New Bifunctional Carbohydrate-Like Thiourea Derivatives – Design and First Application in Organocatalysis

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General Methods: Reactions were generally performed under argon in flame-dried flasks. Solvents and reagents were added by syringes. Solvents were dried using standard procedures. Reagents were purchased and were used as received without further purification unless stated. Reactions were monitored by thin-layer chromatography (TLC). Products were purified by flash chromatography (FLC) on silica gel (32-63 µm). Unless otherwise stated, yields refer to chromatographically homogeneous and spectroscopically pure materials (^{1}H-NMR spectroscopy). NMR spectra were recorded with JEOL (ECX 400, Eclipse 500) instruments. Chemical shifts are reported relative to TMS (^{1}H: δ = 0.00 ppm) and $CDCl_3$ (^{13}C: δ = 77.0 ppm). Integrals are in accordance with assignments; coupling constants are given in Hz. Multiplicity is indicated as follows: s (singlet), d (doublet), t (triplet), m (multiplet), m_c (centered multiplet), dd (doublet of doublet), br s (broad singlet). MS and HRMS analyses were performed with a Varian Ionspec QFT-7 instrument (ESI-FT ICRMS). Elemental analyses were carried out with a Vario EL Elemental Analyzer. Optical

rotations ($[\alpha]_D$) were determined with Perkin–Elmer 141 or Perkin–Elmer 241 polarimeters at the temperatures given. Melting points were measured with a Reichert apparatus (Thermovar) and are uncorrected.

The starting materials **9**,[1] **11**,[2] **13**,[3] and the prolinol derivative **26**[4] were prepared according to literature procedures.

General Procedure 1, Syntheses of Thiourea Derivatives:

The corresponding aminopyran or aminooxepane derivative (1.0 equivalent) and isothiocyanate **14** (1.0 equivalent) were dissolved in methanol or isopropanol (2-8 mL/mmol substrate) at 0 °C. After stirring the mixture for 1.5 h at this temperature, the solvent was removed under reduced pressure. The residue was purified by column chromatography on silica gel (CH_2Cl_2/MeOH, 15:1) to give the corresponding thiourea product.

1-[3,5-Bis(trifluoromethyl)phenyl]-3-[(2*S*,3*R*,4*S*,5*S*)-4-hydroxy-2,5-bis(hydroxyl-methyl)-6,6-dimethyltetrahydro-2*H*-pyran-3-yl]thiourea (15):

According to the general procedure 1, pyran derivative **9** (282 mg, 1.38 mmol), and isothiocyanate **14** (374 mg, 1.38 mmol) in methanol (7 mL) were used. The crude product was purified by column chromatography to give **15** (305 mg, 46%) as colorless crystals, mp. 83-86 °C, and **18** (160 mg, 38%) as colorless wax. Product **15**: [α_D^{20}] +45.0 (*c* 0.5, MeOH). ^{1}H NMR (CD_3OD, 500 MHz): δ = 1.27, 1.46 (2 s, 3 H each, Me), 1.78 (q, *J* = 5.3 Hz, 1 H, 5''-H), 3.56 (dd, *J* = 11.6, 7.1 Hz, 1 H, 2''-CH_2), 3.66-3.72 (m, 2 H, 2''-CH_2, 5''-CH_2), 3.75 (dd, *J* = 11.1, 5.7 Hz, 1 H, 5''-CH_2), 4.05 (t, *J* = 4.7 Hz, 1 H, 4''-H), 4.19-4.25 (m, 1 H, 2''-H), 4.63-4.66 (m, 1 H, 3''-H), 7.63 (s, 1 H, 4'-H), 8.21 ppm (s, 2 H, 2'-H). ^{13}C NMR (CD_3OD, 125.8 MHz): δ = 26.5, 27.6 (2 q, Me), 49.4 (d, C-5''), 58.0 (d, C 3''), 62.8 (t, 2''-CH_2), 63.2 (t, 5''-CH_2), 70.8 (d, C-2''), 72.6 (d, C-4''), 75.8 (s, C-6''), 117.8 (d, C-4'), 123.7 (d, C-2'), 124.7 (q, $^1J_{CF}$ = 271.9 Hz, CF_3), 132.6 (q, $^2J_{CF}$ = 32.9 Hz, C-3'), 141.5 (s, C-1'), 182.8 ppm (s, C-2). ^{19}F NMR (CD_3OD, 376 MHz): δ = -60.4 ppm (s, CF_3). IR (ATR): ν = 3500-3100 (OH, NH), 3100-2895 (=C-H, C-H), 1275 cm^{-1} (C=S). HRMS (ESI-TOF) calcd for $C_{18}H_{23}F_6N_2O_5S$ $[M+H]^+$: 477.1277, found: 477.1325. Elemental analysis calc (%) for $C_{18}H_{22}F_6N_2O_5S$ (476.4): C 45.38, H 4.65, N 5.88, S 6.73; found: C 45.38, H 4.66, N

5.92, S 7.24. Product **18**: ^{1}H NMR (CD_3OD, 400 MHz): δ = 4.07 (s, 3 H, OMe), 7.69 (s, 1 H, 4-H), 8.30 ppm (br s, 2 H, 2-H). ^{13}C NMR (CD_3OD, 125.8 MHz): δ = 56.4 (q, OMe), 117.0 (d, C-4), 121.1 (d, C-2), 123.3 (q, $^{1}J_{CF}$ = 277.2 Hz, CF_3), 131.7 (q, $^{2}J_{CF}$ = 37.4 Hz, C-3'), 189.5 ppm (s, C=S); the signal of C-1' could not be detected. IR (ATR): ν = 3300-3200 (N-H), 3100-2900 (=C-H, C-H), 1280 cm^{-1} (C=S). Elemental analysis calc (%) for $C_{10}H_7F_6NOS$ (303.2): C 39.61, H 2.33, N 4.62, S 10.57; found: C 39.64, H 2.54, N 4.69, S 10.04.

1-[3,5-Bis(trifluoromethyl)phenyl]-3-[(2*S*,3*R*,4*R*,5*S*,6*S*)-4-hydroxy-2,5-bis-(hydroxylmethyl)-6-methoxytetrahydro-2*H*-pyran-3-yl]thiourea (16):

According to the general procedure 1, pyran derivative **11** (79 mg, 0.38 mmol), and isothiocyanate **14** (103 mg, 0.38 mmol) in methanol (3 mL) were used. The crude product was purified by column chromatography to give **16** (83 mg, 45%) as colorless solid, mp. 163-165 °C. [[α_D^{20}] +65.5 (*c* 0.38, MeOH). ^{1}H NMR (CD_3OD, 400 MHz): δ = 1.97-2.02 (m, 1 H, 5''-H), 3.37 (s, 3 H, OMe), 3.62 (dd, *J* = 11.6, 7.0 Hz, 1 H, 2''-CH_2), 3.68-3.82 (m, 3 H, 2''-CH_2, 5''-CH_2), 4.01-4.06 (m, 1 H, 2''-H), 4.22-4.42 (m, 1 H, 4''-H), 4.83 (s, 1 H, 6''-H), 4.97-5.01 (m, 1 H, 3''-H), 7.64 (s, 1 H, 4'-H), 8.13 ppm (s, 2 H, 2'-H). ^{13}C NMR (CD_3OD, 125.8 MHz): δ = 45.3 (d, C-5''), 54.0 (d, C-3''), 54.0 (q, OMe), 57.5 (t, 5''-CH_2), 61.3 (t, 2''-CH_2), 65.8 (d, C-4''), 70.4 (d, C-2''), 100.9 (d, C-6''), 117.0 (d, C-4'), 123.1 (d, C-2'), 123.4 (q, $^{1}J_{CF}$ = 271.8 Hz,CF_3), 131.5 (q, $^{2}J_{CF}$ = 33.9 Hz, C-3'), 141.4 (s, C-1'), 182.4 ppm (s, C-2). ^{19}F NMR (CD_3OD, 376 MHz): δ = -64.3 ppm (s, CF_3). IR (ATR): ν = 3500-3100 (O-H, N-H), 3100-2880 (=C-H, C-H), 1275 cm^{-1} (C=S). HRMS (ESI-TOF) calcd for $C_{17}H_{21}F_6N_2O_5S$ $[M+H]^+$: 479.1070, found: 479.1091. Elemental analysis calc (%) for $C_{17}H_{20}F_6N_2O_5S$ (478): C 42.68, H 4.21, N 5.86, S 6.70; found: C 42.72, H 4.44, N 5.83, S 7.26.

1-[3,5-Bis(trifluoromethyl)phenyl]-3-[(2*S*,3*S*,4*R*,5*S*,6*S*)-3,5-dihydroxy-2,6-bis-(hydroxymethyl)-7,7-dimethyloxepan-4-yl]thiourea (17):

According to the general procedure 1, oxepane derivative **13** (353 mg, 1.50 mmol), and isothiocyanate **14** (407 mg, 1.50 mmol) in methanol (8 mL) were used. The crude product was purified by column chromatography to give **17** (605 mg, 80%) as pale pink solid, mp. 165 °C, [α_D^{20}] -20.5 (*c* 0.7, MeOH). ^{1}H NMR (CD_3OD, 500 MHz, 300

K): δ = 1.35 (2 s, 3 H each, Me), 2.00-2.08 (m, 1 H, 6''-H), 3.53-3.72 (m, 5 H, 2''-H, 2''-CH_2, 6''-CH_2), 3.85 (dd, *J* = 7.8, 2.9 Hz, 1 H, 5''-H), 3.95 (m_c, 1 H, 3''-H), 4.58-4.70 (m, 1 H, 4''-H), 7.56 (s, 1 H, 4'-H), 8.07 ppm (s, 2 H, 2'-H). ^{13}C NMR (CD_3OD, 125.8 MHz, 300 K): δ = 21.2, 31.6 (2 q, Me), 59.8 (d, C-6''), 63.6* (t, 2''-CH_2, 6''-CH_2), 67.7 (d, C-4''), 73.7, 74.9 (2 d, C-2'', C-5''), 77.4 (s, C-7''), 118.1 (d, C-4'), 124.4 (d, C-2'), 124.7 (q, $^1J_{CF}$ = 273.5 Hz, CF_3), 132.8 (q, $^2J_{CF}$ = 40.9 Hz, C-3'), 143.0 (s, C-1'), 184.2 ppm (s, C-2); *intensity of the peak corresponds to two C atoms. ^{19}F NMR (CD_3OD, 376 MHz): δ = -64.3 ppm (s, CF_3). IR (ATR): ν = 3500-3100 (O-H, N-H), 3100-2850 (=C-H, C-H), 1275 cm^{-1} (C=S). HRMS (ESI-TOF): calcd for $C_{19}H_{25}F_6N_2O_5S$ $[M+H]^+$: 507.1400, found: 507.1383. Elemental analysis calc (%) for $C_{19}H_{24}F_6N_2O_5S$ (506.5): C 45.06, H 4.78, N 5.53, S 6.33; found: C 45.00, H 4.79, N 5.46, S 6.48.

[(1*S*,5*R*,8*S*)-2-Benzyl-6,6-dimethyl-9-oxo-3,7-dioxa-2-azabicyclo[3.3.1]nonan-8-yl]methylmethanesulfonate:

To a solution of bicyclic ketone **8** (391 mg, 1.34 mmmol) in dichloromethane (10 mL) mesyl chloride (220 μL, 2.81 mmol) and NEt_3 (940 μL, 6.70 mmol) were added under argon atmosphere at 0 °C. The solution was stirred at this temperature for 4 h. Then, sat. aq. $NaHCO_3$ (30 mL) and water (15 mL) were added and the phases were separated. The aqueous phase was extracted with dichloromethane (4 x 40 mL) and dried (Na_2SO_4). After filtration and removal of the solvent under reduced pressure, the residue was purified by column chromatography on silica gel (hexane/ethyl acetate, 1:1) to yield the mesylate (361 mg, 73%) as pale yellow solid, mp. 123 °C. [α_D^{20}] +86.0 (*c* 1.37, CH_2Cl_2). ^{1}H NMR ($CDCl_3$, 500 MHz): δ = 1.21, 1.44 (2 s, 3 H each, Me), 2.30 (dt, *J* = 4.0, 2.3 Hz, 1 H, 5-H), 2.96 (s, 3 H, SO_2Me), 3.08-3.10 (m, 1 H, 1-H), 3.95, 4.19 (2 d, *J* = 13.0 Hz, 1 H each, NCH_2), 4.18-4.22 (m, 1 H, 8-H), 4.37 (dd, *J* = 10.5, 5.3 Hz, 1 H, 4-H), 4.50-4.57 (m, 2 H, 4-H, 8-CH_2), 4.61 (dd, *J* = 12.4, 4.1 Hz, 1 H, 8-CH_2), 7.27-7.35 ppm (m, 5 H, Ph). ^{13}C NMR ($CDCl_3$, 125.8 MHz): δ = 24.0, 26.65 (2 q, Me), 37.4 (q, SO_2Me), 57.8 (d, C-5), 58.6 (t, NCH_2), 68.3 (d, C-1), 68.9 (t, C-4), 69.3 (t, 8-CH_2), 73.0 (d, C-8), 78.8 (s, C-6), 128.0, 128.6, 129.2, 135.3 (s, 3 d, Ph), 207.6 ppm (s, C-9). IR (ATR): ν = 3095-3030 (=C-H), 2980-2870 (C-H), 1725 cm^{-1} (C=O). HRMS (ESI-TOF): calcd for $C_{17}H_{24}NO_6S$ $[M+H]^+$: 370.1319, found: 370.1328.

(1*S*,5*R*,8*R*)-2-Benzyl-6,6-dimethyl-8-(pyrrolidin-1-ylmethyl)-3,7-dioxa-2-aza-bicyclo[3.3.1]nonan-9-one (19):

A mixture of the above prepared mesylate (200 mg, 0.541 mmol) and pyrrolidine (230 μL, 2.70 mmol) in dry 1,4-dioxane (5 mL) was placed in an ACE-sealed tube and heated at 100 °C for 17 h. The mixture was cooled to room temperature and the solvent was removed under reduced pressure. The residue was purified by column chromatography on silica gel (CH_2Cl_2/methanol, 15:1) to yield compound **19** (133 mg, 71%) as caramel-hued wax, [α_D^{20}] +77.1 (*c* 0.2, CH_2Cl_2). ^{1}H NMR ($CDCl_3$, 500 MHz): δ = 1.14, 1.33 (2 s, 3 H each, Me), 1.71-1.79 (m, 4 H, 3'-H), 2.17-2.30 (m, 1 H, 5-H), 2.64-2.77 (m, 4 H, 2'-H), 2.85 (dd, *J* = 12.0, 6.8 Hz, 1 H, 8-CH_2), 2.99 (dd, *J* = 12.6, 5.4 Hz, 1 H, 8-CH_2), 3.12-3.15 (m, 1 H, 1-H), 3.90, 4.06 (2 d, *J* = 13.5 Hz, 1 H each, 2-CH_2), 4.17-4.22 (m, 1 H, 8-H), 4.41 (dd, *J* = 12.2, 5.1 Hz, 1 H, 4-H), 4.45 (dd, *J* = 12.1, 2.9 Hz, 1 H, 4-H), 7.16-7.28 ppm (m, 5 H, Ph). ^{13}C NMR ($CDCl_3$, 125.8 MHz): δ = 23.5 (t, C-3'), 24.0, 26.9 (2 q, Me), 54.7 (t, C-2'), 56.9 (t, 8-CH_2), 58.0 (d, C-5), 59.8 (t, 2-CH_2), 69.2 (t, C-4), 70.9 (d, C-1), 73.2 (d, C-8), 78.4 (s, C-6), 127.8, 128.5, 129.1, 136.1 (s, 3 d, Ph), 207.9 ppm (s, C-9). IR (ATR): ν = 3090-3020 (=C-H), 2950-2855 (C-H), 1720 cm^{-1} (C=O). HRMS (ESI-TOF): calcd for $C_{20}H_{29}N_2O_3$ $[M+H]^+$: 345.2173, found: 345.2187.

(1*R*,5*S*,8*R*,9*S*)-2-Benzyl-6,6-dimethyl-8-(pyrrolidin-1-ylmethyl)-3,7-dioxa-2-aza-bicyclo[3.3.1]nonan-9-ol (20):

Bicyclic compound **19** (129 mg, 0.375 mmol) was dissolved in ethanol (5 mL) under argon atmosphere and cooled to 0 °C. $NaBH_4$ (28.4 mg, 0.750 mmol) was added in portions and the mixture was stirred at 0 °C to room temperature for 3 h. Then, the solvent was removed under reduced pressure. The resulting residue was dissolved in dichloromethane (5 mL) and water (5 mL). The aqueous phase was extracted with dichloromethane (3 x 5 mL), the combined organic phases were dried ($MgSO_4$), and the solvent was removed under reduced pressure. The obtained product **20** (116 mg, 89%) was used without further purification in the next step. ^{1}H NMR ($CDCl_3$, 500 MHz): δ = 1.30, 1.56 (2 s, 3 H each, Me), 1.53-1.56 (m, 1 H, 5-H), 1.70-1.82 (m, 4 H, 3'-H), 2.36-2.39 (m, 1 H, 1-H), 2.48-2.55 (m, 2 H, 8-CH_2), 2.63-2.76 (m, 4 H, 2'-H), 4.05 (d, *J* = 13.7 Hz, 1 H, 2-CH_2), 4.08-4.19 (m, 2 H, 4-H), 4.26 (d, *J* = 13.6 Hz, 1 H, 2-CH_2), 4.45-4.51 (m, 1 H, 8-H), 4.54 (t, *J* = 3.3 Hz, 1 H, 9-H), 7.15-7.41 ppm (m, 5 H,

Ph); the OH signal could not be observed. ^{13}C NMR ($CDCl_3$, 125.8 MHz): δ = 23.5 (t, C-3'), 26.4, 29.6 (2 q, Me), 42.0 (d, C-5), 54.7 (t, C-2'), 57.9 (t, 2-CH_2), 59.3 (d, C-1), 60.9 (d, C-9), 65.4 (t, 8-CH_2), 67.2 (t, C-4), 67.6 (d, C-8), 73.3 (s, C-6), 127.3, 128.3, 128.5, 138.0 ppm (s, 3 d, Ph).

(3*S*,4*S*,5*R*,6*R*)-5-Amino-3-(hydroxymethyl)-2,2-dimethyl-6-(pyrrolidin-1-yl-methyl)tetrahydro-2*H*-pyran-4-ol (21):

Bicyclic compound **20** (113 mg, 0.326 mmol) was dissolved in isopropanol (10 mL) and Pd/C (10% Pd, 150 mg) was added. The suspension was saturated with H_2 for 1 h and stirred under the H_2 atmosphere for 3.5 d. The suspension was filtered through a shot pad of Celite, washed with isopropanol (5 mL) and subsequently concentrated under reduced pressure affording aminopyran **21** (76 mg, 90%) as caramel-hued foam, [α_D^{20}] +65.7 (*c* 0.14, MeOH). ^{1}H NMR (CD_3OD, 500 MHz, 300 K): δ = 1.37, 1.51 (2 s, 3 H each, Me), 1.81 (dd, *J* = 9.1, 4.6 Hz, 1 H, 3-H), 2.01-2.11 (m, 4 H, 3'-H), 3.21 (br s, 1 H, 5-H), 3.29-3.32 (m, 4 H, 2'-H), 3.34-3.38 (m, 2 H, 6-CH_2), 3.66 (d, *J* = 11.2, 4.0 Hz, 1 H, 3-CH_2), 3.93-3.99 (m, 2 H, 4-H, 3-CH_2), 4.42-4.50 ppm (m, 1 H, 6-H). ^{13}C NMR (CD_3OD, 125.8 MHz, 300 K): δ = 24.1 (t, C-3'), 26.4, 27.7 (2 q, Me), 48.1 (d, C-3), 54.8 (d, C-5), 56.0 (t, C-2'), 57.6 (t, 6-CH_2), 62.6 (t, 3-CH_2), 64.9 (d, C-6), 72.7 (d, C-4), 77.0 ppm (s, C-2). IR (ATR): ν = 3500-3100 (O-H, N-H), 2970-2900 cm^{-1} (C-H). HRMS (ESI-TOF) calcd for $C_{13}H_{27}N_2O_3$ $[M+H]^+$: 259.2016, found: 259.2015.

1-[3,5-Bis(trifluoromethyl)phenyl]-3-[(2*R*,3*R*,4*S*,5*S*)-4-hydroxy-5-(hydroxyl-methyl)-6,6-dimethyl-2-(pyrrolidin-1-ylmethyl)tetrahydro-2*H*-pyran-3-yl]thiourea (22):

Analogous to the general procedure 1, aminopyran derivative **21** (70 mg, 0.132 mmol), and isothiocyanate **14** (37 mg, 0.132 mmol) in isopropanol (3 mL) were used. The mixture was stirred at 0 °C to room temperature for 17 h. The crude product was purified by column chromatography to give **22** (54 mg, 77%) as pale yellow solid, mp. 113-116 °C. [α_D^{20}] +68.5 (*c* 0.72, MeOH). ^{1}H NMR (CD_3OD, 500 MHz, 300 K): δ = 1.37, 1.56 (2 s, 3 H each, Me), 1.86 (q, *J* = 5.4 Hz, 1 H, 5''-H), 2.05-2.20 (m, 4 H, CH_2), 3.25-3.45 (m, 4 H, NCH_2, 6''-CH_2), 3.75 (dd, *J* = 11.1, 5.4 Hz, 1 H, 3''-CH_2), 3.85 (dd, *J* = 11.1, 5.4 Hz, 1 H, 5''-CH_2), 4.10 (m_c, 1 H, 4''-H), 4.56 (br d, *J* ≈ 10.0 Hz,

1 H, 2''-H), 4.75 (m_c, 1 H, 3''-H), 7.67 (s, 1 H, 4'-H), 8.32 ppm (s, 2 H, 2'-H). ^{13}C NMR (CD_3OD, 125.8 MHz, 300 K): δ = 24.0 (t, CH_2), 26.5, 27.7 (2 q, Me), 49.5 (d, C-5''), 55.9 (t, NCH_2), 57.6 (d, C-3''), 58.6 (t, 2''-CH_2), 62.6 (t, 5''-CH_2), 66.8 (d, C-2''), 72.1 (d, C-4''), 76.8 (s, C-6''), 117.8 (d, C-4'), 123.6 (d, C-2'), 124.5 (q, $^1J_{CF}$ = 270 Hz, CF_3), 132.6 (q, $^2J_{CF}$ = 33.6 Hz, C-3'), 143.0 (s, C-1'), 182.3 ppm (s, C-2). IR (ATR): ν = 3500-3100 (O-H, N-H), 3050 (=C-H), 2975 (C-H), 1275 cm^{-1} (C=S). HRMS (ESI-TOF) calcd for $C_{22}H_{30}F_6N_3O_3S$ $[M+H]^+$: 530.1907, found: 530.1911.

Michael addition of acetylacetone to β-nitrostyrene:

To a solution of β-nitrostyrene **23** (30 mg, 0.20 mmmol) in dichloromethane (1 mL) or dichloromethane/methanol (1 mL/0.1 mL) the corresponding organocatalyst (0.20 mmol) was added under argon atmosphere at room temperature. The solution was stirred for 5 min, then acetylacetone **24** (24 μL, 0.23 mmol) was added and stirring was continued for the time indicated in Table 1 of the main text. The solution concentrated under reduced pressure and the crude product was purified by column chromatography on silica gel (hexane/ethyl acetate, 3:1) to give the product **25**. The ratio of the formed enantiomers was determined by chiral HPLC (chiralpak IA, 4.6x250 mm; 5% isopropanol/hexane; flow 1 mL/min, 25 bar; UV 215 nm, RI).

$[\alpha_D^{20}]$ +60 (*c* 0.59, CH_2Cl_2); 39% ee. ^{1}H NMR ($CDCl_3$, 400 MHz): δ = 1.91, 2.25 (2 s, 3 H each, Me), 4.19 (ddd, *J* = 10.9, 8.1, 6.4 Hz, 1 H, PhCH), 4.57 (d, *J* = 10.9 Hz, 1 H, COCH), 4.68-4.75 (m, 2 H, CH_2), 7.11-7.63 ppm (m, 5 H, Ph). The NMR data are in accordance to those reported in the literature.[5]

(*R*)-3-Hydroxy-3-(2-oxopropyl)indolin-2-one (28):

To a solution of isatin **27** (15 mg, 0.10 mmol) dissolved in dichloromethane (2 mL) thiourea derivative **17** (5 mg, 0.01 mmol) was added and the solution was stirred for 15 min at 0 °C. After addition of acetone (587 μL, 8.0 mmol) and pyrrolidine (100 μL, 0.1 mmol) the mixture was stirred for 74 h at 4 °C. The solvent was removed under reduced pressure and the crude product was purified by column chromatography on silica gel (ethyl acetate/hexane, 5:1) to yield **28** (5.4 mg, 28%) beside a mixture of **28** and **17** (6 mg). $[\alpha_D^{20}]$ +34 (*c* 0.12, MeOH); ^{1}H NMR ($CDCl_3$, 400 MHz): δ = 1.57 (s, 1 H, OH), 2.19 (s, 3 H, Me), 2.96 (d, *J* = 16.7 Hz, 1 H, CH_2), 3.18 (d, *J* = 16.7 Hz, 1 H,

CH_2), 6.86 (d, *J* = 7.7 Hz, 1 H, 5-H), 7.05, 7.24 (2 t, *J* = 7.6 Hz, 1 H each, 6-H, 7-H), 7.35 (d, *J* = 7.5 Hz, 1 H, 8-H), 7.51 ppm (s, 1 H, NH). The NMR data are in accordance to those reported in the literature.[6]

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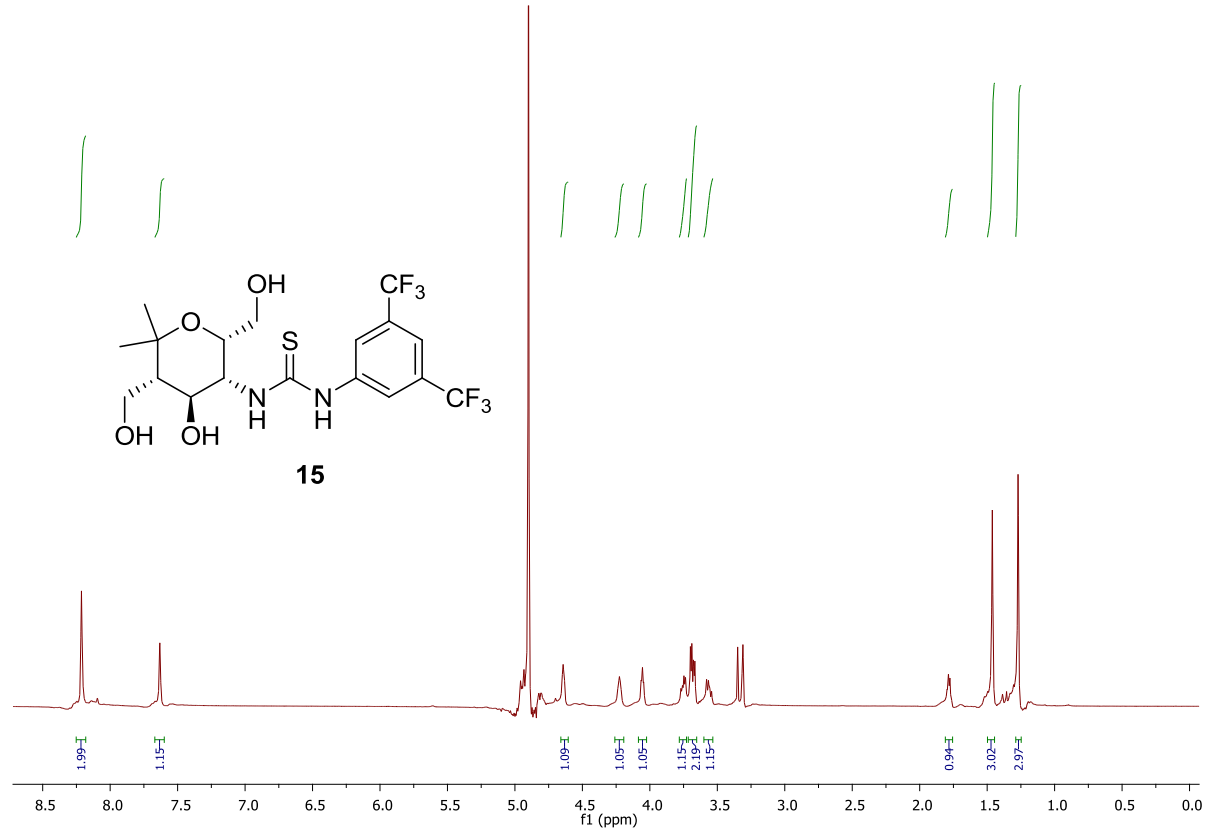
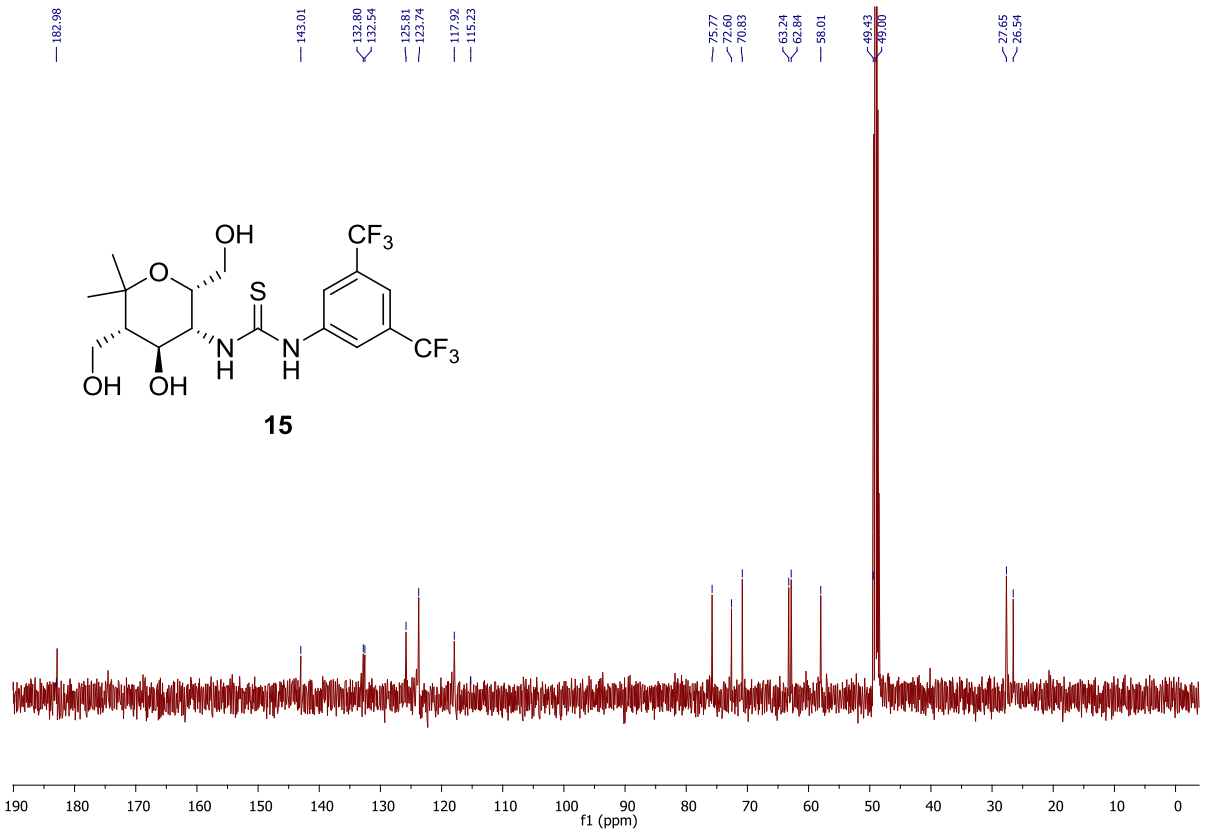
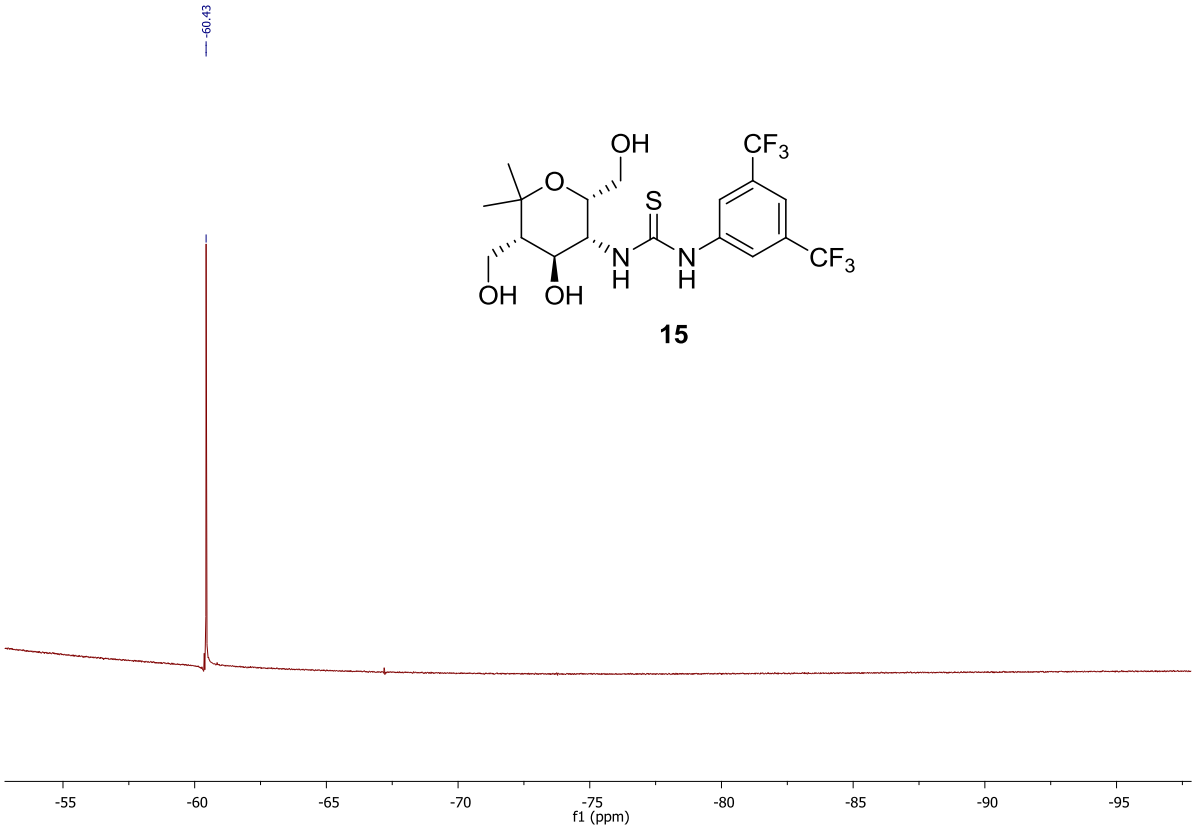
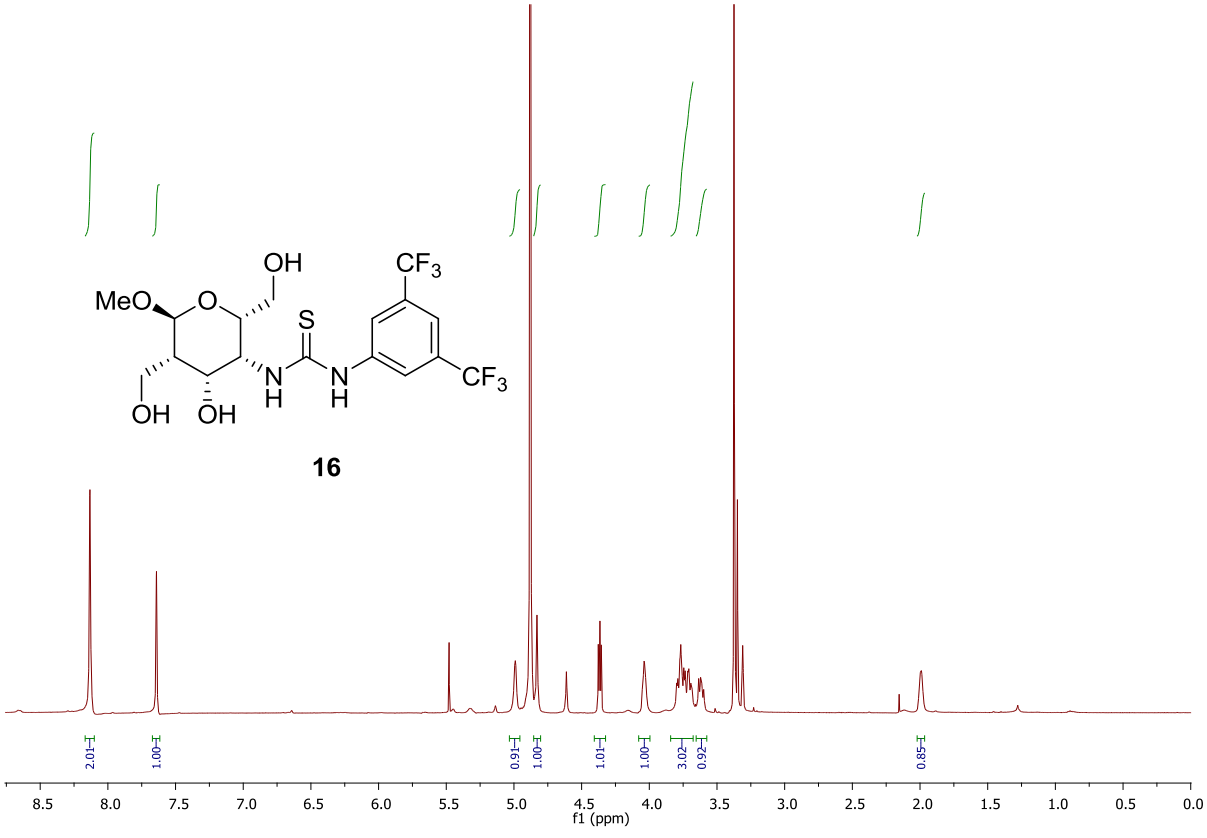
Compound **15** (CD_3OD)

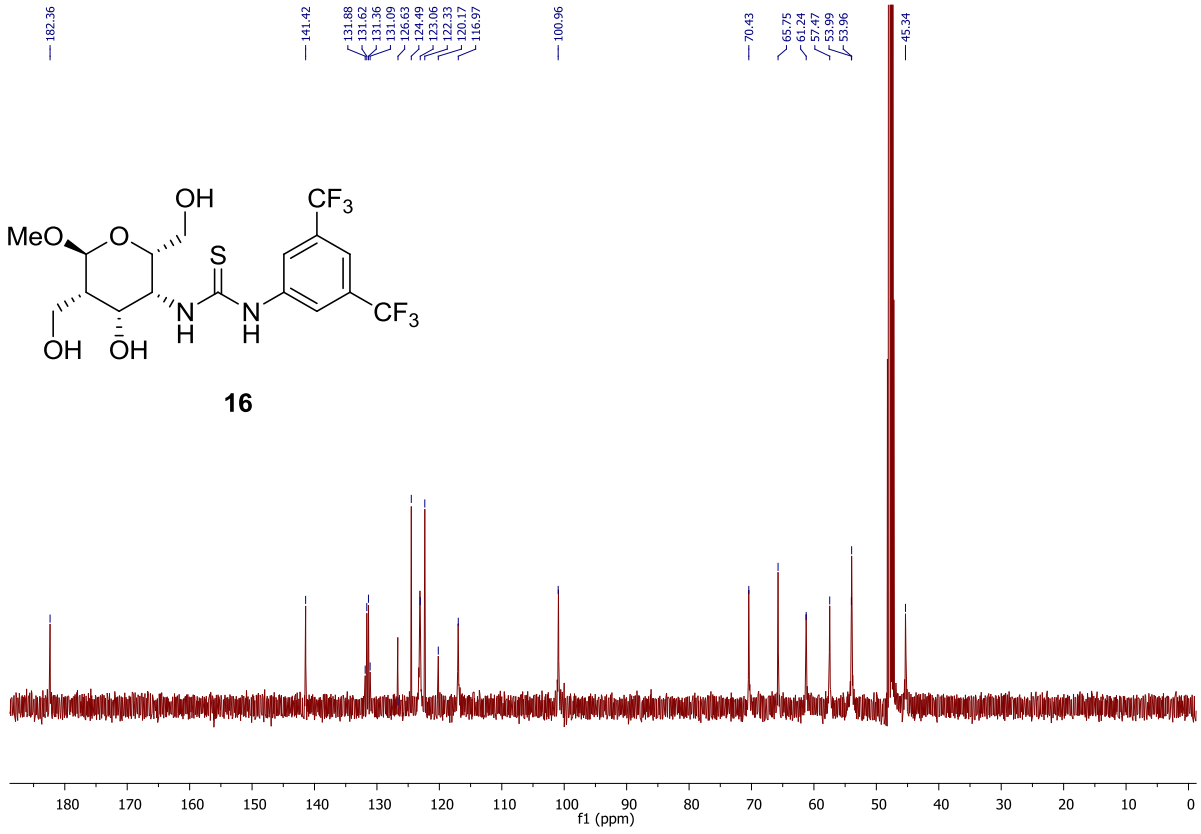




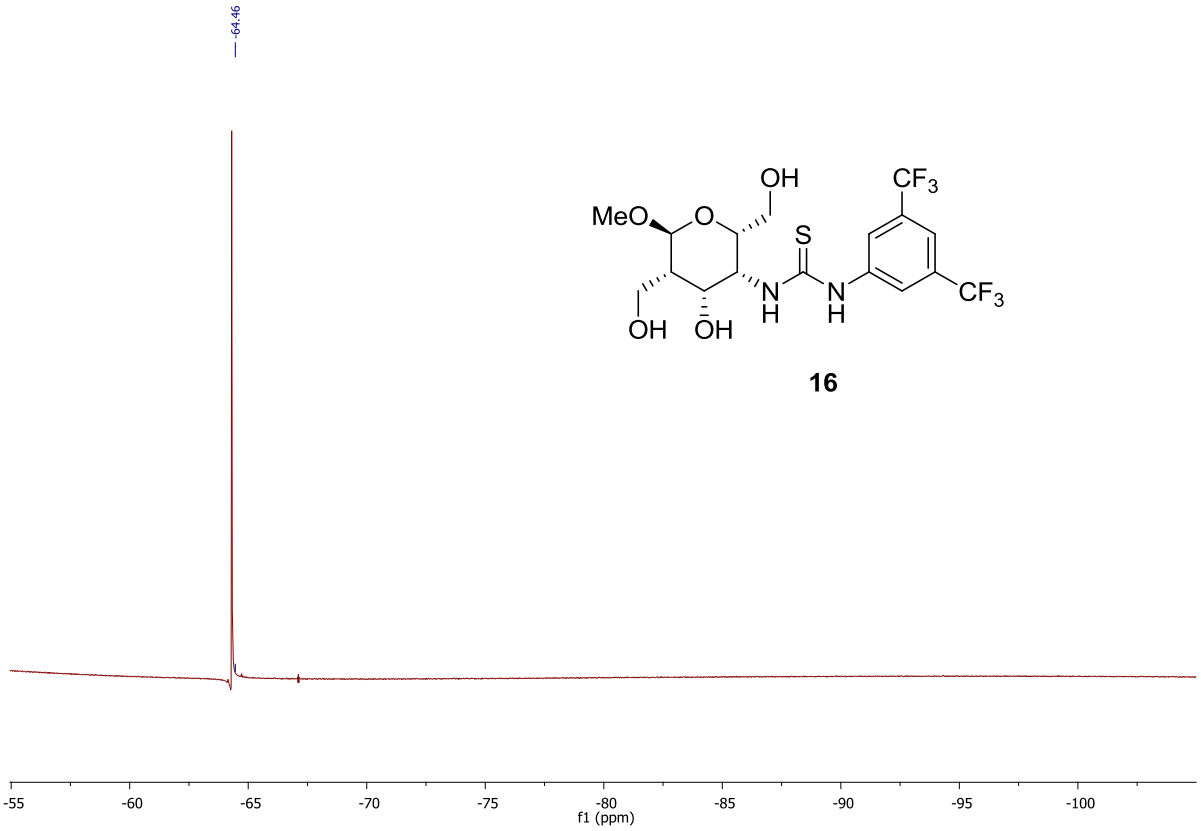


Compound **16** (CD_3OD)




182.36
141.42
131.88
131.62
131.36
131.09
126.63
124.49
123.06
122.33
120.17
116.97
100.96
70.43
65.75
61.24
57.47
53.99
53.96
45.34
MeO
O
OH
S
N
H
N
H
CF3
CF3
OH
OH
180 170 160 150 140 130 120 110 100 90 80 70 60 50 40 30 20 10 0
f1 (ppm)

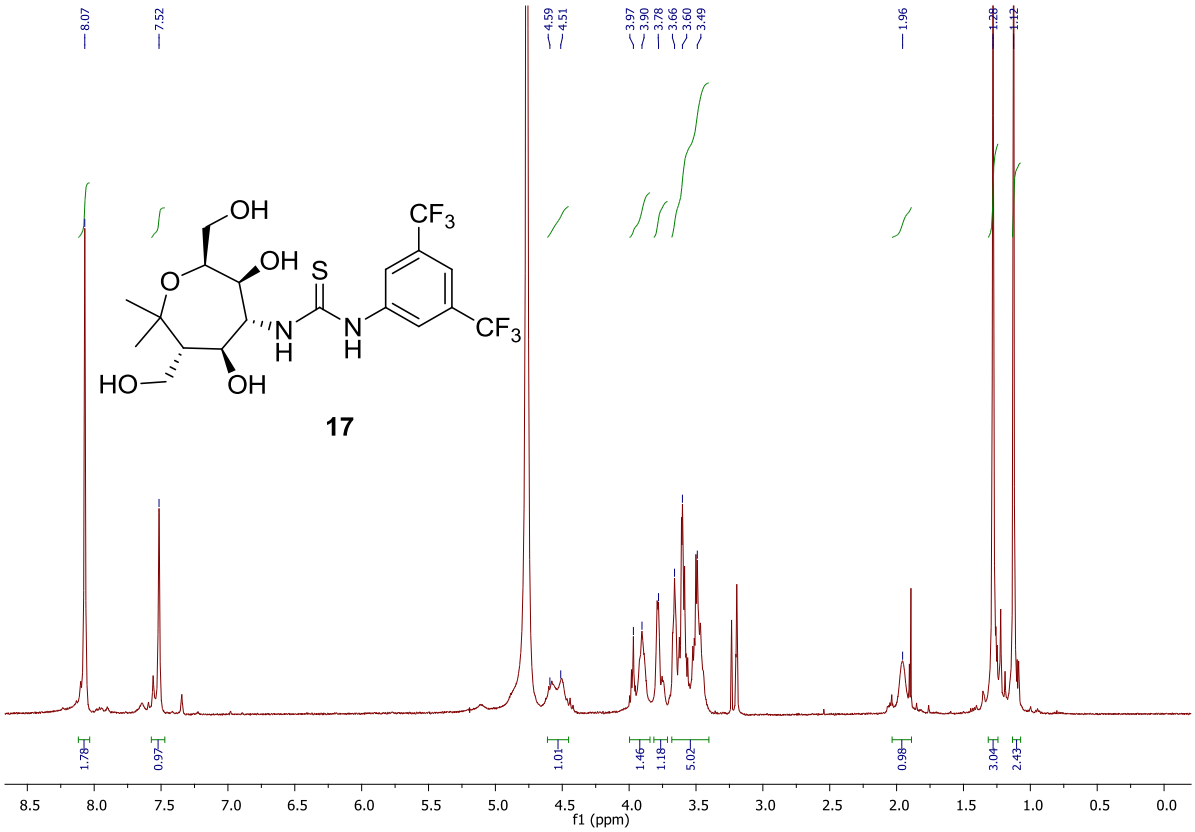
16

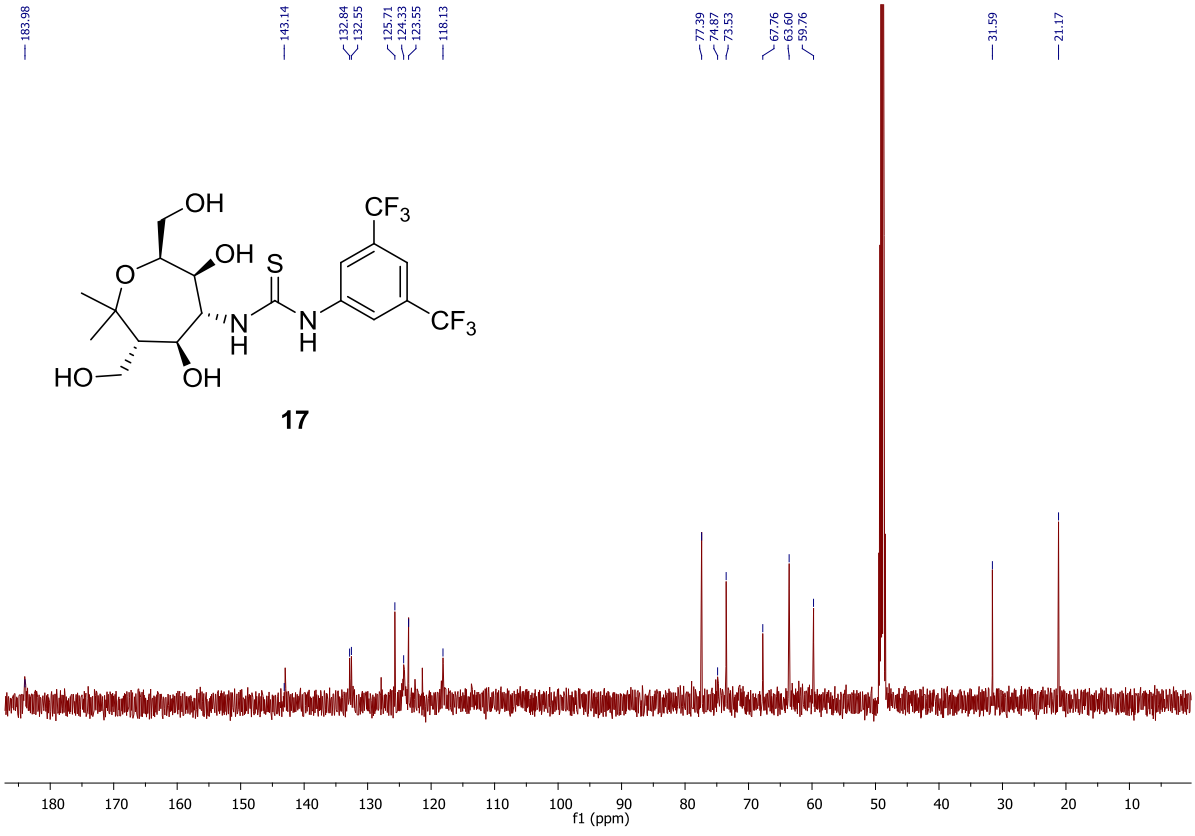

-64.46
-55 -60 -65 -70 -75 -80 -85 -90 -95 -100
f1 (ppm)

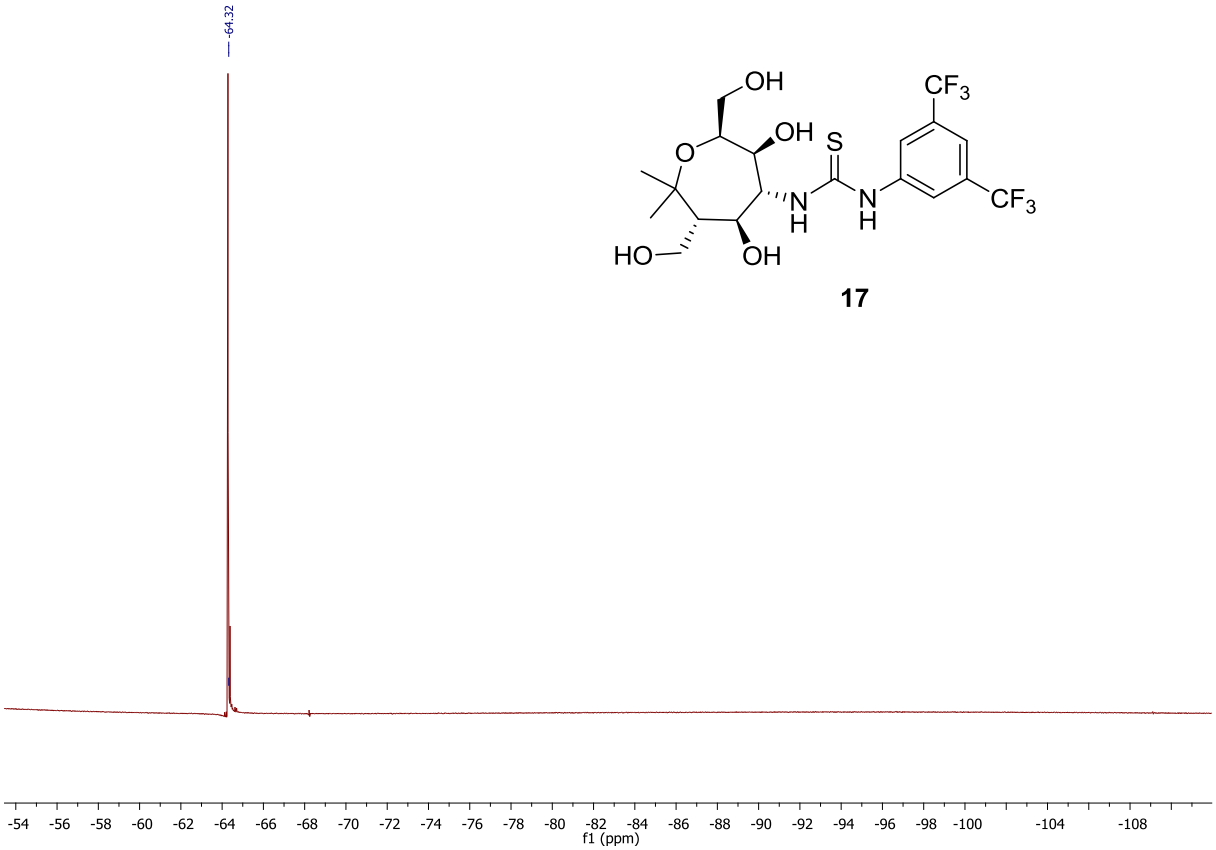
MeO
O
OH
S
N
H
N
H
CF3
CF3
OH
OH

16

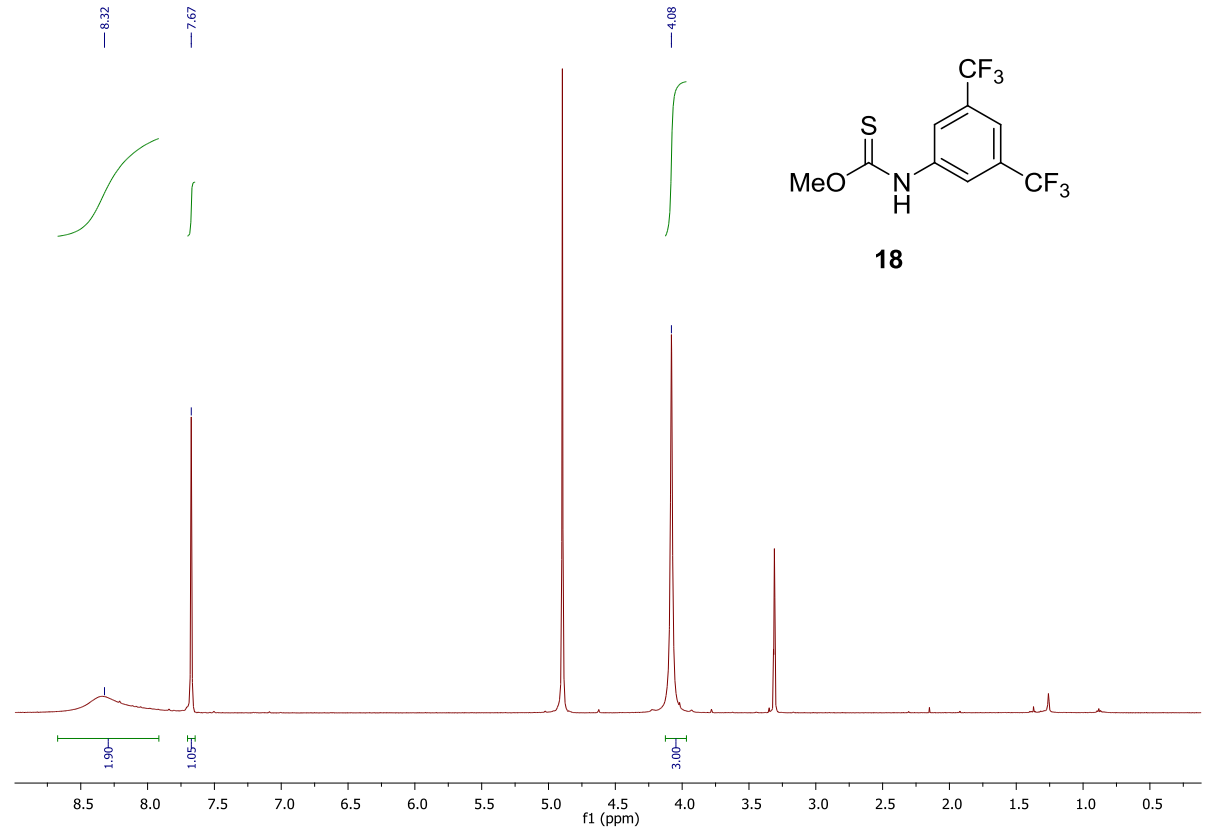
Compound **17** (CD_3OD)

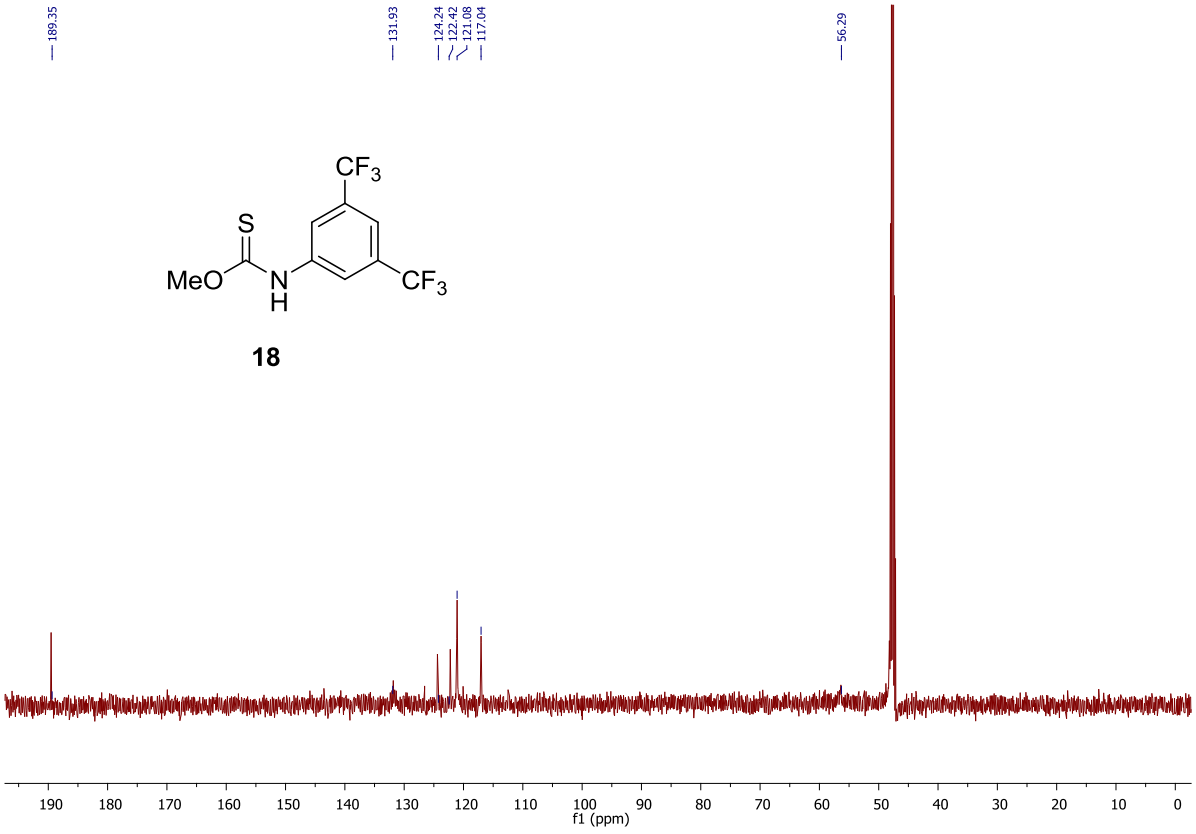




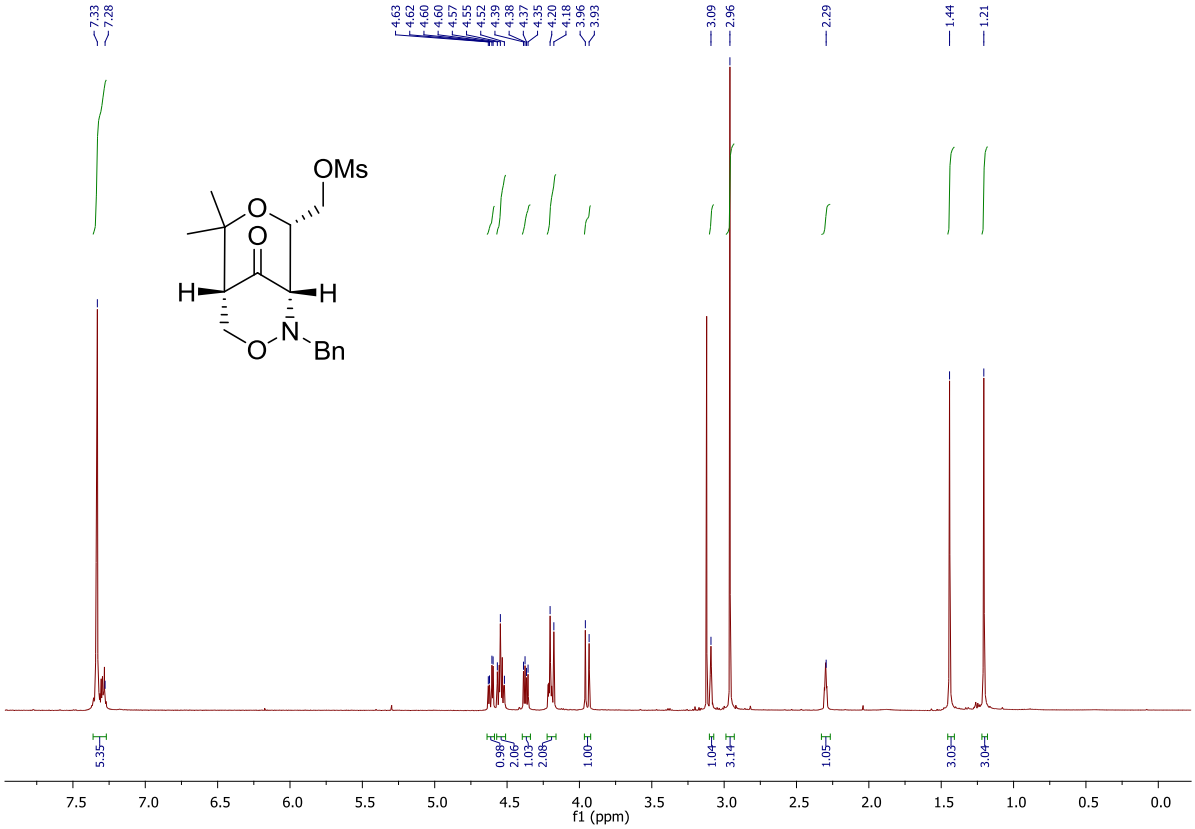


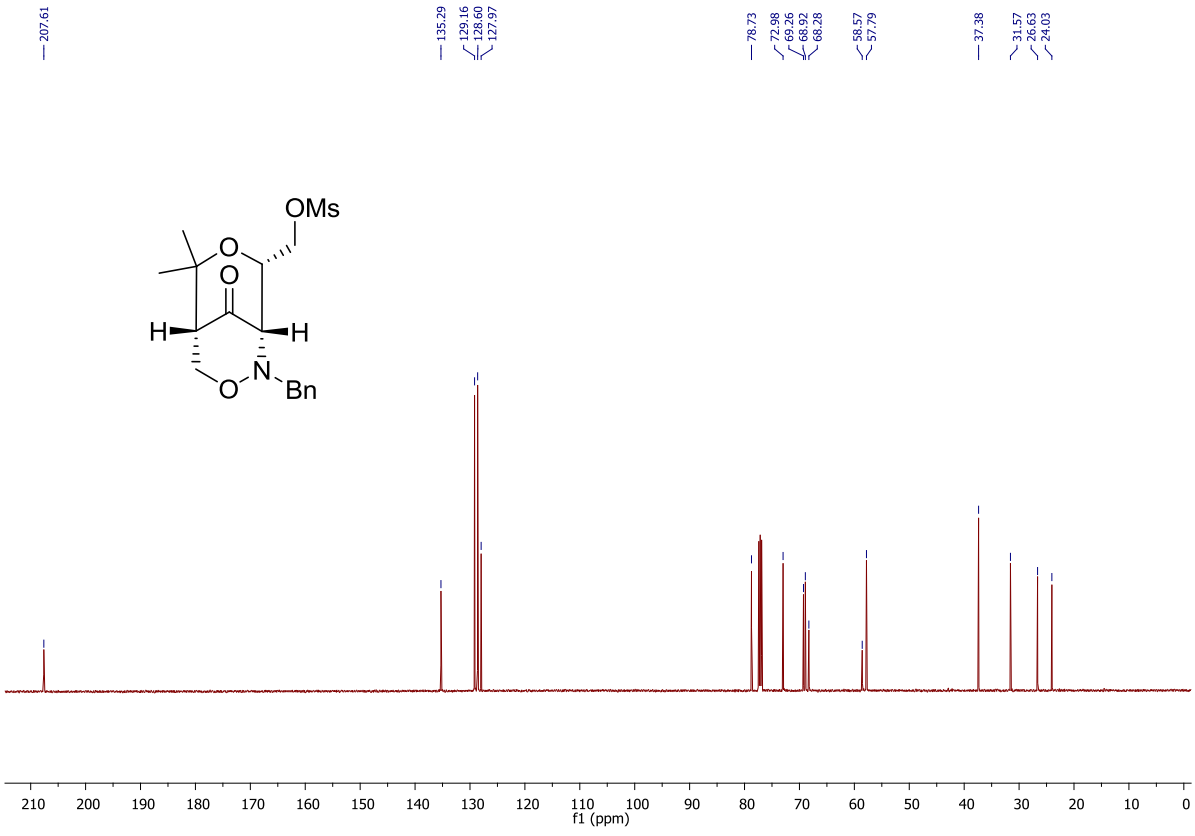
Compound **18** (CD_3OD)



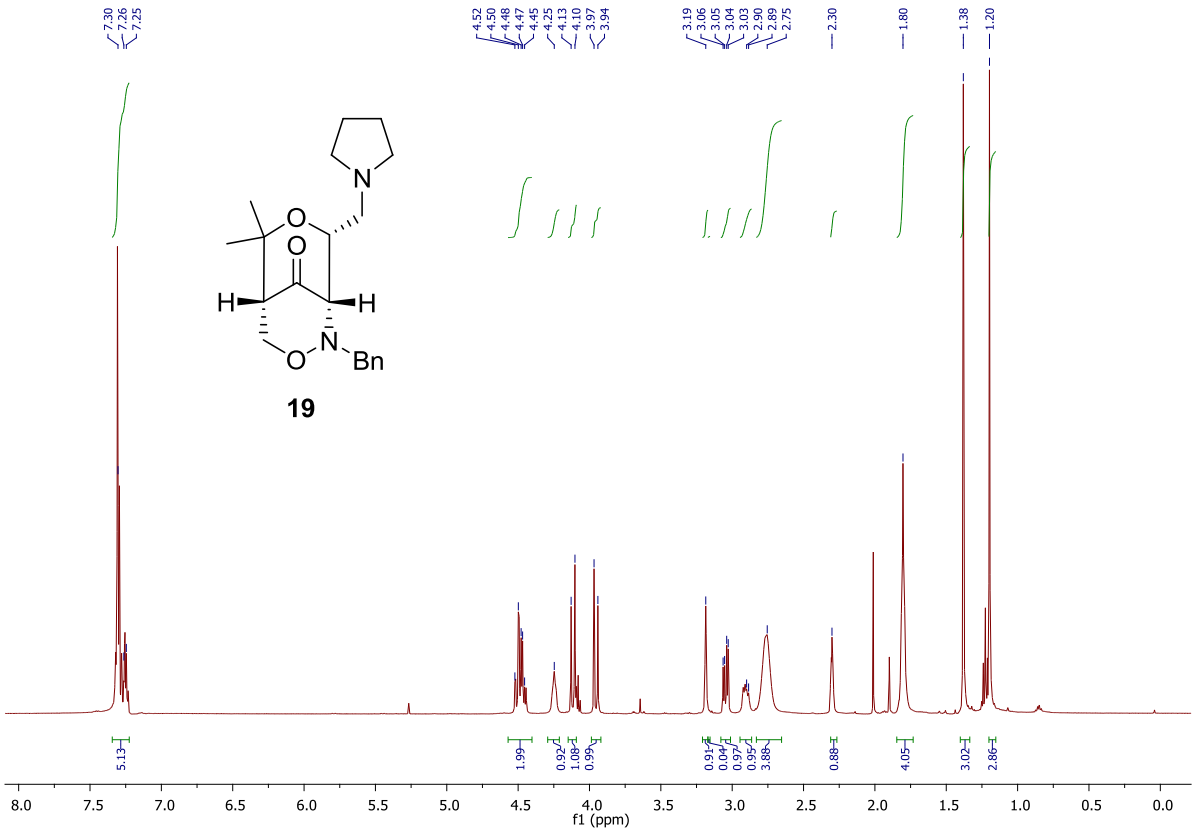

189.35
131.93
124.24
122.42
121.08
117.04
56.29
CF3
S
MeO
N
H
CF3
18
190
180
170
160
150
140
130
120
110
100
90
80
70
60
50
40
30
20
10
0
f1 (ppm)

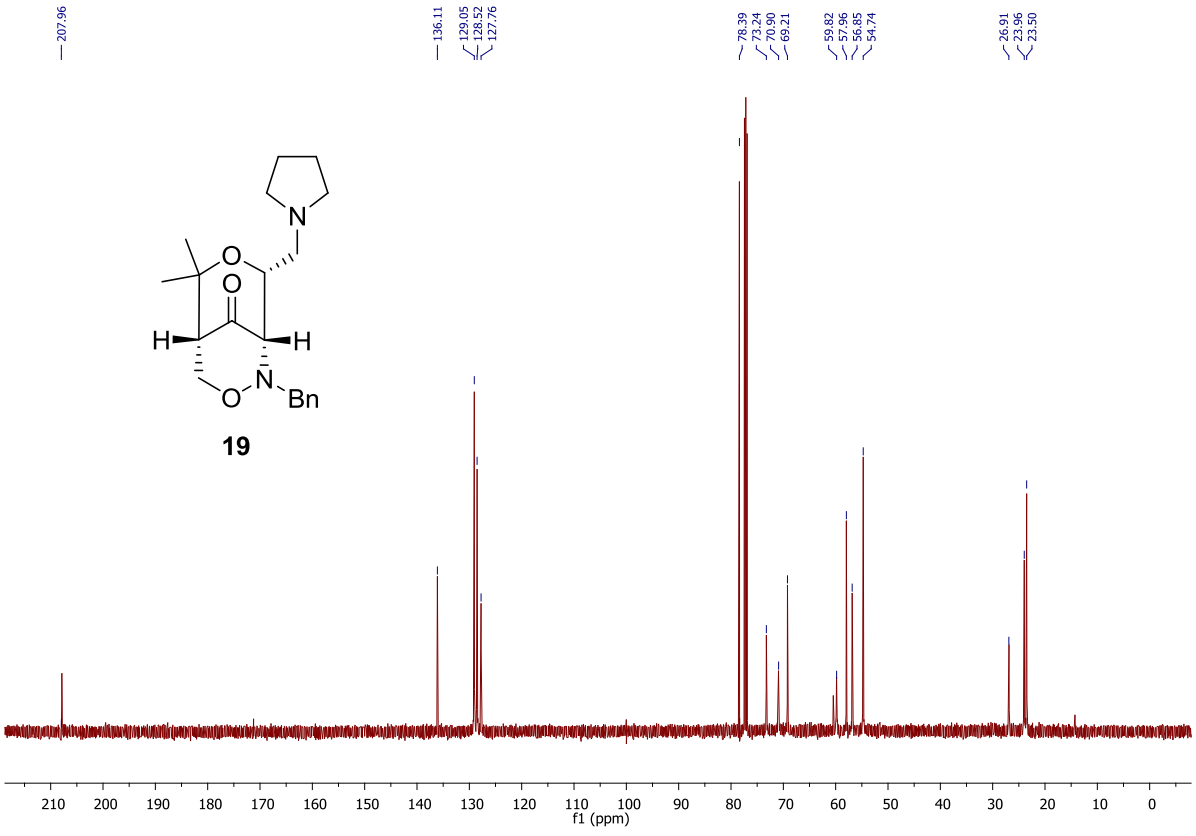
Mesylate ($CDCl_3$)



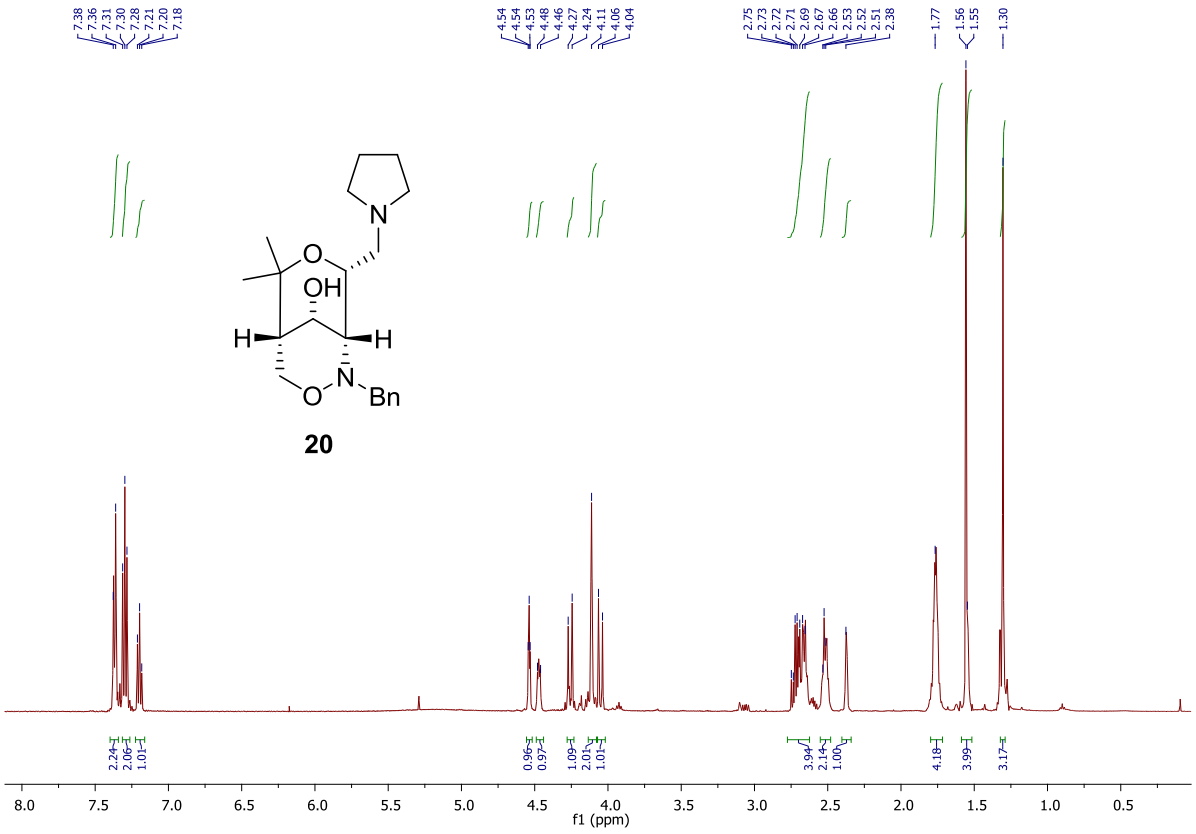


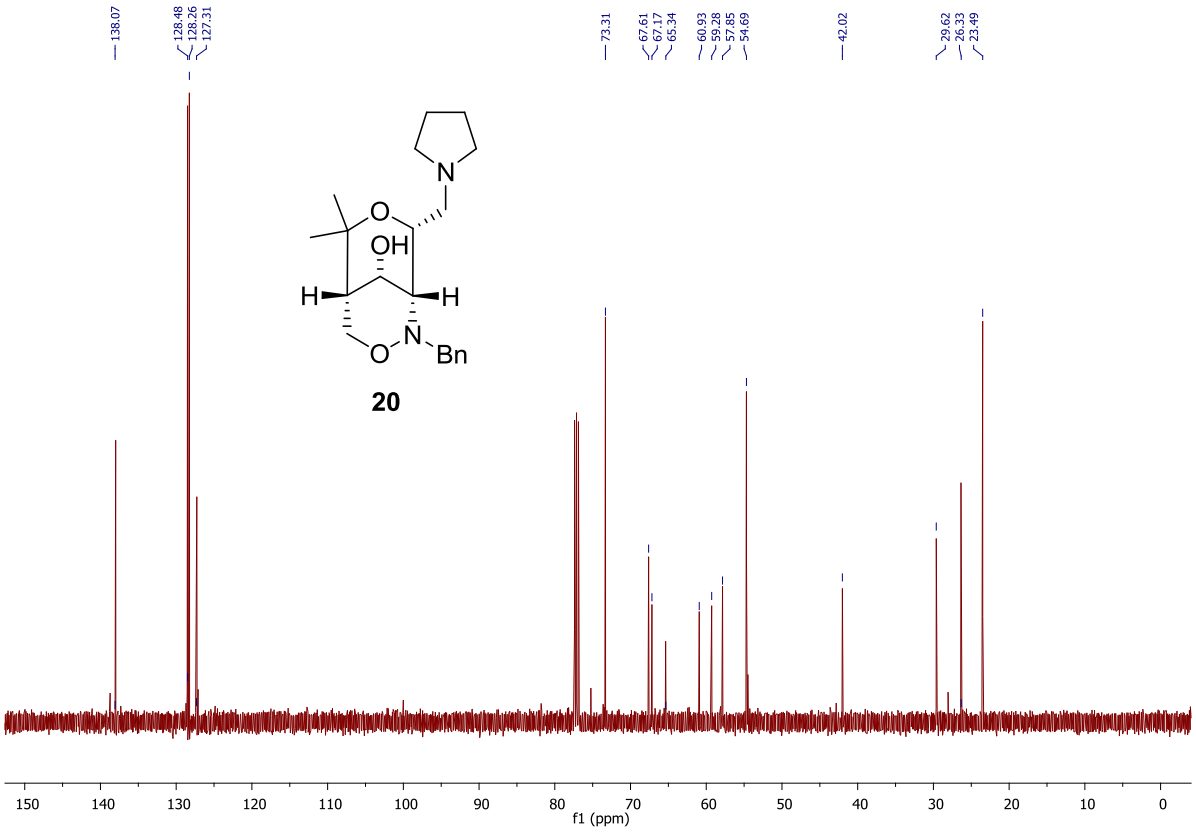
Compound **19** ($CDCl_3$)



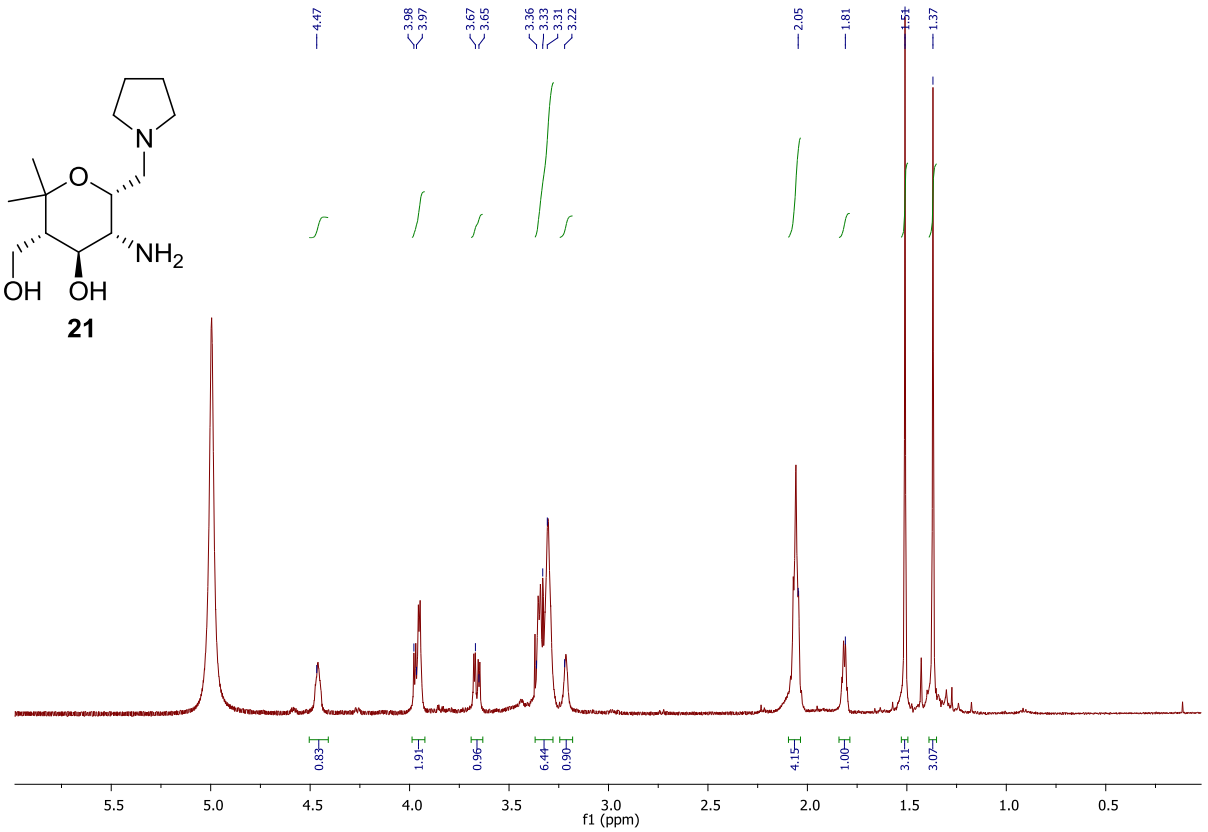


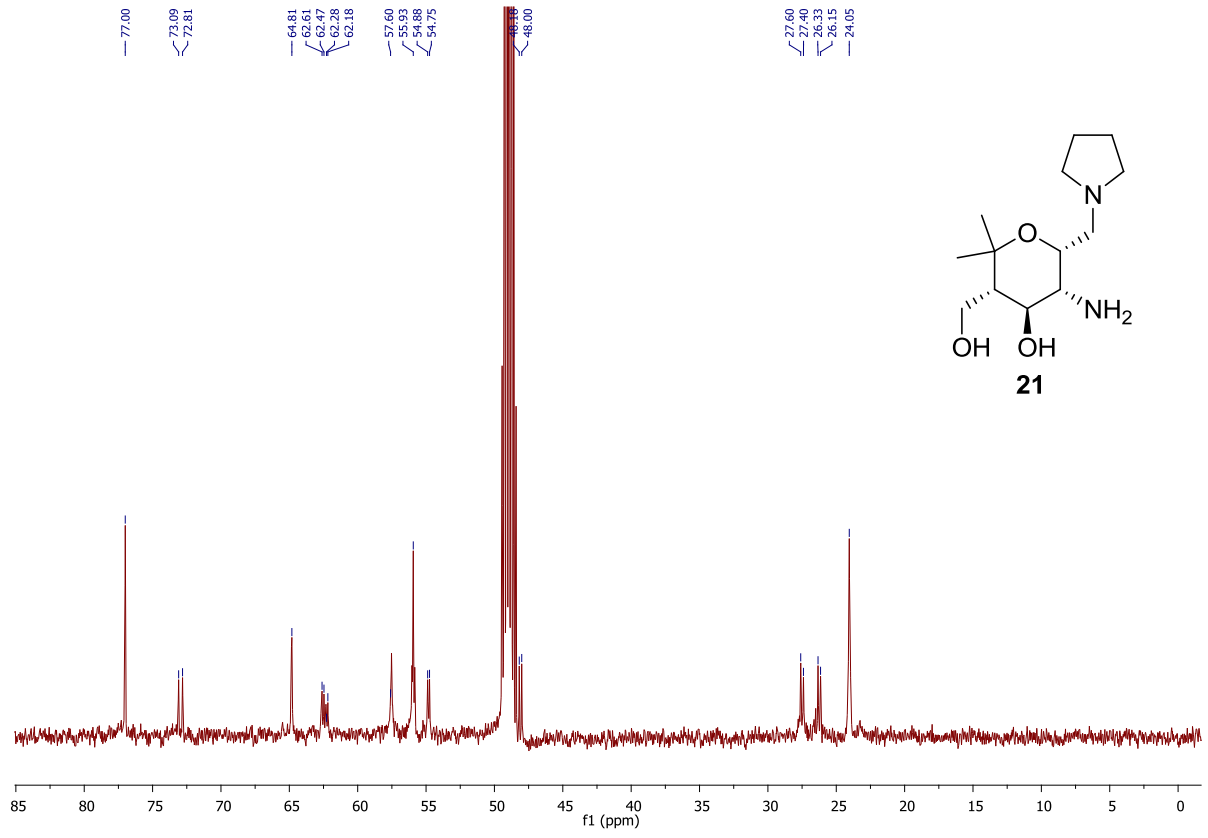
Compound **20** ($CDCl_3$)



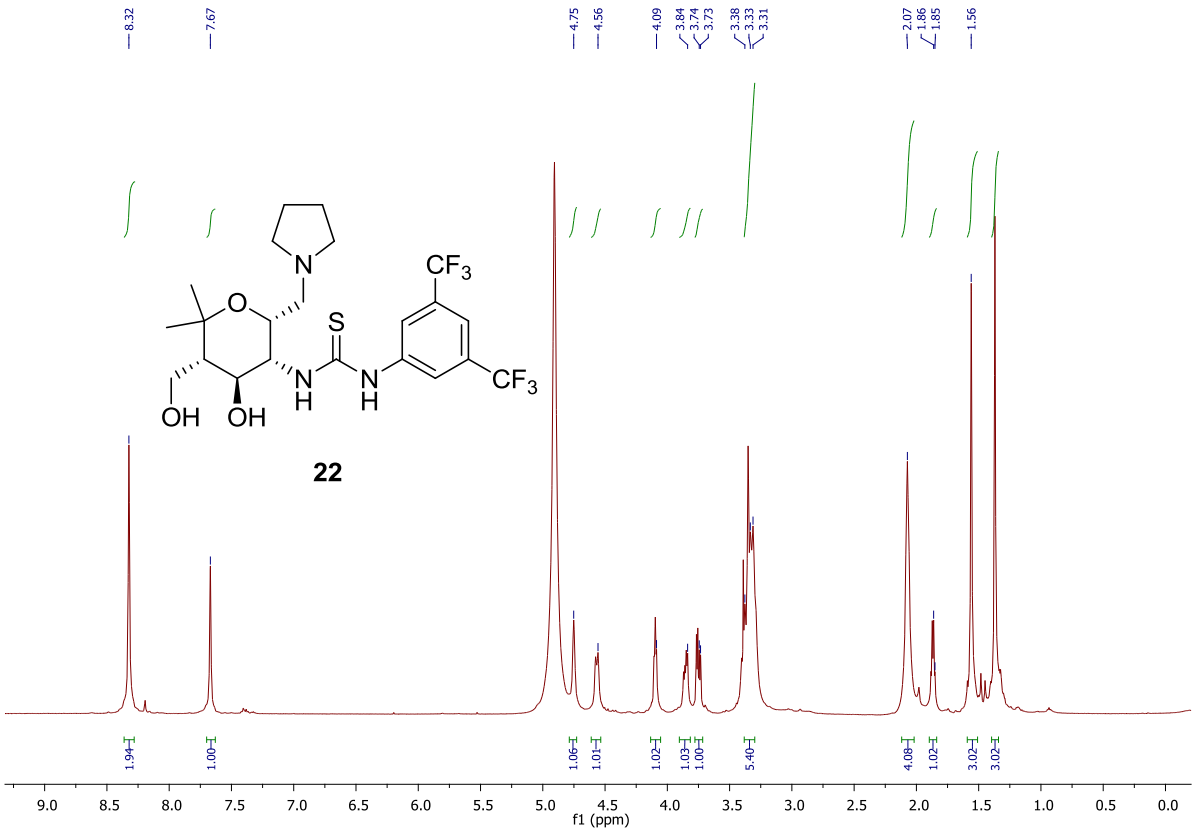


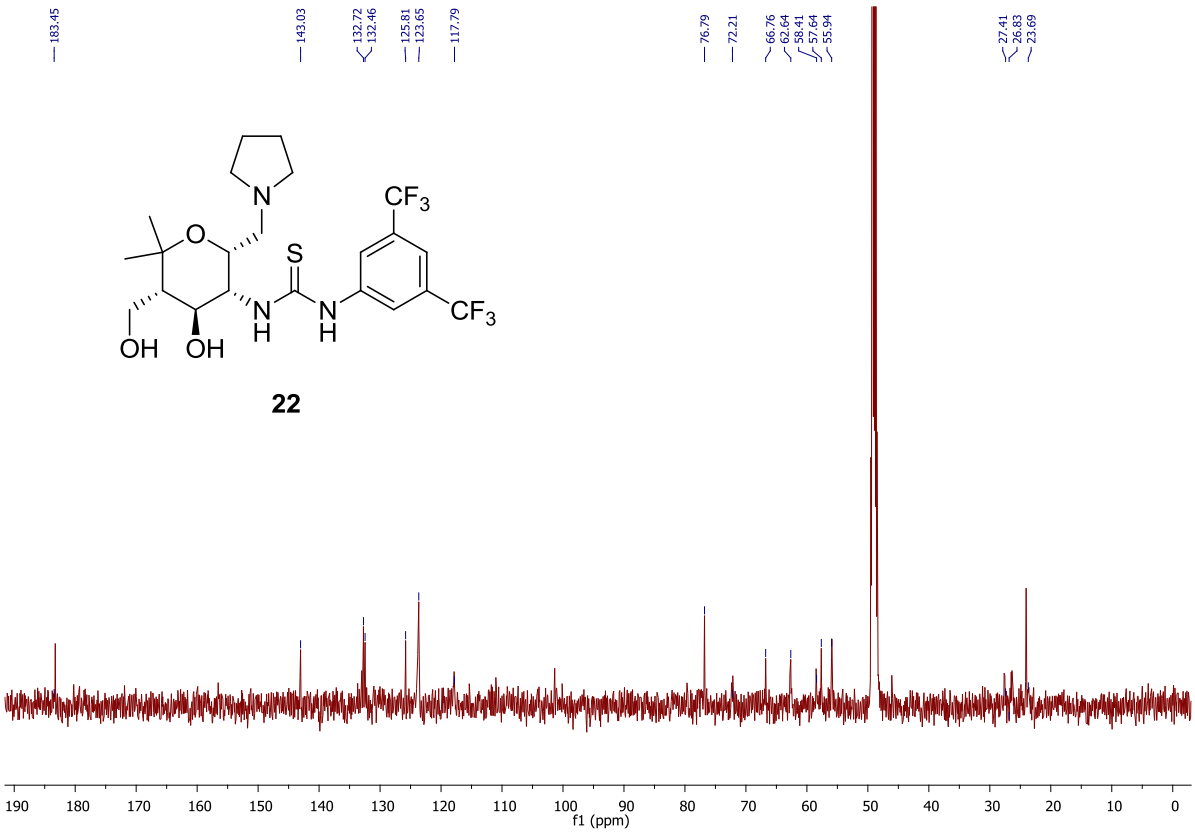
Compound **21** (CD_3OD)



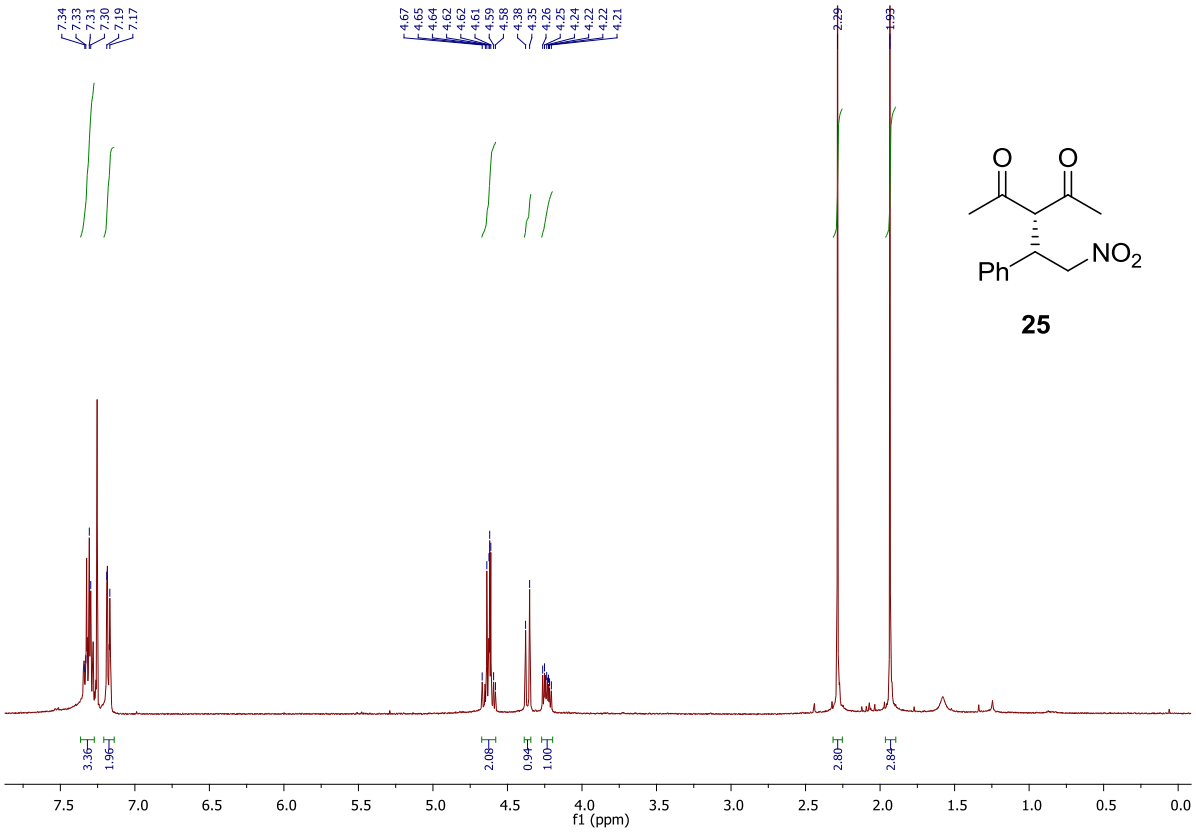


Compound **22** (CD_3OD)





Compound **25** ($CDCl_3$)



25

Compound **28** ($CDCl_3$)