SUPPLEMENTARY MATERIAL

# A convenient synthesis of orthogonally protected 2-deoxystreptamine (2-DOS) as an aminocyclitol scaffold for the development of novel aminoglycoside antibiotic derivatives against bacterial resistance.

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This Supporting Information contains additional experimental procedures and characterization details for the intermediates **1**, **2**, **4**, **5**, **9**, **10**, **11, 11a** and **11b**, as well as full NMR spectra for all the products described in the paper.

## General Information.

Reactions were carried out in flame-dried glassware under an argon atmosphere, unless otherwise noted. All solvents used were of reagent grade. Tetrahydrofuran (THF) was freshly distilled from sodium/benzophenone under argon immediately prior to use. Unless otherwise noted, reactions were magnetically stirred and monitored by thin layer chromatography (TLC) with 0.25 mm Merck pre-coated silica gel plates. Spots were detected under UV (254 nm) and/or by staining with acidic ceric ammonium molybdate unless otherwise noted. Flash chromatography were performed with silica gel 60 (particle size 0.040-0.063 mm) supplied by Merck, Geduran. Yields refer to chromatographically and spectroscopically pure compounds, unless otherwise stated. 1H NMR, 13C NMR, COSY, NOESY, HMQC as well as HMBC spectra were measured on Bruker Avance-300 spectrometer using an internal deuterium lock at ambient temperature. If not otherwise noted, $CDCl_3$ (7.26 ppm relative to residual $CHCl_3$) is the solvent for all NMR experiments. Multiplicities are described using the following abbreviations: s = singlet, d = doublet, t = triplet, q = quartet, m = multiplet, br = broad, ABX = an ABX system. Chemical shift are given in ppm and coupling constant are presented in Hz. $^{13}C$ NMR spectra were calibrated from the central triplet peak, to 77.0 ppm for $CDCl_3$. Optical rotations [α] were recorded on a Polarimeter Model 341 (Perkin Elmer) at a wavelength of 589 nm and are reported as follows: $[\alpha]_D$, concentration (*c* in g/100 mL) and solvent. Elemental analysis were collected at the Service de microanalyse of the University Louis Pasteur of Strasbourg (France).

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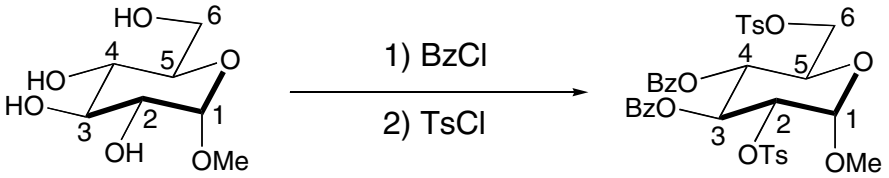
**Experimental Section :**




**1**

**Methyl 3,4-di-*O*-benzoyl-2,6-di-*O*-tosyl-α-D-glucopyranoside (1)**[1]

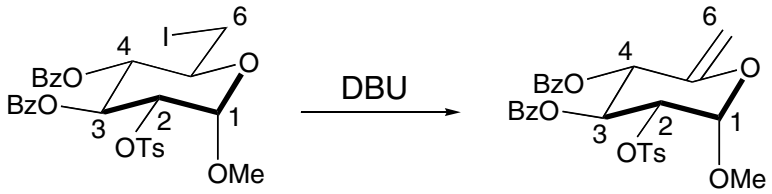
This compound **1** was synthesized from commercially available methyl α-D-glucopyranoside (21 g) according the literature[1] and obtained by simple crystallization in 92% yield (lit.[1a] 38%). Mp = 193 °C (lit.[1a]; 190-191 °C). $[\alpha]_D^{20}$ = + 27.7 (c 1.79 in $CHCl_3$), (lit.[1a]; + 22.5 (c 2.5 in $CHCl_3$)). **$^1$H NMR** (300 MHz, $CDCl_3$), δ (ppm) = 7.76-6.92 (m, 18 H, Ar), 5.82 (dd, 1 H, $J_{3\text{-}2} = J_{3\text{-}4}$ = 9.7 Hz, H-3), 5.27 (dd, 1 H, $J_{4\text{-}3} = J_{4\text{-}5}$ = 9.7 Hz, H-4), 5.02 (d, 1 H, $J_{1\text{-}2}$ = 3.6 Hz, H-1 β anomeric), 4.51 (dd, 1 H, $J_{2\text{-}1}$ = 3.6 Hz, $J_{2\text{-}3}$ = 10 Hz, H-2), 4.20-4.17 (m, 1 H, H-5), 4.19-4.14 (m, 1 H, H-6a), 4.05 (dd, 1 H, $J_{6b\text{-}6a}$ = 11.5 Hz, $J_{6b\text{-}5}$ = 5.9 Hz, H-6b), 3.46 (s, 3 H, MeO), 2.33 (s, 3 H, $CH_3$ of pTs at C6), 2.19 (s, 3 H, $CH_3$ of pTs at C2). **$^{13}$C NMR** (75 MHz, $CDCl_3$), δ (ppm) = 164.9 (CO), 164.8 (CO), 145.0 (Cq Ar), 144.9 (Cq Ar), 133.5 (CH Ar), 133.1 (CH Ar), 132.6 (Cq Ar), 132.2 (Cq Ar), 129.7 (CH Ar), 128.7 (Cq Ar), 128.4 (CH Ar), 128.3 (Cq Ar), 128.1 (CH Ar), 128.0 (CH Ar), 127.6 (CH Ar) (CH Ar), 97.7 (CH anomeric), 76.3 (CH), 69.4 (CH), 68.7 (CH), 67.6 ($CH_2$), 67.2 (CH), 56.2 (MeO), 21.6 (2 x Me of pTs).


**1** **2**

**Methyl 3,4-di-*O*-benzoyl-6-deoxy-6-iodo-2-*O*-tosyl-α-D-glucopyranoside (2)**

This compound **2** was synthesized from **1** (10.8 g) according the literature[1a,2] and obtained by simple crystallization in 93% yield (lit.[1a]; 88 %). Mp = 180 °C (lit.[1a]; 179-180 °C). $[\alpha]_D^{20}$ = + 32.4 (c 1.03 in $CHCl_3$), (lit.[1a]; + 32 (c 3 in $CHCl_3$)). **$^1$H NMR** (300 MHz, $CDCl_3$), δ (ppm) = 7.9-6.9 (m, 14 H, Ar), 5.88 (dd, 1 H, $J_{3\text{-}2} = J_{3\text{-}4}$ = 9.7 Hz, H-3), 5.19 (dd, 1 H, $J_{4\text{-}3} = J_{4\text{-}5}$ = 9.7 Hz, H-4), 5.08 (d, 1 H, $J_{1\text{-}2}$ = 3.7 Hz, H-1 β anomeric), 4.60 (dd, 1 H, $J_{2\text{-}1}$ = 3.7 Hz, $J_{2\text{-}3}$ = 10.1 Hz, H-2), 3.99 (ddd, Hx of ABX, 1 H, $J_{5\text{-}4}$ = 9.7 Hz, $J_{5\text{-}6a}$ = 8.4 Hz, $J_{5\text{-}6b}$ = 2.6 Hz, H-5), 3.56 (s, 3 H, MeO), 3.25 (AB part on an ABX system, 2 H, $J_{AB}$ = 11 Hz, $J_{AX}$ = 8.4 Hz, $J_{BX}$ = 2.6 Hz, Δν = 48 Hz, H-6), 2.20 (s, 3 H, $CH_3$ of pTs). **$^{13}$C NMR** (75 MHz, $CDCl_3$), δ (ppm) = 165.2 (CO), 164.9 (CO), 144.9 (Cq Ar), 133.7 (CH Ar), 133.1 (CH Ar), 132.7 (Cq Ar), 129.8 (CH Ar), 129.7 (CH Ar), 128.7 (Cq Ar), 128.4 (CH Ar), 128.3 (Cq Ar), 128.1 (CH Ar), 127.6

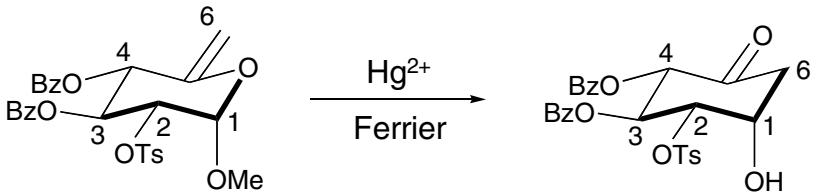
(CH Ar), 97.7 (CH anomeric), 72.5 (CH), 69.0 (CH), 68.9 (CH), 56.3 (MeO), 21.6 (Me of pTs), 3.2 ($CH_2$).




**2** **4**

**Methyl 3,4-Di-*O*-Benzoyl-6-deoxy-2-*O*-tosyl-α-D-xylo-hex-5-enopyranoside (4)**[1a,3]

The iodo glucopyranoside **2** (5.57 g; 8.35 mmol) and DBU (5 mL; 4 equiv.) were heated in dry PhMe (40 mL) for 15 h at ca 80 °C. The resulting deep red mixture was left at room temperature for 1 h without stirring. The upper layer was concentrated in vacuo and then diluted with $CH_2Cl_2$ (80 mL). The organic layer was washed with water (2 x 60 mL), sat. aq. sodium thiosulfate (50 mL), water (2 x 50 mL), brine (20 mL), dried ($MgSO_4$), filtered and concentrated under reduced pressure. The crude product was purified by chromatography column on silica gel (AcOEt/cyclohexane, 1:1) to yield a white powder of the title enone **4**[3] (3.07 g; 68.2%, lit.[1a]; 76%). Mp = 138 °C (lit.[1a]; 132-3 °C). $[\alpha]_D^{20}$ = + 23.2 (c 1.16 in $CHCl_3$), (lit.[1a]; + 24 (c 1.3 in $CHCl_3$)). **$^1$H NMR** (300 MHz, $CDCl_3$), δ (ppm) = 7.96-6.93 (m, 14 H, Ar), 5.90 (dd, 1 H, $J_{3\text{-}2} = J_{3\text{-}4} = 9.7$ Hz, H-3), 5.75 (ddd, 1 H, $J_{4\text{-}3} = 9.6$ Hz, $J_{4\text{-}6a} = J_{4\text{-}6b} = 2.1$ Hz, H-4), 5.15 (d, 1 H, $J_{1\text{-}2} = 3.4$ Hz, H-1 β anomeric), 4.85 (dd, 1 H, $J_{6a\text{-}6b} = J_{6a\text{-}4} = 2.1$ Hz, H-6a), 4.73 (dd, 1 H, $J_{2\text{-}1} = 3.4$ Hz, $J_{2\text{-}3} = 9.8$ Hz, H-2), 4.66 (dd, 1 H, $J_{6b\text{-}6a} = J_{6b\text{-}4} = 2.1$ Hz, H-6b), 3.53 (s, 3 H, MeO), 2.20 (s, 3 H, $CH_3$ of pTs). **$^{13}$C NMR** (75 MHz, $CDCl_3$), δ (ppm) = 165.0 (CO), 164.8 (CO), 149.3 (Cq Ar), 145.0 (Cq Ar), 133.6 (CH Ar), 133.1 (CH Ar), 132.7 (Cq Ar), 129.9 (CH Ar), 129.7 (2 x CH Ar), 128.8 (Cq Ar), 128.6 (Cq Ar), 128.5 (CH Ar), 128.1 (CH Ar), 127.6 (CH Ar), 98.6 (CH anomeric), 98.5 ($CH_2$ vinyl), 76.4 (CH), 69.8 (CH), 69.3 (CH), 56.1 (MeO), 21.6 (Me of pTs).

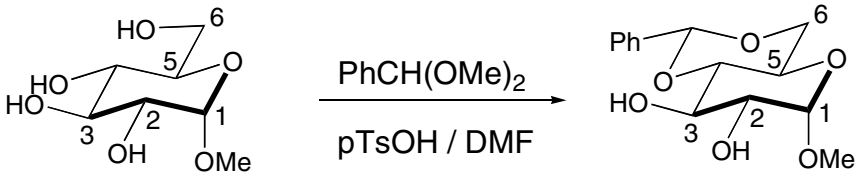



**4** **5**

**Preparation of the cyclohexanone (5)**[1a,4]

To the enone **4** (0.653 g; 1.21 mmol) dissolved in acetone (40 mL) and water (15 mL) were added successively $Hg(OAc)_2$ (680 mg; 1.7 equiv.) and AcOH (5 mL). The medium turned quickly from yellow to colorless and the reaction was heated for 2.5 h at 70 °C. The organic solvent was then evaporated in vacuo and $CH_2Cl_2$ (60 mL) was added to the aqueous residue. The organic layer was filtered on a pad of Celite and rinsed with $CH_2Cl_2$ (2 x 10 mL). The

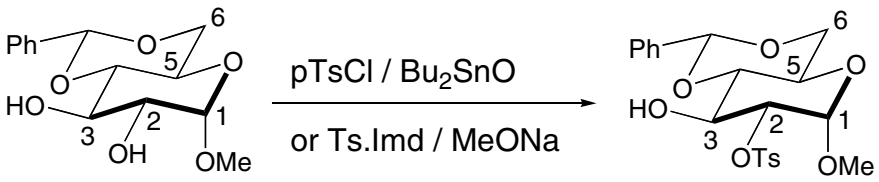
combined organic layers were washed with water (3 x 15 mL), aq. sat. $NaHCO_3$ (2 x 15 mL), water (3 x 15 mL), dried ($MgSO_4$), filtered and the solvent was concentrated to the half of its volume. The desired product crystallized slowly to give white needles of the β-hydroxyketone **5** (0.440 g; 69%). Mp = 178 °C (lit[1a]; 175-6 °C). $[\alpha]_D^{20}$ = – 21.1 (c 1.08; $CHCl_3$. **$^1$H NMR** (300 MHz, $CDCl_3$), δ (ppm) = 7.96-6.92 (m, 14 H, Ar), 6.13 (dd, 1 H, $J_{3\text{-}2} = J_{3\text{-}4}$ = 10.1 Hz, H-3), 5.67 (d, 1 H, $J_{4\text{-}3}$ = 10.4 Hz, H-4), 5.12 (dd, 1 H, $J_{2\text{-}3}$ = 9.8 Hz, $J_{2\text{-}1}$ = 2.5 Hz, H-2), 4.72 (m, X of an ABX system, 1 H, H-1), 2.79 (s br, 1H, OH), 2.88 (AB part on an ABX system, 2 H, $J_{AB}$ = 15.1 Hz, $J_{AX}$ = 3.7 Hz, $J_{BX}$ = 2.7 Hz, Δν = 34 Hz, H-6), 2.18 (s, 3 H, $CH_3$ of pTs). **$^{13}$C NMR** (75 MHz, $CDCl_3$), δ (ppm) = 195.8 (CO), 165.4 (Cq COOBz), 164.5 (Cq COOBz), 145.2 (Cq Ar), 133.5 (CH Ar), 133.3 (CH Ar), 132.7 (Cq Ar), 130.0 (CH Ar), 129.9 (CH Ar), 129.8 (CH Ar), 128.6 (Cq Ar), 128.4 (CH Ar), 128.2 (CH Ar), 127.6 (CH Ar), 81.1 (CH-2), 76.9 (CH-4), 69.9 (CH-3), 68.1 (CH-1), 42.7 ($CH_2$-6), 21.8 (Me of pTs).




Methyl α-D-Glucopyranoside **9**

**Methyl 4,6-*O*-Benzylidene-α-D-glucopyranoside (9)**[5]

A solution of methyl α-D-glucopyranoside[6] (19.40 g; 0.099 mol) and p-toluenesulfonic acid monohydrate (2 g; 1 equiv.) and α,α-dimethoxytoluene (15.4 mL; 1 equiv.) in dry DMF (80 mL) was refluxed at 84 °C under reduced pressure (ca 20 mbar) during 1.5 h. All the solvent was then evaporated by concentration under reduced pressure to leave a white solid product which was finely dispersed in an aqueous saturated solution of $NaHCO_3$ (100 mL) The mixture was stirred for 15 min at 80 °C, diluted with water (100 mL) and filtered. The white cake was washed thoroughly with water (4 x 100 mL), dried under water-aspirator vacuum for 3 h, azeotroped with benzene (3 x 100 mL) and then dried under high reduced pressure. No further purification was necessary for this white powder product of methyl 4,6-*O*-benzylidene-α-D-glucopyranoside **9** (20.6 g; 73%). Mp = 170 °C. (lit.[5a], 168-9 °C). $[\alpha]_D^{20}$ = +104 (c 1.16 in $CHCl_3$), (lit.[5a], + 105 (c 1.1 in $CHCl_3$). **$^1$H NMR** (300 MHz, $CDCl_3$), δ (ppm) = 7.51-7.46 (m, 2 H, Ar), 7.40-7.33 (m, 3 H, Ar), 5.52 (s, 1 H, H-7), 4.77 (d, 1 H, $J_{1\text{-}2}$ = 3.9 Hz, H-1), 4.28 (dd, 1 H, $J_{6e\text{-}6a}$ = 9.1 Hz, $J_{6e\text{-}5}$ = 3.7 Hz, H-6eq), 3.92 (ddd, 1 H, $J_{3\text{-}4} = J_{3\text{-}2}$ = 9.3 Hz, $J_{3\text{-}OH}$ = 1.8 Hz, H-3), 3.81-3.76 (m, 1 H, H-5), 3.73 (dd, 1 H, $J_{6a\text{-}6e} = J_{6a\text{-}5}$ = 9.9 Hz, H-6ax), 3.61 (dd, 1 H, $J_{2\text{-}3} = J_{2\text{-}OH}$ = 9.2 Hz, $J_{2\text{-}1}$ = 3.9 Hz, H-2), 3.49 (dd, 1 H, $J_{4\text{-}5} = J_{4\text{-}3}$ = 9.2 Hz, H-4), 3.44 (s, 3 H, MeO), 3.01 (d, 1 H, $J_{OH\text{-}3}$ = 1.9 Hz, OH) 2.48 (d, 1 H, $J_{OH\text{-}2}$ = 9.2 Hz, OH). **$^{13}$C NMR** (75 MHz, $CDCl_3$), δ (ppm) = 137.0 (Cq Ar), 129.3 (CH Ar), 128.3 (CH Ar), 126.3 (CH Ar), 101.9 (CH benzyl), 99.8 (CH-1), 80.9 (CH-4), 72.8 (CH-2), 71.7 (CH-3), 68.9 ($CH_2$), 62.3 (CH-5), 55.6 (OMe).

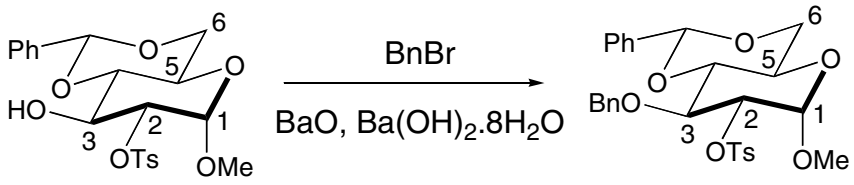



**9** **10**

**Methyl 4,6-*O*-Benzylidene 2-*O*-Tosyl-α-D-glucopyranoside (10)**[7]

Method A[7c] (with $Bu_2SnO$): Methyl 4,6-*O*-benzylidene-α-D-glucopyranoside **9** (4.92 g; 0.0174 mol) and $Bu_2SnO$ (4.77 g; 1.1 equiv.) were added to a solution of toluene and methanol (36 mL : 4 ml). The mixture was heated for 3 h at 85 °C and then the solvents were removed to leave a thick solution that was diluted with toluene (40 mL). To this solution were added p-toluenesulfonyl chloride (6.64 g; 2 equiv.) and triethylamine (0.25 mL). After being stirred for 3.5 h at room temperature, the mixture was treated with a saturated aq. solution of $NaHCO_3$ (40 mL), $CH_2Cl_2$ (100 mL) and water (50 mL). After filtration through a pad of Celite the organic layer was dried ($MgSO_4$), filtered and concentrated under reduced pressure. The crude product was then purified by column chromatography on a silica gel (cyclohexane/AcOEt, 4:1 to 1:1) to afford a crystalline white solid of **10** (6.28 g; 82.3%).

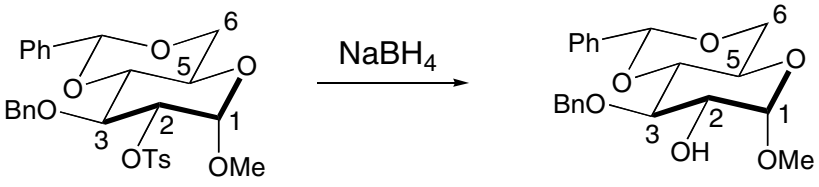
Method B[7b] (with Ts.Im): Methyl 4,6-*O*-benzylidene-α-D-glucopyranoside **9** (11.24 g; 0.0398 mol) and the N-tosylimidazole (13.27 g; 1.5 equiv.) were dissolved in a solution of $CHCl_3$-pentane (250 mL/200 mL). Sodium methanolate (3.2 g; 1.48 equiv.) was then added and the reaction was stirred at 65 °C for 3 h. After cooling the mixture was diluted with $CHCl_3$ (150 mL) and water (150 mL). The organic layer was washed with water (5 x 100 mL), dried ($MgSO_4$), filtered and concentrated under reduced pressure to give a viscous yellow liquid which was crystallized upon trituration with ethanol. Concentration of the mother liquors produced further crops of white crystals of **10** (total yield 9.60 g; 55%). Mp = 154 °C, (lit.[7a,b,c], 153-155 °C). $[\alpha]_D^{20}$ = + 64.6 (c 1.11 in $CHCl_3$), lit.[7a], + 64 (c 1 in $CHCl_3$). **$^1$H NMR** (300 MHz, $CDCl_3$), δ (ppm) = 7.84 (d, 2 H, $J$ = 8.3 Hz, ArCH of pTs), 7.46-7.41 (m, 2 H, Ar), 7.35-7.32 (m, 5 H, Ar), 5.48 (s, 1 H, H-7), 4.84 (d, 1 H, $J_{1\text{-}2}$ = 3.7 Hz, H-1), 4.37 (dd, 1 H, $J_{2\text{-}3}$ = 9.3 Hz, $J_{2\text{-}1}$ = 3.8 Hz, H-2), 4.26 (dd, 1 H, $J_{6e\text{-}6a}$ = 9.9 Hz, $J_{6e\text{-}5}$ = 4.5 Hz, H-6eq), 4.13 (ddd, 1 H, $J_{3\text{-}4}$ = $J_{3\text{-}2}$ = 9.3 Hz, $J_{3\text{-}OH}$ = 3.1 Hz, H-3), 3.81 (ddd, 1 H, $J_{5\text{-}6a}$ = 10.1 Hz, $J_{5\text{-}6e}$ = 4.6 Hz, $J_{5\text{-}4}$ = 9.6 Hz, H-5), 3.70 (dd, 1 H, $J_{6a\text{-}6e}$ = $J_{6a\text{-}5}$ = 10.1 Hz, H-6ax), 3.46 (dd, 1 H, $J_{4\text{-}5}$ = $J_{4\text{-}3}$ = 9.3 Hz, H-4), 3.34 (s, 3 H, MeO), 2.48 (d, 1 H, $J_{OH\text{-}3}$ = 3.1 Hz, OH), 2.43 (s, 3H, Me of pTs). **$^{13}$C NMR** (75 MHz, $CDCl_3$), δ (ppm) = 145.2 (Cq Ar), 136.8 (Cq Ar), 133.2 (Cq Ar), 129.8 (CH Ar), 129.3 (CH Ar), 128.3 (CH Ar), 128.1(CH Ar), 126.2 (CH Ar), 101.9 (CH benzyl), 98.2 (CH-1), 80.9 (CH), 79.5 (CH), 68.7 ($CH_2$), 68.3 (CH), 61.9 (CH), 55.7 (MeO), 21.7 (Me of pTs).




**10** **11**

**Methyl 3-*O*-Benzyl-4,6-*O*-benzylidene-2-*O*-(4-toluenesulfonyl)-α-D-glucopyranoside (11)**[8]

Methyl 4,6-*O*-Benzylidene 2-O-Tosyl-α-D-glucopyranoside **10** (3.152 g; 0.0072 mol) in dry DMF (5 mL) was slowly added at 0 °C to a mixture containing of BaO (8.915; 8.05 equiv.) and $Ba(OH)_2.8H_2O$ (2.315; 1.01 equiv.) in dry DMF (12 mL). Immediately after, benzylbromide (1.9 mL, 2.21 equiv.) was added at the same temperature. The reaction was then stirred 8 h at ambient temperature before addition of Celite and filtration of the mixture. The pad was washed with AcOEt (3 x 30 mL) and the combined solvents were washed with water (4 x 50 mL), brine (20 mL), dried ($MgSO_4$), filtered and concentrated in vacuo to get a white powder. Recrystallization (3 crops) in AcOEt/EtOH (1:2) yielded a white crystalline solid of **11** (total yield 3.31 g; 87%). Mp = 128 °C, (lit.[8] ; 119-21 °C), $[\alpha]_D^{20}$ = + 2 (c 1.31 in $CHCl_3$), lit.[8] + 4 (c 1.6 in $CHCl_3$). **$^1$H NMR** (300 MHz, $CDCl_3$), δ (ppm) = 7.84 (d, 2 H, $J$ = 8.4 Hz, ArCH of pTs), 7.35-7.32 (m, 12 H, Ar), 5.52 (s, 1 H, H-7), 4.96 (d, 1 H, $J_{1\text{-}2}$ = 3.8 Hz, H-1), 4.70 and 4.50 (AB system, 2 H, $J$ = 11.3 Hz, Δν = 58,6 Hz, $PhCH_2O$), 4.41 (dd, 1 H, $J_{2\text{-}3}$ = 9.4 Hz, $J_{2\text{-}1}$ = 3.8 Hz, H-2), 4.29 (dd, 1 H, $J_{6e\text{-}6a}$ = 9.9 Hz, $J_{6e\text{-}5}$ = 4.5 Hz, H-6eq), 4.00 (ddd, 1 H, $J_{3\text{-}4}$ = $J_{3\text{-}2}$ = 9.3 Hz, H-3), 3.85 (ddd, 1 H, $J_{5\text{-}6a}$ = 10.0 Hz, $J_{5\text{-}6e}$ = 4.6 Hz, $J_{5\text{-}4}$ = 9.7 Hz, H-5), 3.72 (dd, 1 H, $J_{6a\text{-}6e}$ = $J_{6a\text{-}5}$ = 10.0 Hz, H-6ax), 3.59 (dd, 1 H, $J_{4\text{-}5}$ = $J_{4\text{-}3}$ = 9.3 Hz, H-4), 3.41 (s, 3 H, MeO), 2.37 (s, 3 H, Me of pTs). **$^{13}$C NMR** (75 MHz, $CDCl_3$), δ (ppm) = 144.9 (Cq Ar), 137.9 (Cq Ar), 137.1 (Cq Ar), 133.2 (Cq Ar), 129.7 (CH Ar), 129.0 (CH Ar), 128.2 (CH Ar), 128.1 (CH Ar), 128.0 (CH Ar), 127.9 (CH Ar), 127.6 (CH Ar), 126.0 (CH Ar) 101.4 (CH-7), 98.6 (CH-1), 81.9 (CH), 79.0 (CH), 75.7 (CH), 75.0 ($CH_2O$ benzyl), 68.8 ($CH_2$-6), 55.7 (MeO), 21.6 (Me of pTs).

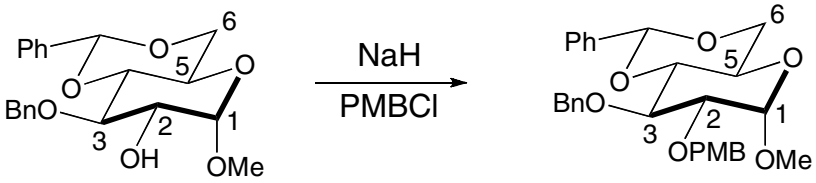



**11** **11a**

**Methyl 3-*O*-Benzyl-4,6-*O*-benzylidene-α-D-glucopyranoside (11a)**[8,9]

To a solution of methyl 3-*O*-Benzyl-4,6-*O*-benzylidene-2-*O*-(4-toluenesulfonyl)-α-D-glucopyranoside **11** (2.122 g; 4.02 mmol) in dry DMSO (12 mL) was added solid $NaBH_4$ (2.17; 14.3 equiv.) at 0 °C (exothermic reaction). The solution was then heated to 160 °C and the reaction was stirred for 3 days (70 to 90 h). After cooling of the medium, water (50 mL) was cautiously added and stirring was continued during 2 h. The precipitate was filtered out, washed with water (30 mL) and azeotroped with benzene (3 x 10 mL) to leave a white solid

of **11a** (1.38 g; 78.1%). Mp = 184 °C, lit.[9]; 176 °C, $[\alpha]_D^{20}$ = + 77.0 (c 0.91 in $CHCl_3$), lit.[9]; + 79 (c 1.2 in $CHCl_3$). **$^1$H NMR** (300 MHz, $CDCl_3$), δ (ppm) = 7.55-7.27 (m, 10 H, Ar), 5.57 (s, 1 H, H-7), 4.96 and 4.79 (AB system, 2 H, $J$ = 11.4 Hz, Δν = 51.8 Hz, $PhCH_2O$), 4.81 (d, 1 H, $J_{1\text{-}2}$ = 3.4 Hz, H-1), 4.30 ((dd, 1 H, $J_{2\text{-}3}$ = 9.2 Hz, $J_{2\text{-}1}$ = 3.8 Hz, H-2), 3.88-3.62 (m, 5 H, H-3, H-4, H-5, H-6), 3.45 (s, 3 H, MeO), 2.28 (broad s, 1 H, OH). **$^{13}$C NMR** (75 MHz, $CDCl_3$), δ (ppm) = 138.4 (Cq Ar), 137.3 (Cq Ar), 129.0 (CH Ar), 128.4 (CH Ar), 128.3 (CH Ar), 128.0 (CH Ar), 127.7 (CH Ar), 126.0 (CH Ar), 101.3 (CH-7), 99.9 (CH-1), 82.0 (CH), 78.8 (CH), 74.8 ($PhCH_2O$), 72.3 (CH), 69.0 ($CH_2$-6), 62.6 (CH), 55.4 (MeO).




**11a** **11b**

**Methyl 3-*O*-Benzyl-4,6-*O*-benzylidene-2-*O*-(*p*-methoxybenzyl-□-D-glucopyranoside (11b).**

Sodium hydride (90 mg ; 1.46 equiv.) was added to a cooled solution (0 °C) of **11a** (0.959 g; 2.57 mmol) in DMF (5.5 mL) containing PMBCl (0.45 mL; 1.29 equiv.) and tetrabutylammonium iodide (12 mg). The reaction was stirred 3 h at ambient temperature and quenched cautiously with water (10 mL) and AcOEt (30 mL). Stirring was continued during 15 min and then the organic layer was separated, washed with water (4 x 20 mL), brine (10 mL), dried ($MgSO_4$), filtered and concentrated under reduced pressure to afford a pale viscous liquid which solidified on standing. The crude product was recrystallized from AcOEt/cyclohexane (1:5) to produced **11b** (640 mg; 50.5%) as a white solid. Mp = 114 °C. $[\square]_D^{20}$ = – 38.1 (c 1.17 in $CHCl_3$). Elemental analysis for $C_{29}H_{32}O_7$ (492.560): Calcd. C, 70.71; H, 6.55. Found : C, 70.83; H, 6.44. **$^1$H NMR** (300 MHz, $CDCl_3$), □ (ppm) = 7.51-7.27 (m, 10 H, ArCH), 7.27 (d, 2 H, $J$ = 8.5 Hz, meta CH of OPMB), 6.86 (d, 2 H, $J$ = 8.6 Hz, ortho CH of OPMB), 5.55 (s, 1 H, H-7), 4.91 and 4.83 (AB system, 2 H, $J$ = 11.5 Hz, □□ = 20.3 Hz, $PhCH_2O$), 4.79 and 4.63 (AB system, 2 H, $J$ = 12.0 Hz, □□ = 46.5 Hz, $MeOPhCH_2O$), 4.54 (d, 1 H, $J_{1\text{-}2}$ = 3.7 Hz, H-1), 4.27 (dd, 1 H, $J_{6e\text{-}6a}$ = 9.9 Hz, $J_{6e\text{-}5}$ = 4.5 Hz, H-6eq), 4.03 (dd, 1 H, $J_{3\text{-}4}$ = $J_{3\text{-}2}$ = 9.3 Hz, H-3), 3.82 (m, 1 H, H-5), 3.81 (s, 3 H, MeO of OPMB), 3.71 (dd, 1 H, $J_{6a\text{-}6e}$ = $J_{6a\text{-}5}$ = 10.0 Hz, H-6ax), 3.60 (dd, 1 H, $J_{4\text{-}5}$ = $J_{4\text{-}3}$ = 9.3 Hz, H-4), 3.54 (dd, 1 H, $J_{2\text{-}3}$ = 9.4 Hz, $J_{2\text{-}1}$ = 3.7 Hz, H-2), 3.40 (s, 3 H, MeO on C1). **$^{13}$C NMR** (75 MHz, $CDCl_3$), □ (ppm) = 159.4 (Cq Ar), 138.7 (Cq Ar), 137.4 (Cq Ar), 130.2 (Cq Ar), 129.8 (CH Ar), 128.9 (CH Ar), 128.3 (CH Ar), 128.2 (CH Ar), 128.0 (CH Ar), 127.6 (CH Ar), 126.0 (CH Ar), 113.8 (ortho CH Ar of OPMB), 101.3 (CH-7), 99.3 (CH-1), 82.1 CH-4), 78.7 CH-2), 78.6 CH-3), 75.3 ($CH_2$ of OBn), 73.4 ($CH_2$ of OPMB), 69.1 ($CH_2$-6), 62.3 CH-5), 55.4 (MeO on C1), 55.3 (MeO of OPMB).

**References**:

(1) (a) Ferrier, R. J. *J. Chem. Soc., Perkin Trans. 1*, **1979**, 1455-1458. (b) Lopez, O. L.; Fernández-Bolaños, J. G.; Lillelund, V. H.; Bols, M. *Org. Biomol. Chem.* **2003**, 1, 478-482.

(2) (a) Blattner, R.; Furneaux, R. H.; Kemmitt, T.; Tyler, P. C.; Ferrier, R. J.; Tiden, A.-K. *J. Chem. Soc., Perkin Trans. 1* **1994**, 3411-3421. (b) Ferrier, R. J.; Prasit, P.; Gainsford, G. J. *J. Chem. Soc., Perkin Trans. 1* **1983**, 1629-1634.

(3) This product was described in 76 % yield with AgF (see ref 1a) and was obtained here with a modified alternative using DBU (ref 3a-d) to eliminate the hydrogen iodide. Attemps elimination with tBuOK (see ref 3e,f) gave only starting material.
(a) Enright, P. M.; O'Boyle, K. M.; Murphy, P. V. *Org. Lett.* **2000**, 3929-3932. (b) O'Brien, J. L.; Tosin, M.; Murphy, P. V. *Org. Lett.* **2001**, 3353-3356, (c) McDonnell, C.; Cronin, L.; O'Brien, J. L.; Murphy, P. V. *J. Org. Chem*. **2004**, 69, 3565-3568. (d) Adam, S. *Tetrahedron Lett.* **1988**, 29, 6589-6592. (e) Ermolenko, M. S.; Shekharam, T.; Lukacs, G.; Potier, P. *Tetrahedron Lett.* **1995**, 2461-2464. (f) Imuta, S.; Ochiai, S.; Kuribayashi, M.; Chida, N. *Tetrahedron Lett.* **2003**, 5047-5051.

(4) This product was obtained in 83% with $HgCl_2$ (ref 1a) or in 89% with $Hg(OAc)_2$. Blattner, R.; Ferrier, R. J.; Haines, S. R. *J. Chem. Soc., Perkin Trans. 1* **1985**, 2413-2416.

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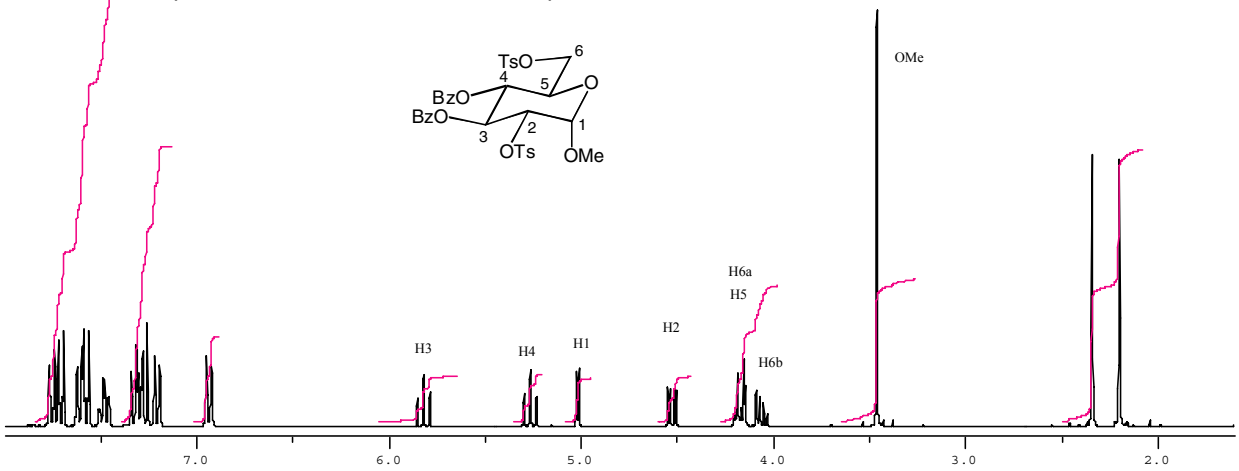
(6) Preparation of methyl α-D-glucopyranoside which is available commercially, can be obtained from D-(+)-glucose (Helferich, B.; Schäfer, W. *Org. Syn. Coll. Vol. I* **1958**, 364-365).

(7) (a) Pelyvas, I. F.; Lindhorst, T. K.; Streicher, H.; Thiem, J. *Synthesis* **1991**, 1015-1018. (b) Hicks, D. R.; Fraser-Reid, B. *Synthesis* **1974**, 203-203. (c) Munavu, R. M.; Szmant, H. H. *J. Org. Chem.* **1976**, 41, 1832-1836.

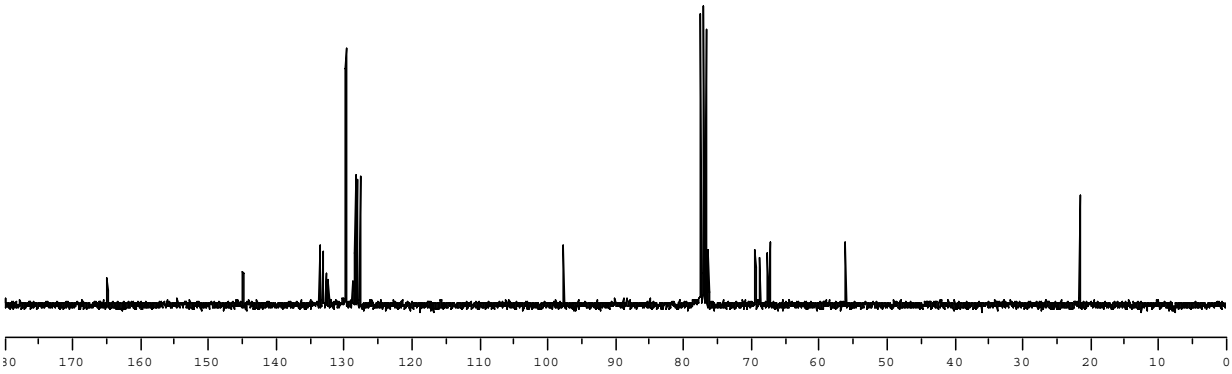
(8) Pozsgay, V.; Dubois, E. P.; Pannell, L. *J. Org. Chem.* **1997**, 62, 2832-2846.

(9) Detosylation with $NaBH_4$ in DMSO was used according the procedure in ref. 8. The same product was obtained by regioselective monobenzylation with $(Bu_3Sn)_2O$. Dasgupta, F.; Garegg, P. J. *Synthesis* **1994**, 1121-1123 [mp = 176-177°C; [α] = +79 (c 1.2 $CHCl_3$)].

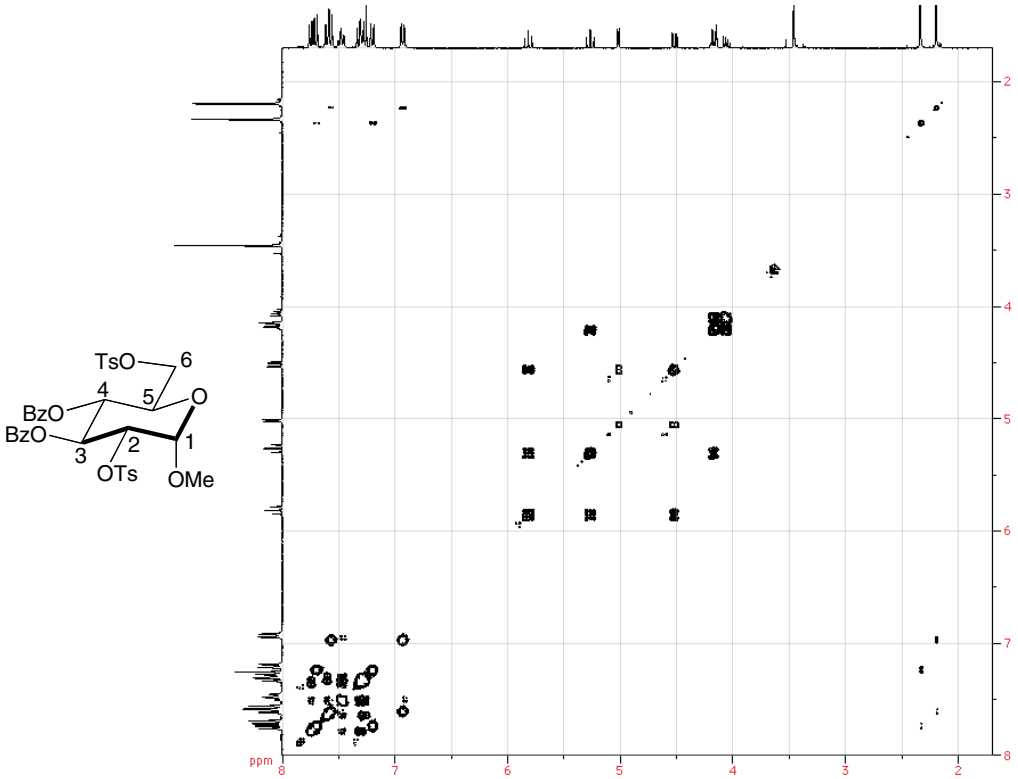
Molecule **1** ($^{1}$H NMR, 300 MHz, $CDCl_3$).



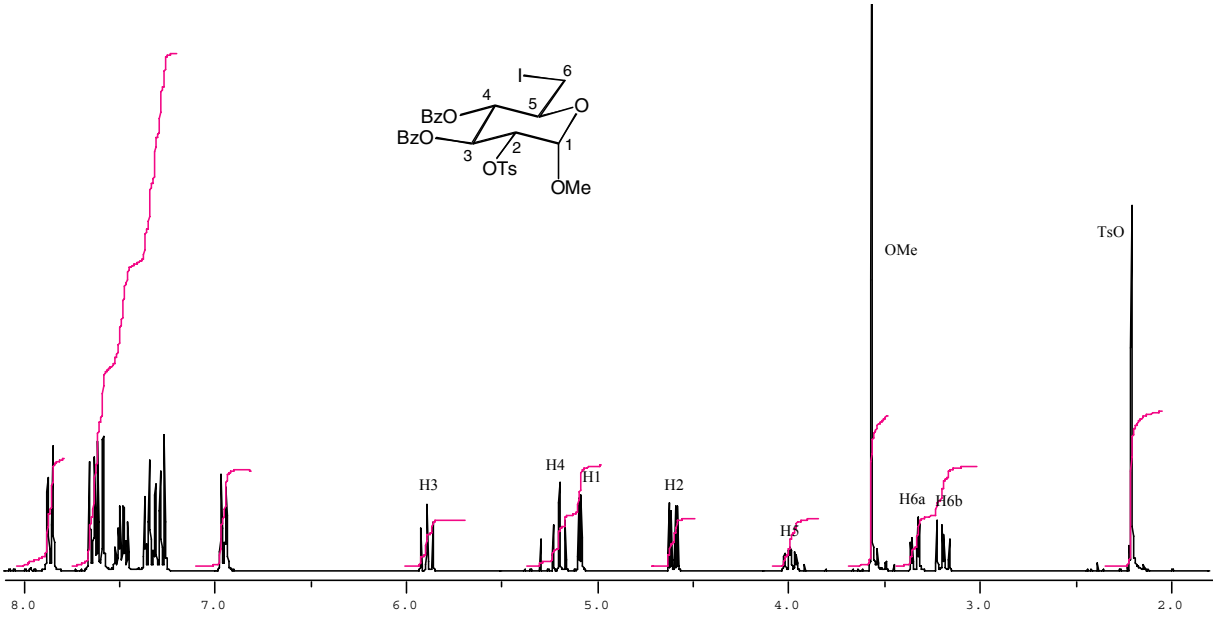

Molecule **1** ($^{13}$C NMR, 75 MHz, $CDCl_3$).



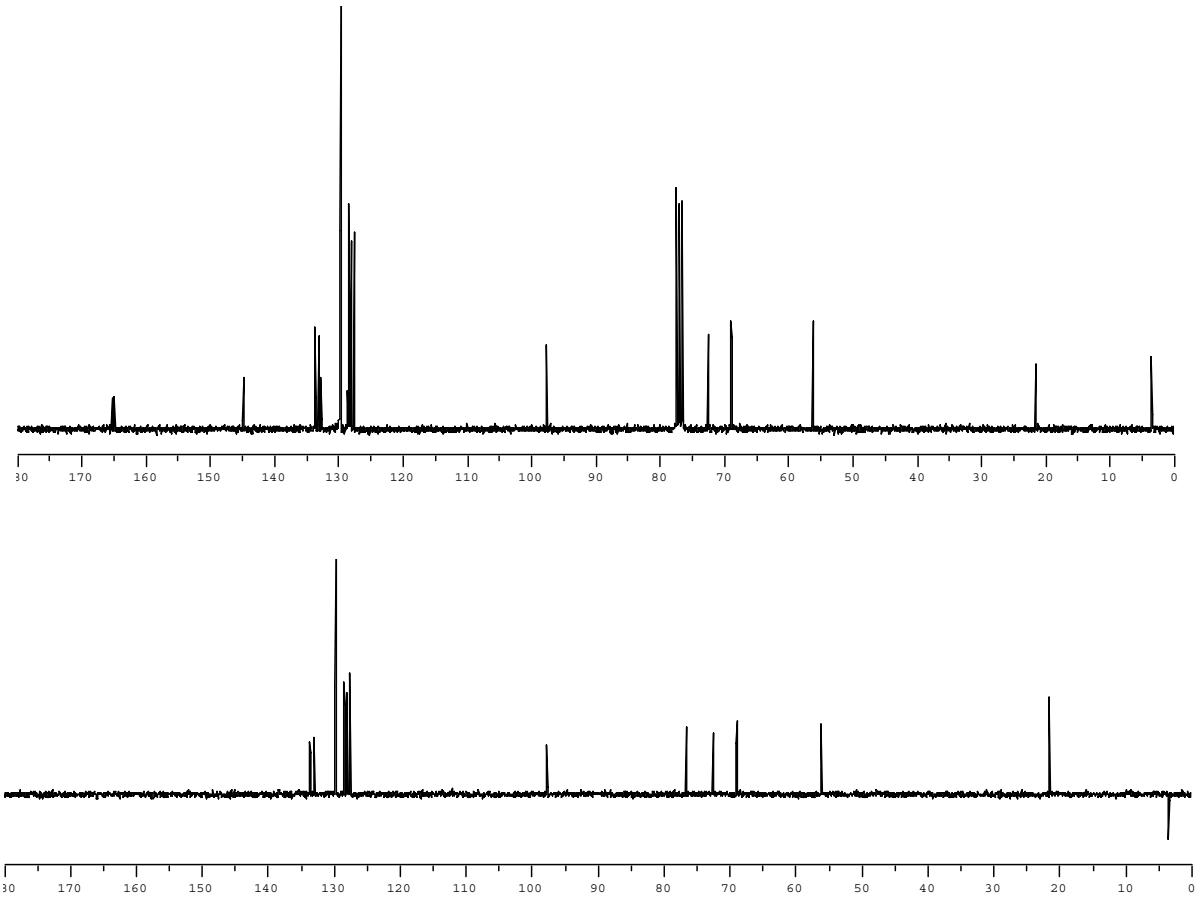

COSY spectrum of molecule **1** (300 MHz; $CDCl_3$)



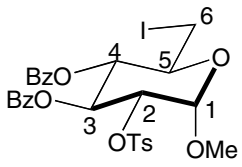
Molecule **2** ($^{1}$H NMR, 300 MHz, $CDCl_3$).

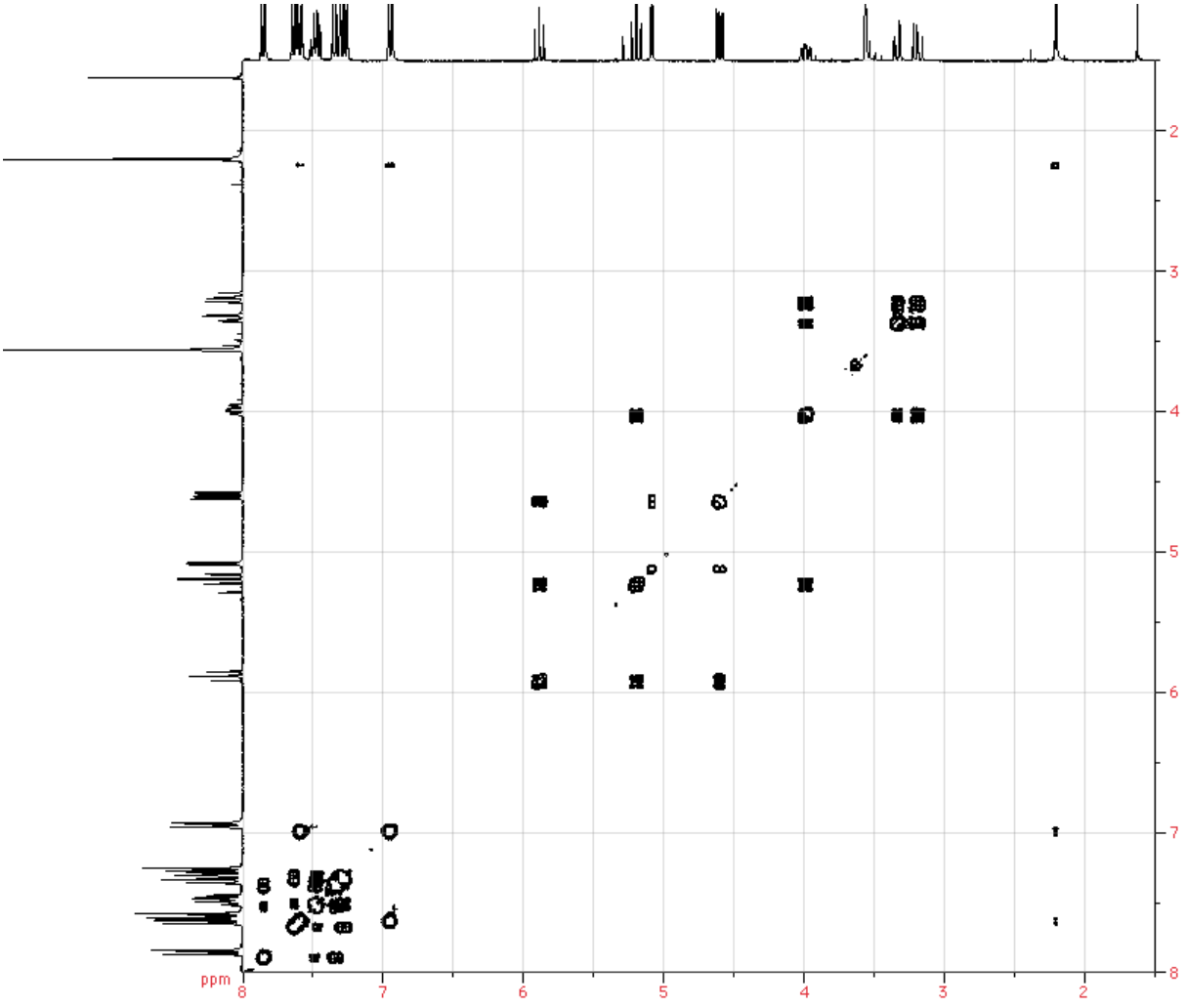



Molecule **2** ($^{13}$C NMR, 75 MHz, $CDCl_3$).

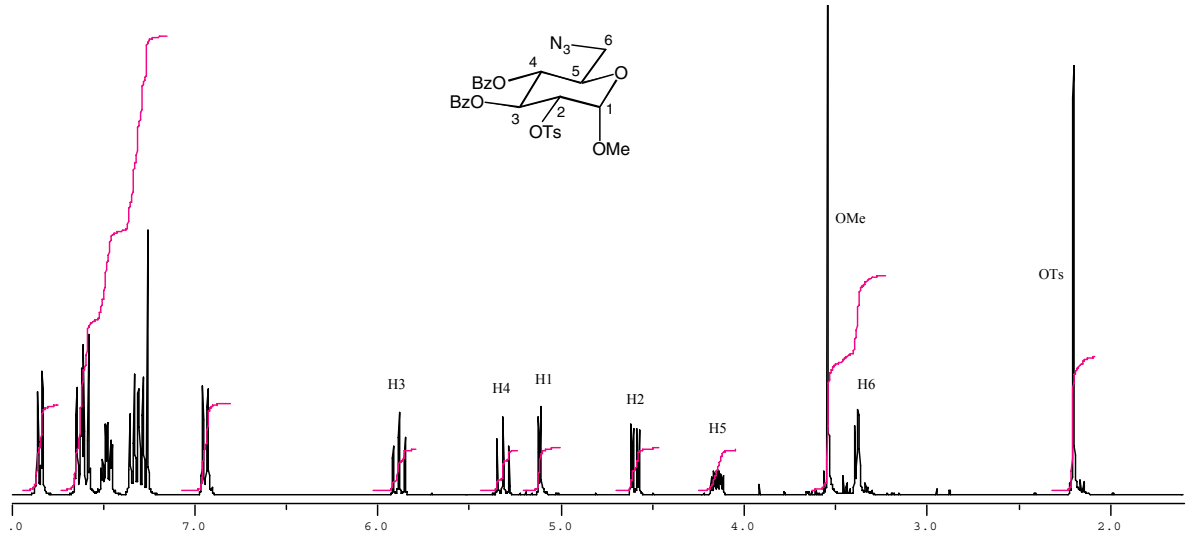


COSY spectrum of molecule **2** (300 MHz; $CDCl_3$)

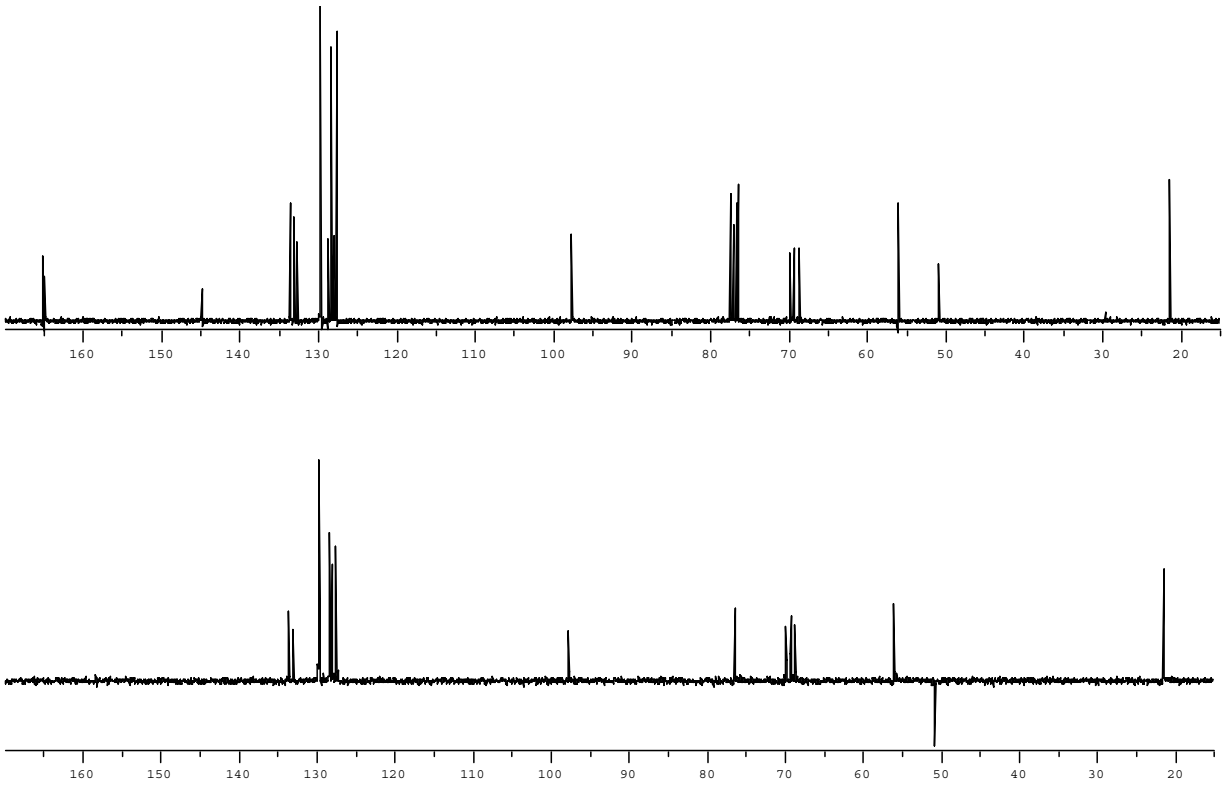


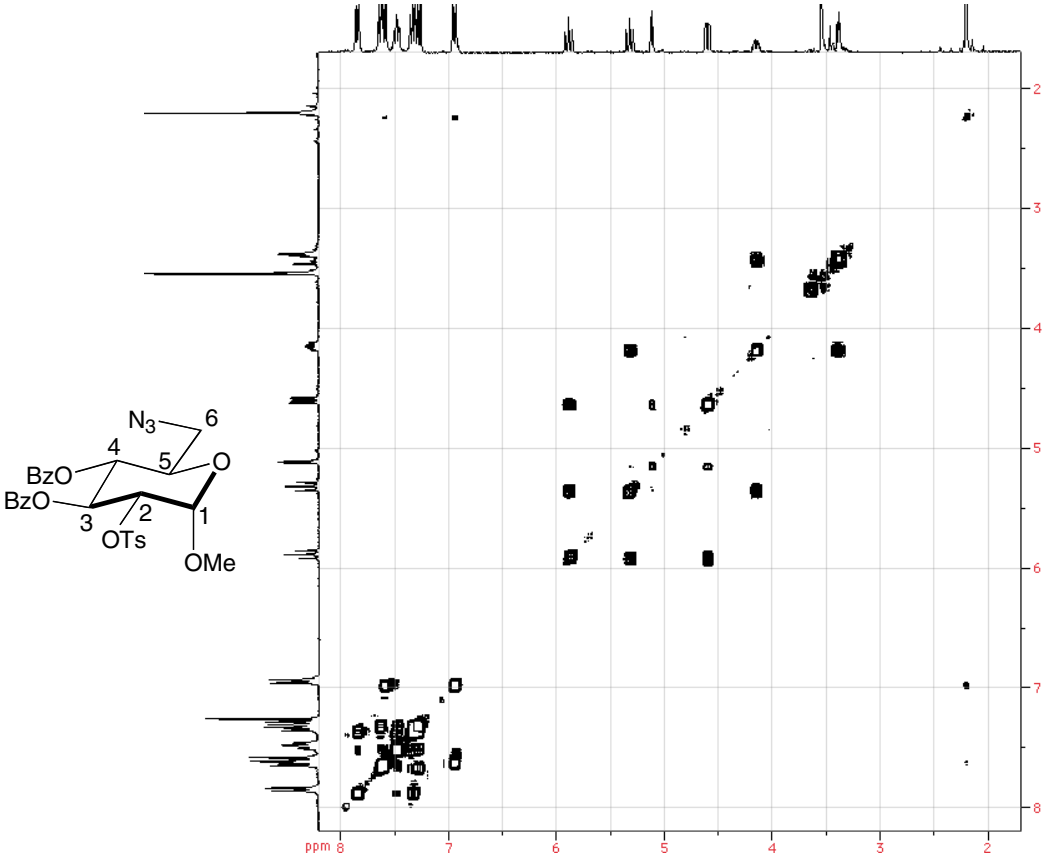
Molecule **3** ($^{1}$H NMR, 300 MHz, $CDCl_3$).



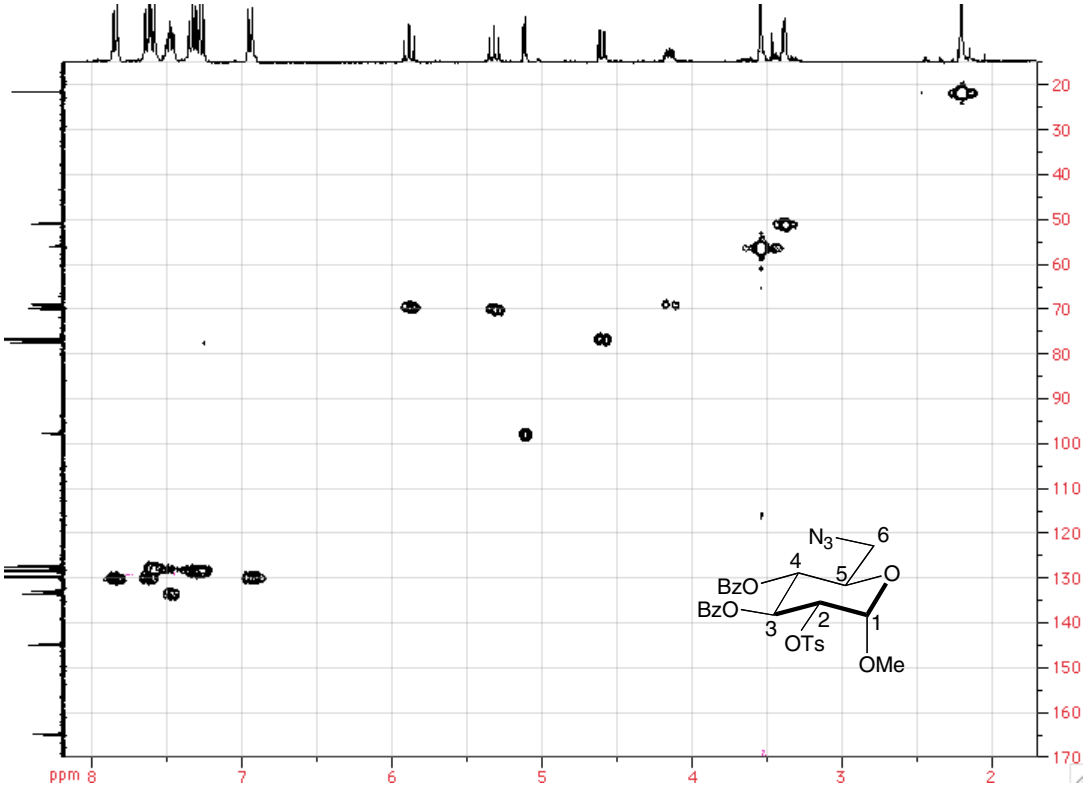

Molecule **3** ($^{13}$C NMR, 75 MHz, $CDCl_3$).



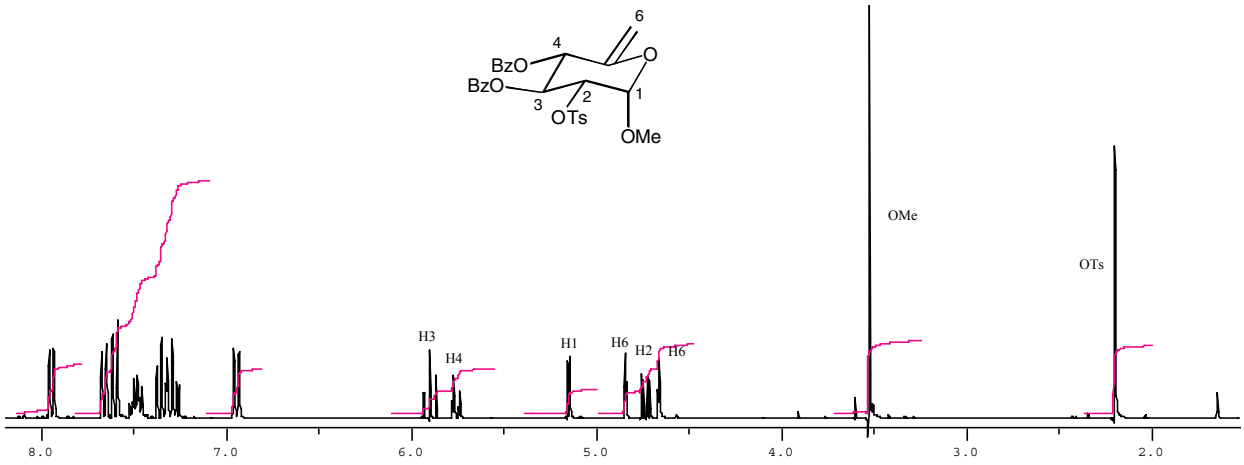
COSY spectrum of molecule **3** (300 MHz; $CDCl_3$)



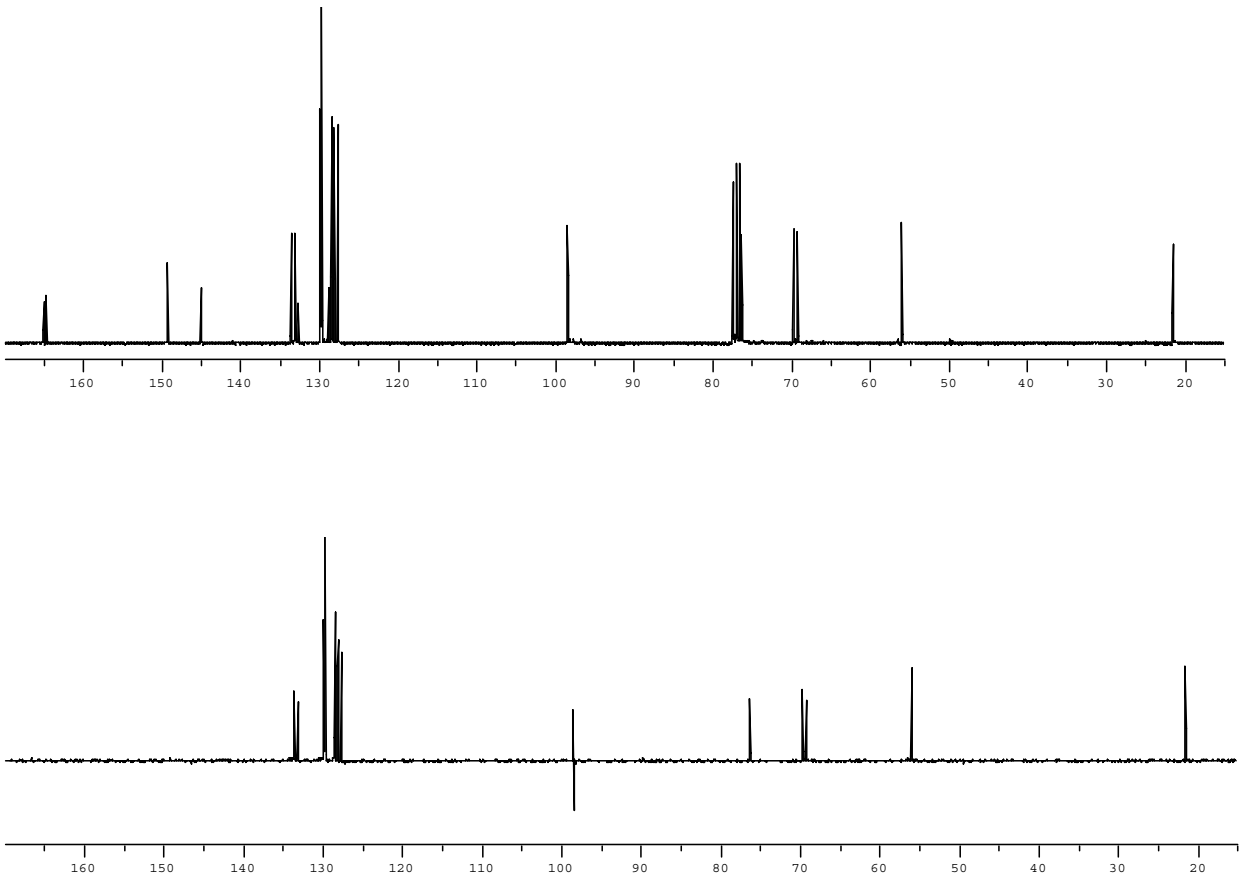

HMQC spectrum of molecule **3** ($CDCl_3$)



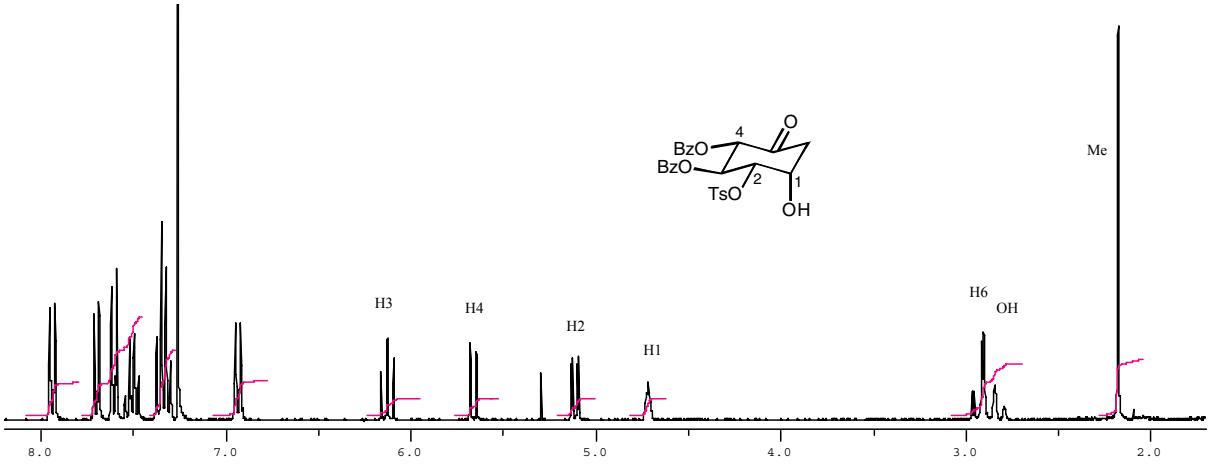
Molecule **4** ($^{1}$H NMR, 300 MHz, $CDCl_3$).



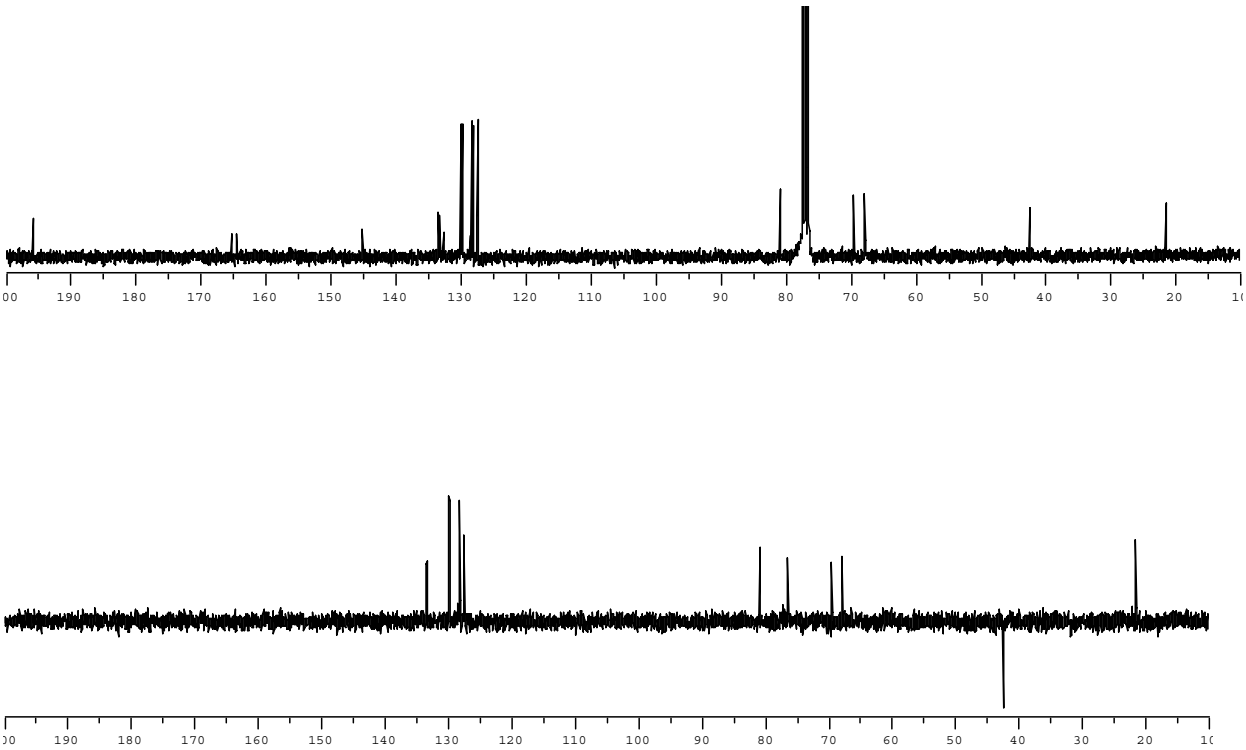

Molecule **4** ($^{13}$C NMR, 75 MHz, $CDCl_3$).



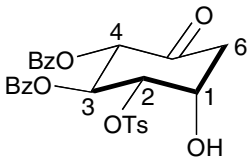
Molecule **5** ($^{1}$H NMR, 300 MHz, $CDCl_3$).

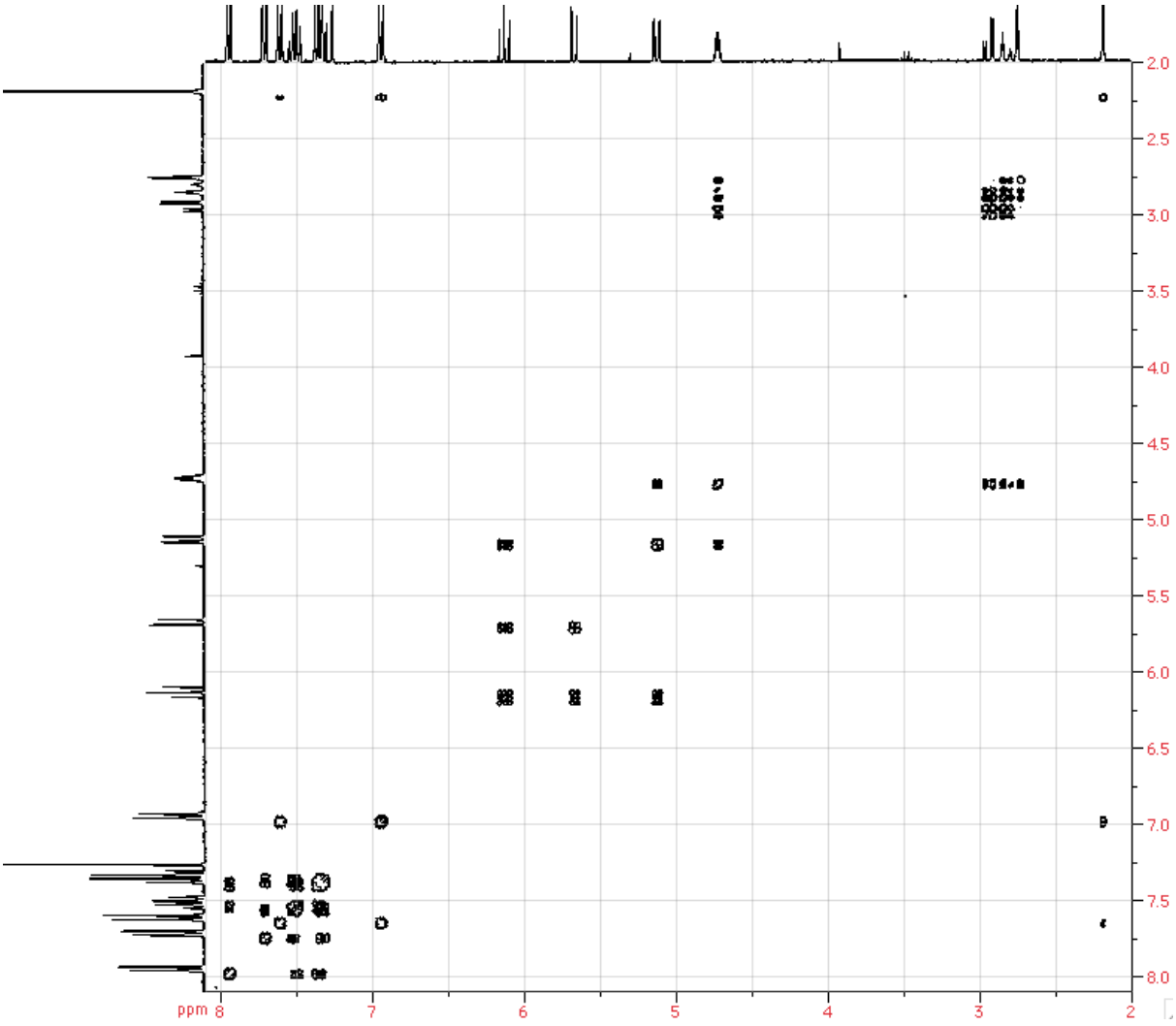



Molecule **5** ($^{13}$C NMR, 75 MHz, $CDCl_3$).

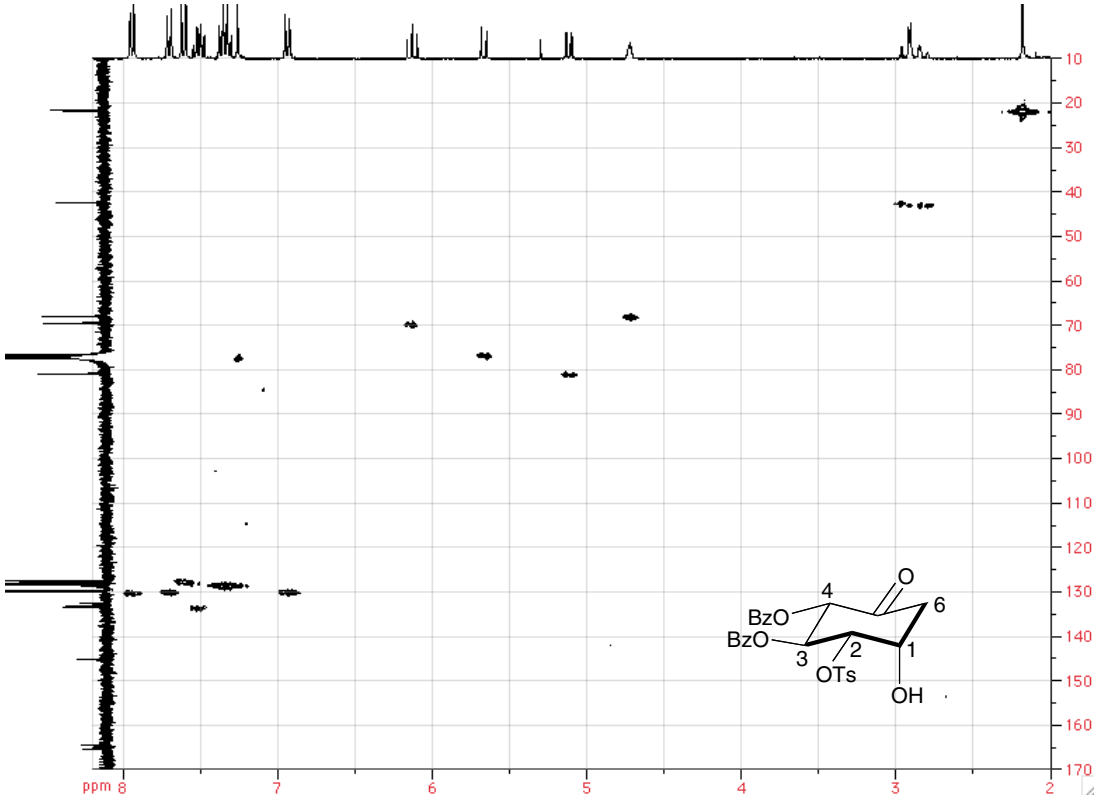


COSY spectrum of molecule **5** (300 MHz; $CDCl_3$).

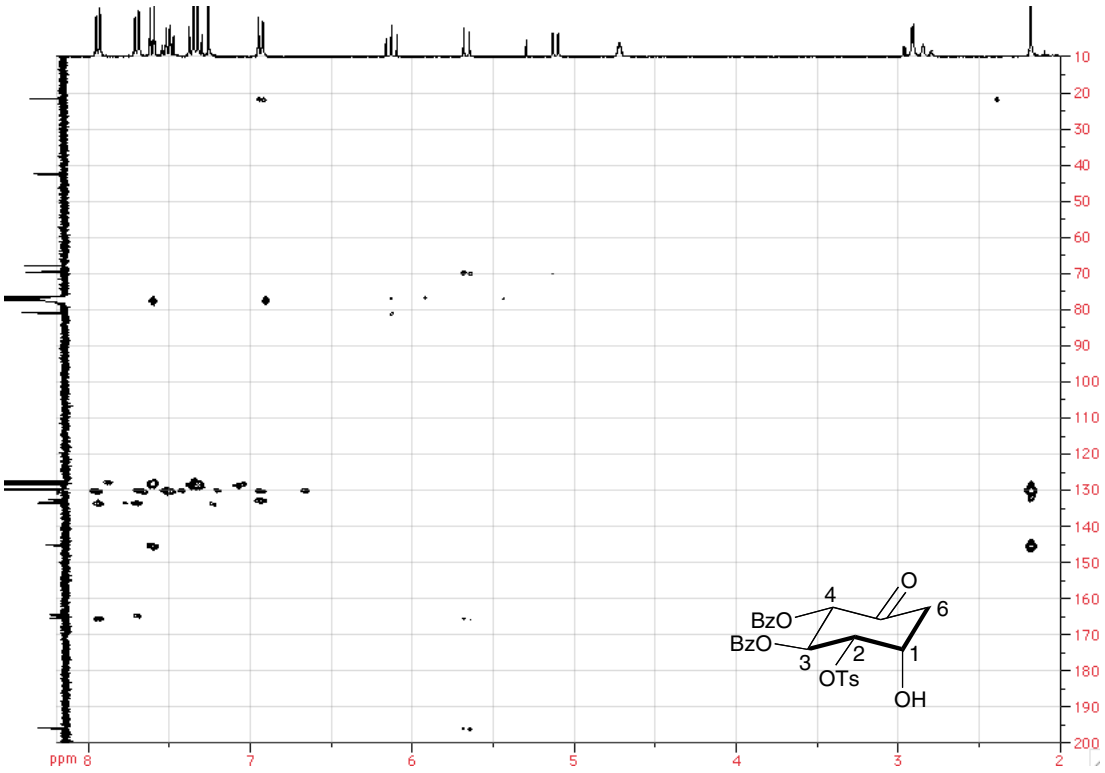


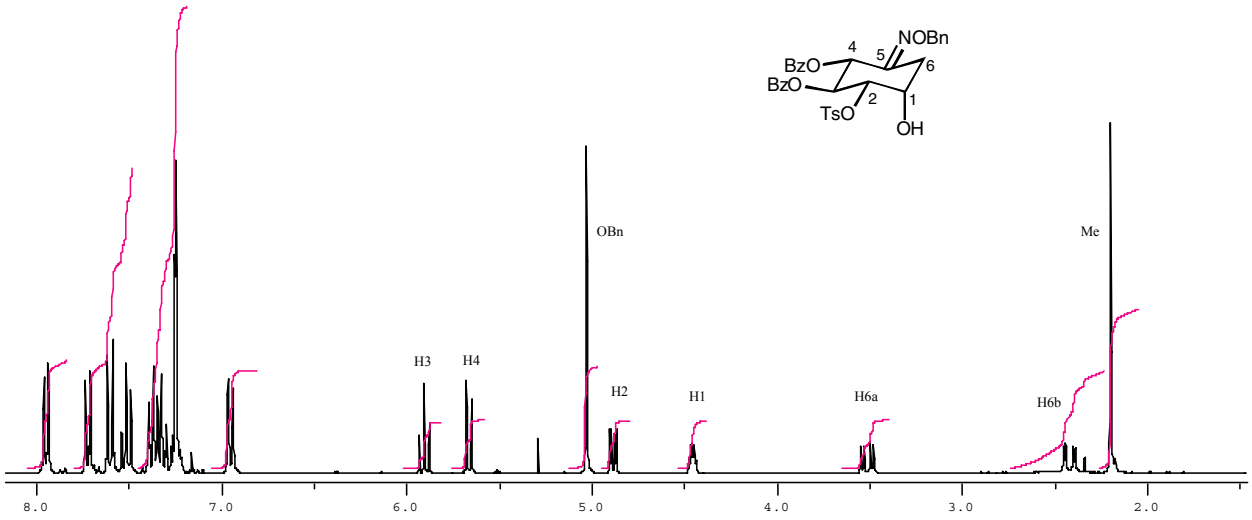
HMQC spectrum of molecule **5** ($CDCl_3$).



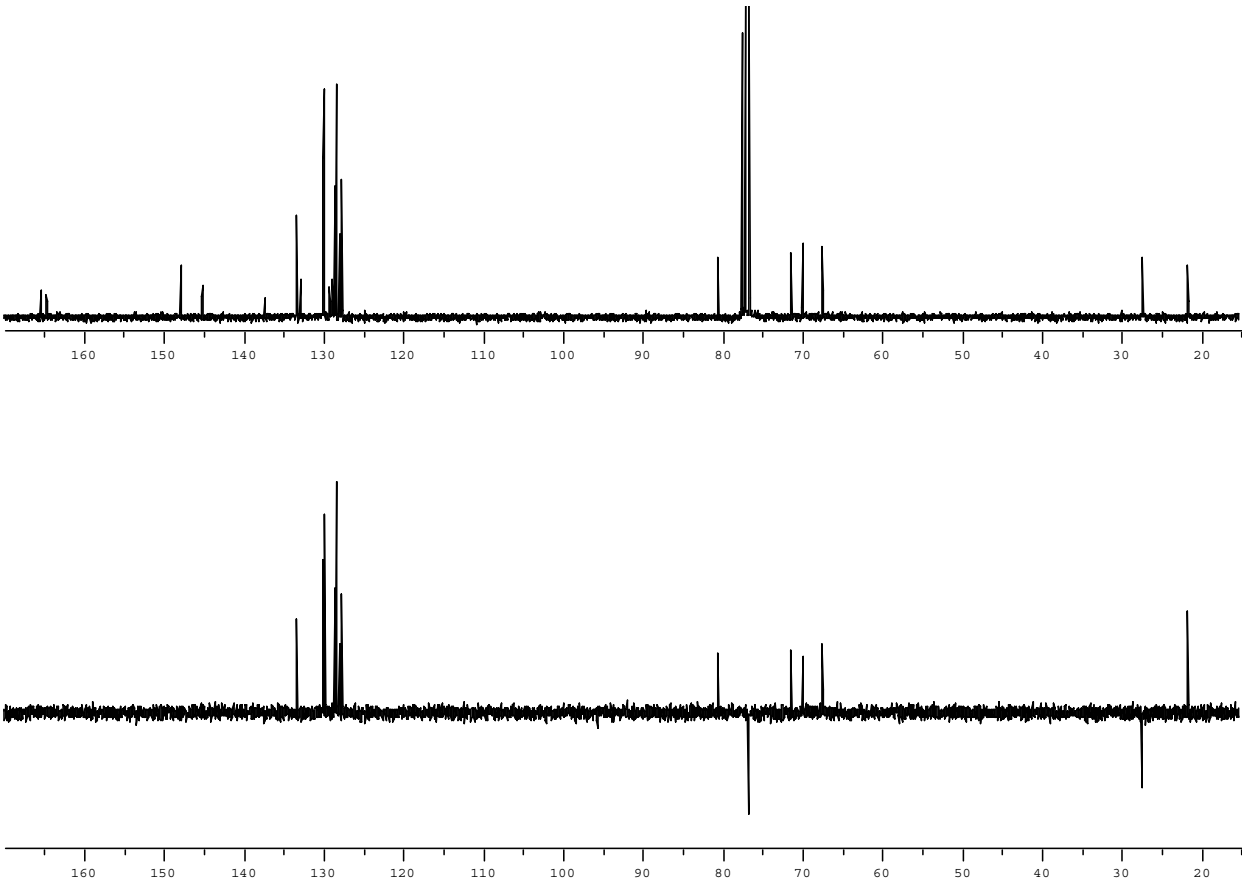

HMBC spectrum of molecule **5** (300 MHz; $CDCl_3$).



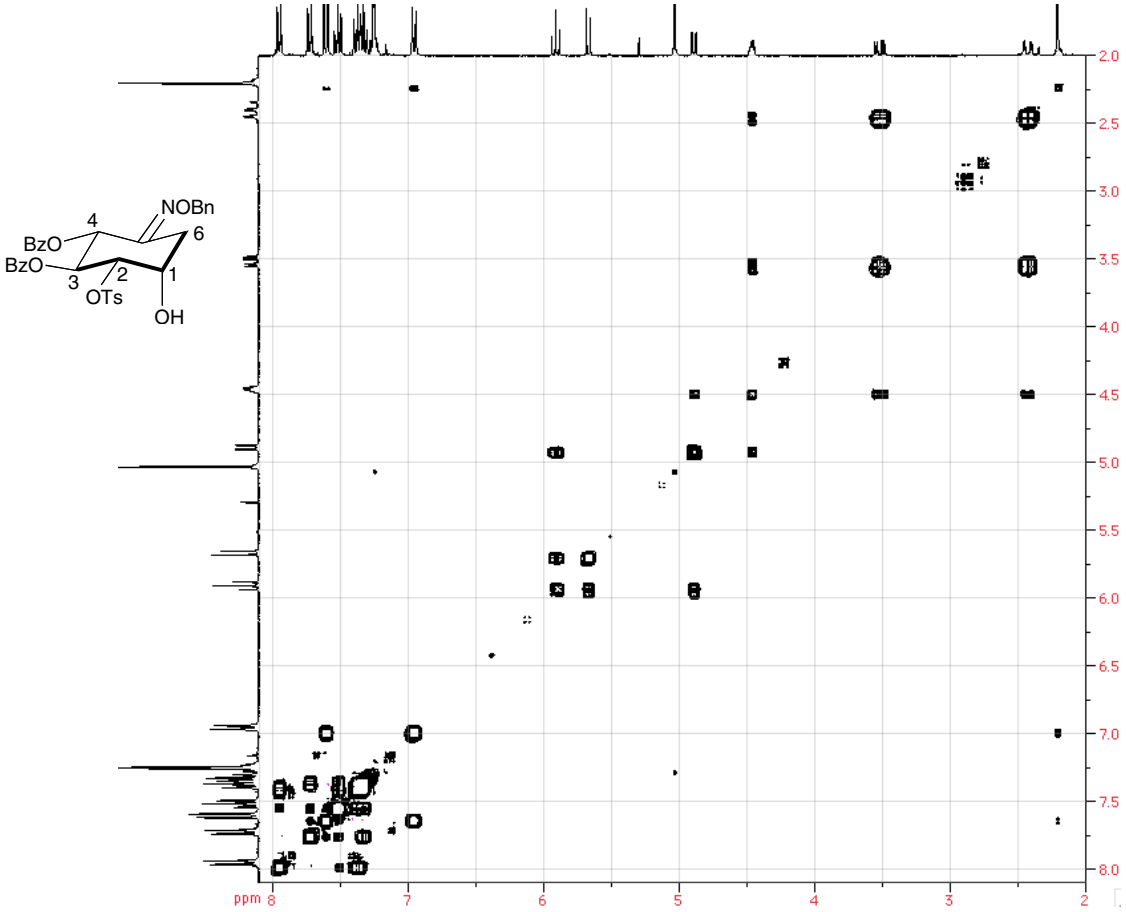
Molecule **6** ($^{1}$H NMR, 300 MHz, $CDCl_3$).



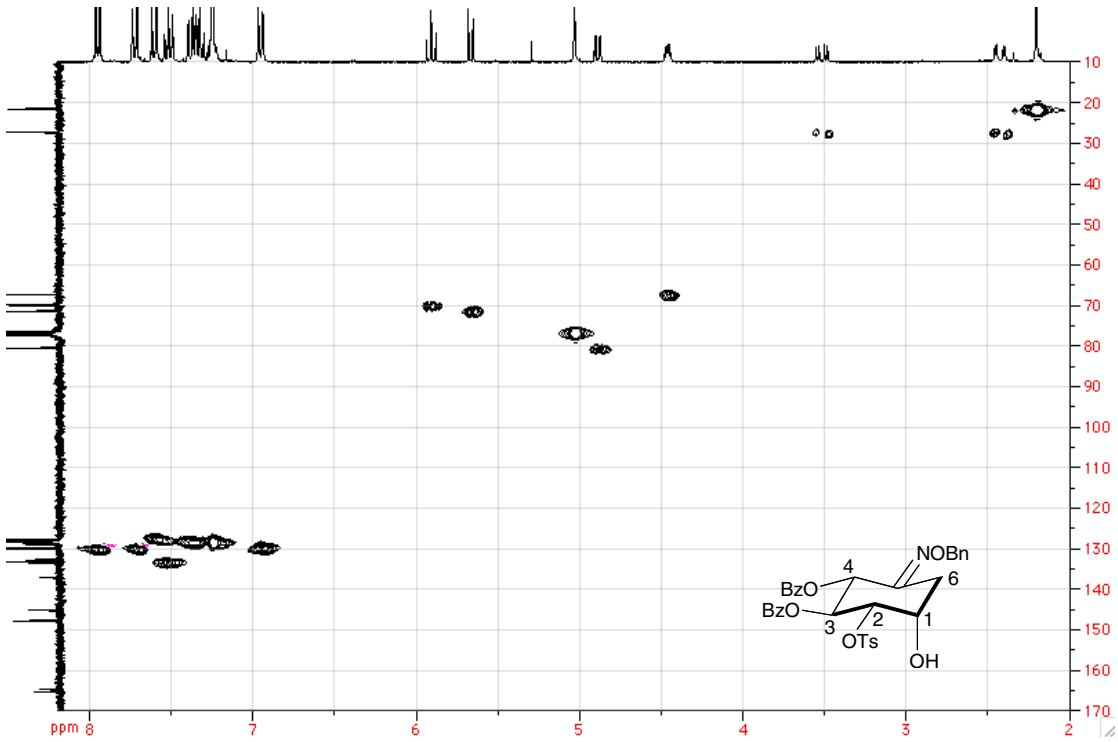

Molecule **6** ($^{13}$C NMR, 75 MHz, $CDCl_3$).



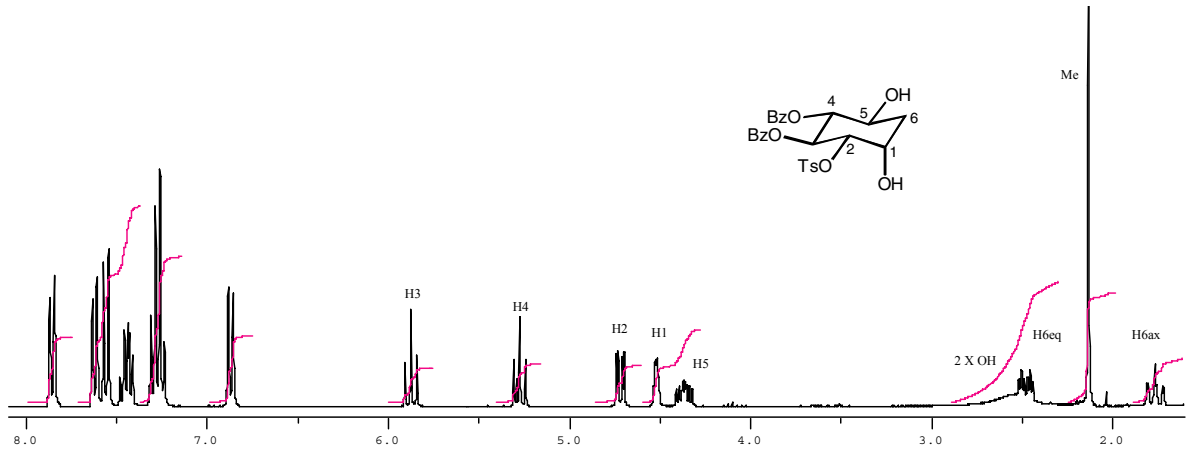
COSY spectrum of molecule **6** (300 MHz; $CDCl_3$).



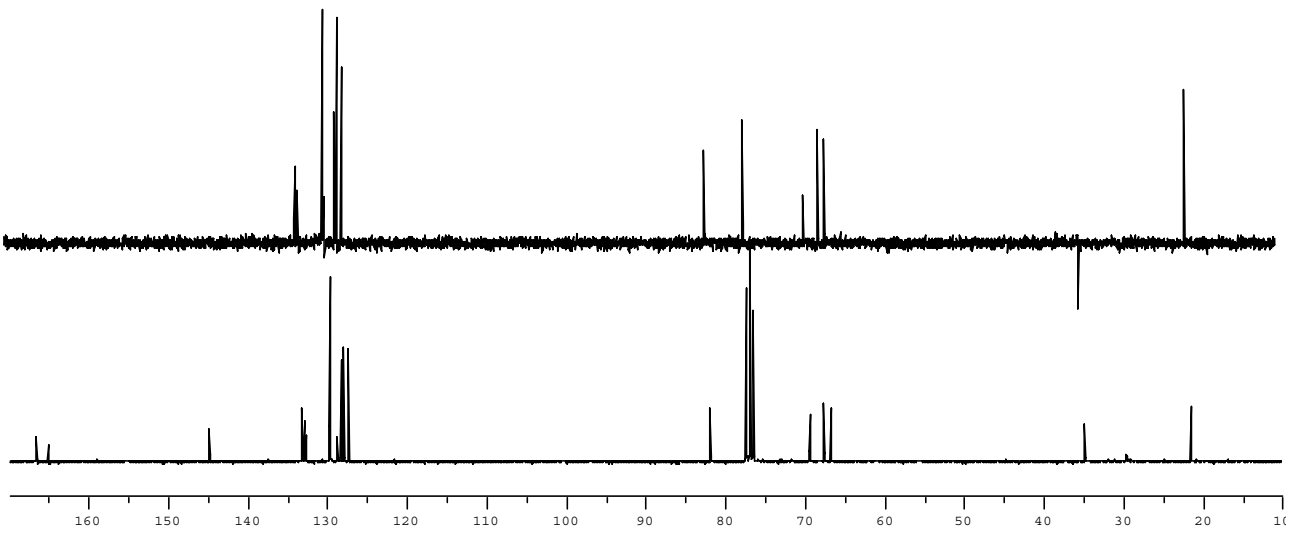

HMQC spectrum of molecule **6** ($CDCl_3$)



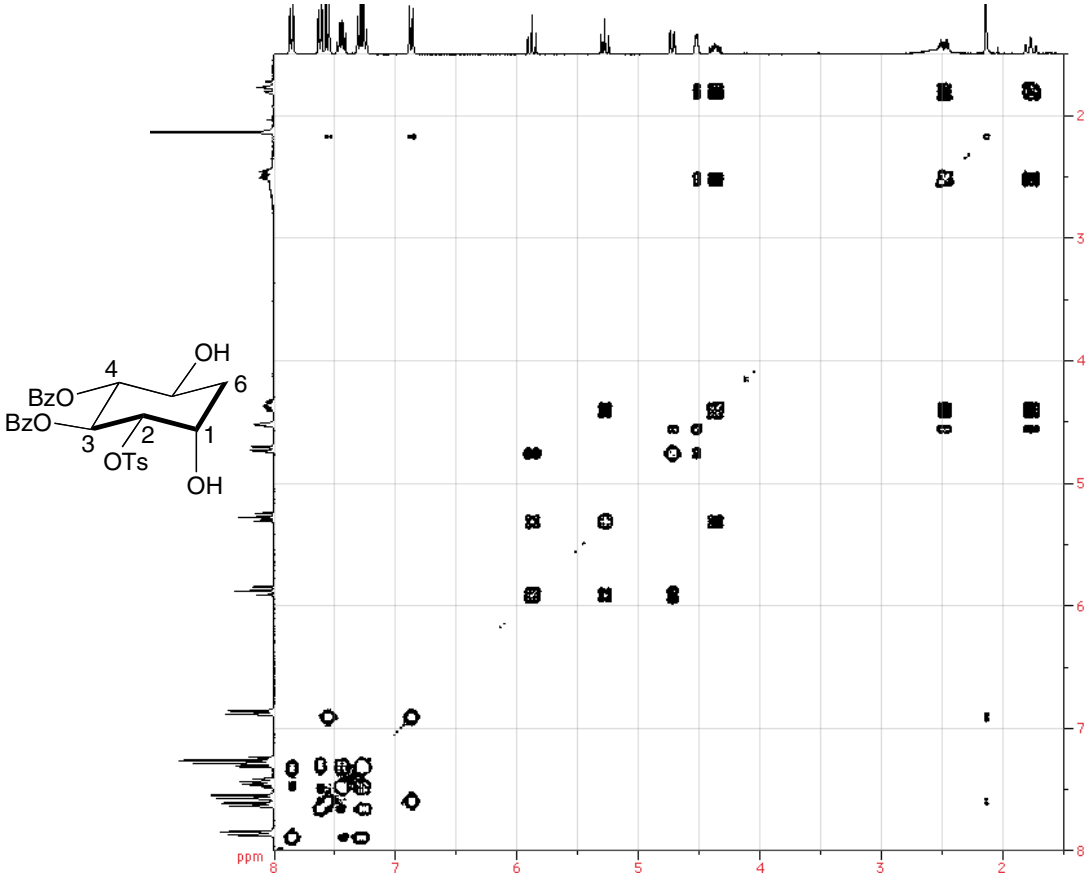
Molecule **7a** ($^{1}$H NMR, 300 MHz, $CDCl_3$).



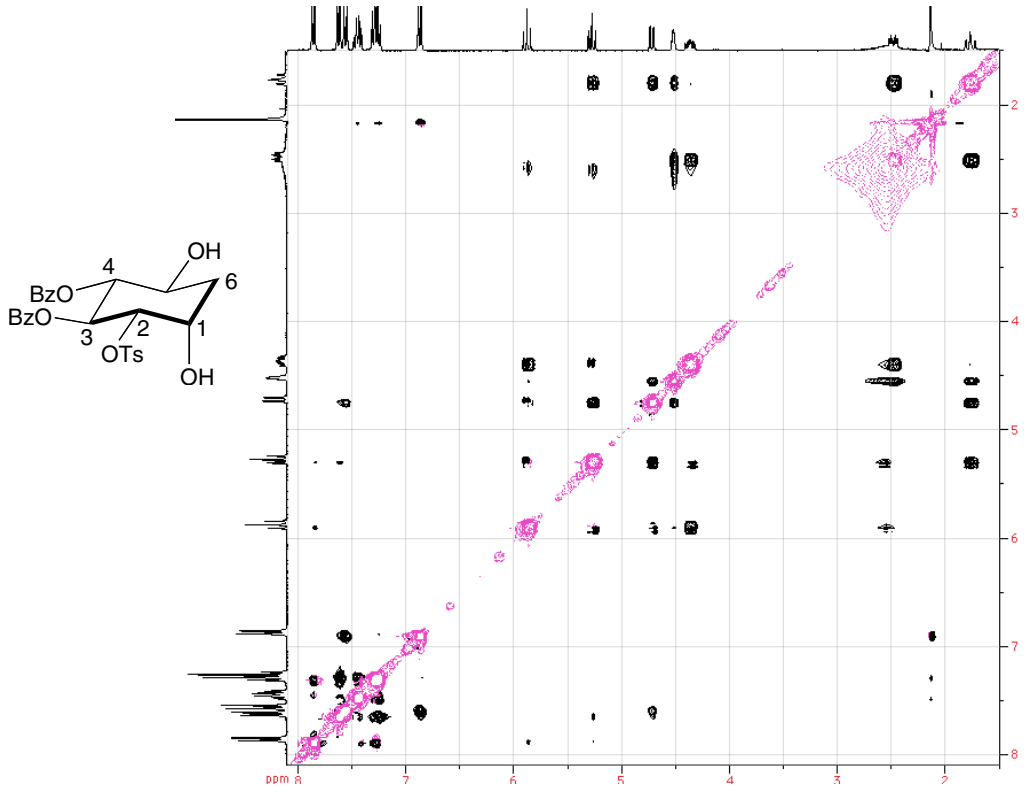

Molecule **7a** ($^{13}$C NMR, 75 MHz, $CDCl_3$).



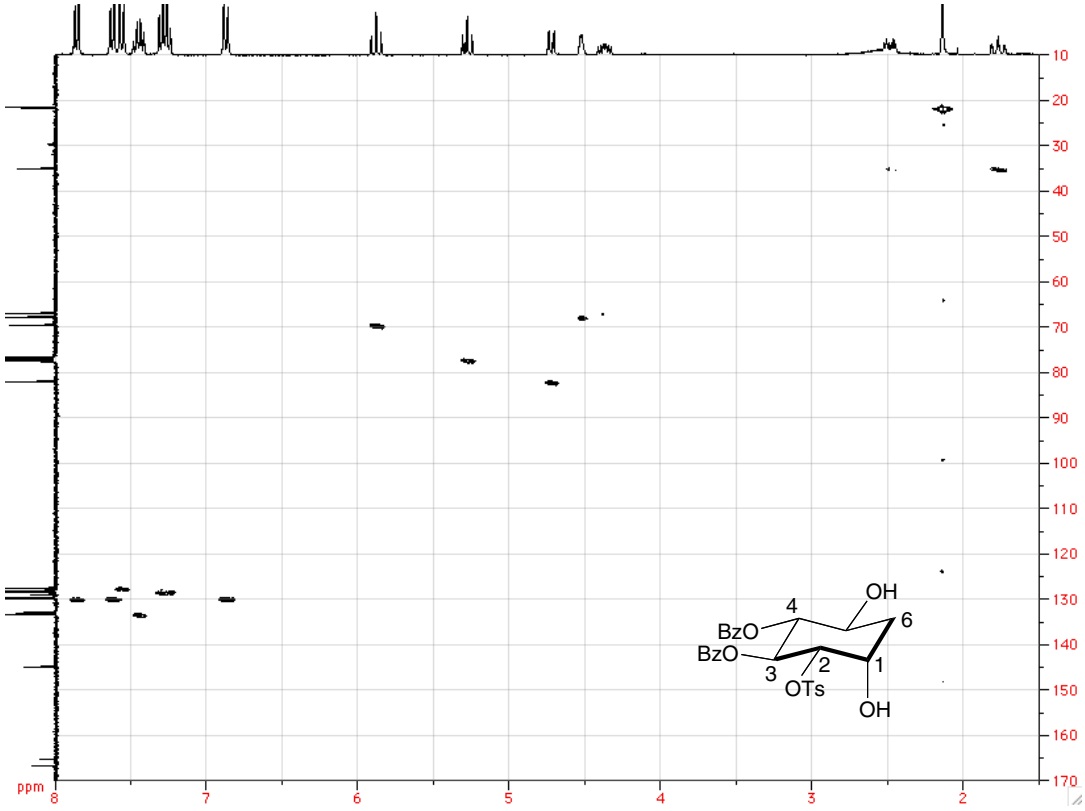
COSY spectrum of molecule **7a** (300 MHz; $CDCl_3$).




NOESY spectrum of molecule **7a** (300 MHz; $CDCl_3$).



HMQC spectrum of molecule **7a** ($CDCl_3$).

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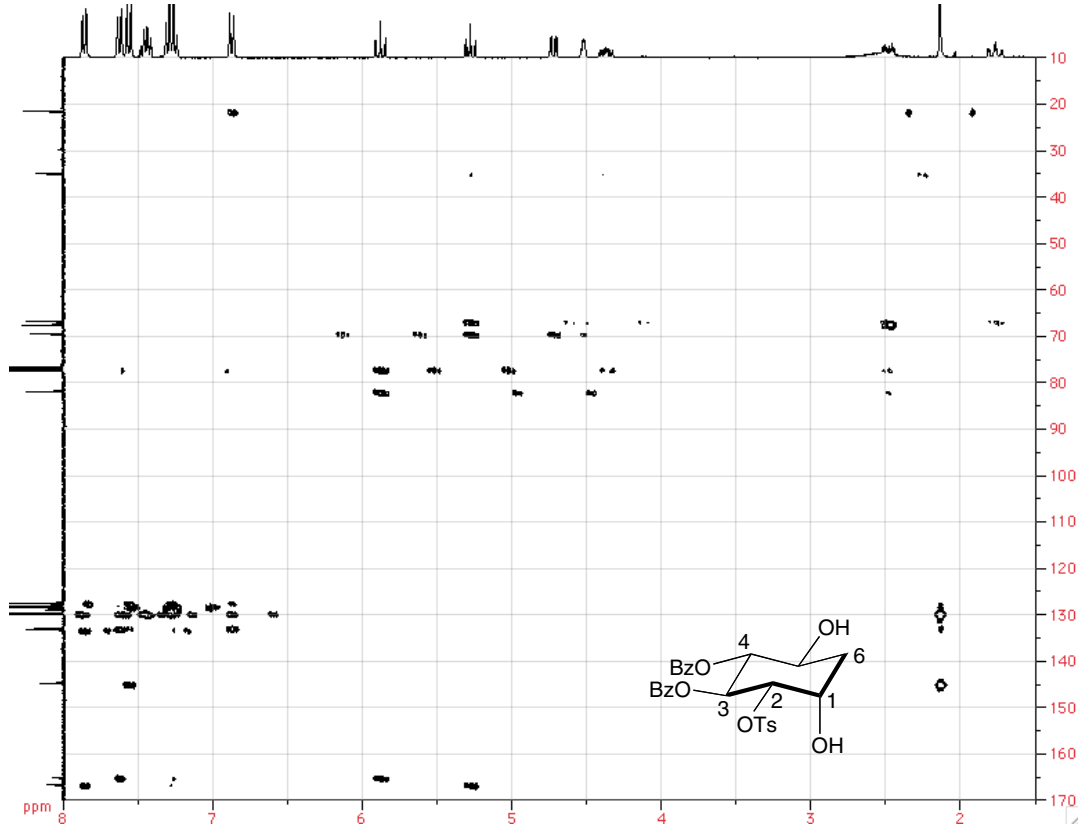
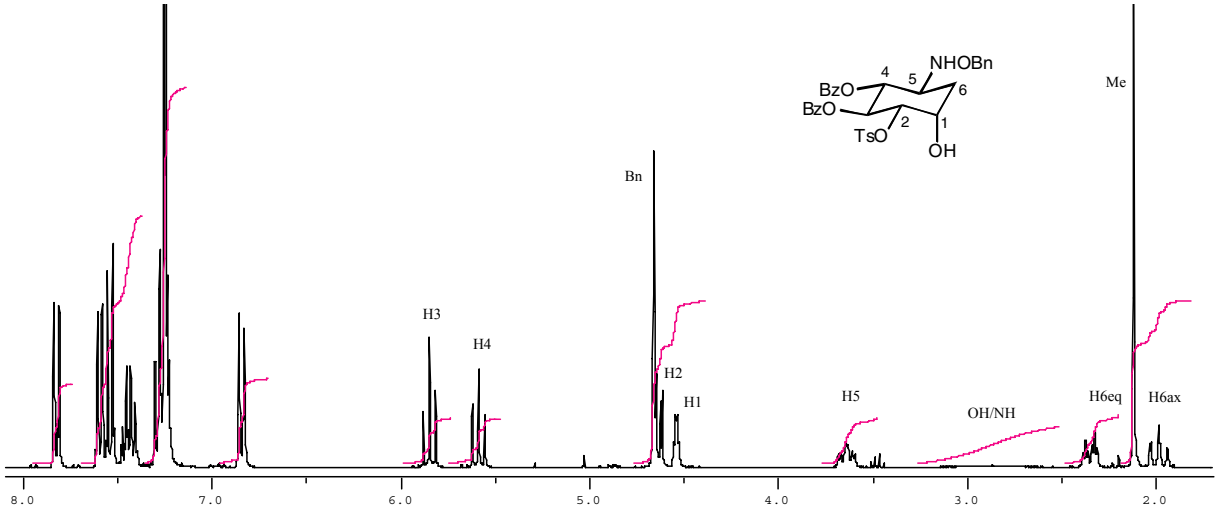
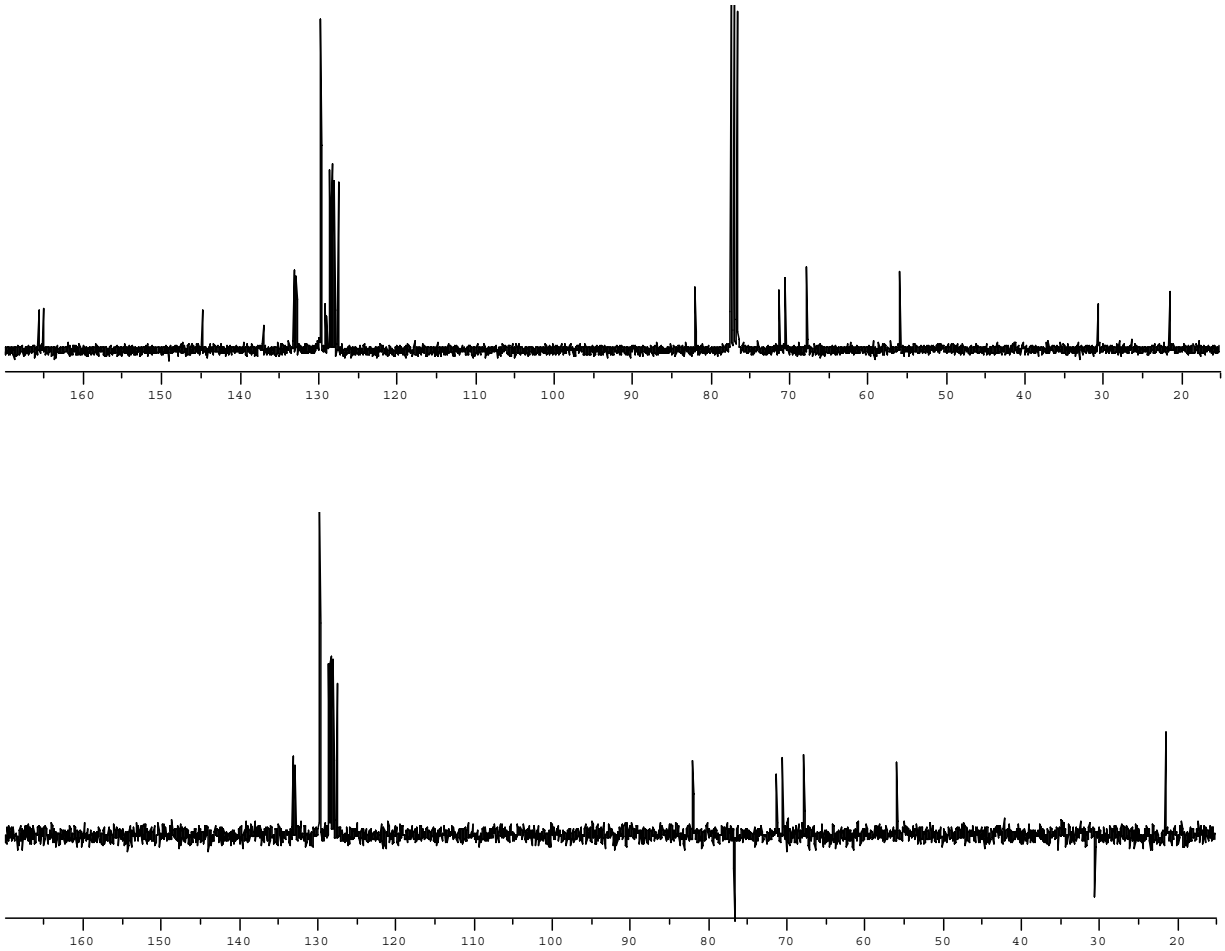


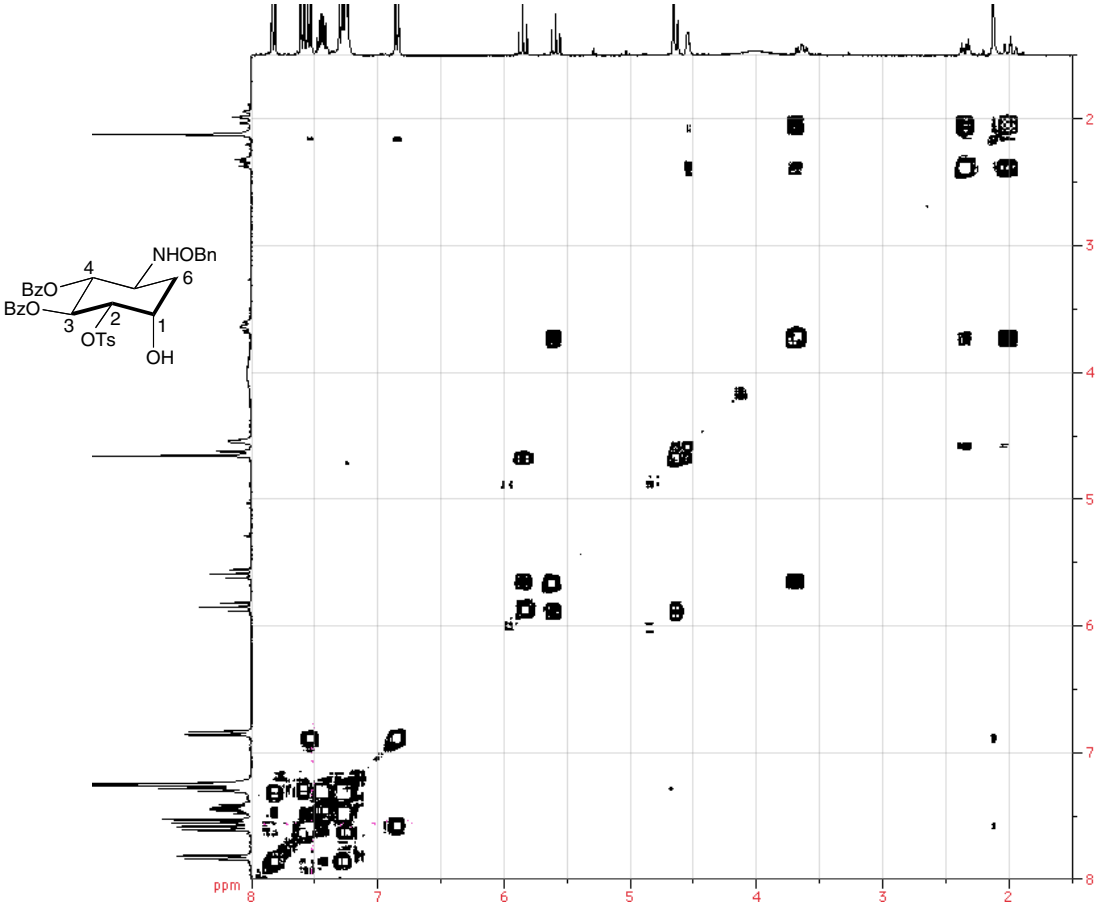
Molecule **7b** ($^{1}$H NMR, 300 MHz, $CDCl_3$).



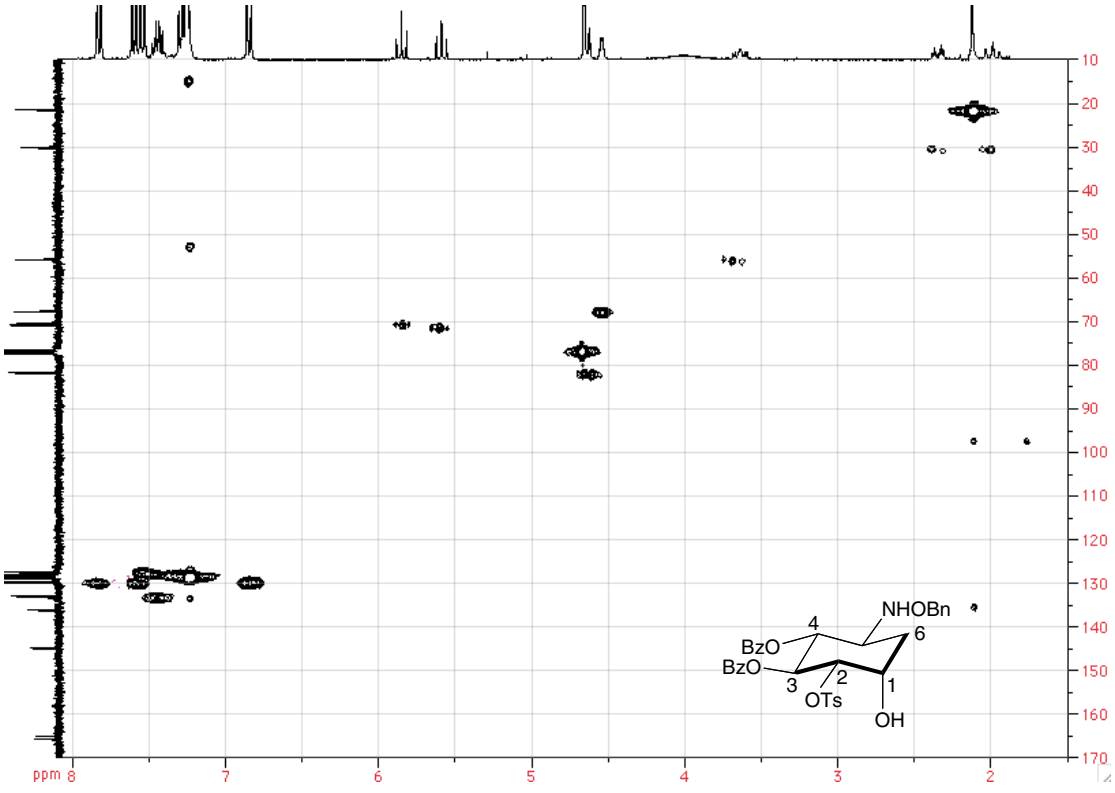

Molecule **7b** ($^{13}$C NMR, 75 MHz, $CDCl_3$).



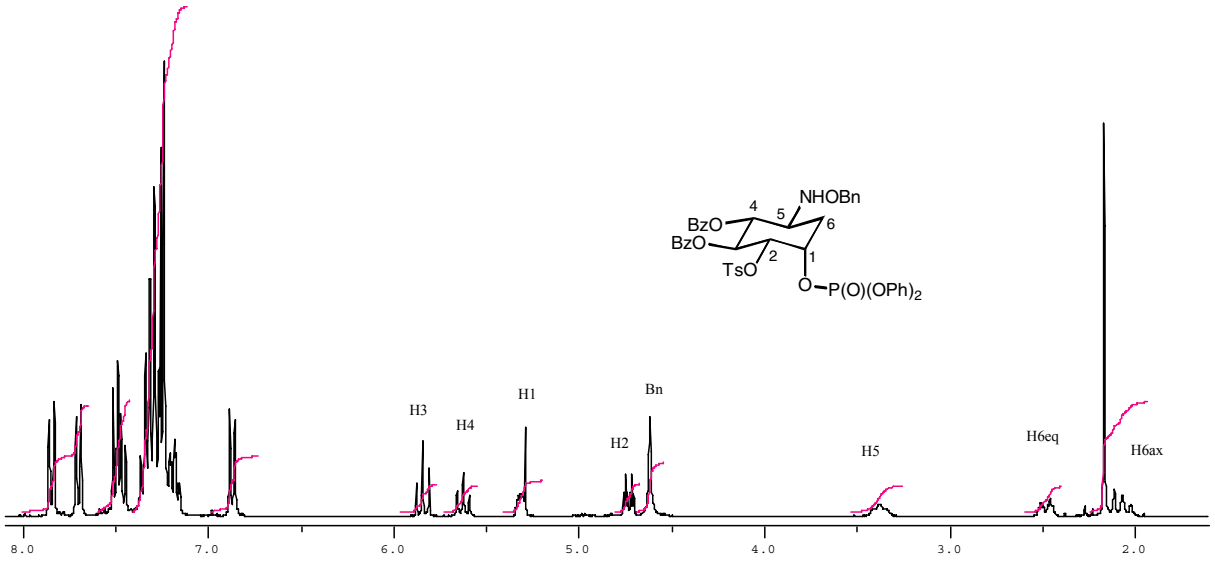
COSY spectrum of molecule **7b** (300 MHz; $CDCl_3$).



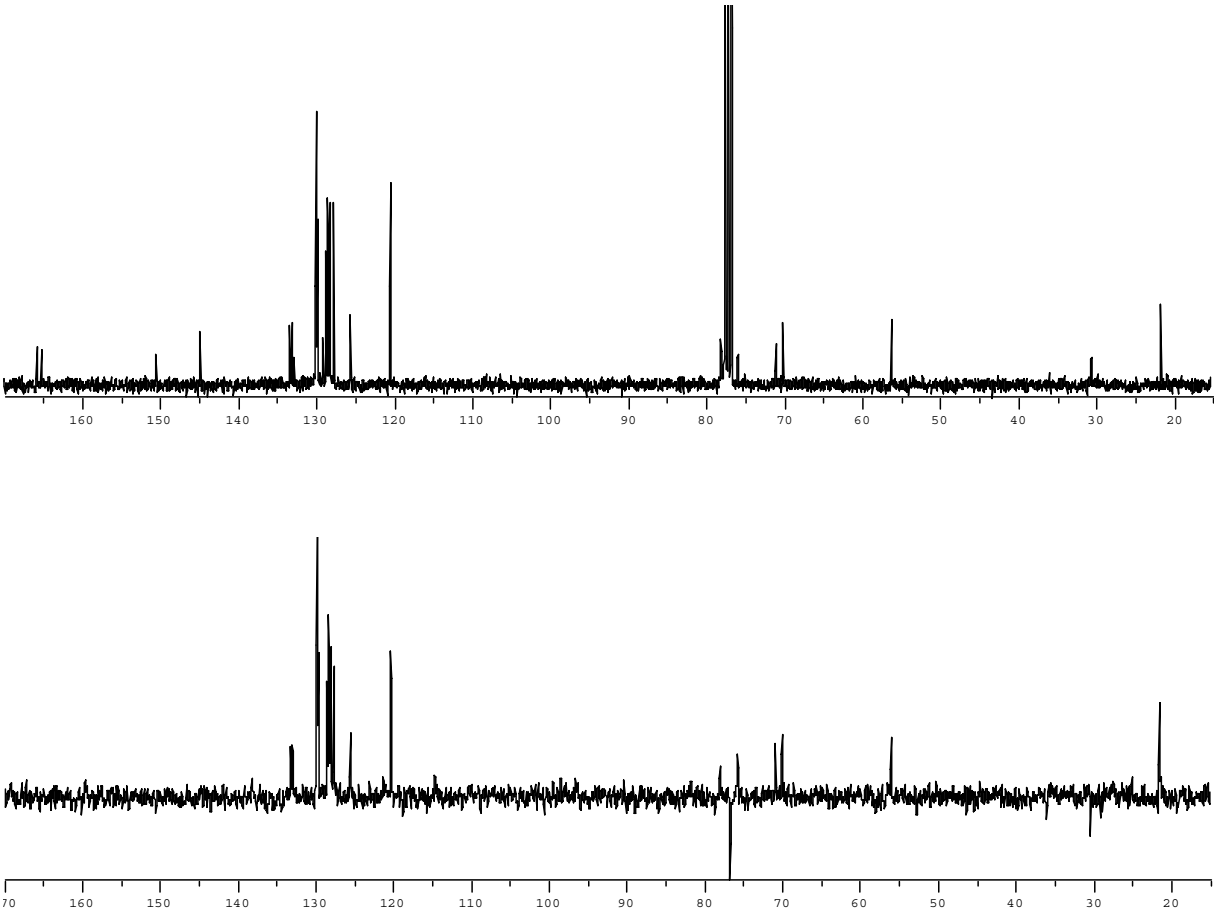

HMQC spectrum of molecule **7b** ($CDCl_3$).



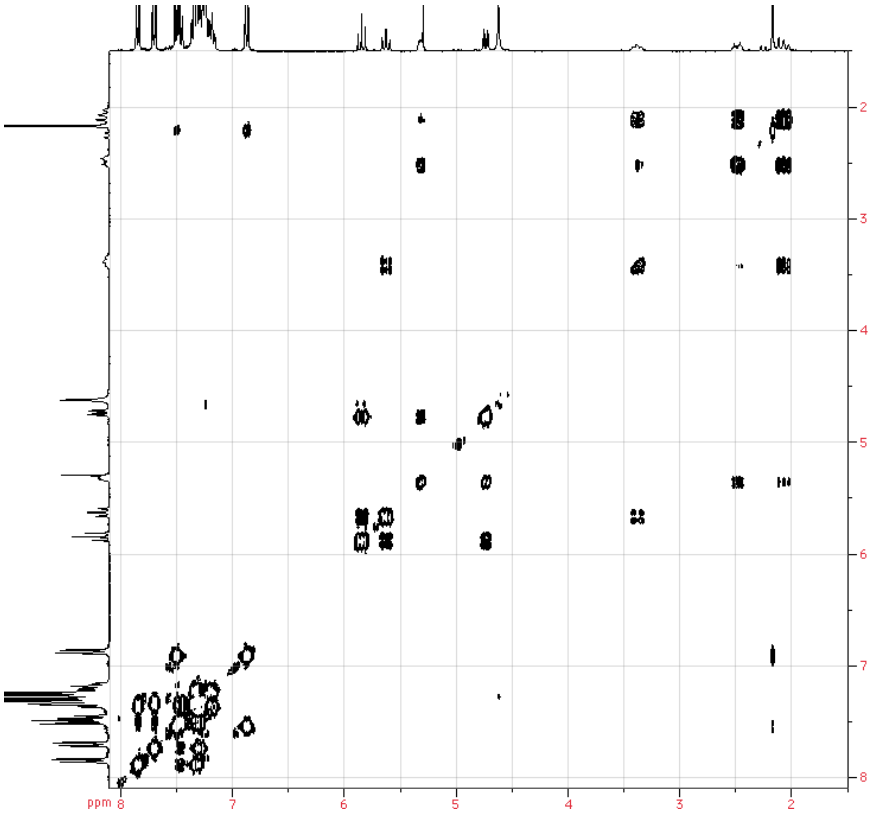
Molecule **7c** ($^{1}$H NMR, 300 MHz, $CDCl_3$).

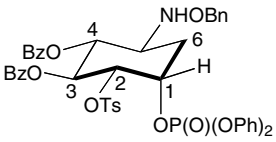



Molecule **7c** ($^{13}$C NMR, 75 MHz, $CDCl_3$).

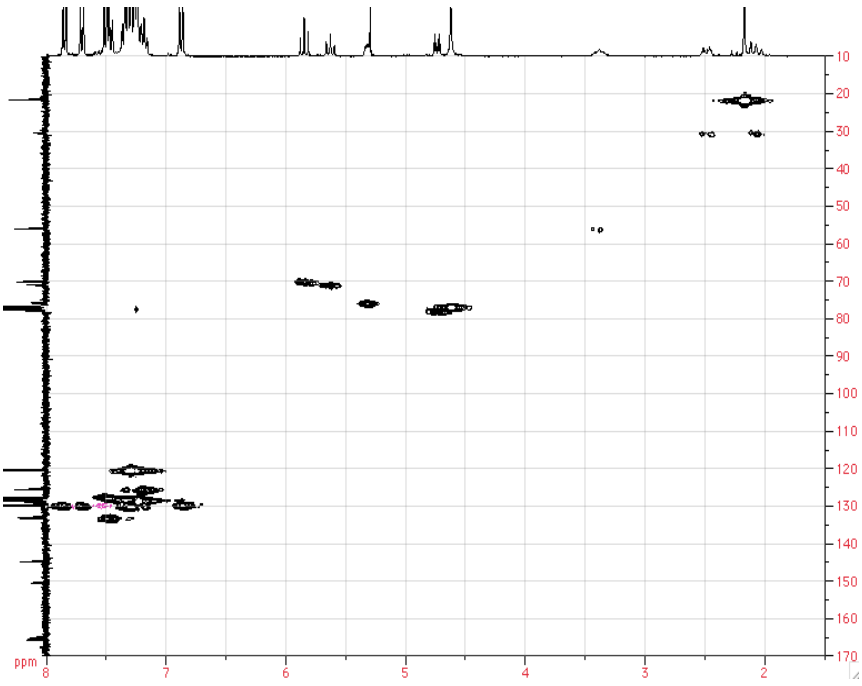


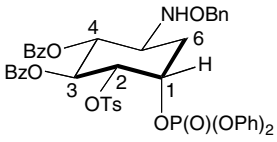
COSY spectrum of molecule **7c** (300 MHz; $CDCl_3$).



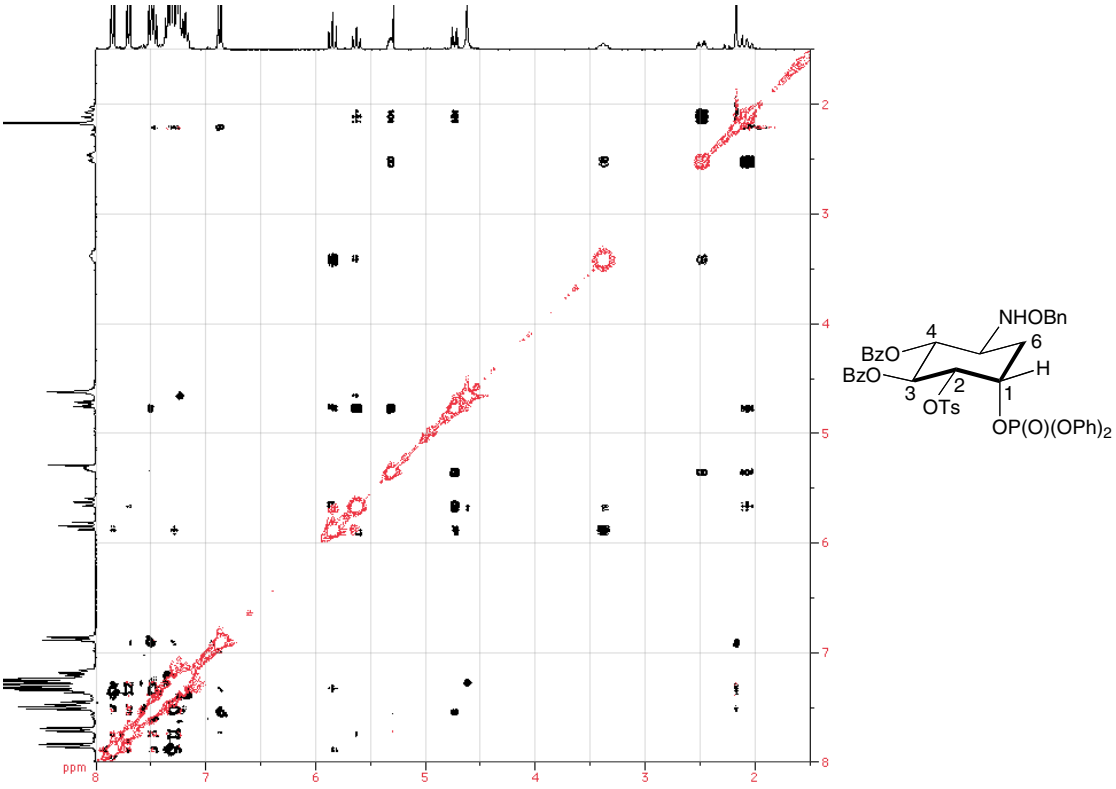




HMQC spectrum of molecule **7c** ($CDCl_3$).

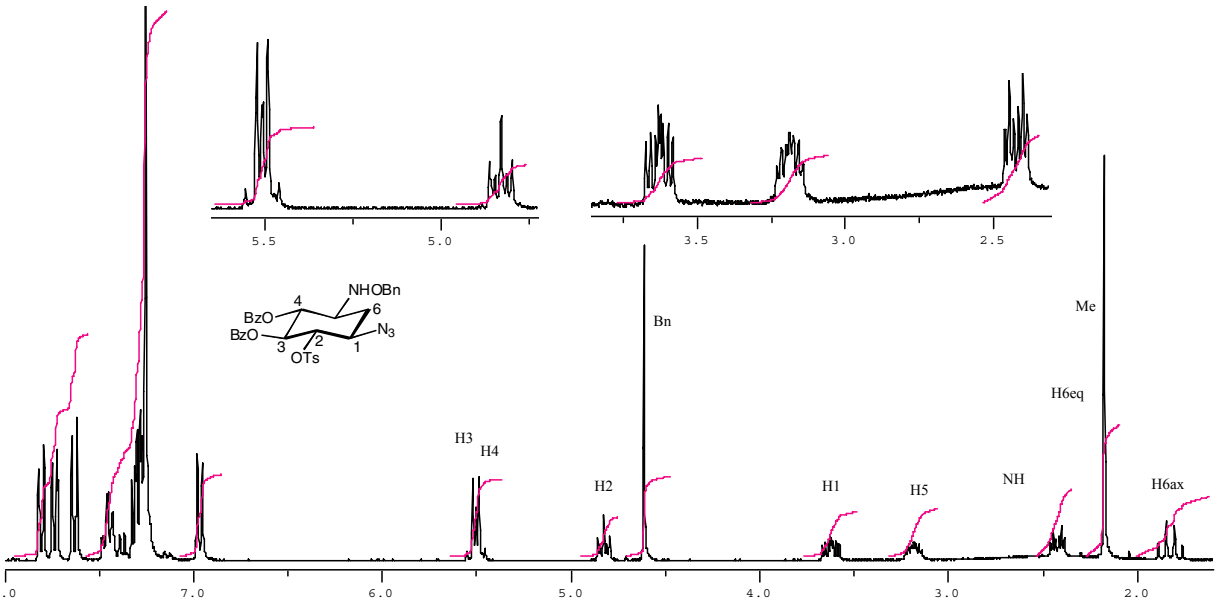


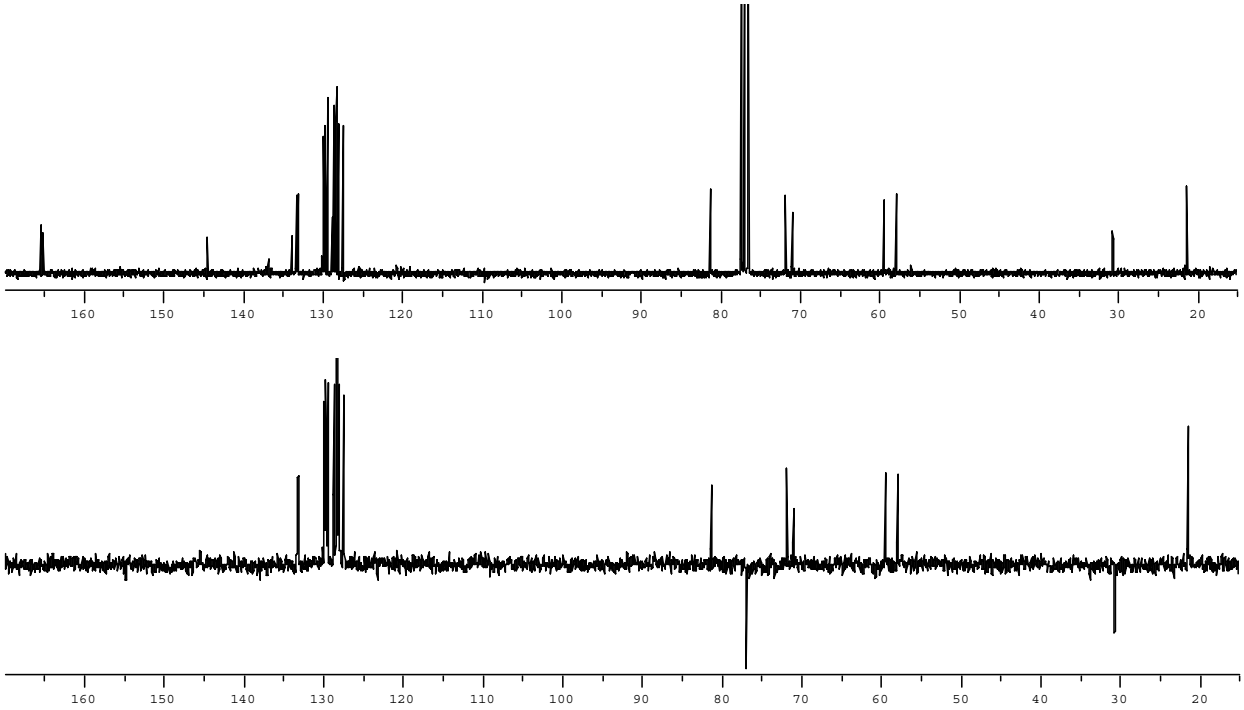
NOESY spectrum of molecule **7c** (300 MHz; $CDCl_3$).



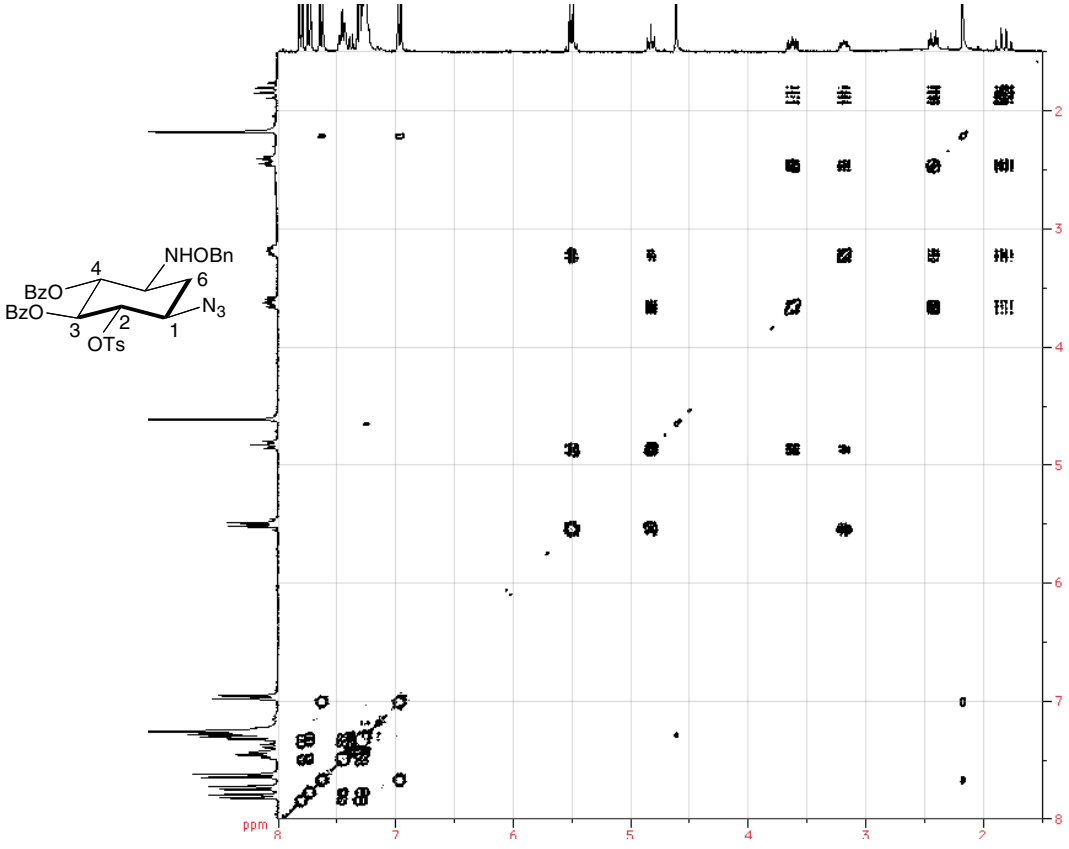

Molecule **8** ($^1$H NMR, 300 MHz, $CDCl_3$).



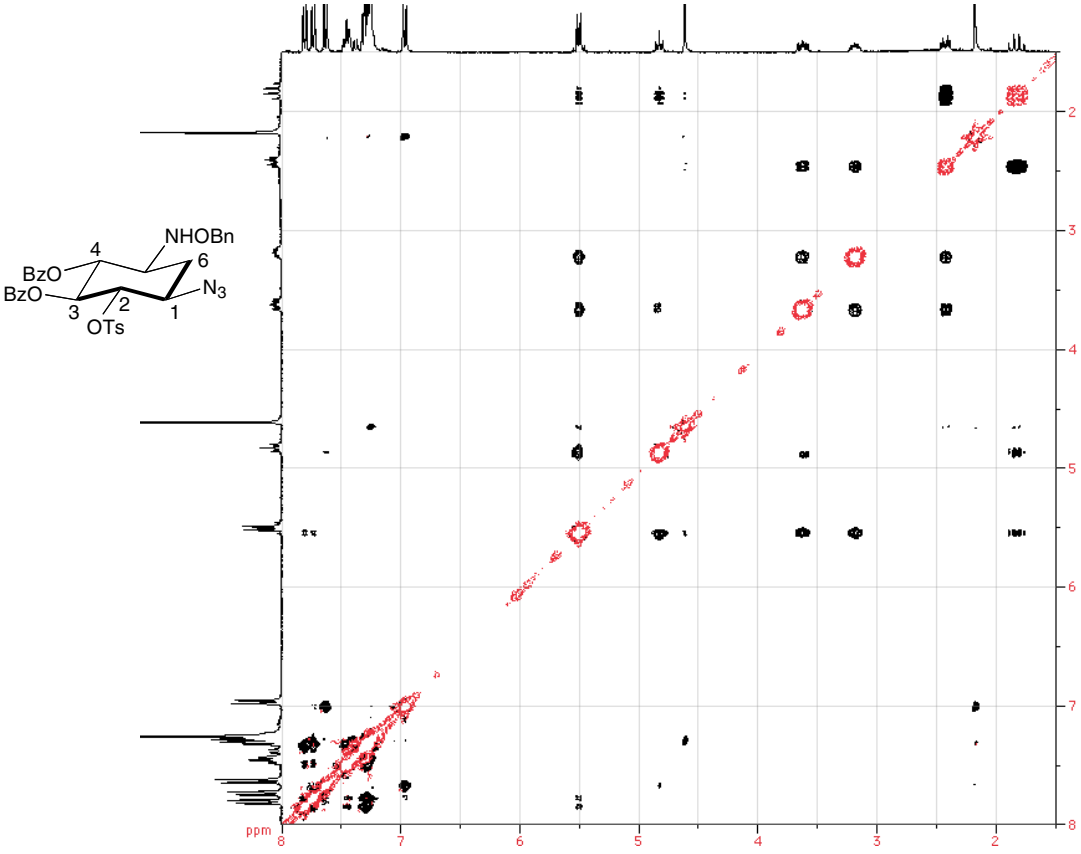
Molecule **8** ($^{13}$C NMR, 75 MHz, $CDCl_3$).



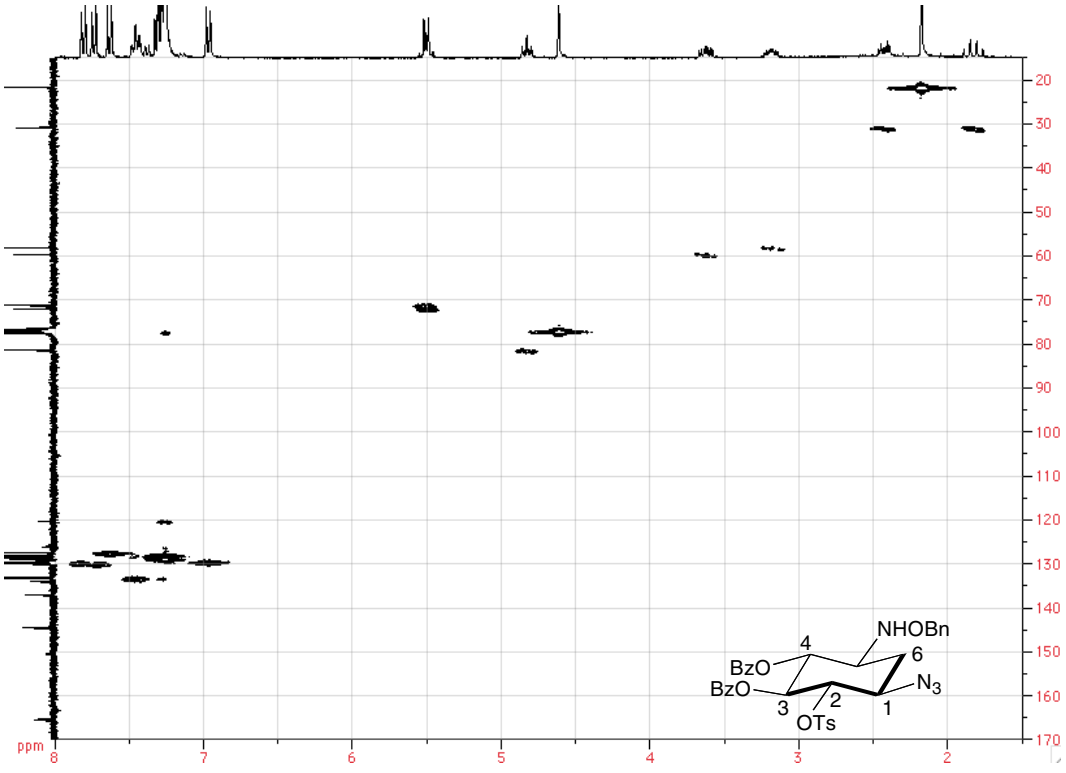

COSY spectrum of molecule **8** (300 MHz; $CDCl_3$).



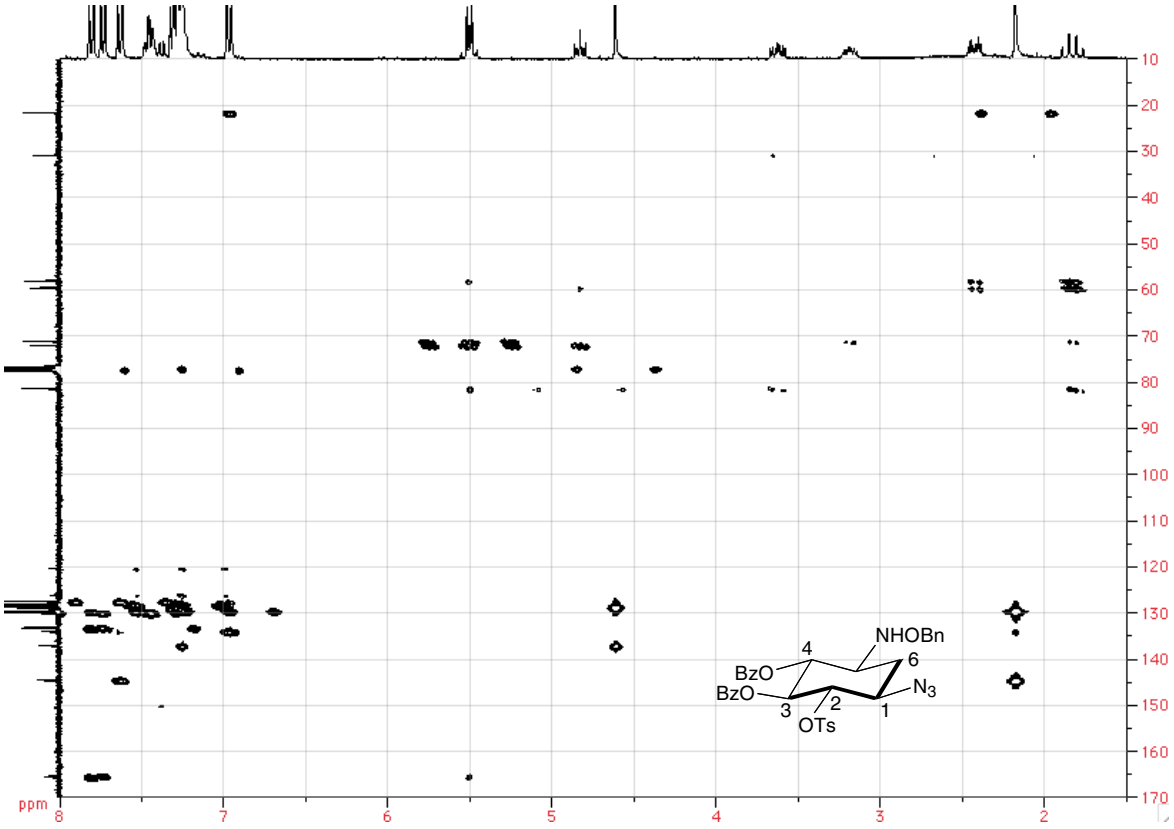
NOESY spectrum of molecule **8** (300 MHz; $CDCl_3$).



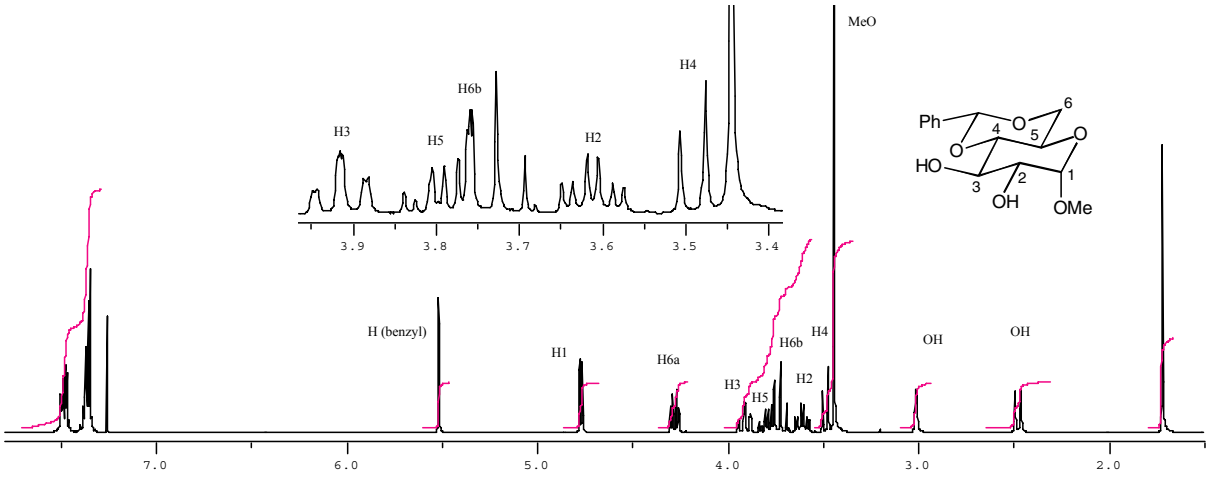

HMQC spectrum of molecule **8** ($CDCl_3$).



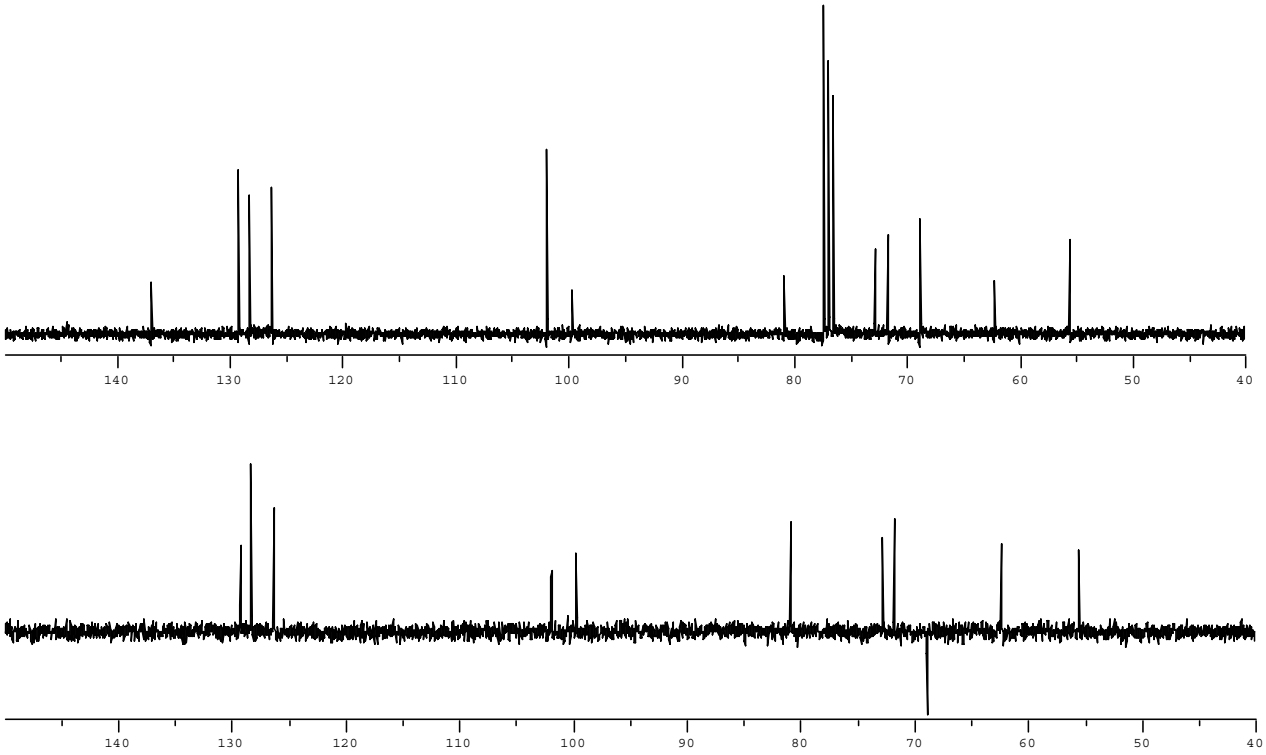
HMBC spectrum of molecule **8** (300 MHz; $CDCl_3$).



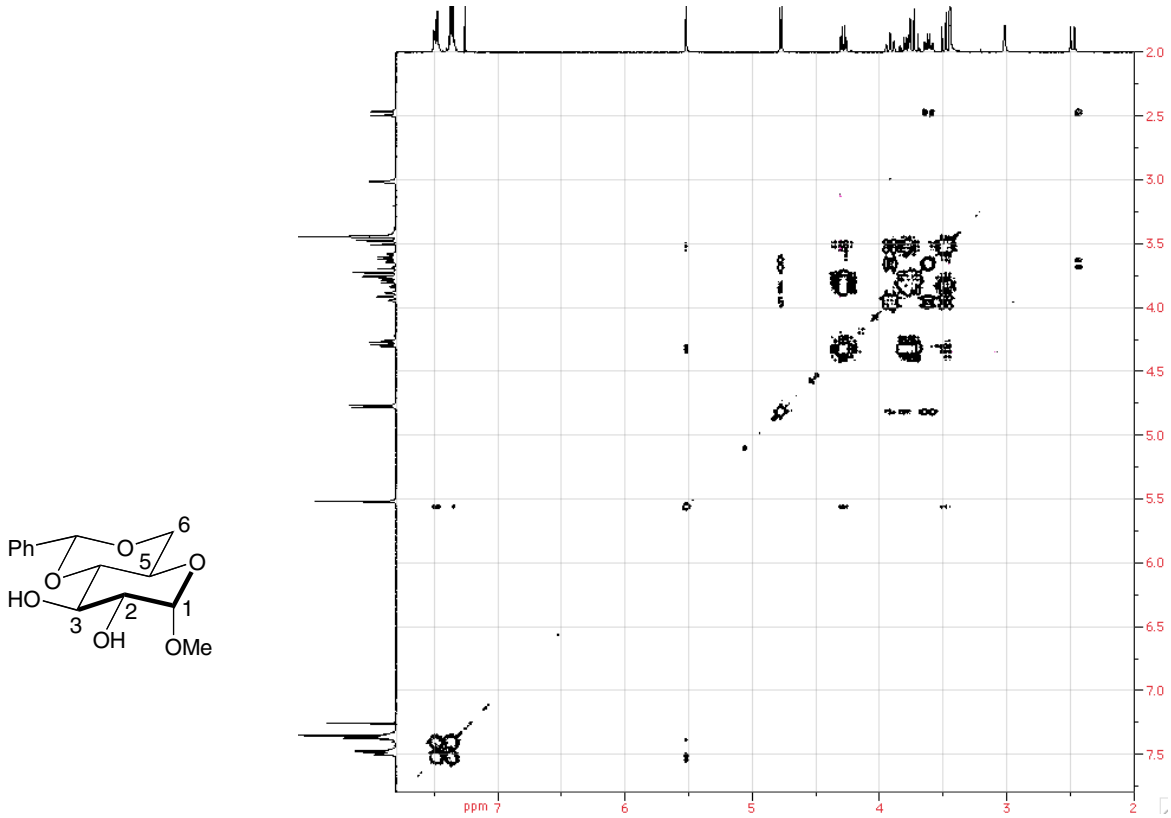

Molecule **9** ($^1$H NMR, 300 MHz, $CDCl_3$).



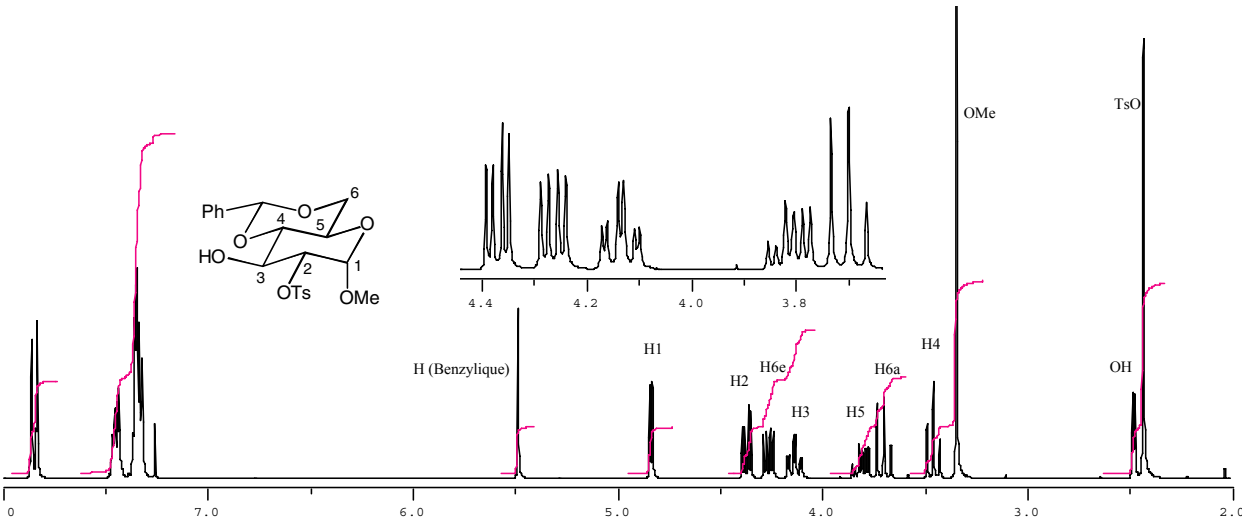
Molecule **9** ($^{13}C$ NMR, 75 MHz, $CDCl_3$).



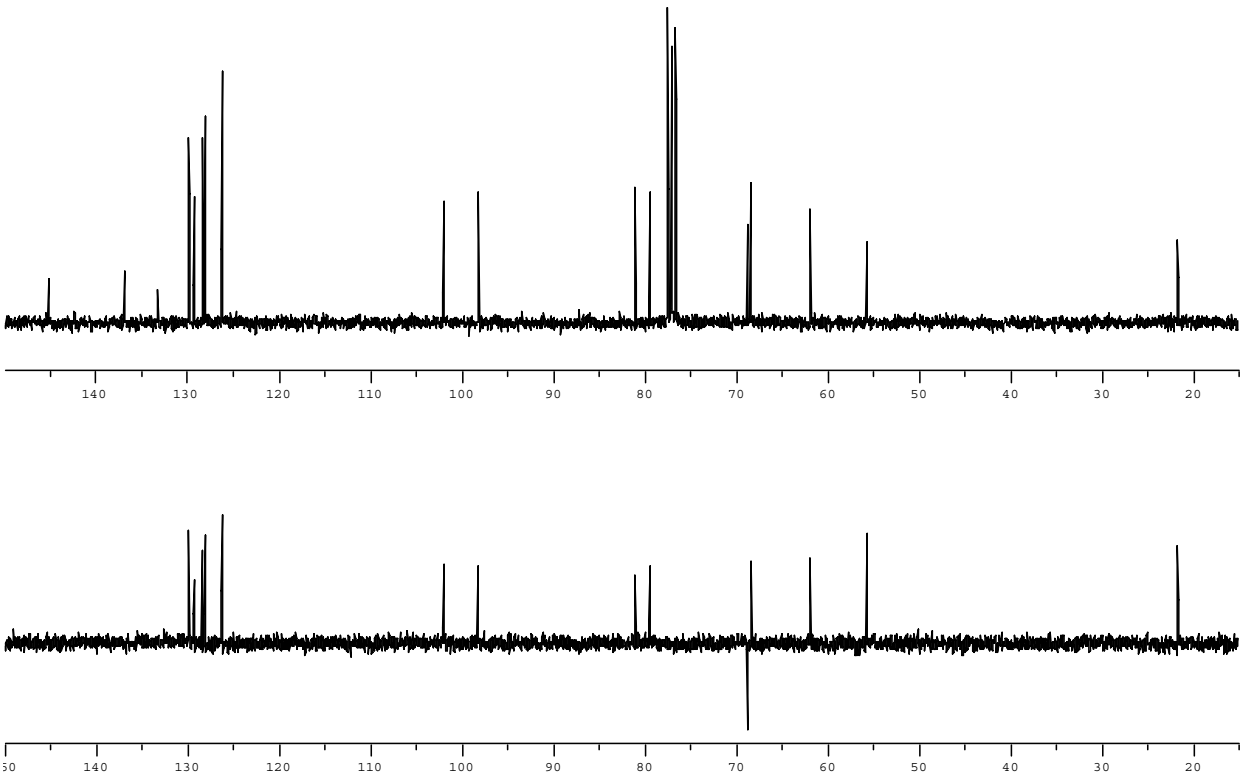

COSY spectrum of molecule **9** (300 MHz; $CDCl_3$).



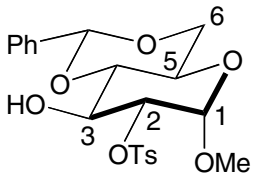
Molecule **10** ($^{1}$H NMR, 300 MHz, $CDCl_3$).

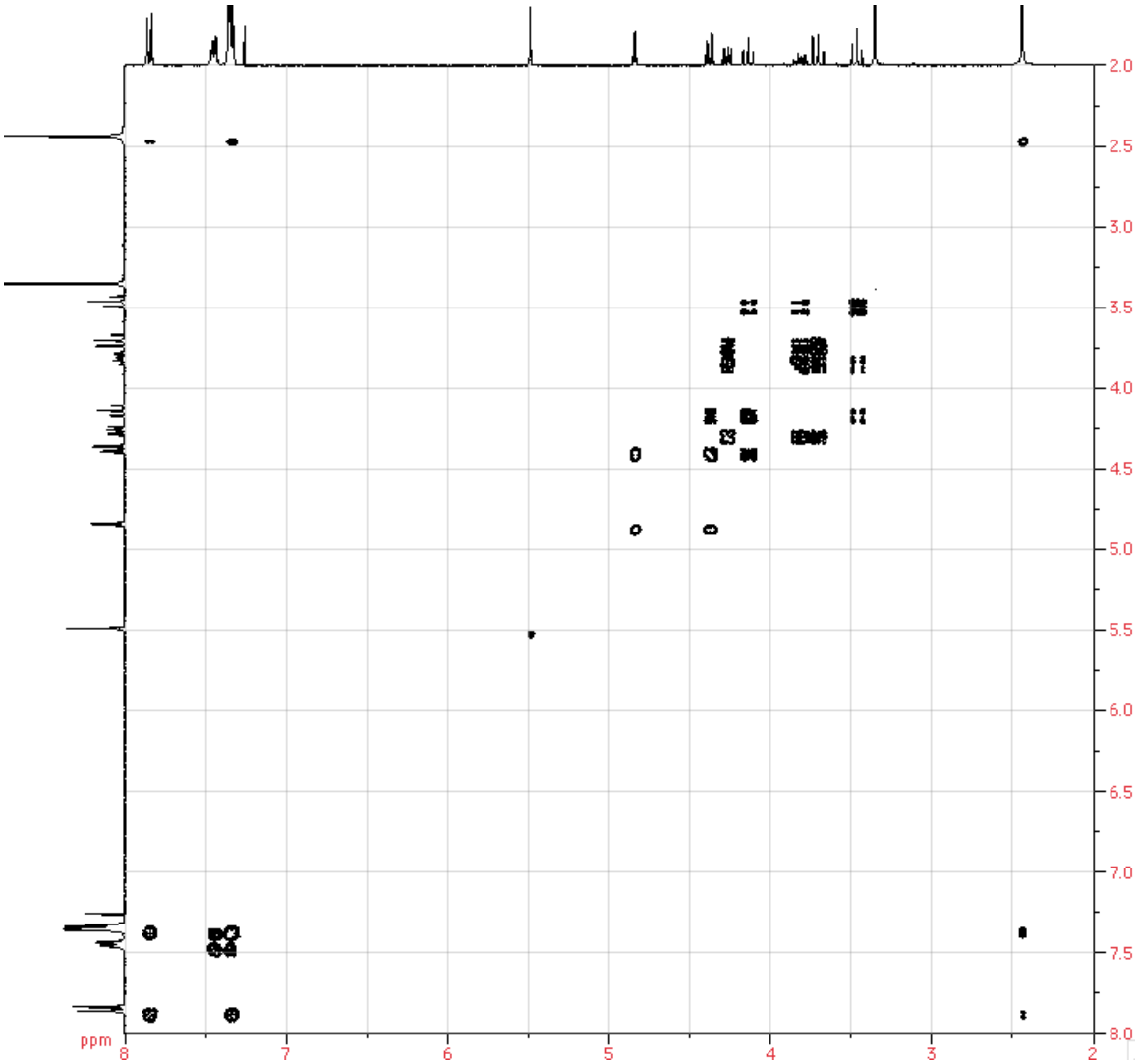



Molecule **10** ($^{13}$C NMR, 75 MHz, $CDCl_3$).

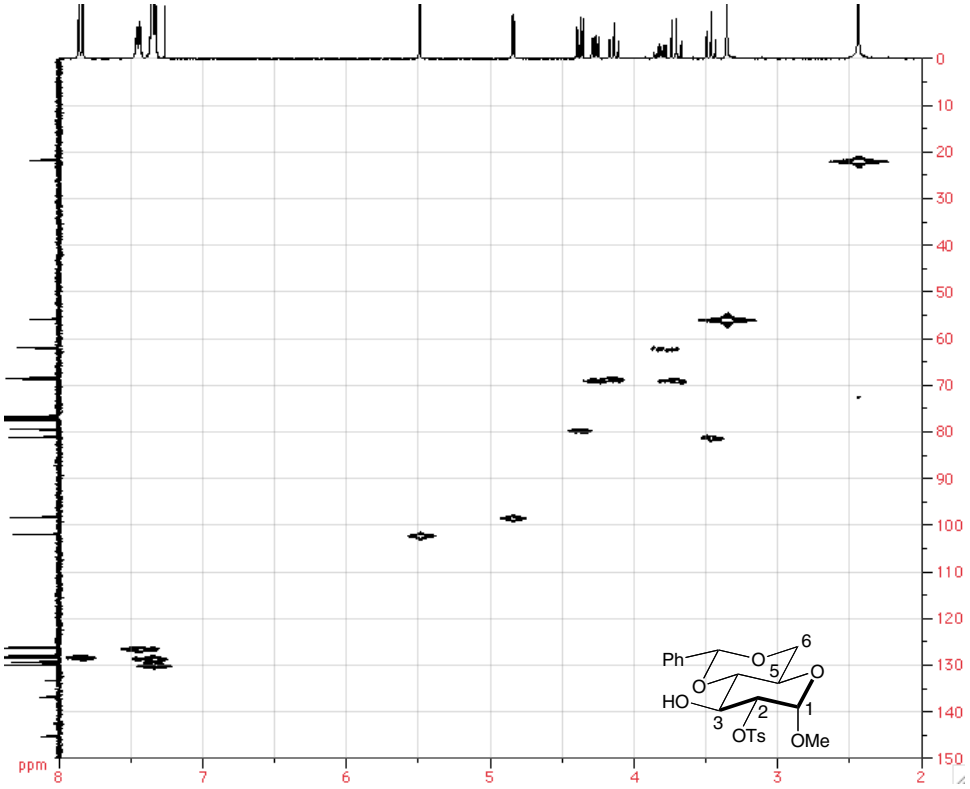


COSY spectrum of molecule **10** (300 MHz; $CDCl_3$).

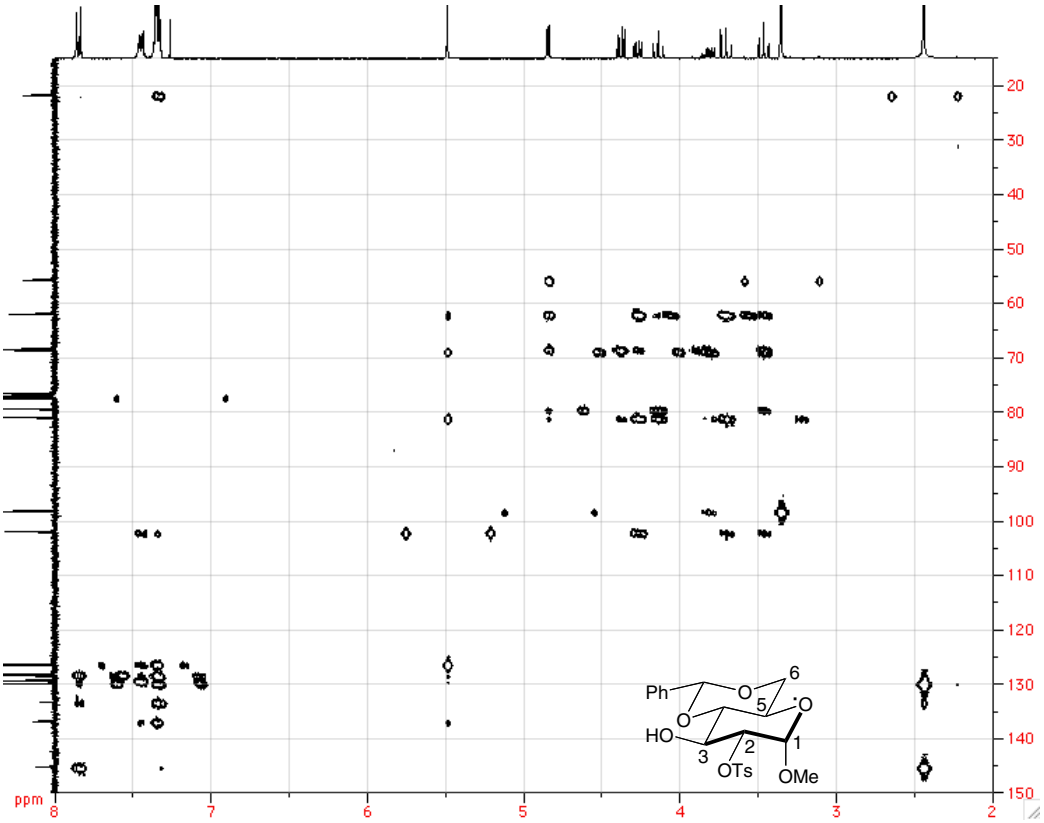


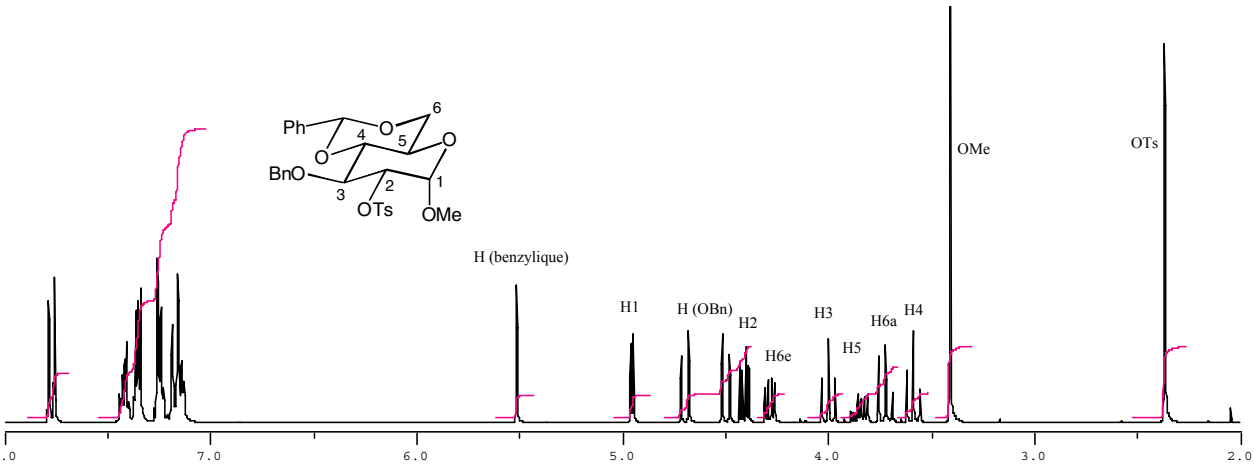
HMQC spectrum of molecule **10** ($CDCl_3$).



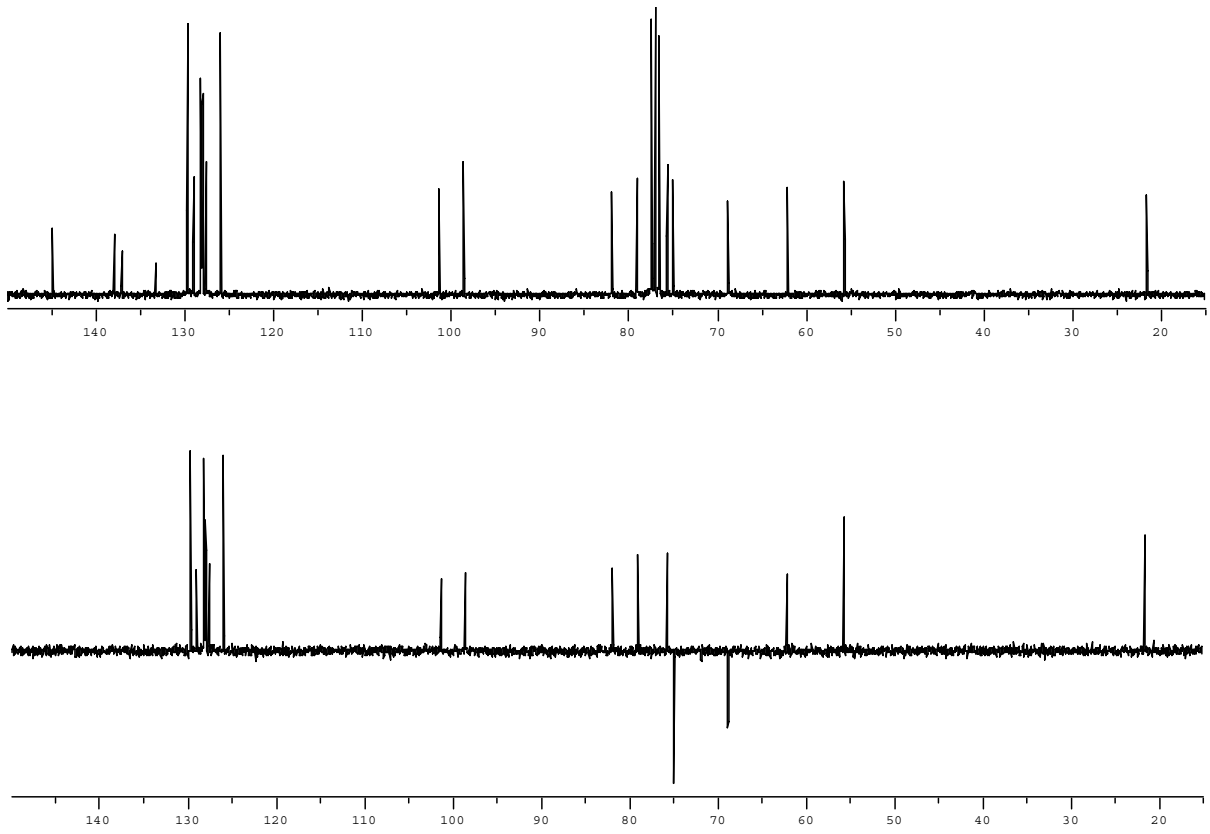

HMBC spectrum of molecule **10** ($CDCl_3$).



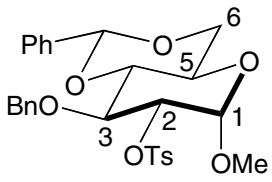
Molecule **11** ($^{1}$H NMR, 300 MHz, $CDCl_3$).

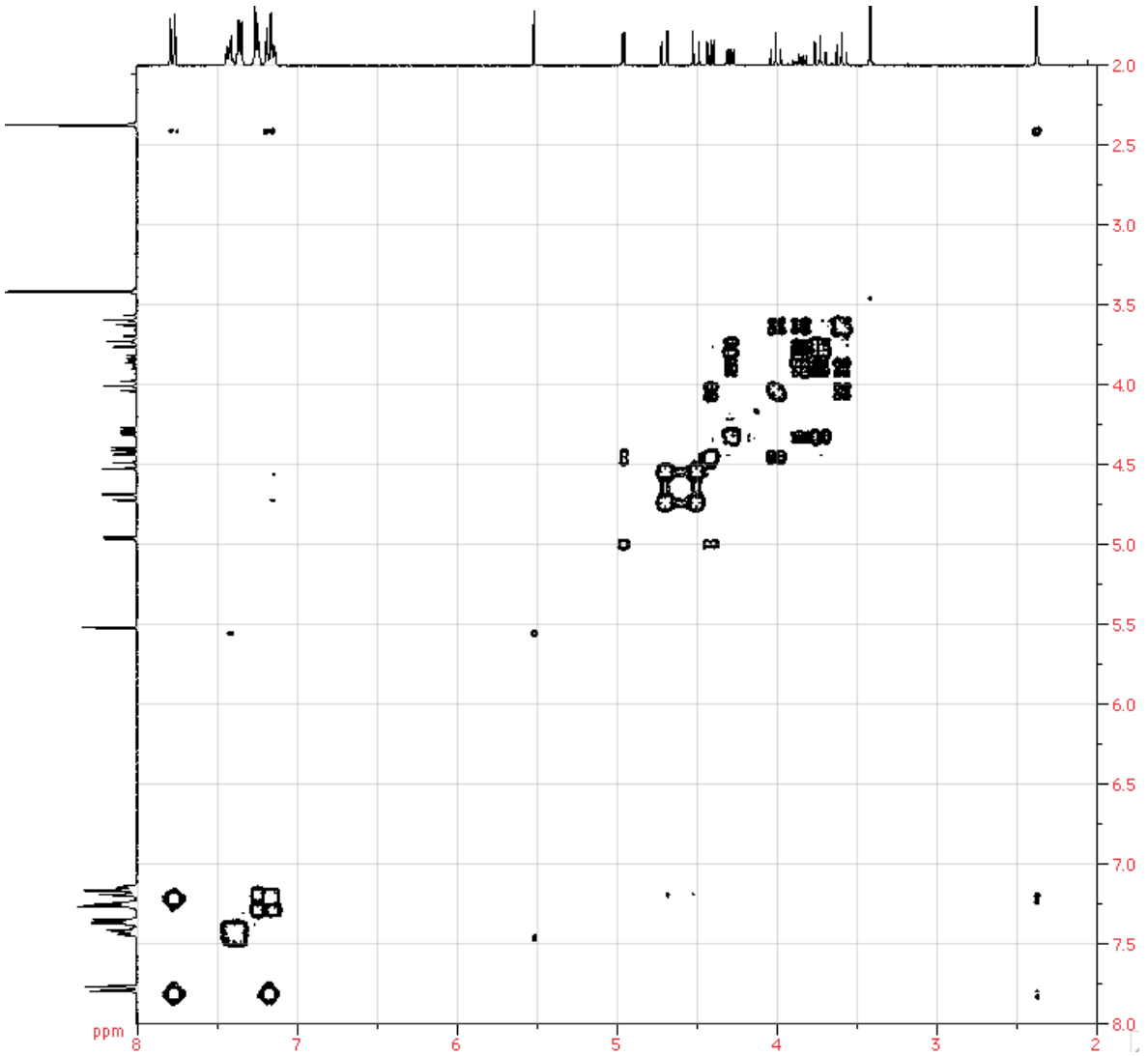



Molecule **11** ($^{13}$C NMR, 75 MHz, $CDCl_3$).

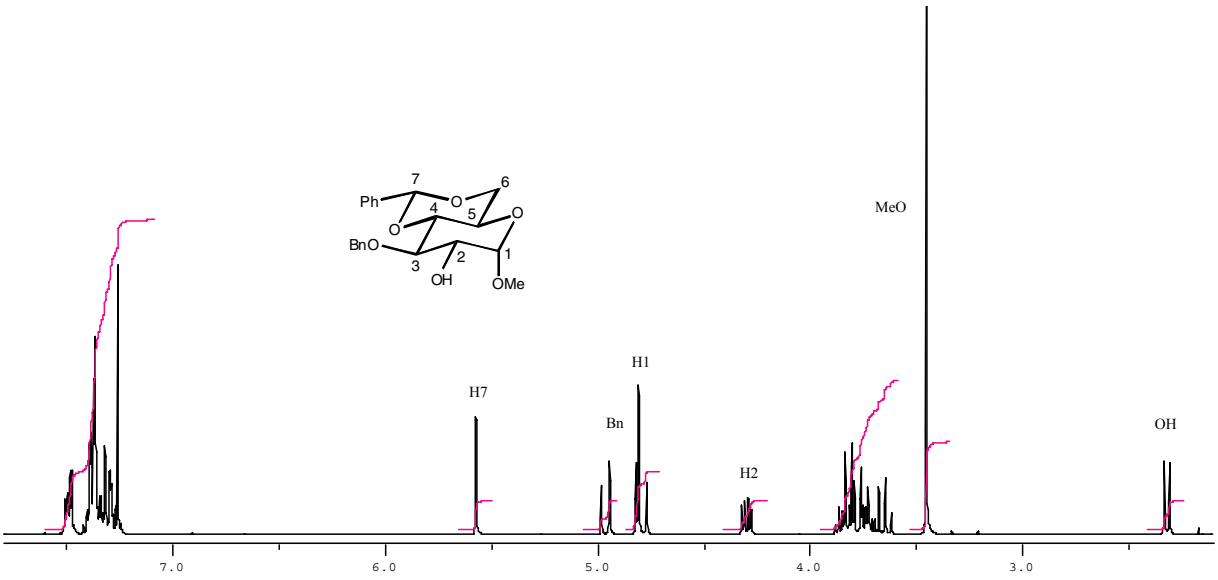



COSY spectrum of molecule **11** (300 MHz; $CDCl_3$).

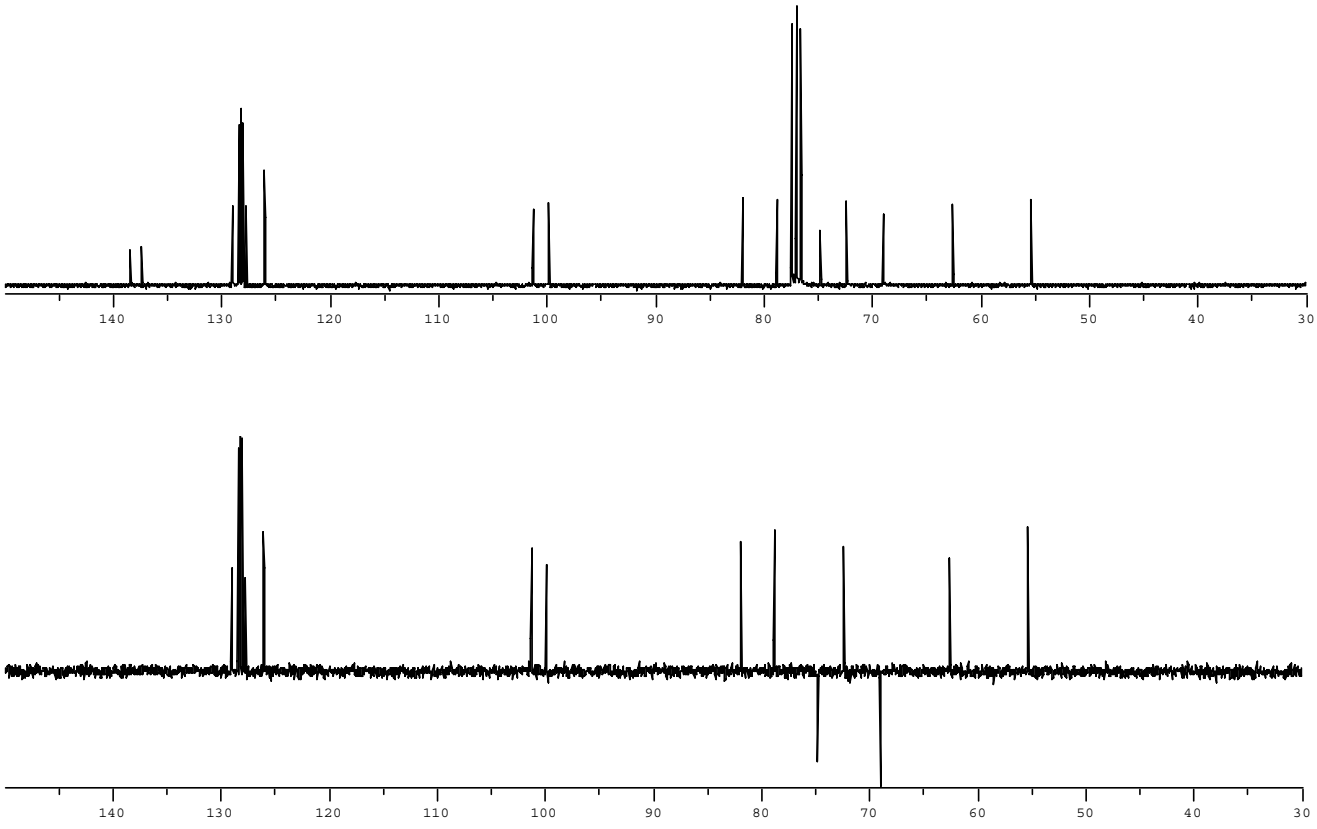


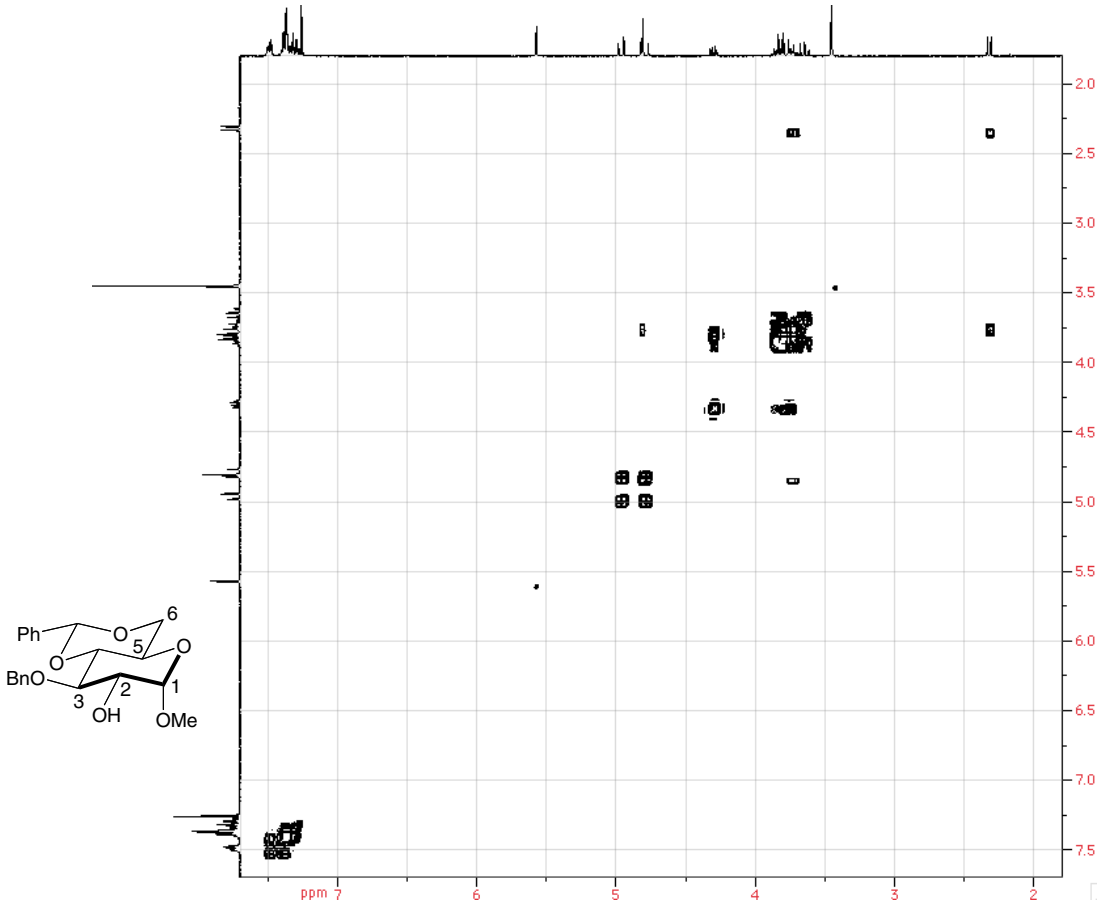

Molecule **11a** ($^{1}$H NMR, 300 MHz, $CDCl_3$)



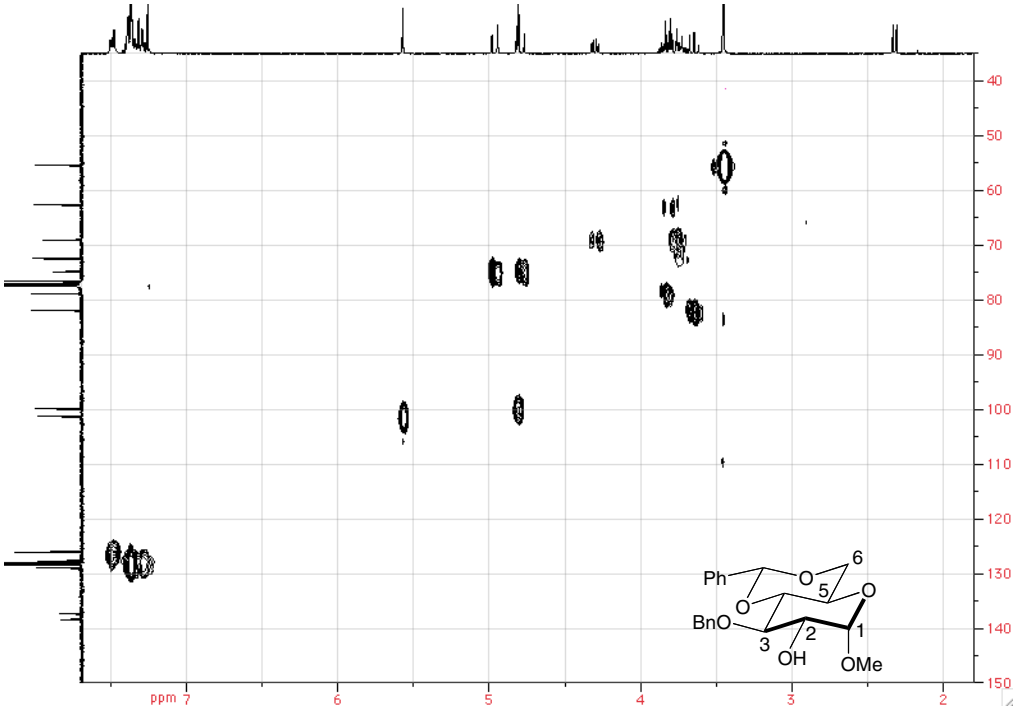

Molecule **11a** ($^{13}$C NMR, 75 MHz, $CDCl_3$).



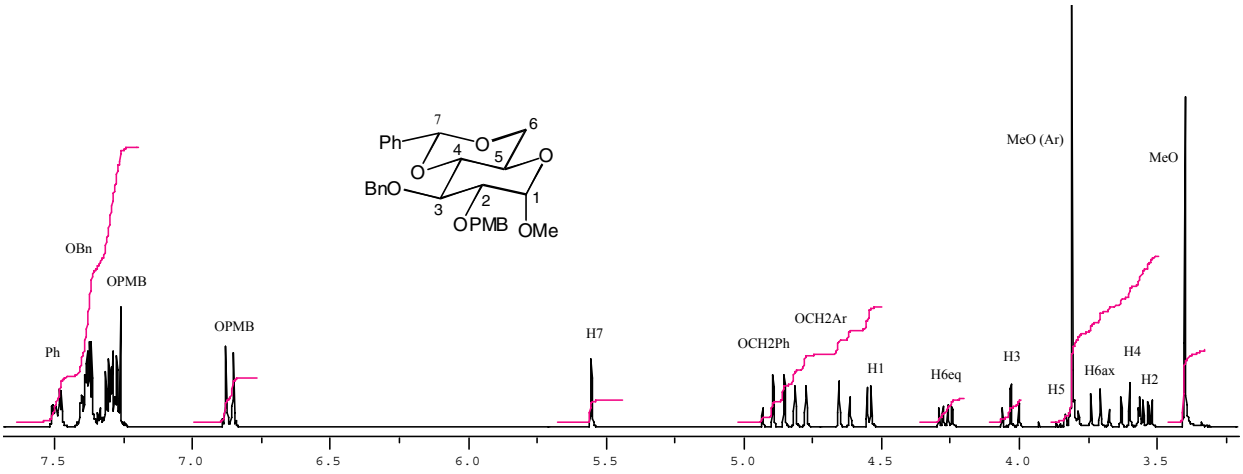

COSY spectrum of molecule **11a** (300 MHz; $CDCl_3$).



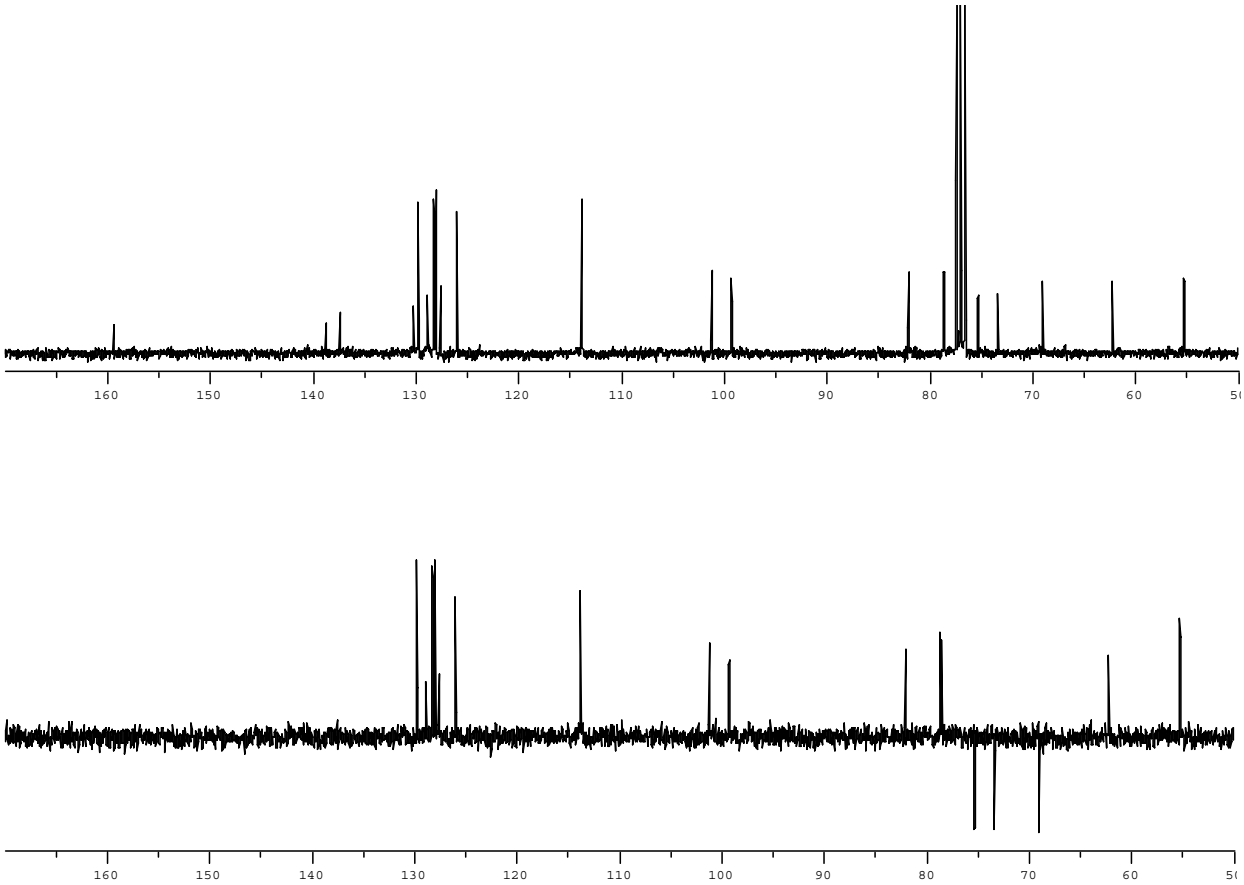

HMQC spectrum of molecule **11a** ($CDCl_3$).



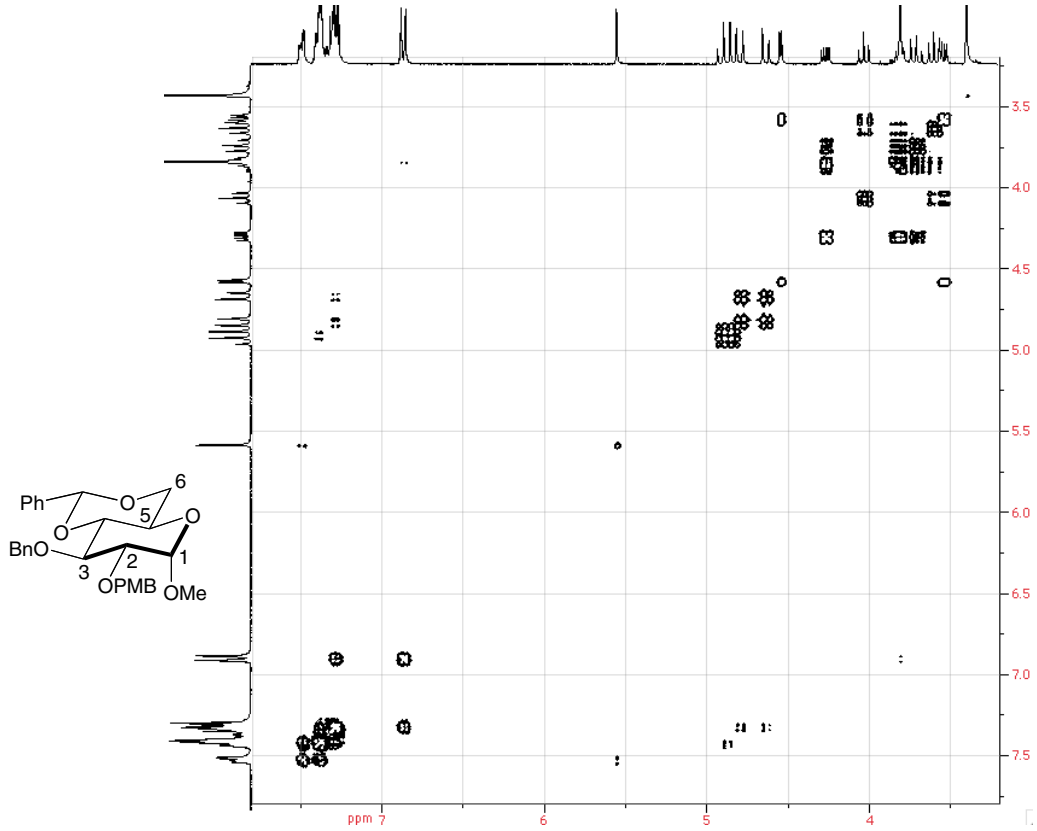

Molecule **11b** ($^1$H NMR, 300 MHz, $CDCl_3$).



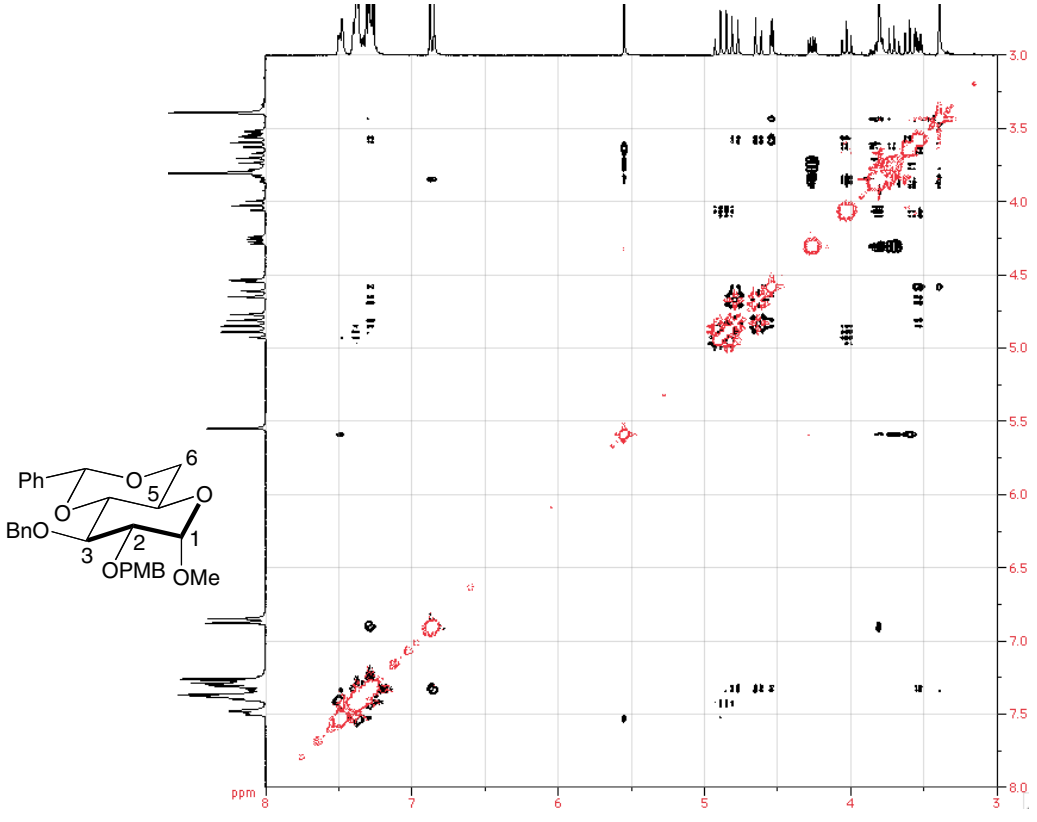

Molecule **11b** ($^{13}$C NMR, 75 MHz, $CDCl_3$).



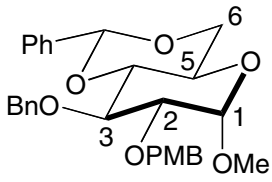

COSY spectrum of molecule **11b** (300 MHz; $CDCl_3$).

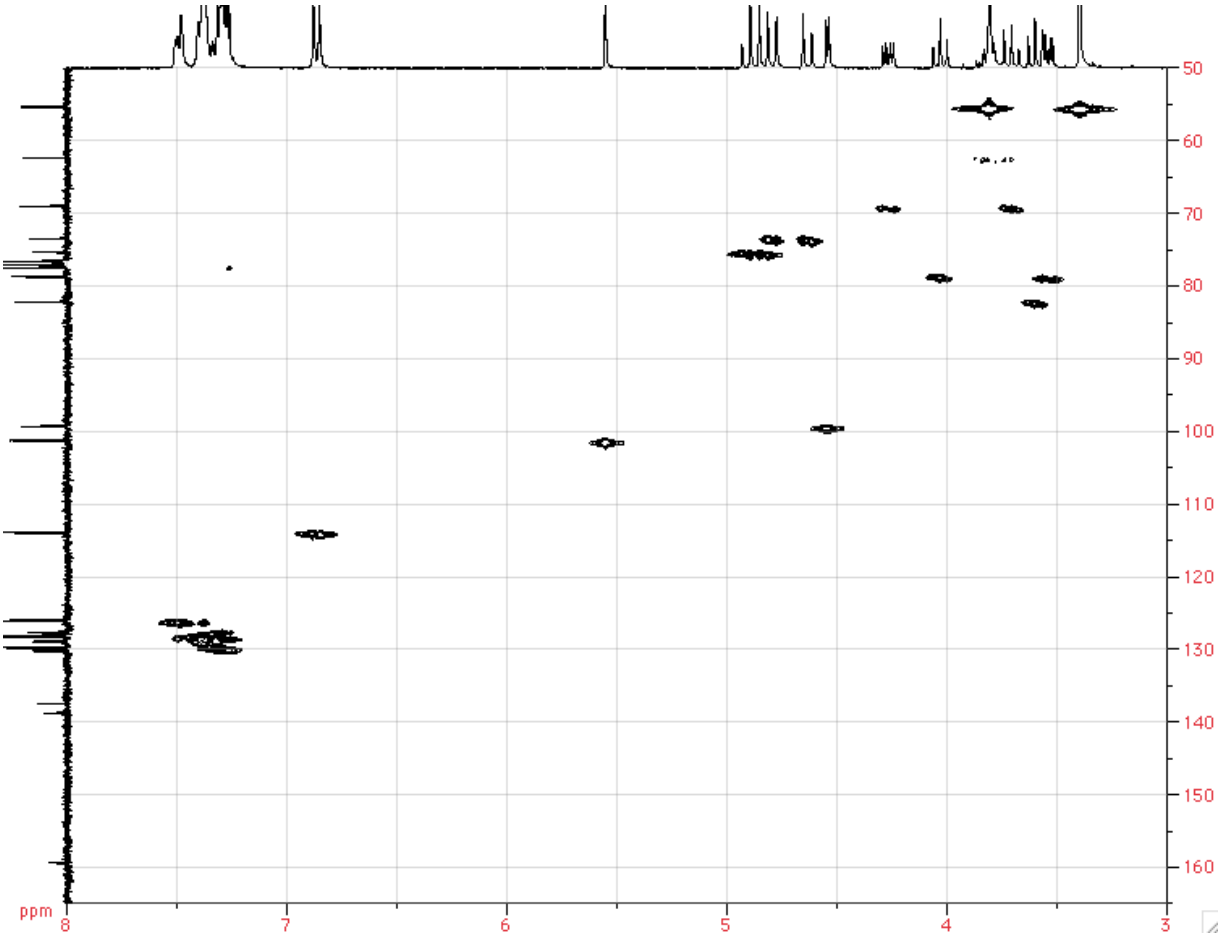



NOESY spectrum of molecule **11b** (300 MHz; $CDCl_3$).

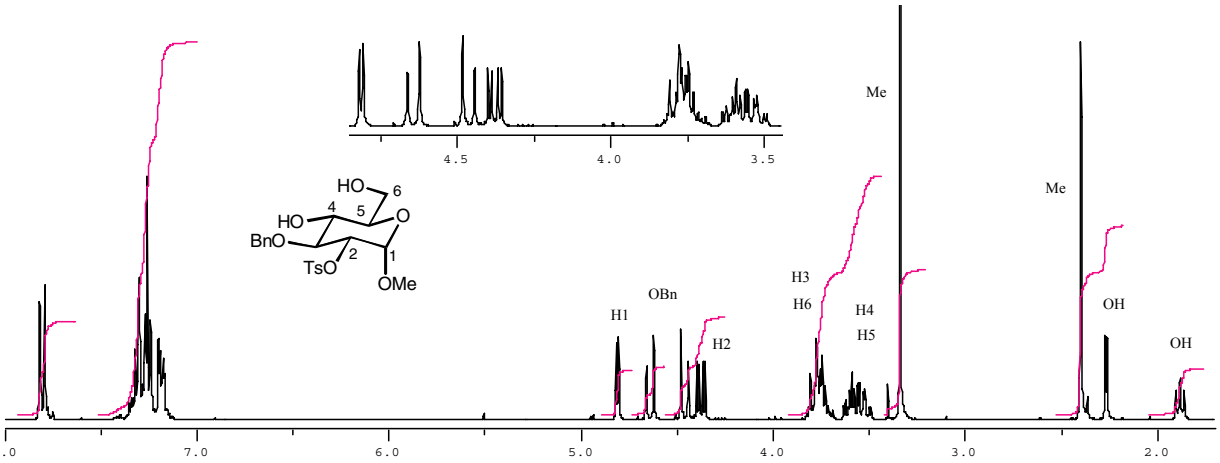



HMQC spectrum of molecule **11b** ($CDCl_3$).

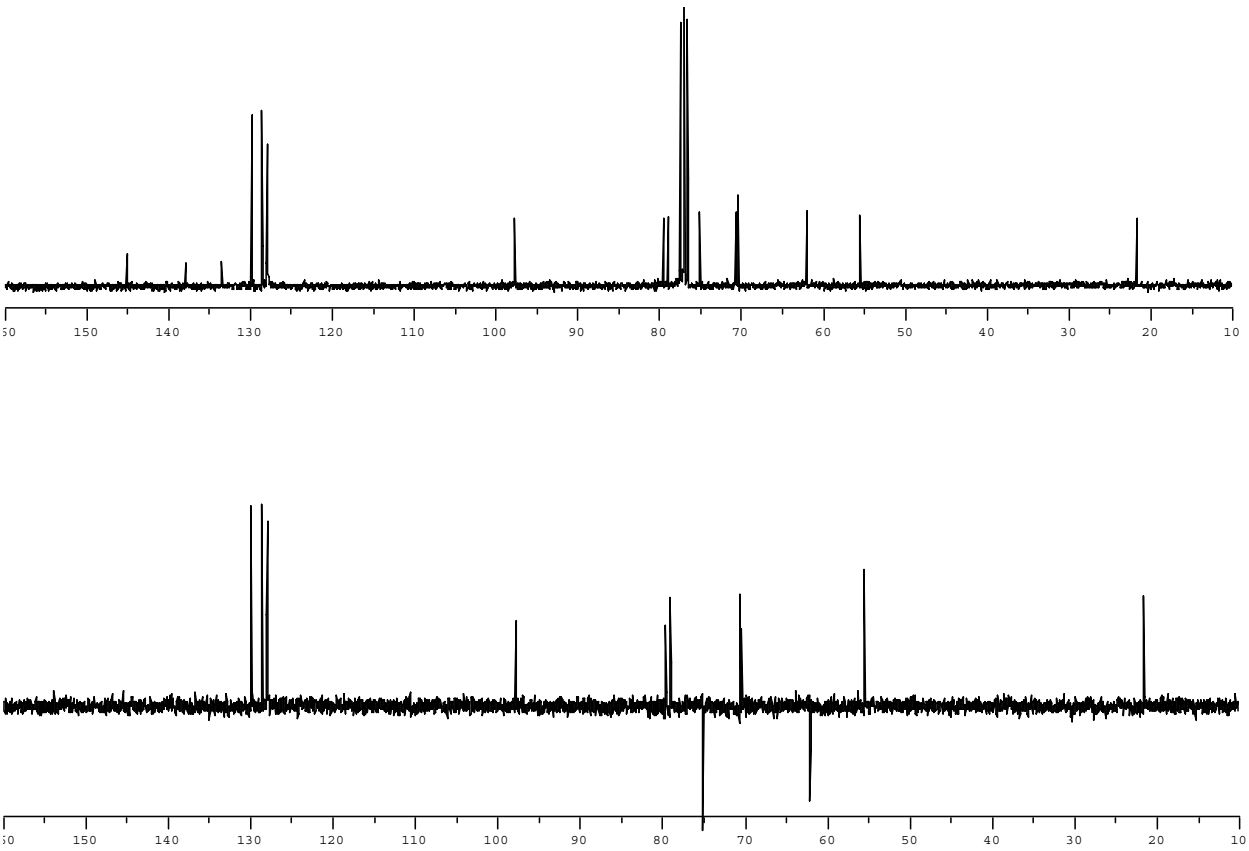


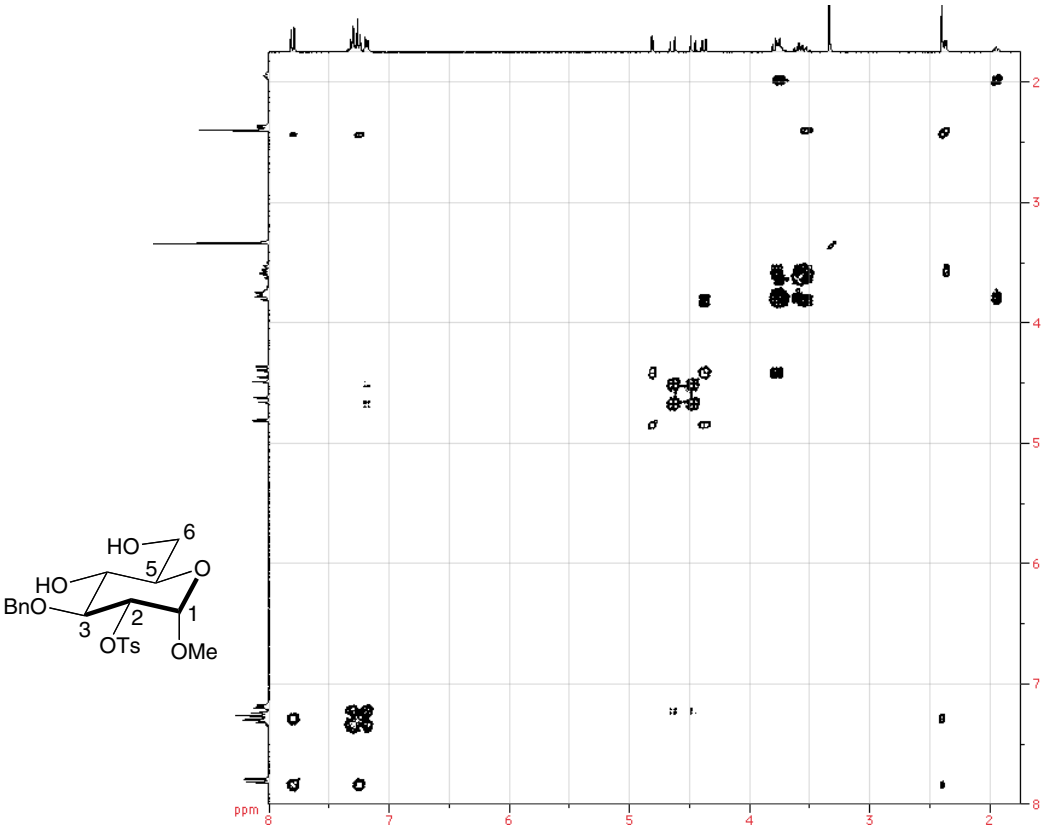

Molecule **12** ($^1$H NMR, 300 MHz, $CDCl_3$).



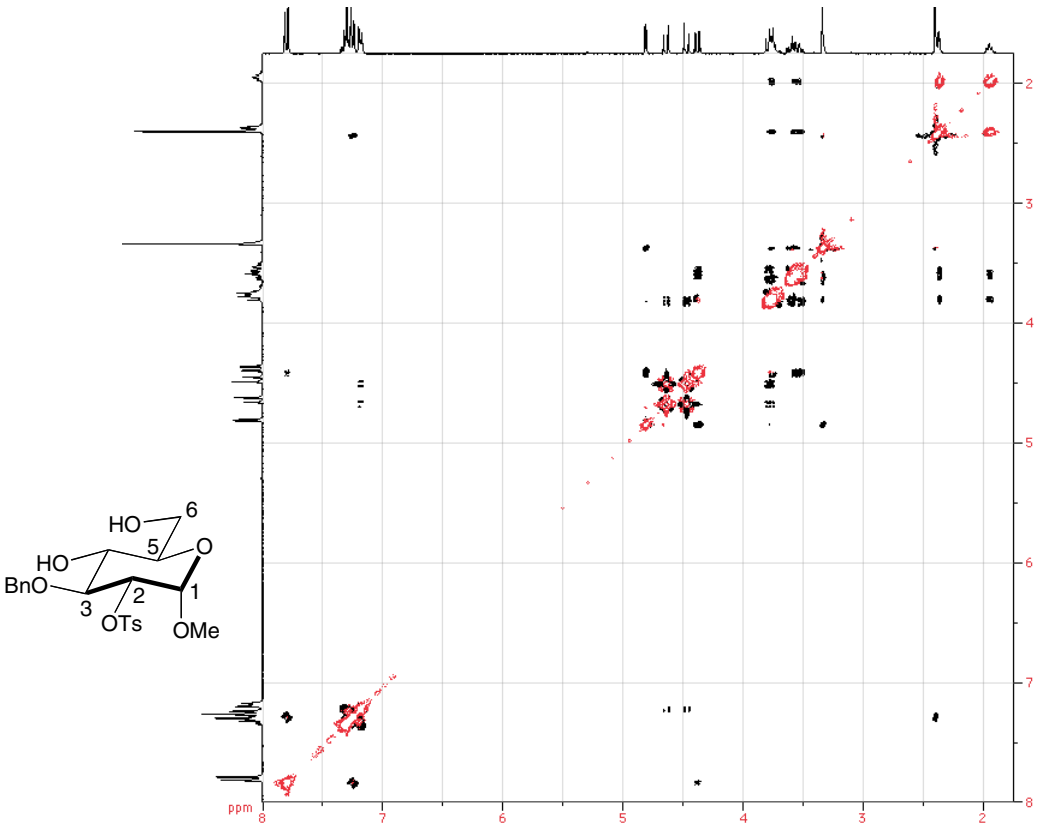

Molecule **12** ($^{13}$C NMR, 75 MHz, $CDCl_3$).



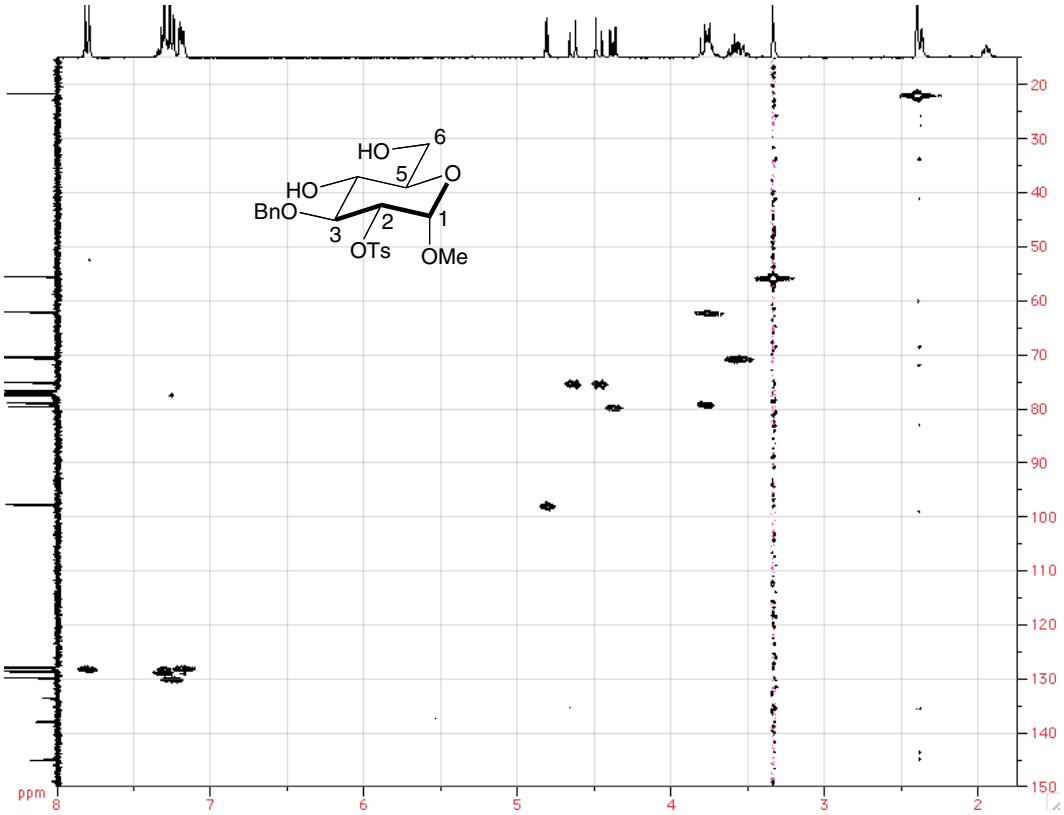
COSY spectrum of molecule **12** (300 MHz; $CDCl_3$).



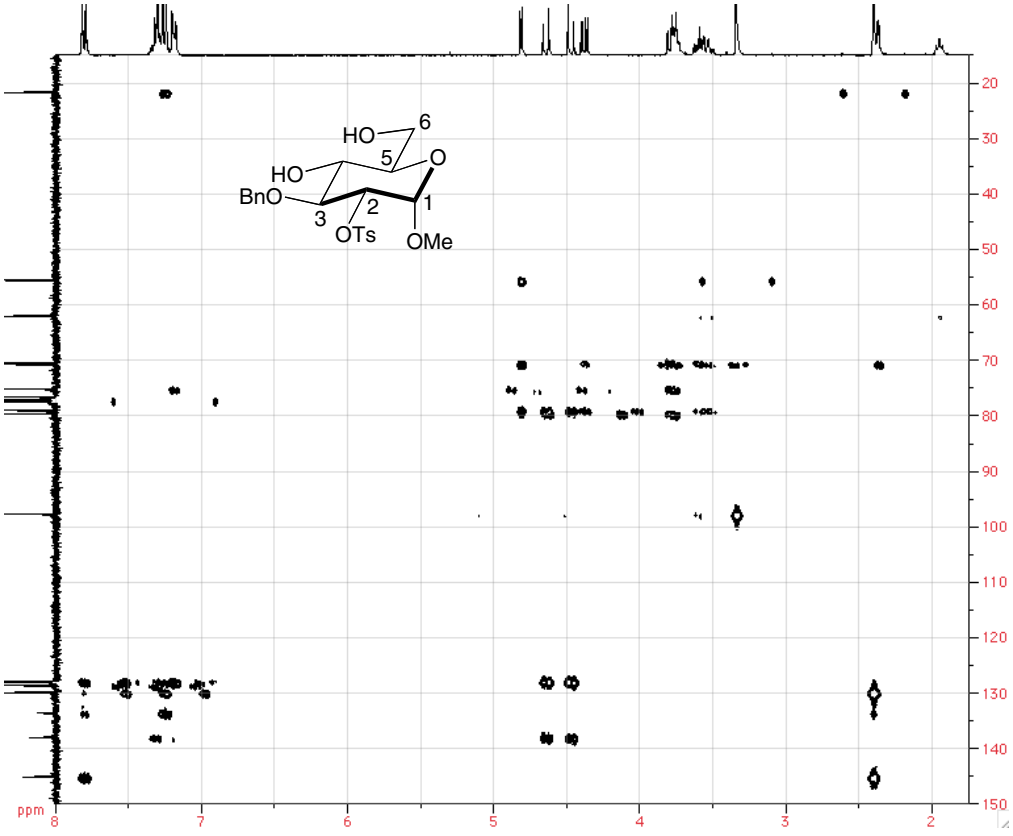

NOESY spectrum of molecule **12** (300 MHz; $CDCl_3$).



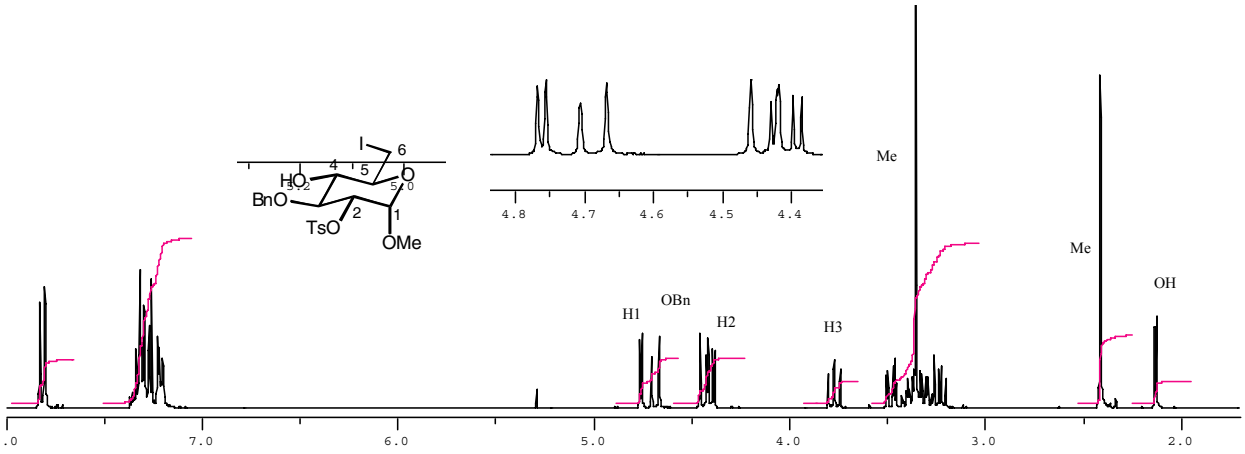

HMQC spectrum of molecule **12** ($CDCl_3$).



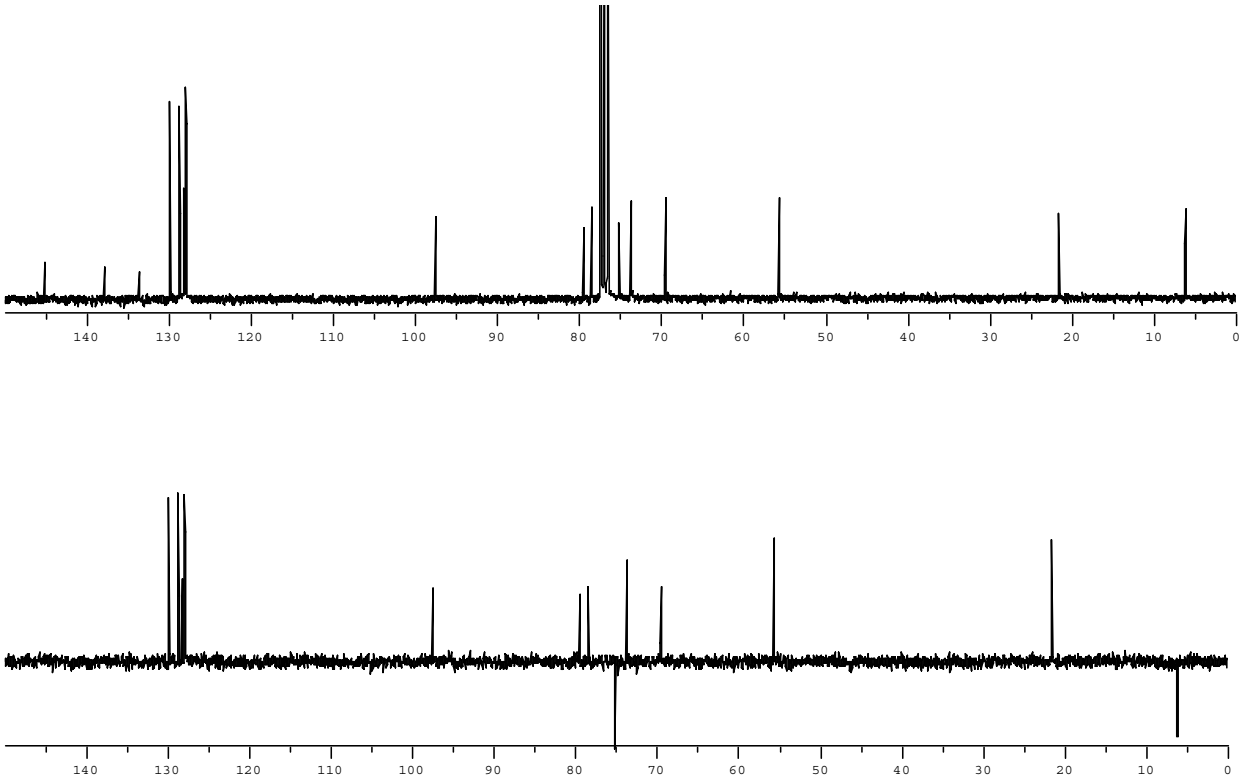

HMBC spectrum of molecule **12** ($CDCl_3$).



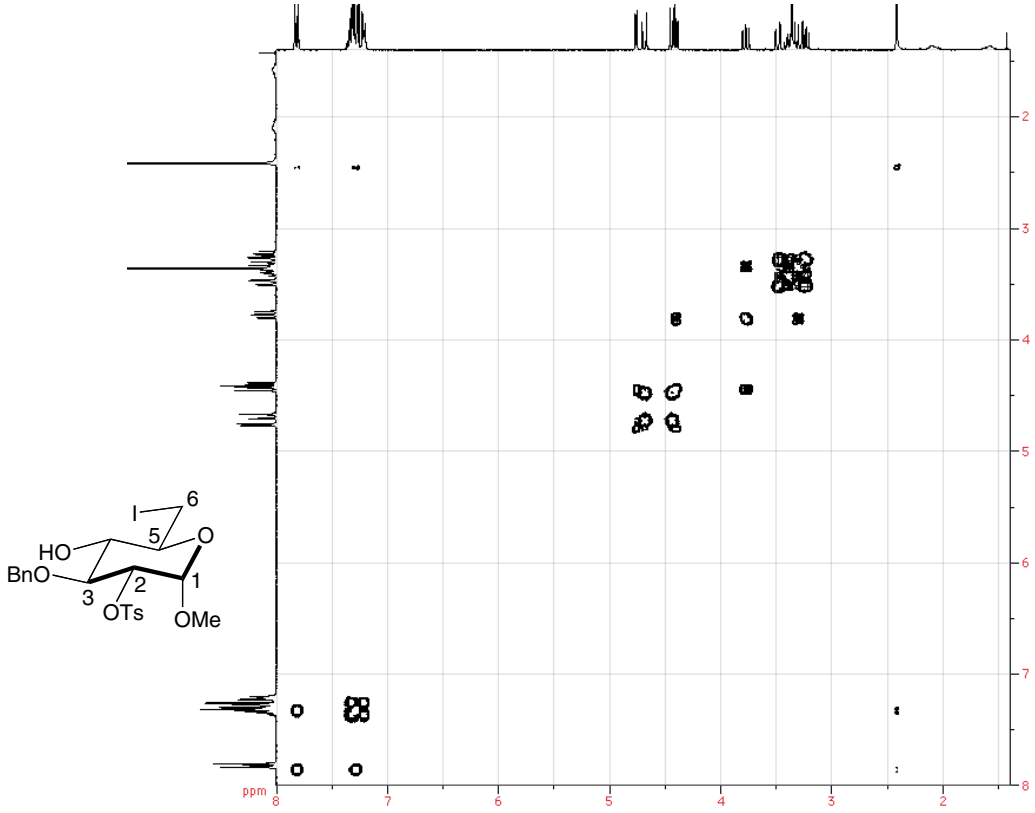

Molecule **13** ($^1$H NMR, 300 MHz, $CDCl_3$).



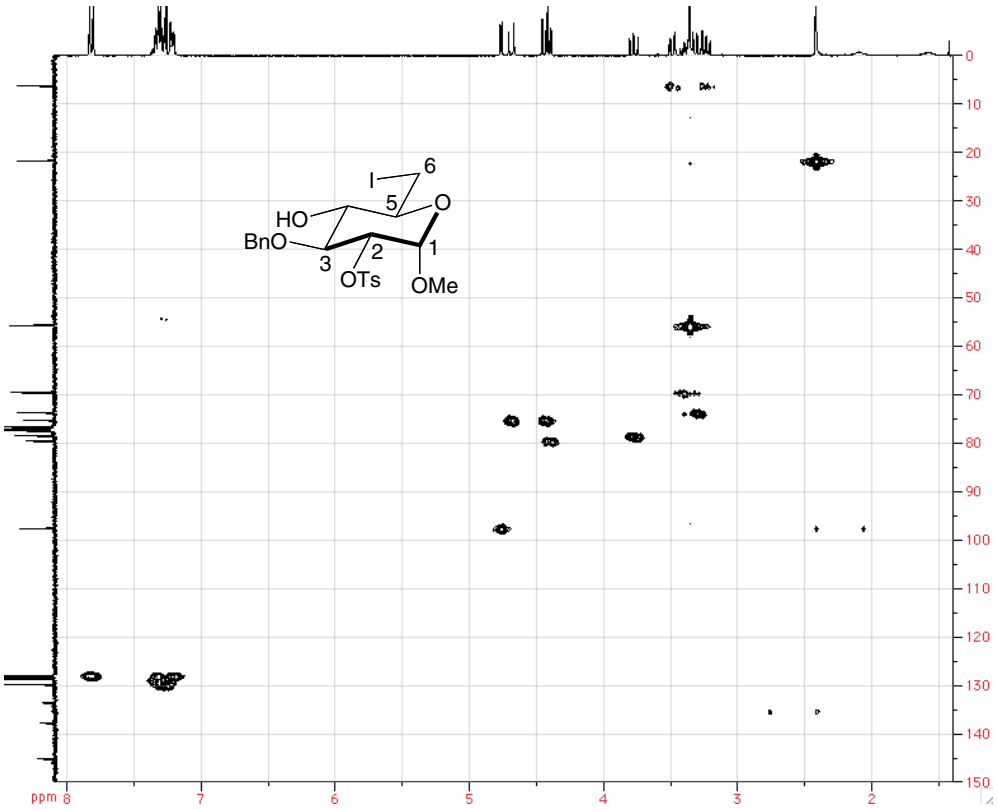

Molecule **13** ($^{13}$C NMR, 75 MHz, $CDCl_3$).



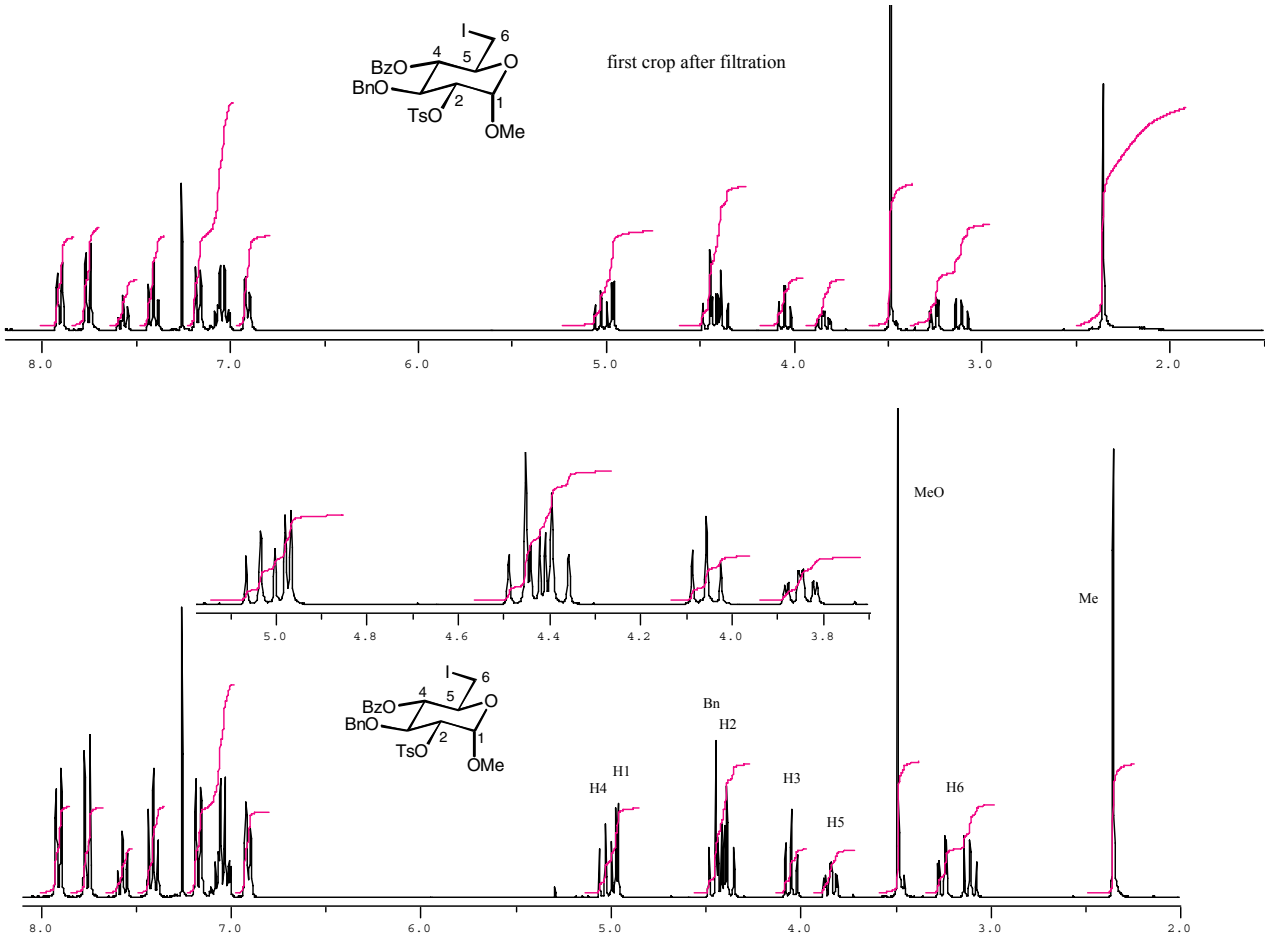
COSY spectrum of molecule **13** (300 MHz; $CDCl_3$).



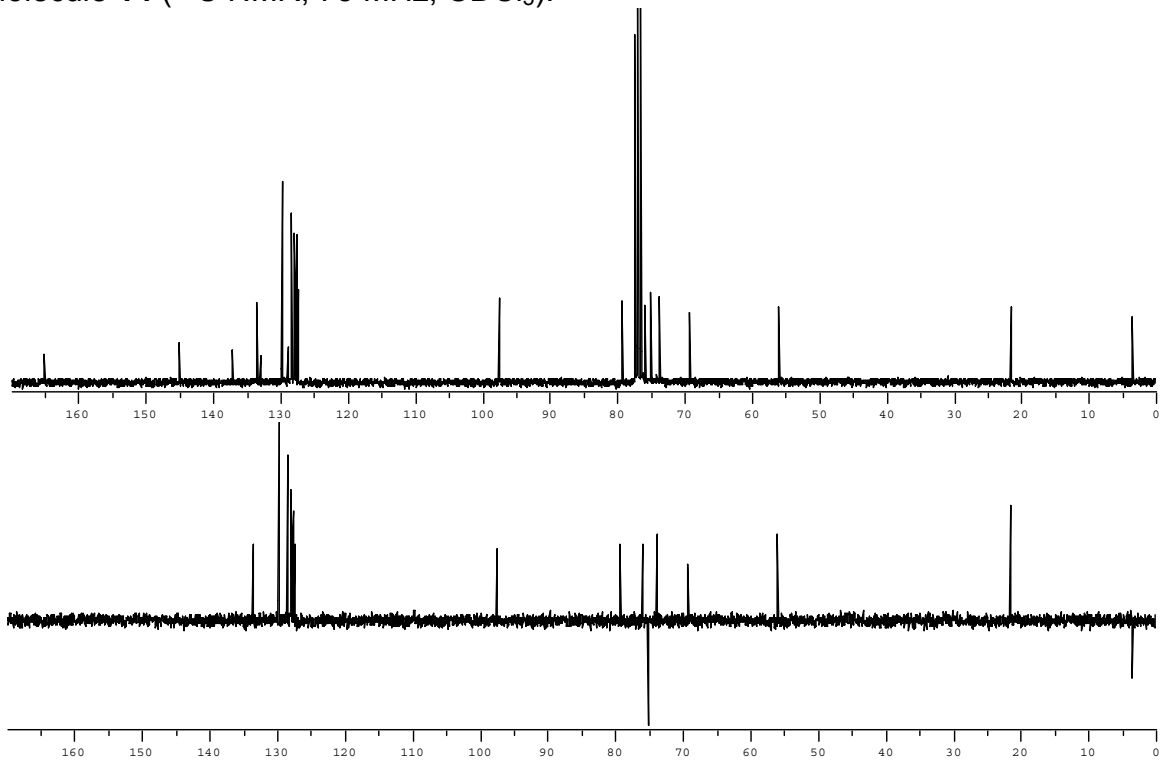

HMQC spectrum of molecule **13** ($CDCl_3$).



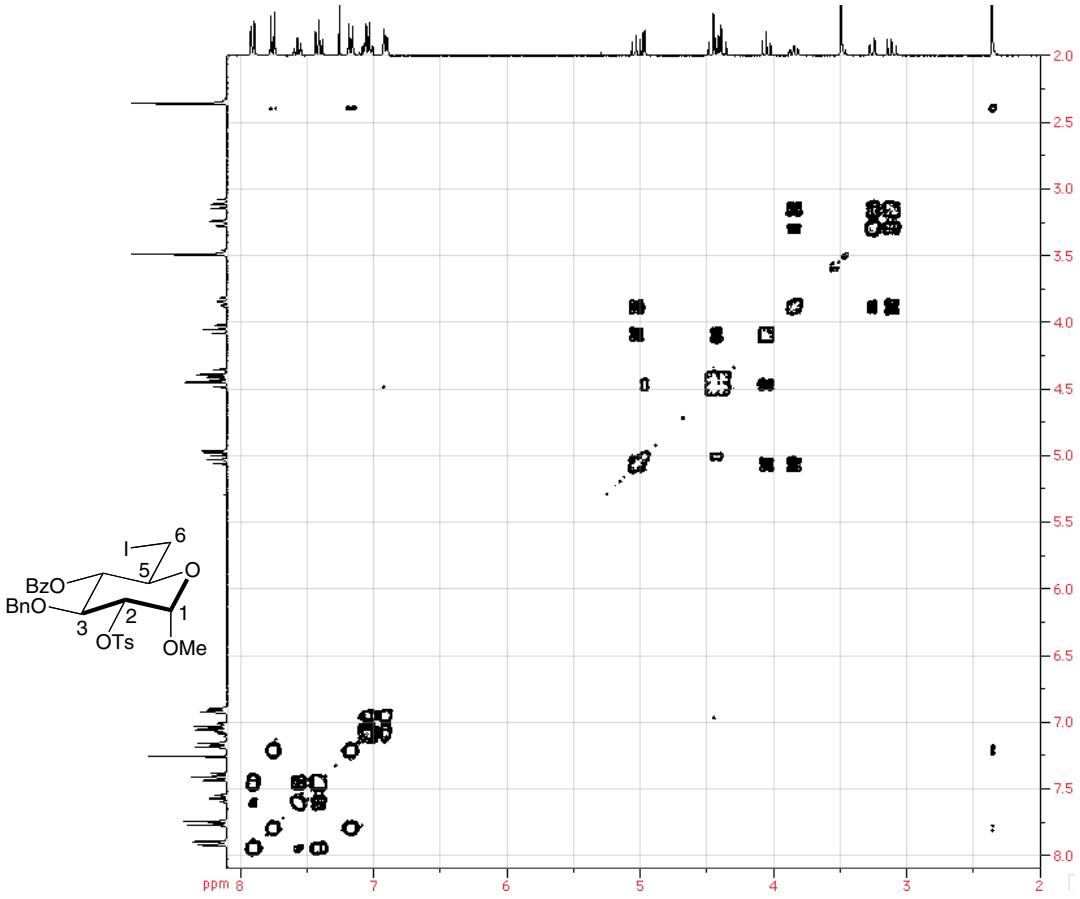

Molecule **14** ($^1$H NMR, 300 MHz, $CDCl_3$).



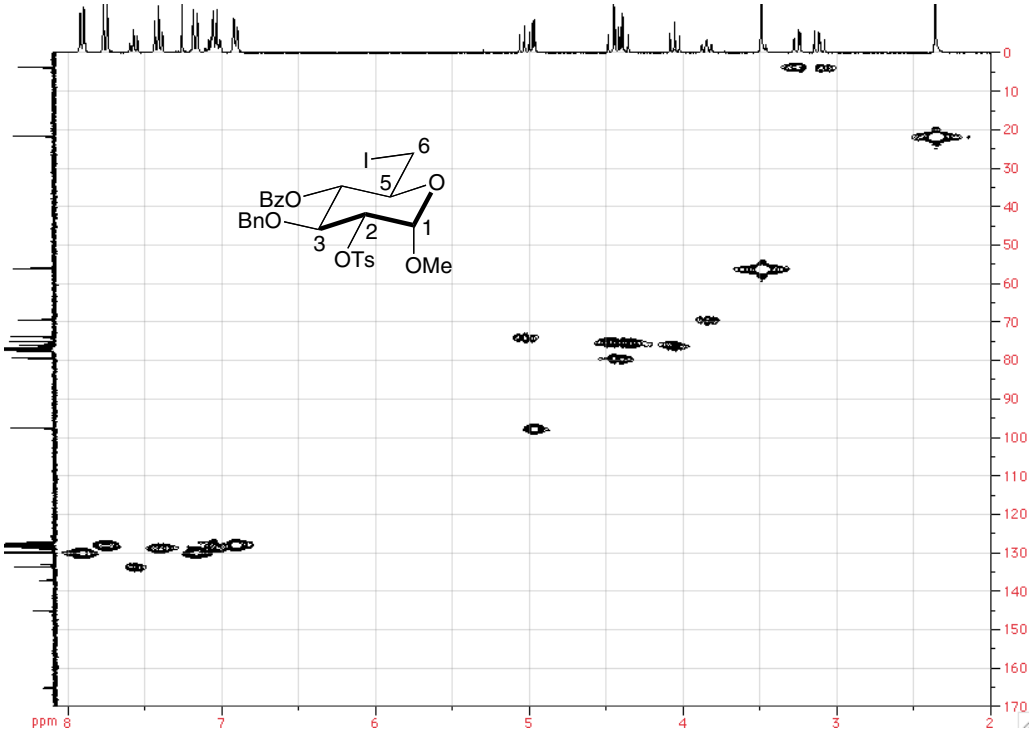

Molecule **14** ($^{13}$C NMR, 75 MHz, $CDCl_3$).



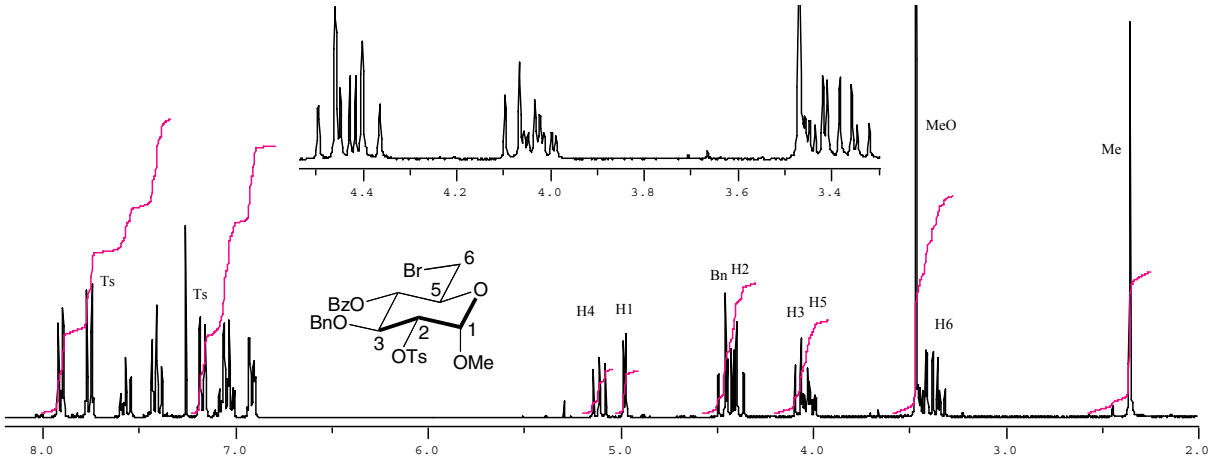
COSY spectrum of molecule **14** (300 MHz; $CDCl_3$).



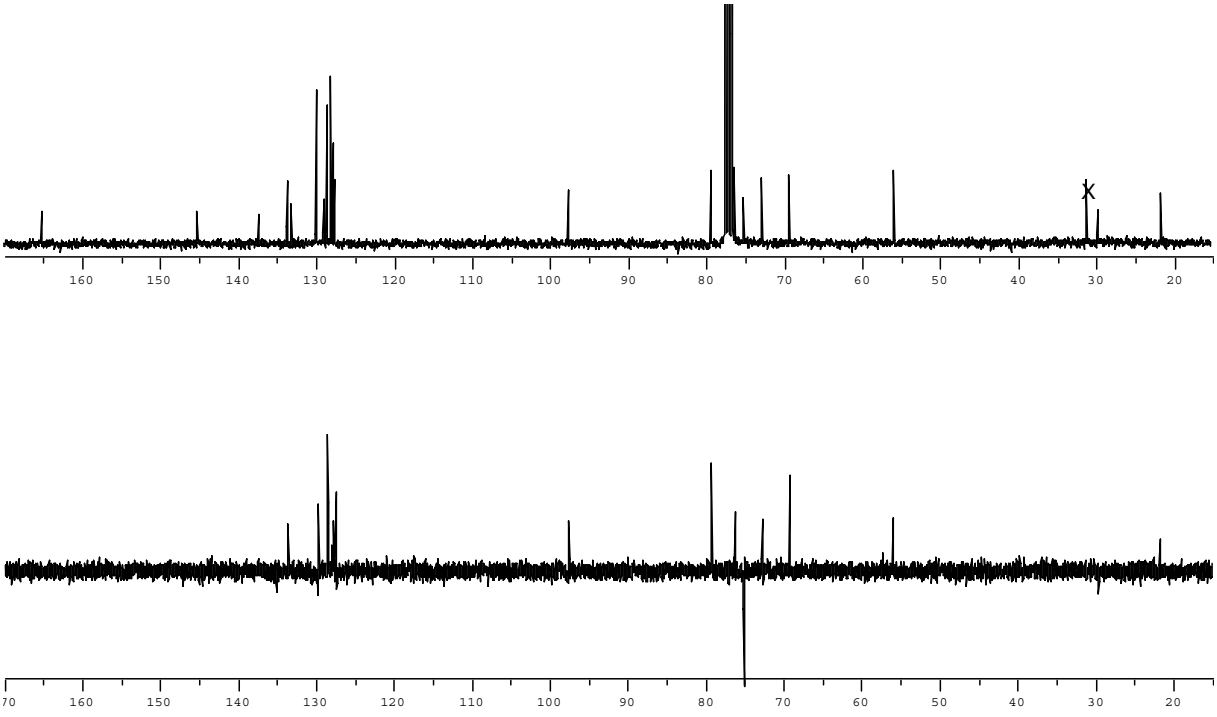

HMQC spectrum of molecule **14** ($CDCl_3$).



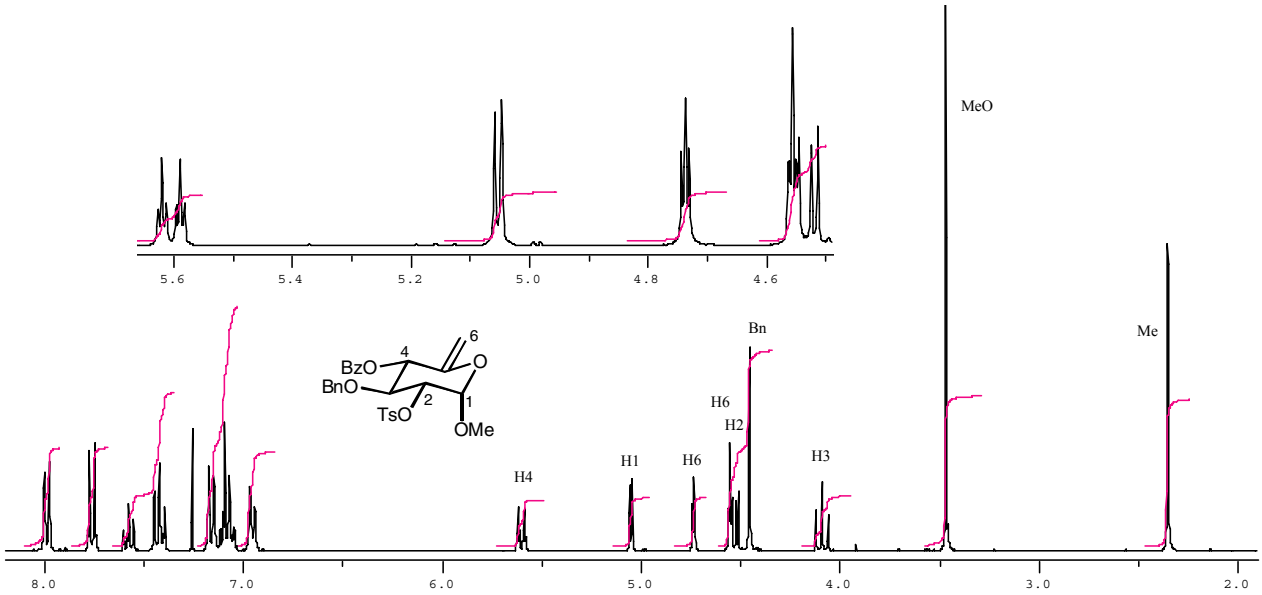

Molecule **14a** ($^1$H NMR, 300 MHz, $CDCl_3$).



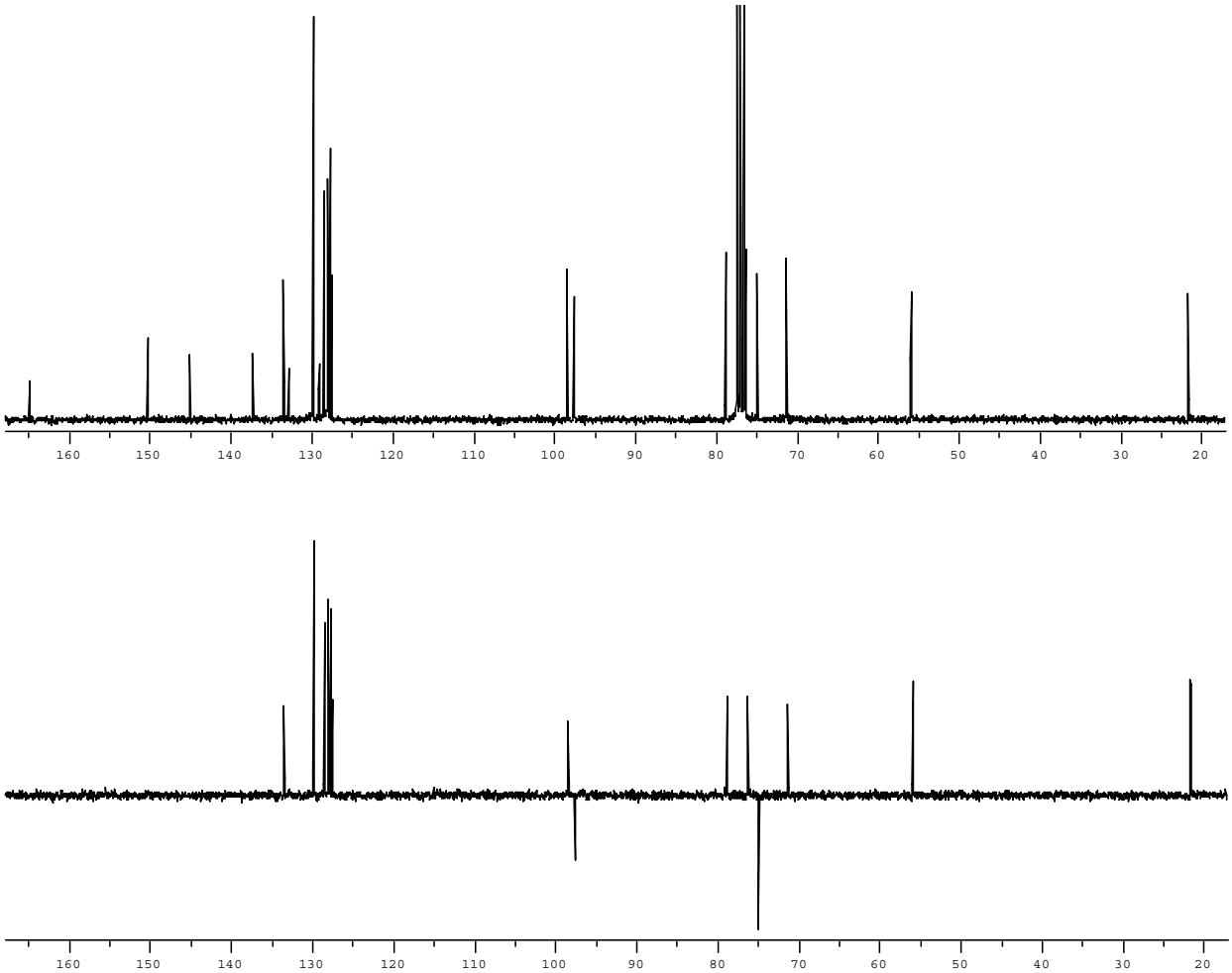

Molecule **14a** ($^{13}$C NMR, 75 MHz, $CDCl_3$).



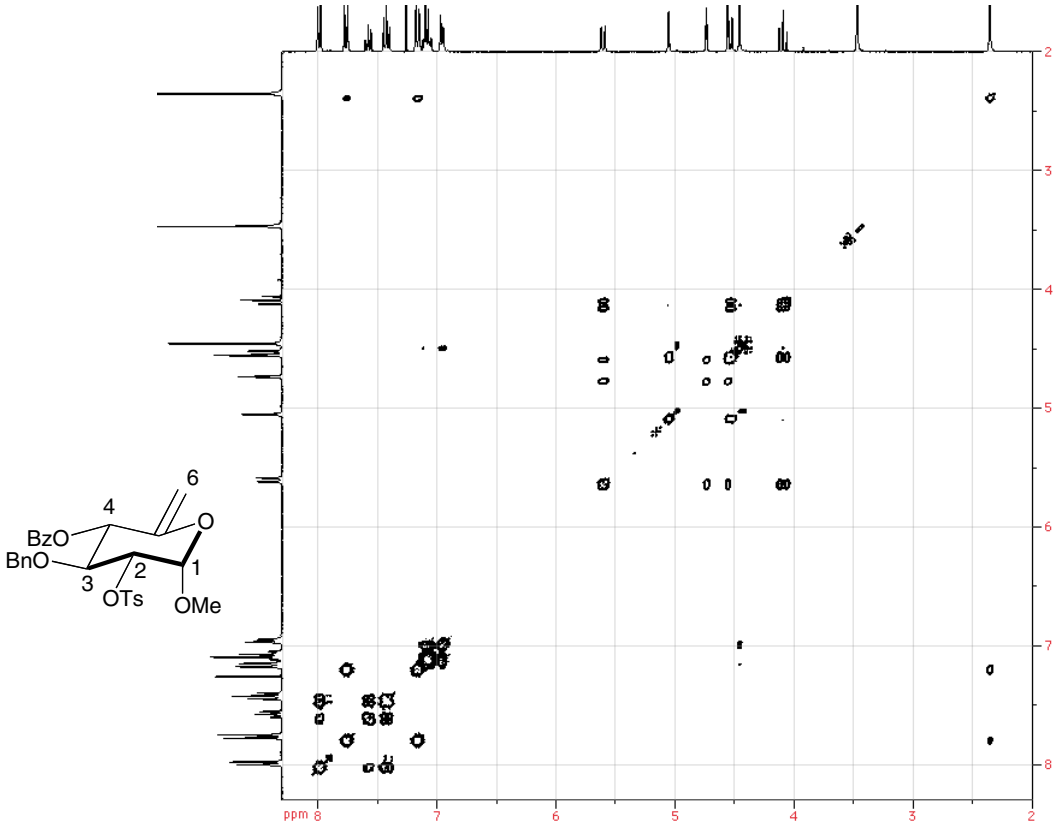

Molecule **15** ($^{1}$H NMR, 300 MHz, $CDCl_3$).



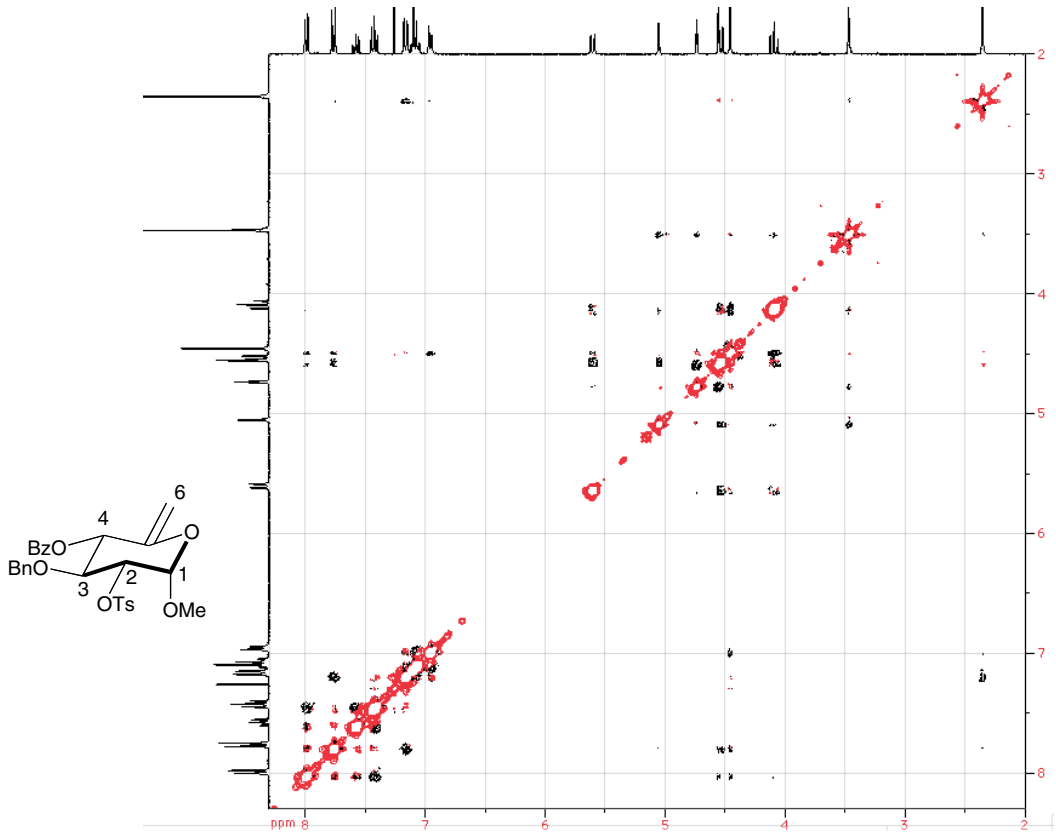

Molecule **15** ($^{13}$C NMR, 75 MHz, $CDCl_3$).



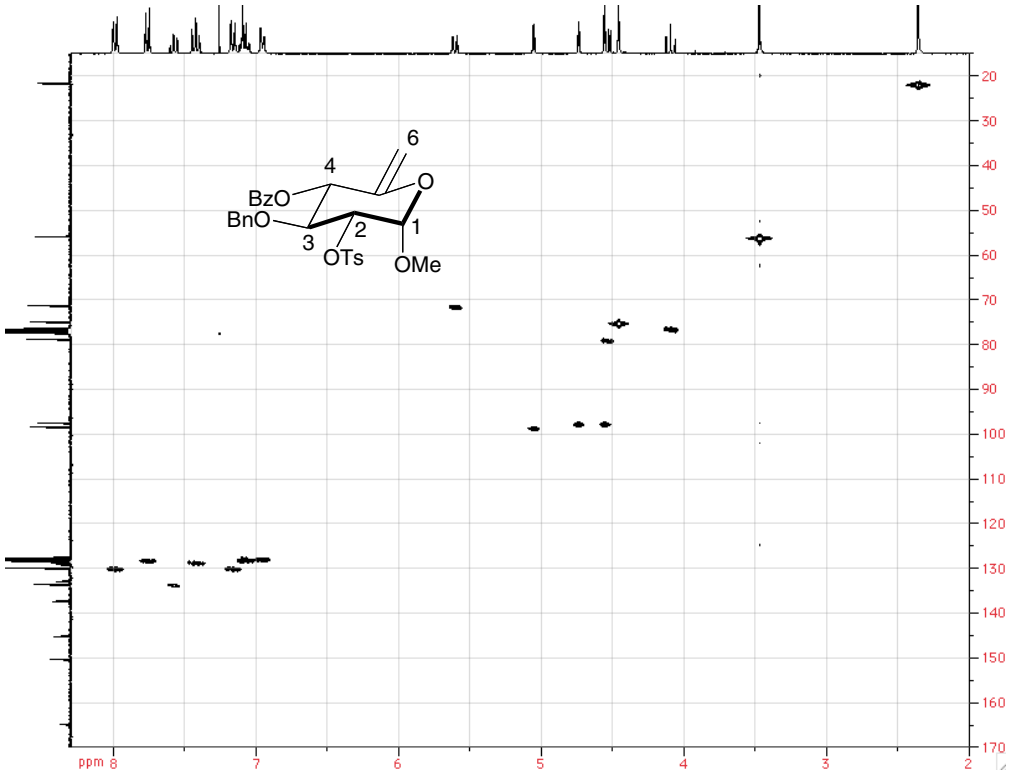
COSY spectrum of molecule **15** (300 MHz; $CDCl_3$).



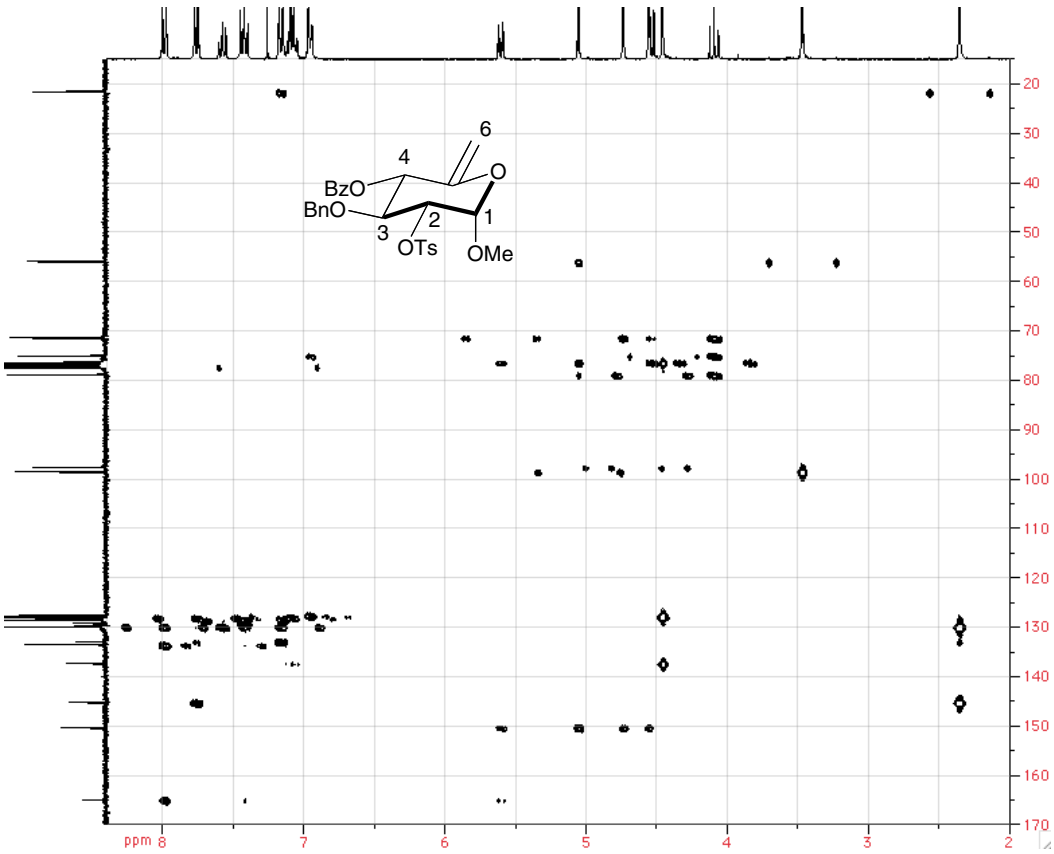

NOESY spectrum of molecule **15** (300 MHz; $CDCl_3$).



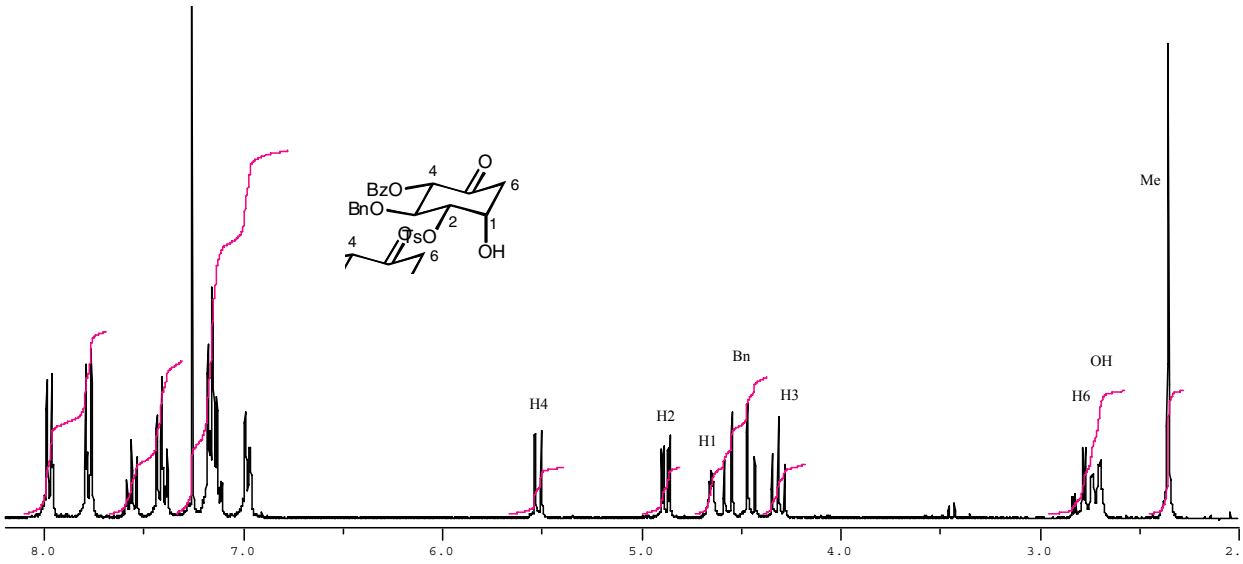

HMQC spectrum of molecule **15** ($CDCl_3$).



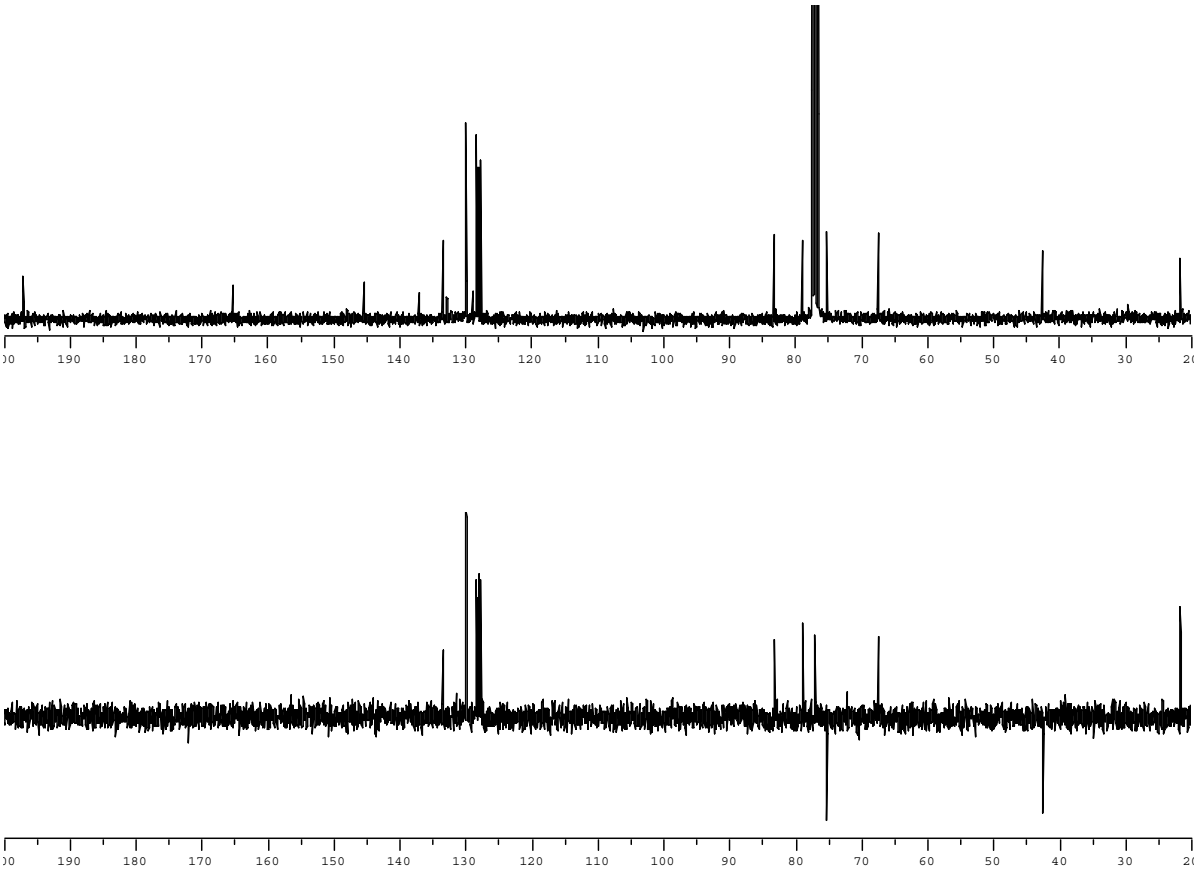

HMBC spectrum of molecule **15** ($CDCl_3$).



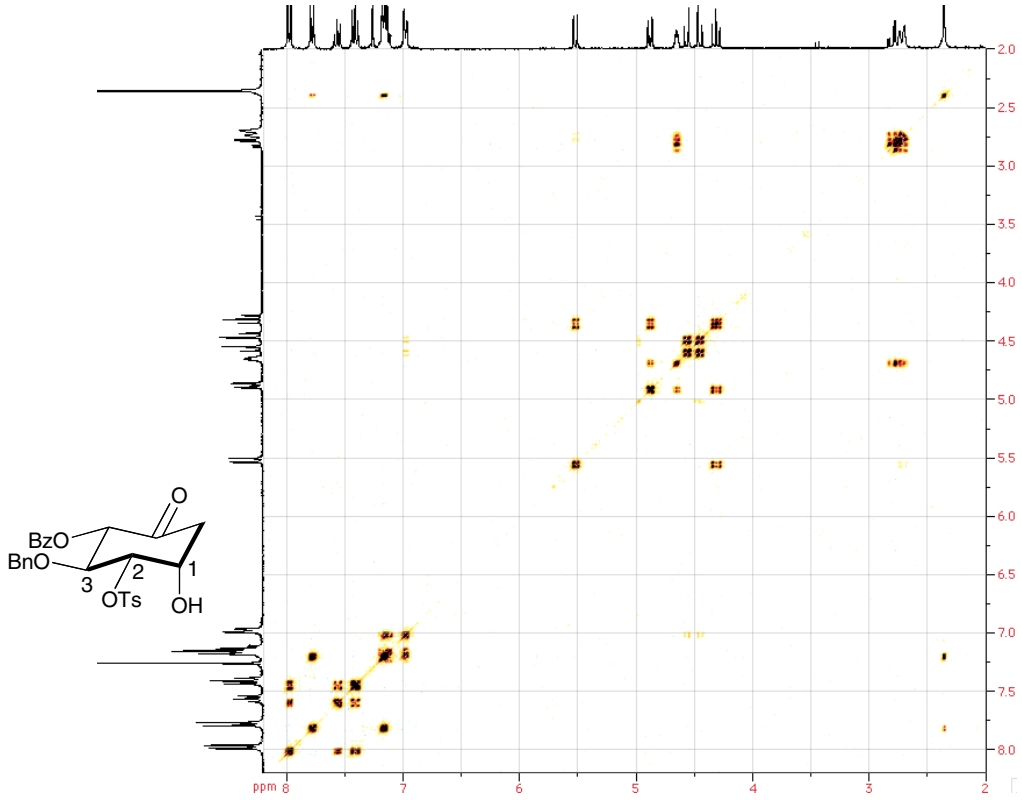

Molecule **16** ($^1$H NMR, 300 MHz, $CDCl_3$).



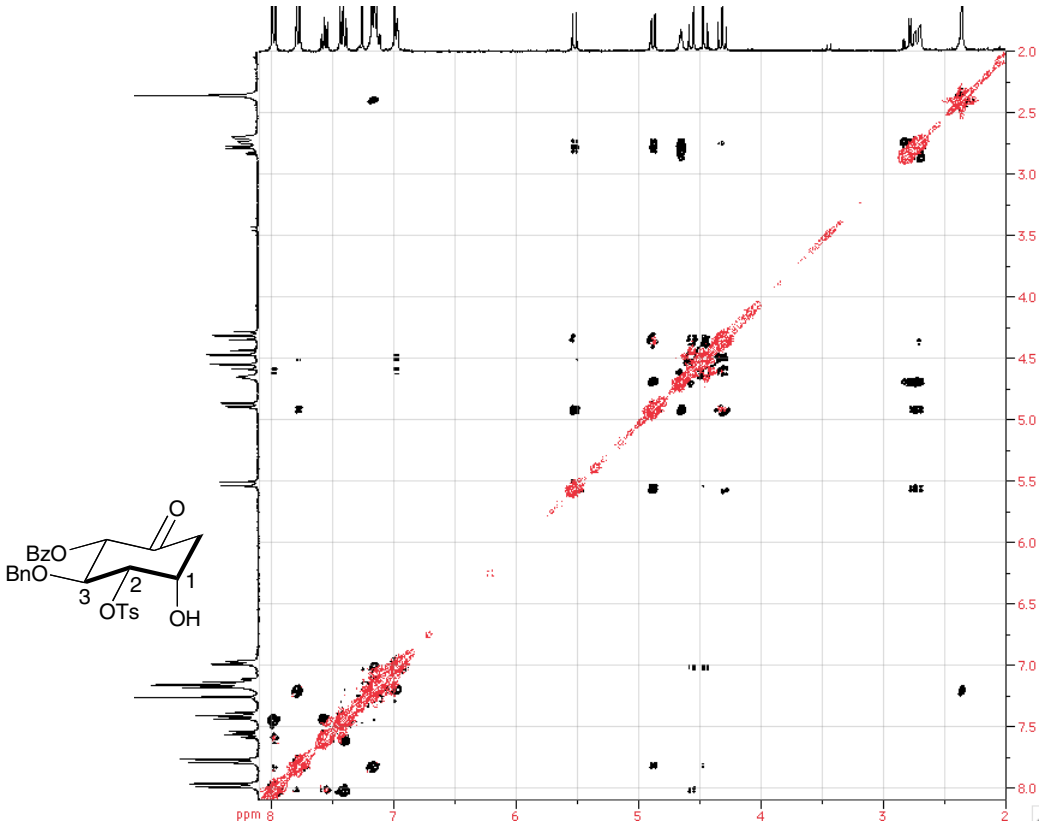

Molecule **16** ($^{13}$C NMR, 75 MHz, $CDCl_3$).



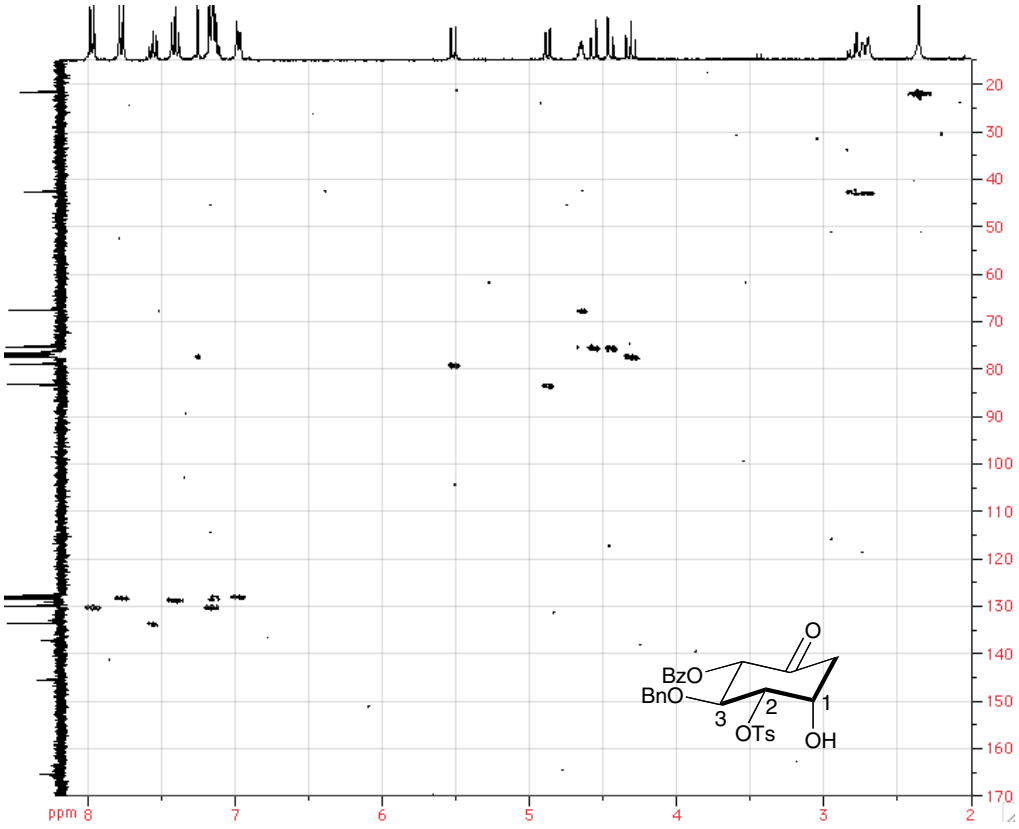
COSY spectrum of molecule **16** (300 MHz; $CDCl_3$).



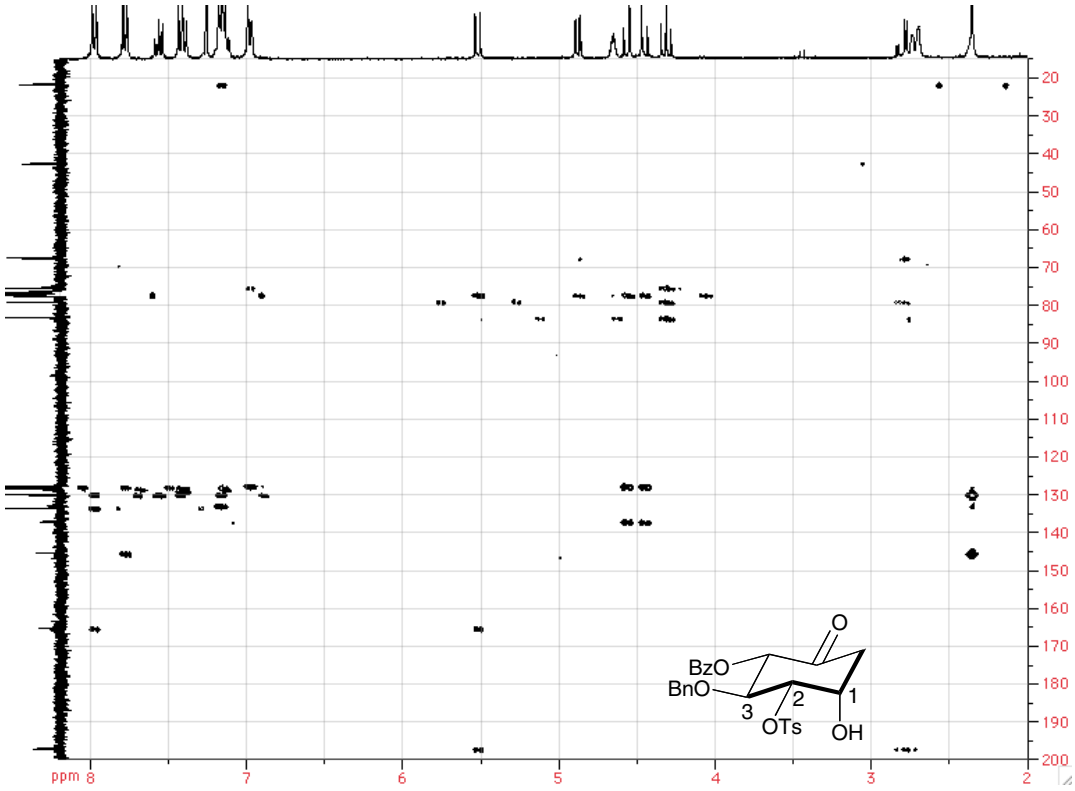

NOESY spectrum of molecule **16** (300 MHz; $CDCl_3$).



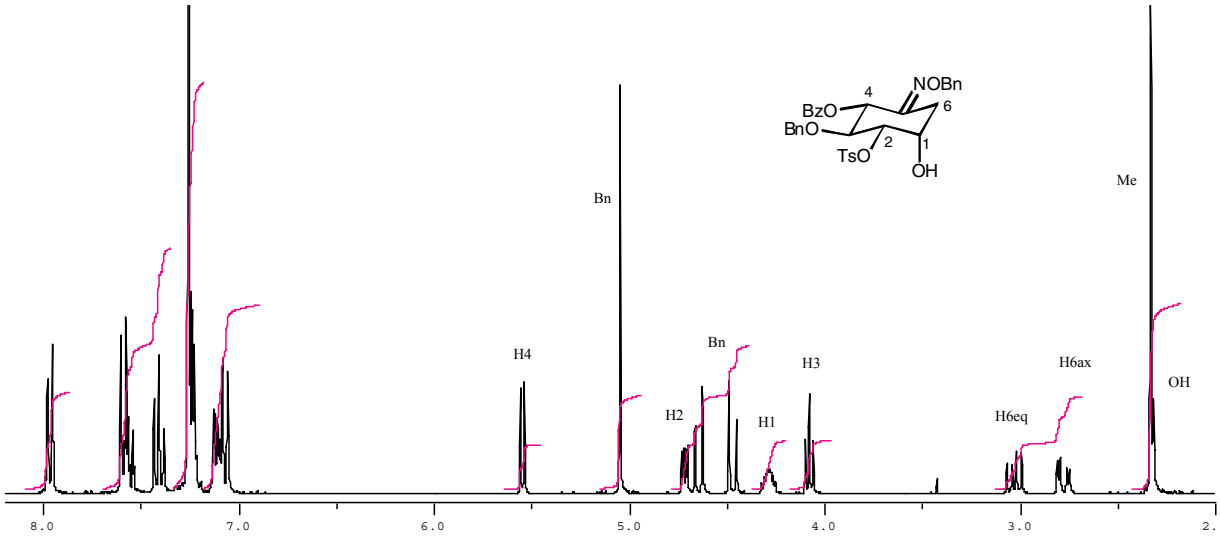

HMQC spectrum of molecule **16** ($CDCl_3$).



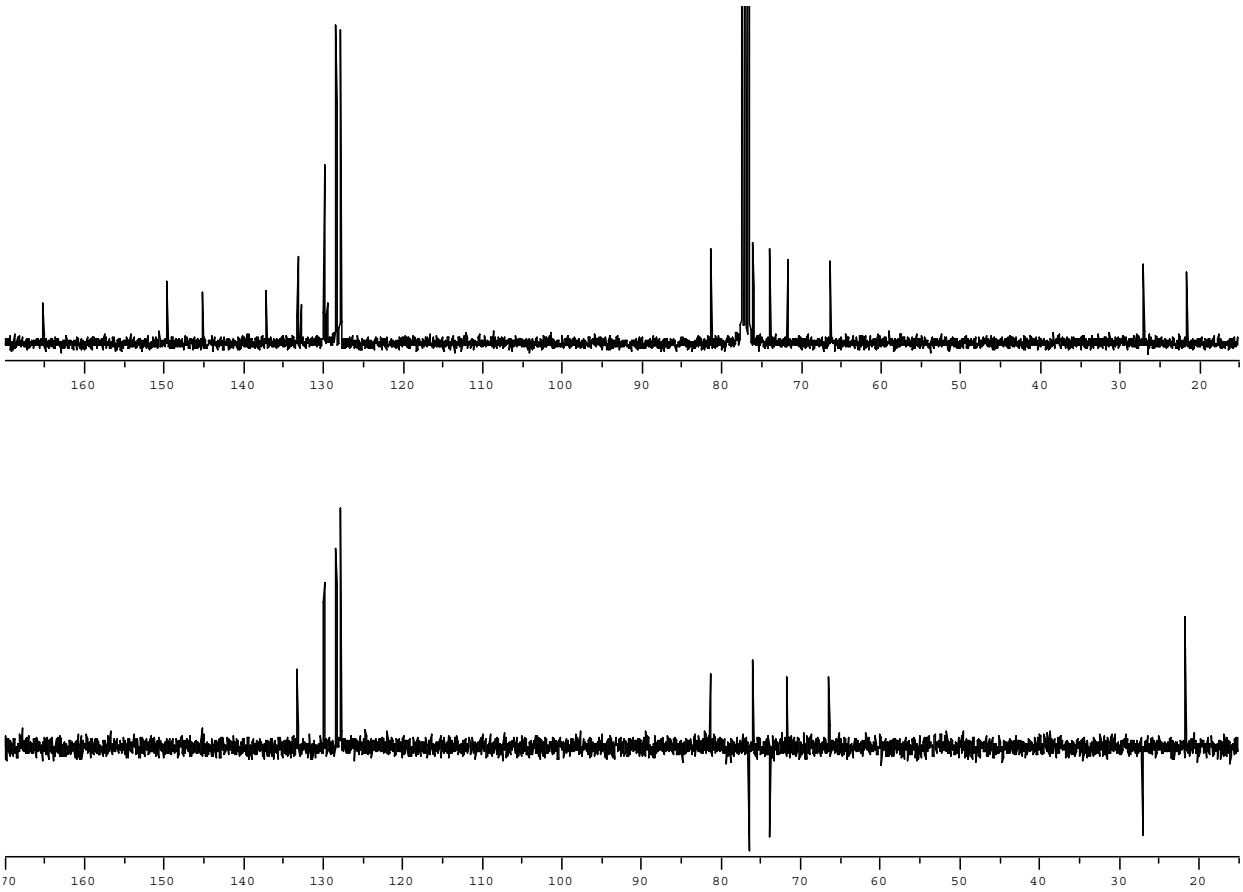

HMBC spectrum of molecule **16** ($CDCl_3$).



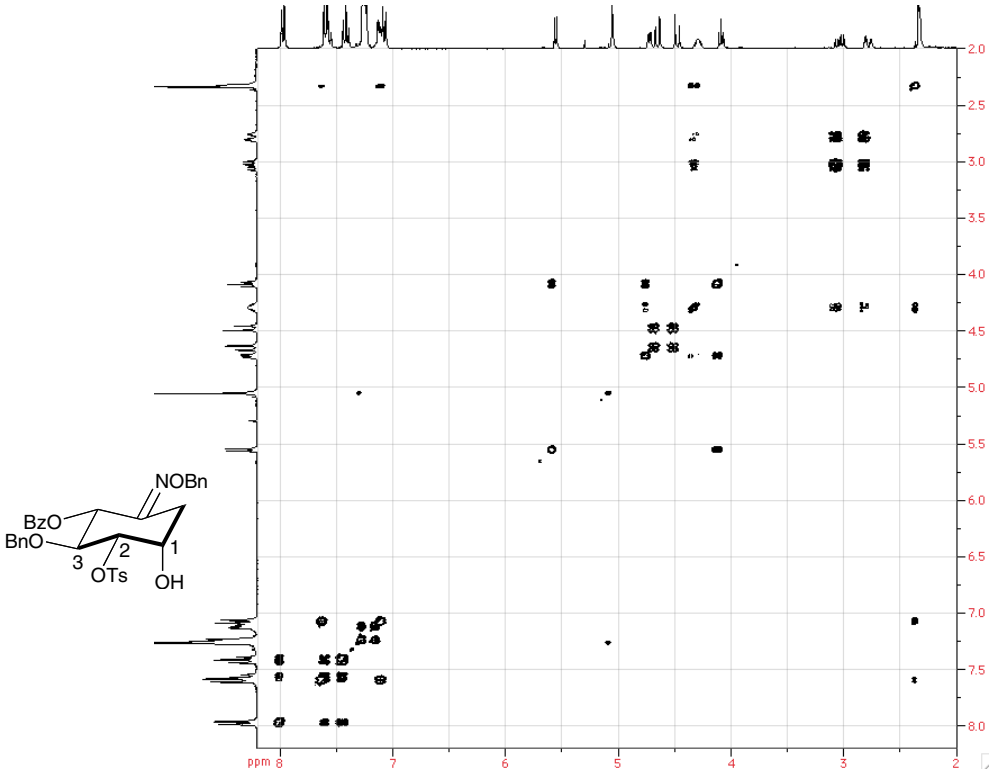

Molecule **17** ($^1$H NMR, 300 MHz, $CDCl_3$).



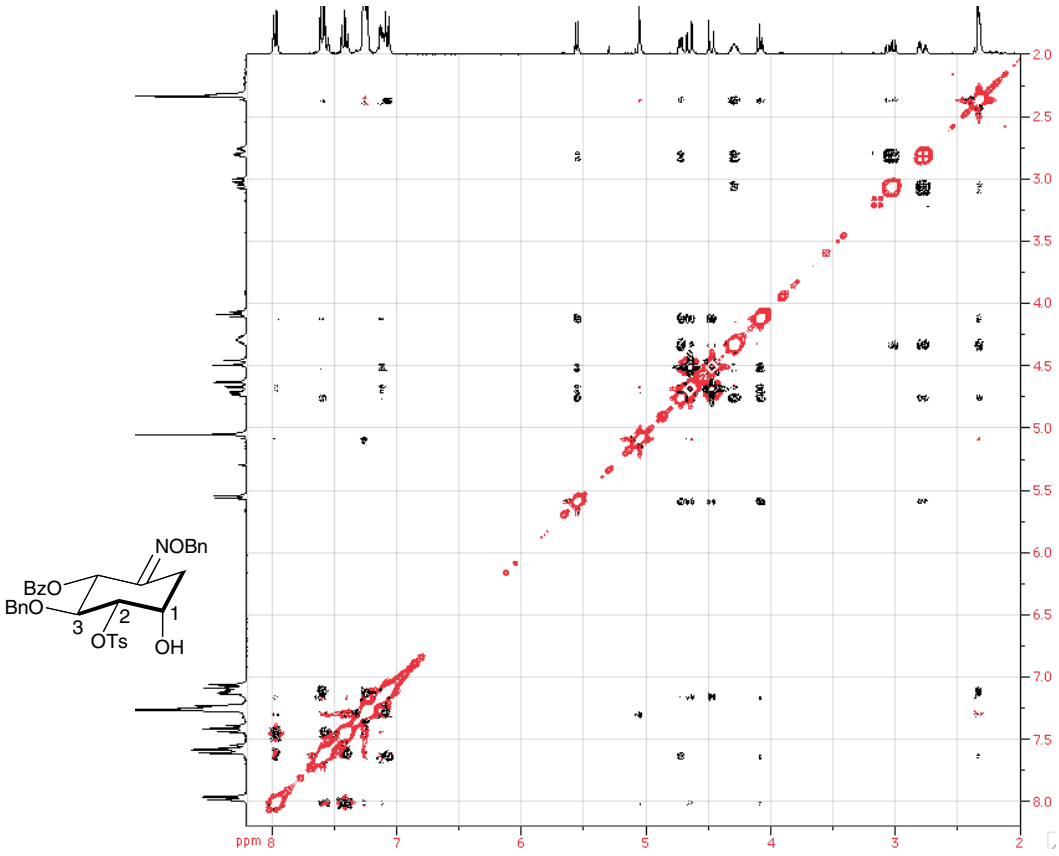

Molecule **17** ($^{13}$C NMR, 75 MHz, $CDCl_3$).



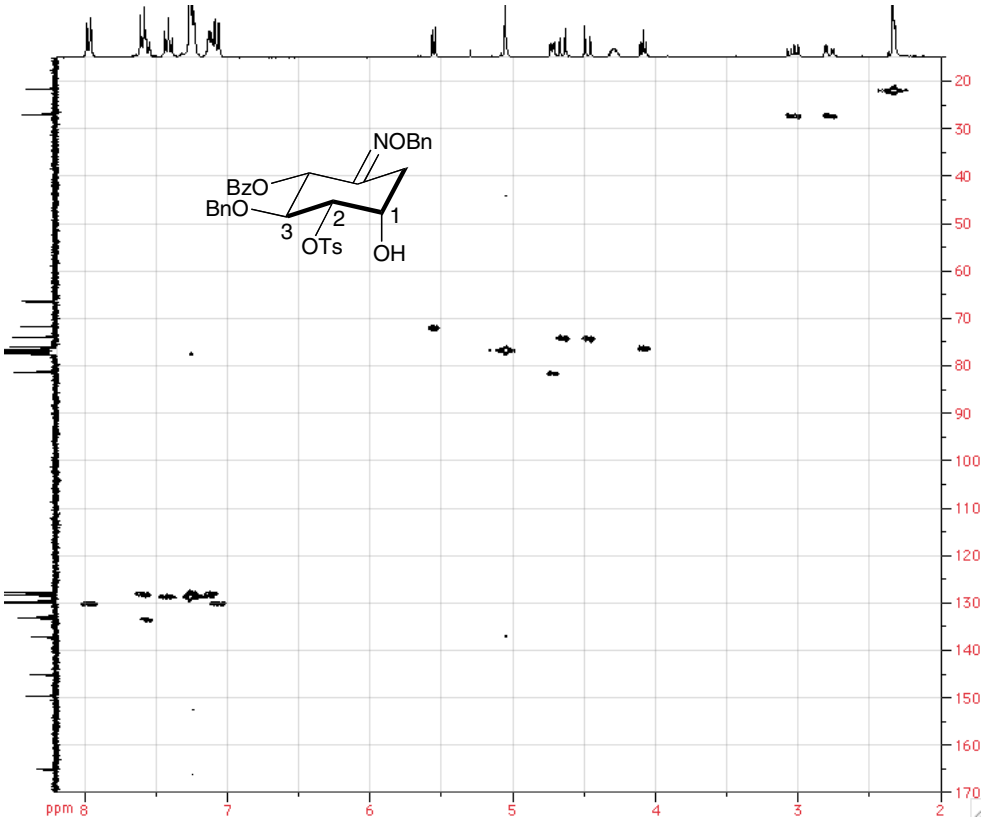

COSY spectrum of molecule **17** (300 MHz; $CDCl_3$).



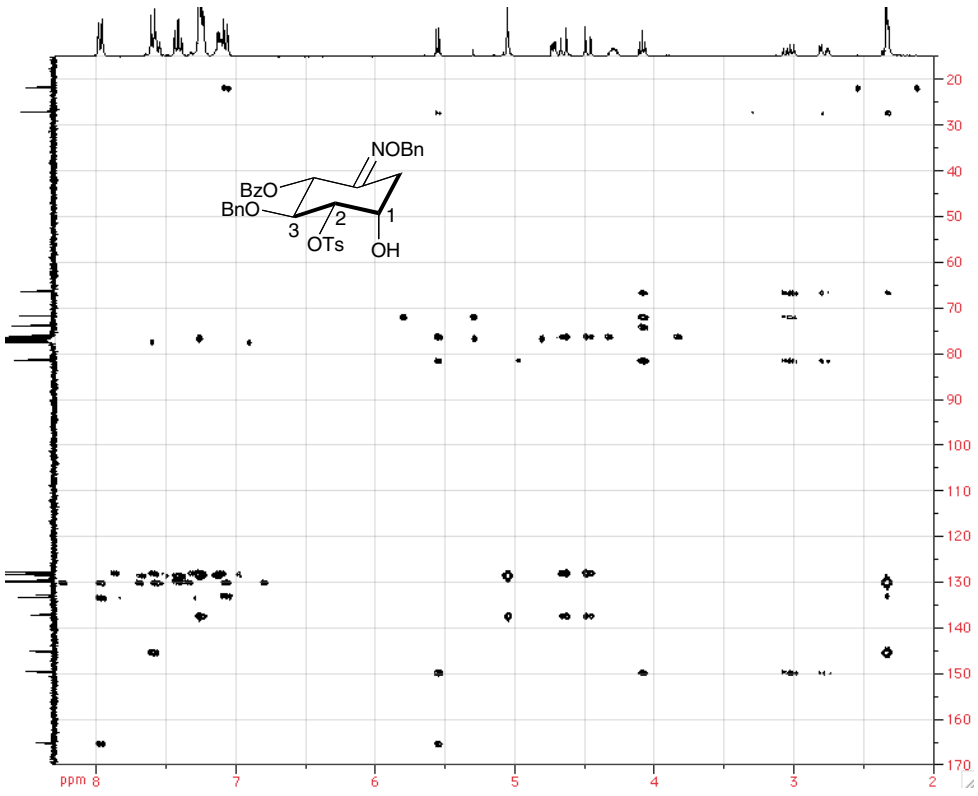

NOESY spectrum of molecule **17** (300 MHz; $CDCl_3$).



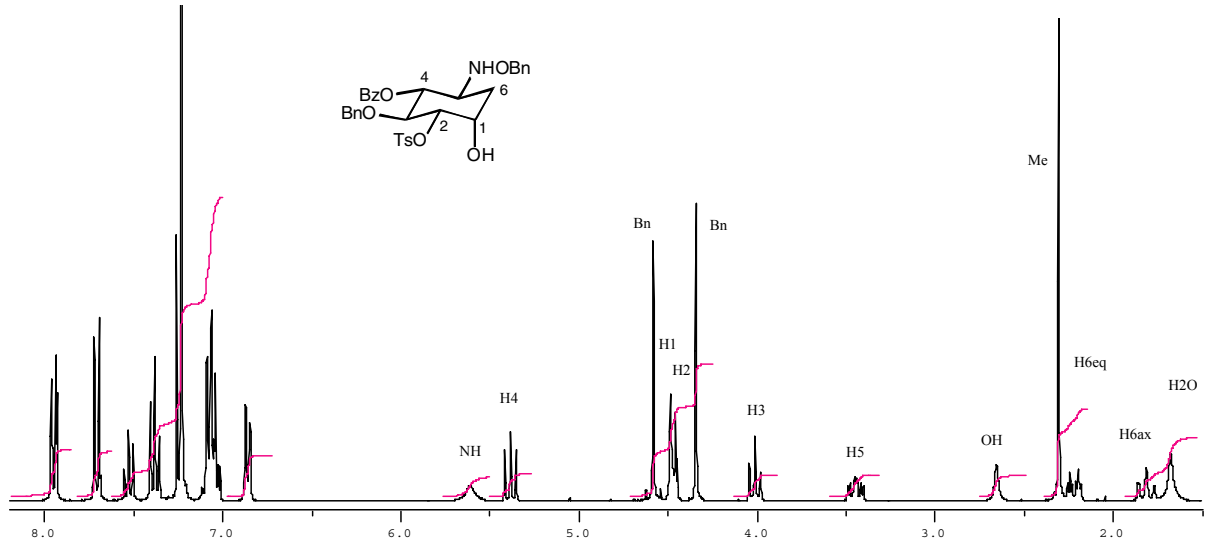

HMQC spectrum of molecule **17** ($CDCl_3$).



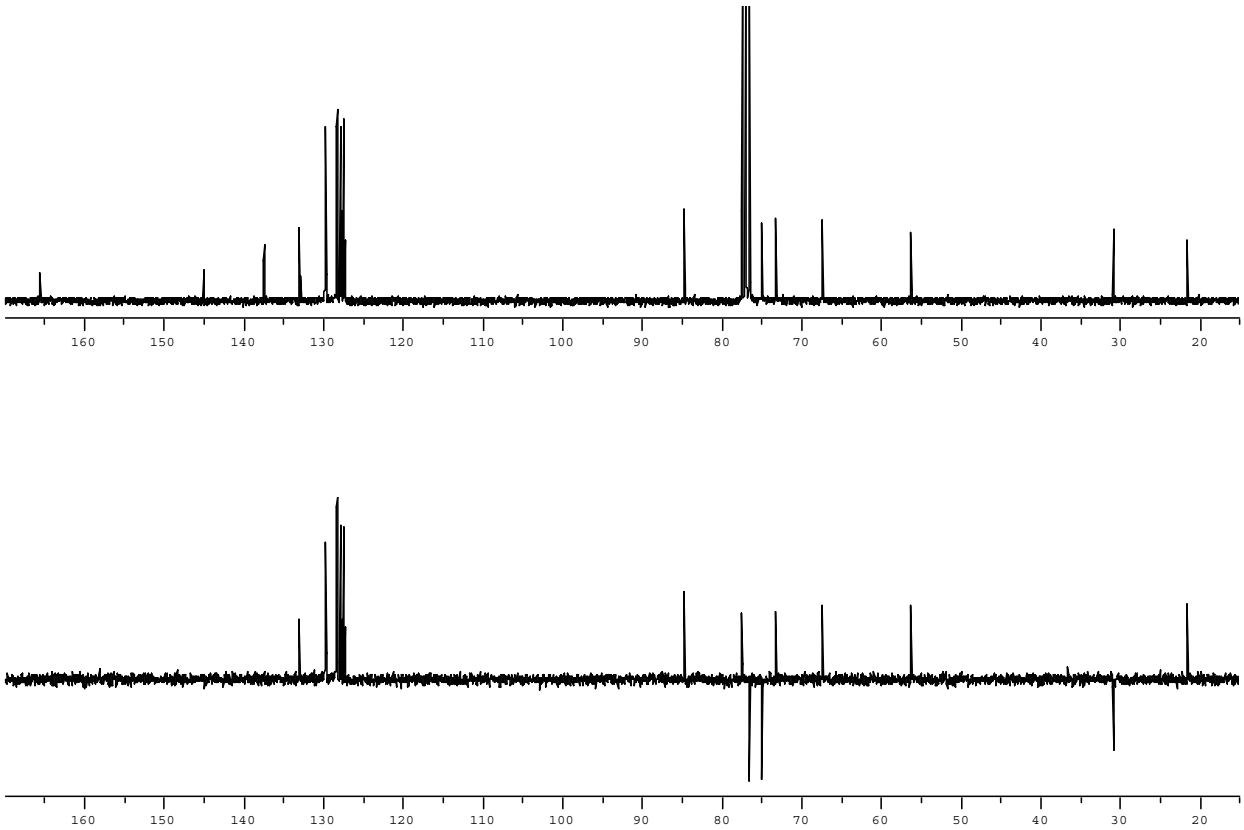

HMBC spectrum of molecule **17** ($CDCl_3$).



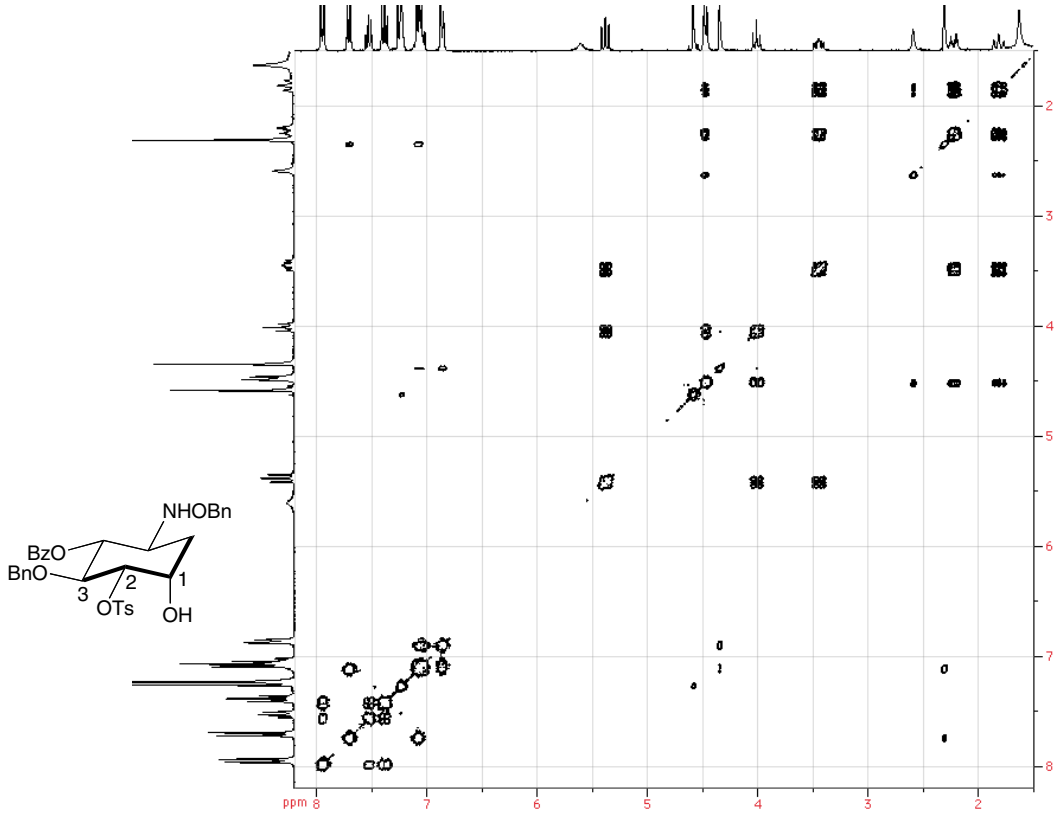

Molecule **18** ($^1$H NMR, 300 MHz, $CDCl_3$).



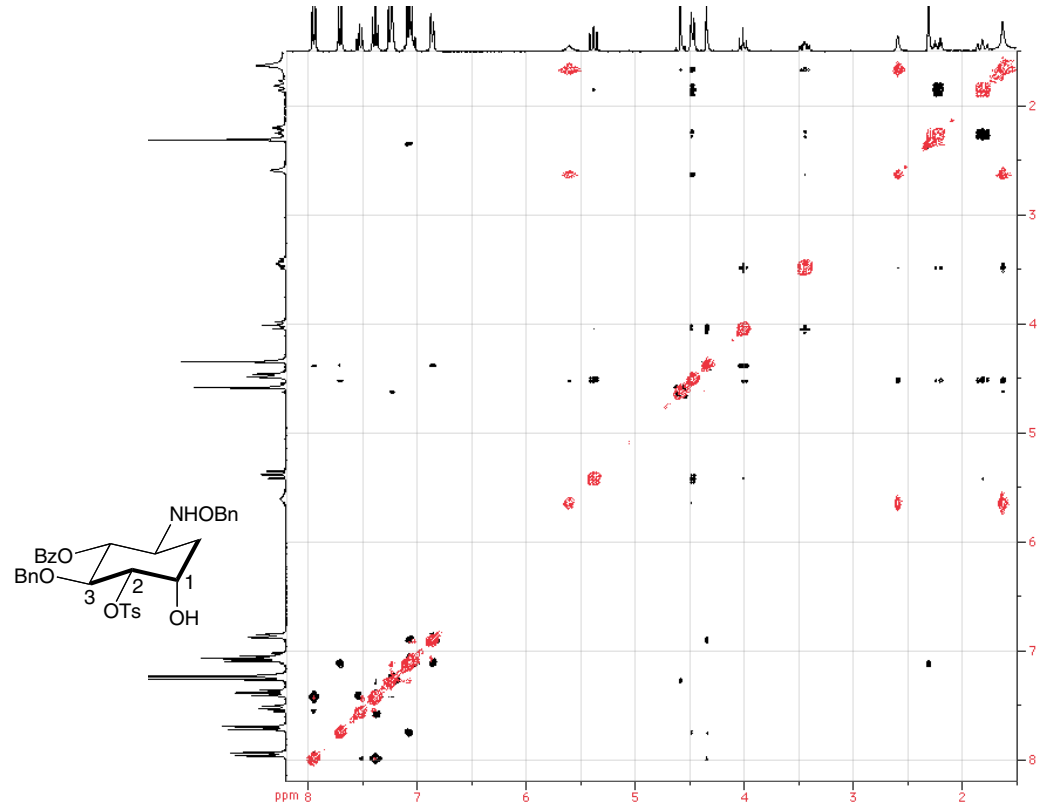

Molecule **18** ($^{13}$C NMR, 75 MHz, $CDCl_3$).



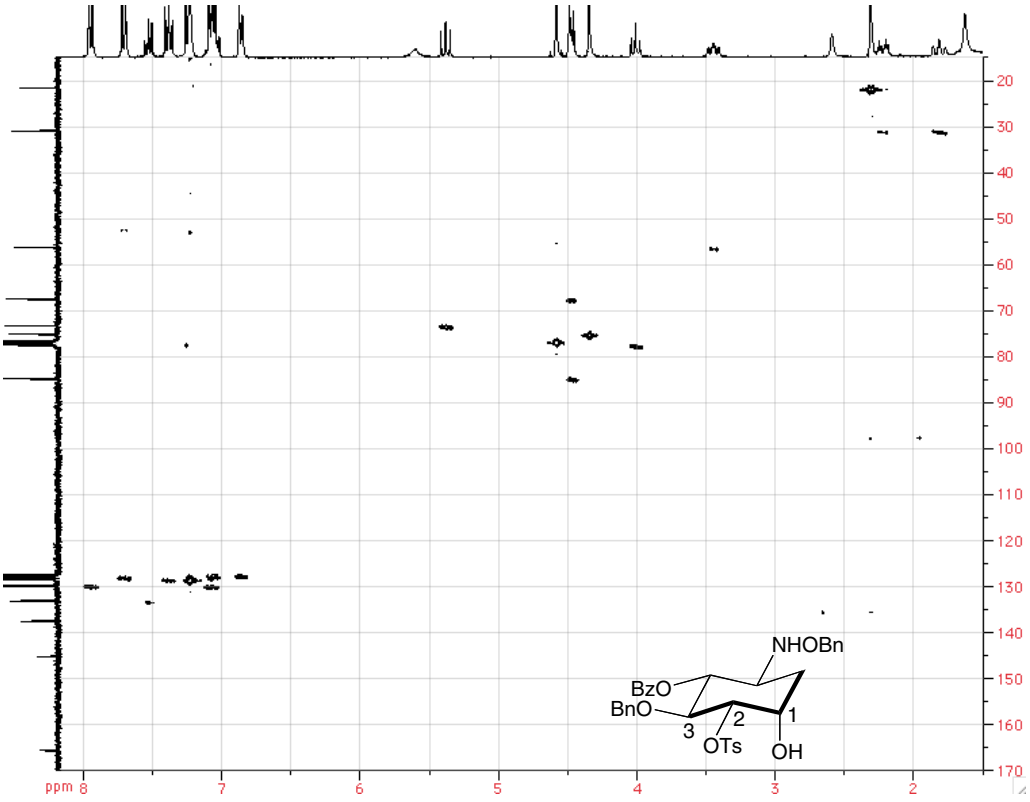

COSY spectrum of molecule **18** (300 MHz; $CDCl_3$).



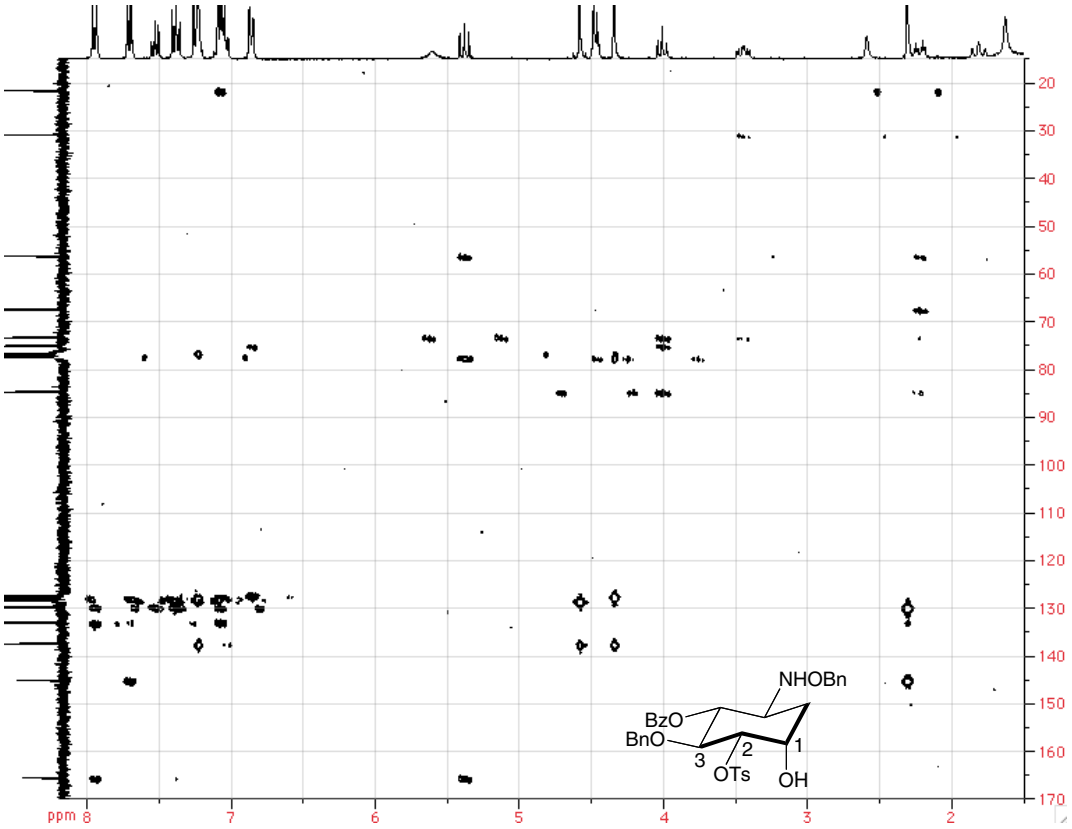

NOESY spectrum of molecule **18** (300 MHz; $CDCl_3$).



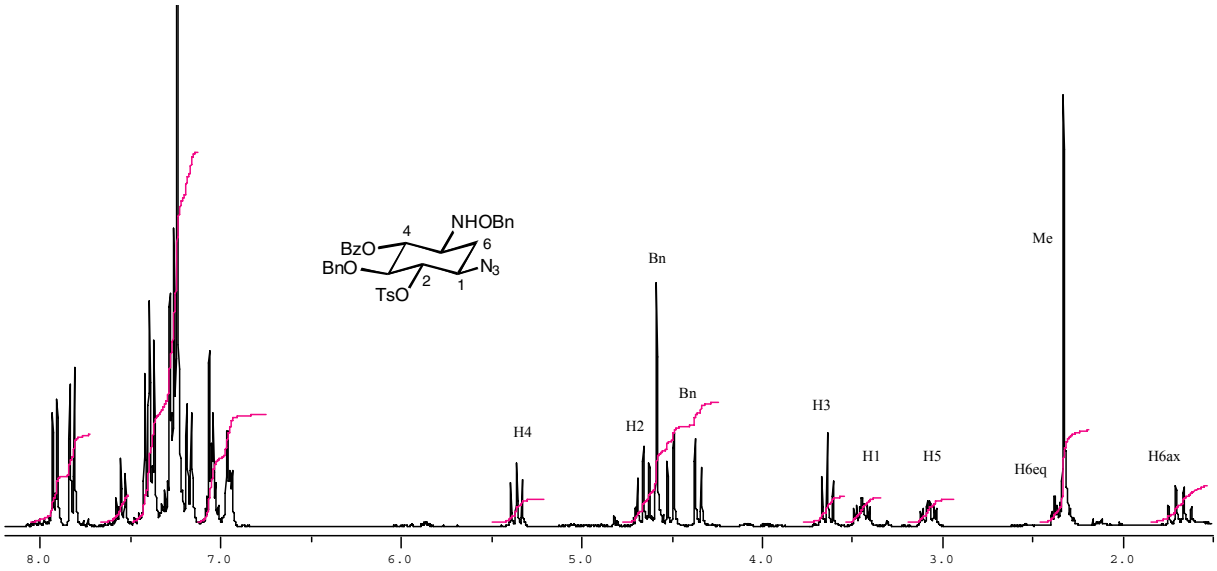

HMQC spectrum of molecule **18** ($CDCl_3$).



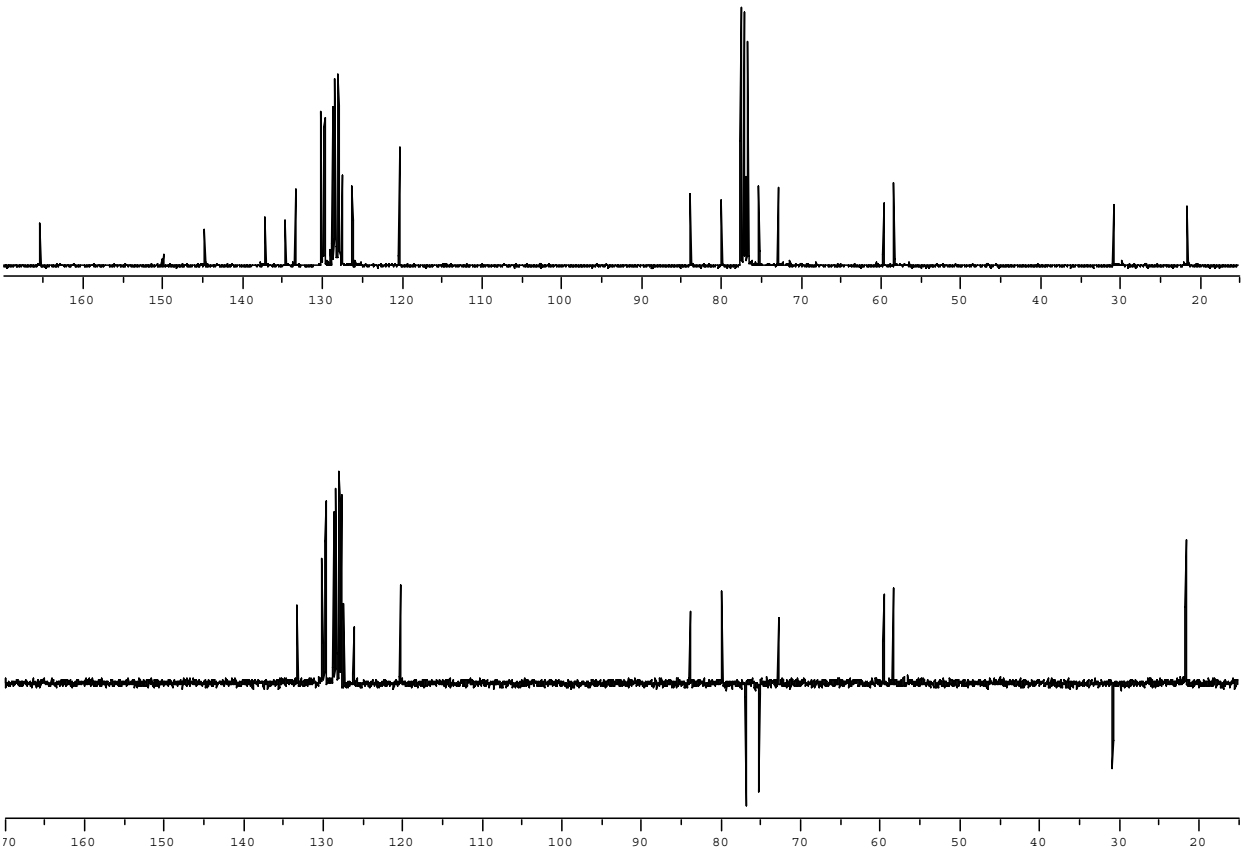

HMBC spectrum of molecule **18** ($CDCl_3$).



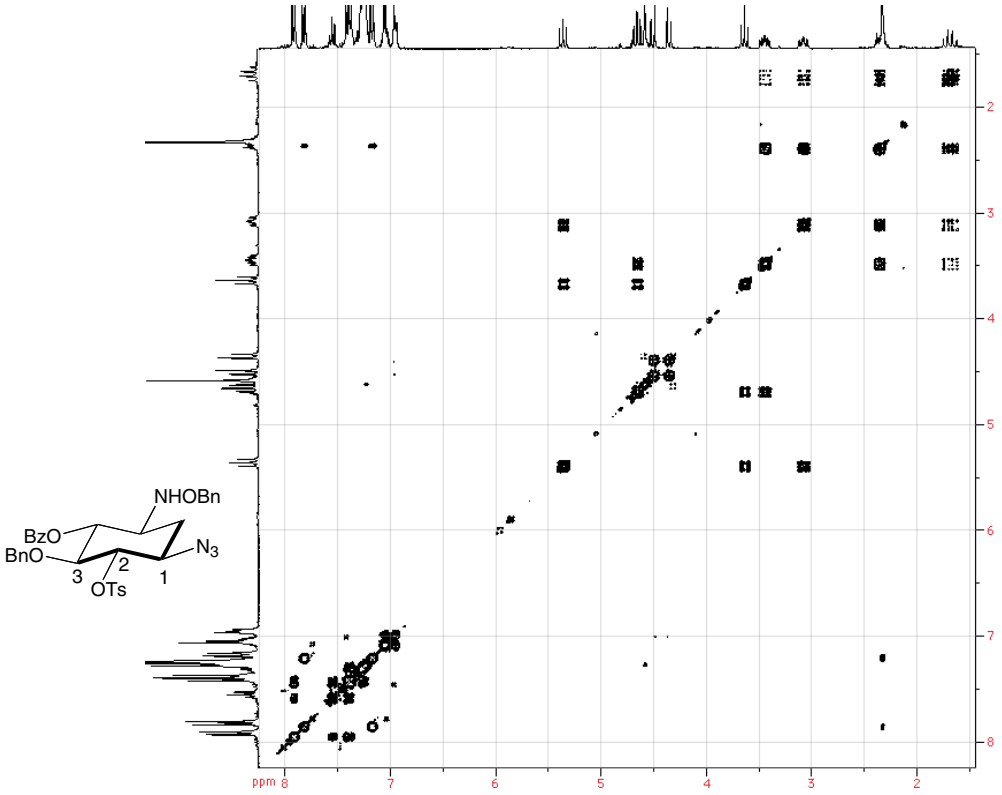

Molecule **19** ($^1$H NMR, 300 MHz, $CDCl_3$).



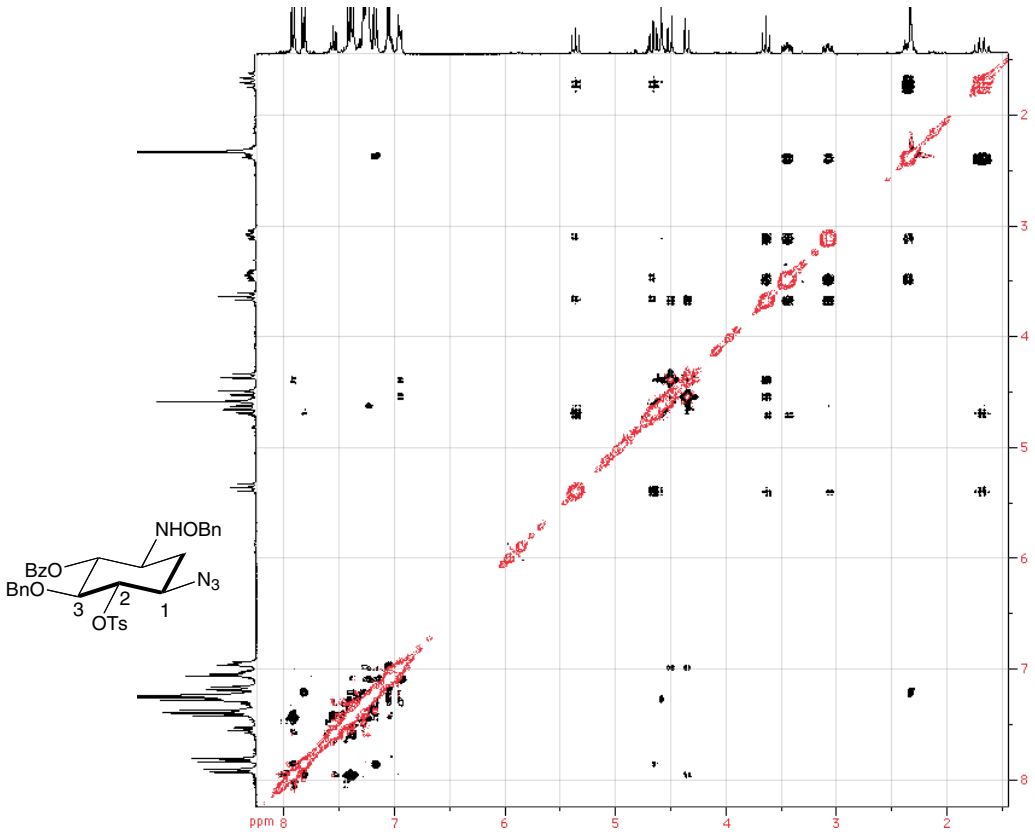

Molecule **19** ($^{13}$C NMR, 75 MHz, $CDCl_3$).



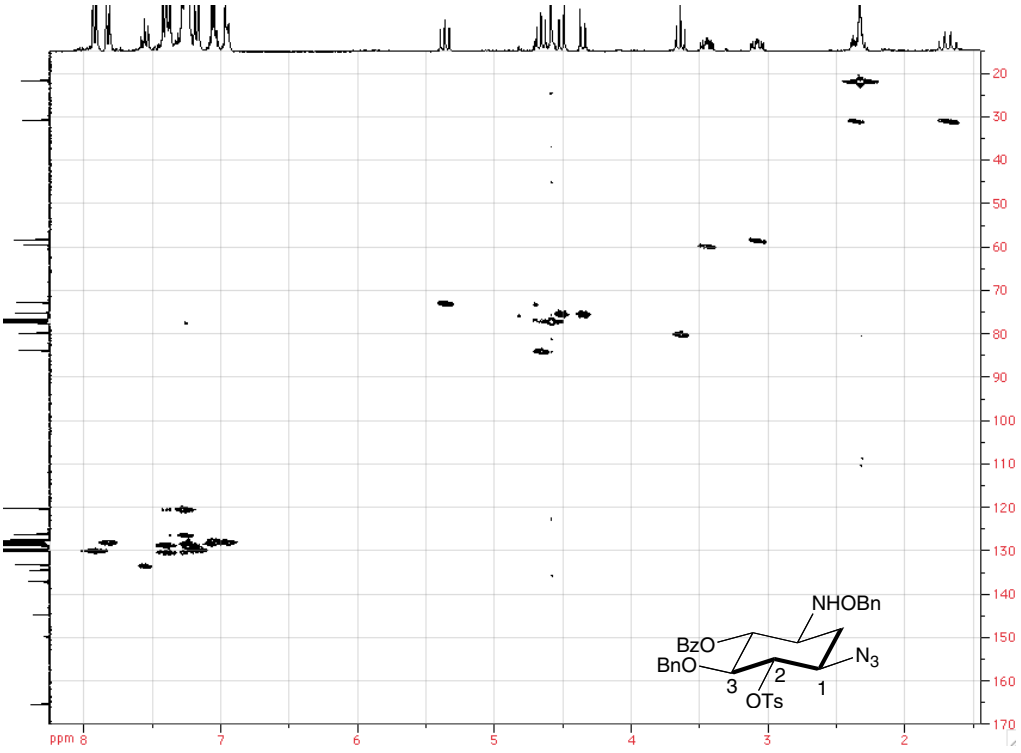

COSY spectrum of molecule **19** (300 MHz; $CDCl_3$).




NOESY spectrum of molecule **19** (300 MHz; $CDCl_3$).




HMQC spectrum of molecule **19** ($CDCl_3$).




HMBC spectrum of molecule **19** ($CDCl_3$).