Electronic Supplementary Material (ESI) for Organic & Biomolecular Chemistry

SUPPORTING INFORMATION

SULFUR-ASSISTED DOMINO ACCESS TO BICYCLIC DIHYDROFURANS: CASE STUDY AND EARLY SYNTHETIC APPLICATIONS

Concetta Paolella, Daniele D'Alonzo,* Giovanni Palumbo and Annalisa Guaragna*

Dipartimento di Scienze Chimiche, Università di Napoli Federico II
via Cintia, 21 I-80126 Napoli, Italy

dandalonzo@unina.it; guaragna@unina.it

COPIES OF ^{1}H AND ^{13}C NMR SPECTRA

Experimental Section

General methods and materials.

All moisture-sensitive reactions were performed under a nitrogen atmosphere using oven-dried glassware. Solvents were dried over standard drying agents and freshly distilled prior to use. Reactions were monitored by TLC (precoated silica gel plate F_{254}, Merck). Column chromatography: Merck Kieselgel 60 (70-230 mesh); flash chromatography: Merck Kieselgel 60 (230-400 mesh). Melting points are uncorrected and were determined with a capillary apparatus. ^{1}H and ^{13}C NMR spectra were recorded on NMR spectrometers operating at 200, 400 or 500 MHz and 50, 100 or 125 MHz, respectively; in all cases, the solvent is meant to be $CDCl_3$ (unless otherwise specified). Combustion analyses were performed using a CHNS analyzer.

Methyl 2-((*tert*-butyl(diphenyl)silyl)-oxy)acetate (6).

To a stirred solution of methyl glycolate (1.5 g, 16.8 mmol) in anhydrous DMF (24 mL), imidazole (1.36 g, 20.0 mmol) and TBDPSCl (5.1 mL, 20.1 mmol) were added at room temperature. After 3h, the solvent was removed under reduced pressure; the resulting residue was diluted with $CHCl_3$ and washed with ice-cold water. The organic layer was dried (Na_2SO_4) and the solvent removed under vacuum. Purification of the crude residue by silica gel chromatography (hexane:EtOAc = 9:1) gave pure **6** (5.4 g, 98% yield) as a colorless oil. ^{1}H NMR (200 MHz): δ 1.09 (s, 9H), 3.68 (s, 3H), 4.25 (s, 2H), 7.38-7.42 (m, 6H), 7.66-7.71 (m, 4H). ^{13}C NMR (50 MHz): ppm 19.5, 26.9, 51.8, 62.4, 128.0, 130.2, 133.0, 135.8, 171.9. Anal. calcd for $C_{19}H_{24}O_3Si$: C 69.47, H 7.36. Found: C 69.67, H 7.33.

2-((*Tert*-butyl(diphenyl)silyl)-oxy)-1-(3-(((4-methoxybenzyl)oxy)methyl)-5,6-dihydro-1,4-dithiin-2-yl)-1-ethanone (7).

To a stirring solution of DIPA (0.8 mL, 5.6 mmol) in anhydrous THF (20 mL) at -78 °C and under nitrogen atmosphere, *n*-BuLi (1.6 m, 0.55 mL, 5.6 mmol) was added. After 10 min, a solution of **1** (1.25 g, 4.66 mmol) in anhydrous THF (20 mL) was added dropwise. The resulting mixture was stirred for 30 min at -78 °C, then a solution of **6** (1.5 g, 4.57 mmol) in anhydrous THF (10 mL) was added. After 20 min, the reaction was quenched by careful addition of 10% aq NH_4Cl. The mixture was extracted with EtOAc, and the combined organic phases were washed with brine, dried (Na_2SO_4) and evaporated under reduced pressure. The resulting crude residue was purified by silica gel column chromatography (hexane:AcOEt = 8:2) to give the pure **7** (2.44 g, 80% yield) as a colorless oil. ^{1}H NMR (200 MHz): δ 1.09 (s, 9H), 2.99-3.05 (m, 2H), 3.19-3.22 (m, 2H), 3.79 (s, 3H), 4.34 (s, 2H), 4.38 (s, 2H), 4.57 (s, 2H), 6.85 (d, *J* = 8.5, 2H), 7.25 (d, *J* = 8.5, 2H), 7.34-7.43 (m, 6H), 7.65-7.71 (m, 4H). ^{13}C NMR (50 MHz): ppm 19.3, 26.3, 26.7, 29.7, 55.2, 68.7, 71.2, 72.3, 113.7, 122.4, 127.7, 129.4, 129.8, 132.9, 135.5, 140.8, 159.2, 195.4. Anal. calcd for $C_{31}H_{36}O_4S_2Si$: C 65.92, H 6.42, S 11.35. Found: C 66.11, H 6.40, S 11.30.

2-((*Tert*-butyl(diphenyl)silyl)-oxy)-1-(3-(((4-methoxybenzyl)oxy)methyl)-5,6-dihydro-1,4-dithiin-2-yl)-1-ethanol (8).

To a stirring solution of ketone **7** (1.0 g, 1.78 mmol) in anhydrous THF (30 mL) at room temperature and under nitrogen atmosphere, a 1 m solution of $BH_3 \cdot THF$ (4.4 mL, 4.4 mmol) was added dropwise. After 5h, MeOH (10 mL) was slowly added, then the solvent was evaporated under reduced pressure. Chromatography of crude residue over silica gel (hexane:EtOAc = 9:1) gave the pure **8**(4.3 g 86% yield) as a colorless oil. ^{1}H NMR (400 MHz): δ 1.05 (s, 9H), 2.86 (bs, 1H), 2.94-3.26 (m, 4H), 3.72 (dd, *J* = 4.7, 10.2, 1H), 3.74-3.82 (m, 4H), 3.92 (d, *J* = 12.2, 1H), 3.96 (d, *J* = 12.2, 1H), 4.31 (d, *J* = 11.6, 1H), 4.36 (d, *J* = 11.6, 1H), 4.86 (dd, *J* = 5.8, 7.9, 1H), 6.87 (d, *J* = 8.6, 2H), 7.25 (d, *J* = 8.6, 2H), 7.36-7.52 (m, 6H), 7.59-7.71 (m, 4H). ^{13}C NMR (50 MHz): ppm 19.1, 26.7, 27.1, 29.2, 55.1, 66.5, 69.5, 71.3, 71.5, 113.6, 124.4, 127.7, 128.9, 129.4, 129.6, 129.7, 132.9, 133.0, 135.4, 159.1. Anal. calcd for $C_{31}H_{38}O_4S_2Si$: C 65.68, H 6.76, S 11.31. Found: C 65.90, H 6.79, S 11.27.

5-((*Tert*-butyl(diphenyl)silyl)-oxy)-7-methoxy-2,3,5,7-tetrahydro-[1,4]dithiino[2,3-c]furan (9).

To a stirred CH_2Cl_2/CH_3OH solution (95/5 v/v, 8.75 mL) containing alcohol **8** (0.50 g, 0.88 mmol), DDQ (0.28 g, 1.06 mmol) was added in one portion at room temperature. After 30 min, H_2O was added and the mixture was extracted with CH_2Cl_2. The organic layer was dried (Na_2SO_4), and the solvent evaporated under reduced pressure. Chromatography of the crude residue over silica gel (hexane:EtOAc = 95:5) gave **9** (0.34 g, 83% yield, α:β = 3.3:1). Data for **9**α: ^{1}H NMR (200 MHz, C_6D_6): δ 1.15 (s, 9H), 2.22-2.59 (m, 4H), 3.21 (s, 3H), 3.74 (dd, *J* = 10.8, 3.8, 1H), 3.80 (dd, *J* = 10.8, 3.9, 1H), 4.85 (q, *J* = 3.8, 1H), 5.89 (d, *J* = 3.9, 1H), 7.14-7.25 (m, 6H), 7.72-7.81 (m, 4H). ^{13}C NMR (50 MHz, C_6D_6): ppm 19.4, 25.7, 26.2, 26.9, 52.0, 65.4, 88.0, 109.9, 120.2, 124.7, 127.2, 129.8, 133.8, 135.9. Anal. calcd for $C_{24}H_{30}O_3S_2Si$: C 62.84, H 6.59, S 13.98. Found: C 62.60, H 6.56, S 14.03. Data for **9**β: ^{1}H NMR (200 MHz, C_6D_6): δ 1.17 (s, 9H), 2.25-2.55 (m, 4H), 3.20 (s, 3H), 3.90 (dd, *J* = 10.8, 5.3, 1H), 3.98 (dd, *J* = 10.8, 4.6, 1H), 4.79 (dt, *J* = 4.9, 1.2, 1H), 5.65 (d, *J* = 1.2, 1H), 6.90-7.20 (m, 6H), 7.70-7.83 (m, 4H). ^{13}C NMR (50 MHz, C_6D_6): ppm 19.4, 25.4, 26.2, 26.8, 52.1, 67.0, 87.8, 110.1, 120.3, 124.9, 127.2, 129.8, 133.7, 136.1. Anal. calcd for $C_{24}H_{30}O_3S_2Si$: C 62.84, H 6.59, S 13.98. Found: C 62.70, H 6.50, S 13.90.

2-(((*Tert*-butyl(diphenyl)silyl)-oxy)methyl)furan (10).

To a stirred C_6H_6/CH_3OH solution (95/5 v/v, 8.75 mL) containing alcohol **8** (0.50 g, 0.88 mmol), DDQ (0.28 g, 1.06 mmol) was added in one portion at room temperature. After 3h, H_2O was added, and the mixture extracted with EtOAc. The organic layer was dried (Na_2SO_4), and the solvent evaporated under reduced pressure. Chromatography of the crude residue over silica gel (hexane:EtOAc = 98:2) gave furan **10** (0.28 g, 75% yield). ^{1}H NMR (200 MHz, C_6D_6): δ 1.28 (s, 9H), 2.48 (s, 4H), 4.71 (s, 2H), 6.92 (s, 1H), 7.31-7.40 (m, 5H), 7.91-7.96 (m, 5H). ^{13}C NMR (100 MHz, C_6D_6): ppm 19.1, 26.1, 26.3, 26.5, 56.9, 127.6, 129.3, 129.5, 133.1, 134.8, 135.6, 136.2. Anal. calcd for $C_{23}H_{26}O_2S_2Si$: C 64.75, H 6.14, S 15.03. Found: C 65.00, H 6.12, S 15.08.

5-((*Tert*-butyl(diphenyl)silyl)-oxy)-5,7-dimethoxy-2,3,5,7-tetrahydro[1,4]dithiino[2,3-c]furan (11α).

Method A: from alcohol 8. To a stirred C_6H_6/CH_3OH solution (3/1 v/v, 8.75 mL) containing alcohol **8** (0.50 g, 0.88 mmol), DDQ (0.37 g, 1.65 mmol) was added in one portion at room temperature. After 3h, H_2O was added, and the mixture was extracted with EtOAc. The organic layer was dried (Na_2SO_4), and the solvent was evaporated under reduced pressure. Chromatography of the crude residue over silica gel (hexane:EtOAc = 95:5) gave acetal **11** (0.39 g, 90% yield, α:β = 6:1). *Method B: from ketone 7*. To a stirred CH_2Cl_2/CH_3OH solution (95/5 v/v, 8.75 mL) containing ketone **7** (0.50 g, 0.88 mmol), DDQ (0.28 g, 1.06 mmol) was added in one portion at room temperature. After 3h, H_2O was added, and the mixture was extracted with CH_2Cl_2. The organic layer was dried (Na_2SO_4), and the solvent was evaporated under reduced pressure. Chromatography of the crude residue over silica gel (hexane:EtOAc = 95:5) gave **11** (0.37 g, 87% yield, α:β = 6:1). Data for **11**α: white crystals, m.p. 88.2-89.7 °C (MeOH); ^{1}H NMR (400 MHz): δ 1.03 (s, 9H), 3.14-3.23 (m, 4H), 3.26 (s, 3H), 3.53 (s, 3H), 3.69 (d, *J* = 10.4, 1H), 3.78 (d, *J* = 10.4, 1H) 5.45 (s, 1H), 7.28-7.42 (m, 6H), 7.62-7.70 (m, 4H). ^{13}C NMR (100 MHz): ppm 19.4, 25.8, 26.7, 49.9, 55.9, 65.8, 107.6, 114.2, 125.2, 127.7, 129.6, 133.4, 133.5, 135.6. Anal. calcd for $C_{25}H_{32}O_4S_2Si$: C 61.44, H 6.60, S 13.12. Found: C 61.20, H 6.63, S 13.17.

*General procedure for trans-acetalization of **11**.* To a stirred CH_2Cl_2/ROH solution (3/1 v/v, 10 mL) containing acetal **11** (1 mmol), DDQ (1.5 mmol) was added in one portion at room temperature. After 24-48h, H_2O was added, and the mixture was extracted with EtOAc. The organic layer was dried (Na_2SO_4), and the solvent was evaporated under reduced pressure. Chromatography of the crude residue over silica gel gave the corresponding trans-acetalization product (71-99% yield).

5-[(*Tert*-butyldiphenyloxy)methyl]-5,7-bis-(trideuteromethoxy)-2,3,5,7-tetrahydro[1,4]dithino[2,3-c]furan (26).

Using CD_3OD as acetalization agent, acetal **26** was obtained quantitatively (> 99% yield) as α/β-mixture (α:β =6:1 by ^{1}H NMR). Data for **26** (α-anomer): oily, ^{1}HNMR (500 MHz): δ1.04 (s, 9H), 3.15-3.32 (m, 4H),3.71 (d, *J* = 10.3, 1H), 3.78 (d, *J* = 10.3, 1H), 5.46 (s, 1H), 7.32-7.43 (m, 6H), 7.63-7.77 (m, 4H).^{13}CNMR (125 MHz): ppm 19.2, 26.6, 29.4, 29.7, 46.8-50.1 (m),65.7, 107.4, 123.5, 127.6, 129.6, 133.4, 135.7. Anal. calcd for $C_{25}H_{26}D_6O_4S_2Si$:C 60.69, H 7.74, S 12.96.Found: C 60.80, H 7.71, S 12.91.

5-[(*Tert*-butyldiphenyloxy)methyl]-5,7-bis-(2,2,2-trifluoroethoxy)-2,3,5,7-tetrahydro[1,4]dithino[2,3-c]furan (27a).

Using CF_3CH_2OH as acetalizing agent, acetal **27a** was obtained (71% yield) mainly as α-anomer (α:β> 20:1 by ^{1}H NMR). Data for **27a**: oily, ^{1}HNMR (500 MHz): δ1.03 (s, 9H), 3.18-3.33 (m, 4H), 3.65-3.80 (m, 2H), 3.85 (d, *J* = 10.6, 1H), 3.89-4.03 (m, 2H), 4.05-4.15 (m, 1H), 5.53 (s, 1H), 7.34-7.47 (m, 6H), 7.66 (d, *J* = 7.1, 4H).^{13}CNMR (50 MHz): ppm 19.3, 26.1, 26.7, 29.7, 65.7, 107.5, 114.3, 123.8, 124.5, 127.6, 129.6, 133.4, 135.5, 135.6.Anal. calcd for $C_{27}H_{30}F_6O_4S_2Si$: C 51.91, H 4.84, F 18.25, S 10.27. Found: C 51.79, H 4.86, F 18.26, S 10.31.

5-[(t-butyldiphenyloxy)methyl]-5,7-bis-(2-propynyloxy)-2,3,5,7-tetrahydro[1,4]dithino[2,3-c]furan (27b).

Using propargyl alcohol as acetalization agent, acetal **27b** was obtained (83% yield) as α/β-mixture (α:β =6:1 by ^{1}H NMR).Data for **27b** (α-anomer): oily,^{1}HNMR (500 MHz): δ1.04 (s, 9H), 2.38 (t, *J* = 2.4, 1H), 2.48 (t, *J* = 2.4, 1H), 3.17-3.31 (m, 4H), 3.74 (d,*J* = 10.5, 1H),3.84 (d, *J* = 10.5, 1H), 4.09 (dd, *J* = 2.4, 14.9, 1H), 4.26 (dd, *J* = 2.4, 14.9, 1H), 4.39 (dd, *J* = 2.4, 15.7,1H), 4.43 (dd, *J* = 2.4, 15.7, 1H), 5.76 (s, 1H), 7.33-7.45 (m, 6H), 7.64-7.71 (m, 4H). ^{13}C NMR (125 MHz): ppm 19.3, 26.0, 26.1, 26.7, 50.9, 55.8, 65.5, 73.7, 75.2, 78.7, 79.9, 104.9, 114.3, 123.5, 125.4, 127.6, 129.6, 133.3, 135.6, 135.9. Anal. calcd for $C_{29}H_{32}O_4S_2Si$: C 64.89, H 6.01, S 11.95.Found: C 65.03, H 5.99, S 11.91.

5-[(*tert*-butyldiphenyloxy)methyl]-5,7-diisopropoxy-2,3,5,7-tetrahydro[1,4]dithino[2,3-c]furan (27c).

Using *i*-PrOH as acetalization agent, acetal **27c** was obtained in 90% yield, mainly as α-anomer (α:β> 20:1 by ^{1}H NMR). Data for **27c**: oily, ^{1}H NMR (500 MHz): δ 1.04 (s, 9H), 1.14 (d, *J* = 6.2, 3H), 1.16 (d, *J* = 6.2, 3H), 1.24 (d, *J* = 6.2, 3H), 1.31 (d, *J* = 6.2, 3H), 3.11-3.32 (m, 4H), 3.65 (d, *J* = 10.4, 1H), 3.79 (d, *J* = 10.4, 1H), 3.98-4.04 (m, 1H), 4.05-4.12 (m, 1H), 5.60 (s, 1H), 7.32-7.45 (m, 5H), 7.66-7.75 (m, 5H). ^{13}C NMR (125 MHz): ppm 19.4, 22.4, 23.6, 23.7, 24.4, 26.1, 26.3, 26.7, 65.7, 66.4, 72.3, 105.7, 114.1, 124.1, 125.2, 127.6, 129.5, 129.6, 133.6, 133.7, 135.6, 135.7. Anal. calcd for $C_{29}H_{40}O_4S_2Si$: C 63.93, H 7.40, S, 11.77. Found: C 63.95, H 7.44, S, 11.78.

2-(((*Tert*-butyl(diphenyl)silyl)-oxy)methyl)-2,5-dimethoxy-2,5-dihydrofuran (18α).

A solution of **11**α (0.30 g, 0.61 mmol) in acetone (7 mL) was added in one portion to a stirring suspension of Raney-Ni (W2) (2.25 g, wet) in the same solvent (7 mL) at 0 °C. The reaction mixture was stirred for 5h, then the solid was filtered off and washed with EtOAc. The filtrate was evaporated under reduced pressure to afford a crude residue which chromatography over silica gel (hexane:EtOAc = 98:2) gave pure olefin **18**α(0.20 g, 82% yield) as white solid; ^{1}H NMR (400 MHz, C_6D_6): δ 1.25 (s, 9H), 3.34 (s, 3H), 3.38 (s, 3H), 4.09 (d, *J* = 10.3, 1H), 4.13 (d, *J* = 10.3, 1H) 5.52 (appt, *J* = 0.8, 1.0, 1H), 5.77 (dd, *J* = 1.0, 5.8, 1H), 5.88 (dd, *J* = 0.8, 5.8, 1H), 7.27-7.35 (m, 6H) 7.80-7.89 (m, 4H). ^{13}C NMR (50 MHz): ppm 19.2, 26.7, 50.2, 56.1, 67.0, 107.5, 113.6, 127.6, 129.6, 131.9, 132.1, 133.4, 134.7, 135.6. Anal. calcd for $C_{23}H_{30}O_4Si$: C 69.31, H 7.59. Found: C 69.52, H 7.56.

*N*1-(1-(7-((*tert*-butyl(diphenyl)silyl)-oxy)methyl)-7-methoxy-2,3,5,7-tetrahydro[1,4]dithiino [2,3-c]furan-5-yl-2-oxo-1,2-dihydro-4-pyrimidinyl)acetamide (28α and 28β).

N-Acetylcytosine (0.02 g, 0.15 mmol) and acetal **11**α (0.05 g, 0.10 mmol) were co-evaporated with anhydrous toluene (3 x 5 mL). The resulting residue was kept at room temperature for 20 min under nitrogen atmosphere, then it was suspended in anhydrous CH_3CN (2mL), and *N,O-bis*-(trimethylsilyl)acetamide (BSA, 0.11 mL, 0.45 mmol) was added in one portion. The mixture was kept at 50 °C until an homogenous solution was observed (about 30 min). Afterwards, the solution was cooled to rt, and DMF (0.05 mL, 0.6 mmol) was added. After 10 min, a catalytic amount of TMSOTf was eventually added dropwise. After 48h at the same temperature, saturated aq. $NaHCO_3$ was added. After 10 min, the solution was extracted with EtOAc and washed with brine. The combined organic phases were dried (Na_2SO_4) and evaporated under reduced pressure; chromatography of the crude residue over silica gel (hexane:EtOAc = 1:1) afforded nucleoside **28** (0.04 g, 65% yield) as mixture of anomers (α:β = 4:1).

Data for **28**α: oily; ^{1}H NMR (400 MHz): δ 1.07 (s, 9H), 2.26 (s, 3H), 3.20-3.31 (m, 7H), 3.78 (d, *J* = 10.6, 1H), 3.83 (d, *J* = 10.6, 1H), 7.08 (s, 1H), 7.34-7.50 (m, 7H), 7.67-7.80 (m, 5H), 9.21 (bs, 1H). ^{13}C NMR (125 MHz): ppm 19.2, 26.1, 26.2, 26.7, 29.7, 50.8, 65.0, 89.5, 97.3, 114.9, 122.9, 126.9, 127.8, 129.8, 132.6, 132.9, 135.3, 135.5, 144.7, 155.8, 162.7, 170.6. Anal. calcd for $C_{30}H_{35}N_3O_5S_2Si$: C 59.09; H 5.78; N 6.89; S 10.52. Found: C 59.30; H 5.76; N 6.86; S 10.56.

Data for **28**β: oily; ^{1}H NMR (400 MHz): δ 1.11 (s, 9H), 2.18 (s, 3H), 3.16-3.32 (m, 7H), 3.92 (d, *J* = 11.2, 1H), 3.97 (d, *J* = 11.2, 1H), 6.61 (bd, *J* = 7.3, 1H), 7.23 (s, 1H), 7.31-7.49 (m, 6H), 7.56-7.68 (m, 4H), 8.10 (d, *J* = 7.5, 1H), 9.03 (bs, 1H). ^{13}C NMR (100 MHz): ppm 19.6, 24.9, 25.9, 26.0, 27.0, 29.7, 49.6, 65.5, 90.4, 97.1, 116.0, 124.4, 124.6, 127.9, 130.0, 132.3, 133.2, 135.3, 135.5, 145.3, 155.8, 162.6, 170.0. Anal. calcd for $C_{30}H_{35}N_3O_5S_2Si$: C 59.09; H 5.78; N 6.89; S 10.52. Found: C 59.28; H 5.80; N 6.91; S 10.55.

***N*1-(1-(5-(((*tert*-butyl(diphenyl)silyl)oxy)methyl)-5-methoxy-2,5-dihydro-2-furanyl)-2-oxo-1,2-dihydro-4-pyrimidinyl)acetamide (30α and 30β).**

N-Acetylcytosine (0.11 g, 0.7 mmol) and olefin **18**α (0.25 g, 0.65 mmol) were co-evaporated with anhydrous toluene (3 x 10 mL). The resulting residue was kept at room temperature for 20 min under nitrogen atmosphere, then it was suspended in anhydrous CH_3CN (3 mL), and *N*,*O*-*bis*-(trimethylsilyl)acetamide (BSA, 0.65 mL, 2.5 mmol) was added. The mixture was kept at 50 °C until an homogenous solution was observed (about 30 min). Afterwards, the solution was cooled to rt, and TMSOTf (0.02 mL, 0.06 mmol) was added dropwise. After 48h at the same temperature, saturated aq. $NaHCO_3$ was added. After 10 min, the solution was extracted with EtOAc and washed with brine. The combined organic phases were dried (Na_2SO_4) and evaporated under reduced pressure. Chromatography of the crude residue over silica gel (hexane:EtOAc = 1:1) afforded nucleoside **30** (0.22 g, 65% yield) as mixture of anomers (α:β = 1:2).
Data for **30**α: white powder; ^1H NMR (400 MHz): δ 1.06 (s, 9H), 2.24 (s, 3H), 3.29 (s, 3H), 3.76 (d, *J* = 10.9, 1H), 3.93 (d, *J* = 10.9, 1H), 6.22 (dd, *J* = 5.9, 1.2, 1H), 6.26 (d, *J* = 5.9, 1H), 6.89 (s, 1H), 7.29-7.50 (m, 7H), 7.64-7.66 (m, 4H), 7.86 (d, *J* = 7.5, 1H), 9.76 (bs, 1H). ^{13}C NMR (125 MHz): ppm 19.2, 24.9, 26.8, 51.0, 64.8, 89.9, 97.1, 114.7, 127.8, 129.8, 129.9, 130.3, 132.8, 132.9, 133.9, 135.5, 135.6, 144.6, 155.3, 163.0, 171.0. Anal. calcd for $C_{28}H_{33}N_3O_5Si$: C 64.71, H 6.40, N 8.09. Found: C 64.97, H 6.38, N 8.06.
Data for **30**β: white crystals, m.p. 178.9 °C (dec.; MeOH); ^1H NMR (400 MHz): δ 1.06 (s, 9H), 2.19 (s, 3H), 3.18 (s, 3H), 3.92 (d, *J* = 11.2, 1H), 4.00 (d, *J* = 11.2, 1H), 5.91 (dd, *J* = 1.8, 5.8, 1H), 6.39 (dd, *J* = 0.9, 5.8, 1H), 6.93 (bd, *J* = 7.4, 1H), 7.15 (s, 1H), 7.37-7.52 (m, 6H), 7.55-7.64 (m, 4H), 8.26 (d, *J* = 7.5, 1H), 8.33 (bs, 1H). ^{13}C NMR (125 MHz): ppm 19.3, 24.8, 26.9, 49.7, 66.8, 90.7, 96.7, 116.2, 127.9, 128.0, 130.1, 132.0, 132.3, 133.7, 135.4, 135.6, 145.1, 155.6, 162.5, 170.2. Anal. calcd for $C_{28}H_{33}N_3O_5Si$: C 64.71, H 6.40, N 8.09. Found: C 64.98, H 6.42, N 8.07.

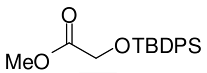
4-Amino-1-(5-(hydroxymethyl)-5-methoxy-2,5-dihydro-2-furanyl)-1,2-dihydro-2-pyrimidinone (31α).

To a stirring solution of **30**α (0.10 g, 0.20 mmol) in THF (1 mL), TBAF (22 µL, 1m solution in THF, 0.22 mmol) was added at room temperature. The reaction was stirred for 18 h, then the solvent was evaporated under vacuum. The crude residue was treated with 2 mL of NH_3/CH_3OH 6m at room temperature. After 2h, the solvent was evaporated and the crude residue purified by chromatography on silica gel ($CHCl_3$:CH_3OH = 8:2) to afford nucleoside **31**α as white crystals (0.05 g, 97 % o.y.). M.p. 203.5 °C (dec.; EtOAc/MeOH); ^1H NMR (400 MHz, CD_3OD): 3.26 (s, 3H), 3.58 (d, *J* = 11.8, 1H), 3.73 (d, *J* = 11.8, 1H), 5.90 (d, *J* = 7.5, 1H), 6.27 (dd, *J* = 1.3, 5.9, 1H), 6.32 (dd, *J* = 1.7, 5.9, 1H), 6.83 (appt, *J* = 1.3, 1H), 7.58 (d, *J* = 7.5, 1H). ^{13}C NMR (100 MHz, CD_3OD): ppm 51.2, 65.3, 90.1, 96.5, 115.5, 131.8, 135.3, 142.8, 158.6, 167.9. Anal. calcd for $C_{10}H_{13}N_3O_4$: C 50.21, H 5.48, N 17.56.Found: C 50.39, H 5.46, N 17.50.

4-Amino-1-(5-(hydroxymethyl)-5-methoxy-2,5-dihydro-2-furanyl)-1,2-dihydro-2-pyrimidinone (31β).

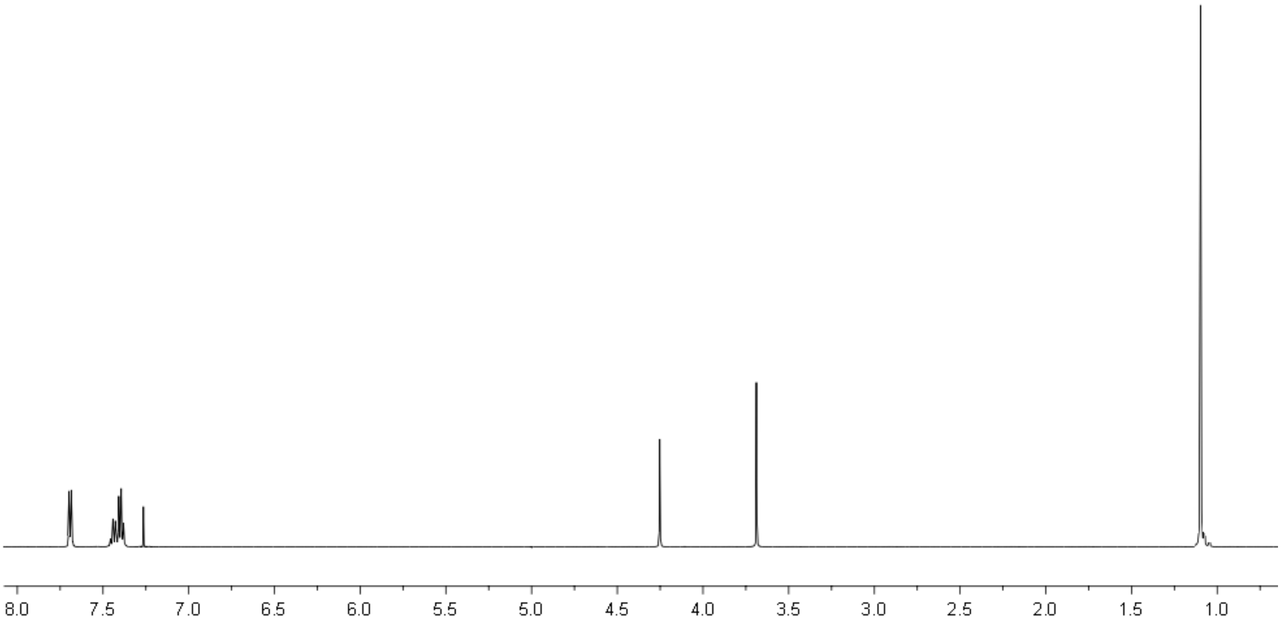
31β was obtained (92% o.y.) under the same conditions reported for **31**α. White crystals, m.p. 213.0 °C (dec.; EtOAc/MeOH);^1H NMR (400 MHz, CD_3OD): 3.21 (s, 3H), 3.60 (d, *J* = 11.9, 1H), 3.73

(d, *J* = 11.9, 1H), 5.84 (d, *J* = 7.5, 1H), 6.12 (dd, *J* = 1.7, 5.8, 1H), 6.31 (d *J* = 5.8, 1H), 7.13 (s, 1H), 7.87 (d, *J* = 7.5, 1H). ^{13}C NMR (100 MHz, CD_3OD): ppm 49.0, 65.8, 91.7, 96.3, 117.1, 133.3, 134.0, 143.1, 158.7, 167.8. Anal. calcd for $C_{10}H_{13}N_3O_4$: C 50.21, H 5.48, N 17.56 Found: C 50.57, H 5.44, N 17.43.

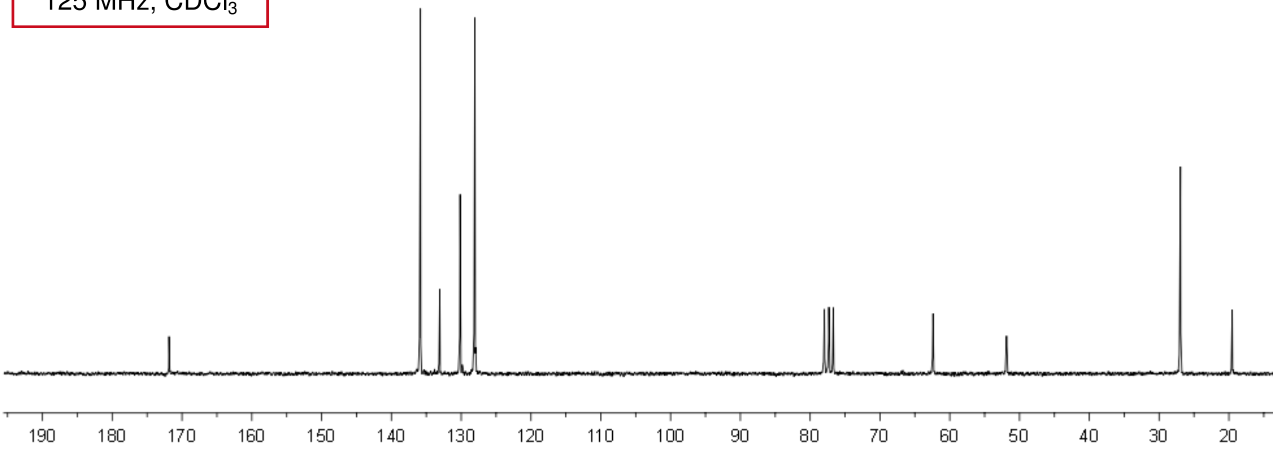


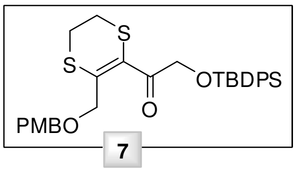
6

500 MHz, $CDCl_3$



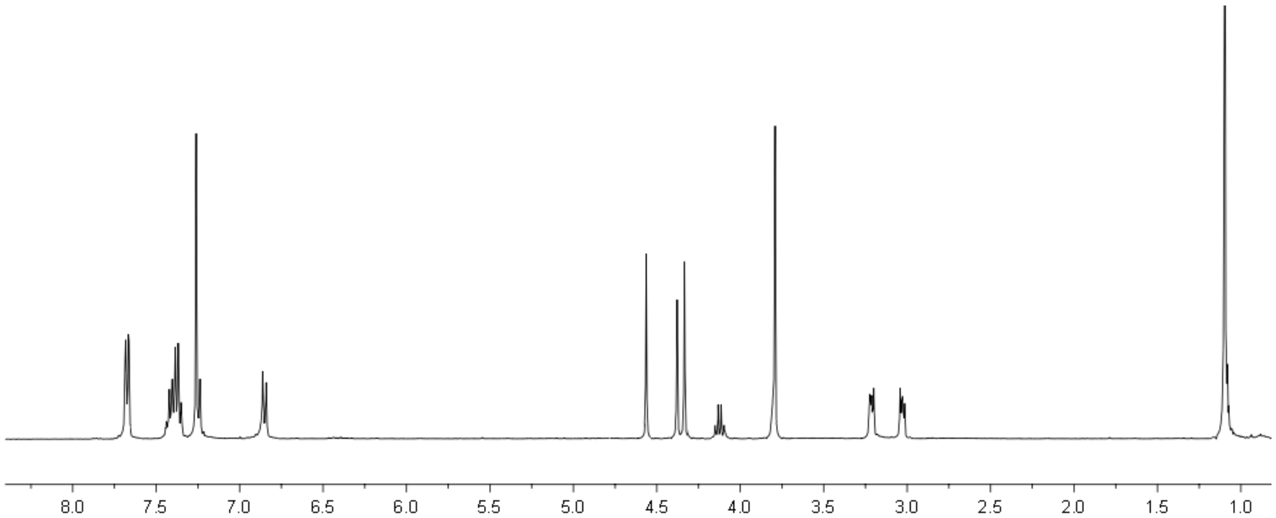
125 MHz, $CDCl_3$



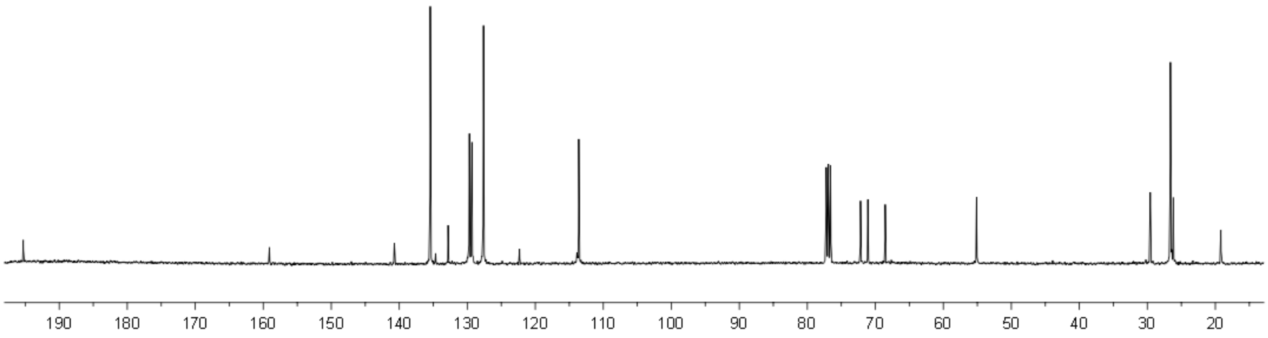


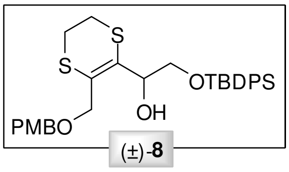
7

400 MHz, $CDCl_3$



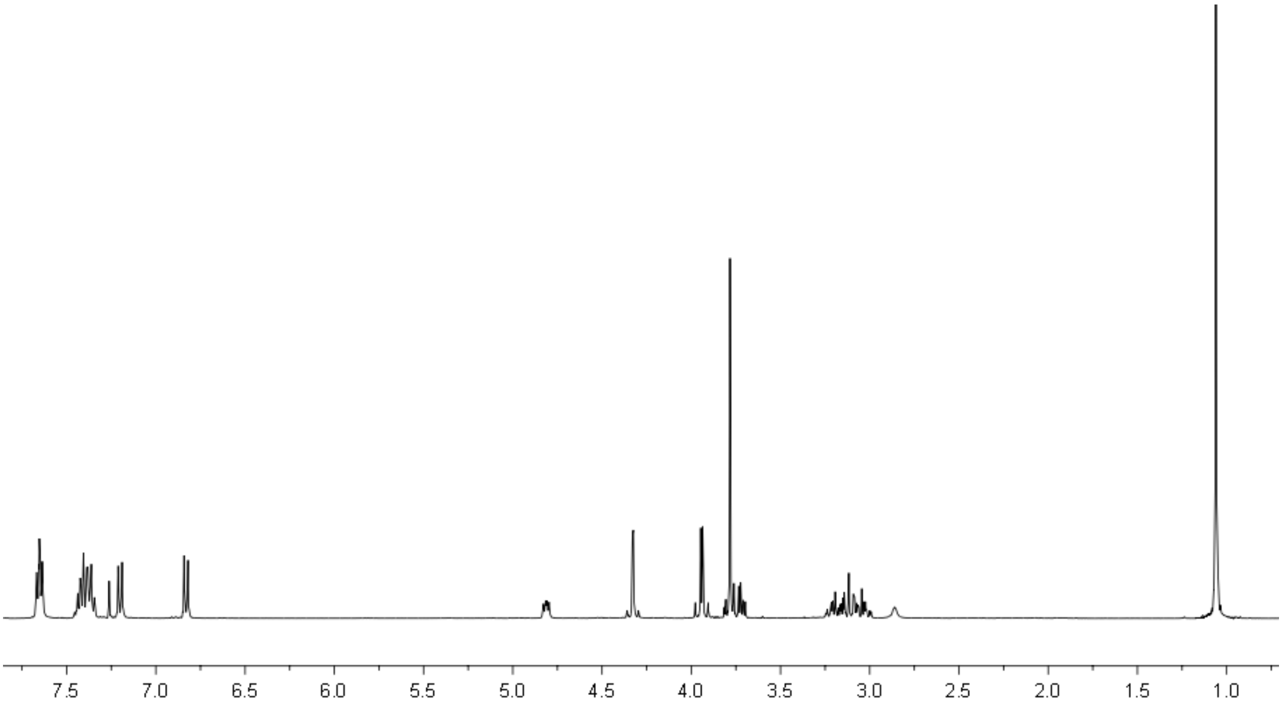
125 MHz, $CDCl_3$



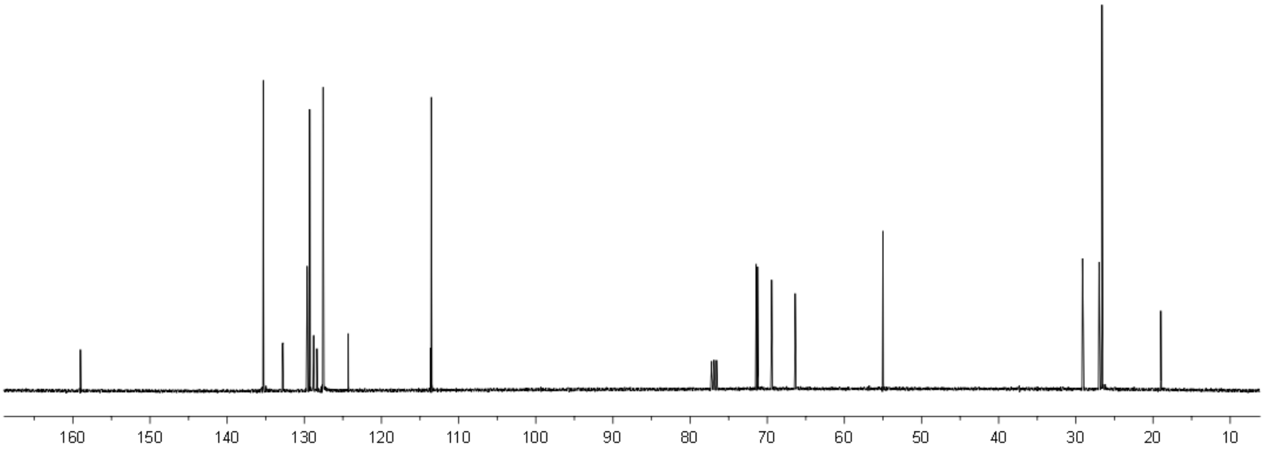


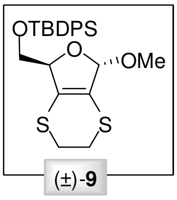
(±)-**8**

500 MHz, $CDCl_3$

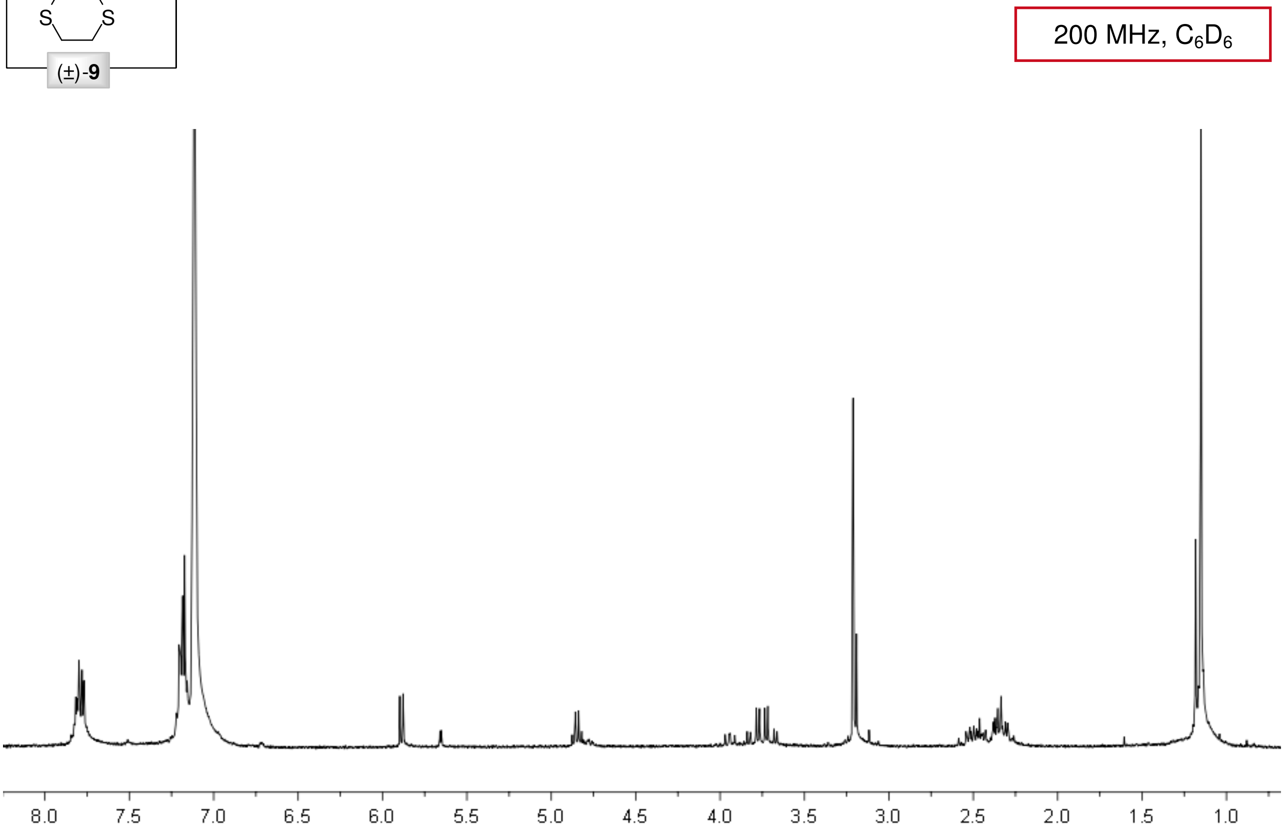


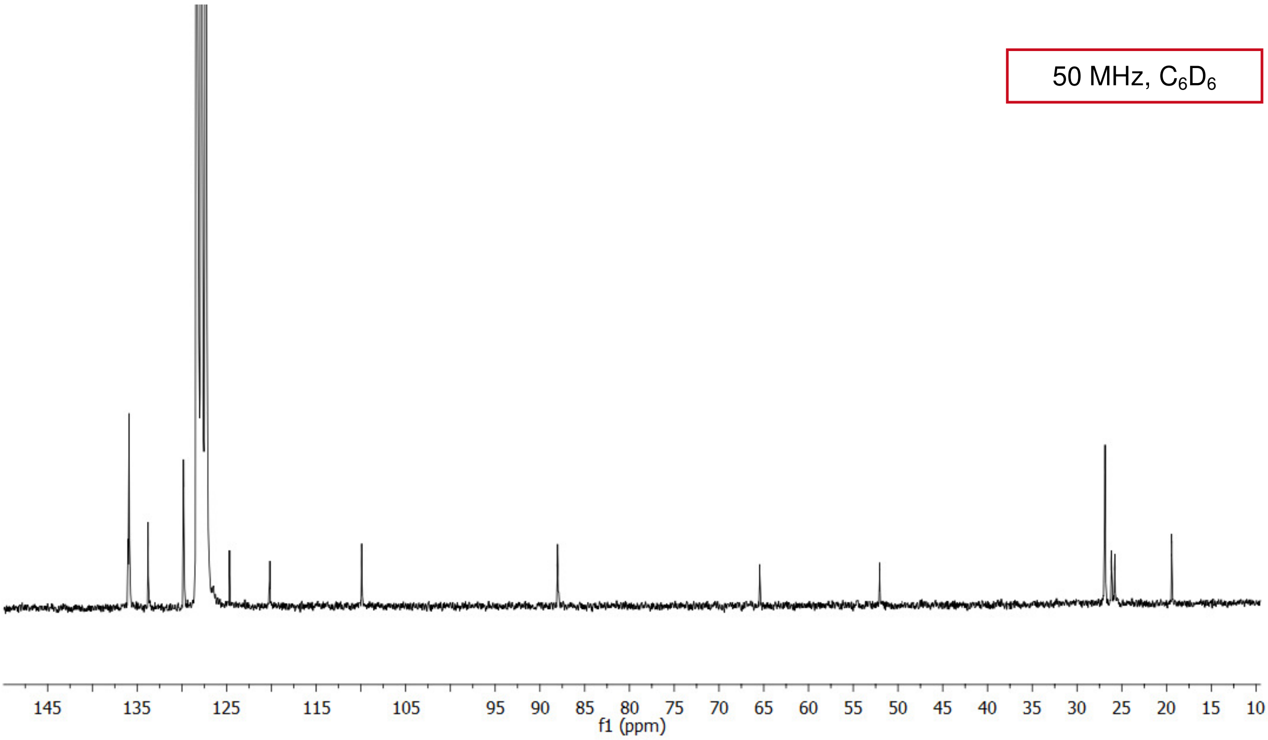
100 MHz, $CDCl_3$

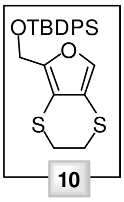



OTBDPS
O
OMe
S
S

(±)-**9**

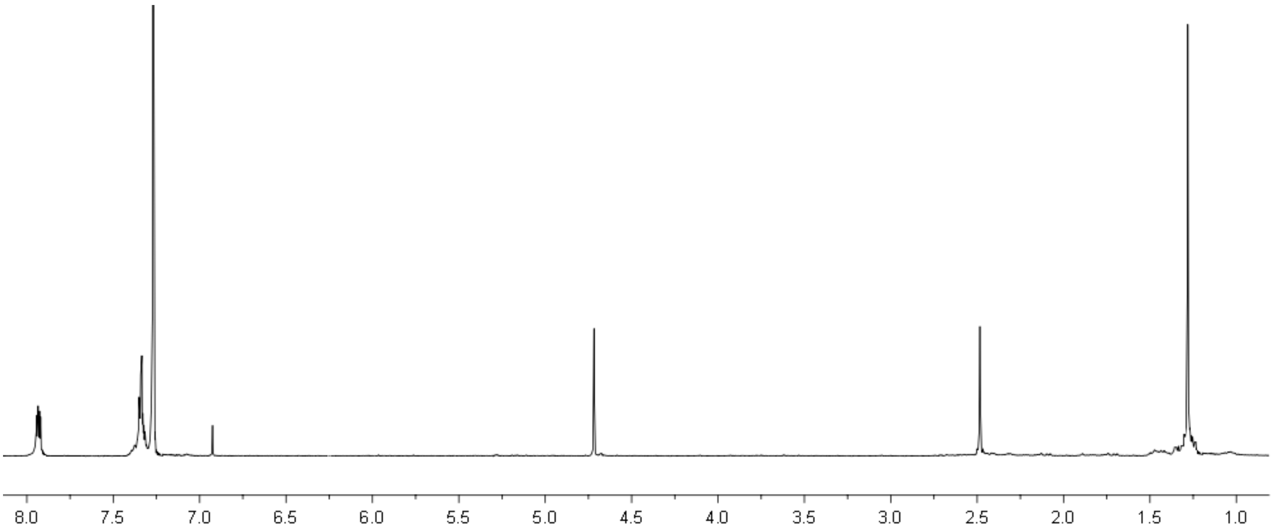

200 MHz, C6D6
8.0
7.5
7.0
6.5
6.0
5.5
5.0
4.5
4.0
3.5
3.0
2.5
2.0
1.5
1.0

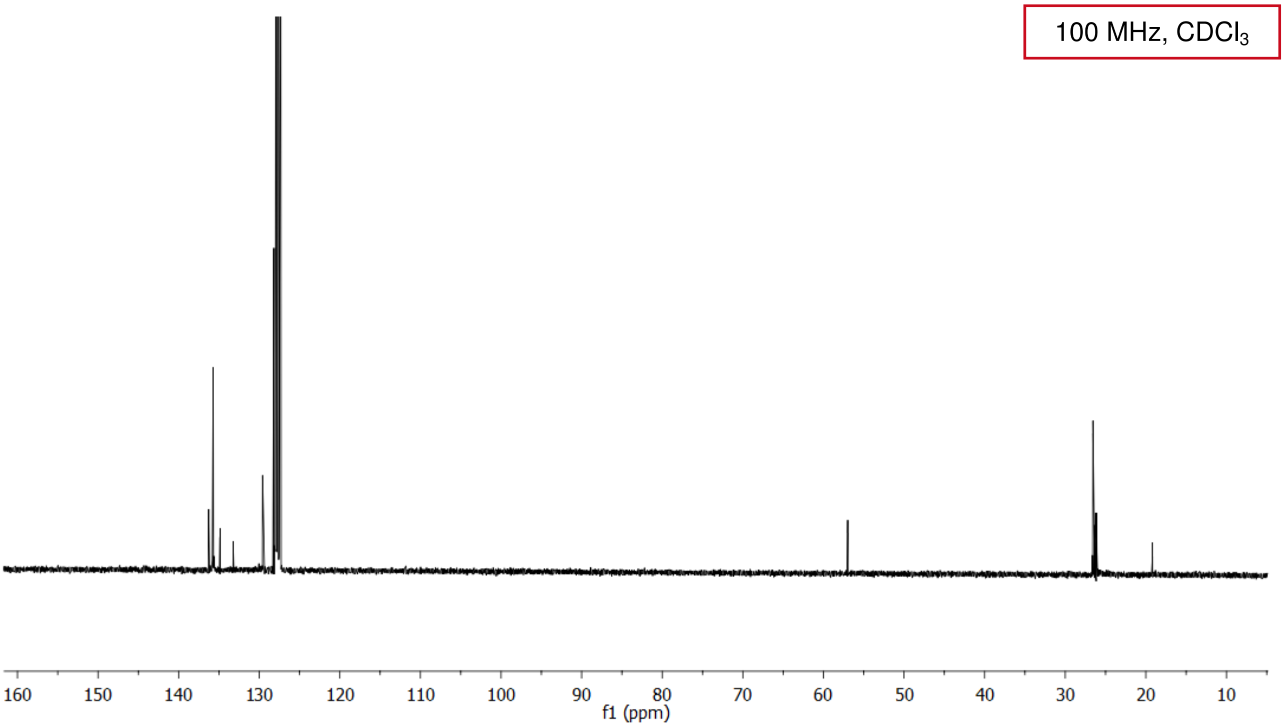

50 MHz, C6D6
145
135
125
115
105
95
90
85
80
75
70
65
60
55
50
45
40
35
30
25
20
15
10
f1 (ppm)

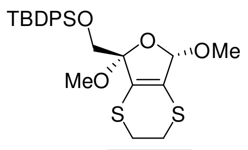


10

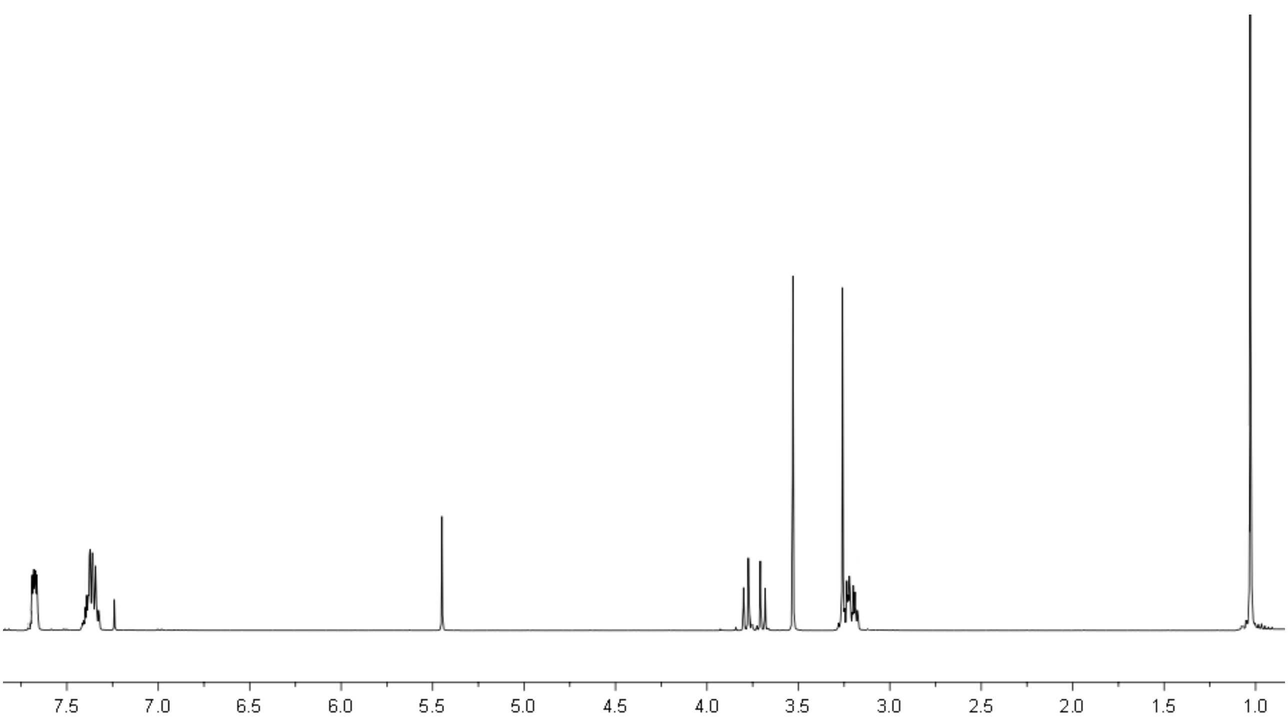
400 MHz, $CDCl_3$

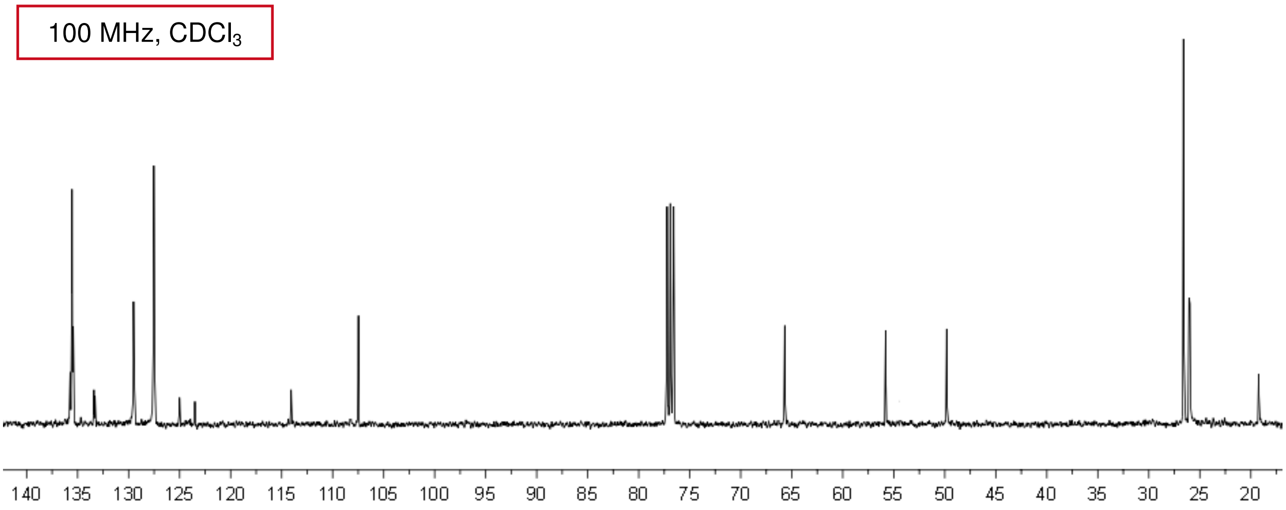


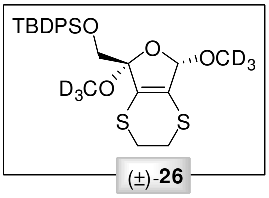



TBDPSO
O
OMe
MeO
S
S

(±)-**11**α

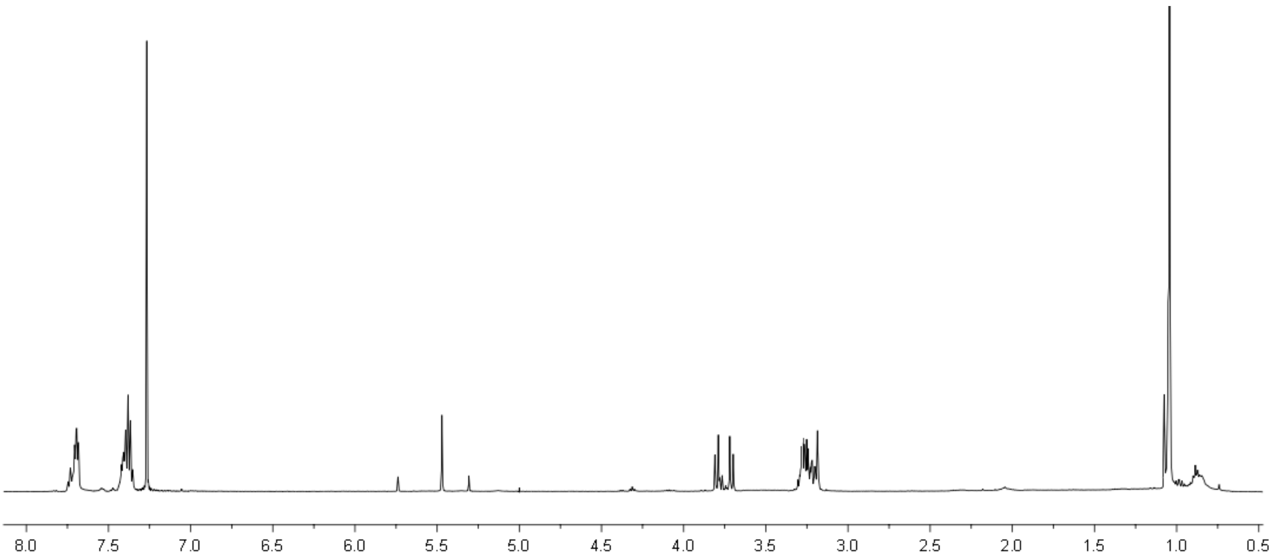

400 MHz, CDCl3
7.5
7.0
6.5
6.0
5.5
5.0
4.5
4.0
3.5
3.0
2.5
2.0
1.5
1.0


100 MHz, CDCl3
140
135
130
125
120
115
110
105
100
95
90
85
80
75
70
65
60
55
50
45
40
35
30
25
20

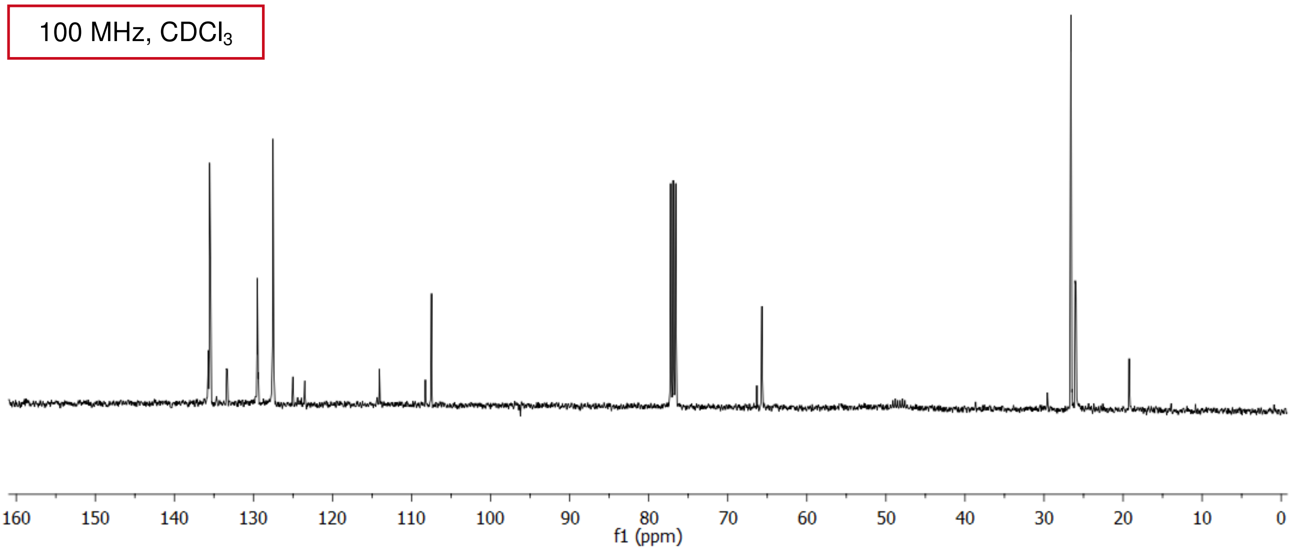


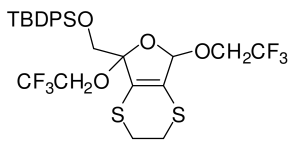
(±)-**26**

500 MHz, CDCl$_3$

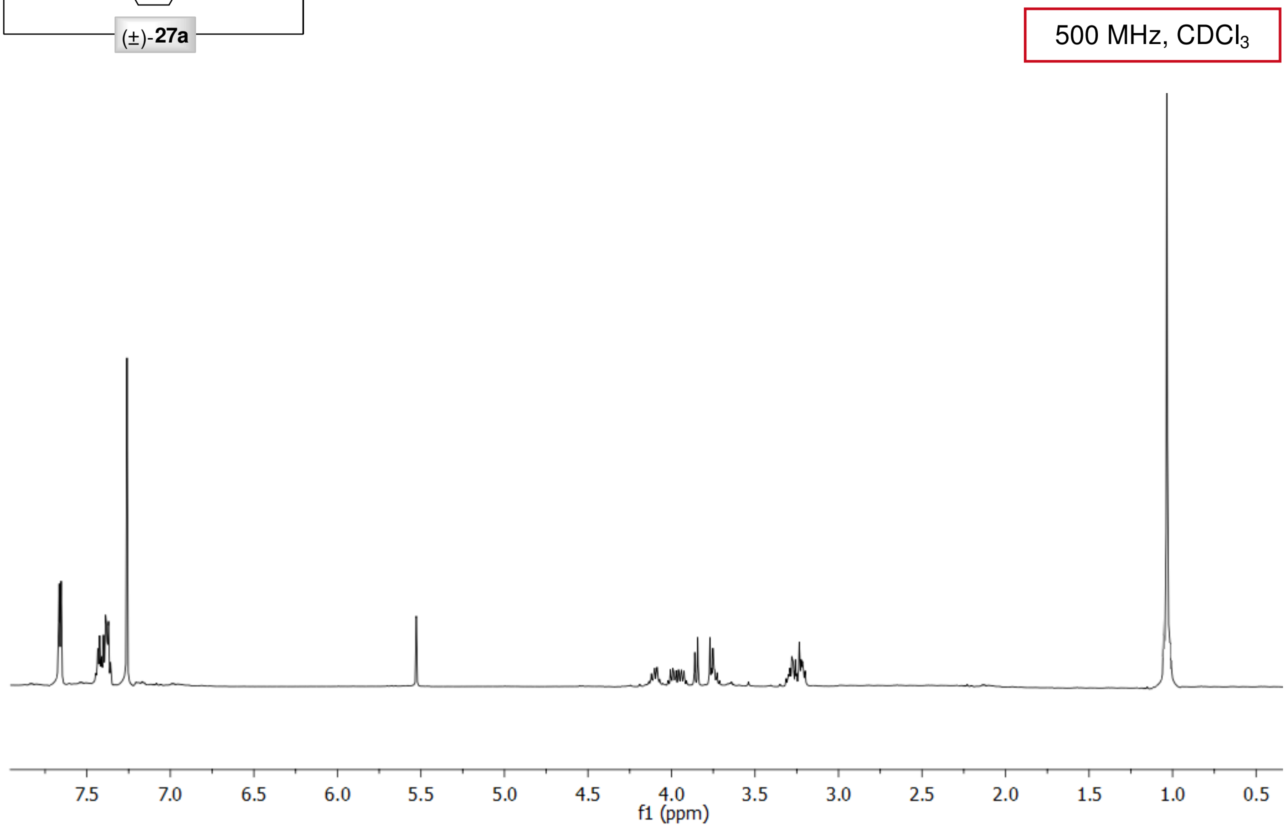


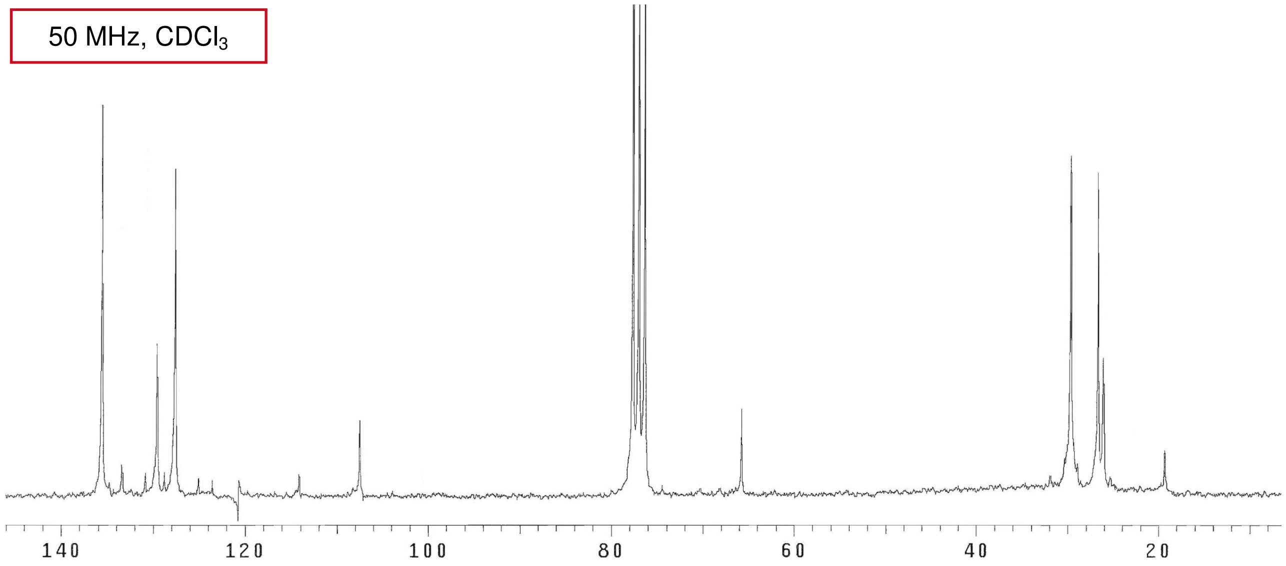
100 MHz, CDCl$_3$

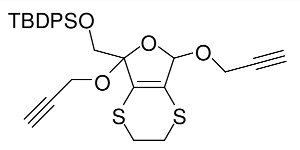



TBDPSO
O
OCH2CF3
CF3CH2O
S
S

(±)-**27a**

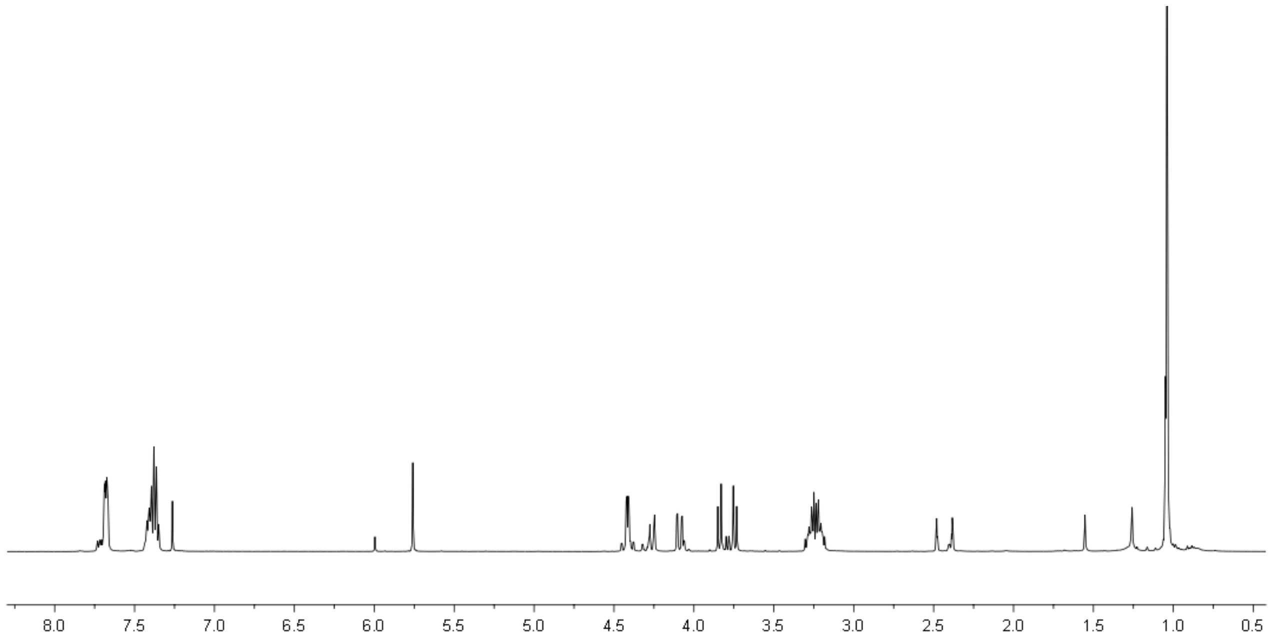

500 MHz, CDCl3
7.5
7.0
6.5
6.0
5.5
5.0
4.5
4.0
3.5
3.0
2.5
2.0
1.5
1.0
0.5
f1 (ppm)


50 MHz, CDCl3
140
120
100
80
60
40
20

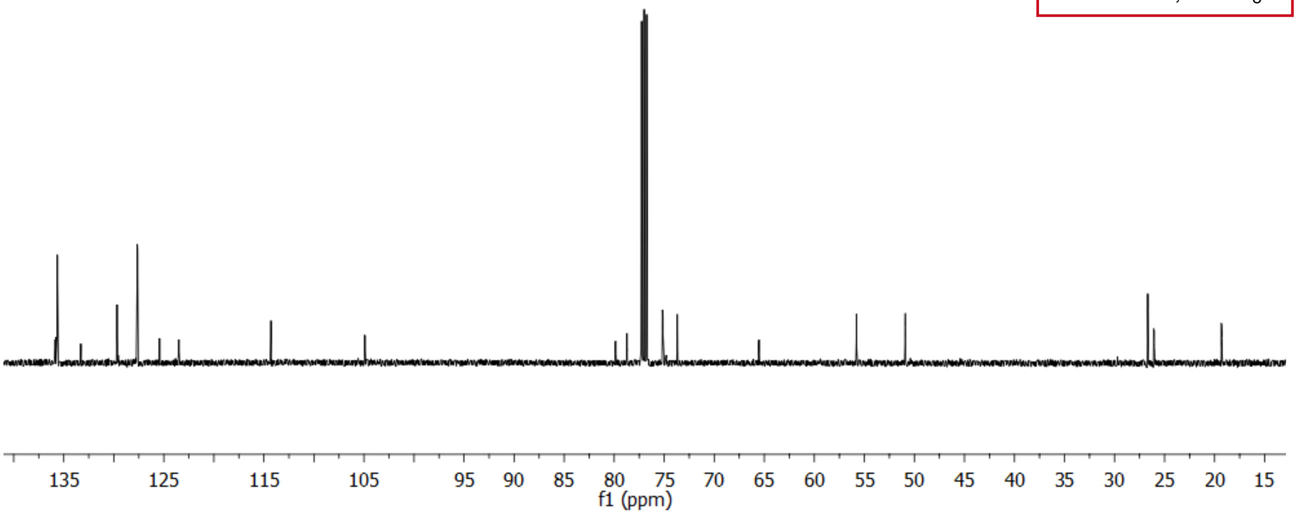


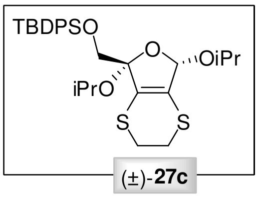
(±)-**27b**

500 MHz, $CDCl_3$



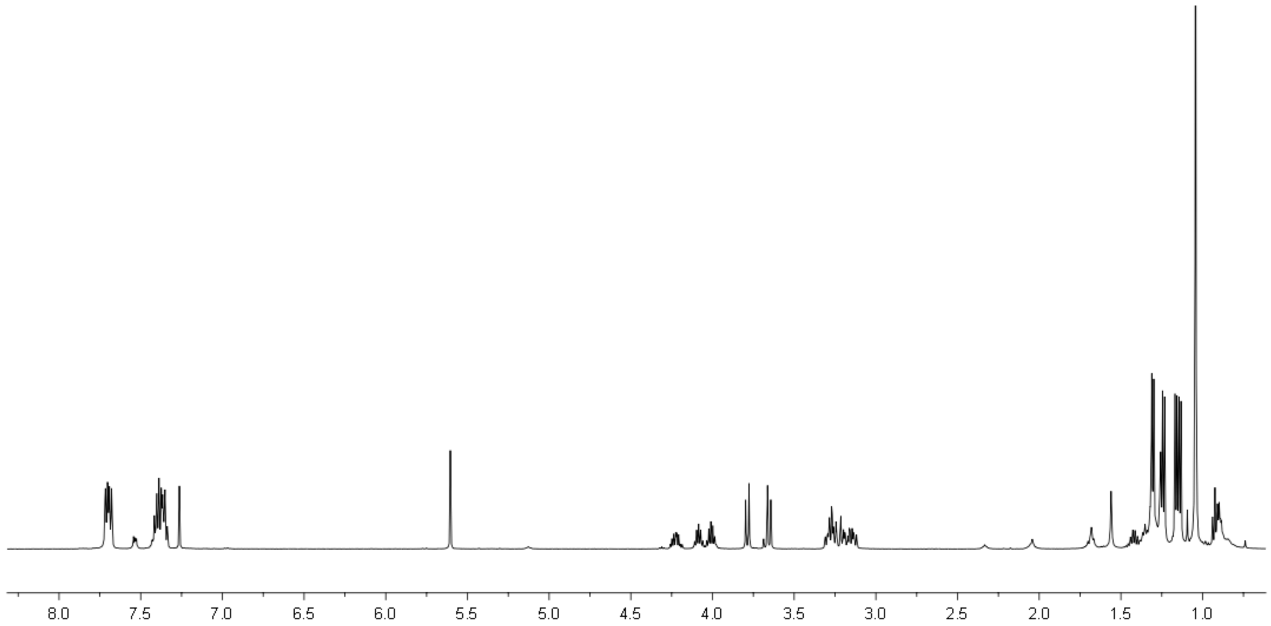
125 MHz, $CDCl_3$



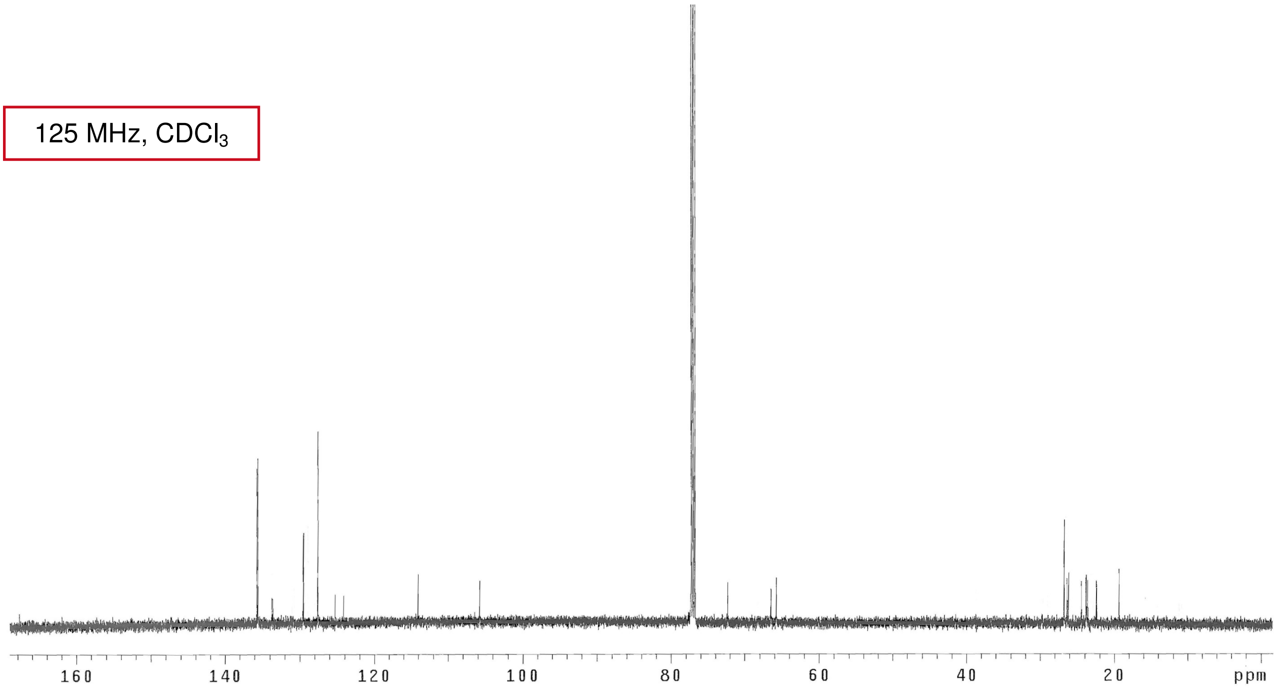


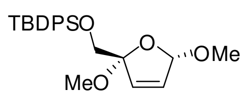
(±)-**27c**

500 MHz, $CDCl_3$



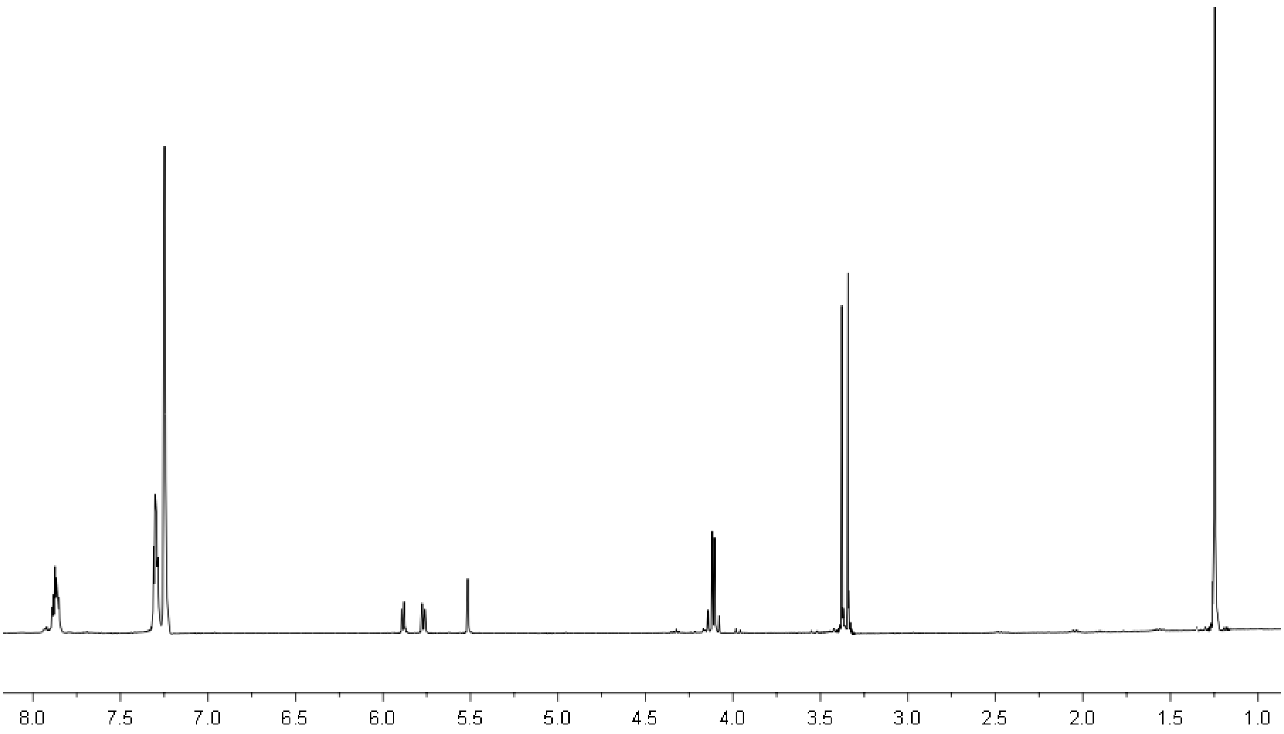
125 MHz, $CDCl_3$



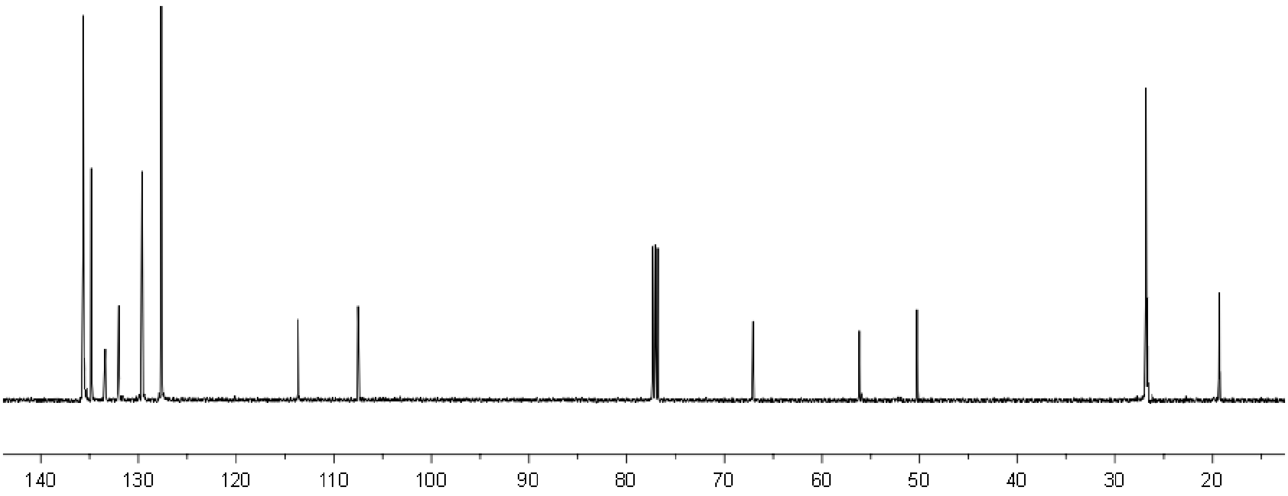


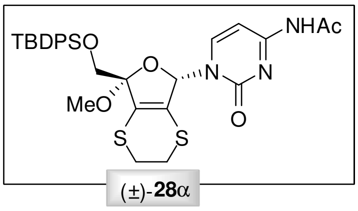
(±)-**18**α

400 MHz, $CDCl_3$

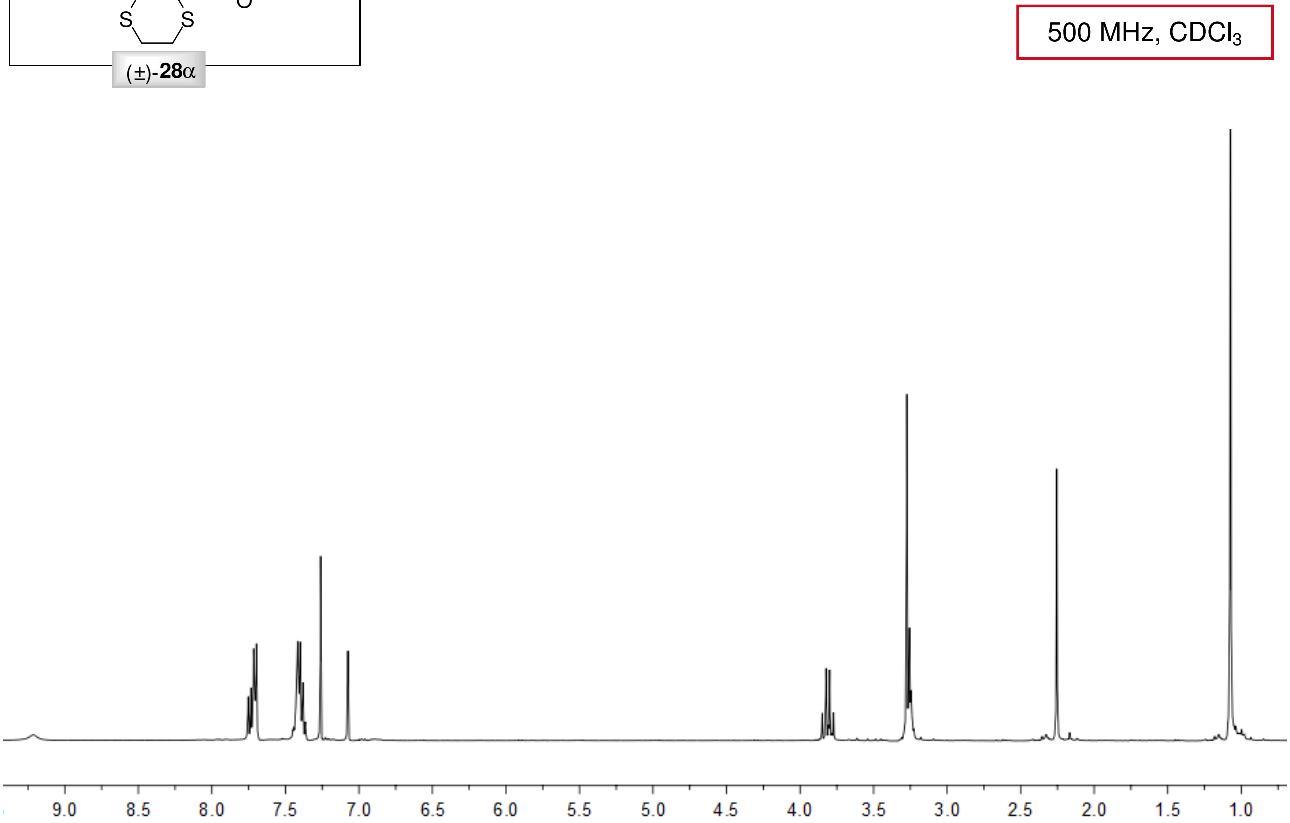


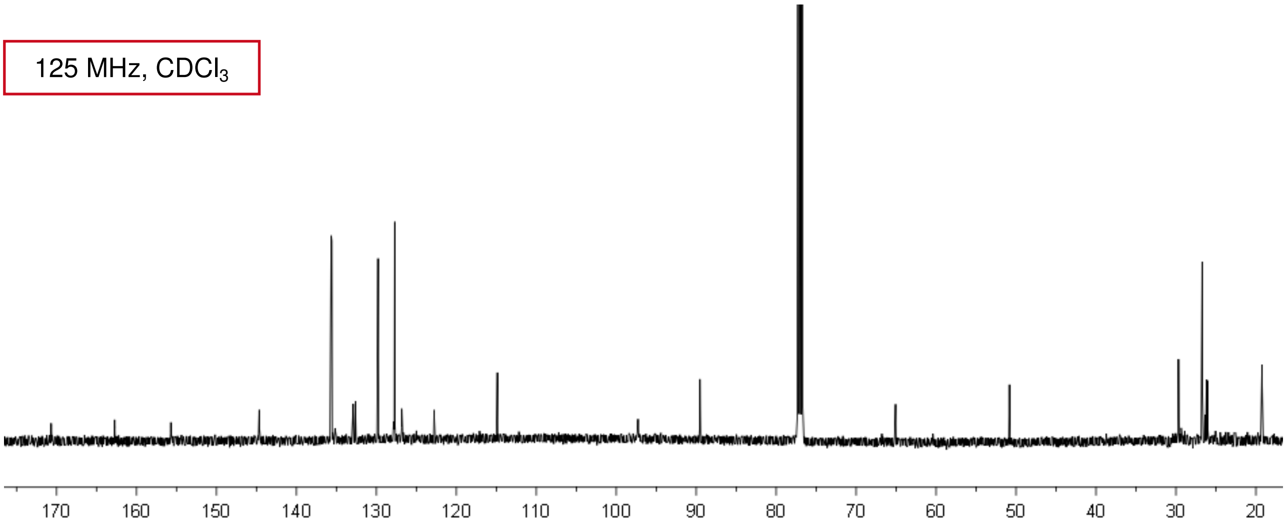
100 MHz, $CDCl_3$

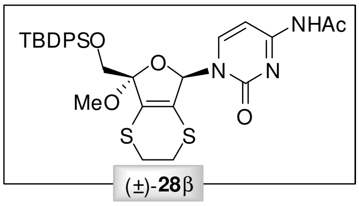



TBDPSO
MeO
O
S
S
N
N
O
NHAc

(±)-**28**α

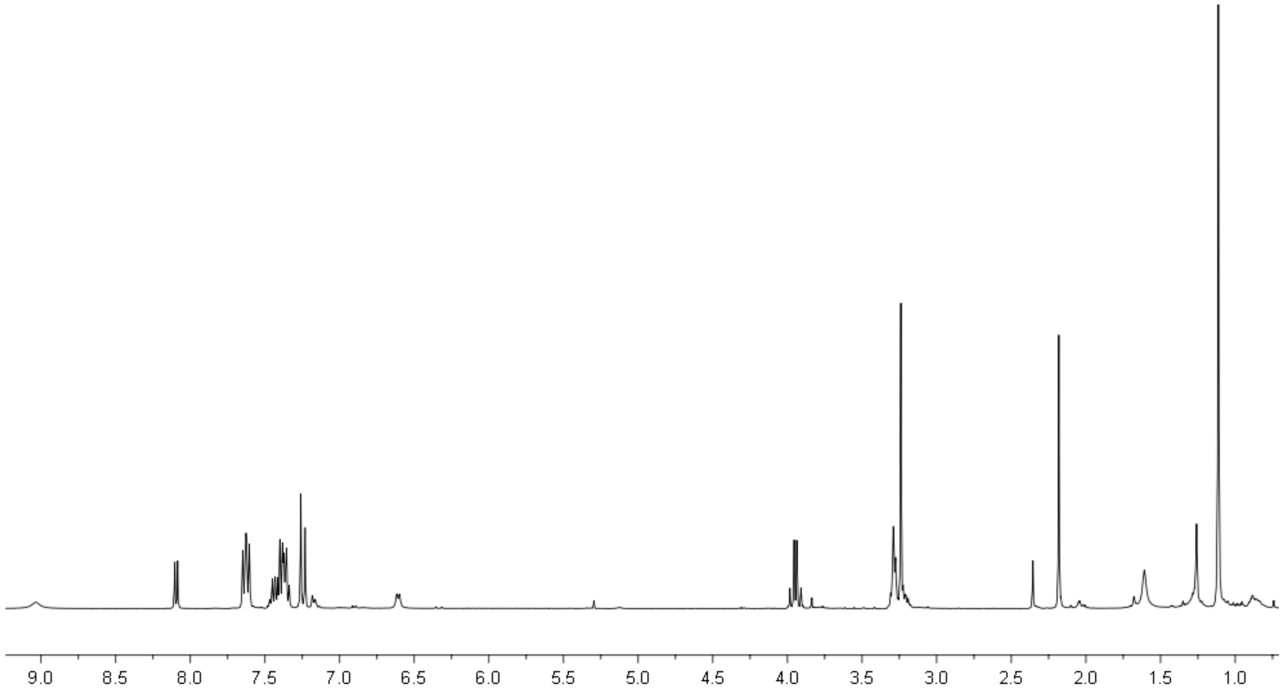

500 MHz, $CDCl_3$
9.0
8.5
8.0
7.5
7.0
6.5
6.0
5.5
5.0
4.5
4.0
3.5
3.0
2.5
2.0
1.5
1.0

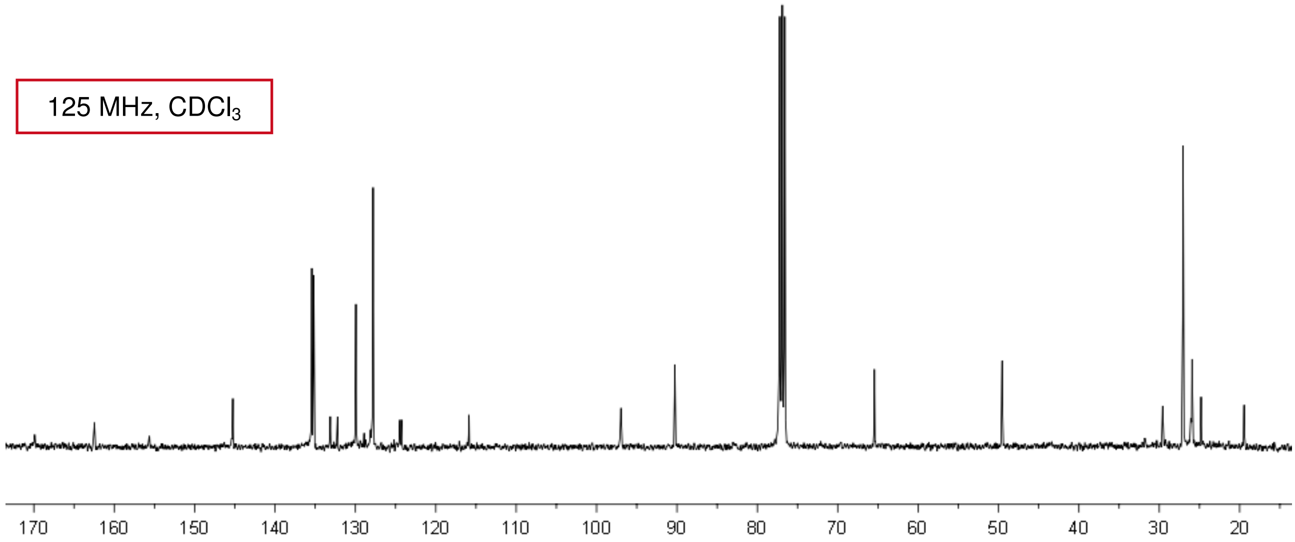

125 MHz, $CDCl_3$
170
160
150
140
130
120
110
100
90
80
70
60
50
40
30
20

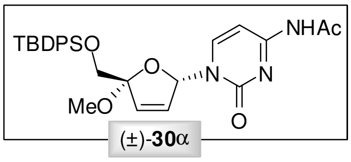


(±)-**28**β

500 MHz, $CDCl_3$

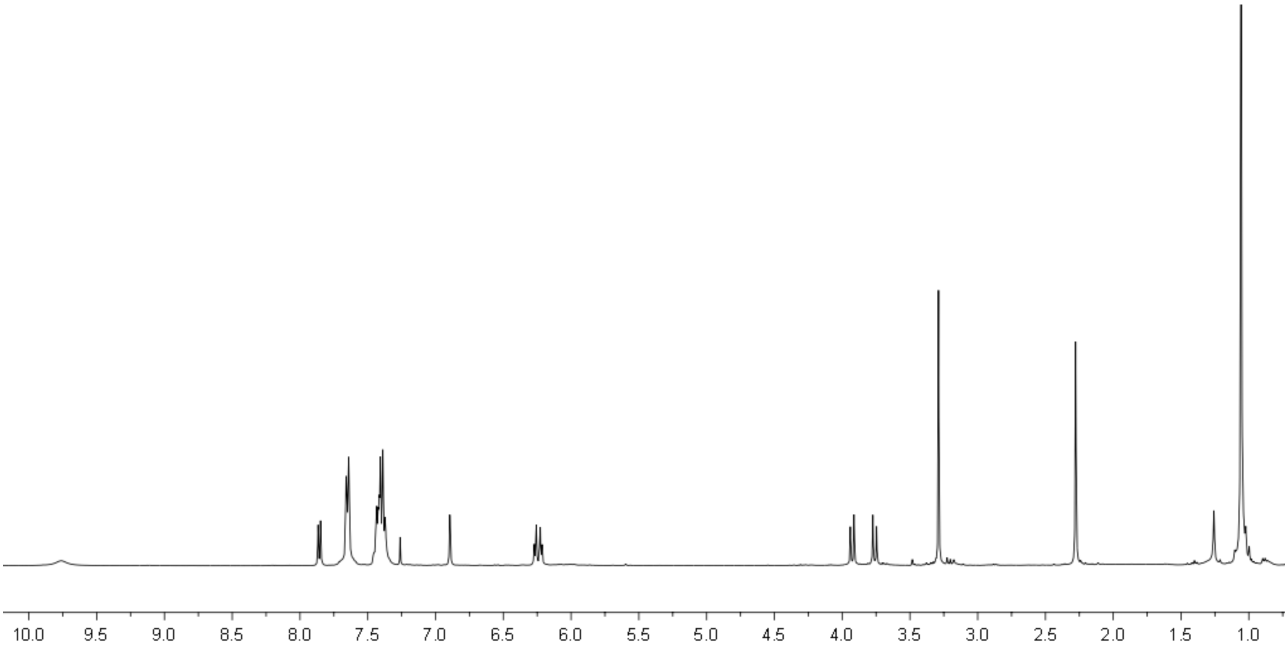




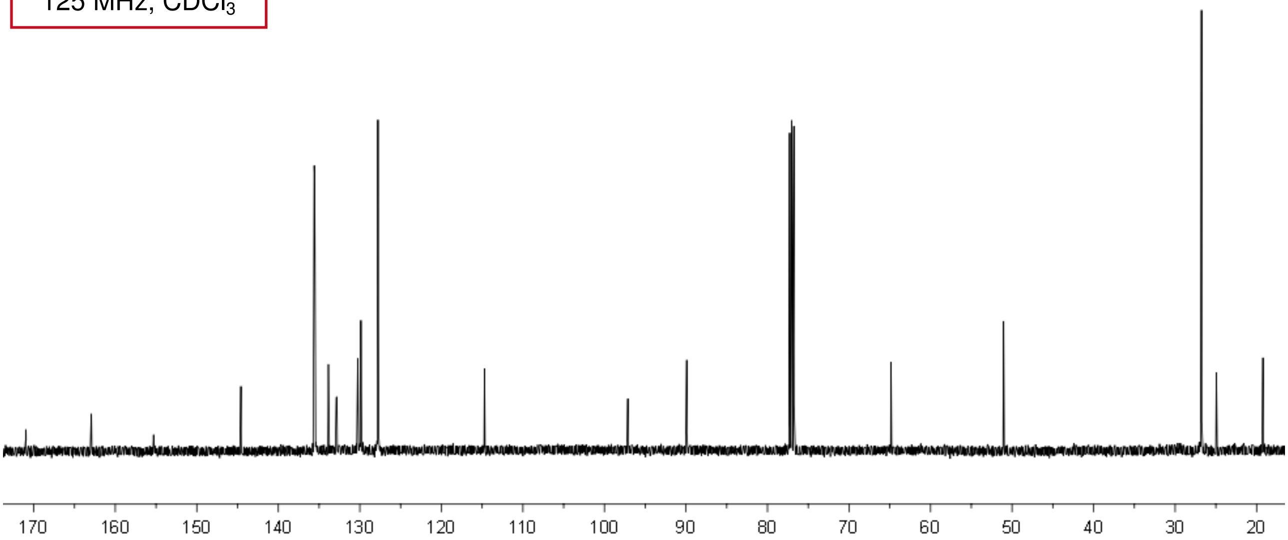


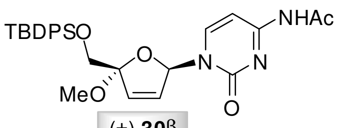
(±)-**30**α

500 MHz, $CDCl_3$



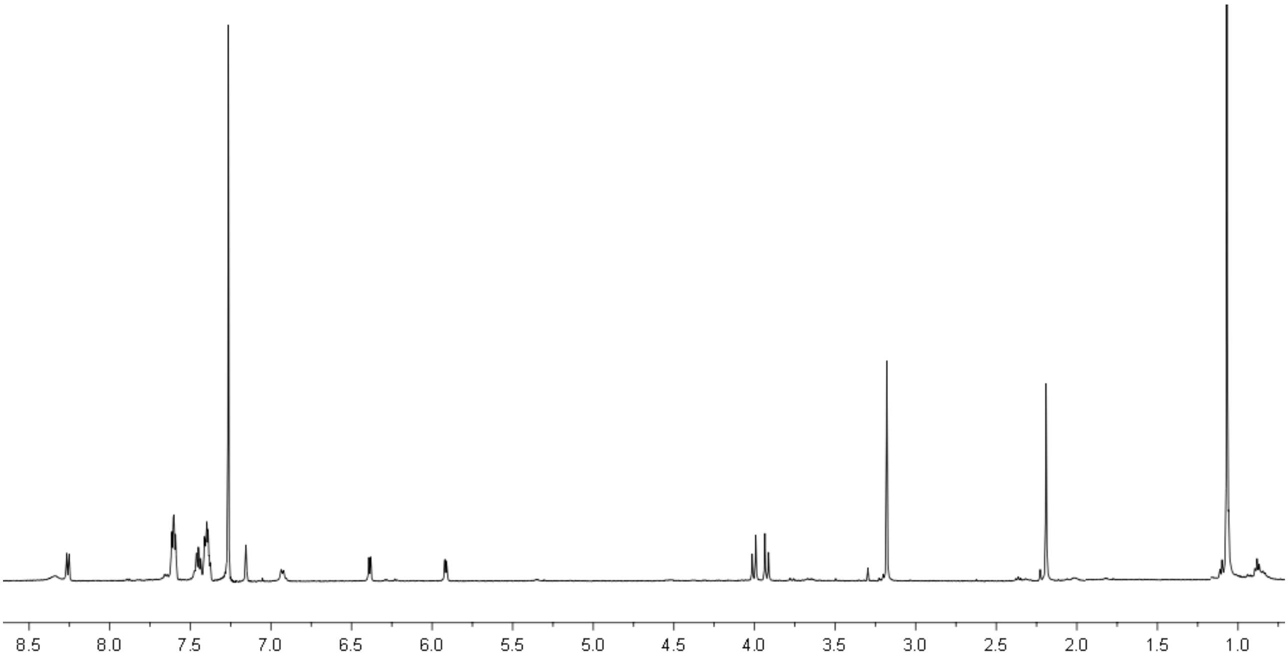
125 MHz, $CDCl_3$



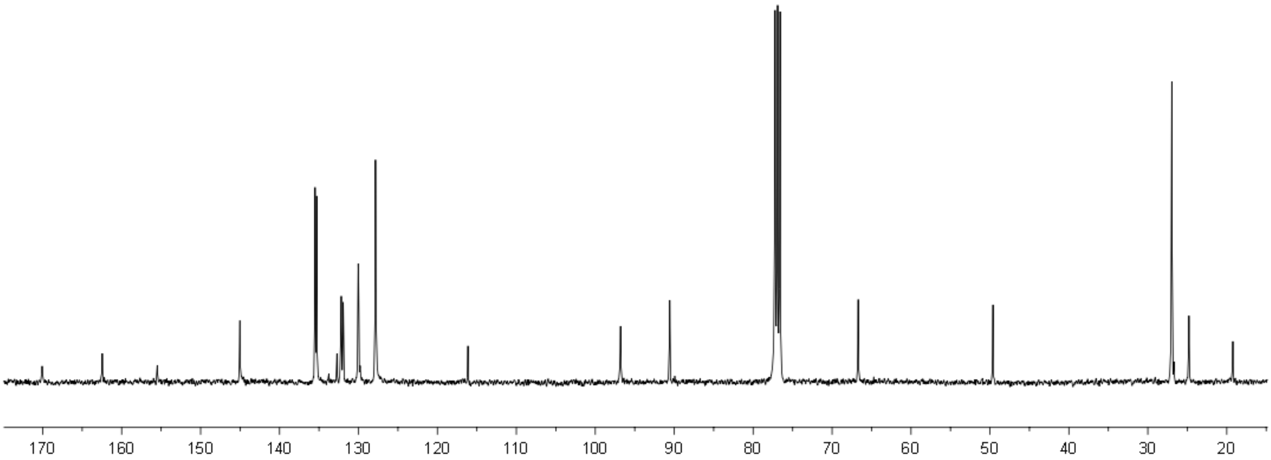


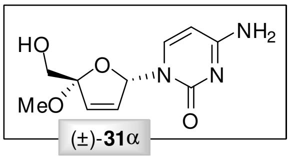
(±)-**30**β

500 MHz, $CDCl_3$

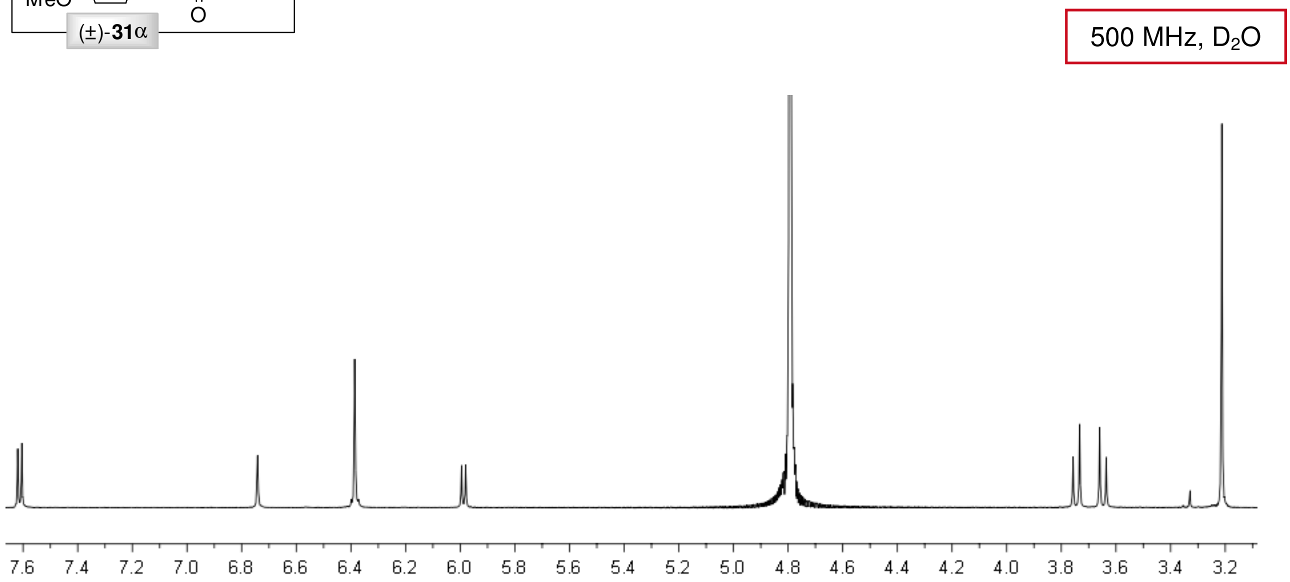


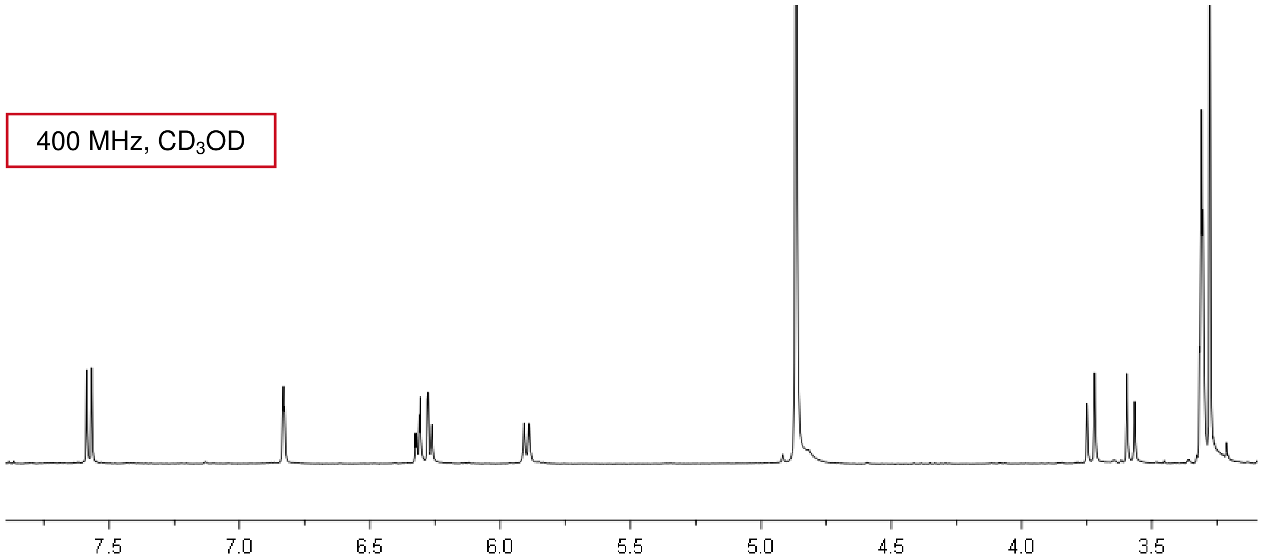
125 MHz, $CDCl_3$

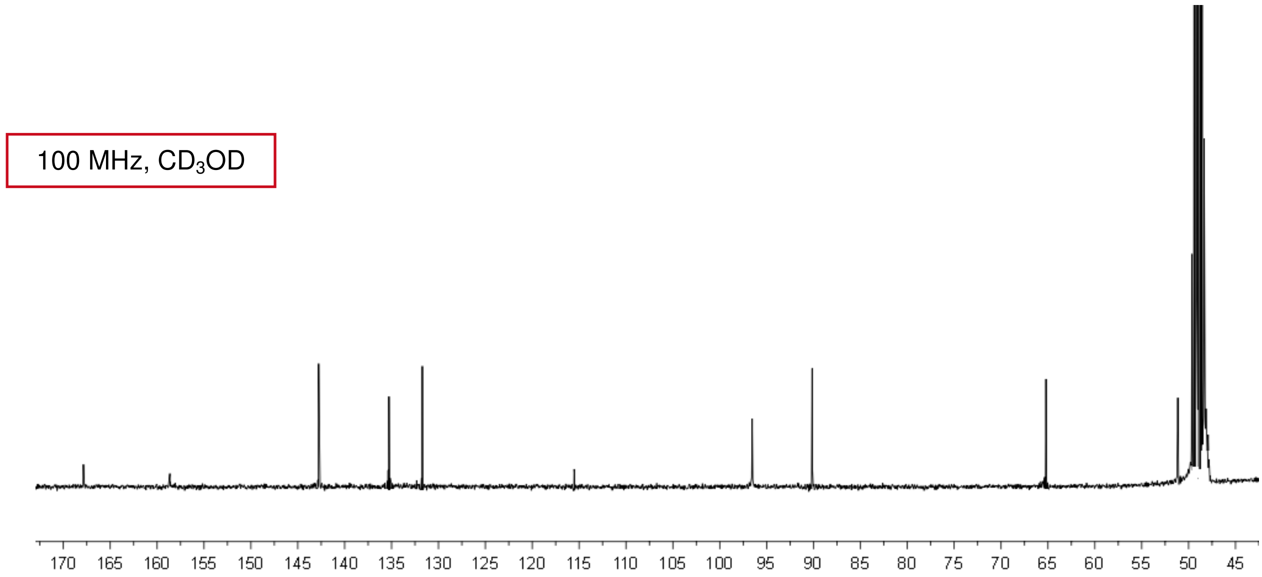


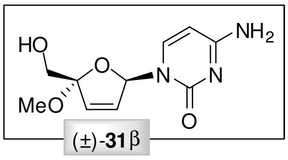

HO
MeO
O
N
N
NH2
O

(±)-**31**α

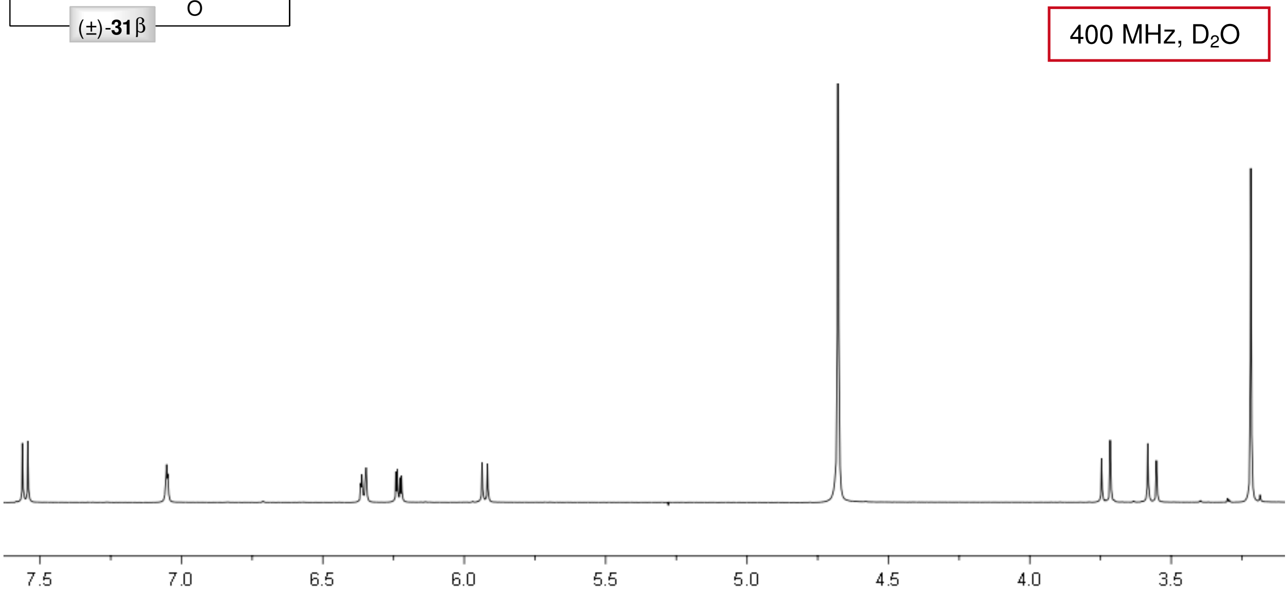

500 MHz, D2O
7.6
7.4
7.2
7.0
6.8
6.6
6.4
6.2
6.0
5.8
5.6
5.4
5.2
5.0
4.8
4.6
4.4
4.2
4.0
3.8
3.6
3.4
3.2

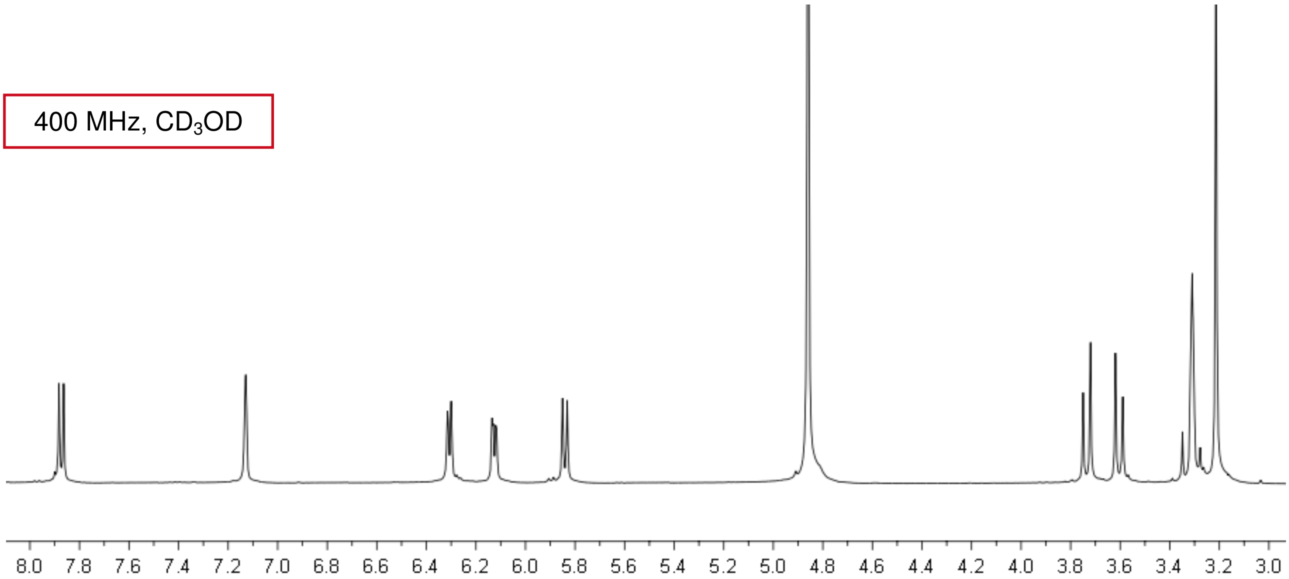

400 MHz, CD3OD
7.5
7.0
6.5
6.0
5.5
5.0
4.5
4.0
3.5

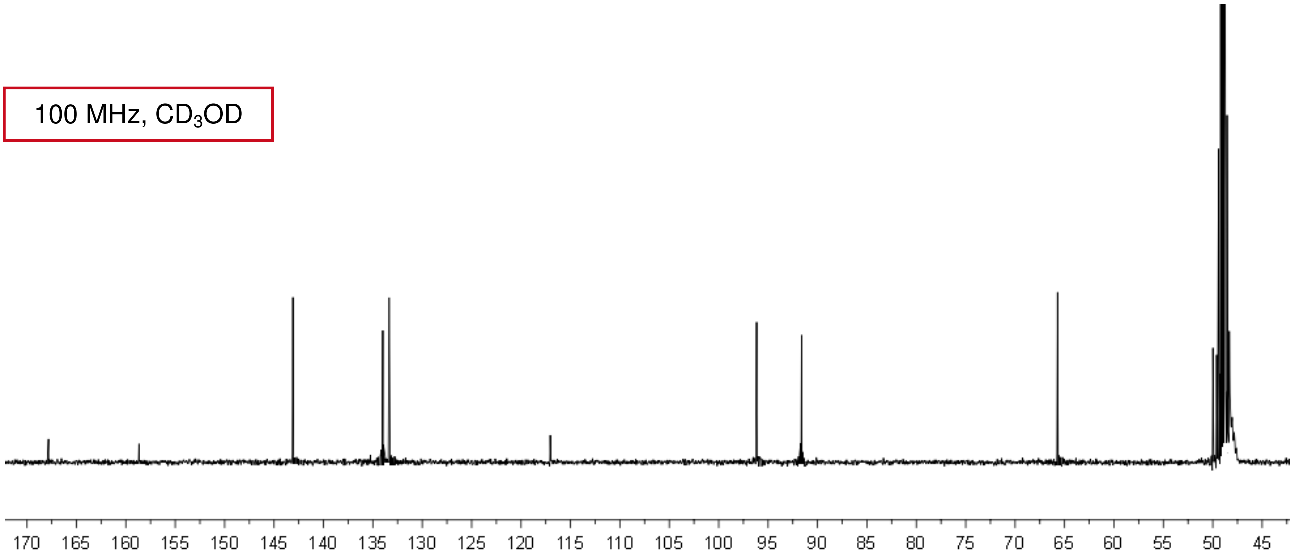

100 MHz, CD3OD
170
165
160
155
150
145
140
135
130
125
120
115
110
105
100
95
90
85
80
75
70
65
60
55
50
45


HO
MeO
O
N
N
NH2
O

(±)-**31**β


400 MHz, D2O
7.5
7.0
6.5
6.0
5.5
5.0
4.5
4.0
3.5


400 MHz, CD3OD
8.0
7.8
7.6
7.4
7.2
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


100 MHz, CD3OD
170
165
160
155
150
145
140
135
130
125
120
115
110
105
100
95
90
85
80
75
70
65
60
55
50
45