Electronic Supplementary Information

The synthesis of a pyridine-*N*-oxide isophthalamide rotaxane utilizing supplementary amide hydrogen bond interactions

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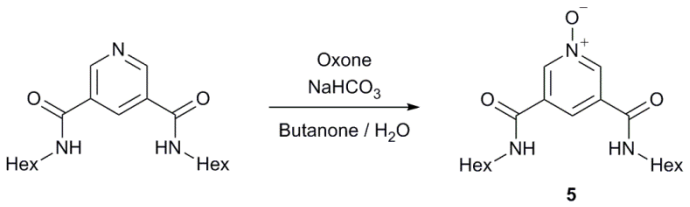
Contents

Part I: Synthesis

Additional Notes on Experimental Procedures

(a) Preparation of pyridine-*N*-oxide bis-hexyl thread **5**

Pyridine-*N*-oxide bis-hexyl thread **5** has been reported previously,[1] but a complete experimental procedure and characterisation was not included.

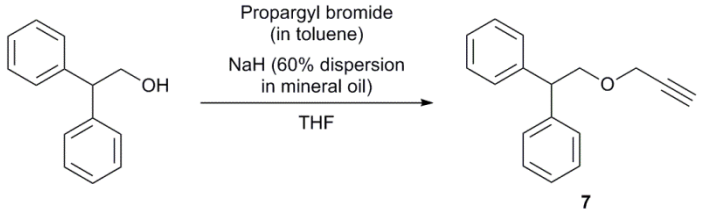


*Scheme ESI-1: Synthesis of pyridine-N-oxide bis-hexyl thread **5***

Dihexylpyridine-3,5-dicarboxamide[2] (250 mg, 0.750 mmol) and $NaHCO_3$ (1.89 g, 22.5 mmol) were dissolved in a 1:1 mixture of H_2O and butanone (60 mL). Then, a saturated solution of Oxone (1.38 g, 2.25 mmol) in H_2O (~ 5 mL) was added to the reaction mixture, and the resulting mixture stirred for 2 h. After this time, NaCl (7.9 g, 135 mmol) was added and the solution extracted with $CHCl_3$ (3 × 30 mL). The combined organic layers were dried ($MgSO_4$), filtered and the solvent removed *in vacuo* to give the title compound as a white solid (246 mg, 94 %). Mp 182–184 °C. υ_{max}/cm^{-1} (neat) 3290 (N–H), 3120 (C–H), 3050 (C–H), 2960 (C–H), 2920 (C–H), 2860 (C–H), 1650 (C=O), 1530 (N–O). δH(400 MHz; $CDCl_3$) 8.94 (2H, s, *ortho*-pyridyl Ar*H*), 8.33 (1H, s, *para*-pyridyl Ar*H*), 7.95 (2H, t, ^3J = 5.4 Hz, N*H*), 3.41–3.46 (4H, NHCH_2), 1.61–1.68 (4H, $NHCH_2CH_2$), 1.29-1.40 (12H, 3 × CH_2), 0.87-0.90 (6H, CH_3). δC(100 MHz; $CDCl_3$) 162.2 (C=O), 140.1, 134.2, 124.8 (3 pyridyl Ar C environments), 40.7, 31.4, 29.3, 26.7, 22.5, 14.0 (6 sp^3 C environments). *m/z* (ES) 350.2421 ($[M + H]^+$, $C_{19}H_{32}N_3O_3$ requires 350.2438).

(b) Preparation of alkyne stopper **7**

A synthesis with full characterisation data has not been previously reported for this compound.



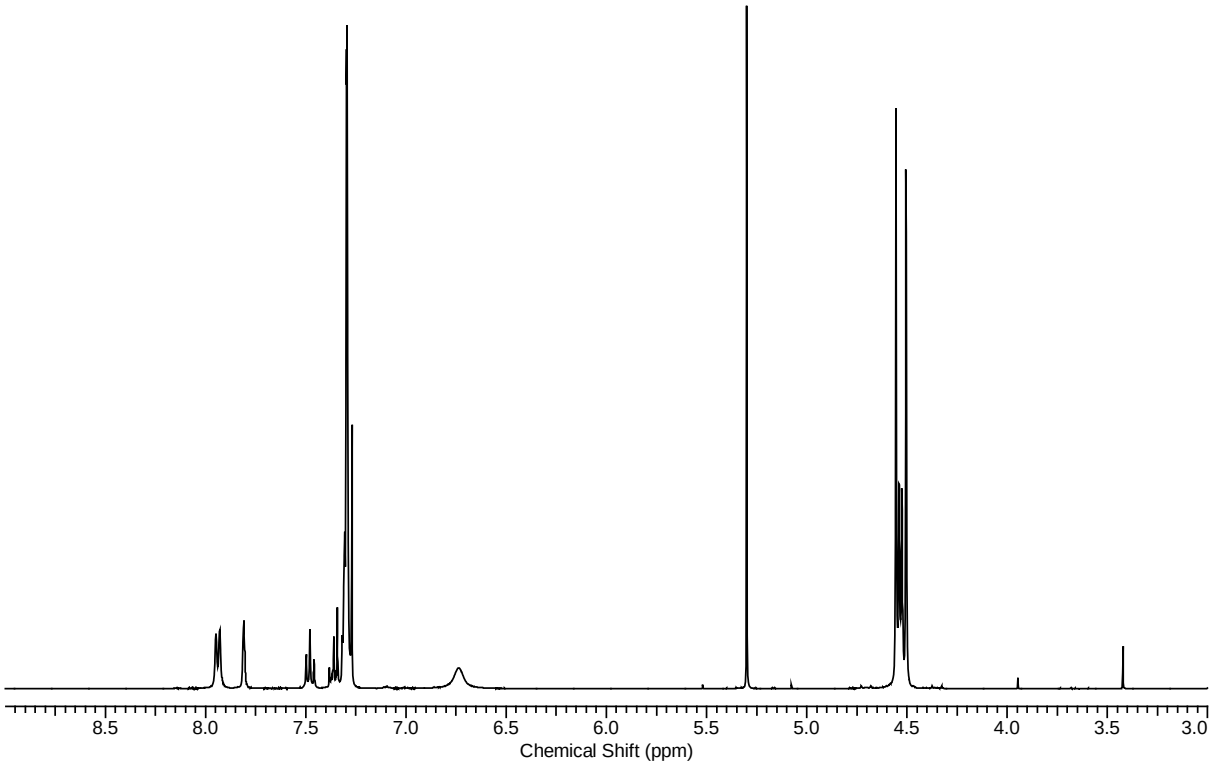
*Scheme ESI-2: Synthesis of alkyne stopper **7***

NaH (60% dispersion in mineral oil, 50 mg, 1.3 mmol) was added to a solution of 2,2'-diphenylethanol (225 mg, 1.1 mmol) in dry THF (3 mL) under an Ar (g) atmosphere. Then propargyl bromide (80% in toluene, 0.18 mL, 2.9 mmol) was stirred for 24 h at RT under an Ar (g) atmosphere. After careful quenching with H_2O, the reaction mixture was extracted with Et_2O (3 × 10 mL). The combined organic layers were dried (Na_2SO_4), filtered and concentrated to give a yellow oil. The crude material was purified by silica gel column chromatography (95 : 5 Petrol 40-60/EtOAc) to yield the title compound as a waxy-white solid (140 mg, 52%). R_f = 0.57, 95 : 5 Petrol 40-60/EtOAc. υ_{max}/cm^{-1} (neat) 3270 (C–H), 3020 (C–H), 3000 (C–H), 2940 (C–H), 2910 (C–H), 2890 (C–H), 2850 (C–H), 2800 (C–H), 2110 (alkyne C–C), 1600 (ring C=C), 1490 (ring C=C), 1450 (ring C=C), 1090 (C–O). δH(400 MHz; $CDCl_3$) 7.17–7.31 (10H, m, aromatic *H*), 4.31 (1H, t, ^3J = 7.3 Hz, C*H*CH_2O), 4.16 (2H, d, ^4J = 2.4 Hz, C*H*$_2$CCH), 4.07 (2H, d, ^3J = 7.3 Hz, CHC*H*$_2$O) 2.42 (1H, t, ^4J = 2.4 Hz, alkyne *H*). δC(100 MHz; $CDCl_3$) 141.8, 128.4, 128.2, 126.5 (4 Ar C environments), 79.6, 74.6, 72.8, 58.2, 50.8 (3 sp^3 C & 2 sp C environments). *m/z* (ES) 254.1540 ([M + NH_4]$^+$, $C_{17}H_{20}NO$ requires 254.1539).

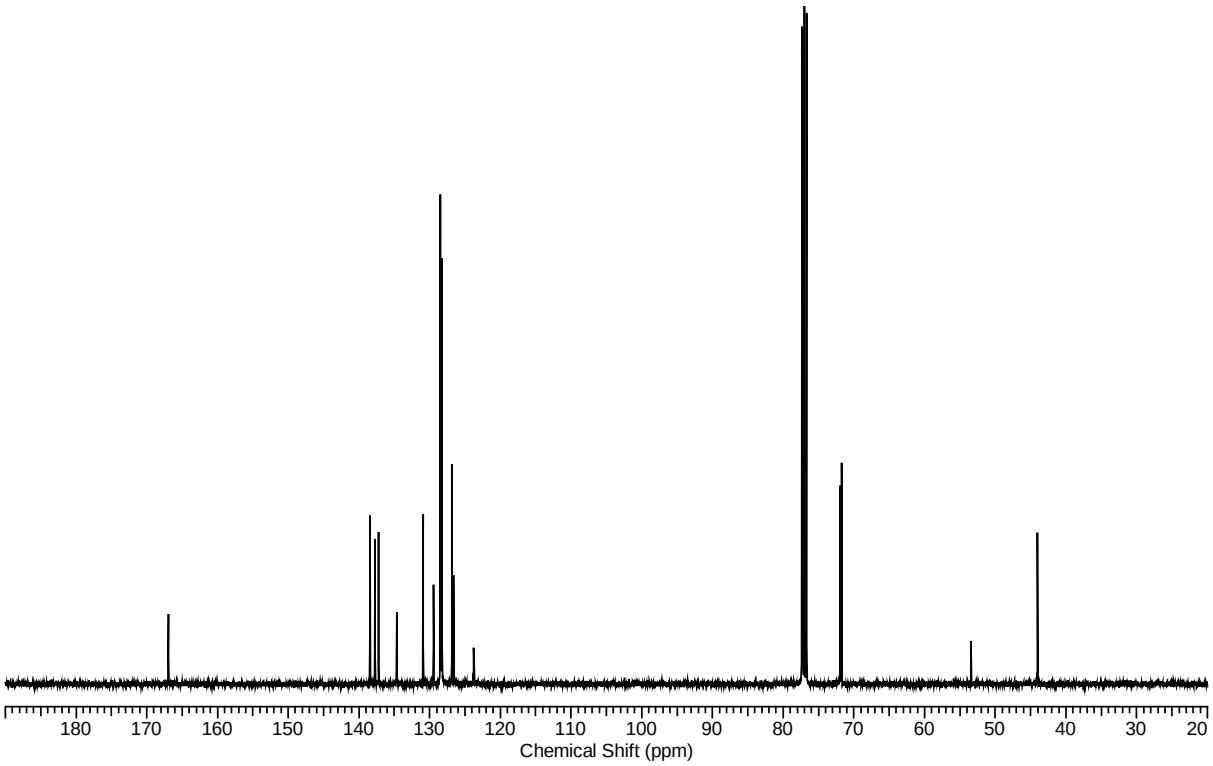
Part II: Spectra

Macrocycle 2

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

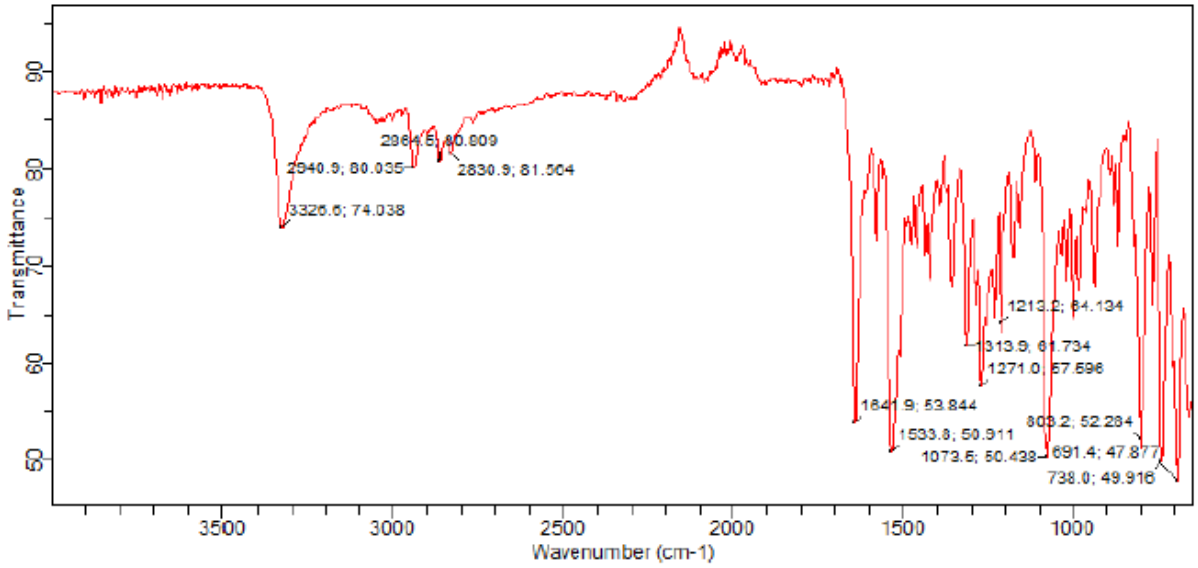


^{13}C NMR ($CDCl_3$, 100 MHz)

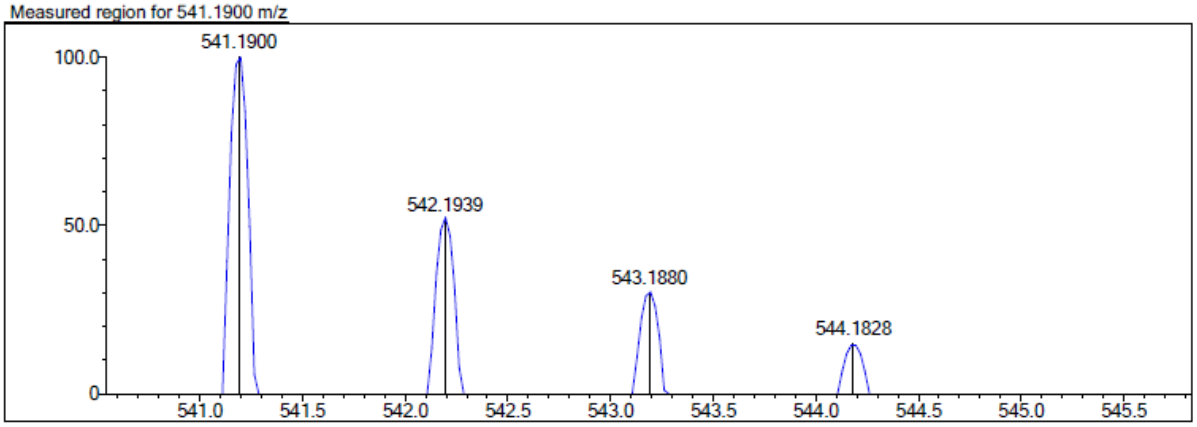


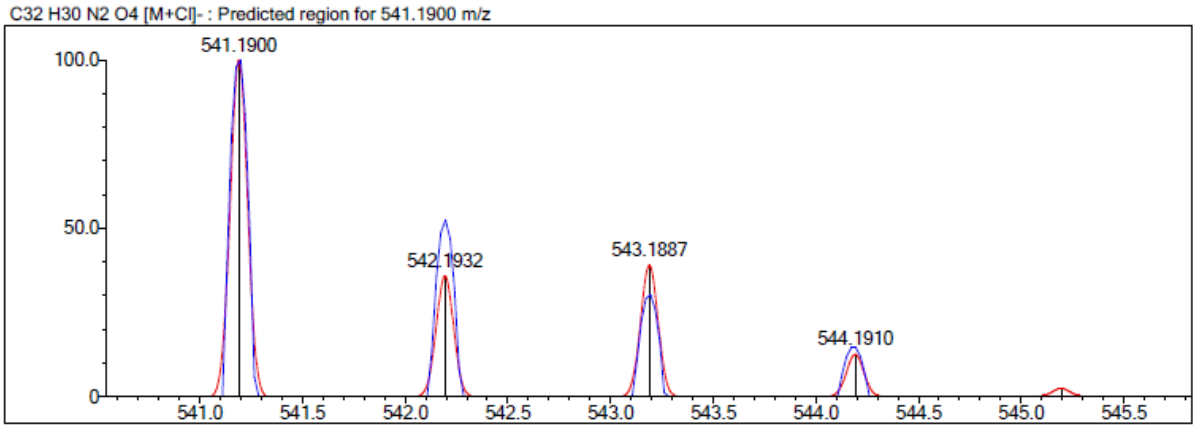
Macrocycle 2

IR Spectrum (neat)



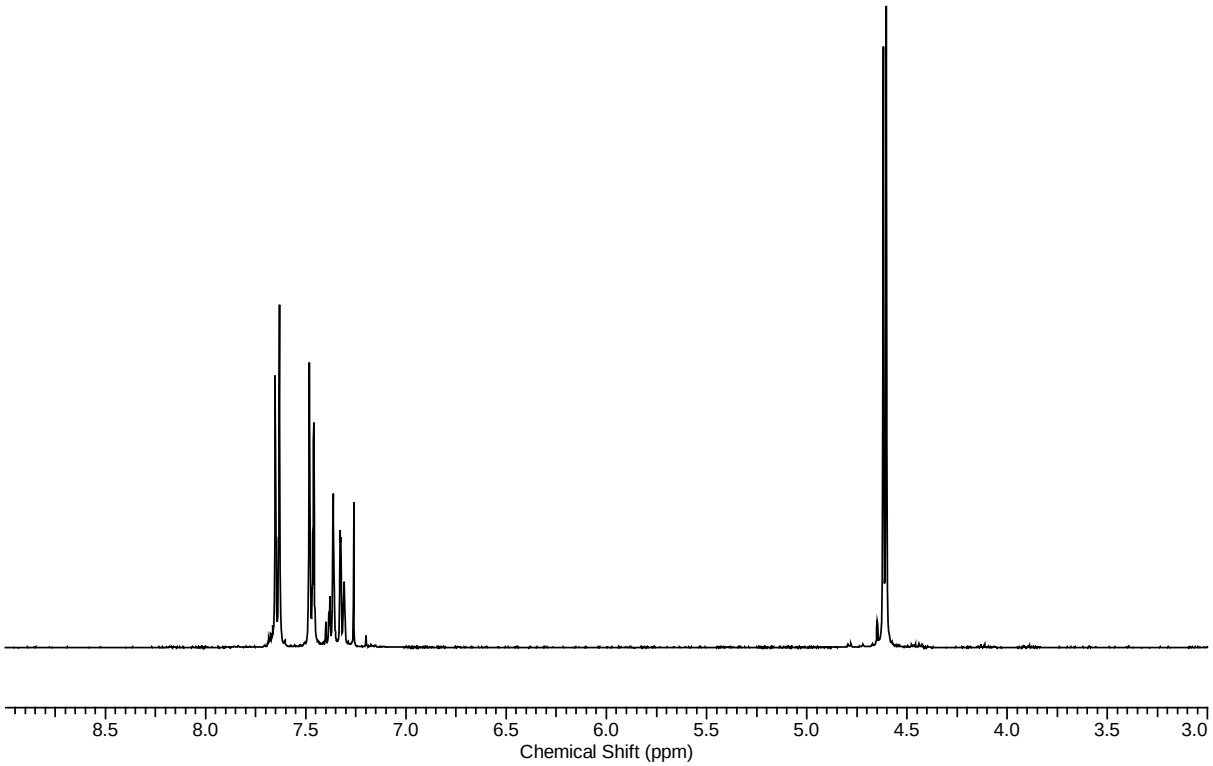
Mass Spectrum (ES −ve)



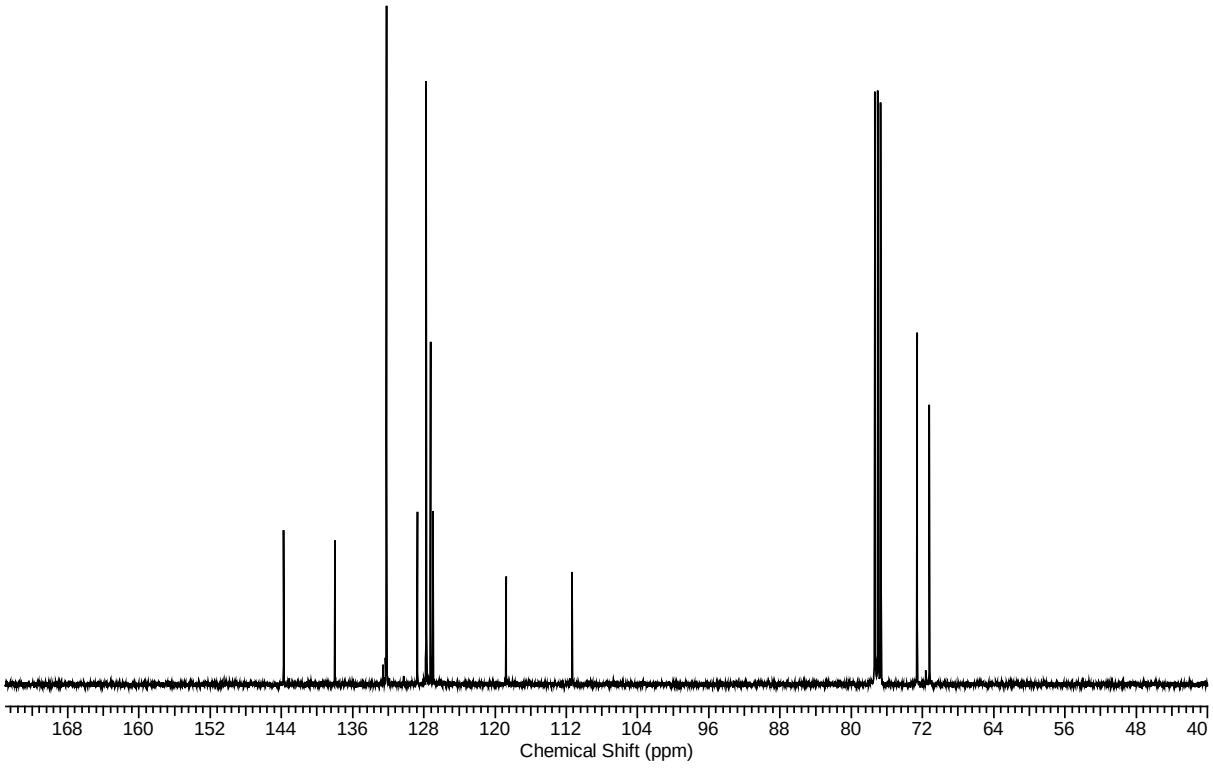


Bis-nitrile 3

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

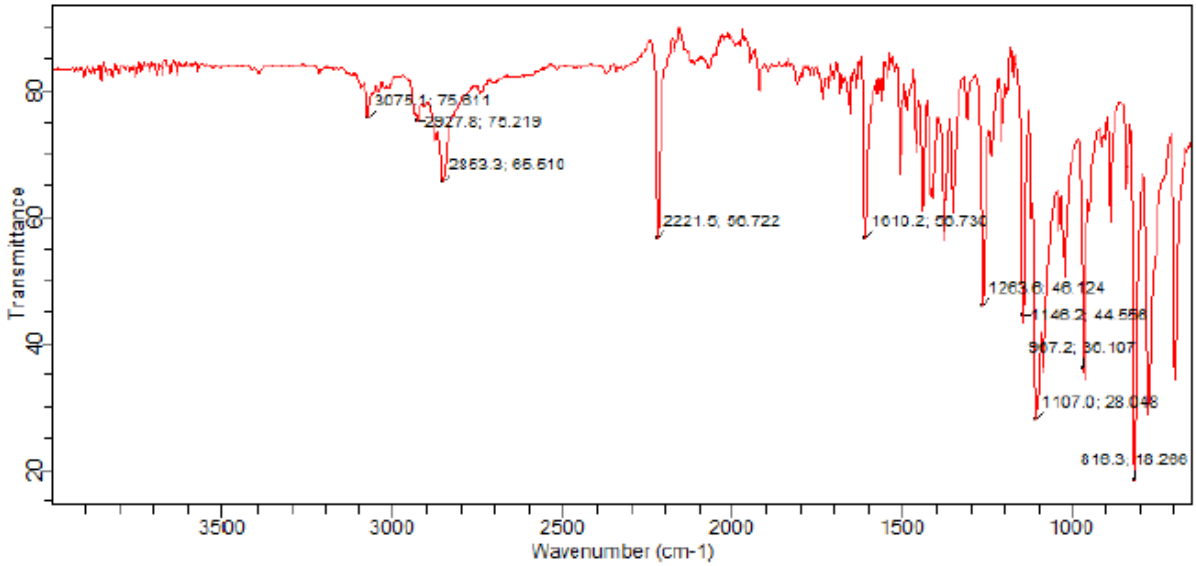


^{13}C NMR ($CDCl_3$, 100 MHz)

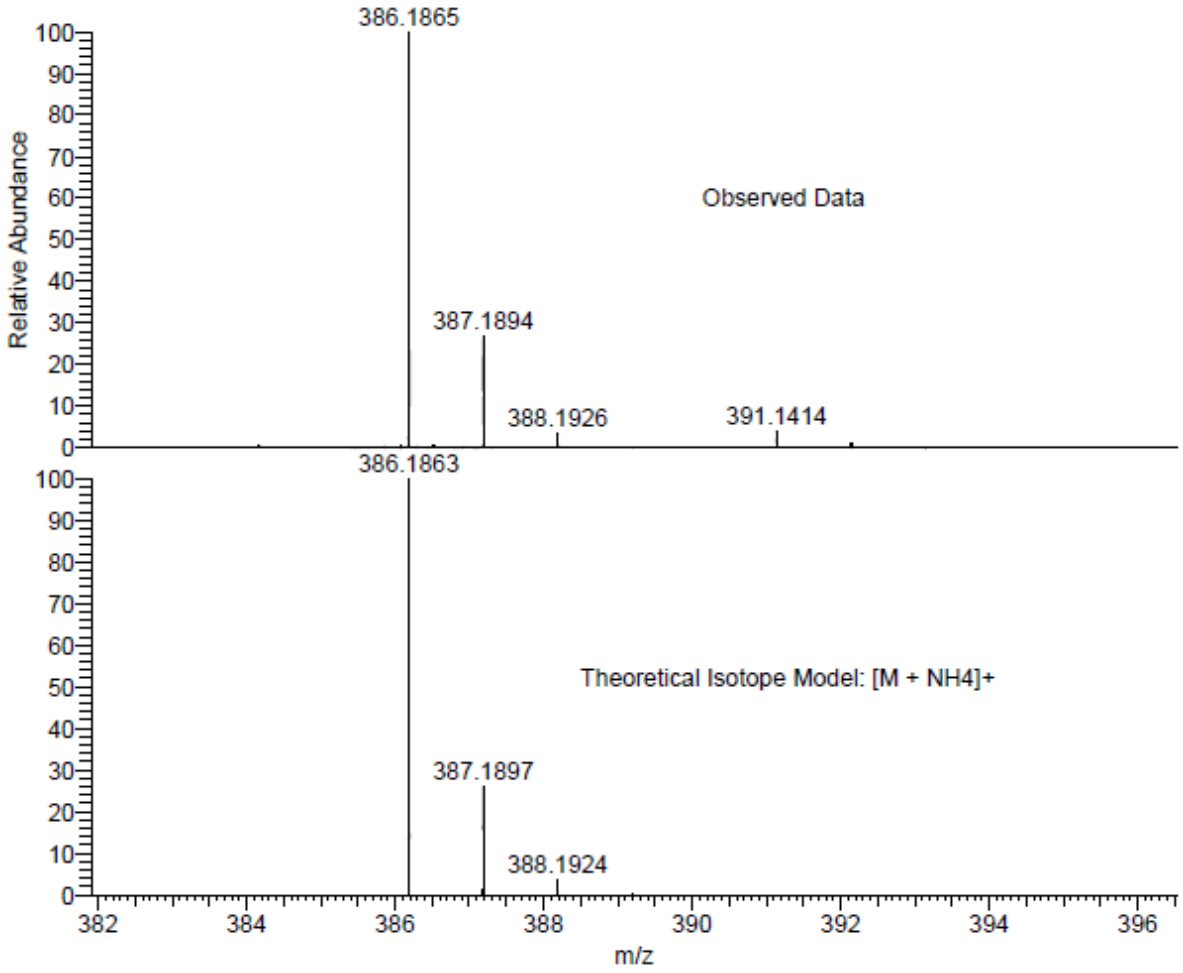


Bis-nitrile 3

IR Spectrum (neat)

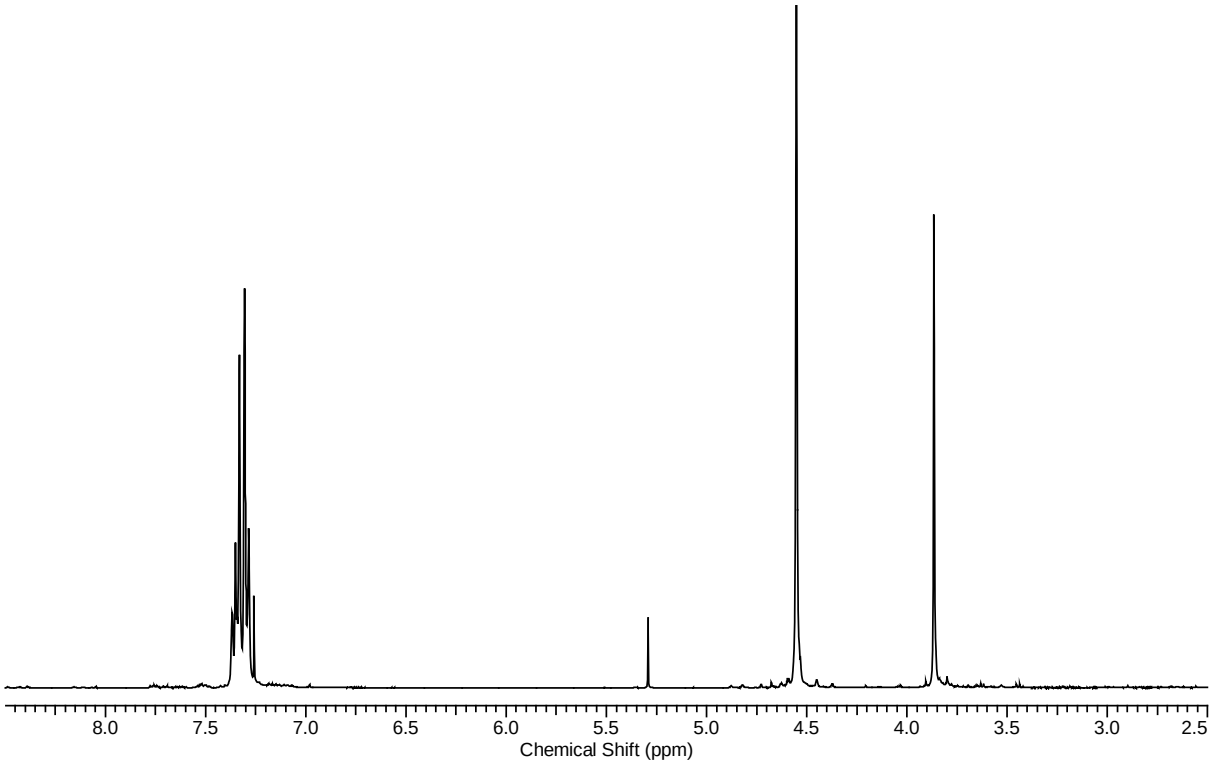


Mass Spectrum (ES +ve)

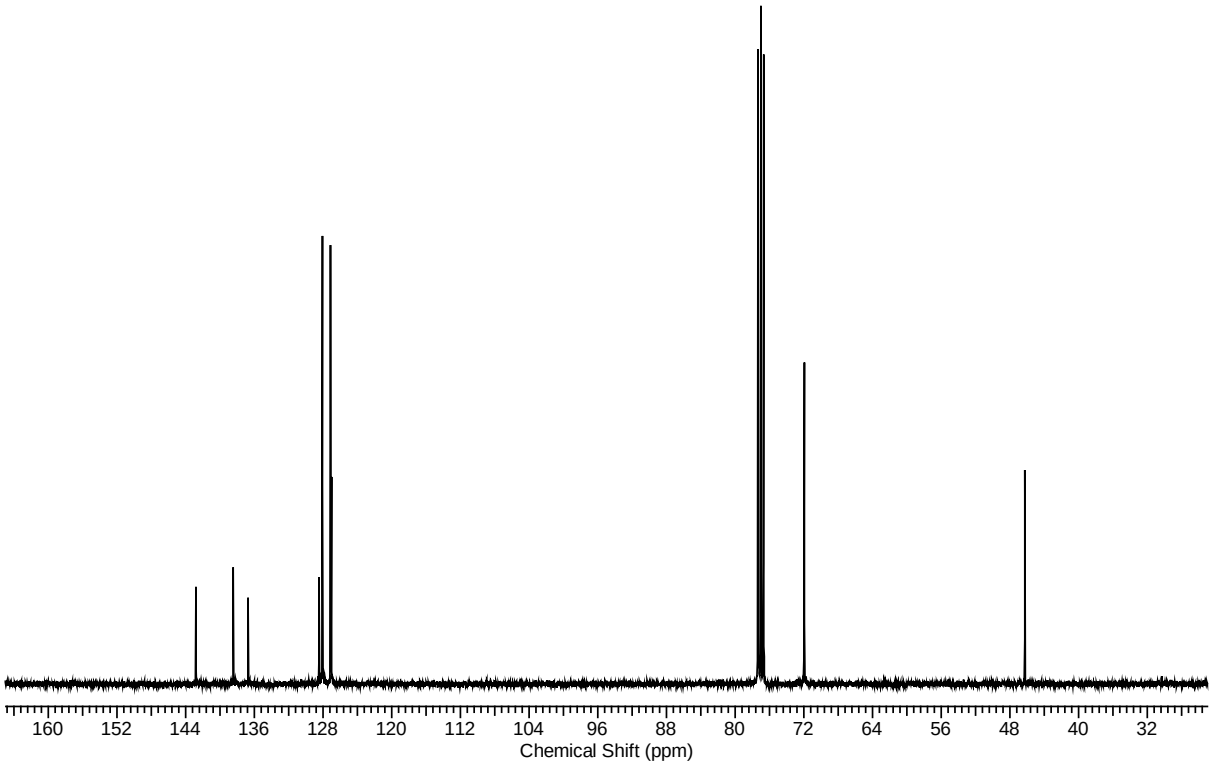


Bis-amine 4

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

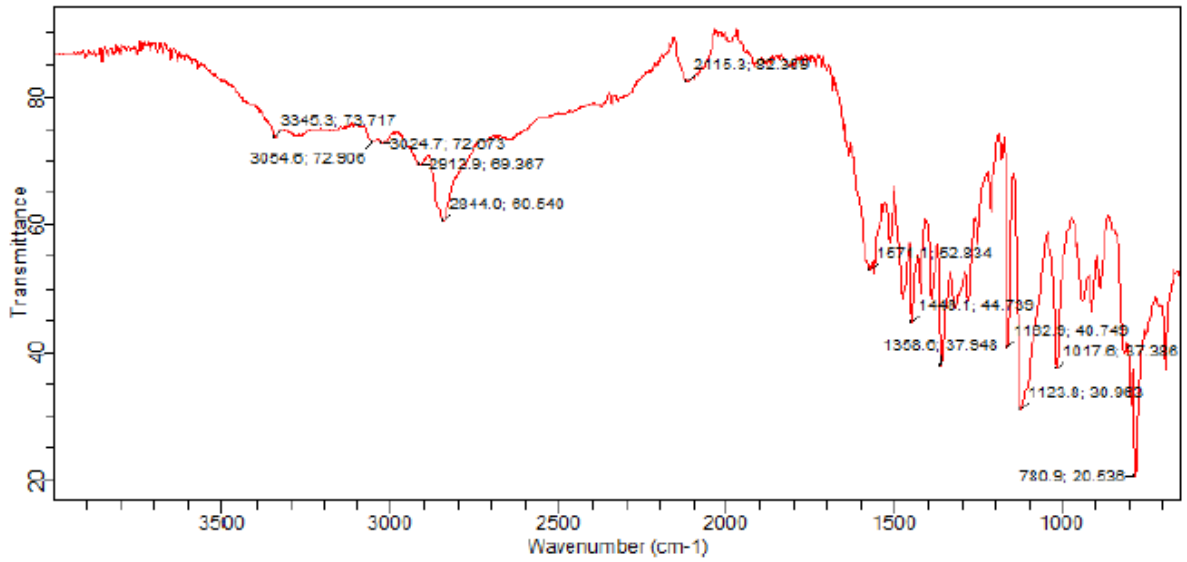


^{13}C NMR ($CDCl_3$, 100 MHz)

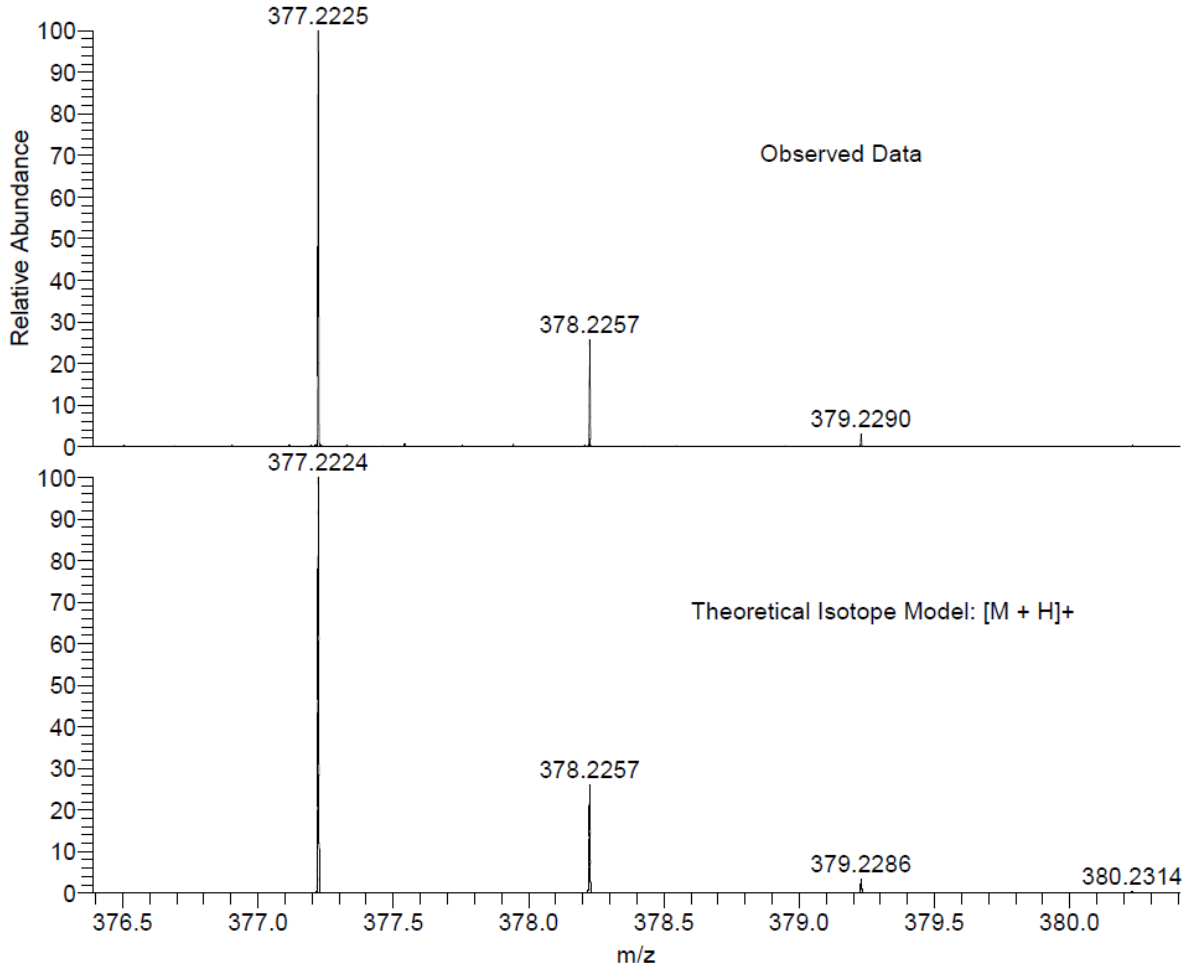


Bis-amine 4

IR Spectrum (neat)

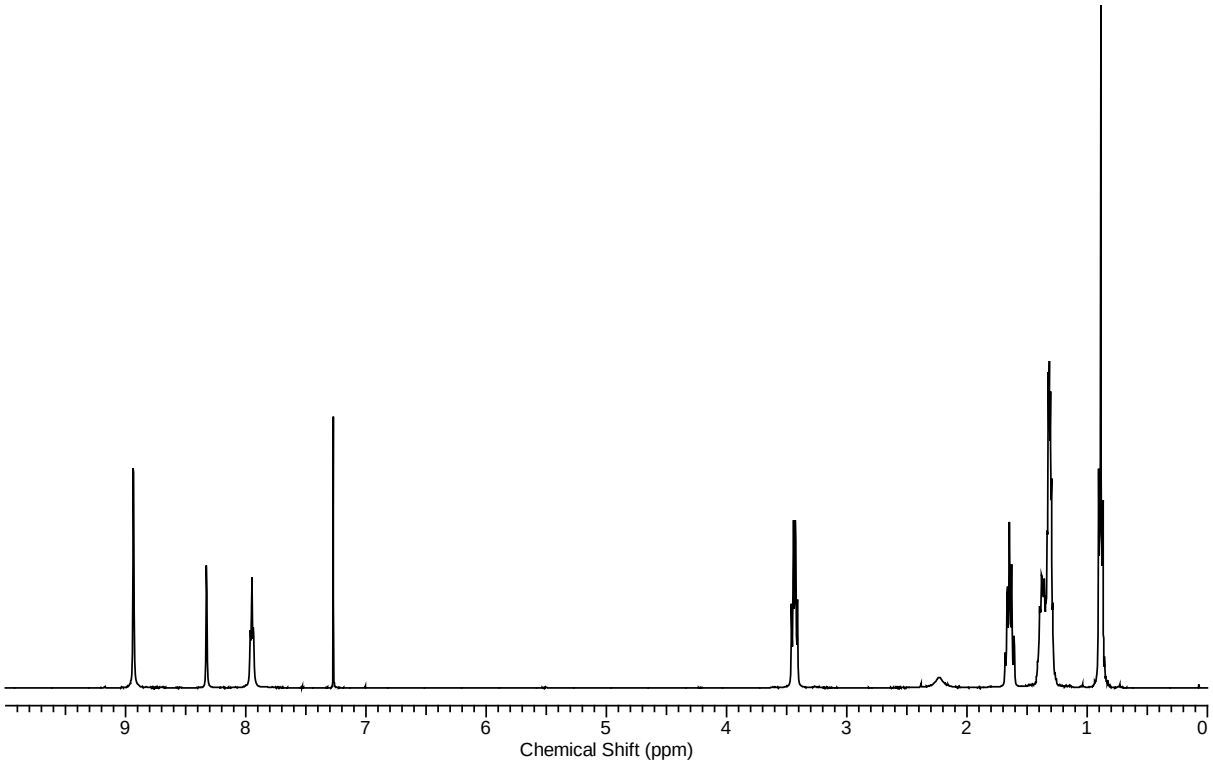


Mass Spectrum (ES +ve)

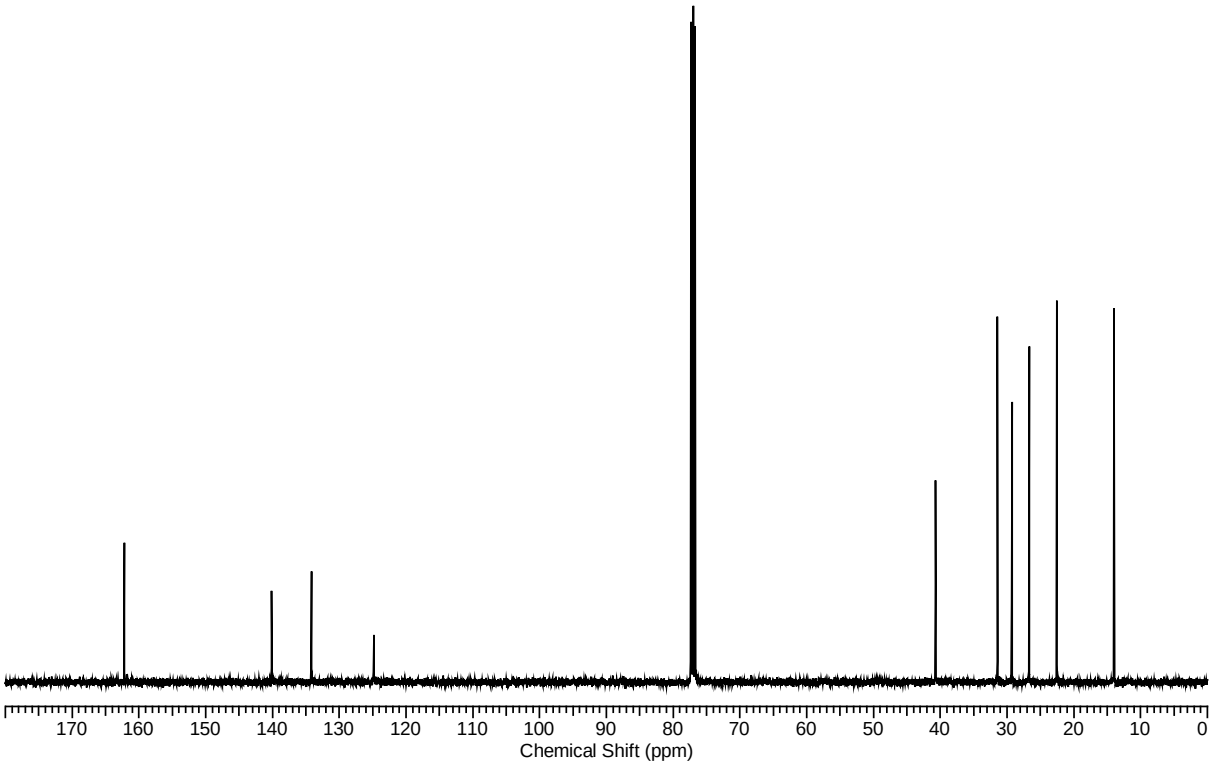


Pyridine-*N*-oxide bis-hexyl thread 5

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

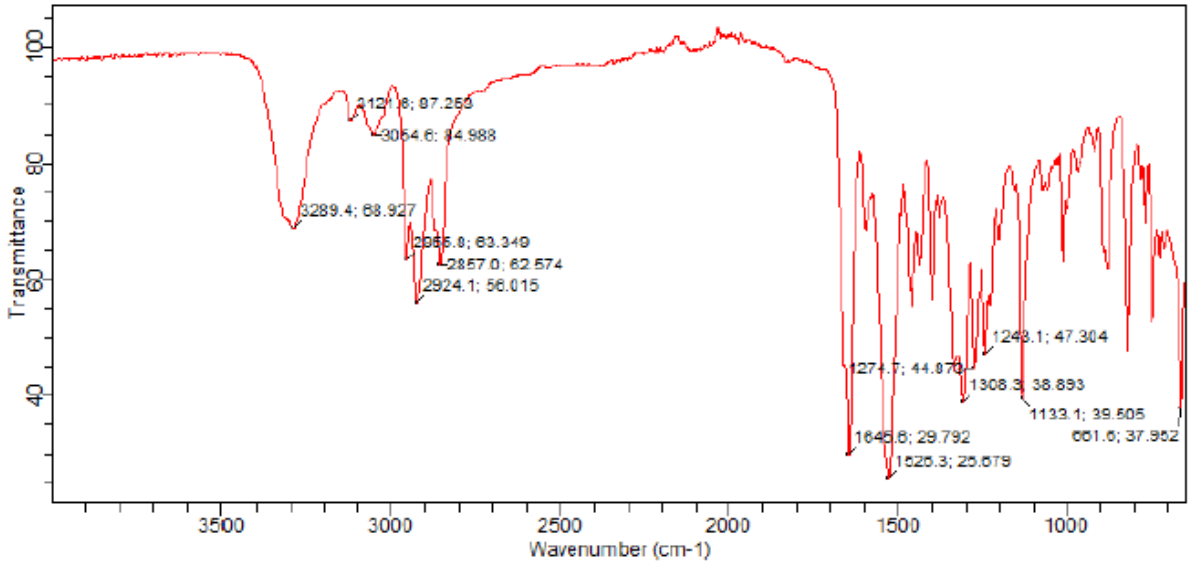


^{13}C NMR ($CDCl_3$, 100 MHz)

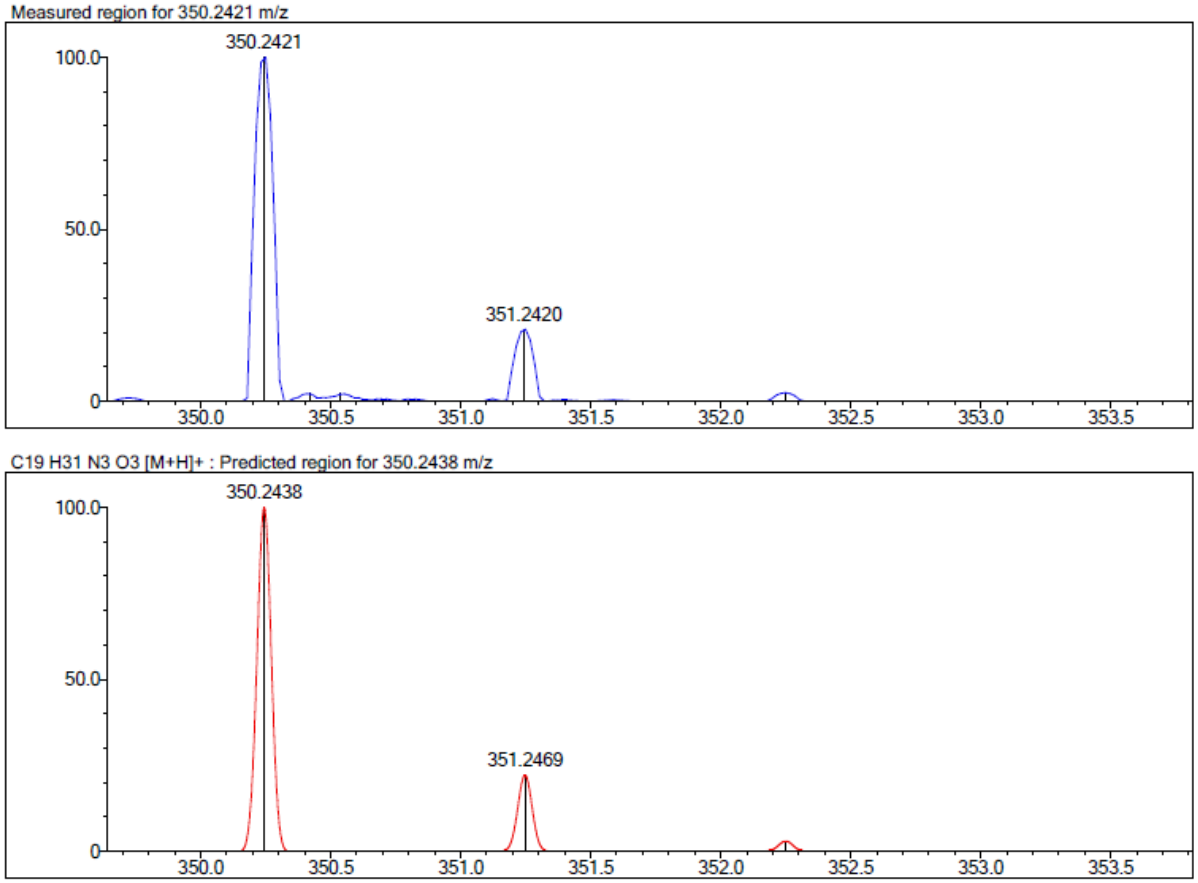


Pyridine-*N*-oxide bis-hexyl thread 5

IR Spectrum (neat)

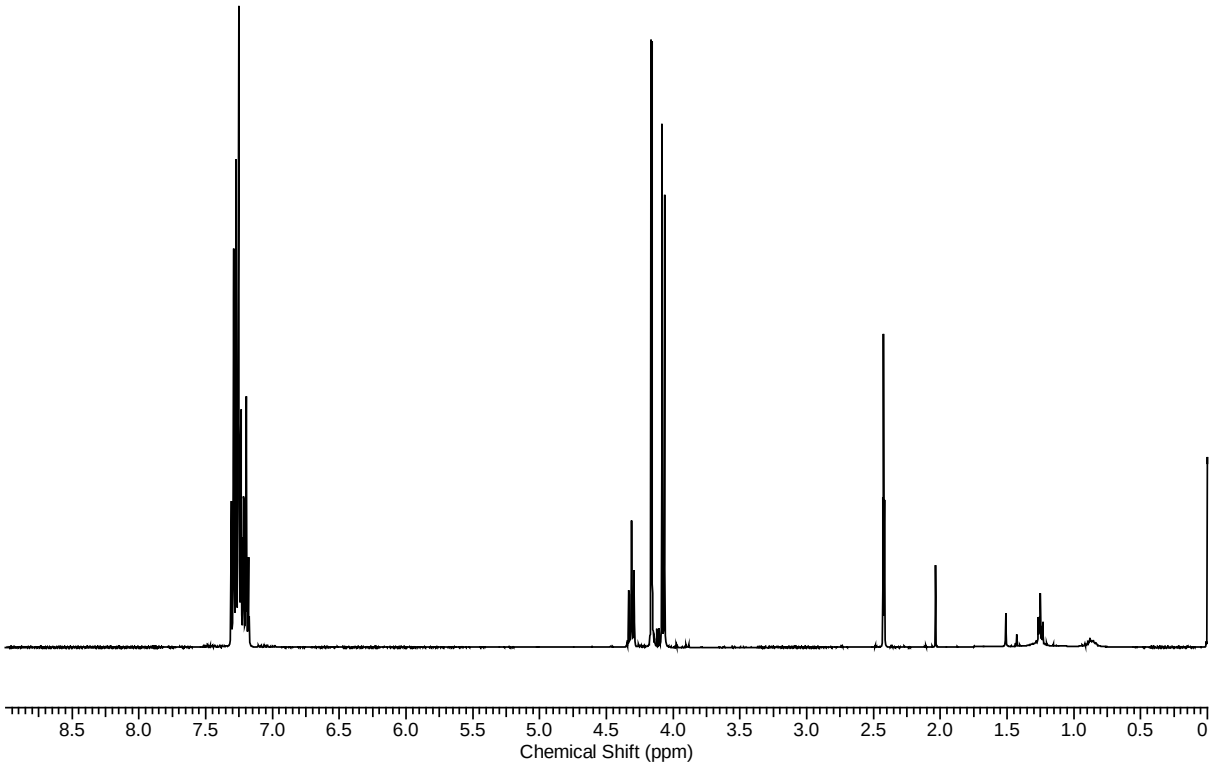


Mass Spectrum (ES +ve)

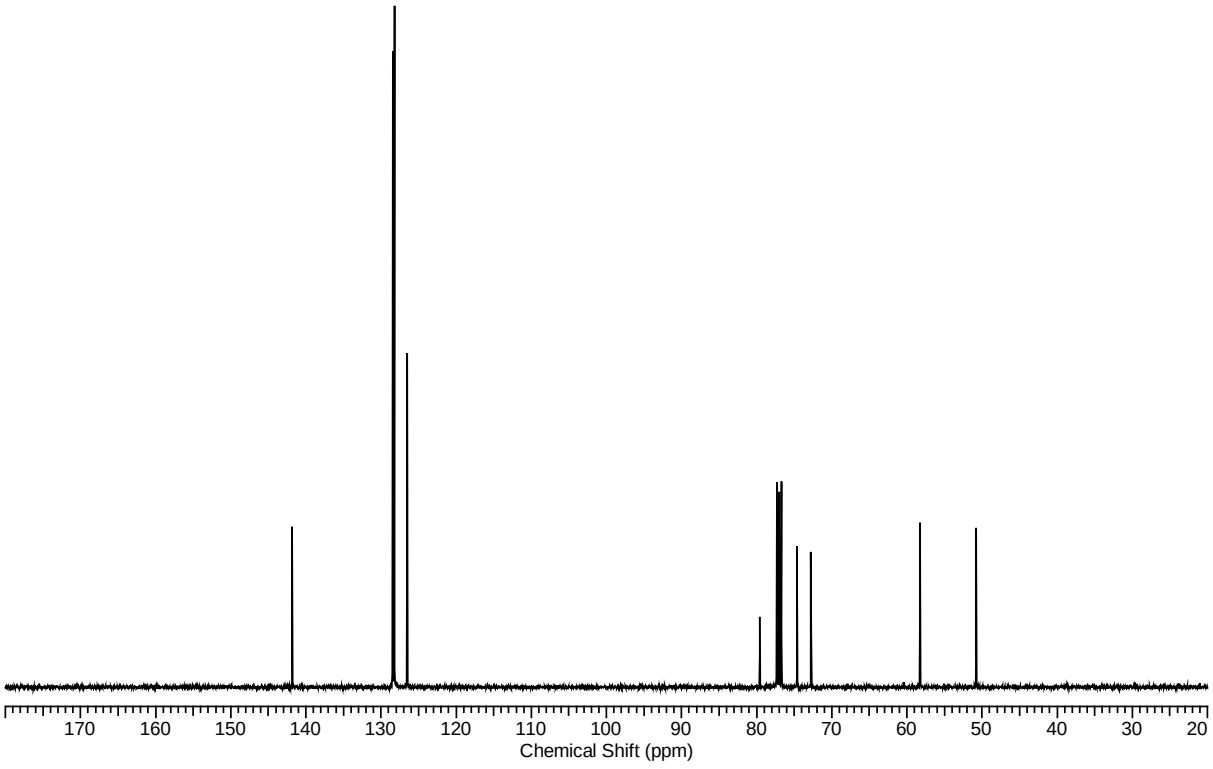


Alkyne stopper 7

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

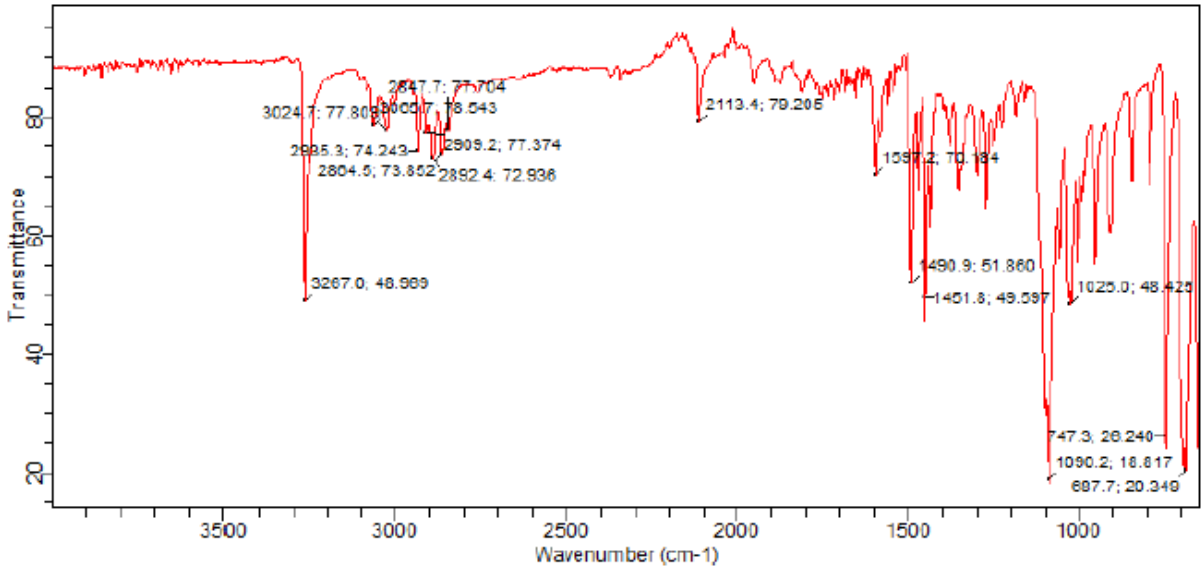


^{13}C NMR ($CDCl_3$, 100 MHz)

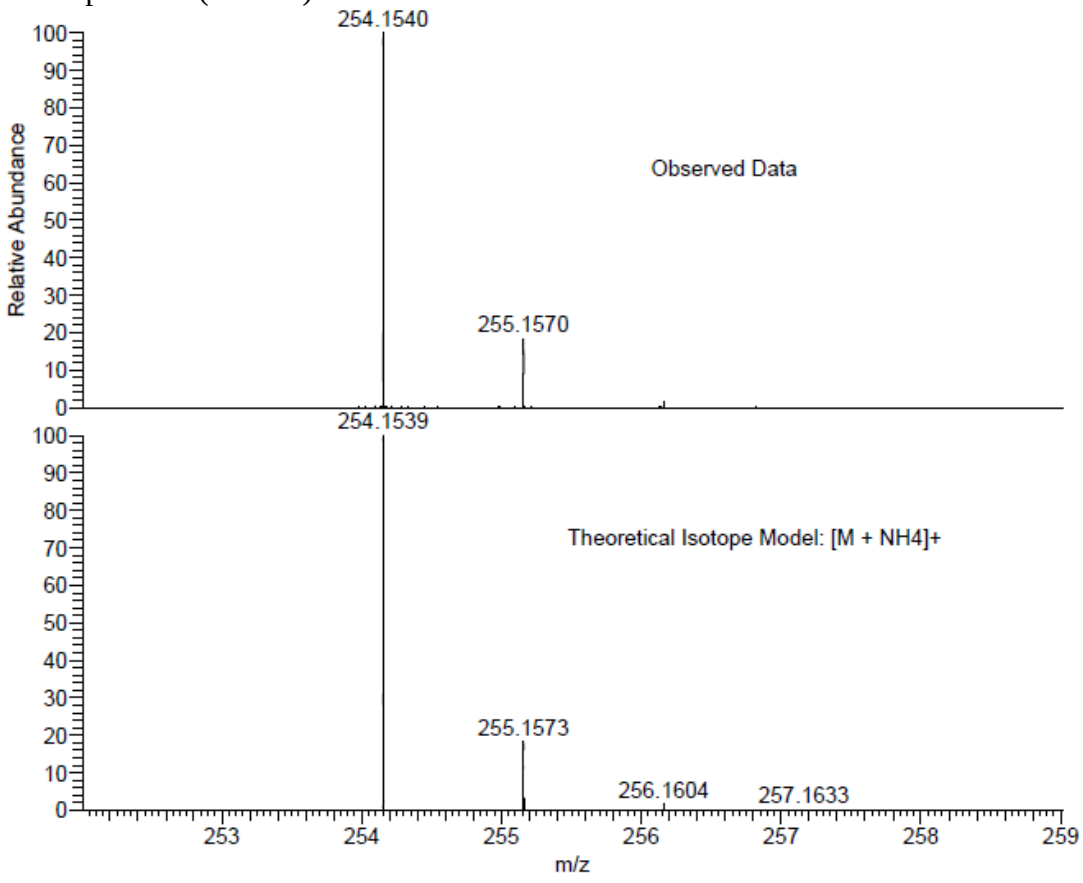


Alkyne stopper 7

IR Spectrum (neat)

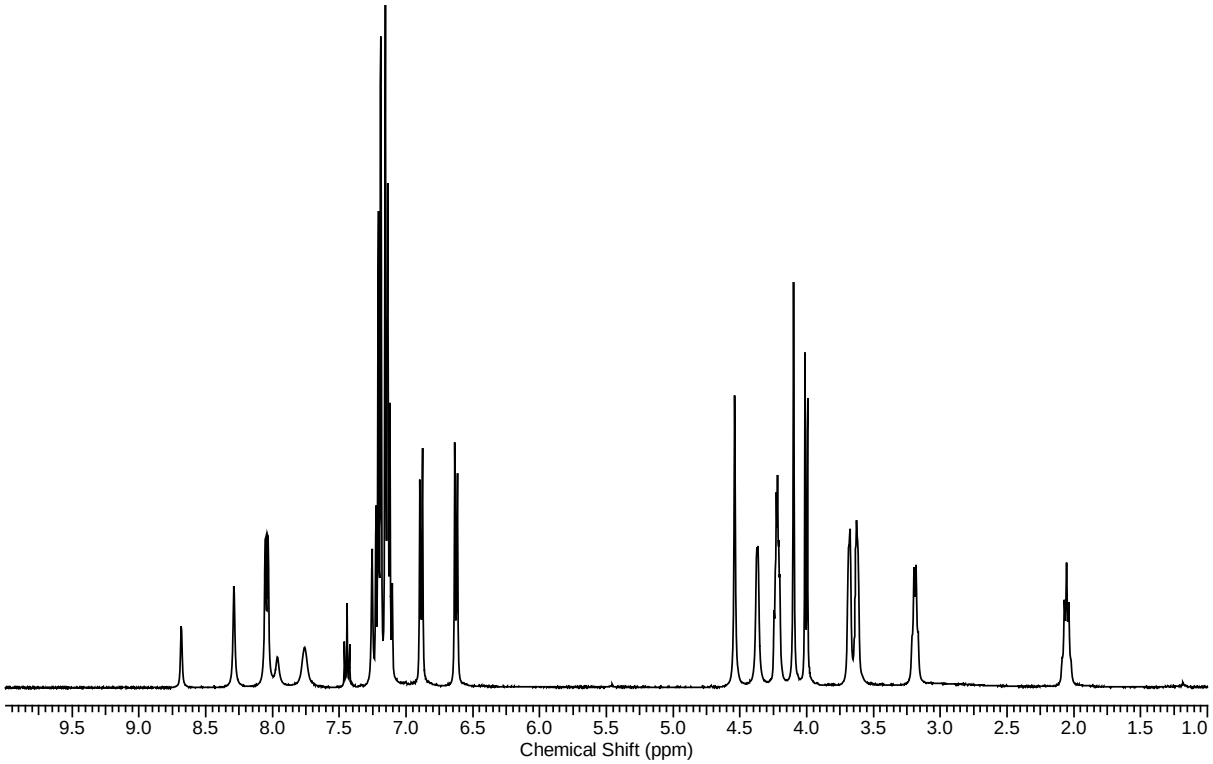


Mass Spectrum (ES +ve)

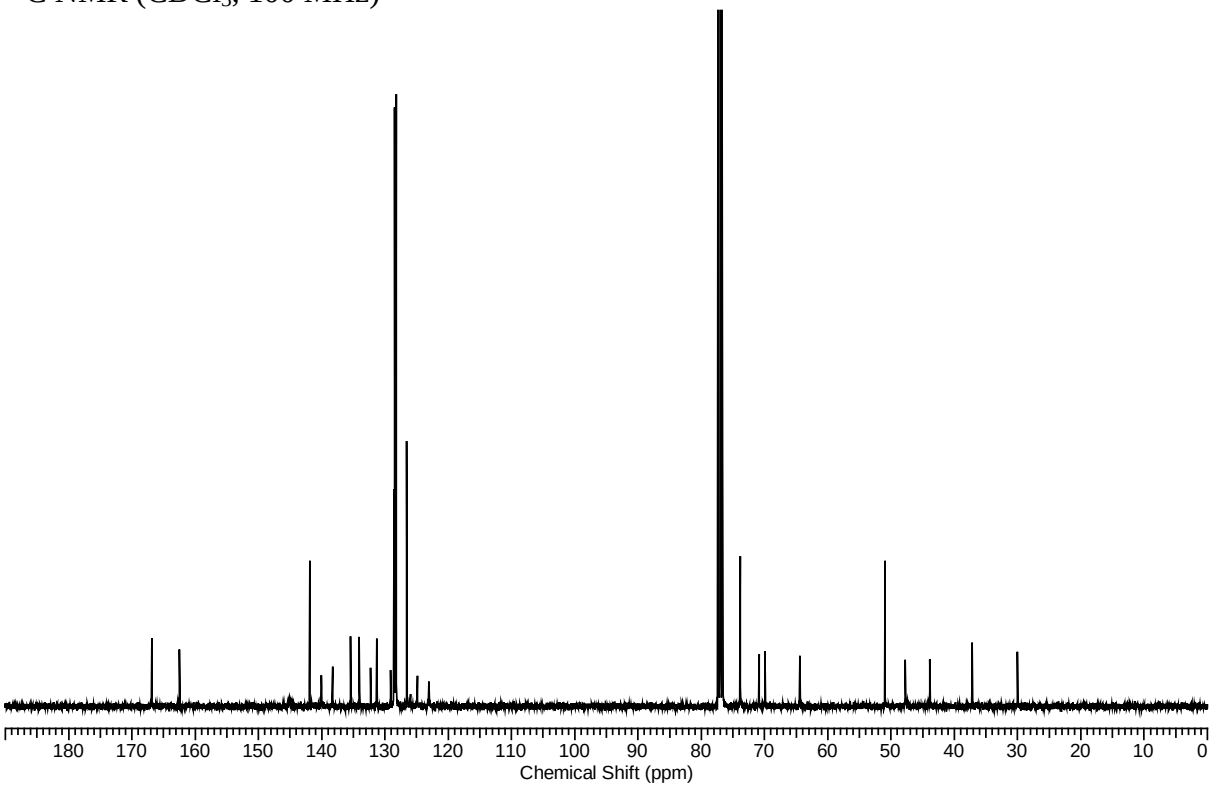


Rotaxane 8

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

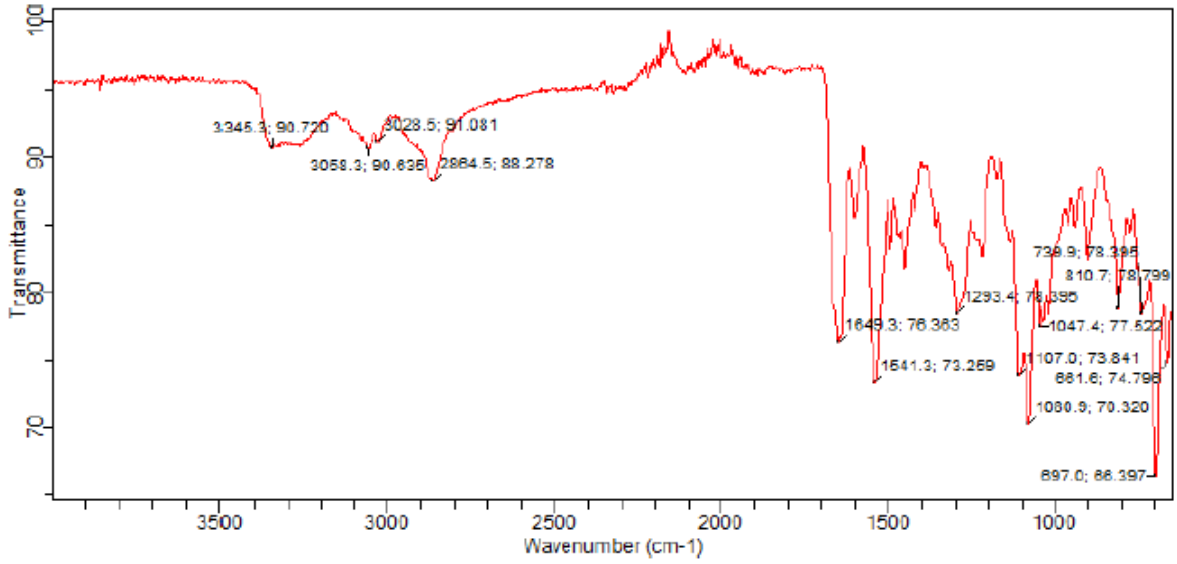


^{13}C NMR ($CDCl_3$, 100 MHz)

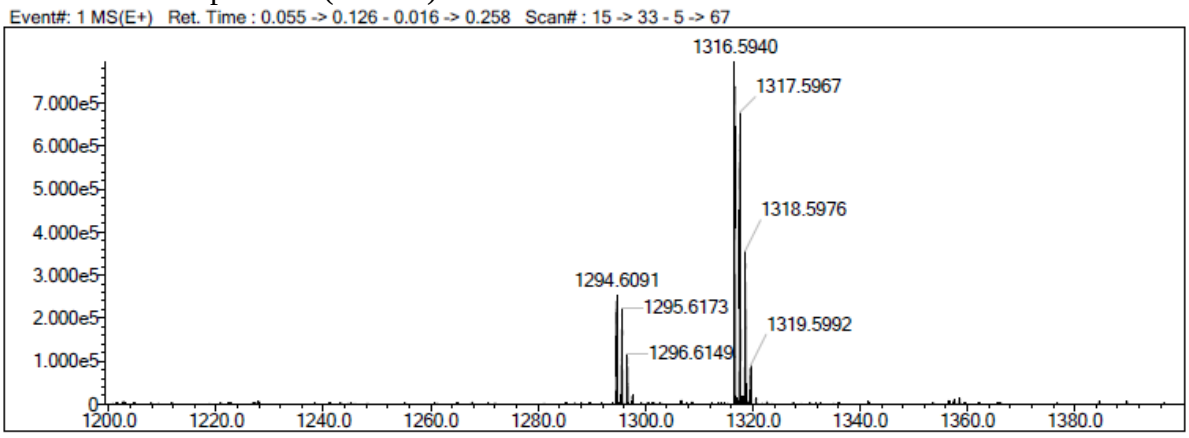


Rotaxane 8

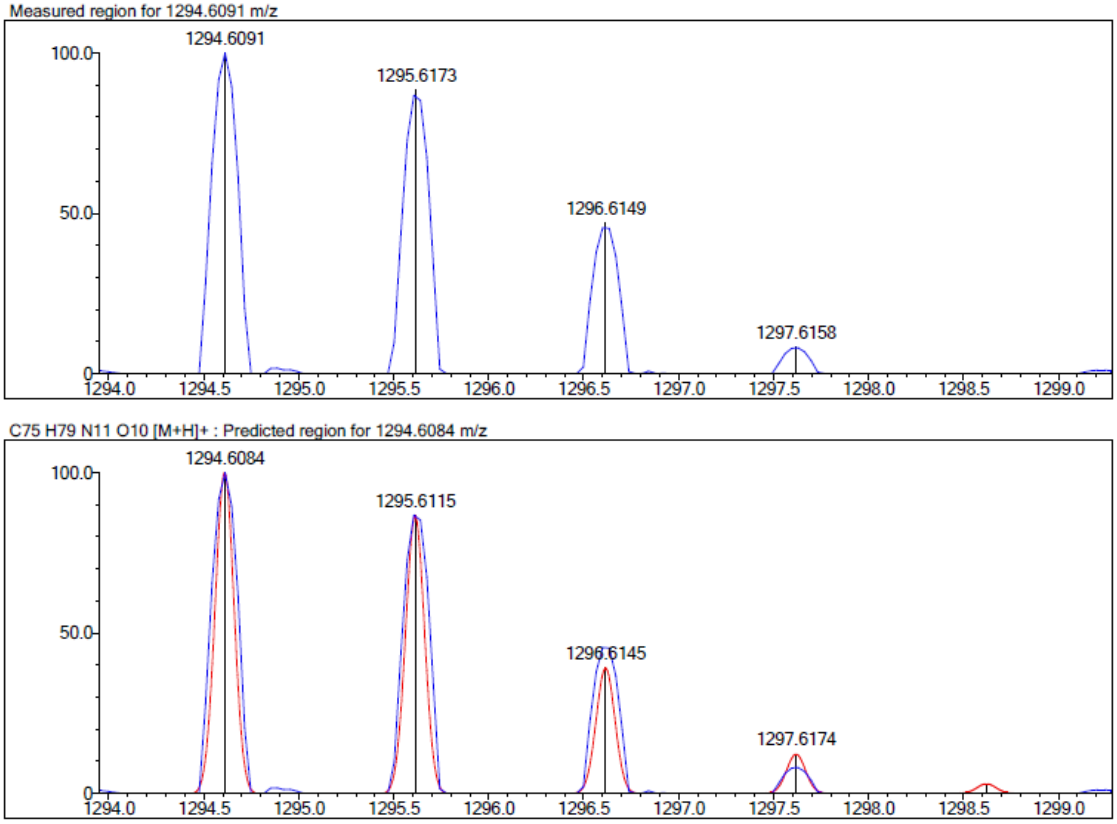
IR Spectrum (neat)

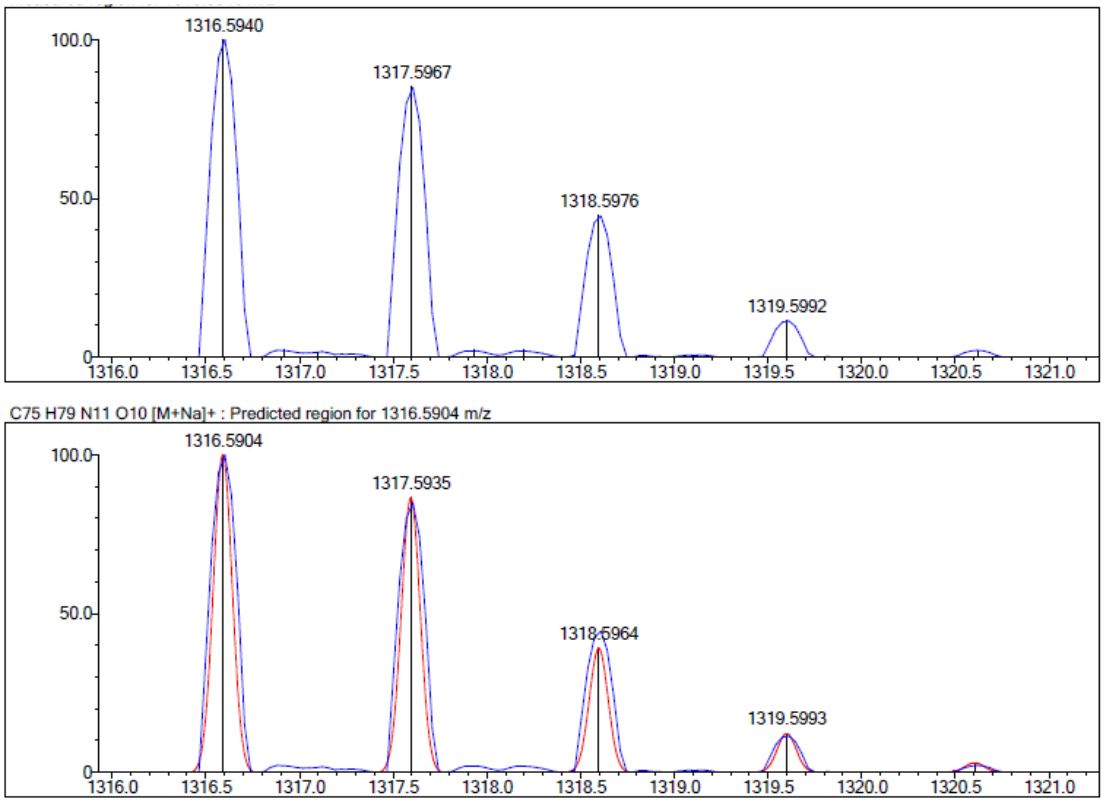


Low Res Mass Spectrum (ES +ve)



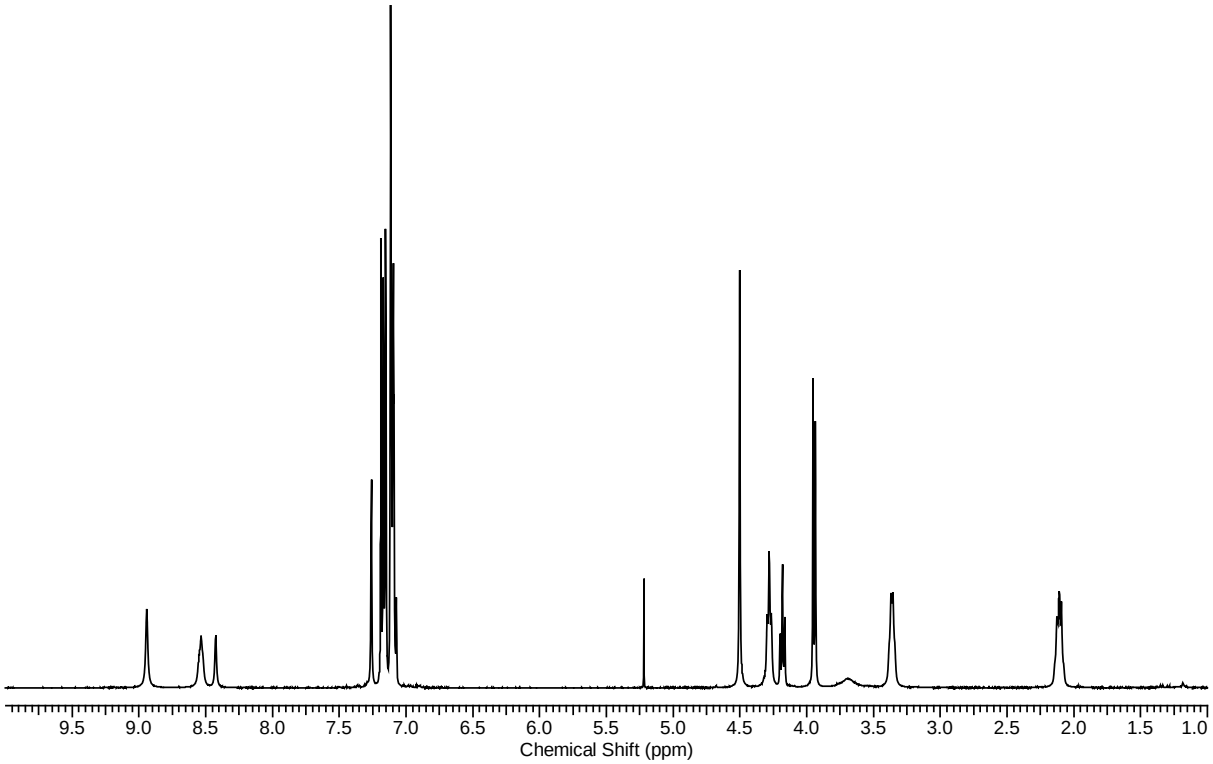
High Res Mass Spectra (ES +ve)



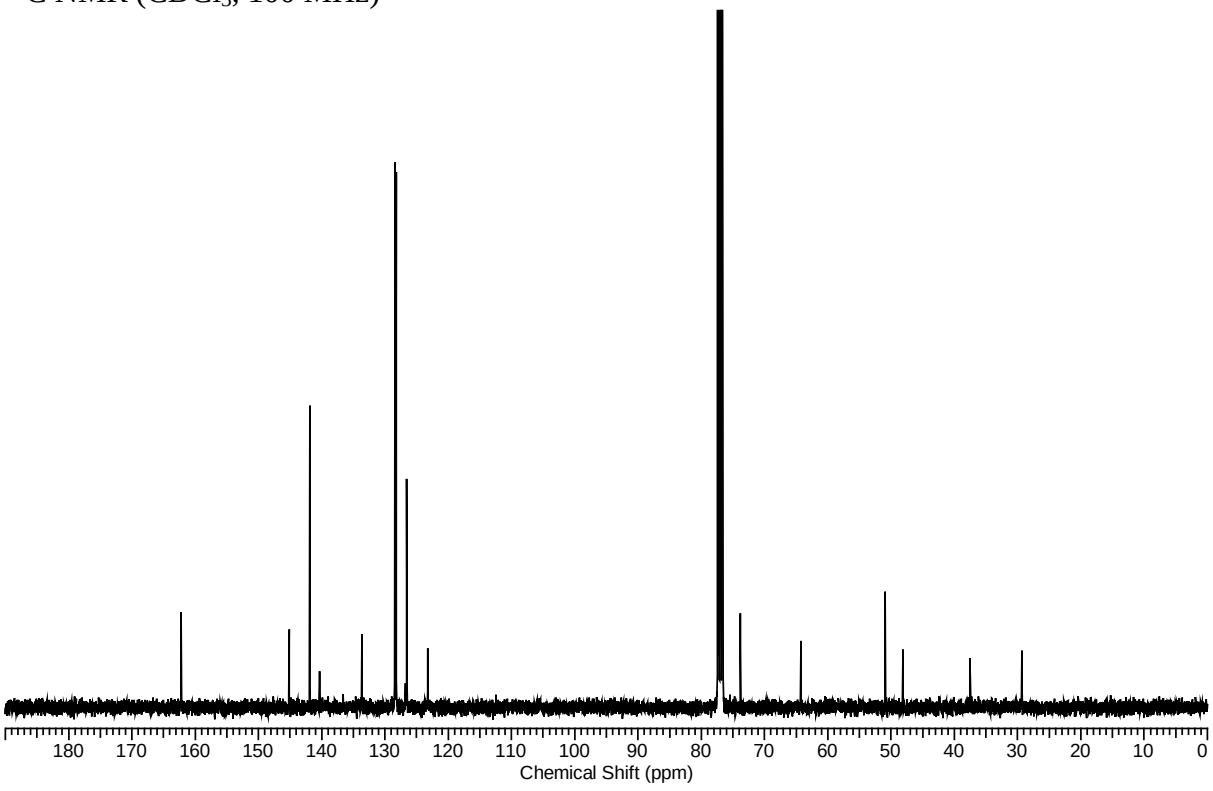


Axle 10

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

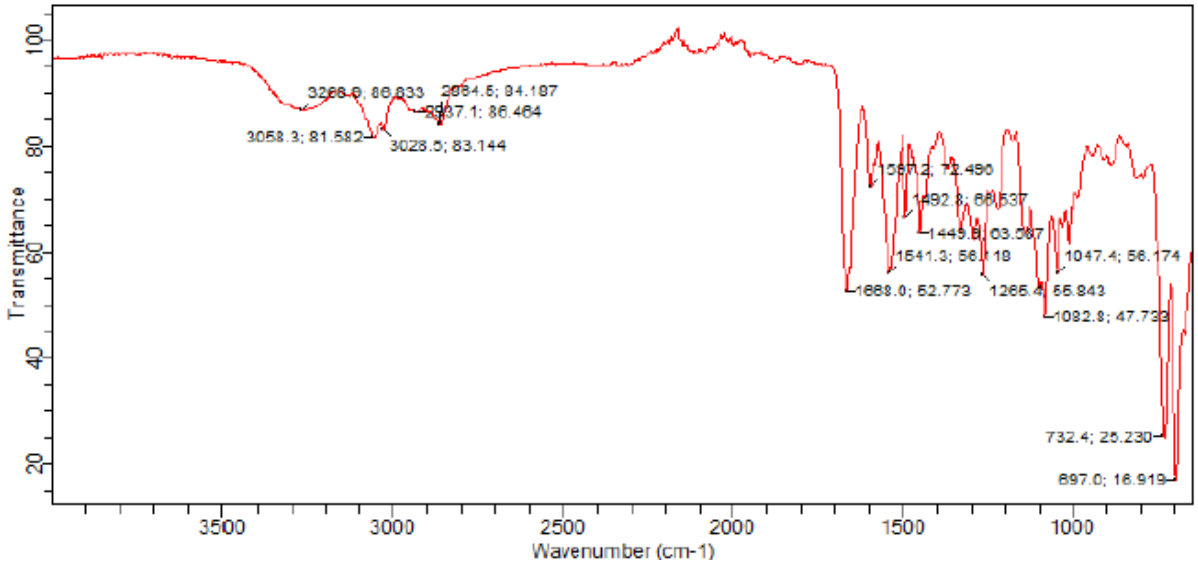


^{13}C NMR ($CDCl_3$, 100 MHz)

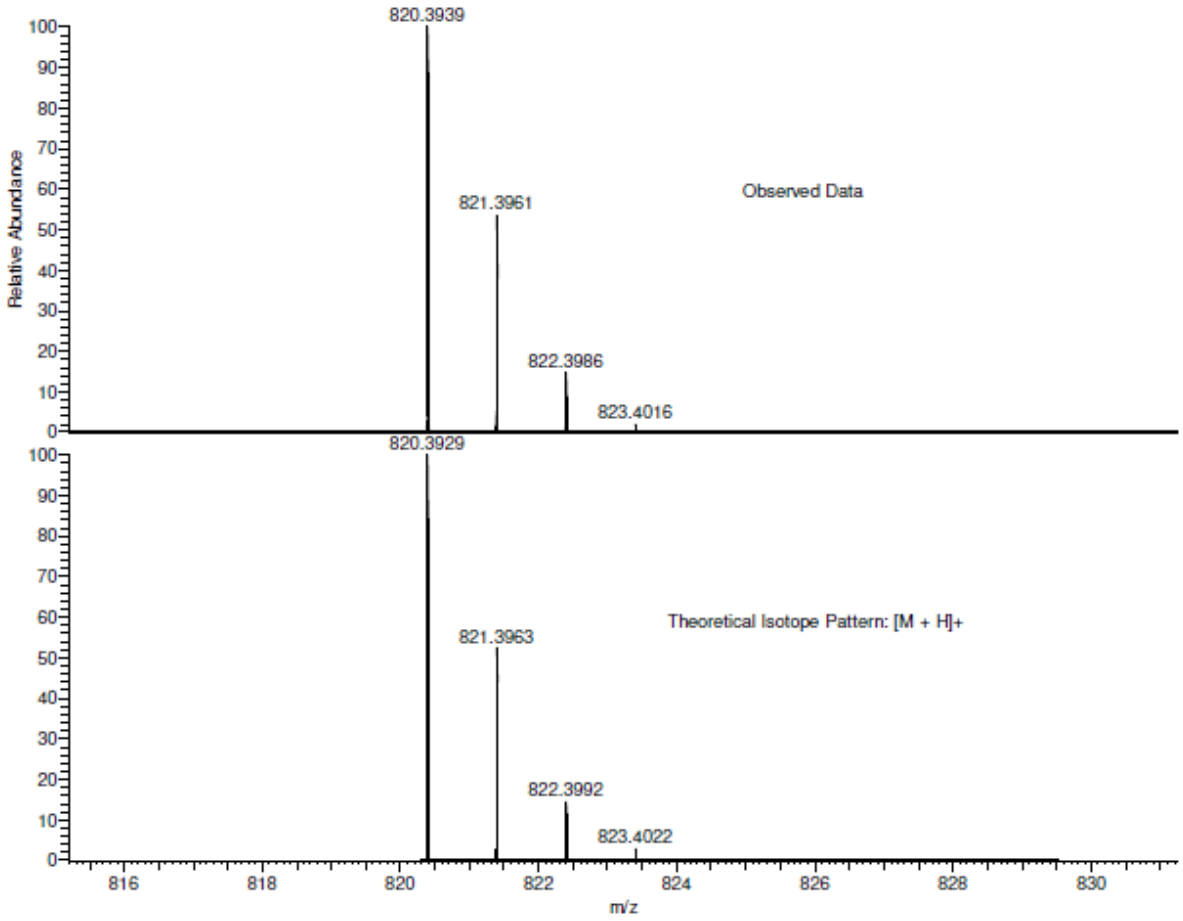


Axle 10

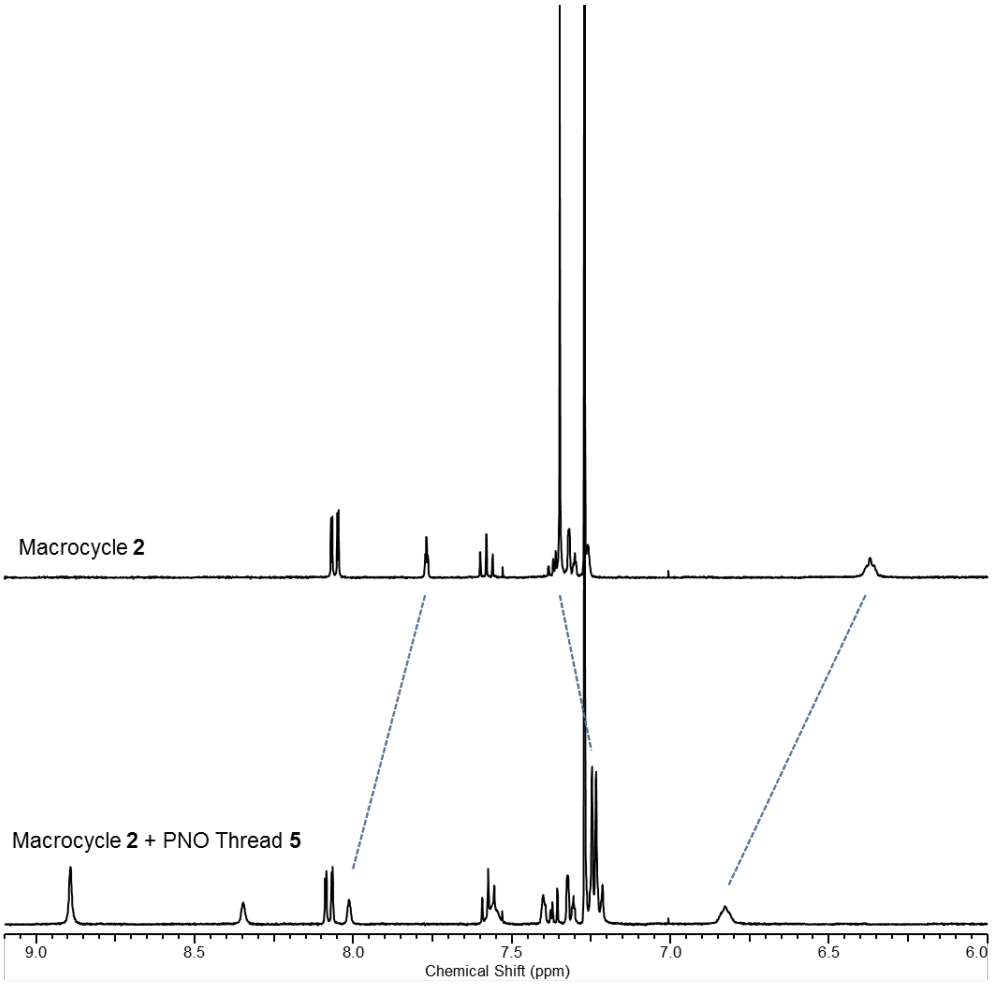
IR Spectrum (neat)



Mass Spectrum (ES +ve)



Attempted formation of pseudo-rotaxane 2·5:
^{1}H NMR spectra ($CDCl_3$, 0.5 mM, 400 MHz, 298 K)



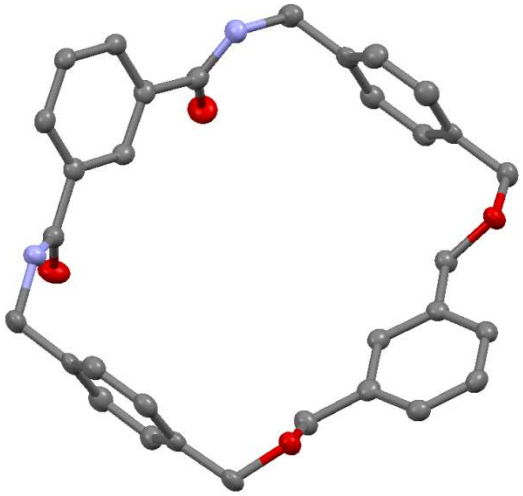
The upfield shift of the aromatic protons of macrocycle **2** is only ~ 0.025 ppm (compared to an average of ~ 0.5 ppm for the equivalent protons of macrocycle **1**).

The significant downfield shifts of the amide and internal isophthalamide proton of **2** are attributed to hydrogen bonding of the pyridine-*N*-oxide thread **5** predominantly *perching on* and **not** *threading through* macrocycle **2**.

Part III: Crystallographic Data

Macrocycle 2

Single crystals of macrocycle **2** were grown by slow evaporation of a chloroform solution. A suitable crystal was selected and the crystal was mounted on a MITIGEN holder using Paratone-N oil on a SuperNova, Dual, Cu at zero, AtlasS2 diffractometer. The crystal was kept at 99.9(2) K during data collection. Using Olex2,[3] the structure was solved with the ShelXT[4] structure solution program using Direct Methods and refined with the ShelXL[5] refinement package using Least Squares minimisation.



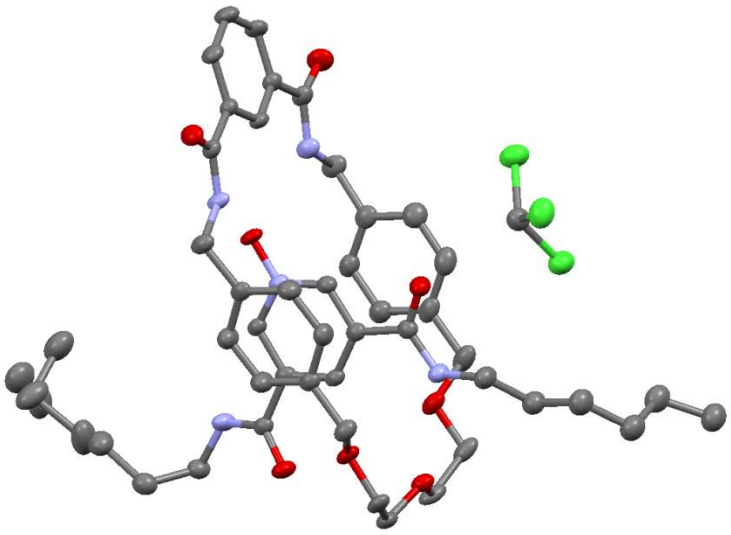
*X-ray crystal structure of macrocycle **2**. Thermal ellipsoids are displayed at 50% probability.*

*Crystal data for macrocycle **2** (CCDC Number: 1473491):*

$C_{32}H_{30}N_2O_4$ (*M* =506.58 g/mol): monoclinic, space group $P2_1$ (no. 4), *a* = 8.7998(4) Å, *b* = 13.3320(6) Å, *c* = 12.0001(6) Å, *β* = 110.314(6)°, *V* = 1320.28(12) $Å^3$, *Z* = 2, *T* = 99.9(2) K, μ(CuKα) = 0.675 mm^{-1}, *Dcalc* = 1.274 g/cm^3, 7970 reflections measured (7.856° ≤ 2Θ ≤ 147.804°), 4647 unique (R_{int} = 0.0340, R_{sigma} = 0.0558) which were used in all calculations. The final R_1 was 0.0434 (I > 2σ(I)) and wR_2 was 0.1040 (all data).

Pseudo-rotaxane 1·5

Single crystals of pseudo-rotaxane **1·5** were grown by slow diffusion of isopropyl ether into a chloroform solution of **1** and **5**. A suitable crystal was selected and mounted on a polyimide loop using Paratone-N oil on a SuperNova, Dual, Cu at zero, AtlasS2 diffractometer. The crystal was kept at T = 99.9(3) K during data collection. Using Olex2,[3] the structure was solved with the ShelXT[4] structure solution program using Direct Methods and refined with the ShelXL[5] refinement package using Least Squares minimisation.



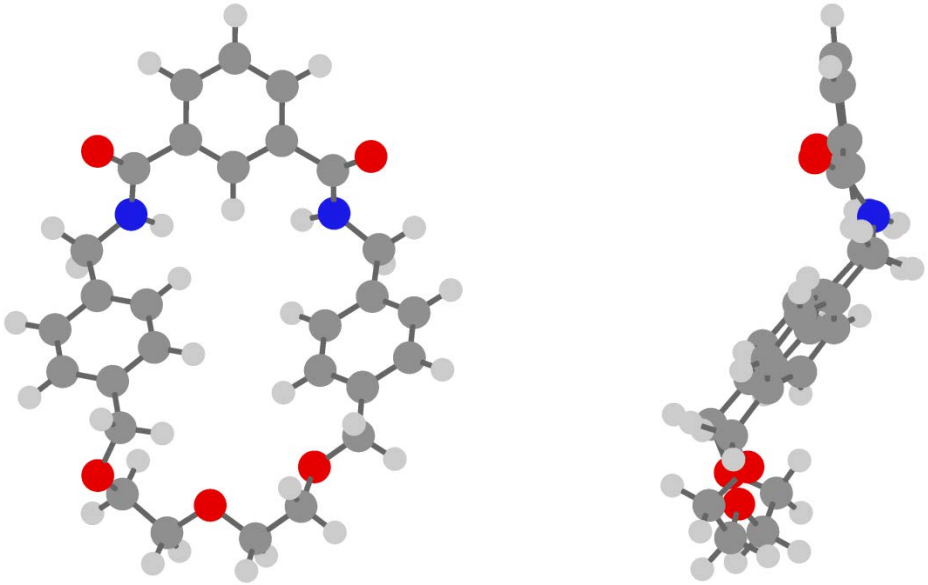
*X-ray crystal structure of pseudo-rotaxane **1·5**. Thermal ellipsoids are displayed at 50% probability.*

*Crystal data for pseudo-rotaxane **1·5** (CCDC Number: 1473492)*

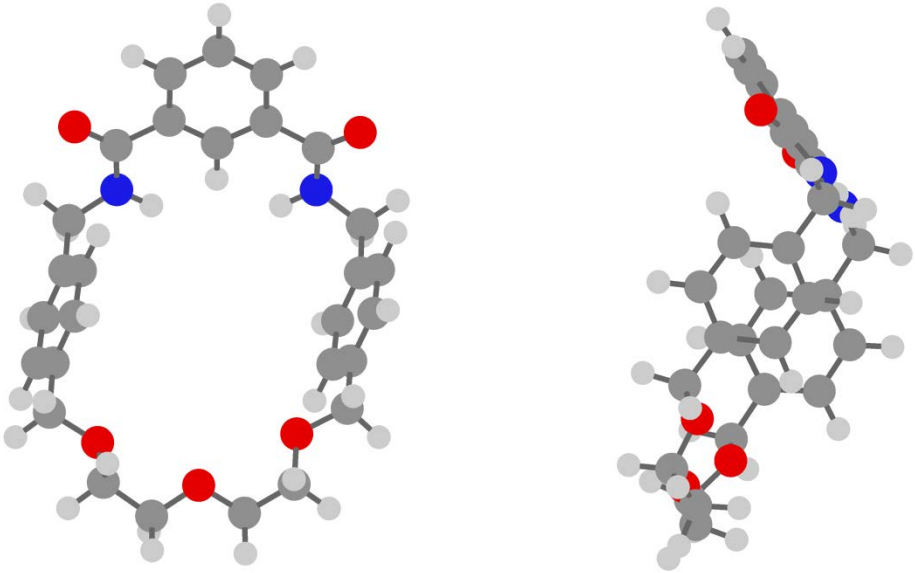
$C_{48}H_{62}Cl_3N_5O_8$, M_r = 943.37, monoclinic, $P2_1/n$ (No. 14), a = 15.0431(3) Å, b = 10.80301(18) Å, c = 29.7705(5) Å, β = 96.8269(17)°, $\alpha = \gamma = 90°$, V = 4803.73(15) Å^3, T = 99.9(3) K, Z = 4, Z' = 1, $\mu(CuK_a)$ = 2.196, 52573 reflections measured, 8552 unique (R_{int} = 0.0550) which were used in all calculations. The final wR_2 was 0.2091 (all data) and R_1 was 0.0692 (I > 2(I)).

Part IV: Computational Modelling

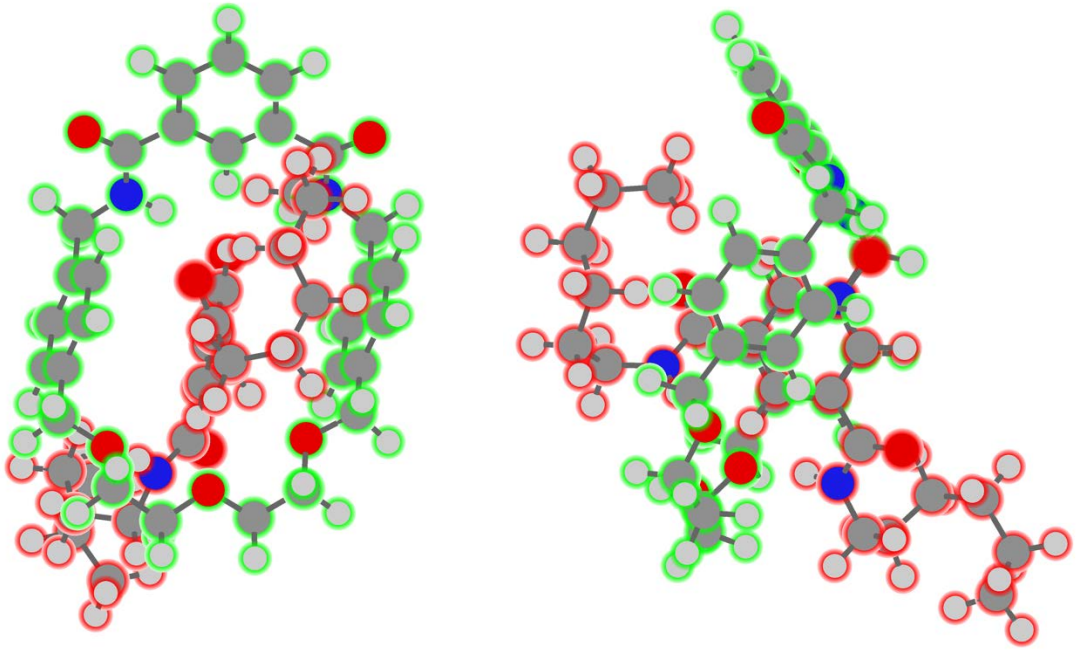
Structural Information



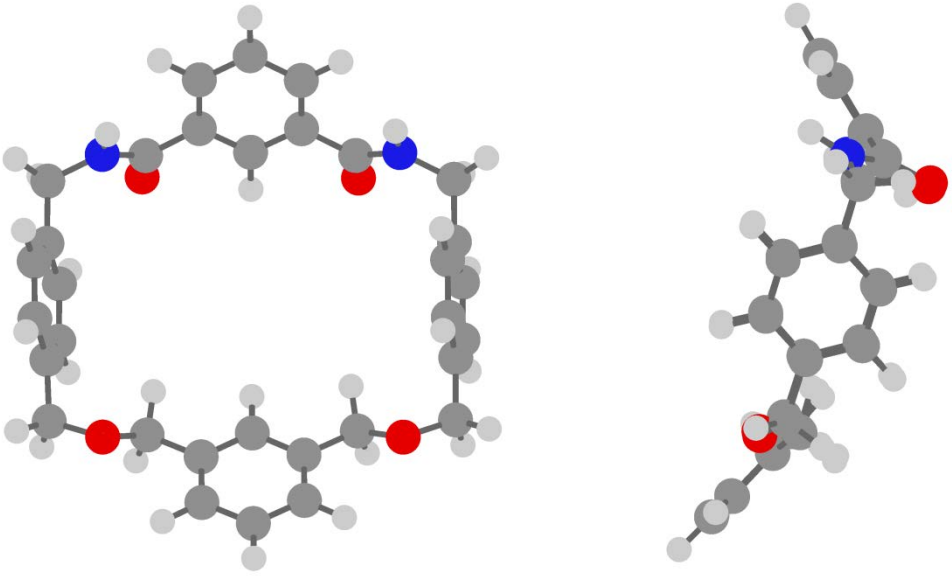
*Two views of the crystal structure of macrocycle **1**.*



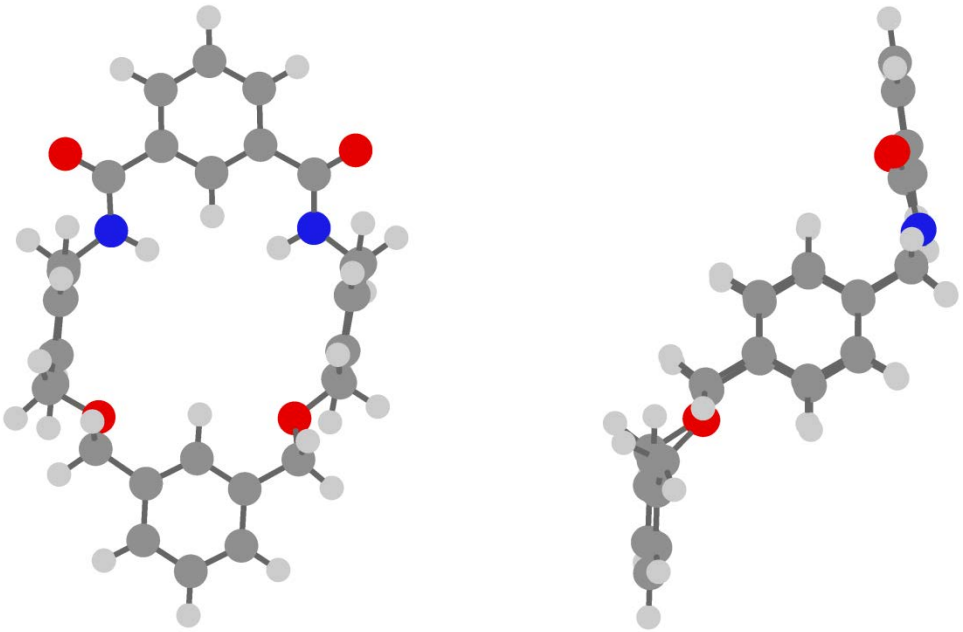
*The same two views of the optimised structure the macrocyclic component of pseudo-rotaxane **1**·**5**, highlighting the change in conformation of the macrocycle for the syn-syn thread conformation. Thread not shown for clarity.*



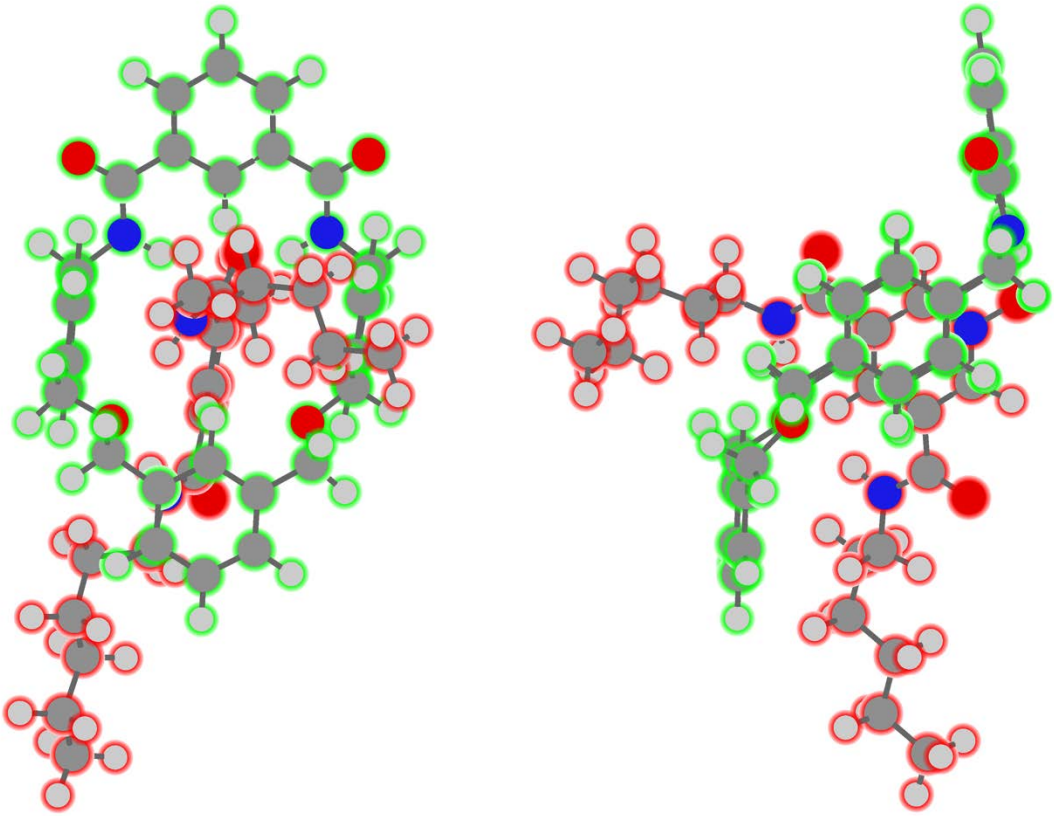
*The same two views of the optimised structure of pseudo-rotaxane **1·5**, highlighting the change in conformation of macrocycle **1** (green) for the syn-syn thread conformation; thread highlighted in red.*



*Two views of the crystal structure of macrocycle **2**.*



*The same two views of the optimised structure the macrocyclic component of pseudo-rotaxane **2·5**, highlighting the change in conformation of the macrocycle for the syn-syn thread conformation. Thread not shown for clarity.*



*The same two views of the optimised structure of pseudo-rotaxane **2·5**, highlighting the change in conformation of macrocycle **2** (green) for the syn-syn thread conformation; thread highlighted in red.*

Energetic Data

Relative energies of the thread in the three conformations considered (energies in kJ mol^{-1}):

syn-syn	5.5
syn-anti	0
anti-anti	8.5

*Relative binding energies of the pseudo-rotaxane for **1·5** and **2·5**, in each of the three thread conformations considered (energies in kJ mol^{-1}):*

	1·5	**2·5**
syn-syn	0.0	0.0
syn-anti	11.2	30.1
anti-anti	31.8	31.7

Atomic Coordinate Files Data

Reference for supplied structure files, including total energies of structures computed as discussed in the manuscript (B3LYP/6-31G with solvent and dispersion corrections) in atomic units (Hartree). It was confirmed that none of the structures had any imaginary frequencies; each is a minimum on its respective potential energy surface.*

Filename	**Structure**	**Energy**
1.mol2	Minimised structure of **1**	–1570.75963666
2.mol2	Minimised structure of **2**	–1647.97900279
5.mol2	Minimised structure of **5**	–1132.67614542
1-5_ss.mol2	Minimised structure of **1·5** with *syn-syn* thread	–2703.52770075
1-5_sa.mol2	Minimised structure of **1·5** with *syn-anti* thread	–2703.52345266
1-5_aa.mol2	Minimised structure of **1·5** with *anti-anti* thread	–2703.51558226
2-5_ss.mol2	Minimised structure of **2·5** with *syn-syn* thread	–2780.74006196
2-5_sa.mol2	Minimised structure of **2·5** with *syn-anti* thread	–2780.72858493
2-5_aa.mol2	Minimised structure of **2·5** with *anti-anti* thread	–2780.72799531

Part V: References

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2) J. A. Wisner, P. D. Beer and M. G. B. Drew, *Angew. Chem. Int. Ed.*, 2001, **40**, 3606-3609.
3) O. V. Dolomanov, L. J. Bourhis, R. J. Gildea, J. A. K. Howard and H. Puschmann, *J. Appl. Cryst.*, 2009, **42**, 339-341.
4) G. M. Sheldrick, *Acta Cryst. A*, 2015, **71**, 3-8.
5) G. M. Sheldrick, *Acta Cryst. A*, 2008, **64**, 112-122.