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Supporting Information

Non-natural Acetogenin Analogues as Potent *Trypanosoma brucei* Inhibitors

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General experimental

Analytical thin layer chromatography was carried out on Merck Kieselgel 60 F254 plates with visualization by ultraviolet light (254 nm) and/or heating the plate after staining with either a solution of 20% ceric ammonium molybdate w/v in H_2O or 20% potassium permanganate w/v in H_2O. Optical rotations were measured with a Perkin-Elmer 341 polarimeter at 589 nm (sodium D line) and concentrations (c) are reported in g/100 mL. Infrared (IR) spectra were recorded on a Perkin-Elmer Paragon series 1000 FTIR spectrophotometer or a Shimadzu IRAffinity-1 fourier transform IR spectrophotometer using Pike MIRacle ATR accessory. Analysis was carried out using Shimadzu IRsolution v1.50. Wavelengths of maximum absorbance (νmax) are quoted in cm^{-1}. Only selected, characteristic IR absorption data are provided for each compound. NMR spectra were recorded using deuterochloroform ($CDCl_3$) as the solvent. Chemical shifts (δ) are given in parts per million (ppm) from tetramethylsilane ($\delta = 0$) and were measured relative to the signal of the solvent in which the sample was analyzed ($CDCl_3$: δ 7.26, ^1H NMR; δ 77.0, ^{13}C NMR). Coupling constants (*J* values) are given in Hertz (Hz) and are reported to the nearest 0.1 Hz. ^1H NMR spectral data are tabulated in the order: number of protons, multiplicity (br, broad; s, singlet; d, doublet; dd, doublet of doublets; t, triplet; q, quartet; m, multiplet), coupling constant and proton assignment using the numbering shown. HPLC analyses were obtained on a a Shimadzu HPLC consisting of a DGU-20A5 degasser, LX-20AT liquid chromatograph, SIL-20AHT autosampler, CMB-20A column oven with variable temperature setting (25−40 °C).

General procedure A: Copper catalyzed azide-alkyne cycloaddition reactions

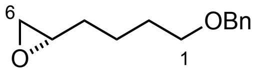
To a solution of alkyne (1 eq) and azide (1 eq) in *t*-BuOH (1 mL) and H_2O (1 mL) was added $CuSO_4{\cdot}5H_2O$ (1.2 eq) and sodium ascorbate (2.4 eq) at RT and the mixture left to stir for 16 h. The reaction mixture was diluted with H_2O (5 mL) and CH_2Cl_2 (5 mL). The organics were extracted with CH_2Cl_2 (3 × 5 mL), dried (Na_2SO_4) and concentrated *in vacuo*. Purification by flash column chromatography provided the desired 1,4-triazoles.

General procedure B: Benzyl ether cleavage

To a solution of benzyl ether (1 eq) in EtOH (4 mL) at RT was added $Pd(OH)_2$ on carbon (0.2 eq, 20% wt on carbon). The reaction system was purged with H_2 and left under a positive pressure of H_2. After 1.5 h, the reaction mixture was filtered through Celite with EtOH (15 mL). The filtrate was concentrated *in vacuo* and purification by flash column chromatography provided the desired alcohols.

The synthesis of **8a, 9a, 10a and 14a** have been described previously.[1]

(2*S*)-2-[4-(benzyloxy)butyl] oxirane (10b)[2]



To a suspension of NaH (3.22 g, 60% dispersion in mineral oil, 134 mmol) in THF (140 mL) at 0 °C was added a solution of 5-hexen-1-ol **276** (8.24 mL, 69.9 mmol) in THF (10 mL) *via* cannula. After 5 min, benzyl bromide (10.0 mL, 84.1 mmol) was added and the reaction mixture allowed to warm to RT. After 16 h, the reaction mixture was quenched by slow addition of MeOH (2 mL), followed by addition of saturated aqueous NH_4Cl (100 mL). The organics were extracted with Et_2O (3 × 50 mL), washed with H_2O (50 mL), brine (50 mL), dried (Na_2SO_4) and concentrated *in vacuo*. Purification by flash column chromatography (5% EtOAc/Hexane) provided 6-(benzyloxy)-hex-1-ene (13.0 g, 98%) as a colourless oil.

R_f 0.74 (10% EtOAc/Hexane); **^{1}H NMR** (300 MHz, $CDCl_3$) δ 7.42-7.27 (5H, m, Ar$\underline{H}$), 5.81 (1H, app ddt, *J* = 16.9, 10.2, 6.7 Hz, $\underline{H}_5$), 5.04-4.92 (2H, m, $\underline{H}_6$), 4.51 (2H, s, OC$\underline{H}_2$Ar), 3.48 (2H, t, *J* = 6.4 Hz, $\underline{H}_1$), 2.11-2.03 (2H, m, $\underline{H}_4$), 1.69-1.56 (2H, m, $\underline{H}_2$), 1.53-1.43 (2H, m, $\underline{H}_3$).

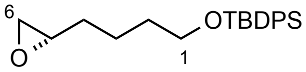
To a solution of 6-(benzyloxy)-hex-1-ene (13.3 g, 69.9 mmol) in CH_2Cl_2 (200 mL) at 0 °C was added m-CPBA (20.5 g, 119 mmol) and the reaction mixture allowed to warm to RT. After 16 h, the reaction mixture was quenched by addition of saturated aqueous $NaHCO_3$ (150 mL). The organics were extracted with CH_2Cl_2 (3 × 100 mL), washed with KOH (100 mL), H_2O (100 mL) and brine (100 mL). The combined organic layers were dried (Na_2SO_4), filtered and concentrated *in vacuo*. Purification by flash column chromatography (1→10% EtOAc/Hexane) provided (±)-epoxide **10b** (10.8 g, 75%) as a colourless oil.

R_f 0.3 (10% EtOAc/Hexane); **^{1}H NMR** (300 MHz, $CDCl_3$) δ 7.38-7.27 (5H, m, Ar$\underline{H}$), 4.51 (2H, s, OC$\underline{H}_2$Ar), 3.49 (2H, t, *J* = 6.2 Hz, $\underline{H}_1$), 2.94-2.88 (1H, m, $\underline{H}_5$), 2.75 (1H, dd, *J* = 5.0, 4.0 Hz, $\underline{H}_{6a}$), 2.46 (1H, dd, *J* = 5.0, 2.7 Hz, $\underline{H}_{6b}$), 1.73-1.51 (6H, m, $\underline{H}_{2-4}$).

To a suspension of (*S*, *S*)-Co-salen catalyst[3] (63.0 mg, 0.11 mmol) in toluene (2 mL) at RT was added acetic acid (63.0 μL, 1.10 mmol). After 1 h open to air, the solvent was removed under reduced pressure and the brown tar residue was dried under vacuum. To the residue was added (±)-**10b** (10.8 g, 52.4 mmol), the reaction mixture was cooled to 0 °C and water (520 μL, 28.8 mmol) was slowly added. After 16 h at RT, purification by flash column chromatography (5% EtOAc/Hexane) provided (*S*)-epoxide **10b** (4.56 g, 42%) as a colourless oil.

R$_f$ 0.3 (10% EtOAc/Hexane); $[\alpha]_D^{20}$ -5.2 (*c* 2.0, $CHCl_3$), lit $[\alpha]_D^{20}$ -5.1 (*c* 2.0, $CHCl_3$)[2]; **^{1}H NMR** (300 MHz, $CDCl_3$) δ 7.38-7.27 (5H, m, Ar$\underline{H}$), 4.51 (2H, s, OC$\underline{H}_2$Ar), 3.49 (2H, t, *J* = 6.2 Hz, $\underline{H}_1$), 2.94-2.88 (1H, m, $\underline{H}_5$), 2.75 (1H, dd, *J* = 5.0, 4.0 Hz, $\underline{H}_{6a}$), 2.46 (1H, dd, *J* = 5.0, 2.7 Hz, $\underline{H}_{6b}$), 1.73-1.51 (6H, m, $\underline{H}_{2\text{-}4}$).

(2*S*)-2-[4-((*tert*-butyldiphenylsilyl)oxy)butyl] oxirane (10c)[4]



To a suspension of NaH (3.36 g, 60% dispersion in mineral oil, 84.0 mmol) in THF (140 mL) at 0 °C was added a solution of 5-hexen-1-ol (8.4 mL, 70.0 mmol) in THF (10 mL) *via* cannula. After 5 min, benzyl bromide (10.0 mL, 84.0 mmol) was added and the reaction mixture allowed to warm to RT. After 16 h, the reaction mixture was quenched by slow addition of MeOH (2 mL), followed by addition of saturated aqueous NH_4Cl (100 mL). The organics were extracted with Et_2O (3 × 50 mL), washed with H_2O (50 mL), brine (50 mL), dried (Na_2SO_4) and concentrated *in vacuo*. Purification by flash column chromatography (0.25→10% Et_2O/Hexane) provided 6-((*tert*-butyldiphenylsilyl)oxy)-hex-1-ene (20.8 g, 87%) as a colourless oil.

R$_f$ 0.81 (10% EtOAc/Hexane); **^{1}H NMR** (300 MHz, $CDCl_3$) δ 7.69-7.65 (4H, m, Ar$\underline{H}$), 7.45-7.35 (6H, m, Ar$\underline{H}$), 5.80 (1H, app ddt, *J* = 16.9, 10.1, 6.6 Hz, $\underline{H}_5$), 5.01-4.92 (2H, m, $\underline{H}_6$), 3.66 (2H, t, *J* = 6.3 Hz, $\underline{H}_1$), 2.04 (2H, app q, *J* = 7.0 Hz, $\underline{H}_4$), 1.63-1.42 (4H, m, $\underline{H}_{2\text{-}3}$), 1.05 (9H, s, SiC(C$\underline{H}_3$)$_3$).

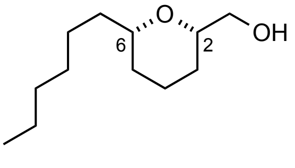
To a solution of 6-((*tert*-butyldiphenylsilyl)oxy)-hex-1-ene (20.8 g, 61.4 mmol) in CH_2Cl_2 (200 mL) at 0 °C was added m-CPBA (18.0 g, 104 mmol) and the reaction mixture allowed to warm to RT. After 2 h, the reaction mixture was quenched by addition of saturated aqueous $NaHCO_3$ (150 mL). The organics were extracted with CH_2Cl_2 (3 × 100 mL), washed with KOH (100 mL), H_2O (100 mL) and brine (100 mL). The combined organic layers were dried ($MgSO_4$), filtered and concentrated *in vacuo*. Purification by flash column chromatography (7.5% Et_2O/Hexane) provided (±)-epoxide **10c** (20.4 g, 94%) as a colourless oil.

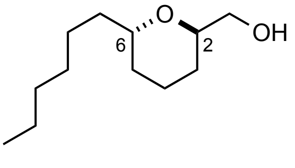
R_f 0.21 (5% Et_2O/Hexane); **^{1}H NMR** (400 MHz, $CDCl_3$) δ 7.68-7.65 (4H, m, Ar$\underline{H}$), 7.45-7.36 (6H, m, Ar$\underline{H}$), 3.67 (2H, t, J = 6.2 Hz, $\underline{H}_1$), 2.97-2.87 (1H, m, $\underline{H}_5$), 2.74 (1H, dd, J = 5.0, 4.0 Hz, $\underline{H}_{6a}$), 2.44 (1H, dd, J = 5.0, 2.7 Hz, $\underline{H}_{6b}$), 1.63-1.50 (6H, m, $\underline{H}_{2-4}$), 1.05 (9H, s, $SiC(C\underline{H}_3)_3$). [4]

To a suspension of (*S*, *S*)-Co-salen catalyst[3] (69.0 mg, 0.12 mmol) in toluene (2 mL) at RT was added acetic acid (67.0 μL, 0.12 mmol). After 1 h open to air, the solvent was removed under reduced pressure and the brown tar residue was dried under vacuum. To the residue was added (±)-epoxide **10c** (20.4 g, 57.5 mmol), the reaction mixture was cooled to 0 °C and water (570 μL, 31.7 mmol) was slowly added. After 16 h at RT, purification by flash column chromatography (5% EtOAc/Hexane) provided (*S*)-epoxide **10c** (11.6 g) as a colourless oil. HPLC analysis indicated an ee of 50%. Hence, more catalyst was prepared as above from (*S*, *S*)-Co-salen catalyst (32.0 mg, 52.0 μmol) and acetic acid (31.0 μL, 52.0 μmol) and this was taken up in THF (13 mL) to improve solubility. (*S*)-epoxide **10c** (11.6 g, 32.7 mmol) was added, the reaction mixture was cooled to 0 °C and water (235.0 μL, 15.9 mmol) was slowly added. After 5 days at 20 °C, the mixture was concentrated *in vacuo* then purified by flash column chromatography (5% EtOAc/Hexane) to provide (*S*)-epoxide **10c** (7.74 g, 48%) as a colourless oil with an ee of 97%.[4]

$[\alpha]_D^{20}$ -3.5 (*c* 1.1, $CHCl_3$), lit $[\alpha]_D^{20}$ +3.8 (*R*-enantiomer, *c* 1.06, $CHCl_3$)[4]; **Chiral HPLC** Daicel Chiralpak IA (hexane, flow rate 1 mL/min, 220 nm, 30 °C) t_R minor = 13.0 min, t_R major = 14.8 min.

(2*S*,6*S*)-6-hexyl-2-(hydroxymethyl)tetrahydropyran (8a) and (2*R*,6*S*)-6-hexyl-2-(hydroxymethyl)tetrahydropyran (9a)[1]





To a solution of magnesium turnings (4.50 g, 191 mmol) and a crystal of iodine in THF (170 mL) was added 2.5 mL of a solution of 4-bromo-1-butene (9.80 mL, 95.5 mmol) in THF (20 mL) and the reaction mixture heated to reflux. Upon initian of the reaction (colour changed from orange to clear), the rest of the solution was added over 1 h at RT. After a further 1 h the reaction was cooled to -78 °C and copper(I) iodide (360 mg, 1.91 mmol) added. After 10 min, a solution of (*S*)-epoxide **10a**[5] (4.90 g, 38.2 mmol) in THF (5 mL) was added in one portion. The reaction was warmed to 0 °C over 1 h then warmed to RT for a further hour. The residual magnesium turnings were decanted and the resulting solution extracted with saturated aqueous NH_4Cl (70 mL) and water (70 mL). The combined aqueous layers were washed with Et_2O (3 x 50 mL) and the combined organic extracts were washed with brine (100 mL), dried (Na_2SO_4), filtered and concentrated *in vacuo*. Purification by flash column chromatography (20% Et_2O/Hexane) provided (6*S*)-dodec-1-en-6-ol (5.90 g, 84%) as a colourless oil.

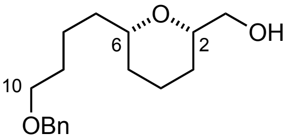
$\mathbf{R_f}$ 0.4 (25% EtOAc/Pet.Ether); $[\alpha]_D^{20}$ +1.0 (*c* 3.5, $CHCl_3$); **^{1}H NMR** (300 MHz, $CDCl_3$) δ 5.81 (1H, app dddd, *J* = 16.9, 13.3, 10.1, 6.7 Hz, $\underline{H}_2$), 5.05-4.92 (2H, m, $\underline{H}_1$), 3.63-3.53 (1H, m, $\underline{H}_6$), 2.10-2.02 (2H, m, $\underline{H}_3$), 1.46-1.37 (6H, m, $\underline{H}_{4-5}$ + $\underline{H}_7$), 1.32-1.25 (8H, m, $\underline{H}_{8-11}$), 0.88 (3H, t, *J* = 6.8 Hz, $\underline{H}_{12}$).

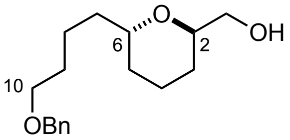
To a solution of (6*S*)-dodec-1-en-6-ol (5.90 g, 32.0 mmol) in CH_2Cl_2 (160 mL) at 0 °C was added *m*-CPBA (8.30 g, 68.9 mmol). The reaction mixture was allowed to warm to RT for 3 h before being re-cooled to 0 ^{o}C, and addition of (±)-CSA (1.49 g, 6.40 mmol) in one portion. The reaction mixture was stirred at RT for an additional 2.5 h prior to the addition of a saturated aqueous solution of $NaHCO_3$ (150 mL). The layers were seperated and the aqueous layer washed with CH_2Cl_2 (2 x 50 mL). The combined organic extracts were washed with brine (100 mL), dried (Na_2SO_4), filtered and concentrated *in vacuo*. Purification by flash column chromatography (10→35% EtOAc/Hexane) gave a separable mixture of *syn*-alcohol **8a** and *anti*-alcohol **9a** as colourless oils, in a combined 95% yield (d.r. **8a** : **9a** = 53 : 47).

8a: $\mathbf{R_f}$ 0.27 (25% EtOAc/Hexane); $[\alpha]_D^{20}$ -3.3 (*c* 1.8, $CHCl_3$); **^{1}H NMR** (300 MHz, $CDCl_3$) δ 3.61-3.39 (3H, m, $\underline{H}_1$ + $\underline{H}_2$), 3.34-3.24 (1H, m, $\underline{H}_6$), 2.13 (1H, br s, O$\underline{H}$), 1.90-1.78 (1H, m, $\underline{H}_{4a}$), 1.64-1.46 (3H, m, $\underline{H}_{3a}$ + $\underline{H}_{4b}$ + $\underline{H}_{5a}$), 1.46-1.24 (10H, m, $\underline{H}_{7-11}$), 1.24-1.09 (2H, m, $\underline{H}_{3b}$ + $\underline{H}_{5b}$), 0.88 (3H, t, *J* = 6.6 Hz, $\underline{H}_{12}$).

9a: $\mathbf{R_f}$ 0.19 (25% EtOAc/Hexane); $[\alpha]_D^{20}$ -16.1 (*c* 2.0, $CHCl_3$); **^{1}H NMR** (300 MHz, $CDCl_3$) δ 3.81-3.70 (2H, m, $\underline{H}_2$ + $\underline{H}_6$), 3.65 (1H, ddd, *J* = 11.0, 8.4, 2.9 Hz, $\underline{H}_{1a}$), 3.45 (1H, ddd, *J* = 11.0, 8.4, 3.6 Hz, $\underline{H}_{1b}$), 2.02 (1H, br s, O$\underline{H}$), 1.75-1.51 (5H, m, $\underline{H}_3$ + $\underline{H}_{4a}$ + $\underline{H}_5$), 1.44-1.27 (11H, m, $\underline{H}_{4b}$ + $\underline{H}_{7-11}$), 0.88 (3H, t, *J* = 7.0 Hz, $\underline{H}_{12}$).

(2*S*,6*S*)-6-[(4-benzyloxy)butyl]-2-(hydroxymethyl)tetrahydropyran (8b) and (2*R*,6*S*)-6-[(4-benzyloxy) butyl]-2-(hydroxymethyl)tetrahydropyran (9b)





To a solution of magnesium turnings (2.15 g, 88.4 mmol) in Et_2O (15 mL) was added slowly a solution of 4-bromo-1-butene (6.70 mL, 66.3 mmol) in THF (20 mL) and the reaction mixture heated to 50 °C. After 2 h, the reaction mixture was allowed to cool to RT. To a stirred solution of (*S*)-epoxide **10b** (4.56 g, 22.1 mmol) and copper(I) iodide (550 mg, 2.87 mmol) in THF (50 mL) at -40 °C was added the freshly prepared homoallylmagnesium bromide solution (35 mL, ~1.89 M solution) *via* cannula and the resulting black solution allowed to warm to RT. After 2 h, the solution was quenched by the addition of a saturated aqueous NH_4Cl (40 mL). The organics were extracted with Et_2O (3 x 40 mL) and the combined organic extracts were dried (Na_2SO_4), filtered and concentrated *in vacuo*. Purification by flash column chromatography (10% EtOAc/Pet. Ether) provided (5*R*)-1-(benzyloxy) dec-9-en-5-ol (5.77 g, 99%) as a colourless oil.

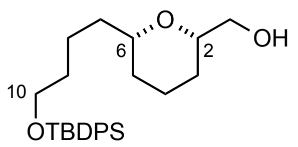
R$_f$ 0.48 (20% EtOAc/Hexane); $[\alpha]_D^{20}$ +0.14 (*c* 1.46, $CHCl_3$); **IR** (thin film) 3399, 2934, 2859, 17.17, 1639, 1454 cm^{-1}; **^{1}H NMR** (300 MHz, $CDCl_3$) δ 7.37-7.27 (5H, m, Ar$\underline{H}$), 5.81 (1H, app ddt, *J* = 16.9, 10.2, 6.7 Hz, $\underline{H}_2$), 5.05-4.93 (2H, m, $\underline{H}_1$), 4.50 (2H, s, OC$\underline{H}_2$Ar), 3.63-3.56 (1H, m, $\underline{H}_6$), 3.48 (2H, t, *J* = 6.4 Hz, $\underline{H}_{10}$), 2.10-2.06 (2H, m, $\underline{H}_3$), 1.69-1.59 (2H, m, $\underline{H}_9$), 1.58-1.36 (8H, m, $\underline{H}_{4\text{-}5}$ + $\underline{H}_{7\text{-}8}$); **^{13}C NMR** (75 MHz, $CDCl_3$) δ 138.7, 138.5, 128.3, 127.6, 127.5, 114.5, 72.9, 71.6, 70.2, 37.2, 36.8, 33.7, 29.7, 24.9, 22.3; **HRMS** (ES$^+$) Calc. for $C_{17}H_{26}O_2Na$ $[M+Na]^+$ 285.1839, found 285.1824.

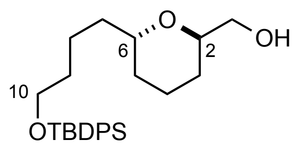
To a solution of (5*R*)-1-(benzyloxy) dec-9-en-5-ol (5.77 g, 22.0 mmol) in CH_2Cl_2 (100 mL) at 0 °C was added *m*-CPBA (6.53 g, 37.8 mmol). The reaction mixture was allowed to warm to RT for 3 h before being re-cooled to 0 °C, and addition of (±)-CSA (1.02 g, 4.40 mmol) in one portion. The reaction mixture was stirred at RT for an additional 6 h prior to the addition of a saturated aqueous solution of $NaHCO_3$ (100 mL). The organics were extracted with CH_2Cl_2 (3 x 50 mL). The combined organic extracts were dried (Na_2SO_4), filtered and concentrated *in vacuo*. Purification by flash column chromatography (5→10% EtOAc/Hexane) gave a separable mixture of *syn*-alcohol **8b** and *anti*-alcohol **9b** as colourless oils, in a combined 77% yield (d.r. **8b** : **9b** = 55 : 44).

8b: **R$_f$** 0.27 (25% EtOAc/Hexane); $[\alpha]_D^{20}$ -2.2 (*c* 1.12, $CHCl_3$); **IR** (thin film) 3447, 2936, 2859, 1454 cm^{-1}; **^{1}H NMR** (400 MHz, $CDCl_3$) δ 7.38-7.27 (5H, m, Ar$\underline{H}$), 4.50 (2H, s, OC$\underline{H}_2$Ar), 3.58-3.55 (1H, m, $\underline{H}_{1a}$), 3.51-3.41 (4H, m, $\underline{H}_{1b}$ + $\underline{H}_2$ + $\underline{H}_{10}$), 3.34-3.28 (1H, m, $\underline{H}_6$), 1.91 (1H, br s, O$\underline{H}$), 1.87-1.82 (2H, m, $\underline{H}_4$), 1.66-1.37 (8H, m, $\underline{H}_{3a}$ + $\underline{H}_{5a}$ + $\underline{H}_{7-9}$), 1.24-1.12 (2H, m, $\underline{H}_{3b}$ + $\underline{H}_{5b}$); **^{13}C NMR** (75 MHz, $CDCl_3$) δ 138.5, 128.3, 127.6, 127.4, 77.9, 77.5, 72.8, 70.2, 66.3, 36.1, 31.5, 29.7, 27.1, 23.1, 22.2; **HRMS** (ES$^+$) Calc. for $C_{17}H_{27}O_3$ $[M+H]^+$ 279.1955, found 279.1960.

9b: **R$_f$** 0.19 (25% EtOAc/Hexane); $[\alpha]_D^{20}$ -24.3 (*c* 1.0, $CHCl_3$); **IR** (thin film) 3447, 2936, 2862, 1456 cm^{-1}; **^{1}H NMR** (400 MHz, $CDCl_3$) δ 7.36-7.27 (5H, m, Ar$\underline{H}$), 4.50 (2H, s, OC$\underline{H}_2$Ar), 3.80-3.74 (2H, m, $\underline{H}_2$ + $\underline{H}_6$), 3.67 (1H, dd, *J* = 11.1, 8.4 Hz, $\underline{H}_{1a}$), 3.50-3.44 (3H, m, $\underline{H}_{1b}$ + $\underline{H}_{10}$), 1.87 (1H, br s, O$\underline{H}$), 1.80-1.52 (8H, m, $\underline{H}_{3a}$ + $\underline{H}_4$ + $\underline{H}_{5a}$ + $\underline{H}_7$ + $\underline{H}_9$), 1.51-1.32 (4H, m, $\underline{H}_{3b}$ + $\underline{H}_{5b}$ + $\underline{H}_8$); **^{13}C NMR** (75 MHz, $CDCl_3$) δ 138.5, 128.2, 127.5, 127.3, 72.7, 71.5, 70.7, 70.1, 64.1, 32.0, 29.5, 29.3, 26.3, 22.4, 18.3; **HRMS** (ES$^+$) Calc. for $C_{17}H_{27}O_3$ $[M+H]^+$ 279.1955, found 279.1960.

(2*S*,6*S*)-6-[((*tert*-butyldiphenylsilyl)oxy)butyl]-2-(hydroxymethyl)tetrahydropyran (8c) and (2*R*,6*S*)-6-[((*tert*-butyldiphenylsilyl)oxy)butyl]-2-(hydroxymethyl) tetrahydropyran (9c)





To a solution of magnesium turnings (2.56 g, 109 mmol) and a crystal of iodine in THF (120 mL) was added 3 mL of a solution of 4-bromo-1-butene (5.50 mL, 54.5 mmol) in THF (20 mL) and the reaction mixture heated to reflux. Upon initian of the reaction (colour changed from orange to clear), the rest of the solution was added over 1 h at RT. After a further 1 h the reaction was cooled to -78 °C and copper(I) iodide (206 mg, 1.08 mmol) added. After 10 min, a solution of (*S*)-epoxide **10c** (4.56 g, 22.1 mmol) in THF (10 mL) was added in one portion. The reaction was warmed to 0 °C over 1 h then warmed to RT for a further hour. The residual magnesium turnings were decanted and the resulting solution extracted with saturated aqueous NH_4Cl (100 mL) and water (50 mL). The combined aqueous layers were washed with Et_2O (3 x 50 mL) and the combined organic extracts were washed with brine (200 mL), dried (Na_2SO_4), filtered and concentrated *in* *vacuo*. Purification by flash column chromatography (15% Et_2O/Hexane) provided (5*R*)-1-((*tert*-butyldiphenylsilyl)oxy)dec-9-en-5-ol (8.00 g, 89%) as a colourless oil.

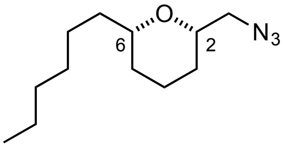
R$_f$ 0.29 (20% Et_2O/Hexane); $[\alpha]_D^{20}$ +0.20 (*c* 2.0, $CHCl_3$); **IR** (thin film) 3400, 2931, 2859, 1637, 1555 cm^{-1}; **^{1}H NMR** (300 MHz, $CDCl_3$) δ 7.72-7.61 (4H, m, Ar$\underline{H}$), 7.49-7.31 (6H, m, Ar$\underline{H}$), 5.81 (1H, app ddt, *J* = 16.9, 10.2, 6.6 Hz, $\underline{H}_2$), 5.08-4.90 (2H, m, $\underline{H}_1$), 3.67 (2H, t, *J* = 6.2 Hz, $\underline{H}_{10}$), 3.60-3.57 (1H, m, $\underline{H}_6$), 2.14-2.00 (2H, m, $\underline{H}_3$), 1.64-1.31 (2H, m, $\underline{H}_9$), 1.58-1.36 (8H, m, $\underline{H}_{4\text{-}5}$ + $\underline{H}_{7\text{-}8}$), 1.05 (9H, s, SiC(C$\underline{H}_3$)$_3$); **^{13}C NMR** (75 MHz, $CDCl_3$) δ 138.9, 135.7, 134.2, 129.7, 127.7, 114.7, 71.9, 63.9, 37.3, 37.0, 33.9, 32.7, 27.0, 25.1, 22.0, 19.4; **HRMS** (ES$^+$) Calc. for $C_{26}H_{39}O_2Si$ $[M+H]^+$ 411.2714, found 411.2712.

To a solution of (5*R*)-1-((*tert*-butyldiphenylsilyl)oxy)dec-9-en-5-ol (8.00 g, 19.5 mmol) in CH_2Cl_2 (150 mL) at 0 °C was added *m*-CPBA (6.53 g, 55.7 mmol). The reaction mixture was allowed to warm to RT for 2 h before being re-cooled to 0 °C, and addition of (±)-CSA (867 mg, 3.90 mmol) in one portion. The reaction mixture was stirred at RT for an additional 18 h prior to the addition of a saturated aqueous solution of $NaHCO_3$ (100 mL). The organics were extracted with CH_2Cl_2 (3 x 50 mL). The combined organic extracts were washed with brine (100 mL), dried (Na_2SO_4), filtered and concentrated *in vacuo*. Purification by flash column chromatography (10→20% EtOAc/Hexane) gave a separable mixture of *syn*-alcohol **8c** and *anti*-alcohol **9c** as colourless oils, in a combined 66% yield (d.r. **8c** : **9c** = 45 : 55).

8c: **R$_f$** 0.34 (20% EtOAc/Hexane); $[\alpha]_D^{20}$ -2.9 (*c* 1.2, $CHCl_3$); **IR** (thin film) 3426, 3071, 2932, 2857, 1589, 1471 cm^{-1}; **^{1}H NMR** (300 MHz, $CDCl_3$) δ 7.69-7.64 (4H, m, Ar$\underline{H}$), 7.45-7.34 (6H, m, Ar$\underline{H}$), 3.66 (2H, t, *J* = 6.3 Hz, $\underline{H}_{10}$), 3.58-3.42 (3H, m, $\underline{H}_1$ + $\underline{H}_2$), 3.32-3.25 (1H, m, $\underline{H}_6$), 1.87-1.81 (1H, m, $\underline{H}_{4a}$), 1.61-1.37 (8H, m, $\underline{H}_{4b}$ + $\underline{H}_{3a}$ + $\underline{H}_{7\text{-}9}$), 1.26-1.04 (3H, m, $\underline{H}_{3b}$ + $\underline{H}_5$); 1.04 (9H, s, SiC(C$\underline{H}_3$)$_3$); **^{13}C NMR** (75 MHz, $CDCl_3$) δ 135.7, 134.2, 129.6, 127.7, 78.1, 77.8, 66.5, 63.9, 36.3, 32.7, 31.7, 27.3, 27.0, 23.3, 21.9, 19.4; **HRMS** (ES$^+$) Calc. for $C_{26}H_{39}O_3Si$ $[M+H]^+$ 427.2663, found 427.2664.

9c: **R$_f$** 0.25 (20% EtOAc/Hexane); $[\alpha]_D^{20}$ -15.7 (*c* 1.0, $CHCl_3$); **IR** (thin film) 3389, 3071, 2934, 2859, 1471 cm^{-1}; **^{1}H NMR** (300 MHz, $CDCl_3$) δ 7.71-7.68 (4H, m, Ar$\underline{H}$), 7.48-7.37 (6H, m, Ar$\underline{H}$), 3.81-3.75 (2H, m, $\underline{H}_2$ + $\underline{H}_6$), 3.69 (2H, t, *J* = 6.4 Hz, $\underline{H}_{10}$), 3.68 (1H, dd, *J* = 10.9, 8.3 Hz, $\underline{H}_{1a}$), 3.49 (1H, dd, *J* = 10.9, 3.5 Hz, $\underline{H}_{1b}$), 1.90 (1H, br s, O$\underline{H}$), 1.72-1.57 (8H, m, $\underline{H}_{3a}$ + $\underline{H}_4$ + $\underline{H}_{5a}$ + $\underline{H}_7$ + $\underline{H}_9$), 1.45-1.29 (4H, m, $\underline{H}_{3b}$ + $\underline{H}_{5b}$ + $\underline{H}_8$), 1.07 (9H, s, SiC(C$\underline{H}_3$)$_3$); **^{13}C NMR** (75 MHz, $CDCl_3$) δ 135.7, 134.2, 130.0, 127.7, 71.8, 70.9, 64.4, 63.9, 32.6, 32.3, 29.6, 27.0, 26.6, 22.3, 19.4, 18.6; **HRMS** (ES$^+$) Calc. for $C_{26}H_{39}O_3Si$ $[M+H]^+$ 427.2663, found 427.2664.

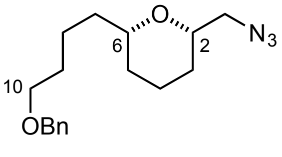
(2*S*,6*S*)-[2-azidomethyl-6-hexyl]tetrahydropyran (11a)



To a solution of alcohol **8a** (52.5 mg, 0.26 mmol) in THF (3 mL) was added PPh_3 (82.5 mg, 0.31 mmol) and $^iPr_2NEt$ (46.0 μL, 0.26 mmol). The solution was then cooled to 10 °C and DIAD (62.0 μL, 0.31 mmol) was added dropwise. After 20 min, DPPA (68.0 μL, 0.31 mmol) was added dropwise and the solution allowed to warm to RT and left to stir for 16 h. The reaction mixture was quenched by the addition of H_2O (3 mL). The organics were extracted with EtOAc (3 × 5 mL), dried over Na_2SO_4 and concentrated *in vacuo*. Purification by flash column chromatography (5% EtOAc/Hexane) provided azide **11a** (42.2 mg, 71%) as a colourless oil.

R$_f$ 0.79 (10% EtOAc/Hexane); $[\alpha]_D^{20}$ -33.8 (*c* 1.62, $CHCl_3$); **IR** (thin film) 2932, 2859, 2170, 2095, 1591, 1489 cm^{-1}; **^{1}H NMR** (400 MHz, $CDCl_3$) δ 3.53 (1H, dddd, *J* = 11.4, 7.5, 3.5, 2.1 Hz, $\underline{H}_2$), 3.34-3.27 (1H, m, $\underline{H}_6$), 3.29 (1H, dd, *J* = 12.8, 7.5 Hz, $\underline{H}_{1a}$), 3.07 (1H, dd, *J* = 12.8, 3.5 Hz, $\underline{H}_{1b}$), 1.90-1.82 (1H, m, $\underline{H}_{4a}$), 1.61-1.33 (7H, m, $\underline{H}_{3a}$ + $\underline{H}_{4b}$ + $\underline{H}_{5a}$ + $\underline{H}_7$ + $\underline{H}_{10}$), 1.32-1.14 (8H, m, $\underline{H}_{3b}$ + $\underline{H}_{5b}$ + $\underline{H}_{8-9}$ + $\underline{H}_{11}$), 0.87 (3H, t, *J* = 6.8 Hz, $\underline{H}_{12}$); **^{13}C NMR** (100 MHz, $CDCl_3$) δ 78.0, 77.0, 55.4, 36.4, 31.8, 31.3, 29.3, 28.7, 25.5, 23.3, 22.6, 14.1; **HRMS** (CI$^+$) Calc. for $C_{12}H_{24}ON_3$ $[M+H]^+$ 226.1914, found 226.1912.

(2*S*,6*S*)-2-(azidomethyl)-6-[4-(benzyloxy)butyl]tetrahydropyran (11b)

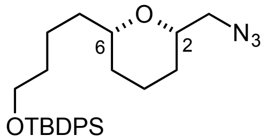


To a solution of alcohol **8b** (403 mg, 1.45 mmol) in THF (10 mL) was added PPh_3 (456 mg, 1.74 mmol) and $^iPr_2NEt$ (250 μL, 1.45 mmol). The solution was then cooled to 10 °C and DIAD (340 μL, 1.74 mmol) was added dropwise. After 20 min, DPPA (370 μL, 1.74 mmol) was added dropwise and the solution allowed to warm to RT and left to stir for 16

h. The reaction mixture was quenched by the addition of H_2O (10 mL). The organics were extracted with EtOAc (3 × 10 mL), dried over Na_2SO_4 and concentrated *in vacuo*. Purification by flash column chromatography (15% EtOAc/Hexane) provided azide **11b** (430 mg, 98%) as a colourless oil.

R$_f$ 0.68 (20% EtOAc/Hexane); $[\alpha]_D^{20}$ -31.6 (*c* 1.04, $CHCl_3$); **IR** (thin film) 2938, 2859, 2093, 1717, 1454 cm^{-1}; **^{1}H NMR** (400 MHz, $CDCl_3$) δ 7.35-7.24 (5H, m, Ar$\underline{H}$), 4.49 (2H, s, OC$\underline{H}_2$Ar), 3.54-3.48 (1H, m, $\underline{H}_2$), 3.47 (2H, t, *J* = 6.5 Hz, $\underline{H}_{10}$), 3.34-3.29 (1H, m, $\underline{H}_6$), 3.26 (1H, dd, *J* = 12.8, 7.5 Hz, $\underline{H}_{1a}$), 3.05 (1H, dd, *J* = 12.8, 3.4 Hz, $\underline{H}_{1b}$), 1.89-1.82 (1H, m, $\underline{H}_{4a}$), 1.68-1.39 (9H, m, $\underline{H}_{3a}$ + $\underline{H}_{4b}$ + $\underline{H}_{5a}$ + $\underline{H}_{7-9}$), 1.29-1.13 (2H, m, $\underline{H}_{3b}$ + $\underline{H}_{5b}$); **^{13}C NMR** (100 MHz, $CDCl_3$) δ 138.5, 128.1, 127.4, 127.2, 77.6, 76.8, 72.6, 70.2, 55.1, 36.0, 31.1, 29.5, 28.5, 23.0, 21.9; **HRMS** (ES$^+$) Calc. for $C_{17}H_{26}O_2N_3$ $[M+H]^+$ 304.2020, found 304.2021.

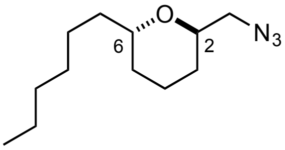
(2*S*,6*S*)-2-(azidomethyl)-6-[4-((*tert*-butyldiphenylsilyl)oxy)butyl]tetrahydropyran (11c)



To a solution of alcohol **8c** (619 mg, 1.45 mmol) in THF (10 mL) was added PPh_3 (456 mg, 1.74 mmol) and $^i Pr_2NEt$ (250 μL, 1.45 mmol). The solution was then cooled to 0 °C and DIAD (340 μL, 1.74 mmol) was added dropwise. After 20 min, DPPA (370 μL, 1.74 mmol) was added dropwise and the solution allowed to warm to RT and left to stir for 24 h. The reaction mixture was quenched by the addition of H_2O (15 mL). The organics were extracted with EtOAc (3 × 10 mL) and the combined organic layers washed with brine (20 mL), dried (Na_2SO_4) and concentrated *in vacuo*. Purification by flash column chromatography (30% EtOAc/Hexane) provided azide **11c** (574 mg, 88%) as a colourless oil.

R$_f$ 0.65 (10% EtOAc/Hexane); $[\alpha]_D^{20}$ -16.7 (*c* 1.1, $CHCl_3$); **IR** (thin film) 3071, 2934, 2859, 2170, 2095, 1716, 1589 cm^{-1}; **^{1}H NMR** (300 MHz, $CDCl_3$) δ 7.68-7.65 (4H, m, Ar$\underline{H}$), 7.44-7.34 (6H, m, Ar$\underline{H}$), 3.66 (2H, t, *J* = 6.3 Hz, $\underline{H}_{10}$), 3.56-3.48 (1H, m, $\underline{H}_2$), 3.35-3.24 (1H, m, $\underline{H}_6$), 3.28 (1H, dd, *J* = 12.7, 7.3 Hz, $\underline{H}_{1a}$), 3.07 (1H, dd, *J* = 12.7, 3.6 Hz, $\underline{H}_{1b}$), 1.90-1.82 (1H, m, $\underline{H}_{4a}$), 1.62-1.37 (8H, m, $\underline{H}_{4b}$ + $\underline{H}_{3a}$ + $\underline{H}_{7-9}$), 1.31-1.09 (3H, m, $\underline{H}_{3b}$ + $\underline{H}_5$); 1.05 (9H, s, SiC(C$\underline{H}_3$)$_3$); **^{13}C NMR** (75 MHz, $CDCl_3$) δ 135.7, 134.3, 129.6, 127.7, 78.0, 77.1, 64.1, 55.6, 36.2, 32.7, 31.4, 28.9, 27.0, 23.4, 21.9, 19.4; **HRMS** (ES$^+$) Calc. for $C_{26}H_{38}O_2N_3Si$ $[M+H]^+$ 452.2728, found 452.2725.

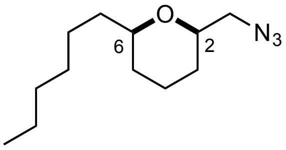
(2*R*,6*S*)-[2-azidomethyl-6-hexyl]tetrahydropyran (12)



To a solution of alcohol **9a** (50 mg, 0.26 mmol) in THF (10 mL) was added PPh_3 (83 mg, 0.32 mmol) and $^iPr_2NEt$ (46 μL, 0.26 mmol). The solution was then cooled to 10 °C and DIAD (62 μL, 0.32 mmol) was added dropwise. After 20 min, DPPA (68 μL, 0.32 mmol) was added dropwise and the solution allowed to warm to RT and left to stir for 16 h. The reaction mixture was quenched by the addition of H_2O (3 mL). The organics were extracted with EtOAc (3 × 7 mL), dried over Na_2SO_4 and concentrated *in vacuo*. Purification by flash column chromatography (2% Et_2O/Hexane) provided azide **12** (22 mg, 37%) as a colourless oil.

R$_f$ 0.75 (10% EtOAc/Hexane); $[\alpha]_D^{20}$ -2.1 (*c* 0.8, $CHCl_3$); **IR** (thin film) 2926, 2855, 2095, 1724, 1458, 1427 cm^{-1}; **^{1}H NMR** (400 MHz, $CDCl_3$) δ 3.85 (1H, app tt, *J* = 7.6, 3.8 Hz, $\underline{H}_2$), 3.81-3.75 (1H, m, $\underline{H}_6$), 3.43 (1H, dd, *J* = 12.7, 8.1 Hz, $\underline{H}_{1a}$), 3.08 (1H, dd, *J* = 12.7, 4.1 Hz, $\underline{H}_{1b}$), 1.75-1.56 (5H, m, $\underline{H}_{3a} + \underline{H}_4 + \underline{H}_{5a} + \underline{H}_{7a}$), 1.41-1.22 (11H, m, $\underline{H}_{3b} + \underline{H}_{5b} + \underline{H}_{7b} + \underline{H}_{8\text{-}11}$), 0.88 (3H, t, *J* = 6.4 Hz, $\underline{H}_{12}$); **^{13}C NMR** (100 MHz, $CDCl_3$) δ 72.0, 69.7, 53.8, 32.2, 31.8, 29.3, 29.2, 27.9, 25.7, 22.6, 18.3, 14.1; **HRMS** (ES$^+$) Calc. for $C_{12}H_{23}O_2N_3Na$ $[M+Na]^+$ 248.1733, found 248.1728.

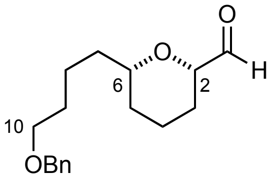
(2*R*,6*R*)-[2-azidomethyl-6-hexyl]tetrahydropyran (13)



Prepared in an identical manner to **11a**.

$[\alpha]_D^{20}$ +35.7 (*c* 0.9, $CHCl_3$).

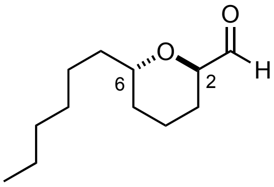
(2*S*,6*S*)-6-[(4-benzyloxy)butyl]-2-(carbaldehyde)tetrahydropyran (14b)



To a solution of dimethyl sulfoxide (310 μL, 4.37 mmol) in CH_2Cl_2 (10 mL) at -78 °C was added oxalyl chloride (310 μL, 3.59 mmol). The reaction mixture was stirred at this temperature for 30 min before the addition of alcohol **8b** (500 mg, 1.80 mmol) as a solution in CH_2Cl_2 (5 mL) *via* cannula. The reaction was stirred for a further 1 h, before the dropwise addition of Et_3N (1.75 mL, 12.6 mmol) and the reaction mixture was warmed to RT over 30 min. After the addition of saturated aqueous NH_4Cl (10 mL), the organics were extracted with CH_2Cl_2 (3 x 15 mL) and the combined organic extracts were dried (Na_2SO_4), filtered and concentrated *in vacuo*. Purification by flash column chromatography (5% EtOAc/Hexane) provided aldehyde **14b** (432 mg, 87%) as a colourless oil.

R$_f$ 0.54 (25% EtOAc/Hexane); $[\alpha]_D^{20}$ -38.7 (*c* 1.6, $CHCl_3$); **IR** (thin film) 3402, 2938, 2859, 1738, 1454, 1362 cm^{-1}; **^{1}H NMR** (300 MHz, $CDCl_3$) δ 9.62 (1H, s, $\underline{H}_1$), 7.36-7.26 (5H, m, Ar$\underline{H}$), 4.50 (2H, s, OC$\underline{H}_2$Ar), 3.78 (1H, ddd, *J* = 11.9, 2.7, 0.6 Hz, $\underline{H}_2$), 3.48 (2H, t, *J* = 6.4 Hz, $\underline{H}_{10}$), 3.41-3.32 (1H, m, $\underline{H}_6$), 1.98-1.89 (1H, m, $\underline{H}_{4a}$), 1.85-1.77 (1H, m, $\underline{H}_{3a}$), 1.69-1.43 (8H, m, $\underline{H}_{4b}$ + $\underline{H}_{5a}$ + $\underline{H}_{7-9}$), 1.41-1.16 (2H, m, $\underline{H}_{3b}$ + $\underline{H}_{5b}$); **^{13}C NMR** (75 MHz, $CDCl_3$) δ 202.3, 138.6, 128.3, 127.6, 127.4, 81.8, 77.9, 72.9, 70.2, 36.0, 31.0, 29.7, 26.1, 22.9, 22.1; **HRMS** (ES$^+$) Calc. for $C_{17}H_{25}O_3$ $[M+H]^+$ 277.1811, found 277.1796.

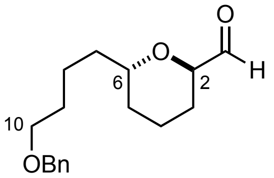
(2*R*,6*S*)-[2-carbaldehyde-6-hexyl]tetrahydropyran (15a)[6]



To a solution of dimethyl sulfoxide (300 μL, 4.23 mmol) in CH_2Cl_2 (8 mL) at -78 °C was added oxalyl chloride (300 μL, 3.47 mmol). The reaction mixture was stirred at this temperature for 30 min before the addition of alcohol **9a** (350 mg, 1.75 mmol) as a solution in CH_2Cl_2 (2 mL) *via* cannula. The reaction was stirred for a further 1 h, before the dropwise addition of Et_3N (1.70 mL, 12.2 mmol) and the reaction mixture was warmed to RT over 30 min. After the addition of saturated aqueous NH_4Cl (10 mL), the organics were extracted with CH_2Cl_2 (3 x 15 mL) and the combined organic extracts were dried (Na_2SO_4), filtered and concentrated *in vacuo*. Purification by flash column chromatography (5% EtOAc/Hexane) provided aldehyde **15a** (305 mg, 88%) as a colourless oil, which was used without further characterization.

R_f 0.35 (5% EtOAc/Hexane); $[\alpha]_D^{20}$ -70.4 (*c* 1.89, $CHCl_3$), lit $[\alpha]_D^{20}$ -24.5 (*c* 1.8, $CHCl_3$)[6]; **^{1}H NMR** (500 MHz, $CDCl_3$) δ 9.84 (1H, br s, $\underline{H}_1$), 4.18 (1H, dd, *J* = 6.0, 2.9 Hz, $\underline{H}_2$), 3.58-3.54 (1H, m, $\underline{H}_6$), 2.02-1.98 (1H, m, $\underline{H}_{3a}$), 1.73-1.65 (2H, m, $\underline{H}_{3b}$ + $\underline{H}_{4a}$), 1.63-1.57 (2H, m, $\underline{H}_{5a}$ + $\underline{H}_{7a}$), 1.49-1.25 (11H, m, $\underline{H}_{4b}$ + $\underline{H}_{5b}$ + $\underline{H}_{7b}$ + $\underline{H}_{8-11}$), 0.88 (3H, t, *J* = 6.7 Hz, $\underline{H}_{12}$).

(2*R*,6*S*)-6-[(4-benzyloxy)butyl]-2-(carbaldehyde)tetrahydropyran (15b)

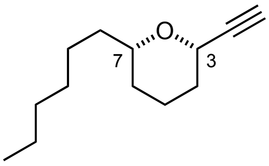


To a solution of dimethyl sulfoxide (360 μL, 5.08 mmol) in CH_2Cl_2 (10 mL) at -78 °C was added oxalyl chloride (370 μL, 4.28 mmol). The reaction mixture was stirred at this temperature for 30 min before the addition of alcohol **9b** (590 mg, 2.12 mmol) as a solution in CH_2Cl_2 (5 mL) *via* cannula. The reaction was stirred for a further 1 h, before the dropwise addition of Et_3N (2.06 mL, 14.8 mmol) and the reaction mixture was warmed to RT over 30 min. After the addition of saturated aqueous NH_4Cl (10 mL), the organics were extracted with CH_2Cl_2 (3 x 15 mL) and the combined organic extracts were dried (Na_2SO_4), filtered and concentrated *in vacuo*. Purification by flash column chromatography (10% EtOAc/Hexane) provided aldehyde **15b** (486 mg, 83%) as a colourless oil.

R_f 0.5 (25% EtOAc/Hexane); $[\alpha]_D^{20}$ -51.0 (*c* 1.75, $CHCl_3$); **IR** (thin film) 2940, 2862, 1732, 1454, 1362 cm^{-1}; **^{1}H NMR** (400 MHz, $CDCl_3$) δ 9.83 (1H, br s, $\underline{H}_1$), 7.36-7.25 (5H, m, Ar$\underline{H}$), 4.50 (2H, s, OC$\underline{H}_2$Ar), 4.17 (1H, dd, *J* = 6.1, 3.0 Hz, $\underline{H}_2$), 3.60-3.54 (1H, m, $\underline{H}_6$), 3.49 (2H, t, *J* = 6.5 Hz, $\underline{H}_{10}$), 2.03-1.97 (1H, m, $\underline{H}_{3a}$), 1.73-1.53 (7H, m, $\underline{H}_{3b}$ + $\underline{H}_{4a}$ + $\underline{H}_{5a}$ + $\underline{H}_{8-9}$), 1.52-1.36 (3H, m, $\underline{H}_{4b}$ + $\underline{H}_7$), 1.34-1.24 (1H, m, $\underline{H}_{5b}$); **^{13}C NMR** (100 MHz, $CDCl_3$) δ

205.2, 138.5, 128.3, 127.6, 127.5, 78.8, 74.7, 72.8, 70.2, 35.4, 30.5, 29.7, 23.9, 22.1, 19.8; **HRMS** (ES^+) Calc. for $C_{17}H_{24}O_3Na$ $[M+Na]^+$ 299.1631, found 299.1616.

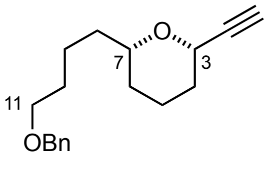
(2*S*,6*S*)-[2-ethynyl-6-hexyl]tetrahydropyran (16a)



To a solution of dimethyldiazo-2-oxopropylphosphonate (160 mg, 0.83 mmol) and K_2CO_3 (190 mg, 1.38 mmol) in MeOH (4 mL) at RT was added a solution of aldehyde **14a** (136 mg, 0.69 mmol) in MeOH (1 mL). After 16 h, the reaction mixture was quenched by addition of saturated aqueous $NaHCO_3$ (5 mL). The organics were extracted with Et_2O (3 × 10 mL), dried (Na_2SO_4) and concentrated *in vacuo*. Purification by flash column chromatography (1% EtOAc/Hexane) provided alkyne **16a** (96.5 mg, 72%) as a colourless oil.

$\mathbf{R_f}$ 0.80 (5% EtOAc/Hexane); $[\alpha]_D^{20}$ -36.5 (*c* 1.55, $CHCl_3$); **IR** (thin film) 2924, 2855, 1456, 1377, 1312 cm^{-1}; ^{1}**H NMR** (400 MHz, $CDCl_3$) δ 4.08 (1H, dt, *J* = 11.3, 2.2 Hz, $\underline{H}_3$), 3.30-3.24 (1H, m, $\underline{H}_7$), 2.44 (1H, d, *J* = 2.2 Hz, $\underline{H}_1$), 1.86-1.78 (2H, m, $\underline{H}_{4a}$ + $\underline{H}_{5a}$), 1.69-1.35 (5H, m, $\underline{H}_{4b}$ + $\underline{H}_{5b}$ + $\underline{H}_{6a}$ + $\underline{H}_8$), 1.34-1.18 (9H, m, $\underline{H}_{6b}$ + $\underline{H}_{9-12}$), 0.87 (3H, t, *J* = 7.0 Hz, $\underline{H}_{13}$); ^{13}**C NMR** (100 MHz, $CDCl_3$) δ 83.6, 78.6, 72.1, 67.8, 36.4, 32.5, 31.8, 30.7, 29.3, 25.4, 23.4, 22.6, 14.1; **HRMS** (EI^+) Calc. for $C_{13}H_{22}O$ $[M]^+$ 194.1665, found 194.1665.

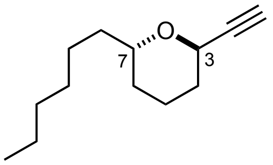
(2*S*,6*S*)-6-[(4-benzyloxy)butyl]-2-(ethynyl)tetrahydropyran (16b)



To a solution of dimethyldiazo-2-oxopropylphosphonate (360 mg, 1.88 mmol) and K_2CO_3 (430 mg, 3.13 mmol) in MeOH (10 mL) at RT was added as a solution of aldehyde **14b** (432 mg, 1.56 mmol) in MeOH (5 mL) and left to stir for 16 h. The reaction mixture was quenched by addition of saturated aqueous $NaHCO_3$ (15 mL). The organics were extracted with Et_2O (3 × 15 mL), dried over Na_2SO_4 and concentrated *in vacuo*. Purification by flash column chromatography (5% EtOAc/Hexane) provided alkyne **16b** (376 mg, 88%) as a colourless oil.

R$_f$ 0.56 (15% EtOAc/Hexane); $[\alpha]_D^{20}$ -28.5 (*c* 0.72, $CHCl_3$); **IR** (thin film) 3289, 2938, 2859, 1717, 1454 cm^{-1}; **^{1}H NMR** (400 MHz, $CDCl_3$) δ 7.36-7.27 (5H, m, Ar$\underline{H}$), 4.49 (2H, s, OC$\underline{H}_2$Ar), 4.08 (1H, dt, *J* = 11.3, 2.2 Hz, $\underline{H}_3$), 3.47 (2H, t, *J* = 6.7 Hz, $\underline{H}_{11}$), 3.31-3.25 (1H, m, $\underline{H}_7$), 2.44 (1H, d, *J* = 2.2 Hz, $\underline{H}_1$), 1.86-1.79 (2H, m, $\underline{H}_{4a}$ + $\underline{H}_{5a}$), 1.69-1.37 (9H, m, $\underline{H}_{4b}$ + $\underline{H}_{5b}$ + $\underline{H}_{6a}$ + $\underline{H}_{8-10}$), 1.28-1.19 (1H, m, $\underline{H}_{6b}$); **^{13}C NMR** (100 MHz, $CDCl_3$) δ 138.6, 128.3, 127.6, 127.5, 83.6, 78.4, 72.9, 72.2, 70.3, 67.8, 36.1, 32.5, 30.7, 29.7, 23.3, 22.1; **HRMS** (ES$^+$) Calc. for $C_{18}H_{25}O_2$ $[M+H]^+$ 273.1849, found 273.1854.

(2*R*,6*S*)-[2-ethynyl-6-hexyl]tetrahydropyran (17a)



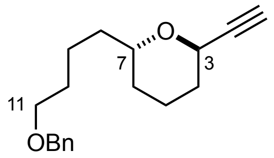
To a solution of CBr_4 (1.19 g, 3.59 mmol) in CH_2Cl_2 (7 mL) at 0 °C was added PPh_3 (1.88 g, 7.17 mmol) and the reaction mixture cooled to -78 °C. After 5 min, a solution of aldehyde **15a** (356 mg, 1.79 mmol) in CH_2Cl_2 (3 mL) was added and the reaction mixture was not allowed to exceed -50 °C over 45 min. The reaction mixture was quenched by addition of saturated aqueous NH_4Cl (10 mL), the organics were extracted with CH_2Cl_2 (3 × 15 mL) and the combined organic extracts were dried ($NaSO_4$), filtered and concentrated *in vacuo*. Purification by flash column chromatography (2% EtOAc/Hexane) provided (2*R*,6*S*)-[2-(2,2-dibromo-ethenyl)-6-(hexyl)]tetrahydropyran (515 mg, 81%) as a colourless oil.

R$_f$ 0.77 (5% Acetone/Hexane); $[\alpha]_D^{20}$ -40.3 (*c* 1.01, $CHCl_3$); **IR** (thin film) 2937, 2857, 1732, 1607, 1458 cm^{-1}; **^{1}H NMR** (400 MHz, $CDCl_3$) δ 6.76 (1H, d, *J* = 7.5 Hz, $\underline{H}_2$), 4.46 (1H, app dt, *J* = 7.5, 4.4 Hz, $\underline{H}_3$), 3.65-3.59 (1H, m, $\underline{H}_7$), 1.78-1.50 (5H, m, $\underline{H}_{4-5}$ + $\underline{H}_{6a}$), 1.43-1.23 (11H, m, $\underline{H}_{6b}$ + $\underline{H}_{8-12}$), 0.88 (3H, t, *J* = 6.7 Hz, $\underline{H}_{13}$); **^{13}C NMR** (100 MHz, $CDCl_3$) δ 137.9, 91.1, 72.4, 72.0, 34.3, 31.8, 30.1, 29.2, 29.0, 25.5, 22.6, 18.9, 14.1; **HRMS** (CI$^+$) Calc. for $C_{13}H_{23}O^{79}Br_2$ $[M+H]^+$ 353.0110, found 353.0110.

To a solution of (2*R*,6*S*)-[2-(2,2-dibromo-ethenyl)-6-(hexyl)]tetrahydropyran (151 mg, 0.43 mmol) in THF (6 mL) at -78 °C was added *n*-BuLi (800 μL, 1.6 M solution in hexane, 1.28 mmol). After 1.5 h, the reaction mixture was quenched by addition of saturated aqueous NH_4Cl (10 mL). The organics were extracted with EtOAc (3 × 15 mL), dried (Na_2SO_4), filtered and concentrated *in vacuo*. Purification by flash column chromatography (1% EtOAc/Hexane) provided alkyne **17a** (57.7 mg, 70%) as a colourless oil.

R$_f$ 0.77 (5% Acetone/Hexane); $[\alpha]_D^{20}$ -11.1 (*c* 1.09, $CHCl_3$); **IR** (thin film) 3310, 2932, 2860, 1466, 1456 cm^{-1}; **^{1}H NMR** (300 MHz, $CDCl_3$) δ 4.77-4.73 (1H, m, $\underline{H}_3$), 3.86-3.78 (1H, m, $\underline{H}_7$), 2.45 (1H, d, *J* = 2.3 Hz, $\underline{H}_1$), 1.91-1.73 (2H, m, $\underline{H}_{4a}$ + $\underline{H}_{5a}$), 1.71-1.57 (3H, m, $\underline{H}_{4b}$ + $\underline{H}_{5b}$ + $\underline{H}_{6a}$), 1.53-1.14 (11H, m, $\underline{H}_{6b}$ + $\underline{H}_{8-12}$), 0.87 (3H, t, *J* = 6.9 Hz, $\underline{H}_{13}$); **^{13}C NMR** (100 MHz, $CDCl_3$) δ 82.5, 74.1, 71.7, 64.8, 36.2, 31.8, 31.4, 30.4, 29.3, 25.3, 22.6, 19.3, 14.1; **HRMS** (CI$^+$) Calc. for $C_{13}H_{23}O$ [M+H]$^+$ 195.1743, found 195.1745.

(2*R*,6*S*)-6-[(4-benzyloxy)butyl]-2-(ethynyl)tetrahydropyran (17b)



To a solution of CBr_4 (1.15 g, 3.47 mmol) in CH_2Cl_2 (5 mL) at 0 °C was added PPh_3 (1.81 g, 6.90 mmol) and the reaction mixture cooled to -78 °C. After 5 min, a solution of aldehyde **15b** (478 mg, 1.73 mmol) in CH_2Cl_2 (5 mL) was added and the reaction mixture was not allowed to exceed -50 °C over 50 min. The reaction mixture was quenched by addition of saturated aqueous NH_4Cl (10 mL), the organics were extracted with CH_2Cl_2 (3 × 15 mL) and the combined organic extracts were dried ($NaSO_4$), filtered and concentrated *in vacuo*. Purification by flash column chromatography (5% EtOAc/Hexane) provided (2*R*,6*S*)-6-[(4-benzyloxy)butyl]-2-[(2,2-dibromo-ethenyl)]tetrahydropyran (687 mg, 92%) as a colourless oil.

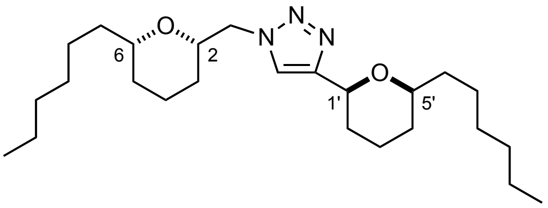
R$_f$ 0.65 (15% EtOAc/Hexane); $[\alpha]_D^{20}$ -37.0 (*c* 0.82, $CHCl_3$); **IR** (thin film) 2938, 2862, 1759, 1717, 1607, 1454 cm^{-1}; **^{1}H NMR** (300 MHz, $CDCl_3$) δ 7.35-7.27 (5H, m, Ar$\underline{H}$), 6.76 (1H, d, *J* = 7.5 Hz, $\underline{H}_2$), 4.50 (2H, s, OC$\underline{H}_2$Ar), 4.45 (1H, app dt, *J* = 7.5, 4.5 Hz, $\underline{H}_3$), 3.66-3.58 (1H, m, $\underline{H}_7$), 3.48 (2H, t, *J* = 6.5 Hz, $\underline{H}_{11}$), 1.80-1.49 (7H, m, $\underline{H}_{4-5}$ + $\underline{H}_{6a}$ + $\underline{H}_{10}$), 1.46-1.24 (5H, m, $\underline{H}_{6b}$ + $\underline{H}_{8-9}$); **^{13}C NMR** (100 MHz, $CDCl_3$) δ 138.6, 137.9, 128.3, 127.6, 127.4, 91.2, 72.8, 72.5, 71.9, 70.3, 34.2, 30.2, 29.7, 29.0, 22.3, 18.9; **HRMS** (CI$^+$) Calc. for $C_{18}H_{25}O_2{}^{79}Br_2$ [M+H]$^+$ 431.0216, found 431.0214.

To a solution of (2*R*,6*S*)-6-[(4-benzyloxy)butyl]-2-[(2,2-dibromo-ethenyl)]tetrahydropyran (636 mg, 1.47 mmol) in THF (15 mL) at -78 °C was added *n*-BuLi (2.80 mL, 1.6 M solution in hexane, 4.48 mmol). After 45 min, the reaction mixture was quenched by addition of saturated aqueous NH_4Cl (15 mL). The organics were extracted with EtOAc (3 × 15 mL), dried (Na_2SO_4), filtered and concentrated *in vacuo*. Purification by flash column chromatography (5% EtOAc/Hexane) provided alkyne **17b** (331 mg, 82%) as a colourless oil.

R

R_f 0.73 (20% EtOAc/Hexane); $[\alpha]_D^{20}$ -6.7 (*c* 1.04, $CHCl_3$); **IR** (thin film) 3290, 2938, 2862, 1734, 1624, 1558 cm^{-1}; **^{1}H NMR** (400 MHz, $CDCl_3$) δ 7.35-7.25 (5H, m, Ar$\underline{H}$), 4.75-4.74 (1H, m, $\underline{H}_3$), 4.50 (2H, s, OC$\underline{H}_2$Ar), 3.87-3.81 (1H, m, $\underline{H}_7$), 3.48 (2H, t, *J* = 6.6 Hz, $\underline{H}_{11}$), 2.45 (1H, d, *J* = 2.3 Hz, $\underline{H}_1$), 1.93-1.74 (2H, m, $\underline{H}_{4a}$ + $\underline{H}_{5a}$), 1.70-1.58 (5H, m, $\underline{H}_{4b}$ + $\underline{H}_{5b}$ + $\underline{H}_{6a}$ + $\underline{H}_{10}$), 1.53-1.38 (4H, m, $\underline{H}_{8\text{-}9}$), 1.27-1.17 (1H, m, $\underline{H}_{6b}$); **^{13}C NMR** (100 MHz, $CDCl_3$) δ 138.6, 128.3, 127.5, 127.4, 82.4, 74.1, 72.8, 71.4, 70.3, 64.8, 35.9, 31.3, 30.3, 29.6, 21.9, 19.2; **HRMS** (CI^+) Calc. for $C_{18}H_{25}O_2$ $[M+H]^+$ 273.1849, found 273.1850.

4-[(2*S*’,6*S*’)-6’-hexyltetrahydropyran-2-yl]-1-[(2*S*’’,6*S*’’)-6’’-(hexyltetrahydropyran-2-yl)methyl]-*1H*-1,2,3-triazole (18a)

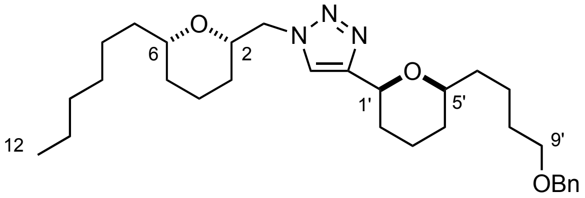


General procedure A was followed with alkyne **16a** (16.0 mg, 82.3 μmol) and azide **11a** (19.0 mg, 84.3 μmol) in *t*-BuOH (0.5 mL) and H_2O (0.5 mL) to which was added $CuSO_4{\cdot}5H_2O$ (25.0 mg, 100 μmol) and sodium ascorbate (40.0 mg, 202 μmol). Standard workup and flash column chromatography (10% EtOAc/Hexane) provided triazole **18a** (25.2 mg, 71%) as a colourless oil.

R_f 0.12 (10% EtOAc/Hexane); $[\alpha]_D^{20}$ -25.6 (*c* 2.38, $CHCl_3$); **IR** (thin film) 2934, 2859, 1456 cm^{-1}; **^{1}H NMR** (400 MHz, $CDCl_3$) δ 7.64 (1H, s, $\underline{H}_{Ar}$), 4.59 (1H, dd, *J* = 11.1, 2.1 Hz, $\underline{H}_{1'}$), 4.45 (1H, dd, *J* = 14.0, 3.1 Hz, $\underline{H}_{1a}$), 4.18 (1H, dd, *J* = 14.1, 8.2 Hz, $\underline{H}_{1b}$), 3.66-3.60 (1H, m, $\underline{H}_2$), 3.49-3.42 (1H, m, $\underline{H}_{5'}$), 3.23-3.17 (1H, m, $\underline{H}_6$), 2.03-1.99 (1H, m, $\underline{H}_{2a'}$), 1.95-1.82 (2H, m, $\underline{H}_{3a'}$ + $\underline{H}_{4a}$), 1.68-1.50 (6H, m, $\underline{H}_{2b'}$ + $\underline{H}_{3a}$ + $\underline{H}_{3b'}$ + $\underline{H}_{4a'}$ + $\underline{H}_{4b}$ + $\underline{H}_{5a}$), 1.49-1.11 (23H, m, $\underline{H}_{3b}$ + $\underline{H}_{4b'}$ + $\underline{H}_{5b}$ + $\underline{H}_{6'\text{-}10'}$ + $\underline{H}_{7\text{-}11}$), 0.89-0.84 (6H, m, $\underline{H}_{11'}$ + $\underline{H}_{12}$); **^{13}C**

NMR (100 MHz, $CDCl_3$) δ 149.9, 122.2, 78.4, 77.8, 76.1, 73.2, 55.0, 36.5, 36.4, 31.8, 31.8, 31.8, 31.2, 31.2, 29.4, 29.3, 28.6, 25.6, 25.5, 23.6, 23.0, 22.6, 22.6, 14.1, 14.1; **HRMS** (ES^+) Calc. for $C_{25}H_{46}O_2N_3$ $[M+H]^+$ 420.3585, found 420.3580

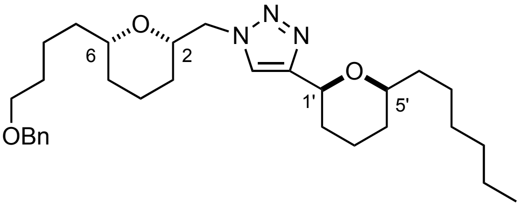
4-[(2*S*',6*S*')-6'-(4-(benzyloxy)butyl)tetrahydropyran-2-yl]-1-[(2*S*'',6*S*'')-6''-(hexyltetrahydropyran-2-yl)methyl]-*1H*-1,2,3-triazole (18b)



General procedure A was followed with alkyne **16b** (59.0 mg, 0.22 mmol) and azide **11a** (48.7 mg, 0.22 mmol) in *t*-BuOH (1 mL) and H_2O (1 mL) to which was added $CuSO_4{\cdot}5H_2O$ (65.0 mg, 0.26 mmol) and sodium ascorbate (103 mg, 0.52 mmol). Standard work-up and purification by flash column chromatography (10→25% EtOAc/Hexane) provided triazole **18b** (75.1 mg, 70%) as a colourless oil.

$\mathbf{R_f}$ 0.47 (30% EtOAc/Hexane); $[\alpha]_D^{20}$ -24.5 (*c* 1.06, $CHCl_3$); **IR** (thin film) 2934, 2857, 1719, 1454 cm^{-1}; ^{1}**H NMR** (300 MHz, $CDCl_3$) δ 7.64 (1H, s, $\underline{H}_{Ar}$), 7.36-7.24 (5H, m, Ar$\underline{H}$), 4.61-4.58 (1H, m, $\underline{H}_{1'}$), 4.48 (2H, s, $OC\underline{H}_2Ar$), 4.48-4.42 (1H, m, $\underline{H}_{1a}$), 4.17 (1H, dd, *J* = 14.0, 8.2 Hz, $\underline{H}_{1b}$), 3.65-3.59 (1H, m, $\underline{H}_2$), 3.51-3.43 (1H, m, $\underline{H}_{5'}$), 3.46 (2H, t, *J* = 6.4 Hz, $\underline{H}_{9'}$), 3.22-3.16 (1H, m, $\underline{H}_6$), 2.03-1.82 (3H, m, $\underline{H}_{3a'}$ + $\underline{H}_4$), 1.66-1.41 (12H, m, $\underline{H}_{2'}$ + $\underline{H}_{3a}$ + $\underline{H}_{3b'}$ + $\underline{H}_{4a'}$ + $\underline{H}_{5a}$ + $\underline{H}_{6'}$ + $\underline{H}_{8'}$ + $\underline{H}_{10}$), 1.38-1.11 (13H, m, $\underline{H}_{3b}$ + $\underline{H}_{4b'}$ + $\underline{H}_{5b}$ + $\underline{H}_{7\text{-}9}$ + $\underline{H}_{7'}$ + $\underline{H}_{11}$), 0.87 (3H, t, *J* = 6.4 Hz, $\underline{H}_{12}$); ^{13}**C NMR** (75 MHz, $CDCl_3$) δ 149.9, 138.7, 128.3, 127.6, 127.4, 122.3, 78.3, 77.8, 76.1, 73.2, 72.9, 70.4, 55.0, 36.4, 36.3, 31.9, 31.8, 31.3, 31.2, 29.8, 29.3, 28.6, 25.6, 23.6, 23.0, 22.6, 22.2, 14.1; **HRMS** (ES^+) Calc. for $C_{30}H_{48}O_3N_3$ $[M+H]^+$ 498.3690, found 498.3693.

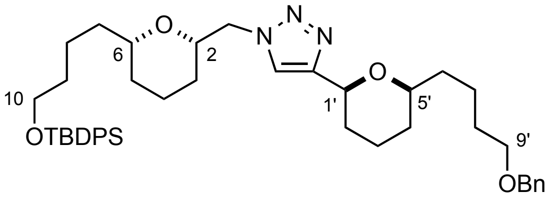
1-[(2*S*’,6*S*’)-6’-(4-(benzyloxy)butyltetrahydropyran-2-yl)methyl]-4-[(2*S*’’,6*S*’’)-6’’-(hexyltetrahydropyran-2-yl)]-*1H*-1,2,3-triazole (18c)



General procedure A was followed with alkyne **16a** (26.0 mg, 0.14 mmol) and azide **11b** (41.0 mg, 0.14 mmol) in *t*-BuOH (2 mL) and H_2O (2 mL) to which was added $CuSO_4{\cdot}5H_2O$ (40.0 mg, 0.16 mmol) and sodium ascorbate (64.0 mg, 0.32 mmol). Standard work-up and purification by flash column chromatography (15% EtOAc/Hexane) provided triazole **18c** (27.0 mg, 41%) as a colourless oil.

$\mathbf{R_f}$ 0.43 (30% EtOAc/Hexane); $[\alpha]_D^{20}$ -23.5 (*c* 1.0, $CHCl_3$); **IR** (thin film) 2934, 2857, 1456 cm^{-1}; ^{1}**H NMR** (500 MHz, $CDCl_3$) δ 7.62 (1H, s, $\underline{H}_{Ar}$), 7.35-7.31 (4H, m, Ar$\underline{H}$), 7.28-7.27 (1H, m, Ar$\underline{H}$), 4.59-4.57 (1H, m, $\underline{H}_{1'}$), 4.49 (2H, s, OC$\underline{H}_2$Ar), 4.44 (1H, dd, *J* = 14.0, 3.2 Hz, $\underline{H}_{1a}$), 4.20 (1H, dd, *J* = 14.0, 7.9 Hz, $\underline{H}_{1b}$), 3.66-3.62 (1H, m, $\underline{H}_2$), 3.46-3.41 (3H, m, $\underline{H}_{5'}$ + $\underline{H}_{10}$), 3.24-3.19 (1H, m, $\underline{H}_6$), 2.02-2.00 (1H, m, $\underline{H}_{2a'}$), 1.91-1.84 (2H, m, $\underline{H}_{3a'}$ + $\underline{H}_{4a}$), 1.65-1.37 (14H, m, $\underline{H}_{2b'}$ + $\underline{H}_{3a}$ + $\underline{H}_{3b'}$ + $\underline{H}_{4a'}$ + $\underline{H}_{4b}$ + $\underline{H}_{5a}$ + $\underline{H}_{6'}$ + $\underline{H}_7$ + $\underline{H}_9$ + $\underline{H}_{9'}$), 1.35-1.12 (11H, m, $\underline{H}_{3b}$ + $\underline{H}_{4b'}$ + $\underline{H}_{5b}$ + $\underline{H}_{7'-8'}$ + $\underline{H}_8$ + $\underline{H}_{10'}$), 0.86 (3H, t, *J* = 6.7 Hz, $\underline{H}_{11'}$); ^{13}**C NMR** (125 MHz, $CDCl_3$) δ 149.9, 138.5, 128.3, 127.5, 127.4, 122.2, 78.4, 77.6, 76.0, 73.1, 72.8, 70.3, 55.0, 36.5, 36.0, 31.8, 31.7, 31.2, 31.1, 29.6, 29.4, 28.5, 25.5, 23.6, 22.9, 22.6, 22.1, 14.1; **HRMS** (CI^+) Calc. for $C_{30}H_{48}O_3N_3$ $[M+H]^+$ 498.3690, found 498.3686.

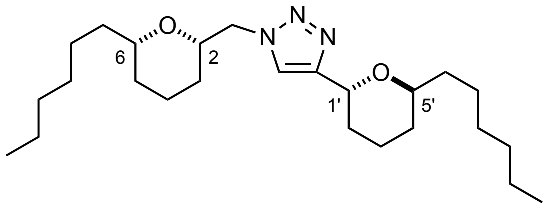
4-[(2*S*’,6*S*’)-6’-(4-(benzyloxy)butyl)tetrahydropyran-2-yl]-1-[(2*S*’’,6*S*’’)-6’’-((4-((*tert*-butyldiphenylsilyl)oxy)butyl)tetrahydropyran-2-yl)methyl]-*1H*-1,2,3-triazole (18d)



General procedure A was followed with alkyne **16b** (250 mg, 0.920 mmol) and azide **11c** (415 mg, 0.920 mmol) in *t*-BuOH (4 mL) and H_2O (4 mL) to which was added $CuSO_4{\cdot}5H_2O$ (276 mg, 1.10 mmol) and sodium ascorbate (437 mg, 2.21 mmol). Standard work-up and purification by flash column chromatography (30% EtOAc/Hexane) provided triazole **18d** (450 mg, 68%) as a colourless oil.

R$_f$ 0.25 (50% EtOAc/Hexane); $[\alpha]_D^{20}$ -13.3 (*c* 0.9, $CHCl_3$); **IR** (thin film) 2933, 2857, 1472 cm^{-1}; **^{1}H NMR** (300 MHz, $CDCl_3$) δ 7.67-7.64 (4H, m, Ar$\underline{H}$), 7.58 (1H, s, $\underline{H}_{Ar}$), 7.42-7.26 (11H, m, Ar$\underline{H}$), 4.56 (1H, dd, *J* = 10.7, 1.8 Hz, $\underline{H}_{1'}$), 4.48 (2H, s, OC$\underline{H}_2$Ar), 4.42 (1H, dd, *J* = 14.0, 3.5 Hz, $\underline{H}_{1a}$), 4.19 (1H, dd, *J* = 14.0, 7.8 Hz, $\underline{H}_{1b}$), 3.64-3.60 (1H, m, $\underline{H}_2$), 3.64 (2H, t, *J* = 6.5 Hz, $\underline{H}_{10}$), 3.47-3.39 (1H, m, $\underline{H}_{5'}$), 3.45 (2H, t, *J* = 6.5 Hz, $\underline{H}_{9'}$), 3.23-3.13 (1H, m, $\underline{H}_6$), 1.99-1.83 (3H, m, $\underline{H}_{3a'}$ + $\underline{H}_4$), 1.66-1.31 (16H, m, $\underline{H}_{2'}$ + $\underline{H}_{3a}$ + $\underline{H}_{3b'}$ + $\underline{H}_{4'}$ + $\underline{H}_5$ + $\underline{H}_7$ + $\underline{H}_{6'-8'}$), 1.31-1.08 (5H, m, $\underline{H}_{3b}$ + $\underline{H}_{8-9}$), 1.04 (9H, s, SiC(C$\underline{H}_3$)$_3$); **^{13}C NMR** (75 MHz, $CDCl_3$) δ 150.0, 138.8, 135.7, 134.2, 129.7, 128.5, 127.8, 127.7, 127.6, 122.4, 78.4, 77.8, 76.2, 73.3, 73.0, 70.5, 63.9, 55.1, 36.4, 36.1, 32.6, 31.8, 31.3, 31.2, 29.9, 28.8, 27.0, 23.7, 23.1, 22.3, 21.8, 19.3; **HRMS** (ES$^+$) Calc. for $C_{44}H_{62}O_4N_3Si$ $[M+H]^+$ 724.4504, found 724.4493.

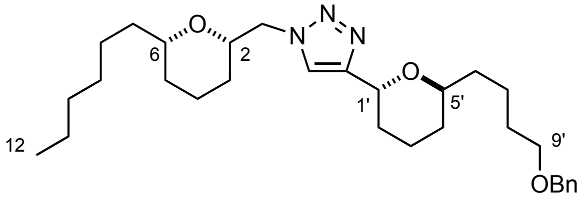
4-[(2*R*',6*S*')-6'-hexyltetrahydropyran-2-yl]-1-[(2*S*'',6*S*'')-6''-(hexyltetrahydropyran-2-yl)methyl]-*1H*-1,2,3-triazole (19a)



General procedure A was followed with alkyne **17a** (12.3 mg, 63.0 μmol) and azide **11a** (14.3 mg, 63.0 μmol) in *t*-BuOH (0.5 mL) and H_2O (0.5 mL) to which was added $CuSO_4{\cdot}5H_2O$ (19.0 mg, 76.0 μmol) and sodium ascorbate (30.0 mg, 150 μmol). Standard work-up and purification by flash column chromatography (5→10% EtOAc/Hexane) provided triazole **19a** (20.0 mg, 75%) as a colourless oil.

R$_f$ 0.14 (15% EtOAc/Hexane); $[\alpha]_D^{20}$ -31.7 (*c* 0.53, $CHCl_3$); **IR** (thin film) 2930, 2857, 1456, 1438, 1377 cm^{-1}; **^{1}H NMR** (400 MHz, $CDCl_3$) δ 7.64 (1H, s, $\underline{H}_{Ar}$), 5.08 (1H, t, *J* = 4.3 Hz, $\underline{H}_{1'}$), 4.48 (1H, dd, *J* = 14.1, 3.1 Hz, $\underline{H}_{1a}$), 4.26 (1H, dd, *J* = 14.1, 7.8 Hz, $\underline{H}_{1b}$), 3.69-3.63 (1H, m, $\underline{H}_2$), 3.59-3.53 (1H, m, $\underline{H}_{5'}$), 3.26-3.20 (1H, m, $\underline{H}_6$), 2.23-2.16 (1H, m, $\underline{H}_{2a'}$), 2.02-1.94 (1H, m, $\underline{H}_{2b'}$), 1.89-1.83 (1H, m, $\underline{H}_{4a}$), 1.77-1.46 (7H, m, $\underline{H}_{3'}$ + $\underline{H}_{4a'}$ + $\underline{H}_{4b}$ + $\underline{H}_{5a}$ + $\underline{H}_{6'}$), 1.43-1.36 (3H, m, $\underline{H}_{4b'}$ + $\underline{H}_7$), 1.33-1.09 (19H, m, $\underline{H}_3$ + $\underline{H}_{5b}$ + $\underline{H}_{7'-10'}$ + $\underline{H}_{8-11}$), 0.88 (6H, t, *J* = 6.6 Hz, $\underline{H}_{11'}$ + $\underline{H}_{12}$); **^{13}C NMR** (125 MHz, $CDCl_3$) δ 148.6, 123.3, 77.9, 76.1, 71.6, 67.8, 55.1, 36.3, 34.9, 31.8, 31.8, 31.2, 30.7, 29.5, 29.3, 28.5, 28.5, 25.7, 25.5, 23.0, 22.7, 22.6, 19.2, 14.1; **HRMS** (ES$^+$) Calc. for $C_{25}H_{46}O_2N_3$ [M+H]$^+$ 420.3585, found 420.3580.

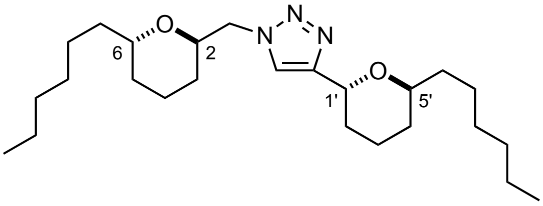
4-[(2*R*',6*S*')-6'-(4-(benzyloxy)butyl)tetrahydropyran-2-yl]-1-[(2*S*'',6*S*'')-6''-(hexyltetrahydropyran-2-yl)methyl]-*1H*-1,2,3-triazole (19b)



General procedure A was followed with alkyne **17b** (50.0 mg, 0.18 mmol) and azide **11a** (41.2 mg, 0.18 mmol) in *t*-BuOH (1 mL) and H_2O (1 mL) to which was added $CuSO_4{\cdot}5H_2O$ (55.0 mg, 0.22 mmol) and sodium ascorbate (87.0 mg, 0.44 mmol). Standard work-up and purification by flash column chromatography (10→30% EtOAc/Hexane) provided triazole **19b** (58.7 mg, 65%) as a colourless oil.

R$_f$ 0.28 (30% EtOAc/Hexane); $[\alpha]_D^{20}$ -22.8 (*c* 1.0, $CHCl_3$); **IR** (thin film) 2932, 2857, 1719, 1454 cm^{-1}; **^{1}H NMR** (300 MHz, $CDCl_3$) δ 7.63 (1H, s, $\underline{H}_{Ar}$), 7.36-7.23 (5H, m, Ar$\underline{H}$), 5.09-5.05 (1H, m, $\underline{H}_{1'}$), 4.49 (2H, s, OC$\underline{H}_2$Ar), 4.49-4.42 (1H, m, $\underline{H}_{1a}$), 4.23 (1H, dd, *J* = 14.0, 7.9 Hz, $\underline{H}_{1b}$), 3.67-3.54 (2H, m, $\underline{H}_2$ + $\underline{H}_{5'}$), 3.46 (2H, t, *J* = 6.5 Hz, $\underline{H}_{9'}$), 3.23-3.17 (1H, m, $\underline{H}_6$), 2.24-2.13 (1H, m, $\underline{H}_{2a'}$), 2.04-1.91 (1H, m, $\underline{H}_{2b'}$), 1.89-1.80 (1H, m, $\underline{H}_{4a}$), 1.77-1.69 (2H, m, $\underline{H}_{3'}$), 1.67-1.34 (10H, m, $\underline{H}_{4'}$ + $\underline{H}_{4b}$ + $\underline{H}_{5a}$ + $\underline{H}_{6'}$ + $\underline{H}_7$ + $\underline{H}_{8'}$), 1.30-1.08 (13H, m, $\underline{H}_3$ + $\underline{H}_{5b}$ + $\underline{H}_{7'}$ + $\underline{H}_{8\text{-}11}$), 0.87 (3H, t, *J* = 6.5 Hz, $\underline{H}_{12}$); **^{13}C NMR** (75 MHz, $CDCl_3$) δ 148.5, 138.6, 128.3, 127.5, 127.4, 123.3, 77.8, 76.0, 72.8, 71.3, 70.3, 67.8, 55.0, 36.3, 34.6, 31.7, 31.2, 30.6, 29.8, 29.2, 28.5, 28.4, 25.4, 23.0, 22.6, 22.2, 19.1, 14.0; **HRMS** (ES$^+$) Calc. for $C_{30}H_{48}O_3N_3$ [M+H]$^+$ 498.3690, found 498.3692.

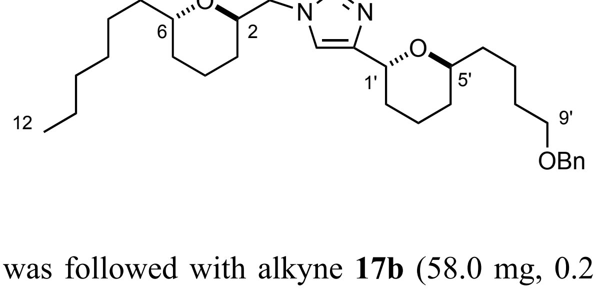
4-[(2*R*',6*S*')-6'-hexyltetrahydropyran-2-yl]-1-[(2*R*'',6*S*'')-6''-(hexyltetrahydropyran-2-yl)methyl]-*1H*-1,2,3-triazole (20a)



General procedure A was followed with alkyne **17a** (16.1 mg, 83.0 μmol) and azide **12** (18.7 mg, 83.0 μmol) in *t*-BuOH (1 mL) and H_2O (1 mL) to which was added $CuSO_4{\cdot}5H_2O$ (25.0 mg, 99.0 μmol) and sodium ascorbate (39.0 mg, 199 μmol). Standard work-up and purification by flash column chromatography (5→10% EtOAc/Hexane) provided triazole **20a** (17.8 mg, 51%) as a colourless oil.

$\mathbf{R_f}$ 0.30 (15% EtOAc/Hexane); $[\alpha]_D^{20}$ -41.4 (*c* 0.73, $CHCl_3$); **IR** (thin film) 2930, 2857, 1772, 1734, 1558, 1456 cm^{-1}; **^{1}H NMR** (400 MHz, $CDCl_3$) δ 7.58 (1H, s, $\underline{H}_{Ar}$), 5.07 (1H, t, *J* = 4.4 Hz, $\underline{H}_{1'}$), 4.43-4.32 (2H, m, $\underline{H}_1$), 4.02-3.96 (1H, m, $\underline{H}_2$), 3.83-3.78 (1H, m, $\underline{H}_{5'}$), 3.61-3.55 (1H, m, $\underline{H}_6$), 2.19-2.12 (1H, m, $\underline{H}_{2a'}$), 2.00-1.92 (1H, m, $\underline{H}_{2b'}$), 1.76-1.59 (7H, m, $\underline{H}_{3a}$ + $\underline{H}_{3'}$ + $\underline{H}_4$ + $\underline{H}_{4a'}$ + $\underline{H}_{5a}$), 1.45-1.34 (5H, m, $\underline{H}_{5b}$ + $\underline{H}_{6'}$ + $\underline{H}_7$), 1.33-1.15 (18H, m, $\underline{H}_{3b}$ + $\underline{H}_{4b'}$ + $\underline{H}_{7'-10'}$ + $\underline{H}_{8-11}$), 0.88-0.83 (6H, m, $\underline{H}_{11'}$ + $\underline{H}_{12}$); **^{13}C NMR** (125 MHz, $CDCl_3$) δ 148.7, 123.1, 72.4, 71.7, 69.0, 67.8, 53.8, 34.6, 31.8, 31.7, 31.6, 30.6, 29.4, 29.2, 28.9, 28.7, 28.0, 25.7, 25.6, 22.6 (2C), 19.1, 18.1, 14.1, 14.0; **HRMS** (ES^+) Calc. for $C_{25}H_{46}O_2N_3$ $[M+H]^+$ 420.3585, found 420.3581.

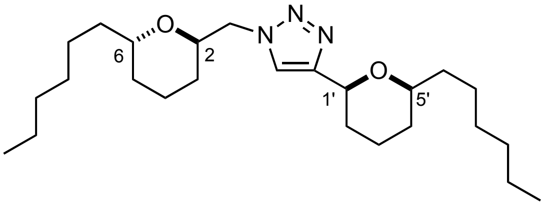
4-[(2*R*',6*S*')-6'-(4-(benzyloxy)butyl)tetrahydropyran-2-yl]-1-[(2*R*'',6*S*'')-6''-(hexyltetrahydropyran-2-yl)methyl]-*1H*-1,2,3-triazole (20b)



General procedure A was followed with alkyne **17b** (58.0 mg, 0.21 mmol) and azide **12** (47.9 mg, 0.21 mmol) in *t*-BuOH (1 mL) and H_2O (1 mL) to which was added $CuSO_4{\cdot}5H_2O$ (64.0 mg, 0.26 mmol) and sodium ascorbate (100 mg, 0.51 mmol). Standard work-up and purification by flash column chromatography (15→25% EtOAc/Hexane) provided triazole **20b** (81.2 mg, 77%) as a colourless oil.

R$_f$ 0.41 (30% EtOAc/Hexane); $[\alpha]_D^{20}$ -34.1 (*c* 1.03, $CHCl_3$); **IR** (thin film) 2932, 2859, 1719, 1454 cm^{-1}; **^{1}H NMR** (300 MHz, $CDCl_3$) δ 7.58 (1H, s, $\underline{H}_{Ar}$), 7.33-7.23 (5H, m, Ar$\underline{H}$), 5.07 (1H, t, *J* = 4.5 Hz, $\underline{H}_{1'}$), 4.49 (2H, s, OC$\underline{H}_2$Ar), 4.43-4.28 (1H, m, $\underline{H}_1$), 4.02-3.94 (1H, m, $\underline{H}_2$), 3.83-3.75 (1H, m, $\underline{H}_{5'}$), 3.62-3.54 (1H, m, $\underline{H}_6$), 3.46 (2H, t, *J* = 6.4 Hz, $\underline{H}_{9'}$), 2.21-2.12 (1H, m, $\underline{H}_{2a'}$), 2.04-1.91 (1H, m, $\underline{H}_{2b'}$), 1.77-1.50 (13H, m, $\underline{H}_{3a}$ + $\underline{H}_{3'}$ + $\underline{H}_{4a'}$ + $\underline{H}_4$ + $\underline{H}_{5a}$ + $\underline{H}_{6'}$ + $\underline{H}_7$ + $\underline{H}_{8'}$), 1.47-1.32 (2H, m, $\underline{H}_{4b'}$ + $\underline{H}_{5b}$), 1.30-1.03 (11H, m, $\underline{H}_{3b}$ + $\underline{H}_{7'}$ + $\underline{H}_{8\text{-}11}$), 0.85 (3H, t, *J* = 6.7 Hz, $\underline{H}_{12}$); **^{13}C NMR** (75 MHz, $CDCl_3$) δ 148.6, 138.6, 128.3, 127.5, 127.4, 123.0, 72.8, 72.3, 71.4, 70.3, 69.0, 67.9, 53.6, 34.5, 31.7, 31.6, 30.6, 29.8, 29.2, 28.9, 28.6, 27.9, 25.6, 22.6, 22.2, 19.1, 18.1, 14.0; **HRMS** (ES$^+$) Calc. for $C_{30}H_{48}O_3N_3$ $[M+H]^+$ 498.3690, found 498.3693.

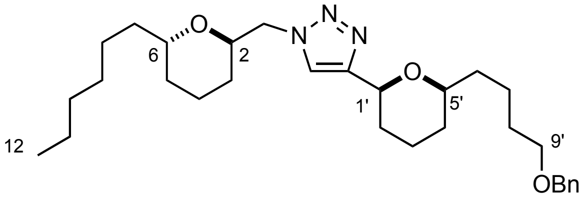
4-[(2*S*’,6*S*’)-6’-hexyltetrahydropyran-2-yl]-1-[(2*R*’’,6*S*’’)-6’’-(hexyltetrahydropyran-2-yl)methyl]-*1H*-1,2,3-triazole (21a)



General procedure A was followed with alkyne **16a** (12.0 mg, 62.0 μmol) and azide **12** (21.1 mg, 93.7 μmol) in *t*-BuOH (0.5 mL) and H_2O (0.5 mL) to which was added $CuSO_4{\cdot}5H_2O$ (19.0 mg, 74.0 μmol) and sodium ascorbate (29.0 mg, 150 μmol). Standard work-up and purification by flash column chromatography (5→10% EtOAc/Hexane) provided triazole **21a** (9.0 mg, 35%) as a colourless oil.

R$_f$ 0.09 (10% EtOAc/Hexane); $[\alpha]_D^{20}$ -45.7 (*c* 0.35, $CHCl_3$); **IR** (thin film) 2926, 2855, 1456 cm^{-1}; **^{1}H NMR** (500 MHz, $CDCl_3$) δ 7.60 (1H, s, $\underline{H}_{Ar}$), 4.58 (1H, d, *J* = 10.6 Hz, $\underline{H}_{1'}$), 4.38 (2H, d, *J* = 6.1 Hz, $\underline{H}_1$), 4.03-3.98 (1H, m, $\underline{H}_2$), 3.83-3.78 (1H, m, $\underline{H}_{5'}$), 3.45 (1H, dtd, *J* = 11.7, 4.9, 1.5 Hz, $\underline{H}_6$), 2.08 (1H, d, *J* = 11.4 Hz, $\underline{H}_{2a'}$), 1.94-1.91 (1H, m, $\underline{H}_{2b'}$), 1.71-1.53 (7H, m, $\underline{H}_{3a}$ + $\underline{H}_{3'}$ + $\underline{H}_4$ + $\underline{H}_{4a'}$ + $\underline{H}_{5a}$), 1.43-1.20 (23H, m, $\underline{H}_{3b}$ + $\underline{H}_{4b'}$ + $\underline{H}_{5b}$ + $\underline{H}_{6'\text{-}10'}$ + $\underline{H}_{7\text{-}11}$), 1.33-1.15 (18H, m,), 0.89-0.85 (6H, m, $\underline{H}_{11'}$ + $\underline{H}_{12}$); **^{13}C NMR** (125 MHz, $CDCl_3$) δ 148.2, 121.9, 78.6, 73.4, 72.3, 69.4, 53.5, 36.7, 32.1, 32.0 (2C), 31.9, 31.4, 29.6, 29.3, 29.2, 28.1, 25.7, 25.6, 23.7, 22.8, 22.7, 18.4, 14.3, 14.2; **HRMS** (ES$^+$) Calc. for $C_{25}H_{45}O_2N_3Na$ $[M+Na]^+$ 442.3404, found 442.3393.

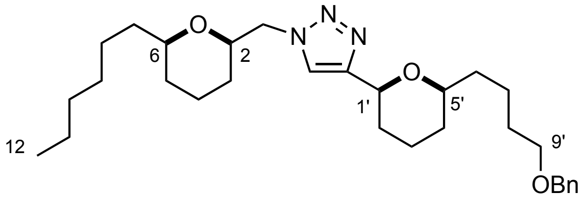
4-[(2*S*',6*S*')-6'-(4-(benzyloxy)butyl)tetrahydropyran-2-yl]-1-[(2*R*'',6*S*'')-6''-(hexyltetrahydropyran-2-yl)methyl]-*1H*-1,2,3-triazole (21b)



General procedure A was followed with alkyne **16b** (57.0 mg, 0.21 mmol) and azide **12** (46.8 mg, 0.21 mmol) in *t*-BuOH (1 mL) and H_2O (1 mL) to which was added $CuSO_4{\cdot}5H_2O$ (62.0 mg, 0.25 mmol) and sodium ascorbate (99.0 mg, 0.50 mmol). Standard work-up and purification by flash column chromatography (15→30% EtOAc/Hexane) provided triazole **21b** (78.6 mg, 76%) as a colourless oil.

R$_f$ 0.22 (30% EtOAc/Hexane); $[\alpha]_D^{20}$ -36.0 (*c* 1.05, $CHCl_3$); **IR** (thin film) 2932, 2857, 1717, 1454 cm^{-1}; **^{1}H NMR** (300 MHz, $CDCl_3$) δ 7.57 (1H, s, $\underline{H}_{Ar}$), 7.33-7.22 (5H, m, Ar$\underline{H}$), 4.59-4.54 (1H, m, $\underline{H}_{1'}$), 4.48 (2H, s, OC$\underline{H}_2$Ar), 4.36-4.34 (2H, m, $\underline{H}_1$), 4.02-3.95 (1H, m, $\underline{H}_2$), 3.81-3.76 (1H, m, $\underline{H}_{5'}$), 3.49-3.41 (1H, m, $\underline{H}_6$), 3.46 (2H, t, J = 6.4 Hz, $\underline{H}_{9'}$), 2.08-2.03 (1H, m, $\underline{H}_{2a'}$), 1.95-1.86 (1H, m, $\underline{H}_{4a}$), 1.65-1.40 (13H, m, $\underline{H}_{2b'} + \underline{H}_{3a} + \underline{H}_{3'} + \underline{H}_{4a'} + \underline{H}_{4b} + \underline{H}_{5a} + \underline{H}_{6'} + \underline{H}_7 + \underline{H}_{8'}$), 1.37-1.04 (13H, m, $\underline{H}_{3b} + \underline{H}_{4b'} + \underline{H}_{5b} + \underline{H}_{7'} + \underline{H}_{8\text{-}11}$), 0.85 (3H, t, J = 6.6 Hz, $\underline{H}_{12}$); **^{13}C NMR** (75 MHz, $CDCl_3$) δ 149.9, 138.5, 128.2, 127.5, 127.3, 121.6, 78.1, 73.2, 72.8, 72.0, 70.3, 69.1, 53.2, 36.2, 31.9, 31.7, 31.5, 31.1, 29.7, 29.1, 29.0, 27.8, 25.5, 23.5, 22.5, 22.1, 18.1, 14.0; **HRMS** (ES$^+$) Calc. for $C_{30}H_{48}O_3N_3$ $[M+H]^+$ 498.3690, found 498.3693.

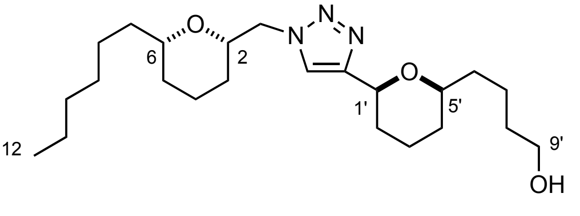
4-[(2*S*',6*S*')-6'-(4-(benzyloxy)butyl)tetrahydropyran-2-yl]-1-[(2*R*'',6*R*'')-6''-(hexyltetrahydropyran-2-yl)methyl]-*1H*-1,2,3-triazole (22)



General procedure A was followed with alkyne **16b** (58.0 mg, 0.21 mmol) and azide **13** (47.9 mg, 0.21 mmol) in *t*-BuOH (1 mL) and H_2O (1 mL) to which was added $CuSO_4{\cdot}5H_2O$ (64.0 mg, 0.26 mmol) and sodium ascorbate (101 mg, 0.51 mmol). Standard work-up and purification by flash column chromatography (10→20% EtOAc/Hexane) provided triazole **22** (45.6 mg, 43%) as a colourless oil.

$\mathbf{R_f}$ 0.43 (30% EtOAc/Hexane); $[\alpha]_D^{20}$ -19.4 (*c* 0.66, $CHCl_3$); **IR** (thin film) 2932, 2857, 1755, 1732, 1454 cm^{-1}; ^{1}**H NMR** (300 MHz, $CDCl_3$) δ 7.64 (1H, s, $\underline{H}_{Ar}$), 7.34-7.27 (5H, m, Ar$\underline{H}$), 4.61-4.57 (1H, m, $\underline{H}_{1'}$), 4.49 (2H, s, OC$\underline{H}_2$Ar), 4.45 (1H, dd, *J* = 14.0, 3.2 Hz, $\underline{H}_{1a}$), 4.21 (1H, dd, *J* = 14.1, 8.0 Hz, $\underline{H}_{1b}$), 3.68-3.60 (1H, m, $\underline{H}_2$), 3.51-3.43 (1H, m, $\underline{H}_{5'}$), 3.47 (2H, t, *J* = 6.5 Hz, $\underline{H}_{9'}$), 3.26-3.18 (1H, m, $\underline{H}_6$), 2.08-2.04 (1H, m, $\underline{H}_{2a'}$), 1.98-1.81 (2H, m, $\underline{H}_{3a'}$ + $\underline{H}_{4a}$), 1.69-1.43 (12H, m, $\underline{H}_{2b'}$ + $\underline{H}_{3a}$ + $\underline{H}_{3b'}$ + $\underline{H}_{4a'}$ + $\underline{H}_{4b}$ + $\underline{H}_{5a}$ + $\underline{H}_{6'}$ + $\underline{H}_7$ + $\underline{H}_{8'}$), 1.41-1.10 (13H, m, $\underline{H}_{3b}$ + $\underline{H}_{4b'}$ + $\underline{H}_{5b}$ + $\underline{H}_{7'}$ + $\underline{H}_{8\text{-}11}$), 0.88 (3H, t, *J* = 6.6 Hz, $\underline{H}_{12}$); ^{13}**C NMR** (125 MHz, $CDCl_3$) δ 149.6, 138.6, 128.3, 127.6, 127.4, 122.3, 78.2, 77.7, 76.0, 73.0, 72.8, 70.3, 55.0, 36.3, 36.2, 31.8, 31.5, 31.1 (2C), 29.8, 29.2, 28.6, 25.4, 23.5, 23.0, 22.6, 22.1, 14.1; **HRMS** (ES^+) Calc. for $C_{30}H_{48}O_3N_3$ $[M+H]^+$ 498.3690, found 498.3680.

1-[(2*S*’,6*S*’)-6’-(hexyltetrahydropyran-2-yl)methyl]-4-[(2*S*’’,6*S*’’)-6’’-(4-hydroxybutyl) tetrahydropyran-2-yl]-*1H*-1,2,3-triazole (23)

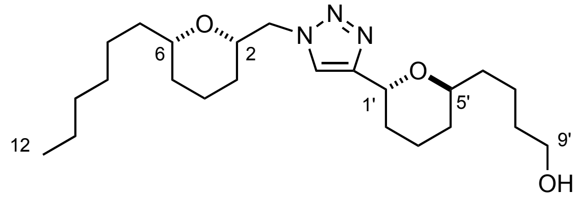


General procedure B was followed with benzyl ether **18b** (17.3 mg, 35.0 μmol) in EtOH (2 mL) to which was added $Pd(OH)_2$ on carbon (4.90 mg, 20% wt on carbon, 6.95 μmol). Standard work-up and purification by flash column chromatography (50→70% EtOAc/Hexane) provided alcohol **23** (13.1 mg, 92%), as a colourless oil.

$\mathbf{R_f}$ 0.14 (50% EtOAc/Hexane); $[\alpha]_D^{20}$ -25.2 (*c* 0.5, $CHCl_3$); **IR** (thin film) 3431, 2934, 2859, 1751, 1456 cm^{-1}; ^{1}**H NMR** (300 MHz, $CDCl_3$) δ 7.64 (1H, s, $\underline{H}_{Ar}$), 4.62-4.58 (1H, m, $\underline{H}_{1'}$), 4.46 (1H, dd, *J* = 14.0, 3.1 Hz, $\underline{H}_{1a}$), 4.18 (1H, dd, *J* = 14.0, 8.3 Hz, $\underline{H}_{1b}$), 3.67-3.59 (3H, m, $\underline{H}_2$ + $\underline{H}_{9'}$), 3.51-3.45 (1H, m, $\underline{H}_{5'}$), 3.22-3.16 (1H, m, $\underline{H}_6$), 2.02-1.74 (3H, m, $\underline{H}_{2a'}$ + $\underline{H}_{3a'}$ + $\underline{H}_{4a}$), 1.67-1.41 (12H, m, $\underline{H}_{2b'}$ + $\underline{H}_{3a}$ + $\underline{H}_{3b'}$ + $\underline{H}_{4a'}$ + $\underline{H}_{4b}$ + $\underline{H}_{5a}$ + $\underline{H}_{6'}$ + $\underline{H}_7$ + $\underline{H}_{8'}$), 1.38-1.14 (13H, m, $\underline{H}_{3b}$ + $\underline{H}_{4b'}$ + $\underline{H}_{5b}$ + $\underline{H}_{7'}$ + $\underline{H}_{8\text{-}11}$), 0.87 (3H, t, *J* = 6.5 Hz, $\underline{H}_{12}$); ^{13}**C NMR** (125

MHz, $CDCl_3$) δ 149.5, 122.6, 78.3, 77.8, 76.0, 72.8, 62.8, 55.2, 36.3, 36.0, 32.6, 31.9, 31.6, 31.2, 31.2, 29.3, 28.6, 25.6, 23.5, 23.0, 22.6, 21.7, 14.1; **HRMS** (ES^+) Calc. for $C_{23}H_{42}O_3N_3$ $[M+H]^+$ 408.3221, found 408.3221.

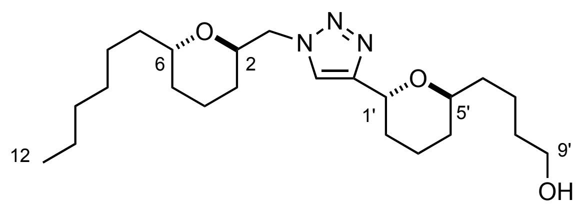
1-[(2*S*',6*S*')-6'-(hexyltetrahydropyran-2-yl)methyl]-4-[(2*R*'',6*S*'')-6''-(4-hydroxybutyl) tetrahydropyran-2-yl]-*1H*-1,2,3-triazole (24)



General procedure B was followed with benzyl ether **19b** (27.5 mg, 55.0 μmol) in EtOH (4 mL) to which was added $Pd(OH)_2$ on carbon (7.70 mg, 20% wt on carbon, 11.0 μmol). Standard work-up and purification by flash column chromatography (50→70% EtOAc/Hexane) provided alcohol **24** (21.3 mg, 95%), as a colourless oil.

R_f 0.59 (50% EtOAc/Hexane); $[\alpha]_D^{20}$ -28.1 (*c* 1.05, $CHCl_3$); **IR** (thin film) 3421, 2934, 2860, 1456, 1441, 1381 cm^{-1}; **^{1}H NMR** (500 MHz, $CDCl_3$) δ 7.66 (1H, s, $\underline{H}_{Ar}$), 5.09-5.05 (1H, m, $\underline{H}_{1'}$), 4.47 (1H, dd, *J* = 13.9, 2.6 Hz, $\underline{H}_{1a}$), 4.25 (1H, dd, *J* = 14.0, 8.0 Hz, $\underline{H}_{1b}$), 3.68-3.57 (4H, m, $\underline{H}_2 + \underline{H}_{5'} + \underline{H}_{9'}$), 3.24-3.19 (1H, m, $\underline{H}_6$), 2.18-2.15 (1H, m, $\underline{H}_{2a'}$), 2.01-1.93 (1H, m, $\underline{H}_{2b'}$), 1.87-1.34 (14H, m, $\underline{H}_{3a} + \underline{H}_{3'-4'} + \underline{H}_4 + \underline{H}_{5a} + \underline{H}_{6'} + \underline{H}_7 + \underline{H}_{8'}$), 1.30-1.09 (12H, m, $\underline{H}_{3b} + \underline{H}_{5b} + \underline{H}_{7'} + \underline{H}_{8-11}$), 0.87 (3H, t, *J* = 6.6 Hz, $\underline{H}_{12}$); **^{13}C NMR** (125 MHz, $CDCl_3$) δ 148.4, 123.3, 77.8, 76.1, 71.3, 67.7, 62.7, 55.0, 36.3, 34.4, 32.7, 31.8, 31.2, 30.7, 29.2, 28.5, 28.3, 25.5, 23.0, 22.6, 21.8, 19.1, 14.1; **HRMS** (ES^+) Calc. for $C_{23}H_{42}O_3N_3$ $[M+H]^+$ 408.3221, found 408.3221.

1-[(2*R*',6*S*')-6'-(hexyltetrahydropyran-2-yl)methyl]-4-[(2*R*'',6*S*'')-6''-(4-hydroxybutyl) tetrahydropyran-2-yl]-1H-1,2,3-triazole (25)

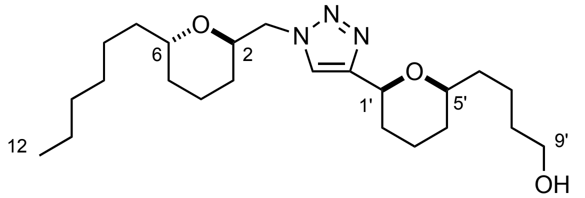


General procedure B was followed with benzyl ether **20b** (10.0 mg, 20.0 μmol) in EtOH (2 mL) to which was added $Pd(OH)_2$ on carbon (2.80 mg, 20% wt on carbon, 4.02 μmol).

Standard work-up and purification by flash column chromatography (50→70% EtOAc/Hexane) provided alcohol **25** (7.60 mg, 93%), as a colourless oil.

R$_f$ 0.03 (50% EtOAc/Hexane); $[\alpha]_D^{20}$ -48.3 (*c* 0.84, CHCl$_3$); **IR** (thin film) 3422, 2934, 2860, 1749, 1456 cm^{-1}; **^{1}H NMR** (500 MHz, CDCl$_3$) δ 7.61 (1H, s, $\underline{H}_{Ar}$), 5.08 (1H, t, *J* = 4.4 Hz, $\underline{H}_{1'}$), 4.42 (1H, dd, *J* = 14.0, 3.5 Hz, $\underline{H}_{1a}$), 4.32 (1H, dd, *J* = 14.1, 8.6 Hz, $\underline{H}_{1b}$), 4.00 (1H, app tt, *J* = 8.7, 3.1 Hz, $\underline{H}_{2}$), 3.83-3.79 (1H, m, $\underline{H}_{5'}$), 3.67-3.58 (1H, m, $\underline{H}_{9'}$), 3.58-3.54 (1H, m, $\underline{H}_{6}$), 2.19 (1H, app dq, *J* = 13.1, 4.3 Hz, $\underline{H}_{2a'}$), 1.99-1.92 (1H, m, $\underline{H}_{2b'}$), 1.75-1.62 (8H, m, $\underline{H}_{3a}$ + $\underline{H}_{3'}$ + $\underline{H}_{5a}$ + $\underline{H}_{6'}$ + $\underline{H}_{7}$), 1.59-1.28 (9H, m, $\underline{H}_{3b}$ + $\underline{H}_{4a'}$ + $\underline{H}_{4}$ + $\underline{H}_{5b}$ + $\underline{H}_{7'-8'}$), 1.27-1.12 (8H, m, $\underline{H}_{4b'}$ + $\underline{H}_{8a}$ + $\underline{H}_{9-11}$), 1.10-1.03 (1H, m, $\underline{H}_{8b}$), 0.84 (3H, t, *J* = 7.1 Hz, $\underline{H}_{12}$); **^{13}C NMR** (125 MHz, CDCl$_3$) δ 148.4, 123.2, 72.5, 71.0, 69.1, 68.0, 62.8, 53.7, 34.5, 32.6, 31.7, 31.4, 30.9, 29.2, 28.9, 28.3, 28.0, 25.6, 22.6, 21.6, 19.2, 18.1, 14.0; **HRMS** (ES$^+$) Calc. for $C_{23}H_{42}O_3N_3$ [M+H]$^+$ 408.3221, found 408.3218.

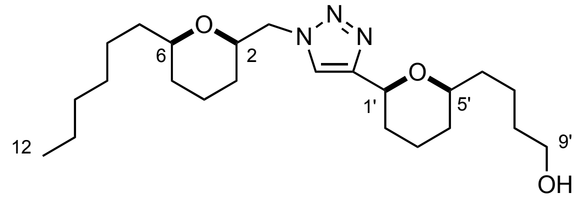
1-[(2*R*',6*S*')-6'-(hexyltetrahydropyran-2-yl)methyl]-4-[(2*S*'',6*S*'')-6''-(4-hydroxybutyl) tetrahydropyran-2-yl]-1H-1,2,3-triazole (26)



General procedure B was followed with benzyl ether **21b** (17.2 mg, 35.0 μmol) in EtOH (4 mL) to which was added Pd(OH)$_2$ on carbon (4.80 mg, 20% wt on carbon, 6.91 μmol). Standard work-up and purification by flash column chromatography (50→70% EtOAc/Hexane) provided alcohol **26** (13.0 mg, 92%), as a colourless oil.

R$_f$ 0.16 (60% EtOAc/Hexane); $[\alpha]_D^{20}$ -41.7 (*c* 1.04, CHCl$_3$); **IR** (thin film) 3424, 2932, 2859, 1742, 1458 cm^{-1}; **^{1}H NMR** (400 MHz, CDCl$_3$) δ 7.61 (1H, s, $\underline{H}_{Ar}$), 4.59-4.56 (1H, m, $\underline{H}_{1'}$), 4.38-4.37 (2H, m, $\underline{H}_{1}$), 4.03-3.97 (1H, m, $\underline{H}_{2}$), 3.82-3.78 (1H, m, $\underline{H}_{5'}$), 3.64 (2H, m, $\underline{H}_{9'}$), 3.50-3.45 (1H, m, $\underline{H}_{6}$), 2.07-2.04 (1H, m, $\underline{H}_{2a'}$), 1.94-1.92 (1H, m, $\underline{H}_{3a'}$), 1.74-1.45 (11H, m, $\underline{H}_{2b'}$ + $\underline{H}_{3a}$ + $\underline{H}_{3b'}$ + $\underline{H}_{4a'}$ + $\underline{H}_{4}$ + $\underline{H}_{5a}$ + $\underline{H}_{7}$ + $\underline{H}_{8'}$), 1.40-1.08 (15H, m, $\underline{H}_{3b}$ + $\underline{H}_{4b'}$ + $\underline{H}_{5b}$ + $\underline{H}_{6'-7'}$ + $\underline{H}_{8-11}$), 0.86 (3H, t, *J* = 6.8 Hz, $\underline{H}_{12}$); **^{13}C NMR** (125 MHz, CDCl$_3$) δ 149.6, 121.9, 78.3, 73.0, 72.2, 69.1, 62.8, 53.5, 36.0, 32.7, 31.9, 31.8, 31.5, 31.2, 29.1, 29.0, 27.8, 25.6, 23.5, 22.6, 21.7, 18.2, 14.1; **HRMS** (ES$^+$) Calc. for $C_{23}H_{42}O_3N_3$ [M+H]$^+$ 408.3221, found 408.3217.

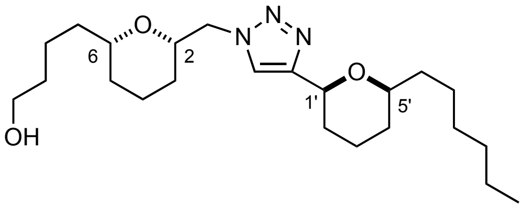
1-[(2*R*',6*R*')-6'-(hexyltetrahydropyran-2-yl)methyl]-4-[(2*S*'',6*S*'')-6''-(4-hydroxybutyl) tetrahydropyran-2-yl]-1H-1,2,3-triazole (27)



General procedure B was followed with benzyl ether **22** (23.1 mg, 46.0 μmol) in EtOH (4 mL) to which was added Pd(OH)$_2$ on carbon (6.50 mg, 20% wt on carbon, 9.00 μmol). Standard work-up and purification by flash column chromatography (50→70% EtOAc/Hexane) provided alcohol **27** (17.1 mg, 90%), as a colourless oil.

R_f 0.06 (60% EtOAc/Hexane); $[\alpha]_D^{20}$ -20.3 (*c* 1.71, CHCl$_3$); **IR** (thin film) 2297, 2932, 2859, 1792, 1734, 1628, 1559 cm^{-1}; **^{1}H NMR** (500 MHz, CDCl$_3$) δ 7.67 (1H, s, $\underline{H}_{Ar}$), 4.64-4.60 (1H, m, $\underline{H}_{1'}$), 4.47 (1H, dd, *J* = 14.1, 3.1 Hz, $\underline{H}_{1a}$), 4.22 (1H, dd, *J* = 14.0, 8.1 Hz, $\underline{H}_{1b}$), 3.67-3.63 (3H, m, $\underline{H}_2$ + $\underline{H}_{9'}$), 3.52-3.47 (1H, m, $\underline{H}_{5'}$), 3.26-3.20 (1H, m, $\underline{H}_6$), 2.09-2.05 (1H, m, $\underline{H}_{2a'}$), 2.01-1.84 (2H, m, $\underline{H}_{3a'}$ + $\underline{H}_{4a}$), 1.72-1.41 (10H, m, $\underline{H}_{2b'}$ + $\underline{H}_{3a}$ + $\underline{H}_{3b'}$ + $\underline{H}_{4a'}$ + $\underline{H}_{4b}$ + $\underline{H}_{5a}$ + $\underline{H}_{6'}$ + $\underline{H}_{8'}$), 1.40-1.11 (15H, m, $\underline{H}_{3b}$ + $\underline{H}_{4b'}$ + $\underline{H}_{5b}$ + $\underline{H}_{7'}$ + $\underline{H}_{7\text{-}11}$), 0.88 (3H, t, *J* = 6.7 Hz, $\underline{H}_{12}$); **^{13}C NMR** (125 MHz, CDCl$_3$) δ 149.6, 122.2, 78.3, 77.8, 76.0, 73.0, 62.8, 55.0, 36.3, 36.1, 32.7, 31.9, 31.4, 31.2, 31.1, 29.3, 28.6, 25.5, 23.5, 23.0, 22.6, 21.7, 14.1; **HRMS** (ES$^+$) Calc. for $C_{23}H_{42}O_3N_3$ $[M+H]^+$ 408.3221, found 408.3220.

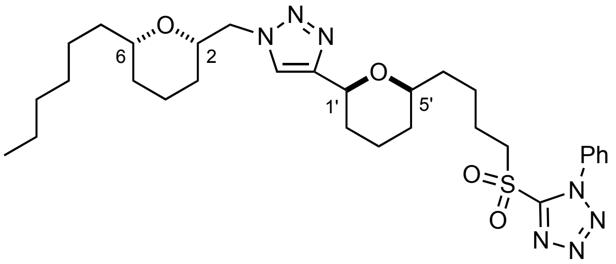
4-[(2*S*',6*S*')-6'-(hexyltetrahydropyran-2-yl)]-1-[(2*S*'',6*S*'')-6''-(4-hydroxybutyl tetrahydropyran-2-yl)methyl]-*1H*-1,2,3-triazole (28)



General procedure B was followed with benzyl ether **18c** (26.2 mg, 53.0 μmol) in EtOH (4 mL) to which was added Pd(OH)$_2$ on carbon (7.40 mg, 20% wt on carbon, 11.0 μmol). Standard work-up and purification by flash column chromatography (60% EtOAc/Hexane) provided alcohol **28** (21.5 mg, 100%), as a colourless oil.

R$_\mathrm{f}$ 0.2 (60% EtOAc/Hexane); $[\alpha]_D^{20}$ -20.3 (*c* 0.39, $CHCl_3$); **IR** (thin film) 3395, 2932, 2859, 1456, 1439 cm^{-1}; **^{1}H NMR** (500 MHz, $CDCl_3$) δ 7.63 (1H s, $\underline{H}_{Ar}$), 4.60-4.58 (1H, m, $\underline{H}_{1'}$), 4.44 (1H, dd, *J* = 14.0, 2.8 Hz, $\underline{H}_{1a}$), 4.19 (1H, dd, *J* = 14.0, 8.4 Hz, $\underline{H}_{1b}$), 3.67-3.63 (1H, m, $\underline{H}_2$), 3.61-3.56 (2H, m, $\underline{H}_{10}$), 3.48-3.44 (1H, m, $\underline{H}_{5'}$), 3.24-3.20 (1H, m, $\underline{H}_6$), 2.05-2.03 (1H, m, $\underline{H}_{2a'}$), 1.94-1.84 (2H, m, $\underline{H}_{3a'}$ + $\underline{H}_{4a}$), 1.66-1.40 (14H, m, $\underline{H}_{2b'}$ + $\underline{H}_{3a}$ + $\underline{H}_{3b'}$ + $\underline{H}_{4a'}$ + $\underline{H}_{4b}$ + $\underline{H}_{5a}$ + $\underline{H}_{6'}$ + $\underline{H}_7$ + $\underline{H}_9$ + $\underline{H}_{9'}$), 1.35-1.17 (11H, m, $\underline{H}_{3b}$ + $\underline{H}_{4b'}$ + $\underline{H}_{5b}$ + $\underline{H}_{7'-8'}$ + $\underline{H}_8$ + $\underline{H}_{10'}$), 0.86 (3H, t, *J* = 6.1 Hz, $\underline{H}_{11'}$); **^{13}C NMR** (125 MHz, $CDCl_3$) δ 149.8, 122.2, 78.6, 77.6, 76.1, 73.3, 62.6, 55.0, 36.5, 35.7, 32.5, 31.8, 31.7, 31.2, 31.2, 29.4, 28.6, 25.5, 23.6, 23.0, 22.6, 21.7, 14.1; **HRMS** (CI$^+$) Calc. for $C_{23}H_{42}O_3N_3$ [M+H]$^+$ 408.3221, found 408.3218.

1-[(2*S*',6*S*')-6'-(hexyltetrahydropyran-2-yl)methyl]-4-[(2*S*'',6*S*'')-6''-(4-(sulfonyl-1-phenyl-*1H*-1,2,3,4-tetrazolyl)butyl)tetrahydropyran-2-yl]-*1H*-1,2,3-triazole (29)



To a solution of alcohol **23** (38.2 mg, 94.0 μmol) in THF (2 mL) at 0 °C was added 1-phenyl-*1H*-tetrazole-5-thiol (21.7 mg, 120 μmol) and PPh_3 (32.0 mg, 120 μmol) followed by DIAD (24.0 μL, 120 μmol) dropwise. The reaction mixture was warmed to RT over 3 h, then quenched by the addition of saturated aqueous NH_4Cl (5 mL) and EtOAc (5 mL). The organics were extracted with EtOAc (3 × 5 mL), dried (Na_2SO_4), filtered and concentrated *in vacuo*. Purification by flash column chromatography (20→50% EtOAc/Hexane) provided 1-[(2*S*',6*S*')-6'-(hexyltetrahydropyran-2-yl)methyl]-4-[(2*S*'',6*S*'')-6''-(4-(sulfanyl-1-phenyl-*1H*-1,2,3,4-tetrazolyl)butyl)tetrahydropyran-2-yl]-*1H*-1,2,3-triazole (35.8 mg, 67%), as a colourless oil.

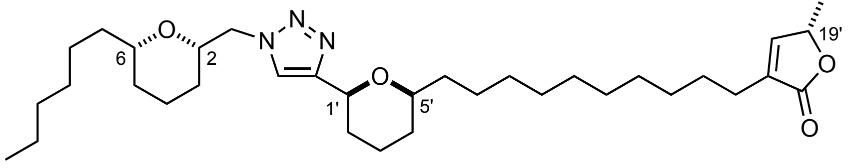
R$_\mathrm{f}$ 0.46 (30% Acetone/Hexane); $[\alpha]_D^{20}$ -26.1 (*c* 1.01, $CHCl_3$); **IR** (thin film) 2932, 2857, 1728, 1499, 1385, 1086 cm^{-1}; **^{1}H NMR** (300 MHz, $CDCl_3$) δ 7.68 (1H, s, $\underline{H}_{Ar}$), 7.61-7.51 (5H, m, Ar$\underline{H}$), 4.66-4.62 (1H, m, $\underline{H}_{1'}$), 4.48 (1H, dd, *J* = 13.9, 3.0 Hz, $\underline{H}_{1a}$), 4.20 (1H, dd, *J* = 14.0, 8.4 Hz, $\underline{H}_{1b}$), 3.68-3.60 (1H, m, $\underline{H}_2$), 3.51-3.44 (1H, m, $\underline{H}_{5'}$), 3.38 (2H, t, *J* = 7.3 Hz, $\underline{H}_{9'}$), 3.23-3.16 (1H, m, $\underline{H}_6$), 2.10-2.07 (1H, m, $\underline{H}_{2a'}$), 1.97-1.79 (4H, m, $\underline{H}_4$ + $\underline{H}_{8'}$), 1.68-1.42 (10H, m, $\underline{H}_{2b'}$ + $\underline{H}_{3a}$ + $\underline{H}_{3'}$ + $\underline{H}_{4a'}$ + $\underline{H}_{5a}$ + $\underline{H}_{6'}$ + $\underline{H}_7$), 1.37-1.14 (13H, m, $\underline{H}_{3b}$ + $\underline{H}_{4b'}$ +

$\underline{H}_{5b}$ + $\underline{H}_{7'}$ + $\underline{H}_{8-11}$), 0.86 (3H, t, J = 6.4 Hz, $\underline{H}_{12}$); **^{13}C NMR** (75 MHz, $CDCl_3$) δ 154.4, 149.5, 133.7, 130.0, 129.7, 123.8, 122.3, 77.9, 77.8, 76.0, 73.1, 55.0, 36.3, 35.7, 33.2, 31.8, 31.6, 31.2, 31.1, 29.3, 29.1, 28.6, 25.5, 24.6, 23.5, 22.9, 22.6, 14.1; **HRMS** (ES$^+$) Calc. for $C_{30}H_{45}O_2N_7S_1Na$ [M+Na]$^+$ 590.3261, found 590.3245.

To a solution of 1-[(2*S*',6*S*')-6'-(hexyltetrahydropyran-2-yl)methyl]-4-[(2*S*'',6*S*'')-6''-(4-(sulfanyl-1-phenyl-*1H*-1,2,3,4-tetrazolyl)butyl)tetrahydropyran-2-yl]-*1H*-1,2,3-triazole (35.8 mg, 63.0 μmol) in MeOH (1 mL) at 0 °C was added a mixture of ammonium molybdate (39.0 mg, 32.0 μmol) and H_2O_2 (143 μL, 30% v/v solution in H_2O, 1.26 mmol). After 16 h at RT, the reaction mixture was diluted with MeOH (3 mL) and H_2O (3 mL). The organics were extracted with CH_2Cl_2 (3 × 5 mL), dried (Na_2SO_4), filtered and concentrated *in vacuo*. Purification by flash column chromatography (20% Acetone/Hexane) provided sulfone **29** (34.3 mg, 91%), as a colourless oil.

R$_f$ 0.43 (30% Acetone/Hexane); $[\alpha]_D^{20}$ -20.1 (*c* 1.00, $CHCl_3$); **IR** (thin film) 2932, 2857, 1732, 1595, 1499, 1340 cm^{-1}; **^{1}H NMR** (400 MHz, $CDCl_3$) δ 7.72-7.55 (6H, m, Ar$\underline{H}$ + $\underline{H}_{Ar}$), 4.60-4.57 (1H, m, $\underline{H}_{1'}$), 4.44 (1H, dd, J = 14.0, 3.2 Hz, $\underline{H}_{1a}$), 4.18 (1H, dd, J = 14.0, 8.3 Hz, $\underline{H}_{1b}$), 3.72-3.68 (2H, m, $\underline{H}_{9'}$), 3.65-3.59 (1H, m, $\underline{H}_{2}$), 3.51-3.45 (1H, m, $\underline{H}_{5'}$), 3.21-3.16 (1H, m, $\underline{H}_{6}$), 2.01-1.91 (3H, m, $\underline{H}_{2a'}$ + $\underline{H}_{8'}$), 1.86-1.82 (1H, m, $\underline{H}_{4a}$), 1.70-1.42 (11H, m, $\underline{H}_{2b'}$ + $\underline{H}_{3a}$ + $\underline{H}_{3'}$ + $\underline{H}_{4a'}$ + $\underline{H}_{4b}$ + $\underline{H}_{5a}$ + $\underline{H}_{6'}$ + $\underline{H}_{10}$), 1.39-1.10 (13H, m, $\underline{H}_{3b}$ + $\underline{H}_{4b'}$ + $\underline{H}_{5b}$ + $\underline{H}_{7'}$ + $\underline{H}_{7-9}$ + $\underline{H}_{11}$), 0.86 (3H, t, J = 6.7 Hz, $\underline{H}_{12}$); **^{13}C NMR** (75 MHz, $CDCl_3$) δ 153.4, 149.4, 133.0, 131.4, 129.6, 125.0, 122.3, 77.8, 77.7, 76.1, 73.1, 55.9, 55.0, 36.3, 35.5, 31.8, 31.6, 31.2, 31.2, 29.3, 28.6, 25.5, 24.2, 23.5, 23.0, 22.6, 22.0, 14.1; **HRMS** (ES$^+$) Calc. for $C_{30}H_{46}O_4N_7S_1$ [M+H]$^+$ 600.3340, found 600.3320.

1-[(2*S*',6*S*')-6'-(hexyltetrahydropyran-2-yl)methyl]-4-[(2*S*'',6*S*'')-6''-[10-[(5*S*)-3-(5-methyl-2,5-dihydrofuran-2-one)decyl)-tetrahydropyran-2-yl]-*1H*-1,2,3-triazole (31)



To a solution of sulfone **29** (31.5 mg, 53.0 μmol) in THF (3 mL) at -78 °C was added NaHMDS (410 μL, 0.2 M solution in THF, 82.0 μmol). After 10 min, a solution of aldehyde **30** (37.0 mg, 190 μmol) in THF (1 mL) was added dropwise *via* cannula. After 1.25 h, saturated aqueous NH_4Cl (4 mL) was added, and the reaction mixture was warmed to RT. The organics were extracted with EtOAc (3 x 5 mL) and the combined organic extracts were washed with brine (10 mL), dried (Na_2SO_4), filtered and concentrated *in vacuo*. Purification by flash column chromatography (3% EtOAc/CH_2Cl_2) provided 1-[(2*S*',6*S*')-6'-(hexyltetrahydropyran-2-yl)methyl]-4-[(2*S*'',6*S*'')-6''-[(4*E*)-10-[(5*S*)-3-(5-methyl-2,5-dihydrofuran-2-one)dec-4-ene)-tetrahydropyran-2-yl]-*1H*-1,2,3-triazole (18.4 mg, 61%) as a colourless oil.

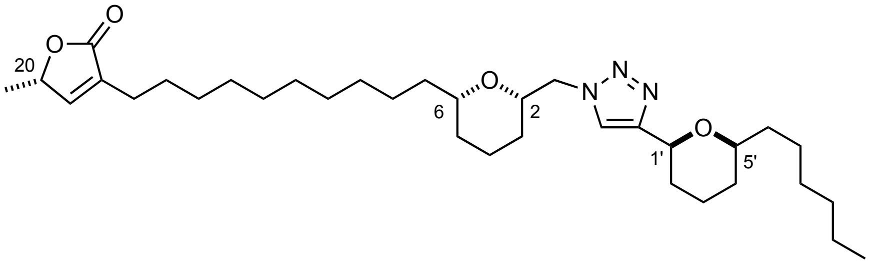
R_f 0.61 (30% Acetone/Hexane); $[\alpha]_D^{20}$ -9.40 (*c* 1.84, $CHCl_3$); **IR** (thin film) 2934, 2856, 1751, 1456, 1084 cm^{-1}; **^{1}H NMR** (400 MHz, $CDCl_3$) δ 7.64 (1H, s, $\underline{H}_{Ar}$), 6.97 (1H, app q, *J* = 1.5 Hz, $\underline{H}_{18'}$), 5.37-5.31 (2H, m, $\underline{H}_{9'-10'}$), 4.98 (1H, qq, *J* = 6.7, 1.7 Hz, $\underline{H}_{19'}$), 4.60 (1H, dd, *J* = 11.1, 1.9 Hz, $\underline{H}_{1'}$), 4.46 (1H, dd, *J* = 14.0, 3.0 Hz, $\underline{H}_{1a}$), 4.18 (1H, dd, *J* = 14.1, 8.3 Hz, $\underline{H}_{1b}$), 3.62 (1H, app ddt, *J* = 11.3, 8.5, 2.5 Hz, $\underline{H}_{2}$), 3.49-3.43 (1H, m, $\underline{H}_{5'}$), 3.23-3.16 (1H, m, $\underline{H}_{6}$), 2.27-2.22 (2H, m, $\underline{H}_{15'}$), 2.02-1.83 (7H, m, $\underline{H}_{2a'}$ + $\underline{H}_{3a'}$ + $\underline{H}_{4a}$ + $\underline{H}_{8'}$ + $\underline{H}_{11'}$), 1.64-1.43 (10H, m, $\underline{H}_{2b'}$ + $\underline{H}_{3a}$ + $\underline{H}_{3b'}$ + $\underline{H}_{4a'}$ + $\underline{H}_{4b}$ + $\underline{H}_{5a}$ + $\underline{H}_{10}$ + $\underline{H}_{14'}$), 1.41-1.30 (8H, m, $\underline{H}_{6'-7'}$ + $\underline{H}_{7}$ + $\underline{H}_{12'}$), 1.39 (3H, d, *J* = 6.8 Hz, $\underline{H}_{20'}$), 1.29-1.11 (11H, m, $\underline{H}_{3b}$ + $\underline{H}_{4b'}$ + $\underline{H}_{5b}$ + $\underline{H}_{8-9}$ + $\underline{H}_{11}$ + $\underline{H}_{13'}$), 0.87 (3H, t, *J* = 6.7 Hz, $\underline{H}_{12}$); **^{13}C NMR** (125 MHz, $CDCl_3$) δ 173.9, 149.7, 148.9, 134.2, 130.3, 130.2, 122.4, 78.3, 77.8, 77.3, 76.1, 73.0, 55.1, 36.3, 36.0, 32.6, 32.3, 31.8, 31.7, 31.2, 31.1, 29.3, 29.2, 28.6, 28.6, 27.2, 25.6, 25.5, 25.1, 23.5, 23.0, 22.6, 19.2, 14.1; **HRMS** (ES$^+$) Calc. for $C_{34}H_{55}O_4N_3Na$ $[M+Na]^+$ 592.4099, found 592.4079.

To a solution of 1-[(2*S*',6*S*')-6'-(hexyltetrahydropyran-2-yl)methyl]-4-[(2*S*'',6*S*'')-6''-[(4*E*)-10-[(5*S*)-3-(5-methyl-2,5-dihydrofuran-2-one)dec-4-ene)-tetrahydropyran-2-yl]-*1H*-1,2,3-triazole (17.1 mg, 30.0 μmol) and $TsNHNH_2$ (340 mg, 1.80 mmol) in DME (3 mL) at reflux was added a solution of NaOAc (240 mg, 1.80 mmol) in H_2O (3 mL) over 3 h. The reaction mixture was cooled and diluted with H_2O (3 mL) and EtOAc (5 mL) and the organics were extracted with EtOAc (3 x 10 mL). The combined organic extracts were washed with 3 N HCl (3 x 5 mL), $NaHCO_3$ (10 mL), brine (10 mL), dried (Na_2SO_4), filtered and concentrated *in vacuo*. Purification by flash column chromatography (8% EtOAc/CH_2Cl_2) provided alkane **31** (14.7 mg, 86%) as a colourless oil.

R_f 0.22 (3% EtOAc/CH_2Cl_2); $[\alpha]_D^{20}$ -8.1 (*c* 1.47, $CHCl_3$); **IR** (thin film) 2928, 2855, 1755, 1456, 1317, 1198 cm^{-1}; **^{1}H NMR** (400 MHz, $CDCl_3$) δ 7.64 (1H, s, $\underline{H}_{Ar}$), 6.98 (1H, app q, *J* = 1.5 Hz, $\underline{H}_{18'}$), 4.98 (1H, qq, *J* = 6.8, 1.8 Hz, $\underline{H}_{19'}$), 4.61-4.58 (1H, m, $\underline{H}_{1'}$), 4.46 (1H, dd, *J* = 14.1, 3.0 Hz, $\underline{H}_{1a}$), 4.18 (1H, dd, *J* = 14.1, 8.2 Hz, $\underline{H}_{1b}$), 3.65-3.60 (1H, m, $\underline{H}_{2}$), 3.48-3.43 (1H, m, $\underline{H}_{5'}$), 3.22-3.17 (1H, m, $\underline{H}_{6}$), 2.27-2.23 (2H, m, $\underline{H}_{15'}$), 2.02-1.83 (3H, m, $\underline{H}_{2a'}$ + $\underline{H}_{3a'}$ + $\underline{H}_{4a}$), 1.66-1.45 (9H, m, $\underline{H}_{2b'}$ + $\underline{H}_{3a}$ + $\underline{H}_{3b'}$ + $\underline{H}_{4a'}$ + $\underline{H}_{4b}$ + $\underline{H}_{10}$ + $\underline{H}_{14'}$), 1.43-1.32 (5H, m,

$\underline{H}_{5a}$ + $\underline{H}_{6'}$ + $\underline{H}_{7}$), 1.39 (3H, d, *J* = 6.8 Hz, $\underline{H}_{20'}$), 1.32-1.11 (23H, m, $\underline{H}_{3b}$ + $\underline{H}_{4b'}$ + $\underline{H}_{5b}$ + $\underline{H}_{7'-13'}$ + $\underline{H}_{8-9}$ + $\underline{H}_{11}$), 0.87 (3H, t, *J* = 6.5 Hz, $\underline{H}_{12}$); **^{13}C NMR** (125 MHz, CDCl$_3$) δ 173.9, 149.9, 148.9, 134.3, 122.3, 78.4, 77.8, 77.4, 76.1, 73.1, 55.0, 36.5, 36.4, 31.9, 31.8, 31.2, 31.2, 29.7, 29.6 (2C), 29.5, 29.3, 29.3, 29.2, 28.6, 27.4, 25.6, 25.5, 25.1, 23.6, 23.0, 22.6, 19.2, 14.1; **HRMS** (ES$^+$) Calc. for $C_{34}H_{58}O_4N_3$ [M+H]$^+$ 572.4435, found 572.4405.

4-[(2*S*’,6*S*’)-6’-(hexyltetrahydropyran-2-yl)]-1-[(2*S*’’,6*S*’’)-6’’-[10-[(5*S*)-3-(5-methyl-2,5-dihydrofuran-2-one)decyl-(tetrahydropyran-2-yl)methyl]-*1H*-1,2,3-triazole (32)



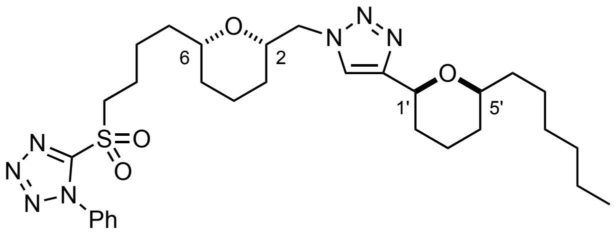
To a solution of sulfone **33** (21.9 mg, 37.0 μmol) in THF (2 mL) at -78 °C was added NaHMDS (220 μL, 0.20 M solution in THF, 44.0 μmol). After 10 min, a solution of aldehyde **30** (11.0 mg, 55.0 μmol) in THF (1 mL) was added dropwise *via* cannula. After 1.5 h, saturated aqueous NH_4Cl (5 mL) was added, and the reaction mixture was warmed to RT. The organics were extracted with EtOAc (3 x 5 mL) and the combined organic extracts were washed with brine (10 mL), dried (Na_2SO_4), filtered and concentrated *in vacuo*. Purification by flash column chromatography (3% EtOAc/CH_2Cl_2) provided 4-[(2*S*’,6*S*’)-6’-(hexyltetrahydropyran-2-yl)]-1-[(2*S*’’,6*S*’’)-6’’-[(4*E*)-10-[(5*S*)-3-(5-methyl-2,5-dihydrofuran-2-one)dec-4-ene-(tetrahydropyran-2-yl)methyl]-*1H*-1,2,3-triazole (9.20 mg, 44%) as a colourless oil.

R_f 0.43 (30% EtOAc/Hexane); $[\alpha]_D^{20}$ -5.7 (*c* 0.92, CHCl$_3$); **IR** (thin flm) 2932, 2859, 2097, 1755 cm^{-1}; **^{1}H NMR** (300 MHz, CDCl$_3$) δ 7.63 (1H, s, $\underline{H}_{Ar}$), 7.00-6.97 (1H, m, $\underline{H}_{19}$), 5.43-5.29 (2H, m, $\underline{H}_{10-11}$), 5.03-4.95 (1H, m, $\underline{H}_{20}$), 4.61-4.58 (1H, m, $\underline{H}_{1'}$), 4.45 (1H, dd, *J* = 14.1, 3.1 Hz, $\underline{H}_{1a}$), 4.20 (1H, dd, *J* = 14.0, 8.0 Hz, $\underline{H}_{1b}$), 3.69-3.60 (1H, m, $\underline{H}_{2}$), 3.50-3.42 (1H, m, $\underline{H}_{5'}$), 3.26-3.17 (1H, m, $\underline{H}_{6}$), 2.29-2.23 (2H, m, $\underline{H}_{16}$), 2.04-1.83 (7H, m, $\underline{H}_{2a'}$ + $\underline{H}_{3a'}$ + $\underline{H}_{4a}$ + $\underline{H}_{9}$ + $\underline{H}_{12}$), 1.71-1.48 (7H, m, $\underline{H}_{2b'}$ + $\underline{H}_{3a}$ + $\underline{H}_{3b'}$ + $\underline{H}_{4a'}$ + $\underline{H}_{4b}$ + $\underline{H}_{15}$), 1.46-1.32 (9H, m, $\underline{H}_{5a}$ + $\underline{H}_{6'}$ + $\underline{H}_{7-8}$ + $\underline{H}_{13}$), 1.40 (3H, d, *J* = 6.8 Hz, $\underline{H}_{21}$), 1.30-1.11 (13H, m, $\underline{H}_{3b}$ + $\underline{H}_{4b'}$ + $\underline{H}_{5b}$ + $\underline{H}_{7'-10'}$ + $\underline{H}_{14}$), 0.86 (3H, t, *J* = 6.9 Hz, $\underline{H}_{11'}$); **^{13}C NMR** (125 MHz, CDCl$_3$) δ 173.8, 149.9, 148.9, 134.2, 130.3, 130.2, 122.3, 78.4, 77.7, 77.4, 76.1, 73.1, 55.0, 36.5, 35.8, 32.5, 32.4, 31.8, 31.7, 31.2 (2C), 29.4, 29.2, 28.7, 28.6, 27.3, 25.5 (2C), 25.1, 23.6, 23.0, 22.6, 19.2, 14.1; **HRMS** (ES^+) Calc. for $C_{34}H_{56}O_4N_3$ $[M+H]^+$ 570.4279, found 570.4262.

To a solution of 4-[(2*S*',6*S*')-6'-(hexyltetrahydropyran-2-yl)]-1-[(2*S*'',6*S*'')-6''-[(4*E*)-10-[(5*S*)-3-(5-methyl-2,5-dihydrofuran-2-one)dec-4-ene-(tetrahydropyran-2-yl)methyl]-*1H*-1,2,3-triazole (9.20 mg, 16.0 μmol) and $TsNHNH_2$ (180 mg, 970 μmol) in DME (1 mL) at reflux was added a solution of NaOAc (131 mg, 970 μmol) in H_2O (1 mL) over 3 h. The reaction mixture was cooled and diluted with H_2O (3 mL) and EtOAc (5 mL) and the organics were extracted with EtOAc (3 x 5 mL). The combined organic extracts were washed with 3 N HCl (3 x 5 mL), $NaHCO_3$ (10 mL), brine (10 mL), dried (Na_2SO_4), filtered and concentrated *in vacuo*. Purification by flash column chromatography (8% EtOAc/CH_2Cl_2) provided alkane **32** (6.90 mg, 75%) as a colourless oil.

$\mathbf{R_f}$ 0.43 (30% EtOAc/Hexane); $[\alpha]_D^{20}$ -6.4 (*c* 0.67, $CHCl_3$); **IR** (thin film) 2930, 2855, 1757, 1456, 1373, 1317 cm^{-1}; ^{1}**H NMR** (400 MHz, $CDCl_3$) δ 7.67 (1H, s, $\underline{H}_{Ar}$), 6.99-6.98 (1H, m, $\underline{H}_{19}$), 5.03-4.96 (1H, m, $\underline{H}_{20}$), 4.68-4.61 (1H, m, $\underline{H}_{1'}$), 4.47 (1H, dd, *J* = 14.0, 3.2 Hz, $\underline{H}_{1a}$), 4.21 (1H, dd, *J* = 13.9, 8.1 Hz, $\underline{H}_{1b}$), 3.37-3.62 (1H, m, $\underline{H}_2$), 3.49-3.44 (1H, m, $\underline{H}_{5'}$), 3.26-3.18 (1H, m, $\underline{H}_6$), 2.28-2.24 (2H, m, $\underline{H}_{16}$), 2.09-2.04 (1H, m, $\underline{H}_{2a'}$), 1.95-1.84 (2H, m, $\underline{H}_{3a'}$ + $\underline{H}_{4a}$), 1.67-1.46 (10H, m, $\underline{H}_{2b'}$ + $\underline{H}_{3a}$ + $\underline{H}_{3b'}$ + $\underline{H}_{4a'}$ + $\underline{H}_{4b}$ + $\underline{H}_{5a}$ + $\underline{H}_{9'}$ + $\underline{H}_{15}$), 1.43-1.36 (4H, m, $\underline{H}_{6'}$ + $\underline{H}_7$), 1.40 (3H, d, *J* = 6.8 Hz, $\underline{H}_{21}$), 1.32-1.12 (23H, m, $\underline{H}_{3b}$ + $\underline{H}_{4b'}$ + $\underline{H}_{5b}$ + $\underline{H}_{7'-8'}$ + $\underline{H}_{8-14}$ + $\underline{H}_{10'}$), 0.87 (3H, t, *J* = 6.9 Hz, $\underline{H}_{11'}$); ^{13}**C NMR** (125 MHz, $CDCl_3$) δ 173.9, 149.2, 148.9, 134.3, 122.9, 78.4, 77.9, 77.4, 75.9, 72.7, 55.4, 36.5, 36.3, 31.8 (2C), 31.2, 31.1, 29.7, 29.6 (2C), 29.5, 29.4, 29.3, 29.2, 28.5, 27.4, 25.6, 25.5, 25.2, 23.5, 22.9, 22.6, 19.2, 14.1; **HRMS** (ES^+) Calc. for $C_{34}H_{58}O_4N_3$ $[M+H]^+$ 572.4435, found 572.4413.

4-[(2*S*',6*S*')-6'-(hexyltetrahydropyran-2-yl)]-1-[(2*S*'',6*S*'')-6''-(4-(sulfonyl-1-phenyl-*1H*-1,2,3,4-tetrazolyl)butyltetrahydropyran-2-yl)methyl]-*1H*-1,2,3-triazole (33)



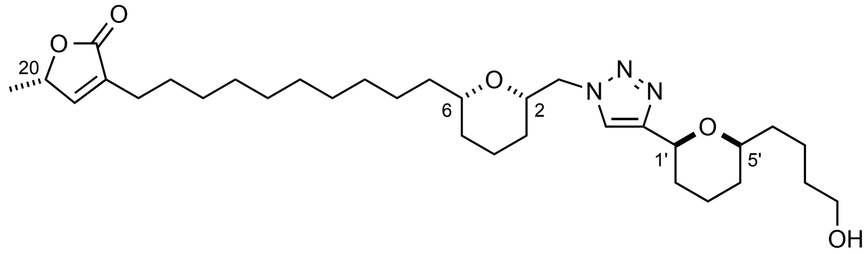
To a solution of alcohol **28** (21.9 mg, 54.0 μmol) in THF (2 mL) at 0 °C was added 1-phenyl-*1H*-tetrazole-5-thiol (12.0 mg, 70.0 μmol) and PPh_3 (18.0 mg, 70.0 μmol) followed by DIAD (14.0 μL, 70.0 μmol) dropwise. The reaction mixture was warmed to RT over 3 h, then quenched by the addition of saturated aqueous NH_4Cl (5 mL) and EtOAc (5 mL). The organics were extracted with EtOAc (3 × 5 mL), dried (Na_2SO_4), filtered and concentrated *in vacuo*. Purification by flash column chromatography (15→30% EtOAc/Hexane) provided 4-[(2*S*',6*S*')-6'-(hexyltetrahydropyran-2-yl)]-1-[(2*S*'',6*S*'')-6''-(4-(sulfanyl-1-phenyl-*1H*-1,2,3,4-tetrazolyl)butyltetrahydropyran-2-yl)methyl]-*1H*-1,2,3-triazole (23.1 mg, 76%), as a colourless oil.

R$_f$ 0.57 (30% Acetone/Hexane); $[\alpha]_D^{20}$ -15.4 (*c* 1.0, $CHCl_3$); **IR** (thin film) 2932, 2857, 1499, 1456, 1387 cm^{-1}; **^{1}H NMR** (500 MHz, $CDCl_3$) δ 7.60 (1H, s, $\underline{H}_{Ar}$), 7.58-7.52 (5H, m, Ar$\underline{H}$), 4.59 (1H, dd, J = 11.1, 1.9 Hz, $\underline{H}_{1'}$), 4.43 (1H, dd, J = 14.1, 3.3 Hz, $\underline{H}_{1a}$), 4.20 (1H, dd, J = 14.1, 8.0 Hz, $\underline{H}_{1b}$), 3.67-3.62 (1H, m, $\underline{H}_{2}$), 3.46-3.42 (1H, m, $\underline{H}_{5'}$), 3.41-3.31 (2H, m, $\underline{H}_{10}$), 3.24-3.20 (1H, m, $\underline{H}_{6}$), 2.04-2.02 (1H, m, $\underline{H}_{2a'}$), 1.90-1.76 (4H, m, $\underline{H}_{4}$ + $\underline{H}_{9}$), 1.64-1.36 (12H, m, $\underline{H}_{2b'}$ + $\underline{H}_{3a}$ + $\underline{H}_{3'}$ + $\underline{H}_{4a'}$ + $\underline{H}_{5a}$ + $\underline{H}_{6'}$ + $\underline{H}_{7\text{-}8}$), 1.31-1.12 (11H, m, $\underline{H}_{3b}$ + $\underline{H}_{4b'}$ + $\underline{H}_{5b}$ + $\underline{H}_{7'\text{-}10'}$), 0.85 (3H, t, J = 6.6 Hz, $\underline{H}_{11'}$); **^{13}C NMR** (125 MHz, $CDCl_3$) δ 154.3, 149.8, 133.6, 130.0, 129.7, 123.7, 122.2, 78.4, 77.3, 76.1, 73.1, 54.9, 36.5, 35.4, 33.1, 31.8, 31.7, 31.2, 31.1, 29.3, 28.9, 28.5, 25.5, 24.5, 23.5, 22.9, 22.6, 14.1; **HRMS** (CI$^+$) Calc. for $C_{30}H_{46}O_2N_7S$ $[M+H]^+$ 568.3428, found 568.3425.

To a solution of 4-[(2*S*',6*S*')-6'-(hexyltetrahydropyran-2-yl)]-1-[(2*S*'',6*S*'')-6''-(4-(sulfanyl-1-phenyl-*1H*-1,2,3,4-tetrazolyl)butyltetrahydropyran-2-yl)methyl]-*1H*-1,2,3-triazole (22.0 mg, 39.0 μmol) in MeOH (1 mL) at 0 °C was added a mixture of ammonium molybdate (24.0 mg, 19.0 μmol) and H_2O_2 (90.0 μL, 30% v/v solution in H_2O, 770 μmol). After 16 h at RT, the reaction mixture was diluted with MeOH (3 mL) and H_2O (3 mL). The organics were extracted with CH_2Cl_2 (3 × 5 mL), dried (Na_2SO_4), filtered and concentrated *in vacuo*. Purification by flash column chromatography (15% Acetone/Hexane) provided sulfone **33** (21.9 mg, 94%), as a colourless oil.

R$_f$ 0.5 (30% Acetone/Hexane); $[\alpha]_D^{20}$ -15.0 (*c* 0.98, $CHCl_3$); **IR** (thin film) 2936, 2859, 1499, 1456, 1339 cm^{-1}; **^{1}H NMR** (500 MHz, $CDCl_3$) δ 7.72-7.68 (2H, m, Ar$\underline{H}$), 7.64-7.54 (4H, m, Ar$\underline{H}$ + $\underline{H}_{Ar}$), 4.60-4.58 (1H, m, $\underline{H}_{1'}$), 4.43 (1H, dd, J = 13.9, 3.2 Hz, $\underline{H}_{1a}$), 4.22 (1H, dd, J = 13.8, 8.0 Hz, $\underline{H}_{1b}$), 3.76-3.65 (3H, m, $\underline{H}_{2}$ + $\underline{H}_{10}$), 3.48-3.43 (1H, m, $\underline{H}_{5'}$), 3.25-3.21 (1H, m, $\underline{H}_{6}$), 2.05-2.03 (1H, m, $\underline{H}_{2a'}$), 1.94-1.84 (4H, m, $\underline{H}_{3a'}$ + $\underline{H}_{4a}$ + $\underline{H}_{9}$), 1.65-1.39 (12H, m, $\underline{H}_{2b'}$ + $\underline{H}_{3a}$ + $\underline{H}_{3b'}$ + $\underline{H}_{4a'}$ + $\underline{H}_{4b}$ + $\underline{H}_{5a}$ + $\underline{H}_{6'}$ + $\underline{H}_{7\text{-}8}$), 1.31-1.15 (11H, m, $\underline{H}_{3b}$ + $\underline{H}_{4b'}$ + $\underline{H}_{5b}$ + $\underline{H}_{7'\text{-}10'}$), 0.85 (3H, t, J = 6.5 Hz, $\underline{H}_{11'}$); **^{13}C NMR** (125 MHz, $CDCl_3$) δ 153.4, 149.9, 133.0, 131.4, 129.7, 125.0, 121.2, 78.4, 77.0, 76.1, 73.2, 55.8, 54.9, 36.5, 35.2, 31.8, 31.7, 31.2, 31.1, 29.3, 28.4, 25.5, 24.1, 23.5, 22.8, 22.6, 21.9, 14.1; **HRMS** (ES$^+$) Calc. for $C_{30}H_{45}O_4N_7SNa$ $[M+Na]^+$ 622.3160, found 622.3138.

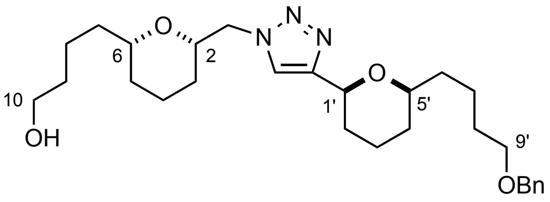
4-[(2*S*’,6*S*’)-6’-(4-hydroxybutyl tetrahydropyran-2-yl)]-1-[(2*S*’’,6*S*’’)-6’’-[10-[(5*S*)-3-(5-methyl-2,5-dihydrofuran-2-one)decyl-(tetrahydropyran-2-yl)methyl]-*1H*-1,2,3-triazole (34)



To a solution of benzyl ether **37** (11.0 mg, 16.9 μmol) in CH_2Cl_2 (2 mL) at -15 °C was added BCl_3·DMS (30 μL, 2.0 M solution in CH_2Cl_2, 60 μmol) dropwise. TLC analysis after 3.5 h indicated incomplete reaction therefore further BCl_3·DMS (30 μL, 2.0 M solution in CH_2Cl_2, 60 μmol) was added dropwise and the reaction allowed to warm to RT overnight. The reaction was quenched by the addition of saturated aqueous $NaHCO_3$ (5 mL) and the organics were extracted with Et_2O (3 x 5 mL). The combined organic extracts were dried (Na_2SO_4), filtered and concentrated *in vacuo*. Purification by flash column chromatography (50%→100% EtOAc/Hexane) provided alcohol **34** (2.2 mg, 23%), as a colourless oil.

R$_f$ 0.16 (50% EtOAc/Hexane); $[\alpha]_D^{20}$ -6.5 (*c* 0.2, $CHCl_3$); **IR** (thin film) 2924, 2853, 1751, 1456, 1439 cm^{-1}; **^{1}H NMR** (500 MHz, $CDCl_3$) δ 7.64 (1H, s, $\underline{H}_{Ar}$), 6.99 (1H, s, $\underline{H}_{19}$), 5.00 (1H, q, *J* = 6.8 Hz, $\underline{H}_{20}$), 4.61 (1H, m, $\underline{H}_{1'}$), 4.46 (1H, dd, *J* = 14.0, 3.0 Hz, $\underline{H}_{1a}$), 4.19 (1H, dd, *J* = 14.0, 8.2 Hz, $\underline{H}_{1b}$), 3.66-3.62 (1H, m, $\underline{H}_2$), 3.64 (t, *J* = 6.4 Hz, $\underline{H}_{9'}$), 3.51-3.47 (1H, m, $\underline{H}_{5'}$), 3.25-3.19 (1H, m, $\underline{H}_6$), 2.26 (2H, t, *J* 7.6 Hz, $\underline{H}_{16}$), 2.01 (1H, app d, *J* 13.5 Hz, $\underline{H}_{2a'}$), 1.94-1.92 (1H, m, $\underline{H}_{2b'}$), 1.87-1.84 (1H, m, $\underline{H}_{3a'}$), 1.66-1.18 (33H, m, $\underline{H}_{3\text{-}5}$ + $\underline{H}_{3b'}$ + $\underline{H}_{4'}$ + $\underline{H}_{6'\text{-}8'}$ + $\underline{H}_{7\text{-}15}$), 1.40 (3H, d, *J* = 6.8 Hz, $\underline{H}_{21}$); **^{13}C NMR** (125 MHz, $CDCl_3$) δ 174.0, 149.6, 149.1, 134.4, 122.7, 78.5, 78.0, 77.6, 76.2, 73.1, 63.0, 55.4, 36.5, 36.2, 32.9, 31.8, 31.4, 31.3, 29.8 (2C), 29.7, 29.5, 29.4, 28.8, 27.6, 25.8, 25.3, 23.7, 23.1, 21.9, 19.4; **HRMS** (ES$^+$) Calc. for $C_{32}H_{54}O_5N_3$ $[M+H]^+$ 560.4058, found 560.4046.

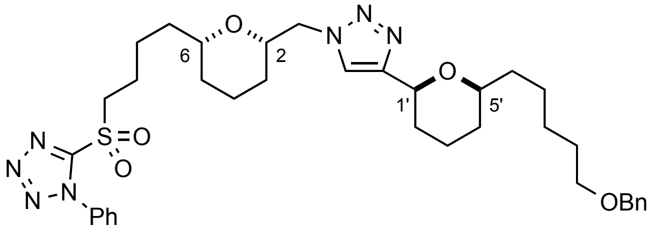
4-[(2*S*’,6*S*’)-6’-(4-(benzyloxy)butyl)tetrahydropyran-2-yl]-1-[(2*S*’’,6*S*’’)-6’’-(4-hydroxybutyltetrahydropyran-2-yl)methyl]-*1H*-1,2,3-triazole (35)



To a solution of triazole **18d** (150 mg, 0.210 mmol) in THF (5 mL) at 0 °C was TBAF (2.10 mL, 1.0 M solution in THF, 2.10 mmol) dropwise. The reaction mixture was stirred at RT for 4 h, then quenched by the addition of saturated aqueous $NaHCO_3$ (15 mL). The mixture was extracted with CH_2Cl_2 (3 x 15 mL) and the combined organics dried ($MgSO_4$), filtered and concentrated *in vacuo*. Purification by flash column chromatography (70% EtOAc/Hexane) provided alcohol **35** (84.0 mg, 83%), as a colourless oil.

$\mathbf{R_f}$ 0.21 (50% EtOAc/Hexane); $[\alpha]_D^{20}$ -94.6 (*c* 2.6, $CHCl_3$); **IR** (thin film) 3005, 2939, 2860, 1558, 1541 cm^{-1}; ^{1}**H NMR** (300 MHz, $CDCl_3$) δ 7.56 (1H, s, $\underline{H}_{Ar}$), 7.30-7.17 (5H, m, Ar$\underline{H}$), 4.53 (1H, dd, *J* = 10.8, 1.8 Hz, $\underline{H}_{1'}$), 4.43 (2H, s, OC$\underline{H}_2$Ar), 4.38 (1H, dd, *J* = 14.0, 2.8 Hz, $\underline{H}_{1a}$), 4.12 (1H, dd, *J* = 14.0, 8.3 Hz, $\underline{H}_{1b}$), 3.59 (1H, app qt, *J* = 8.3, 2.8 Hz, $\underline{H}_2$), 3.51 (2H, t, *J* = 6.3 Hz, $\underline{H}_{10}$), 3.47-3.43 (1H, m, $\underline{H}_{5'}$), 3.40 (2H, t, *J* = 6.5 Hz, $\underline{H}_{9'}$), 3.15 (1H, app t, *J* = 9.3 Hz, $\underline{H}_6$), 2.00-1.70 (5H, m, $\underline{H}_{3a'}$ + $\underline{H}_4$ + $\underline{H}_9$), 1.62-1.14 (19H, m, $\underline{H}_{2'}$ + $\underline{H}_3$ + $\underline{H}_{3b'}$ + $\underline{H}_{5\text{-}8}$ + $\underline{H}_{4'\text{-}8'}$); ^{13}**C NMR** (75 MHz, $CDCl_3$) δ 149.9, 138.7, 128.5, 127.7, 127.6, 122.4, 78.5, 77.7, 76.3, 73.5, 73.0, 70.5, 62.8, 55.1, 36.4, 35.9, 32.6, 31.8, 31.4, 31.3, 29.9, 28.7, 23.7, 23.1, 22.3, 21.8; **HRMS** (ES^+) Calc. for $C_{28}H_{44}O_4N_3$ $[M+H]^+$ 486.3326, found 486.3315.

4-[(2*S*',6*S*')-6'-(4-(benzyloxy)butyltetrahydropyran-2-yl)]-1-[(2*S*'',6*S*'')-6''-(4-(sulfonyl-1-phenyl-*1H*-1,2,3,4-tetrazolyl)butyltetrahydropyran-2-yl)methyl]-*1H*-1,2,3-triazole (36)



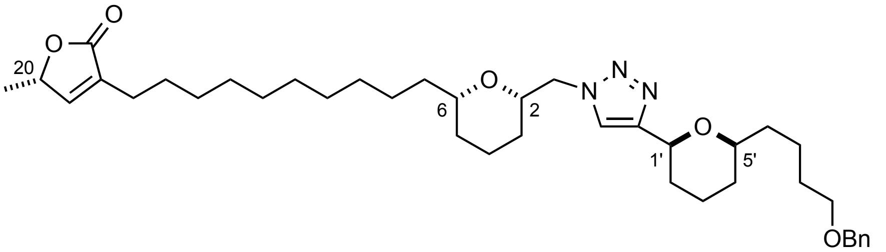
To a solution of alcohol **35** (84.0 mg, 173 µmol) in THF (2 mL) at 0 °C was added 1-phenyl-*1H*-tetrazole-5-thiol (46.0 mg, 260 µmol) and PPh_3 (68.0 mg, 260 µmol) followed by DIAD (51.0 µL, 260 µmol) dropwise. The reaction mixture was warmed to RT overnight then quenched by the addition of saturated aqueous NH_4Cl (10 mL) and EtOAc

(10 mL). The organics were extracted with EtOAc (2 × 10 mL), dried (Na_2SO_4), filtered and concentrated *in vacuo*. Purification by flash column chromatography (40→50% EtOAc/Hexane) provided 4-[(2*S*',6*S*')-6'-(4-(benzyloxy)butyltetrahydropyran-2-yl)]-1-[(2*S*'',6*S*'')-6''-(4-(sulfanyl-1-phenyl-1*H*-1,2,3,4-tetrazolyl)butyltetrahydropyran-2-yl)methyl]-*1H*-1,2,3-triazole (100 mg) as a colourless oil.

To a solution of 4-[(2*S*',6*S*')-6'-(4-(benzyloxy)butyltetrahydropyran-2-yl)]-1-[(2*S*'',6*S*'')-6''-(4-(sulfanyl-1-phenyl-*1H*-1,2,3,4-tetrazolyl)butyltetrahydropyran-2-yl)methyl]-*1H*-1,2,3-triazole (100 mg, 154 μmol) in MeOH (3 mL) at 0 °C was added a mixture of ammonium molybdate (95.0 mg, 77.0 μmol) and H_2O_2 (350 μL, 30% v/v solution in H_2O, 3.08 mmol). After 16 h at RT, the reaction mixture was diluted with MeOH (5 mL) and H_2O (5 mL). The organics were extracted with CH_2Cl_2 (3 × 10 mL) and the cobined organic layers washed with brine (30 mL), dried ($MgSO_4$), filtered and concentrated *in vacuo*. Purification by flash column chromatography (40% EtOAc/Hexane) provided sulfone **36** (82.0 mg, 68%, 2 steps), as a colourless oil.

R$_f$ 0.45 (50% Acetone/Hexane); $[\alpha]_D^{20}$ -12.9 (*c* 1.6, $CHCl_3$); **IR** (thin film) 2934, 2918, 2859, 1595, 1497, 1339 cm^{-1}; **^{1}H NMR** (500 MHz, $CDCl_3$) δ 7.69 (2H, dt, *J* = 6.5, 1.5 Hz, Ar$\underline{H}$), 7.63-7.57 (4H, m, Ar$\underline{H}$ + $\underline{H}_{Ar}$), 7.34-7.31 (4H, m, Ar$\underline{H}$), 7.29-7.24 (1H, m, Ar$\underline{H}$), 4.59 (1H, dd, *J* = 10.9, 1.7 Hz, $\underline{H}_{1'}$), 4.48 (2H, s, OC$\underline{H}_2$Ar), 4.42 (1H, dd, *J* = 14.0, 3.5 Hz, $\underline{H}_{1a}$), 4.20 (1H, dd, *J* = 14.0, 8.1 Hz, $\underline{H}_{1b}$), 3.73-3.64 (3H, m, $\underline{H}_2$ + $\underline{H}_{10}$), 3.49-3.44 (1H, m, $\underline{H}_{5'}$), 3.45 (2H, t, *J* = 6.6 Hz, $\underline{H}_{9'}$), 3.22 (1H, app t, *J* = 8.3 Hz, $\underline{H}_6$), 2.04-2.01 (1H, m, $\underline{H}_{2a'}$), 1.96-1.83 (4H, m, $\underline{H}_{3a'}$ + $\underline{H}_{4a}$ + $\underline{H}_9$), 1.70-1.38 (15H, m, $\underline{H}_{2b'}$ + $\underline{H}_3$ + $\underline{H}_{3b'}$ + $\underline{H}_{4'}$ + $\underline{H}_{4b}$ + $\underline{H}_5$ + $\underline{H}_{6'}$ + $\underline{H}_{7\text{-}8}$), 1.32-1.13 (4H, m, $\underline{H}_{7'\text{-}8'}$); **^{13}C NMR** (125 MHz, $CDCl_3$) δ 153.5, 150.0, 138.8, 133.1, 131.6, 129.9, 128.5, 127.8, 127.6, 125.1, 122.3, 78.5, 77.2, 76.3, 73.3, 73.0, 70.5, 56.0, 55.1, 36.4, 35.4, 31.9, 31.3, 31.2, 29.9, 28.6, 24.2, 23.7, 23.0, 22.3, 22.1; **HRMS** (ES$^+$) Calc. for $C_{35}H_{48}O_5N_7S$ $[M+H]^+$ 678.3432, found 678.3429.

4-[(2*S*',6*S*')-6'-(4-(benzyloxy)butyl tetrahydropyran-2-yl)]-1-[(2*S*'',6*S*'')-6''-[10-[(5*S*)-3-(5-methyl-2,5-dihydrofuran-2-one)decyl-(tetrahydropyran-2-yl)methyl]-*1H*-1,2,3-triazole (37)



Sulfone **36** (53.0 mg, 78.2 μmol) was azeotroped 3 times with toluene then suspended in THF (2 mL) at -78 °C and NaHMDS (235 μL, 0.40 M solution in THF, 94.0 μmol) was added. After 10 min, a solution of aldehyde **30** (45.0 mg, 229 μmol) in THF (1 mL) was added dropwise *via* cannula. After 1 h, the reaction was allowed to come up to RT. After 2 h further stirring, saturated aqueous NH_4Cl (5 mL) was added. The organics were extracted with EtOAc (3 x 5 mL) and the combined organic extracts were washed with brine (10 mL), dried ($MgSO_4$), filtered and concentrated *in vacuo*. Purification by flash column chromatography (30→40% EtOAc/Hexane) provided 4-[(2*S*',6*S*')-6'-(4-(benzyloxy)butyltetrahydropyran-2-yl)]-1-[(2*S*'',6*S*'')-6''-[(4*E*)-10-[(5*S*)-3-(5-methyl-2,5-dihydrofuran-2-one)dec-4-ene-(tetrahydropyran-2-yl)methyl]-*1H*-1,2,3-triazole (34.0 mg, 67%) as a colourless oil.

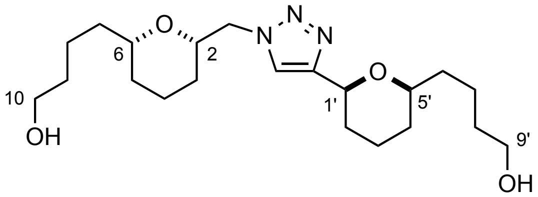
R_f 0.61 (50% EtOAc/Hexane); $[\alpha]_D^{20}$ -5.8 (*c* 0.5, $CHCl_3$); **IR** (thin flm) 2930, 2855, 1749 cm^{-1}; **^{1}H NMR** (300 MHz, $CDCl_3$) δ 7.62 (1H, s, $\underline{H}_{Ar}$), 7.33-7.30 (4H, m, Ar$\underline{H}$), 7.29-7.24 (1H, m, Ar$\underline{H}$), 6.97 (1H, app q, *J* = 1.6 Hz, $\underline{H}_{19}$), 5.37-5.33 (2H, m, $\underline{H}_{10\text{-}11}$), 4.98 (1H, app qq, 1.66, *J* = 6.7, 1.6 Hz, $\underline{H}_{20}$), 4.59 (1H, dd, *J* = 10.7, 1.8 Hz, $\underline{H}_{1'}$), 4.48 (2H, s, OC$\underline{H}_2$Ar), 4.44 (1H, dd, *J* = 14.0, 3.4 Hz, $\underline{H}_{1a}$), 4.19 (1H, dd, *J* = 14.0, 8.1 Hz, $\underline{H}_{1b}$), 3.67-3.59 (1H, m, $\underline{H}_2$), 3.50-3.42 (1H, m, $\underline{H}_{5'}$), 3.46 (2H, t, *J* = 6.5 Hz, $\underline{H}_{9'}$), 3.22-3.17 (1H, m, $\underline{H}_6$), 2.28-2.22 (2H, m, $\underline{H}_{16}$), 2.03-1.83 (7H, m, $\underline{H}_{2a'}$ + $\underline{H}_{3a'}$ + $\underline{H}_{4a}$ + $\underline{H}_9$ + $\underline{H}_{12}$), 1.69-1.14 (25H, m, $\underline{H}_{2b'}$ + $\underline{H}_3$ + $\underline{H}_{3b'}$ + $\underline{H}_{4b}$ + $\underline{H}_{4'}$ + $\underline{H}_5$ + $\underline{H}_{7\text{-}8}$ + $\underline{H}_{6'\text{-}8'}$ + $\underline{H}_{13\text{-}15}$), 1.39 (3H, d, *J* = 6.7 Hz, $\underline{H}_{21}$); **^{13}C NMR** (75 MHz, $CDCl_3$) δ 173.6, 150.0, 149.0, 138.8, 134.4, 130.5, 130.3, 129.9, 127.8, 127.6, 122.5, 78.4, 77.8, 77.4, 76.3, 73.3, 73.0, 70.5, 55.1, 36.4, 35.9, 32.6, 32.5, 31.9, 31.4, 29.9, 29.4, 28.9, 28.8, 27.4, 25.7, 25.3, 23.8, 23.1, 22.3, 19.4; **HRMS** (ES^+) Calc. for $C_{39}H_{58}O_5N_3$ $[M+H]^+$ 648.4371, found 648.4365.

To a solution of 4-[(2*S*',6*S*')-6'-(4-(benzyloxy)butyltetrahydropyran-2-yl)]-1-[(2*S*'',6*S*'')-6''-[(4*E*)-10-[(5*S*)-3-(5-methyl-2,5-dihydrofuran-2-one)dec-4-ene-(tetrahydropyran-2-yl)methyl]-*1H*-1,2,3-triazole (34.0 mg, 52.5 μmol) and $TsNHNH_2$ (595 mg, 3.19 mmol) in DME (2 mL) at reflux was added a solution of NaOAc (432 mg, 3.19 mmol) in H_2O (1.5 mL) over 3 h. The reaction mixture was cooled and diluted with H_2O (3 mL) and

EtOAc (5 mL) and the organics were extracted with EtOAc (2 x 5 mL). The combined organic extracts were washed with 3 N HCl (3 x 5 mL), $NaHCO_3$ (10 mL), brine (10 mL), dried ($MgSO_4$), filtered and concentrated *in vacuo*. Purification by flash column chromatography (40% EtOAc/Hexane) then a second column (75→90% Et_2O/Hexane) provided alkane **37** (22.0 mg, 65%) as a colourless oil.

R$_f$ 0.12 (30% EtOAc/Hexane); $[\alpha]_D^{20}$ -7.2 (*c* 0.5, $CHCl_3$); **IR** (thin film) 2926, 2853, 1751, 1717, 1454, 1439 cm^{-1}; **^{1}H NMR** (500 MHz, $CDCl_3$) δ 7.65 (1H, s, $\underline{H}_{Ar}$), 7.33-7.30 (4H, m, Ar$\underline{H}$), 7.29-7.24 (1H, m, Ar$\underline{H}$), 6.98 (1H, s, $\underline{H}_{19}$), 4.99 (1H, q, *J* = 6.9 Hz, $\underline{H}_{20}$), 4.61 (1H, d, *J* = 10.7 Hz, $\underline{H}_{1'}$), 4.49 (2H, s, OC$\underline{H}_2$Ar), 4.45 (1H, dd, *J* = 14.0, 2.9 Hz, $\underline{H}_{1a}$), 4.19 (1H, dd, *J* = 14.0, 8.2 Hz, $\underline{H}_{1b}$), 3.64 (1H, app t, *J* = 9.6 Hz, $\underline{H}_2$), 3.50-3.45 (1H, m, $\underline{H}_{5'}$), 3.46 (2H, t, *J* = 6.5 Hz, $\underline{H}_{9'}$), 3.20 (1H, app t, *J* = 9.1 Hz, $\underline{H}_6$), 2.27-2.24 (2H, m, $\underline{H}_{16}$), 2.09-2.00 (1H, m, $\underline{H}_{2a'}$), 1.93-1.79 (6H, m, $\underline{H}_{2b'}$ + $\underline{H}_{3a'}$ + $\underline{H}_9$ + $\underline{H}_{12}$), 1.65-1.13 (29H, m, $\underline{H}_{3b'}$ + $\underline{H}_{4\text{-}5}$ + $\underline{H}_{4'}$ + $\underline{H}_{6'\text{-}9'}$ + $\underline{H}_{7\text{-}8}$ + $\underline{H}_{10\text{-}11}$ + $\underline{H}_{13\text{-}15}$), 1.40 (3H, d, *J* = 6.9 Hz, $\underline{H}_{21}$); **^{13}C NMR** (125 MHz, $CDCl_3$) δ 174.1, 149.7, 149.0, 138.8, 134.4, 128.5, 127.8, 127.6, 122.7, 78.4, 78.0, 77.6, 76.2, 73.2, 73.0, 70.5, 55.3, 36.5, 36.4, 31.9, 31.4, 31.3, 29.9, 29.8 (2C), 29.7, 29.5, 29.4, 27.6, 25.8, 23.1, 22.3, 19.4, 14.1; **HRMS** (ES$^+$) Calc. for $C_{39}H_{60}O_5N_3$ $[M+H]^+$ 650.4527, found 650.4511.

4-[(2*S*',6*S*')-6'-(4-hydroxybutyl)tetrahydropyran-2-yl]-1-[(2*S*'',6*S*'')-6''-(4-hydroxybutyltetrahydropyran-2-yl)methyl]-*1H*-1,2,3-triazole (38)



General procedure B was followed with benzyl ether **35** (12.0 mg, 24.7 μmol) in EtOH (2 mL) to which was added $Pd(OH)_2$ on carbon (3.50 mg, 20% wt on carbon, 4.90 μmol). Standard work-up and purification by flash column chromatography (1% MeOH/EtOAc) provided alcohol **38** (7.0 mg, 71%), as a colourless oil.

R$_f$ 0.13 (EtOAc); $[\alpha]_D^{20}$ -22.6 (*c* 0.7, $CHCl_3$); **IR** (thin film) 3402, 3017, 2940, 2862 cm^{-1}; **^{1}H NMR** (400 MHz, $CDCl_3$) δ 7.65 (1H, s, $\underline{H}_{Ar}$), 4.60 (1H, d, *J* = 10.7 Hz, $\underline{H}_{1'}$), 4.45 (1H, dd, *J* = 14.0, 2.8 Hz, $\underline{H}_{1a}$), 4.21 (1H, dd, *J* = 14.0, 8.4 Hz, $\underline{H}_{1b}$), 3.71-3.64 (3H, m, $\underline{H}_2$ + $\underline{H}_{9'}$), 3.58 (2H, t, *J* = 6.4 Hz, $\underline{H}_{10}$), 3.54-3.46 (1H, m, $\underline{H}_{5'}$), 3.23 (1H, app t, *J* = 9.5 Hz, $\underline{H}_6$), 2.08-1.85 (5H, m, $\underline{H}_{3a'} + \underline{H}_{4} + \underline{H}_{9}$), 1.62-1.17 (19H, m, $\underline{H}_{2'} + \underline{H}_{3} + \underline{H}_{3b'} + \underline{H}_{5\text{-}8} + \underline{H}_{4'\text{-}8'}$); **^{13}C NMR** (125 MHz, $CDCl_3$) δ 149.7, 122.4, 78.6, 77.7, 76.3, 73.5, 62.7 (2C), 55.2, 36.0, 35.9, 32.7, 32.6, 31.7, 31.4, 31.3, 28.7, 23.7, 23.1, 21.8 (2C); **HRMS** (ES$^+$) Calc. for $C_{21}H_{38}O_4N_3$ $[M+H]^+$ 396.2857, found 396.2852.

References

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[1] a) G. J. Florence, J. C. Morris, R. G. Murray, R. R. Vanga, J. D. Osler, T. K. Smith, *Org. Lett.* **2011**, *13*, 514-517; b) G. J. Florence, J. C. Morris, R. G. Murray, R. R. Vanga, J. D. Osler, T. K. Smith, *Chem. Eur. J.* **2013**, *19*, 8309-8320.

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[3] S. E. Schaus, B. D. Brandes, J. F. Larrow, M. Tokunaga, K. B. Hansen, A. E. Gould, M. E. Furrow, E. N. Jacobsen, *J. Am. Chem. Soc* **2002**, *124*, 1307-1315.

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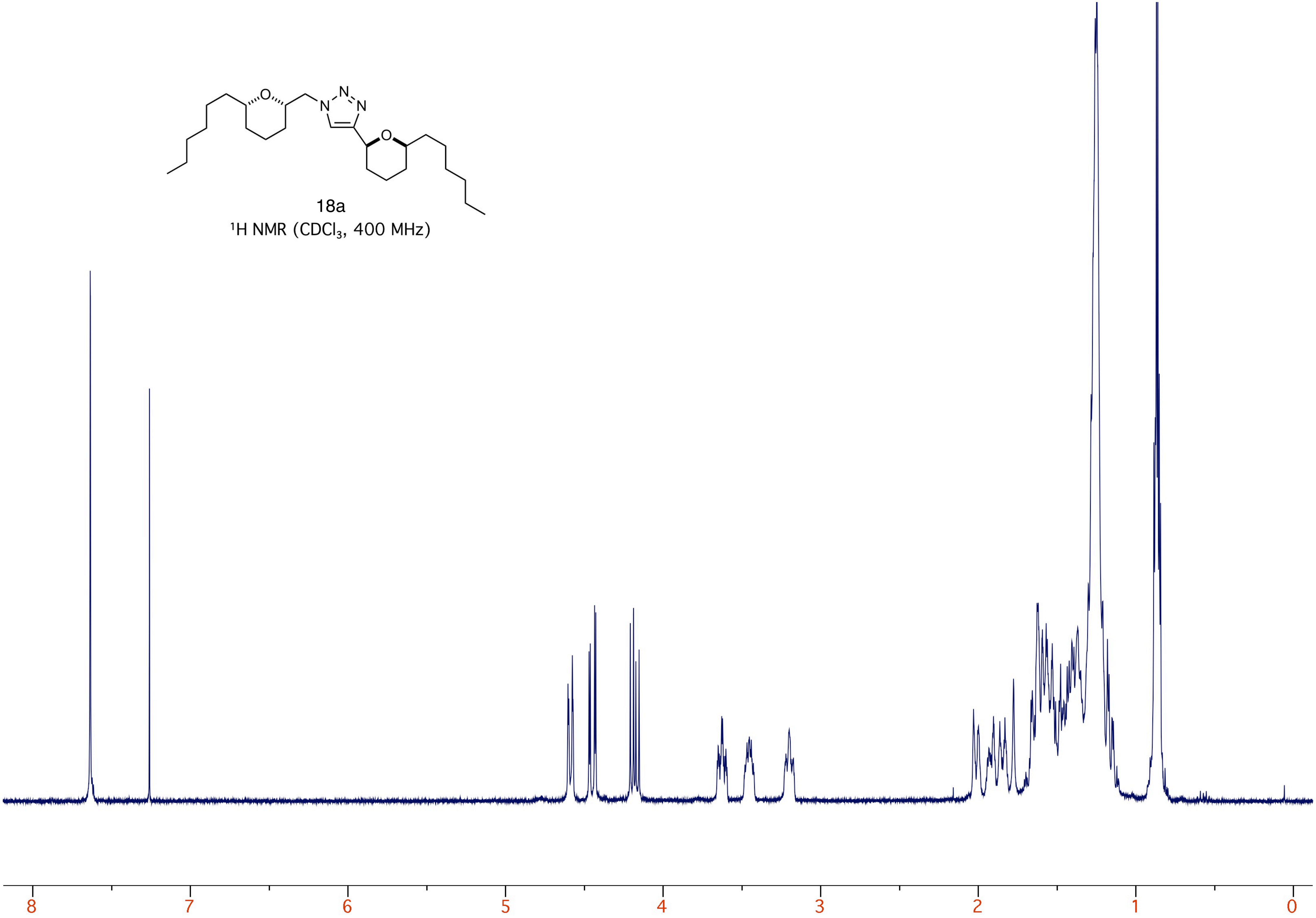
[6] R. V. Reddy, University of St Andrews, PhD thesis, **2009**.

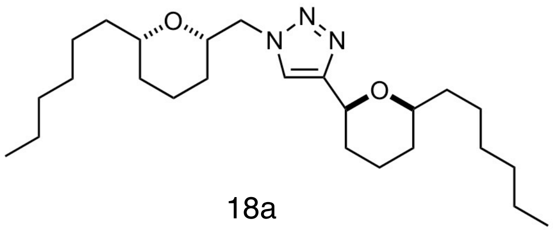
Appendix

^{1}H and ^{13}C NMR spectra for selected novel compounds



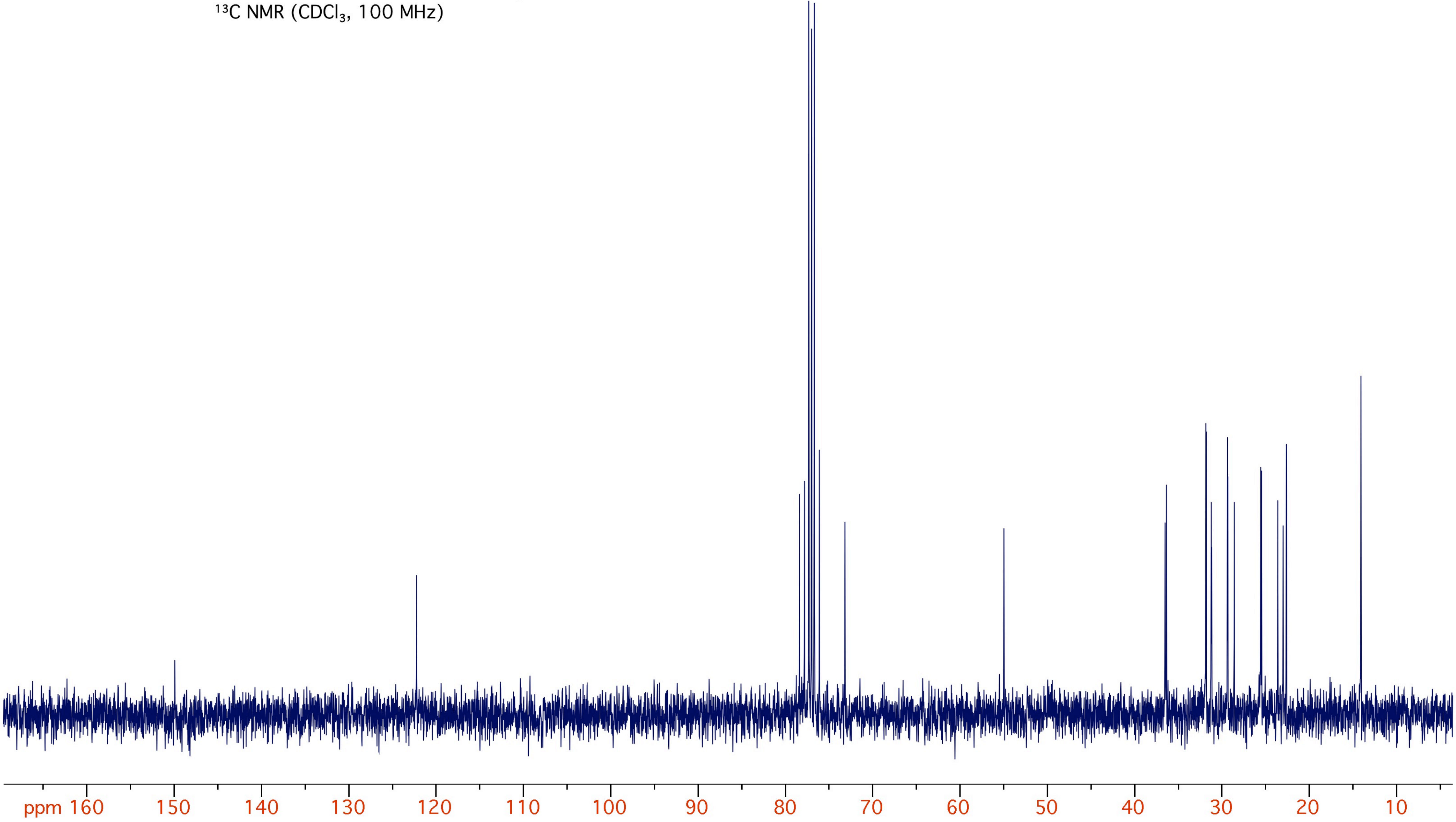
18a

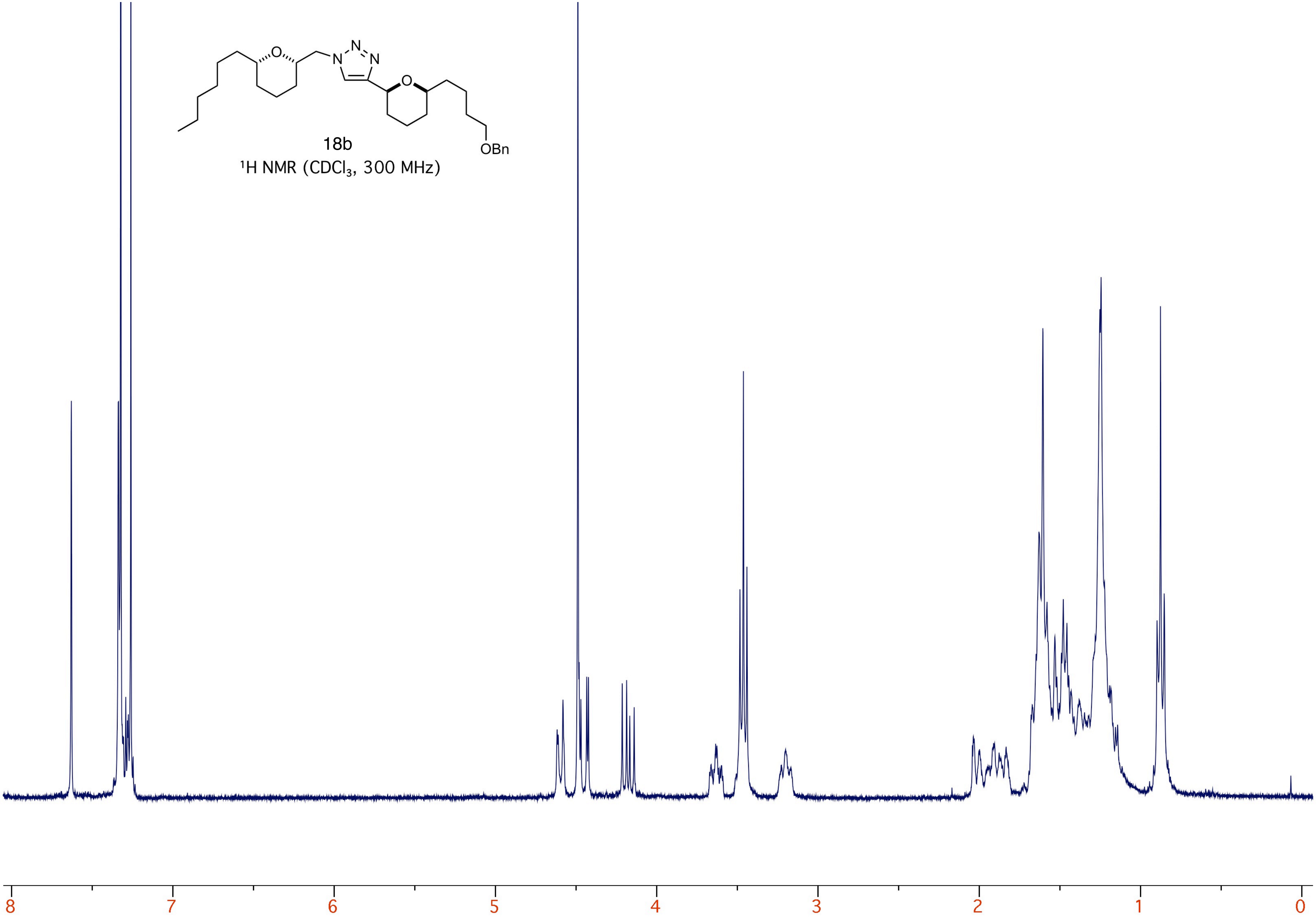
^{1}H NMR (CDCl$_3$, 400 MHz)



18a

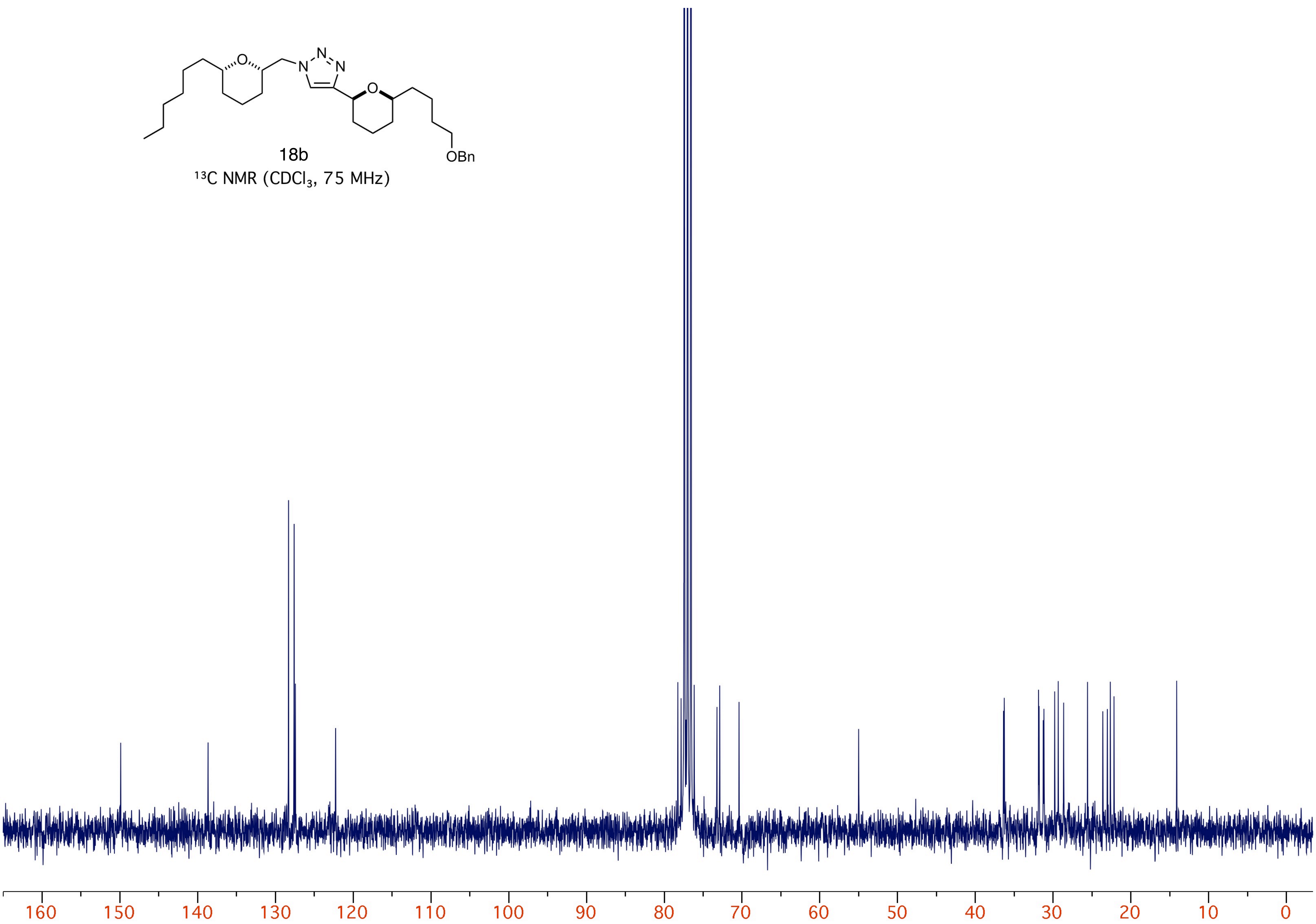
^{13}C NMR (CDCl$_3$, 100 MHz)





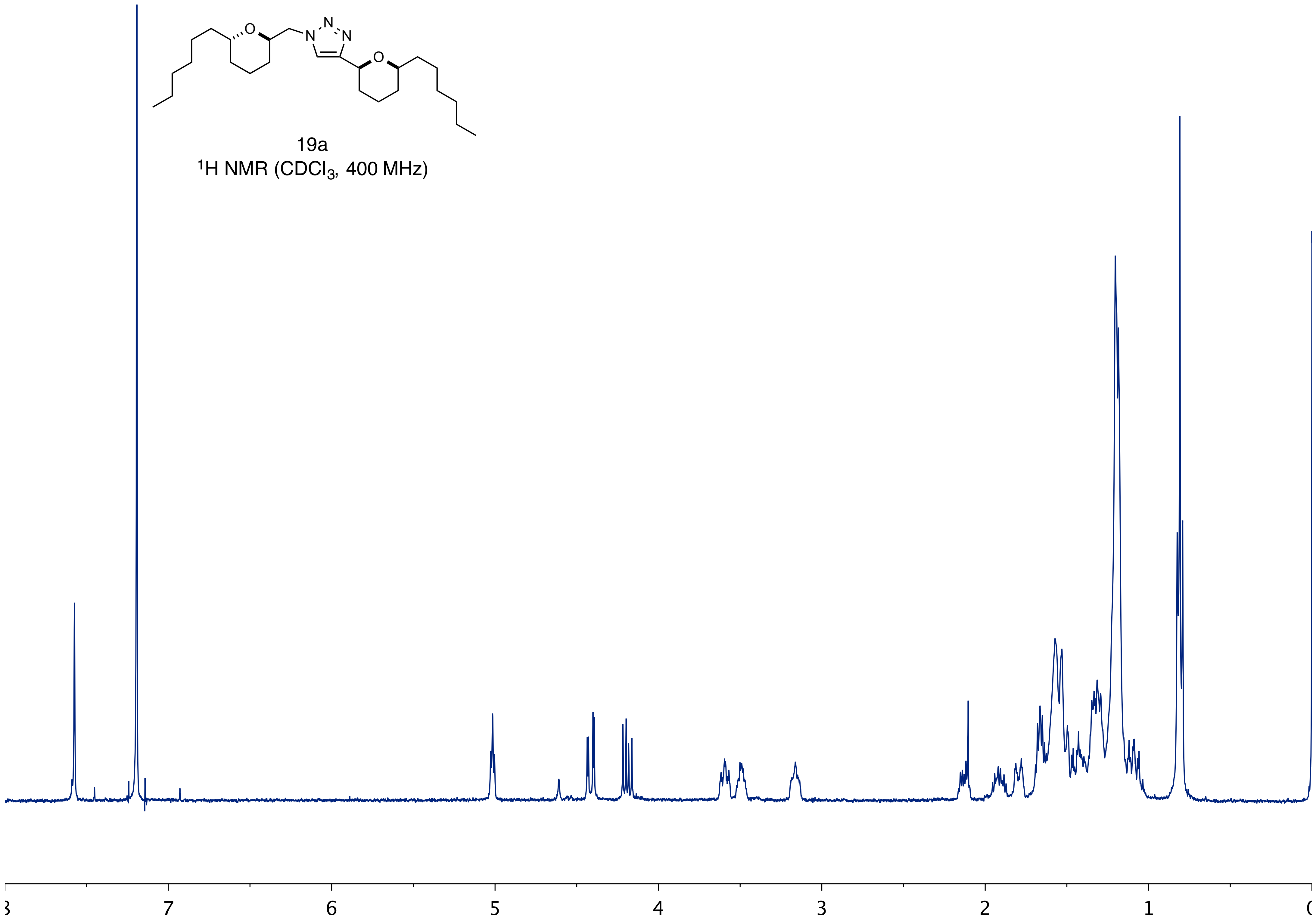
18b

^{1}H NMR (CDCl$_3$, 300 MHz)



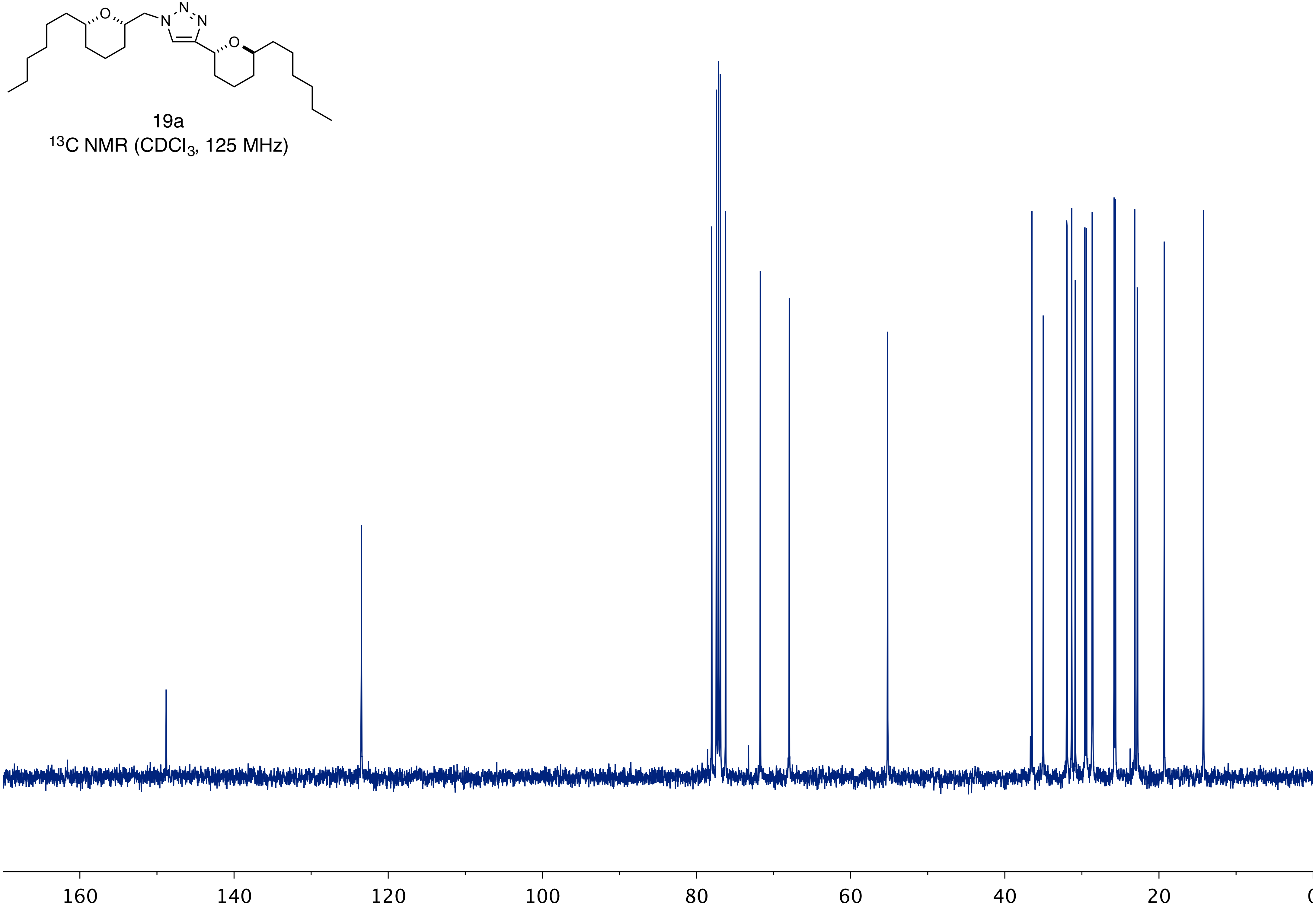
18b

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



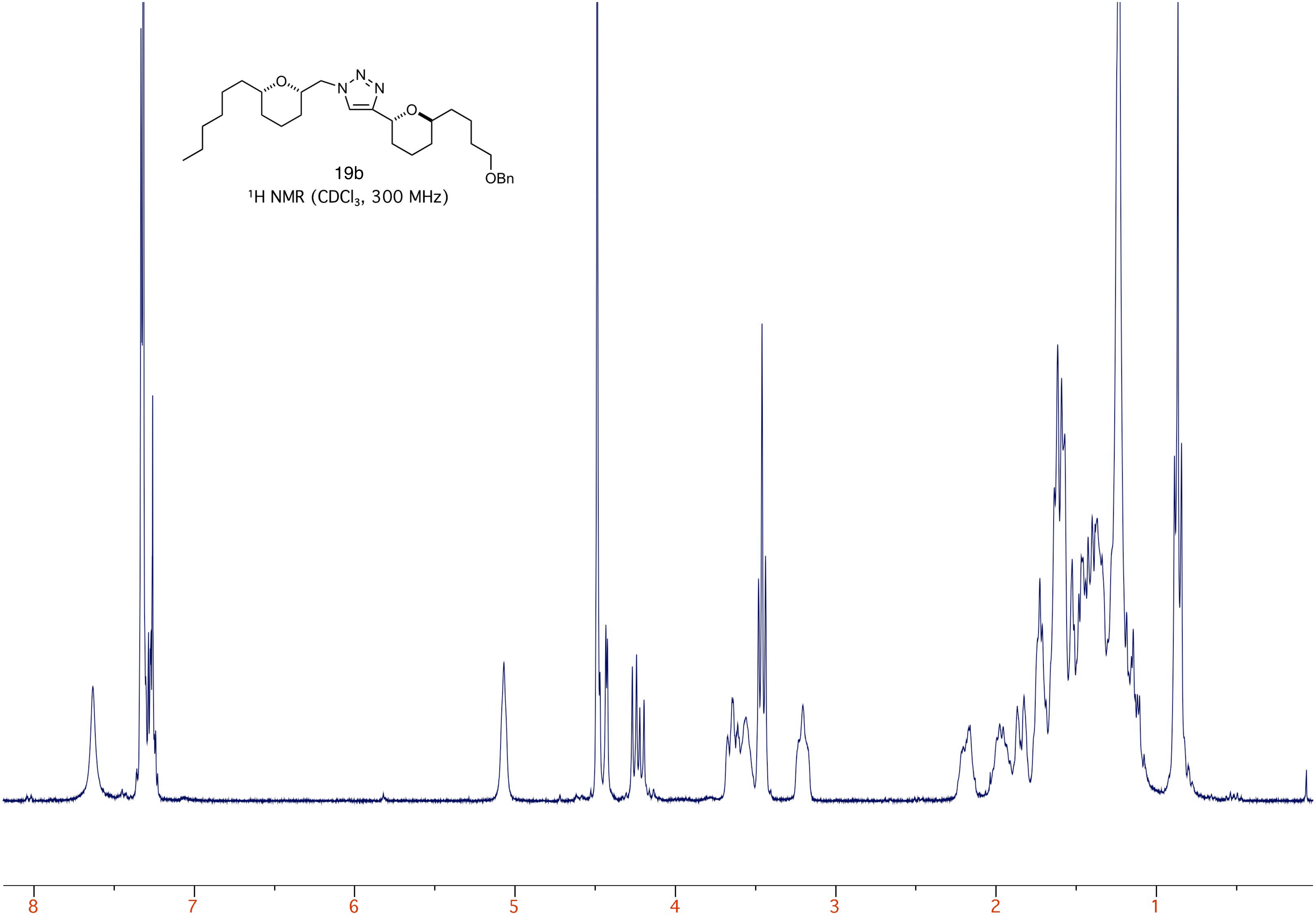
19a

^{1}H NMR ($CDCl_3$, 400 MHz)

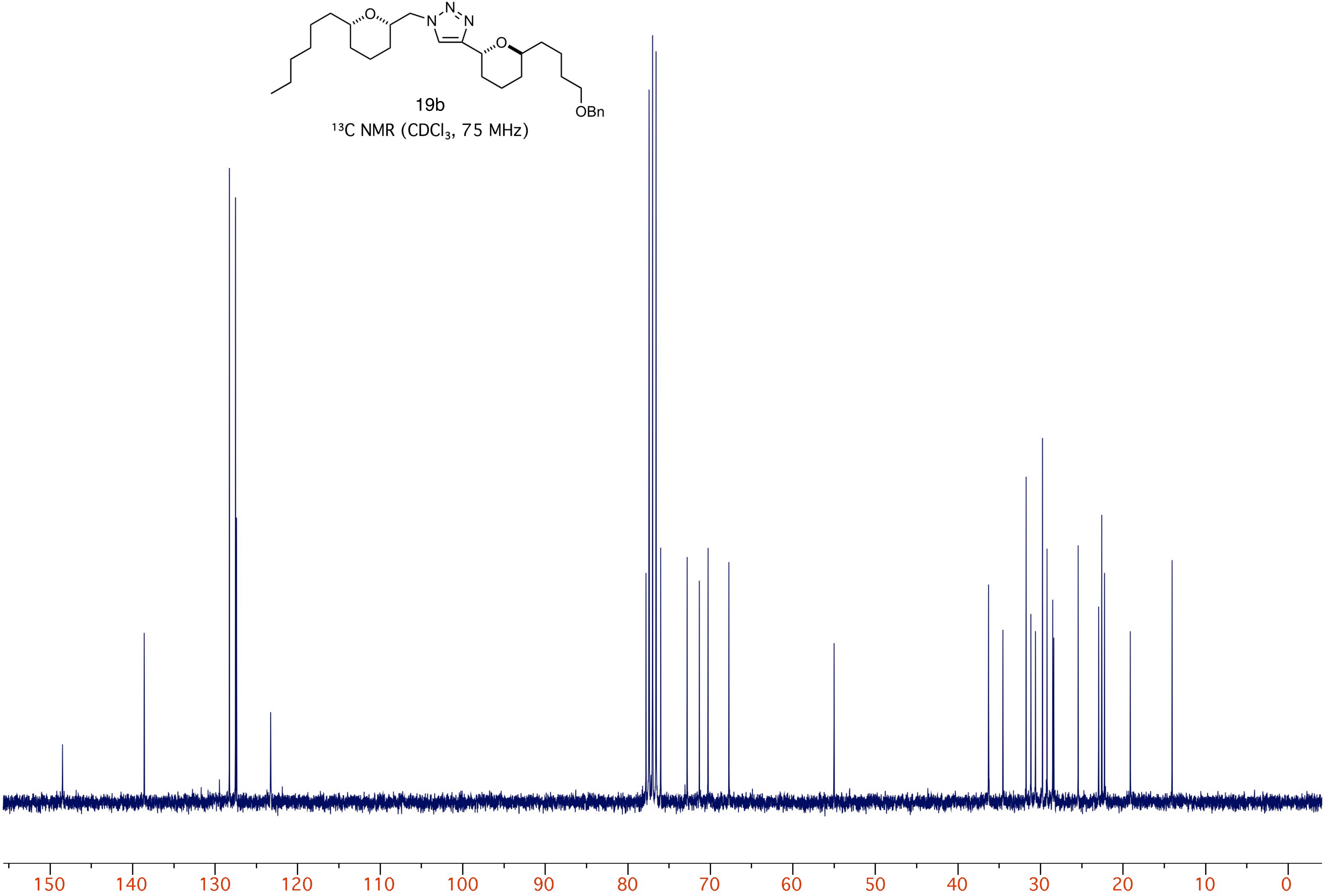


19a

^{13}C NMR (CDCl$_3$, 125 MHz)

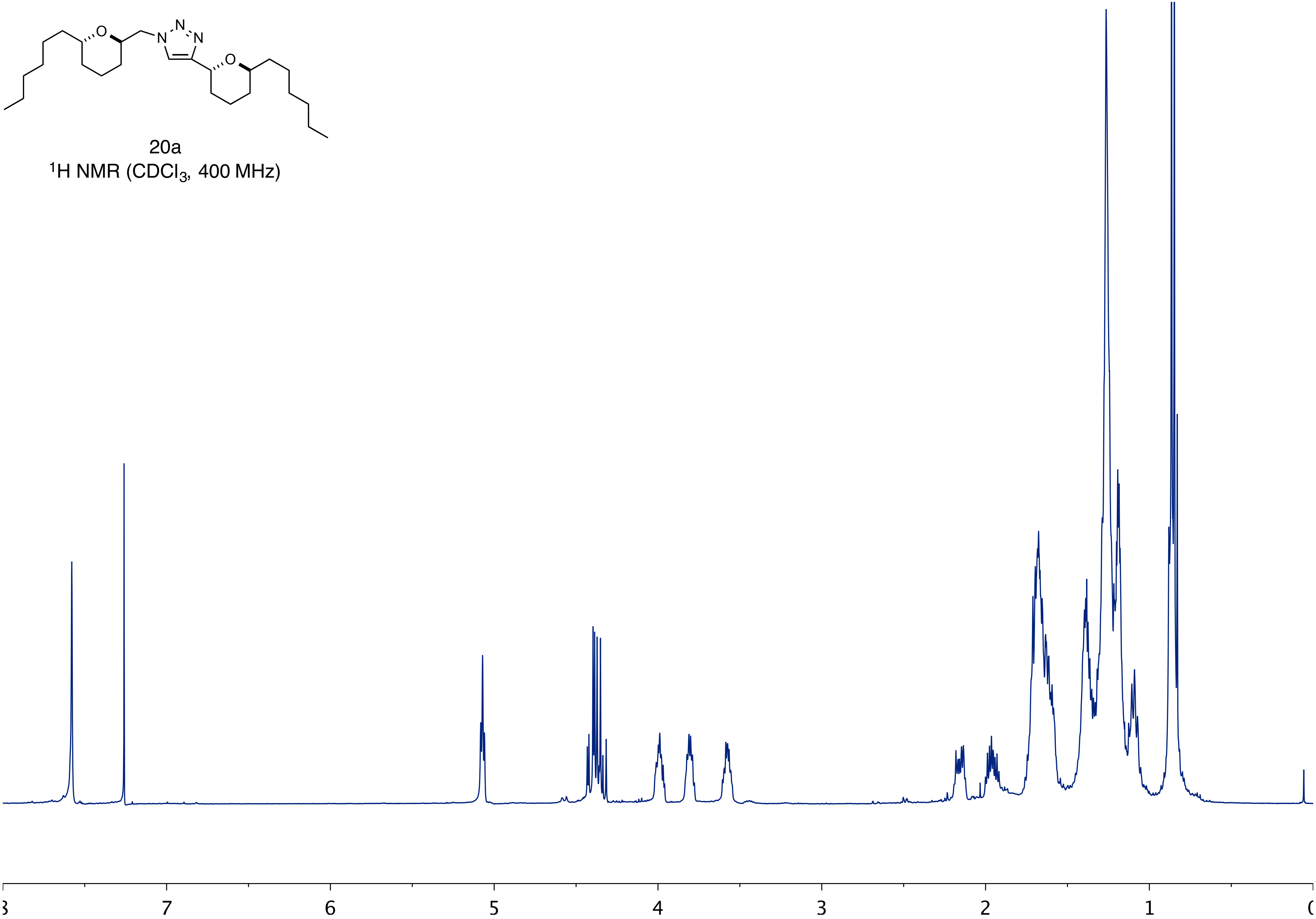

19b

^{1}H NMR (CDCl$_3$, 300 MHz)



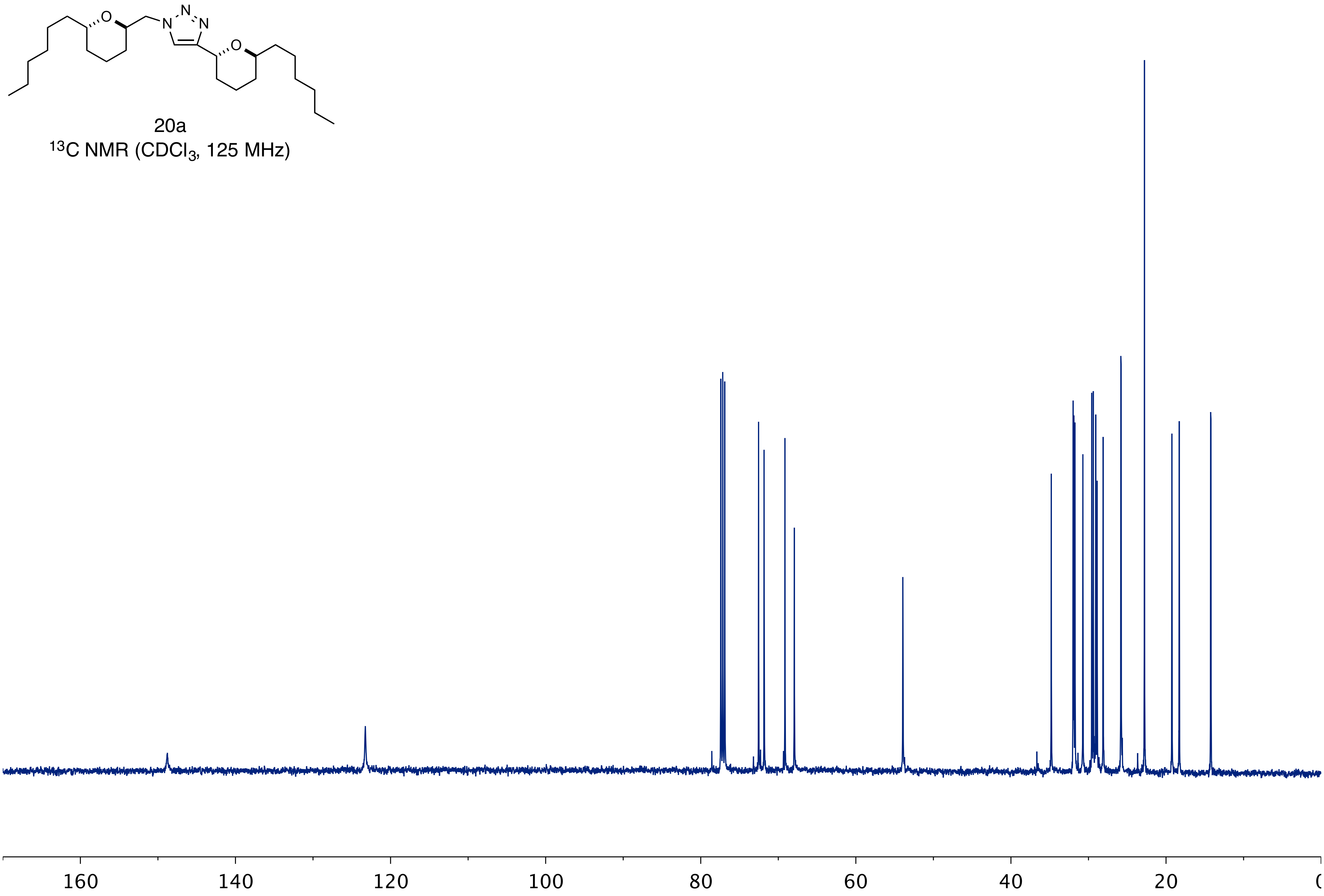
19b

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



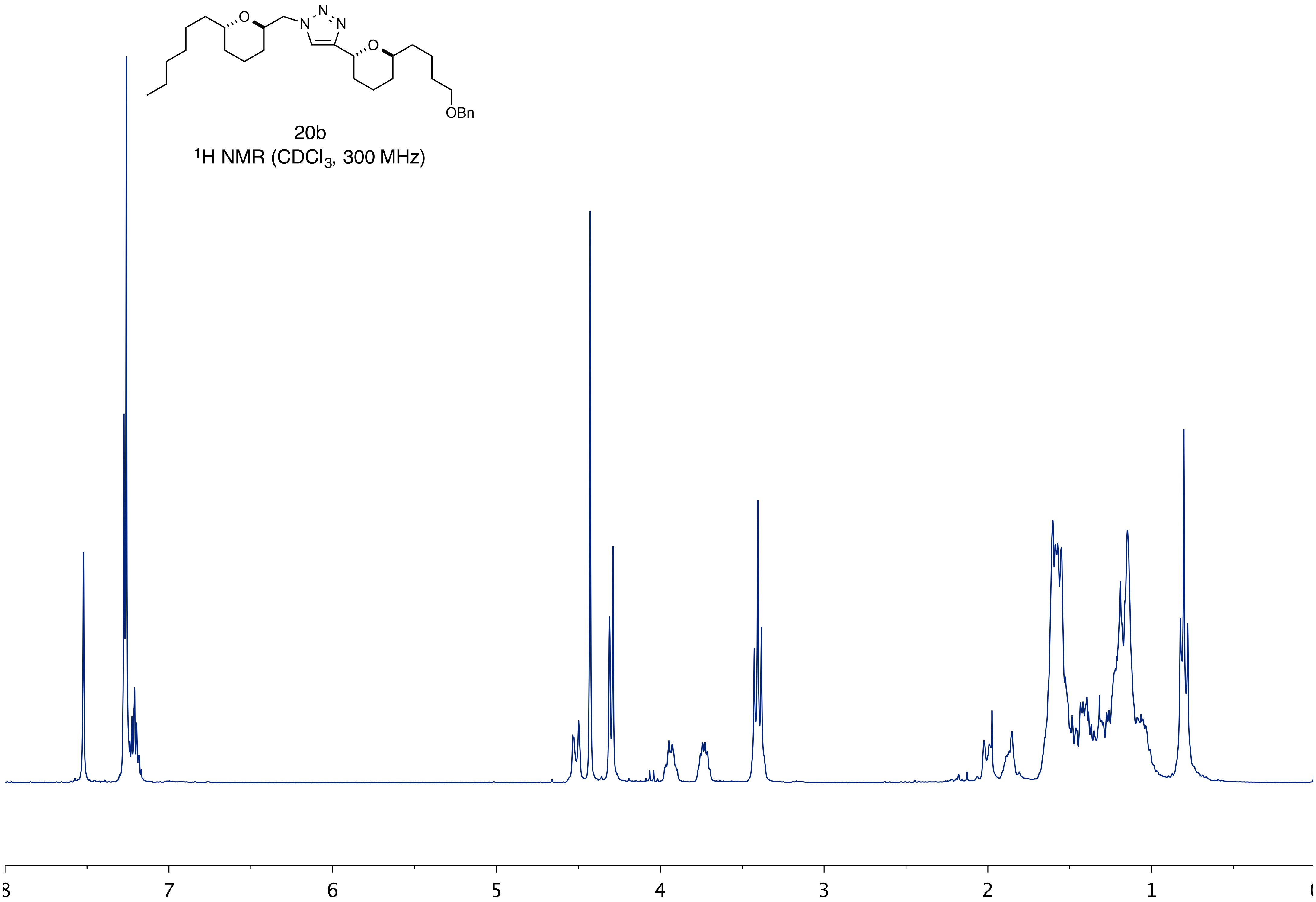
20a

^{1}H NMR (CDCl$_3$, 400 MHz)



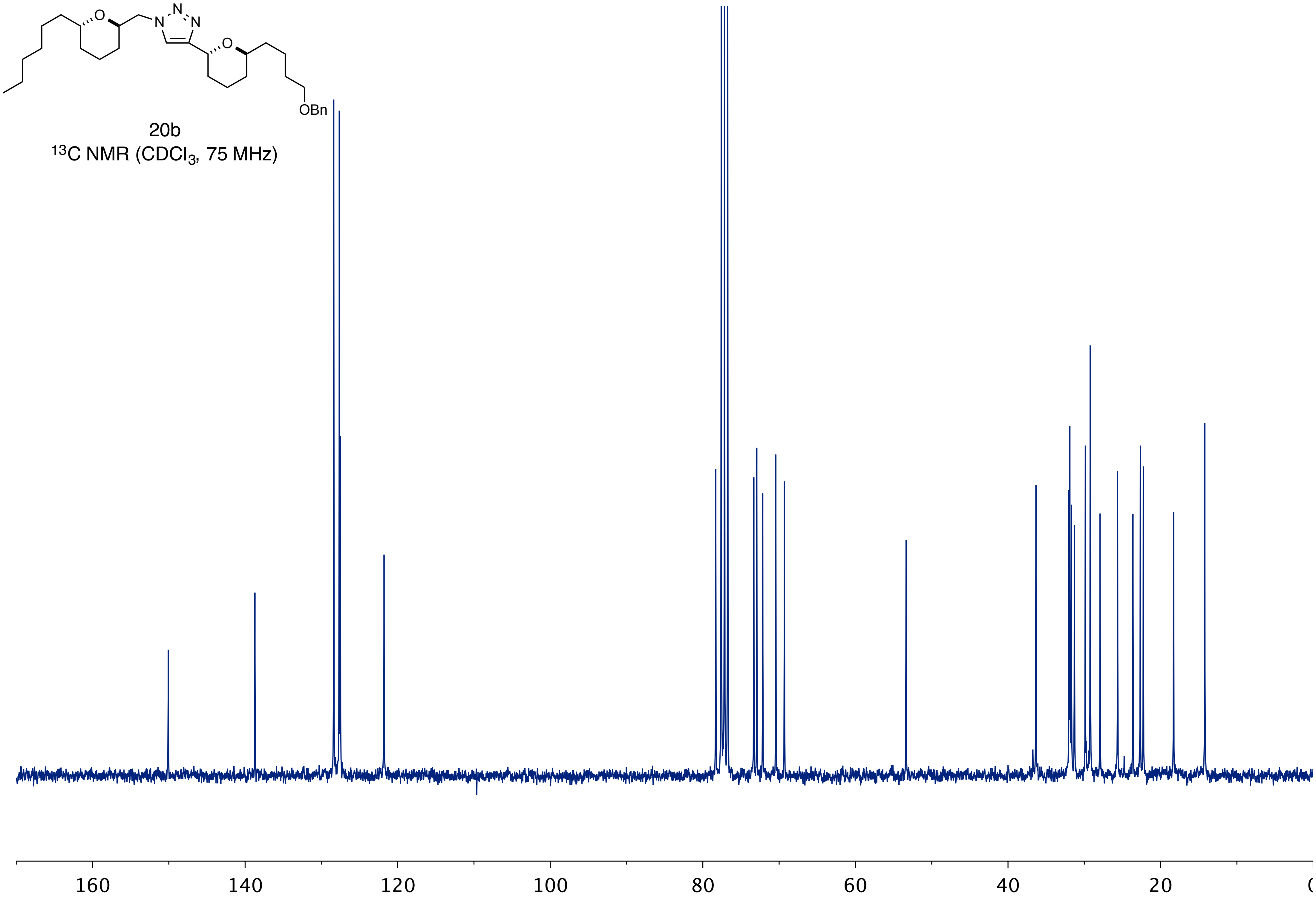
20a

^{13}C NMR ($CDCl_3$, 125 MHz)



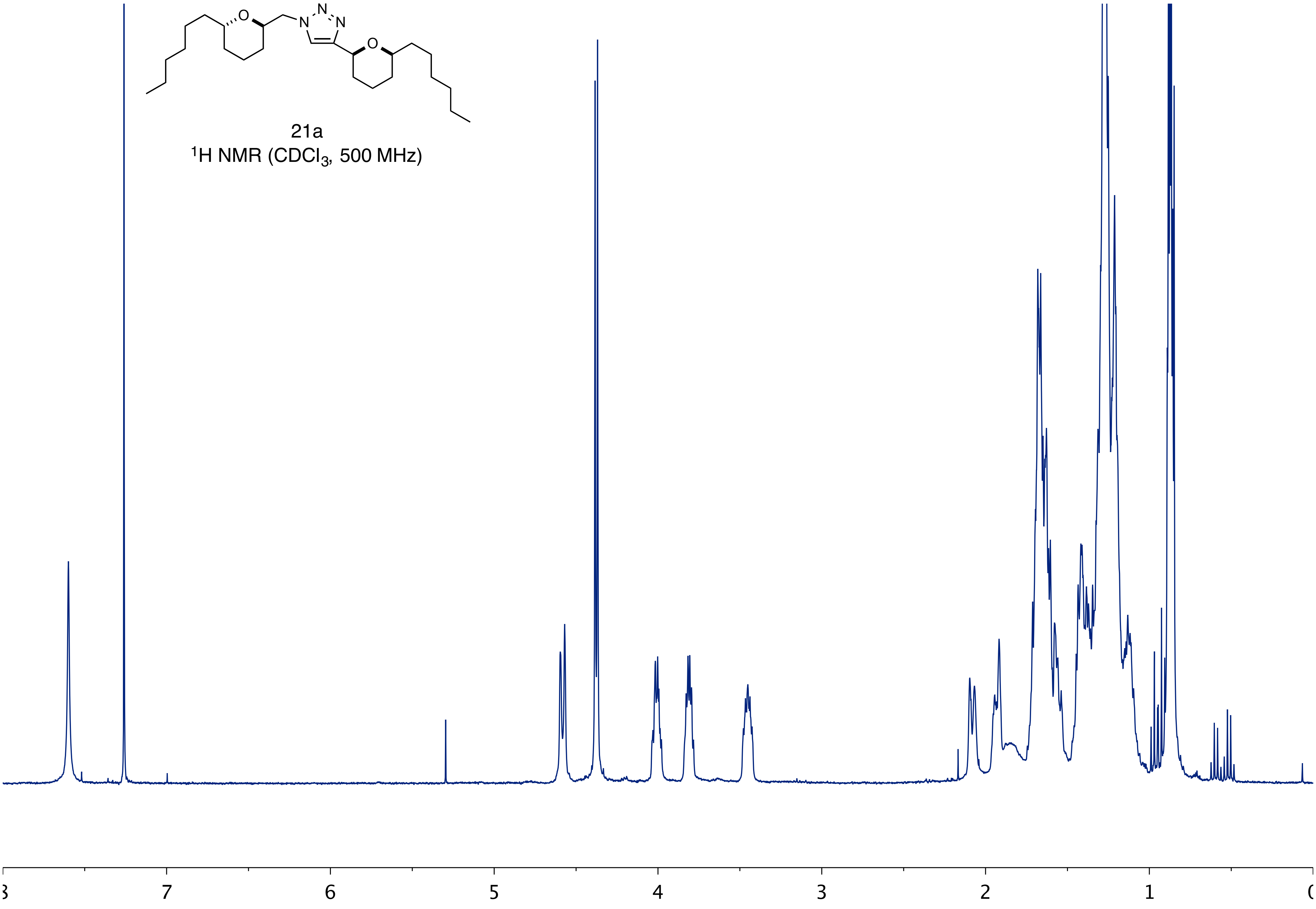
20b

^{1}H NMR (CDCl$_3$, 300 MHz)



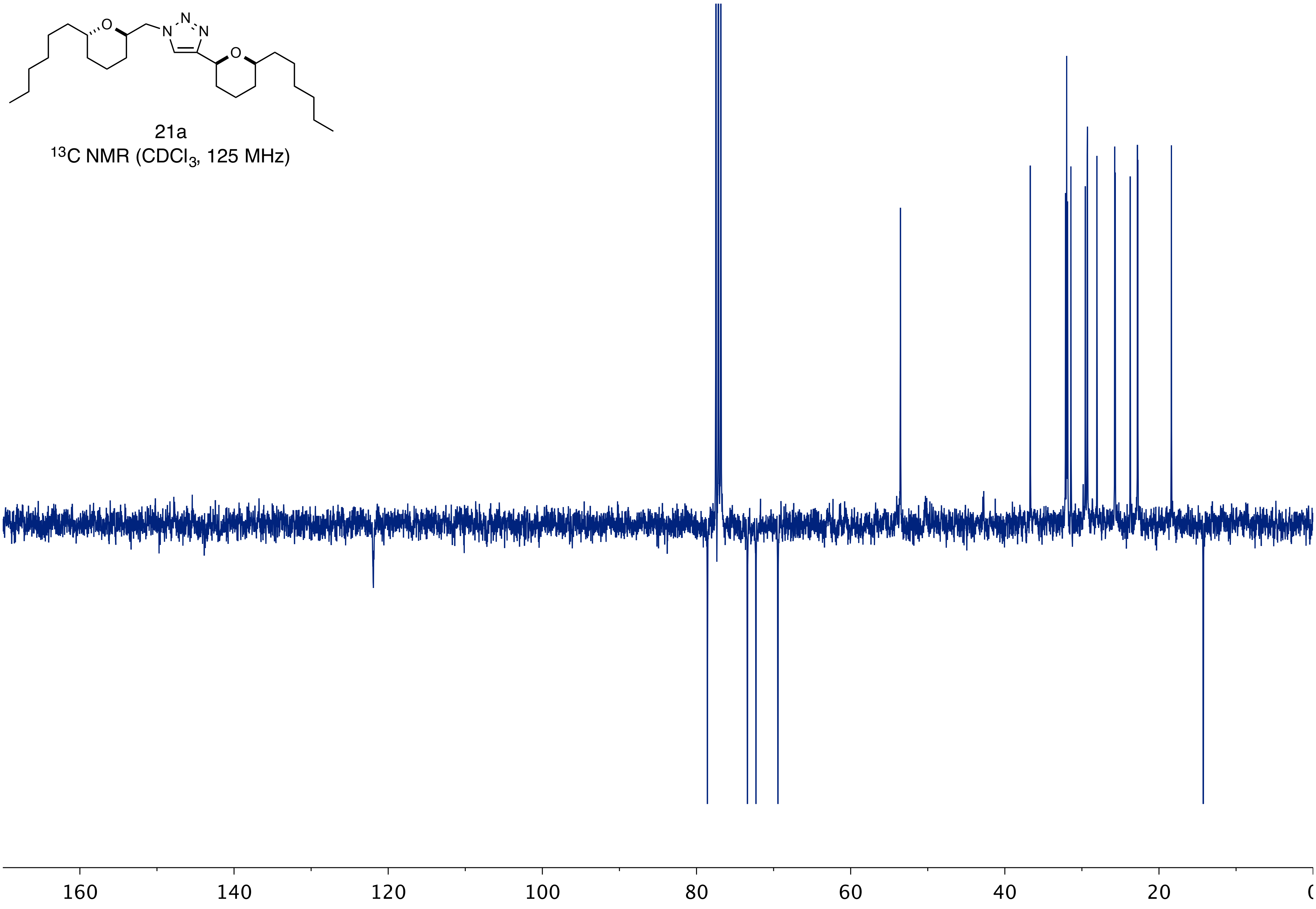
20b

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



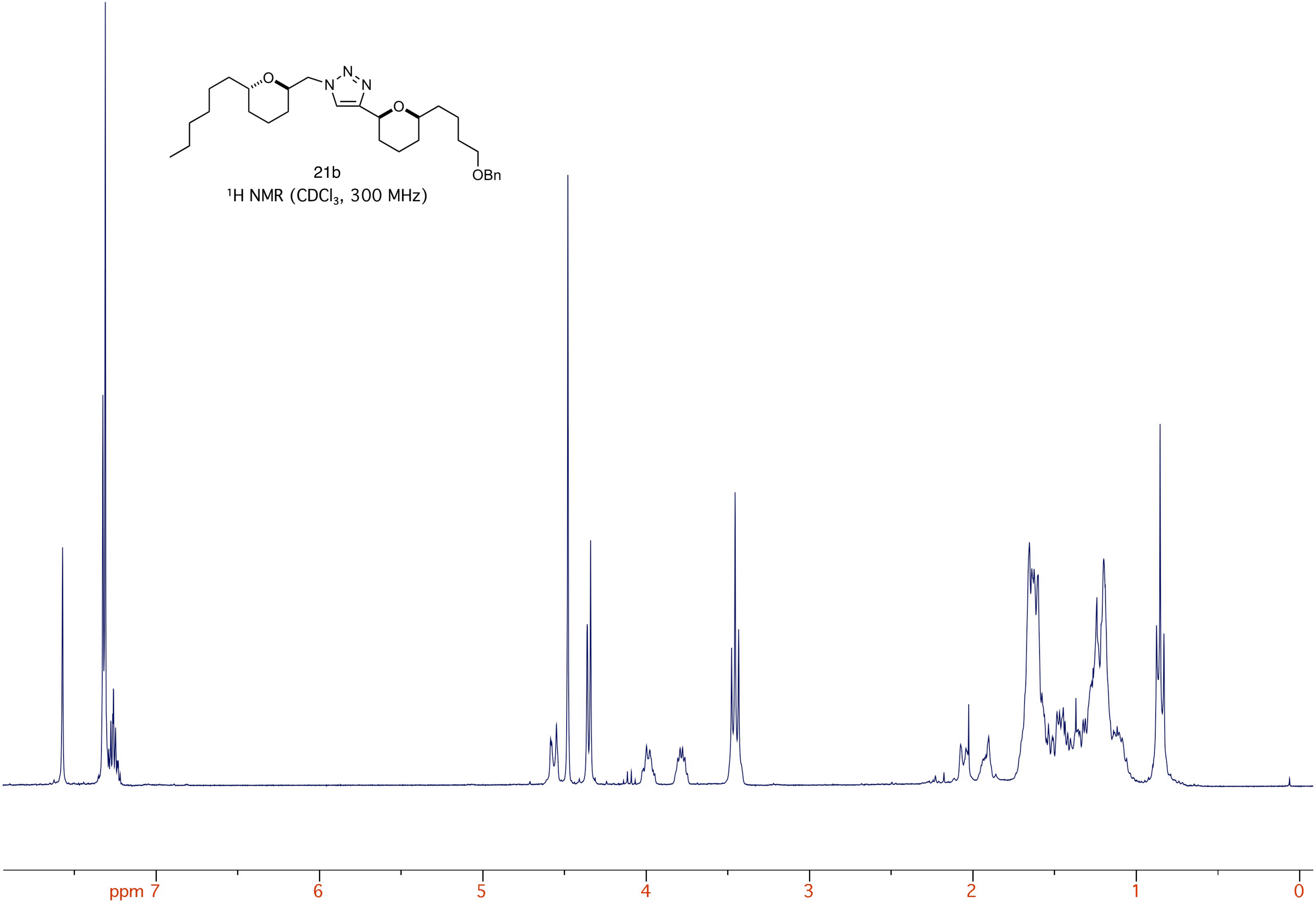
21a

^{1}H NMR (CDCl$_3$, 500 MHz)



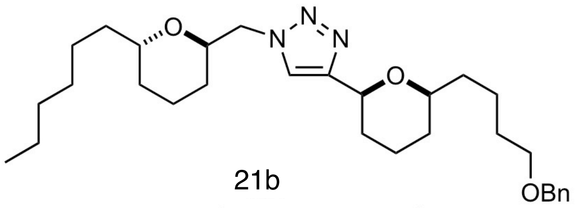
21a

^{13}C NMR ($CDCl_3$, 125 MHz)



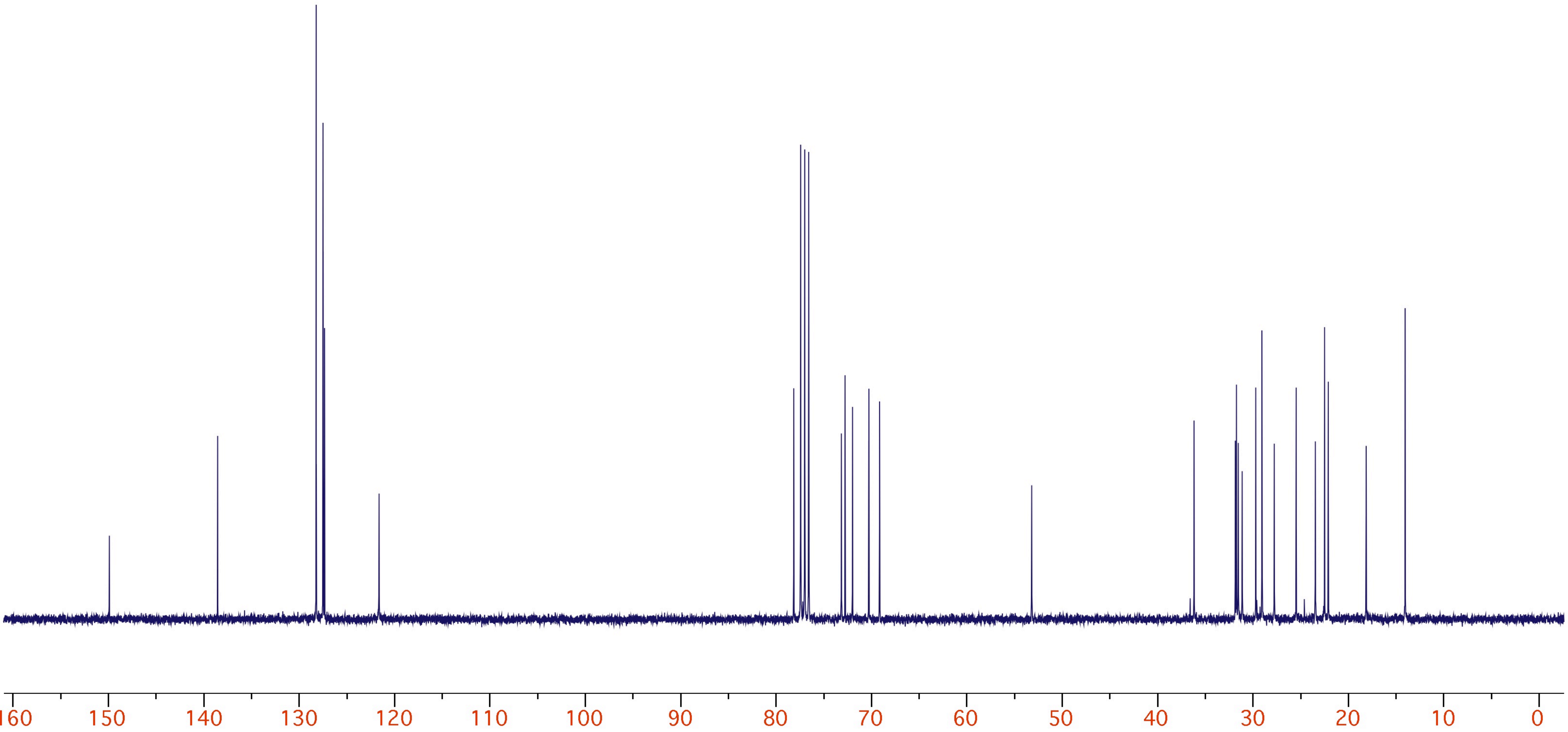
21b

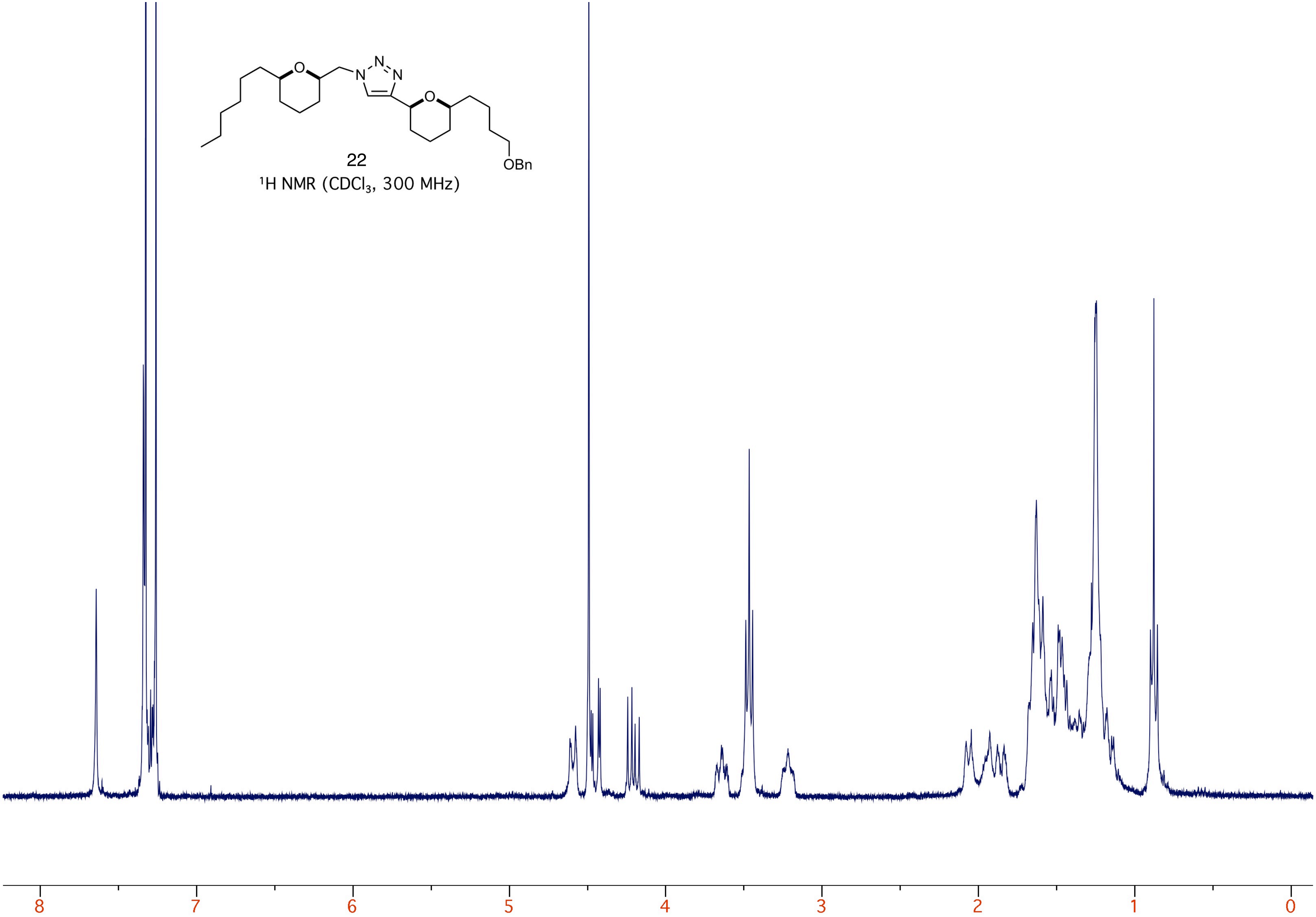
^{1}H NMR (CDCl$_3$, 300 MHz)



21b

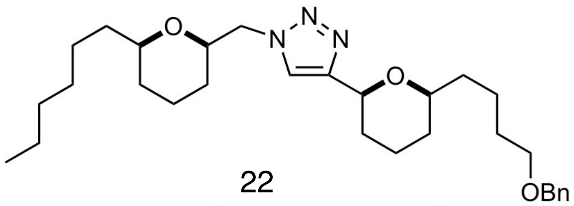
^{13}C NMR (CDCl$_3$, 75 MHz)





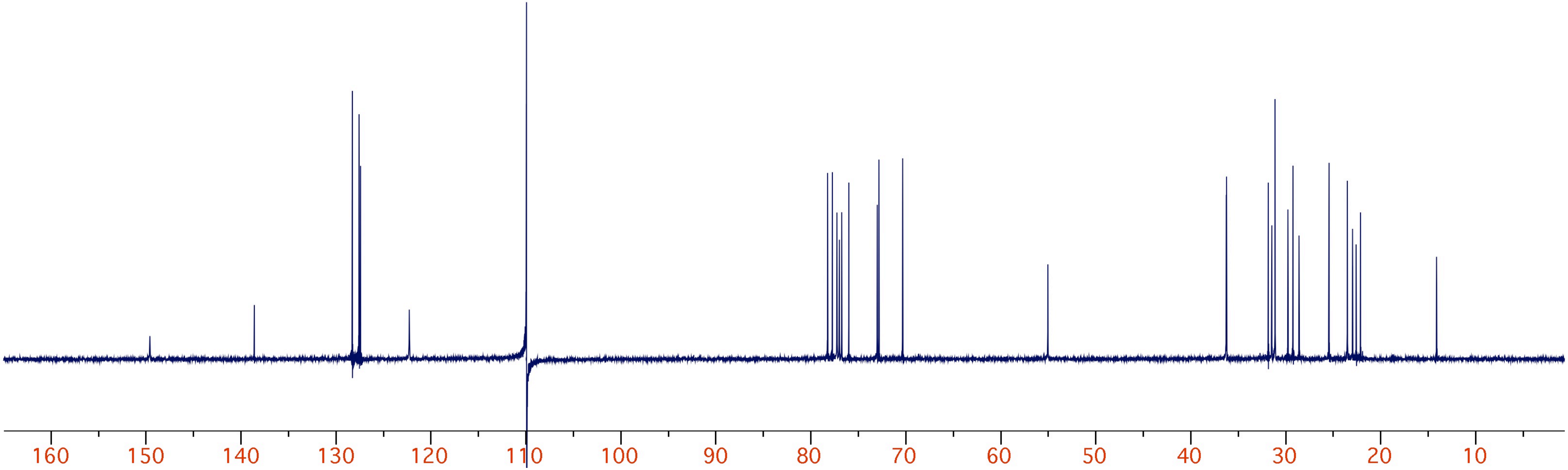
22

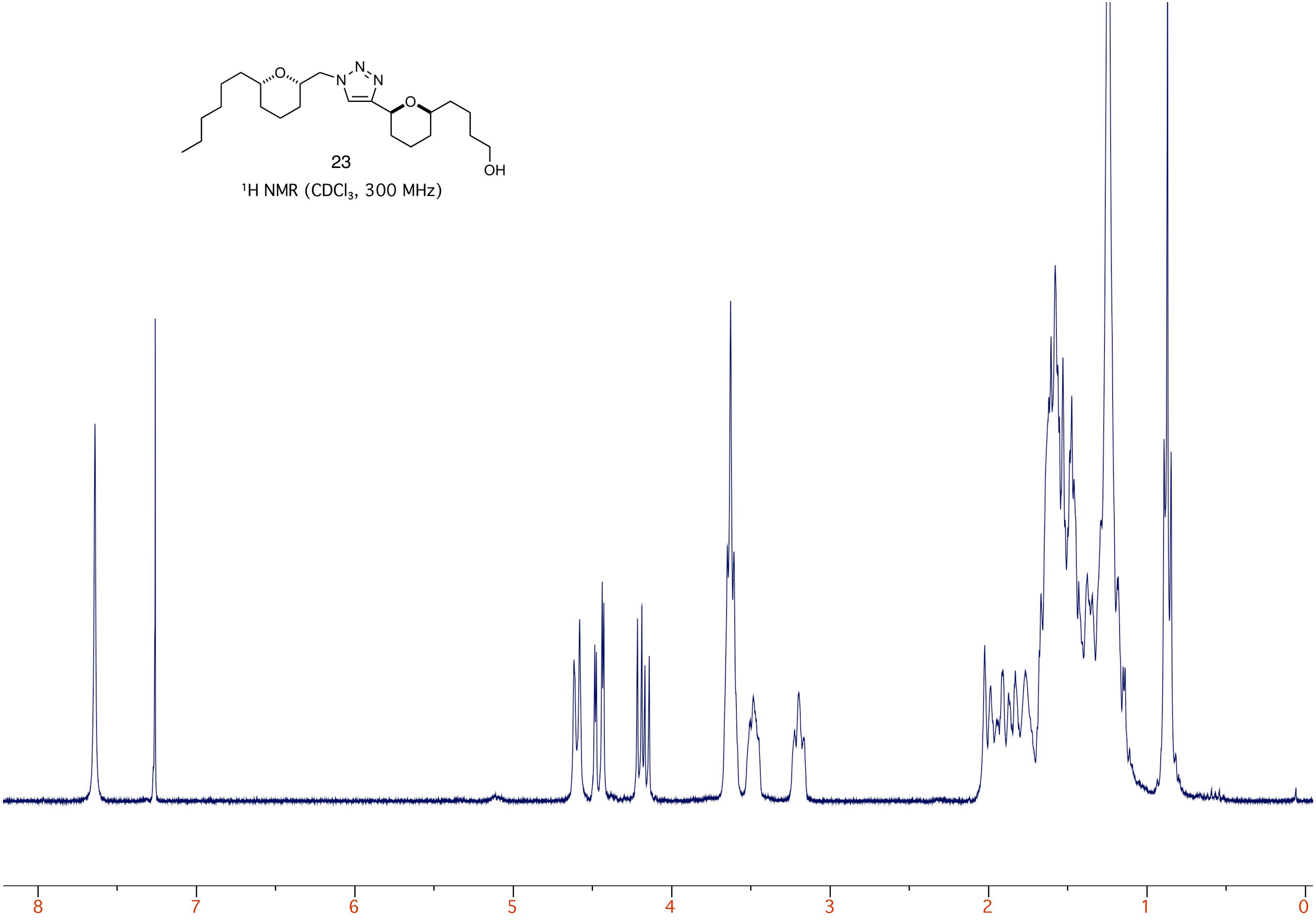
^{1}H NMR (CDCl$_3$, 300 MHz)



22

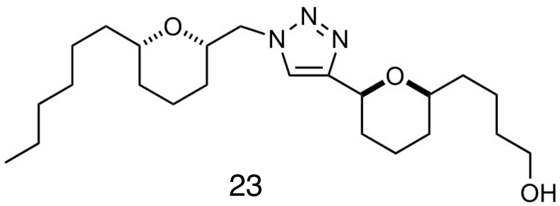
^{13}C NMR (CDCl$_3$, 125 MHz)





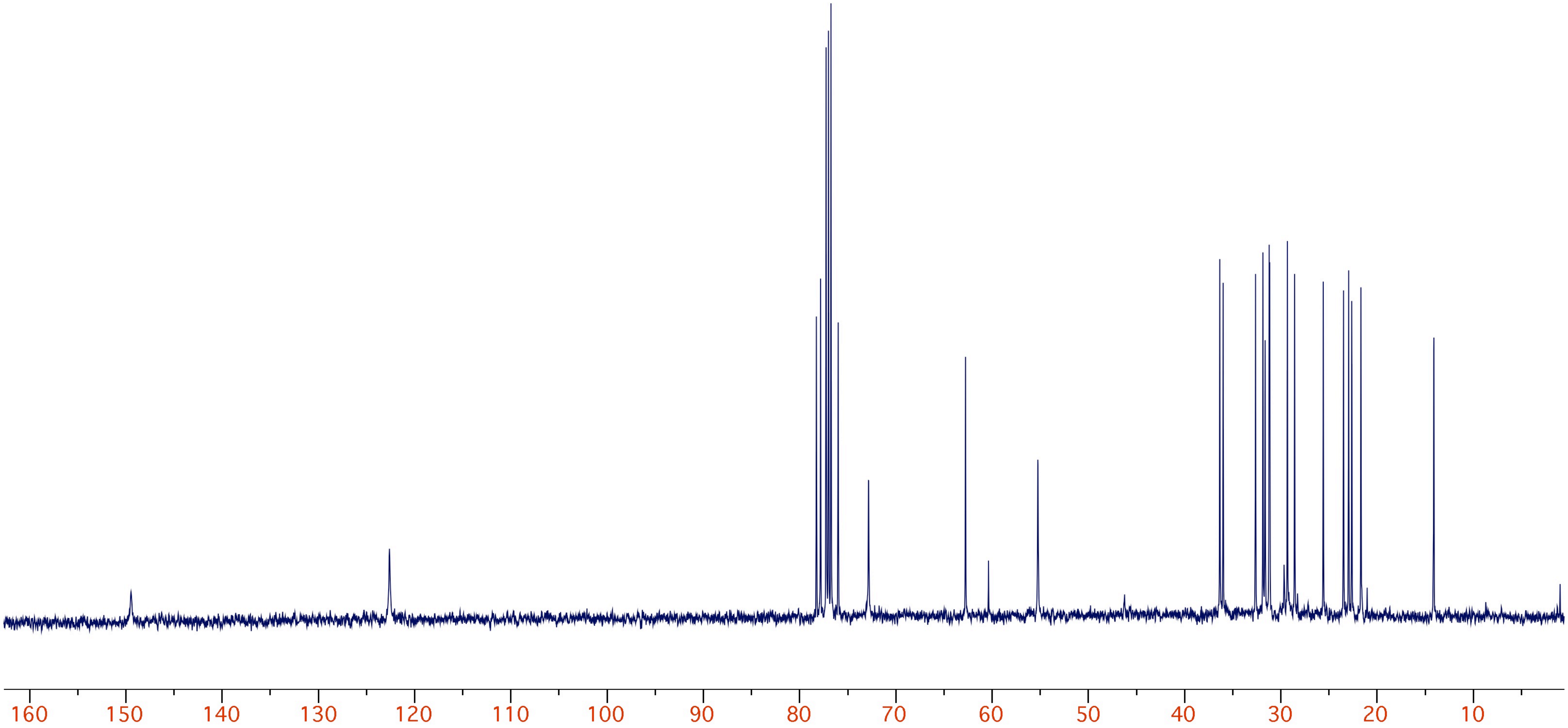
23

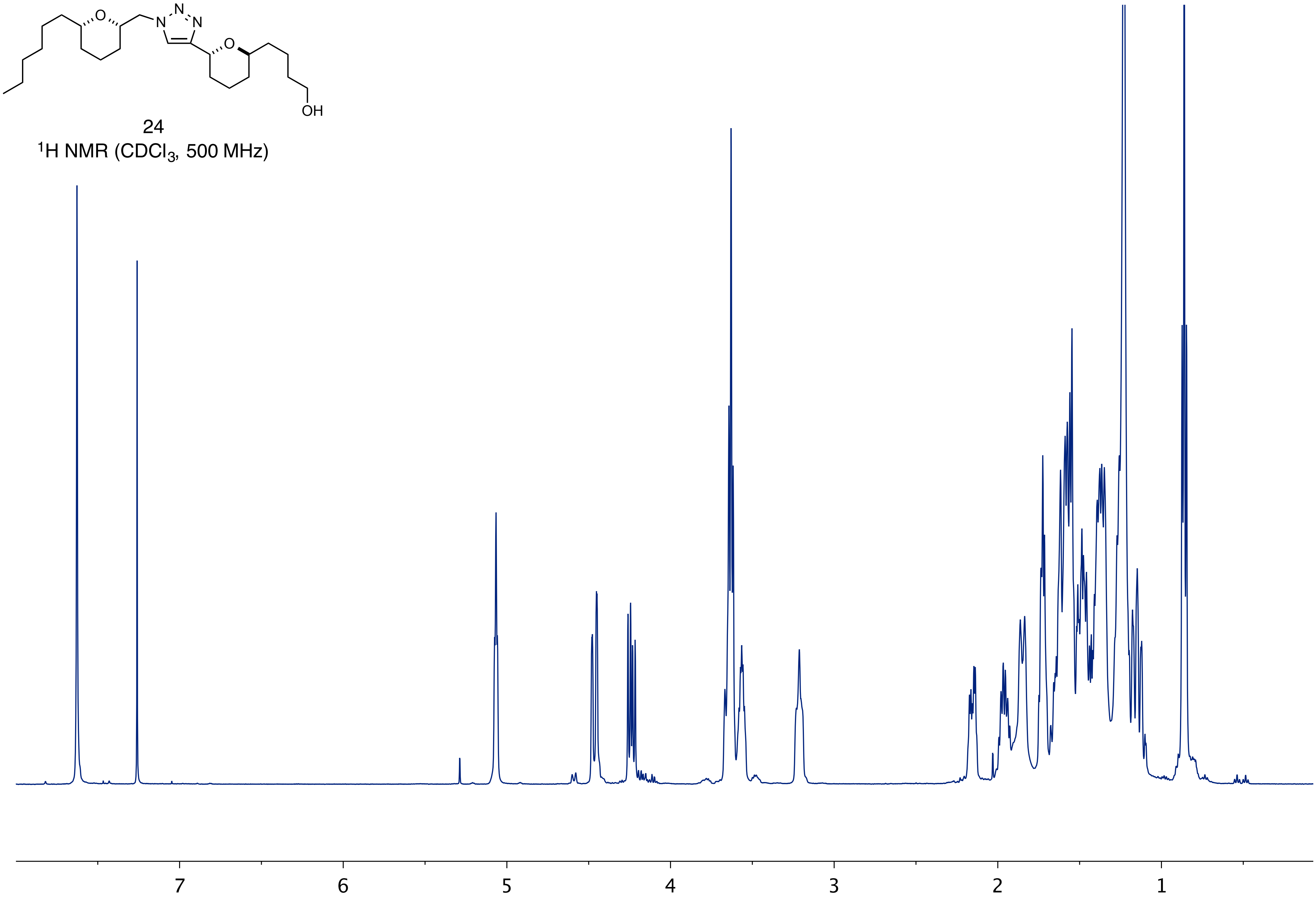
^1H NMR ($CDCl_3$, 300 MHz)



23

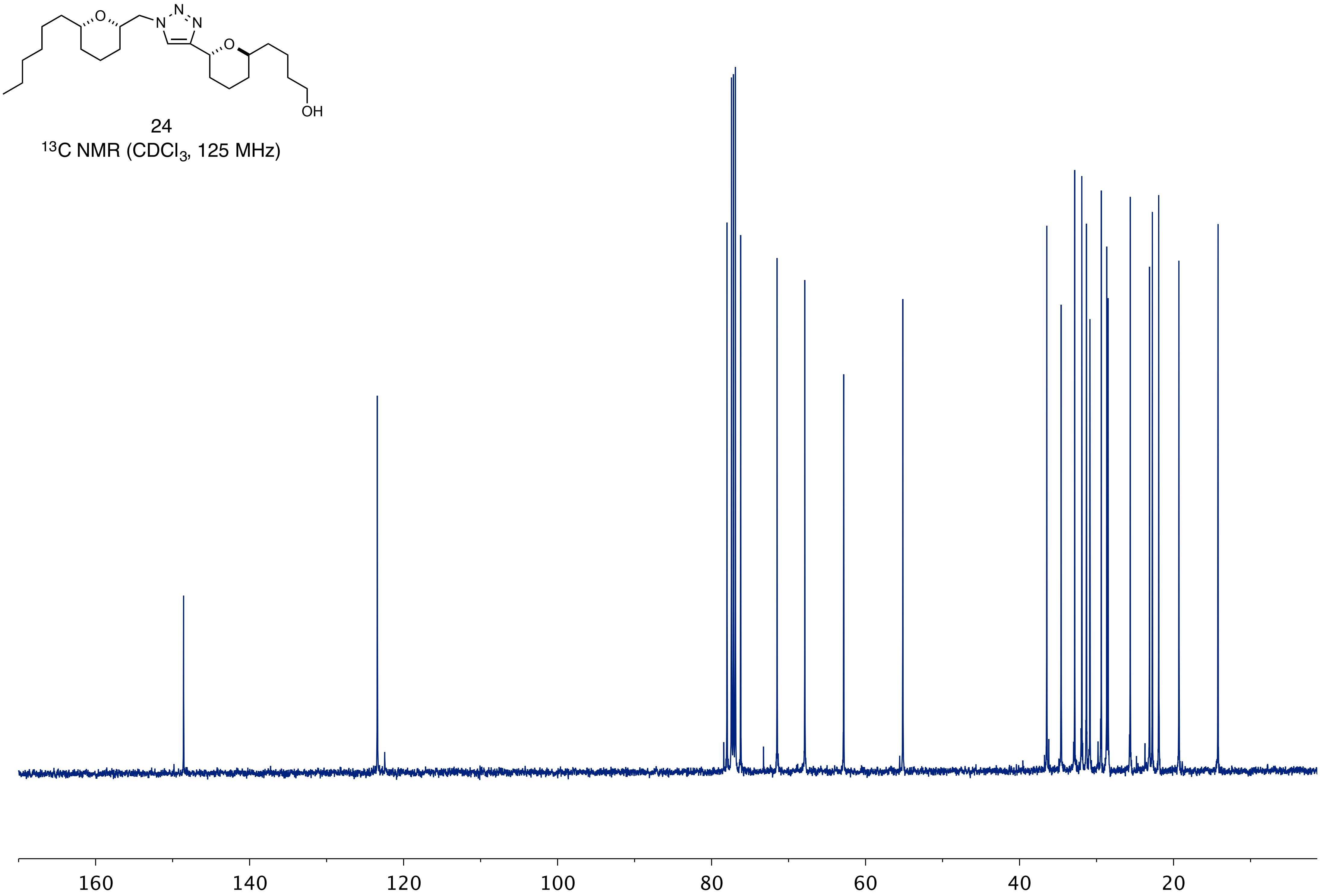
^{13}C NMR ($CDCl_3$, 125 MHz)





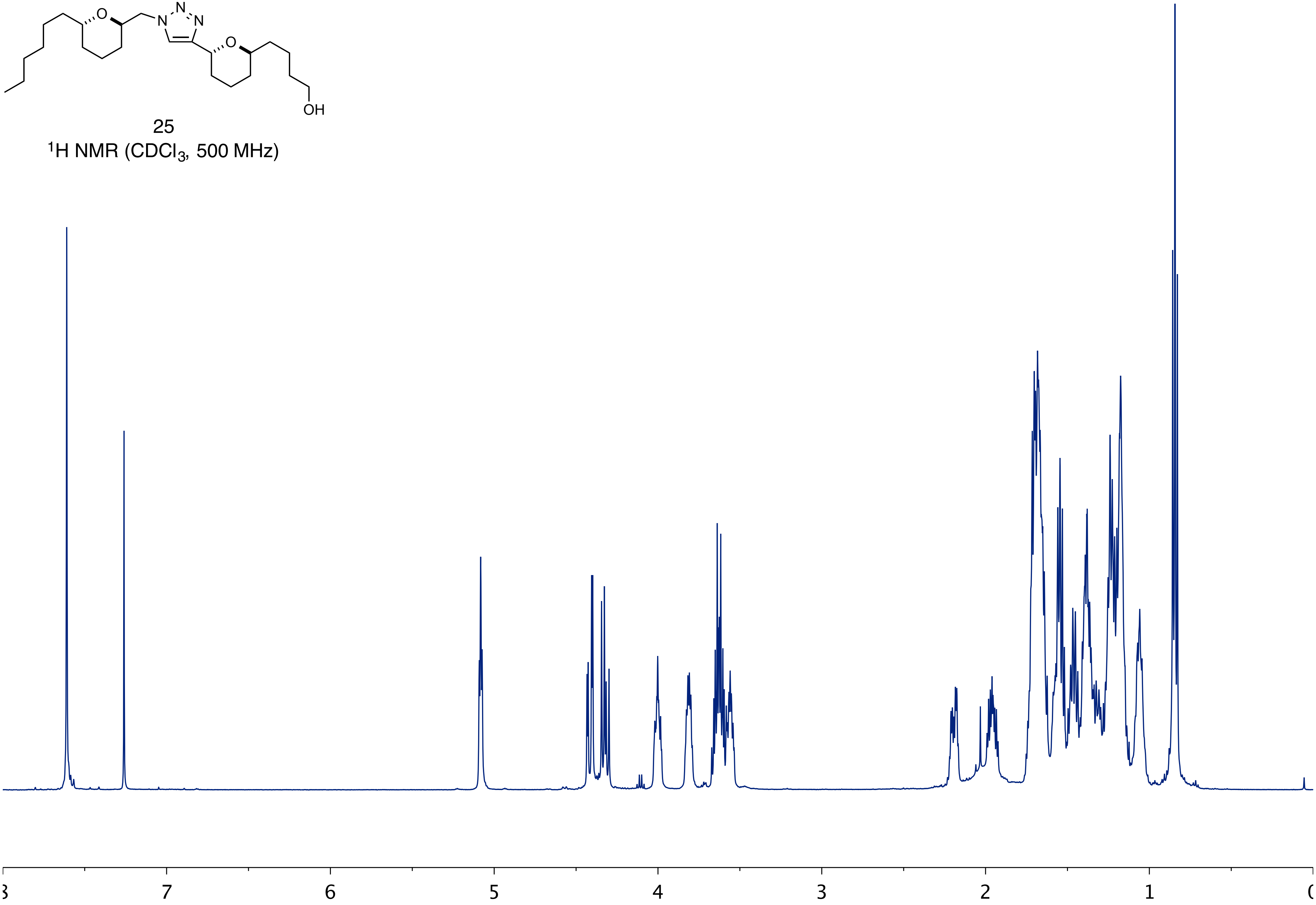
24

^1H NMR ($CDCl_3$, 500 MHz)



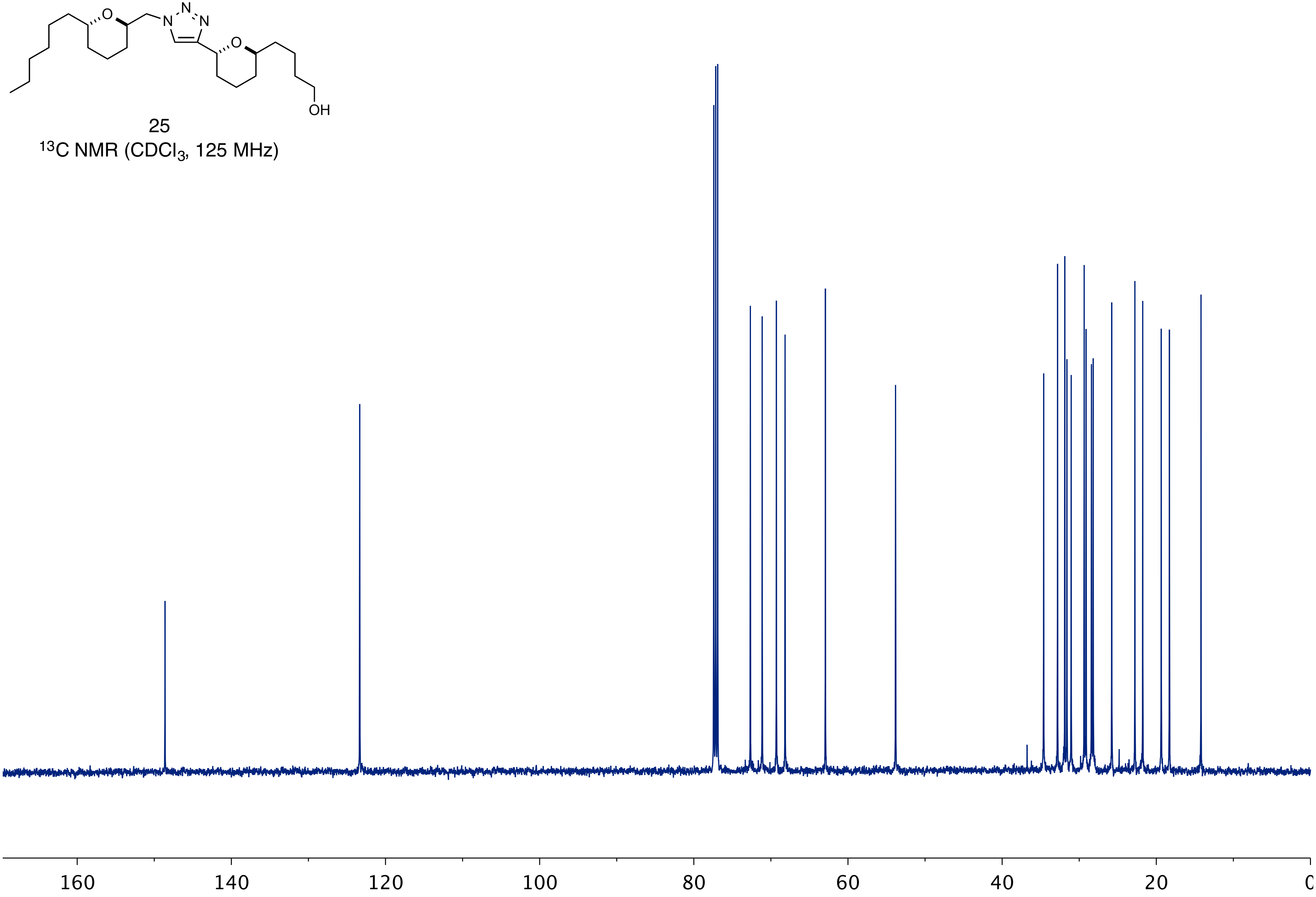
24

^{13}C NMR (CDCl$_3$, 125 MHz)



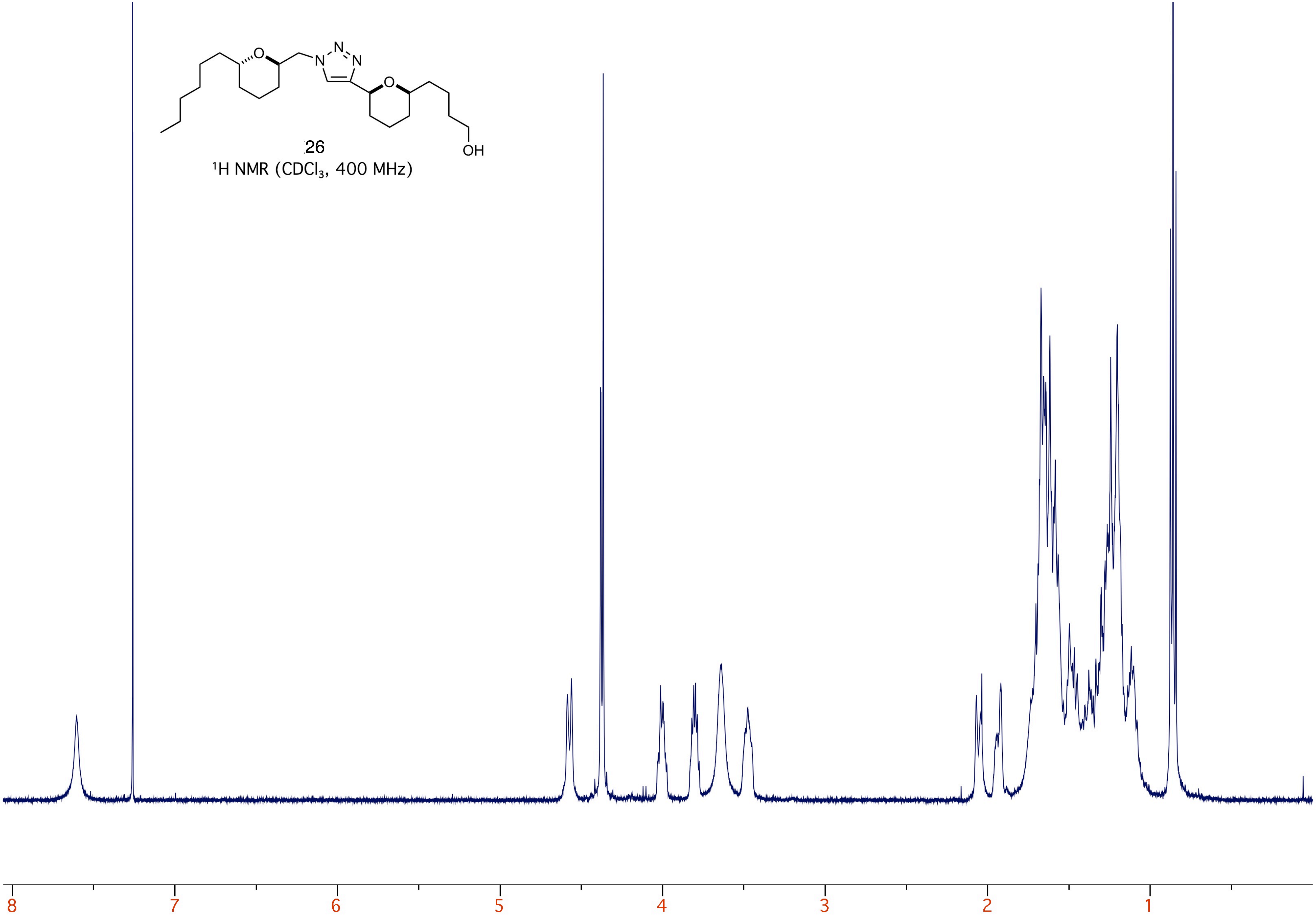
25

^{1}H NMR (CDCl$_3$, 500 MHz)



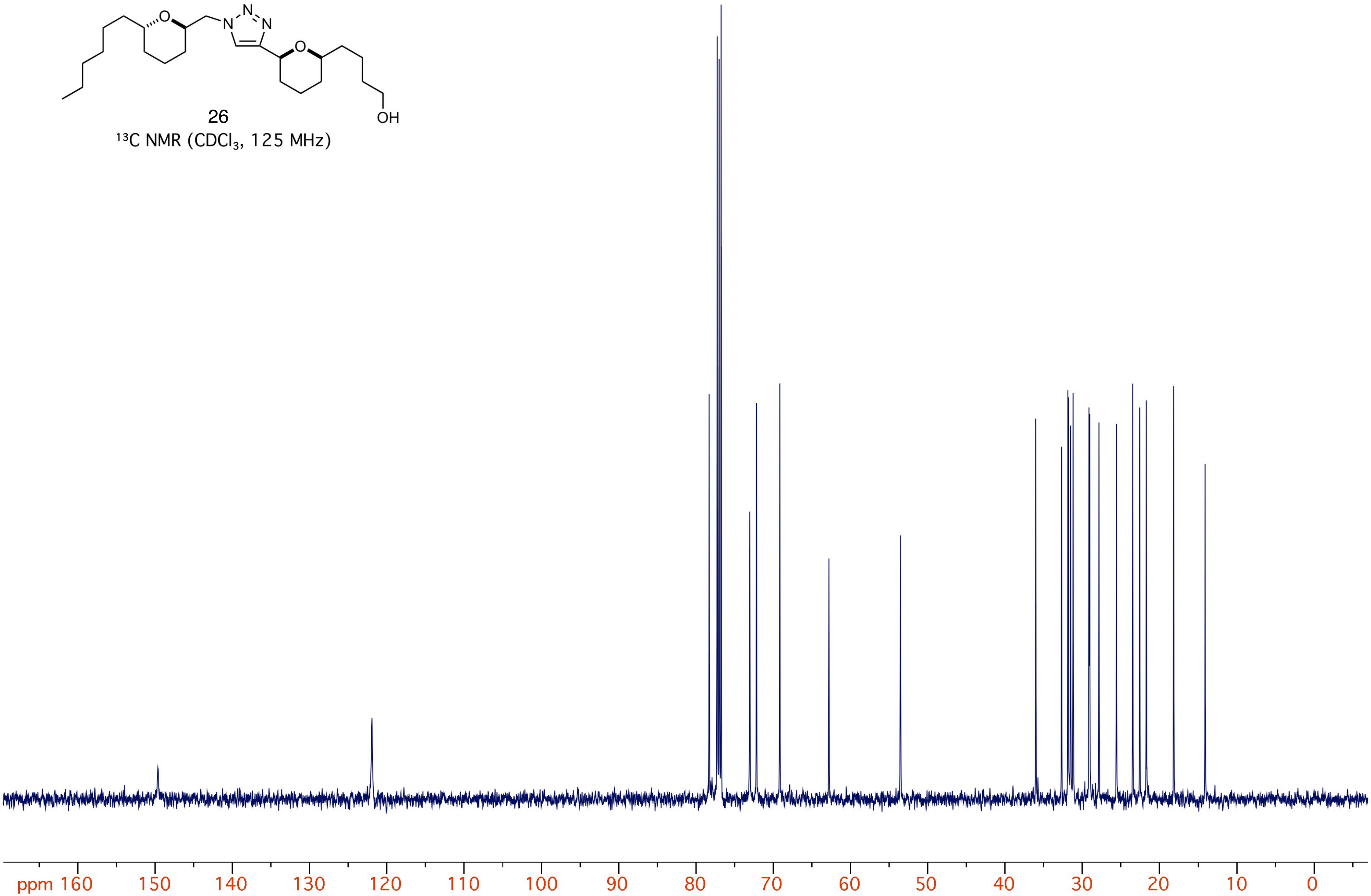
25

^{13}C NMR ($CDCl_3$, 125 MHz)

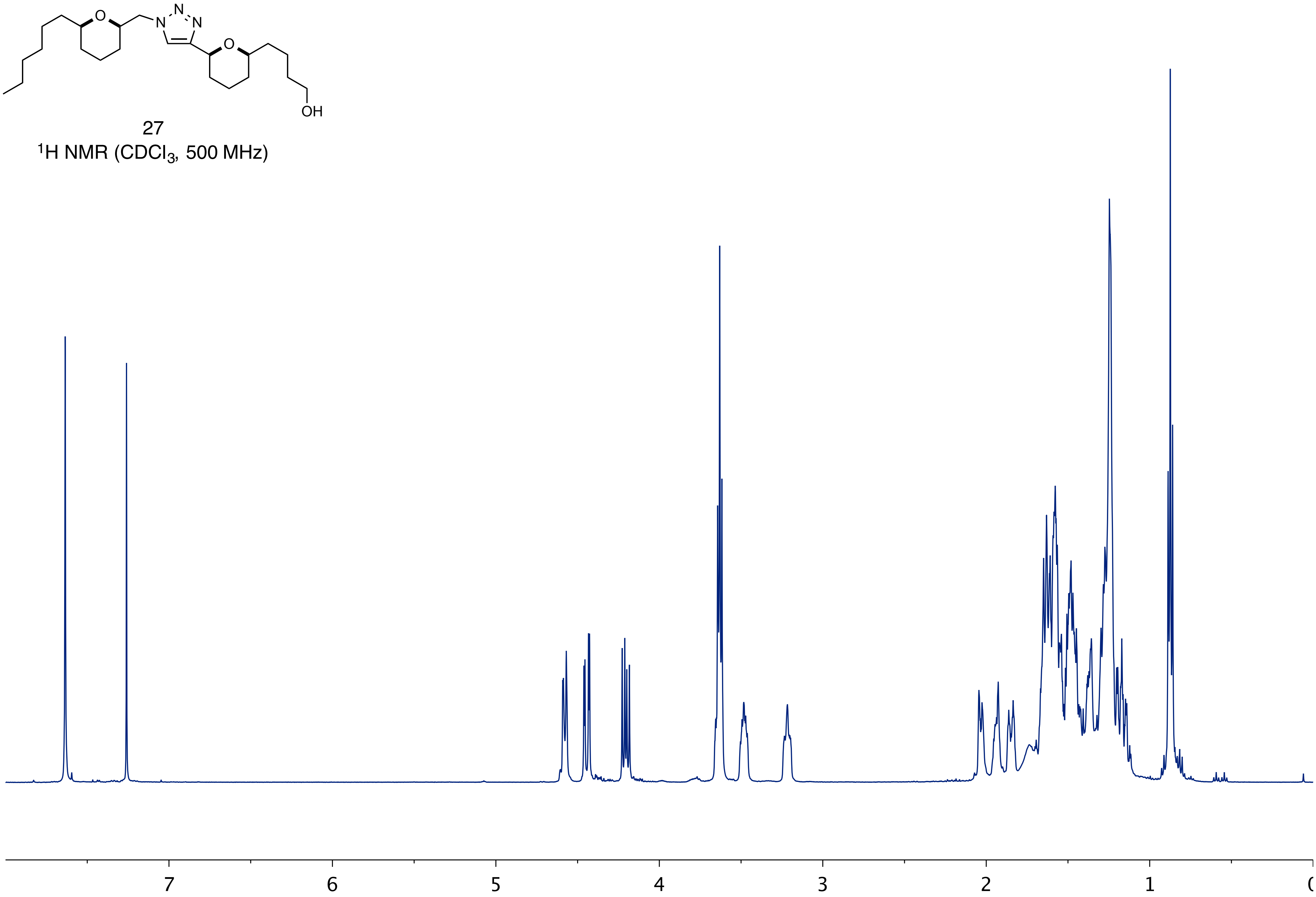


26

^{1}H NMR (CDCl$_3$, 400 MHz)

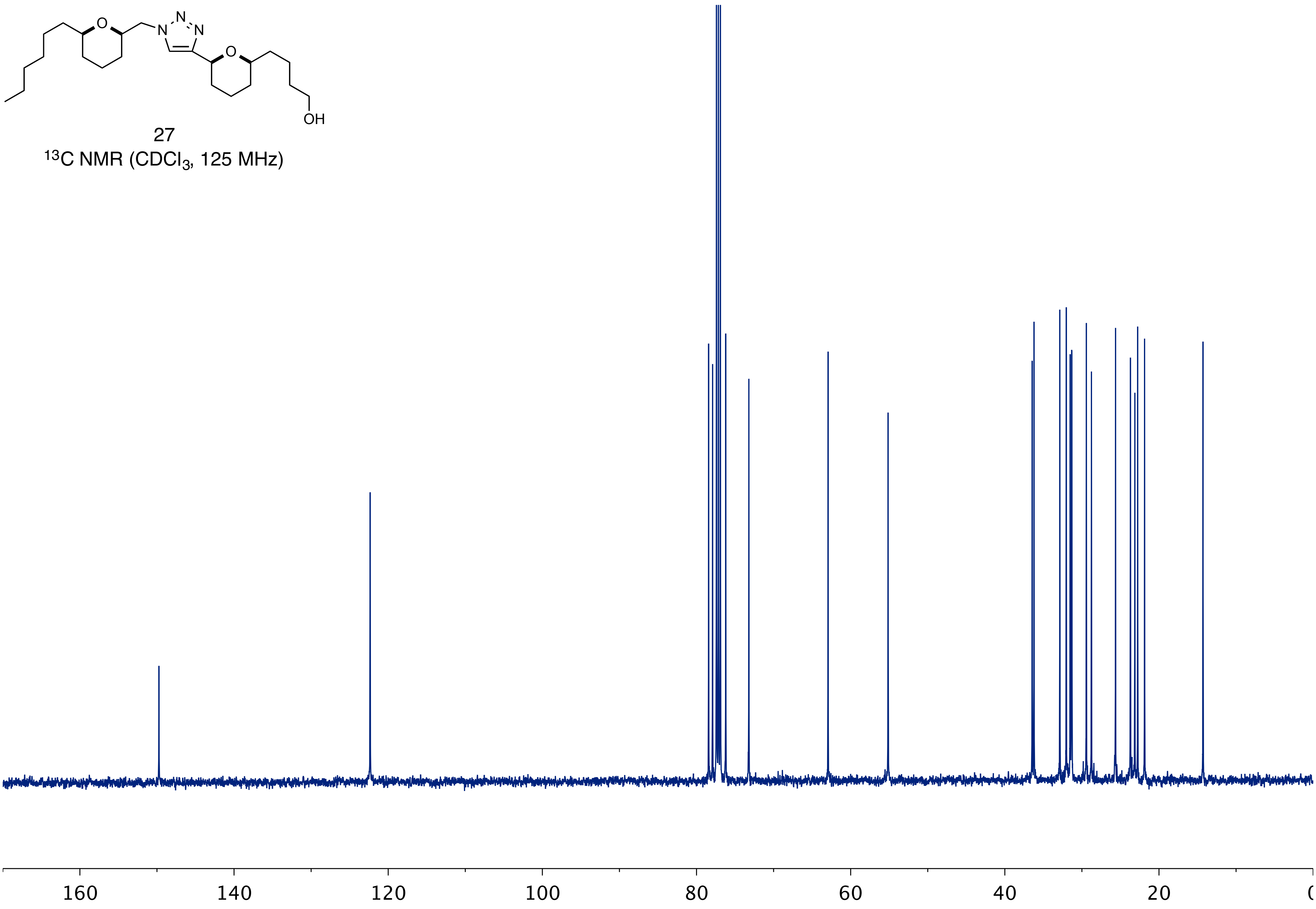

26

^{13}C NMR ($CDCl_3$, 125 MHz)



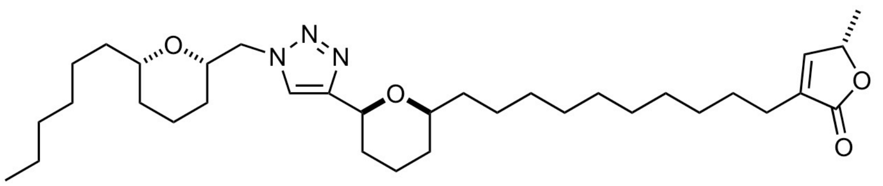
27

^{1}H NMR ($CDCl_3$, 500 MHz)



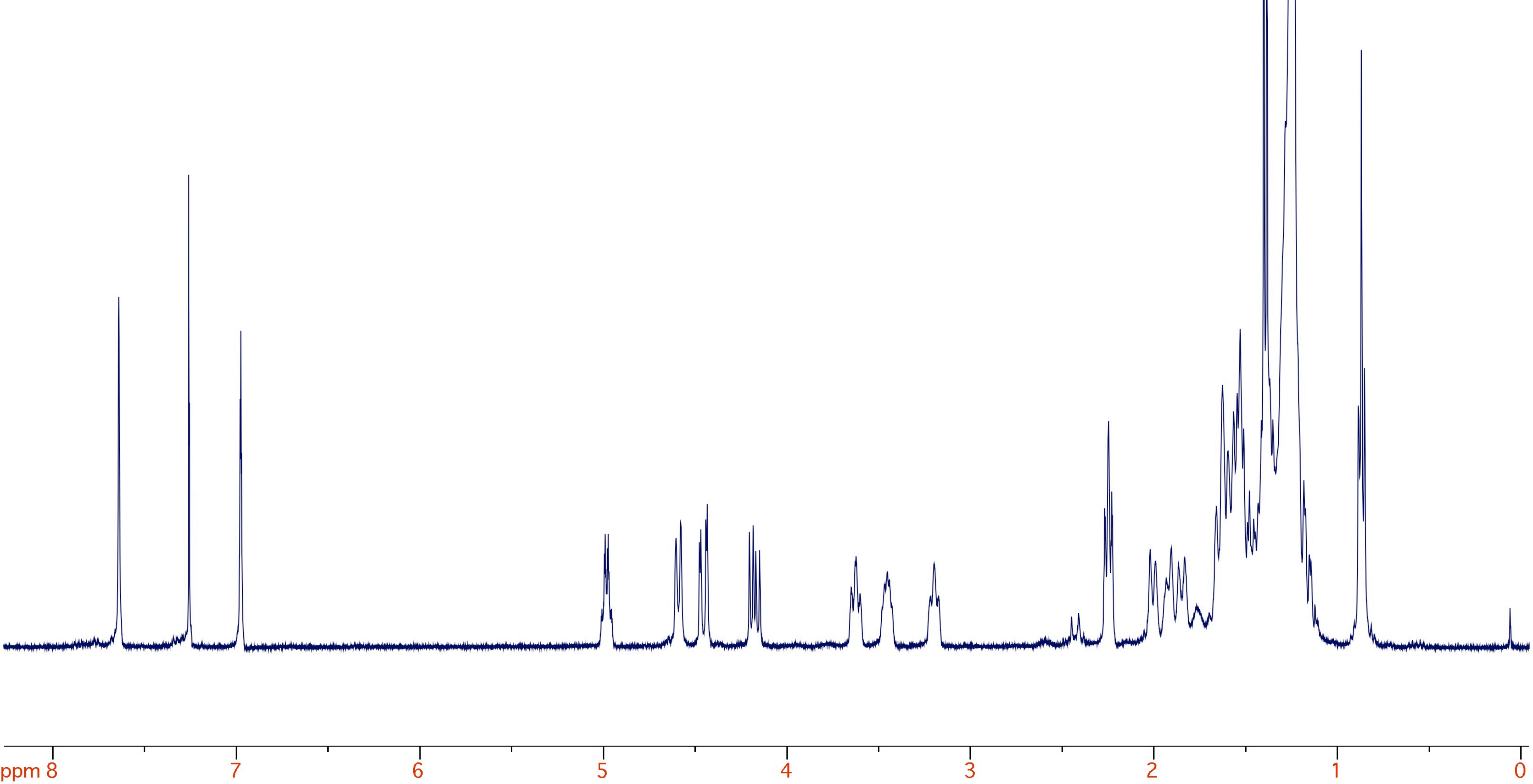
27

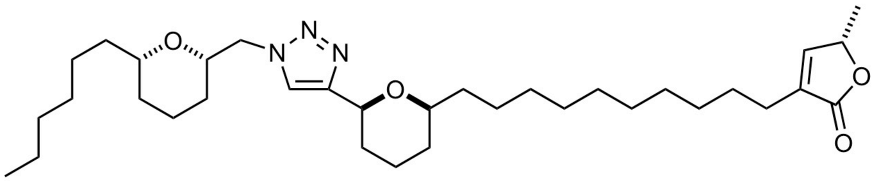
^{13}C NMR (CDCl$_3$, 125 MHz)



31

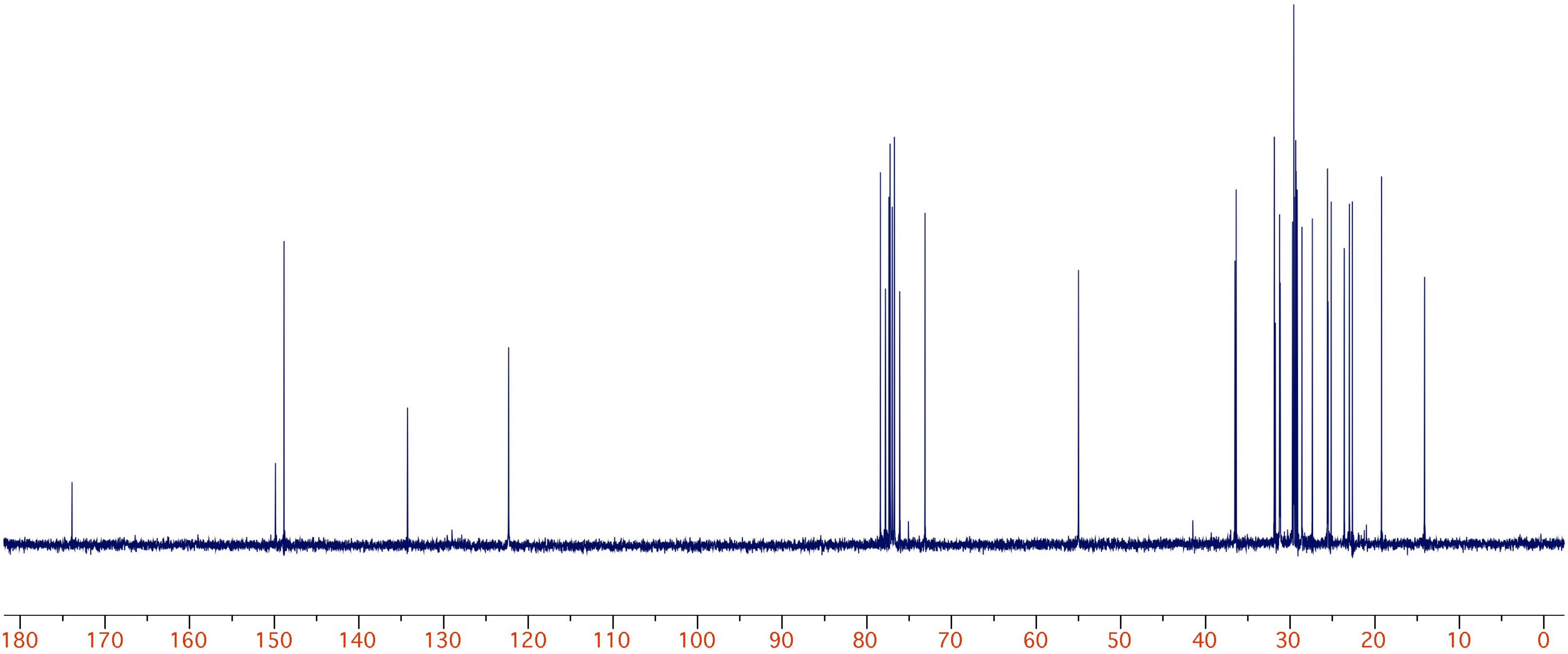
^{1}H NMR (CDCl$_3$, 400 MHz)

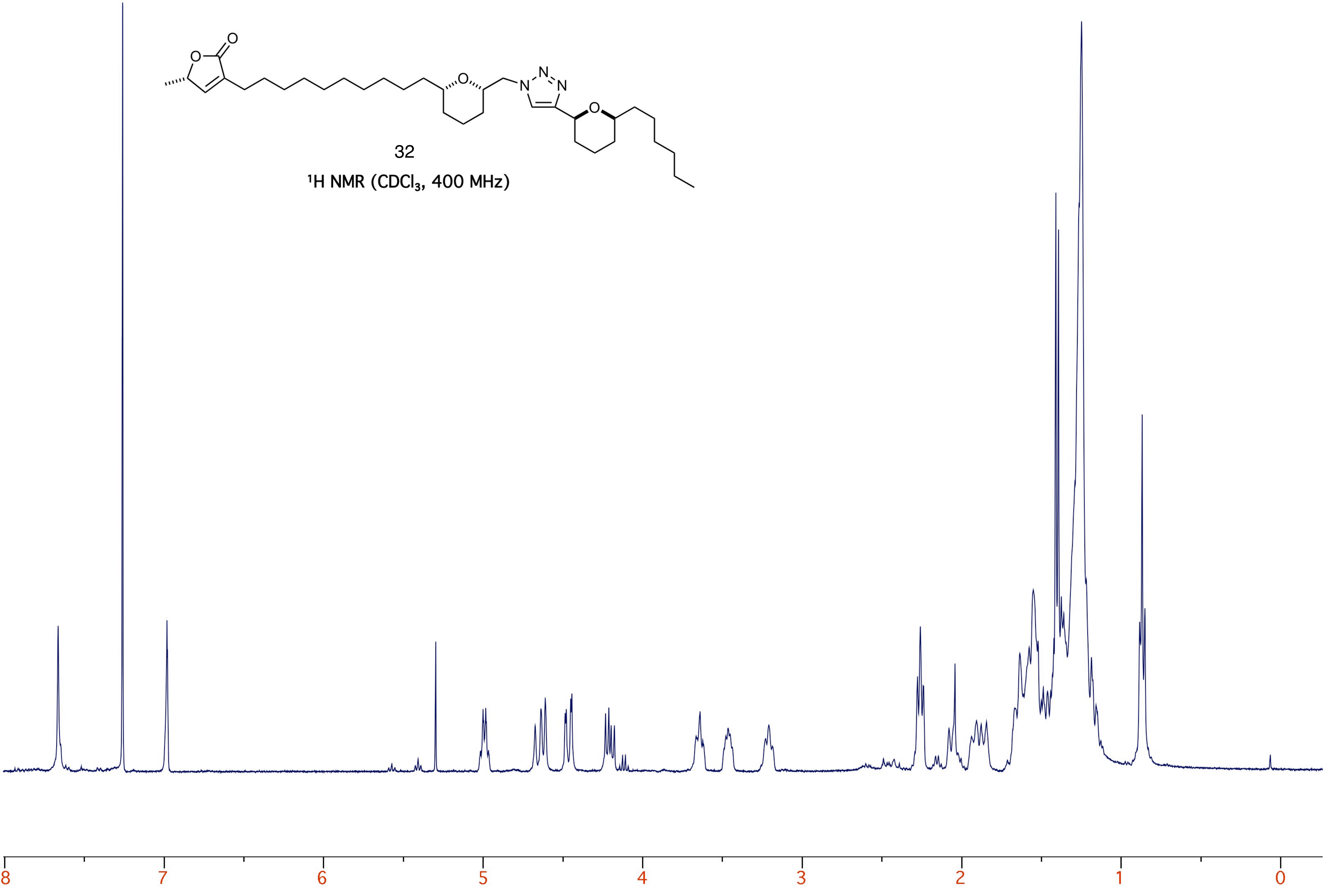




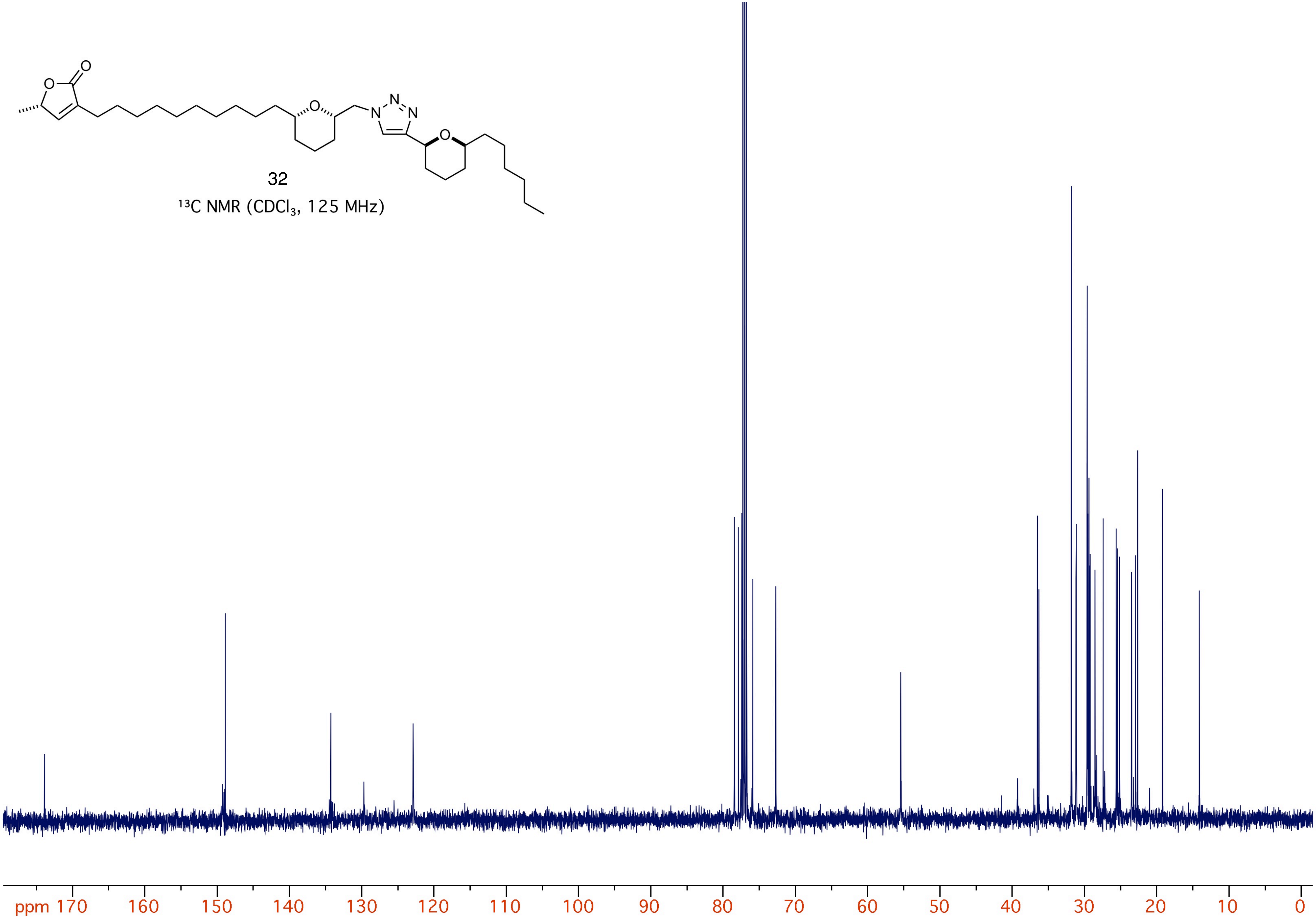
31

^{13}C NMR (CDCl$_3$, 125 MHz)



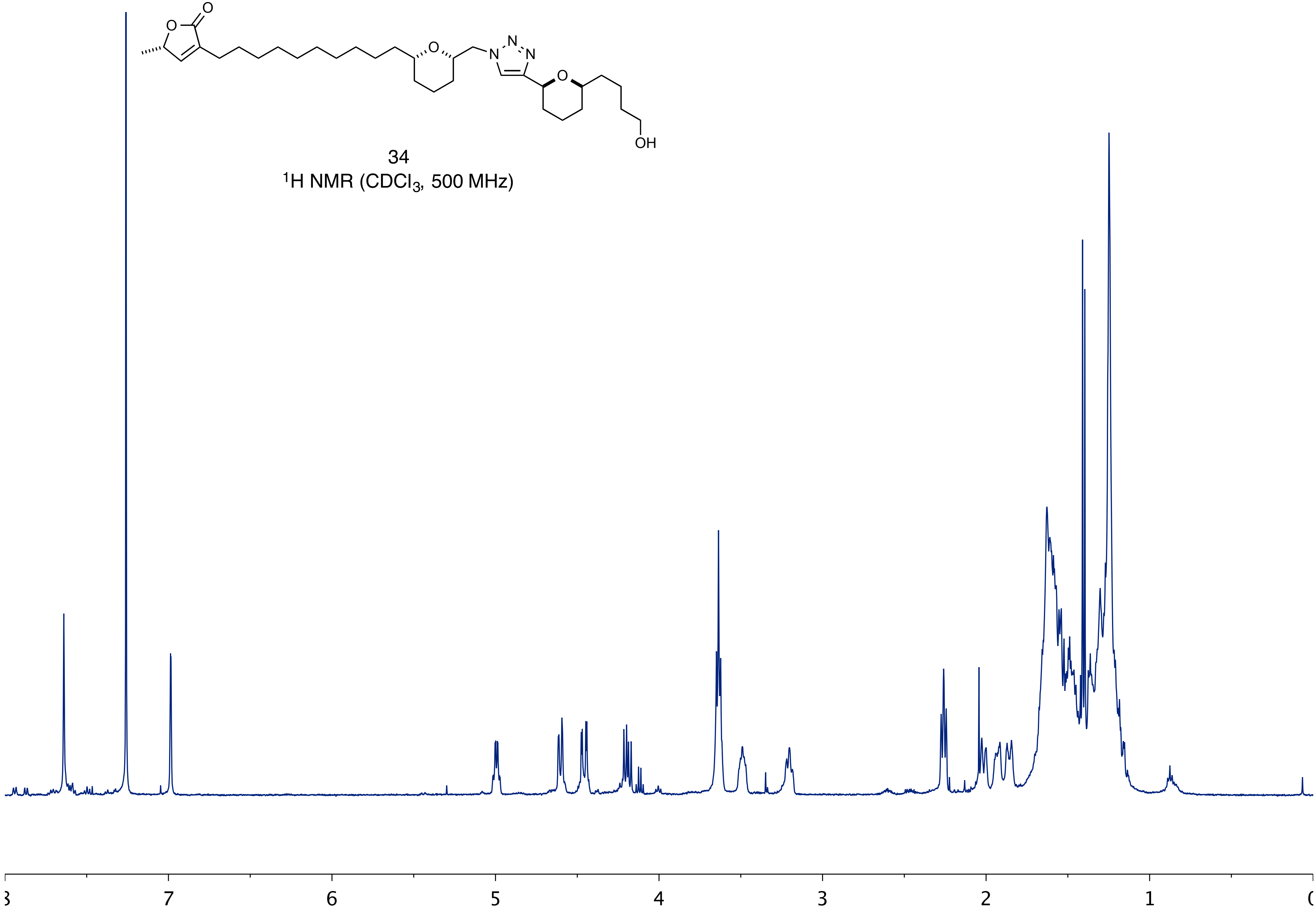

32

^{1}H NMR (CDCl$_3$, 400 MHz)

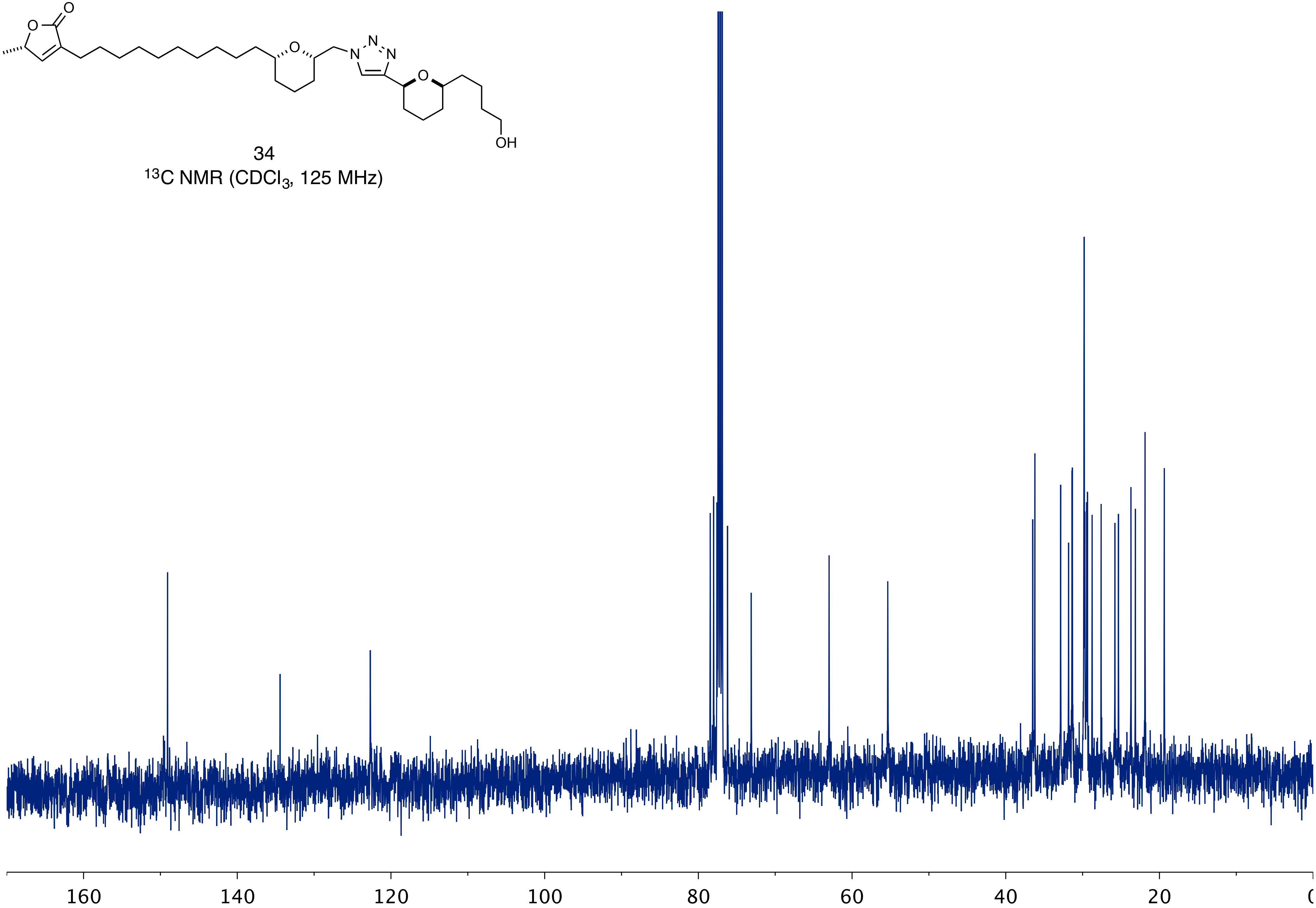


32

^{13}C NMR (CDCl$_3$, 125 MHz)

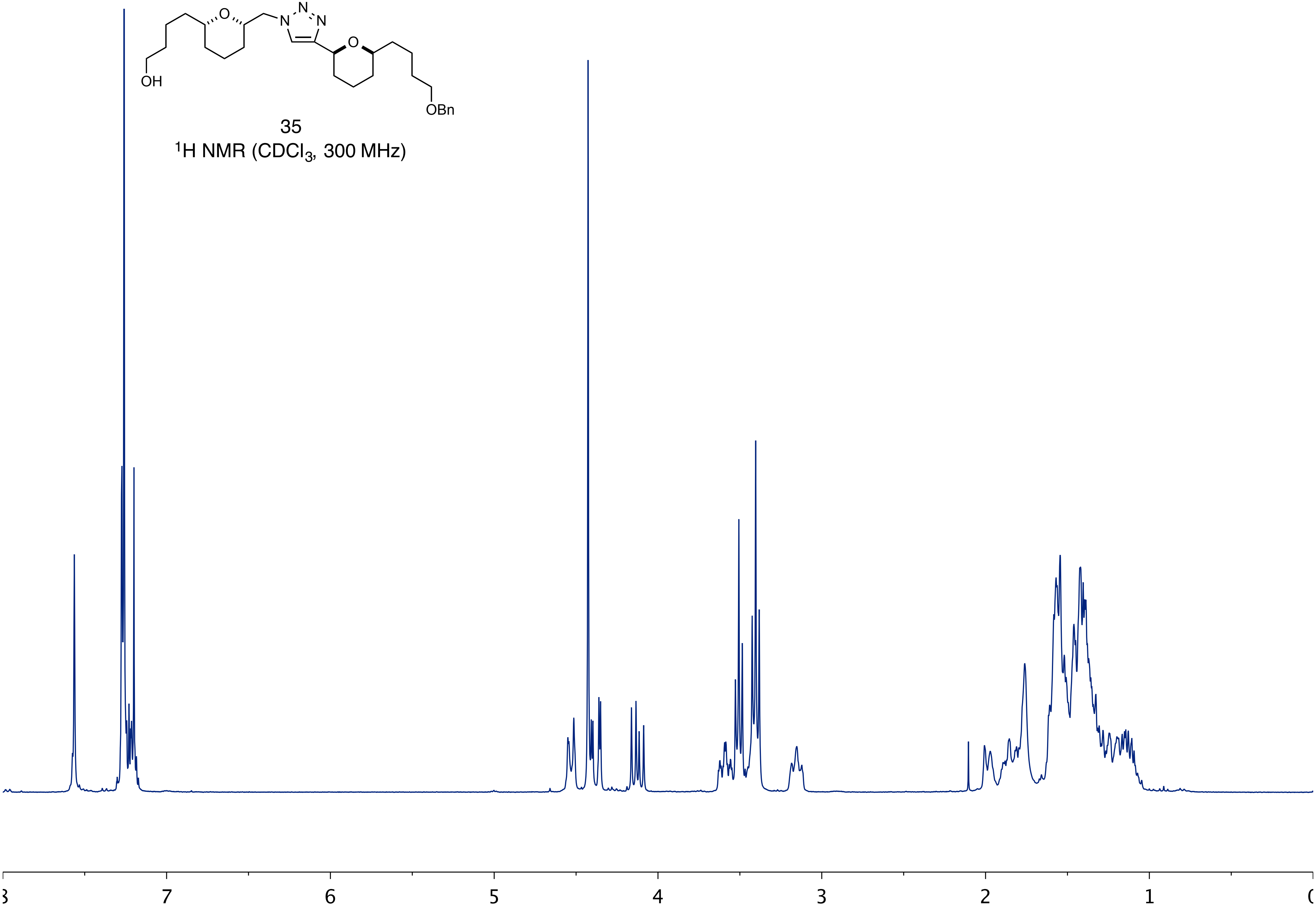


34
^{1}H NMR ($CDCl_3$, 500 MHz)



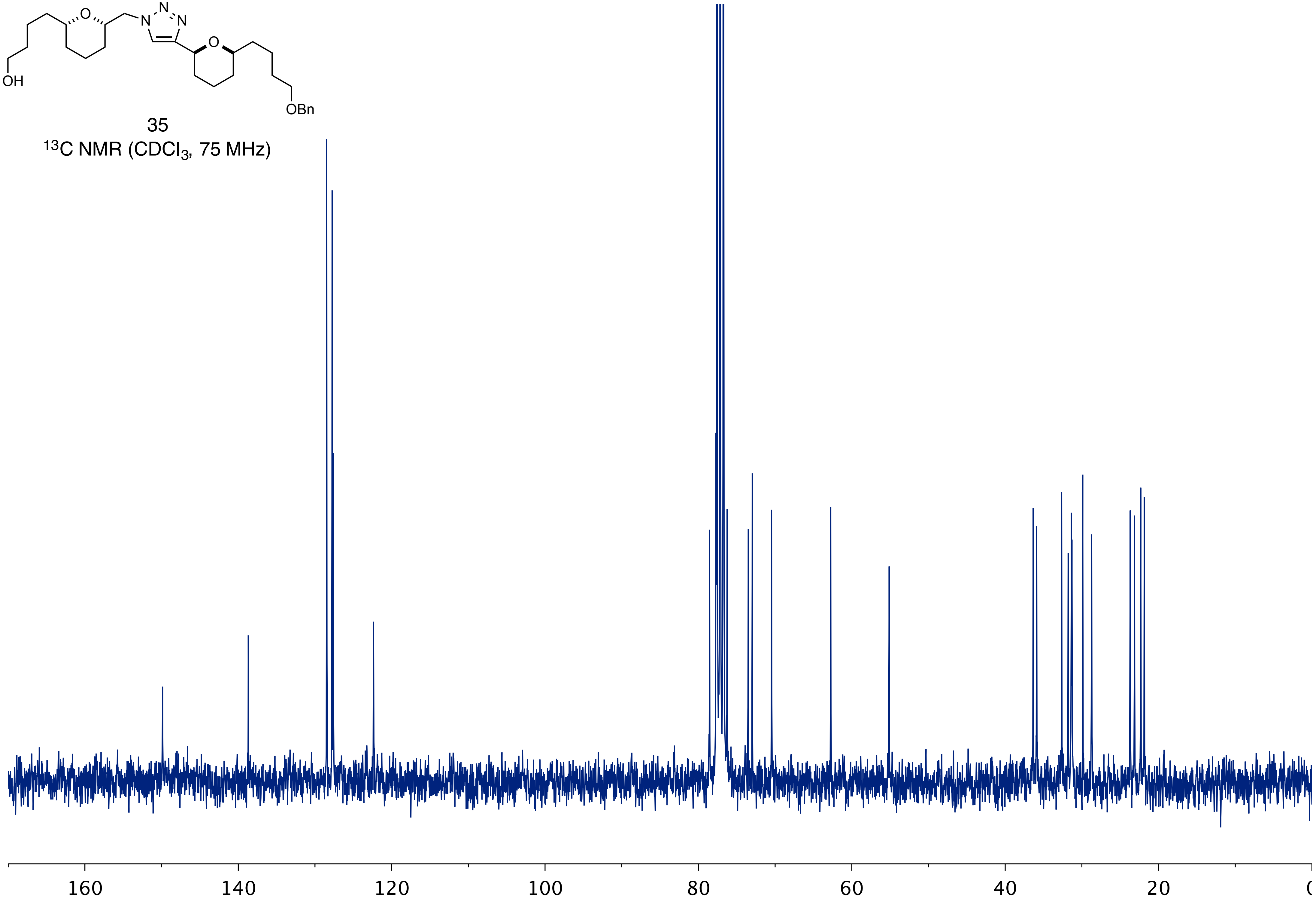
34

^{13}C NMR ($CDCl_3$, 125 MHz)



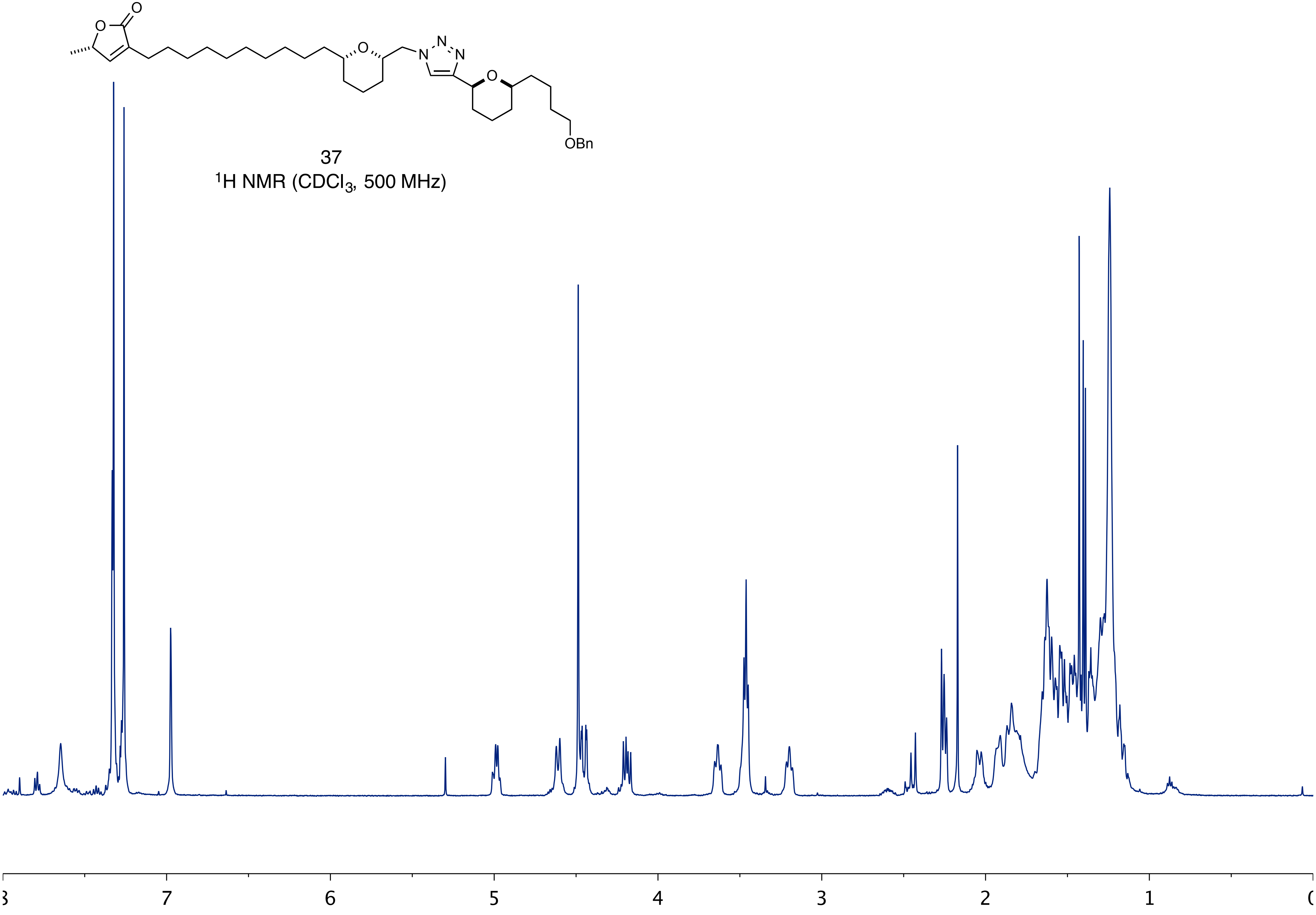
35

^{1}H NMR (CDCl$_3$, 300 MHz)



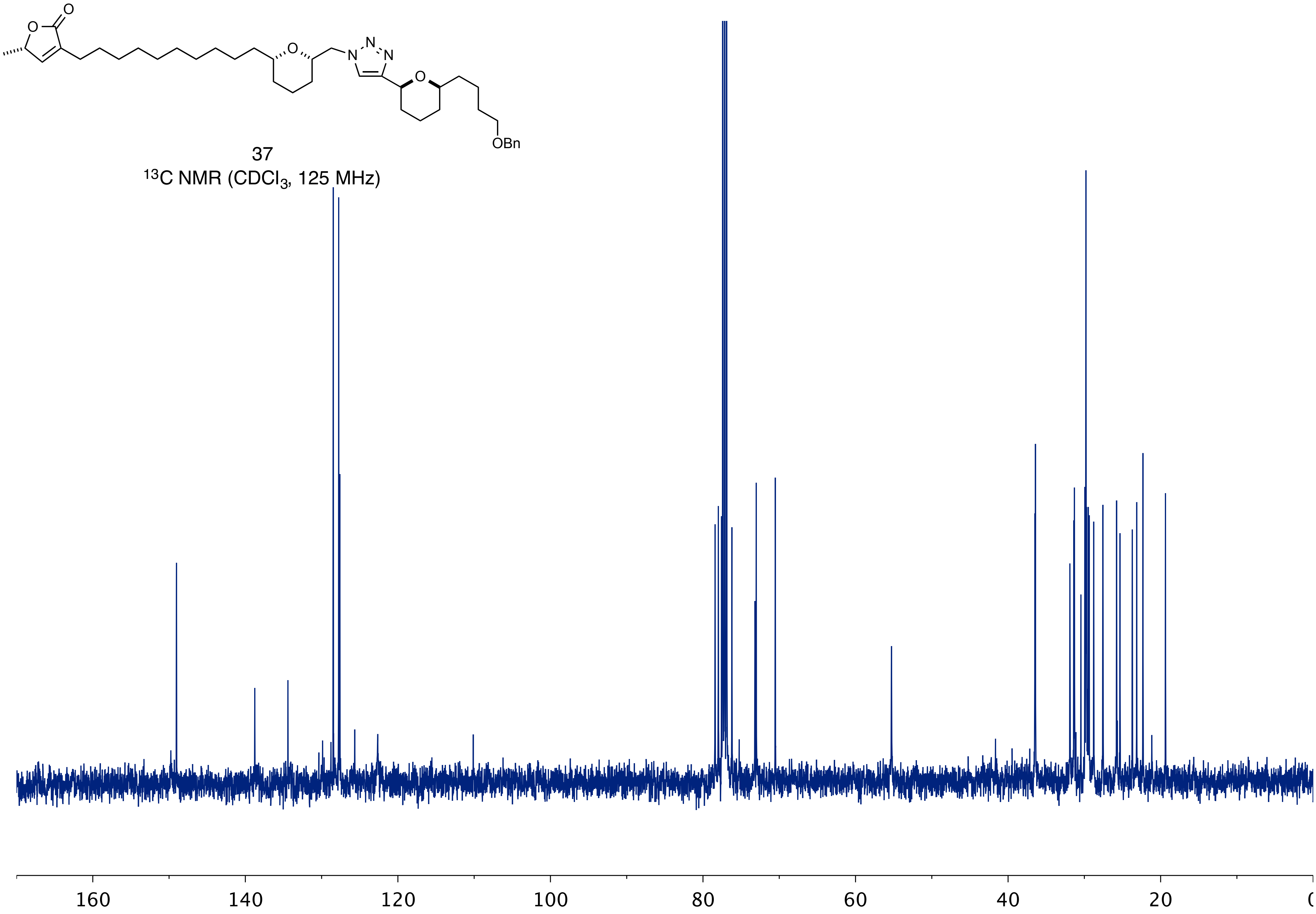
35

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



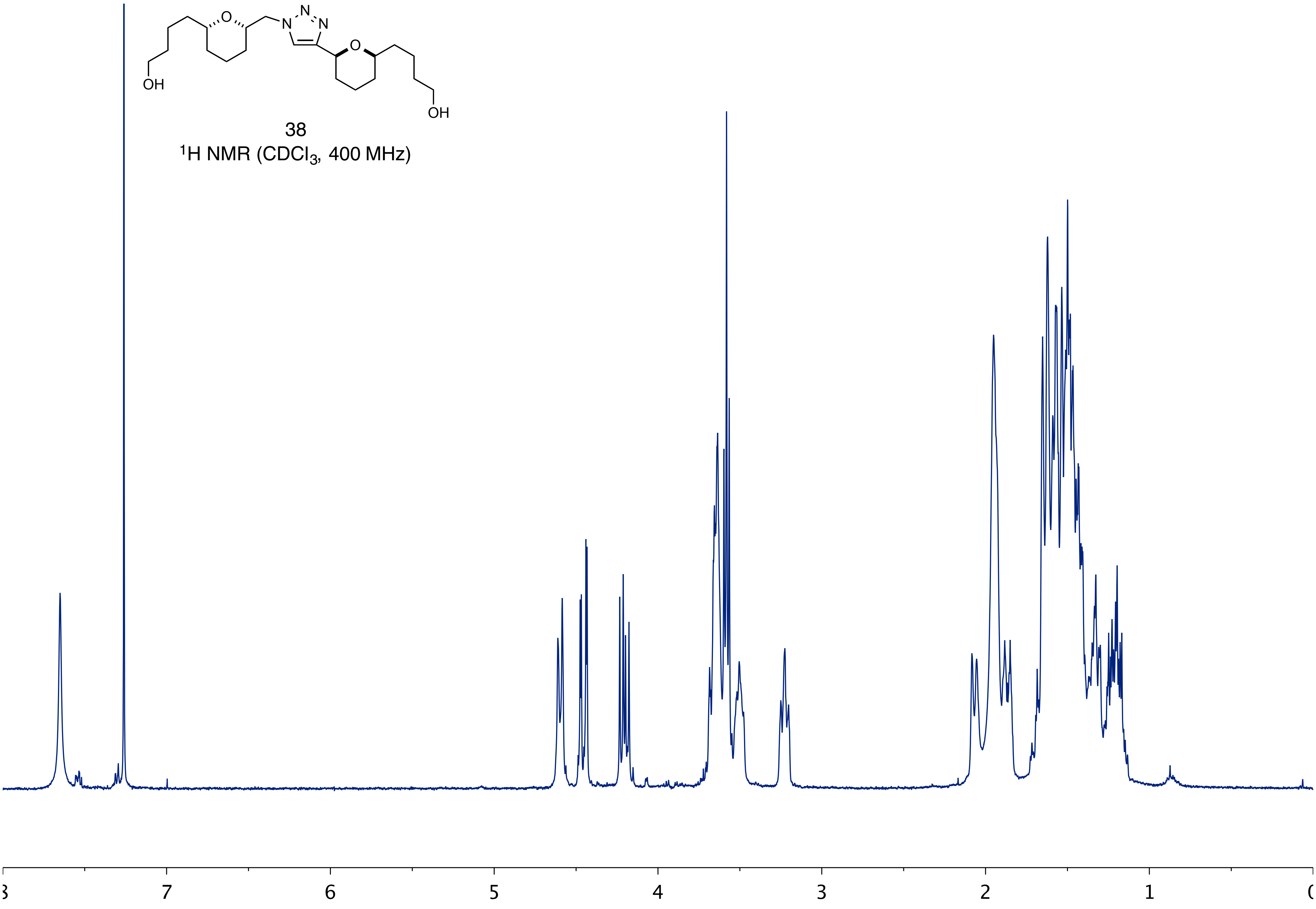
37

^{1}H NMR ($CDCl_3$, 500 MHz)



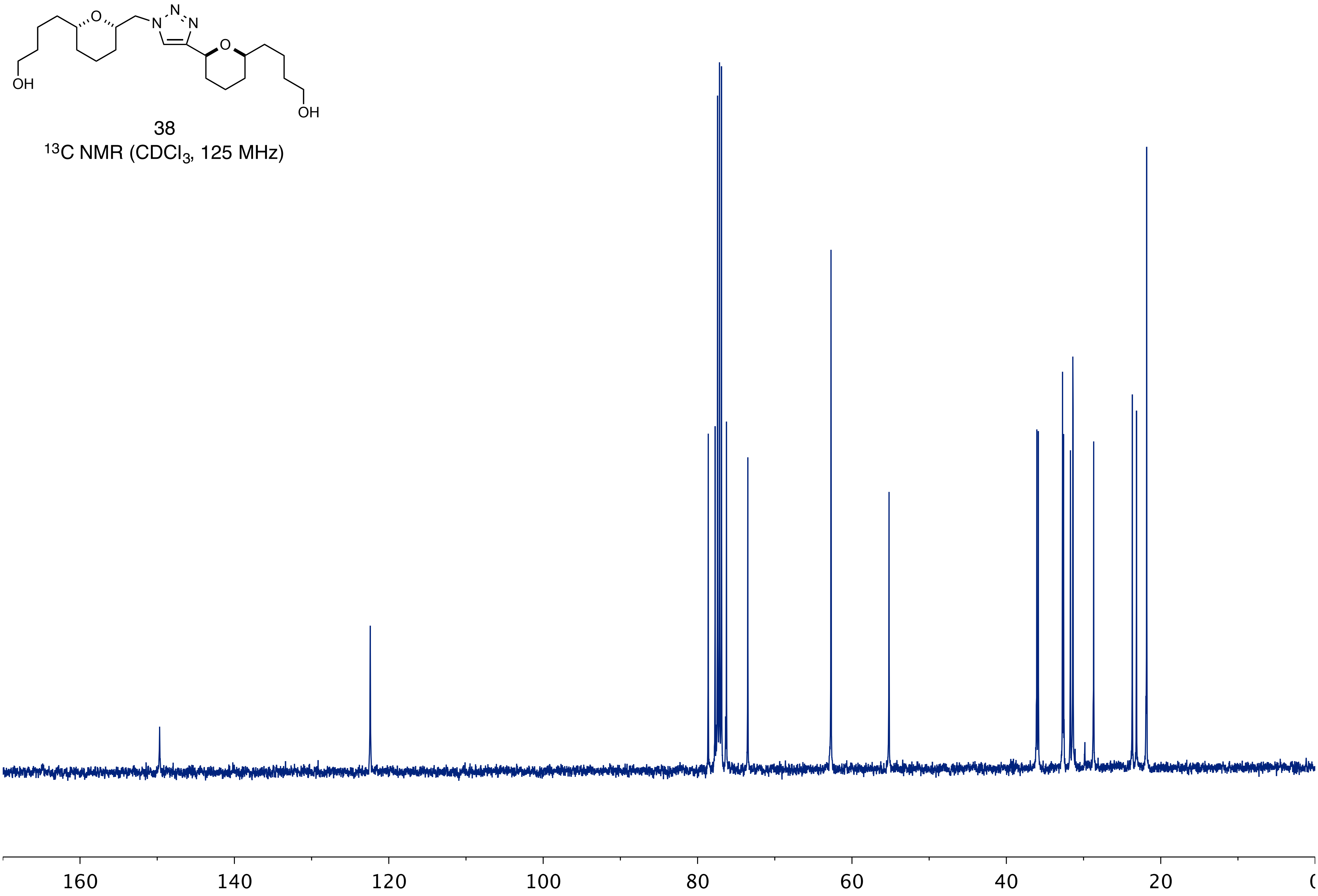
37

^{13}C NMR ($CDCl_3$, 125 MHz)



38

^{1}H NMR (CDCl$_3$, 400 MHz)



38

^{13}C NMR ($CDCl_3$, 125 MHz)