

Supporting Information for

Harnessing Solid-state Packing for Selective Detection of Chloride in a Macrocyclic Anionophore

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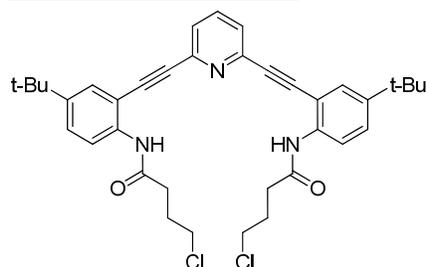
Table of Contents

General Methods	S2
Synthetic Information	S2
X-ray Diffraction Studies	S4
Fluorescence Spectra in Chloroform.....	S6
Solution State Titration Data	S6
References	S8
Copies of ¹ H & ¹³ C NMR Spectra	S9

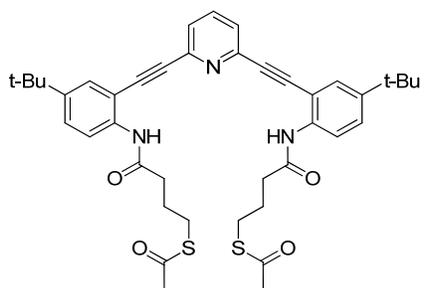
General Methods

^1H and ^{13}C NMR spectra were obtained on an Inova 500 MHz spectrometer (^1H : 500.10 MHz, ^{13}C : 125.75 MHz). Chemical shifts (δ) are expressed in ppm using non-deuterated solvent present in the bulk deuterated solvent (CDCl_3 : ^1H 7.26 ppm, ^{13}C 77.16 ppm). Solvents and reagents were used as purchased from suppliers, unless anhydrous conditions were employed, in which solvents were freshly distilled from sodium/benzophenone under N_2 atmosphere (THF) or as purchased in sealed, DriSolv containers (pyridine, DMF). Mass spectra were acquired with a Waters LCT Premier ESI-MS in positive mode. UV-Vis spectra were acquired with a Hewlett-Packard 8453 UV-Visible spectrophotometer. Fluorescence data was acquired with a Horiba Jobin-Yvon FluoroMax-4 fluorescence spectrophotometer. IR spectra were acquired with a Thermo Nicolet 4700 FT-IR Spectrometer with a Smart iTR™ Attenuated Total Reflectance (ATR) attachment. Melting points determined with a MEL-TEMP capillary melting point apparatus. HPLC performed using a JAI Recycling Preparative HPLC (Model LC-9101) with a JAIGEL-1H preparative column. Compound **3** was prepared as previously described.¹

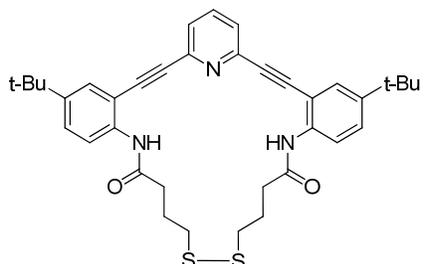
Synthetic Information



Amide 4. 4-chlorobutanoyl chloride (0.15 mL, 1.34 mmol) was added to a solution of **3** (100 mg, 0.24 mmol) in anhydrous THF (10 mL). The reaction was stirred for 1 h at rt before being quenched with MeOH (10 mL). The volatiles were removed *in vacuo*, redissolved in 5 mL CH_2Cl_2 and treated with pyridine (0.5 mL) to form the free base. Volatiles were removed once more *in vacuo*, and filtration of the crude solid through a 3-inch silica plug (1:1 hexanes:EtOAc) afforded **4** (147 mg, 97%) as a white, crystalline solid. ^1H NMR (500 MHz, CDCl_3) δ 8.28 (d, J = 8.8 Hz, 2H), 8.04 (s, 2H), 7.76 (t, J = 7.8 Hz, 1H), 7.58 (d, J = 2.4 Hz, 2H), 7.54 (d, J = 7.8 Hz, 2H), 7.43 (dd, J = 8.8, 2.4 Hz, 2H), 3.67 (t, J = 6.2 Hz, 4H), 2.67 (t, J = 7.1 Hz, 4H), 2.23 (p, J = 6.7 Hz, 4H), 1.31 (s, 18H). ^{13}C NMR (126 MHz, CDCl_3) δ 170.14, 146.89, 143.50, 137.04, 137.00, 129.30, 128.15, 126.63, 119.93, 110.68, 94.46, 85.77, 44.53, 34.58, 34.56, 31.33, 28.21. HRMS (EI+) calcd for $\text{C}_{37}\text{H}_{42}\text{N}_3\text{O}_2\text{Cl}_2$ [MH^+]: 630.2654, found 630.2667. IR (ATR, cm^{-1}): 3280, 2960, 2867, 2208, 1662, 1582, 1554, 1512, 1480, 1442, 1301, 1171, 799. mp: 89-91 °C.



Thioacetate 5. Potassium thioacetate (110 mg, 0.96 mmol) was added to a solution of **4** (100 mg, 0.19 mmol) in anhydrous DMF (10 mL). After stirring for 4 h at rt, the reaction was quenched with saturated aqueous NH_4Cl soln (20 mL). The reaction mixture was extracted with EtOAc (40 mL), washed with brine (3 x 30mL), dried (MgSO_4) and filtered. The volatiles were removed *in vacuo* and filtration of the crude solid through a 3-inch silica plug (3:1 hexanes: EtOAc) furnished **5** (119 mg, 88%) as an orange solid. ^1H NMR (500 MHz, CDCl_3) δ 8.28 (d, $J = 8.7$ Hz, 2H), 7.98 (s, 2H), 7.79 (t, $J = 7.8$ Hz, 1H), 7.58 (d, $J = 1.9$ Hz, 2H), 7.55 (d, $J = 7.8$ Hz, 2H), 7.43 (dd, $J = 8.8, 2.2$ Hz, 2H), 2.99 (t, $J = 7.1$ Hz, 4H), 2.54 (t, $J = 7.3$ Hz, 4H), 2.27 (s, 6H), 2.06 (p, $J = 7.2$ Hz, 4H), 1.31 (s, 18H). ^{13}C NMR (126 MHz, CDCl_3) δ 195.83, 170.29, 146.83, 143.63, 137.04, 136.99, 129.30, 128.17, 126.68, 119.99, 110.68, 94.48, 85.83, 36.51, 34.56, 31.34, 30.73, 28.56, 25.67. HRMS (EI+) calcd for $\text{C}_{41}\text{H}_{48}\text{N}_3\text{O}_4\text{S}_2$ [MH^+]: 710.3086, found 710.3112. IR (ATR, cm^{-1}): 3265, 2956, 2921, 2852, 2208, 1685, 1660, 1582, 1515, 1442, 1170, 1131. mp: 128-129 °C.



Macrocycle 1. To a stirred solution of **5** (100 mg, 0.168 mmol) in rigorously degassed MeOH (100 mL) was added K_2CO_3 (115 mg, 0.83 mmol) under an N_2 atmosphere. After stirring for 1 h at rt, a N_2 -degassed solution of 20% aqueous NH_4Cl (100 mL) was cannula transferred into the flask under inert conditions to precipitate the intermediate thiol. The solid was collected and washed thoroughly with deionized water, dried, and immediately dissolved in CH_2Cl_2 (100 mL). Solid elemental iodine was then added slowly until iodine coloration remained. The reaction was quenched with 10% Na_2SO_3 (15 mL), washed with brine solution (2 x 30 mL), and dried over MgSO_4 . The volatiles were removed *in vacuo* and the crude product purified via flash chromatography (3:1 hexanes:EtOAc) affording **1** (62 mg, 59%) as a light yellow solid. Further purification by preparative HPLC with a gel permeation column was sometimes needed to remove trace oligomers and small polymers. ^1H NMR (500 MHz, CDCl_3) δ 8.30 (d, J

= 8.7 Hz, 2H), 8.19 (s, 2H), 7.76 (t, $J = 7.8$ Hz, 1H), 7.56 (d, $J = 7.8$ Hz, 2H), 7.54 (d, $J = 2.0$ Hz, 2H), 7.43 (dd, $J = 8.8, 2.3$ Hz, 2H), 2.78 (t, $J = 6.6$ Hz, 4H), 2.64 (t, $J = 6.8$ Hz, 4H), 2.17 (q, $J = 6.8$ Hz, 4H), 1.32 (s, 18H). ^{13}C NMR (126 MHz, CDCl_3) δ 170.81, 146.69, 143.43, 137.15, 136.93, 129.05, 128.12, 127.03, 119.96, 110.65, 94.25, 85.91, 37.91, 35.79, 34.51, 31.32, 24.79. HRMS (EI+) calcd for $\text{C}_{37}\text{H}_{42}\text{N}_3\text{O}_2\text{S}_2$ $[\text{MH}^+]$: 624.2718, found 624.2747. IR (ATR, cm^{-1}): 3266, 2957, 2920, 2850, 2208, 1664, 1512, 1443, 1172. mp: 181 °C (d).

X-ray Diffraction Studies

General Information. Diffraction intensities were collected at 173 K (**1•HCl**) and 200 K (**1•H₂O**) on a Bruker Apex2 CCD diffractometer using $\text{CuK}\alpha$ radiation, $\lambda = 1.54178$ Å. Space groups determined based on systematic absences. Absorption corrections applied by SADABS.² Structures solved by direct methods and Fourier techniques and refined on F^2 using full matrix least-squares procedures. All non-H atoms were refined with anisotropic thermal parameters. H atoms were treated in calculated positions in a rigid group model except those at N atoms and in solvent water molecules in **1•H₂O** involved in H-bonds. Those H atoms were found from the residual density maps and refined with isotropic thermal parameters. The structure of **1•HCl** has four symmetrically independent structural units and five solvent molecules (CH_2Cl_2). One of the solvent molecules was refined as disordered over two positions, another one is highly disordered and was treated by SQUEEZE;³ correction of the X-ray data was 199 electrons/unit cell; the required value is 168 electrons/unit cell for four CH_2Cl_2 molecules in the full unit cell. Crystals of **1•HCl** are very thin plates and reflections at high angles were very weak even with using a strong *Incoatec* Cu μS source. The X-ray diffraction data for **1•HCl** were collected up to $2\theta_{\text{max}} = 126.0^\circ$, but only reflections with $2\theta_{\text{max}} = 100.0^\circ$ were used in the final refinement. All calculations were performed by the Bruker SHELXTL (v. 6.10)⁴ and SHELXL-2013 packages.⁵ CCDC-1422046 (**1•H₂O**) and 1422049 (**1•HCl**) contain the supplementary crystallographic data for this paper. These data can be obtained free of charge from The Cambridge Crystallographic Data Centre via www.ccdc.cam.ac.uk/data_request/cif.

Crystallographic Data for **1•H₂O**: $\text{C}_{37}\text{H}_{43}\text{N}_3\text{O}_3\text{S}_2$, $M = 641.86$, $0.16 \times 0.12 \times 0.03$ mm, $T = 200$ K, Monoclinic, space group $P2_1/c$, $a = 14.0664(12)$ Å, $b = 27.410(2)$ Å, $c = 9.4754(7)$ Å, $\beta = 107.434(5)^\circ$, $V = 3485.5(5)$ Å³, $Z = 4$, $D_c = 1.223$ Mg/m³, $\mu(\text{Cu}) = 1.690$ mm⁻¹, $F(000) = 1368$, $2\theta_{\text{max}} = 136.71^\circ$, 24228 reflections, 6295 independent reflections [$R_{\text{int}} = 0.0605$], $R1 = 0.0556$, $wR2 = 0.1365$ and $\text{GOF} = 1.034$ for 6295 reflections

(422 parameters) with $I > 2\sigma(I)$, $R1 = 0.0801$, $wR2 = 0.1504$ and $GOF = 1.035$ for all reflections, max/min residual electron density $+0.373/-0.328 \text{ e}\text{\AA}^3$.

Crystallographic Data for **1**•HCl: $C_{38.25}H_{44.5}Cl_{3.5}N_3O_2S_2$, $C_{37}H_{42}ClN_3O_2S_2 \cdot 1.25(CH_2Cl_2)$, $M = 766.46$, $0.13 \times 0.12 \times 0.02 \text{ mm}$, $T = 173 \text{ K}$, Monoclinic, space group $P2_1/n$, $a = 20.7737(8) \text{ \AA}$, $b = 31.7155(12) \text{ \AA}$, $c = 24.6016(10) \text{ \AA}$, $\beta = 98.088(3)^\circ$, $V = 16047.5(11) \text{ \AA}^3$, $Z = 16$, $Z' = 4$, $D_c = 1.269 \text{ Mg/m}^3$, $\mu(\text{Cu}) = 3.627 \text{ mm}^{-1}$, $F(000) = 6440$, $2\theta_{\text{max}} = 100.0^\circ$, 101170 reflections, 16467 independent reflections [$R_{\text{int}} = 0.0880$], $R1 = 0.1091$, $wR2 = 0.3280$ and $GOF = 1.007$ for 16467 reflections (1774 parameters) with $I > 2\sigma(I)$, $R1 = 0.1299$, $wR2 = 0.3530$ and $GOF = 1.008$ for all reflections, max/min residual electron density $+1.143/-0.955 \text{ e}\text{\AA}^3$.

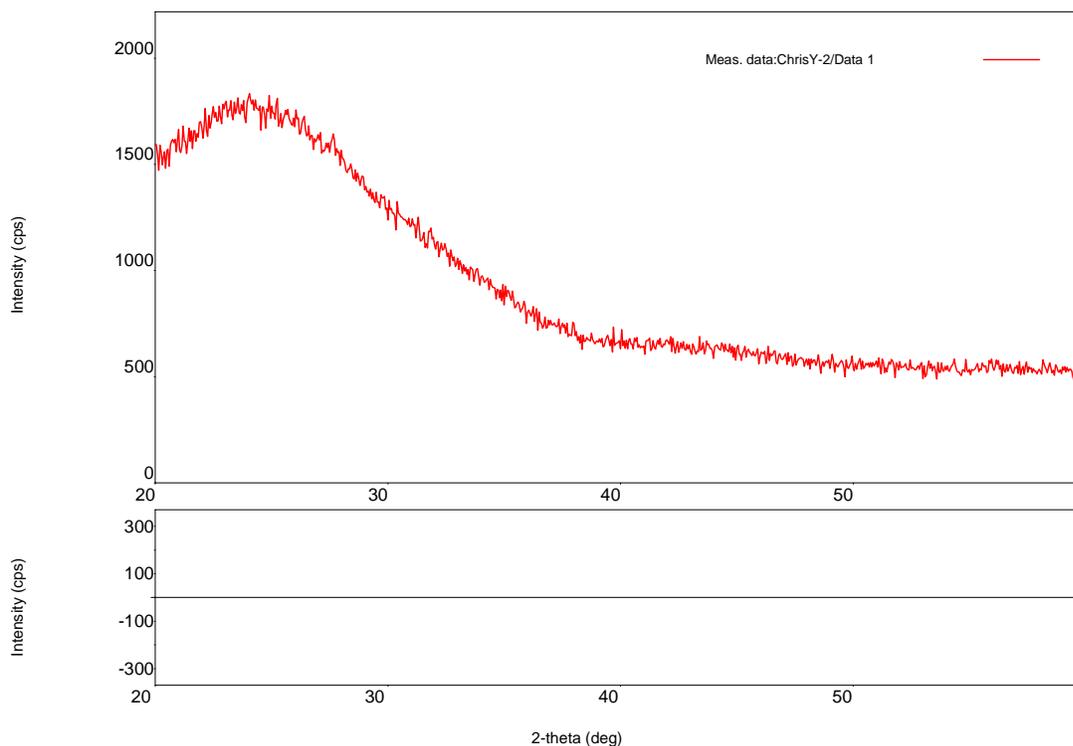
X-Ray Diffraction of films

Films of **1** were formed on glass slides by drop-casting 1 mL of a solution of **1** in CH_2Cl_2 at a concentration of 1 mg/mL. The X-ray powder diffractions from the films were obtained by an Ultima IV thin film & powder diffractometer (Cu-radiation, $\theta/2\theta$ –scan in the range of 20-60 degrees), and there were no diffraction peaks visible, indicating that the films are amorphous.

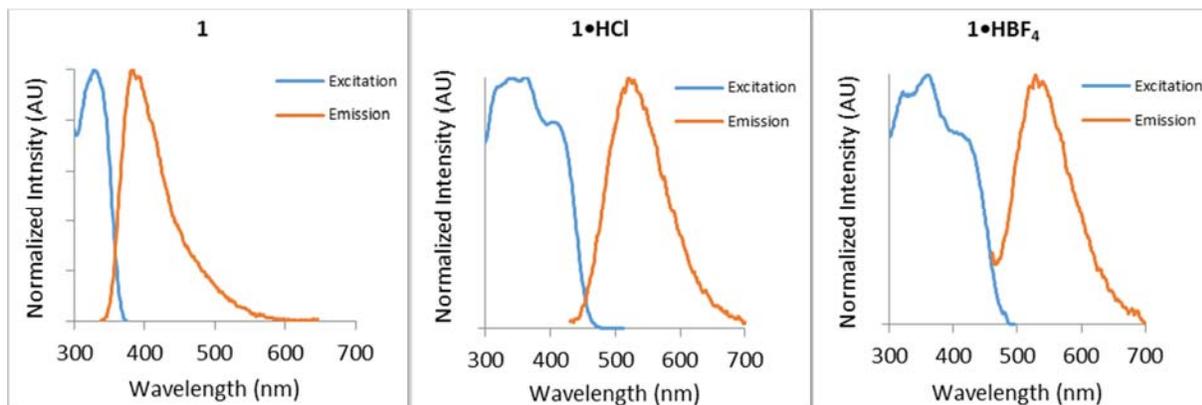
Measurement conditions

X-Ray	40 kV , 40 mA	Scan speed / Duration time	2.0000 deg./min.
Goniometer		Step width	0.0500 deg.
Attachment	-	Scan axis	2Theta/Omega
Filter		Scan range	20.0000 - 60.0000 deg.
CBO selection slit	PB	Incident slit	1.0mm
Detector	Scintillation counter	Receiving slit #1	1.0mm
Scan mode	CONTINUOUS	Receiving slit #2	2.0mm

Measurement profile



Fluorescence Spectra in Chloroform



Solution State Titration Data

An example fit from treatment of **1•TFA** with TBACl in acetonitrile with 15% H₂O is presented.

1•TFA was prepared through dissolution of **1** in CH₂Cl₂ and then bubbling TFA vapors through the solution. This was then dried under vacuum, and the solid remaining was used to prepare solutions of **1•TFA** for analysis.

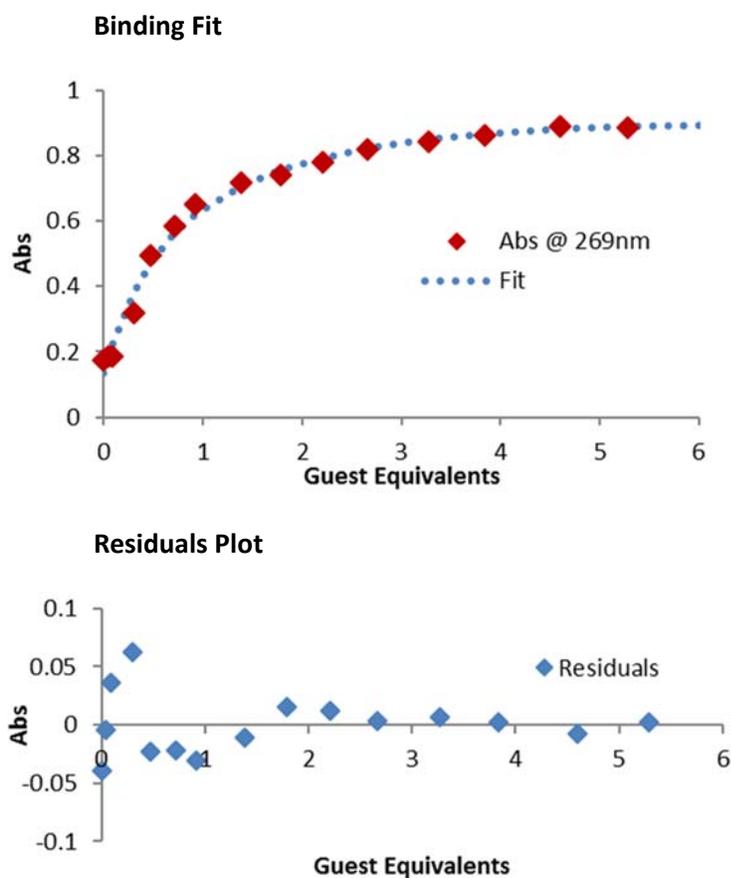
2.0 mg **1•TFA** was dissolved in 3 mL acetonitrile with 15% H₂O, and the UV/Vis absorption spectrum was measured after every addition of a stock solution of TBACl (18.3 mM in acetonitrile with 15% H₂O).

The results obtained from these studies yielded variable association constants depending on the period of time the solutions stood prior to analysis, leading us to believe the macrocycles were structurally dynamic in the partially aqueous solutions. The titration presented here is the result of the measurement occurring as quickly as possible after solution preparation.

The highest quality fits for association in solution resulted from calculation as a 2:1 host:guest ratio.

The relative amounts of host and guest were correlated to the absorbance values of a peak at 269 nm, and fitted with the Thordarson host-guest association program provided at <http://supramolecular.org/>.

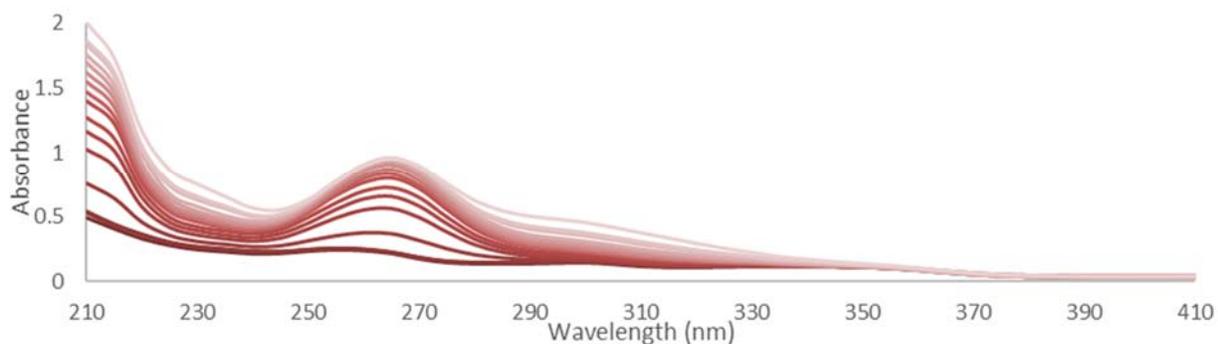
The result of an example titration and the resultant association constant fitting are provided below.



Results:

K_{11}	$3 * 10^1 M^{-1}$
K_{21}	$2 * 10^9 M^{-1}$
RMS: 269.0	0.024338132
Covariance: 269.0	0.008608199

Stacked UV/Vis absorption plots of titration of **1•TFA** with TBACl.

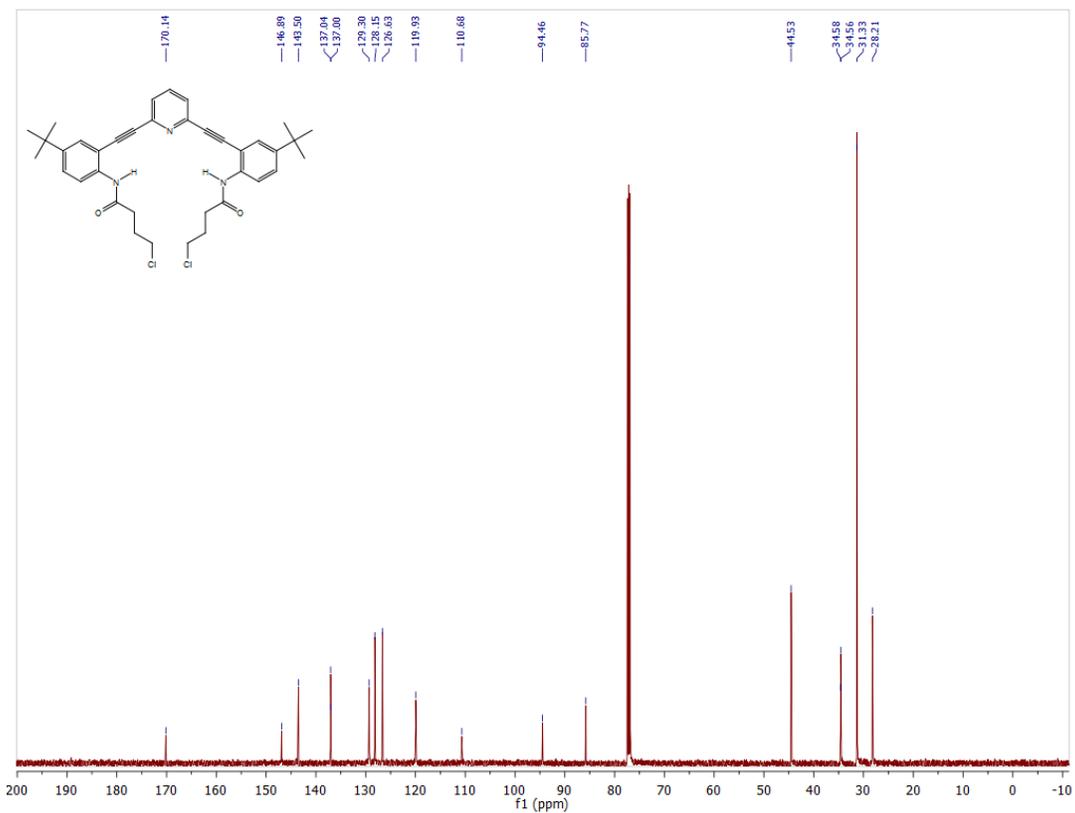
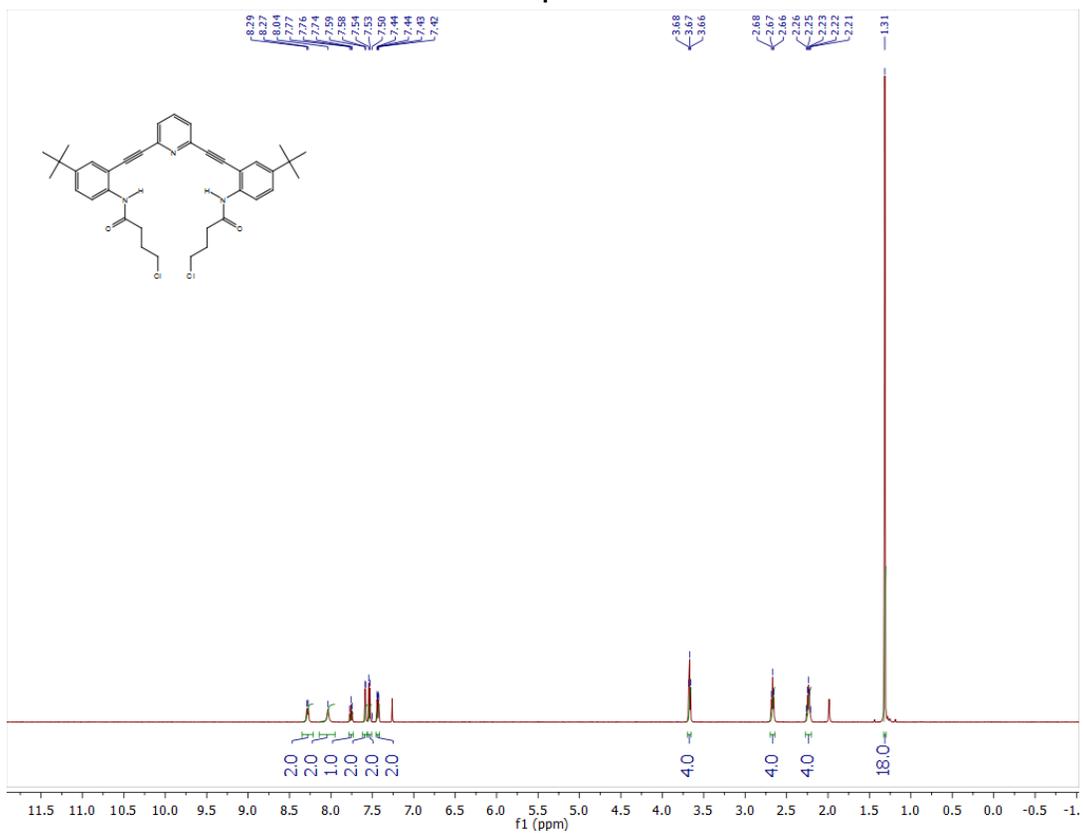


References

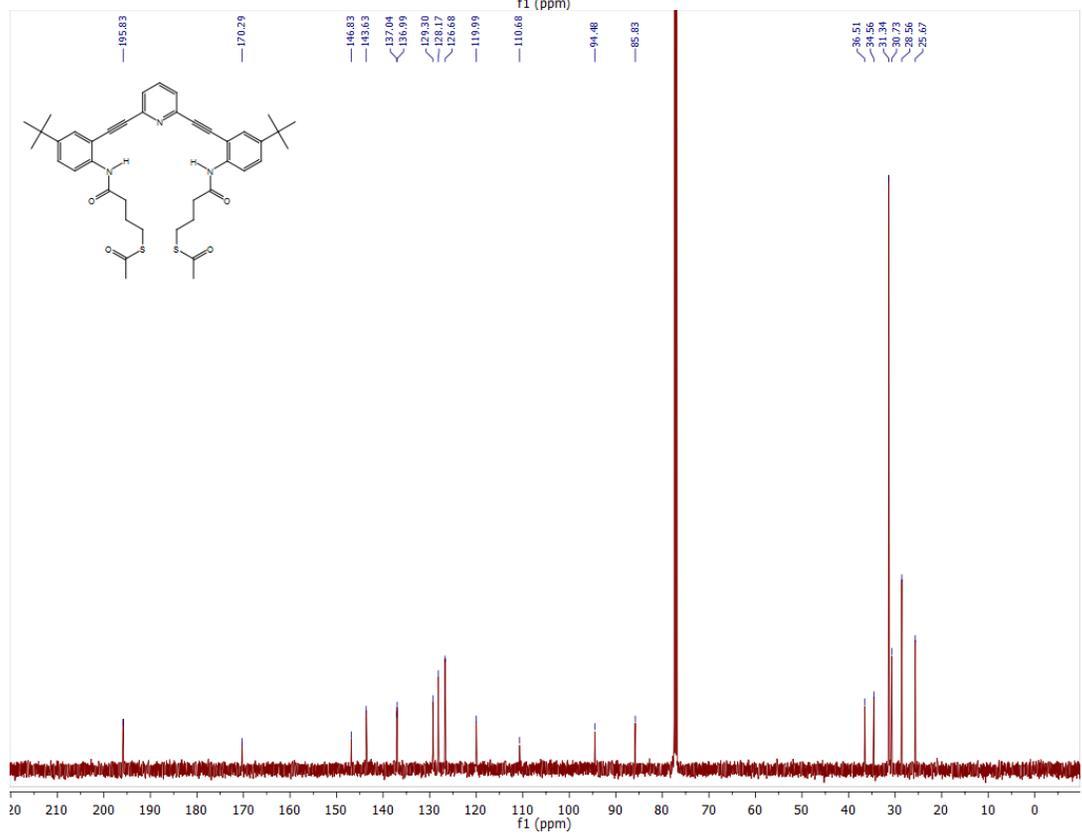
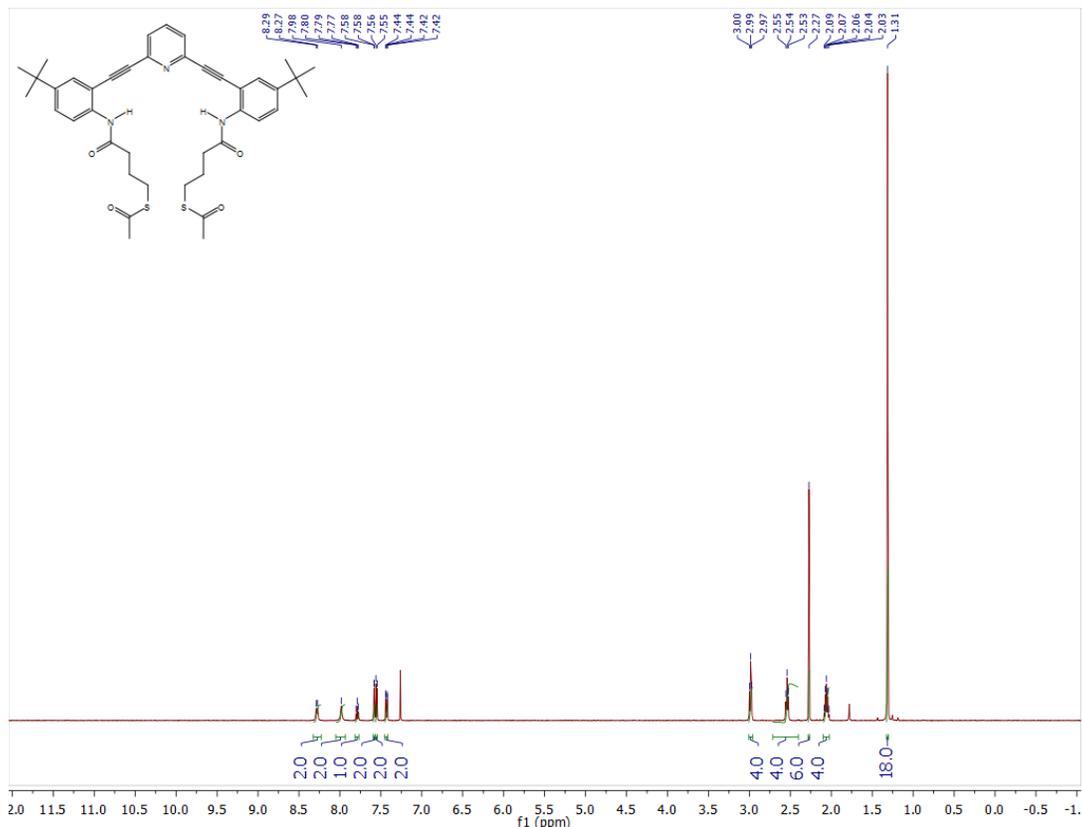
1. Engle, J. M.; Carroll, C. N.; Johnson, D. W.; Haley, M. M. *Chem. Sci.* **2012**, *3*, 1105.
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3. Van der Sluis, P.; Spek, A. L. *Acta Cryst. A* **1990** *A46*, 194-201.
4. SHELXTL-6.10 "Program for Structure Solution, Refinement and Presentation" BRUKER AXS Inc., 5465 East Cheryl Parkway, Madison, WI 53711-5373 USA.
5. Sheldrick, G. M. *Acta Cryst. A* **2008**, *64*, 112–122.

Copies of ^1H & ^{13}C NMR Spectra

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1

