

Supplementary Materials

Synthesis and anticancer and antiviral activities of C-2'-branched arabinonucleosides

Miklós Bege, Alexandra Kiss, Ilona Bereczki, Jan Hodek, Lenke Polyák, Gábor Szemán-Nagy, Lieve Naesens, Jan Weber, Anikó Borbás

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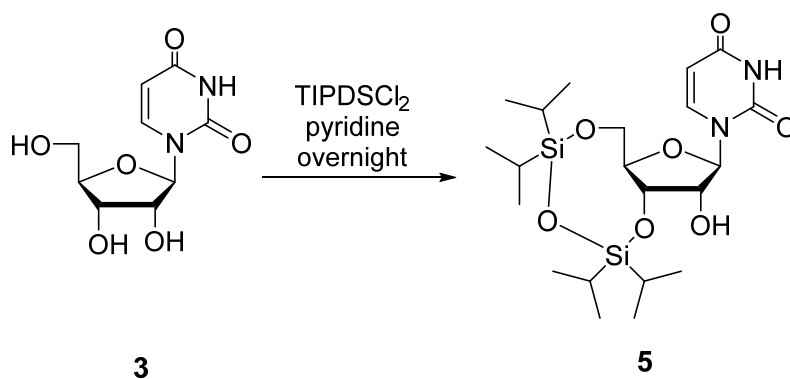
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General information

Compounds **9f**¹ and **9g**¹ were prepared according to literature procedures. 2,2-Dimethoxy-2-phenylacetophenone (DPAP), 4-methoxyacetophenone (MAP), thioacetic acid, *n*-propyl-mercaptane, *n*-butyl-mercaptane and *n*-hexyl-mercaptane were purchased from Sigma-Aldrich Chemical Co. and used without further purification. Optical rotations were measured at room temperature with a Perkin-Elmer 241 automatic polarimeter. TLC was performed on Kieselgel 60 F₂₅₄ (Merck) with detection by UV-light (254 nm) and immersing into sulfuric acidic ammonium molybdate solution or 5% ethanolic sulfuric acid followed by heating. Flash column chromatography was performed on silica gel 60 (Merck, 0.040-0.063 mm). Organic solutions were dried over anhydrous Na₂SO₄ and concentrated in vacuum. The ¹H NMR (360, 400 and 500 MHz) and ¹³C NMR (90, 100 and 125 MHz) spectra were recorded with Bruker DRX-360, Bruker DRX-400 and Bruker Avance II 500 spectrometers at 25 °C. Chemical shifts are referenced to Me₄Si (0.00 ppm for ¹H) and to the residual solvent signals (CDCl₃: 77.2, DMSO-*d*₆: 39.5, CD₃OD: 49.0 for ¹³C). Two-dimensional COSY and ¹H–¹³C HSQC experiments were used to assist NMR assignments. MALDI-TOF MS analyses of the compounds were carried out in the positive reflectron mode using a BIFLEX III mass spectrometer or with a Bruker Autoflex Speed mass spectrometer equipped with a time-of-flight (TOF) mass analyzer. 2,5-Dihydroxybenzoic acid (DHB) was used as matrix and F₃CCOONa as cationising agent in DMF.

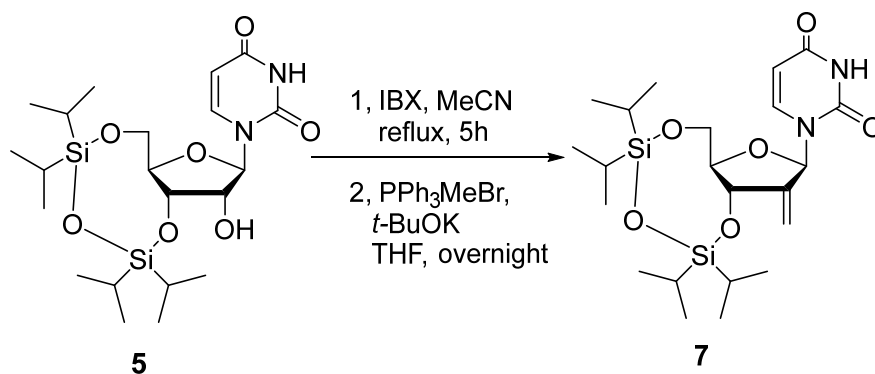
The photoinitiated reactions were carried out in a borosilicate vessel by irradiation with a low-pressure Hg-lamp (Osram Supratec UV, HTC 150-211, 150 W, 230 V, R7s) giving maximum emission at 365 nm, without any caution to exclude air or moisture.

Synthesis of furanosyl exomethylenes



3',5'-O-(1,1,3,3-Tetraisopropylidisiloxane-1,3-diyl)-β-D-ribofuranosyl-uracil (5)²

Uridine (1.68 g, 6.87 mmol) was dissolved in dry pyridine (20 ml). 1,3-dichloro-1,1,3,3-tetraisopropylidisiloxane (2.3 ml, 7.2 mmol, 1.05 equiv.) was added and the reaction mixture was stirred overnight. Next day, water (10 ml) was added and the solvent was evaporated under reduced pressure. The residue was dissolved in EtOAc (100 ml) and extracted with H₂O (2x), 10% aq. solution of NaHSO₄ (2x) H₂O (1x) and brine (1x). The organic phase was dried over Na₂SO₄, filtered and concentrated *in vacuo*. The crude product was purified by flash column chromatography (hexane/acetone 8/2→7/3) to give compound **5** (2.54 g, 76%) as a white solid. $[\alpha]_D = +10.8$ (c = 0.12, CHCl₃), R_f = 0.15 (hexane/acetone 8/2), ¹H NMR (500 MHz, CDCl₃) δ (ppm) 9.98 (s, 1H, NH), 7.80 (d, *J* = 8.1 Hz, 1H, H-6), 5.75 (s, 1H, H-1'), 5.71 (d, *J* = 8.1 Hz, 1H, H-5), 4.31 (dd, *J* = 8.8, 4.6 Hz, 1H), 4.20 (dd, *J* = 16.4, 12.1 Hz, 3H), 4.01 (dd, *J* = 13.2, 2.2 Hz, 1H), 3.87 (br s, 1H), 1.12 – 1.00 (m, 28H, 8x *i*-PrCH₃ and 4x *i*-PrCH). ¹³C NMR (125 MHz, CDCl₃) δ (ppm) 163.8, 150.5 (2C, 2xCO), 140.0 (1C, C-6), 102.1 (1C, C-5), 91.1, 82.0, 75.2, 68.8 (4C, C-1', C-2', C-3', C-4'), 60.2 (1C, C-5'), 17.6, 17.5, 17.4, 17.3, 17.1, 17.0, 17.0, 16.9 (8C, 8x *i*-PrCH₃), 13.5, 13.1, 13.0, 12.6 (4C, 4x *i*-PrCH). MALDI-ToF MS *m/z* calcd for C₂₁H₃₈N₂O₇Si₂Na⁺: 509.212 [M+Na]⁺, found 509.167.



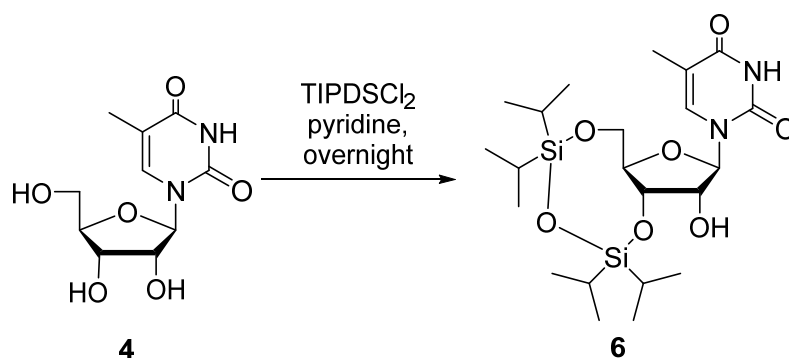
2'-Deoxy-2'-methylene-3',5'-O-(1,1,3,3-tetraisopropylidisiloxane-1,3-diyl)-β-D-ribofuranosyl-uracil (7**)³**

Compound **5** (1.54 g, 3.17 mmol) and IBX (2.67 g, 9.52 mmol, 3.0 equiv.) were suspended in MeCN (25 ml) and stirred at 100 °C for 5 h. After 5 h, the reaction mixture was diluted with EtOAc (100 ml), filtered and evaporated under reduced pressure.

Methyltriphenylphosphonium-bromide (2.8 g, 7.92 mmol, 2.5 equiv) was suspended in dry THF (20 ml) under Ar. T-BuOK (0.89 g, 7.92 mmol, 2.5 equiv) was added and stirred for 2 h at room temperature. After 2 h, the reaction mixture was cooled to -78 °C, and the keton crude product was added to this suspension. The reaction mixture was allowed to warm to -10 °C

over 1 h and stored at 0–4 °C overnight. The reaction mixture was diluted with CH₂Cl₂ (200 ml) and washed with saturated aq. NH₄Cl solution (3 x 50 ml) and brine (1 x 50ml). The organic phase was dried over anhydrous Na₂SO₄ and concentrated in *vacuo*. The residue was purified by flash column chromatography (gradient elution hexane/acetone 9/1→85/15) to yield compound **7** (641 mg, 43%) as a yellow syrup.

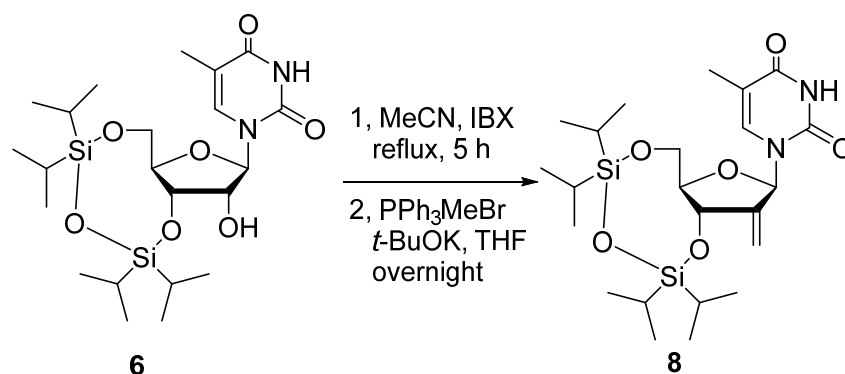
$[\alpha]_D = -9.6$ ($c = 0.30$, CHCl₃), $R_f = 0.13$ (hexane/acetone 8/1), ¹H NMR (360 MHz, CDCl₃) δ (ppm) 10.18 (s, 1H, NH), 7.49 (d, $J = 8.1$ Hz, 1H, H-6), 6.53 (s, 1H, H-1'), 5.74 (d, $J = 8.1$ Hz, 1H, H-5), 5.56 (s, 1H, exomethylene H_a), 5.45 (s, 1H, exomethylene H_b), 4.82 (d, $J = 8.6$ Hz, 1H, H-3'), 4.16 (dd, $J = 13.1, 1.4$ Hz, 1H, H-5'a), 4.05 (dd, $J = 13.2, 2.4$ Hz, 1H, H-5'b), 3.70 (d, $J = 8.8$ Hz, 1H, H-4'), 1.07 (m, 28H, 8x *i*-PrCH₃ and 4x *i*-PrCH). ¹³C NMR (90 MHz, CDCl₃) δ (ppm) 164.0 (1C, C-4), 150.8 (1C, C-2), 146.6 (1C, C-2'), 139.9 (1C, C-6), 112.2 (1C, exomethyleneCH₂), 102.7 (1C, C-5), 83.9 (1C, C-1'), 83.1 (1C, C-4'), 69.8 (1C, C-3'), 60.4 (1C, C-5'), 17.5, 17.4, 17.3, 17.0, 17.0, 16.9, 16.9 (8C, 8x *i*-PrCH₃), 13.6, 13.0, 12.9, 12.5 (4C, 4x *i*-PrCH). MALDI-ToF MS: m/z calcd for C₂₂H₃₈N₂O₆Si₂Na⁺: 505.217 [M+Na]⁺, found 505.182.



3',5'-O-(1,1,3,3-Tetraisopropylidisiloxane-1,3-diyl)-β-D-ribofuranosyl-thymine (**6**)⁴

Ribothymidine (3.54 g, 13.74 mmol) was dissolved in dry pyridine (40 ml). 1,3-dichloro-1,1,3,3-tetraisopropylidisiloxane (4.6 ml, 14.4 mmol, 1.05 equiv.) was added and the reaction mixture was stirred overnight. Next day, water (20 ml) was added and the solvent was evaporated under reduced pressure. The residue was dissolved in EtOAc (400 ml) and extracted with, 10% aq. solution of NaHSO₄ (2x) and brine (1x). The organic phase was dried over Na₂SO₄, filtered and concentrated in *vacuo*. The crude product was purified by flash column chromatography (hexane/acetone 8/2→7/3) to give compound **6** (5.81 g, 84%) as a white foam. $[\alpha]_D = -15.0$ ($c = 0.18$, CHCl₃), $R_f = 0.26$ (hexane/acetone 8/2), ¹H NMR (360 MHz, CDCl₃) δ (ppm) 10.22 (s, 1H, NH), 7.56 (s, 1H, H-6), 5.73 (s, 1H, H-1'), 4.37 – 4.27 (m, 2H), 4.26 – 4.18 (m, 3H), 4.01 (dd, $J = 13.4, 2.6$ Hz, 1H, H-5'a), 1.91 (s, 3H, thymineCH₃), 1.12 – 0.96 (m, 28H,

6*xi*-PrCH₃ & 4*xi*-PrCH). ¹³C NMR (90 MHz, CDCl₃) δ (ppm) 164.4, 150.6 (2C, 2xCO), 135.6 (1C, C-6), 110.6 (1C, C-5), 91.3, 81.9, 75.1, 68.7 (4C, C-1', C-2', C-3', C-4'), 60.1 (1C, C-5'), 17.5, 17.4, 17.3, 17.1, 17.0, 16.9 (8C, 8x *i*-PrCH₃), 13.5, 13.0, 12.8, 12.7, 12.5 (5C, 4x *i*-PrCH & thymine CH₃). MALDI-ToF MS: *m/z* calcd for C₂₂H₄₀N₂O₇Si₂Na⁺: 523.227 [M+Na]⁺, found 523.172.



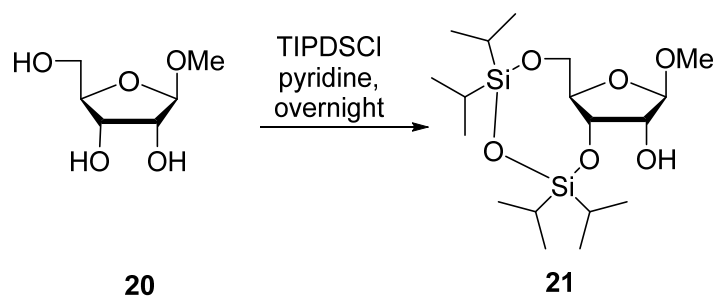
2'-Deoxy-2'-methylene-3',5'-O-(1,1,3,3-tetraisopropylidisiloxane-1,3-diyl)-β-D-ribofuranosyl-thymine (8)³

Compound **6** (5.5 g, 10.9 mmol) and IBX (9.2 g, 32.9 mmol, 3.0 equiv.) were suspended in MeCN (40 ml) and stirred for 5 h at 100 °C. The suspension was diluted with EtOAc (200 ml), filtered, and concentrated under reduced pressure.

Methyltriphenylphosphonium bromide (11.8 g, 32.9 mmol, 3.0 equiv.) was suspended in dry THF (30 ml). Under Ar *t*-BuOK (3.7 g, 32.9 mmol, 3.0 equiv.) was added and stirred for 2 h. After 2 h, the reaction mixture was cooled to -78 °C, and the keton crude product (dissolved in dry THF) was added. The reaction mixture was allowed to warm to -10 °C over 1 h and stored at 0–4 °C overnight. The reaction mixture was diluted with CH₂Cl₂ (350 ml) and washed with saturated aq. NH₄Cl solution (3 x 10 ml) and brine (1 x 10ml). The organic phase was dried over anhydrous Na₂SO₄ and concentrated in *vacuo*. The residue was purified by flash column chromatography (gradient elution hexane/acetone 9/1→85/15→8/2) to yield compound **8** (2.7 g, 48%) as a yellow syrup.

[α]_D = -36.1 (c = 0.18, CHCl₃), R_f = 0.27 (hexane/acetone 8/2), ¹H NMR (400 MHz, CDCl₃) δ (ppm) 9.49 (s, 1H, NH), 7.12 (s, 1H, H-6), 6.58 (d, *J* = 1.5 Hz, 1H, H-1'), 5.49 (dd, *J* = 2.6, 1.3 Hz, 1H, exomethyleneH_a), 5.48 – 5.45 (m, 1H, exomethyleneH_b), 4.86 (dd, *J* = 8.8, 1.7 Hz, 1H, H-3'), 4.15 (dd, *J* = 13.3, 2.0 Hz, 1H, H-5'_a), 4.05 (dd, *J* = 13.2, 2.8 Hz, 1H, H-5'_b), 3.67 (dt, *J* = 8.8, 2.4 Hz, 1H, H-4'), 1.89 (s, 3H, thymineCH₃), 1.08 (dd, *J* = 19.6, 4.7 Hz, 28H, 28H, 8x *i*-

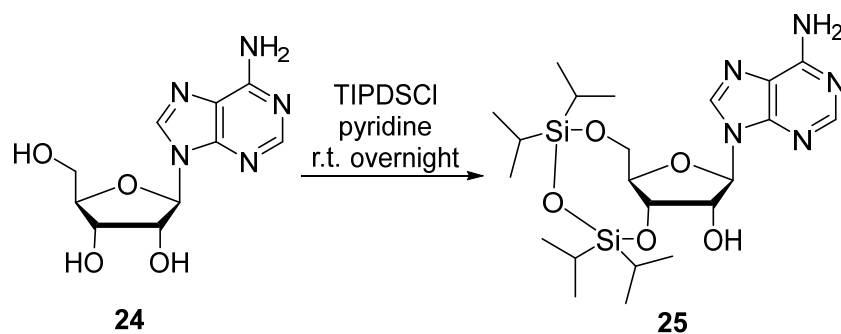
PrCH₃ and 4x *i*-PrCH). ¹³C NMR (100 MHz, CDCl₃) δ (ppm) 164.0, 150.9 (2C, 2xCO), 147.1 (1C, C-2'), 135.6 (1C, C-6), 112.1, 111.5 (2C, exomethyleneCH₂ & C-5), 83.5, 82.8, 70.2 (3C, C-1', C-4', C-3'), 60.2 (1C, C-5'), 17.5, 17.3, 17.1, 17.1, 17.1, 16.9 (8C, 8x *i*-PrCH₃), 13.7, 13.1, 12.7, 12.6, 12.6 (5C, 4x4x *i*-PrCH & thymineCH₃). MALDI-ToF MS: *m/z* calcd for C₂₃H₄₀N₂O₆Si₂Na⁺: 519.232 [M+Na]⁺, found 519.171.



Methyl 3,5-*O*-(1,1,3,3-tetraisopropylidisiloxane-1,3-diyl)-β-D-ribofuranoside (**21**)⁵

Methyl-β-D-ribofuranoside (5.0 g, 30.5 mmol) was dissolved in dry Pyridine (50 mL), and cooled to 0 °C. Then, 1,3-dichloro-1,1,3,3-tetraisopropylidisiloxane (10 mL, 32 mmol, 1.05 equiv.) was added and stirred overnight at r.t. Next day, water (40 mL, was added and the solvent was evaporated under reduced pressure. The residue was dissolved in EtOAc, and extracted with 10% aq.NaHSO₄ and brine. The organic phase was dried over Na₂SO₄, filtered and concentrated *in vacuo*. The crude product was purified by flash chromatography (hexane/acetone 98/2) to give compound **21** (9.4 g, 84%).

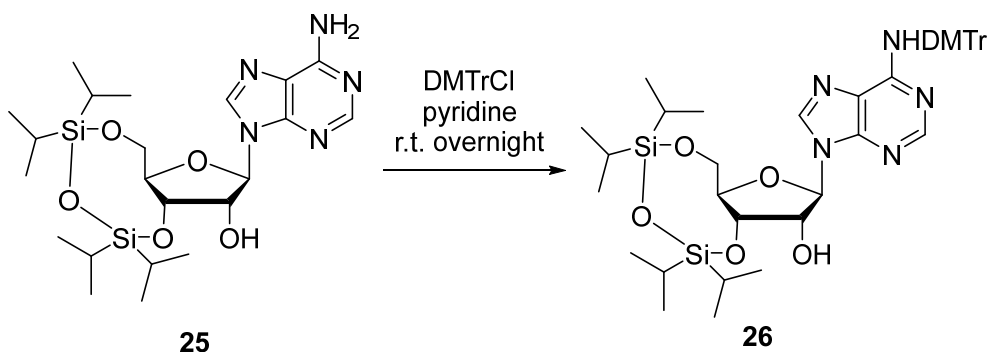
R_f= 0.68 (hexane/acetone 9/1), ¹H NMR (360 MHz, CDCl₃) δ (ppm) 4.82 (s, 1H, H-1), 4.50 (t, *J* = 5.4 Hz, 1H), 4.09 – 3.99 (m, 3H), 3.75 (dd, *J* = 10.5, 8.8 Hz, 1H, H-5b), 3.32 (s, 3H, OMe), 2.99 (s, 1H), 1.15 – 0.97 (m, 28H, 8xi-PrCH₃ & 4x *i*-PrCH). ¹³C NMR (90 MHz, CDCl₃) δ (ppm) 107.4 (1C, C-1), 82.8, 75.9, 75.2 (3C, C-2, C-3, C-4), 66.3 (1C, C-5), 55.0 (1C, OMe), 17.6, 17.5, 17.3, 17.1 (8C, 8xi-PrCH₃), 13.4, 12.9, 12.7 (4C, 4xi-PrCH).



3',5'-O-(1,1,3,3-Tetraisopropylidisiloxy)-adenosine (**25**)⁶

Adenosine (2.0 g, 7.5 mmol) was dissolved in dry pyridine (50 mL) and cooled to 0 °C. TIPDSCI₂ (2.5 mL, 7.85 mmol, 1.05 equiv.) was added, the reaction mixture was allowed to warm up to room temperature and stirred for 2 days. The solvent was evaporated under reduced pressure, the residue was dissolved in EtOAc (500 mL) and washed with water (100 mL), 10% aq. NaHSO₄ solution (3x100 mL) and brine (100 mL). The organic phase was dried over Na₂SO₄, filtered and evaporated under reduced pressure. The crude product was purified by flash column chromatography (CH₂Cl₂/MeOH 95/5) to give compound **25** (3.52 g, 93%) as white solid.

$[\alpha]_D^{25} = +10.8$ ($c = 0.12$, DMSO), $R_f = 0.32$ (CH₂Cl₂/MeOH 95/5), ¹H NMR (400 MHz, DMSO) δ (ppm) 8.22, 8.08 (2xs, 2x1H, H-2, H-8), 7.34 (s, 2H, NH₂), 5.88 (s, 1H), 5.65 (d, $J = 4.6$ Hz, 1H, H-1'), 4.80 (dd, $J = 8.5, 5.1$ Hz, 1H, H-3'), 4.52 (t, $J = 4.6$ Hz, 1H, H-2'), 4.07 (dd, $J = 12.6, 3.2$ Hz, 1H, H-5'a), 4.01 (dt, $J = 8.5, 2.8$ Hz, 1H, H-4'), 3.93 (dd, $J = 12.6, 2.6$ Hz, 1H, H-5'b), 1.04 (s, 28H, 4xi-PrCH, 8xi-PrCH₃). ¹³C NMR (100 MHz, DMSO) δ (ppm) 156.1, 148.6, 119.3 (3C, 3x adenine C_q), 152.5 (1C, adenine CH), 89.4, 80.8, 73.7, 69.8 (4C, C-1', C-2', C-3', C-4'), 60.8 (1C, C-5'), 17.4, 17.2, 17.0, 16.9, 16.8 (8C, 8x *i*-PrCH₃), 12.8, 12.5, 12.3, 12.1 (4C, 4x *i*-PrCH). MALDI-ToF MS: m/z calcd for C₂₂H₃₉N₅O₅Si₂Na⁺: 532.239 [M+Na]⁺, found 532.279.

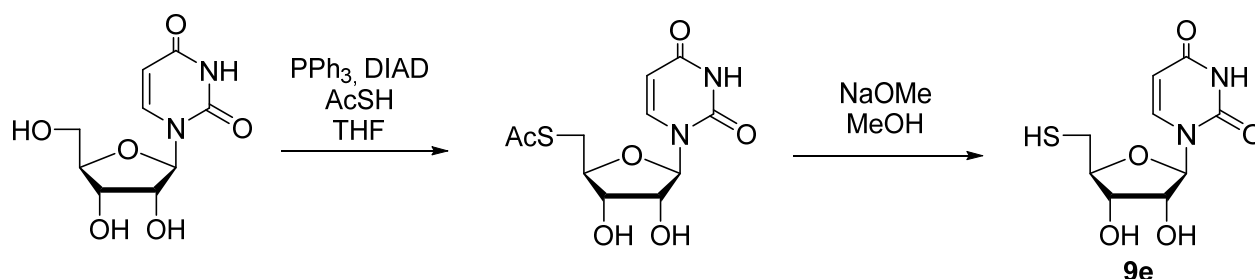


3',5'-O-(1,1,3,3-Tetraisopropylidisiloxy)-N-dimethoxytrityl-adenosine (**26**)⁷

Compound **25** (410 mg, 0.80 mmol) was dissolved in dry pyridine (5 mL) and DMTrCl (553 mg, 1.6 mmol, 2.0 equiv.) was added, the reaction mixture was stirred at r.t. overnight. Next day, the was diluted with CH₂Cl₂ (200 mL) and washed with 10% aq. NaHSO₄ solution. The organic phase was dried over Na₂SO₄, filtered and evaporated under reduced pressure. The crude product was purified by flash column chromatography (hexane/acetone 9/1→8/2) to give compound **26** (498 mg, 77%) as white foam.

[α]_D = -35.7 (c = 0.21, CHCl₃), R_f = 0.54 (hexane/acetone 6/4), ¹H NMR (400 MHz, CDCl₃) δ (ppm) 7.99, 7.86 (2xs, 2x1H, H-2, H-8), 7.33 (dd, *J* = 8.2, 1.3 Hz, 2H, arom), 7.28 – 7.20 (m, 7H, arom), 6.91 (s, 1H, NH), 6.82 – 6.75 (m, 4H, arom), 5.89 (d, *J* = 1.0 Hz, 1H, H-1'), 5.15 (dd, *J* = 7.6, 5.6 Hz, 1H, H-3'), 4.61 (d, *J* = 5.5 Hz, 1H, H-2'), 4.12 (dd, *J* = 11.6, 4.1 Hz, 1H, H-5'a), 4.07 (dd, *J* = 7.7, 3.0 Hz, 1H, H-4'), 4.05 – 4.00 (m, 1H, H-5'b), 3.77 (s, 6H, 2x OMe), 3.52 (s, 1H, OH) 1.12 – 1.03 (m, 28H, 4xi-PrCH, 8xi-PrCH₃). ¹³C NMR (100 MHz, CDCl₃) δ (ppm) 158.4 (2C, 2x arom C_q), 152.4 (1C, adenine CH), 154.3, 148.1 (2C, 2x adenine C_q), 145.5 (1C, Trt C_q), 137.6 (2C, 2x Trt C_q), 130.2, 128.9, 127.9, 126.9, 113.2 (13C, arom.), 121.7 (1C, adenine C_q), 89.9, 82.2, 75.0, 70.9 (4C, C-1', C-2', C-3', C-4'), 70.7 (1C, Trt C_q), 61.8 (1C, C-5'), 55.3 (2C, 2x OMe), 17.6, 17.4, 17.2, 17.1 (8C, 8x *i*-PrCH₃), 13.4, 13.2, 12.8, 12.7 (4C, 4x *i*-PrCH). MALDI-ToF MS: *m/z* calcd for C₄₃H₅₇N₅O₇Si₂Na⁺: 834.369 [M+Na]⁺, found 834.464.

Synthesis of 5'-thiouridine



5'-S-acetyl-5'-thiouridine

PPh₃ (6.5 g, 24.6 mmol, 2.0 equiv.) was suspended in dry THF (50 mL). The reaction mixture was cooled to 0 °C and diisopropyl azodicarboxylate (DIAD) (5.0 mL, 24.6 mmol, 2.0 equiv.) was added dropwise and stirred for 30 min at 0 °C. Uridine (3.02 g, 12.3 mmol) and AcSH (1.8 mL, 24.6 mmol, 2.0 equiv.) were dissolved in dry DMF (50 mL) and the solution was added to the reaction mixture dropwise, then stirred for 30 min at 0 °C and for 30 min at r.t. The solvent was evaporated under reduced pressure and the crude product was purified by flash chromatography (CH₂Cl₂/MeOH 97.5/2.5→95/5→9/1→8/2) to give **5'-S-acetyl-5'-thiouridine** (2.5 g, 70%) as a yellowish solid.

$[\alpha]_D^{25} = +17.8$ ($c = 0.23$, DMSO), $R_f = 0.16$ (CH₂Cl₂/MeOH 95/5), ¹H NMR (400 MHz, DMSO) δ (ppm) 11.36 (s, 1H, NH), 7.63 (d, $J = 8.1$ Hz, 1H, H-6), 5.73 (d, $J = 5.6$ Hz, 1H, H-1'), 5.67 (dd, $J = 8.0, 2.1$ Hz, 1H, H-5), 5.43 (d, $J = 5.6$ Hz, 1H, 2'-OH), 5.29 (d, $J = 4.5$ Hz, 1H, 3'-OH), 4.14 (dd, $J = 10.2, 5.1$ Hz, 1H, H-2'), 3.87 – 3.78 (m, 2H, H-4', H-3'), 3.27 (dd, $J = 13.8, 5.0$ Hz, 1H, H-5'a), 3.10 (dd, $J = 13.8, 7.0$ Hz, 1H, H-5'b), 2.36 (s, 3H, AcCH₃). ¹³C NMR (100 MHz, DMSO) δ (ppm) 194.8 (1C, AcCO), 163.1, 150.7 (2C, C-2, C-4), 141.2 (1C, C-6), 102.2 (1C, C-5), 88.4, 82.3, 72.3, 72.2 (4C, C-1', C-2', C-3', C-4'), 31.0 (1C, C-5'), 30.5 (1C, AcCH₃). MALDI-ToF MS: m/z calcd for C₁₁H₁₄N₂O₆SN⁺: 325.0470 [M+Na]⁺, found 325.0423.

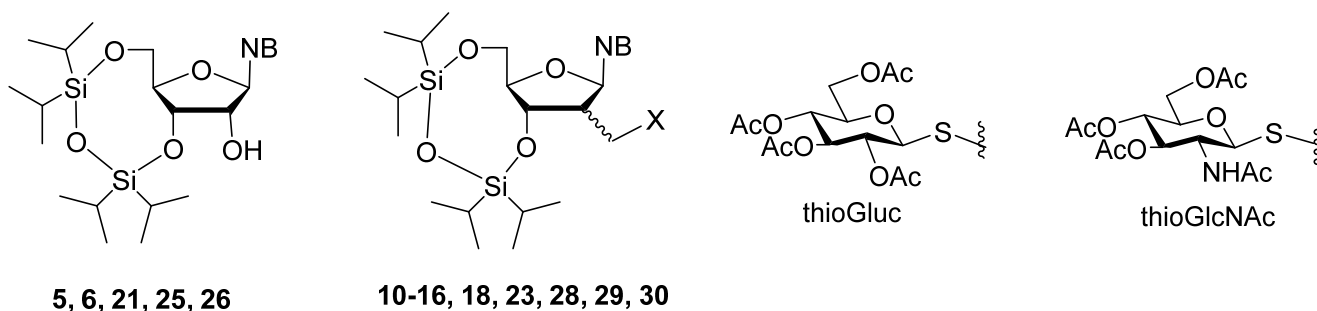
5'-thiouridine (9e)⁸

5'-S-acetyl-5'-thiouridine (2.4 g, 8.0 mmol) was dissolved in dry MeOH (50 mL) under Ar, and NaOMe (648 mg, 12 mmol, 1.5 equiv.) was added and stirred at r.t. for 1 h. The reaction mixture was neutralized with Amberlite IR 120 ion exchanger resins, filtered off, and evaporated under reduced pressure. The crude product was purified by flash column chromatography (CH₂Cl₂/MeOH 9/1) to give compound **9e** (1.47 g, 71%) as a white solid.

$[\alpha]_D = -40.8$ ($c = 0.13$, DMSO), $R_f = 0.24$ ($\text{CH}_2\text{Cl}_2/\text{MeOH } 95/5$), $^1\text{H NMR}$ (400 MHz, DMSO) δ (ppm) 11.35 (s, 1H, *NH*), 7.67 (d, $J = 8.1$ Hz, 1H, H-6), 5.78 (d, $J = 6.0$ Hz, 1H, H-1'), 5.67 (d, $J = 8.1$ Hz, 1H, H-6), 5.41 (d, $J = 5.8$ Hz, 1H, H-3'), 5.22 (d, $J = 5.0$ Hz, 1H), 4.13 (dd, $J = 11.3, 5.7$ Hz, 1H, H-2'), 3.96 – 3.90 (m, 1H), 3.85 (dd, $J = 9.5, 5.8$ Hz, 1H, H-4'), 2.81 (dd, $J = 13.6, 5.5$ Hz, 1H, H-5'a), 2.73 (dd, $J = 13.8, 6.0$ Hz, 1H, H-5'b), 2.46 (s, 1H). $^{13}\text{C NMR}$ (100 MHz, DMSO) δ (ppm) 163.1, 150.8 (2C, C-2, C-4), 141.2 (1C, C-6), 102.2 (1C, C-5), 88.0, 84.6, 72.4, 71.5 (4C, C-1', C-2', C-3', C-4'), 26.3 (1C, C-5'). MALDI-ToF MS: m/z calcd for $\text{C}_9\text{H}_{12}\text{N}_2\text{O}_5\text{SNa}^+$: 283.0365 $[\text{M}+\text{Na}]^+$, found 283.0306.

Characteristic NMR signals of the compounds

Table S1. Characteristic NMR signals of ribonucleoside (**5**, **6**, **21**, **25**, **26** and **29ribo**) and arabinonucleoside (**10-16**, **18**, **23**, **28**, **29arabino** and **30**) derivatives



Product	NB	X	H-1'	H-2'	H-3'	H-4'	C-1'	C-2'	C-3'	C-4'
5	U	-	5.75 s	N.A.	N.A.	N.A.	91.1	N.A.	N.A.	N.A.
6	T	-	5.73 s	N.A.	N.A.	N.A.	91.3	N.A.	N.A.	N.A.
10	U	-SPr	6.23 d $J = 4.7$ Hz	2.86 m^a	4.35 t $J = 8.8$ Hz	3.75 d $J = 8.1$ Hz	84.2	49.3	N.A.	84.2
11	U	-SBu	6.23 d $J = 4.4$ Hz	2.89- 2.81 m^a	4.35 t $J = 8.8$ Hz	3.75 d $J = 8.1$ Hz	84.2	49.3	N.A.	84.2
12	U	-SHex	6.24 d $J = 5.2$ Hz	2.91- 2.83 m^a	4.36 t $J = 8.8$ Hz	3.77 dt $J = 8.1, 2.2$ Hz	84.3	49.4	N.A.	84.3

13	U	-SAc	6.26 d J= 6.2 Hz	2.90- 2.78 m ^a	4.24 t J= 8.9 Hz	3.77 d J= 8.2 Hz	84.2	49.7	N.A.	84.2
16	T	-5'-thiouridine	6.23 s	3.00- 2.91 m	4.47 s	3.89- 3.81 m	N.A.	50.7	74.5	85.2
14	T	-SPr	6.24 d J= 4.1 Hz	2.82 d J= 4.1 Hz	4.38 t J= 8.6 Hz	3.76 d J= 7.9 Hz	84.1	49.4	71.3	84.1
15	T	-SBu	6.12 s	2.84- 2.79 m ^a	4.35 t J= 8.3 Hz	3.73 d J= 7.9 Hz	84.3	49.3	N.A.	84.0
18 major	T	-thioGlcNAc	6.36 d J= 7.2 Hz	N.A.	N.A.	N.A.	84.1	N.A.	N.A.	N.A.
18minor	T	-thioGlcNAc	5.85 s	N.A.	N.A.	N.A.	89.2	N.A.	N.A.	N.A.
21	OMe	-	4.82 s	N.A.	N.A.	N.A.	107.4	N.A.	N.A.	N.A.
23	OMe	-SBu	4.88 d J= 3.9 Hz	2.44 td J= 9.4, 4.6 Hz	4.19 dd J= 8.8, 5.5 Hz	3.96- 3.89 m	103.8	53.6	N.A.	N.A.
25	A	-	5.65 d J= 4.6 Hz	4.52 t J= 4.6 Hz	4.80 dd J= 8.5, 5.1 Hz	4.01 dt J= 8.5, 2.8 Hz	89.4	N.A.	N.A.	N.A.
26	A ^{DMTr}	-	5.89 d J= 1.0 Hz	4.61 d J= 5.5 Hz	5.15 dd J= 7.6, 5.6 Hz	4.07 dd J= 7.7, 3.0 Hz	89.9			
28	A ^{DMTr}	-SBu	6.25 d J= 7.6 Hz	2.96 ddd J= 13.5, 11.2, 4.0 Hz	5.14- 5.05 m	3.89 t J= 6.7, 3.0 Hz	85.7	51.4	74.9	85.0
30	A ^{DMTr}	-thioGluc	6.25 d J= 7.5 Hz	3.23- 3.12 m	5.16- 5.08	3.89 t J= 6.7, 3.0 Hz	85.5	52.3	75.3	82.6

29 ribo	A ^{DMTr}	-SAc	5.89 s	2.78 d J= 14.3 Hz	5.12 d J= 7.6 Hz	4.09 ddd 7.7, 6.0, 3.1 Hz	90.8	55.4	75.3	82.6
29 arabino	A ^{DMTr}	-SAc	6.25 d, 7.5 Hz	3.02- 2.90 m	4.99- 4.91 m	3.87 ddd 7.9, 4.9, 3.3 Hz	84.9	51.1	74.2	84.7

a: overlapping signals

N.A.: not assigned

Cytotoxic activity of compounds 6, 8, 10, 12, 14, 16, 28 and 29ara

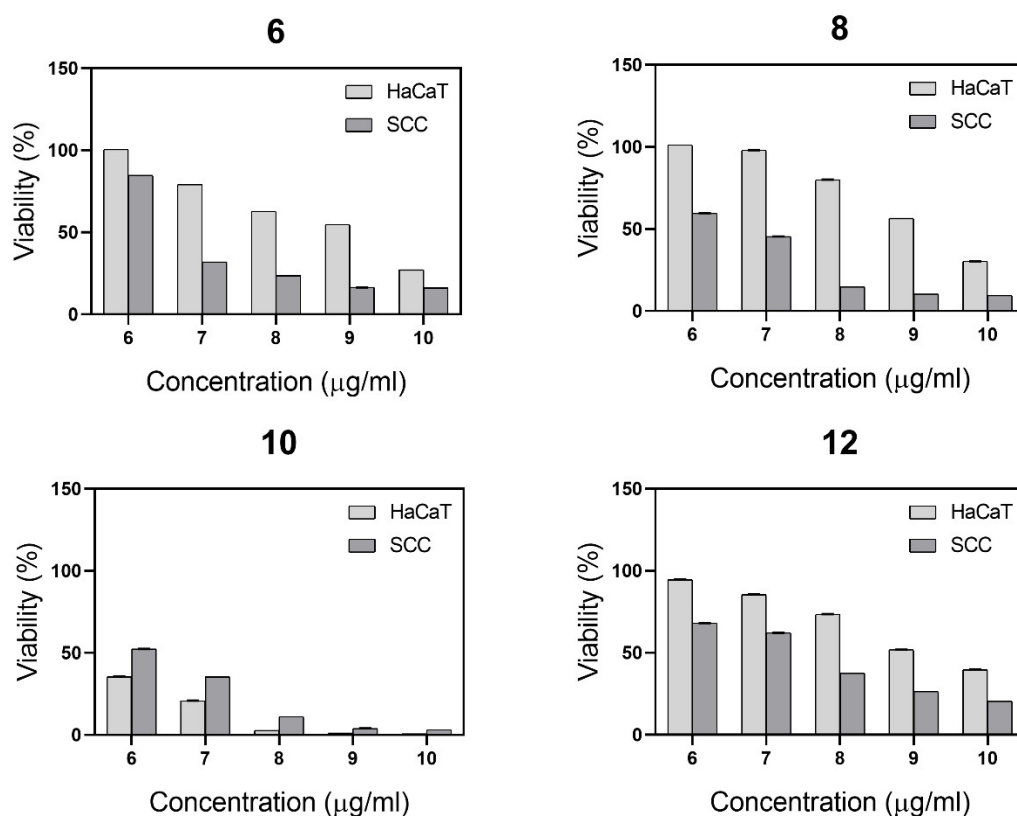


Figure S1. Effect of compounds **6**, **8**, **10** and **12** on viability of HaCaT and SCC cells by MTT assay

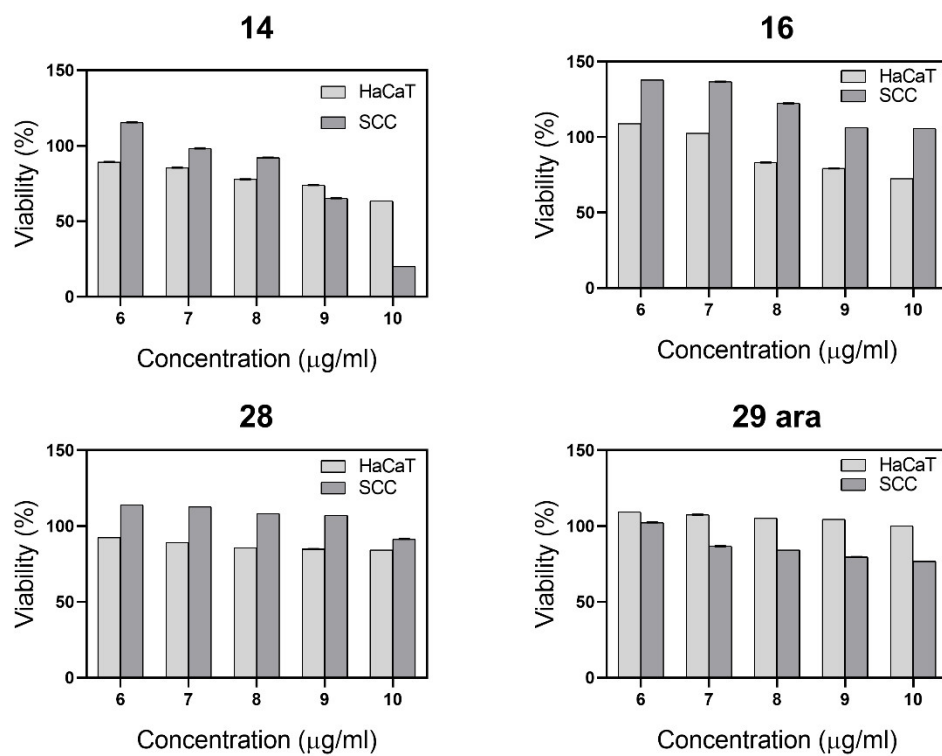


Figure S2. Effect of compounds **14**, **16**, **28** and **29ara** on viability of HaCaT and SCC cells by MTT assay

Anti-SARS-CoV-2 activity determination in VERO E6 cells

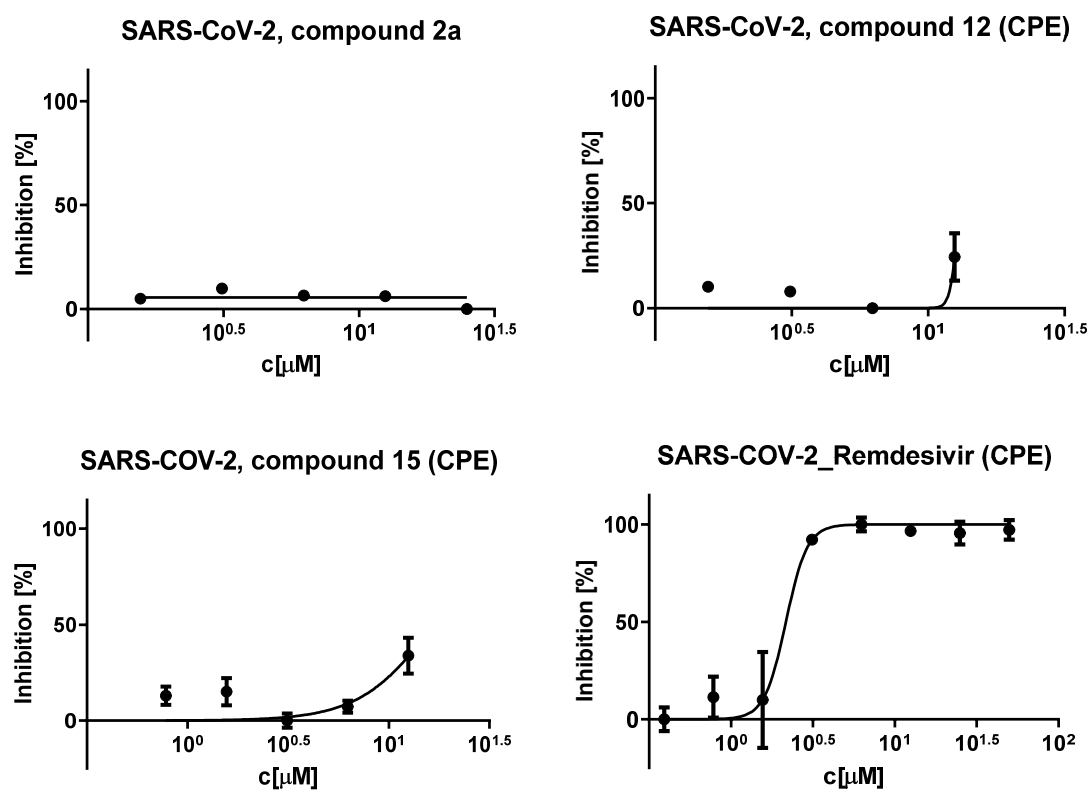


Figure S3. Inhibition of SARS-CoV-2-induced cytopathic effect in Vero E6 cells

Cytotoxicity in VERO E6 cells

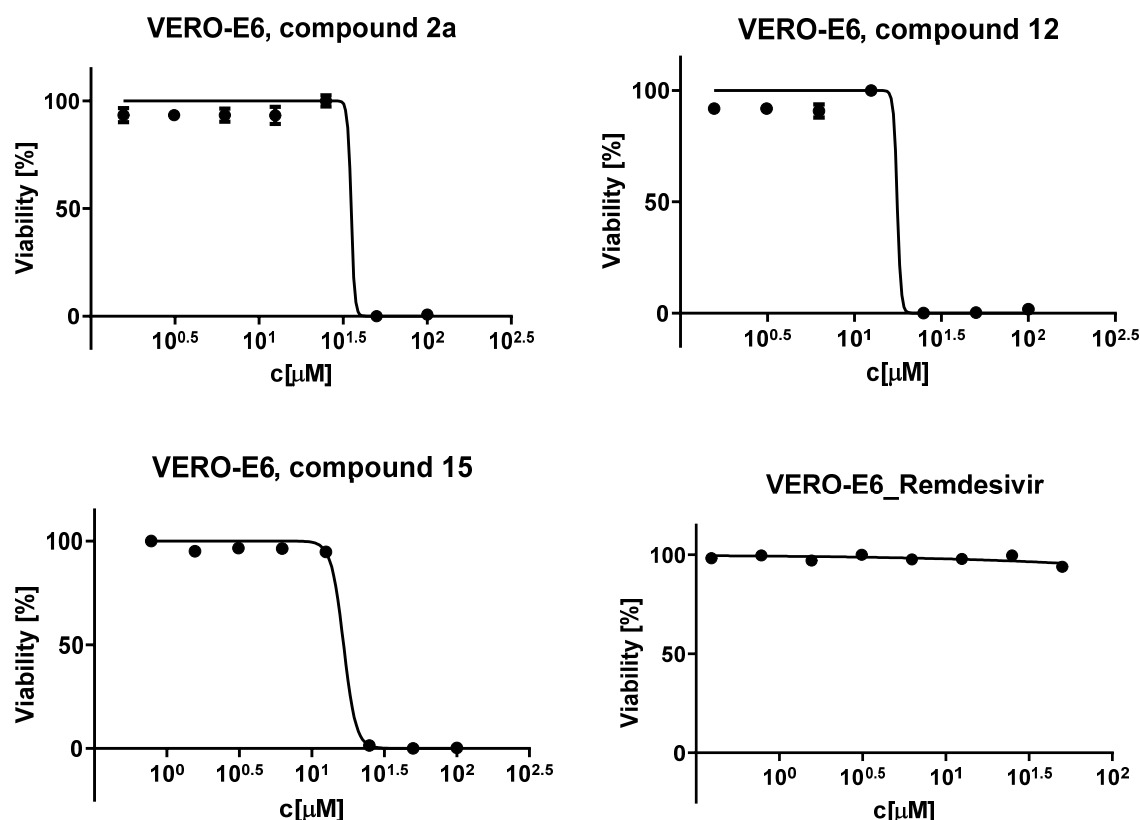


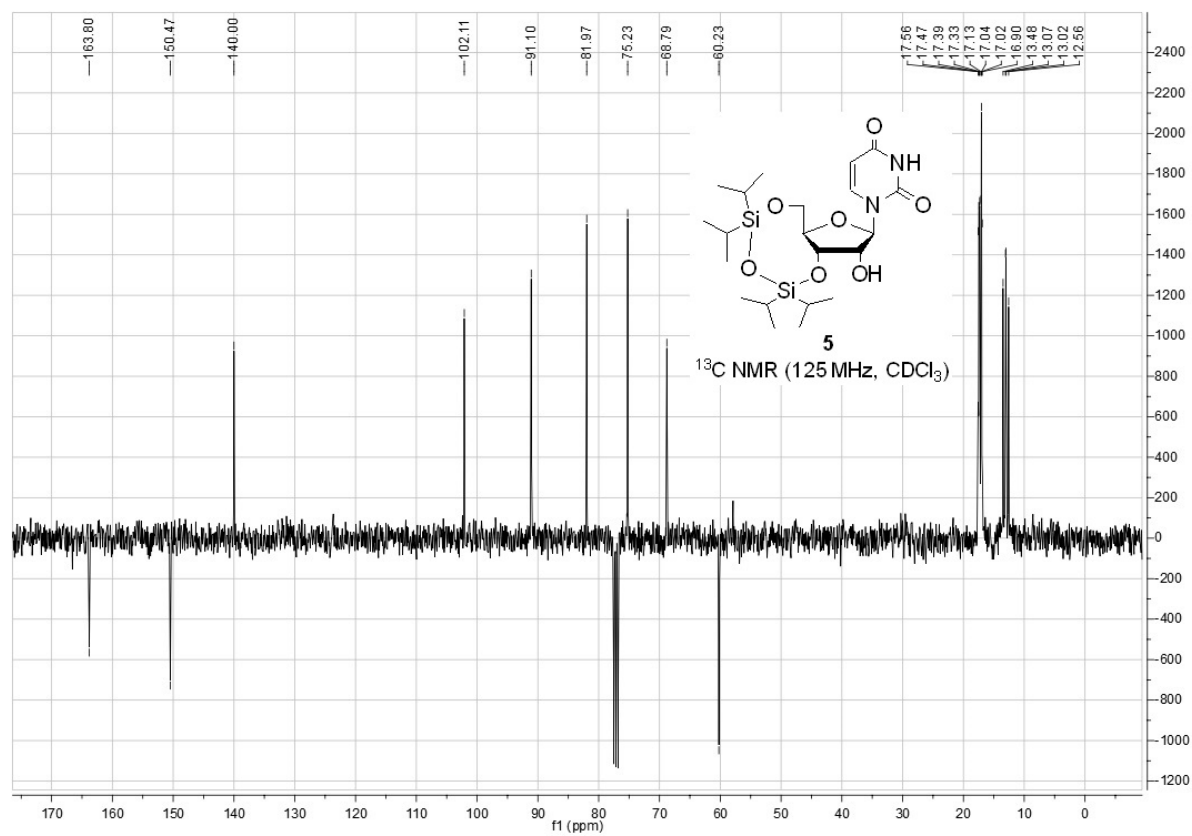
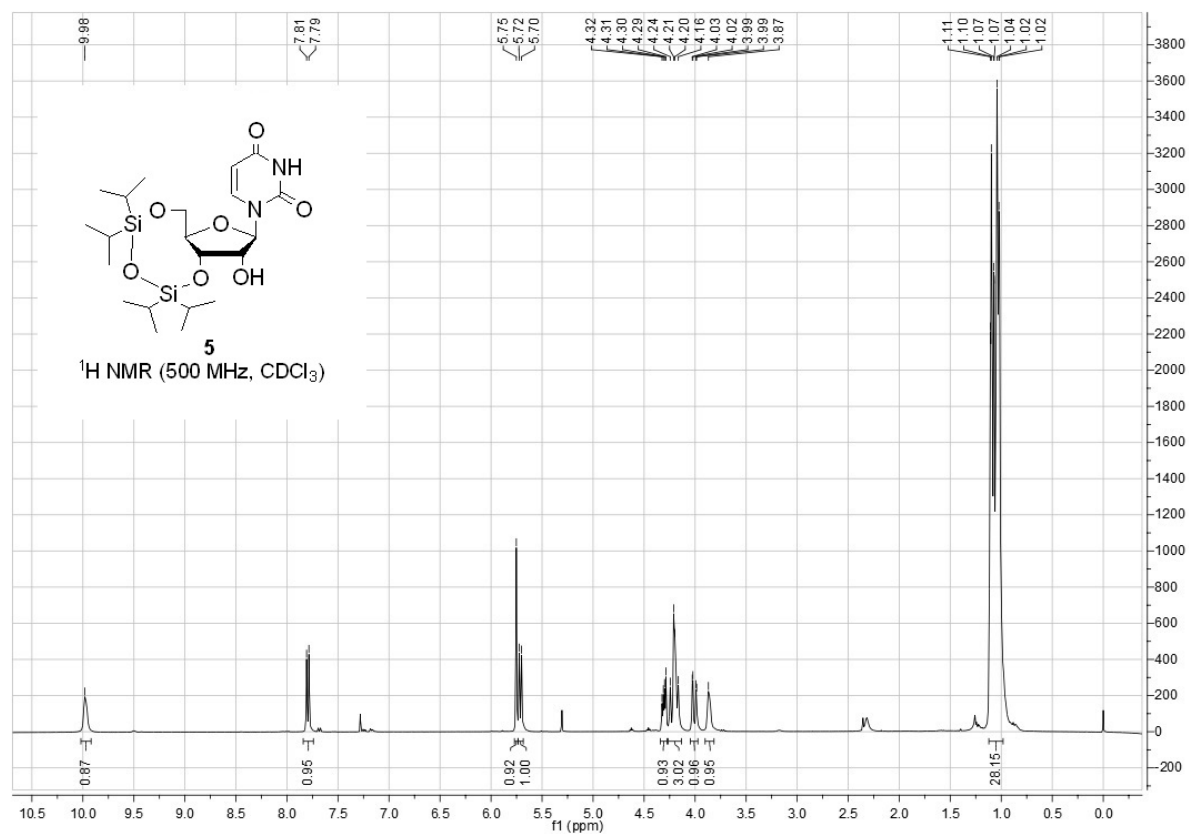
Figure S4. Cytotoxicity determination in Vero E6 cells

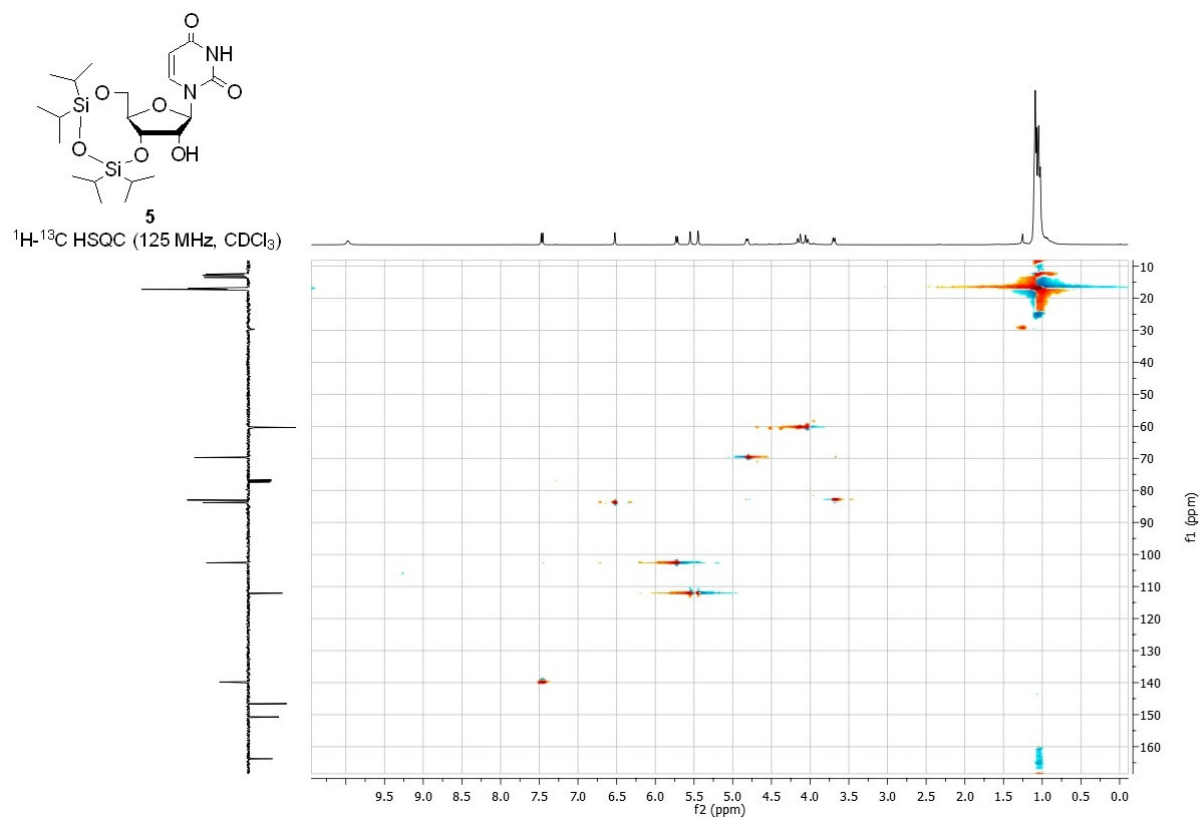
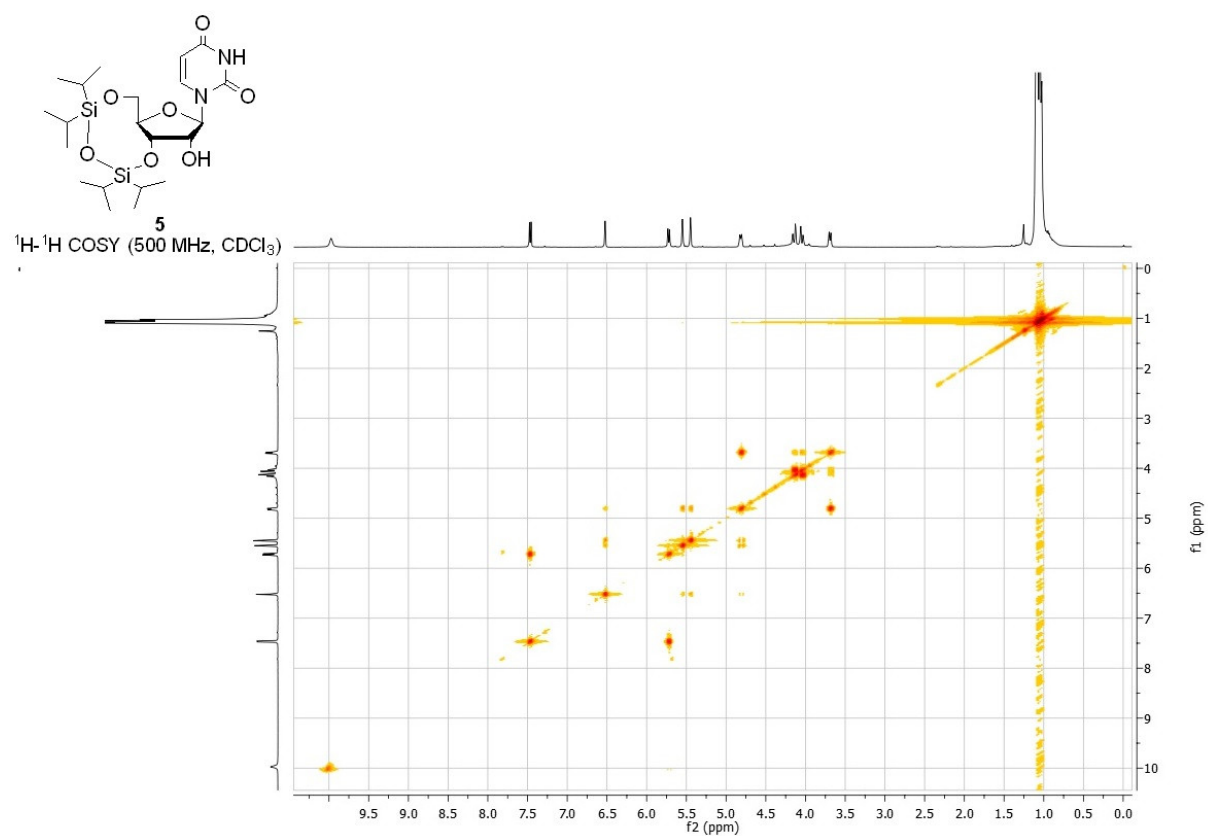
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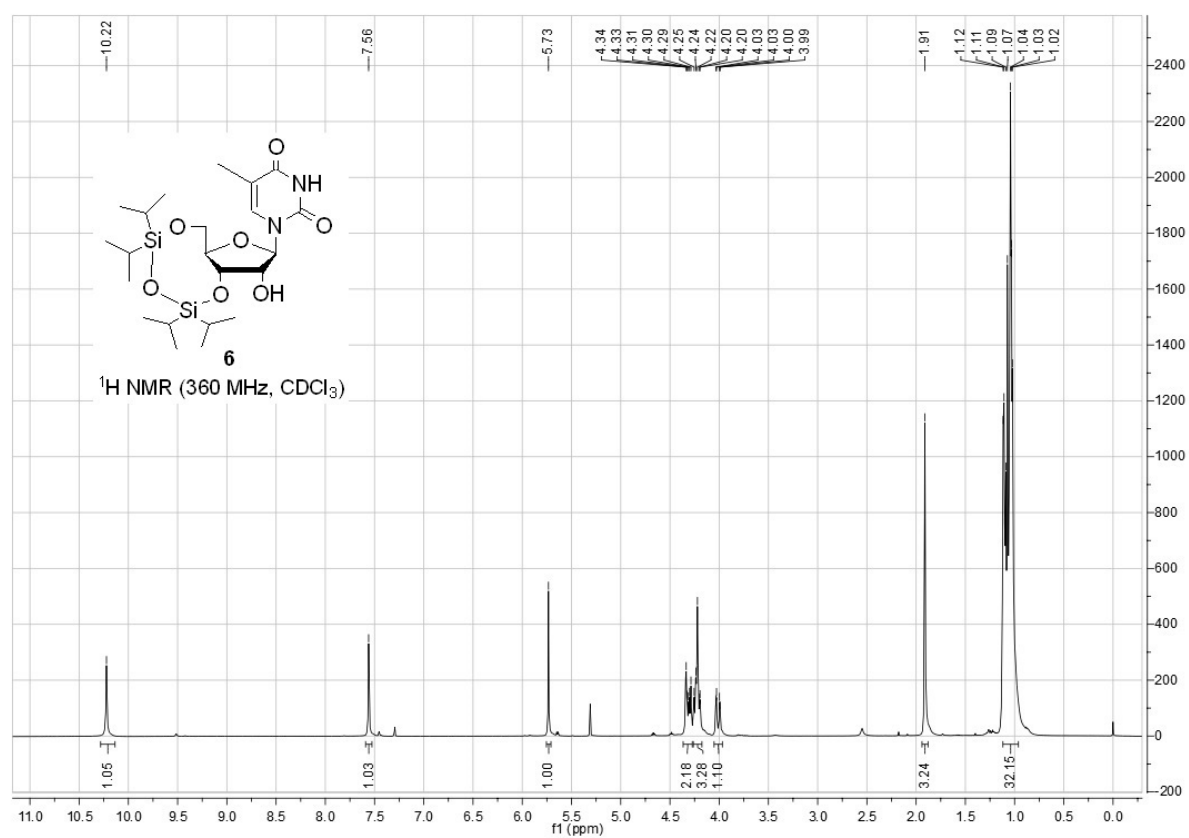
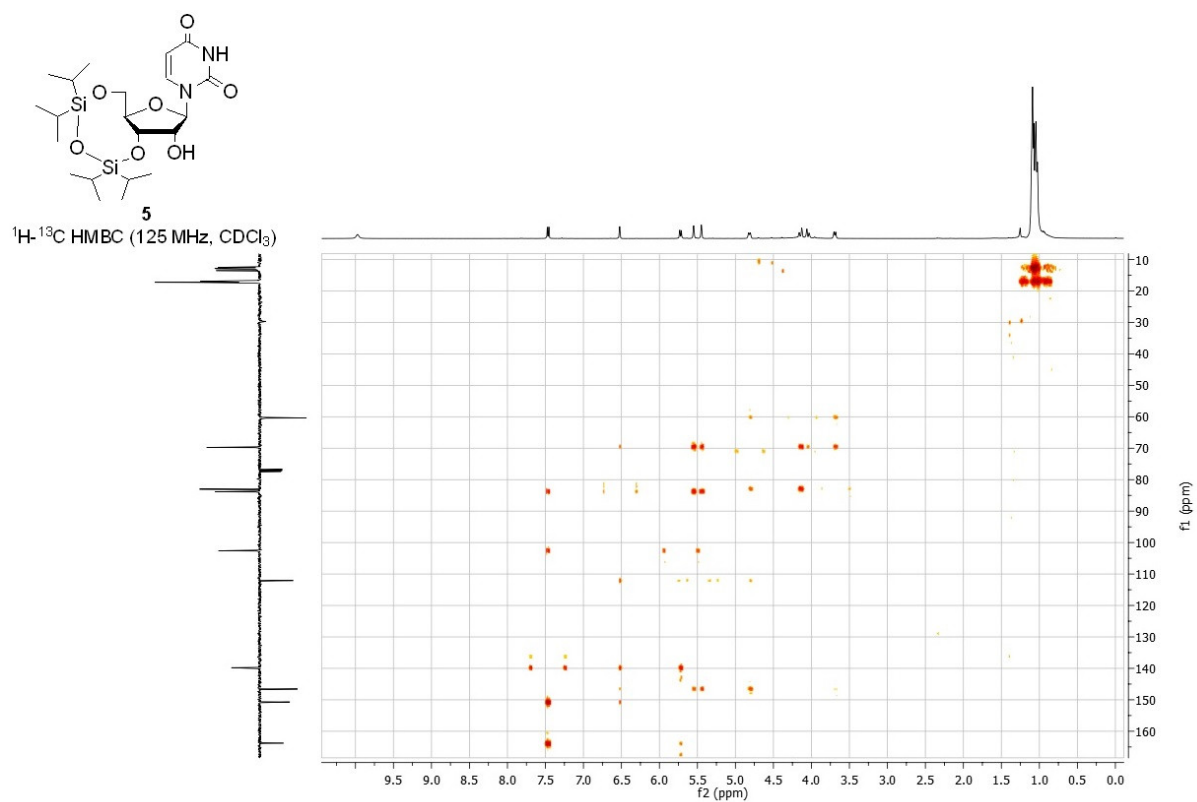
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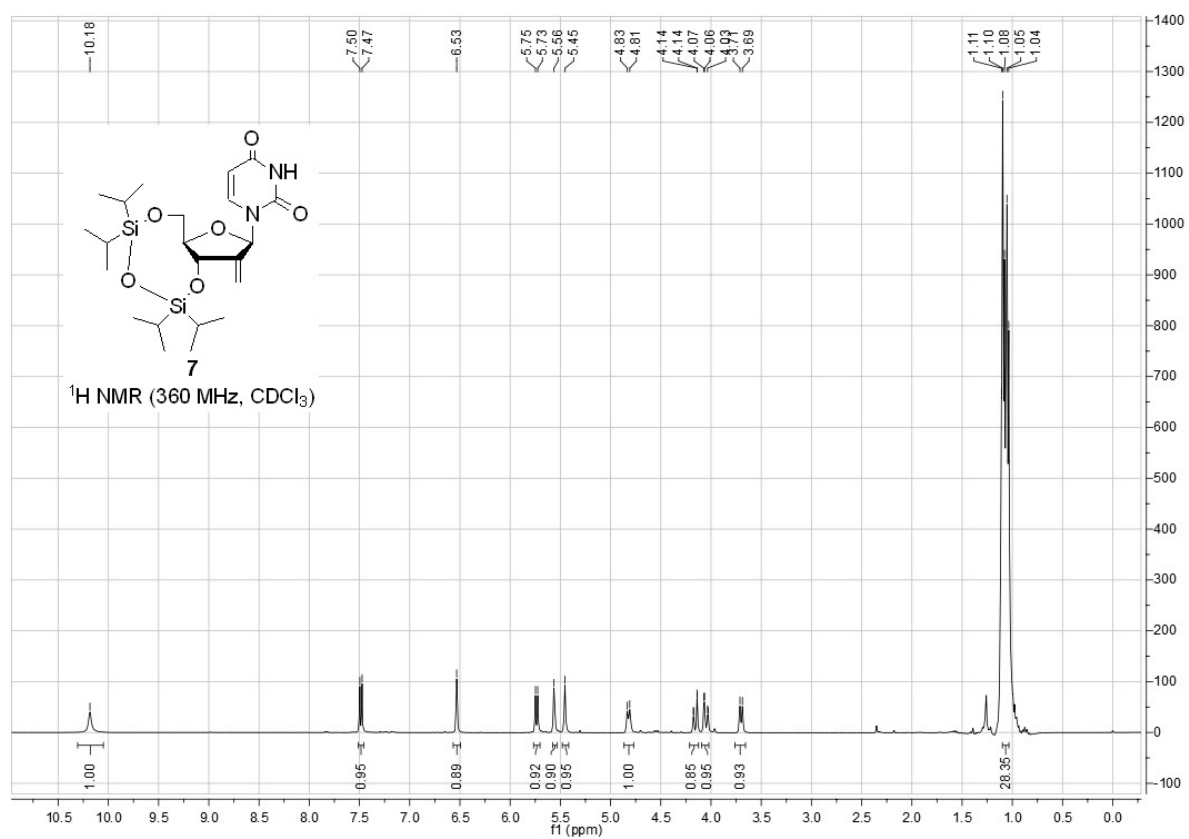
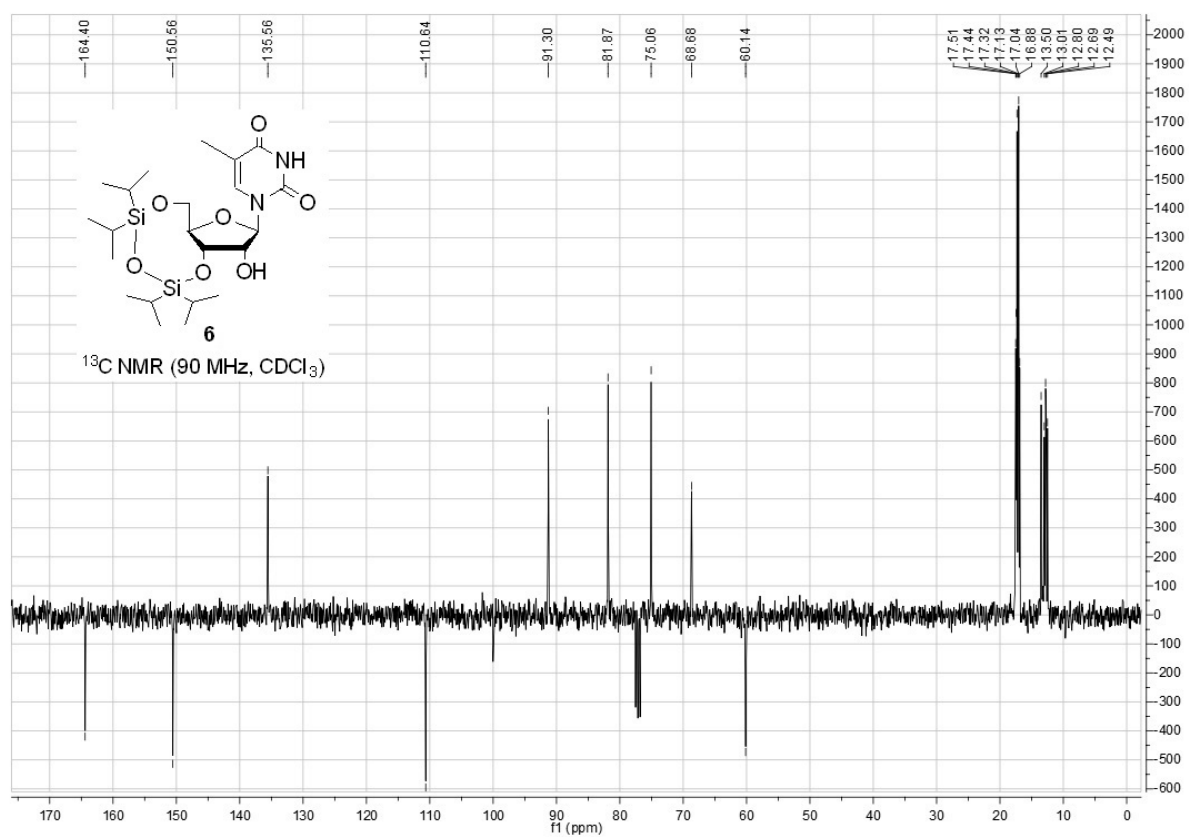
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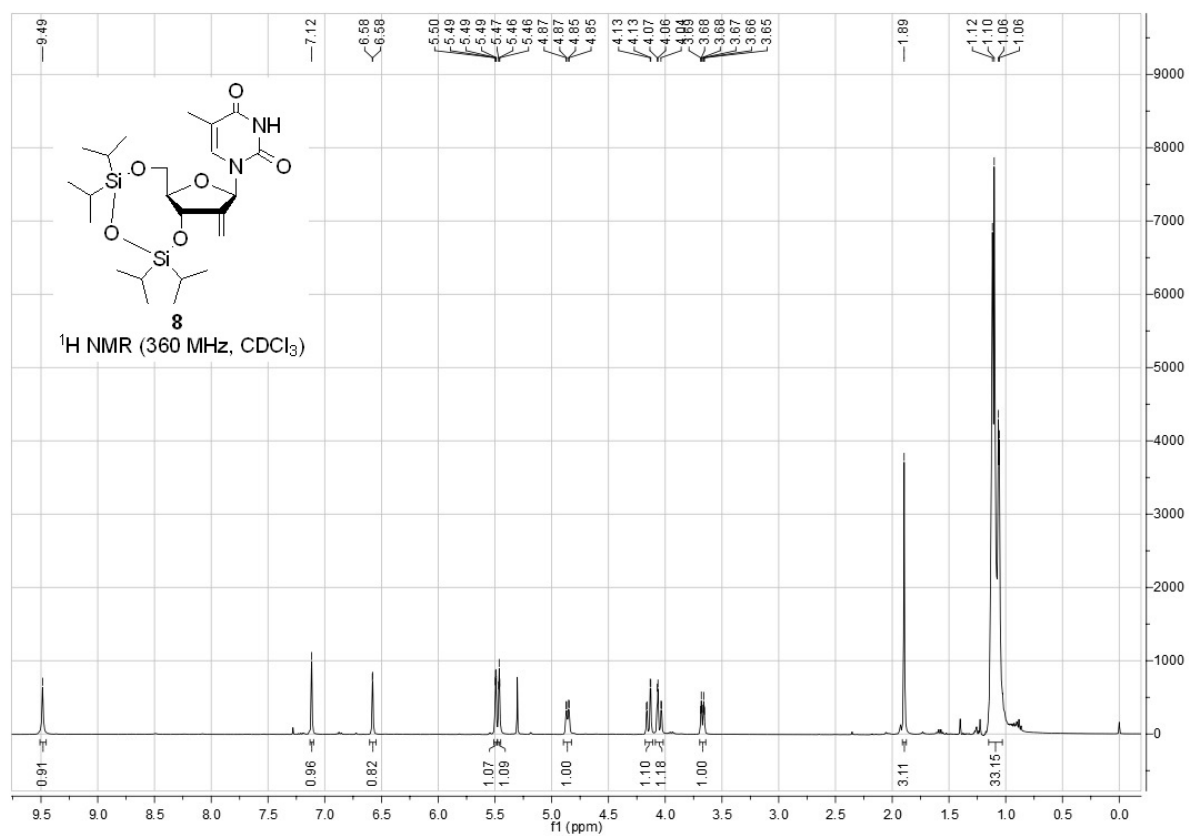
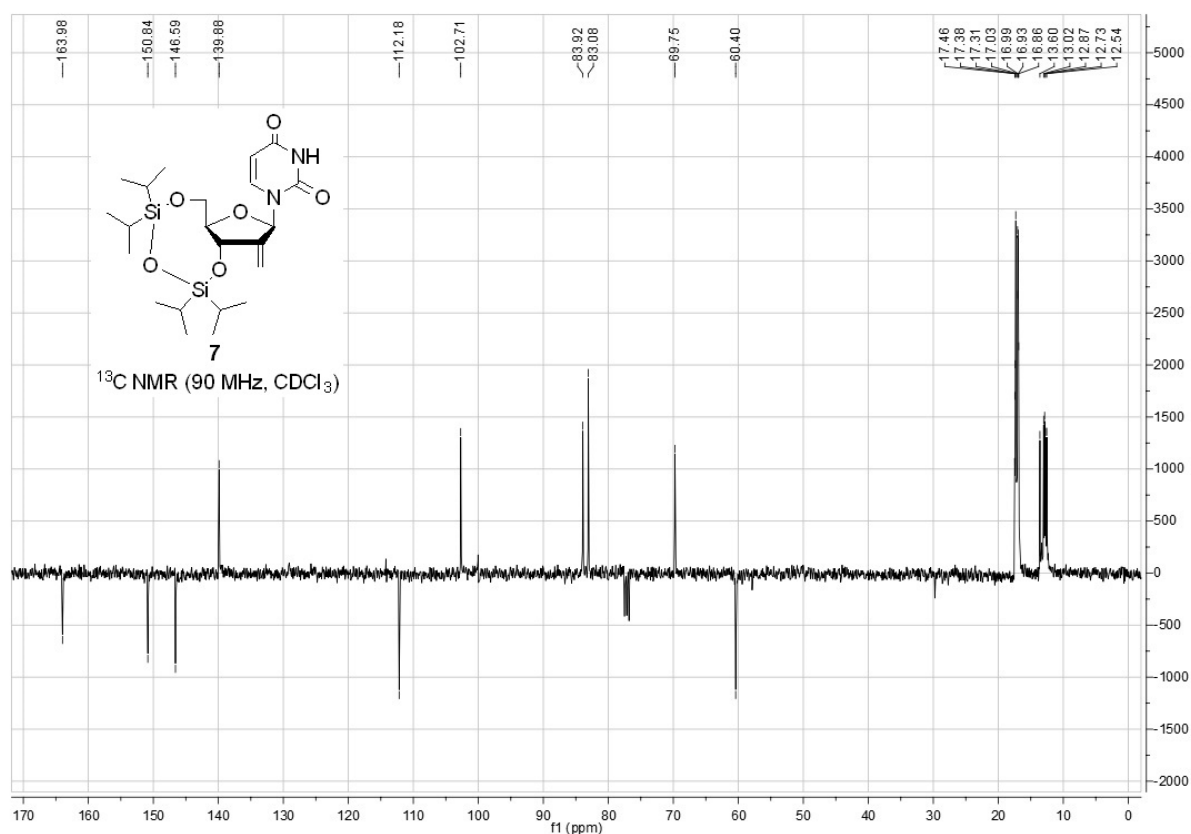
NMR spectra of the compounds

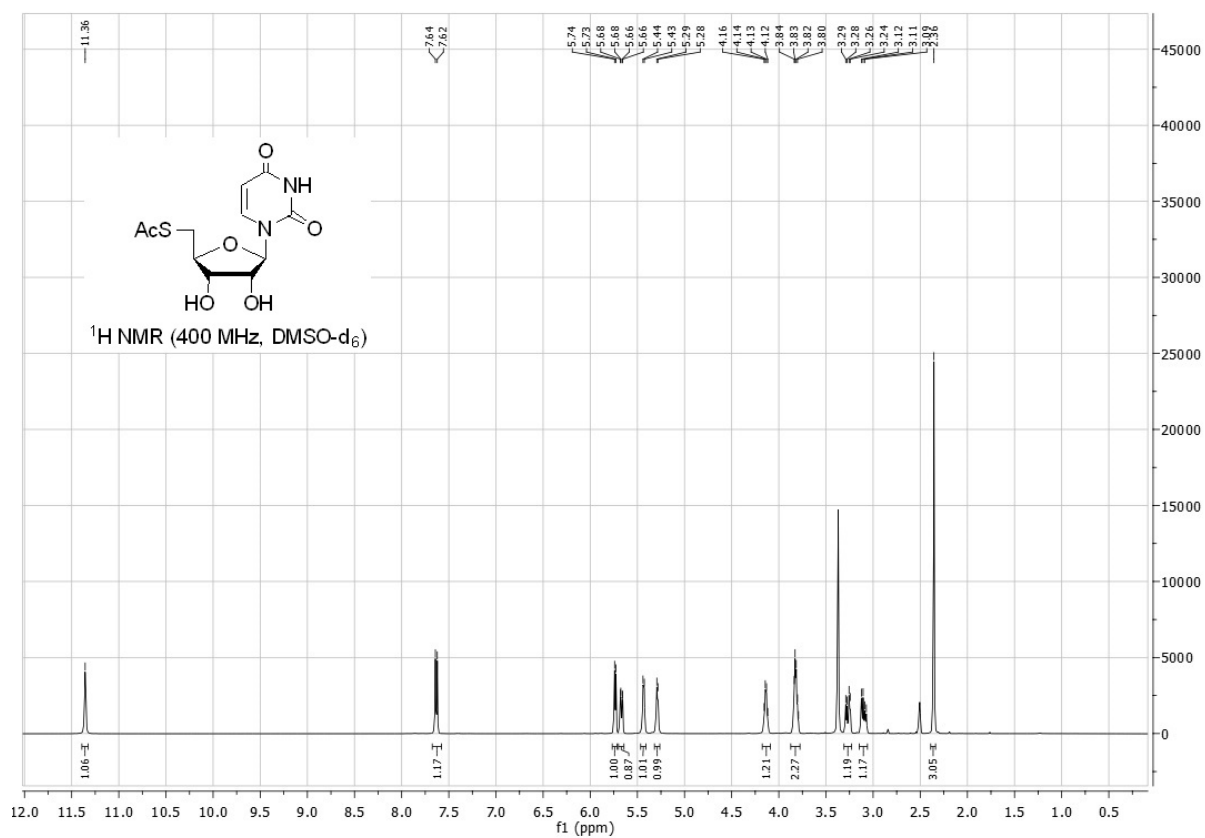
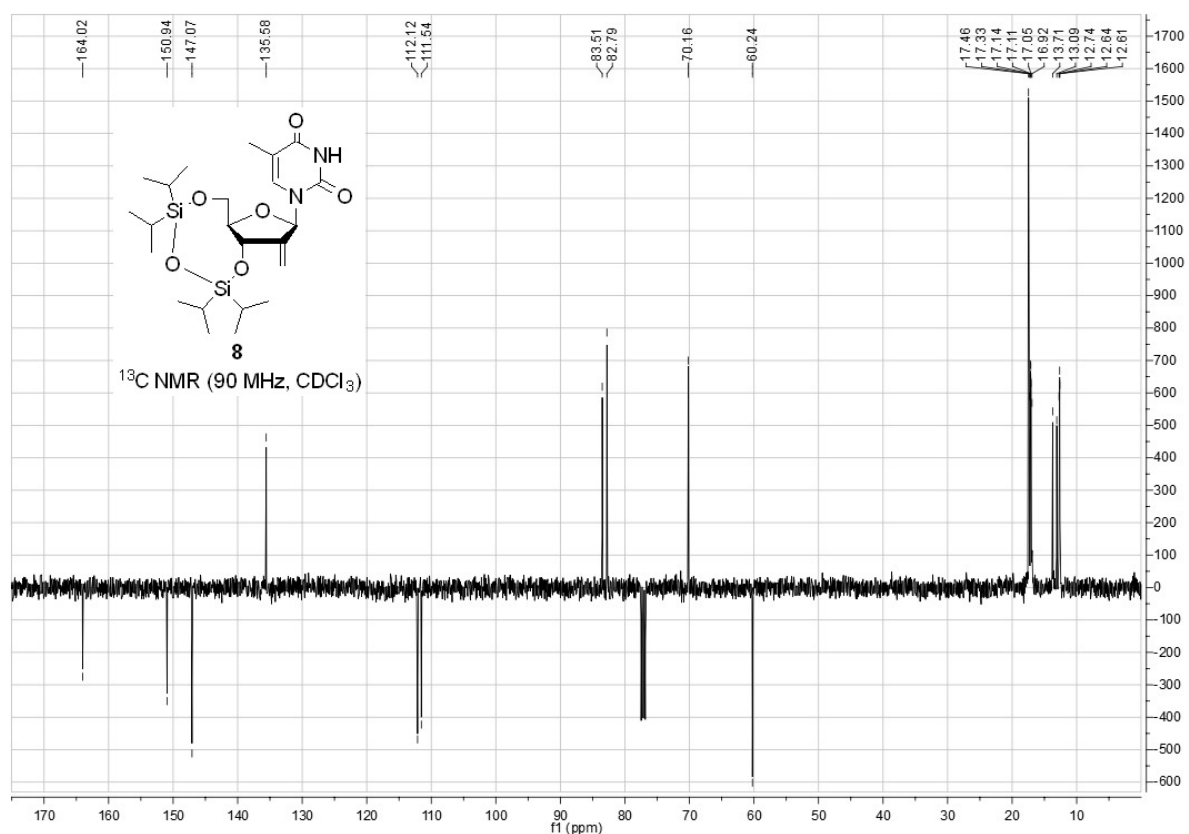


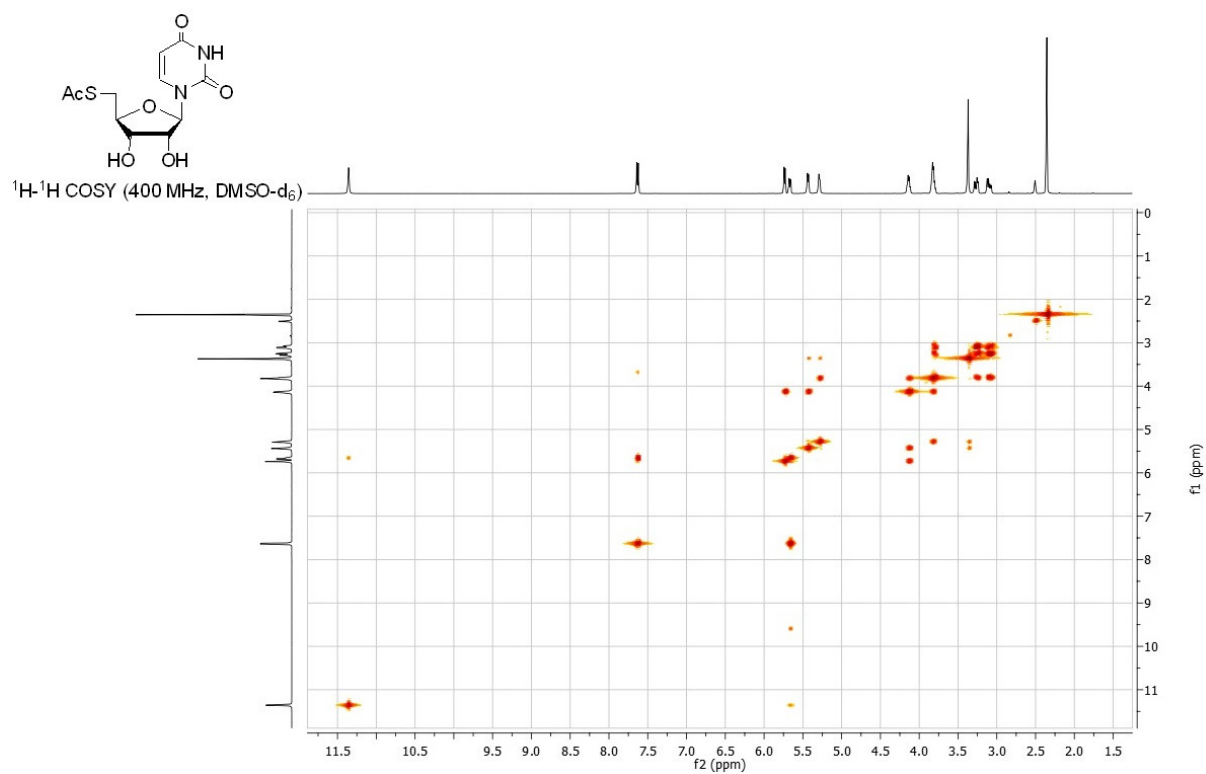
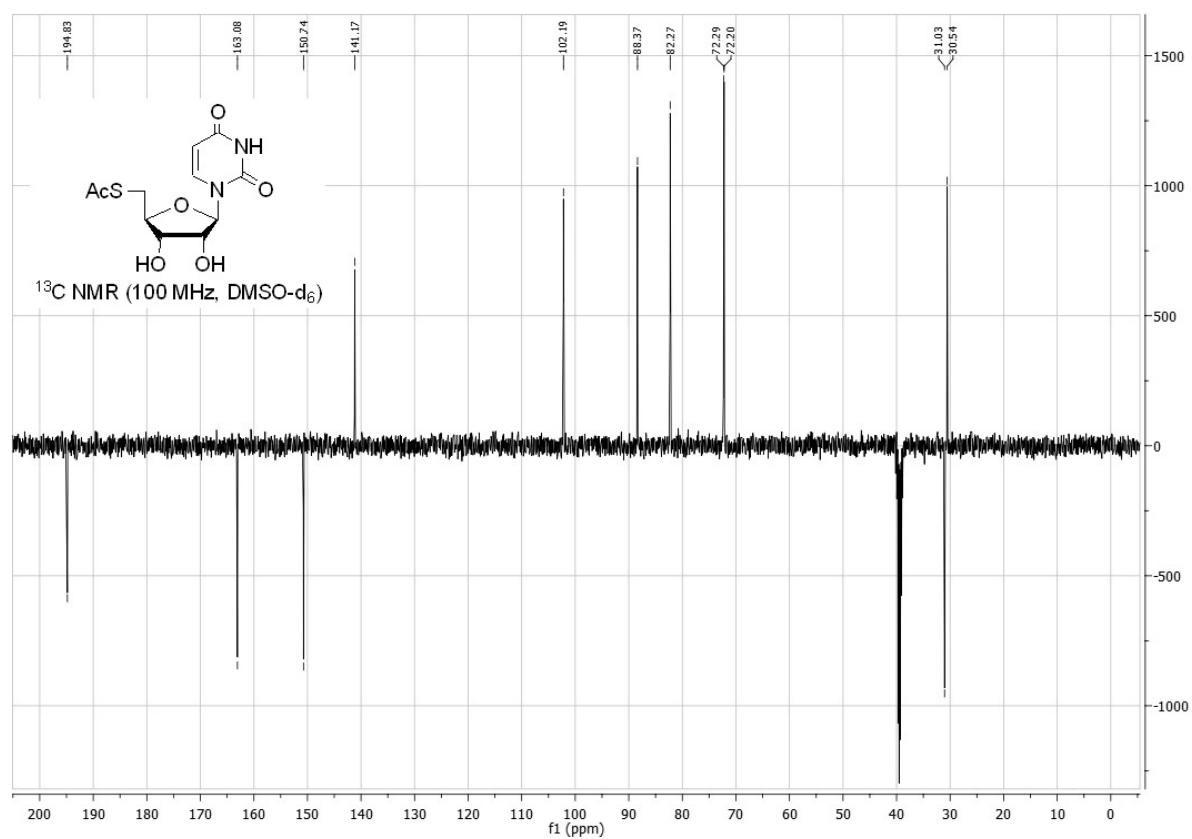


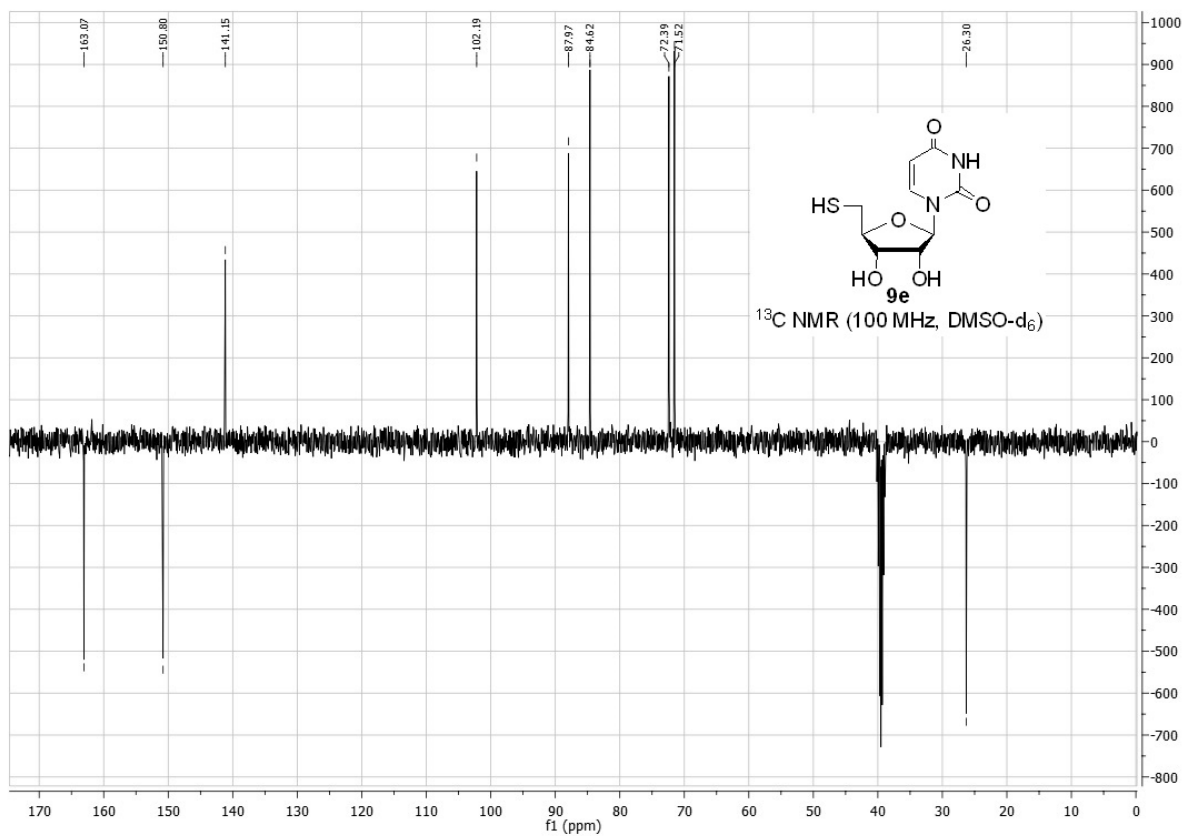
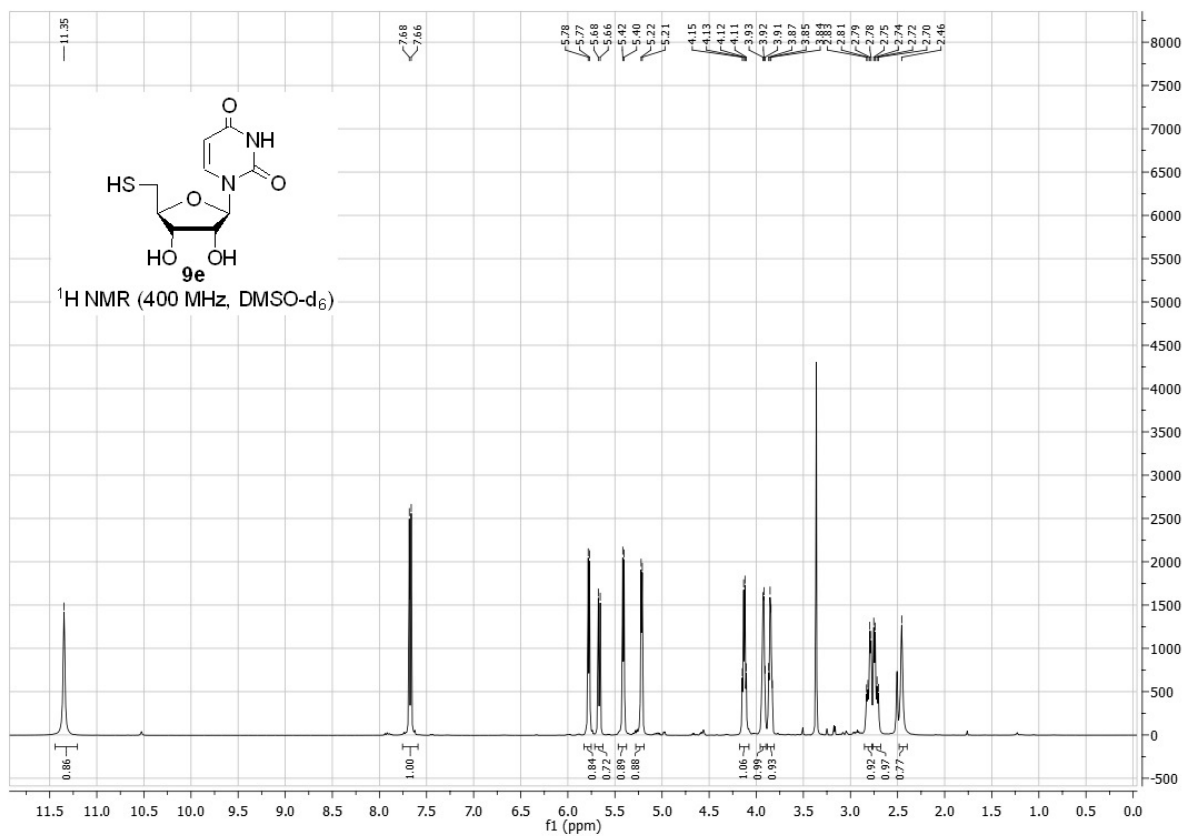


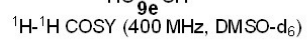


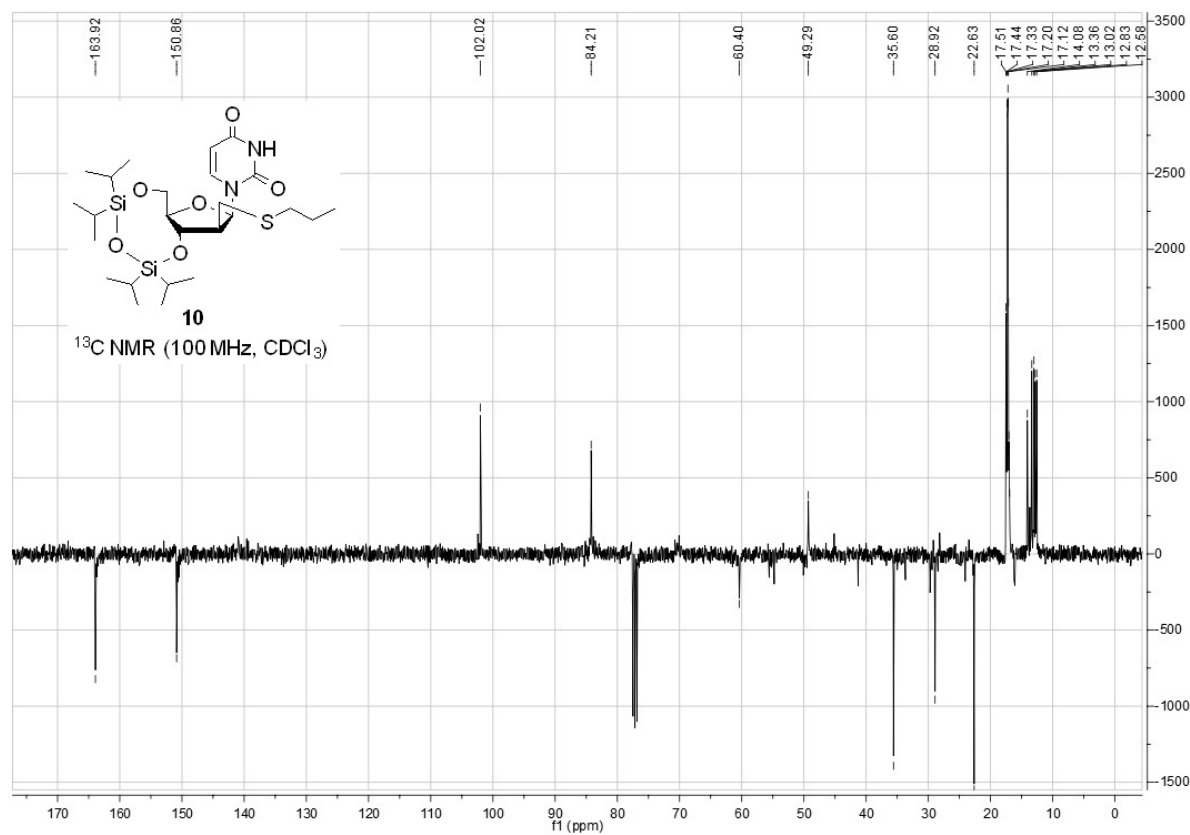
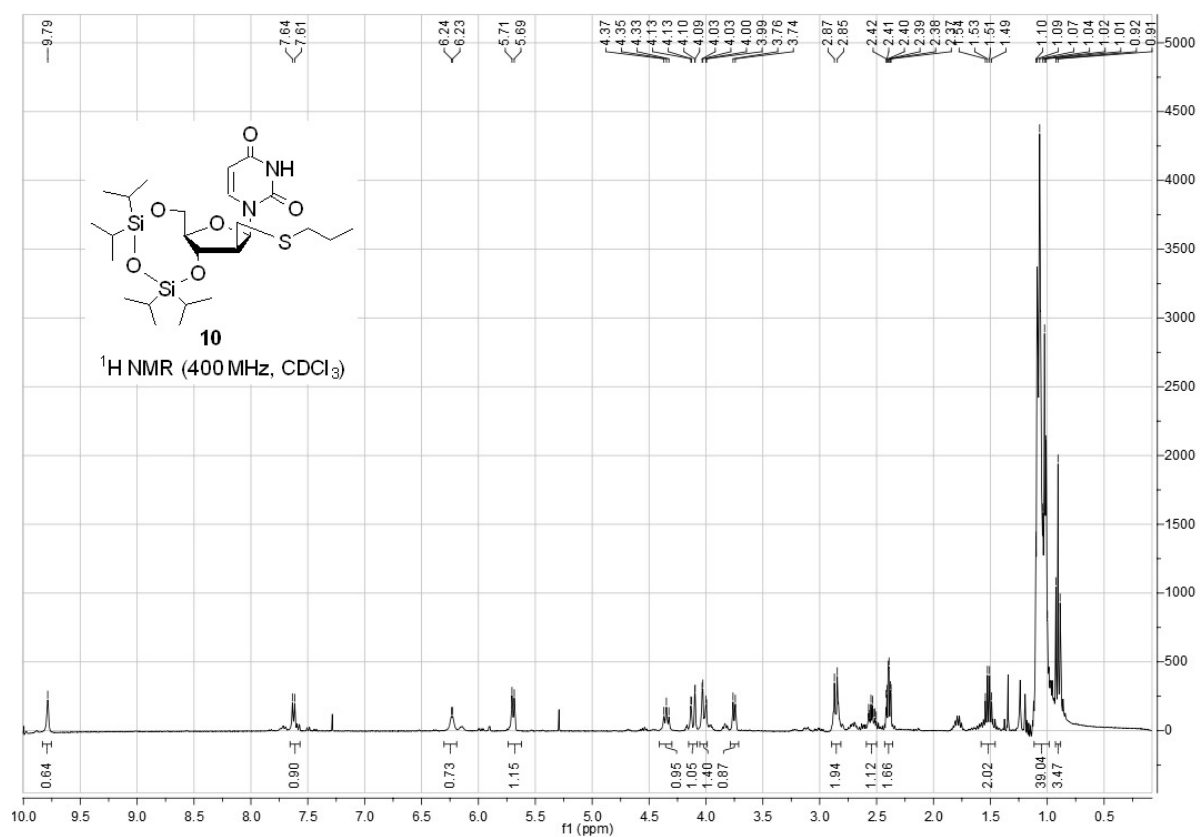


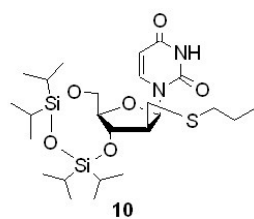




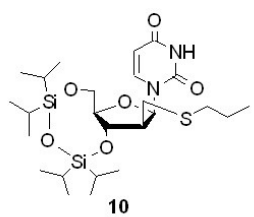
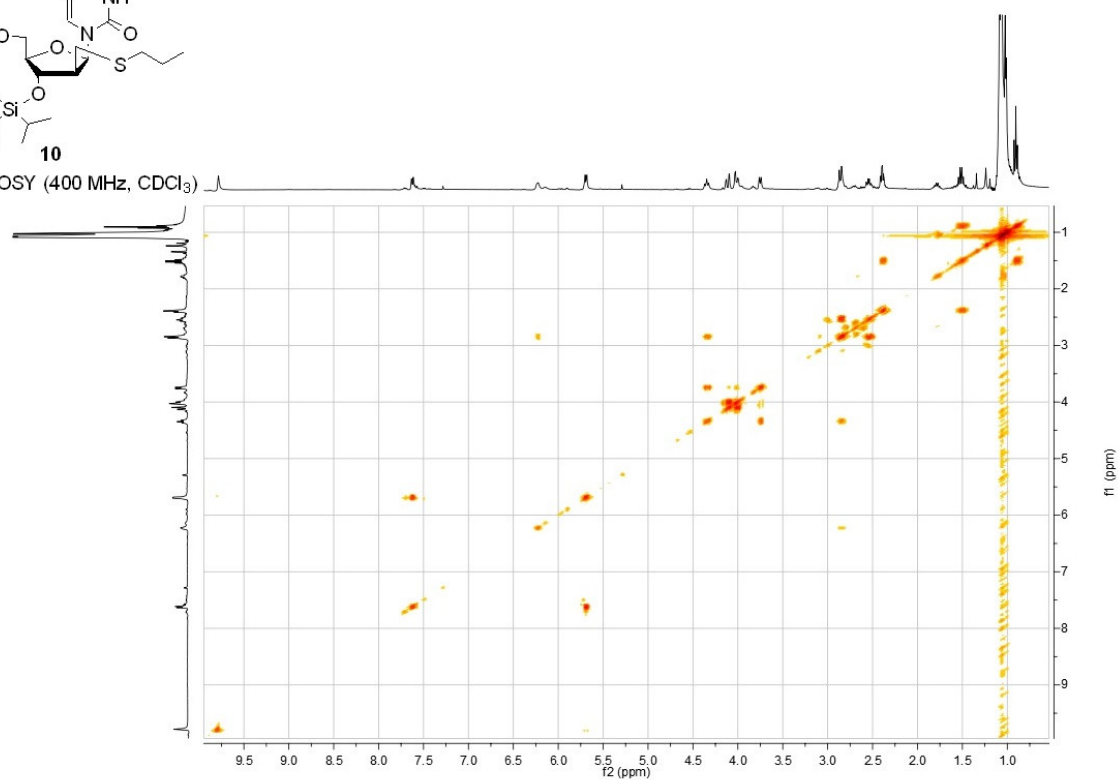




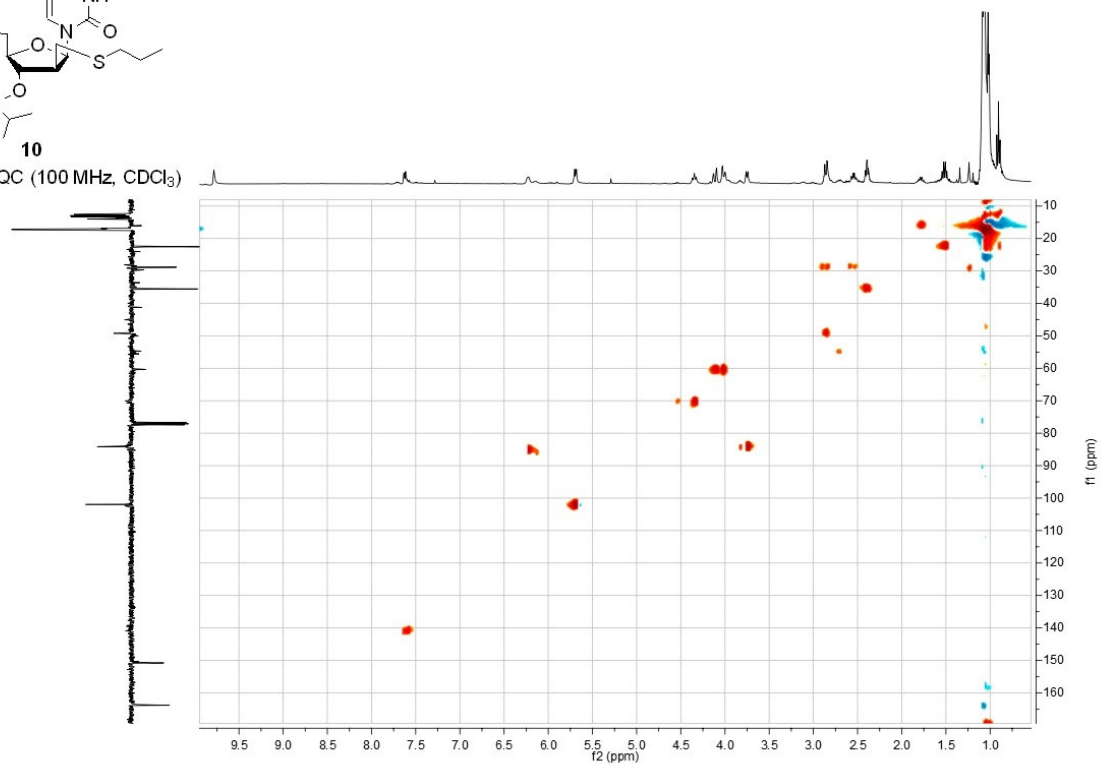


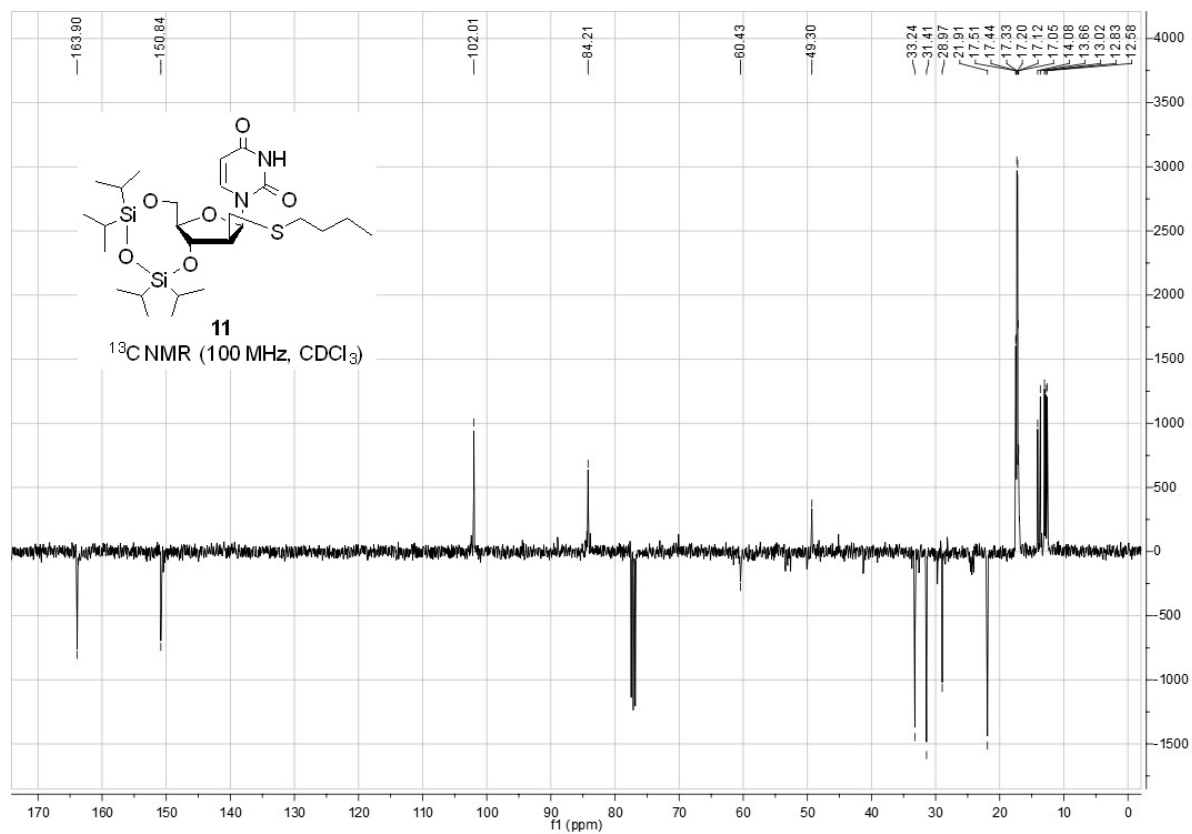
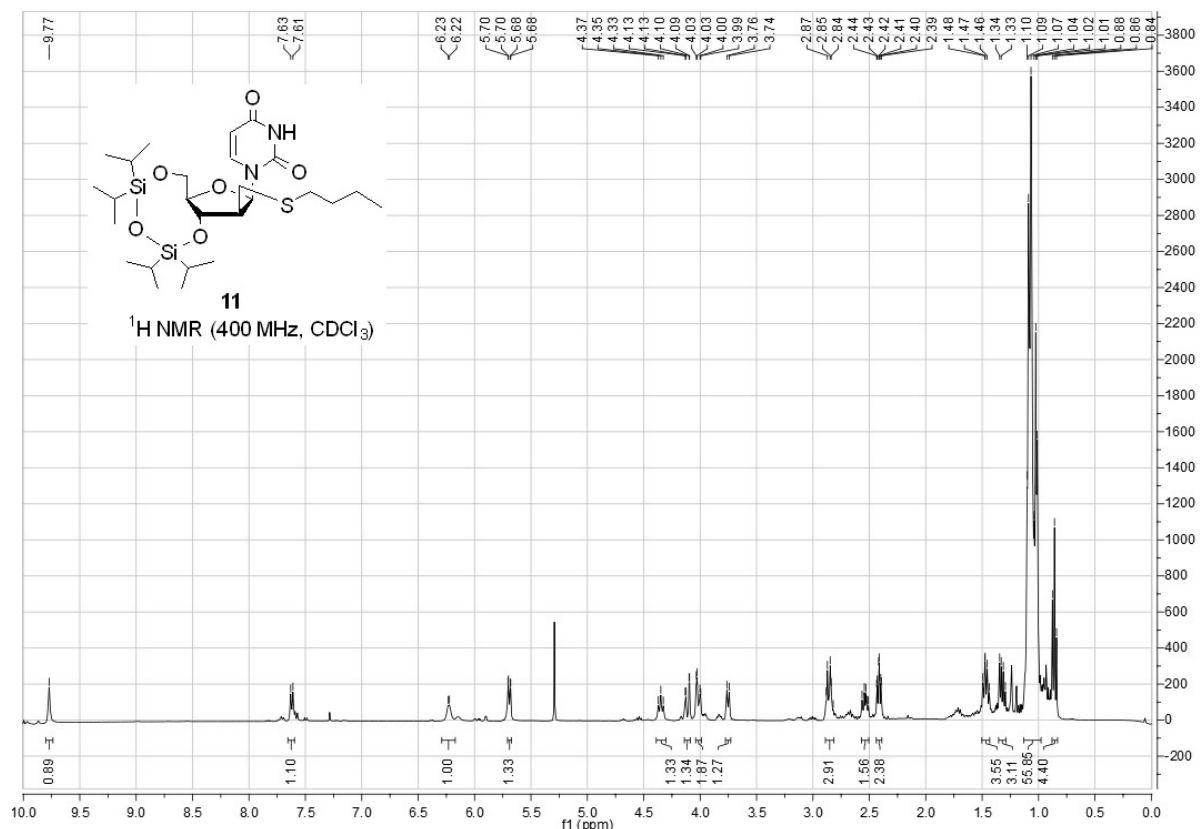


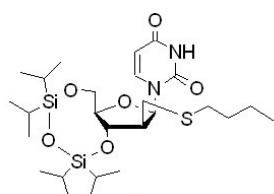
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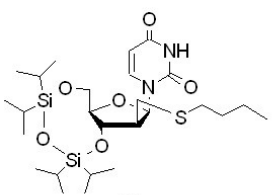
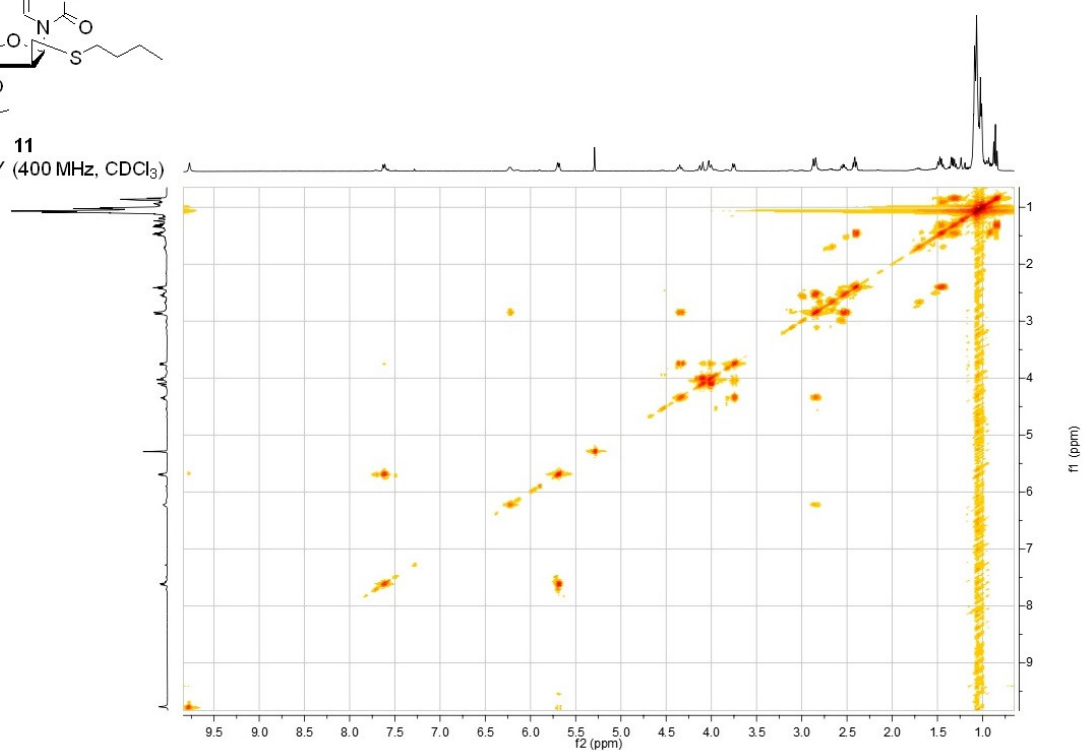
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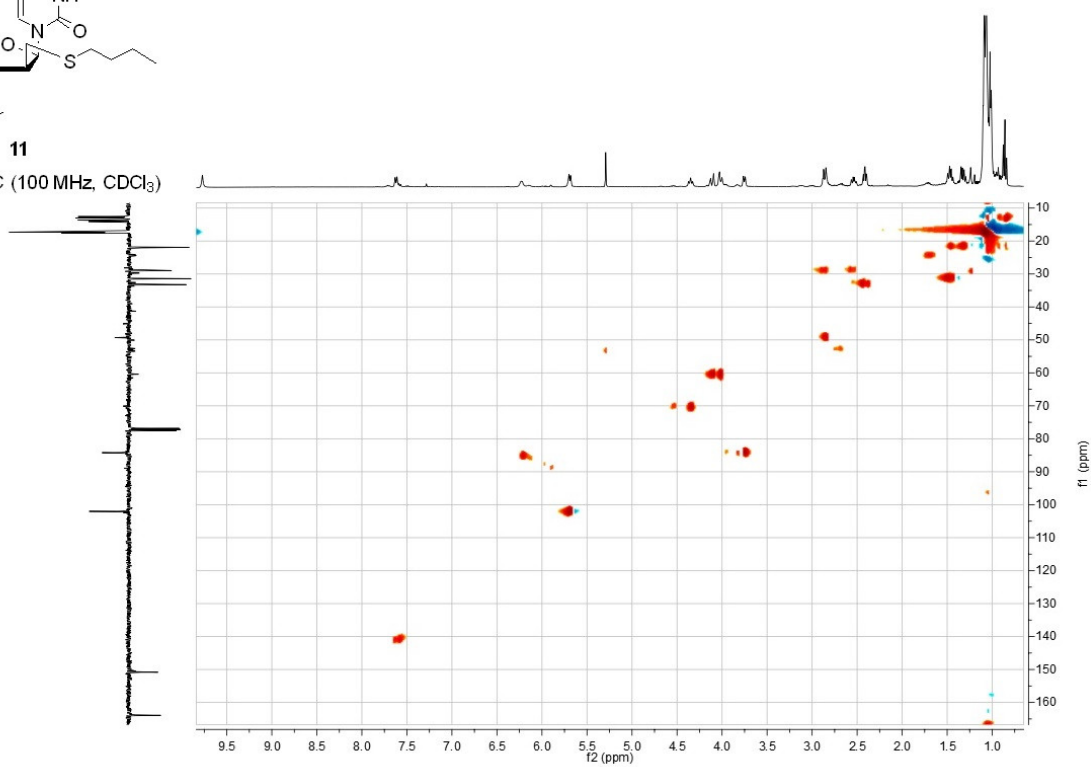


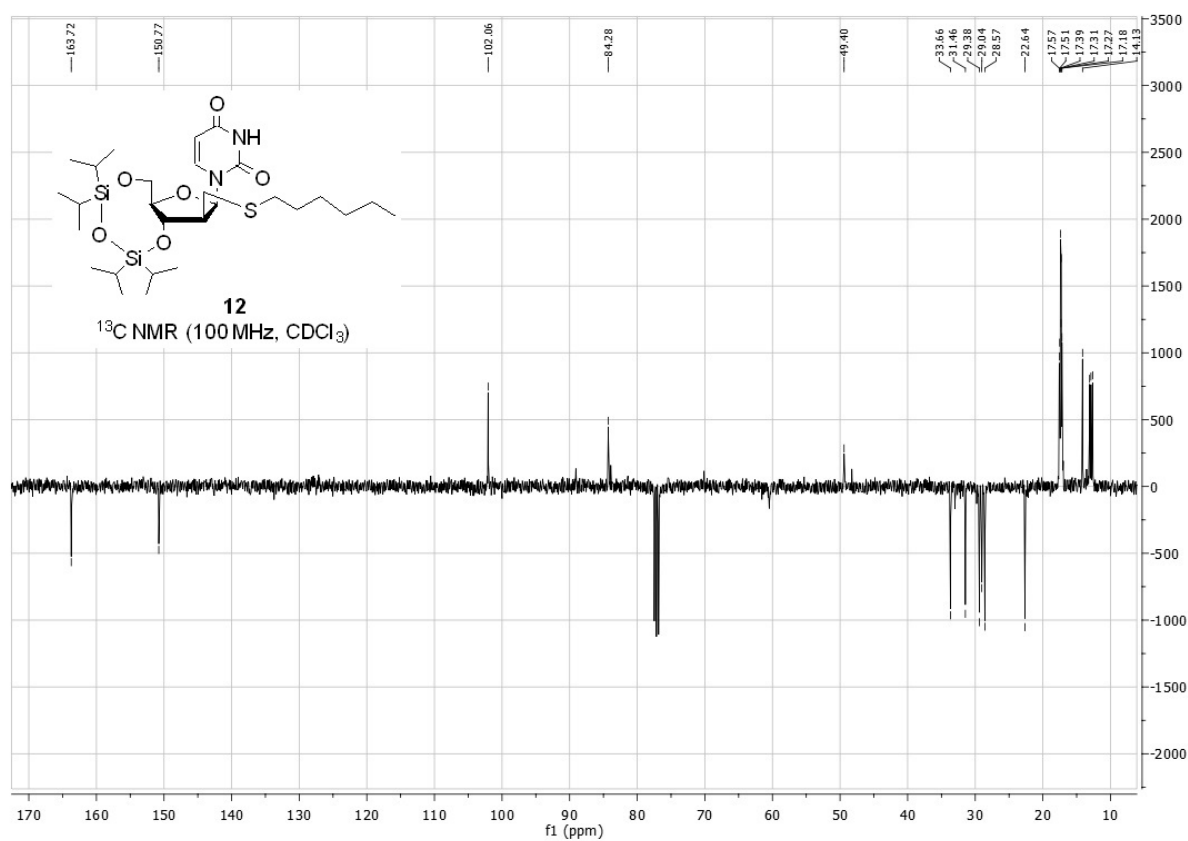
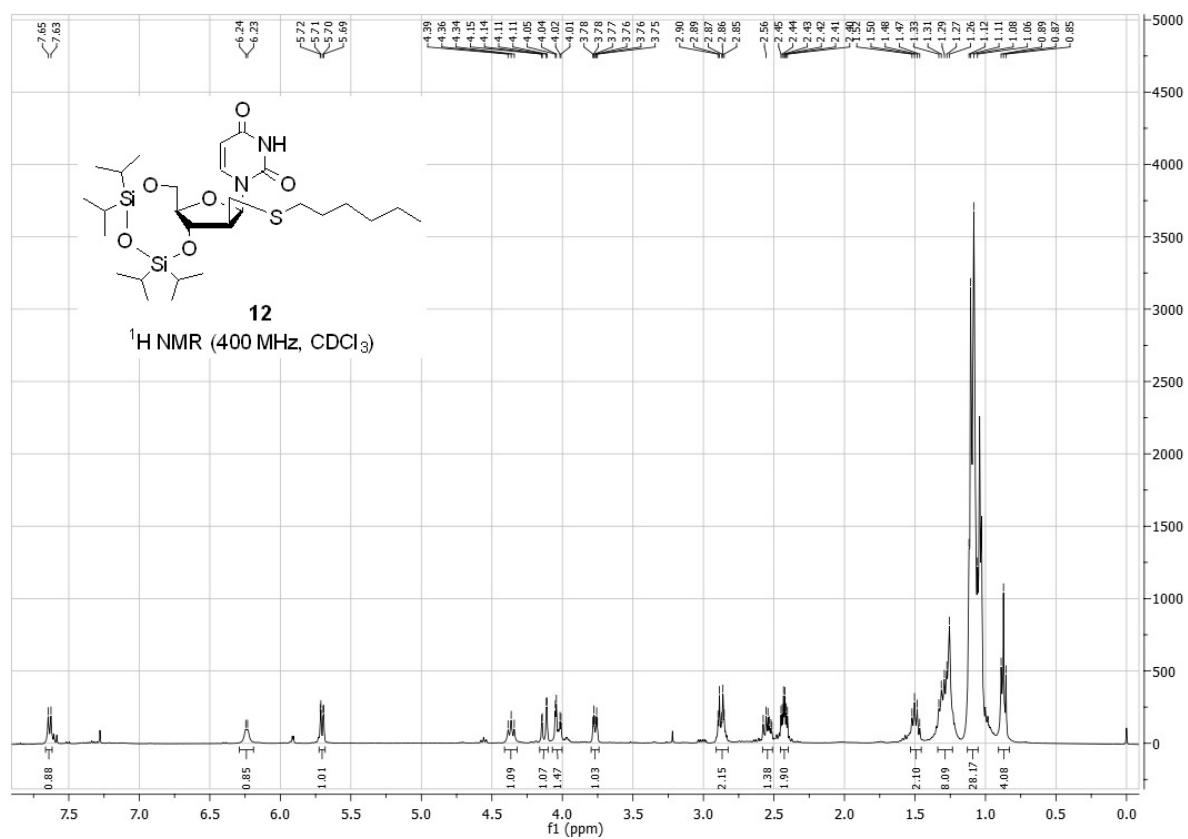


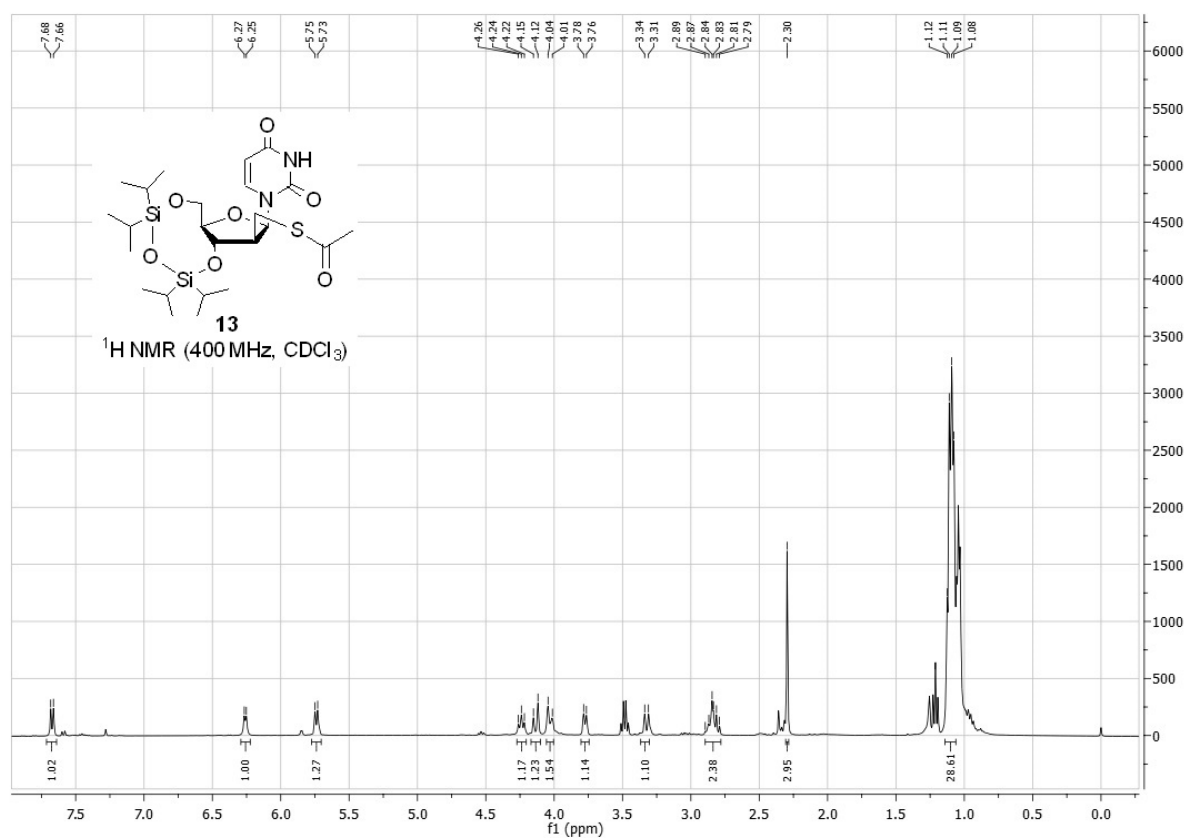
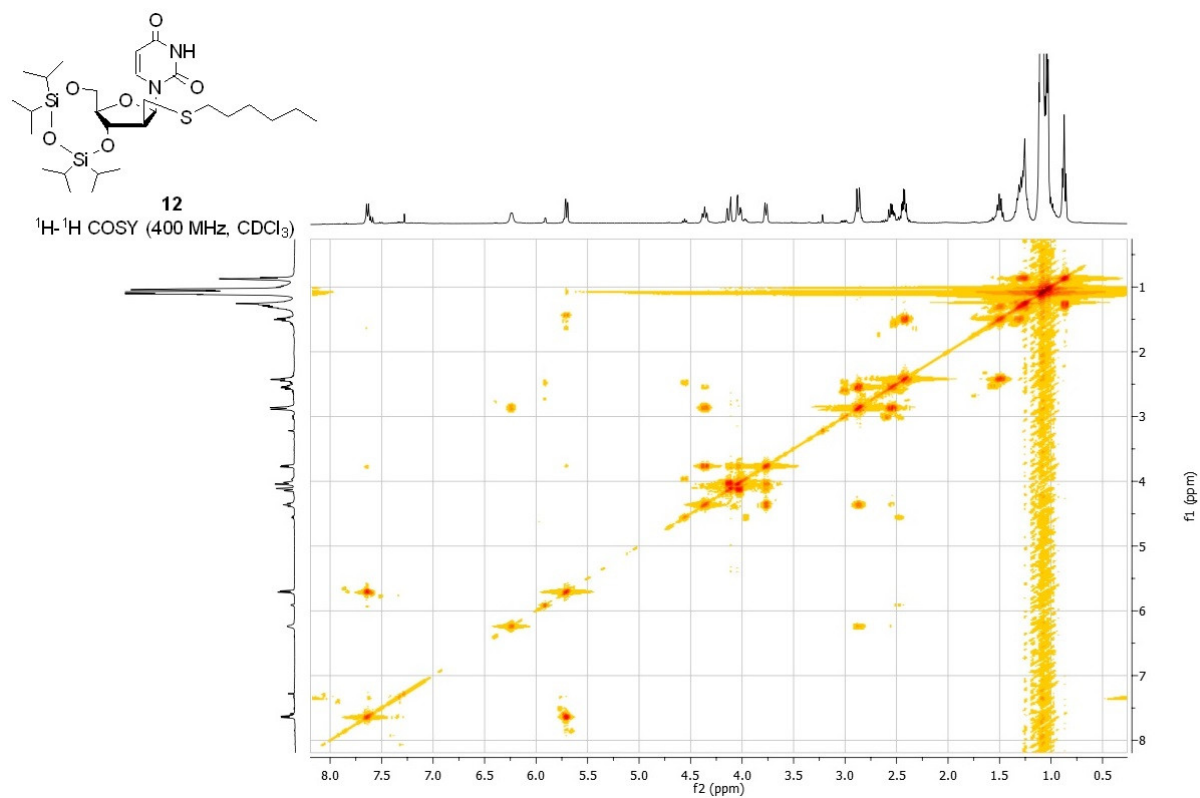
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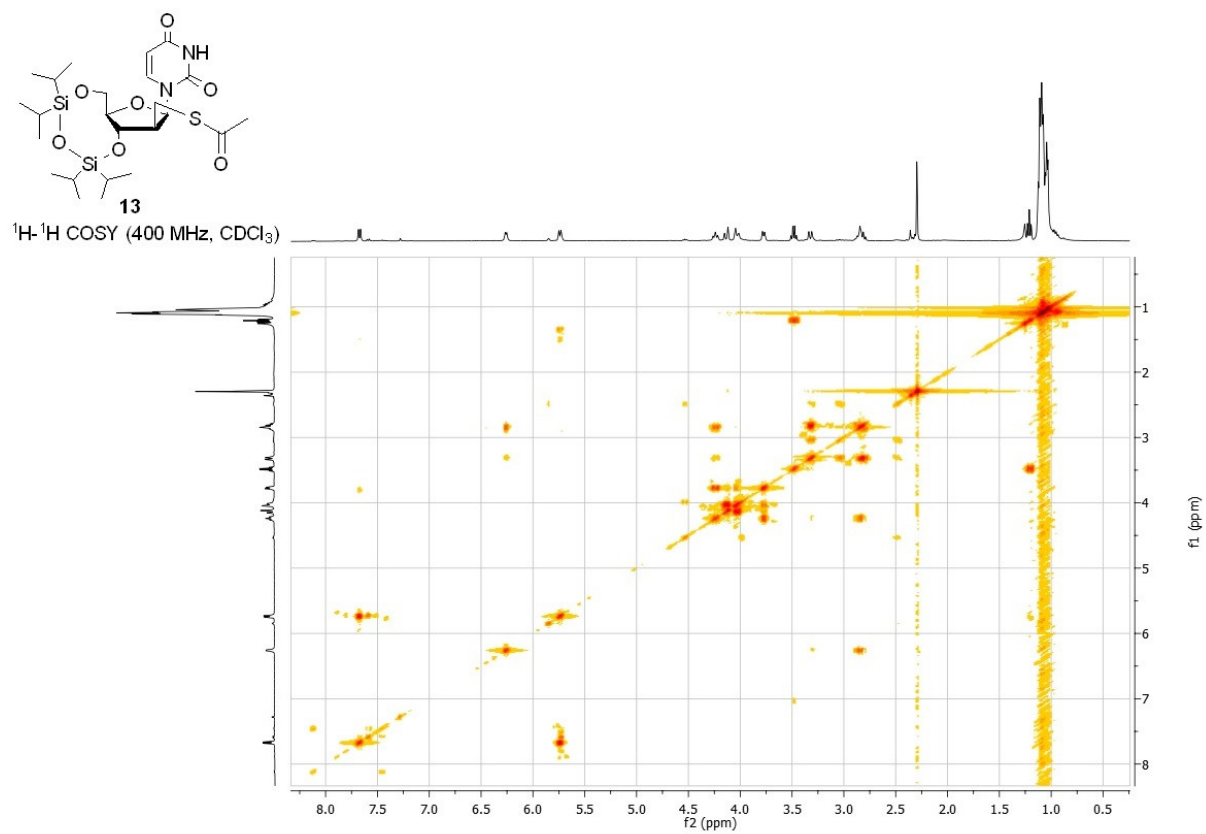
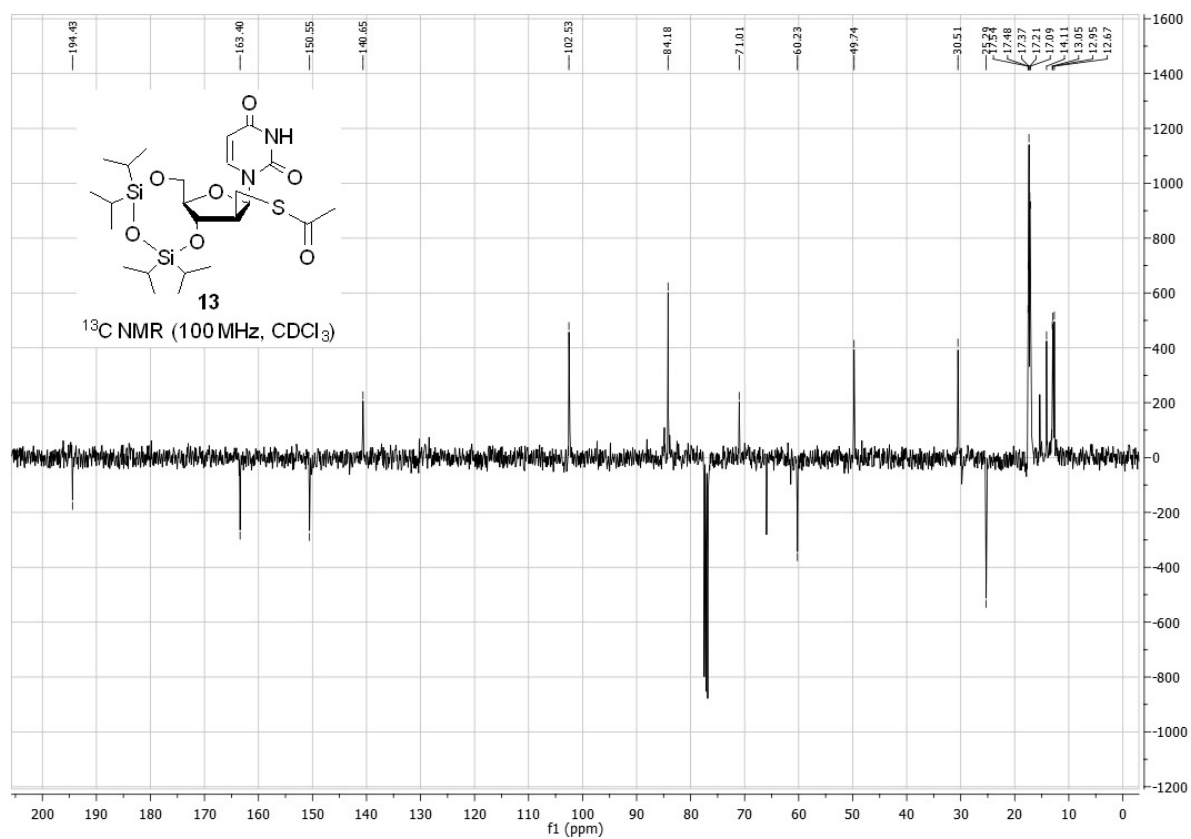


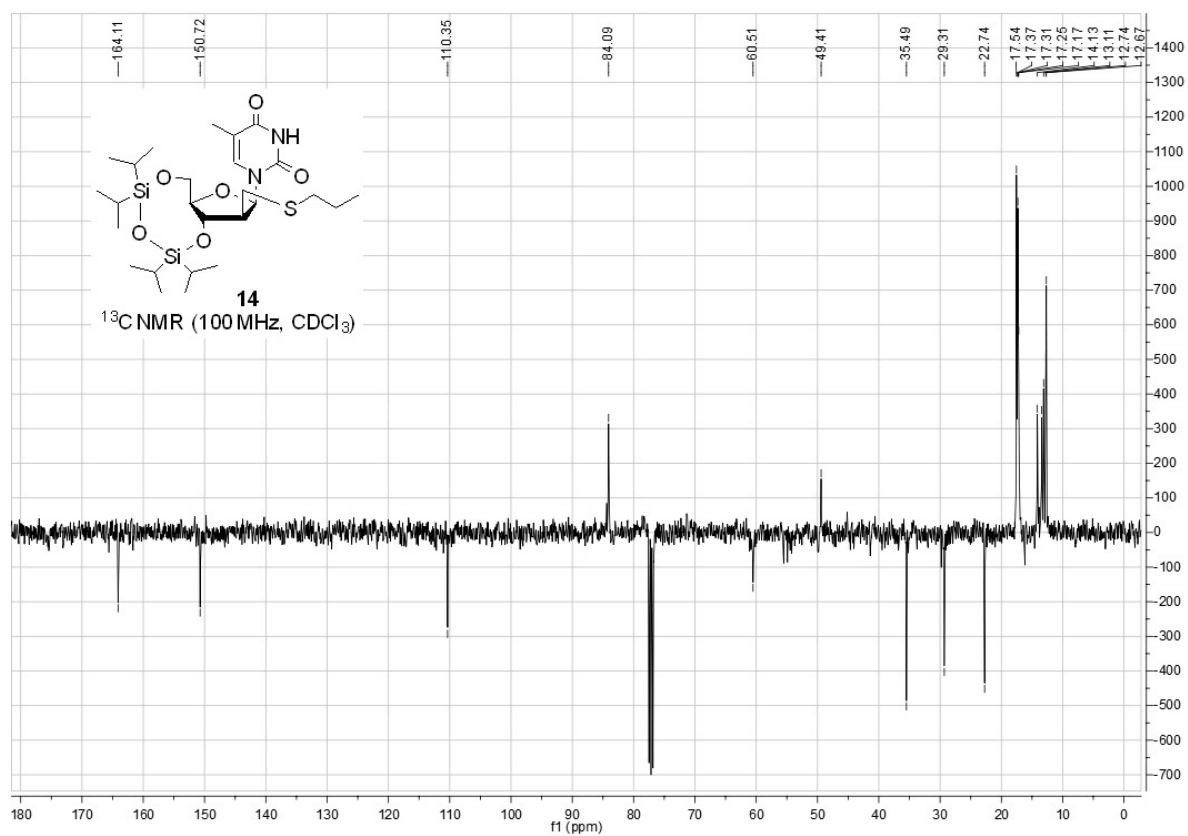
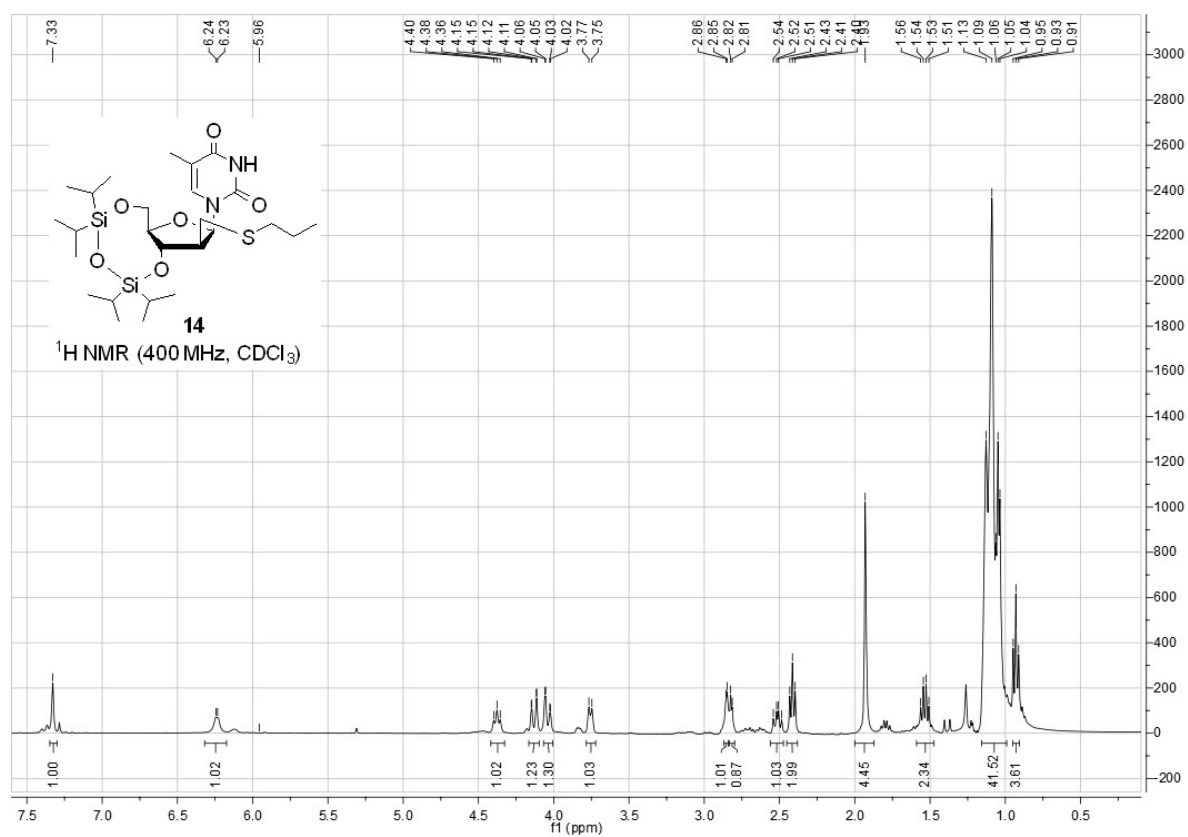
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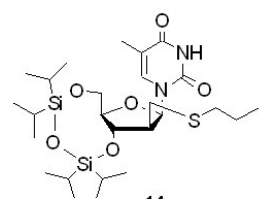




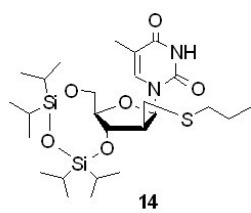
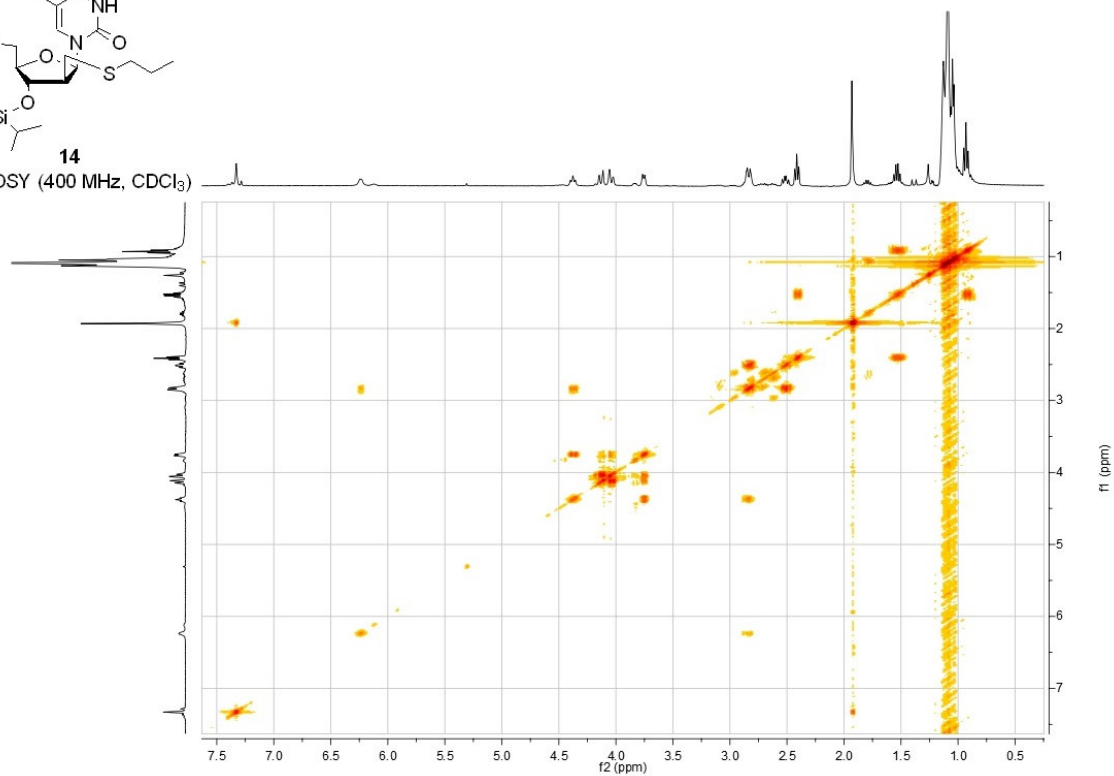




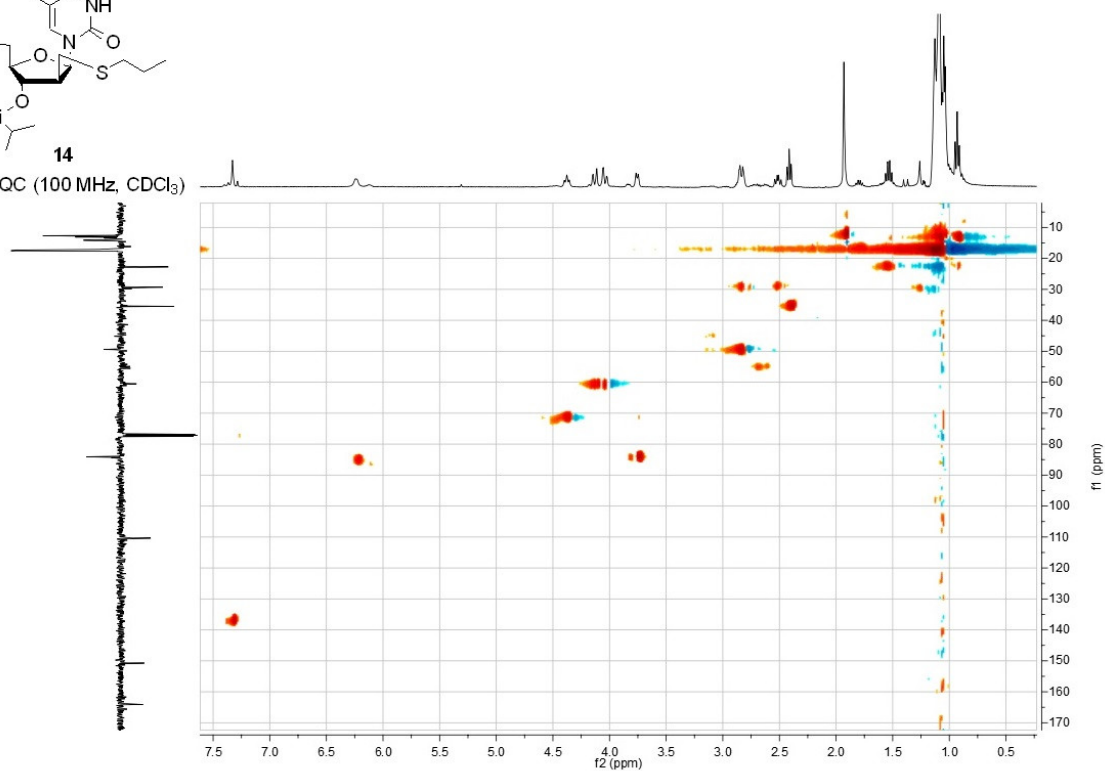


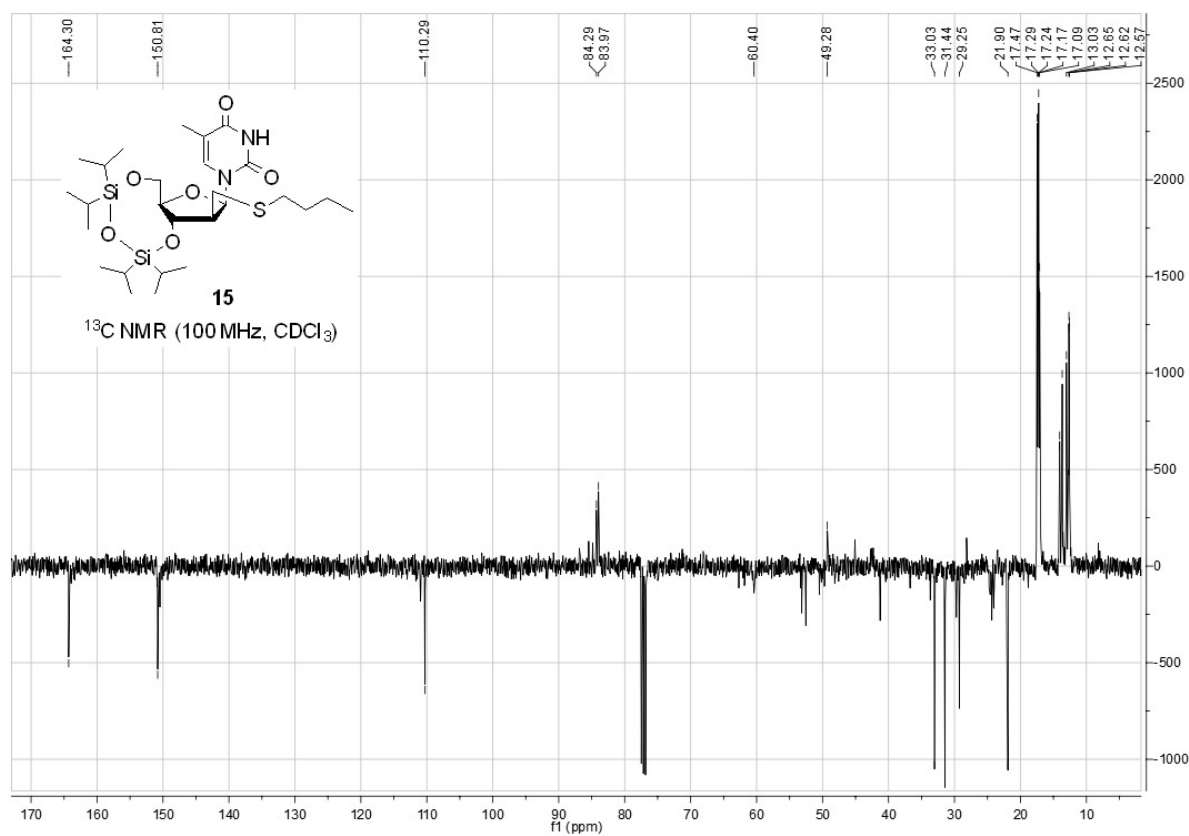
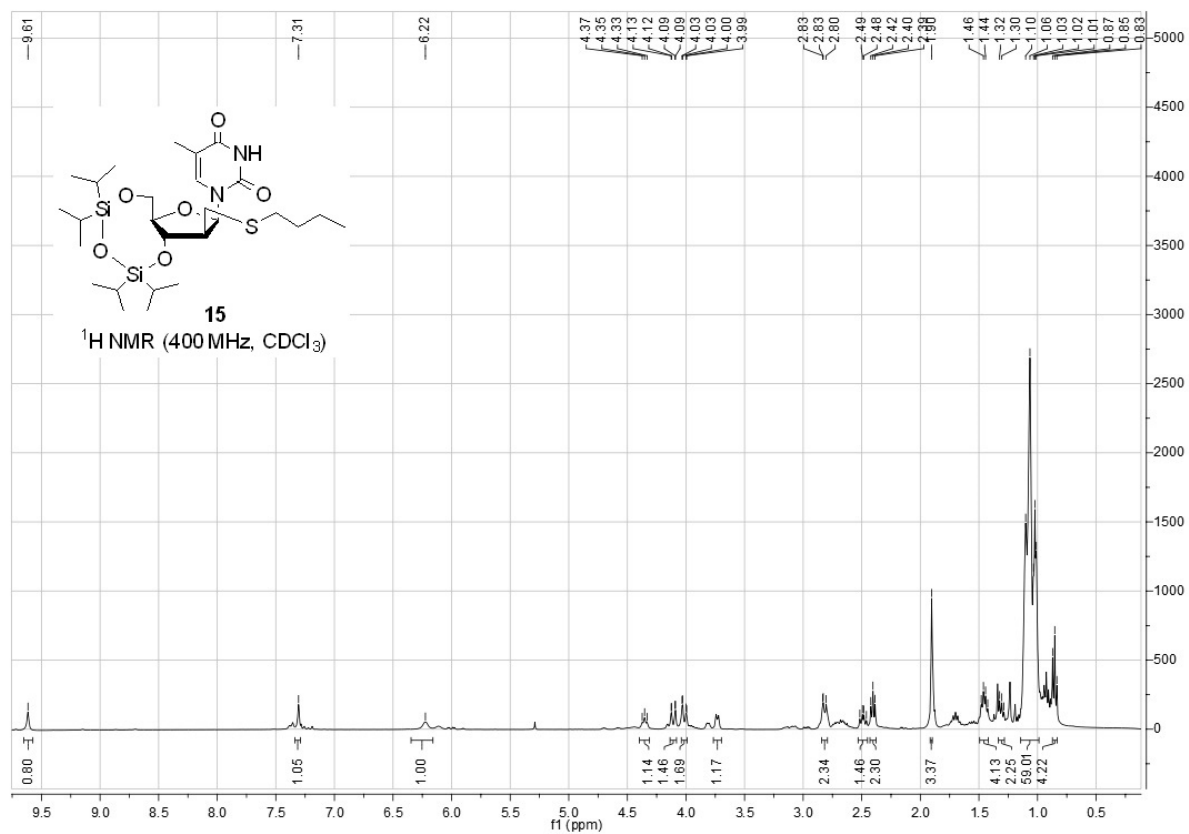


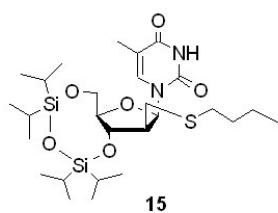
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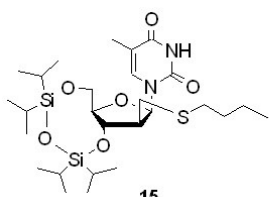
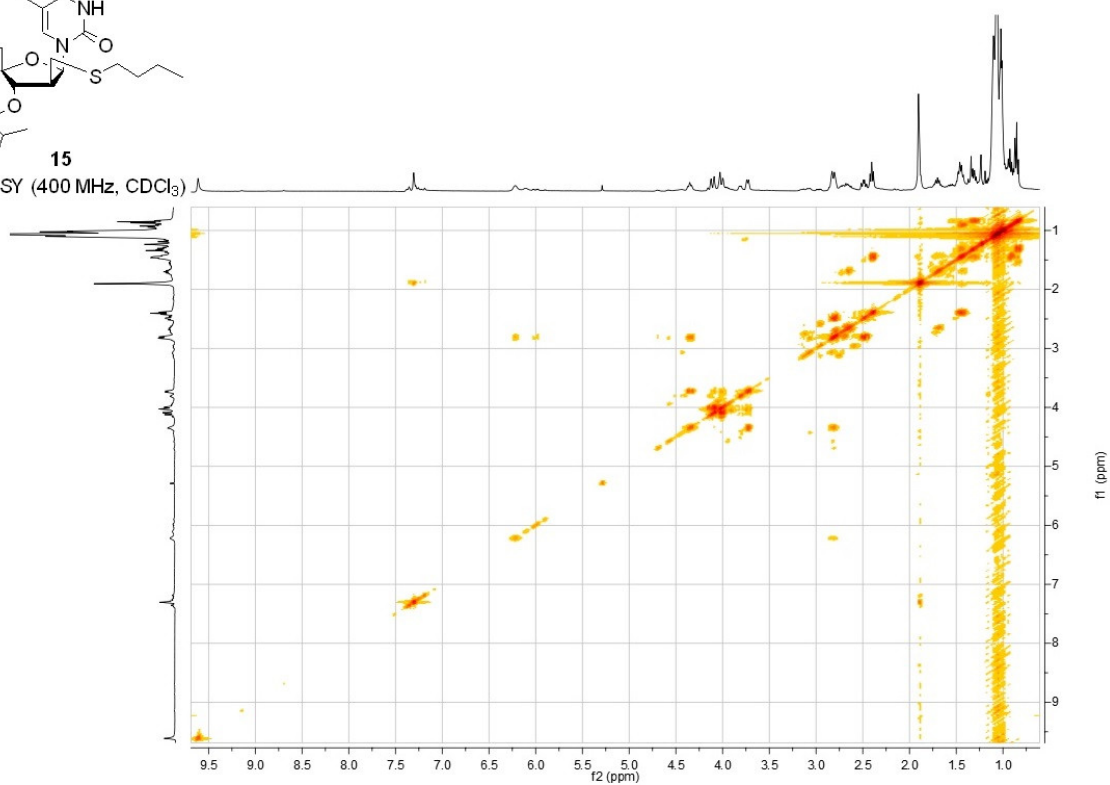
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^1H - ^1H COSY (400 MHz, CDCl_3)



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