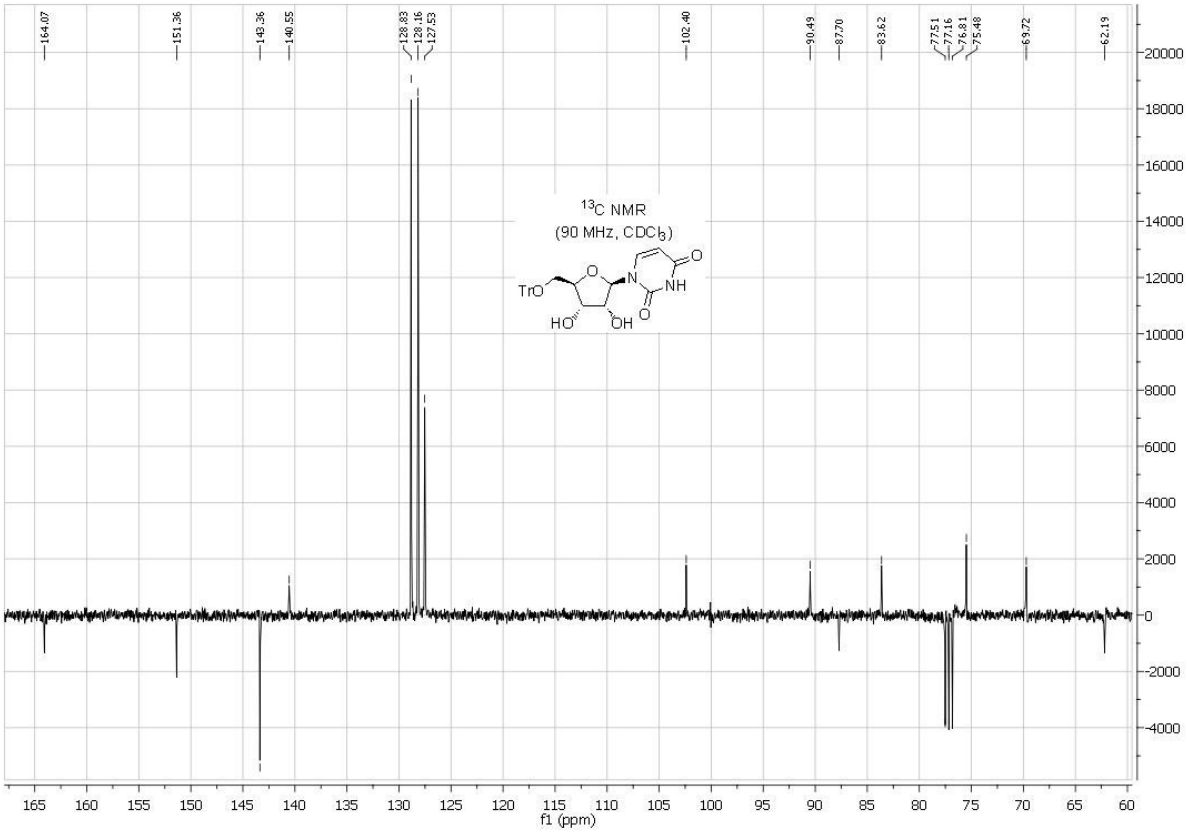


Figure S10. ^{13}C spectrum of compound 2c

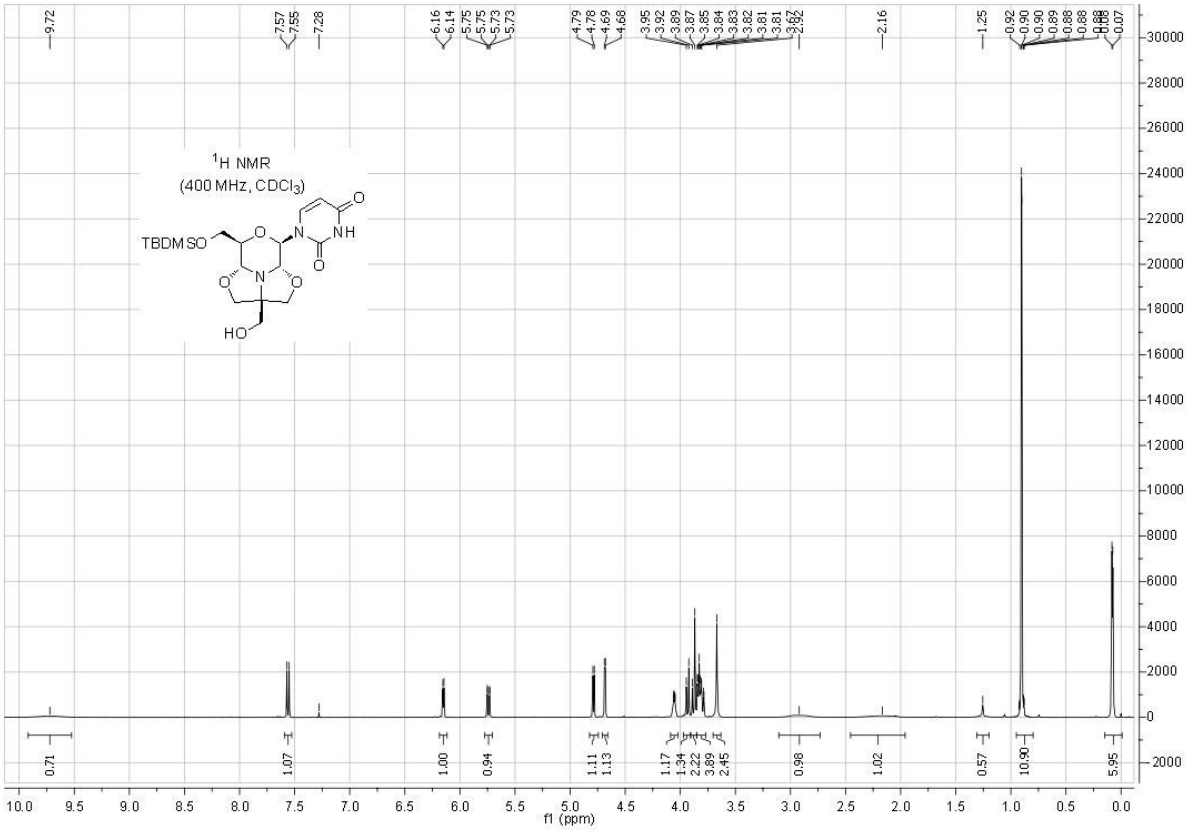


Figure S11. ^{1}H spectrum of compound 3a

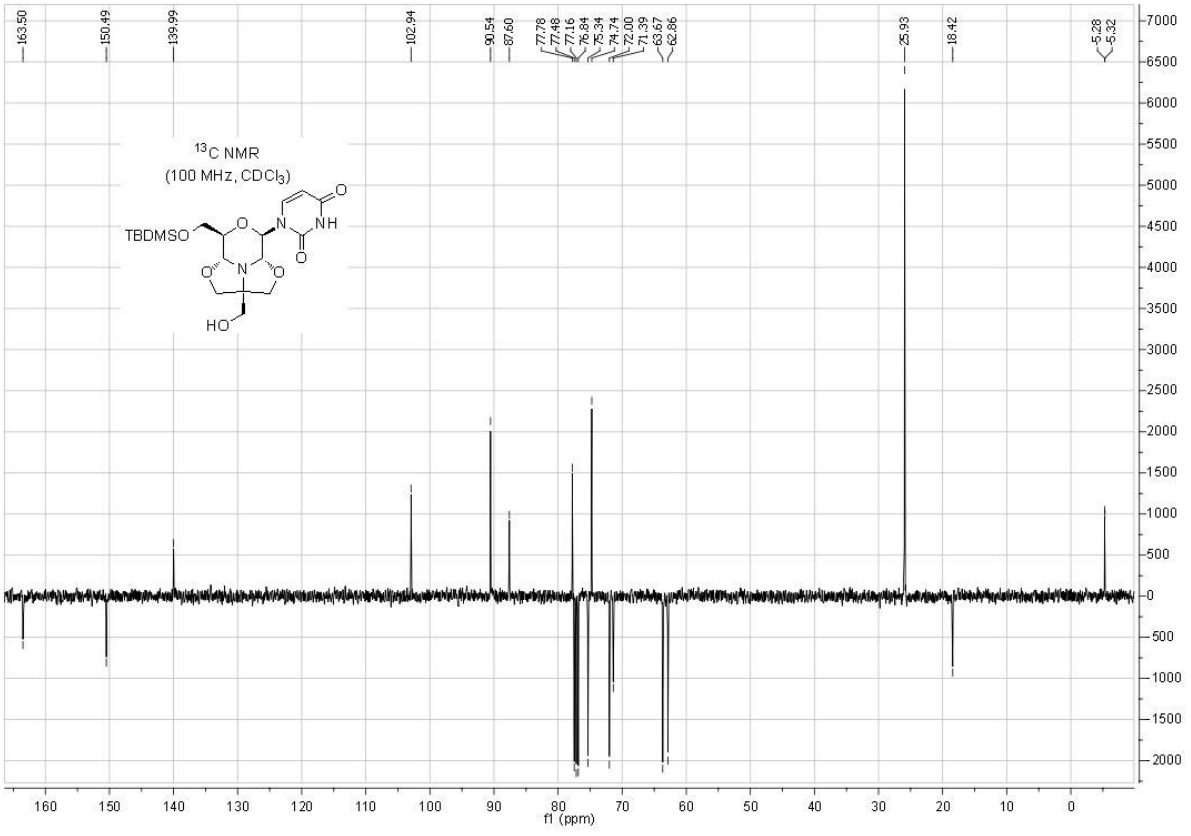


Figure S12. ^{13}C spectrum of compound 3a

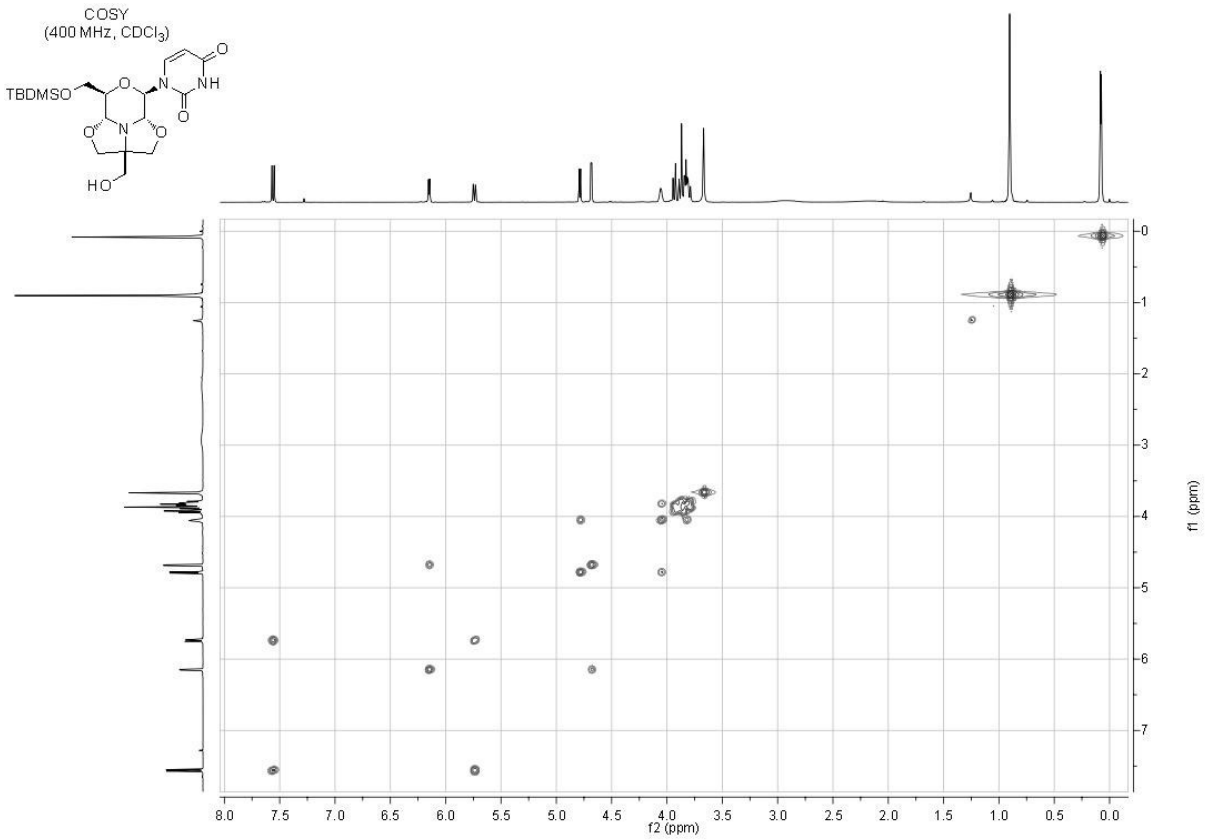


Figure S13. ^{1}H-^{1}H COSY spectrum of compound 3a

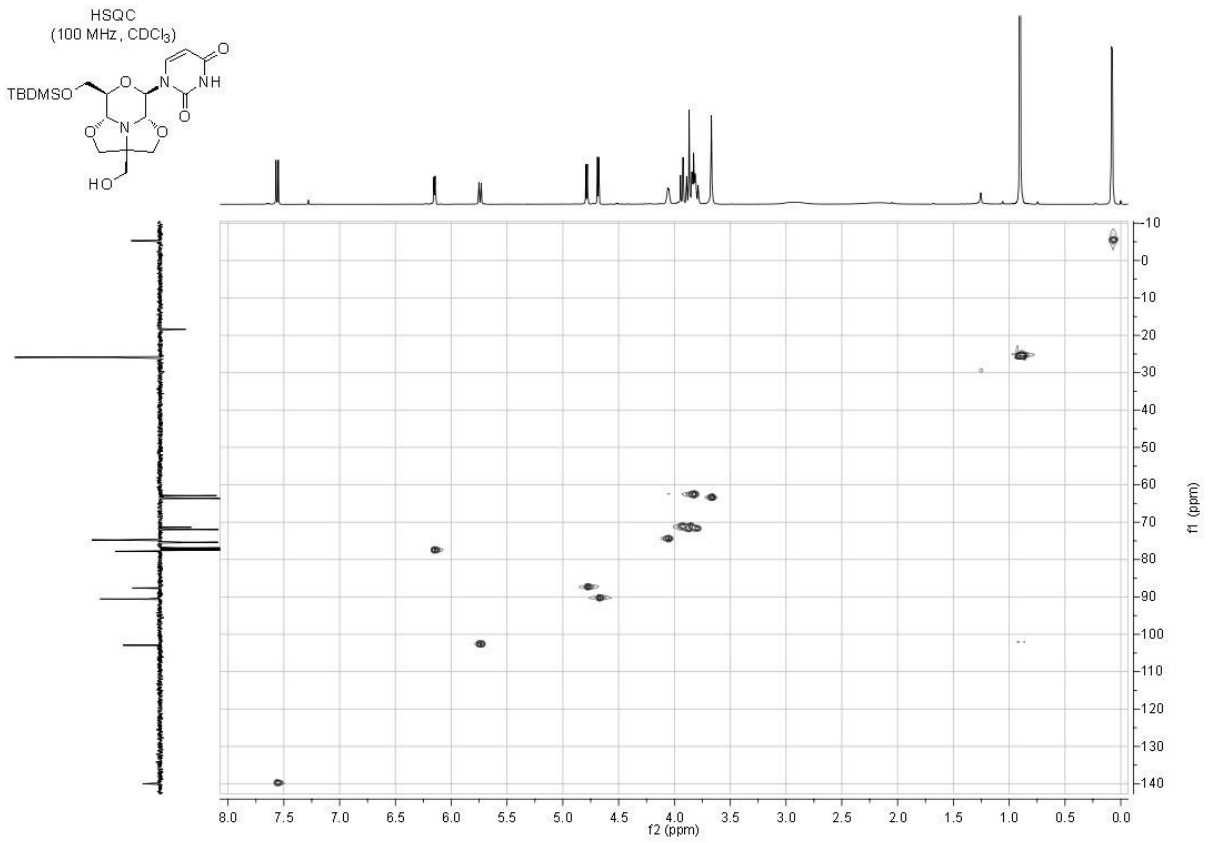


Figure S14. ^{1}H-^{13}C HSQC spectrum of compound 3a

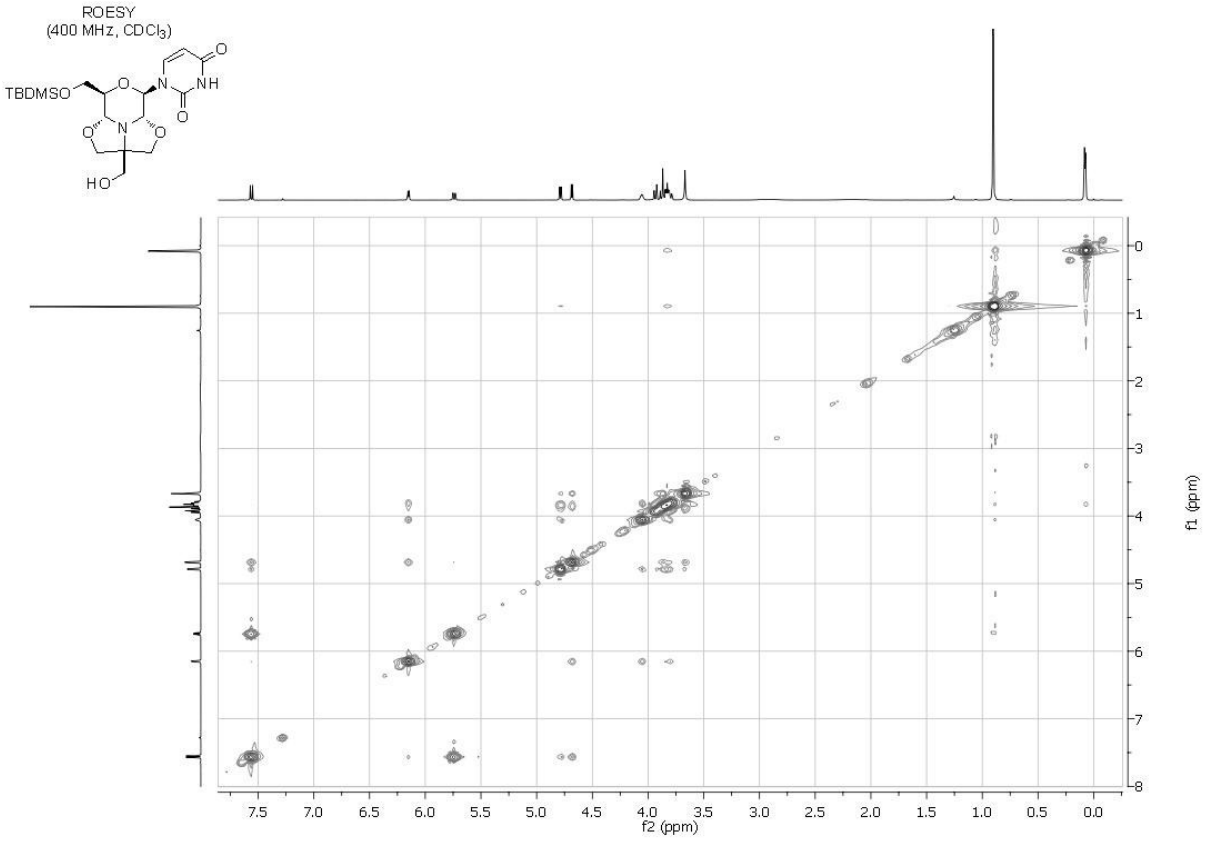


Figure S15. ^{1}H-^{1}H ROESY spectrum of compound 3a

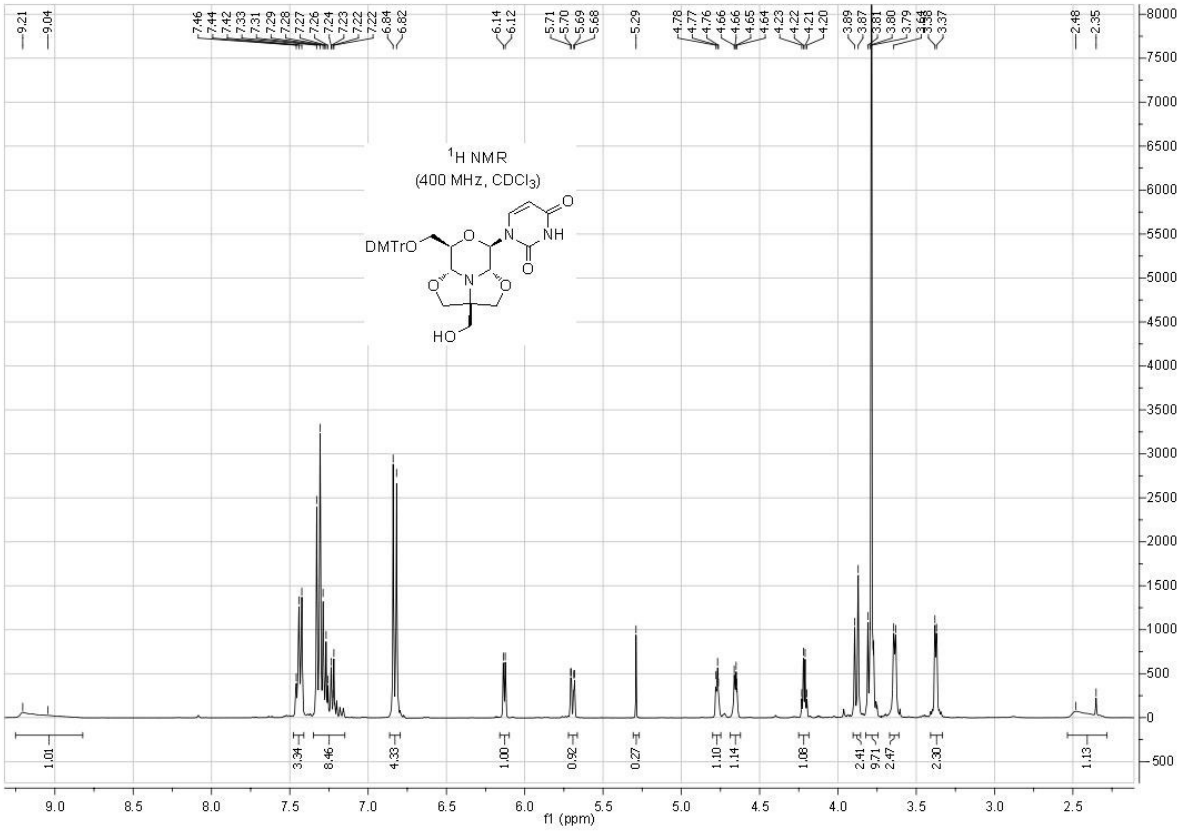


Figure S16. ^{1}H spectrum of compound 3b

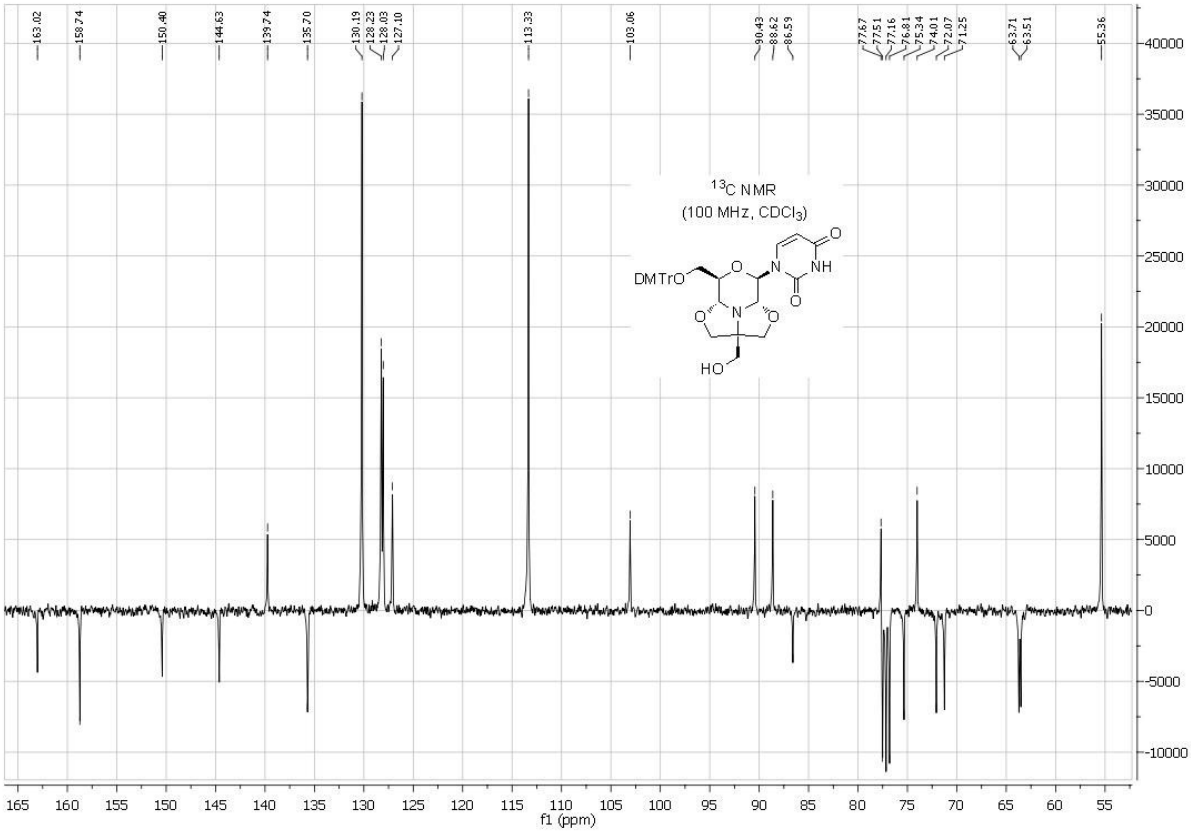


Figure S17. ^{13}C spectrum of compound 3b

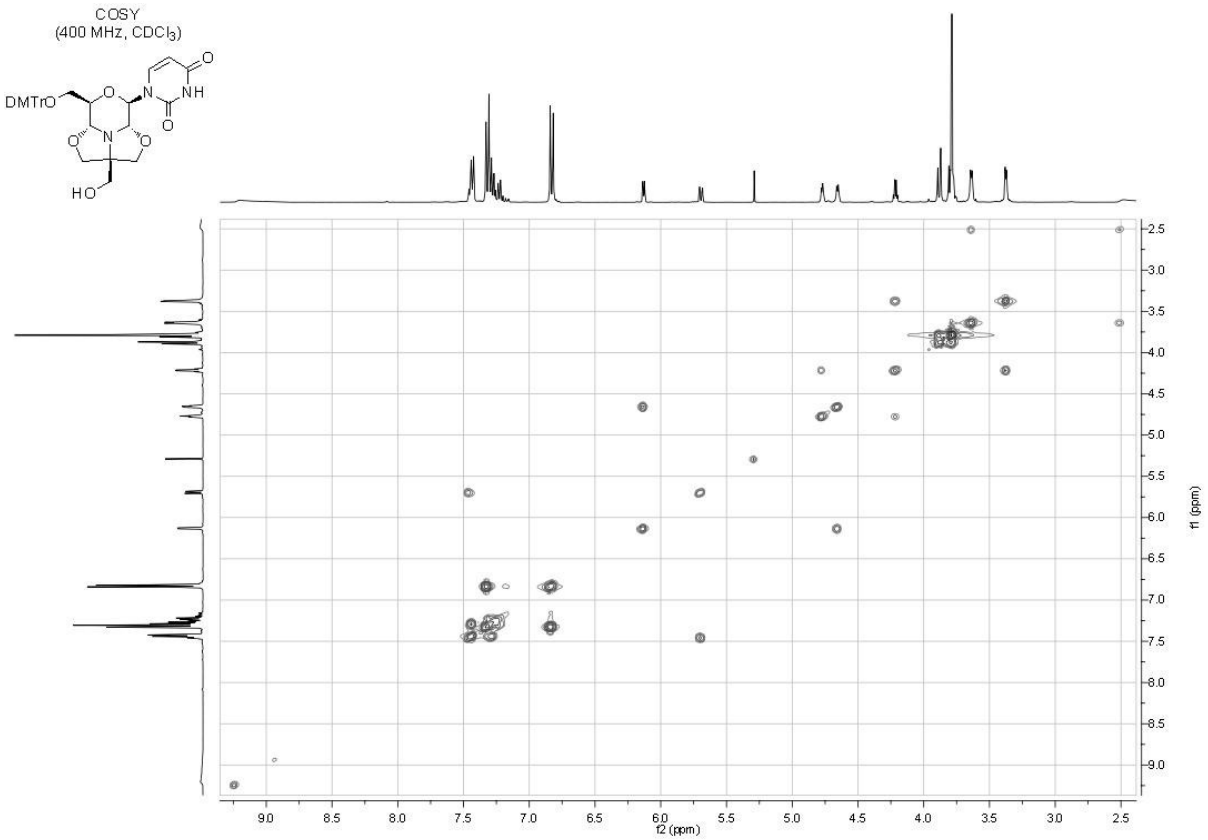


Figure S18. ^{1}H-^{1}H COSY spectrum of compound 3b

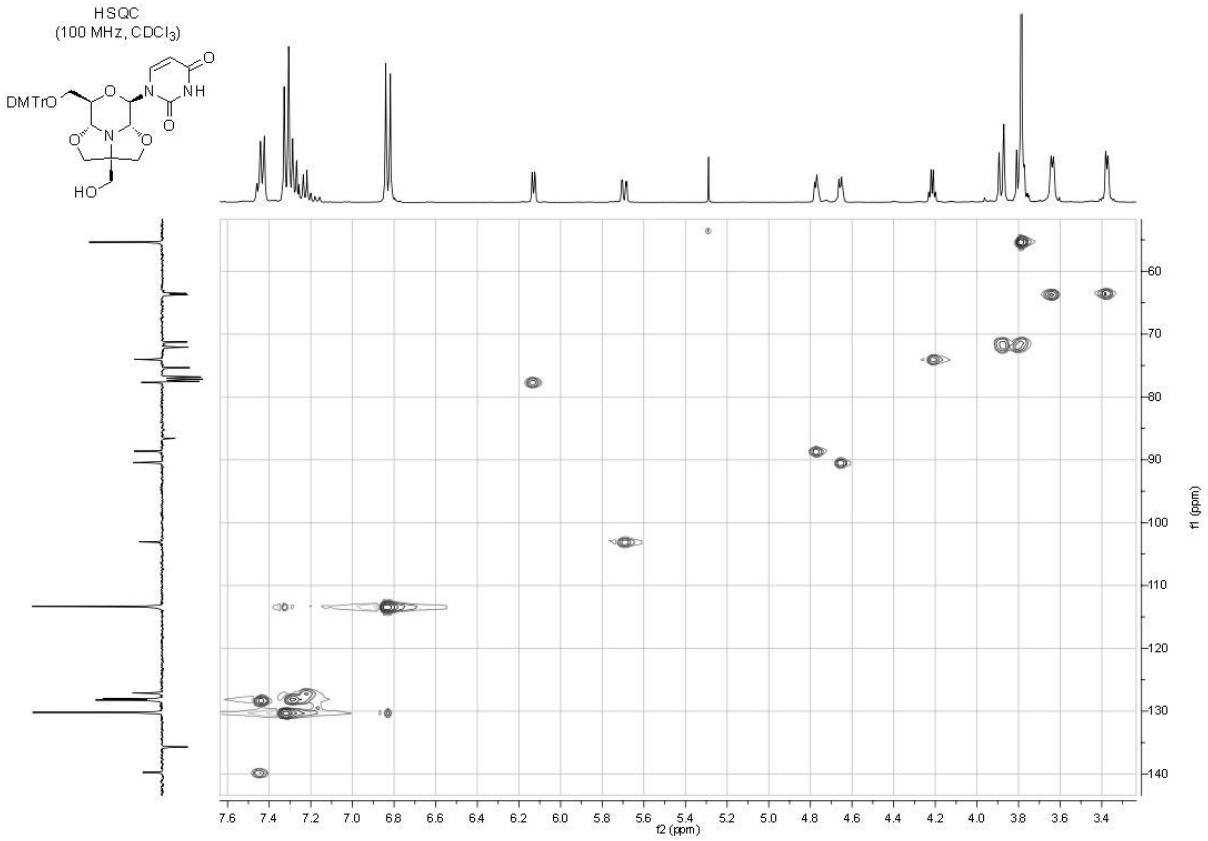


Figure S19. ^{1}H-^{13}C HSQC spectrum of compound 3b

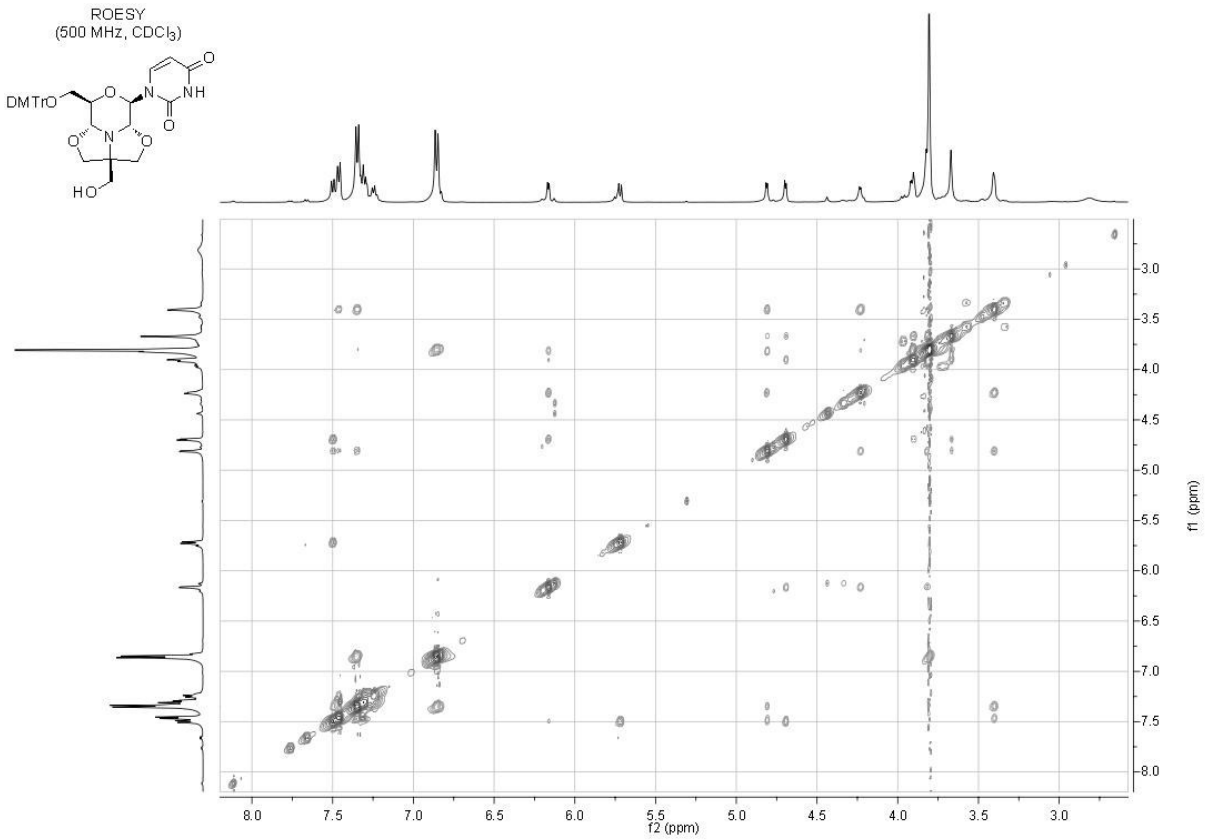


Figure S20. ^{1}H-^{1}H ROESY spectrum of compound 3b

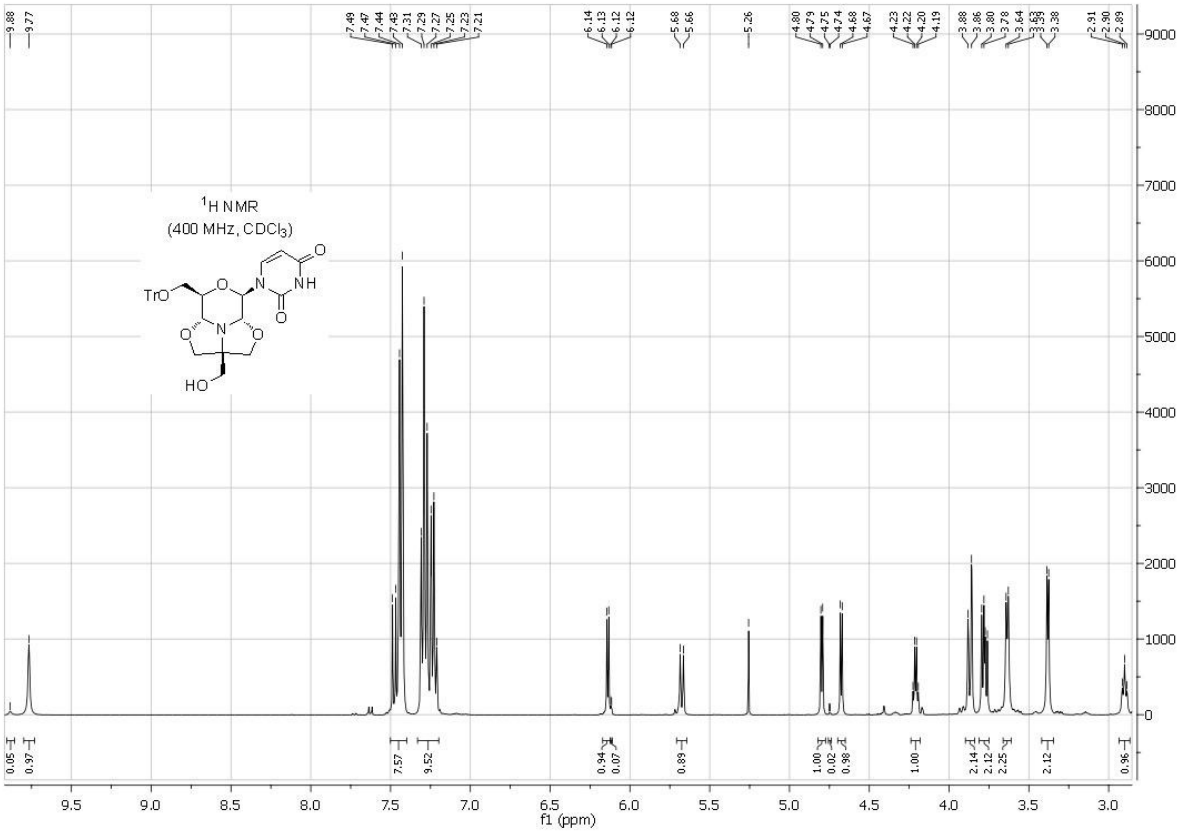


Figure S21. ^{1}H spectrum of compound 3c

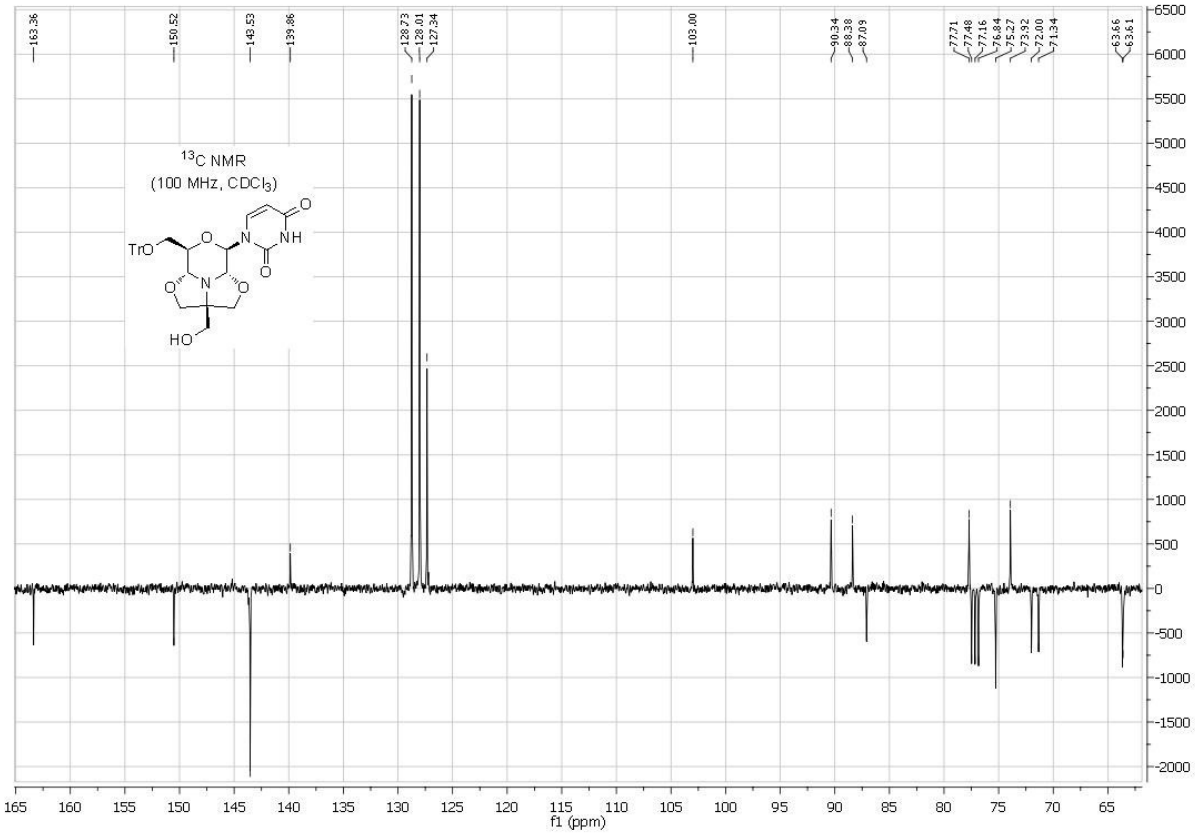


Figure S22. ^{13}C spectrum of compound 3c

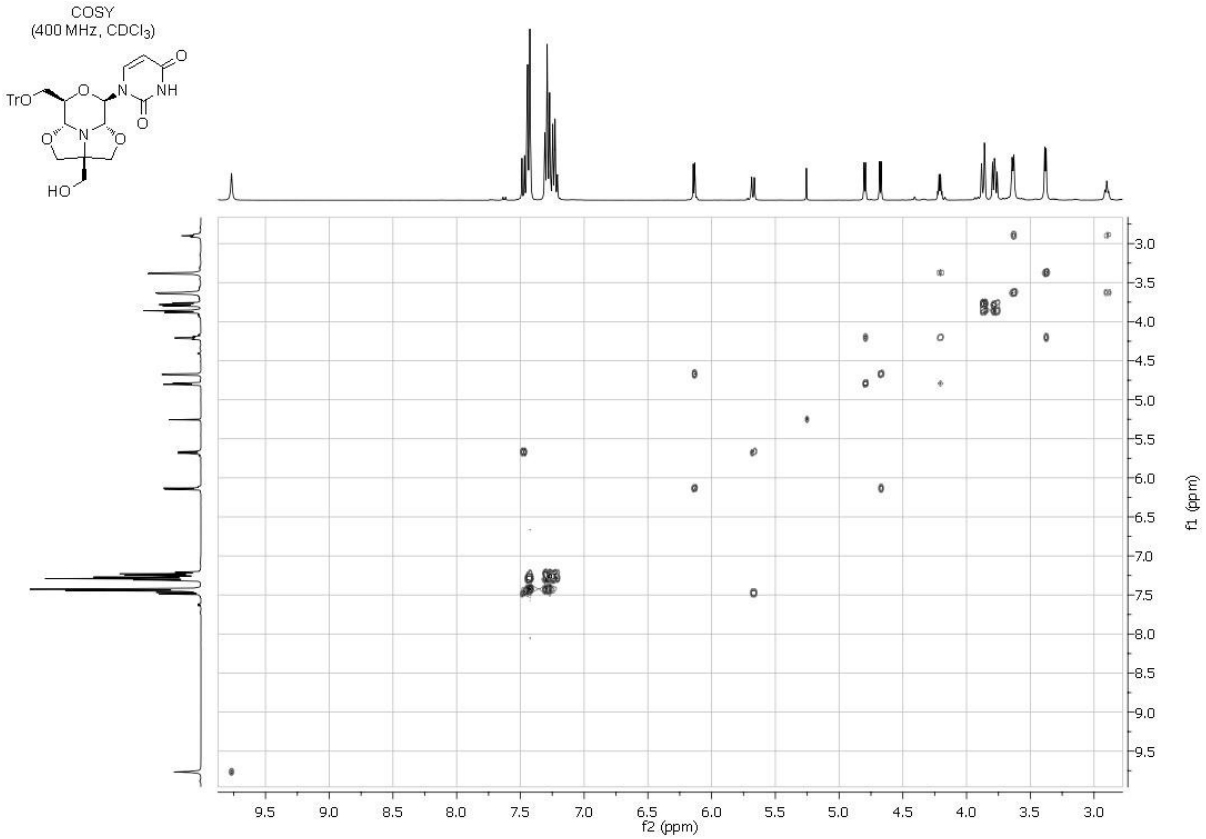


Figure S23. ^{1}H-^{1}H COSY spectrum of compound 3c

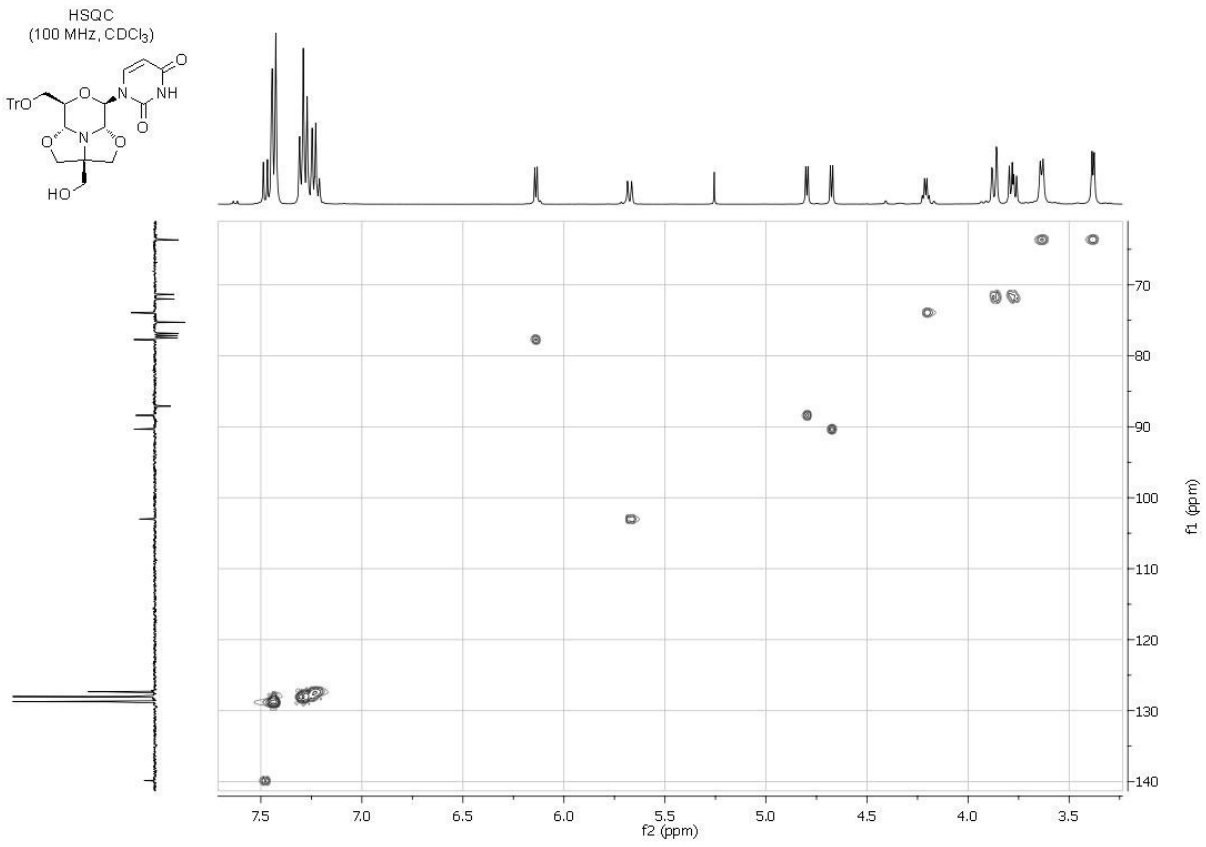


Figure S24. ^{1}H-^{13}C HSQC spectrum of compound 3c

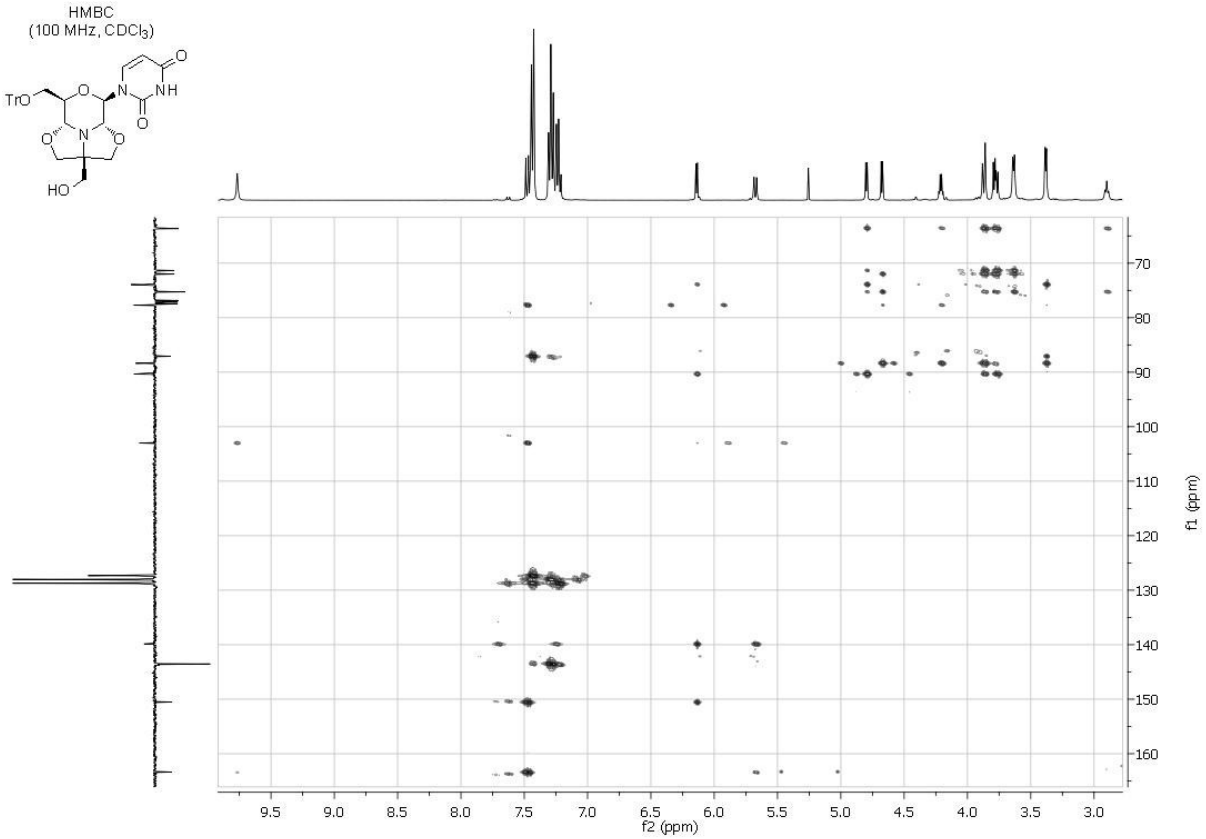


Figure S25. ^{1}H-^{13}C HMBC spectrum of compound 3c

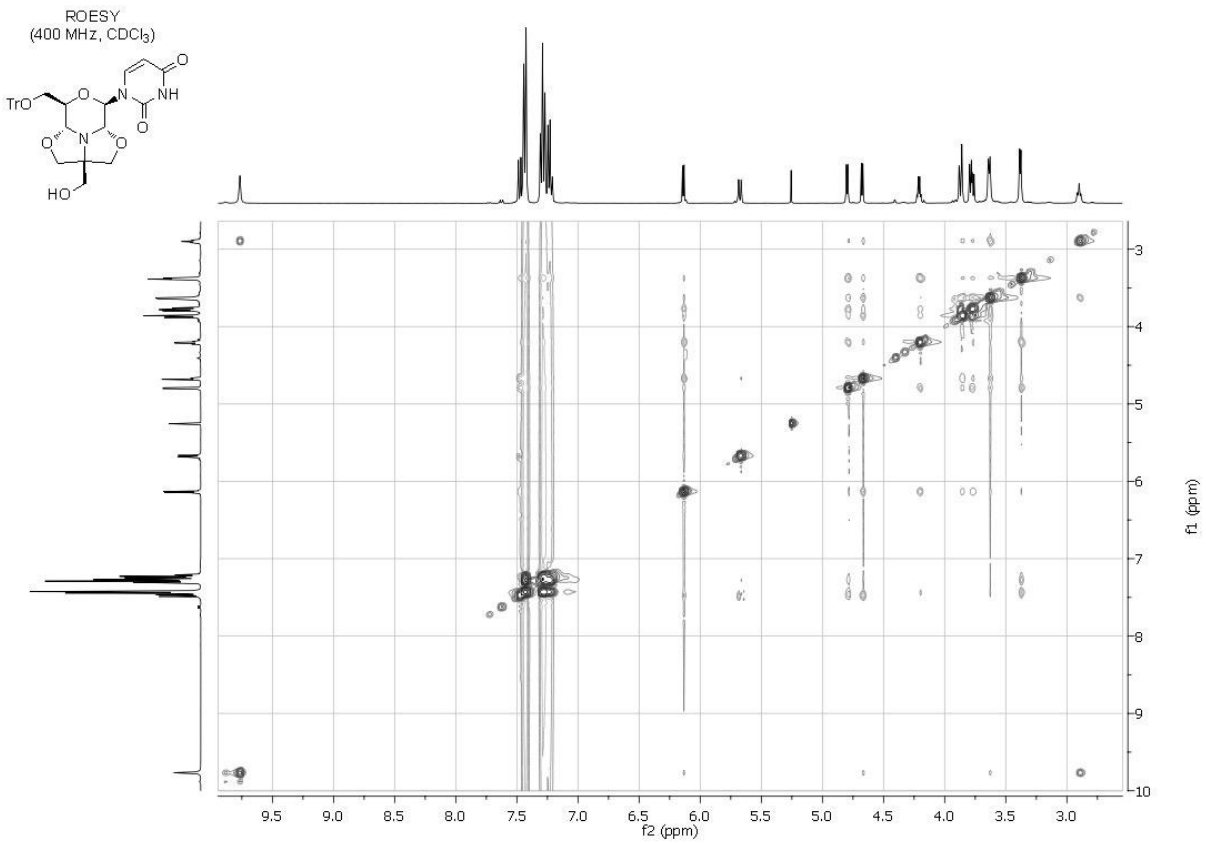


Figure S26. ^{1}H-^{1}H ROESY spectrum of compound 3c

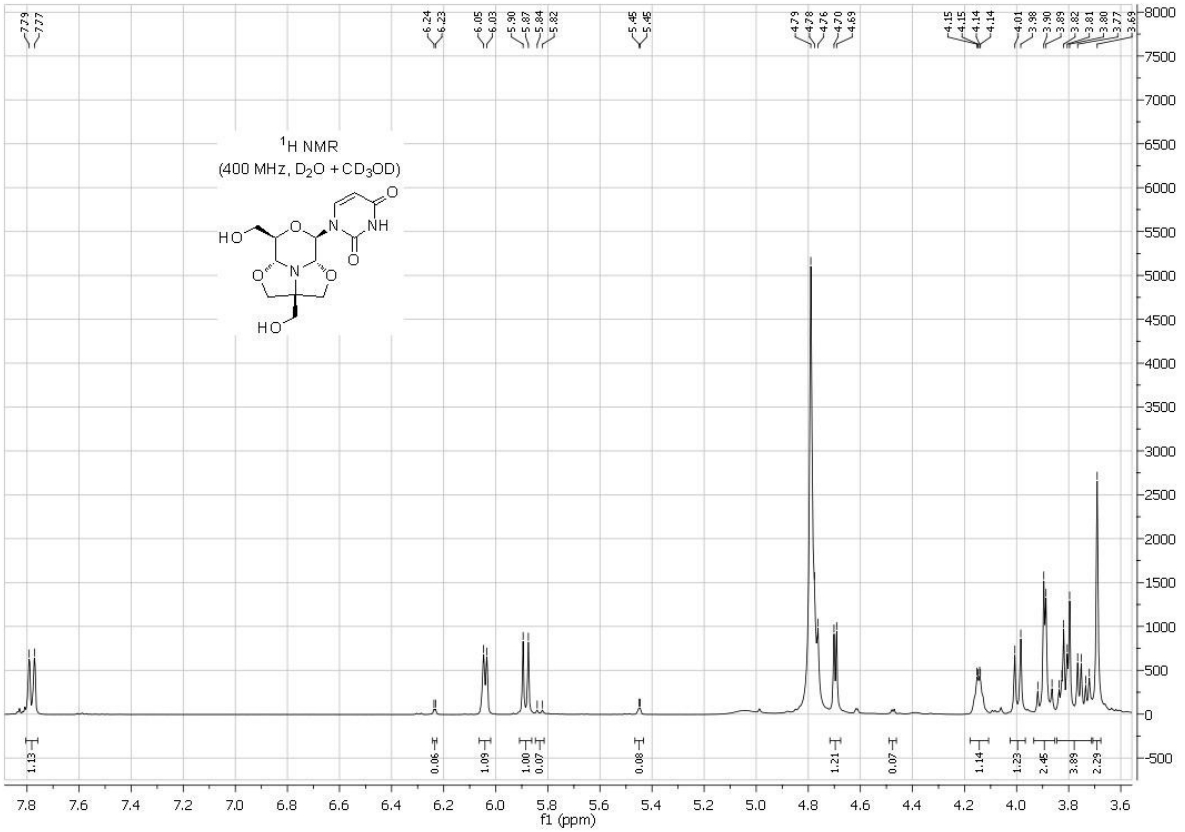


Figure S27. ^{1}H spectrum of compound 4– Deprotection of compound 3c

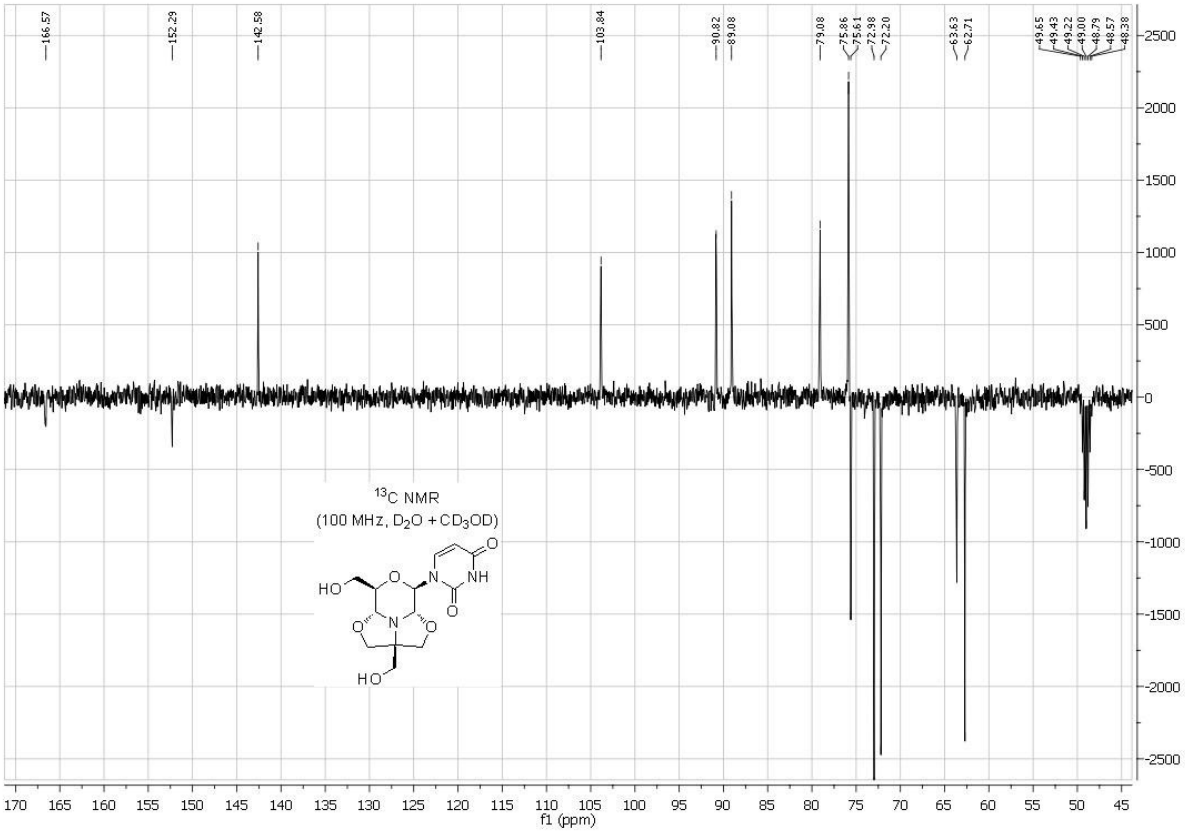


Figure S28. ^{13}C spectrum of compound 4 – Deprotection of compound 3c

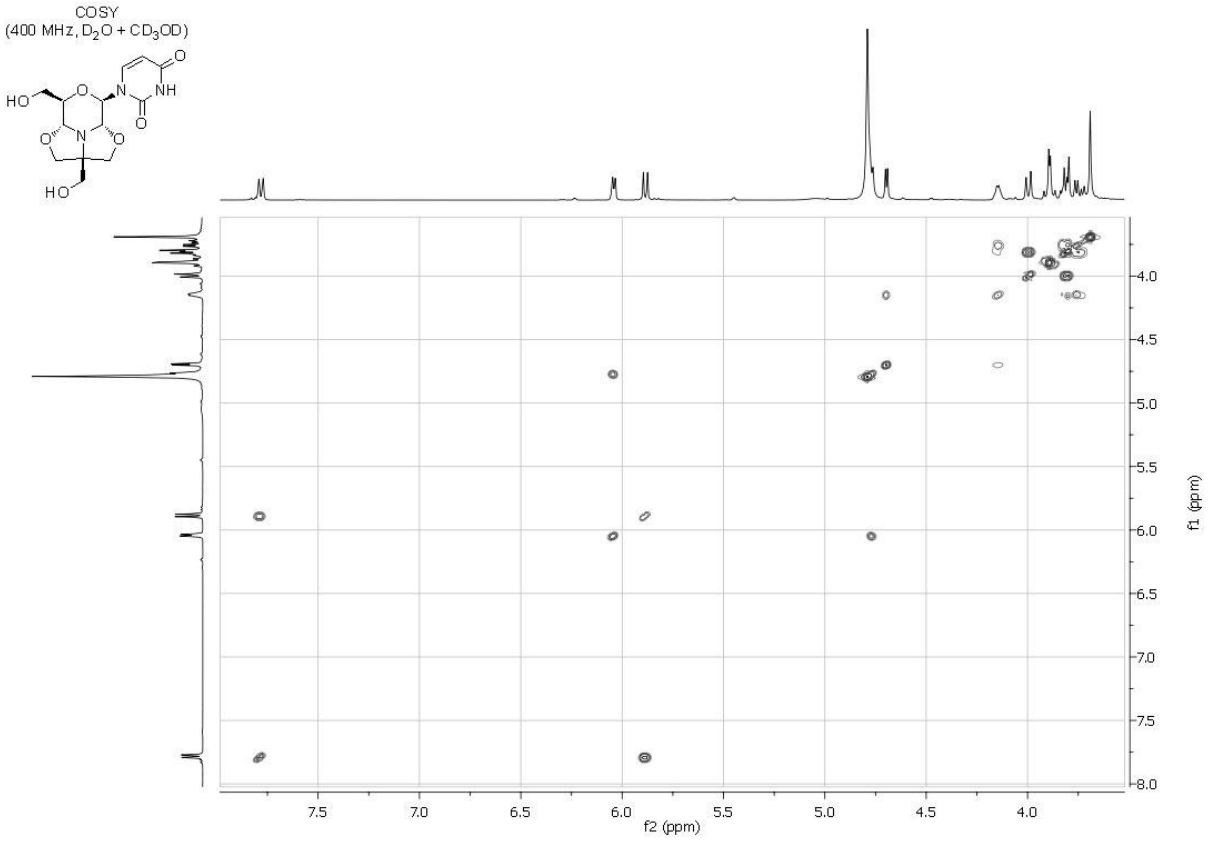


Figure S29. ^{1}H-^{1}H COSY spectrum of compound 4 – Deprotection of compound 3c

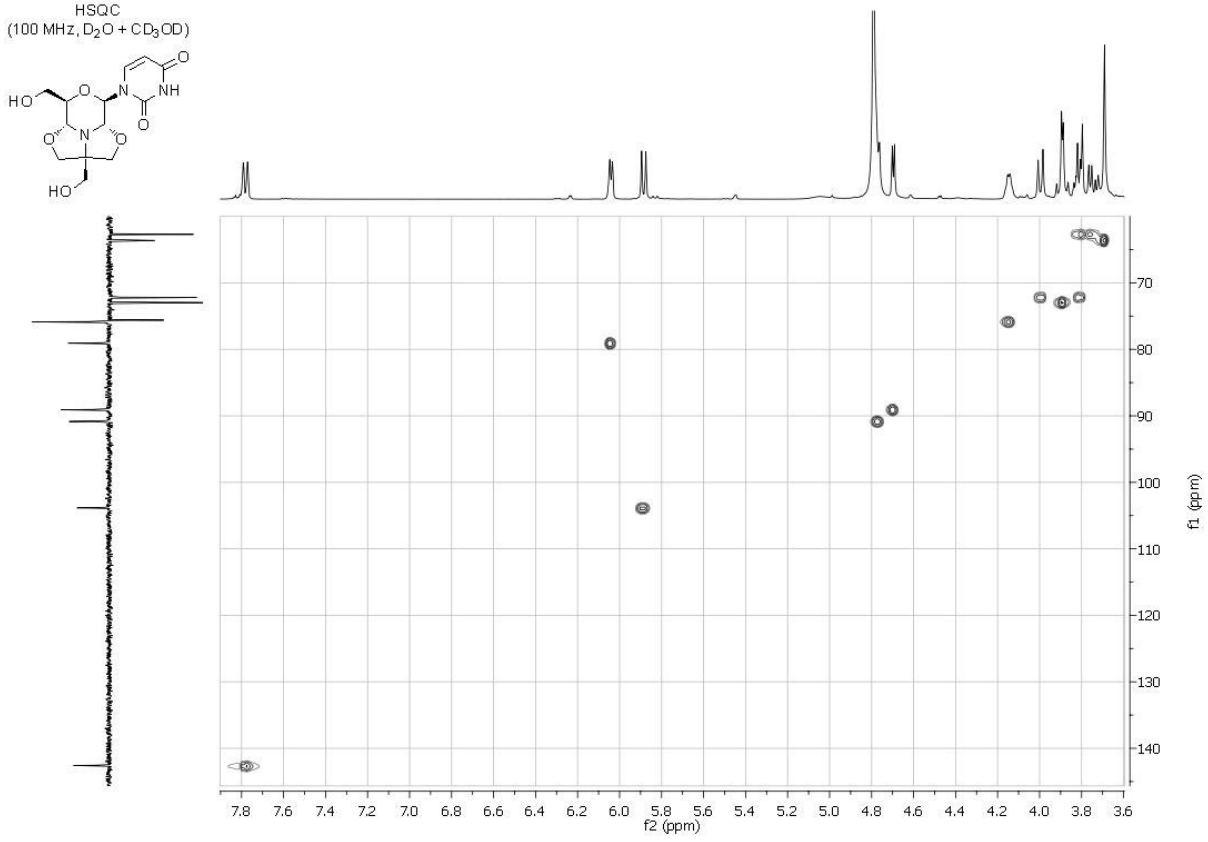


Figure S30. ^{1}H-^{13}C HSQC spectrum of compound 4 – Deprotection of compound 3c

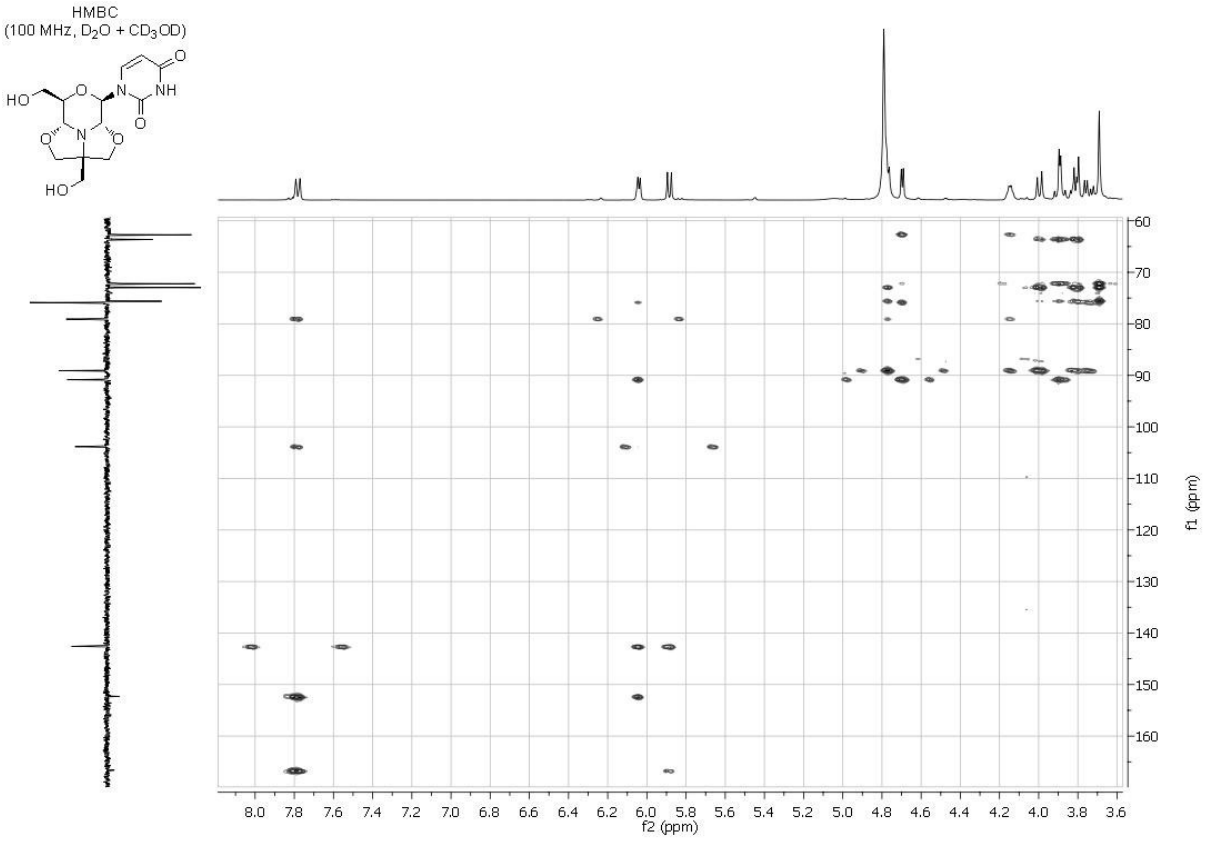


Figure S31. ^{1}H-^{13}C HMBC spectrum of compound 4 – Deprotection of compound 3c

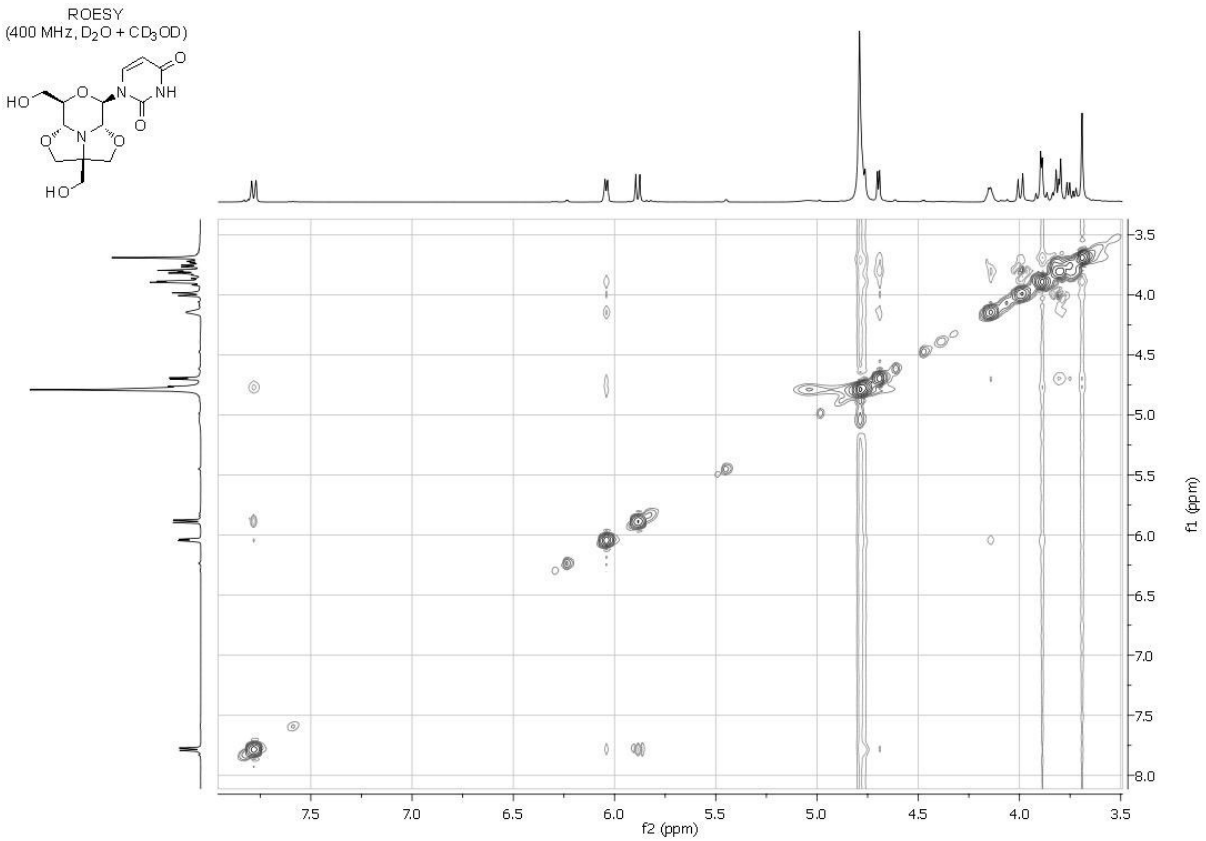


Figure S32. ^{1}H-^{1}H ROESY spectrum of compound 4 – Deprotection of compound 3c

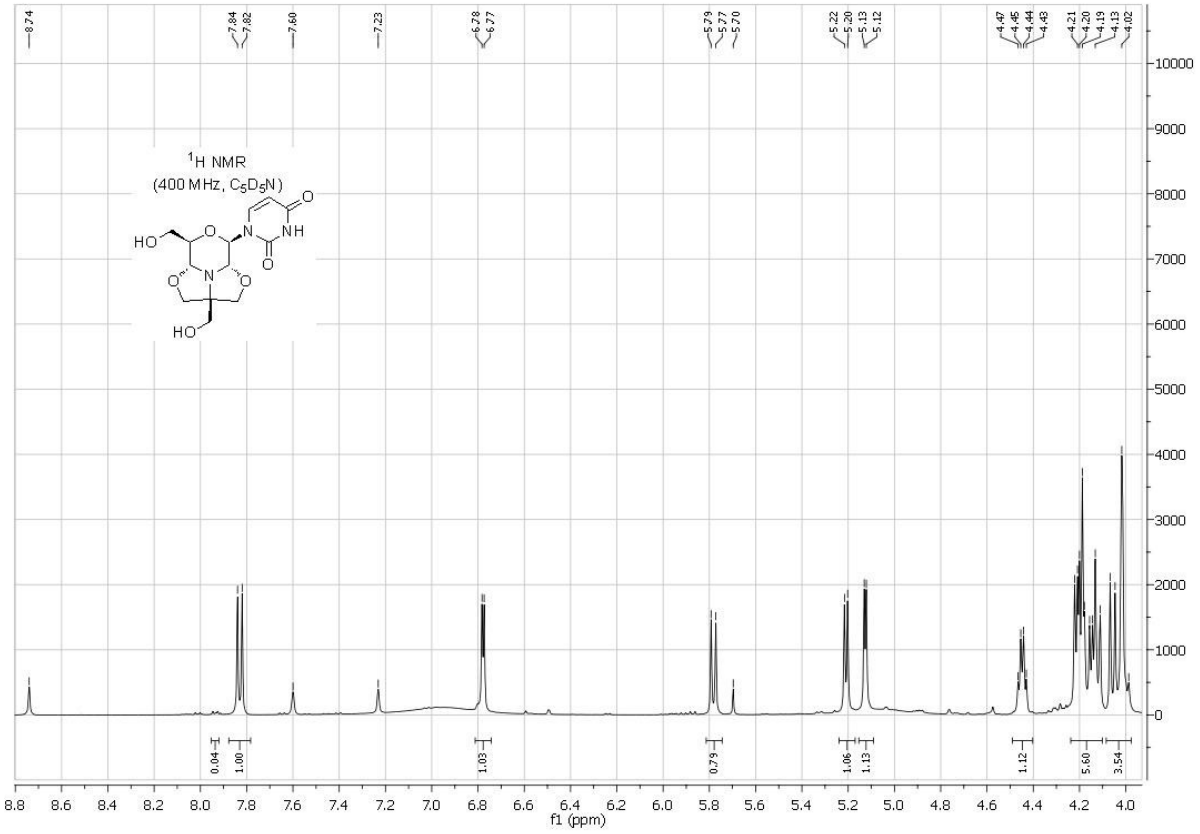


Figure S33. ^{1}H spectrum of compound 4 – Synthesis without protecting groups

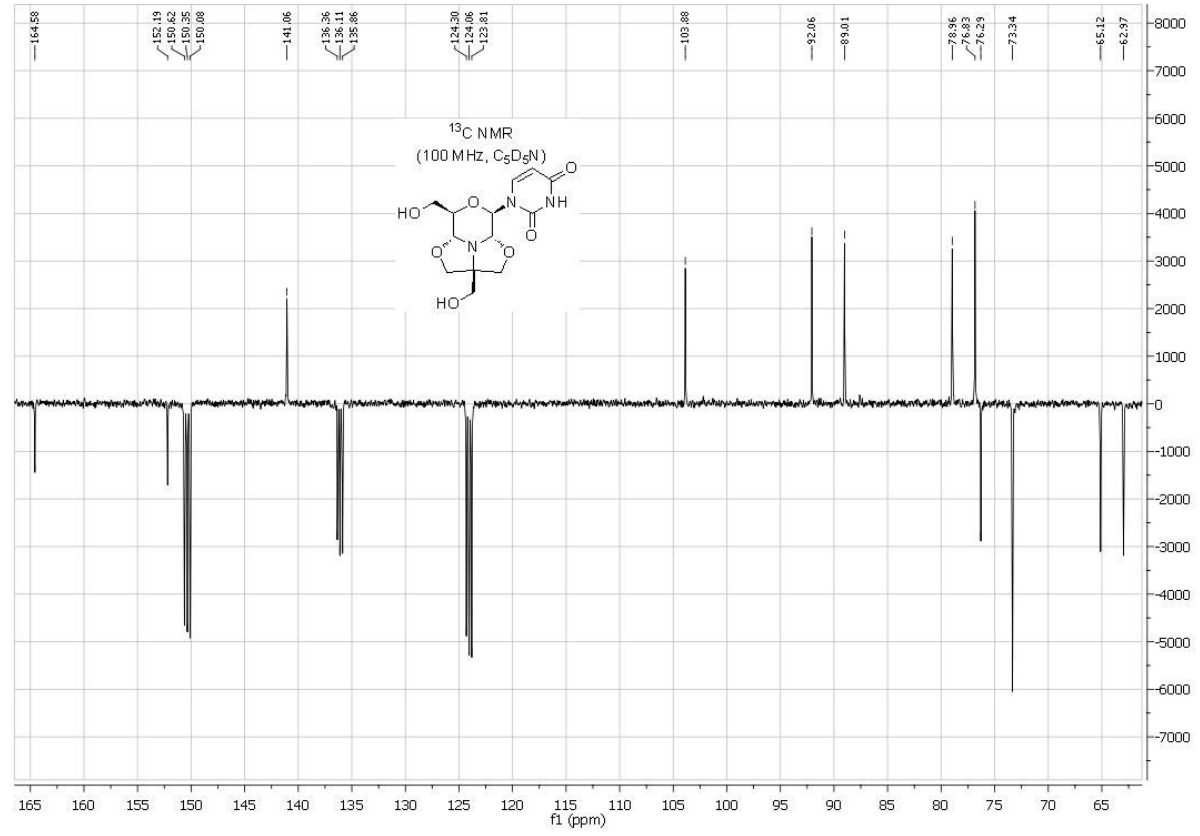


Figure S34. ^{13}C spectrum of compound 4 – Synthesis without protecting groups

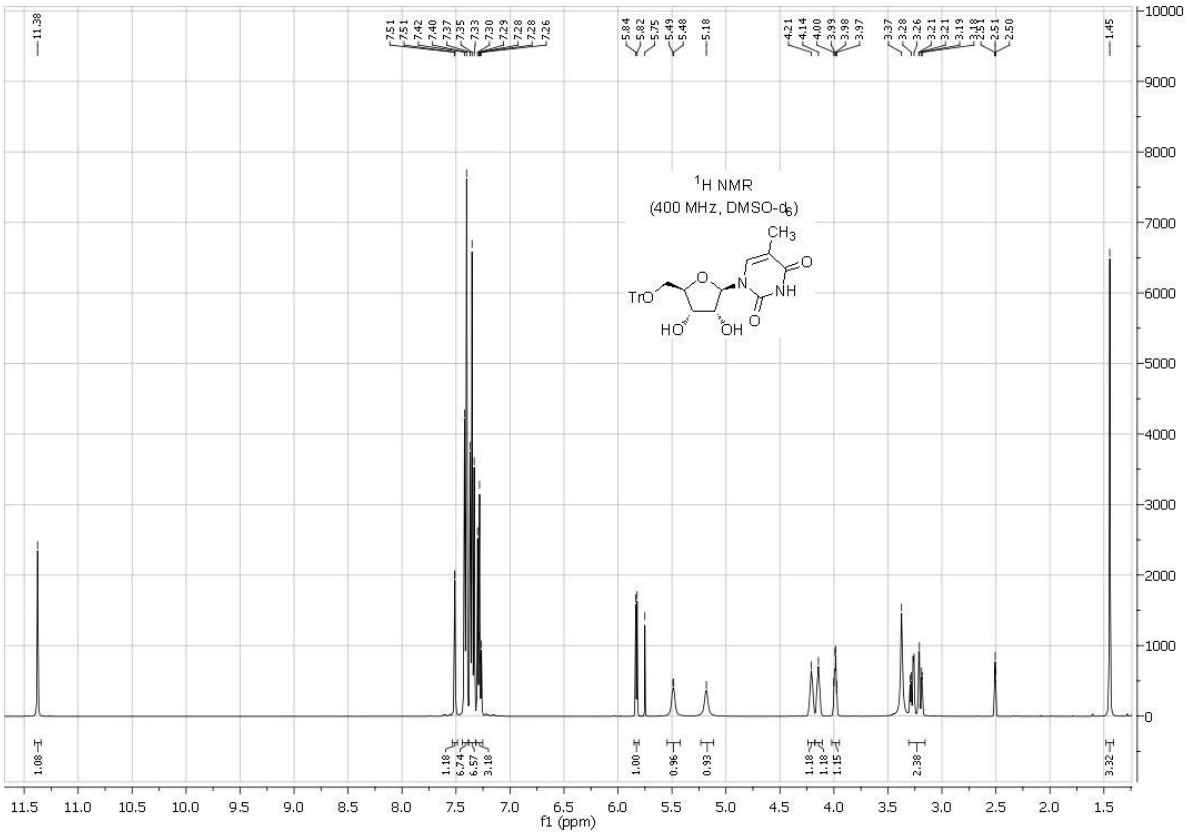


Figure S35. ^{1}H spectrum of compound 6

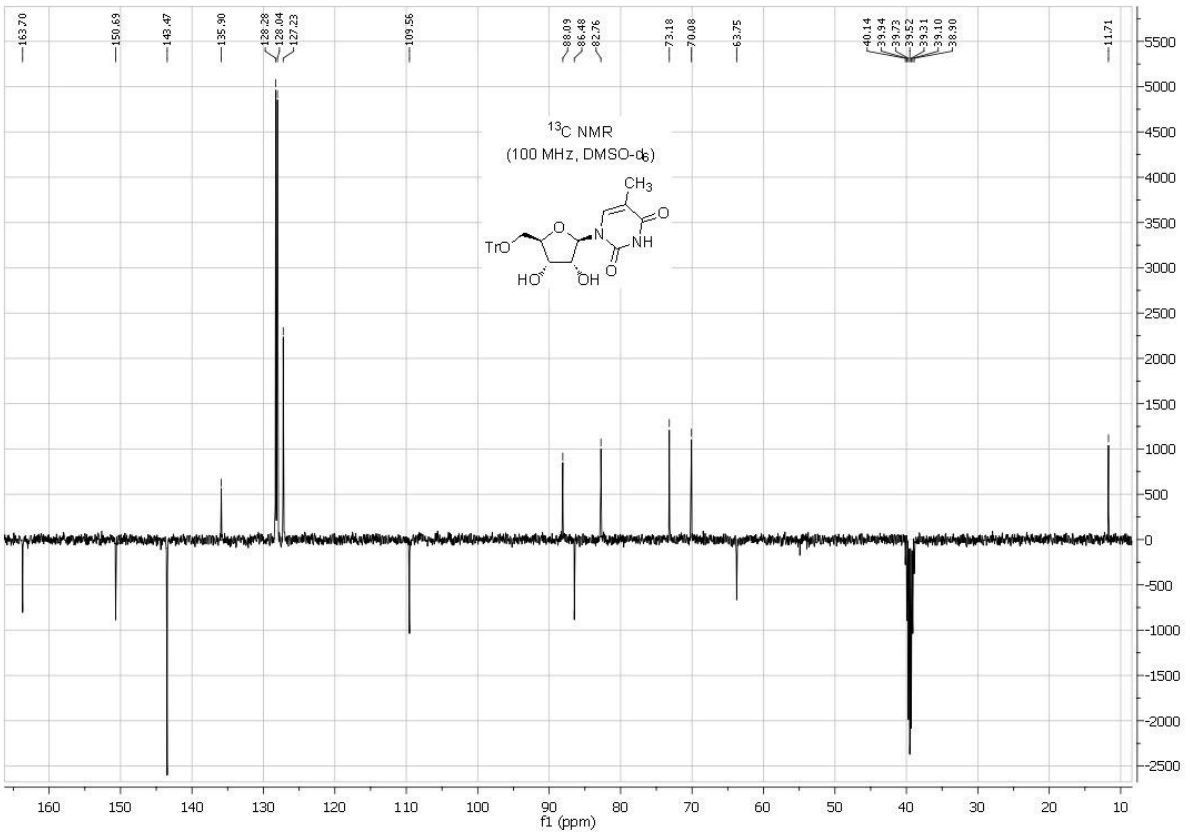


Figure S36. ^{13}C spectrum of compound 6

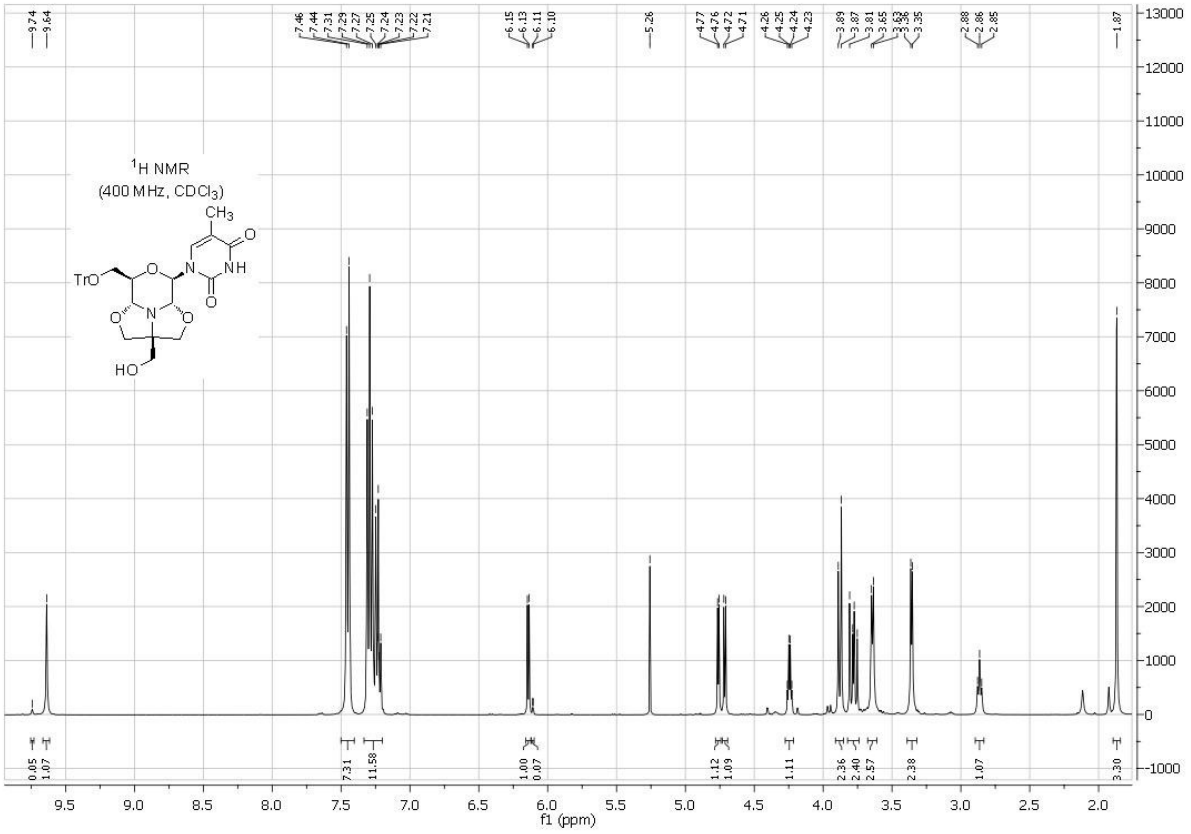


Figure S37. ^{1}H spectrum of compound 7

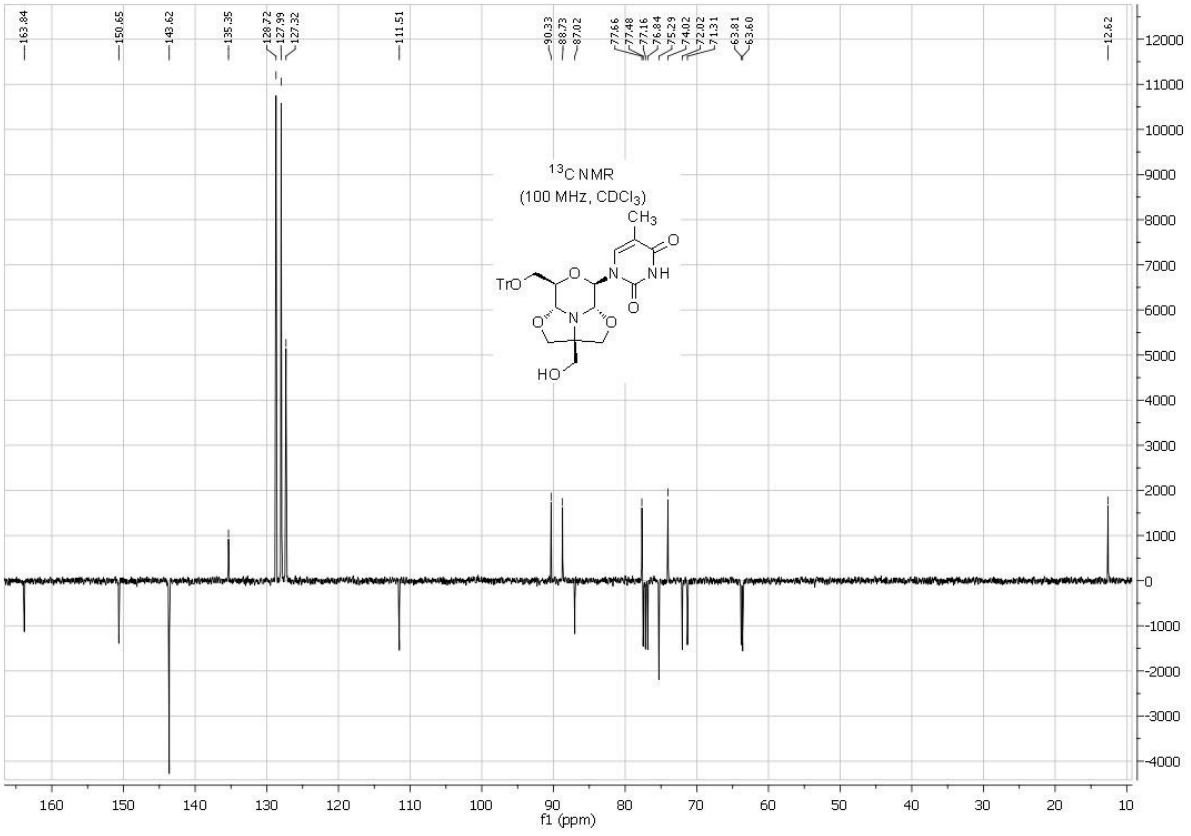


Figure S38. ^{13}C spectrum of compound 7

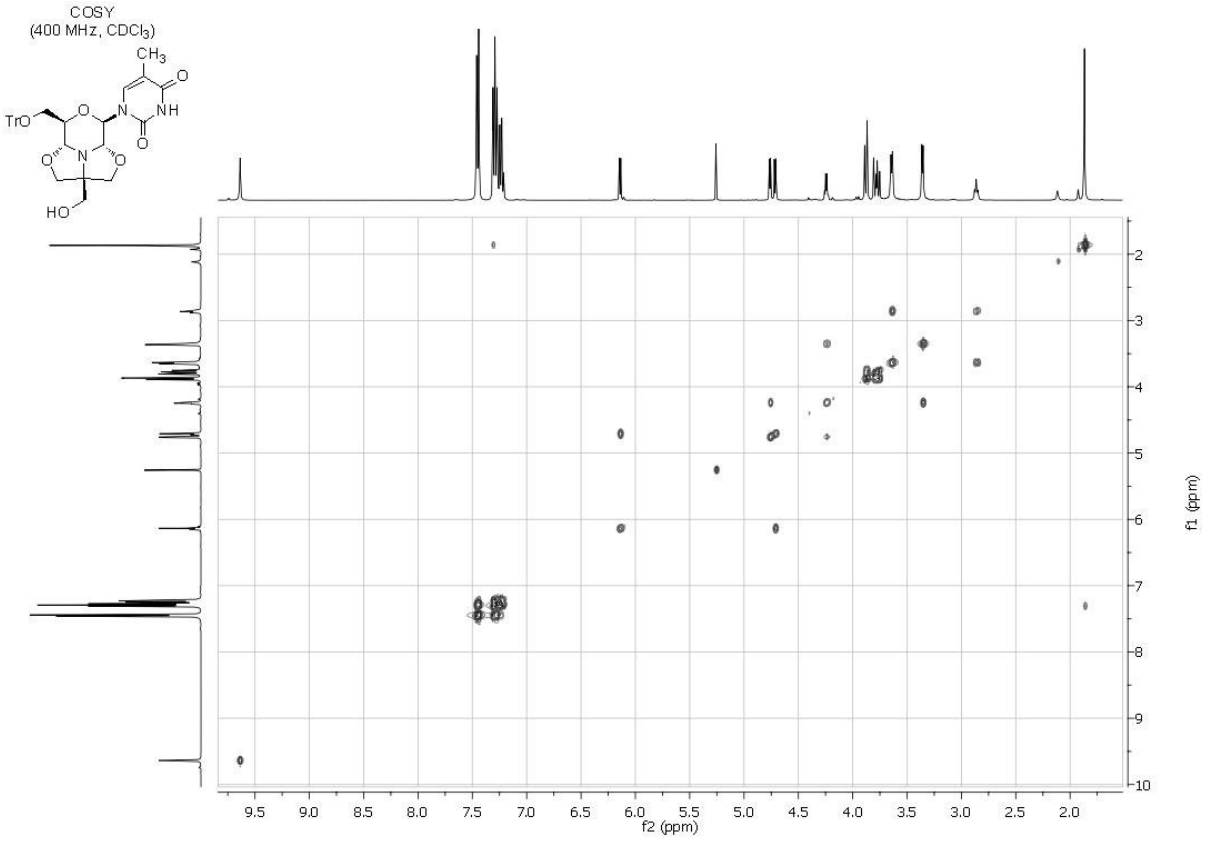


Figure S39. ^{1}H-^{1}H COSY spectrum of compound 7

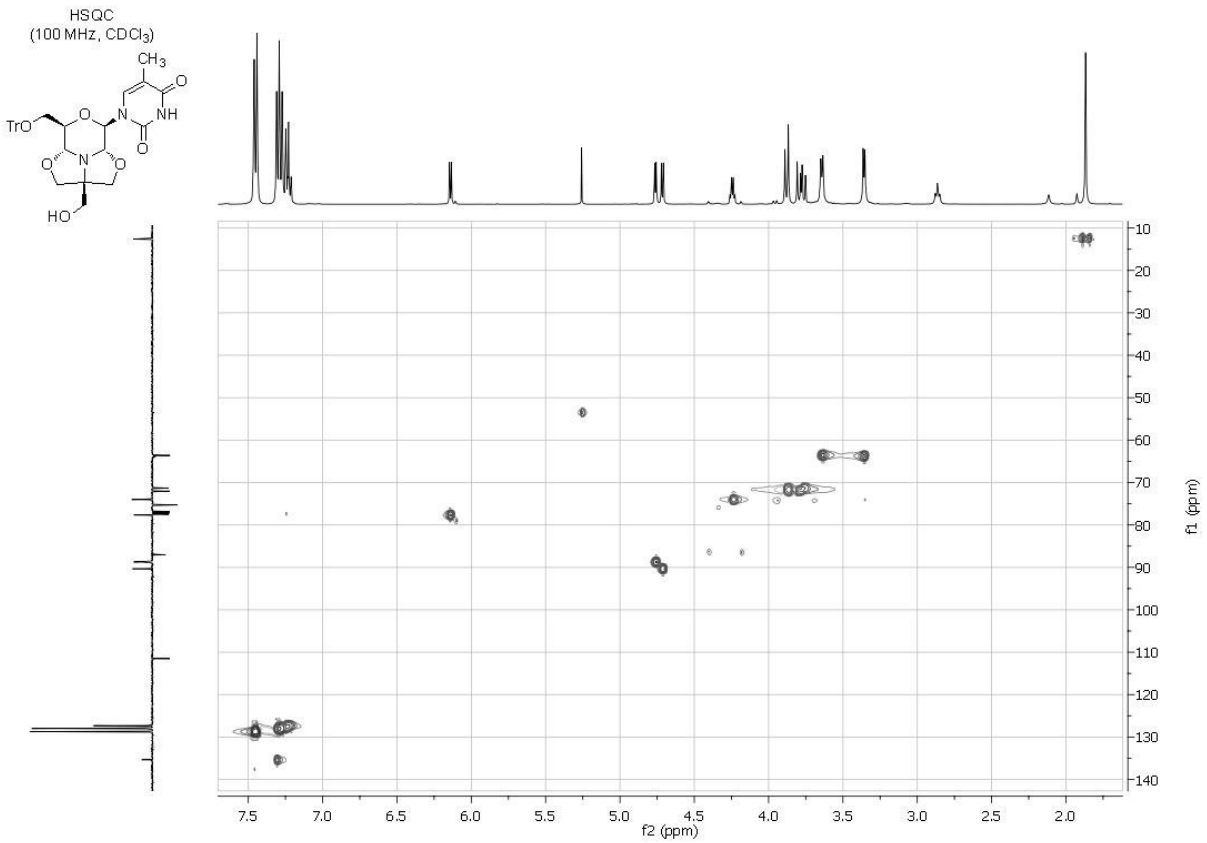


Figure S40. ^{1}H-^{13}C HSQC spectrum of compound 7

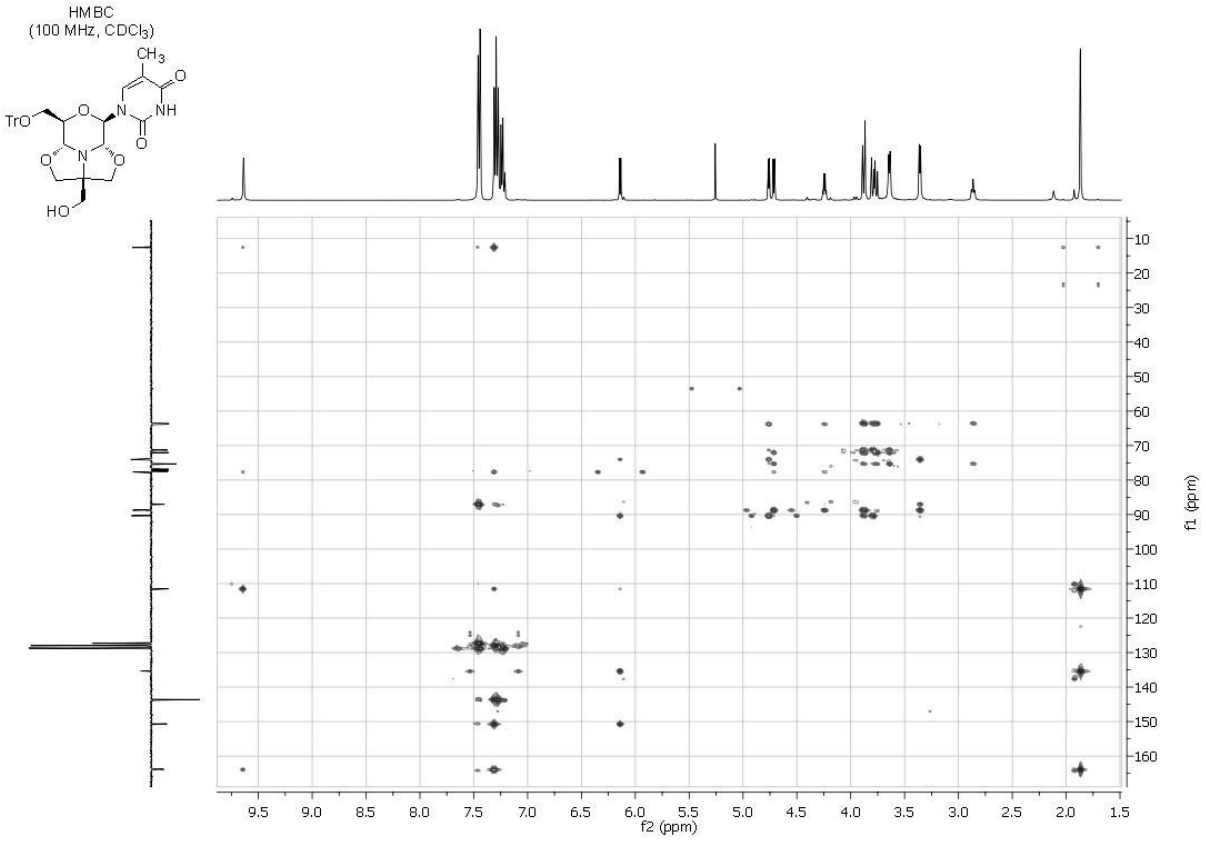


Figure S41. ^{1}H-^{13}C HMBC spectrum of compound 7

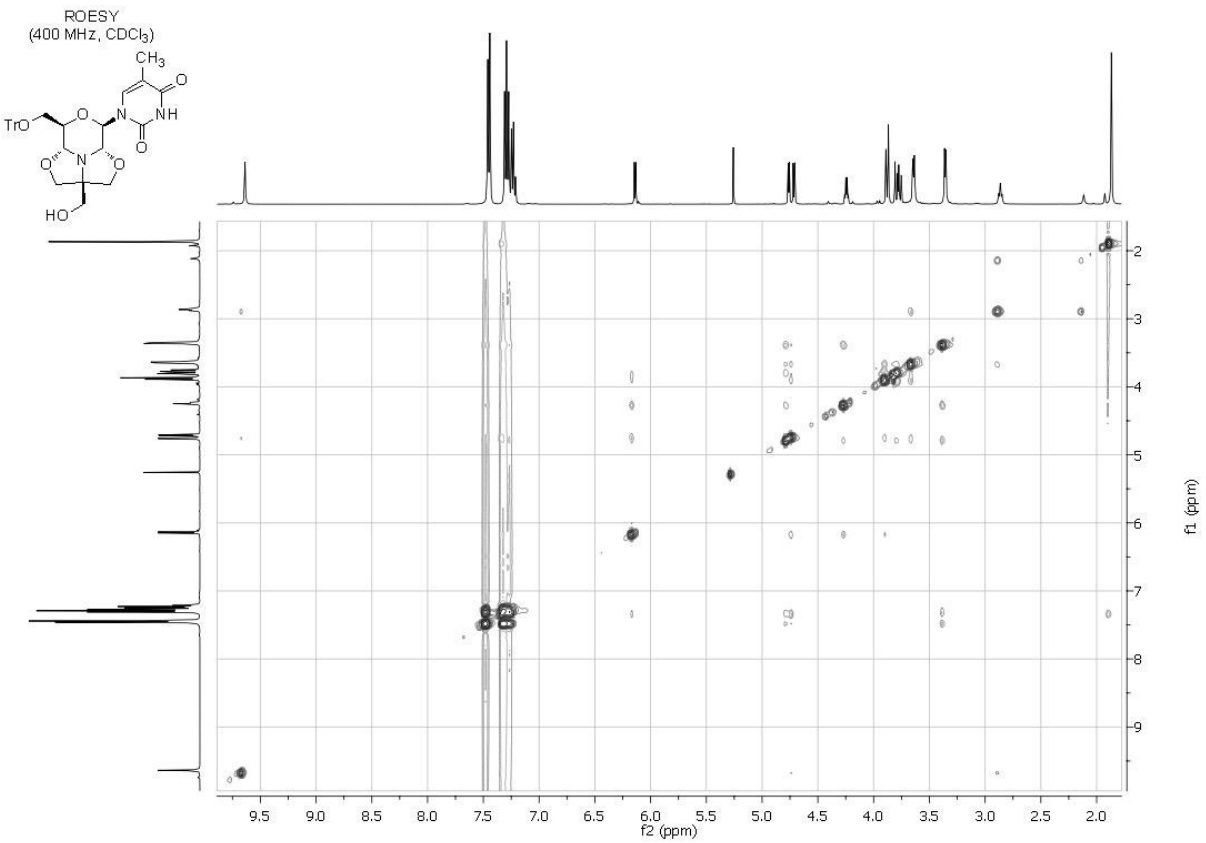


Figure S42. ^{1}H-^{1}H ROESY spectrum of compound 7

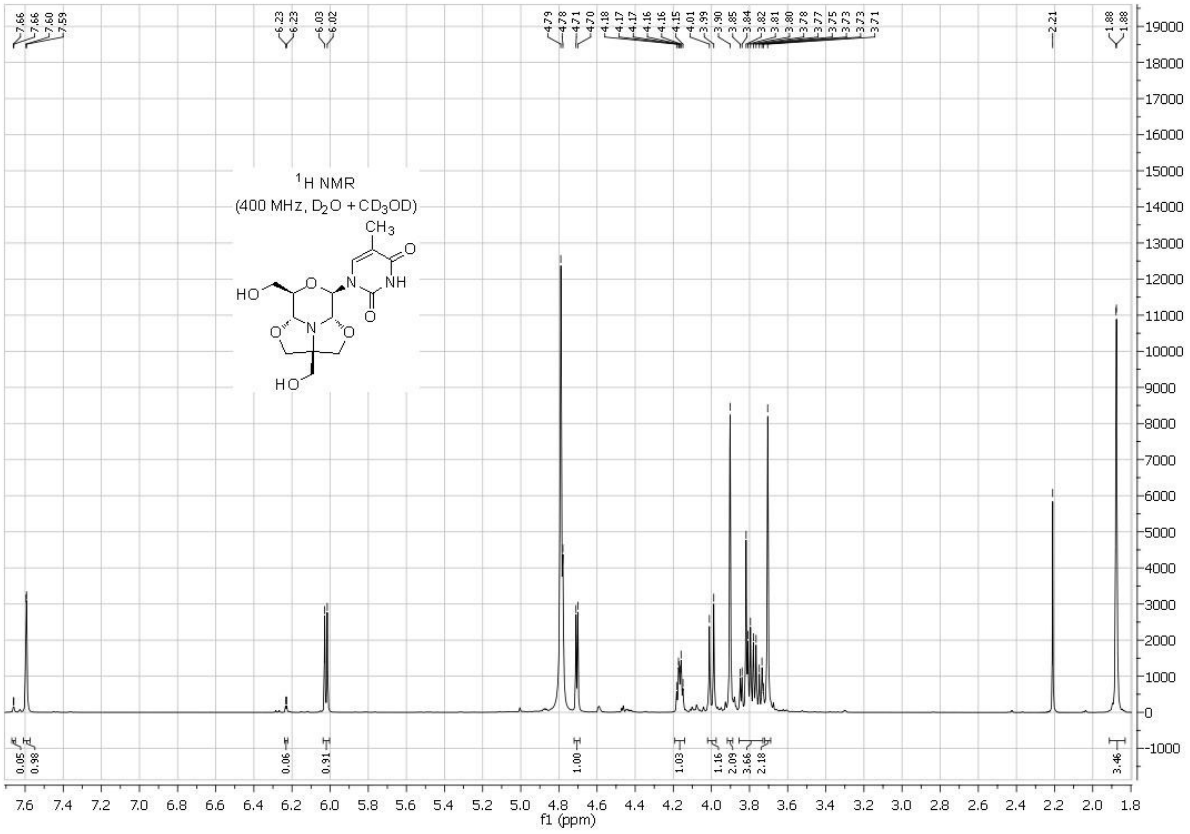


Figure S43. ^{1}H spectrum of compound 8

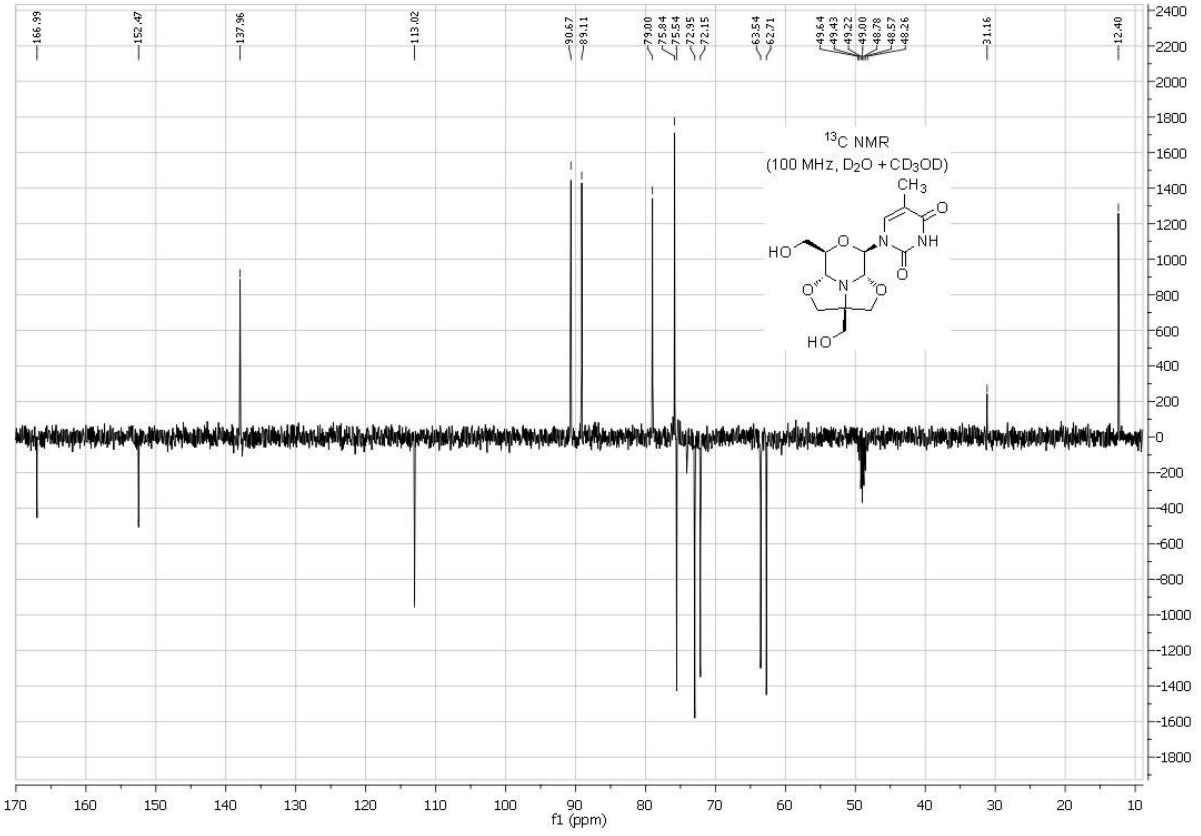


Figure S44. ^{13}C spectrum of compound 8

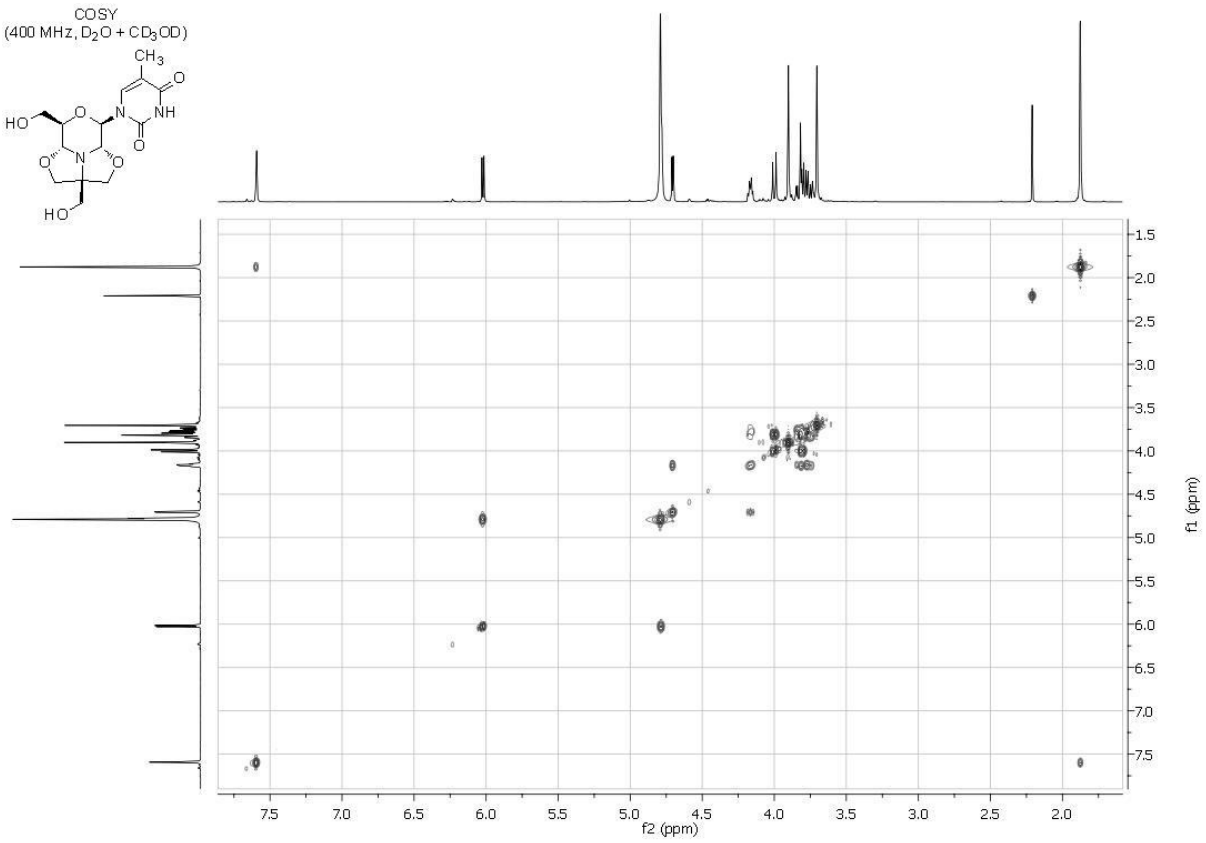


Figure S45. ^{1}H-^{1}H COSY spectrum of compound 8

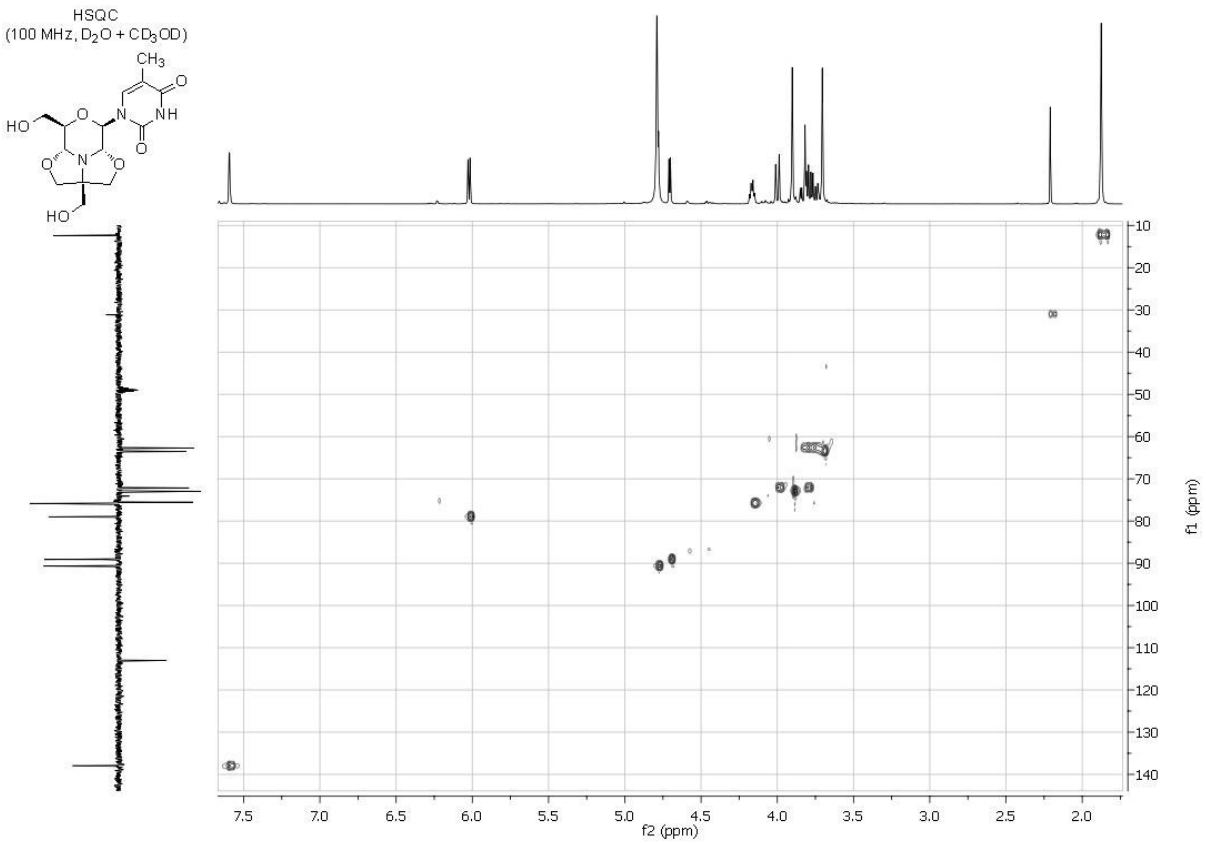


Figure S46. ^{1}H-^{13}C HSQC spectrum of compound 8

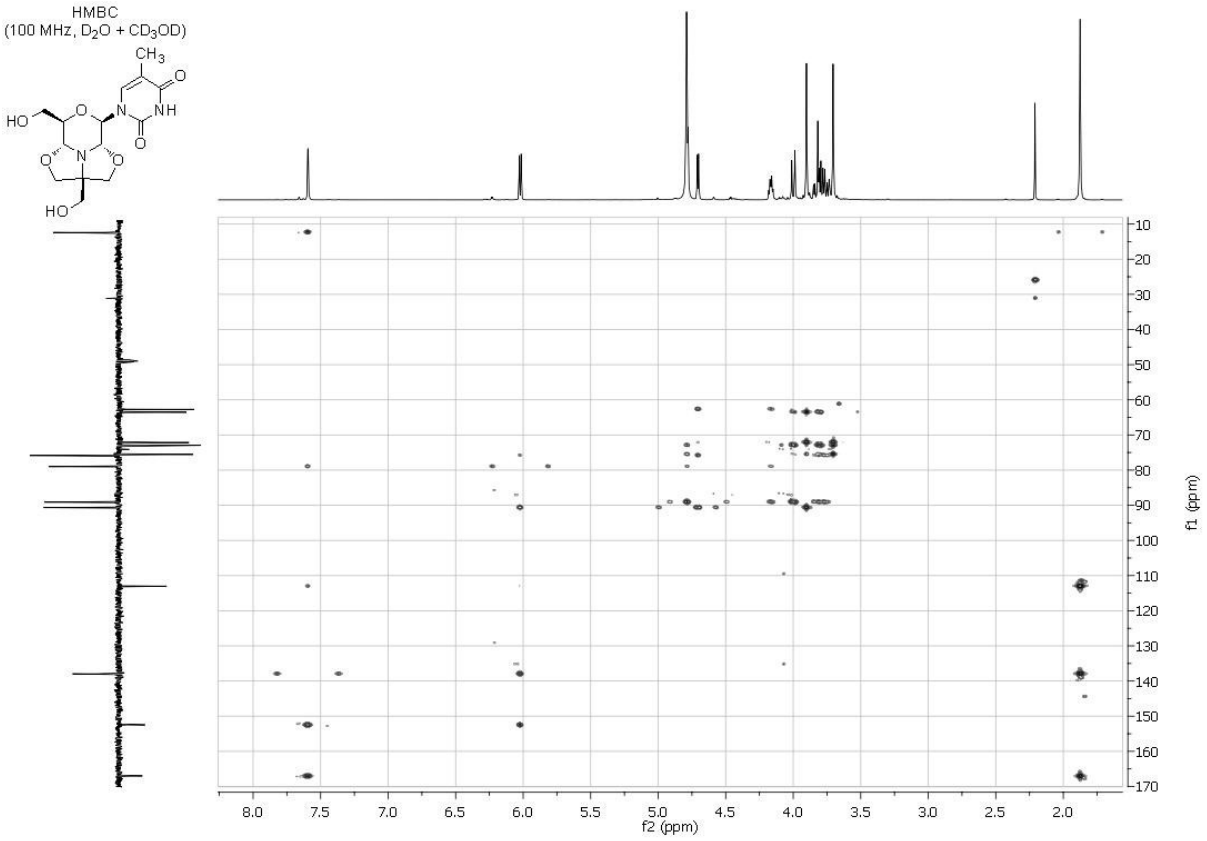


Figure S47. ^{1}H-^{13}C HMBC spectrum of compound 8

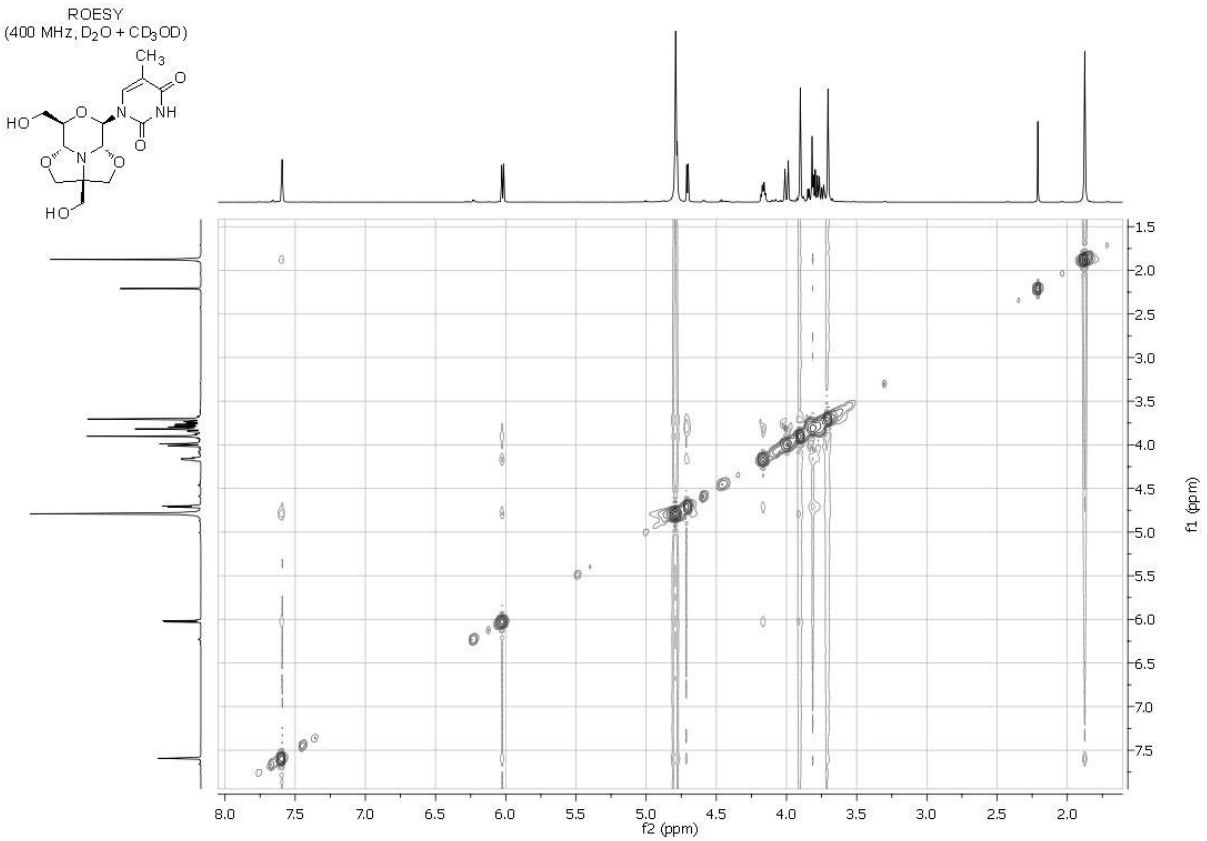


Figure S48. ^{1}H-^{1}H ROESY spectrum of compound 8

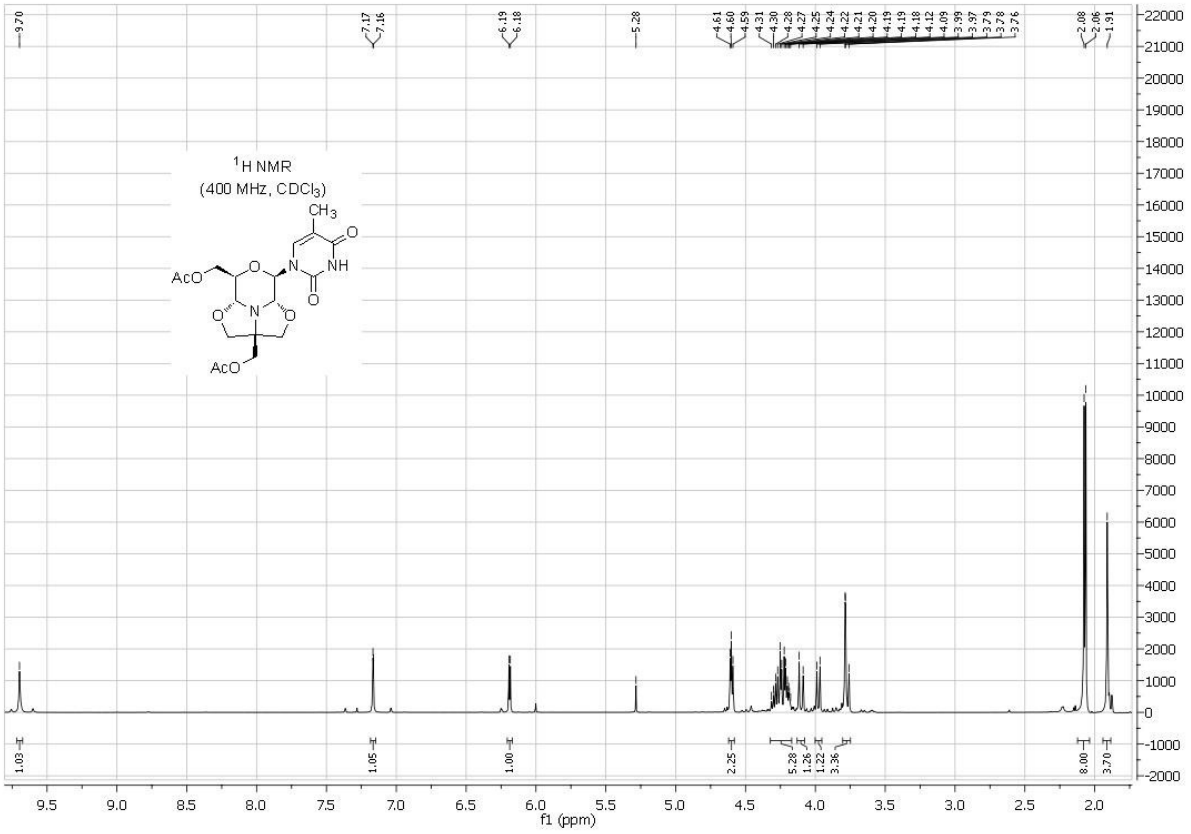


Figure S49. ^{1}H spectrum of compound 9

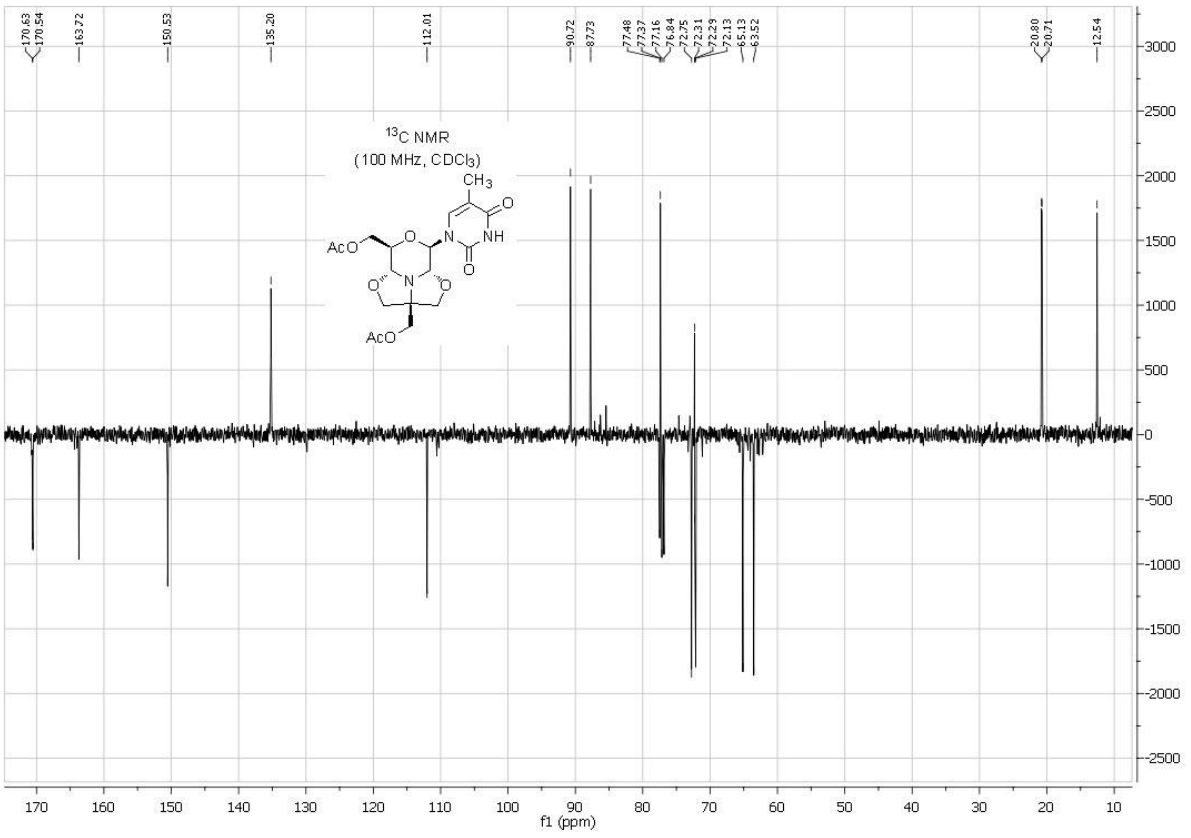


Figure S50. ^{13}C spectrum of compound 9

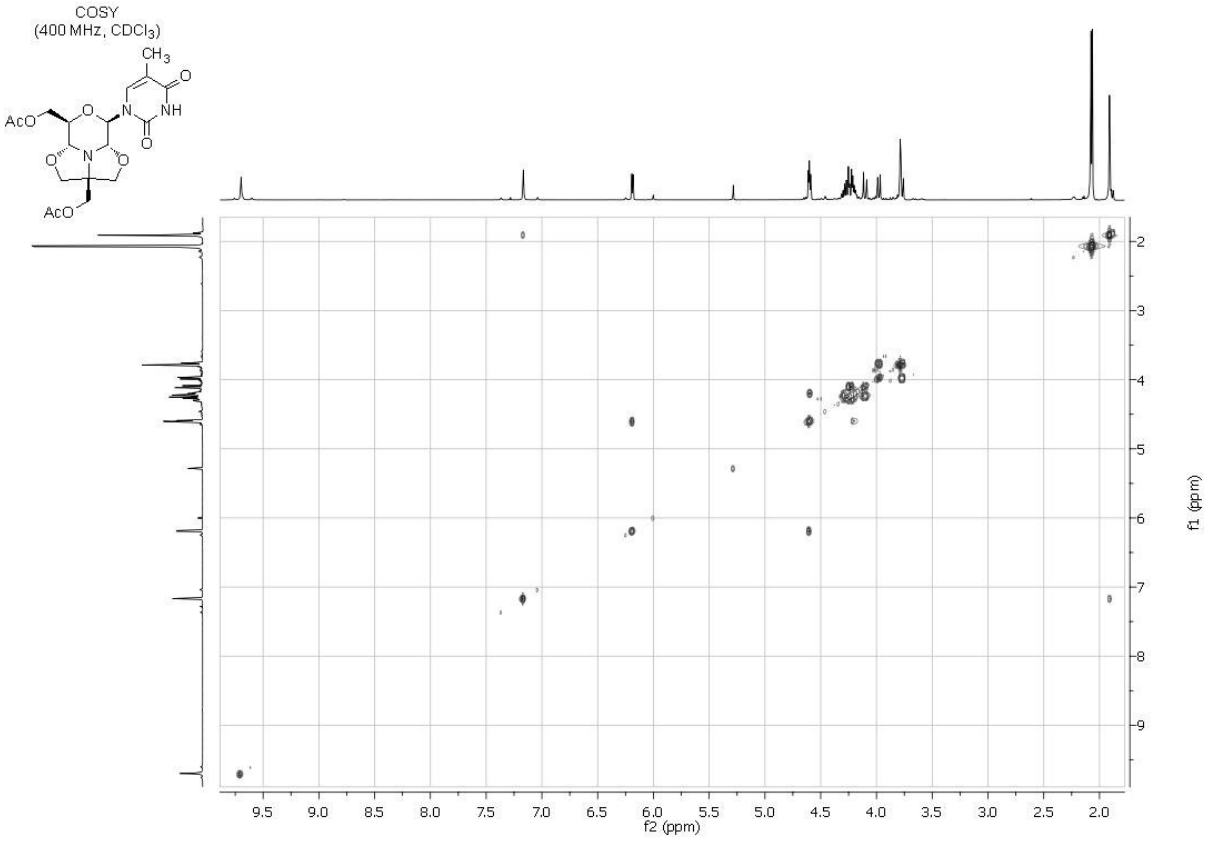


Figure S51. ^{1}H-^{1}H COSY spectrum of compound 9

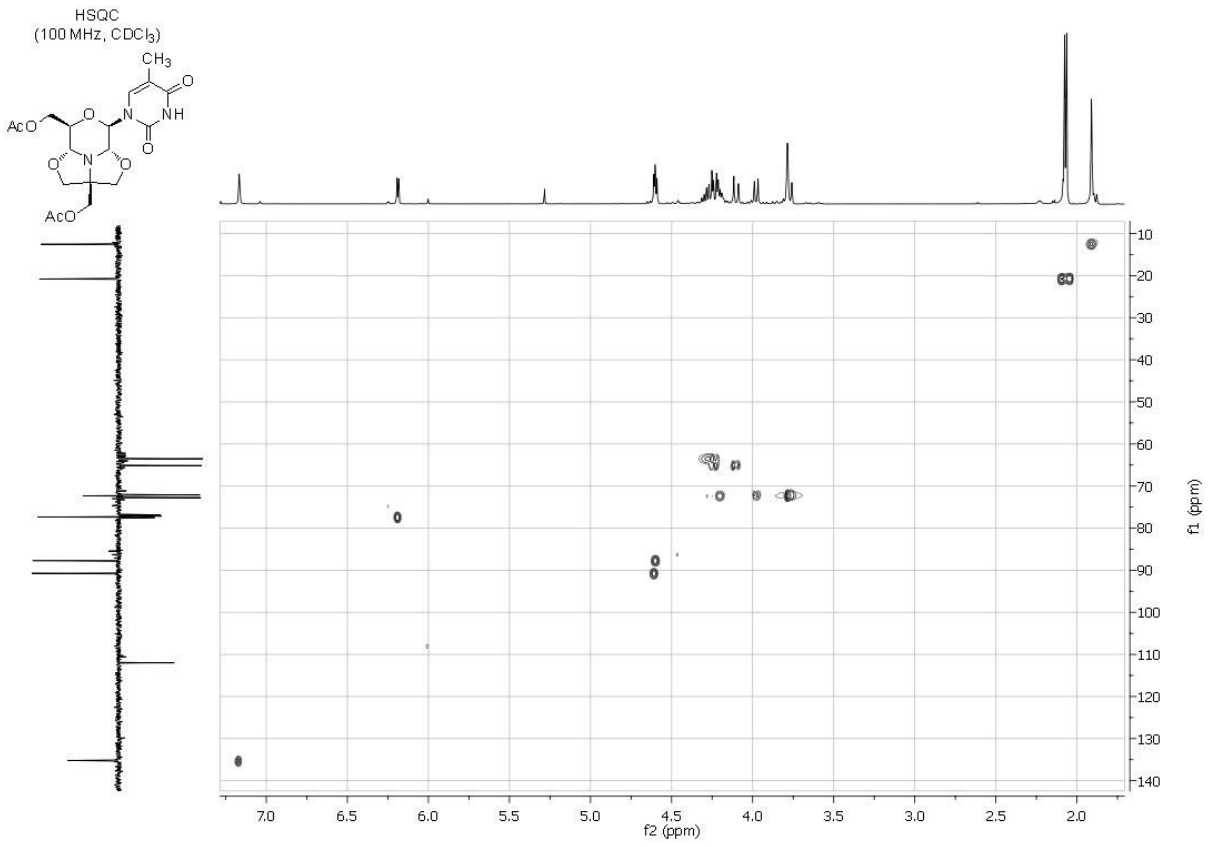


Figure S52. ^{1}H-^{13}C HSQC spectrum of compound 9

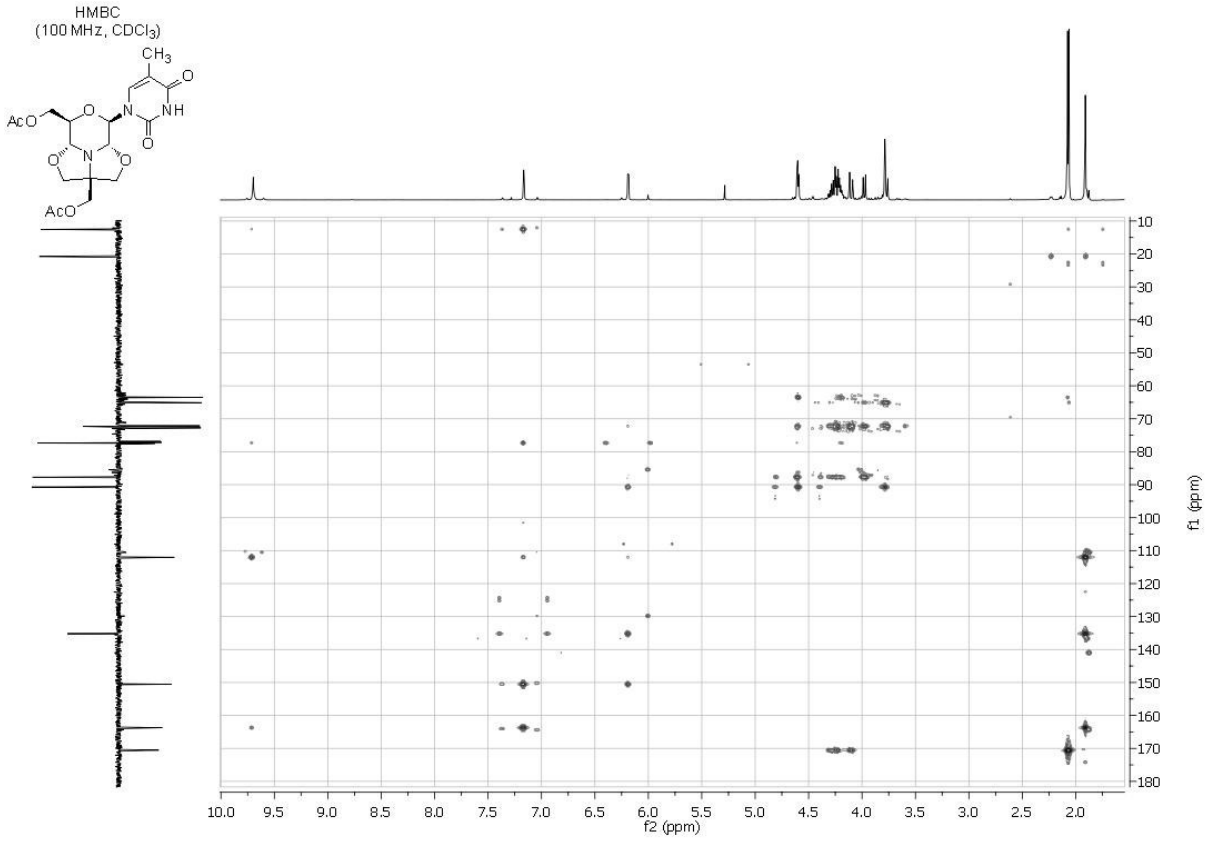


Figure S53. ^{1}H-^{13}C HMBC spectrum of compound 9

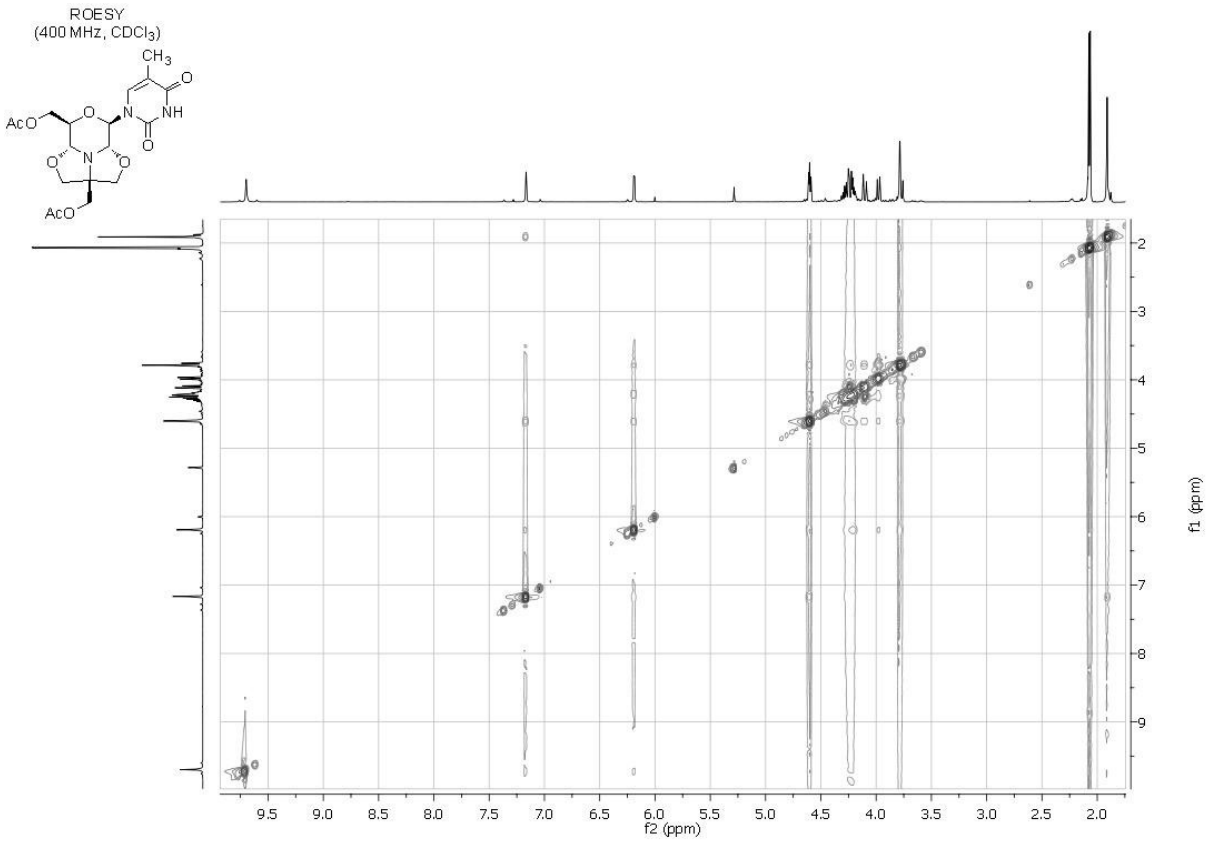


Figure S54. ^{1}H-^{1}H ROESY spectrum of compound 9

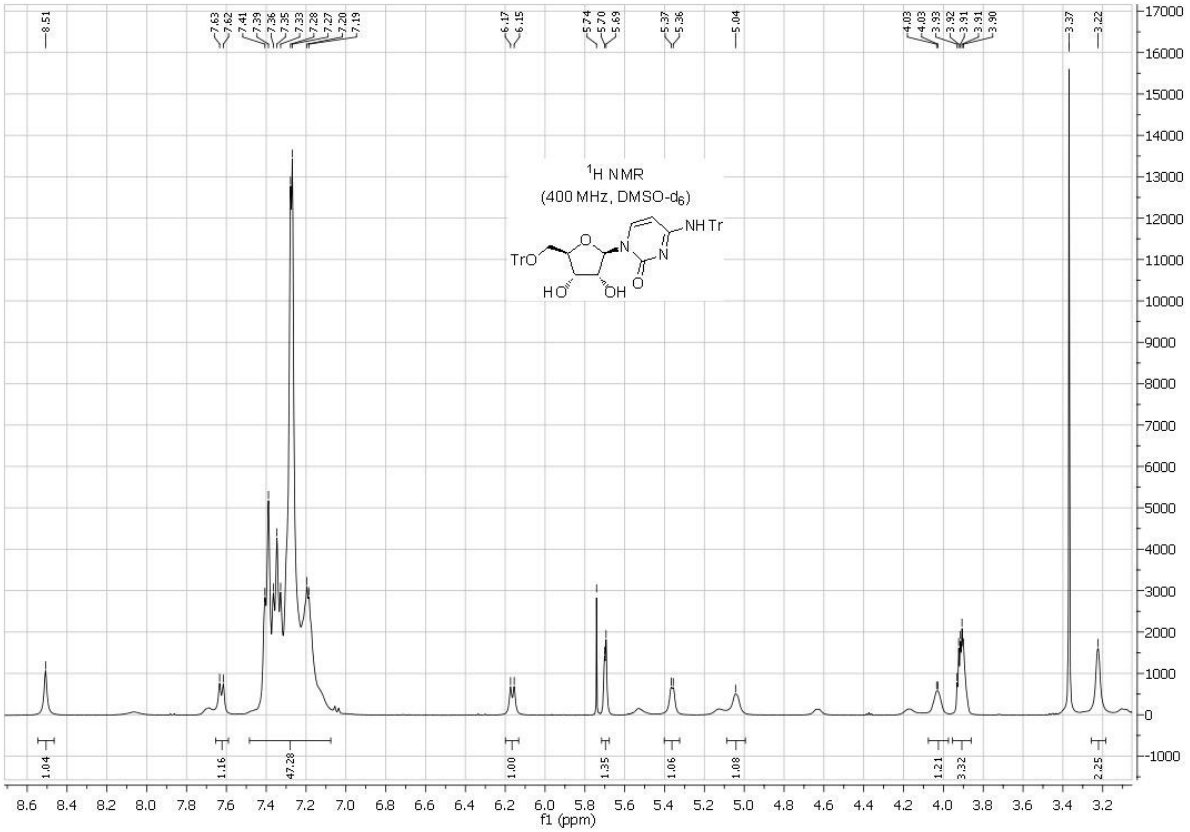


Figure S55. ^{1}H spectrum of compound 11a

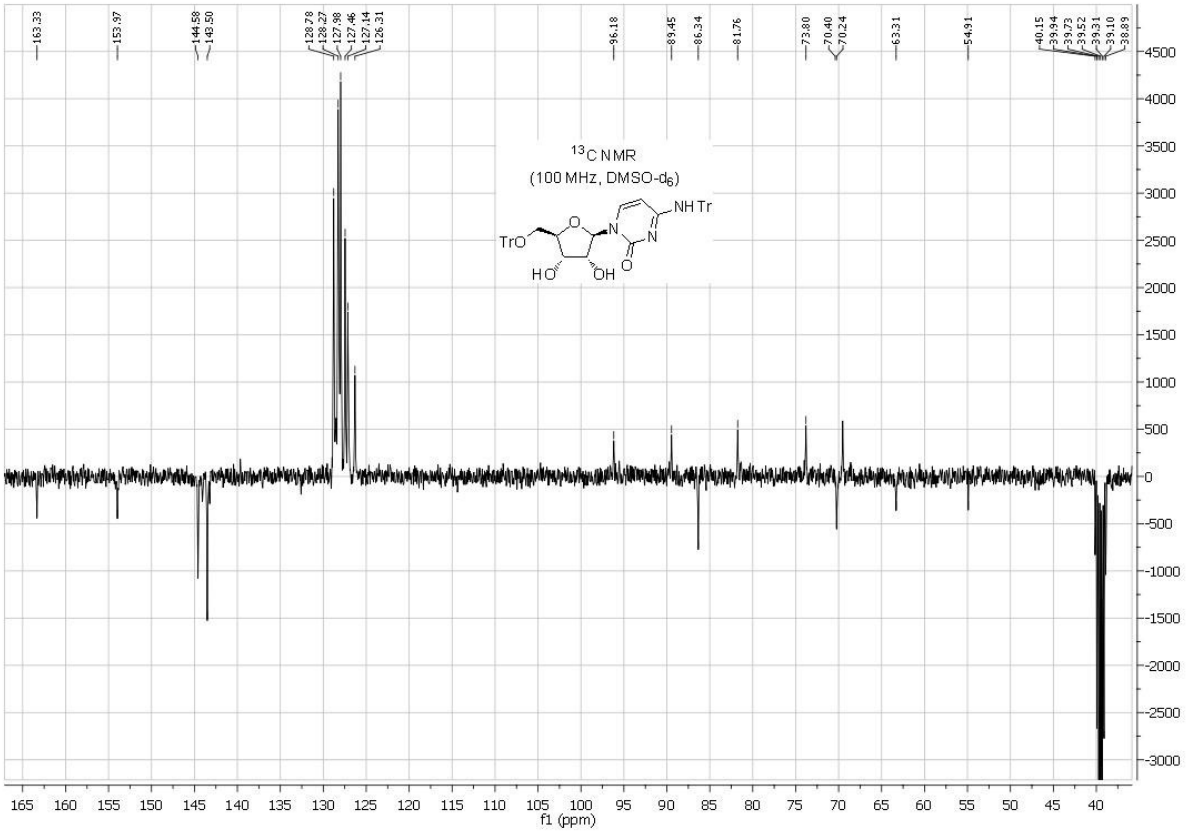


Figure S56. ^{13}C spectrum of compound 11a

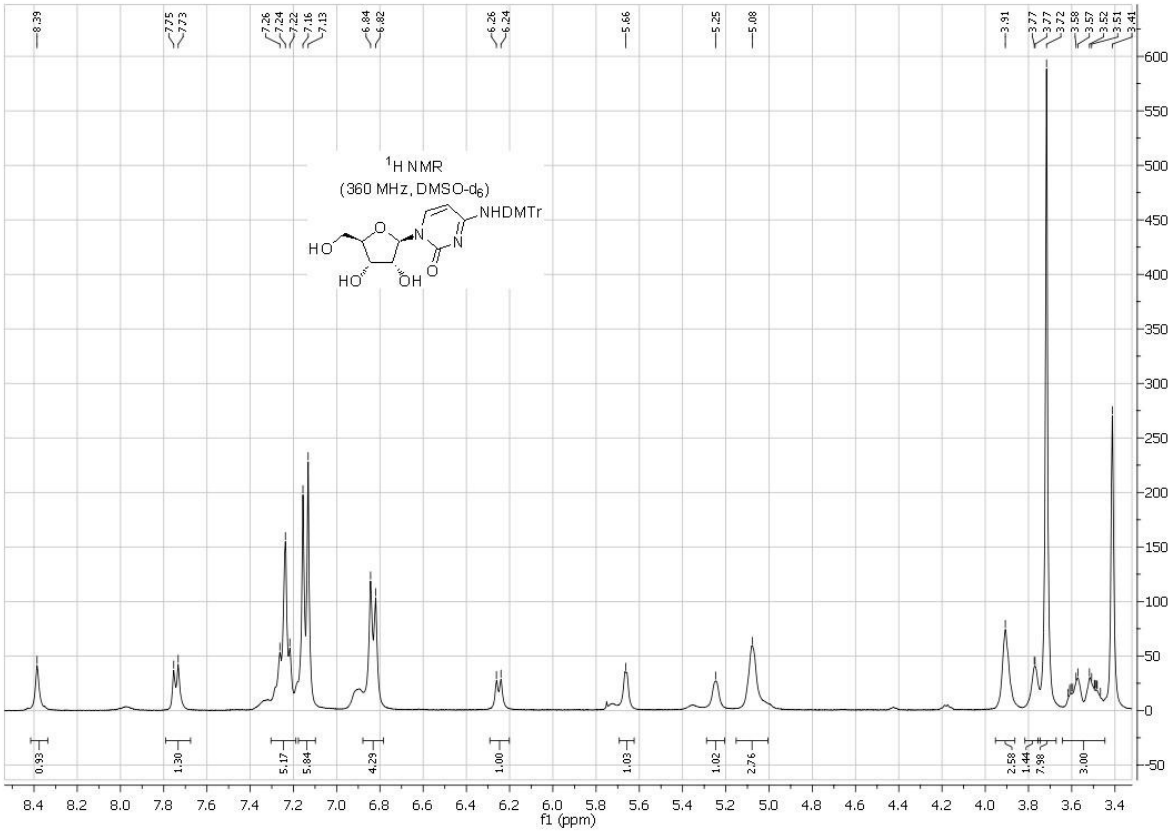


Figure S57. ^{1}H spectrum of compound 11b

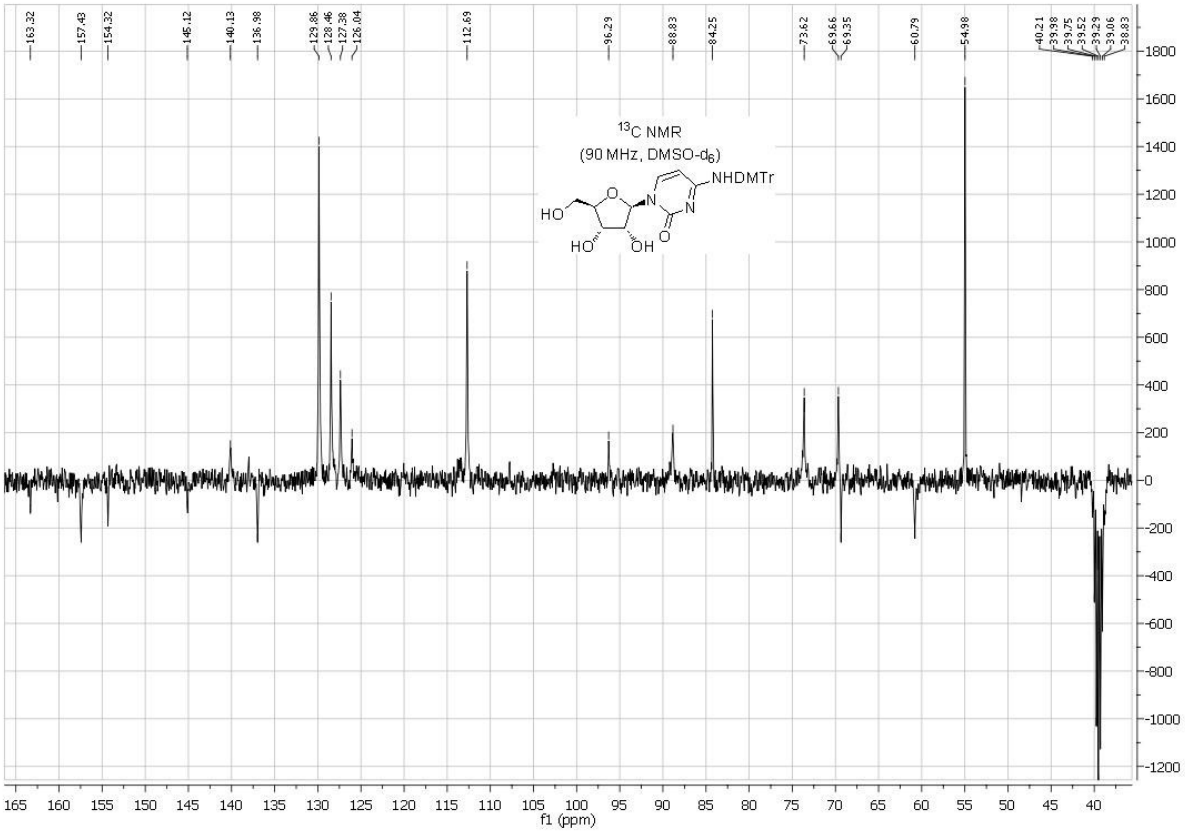


Figure S58. ^{13}C spectrum of compound 11b

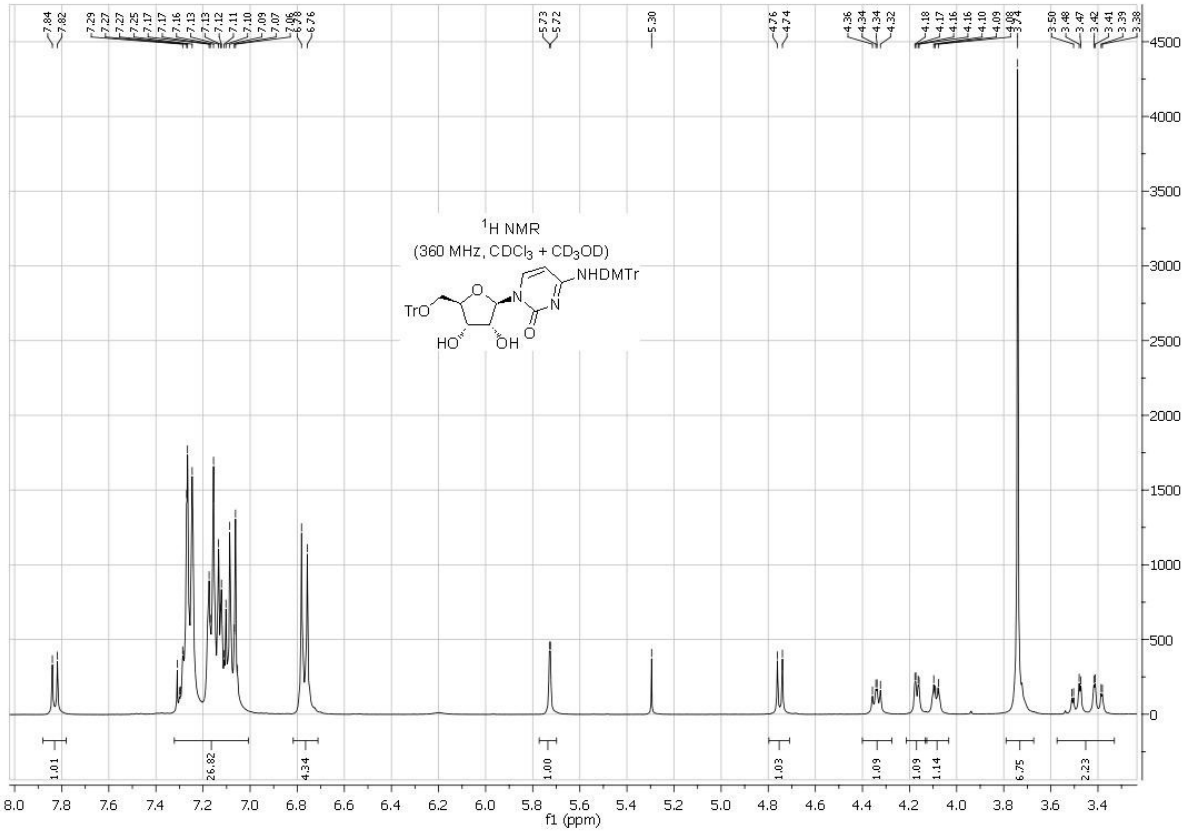


Figure S59. ^{1}H spectrum of compound 12b

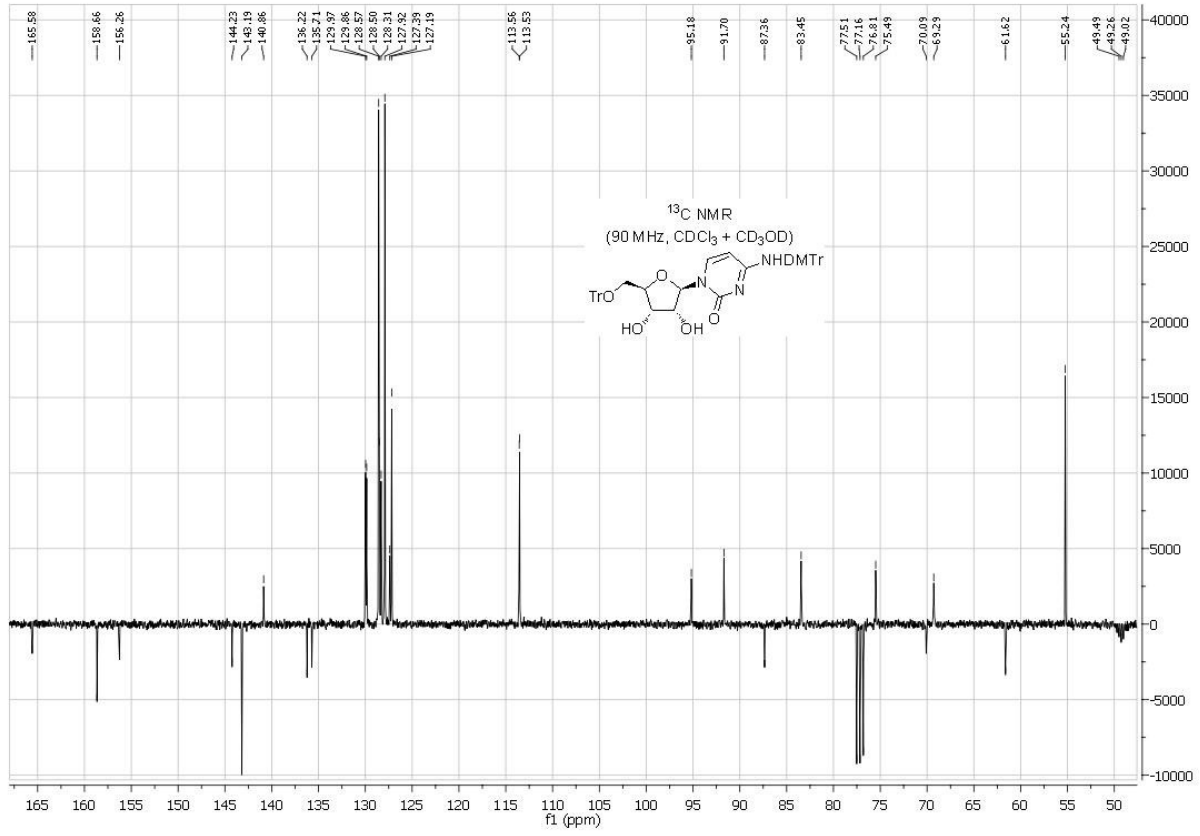


Figure S60. ^{13}C spectrum of compound 12b

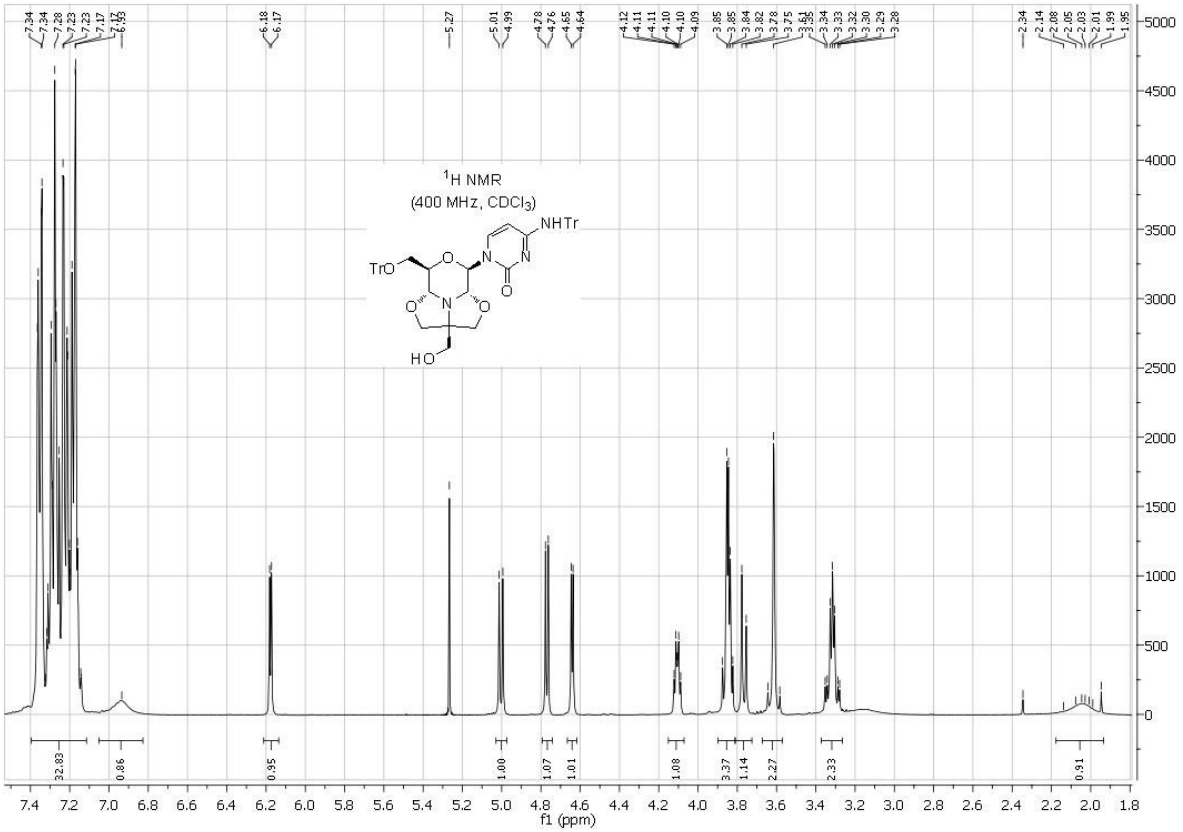


Figure S61. ^{1}H spectrum of compound 13a

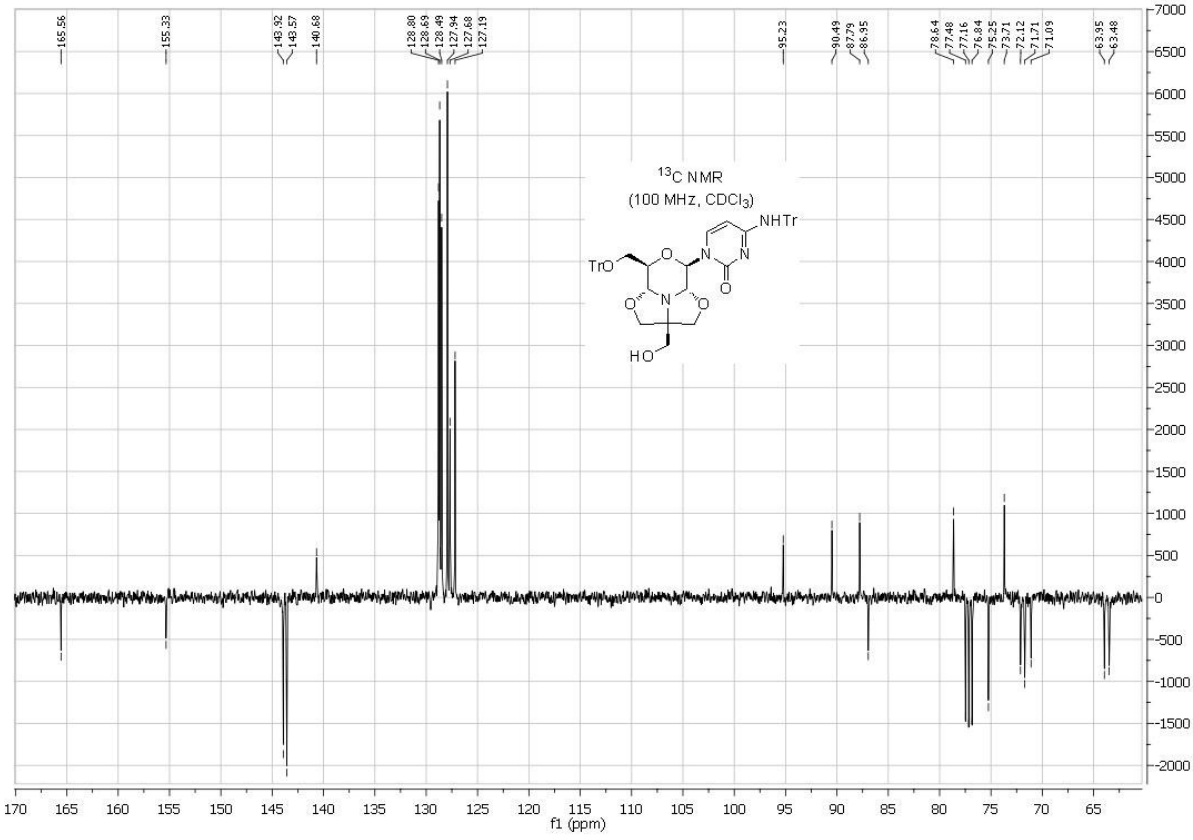


Figure S62. ^{13}C spectrum of compound 13a

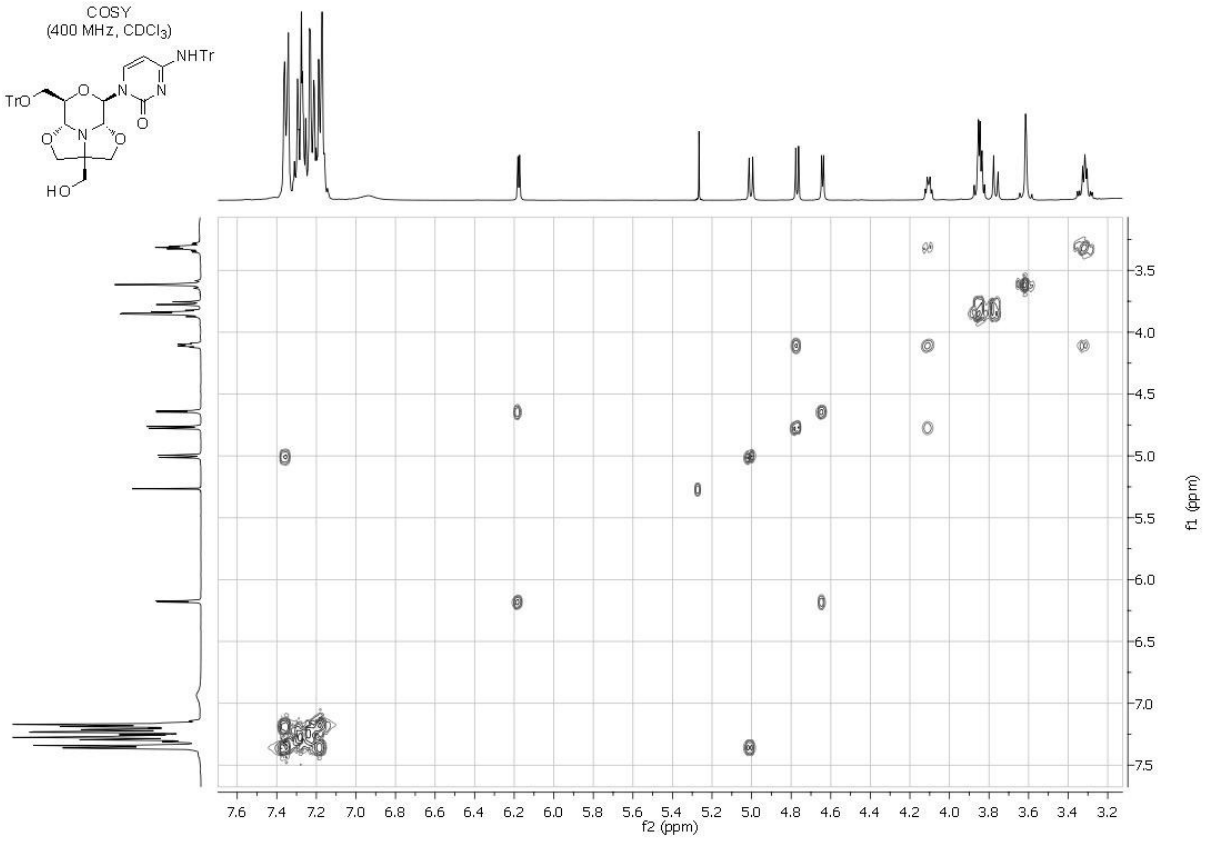


Figure S63. ^{1}H-^{1}H COSY spectrum of compound 13a

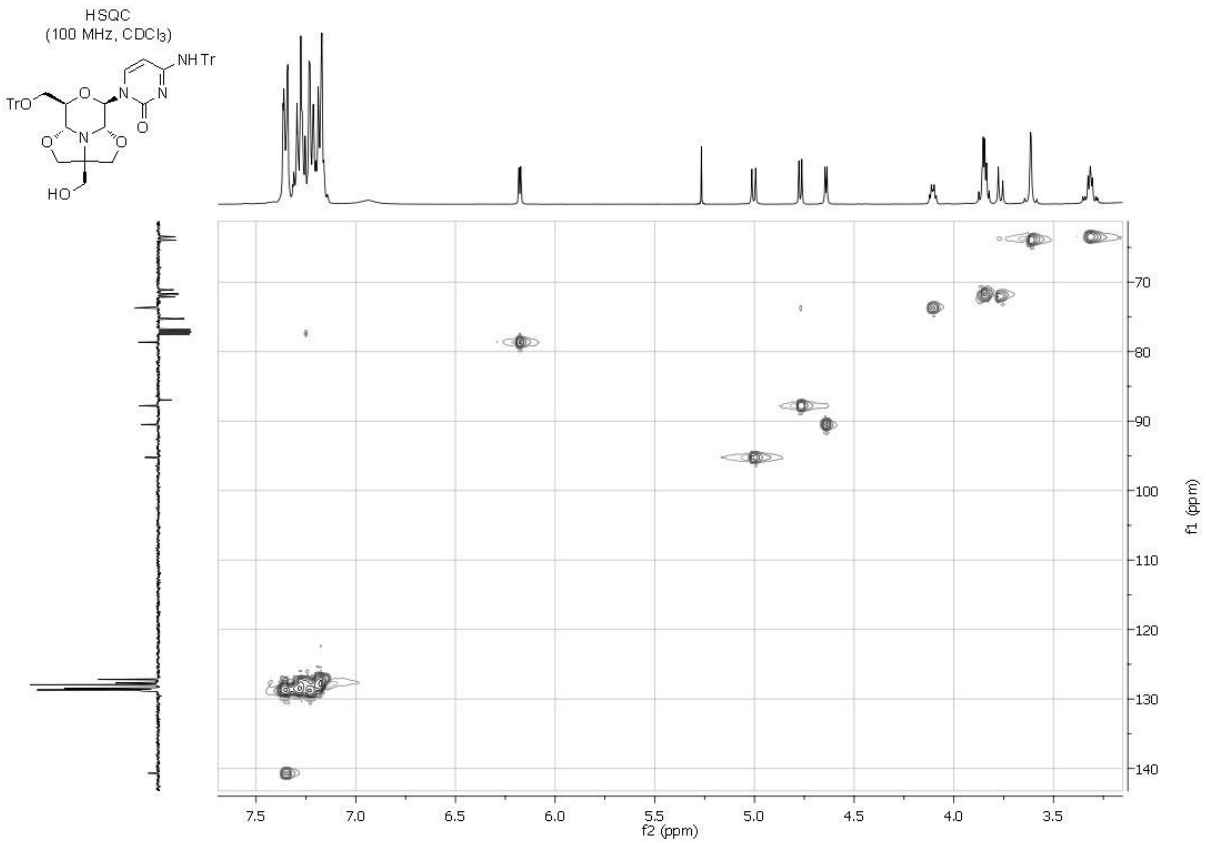


Figure S64. ^{1}H-^{13}C HSQC spectrum of compound 13a

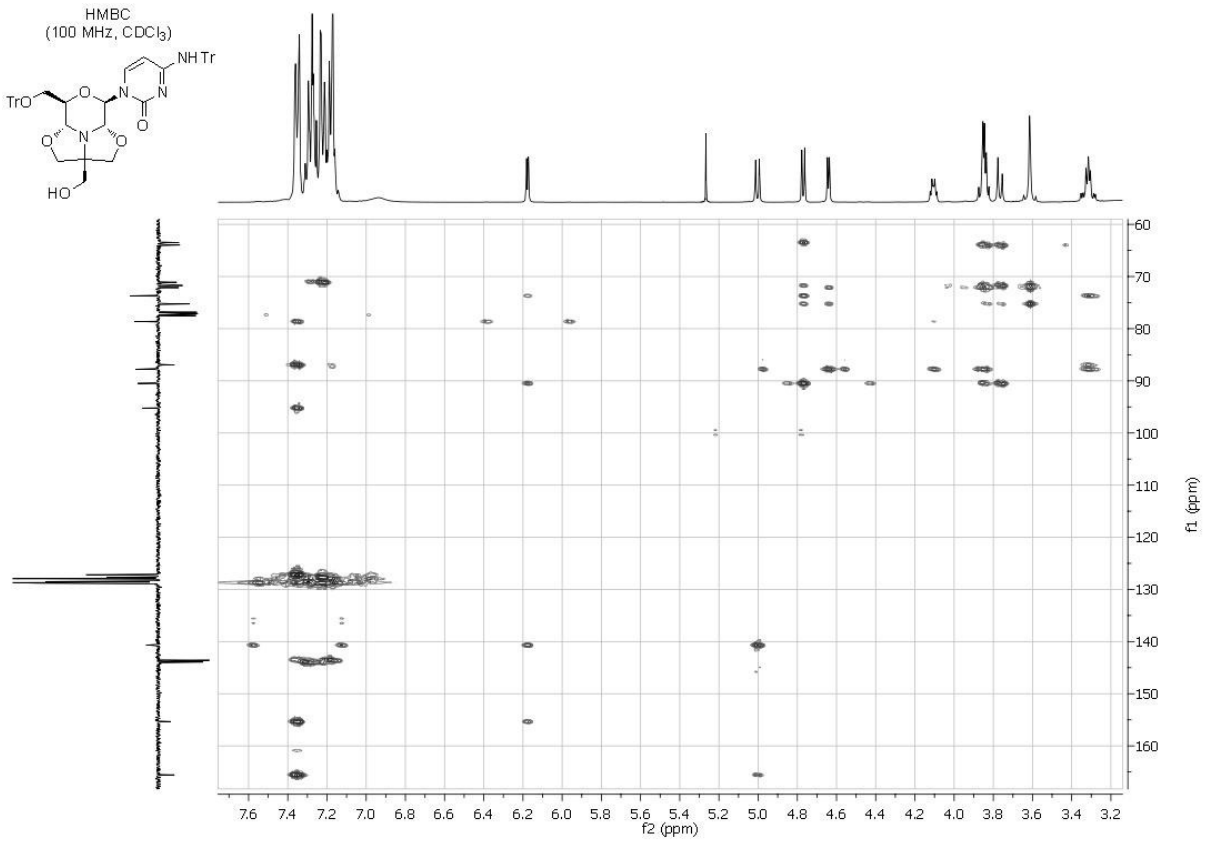


Figure S65. ^{1}H-^{13}C HMBC spectrum of compound 13a

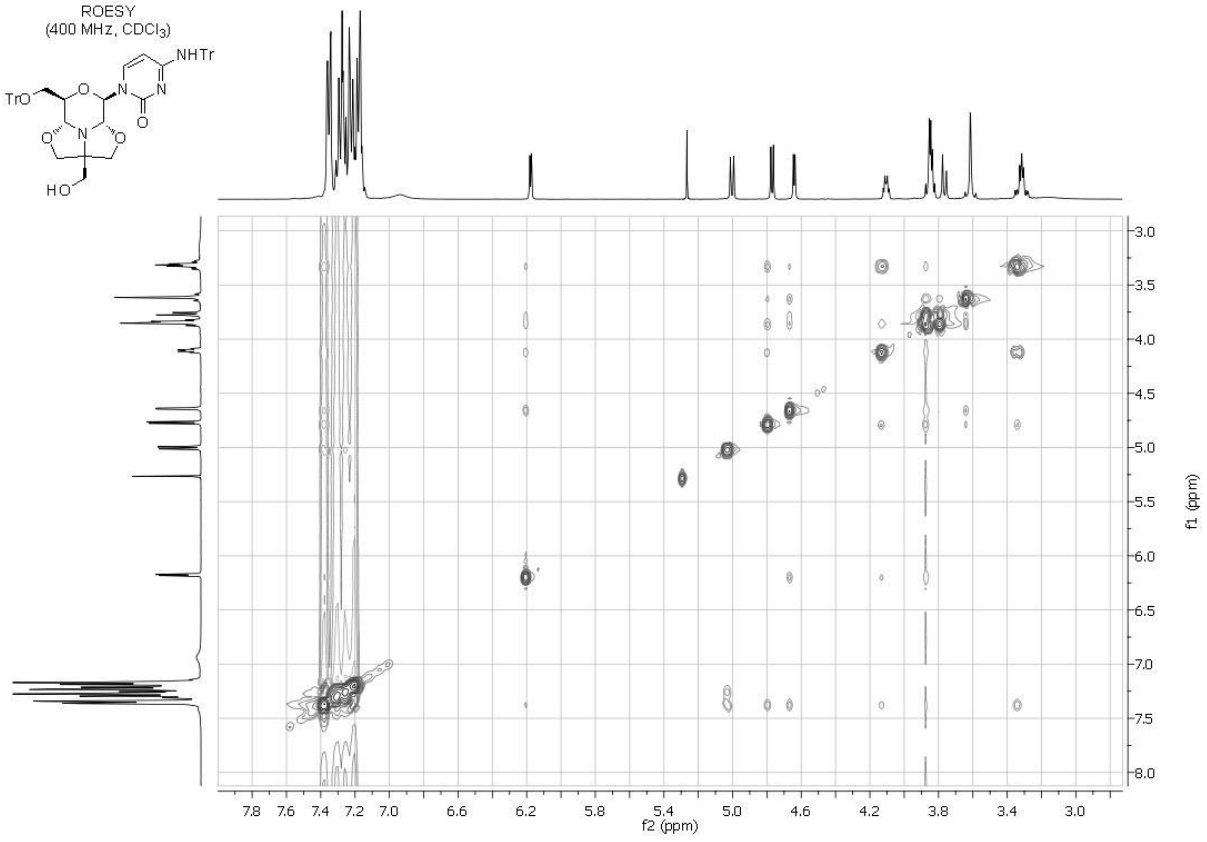


Figure S66. ^{1}H-^{1}H ROESY spectrum of compound 13a

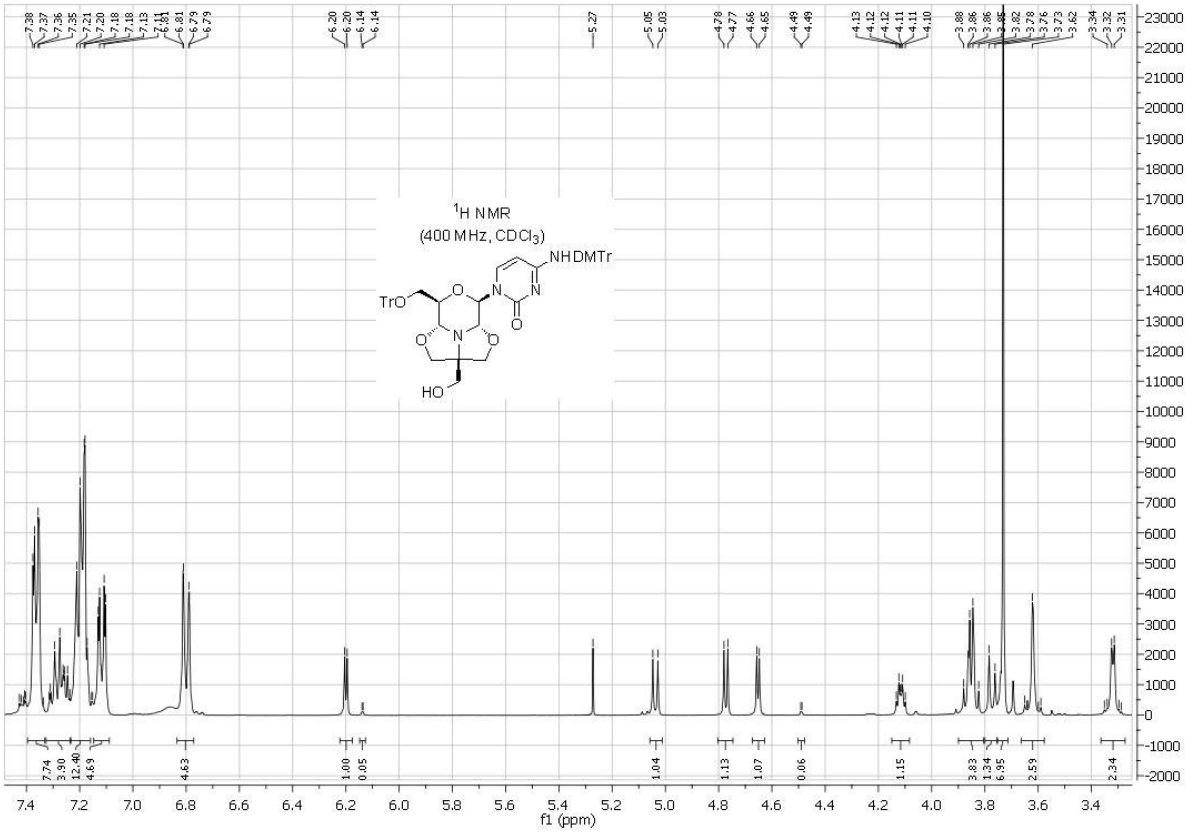


Figure S67. ^{1}H spectrum of compound 13b

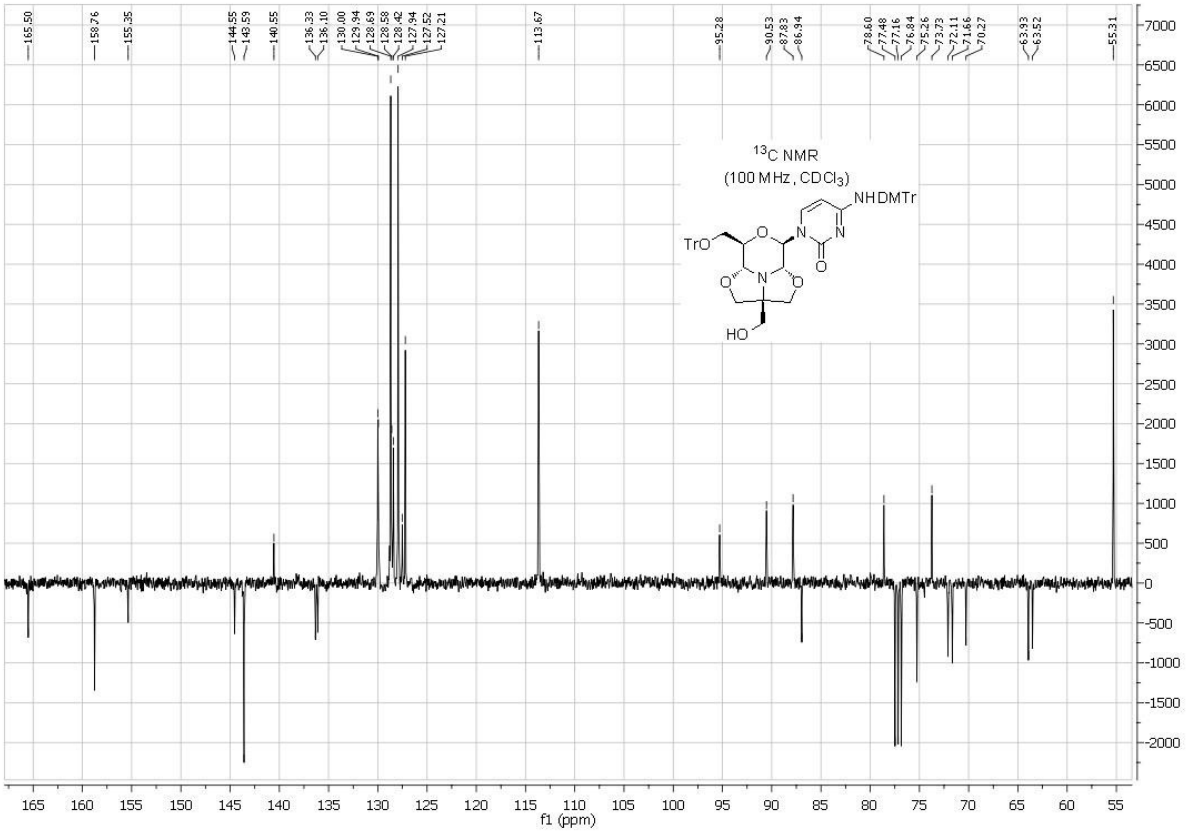


Figure S68. ^{13}C spectrum of compound 13b

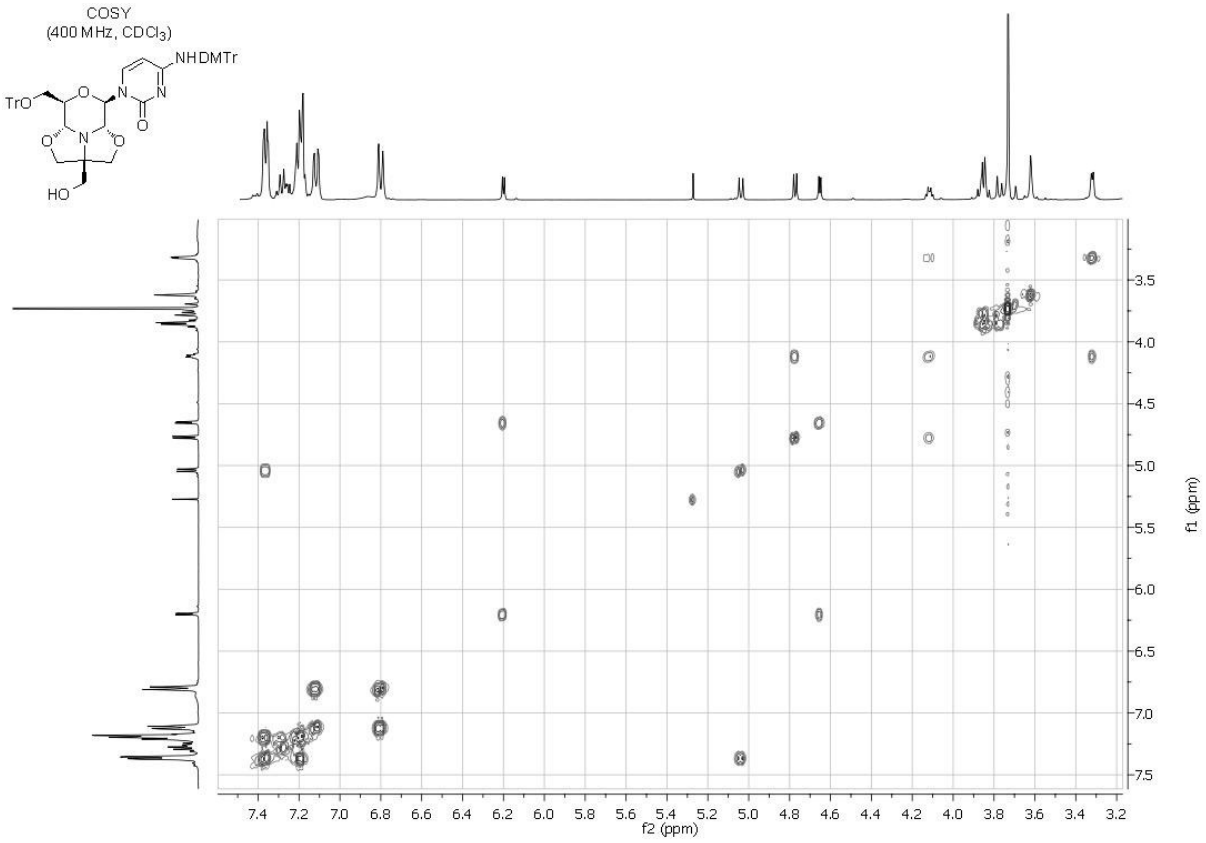


Figure S69. ^{1}H-^{1}H COSY spectrum of compound 13b

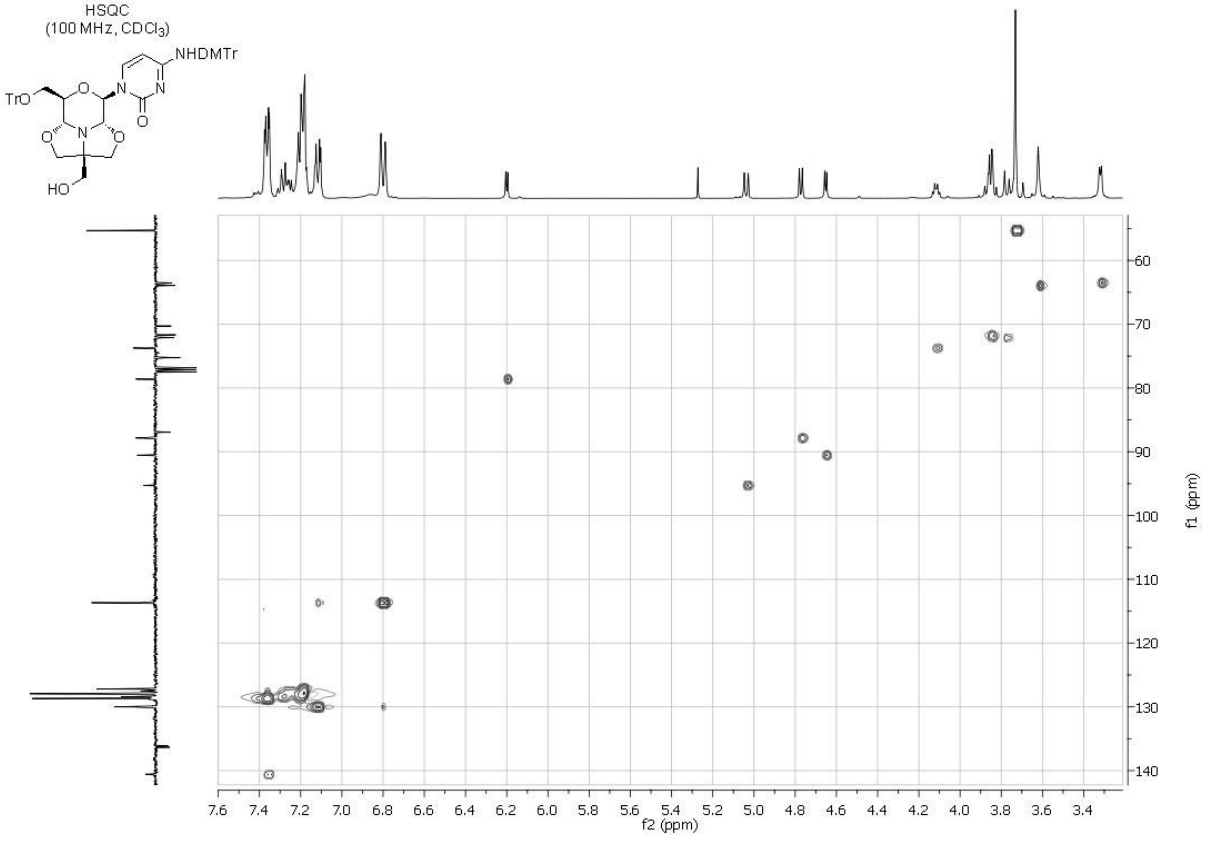


Figure S70. ^{1}H-^{13}C HSQC spectrum of compound 13b

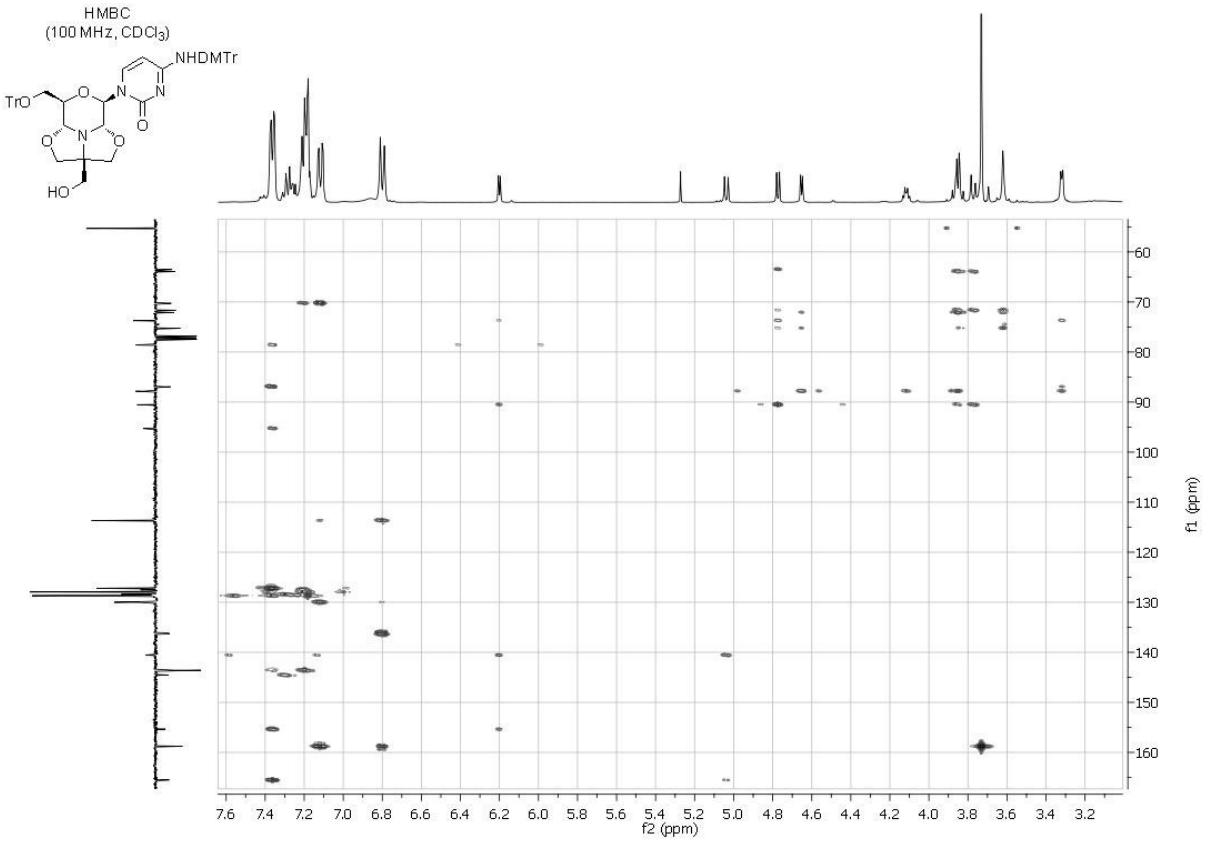


Figure S71. ^{1}H-^{13}C HMBC spectrum of compound 13b

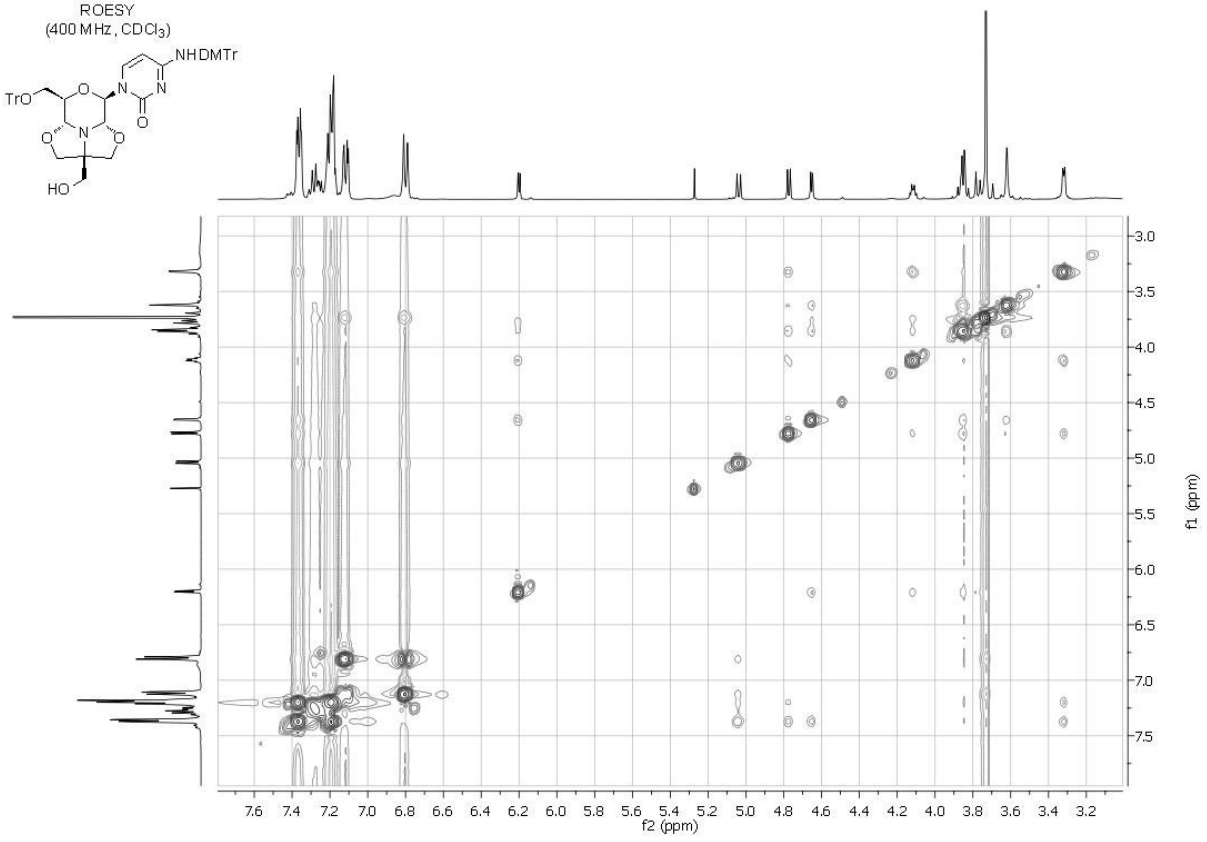


Figure S72. ^{1}H-^{1}H ROESY spectrum of compound 13b

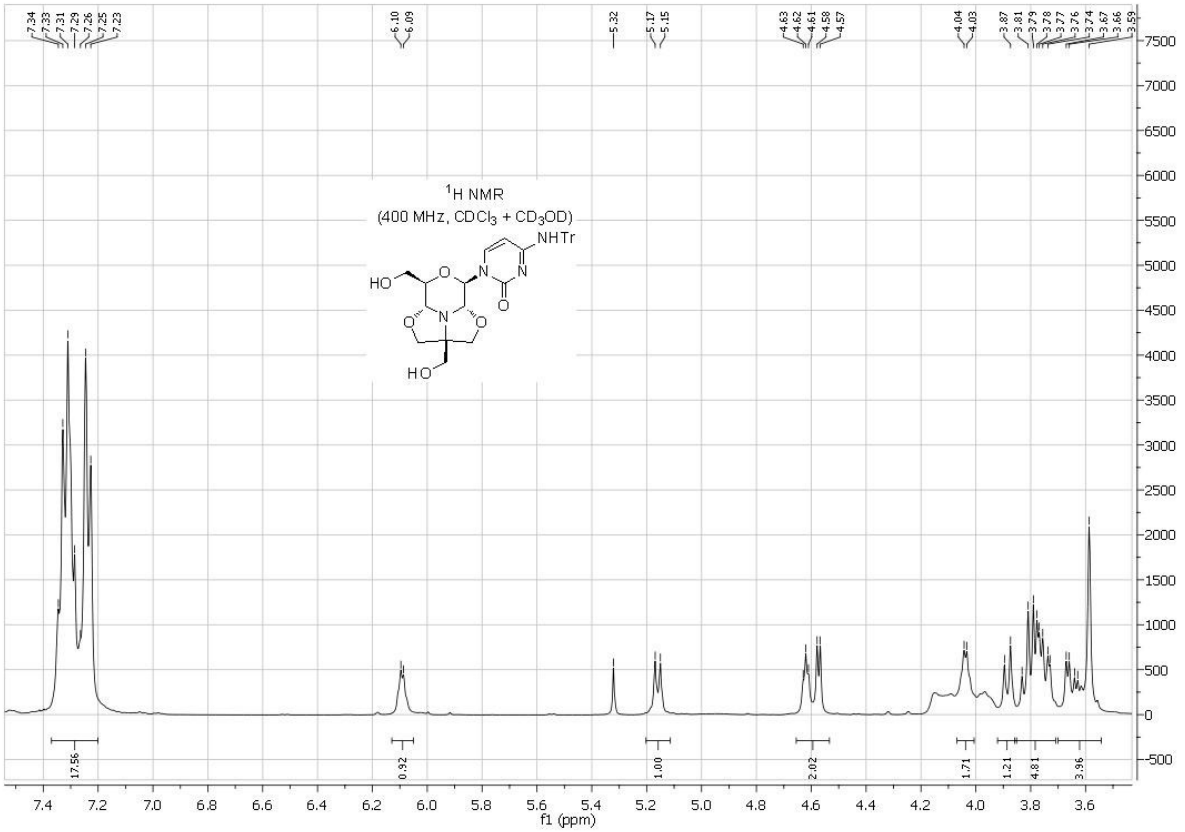


Figure S73. ^{1}H spectrum of compound 14a

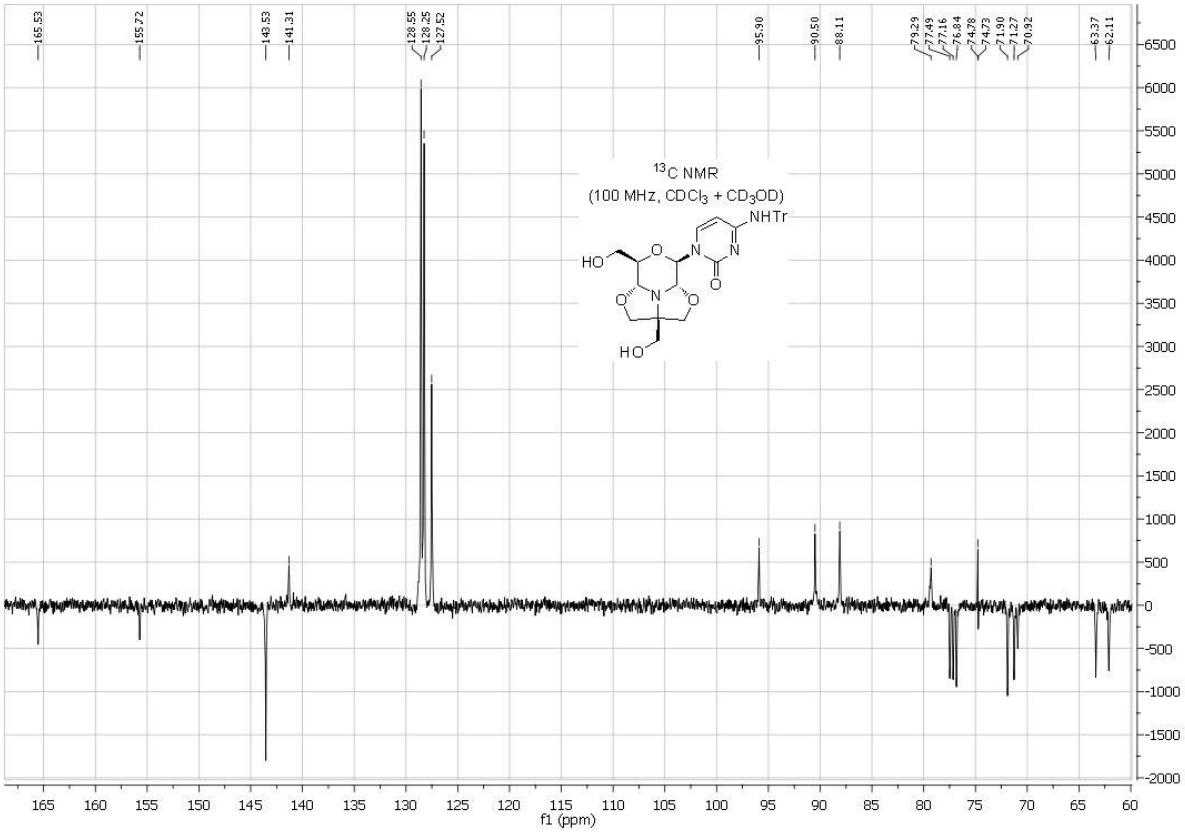


Figure S74. ^{13}C spectrum of compound 14a

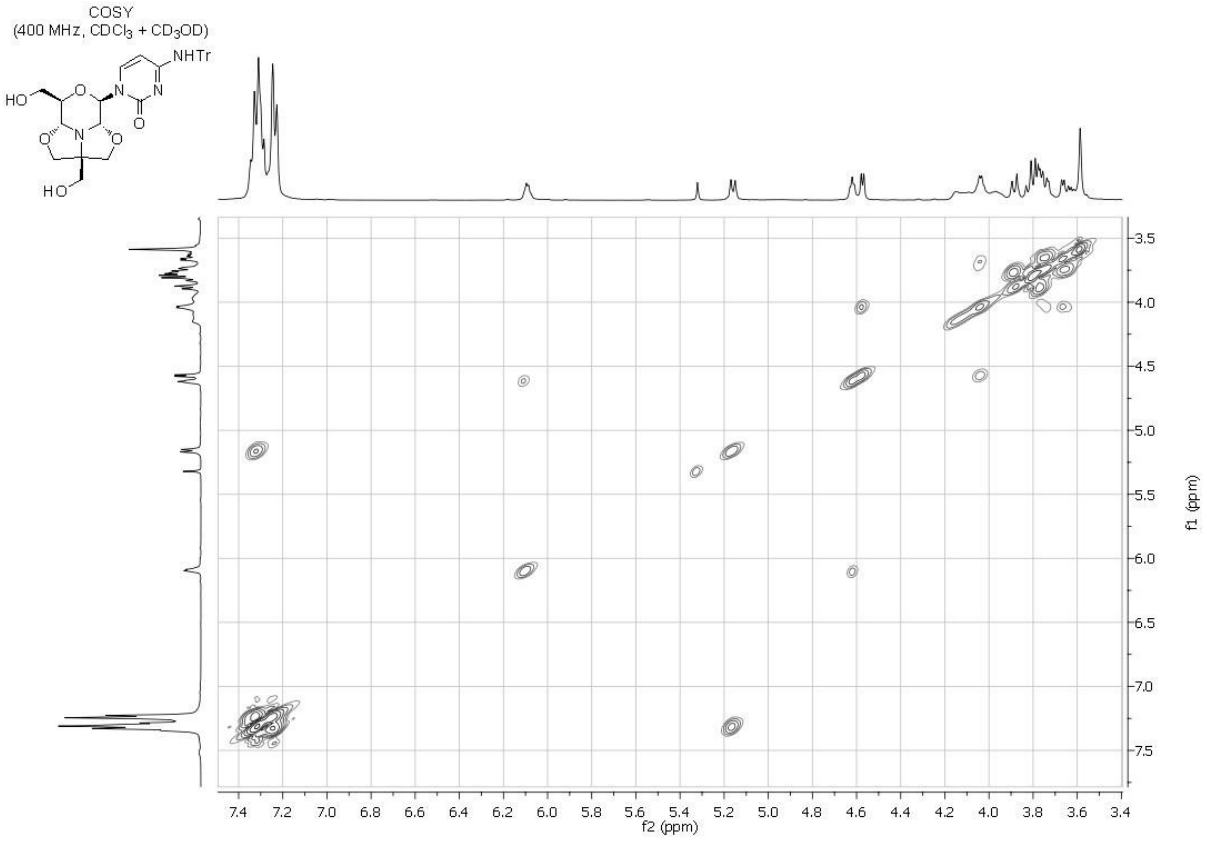


Figure S75. ^{1}H-^{1}H COSY spectrum of compound 14a

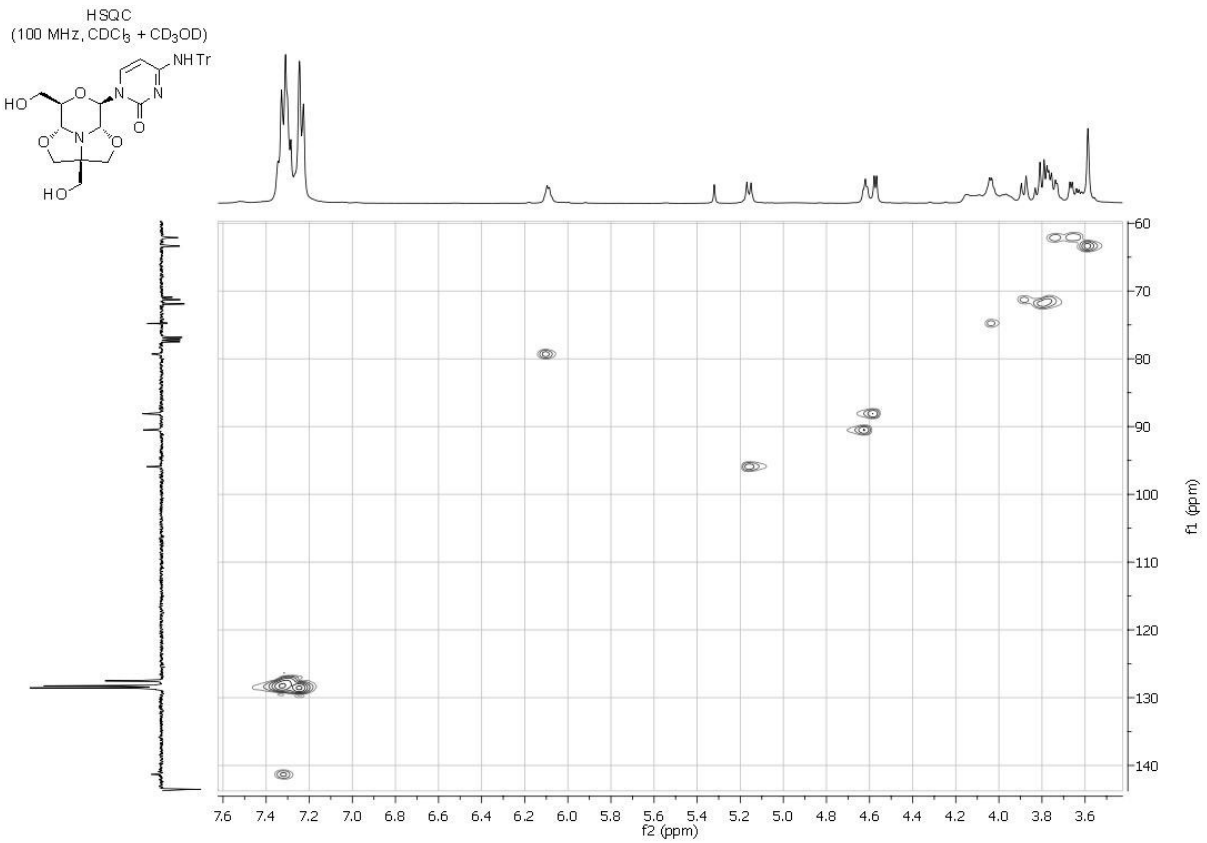


Figure S76. ^{1}H-^{13}C HSQC spectrum of compound 14a

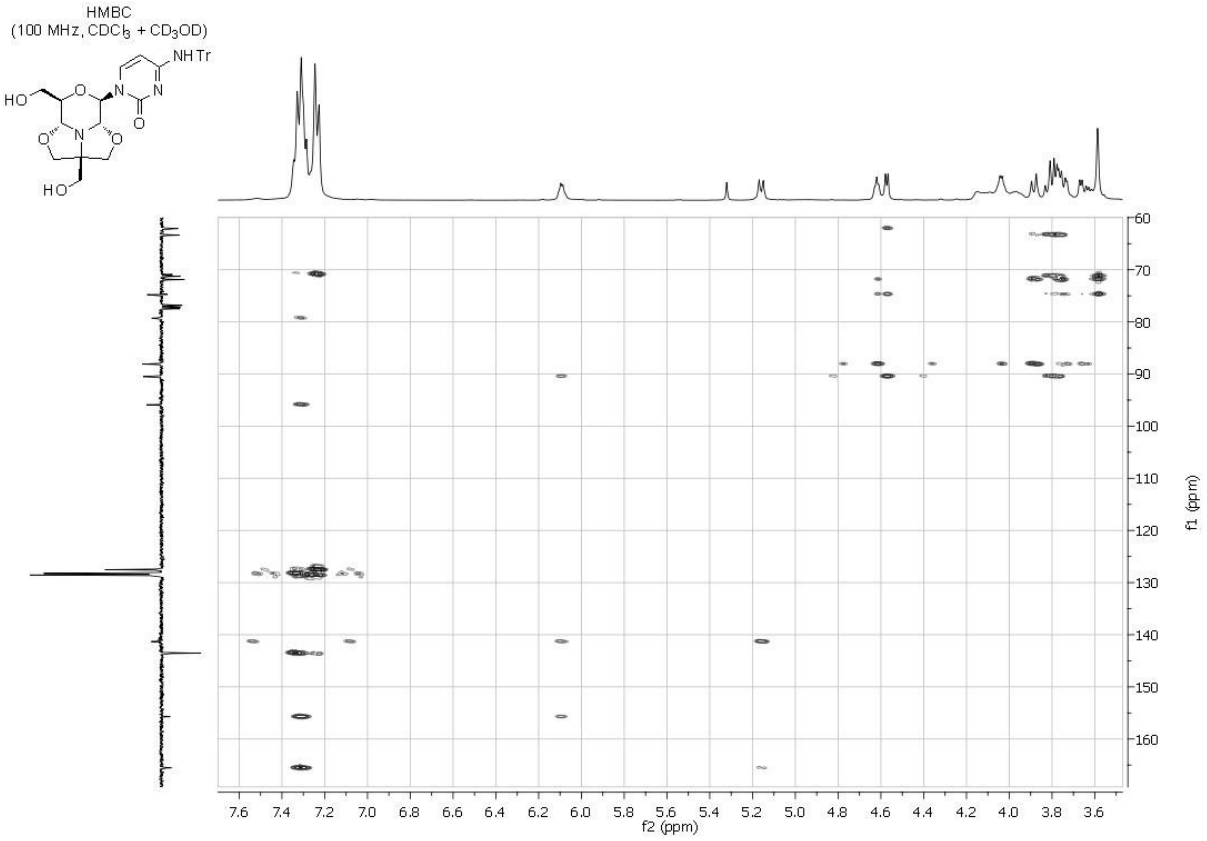


Figure S77. ^{1}H-^{13}C HMBC spectrum of compound 14a

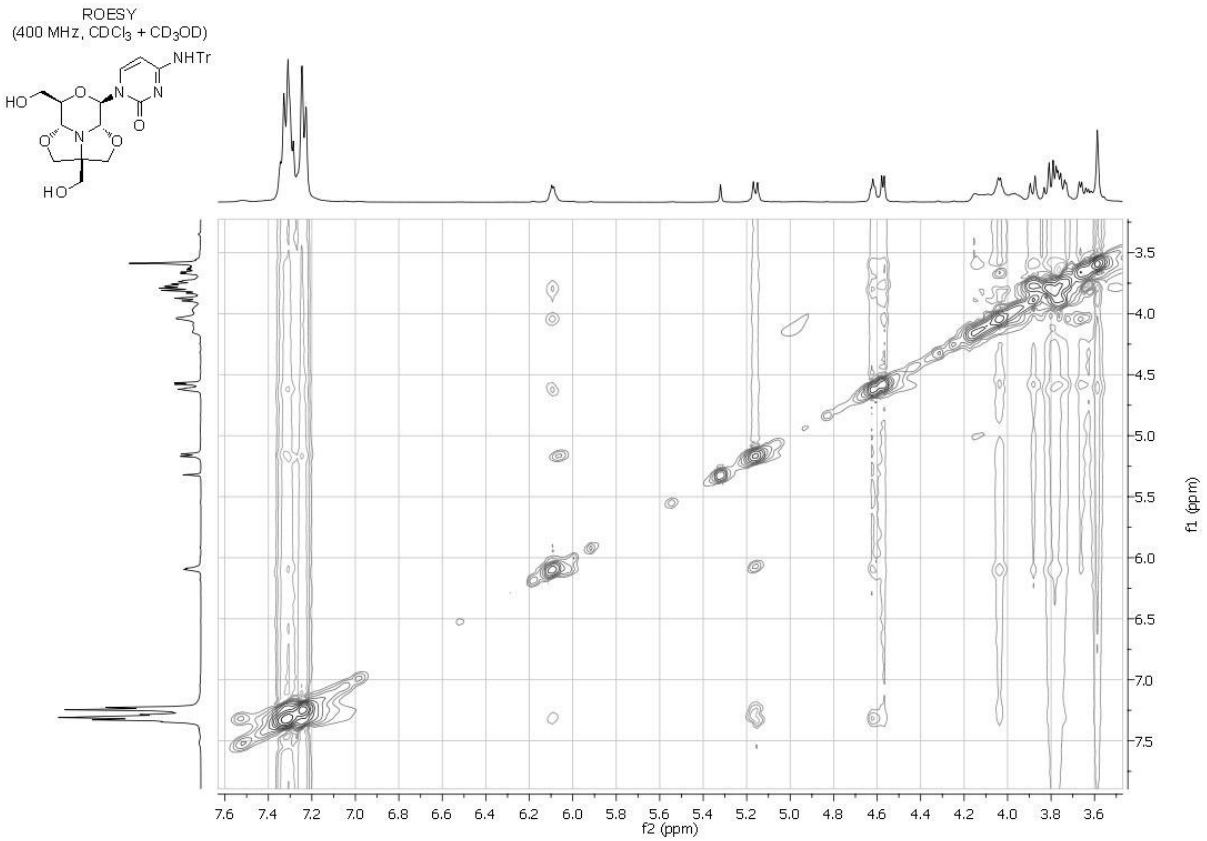


Figure S78. ^{1}H-^{1}H ROESY spectrum of compound 14a

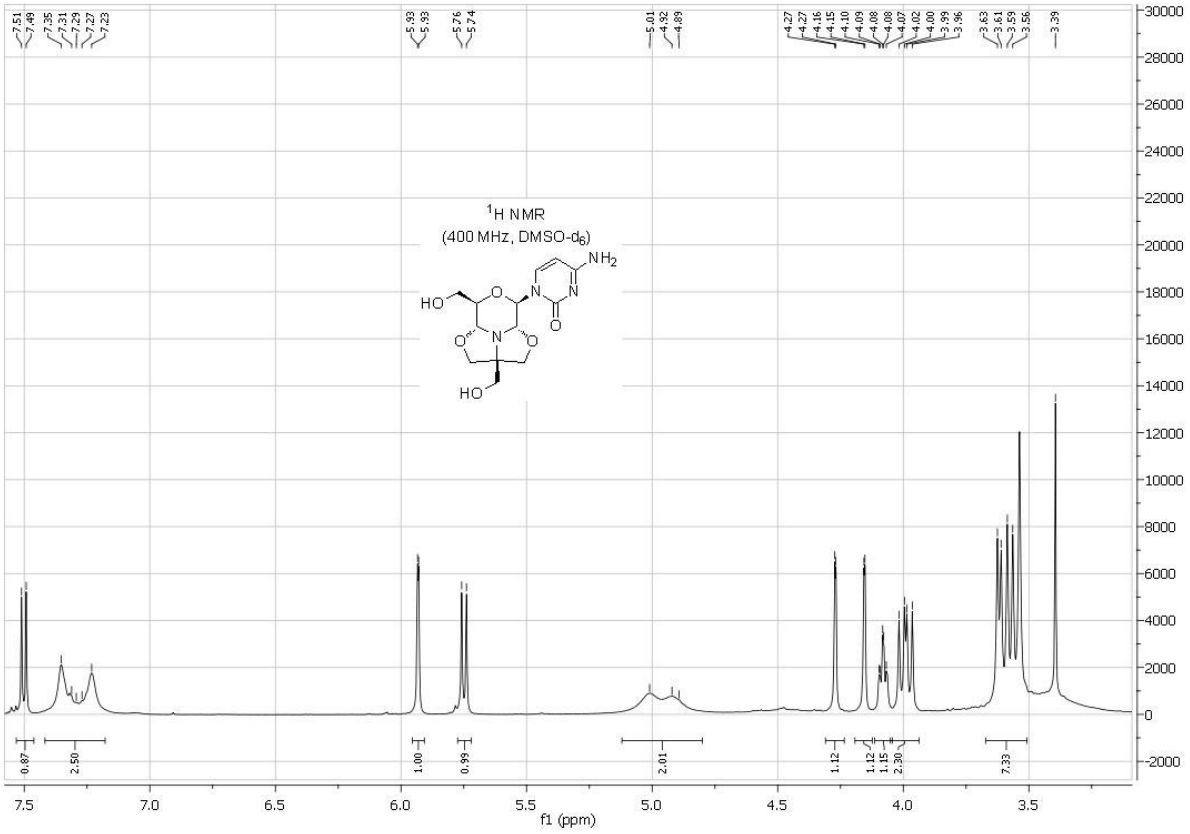


Figure S79. ^{1}H spectrum of compound 14b

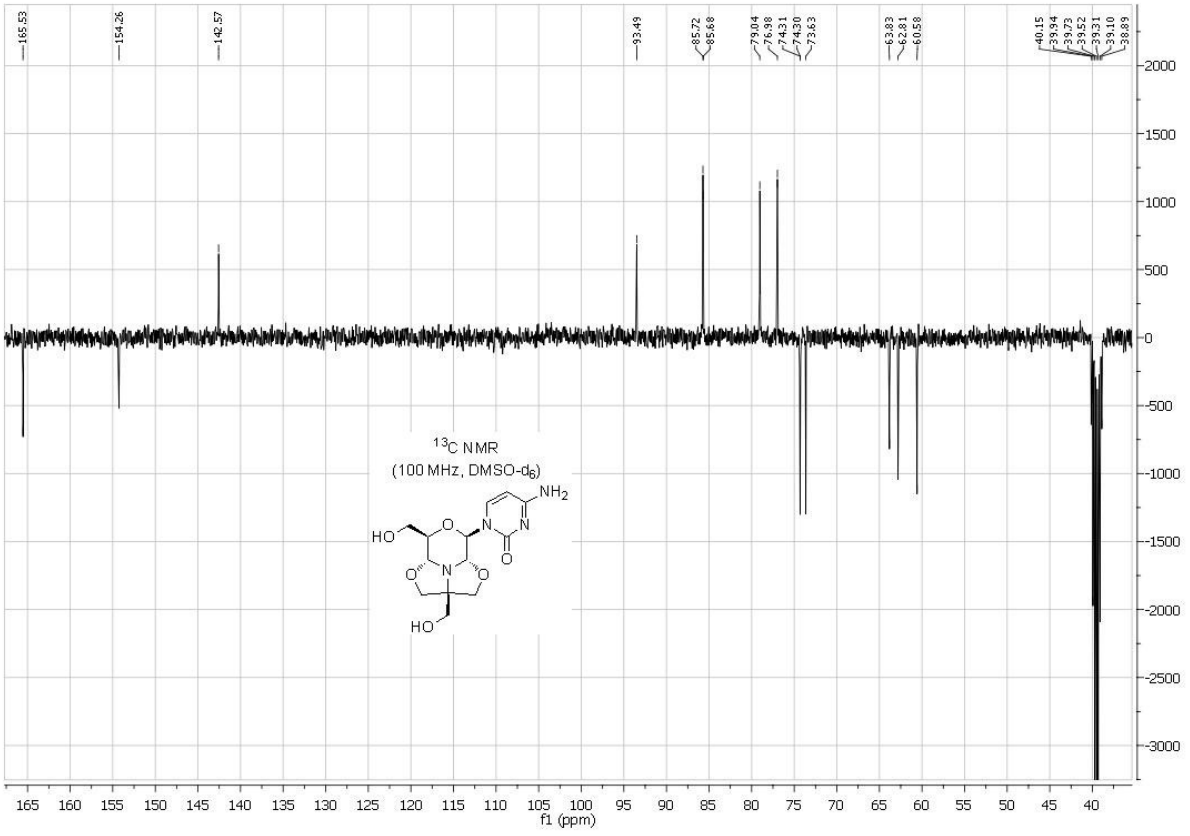


Figure S80. ^{13}C spectrum of compound 14b

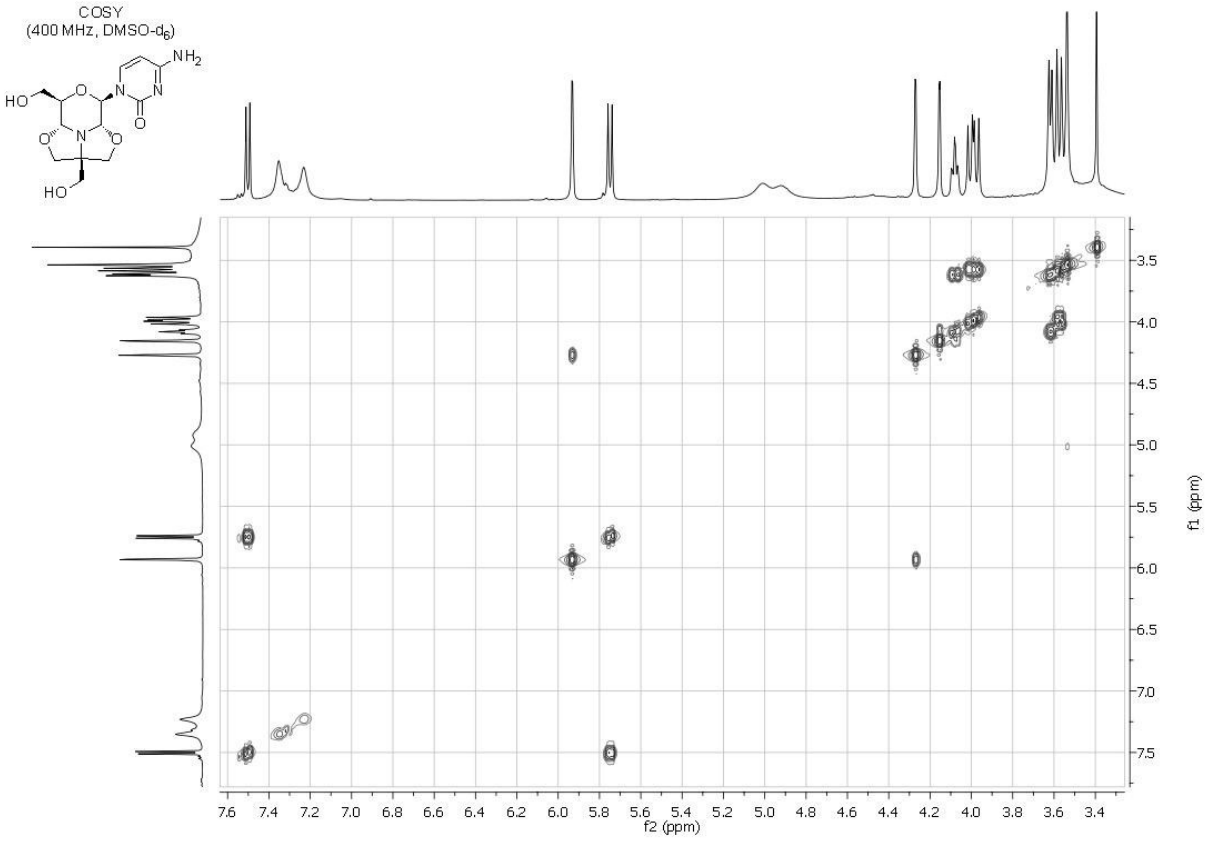


Figure S81. ^{1}H-^{1}H COSY spectrum of compound 14b

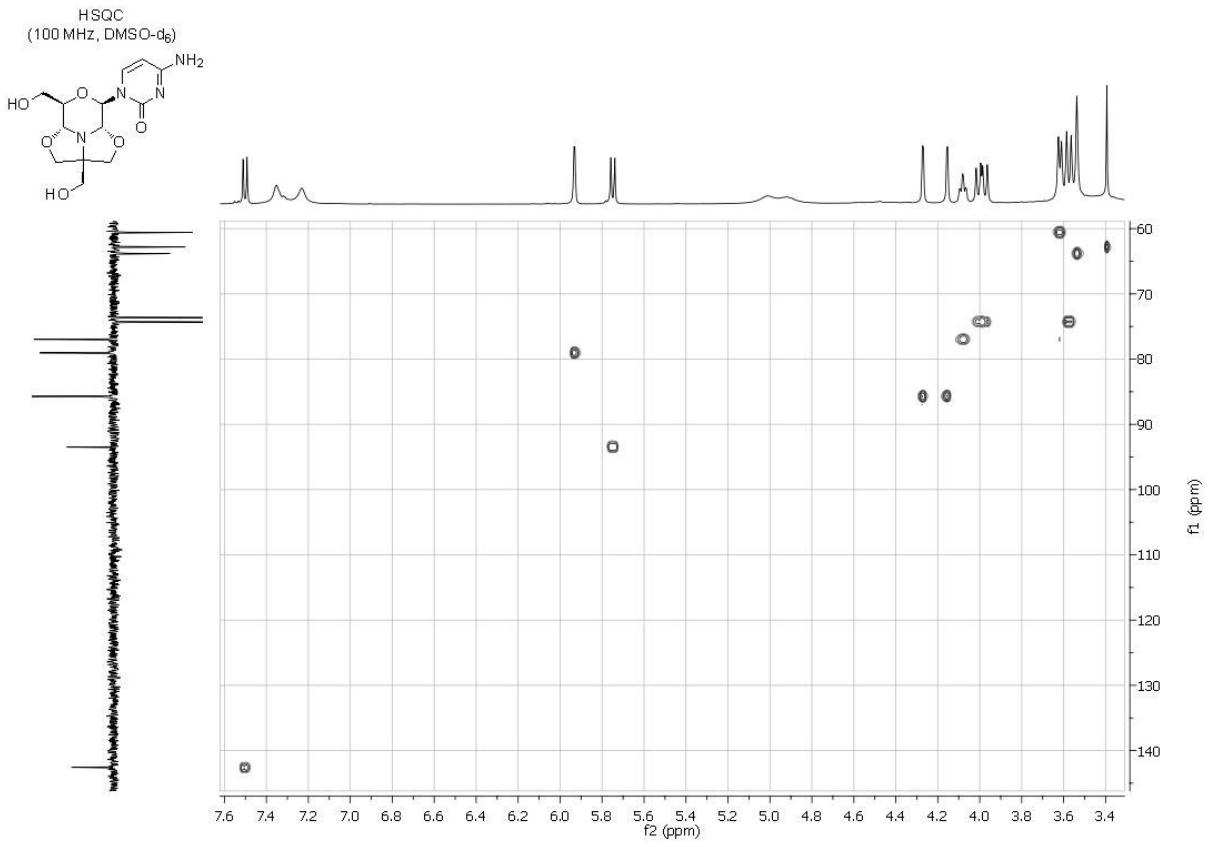


Figure S82. ^{1}H-^{13}C HSQC spectrum of compound 14b

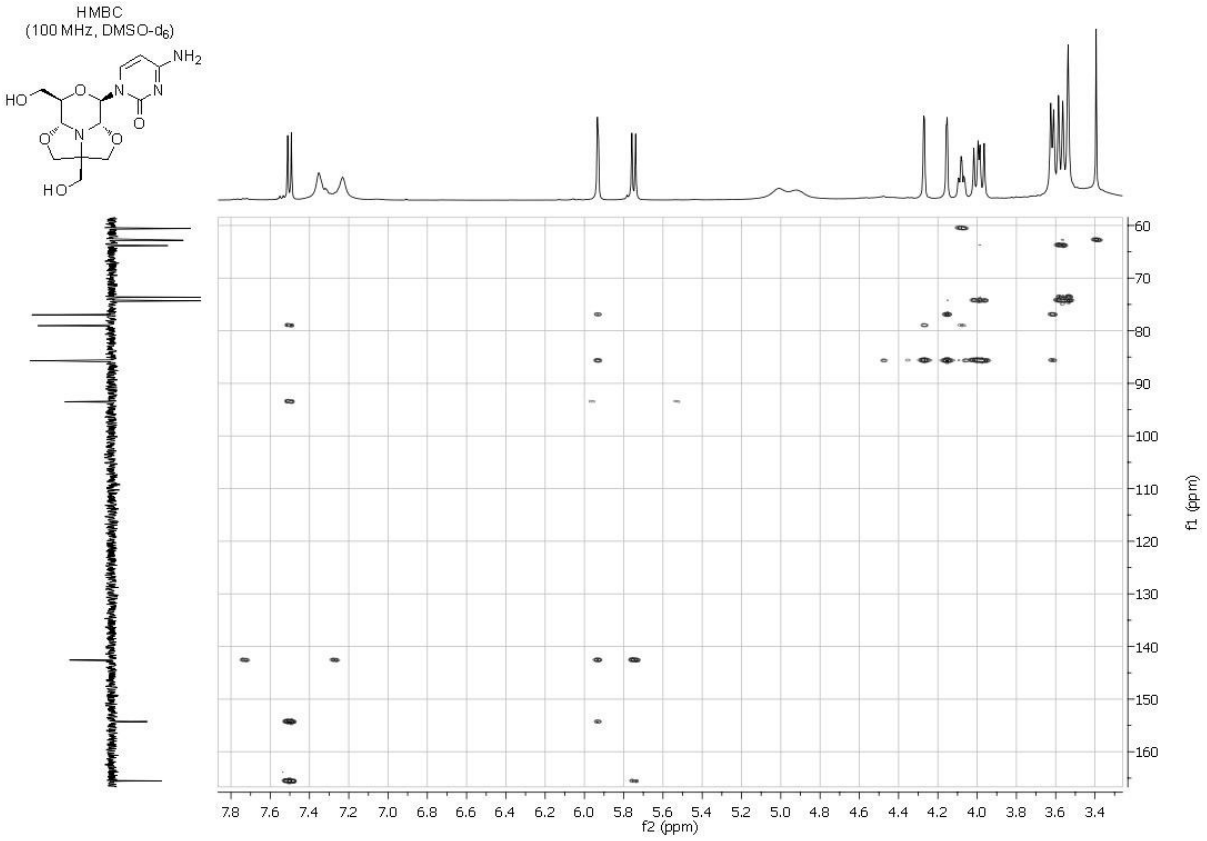


Figure S83. ^{1}H-^{13}C HMBC spectrum of compound 14b

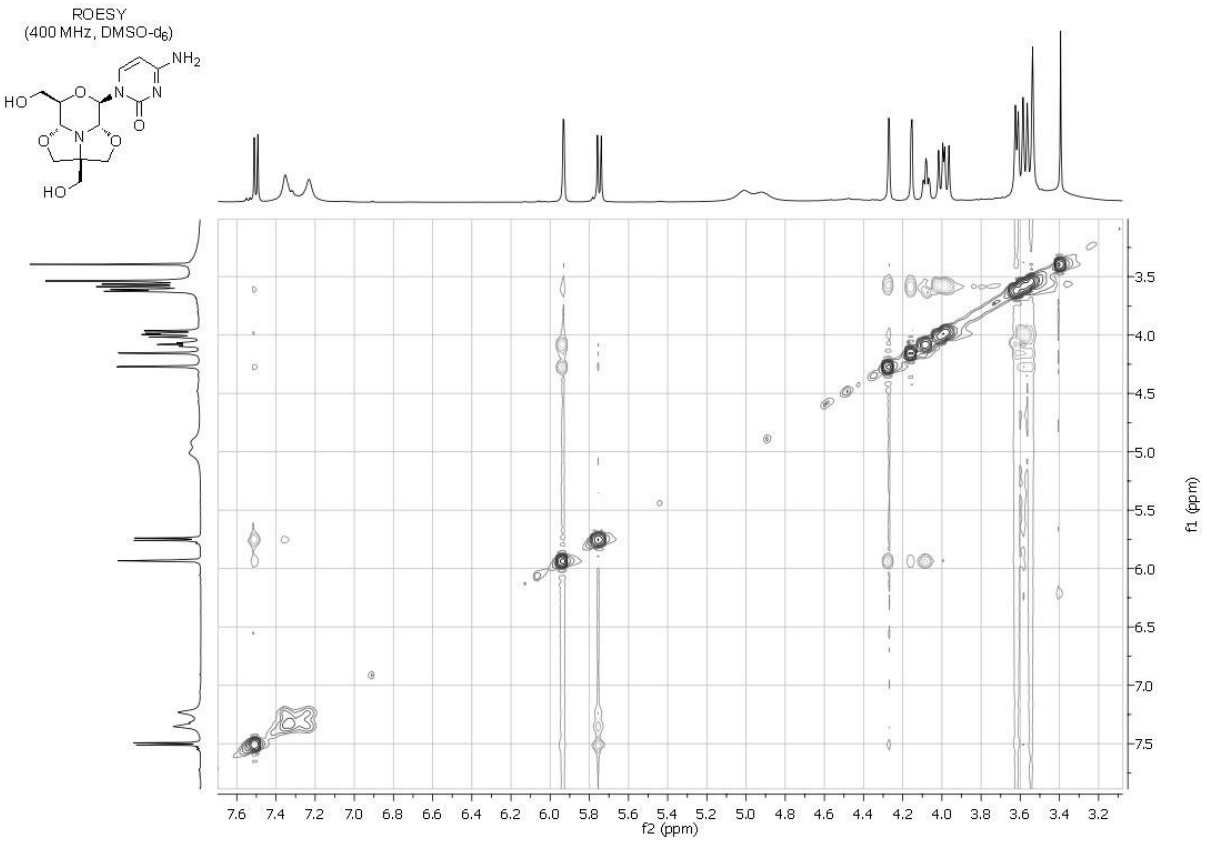


Figure S84. ^{1}H-^{1}H ROESY spectrum of compound 14b

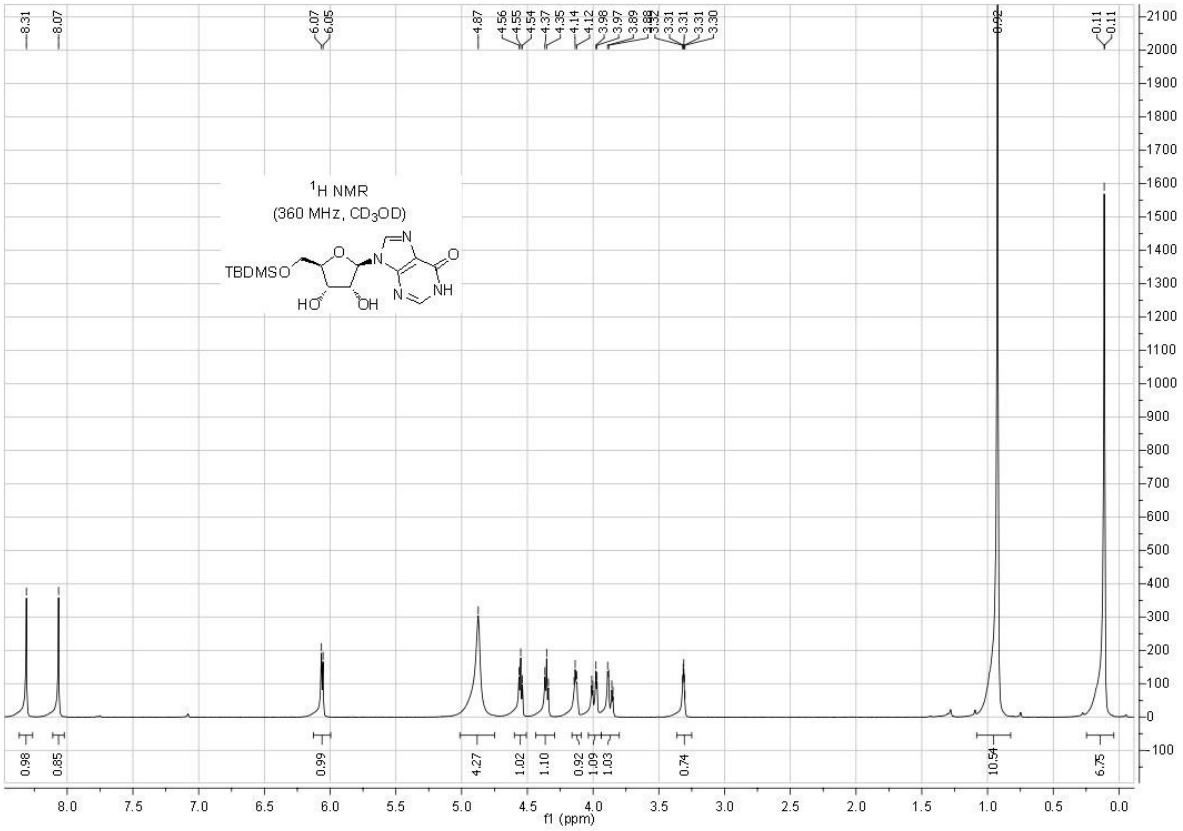


Figure S85. ^{1}H spectrum of compound 16a

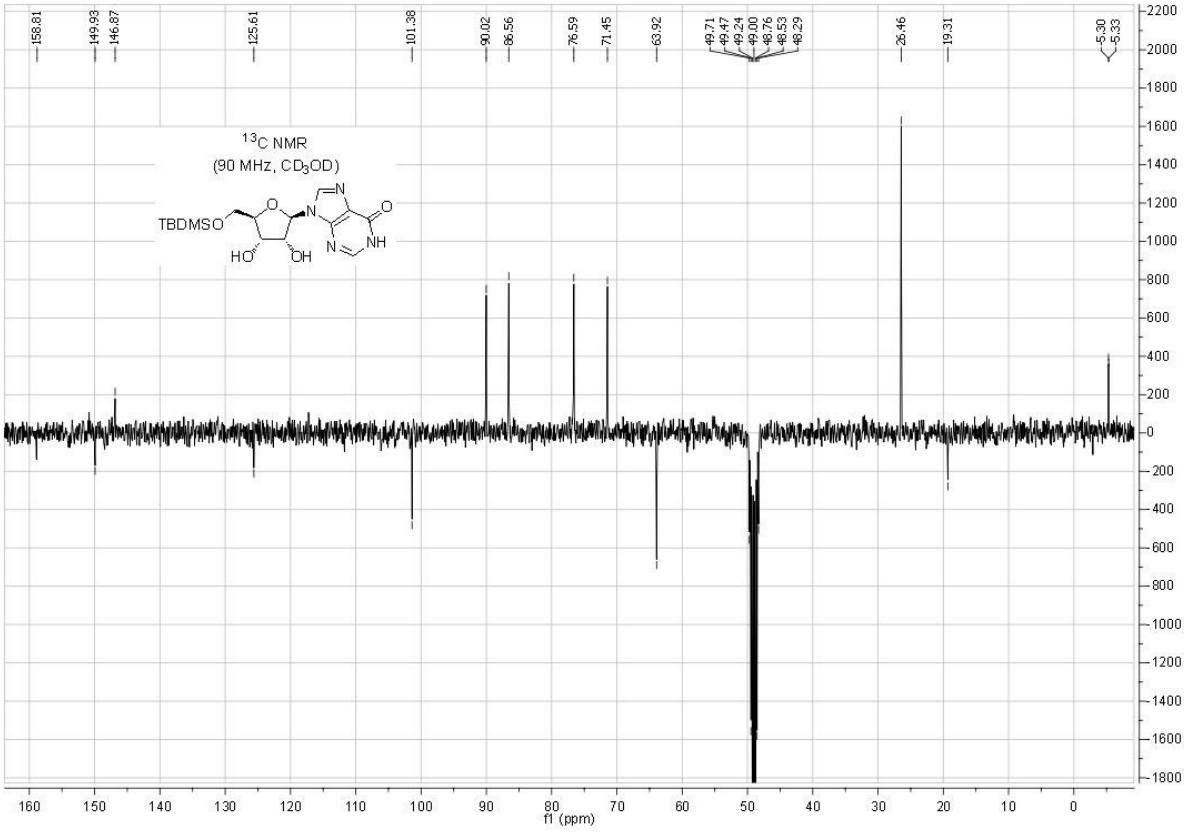


Figure S86. ^{13}C spectrum of compound 16a

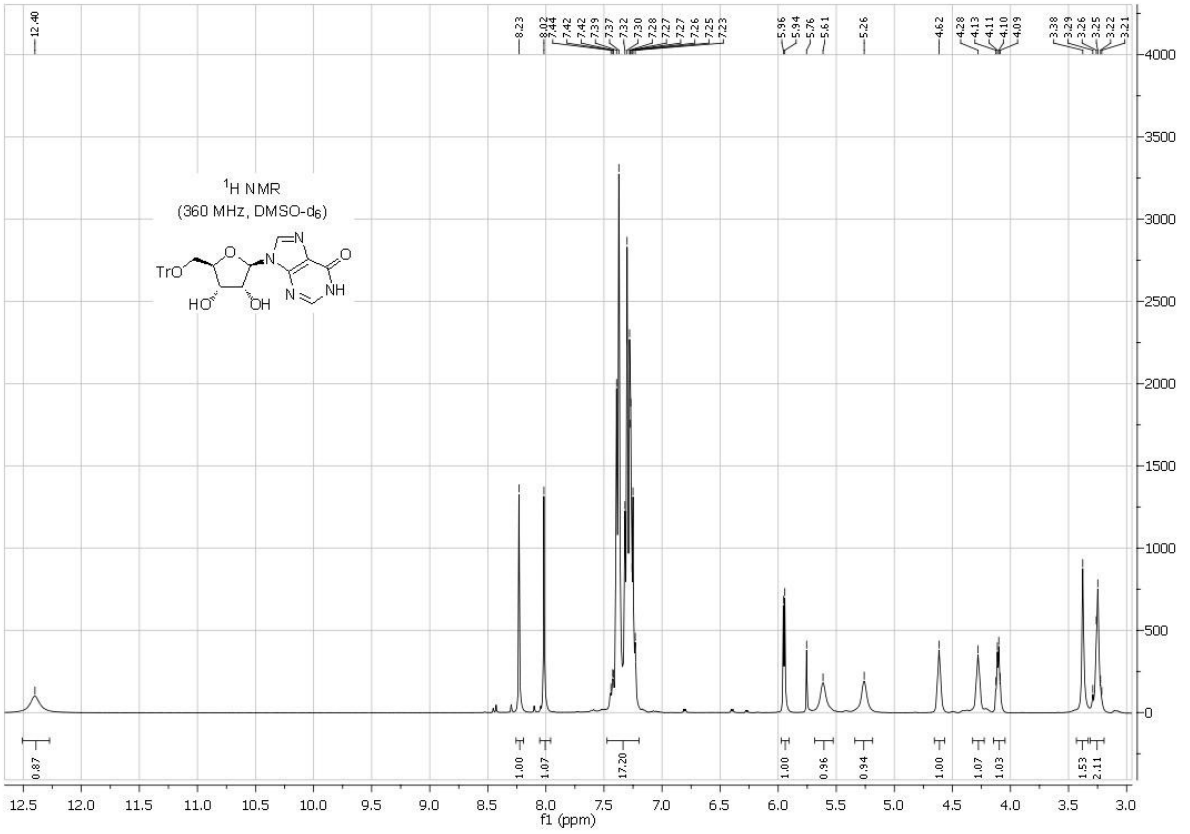


Figure S87. ^{1}H spectrum of compound 16b

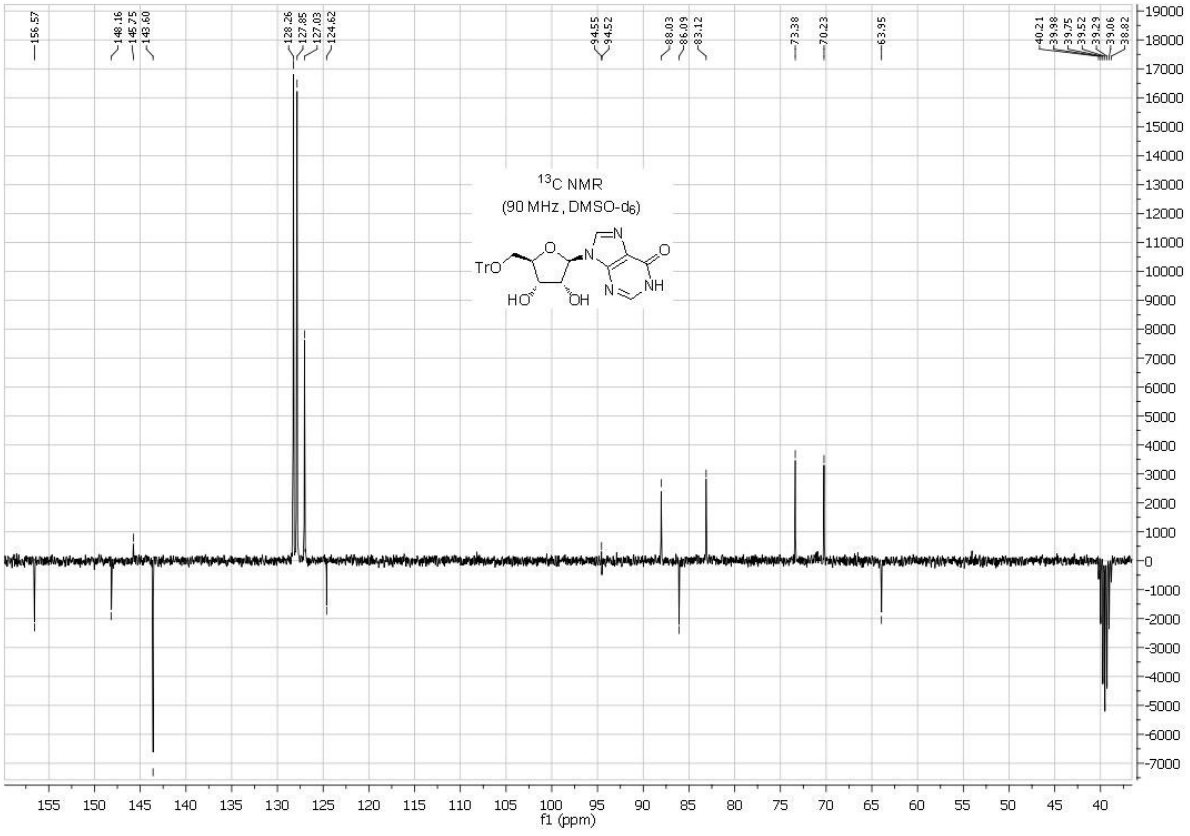


Figure S88. ^{13}C spectrum of compound 16b

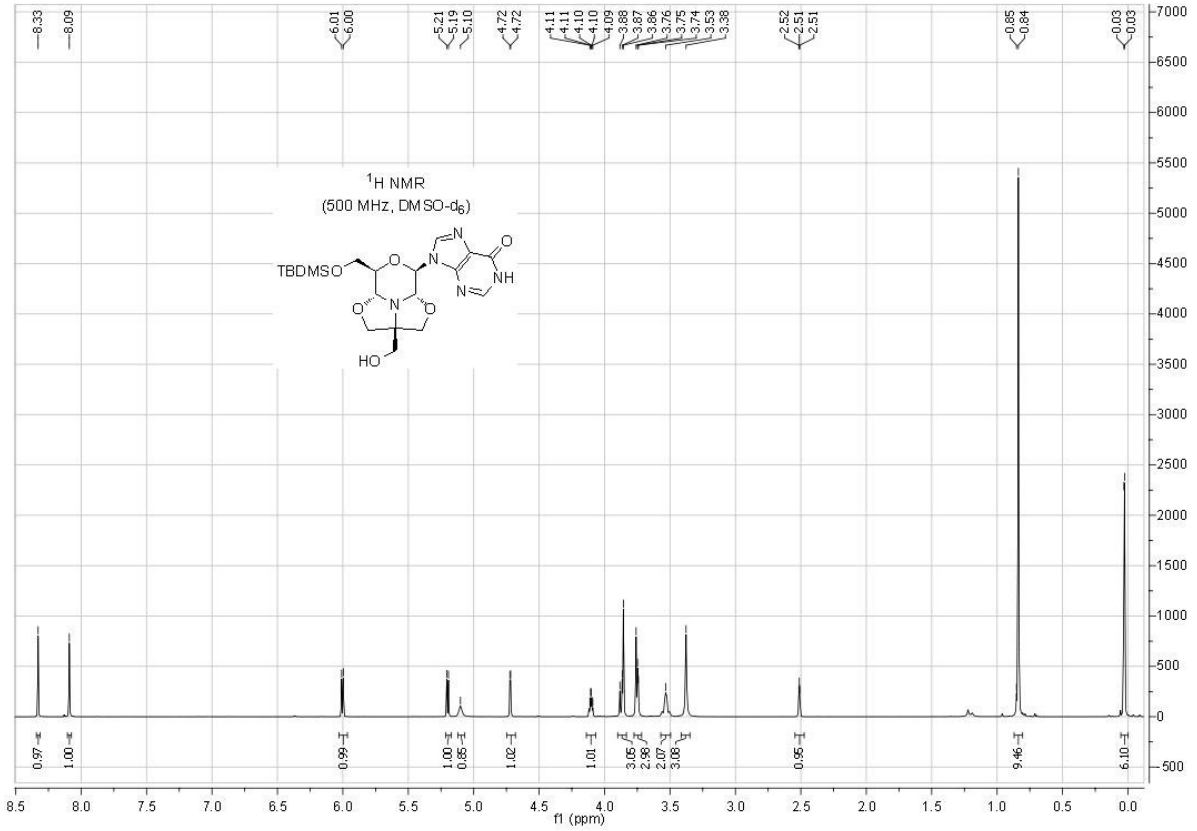


Figure S89. ^{1}H spectrum of compound 17a

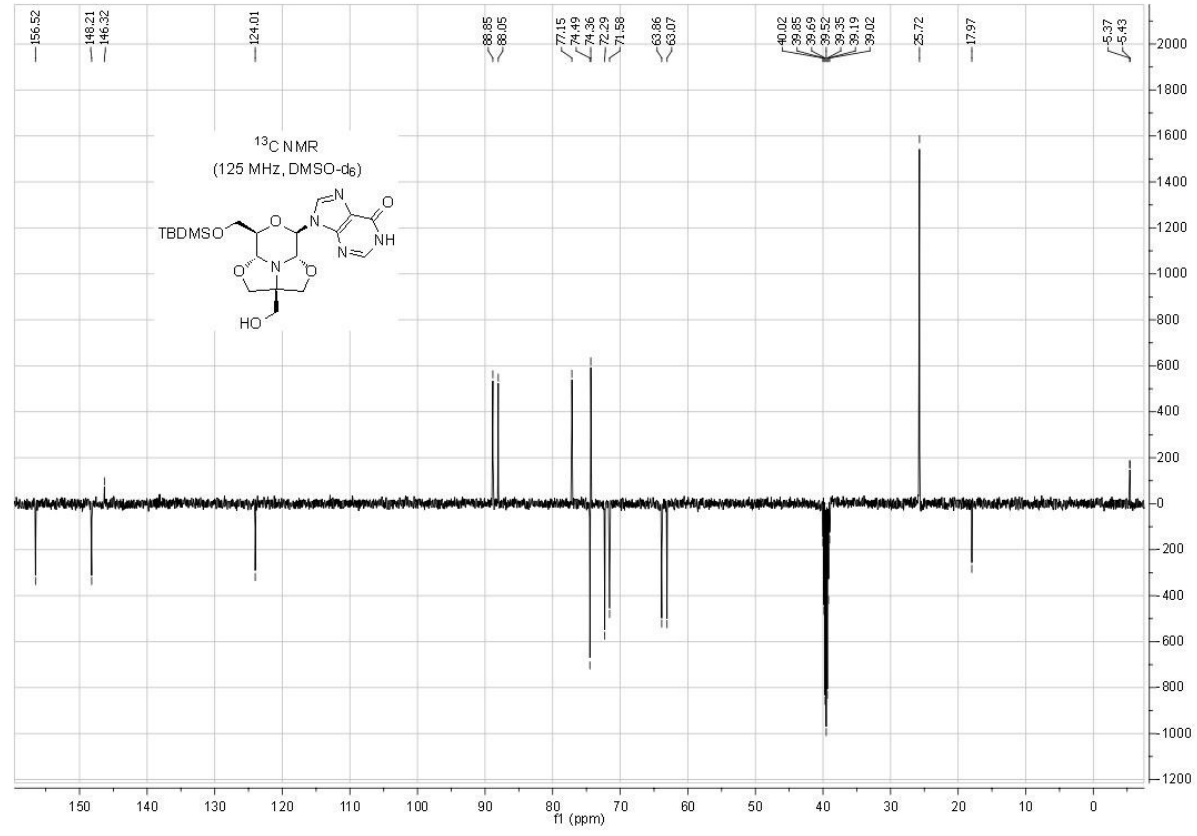


Figure S90. ^{13}C spectrum of compound 17a

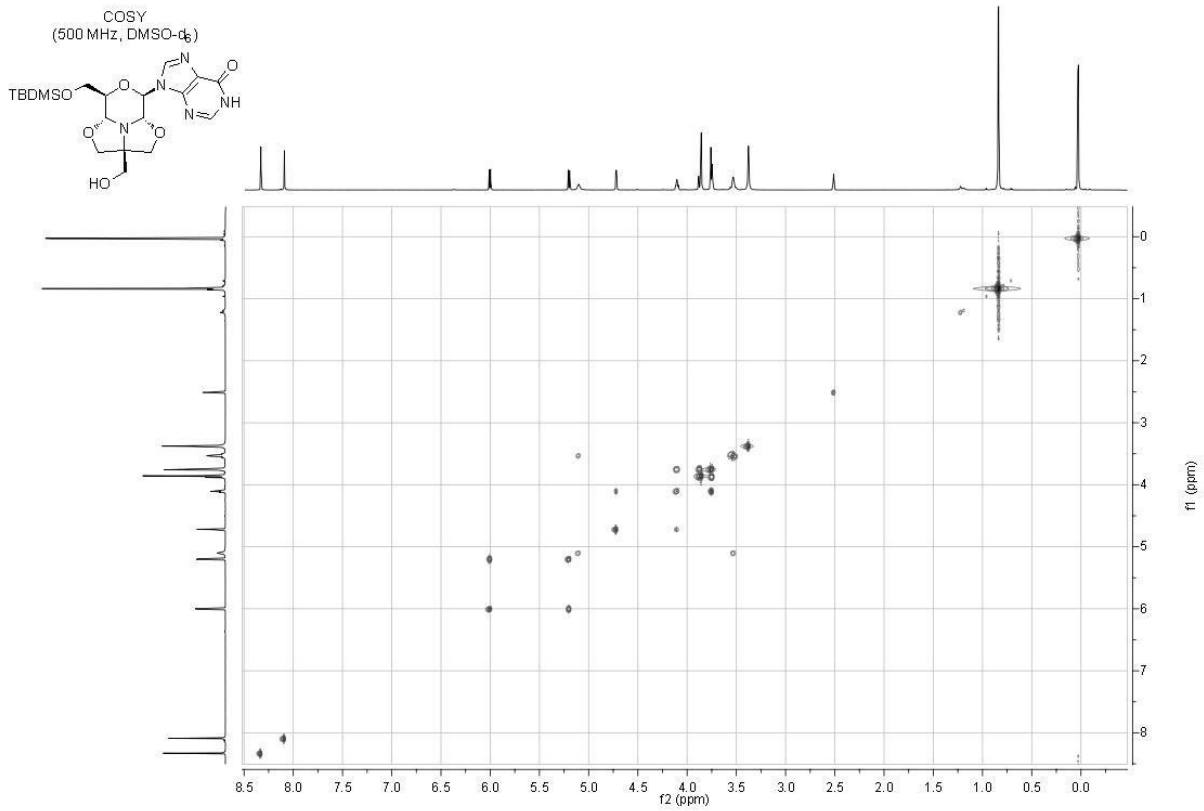


Figure S91. ^{1}H-^{1}H COSY spectrum of compound 17a

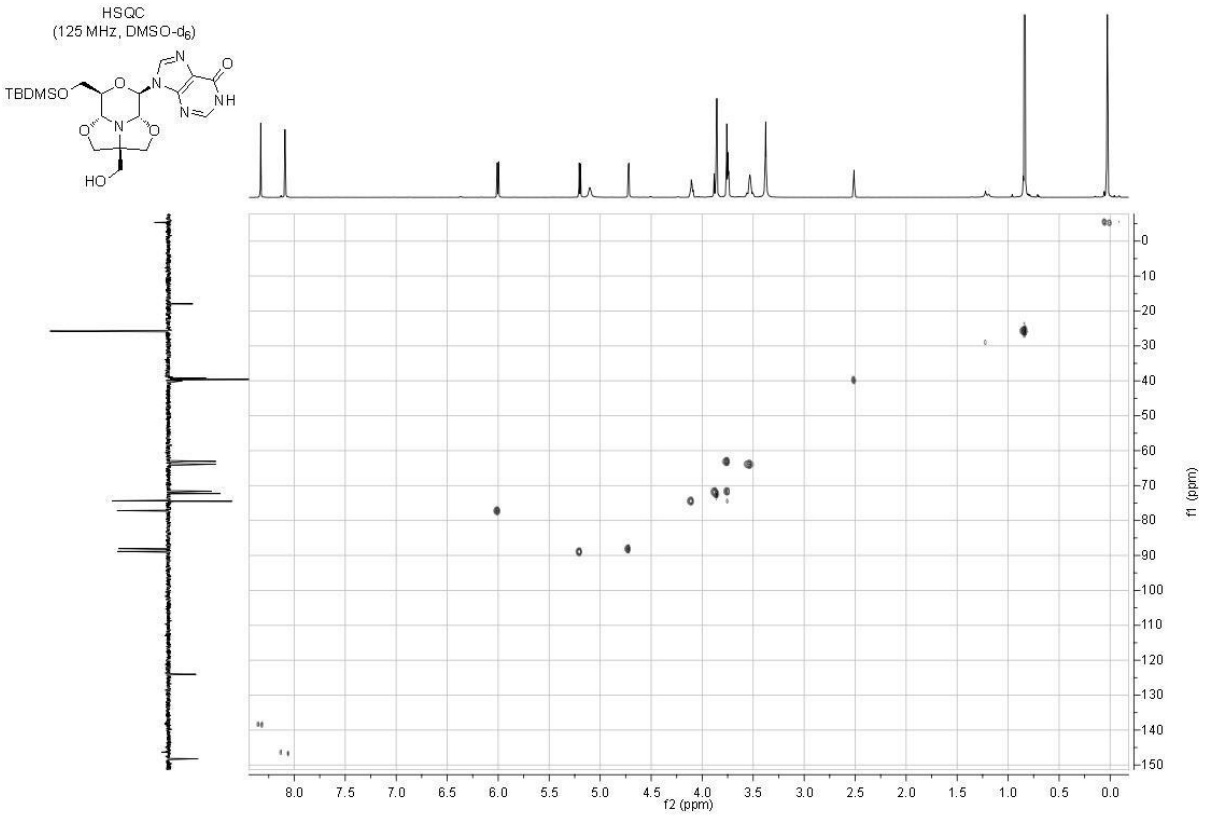


Figure S92. ^{1}H-^{13}C HSQC spectrum of compound 17a

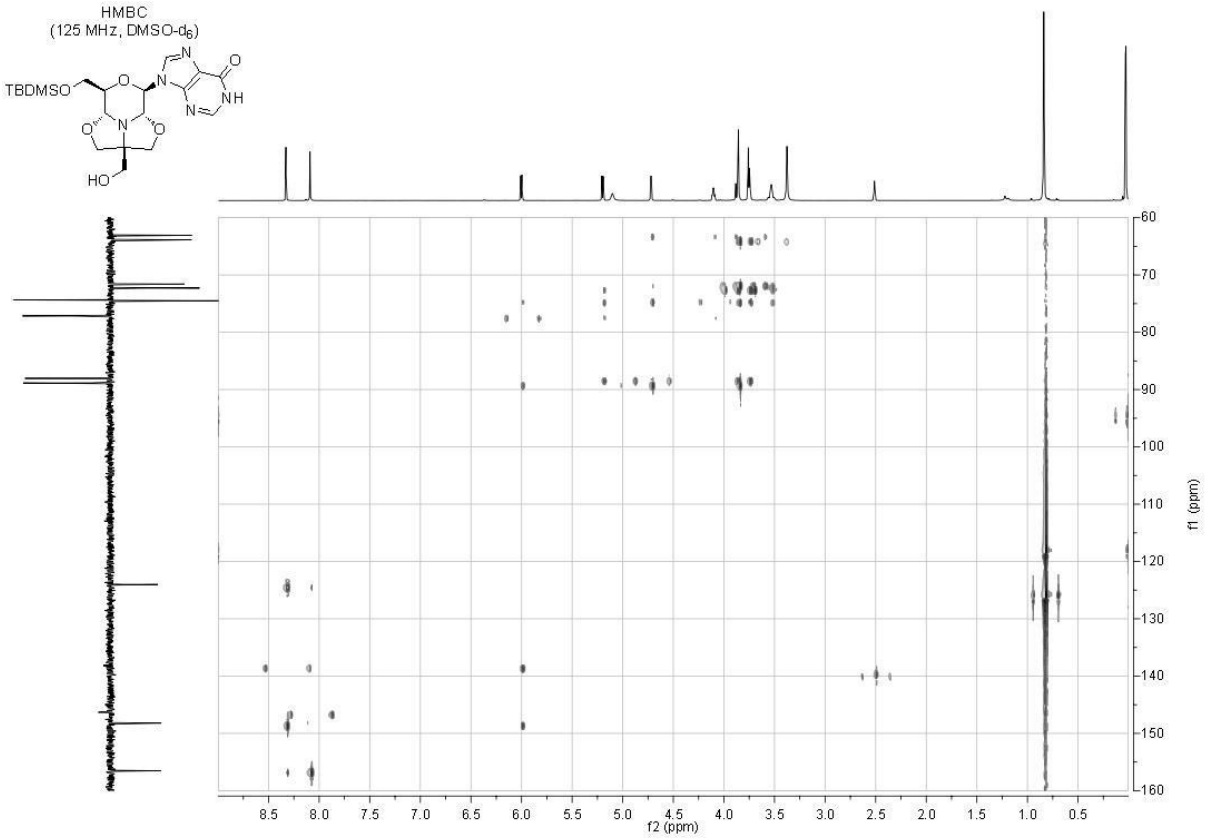


Figure S93. ^{1}H-^{13}C HMBC spectrum of compound 17a

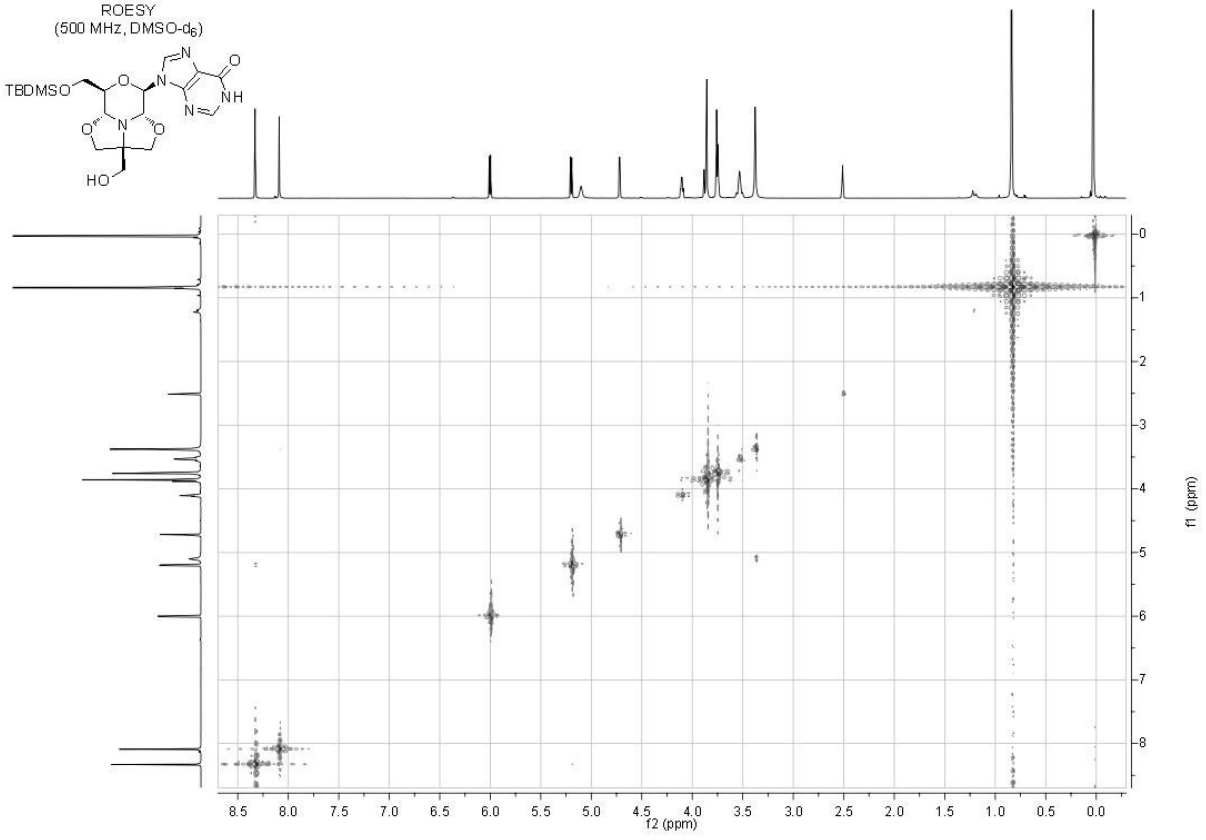


Figure S94. ^{1}H-^{1}H ROESY spectrum of compound 17a

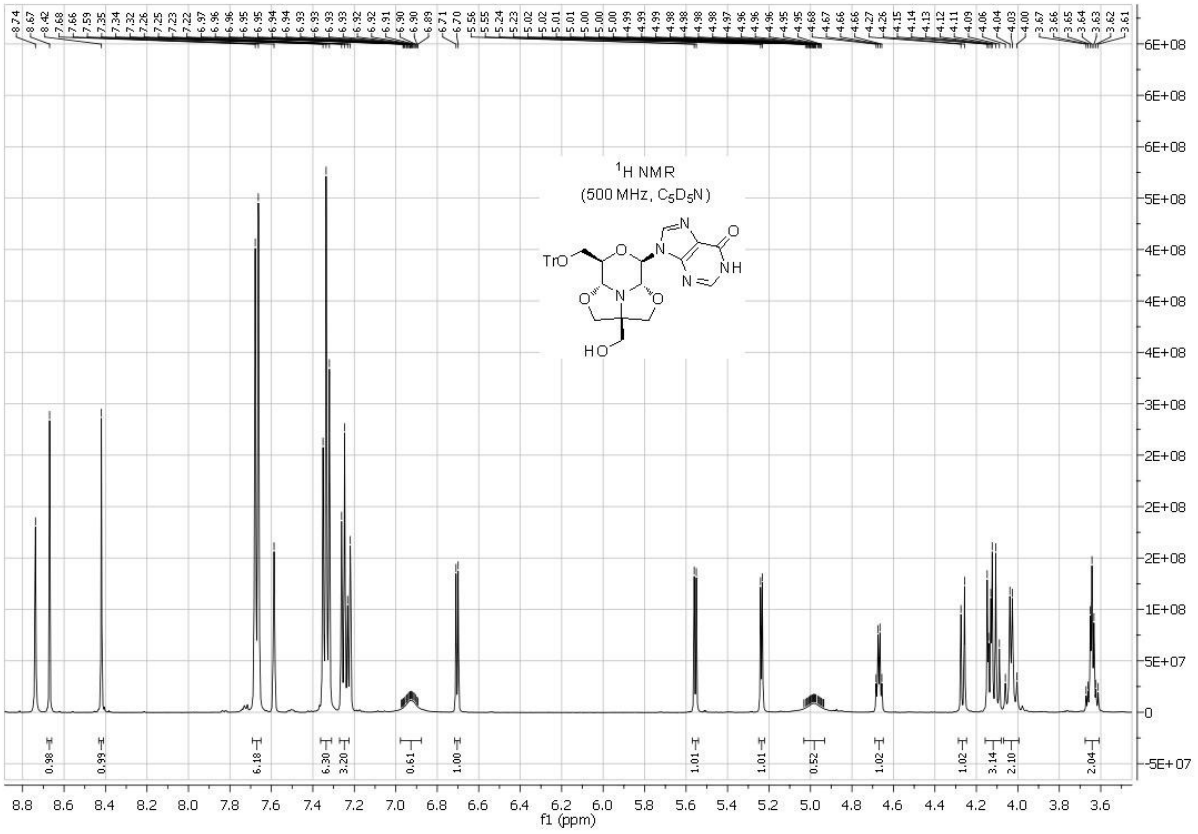


Figure S95. ^{1}H spectrum of compound 17b

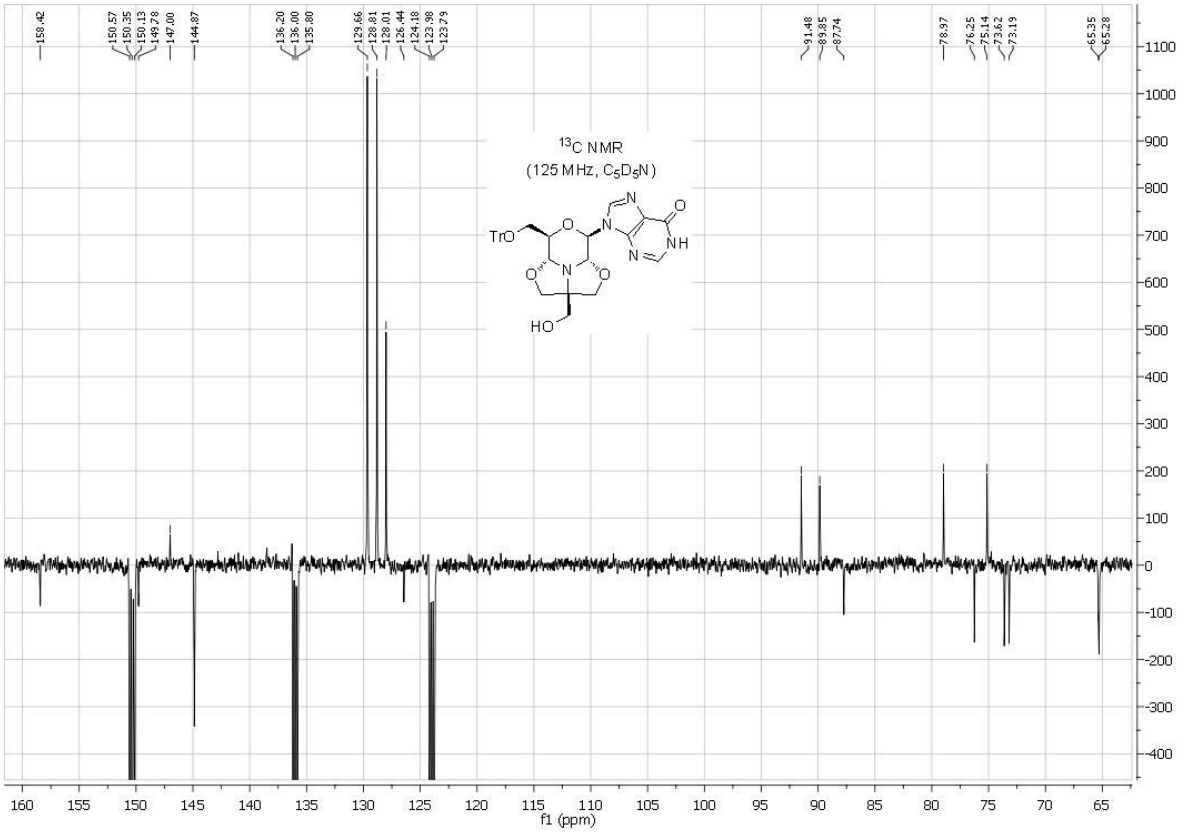


Figure S96. ^{13}C spectrum of compound 17b

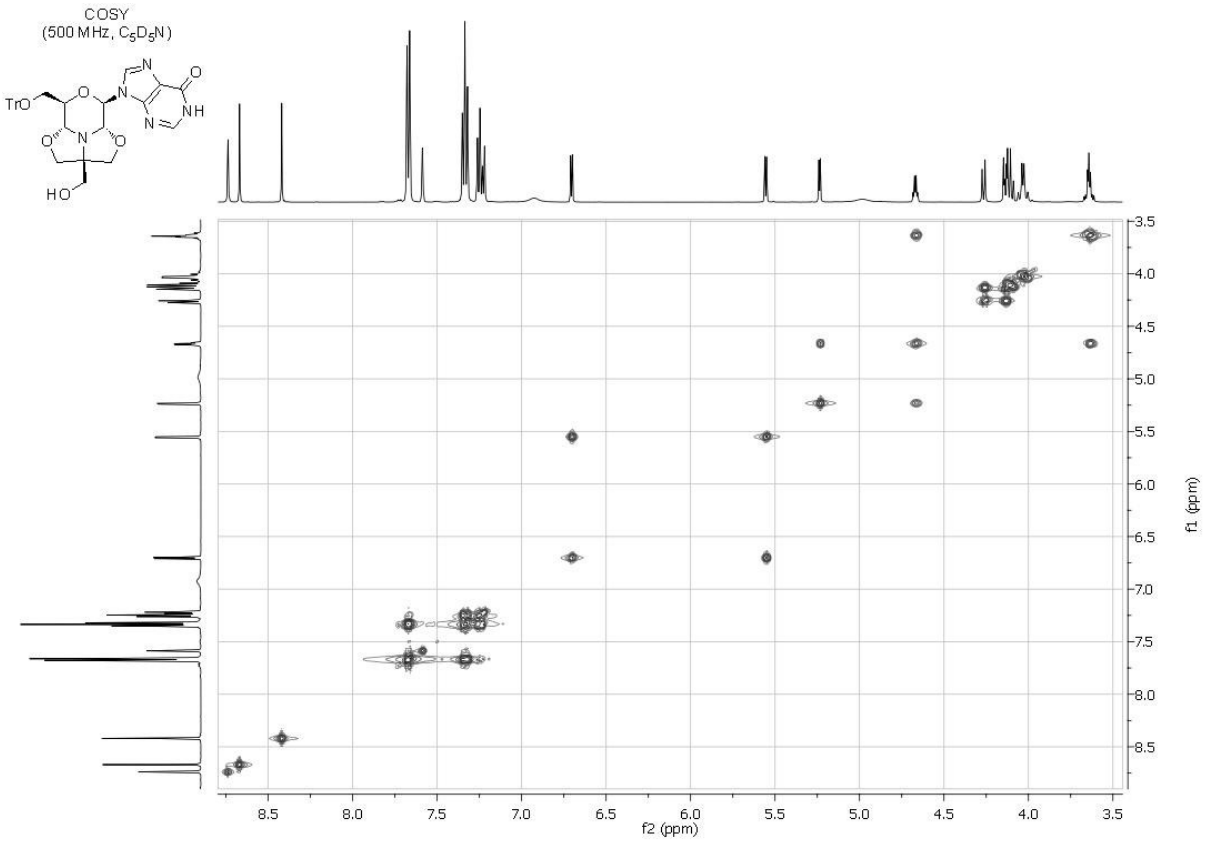


Figure S97. ^{1}H-^{1}H COSY spectrum of compound 17b

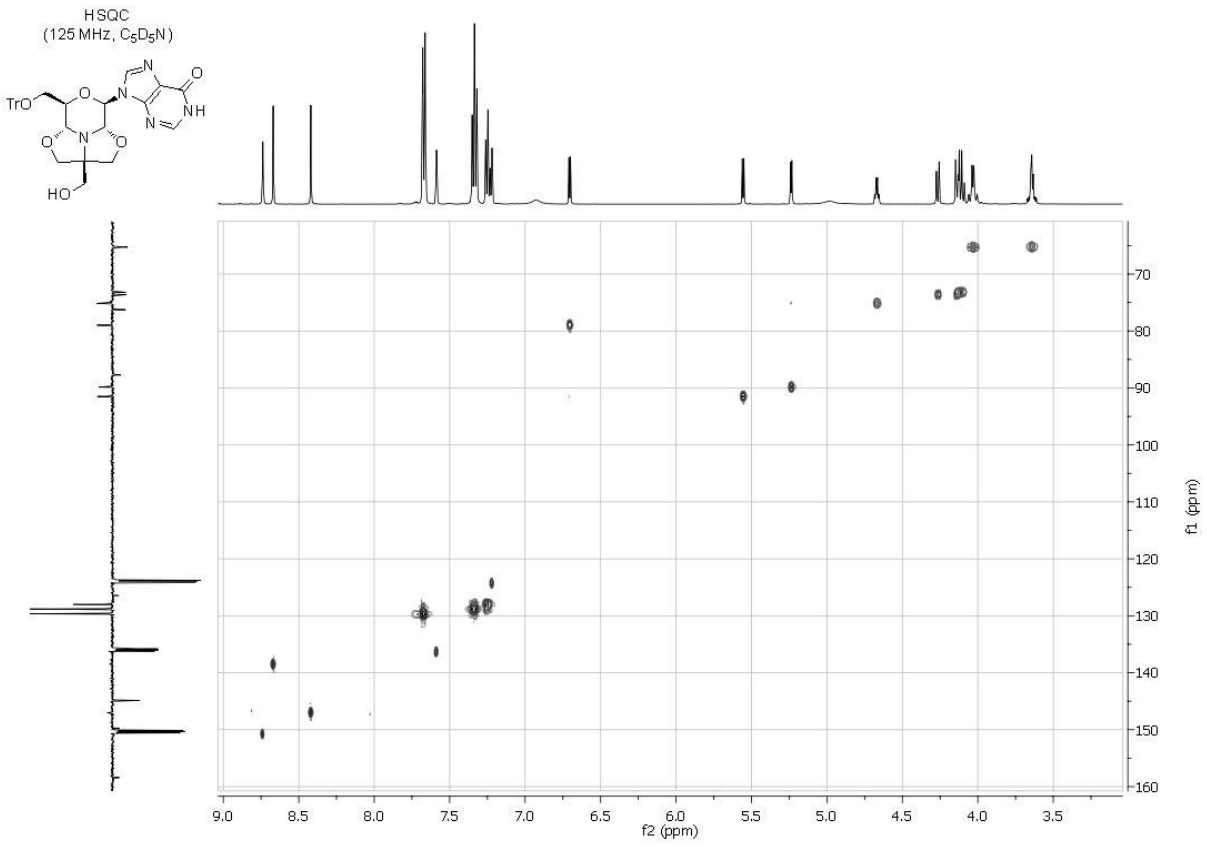


Figure S98. ^{1}H-^{13}C HSQC spectrum of compound 17b

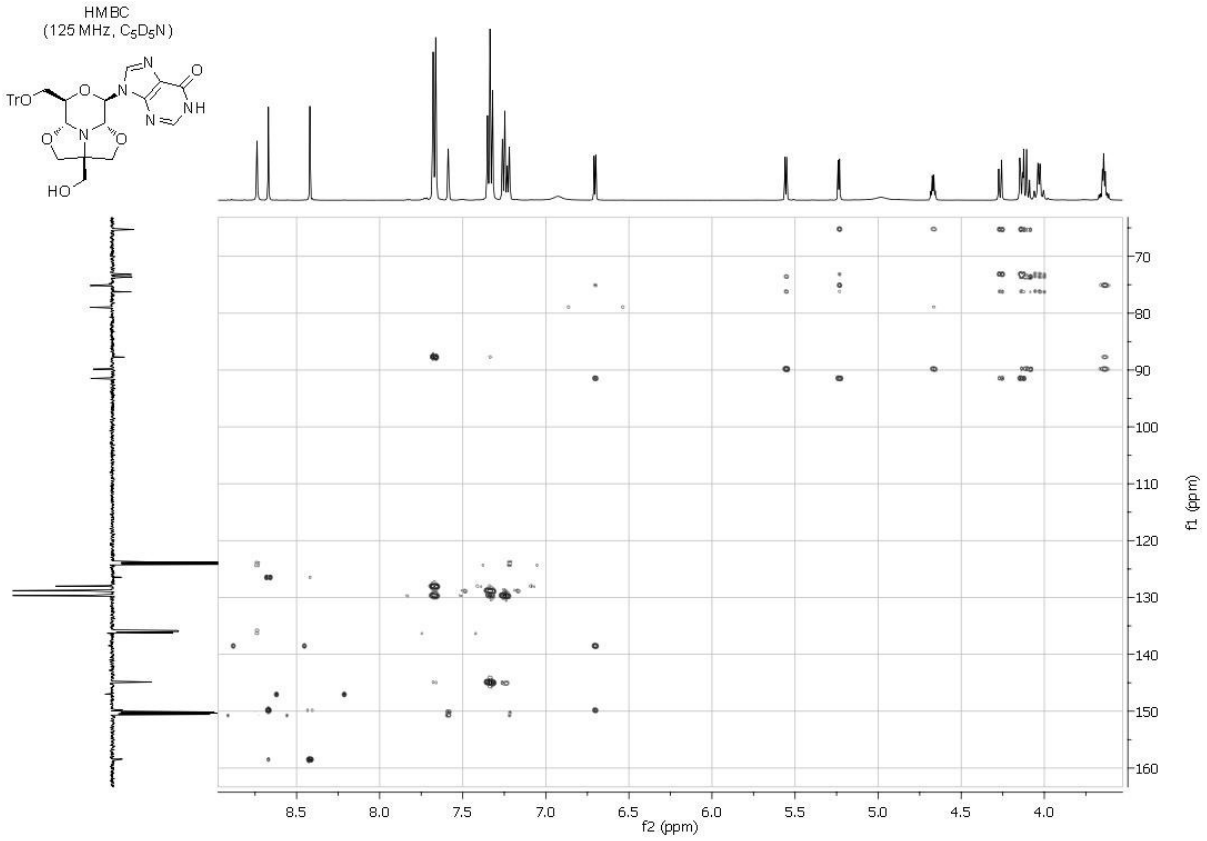


Figure S99. ^{1}H-^{13}C HMBC spectrum of compound 17b

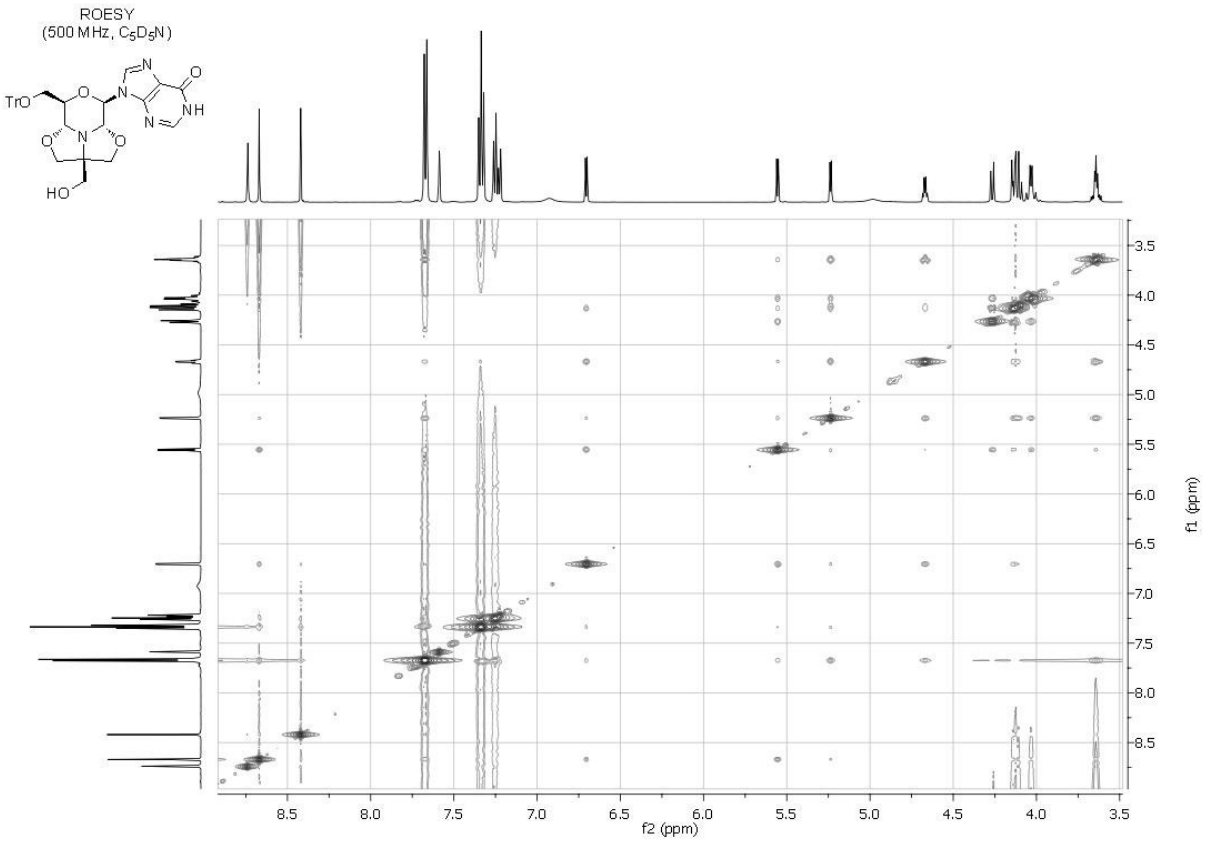


Figure S100. ^{1}H-^{1}H ROESY spectrum of compound 17b

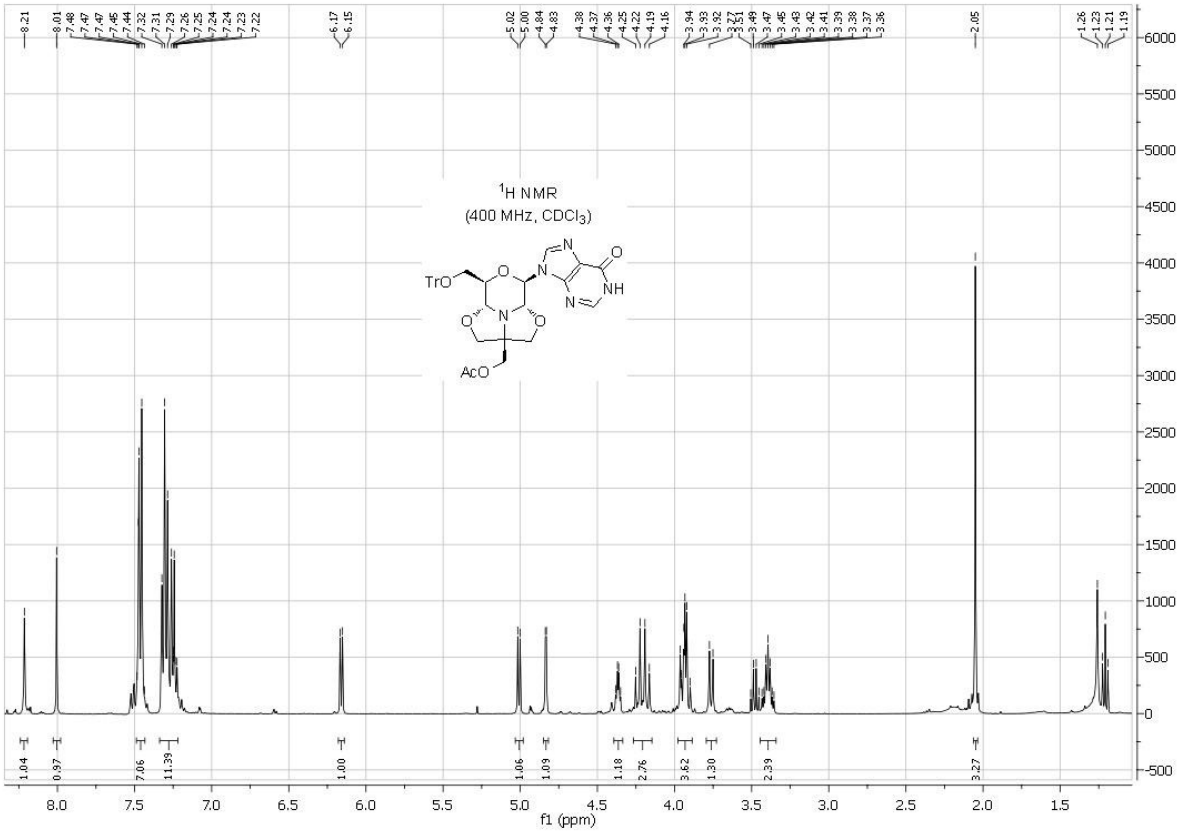


Figure S101. ^{1}H spectrum of compound 18b

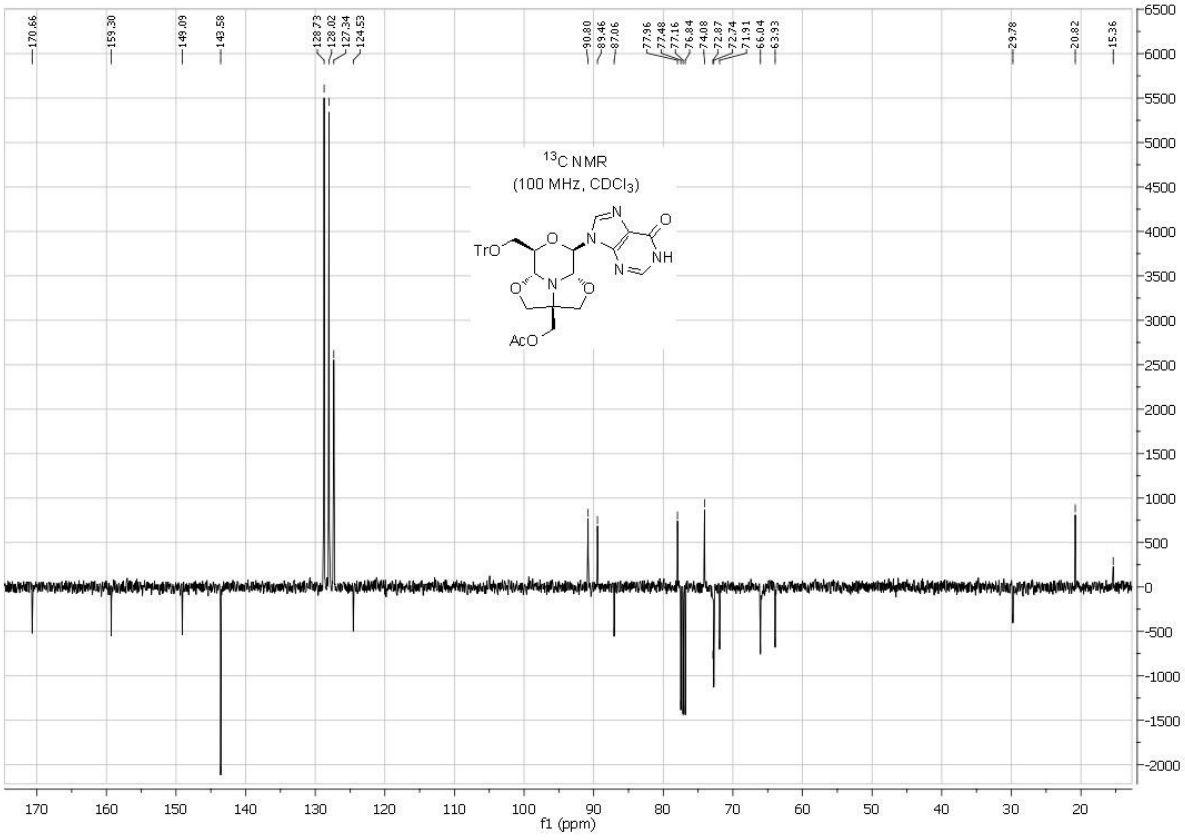


Figure S102. ^{13}C spectrum of compound 18b

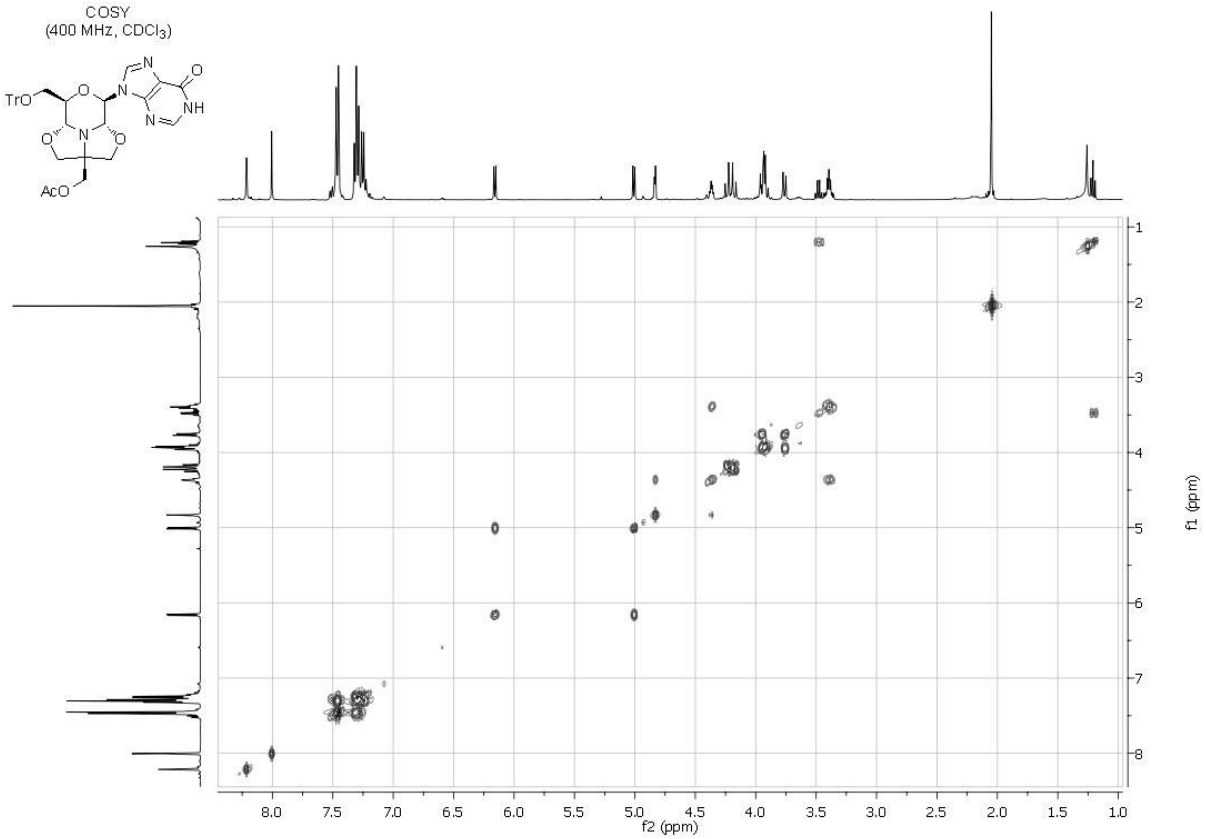


Figure S103. ^{1}H-^{1}H COSY spectrum of compound 18b

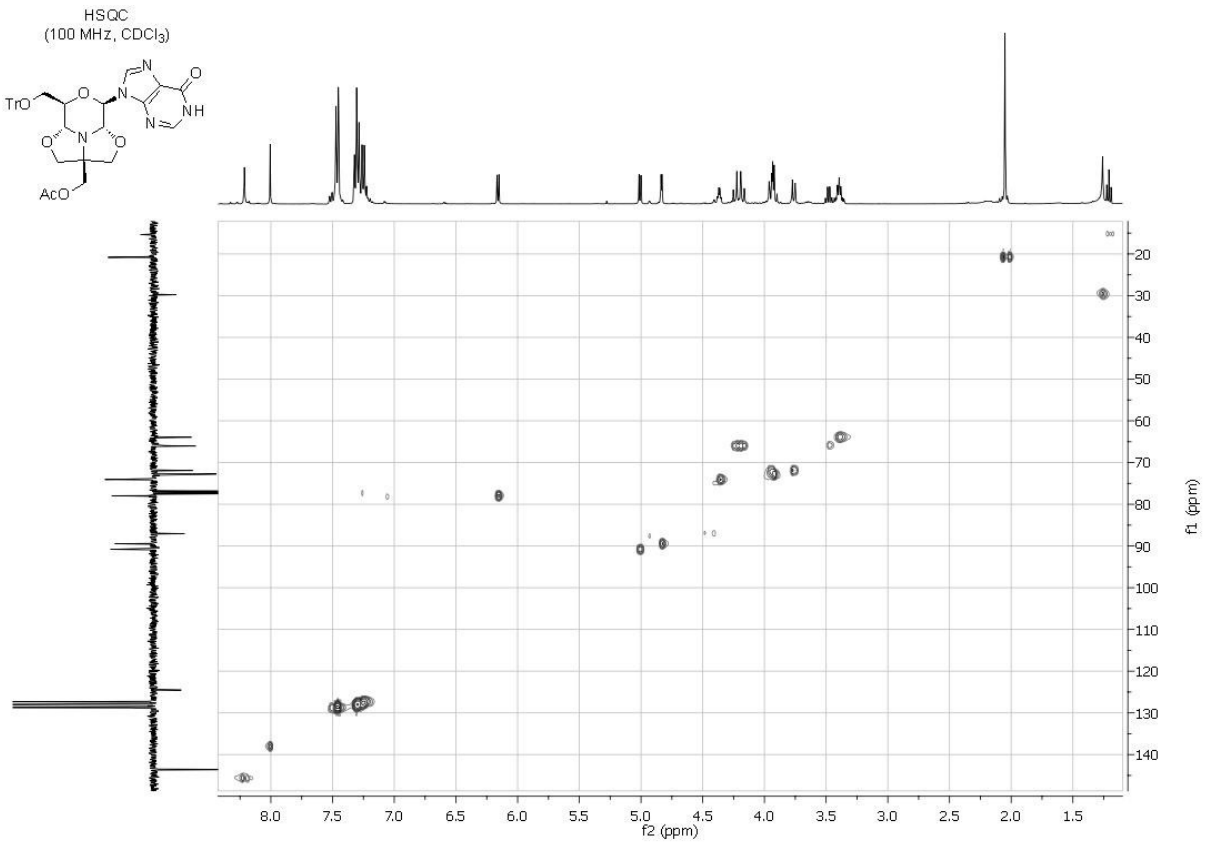


Figure S104. ^{1}H-^{13}C HSQC spectrum of compound 18b

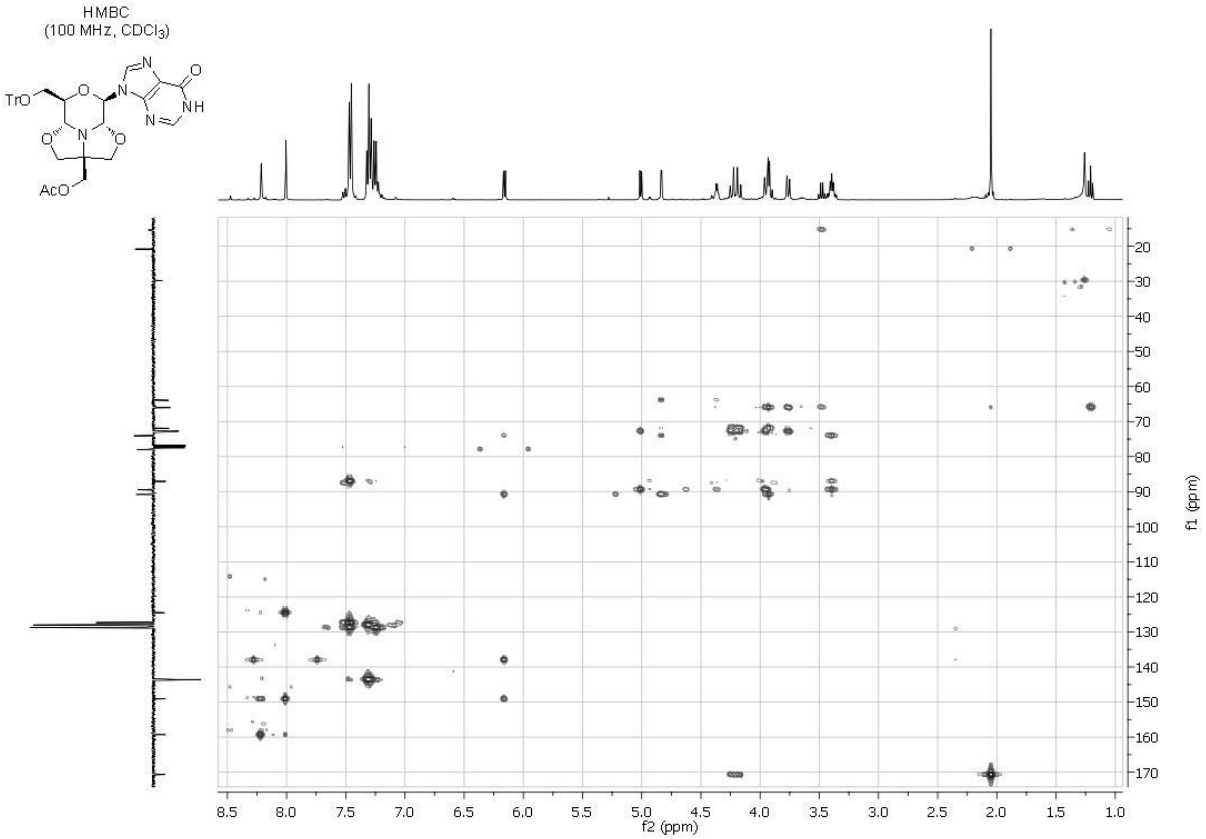


Figure S105. ^{1}H-^{13}C HMBC spectrum of compound 18b

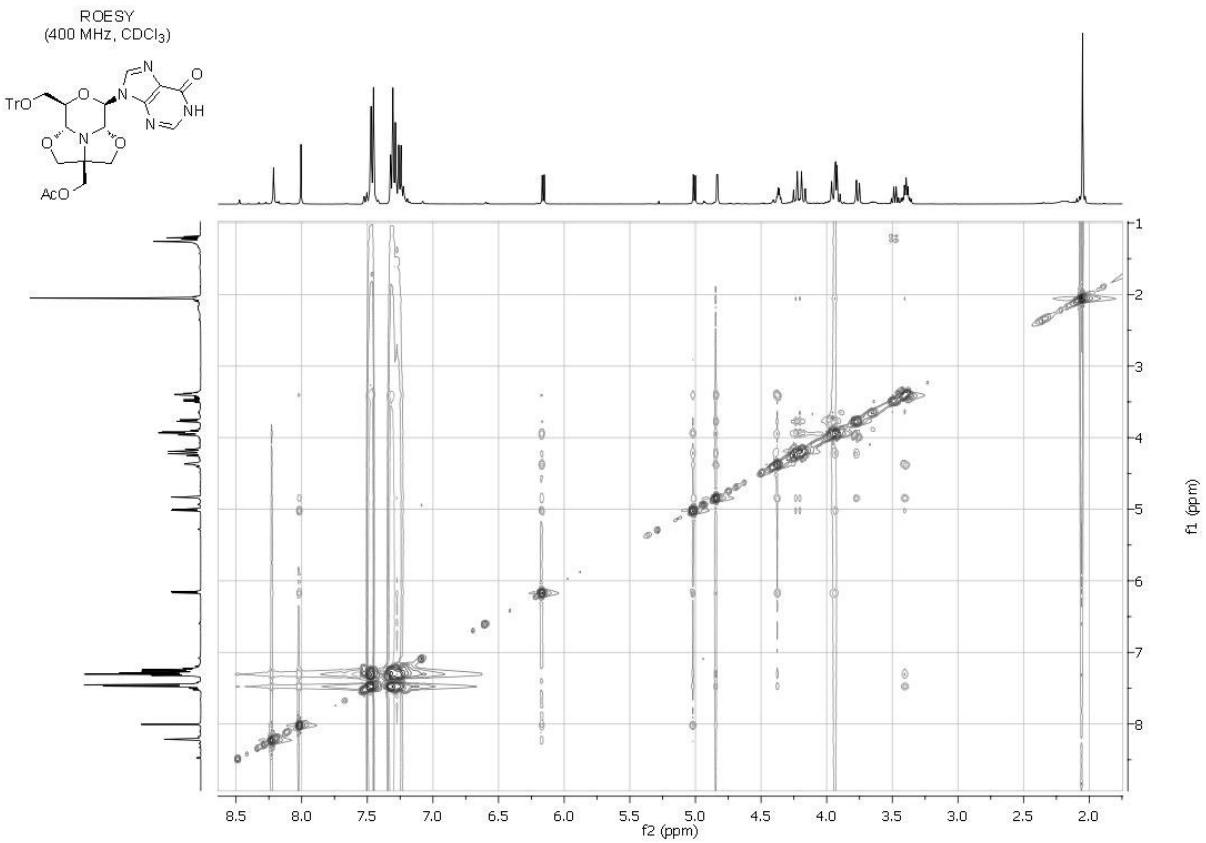


Figure S106. ^{1}H-^{1}H ROESY spectrum of compound 18b

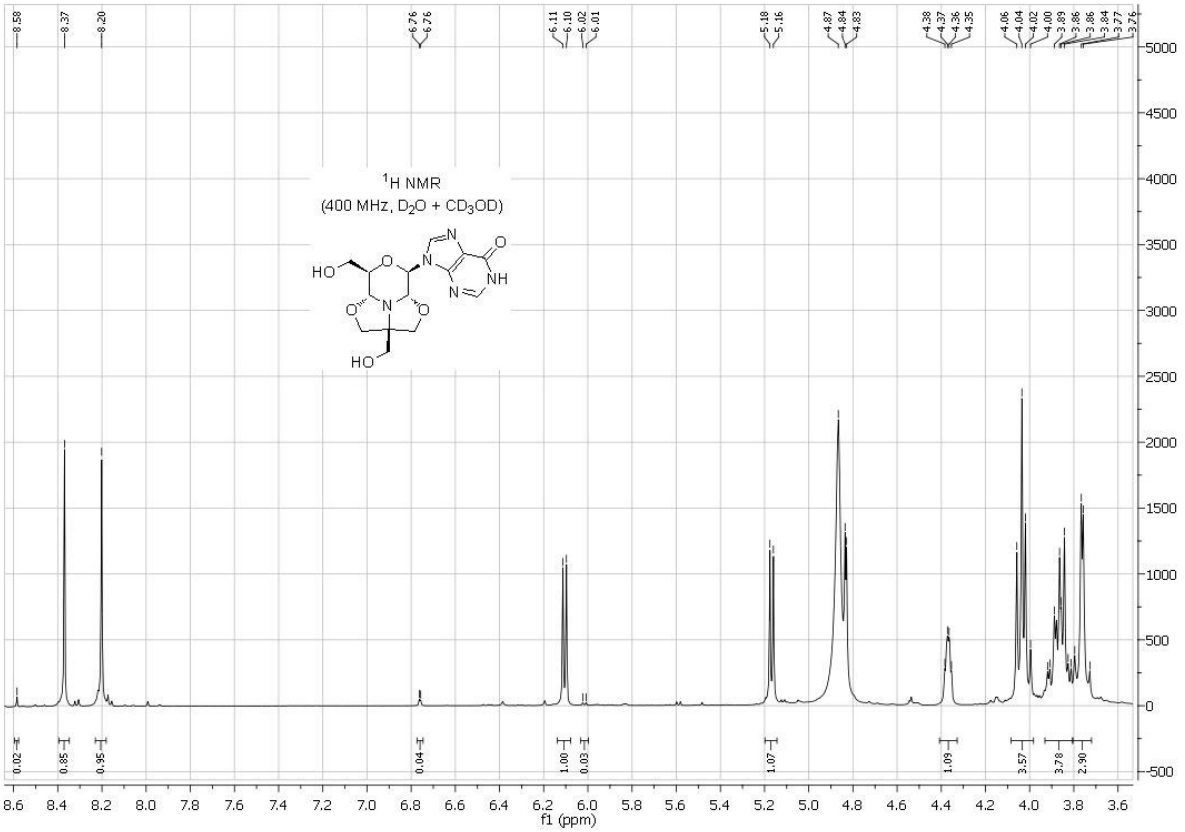


Figure S107. ^{1}H spectrum of compound 19 – Deprotection of compound 17b

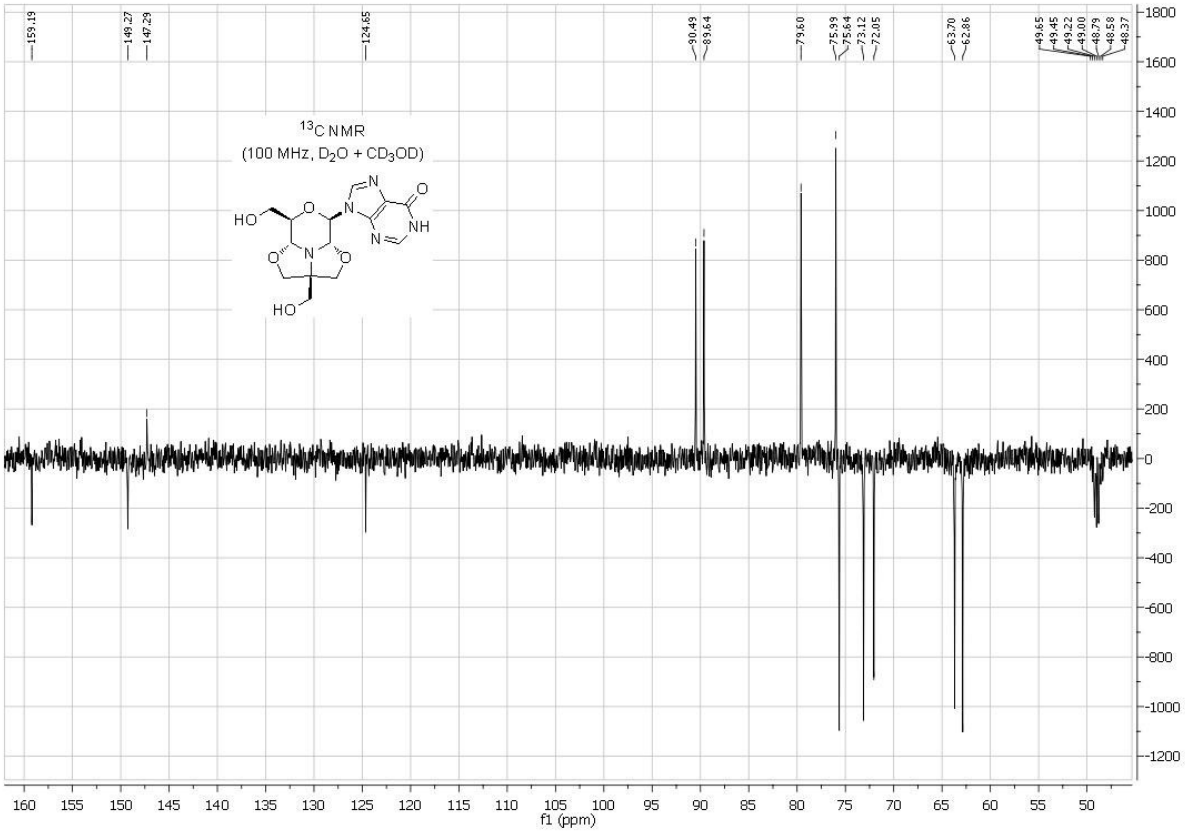


Figure S108. ^{13}C spectrum of compound 19 – Deprotection of compound 17b

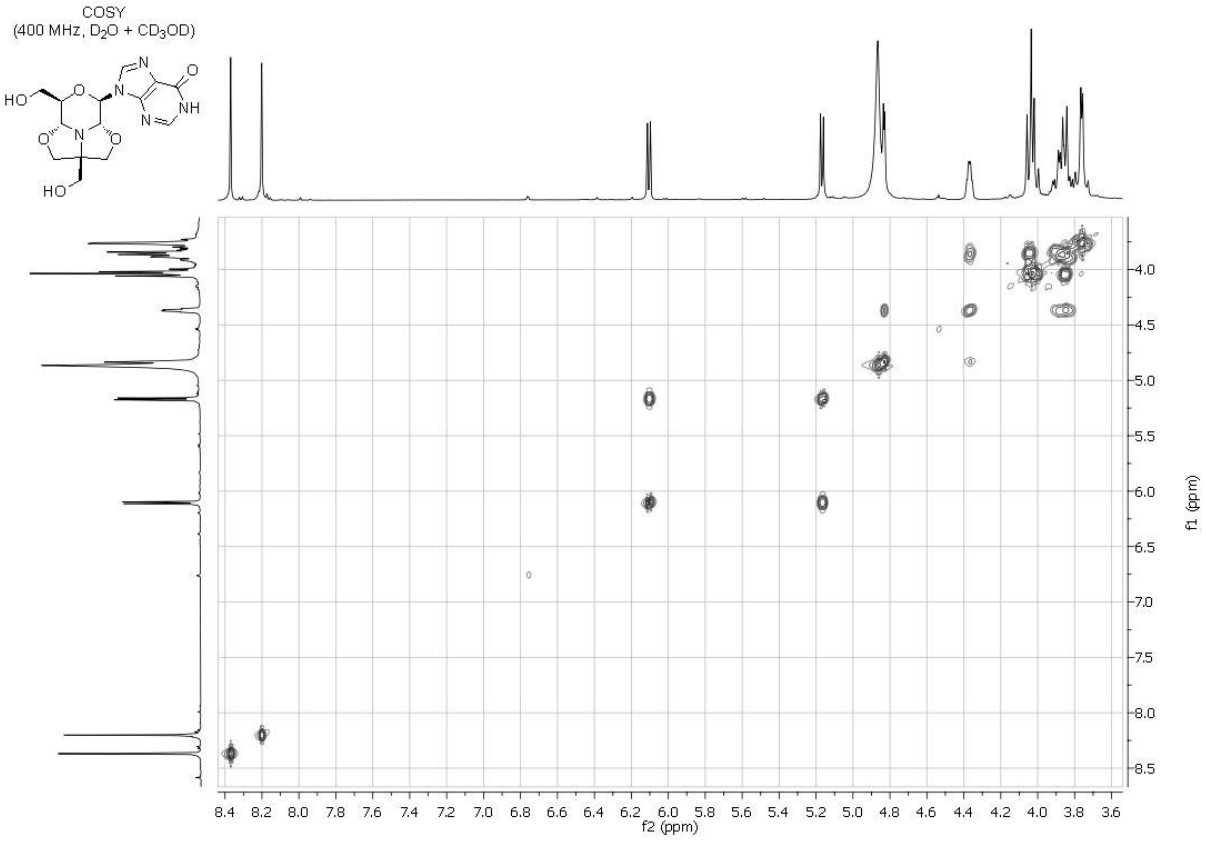


Figure S109. ^{1}H-^{1}H COSY spectrum of compound 19 – Deprotection of compound 17b

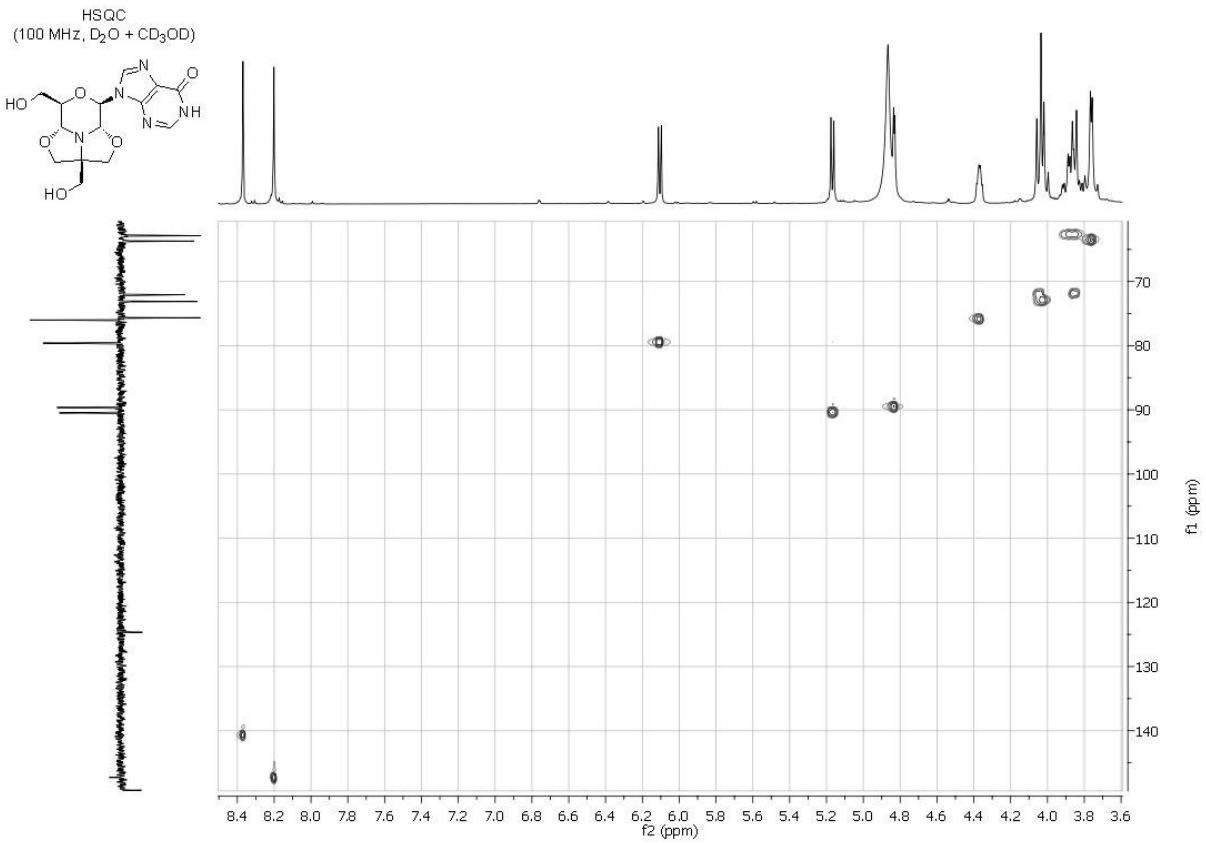


Figure S110. ^{1}H-^{13}C HSQC spectrum of compound 19 – Deprotection of compound 17b

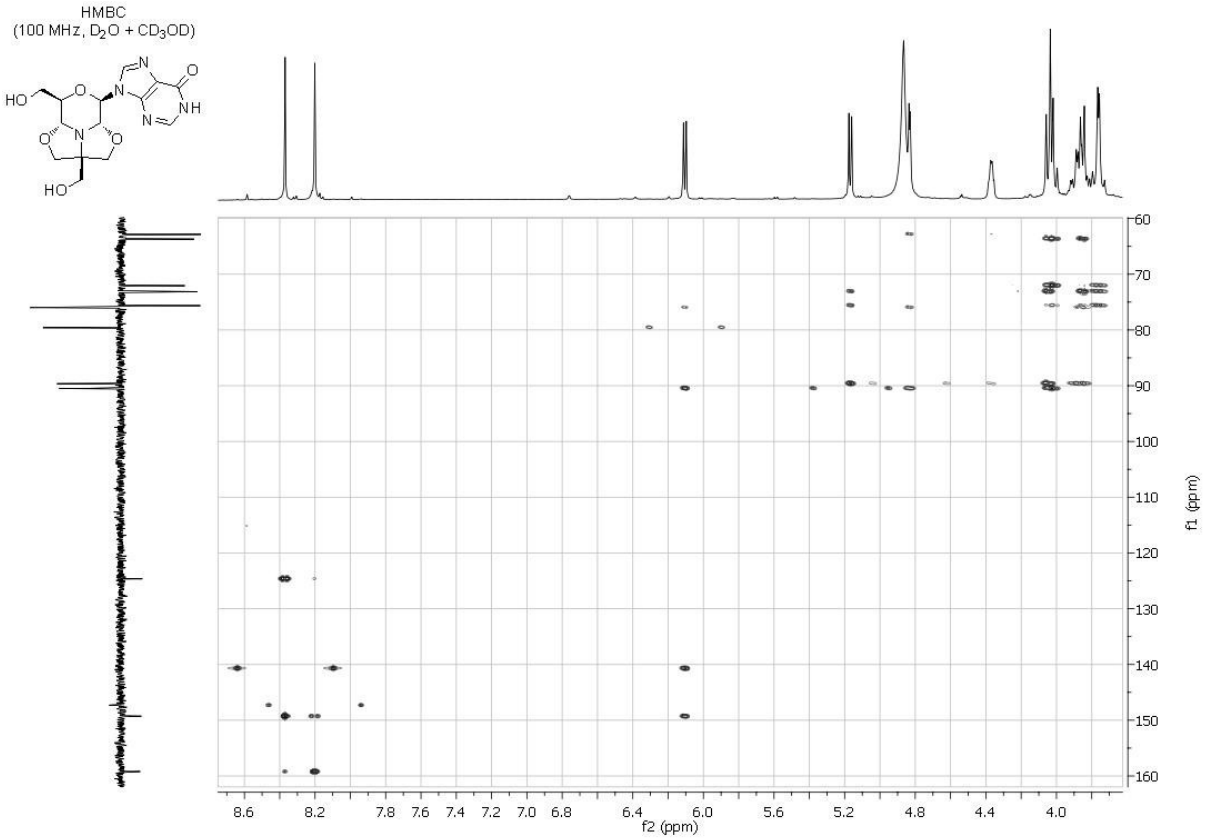


Figure S111. ^{1}H-^{13}C HMBC spectrum of compound 19 – Deprotection of compound 17b

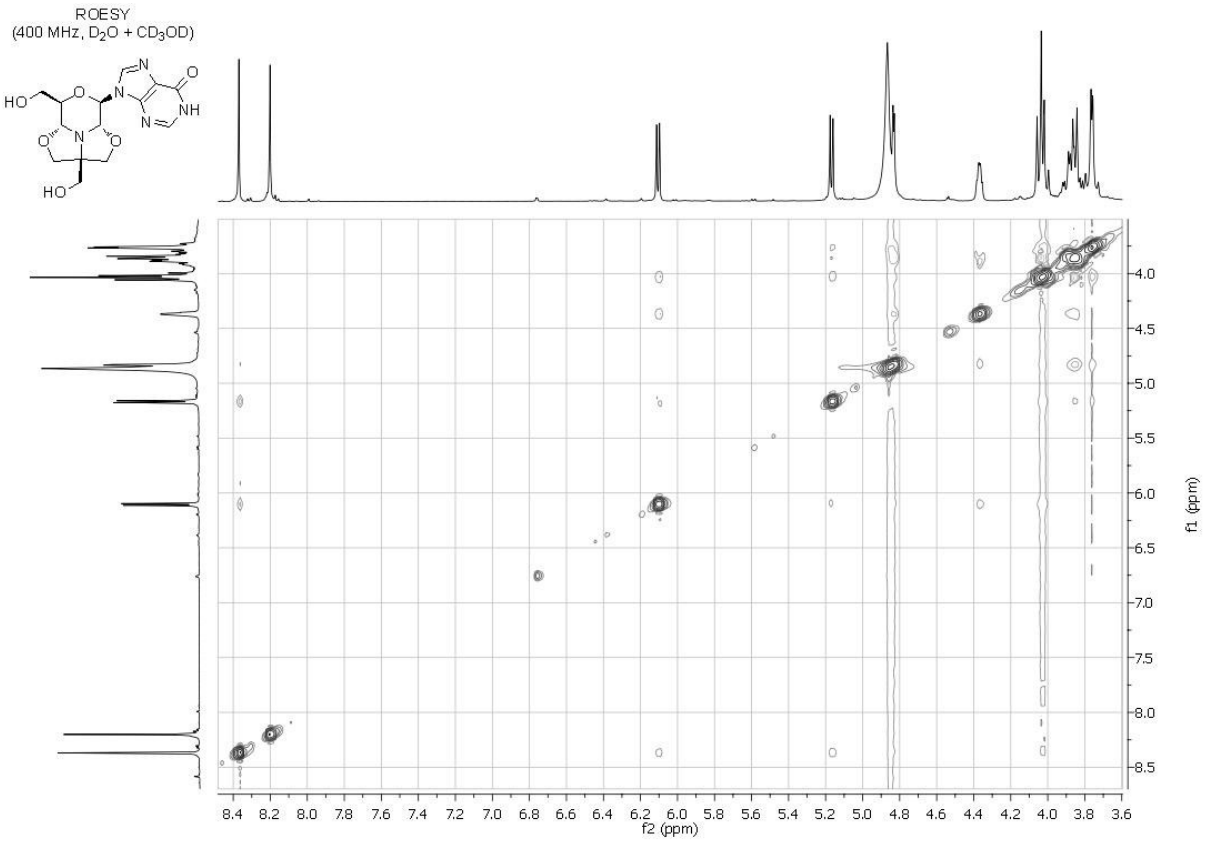


Figure S112. ^{1}H-^{1}H ROESY spectrum of compound 19 – Deprotection of compound 17b

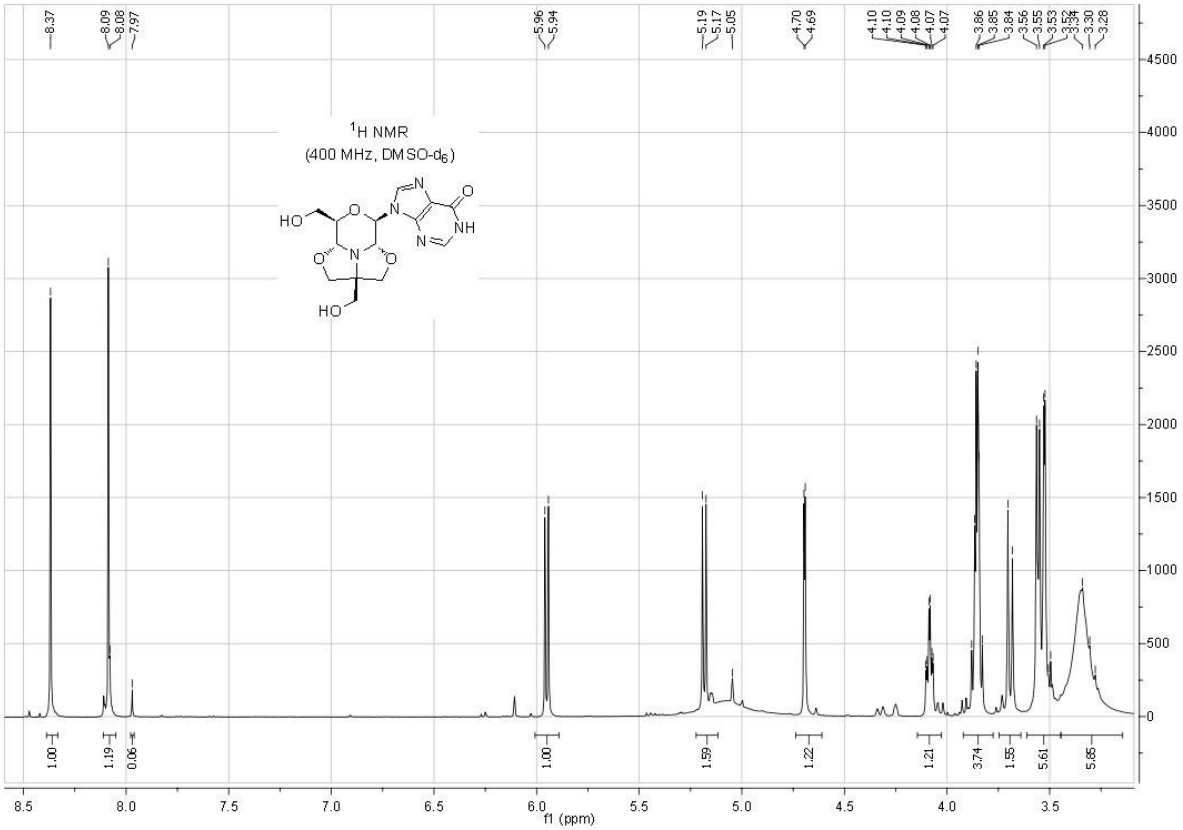


Figure S113. ^{1}H spectrum of compound 19 – Synthesis without protecting group

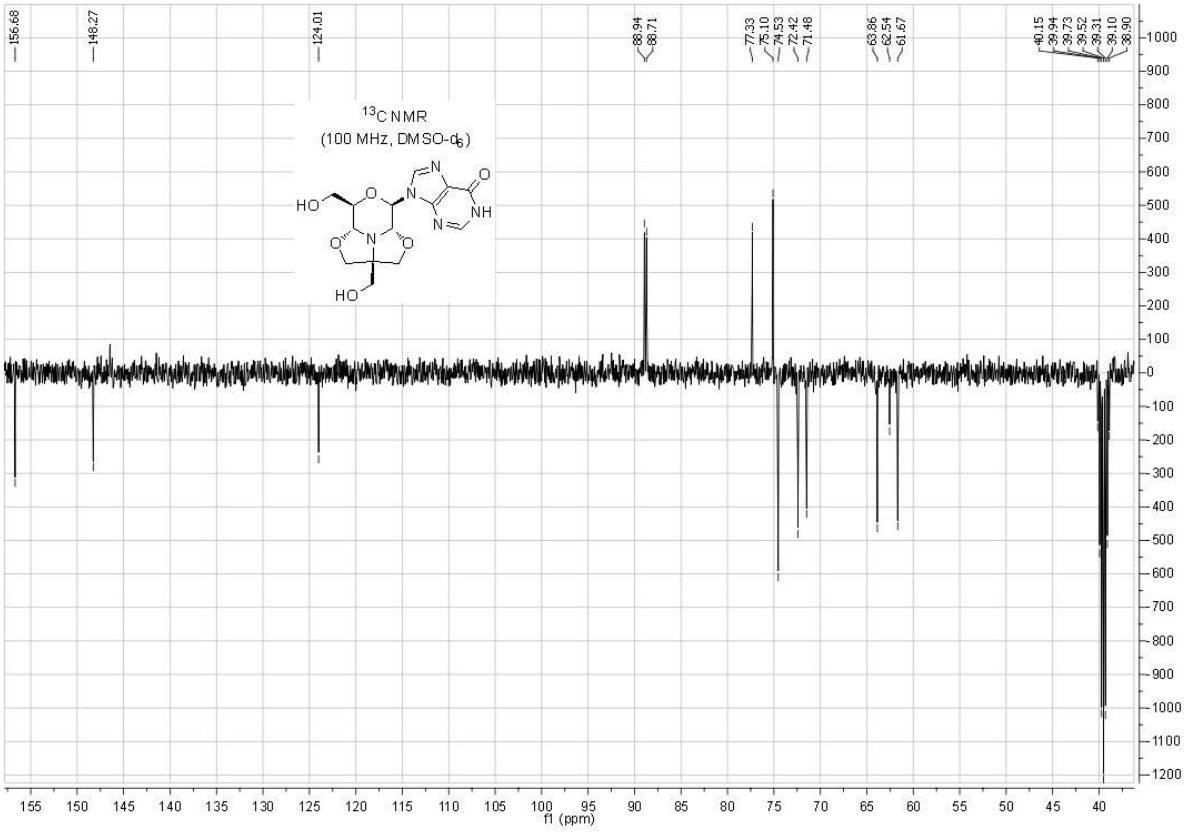


Figure S114. ^{13}C spectrum of compound 19 – Synthesis without protecting group

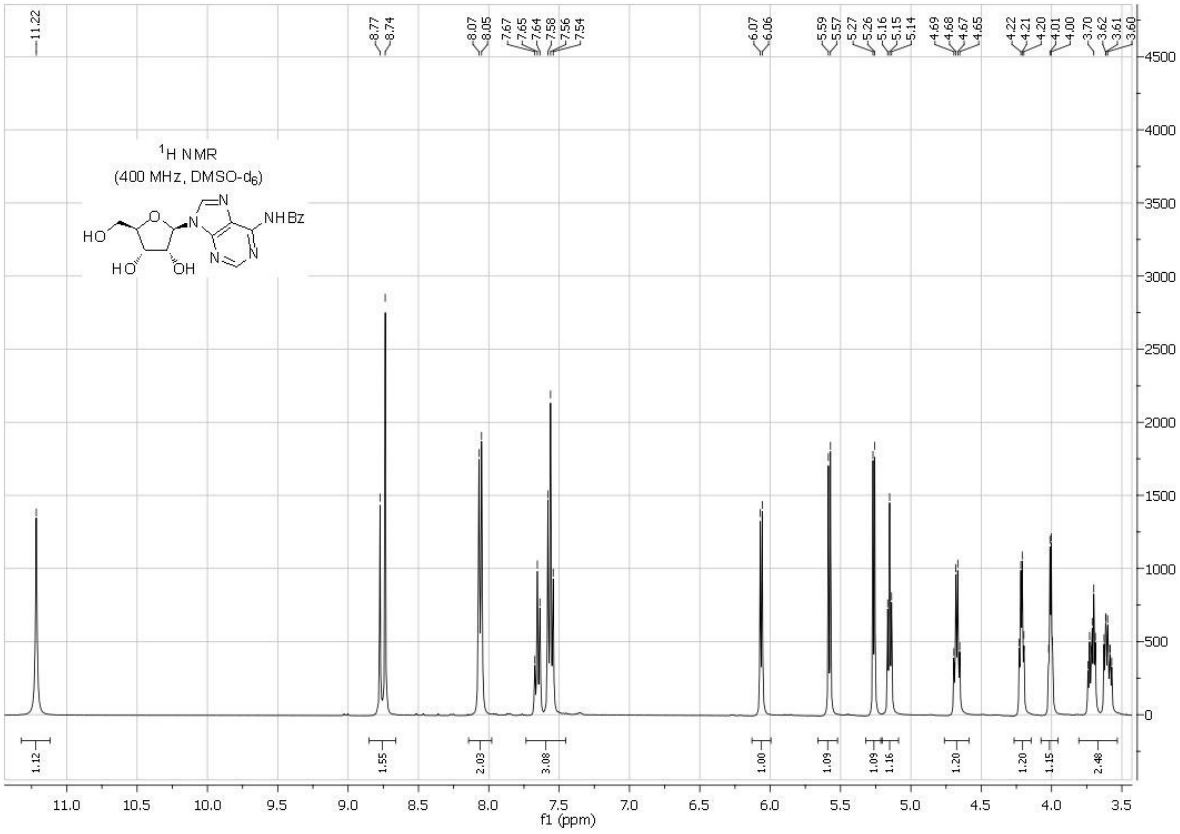


Figure S115. ^{1}H spectrum of compound 21

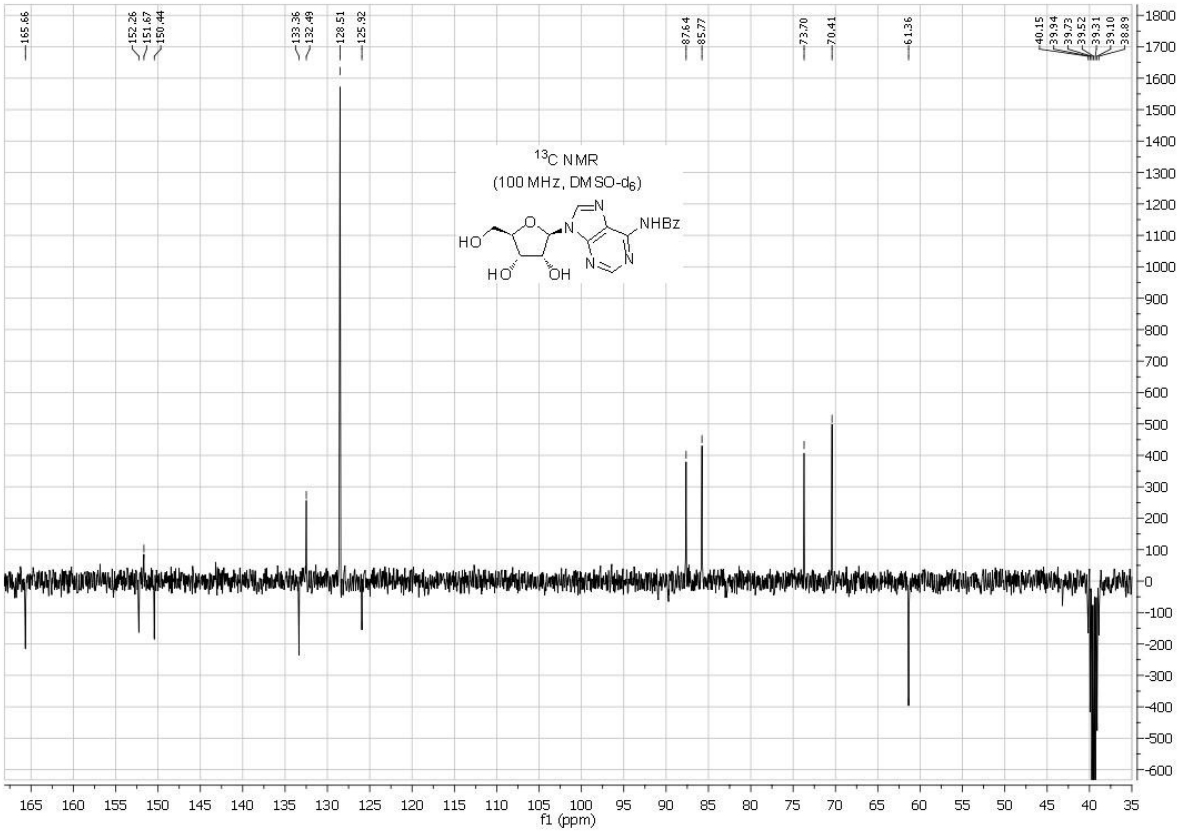


Figure S116. ^{13}C spectrum of compound 21

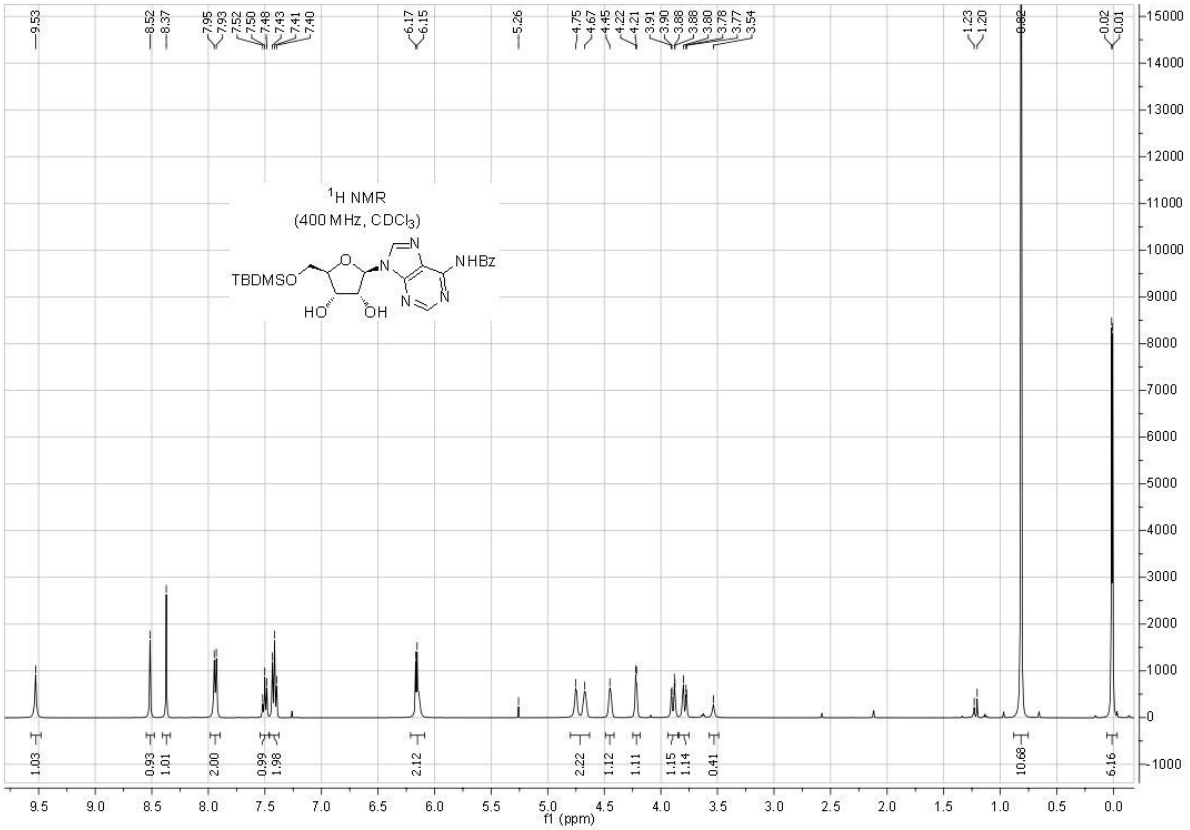


Figure S117. ^{1}H spectrum of compound 22a

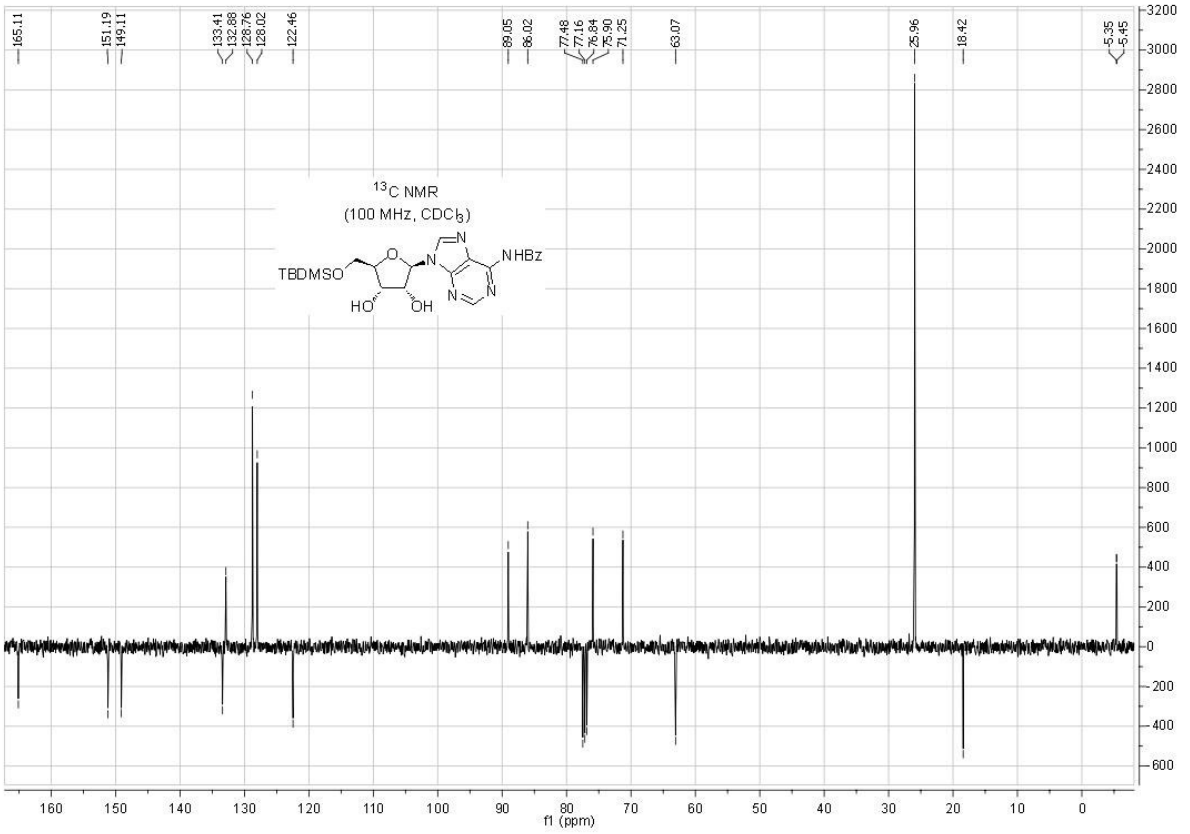


Figure S118. ^{13}C spectrum of compound 22a

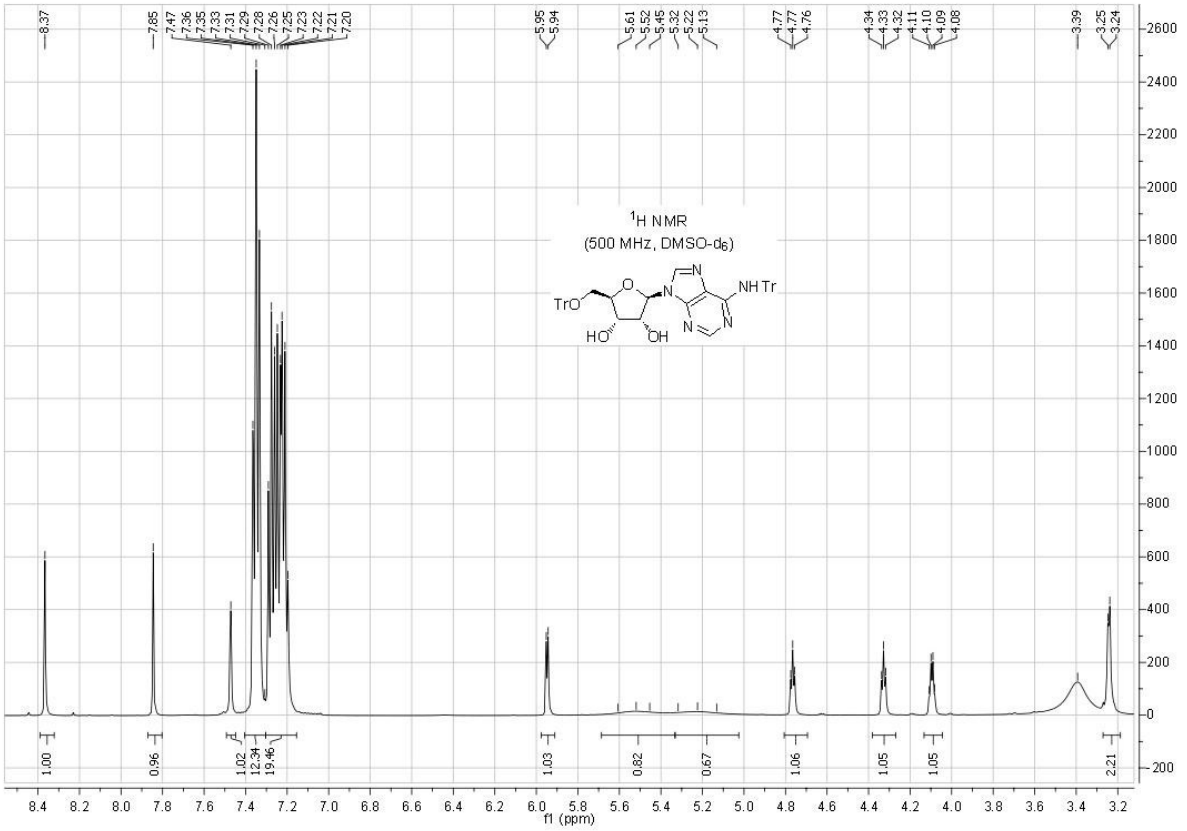


Figure S119. ^{1}H spectrum of compound 22b

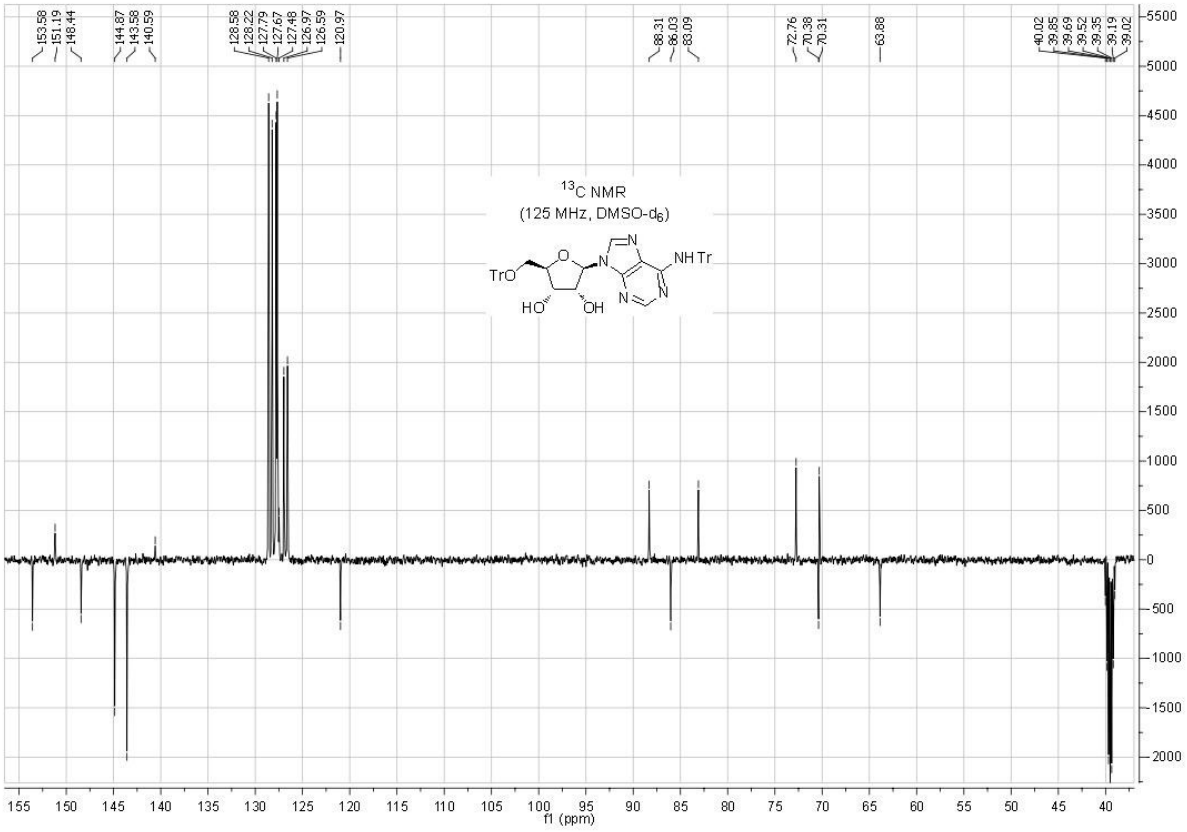


Figure S120. ^{13}C spectrum of compound 22b

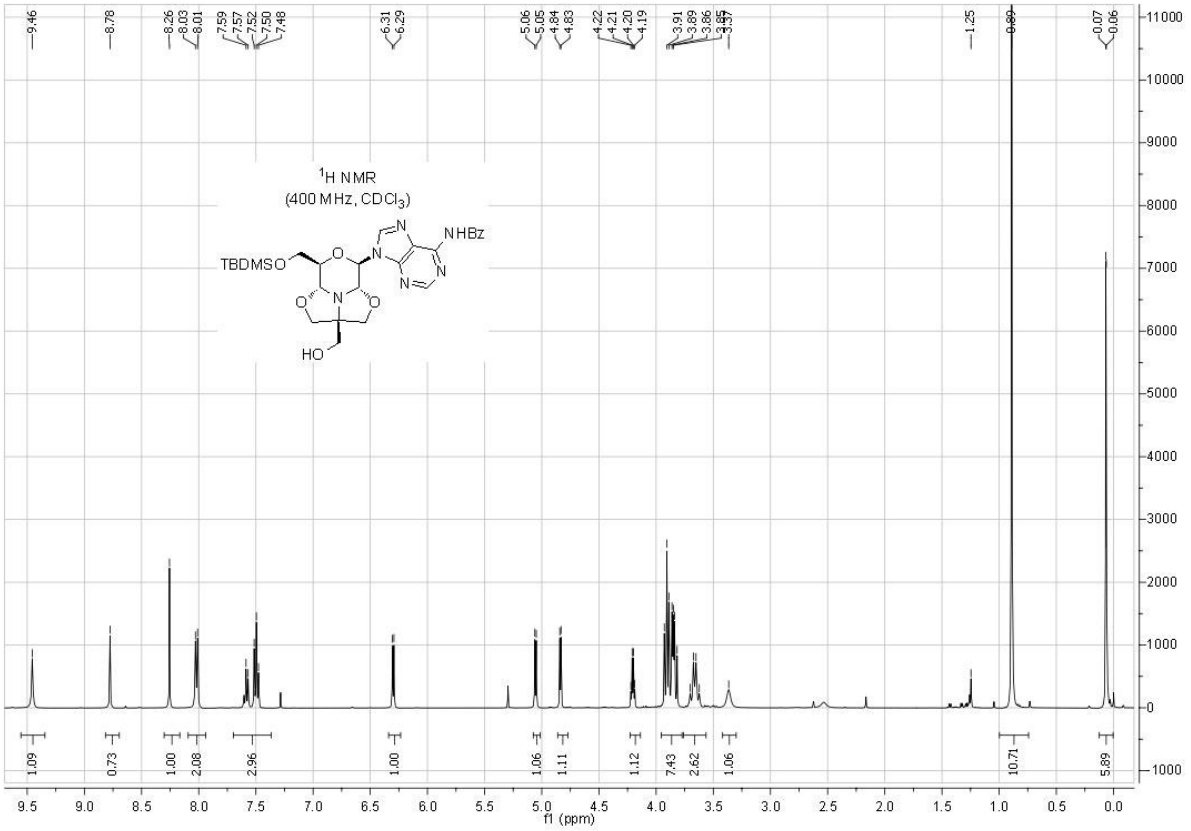


Figure S121. ^{1}H spectrum of compound 23a

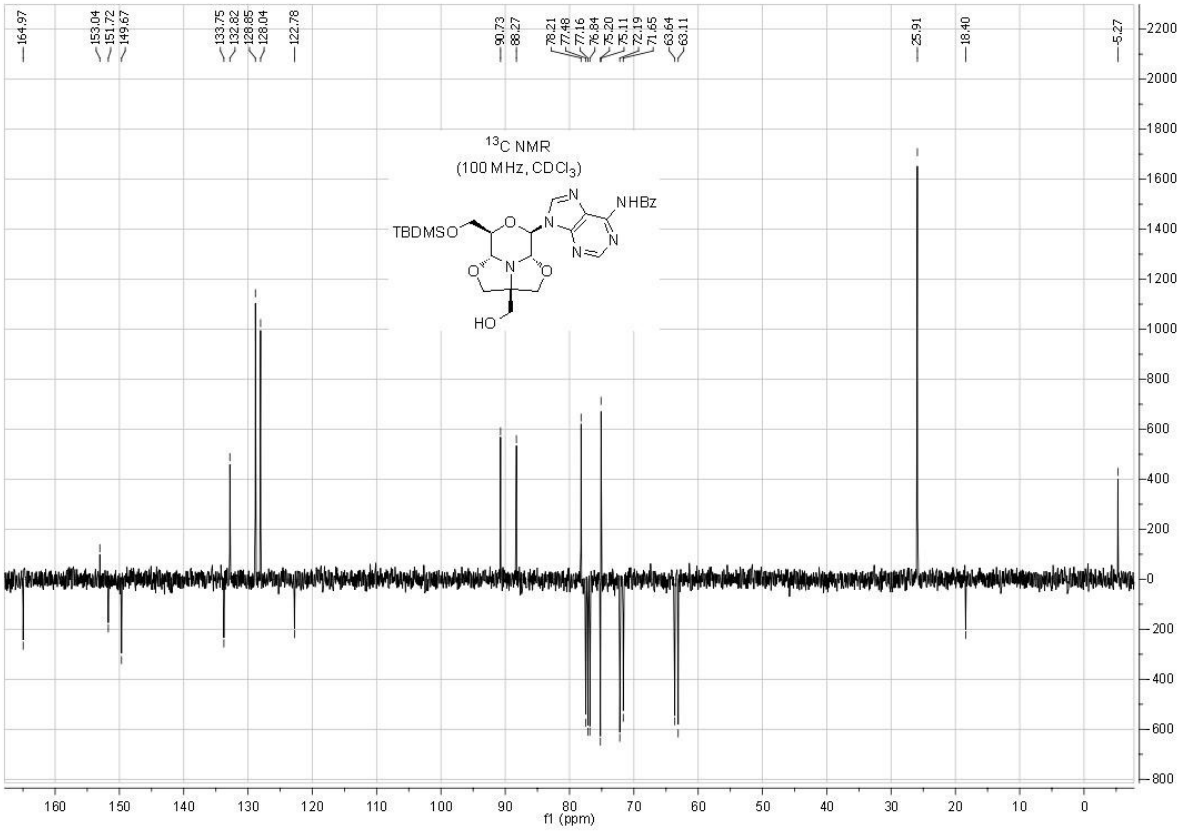


Figure S122. ^{13}C spectrum of compound 23a

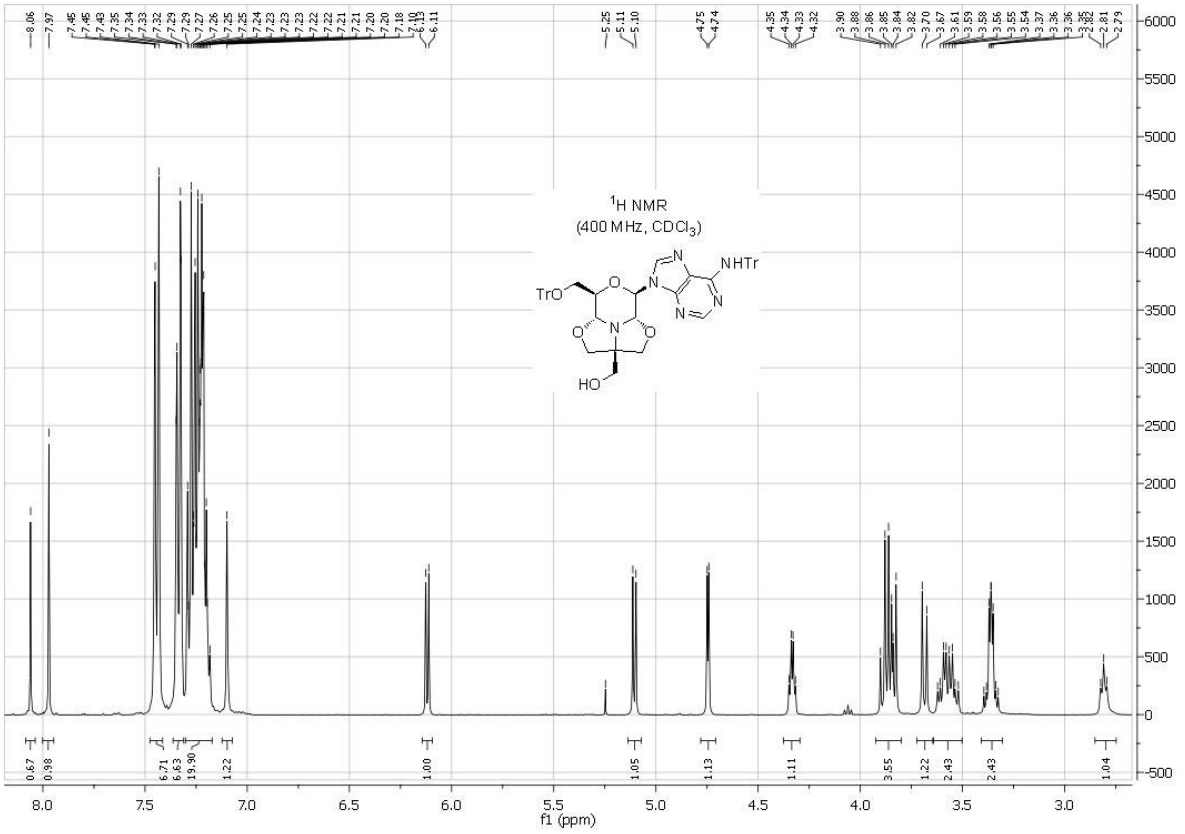


Figure S123. ^{1}H spectrum of compound 23b

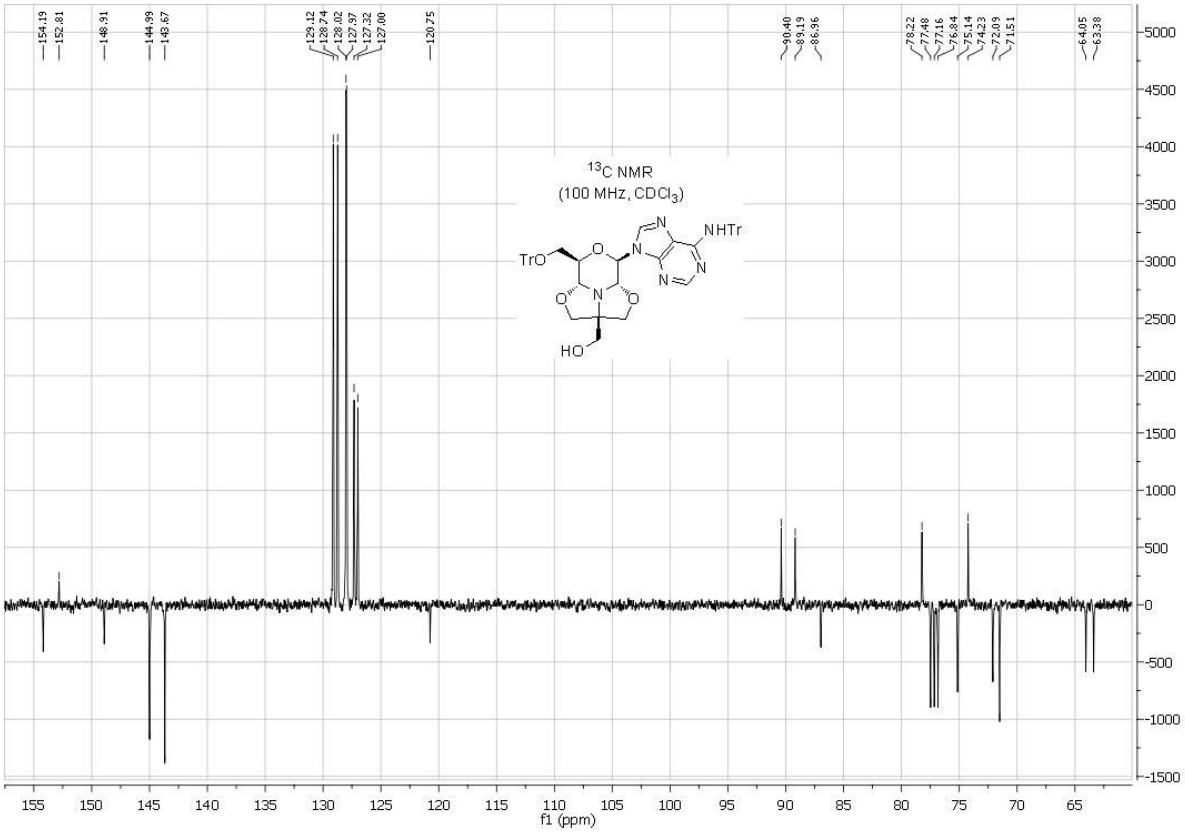


Figure S124. ^{13}C spectrum of compound 23b

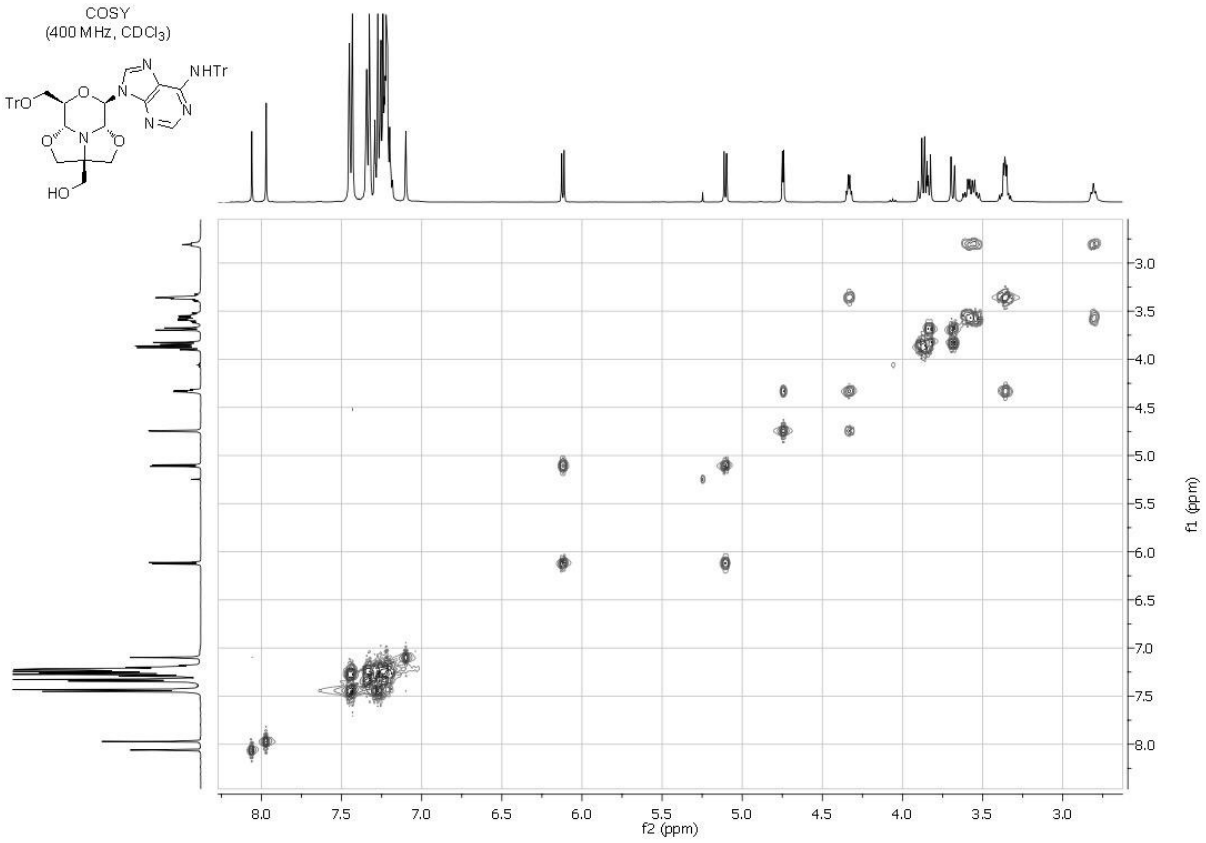


Figure S125. ^{1}H-^{1}H COSY spectrum of compound 23b

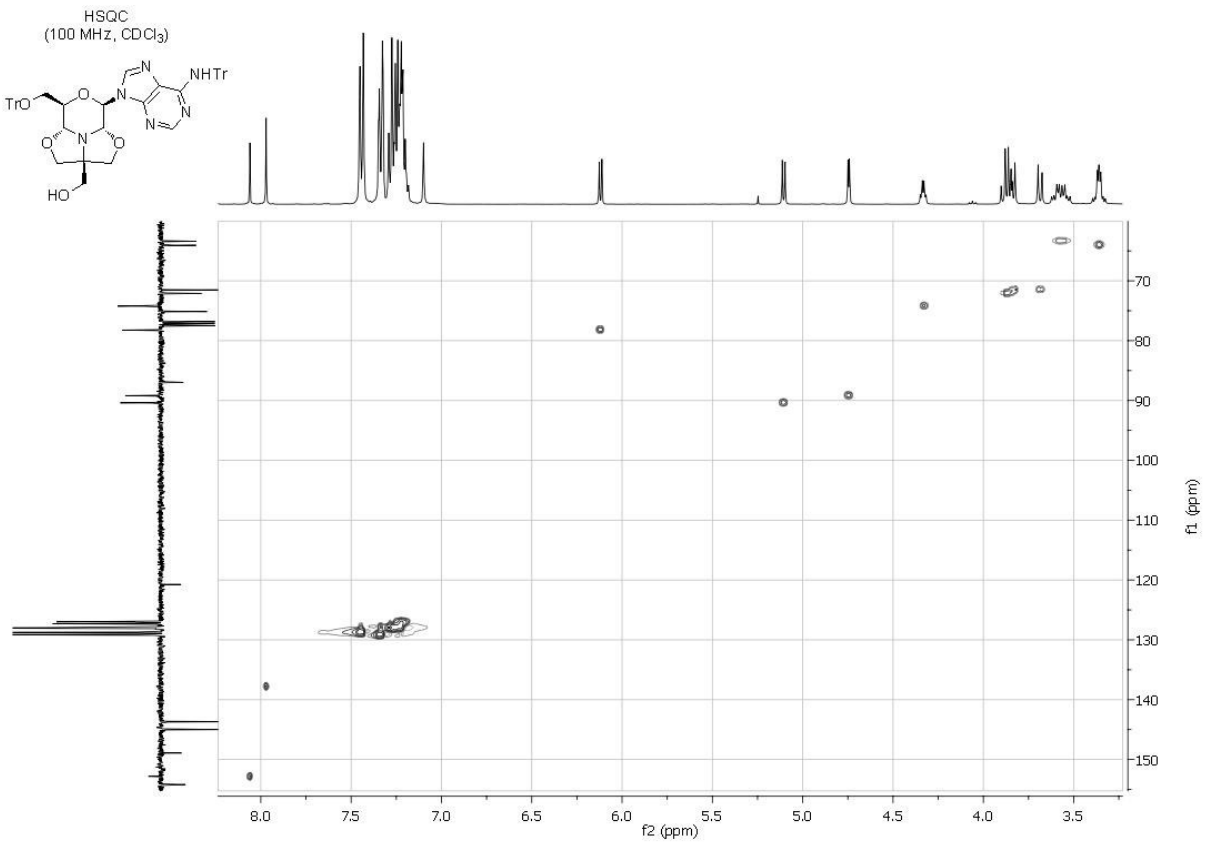


Figure S126. ^{1}H-^{13}C HSQC spectrum of compound 23b

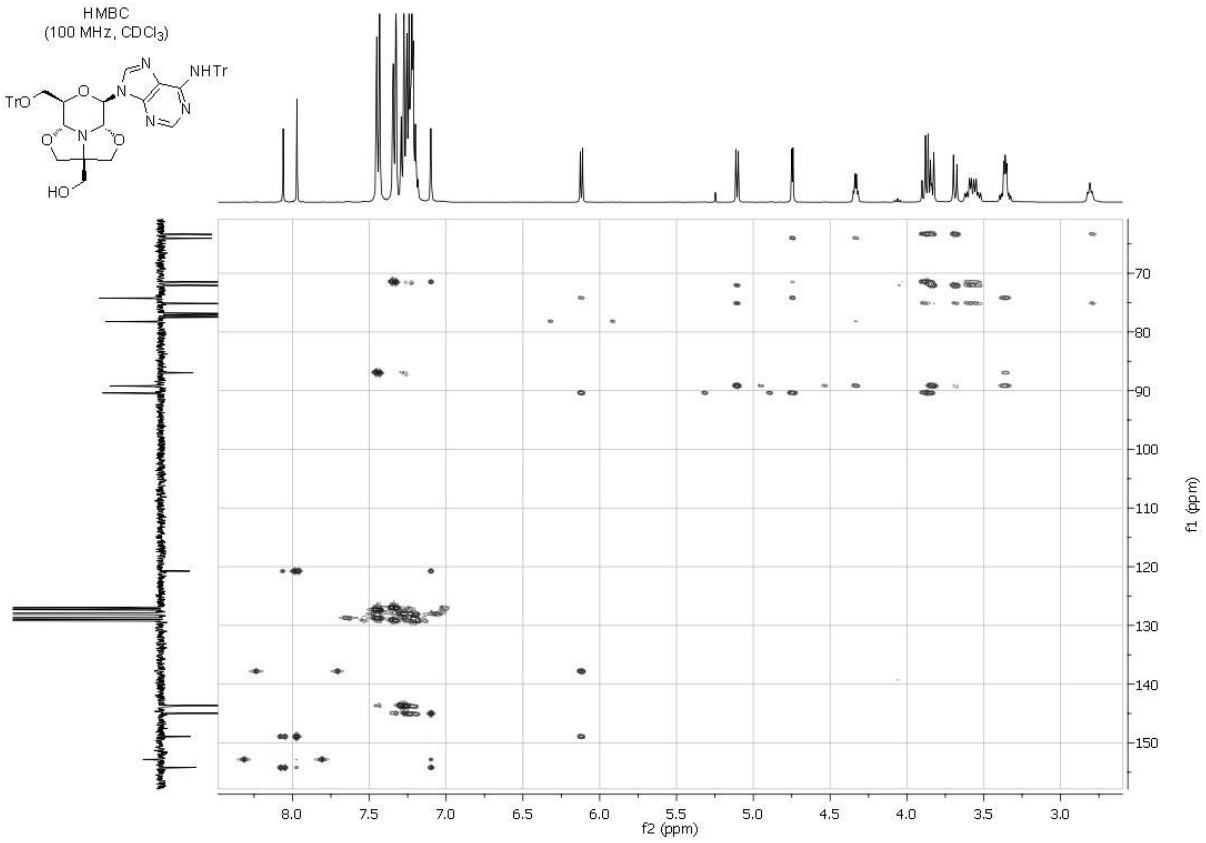


Figure S127. ^{1}H-^{13}C HMBC spectrum of compound 23b

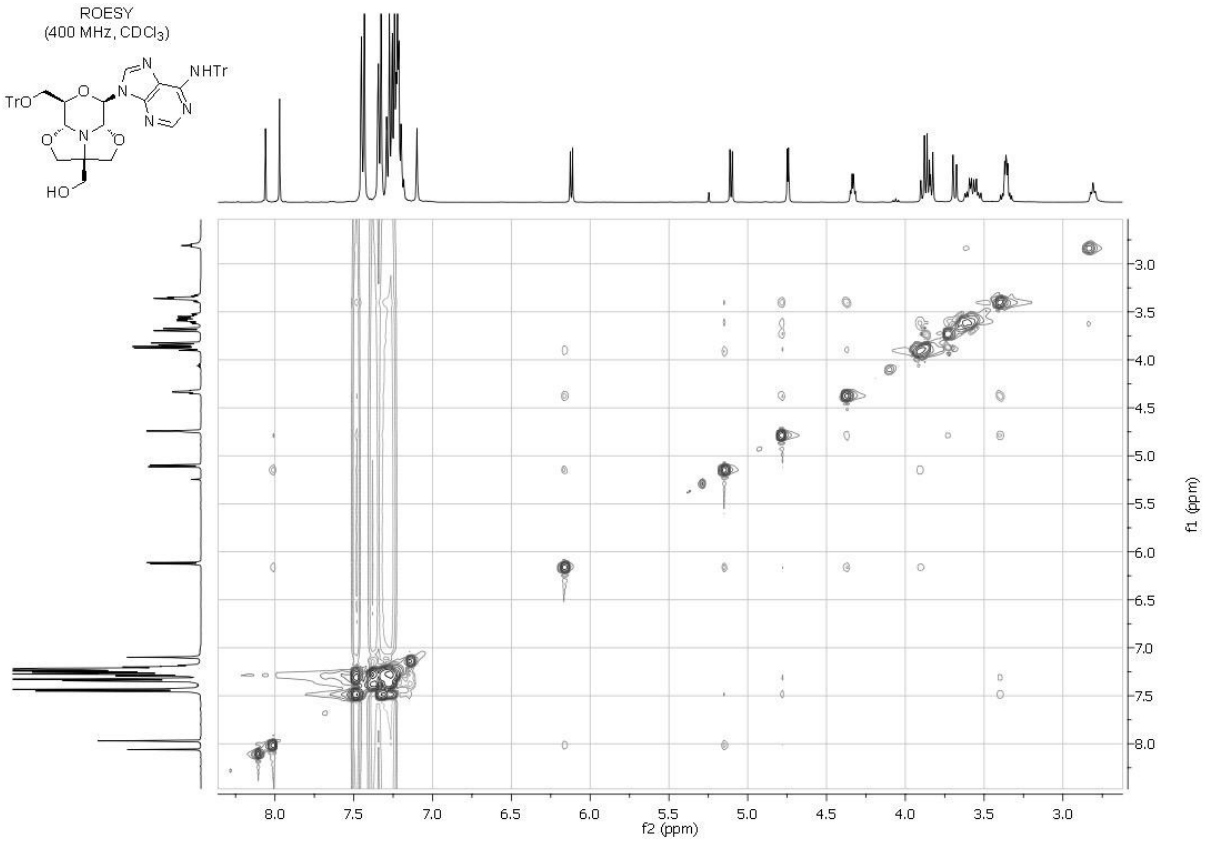


Figure S128. ^{1}H-^{1}H ROESY spectrum of compound 23b

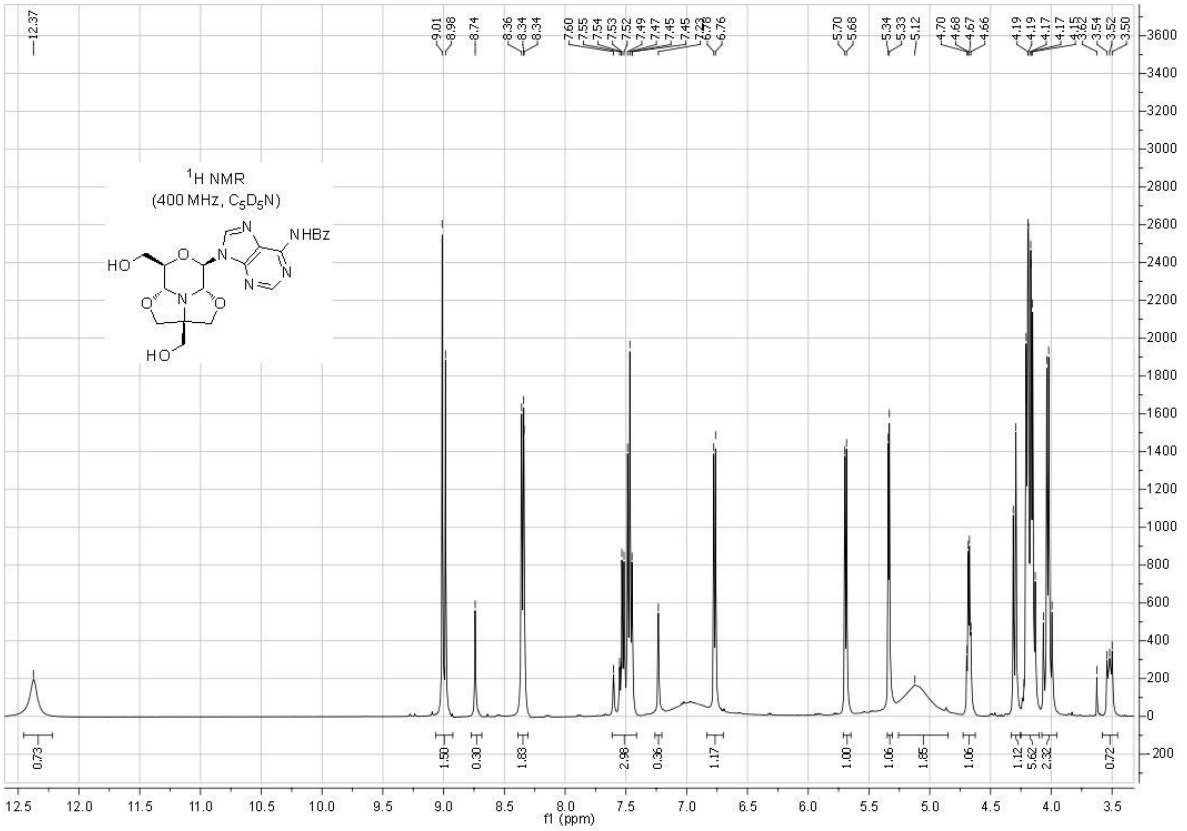


Figure S129. ^{1}H spectrum of compound 24a

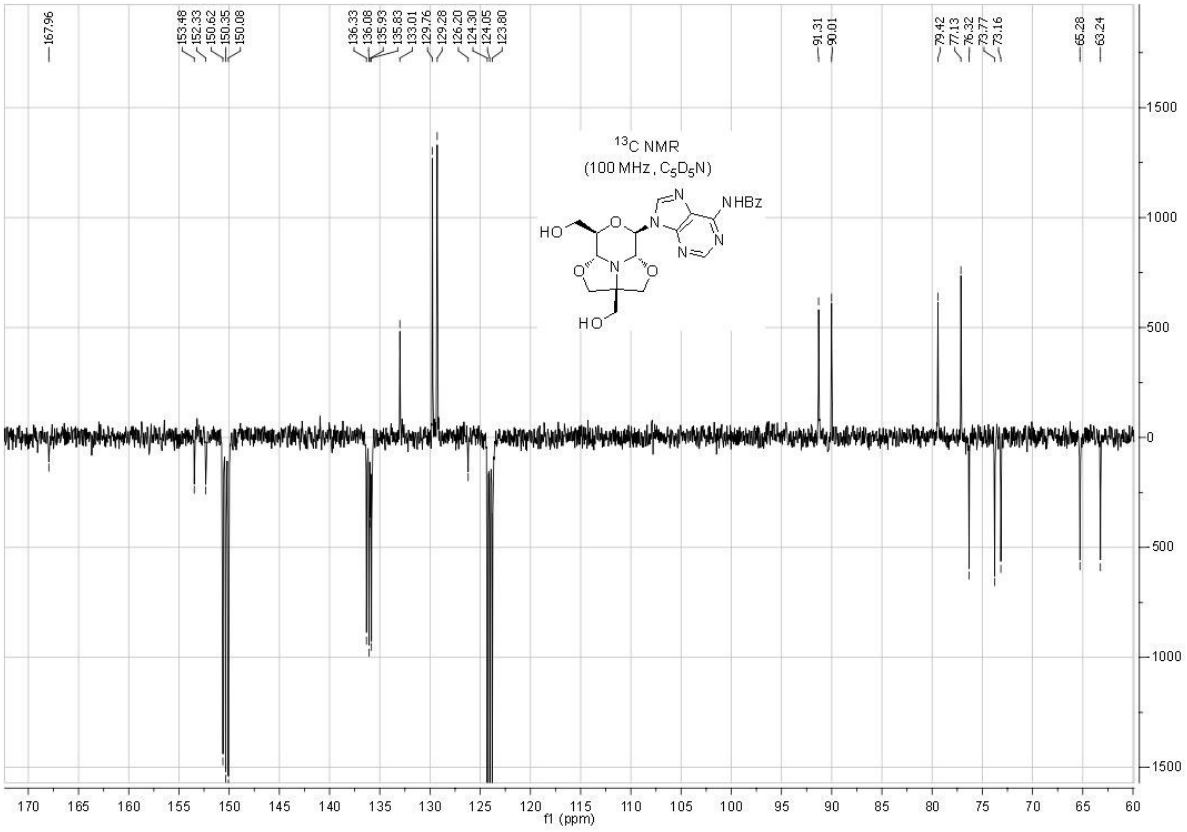


Figure S130. ^{13}C spectrum of compound 24a

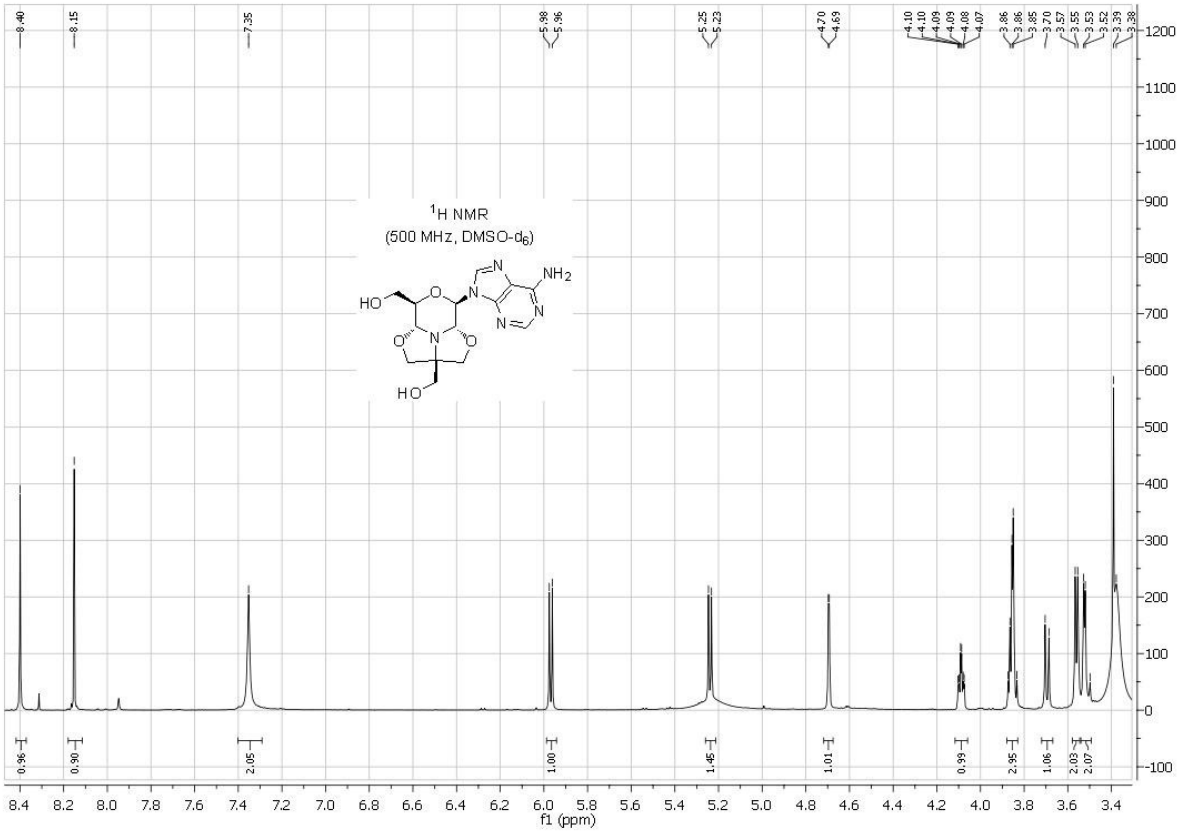


Figure S131. ^{1}H spectrum of compound 25

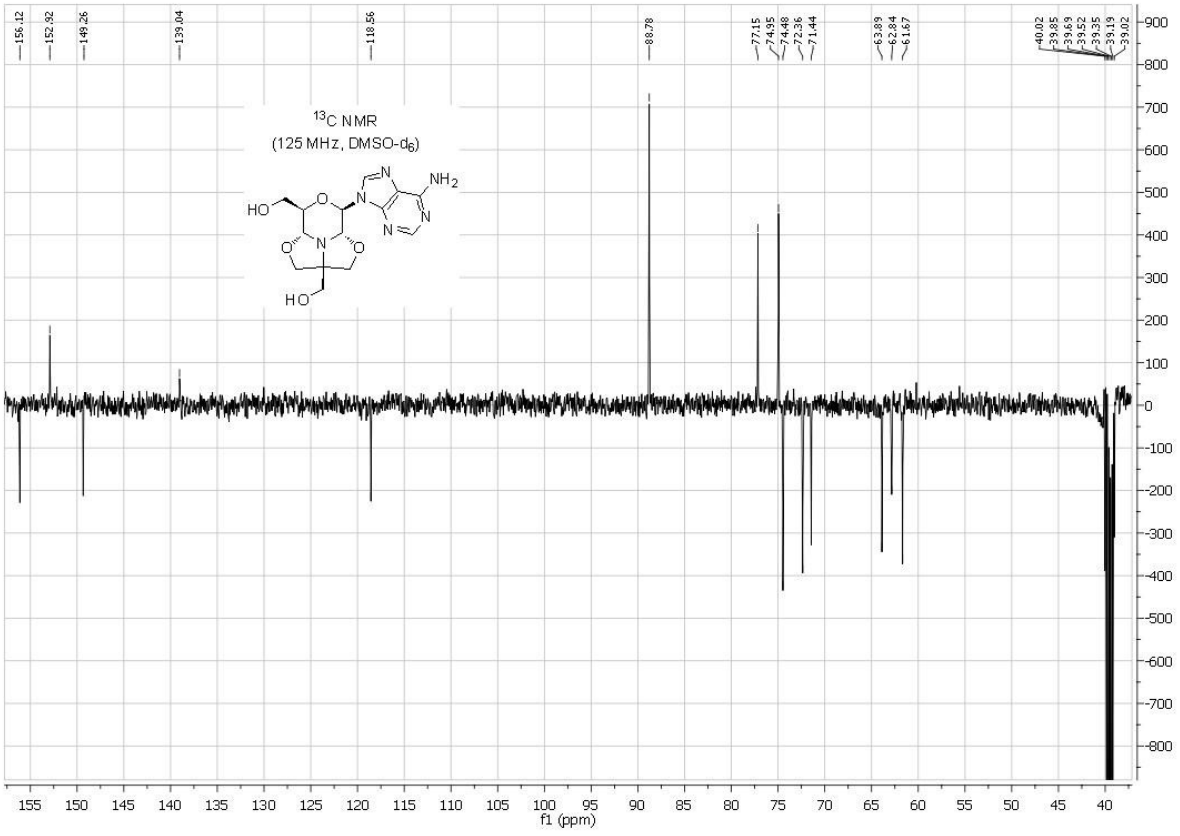


Figure S132. ^{13}C spectrum of compound 25

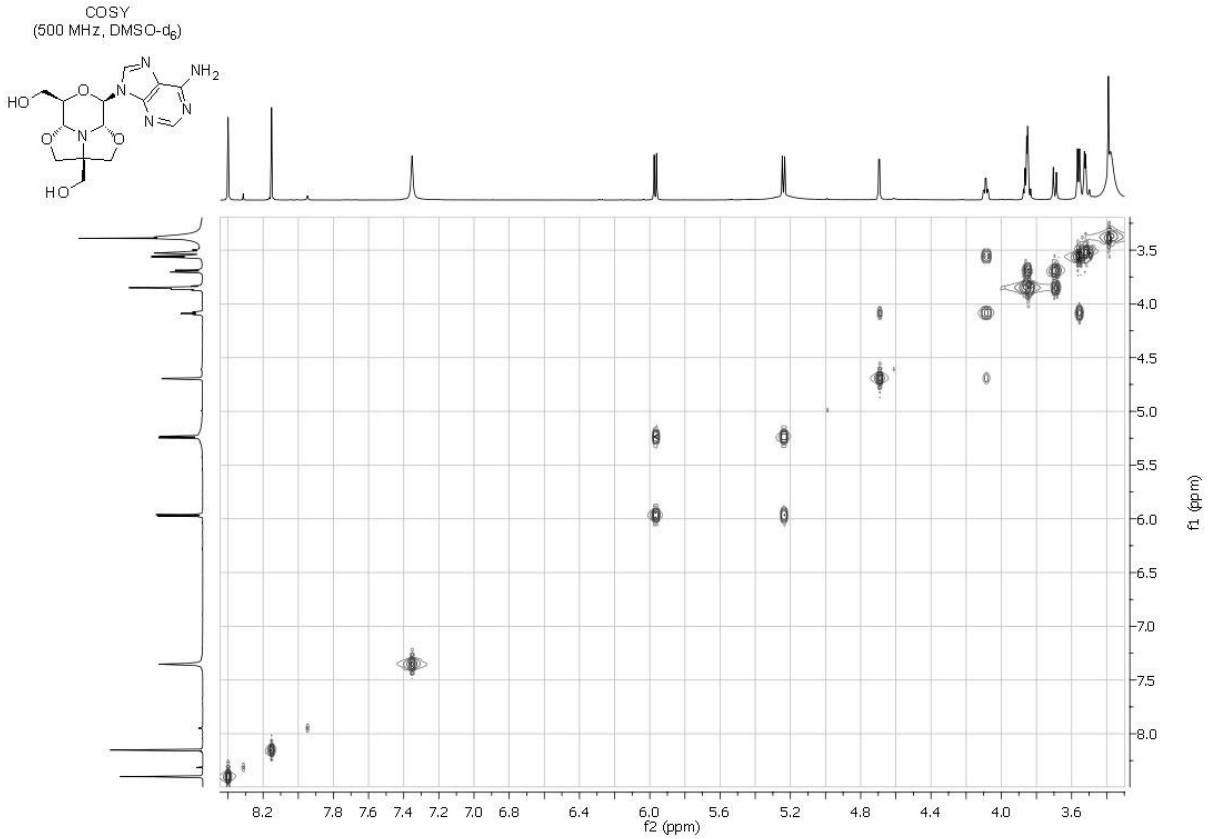


Figure S133. ^{1}H-^{1}H COSY spectrum of compound 25

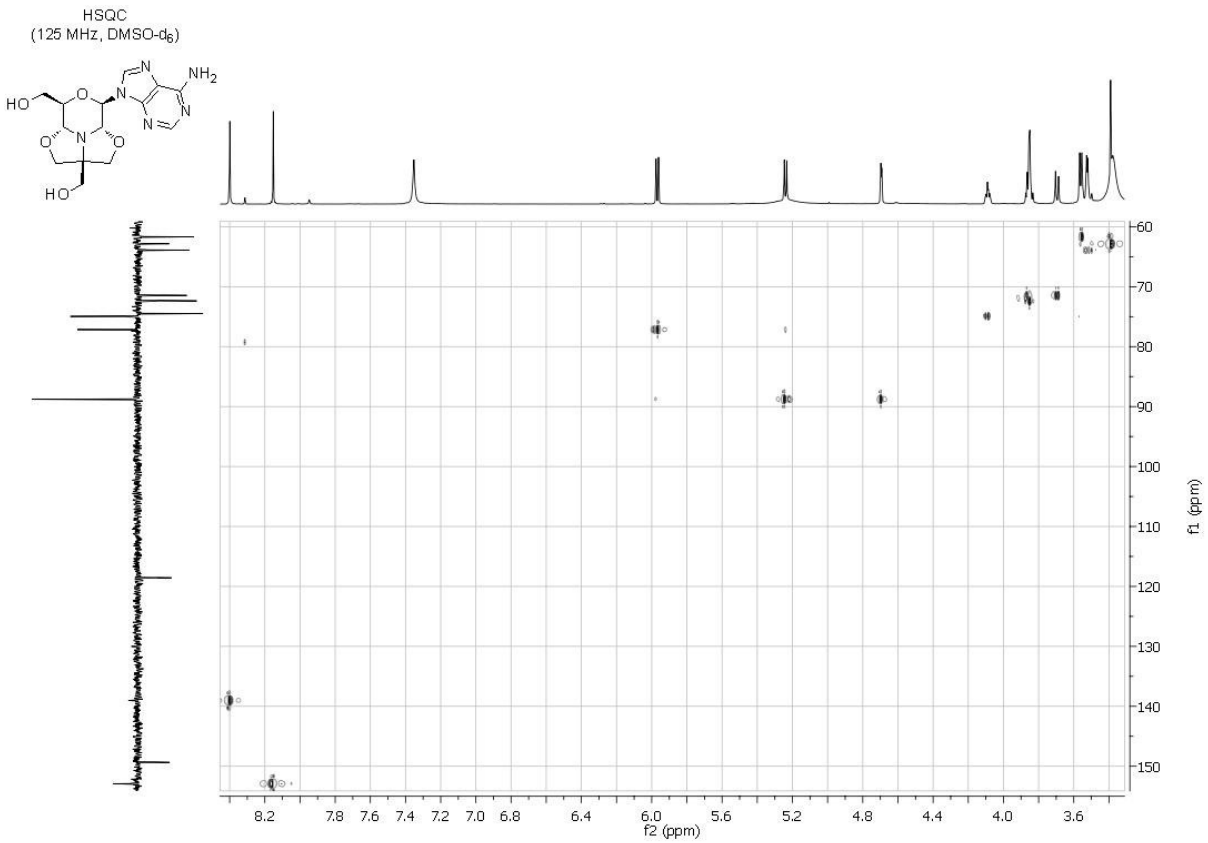


Figure S134. ^{1}H-^{13}C HSQC spectrum of compound 25

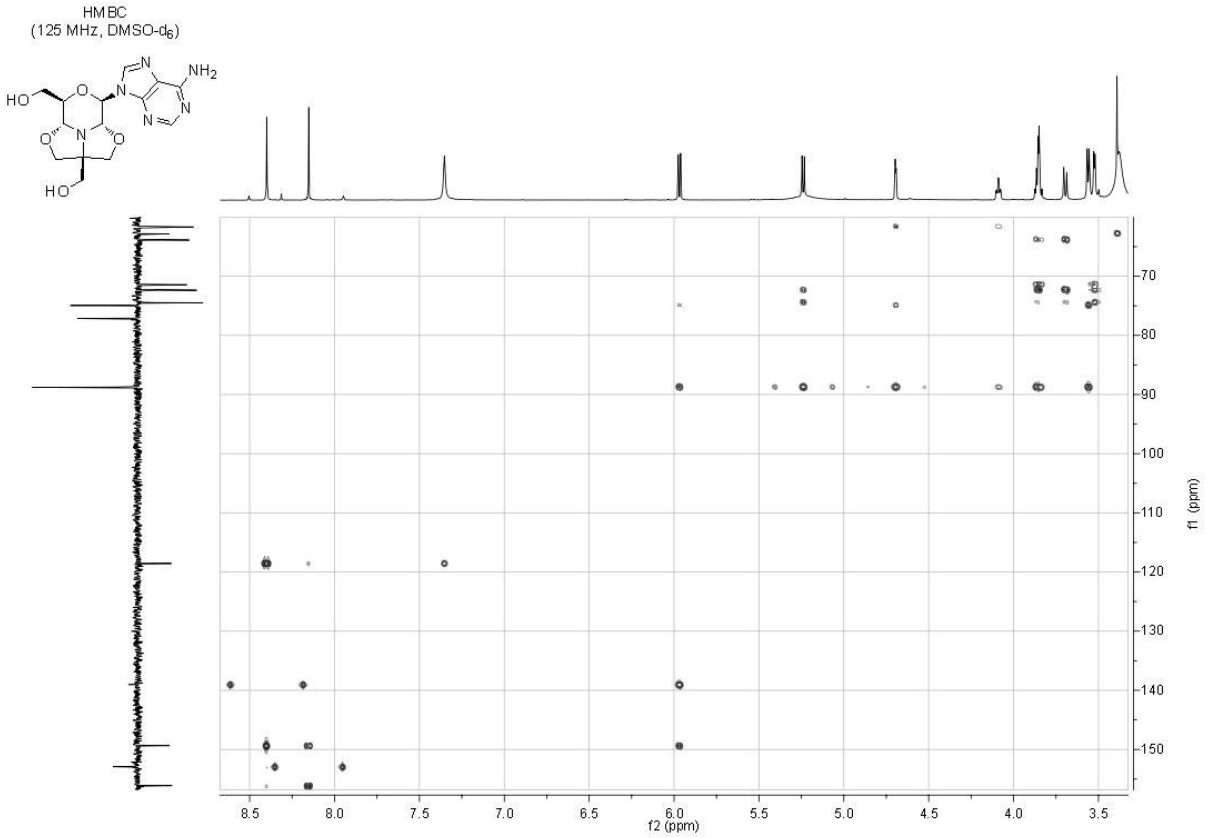


Figure S135. ^{1}H-^{13}C HMBC spectrum of compound 25

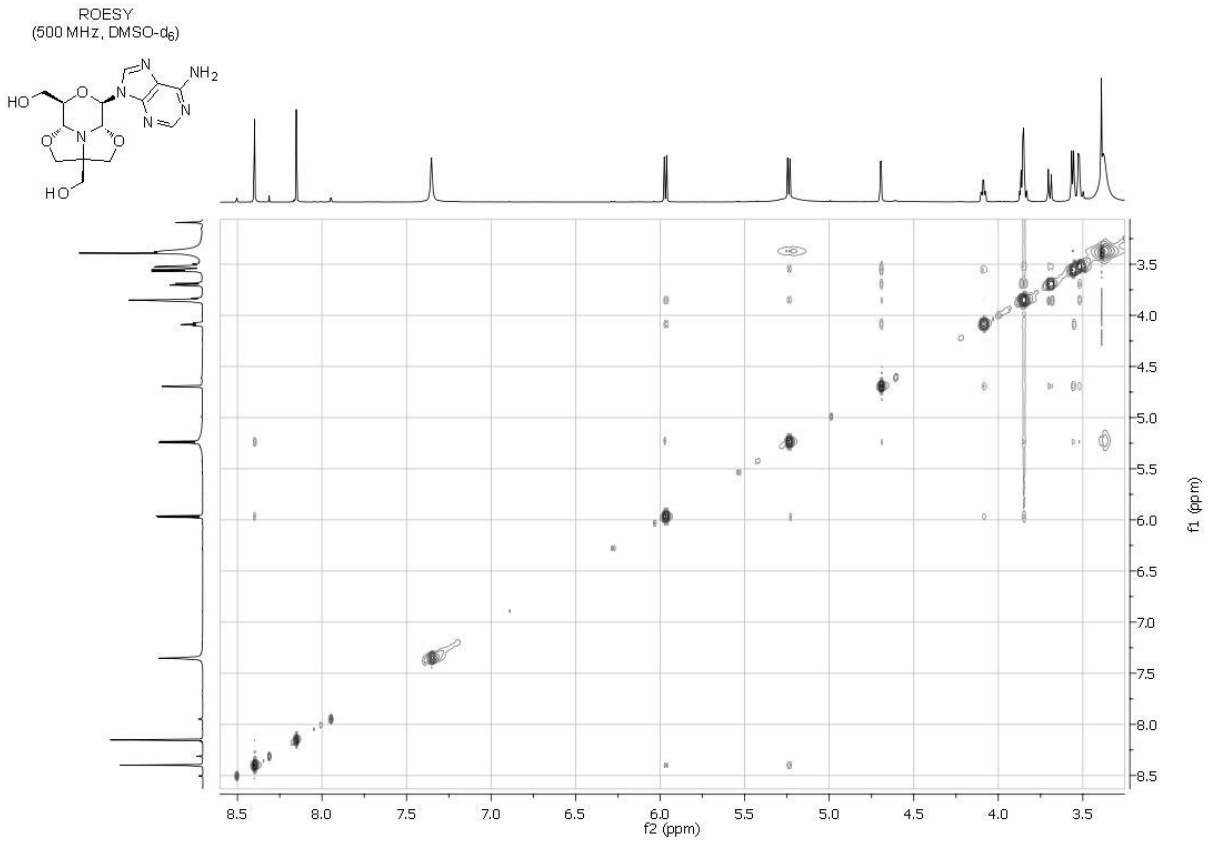


Figure S136. ^{1}H-^{1}H ROESY spectrum of compound 25

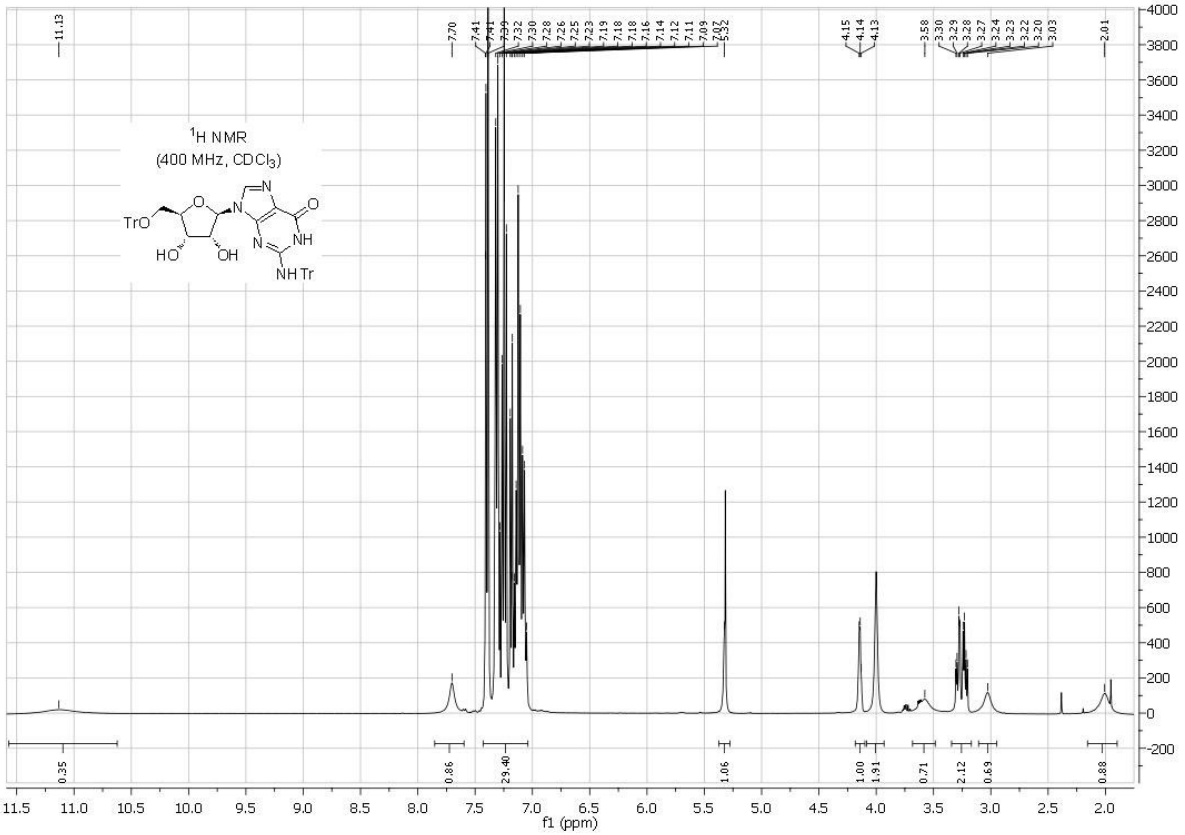


Figure S137. ^{1}H spectrum of compound 27a

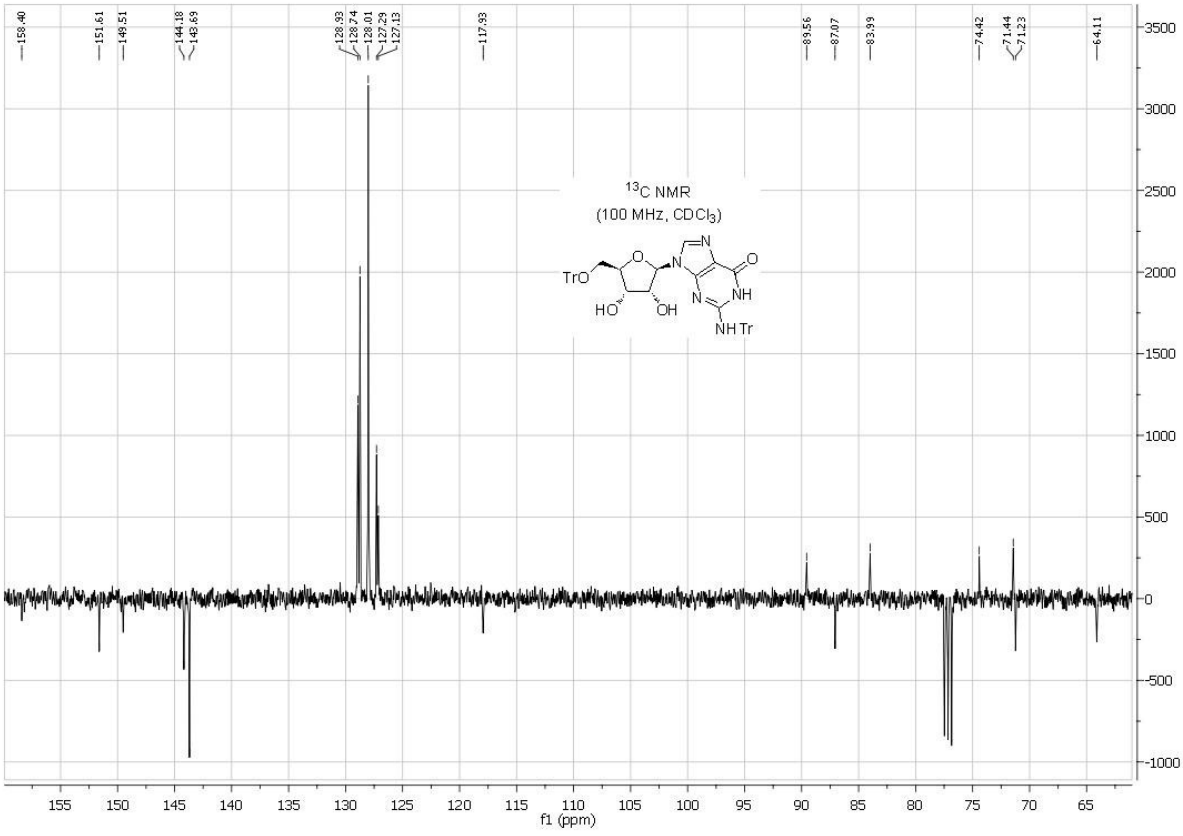


Figure S138. ^{13}C spectrum of compound 27a

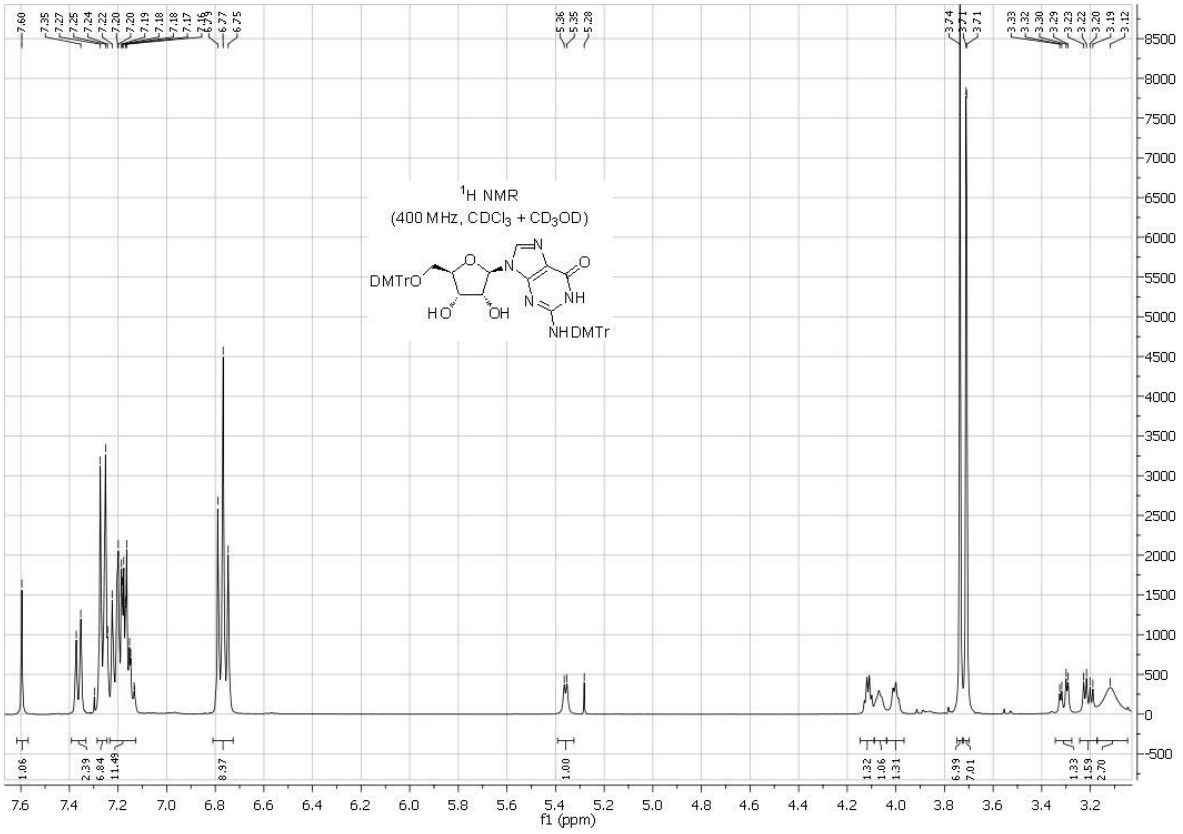


Figure S139. ^{1}H spectrum of compound 27b

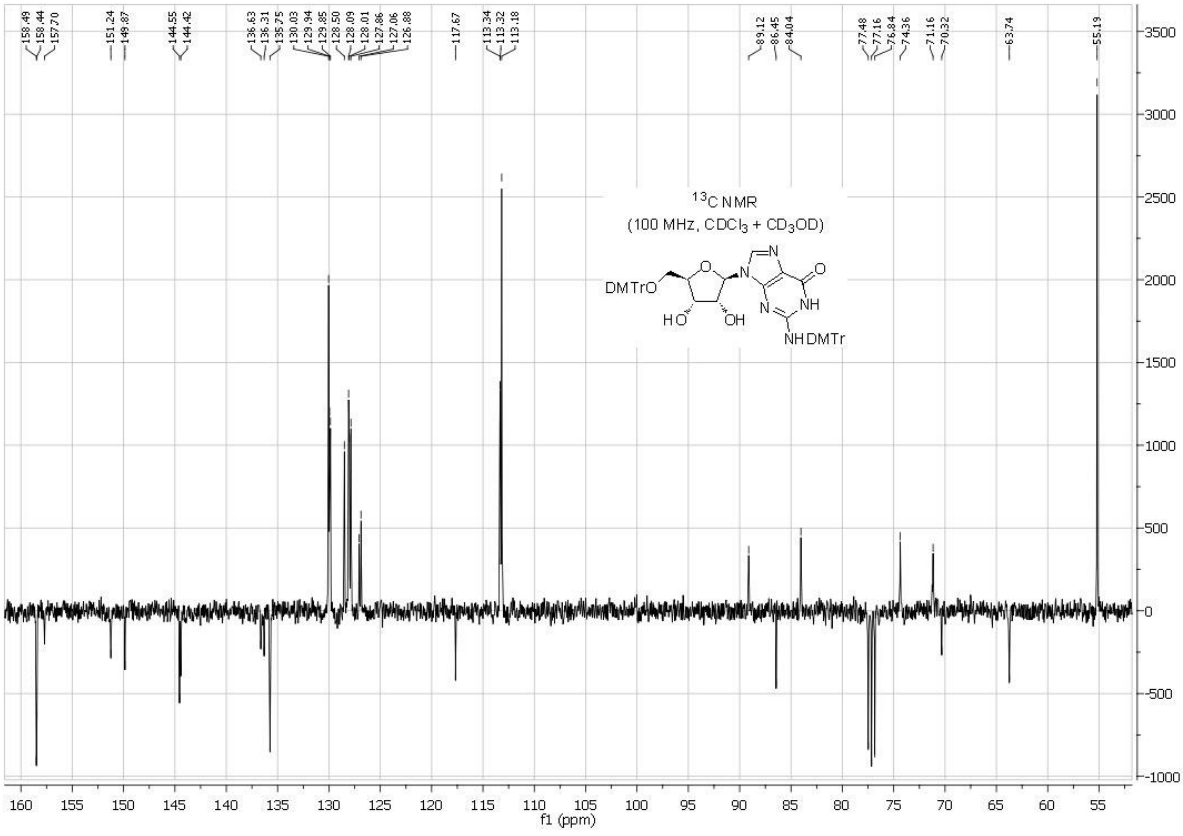


Figure S140. ^{13}C spectrum of compound 27b

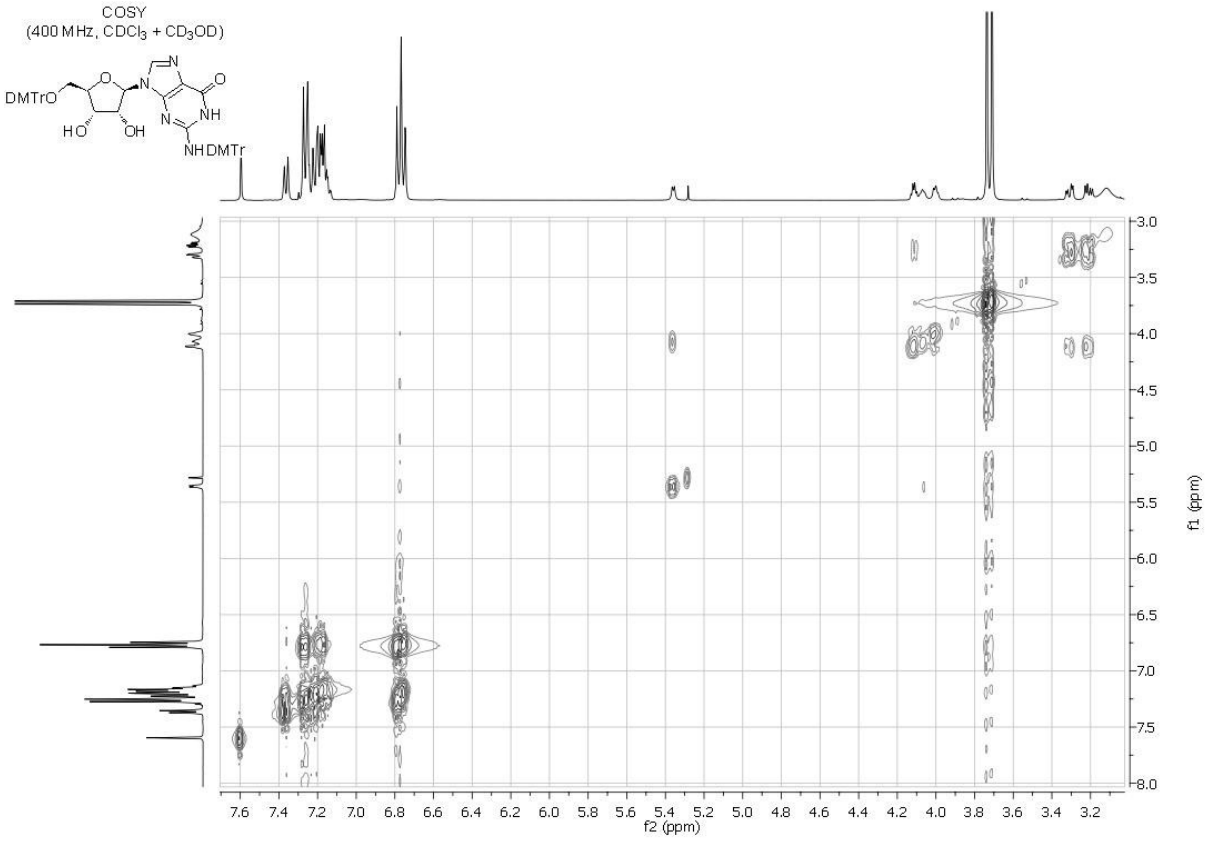


Figure S141. ^{1}H-^{1}H COSY spectrum of compound 27b

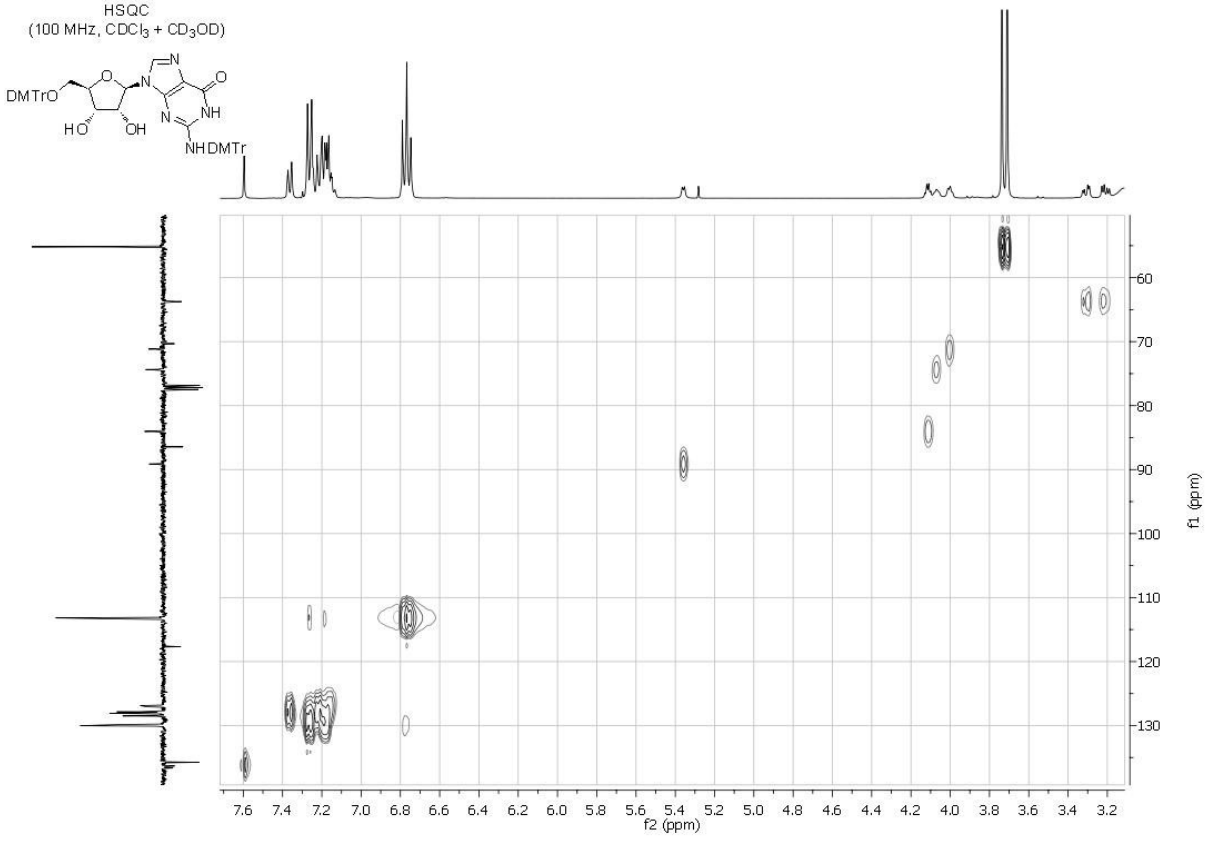


Figure S142. ^{1}H-^{13}C HSQC spectrum of compound 27b

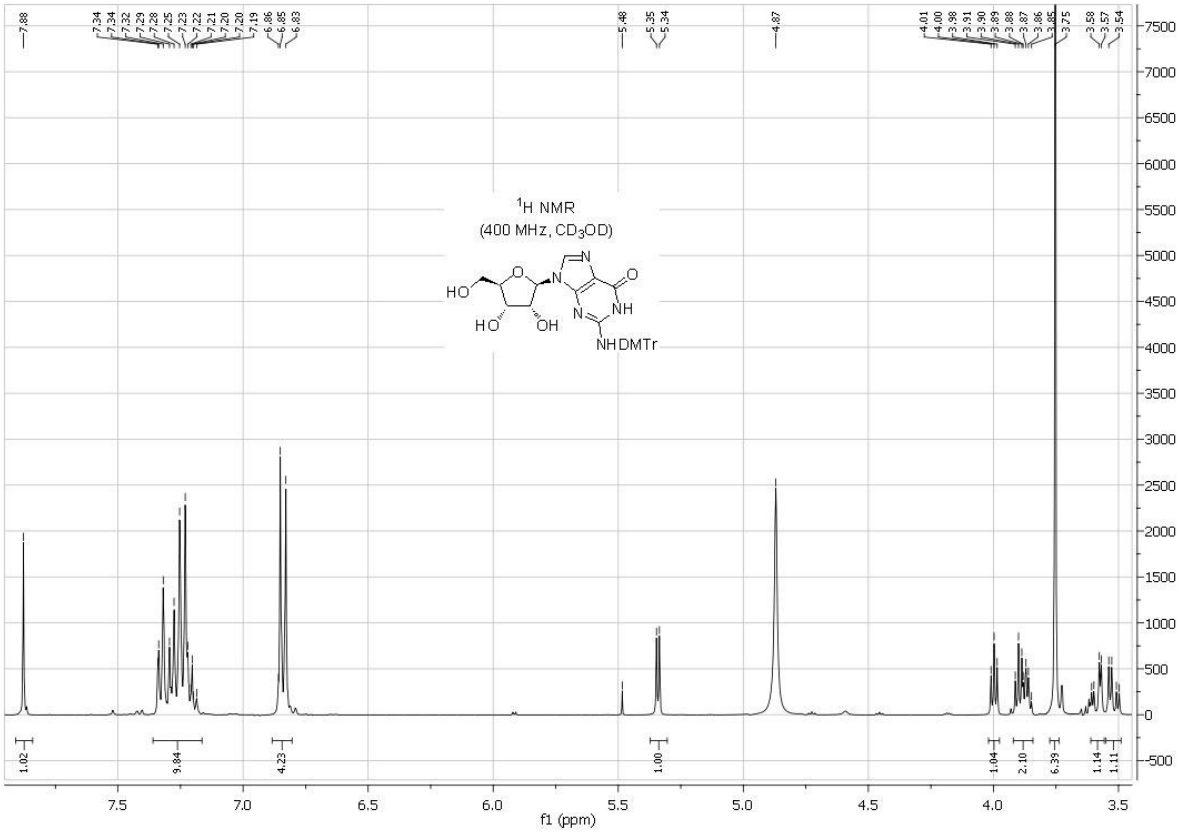


Figure S143. ^{1}H spectrum of compound 27c

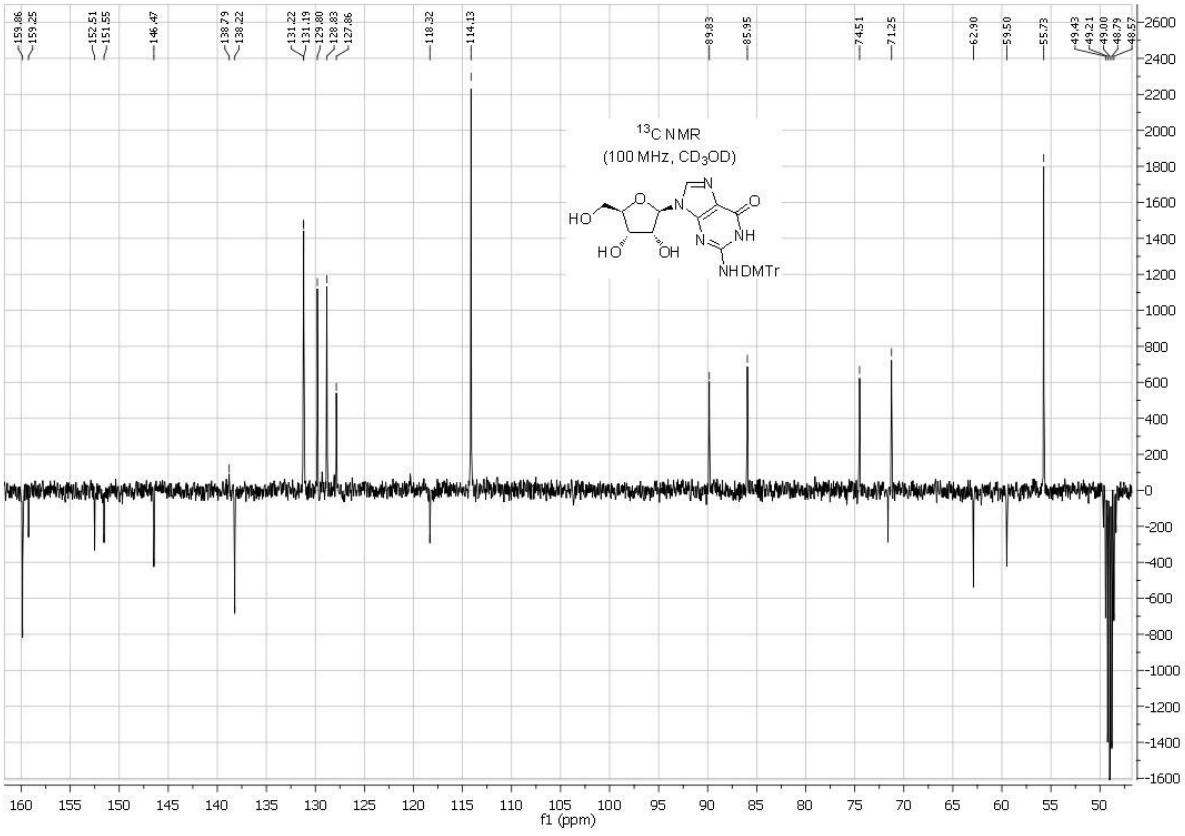


Figure S144. ^{13}C spectrum of compound 27c

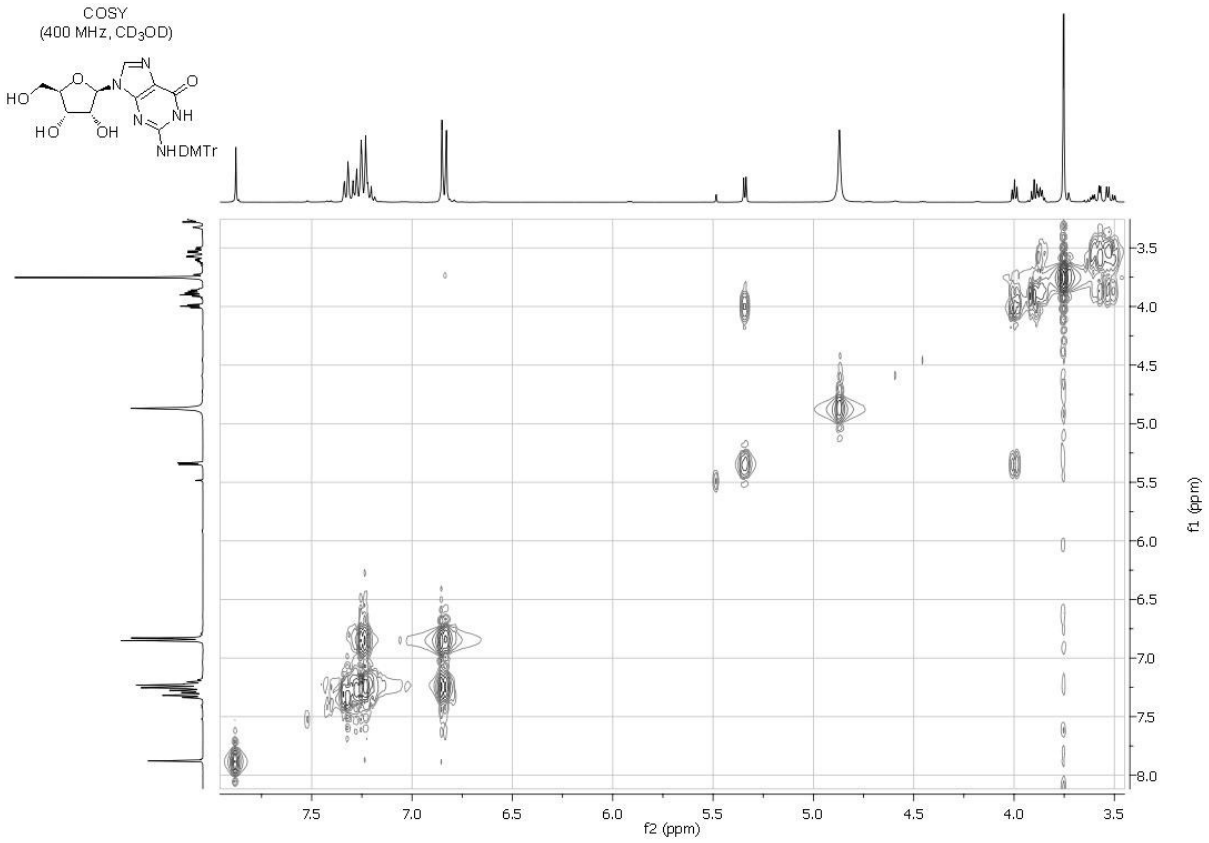


Figure S145. ^{1}H-^{1}H COSY spectrum of compound 27c

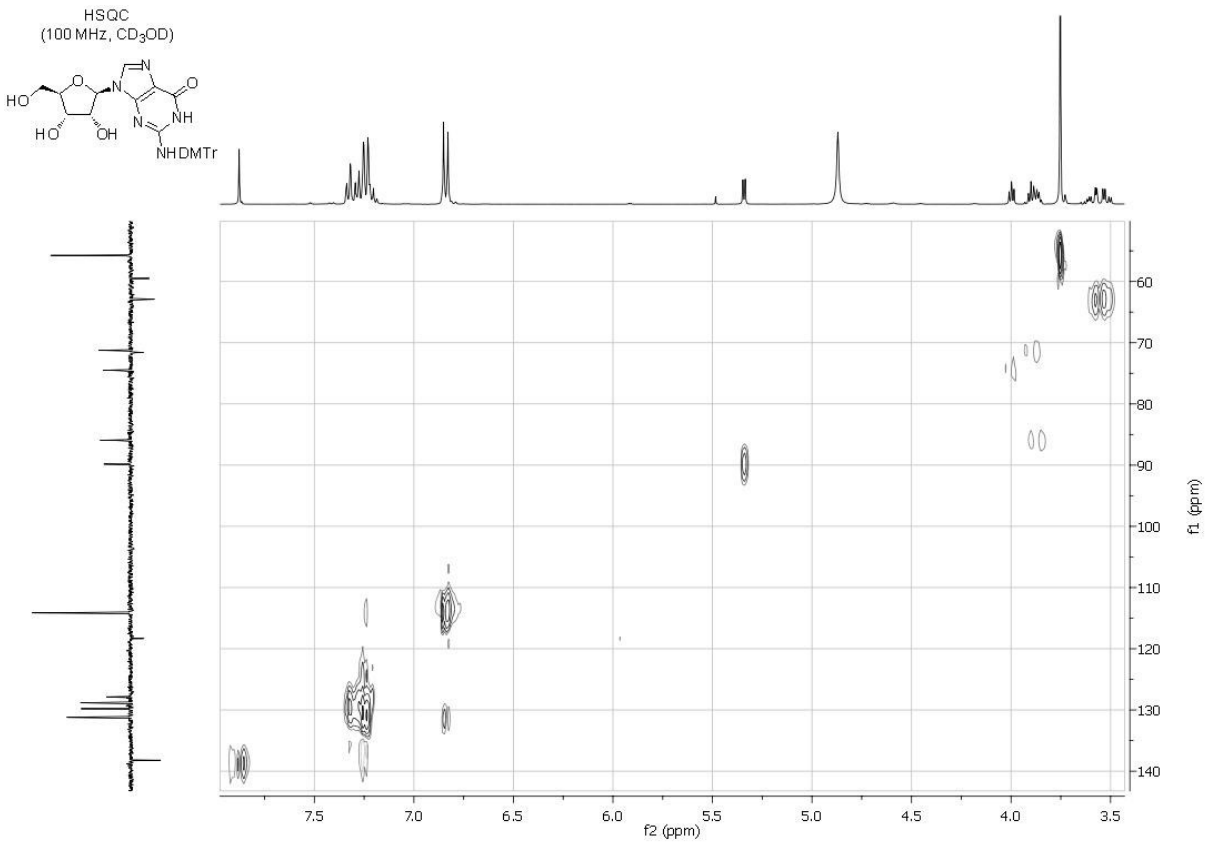


Figure S146. ^{1}H-^{13}C HSQC spectrum of compound 27c

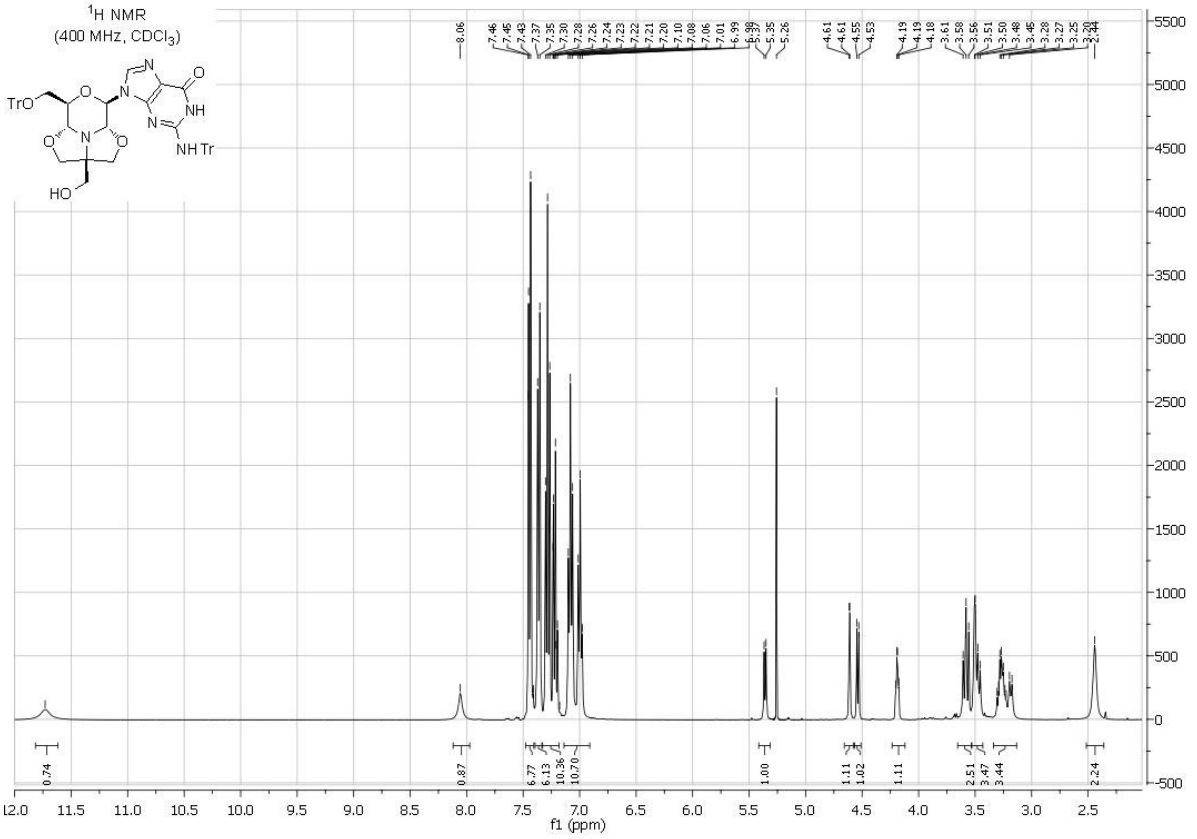


Figure S147. ^{1}H spectrum of compound 28a

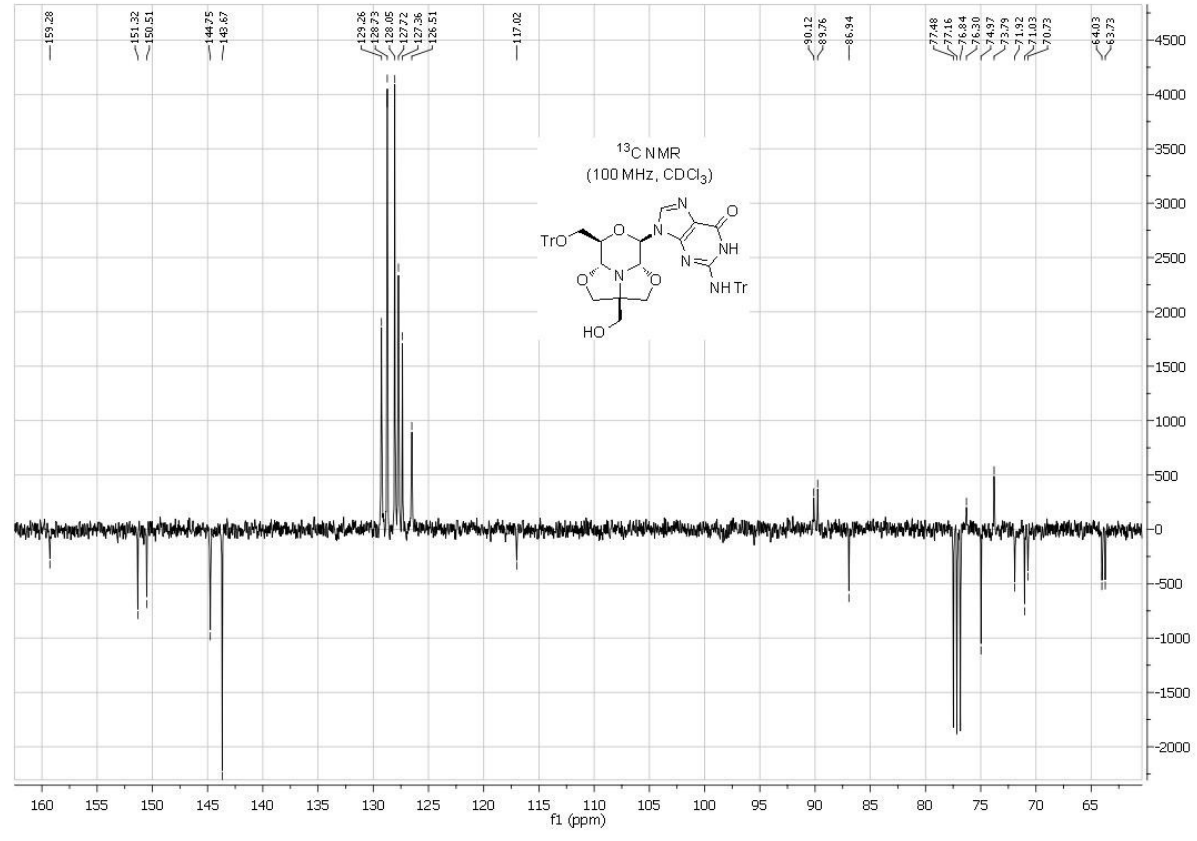


Figure S148. ^{13}C spectrum of compound 28a

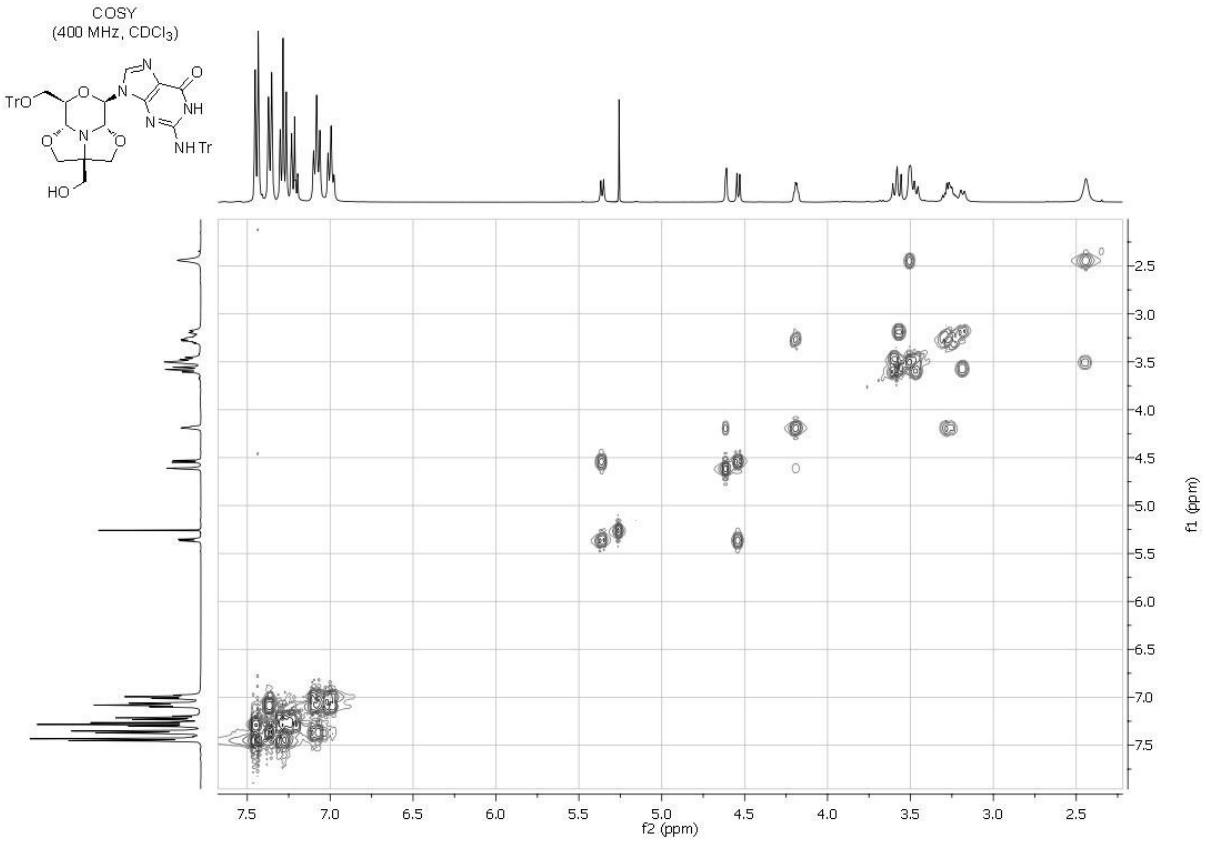


Figure S149. ^{1}H-^{1}H COSY spectrum of compound 28a

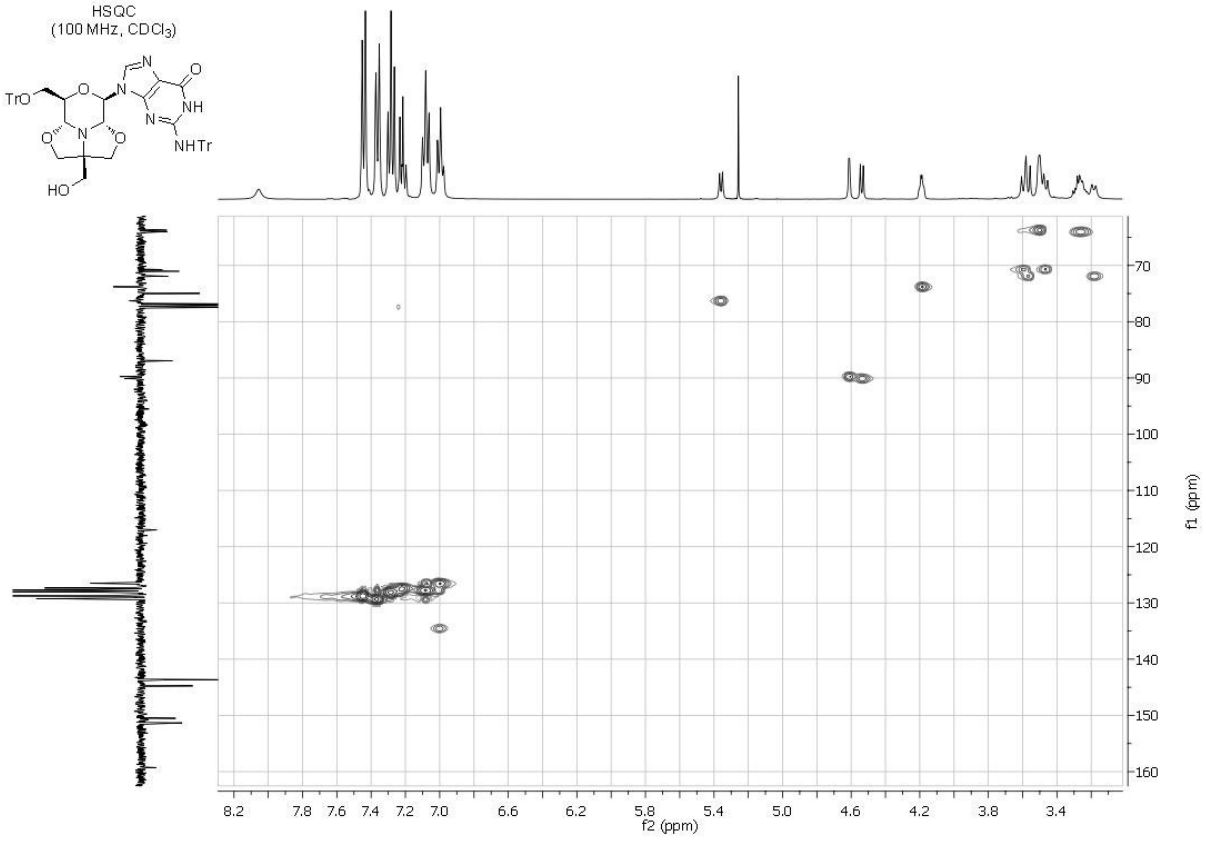


Figure S150. ^{1}H-^{13}C HSQC spectrum of compound 28a

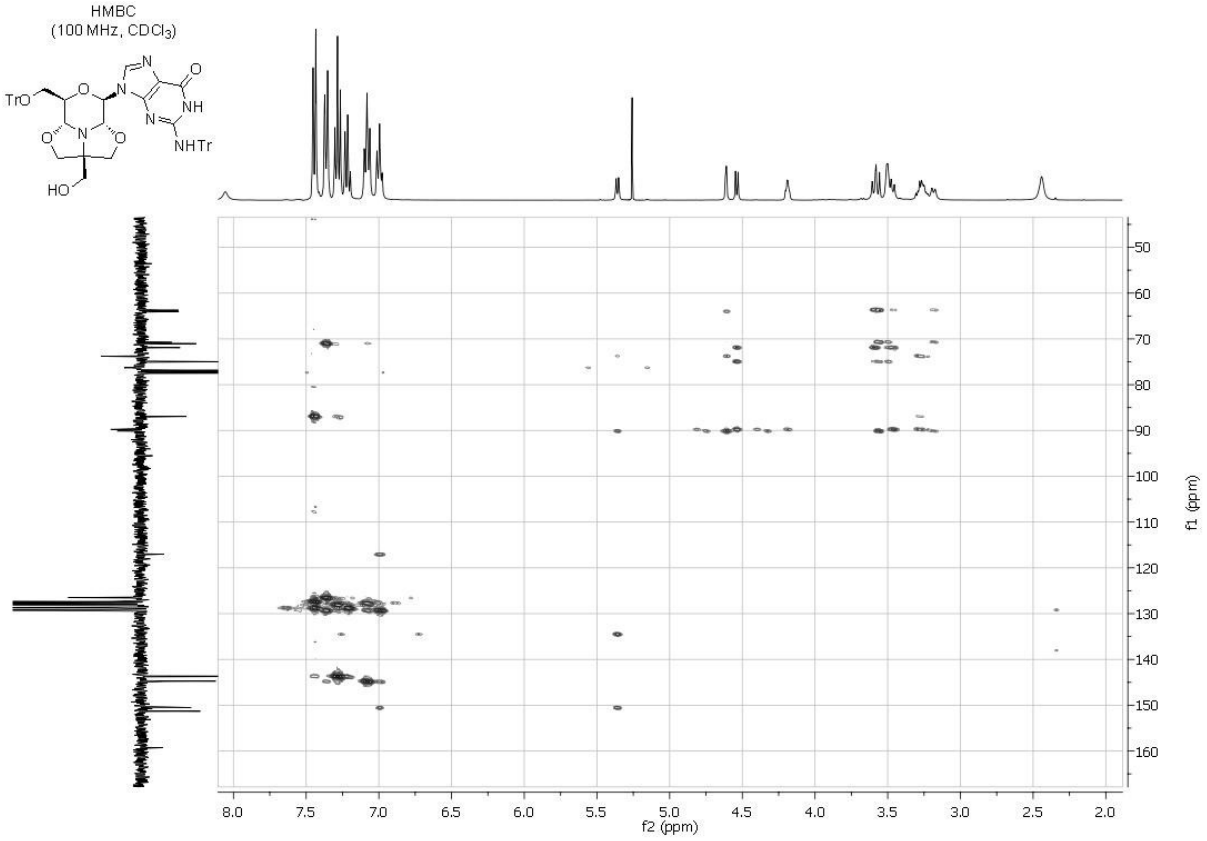


Figure S151. ^{1}H-^{13}C HMBC spectrum of compound 28a

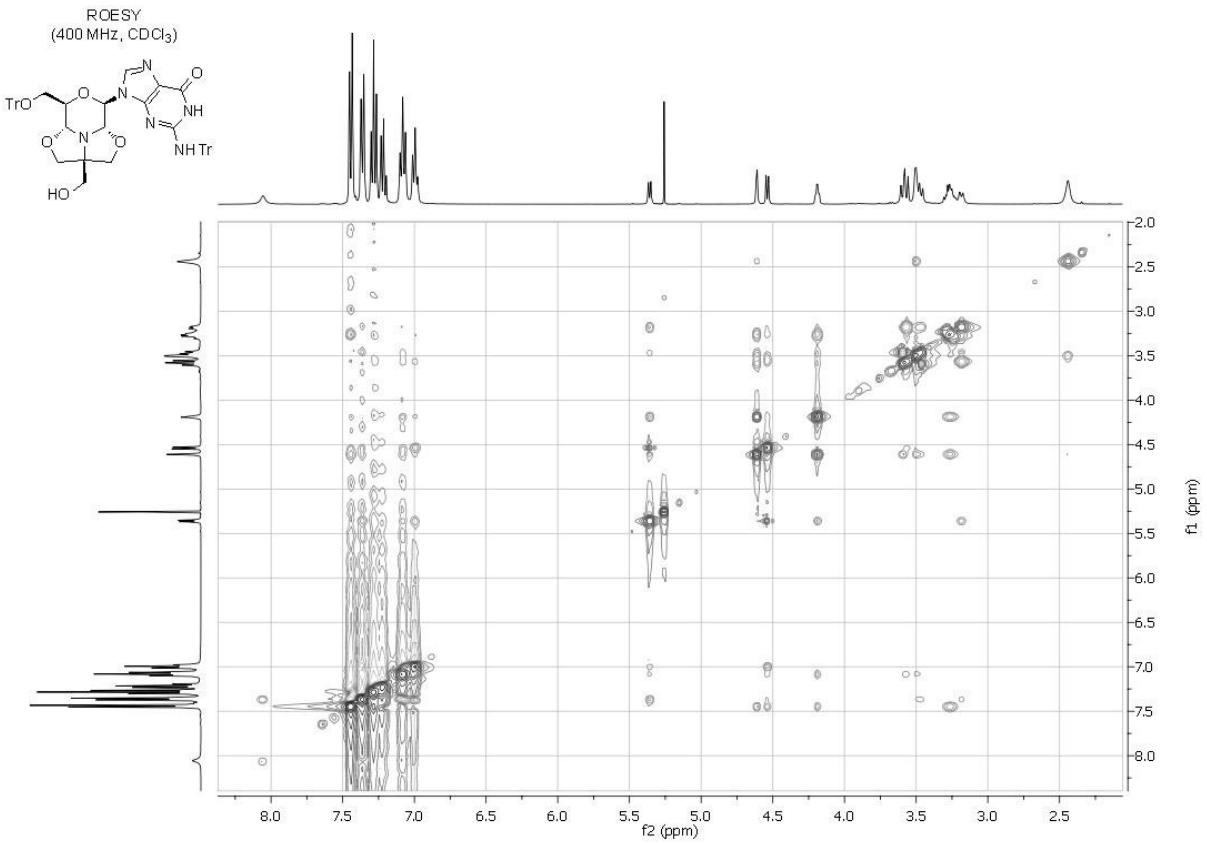


Figure S152. ^{1}H-^{1}H ROESY spectrum of compound 28a

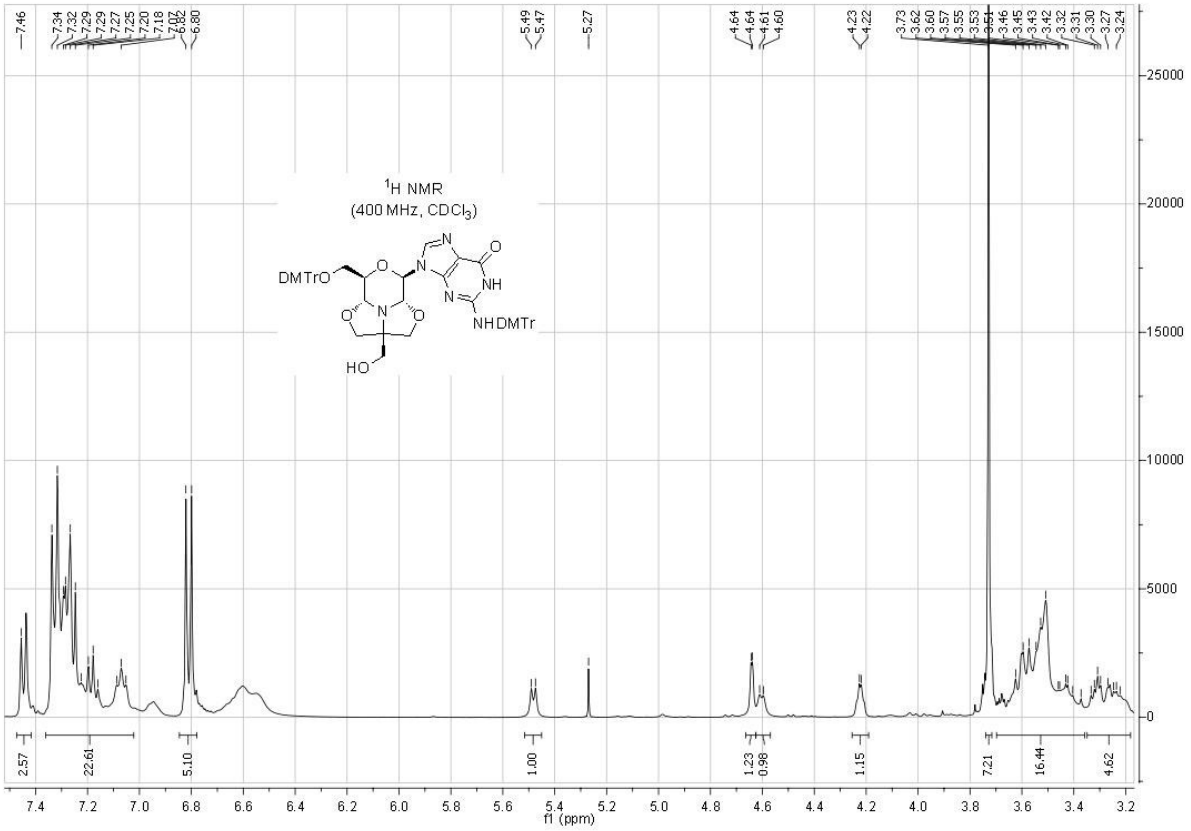


Figure S153. ^{1}H spectrum of compound 28b

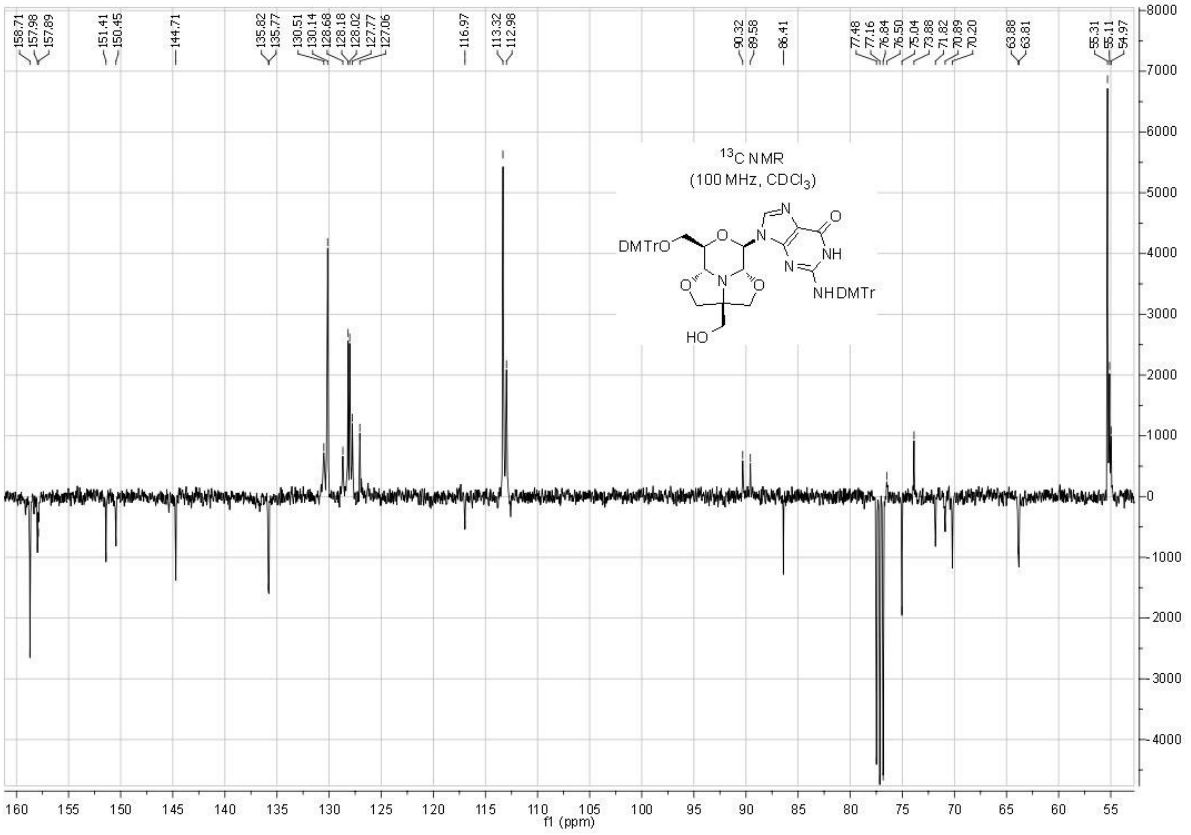


Figure S154. ^{13}C spectrum of compound 28b

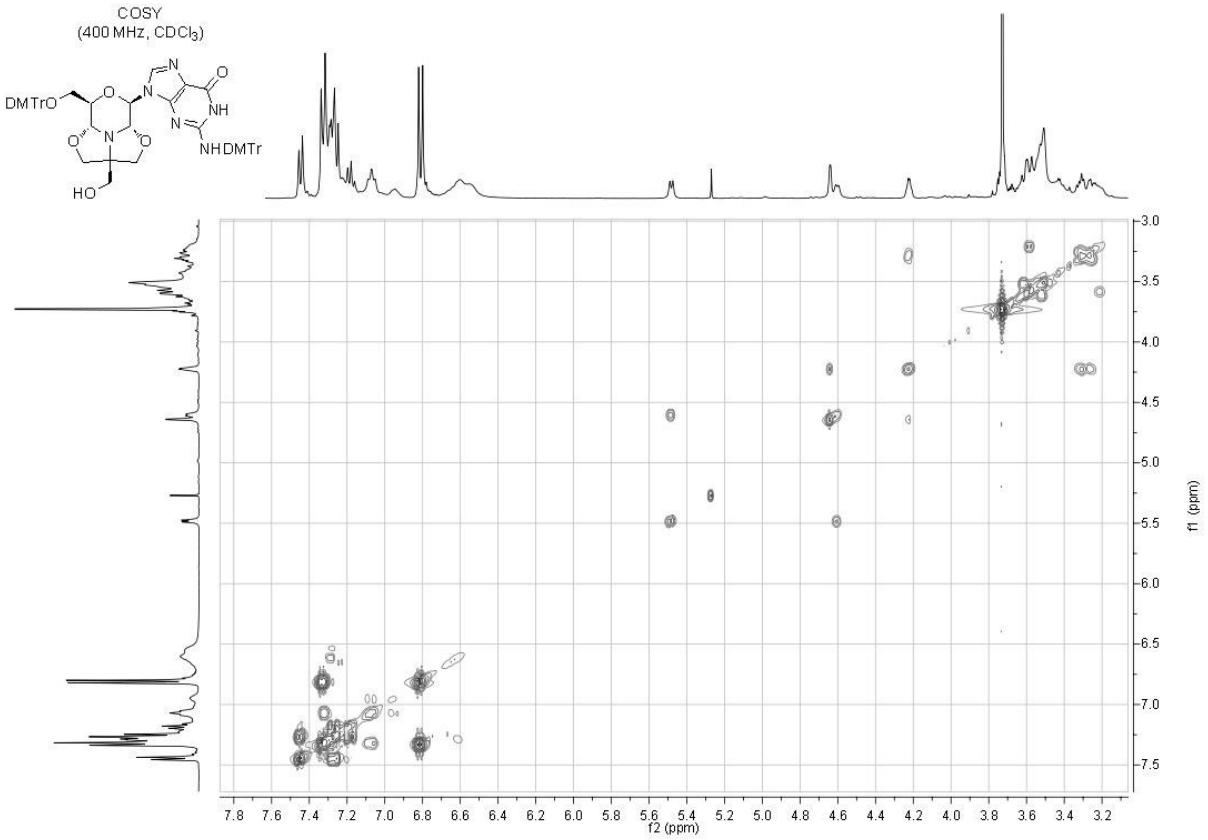


Figure S155. ^{1}H-^{1}H COSY spectrum of compound 28b

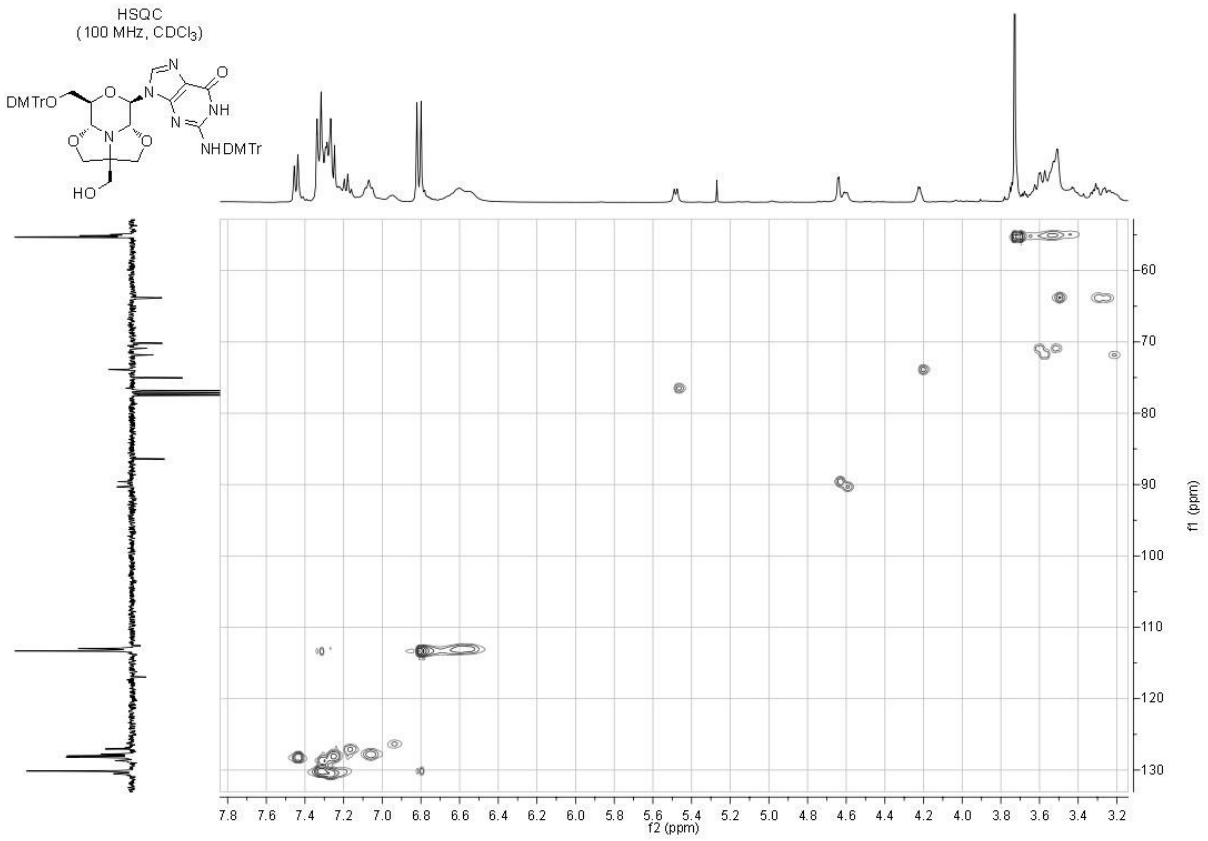


Figure S156. ^{1}H-^{13}C HSQC spectrum of compound 28b

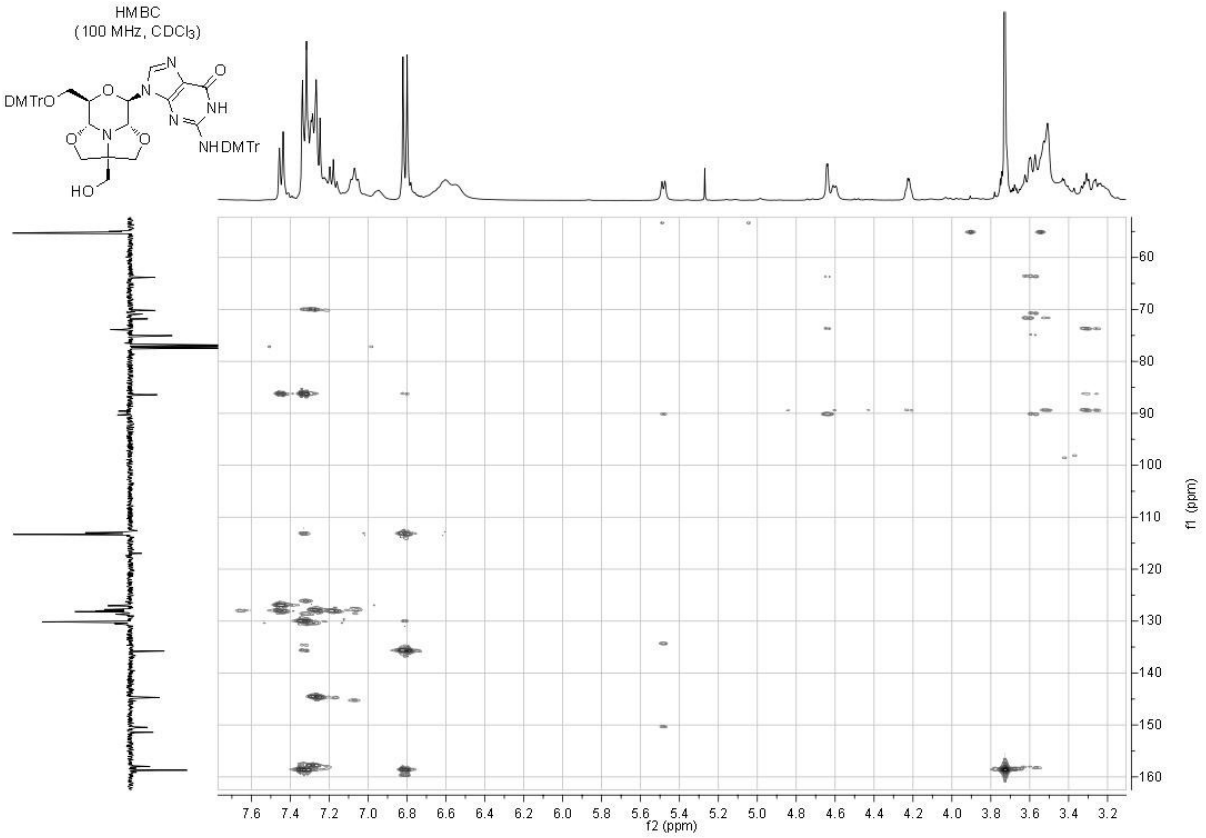


Figure S157. ^{1}H-^{13}C HMBC spectrum of compound 28b

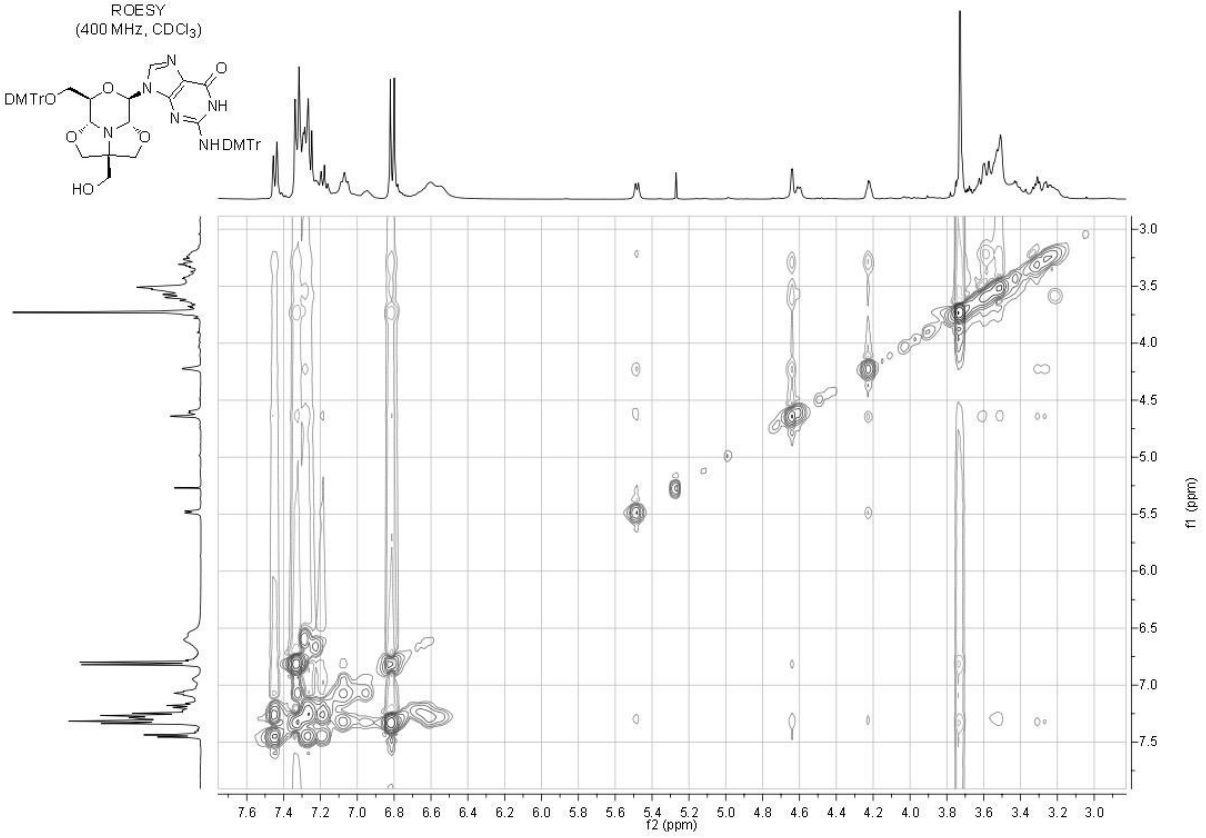


Figure S158. ^{1}H-^{1}H ROESY spectrum of compound 28b

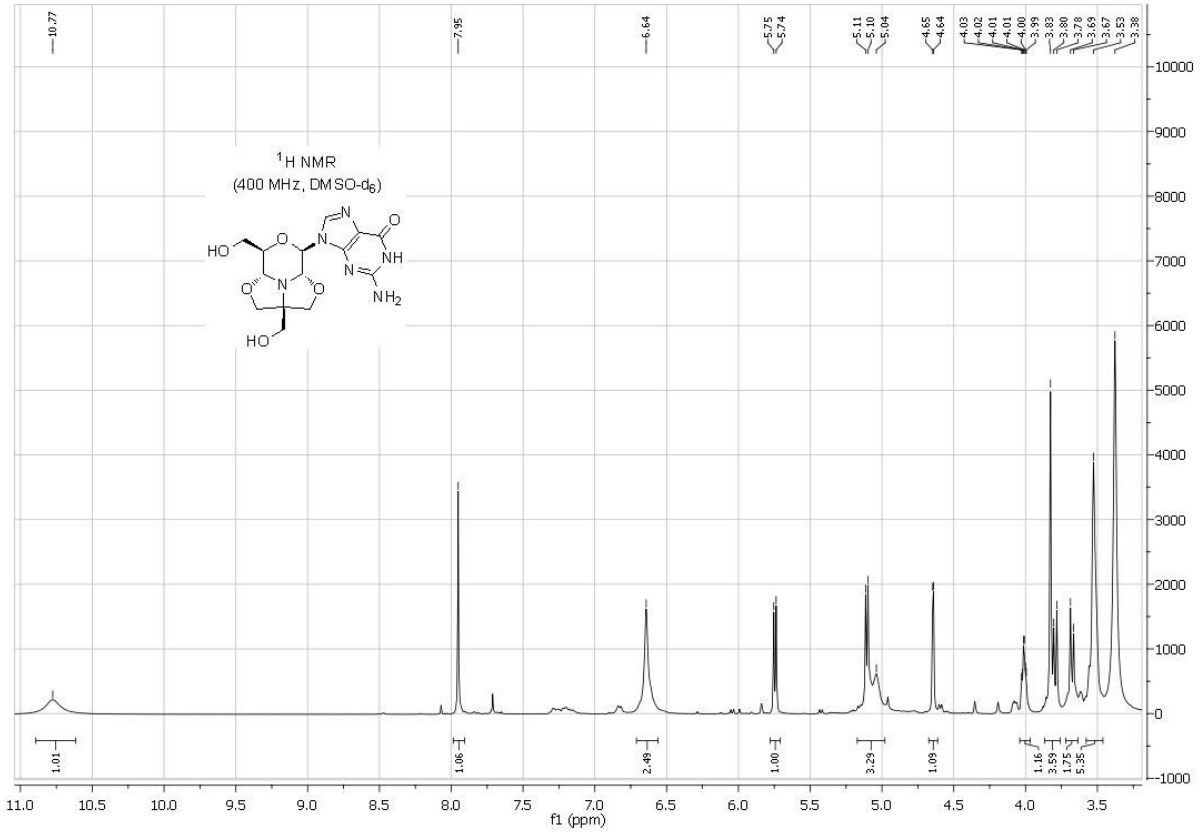


Figure S159. ^{1}H spectrum of compound 29

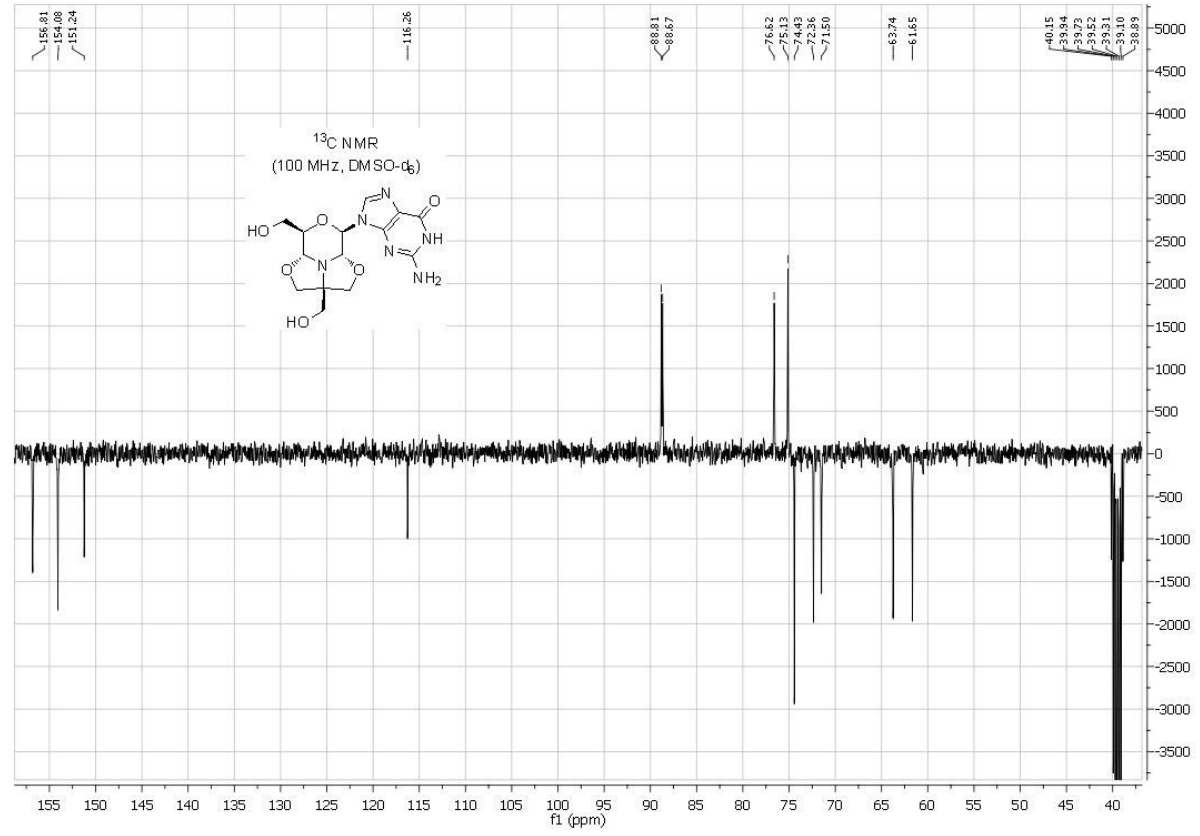


Figure S160. ^{13}C spectrum of compound 29

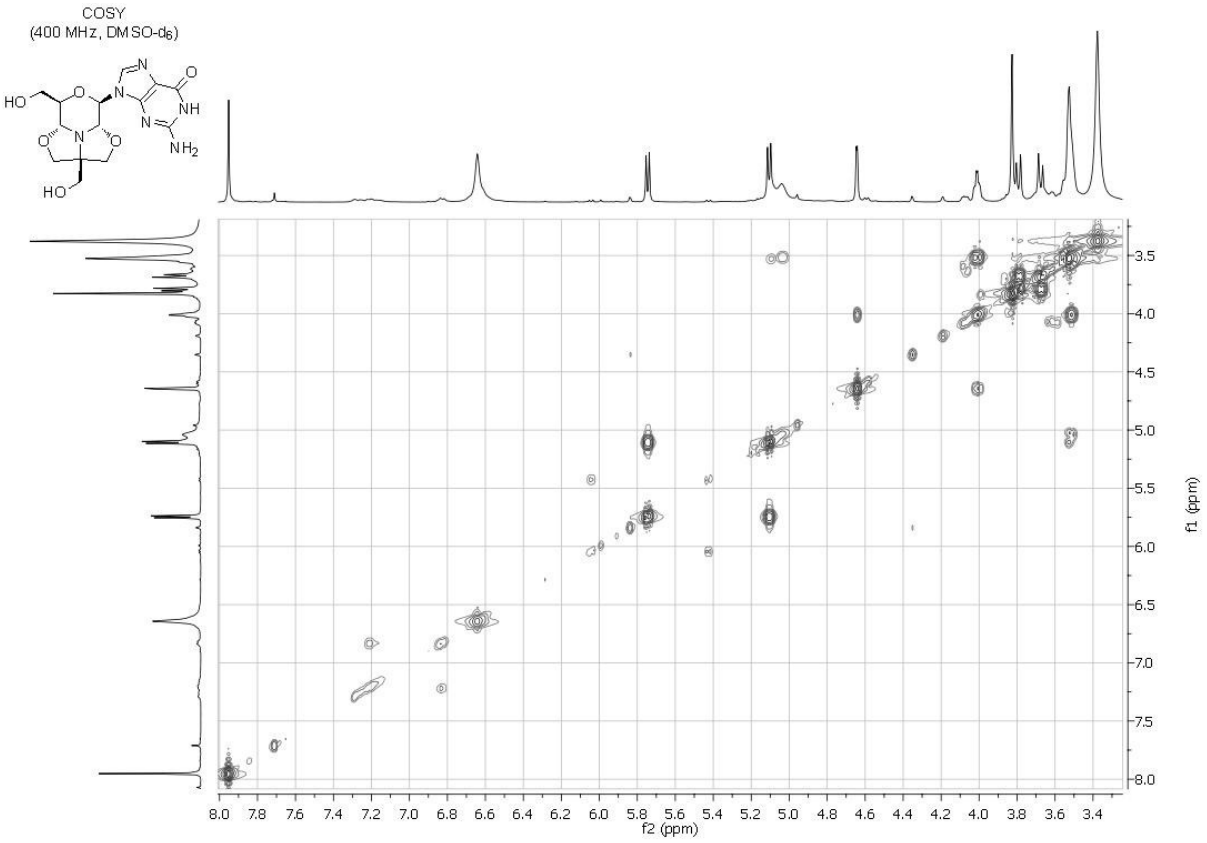


Figure S161. ^{1}H-^{1}H COSY spectrum of compound 29

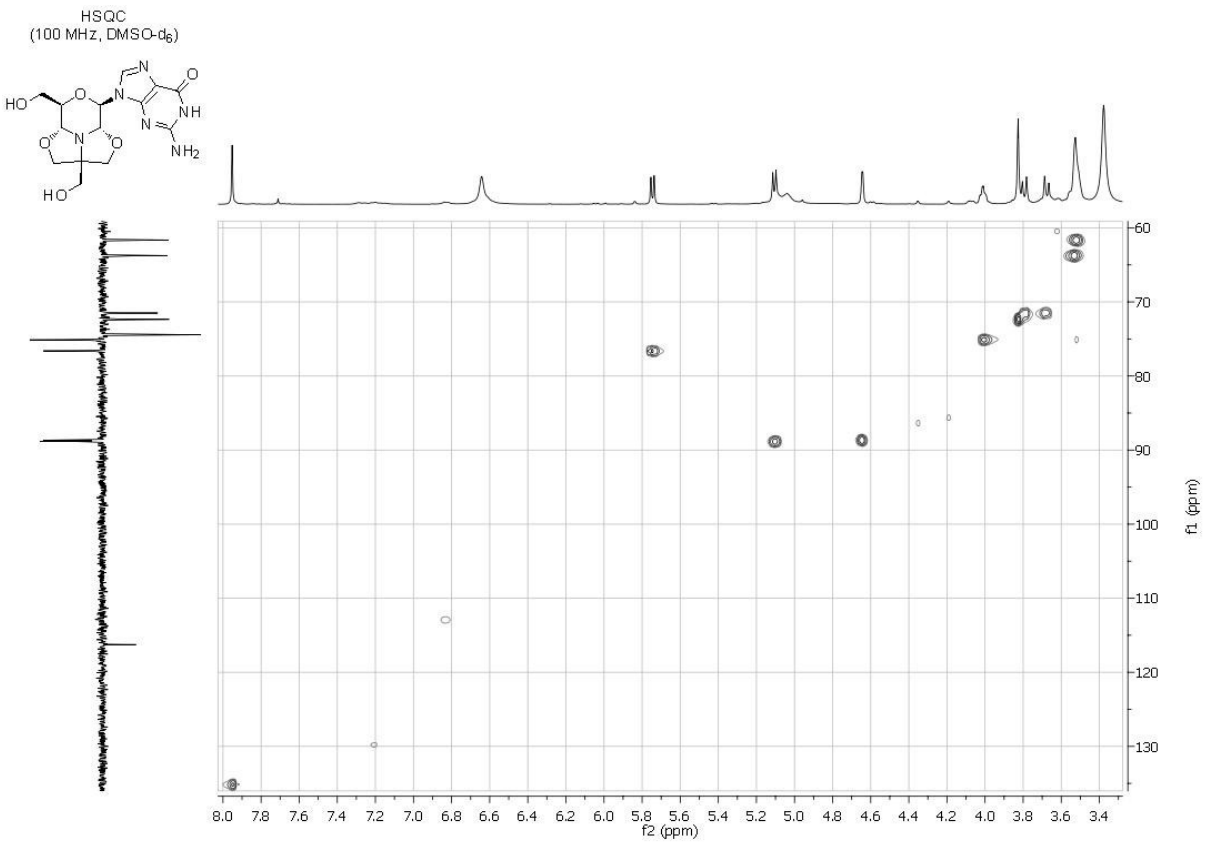


Figure S162. ^{1}H-^{13}C HSQC spectrum of compound 29

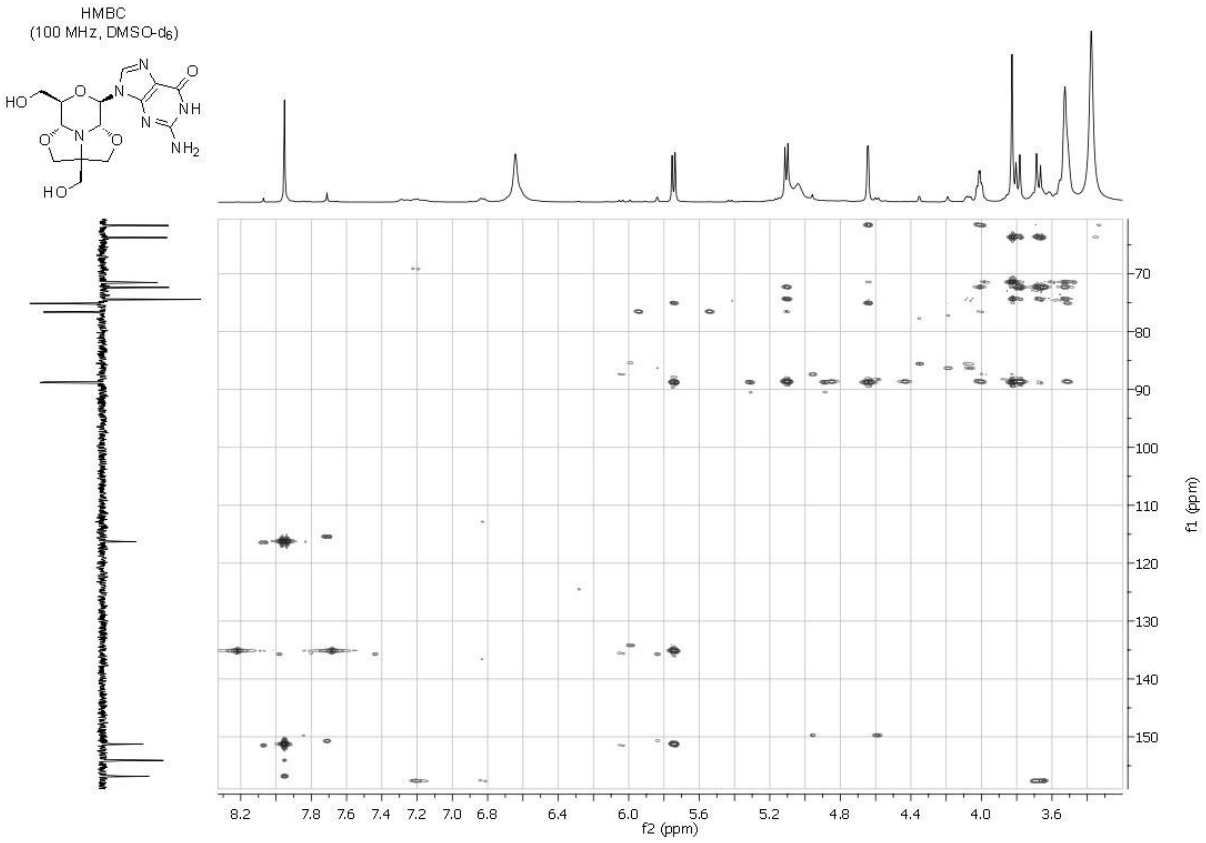


Figure S163. ^{1}H-^{13}C HMBC spectrum of compound 29

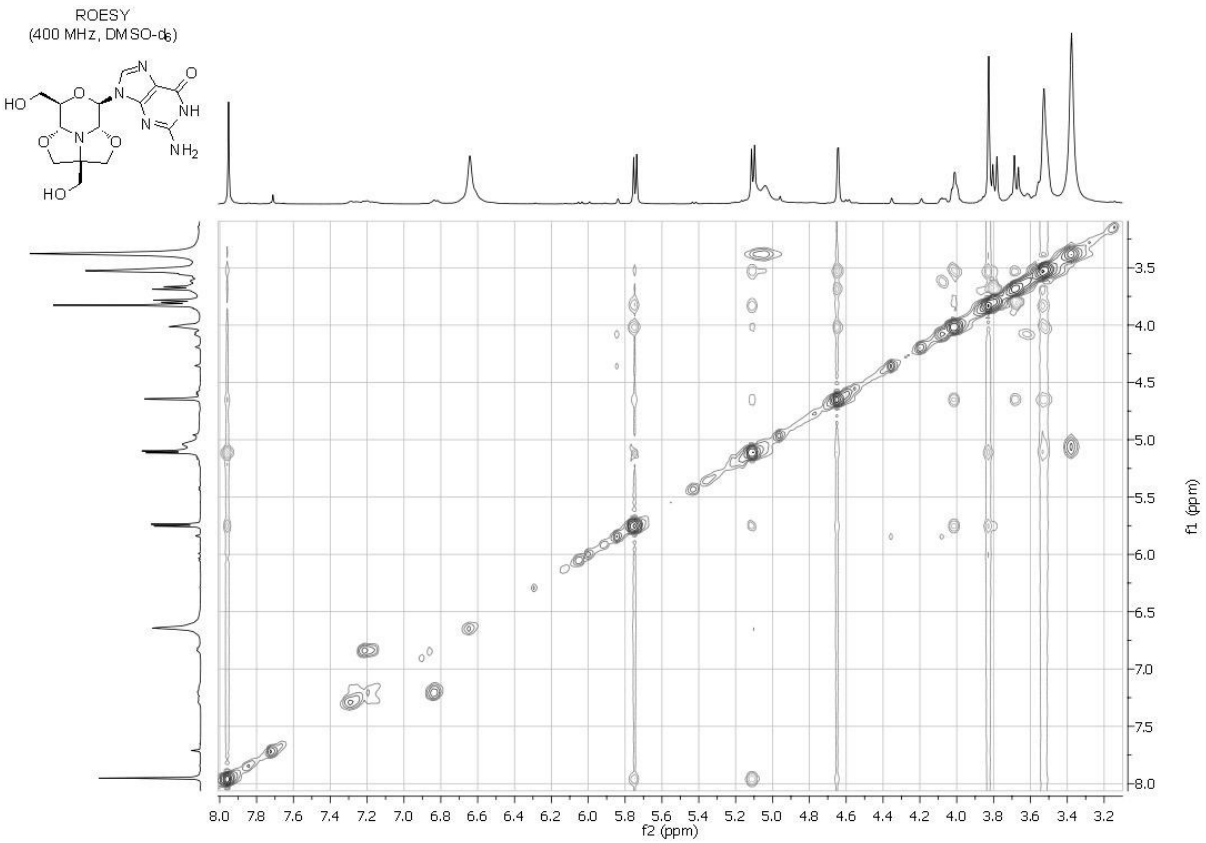


Figure S164. ^{1}H-^{1}H ROESY spectrum of compound 29

X-ray data

Table S1. *Experimental details*

Crystal data	
Chemical formula	$2(C_{35}H_{33}N_5O_7)\cdot 2(C_3H_8O)$
M_r	1391.51
Crystal system, space group	Orthorhombic, $P2_12_12_1$
Temperature (K)	293
a, b, c (Å)	10.8476 (3), 17.3220 (4), 37.2345 (9)
V (Å^3)	6996.4 (3)
Z	4
Radiation type	Cu $K\alpha$
μ (mm^{-1})	0.77
Crystal size (mm)	0.11 × 0.03 × 0.02
Data collection	
Diffractometer	Synergy, Dualflex, Pilatus 200K
Absorption correction	Multi-scan *CrysAlis PRO* 1.171.39.6a (Rigaku Oxford Diffraction, 2015) Empirical absorption correction using spherical harmonics, implemented in SCALE3 ABSPACK scaling algorithm.
T_{min}, T_{max}	0.623, 1
No. of measured, independent and observed [$I > 2\sigma(I)$] reflections	43348, 14689, 11384
R_{int}	0.056
$(\sin\theta/\lambda)_{max}$ (Å^{-1})	0.637
Refinement	
$R[F^2 > 2\sigma(F^2)]$, $wR(F^2)$, S	0.067, 0.186, 1.05
No. of reflections	14689
No. of parameters	933
No. of restraints	8
H-atom treatment	H atoms treated by a mixture of independent and constrained refinement

$\Delta\rangle_{max}$, $\Delta\rangle_{min}$ (e Å^{-3})	0.64, -0.44
Absolute structure	Flack x determined using 4034 quotients [(I+)-(I-)]/[(I+)+(I-)] (Parsons, Flack and Wagner, Acta Cryst. B69 (2013) 249-259).
Absolute structure parameter	0.03 (12)

Table S2. *Selected bond length data (Å) for* **18b**

C1—O10	1.403 (6)	C51—O60	1.410 (6)
C1—N14	1.441 (6)	C51—N64	1.447 (6)
C1—C2	1.516 (7)	C51—C52	1.516 (7)
C2—O3	1.406 (6)	C52—O53	1.399 (6)
C2—N11	1.468 (6)	C52—N61	1.475 (6)
C4—O3	1.431 (7)	C54—O53	1.431 (7)
C4—C5	1.524 (7)	C54—C55	1.529 (8)
C5—N11	1.489 (6)	C55—N61	1.493 (7)
C5—C13	1.514 (7)	C55—C63	1.495 (8)
C5-C6	1.524 (7)	C55—C56	1.523 (8)
C6—O7	1.429 (6)	C56—O57	1.412 (8)
C8—O7	1.433 (5)	C58—O57	1.446 (6)
C8—N11	1.461 (6)	C58—N61	1.469 (7)
C8—C9	1.529 (7)	C58—C59	1.508 (8)
C9—O10	1.442 (6)	C59—O60	1.439 (6)
C9—C12	1.516 (7)	C59—C62	1.518 (7)
C12—O24	1.422 (6)	C62—O74	1.414 (6)
C13—O44	1.433 (7)	C63—O94	1.475 (8)
C15—N16	1.307 (6)	C65—N66	1.300 (6)
C15—N14	1.380 (6)	C65—N64	1.380 (6)
C17—C23	1.369 (6)	C67—C73	1.373 (6)
C17—N16	1.390 (5)	C67—N66	1.388 (6)
C17—C18	1.424 (6)	C67—C68	1.417 (6)
C18—O19	1.229 (6)	C68—O69	1.225 (6)
C18—N20	1.396 (6)	C68—N70	1.411 (6)
C21—N22	1.310 (6)	C71—N72	1.302 (6)
C21—N20	1.356 (6)	C71—N70	1.367 (6)

C23—N22	1.366 (6)	C73—N72	1.360 (5)
C23—N14	1.372 (5)	C73—N64	1.367 (6)
C25—O24	1.435 (6)	C75—O74	1.447 (5)
C25—C26	1.528 (7)	C75—C76	1.530 (7)
C25—C32	1.538 (7)	C75—C82	1.536 (7)
C25—C38	1.539 (7)	C75—C88	1.528 (6)
C26—C27	1.383 (8)	C76—C77	1.390 (7)
C26—C31	1.406 (7)	C76—C81	1.389 (7)
C27—C28	1.383 (8)	C77—C78	1.393 (8)
C28—C29	1.365 (9)	C78—C79	1.387 (9)
C29—C30	1.398 (10)	C79—C80	1.372 (9)
C30—C31	1.367 (9)	C80—C81	1.387 (7)
C32—C33	1.382 (8)	C82—C83	1.390 (8)
C32—C37	1.398 (8)	C82—C87	1.383 (9)
C33—C34	1.389 (8)	C83—C84	1.360 (10)
C34—C35	1.365 (12)	C84—C85	1.387 (14)
C35—C36	1.367 (12)	C85—C86	1.369 (14)
C36—C37	1.385 (9)	C86—C87	1.382 (9)
C38—C39	1.390 (7)	C88—C89	1.378 (7)
C38—C43	1.394 (7)	C88—C93	1.397 (7)
C39—C40	1.394 (7)	C89—C90	1.382 (7)
C40—C41	1.391 (9)	C90—C91	1.386 (9)
C41—C42	1.379 (9)	C91—C92	1.378 (9)
C42—C43	1.399 (7)	C92—C93	1.383 (8)
C45—O46	1.212 (9)	C95—O96	1.222 (11)
C45—O44	1.299 (8)	C95—O94	1.275 (9)
C45—C47	1.529 (11)	C95—C97	1.496 (12)
C110—O111	1.298 (15)	C100—O101	1.229 (16)
C110—C111	1.408 (14)	C100—C101	1.455 (14)
C110—C112	1.485 (14)	C100—C102	1.503 (19)
N20—H20	0.85 (3)	N70—H70	0.85 (3)

Table S3. *Selected bond angle and torsion angle data (º) for* **18b**

O10—C1—N14	108.4 (4)	C59—C58—H58	108.5

O10—C1—C2	108.1 (4)	O60—C59—C58	114.4 (4)
N14—C1—C2	110.7 (4)	O60—C59—C62	107.9 (4)
O10—C1—H1	109.9	C58—C59—C62	112.7 (4)
N14—C1—H1	109.9	O60—C59—H59	107.1
C2—C1—H1	109.9	C58—C59—H59	107.1
O3—C2—N11	105.9 (4)	C62—C59—H59	107.1
O3—C2—C1	112.6 (4)	O74—C62—C59	106.4 (4)
N11—C2—C1	110.7 (4)	O74—C62—H62A	110.4
O3—C2—H2	109.2	C59—C62—H62A	110.4
N11—C2—H2	109.2	O74—C62—H62B	110.5
C1—C2—H2	109.2	C59—C62—H62B	110.4
O3—C4—C5	104.2 (4)	H62A—C62—H62B	108.6
O3—C4—H4A	110.9	O94—C63—C55	104.6 (5)
C5—C4—H4A	110.9	O94—C63—H63A	110.8
O3—C4—H4B	110.9	C55—C63—H63A	110.8
C5—C4—H4B	110.9	O94—C63—H63B	110.8
H4A—C4—H4B	108.9	C55—C63—H63B	110.8
N11—C5—C13	107.7 (4)	H63A—C63—H63B	108.9
N11—C5—C6	103.7 (4)	N66—C65—N64	113.0 (4)
C13—C5—C6	114.0 (4)	N66—C65—H65	123.5
N11—C5—C4	103.5 (4)	N64—C65—H65	123.5
C13—C5—C4	113.1 (5)	C73—C67—N66	109.4 (4)
C6—C5—C4	113.5 (4)	C73—C67—C68	120.5 (4)
O7—C6—C5	104.8 (4)	N66—C67—C68	130.1 (4)
O7—C6—H6A	110.8	O69—C68—N70	120.4 (4)
C5—C6—H6A	110.8	O69—C68—C67	129.5 (4)
O7—C6—H6B	110.8	N70—C68—C67	110.2 (4)
C5—C6—H6B	110.8	N72—C71—N70	125.6 (4)
H6A—C6—H6B	108.9	N72—C71—H71	117.2
O7—C8—N11	106.0 (4)	N70—C71—H71	117.2
O7—C8—C9	109.0 (4)	N72—C73—N64	125.3 (4)
N11—C8—C9	116.7 (4)	N72—C73—C67	127.6 (4)
O7—C8—H8	108.3	N64—C73—C67	107.1 (4)
N11—C8—H8	108.3	O74—C75—C88	101.7 (3)
C9—C8—H8	108.3	O74—C75—C76	110.5 (4)

O10—C9—C12	107.3 (4)	C88—C75—C76	110.7 (4)
O10—C9—C8	113.7 (4)	O74—C75—C82	111.0 (4)
C12—C9—C8	111.3 (4)	C88—C75—C82	111.6 (4)
O10—C9—H9	108.1	C76—C75—C82	111.0 (4)
C12—C9—H9	108.1	C81—C76—C77	118.0 (5)
C8—C9—H9	108.1	C81—C76—C75	121.6 (4)
O24—C12—C9	106.1 (4)	C77—C76—C75	120.3 (4)
O24—C12—H12A	110.5	C76—C77—C78	121.2 (5)
C9—C12—H12A	110.5	C76—C77—H77	119.4
O24—C12—H12B	110.5	C78—C77—H77	119.4
C9—C12—H12B	110.5	C79—C78—C77	119.6 (5)
H12A—C12—H12B	108.7	C79—C78—H78	120.2
O44—C13—C5	108.2 (4)	C77—C78—H78	120.2
O44—C13—H13A	110.1	C80—C79—C78	119.7 (5)
C5—C13—H13A	110.1	C80—C79—H79	120.2
O44—C13—H13B	110.1	C78—C79—H79	120.2
C5—C13—H13B	110.1	C79—C80—C81	120.6 (5)
H13A—C13—H13B	108.4	C79—C80—H80	119.7
N16—C15—N14	113.1 (4)	C81—C80—H80	119.7
N16—C15—H15	123.5	C80—C81—C76	120.9 (5)
N14—C15—H15	123.5	C80—C81—H81	119.6
C23—C17—N16	110.5 (4)	C76—C81—H81	119.6
C23—C17—C18	119.2 (4)	C87—C82—C83	117.5 (5)
N16—C17—C18	130.2 (4)	C87—C82—C75	122.3 (5)
O19—C18—N20	121.5 (4)	C83—C82—C75	120.3 (5)
O19—C18—C17	128.0 (4)	C84—C83—C82	122.0 (8)
N20—C18—C17	110.4 (4)	C84—C83—H83	119
N22—C21—N20	125.3 (4)	C82—C83—H83	119
N22—C21—H21	117.4	C83—C84—C85	120.0 (8)
N20—C21—H21	117.4	C83—C84—H84	120
N22—C23—C17	128.6 (4)	C85—C84—H84	120
N22—C23—N14	125.0 (4)	C86—C85—C84	118.8 (6)
C17—C23—N14	106.4 (4)	C86—C85—H85	120.6
O24—C25—C26	109.0 (4)	C84—C85—H85	120.6
O24—C25—C32	103.9 (4)	C85—C86—C87	121.0 (8)

C26—C25—C32	110.6 (4)	C85—C86—H86	119.5
O24—C25—C38	109.7 (4)	C87—C86—H86	119.5
C26—C25—C38	114.8 (4)	C86—C87—C82	120.6 (7)
C32—C25—C38	108.3 (4)	C86—C87—H87	119.7
C27—C26—C31	117.7 (5)	C82—C87—H87	119.7
C27—C26—C25	124.2 (4)	C89—C88—C93	118.2 (5)
C31—C26—C25	117.9 (5)	C89—C88—C75	123.1 (4)
C28—C27—C26	120.9 (5)	C93—C88—C75	118.7 (4)
C28—C27—H27	119.6	C88—C89—C90	121.3 (5)
C26—C27—H27	119.6	C88—C89—H89	119.3
C29—C28—C27	121.1 (6)	C90—C89—H89	119.3
C29—C28—H28	119.4	C89—C90—C91	120.1 (5)
C27—C28—H28	119.4	C89—C90—H90	119.9
C28—C29—C30	118.8 (5)	C91—C90—H90	119.9
C28—C29—H29	120.6	C92—C91—C90	119.2 (5)
C30—C29—H29	120.6	C92—C91—H91	120.4
C31—C30—C29	120.4 (6)	C90—C91—H91	120.4
C31—C30—H30	119.8	C91—C92—C93	120.6 (5)
C29—C30—H30	119.8	C91—C92—H92	119.7
C30—C31—C26	121.0 (6)	C93—C92—H92	119.7
C30—C31—H31	119.5	C92—C93—C88	120.5 (5)
C26—C31—H31	119.5	C92—C93—H93	119.7
C33—C32—C37	118.8 (5)	C88—C93—H93	119.7
C33—C32—C25	120.8 (5)	O96—C95—O94	123.6 (8)
C37—C32—C25	120.4 (5)	O96—C95—C97	122.5 (8)
C32—C33—C34	120.1 (6)	O94—C95—C97	113.7 (8)
C32—C33—H33	119.9	C95—C97—H97A	109.5
C34—C33—H33	119.9	C95—C97—H97B	109.5
C35—C34—C33	120.7 (8)	H97A—C97—H97B	109.5
C35—C34—H34	119.6	C95—C97—H97C	109.5
C33—C34—H34	119.6	H97A—C97—H97C	109.5
C34—C35—C36	119.6 (6)	H97B—C97—H97C	109.5
C34—C35—H35	120.2	O101—C100—C101	108.3 (13)
C36—C35—H35	120.2	O101—C100—C102	132.3 (15)
C35—C36—C37	120.8 (7)	C101—C100—C102	115.5 (10)

C35—C36—H36	119.6	O101—C100—H100	96.4
C37—C36—H36	119.6	C101—C100—H100	96.4
C36—C37—C32	119.8 (7)	C102—C100—H100	96.4
C36—C37—H37	120.1	C100—C101—H10A	109.5
C32—C37—H37	120.1	C100—C101—H10B	109.5
C39—C38—C43	117.9 (5)	H10A—C101—H10B	109.5
C39—C38—C25	121.5 (5)	C100—C101—H10C	109.5
C43—C38—C25	120.4 (4)	H10A—C101—H10C	109.5
C38—C39—C40	121.3 (5)	H10B—C101—H10C	109.5
C38—C39—H39	119.3	C100—C102—H10D	109.5
C40—C39—H39	119.3	C100—C102—H10E	109.5
C41—C40—C39	120.0 (5)	H10D—C102—H10E	109.5
C41—C40—H40	120	C100—C102—H10F	109.5
C39—C40—H40	120	H10D—C102—H10F	109.5
C42—C41—C40	119.4 (5)	H10E—C102—H10F	109.5
C42—C41—H41	120.3	O111—C110—C111	121.7 (14)
C40—C41—H41	120.3	O111—C110—C112	115.8 (14)
C41—C42—C43	120.2 (5)	C111—C110—C112	118.6 (9)
C41—C42—H42	119.9	O111—C110—H110	96.5
C43—C42—H42	119.9	C111—C110—H110	96.5
C38—C43—C42	121.1 (5)	C112—C110—H110	96.5
C38—C43—H43	119.5	C110—C111—H11A	109.5
C42—C43—H43	119.5	C110—C111—H11B	109.5
O46—C45—O44	123.5 (6)	H11A—C111—H11B	109.5
O46—C45—C47	125.9 (7)	C110—C111—H11C	109.5
O44—C45—C47	110.6 (7)	H11A—C111—H11C	109.5
C45—C47—H47A	109.5	H11B—C111—H11C	109.5
C45—C47—H47B	109.5	C110—C112—H11D	109.5
H47A—C47—H47B	109.5	C110—C112—H11E	109.5
C45—C47—H47C	109.5	H11D—C112—H11E	109.5
H47A—C47—H47C	109.5	C110—C112—H11F	109.5
H47B—C47—H47C	109.5	H11D—C112—H11F	109.5
O60—C51—N64	106.7 (4)	H11E—C112—H11F	109.5
O60—C51—C52	109.1 (4)	C8—N11—C2	115.4 (4)
N64—C51—C52	112.6 (4)	C8—N11—C5	105.3 (4)

O60—C51—H51	109.4	C2—N11—C5	106.8 (4)
N64—C51—H51	109.4	C23—N14—C15	105.7 (3)
C52—C51—H51	109.4	C23—N14—C1	124.7 (4)
O53—C52—N61	105.4 (4)	C15—N14—C1	128.9 (4)
O53—C52—C51	112.3 (4)	C15—N16—C17	104.4 (4)
N61—C52—C51	111.6 (4)	C21—N20—C18	125.4 (4)
O53—C52—H52	109.2	C21—N20—H20	128 (10)
N61—C52—H52	109.2	C18—N20—H20	105 (10)
C51—C52—H52	109.2	C21—N22—C23	110.8 (4)
O53—C54—C55	104.1 (4)	C58—N61—C52	114.2 (4)
O53—C54—H54A	110.9	C58—N61—C55	104.9 (4)
C55—C54—H54A	110.9	C52—N61—C55	106.4 (4)
O53—C54—H54B	110.9	C73—N64—C65	105.4 (4)
C55—C54—H54B	110.9	C73—N64—C51	126.5 (4)
H54A—C54—H54B	109	C65—N64—C51	127.9 (4)
N61—C55—C63	110.4 (4)	C65—N66—C67	105.2 (4)
N61—C55—C56	103.3 (5)	C71—N70—C68	124.5 (4)
C63—C55—C56	113.5 (5)	C71—N70—H70	113 (10)
N61—C55—C54	102.8 (4)	C68—N70—H70	121 (10)
C63—C55—C54	111.5 (5)	C71—N72—C73	111.6 (4)
C56—C55—C54	114.3 (5)	C2—O3—C4	106.5 (4)
O57—C56—C55	105.5 (4)	C6—O7—C8	102.8 (4)
O57—C56—H56A	110.6	C1—O10—C9	113.1 (4)
C55—C56—H56A	110.6	C12—O24—C25	117.9 (4)
O57—C56—H56B	110.6	C45—O44—C13	116.5 (5)
C55—C56—H56B	110.6	C52—O53—C54	105.3 (4)
H56A—C56—H56B	108.8	C56—O57—C58	102.0 (4)
O57—C58—N61	105.8 (4)	C51—O60—C59	115.0 (4)
O57—C58—C59	109.6 (4)	C62—O74—C75	120.0 (4)
N61—C58—C59	115.8 (4)	C95—O94—C63	118.0 (6)
O57—C58—H58	108.5	C100—O101—H101	124 (3)
N61—C58—H58	108.5	C110—O111—H111	118 (3)
O10—C1—C2—O3	-179.5 (4)	C83—C84—C85—C86	1.3 (11)
N14—C1—C2—O3	-60.9 (5)	C84—C85—C86—C87	-1.3 (11)

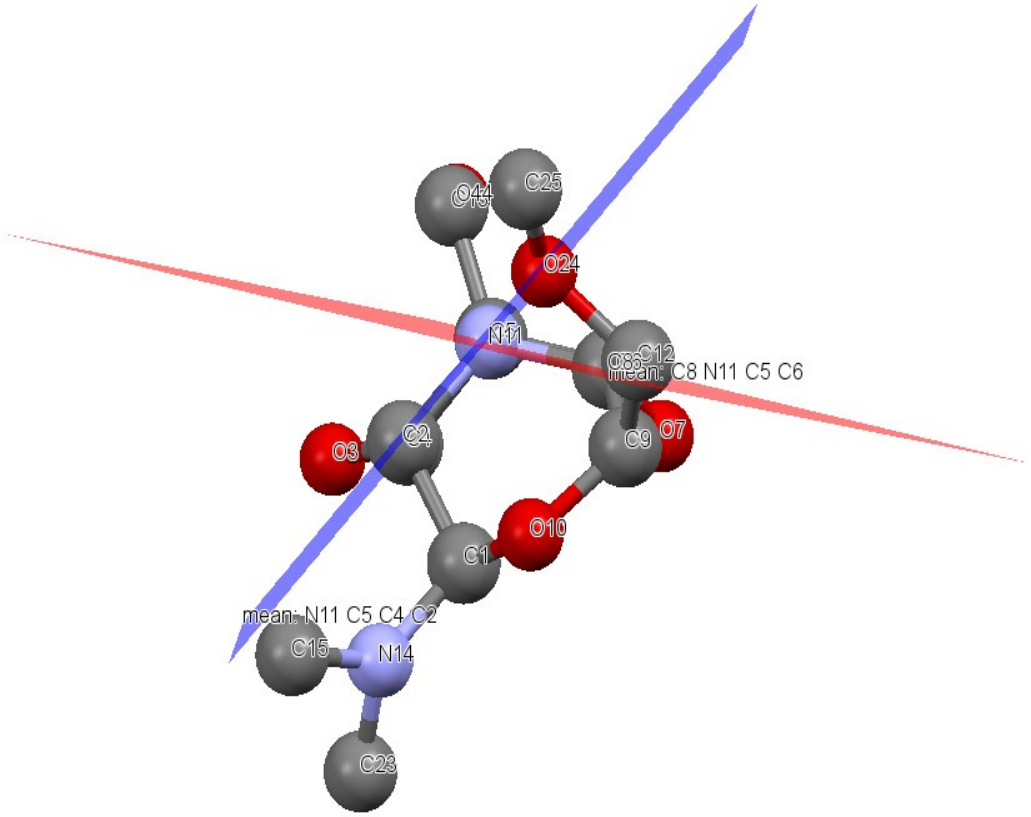
O10—C1—C2—N11	62.1 (5)	C85—C86—C87—C82	0.0 (11)
N14—C1—C2—N11	-179.3 (4)	C83—C82—C87—C86	1.1 (9)
O3—C4—C5—N11	22.9 (5)	C75—C82—C87—C86	-179.4 (6)
O3—C4—C5—C13	-93.4 (5)	O74—C75—C88—C89	146.1 (5)
O3—C4—C5—C6	134.7 (4)	C76—C75—C88—C89	28.6 (6)
N11—C5—C6—O7	23.1 (5)	C82—C75—C88—C89	-95.5 (6)
C13—C5—C6—O7	140.0 (4)	O74—C75—C88—C93	-35.8 (6)
C4—C5—C6—O7	-88.5 (5)	C76—C75—C88—C93	-153.3 (4)
O7—C8—C9—O10	-91.4 (5)	C82—C75—C88—C93	82.6 (5)
N11—C8—C9—O10	28.6 (6)	C93—C88—C89—C90	-3.0 (8)
O7—C8—C9—C12	147.3 (4)	C75—C88—C89—C90	175.1 (5)
N11—C8—C9—C12	-92.7 (5)	C88—C89—C90—C91	1.8 (9)
O10—C9—C12—O24	-74.9 (4)	C89—C90—C91—C92	0.2 (10)
C8—C9—C12—O24	50.0 (5)	C90—C91—C92—C93	-0.9 (10)
N11—C5—C13—O44	178.6 (4)	C91—C92—C93—C88	-0.3 (10)
C6—C5—C13—O44	64.1 (6)	C89—C88—C93—C92	2.3 (8)
C4—C5—C13—O44	-67.6 (6)	C75—C88—C93—C92	-175.9 (5)
C23—C17—C18—O19	-172.6 (5)	O7—C8—N11—C2	91.2 (4)
N16—C17—C18—O19	3.0 (8)	C9—C8—N11—C2	-30.3 (6)
C23—C17—C18—N20	6.1 (6)	O7—C8—N11—C5	-26.3 (4)
N16—C17—C18—N20	-178.3 (4)	C9—C8—N11—C5	-147.8 (4)
N16—C17—C23—N22	179.2 (4)	O3—C2—N11—C8	-135.9 (4)
C18—C17—C23—N22	-4.4 (7)	C1—C2—N11—C8	-13.5 (5)
N16—C17—C23—N14	0.7 (5)	O3—C2—N11—C5	-19.2 (5)
C18—C17—C23—N14	177.1 (4)	C1—C2—N11—C5	103.2 (4)
O24—C25—C26—C27	-111.9 (5)	C13—C5—N11—C8	-119.3 (4)
C32—C25—C26—C27	134.4 (5)	C6—C5—N11—C8	1.8 (5)
C38—C25—C26—C27	11.5 (7)	C4—C5—N11—C8	120.6 (4)
O24—C25—C26—C31	63.4 (6)	C13—C5—N11—C2	117.5 (4)
C32—C25—C26—C31	-50.2 (6)	C6—C5—N11—C2	-121.4 (4)
C38—C25—C26—C31	-173.2 (5)	C4—C5—N11—C2	-2.6 (5)
C31—C26—C27—C28	1.9 (8)	N22—C23—N14—C15	-179.1 (4)
C25—C26—C27—C28	177.3 (5)	C17—C23—N14—C15	-0.5 (5)
C26—C27—C28—C29	-2.2 (8)	N22—C23—N14—C1	10.0 (7)
C27—C28—C29—C30	1.8 (9)	C17—C23—N14—C1	-171.5 (4)

C28—C29—C30—C31	-1.2 (10)	N16—C15—N14—C23	0.2 (5)
C29—C30—C31—C26	1.0 (10)	N16—C15—N14—C1	170.6 (4)
C27—C26—C31—C30	-1.3 (9)	O10—C1—N14—C23	-130.4 (4)
C25—C26—C31—C30	-177.0 (6)	C2—C1—N14—C23	111.2 (5)
O24—C25—C32—C33	16.7 (6)	O10—C1—N14—C15	60.8 (6)
C26—C25—C32—C33	133.5 (5)	C2—C1—N14—C15	-57.6 (6)
C38—C25—C32—C33	-99.9 (6)	N14—C15—N16—C17	0.2 (5)
O24—C25—C32—C37	-163.7 (5)	C23—C17—N16—C15	-0.6 (5)
C26—C25—C32—C37	-46.9 (6)	C18—C17—N16—C15	-176.5 (5)
C38—C25—C32—C37	79.7 (6)	N22—C21—N20—C18	1.7 (8)
C37—C32—C33—C34	-1.2 (9)	O19—C18—N20—C21	173.7 (5)
C25—C32—C33—C34	178.3 (5)	C17—C18—N20—C21	-5.2 (7)
C32—C33—C34—C35	-1.4 (10)	N20—C21—N22—C23	1.0 (7)
C33—C34—C35—C36	3.1 (11)	C17—C23—N22—C21	0.4 (7)
C34—C35—C36—C37	-2.2 (10)	N14—C23—N22—C21	178.7 (4)
C35—C36—C37—C32	-0.4 (10)	O57—C58—N61—C52	89.7 (5)
C33—C32—C37—C36	2.1 (9)	C59—C58—N61—C52	-31.8 (6)
C25—C32—C37—C36	-177.5 (5)	O57—C58—N61—C55	-26.3 (5)
O24—C25—C38—C39	179.9 (5)	C59—C58—N61—C55	-147.9 (4)
C26—C25—C38—C39	56.8 (6)	O53—C52—N61—C58	-138.1 (4)
C32—C25—C38—C39	-67.3 (6)	C51—C52—N61—C58	-16.0 (5)
O24—C25—C38—C43	-4.7 (6)	O53—C52—N61—C55	-22.9 (5)
C26—C25—C38—C43	-127.8 (5)	C51—C52—N61—C55	99.2 (5)
C32—C25—C38—C43	108.1 (5)	C63—C55—N61—C58	-120.5 (5)
C43—C38—C39—C40	-0.2 (8)	C56—C55—N61—C58	1.2 (5)
C25—C38—C39—C40	175.3 (5)	C54—C55—N61—C58	120.4 (5)
C38—C39—C40—C41	-0.6 (8)	C63—C55—N61—C52	118.2 (5)
C39—C40—C41—C42	1.3 (8)	C56—C55—N61—C52	-120.1 (4)
C40—C41—C42—C43	-1.2 (8)	C54—C55—N61—C52	-0.9 (5)
C39—C38—C43—C42	0.3 (7)	N72—C73—N64—C65	-179.7 (5)
C25—C38—C43—C42	-175.3 (5)	C67—C73—N64—C65	0.0 (5)
C41—C42—C43—C38	0.4 (8)	N72—C73—N64—C51	-5.4 (8)
O60—C51—C52—O53	179.2 (4)	C67—C73—N64—C51	174.3 (4)
N64—C51—C52—O53	-62.5 (5)	N66—C65—N64—C73	0.3 (6)
O60—C51—C52—N61	61.2 (5)	N66—C65—N64—C51	-173.9 (4)

N64—C51—C52—N61	179.5 (4)	O60—C51—N64—C73	-121.0 (5)
O53—C54—C55—N61	23.7 (6)	C52—C51—N64—C73	119.3 (5)
O53—C54—C55—C63	-94.6 (5)	O60—C51—N64—C65	52.0 (6)
O53—C54—C55—C56	134.9 (5)	C52—C51—N64—C65	-67.7 (6)
N61—C55—C56—O57	24.8 (5)	N64—C65—N66—C67	-0.5 (6)
C63—C55—C56—O57	144.4 (5)	C73—C67—N66—C65	0.5 (6)
C54—C55—C56—O57	-86.1 (6)	C68—C67—N66—C65	178.1 (5)
O57—C58—C59—O60	-81.6 (5)	N72—C71—N70—C68	0.6 (8)
N61—C58—C59—O60	37.9 (6)	O69—C68—N70—C71	-179.5 (5)
O57—C58—C59—C62	154.6 (4)	C67—C68—N70—C71	-0.1 (7)
N61—C58—C59—C62	-85.9 (5)	N70—C71—N72—C73	0.0 (8)
O60—C59—C62—O74	-67.0 (5)	N64—C73—N72—C71	178.6 (5)
C58—C59—C62—O74	60.3 (5)	C67—C73—N72—C71	-1.0 (7)
N61—C55—C63—O94	173.4 (5)	N11—C2—O3—C4	34.9 (5)
C56—C55—C63—O94	58.0 (6)	C1—C2—O3—C4	-86.3 (5)
C54—C55—C63—O94	-72.9 (6)	C5—C4—O3—C2	-36.2 (5)
C73—C67—C68—O69	178.5 (5)	C5—C6—O7—C8	-39.5 (5)
N66—C67—C68—O69	1.1 (9)	N11—C8—O7—C6	41.4 (4)
C73—C67—C68—N70	-0.8 (6)	C9—C8—O7—C6	167.7 (4)
N66—C67—C68—N70	-178.2 (5)	N14—C1—O10—C9	174.4 (3)
N66—C67—C73—N72	179.4 (5)	C2—C1—O10—C9	-65.5 (5)
C68—C67—C73—N72	1.5 (8)	C12—C9—O10—C1	143.8 (4)
N66—C67—C73—N64	-0.3 (5)	C8—C9—O10—C1	20.3 (5)
C68—C67—C73—N64	-178.1 (4)	C9—C12—O24—C25	171.2 (4)
O74—C75—C76—C81	154.1 (4)	C26—C25—O24—C12	47.7 (5)
C88—C75—C76—C81	-94.0 (5)	C32—C25—O24—C12	165.6 (4)
C82—C75—C76—C81	30.5 (6)	C38—C25—O24—C12	-78.7 (5)
O74—C75—C76—C77	-29.9 (6)	O46—C45—O44—C13	8.2 (11)
C88—C75—C76—C77	82.1 (5)	C47—C45—O44—C13	-172.8 (6)
C82—C75—C76—C77	-153.4 (5)	C5—C13—O44—C45	-174.0 (5)
C81—C76—C77—C78	0.1 (8)	N61—C52—O53—C54	39.1 (5)
C75—C76—C77—C78	-176.1 (5)	C51—C52—O53—C54	-82.6 (5)
C76—C77—C78—C79	1.2 (8)	C55—C54—O53—C52	-39.3 (5)
C77—C78—C79—C80	-1.4 (8)	C55—C56—O57—C58	-41.0 (5)
C78—C79—C80—C81	0.2 (8)	N61—C58—O57—C56	42.3 (5)

C79—C80—C81—C76	1.2 (8)	C59—C58—O57—C56	167.8 (4)
C77—C76—C81—C80	-1.3 (7)	N64—C51—O60—C59	-178.5 (4)
C75—C76—C81—C80	174.8 (5)	C52—C51—O60—C59	-56.5 (5)
O74—C75—C82—C87	106.3 (6)	C58—C59—O60—C51	8.1 (6)
C88—C75—C82—C87	-6.4 (7)	C62—C59—O60—C51	134.4 (4)
C76—C75—C82—C87	-130.4 (5)	C59—C62—O74—C75	171.8 (4)
O74—C75—C82—C83	-74.2 (6)	C88—C75—O74—C62	179.3 (4)
C88—C75—C82—C83	173.1 (5)	C76—C75—O74—C62	-63.1 (5)
C76—C75—C82—C83	49.1 (6)	C82—C75—O74—C62	60.5 (6)
C87—C82—C83—C84	-1.1 (9)	O96—C95—O94—C63	-4.6 (14)
C75—C82—C83—C84	179.4 (5)	C97—C95—O94—C63	179.4 (8)
C82—C83—C84—C85	-0.1 (10)	C55—C63—O94—C95	172.0 (7)

Figure S165. Conformation of N11-C2-O3-C4-C5 (envelope on O3) and N11-C8-O7-C6-C5 (envelope on O7) oxazolidine rings of **18b** with the calculated data



PLATON DATA

18b ("km-151 ") PLATON-GEOMETRY Page 25

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5-Membered Ring (1) O(3) --> C(2) --> N(11) --> C(5) --> C(4) -->

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	sp3	sp3	sp3	sp3	sp3
Dev. (Ang)	-0.2081	0.1574	-0.0466	-0.0820	0.1793
Cs(I)-Asym-Par (Deg)	2.76	29.55	43.73	41.74	24.73
C2(I)-Asym-Par (Deg)	58.46	45.08	14.52	21.65	49.50
Ring Bond Angle(Deg)	106.47	105.94	106.78	103.52	104.20
Tors(I-J) (Deg)	34.94	-19.24	-2.56	22.94	-36.17
Cs(I-J)-Asym-Par (Deg)	41.74	24.73	2.76	29.55	43.73
C2(I-J)-Asym-Par (Deg)	21.65	49.50	58.46	45.08	14.52
Ring Bond Distance (Ang)	1.4057(1)	1.4682(1)	1.4901(1)	1.5240(1)	1.4308(1)

Weighted Average Ring Bond Distance = 1.4638(0,210) Ang. - NOTE: 1st esd. Internal, 2nd esd External.

Weighted Average Abs. Torsion Angl. = 23.17(45,611) Deg. see: e.g. Domenicano et al., Acta Cryst.(1975), B31, 221-234.

Cremer & Pople Puckering Parameters [D. Cremer & J.A. Pople, J.Amer.Chem.Soc., 97, (1975), 1354-1358]

Q(2) = 0.3303 Ang., Phi(2) =174.8858 Deg

* NOTE * - A Change of the Absolute Configuration Transforms Phi(2) into 180 + Phi(2).
- A Cyclic Forward Shift of the Pivot Atom from At1 to At2 Transforms Phi(2) into Phi(2) + 144.
- A Change of the Sense Transforms Phi(2) into 180 - Phi(2).

Pseudorotation Parameters P and Tau(M), (S.T.Rao, E.Westhof & M.Sundaralingam, Acta Cryst (1981), A37, 421-425)

P = 266.3 Degree, Tau(M) = 37.0 Deg. for Reference Bond N(11) --> C(5) [add 144 Deg. to P for each shift to next Bond]

[Ring-Sequence Change of Sense : P ----->>> - P]

Note: DELTA [Defined in Altona,C., Geise,H.J. & Romers,C. (1968). Tetrahedron, 24, 13-32] = 2 * P = 532.6 Deg.

Closest Pucker Descriptor: Envelope on O(3)

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5-Membered Ring (2) O(7) --> C(6) --> C(5) --> N(11) --> C(8) -->

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	sp3	sp3	sp3	sp3	sp3
Dev. (Ang)	0.2423	-0.1915	0.0675	0.0822	-0.2006
Cs(I)-Asym-Par (Deg)	2.62	32.65	49.72	48.83	28.68
C2(I)-Asym-Par (Deg)	67.01	52.38	17.73	23.69	56.06
Ring Bond Angle(Deg)	102.79	104.77	103.67	105.30	106.05
Tors(I-J) (Deg)	-39.44	23.16	1.80	-26.30	41.41
Cs(I-J)-Asym-Par (Deg)	48.83	28.68	2.62	32.65	49.72
C2(I-J)-Asym-Par (Deg)	23.69	56.06	67.01	52.38	17.73
Ring Bond Distance (Ang)	1.4292(1)	1.5243(1)	1.4901(1)	1.4607(1)	1.4337(1)

Weighted Average Ring Bond Distance = 1.4676(0,179) Ang. - NOTE: 1st esd. Internal, 2nd esd External.
Weighted Average Abs. Torsion Angl. = 26.42(45,711) Deg. see: e.g. Domenicano et al., Acta Cryst.(1975), B31, 221-234.

Cremer & Pople Puckering Parameters [D. Cremer & J.A. Pople, J.Amer.Chem.Soc., 97, (1975), 1354-1358]

Q(2) = 0.3833 Ang., Phi(2) =358.1732 Deg

* NOTE * - A Change of the Absolute Configuration Transforms Phi(2) into 180 + Phi(2).
- A Cyclic Forward Shift of the Pivot Atom from At1 to At2 Transforms Phi(2) into Phi(2) + 144.
- A Change of the Sense Transforms Phi(2) into 180 - Phi(2).

Pseudorotation Parameters P and Tau(M), (S.T.Rao, E.Westhof & M.Sundaralingam, Acta Cryst (1981), A37, 421-425)

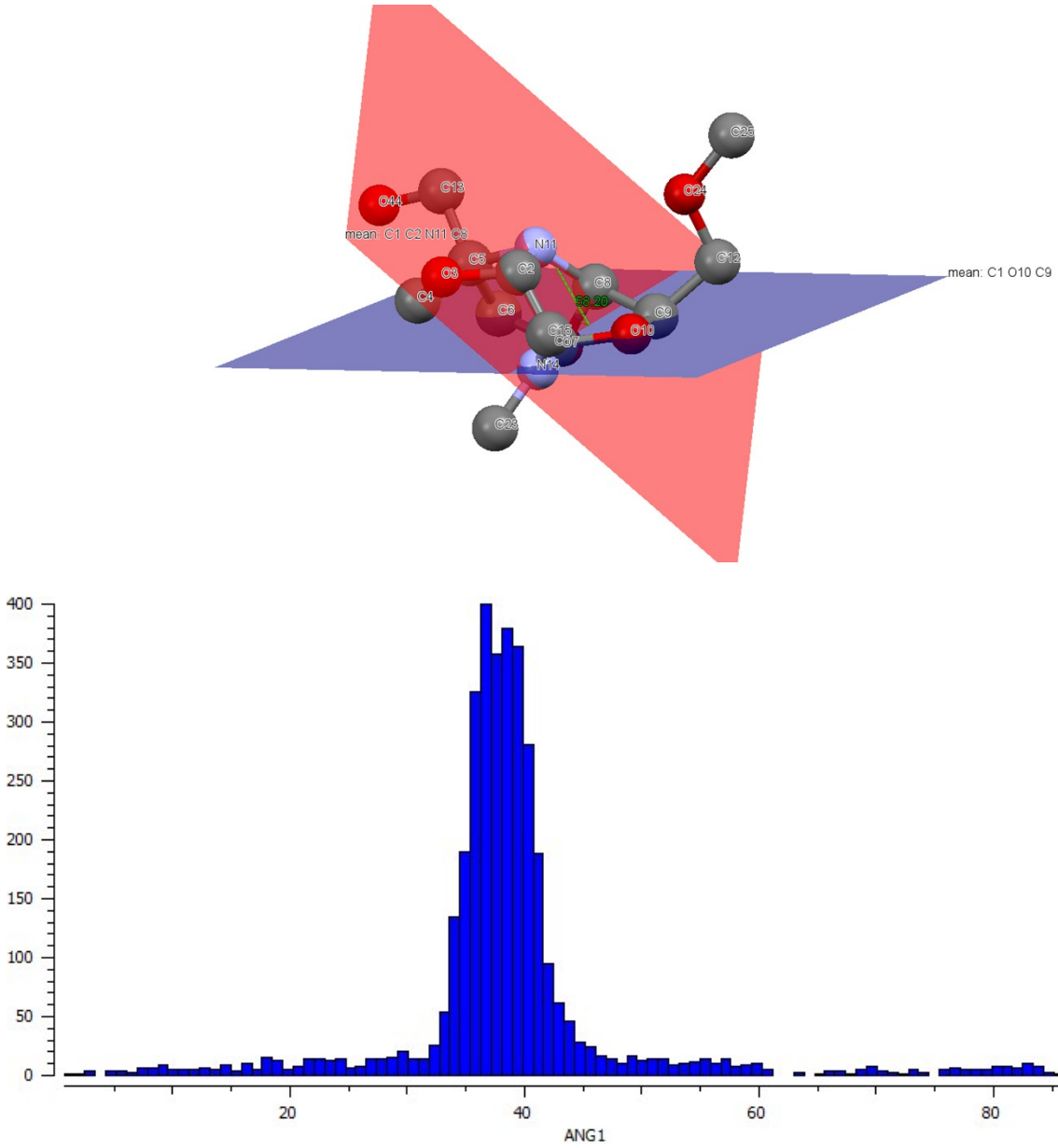
P = 87.3 Degree, Tau(M) = 42.4 Deg. for Reference Bond C(5) --> N(11) [add 144 Deg. to P for each shift to next Bond]

[Ring-Sequence Change of Sense : P ----->>> - P]

Note: DELTA [Defined in Altona,C., Geise,H.J. & Romers,C. (1968). Tetrahedron, 24, 13-32] = 2 * P = 174.6 Deg.

Closest Pucker Descriptor: Envelope on O(7)

Figure S166. View (up)of C1-O10-C9 and C1-C2-N11-C8 planes for one of the molecules in structure **18b** and histogram (down) for the angle of C1-O10-C9 and C1-C2-N11-C8 planes of morpholine ring moiety in organic compounds deposited in Cambridge Structural Database



NMR Tables

Table S4. Interproton distances (Å) in compound **18b**

Peak	Annot. pair	ROE (average)	X-ray
1	Hx-Hy		
2	1,2	2.76±0.03	2.85
3	1,4	2.85±0.16	2.75
4	1,9	2.55±0.06	2.85
5	2,4	2.89±0.1	3.1
6	2,12	3.67±0.5	4.1
7	4,13	2.81±0.23	2.5
8	6a,6b	1.75±0.01	1.6
9	6b,8	2.49±0.02	2.5
10	6b,13	2.52±0.01	2.5
11	8,9	2.53±0.07	2.45
12	8,12	2.53±0.05	2.5
13	8,13	3.33±0.2	3.1
14	9,4	3.93±0.8	4.7
15	9,12	2.31±0.02	2.3

ROE distances were determined from the two symmetric peaks around the diagonal and evaluated by two different integration methods yielding generally four peak volumes for distance determination and averaging (in case of CH_2 groups, the shorter (shortest) distance is given, and the overlap of the CH_2 peak integral is considered). As reference distance the anisochronous CH_2 group (6a, 6b = 1.75 Å) served. Evaluation was carried out as described in ref. 42 in the main text.

Figure S167. NMR−X-Ray correlation of **18b** (for **Table S4**)

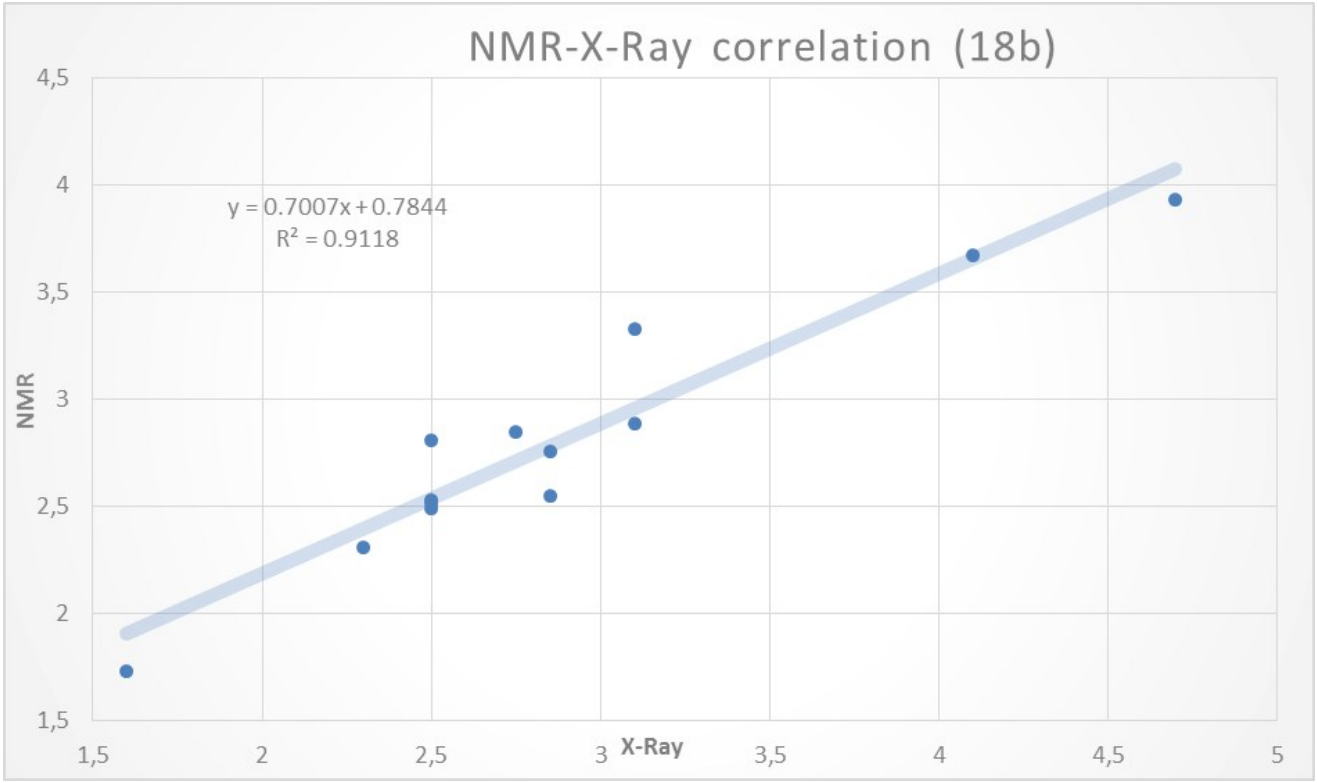


Figure S168. ZQF Easy-ROESY spectrum of **18b** (for **Table S4**)

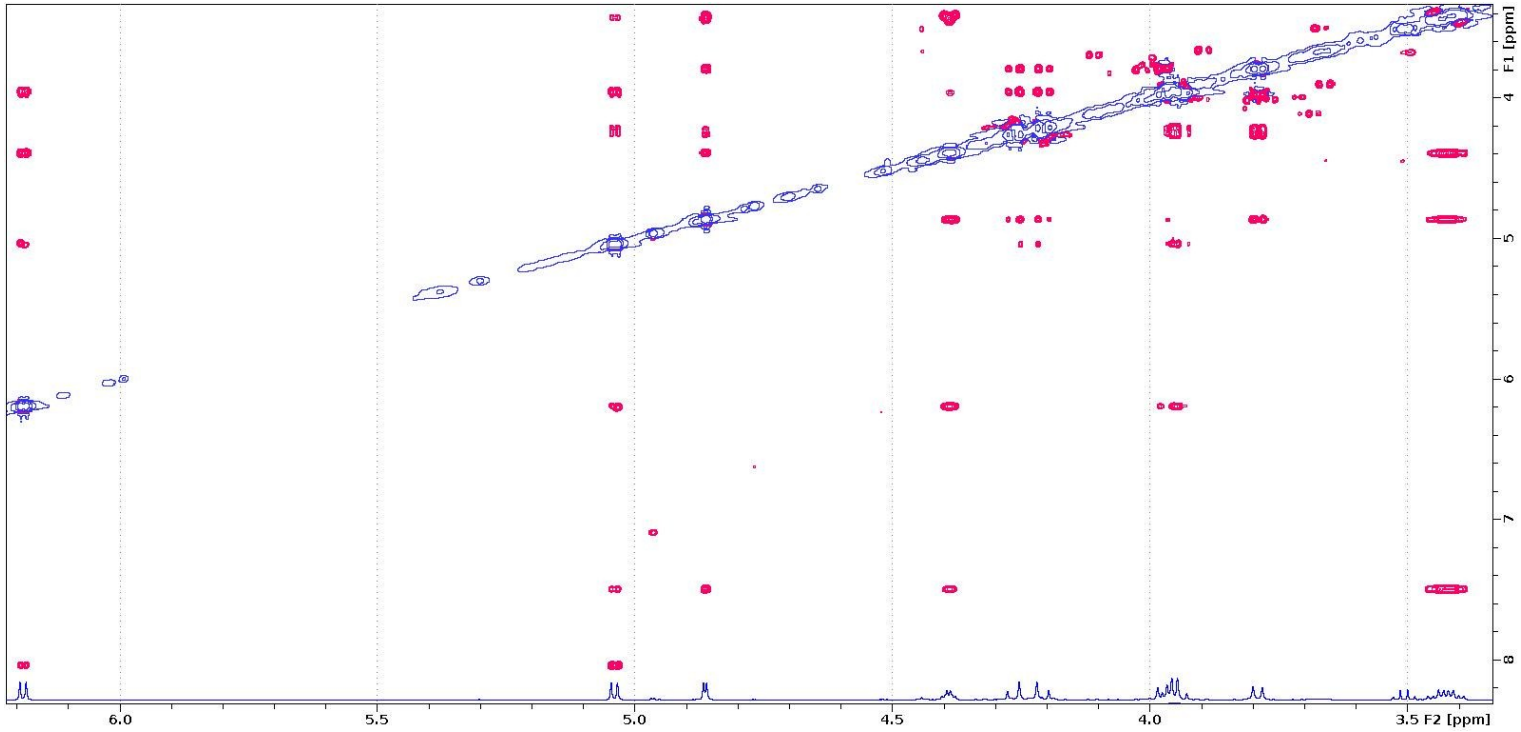


Figure S169. Detailed ROESY spectrum of **18b** with the relevant NOE cross-peaks

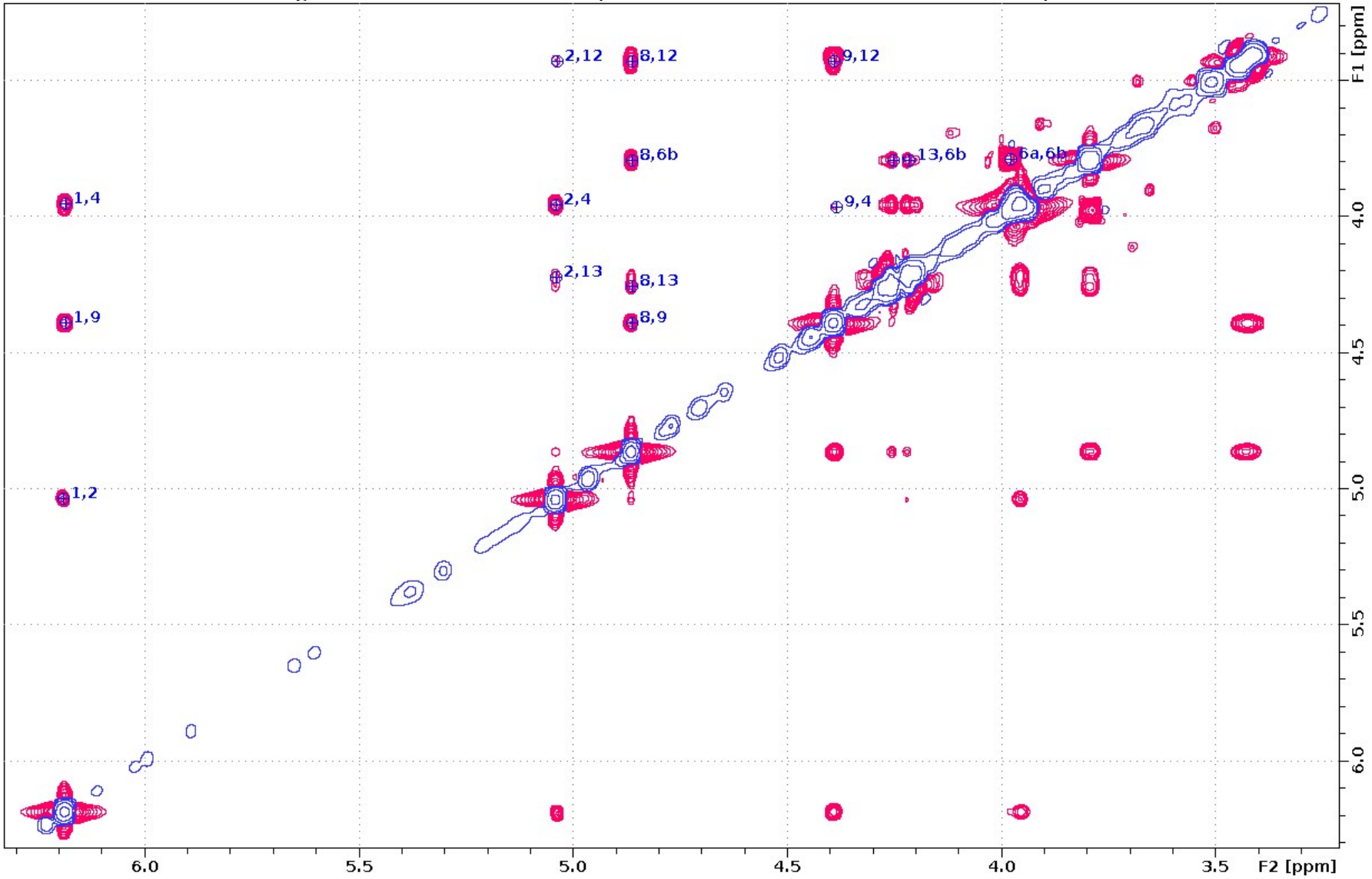


Table S5. Comparison of the computed ^{13}C NMR data of the eight possible stereoisomers of **3c** in the vicinity of the core part (C-1', C-2', C-4', C-5', C-6', C-8', C-9', C-12' and C-13') with the experimental data. Corrected mean absolute error values are listed for both the core part ($CMAE_{Core}$) and for all carbon atoms (CMAE). For better comparison $\Delta\delta$ values ≥ 2 are highlighted with yellow and ≥ 4 with red.

Numbering	Exp.	D1	Δδ1	D2	Δδ2	D3	Δδ3	D4	Δδ4	D5	Δδ5	D6	Δδ6	D7	Δδ7	D8	Δδ8
C-1'	77.7	77.77	0.07	85.11	7.41	78.88	1.18	79.19	1.49	77.48	0.22	78.28	0.58	82.09	4.39	76.14	1.56
C-2'	90.3	86.88	3.42	79.89	10.51	87.82	2.58	93.13	2.73	89.40	1.00	85.84	4.56	90.24	0.16	90.86	0.46
C-4'	72.0	73.33	1.33	70.41	0.89	74.00	2.70	73.33	2.03	72.22	0.92	76.53	5.23	75.11	3.81	71.21	0.09
C-5'	75.3	76.34	1.04	74.93	0.37	74.42	0.88	73.28	2.02	74.38	0.92	73.08	2.22	71.18	4.12	77.24	1.94
C-6'	71.3	73.40	2.10	69.77	2.23	72.12	0.12	77.16	5.16	74.27	2.27	73.46	1.46	74.71	2.71	69.27	2.73
C-8'	88.4	86.74	1.66	80.52	7.88	89.23	0.83	86.40	2.00	87.11	1.29	89.82	1.42	88.27	0.13	88.88	0.48
C-9'	73.9	76.14	2.24	83.01	9.11	76.11	2.21	75.57	1.67	78.78	4.88	75.90	2.00	83.76	9.86	74.83	0.93
C-12'	63.6	61.86	1.74	59.85	3.75	61.38	2.22	59.61	3.99	61.52	2.08	62.57	1.03	61.32	2.28	61.60	2.00
C-13'	63.7	63.07	0.63	63.45	0.15	60.85	2.75	62.26	1.34	60.48	3.12	61.98	1.62	67.95	4.35	62.05	1.55
$CMAE_{Core}$			1.58		4.70		1.72		2.49		1.85		2.24		3.53		1.31
CMAE			1.46		2.51		1.37		1.80		1.63		1.57		1.83		1.15

Table S6. Comparison of the computed ^{1}H NMR data of the eight possible stereoisomers of **3c** in the vicinity of the core part (belonging to C-1', C-2', C-4', C-6', C-8', C-9', C-12' and C-13') with the experimental data. Corrected mean absolute error values are listed for both the core part ($CMAE_{Core}$) and for all hydrogen atoms but the NH and OH hydrogens (CMAE). For better comparison $\Delta\delta$ values ≥ 0.3 are highlighted with yellow and ≥ 0.6 with red.

Numbering	Exp	D1	Δδ1	D2	Δδ2	D3	Δδ3	D4	Δδ4	D5	Δδ5	D6	Δδ6	D7	Δδ7	D8	Δδ8
H-1'	6.14	6.03	0.11	5.22	0.92	5.91	0.23	6.07	0.07	6.35	0.21	6.42	0.28	6.28	0.14	6.18	0.04
H-2'	4.68	4.20	0.48	5.00	0.33	4.15	0.52	4.46	0.21	4.48	0.19	4.54	0.13	4.40	0.27	4.44	0.23
H-4'a	3.87	3.74	0.13	3.58	0.24	3.74	0.08	3.79	0.03	3.82	0.00	3.86	0.04	3.80	0.02	3.63	0.19
H-4'b	3.77	3.74	0.03	3.92	0.10	4.48	0.66	3.30	0.52	3.37	0.45	4.58	0.76	4.01	0.19	3.59	0.23
H-6'a	3.78	3.72	0.06	3.49	0.33	3.77	0.05	3.92	0.10	3.77	0.05	3.74	0.08	3.74	0.08	3.59	0.23
H-6'b	3.87	3.71	0.16	3.99	0.17	3.39	0.43	4.64	0.82	4.41	0.59	3.30	0.52	3.80	0.02	3.74	0.08
H-8'	4.80	4.08	0.72	4.54	0.25	4.48	0.31	4.70	0.09	4.33	0.46	4.64	0.15	4.50	0.29	4.59	0.20
H-9'	4.21	3.96	0.25	3.83	0.38	3.97	0.24	4.35	0.14	3.89	0.32	4.00	0.21	3.93	0.28	4.25	0.04
H-12'a	3.38	3.14	0.24	3.64	0.26	3.35	0.03	3.74	0.36	3.26	0.12	3.19	0.19	3.23	0.15	3.25	0.13
H-12'b	3.38	3.50	0.12	3.02	0.36	3.36	0.02	2.96	0.42	3.08	0.30	3.20	0.18	3.04	0.34	3.18	0.20

H-13'a	3.64	3.40	0.24	3.67	0.03	3.56	0.08	3.08	0.56	3.10	0.54	3.49	0.15	3.56	0.08	3.29	0.35
H-13'b	3.64	3.40	0.24	3.83	0.19	3.13	0.51	3.44	0.20	3.53	0.11	3.04	0.60	3.55	0.09	3.45	0.19
$CMAE_{Core}$			0.23		0.30		0.26		0.29		0.28		0.27		0.16		0.17
CMAE			0.18		0.24		0.22		0.23		0.22		0.22		0.16		0.16

Table S7. Comparison of the computed ^{13}C NMR data of the eight possible stereoisomers of **9** in the vicinity of the core part (C-1', C-2', C-4', C-5', C-6', C-8', C-9', C-12' and C-13') with the experimental data. Corrected mean absolute error values are listed for both the core part ($CMAE_{Core}$) and for all carbon atoms (CMAE). For better comparison $\Delta\delta$ values ≥ 2 are highlighted with yellow and ≥ 4 with red.

Numbering	Exp	D1	Δδ1	D2	Δδ2	D3	Δδ3	D4	Δδ4	D5	Δδ5	D6	Δδ6	D7	Δδ7	D8	Δδ8
C-1'	77.4	77.22	0.18	85.52	8.12	78.76	1.36	78.86	1.46	76.97	0.43	76.31	1.09	80.78	3.38	76.02	1.38
C-2'	90.7	86.52	4.18	78.63	12.07	88.05	2.65	93.97	3.27	91.14	0.44	86.09	4.61	82.96	7.74	91.49	0.79
C-4'	72.3	75.44	3.14	69.43	2.87	75.47	3.17	73.82	1.52	72.70	0.40	78.22	5.92	71.75	0.55	72.41	0.11
C-5'	72.8	72.73	0.07	73.50	0.70	72.07	0.73	70.83	1.97	71.32	1.48	70.20	2.60	69.52	3.28	74.30	1.50
C-6'	72.1	75.68	3.58	69.21	2.89	72.43	0.33	78.86	6.76	76.68	4.58	74.11	2.01	72.28	0.18	71.74	0.36
C-8'	87.7	85.76	1.94	79.26	8.44	90.01	2.31	85.94	1.76	87.13	0.57	91.40	3.70	81.65	6.05	88.06	0.36
C-9'	72.3	74.49	2.19	80.27	7.97	74.60	2.30	73.25	0.95	75.98	3.68	73.39	1.09	80.40	8.10	72.44	0.14
C-12'	63.5	63.85	0.35	60.93	2.57	62.62	0.88	61.69	1.81	63.09	0.41	64.45	0.95	61.86	1.64	63.77	0.27
C-13'	65.1	68.24	3.14	65.93	0.83	64.05	1.05	65.72	0.62	66.32	1.22	65.67	0.57	64.31	0.79	65.65	0.55
$CMAE_{Core}$			2.08		5.16		1.64		2.23		1.47		2.50		3.52		0.61
CMAE			1.81		3.09		1.46		1.93		1.47		1.94		2.35		1.04

Table S8. Comparison of the computed ^{1}H NMR data of the eight possible stereoisomers of **9** in the vicinity of the core part (belonging to C-1', C-2', C-4', C-6', C-8', C-9', C-12' and C-13') with the experimental data. Corrected mean absolute error values are listed for both the core part ($CMAE_{Core}$) and for all hydrogen atoms but the NH hydrogen (CMAE). For better comparison $\Delta\delta$ values ≥ 0.3 are highlighted with yellow and ≥ 0.6 with red.

Numbering	Exp	D1	Δδ1	D2	Δδ2	D3	Δδ3	D4	Δδ4	D5	Δδ5	D6	Δδ6	D7	Δδ7	D8	Δδ8
H-1'	6.19	5.97	0.22	5.01	1.18	5.90	0.29	6.13	0.06	6.26	0.07	6.34	0.15	5.63	0.56	6.23	0.04
H-2'	4.60	4.22	0.38	4.99	0.39	4.11	0.49	4.67	0.07	4.59	0.01	4.53	0.07	4.54	0.06	4.49	0.11
H-4'a	3.78	3.83	0.05	3.59	0.19	4.07	0.29	3.80	0.02	3.75	0.03	3.92	0.14	3.99	0.21	3.71	0.07
H-4'b	3.78	3.78	0.00	3.62	0.16	3.81	0.03	3.64	0.14	3.85	0.07	4.14	0.36	3.65	0.13	3.68	0.10
H-6'a	3.98	3.65	0.33	3.63	0.35	3.66	0.32	3.97	0.01	4.05	0.07	3.83	0.15	3.84	0.14	3.83	0.15

H-6'b	3.78	3.94	0.16	3.82	0.04	3.76	0.02	4.21	0.43	3.92	0.14	3.74	0.04	3.71	0.07	3.74	0.04
H-8'	4.60	4.15	0.45	4.77	0.17	4.57	0.03	4.67	0.07	4.19	0.41	4.57	0.03	4.48	0.12	4.44	0.16
H-9'	4.25	4.16	0.09	3.77	0.48	4.28	0.03	4.31	0.06	3.98	0.27	3.97	0.28	3.74	0.51	4.11	0.14
H-12'a	4.25	4.35	0.10	4.70	0.45	4.14	0.11	3.75	0.50	4.16	0.09	4.02	0.23	3.98	0.27	3.84	0.41
H-12'b	4.25	4.00	0.25	3.89	0.36	4.34	0.09	5.10	0.85	3.95	0.30	4.08	0.17	4.19	0.06	4.51	0.26
H-13'a	4.10	3.95	0.15	4.15	0.05	3.59	0.51	3.70	0.40	4.09	0.01	3.98	0.12	4.49	0.39	3.73	0.37
H-13'b	4.25	3.95	0.30	4.17	0.08	4.36	0.11	4.18	0.07	3.77	0.48	3.97	0.28	4.08	0.17	4.32	0.07
$CMAE_{Core}$			0.21		0.32		0.19		0.22		0.16		0.17		0.22		0.16
CMAE			0.15		0.21		0.15		0.15		0.13		0.14		0.16		0.11

Table S9. Comparison of the computed ^{13}C NMR data of the assumed stereoisomer of **13a** in the vicinity of the core part (C-1', C-2', C-4', C-5', C-6', C-8', C-9', C-12' and C-13') with the experimental data. Corrected mean absolute error values are listed for both the core part ($CMAE_{Core}$) and for all carbon atoms (CMAE). $\Delta\delta$ values ≥ 2 are highlighted with yellow.

Numbering	Exp	D8	Δδ8
C-1'	78.64	76.22	2.42
C-2'	90.49	91.73	1.24
C-4'	72.12	71.30	0.82
C-5'	75.25	77.03	1.78
C-6'	71.71	68.73	2.98
C-8'	87.79	89.59	1.80
C-9'	73.71	74.90	1.19
C-12'	63.48	62.42	1.06
C-13'	63.95	62.76	1.19
$CMAE_{Core}$			1.61
CMAE			1.44

Table S10. Comparison of the computed ^{1}H NMR data of the assumed stereoisomer of **13a** in the vicinity of the core part (belonging to C-1', C-2', C-4', C-6', C-8', C-9', C-12' and C-13') with the experimental data. Corrected mean absolute error values are listed for both the core part ($CMAE_{Core}$) and for all hydrogen atoms but the NH and OH hydrogens (CMAE). $\Delta\delta$ values ≥ 0.3 are highlighted with yellow.

Numbering	Exp	D8	Δδ8
H-1’	6.18	6.28	0.10
H-2’	4.64	4.36	0.28
H-4’a	3.85	3.71	0.14
H-4’b	3.77	3.50	0.27
H-6’	3.85	3.68	0.17
H-6’	3.85	3.56	0.29
H-8’	4.77	4.36	0.41
H-9’	4.11	4.27	0.16
H-12’	3.32	3.08	0.24
H-12’	3.32	3.13	0.19
H-13’	3.61	3.43	0.18
H-13’	3.61	3.21	0.40
$CMAE_{Core}$			0.23
CMAE			0.16

Table S11. Comparison of the computed ^{13}C NMR data of the assumed stereoisomer of **18b** in the vicinity of the core part (C-1’, C-2’, C-4’, C-5’, C-6’, C-8’, C-9’, C-12’ and C-13’) with the experimental data. Corrected mean absolute error values are listed for both the core part ($CMAE_{Core}$) and for all carbon atoms but C-2 (CMAE).

Numbering	Exp	D8	Δδ8
C1	77.96	77.34	0.62
C2	90.80	91.44	0.64
C4	72.74	72.01	0.73
C5	72.87	74.25	1.38
C6	71.91	71.25	0.66
C8	89.46	88.45	1.01
C9	74.08	75.80	1.72
C12	63.93	62.43	1.50
C13	66.04	65.07	0.97
$CMAE_{Core}$			1.02
CMAE			1.30

Table S12. Comparison of the computed ^{1}H NMR data of the assumed stereoisomer of **18b** in the vicinity of the core part (belonging to C-1', C-2', C-4', C-6', C-8', C-9', C-12' and C-13') with the experimental data. Corrected mean absolute error values are listed for both the core part ($CMAE_{Core}$) and for all hydrogen atoms but the NH hydrogen (CMAE). $\Delta\delta$ values ≥ 0.3 are highlighted with yellow.

Numbering	Exp	D8	Δδ8
H1'	6.16	6.08	0.08
H2'	5.01	5.06	0.05
H4'	3.93	3.77	0.16
H4'	3.93	3.70	0.23
H6'a	3.95	3.68	0.27
H6'b	3.76	3.65	0.11
H8'	4.83	4.70	0.13
H9'	4.37	4.17	0.20
H12'	3.34	3.01	0.33
H12'	3.44	3.38	0.06
H13'	4.21	4.02	0.19
H13'	4.21	4.09	0.12
$CMAE_{Core}$			0.16
CMAE			0.17