Electronic Supplementary Material (ESI) for Chemical Communications

Photodimerisation of glycothymidines in solution and in micelles

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Supporting Information

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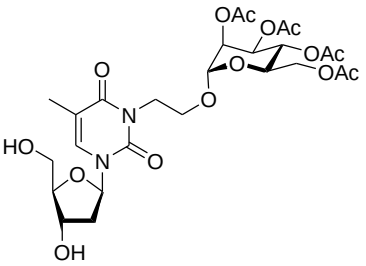
General Experimental Section. Commercially available starting materials and reagents were used without further purification. Reactions requiring dry conditions were performed under an atmophere of nitrogen using oven-dried glassware. Acetonitrile and dichloromethane (DCM) were dried over CaH_2, methanol was dried over magnesium, and tetrahydrofurane was dried over lithium aluminium hydride. (2-Bromoethyl)-2,3:4,6-di-*O*-isopropylidene-α-D-manno-pyranoside (**2**)[1, 2] and 5'-azido-5',2'-dideoxythymidine (**6**)[3] were prepared according to the literature. All reactions were monitored by thin-layer chromatography on silica gel 60 GF_{254} on aluminium foil (Merck) with detection by UV light and charring with sulfuric acid in EtOH (10 %). Silica gel 60 Å (Merck, 230-400 mesh) was used for flash chromatography. Gel permeation chromatography (GPC) was carried out on Sephadex LH-20 from Pharmacia-Biotech. ^1H and ^{13}C NMR spectra were recorded using a Bruker DRX-500 or a Bruker AV-600 spectrometer. NMR spectra were calibrated with respect to the solvent peak (in case of $CDCl_3$ the reference was tetramethylsilane (TMS)). 2D NMR techniques (COSY, HSQC, HMBC) were used for full assignment of the spectra. Assignments marked with an asterix are interchangeable. ESI MS measurements were performed on a Mariner ESI-ToF 5280 instrument. MALDI-TOF mass spectra were recorded on a Bruker Biflex-III 19 kV instrument with CCA as matrix. Optical rotation was measured on a Perkin-Elmer polarimeter 341. IR spectra were recorded on a Perkin-Elmer Paragon 1000 FT-IR spectrometer.

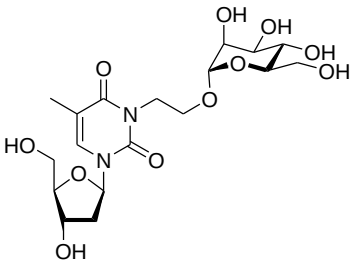
***N*^{3}-[2-(2,3,4,6-Tetra-*O*-acetyl-α-D-mannopyranosyloxy)-ethyl]-2'-deoxythymidine (3)**



2'-Deoxythymidine (**1**, 100 mg, 0.446 mmol, 1.0 equiv) and 2-bromoethyl mannoside (**2,** 203 mg, 0.446 mmol, 1.0 equiv) were dissolved in 6 mL of anhydrous DMF and 15 mL of anhydrous acetonitrile under nitrogen. DBU (66 µL, 0.446 mmol, 1.0 equiv) and TBAI (165 mg, 0.446 mmol, 1.0 equiv) were added and the reaction mixture was stirred at room temperature for 16 h. After the solvent was evaporated under reduced pressure, the residue was taken up in 10 mL of DCM. The solution was washed with saturated aqueous $NaHCO_3$, dried over $MgSO_4$, filtered and concentrated under reduced pressure. Purification by column chromatography on silica gel (EtOAc) gave 153 mg (0.255 mmol, 57 %) of **3** as a colourless solid. $\mathbf{R_f}$: 0.45 (EtOAc / MeOH, 9:1); $[\alpha]_D^{22}$ = + 64.4 (c = 0.96, MeOH); **mp.**: 57 C; **^{1}H NMR** (500 MHz, $CDCl_3$, 300 K, TMS): δ = 7.40 (q, ^4J = 1.2 Hz, 1H, $H6_{thy}$), 6.12 (dd~t, ^3J = 6.4 Hz, 1H, $H1_{ribo}$), 5.25 (dd~t, ^3J = 10.0 Hz, 1H, $H4_{man}$), 5.22 (dd, ^3J = 3.5 Hz, ^3J = 10.0 Hz, 1H, $H3_{man}$),

5.19 (dd, ^3J = 1.7 Hz, ^3J = 3.1 Hz, 1H, $H2_{man}$), 4.91 (d, ^3J = 1.5 Hz, 1H, $H1_{man}$), 4.58 (ddd~dt, ^3J = 4.6 Hz, ^3J = 4.6 Hz, ^3J = 6.3 Hz, 1H, $H3_{ribo}$), 4.31 (ddd, ^3J = 5.2 Hz, ^3J = 7.8 Hz, ^2J = 13.5 Hz, 1H, NCH_2), 4.26 (dd, ^3J = 5.3 Hz, ^2J = 12.3 Hz, 1H, $H6_{man}$), 4.13 (ddd~dt, ^3J = 5.0 Hz, ^3J = 5.0 Hz, ^2J = 13.4 Hz, 1H, NCH_2), 4.09 (dd, ^3J = 2.4 Hz, ^2J = 12.2 Hz, 1H, $H6_{man}$), 4.00 (ddd~dt, ^3J = 3.3 Hz, ^3J = 3.3 Hz, ^3J = 4.3 Hz, 1H, $H4_{ribo}$), 3.96 (ddd, ^3J = 2.4 Hz, ^3J = 5.2 Hz, ^3J = 10.0 Hz, 1H, $H5_{man}$), 3.94 (dd, ^3J = 3.0 Hz, ^2J = 11.2 Hz, 1H, $H5_{ribo}$), 3.89 (ddd, ^3J = 5.0 Hz, ^3J = 7.8 Hz, ^2J = 10.8 Hz, 1H, NCH_2CH_2O), 3.84 (dd, ^3J = 3.3 Hz, ^2J = 11.8 Hz, 1H, $H5_{ribo}$), 3.76 (ddd~dt, ^3J = 5.1 Hz, ^3J = 5.1 Hz, ^2J = 10.8 Hz, 1H, NCH_2CH_2O), 2.55 (br s, 1H, OH), 2.45 (br s, 1H, OH), 2.43 (ddd~dt, ^3J = 6.4 Hz, ^3J = 6.4 Hz, ^2J = 13.8 Hz, 1H, $H2_{ribo}$), 2.38 (ddd, ^3J = 4.8 Hz, ^3J = 6.6 Hz, ^2J = 13.8 Hz, 1H, $H2_{ribo}$), 2.15 (s, 3H, $C(O)CH_3$), 2.11 (s, 3H, $C(O)CH_3$), 2.04 (s, 3H, $C(O)CH_3$), 1.97 (s, 3H, $C(O)CH_3$), 1.95 (d, ^4J = 1.1 Hz, 3H, $C5_{thy}$-CH_3) ppm; **^{13}C NMR** (125 MHz, $CDCl_3$, 300 K, TMS): δ = 170.8 ($C(O)CH_3$), 170.2 ($C(O)CH_3$), 170.1 ($C(O)CH_3$), 169.7 ($C(O)CH_3$), 163.3 ($C4_{thy}$), 151.0 ($C2_{thy}$), 135.1 ($C6_{thy}$), 110.1 ($C5_{thy}$), 96.8 ($C1_{man}$), 87.5 ($C1_{ribo}$), 86.7 ($C4_{ribo}$), 71.0 ($C3_{ribo}$), 69.4 ($C3_{man}$), 69.4 ($C2_{man}$), 68.7 ($C5_{man}$), 66.1 ($C4_{man}$), 63.6 (NCH_2CH_2O), 62.5 ($C6_{man}$), 62.3 ($C5_{ribo}$), 40.6 ($C2_{ribo}$), 39.4 (NCH_2), 20.9 ($C(O)CH_3$), 20.8 ($C(O)CH_3$), 20.8 ($C(O)CH_3$), 20.7 ($C(O)CH_3$), 13.2 ($C5_{thy}$-CH_3) ppm; **ESI MS**: calcd for $C_{26}H_{36}N_2O_{15}$: *m/z* 639.2013 $[M+Na]^+$; found: *m/z* 639.2043 $[M+Na]^+$; **IR** (ATR-IR): $\tilde{\nu}$ = 3343, 2921, 1743, 1699, 1662, 1634, 1469, 1368, 1217, 1136, 1085, 1042, 977, 768 cm^{-1}; **EA** $C_{26}H_{36}N_2O_{15}$ (M = 616.57 g/mol): calcd: C 50.65, H 5.89, N 4.54; found: C 49.40, H 6.15, N 4.46.

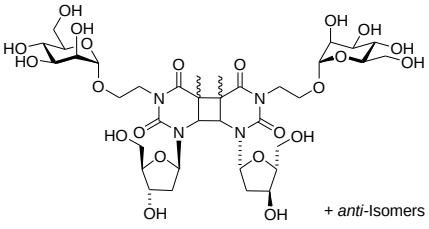
N^3-[2-(α-D-Mannopyranosyloxy)-ethyl]-2'-deoxythymidine (4)



Acetyl-protected glycothymidine **3** (100 mg, 0.156 mmol, 1.0 equiv) was dissolved in 6 mL of anhydrous methanol, sodium methanolate (68 mg, 1.25 mmol, 8.0 equiv) was added and the reaction mixture was stirred at room temperature for 16 h. After neutralisation with Amberlite IR-120 and filtration, the solvent was evaporated under reduced pressure to give 70.0 mg (156 mmol, quant.) of **4** as a colourless solid. **R_f**: 0.27 (EtOAc / MeOH, 3:1); $[\alpha]_D^{22}$ = + 72.0 (c = 1.08, MeOH); **mp.**: 62-68 °C; **^{1}H NMR** (500 MHz, MeOD, 297 K): δ = 7.87 (q, ^4J = 1.3 Hz, 1H, $H6_{thy}$), 6.32 (dd~t, ^3J = 6.7 Hz, 1H, $H1_{ribo}$), 4.82 (d, ^3J = 1.2 Hz, 1H, $H1_{man}$), 4.43 (ddd~dt, ^3J = 3.5 Hz, ^3J = 3.5 Hz, ^3J = 6.2 Hz, 1H, $H3_{ribo}$), 4.34 (ddd, ^3J = 5.4 Hz, ^3J = 8.0 Hz, ^2J = 13.4 Hz, 1H, NCH_2), 4.08 (ddd~dt, ^3J = 4.9 Hz, ^3J = 4.9 Hz, ^2J = 13.4 Hz,

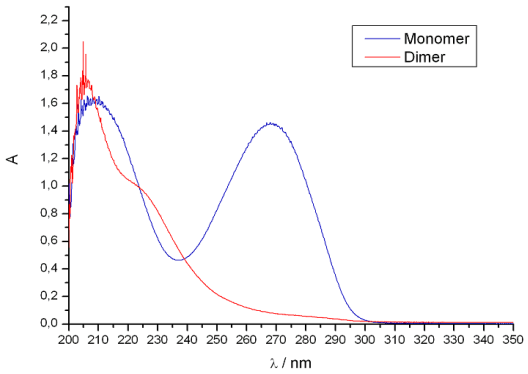
1H, NCH_2), 3.95 (ddd~dt, ^3J = 3.5 Hz, ^3J = 3.5 Hz, ^3J = 3.5 Hz, 1H, $H4_{ribo}$), 3.91 (ddd, ^3J = 5.2 Hz, ^3J = 8.0 Hz, ^2J = 10.5 Hz, 1H, OCH_2), 3.84 (dd, ^3J = 3.2 Hz, ^2J = 12.1 Hz, 1H, $H5_{ribo}$), 3.78* (dd, ^3J = 2.5 Hz, ^2J = 12.1 Hz, 1H, $H5_{ribo}$), 3.77* (dd, ^3J = 3.7 Hz, ^2J = 12.1 Hz, 1H, $H6_{man}$), 3.78-3.76 (m, 1H, $H2_{man}$), 3.76* (dd, ^3J = 3.7 Hz, ^2J = 12.1 Hz, 1H, $H6_{man}$), 3.74 (ddd~dt, ^3J = 5.2 Hz, ^3J = 5.2 Hz, ^2J = 10.4 Hz, 1H, OCH_2), 3.72 (dd, ^3J = 5.3 Hz, ^2J = 11.8 Hz, 1H, $H6_{man}$), 3.67-3.61 (m, 2H, $H3_{man}$, $H4_{man}$), 3.39-3.37 (m, 1H, $H5_{man}$), 2.33 (ddd, ^3J = 3.7 Hz, ^3J = 6.2 Hz, ^2J = 13.6 Hz, 1H, $H2_{ribo}$), 2.27 (ddd~dt, ^3J = 6.8 Hz, ^3J = 6.8 Hz, ^2J = 13.6 Hz, 1H, $H2_{ribo}$), 1.94 (d, ^4J = 1.1 Hz, 3H, $C5_{thy}$-CH_3) ppm; **^{13}C NMR** (150 MHz, MeOD, 300 K): δ = 165.4 ($C4_{thy}$), 152.4 ($C2_{thy}$), 136.7 ($C6_{thy}$), 110.7 ($C5_{thy}$), 101.0 ($C1_{man}$), 88.9 ($C4_{ribo}$), 87.3 ($C1_{ribo}$), 74.8 ($C5_{man}$), 72.5 ($C4_{man}$), 72.1, 72.0 ($C3_{ribo}$, $C2_{man}$), 68.4 ($C3_{man}$), 64.4 (OCH_2), 62.8, 62.7 ($C6_{man}$, $C5_{ribo}$), 41.4, 41.2 (NCH_2, $C2_{ribo}$), 13.3 ($C5_{thy}$-*C*H_3) ppm; **ESI MS**: calcd for $C_{18}H_{28}N_2O_{11}$: *m/z* 471.1585 $[M+Na]^+$; found: *m/z* 471.1556 $[M+Na]^+$; **IR** (ATR-IR): $\tilde{\nu}$ = 3336, 2921, 1694, 1661, 1623, 1470, 1334, 1267, 1131, 1088, 1052, 975, 769 cm^{-1}; **EA** $C_{18}H_{28}N_2O_{11} \cdot 2/3\ H_2O$ (M = 448.4217 g/mol): calcd: C 46.95, H 6.08, N 6.42; found: C 46.98, H 6.50, N 6.03.

N^3-[2-(α-D-Mannopyranosyloxy)-ethyl]-2'-deoxythymidine dimer (5)

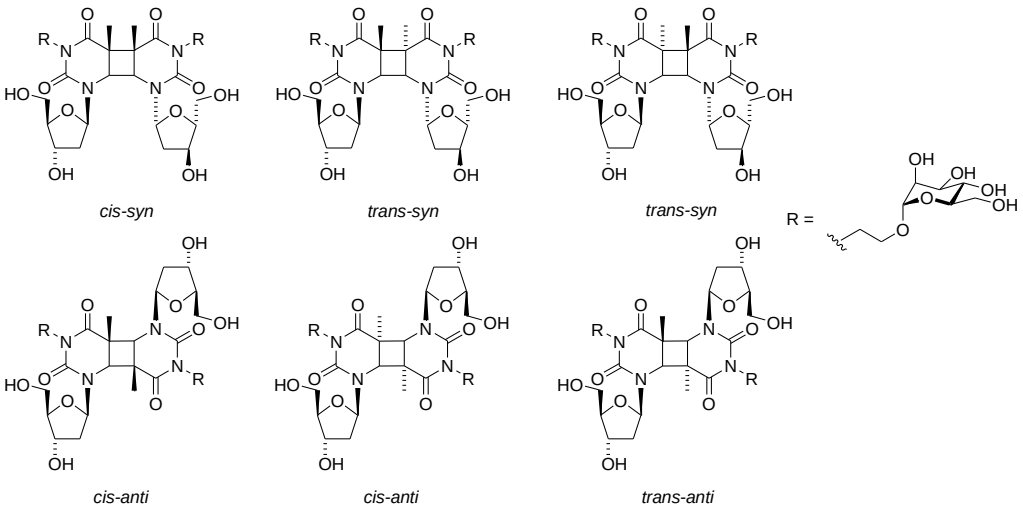


In a quarz glass cuvette glycothymidine **4** (20 mg, 0.045 mmol) was dissolved in 1 mL of H_2O and 1 mL of acetone was added as triplet sensitizer. The solution was degased by treatment with nitrogen for 30 min and subsequently irradiated for 6 h with a 150 W medium pressure mercury lamp and a cut off filter for wave lengths of $\lambda \geq 295$ nm. The solvent was evaporated under reduced pressure. The reaction mixture was purified using gel permeation chromatography (Sephadex, LH-20, H_2O) giving 14 mg (0.015 mmol, 70 %) of the product mixture as a colourless solid. **^{1}H NMR** (600 MHz, D_2O, 300 K): δ = 6.27 (dd, ^3J = 6.4 Hz, ^3J = 9.0 Hz, $H1_{ribo}$), 6.11 (t, ^3J = 6.6 Hz, $H1_{ribo}$), 6.06 (dd, ^3J = 6.0 Hz, ^3J = 8.4 Hz, $H1_{ribo}$), 6.00 (t, ^3J = 6.4 Hz, $H1_{ribo}$), 5.88 (t, ^3J = 7.3 Hz, 0.25H, $H1_{ribo}$), 5.77 (t, ^3J = 6.8 Hz, $H1_{ribo}$), 5.54 (t, ^3J = 7.3 Hz, $H1_{ribo}$), 4.92-4.86 (m, 2H, $H1_{man}$), 4.52-4.38 (m, 4H, $H3_{ribo}$, NCH_2), 4.36, 4.35 4.31, 4.30, 4.28 (each s, 1H, $H6_{thy}$), 4.20-3.55 (m, 24H, NCH_2, 2 x OCH_2, $H4_{ribo}$, 2 x $H5_{ribo}$, 2 x $H6_{man}$, $H2_{man}$, $H3_{man}$, $H4_{man}$, $H5_{man}$), 2.55-2.15 (m, 4H, $H2_{ribo}$), 1.59, 1.55, 1.53, 1.53, 1.48 (each s, $C5_{thy}$-CH_3) ppm; **MALDI-ToF MS**: calcd. for $C_{36}H_{56}N_4O_{22}$: *m/z* 919.33

$[M+Na]^+$; found: *m/z* 919.44 $[M+Na]^+$; **IR** (ATR-IR): $\tilde{\nu}$ = 3344, 2928, 1702, 1655, 1449, 1390, 1332, 1203, 1132, 1086, 1051, 1024, 877, 809, 754, 670, 649, 528, 459 cm^{-1}.

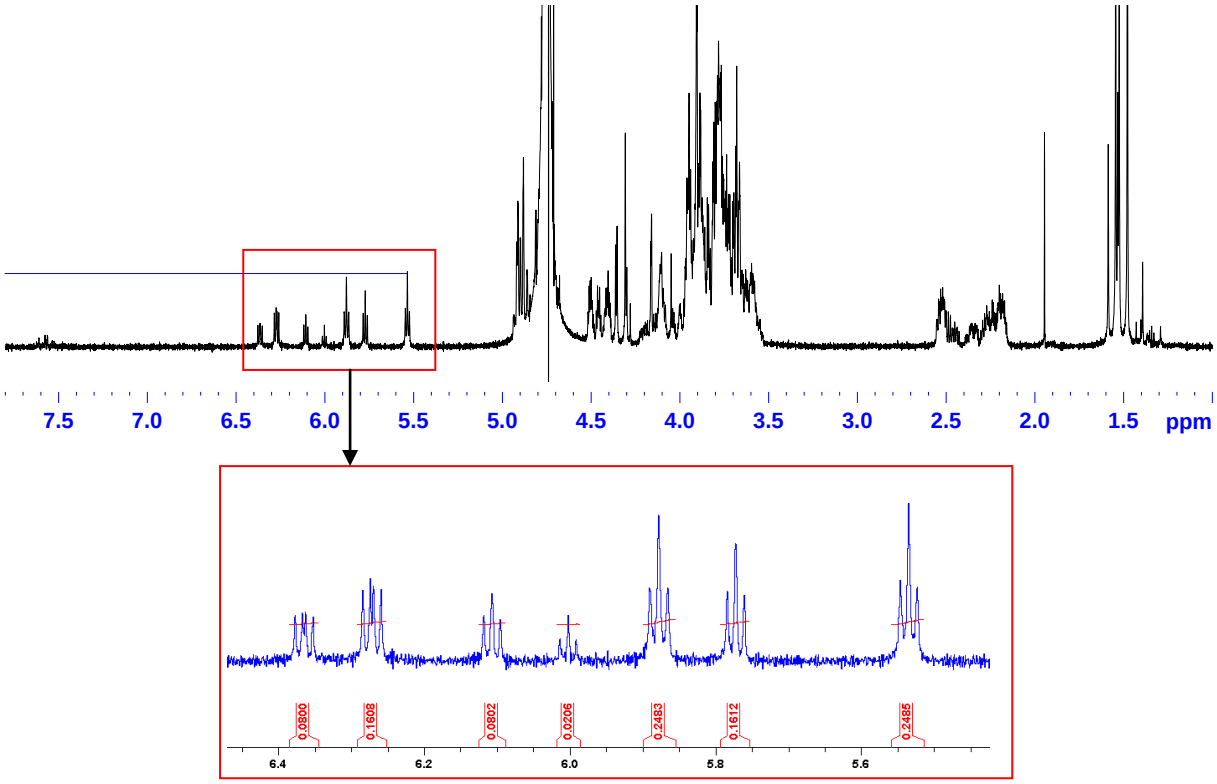


Scheme 5: UV spectra of glycothymidine 4 (blue) and dimer 5 (red).



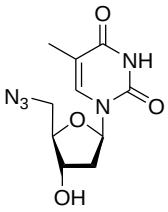
Scheme 6: Stereoisomeric structures of the dimer 5.

The *trans-syn* and *cis-anti* isomers include a C_2 axis symmetry, so the two thymidine units of the dimer are identical and there is only one signal for both anomeric protons, whereas the *cis-syn* and *trans-anti* products do not have any symmetry axis and the ^1H spectrum shows two different signals for the two anomeric protons of the ribose. The effect which is described here for the anomeric proton of the ribose is also valid for the other protons. As there are more than four signals for each proton occuring in the ^1H NMR spectrum, the isomeric mixture includes *cis*- as well as *trans*-cycloaddition products.



Scheme 7: ^{1}H NMR spectra of glycothymidine dimer 5. The anomeric protons of the ribose are highlighted and expanded for clarity.

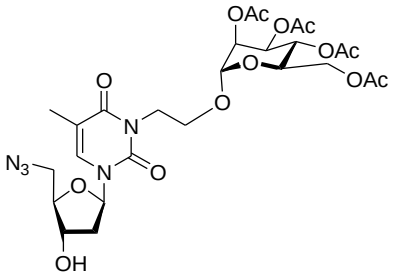
5'-Azido-2',5'-dideoxythymidine (6)[3]



2'-Deoxythymidine (**1**, 1.00 g, 4.13 mmol, 1.0 equiv.) was suspended in pyridine (5 mL) and evaporated. This was repeated with toluene (5 mL). The residue was taken up in DMF (15 mL), and Ph_3P (1.08 g, 4.13 mmol, 1.0 equiv.), sodium azide (1.34 g, 20.7 mmol, 5 equiv.) and tetrabromo methane (1.37 g, 4.13 mmol, 1.0 equiv.) were added. The mixture was stirred at room temperature for 23 h and then treated with methanol (1.5 mL). Stirring was continued for another hour. After evaporation of the solvent the crude product was purified by column chromatography on silica gel (CH_2Cl_2 / EtOH, 98:2 → 90:10) giving 893 mg (3.34 mmol, 76 %) of **6** as a colourless solid. $\mathbf{R_f}$: 0.16 (CH_2Cl_2 / EtOH, 98:2); $[\alpha]_D^{22}$ = + 89.5 (c = 0.94, MeOH); **mp.**: 149 °C; **^{1}H NMR** (500 MHz, $CDCl_3$, 300 K, TMS): δ = 7.57 (q, ^{4}J = 1.2 Hz, 1H, $H6_{thy}$), 6.30 (dd~t, ^{3}J = 6.8 Hz, 1H, $H1_{ribo}$), 4.38 (ddd~dt, ^{3}J = 4.0 Hz, ^{3}J = 4.0 Hz, ^{3}J = 6.6 Hz, 1H, $H3_{ribo}$), 4.00 (ddd~dt, ^{3}J = 3.8 Hz, ^{3}J = 3.8 Hz, ^{3}J = 5.1 Hz, 1H, $H4_{ribo}$), 3.67 (dd, ^{3}J = 3.7 Hz, ^{2}J = 13.2 Hz, 1H, $H5_{ribo}$), 3.61 (dd, ^{3}J = 5.1 Hz, ^{2}J = 13.3 Hz, 1H, $H5_{ribo}$), 2.34 (ddd, ^{3}J = 6.9 Hz, ^{3}J = 6.9 Hz, ^{2}J = 13.8 Hz, 1H, $H2_{ribo}$), 2.29 (ddd, ^{3}J = 4.2 Hz, ^{3}J = 6.6 Hz, ^{2}J = 13.8 Hz, 1H, $H2_{ribo}$), 1.90 (d, ^{4}J = 1.2 Hz, 3H, $C5_{thy}$-CH_3) ppm; **^{13}C NMR**

(150 MHz, $CDCl_3$, 300 K, TMS): δ = 166.3 ($C4_{thy}$), 152.3 ($C2_{thy}$), 137.7 ($C6_{thy}$), 111.9 ($C5_{thy}$), 86.3 ($C4_{ribo}$, $C1_{ribo}$), 72.5 ($C3_{ribo}$), 53.5 ($C5_{ribo}$), 40.3 ($C2_{ribo}$), 12.5 ($C5_{thy}$-CH_3) ppm; **ESI MS**: calcd. for $C_{10}H_{13}N_5O_4$: *m/z* 290.0865 $[M+Na]^+$; found: *m/z* 290.0927 $[M+Na]^+$; **IR** (KBr): $\tilde{\nu}$ = 3388, 3186, 2924, 2100, 1721, 1654 cm^{-1}.

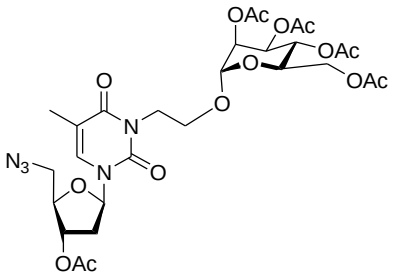
N^3-[2-(2,3,4,6-Tetra-*O*-acetyl-α-D-mannopyranosyloxy)-ethyl]-5'-azido-2',5'-dideoxythymidine (7)



Azidothymidine **6** (150 mg, 0.561 mmol, 1.0 equiv.) was dissolved in anhydrous DMF (3 mL), 2-bromoethyl mannoside (255 mg, 0.561 mmol, 1.0 equiv.), DBU (84 µL, 0.56 mmol, 1.0 equiv.) and TBAI (207 mg, 0.561 mmol, 1.0 equiv.) were added and the solution was stirred at room temperature for 24 h. The solvent was evaporated under reduced pressure and the residue was taken up in dichloromethane (30 mL). The solution was washed with saturated aqueous $NaHCO_3$, dried over $MgSO_4$, filtered and concentrated under reduced pressure. Purification by column chromatography on silica gel (EtOAc) gave 245 mg (0.396 mmol, 71 %) of **7** as a colourless solid. $\mathbf{R}_f$: 0.48 (EtOAc); **mp.**: 52 °C; $[\alpha]_D^{22}$ = + 103.4° (c = 0.95, CH_2Cl_2); **^{1}H NMR** (500 MHz, $CDCl_3$, 300 K, TMS): δ = 7.38 (q, ^4J = 1.2 Hz, 1H, $H6_{thy}$), 6.21 (dd~t, ^3J = 6.4 Hz, ^3J = 6.4 Hz, 1H, $H1_{ribo}$), 5.25 (dd~t, ^3J = 9.8 Hz, 1H, $H4_{man}$), 5.21 (dd, ^3J = 3.1 Hz, ^3J = 9.3 Hz, 1H, $H3_{man}$), 5.19 (dd, ^3J = 1.7 Hz, ^3J = 3.1 Hz, 1H, $H2_{man}$), 4.94 (d, ^3J = 1.5 Hz, 1H, $H1_{man}$), 4.44 (ddd~dt, ^3J = 4.5 Hz, ^3J = 4.5 Hz, ^3J = 6.7 Hz, 1H, $H3_{ribo}$), 4.33 (ddd, ^3J = 5.2 Hz, ^3J = 8.3 Hz, ^2J = 13.5 Hz, 1H, NCH_2), 4.26 (dd, ^3J = 5.3 Hz, ^2J = 12.3 Hz, 1H, $H6_{man}$), 4.11 (ddd~dt, ^3J = 4.7 Hz, ^3J = 4.7 Hz, ^2J = 12.7 Hz, 1H, NCH_2), 4.09 (dd, ^3J = 2.3 Hz, ^2J = 12.2 Hz, 1H, $H6_{man}$), 4.05 (ddd~dt, ^3J = 4.0 Hz, ^3J = 4.0 Hz, ^3J = 4.0 Hz, 1H, $H4_{thy}$), 3.95 (ddd, ^3J = 2.3 Hz, ^3J = 5.3 Hz, ^3J = 8.7 Hz, 1H, $H5_{man}$), 3.88 (ddd, ^3J = 5.0 Hz, ^3J = 8.4 Hz, ^2J = 10.9 Hz, 1H, OCH_2), 3.76 (ddd~dt, ^3J = 4.8 Hz, ^3J = 4.8 Hz, ^2J = 10.7 Hz, 1H, OCH_2), 3.74 (dd, ^3J = 3.6 Hz, ^2J = 13.3 Hz, 1H, $H5_{ribo}$), 3.59 (dd, ^3J = 4.0 Hz, ^2J = 13.2 Hz, 1H, $H5_{ribo}$), 2.43 (ddd, ^3J = 4.5 Hz, ^3J = 6.3 Hz, ^2J = 13.9 Hz, 1H, $H2_{ribo}$), 2.27 (ddd, ^3J = 6.7 Hz, ^3J = 6.7 Hz, ^2J = 13.6 Hz, 1H, $H2_{ribo}$), 2.15 (s, 3H, $C(O)CH_3$), 2.11 (s, 3H, $C(O)CH_3$), 2.04 (s, 3H, $C(O)CH_3$), 1.97 (s, 3H, $C(O)CH_3$), 1.97 (s, 3H, $C5_{thy}$-CH_3) ppm; **^{13}C NMR** (125 MHz, $CDCl_3$, 300 K, TMS): δ = 170.7 ($C(O)CH_3$), 170.2 ($C(O)CH_3$), 170.1 ($C(O)CH_3$), 169.7 ($C(O)CH_3$), 163.2 ($C4_{thy}$), 150.9 ($C2_{thy}$), 133.8 ($C6_{thy}$), 110.2 ($C5_{thy}$), 96.6 ($C1_{man}$), 86.0 ($C1_{ribo}$), 84.4 ($C4_{ribo}$), 71.4 ($C3_{ribo}$), 69.4 ($C3_{man}$), 69.4 ($C2_{man}$), 68.7 ($C5_{man}$),

66.1 ($C4_{man}$), 63.5 (OCH_2), 62.4 ($C6_{man}$), 52.2 ($C5_{ribo}$), 40.7 ($C2_{ribo}$), 39.3 (NCH_2), 20.9 (C(O)CH_3), 20.7 (C(O)CH_3), 20.7 (C(O)CH_3), 20.7 (C(O)CH_3), 13.2 ($C5_{thy}$-CH_3) ppm; **ESI MS**: calcd for $C_{26}H_{35}N_5O_{14}$: *m/z* 664.2107 $[M+Na]^+$; found: *m/z* 664.1952 $[M+Na]^+$; **IR** (ATR-IR): $\tilde{\nu}$ = 3464, 2933, 2103, 1744, 1704, 1667, 1643, 1468, 1368, 1218, 1136, 1082, 1042, 975, 899, 768 cm^{-1}; **EA** $C_{26}H_{35}N_5O_{14}$ (M = 641.58 g/mol): calcd: C 48.67, H 5.50, N 10.92; found: C 48.76, H 5.69, N 10.65.

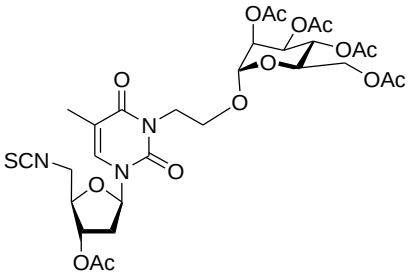
N^3-[2-(2,3,4,6-Tetra-*O*-acetyl-α-D-mannopyranosyloxy)-ethyl]-3'-*O*-acetyl-5'-azido-2',5'-dideoxythymidine (8)



Azidoglycothymidine **7** (50 mg, 0.078 mmol) was dissolved in anhydrous pyridine (0.3 mL) and treated with acetic anhydride (0.1 mL). The reaction mixture was stirred at room temperature for 18 h. The solvent was evaporated under reduced pressure to give without further purification 523 mg (0.765 mmol, 95 %) of the pure product as a colourless solid. **R_f**: 0.75 (EtOAc); **mp**.: 66 °C; $[\alpha]_D^{22}$ = + 83.1° (c = 1.01, CH_2Cl_2); **^{1}H NMR** (500 MHz, $CDCl_3$, 300 K, TMS): δ = 7.38 (q, ^4J = 1.2 Hz, 1H, $H6_{thy}$), 6.34 (dd, ^3J = 5.5 Hz, ^3J = 8.9 Hz, 1H, $H1_{ribo}$), 5.26 (dd~t, ^3J = 10.0 Hz, 1H, $H4_{man}$), 5.24 (dd, ^3J = 3.1 Hz, ^3J = 10.0 Hz, 1H, $H3_{man}$), 5.19 (ddd~dt, ^3J = 2.2 Hz, ^3J = 2.2 Hz, ^3J = 7.0 Hz, 1H, $H3_{ribo}$), 5.19 (dd, ^3J = 1.8 Hz, ^3J = 3.0 Hz, 1H, $H2_{man}$), 4.92 (d, ^3J = 1.6 Hz, 1H, $H1_{man}$), 4.33 (ddd, ^3J = 5.9 Hz, ^3J = 7.8 Hz, ^2J = 13.4 Hz, 1H, NCH_2), 4.27 (dd, ^3J = 5.2 Hz, ^2J = 12.3 Hz, 1H, $H6_{man}$), 4.13 (m_c, 1H, NCH_2), 4.12 (m_c, 1H, $H4_{ribo}$), 4.08 (dd, ^3J = 2.3 Hz, ^2J = 12.3 Hz, 1H, $H6_{man}$), 3.94 (ddd, ^3J = 2.3 Hz, ^3J = 5.1 Hz, ^3J = 9.8 Hz, 1H, $H5_{man}$), 3.89 (ddd, ^3J = 5.7 Hz, ^3J = 7.8 Hz, ^2J = 10.5 Hz, 1H, OCH_2), 3.77 (dd, ^3J = 3.1 Hz, ^2J = 13.1 Hz, 1H, $H5_{ribo}$), 3.75 (ddd, ^3J = 4.9 Hz, ^3J = 5.7 Hz, ^2J = 10.5 Hz, 1H, OCH_2), 3.69 (dd, ^3J = 3.4 Hz, ^2J = 13.1 Hz, 1H, $H5_{ribo}$), 2.49 (ddd, ^3J = 1.8 Hz, ^3J = 5.6 Hz, ^2J = 14.3 Hz, 1H, $H2_{ribo}$), 2.24 (ddd, ^3J = 7.0 Hz, ^3J = 8.9 Hz, ^2J = 14.3 Hz, 1H, $H2_{ribo}$), 2.15 (s, 3H, C(O)CH_3), 2.11 (s, 3H, C(O)CH_3), 2.11 (s, 3H, C(O)CH_3), 2.04 (s, 3H, C(O)CH_3), 1.98 (d, ^4J = 1.2 Hz, 3H, $CH_{3,thy}$); 1.97 (s, 3H, C(O)CH_3) ppm; **^{13}C NMR** (125 MHz, $CDCl_3$, 300 K, TMS): δ = 170.7 (*C*(O)CH_3),170.6 (*C*(O)CH_3), 169.9 (*C*(O)CH_3), 169.8 (*C*(O)CH_3), 169.8 (*C*(O)CH_3), 163.0 ($C4_{thy}$), 150.9 ($C2_{thy}$), 133.1 ($C6_{thy}$), 110.9 ($C5_{thy}$), 96.7 ($C1_{man}$), 85.2 ($C1_{ribo}$), 82.5 ($C4_{ribo}$), 74.6 ($C3_{ribo}$), 69.3 ($C2_{man}$), 69.1 ($C3_{man}$), 68.7 ($C5_{man}$), 66.0 ($C4_{man}$), 63.4 (OCH_2), 62.4 ($C6_{man}$), 52.6 ($C5_{ribo}$), 39.5 (NCH_2), 37.2 ($C2_{ribo}$), 20.9 (C(O)CH_3), 20.9 (C(O)CH_3), 20.8 (C(O)CH_3), 20.7 (C(O)CH_3), 20.7 (C(O)CH_3), 13.4

($CH_{3,thy}$) ppm; **ESI-MS**: calcd for $C_{28}H_{37}N_5O_{15}$: *m/*z 706.2178 $[M+Na]^+$; found: *m/z* 706.2089 $[M+Na]^+$; **IR** (ATR-IR): $\tilde{\nu}$ = 2940, 2103, 1739, 1705, 1668, 1645, 1466, 1368, 1217, 1136, 1084, 1043, 973, 895, 768 cm^{-1}; **EA** $C_{28}H_{37}N_5O_{15}$ (M = 683.62 g/mol): calcd: C 49.19, H 5.46, N 10.24; found: C 49.46, H 5.51, N 9.87.

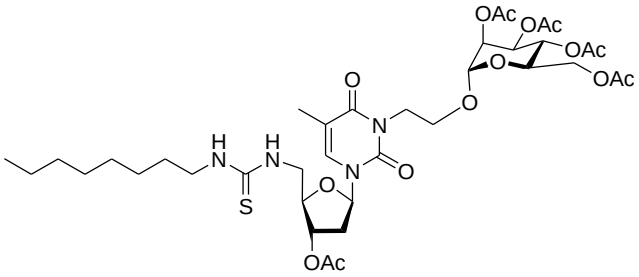
N^3-[2-(2,3,4,6-Tetra-*O*-acetyl-α-D-mannopyranosyloxy)-ethyl]-3'-*O*-acetyl-5'-isothiocyanato-2',5'-dideoxythymidine (9)



Glycothymidine **8** (15 mg, 0.022 mmol, 1.0 equiv.) was dissolved in anhydrous THF (2 mL), carbon disulfide (20 µL, 0.329 mmol, 15 equiv.) and Ph_3P (6.3 mg, 0.024 mmol, 1.1 eqiuv.) were added and the reaction mixture was stirred at room temperature for 70 h. The solvent was evaporated under reduced pressure and the crude product was purified by column chromatography on silica gel (Cy / EtOAc 2:1 → 0:1) to give 14 mg (0.020 mmol, 91 %) of **9** as a colourless solid. $\mathbf{R_f}$: 0.28 (EtOAc / Cy, 2:1); **mp.**: 60-62 °C; $[\alpha]_D^{22}$ = + 12.9° (c = 1.07, CH_2Cl_2); **^{1}H NMR** (500 MHz, $CDCl_3$, 300 K, TMS): δ = 7.37 (q, ^4J = 1.1 Hz, 1H, $H6_{thy}$), 6.39 (dd, ^3J = 5.4 Hz, ^3J = 9.2 Hz, 1H, $H1_{ribo}$), 5.27 (dd~t, ^3J = 10.0 Hz, ^3J = 10.0 Hz, 1H, $H4_{man}$), 5.23 (dd, ^3J = 2.6 Hz, ^3J = 10.0 Hz, 1H, $H3_{man}$), 5.23 (m_c, 1H, $H3_{ribo}$), 5.19 (dd, ^3J = 1.7 Hz, ^3J = 2.7 Hz, 1H, $H2_{man}$), 4.92 (d, ^3J = 1.6 Hz, 1H, $H1_{man}$), 4.35 (ddd, ^3J = 5.8 Hz, ^3J = 7.9 Hz, ^2J = 13.4 Hz, 1H, NCH_2), 4.27 (dd, ^3J = 5.2 Hz, ^2J = 12.3 Hz, 1H, $H6_{man}$), 4.15-4.08 (m, 2H, NCH_2, $H4_{ribo}$), 4.08 (dd, ^3J = 2.4 Hz, ^2J = 12.3 Hz, 1H, $H6_{man}$), 4.02 (dd, ^3J = 3.1 Hz, ^2J = 14.9 Hz, 1H, $H5_{ribo}$), 3.94 (dd, ^3J = 2.9 Hz, ^2J = 14.9 Hz, 1H, $H5_{ribo}$), 3.93 (m_c, 1H, $H5_{man}$), 3.90 (ddd, ^3J = 5.6 Hz, ^3J = 7.9 Hz, ^2J = 10.5 Hz, 1H, OCH_2), 3.75 (ddd, ^3J = 4.8 Hz, ^3J = 5.7 Hz, ^2J = 10.5 Hz, 1H, OCH_2), 2.53 (ddd, ^3J = 1.6 Hz, ^3J = 5.5 Hz, ^2J = 14.4 Hz, 1H, $H2_{ribo}$), 2.29 (ddd, ^3J = 7.3 Hz, ^3J = 9.1 Hz, ^2J = 14.4 Hz, 1H, $H2_{ribo}$), 2.15 (s, 3H, $C(O)CH_3$), 2.12 (s, 3H, $C(O)CH_3$), 2.11 (s, 3H, $C(O)CH_3$), 2.04 (s, 3H, $C(O)CH_3$), 2.02 (d, ^4J = 1.1 Hz, 3H, $CH_{3,thy}$); 1.97 (s, 3H, $C(O)CH_3$) ppm; **^{13}C NMR** (125 MHz, $CDCl_3$, 300 K, TMS): δ = 170.7 ($C(O)CH_3$), 170.7 ($C(O)CH_3$), 169.9 ($C(O)CH_3$), 169.8 ($C(O)CH_3$), 169.7 ($C(O)CH_3$), 163.0 ($C4_{thy}$), 151.0 ($C2_{thy}$), 133.0 ($C6_{thy}$), 111.4 ($C5_{thy}$), 96.7 ($C1_{man}$), 84.9 ($C1_{ribo}$), 81.7 ($C4_{ribo}$), 74.6 ($C3_{ribo}$), 69.3 ($C2_{man}$), 69.1 ($C3_{man}$), 68.7 ($C5_{man}$), 66.0 ($C4_{man}$), 63.4 (OCH_2), 62.4 ($C6_{man}$), 47.1 ($C5_{ribo}$), 39.6 (NCH_2), 36.8 ($C2_{ribo}$), 20.9 ($C(O)CH_3$), 20.8 ($C(O)CH_3$), 20.8 ($C(O)CH_3$), 20.7 ($C(O)CH_3$), 20.7 ($C(O)CH_3$), 13.2 ($C5_{thy}$-CH_3) ppm; **ESI MS**: calcd for $C_{29}H_{37}N_3O_{15}S$:

m/z 722.1838 $[M+Na]^+$; found: *m/z* 722.1725 $[M+Na]^+$; **IR** (ATR-IR): $\tilde{\nu}$ = 2956, 2097, 1736, 1704, 1665, 1647, 1465, 1450, 1367, 1216, 1135, 1083, 1041, 973, 894, 767 cm^{-1}; **EA** $C_{29}H_{37}N_3O_{15}S$ (M = 699.68 g/mol): calcd: C 49.78, H 6.01, N 5.33, S 4.58; found: C 49.87, H 5.47, N 5.81, S 4.13.

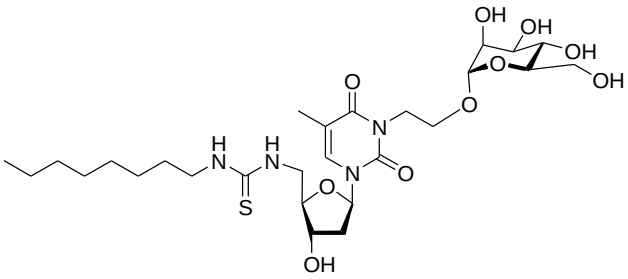
N^3-[2-(2,3,4,6-Tetra-*O*-acetyl-α-D-mannopyranosyloxy)-ethyl]-3'-*O*-acetyl-5'-octyl-thioureido-2',5'-dideoxythymidine (10)



Octylamine (19.3 µl, 0.15 mmol, 1.5 equiv.) was dissolved in anhydrous DMF (5 mL). Glycothymidine **9** (69.9 mg, 0.10 mmol, 1.0 equiv.) was added at 0 °C and the reaction mixture was stirred at room temperature for 16 h. The solvent was evaporated under reduced pressure. Purification by column chromatography on silica gel (EtOAc) gave 68.2 mg (0.082 mmol, 82 %) of **10** as a colourless solid. **R_f**: 0.48 (EtOAc) ; **mp**.: 79 °C; **^{1}H NMR** (500 MHz, $CDCl_3$, 300 K, TMS): δ = 7.17 (br s, 1H, $H6_{thy}$), 6.60-6.40 (br s, NH), 6.40-6.15 (br s, NH), 6.24 (dd, ^3J = 6.2 Hz, ^3J = 8.0 Hz, 1H, $H1_{ribo}$), 5.25 (dd~t, ^3J = 9.8 Hz, ^3J = 9.8 Hz, 1H, $H4_{man}$), 5.21 (dd, ^3J = 3.3 Hz, ^3J = 9.8 Hz, 1H, $H3_{man}$), 5.18 (dd, ^3J = 1.7 Hz, ^3J = 3.3 Hz, 1H, $H2_{man}$), 5.15 (ddd~dt, ^3J = 3.1 Hz, ^3J = 3.1 Hz, ^3J = 7.0 Hz, 1H, $H3_{ribo}$), 4.89 (d, ^3J = 1.7 Hz, 1H, $H1_{man}$), 4.36 (ddd, ^3J = 5.4 Hz, ^3J = 7.9 Hz, ^2J = 13.4 Hz, 1H, NCH_2), 4.26 (dd, ^3J = 5.1 Hz, ^2J = 12.3 Hz, 1H, $H6_{man}$), 4.16-4.11 (m, 1H, $H4_{ribo}$), 4.10 (ddd~dt, ^3J = 5.0 Hz, ^3J = 5.0 Hz, ^2J = 13.5 Hz, 1H, NCH_2), 4.06 (dd, ^3J = 2.4 Hz, ^2J = 12.3 Hz, 1H, $H6_{man}$), 3.98-3.81 (m, 3H, 2x $H5_{ribo}$, $H5_{man}$), 3.91 (ddd, ^3J = 5.2 Hz, ^3J = 7.8 Hz, ^2J = 10.6 Hz, 1H, OCH_2), 3.75 (ddd~dt, ^3J = 5.1 Hz, ^3J = 5.1 Hz, ^2J = 10.5 Hz, 1H, OCH_2), 3.60-3.25 (m, br, 2H, $NHCH_2$), 2.47 (ddd, ^3J = 2.6 Hz, ^3J = 6.1 Hz, ^2J = 14.2 Hz, 1H, $H2_{ribo}$), 2.38 (ddd, ^3J = 7.6 Hz, ^3J = 7.6 Hz, ^2J = 14,7 Hz, 1H, $H2_{ribo}$), 2.15 (s, 3H, $C(O)CH_3$), 2.12 (s, 3H, $C(O)CH_3$), 2.11 (s, 3H, $C(O)CH_3$), 2.03 (s, 3H, $C(O)CH_3$), 1.99 (d, ^4J = 1.2 Hz, 3H, $CH_{3,thy}$); 1.96 (s, 3H, $C(O)CH_3$), 1.57 (dddd~pent., ^3J = 7.2 Hz, 2H, $NHCH_2CH_2$), 1.36-1.20 (m, 10H, $CH_{2,\,alkyl}$), 0.88 (t, ^3J = 7.0 Hz, 3H, CH_2CH_3) ppm; **^{13}C NMR** (125 MHz, $CDCl_3$, 300K, TMS): δ = 171.0 ($C(O)CH_3$), 170.0 ($C(O)CH_3$), 169.9 ($C(O)CH_3$), 169.8 ($C(O)CH_3$), 169.7 ($C(O)CH_3$), 162.9 ($C4_{thy}$), 151.0 ($C2_{thy}$), 133.7 ($C6_{thy}$), 111.3 ($C5_{thy}$), 96.7 ($C1_{man}$), 86.1 ($C1_{ribo}$), 82.7 ($C4_{ribo}$), 74.6 ($C3_{ribo}$), 69.3 ($C2_{man}$), 69.1 ($C3_{man}$), 68.6 ($C5_{man}$), 65.9 ($C4_{man}$), 63.5 (OCH_2), 62.4 ($C6_{man}$), 46.8 ($C5_{ribo}$), 44.5

(C(S)NH*C*H$_2$), 39.6 (NCH$_2$), 36.2 (C2$_{ribo}$), 31.8 (CH$_{2,alkyl}$), 29.2 (CH$_{2,alkyl}$), 29.2 (CH$_{2,alkyl}$), 28.9 (CH$_{2,alkyl}$), 26.9 (CH$_{2,alkyl}$), 22.6 (CH$_{2,alkyl}$), 21.0 (C(O)*C*H$_3$), 20.9 (C(O)*C*H$_3$), 20.8 (C(O)*C*H$_3$), 20.7 (C(O)*C*H$_3$), 20.7 (C(O)*C*H$_3$), 14.0 (CH$_2$)$_7$*C*H$_3$) 13.3 (C5$_{thy}$-*C*H$_3$) ppm; **ESI MS**: calcd for $C_{37}H_{56}N_4O_{15}S$.: *m/z* 851.3355 $[M+Na]^+$; found: *m/z* 851.3269 $[M+Na]^+$; **IR** (ATR-IR): $\tilde{\nu}$ = 3352, 2928, 1772, 1705, 1644, 1548, 1466, 1366, 1218, 1136, 1082, 1042, 977, 897, 768 cm^{-1};

***N*^{3}-[2-(α-D-Mannopyranosyloxy)-ethyl]-5'-octyl-thioureido-2',5'-dideoxythymidine (11)**

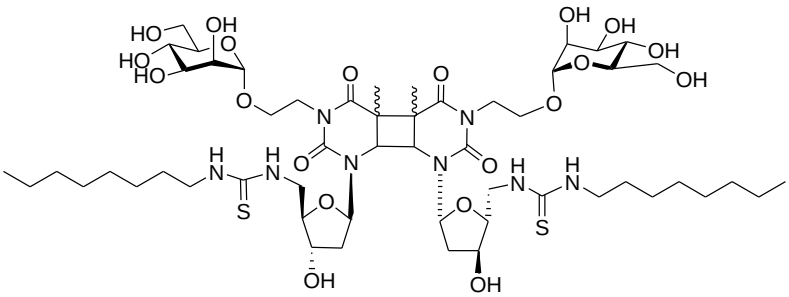


Glycothymidine **10** (38 mg, 0.046 mmol) was dissolved in anhydrous methanol (1 mL), sodium methanolate (13.3 mg, 0.246 mmol) was added and the reaction mixture was stirred at room temperature for 16 h. The solution was neutralized with amberlite IR-120 and filtered. The solvent was removed under reduced pressure to give 16.1 mg (0.026 mmol, 57 %) of **11** as a colourless solid. **R$_f$**: 0.26 (EtOAc / MeOH, 5:1); $[\alpha]_D^{22}$ = + 64.5 (c = 0.45, MeOH); **mp.**: 92 °C; **^{1}H NMR** (500 MHz, CD$_3$OD, 300 K): δ = 7.54 (s, br, 1H, H6$_{thy}$), 6.23 (dd~t, ^3J = 6.8 Hz, ^3J = 6.8 Hz, 1H, H1$_{ribo}$), 4.80 (d, ^3J = 1.9 Hz, 1H, H1$_{man}$), 4.37-4.33 (m, 1H, H3$_{ribo}$), 4.31 (ddd, ^3J = 5.4 Hz, ^3J = 8.0 Hz, ^2J = 13.4 Hz, 1H, NCH$_2$), 4.05 (ddd~dt, ^3J = 4.9 Hz, ^3J = 4.9 Hz, ^2J = 13.4 Hz, 1H, NCH$_2$), 4.04-3.98 (m, 1H, H4$_{ribo}$), 4.12-4.20 (br m, 4H, C(S)NHC*H*$_2$), 2x H5$_{ribo}$), 3.89 (ddd, ^3J = 5.2 Hz, ^3J = 8.0 Hz, ^2J = 10.5 Hz, 1H, OCH$_2$), 3.75 (dd, ^3J = 2.5 Hz, ^2J = 11.8 Hz, 1H, H6$_{man}$), 3.73 (dd, ^3J = 1.8 Hz, ^3J = 2.7 Hz, 1H, H2$_{man}$), 3.69 (ddd~dt, ^3J = 5.0 Hz, ^3J = 5.0 Hz, ^2J = 10.5 Hz, OCH$_2$), 3.68 (dd, ^3J = 5.5 Hz, ^2J = 11.8 Hz, 1H, H6$_{man}$), 3.61-3.59 (m, 2H, H3$_{man}$, H4$_{man}$), 3.35 (m$_c$, 1H, H5$_{man}$), 2.31 (ddd, ^3J = 4.3 Hz, ^3J = 6.5 Hz, ^2J = 13.9 Hz, H2$_{ribo}$), 2.31-2.25 (m, 1H, H2$_{ribo}$), 1.94 (d, ^4J = 1.2 Hz, 3H, C5$_{thy}$-CH$_3$), 1.59-1.52 (m, 2H, NHCH$_2$C*H*$_2$), 1.35-1.26 (m, 10H, (C*H*$_2$)$_5$CH$_3$), 0.90 (t, ^3J = 7.0 Hz, 1H, (CH$_2$)$_7$C*H*$_3$) ppm; **^{13}C NMR** (125 MHz, CD$_3$OD, 300K): δ = 165.4 (C4$_{thy}$), 152.4 (C2$_{thy}$), 136.7 (C6$_{thy}$), 111.1 (C5$_{thy}$), 101.0 (C1$_{man}$), 87.9 (C1$_{ribo}$), 86.7 (C4$_{ribo}$), 74.8 (C5$_{man}$), 72.9 (C3$_{ribo}$), 72.5 (C3$_{man}$), 72.1 (C2$_{man}$), 68.4 (C4$_{man}$), 64.4 (OCH$_2$), 62.8 (C6$_{man}$), 41.3 (NCH$_2$), 40.2 (C2$_{ribo}$), 33.0 (CH$_{2,alkyl}$), 30.5 (CH$_{2,alkyl}$), 30.4 (CH$_{2,alkyl}$), 30.2 (CH$_{2,alkyl}$), 28.0 (CH$_{2,alkyl}$), 23.8 (CH$_{2,alkyl}$), 14.5 (CH$_2$)$_7$*C*H$_3$) 13.3 (C5$_{thy}$-*C*H$_3$) ppm; **ESI-MS**: calcd for $C_{27}H_{46}N_4O_{10}S$: *m/z* = 641.2827 $[M+Na]^+$; found: *m/z* = 641.2827

$[M+Na]^+$; **IR** (ATR-IR): $\tilde{\nu}$ = 3319, 2925, 2855, 1696, 1628, 1551, 1466, 1339, 1269, 1225, 1188, 1131, 1049, 1028, 975, 768 cm^{-1}; **EA** $C_{27}H_{46}N_4O_{10}$ (M = 618.7399 g/mol): calcd: C 52.41, H 7.49, N 9.05, S 5.18; found: C 50.86, H 7.95, N 8.72, S 4.83.

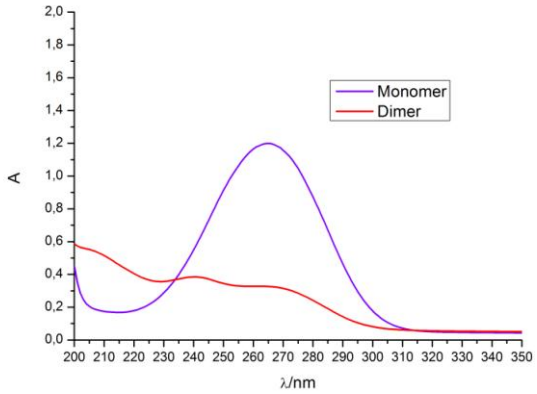
N^3-[2-(α-D-Mannopyranosyloxy)-ethyl]-5'-octyl-thioureido-2',5'-dideoxythymidine dimer (12)

In a quarz glass cuvette glycothymidine **11** (26 mg, 0.042 mmol) was dissolved in 1.5 mL of H_2O and 1.5 mL of acetone was added as triplet sensitizer. The solution was



+ *anti*-Isomere

degased by treatment with nitrogen for 30 min and subsequently irradiated for 230 min with a 150 W medium pressure mercury lamp and a cut off filter for wave lengths of $\lambda \geq 295$ nm. The solvent was evaporated under reduced pressure. The reaction mixture was purified using gel permeation chromatography (Sephadex, LH-20, H_2O) giving 19.6 mg (0.016 mmol, 75 %) of the product mixture as a colourless solid. **MALDI-ToF MS**: calcd. for $C_{54}H_{92}N_8O_{20}S_2$: *m/z* 1259.58 $[M+Na]^+$; found: *m/z* 1259.62 $[M+Na]^+$



Scheme 8: UV spectra of glycothymidine 11 (blue) and dimer 12 (red).

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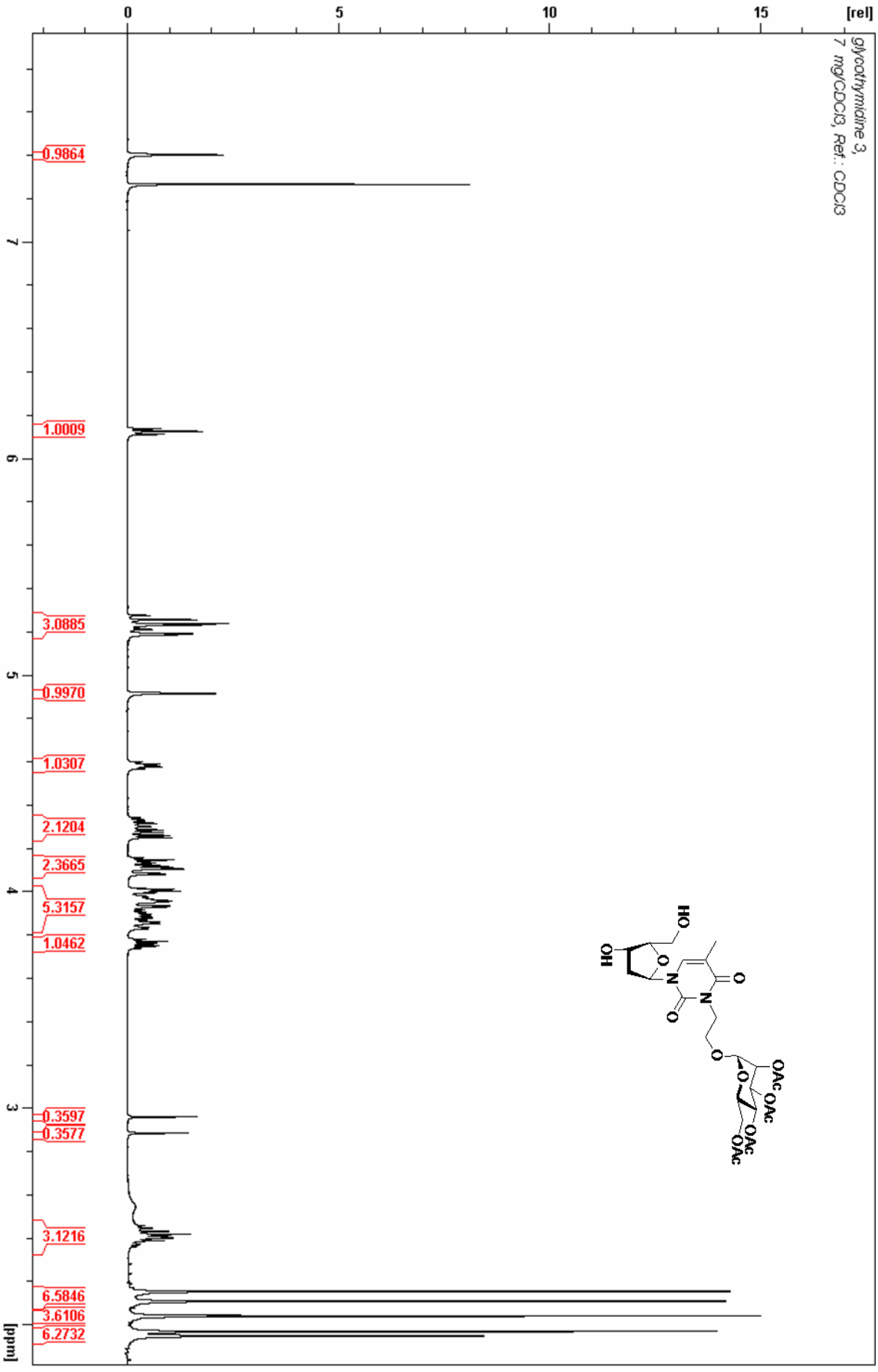
[3] R. Lucas, R. Zerrouki, R. Granet, P. Krausz, Y. Champavier, *Tetrahedron* 2008, **64**, 5467-5471; W. Bannwarth, *Helv. Chim. Acta* 1988, **71**, 1517-1527.

NMR spectra following: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6.5846
3.6106
6.2732
7
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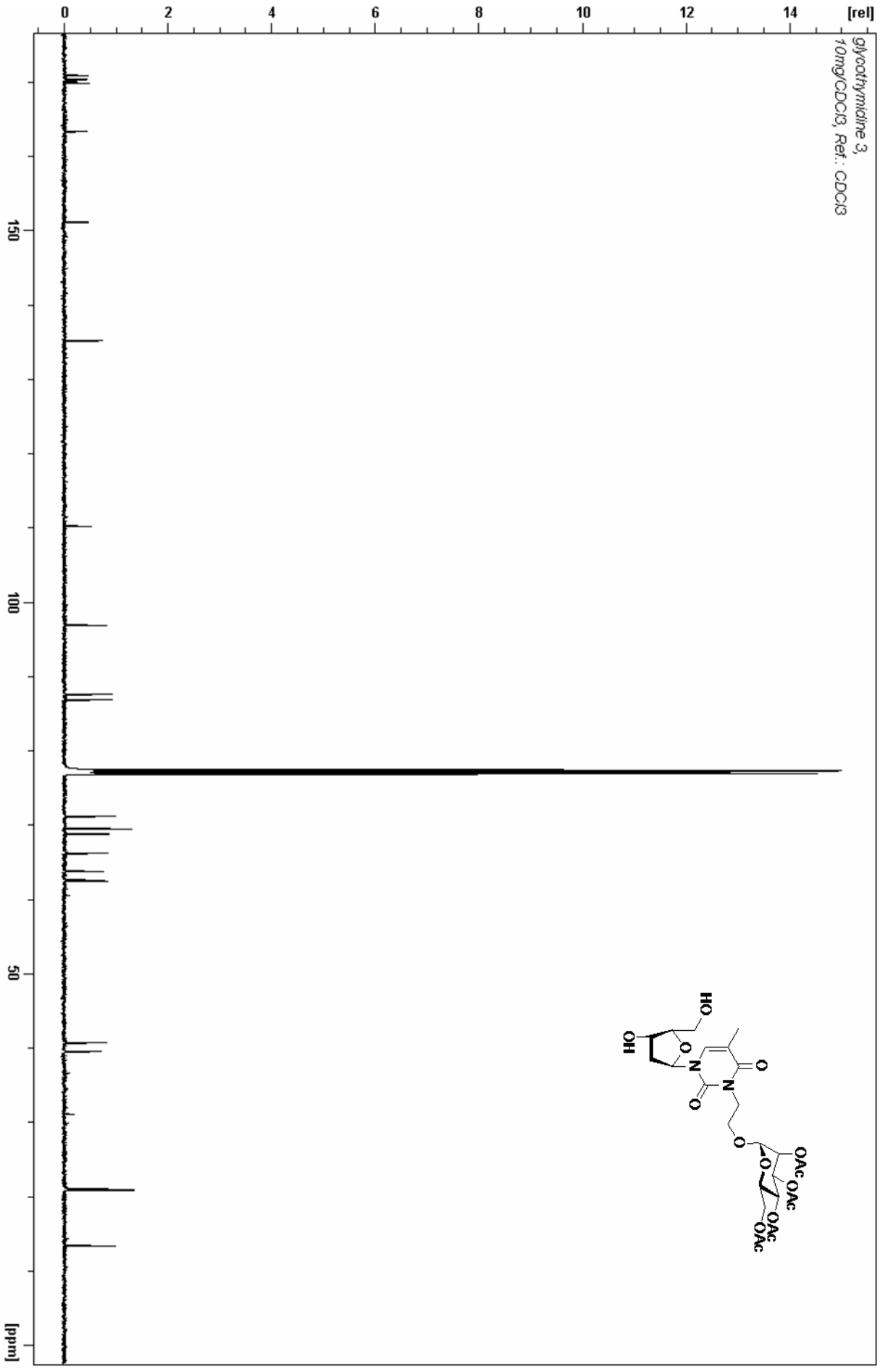
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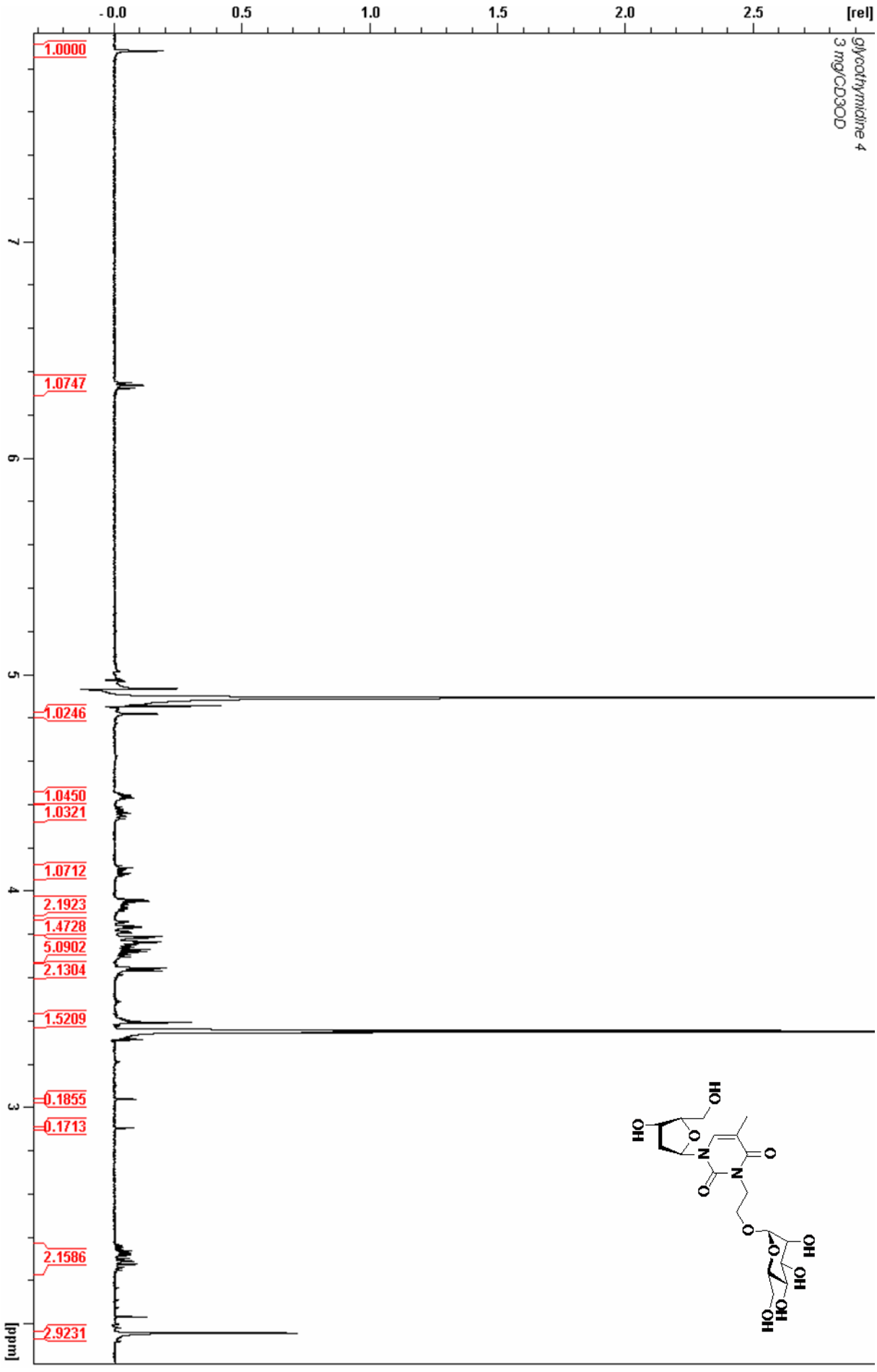
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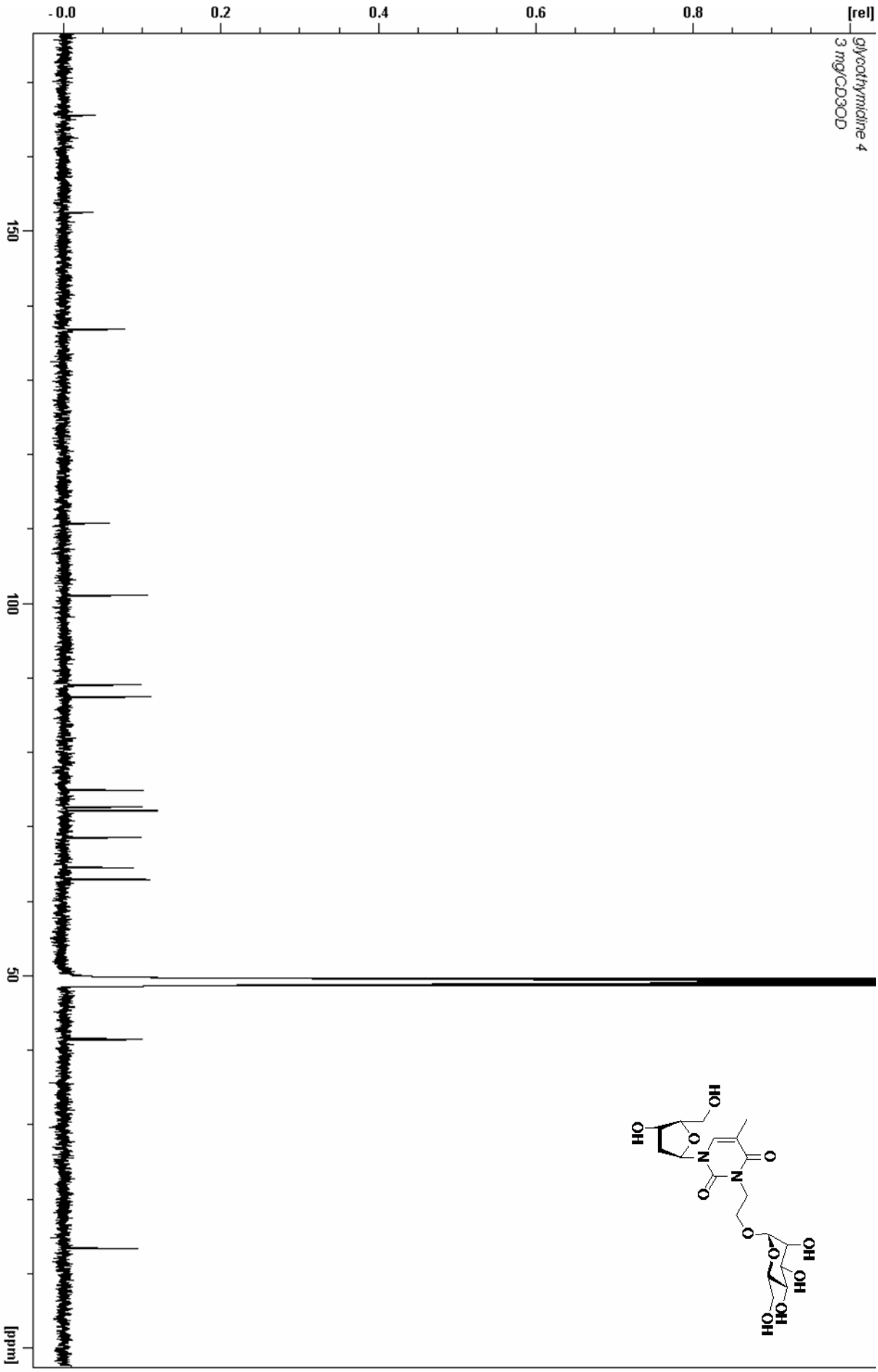
OH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0.4
0.6
0.8
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OH
O
N
O
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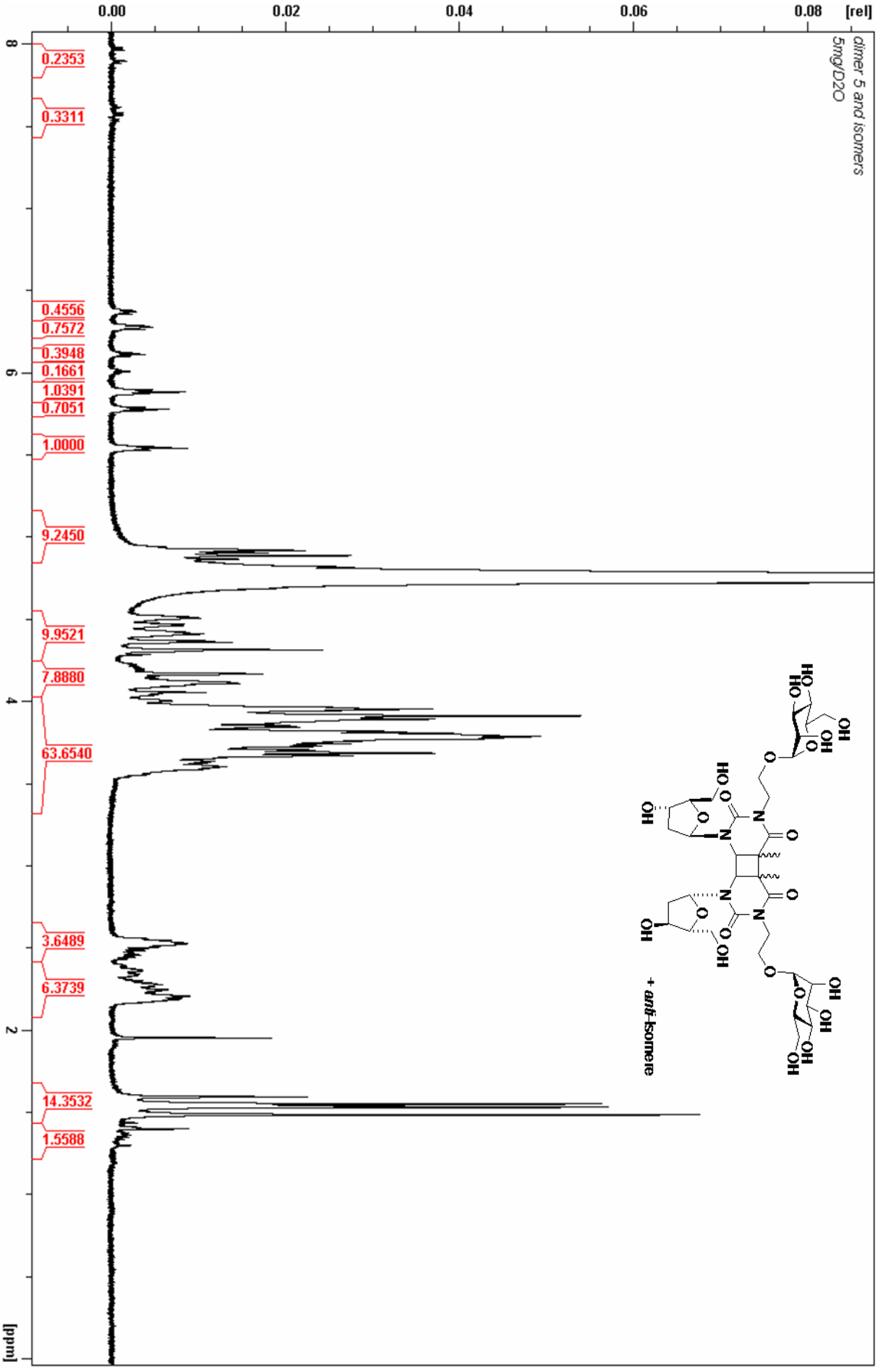
O
O
OH
HO
HO
HO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0.02
0.04
0.06
0.08
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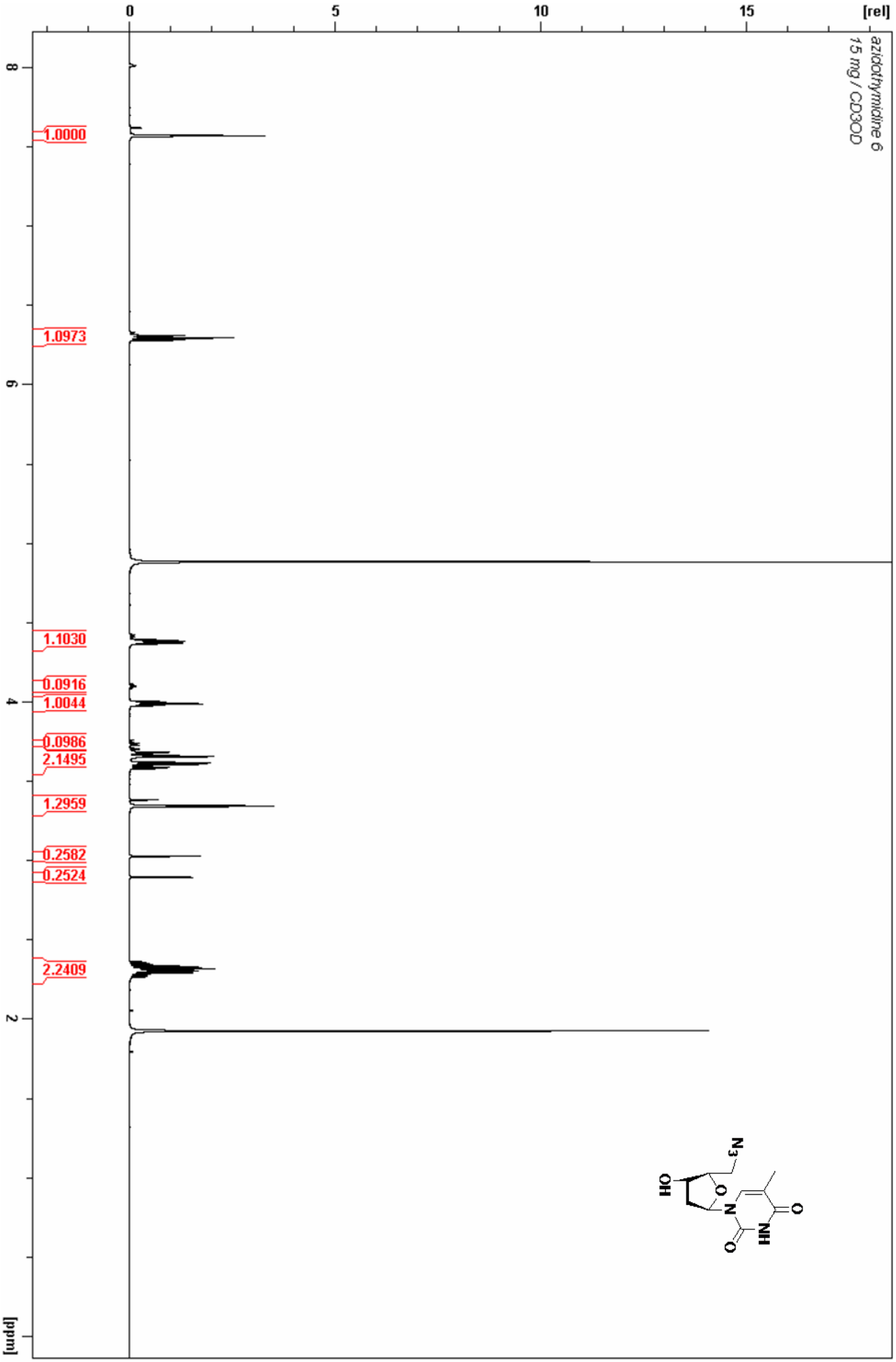
0.4556
0.7572
0.3948
0.1661
1.0391
0.7051
1.0000
9.2450
9.9521
7.8880
63.6540
3.6489
6.3739
14.3532
1.5588
8
6
4
2
[ppm]
+ anti-isomere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[ppm]
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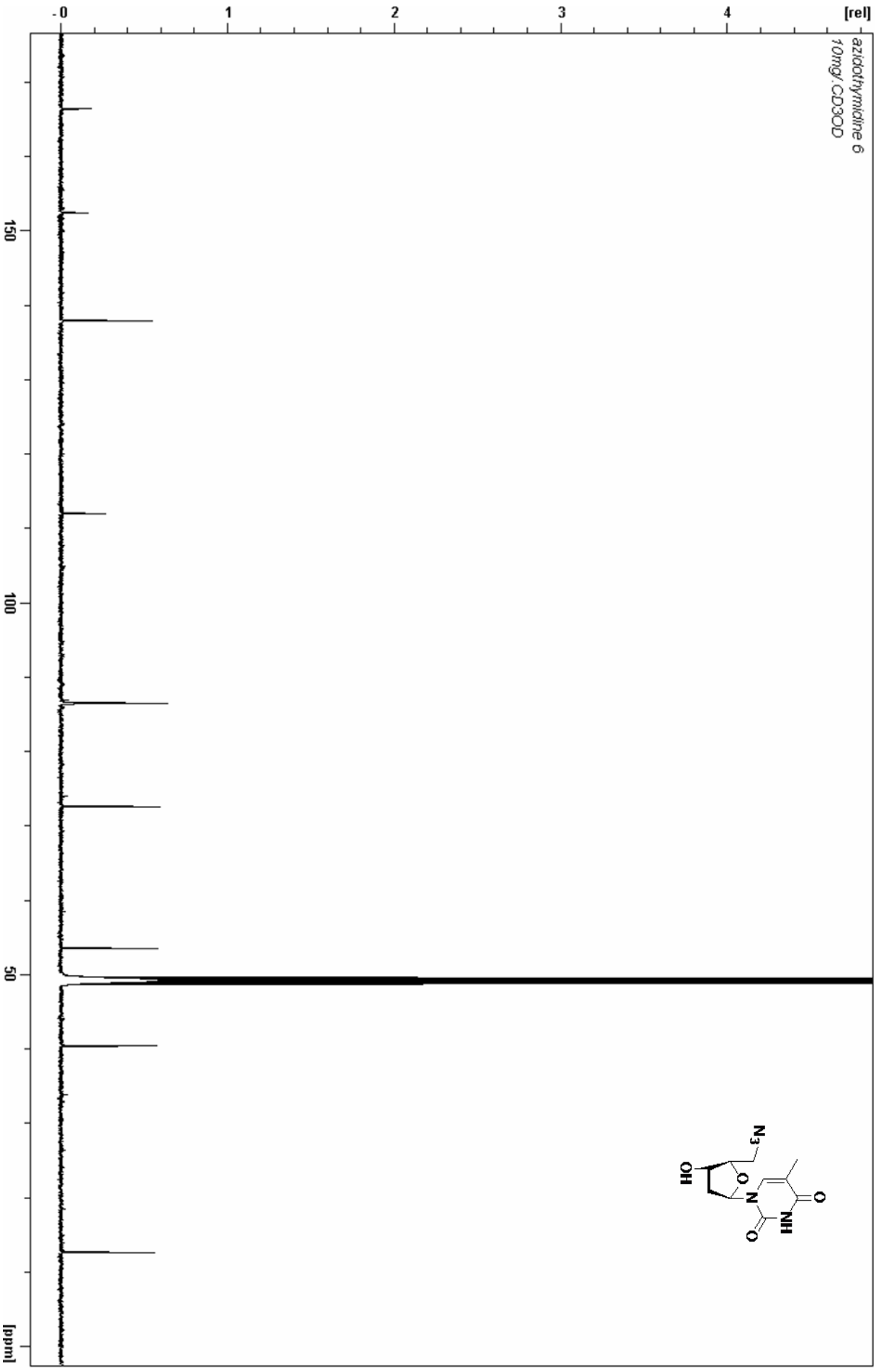
N
N3
O
HN
O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1
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150
100
50
[ppm]
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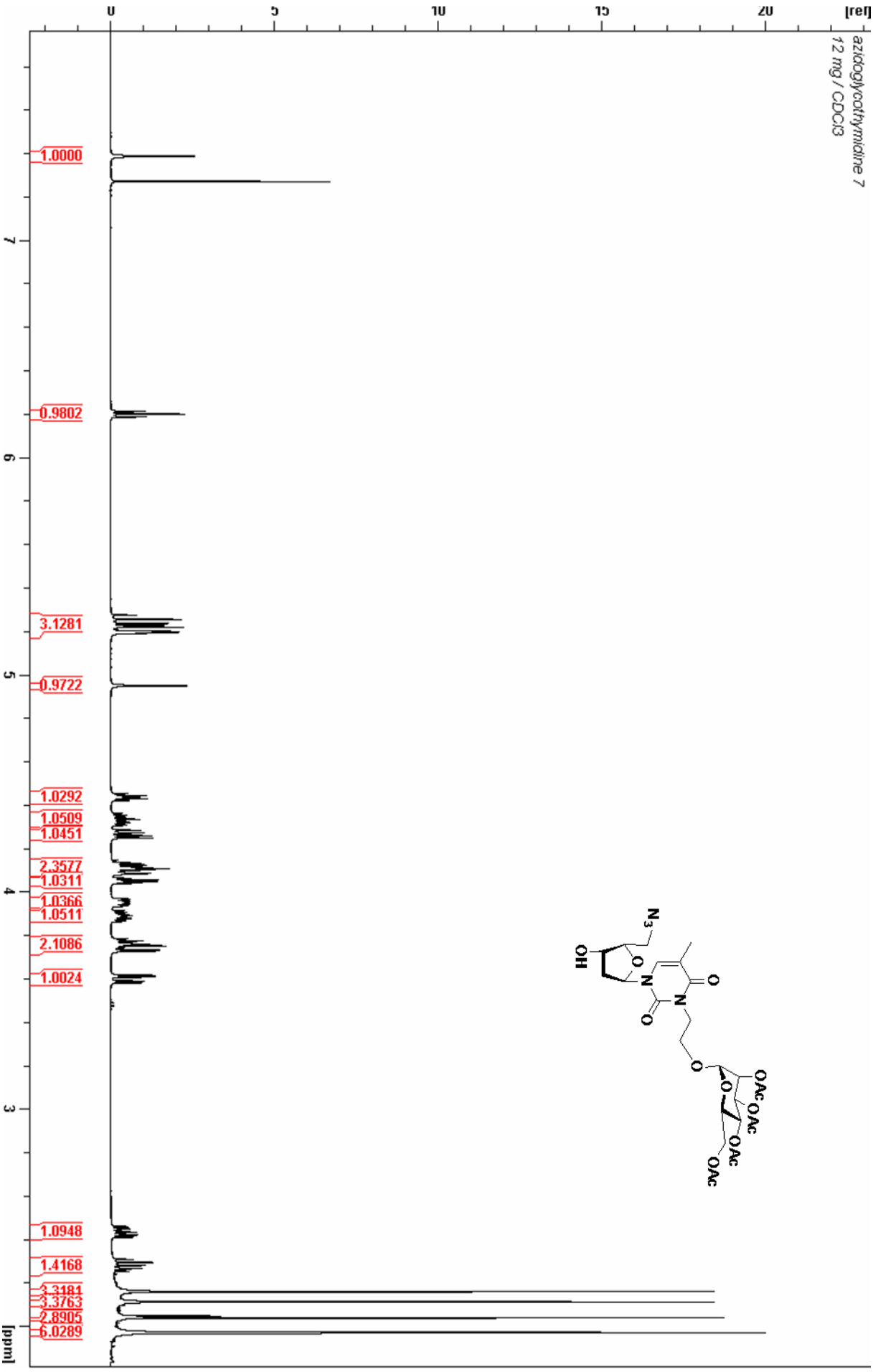
N
O
NH
N3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12 mg / CDCl3
[ref]
[ppm]
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0.9722
1.0292
1.0509
1.0451
2.3577
1.0311
1.0366
1.0511
2.1086
1.0024
1.0948
1.4168
3.3181
3.3763
2.8905
6.0289
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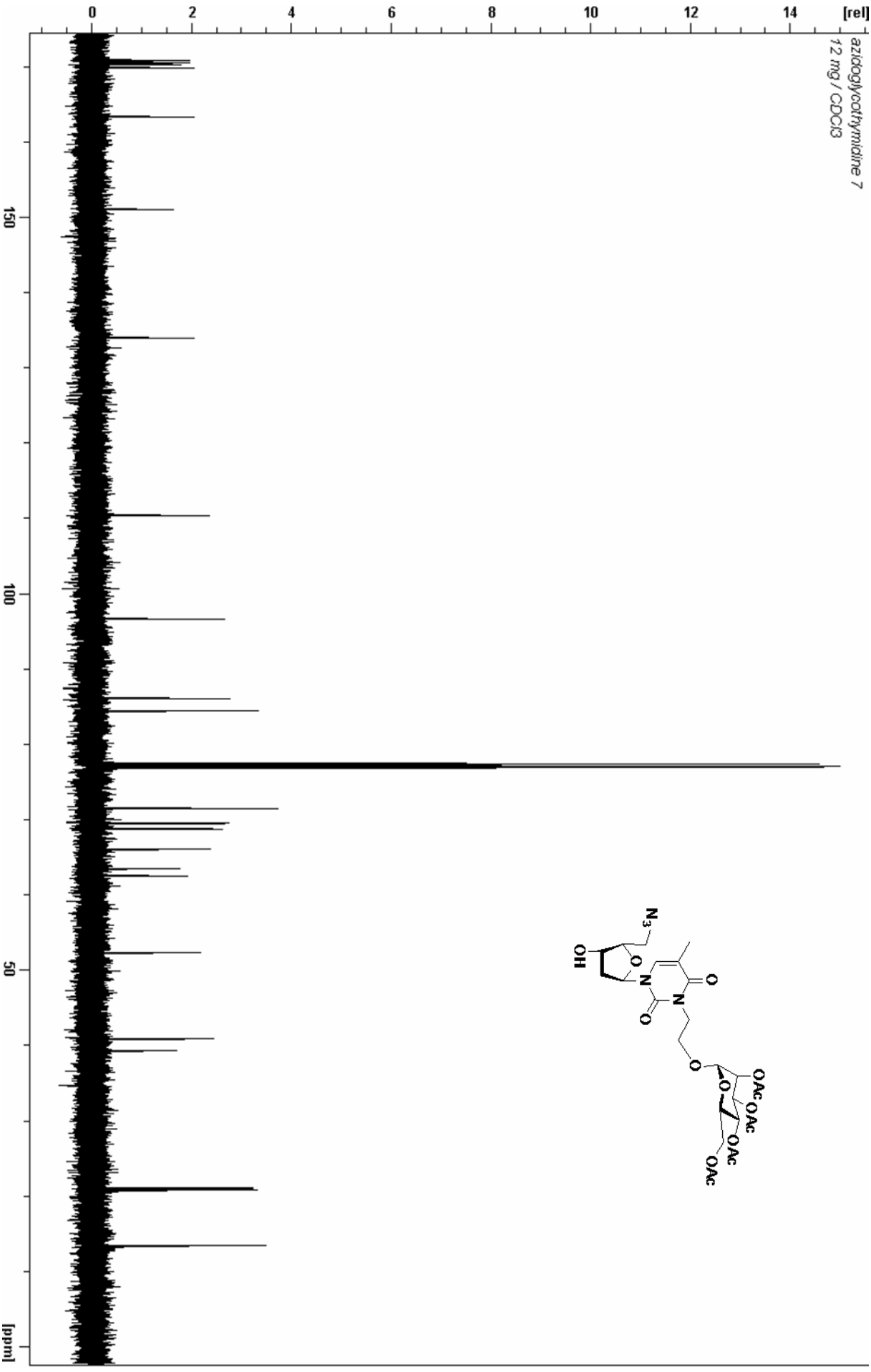
OH
O
N
OAc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12 mg / CDCl3
[rel]
[ppm]
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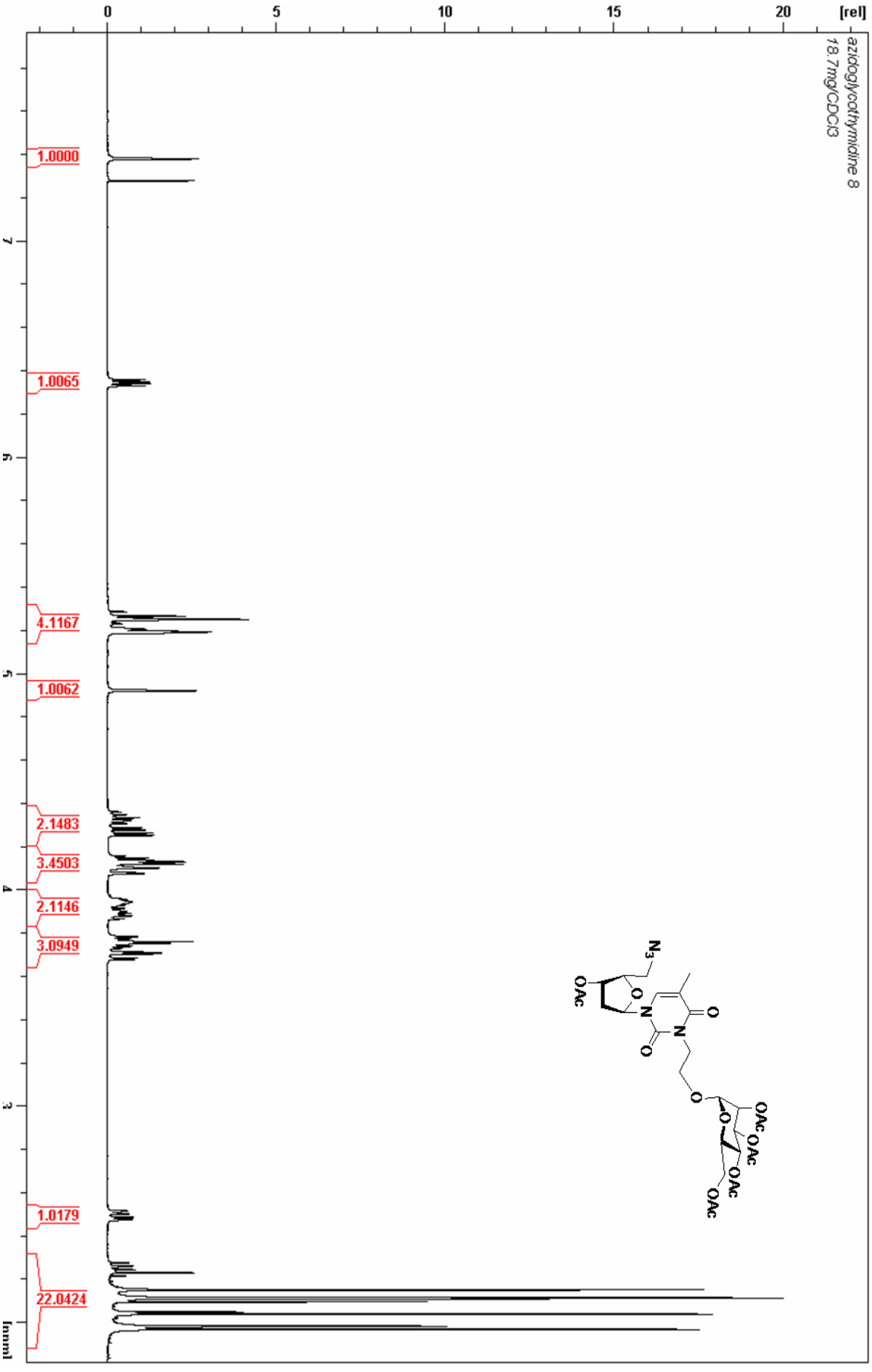
N3
OAc
OAc
OAc
OAc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5
10
15
20
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2.1483
3.4503
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[ppm]
N3
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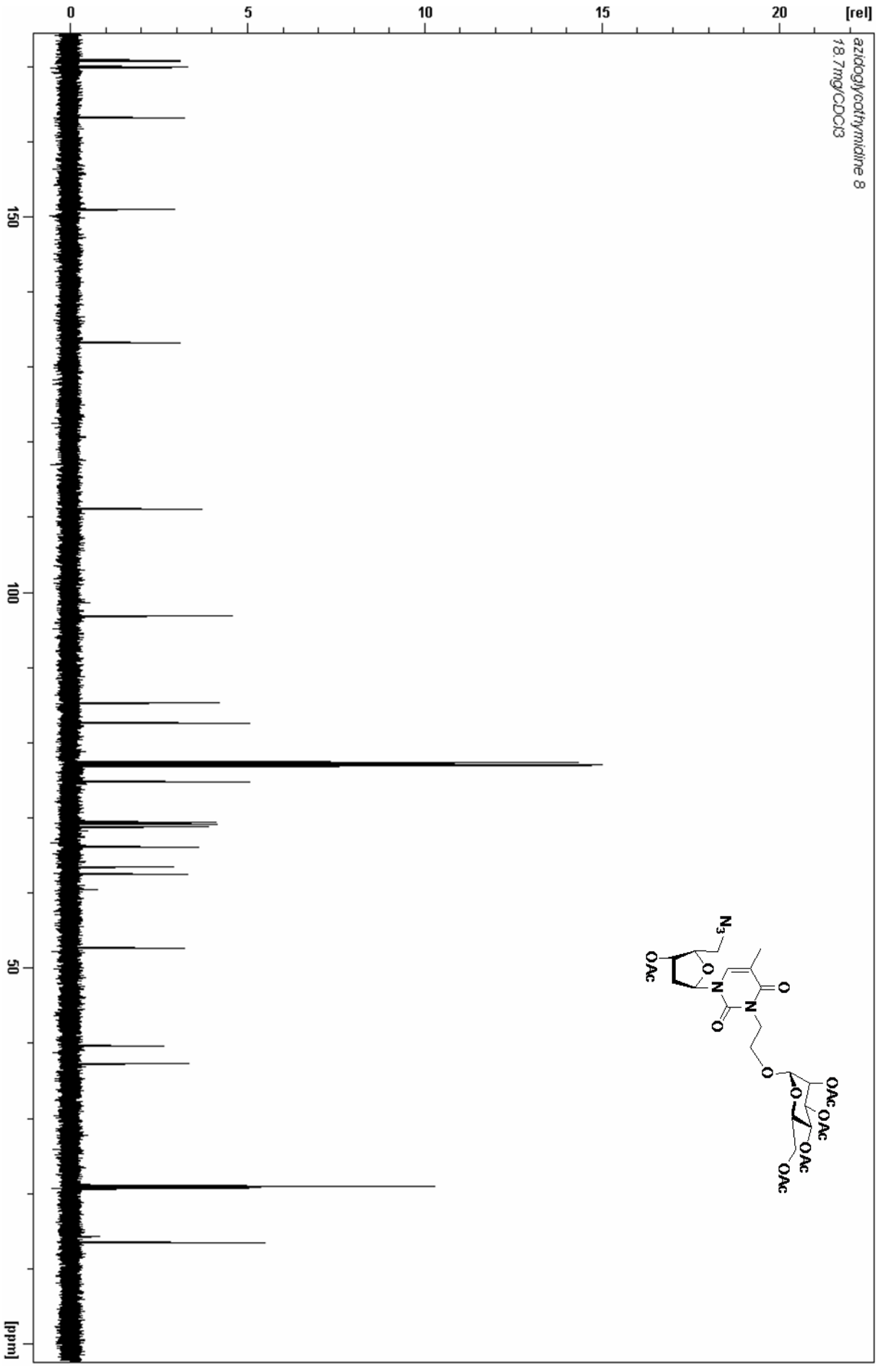
O
N
OAc
OAc
OAc
OAc


0
5
10
15
20
[rel]
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50
[ppm]
N3
OAc
O
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O
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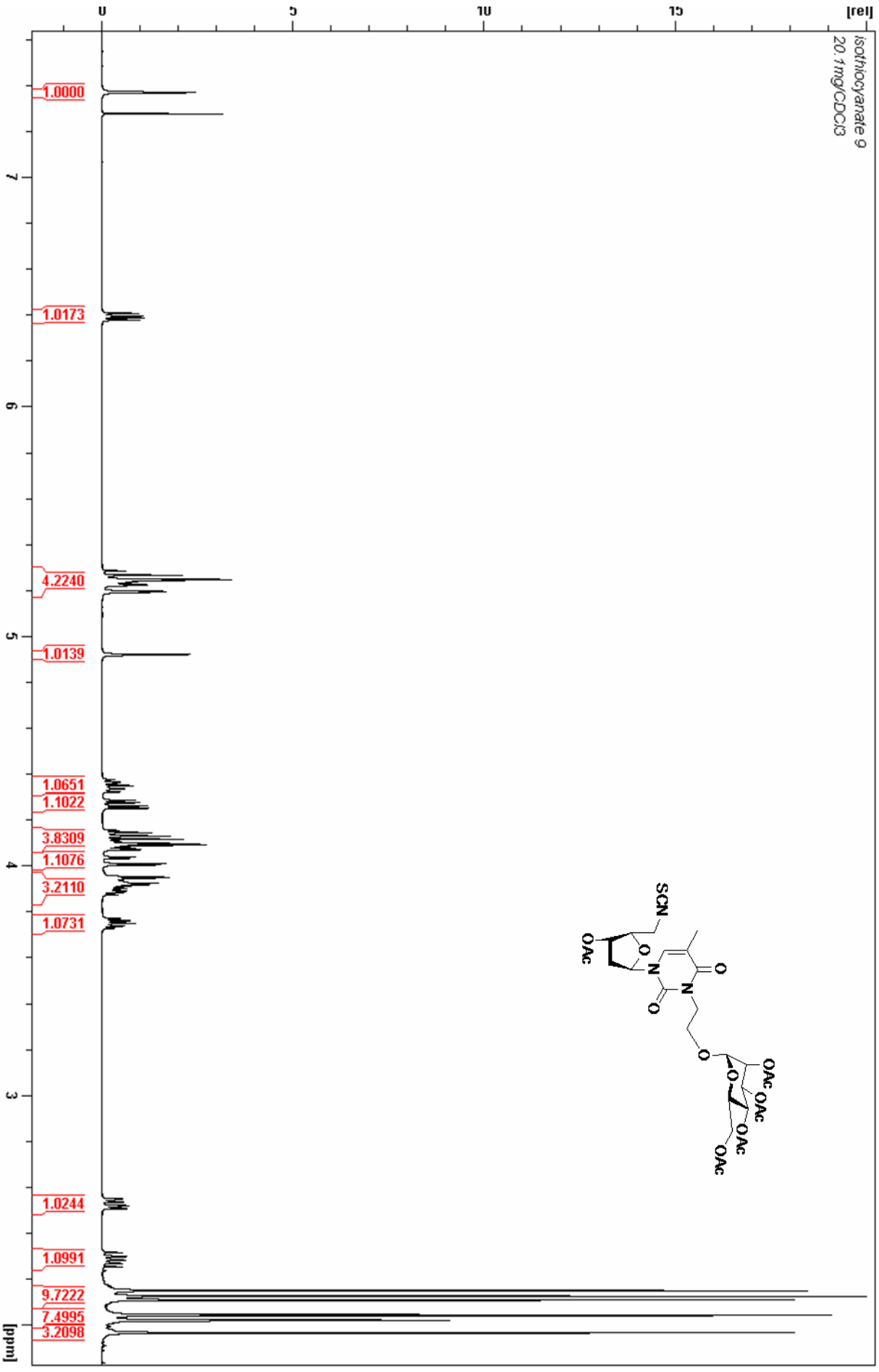
O
OAc
OAc
OAc
OAc
OAc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5
10
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[ppm]
7
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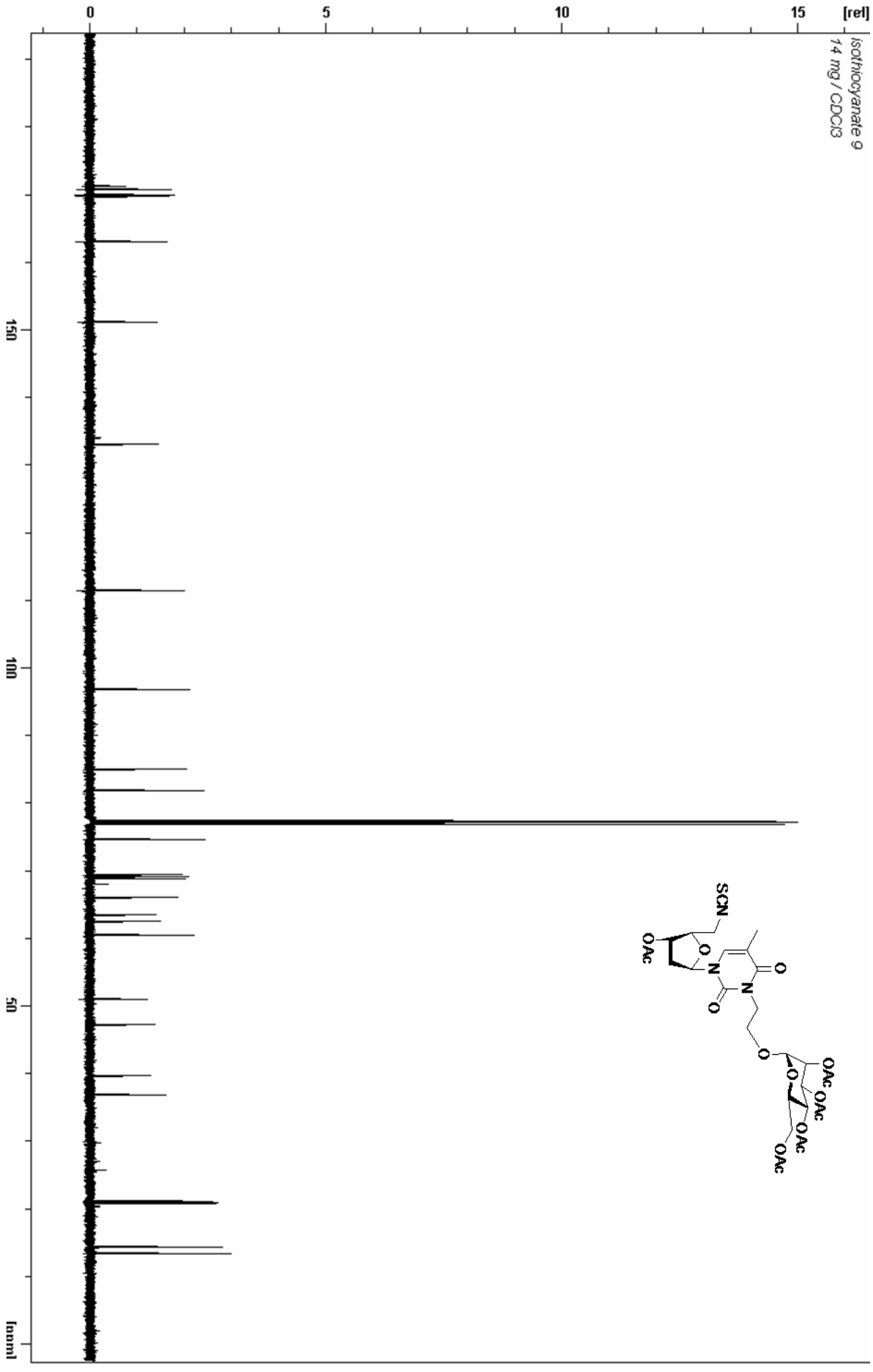
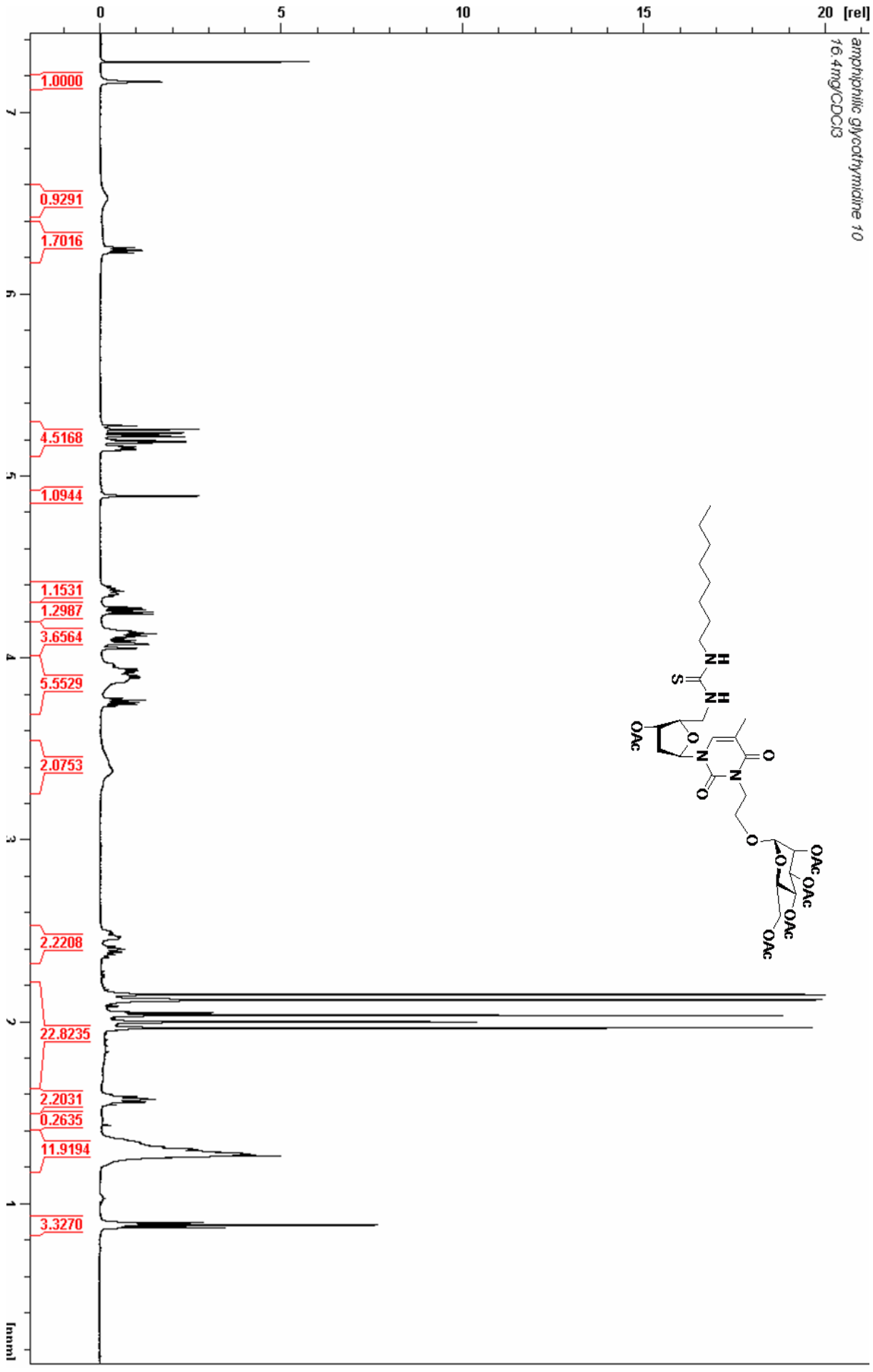
1.0139
1.0651
1.1022
3.8309
1.1076
3.2110
1.0731
1.0244
1.0991
9.7222
7.4995
3.2098
SCN
OAc
O
N
O
OAc
OAc
OAc
OAc


0
5
10
15
[rel]
isothiocyanate 9
14 mg / CDCl3
150
100
50
[ppm]
SCN
OAc
O
N
O
N
O
O
OAc
OAc
OAc
OAc
O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16.4mg/CDCl3
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1.0944
1.1531
1.2987
3.6564
5.5529
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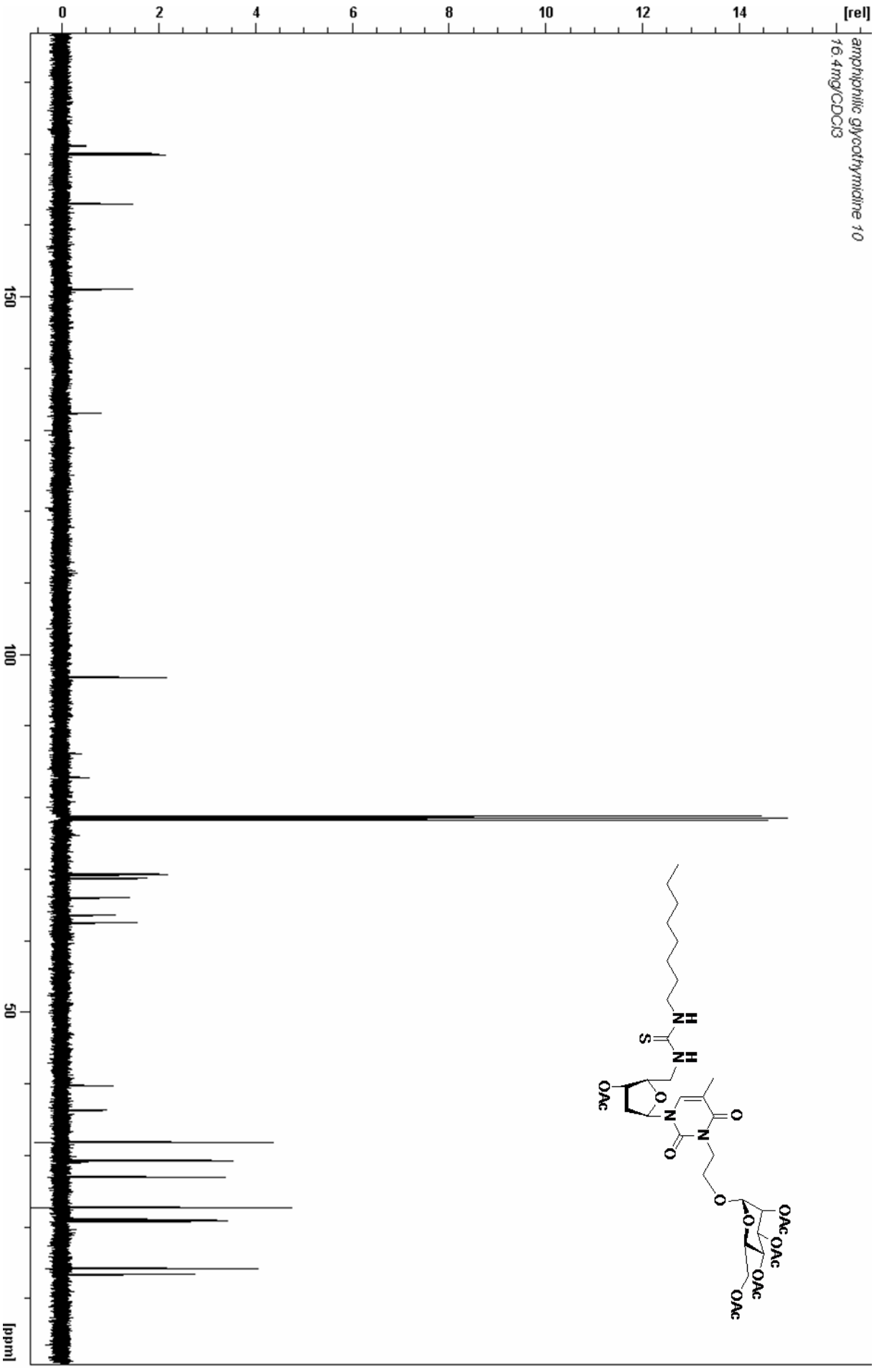
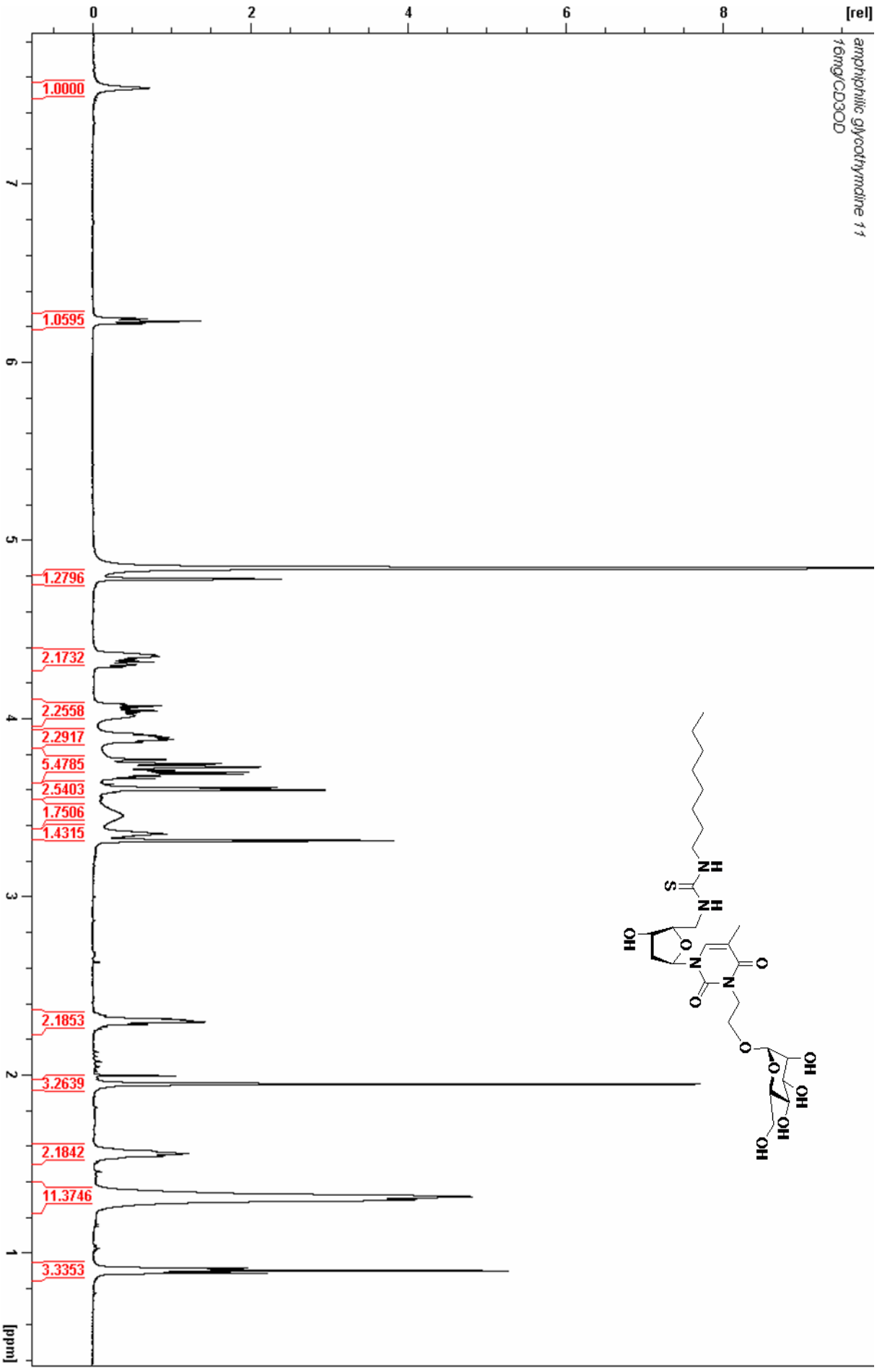
22.8235
2.2031
0.2635
11.9194
3.3270
OAc
S
N
H
O


0
2
4
6
8
10
12
14
[rel]
amphiphilic glycothymidine 10
16.4mg/CDCl3
150
100
50
[ppm]
NH
S
NH
OAc
O
N
O
N
O
O
OAc
OAc
OAc
OAc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16mg/CD3OD
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[ppm]
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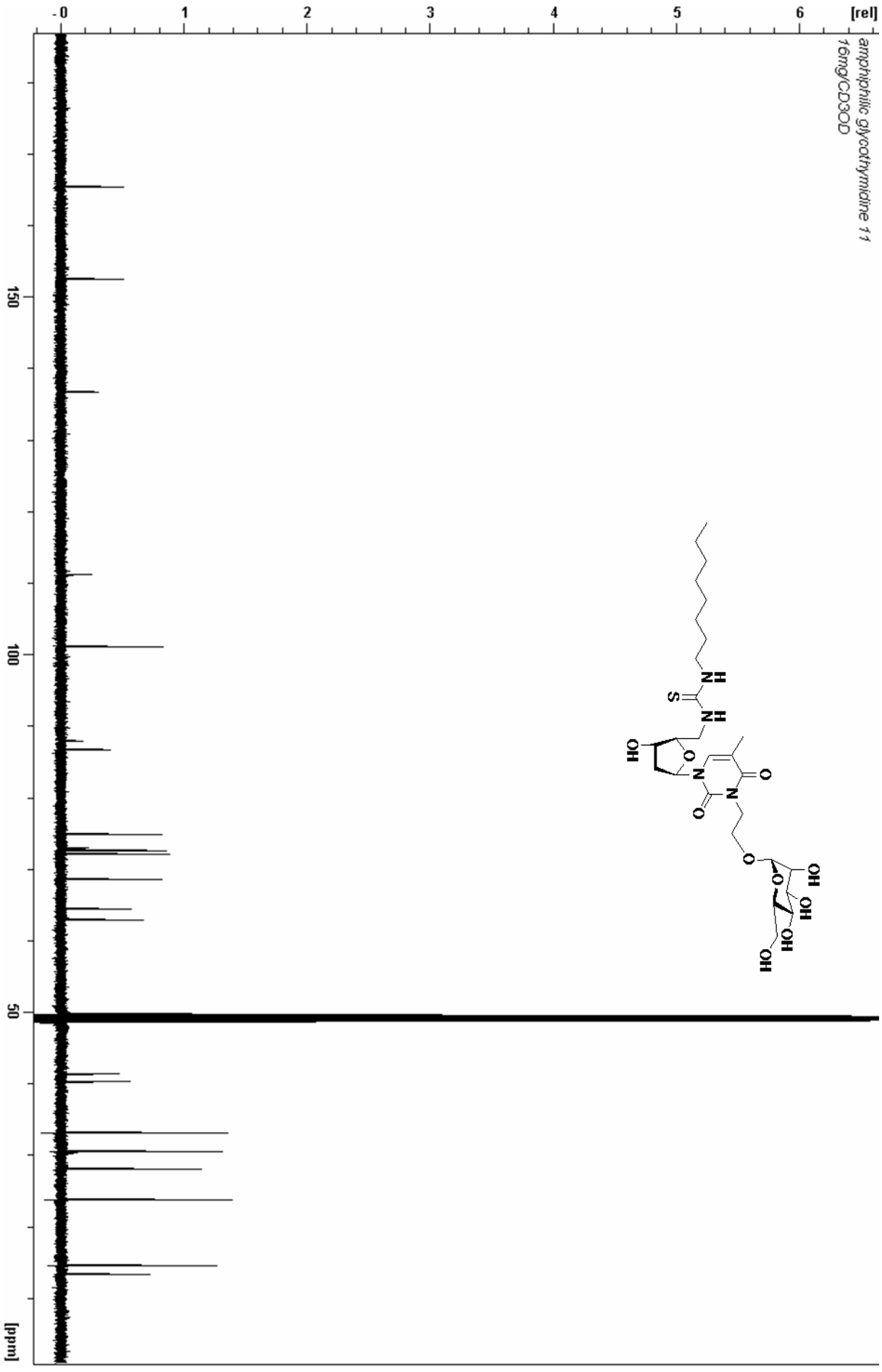
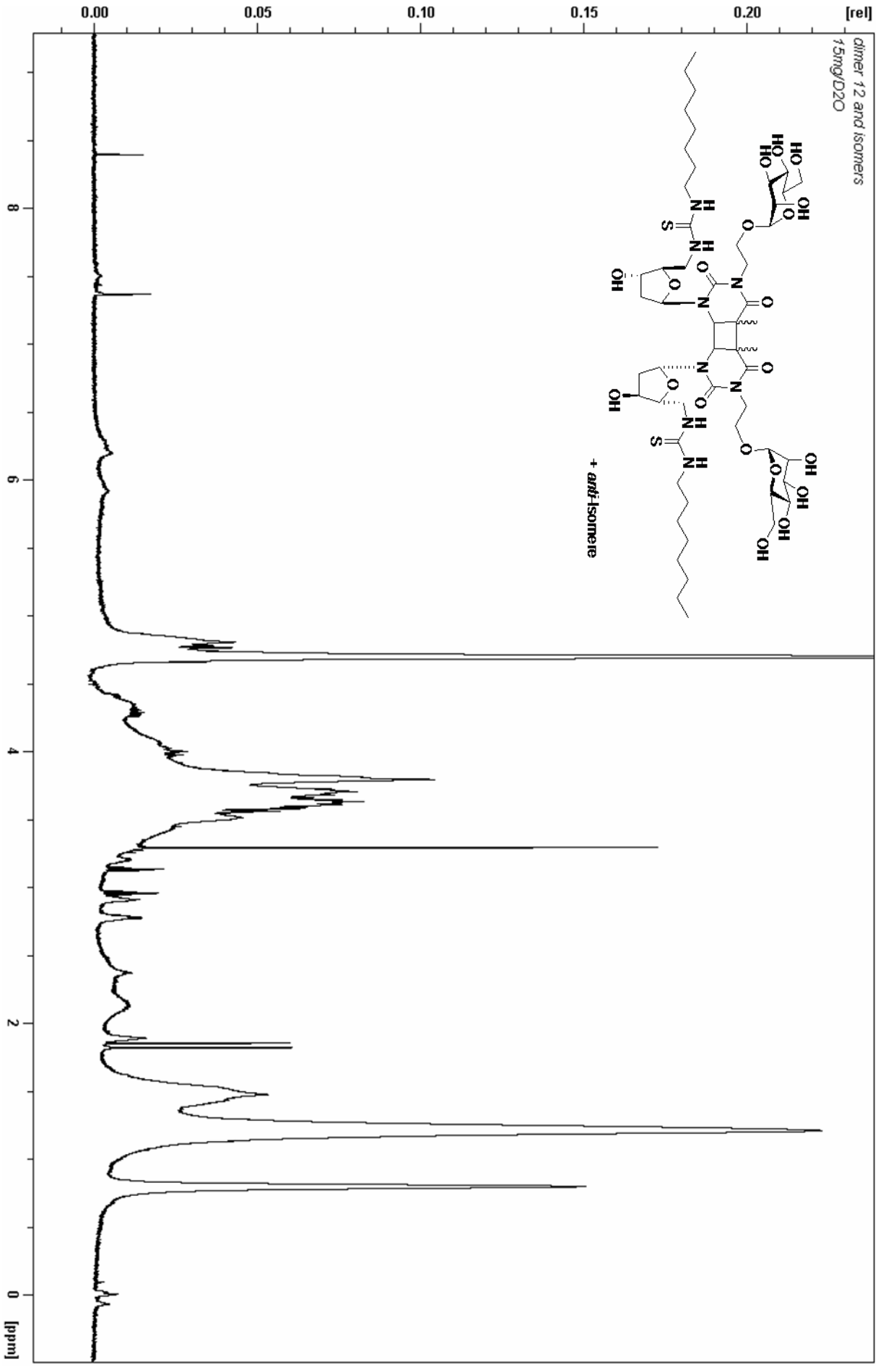
3.2639
2.1842
11.3746
3.3353


- 0
1
2
3
4
5
6
[rel]
150
100
50
[ppm]
amphiphilic glycothymidine 11
16mg/CD3OD
HO
O
N
H
S
O
OH


0.00
0.05
0.10
0.15
0.20
[rel]
dimer 12 and isomers
15mg/D2O
+ anti-isomere
8
6
4
2
0
[ppm]

^{1}H PFG NMR diffusion measurements

These spectra were acquired using a Bruker Avance II 600 spectrometer incorporating a triple-resonance cryoprobe head with actively shielded z-gradient coil. For convection compensation, a double stimulated echo pulse sequence [G. H. Sørland, J. G. Seland, J. Krane,H. W. Anthonsen, *J. Magn. Reson*. 2000, **142**, 323-325] with sine shaped bipolar gradient pairs, longitudinal eddy current delay (5 ms), spoil gradients during the longitudinal delay, and solvent presaturation was used. The gradient amplitude was incremented linearly in each experiment from 2 G/cm up to 34 G/cm in 32 steps. The diffusion time was kept constant at 100 ms, while the gradient pulse duration varied between 4000 ms and 4500 ms for each gradient in the bipolar pair to achieve a signal attenuation of at least 90 %. For each spectra in a series, 256 scans were recorded with an acquisition time of 2.5 s and a relaxation delay of 1 s. All spectra were recorded at 298 K without sample rotation.

Evaluation of PFG NMR spectra

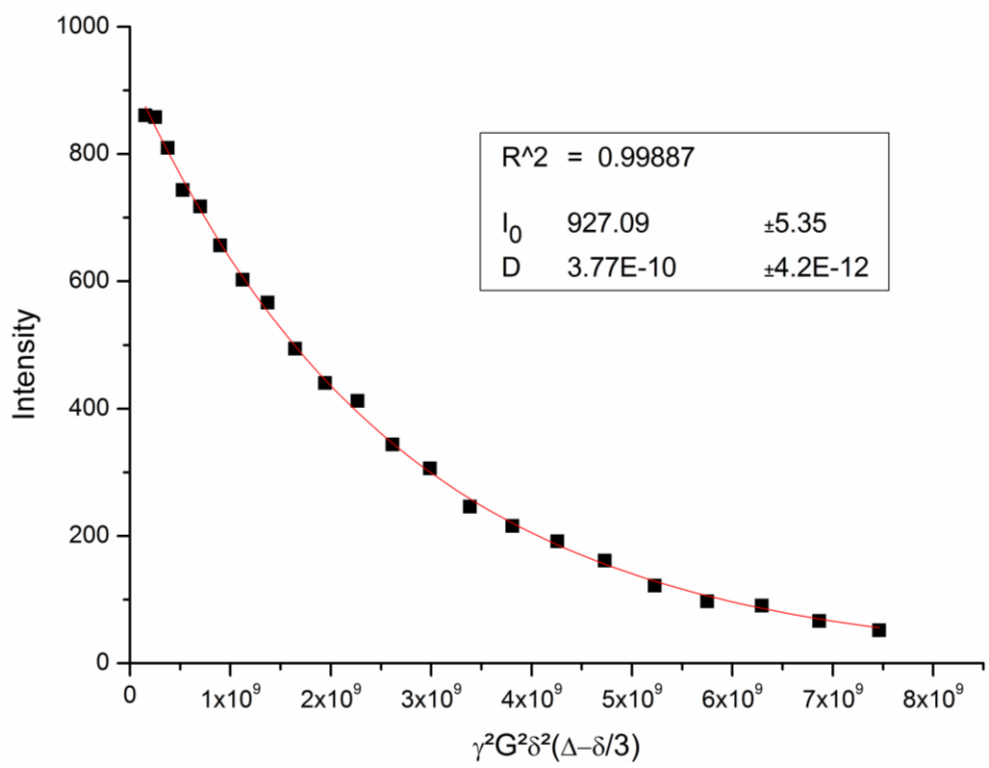


Fig. 1: Evaluation of PFG NMR measurement of pure **4**.

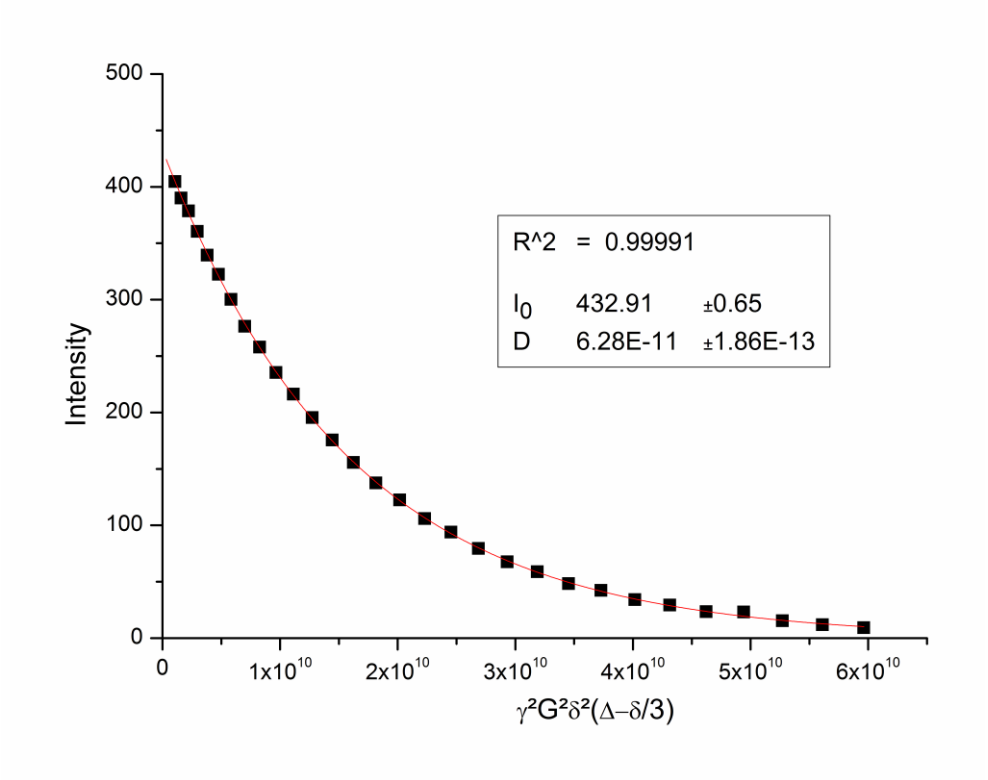


Fig. 2: Evaluation of PFG NMR measurement of pure SDS.

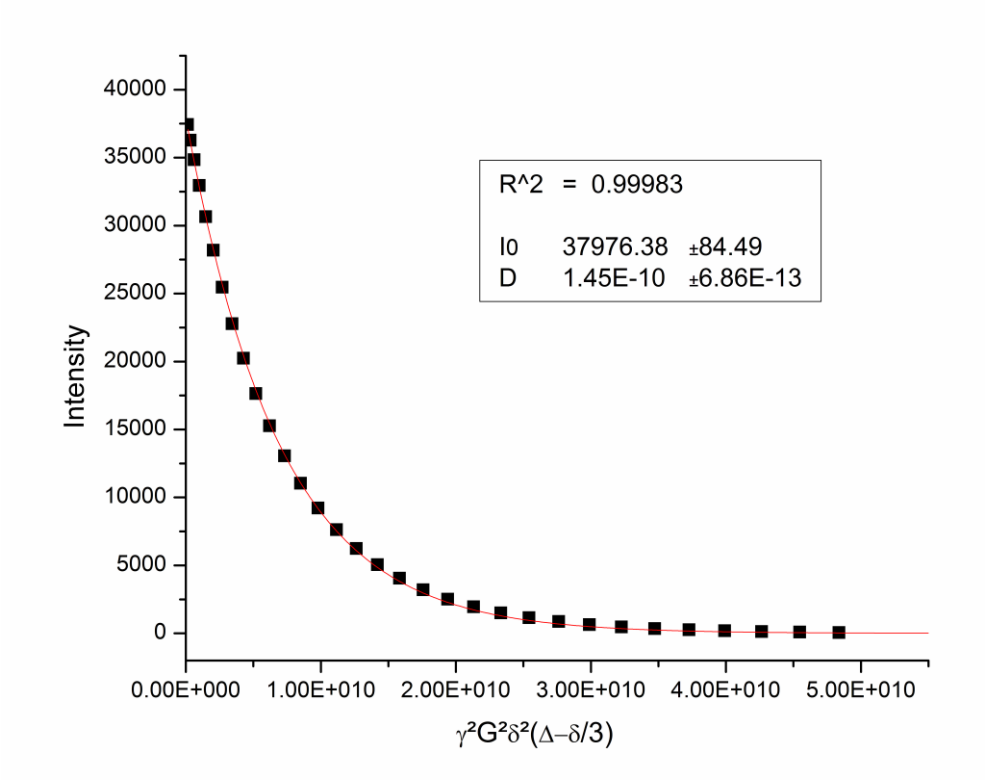


Fig. 3: Evaluation of PFG NMR measurement of pure **11** without irradiation.

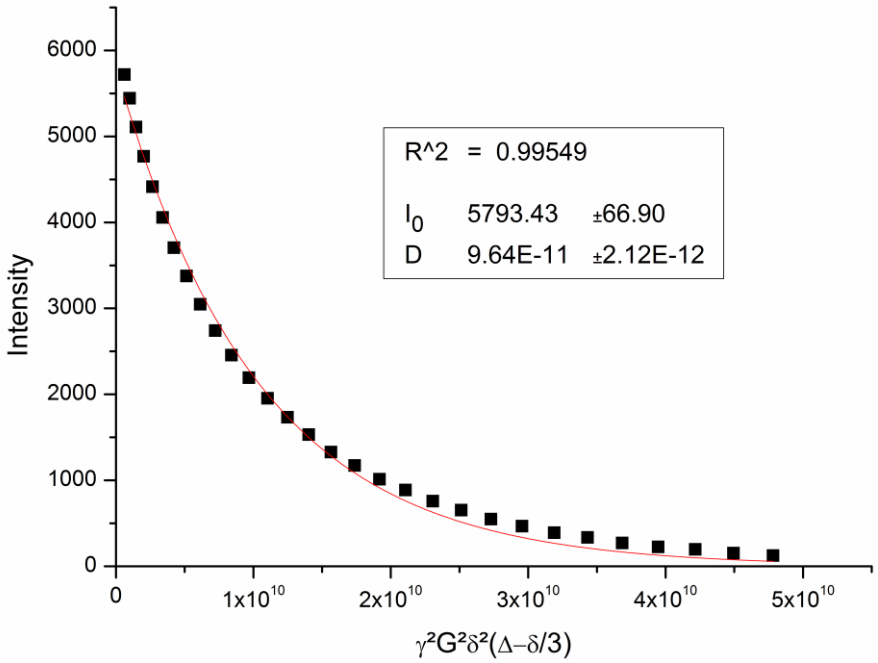


Fig. 4: Evaluation of PFG NMR measurement of pure **11** after 230 min of irradiation.

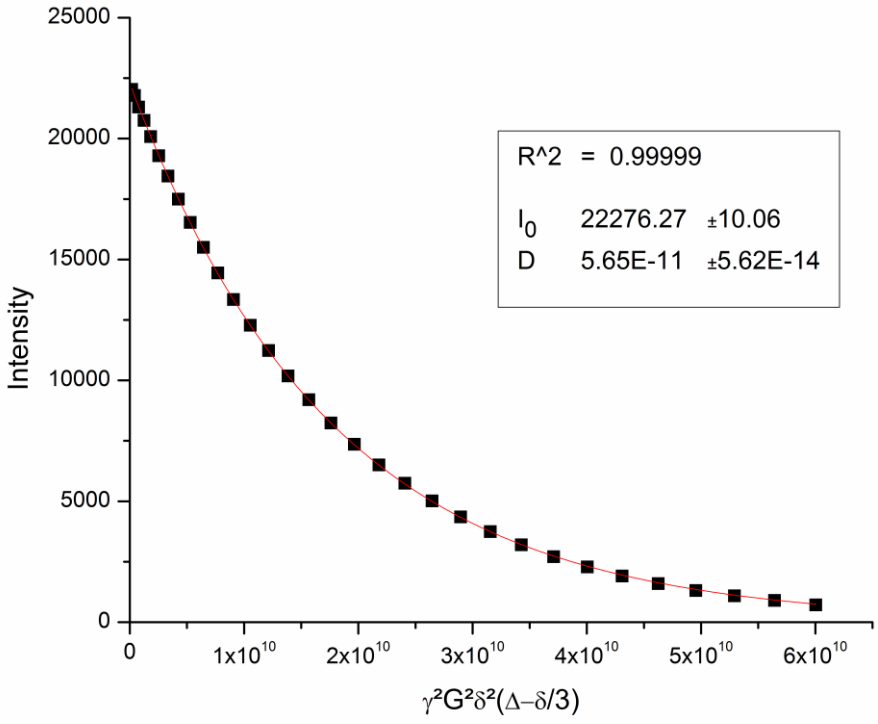


Fig. 5: Evaluation of PFG NMR measurement of **11**
(two molecules per SDS-micelle) before irradiation.

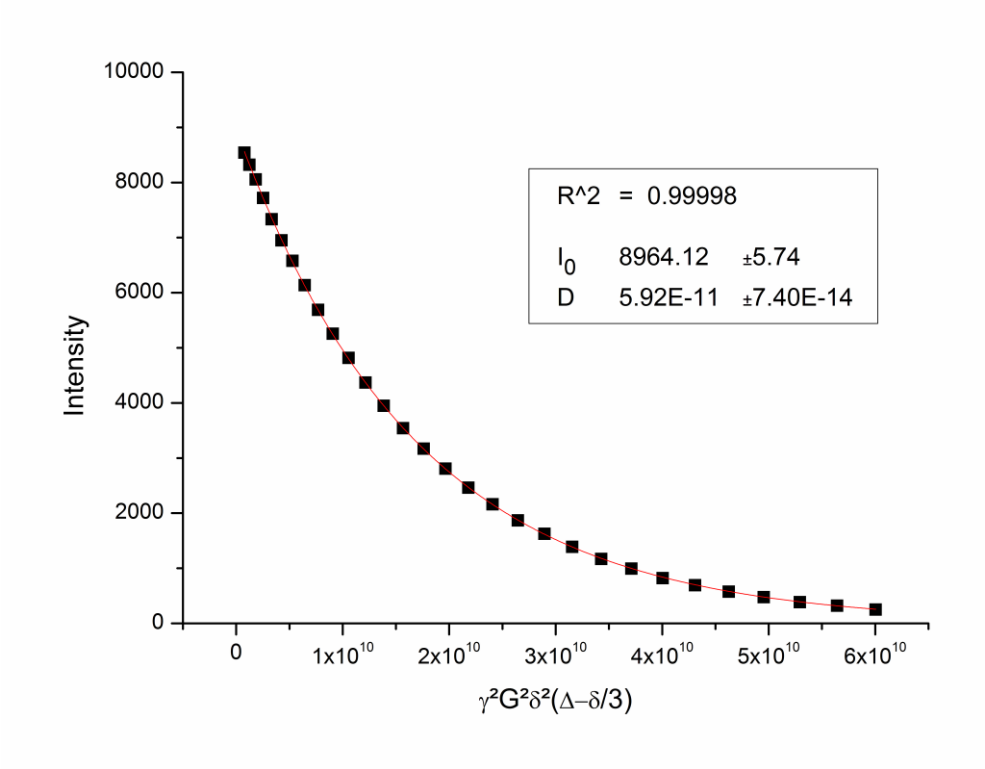


Fig. 6: Evaluation of PFG NMR measurement of SDS (two molecules **11** per SDS-micelle) before irradiation.

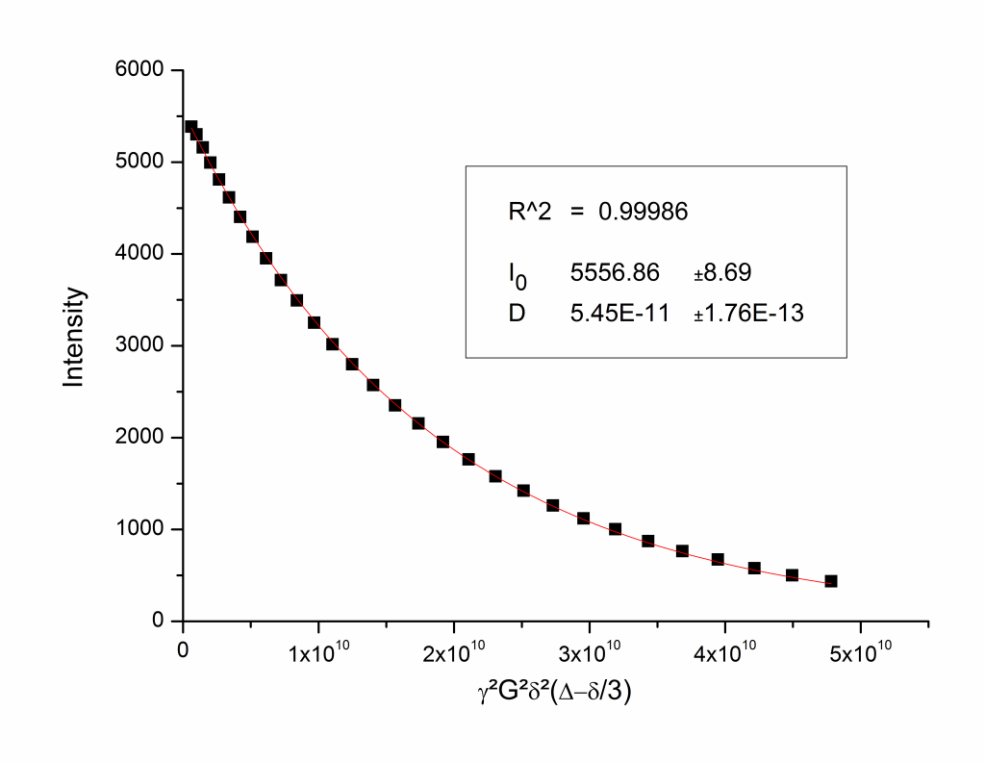


Fig. 7: Evaluation of PFG NMR measurement of **11** (two molecules per SDS-micelle) after 230 min of irradiation.

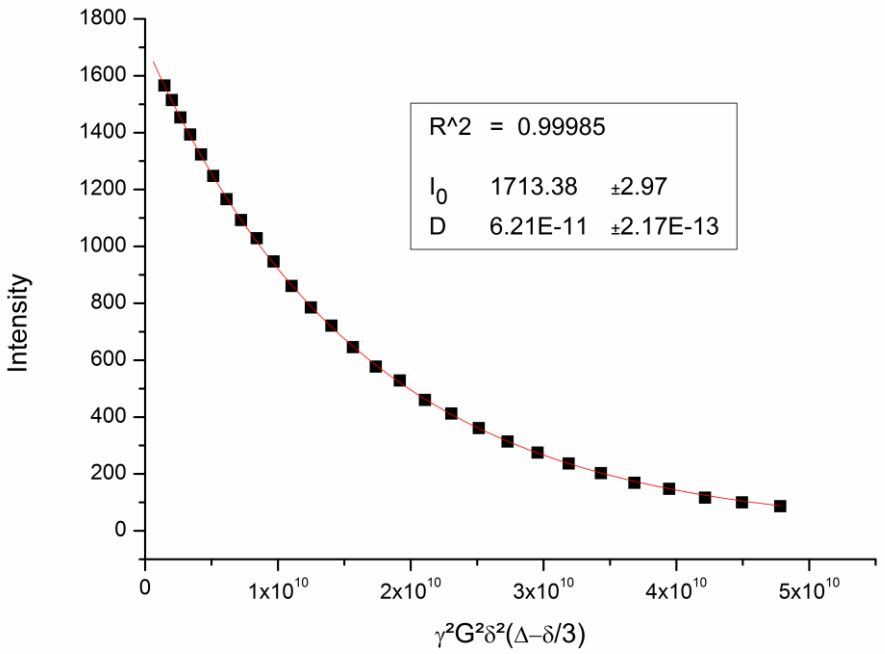


Fig. 8: Evaluation of PFG NMR measurement of SDS (two molecules **11** per SDS micelle) after 230 min irradiation.

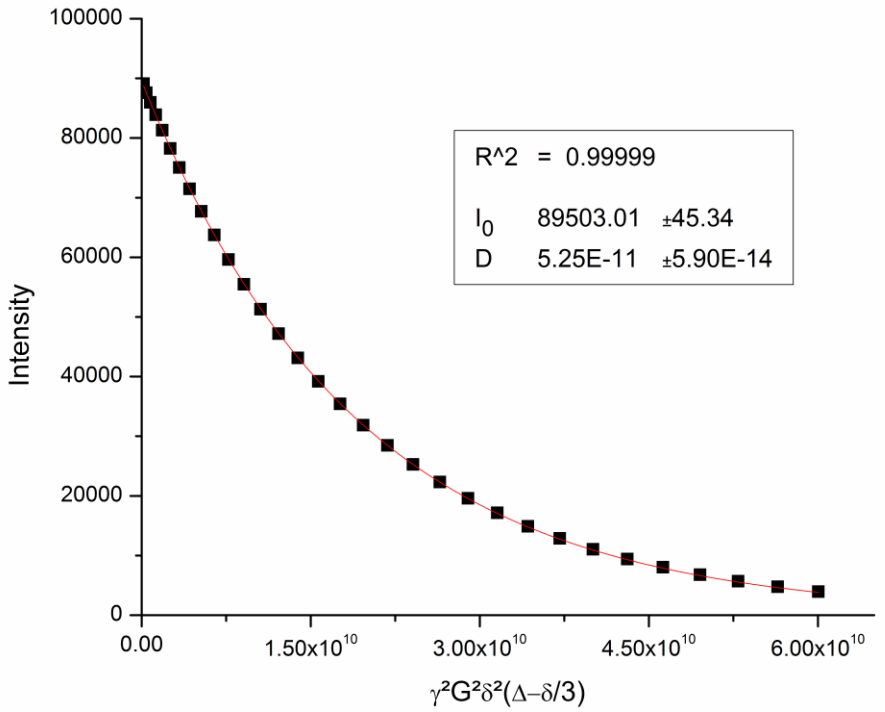


Fig. 9: Evaluation of PFG NMR measurement of **11** (eight molecules per SDS micelle) before irradiation.

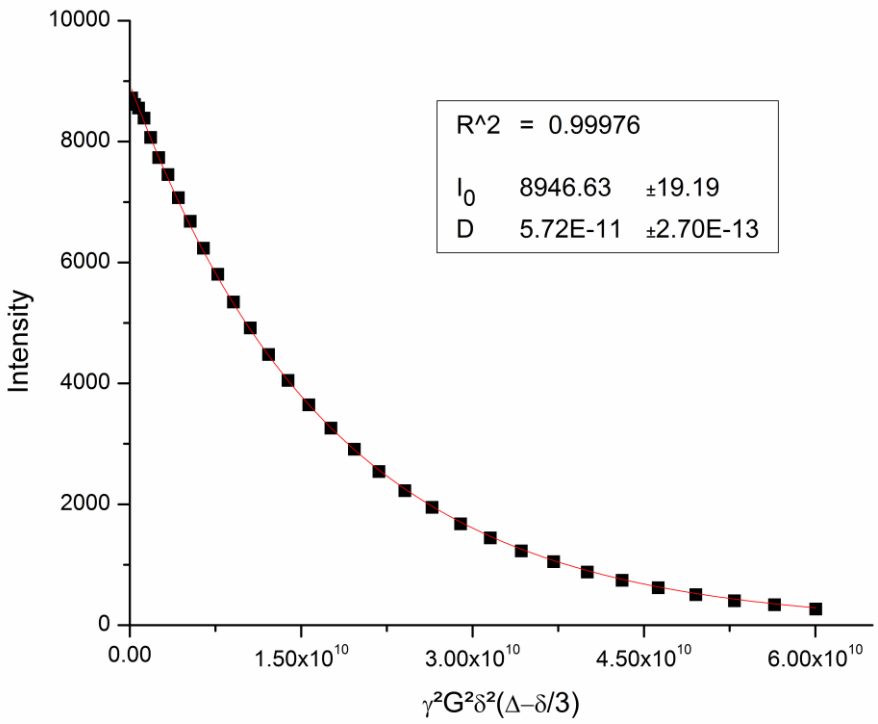


Fig. 10: Evaluation of PFG NMR measurement of SDS (eight molecules of **11** per SDS-micelle) before irradiation.

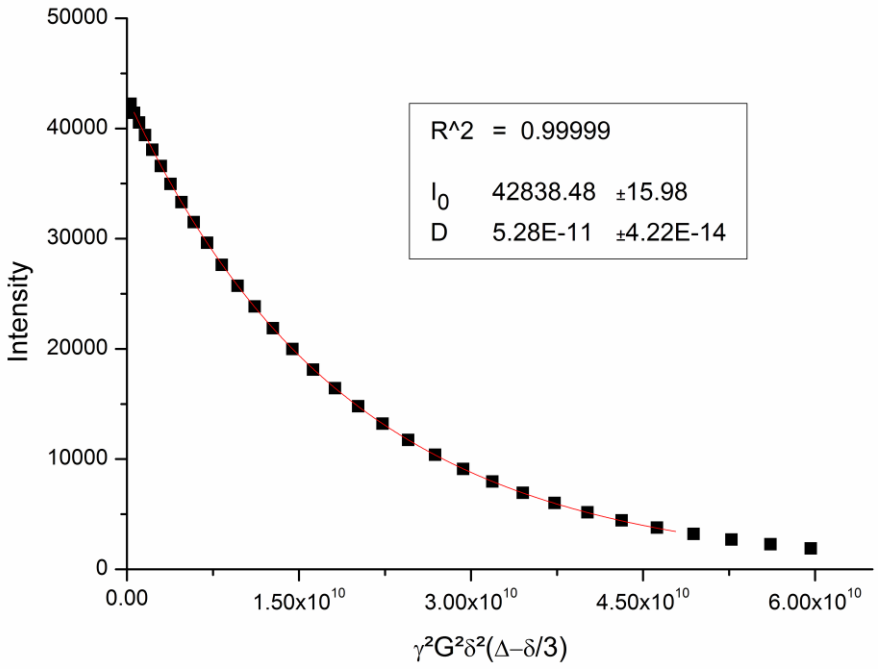


Fig. 11: Evaluation of PFG NMR measurement of **11** (eight molecules per SDS-micelle) after 230 min of irradiation.

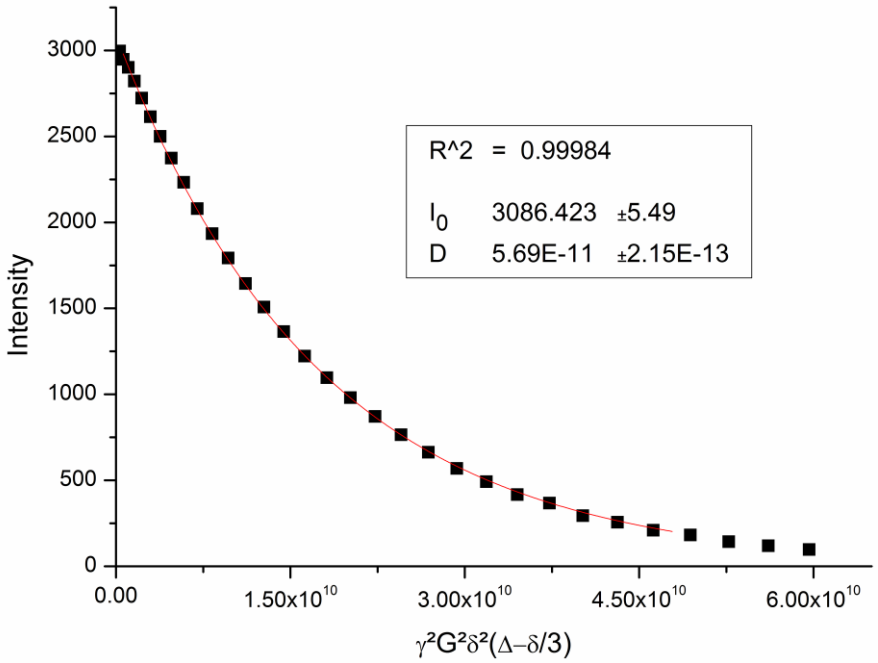


Fig. 12: Evaluation of PFG NMR measurement of **SDS**
(eight molecules of **11** per SDS-micelle) after 230 min of irradiation.

^{1}H-^{1}H gCOSY NMR experiments after relaxation broadening titrations

Titrations:

SDS conc.	0.164 mol/L	25 mg in 500µL
glycothymidine	2.6 mmol/L	0.8 mg in 500µL
MnCl2+EDTA	3.0 mg MnCl2, 7.0mg EDTA in 2mL	11.9 mmol/L MnCl2; 12.0 mmol/L EDTA

Monomer **11**

Addition of MnCl2/EDTA [µL]	Total Volume [µL]	Mn2+ conc. [mM]	EDTA conc. [mM]	SDS conc. [mol/L]	conc. Monomer **11**
0	500	0	0	0.16	2.6
10	510	0.23	0.24	0.16	2.55
15	515	0.35	0.35	0.16	2,52
20	520	0.46	0.46	0.16	2.50
30	530	0.67	0.68	0.15	2.45
40	540	0.88	0.89	0.15	2.41
60	560	1.28	1.29	0.15	2.32
80	580	1.64	1.66	0.14	2.24
100	600	1.98	2	0.14	2.17
140	640	2.60	2.63	0.13	2.03
180	680	3.15	3.18	0.12	1.91
220	720	3.64	3.67	0.11	1.81

Dimer **12**

Addition of MnCl2/EDTA [µL]	Total Volume [µL]	Mn2+ conc. [mM]	EDTA conc. [mM]	SDS conc. [mol/L]	conc. Monomer **11**
0	500	0	0	0.16	2.60
20	520	0.46	0.46	0.16	2.50
60	560	1.28	1.29	0.15	2.32
100	600	1.98	2.00	0.14	2.17

Monomer **11**:

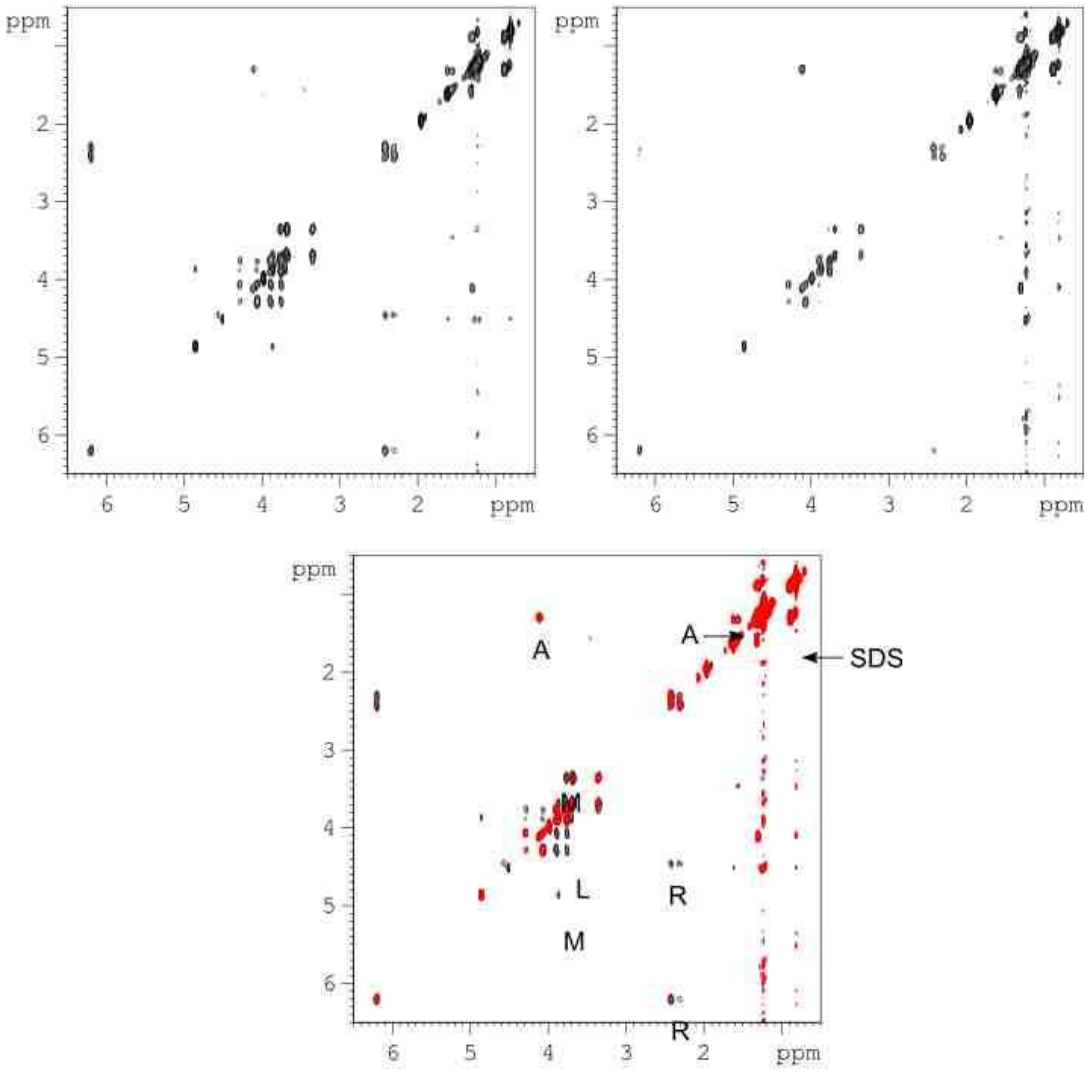


Fig. 13: Overlay of ^{1}H,^{1}H-gCOSY experiments of **11** in SDS detergent micelles:

- in the absence (upper left graph and black contours in overlayed plot) and
- in the presence of 2.6 mM Mn^{2+}-EDTA (upper right graph and red contours in overlayed plot). Correlations are labeled as follows: R: deoxyribose, M: mannose, A: octyl chain, L: ethyl linker, SDS: cross peaks of the residual protons in the deuterated SDS.

Dimer **12**:

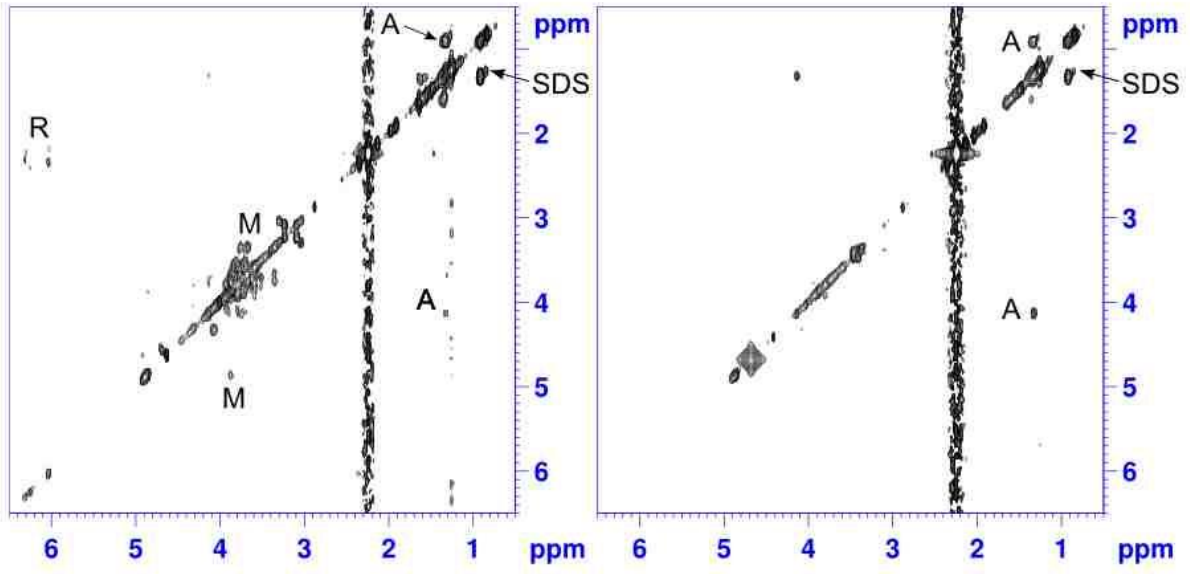


Fig. 14: Regions of the $^{1}H,^{1}H$-gCOSY experiments of **12** in SDS detergent micelles.

Left: in the absence and
Right: in the presence of 2 mM Mn^{2+}-EDTA.

Correlations are labeled as follows: R: deoxyribose, M: mannose, A: octyl chain, SDS: cross peaks of the residual protons in the deuterated SDS. Resonances of the alkyl chain and SDS are unaffected by the paramagnetic broadening of the water-soluble manganese complex, while the broadening of all resonances in the hydrophilic portion of the glycothymidine dimer indicates the water-accessibility of this portion, and confirms its presentation / orientation to the solvent.