Supporting Information

De Novo synthesis of Sugar-Aza-Crown Ethers by a Domino Staudinger Aza-Wittig Reaction

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General Methods

^{1}H and ^{13}C NMR spectra were recorded on a 250 MHz spectrometer. Column chromatography was performed on Silica Gel 60 (230-400 mesh). Analytical thin-layer chromatography was performed on aluminum percolated plates of Silica Gel 60F-254 with detection by UV and by spraying with 6 N H_2SO_4 and heating about 2 min at 300 °C. Dichloromethane and pyridine were distilled over CaH_2. Tetrahydrofurane was distilled over Na and benzophenone. MALDI mass spectra were recorded with a time-of-flight mass spectrometer equipped with a 337 nm nitrogen laser. It was operated in the reflectron delayed extraction mode at an acceleration voltage of 20 kV. Fast atom bombardement mass spectra (FAB-MS) were recorded on a JMS-700 spectrometer at the Service de Spectromètrie de Masse de l'Ecole Normale Supérieure de Paris.

General procedure for oxidation of allyl to aldehyde: to a solution of *C*-allyl glucoside (1 équiv) in a mixture of 1,4-dioxane/H_2O (3:1, 0.1 M), were added 2,6-lutidine (2 equiv), OsO_4 (2.5 % in *t*-BuOH, 0.02 equiv) and $NaIO_4$ (4 equiv). After stirring for 30 min at room temperature, the reaction media is diluted in a mixture of CH_2Cl_2, H_2O and a few drops of HCl 10 % then stirred for an additional period of 10 min. Finally, the mixture is extracted three times with CH_2Cl_2, washed with brine, dried over $MgSO_4$, filtered, evaporated under vacuum and purified over silica gel to afford the desired aldehyde.

(6'-Azido-3'-*O*-benzyl-6'-deoxy-2',4'-di-*O*-methoxymethyl-α-D-glucopyranosyl)-acetaldehyde 5: 3-(6'-azido-3'-*O*-benzyl-6'-deoxy-2',4'-di-*O*-methoxymethyl-α-D-glucopyranosyl)-1-propene **1** (1.200 g, 2.948 mmol) was oxidized and purified over silica gel (EtOAc/cyclohexane, 1:9 then 2:8), affording the aldehyde **5** (778 mg, 1.902 mmol, 65 %) as colourless oil, R_f 0.43 (6:4 EtOAc/cyclohexane), $[\alpha]_D$ +48.7 (*c* 1, CH_2Cl_2). ^{1}H NMR (250 MHz, $CDCl_3$) δ 2.67 (ddd, J = 16.3, 2.8, 8.3 Hz, 1H), 2.84 (ddd, J = 16.3, 1.8, 6.3 Hz, 1H), 3.33 (s, 3H), 3.34 (s, 3H), 3.43 (dd, J = 13.0, 5.0 Hz, 1H), 3.48 (dd, J = 13.0, 3.3 Hz, 1H), 3.53 (t, J = 8.3 Hz, 1H), 3.62 (t, J = 8.3 Hz, 1H), 3.68 (ddd, J = 8.3, 5.0, 3.3 Hz, 1H), 3.82 (dd, J = 5.5, 8.3 Hz, 1H), 4.60 (d, J = 6.5 Hz, 1H), 4.62 (d, J = 6.5 Hz, 1H), 4.67-4.78 (m, 1H), 4.70 (d, J = 11.0 Hz, 1H), 4.74 (d, J = 6.5 Hz, 1H), 4.80 (d, J = 11.0 Hz, 1H), 4.82 (d, J = 6.5 Hz, 1H), 7.27-7.42 (m,

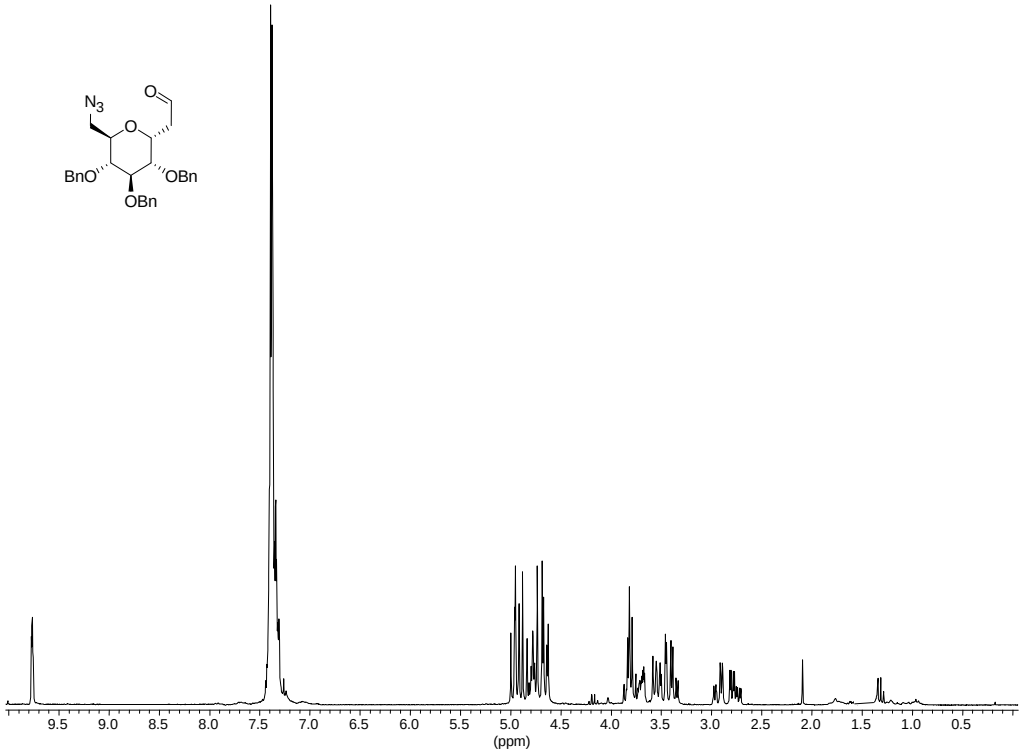
5H), 9.80 (dd, *J* = 2.8, 1.8 Hz, 1H). ^{13}C NMR (62.9 MHz, $CDCl_3$) δ 41.7, 51.3, 56.2, 56.4, 69.6, 72.4, 75.0, 76.2, 76.6, 80.5, 97.5, 98.1, 127.8, 128.0, 128.6, 138.0, 199.8. Anal. Calcd for $C_{19}H_{27}N_3O_7$ (409.43): C, 55.74; H, 6.65; N, 10.26. Found C, 55.86; H, 6.69; N, 10.12.

(6'-Azido-2',3',4'-tri-*O*-benzyl-6'-deoxy-α-D-glucopyranosyl)-acetaldehyde 6: 3-(6'-azido-2',3',4'-tri-*O*-benzyl-6'-deoxy-α-D-glucopyranosyl)-1-propene **3** (300 mg, 0.602 mmol) was oxidized and purified over silica gel (EtOAc/cyclohexane, 1:9 then 2:8), affording the desired aldehyde (250 mg, 0.499 mmol, 83 %) as colourless oil, R_f 0.72 (2:3 EtOAc/cyclohexane), $[\alpha]_D$ +58.5 (*c* 1, CH_2Cl_2). ^{1}H NMR (250 MHz, $CDCl_3$) δ 2.76 (ddd, *J* = 16.2, 2.9, 8.5 Hz, 1H), 2.93 (ddd, *J* = 16.2, 1.4, 5.7 Hz, 1H), 3.32 (dd, *J* = 13.3, 4.9 Hz , 1H), 3.43 (dd, *J* = 13.3, 2.8 Hz , 1H), 3.50 (dd, *J* = 9.6, 8.3 Hz, 1H), 3.60-3.69 (m, 1H), 3.69-3.84 (m, 2H), 4.60 (d, *J* = 11.1 Hz, 1H), 4.61 (d, *J* = 11.4 Hz, 1H), 4.68-4.78 (m, 1H), 4.71 (d, *J* = 11.4 Hz, 1H), 4.81 (d, *J* = 11.8 Hz , 1H), 4.89 (d, *J* = 11.8 Hz , 1H), 4.93 (d, *J* = 11.1 Hz, 1H), 7.23-7.40 (m , 15 H), 9.72 (dd, *J* = 2.9, 1.4 Hz, 1H). ^{13}C NMR (62.9 MHz, $CDCl_3$) δ 41.5, 51.5, 69.7, 72.2, 73.6, 75.2, 75.5, 78.2, 79.0, 81.9, 128.1, 128.2, 128.0, 128.7, 137.9, 138.4, 199.6. Anal. Calcd for $C_{29}H_{31}N_3O_5$ (501.57): C, 69.44; H, 6.23; N, 8.38. Found C, 69.62; H, 6.12; N, 8.27.

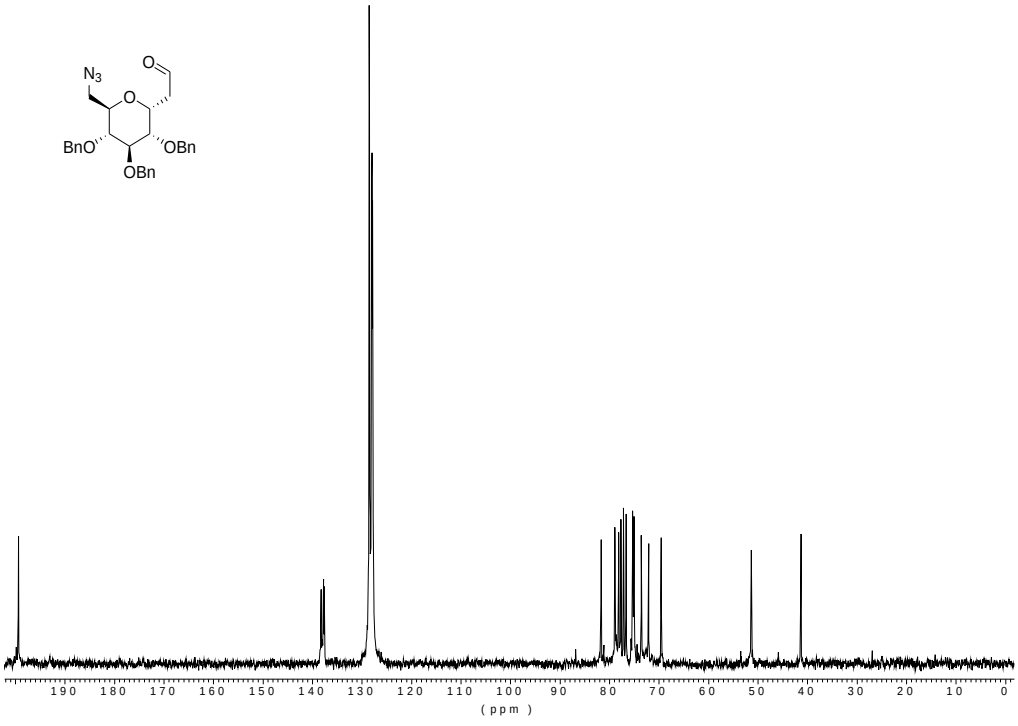
(6'-Azido-3'-*O*-benzyl-6'-deoxy-2',4'-di-*O*-methyl-α-D-glucopyranosyl)-acetaldehyde 7: 3-(6'-azido-3'-*O*-benzyl-6'-deoxy-2',4'-di-*O*-methyl-α-D-glucopyranosyl)-1-propene **4** (2.000 g, 5.764 mmol) was oxidized and purified over silica gel (EtOAc/cyclohexane, 1:9 then 3:7), affording the desired aldehyde (1.526 g, 4.372 mmol, 76 %) as colourless oil, *Rf* 0.48 (6:4 EtOAc/cyclohexane), $[\alpha]_D$ +60.2 (*c* 1, CH_2Cl_2). ^{1}H NMR (250 MHz, $CDCl_3$) δ 2.64 (ddd, *J* = 16.2, 8.3, 2.8 Hz, 1H), 2.80 (ddd, *J* = 16.2, 5.9, 1.5 Hz, 1H), 3.16 (dd, *J* = 9.4, 8.2 Hz, 1H), 3.34 (dd, *J* = 13.1, 5.1 Hz, 1H), 3.43 (s, 3H), 3.51 (s, 3H), 3.39-3.59 (m, 4H), 4.69-4.79 (m, 1H), 4.74 (d, *J* = 11.1 Hz, 1H), 4.83 (d, *J* = 11.1 Hz, 1H), 7.22-7.41 (m, 5H), 9.74 (dd, *J* = 2.8, 1.5 Hz, 1H). ^{13}C NMR (62.9 MHz, $CDCl_3$) δ 41.1, 51.3, 59.0, 60.6, 69.0, 72.1, 74.9, 79.9, 80.9, 81.2, 127.7, 127.8, 128.3, 138.3, 199.3. Anal. Calcd for $C_{17}H_{23}N_3O_5$ (349.16): C, 58.44; H, 6.64; N, 12.03. Found C, 58.56; H, 6.58; N, 12.09.

(6'-Azido-3'-*O*-benzyl-6'-deoxy-2',4'-di-*O*-methoxy-β-D-glucopyranosyl)-acetaldehyde 14: To a solution of α-aldehyde **7** (595 mg, 1.705 mmol) in 0.6 M MeONa in MeOH (24 mL), was added $Zn(OAc)_2$ (1.561 g, 8.524 mmol). After stirring for three days at room temperature, the mixture was acidified with a few drops of AcOH in order to get a clear solution, diluted in water, extracted three times with EtOAc and washed with brine. Then, the solution was dried ($MgSO_4$), filtrated, evaporated under vacuum and purified over silica gel (EtOAc/cyclohexane, 3:7), affording the desired aldehyde **14** (499 mg, 1.430 mmol, 84 %) as colourless oil, R_f 0.48 (6:4 EtOAc/cyclohexane), $[\alpha]_D$ +36.0 (*c* 1, CH_2Cl_2). ^{1}H NMR (250 MHz, $CDCl_3$) δ 2.59 (ddd, *J* = 16.0, 2.3, 7.6 Hz, 1H), 2.72 (ddd, *J* = 16.0, 2.2, 4.6 Hz, 1H), 2.96 (t, *J* = 9.2 Hz, 1H), 3.15 (t, *J* = 9.1 Hz, 1H), 3.24-3.47 (m, 4H), 3.50 (s, 3H), 3.52 (s, 3H), 3.73 (ddd, *J* = 7.6, 4.6, 9.2 Hz, 1H), 4.83 (s, 2H), 7.23-7.42 (m, 5H), 9.72 (dd, *J* = 2.3, 2.2 Hz, 1H). ^{13}C NMR (62.9 MHz, $CDCl_3$) δ 46.1, 51.1, 60.8, 60.9, 74.2, 75.3, 78.5, 80.6, 83.5, 86.3, 127.8, 127.9, 128.4, 138.3, 199.5. Anal. Calcd for $C_{17}H_{23}N_3O_5$ (349.16): C, 58.44; H, 6.64; N, 12.03. Found C, 58.64; H, 6.55; N, 11.95.

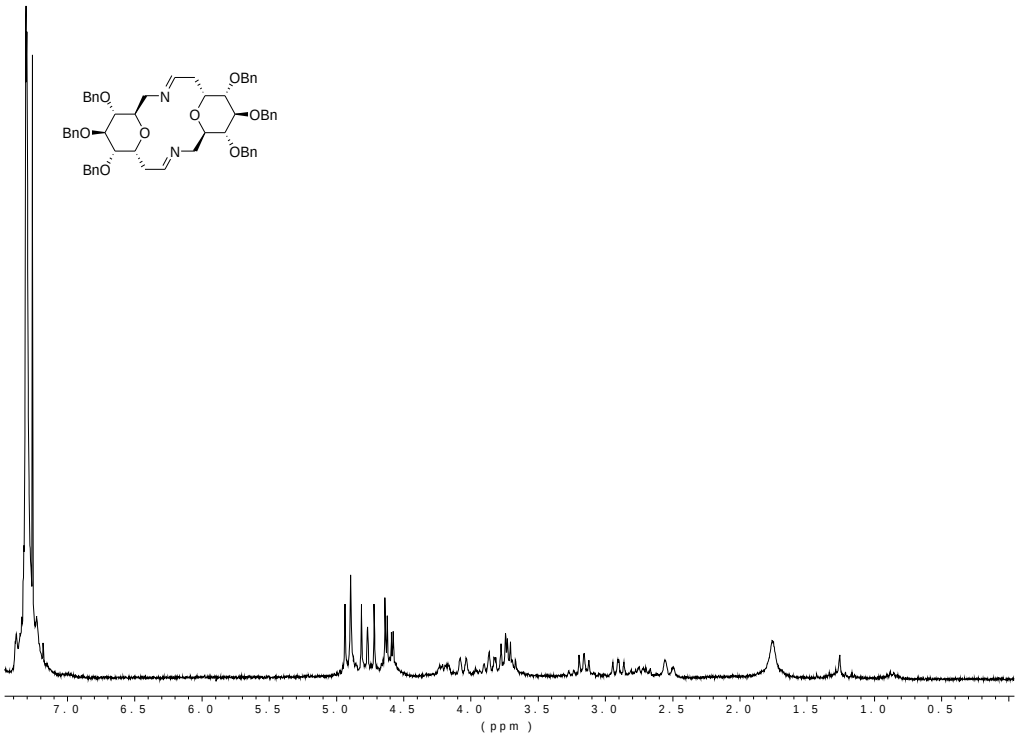
^{1}H NMR of Aldehyde **6** in $CDCl_3$



^{13}C NMR of Aldehyde **6** in $CDCl_3$



^{1}H NMR of Imine cyclodimer **11** in $CDCl_3$



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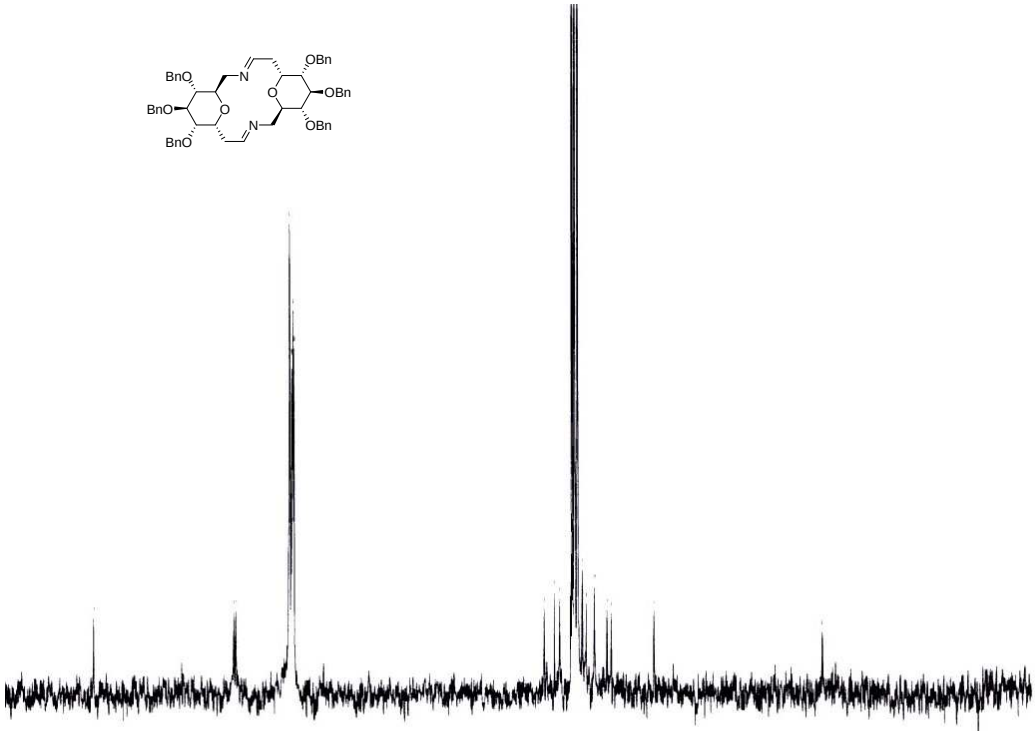

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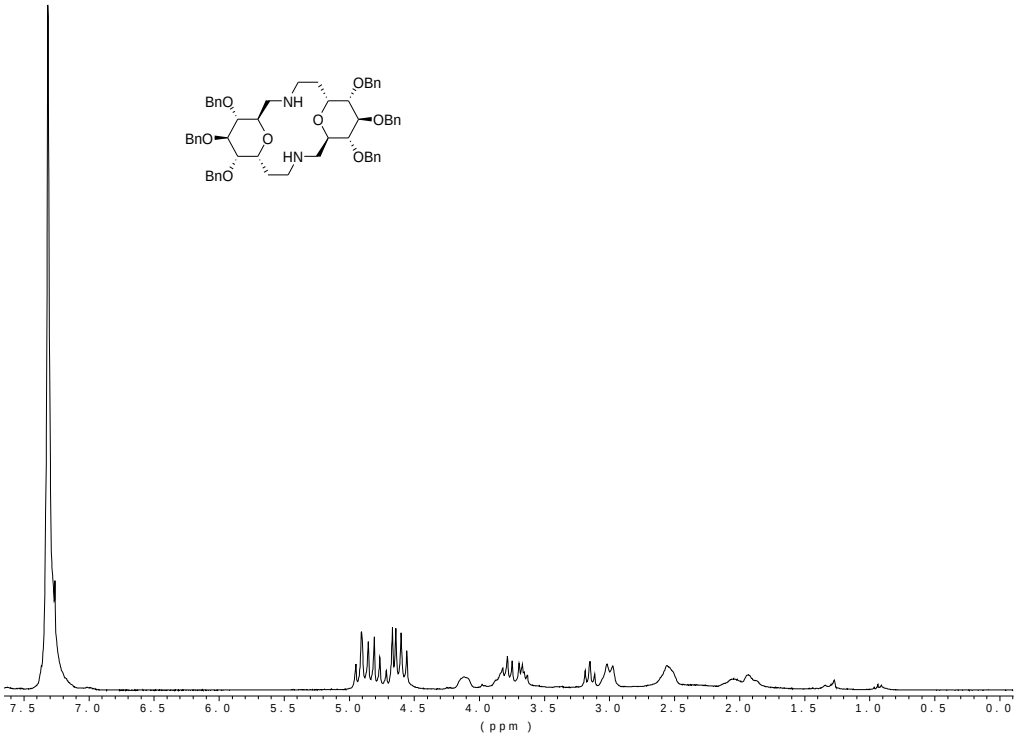
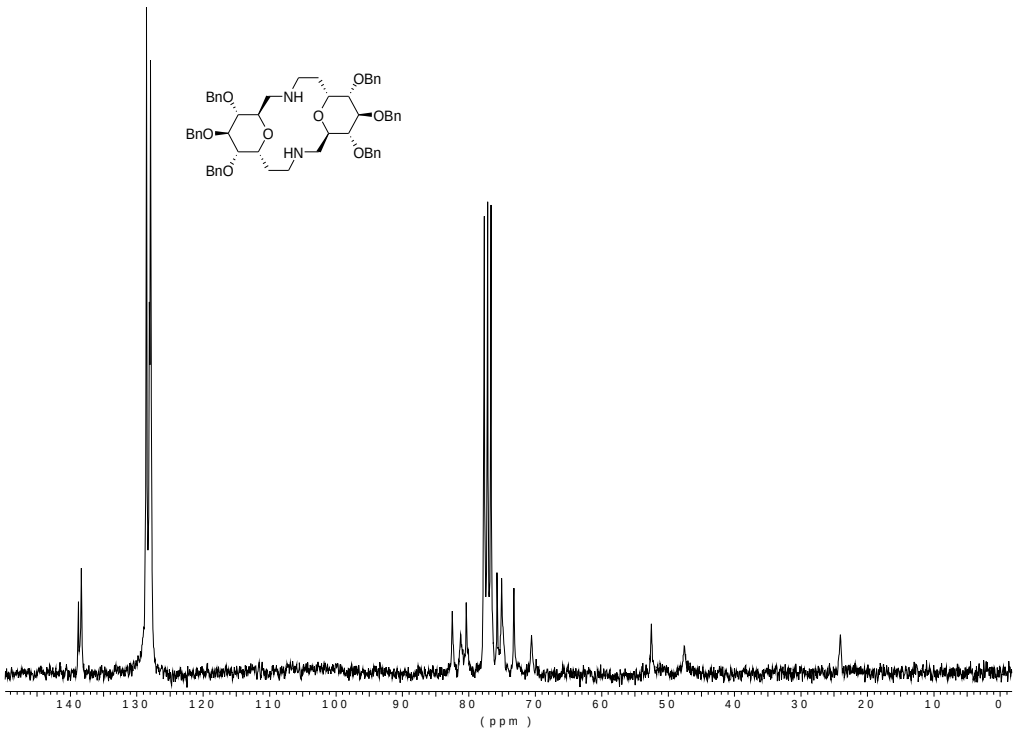


^{13}C NMR of SAC **12** in $CDCl_3$



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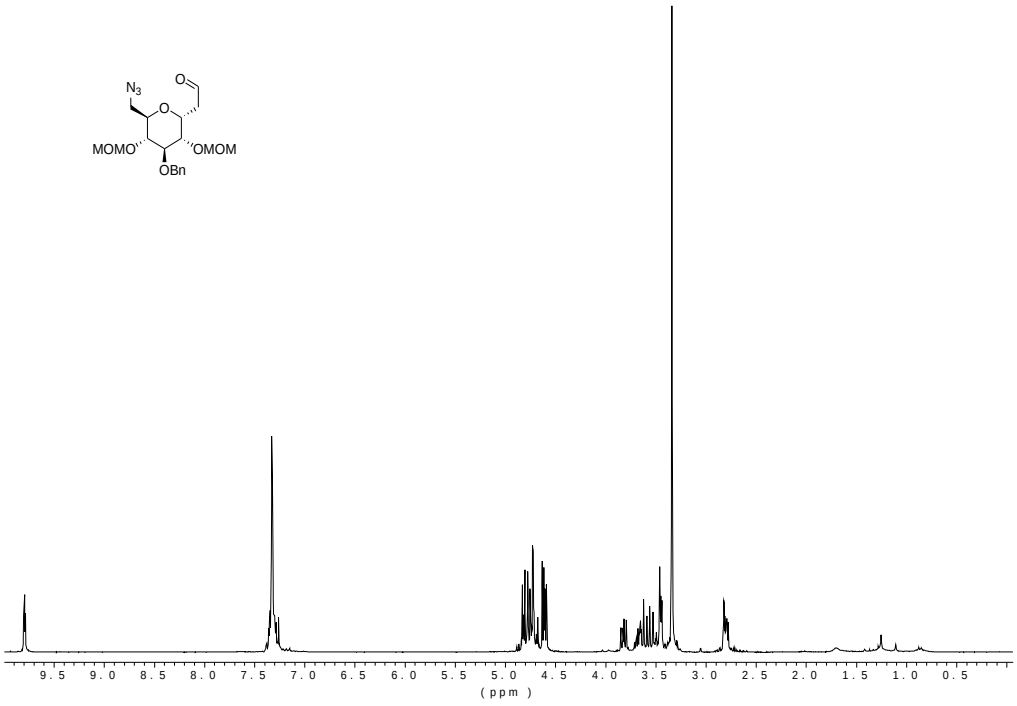
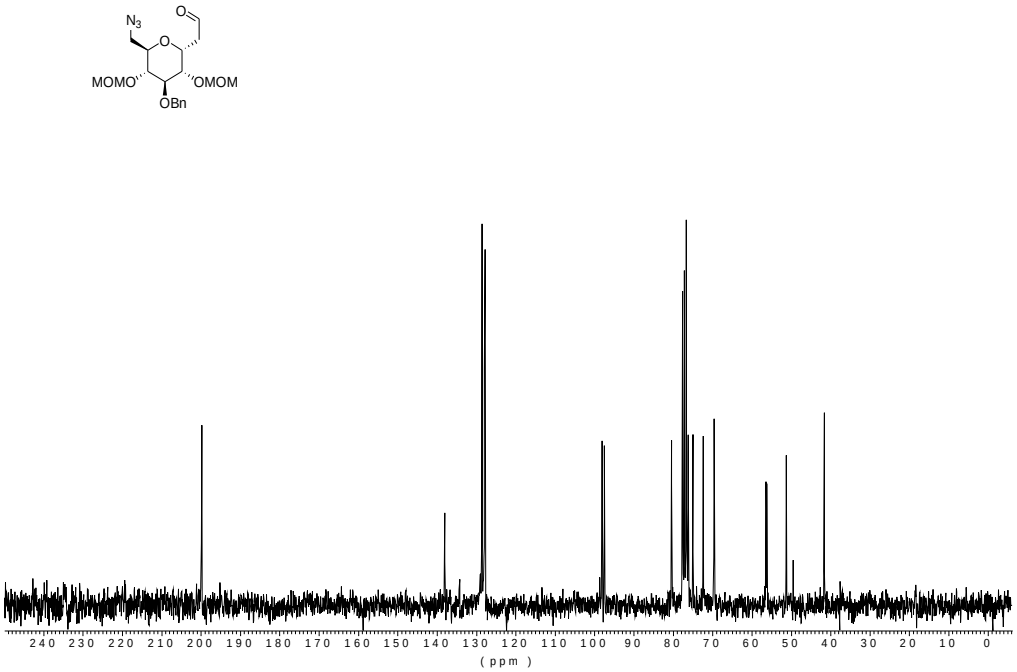


^{13}C NMR of Aldehyde **5** in $CDCl_3$



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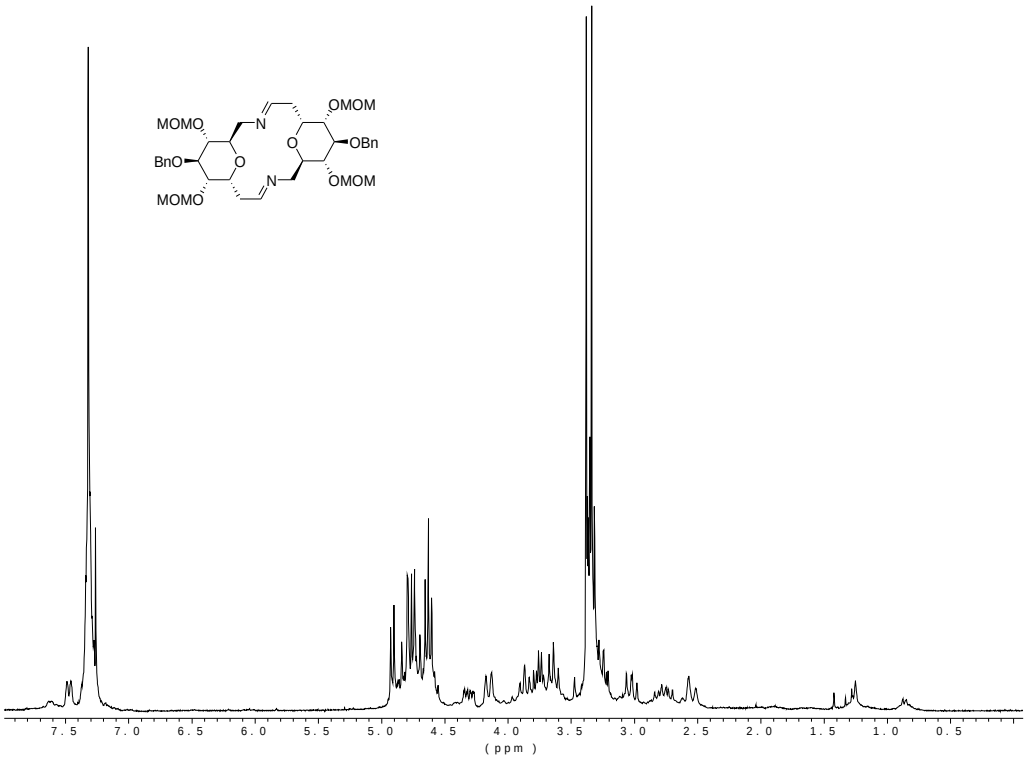

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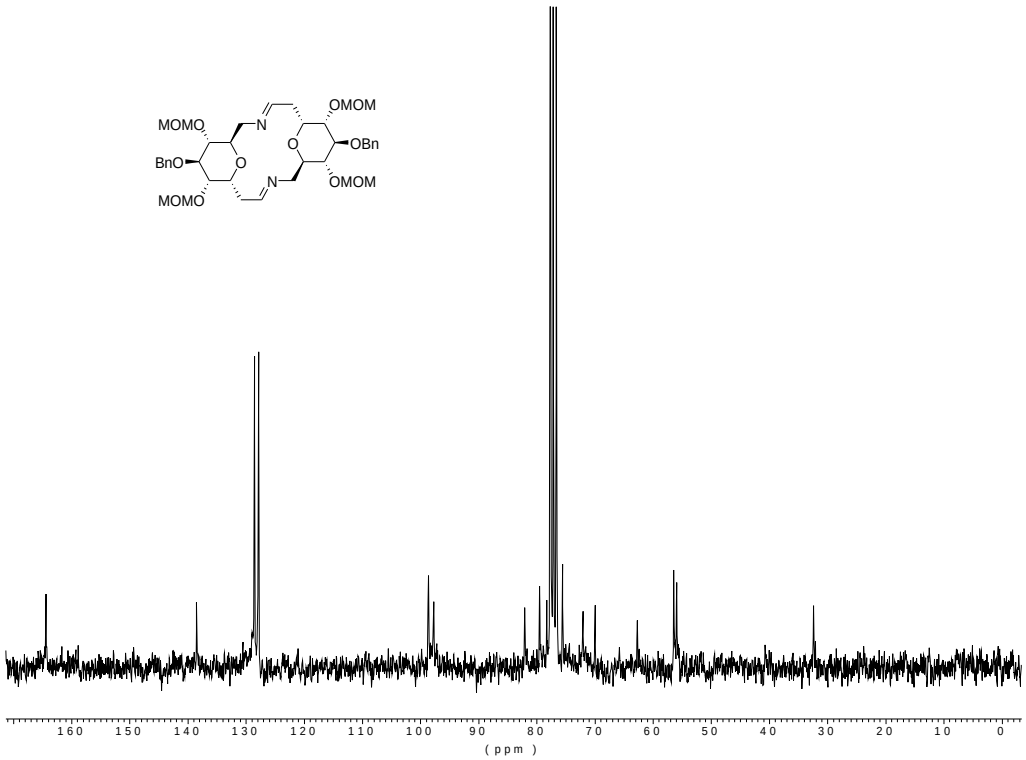
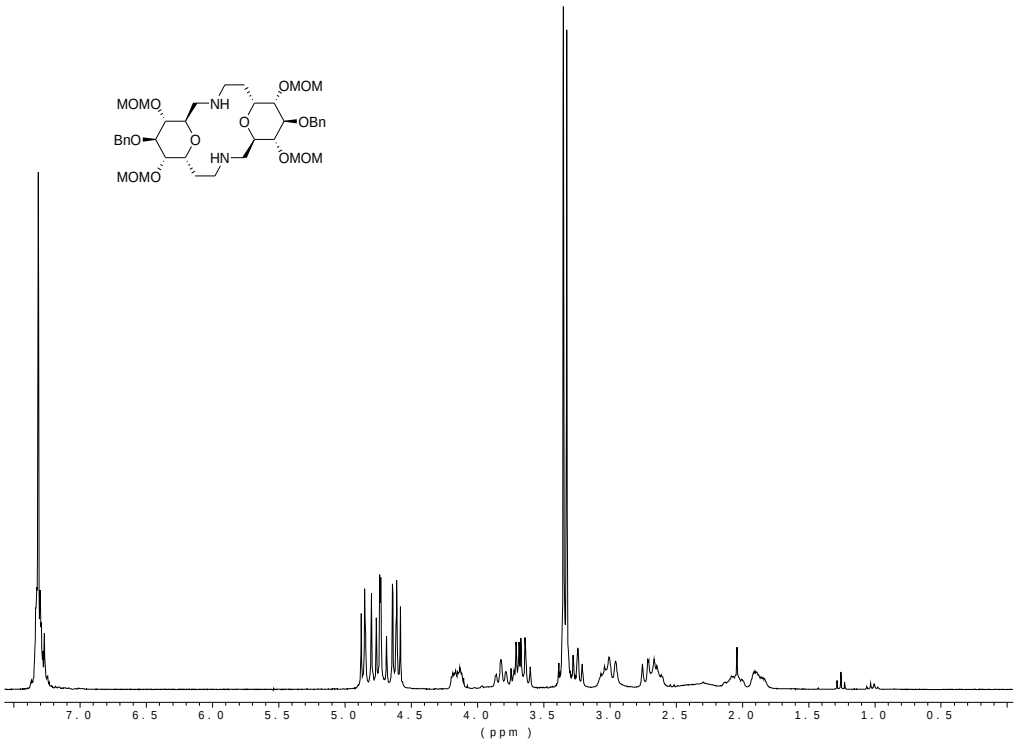
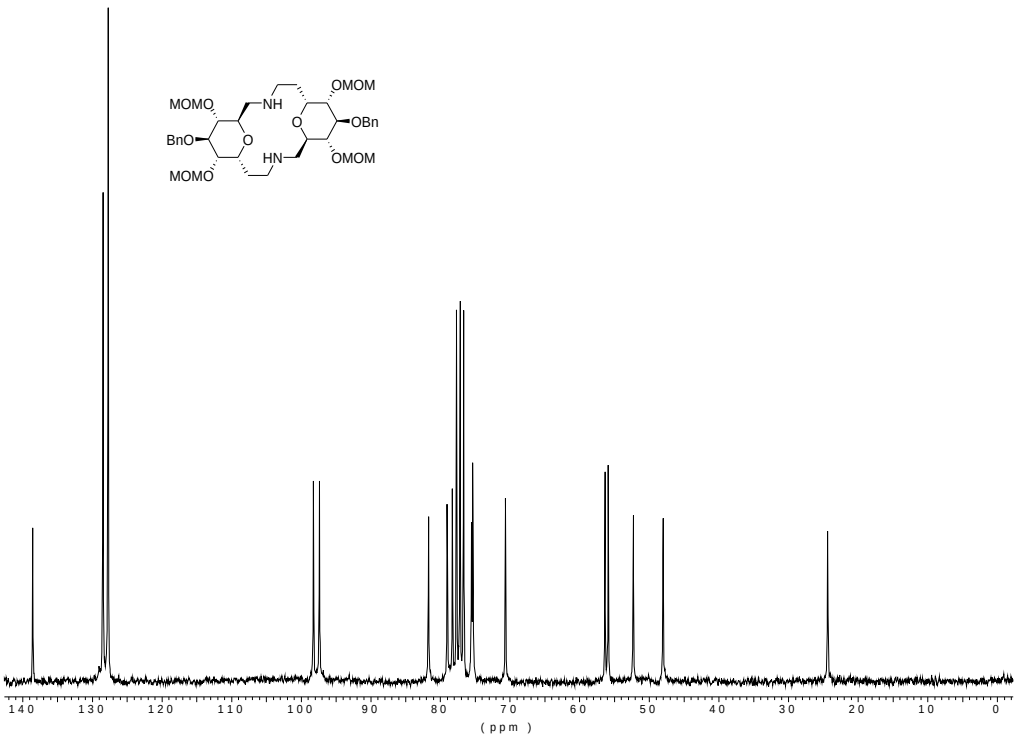


^{1}H NMR of SAC **2** in $CDCl_3$



^{13}C NMR of SAC **2** in $CDCl_3$



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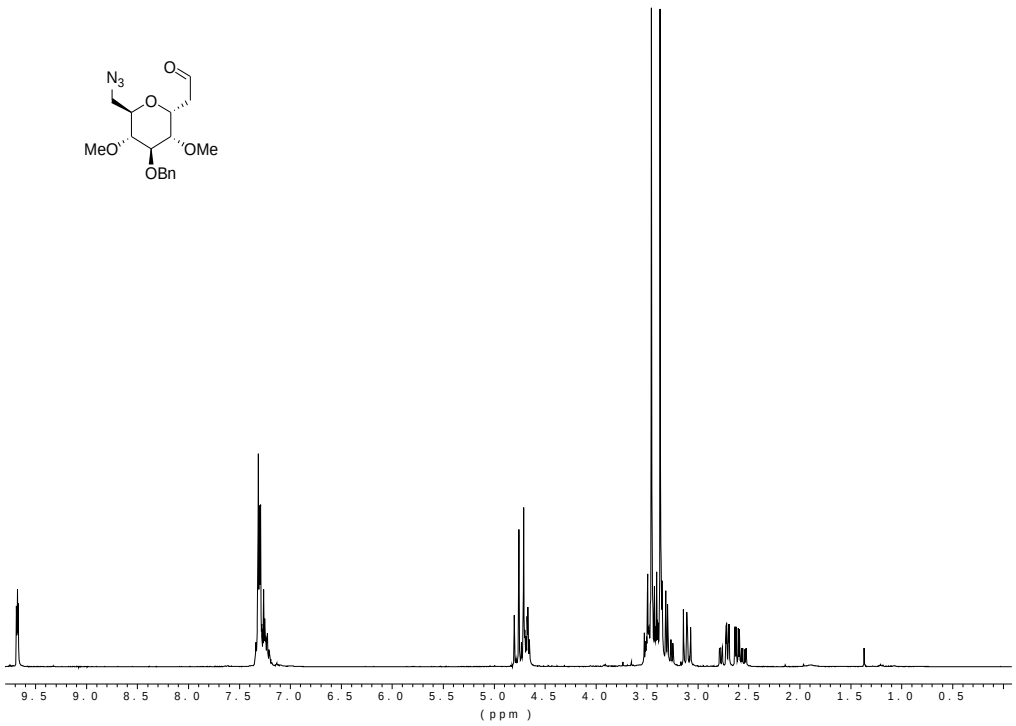
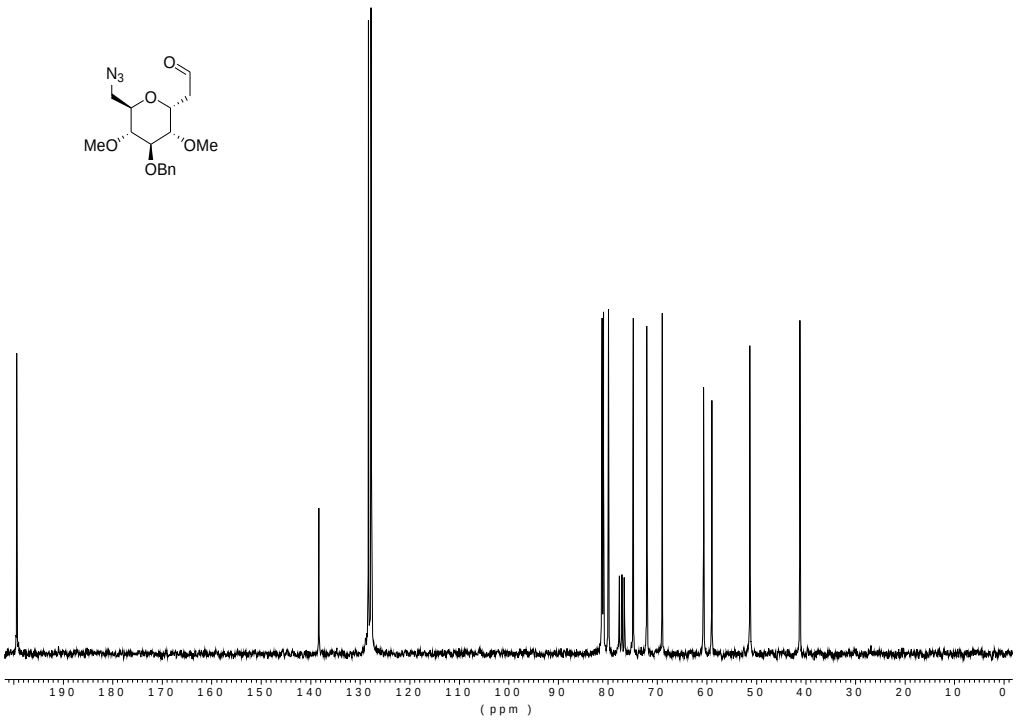


^{13}C NMR of Aldehyde **7** in $CDCl_3$



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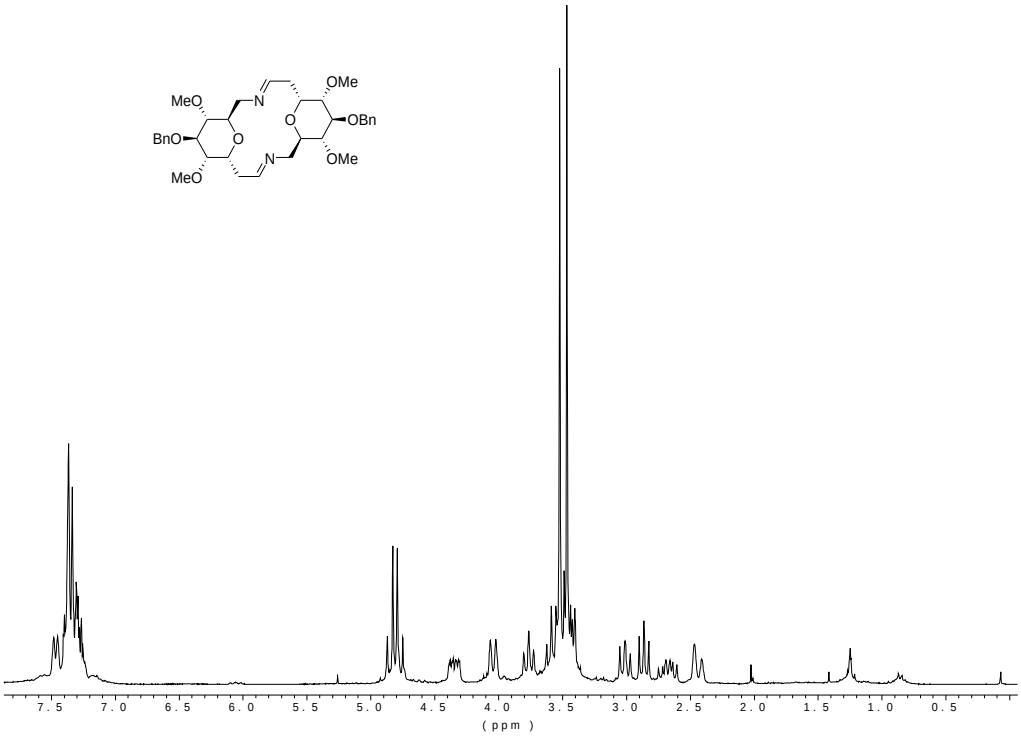
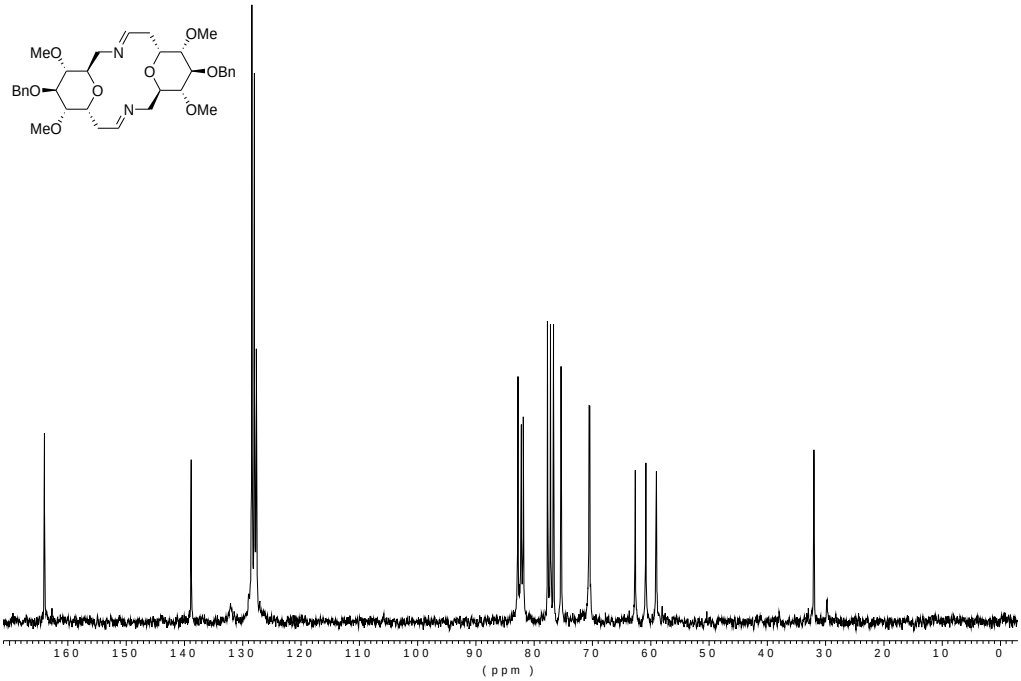
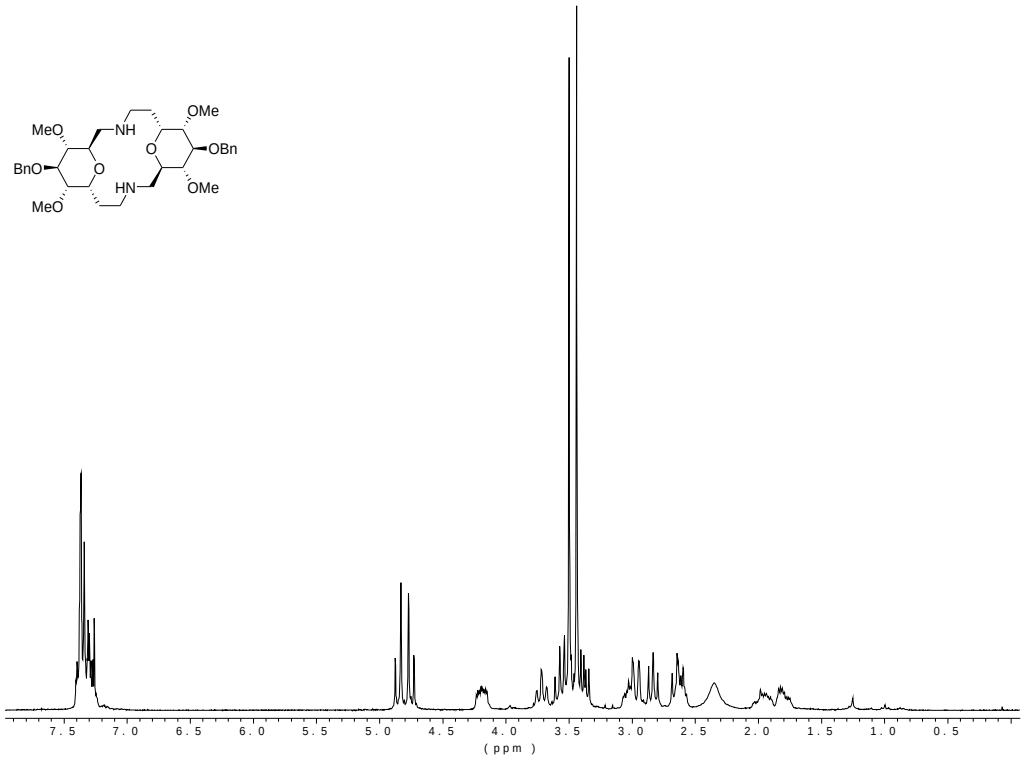


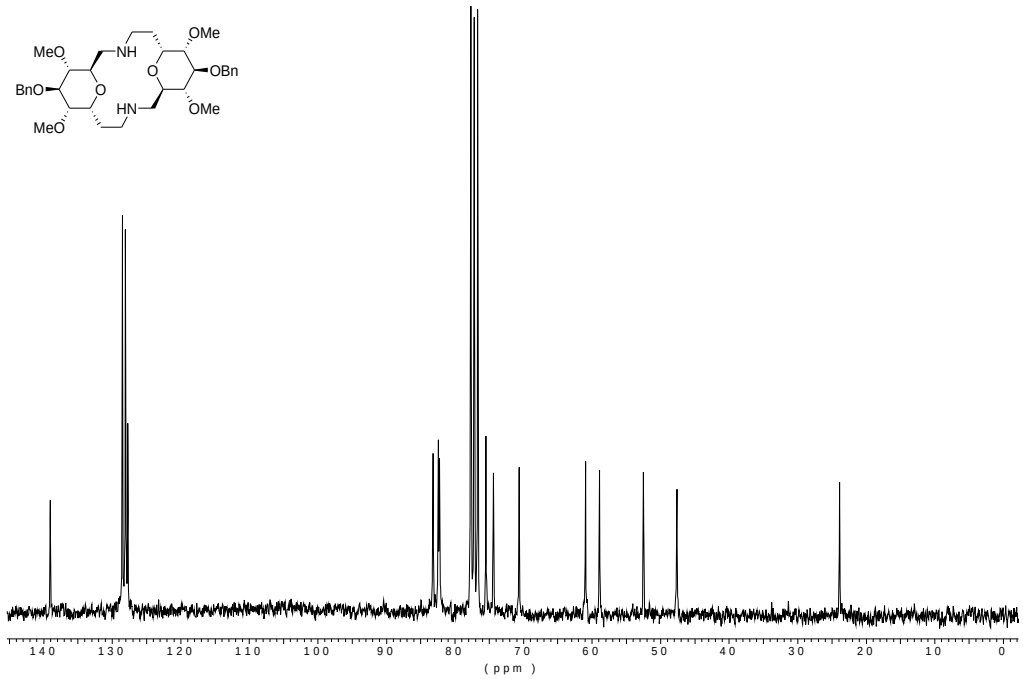
^{13}C NMR of Imine cyclodimer **8** in $CDCl_3$



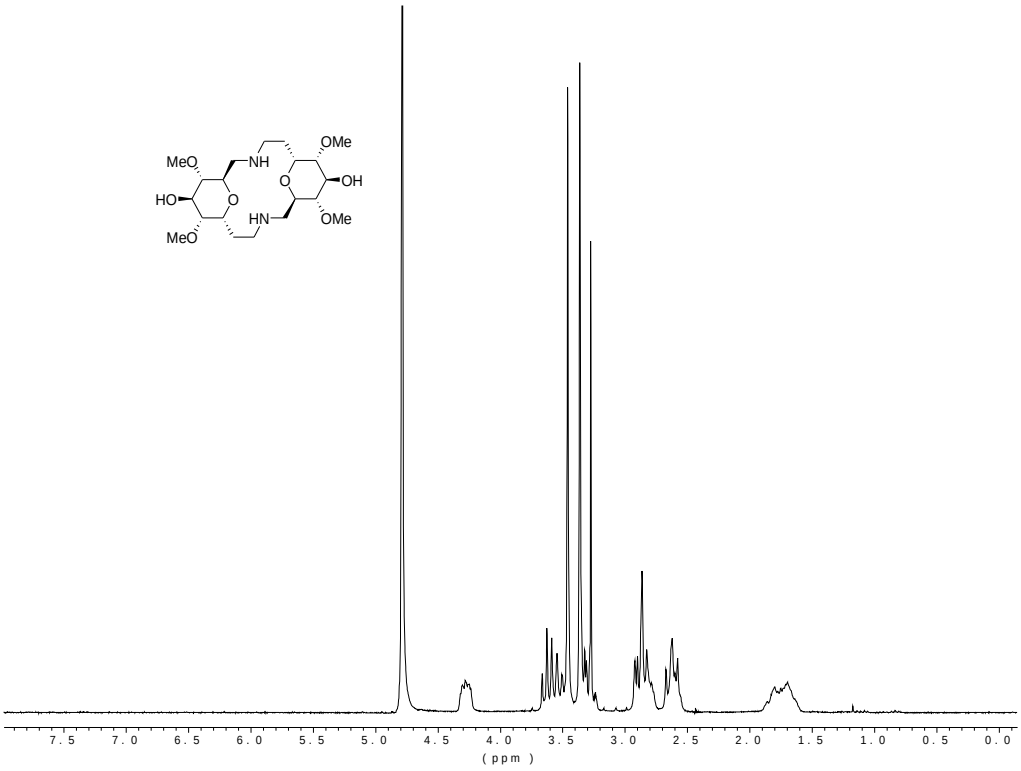
^{1}H NMR of SAC **9** in $CDCl_3$



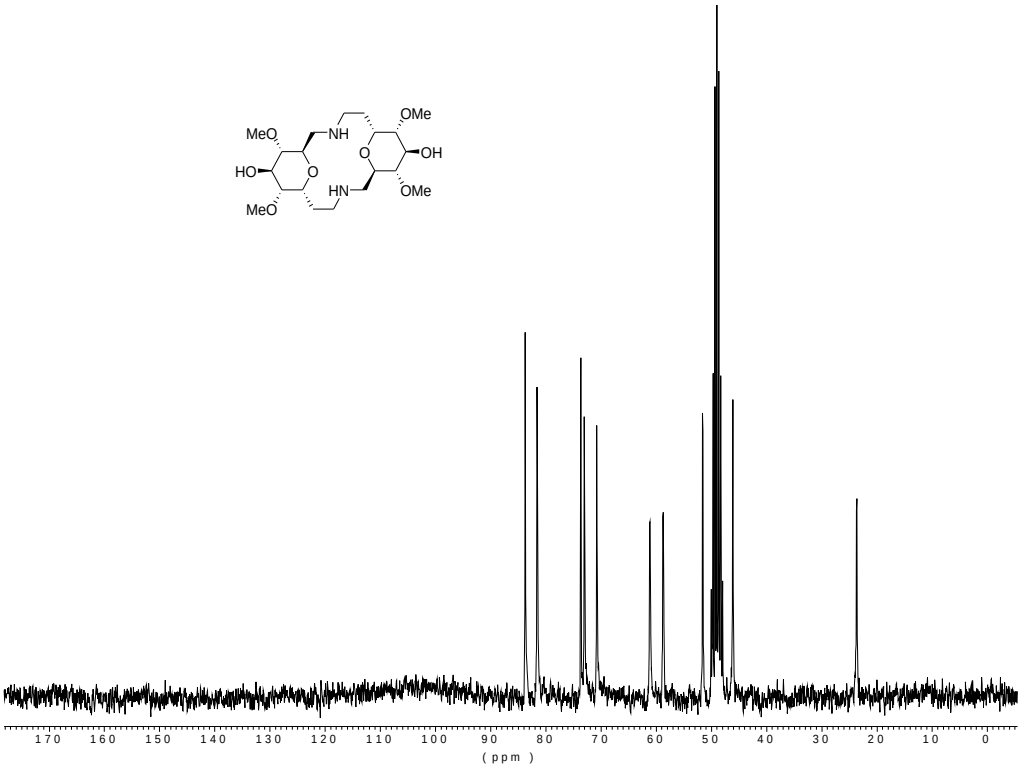
^{13}C NMR of SAC **9** in $CDCl_3$



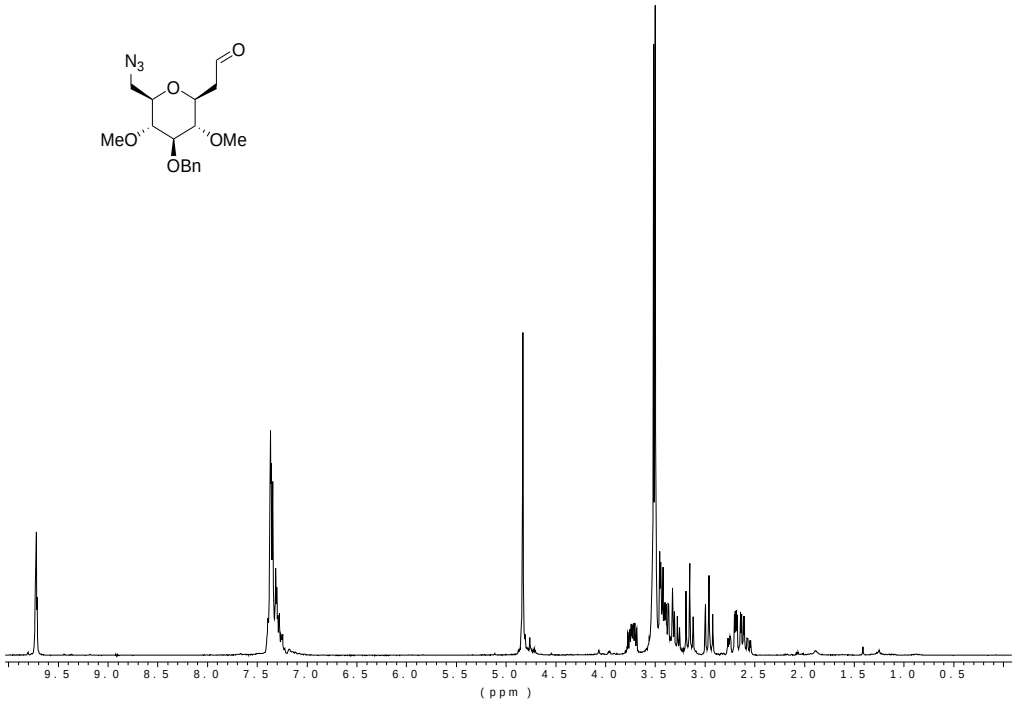
^{1}H NMR of SAC **13** in D_2O with 20% CD_3OD



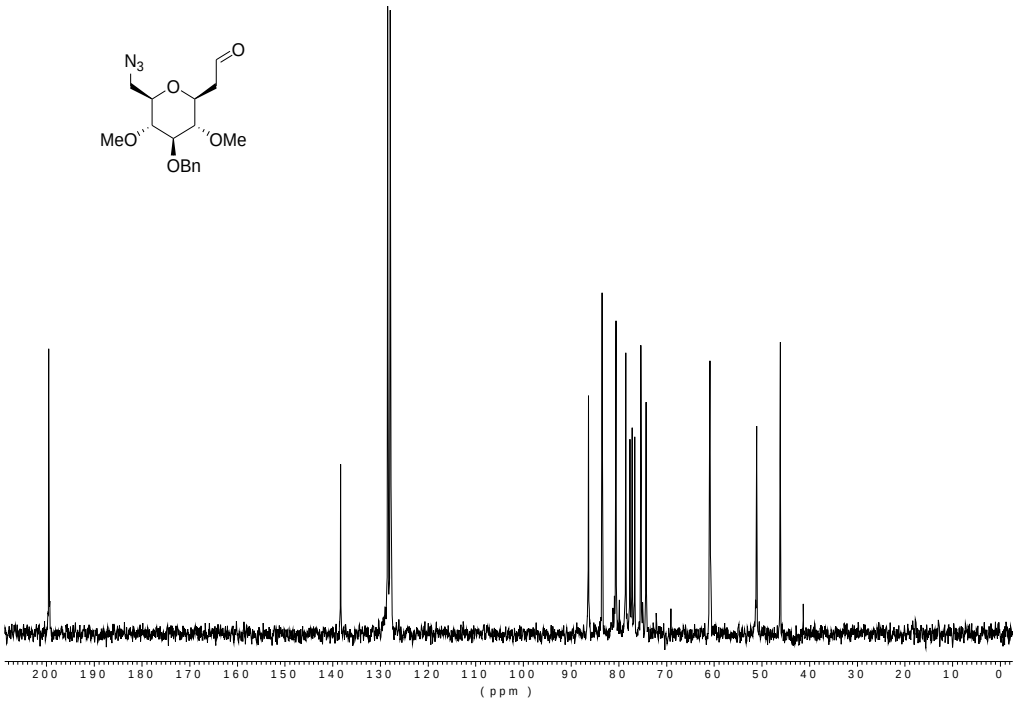
^{13}C NMR of SAC **13** in D_2O with 20% CD_3OD



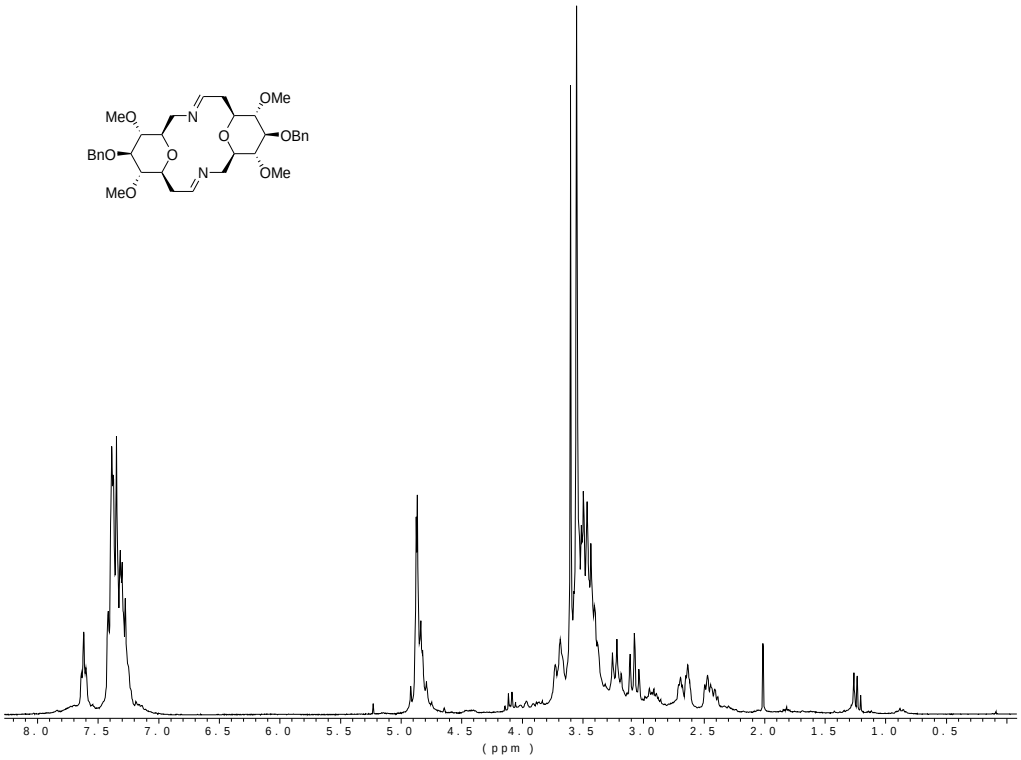
^{1}H NMR of Aldehyde **14** in $CDCl_3$



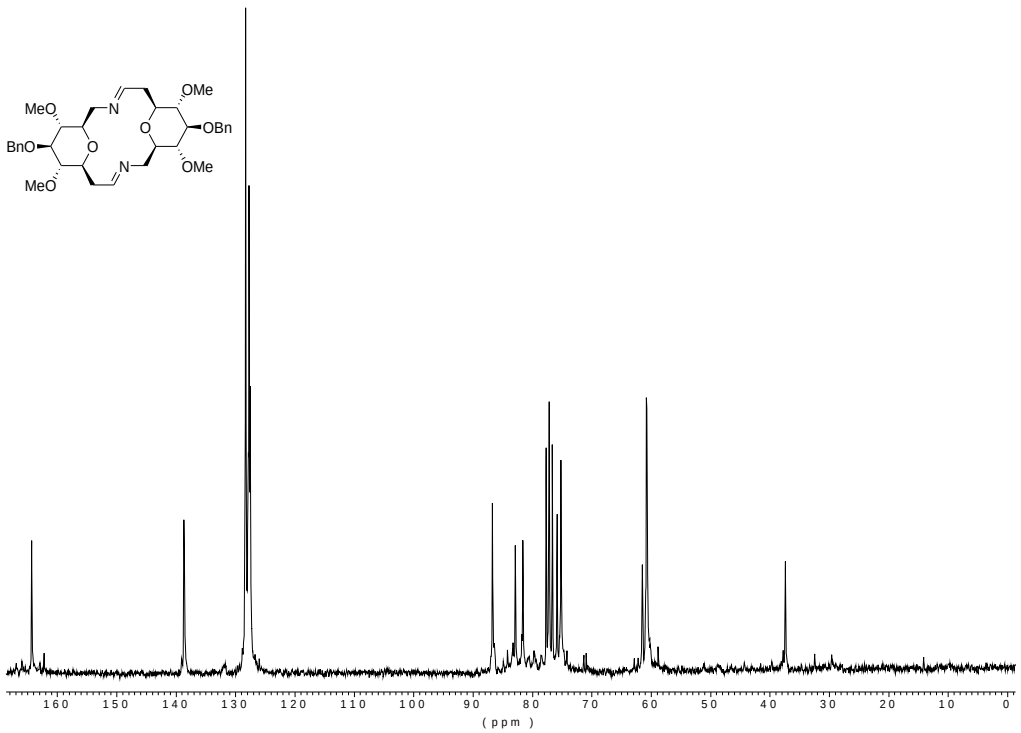
^{13}C NMR of Aldehyde **14** in $CDCl_3$



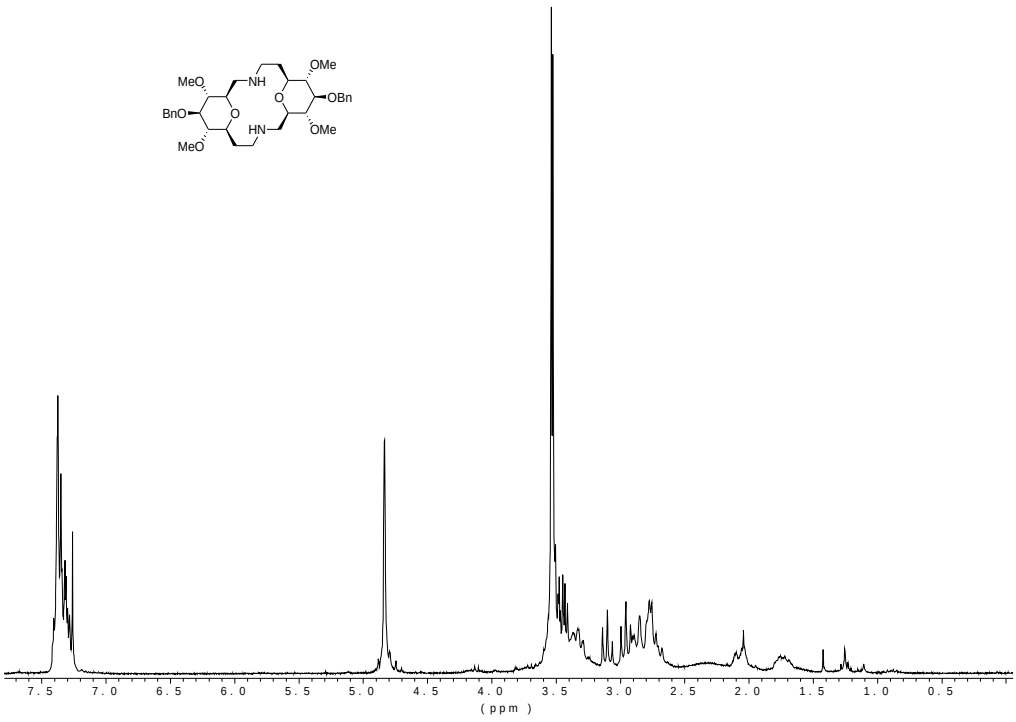
^{1}H NMR of Imine cyclodimer **15** in $CDCl_3$



^{13}C NMR of Imine cyclodimer **15** in $CDCl_3$



^{1}H NMR of SAC **16** in $CDCl_3$



^{13}C NMR of SAC **16** in $CDCl_3$