Electronic Supplementary Information

Rapid Synthesis of Hydrogen Bond Templated Handcuff Rotaxanes

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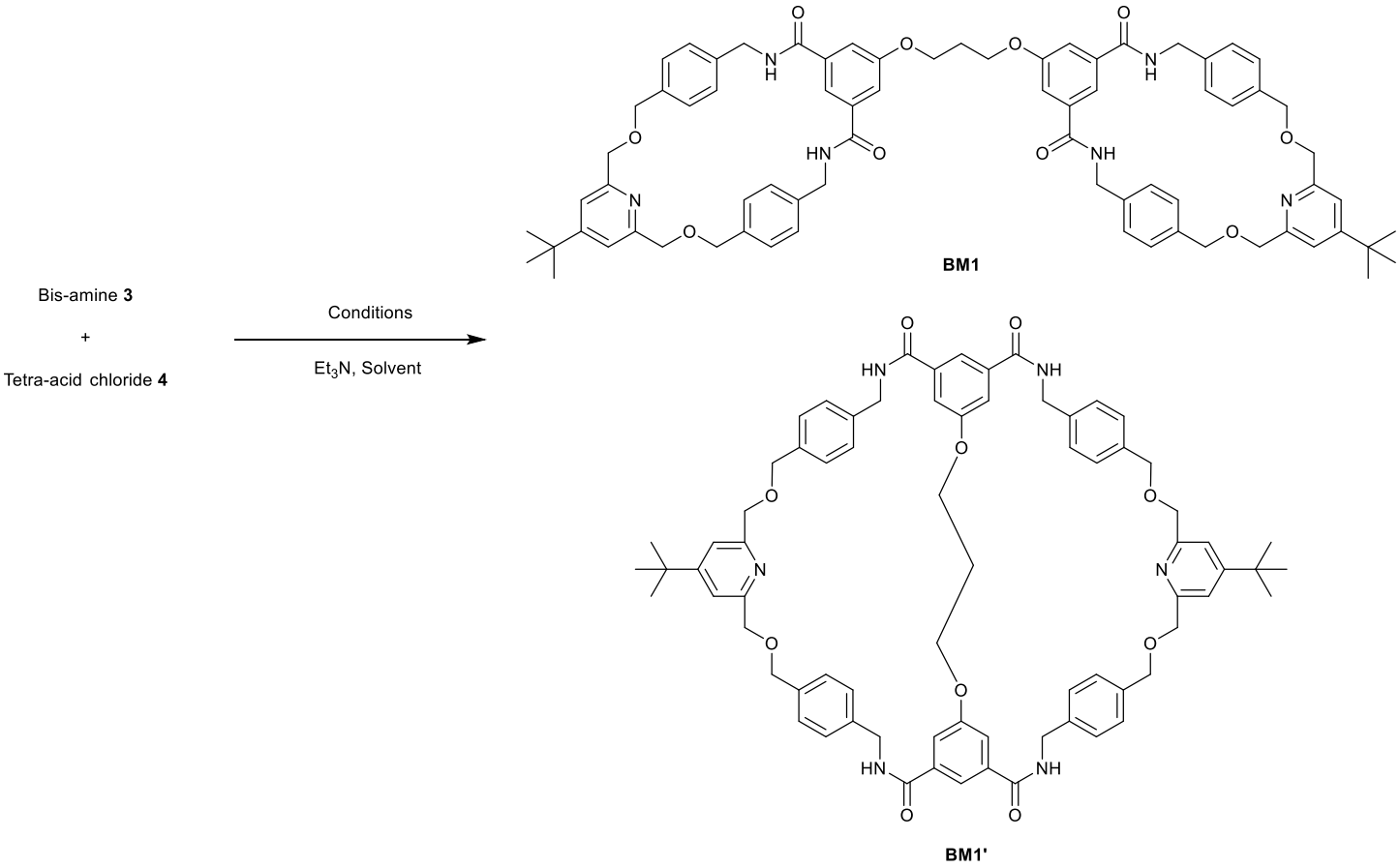
Part 1: Further details on attempted synthesis of bis-macrocycle BM1



Attempt	Solvent	Template	High[a] / Semi-high[b] dilution	(%) Yield **BM1**	(%) Yield **BM1'**
1	CH_2Cl_2	**5.Cl**	Semi-high dilution	2	5
2	CH_2Cl_2	**5.Cl**	High dilution	< 2	3
3	CH_2Cl_2	-	High dilution	-	-
4	$CHCl_3$	**5.Cl**	Semi-high dilution	< 2	6
5	$CHCl_3$	-	High dilution	-	5

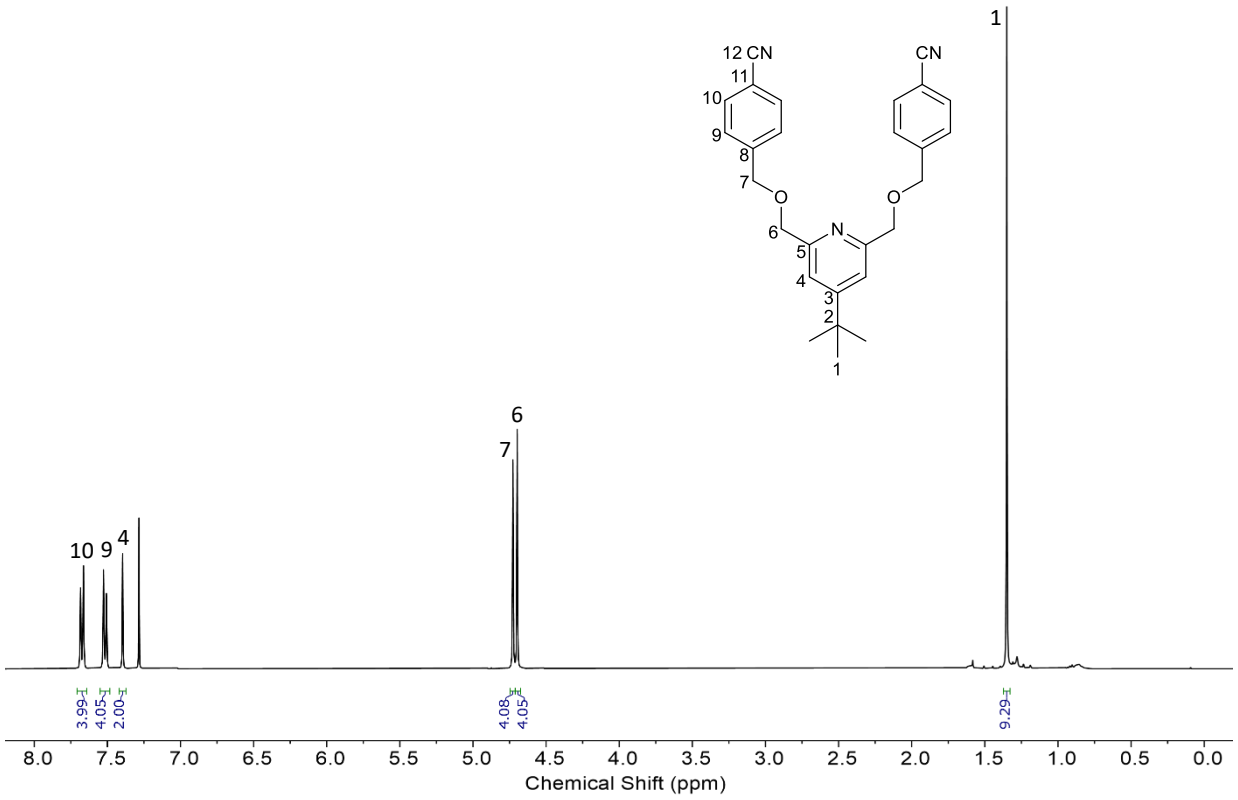
[a]*High dilution attempts were conducted as follows:* Et_3N (5.0 eq) was dissolved in dry solvent (100 mL). Solutions of tetra-acid chloride **4** (1.0 eq) in dry solvent (100 mL) and bis-amine **3** (2.0 eq, with or without the presence of template **5.Cl**, 2.0 eq) in dry solvent (100 mL) were added dropwise simultaneously to the above basic solution. The reaction was stirred for 16 hours, then washed with 10% critic acid (2 x 100 mL) and brine (1 x 100 mL). The organic layer was dried ($MgSO_4$) and concentrated *in vacuo*. The crude material was then purified by silica gel column chromatography.

[b]*Semi-high dilution attempts were conducted as follows:* Bis-amine **3** (2.0 eq) and template **5.Cl** (2.0 eq) were dissolved in dry solvent (60 mL). Et_3N (5.0 eq) was added followed immediately by a dropwise solution of tetra-acid chloride **4** (1.0 eq) in dry solvent (30 mL). Following addition, the solution was allowed to stir for 4 hours. Then the reaction mixture was washed with 10% critic acid (2 x 100 mL) and brine (1 x 100 mL). The organic layer was dried ($MgSO_4$) and concentrated *in vacuo*. The crude material was then purified by silica gel column chromatography.

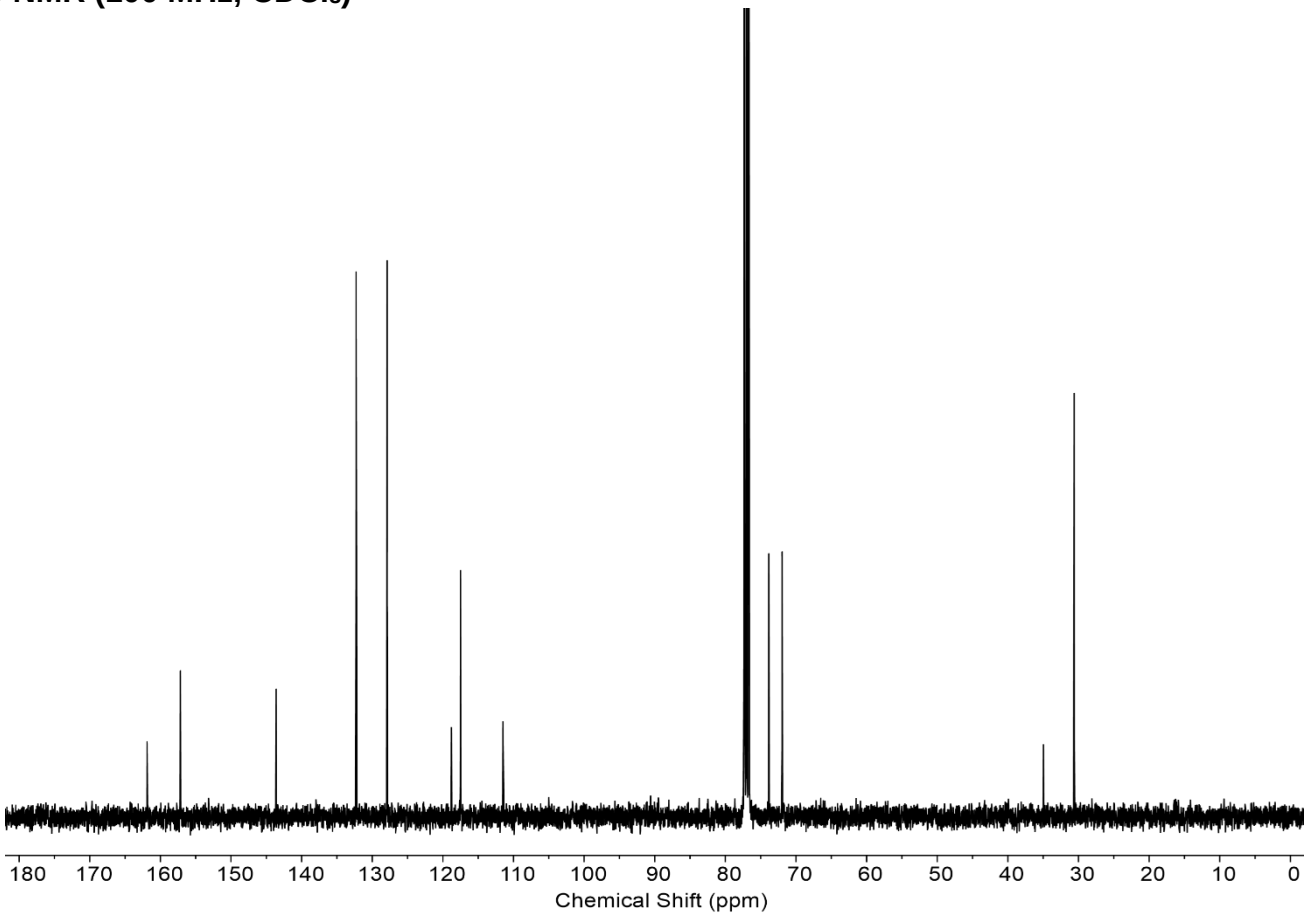
Part 2: Characterization Spectra

Bis-Nitrile 2

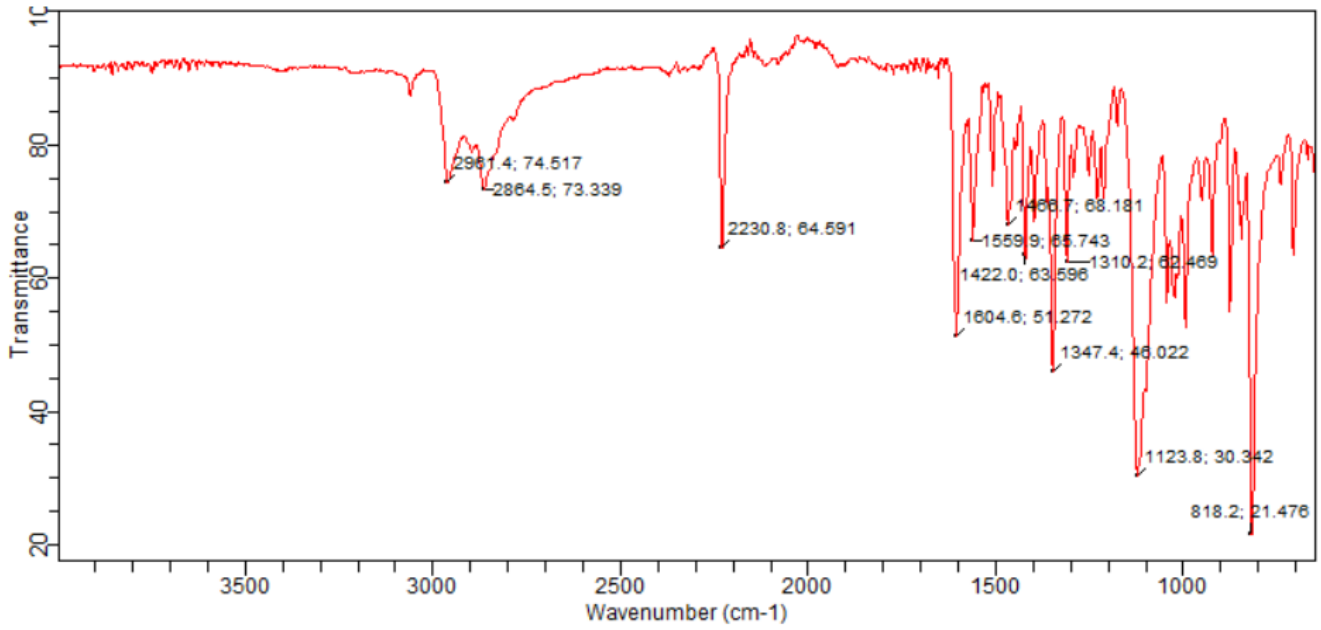
^{1}H NMR (400 MHz, $CDCl_3$)



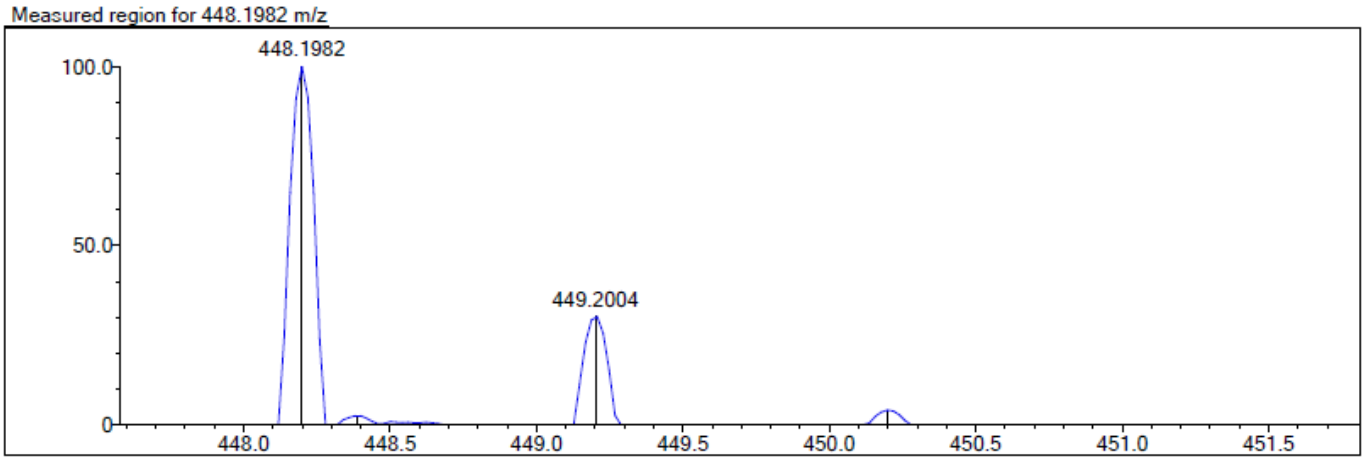
^{13}C NMR (100 MHz, $CDCl_3$)

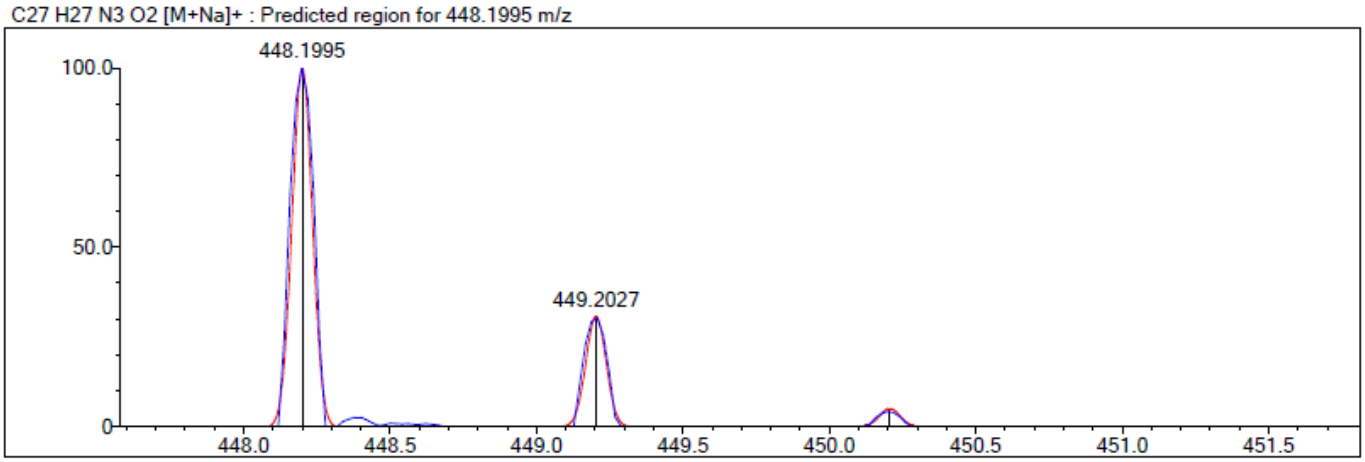


IR Spectrum (neat)



HRMS (ES +ve)

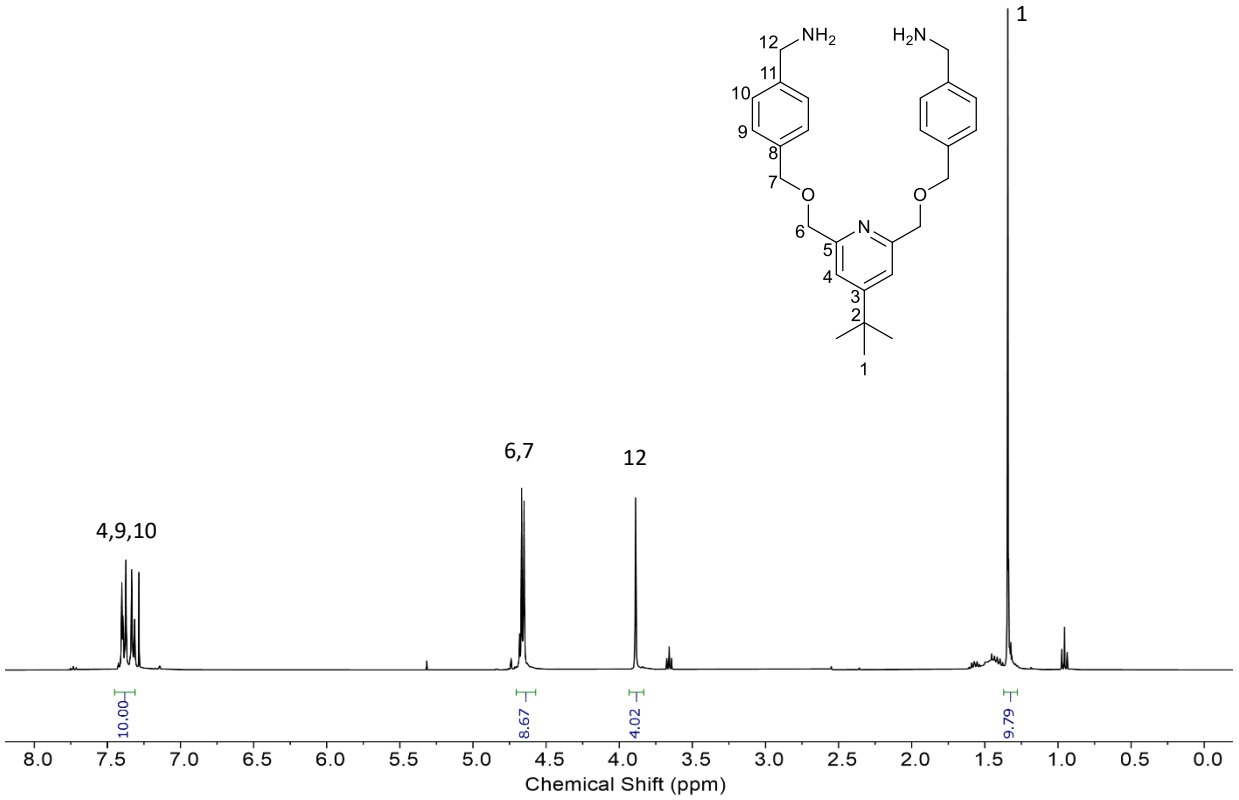




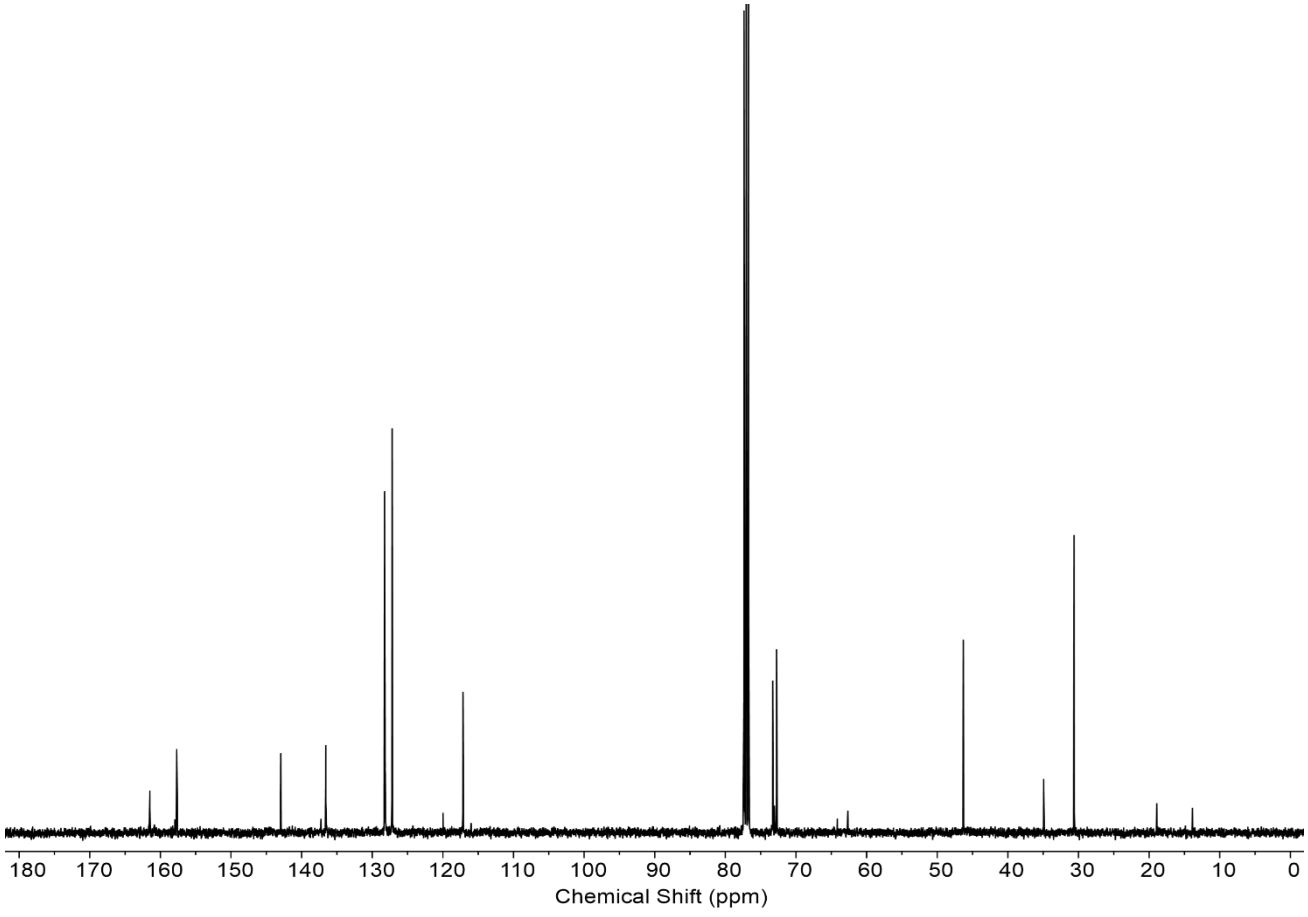
Rank	Score	Formula (M)	Ion	Meas. m/z	Pred. m/z	Df. (mDa)	Df. (ppm)	Iso	DBE
1	95.25	C27 H27 N3 O2	[M+Na]+	448.1982	448.1995	-1.3	-2.90	100.00	16.0

Bis-Amine 3

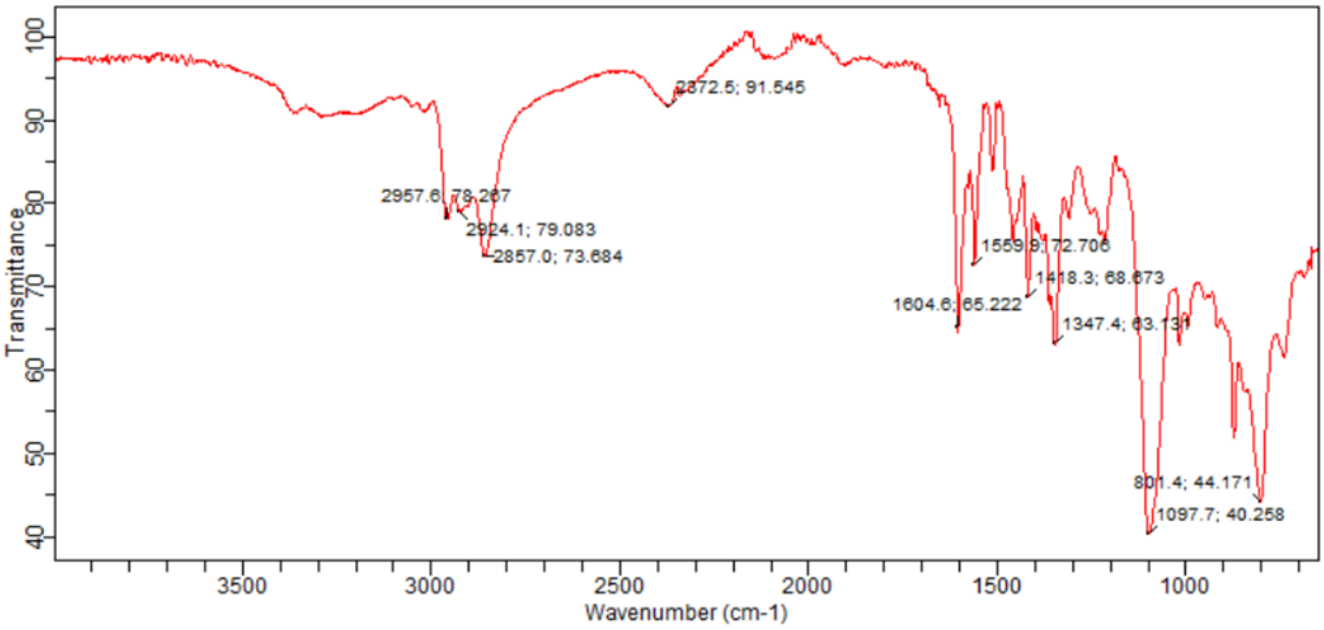
^{1}H NMR (400 MHz, $CDCl_3$)



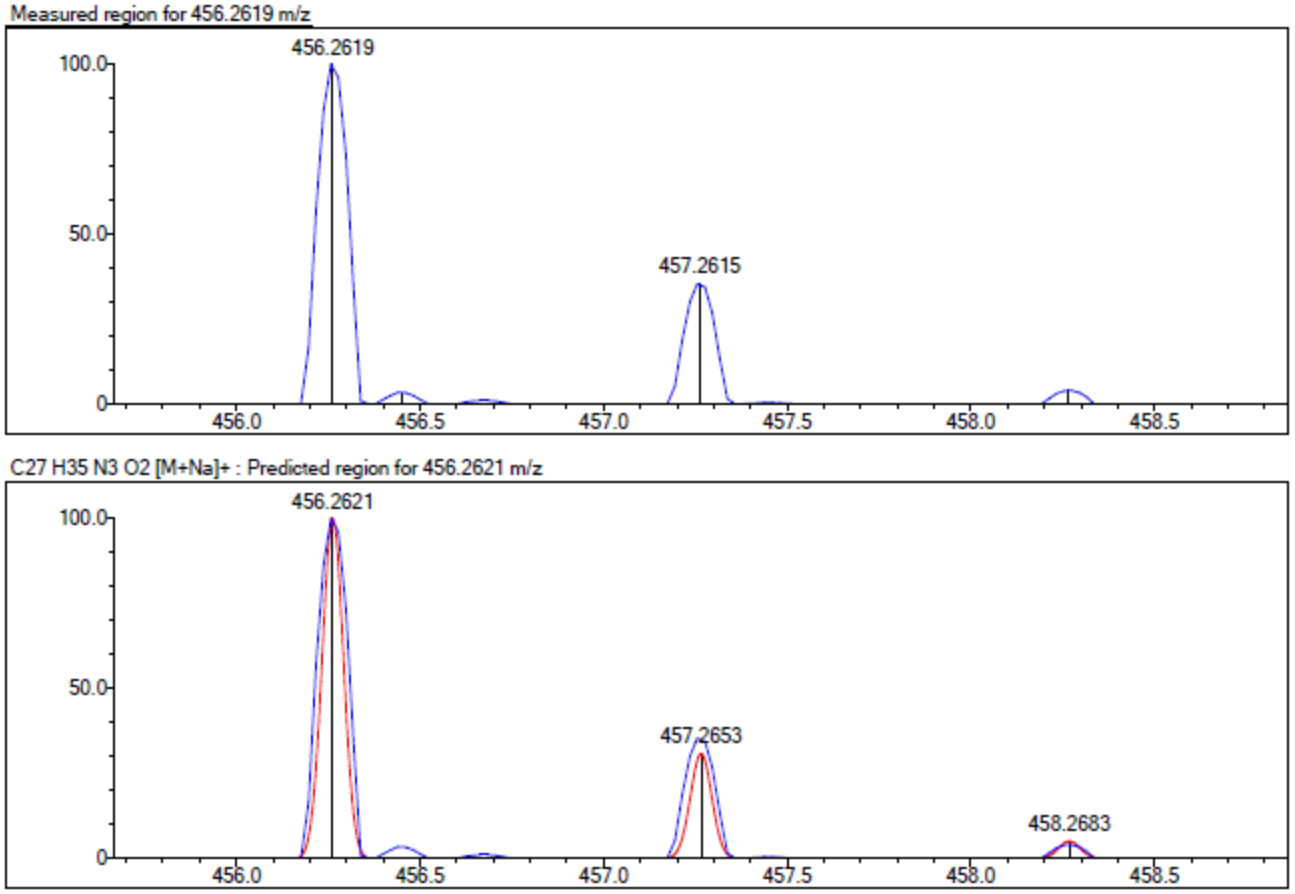
^{13}C NMR (100 MHz, $CDCl_3$)



IR Spectrum (neat)



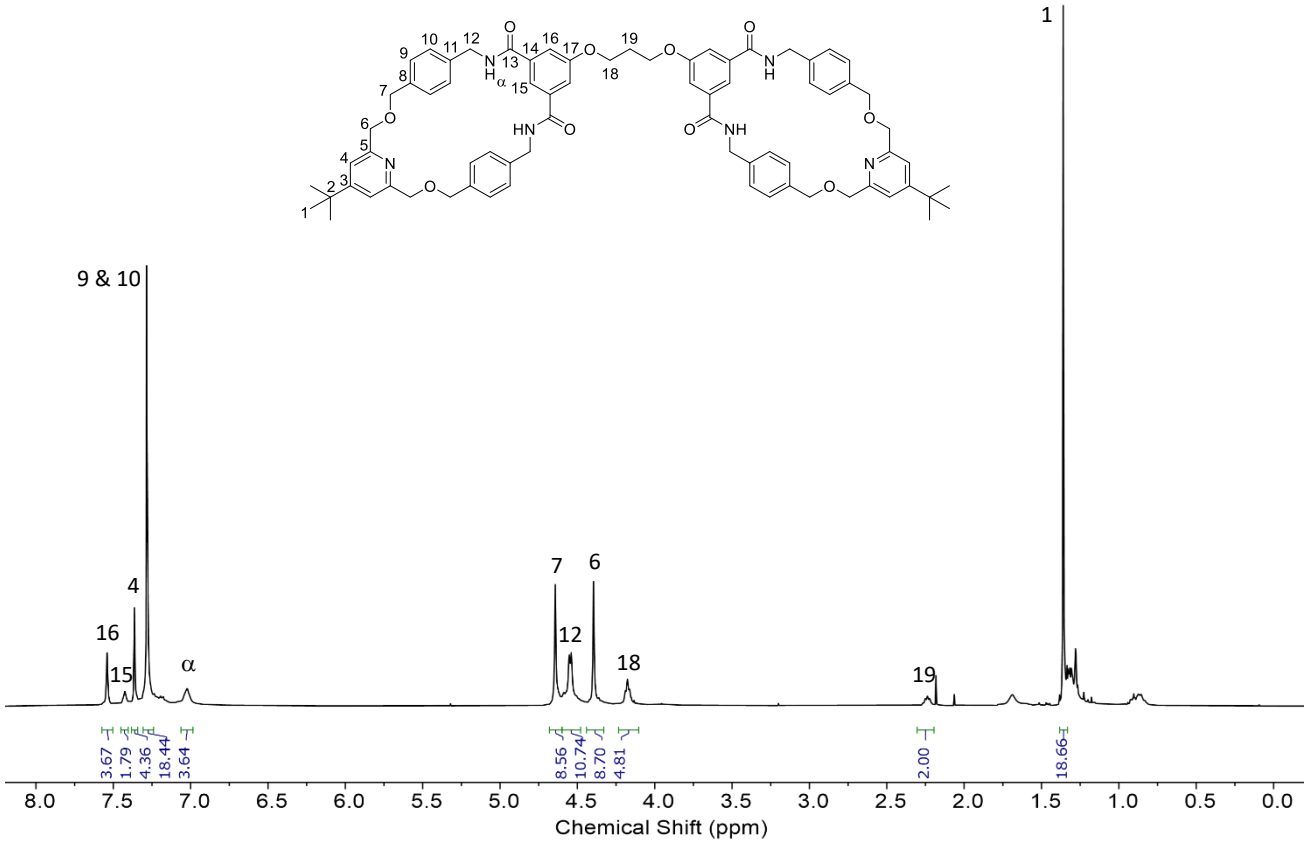
HRMS (ES +ve)



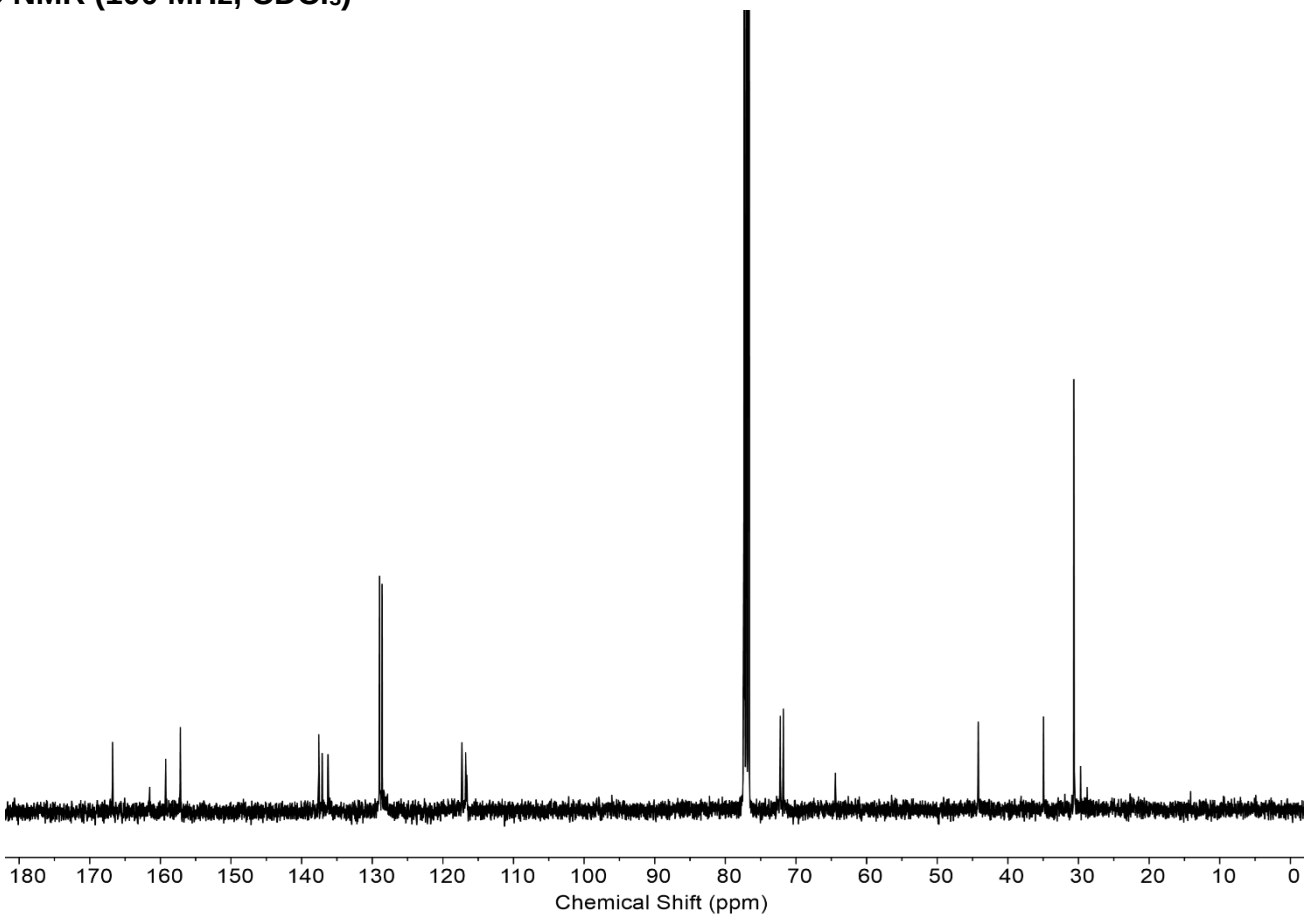
Rank	Score	Formula (M)	Ion	Meas. m/z	Pred. m/z	Df. (mDa)	Df. (ppm)	Iso	DBE
1	95.60	C27 H35 N3 O2	[M+Na]+	456.2619	456.2621	-0.2	-0.44	95.60	12.0

Bis-Macrocycle BM1

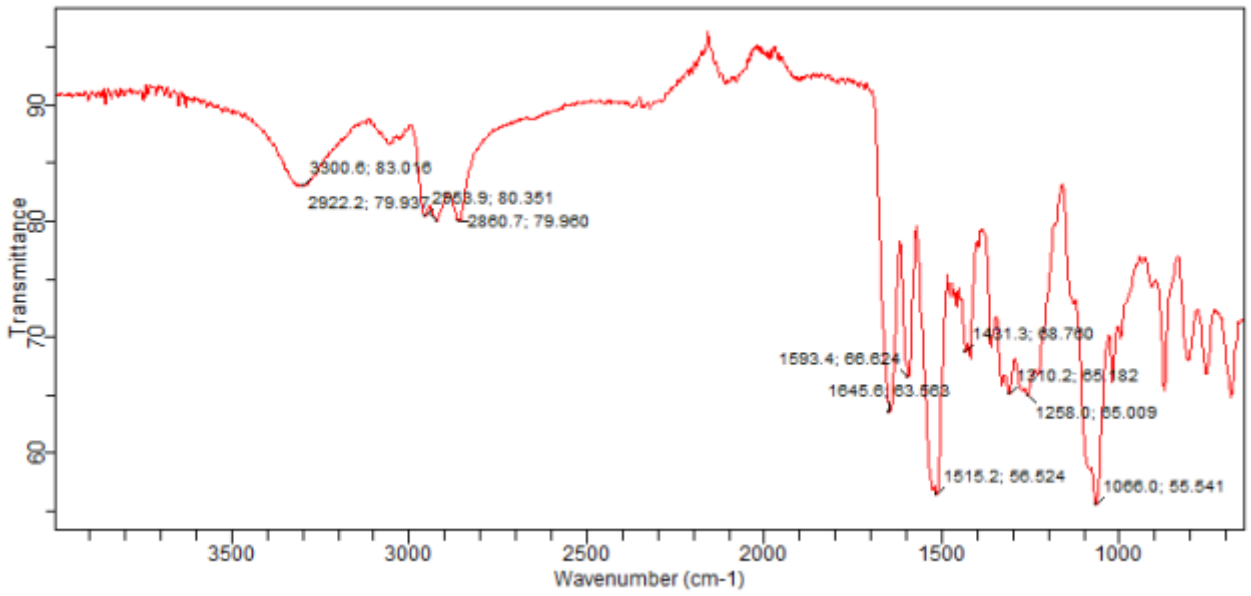
^{1}H NMR (400 MHz, $CDCl_3$)



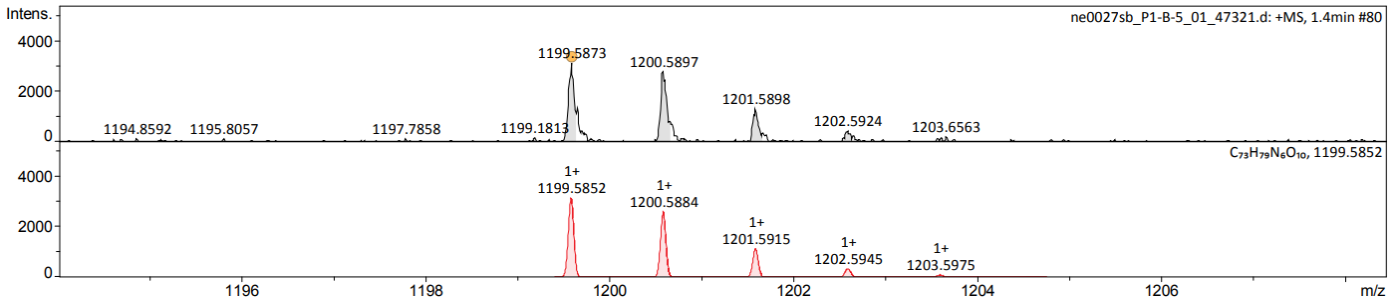
^{13}C NMR (100 MHz, $CDCl_3$)



IR Spectrum (neat)



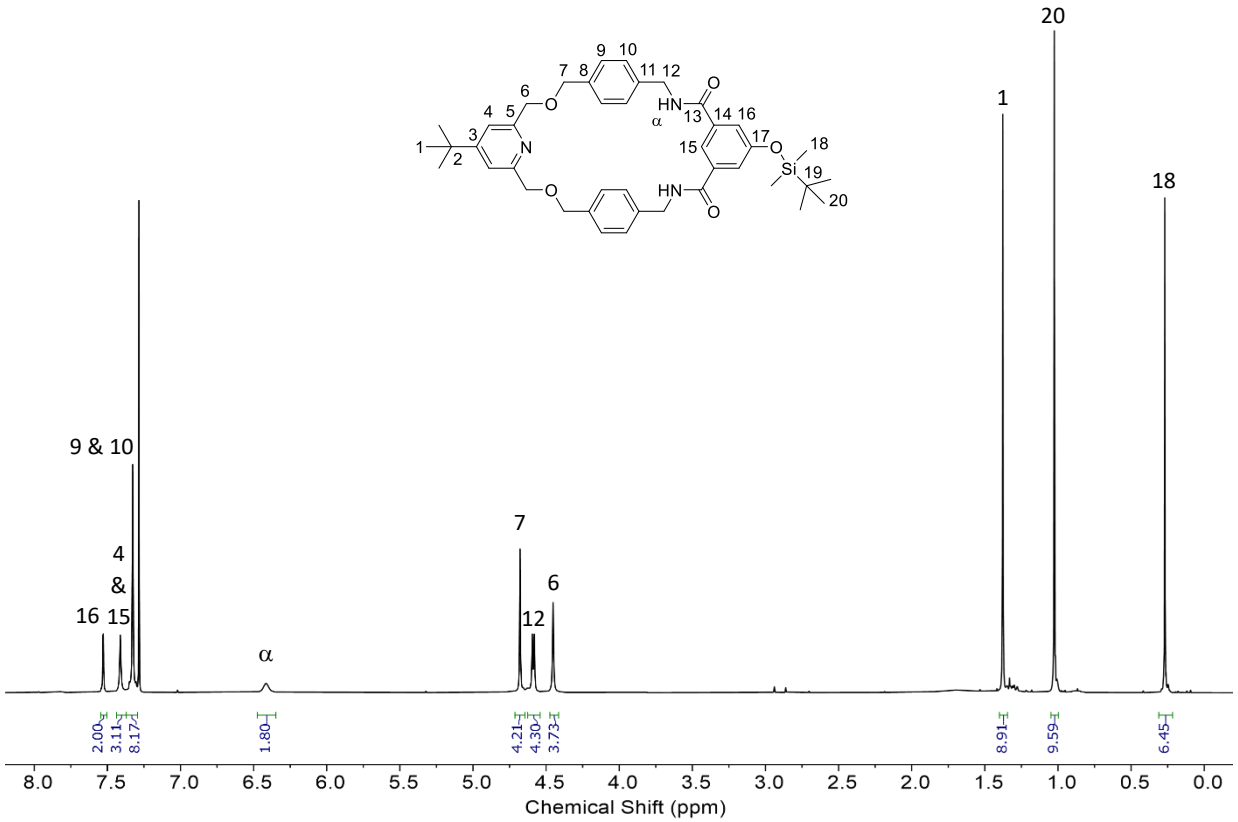
HRMS (ES +ve)



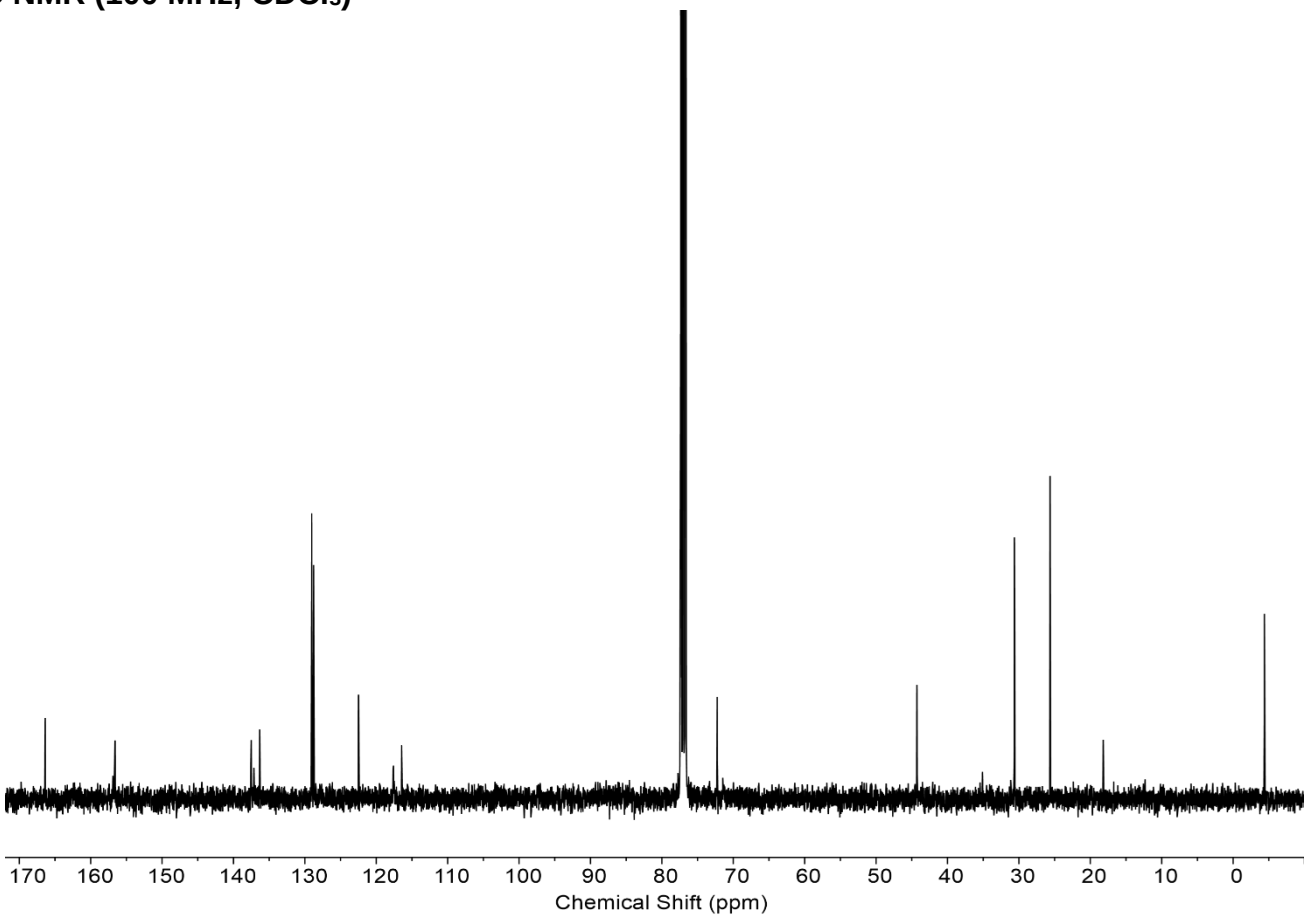
Meas. m/z	#	Ion Formula	m/z	err [ppm]	err [mDa]	mSigma	Mean err [ppm]
1199.5873	1	C73H79N6O10	1199.5852	-1.7	-2.0	45.1	-0.4

TBDMS Protected Macrocycle 7

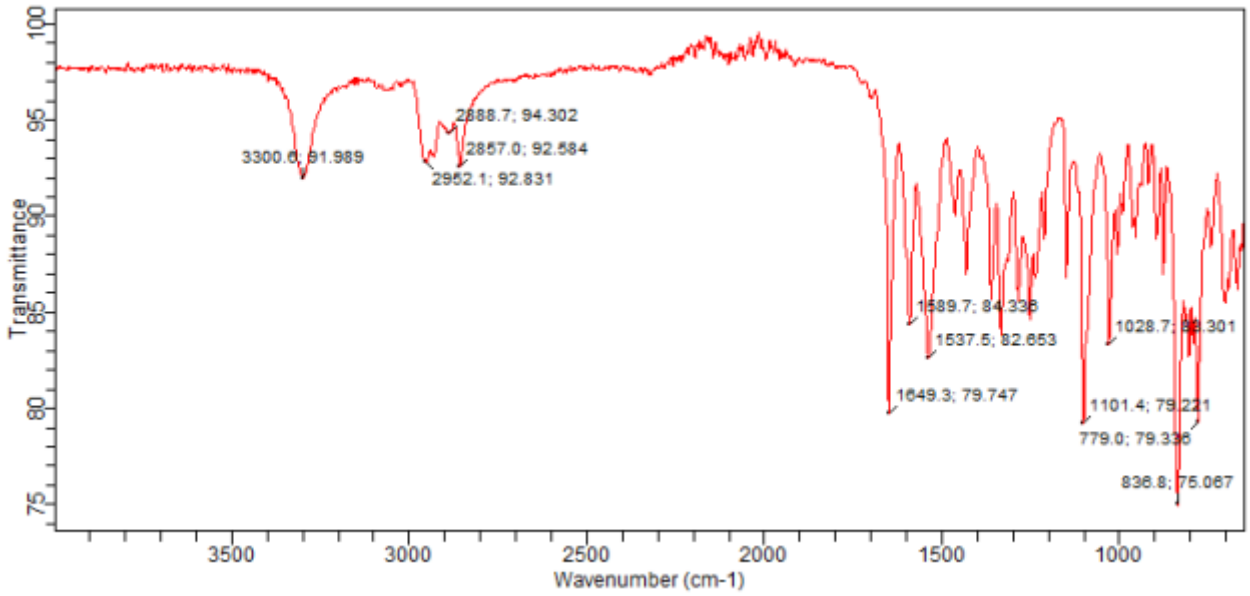
^{1}H NMR (400 MHz, $CDCl_3$)



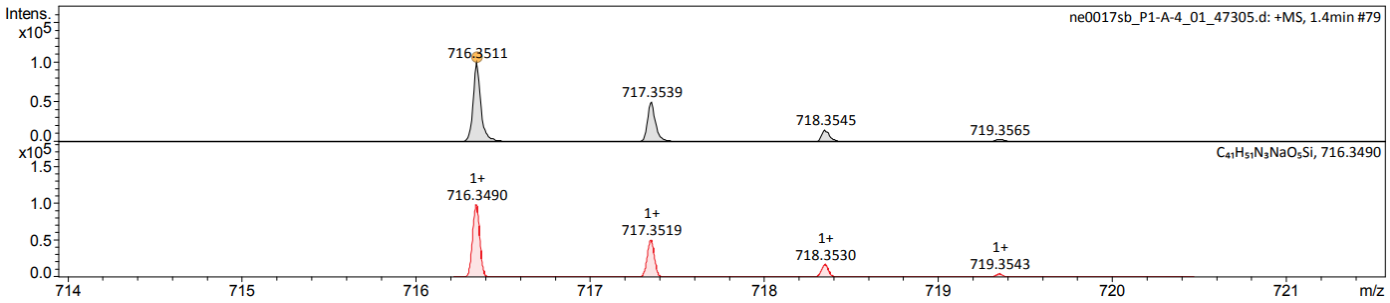
^{13}C NMR (100 MHz, $CDCl_3$)



IR Spectrum (neat)



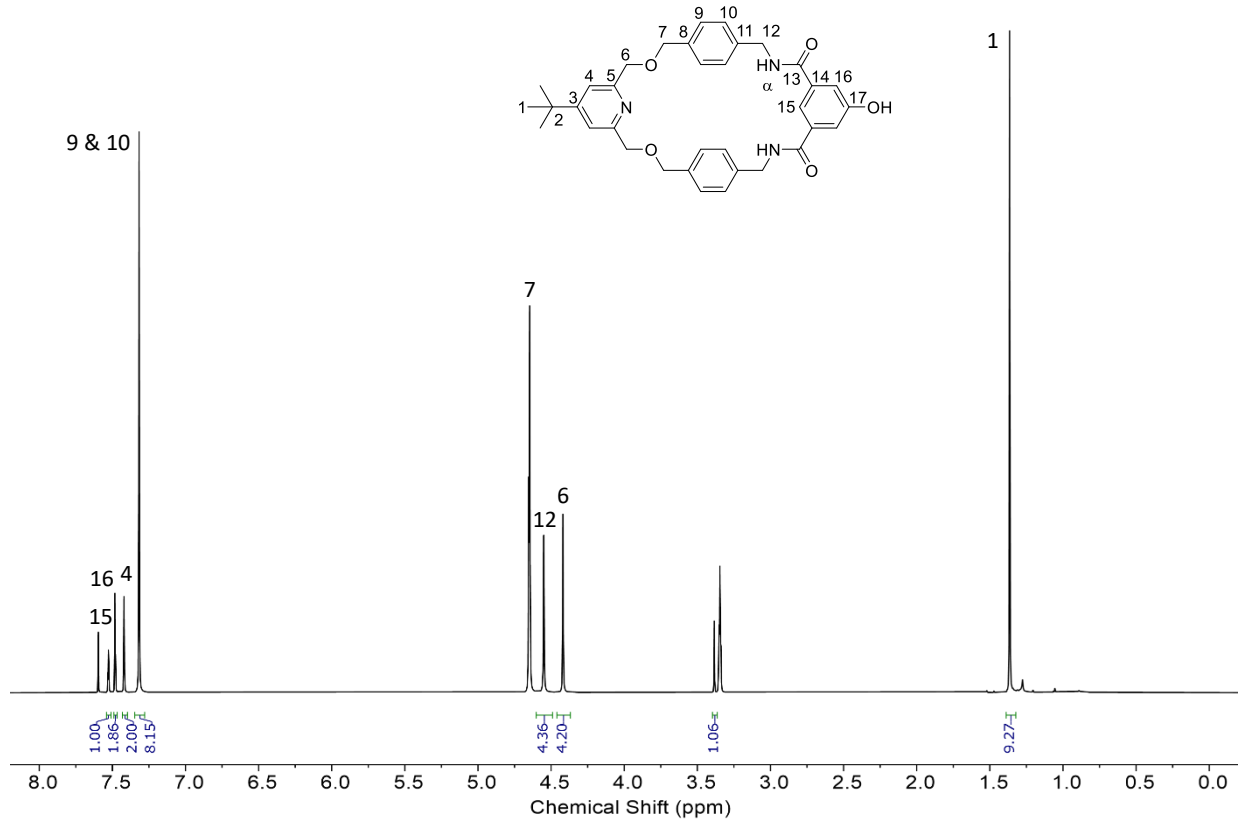
HRMS (ES +ve)



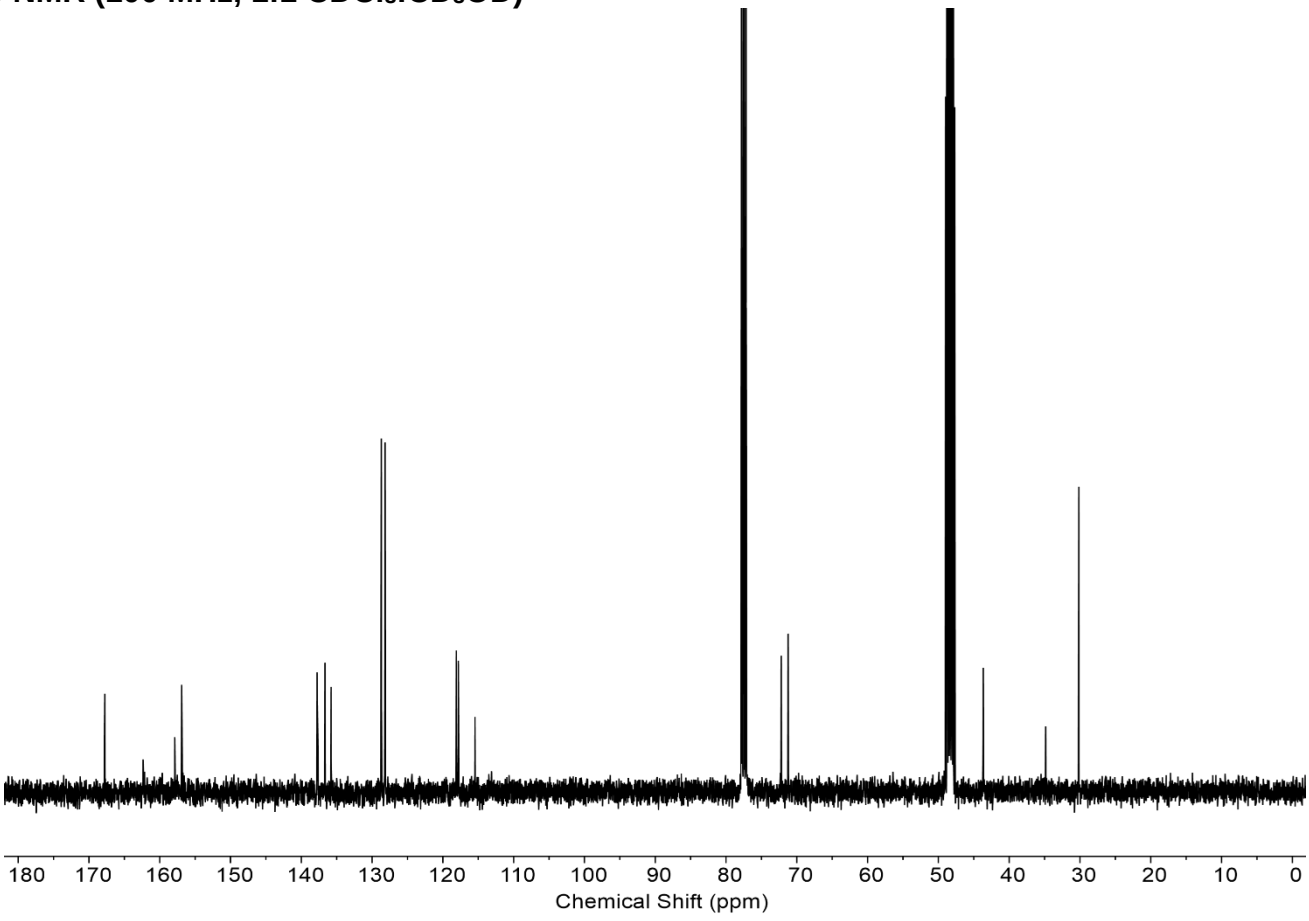
Meas. m/z	#	Ion Formula	m/z	err [ppm]	err [mDa]	mSigma	Mean err [ppm]
694.3684	1	C41H52N3O5Si	694.3671	-1.9	-1.3	6.0	-3.9
716.3511	1	C41H51N3NaO5Si	716.3490	-2.9	-2.1	10.2	-3.5

Phenol Macrocycle 8

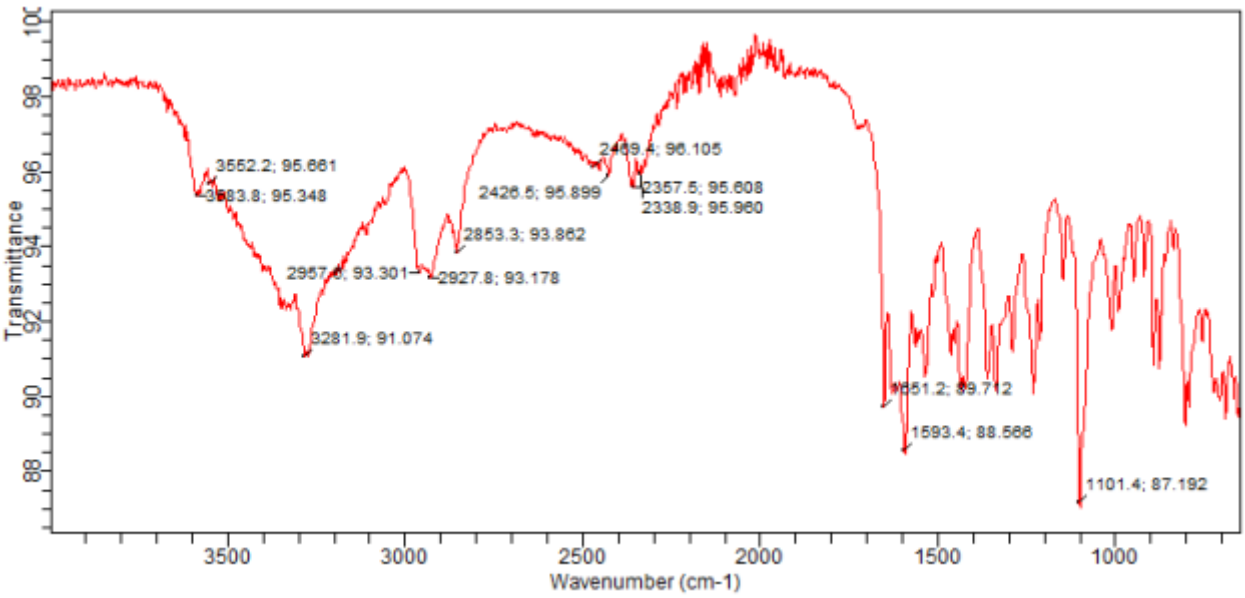
^{1}H NMR (400 MHz, 1:1 $CDCl_3$:CD_3OD)



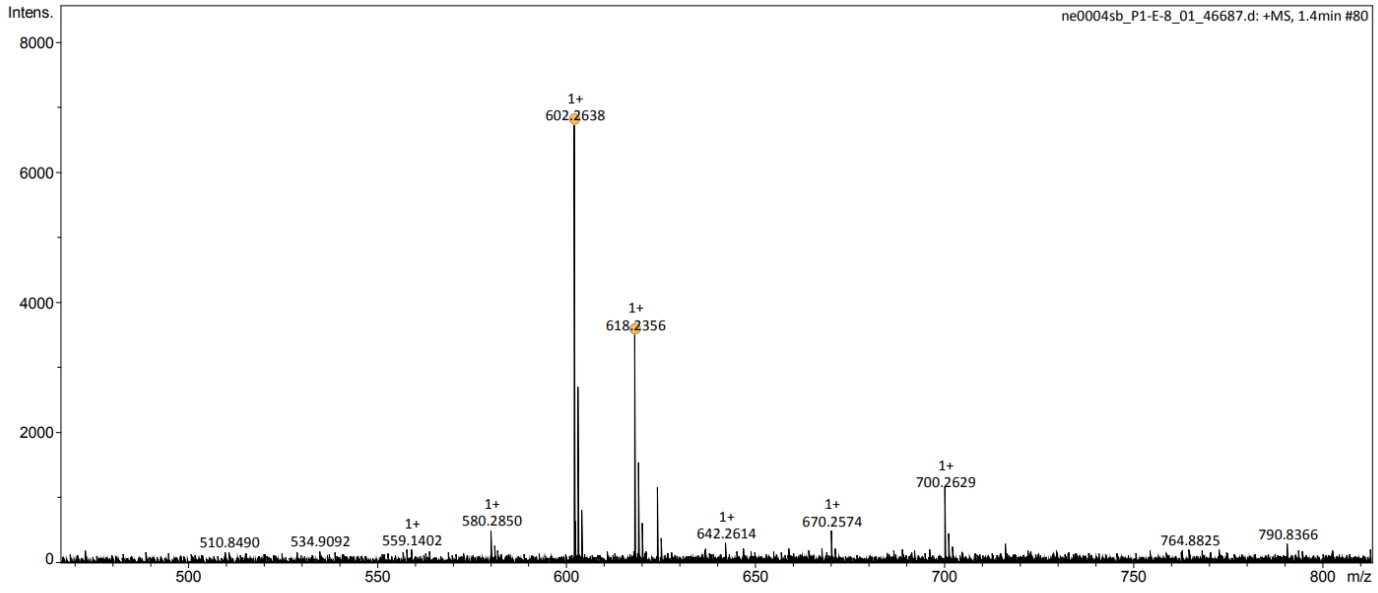
^{13}C NMR (100 MHz, 1:1 $CDCl_3$:CD_3OD)



IR Spectrum (neat)



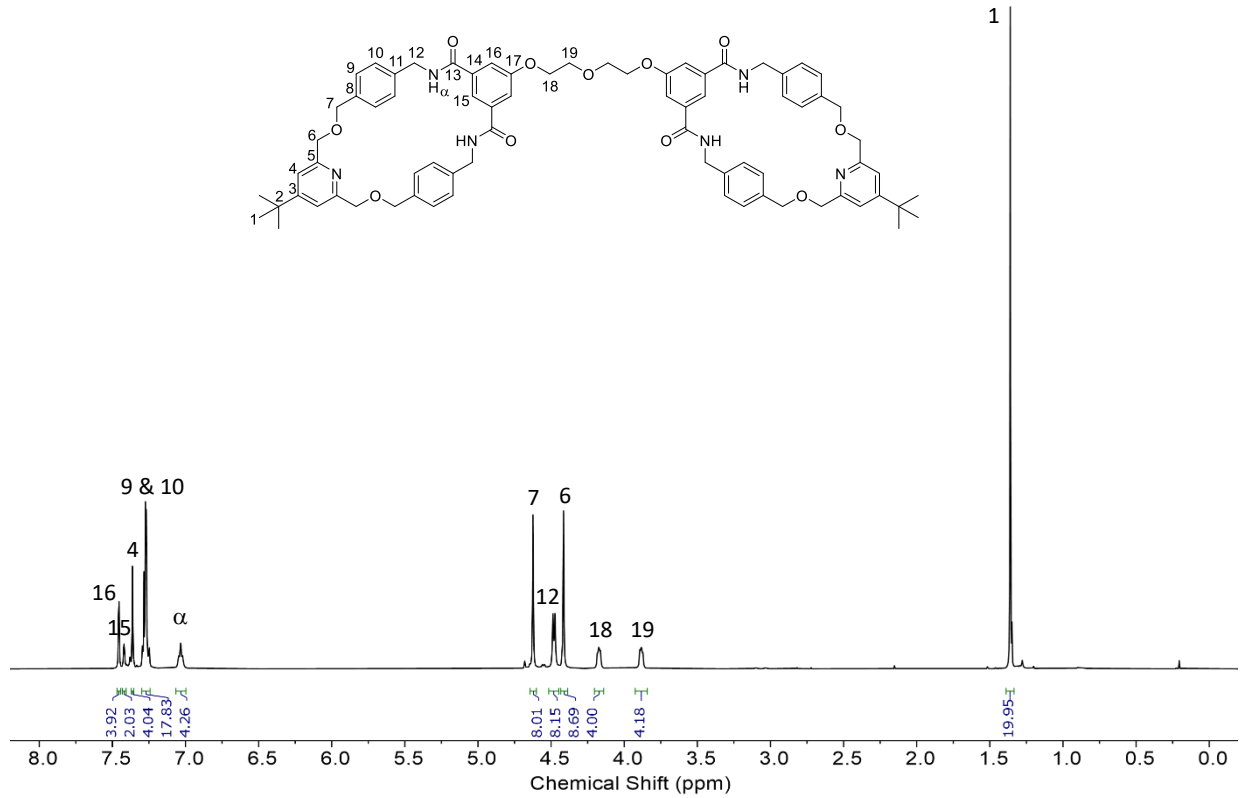
HRMS (ES +ve)



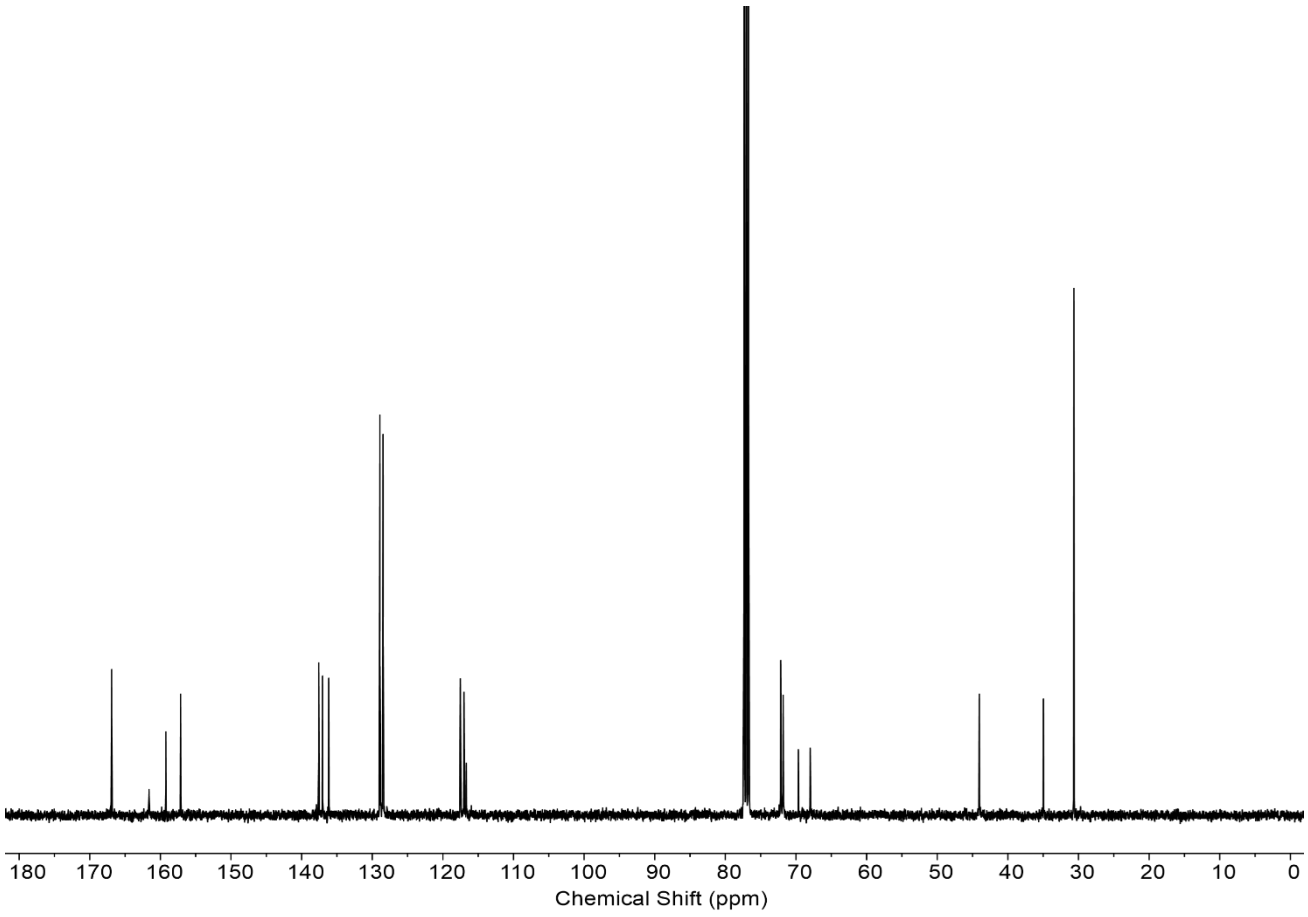
Meas. m/z	#	Ion Formula	m/z	err [ppm]	err [mDa]	mSigma	Mean err [ppm]
602.2638	1	C35H37N3NaO5	602.2625	-2.1	-1.3	19.4	-2.1

Bis-Macrocycle BM2

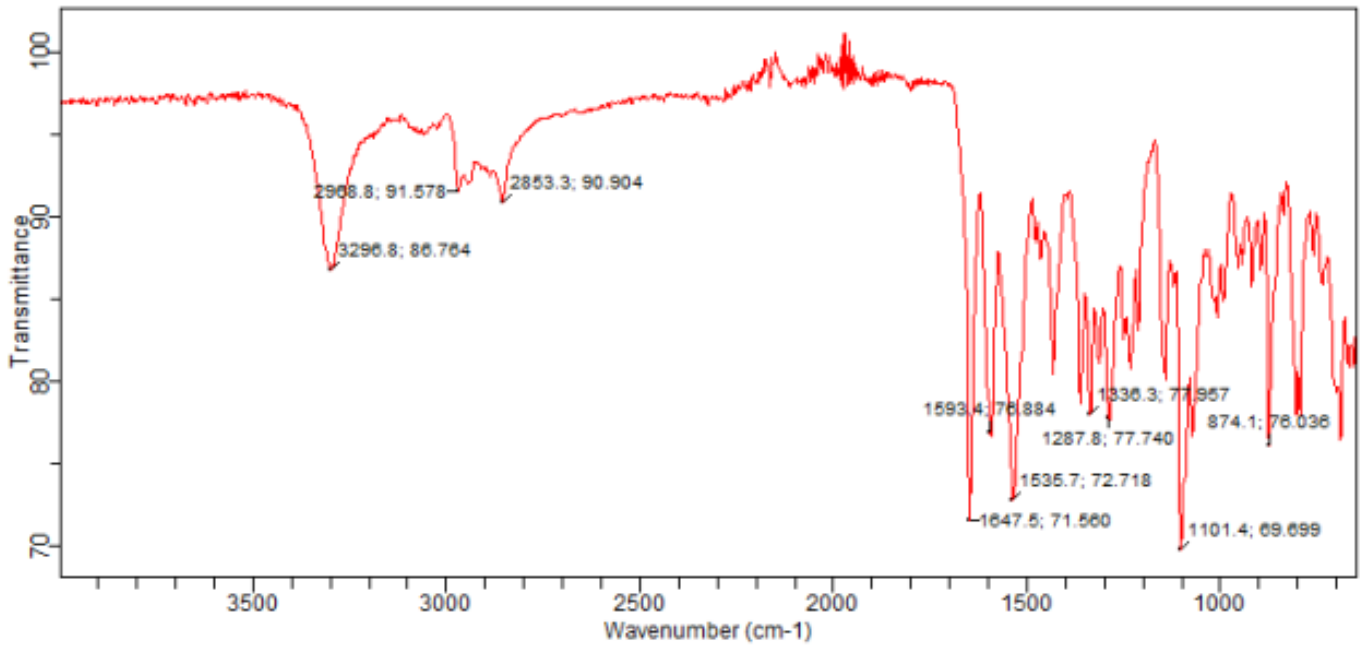
^{1}H NMR (400 MHz, $CDCl_3$)



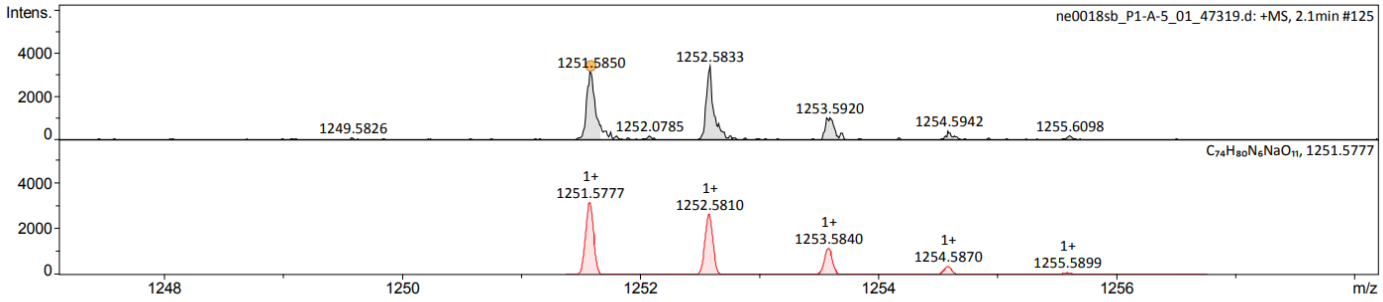
^{13}C NMR (100 MHz, $CDCl_3$)



IR Spectrum (neat)



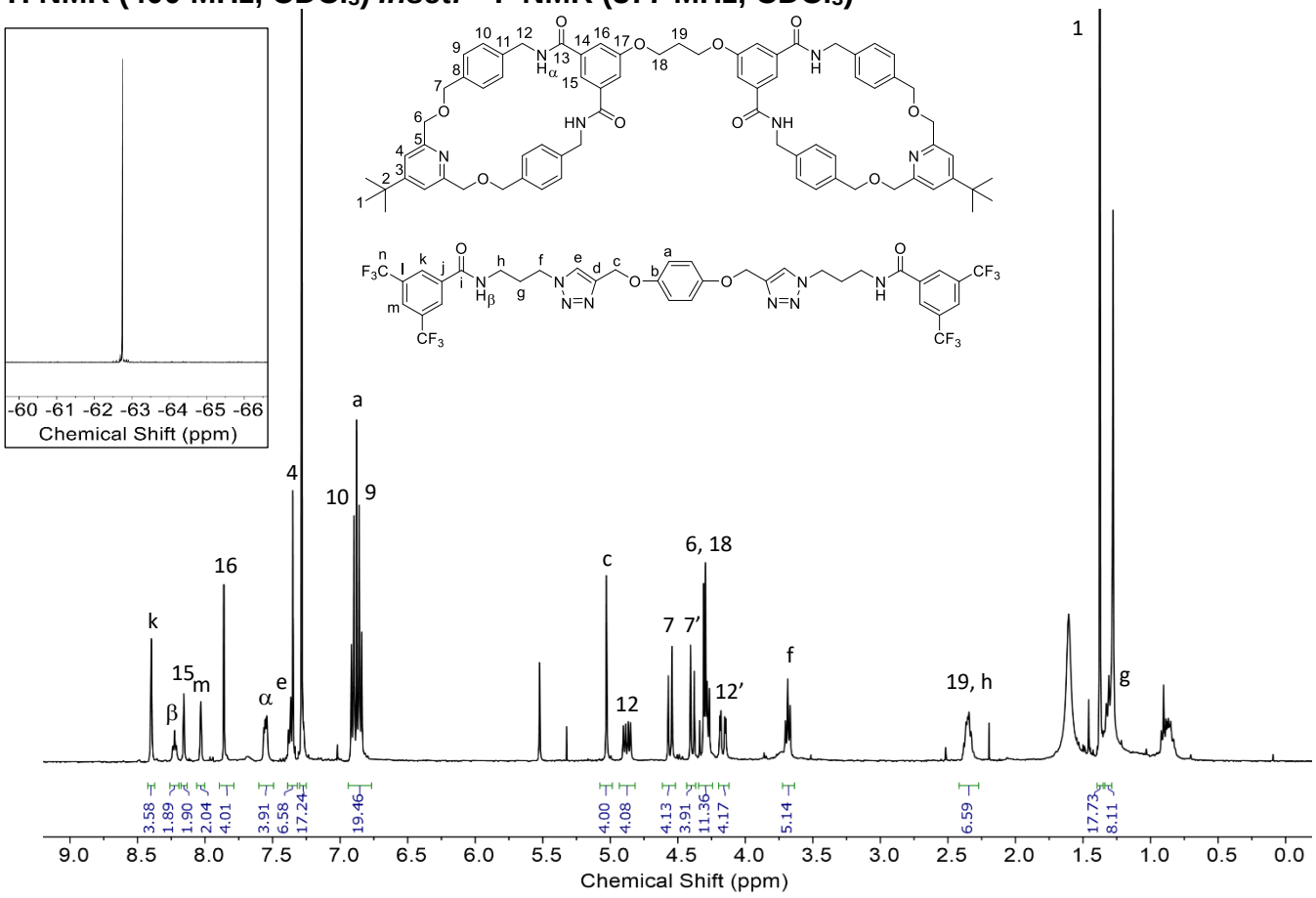
HRMS (ES +ve)



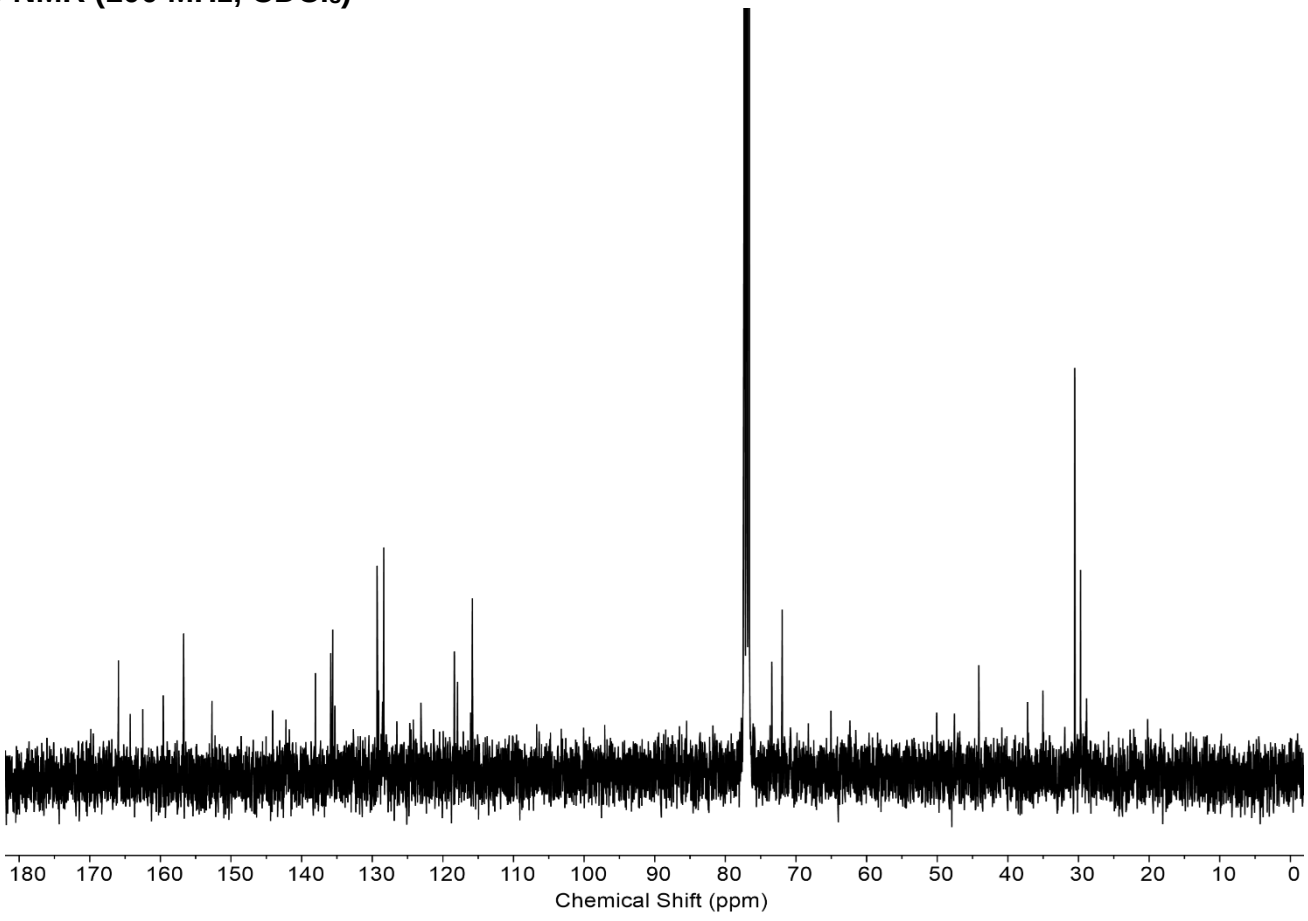
Meas. m/z	#	Ion Formula	m/z	err [ppm]	err [mDa]	mSigma	Mean err [ppm]
1229.5958	1	C74H81N6O11	1229.5958	-0.0	-0.0	93.3	-2.5
1251.5850	1	C74H80N6NaO11	1251.5777	-5.8	-7.3	88.1	-4.2

Handcuff Rotaxane HR1

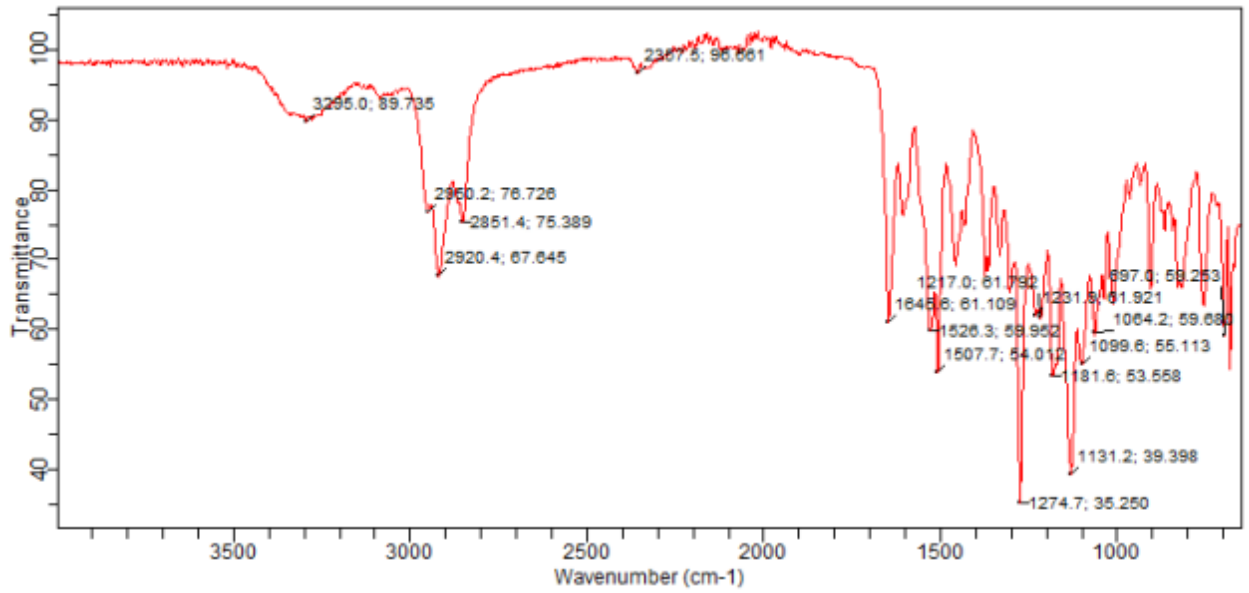
^{1}H NMR (400 MHz, $CDCl_3$) *Inset:* ^{19}F NMR (377 MHz, $CDCl_3$)



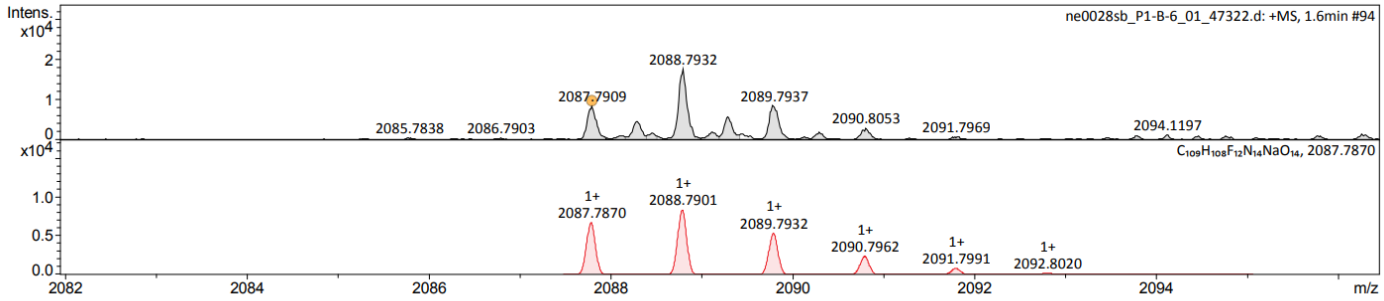
^{13}C NMR (100 MHz, $CDCl_3$)



IR Spectrum (neat)

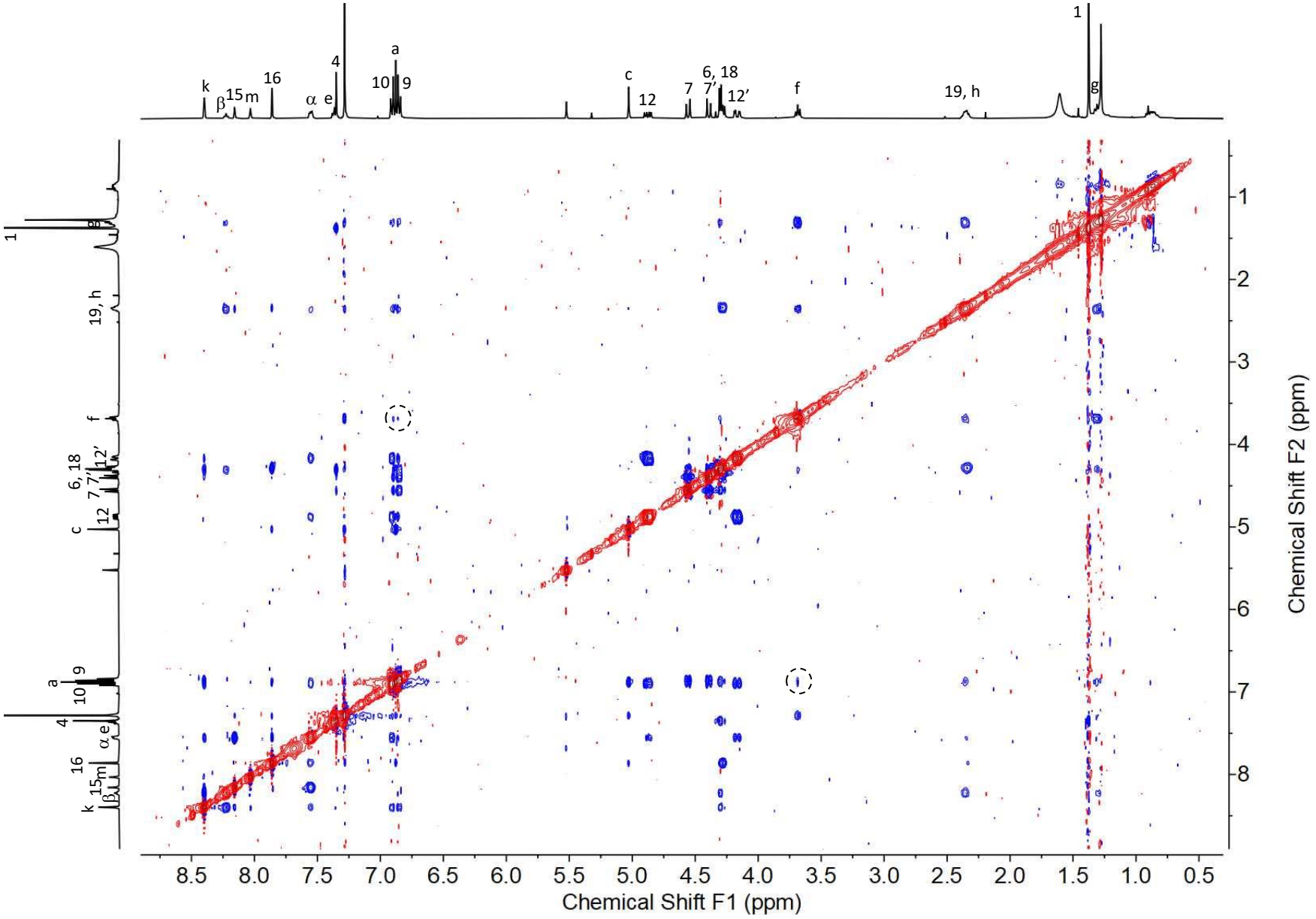


HRMS (ES +ve)



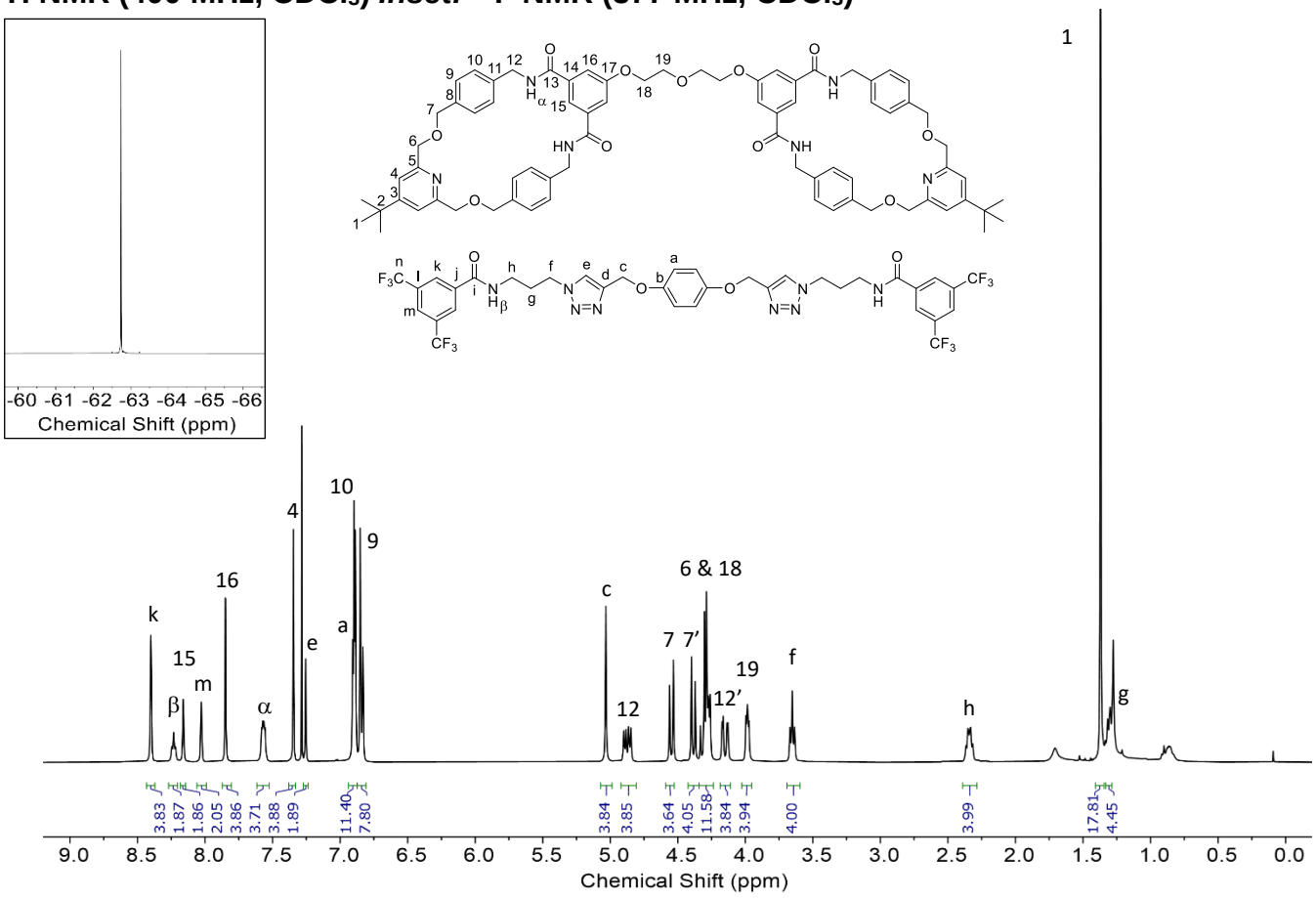
Meas. m/z	#	Ion Formula	m/z	err [ppm]	err [mDa]	mSigma	Mean err [ppm]
2087.7909	1	C109H108F12N14NaO14	2087.7870	-1.9	-3.9	159.2	-1.3

^{1}H-^{1}H ROESY NMR (400 MHz, $CDCl_3$) of HR1 (with intercomponent couplings highlighted)

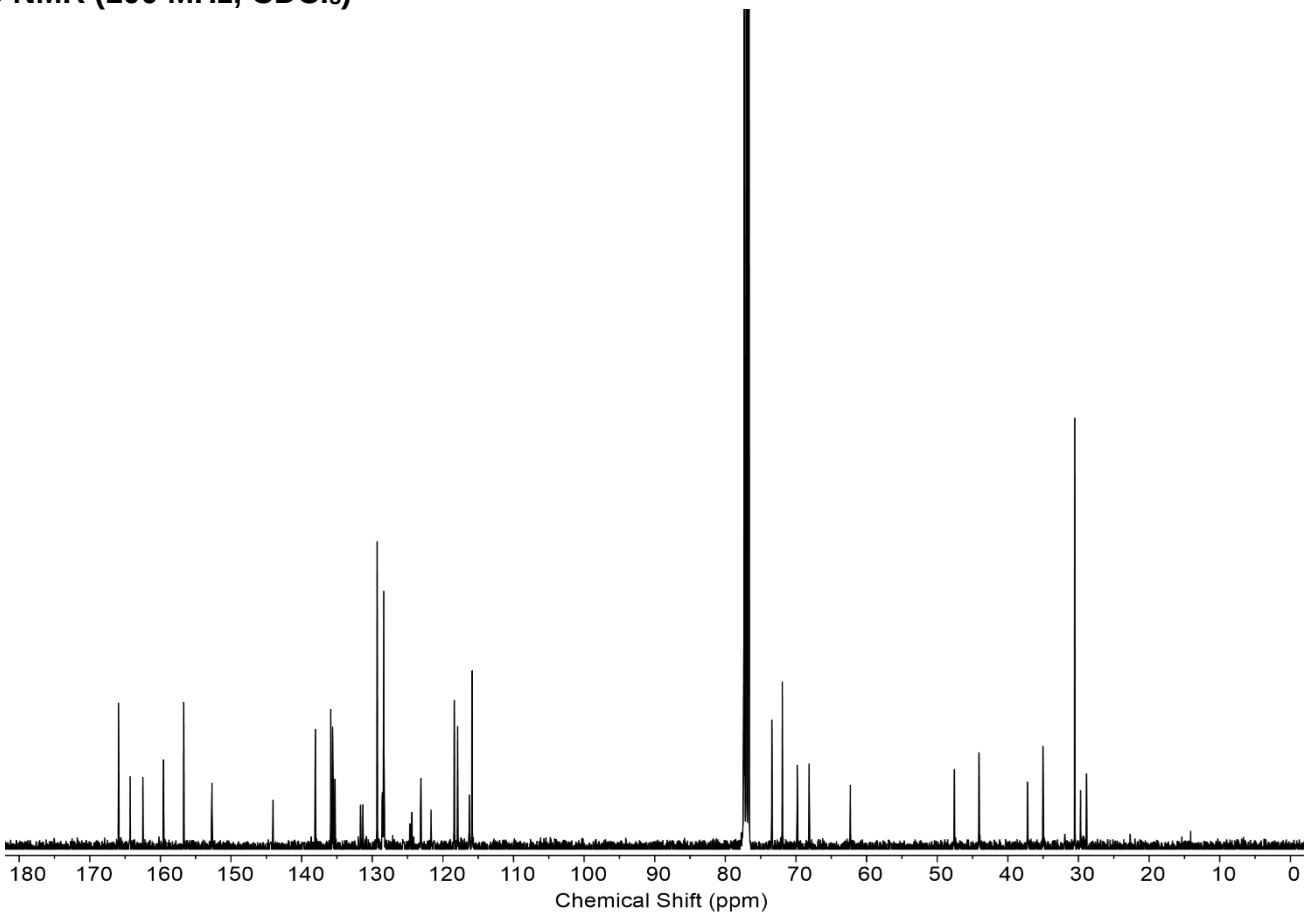


Handcuff Rotaxane HR2

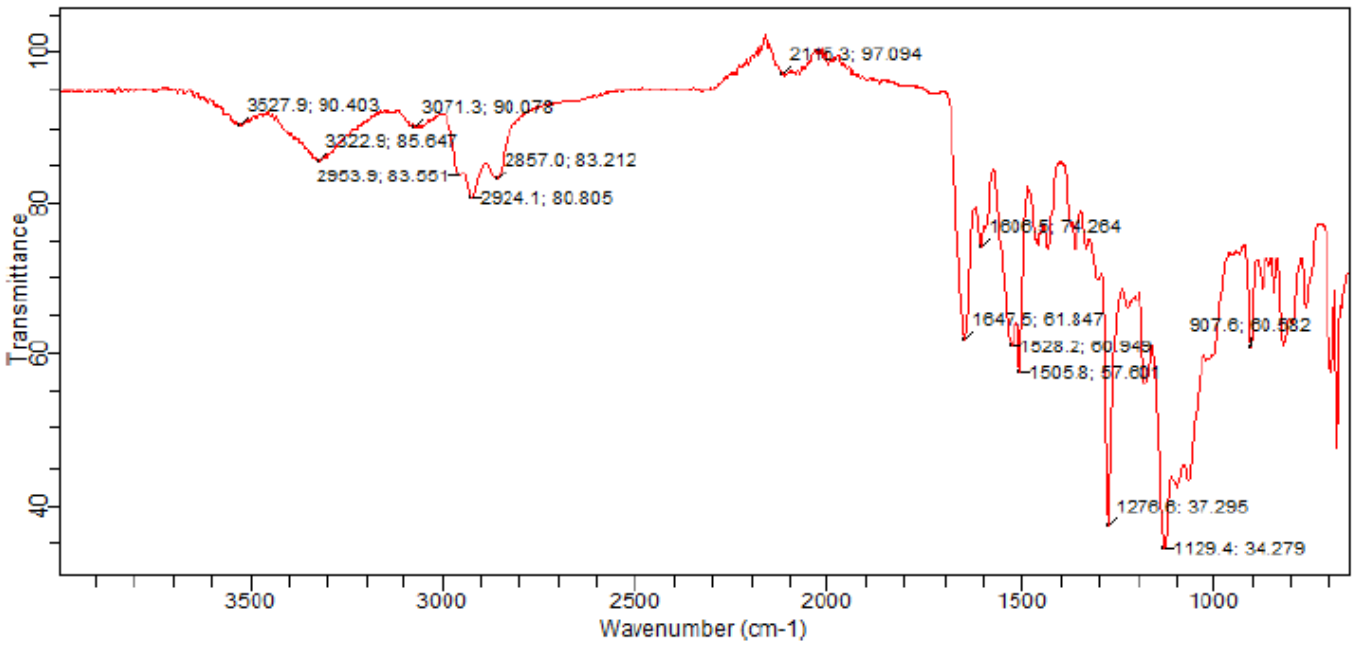
^{1}H NMR (400 MHz, $CDCl_3$) *Inset:* ^{19}F NMR (377 MHz, $CDCl_3$)



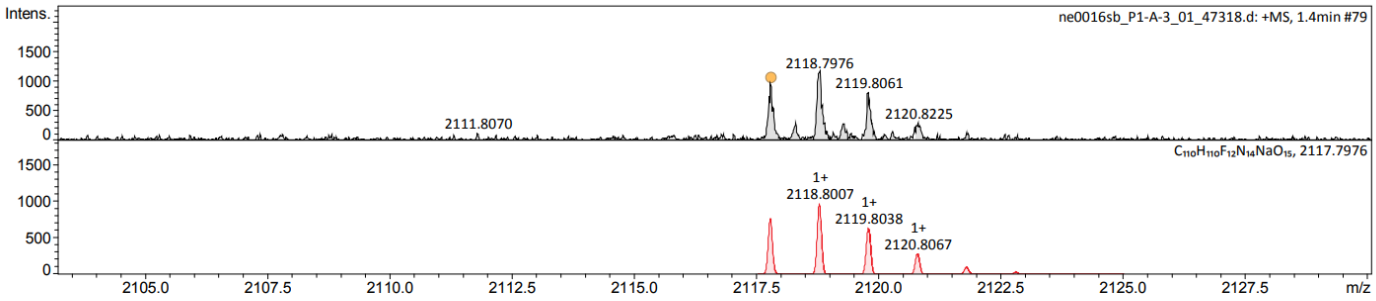
^{13}C NMR (100 MHz, $CDCl_3$)



IR Spectrum (neat)

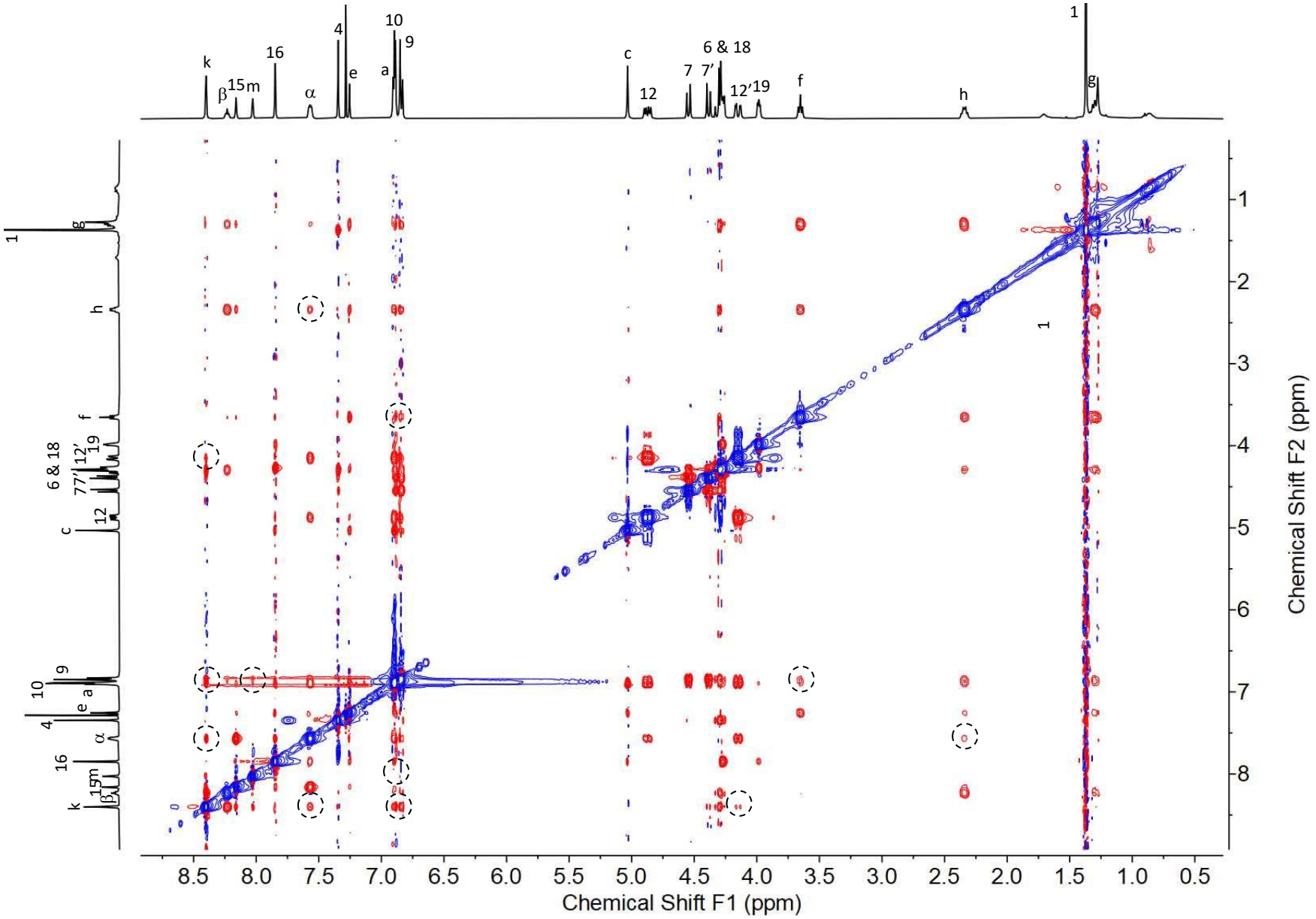


HRMS (ES +ve)



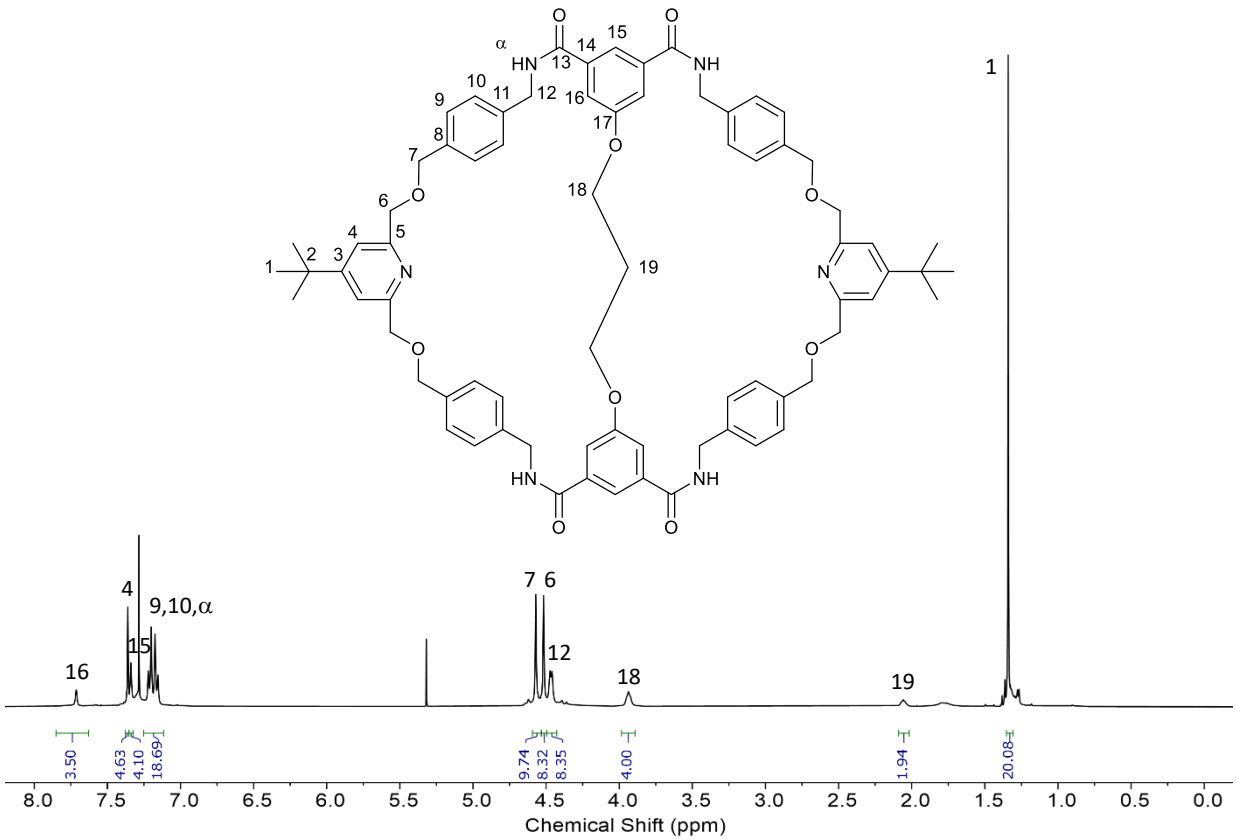
Meas. m/z	#	Ion Formula	m/z	err [ppm]	err [mDa]	mSigma	Mean err [ppm]
2095.8070	1	C110H111F12N14O15	2095.8156	4.1	8.6	442.3	0.9
2117.8048	1	C110H110F12N14NaO15	2117.7976	-3.4	-7.2	33.7	-2.2

^{1}H-^{1}H ROESY NMR (400 MHz, $CDCl_3$) of HR2 (with intercomponent couplings highlighted)

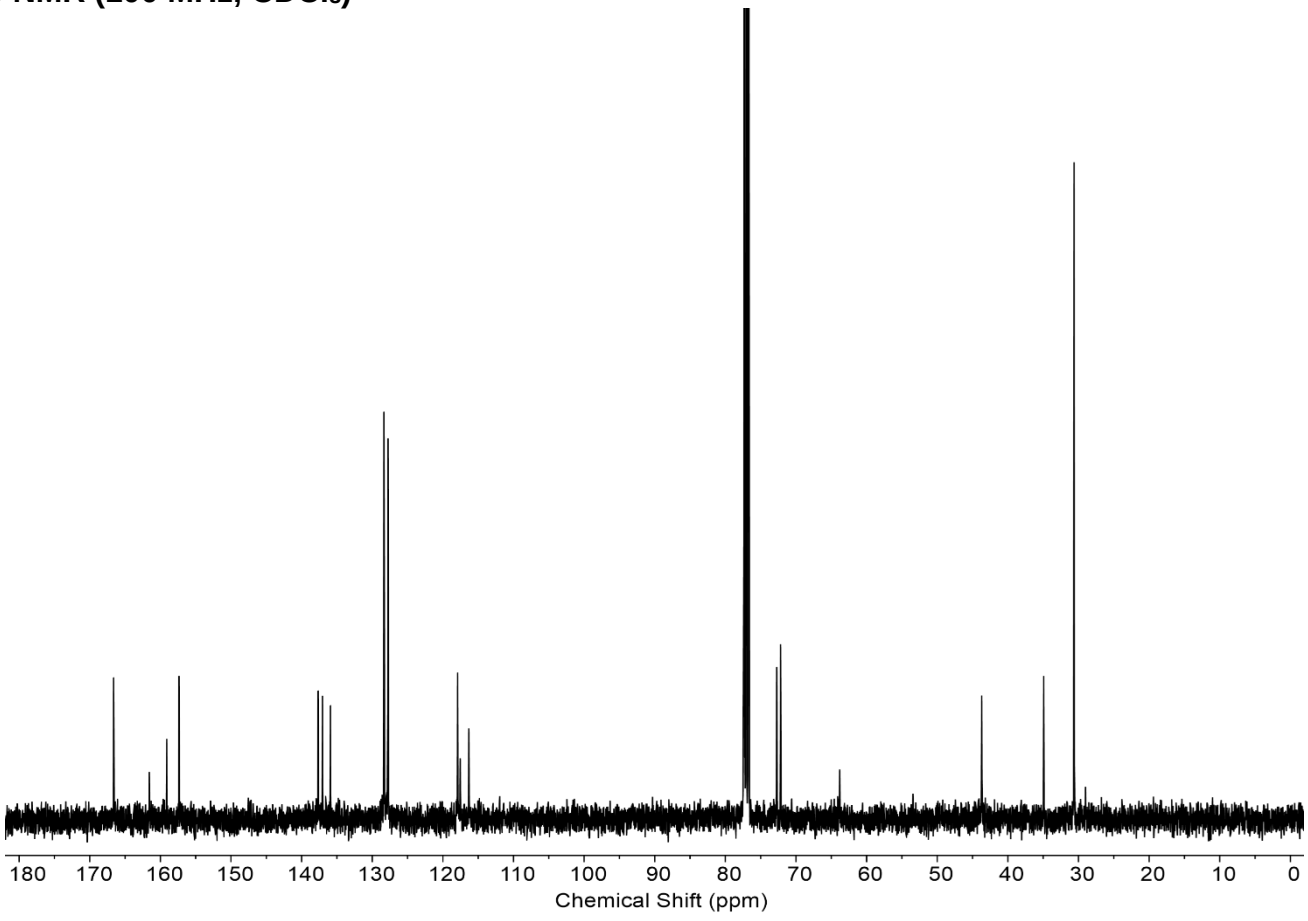


Bis-Macrocycle BM1’

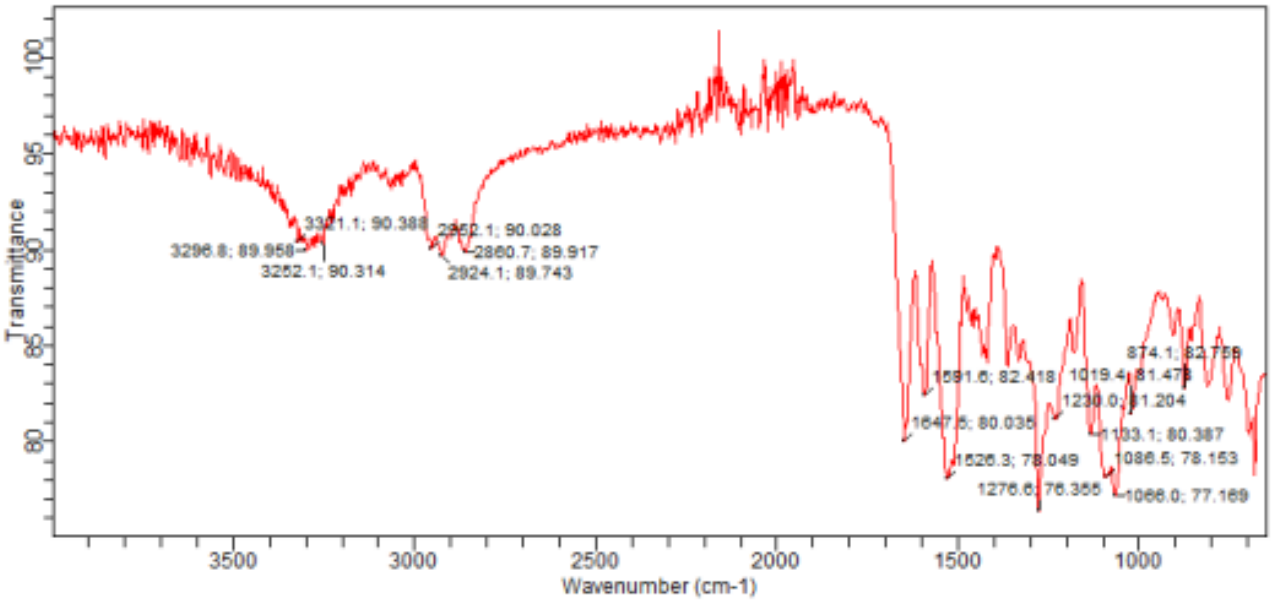
^{1}H NMR (400 MHz, $CDCl_3$)



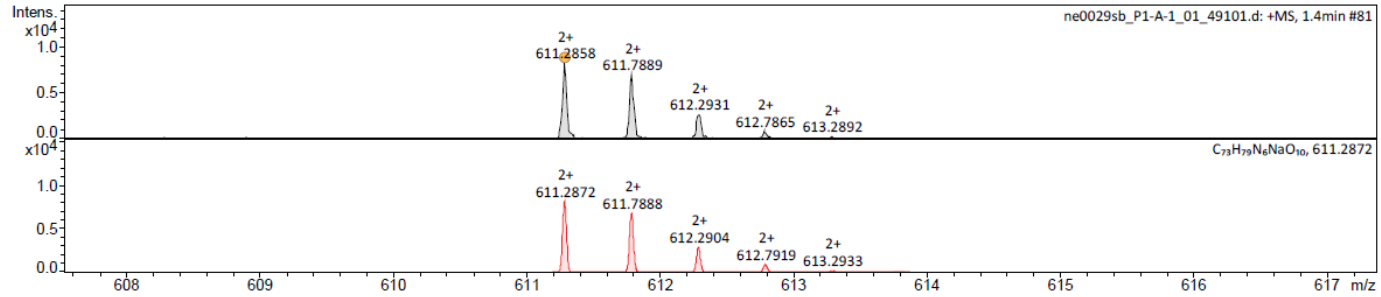
^{13}C NMR (100 MHz, $CDCl_3$)



IR Spectrum (neat)



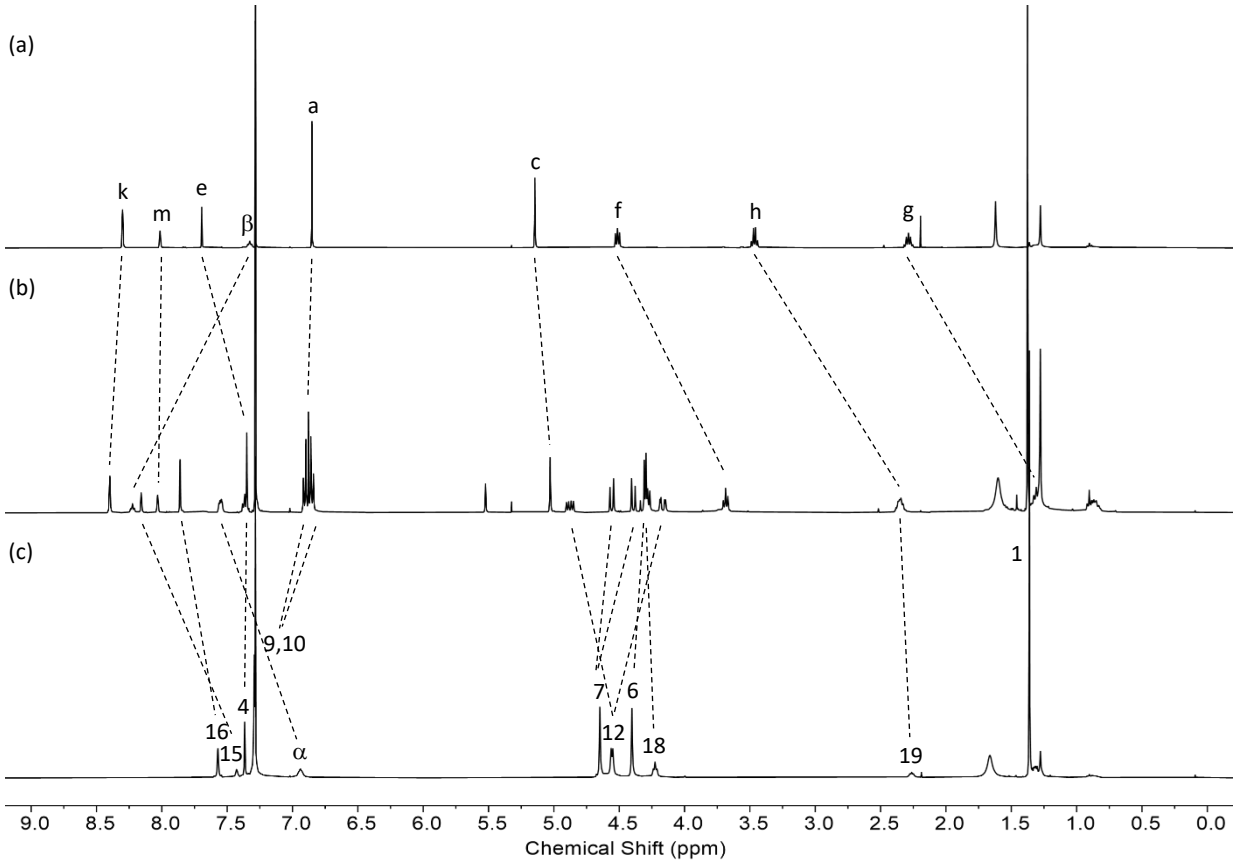
HRMS (ES +ve)



Meas. m/z	#	Ion Formula	m/z	err [ppm]	err [mDa]	mSigma	Mean err [ppm]
611.2858	1	C73H79N6NaO10	611.2872	2.4	1.5	20.4	1.9
622.2761	1	C73H78N6Na2O10	622.2782	3.3	2.1	16.9	1.8
1199.5863	1	C73H79N6O10	1199.5852	-0.9	-1.1	51.9	-2.7
1221.5740	1	C73H78N6NaO10	1221.5672	-5.6	-6.8	181.0	-1.9

NB: Depicted molecular ion peak corresponds to $[M+H+Na]^{2+}$

Stacked ^{1}H NMR Spectra of Handcuff Rotaxane HR1

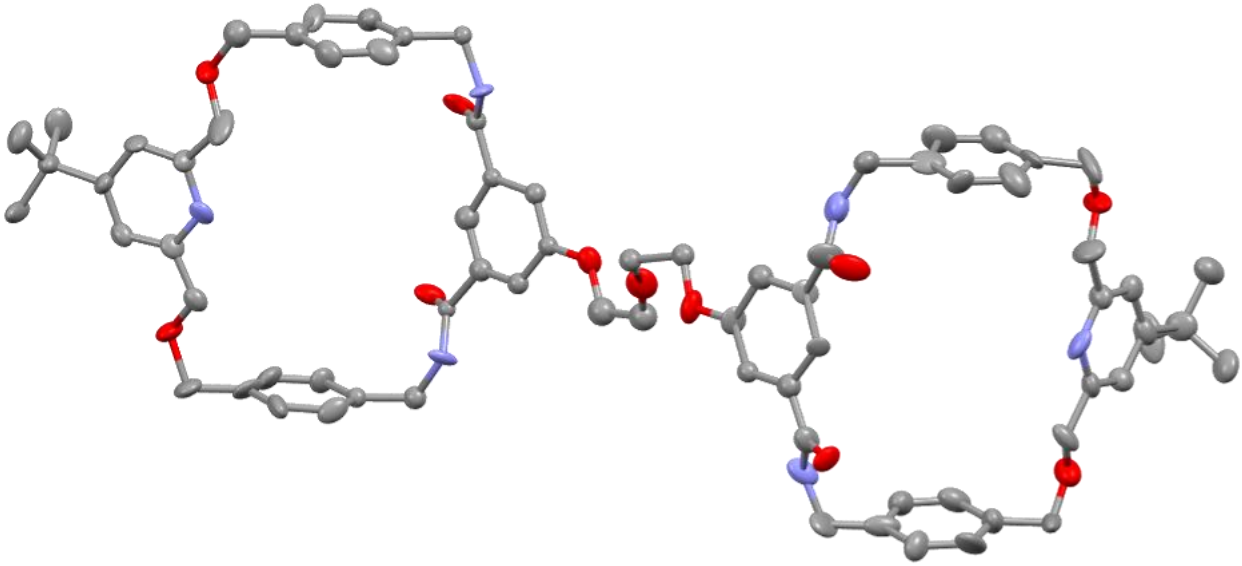


Stacked ^{1}H NMR spectra of (a) axle **Ax**, (b) handcuff rotaxane **HR1** and (c) bis-macrocycle **BM1**.

Part 3: Crystallographic Data

Bis-macrocycle **BM2**:

Single crystals of bis-macrocycle **BM2** were grown by slow evaporation of a chloroform solution. A suitable crystal was selected and studied using an Agilent SuperNova AtlasS2 diffractometer. Using Olex2[1] the structure was solved with the ShelXT[2] structure solution program using Intrinsic Phasing and refined with the ShelXL[3] refinement package using Least Squares minimisation.



X-ray crystal structure of bis-macrocycle **BM2**. Thermal ellipsoids are displayed at 50% probability.

Crystal data and structural refinement for bis-macrocycle **BM2**:

CCDC Number	2343052
Empirical formula	$C_{74}H_{80}N_6O_{11}$
Formula weight	1229.44
Temperature/K	100.01(10)
Crystal system	monoclinic
Space group	Pc
a/Å	27.7031(18)
b/Å	13.0253(10)
c/Å	9.5007(5)
α/°	90
β/°	93.854(6)
γ/°	90
Volume/Å^3	3420.5(4)
Z	2
ρ_{calc}g/cm^3	1.194
μ/mm^{-1}	0.648
F(000)	1308.0
Crystal size/mm^3	0.17 × 0.08 × 0.03
Radiation	Cu Kα (λ = 1.54184)
2Θ range for data collection/°	7.502 to 145.604
Index ranges	-34 ≤ h ≤ 33, -16 ≤ k ≤ 16, -11 ≤ l ≤ 11
Reflections collected	8629
Independent reflections	8629 [R_{int} = ?, R_{sigma} = 0.0577]
Data/restraints/parameters	8629/187/828
Goodness-of-fit on F^2	1.220
Final R indexes [I>=2σ (I)]	R_1 = 0.1052, wR_2 = 0.3054
Final R indexes [all data]	R_1 = 0.1300, wR_2 = 0.3275
Largest diff. peak/hole / e Å^{-3}	1.14/-0.44

Part 4: References

1 O. V. Dolomanov, L. J. Bourhis, R. J. Gildea, J. A. K. Howard and H. Puschmann, *J. Appl. Cryst*., 2009, **42**, 339-341.

2 G. M. Sheldrick, *Acta Cryst. A*, 2015, **71**, 3-8.

3 G. M. Sheldrick, *Acta Cryst. C*, 2015, **71**, 3-8.