Electronic Supplementary Material (ESI) for Organic & Biomolecular Chemistry.
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Electronic Supplementary Information

Rapidly accessible "click" rotaxanes utilizing a single amide hydrogen bond motif

Beth E. Fletcher, Michael J. G. Peach and Nicholas H. Evans*

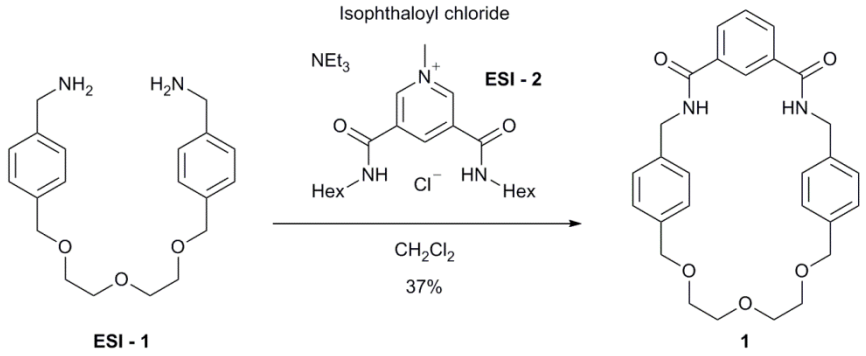
Contents

Part I: Synthesis

Additional Notes on Experimental Procedures

Preparation of macrocycle **1**

The synthesis of macrocycle **1** using semi-high dilution macrocyclisation conditions in 12% yield has been reported previously.[1] We have since adapted the template synthesis method of Hancock and Beer.[2]



*Scheme ESI-1: Templated synthesis of macrocycle **1***

Dimethanamine **ESI-1**[3] (169 mg, 0.49 mmol) and methyl pyridinium chloride template **ESI-2**[4, 5] (188 mg, 0.49 mmol) were dissolved in dry CH_2Cl_2 (15 mL) under an Ar (g) atmosphere. Then NEt_3 (0.14 mL, 99 mg, 0.98 mmol) was added, immediately followed by the dropwise addition of a solution of isophthaloyl chloride (100 mg, 0.49 mmol) in dry CH_2Cl_2 (10 mL). The reaction was stirred for 30 minutes under an Ar (g) atmosphere. Then, the reaction mixture was washed with 10% HCl (aq) (2 × 25 mL) and H_2O (2 × 25 mL). The organic layer was dried ($MgSO_4$), filtered and solvent removed *in vacuo*. The crude material was submitted to silica gel column chromatography (9:1 EtOAc/CH_2Cl_2) to yield the title compound as a white solid (86 mg, 37%).

Mp 192-196 °C (Lit: 198-200 °C).[1]

R_f = 0.54, 9:1 EtOAc/CH_2Cl_2 (Lit: R_f = 0.55, 9:1 EtOAc/CH_2Cl_2).[1]

δH(400 MHz; $CDCl_3$) 7.97 (2H, dd, ^3J = 7.7 Hz ^4J = 0.9 Hz), 7.79 (1H, s), 7.50 (1H, t, ^3J = 7.7 Hz, C^1H), 7.25-7.30 (8H, m), 6.76 (2H, br s), 4.49-4.53 (8H, m), 3.60-3.69 (8H, m).

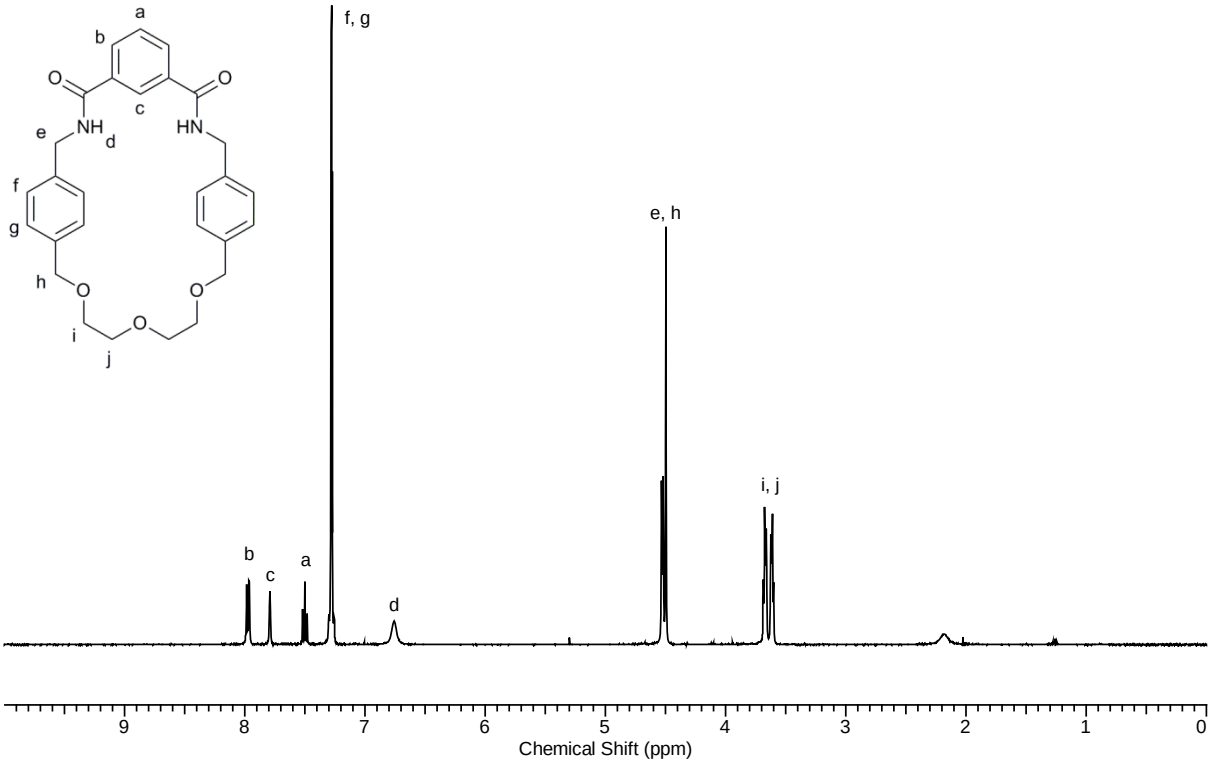
δC(100 MHz; $CDCl_3$) 166.9, 137.5, 137.2, 134.6, 131.0, 129.5, 128.6, 128.3, 123.7, 72.9, 70.5, 69.5, 44.1.

^{1}H and ^{13}C NMR data are consistent with literature values.[1]

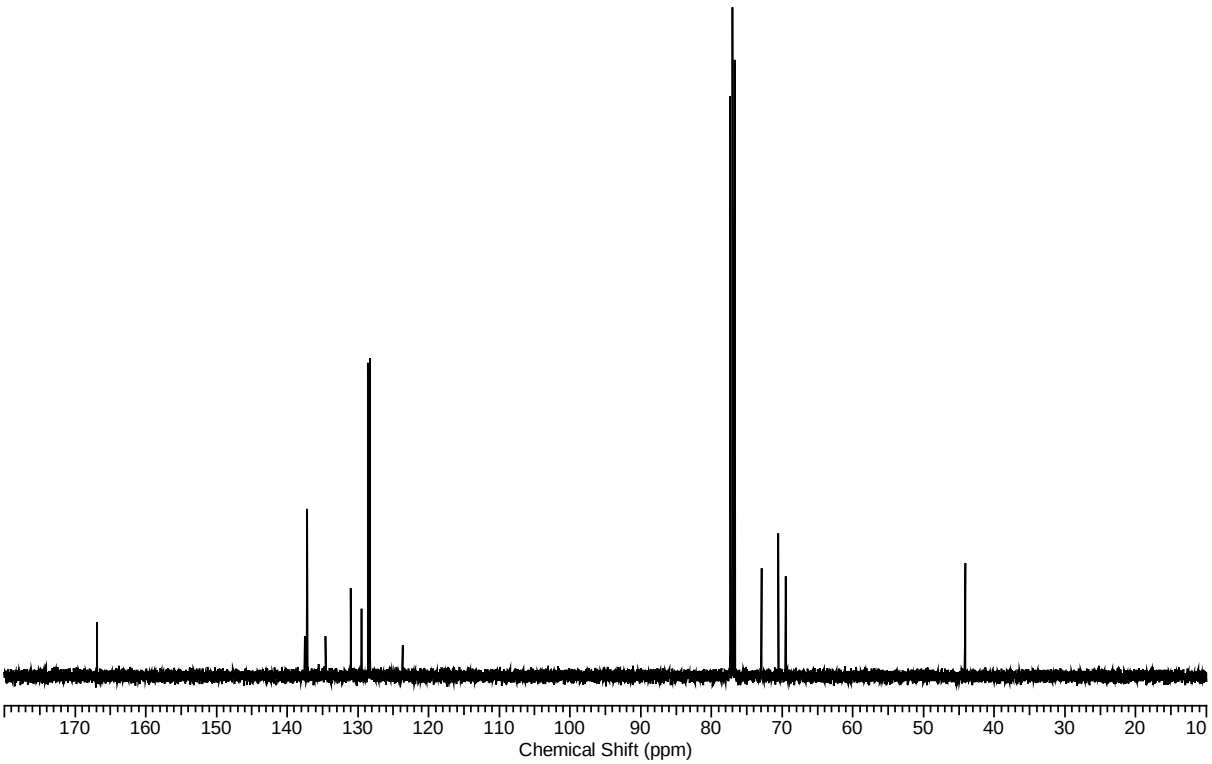
Part II: Characterisation Spectra

Macrocycle 1

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

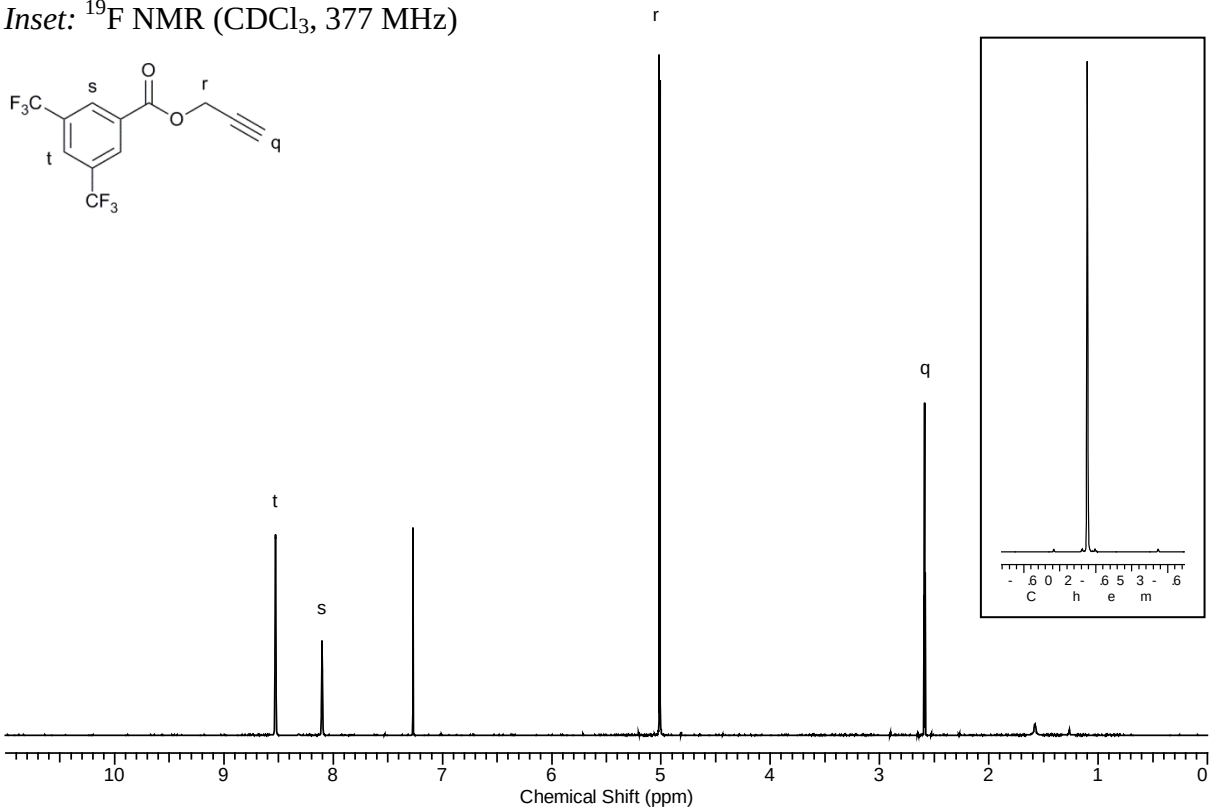


^{13}C NMR ($CDCl_3$, 100 MHz)

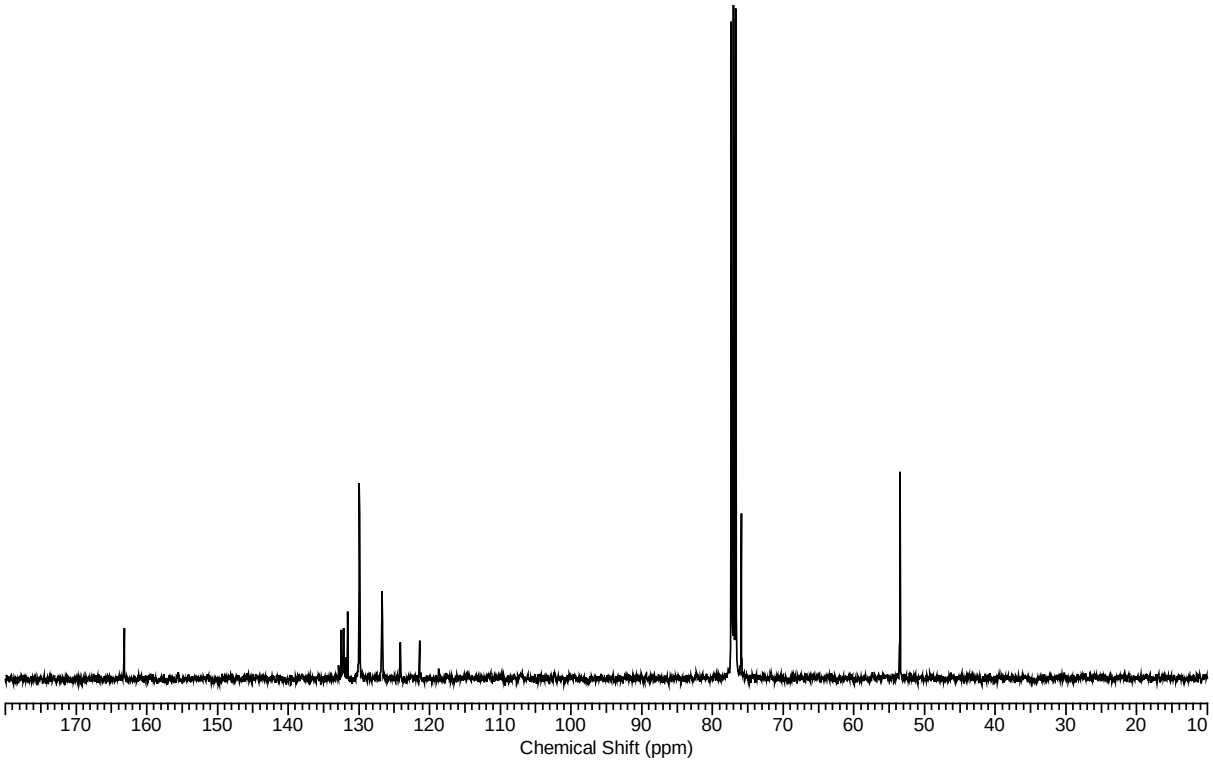


Alkyne 3

^{1}H NMR ($CDCl_3$, 400 MHz)
Inset: ^{19}F NMR ($CDCl_3$, 377 MHz)

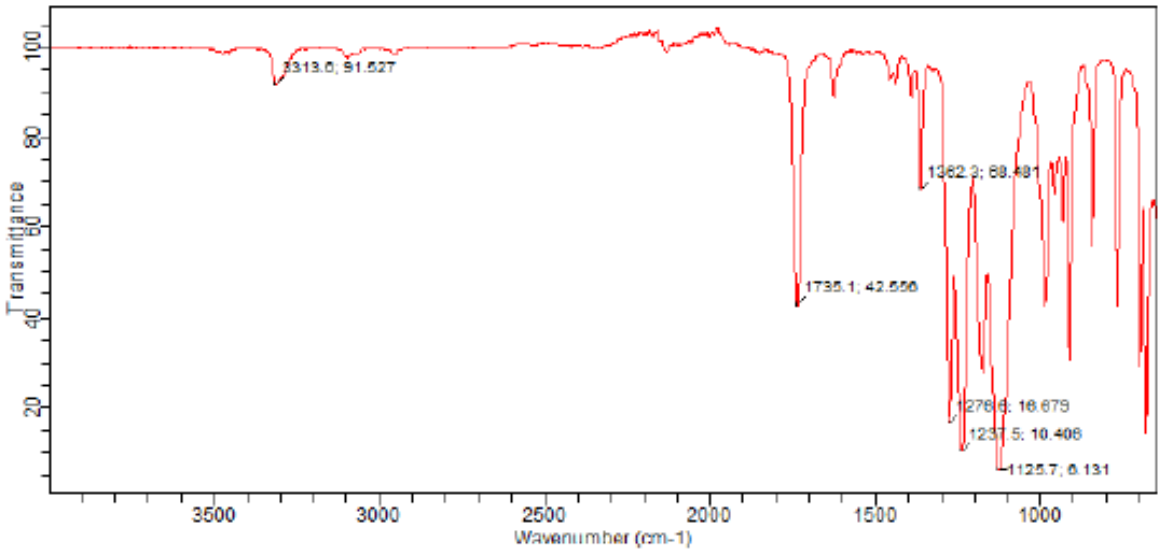


^{13}C NMR ($CDCl_3$, 100 MHz)

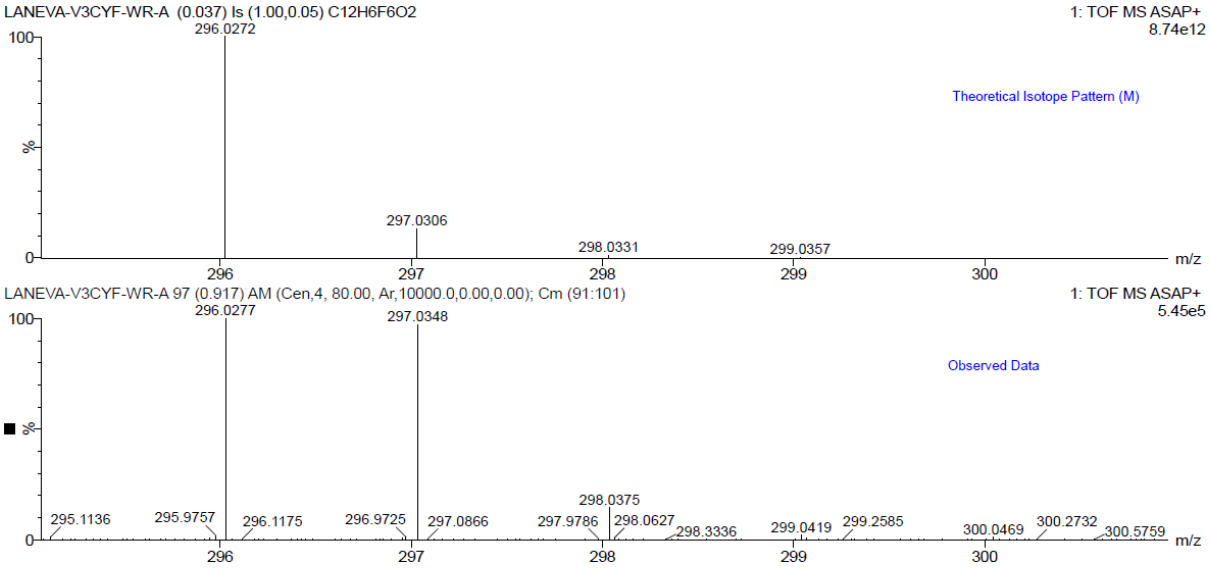


Alkyne 3

IR Spectrum (neat)

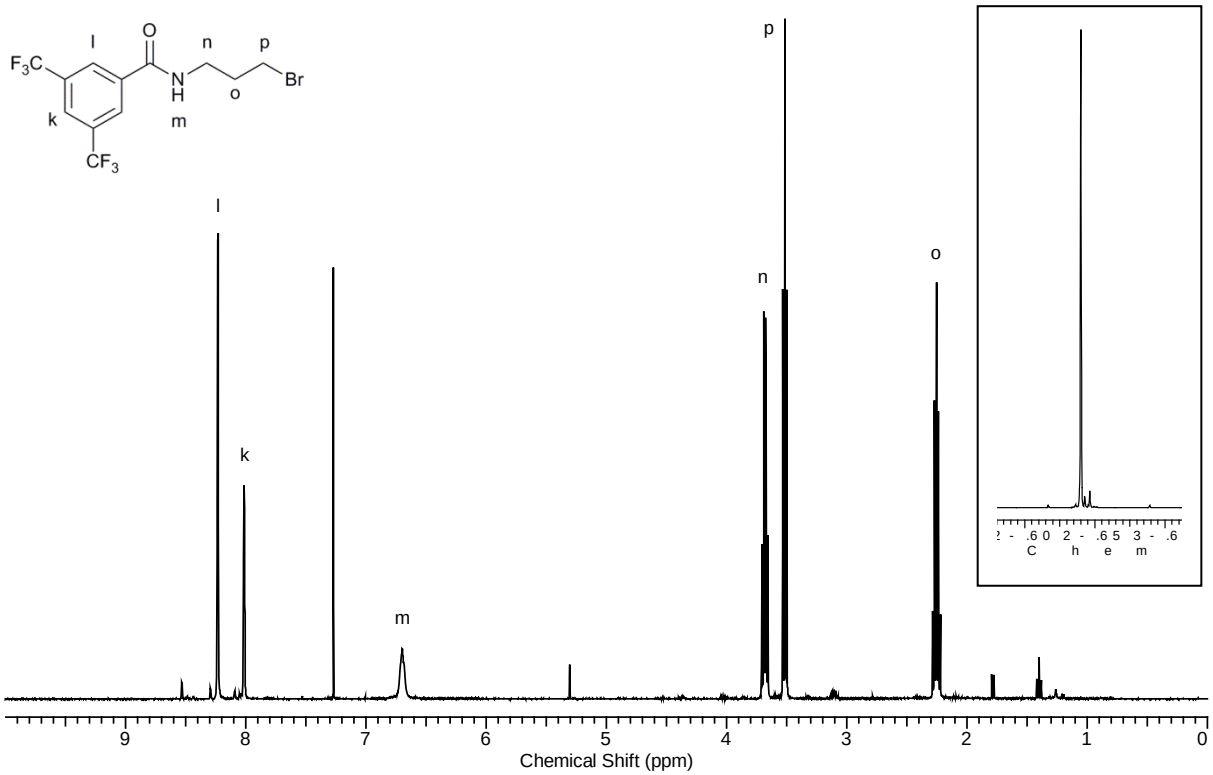


Mass Spectrum (ASAP +ve)

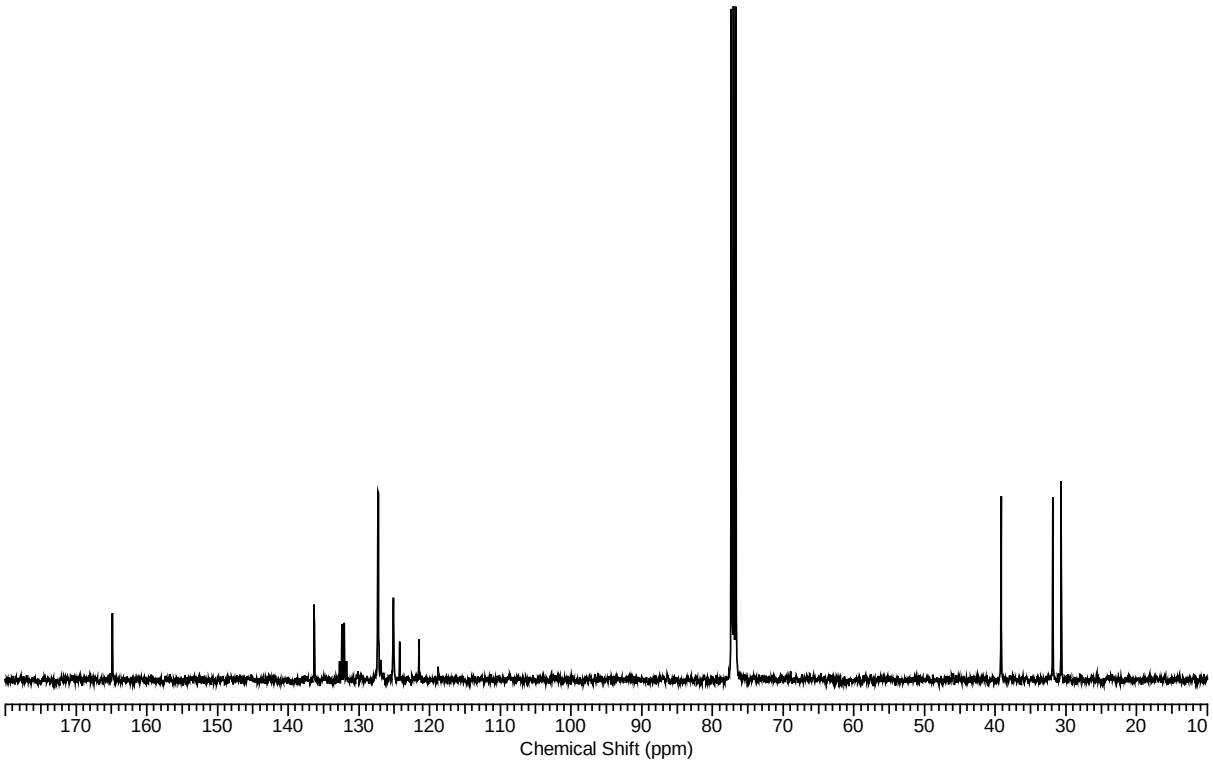


Bromo-amide 4

^{1}H NMR ($CDCl_3$, 400 MHz)
Inset: ^{19}F NMR ($CDCl_3$, 377 MHz)

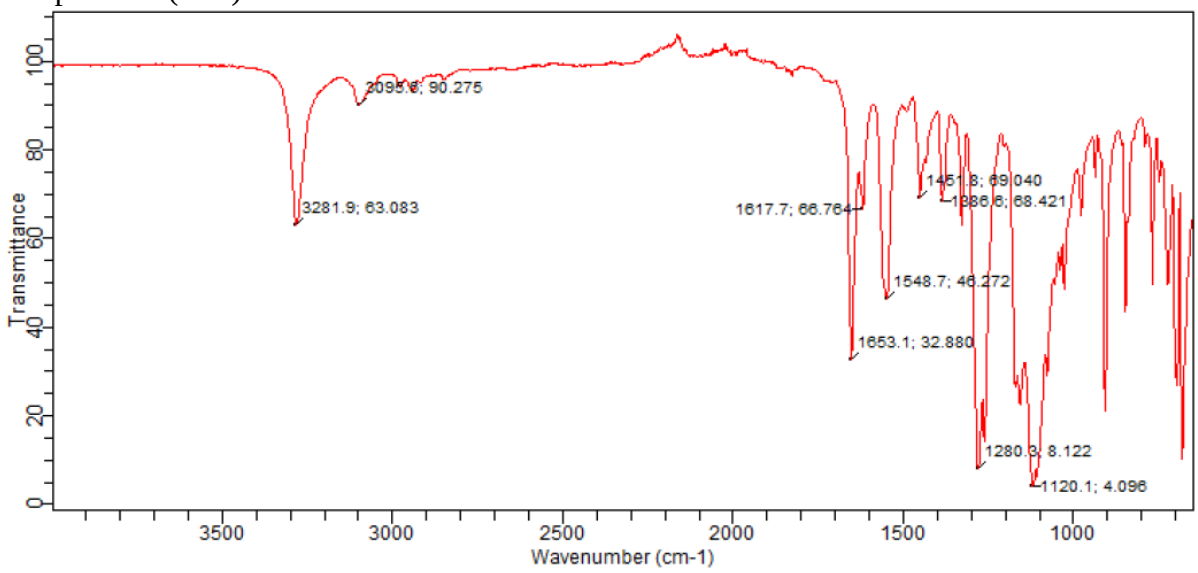


^{13}C NMR ($CDCl_3$, 100 MHz)

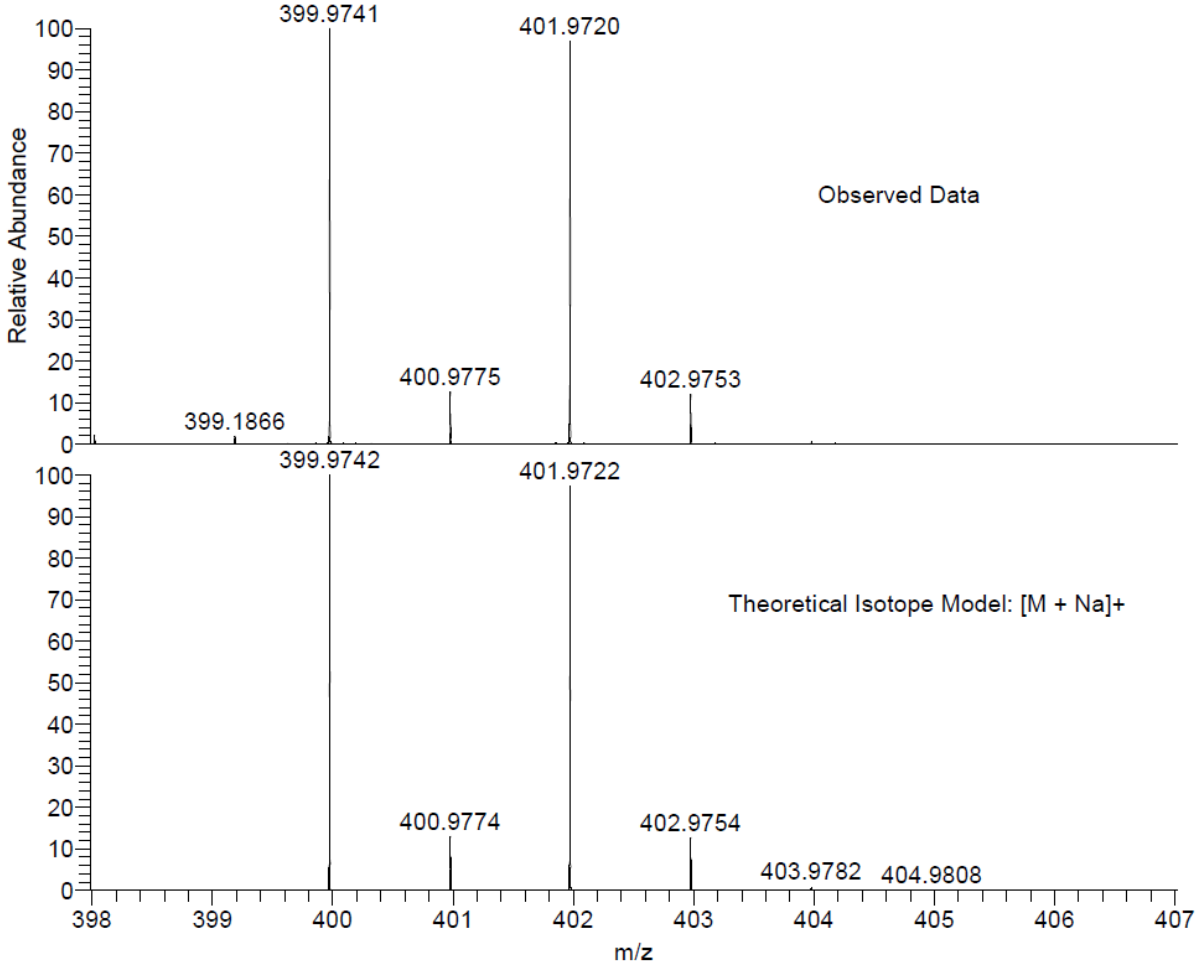


Bromo-amide 4

IR Spectrum (neat)

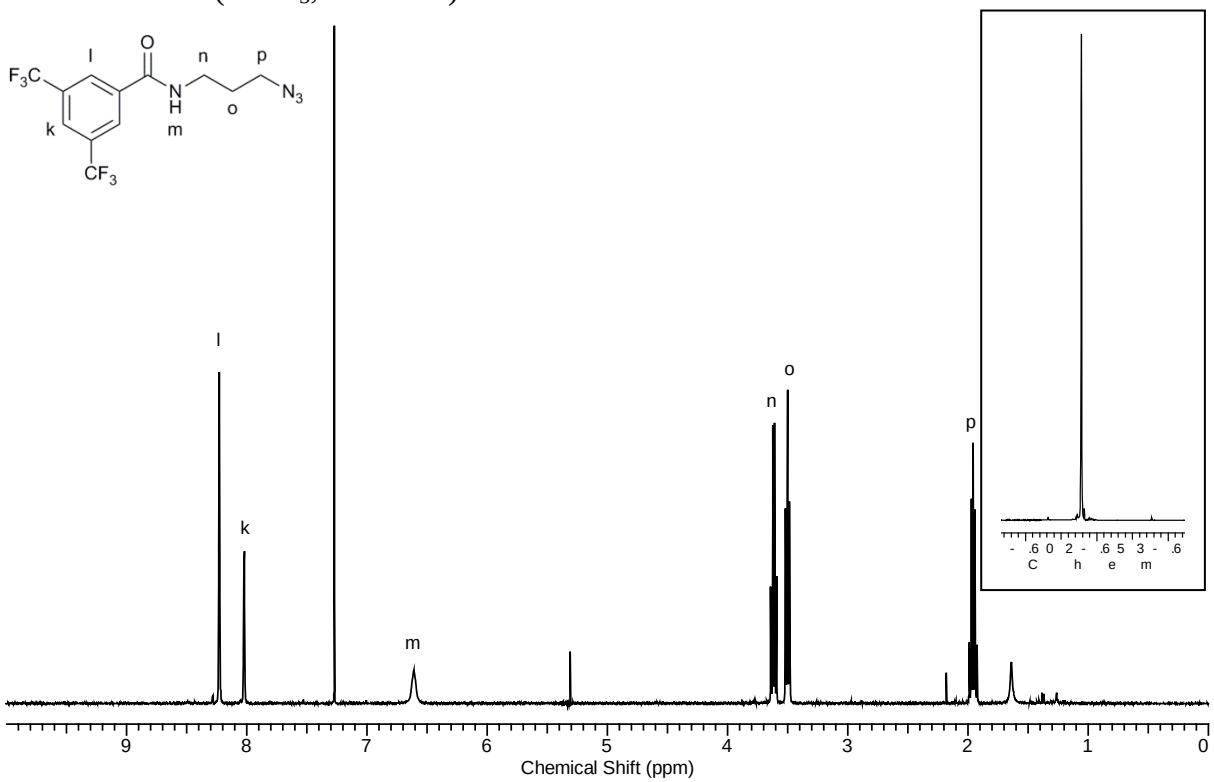


Mass Spectrum (ES +ve)

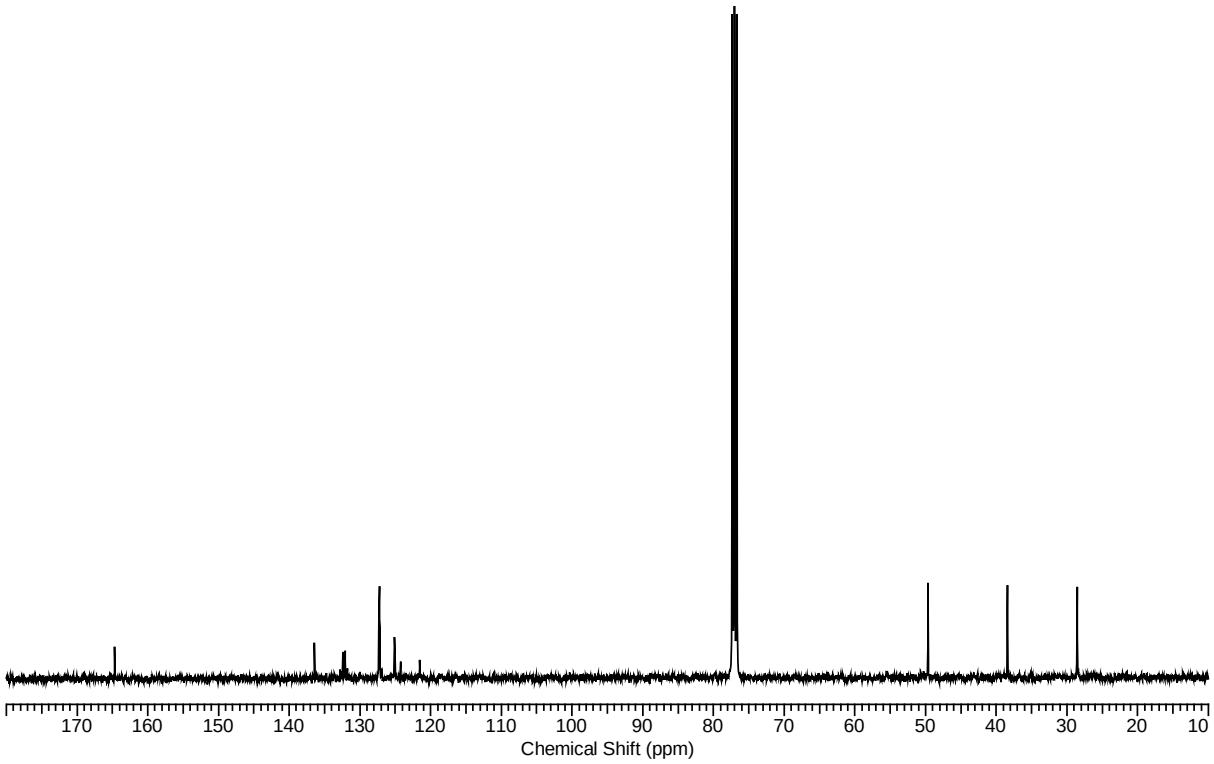


Azide 5

^{1}H NMR ($CDCl_3$, 400 MHz)
Inset: ^{19}F NMR ($CDCl_3$, 377 MHz)

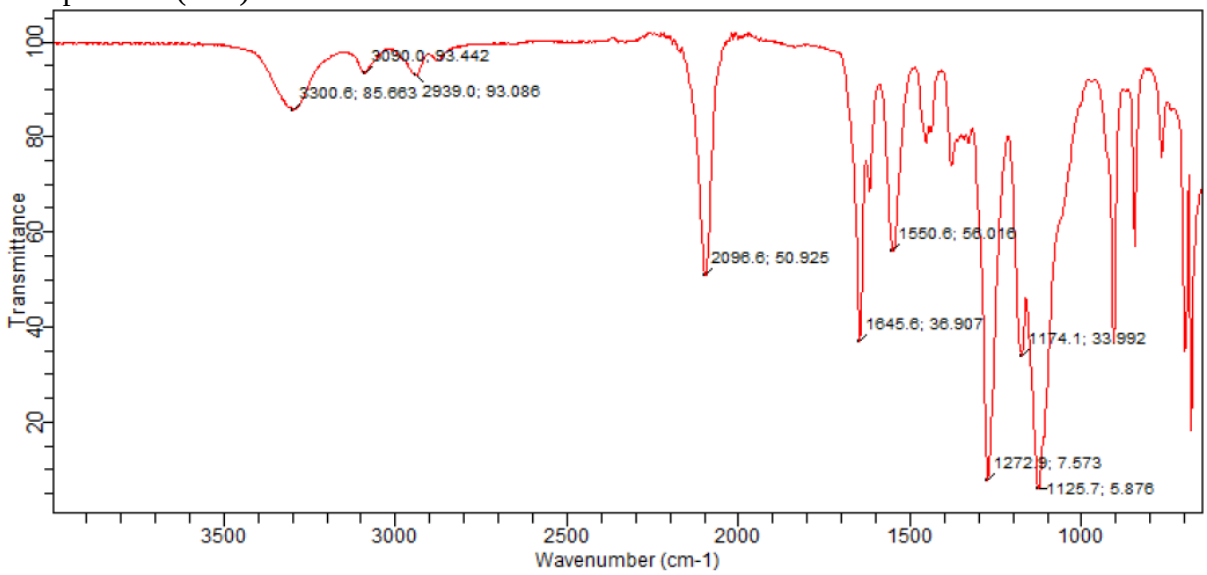


^{13}C NMR ($CDCl_3$, 100 MHz)

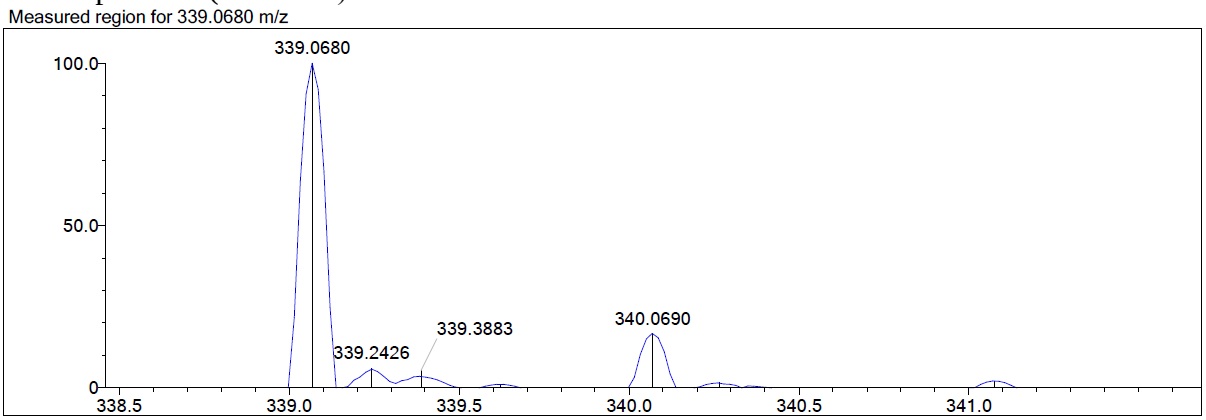


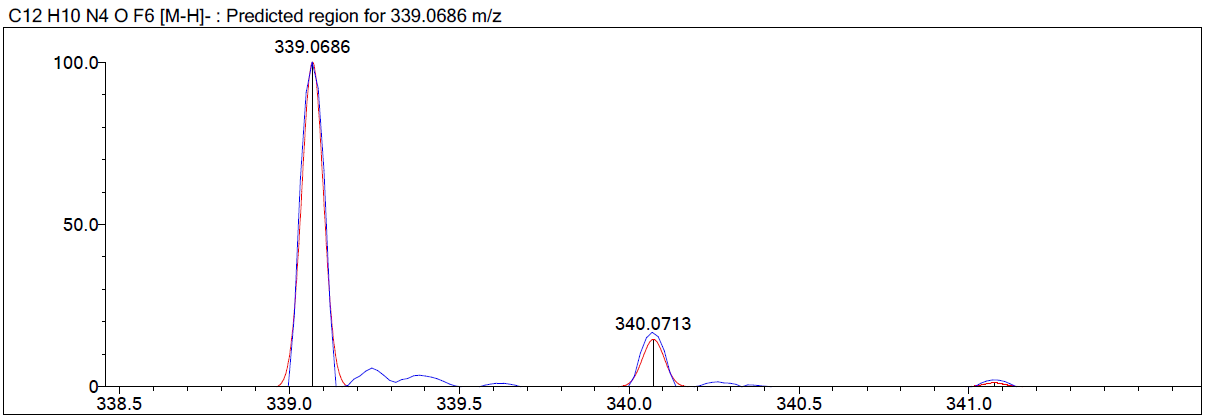
Azide 5

IR Spectrum (neat)



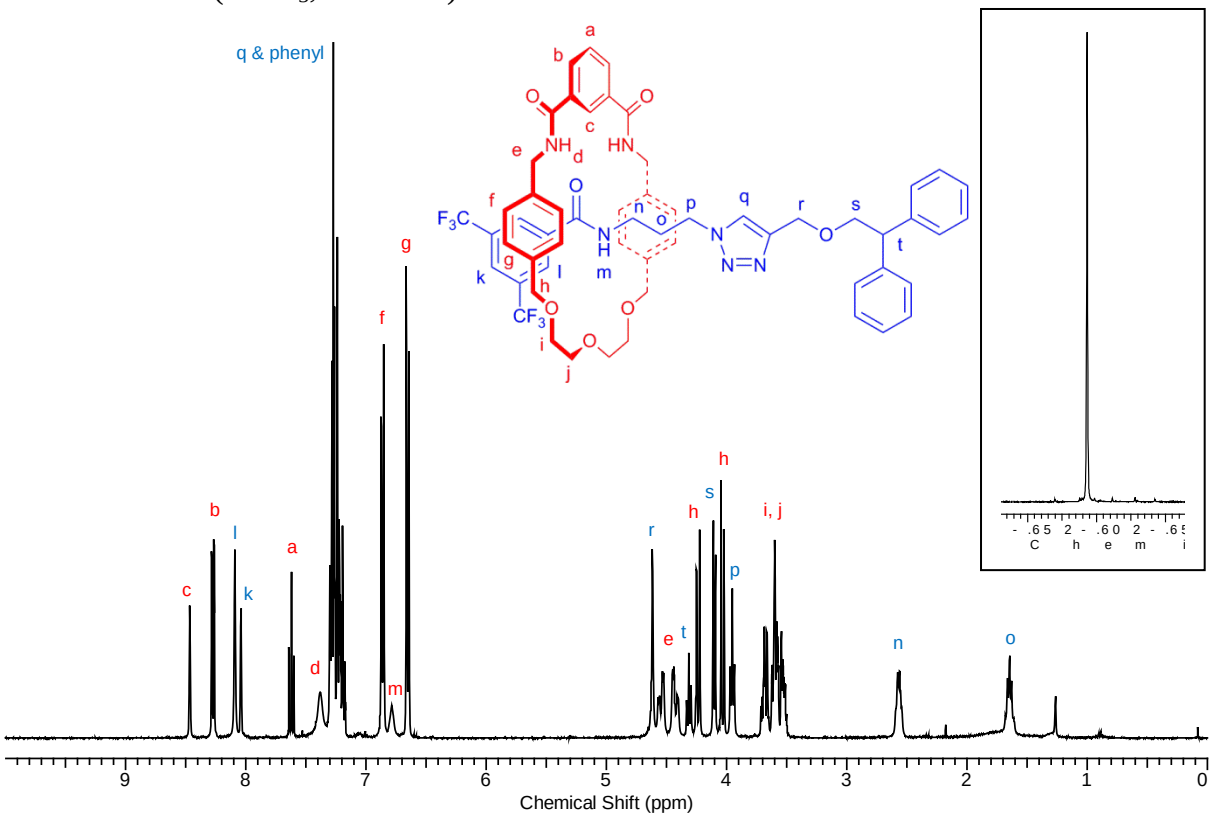
Mass Spectrum (APC −ve)



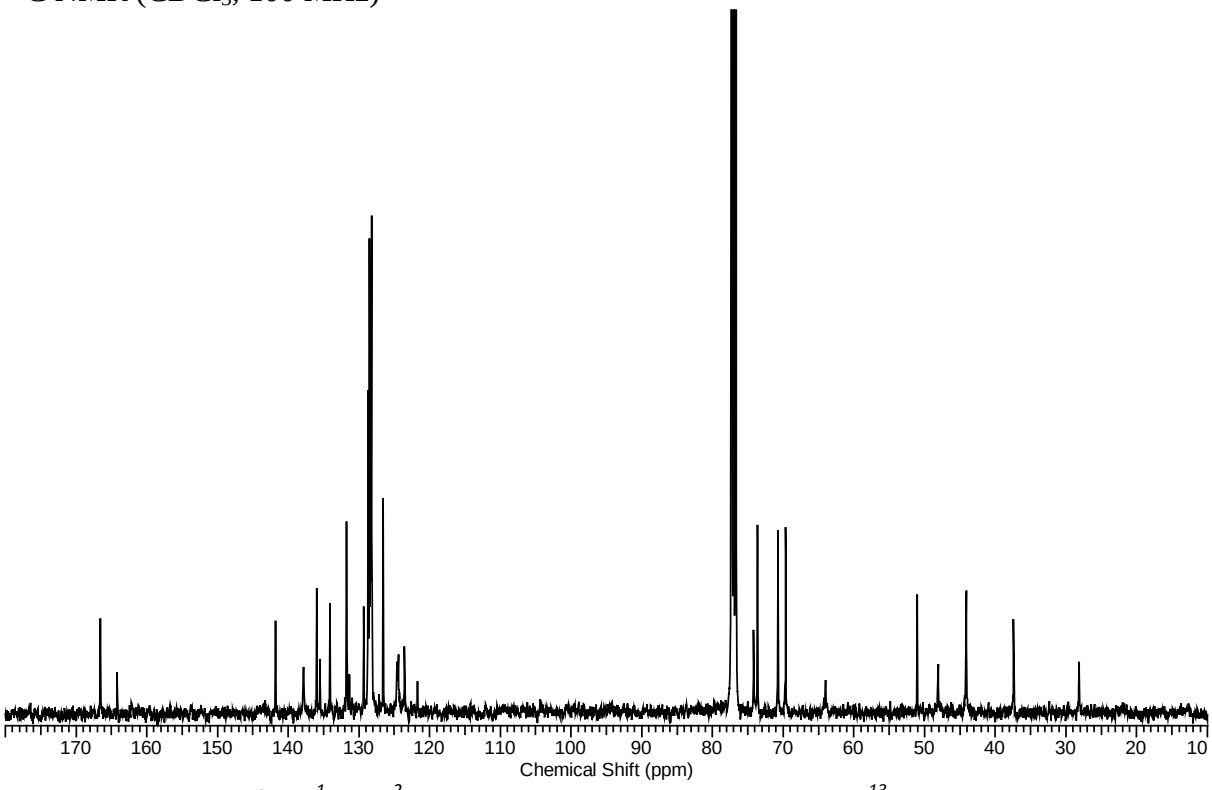


Rotaxane 6

^{1}H NMR ($CDCl_3$, 400 MHz)
Inset: ^{19}F NMR ($CDCl_3$, 377 MHz)



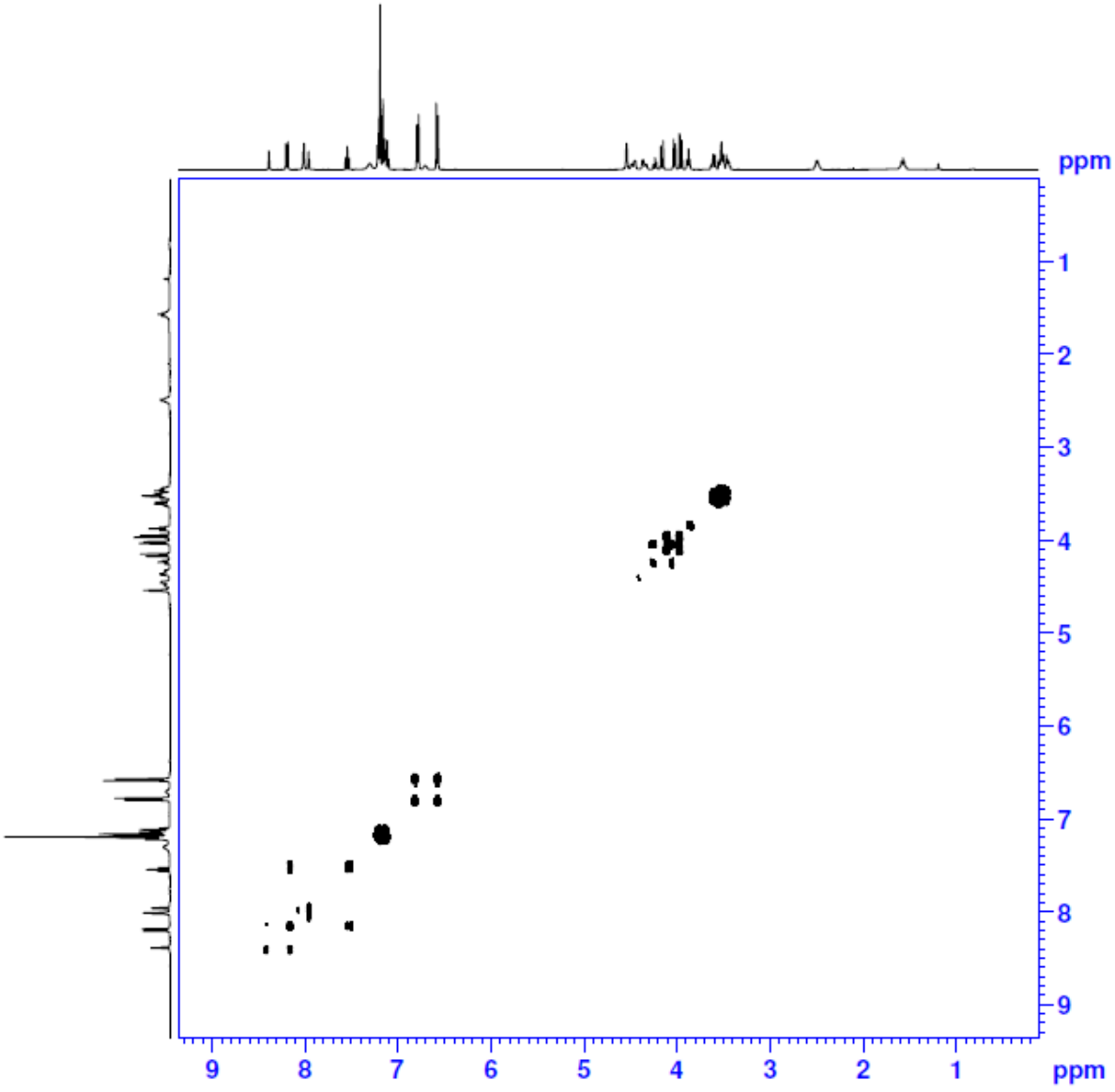
^{13}C NMR ($CDCl_3$, 100 MHz)



NB: Quartets arising from ^{1}J and ^{2}J C-F couplings not well resolved in this ^{13}C NMR spectrum, and broad peaks in aromatic region provides evidence of coincident resonances.

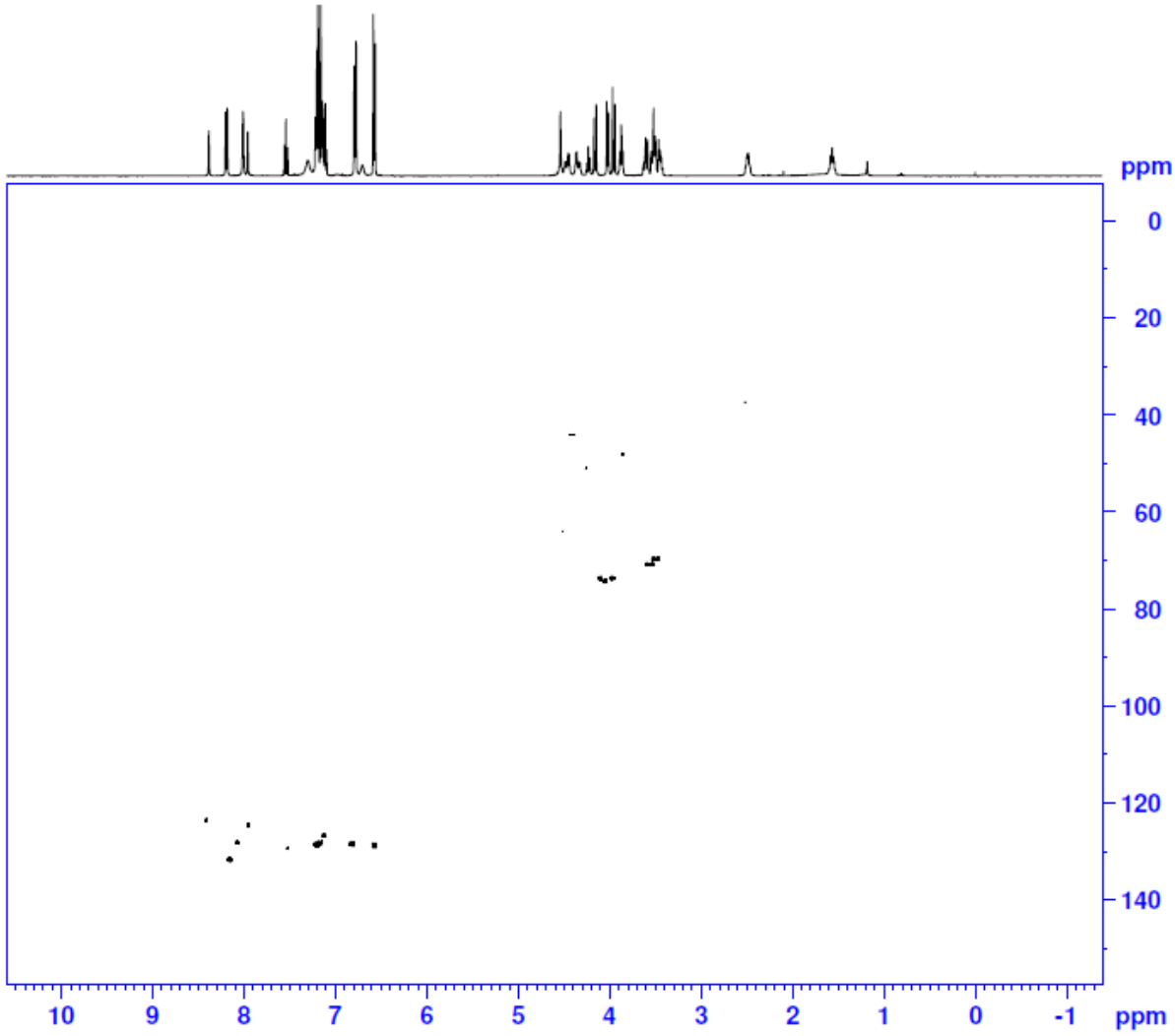
Rotaxane 6

^{1}H-^{1}H COSY NMR ($CDCl_3$)



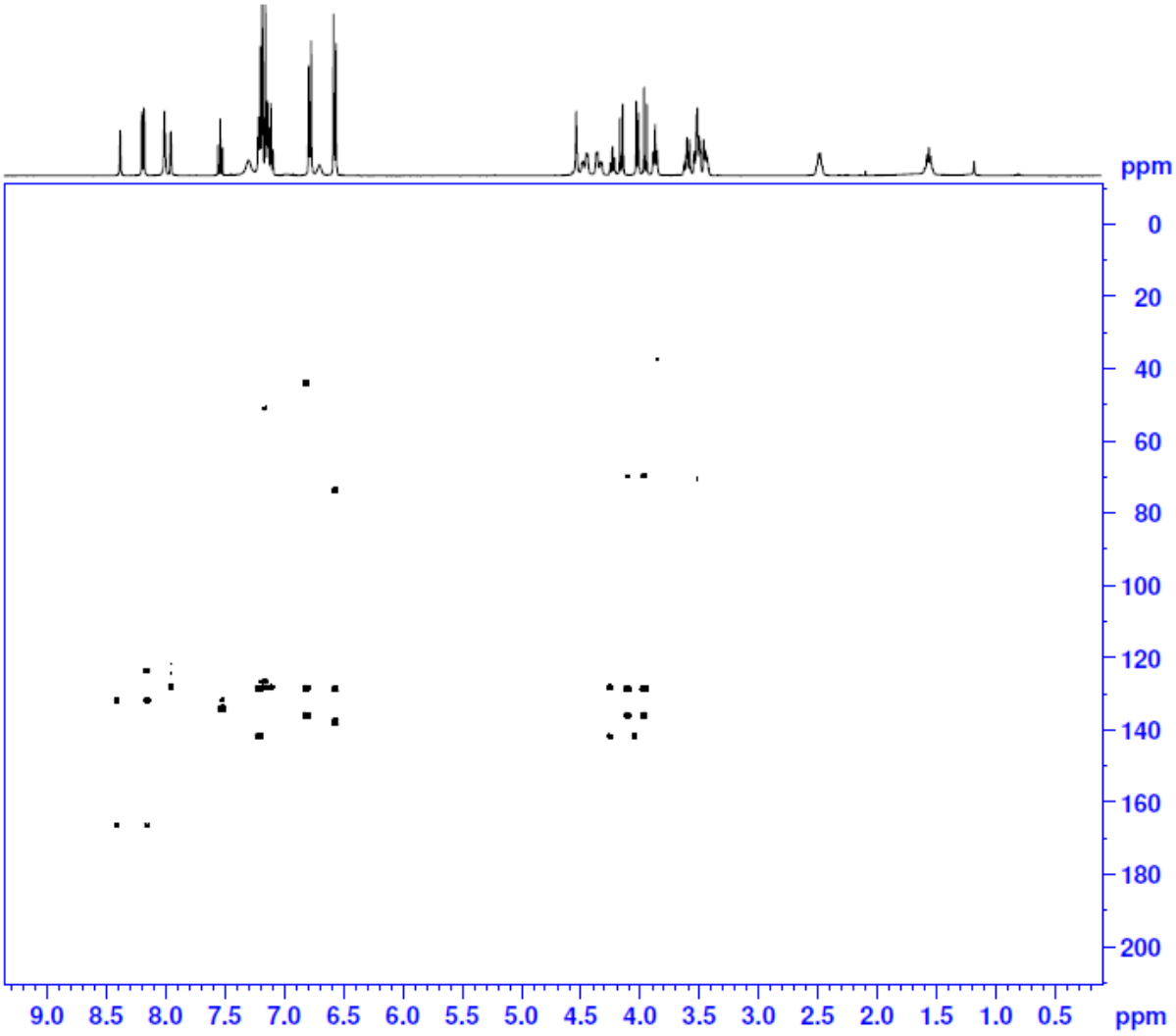
Rotaxane 6

^{1}H-^{13}C HSQC NMR ($CDCl_3$)



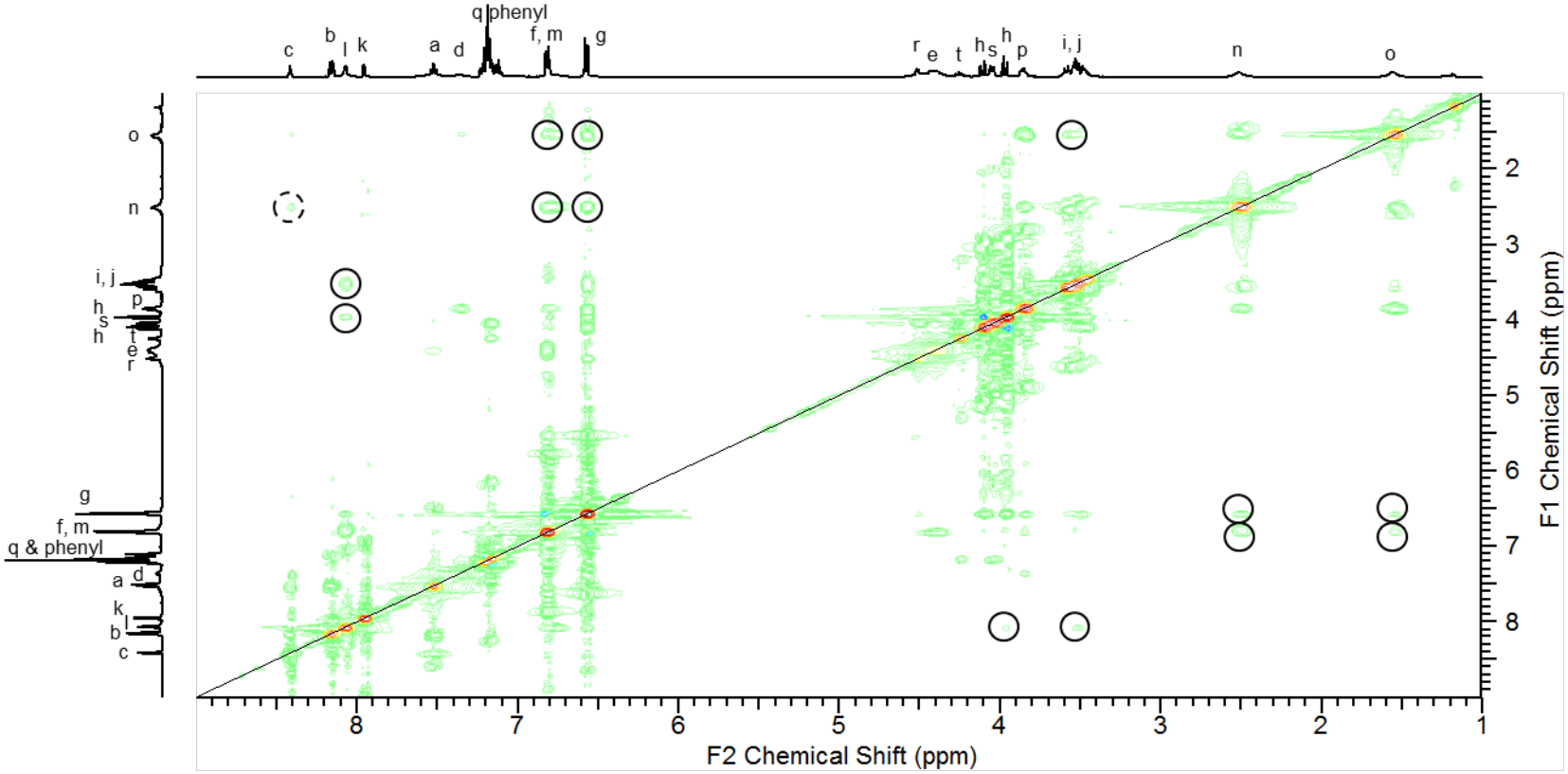
Rotaxane 6

^{1}H-^{13}C HMBC NMR ($CDCl_3$)



Rotaxane 6

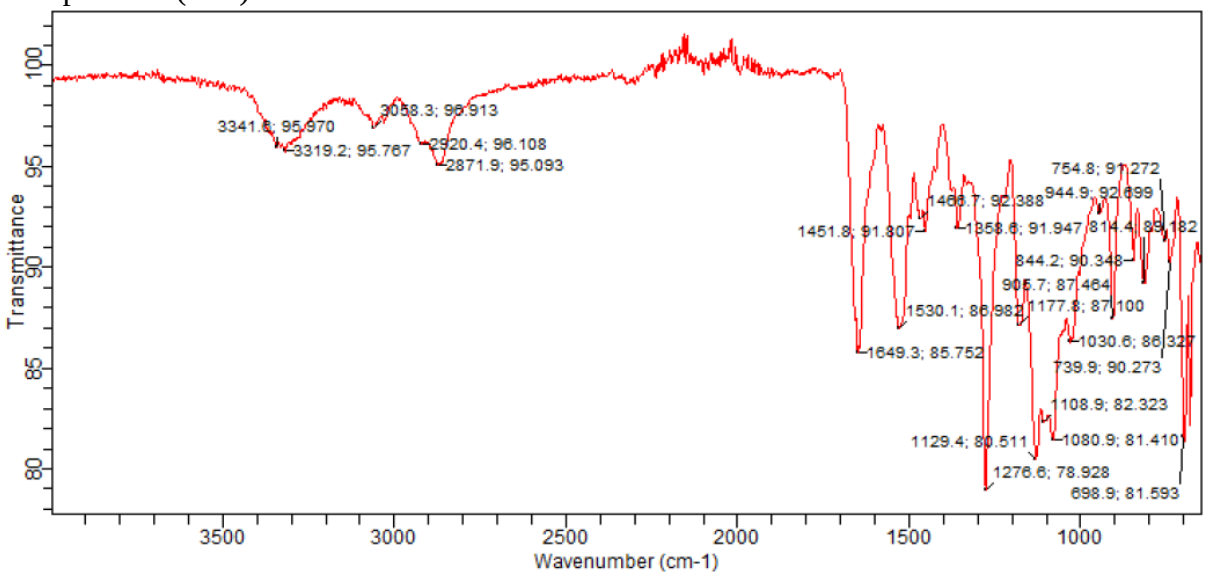
^{1}H-^{1}H ROESY NMR ($CDCl_3$)



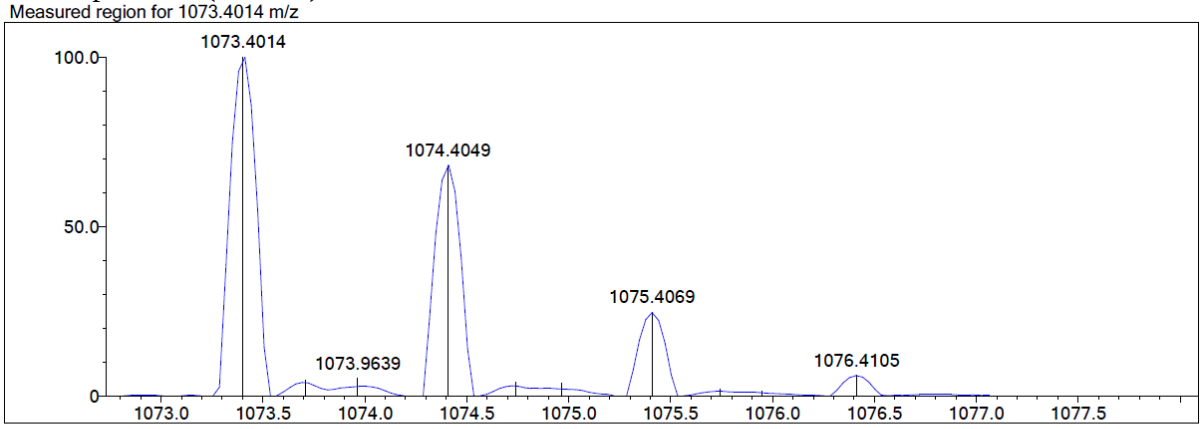
Inter-component through-space cross-peaks are circled. Cross-peaks that appear on only one side of the diagonal are enclosed by a dashed circle.

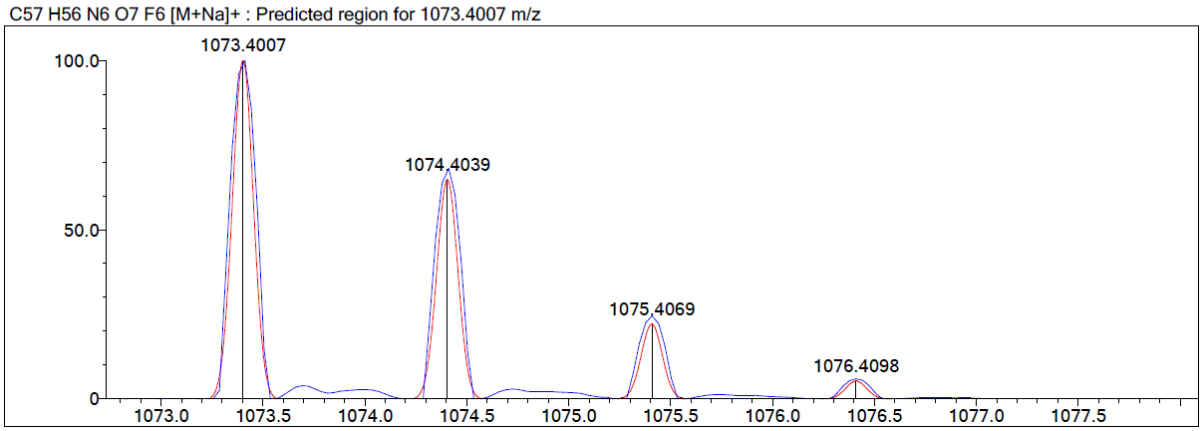
Rotaxane 6

IR Spectrum (neat)



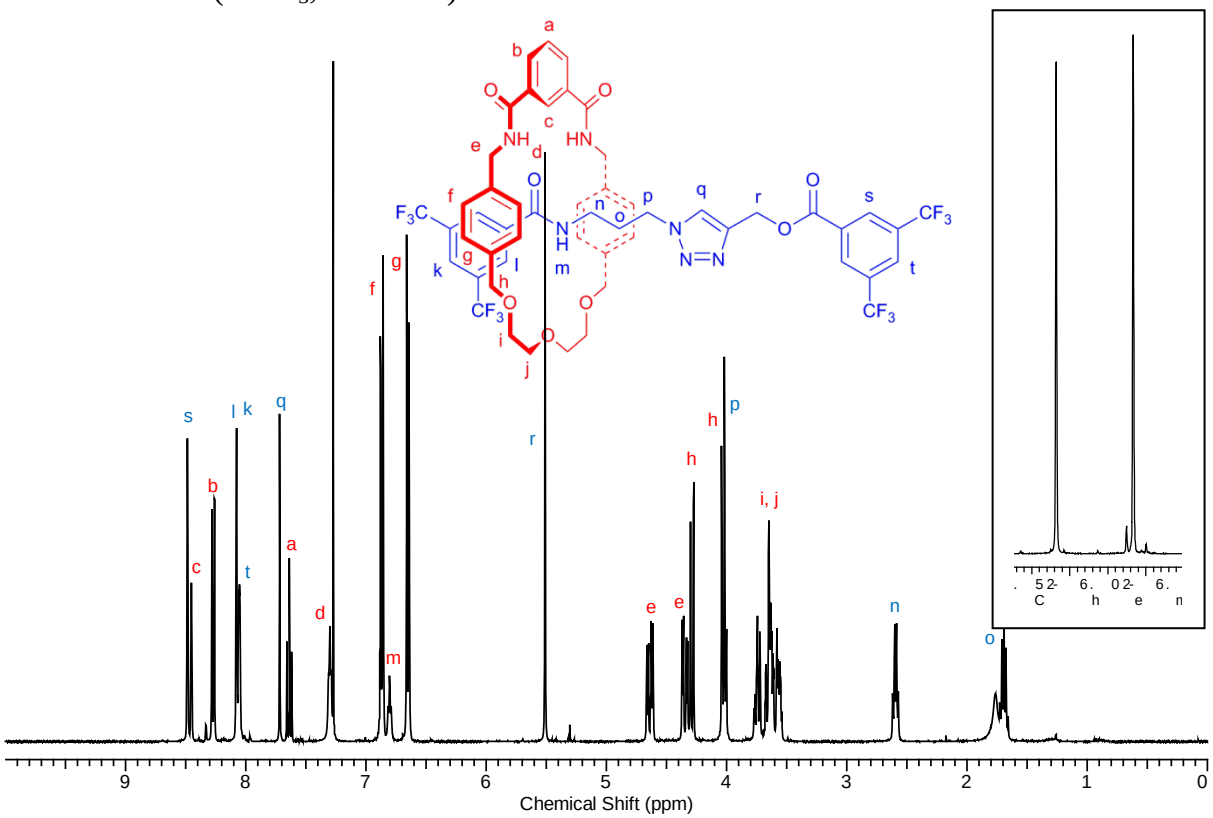
Mass Spectrum (ES +ve)



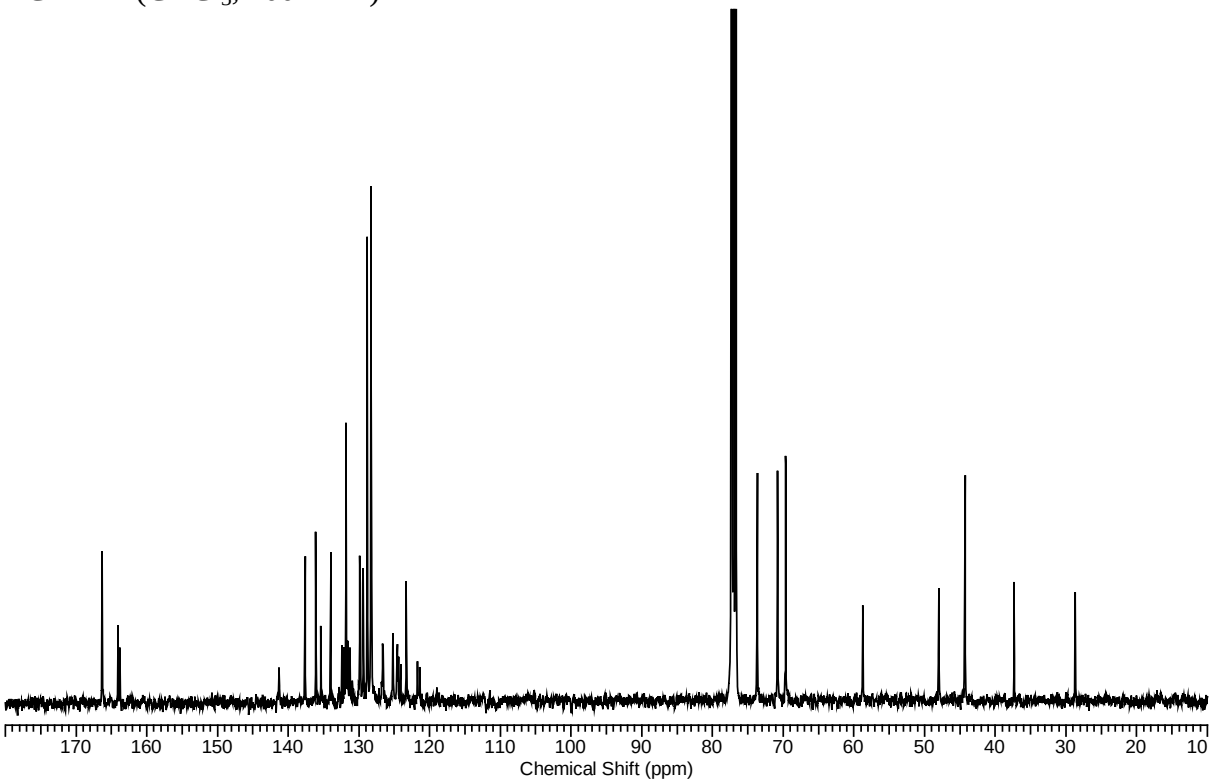


Rotaxane 7

^{1}H NMR ($CDCl_3$, 400 MHz)
Inset: ^{19}F NMR ($CDCl_3$, 377 MHz)



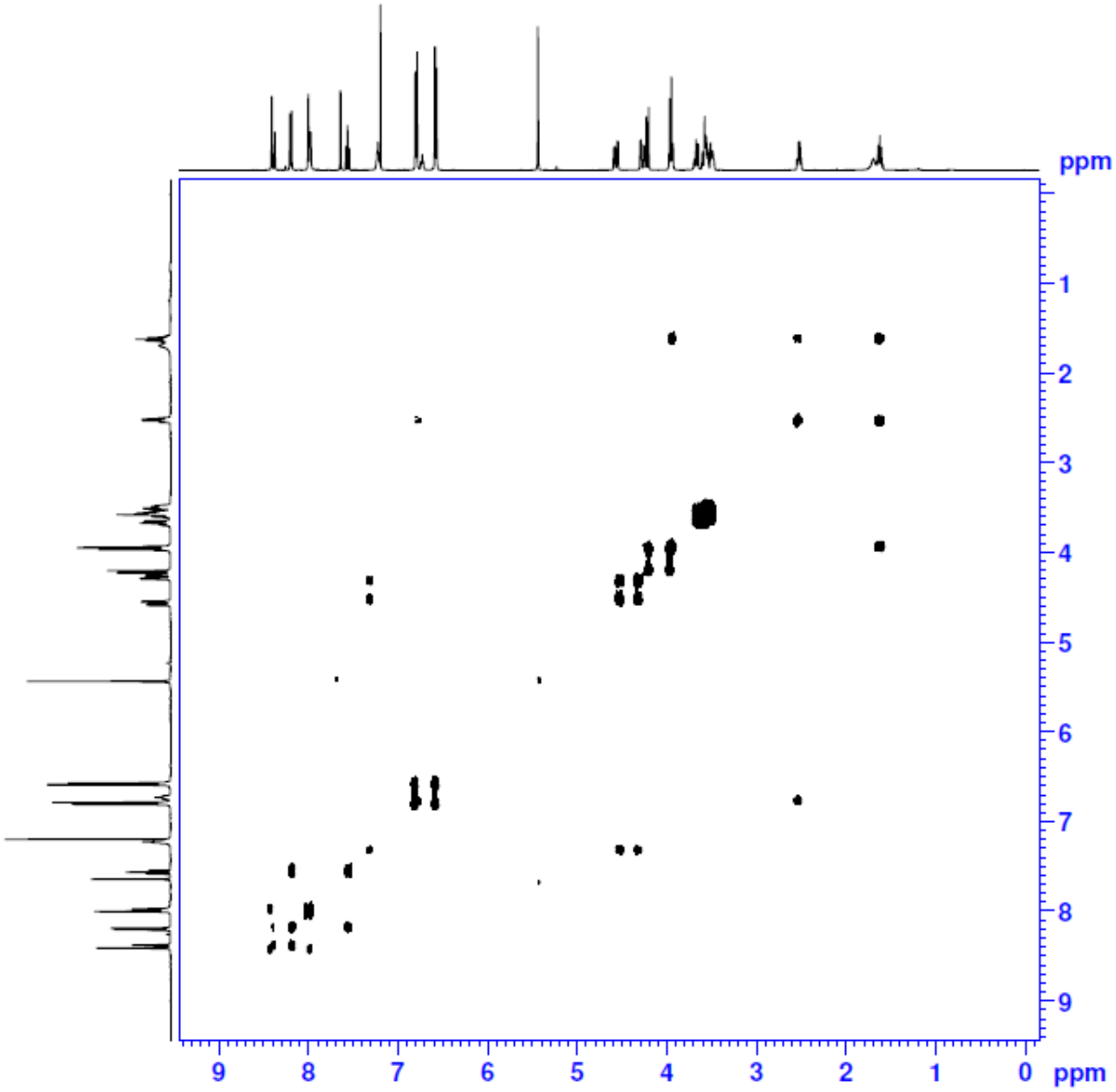
^{13}C NMR ($CDCl_3$, 100 MHz)



NB: In this ^{13}C NMR spectrum, broad peaks in aromatic region provides evidence of coincident resonances.

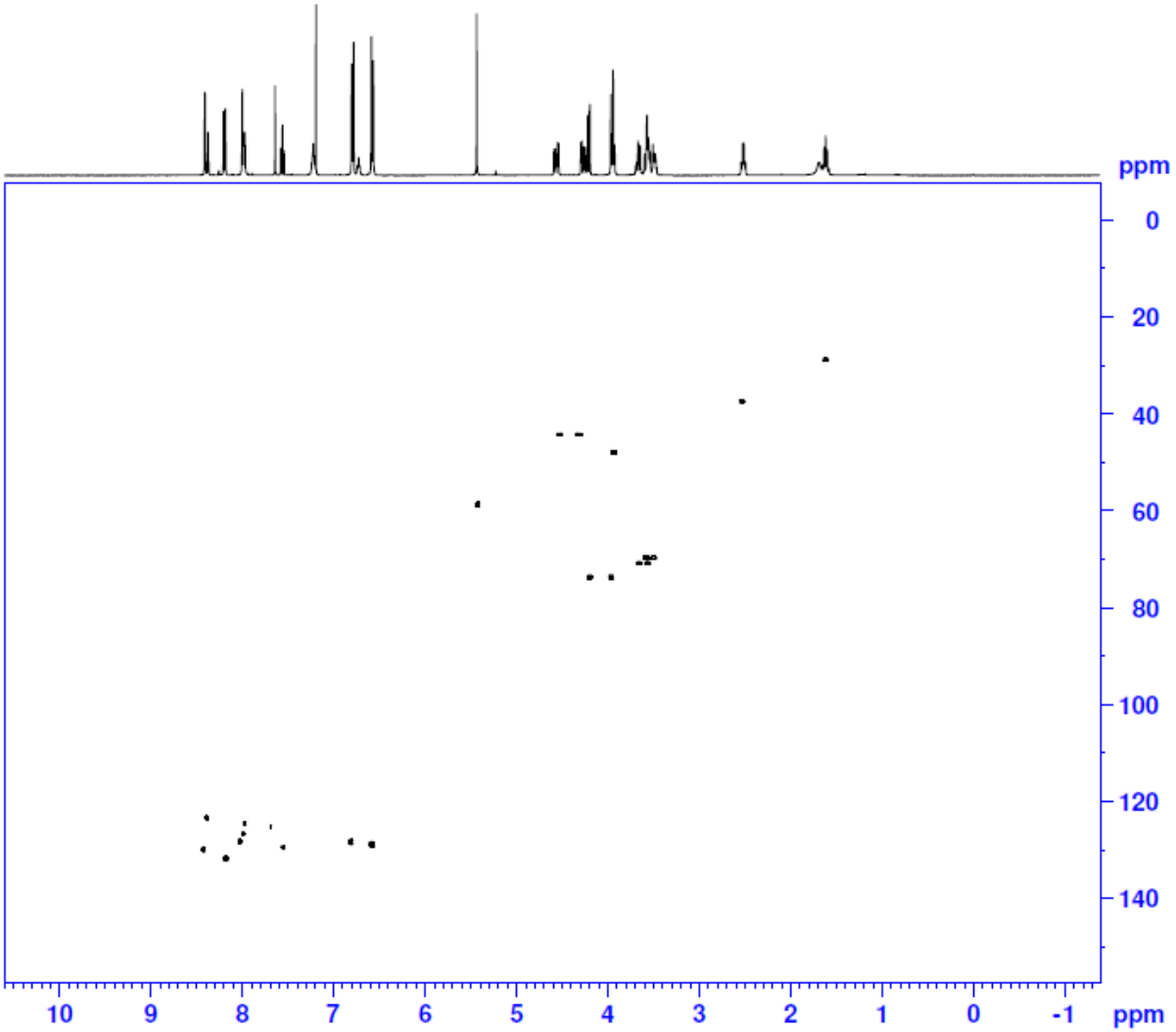
Rotaxane 7

^{1}H-^{1}H COSY NMR ($CDCl_3$)



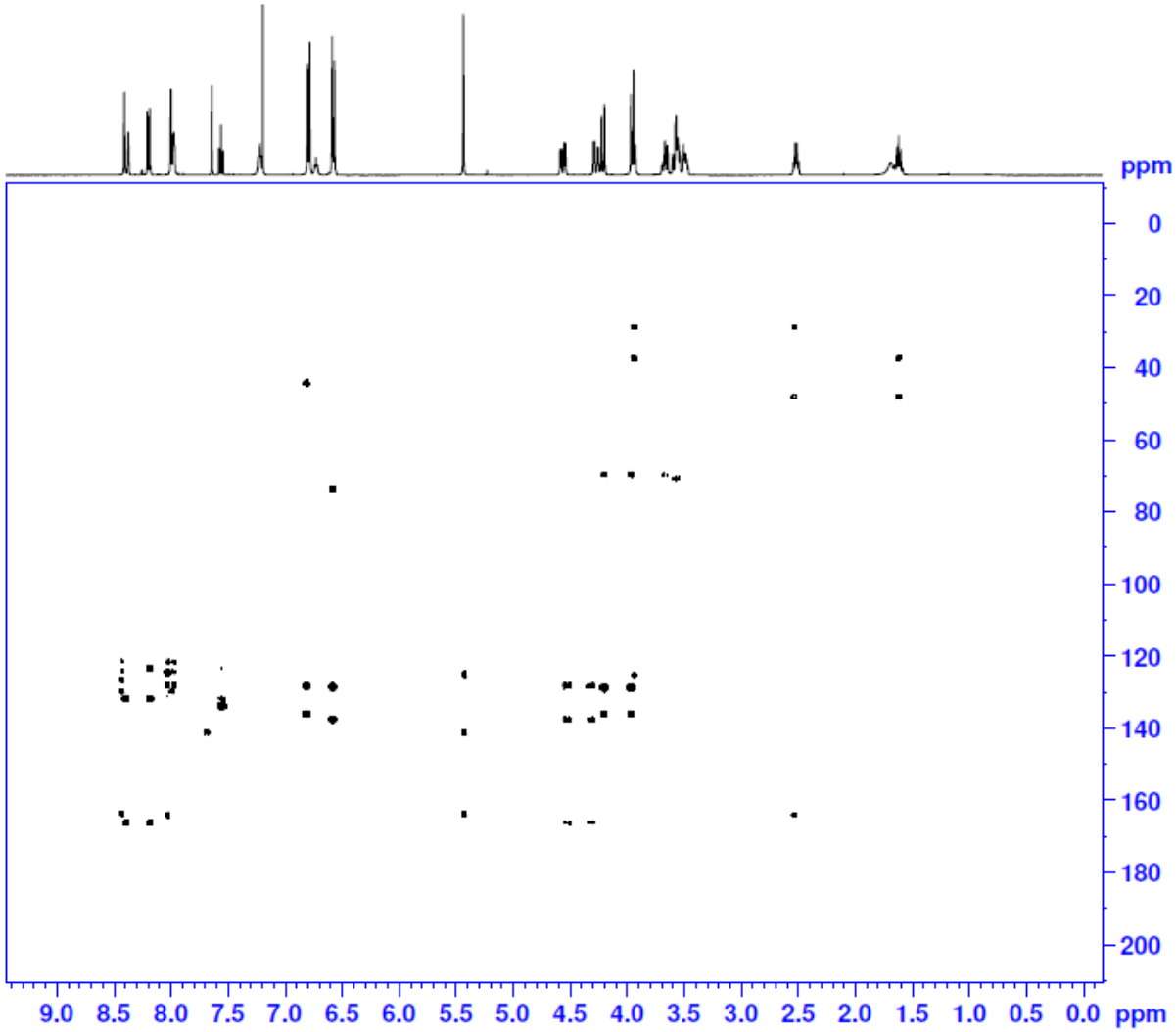
Rotaxane 7

^{1}H-^{13}C HSQC NMR ($CDCl_3$)



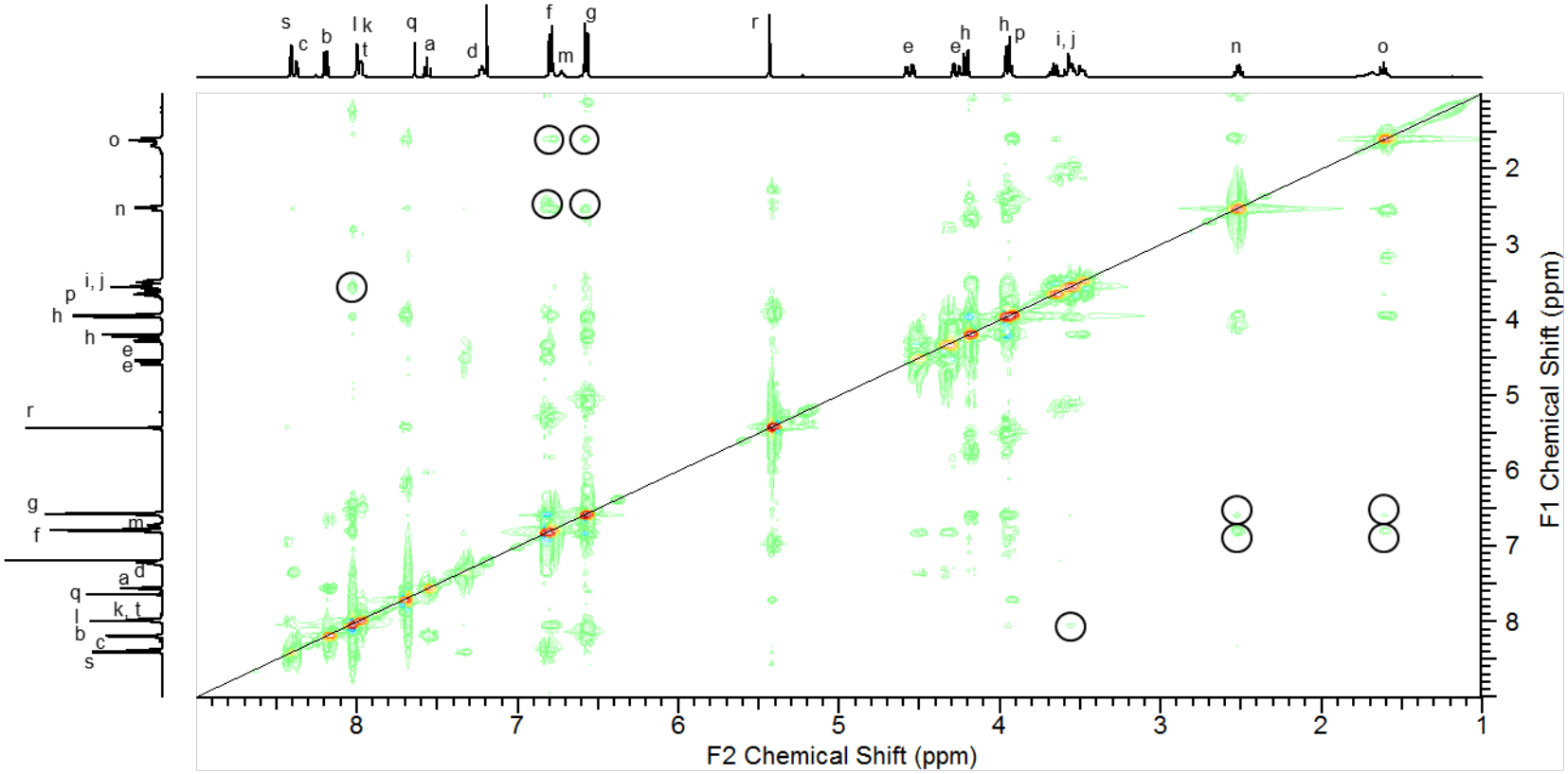
Rotaxane 7

^{1}H-^{13}C HMBC NMR ($CDCl_3$)



Rotaxane 7

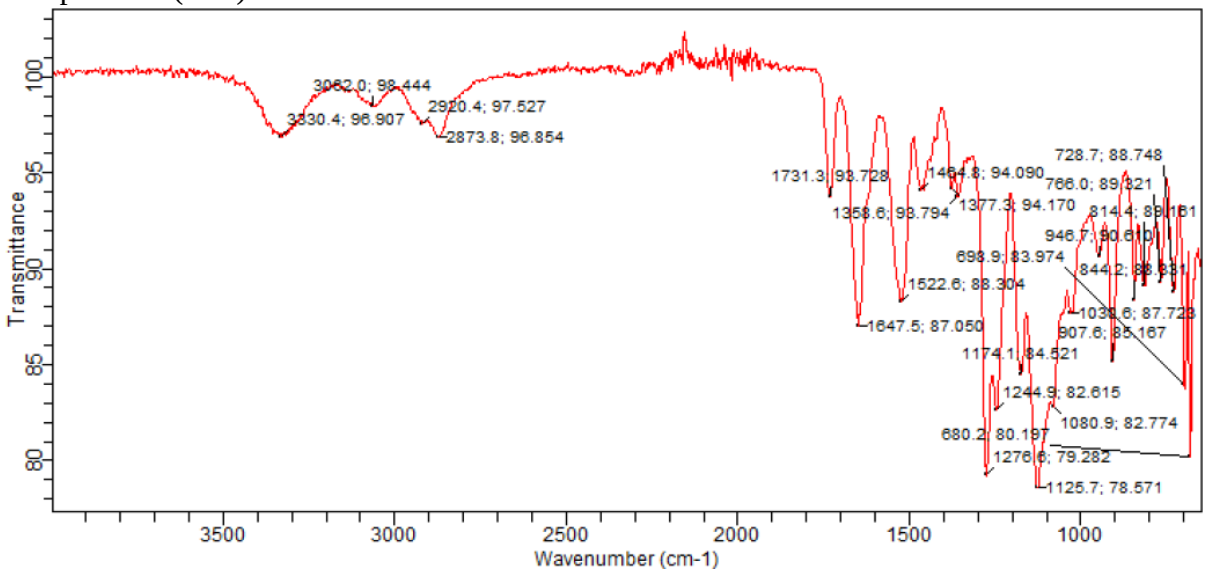
^{1}H-^{1}H ROESY NMR ($CDCl_3$)



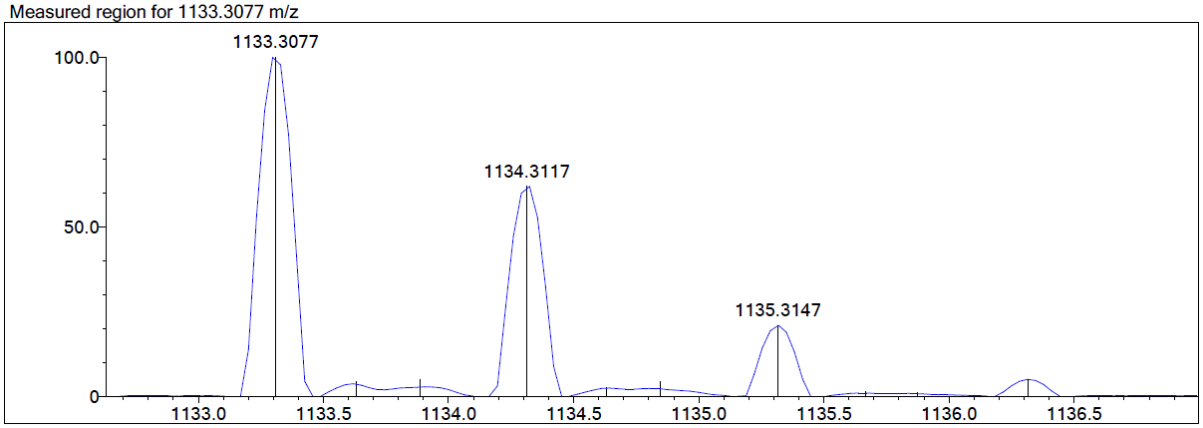
Inter-component through-space cross-peaks are circled.

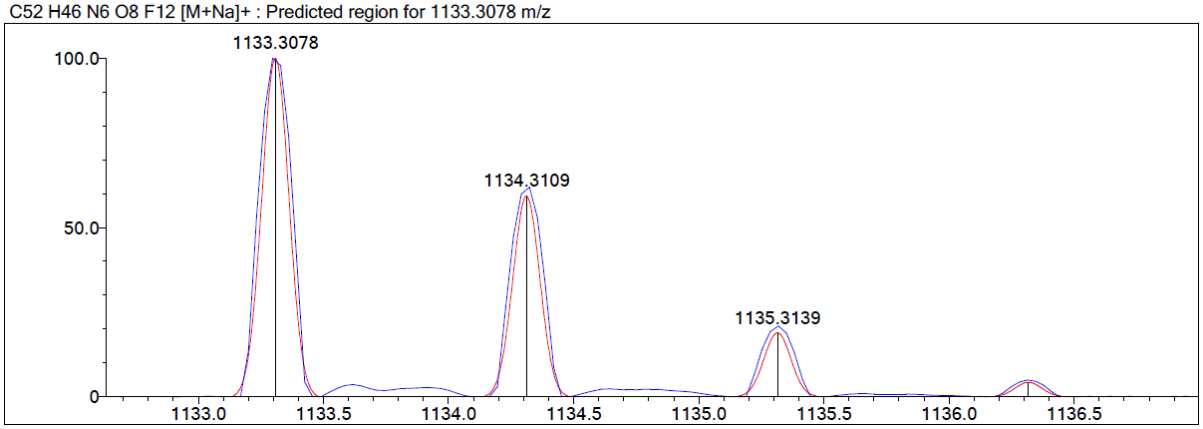
Rotaxane 7

IR Spectrum (neat)



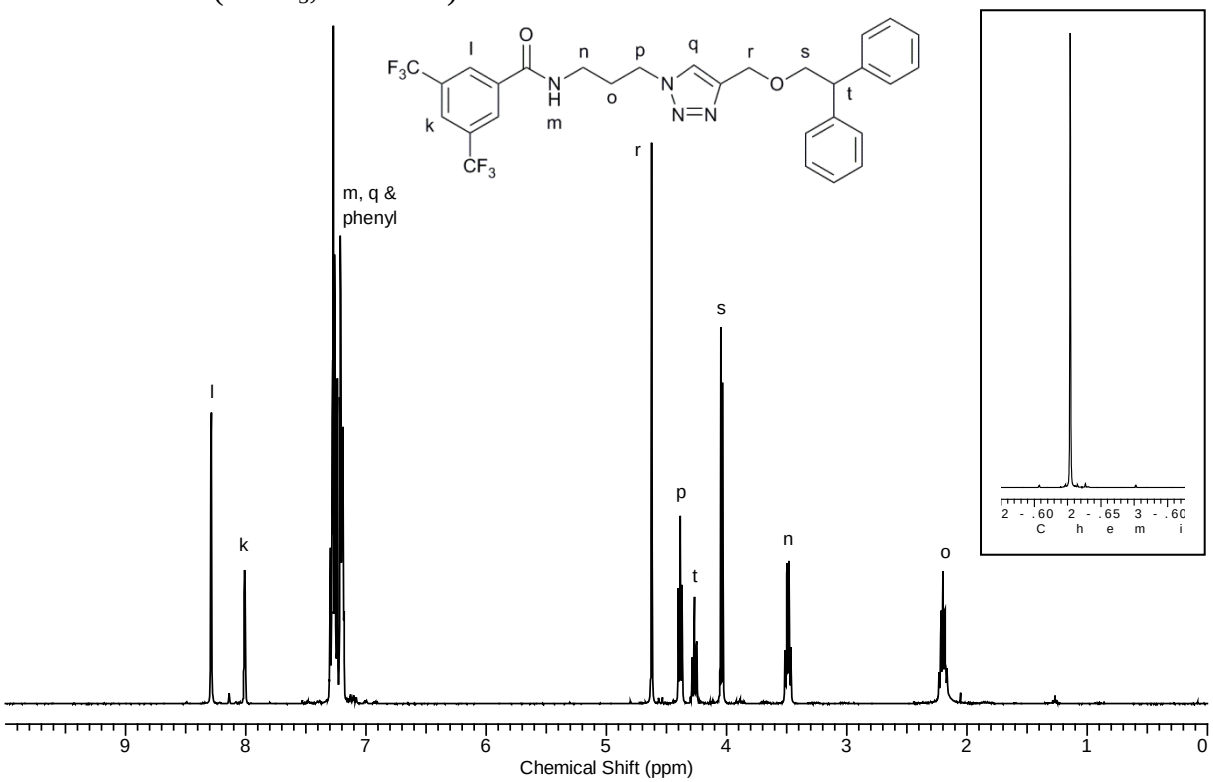
Mass Spectrum (ES +ve)



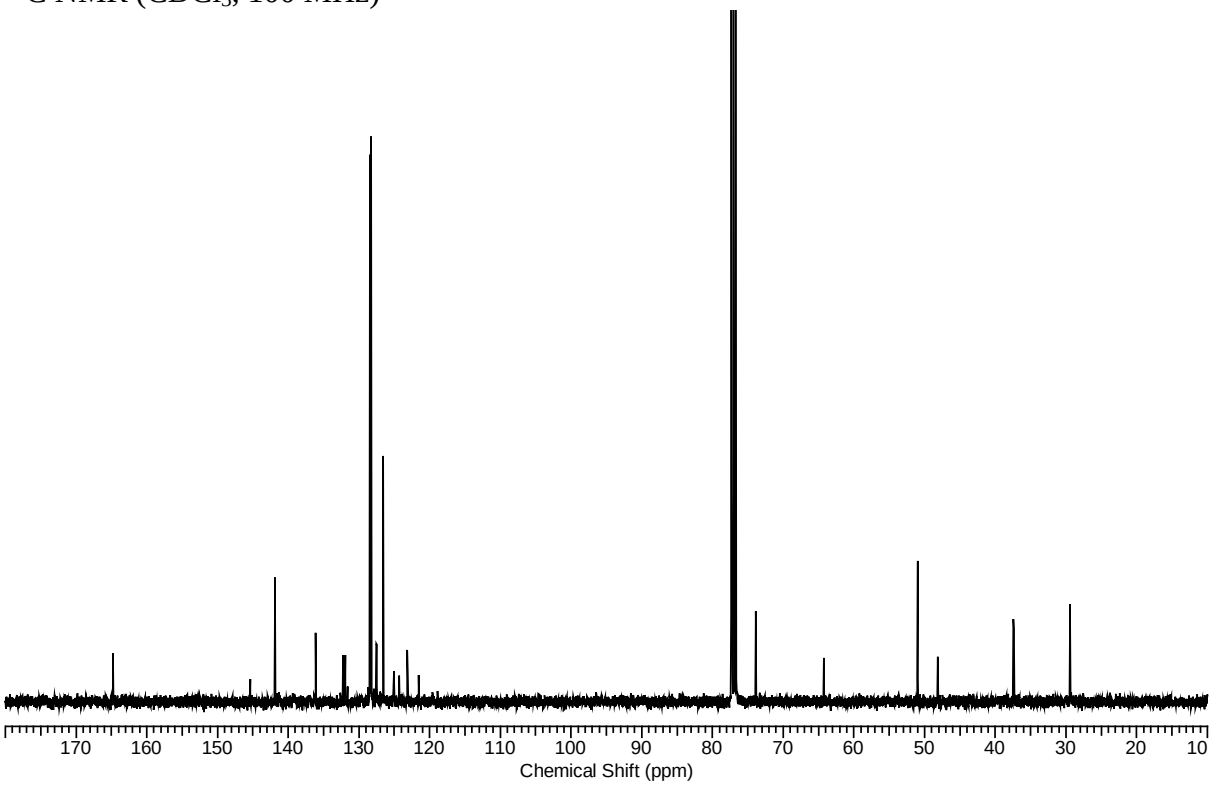


Axle 8

^{1}H NMR ($CDCl_3$, 400 MHz)
Inset: ^{19}F NMR ($CDCl_3$, 377 MHz)

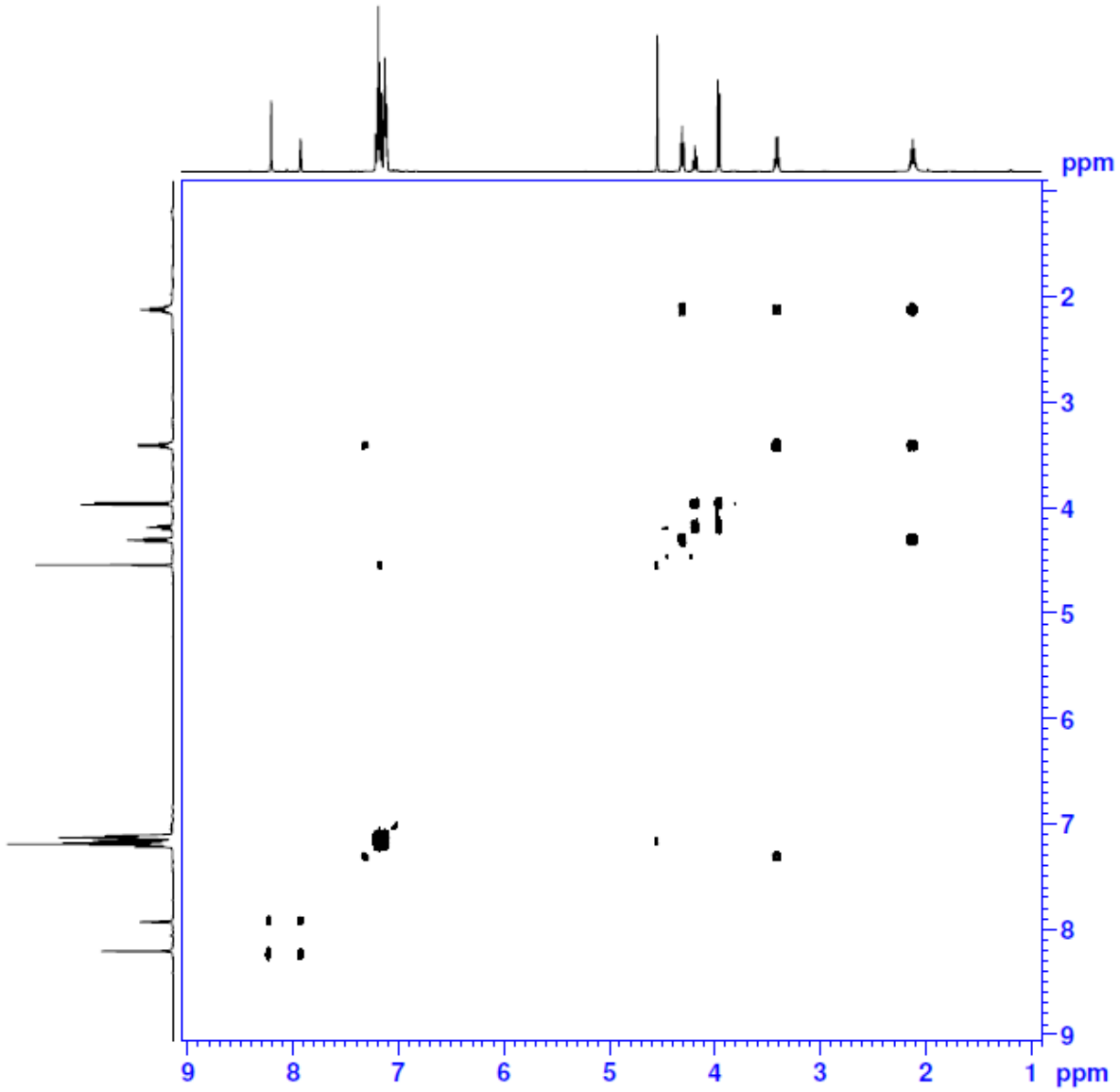


^{13}C NMR ($CDCl_3$, 100 MHz)



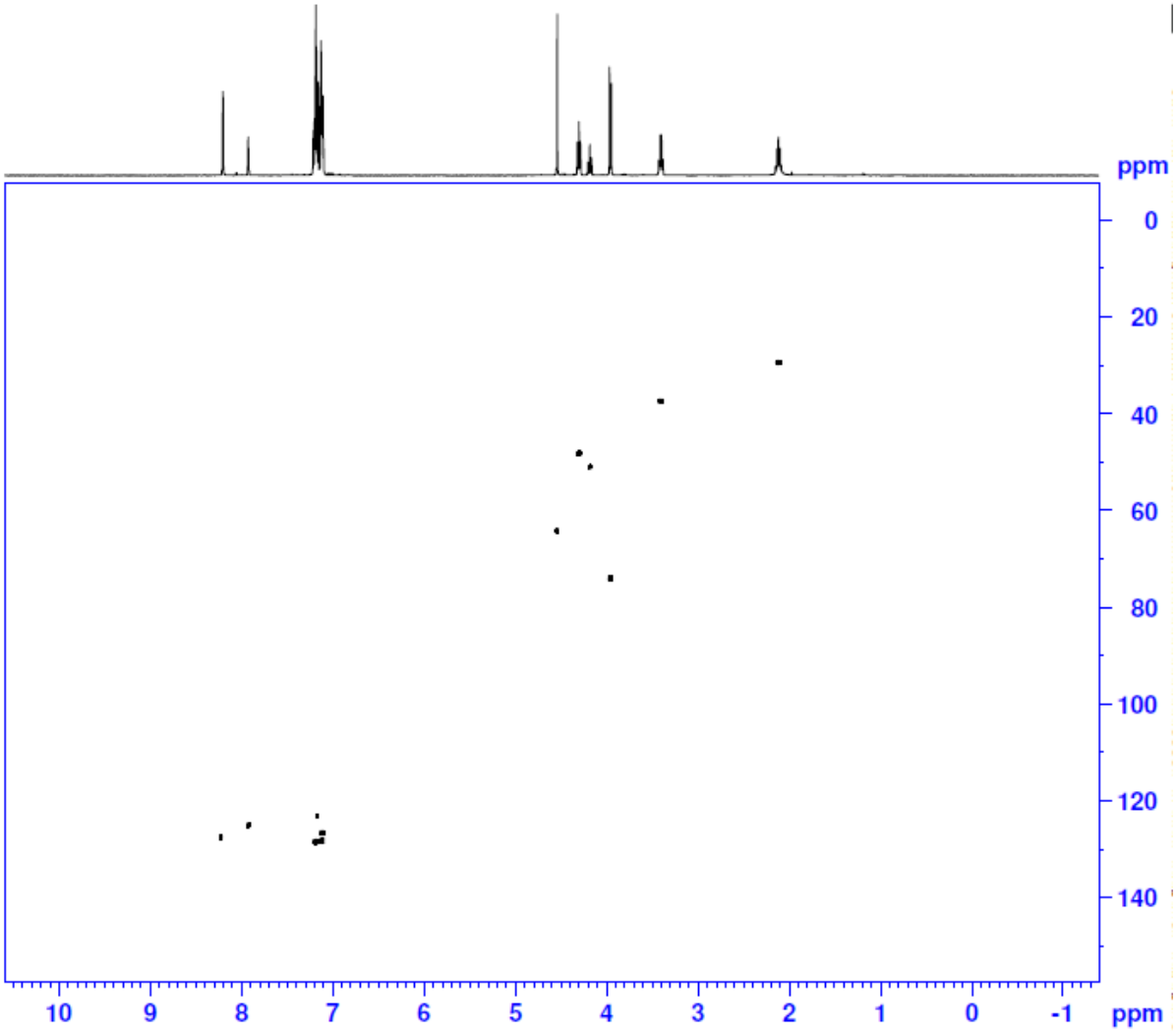
Axle 8

^{1}H-^{1}H COSY NMR ($CDCl_3$)



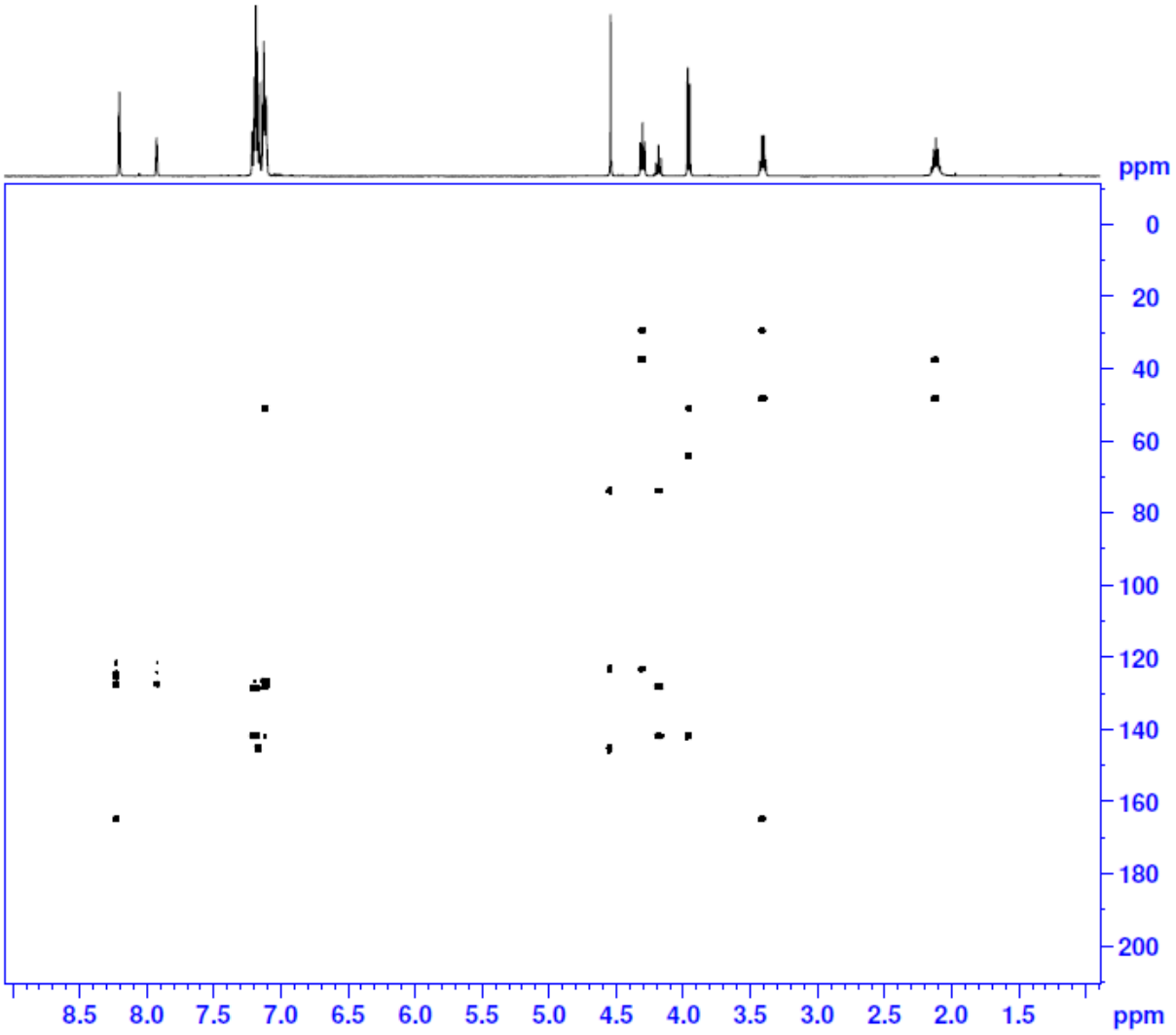
Axle 8

^{1}H-^{13}C HSQC NMR ($CDCl_3$)



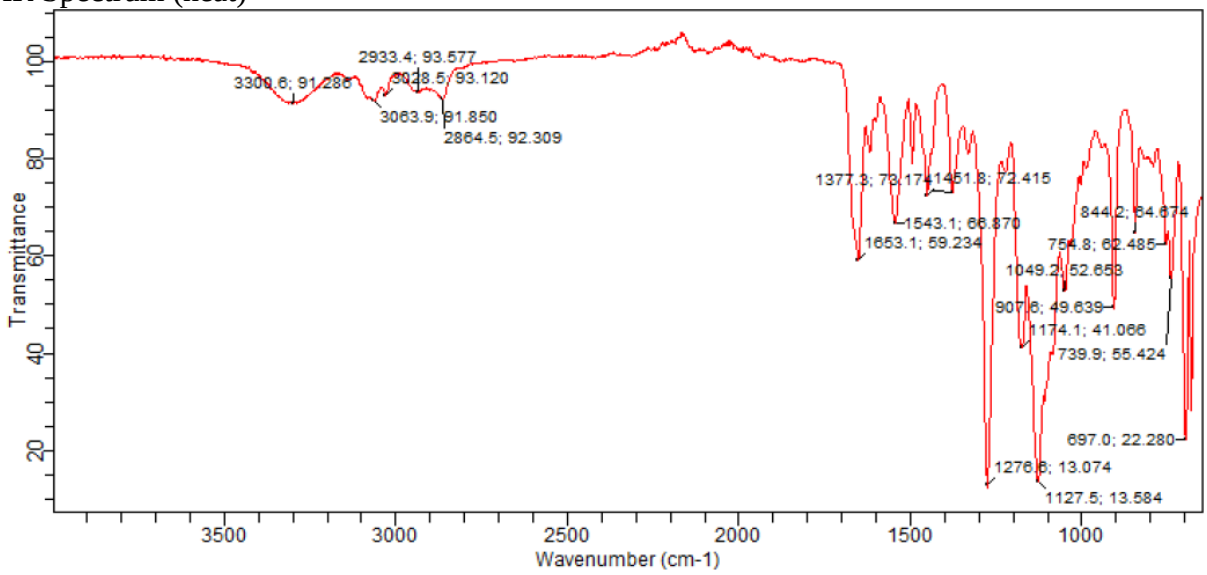
Axle 8

^{1}H-^{13}C HMBC NMR ($CDCl_3$)

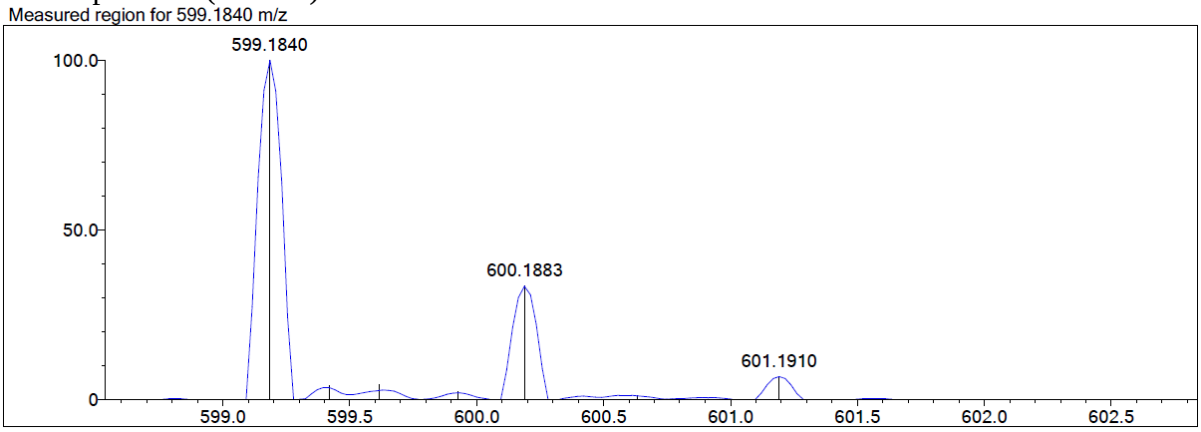


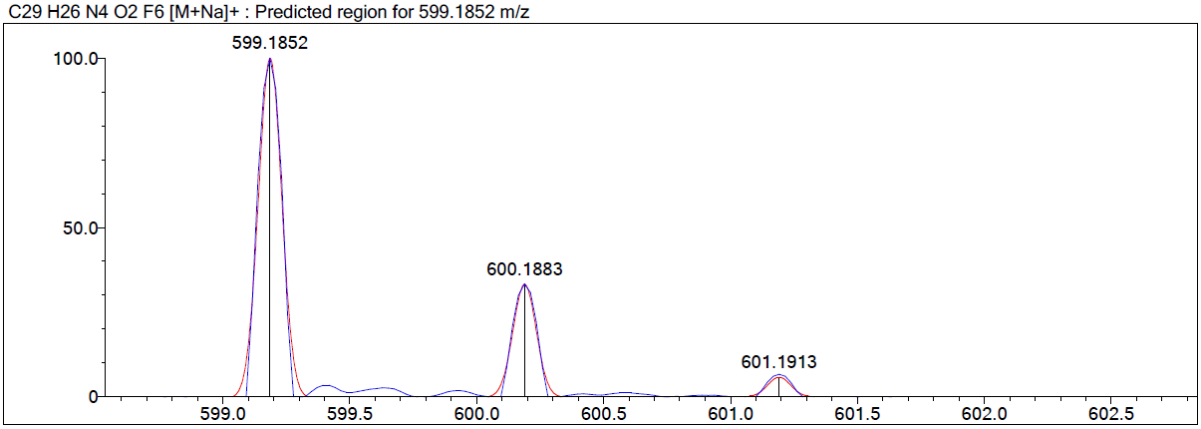
Axle 8

IR Spectrum (neat)



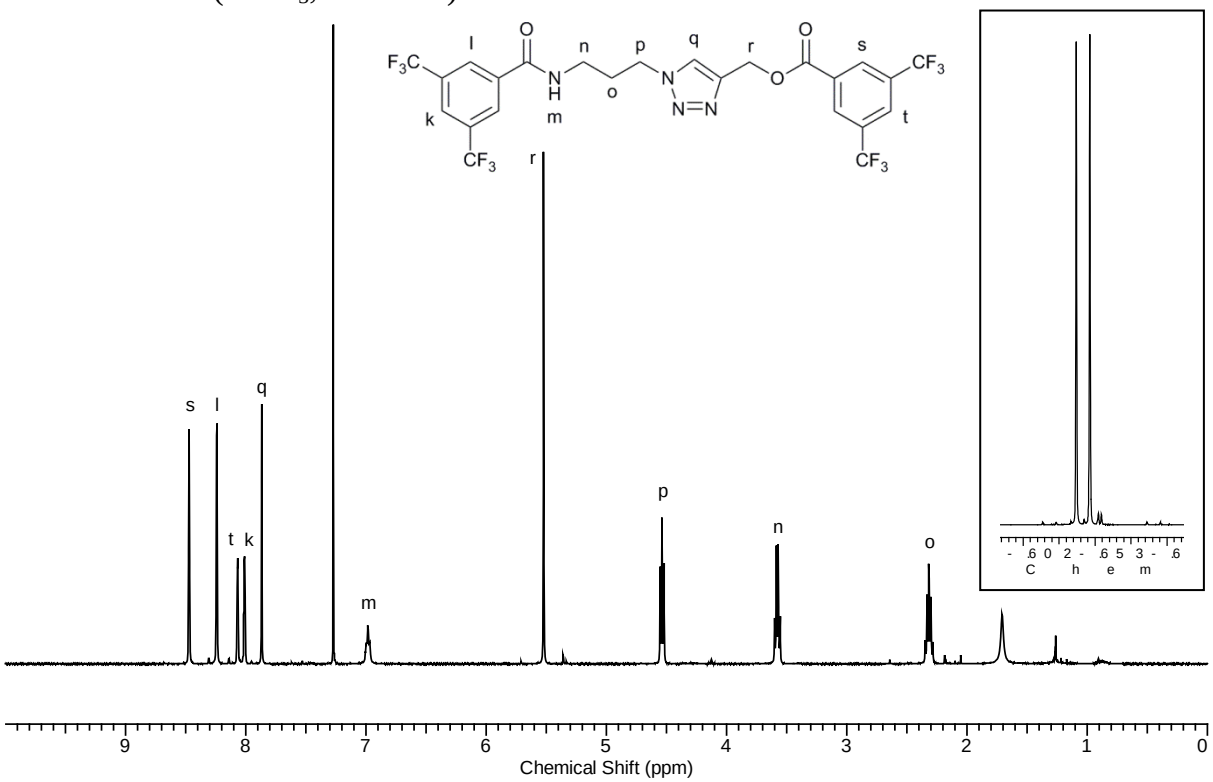
Mass Spectrum (ES +ve)



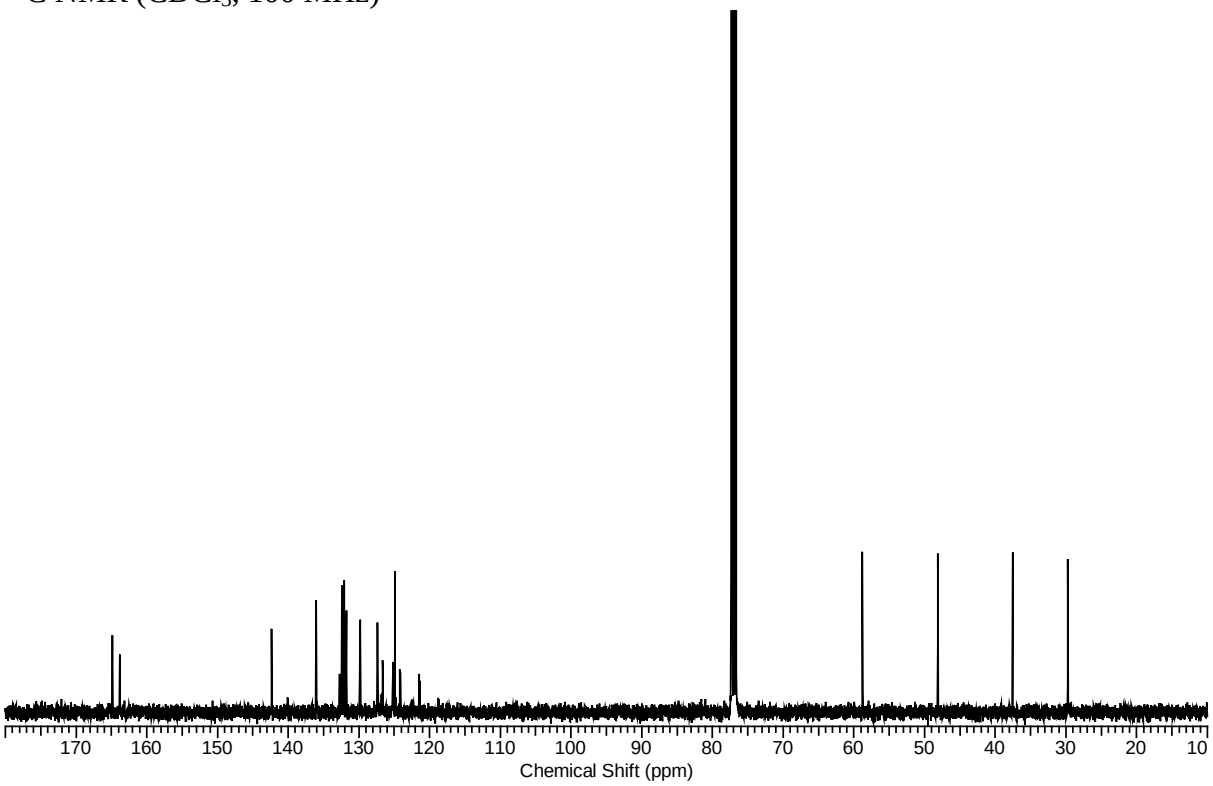


Axle 9

^{1}H NMR ($CDCl_3$, 400 MHz)
Inset: ^{19}F NMR ($CDCl_3$, 377 MHz)

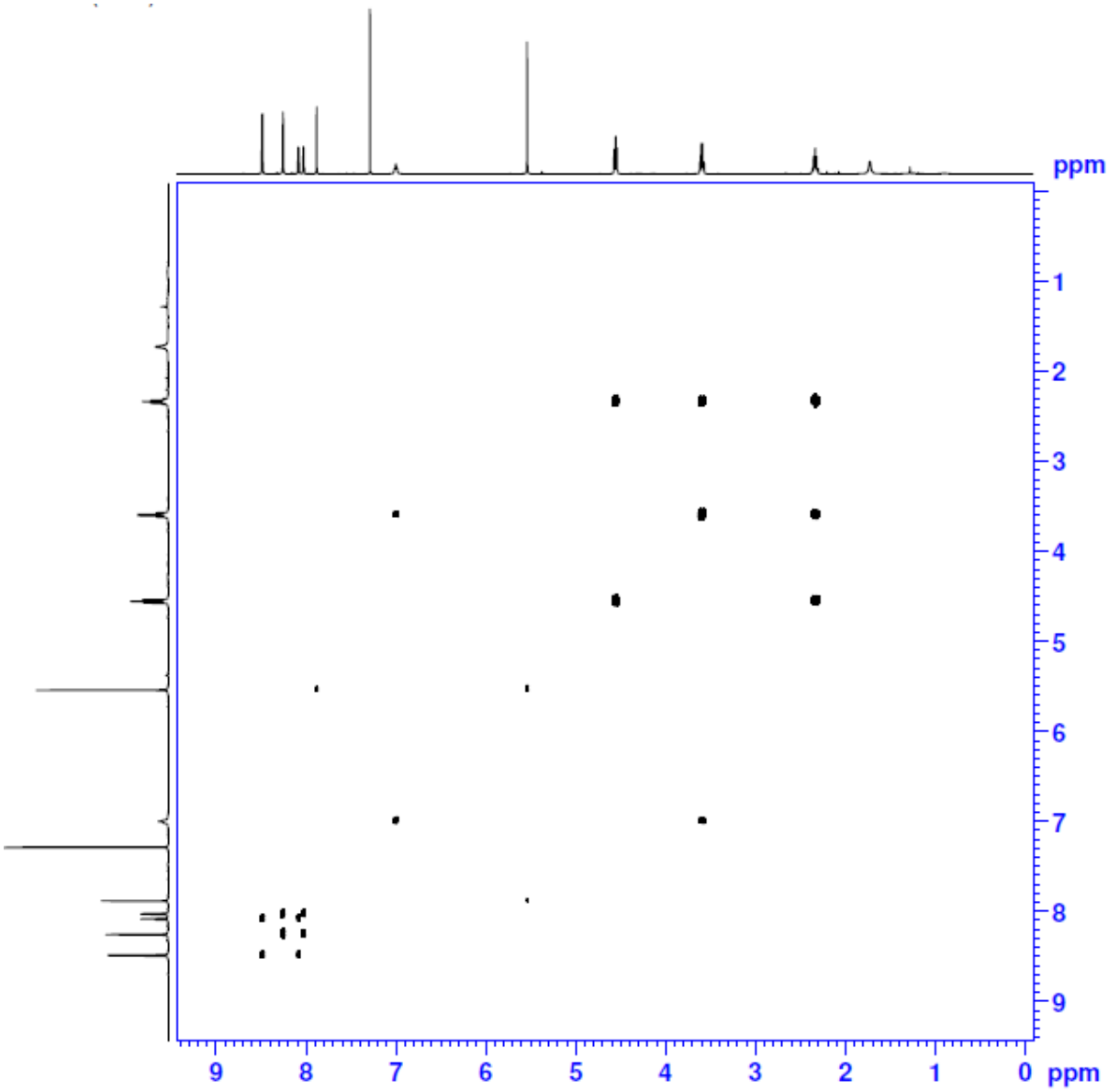


^{13}C NMR ($CDCl_3$, 100 MHz)



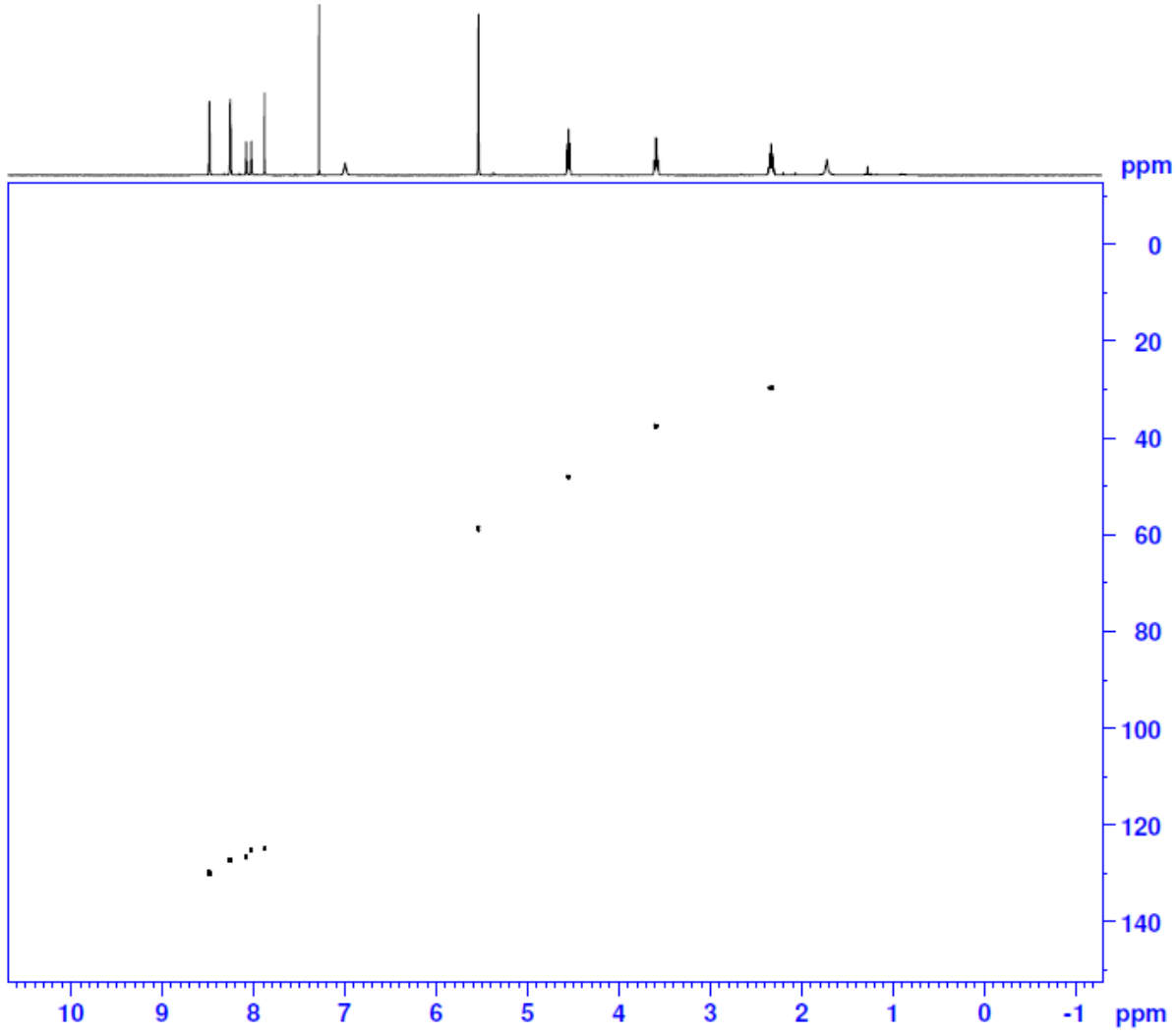
Axle 9

^{1}H-^{1}H COSY NMR ($CDCl_3$)



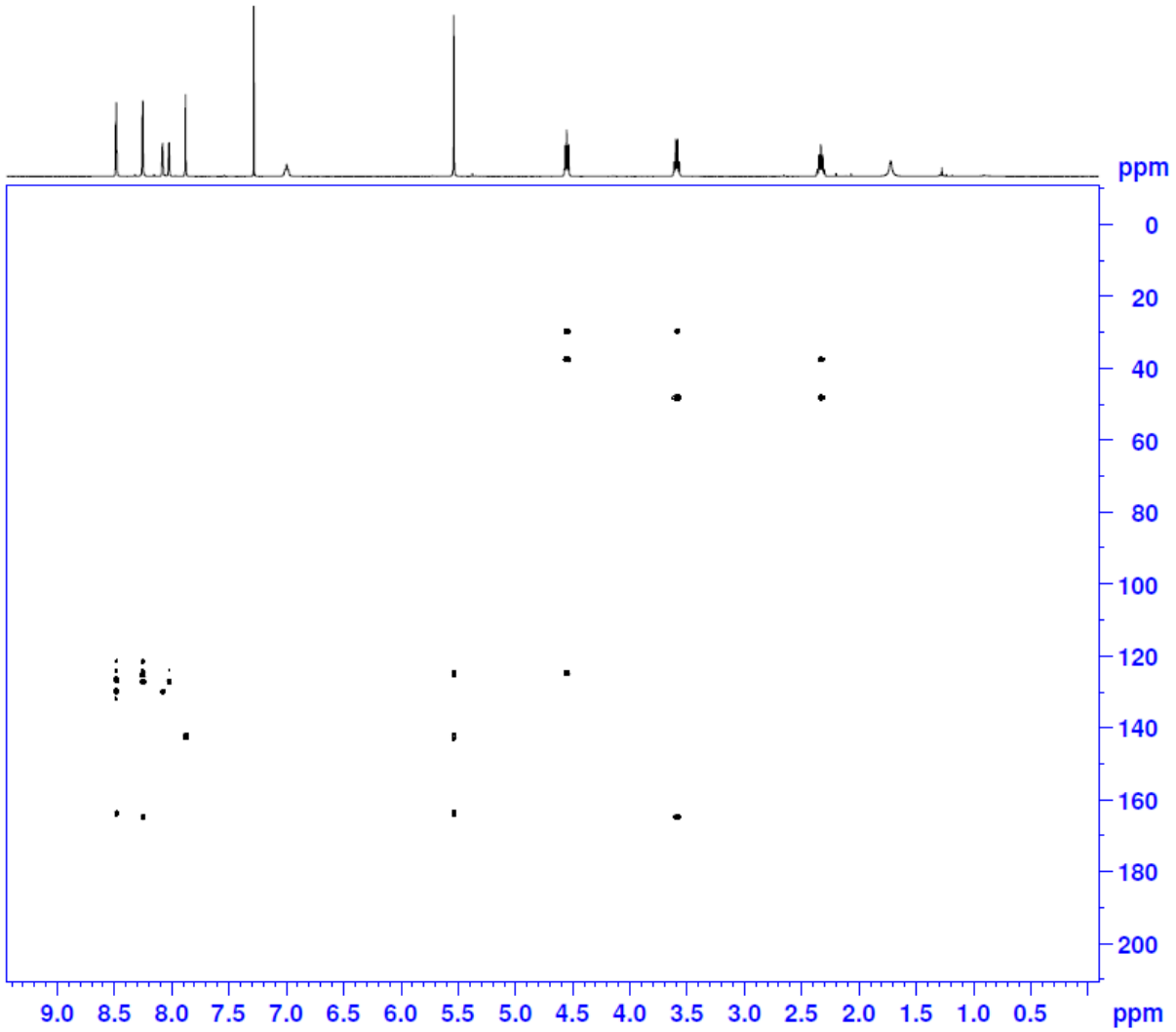
Axle 9

^{1}H-^{13}C HSQC NMR ($CDCl_3$)



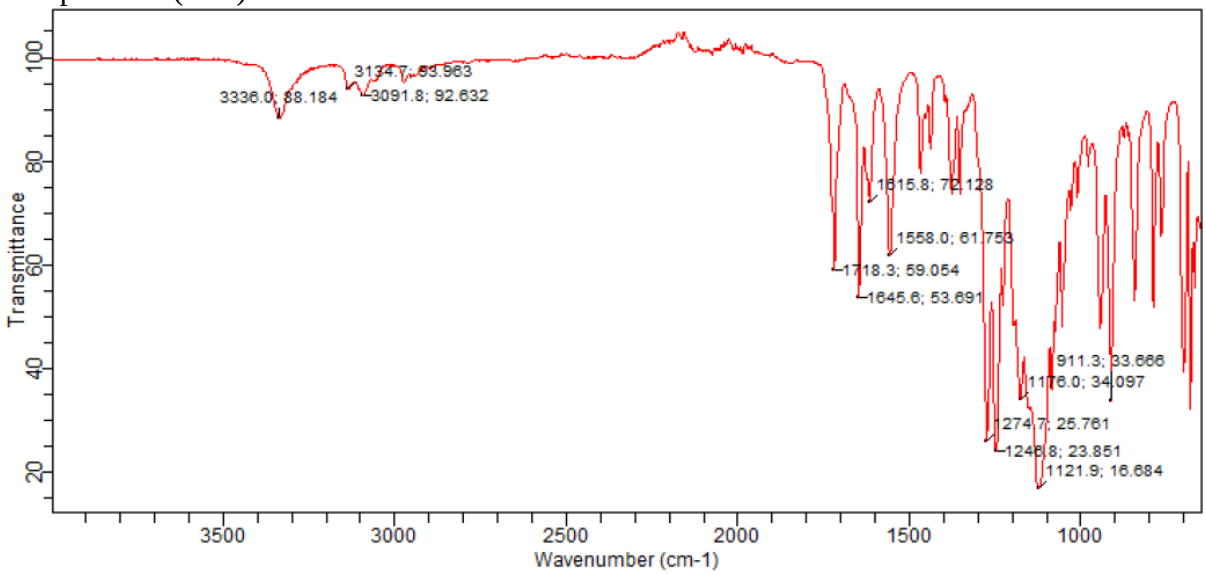
Axle 9

^{1}H-^{13}C HMBC NMR ($CDCl_3$)

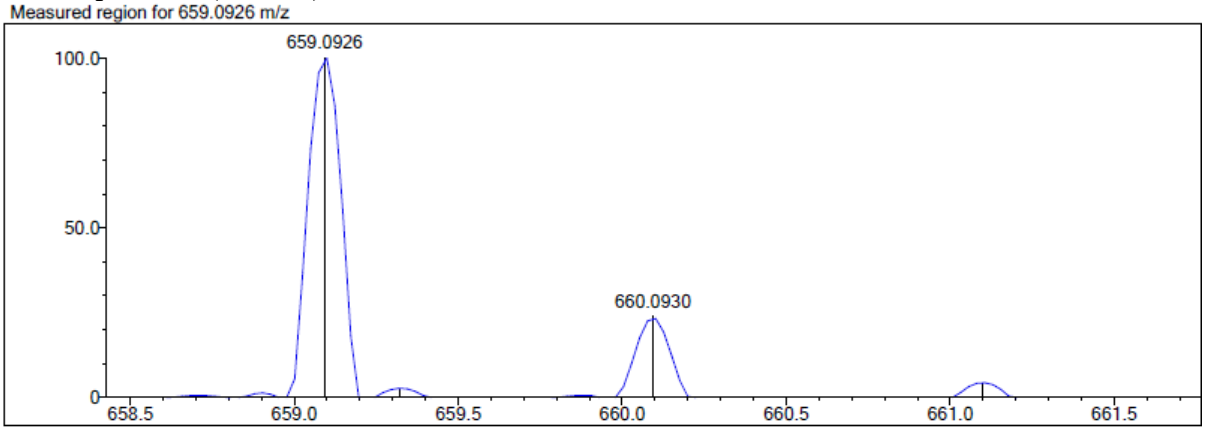


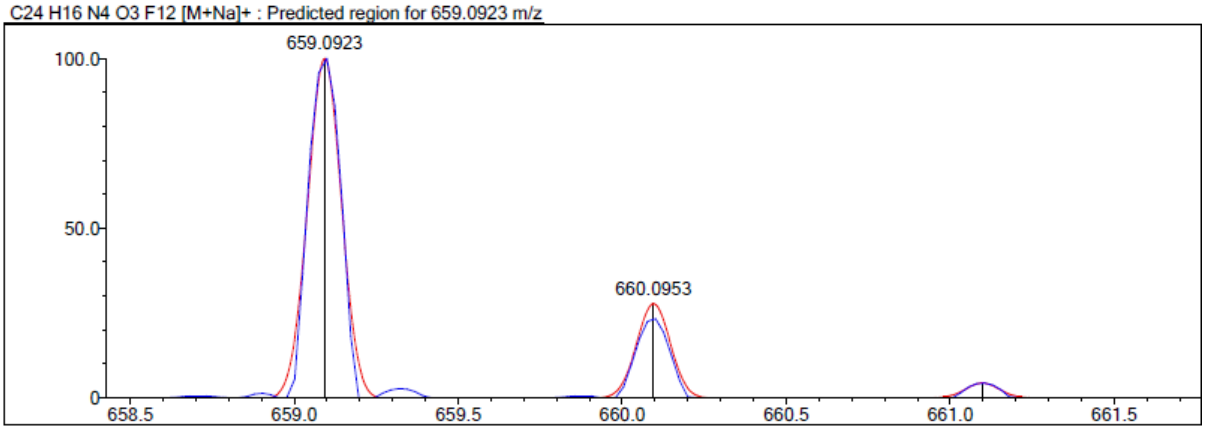
Axle 9

IR Spectrum (neat)

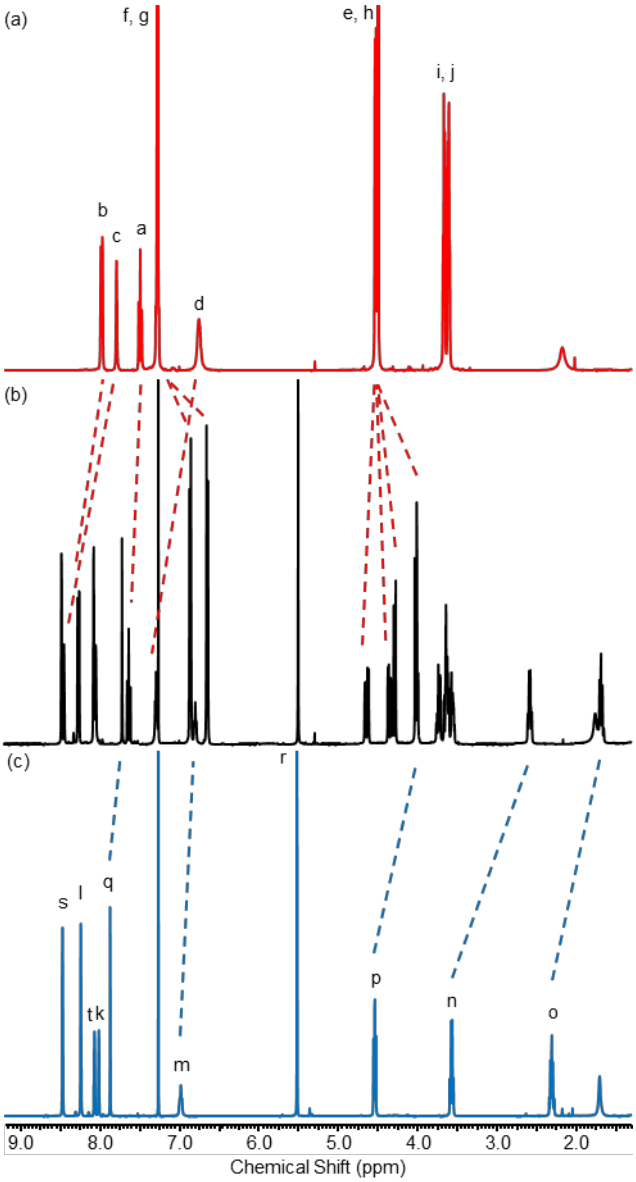


Mass Spectrum (ES +ve)





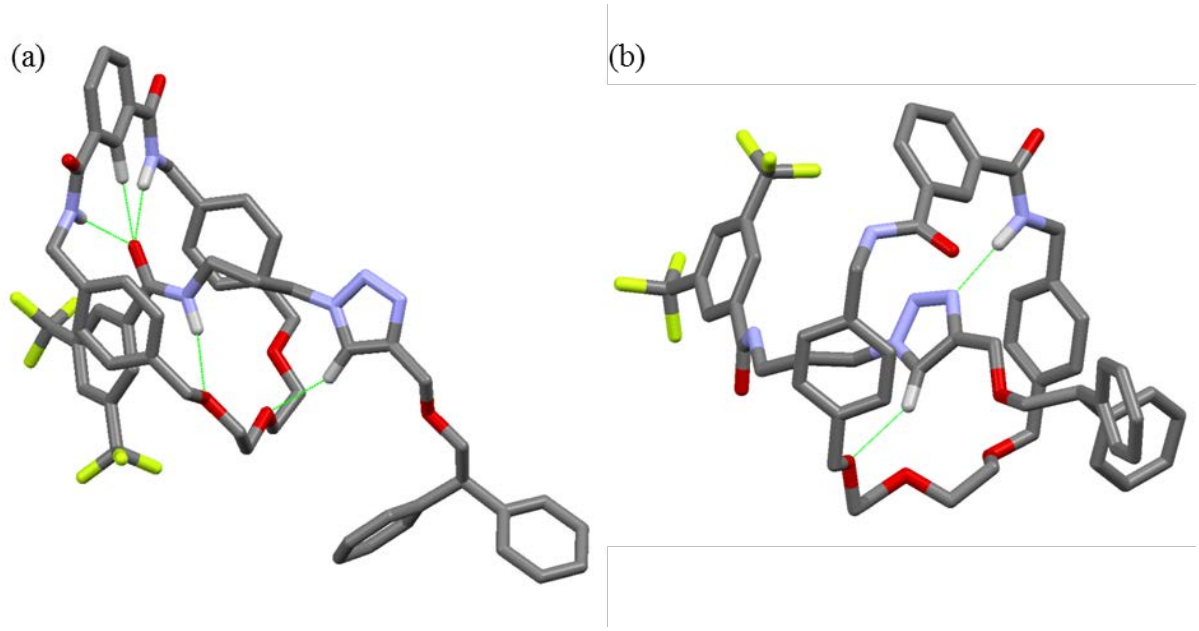
^{1}H NMR Spectral Comparison of (a) Macrocycle 1, (b) Rotaxane 7 and (c) Axle 9 ($CDCl_3$, 400 MHz)



While both the axle amide proton *m* and triazole proton *q* are further upfield in rotaxane **7** compared to free axle **9**, it is noted that alkyl proton *n* (adjacent to the amide) is very much further upfield in the rotaxane compared to the free axle, while alkyl proton *r* (adjacent to the triazole) has the same chemical shift in the rotaxane and free axle. These observations support the macrocycle residing over the amide rather than the triazole in rotaxane **7**.

Part III: Computational Modelling

Minimium Energy Structures of Rotaxane 6



Energies of Minimised Structures of Rotaxanes 6 and 7

"Station" occupied	Rotaxane **6**	Rotaxane **7**
amide	−9609241 kJ mol^{-1}	−10863599 kJ mol^{-1}
triazole	−9609200 kJ mol^{-1}	−10863523 kJ mol^{-1}
difference	41 kJ mol^{-1}	76 kJ mol^{-1}

NB: The four relevant structure files are supplied as part of the ESI.

Hydrogen Bond Distances in Minimised Structures of Rotaxanes 6 and 7

Macrocycle residing over amide of axle component

	Rotaxane **6**	Rotaxane **7**
isophthalamide N-H···O of axle amide	2.134 Å, 2.500 Å	2.195 Å, 2.385 Å
isophthalamide C-H···O of axle amide	2.205 Å	2.195 Å
axle N-H···O polyether	2.629 Å	2.762 Å
triazole C-H···O polyether	2.355 Å	2.316 Å

Macrocycle residing over triazole of axle component

	Rotaxane **6**	Rotaxane **7**
isophthalamide N-H···N of triazole	1.973 Å	1.993 Å
triazole C-H···O polyether	2.376 Å	2.286 Å

Part IV: References and Notes

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4) J. A. Wisner, P. D. Beer and M. G. B. Drew, *Angew. Chem. Int. Edit.*, 2001, **40**, 3606-3609.
5) L. M. Hancock, DPhil Thesis, University of Oxford, 2011.