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Synthesis Of Cryptands For Eu2+-Containing Complexes

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SYNTHESIS OF CRYPTANDS FOR Eu^{2+}-CONTAINING COMPLEXES

by

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DEDICATION

To my parents

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It has been a wonderful journey!

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TABLE OF CONTENTS

LIST OF TABLES

LIST OF FIGURES

LIST OF SCHEMES

LIST OF ABBREVIATIONS

Abbreviation	Term
br	broad
calcd	calculated
d	doublet
dd	doublet of doublets
DEPT	distortionless enhancement polarization transfer
DMSO	dimethyl sulfoxide
equiv	equivalents
GCOSY	gradient correlation spectroscopy
GHMBC	gradient heteronuclear multiple bond correlation
GHMQC	gradient heteronuclear multiple quantum correlation
HRESIMS	high resolution electrospray ionization mass spectra
m	multiplet
R_f	retention factor
s	singlet
SMM	single molecule magnet
t	triplet
THF	tetrahydrofuran
TLC	thin-layer chromatography

Chapter 1: Introduction to the Developments in the Coordination Chemistry of Eu^{2+}

1.1 Introduction

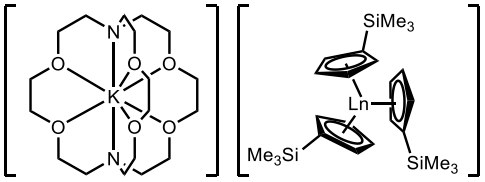
The divalent oxidation states of the lanthanide ions (Ln^{2+}) are less stable compared to their well-known trivalent oxidation states (Ln^{3+}). Before the 1990s, only Eu^{2+}, Yb^{2+}, and Sm^{2+} were known both in solution and in the solid state.[1–4] The calculated reduction potentials (versus normal hydrogen electrode) of Ln^{3+}/Ln^{2+} are shown in **Table 1.1**.[5] As you can see, europium has the most positive reduction potential due to its half-filled 4f orbitals.

Table 1.1 Calculated Ln^{3+}/Ln^{2+} reduction potentials (versus normal hydrogen electrode) of lanthanides[5]

Ln	Potential (V)	Ln	Potential (V)
Eu	−0.35	Pr	−2.9
Yb	−1.15	Ho	−2.9
Sm	−1.55	Er	−3.1
Tm	−2.3	La	−3.1
Dy	−2.5	Ce	−3.2
Nd	−2.6	Tb	−3.7
Pm	−2.7	Gd	−3.9
Lu	−2.7		

Recently, Evans and coworkers synthesized divalent lanthanide complexes [K(2.2.2-cryptand)][$(C_5H_4SiMe_3)_3Ln$] (**1.1**) (**Figure 1.1**) in which Ln includes all lanthanides except the radioactive element Pm.[5,6] Among these compounds, Eu^{2+},

Yb^{2+}, Sm^{2+}, and Tm^{2+} have $4f^{n+1}$ ground state electronic configurations; La^{2+}, Ce^{2+}, Pr^{2+}, Gd^{2+}, Tb^{2+}, Ho^{2+}, Y^{2+}, Er^{2+}, and Lu^{2+} have $4f^n5d^1$ ground state electronic configurations; and Dy^{2+} and Nd^{2+} also have $4f^n5d^1$ ground state electronic configurations even though traditionally they were reported as $4f^{n+1}$.[5] Research in the Evans laboratory challenged traditional thoughts that Eu^{2+}, Yb^{2+}, Sm^{2+}, Tm^{2+}, Dy^{2+}, and Nd^{2+} are the only divalent lanthanide ions that can be isolated in molecular compounds.[7,8]



1.1

Figure 1.1 Chemical Structure of complex **1.1**.

1.2 Properties and applications of Eu^{2+}-containing complexes.

Among the divalent lanthanides, europium has the most positive reduction potential (**Table 1.1**). Therefore, it has the most accessible divalent oxidation state. In its ground state, Eu^{2+} ion has seven unpaired electrons in 4f orbitals. It is isoelectronic with Gd^{3+} and has a faster water-exchange rate. These 4f electrons also produce a large spin magnetic moment of 7 μB.[9] Eu^{2+}-containing complexes have characteristic broad emissions (390–580 nm) in addition to sharp emission bands between 354 and 376 nm that are similar to those observed in Eu^{3+}.[10] In protic solvents such as H_2O and CH_3OH, the luminescence of Eu^{2+} can be quenched by the O–H oscillators of solvent molecules in the first coordination sphere. Macrocyclic ligands are known to have an "insulation effect", and they are able to enhance the emission of Eu^{2+} compared to free Eu^{2+} because of a decrease in the non-radiative rate constant.[11]

Eu^{2+}-containing complexes have considerable applications in synthetic chemistry, medical diagnosis, and materials science.[10] For example, complex **1.2** (**Figure 1.2**) serves as a single-electron reductant when reacting with PhSeSePh;[12] complex **1.3** (**Figure 1.2**) that contains indenyl ligands initiates the polymerization of methyl methacrylate;[13] and complex **1.4** (**Figure 1.2**) is found to be a more efficient MRI contrast agent at ultra-high field strengths than at lower fields.[14]

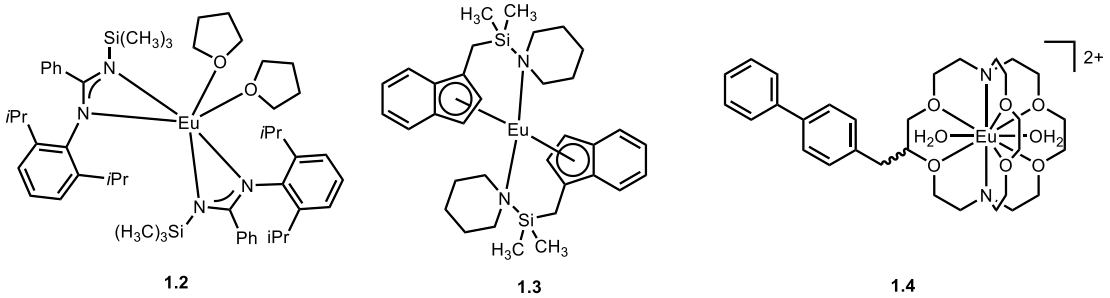


Figure 1.2 Structures of Eu^{2+}-containing complexes **1.2**–**1.4**.

1.3 Methods to stabilize Eu^{2+}

In spite of the greater stability compared to other divalent lanthanides, Eu^{2+} is easily oxidized in solution when exposed to air. The application of Eu^{2+} in solution is largely limited by the lack of suitable ligands to stabilize its divalent state. For example, while Eu^{2+} is widely used in solid-state lighting materials,[15] its luminescence properties in solution are less studied due to the tendency to be oxidized to Eu^{3+}.[11]

To take advantage of the interesting magnetic, catalytic, and luminescence properties of Eu^{2+}, efficient methods must be developed to prevent oxidation. One promising way is to use macrocyclic ligands to encapsulate Eu^{2+}. The Allen research group has studied the oxidative stability of a series of Eu^{2+}-containing cryptates (**1.5**–**1.10**) (**Figure 1.3**).[16] Notably, complex **1.10** is the most oxidatively stable

Eu^{2+}-containing complex in aqueous solution to date. It possesses an oxidative potential that is 35 mV more positive than Fe^{2+} in hemoglobin. The rationale for this design are that (1) the phenyl ring reduces the cryptand cavity size (better matching with the size of Eu^{2+}); (2) the phenyl ring reduces the Lewis basicity of adjacent oxygen atoms (better for electron-rich Eu^{2+}); and (3) the sulfur atoms are softer than oxygen atoms (better matching with soft Eu^{2+} based on hard–soft acid–base theory). Their study demonstrated that stabilization of Eu^{2+} can be achieved by manipulating the electronic and steric properties of the coordinating ligands.

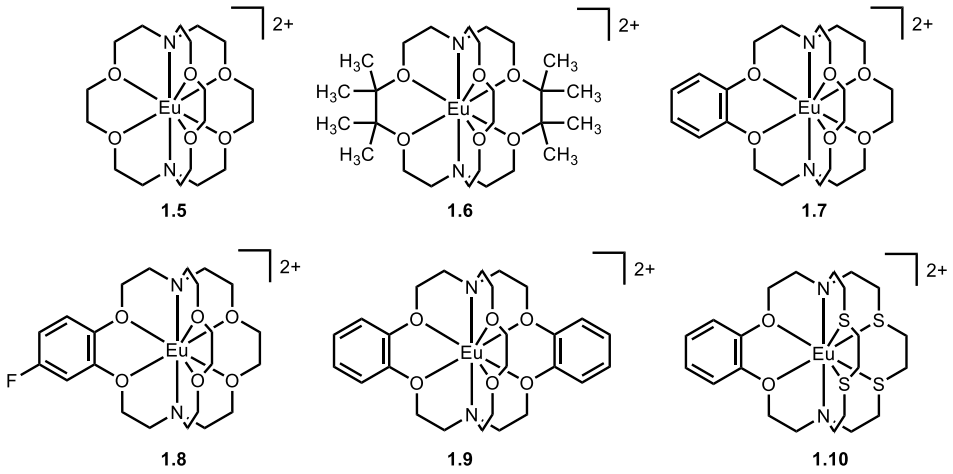


Figure 1.3 Chemical structures of unfunctionalized Eu^{2+}-containing cryptate **1.5** and functionalized Eu^{2+}-containing cryptates **1.6–1.10** (coordinated water molecules and counter ions are not shown for clarity).

1.4 Aims of my research

The goal of my research was to synthesize new ligands which can stabilize Eu^{2+}. Through fine-tuning of ligand properties, we envisioned that the resulting Eu^{2+}-containing complexes would have applications as MRI contrast agents, luminescence materials, and magnetic materials. Inspired by the previous success using functionalized cryptands, I focused my work on modifying cryptands. The second chapter of this thesis discusses the synthesis of a cryptand linked with an

isophthalic acid through a thiourea bridge (**1.11**). In the third chapter, synthesis of an azacryptand **1.12**, and progress towards synthesizing its derivative **1.13** are described. Ligand **1.14** in which two cryptands are bridged by tetraoxolene is discussed in the fourth chapter.

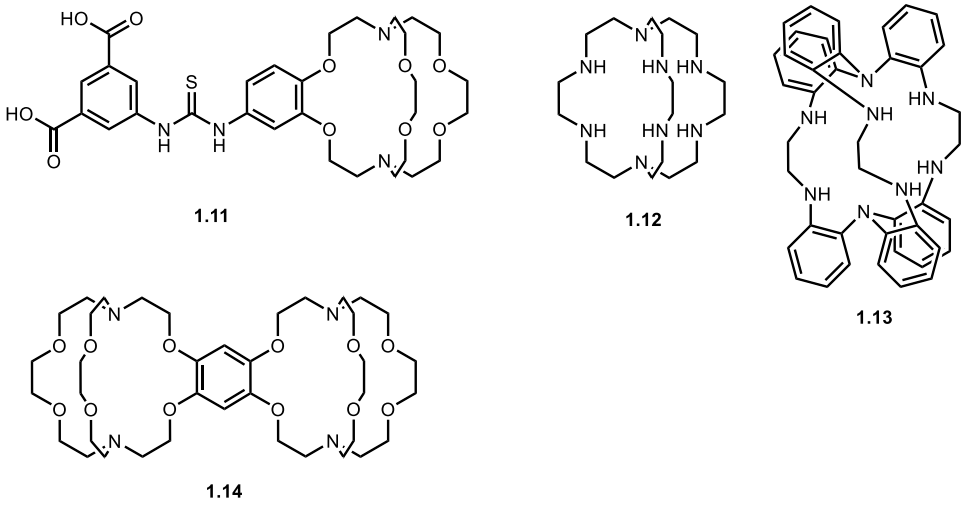


Figure 1.4 Chemical structures of compounds **1.11–1.14**.

Chapter 2: Synthesis of Cryptand Ligands for Eu^{2+}-Containing Complexes as Potential Contrast Agents

2.1 Introduction

Magnetic resonance imaging (MRI) is a powerful technique used in medical diagnoses. It is non-invasive and has excellent spatial resolution.[17,18] Most clinical scanners operate at 1.5–3 T, but higher field strengths provide considerable improvements in spatial and temporal resolution. Thus, there is a tendency in the MRI community to increase magnetic field strength.[19,20] However, common T_1-shortening Gd^{3+}-based contrast agents become less efficient as field strength increases.[21,22] The Allen research group has investigated Eu^{2+}-containing cryptates as alternatives to Gd^{3+}-containing complexes because Eu^{2+} is isoelectronic to Gd^{3+} with a faster water-exchange rate and two inner-sphere water molecules.[23,24] These properties are ideal for ultra high field strength (≥7 T) MRI, and consequently, the Allen research group has shown that Eu^{2+}-containing [2.2.2]cryptates **2.1**–**2.3** (**Figure 2.1**) are more effective at ultra-high field strengths than at lower fields.[14]

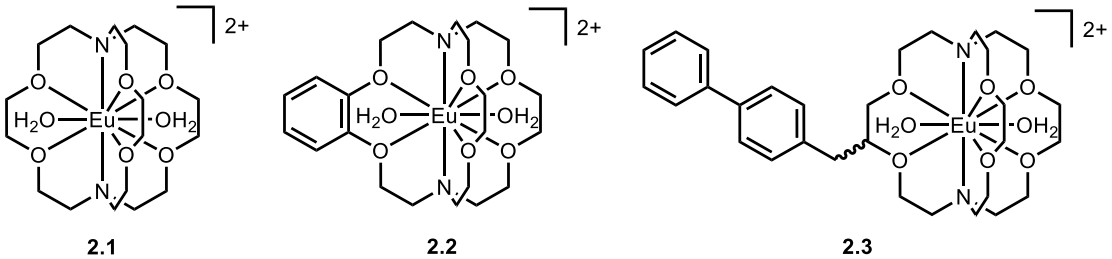
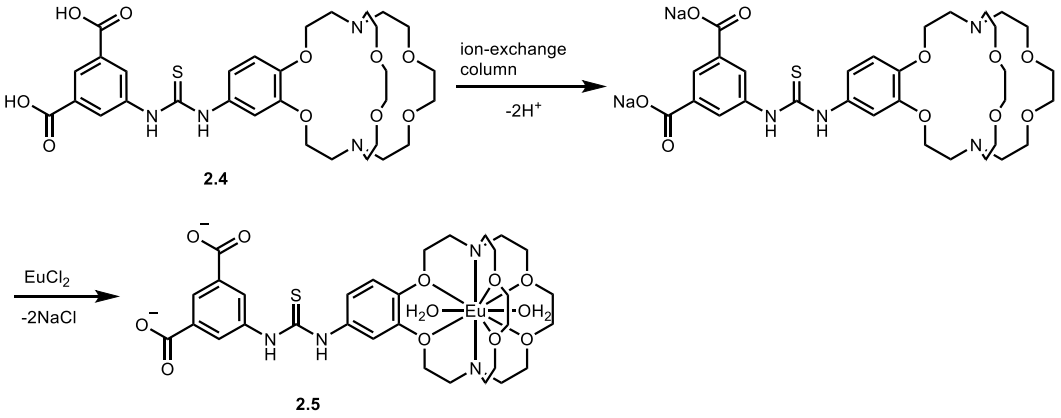


Figure 2.1 Examples of Eu^{2+}-containing [2.2.2]cryptates (**2.1**–**2.3**) that are more effective contrast agents for magnetic resonance imaging at ultra-high field strengths compared to lower fields.[14]

However, the inherent positive charges of cryptates **2.1**–**2.3** might limit their applications. Srinivasan and Sawyer indicated that the blood vessel wall and blood cells are negatively charged under normal conditions.[25] Thus, positively charged **2.1**–

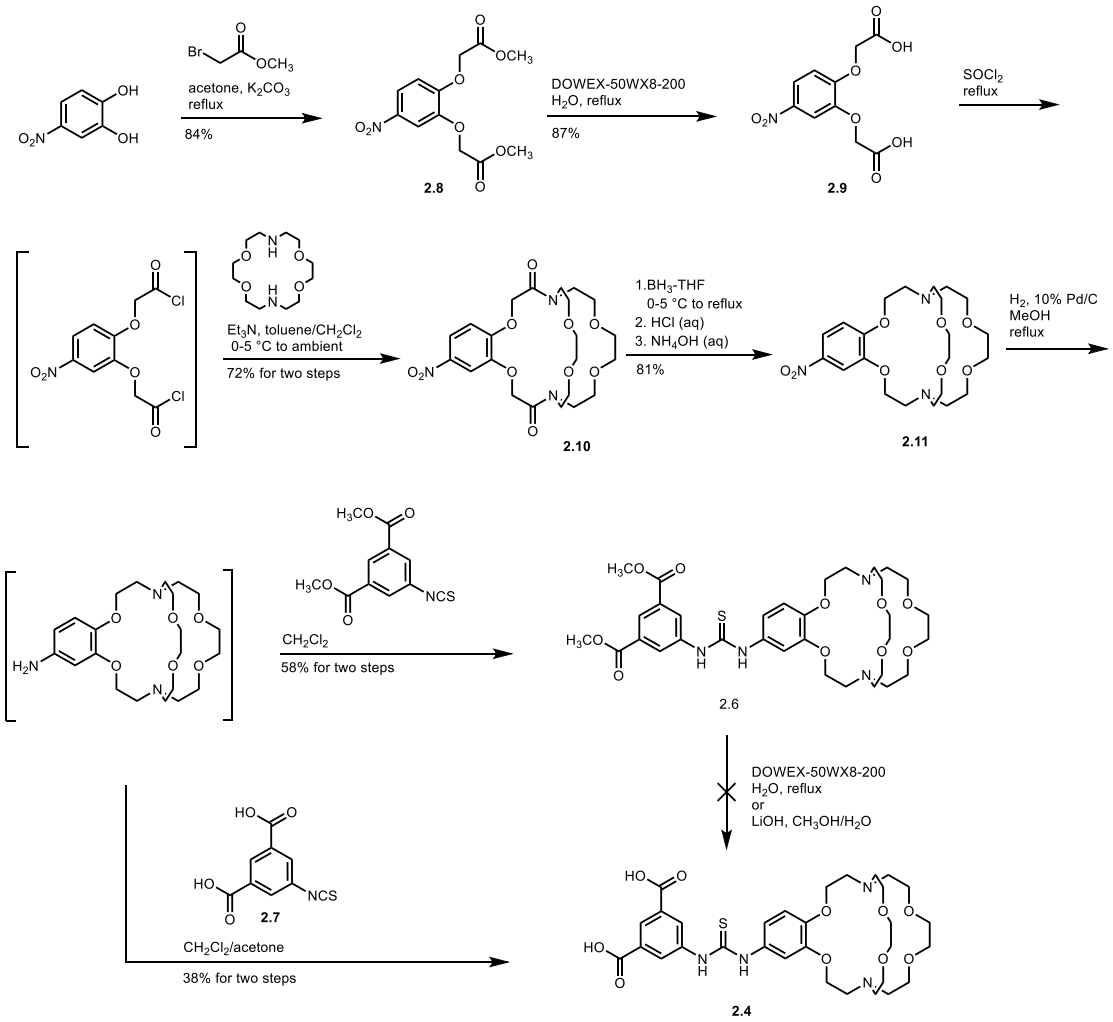
2.3 might interact with the blood vessel walls and blood cells and hinder their in vivo delivery. Based on this idea, ligand **2.4** was designed in which the cryptand ring and isophthalic acid are joined together by a thiourea linker. The rationale for this ligand is that, upon metalation with Eu^{2+}, it will produce a neutral complex **2.5** that will have a low tendency to interact with blood vessel walls and blood cells (**Scheme 2.1**).

Scheme 2.1 Metalation of **2.4** to form neutral Eu^{2+}-containing complex **2.5**.



Initially, I synthesized cryptand **2.6** (**Scheme 2.2**), which contains two methyl ester groups instead of two carboxyl groups, because dimethyl 5-isothiocyanatoisophthalate is commercially available. However, neither acid nor base hydrolysis of **2.6** produced the desired product **2.4**. I then prepared 5-isothiocyanatoisophthalic acid (**2.7**) by following a published procedure.[26] This effort afforded cryptand **2.4**. The synthetic procedures of cryptand **2.4** and **2.6** are same except for the last step (**Scheme 2.2**). Compounds **2.8**–**2.11** were prepared using similar methods to those described by Gansow and coworkers.[27]

Scheme 2.2 Synthesis of cryptands **2.4** and **2.6**.



2.2 Experimental Procedures

2.2.1 Materials

Commercially available chemicals were of reagent-grade purity or better and were used as received unless otherwise noted. Triethylamine was dried over calcium hydride and distilled under an argon atmosphere. Water was purified using a PURELAB Ultra Mk2 purification system. Flash chromatography was performed using silica gel 60, 230–400 mesh. Analytical thin-layer chromatography (TLC) was carried out on TLC plates precoated with silica gel 60 F_{254} (250 μm layer thickness). TLC plates visualization was accomplished with a UV lamp or by charring with

potassium permanganate stain (1.5 g $KMnO_4$, 10 g K_2CO_3, 2.5 mL 5% w/v aqueous NaOH, and 150 mL H_2O).

2.2.2 Characterization

^{1}H- and ^{13}C-NMR spectra were recorded at ambient temperature on a Varian Unity 400 spectrometer (400 MHz for ^{1}H and 101 MHz for ^{13}C). Chemical shifts were referenced to solvent residual signals ($CDCl_3$: ^{1}H δ 7.26 ppm, ^{13}C δ 77.16; CD_3CN: ^{1}H δ 1.94, ^{13}C δ 118.26, 1.32; DMSO-d_6: ^{1}H δ 2.50, ^{13}C δ 39.52; D_2O: ^{1}H δ 4.79, ^{13}C was referenced to 5% DMSO-d_6 added δ 39.52; CD_2Cl_2: ^{1}H δ 5.32, ^{13}C δ 53.84). ^{1}H-NMR data are assumed to be first order, and the apparent multiplicities are reported as follows: ‘‘s’’ = singlet, ‘‘d’’ = doublet, “t” = triplet, ‘‘dd’’ = doublet of doublets, “m” = multiplet, and ‘‘br’’ = broad. Italicized elements are those that are responsible for the shifts. High resolution electrospray ionization mass spectra (HRESIMS) were recorded on a Waters LCT Premiere Xe TOF mass spectrometer. Low resolution mass spectra (MS) of known compounds were recorded on a Shimadzu LCMS-2010EV mass spectrometer.

2.2.3 Synthesis

5-Isothiocyanatoisophthalic acid (2.7): Compound **2.7** was synthesized according to the literature procedure.[26] 5-Aminoisophthalic acid (2.12 g, 11.7 mmol, 1 equiv), sodium acetate trihydrate (6.83 g, 50.2 mmol), and NaOH (1.05 g, 26.2 mmol) were dissolved in a mixed solvent of water (50 mL) and acetone (25 mL) while stirring. The resulting solution was cooled to 0 ℃. Thiophosgene (1.50 g, 13.0 mmol, 1.1 equiv) was added to the cold solution in one shot. A yellow suspension formed, and it

turned into a white cloudy mixture after 30 min. After stirring for 2 h, concentrated HCl was added dropwise to adjust the pH of the reaction to 3. The crude product precipitated as a white solid. The solid was isolated by filtration using a medium porosity glass frit and washed with 0.1 M hydrochloric acid (3 × 10 mL). Acetone (100 mL) was added and the soluble part was isolated and concentrated under reduced pressure to yield 1.05 g (40%) of **2.7** as white powder. ^{1}H- and ^{13}C-NMR spectra were assigned by comparison with literature.[26] ^{1}H NMR (400 MHz, DMSO-d_6) δ 13.63 (brs, 2H), 8.37 (t, J = 1.5 Hz, 1H), 8.08 (d, J = 1.5 Hz, 2H); ^{13}C NMR (101 MHz, DMSO-d_6) δ 165.4, 136.2, 133.1, 131.4, 130.2, 128.6; MS (*m/z*): $[M - H]^-$ calcd for $C_9H_4NO_4S$, 222.0; found, 222.0.

Dimethyl 2,2'-((4-nitro-1,2-phenylene)bis(oxy))diacetate (2.8): Compound **2.8** was prepared using similar methods to those described by Gansow and coworkers.[27] To a stirred mixture of anhydrous K_2CO_3 (5.40 g, 39.1 mmol, 3 equiv) in acetone (100 mL) was slowly (over 30min) added methyl bromoacetate (5.98 g, 39.1 mmol, 3 equiv) at ambient temperature. A solution of 4-nitrocatecol (2.06 g, 13.3 mmol, 1 equiv) in acetone (30 mL) was added dropwise to the resulted reaction mixture. After the addition, the mixture was refluxed for 12 h. After cooling to ambient temperature, solid were removed by filtration and the solvent was removed under reduced pressure. The solid obtained was recrystallized from ethanol to yield 3.34 g (84%) of **2.8** as light yellow solid. ^{1}H- and ^{13}C-NMR spectra were assigned by comparison with literature.[28] ^{1}H NMR (400 MHz, $CDCl_3$) δ 7.92 (dd, J = 9.0, 2.5 Hz, 1H), 7.73 (d, J = 2.5 Hz, 1H), 6.88 (d, J = 9.0 Hz, 1H), 4.83 (s, 2H), 4.80 (s, 2H), 3.82 (s, 3H), 3.81 (s,

3H). ^{13}C NMR (101 MHz, $CDCl_3$) δ 168.5, 168.3, 153.2, 147.6, 142.4, 118.9 113.2, 110.1, 66.4, 66.2, 52.7, 52.6; MS (*m/z*): $[M + Na]^+$ calcd for $C_{12}H_{13}NO_8Na$, 322.0; found, 322.1.

2,2'-((4-Nitro-1,2-phenylene)bis(oxy))diacetic acid (2.9): Compound **2.9** was prepared using similar methods to those described by Gansow and coworkers.[27] Dowex 50WX8 (hydrogen form, 200–400 mesh, 0.22 g) was added into a mixture of **2.8** (2.02 g, 6.75 mmol) in H_2O (130 mL). The reaction mixture was heated at reflux for 20 h then filtered while hot. The yellow filtrate was cooled to ambient temperature to yield 1.59 g (87%) of **2.9** as white solid. ^{1}H- and ^{13}C-NMR spectra were assigned by comparison with literature.[27] ^{1}H NMR (400 MHz, DMSO-d_6) δ 13.19 (brs, 2H), 7.89 (dd, *J* = 9.0, 2.6 Hz, 1H), 7.69 (d, *J* = 2.6 Hz, 1H), 7.11 (d, *J* = 9.1 Hz, 1H), 4.91 (s, 2H), 4.88 (s, 2H); ^{13}C NMR (101 MHz, DMSO-d_6) δ 169.7, 169.4, 153.2, 147.0, 140.8, 117.9, 112.6, 108.4, 65.3, 65.2; MS (*m/z*): $[M - H]^-$ calcd for $C_{10}H_8NO_8$, 270.0; found, 270.1.

5,6-(4-Nitrobenzo)-4,7,13,16,21,24-hexaoxa-1,10-diazabicyclo[8.8.8]hexacosane-2, 9-dione (2.10): Compound **2.10** was prepared using similar methods to those described by Gansow and coworkers.[27] A mixture of **2.9** (1.02 g, 3.76 mmol, 1 equiv) in thionyl chloride (10 mL) was heated at reflux under argon for 3 h to produce a clear, light yellow solution. Excess thionyl chloride was removed under reduced pressure to yield a light yellow solid. Next, a 500 mL three neck flask equipped with two dropping funnels was evacuated and filled with argon. Then 150 mL anhydrous toluene was added to the three neck flask. The solution was cooled to 0 ℃. After that,

to one dropping funnel was added a solution of the above light yellow solid in a mixture of anhydrous toluene (20 mL) and anhydrous CH_2Cl_2 (20 mL). To the other dropping funnel was added a solution of triethylamine (1.09 g, 10.8 mmol) and 1,4,10,13-tetraoxa-7,16-diazacyclooctadecane (0.940 g, 3.58 mmol, 0.95 equiv) in a mixture of anhydrous toluene (30 mL) and anhydrous CH_2Cl_2 (10 mL). The two solutions were added dropwise simultaneously to the three neck flask while stirring. After the additions, the turbid light yellow mixture was stirred at ambient temperature for 24 h. The resulting solid was filtered, and solvents were removed under reduced pressure to produce a yellow solid that was purified using silica gel chromatography (20:1 CH_2Cl_2/CH_3OH) to yield 1.29 g (72%) of **2.10** as light yellow fluffy solid. ^{1}H- and ^{13}C-NMR spectra were assigned by comparison with literature.[29] ^{1}H NMR (400 MHz, $CDCl_3$) δ 7.82 (dd, *J* = 8.9, 2.6 Hz, 1H), 7.77 (d, *J* = 2.6 Hz, 1H), 7.01 (d, *J* = 8.9 Hz, 1H), 5.63 (d, *J* = 15.0 Hz, 1H), 5.47 (d, *J* = 15.0 Hz, 1H), 4.80 (dd, *J* = 17.4, 15.0 Hz, 2H), 4.44–4.20 (m, 2H), 3.99–3.41 (m, 18H), 3.34–3.12 (m, 2H), 2.88–2.71 (m, 2H); ^{13}C NMR (101 MHz, $CDCl_3$) δ 168.70 ,154.0, 148.2, 142.1, 118.5, 117.0, 112.0, 71.5, 71.33, 71.31, 71.2, 69.8, 69.5, 69.2, 68.9, 67.9, 67.3, 49.6, 49.5, 49.2, 49.0; MS (*m/z*): $[M + H]^+$ calcd for $C_{22}H_{32}N_3O_{10}$, 498.2; found, 498.3; TLC: R_f = 0.25 (20:1 CH_2Cl_2/CH_3OH).

5,6-(4-Nitrobenzo)-4,7,13,16,21,24-hexaoxa-1,10-diazabicyclo[8.8.8]hexacosane (2.11): Compound **2.11** was prepared using similar methods to those described by Gansow and coworkers.[27] Compound **2.10** (1.17 g, 2.34 mmol, 1 equiv) was dissolved in anhydrous tetrahydrofuran (THF) (10 mL) under an argon atmosphere. The

solution was cooled 0 ℃. Next, BH_3 (1 M in THF, 11.0 mL, 4.7 equiv) was added at a speed of 30 mL/h using a syringe pump. After the addition, the solution was heated at reflux for 24 h. The reaction was cooled to ambient temperature, and water was added dropwise to destroy the excess borane. Hydrochloric acid (6 M, 11.0 mL) was added, and the mixture was heated at refluxed for 12 h. Ammonium hydroxide (28% NH_3 in H_2O, 10 mL) was added to adjust the pH of the solution to 9. Solvents were removed under reduced pressure, and the residue was dissolved in CH_2Cl_2 and washed with H_2O. The organic layer was collected, and the solvent was removed under reduced pressure. The crude product was purified using silica gel chromatography (20:1 CH_2Cl_2/CH_3OH) to yield 0.891 g (81%) of **2.11** as yellow fluffy solid. ^{1}H- and ^{13}C-NMR spectra were assigned by comparison with literature.[30] ^{1}H NMR (400 MHz, CD_3CN) δ 7.95 (dd, *J* = 9.0, 2.6 Hz, 1H), 7.83 (d, *J* = 2.6 Hz, 1H), 7.16 (d, *J* = 9.0 Hz, 1H), 4.30 (dd, *J* = 9.1, 4.0 Hz, 4H), 3.68–3.46 (m, 12H), 3.44–3.32 (m, 4H), 2.85–2.77 (m, 4H), 2.75–2.55 (m, 8H); ^{13}C NMR (101 MHz, CD_3CN) δ 153.1, 147.2, 142.6, 118.9, 112.8, 108.5, 68.7, 68.2, 67.2, 66.8, 53.3, 53.1, 53.0; MS (*m/z*): $[M + H]^+$ calcd for $C_{22}H_{36}N_3O_8$, 470.3; found, 470.3; TLC: R_f = 0.11 (20:1 CH_2Cl_2/CH_3OH).

5,6-(4-(3-(3,5-Dicarboxyphenyl)thioureido)benzo)-4,7,13,16,21,24-hexaoxa-1,10-diazabicyclo[8.8.8]hexacosane (2.4): A solution of **2.11** (0.612 g, 1.30 mmol, 1 equiv) in CH_3OH (40 mL) was degassed and back filled with Ar. To the solution was added 10% Pd/C (0.0666 g, 0.0626 mmol) quickly. The resulting mixture was hydrogenated using a hydrogen balloon and heating at reflux for 12h. The Pd/C was removed using a 0.2 μm hydrophobic filter, and the filtrate was concentrated under reduced pressure

to produce a pink paste. The pink paste was then dissolved in a mixture of acetone (50 mL) and CH_2Cl_2 (20 mL). To the resulting solution was added 5-isothiocyanatoisophthalic acid (**2.7**) (0.295 g, 1.32 mmol, 1 equiv). The resulting white cloudy mixture was stirred under Ar at ambient temperature for 24 h. The reaction mixture was filtered, and the resulting off-white solid was washed with acetone (10 mL) and CH_2Cl_2 (10 mL). The solid was then dissolved in a minimum amount of boiling water, and a white solid precipitated upon cooling to ambient temperature. The solid was collected and dried under vacuum to yield 0.329 g (38%) of **2.4** as a white solid. ^{1}H- and ^{13}C-NMR spectra were assigned using distortionless enhancement polarization transfer (DEPT), gradient correlation spectroscopy (GCOSY), gradient heteronuclear multiple quantum correlation (GHMQC), and gradient heteronuclear multiple bond correlation (GHMBC) experiments. ^{1}H NMR (400 MHz, D_2O) δ 8.13 (s, C*H*, 1H), 7.84 (s, C*H*, 2H), 7.05–6.86 (m, C*H*, 3H), 4.35 (d, J = 24.9 Hz, CH_2, 4H), 3.92–3.35 (m, CH_2, 28H); ^{13}C NMR (101 MHz, D_2O–DMSO-d_6) δ 181.2, 174.7, 147.6, 146.4, 139.4, 139.0, 133.1, 129.5 (*C*H), 128.6 (*C*H), 120.7 (*C*H), 113.8 (*C*H), 112.3 (*C*H), 71.40 (*C*H_2), 71.38 (*C*H_2), 65.7 (*C*H_2), 63.4 (*C*H_2), 57.4 (*C*H_2), 57.3 (*C*H_2), 57.0 (*C*H_2); HRESIMS (*m/z*): $[M + Na]^+$ calcd for $C_{31}H_{42}N_4O_{10}SNa$, 685.2519; found, 685.2517.

5,6-(4-(3-(3,5-Dimethoxycarbonylphenyl)thioureido)benzo)-4,7,13,16,21,24-hexaoxa-1,10-diazabicyclo[8.8.8]hexacosane (2.6): A solution of **2.11** (0.128 g, 0.273 mmol, 1 equiv) in CH_3OH (30 mL) was degassed and back filled with Ar. To the resulted solution was quickly added 10% Pd/C (0.0202 g, 0.0190 mmol). The

resulting mixture was hydrogenated using a hydrogen balloon and heating at reflux for 12 h. The Pd/C was removed using a 0.2 μm hydrophobic filter, and the filtrate was concentrated under reduced pressure to produce a pink paste. The pink paste was dissolved in CH_2Cl_2 (10 mL) under Ar. To the resulting solution was added a solution of dimethyl 5-isothiocyanatoisophthalate (0.0801 g, 0.319 mmol, 1.2 equiv) in CH_2Cl_2 (5 mL) dropwise. The reaction was stirred at ambient temperature under Ar for 24 h. The solvent was removed under reduced pressure, and the resulting solid was purified using silica gel chromatography (15:1 CH_2Cl_2/CH_3OH) to yield 0.109 g (58%) of **2.6** as light yellow solid. ^{1}H- and ^{13}C-NMR spectra were assigned using DEPT, GCOSY, GHMQC, and GHMB experiments. ^{1}H NMR (400 MHz, CD_2Cl_2) δ 11.45 (s, N*H*, 1H), 11.40 (s, N*H*, 1H), 8.60 (d, *J* = 1.5 Hz, C*H*, 2H), 8.34 (t, *J* = 1.5 Hz, C*H*, 1H), 7.68 (d, *J* = 2.3 Hz, C*H*, 1H), 7.25 (dd, *J* = 8.7, 2.3 Hz, C*H*, 1H), 6.87 (d, *J* = 8.7 Hz, C*H*, 1H), 4.21 (t, *J* = 4.7 Hz, CH_2, 2H), 4.13 (t, *J* = 4.7 Hz, CH_2, 2H), 3.92 (s, CH_3, 6H), 3.64–3.38 (m, CH_2, 16H), 2.87 (t, *J* = 4.7 Hz, CH_2, 2H), 2.80 (t, *J* = 4.7 Hz, CH_2, 2H), 2.73– 2.57 (m, CH_2, 8H); ^{13}C NMR (101 MHz, CD_2Cl_2) δ 181.2, 166.5, 145.5, 143.6, 141.3, 134.7, 130.9, 128.8 (*C*H), 126.1 (*C*H), 117.1 (*C*H), 112.6 (*C*H), 110.9 (*C*H), 68.8 (*C*H_2), 68.7 (*C*H_2), 68.2 (*C*H_2), 68.1 (*C*H_2), 65.9 (*C*H_2), 65.8 (*C*H_2), 53.7 (*C*H_2), 53.4 (*C*H_2), 53.2 (*C*H_2), 52.6 (*C*H_3); HRESIMS (*m/z*): $[M + Na]^+$ calcd for $C_{33}H_{46}N_4O_{10}SNa$, 713.2832; found, 713.2829; TLC: R_f = 0.11 (15:1 CH_2Cl_2/CH_3OH).

2.3 ^{1}H- and ^{13}C-NMR Spectra of 2.4 and 2.6–2.11

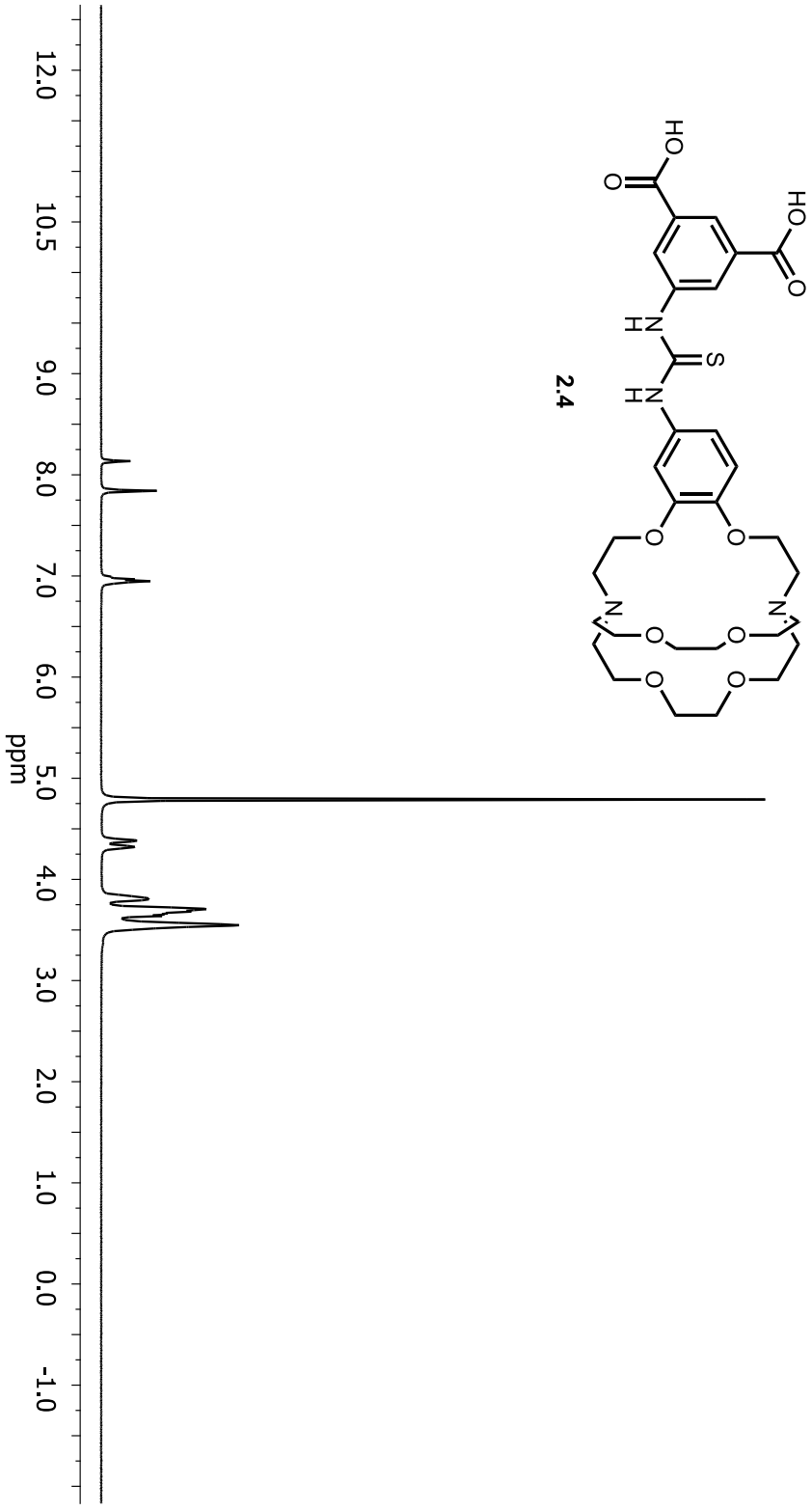
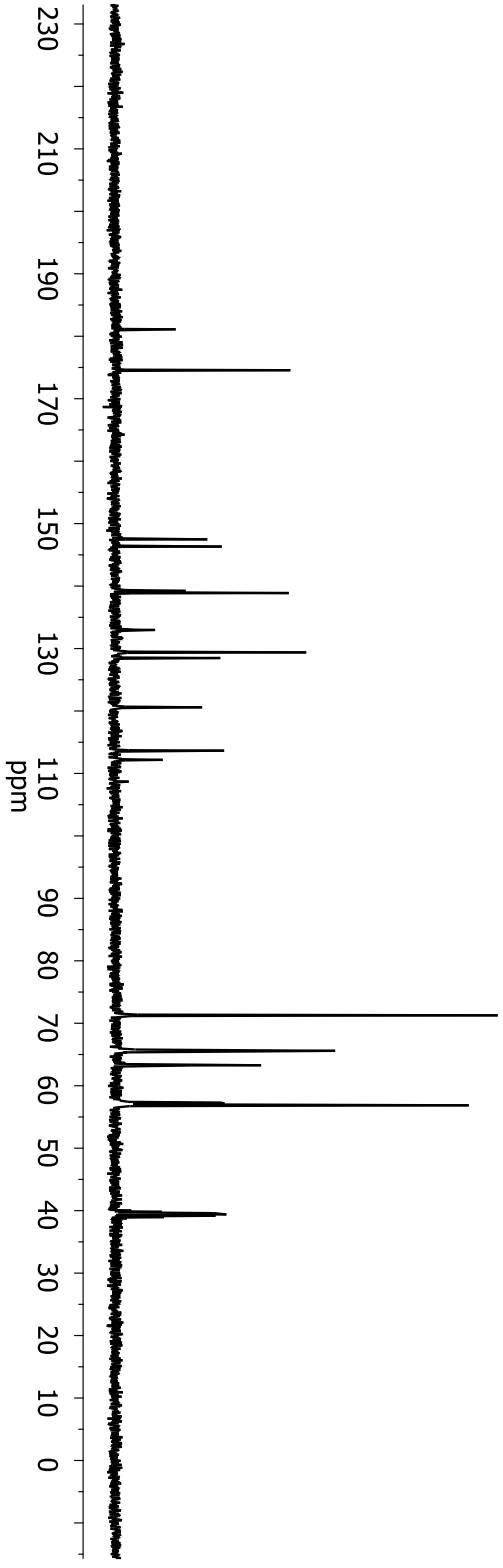
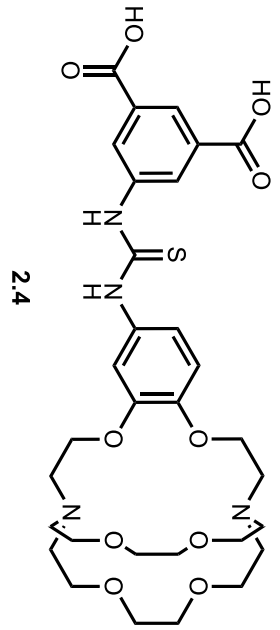


Figure 2.2 ^{1}H-NMR spectrum of **2.4**.





2.4

Figure 2.3 ^{13}C-NMR spectrum of **2.4**.

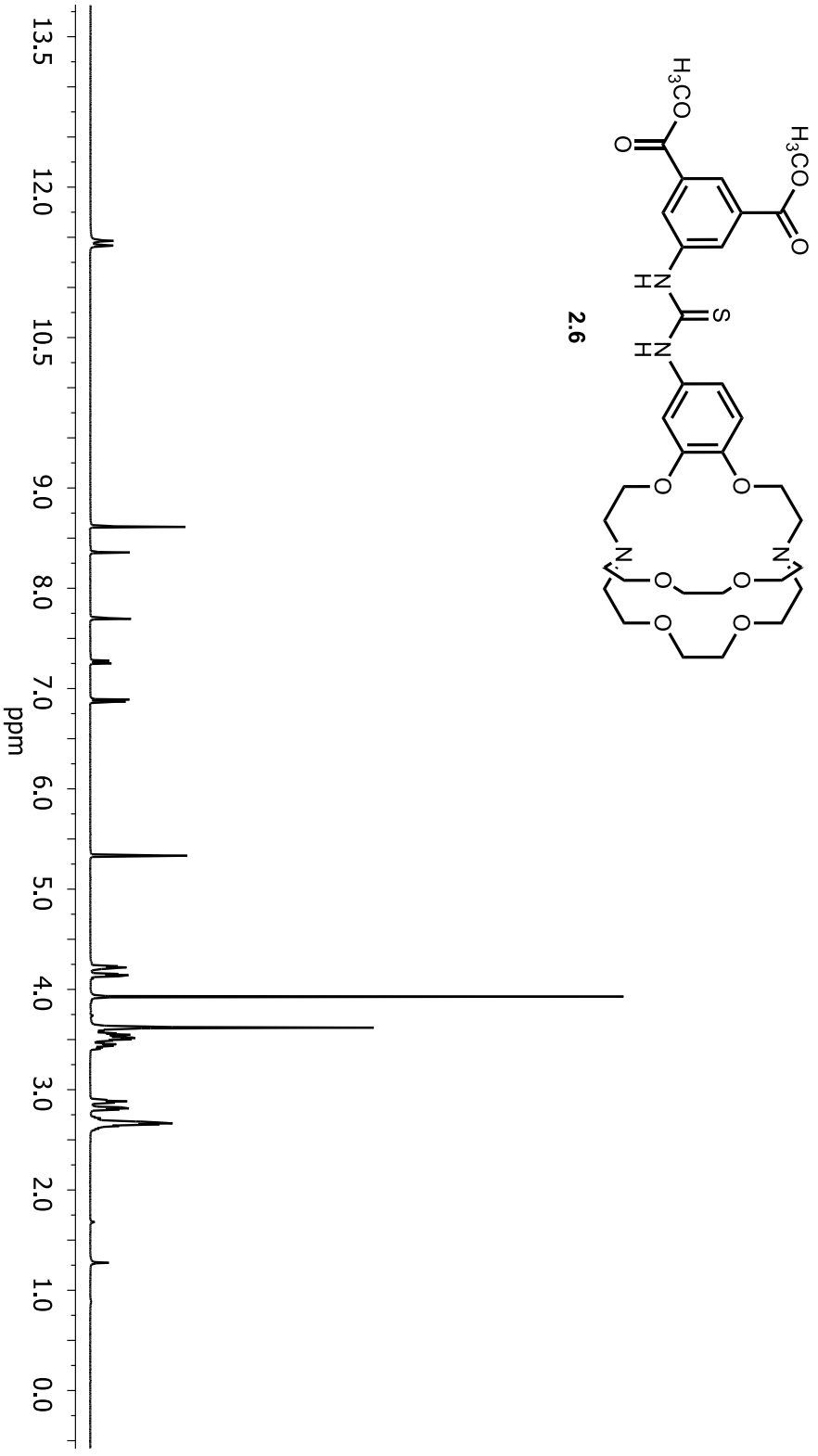


Figure 2.4 ^{1}H-NMR spectrum of **2.6**.

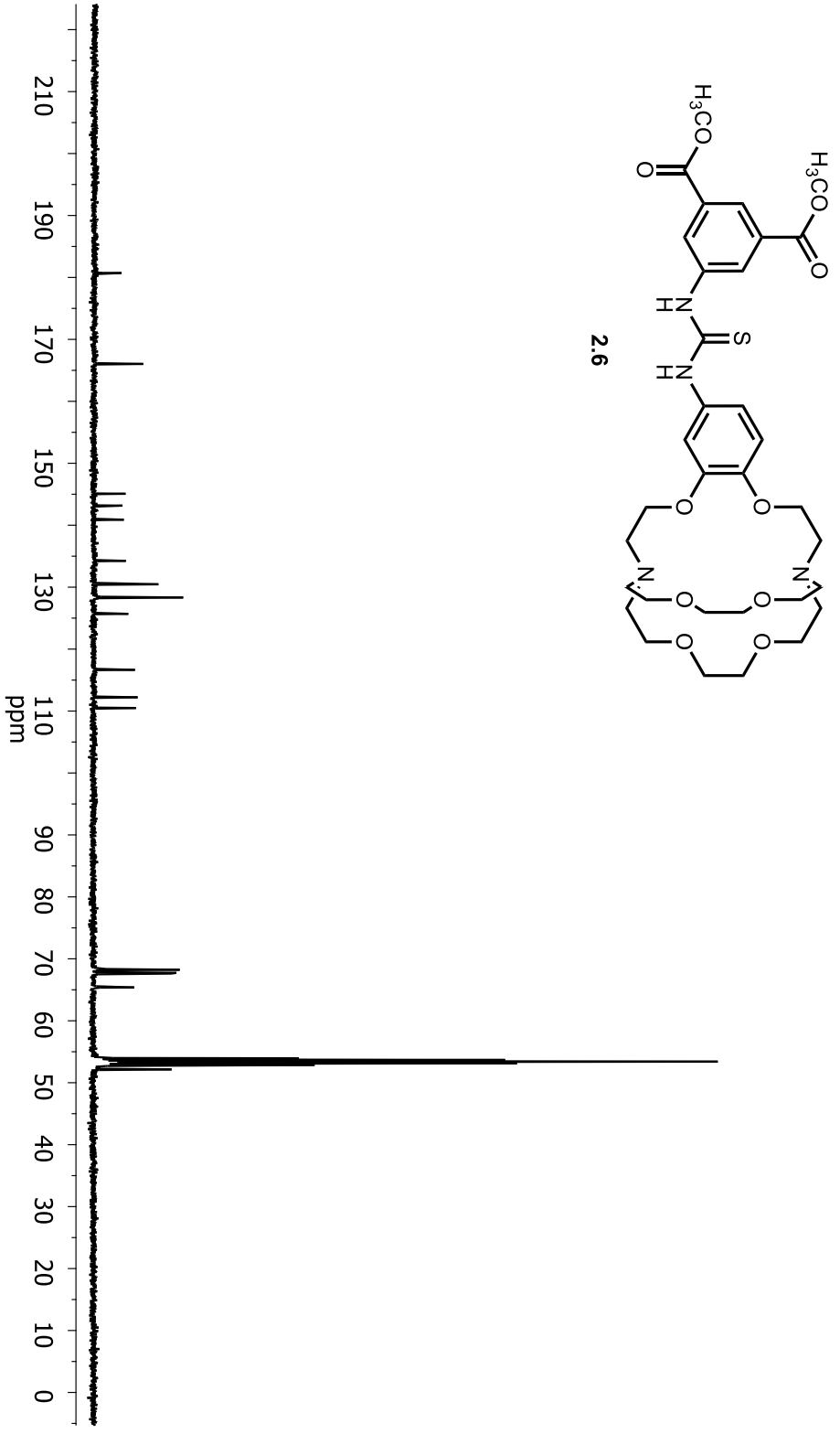
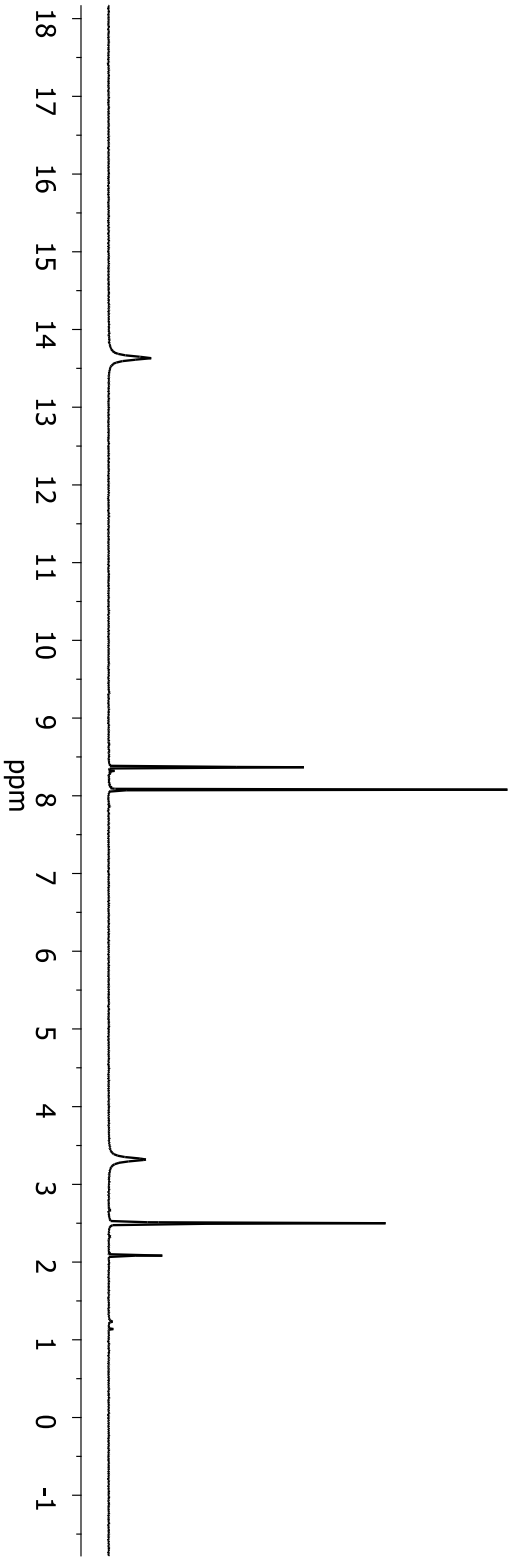


Figure 2.5 ^{13}C-NMR spectrum of **2.6**.



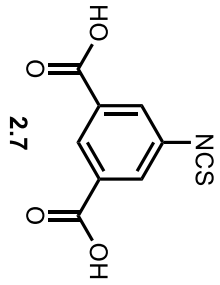


Figure 2.6 ^{1}H-NMR spectrum of **2.7**.

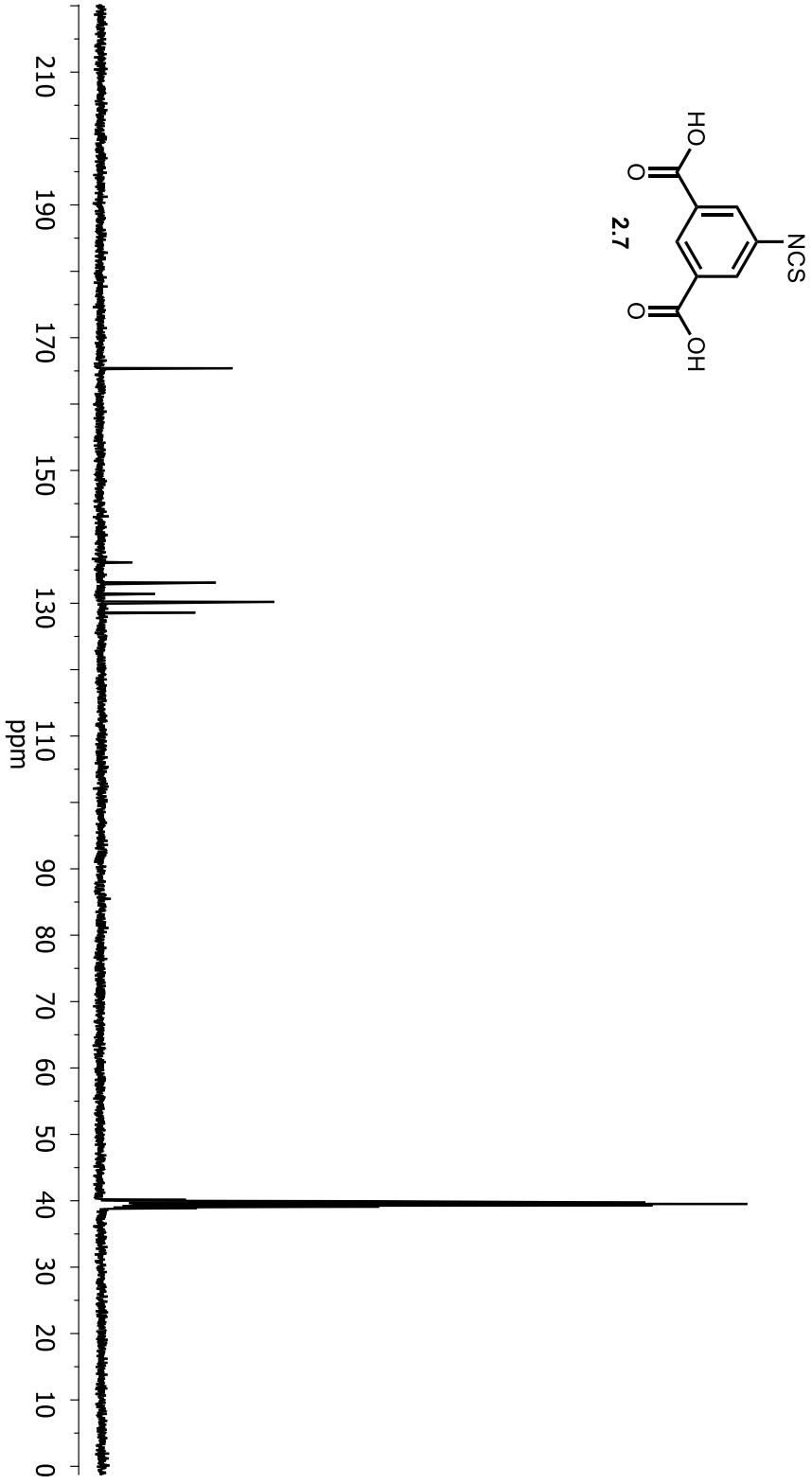


Figure 2.7 ^{13}C-NMR spectrum of **2.7**.

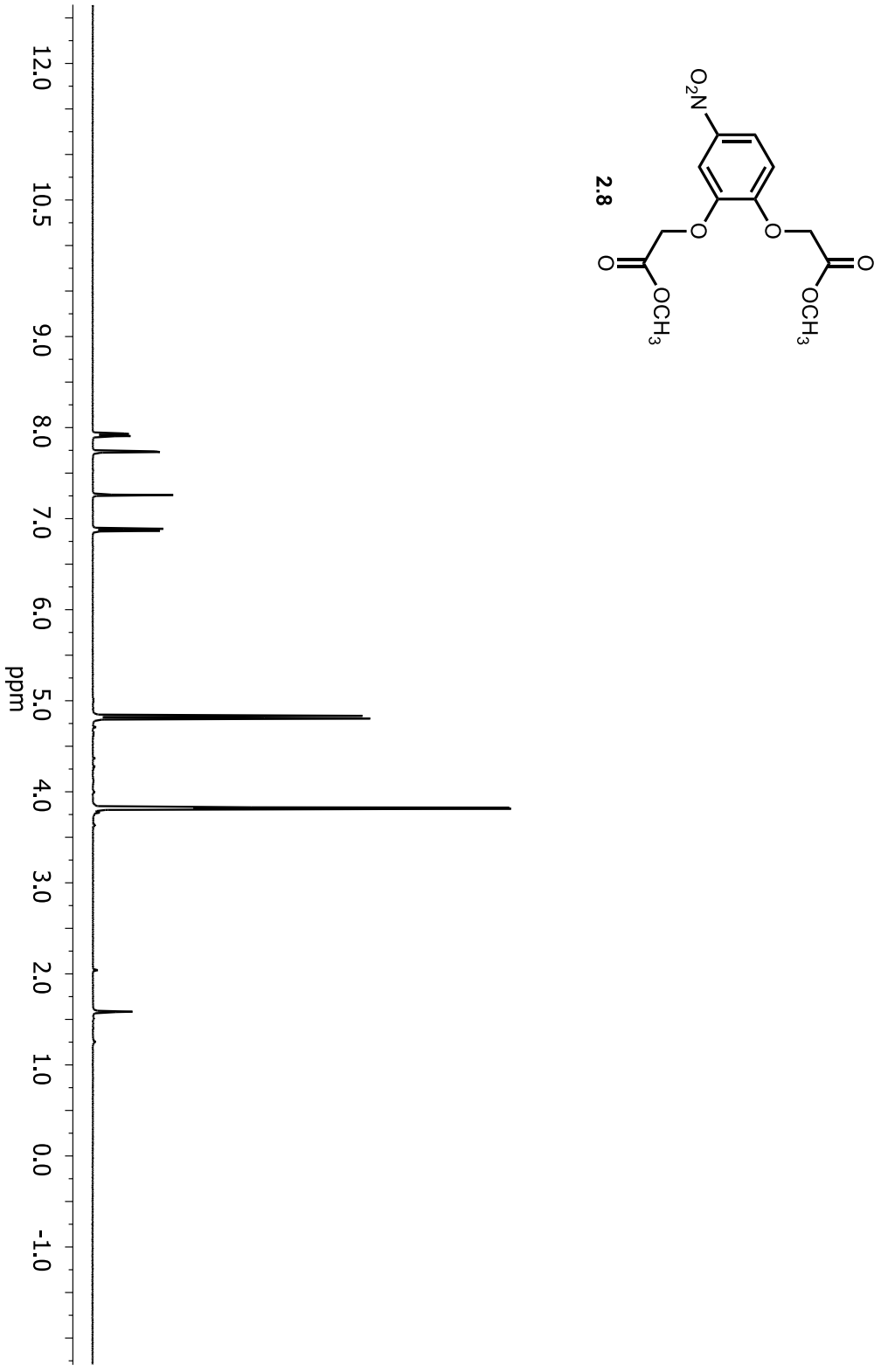
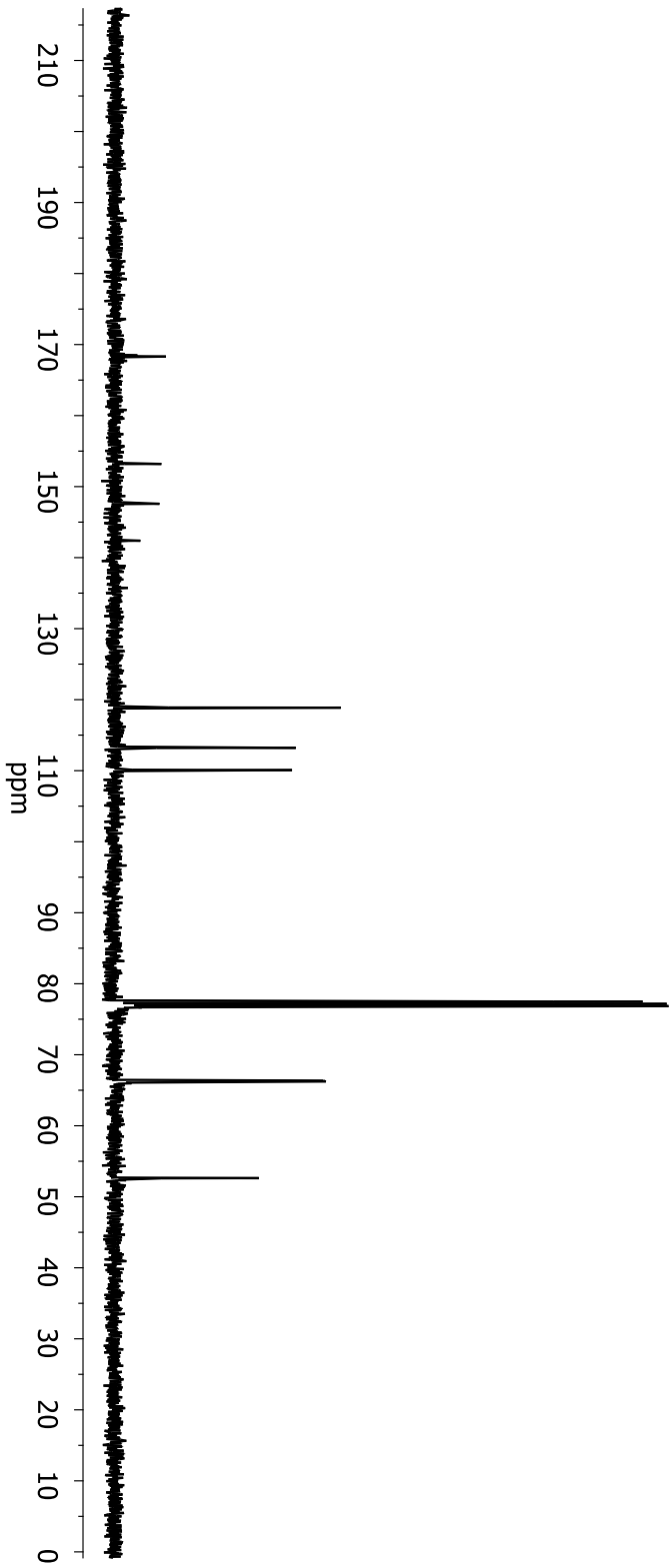
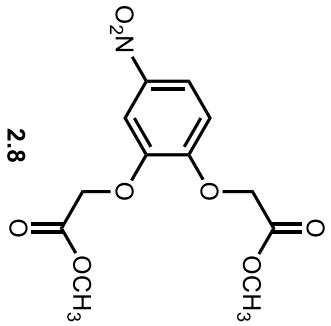


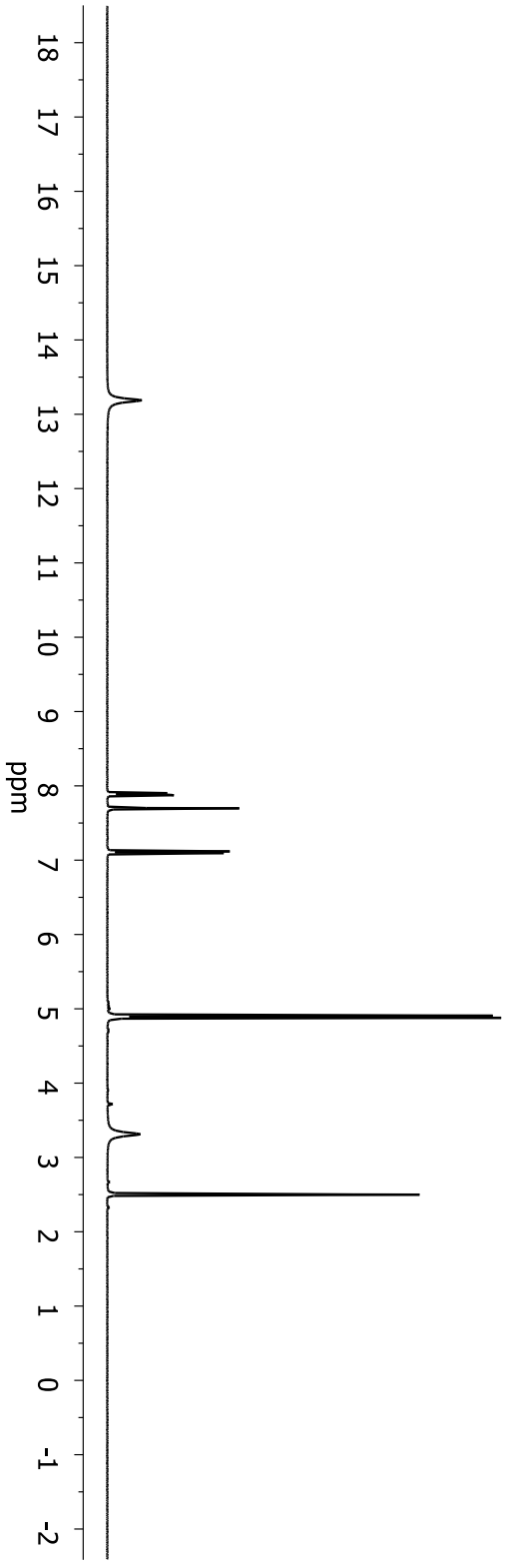
Figure 2.8 ^{1}H-NMR spectrum of **2.8**.

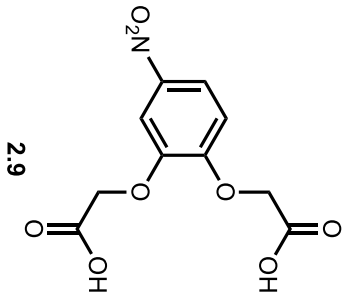




2.8

Figure 2.9 ^{13}C-NMR spectrum of **2.8**.





2.9

Figure 2.10 ^{1}H-NMR spectrum of **2.9**.

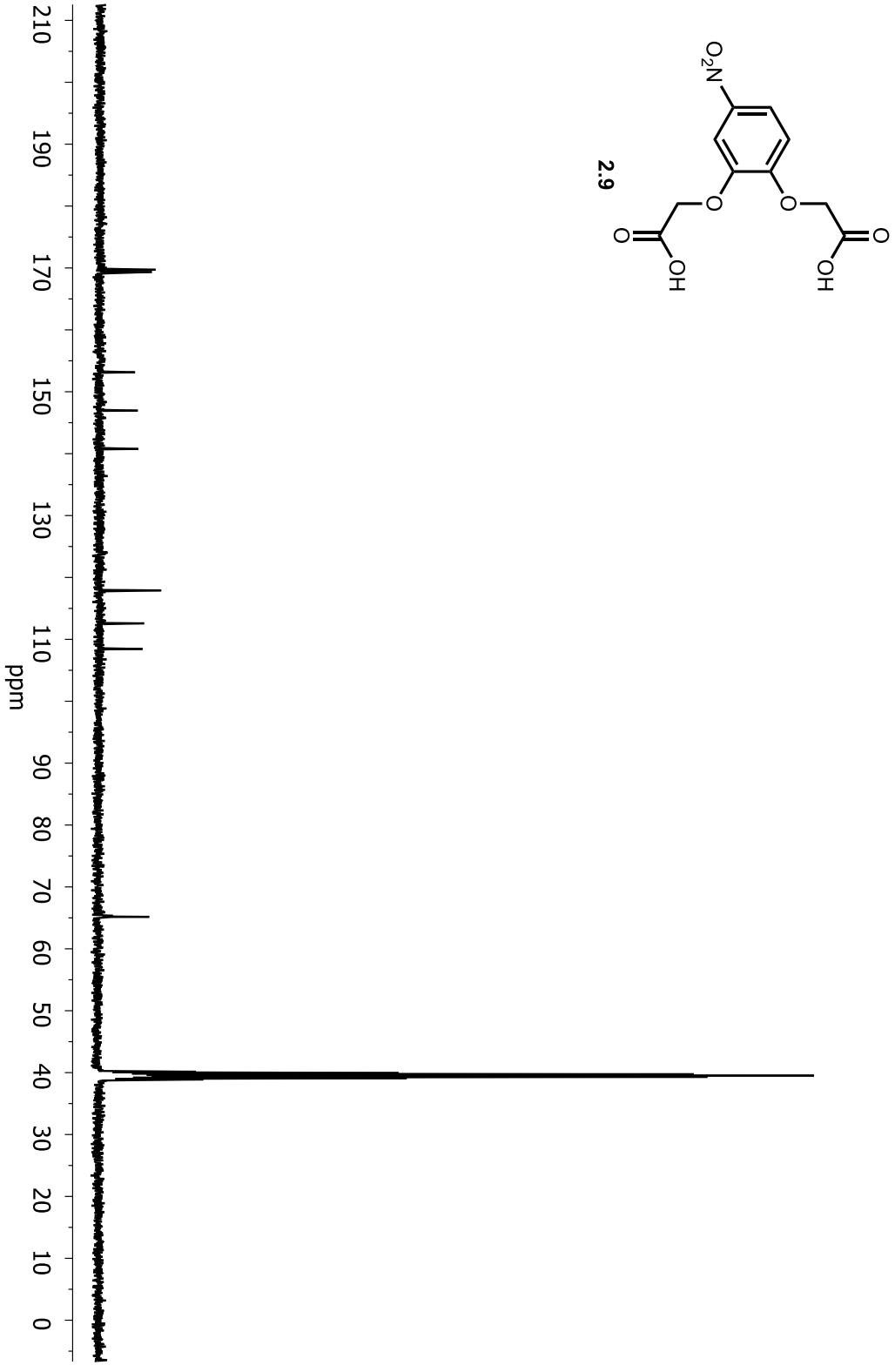


Figure 2.11 ^{13}C-NMR spectrum of **2.9**.

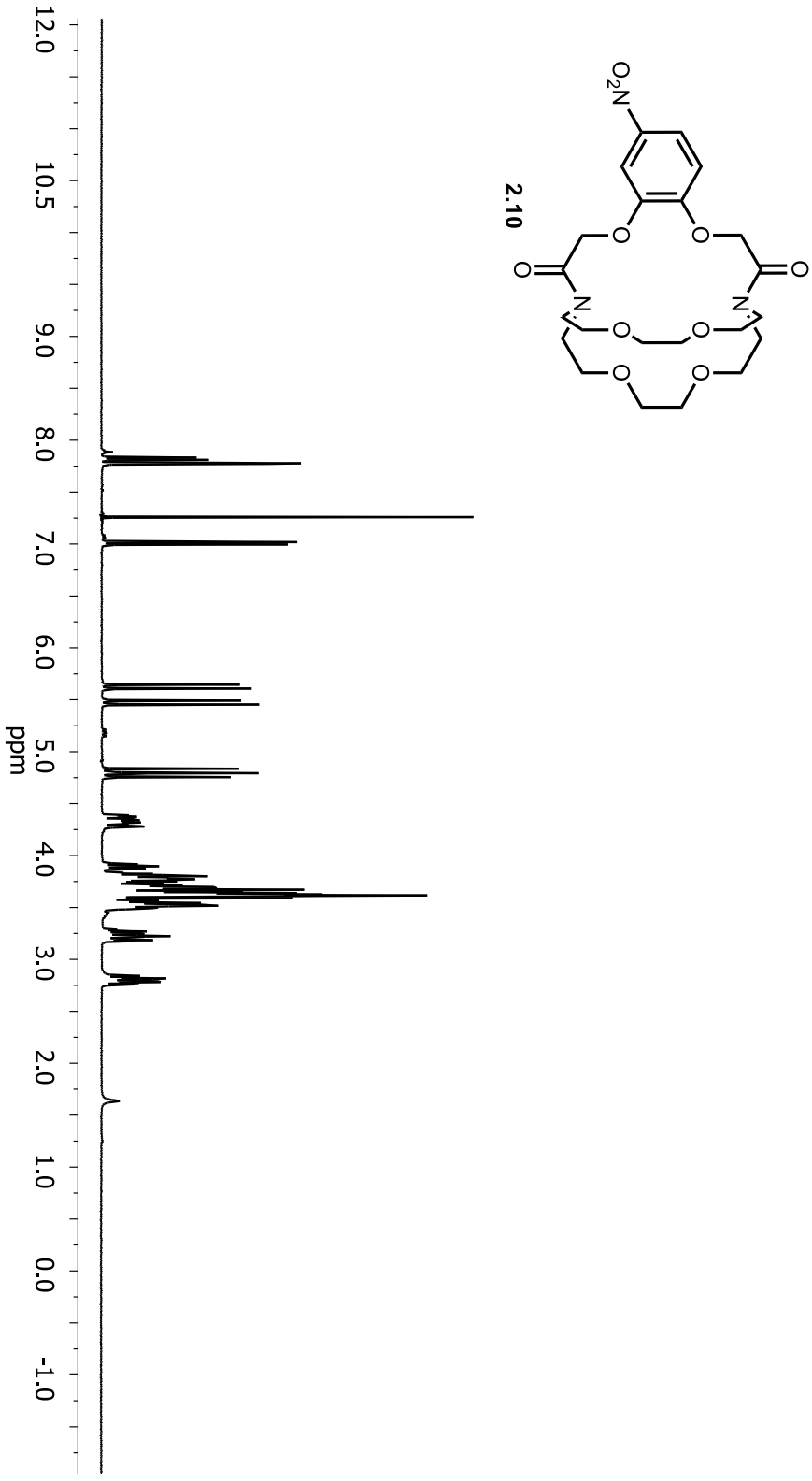
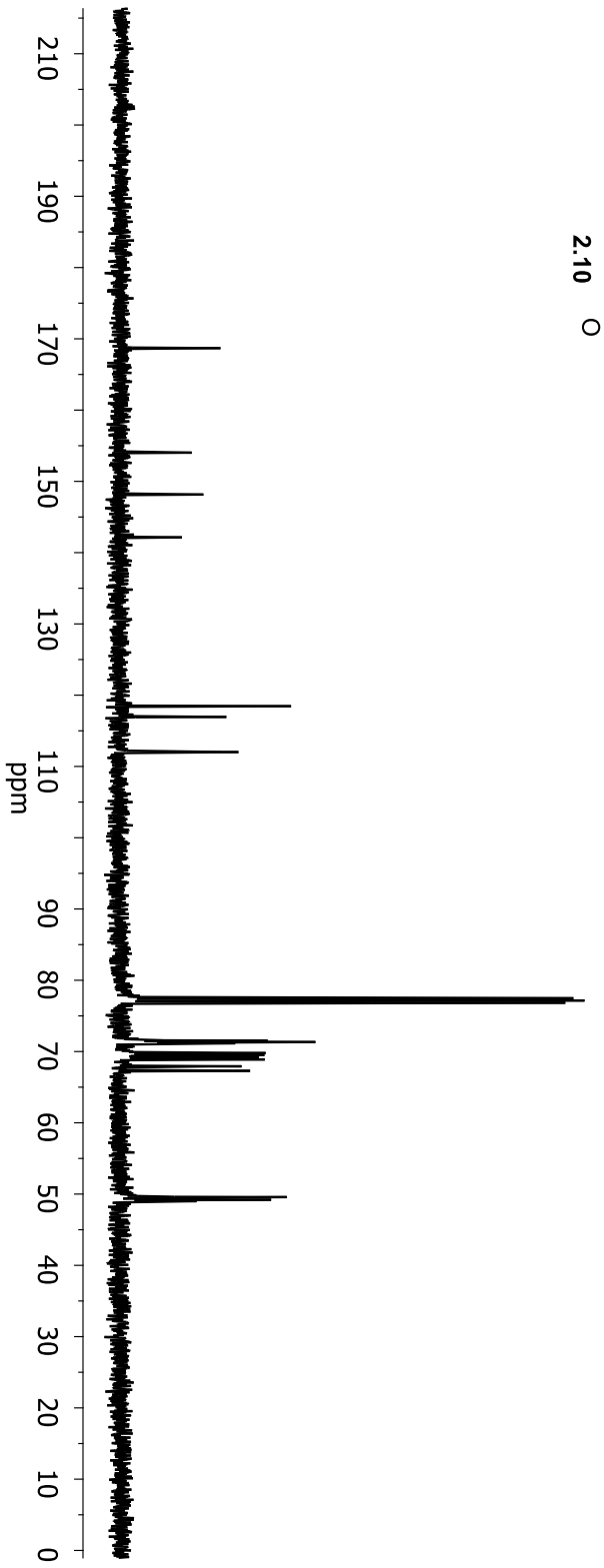
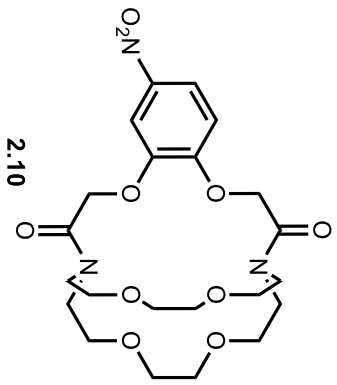


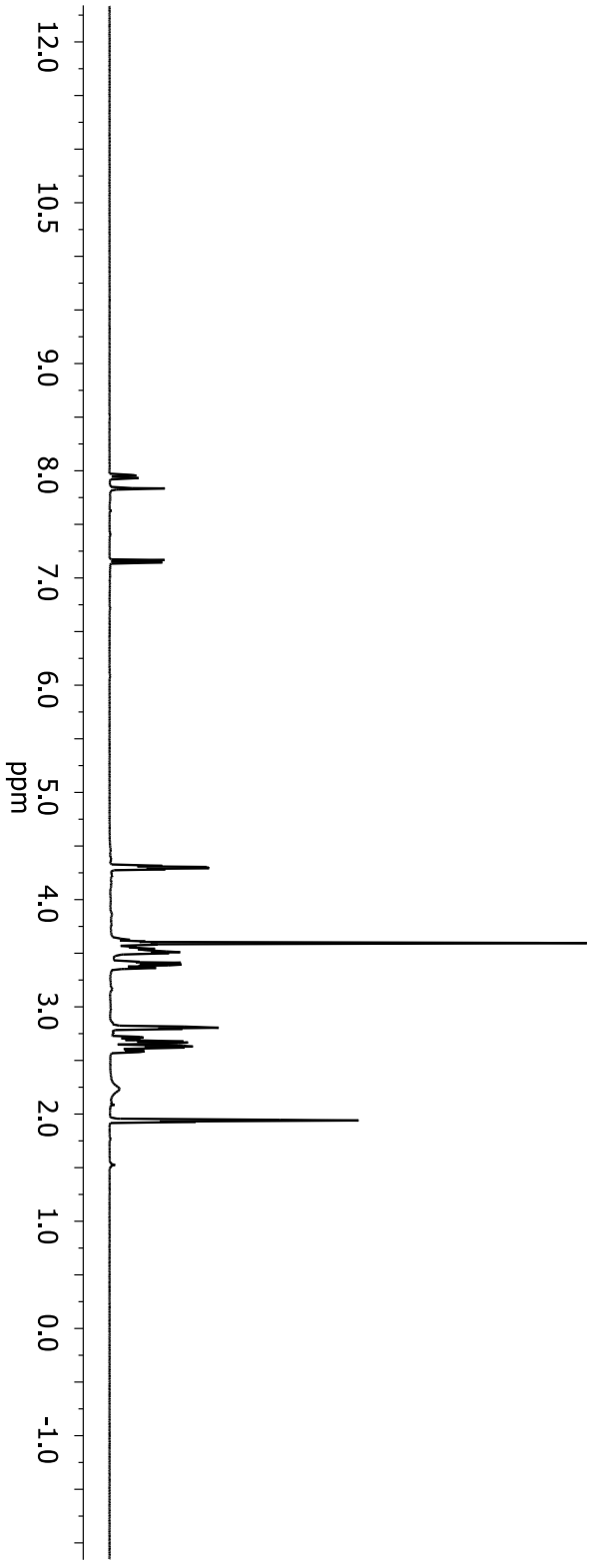
Figure 2.12 ^{1}H-NMR spectrum of **2.10**.

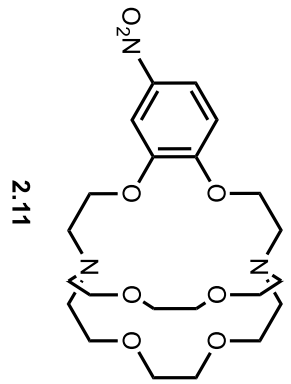




2.10

Figure 2.13 ^{13}C-NMR spectrum of **2.10**.





2.11

Figure 2.14 ^{1}H-NMR spectrum of **2.11**.

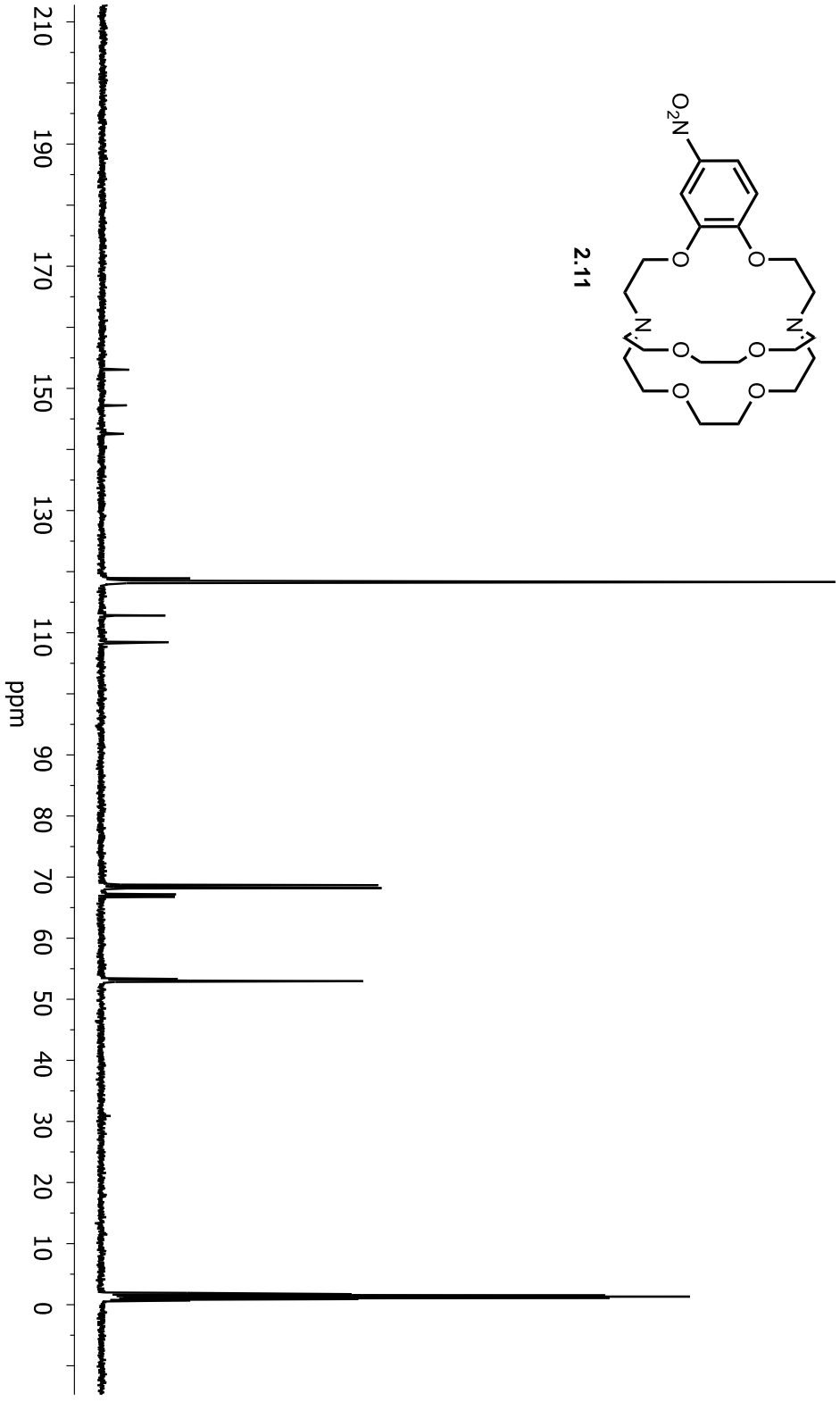


Figure 2.15 ^{13}C-NMR spectrum of **2.11**.

Chapter 3: Synthesis of Azacryptand Ligands for Luminescence Studies of Eu^{2+}

3.1 Introduction

The relative stability of half-filled 4f orbitals compared to other electronic configurations enables europium to access a divalent oxidation state (Eu^{2+}) in addition to its common trivalent oxidation state. In its first excited state, Eu^{2+} has the electron configuration of $4f^6 5d^1$. Unlike the 4f orbitals, which are shielded from the outside by the full 5s and 5p orbitals, the 5d orbitals are readily influenced by ligands. This access to d orbitals enables Eu^{2+} to behave differently from Eu^{3+} with respect to luminescence.[11] Eu^{2+}-containing complexes have characteristic broad emissions (390–580 nm) in addition to sharp emission bands between 354 and 376 nm that are similar to those observed in Eu^{3+}.[10] In protic solvents, macrocyclic ligands are needed to prevent quenching of the luminescence of Eu^{2+} by solvent molecules.[11] However, the study and application of coordination compounds of Eu^{2+} are largely limited by its tendency to be oxidized to Eu^{3+}. The Allen research group has used modified cryptands (**Figure 3.1**) to stabilize the Eu^{2+}.[16] Their study suggests that further stabilization of Eu^{2+} is possible.

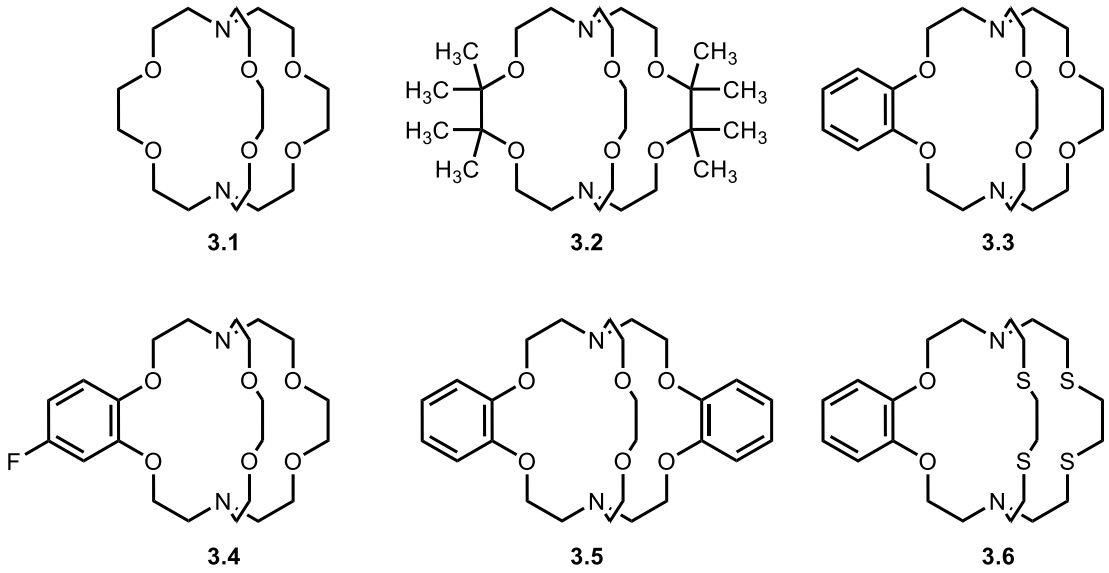


Figure 3.1 Unfunctionalized cryptand **3.1** and modified cryptands **3.2–3.6**

Eu^{2+} is soft and electron-rich. Therefore, substitution of the oxygen atoms in the cryptand ring with the softer nitrogen atoms and introducing electron-withdrawing phenyl groups near the donors were two strategies pursued by me to further stabilize Eu^{2+}. Based on these ideas the azacryptand ligands **3.7** and **3.8** were the targets of my research (**Figure 3.2**).

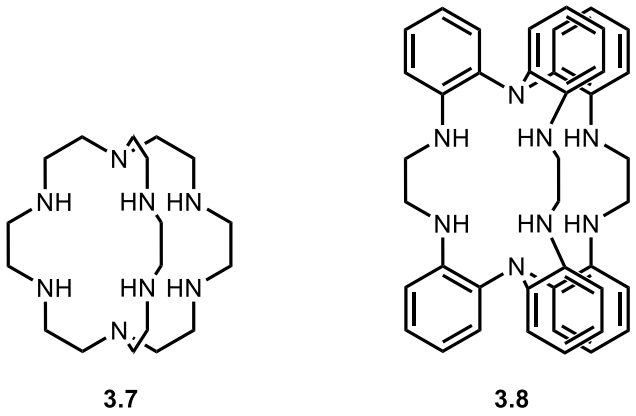
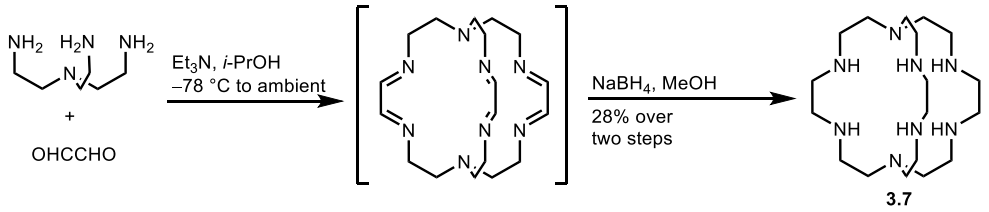


Figure 3.2 Structures of ligands **3.7** and **3.8**.

Ligand **3.7** was prepared according to the published procedures.[31,32] The synthetic procedures are shown in **Scheme 3.1**. Briefly, tris(2-aminoethyl)amine and glyoxal solution were reacted in the presence of triethylamine to give the imine

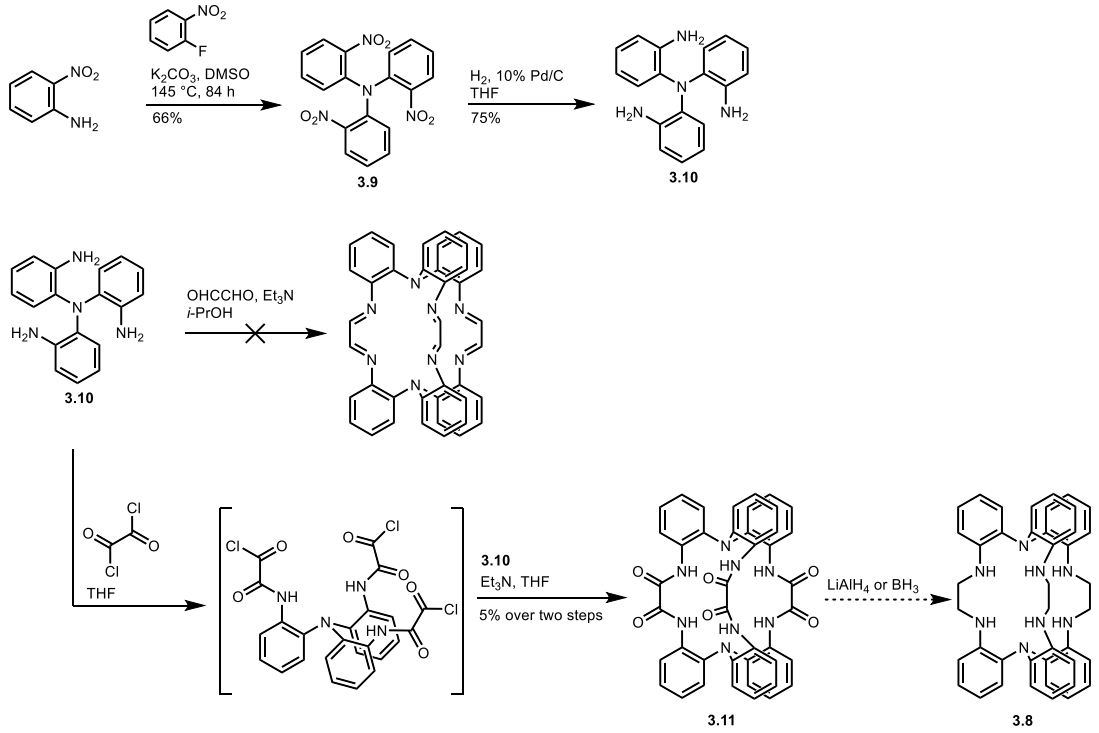
intermediate. This imine was reduced by $NaBH_4$ to give the azacryptand as a white solid.

Scheme 3.1 Synthesis of azacryptand **3.7**.



The proposed synthetic procedures for compound **3.8** are shown in Scheme **3.2**. I synthesized compound **3.10** according to the literature procedures.[33] Starting from compound **3.10**, initially I tried the similar method that was used in the synthesis of compound **3.7**, but the reaction didn't work. Then I used oxalyl chloride, and reaction afforded compound **3.11** in a very low yield (5%). Due to the low solubility of compound **3.11**, only high resolution electrospray ionization mass spectrometry (HRESIMS) was performed for characterization of this compound.

Scheme 3.2 Proposed synthetic procedures for azacryptand **3.8**.



Reduction of compound **3.11** with $LiAlH_4$ did not afford a clean reaction. In the mass spectrometry of the reaction mixture, I observed the product peak as well as peaks from many partially reduced products. Increasing the reaction time and the amount of $LiAlH_4$ did not help. Reduction with BH_3-THF afforded less partially reduced products in the mass spectrometry.

3.2 Experimental Procedures

3.2.1 Materials

Commercially available chemicals were of reagent-grade purity or better and were used as received unless otherwise noted. Triethylamine was dried over calcium hydride and distilled under an argon atmosphere. Water was purified using a PURELAB Ultra Mk2 purification system. Flash chromatography was performed using silica gel 60, 230–400 mesh. Analytical thin-layer chromatography (TLC) was carried out on TLC plates precoated with silica gel 60 F_{254} (250 μm layer thickness). TLC plates visualization was accomplished with a UV lamp or by charring with potassium permanganate stain (1.5 g $KMnO_4$, 10 g K_2CO_3, 2.5 mL 5% w/v aqueous NaOH, and 150 mL H_2O).

3.2.2 Characterization

^{1}H- and ^{13}C-NMR spectra were recorded at ambient temperature on a Varian Unity 400 spectrometer (400 MHz for ^{1}H and 101 MHz for ^{13}C). Chemical shifts were referenced to solvent residual signals ($CDCl_3$: ^{1}H δ 7.26 ppm, ^{13}C δ 77.16; D_2O: ^{1}H δ 4.79, ^{13}C was referenced to 5% DMSO-d_6 added δ 39.52;). ^{1}H-NMR data are assumed to be first order, and the apparent multiplicities are reported as follows: ‘‘s’’ = singlet,

‘‘d’’ = doublet, “t” = triplet, “m” = multiplet, and ‘‘br’’ = broad. High resolution electrospray ionization mass spectra (HRESIMS) were recorded on a Waters LCT Premiere Xe TOF mass spectrometer. Low resolution mass spectra (MS) of known compounds were recorded on a Shimadzu LCMS-2010EV mass spectrometer to confirm identity.

3.2.3 Synthesis

1,4,7,10,13,16,21,24-Octaazabicyclo[8.8.8]hexacosane (3.7): Compound **3.7** was prepared by following literature procedures.[31,32] A solution of tris(2-aminoethyl)amine (1.95 g, 13.3 mmol, 1 equiv) and triethylamine (5.0 mL) in *i*-PrOH (90 mL) was cooled to –78 ℃ , and to the resulting solution was added a solution of glyoxal (40% in H_2O; 2.91 g, 20.0 mmol, 1.5 equiv) in *i*-PrOH (50 mL) dropwise while stirring. After the addition, the reaction mixture was warmed to ambient temperature. Solvent was removed under reduced pressure to produce a yellowish brown solid that was extracted with $CHCl_3$ (100 mL). Solvent was removed under reduced pressure to produce a yellow solid that was dissolved in CH_3OH (80 mL). To the resulting solution was added $NaBH_4$ (2.58 g, 68.2 mmol). The resulting mixture was stirred at ambient temperature under Ar for 4 h. Solvent was removed under reduced pressure to produce a white powder that was recrystallized twice from water to yield 0.702 g (28%) of **3.7** as white solid. ^{1}H- and ^{13}C-NMR spectra were assigned by comparison with the literature.[32] ^{1}H NMR (400 MHz, D_2O) δ 2.76 (s, 12H), 2.69 (brs, 12H), 2.51 (brs, 12H); ^{13}C NMR (101 MHz, D_2O–DMSO-d_6) δ 53.7, 50.4, 47.7; $[M + H]^+$ calcd for $C_{18}H_{43}N_8$, 371.4; found, 371.4.

Tris(2-nitrophenyl)amine (3.9): Compound **3.9** was prepared by following a literature procedure.[33] A mixture of 2-nitroaniline (1.99 g, 14.4 mmol, 1 equiv), 2-fluoro-nitrobenzene (8.16 g, 57.8 mmol, 4 equiv), and K_2CO_3 (12.2 g, 88.3 mmol, 6 equiv) in dimethyl sulfoxide (DMSO) (12 mL) was stirred under Ar at 145 ℃ for 84 h. The reaction mixture was cooled to ambient temperature and diluted with water (200 mL). The resulting mixture was sonicated for 10 min and filtered using a medium frit to produce a brown solid. The brown solid was dissolved in CH_3OH (200 mL), and the resulting mixture was heated at reflux for 20 min. The mixture was filtered while hot, and the resulting solid was washed with CH_3OH (3 × 20 mL, ambient temperature) and dried under vacuum to produce 3.61 g (66%) of **3.9** as yellow solid. ^{1}H- and ^{13}C-NMR spectra were assigned by comparison with the literature.[33] ^{1}H NMR (400 MHz, $CDCl_3$) δ 7.83 (d, *J* = 8.2, 3H), 7.53 (t, *J* = 7.8, 3H), 7.30 (t, *J* = 7.8, 3H), 7.21 (d, *J* = 8.2, 3H); ^{13}C NMR (101 MHz, $CDCl_3$) δ 144.0, 138.9, 134.0, 128.5, 126.4, 126.2; $[M + Na]^+$ calcd for $C_{18}H_{12}N_4O_6Na$, 403.1; found, 403.1.

Tris(2-aminophenyl)amine (3.10): Compound **3.10** was prepared by following a literature procedure.[33] To a solution of **3.9** (1.47 g, 3.87 mmol) in THF (100 mL) under argon was quickly added Pd/C (10%, 0.236 g, 0.222 mmol). The resulting reaction mixture was degassed under vacuum and back filled with H_2 using a H_2 balloon. The reaction mixture was stirred at ambient temperature for 48 h, and then filtered through a pad of celite on a medium frit. The filtrate was concentrated under reduced pressure to produce an off-white solid. This solid was washed with diethyl ether (3 × 15 mL) and dried under vacuum to yield 0.842 g (75%) of **3.10** as an

off-white solid. ^{1}H- and ^{13}C-NMR spectra were assigned by comparison with the literature.[33] ^{1}H NMR (400 MHz, $CDCl_3$) δ 6.99 (t, *J* = 7.6 Hz, 3H), 6.91 (d, *J* = 7.7 Hz, 3H), 6.77–6.63 (m, 6H), 3.47 (brs, 6H); ^{13}C NMR (101 MHz, $CDCl_3$) δ 141.4, 132.5, 125.8, 125.7, 119.0, 116.6; $[M + H]^+$ calcd for $C_{18}H_{19}N_4$, 291.2; found, 291.2.

2,3,8,9,11,12,17,18,19,20,25,26-hexabenzo-1,4,7,10,13,16,21,24-Octaazabicyclo[8.8.8]hexacosane-5,614,15,22,23-hexaone (3.11): Compound **3.11** was synthesized using similar methods to those described in the literature.[34] A solution of compound **3.10** (0.810 g, 2.79 mmol, 1 equiv) in THF (80 mL) was added dropwise to oxalyl chloride (12.0 g, 94.5 mmol) at 0 ℃ under Ar. After the addition, the reaction mixture was stirred at ambient temperature for 12 h. The excess oxalyl chloride was removed under reduced pressure to produce a yellow solid that was dissolved in THF (100 mL). The resulting solution and a solution of triethylamine (1.67 g, 16.5 mmol) and compound **3.10** (0.732 g, 2.52 mmol, 0.9 equiv) in THF (100 mL) were added simultaneously to THF (200 mL) at 0 ℃. After the additions, the resulting turbid mixture was stirred at ambient temperature for 24 h. The resulting solid was removed by filtration, and solvents were removed under reduced pressure to produce brown solid that was purified using silica gel chromatography (CH_2Cl_2) to yield 0.0900 g (4.8%) of **3.11** as white solid. HRESIMS (*m/z*): $[M + Na]^+$ calcd for $C_{42}H_{30}N_8O_6Na$, 765.2186; found, 765.2168; TLC: R_f = 0.08 (CH_2Cl_2).

3.3 ^{1}H- and ^{13}C-NMR Spectra of compounds 3.7, 3.9, and 3.10.

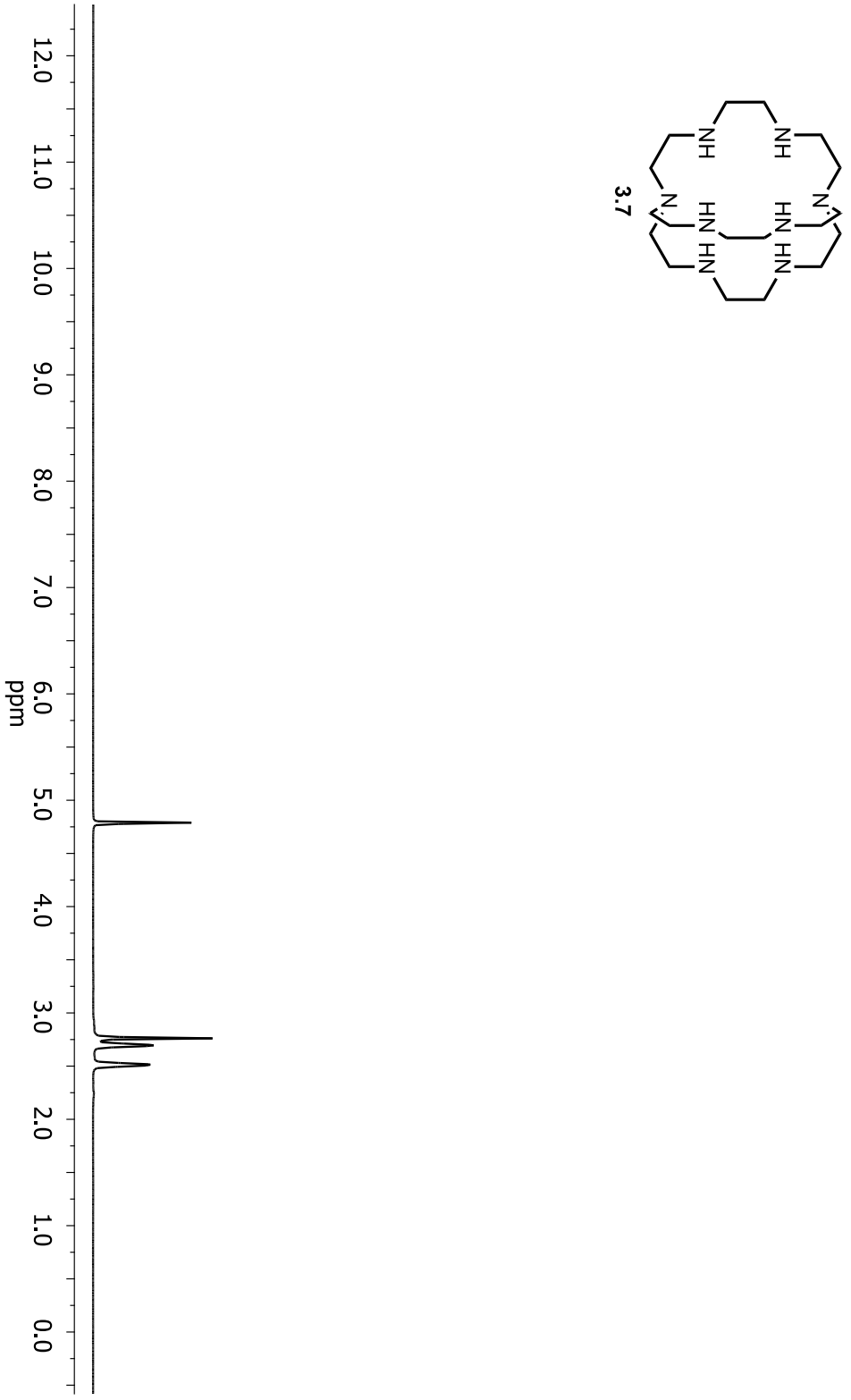
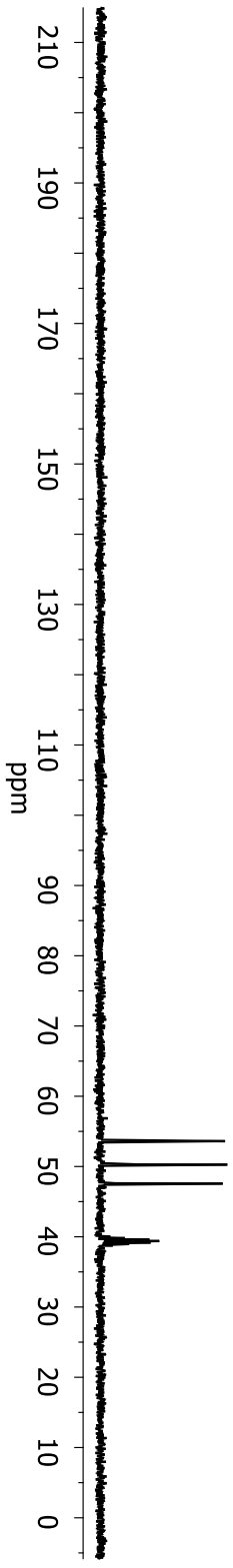


Figure 3.3 ^{1}H-NMR spectrum of **3.7**.



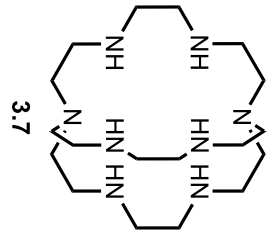


Figure 3.4 ^{13}C-NMR spectrum of **3.7**.

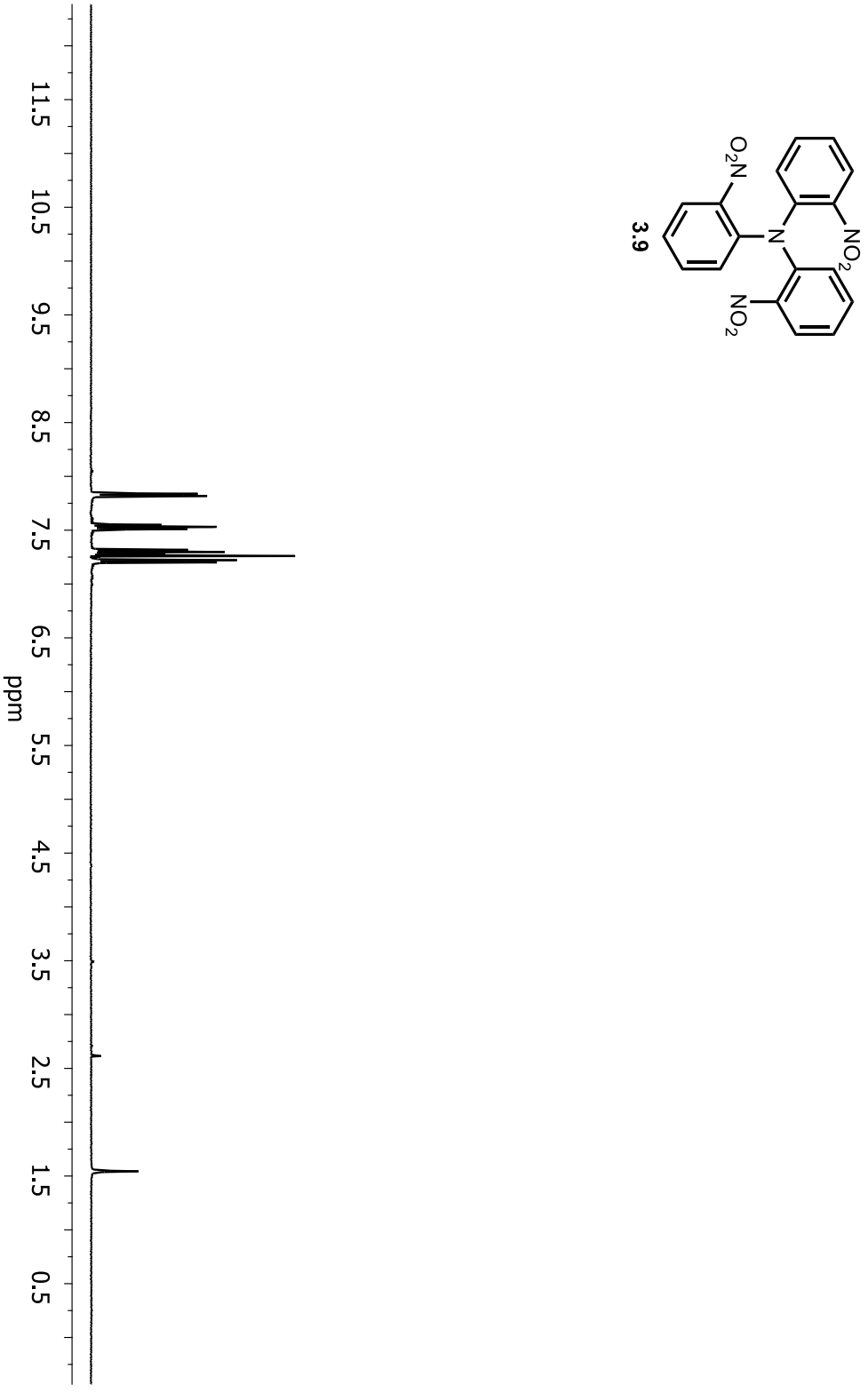
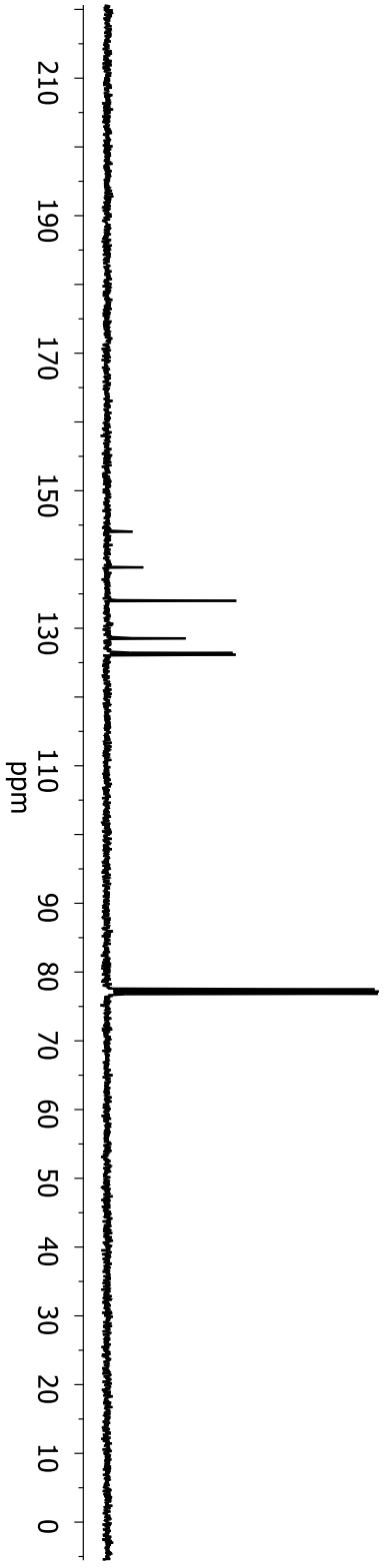
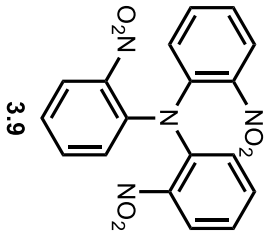


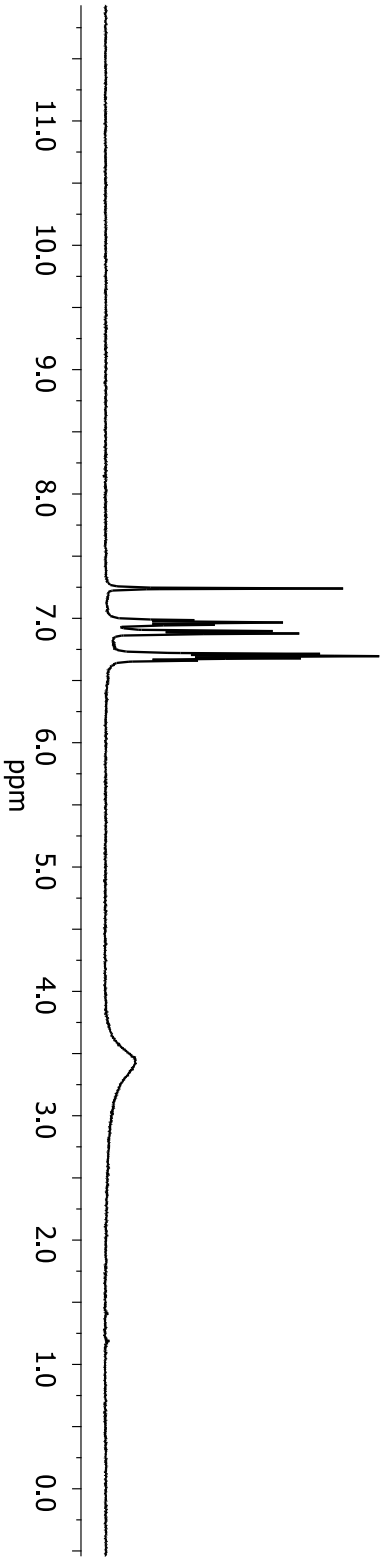
Figure 3.5 ^{1}H-NMR spectrum of **3.9**.

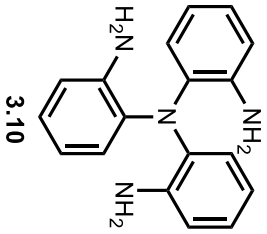




3.9

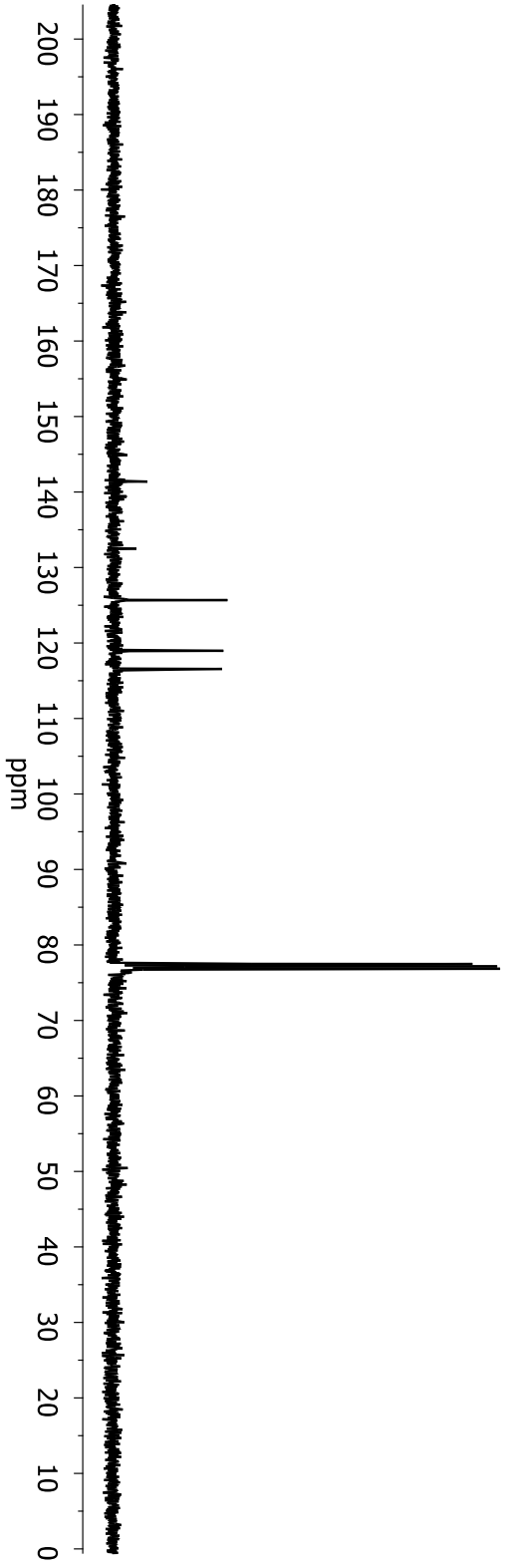
Figure 3.6 ^{13}C-NMR spectrum of **3.9**.

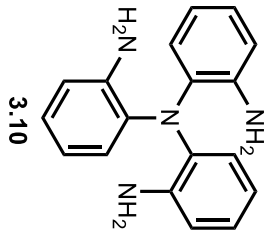




3.10

Figure 3.7 ^{1}H-NMR spectrum of **3.10**.





3.10

Figure 3.8 ^{13}C-NMR spectrum of **3.10**.

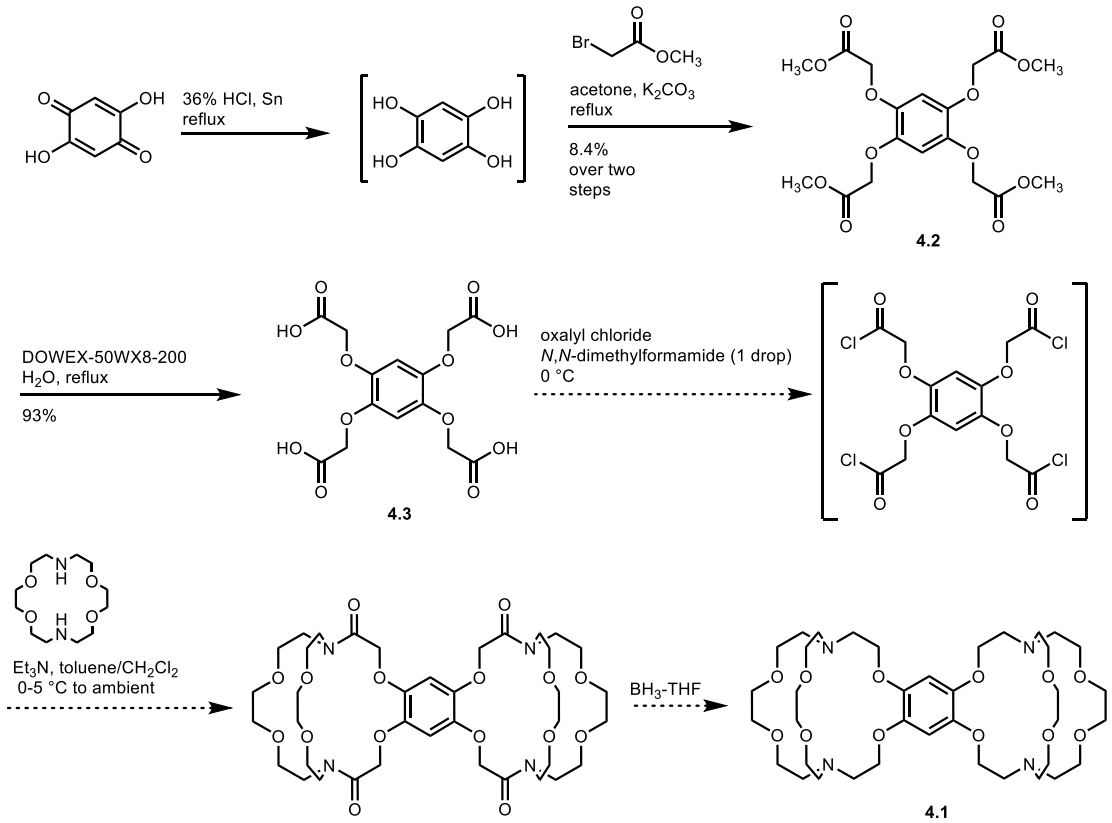
Chapter 4: Synthesis of Tetraoxolene-Bridged Cryptand Ligands for Magnetic Studies of Divalent Lanthanides

4.1 Introduction

Divalent europium (Eu^{2+}) has a large magnetic moment that is partially due to its 7 half-filled 4f orbitals. The interesting magnetic properties of Eu^{2+} make it a suitable candidate for fabricating novel magnetic materials. Among the interesting magnetic materials there is a class of compounds that were discovered twenty years ago known as single molecule magnets (SMMs).[35] These compounds possess energy barriers that are large enough to allow retention of magnetization upon removal from an external magnetic field. Early studies on SMMs were dominated by 3d transition metals, especially Mn^{3+}.[36] However, the development of SMMs was hindered by the inability to increase total spin *S* and axial anisotropy *D* simultaneously.[37] Recently, there has been an increasing agreement that single ion anisotropy is crucial to obtain large energy barrier SMMs.[38] Thus, considerable attention has been paid to lanthanides and actinides whose single-ion anisotropies are unrivalled in the periodic table.[37] A third way to further maximize the energy barrier besides increasing *S* and *D* is to increase exchange coupling by incorporating a radical bridge between multiple metals in the complex. Long, Evans, and coworkers have synthesized a series of N_2^{3-}, bipyrimidyl, and 2,3,5,6-tetra(2-pyridyl)pyrazine) radical-bridged di-lanthanide complexes.[39] These complexes show single molecule magnet properties. Based on these ideas, we designed ligand **4.1** (**Scheme 4.1**), in which two cryptands are bridged by tetraoxolene, which is a multi-electron redox-active ligand. The cryptand can form complexes with

divalent lanthanides such as Eu^{2+}, Sm^{2+}, and Yb^{2+}, which are less studied compared to trivalent lanthanides. The proposed synthetic procedures for ligand 4.1 are shown in **Scheme 4.1**. Dihydroxybenzoquinone was reduced using tin in concentrated hydrochloric acid,[40] and reacted with methyl bromoacetate to give ester **4.2**. It was hydrolyzed using DOWEX to give the corresponding acid **4.3**. Reaction of this acid with oxalyl chloride afforded the acid chloride which was further reacted with aza-crown ether to give the corresponding amide. In the mass spectrometry I observed the peak of the amide, but I was not able to purify it using silica gel chromatography.

Scheme 4.1 Proposed synthetic procedures for ligand **4.1**



4.2 Experimental Procedures

4.2.1 Materials

Commercially available chemicals were of reagent-grade purity or better and were used as received unless otherwise noted. Water was purified using a PURELAB Ultra Mk2 purification system.

4.2.2 Characterization

^{1}H- and ^{13}C-NMR spectra were recorded at ambient temperature on a Varian Unity 400 spectrometer (400 MHz for ^{1}H and 101 MHz for ^{13}C). Chemical shifts were referenced to solvent residual signals ($CDCl_3$: ^{1}H δ 7.26 ppm, ^{13}C δ 77.16; DMSO-d_6: ^{1}H δ 2.50, ^{13}C δ 39.52). ^{1}H-NMR data are assumed to be first order, and the apparent multiplicities are reported as follows: ‘‘s’’ = singlet and ‘‘br’’ = broad. Italicized elements are those that are responsible for the shifts. High resolution electrospray ionization mass spectra (HRESIMS) were recorded on a Waters LCT Premiere Xe TOF mass spectrometer. Low resolution mass spectra (MS) of known compounds were recorded on a Shimadzu LCMS-2010EV mass spectrometer.

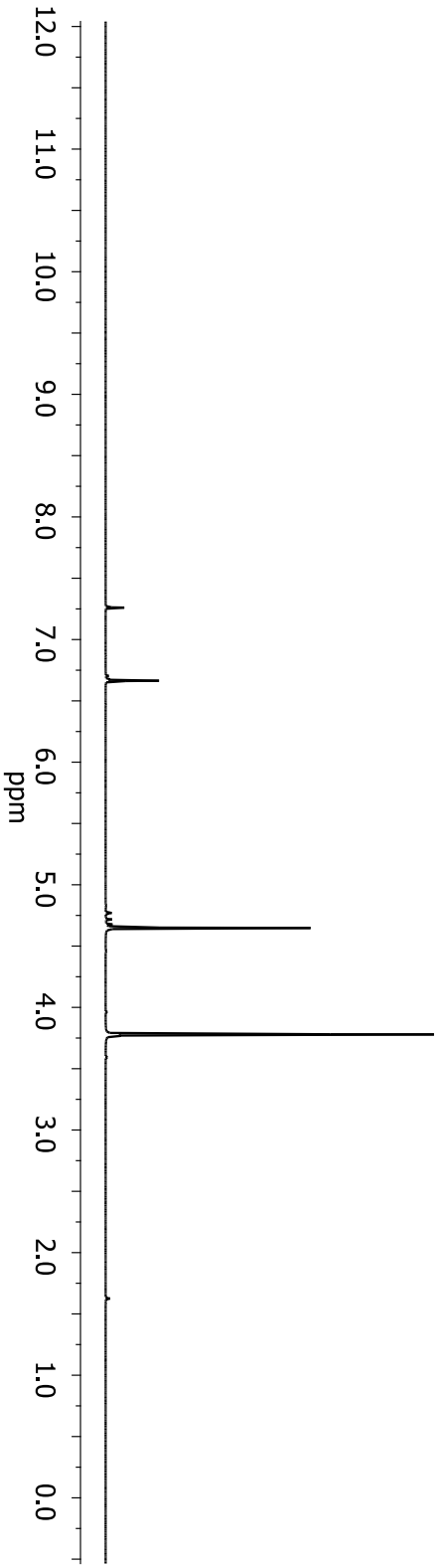
4.2.3 Synthesis

Tetramethyl 2,2',2'',2'''-(benzene-1,2,4,5-tetrayltetrakis(oxy))tetraacetate (4.2): To a stirred mixture of 2,5-dihydroxy-1,4-benzoquinone (1.98 g, 14.1 mmol, 1 equiv) in HCl (36%, aqueous, 50 mL) was slowly added granular tin metal (2.12 g, 17.8 mmol, 1.3 equiv).[40] The reaction mixture was heated at reflux for 1 h then filtered while hot. The filtrate was cooled to 0 ℃ to produce an off-white solid that was crystallized from tetrahydrofuran to yield 0.776 g of a white solid. The solid was dissolved in acetone (20 mL), and added dropwise into a stirred mixture of K_2CO_3 (7.80 g, 56.4 mmol) and methyl bromoacetate (8.56 g, 56.0 mmol) in acetone (130

mL). The reaction mixture was stirred at reflux under Ar for 24 h. After cooling to ambient temperature, solids were removed by filtration, and the solvent was removed under reduced pressure to produce an orange oil. The oil was dissolved in ethyl acetate (50 mL), washed with water (3 × 50 mL) and dried over anhydrous Na_2SO_4. The solvent was removed under reduced pressure to produce a yellow solid that was recrystallized twice from ethanol to yield 0.508 g (8.4%) of **4.2** as white solid. ^{1}H- and ^{13}C-NMR spectra were assigned using DEPT, GCOSY, GHMQC, and GHMBC experiments. ^{1}H NMR (400 MHz, $CDCl_3$) δ 6.66 (s, C*H*, 2H), 4.65 (s, CH_2, 8H), 3.78 (s, CH_3, 12H); ^{13}C NMR (101 MHz, $CDCl_3$) δ 169.5, 143.6, 107.8 (*C*H), 67.8 (*C*H_2), 52.3 (*C*H_3); HRESIMS (*m/z*): $[M + Na]^+$ calcd for $C_{18}H_{22}O_{12}Na$, 453.1009; found, 453.1009.

2,2',2'',2'''-(Benzene-1,2,4,5-tetrayltetrakis(oxy))tetraacetic acid (4.3): Dowex 50WX8 (hydrogen form, 200–400 mesh, 0.22 g) was added to a mixture of **4.2** (1.05 g, 2.44 mmol) in H_2O (100 mL). The reaction mixture was heated at reflux for 24 h then filtered while hot. The filtrate was cooled to ambient temperature to yield 0.847 g (93%) of **4.3** as white solid. ^{1}H- and ^{13}C-NMR spectra were assigned by comparison with published assignments.[41] ^{1}H NMR (400 MHz, DMSO-d_6) δ 12.90 (brs, 4H), 6.70 (s, 2H), 4.62 (s, 8H); ^{13}C NMR (101 MHz, DMSO-d_6) δ 170.4, 142.0, 105.3, 66.4; MS (*m/z*): $[M + Na]^+$ calcd for $C_{14}H_{14}O_{12}Na$, 397.0; found, 397.0 .

4.3 ^{1}H- and ^{13}C-NMR Spectra of compounds 4.2 and 4.3.



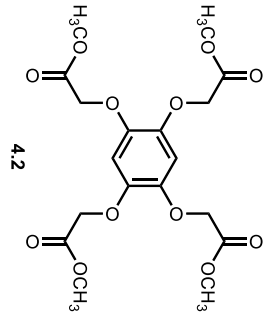
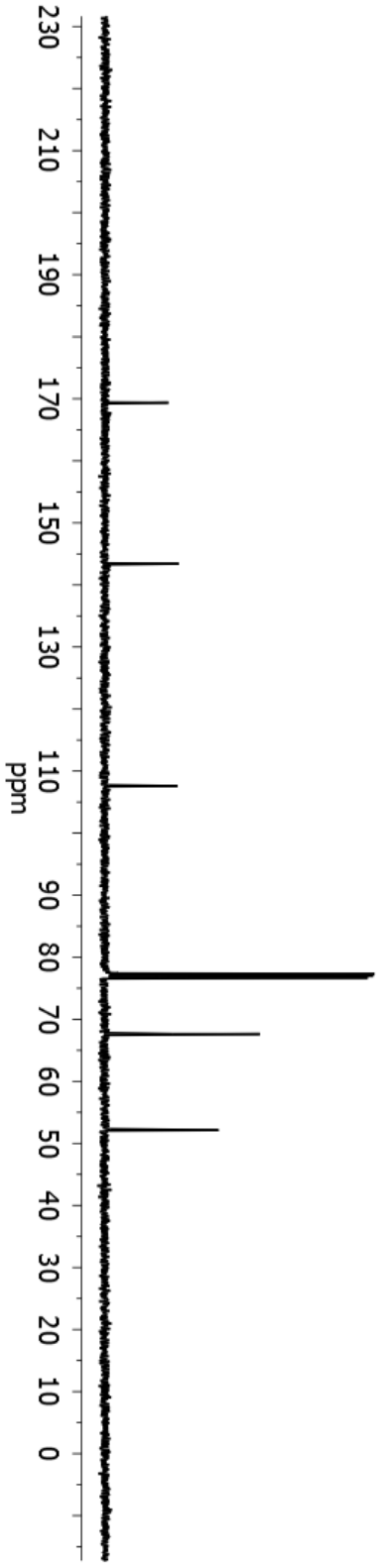
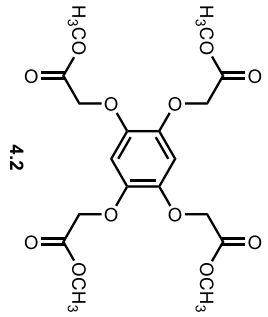


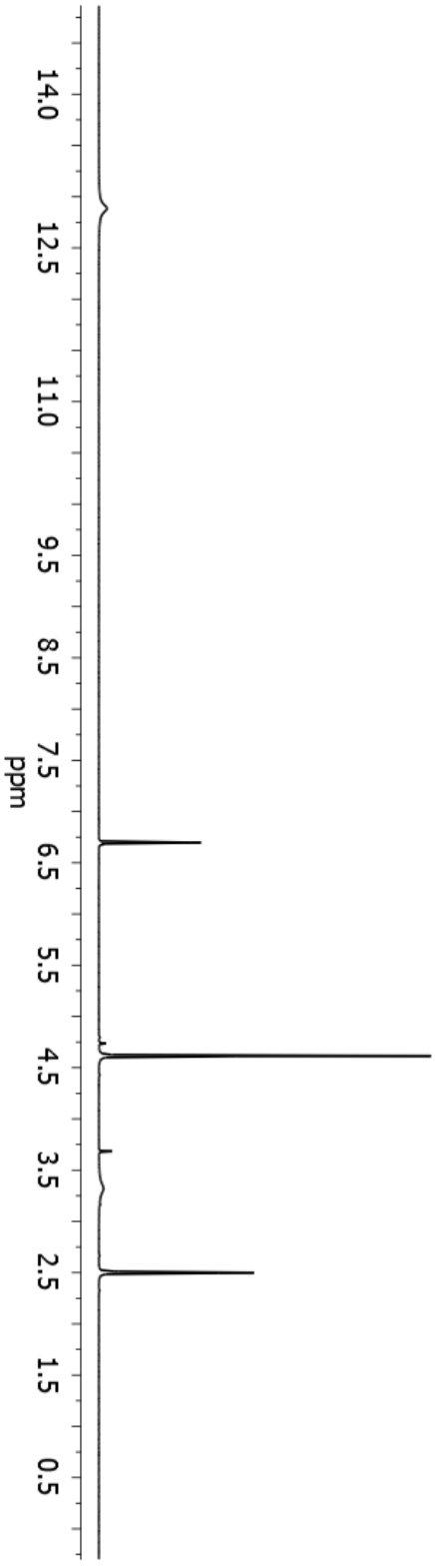
Figure 4.1 ^{1}H-NMR spectrum of **4.2**.





4.2

Figure 4.2 ^{13}C-NMR spectrum of **4.2**.



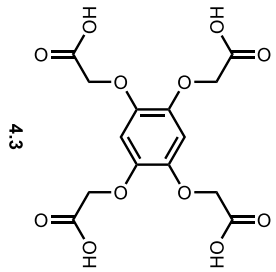
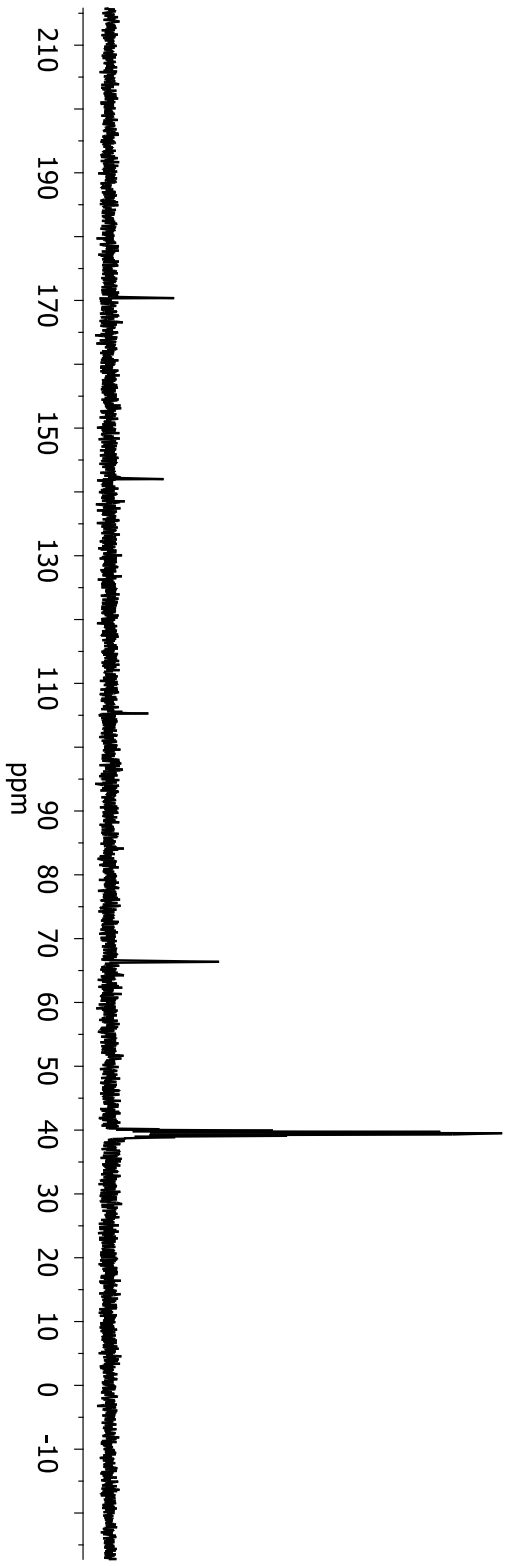
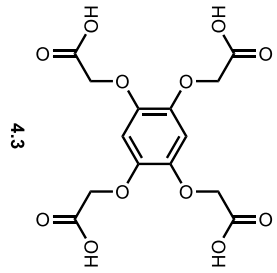


Figure 4.3 [1]H-NMR spectrum of **4.3**.





4.3

Figure 4.4 ^{13}C-NMR spectrum of **4.3**.

Chapter 5: Summary and Future Outlook

5.1 Summary and Future Outlook

Coordination chemistry is one of the most important fields in modern inorganic chemistry. Ligand synthesis using organic techniques plays an important role in coordination chemistry. This thesis describes my efforts to synthesize different cryptands for Eu^{2+}-containing complexes. Subsequent metalation with Eu^{2+} will produce Eu^{2+}-containing cryptates. Cyclic voltammetry experiment can be performed to study the oxidative stability of these complexes.

As with the ligand for MRI application, 5,6-(4-(3-(3,5-dicarboxyphenyl)thioureido)benzo)-4,7,13,16,21,24-hexaoxa-1,10-diaz abicyclo[8.8.8]hexacosane, a series of molecules with two carboxylic groups can be attached to cryptand unit through thiourea linkage. For example, the positions of two carboxylic groups can be changed in phenyl ring; amino acids such as aspartic acid and glutamic acid can also be used.

The Allen group has studied Eu^{2+} complexes of ligand 1,4,7,10,13,16,21,24-octaazabicyclo[8.8.8]hexacosane (aza222). It was found that this complex has bright yellow luminescence.[42] Based on this result, I did a literature search to find ways to incorporate the aza222 ligand into polymers. Jackson and coworkers recently reported methods to synthesize aza222-based polymers.[43] Thus, future work based on this ligand could include synthesizing Eu^{2+}-containing aza222-based polymers, and measuring their luminescence properties.

In the process of synthesizing phenyl derivatives of aza222, the synthetic methods need to be modified to increase the yield to produce one of the intermediates 2,3,8,9,11,12,17,18,19,20,25,26-hexabenzo-1,4,7,10,13,16,21,24-octaazabicyclo[8.8.8]hexacosane-5,614,15,22,23-hexaone. Also, the low solubility of the intermediate in common organic solvents prevents further characterizations except high resolution electrospray ionization mass spectra. One possible solution is to grow single crystals by slow vaporization of its concentrated CH_2Cl_2 or THF solution.

Finally, efforts are needed to synthesize the tetraoxolene bridged dicryptand ligand. Lower reaction yields are expected compared to the synthesis of ligand that has only one cryptand. In addition, functionalized tetraoxolene such as hydrochloranilic acid can also be used as bridging ligand.

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ABSTRACT

SYNTHESIS OF CRYPTANDS FOR Eu^{2+}-CONTAING COMPLEXES

by

CHENGCHENG WANG

May 2015

Advisor: Dr. Matthew J. Allen

Major: Chemistry

Degree: Master of Science

Eu^{2+}-containing complexes have considerable applications in synthetic chemistry, medical diagnosis, and materials science. However, Eu^{2+} is easily oxidized in solution when exposed to air. Allen and coworkers have demonstrated that Eu^{2+} can be stabilized by functionalized cryptands. Based on this idea, I focused my research on synthesizing cryptands. The progress towards synthesizing several modified cryptands is described in the thesis. The Eu^{2+}-containing complexes of these cryptates have potential applications as magnetic resonance imaging contrast agents, luminescent materials, and magnetic materials.

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