SUPPORTING INFORMATION

First general synthesis of 2-*C*-(β-D-glycopyranosyl)pyrimidines and their evaluation as inhibitors of some glycoenzymes

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1. Synthetic details

1.1. General Methods

Melting points were measured on a Kofler hot-stage and are uncorrected. Optical rotations were determined with a Jasco P-2000 polarimeter at rt. NMR spectra were recorded with Bruker 360 (360/90 MHz for $^{1}H/^{13}C$) or Bruker 400 (400/100 MHz for $^{1}H/^{13}C$) spectrometers. Chemical shifts are referenced to the internal TMS (^{1}H), or to the residual solvent signals (^{13}C). Proton-signal assigments for compounds **3, 5, 7** are based on COSY correlations. IR spectra were recorded with a Jasco FT-IR 4100 spectrophotometer. Mass spectra were obtained by Thermo Scientific LTQ XL or 284 MicroTOF-Q type Qq-TOF MS (Bruker Daltonik, Bremen, 285 Germany) instruments. TLC was performed on DC-Alurolle Kieselgel 60 F_{254} (Merck), and the plates were visualised under UV light and by gentle heating (generally no spray reagent was used but, if more intense charring was necessary, the plate was sprayed with the following solution: abs. EtOH (95 mL), ccH_2SO_4 (5 mL) anisaldehyde (1 mL)). For column chromatography Kieselgel 60 (Merck, particle size 0.063-0.200 mm) was used. EtOAc, $CHCl_3$ and CH_2Cl_2 were distilled from P_4O_{10} and stored over 4 Å molecular sieves. MeOH was purified by distillation after refluxing for a couple of hours with magnesium turnings and iodine. EtOH and DMF were purchased from Sigma-Aldrich. 1M solution of NaOMe in anhydrous MeOH and NaOEt in anhydrous EtOH was freshly prepared before using. Organic solutions were dried over anhydrous $MgSO_4$ and concentrated under diminished pressure at 40-60 ºC (water bath). *C*-(2,3,4,6-Tetra-*O*-benzyl-β-D-glucopyranosyl)formamidine hydrochloride[1, 2] (**1**) and *O*-peracylated glycosyl cyanides (**11**,[3] **15**,[4] **16**,[5] **17**,[6] **18**[7]) were synthesized based on literature procedures. The α,β-unsaturated β-chloroketones were obtained by chlorination of the corresponding 1,3-diketones (pentane-2,4-dione/PCl_5,[8] 1,1,1-trifluoropentane-2,4-

dione/$(COCl)_2$,[9] 1-phenylbutane-1,3-dione/$(COCl)_2$,[10] 4,4,4-trifluoro-1-phenylbutane-1,3-dione/$SOCl_2$[9]) according to the cited protocols.

1.2. General procedure I for the synthesis of 2-(β-D-glucopyranosyl)-pyrimidin-4(3*H*)-ones (3, 4) by cyclocondensation of *C*-(β-D-glucopyranosyl)formamidines (1, 2)

The corresponding *C*-(β-D-glucopyranosyl)formamidine hydrochloride (**1**[1, 2] or **2**) was dissolved in anhydrous MeOH (2 mL/100 mg amidine), and a 1M solution of NaOMe in MeOH (3 equiv) was added. After 10 min, the appropriate 3-ketoester (2 equiv) was added to the reaction mixture and the stirring was continued at rt until the TLC showed complete conversion of the starting material (9 : 1 $CHCl_3$-MeOH and 1 : 1 hexane-EtOAc for compounds **1**, **3**, and 7 : 3 $CHCl_3$-MeOH for compounds **2**, **4**, respectively). The reaction mixture was then neutralized with glacial AcOH, and concentrated under diminished pressure. The crude product was purified by column chromatography.

1.3. General procedure II for the removal of *O*-benzyl protecting groups by catalytic hydrogenation under neutral conditions to get compounds 4, 6, 10

To a solution of the corresponding *O*-perbenzylated *C*-(β-D-glucopyranosyl)pyrimidine (**3**, **5** or **8**) in a mixture of anhydrous EtOAc (2 mL/100 mg substrate) and EtOH (4 mL/100 mg substrate) 20 % $Pd(OH)_2$/C (50 weight % of substrate) was added. The reaction mixture was then vigorously stirred at reflux temperature under H_2 atmosphere. After completion of the reaction monitored by TLC (1 : 1 hexane-EtOAc and 3 : 1 EtOAc-MeOH), the hot mixture was filtered through a pad of celite, and washed thoroughly with MeOH. The solvent was then evaporated under reduced pressure and the crude product was purified by column chromatography.

1.4. General procedure III for the reaction of *C*-(2,3,4,6-tetra-*O*-benzyl-β-D-glucopyranosyl)formamidine (1) with malononitrile and ethyl cyanoacetate to get compounds 7a,b

To a solution of *C*-(2,3,4,6-tetra-*O*-benzyl-β-D-glucopyranosyl)formamidine hydrochloride[1, 2] (**1**, 200 mg, 0.33 mmol) in anhydrous EtOH (5 mL) a 1M solution of NaOEt in EtOH (2 or 10 equiv, depending on the quantity of the reagent, see below) was added. After stirring the reaction mixture for 15 min at rt malononitrile (2 equiv) or ethyl cyanoacetate (10 equiv) was added. The stirring was continued at rt until the TLC (9 : 1 $CHCl_3$-MeOH, 1 : 1 hexane-EtOAc) indicated complete conversion of the starting material. The reaction mixture was then neutralized with glacial AcOH, and evaporated under diminished pressure. The resulting crude product was purified by column chromatography.

1.5. General procedure IV for the synthesis of 4,6-disubstituted-2-(β-D-glucopyranosyl)-pyrimidines (8, 10) by cyclocondensation of *C*-(β-D-glucopyranosyl)formamidines (1, 2)

The corresponding *C*-(β-D-glucopyranosyl)formamidine hydrochloride (**1**[1, 2] or **2**) and K_2CO_3 (4 equiv) in the presence of activated molecular sieves (4 Å) were suspended in anhydrous DMF (3 mL/100 mg substrate). This mixture was then cooled to 0 °C and the freshly prepared α,β-unsaturated β-chloroketone (1.2 equiv) obtained from the corresponding 1,3-diketone was added. The reaction mixture was allowed to warm up to rt and the stirring was continued. After completion of the reaction (~ 2 d) monitored by TLC (9 : 1 $CHCl_3$-MeOH and 1 :1 hexane-EtOAc for compounds **1**, **8**, and 7 : 3 $CHCl_3$-MeOH for compounds **2**, **10**, respectively), the inorganic precipitates were filtered off, washed with MeOH, and the solvent was evaporated under reduced pressure. The crude product was purified by column chromatography.

1.6. General procedure V for the removal of *O*-benzyl protecting groups by catalytic hydrogenation under acidic conditions to get compounds 9c,d

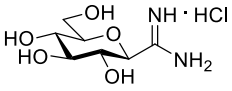
A degassed, vigorously stirred suspension of 20 % $Pd(OH)_2/C$ (50 weight % of substrate) in a mixture of anhydrous EtOAc (2 mL/100 mg substrate) and EtOH (5 mL/100 mg substrate) was saturated with H_2. To this mixture a solution of the corresponding *O*-perbenzylated *C*-β-D-glucopyranosyl derivative in anhydrous EtOAc (3 mL/100 mg substrate), and a drop of ccHCl were added. The reaction mixture was then stirred under H_2 atmosphere at rt overnight. The completion of the reaction was judged by TLC (1 :1 hexane-EtOAc and 7 : 3 $CHCl_3$-MeOH) and the mixture was neutralized by the addition of $NaHCO_3$. The catalyst and the inorganic salts were filtered off through a pad of celite, and washed with MeOH. The solvent was removed under diminished pressure, and the resulting crude product was purified by column chromatography.

1.7. General procedure VI for the synthesis of 2-glycosyl-6-methylpyrimidin-4(3*H*)-ones (19-22) from glycosyl cyanides (15-18) by a *one-pot* three-step procedure

To a stirred solution of the corresponding cyanide (**15-18**) in a mixture of anhydrous $CHCl_3$ (2 mL / 1 g substrate) and MeOH (15 mL / 1 g substrate) a 1M solution of NaOMe in MeOH (20 mol %) was added at rt. After conversion of the starting material into the unprotected methyl *C*-glycopyranosyl formimidate (1 day) NH_4Cl (1.2 equiv) was added to the reaction mixture and the stirring was continued at rt. When TLC (7 : 3 $CHCl_3$-MeOH) indicated complete conversion of formimidate into the appropriate formamidine derivative (1 day) ethyl acetoacetate (2 equiv) and a 1M solution of NaOMe in MeOH (3 equiv) were added to the stirred reaction mixture. After 8 h the solution was neutralized with glacial acetic acid and the solvents were removed under reduced pressure. The residual crude product was purified either by column chromatography or by crystallization.

1.8. Synthesis and characterization of the compounds

***C*-(β-D-Glucopyranosyl)formamidine hydrochloride (2,6-anhydro-D-*glycero*-D-*gulo*-heptonimidamide hydrochloride, 2)**

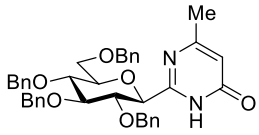


A) A degassed, vigorously stirred suspension of 20 % $Pd(OH)_2/C$ (300 mg) in a mixture of anhydrous EtOAc (10 mL) and EtOH (30 mL) was saturated with H_2. To this mixture a solution of *C*-(2,3,4,6-tetra-*O*-benzyl-β-D-glucopyranosyl)formamidine hydrochloride[1, 2] (**1**, 3.00 g, 4.5 mmol) in anhydrous EtOAc (20 mL) and a drop of ccHCl were added. After stirring the reaction mixture under H_2 atmosphere at rt overnight (the completion of the reaction was judged by TLC (9 : 1 $CHCl_3$-MeOH and MeOH)), it was neutralized with $NaHCO_3$. The catalyst and the inorganic salts were filtered off through a pad of celite and washed thoroughly with MeOH (3 × 10 mL). The solvent was evaporated under diminished pressure and the residual crude product was purified by column chromatography (2 : 1 EtOAc-MeOH → MeOH) to yield 1.19 g (99 %) colourless syrup. R_f = 0.21 (MeOH); $[\alpha]_D$ = +40 (c 0.24, DMSO);^{1}H NMR (400 MHz, CD_3OD) δ (ppm): 4.11 (1H, d, *J* = 9.2 Hz, H-1), 3.87 (1H, dd, *J* = 12.2, 2.0 Hz, H-6a), 3.78 (1H, dd, *J* = 12.2, 4.3 Hz, H-6b), 3.45-3.55 (4H, m, H-2, H-3, H-4, H-5); ^{13}C NMR (90 MHz, CD_3OD) δ (ppm): 169.8 (*C*=N), 81.8, 79.2, 76.8, 73.7, 70.1 (C-1 – C-5), 61.9 (C-6). ESI-MS positive mode (m/z): calcd for $C_7H_{15}N_2O_5^+$ $[M+H]^+$: 207.10. Found: 207.12.

B) To a solution of 2,3,4,6-tetra-*O*-benzoyl-β-D-glucopyranosyl cyanide[3] (**13**, 1.00 g, 1.65 mmol) in a mixture of anhydrous $CHCl_3$ (5 mL) and MeOH (15 mL) a 1M solution of NaOMe in MeOH (0.33 mL, 0.33 mmol, 20 mol %) was added. The mixture was stirred at rt and monitored by TLC (7 : 3 $CHCl_3$-MeOH). After conversion of the starting material (1 d) into the imidate **11** (R_f = 0.51, 7 : 3 $CHCl_3$-MeOH) the reaction mixture was neutralized with a cation exchange resin Amberlist 15 (H^+ form). The resin was filtered off, and the solvent was removed.

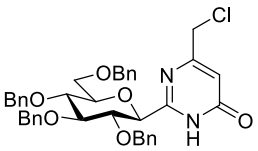
The resulting oil was dissolved in a saturated NH_3 solution in MeOH (10 mL), NH_4Cl (88 mg, 1 equiv) was added, and stirred at rt. When TLC (7 : 3 $CHCl_3$-MeOH) indicated the disappearance of **11** (1 day) the solvent was removed under diminished pressure. Column chromatographic purification of the residue (7 : 3 $CHCl_3$-MeOH) yielded the title compound **2** contaminated with the *C*-(2-deoxy-D-*arabino*-hex-1-enopyranosyl)formamidine hydrochloride **12** (167 mg, **2** : **12** = 9 : 1).

6-Methyl-2-(2',3',4',6'-tetra-*O*-benzyl-β-D-glucopyranosyl)-pyrimidin-4(3*H*)-one (3a)



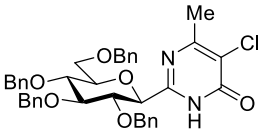
Prepared from compound **1**[1, 2] (400 mg, 0.66 mmol) and ethyl acetoacetate (168 µL, 1.33 mmol) according to general procedure I. Reaction time: 1 day. Purified by column chromatography (1 : 1 hexane-EtOAc) to yield 332 mg (79 %) white amorphous solid. R_f = 0.18 (2 : 3 hexane-EtOAc); $[\alpha]_D$ = +71 (c 0.24, CH_2Cl_2); IR (KBr) ν_{max} (cm^{-1}): 1682 (C=O); ^1H NMR (400 MHz, $CDCl_3$) δ (ppm): 11.48 (1H, broad s, NH), 7.33-7.10 (20H, m, aromatics), 6.10 (1H, s, Py-H-5), 4.92, 4.87 (2 × 1H, 2 d, *J* = 11.0 Hz, Ph*CH*$_2$), 4.85, 4.57 (2 × 1H, 2 d, *J* = 10.8 Hz, Ph*CH*$_2$), 4.66, 4.40 (2 × 1H, 2 d, *J* = 11.0 Hz, Ph*CH*$_2$), 4.56, 4.47 (2 × 1H, 2 d, *J* = 12.1 Hz, Ph*CH*$_2$), 4.26 (1H, d, *J* = 9.2 Hz, H-1'), 3.81-3.78 (2H, m, H-2', H-3'), 3.76-3.71 (3H, m, H-4', H-6'a, H-6'b), 3.64 (1H, ddd, *J* = 9.4, 3.5, 2.0 Hz, H-5'), 2.23 (3H, s, CH_3); ^{13}C NMR (100 MHz, $CDCl_3$) δ (ppm): 165.0, 163.2, 156.8 (Py-C-2, Py-C-4, Py-C-6), 138.4, 138.0, 137.8, 137.5 (aromatics, C_q), 128.6-127.9 (aromatics), 112.7 (Py-C-5), 86.4, 80.1, 79.2, 78.8, 77.5 (C-1' – C-5'), 75.7, 75.2, 74.9, 73.5 (4 × Ph*C*H$_2$), 68.8 (C-6'), 24.0 (CH_3). ESI-MS positive mode (m/z): calcd for $C_{39}H_{41}N_2O_6^+$ $[M+H]^+$: 633.3. Found: 633.5.

6-(Chloromethyl)-2-(2',3',4',6'-tetra-*O*-benzyl-β-D-glucopyranosyl)-pyrimidin-4(3*H*)-one (3b)



Prepared from compound **1**[1, 2] (200 mg, 0.33 mmol) and ethyl 4-chloroacetoacetate (90 μL, 0.66 mmol) according to general procedure I. Reaction time: 2 day. Purified by column chromatography (1 : 1 hexane-EtOAc) to yield 193 mg (87 %) white amorphous solid. R_f = 0.42 (2 : 3 hexane-EtOAc); $[\alpha]_D$ = –2 (c 0.28, CH_2Cl_2); IR (KBr) ν_{max} (cm^{-1}): 1682 (C=O); ^{1}H NMR (400 MHz, $CDCl_3$) δ (ppm): 11.96 (1H, broad s, NH), 7.33-7.09 (20H, m, aromatics), 6.42 (1H, s, Py-H-5), 4.92, 4.88 (2 × 1H, 2 d, *J* = 11.1 Hz, Ph*CH*$_2$), 4.86, 4.58 (2 × 1H, 2 d, *J* = 10.8 Hz, Ph*CH*$_2$), 4.69, 4.46 (2 × 1H, 2 d, *J* = 11.3 Hz, Ph*CH*$_2$), 4.56, 4.47 (2 × 1H, 2 d, *J* = 12.1 Hz, Ph*CH*$_2$), 4.28 (1H, d, *J* = 9.2 Hz, H-1'), 4.26 (2H, s, *CH*$_2$Cl), 3.87-3.80 (2H, m, H-2', H-3'), 3.76-3.72 (3H, m, H-4', H-6'a, H-6'b), 3.66 (1H, ddd, *J* = 9.1, 3.4, 2.1 Hz, H-5'); ^{13}C NMR (100 MHz, $CDCl_3$) δ (ppm): 163.4 (Py-C-4), 162.3 (Py-C-6), 157.8 (Py-C-2), 138.3, 137.9, 137.7, 137.4 (aromatics, C_q), 128.5-127.8 (aromatics), 112.8 (Py-C-5), 86.4, 79.6, 79.2, 78.8, 77.5 (C-1' – C-5'), 75.7, 75.1, 74.8, 73.5 (4 × Ph*C*H$_2$), 68.8 (C-6'), 44.9 (*C*H$_2$Cl). ESI-MS positive mode (m/z): calcd for $C_{39}H_{40}ClN_2O_6^+$ $[M+H]^+$: 667.3. Found: 667.5.

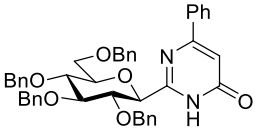
5-Chloro-6-methyl-2-(2',3',4',6'-tetra-*O*-benzyl-β-D-glucopyranosyl)-pyrimidin-4(3*H*)-one (3c)



Prepared from compound **1**[1, 2] (200 mg, 0.33 mmol) and ethyl 2-chloroacetoacetate (90 μL, 0.66 mmol) according to general procedure I. Reaction time: 2 day. Purified by column chromatography (3 : 2 hexane-EtOAc) to yield 133 mg (60 %) white amorphous solid. R_f =

0.58 (2 : 3 hexane-EtOAc); $[\alpha]_D$ = –5 (c 0.25, CH_2Cl_2); IR (KBr) ν_{max} (cm^{-1}): 1666 (C=O); ^1H NMR (400 MHz, $CDCl_3$) δ (ppm): 11.67 (1H, broad s, NH), 7.35-7.08 (20H, m, aromatics), 4.93, 4.89 (2 × 1H, 2 d, *J* = 11.2 Hz, Ph*CH*$_2$), 4.85, 4.56 (2 × 1H, 2 d, *J* = 10.8 Hz, Ph*CH*$_2$), 4.70, 4.44 (2 × 1H, 2 d, *J* = 11.4 Hz, Ph*CH*$_2$), 4.54, 4.48 (2 × 1H, 2 d, *J* = 12.2 Hz, Ph*CH*$_2$), 4.25 (1H, d, *J* = 9.1 Hz, H-1'), 3.83-3.73 (5H, m, H-2', H-3', H-4', H-6'a, H-6'b), 3.66 (1H, ddd, *J* = 9.4, 3.6, 1.9 Hz, H-5'), 2.37 (3H, s, CH_3); ^{13}C NMR (100 MHz, $CDCl_3$) δ (ppm): 160.7, 159.1 (Py-C-4, Py-C-6), 154.1 (Py-C-2), 138.3, 137.9, 137.6, 137.3 (aromatics, C_q), 128.6-127.9 (aromatics), 120.6 (Py-C-5), 86.4, 79.5, 79.0, 78.4, 77.6 (C-1' – C-5'), 75.7, 75.3, 74.8, 73.5 (4 × Ph*C*H_2), 68.9 (C-6'), 22.2 (CH_3). ESI-MS positive mode (m/z): calcd for $C_{39}H_{40}ClN_2O_6^+$ $[M+H]^+$: 667.3. Found: 667.5.

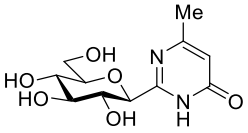
6-Phenyl-2-(2',3',4',6'-tetra-*O*-benzyl-β-D-glucopyranosyl)-pyrimidin-4(3*H*)-one (3d)



Prepared from compound **1**[1, 2] (400 mg, 0.66 mmol) and ethyl benzoylacetate (230 µL, 1.33 mmol) according to general procedure I. Reaction time: 2 day. Purified by column chromatography (1 : 1 hexane-EtOAc) to yield 200 mg (43 %) colourless syrup. R_f = 0.39 (2 : 3 hexane-EtOAc); $[\alpha]_D$ = +32 (c 0.26, CH_2Cl_2); IR (KBr) ν_{max} (cm^{-1}): 1658 (C=O); ^1H NMR (400 MHz, $CDCl_3$) δ (ppm): 12.11 (1H, broad s, NH), 7.97 (2H, d, *J* = 7.9 Hz, aromatics), 7.47-7.41 (3H, aromatics), 7.35-7.01 (20H, m, aromatics), 6.73 (1H, s, Py-H-5), 4.95, 4.90 (2 × 1H, 2 d, *J* = 11.0 Hz, Ph*CH*$_2$), 4.88, 4.62 (2 × 1H, 2 d, *J* = 10.1 Hz, Ph*CH*$_2$), 4.69, 4.42 (2 × 1H, 2 d, *J* = 10.8 Hz, Ph*CH*$_2$), 4.59, 4.49 (2 × 1H, 2 d, *J* = 12.1 Hz, Ph*CH*$_2$), 4.44 (1H, d, *J* = 9.1 Hz, H-1'), 3.97 (1H, pseudo t, *J* = 9.3, 9.1 Hz, H-2'), 3.87 (1H, pseudo t, *J* = 9.4, 9.3 Hz, H-3'), 3.81 (1H, pseudo t, *J* = 9.4, 9.1 Hz, H-4'), 3.78-3.75 (2H, m, H-6'a, H-6'b), 3.72 (1H, ddd, *J* = 9.1, 3.4, 2.0 Hz, H-5'); ^{13}C NMR (100 MHz, $CDCl_3$) δ (ppm): 164.1 (Py-C-4), 162.0 (Py-C-6),

157.4 (C-2), 138.4, 138.0, 137.8, 137.3, 136.1 (aromatics, C_q), 130.7, 128.7-127.8, 127.4 (aromatics), 109.3 (Py-C-5), 86.4, 80.1, 79.2, 79.1, 77.6 (C-1' – C-5'), 75.8, 75.1, 75.0, 73.5 (4 × Ph*C*H_2), 68.9 (C-6'). ESI-MS positive mode (m/z): calcd for $C_{44}H_{43}N_2O_6^+$ $[M+H]^+$: 695.3. Found: 695.4.

2-(β-D-Glucopyranosyl)-6-methylpyrimidin-4(3*H*)-one (4a)



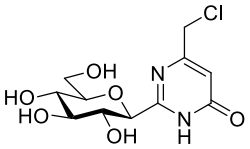
A) From compound **2** (100 mg, 0.41 mmol) and ethyl acetoacetate (104 µL, 0.82 mmol) according to general procedure I. Reaction time: 6 h. Purified by column chromatography (5 : 1 EtOAc-MeOH) to yield 98 mg (88 %) white amorphous solid.

B) From compound **3a** (300 mg, 0.47 mmol) according to general procedure II. Reaction time: 6 h. Purified by column chromatography (5 : 1 EtOAc-MeOH) to yield 80 mg (62 %) white amorphous solid.

C) 2,3,4,6-Tetra-*O*-benzoyl-β-D-glucopyranosyl cyanide[3] (**13**, 3.00 g, 5 mmol) was converted into compounds **2** and **12** via imidate **11** in a two-step procedure as described for compound **2** in method **B**. Without column chromatographic purification the crude mixture of **2** and **12** was dissolved in anhydrous MeOH (10 mL), ethyl acetoacetate (1.12 mL, 9.9 mmol) and a 1M solution of NaOMe in MeOH (15 mL, 14.85 mmol) were added. The reaction mixture was stirred at rt until the TLC (7 : 3 $CHCl_3$-MeOH) showed disappearance of the amidine intermediates. Upon neutralization of the reaction mixture by a cation exchange resin Amberlist 15 (H^+ form) a white solid started to precipitate. By heating the reaction mixture at boiling temperature the precipitates were redissolved and the resin was filtered off from the hot mixture. The reaction mixture was then cooled to rt and the precipitated white solid was filtered off. Yield: 575 mg (43 % for three steps). R_f = 0.43 (2 : 1 EtOAc-MeOH); $[\alpha]_D$ = +13 (c 0.17,

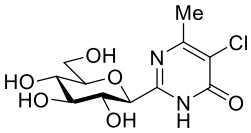
DMSO); ^{1}H NMR (400 MHz, DMSO-d_6) δ (ppm): 12.25 (1H, broad s, NH), 6.12 (1H, s, Py-H-5), 5.13-4.57 (broad signals, OH), 3.96 (1H, d, *J* = 9.5 Hz, H-1'), 3.67 (1H, dd, *J* = 12.0, 2.1 Hz, H-6'a), 3.52 (1H, pseudo t, *J* = 9.5, 9.3 Hz, H-2'), 3.44 (1H, dd, *J* = 12.0, 5.2 Hz, H-6'b), 3.25-3.13 (3H, m, H-3', H-4', H-5'), 2.17 (3H, s, CH_3); ^{13}C NMR (100 MHz, DMSO-d_6) δ (ppm): 163.8, 162.1, 158.4 (Py-C-2, Py-C-4, Py-C-6), 111.7 (Py-C-5), 81.4, 79.0, 77.6, 71.8, 69.5 (C-1' – C-5'), 61.1 (C-6'), 23.3 (CH_3). ESI-MS positive mode (m/z): calcd for $C_{11}H_{17}N_2O_6^+$ $[M+H]^+$: 273.11. Found: 273.12.

6-Chloromethyl-2-(β-D-glucopyranosyl)-pyrimidin-4(3*H*)-one (4b)



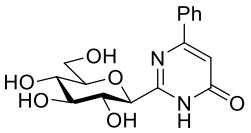
Prepared from compound **2** (100 mg, 0.41 mmol) and ethyl 4-chloroacetoacetate (112 µL, 0.82 mmol) according to general procedure I. Reaction time: 6 h. Purified by column chromatography (5 : 1 EtOAc-MeOH) to yield 74 mg (59 %) white amorphous solid. R_f = 0.29 (3 : 1 EtOAc-MeOH); $[\alpha]_D$ = +95 (c 0.16, DMSO); ^{1}H NMR (400 MHz, DMSO-d_6) δ (ppm): 12.28 (1H, broad s, NH), 6.40 (1H, s, Py-H-5), 5.10-4.62 (broad signals, OH), 4.50 (2H, s, *CH*$_2$Cl), 4.00 (1H, d, *J* = 9.6 Hz, H-1'), 3.67 (1H, dd, *J* = 11.9, 2.0 Hz, H-6'a), 3.54 (1H, pseudo t, *J* = 9.6, 9.4 Hz, H-2'), 3.45 (1H, dd, *J* = 11.9, 5.2 Hz, H-6'b), 3.28-3.16 (3H, m, H-3', H-4', H-5'); ^{13}C NMR (100 MHz, DMSO-d_6) δ (ppm): 162.8, 161.5, 159.9 (Py-C-2, Py-C-4, Py-C-6), 112.0 (Py-C-5), 81.4, 79.2, 77.5, 71.8, 69.5 (C-1' – C-5'), 61.1 (C-6'), 45.2 (*C*H$_2$Cl). ESI-MS positive mode (m/z): calcd for $C_{11}H_{16}ClN_2O_6^+$ $[M+H]^+$: 307.1. Found: 307.2.

5-Chloro-2-(β-D-glucopyranosyl)-6-methylpyrimidin-4(3*H*)-one (4c)



Prepared from compound **2** (100 mg, 0.41 mmol) and ethyl 2-chloroacetoacetate (115 µL, 0.82 mmol) according to general procedure I. Reaction time: 6 h. Purified by column chromatography (5 : 1 EtOAc-MeOH) to yield 92 mg (73 %) white amorphous solid. R_f = 0.29 (3 : 1 EtOAc-MeOH); $[\alpha]_D$ = +11 (c 0.13, DMSO); ^{1}H NMR (400 MHz, DMSO-d_6) δ (ppm): 12.90 (1H, broad s, NH), 5.16-4.15 (broad signals, OH), 3.97 (1H, d, *J* = 9.6 Hz, H-1'), 3.67 (1H, dd, *J* = 12.0, 2.0 Hz, H-6'a), 3.51 (1H, pseudo t, *J* = 9.6, 9.4 Hz, H-2'), 3.45 (1H, dd, *J* = 12.0, 4.6 Hz, H-6'b), 3.27-3.16 (3H, m, H-3', H-4', H-5'), 2.33 (3H, s, CH_3); ^{13}C NMR (90 MHz, DMSO-d_6) δ (ppm): 159.2, 158.5, 156.3 (Py-C-2, Py-C-4, Py-C-6), 118.8 (Py-C-5), 81.3, 79.1, 77.4, 71.8, 69.4 (C-1' – C-5'), 61.1 (C-6'), 21.7 (CH_3). ESI-MS positive mode (m/z): calcd for $C_{11}H_{16}ClN_2O_6^+$ $[M+H]^+$: 307.1. Found: 307.2.

2-(β-D-Glucopyranosyl)-6-phenylpyrimidin-4(3*H*)-one (4d)



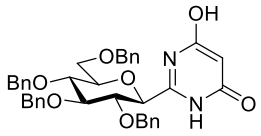
A) From compound **2** (100 mg, 0.41 mmol) and ethyl benzoylacetate (143 µL, 0.82 mmol) according to general procedure I. Reaction time: 6 h. Purified by column chromatography (5 : 1 EtOAc-MeOH) to yield 90 mg (65 %) white amorphous solid.

B) From compound **3d** (100 mg, 0.14 mmol) according to general procedure II. Reaction time: 5 h. Purified by column chromatography (5 : 1 EtOAc-MeOH) to yield 37 mg (77 %) white amorphous solid.

C) 2,3,4,6-Tetra-*O*-benzoyl-β-D-glucopyranosyl cyanide[3] (**13**, 1.00 g, 1.65 mmol) was converted into compounds **2** and **12** via imidate **11** in a two-step procedure as described for

compound **2** in method **B**. Without column chromatographic purification the crude mixture of **2** and **12** was dissolved in anhydrous MeOH (10 mL), ethyl benzoylacetate (0.57 mL, 3.3 mmol) and a 1M solution of NaOMe in MeOH (5 mL, 4.95 mmol) were added. The reaction mixture was stirred at rt until the TLC (7 : 3 $CHCl_3$-MeOH) showed disappearance of the amidine intermediates. The reaction mixture was neutralized with a cation exchange resin Amberlist 15 (H^+ form), filtered and concentrated to quarter of its volume. After addition of Et_2O (20 mL) the precipitated crude product was filtered off and subsequently purified by column chromatography (5 : 1 EtOAc-MeOH). Yield: 137 mg (25 % for three steps). R_f = 0.39 (3:1 EtOAc-MeOH); $[\alpha]_D$ = +31 (c 0.21, DMSO); ^{1}H NMR (400 MHz, DMSO-d_6) δ (ppm): 12.46 (1H, broad s, NH), 8.05 (2H, d, *J* = 7.1 Hz, Ph), 7.50-7.48 (3H, m, Ph), 6.83 (1H, s, Py-H-5), 5.09-4.58 (broad signals, OH), 4.09 (1H, d, *J* = 9.6 Hz, H-1'), 3.70 (1H, dd, *J* = 12.0, 2.1 Hz, H-6'a), 3.66 (1H, pseudo t, *J* = 9.6, 9.4 Hz, H-2'), 3.48 (1H, dd, *J* = 12.0, 5.3 Hz, H-6'b), 3.31-3.20 (3H, m, H-3', H-4', H-5'); ^{13}C NMR (100 MHz, DMSO-d_6) δ (ppm): 163.0, 160.2, 158.9 (Py-C-2, Py-C-4, Py-C-6), 136.1, 130.5, 128.7 (2), 127.0 (2) (Ph), 108.5 (Py-C-5), 81.4, 79.5, 77.6, 71.7, 69.5 (C-1' – C-5'), 61.1 (C-6'). ESI-MS positive mode (m/z): calcd for $C_{16}H_{19}N_2O_6^+$ $[M+H]^+$: 335.1. Found: 335.3.

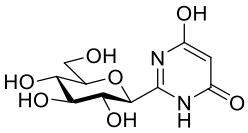
6-Hydroxy-2-(2',3',4',6'-tetra-*O*-benzyl-β-D-glucopyranosyl)-pyrimidin-4(3*H*)-one (5)



To a solution of compound **1**[1, 2] (200 mg, 0.33 mmol) in anhydrous MeOH (2 mL) dimethyl malonate (379 µL, 3.32 mmol, 10 equiv) and a 1M solution of NaOMe in MeOH (3.32 mL, 3.32 mmol, 10 equiv) were added. The reaction mixture was stirred at rt until the TLC (9:1 $CHCl_3$-MeOH) showed total consumption of the starting material (1 d). The reaction mixture was then neutralized with glacial AcOH and the solvent was removed under reduced pressure.

The residue was purified by column chromatography (1 : 2 → 1 : 4 hexane-EtOAc) to yield 172 mg (82 %) white amorphous solid. R_f = 0.63 (9 : 1 $CHCl_3$-MeOH); $[\alpha]_D$ = +34 (c 0.24, CH_2Cl_2); IR (KBr) ν_{max} (cm^{-1}): 1650 (C=O); ^{1}H NMR (400 MHz, $CDCl_3$) δ (ppm): 11.01 (2H, 2 broad s, exchangeable protons), 7.31-7.07 (20H, m, aromatics), 5.54 (1H, s, Py-H-5), 4.92, 4.88 (2 × 1H, 2 d, *J* = 11.1 Hz, Ph*CH*$_2$), 4.83, 4.56 (2 × 1H, 2 d, *J* = 10.9 Hz, Ph*CH*$_2$), 4.64, 4.38 (2 × 1H, 2 d, *J* = 11.2 Hz, Ph*CH*$_2$), 4.51, 4.46 (2 × 1H, 2 d, *J* = 12.3 Hz, Ph*CH*$_2$), 4.21 (1H, d, *J* = 9.1 Hz, H-1'), 3.85 (1H, pseudo t, *J* = 9.3, 9.0 Hz, H-3'), 3.72-3.65 (5H, m, H-2', H-4', H-5', H-6'a, H-6'b); ^{13}C NMR (100 MHz, $CDCl_3$) δ (ppm): 166.8, 158.9 (Py-C-2, Py-C-4, Py-C-6), 138.2, 137.9, 137.7, 136.9 (aromatics, C_q), 128.6-127.9 (aromatics), 91.3 (Py-C-5), 86.4, 79.5, 79.1, 77.6 (2) (C-1' – C-5'), 75.8, 75.1, 74.9, 73.5 (4 × Ph*C*H$_2$), 69.0 (C-6'). ESI-MS positive mode (m/z): calcd for $C_{38}H_{39}N_2O_7^+$ $[M+H]^+$: 635.3. Found: 635.5.

2-(β-D-Glucopyranosyl)-6-hydroxy-pyrimidin-4(3*H*)-one (6)

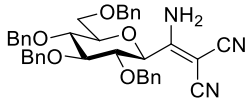


A) Compound **2** (100 mg, 0.41 mmol) and dimethyl malonate (471 μL, 4.12 mmol, 10 equiv) were dissolved in anhydrous MeOH (1 mL), and a 1M solution of NaOMe in MeOH (4.12 mL, 4.12 mmol, 10 equiv) was added. The reaction mixture was stirred at rt overnight. The completion of the reaction was monitored by TLC (7:3 $CHCl_3$-MeOH and 1 : 2 $CHCl_3$-MeOH), then the mixture was neutralized with glacial AcOH, and concentrated under diminished pressure. The residue was purified by column chromatography (1 : 1 $CHCl_3$-MeOH) to yield 80 mg (71 %) white amorphous solid.

B) From compound **5** (100 mg, 0.16 mmol) according to general procedure II. Reaction time: 4 h. Purified by column chromatography (1 : 1 $CHCl_3$-MeOH) to yield 20 mg (47 %) colourless syrup. R_f = 0.35 (1 : 2 $CHCl_3$-MeOH); $[\alpha]_D$ = +60 (c 0.16, H_2O); ^{1}H NMR (400 MHz, DMSO-

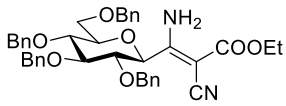
d_6) δ (ppm): 5.78-5.13 (broad signals, OH), 4.57 (1H, s, Py-H-5), 3.88 (1H, d, *J* = 9.3 Hz, H-1'), 3.67 (1H, dd, *J* = 12.0, 2.3 Hz, H-6'a), 3.42 (1H, dd, *J* = 12.0, 6.5 Hz, H-6'b), 3.33 (1H, pseudo t, *J* = 9.3, 9.1 Hz, H-2'), 3.25 (1H, pseudo t, *J* = 9.2, 9.1 Hz, H-3' or H-4'), 3.22 (1H, ddd, *J* = 9.1, 6.5, 2.3 Hz, H-5'), 3.06 (1H, pseudo t, *J* = 9.2, 9.1 Hz, H-3' or H-4'); ^{13}C NMR (90 MHz, D_2O + 1 drop of CD_3OD) δ (ppm): 171.4 (Py-C-4, Py-C-6), 158.8 (Py-C-2), 90.1 (Py-C-5), 80.8, 78.6, 77.5, 73.1, 69.9 (C-1' – C-5'), 61.5 (C-6'). ESI-MS positive mode (m/z): calcd for $C_{10}H_{15}N_2O_7^+$ $[M+H]^+$: 275.09. Found: 275.08.

2-(Amino(2',3',4',6'-tetra-*O*-benzyl-β-D-glucopyranosyl)methylene)malononitrile (7a)



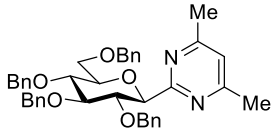
Prepared from compound **1**[1, 2] (200 mg, 0.33 mmol) and malononitrile (44 mg, 0.66 mmol, 2 equiv) according to general procedure III. Reaction time: 2 h. Purified by column chromatography (2 : 1 hexane-EtOAc) to yield 162 mg (79 %) pale yellow amorphous solid. R_f = 0.38 (1 : 1 hexane-EtOAc); $[\alpha]_D$ = +87 (c 0.24, CH_2Cl_2); ^{1}H NMR (400 MHz, $CDCl_3$) δ (ppm): 7.31-7.16 (20H, m, aromatics), 6.33, 5.87 (2 × 1H, 2 broad s, NH_2), 4.88, 4.83 (2 × 1H, 2 d, *J* = 10.9 Hz, Ph*CH*$_2$), 4.85, 4.55 (2 × 1H, 2 d, *J* = 11.0 Hz, Ph*CH*$_2$), 4.77, 4.60 (2 × 1H, 2 d, *J* = 11.3 Hz, Ph*CH*$_2$), 4.49, 4.45 (2 × 1H, 2 d, *J* = 12.2 Hz, Ph*CH*$_2$), 4.34 (1H, d, *J* = 9.2 Hz, H-1'), 3.78 (1H, pseudo t, *J* = 9.4, 9.0 Hz, H-3'), 3.72-3.65 (3H, m, H-4', H-6'a, H-6'b), 3.55 (1H, ddd, *J* = 9.5, 3.5, 2.0 Hz, H-5'), 3.47 (1H, pseudo t, *J* = 9.4, 9.2 Hz, H-2'); ^{13}C NMR (100 MHz, $CDCl_3$) δ (ppm): 170.1 (*C*=C(CN)$_2$), 138.1, 137.9, 137.5, 136.9 (aromatics, C_q), 128.7-127.9 (aromatics), 113.9, 113.7 (2 × *C*≡N), 86.1, 80.1, 78.7, 77.0, 76.3 (C-1' – C-5'), 75.9, 75.2, 75.1, 73.7 (4 × Ph*C*H$_2$), 68.5 (C-6'), 55.0 (C=*C*(CN)$_2$). ESI-MS positive mode (m/z): calcd for $C_{38}H_{37}N_3NaO_5^+$ $[M+Na]^+$: 638.263. Found: 638.266; $C_{38}H_{37}KN_3O_5^+$ $[M+K]^+$: 654.236. Found: 654.238.

(*Z*)-Ethyl 3-amino-2-cyano-3-(2',3',4',6'-tetra-*O*-benzyl-β-D-glucopyranosyl)acrylate (7b)



Prepared from compound **1**[1, 2] (200 mg, 0.33 mmol) and ethyl cyanoacetate (354 µL, 0.66 mmol, 10 equiv) according to general procedure III. Reaction time: 6 h. Purified by column chromatography (2 : 1 hexane-EtOAc) to yield 92 mg (42 %) pale yellow amorphous solid. R_f = 0.51 (1 : 1 hexane-EtOAc); $[\alpha]_D$ = +35 (c 0.24, CH_2Cl_2); ^{1}H NMR (400 MHz, $CDCl_3$) δ (ppm): 8.89 (1H, broad s, NH_2), 7.33-7.16 (20H, m, aromatics), 6.37 (1H, broad s, NH_2), 4.87, 4.80 (2 × 1H, 2 d, *J* = 10.9 Hz, Ph*CH*$_2$), 4.72, 4.60 (2 × 1H, 2 d, *J* = 11.2 Hz, Ph*CH*$_2$), 4.82, 4.56 (2 × 1H, 2 d, *J* = 11.6 Hz, Ph*CH*$_2$), 4.51, 4.47 (2 × 1H, 2 d, *J* = 12.2 Hz, Ph*CH*$_2$), 4.46 (1H, d, *J* = 9.0 Hz, H-1'), 4.21 (2H, q, *J* = 7.1 Hz, *CH*$_2$CH$_3$), 3.80 (1H, pseudo t, *J* = 9.2, 9.1 Hz, H-3'), 3.73-3.65 (3H, m, H-4', H-6'a, H-6'b), 3.58 (1H, ddd, *J* = 9.5, 3.5, 1.9 Hz, H-5'), 3.52 (1H, pseudo t, *J* = 9.1, 9.0 Hz, H-2'), 1.31 (3H, t, *J* = 7.1 Hz, CH$_2$*CH*$_3$); ^{13}C NMR (100 MHz, $CDCl_3$) δ (ppm): 168.3 (*C*=CCN(COOEt)), 167.5 (*C*=O), 138.3, 138.0, 137.8, 137.3 (aromatics, C_q), 128.6-127.8 (aromatics), 117.5 (*C*≡N), 86.1, 81.3, 78.5, 77.2 (2) (C-1' – C-5'), 75.7, 75.3, 75.0 (3 × Ph*C*H$_2$), 74.1 (C=*C*CN(COOEt)), 73.6 (Ph*C*H$_2$), 68.7 (C-6'), 60.8 (*C*H$_2$CH$_3$), 14.5 (CH$_2$*C*H$_3$). ESI-MS positive mode (m/z): calcd for $C_{40}H_{42}N_2NaO_7^+$ $[M+Na]^+$: 685.288. Found: 685.291; $C_{40}H_{42}KN_2O_7^+$ $[M+K]^+$: 701.262. Found: 701.266.

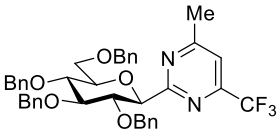
4,6-Dimethyl-2-(2',3',4',6'-tetra-*O*-benzyl-β-D-glucopyranosyl)-pyrimidine (8a)



Prepared from compound **1**[1, 2] (400 mg, 0.66 mmol) and the α,β-unsaturated β-chloroketone (94 mg, 0.80 mmol) obtained from pentane-2,4-dione[8] according to general procedure IV. Purified

by column chromatography (2 : 1 hexane-EtOAc) to yield 270 mg (65 %) colourless syrup. R_f = 0.33 (1 : 1 hexane-EtOAc); $[\alpha]_D$ = +3 (c 0.21, CH_2Cl_2); ^{1}H NMR (400 MHz, $CDCl_3$) δ (ppm): 7.36-6.84 (20H, m, aromatics), 6.86 (1H, s, Py-H-5), 4.94, 4.91 (2 × 1H, 2 d, *J* = 11.2 Hz, Ph*CH*$_2$), 4.84, 4.56 (2 × 1H, 2 d, *J* = 10.7 Hz, Ph*CH*$_2$), 4.62, 4.23 (2 × 1H, 2 d, *J* = 11.1 Hz, Ph*CH*$_2$), 4.59, 4.49 (2 × 1H, 2 d, *J* = 12.2 Hz, Ph*CH*$_2$), 4.49 (1H, d, *J* = 9.1 Hz, H-1'), 4.20 (1H, pseudo t, *J* = 9.4, 9.1 Hz, H-2'), 3.88 (1H, pseudo t, *J* = 9.4, 9.0 Hz, H-4'), 3.81 (1H, pseudo t, *J* = 9.5, 9.0 Hz, H-4'), 3.78-3.72 (2H, m, H-6'a, H-6'b), 3.71-3.66 (1H, m, H-5'), 2.45 (6H, s, 2 × CH_3); ^{13}C NMR (100 MHz, $CDCl_3$) δ (ppm): 167.0 (2), 165.4 (Py-C-2, Py-C-4, Py-C-6), 138.9, 138.4, 138.2 (2) (aromatics, C_q), 128.5-127.4 (aromatics), 119.6 (Py-C-5), 87.2, 83.3, 81.3, 79.7, 78.2 (C-1' – C-5'), 75.6, 75.2, 74.6, 73.5 (4 × Ph*C*H_2), 69.0 (C-6'), 24.0 (2) (2 × CH_3). ESI-MS positive mode (m/z): calcd for $C_{40}H_{43}N_2O_5^+$ $[M+H]^+$: 631.3. Found: 631.5.

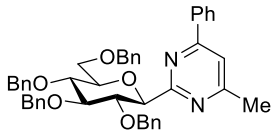
4-Methyl-2-(2',3',4',6'-tetra-*O*-benzyl-β-D-glucopyranosyl)-6-trifluoromethyl-pyrimidine (8b)



Prepared from compound **1**[1, 2] (400 mg, 0.66 mmol) and the α,β-unsaturated β-chloroketone (137 mg, 0.80 mmol) obtained from 1,1,1-trifluoropentane-2,4-dione[9] according to general procedure IV. Purified by column chromatography (5 : 1 hexane-EtOAc) to yield 309 mg (68 %) pale yellow syrup. R_f = 0.43 (3 : 1 hexane-EtOAc); $[\alpha]_D$ = +1 (c 0.30, CH_2Cl_2); ^{1}H NMR (400 MHz, $CDCl_3$) δ (ppm): 7.37-6.83 (21H, m, aromatics, Py-H-5), 4.96, 4.93 (2 × 1H, 2 d, *J* = 11.1 Hz, Ph*CH*$_2$), 4.85, 4.59 (2 × 1H, 2 d, *J* = 10.7 Hz, Ph*CH*$_2$), 4.71, 4.31 (2 × 1H, 2 d, *J* = 11.4 Hz, Ph*CH*$_2$), 4.59, 4.50 (2 × 1H, 2 d, *J* = 12.2 Hz, Ph*CH*$_2$), 4.59 (1H, d, *J* = 9.1 Hz, H-1'), 4.23 (1H, pseudo t, *J* = 9.4, 9.1 Hz, H-2'), 3.90 (1H, pseudo t, *J* = 9.4, 9.0 Hz, H-3'), 3.81 (1H, pseudo t, *J* = 9.5, 9.0 Hz, H-4'), 3.78-3.72 (2H, m, H-6'a, H-6'b), 3.70 (1H, ddd, *J* = 9.5, 4.0,

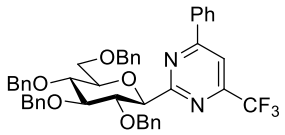
2.2 Hz, H-5'), 2.56 (3H, s, CH_3); ^{13}C NMR (100 MHz, $CDCl_3$) δ (ppm): 170.7, 166.8 (Py-C-2, Py-C-4), 155.4 (q, $^2J_{C\text{-}F}$ = 36.3 Hz, Py-C-6), 138.7, 138.2, 138.2, 138.1 (aromatics, C_q), 128.6-127.5 (aromatics), 120.7 (q, $^1J_{C\text{-}F}$ = 275.3 Hz, CF_3), 115.9 (q, $^3J_{C\text{-}F}$ = 2.1 Hz, Py-C-5), 87.3, 82.6, 80.8, 79.9, 78.2 (C-1' – C-5'), 75.7, 75.3, 74.7, 73.6 (4 × Ph*C*H_2), 68.9 (C-6'), 24.7 (CH_3). ESI-MS positive mode (m/z): calcd for $C_{40}H_{40}F_3N_2O_5^+$ $[M+H]^+$: 685.3. Found: 685.4.

4-Methyl-6-phenyl-2-(2',3',4',6'-tetra-*O*-benzyl-β-D-glucopyranosyl)-pyrimidine (8c)



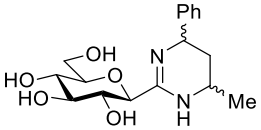
Prepared from compound **1** (400 mg, 0.66 mmol) and the α,β-unsaturated β-chloroketone (144 mg, 0.80 mmol) obtained from 1-phenylbutane-1,3-dione[10] according to general procedure IV. Purified by column chromatography (3 : 1 hexane-EtOAc) to yield 340 mg (74 %) pale yellow syrup. R_f = 0.47 (1 : 1 hexane-EtOAc); $[\alpha]_D$ = +19 (c 0.24, CH_2Cl_2); ^1H NMR (400 MHz, $CDCl_3$) δ (ppm): 8.10 (2H, d, *J* = 7.0 Hz, aromatics), 7.48-7.44 (4H, m, aromatics, Py-H-5), 7.38-6.81 (20H, m, aromatics), 4.98, 4.95 (2 × 1H, 2 d, *J* = 11.1 Hz, Ph*C*H_2), 4.88, 4.62 (2 × 1H, 2 d, *J* = 10.7 Hz, Ph*C*H_2), 4.62, 4.26 (2 × 1H, 2 d, *J* = 11.1 Hz, Ph*C*H_2), 4.65, 4.50 (2 × 1H, 2 d, *J* = 12.1 Hz, Ph*C*H_2), 4.62 (1H, d, *J* = 9.0 Hz, H-1'), 4.36 (1H, pseudo t, *J* = 9.4, 9.0 Hz, H-2'), 3.93 (1H, pseudo t, *J* = 9.4, 9.0 Hz, H-3'), 3.88 (1H, pseudo t, *J* = 9.5, 9.0 Hz, H-4'), 3.81 (1H, dd, *J* = 11.1, 4.2 Hz, H-6'a), 3.77 (1H, dd, *J* = 11.1, 2.0 Hz, H-6'b), 3.73 (1H, ddd, *J* = 9.5, 4.2, 2.0 Hz, H-5'), 2.54 (3H, s, CH_3); ^{13}C NMR (100 MHz, $CDCl_3$) δ (ppm): 168.0, 165.9, 164.0 (Py-C-2, Py-C-4, Py-C-6), 138.9, 138.3, 138.2 (2), 136.7 (aromatics, C_q), 130.9, 128.9, 128.5-127.4 (aromatics), 115.5 (Py-C-5), 87.2, 83.4, 81.4, 79.8, 78.3 (C-1' – C-5'), 75.6, 75.2, 74.7, 73.5 (4 × Ph*C*H_2), 69.0 (C-6'), 24.4 (CH_3). ESI-MS positive mode (m/z): calcd for $C_{45}H_{45}N_2O_5^+$ $[M+H]^+$: 693.3. Found: 693.4.

4-Phenyl-2-(2',3',4',6'-tetra-*O*-benzyl-β-D-glucopyranosyl)-6-trifluoromethyl-pyrimidine (8d)



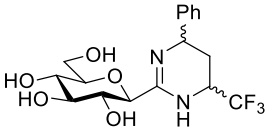
Prepared from compound **1**[1, 2] (400 mg, 0.66 mmol) and the α,β-unsaturated β-chloroketone (187 mg, 0.80 mmol) obtained from 4,4,4-trifluoro-1-phenylbutane-1,3-dione[9] according to general procedure IV. Purified by column chromatography (7 : 1 hexane-EtOAc) to yield 356 mg (72 %) colourless syrup. R_f = 0.38 (5 : 1 hexane-EtOAc); $[\alpha]_D$ = +27 (c 0.29, CH_2Cl_2); ^{1}H NMR (400 MHz, $CDCl_3$) δ (ppm): 8.12 (2H, d, *J* = 7.0 Hz, aromatics), 7.85 (1H, s, Py-H-5), 7.56-7.48 (3H, m, aromatics) 7.38-6.79 (20H, m, aromatics), 4.98, 4.96 (2 × 1H, 2 d, *J* = 11.1 Hz, Ph*CH*$_2$), 4.89, 4.65 (2 × 1H, 2 d, *J* = 10.7 Hz, Ph*CH*$_2$), 4.73, 4.31 (2 × 1H, 2 d, *J* = 11.3 Hz, Ph*CH*$_2$), 4.64, 4.51 (2 × 1H, 2 d, *J* = 12.1 Hz, Ph*CH*$_2$), 4.71 (1H, d, *J* = 9.1 Hz, H-1'), 4.36 (1H, pseudo t, *J* = 9.4, 9.1 Hz, H-2'), 3.95 (1H, pseudo t, *J* = 9.4, 9.0 Hz, H-3'), 3.88 (1H, pseudo t, *J* = 9.6, 9.0 Hz, H-4'), 3.82 (1H, dd, *J* = 11.2, 4.3 Hz, H-6'a), 3.77 (1H, dd, *J* = 11.2, 1.9 Hz, H-6'b), 3.73 (1H, ddd, *J* = 9.6, 4.3, 1.9 Hz, H-5'); ^{13}C NMR (100 MHz, $CDCl_3$) δ (ppm): 167.4, 166.9 (Py-C-2, Py-C-4), 156.5 (q, $^2J_{C\text{-}F}$ = 35.9 Hz, Py-C-6), 138.7, 138.3, 138.2, 138.1, 135.4 (aromatic, C_q), 132.2, 129.2, 128.6-127.5 (aromatics), 120.8 (q, $^1J_{C\text{-}F}$ = 275.1 Hz, CF_3), 111.6 (q, $^3J_{C\text{-}F}$ = 1.9 Hz, Py-C-5), 87.2, 82.7, 81.2, 80.0, 78.3 (C-1' – C-5'), 75.8, 75.3, 74.9, 73.6 (4 × Ph*C*H$_2$), 69.0 (C-6'). ESI-MS positive mode (m/z): calcd for $C_{45}H_{43}F_3N_2O_5^+$ $[M+H]^+$: 747.3. Found: 747.4.

(4*R*,6*R*)- and (4*S*,6*S*)-2-(β-D-Glucopyranosyl)-6-methyl-4-phenyl-1,4,5,6-tetrahydropyrimidines (9c)



Prepared from compound **8c** (300 mg, 0.43 mmol) according to general procedure V. Purified by column chromatography (5 : 1 $CHCl_3$-MeOH) to yield 120 mg (82 %) colourless syrup. R_f = 0.46 (3 : 1 $CHCl_3$-MeOH). NMR assignment of the major component: ^{1}H NMR (400 MHz, CD_3OD) δ (ppm): 7.46-7.35 (5H, m, aromatics), 4.79 (1H, dd, *J* = 11.2, 3.8 Hz, Py-H-4), 4.12 (1H, d, *J* = 9.0 Hz, H-1'), 3.95-3.81 (3H, m, Py-H-6, H-6'a, H-6'b), 3.54-3.39 (4H, m, H-2', H-3', H-4', H-5'), 2.36 (1H, dt, *J* = 13.4, 3.8 Hz, Py-H-5_{eq}), 1.72 (1H, dt, *J* = 13.4, 11.2 Hz, Py-H-5_{ax}), 1.39 (3H, d, *J* = 6.6 Hz, CH_3); ^{13}C NMR (90 MHz, CD_3OD) δ (ppm): 162.7 (Py-C-2), 140.1, 130.0 (2), 129.7, 127.9 (2) (Ph), 81.7, 78.8, 77.7, 73.9, 69.8 (C-1' – C-5'), 61.3 (C-6'), 56.0, 47.7 (Py-C-4, Py-C-6), 38.1 (Py-C-5), 19.7 (CH_3). ESI-MS positive mode (m/z): calcd for $C_{17}H_{25}N_2O_5^+$ $[M+H]^+$: 337.18. Found:337.17.

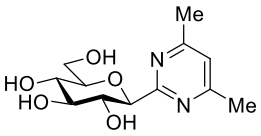
(4*R*,6*S*)- and (4*S*,6*R*)-2-(β-D-Glucopyranosyl)-4-phenyl-6-trifluoromethyl-1,4,5,6-tetrahydropyrimidines (9d)



Prepared from compound **8d** (200 mg, 0.27 mmol) according to general procedure V. Purified by column chromatography (5 : 1 $CHCl_3$-MeOH) to yield 83 mg (79 %) colourless syrup. R_f = 0.51 (3 : 1 $CHCl_3$-MeOH); ^{1}H NMR (400 MHz, CD_3OD) δ (ppm): 7.41-7.29 (2 × 5H, m, aromatics), 4.62-4.57 (2 × 1H, 2 dd, *J* = 11.3, 3.8 Hz in each, 2 × Py-H-4), 4.29-4.17 (2H, m, 2 × Py-H-6), 3.91-3.79 (4H, m, 2 × H-1', 2 × H-6'a), 3.66, 3.63 (2 × 1H, 2 dd, *J* = 11.7, 4.9 Hz in each, 2 × H-6'b), 3.50, 3.48 (2 × 1H, 2 pseudo t, *J* = 9.4, 9.2 Hz in each, 2 × H-2'), 3.42, 3.41

(2 × 1H, 2 pseudo t, J = 9.4, 9.2 Hz in each, 2 × H-3'), 3.36-3.26 (4H, m, 2 × H-4', 2 × H-5'), 2.32-2.25 (2 × 1H, 2 dt, J = 13.0, 3.8 Hz in each, 2 × Py-H-5_{eq}), 1.81-1.67 (2 × 1H, 2 dt, J = 13.0, 11.3 Hz in each, 2 × Py-H-5_{ax}); ^{13}C NMR (100 MHz, CD_3OD) δ (ppm): ^{13}C NMR (100 MHz, $CDCl_3$) δ (ppm): 162.0, 161.8 (2 × Py-C-2), 142.1, 142.0, 130.0 (2), 129.9 (2), 129.5, 129.4, 127.8 (4) (aromatics), 127.0, 126.9 (2 q, $^1J_{C\text{-}F}$ = 278.0 Hz in each, 2 × CF_3), 82.0, 81.9, 78.9, 78.7, 78.4, 77.9, 74.4, 74.1, 70.8, 70.7 (2 × C-1' – C-5'), 62.4, 62.2 (2 × C-6'), 56.2, 56.1 (2 q, $^2J_{C\text{-}F}$ = 30.6 Hz in each, 2 × Py-C-6), 54.2, 54.0 (2 × Py-C-4), 30.8, 30.6 (2 × Py-C-5). ESI-MS positive mode (m/z): calcd for $C_{17}H_{22}F_3N_2O_5^+$ $[M+H]^+$: 391.2. Found: 391.3.

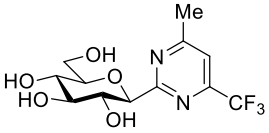
2-(β-D-Glucopyranosyl)-4,6-dimethylpyrimidine (10a)



A) From compound **2** (100 mg, 0.41 mmol) and the α,β-unsaturated β-chloroketone (58 mg, 0.50 mmol) obtained from pentane-2,4-dione[8] according to general procedure IV. Purified by column chromatography (9 : 1 $CHCl_3$-MeOH) to yield 69 mg (62 %) pale yellow syrup.

B) From compound **8a** (200 mg, 0.32 mmol) according to general procedure II. Reaction time: 3 h. Purified by column chromatography (5 : 1 EtOAc-MeOH) to yield 68 mg (79 %) colourless syrup. R_f = 0.34 (5 : 1 $CHCl_3$-MeOH); $[\alpha]_D$ = –62 (c 0.09, MeOH); ^{1}H NMR (400 MHz, CD_3OD) δ (ppm): 7.23 (1H, s, Py-H-5), 4.34 (1H, d, J = 9.5 Hz, H-1'), 3.87 (1H, dd, J = 12.1, 2.2 Hz, H-6'a), 3.75 (1H, pseudo t, J = 9.5, 9.2 Hz, H-2'), 3.72 (1H, dd, J = 12.1, 5.2 Hz, H-6'b), 3.55 (1H, pseudo t, J = 9.4, 9.2 Hz, H-3'), 3.51 (1H, pseudo t, J = 9.4, 9.4 Hz, H-4'), 3.44 (1H, ddd, J = 9.4, 5.2, 2.2 Hz, H-5'), 2.51 (6H, s, 2 × CH_3); ^{13}C NMR (100 MHz, CD_3OD) δ (ppm): 168.9 (2), 167.1 (Py-C-2, Py-C-4, Py-C-6), 120.9 (Py-C-5), 83.6, 82.4, 79.4, 74.7, 71.2 (C-1' – C-5'), 62.8 (C-6'), 23.6 (2) (2 × CH_3). ESI-MS positive mode (m/z): calcd for $C_{12}H_{19}N_2O_5^+$ $[M+H]^+$: 271.1. Found: 271.2.

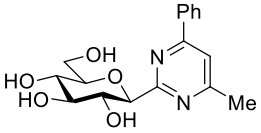
2-(β-D-Glucopyranosyl)-4-methyl-6-trifluoromethyl-pyrimidine (10b)



A) From compound **2** (100 mg, 0.41 mmol) and the α,β-unsaturated β-chloroketone (85 mg, 0.50 mmol) obtained from 1,1,1-trifluoropentane-2,4-dione[9] according to general procedure IV. Purified by column chromatography (9 : 1 $CHCl_3$-MeOH) to yield 84 mg (63 %) pale yellow syrup.

B) From compound **8b** (200 mg, 0.29 mmol) according to general procedure II. Reaction time: 6 h. Purified by column chromatography (5 : 1 EtOAc-MeOH) to yield 87 mg (92 %) colourless syrup. R_f = 0.36 (5 : 1 $CHCl_3$-MeOH); $[\alpha]_D$ = –32 (c 0.19, MeOH); ^{1}H NMR (400 MHz, CD_3OD) δ (ppm): 7.76 (1H, s, Py-H-5), 4.47 (1H, d, *J* = 9.7 Hz, H-1'), 3.89 (1H, pseudo t, *J* = 9.7, 9.2 Hz, H-2'), 3.88 (1H, dd, *J* = 12.1, 2.0 Hz, H-6'a), 3.71 (1H, dd, *J* = 12.1, 5.0 Hz, H-6'b), 3.56 (1H, pseudo t, *J* = 9.4, 9.2 Hz, H-3'), 3.52-3.47 (2H, m, H-4', H-5'), 2.68 (3H, s, CH_3); ^{13}C NMR (90 MHz, CD_3OD) δ (ppm): 172.9, 168.4 (Py-C-2, Py-C-4), 156.4 (q, $^2J_{C\text{-}F}$ = 35.7 Hz, Py-C-6), 125.2 (q, $^1J_{C\text{-}F}$ = 274.9 Hz, CF_3), 117.3 (q, $^3J_{C\text{-}F}$ = 2.4 Hz, Py-C-5), 84.2, 82.7, 79.4, 74.4, 71.4 (C-1' – C-5'), 62.9 (C-6'), 24.3 (CH_3). ESI-MS positive mode (m/z): calcd for $C_{12}H_{16}F_3N_2O_5^+$ $[M+H]^+$: 325.10. Found: 325.08.

2-(β-D-Glucopyranosyl)-4-methyl-6-phenylpyrimidine (10c)



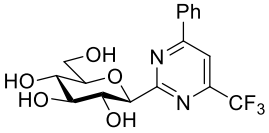
A) From compound **2** (100 mg, 0.41 mmol) and the α,β-unsaturated β-chloroketone (89 mg, 0.50 mmol) obtained from 1-phenylbutane-1,3-dione[10] according to general procedure IV. The crude product was purified by column chromatography (19 : 1 $CHCl_3$-MeOH) to yield 95 mg

(69 %) pale yellow syrup. R_f = 0.50 (5 : 1 $CHCl_3$-MeOH); $[\alpha]_D$ = –42 (c 0.12, MeOH); ^{1}H NMR (400 MHz, CD_3OD) δ (ppm): 8.28-8.26 (2H, m, Ph), 7.90 (1H, s, Py-H-5), 7.62-7.60 (3H, m, Ph), 4.46 (1H, d, *J* = 9.5 Hz, H-1'), 4.04 (1H, pseudo t, *J* = 9.5, 9.2 Hz, H-2'), 3.88 (1H, dd, *J* = 12.1, 1.9 Hz, H-6'a), 3.69 (1H, dd, *J* = 12.1, 5.0 Hz, H-6'b), 3.57 (1H, pseudo t, *J* = 9.4, 9.2 Hz, H-3'), 3.51-3.45 (2H, m, H-4', H-5'), 2.66 (3H, s, CH_3); ^{13}C NMR (100 MHz, CD_3OD + 1 drop of DMSO-d_6) δ (ppm): 169.6, 167.6, 165.0 (Py-C-2, Py-C-4, Py-C-6), 137.9, 132.3, 130.2 (2), 128.6 (2) (Ph), 116.8 (Py-C-5), 84.8, 82.9, 79.6, 74.2, 71.6 (C-1' – C-5'), 62.9 (C-6'), 24.4 (CH_3). ESI-MS positive mode (m/z): calcd for $C_{17}H_{21}N_2O_5^+$ $[M+H]^+$: 333.14. Found: 333.17.

B) From compound **8c** (200 mg, 0.29 mmol) according to general procedure II. Reaction time: 6 h. Purification by column chromatography (5 : 1 EtOAc-MeOH, then 1 : 1 EtOAc-MeOH) yielded the title compound **10c** as the first (35 mg, 36 %) and compound **9c** as the second fraction (26 mg, 27 %). Compound characterization data for both products were identical with those described above.

C) 2,3,4,6-Tetra-*O*-benzoyl-β-D-glucopyranosyl cyanide[3] (**13**, 1.00 g, 1.65 mmol) was converted into compounds **2** and **12** via imidate **11** in a two-step procedure as described for compound **2** in method **B**. Without column chromatographic purification the crude mixture of **2** and **12** was dissolved in anhydrous DMF (10 mL), K_2CO_3 (0.91 g, 6.61 mmol) and activated molecular sieves (4 Å) were added. The reaction mixture was then cooled to 0 °C and the freshly prepared α,β-unsaturated β-chloroketone (358 mg, 1.98 mmol) obtained from 1-phenylbutane-1,3-dione[10] was added. The reaction mixture was allowed to warm up to rt and the stirring was continued. After completion of the reaction (1 d) monitored by TLC (7 : 3 $CHCl_3$-MeOH) the inorganic precipitates were filtered off, washed with MeOH, and the solvent was evaporated under reduced pressure. Column chromatographic purification of the residual oil gave compound **14c** as the first (20 mg, 3.9 % for three steps) and the title compound **10c** as the second fraction (163 mg, 30 % for three steps).

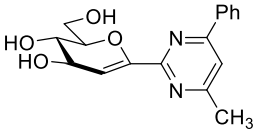
2-(β-D-Glucopyranosyl)-4-phenyl-6-trifluoromethyl-pyrimidine (10d)



A) From compound **2** (100 mg, 0.41 mmol) and the α,β-unsaturated β-chloroketone (116 mg, 0.50 mmol) obtained from 4,4,4-trifluoro-1-phenylbutane-1,3-dione[9] according to general procedure IV. Purified by column chromatography (19 : 1 $CHCl_3$-MeOH) to yield 120 mg (75 %) pale yellow syrup. R_f = 0.56 (5 : 1 $CHCl_3$-MeOH); $[\alpha]_D$ = –33 (c 0.15, MeOH); ^{1}H NMR (400 MHz, CD_3OD) δ (ppm): 8.27 (2H, d, *J* = 7.5 Hz, Ph), 8.25 (1H, s, Py-H-5), 7.60-7.52 (3H, m, Ph), 4.60 (1H, d, *J* = 9.7 Hz, H-1'), 4.10 (1H, pseudo t, *J* = 9.7, 9.3 Hz, H-2'), 3.93 (1H, dd, *J* = 12.1, 1.9 Hz, H-6'a), 3.75 (1H, dd, *J* = 12.1, 5.1 Hz, H-6'b), 3.63 (1H, pseudo t, *J* = 9.4, 9.3 Hz, H-3'), 3.58-3.54 (2H, m, H-4', H-5'); ^{13}C NMR (100 MHz, CD_3OD) δ (ppm): 168.8, 168.7 (Py-C-2, Py-C-4), 157.5 (q, $^2J_{C\text{-}F}$ = 35.7 Hz, Py-C-6), 136.6, 133.2, 130.2 (2), 128.8 (2) (Ph), 122.2 (q, $^1J_{C\text{-}F}$ = 274.6 Hz, CF_3), 113.1 (q, $^3J_{C\text{-}F}$ = 2.0 Hz, Py-C-5), 84.5, 82.8, 79.5, 74.3, 71.6 (C-1' – C-5'), 62.9 (C-6'). ESI-MS positive mode (m/z): calcd for $C_{17}H_{18}F_3N_2O_5^+$ $[M+H]^+$: 387.12. Found: 387.14.

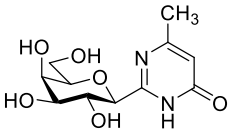
B) From compound **8d** (200 mg, 0.27 mmol) according to general procedure II. Reaction time: 6 h. Purification by column chromatography (5 : 1 EtOAc-MeOH, then 1 : 1 EtOAc-MeOH) yielded the title compound **10d** as the first (20 mg, 19 %) and compound **9d** as the second fraction (45 mg, 43 %). Compound characterization data for both products were identical with those described above.

2-(2'-Deoxy-D-*arabino*-hex-1'-enopyranosyl)-4-methyl-6-phenylpyrimidine (14c)



The title compound was obtained as by-product upon formation of **10c** starting from glucosyl cyanide **13** (see synthetic details of compound **10c**, method **C**). R_f = 0.67 (4 : 1 $CHCl_3$-MeOH); $[\alpha]_D$ = +138 (c 0.12, MeOH); ^{1}H NMR (400 MHz, CD_3OD) δ (ppm): 8.17-8.14 (2H, m, Ph), 7.73 (1H, s, Py-H-5), 7.53-7.50 (3H, m, Ph), 6.43 (1H, d, *J* = 2.6 Hz, H-2'), 4.39 (1H, dd, *J* = 7.5, 2.6 Hz, H-3'), 4.06 (1H, dd, *J* = 12.1, 1.7 Hz, H-6'a), 3.98 (1H, ddd, *J* = 9.8, 6.2, 1.7 Hz, H-5'), 3.92 (1H, dd, *J* = 12.1, 6.2 Hz, H-6'b), 3.66 (1H, dd, *J* = 9.8, 7.5 Hz, H-4'), 2.60 (3H, s, CH_3); ^{13}C NMR (100 MHz, CD_3OD) δ (ppm): 169.2, 165.4, 161.1 (Py-C-2, Py-C-4, Py-C-6), 150.6 (C-1'), 137.7, 132.3, 130.0 (2), 128.4 (2) (Ph), 116.4 (Py-C-5), 109.2 (C-2'), 81.7, 71.3, 70.6 (C-3' – C-5'), 62.7 (C-6'), 23.8 (CH_3). ESI-MS positive mode (m/z): calcd for $C_{17}H_{19}N_2O_4^+$ $[M+H]^+$: 315.13. Found: 315.17.

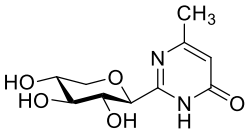
2-(β-D-Galactopyranosyl)-6-methylpyrimidin-4(3*H*)-one (19)



Prepared from cyanide **15**[4] (1.00 g, 2.80 mmol) according to general procedure VI. Purified by column chromatography (4 : 1 $CHCl_3$-MeOH) to yield 537 mg (70 % for three steps) white amorphous solid. R_f = 0.33 (7 : 3 $CHCl_3$-MeOH); $[\alpha]_D$ = +27 (c 0.28, H_2O); ^{1}H NMR (360 MHz, CD_3OD) δ (ppm): 6.22 (1H, s, Py-H-5), 4.10 (1H, d, *J* = 9.6 Hz, H-1'), 3.93 (1H, d, *J* = 3.3 Hz, H-4'), 3.83 (1H, pseudo t, *J* = 9.6, 9.2 Hz, H-2'), 3.81-3.67 (3H, m, H-5', H-6'a, H-6'b), 3.59 (1H, dd, *J* = 9.2, 3.2 Hz, H-3'), 2.30 (3H, s, CH_3); ^{13}C NMR (90 MHz, DMSO-d_6) δ (ppm): 163.5, 162.9, 158.8 (Py-C-2, Py-C-4, Py-C-6), 111.5 (Py-C-5), 80.3, 80.1, 74.3, 69.2,

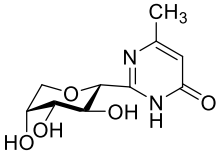
69.1 (C-1' – C-5'), 60.7 (C-6'), 23.2 (CH_3). ESI-MS positive mode (m/z): calcd for $C_{11}H_{17}N_2O_6^+$ $[M+H]^+$: 273.1. Found: 273.2.

2-(β-D-Xylopyranosyl)-6-methylpyrimidin-4(3*H*)-one (20)



Prepared from cyanide **16**[5] (1.00 g, 2.12 mmol) according to general procedure VI. Purified by column chromatography (4 : 1 $CHCl_3$-MeOH) to yield 141 mg (27 % for three steps) white amorphous solid. R_f = 0.49 (7 : 3 $CHCl_3$-MeOH); $[\alpha]_D$ = –14 (c 0.25, H_2O); ^{1}H NMR (360 MHz, CD_3OD) δ (ppm): 6.19 (1H, s, Py-H-5), 4.01 (1H, d, *J* = 9.6 Hz, H-1'), 4.00 (1H, dd, *J* = 11.1, 5.5 Hz, H-5'$_{eq}$), 3.64-3.57 (2H, m, H-4', H-2' or H-3'), 3.39 (1H, pseudo t, *J* = 9.1, 9.0 Hz, H-2' or H-3'), 3.29 (1H, dd, *J* = 11.1, 10.0 Hz, H-5'$_{ax}$), 2.27 (3H, s, CH_3); ^{13}C NMR (90 MHz, CD_3OD) δ (ppm): 167.6, 165.0, 161.1 (Py-C-2, Py-C-4, Py-C-6), 112.1 (Py-C-5), 81.3, 79.2, 73.9, 71.3, 70.8 (C-1' – C-5'), 22.8 (CH_3). ESI-MS positive mode (m/z): calcd for $C_{10}H_{15}N_2O_5^+$ $[M+H]^+$: 243.10. Found: 243.17.

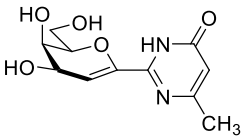
2-(α-D-Arabinopyranosyl)-6-methylpyrimidin-4(3*H*)-one (21)



Prepared from cyanide **17**[6] (1.00 g, 3.51 mmol) according to general procedure VI. Purified by crystallization from MeOH to yield 361 mg (43 % for three steps) white solid. R_f = 0.46 (7 : 3 $CHCl_3$-MeOH); Mp: 153-154 ºC. $[\alpha]_D$ = –3 (c 0.20, H_2O); ^{1}H NMR (360 MHz, CD_3OD) δ (ppm): 6.23 (1H, s, Py-H-5), 4.01 (1H, d, *J* = 9.6 Hz, H-1'), 4.00 (1H, dd, *J* = 12.5, 2.3 Hz, H-5'$_{eq}$), 3.93-3.92 (1H, m, H-4'), 3.81 (1H, pseudo t, *J* = 9.6, 9.2 Hz, H-2'), 3.72 (1H, dd, *J* = 12.5,

1.1 Hz, H-5'$_{ax}$), 3.59 (1H, dd, *J* = 9.2, 3.3 Hz, H-3'), 2.30 (3H, s, CH_3); ^{13}C NMR (90 MHz, DMSO-d_6) δ (ppm): 164.0, 162.3, 158.2 (Py-C-2, Py-C-4, Py-C-6), 111.7 (Py-C-5), 80.9, 73.7, 69.1, 68.9 (C-1' – C-4'), 70.9 (C-5'), 23.3 (CH_3). ESI-MS positive mode (m/z): calcd for $C_{10}H_{15}N_2O_5^+$ $[M+H]^+$: 243.10. Found: 243.17.

2-(2'-Deoxy-D-*lyxo*-hex-1'-enopyranosyl)-6-methylpyrimidin-4(3*H*)-one (22)



Prepared from cyanide **18**[7] (500 mg, 1.68 mmol) according to general procedure VI. The product which precipitated from the reaction mixture upon neutralization with glacial AcOH was filtered and washed with MeOH to yield 403 mg (94 % for three steps) white solid. R_f = 0.62 (7 : 3 $CHCl_3$-MeOH); Mp: decomposition above 200 ºC, no melting till 360 ºC. $[\alpha]_D$ = +68 (c 0.14, DMSO); ^{1}H NMR (360 MHz, DMSO-d_6) δ (ppm): 6.10 (1H, s, Py-H-5), 5.94 (1H, broad signal, H-2'), 5.05-4.71 (broad signals, OH), 4.40 (1H, broad signal, H-3' or H-4'), 4.01 (1H, dd, $J_{5',6'a}$ = 8.5), 3.87 (1H, dd, $J_{6'a,6'b}$ = 12.1 Hz, H-6'a), 3.71 (1H, broad d, $J_{3',4'}$ = 4 Hz, H-3' or H-4'), 3.51 (1H, dd, $J_{5',6'b}$ = 2.3 Hz, H-6'b), 2.19 (3H, s, CH_3). ^{13}C NMR (90 MHz, DMSO-d_6) δ (ppm): 163.9, 162.0, 151.2 (Py-C-2, Py-C-4, Py-C-6), 143.4 (C-1'), 110.9 (Py-C-5), 109.0 (C-2'), 80.1, 64.6, 64.0 (C-3' – C-5'), 61.7 (C-6'), 23.4 (CH_3). ESI-MS positive mode (m/z): calcd for $C_{11}H_{15}N_2O_5^+$ $[M+H]^+$: 255.10. Found: 255.17.

2. Enzyme assays

Glycogen phoshorylase *b* was obtained from rabbit skeletal muscle by a slight modification (application of 2-mercaptoethanol instead of L-cysteine, and recrystallization at least three times before use) of the purification protocol developed by Fischer and Krebs.[11] The kinetic measurements were carried out in the direction of glycogen synthesis as described earlier[12] with maximal inhibitor concentrations of 625 μM.

The glycosidase enzymes used were purchased from Sigma-Aldrich. Typically, (in the case of glycosidases) a 10 μL aliquot for each of different inhibitor stock solutions was mixed with 370 μL of the buffer and 20 μL enzyme stock solution in a plastic UV cuvette. After equilibration at 37 °C for 5 min, a 100 μL aliquot of the substrate stock solution was added. The resulting solutions were thoroughly mixed, and the change in absorbance was followed at 400 nm over 240 s in 2 s intervals using the Parallel Kinetics Analysis program of a JASCO V550 (JASCO Tokyo, Japan) spectrophotometer. Progress curves were plotted and fitted to a straight line. ΔA/min values, proportional to initial rate, were considered to be enzyme activities. In a control experiment, the aliquot of the inhibitor solution was replaced by the same amount of buffer. The initial rate data for the enzymatic substrate hydrolysis in presence and absence of inhibitor were transferred into percentages of overall inhibition, and plotted against the inhibitor concentration in logarithmic scale for IC_{50} determination.

Specific assay conditions for each glycosidase enzyme:

β-Glucosidase from almonds (Sigma-Aldrich): 2.5 mM PNP-β-Glc substrate in citrate-phosphate buffer pH 5.2 using 0.25 mg/mL of enzyme.

α-Glucosidase from *Saccharomyces cerevisiae* (Sigma-Aldrich): 0.5 mM PNP-α-Glc in glycerophosphate buffer pH 6.9 using 0.02 mg/mL of enzyme.

Bovine liver β-galactosidase (Sigma-Aldrich): 1 mM PNP-β-Gal in citrate-phosphate buffer pH 7.3 using 0.12 mg/mL of enzyme.

3. References

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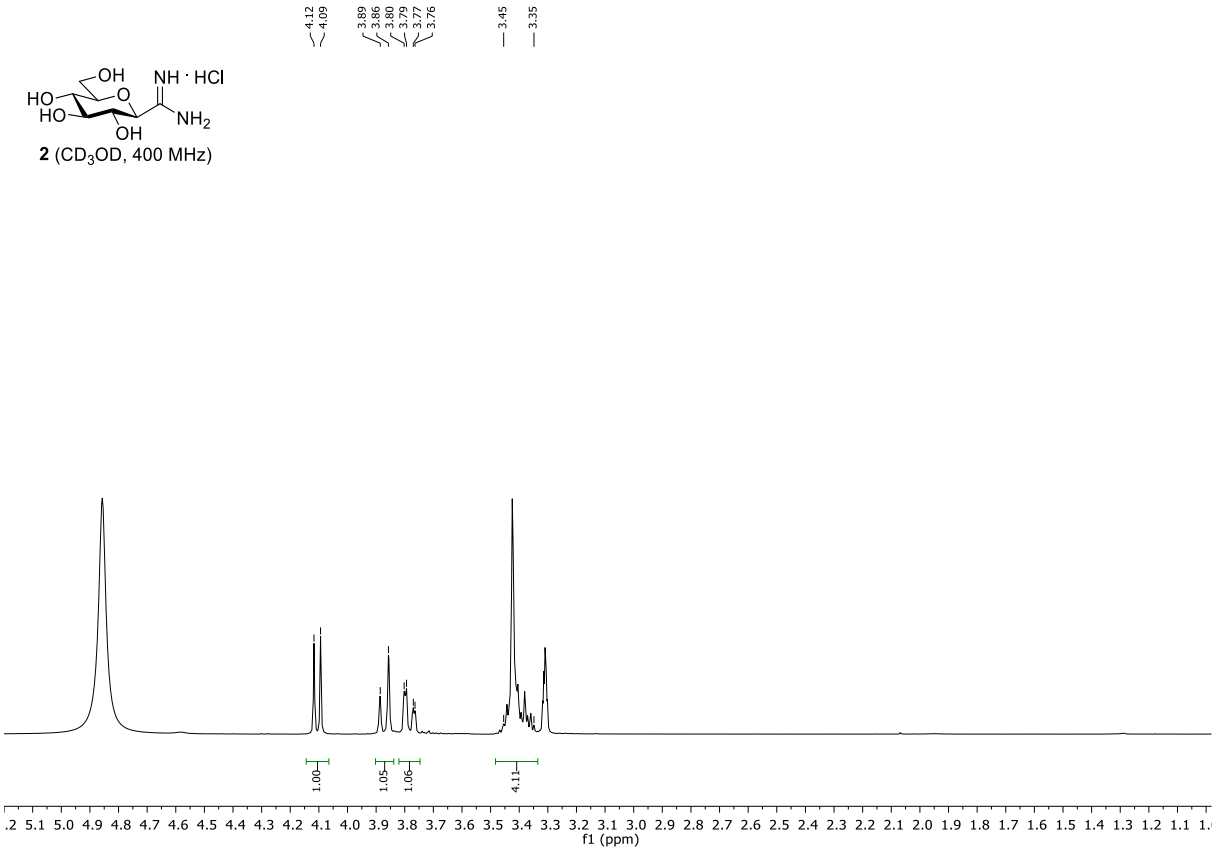
4. Copies of NMR and IR spectra of the new compounds



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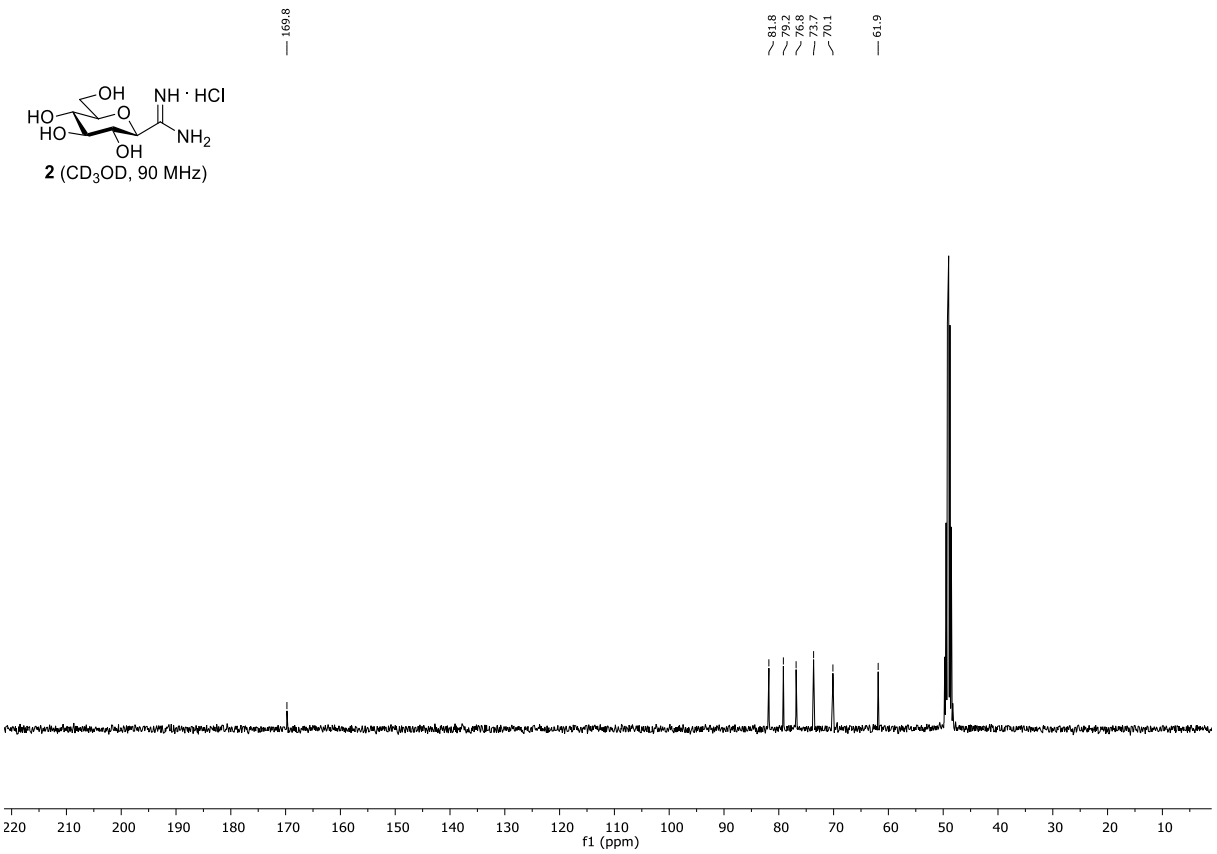

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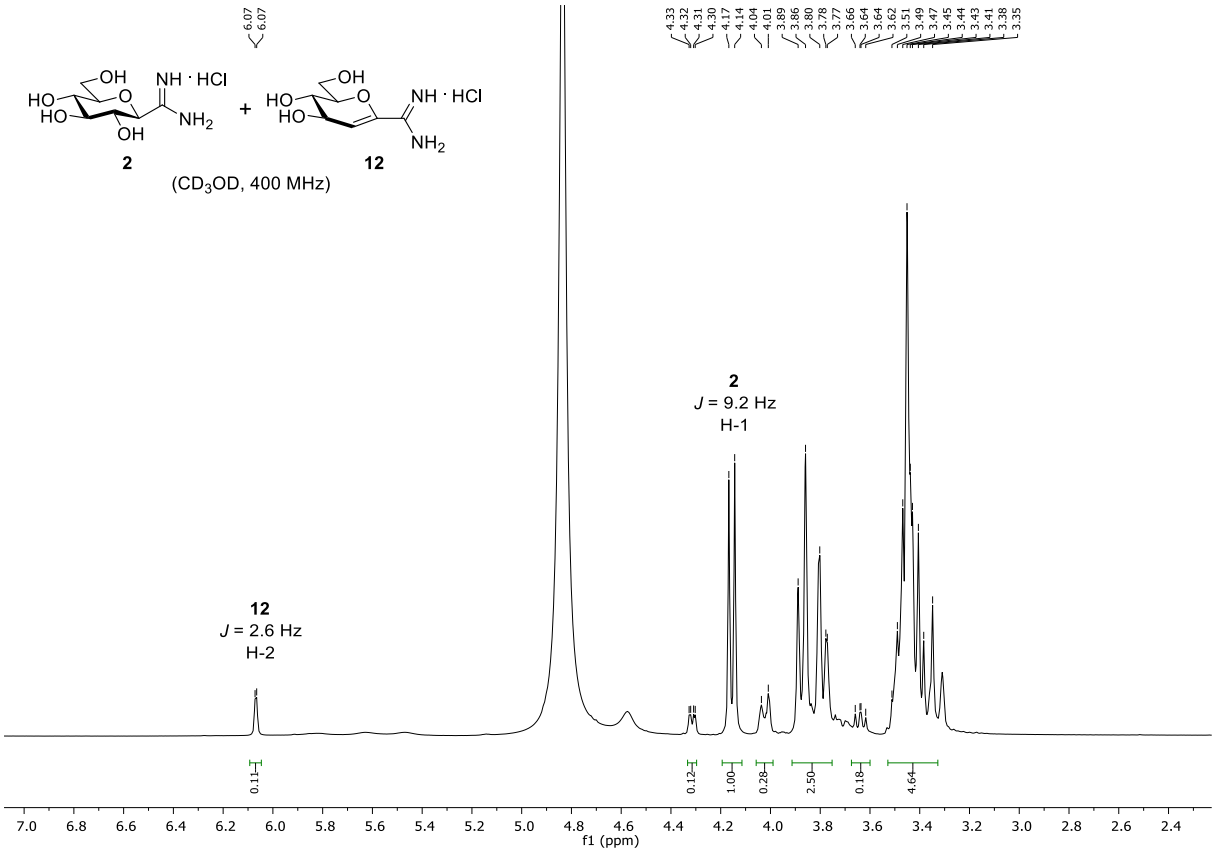
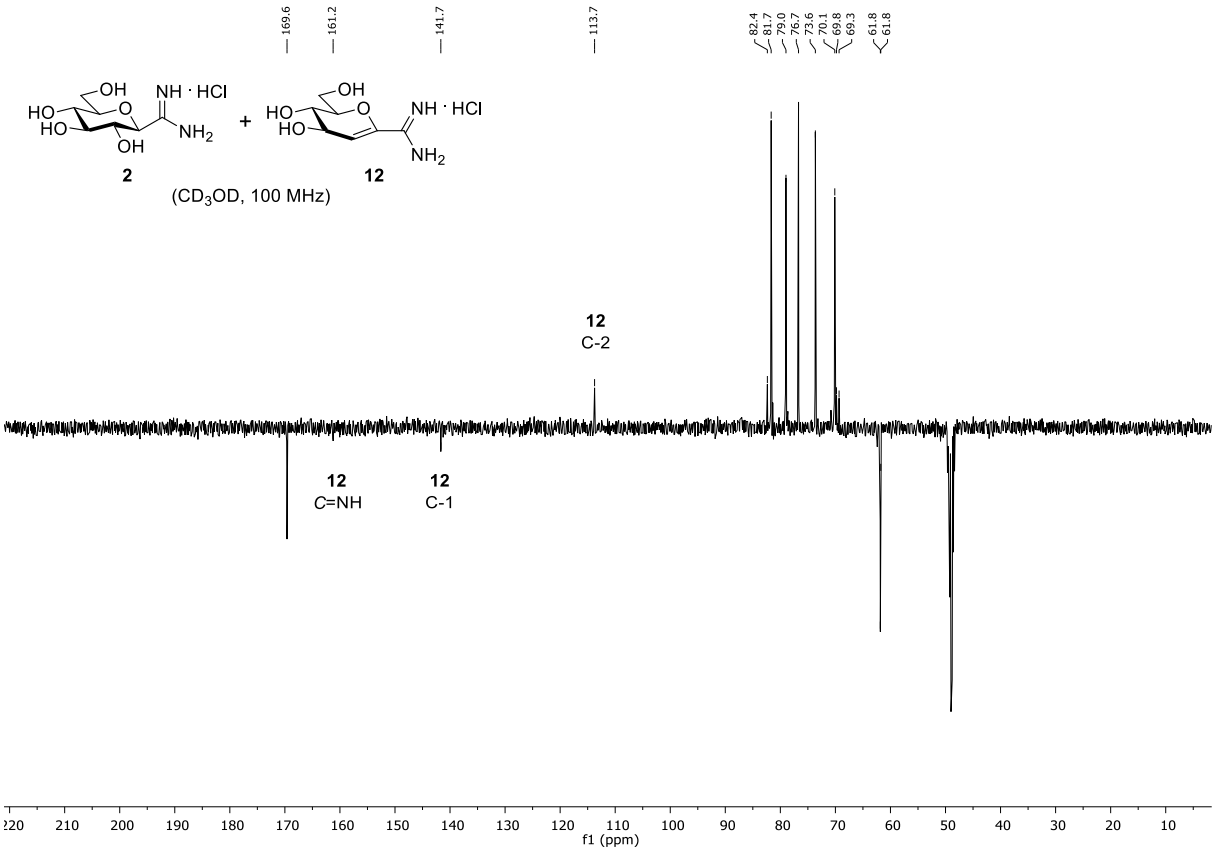
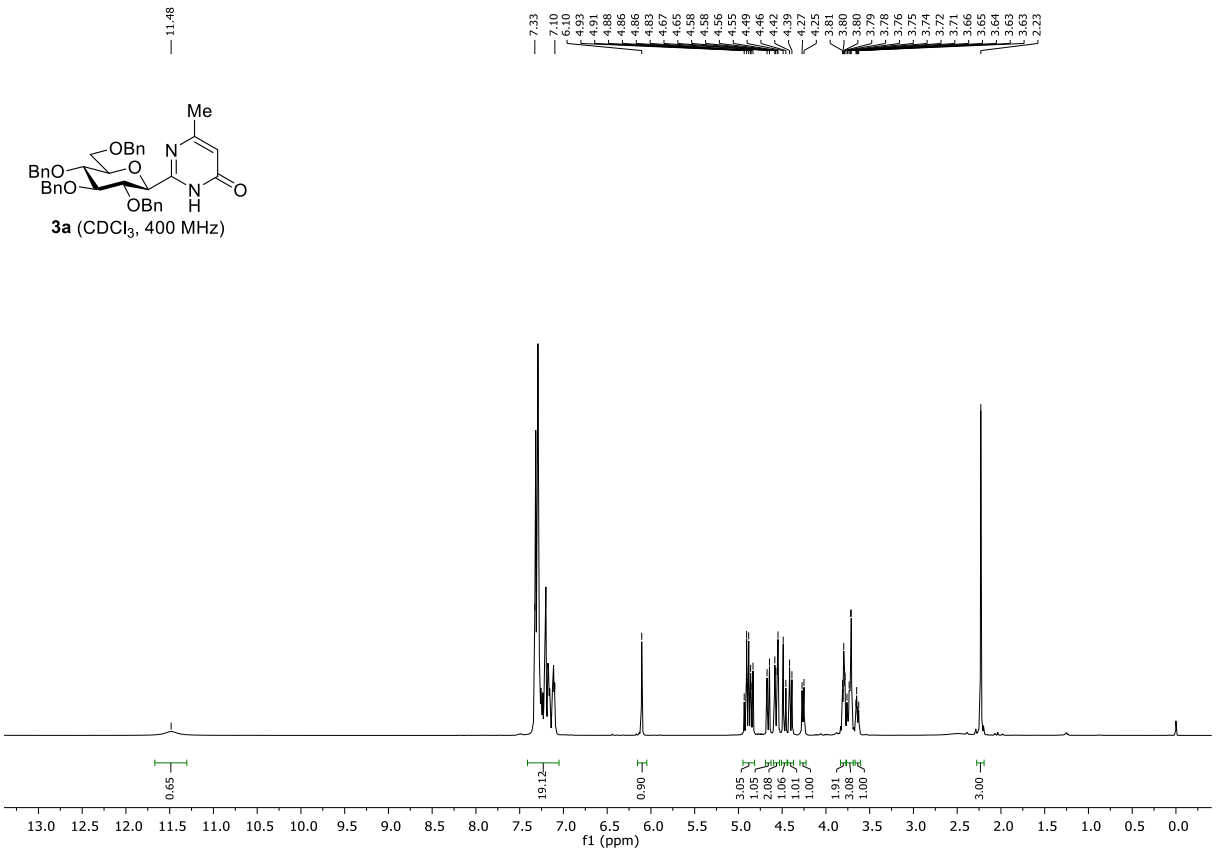

6.07
6.07
4.33
4.32
4.31
4.30
4.17
4.14
4.04
4.01
3.89
3.86
3.80
3.78
3.77
3.66
3.64
3.64
3.62
3.51
3.49
3.47
3.45
3.44
3.43
3.41
3.38
3.35
OH
NH · HCl
HO
HO
O
NH2
OH
2
+
OH
NH · HCl
HO
HO
O
NH2
12
(CD3OD, 400 MHz)
2
J = 9.2 Hz
H-1
12
J = 2.6 Hz
H-2
0.11
0.12
1.00
0.28
2.50
0.18
4.64
7.0
6.8
6.6
6.4
6.2
6.0
5.8
5.6
5.4
5.2
5.0
4.8
4.6
4.4
4.2
4.0
3.8
3.6
3.4
3.2
3.0
2.8
2.6
2.4
f1 (ppm)


169.6
161.2
141.7
113.7
82.4
81.7
79.0
76.7
75.6
70.1
69.8
69.3
61.8
61.8
OH
NH · HCl
HO
HO
O
NH2
OH
2
+
OH
NH · HCl
HO
HO
O
NH2
12
(CD3OD, 100 MHz)
12
C-2
12
C=NH
12
C-1
220
210
200
190
180
170
160
150
140
130
120
110
100
90
80
70
60
50
40
30
20
10
f1 (ppm)


11.48
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7.10
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4.91
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4.86
4.83
4.67
4.65
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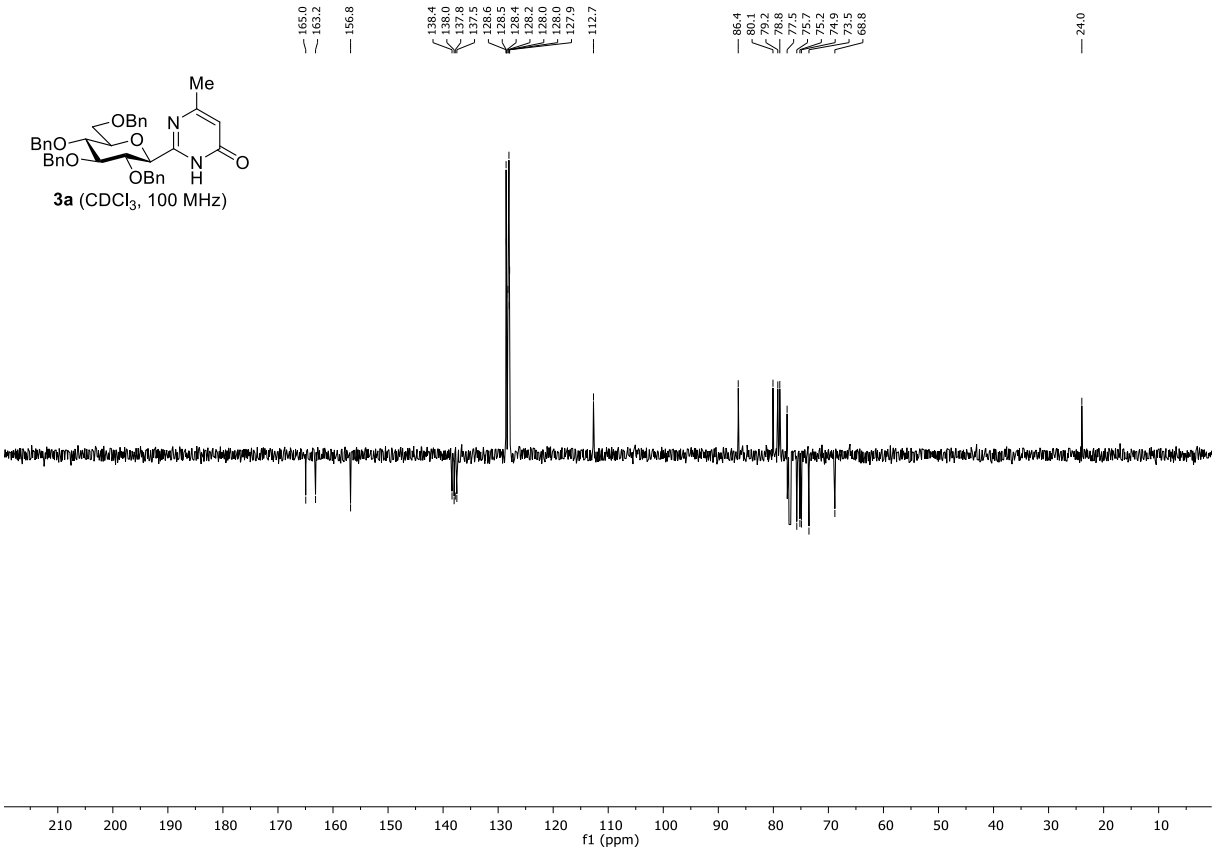
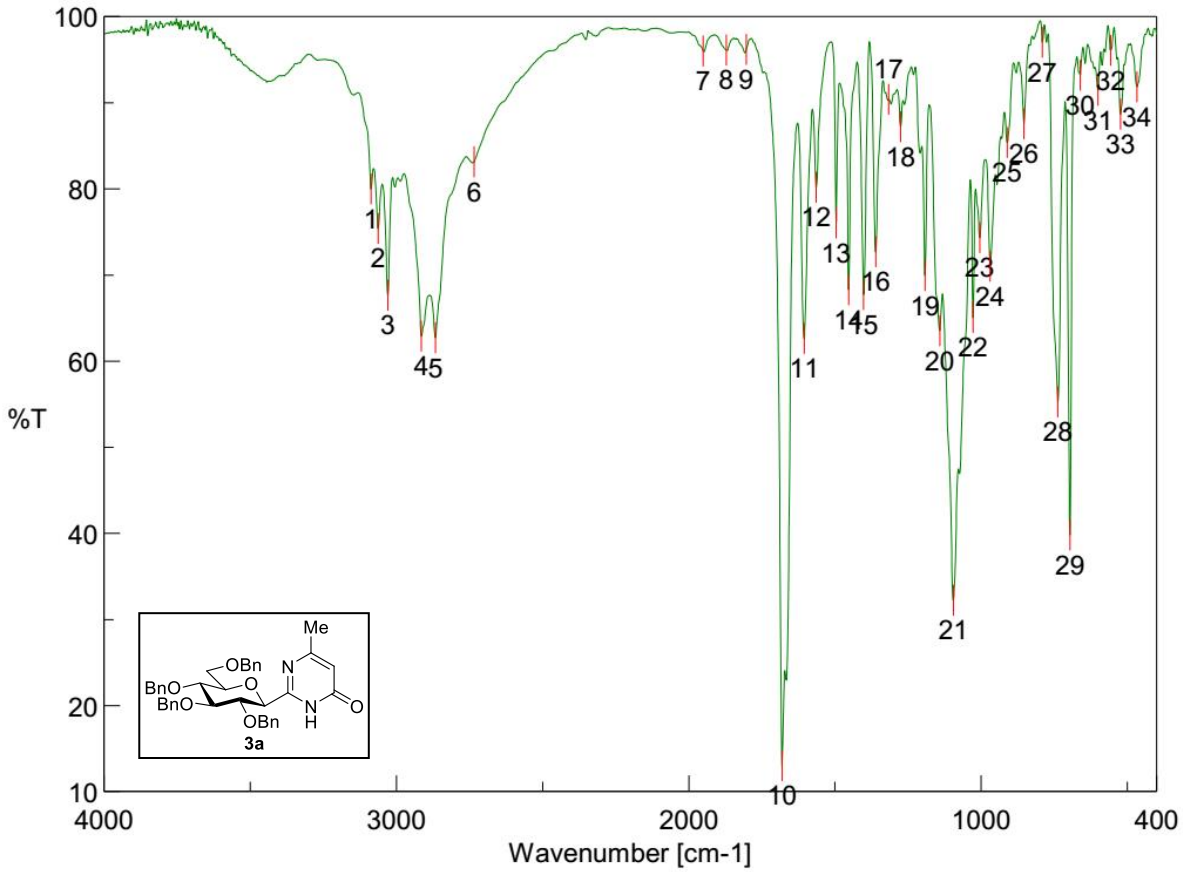
4.58
4.56
4.55
4.49
4.46
4.42
4.39
4.27
4.25
3.81
3.80
3.80
3.79
3.78
3.76
3.75
3.74
3.72
3.71
3.66
3.65
3.64
3.63
3.63
2.23
Me
OBn
N
BnO
O
BnO
N
O
OBn
H
3a (CDCl3, 400 MHz)
0.65
19.12
0.90
3.05
1.05
2.08
1.06
1.01
1.00
1.91
3.08
1.00
3.00
13.0 12.5 12.0 11.5 11.0 10.5 10.0 9.5 9.0 8.5 8.0 7.5 7.0 6.5 6.0 5.5 5.0 4.5 4.0 3.5 3.0 2.5 2.0 1.5 1.0 0.5 0.0
f1 (ppm)


165.0
163.2
156.8
138.4
138.0
137.8
137.5
128.6
128.5
128.4
128.2
128.0
128.0
127.9
112.7
86.4
80.1
79.2
78.8
77.5
75.7
75.2
74.9
73.5
68.8
24.0
Me
OBn
N
BnO
O
BnO
N
O
OBn
H
3a (CDCl3, 100 MHz)
210 200 190 180 170 160 150 140 130 120 110 100 90 80 70 60 50 40 30 20 10
f1 (ppm)



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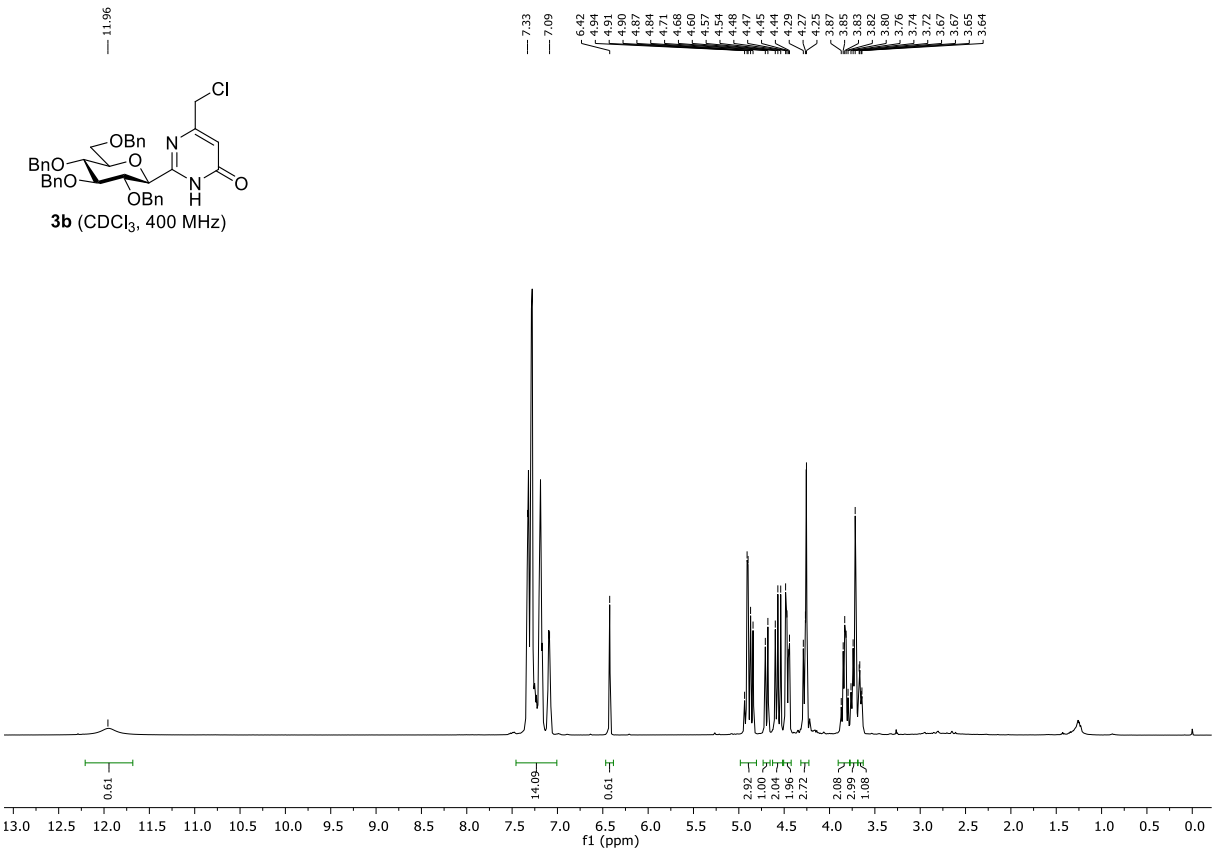
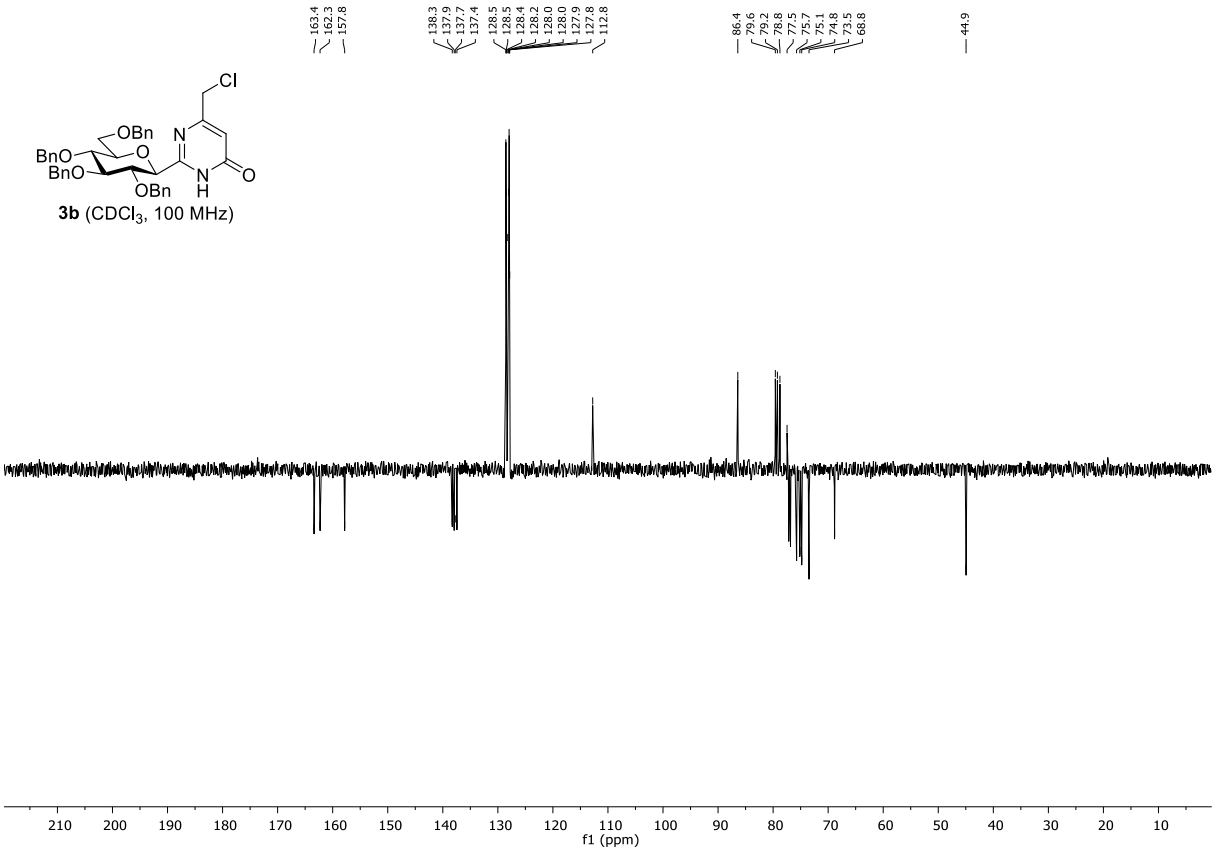
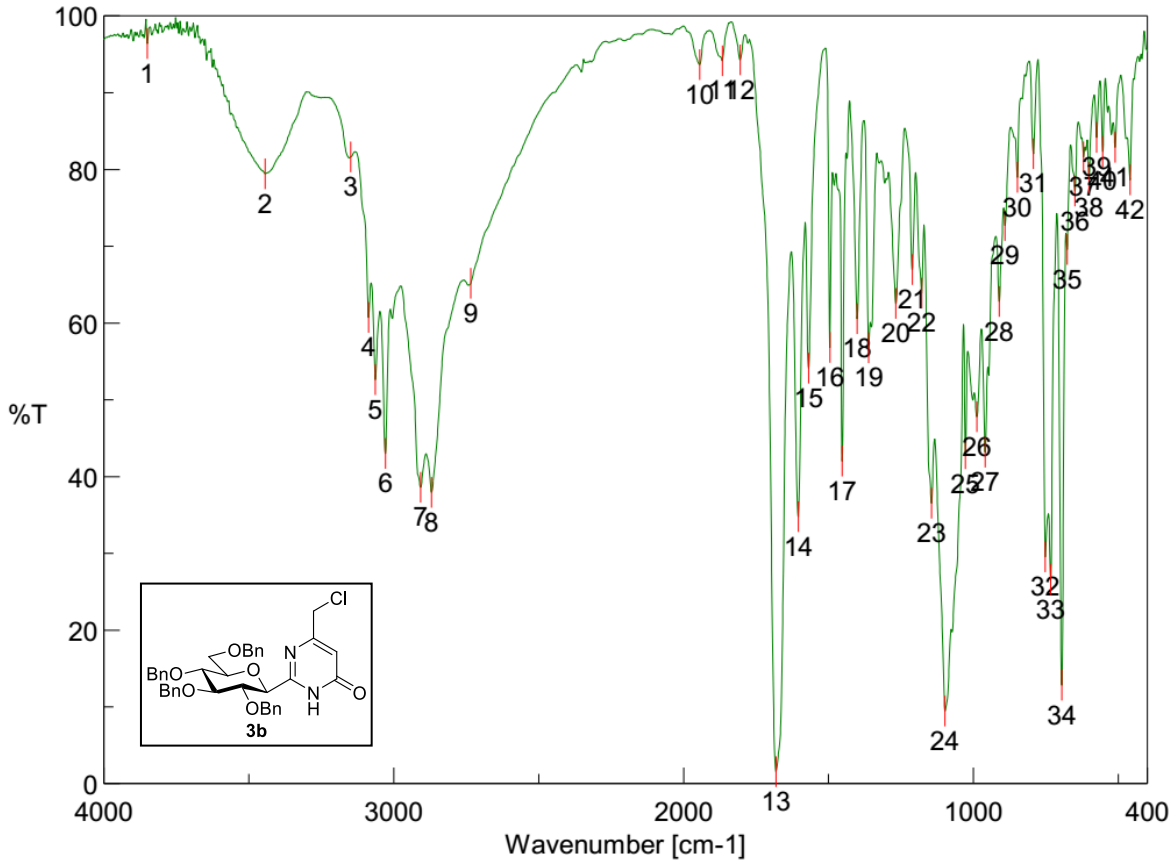
5	2866.67	62.7027	6	2734.57	83.1234
7	1950.64	95.9811	8	1871.58	96.1086
9	1803.12	96.1785	10	1681.62	12.9951
11	1605.45	62.598	12	1563.99	80.1732
13	1496.49	76.0209	14	1453.1	68.2782
15	1402	67.7107	16	1360.53	72.6788
17	1316.18	90.3765	18	1275.68	87.2047
19	1191.79	69.9142	20	1141.65	63.5128
21	1095.37	32.1777	22	1027.87	65.0415
23	1004.73	74.3133	24	969.055	71.0058
25	911.201	85.3616	26	853.347	87.536
27	790.671	97.0056	28	737.639	55.2576
29	696.177	39.7771	30	661.464	93.2034
31	600.717	91.426	32	557.327	96.0588
33	523.579	88.6547	34	466.689	91.8324



3b ($CDCl_3$, 400 MHz)



3b ($CDCl_3$, 100 MHz)



No.	Position	Intensity	No.	Position	Intensity
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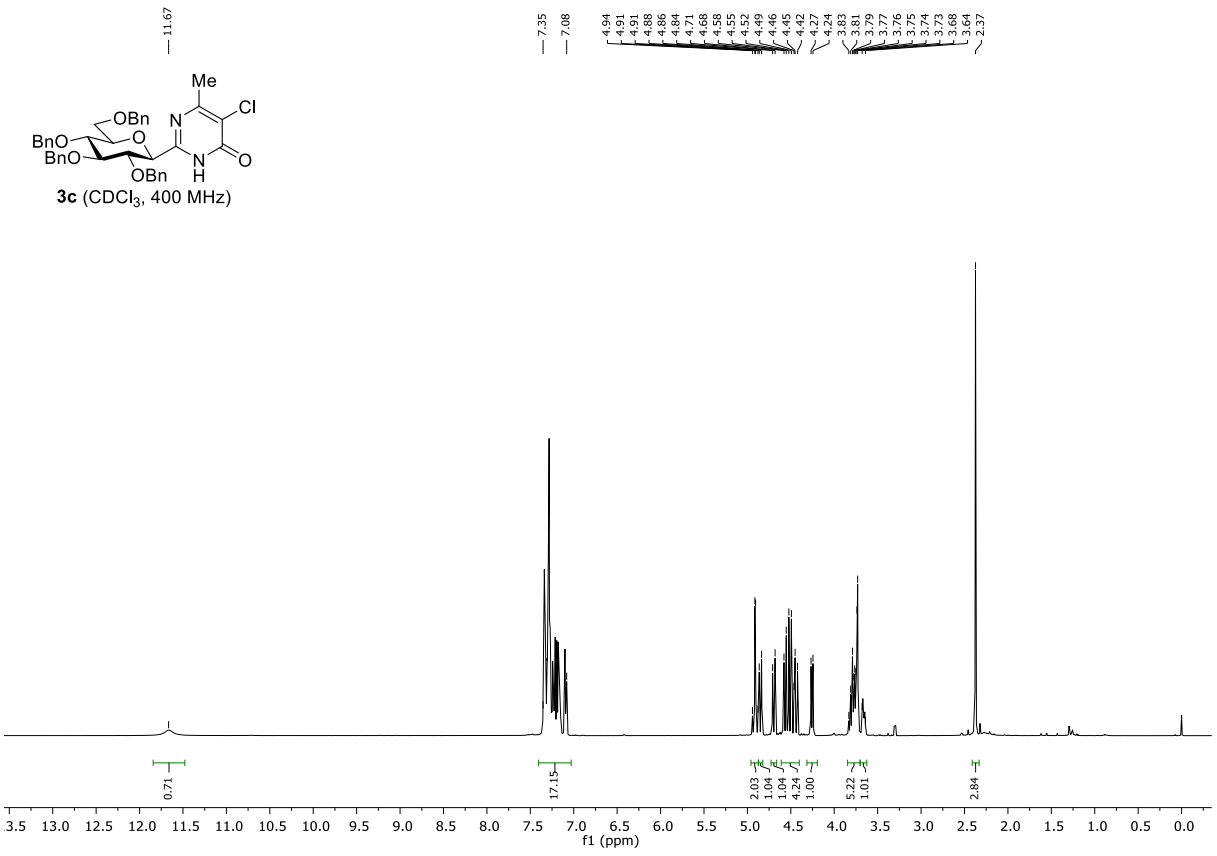
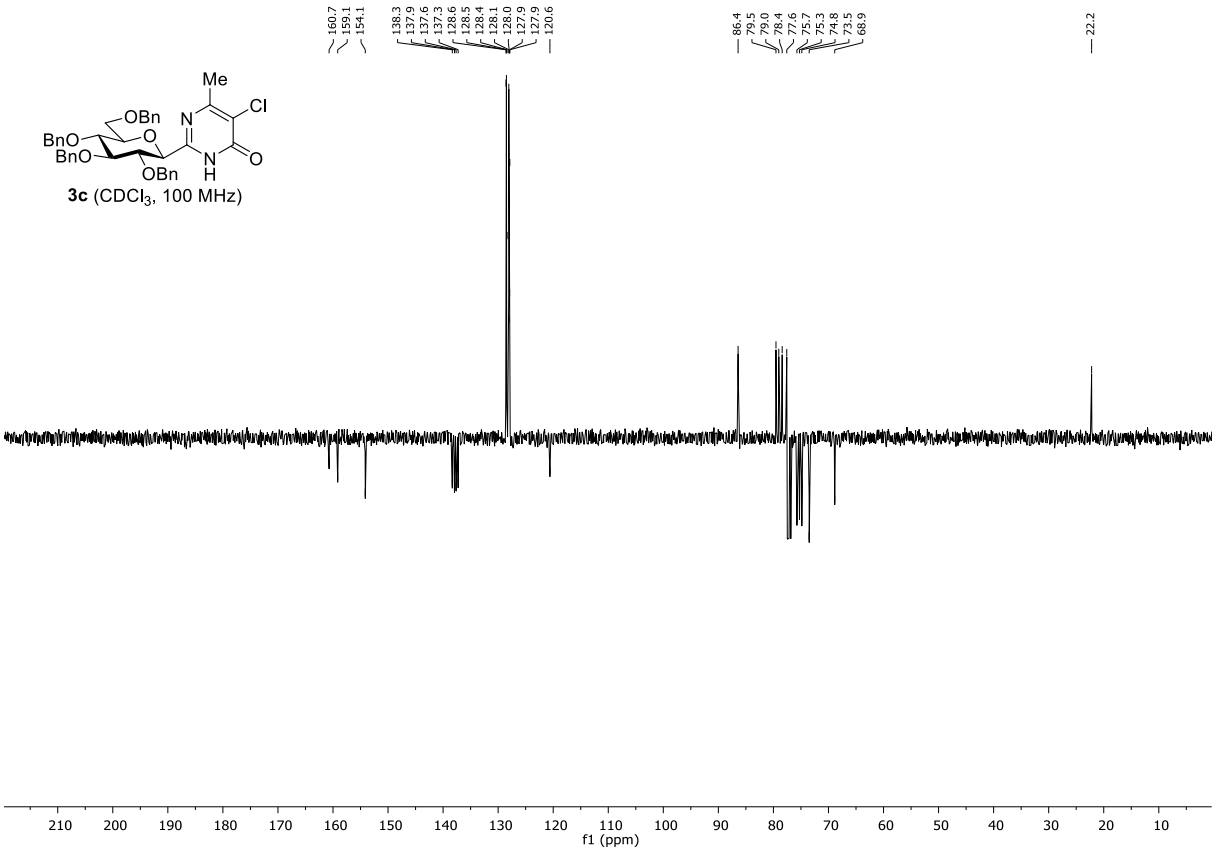
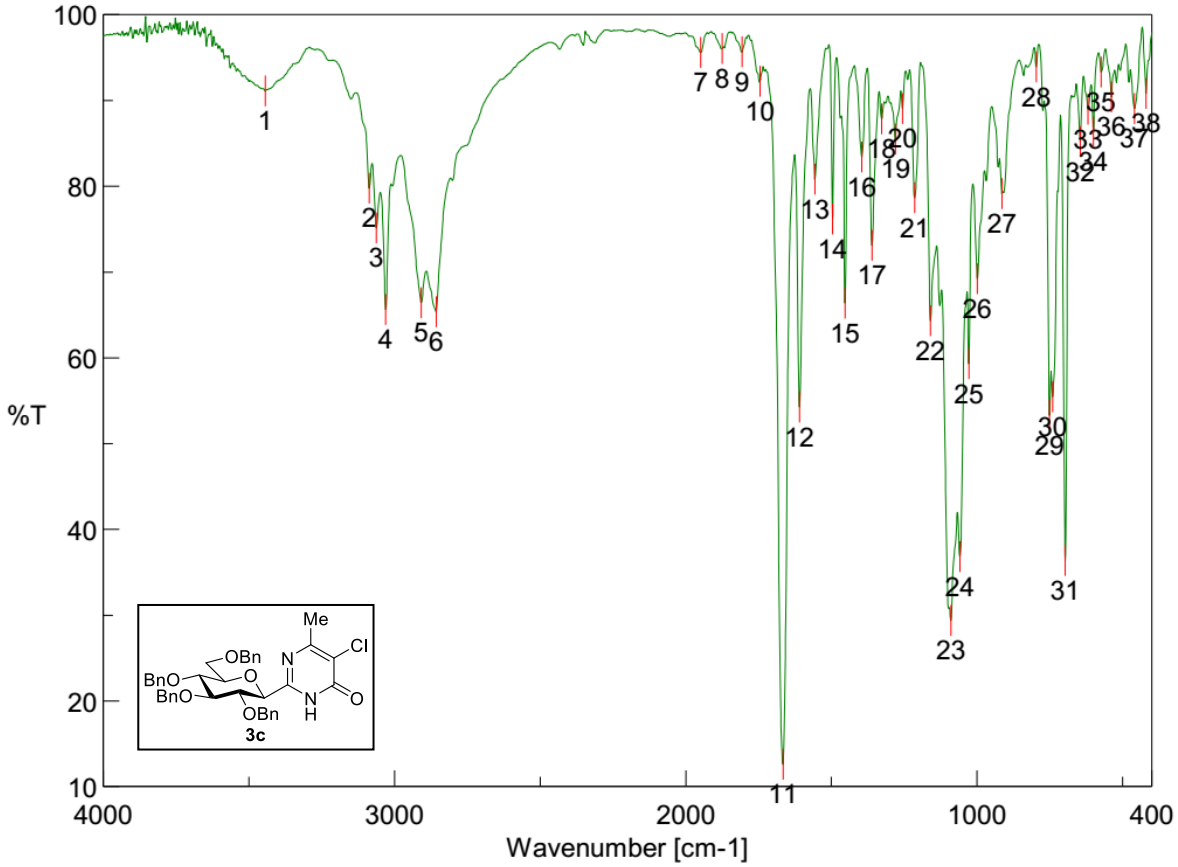
5	3063.37	52.6077	6	3028.66	42.9912
7	2907.16	38.5732	8	2869.56	37.9283
9	2734.57	65.1576	10	1944.86	93.643
11	1866.76	94.1525	12	1805.05	94.2474
13	1681.62	1.53377	14	1604.48	34.747
15	1568.81	54.0821	16	1495.53	56.7883
17	1453.1	41.9976	18	1401.03	60.5379
19	1361.5	56.7725	20	1267.97	62.5433
21	1211.08	66.93	22	1178.29	63.851
23	1144.55	36.5252	24	1098.26	9.42294
25	1027.87	42.9657	26	988.339	47.7587
27	959.412	43.1435	28	911.201	62.801
29	890.952	72.6992	30	848.525	78.9534
31	793.564	82.0339	32	752.102	29.5272
33	733.782	26.5758	34	695.212	12.8177
35	676.892	69.5706	36	649.893	77.1929
37	620.002	81.6041	38	601.682	78.9155
39	575.647	84.1764	40	554.434	82.3439
41	511.044	82.872	42	459.939	78.6408



3c ($CDCl_3$, 400 MHz)



3c ($CDCl_3$, 100 MHz)



No.	Position	Intensity	No.	Position	Intensity
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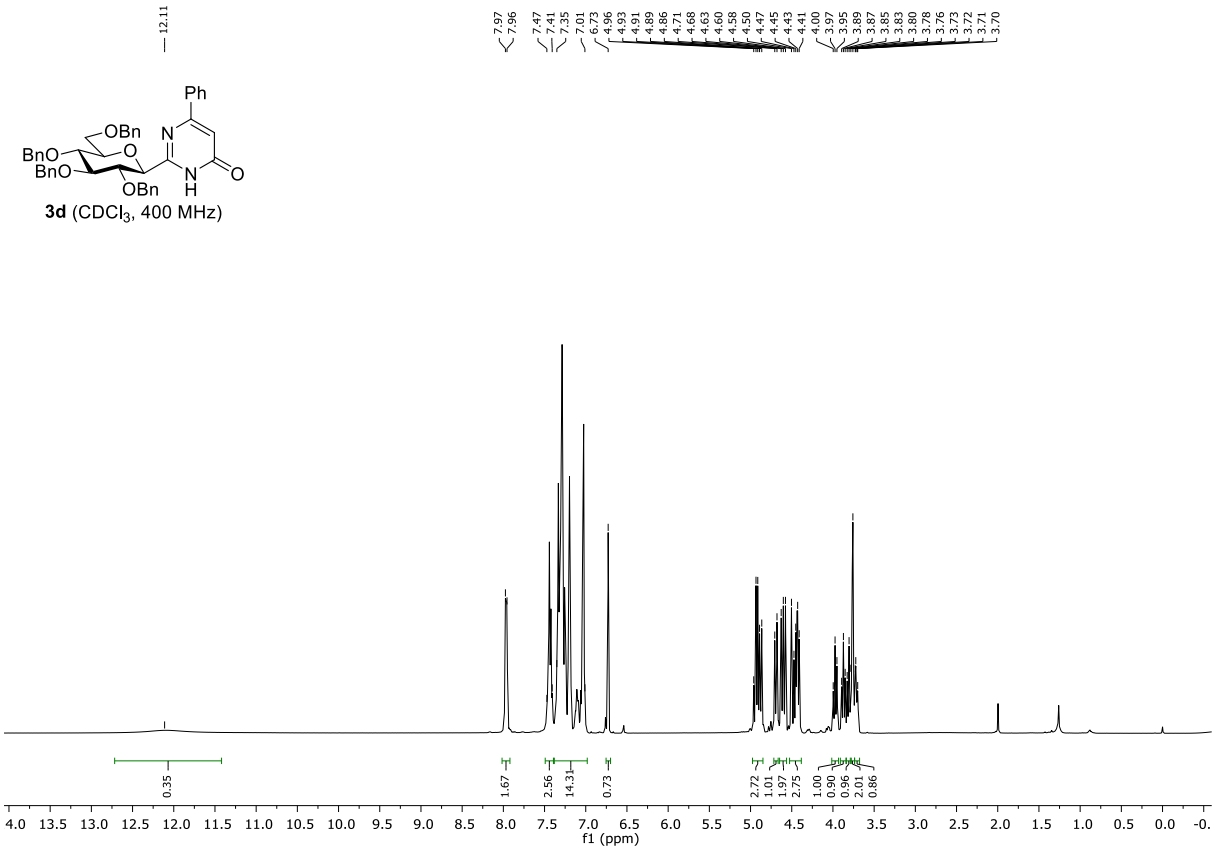
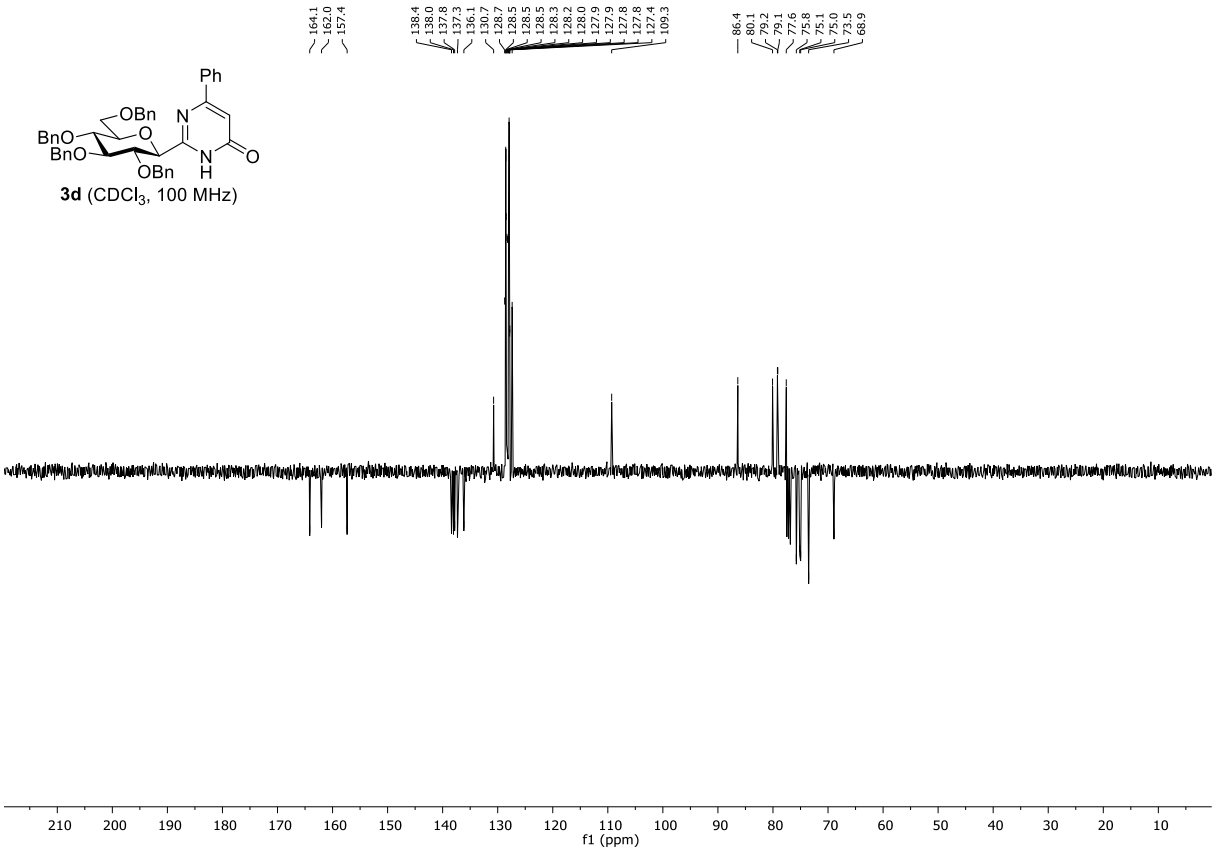
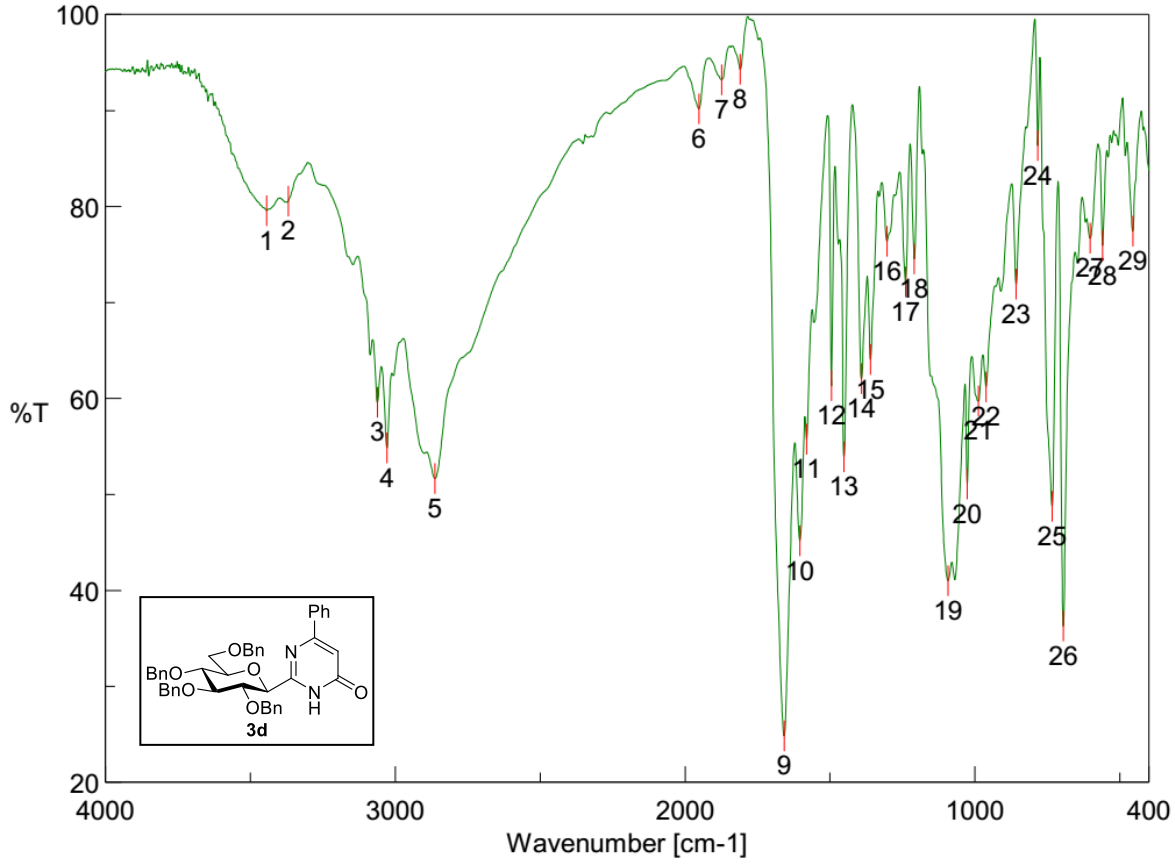
5	2908.13	66.4035	6	2857.02	65.3503
7	1948.72	95.5751	8	1875.43	96.021
9	1806.97	95.6562	10	1745.26	92.2157
11	1666.2	12.5773	12	1609.31	54.2417
13	1556.27	80.7978	14	1496.49	76.1568
15	1453.1	66.3498	16	1396.21	83.3999
17	1360.53	73.0875	18	1327.75	87.8492
19	1280.5	85.4979	20	1256.4	89.046
21	1213.97	78.6479	22	1159.97	64.3171
23	1089.58	29.3481	24	1058.73	36.7998
25	1027.87	59.2854	26	998.946	69.1992
27	914.093	79.1321	28	796.457	93.8972
29	751.138	53.261	30	740.531	55.4211
31	697.141	36.3466	32	646.036	85.1934
33	619.038	88.9628	34	600.717	86.2938
35	573.719	93.2866	36	539.007	90.3808
37	458.975	89.041	38	419.442	90.7933



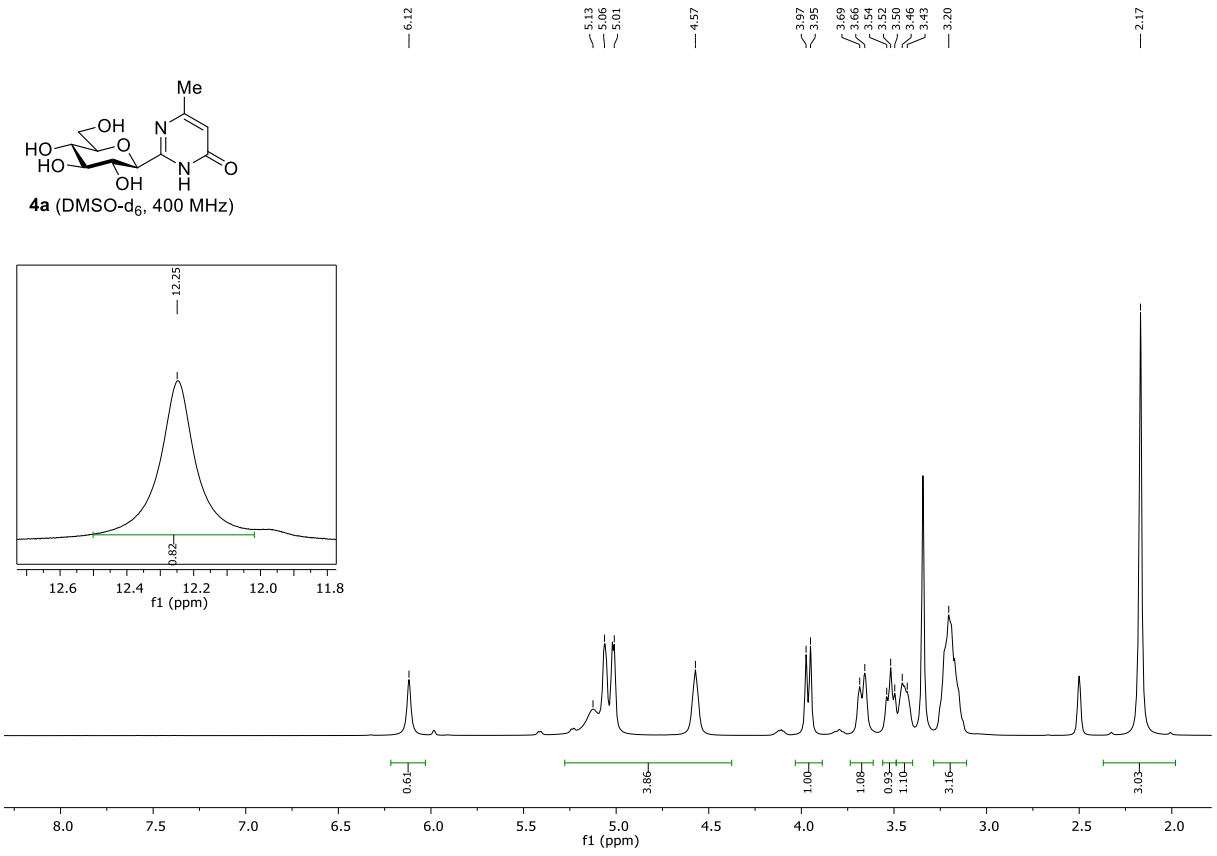
3d ($CDCl_3$, 400 MHz)

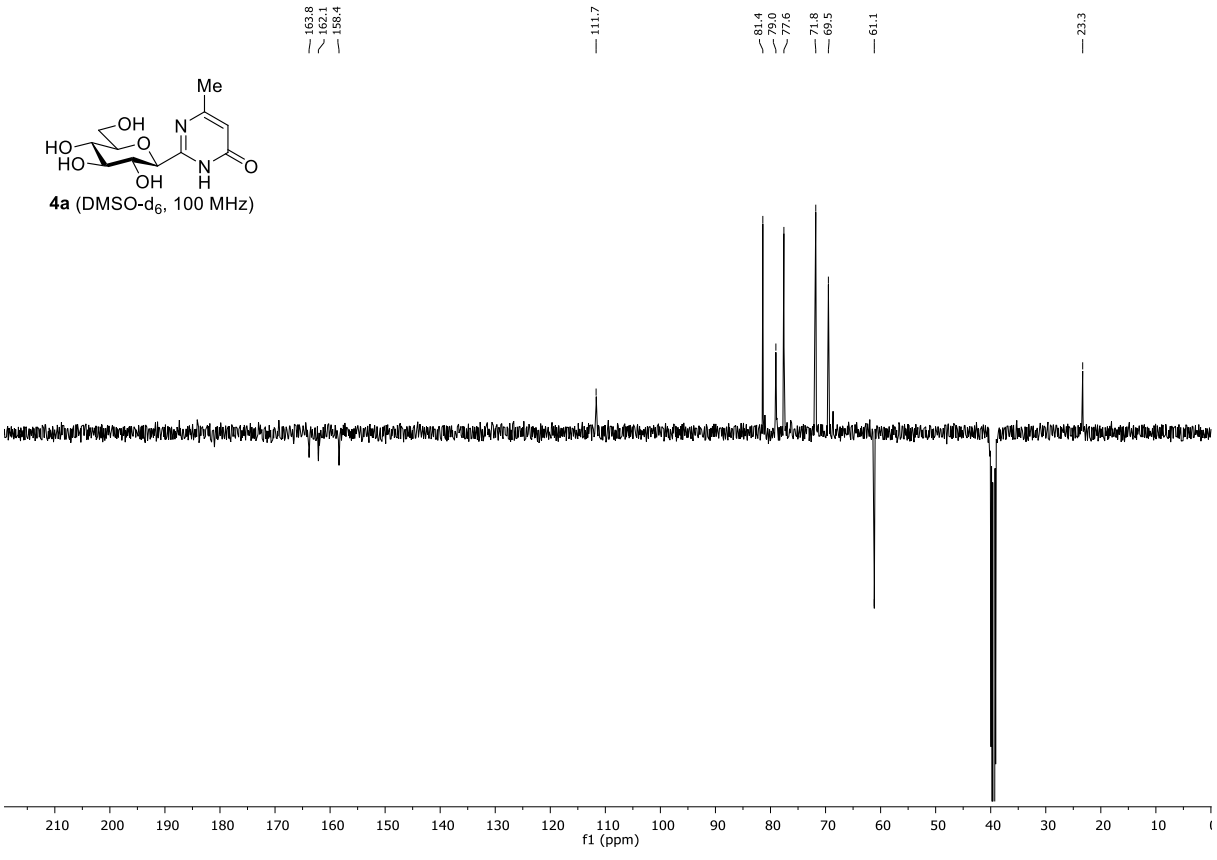


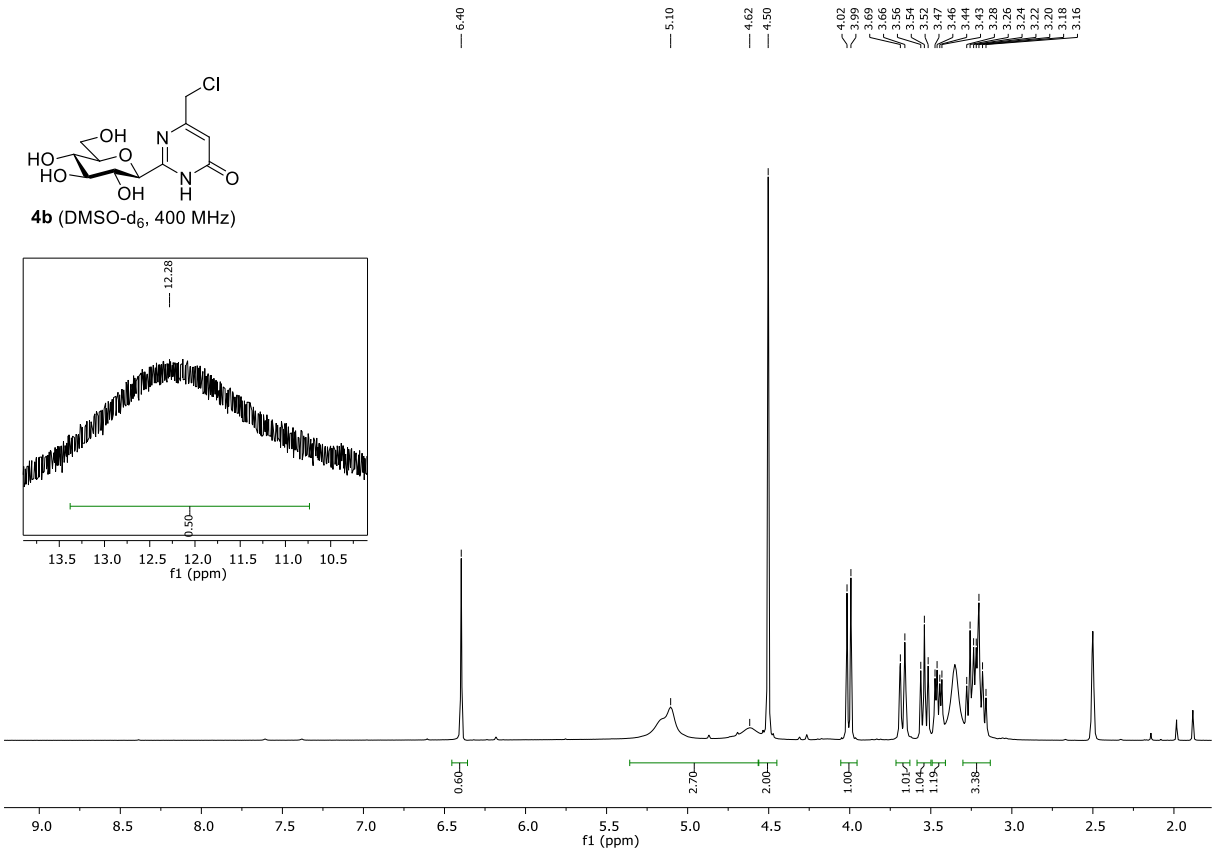
3d ($CDCl_3$, 100 MHz)

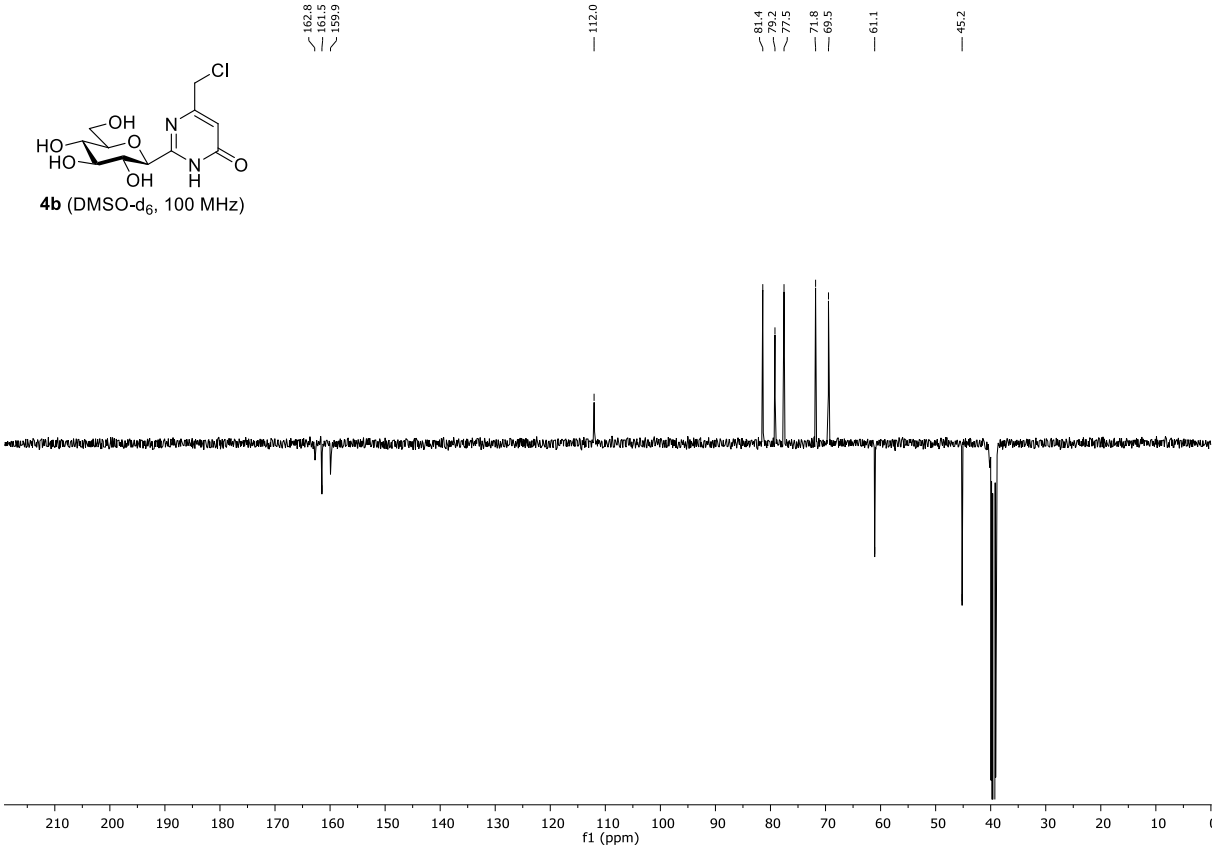


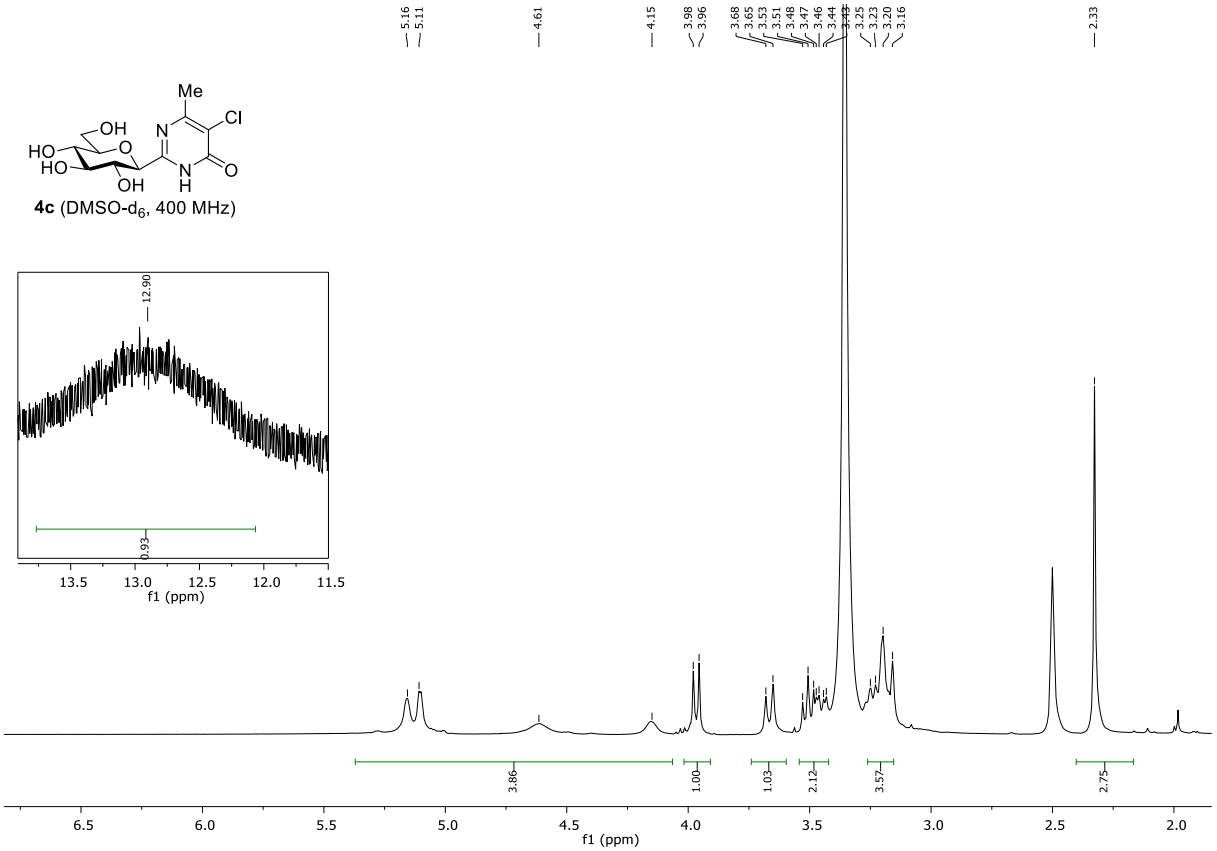
No.	Position	Intensity	No.	Position	Intensity
1	3444.24	79.5552	2	3369.03	80.552
3	3061.44	59.5779	4	3028.66	54.8183
5	2862.81	51.6177	6	1952.57	90.1643
7	1874.47	93.1721	8	1809.87	94.2807
9	1658.48	24.8334	10	1604.48	45.1508
11	1580.38	55.7412	12	1495.53	61.314
13	1452.14	53.8827	14	1391.39	62.0562
15	1360.53	64.0483	16	1303.64	76.335
17	1239.04	72.1257	18	1209.15	74.5134
19	1093.44	40.9773	20	1026.91	51.0745
21	988.339	59.727	22	961.341	61.1732
23	858.168	71.8962	24	782.958	86.3288
25	733.782	48.7556	26	695.212	36.2724
27	602.646	76.6772	28	560.22	75.9203
29	455.118	77.4			


6.12
5.13
5.06
5.01
4.57
3.97
3.95
3.69
3.66
3.54
3.52
3.50
3.46
3.43
3.20
2.17
Me
OH
HO
HO
OH
N
O
N
H
O
4a (DMSO-d6, 400 MHz)
12.25
0.82
12.6
12.4
12.2
12.0
11.8
f1 (ppm)
0.61
3.86
1.00
1.08
0.93
1.10
3.16
3.03
8.0
7.5
7.0
6.5
6.0
5.5
5.0
4.5
4.0
3.5
3.0
2.5
2.0
f1 (ppm)

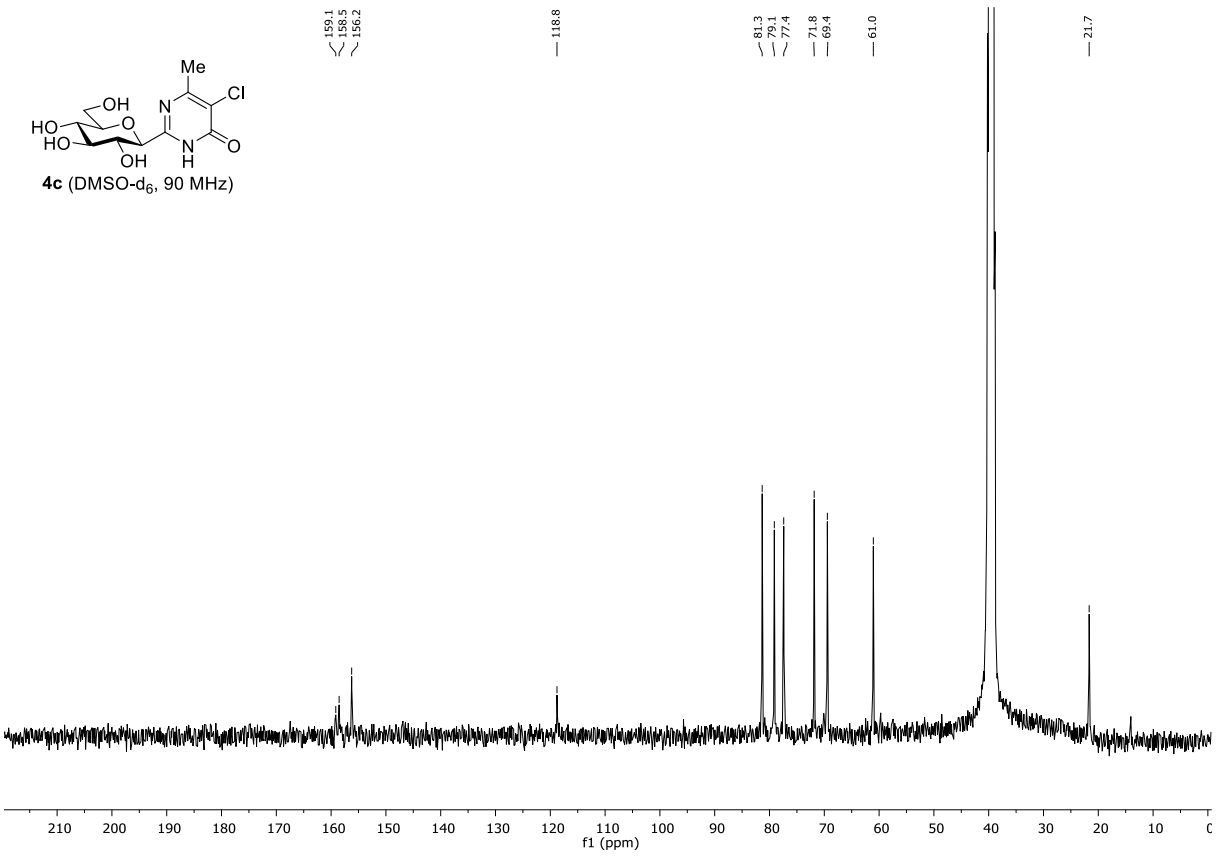

163.8
162.1
158.4
111.7
81.4
79.0
77.6
71.8
69.5
61.1
23.3
Me
OH
HO
HO
OH
N
O
N
H
O
4a (DMSO-d6, 100 MHz)
210
200
190
180
170
160
150
140
130
120
110
100
90
80
70
60
50
40
30
20
10
f1 (ppm)


6.40
5.10
4.62
4.50
4.02
3.99
3.69
3.66
3.56
3.54
3.52
3.47
3.46
3.44
3.43
3.28
3.26
3.24
3.22
3.20
3.18
3.16
Cl
OH
N
HO
O
HO
N
O
OH
H
4b (DMSO-d6, 400 MHz)
12.28
0.50
13.5 13.0 12.5 12.0 11.5 11.0 10.5
f1 (ppm)
0.60
2.70
2.00
1.00
1.01
1.04
1.19
3.38
9.0 8.5 8.0 7.5 7.0 6.5 6.0 5.5 5.0 4.5 4.0 3.5 3.0 2.5 2.0
f1 (ppm)

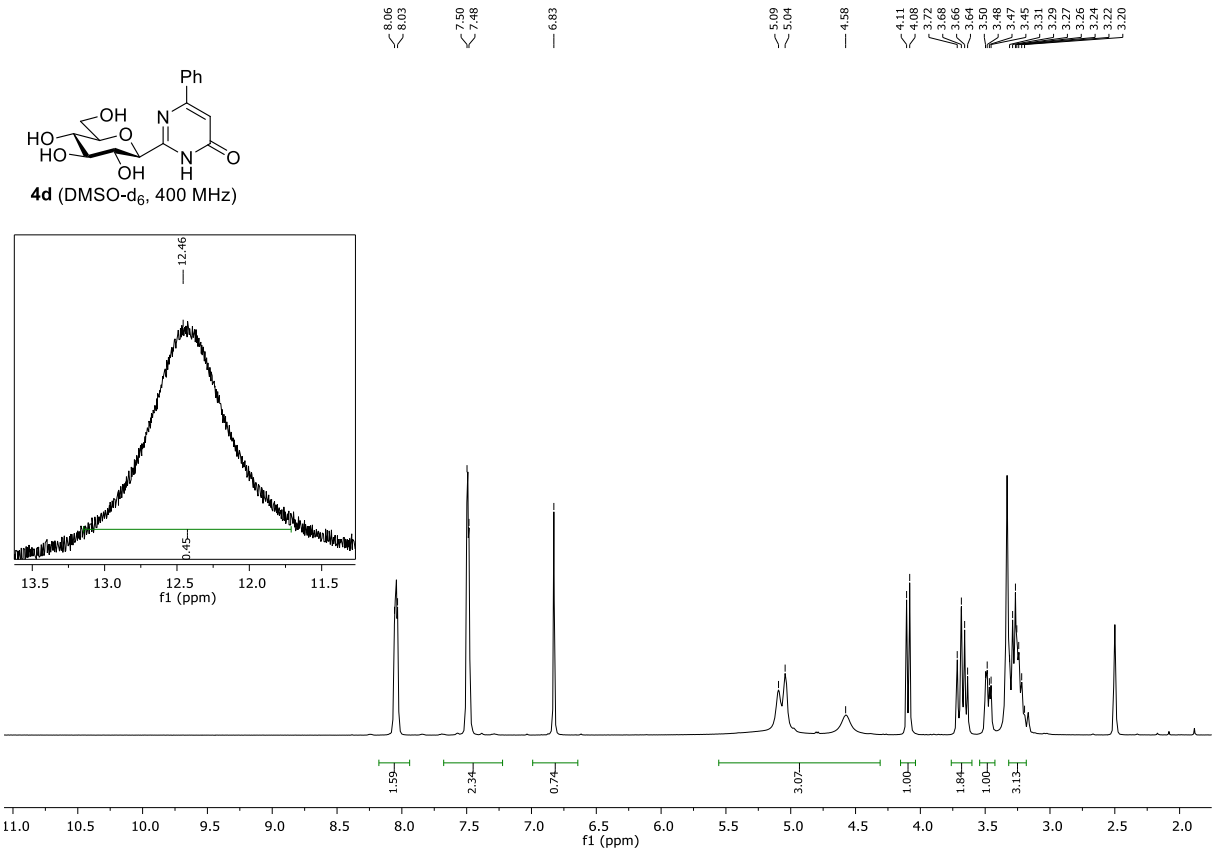

162.8
161.5
159.9
112.0
81.4
79.2
77.5
71.8
69.5
61.1
45.2
Cl
OH
N
HO
O
HO
N
O
OH
H
4b (DMSO-d6, 100 MHz)
210 200 190 180 170 160 150 140 130 120 110 100 90 80 70 60 50 40 30 20 10
f1 (ppm)

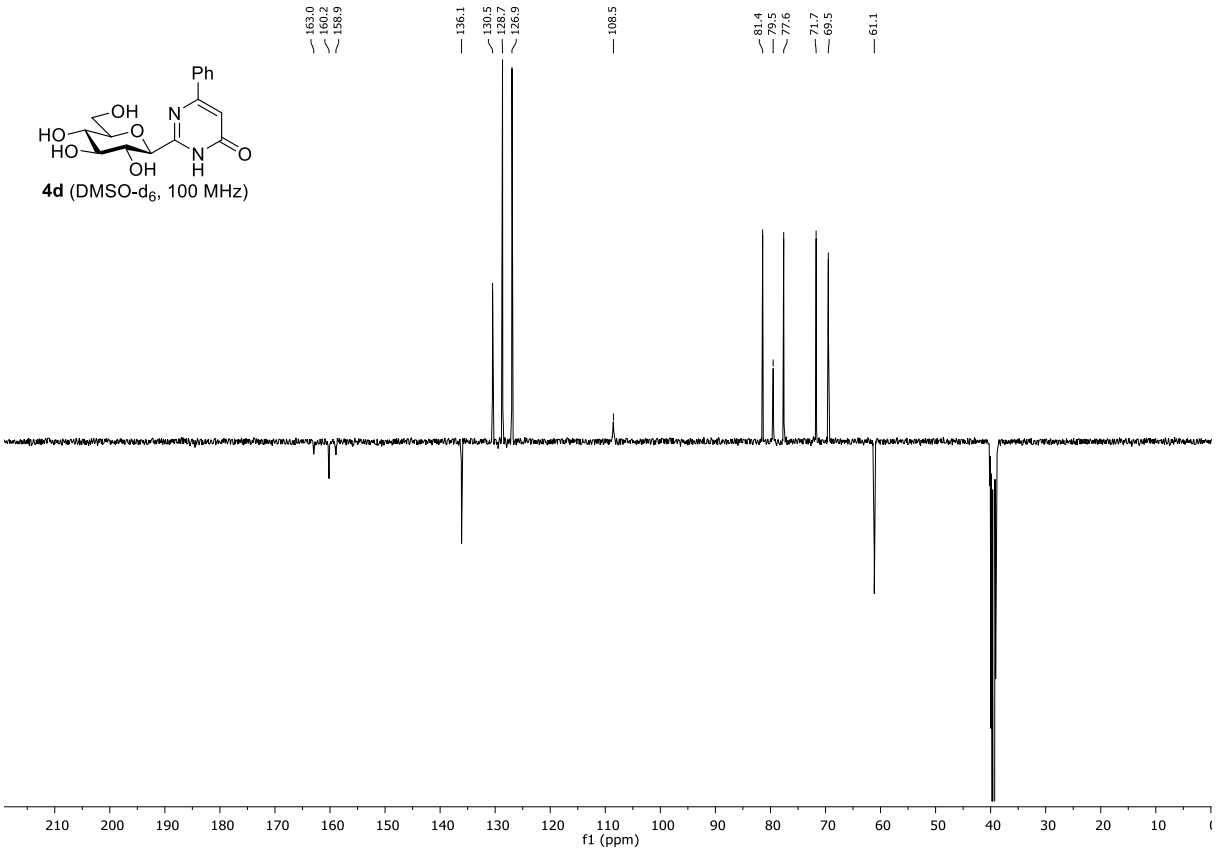


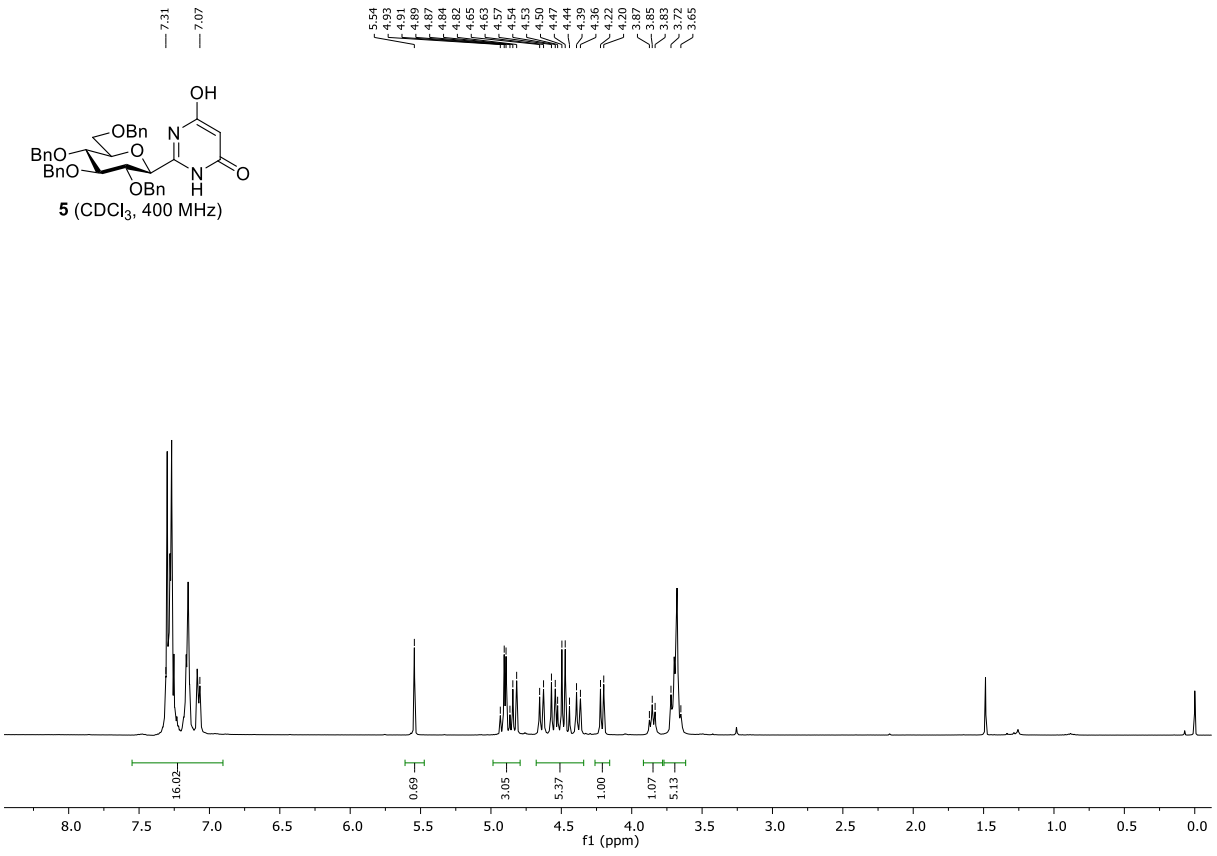
4c (DMSO-d_6, 400 MHz)



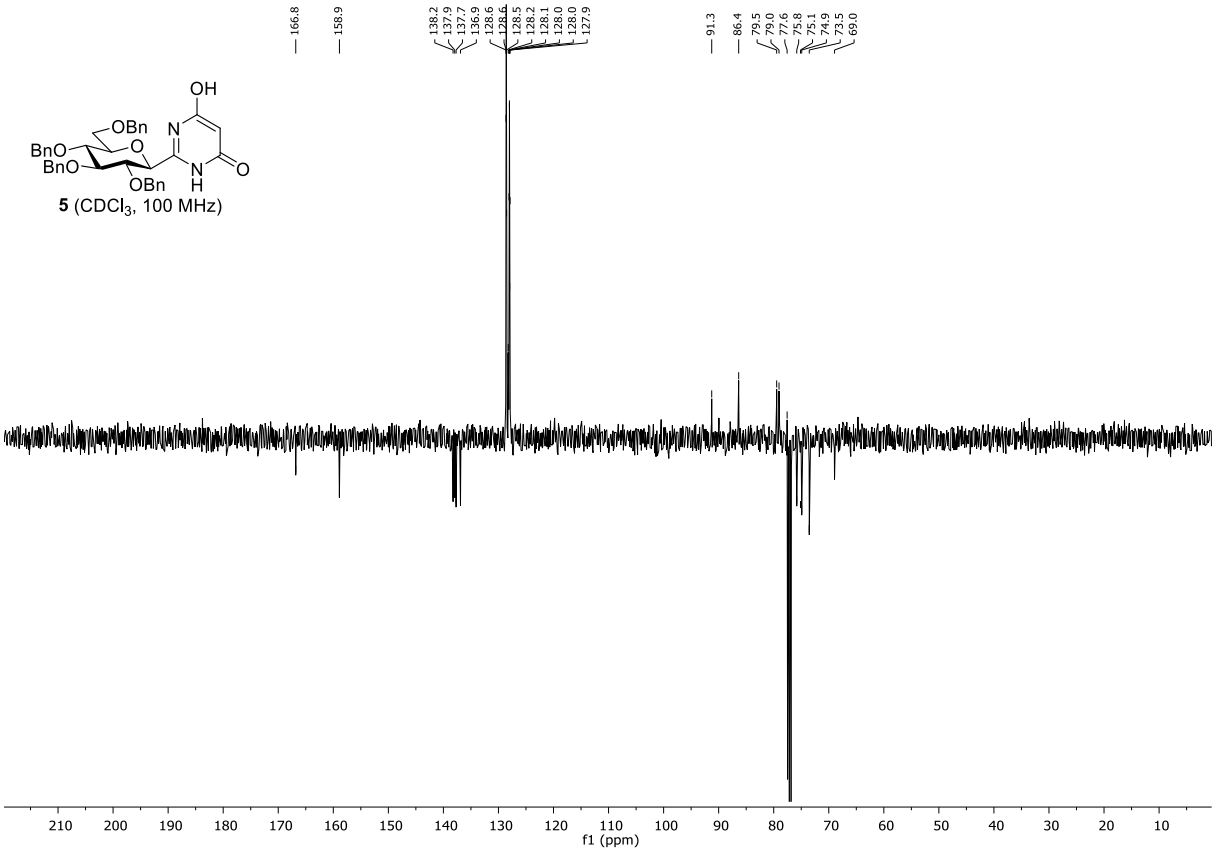
4c (DMSO-d_6, 90 MHz)


8.06
8.03
7.50
7.48
6.83
5.09
5.04
4.58
4.11
4.08
3.72
3.68
3.66
3.64
3.50
3.48
3.47
3.45
3.31
3.29
3.27
3.26
3.24
3.22
3.20
Ph
OH
N
HO
O
HO
N
O
OH
H
4d (DMSO-d6, 400 MHz)
12.46
0.45
13.5
13.0
12.5
12.0
11.5
f1 (ppm)
1.59
2.34
0.74
3.07
1.00
1.84
1.00
3.13
11.0
10.5
10.0
9.5
9.0
8.5
8.0
7.5
7.0
6.5
6.0
5.5
5.0
4.5
4.0
3.5
3.0
2.5
2.0
f1 (ppm)

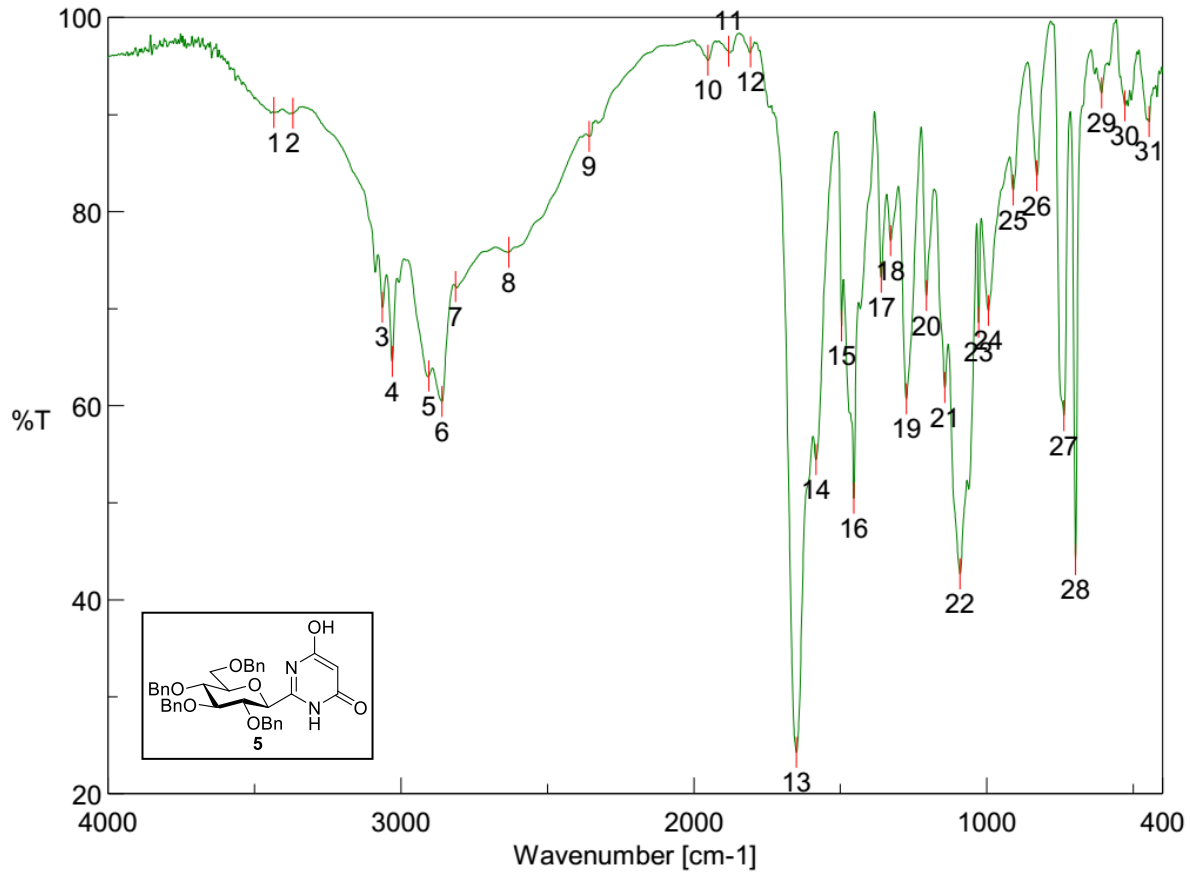

163.0
160.2
158.9
136.1
130.5
128.7
126.9
108.5
81.4
79.5
77.6
71.7
69.5
61.1
Ph
OH
N
HO
O
HO
N
O
OH
H
4d (DMSO-d6, 100 MHz)
210
200
190
180
170
160
150
140
130
120
110
100
90
80
70
60
50
40
30
20
10
f1 (ppm)



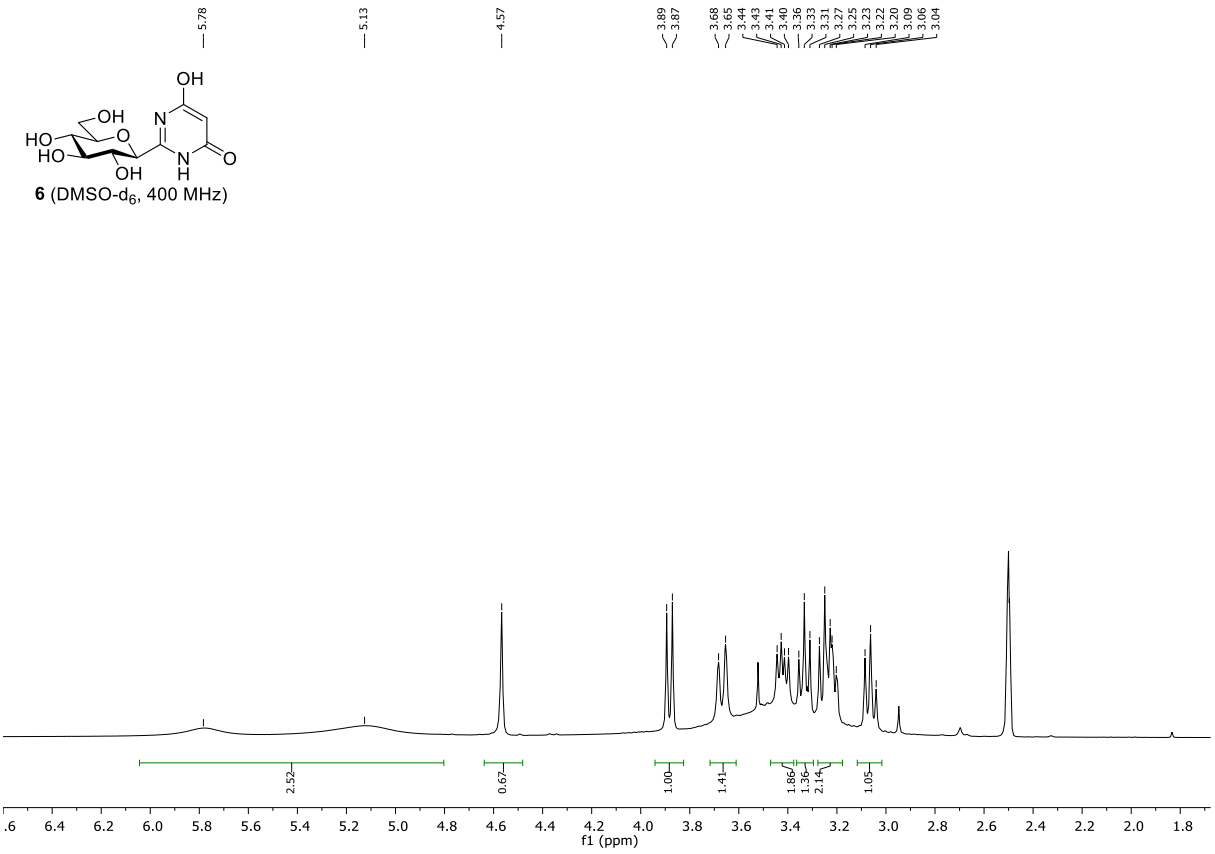
5 ($CDCl_3$, 400 MHz)



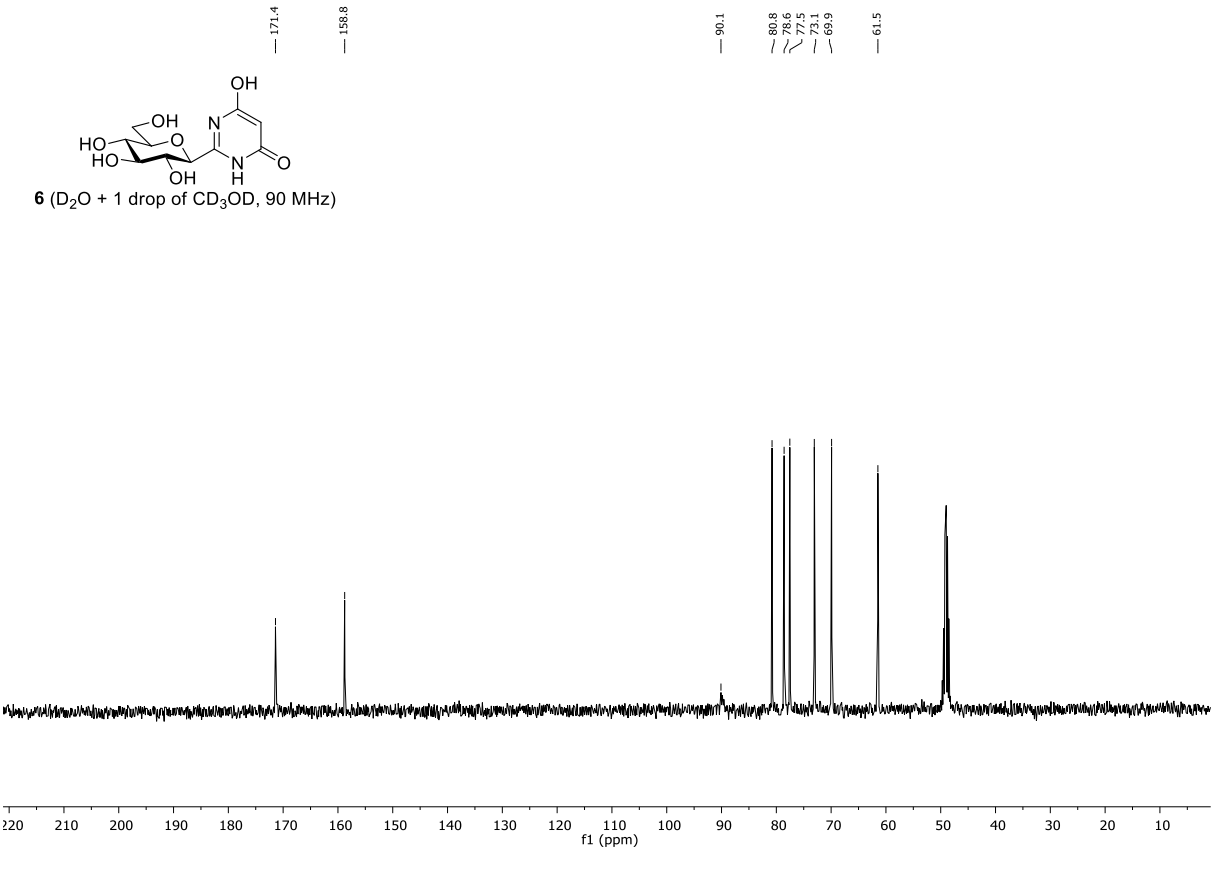
5 ($CDCl_3$, 100 MHz)



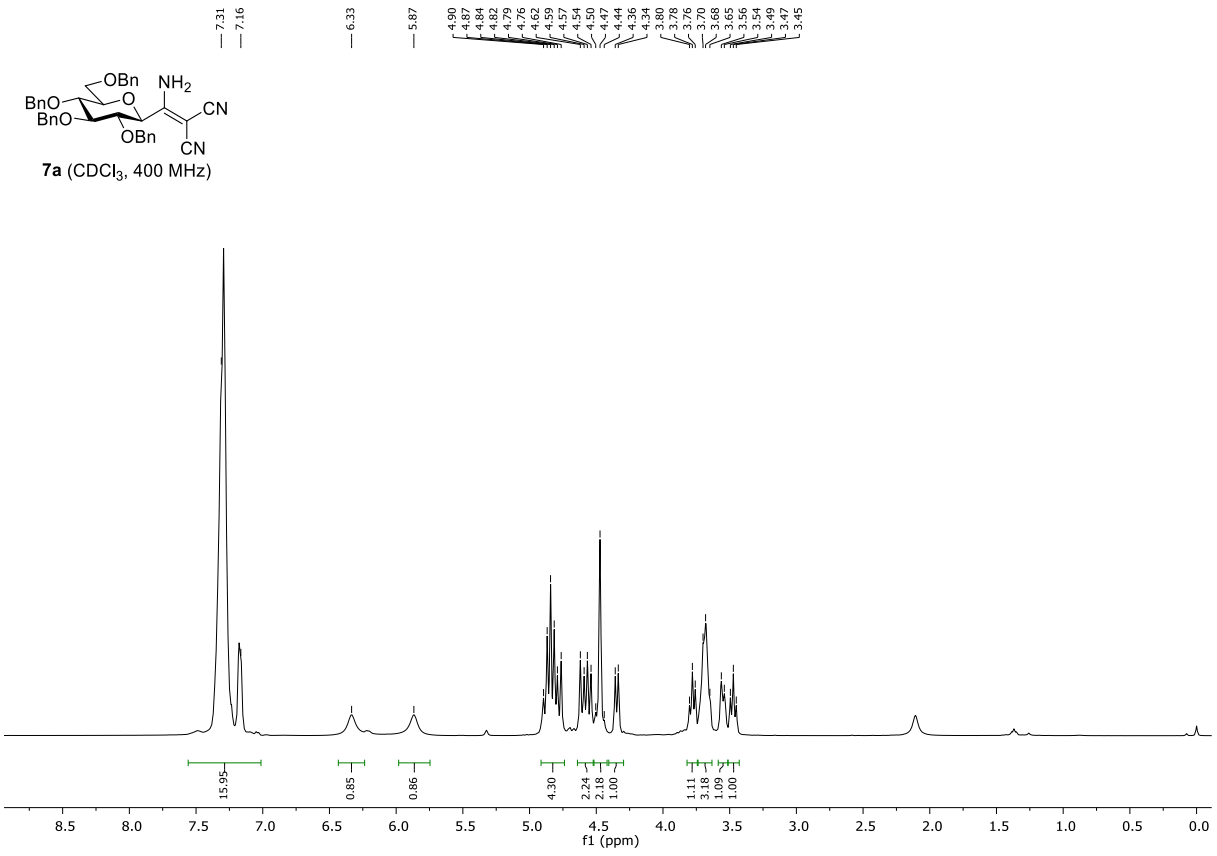
No.	Position	Intensity	No.	Position	Intensity
1	3433.64	90.1909	2	3369.03	90.1202
3	3063.37	70.1148	4	3029.62	64.5562
5	2905.24	63.034	6	2859.92	60.409
7	2813.63	72.2729	8	2631.39	75.7961
9	2357.55	87.7385	10	1951.61	95.5841
11	1882.18	96.5159	12	1806.97	96.4483
13	1649.8	24.2484	14	1583.27	54.4431
15	1496.49	68.1977	16	1454.06	50.4453
17	1360.53	73.2223	18	1328.71	76.9824
19	1274.72	60.684	20	1206.26	71.3217
21	1143.58	61.8316	22	1091.51	42.653
23	1027.87	68.5581	24	995.089	69.7957
25	910.236	82.1882	26	829.241	83.6782
27	736.674	58.9551	28	697.141	44.1155
29	608.431	92.223	30	528.4	90.888
31	446.44	89.2407			



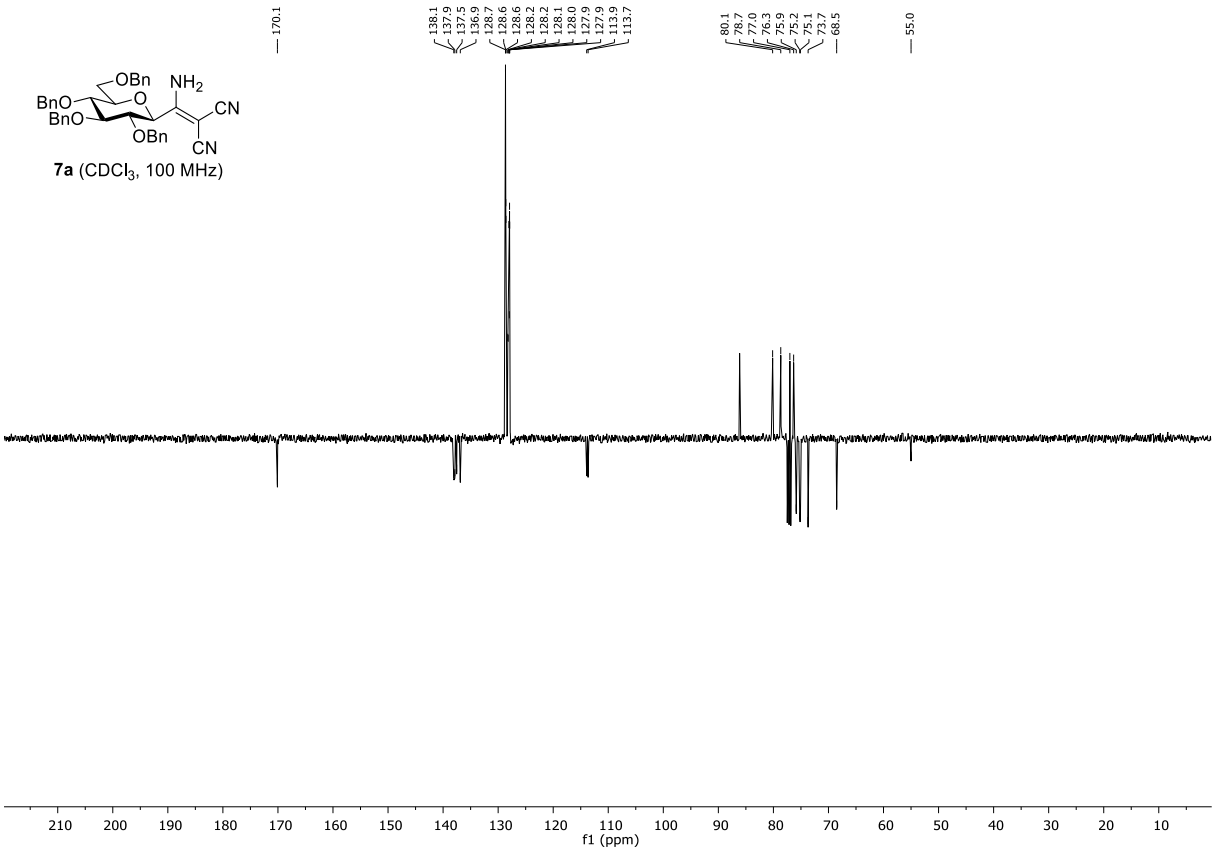
6 (DMSO-d_6, 400 MHz)



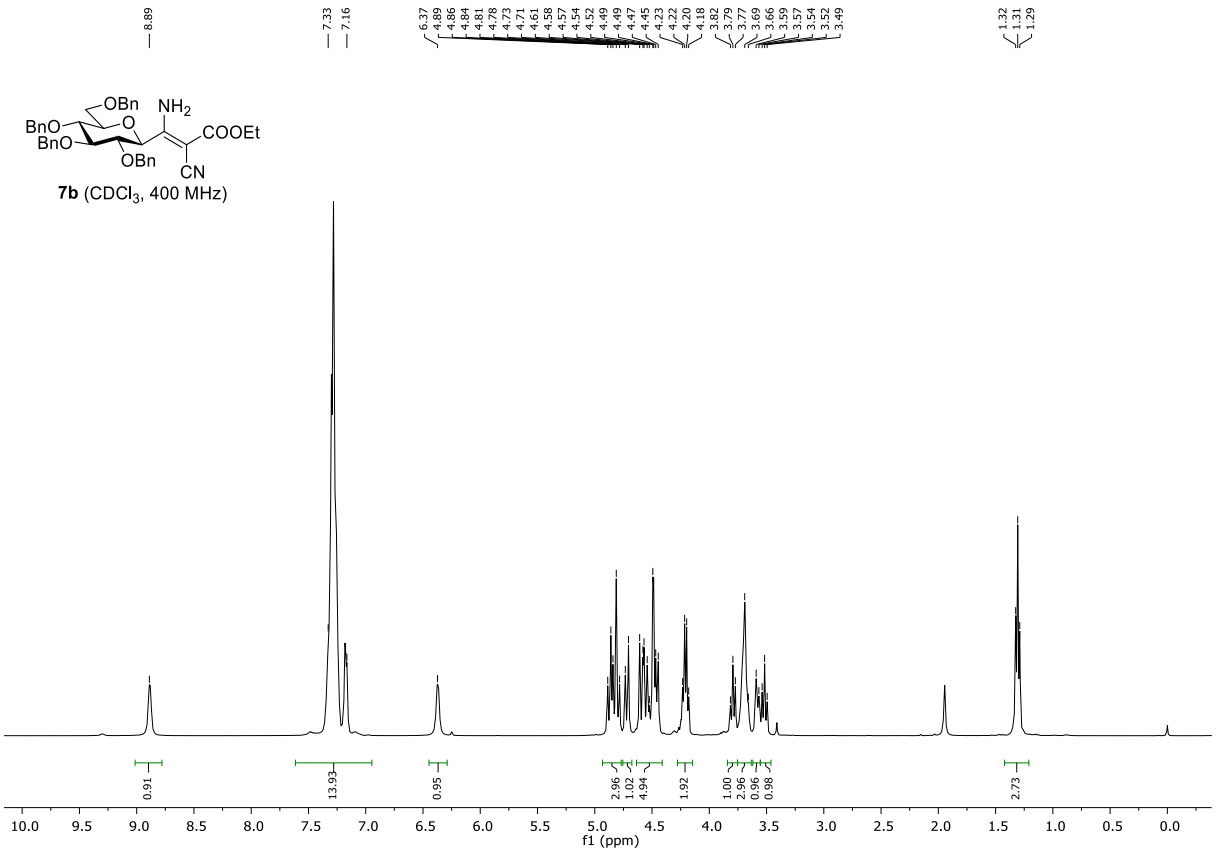
6 (D_2O + 1 drop of CD_3OD, 90 MHz)



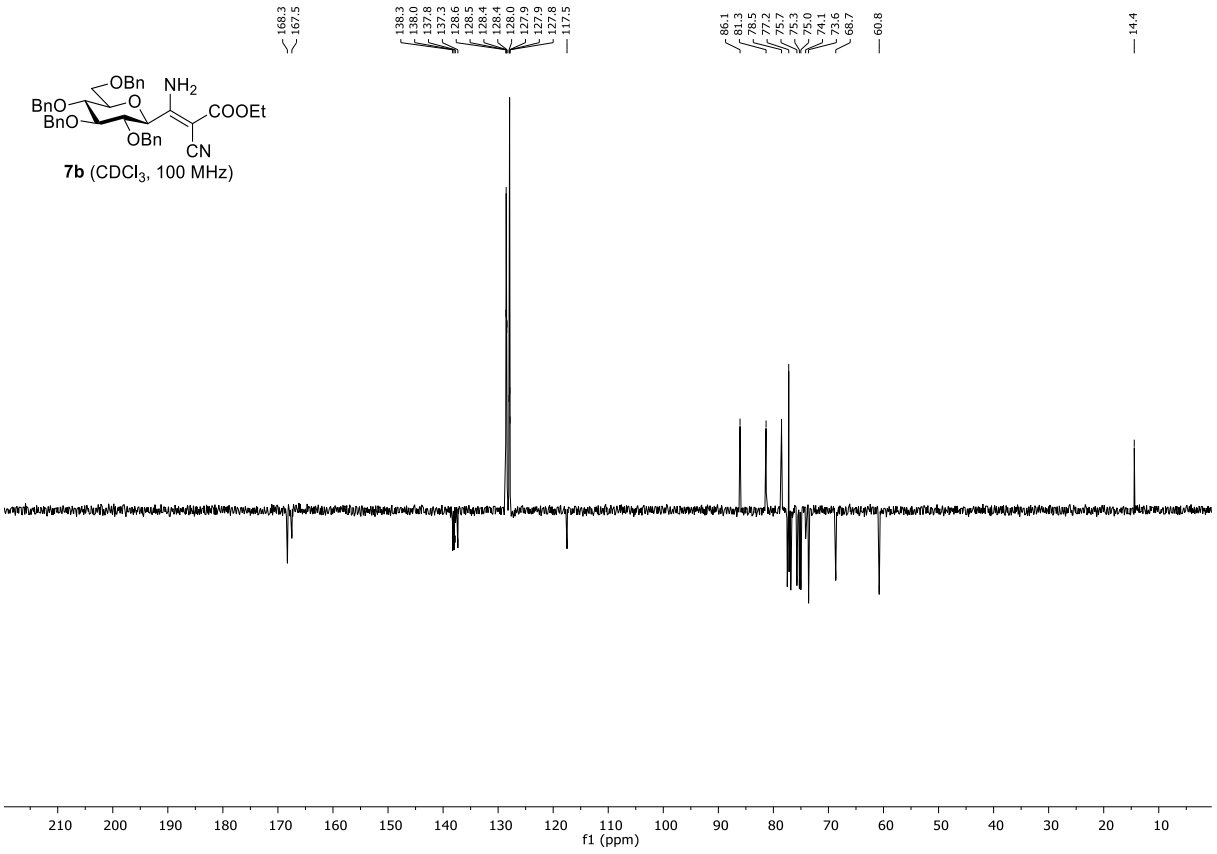
7a ($CDCl_3$, 400 MHz)



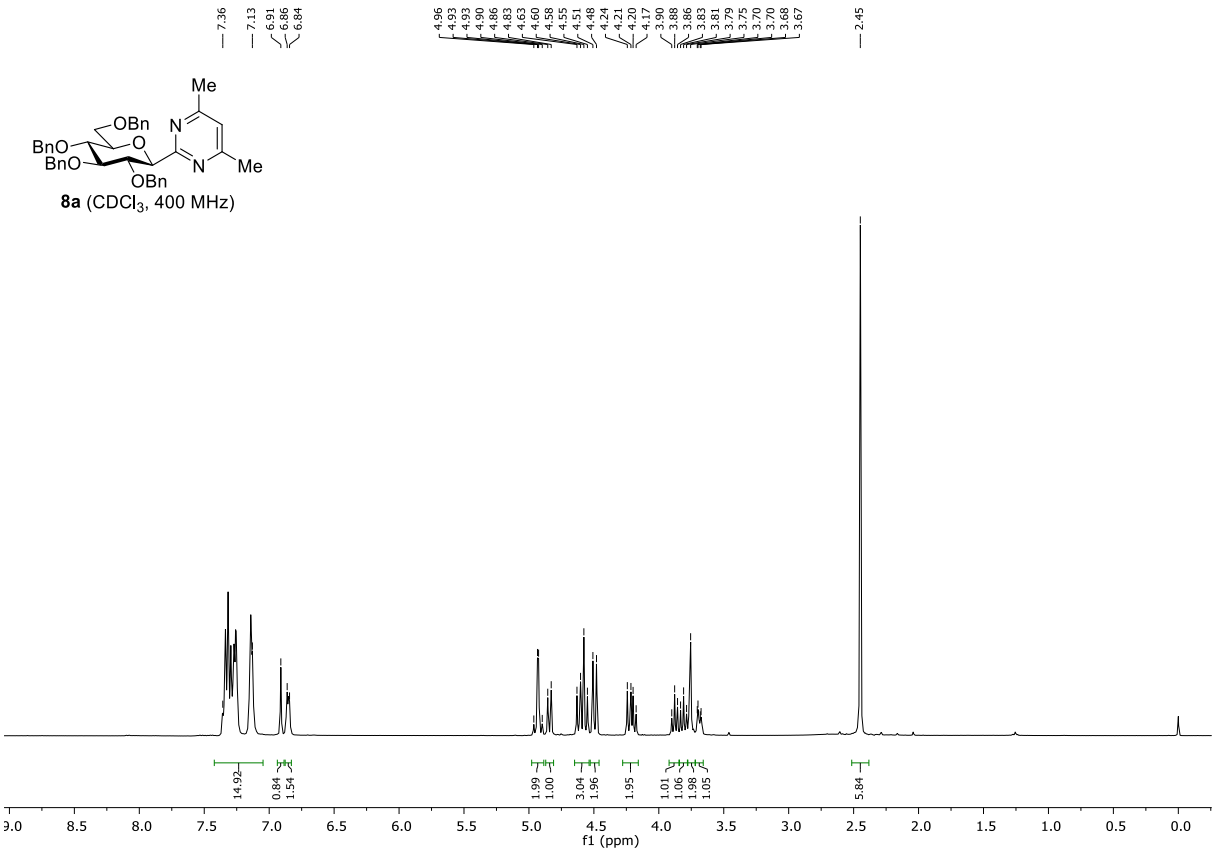
7a ($CDCl_3$, 100 MHz)



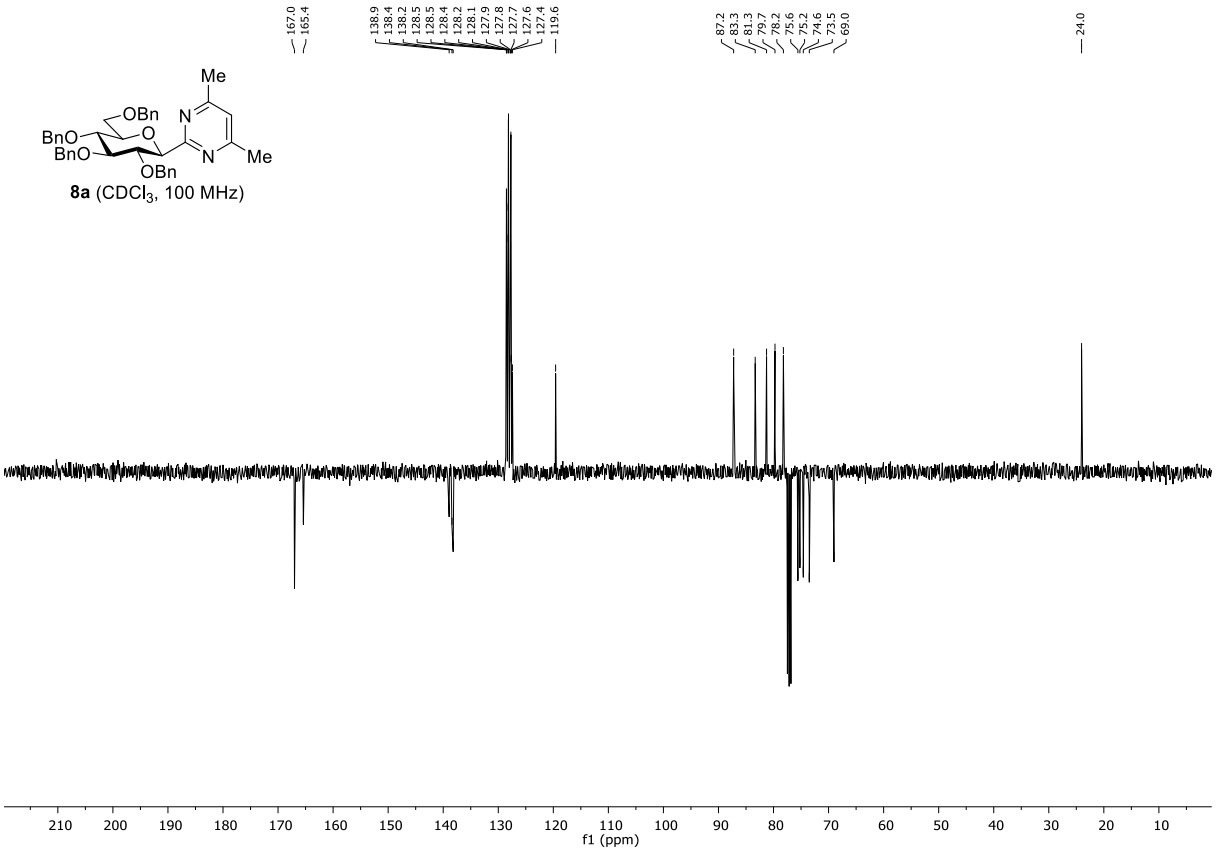
7b ($CDCl_3$, 400 MHz)



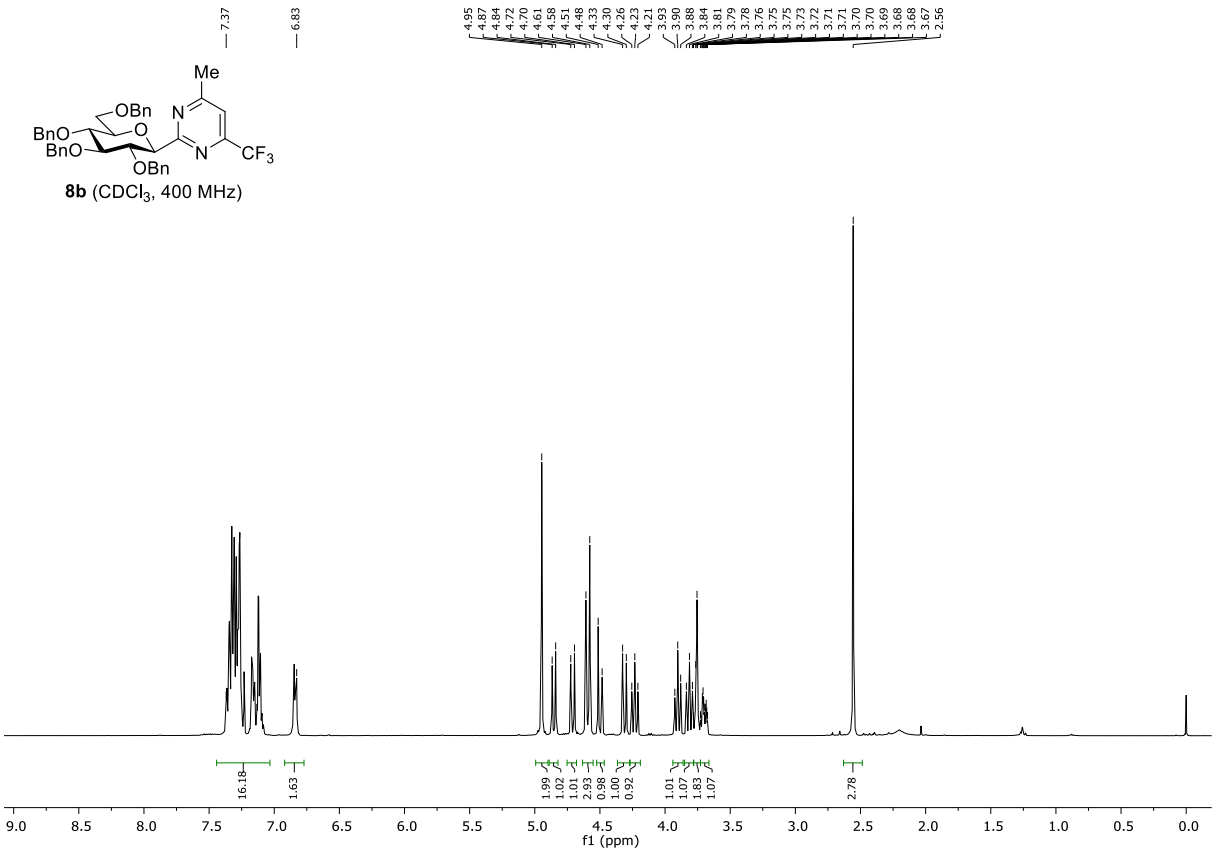
7b ($CDCl_3$, 100 MHz)



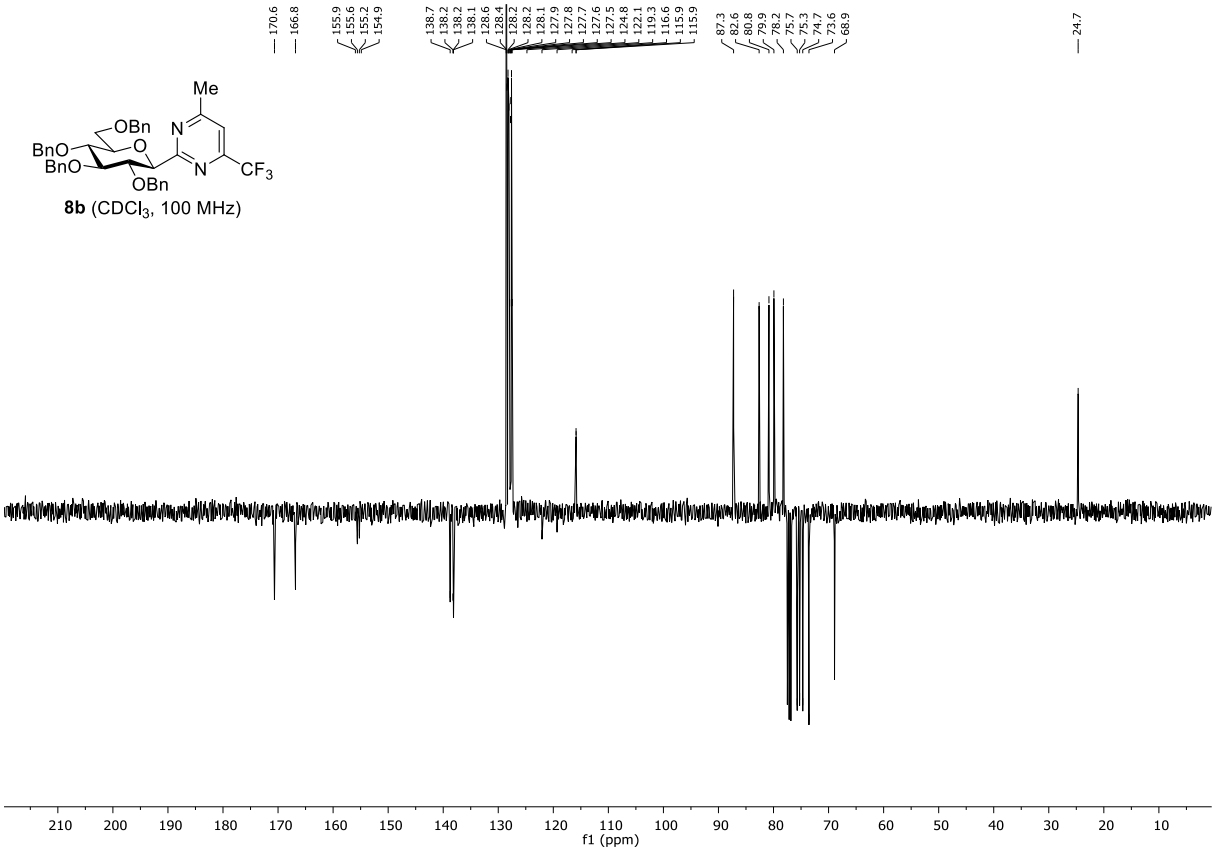
8a ($CDCl_3$, 400 MHz)



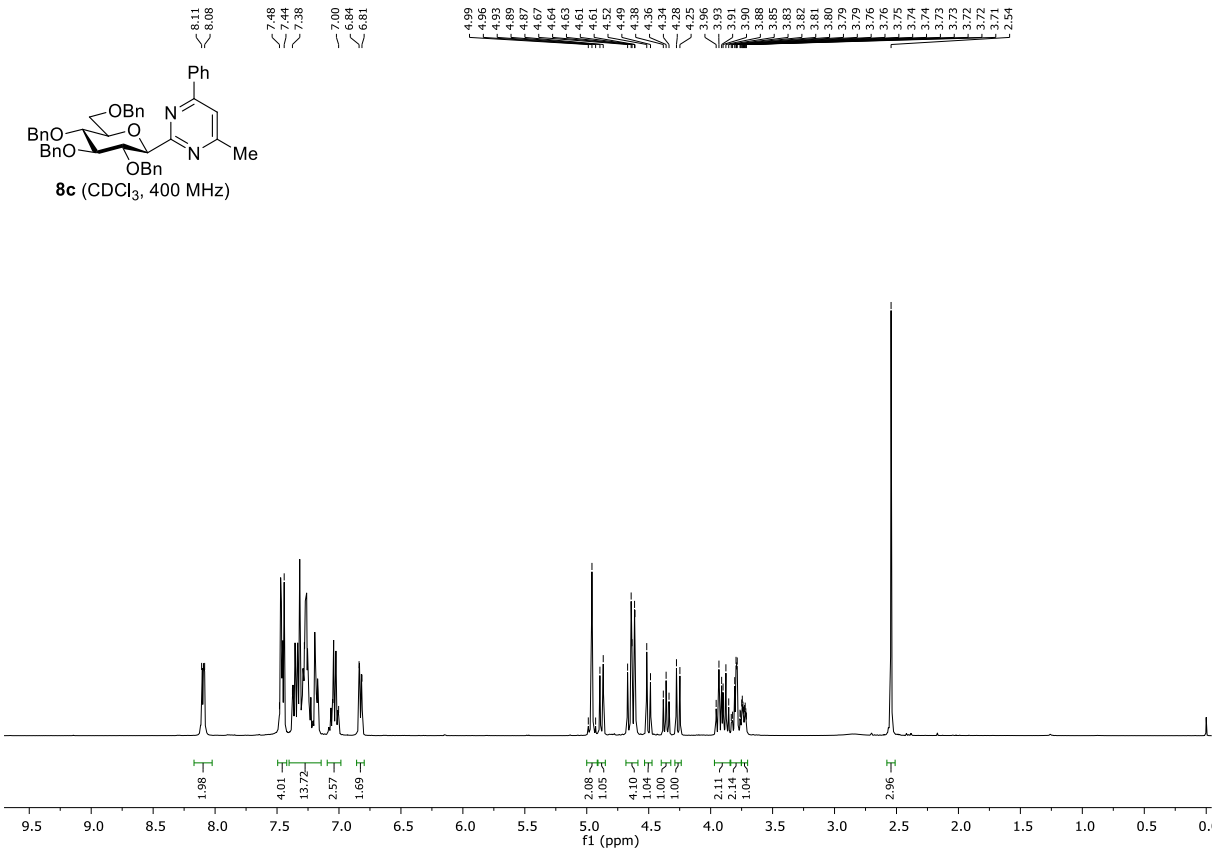
8a ($CDCl_3$, 100 MHz)

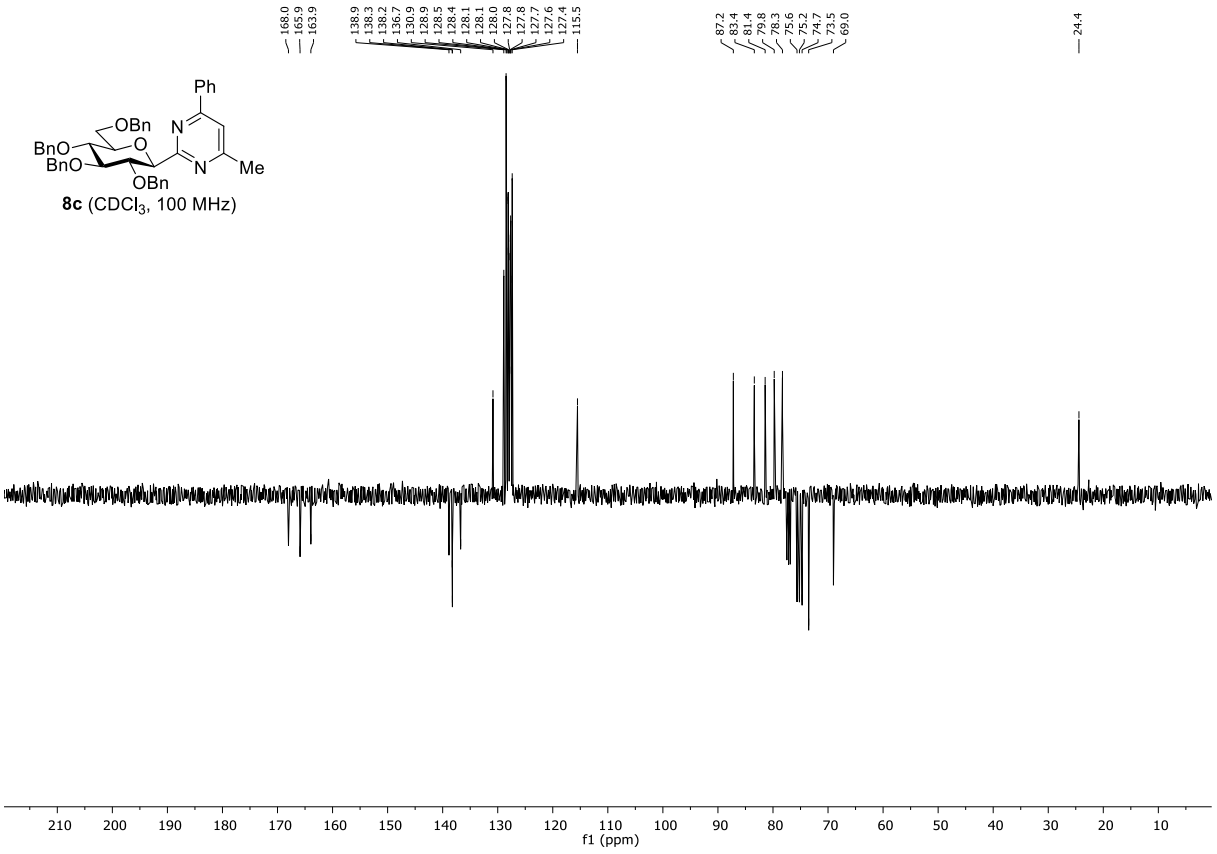


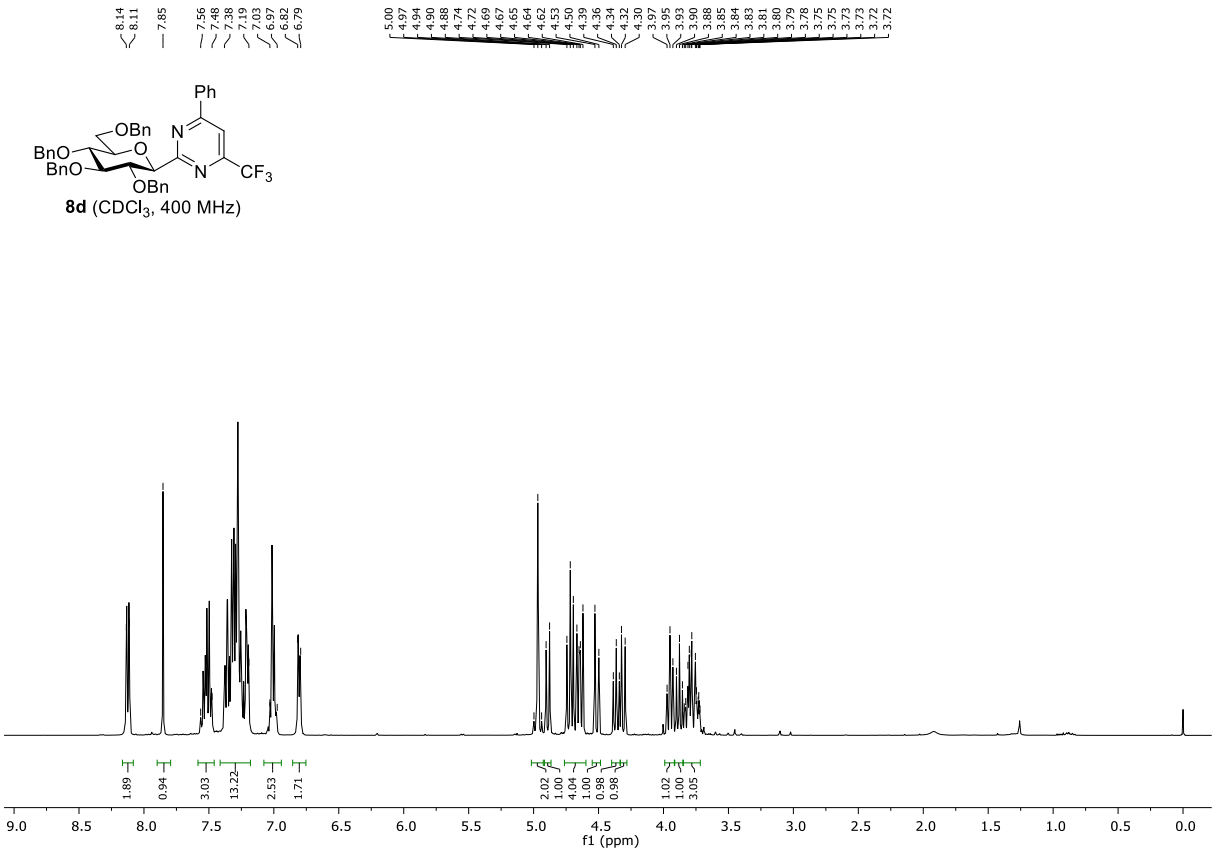
8b ($CDCl_3$, 400 MHz)

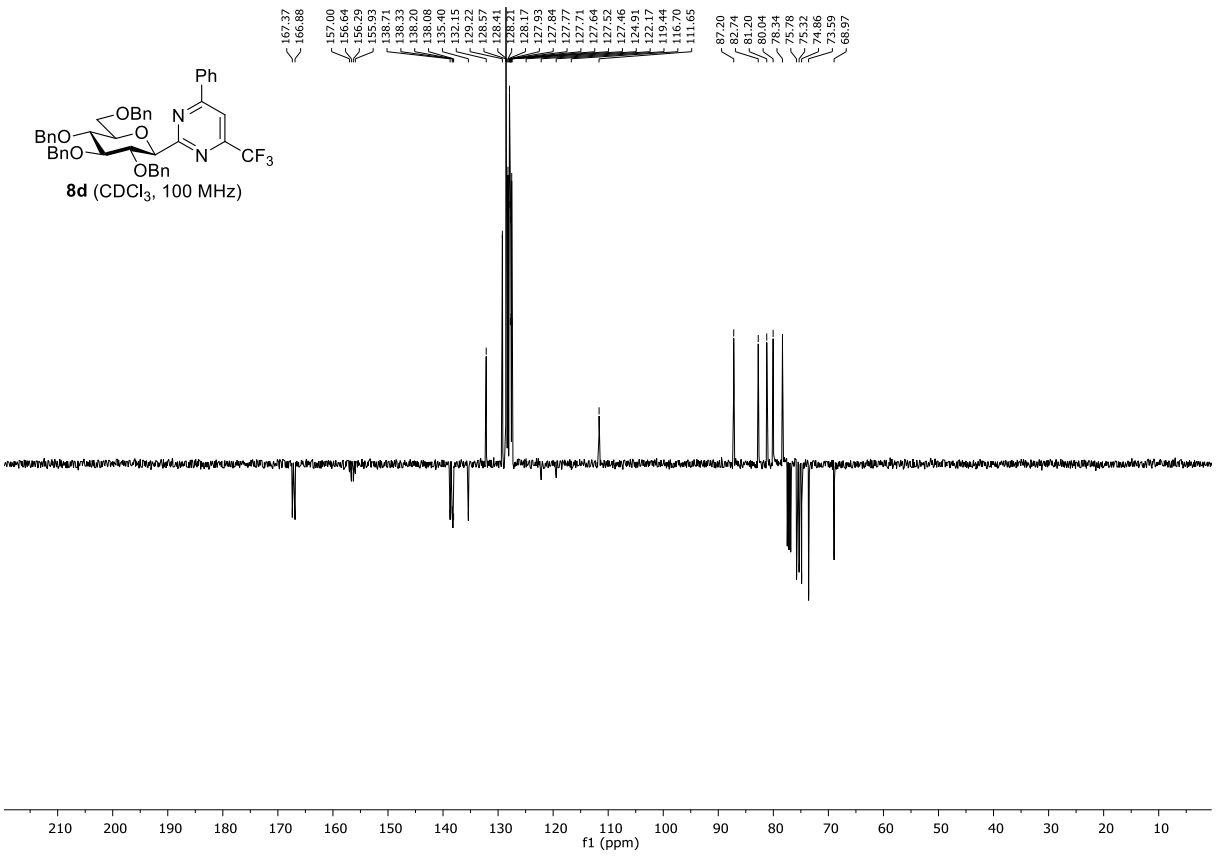


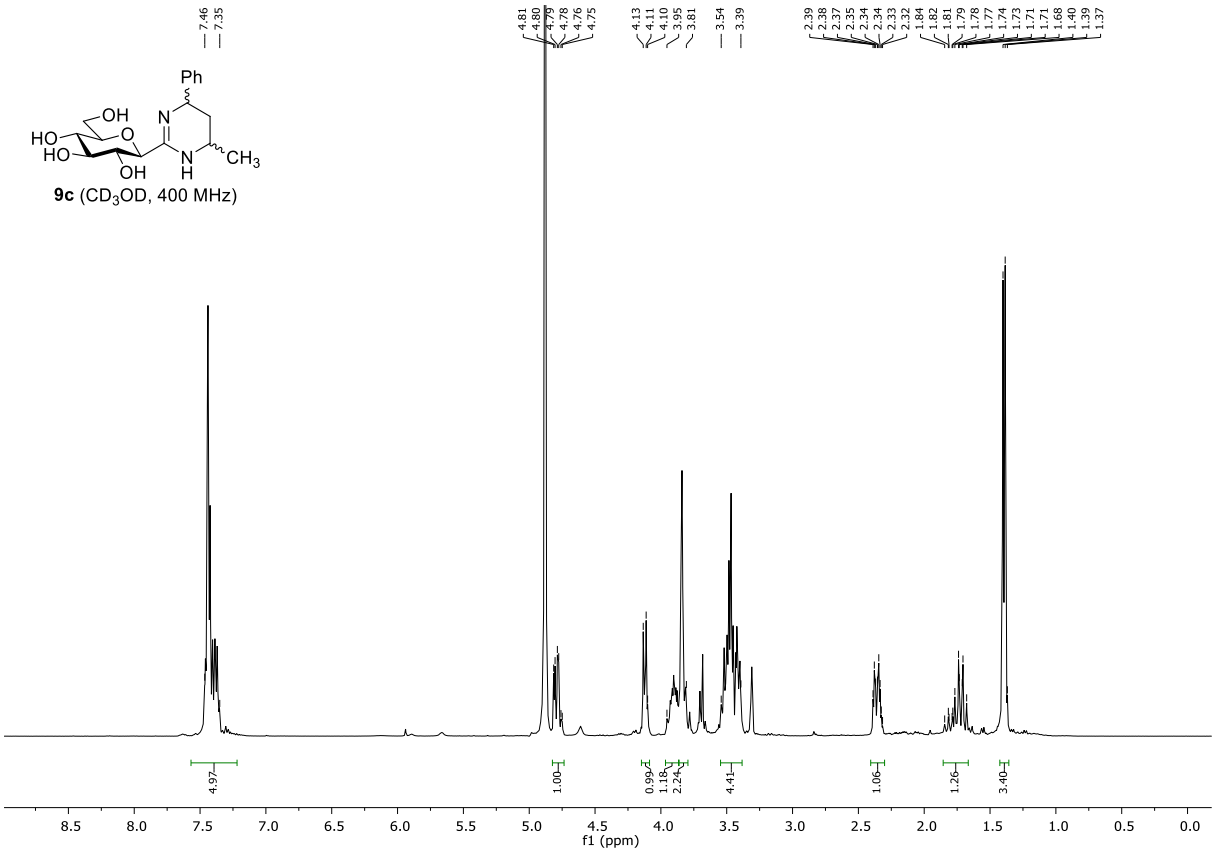
8b ($CDCl_3$, 100 MHz)

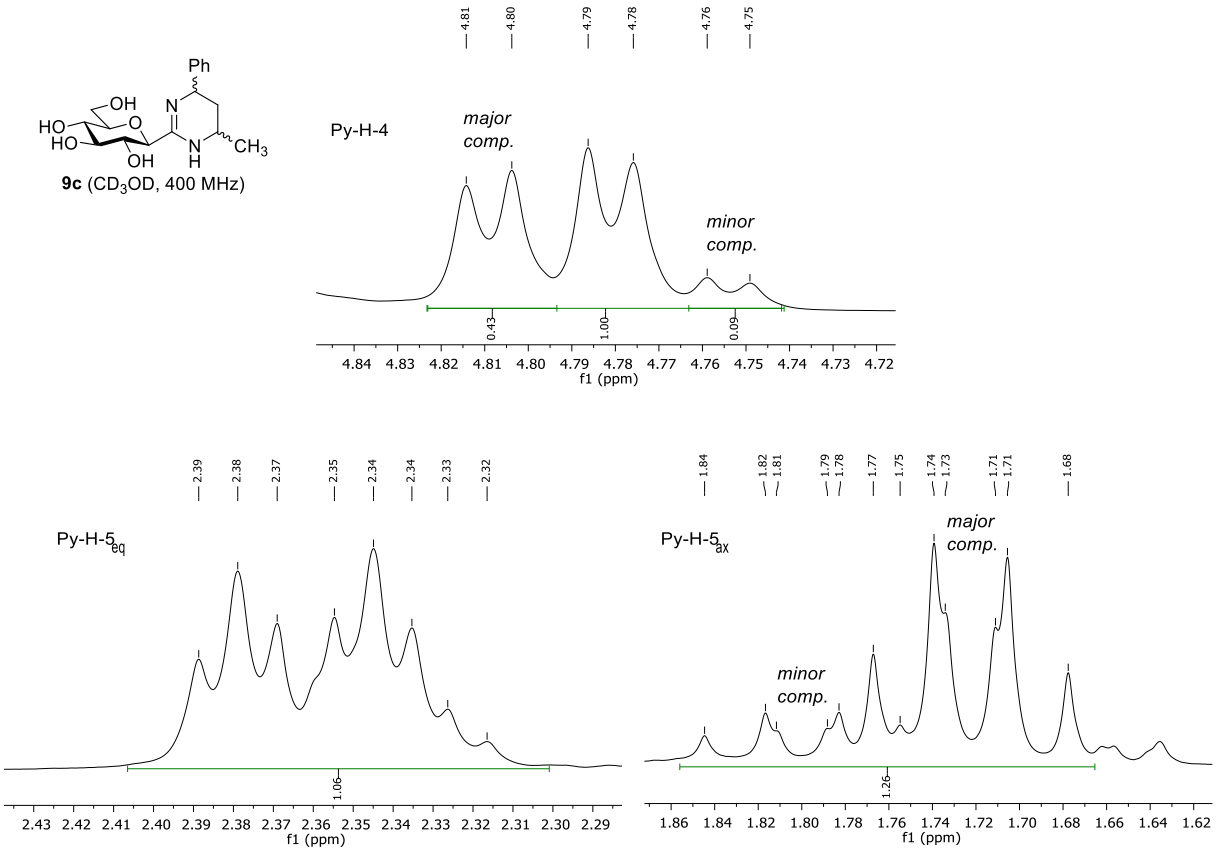

8.11
8.08
7.48
7.44
7.38
7.00
6.84
6.81
4.99
4.96
4.93
4.89
4.87
4.67
4.64
4.63
4.61
4.61
4.52
4.49
4.38
4.36
4.34
4.28
4.25
3.96
3.93
3.91
3.90
3.88
3.85
3.83
3.82
3.81
3.80
3.79
3.79
3.76
3.76
3.75
3.74
3.74
3.73
3.73
3.72
3.72
3.71
2.54
Ph
OBn
N
BnO
O
BnO
N
Me
OBn
8c (CDCl3, 400 MHz)
1.98
4.01
13.72
2.57
1.69
2.08
1.05
4.10
1.04
1.00
1.00
2.11
2.14
1.04
2.96
9.5
9.0
8.5
8.0
7.5
7.0
6.5
6.0
5.5
5.0
4.5
4.0
3.5
3.0
2.5
2.0
1.5
1.0
0.5
f1 (ppm)

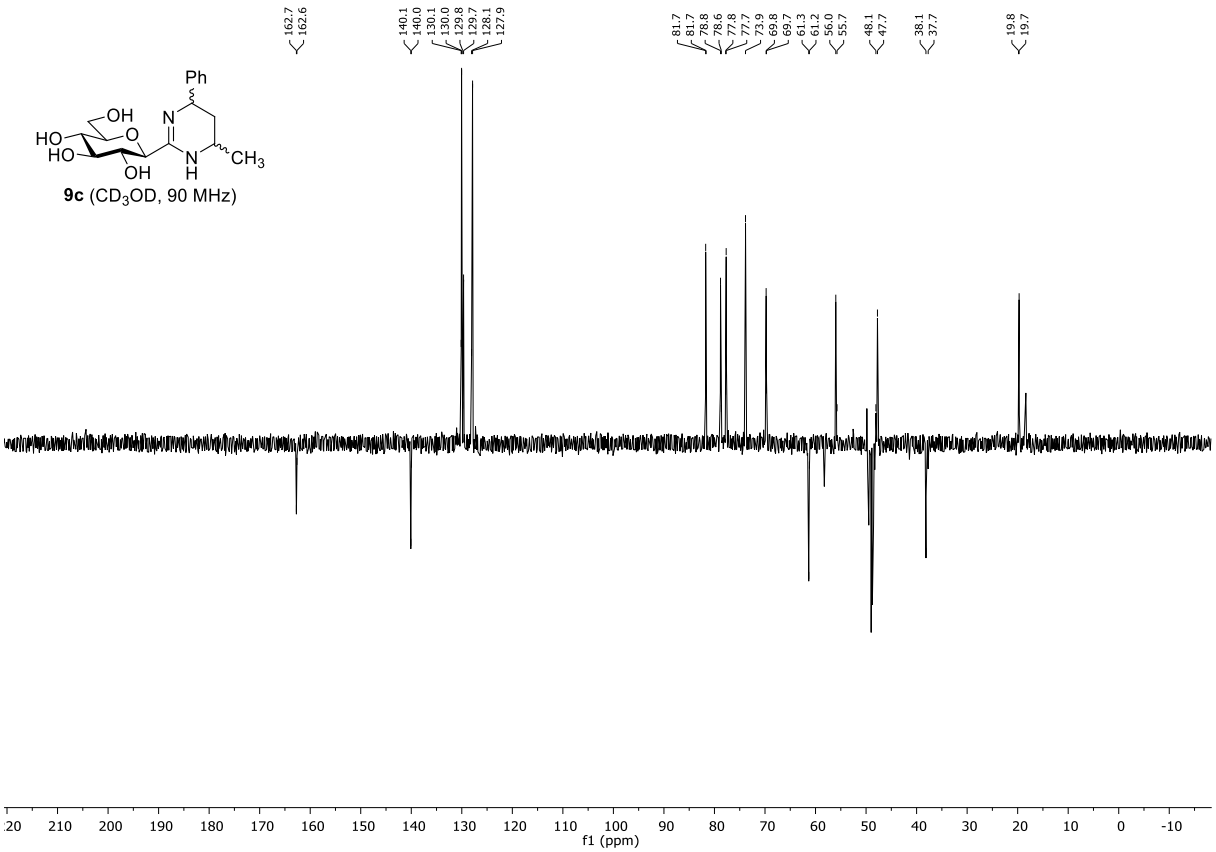

168.0
165.9
163.9
138.9
138.3
138.2
136.7
130.9
128.9
128.5
128.4
128.1
128.1
128.0
127.8
127.8
127.7
127.6
127.4
115.5
87.2
83.4
81.4
79.8
78.3
75.6
75.2
74.7
73.5
69.0
24.4
Ph
OBn
N
BnO
O
BnO
N
Me
OBn
8c (CDCl3, 100 MHz)
210
200
190
180
170
160
150
140
130
120
110
100
90
80
70
60
50
40
30
20
10
f1 (ppm)

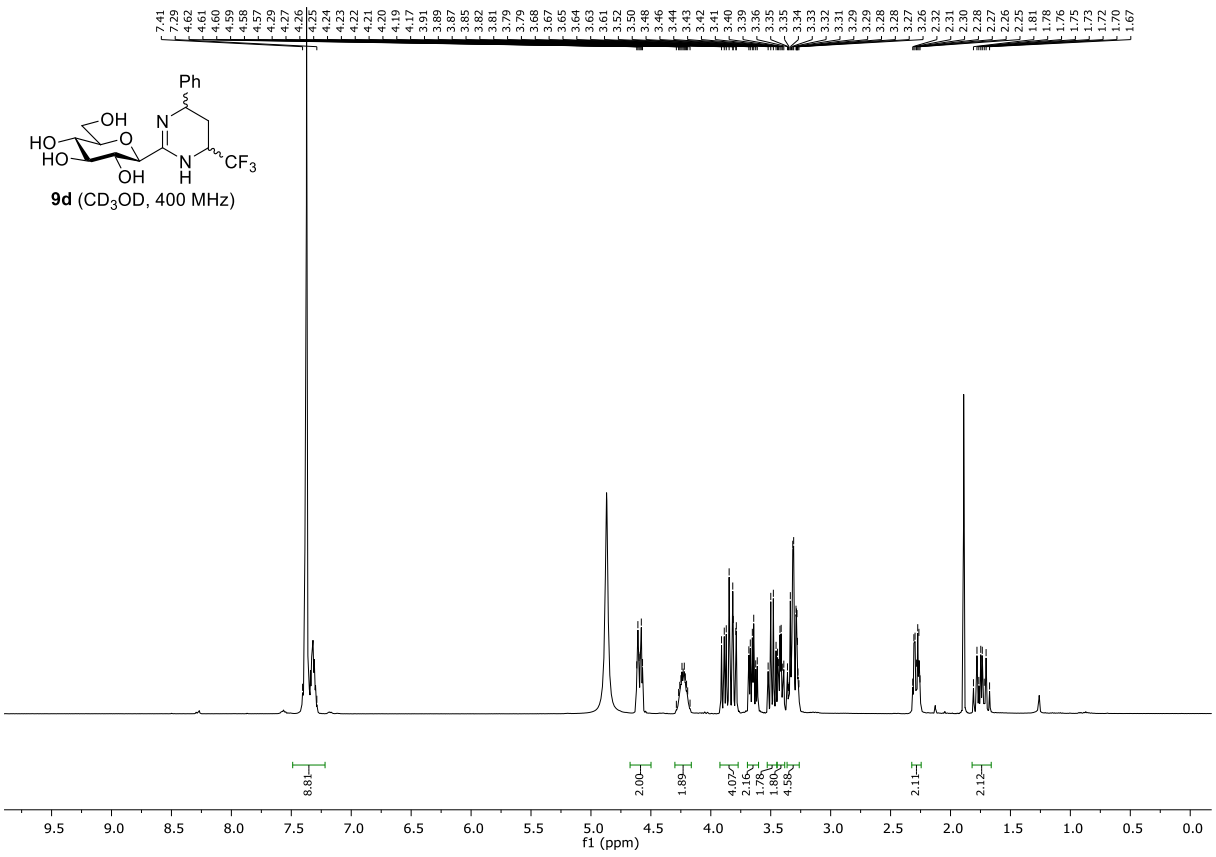

8.14
8.11
7.85
7.56
7.48
7.38
7.19
7.03
6.97
6.82
6.79
5.00
4.97
4.94
4.90
4.88
4.74
4.72
4.69
4.67
4.65
4.64
4.62
4.53
4.50
4.39
4.36
4.34
4.32
4.30
3.97
3.95
3.93
3.90
3.88
3.85
3.84
3.83
3.81
3.80
3.79
3.78
3.75
3.73
3.73
3.72
3.72
Ph
OBn
N
BnO
O
BnO
N
CF3
OBn
8d (CDCl3, 400 MHz)
1.89
0.94
3.03
13.22
2.53
1.71
2.02
1.00
4.04
1.00
0.98
0.98
1.02
1.00
3.05
9.0
8.5
8.0
7.5
7.0
6.5
6.0
5.5
5.0
4.5
4.0
3.5
3.0
2.5
2.0
1.5
1.0
0.5
0.0
f1 (ppm)

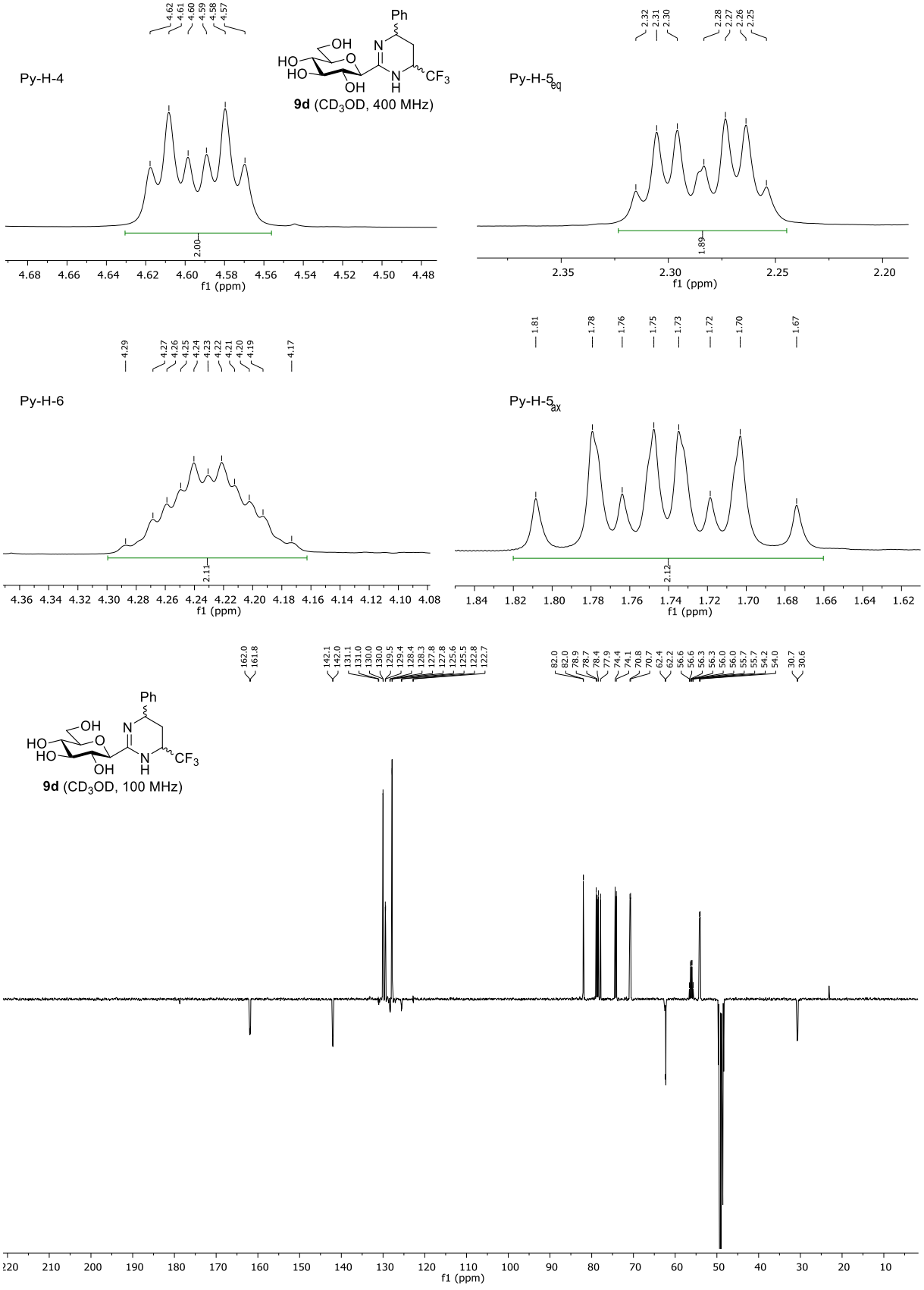

167.37
166.88
157.00
156.64
156.29
155.93
138.71
138.33
138.20
138.08
135.40
132.15
129.22
128.57
128.41
128.21
128.17
127.93
127.84
127.77
127.71
127.64
127.52
127.46
124.91
122.17
119.44
116.70
111.65
87.20
82.74
81.20
80.04
78.34
75.78
75.32
74.86
73.59
68.97
Ph
OBn
N
BnO
O
BnO
N
CF3
OBn
8d (CDCl3, 100 MHz)
210
200
190
180
170
160
150
140
130
120
110
100
90
80
70
60
50
40
30
20
10
f1 (ppm)

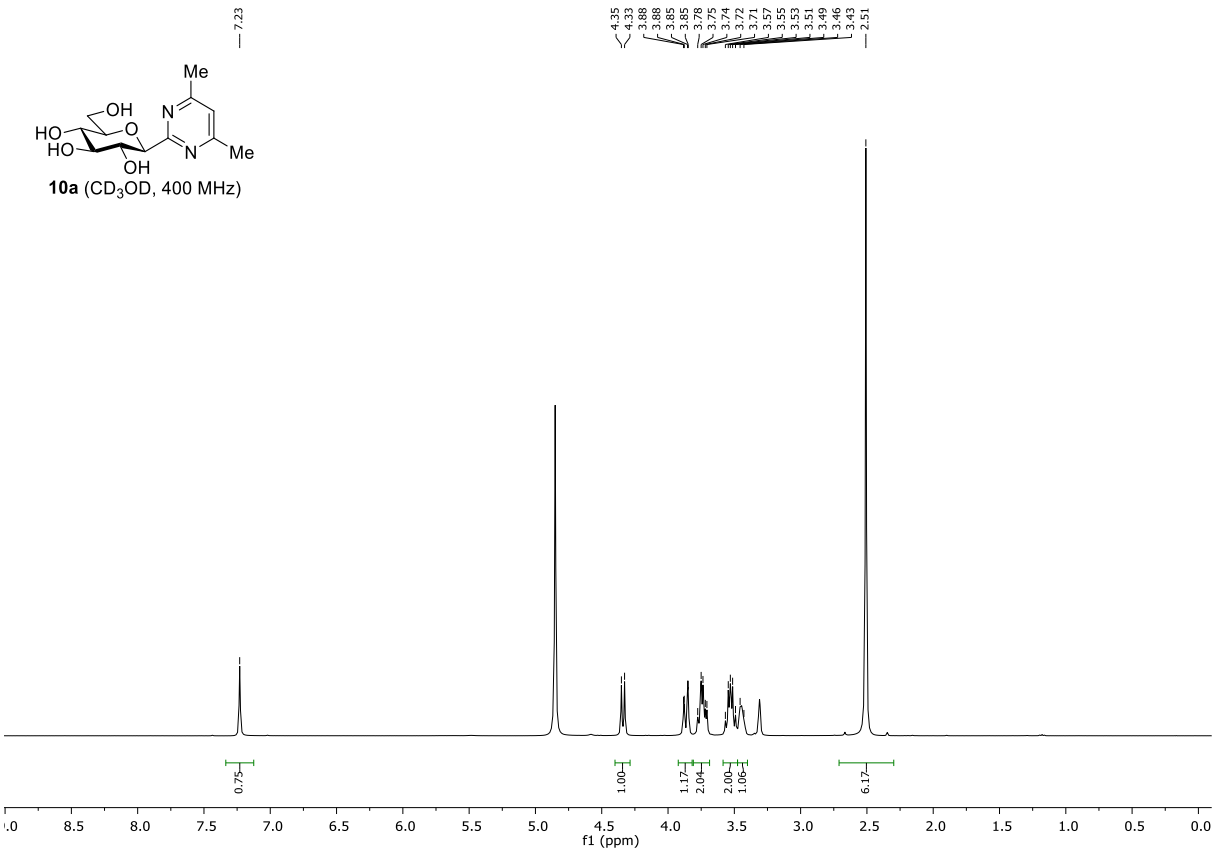

Ph
OH
N
HO
O
HO
OH
N
H
CH3
9c (CD3OD, 400 MHz)
f1 (ppm)


Ph
OH
N
HO
O
HO
OH
N
H
CH3
9c (CD3OD, 400 MHz)
Py-H-4
major comp.
minor comp.
f1 (ppm)
Py-H-5eq
Py-H-5ax
major comp.
minor comp.
f1 (ppm)
f1 (ppm)

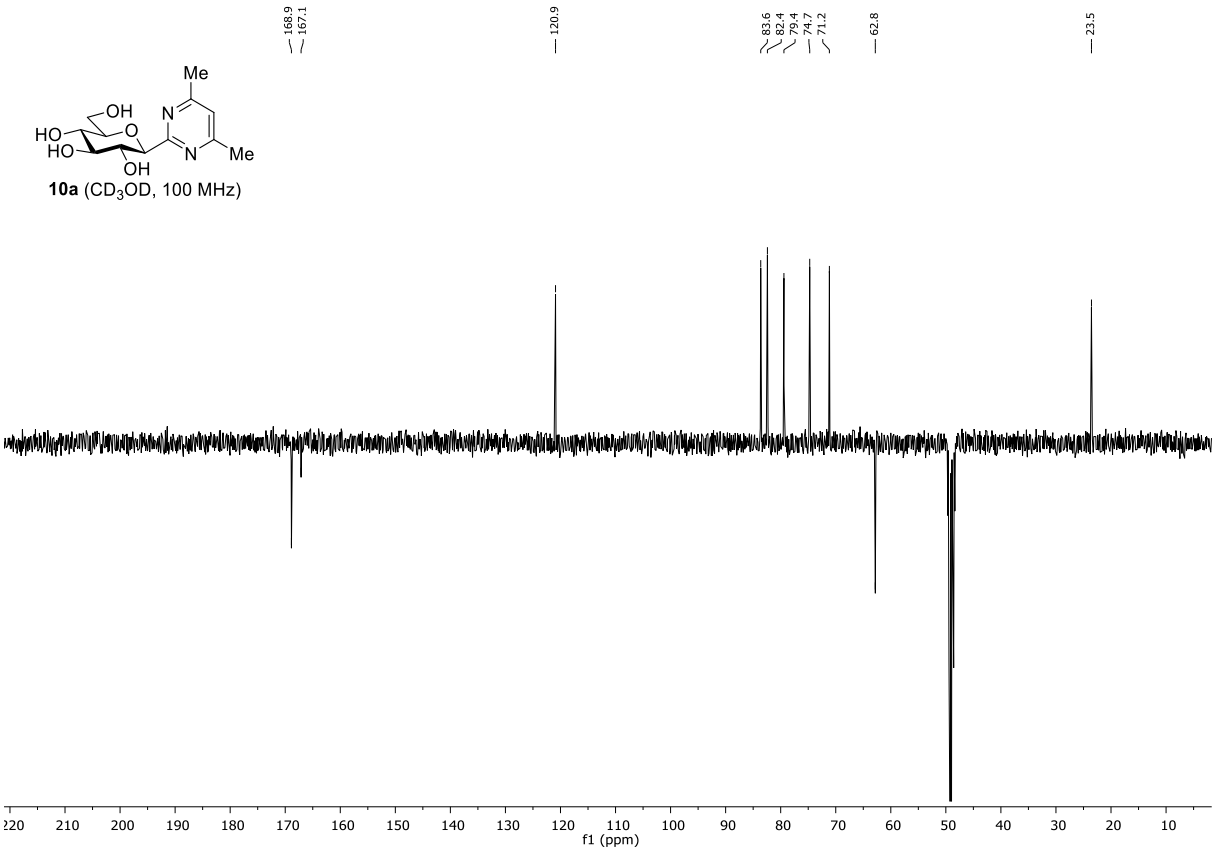

162.7
162.6
140.1
140.0
130.1
130.0
129.8
128.7
128.1
127.9
81.7
81.7
78.8
78.6
77.8
77.7
73.9
69.8
69.7
61.3
61.2
56.0
55.7
48.1
47.7
38.1
37.7
19.8
19.7
Ph
OH
N
HO
O
HO
N
CH3
OH
H
9c (CD3OD, 90 MHz)
f1 (ppm)


7.41
7.29
4.62
4.61
4.60
4.59
4.58
4.57
4.29
4.27
4.26
4.25
4.24
4.23
4.22
4.21
4.20
4.19
4.17
3.91
3.89
3.87
3.85
3.82
3.81
3.79
3.79
3.68
3.67
3.65
3.64
3.63
3.61
3.52
3.50
3.48
3.46
3.44
3.43
3.42
3.41
3.40
3.39
3.36
3.35
3.35
3.34
3.33
3.32
3.31
3.29
3.29
3.28
3.28
3.27
3.26
2.32
2.31
2.30
2.28
2.27
2.26
2.25
1.81
1.78
1.76
1.75
1.73
1.72
1.70
1.67
Ph
OH
N
HO
O
HO
N
CF3
OH
H
9d (CD3OD, 400 MHz)
8.81
2.00
1.89
4.07
2.16
1.78
1.80
4.58
2.11
2.12
f1 (ppm)

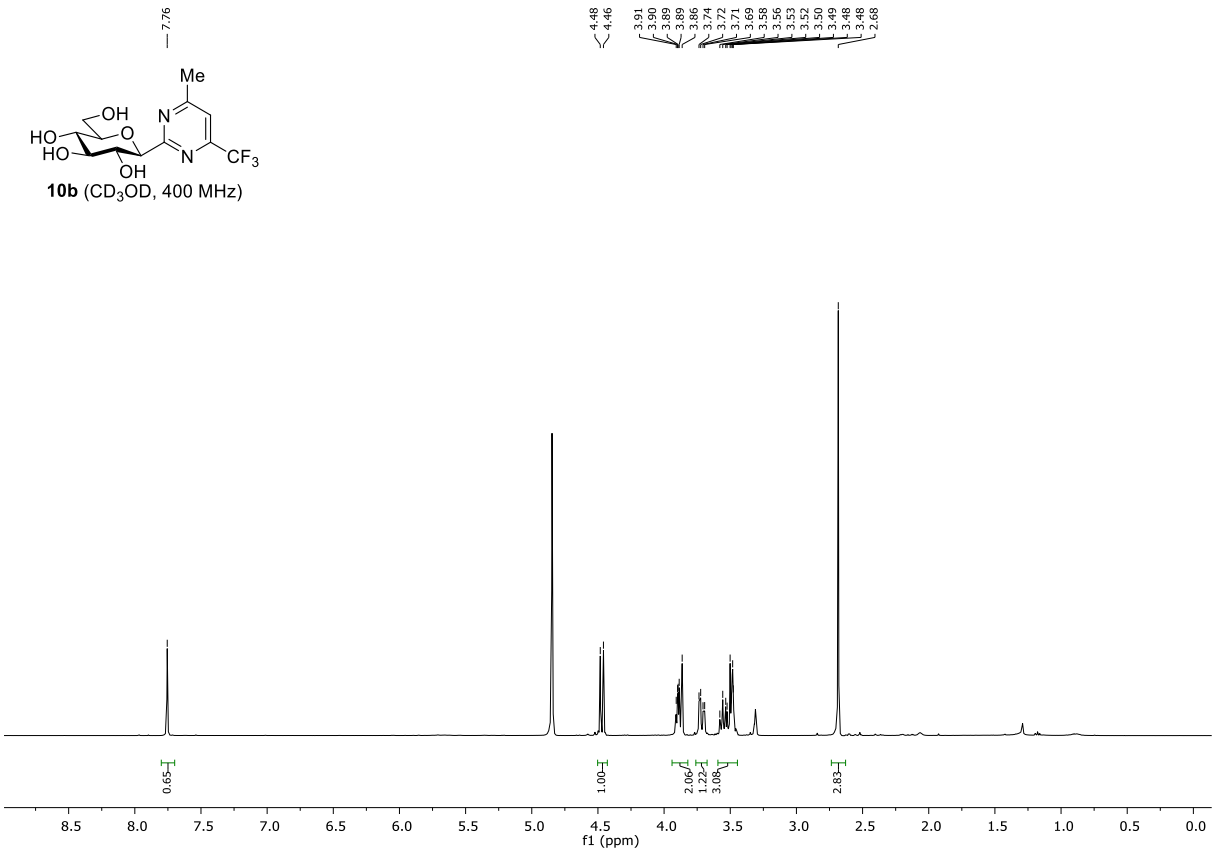

Py-H-4
4.62
4.61
4.60
4.59
4.58
4.57
Ph
OH
N
HO
O
HO
N
CF3
OH
H
9d (CD3OD, 400 MHz)
2.00
4.68 4.66 4.64 4.62 4.60 4.58 4.56 4.54 4.52 4.50 4.48
f1 (ppm)
Py-H-5eq
2.32
2.31
2.30
2.28
2.27
2.26
2.25
1.89
2.35 2.30 2.25 2.20
f1 (ppm)
4.29
4.27
4.26
4.25
4.24
4.23
4.22
4.21
4.20
4.19
4.17
Py-H-6
2.11
4.36 4.34 4.32 4.30 4.28 4.26 4.24 4.22 4.20 4.18 4.16 4.14 4.12 4.10 4.08
f1 (ppm)
1.81
1.78
1.76
1.75
1.73
1.72
1.70
1.67
Py-H-5ax
2.12
1.84 1.82 1.80 1.78 1.76 1.74 1.72 1.70 1.68 1.66 1.64 1.62
f1 (ppm)
162.0
161.8
142.1
142.0
131.1
131.0
130.0
130.0
129.5
129.4
128.4
128.3
127.8
127.8
125.6
125.5
122.8
122.7
82.0
82.0
78.9
78.7
78.4
77.9
74.4
74.1
70.8
70.7
62.4
62.2
56.6
56.6
56.3
56.3
56.0
56.0
55.7
55.7
54.2
54.0
30.7
30.6
Ph
OH
N
HO
O
HO
N
CF3
OH
H
9d (CD3OD, 100 MHz)
220 210 200 190 180 170 160 150 140 130 120 110 100 90 80 70 60 50 40 30 20 10
f1 (ppm)



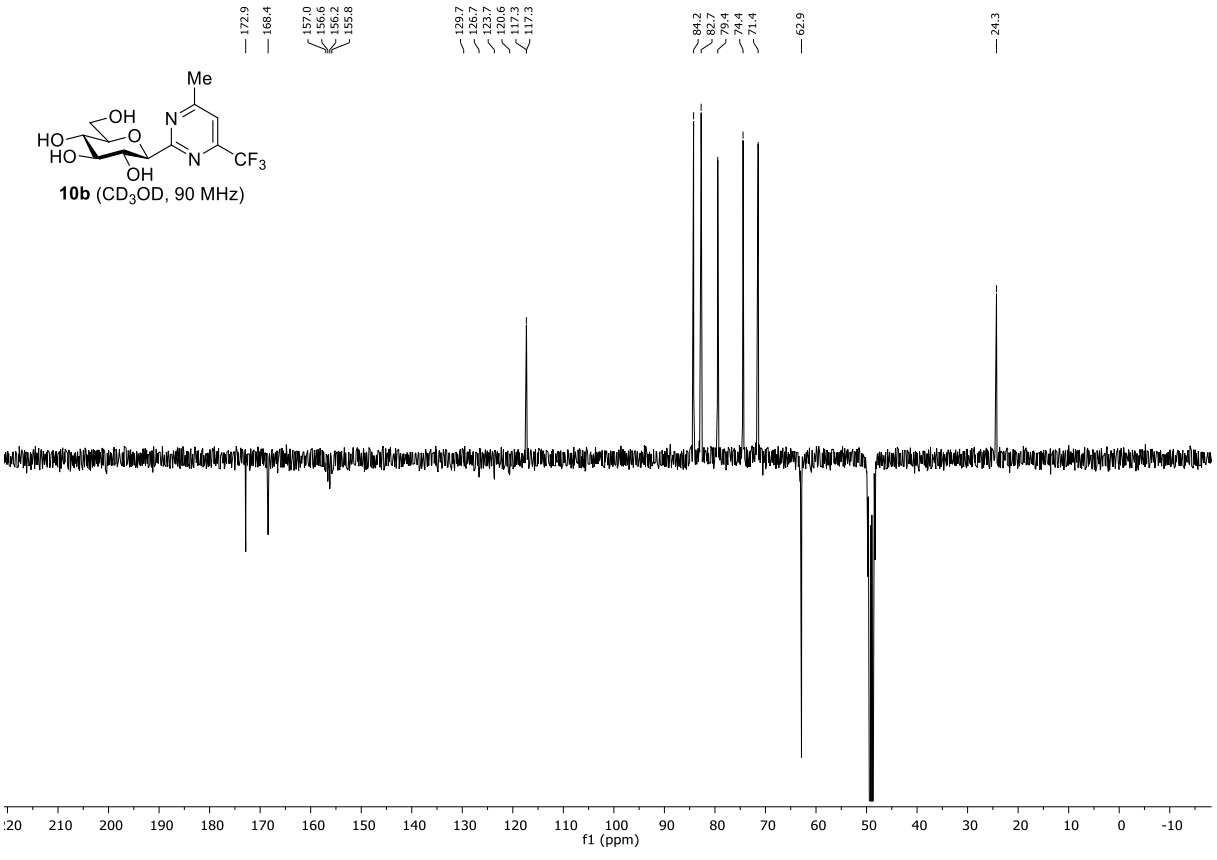
10a (CD_3OD, 400 MHz)



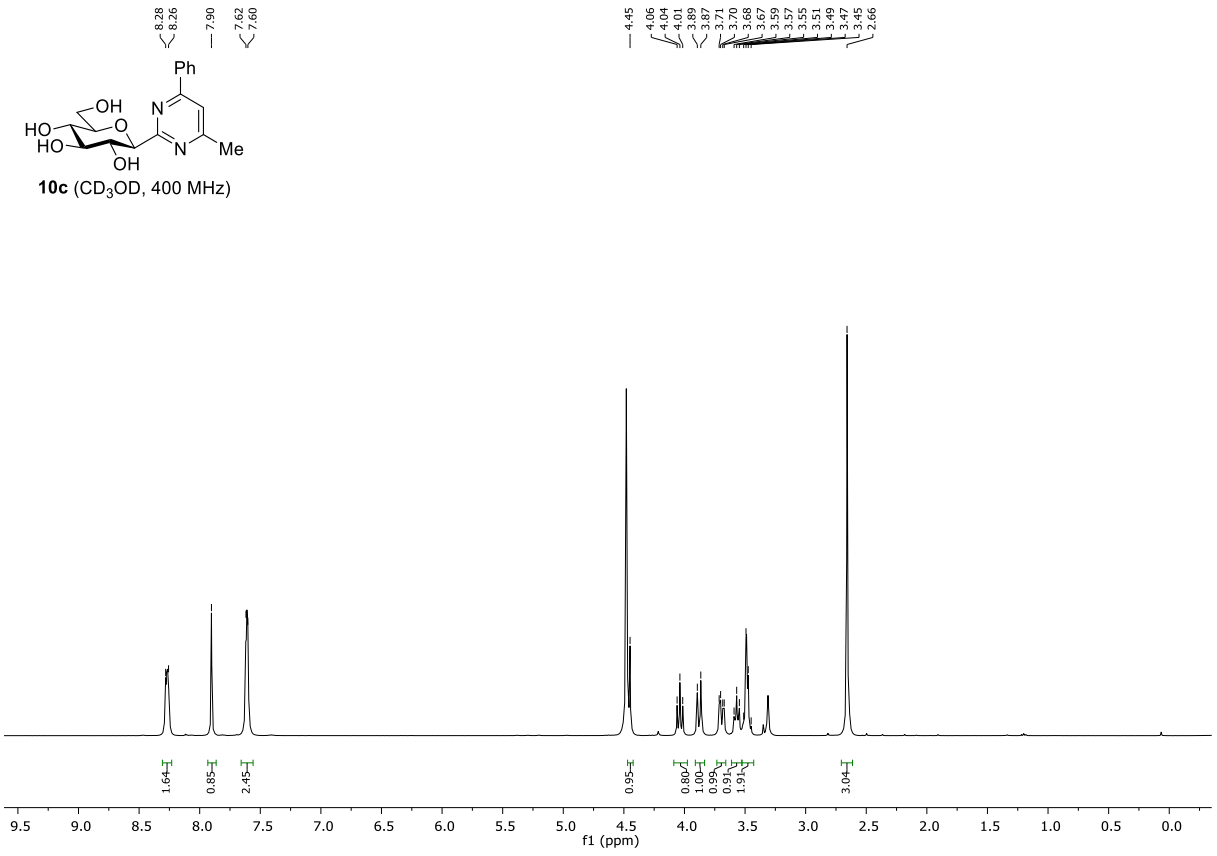
10a (CD_3OD, 100 MHz)



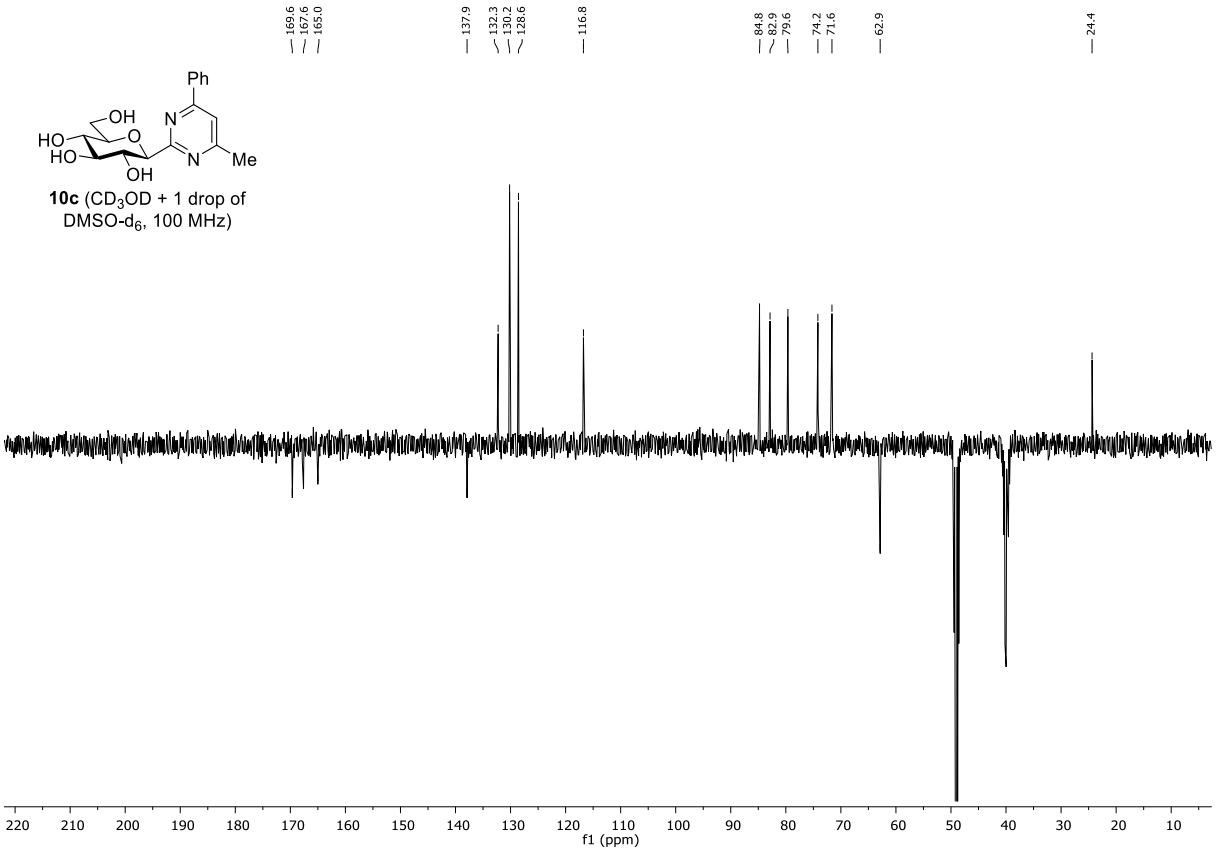
10b (CD_3OD, 400 MHz)



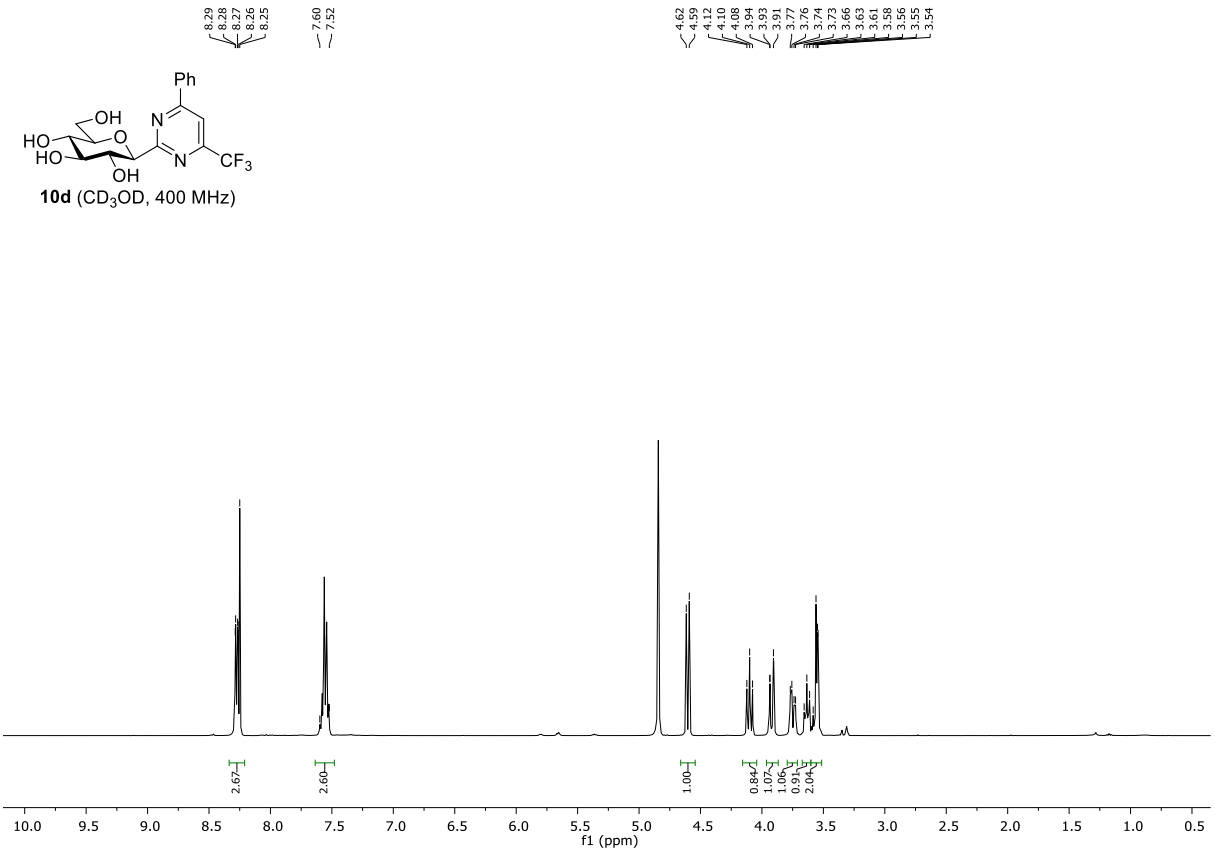
10b (CD_3OD, 90 MHz)

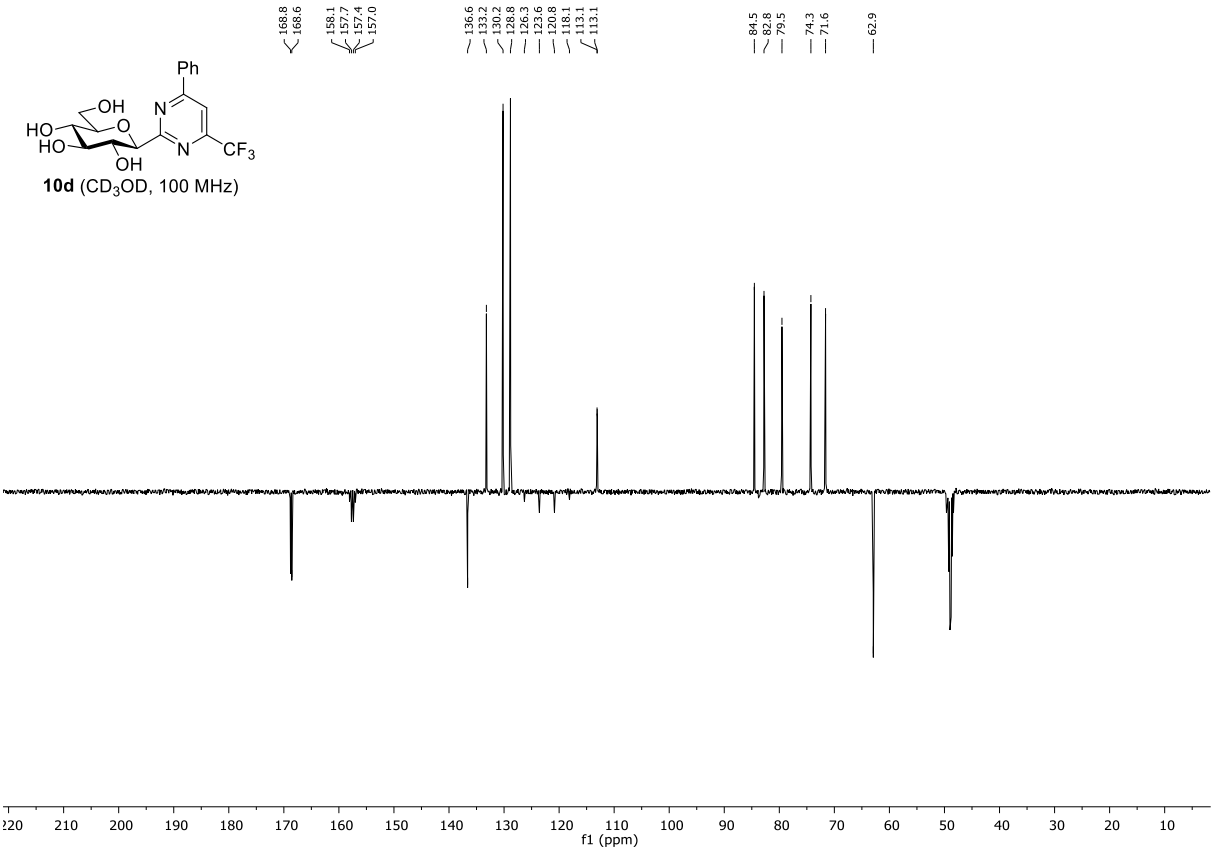


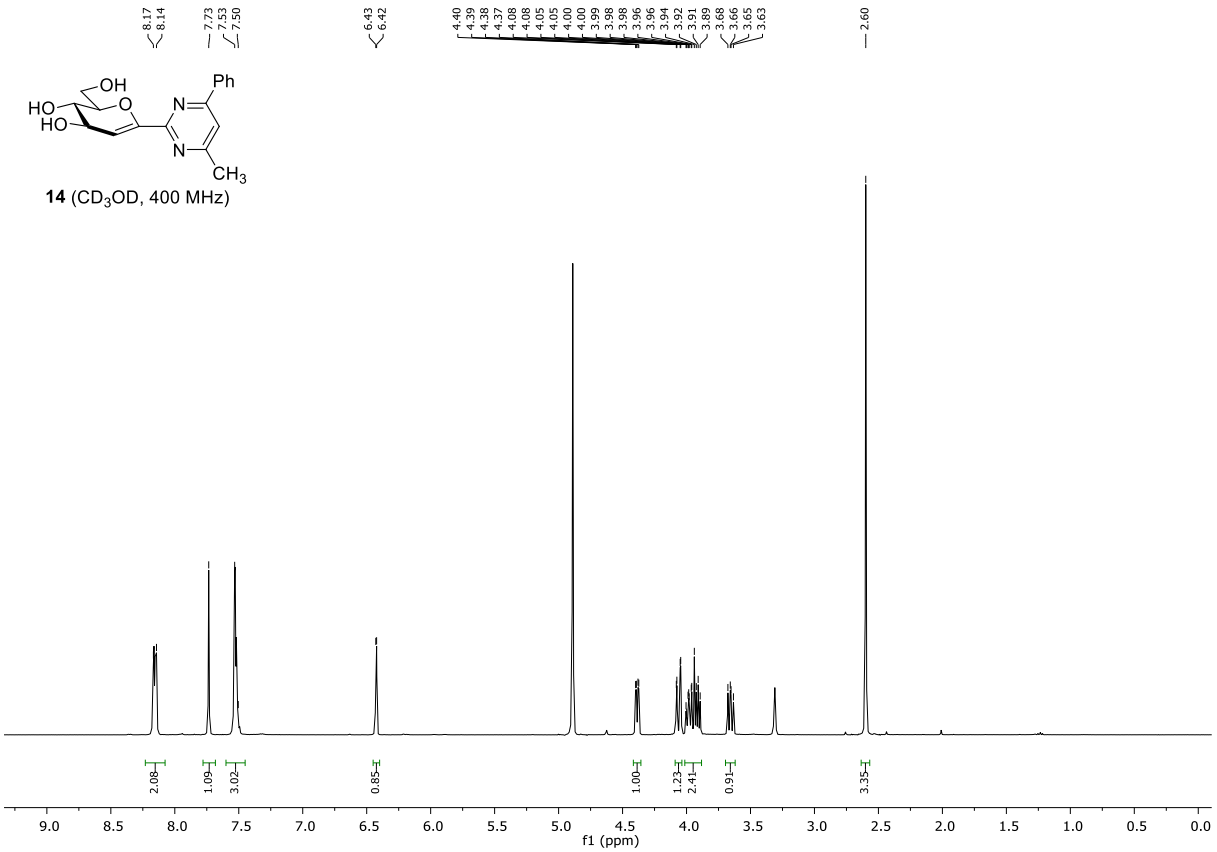
10c (CD_3OD, 400 MHz)

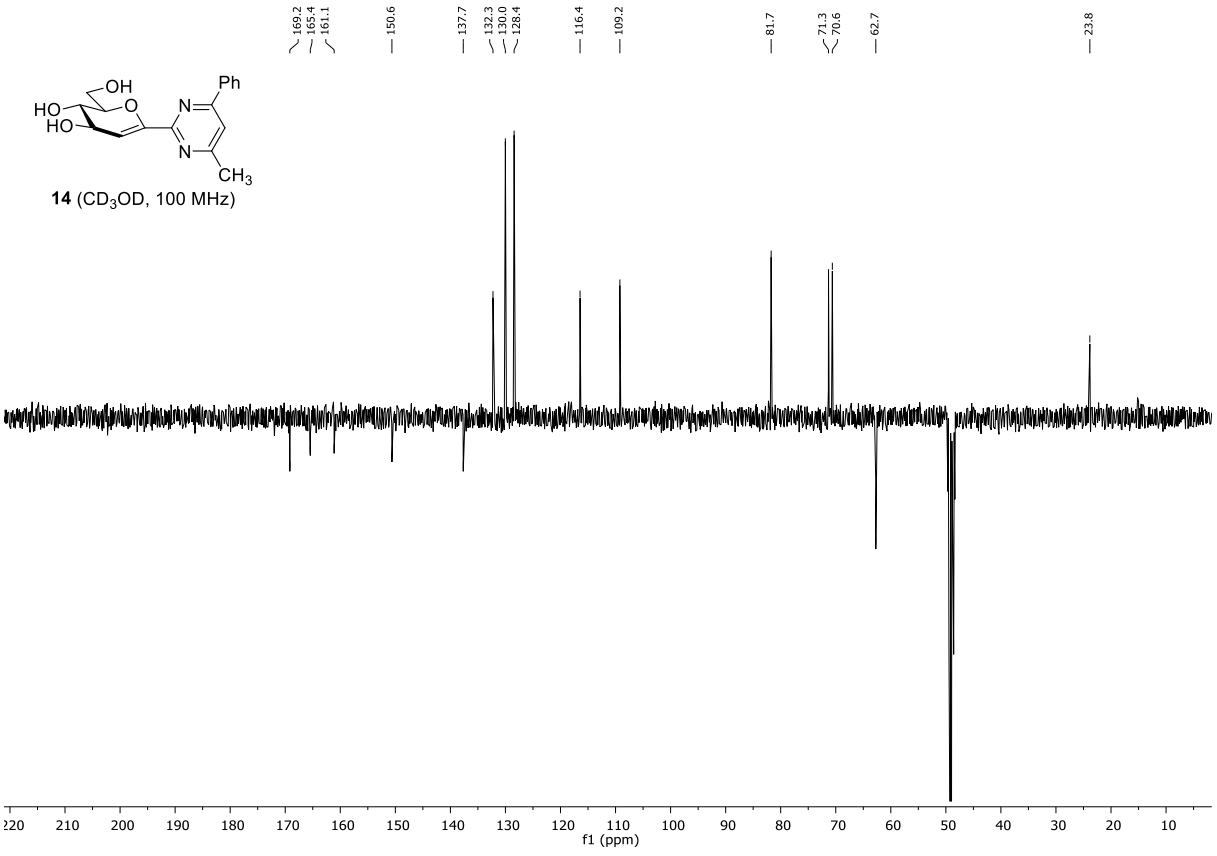


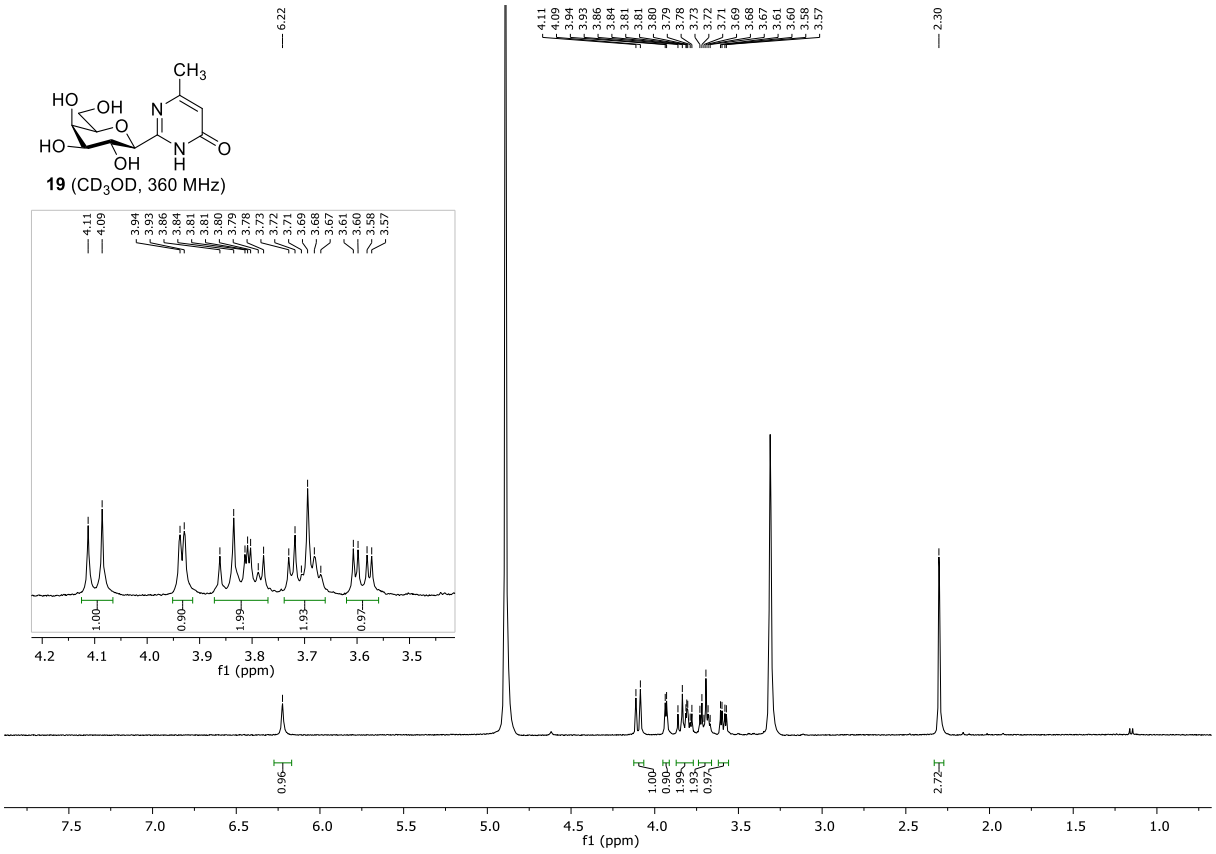
10c (CD_3OD + 1 drop of DMSO-d_6, 100 MHz)

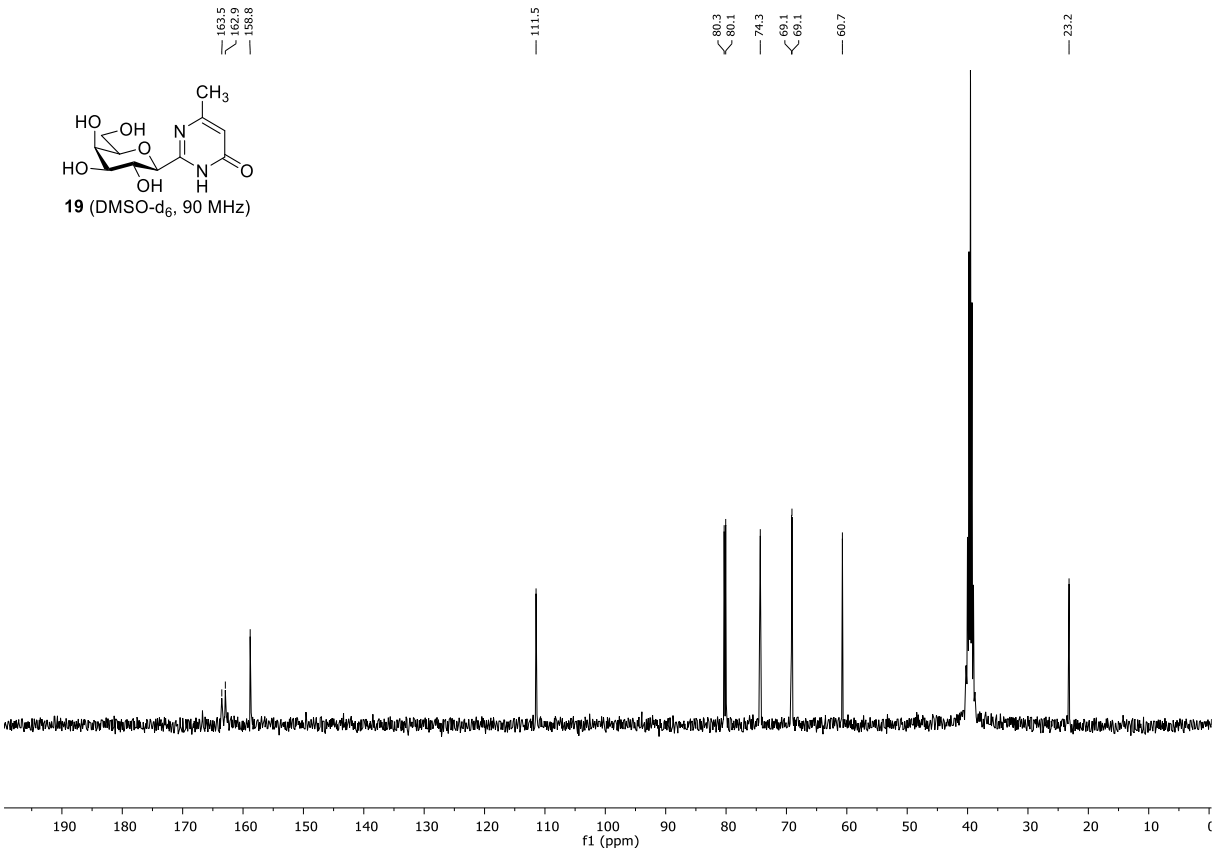

8.29
8.28
8.27
8.26
8.25
7.60
7.52
4.62
4.59
4.12
4.10
4.08
3.94
3.93
3.91
3.77
3.76
3.74
3.73
3.66
3.63
3.61
3.58
3.56
3.55
3.54
Ph
OH
HO
HO
OH
O
N
N
CF3
10d (CD3OD, 400 MHz)
2.67
2.60
1.00
0.84
1.07
1.06
0.91
2.04
10.0
9.5
9.0
8.5
8.0
7.5
7.0
6.5
6.0
5.5
5.0
4.5
4.0
3.5
3.0
2.5
2.0
1.5
1.0
0.5
f1 (ppm)

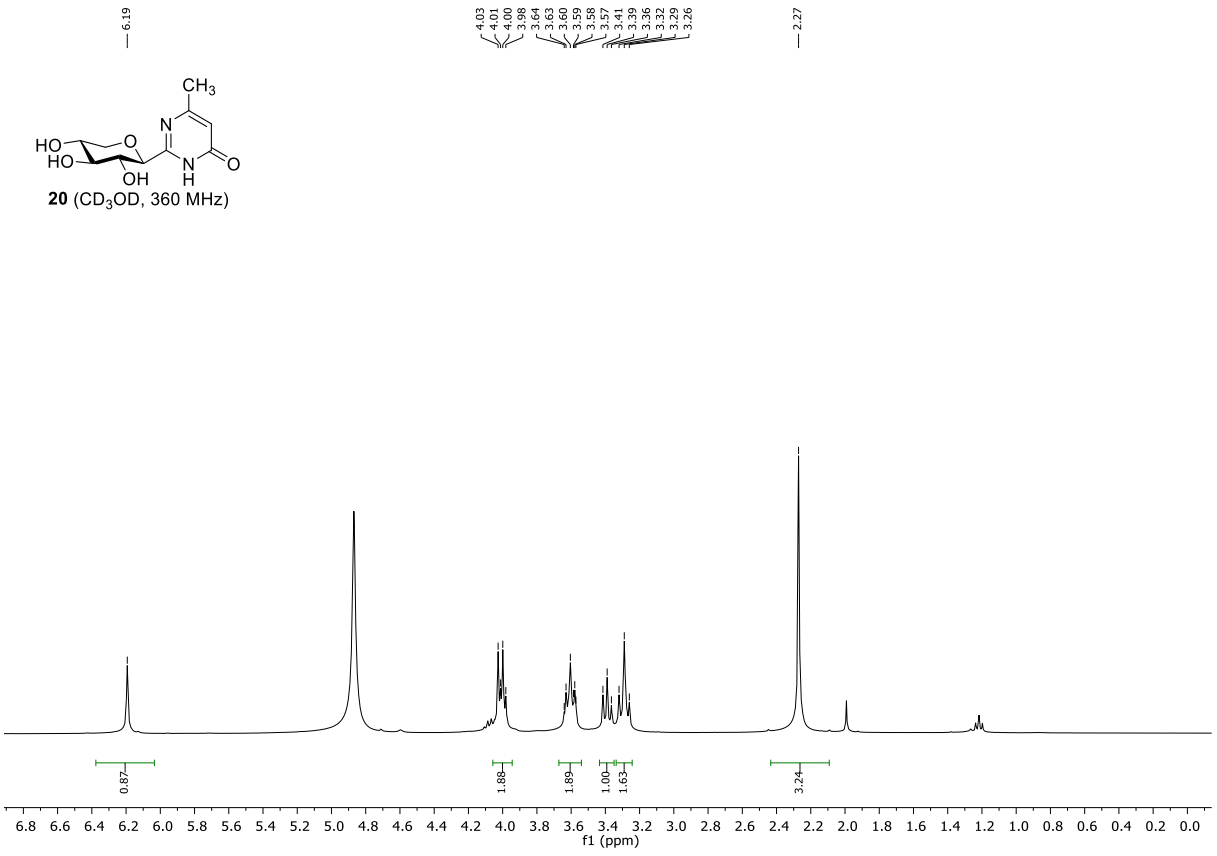

168.8
168.6
158.1
157.7
157.4
157.0
136.6
133.2
130.2
128.8
126.3
123.6
120.8
118.1
113.1
113.1
84.5
82.8
79.5
74.3
71.6
62.9
Ph
OH
HO
HO
OH
O
N
N
CF3
10d (CD3OD, 100 MHz)
220
210
200
190
180
170
160
150
140
130
120
110
100
90
80
70
60
50
40
30
20
10
f1 (ppm)


8.17
8.14
7.73
7.53
7.50
6.43
6.42
4.40
4.39
4.38
4.37
4.08
4.08
4.05
4.05
4.00
4.00
3.99
3.98
3.98
3.96
3.96
3.94
3.92
3.91
3.89
3.68
3.66
3.65
3.63
2.60
OH
HO
HO
O
N
N
Ph
CH3
14 (CD3OD, 400 MHz)
2.08
1.09
3.02
0.85
1.00
1.23
2.41
0.91
3.35
9.0
8.5
8.0
7.5
7.0
6.5
6.0
5.5
5.0
4.5
4.0
3.5
3.0
2.5
2.0
1.5
1.0
0.5
0.0
f1 (ppm)

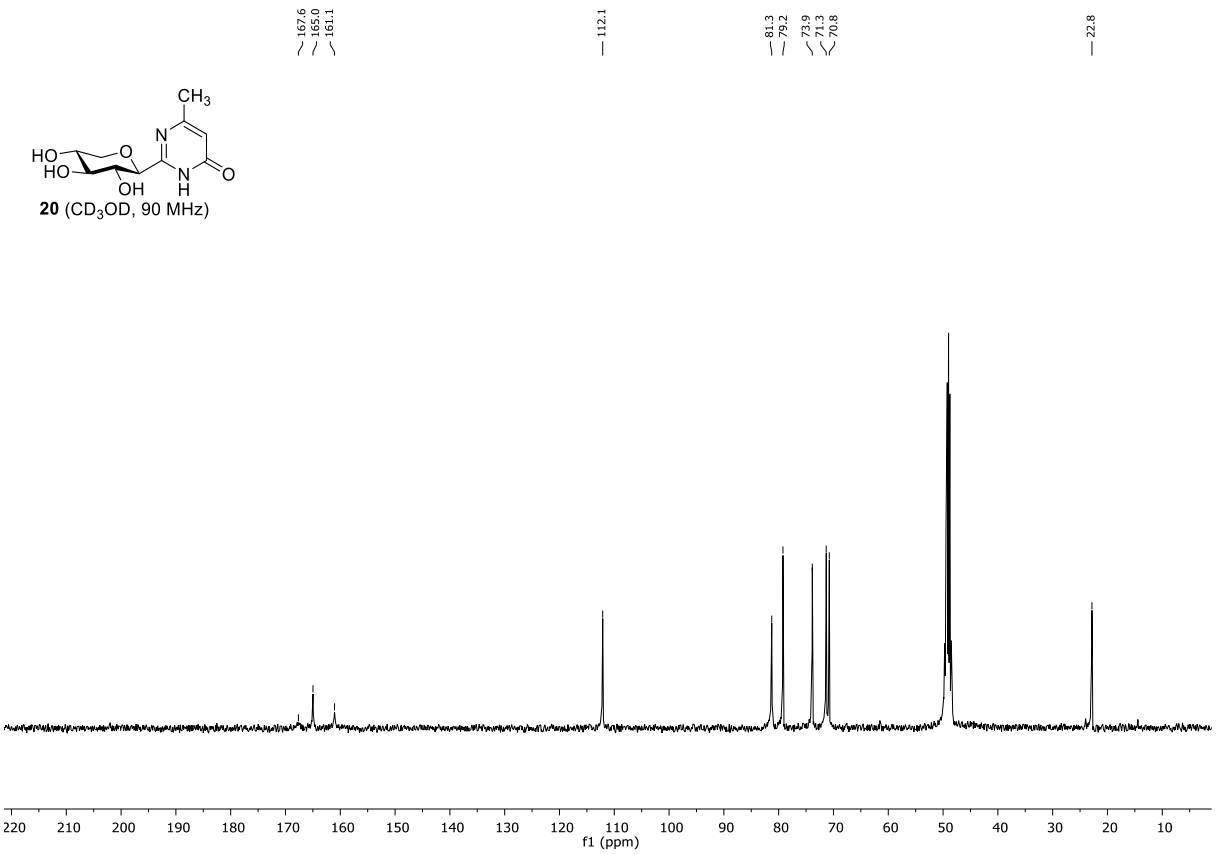

169.2
165.4
161.1
150.6
137.7
132.3
130.0
128.4
116.4
109.2
81.7
71.3
70.6
62.7
23.8
OH
HO
HO
O
N
N
Ph
CH3
14 (CD3OD, 100 MHz)
220
210
200
190
180
170
160
150
140
130
120
110
100
90
80
70
60
50
40
30
20
10
f1 (ppm)


19 (CD3OD, 360 MHz)
f1 (ppm)

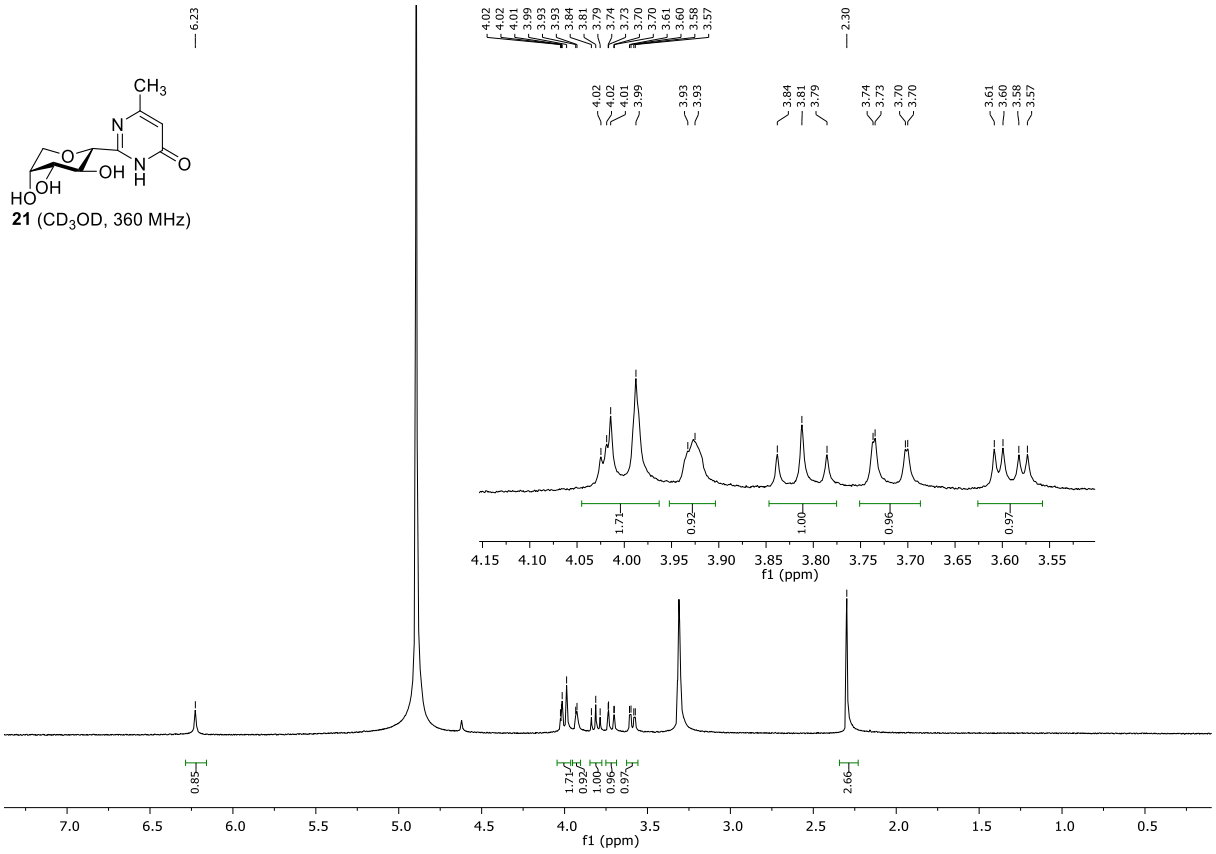

19 (DMSO-d6, 90 MHz)
f1 (ppm)

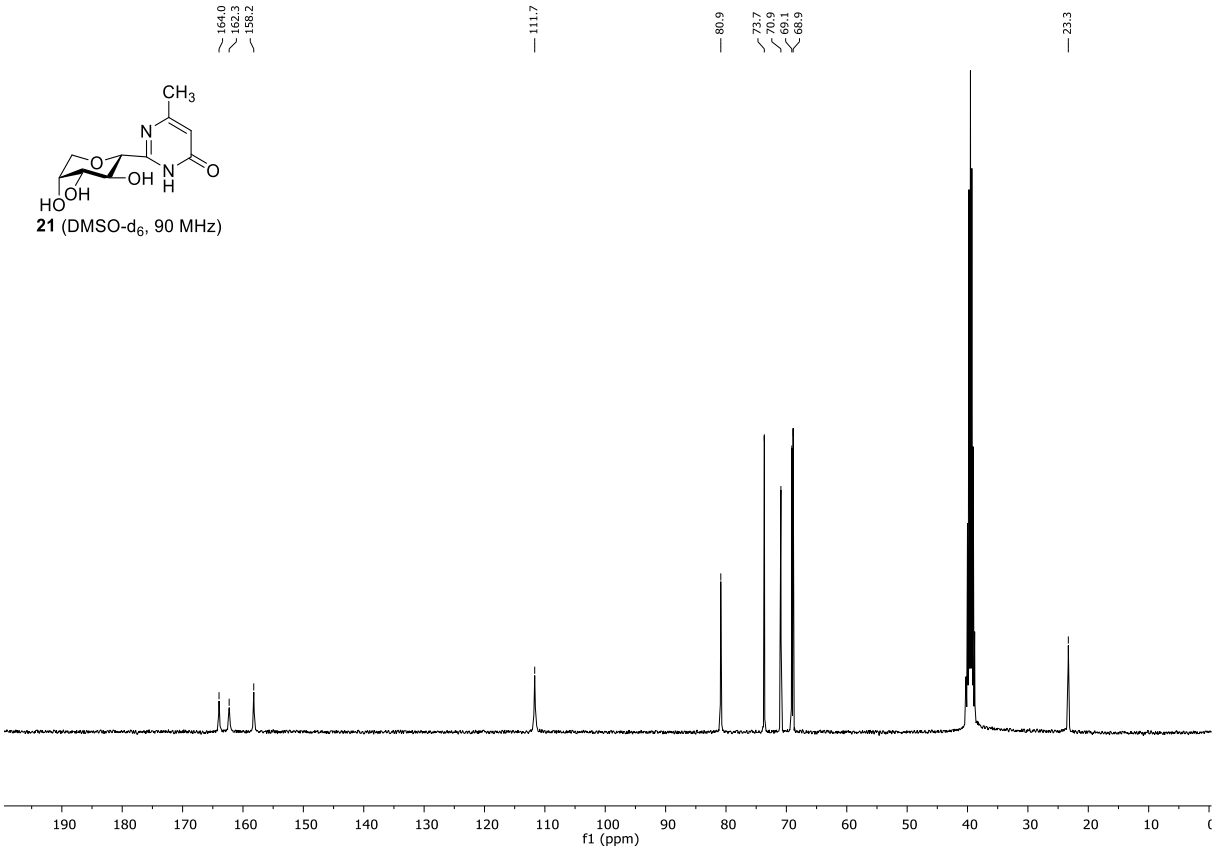


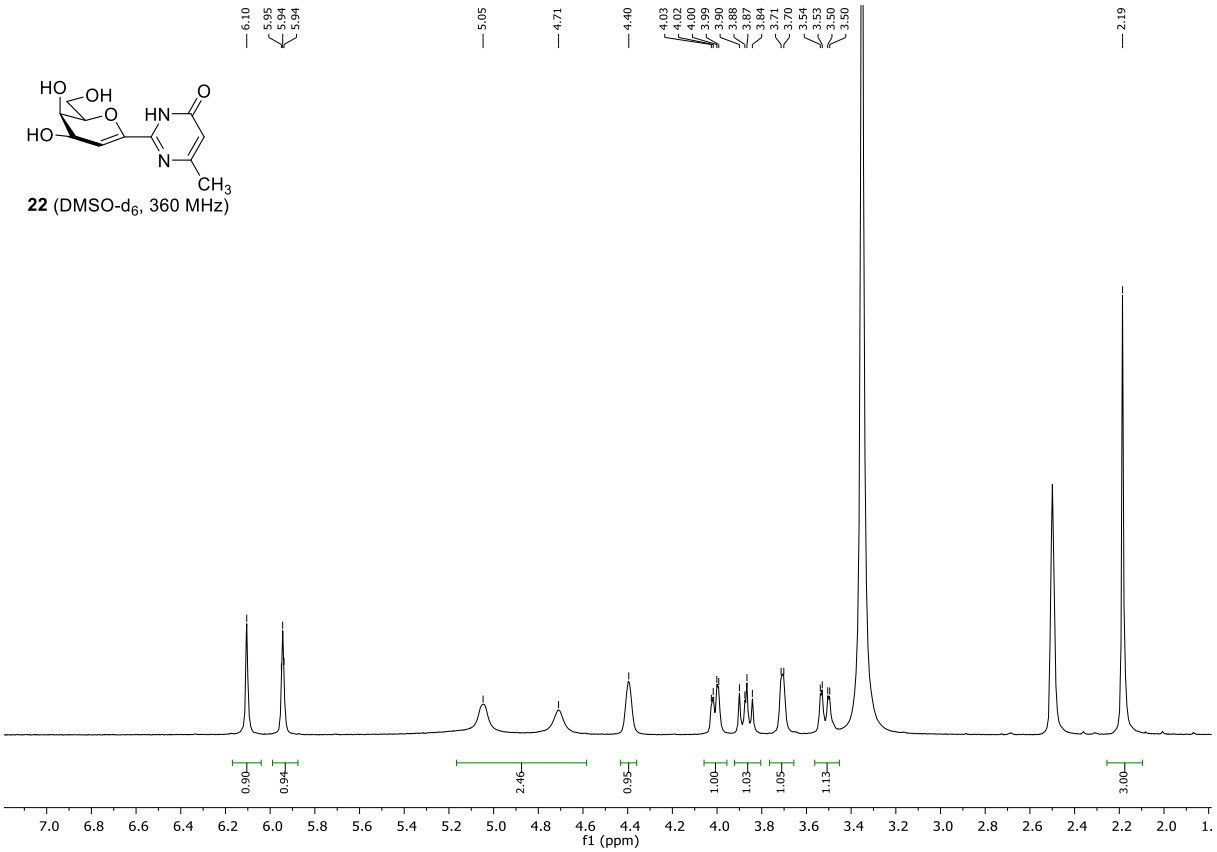
20 (CD_3OD, 360 MHz)



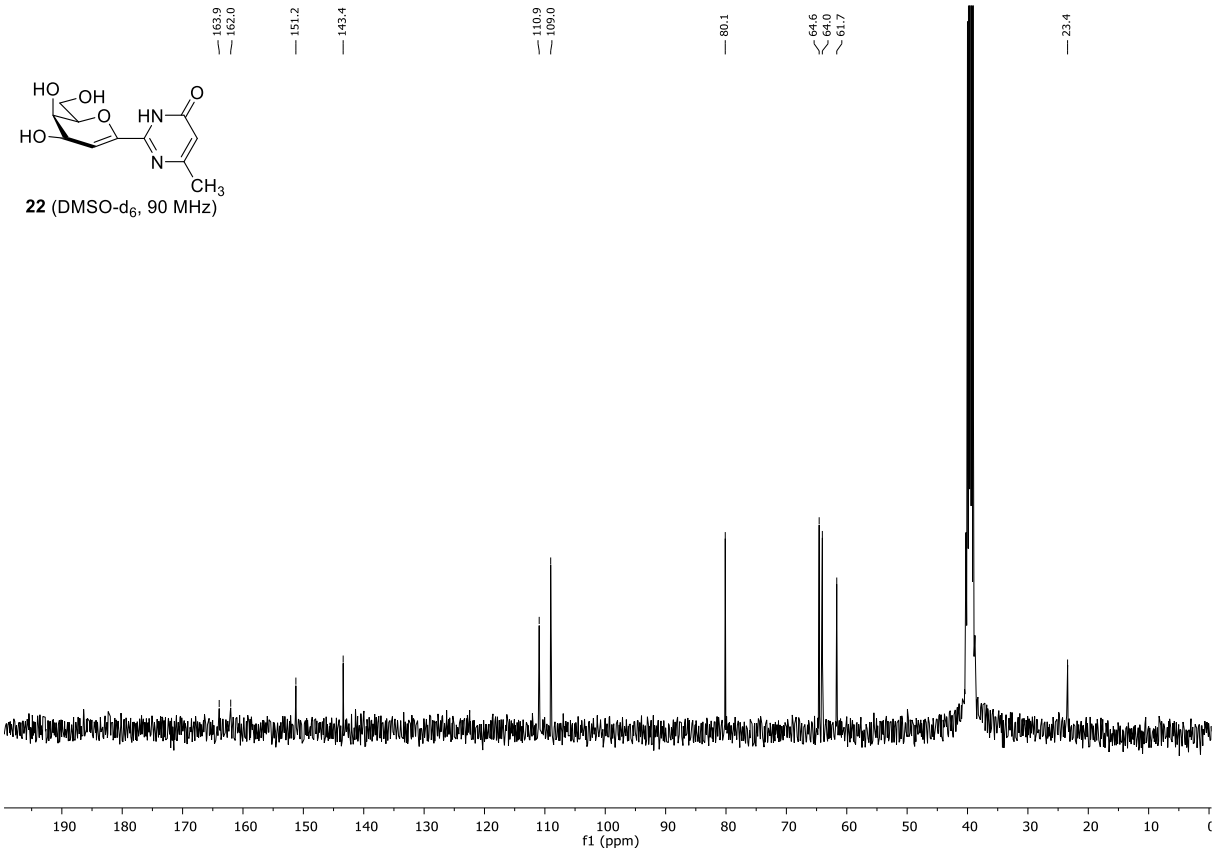
20 (CD_3OD, 90 MHz)


6.23
4.02
4.02
4.01
3.99
3.93
3.93
3.84
3.81
3.79
3.74
3.73
3.70
3.70
3.61
3.60
3.58
3.57
2.30
CH3
N
O
OH
N
H
O
HO
OH
21 (CD3OD, 360 MHz)
1.71
0.92
1.00
0.96
0.97
0.85
2.66
f1 (ppm)


164.0
162.3
158.2
111.7
80.9
73.7
70.9
69.1
68.9
23.3
CH3
N
O
OH
N
H
O
HO
OH
21 (DMSO-d6, 90 MHz)
f1 (ppm)



22 (DMSO-d_6, 360 MHz)



22 (DMSO-d_6, 90 MHz)