Investigation of Disassembling Polymers and Molecular Dynamics Simulations in Molecular Gelation, and Implementation of a Class-Project Centered on Editing Wikipedia

by

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Table of Contents

List of Figures

Figure 5-3. Polyfluorene is an example of a stub article that the students expanded. At the top of the page is a box that reads "This article needs attention from an expert on the

List of Tables

List of Appendices

Chapter 1

Introduction

A. Part 1: Molecular Gels

Gels are materials that trap liquid within a solid network, and the liquid is the major component of the mass of these materials. Gels are categorized based on their solid components into two groups: polymer gels and molecular gels. Polymer gels (polyamides, polyacrylates, or poly(vinyl alcohols)) are most often found in commercial applications like personal care products and food.[1] These gels are polymers that are chemically cross-linked though covalent bonds, and eventually the chains become an interconnected network that entraps the solvent.[2, 3] Molecular gels are different from polymer gels, in that they self-assemble through non-covalent interactions to form large fibers. Molecular gels have been studied for 160 years, and are interesting due to the number of exciting applications. For example, these materials are used in environmental remediation such as the separation of water and oil,[4] the regeneration of neurons,[5] in vitro enzyme sensing,[6] and as reversible liquid crystalline materials.[7]

The biggest limitation in the field of molecular gels is that the exact mechanism of gel formation is largely unknown, which leads to difficulty in developing application-specific gelators or pre-determining appropriate gel-inducing solvents. The formation of fibers rather than all other solid forms is hypothesized to be due to strong unidirectional

1

(1D) aggregation[8] directed by non-covalent interactions, such as π–stacking, hydrogen bonding, metal coordination, and van der Waal interactions (Figure 1-1).[9] Many research groups, including ours, have focused on identifying molecules that have these strong unidirectional intermolecular interactions to design new gelators.[10, 15] These investigations attempt to elucidate the impact of molecular structure on 1D aggregation and gel properties to better understand the mechanism of gel formation, only to find that modifications to a working gelator scaffold are likely to destroy gelation ability rather than lead to a new gelator[11, 12, 13] The opportunity to design gelators, rather than the time-consuming process of screening for a new gelators, can lead to a number of new and exciting applications such as portable sensors explored later in this thesis.
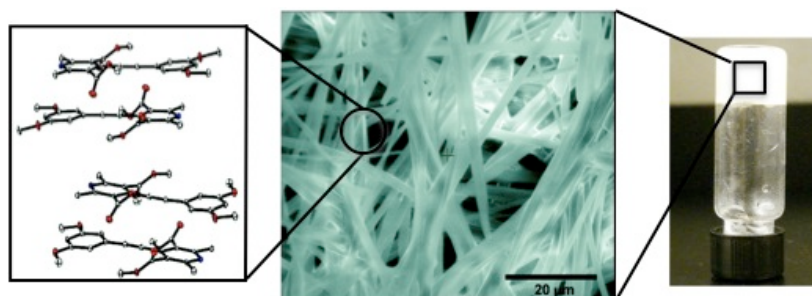
Figure 1-1. Crystal structure of pyridine-based gelator developed in the McNeil lab, showcasing the π–stacking direction, which is coincident with the direction of fiber growth (as shown by polarized Raman spectroscopy).[14]

Gel discovery has proven to be largely serendipitous with many factors that affect a molecule's gelation ability, and few reliable generalizations available to base predictions. Many research groups have worked on gaining a better understanding of the process of gel formation through extensive structure-property relationships.[15] The most well studied gel scaffolds are peptide-based gelators wherein the gelation ability is investigated through a variety of modifications such as appending aromatic moieties and

altering the number and order of amino acid subunits.[16, 17] In general, modifications that increase π-stacking interactions (through appending pyrene, fluorene, and naphthalene moieties) and increase the hydrophobicity (through appending long alkyl chains) have increased the likelihood of these scaffolds form gels.[13] (Figure 1-2).
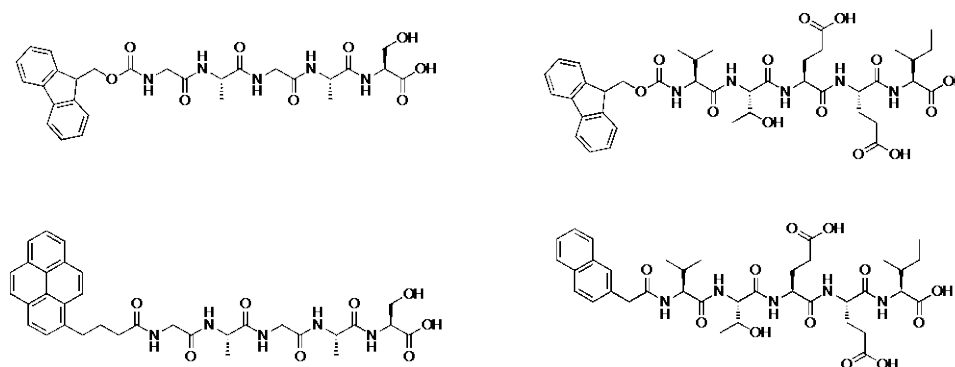
Figure 1-2. Examples of pentapeptide gelators modified to include pyrene, fluorene, or naphthalene moieties.

These modifications to the gelator structure, are not always successful, in some cases it can also disrupt gelation and increase the cgc, indicating that there is a delicate balance of intermolecular interactions for gel formation. However in each of these cases the conclusions are specific to peptide-based systems and are difficult to extend to the design of new types of gelator scaffolds.

In this work, we attempted to elucidate what structural features are important for aryl trihydroxyborate salt gelators (Figure 1-3). Prior to this work, there were no examples of aryl trihydroxyborate salt gelators.
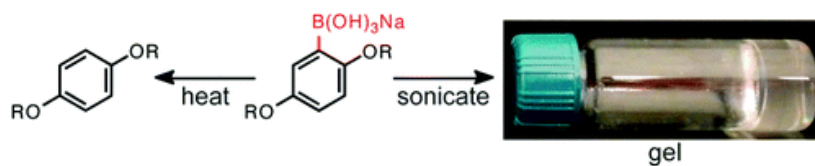
Figure 1-3. Aryl trihydroxyborate salts (center) form gels when sonicated, but undergo protodeboronation when heated.

3

We discovered that aryl trihydroxyborate salts were gelators in aromatic solvents when studying these scaffolds as monomers in metal-catalyzed π−conjugated polymerizations. We varied the alkoxy chain length and investigated the effect alkyl chain-length had on the cgc. We also added a bromine substituent in the position *para-* to the trihydroxyborate substituent to see its affect on gelation ability. These modifications enabled us discover an unusual dependence of gelation on alkoxy chain length. Although chain-length dependent cgcs have previously been observed, they typically are 1.) increasing chain lengths correlate with decreasing cgc[18] or 2.) odd-even effects are observed.[19] Therefore this finding with aryl trihydroxyborate salt gelators highlights that there are a number of unknown interactions that drive gel formation.

This example and previously mentioned peptide-gelators attempt to rationalize observed gel formation to design new gelators, require an initial successful gelator and the characteristics that are attributed to gel formation are potentially specific to the scaffold being studied. Molecular modeling techniques have been applied to gelators to elucidate more universal driving forces for gel formation. There have been a few examples of molecular modeling simulations done by Feringa and coworkers to study the 1D aggregates that may correspond to gel formation.[20] However, these calculations are done in the gas phase, and do not account for the interactions with solvent during the gelation process. Solvent interactions may also play a key role in gel formation as there are very few correlations as to why some solvents induce gelation while other related solvents can inhibit gelation.[21] Through studies in our lab to correlate gelation ability with molecular structure, we were able to correlate the strength of intermolecular

4

interactions in a number of solvents to gelation ability.[22] By comparing pyridine and dipeptide gelators and nongelators, these investigations found that although there was no correlation to room temperature solubilities, gelators were found to have higher dissolution enthalpies and entropies than nongelators in two different solvent systems. If general, this parameter can help distinguish gelators from nongelators and has potential for predicting if a molecular structure will form gels. Therefore, this thesis, in part, will address efforts towards exploring the use of molecular mechanics simulations to model dissolution enthalpies of gelators and nongelators. Along with modeling efforts by Feringa, other research groups in the gel literature have focused on the process of fiber formation.[5] A recent example by Stupp and coworkers modeled the self-assembly of peptide amphiphiles into fibers where the radius is the length of the peptide amphiphiles. Unfortunately, not all gelators aggregate into such thin fibers, and therefore these interactions for fiber formation are difficult to extend to other systems. We focused on developing models that simulate the molecular solid-solid and solute-solvent interactions to calculate the dissolution enthalpies. Several models were developed, including modeling solid-state interactions as a liquid-like state, unfortunately this did not reproduce the experimental observations, suggesting that this model underestimated the solid-state interactions that are important in gelation.

One specific application for gels that is being explored by both our research group as well as others[23] is their use in the detection of target analytes because of the easily distinguishable solution-to-gel phase transition (Figure 1-4).

Figure 1-4. Easily distinguishable solution-to-gel phase transition for chemical sensing.

Inducing this evident phase transition (liquid-to-gel) when an analyte of interest is added can be a portable, inexpensive, stimuli-responsive system for on-site detection of explosives, toxic metals, and to diagnose disease.[14, 24] The key is the design a soluble pre-gelator that can undergo a chemical change in the presence of an analyte, and the resulting compound then self-assembles into a gel. Most examples of analyte-triggered gel-based sensors are plagued by low sensitivity because they require one analyte molecule for each precursor to be transformed into a gelator (Figure 1-5).[9] However, the exceptions to this limitation are systems that use enzymes as the target analyte. In these systems, gelator molecules are generated when enzymes catalytically cleave appended solubilizing units on known gelators thereby inducing gel formation.[25] The inherent selectivity of enzymes make these systems valuable for biomedical applications.[26] Enzyme-triggered systems can obtain high sensitivity through multiple conversions once activated, thereby increasing the gelator concentration. For example, once an enzyme is activated it can repetitively initiate a phosphorylation or a hydrolysis reaction to release gelators.[6b-c,27] However, there are several limitations to these systems; enzymes are thermally and chemically unstable and we anticipate developing a system to detect a range of analytes that may not have a complementary enzymatic activity.

Figure 1-5. One analyte molecule to transform one precursor into a gelator.

An alternative approach to addressing the low sensitivity of analyte-triggered gelation is to take advantage of a disassembling polymer to generate a large number of gelators relative to the analyte signal. In this approach, the analyte would release a trigger that end-caps the polymer and initiate the spontaneous disassembly of the polymer backbone into its individual units that then go on to form a gel (Figure 1-6). An analyte-triggered disassembling polymer has not yet been illustrated for a gel-based sensor. These depolymerization/amplification systems have an additional advantage in that the trigger can be easily exchanged to develop a sensor array with minimal modification to the system. Poly(carbamates)[28] and poly(phthalaldehydes),[29] two common disassembling polymer backbones were explored and modified to form gelator that had polymerizable functional groups. For example, to the carbamate monomeric units, we appended amino acid substituents to increase hydrogen-bonding interactions and promote gelation. Several attempts at synthesizing monomers with gelation abilities are described. Overall, these efforts illustrate the challenges of modifying a nongelling scaffold into a gelator.
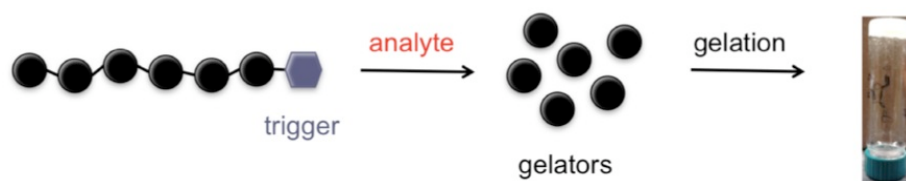
Figure 1-6. Depolymerization initiated by the release of an analyte-sensitive trigger and subsequent gelation of the monomeric units.

B.Part 2: Teaching with Wikipedia

Traditional lecture is the primary resource for instructors to convey information to students. However due to time constraints, instructors often cannot go in depth into topics, and instead choose to provide students with a breath of knowledge during lecture. Therefore, homework assignments are given to support topics presented in lectures, provide the opportunity for students to explore a topic more in depth, and enable students to gain skills that cannot be taught through lecture. A common assignment is for students to write a literature review on a topic presented in class.[30] Through writing assignments, students are required to not only gather relevant information, but need to also reconstruct and revise the information to fit it into their own understanding, leading to learning and deep conceptual understanding.[31]

Specifically, we were interested in taking advantage of Wikipedia's broad audience and ease of contributing to enable students to explore advanced concepts in chemistry and learn how to communicate science to a diverse audience. The primary objective was for students to learn advanced topics in chemistry, and we further hypothesized that working collaboratively and Wikipedia's prominent use as a resource would motivate their efforts to learn and explain advanced topics in chemistry. Therefore we designed a graduate-level project centered on editing Wikipedia.

Wikipedia, the online encyclopedia, is a highly visible and open platform on the Internet to communicate information to both general and technical audiences. English

language Wikipedia alone has 3 million articles and just over 17 billion page views a month.[32] The exponential growth of the online encyclopedia is attributed to Wikipedia capability for anyone to make edits and contribute. However, its ease of editing not only enables legitimate edits, but also makes it prone to vandalism, biased contributions, and questionable accuracy. Despite these natural pitfalls of an open collaborative network, Wikipedia is still reasonably accurate[33] in comparison to other encyclopedias, and continues to be a starting point for information,[34] especially for popular topics that appear in the news.

When we started this project, there were only a handful of known projects incorporating Wikipedia editing in the classroom, and even fewer science courses.[35] When students edit a Wikipedia entry as oppose to writing a traditional literature review, there are additional challenges as Wikipedia has its own markup language and due to an underlying community of seasoned editors, the potential for students' work to be edited. The project's potential for students to learn themselves, while increasing the public understanding, has encouraged other instructors to implement the project. To help other instructors carry out the project in their own courses with minimal editing instruction, we developed tutorials and a manual on editing, and made available the project designs. We have implemented this project over five semesters and each semester we have tried to improve the project to maximize the learning that the students gained through the project. Through informal open-response surveys and retrospective panel surveys, the students' responses indicated that teaching with Wikipedia is an effective method for students to explore advanced topics and learn how to communicate science to a diverse audience. We have also modified the project for undergraduate courses in chemistry.

9

As more courses incorporate the use of Wikipedia, there will need to be a body of Wikipedia editors willing to go into classrooms and teach students how to edit. In efforts to pass along editing knowledge as students graduate, and potentially develop a centralized location for activities involving Wikipedia editing at the University of Michigan, a student organization centered on editing Wikipedia was developed. Through this internal organization we found that students who learn to edit Wikipedia through the student club have a different editing contribution pattern than the general population, and students who are taught to edit through a class project. This preliminary data prompts further investigation into whether or not a student organization can create an effective situated learning environment thereby being able to guide students and encourage them to remain in a community or activity, such as editing Wikipedia.

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Chapter 2

Aryl Trihydroxyborate Salts: Thermally Unstable Species with Unusual Gelation

Abilities[a]

A. Introduction

Aryl trihydroxyborate salts have recently emerged as convenient reagents for a variety of metal-catalyzed reactions,[1] including Pd-catalyzed Suzuki-Miyaura cross-couplings and Rh-catalyzed conjugate additions. Aryl trihydroxyborate salts were first utilized by Vaultier and co-workers in solid-phase reactions in 2001.[2] More recently, Cammidge and co-workers reported a simple procedure for synthesizing aryl trihydroxyborate salts, and provided examples of their use in solution-phase reactions.[3] Since these early reports, a number of other researchers have used aryl trihydroxyborate salts in a variety of synthetic transformations.[1] Aryl trihydroxyborate salts have also been postulated to be the active, transmetalating species in base-mediated Suzuki-Miyaura cross-couplings using either boronic acids[4,5] or trifluoroborates[6] in the presence of water, although this hypothesis has recently come into question.[7]

Given their synthetic utility, we recently prepared a series of brominated aryl trihydroxyborates (**2a**-**e**, Figure 2-1) and investigated their use as difunctional monomers for preparing π-conjugated polymers. During these studies we discovered that these aryl trihydroxyborate salts are unstable to prolonged heating, and readily undergo protodeboronation. In addition, we observed that these complexes formed gels in aromatic solvents. As such, these compounds join a growing class of organometallic gelators.[8,9,10] Gelation typically occurs when molecules self-assemble to form anisotropic fibers, which entangle and entrap solvent through surface tension and capillary forces.[11,12] Because molecular gels can be stimuli-responsive and have nano- and micron-scale architectures, they are being explored for many different applications, including sensing,[13] remediation,[14] and materials synthesis.[15]
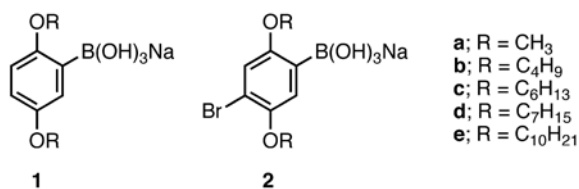
Figure 2-1. Aryl trihydroxyborates synthesized and studied.

B. Results and Discussion

Herein, we report the synthesis, thermal instability and unusual gelation ability of aryl trihydroxyborate salts. Compounds **1a**-**e** and **2a**-**e** were synthesized in quantitative yields from their corresponding boronic acids via treatment with 1 equiv NaOH in benzene. ^{11}B NMR spectroscopic studies revealed the anticipated upfield shift for the

14

tetravalent boron (0-5 ppm) compared to the boronic acids (25-30 ppm), supporting formation of the aryl trihydroxyborate salts.[2] During these studies we observed evidence of decomposition, including changes in the aromatic region of the ^{1}H NMR spectrum and brown discoloration of the NMR sample. We suspected protodeboronation was occurring because it was previously reported for *boronic acids* under base-catalyzed conditions.[16,17] Fields and Doyle first reported on the instability of isolated *aryl trihydroxborate salts* in 1974.[18] They observed an onset of weight-loss for the sodium salt of benzene trihydroxyborate at 170 °C using thermal gravimetric analysis. Consistent with these earlier reports, heating **1c** in the solid-state for 30 min at 200 °C led to quantitative conversion to 1,4-bis(hexyloxy)benzene (Figure 2-2). To determine the decomposition rate in solution, the formation of 1,4-bis(butyloxy)benzene was monitored via HPLC analysis (relative to an internal standard) for samples of **1b** and **2b** heated in benzene. While **2b** was 70% decomposed within 1 h at 60 °C, **1b** was remarkably more stable. However, heating **1b** at an elevated temperature (100 °C) for 1 h lead to a 64% conversion to 1,4-bis(butyloxy)benzene. These results are consistent with Frohn and co-workers, who observed that the rates of base-catalyzed protodeboronation of boronic acids in solution depended on both the number and position of fluorine atoms on the aromatic ring.[16c]
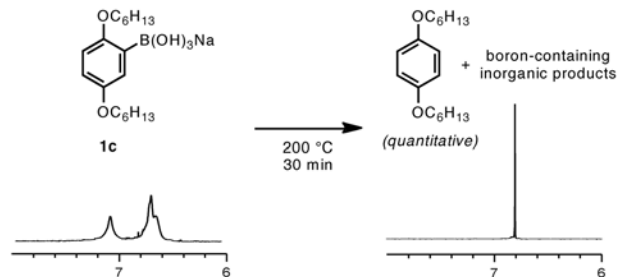
Figure 2-2. ^{1}H NMR spectra of compound **1c** in CD_3OD before (left) and after (right) heating in the solid-state at 200 °C for 30 min.

Compounds **1a**-**e** and **2b**-**d** form gels by heating and cooling samples in benzene. However, this method was not reproducible due to the thermal instability of these materials. To induce gelation without heating, an alternative sonication-based procedure was explored.[19] Indeed, gels were formed by adding solid sodium hydroxide to a vial, followed by a benzene solution of the boronic acid precursor and sonication for 5 min at rt (Figure 2-3). Using this procedure, aryl trihydroxyborate salts **1a**-**e** and **2b**-**d** also form gels in other solvents, including toluene, *p*-cymene, styrene, and cyclohexane. Compounds **2a** and **2e** did not form gels under any conditions examined.

Figure 2-3. Gels of **1c** (12 mg) form in benzene (1 mL) with sonication for 5 min at rt.

As seen in Table 2-1 and Figure 2-4A, the critical gel concentration (cgc), which is the minimum concentration needed to form a stable gel, for **1a**-**e** shows an unusual dependence on alkyl chain length. For example, when the alkyl chain is changed from methyl to hexyl, the cgc drops from 22 to 10 mg/mL. However, the trend does not

16

continue as further increases in chain length (decyl) led to a substantial increase in cgc (44 mg/mL). Chain-length dependent cgcs have previously been observed, however, they typically fall into one of two classes: (1) Increasing chain lengths correlate with decreasing cgcs, which is generally attributed to increased van der Waals interactions and/or hydrophobic interactions.[20] (2) Odd-even effects of chain length are observed.[21] For example, Steed, Clarke and co-workers reported that bis(ureas) with odd-numbered linkers did not form gels whereas molecules with even-numbered linkers did.[21a] These results are generally attributed to differences in packing densities for odd and even-length alkyl chains.[22] Neither of these trends is observed herein. However, Dey and co-workers recently reported a similar trend in cgcs for histidine-based gelators in water, with a C8 chain giving the lowest cgc compared to C6 and C10.[23] They attributed this result to the hydrophilic-lipophilic balance of the amphiphilic gelator. Given that the gels reported herein are formed in benzene, the observed relationship between cgc and chain-length is not easily rationalized. It is interesting to note that the same chain-length dependence is not observed with brominated aryl trihydroxyborate salts **2b-d**, suggesting that the bromine atoms alter the molecular packing in the gel.

Gelator	Chain	cgc (mg/mL)	cgc (mM)	G′/G″ (Pa)
1a	CH_3	22 ± 2	100 ± 10	200/70
1b	C_4H_9	15 ± 1	49 ± 3	300/200
1c	C_6H_{13}	10 ± 2	28 ± 6	4000/1000
1d	C_7H_{15}	26 ± 1	67 ± 3	6000/1500
1e	$C_{10}H_{21}$	44 ± 2	98 ± 4	250/40
2b	C_4H_9	24 ± 2	62 ± 5	15000/9000
2c	C_6H_{13}	30 ± 2	68 ± 5	1400/220
2d	C_7H_{15}	32 ± 2	68 ± 4	4000/900

Table 2-1. Characterization data for gelators 1a-e and 2b-d. All data represent an average of three runs. The G′/G″ measurements were performed at concentrations of 2 x cgc.
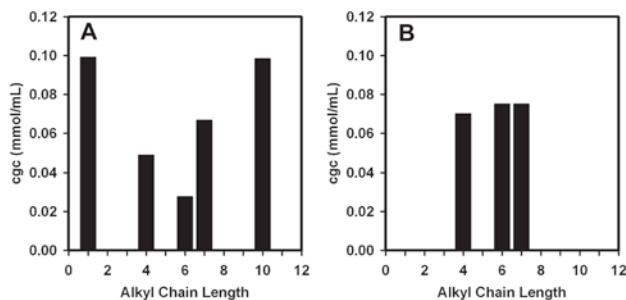
Figure 2-4. Plot of the cgc (in benzene) versus alkyl chain length for aryl trihydroxyborate salts (A) **1a-e** and (B) **2b-d.**

The strength and resilience of a gel to deformation by an external force is characterized by the loss (G′) and storage (G″) moduli. The majority of the aryl trihydroxyborate gels reported herein show relatively large values for the modulus (G′ > 1000 Pa), when compared to other organometallic gelators.[9] Strong gels typically result from highly cross-linked microstructures. To understand this effect, the gel structure was examined via microscopy. Scanning electron microscope images were unreliable because the gel samples decomposed when exposed to the electron beam (Appendix X). Instead, atomic force microscopy (AFM) was used to generate high-resolution images of the aryl trihydroxyborate gels. The AFM images for gels **1a**-**e** and **2b**-**d** revealed that the gel microstructures contain physically crosslinked fibers (see **Figure 2-5** and Appendix X). This dense fibrous network is consistent with the unusually strong gels observed via rheology. Despite these results, it was surprising that the gel-to-solution transition temperatures (measured by the falling-ball method) had almost no correlation with the gel strength (Appendix X). These differences are likely due to the low melting temperature of the salts, and competing decomposition reactions occurring during the T_{gel} measurements.
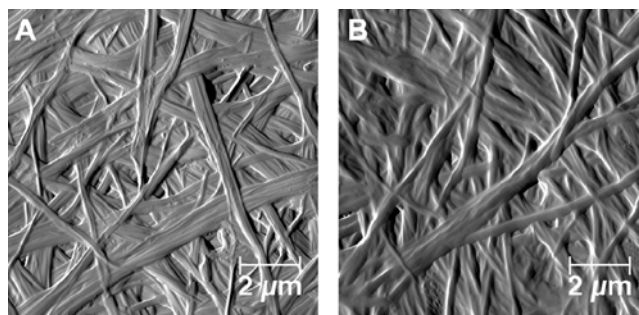
Figure 2-5. AFM images of gels from (A) 1c (12 mg/mL) and (B) 2c (32 mg/mL) in benzene.

The 3D orientation of molecules within the gel fiber can be elucidated if the powder X-ray diffraction (PXRD) pattern of the gel matches a single-crystal diffraction pattern of the gelator. Although we were unable to grow single crystals of **1a-e** and **2b-d** from benzene, Cammidge and co-workers obtained a single-crystal of a structurally related compound, sodium 4-methoxyphenylborate salt, from H_2O.[3] In this compound, the sodium ions formed a linear hydrated chain $[Na(H_2O)_5]_n$ wherein significant hydrogen-bonding interactions between the H_2O and the B-OH were observed. We hypothesize that a similar chain-like structure may be present in our gel fibers because the PXRD pattern for the xerogel of **1a** exhibited a Bragg reflection at a *d*-spacing of 15.6 Å, which is similar to the (002) peak that corresponds to the distance between the chains of sodium ions in the reported structure (Appendix X).[3,24]

C. Conclusion

In summary, a series of aryl trihydroxyborate salts with increasing alkyl chain lengths were synthesized. These compounds were found to be thermally unstable, undergoing quantitative protodeboronation with heating both in solution and the solid

state. These results suggest a limited utility for these compounds as stoichiometric reagents in metal-catalyzed reactions. Some of these salts formed gels in organic solvents. The resulting gels are interesting because of their unusual strength and the observed chain-length dependence on gel properties. The origins of the chain-length dependence remain unclear at this time. Excitingly, these novel gelators may prove useful for preparing new materials, as the localization of difunctional gelators **2b**-**d** may lead to higher molecular weight polymers via Suzuki-Miyaura cross-coupling polymerizations in the gel state. Alternatively, free-radical polymerization of a styrene- or divinylbenzene-based solvent could lead to porous materials after removal of the aryl trihydroxyborate salt.

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Chapter 3

Molecular Dynamic Simulations of Gelator and Nongelator Dissolution Enthalpies

A. Background

The current limitation in the field of molecular gelators is that the process for gel formation and the impact of structure on this process is largely unknown, leading to the difficulty in developing application-specific gelators or pre-determine appropriate gel-inducing solvents. Most efforts towards discovering new gelators have focused on screening a range of solvent combinations or appending alternative functional groups to a gelator scaffold. But screening methods can be time-consuming as each target molecule needs to be synthesized and tested for gelation. To streamline solvent screening efforts, Raynal and Bouteiller reported a method that focused on using Hansen solubility parameters to determine a sphere where potentially gelling solvents fell inside the sphere and outside the sphere were solvents that would not lead to gelation.[1] Hansen solubility parameters are comprised of a solvent's dispersion forces, polar forces, and H-bonding forces, and is often used to determine potential solublizing solvents for a molecule. Because the definition of solubility is subjective when using the program[2], Raynal and Boutiller found that after identifying a few solvents that lead to gel formation, they could use the program to find solvents that have similar Hansen solubility parameters to direct their solvent screen for gelation. However, to use this method, it does require at least two

or three solvents that have been tested and do form gels, which in some cases, finding a sufficient number of solvents may be difficult. Similarly, Feng and coworkers related solubility parameters and molecular size to predict gel-forming solvents. They also plotted the Hanson solubility parameters of alcohol and aromatic solvents in a Teas plot for a series of methyl 4,6,*O*-(*p*-chlorobenzylidene)-α-D-glucopryanoside gelators, and again knowing a few solvents that fell into the categories of gel forming, soluble, and insoluble, they were able to group solvents into these categories. Then adding untested solvents into the Teas plot based on Hanson solubility parameters, they found that some of the untested solvents aggregated around the gel-forming solvent group, and were able to predict solvents that lead to gel formation.[3] The authors note that the predicted solvents and tested solvents that aggregated together in a Teas plot had solvent viscosity in common, potentially indicating that solvent viscosity may play a key role in gel-aggregate formation. These efforts to streamline the gel solvent screening process still require some screening to find an appropriate solvent for the solubility parameters. However, they do suggest that solvent and its interaction with the gelator plays a vial role in forming gels. These methods of gel discovery focus on solvents and require an already existing gel scaffold. As a consequence, they cannot be used for discovering new scaffolds.

An alternative method for discovering application-specific gelators is to begin with a gelator scaffold, append solubilizing units that is selectively cleaved in the presence of an appropriate enzyme, leading to subsequent stimuli-responsive gelation. For example, Xu and coworkers developed an enzymatic hydrogelator that responds to β-

lactamases by appending a substrate with a β-lactam ring to a napthalene-functionalized dipeptide gelator.[4]

Alternatively, to design new gelator scaffolds, our research group has focused on identifying molecules that have strong unidirectional intermolecular interactions.[5] The focus on unidirectional intermolecular interactions is due to the hypothesis that this feature will promote 1D self-assembly leading to the fibrous network that is often characteristic of molecular gels. For example, McNeil and coworkers illustrated that searching the CSD (Cambridge Structural Database) for molecules that exhibited 1D cation-π interactions could streamline the design of a new gelator scaffold. In taking a similar structure reported by Goodgame and coworkers, our research group discovered a di-quinoxalinalone-Hg^{2+} complex formed gels in MeOH/H_2O solvent systems. However, 1D interactions cannot be the only driving force for gel formation as not all molecules that exhibit strong 1D interactions in the solid state are gelators, and there are nongelators exhibit 1D interactions in the solid state.[11] In addition, small structural modifications to a working gelator scaffold have been seen to destroy gelation ability rather than lead to a new gelator.[6, 7] Therefore, modeling the molecular interactions important in gelation can help elucidate the additional interactions that can influence gel formation.

Molecular modeling techniques have been applied to gelators to elucidate the driving forces for gel formation. Molecular modeling simulations, can be used to compare molecular structure to parameters that are anticipated to correlate with gelation ability, leading to a method for designing gelators and determining *a priori* if a molecule will form gels. Molecular mechanics is an economical and fast quantitative method to

estimate simple energy functions of large molecules. Molecular mechanics are able to simulate a potential energy surface, calculate free energies and thermodynamic values.

Stupp and coworkers recently modeled the self-assembly of peptide amphiphiles into nanofibers using molecular mechanics calculations. These studies determined that the electrostatic interactions between the peptide amphiphiles and sodium ions stabilize the nanofiber. Their simulations revealed that the peptide sequences appended to the amphiphiles to promote neurite growth, are exposed on the surface of the fiber. This atomistic level approach to simulate the structural features of these nanofibers can be useful for designing other peptide amphiphile-based gelators. However, these molecular models are specific to these gelators as the fiber radius is approximately 44 Å, which is the length of a single peptide amphiphile. In comparison, the fibers formed by other small molecular weight gelators are typically much larger, with diameters of 2-3 μm by scanning electron microscopy and 2000-3000 molecules across.[8] Therefore these aggregation models, that form stable fibers within 20 – 40 ns simulations, are too short for aggregation of most small molecule gelators and in general are not easily generalized to other gelator scaffolds.

Feringa and coworkers also performed molecular mechanics calculations on bis-urea gelators in the gas phase to look at the aggregation process of their gelators. One-dimensional aggregates through non-covalent interactions of gelator molecules are hypothesized to be the driving force for fiber formation and subsequent gel formation. Therefore, molecular modeling techniques looking at energy minimized conformations directed the researchers to design a number of 1,2-bis(urea)cyclohexane and 1,2-bis(urea)benzene gelators that would not only enforce 1D hydrogen bonding by arranging

the urea functionality to be coplanar, but this arrangement of the urea functionality would also be the lowest energy conformations (Figure 3-1).[9]
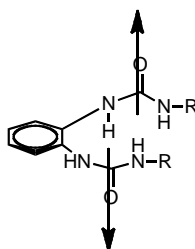
Figure 3-1. Hypothesized 1D hydrogen bonding arrangement for 1,2-bis(urea)benzene gelators.

To further support their hypothesis that 1D hydrogen bonding directed unidirectional aggregation, they carried out docking experiments with a second molecule of 1,2-bis(urea)cyclohexane and found that for the conformations with the urea groups coplanar, the preferred sites of interaction were below and above the urea groups. Then, constructing models of one-dimensional aggregates they found that in all cases, the aggregates were more stable than the lowest energy conformation of a single molecule. However, the gas-phase nature of these computational studies means that solvent contributions were neglected, and the dominant force for aggregation could be different in solution or during gelation. Their gelators form gels in a variety of organic solvents ranging from hexyldecane, toluene, cyclohexanone, dimethyl sulfoxide, ethanol, and 2-propanol. Taking into account the solvent in the simulations is important as some of these solvents are likely to competitively hydrogen bond, such as ethanol and 2-propanol. In another case, Feringa and coworkers use molecular modeling to again look at potential surface interactions of geminal bis-urea gelators.[10] However, in efforts to reduce the complications that large degrees of conformational freedom can contribute to the models, they choose a model compound (1,1'-(phenylmethylene)bis(3-methylurea)), (Figure 3-2)

in which it is unclear whether or not it is a gelator because it was not synthesized or screened for gelation.
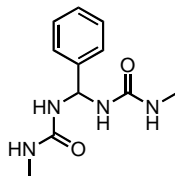
Figure 3-2. (1,1'-(phenylmethylene)bis(3-methylurea)) in lowest energy conformation due to intramolecular hydrogen bond

Similar to the bis(urea)cyclohexane case mentioned above, the authors were able to model a conformational change of (1,1'-(phenylmethylene)bis(3-methylurea)) forming intramolecular hydrogen bonds to intermolecular hydrogen-bonding aggregates that were lower in energy through forming the greatest number of intermolecular hydrogen bonds possible. Then through ^{1}H NMR spectroscopy experiments of a different geminal bis-urea gelator (not the model compound) they are able observe this conformational change from the low energy intramolecular hydrogen bonding monomer to the higher energy intermolecular hydrogen bonding conformer at higher concentrations (Figure 3-3).
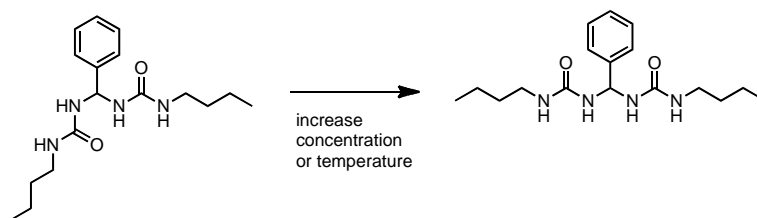
Figure 3-3. Conformational change from intramolecular hydrogen bond to intermolecular hydrogen bonds

They correlate the formation of hydrogen-bonded aggregates seen by NMR spectroscopy at higher concentrations and anticipate that this aggregation also happens in the gel state. The authors were unable to take ^{1}H NMR spectra of the gels due to excessive dipolar broadening. The computational models allowed the researcher to recognize that

28

aggregations in the gel state may not be the compound's lowest energy conformation as a single molecule. However, is inaccessibility to the energy conformation that allows for the greatest number of hydrogen-bonds possible is the only criteria for gel formation in these systems. For the same bis-urea scaffold, the authors synthesized and screened 1-butyl-3-[(3-butylureido)phenylmethyl]urea and 1-benzyl-3-[(3-butylureido)phenylmethyl]urea, and the latter compound does not form gels, even though for both compounds, it is anticipated that they have the potential to form 1D hydrogen bonds.

gelator   non-gelator
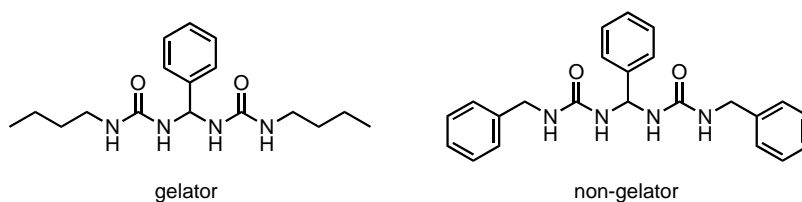
Figure 3-4. 1-butyl-3-[(3-butylureido)phenylmethyl]urea is a gelator, but 1-benzyl-3-[(3-butylureido)phenylmethyl]urea is not a gelator.

Therefore, there is a possibility that the *n*-butyl chains and or the arrangement of adjacent molecules for the optimal number of hydrogen bonds plays a key role in the gelation process that is not addressed through the molecular mechanics studies with a model scaffold.

To relate molecular structure to gel formation, the our research lab looked at a series of pyridine-based (Figure 3-5) and dipeptide-based (Figure 3-6) gelators and nongelators and compared the room temperature solubility, types of interactions, dimensionality of the interactions, critical gel concentration (cgc), and dissolution enthalpies of pyridine-based gelators and nongelators and found that of those properties,

only dissolution enthalpies correlated with gelation ability.[11] Within the same solvent system, gelators exhibited higher dissolution enthalpies relative to their nongelator counterparts.

1a R = Ot-Bu;
1b R = Me;

2a R = OMe;
2b R = Cl;
2c R = Me;

3a R = OMe;
3b R = Cl;

4

5a R = OEt;
5b R = Oi-Pr;
5c R = OBn;

6a R = H;
6b R = OC_4H_9;
6c R = CF_3;
6d R = NO_2

7a $R_1 = R_2 = H$;
7b $R_1 = CN, R_2 = Me$;

8a R = 4-OMe;
8b R = 3, 4, 5-OMe;
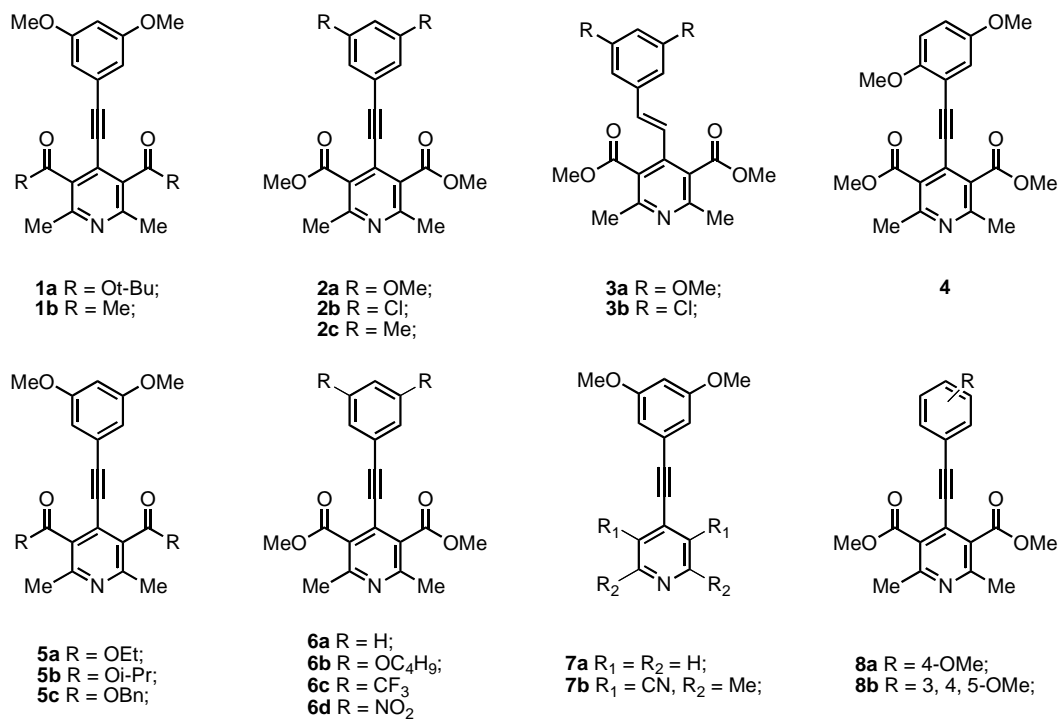
Figure 3-5. Pyridine-based gelators (**1a-b, 2a-c, 3a-b, 4**) and nongelators (**5a-c, 6a-d, 7a-b, 8a-b**)

9a R=H
9b R=CH_3
9c R=CH_2OH
9d R=$CH(CH_3)_2$
9e R=$CH_2(CH_3)_2$

10a R=H
10b R=CH_3
10c R=CH_2OH

11a R=H
11b R=CH_3
11c R=CH_2OH
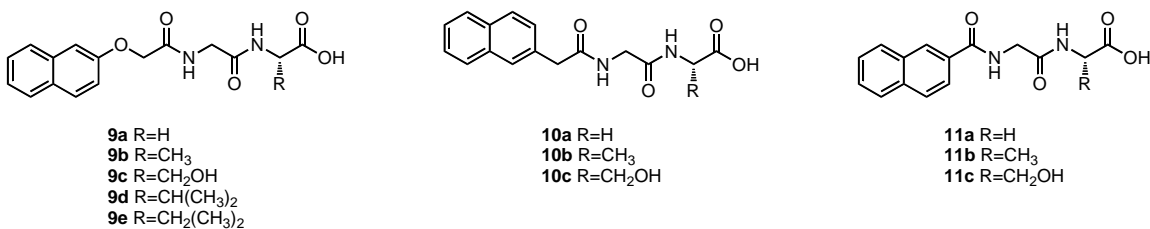
Figure 3-6. Dipeptide-based gelators (**9a-c, 10a-c**) and nongelators (**9d, e; 11a-c**)

Similar to work done in our lab, Miravet has studied the thermodynamic interactions that drive the aggregation of bolaform amino acid hydrogelators in both aqueous media and acetonitrile (Figure 3-7).[12]
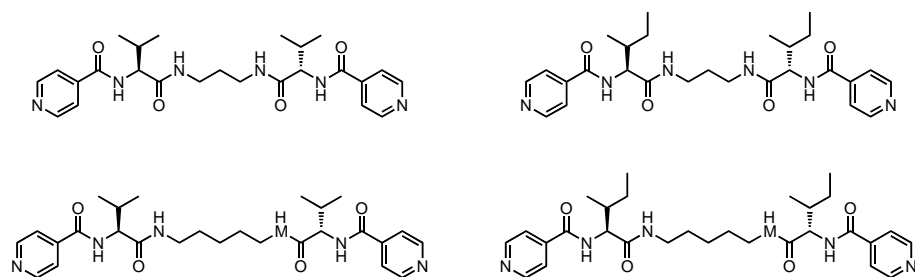
Figure 3-7. Bolaform amino acid hydrogelators

Overall they observe that these molecules assemble in water with low or zero enthalpic gain, but that self-assembly is driven by entropy. That is, the gelators disrupt the highly organized solvent, water, and the entropy gain is due to the hydrophobic effect. The entropic gain of bolaform amino acid hydrogelators is the driving force for self-assembly in water but in a mixed solvent, this might not be the case. In the pyridine-based gelators, we studied the opposite thermodynamic cycle, solubility, rather than aggregation, therefore we cannot directly compare the systems. However, the entropy of dissolution in the pyridine-based systems contribution is small and is not the driving force for dissolution. It is also interesting to note that the bolaform amino acid hydrogelators have a number of hydrogen-bonding moieties and the authors attribute a shift in the NH NMR signals to hydrogen bonding driving the aggregation in acetonitrile. The authors rationalized that gelators require a balance of hydrophobic effects and hydrogen bonding units, and using these principles were able to design isoleucine and longer alkyl chain derivatives that are also gelators (Figure 3-7). Nevertheless, this method again requires an existing gelator molecule scaffold to modify, synthesize, and screen solvents to find gel conditions.

Overall, the above-mentioned methods do not predict gel formation of new gelator scaffolds. Given that finding new gelators is both time-consuming and expensive, it is desirable to develop alternative methods of prediction. In collaboration with Professor Charles Brooks III and Professor Anne McNeil, we used molecular mechanics simulations to develop a model that would support the relationship between dissolution enthalpies and molecular gel structure found experimentally.

The early examples outline efforts to rationalize observed gel formation, yet they require an existing gelator scaffold and these characteristics are potentially specific to the scaffold being studied. The docking simulations used by Feringa and coworkers are good models for calculating the interactions of the molecules and possible 1D aggregates that may correspond to gel formation. But in carrying out gas phase calculations, the interactions with solvent during the gelation process are not accounted. In the previously mentioned studies where researchers attempt to predict potential gelling solvents, it illustrates that solvent interactions may also play a key role in gel formation. In our efforts outlined in this chapter, we will attempt to model both the solute-solvent interactions and solid-state interactions to consider the role of solvent and intermolecular interactions. We will focus on using the molecular structure of both gelators and nongelators in attempts to develop a model that can differentiate them.

B. Computational Details

All simulations were performed using Chemistry at HARvard Molecular Mechanics[13] macromolecular modeling package version c36b2 on an Apple iMac computer with 3.33 GHz Intel core 2 Duo. The crystallographic information file (CIF) provided the molecular structures for (**1a, 1b, 3a, 2c, 3a, 5b, 6a, 6d, 7b, 8a, 8b**) and molecules that did not have crystal structures (**3b, 4, 5a, 5c, 6b, 6c, 7a**) were generated using ChemAxon's Marvin Sketch software version 5.6.0.1 and were initially minimized using Marvin Sketch internal software for basic quantum mechanical calculations. The partial charges and parameters for molecules **1a-8b** (Figure 3-5, above) were assigned using the MATCH parameterization toolset.[14] Parameters for dimethyl sulfoxide (DMSO) were taken from the CHARMM Generalized Force Field (CGenFF)[15], and the TIP3P model represented water molecules. Simulations were carried out at 350 K and constant pressure using the Verlet leapfrog integration method with a 1 – 1.5 fs time step and periodic boundary conditions on a cubic simulation box.

Experimentally, our research group found that pyridine and dipeptide-based gelators had higher dissolution enthalpies and entropies than their nongelator counterparts.[11] We attempted to develop a computational model to examine the experimental trend in dissolution enthalpies, choosing to focus initially on the pyridine-based scaffold because these molecules have a lower degree of conformational freedom[10] than the dipeptide-based scaffold. Experimentally, dissolution enthalpies were determined by measuring the solubility of **1-8** over a range of temperatures and ΔH_d was calculated by the van't Hoff equation (eq 1).[11, 16] Plotting $1/T$ over the $\ln x$ (where x is the mole fraction of **1-8** in solution), ΔH_d is derived from the slope and ΔS_d is from the y-intercept.

$$\ln x = -\frac{\Delta H_d}{RT} + \frac{\Delta S_d}{R} \tag{1}$$

Computationally, we will be looking at heats of dissolution, the enthalpy of a solid going into solution (eq 2).

$$H_{solid} \longrightarrow H_{solution} \tag{2}$$

Enthalpy of dissolution (ΔH_d) is then solved for by subtracting the enthalpy of solid (H_{solid}) from the enthalpy of the solution ($H_{solution}$). (eq 3)

$$H_{solution} - H_{solid} = \Delta H_d \tag{3}$$

Experimentally, the ΔH_d and ΔS_d values for all of the compounds are positive and gelators have both higher dissolution enthalpies and entropies. However, for this computational work we will only focus on comparing to the experimental enthalpy values because there is a broad range of values between gelators and nongelators in the enthalpy values of the molecules. The gelators having higher dissolution enthalpies means that they have a higher preference for solid-state interactions or potentially weaker solute-solvent interactions than nongelators (Table 3-1).

Table 3-1. Experimental dissolution enthalpy values. Shaded compounds are gelators

Pyridines	ΔH_d (kcal/mol)	ΔS_d (kcal/mol*K)
1a	21 ± 2	0.037 ± 0.006
1b	14 ± 2	0.026 ± 0.005
2a	16 ± 2	0.029 ± 0.006
2b	17 ± 2	0.025 ± 0.007
2c	13.7 ± 0.4	0.022 ± 0.001
3a	14 ± 1	0.025 ± 0.004
3b	20 ± 1	0.036 ± 0.003
4	18.3 ± 0.6	0.04 ± 0.002
5a	10.4 ± 0.1	0.0137 ± 0.0004
5b	13 ± 2	0.018 ± 0.005
5c	10 ± 1	$7 \pm 3 \times 10^{-3}$
6a	10 ± 1	---

6b	13 ± 1	0.016 ± 0.004
6c	10 ± 1	$6 \pm 3 \times 10^{-3}$
6d	15 ± 2	0.018 ± 0.005
7a	8.0 ± 0.7	$9 \pm 2 \times 10^{-3}$
7b	10 ± 2	$4 \pm 7 \times 10^{-3}$
8a	15.7 ± 0.7	0.029 ± 0.002
8b	12 ± 2	0.018 ± 0.005

The enthalpy values for the transition from solid to solution, which is the enthalpy of dissolution (ΔH_d), can be determined by modeling the interactions of that compound in a box of solvent (solute-solvent, represented by $H_{solution}$) and the molecular interactions between the compound with itself (solid-solid, represented by $H_{pure\ liquid}$). (Figure 3-8) We are not modeling the entire process of transitioning from solution-to-gel or gel-to-solution, but rather differentiating the interactions that could play a role in gelation, which are the solid-solid, and solute-solvent, to calculate the enthalpy for dissolving the molecule (ΔH_d).

a.   b.
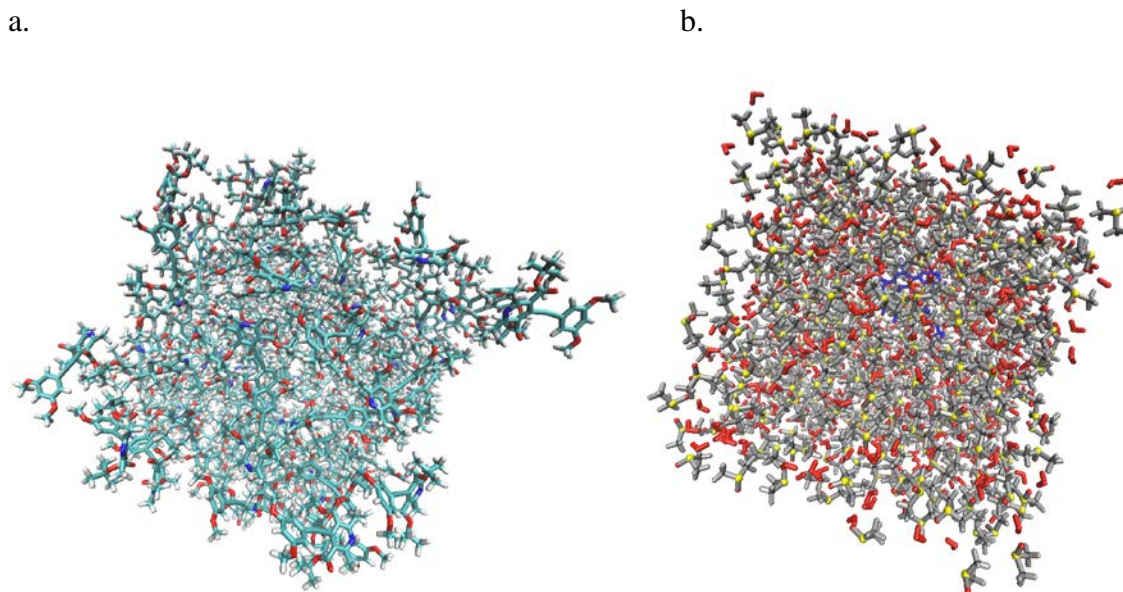
Figure 3-8. Representations of a.) $H_{pure\ liquid}$ and b.) $H_{solution}$

C. Primary Solid Model

The solid-solid interactions (H_{solid}) were initially modeled as a hypothetical liquid represented as $H_{pure\ liquid}$. $H_{pure\ liquid}$ is a surrogate for molecular interactions that we hypothesized are in the gel state. We hypothesized that a liquid representation for the enthalpies in the solid-state would be adequate because the trend in enthalpy values remains consistent when the enthalpy of melting[17] is accounted (Table 3-2). Although these values are not an exact comparison as the ΔH_d and ΔH_{melt} values were measured through different techniques, it illustrates that ΔH_{melt} does not drastically influence the general trend of gelators having higher enthalpies than nongelators.

Table 3-2. Influence on the enthalpy trend when accounting for ΔH_{melt}, measured by DSC.[17]

Pyridines	ΔH_d (kcal/mol)	ΔH_{melt}	ΔH_d - ΔH_{melt}
1a	21 ± 2	5.8	15.2
1b	14 ± 2	4.58	9.42
2a	16 ± 2	8.23	7.77
2b	17 ± 2	7.68	9.32

2c	13.7 ± 0.4	3.63	10.07
3a	14 ± 1	9.43	4.57
3b	20 ± 1	6.73	13.27
4	18.3 ± 0.6	5.94	12.36
5b	13 ± 2	5.94	7.06
6b	13 ± 1	6.92	6.08
6c	10 ± 1	6.06	3.94
6d	15 ± 2	7.57	7.43
7a	8.0 ± 0.7	5.3	2.7
8a	15.7 ± 0.7	6.6	9.1
8b	12 ± 2	5.42	7.06

In addition, there is a greater entropic difference in the transition from solid-state to liquid-state rather than an enthalpic difference, which is the focus for these studies. Therefore, we are assuming that the densities for these molecules in the solid-state are the same in the liquid-state. For a few of the molecules, we crudely measured the melt densities and compared them to the density in the solid-state determined from the x-ray crystal structure (Table 3-3).

Compound	Melt density	Solid-state density
2a	1.3	1.35
6a	1.5	1.306*

Table 3-3. Comparison on melt density and density determined by the x-ray crystal structure. *designates crystal structure with H_2O in the lattice.

The molecular interactions were also modeled as a liquid to develop a predictive model that will not require a single-crystal structure as the input. There are instances where the packing within the crystal structure does not correspond to gel packing.[11, 18, 19] Generating a model that required a single crystal as the input would also limit the model's versatility in general as not every molecule has a known crystal structure. In addition, CHARMM parameters are optimized using hydration free energy data, and modeling the system as a

liquid best matches the degrees of freedom assumed and optimized in the force field. We hypothesized that modeling the molecule in a hypothetical liquid state would enable us to run dynamics to reach equilibrium, and then calculate the enthalpy of the system absent of a crystal structure. However, in the cases where there are crystal structures for the molecules, those structures were converted to a format where all of the atoms and bond types are well defined, using the MATCH algorithm,[14] which is also a good predictor of the solid-solid interactions optimized using hydration free energies.[20] To set up the simulation, the hypothetical liquid state was explored by initially arranging the molecules in a randomly oriented array of 125 molecules, within a 35 - 40 Å box at a density of 1.3 g/mL. Equilibrium was facilitated by ramping the temperature to 500 K before cooling to a final temperature of 350 K. The temperature of 350 K was chosen because preliminary computational results indicated that at room temperature the molecules did not exhibit the properties of a disordered, free-flowing liquid, but were trapped in a glassy state. In addition, it is common to perform self-assembly experiments at a higher temperature than room temperature to allow the molecules to gain enough kinetic energy, thereby decreasing the computation time.[21] The initial coordinates of the system were setup by applying a steepest decent minimization algorithm. The arrangement of these molecules as a liquid was a challenging and unique situation as molecules modeled as a liquid are often solvents and are liquids of relatively low density, especially at higher temperatures, but these pyridine-based molecules are much larger than solvent molecules commonly used for molecular mechanics, and have higher densities. Therefore, initialization of the system often resulted in a large number of steric overlaps between molecules resulting in extremely high energies, making equilibration very difficult. To simulate the appropriate

densities for the organic liquid, we shrunk the molecules to allow the molecules to equilibrate with fewer collisions, then expanded the molecules back to full size to run the dynamic calculations. Scaling the molecules reduced the bond lengths and van der waal radii. During the process of setting up the initial coordinate system, the molecules were scaled down to 50% of full size. With the molecules at half-size, dynamics were run at 500 K and at the completion of the calculations at annealing temperatures, the size of the box was noted, and inputted into the next set of calculations that increased the molecules by 15%. The box size in these calculations were important to note because these computations were run at constant pressure, and the volume of the box expanded and contracted to maintain the density. Again, after the calculations were completed, the box size of the molecules at 65% was inputted into the next set of calculations at 500 K for the molecules at 80% of full size. These iterations were done for each molecule until the structure was scaled up to full size, which was 4 steps in total, to get to a liquid phase, and then dynamics were run at 350 K. The results of these calculations are in Table 3-4. As a control, molecules with known CIF were also modeled and compared to those obtained through ChemAxon's Marvin Sketch.

Table 3-4. $H_{pure\ liquid}$ hypothetical liquid model

CIF originated structure?	Pyridine	$H_{pure\ liquid}$ (kcal/mol)
yes	1a	-220
yes	2a	-47
no	2a	-47
no	2b	-70
yes	2c	-55
yes	3a	1.2
no	3b	-24
no	4	-10
no	5a	-81

yes	**5b**	-140
no	**5c**	-25
yes	**6a**	-38
no	**6b**	-31
no	**6c**	-11
yes	**6d**	-29
no	**7a**	6.5
yes	**7b**	-40
yes	**8a**	-27
yes	**8b**	21

These values represent enthalpy values for the solid-solid interactions as a pure liquid. Because we anticipate that the solute-solvent interactions play a significant role in the dissolution enthalpy, we cannot interpret these values without the $H_{solution}$ half of the thermodynamic process we are attempting to model (eq 2). In general, these values indicate that the molecules have favorable solid-solid interactions as we would expect that these molecules are solids at room temperature. The positive enthalpy values for **3a, 7a,** and **8b** were a concern, and the number of steps for the computation was increased to ensure convergence, but this increase in run time did not significantly alter the values listed in the table.

D. Initial Solvated Compound Model

The calculations for the compound in solution initially required setting up the solvent box. A single molecule of the solute was solvated by in 45 Å cubic box of H_2O and DMSO to simulate the molecule solvated in solution. The hypothetical gelator liquid model only calculated the solid-solid interactions, there are now several different interactions to consider in these solvated simulations: solute-DMSO/H_2O, DMSO-

DMSO, H_2O-H_2O and H_2O-DMSO. We are specifically interested in the solute-DMSO/H_2O interactions, which will allow us to determine ΔH_d. These calculations will provide the values for the second half of the thermodynamic cycle (eq 2), which are the $H_{solution}$ interactions. Several solvent boxes of varying DMSO and H_2O ratios were explored: $H_{solution}$ (1:1 H_2O:DMSO mole ratio), $H_{solution}$ (H_2O), $H_{solution}$ (DMSO), $H_{solution}$ (1:1 H_2O:DMSO volume ratio). The solvent boxes that were a mixture of H_2O and DMSO were built by starting with a box of 144 water molecules and deleting 2 water molecules for every DMSO molecule placed in the box, given that each DMSO molecule is about twice the size of water. The boxes and number of molecules were then expanded to 8 times its original size to fill a 46 Å box. The values for the enthalpy of **1a** (gelator) and **5b** (nongelator) in solution in the different solvent boxes are in Table 3-5.

Table 3-5. Influence of H_2O and DMSO ratio on $H_{solution}$

Solvent Box	1a	5b
$H_{solution}$ (1:1 H_2O:DMSO mole ratio)	-260	-180
$H_{solution}$ (H_2O)	-260	-180
$H_{solution}$ (DMSO)	-250	-170
$H_{solution}$ (1:1 H_2O:DMSO volume ratio)	-260	-190

The values for the different solvent boxes are all similar because the focus is on enthalpy values. The enthalpy contribution for varying the solvent is very small, while the entropy contributions are where one would see the influence of solvent ratio.

Experimentally, the enthalpy of dissolution was determined in 1:1 H_2O:DMSO volume ratio, therefore calculations for $H_{solution}$ were also done in 1:1 H_2O:DMSO volume ratio (Table 3-6).

41

Table 3-6. $H_{solution}$ (1:1 H_2O:DMSO volume ratio).
Gelators are shaded.

Pyridine	$H_{solution}$ (1:1 H_2O: DMSO volume ratio) (kcal/mol)
1a	-250
2b	-100
2c	-94
3a	-44
3b	-63
4	-55
5a	-120
5b	-180
5c	-79
6a	-73
6b	-90
6c	-55
6d	-76
7a	-19
7b	-75
8a	-70
8b	-34

In general, in the simulations thus far the $H_{solution}$ values are describing that the solute-solvent interactions are stronger than the solid-solid interactions ($|H_{solution}| > |H_{pure\ liquid}|$). These values are unexpected as these molecules experimentally are very insoluble and we would hypothesize that the enthalpy values for $H_{solution}$ would be higher in energy than $H_{pure\ liquid}$. At the moment, the computational models are representing the two extremes of the process of dissolution, modeling the point at which there is no solvent, to modeling the other side of the equation with only a single molecule, completely surrounded by solvent. These models at the extreme conditions are potentially either overestimating the solute-solvent interactions or underestimating the solid-state interactions. A potential model to try to mediate the extreme conditions is to run $H_{solution}$ simulations with two

randomly placed molecules, and perform long simulations, on the time scale of 10 ns, to see how the additional molecule changes the $H_{solution}$ values. These conditions may better represent experimental conditions.

E. ΔH of Dissolution Model

As described above, the enthalpy of dissolution (ΔH_d) can be calculated by the enthalpy of the compound in solution ($H_{solution}$) minus the enthalpy of the solid ($H_{pure\ liquid}$, calculated from a hypothetical liquid) from (eq 4).

$$H_{solution} - H_{pureliquid} = \Delta H_d \qquad (4)$$

Tabulated calculations are in Table 3-7. We hypothesized that through molecular mechanics we would be able to model the enthalpy dissolution trend we observed experimentally, that gelators have higher dissolution enthalpies than nongelators. Experimentally the values were also positive, favoring the solid-solid interactions for the process of dissolution. Looking at the absolute values in Table 3-7, gelators are not distinguishable from nongelators.

Table 3-7. Computational dissolution enthalpy values. Shaded are gelators.

Pyridine	$H_{solution}$ (kcal/mol)	$H_{pure\ liquid}$ (kcal/mol)	ΔH_d (kcal/mol)
1a	-260	-220	-40
2a	---	-47	---
2b	-100	-77	-30
2c	-94	-55	-39
3a	-44	1.2	-45
3b	-63	-24	-39

4	-54	-10	-44
5a	-130	-81	-49
5b	-180	-140	-40
5c	-79	-25	-54
6a	-73	-38	-35
6b	-90	-31	-59
6c	-55	-11	-44
6d	-76	-29	-47
7a	-19	6.4	-13
7b	-75	-40	-35
8a	-70	-27	-43
8b	-34	21	-55

The negative dissolution enthalpy values from this initial model indicate that the compounds have stronger solute-solvent ($H_{solution}$) interactions. At this point, the model needed to be revised because experimentally, through solubility data, dissolution enthalpy values are positive and indicate that the compounds have strong solid-solid interactions rather than solute-solvent interactions. Therefore, we reconsidered the hypothetical liquid model to solve for $H_{pure\ liquid}$, and we anticipated that this system might not capture the strength of the solid-state interactions because the molecules could be trapped in a disordered state during the calculations and never reach equilibrium.

F. Secondary Solid Model

The initial $H_{pure\ liquid}$ model is potentially an inadequate representation of the interactions in the solid state as overall these values are less favorable then $H_{solution}$. Therefore, we looked at the molecule's asymmetric unit. The asymmetric unit includes all

of the crystal graphic symmetry information and is repeated several times to accomidate all interactions. We anticipate that starting within a molecule's crystal lattice we will be able to better model the solid-solid interactions than our hypothetical liquid system. Developing a model that requires a crystal structure does limit the extension of this model to predicting gelators, however we do need a starting point for the solid-state interactions.

These calculations required setting up the crystal lattice for each molecule that had a crystal structure, then running an energy minimization step. After minimization, simulations were again carried out at constant pressure and temperature, with the temperature fixed at 350 K. The values in Table 3-8 are for derivatives that have a single molecule within its asymmetric unit.

Table 3-8. H_{xtl} values using crystal lattice

Pyridine	H_{xtl} (kcal/mol)
1a	-260
2c	-80
5b	-170
6a	-40
6d	-42
7b	-56
8a	-63
8b	-13

For all the H_{xtl} values (Table 3-8), they indicate stronger solid-solid interactions than the previous H_{xtl} values (Table 3-4). This is exciting as we anticipated that the previous model (hypothetical liquid) was underestimating the strength of the solid-solid interactions.

Table 3-9. Computational dissolution enthalpy values with new H_{xtl} values.

Pyridine	$H_{solution}$ (kcal/mol)	H_{xtl} (kcal/mol)	ΔH_d (kcal/mol)
1a	-260	-260	0
2c	-94	-80	-14
5b	-180	-170	-10

6a	-73	-40	-33
6d	-76	-42	-34
7b	-75	-56	-19
8a	-70	-63	-7
8b	-34	-13	-21

Although the new H_{xtl} values are moving in the right direction, the majority of the ΔH_d values (Table 3-9) still indicate that in our model, the solute-solvent interactions are still stronger than the solid-solid interactions.

G. Conclusions and Future Work

We explored the use of molecular mechanics simulations to model the relationship between dissolution enthalpies and molecular gel structure. Through these preliminary results we learned that we are unable to model the solid-solid interactions accurately in simulating the molecules as a hypothetical liquid. The immediate next steps for these calculations are to find methods of improving upon our secondary solid model. One method of improving the model is to fit the molecules into another molecule's crystal lattice to see if lattices parameters are exchangeable and/or be relaxed to develop a simulated lattice. This will guide our efforts in developing a model absent of a crystal structure. Eventually, we would like to develop a model that can be used to predict if a molecule will form gels.

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Chapter 4

Sensing via Gelation: Analyte-Triggered Disassembling Polymers for Signal

Amplification

A. Background

Sensors are essential to maintaining safety and security, establishing environmental regulations, and offering lifesaving diagnosis. There has been significant research in developing and improving a variety of sensors, most of which are spectrophotometric in nature. However, these detection methods are limited by their lack of portability, high cost, and complexity of instrumentation for data collection and analysis.[1]

Analyte-triggered gelations have the potential to be portable, accurate, and relatively inexpensive detection methods. A chemical interaction with a target analyte that induces the solution-to-gel phase transition makes these gelators intriguing as molecular sensors. The key is to design a soluble pre-gelator that undergoes a chemical change in the presence of an analyte that that leads to the self-assembly of a gel. In most examples of analyte-triggered gelations, the system is limited by their poor sensitivity.[2,3]

Disassembling polymers have the potential to improve upon the sensitivity of analyte-triggered gelations because the monomeric units act as reporter molecules amplifying the event that initiated the depolymerization. We anticipate that an analyte-

triggered depolymerization of a soluble linear polymer to release multiple gelator molecules will amplify the signal from the initial trigger-releasing event (Figure 4-1). The sensitivity of the system is correlated to the degree of polymerization and the critical gelation concentration of the gelator. Analyte selectivity can also be tuned by modifying the trigger, leaving the polymer backbone or signal output (gelation) intact. This system offers the potential to quickly design indicators for a wide range of analytes by simply replacing the trigger.
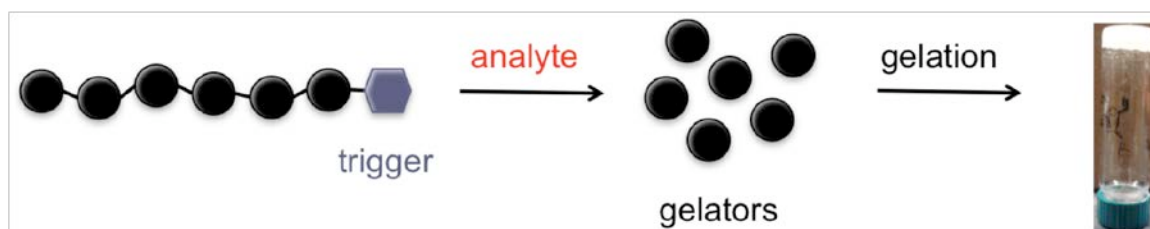
Figure 4-1. Depolymerization initiated by the release of an analyte-sensitive trigger and subsequent gelation of the monomeric units.

Disassembling polymers undergo a cascade of cleavage reactions that release the monomeric units when the trigger-end of the polymer comes in contact with the analyte. The driving force for depolymerization can be driven by the release of a volatile small molecule such as CO_2. Poly(aryl)carbamates are an example of an entropy-driven depolymerization scaffold, releasing CO_2 during polymerization and were initially introduced as a means of connecting a releasable molecule to an active drug to add specificity or to introduce a prodrug form.[4] An alternative driving force for depolymerization is when the polymer is above its ceiling temperature. The ceiling temperature is the temperature at which the rate of polymerization and depolymerization are in equilibrium. Poly(phthalaldehydes) take advantage the polymer's low ceiling

49

temperature to depolymerize when the oxygen anion is unprotected at room temperature because, the equilibrium favors depolymerization.

B. Polyurethanes as the Depolymerization Scaffold

We initially choose to look at poly(aryl)carbamates (aka polyurethanes), which were developed as signal amplification systems by Shabat[5] and coworkers (Figure 4-2).
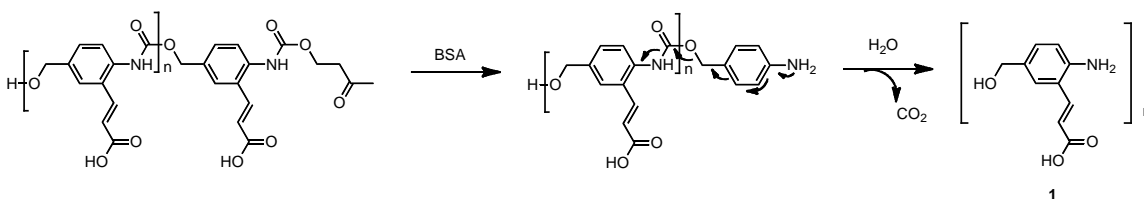
Figure 4-2. Poly(aryl)carbamate disassembling backbone

He showed that a β-elimination of the oxobutoxycarbonyl trigger, catalyzed by bovine serum albumin (BSA) protein, resulted in the polyurethane backbone undergoing spontaneous 1,6-benzyl elimination (to generate an azaquinone methide intermediate) and a decarboxylation reactions to generate CO_2. Immediate hydrolysis of the azaquinone methide forms a 4-aminobenzylalcohol derivative (**1**). Complete depolymerization of 15-20 repeat units occurs within 10 h. The authors note that the rate-limiting step was the enzymatic cleavage and subsequent β-elimination.[6] Disassembling polymers as a system for signal amplification is an extension of the dendrimer work developed around the same time by three independent research groups, Doron Shabat, Dominic McGrath, and Franciscus de Groot.[7, 8, 9] They developed dendrimers that undergo a cascade-release of the dendritic building blocks upon cleavage of the central trigger. Using this method, the drug molecules located at the periphery were rapidly released. Shabat has expanded this

system by introducing components for further signal amplification. For example they developed a cascade systems for the detection of hydrogen peroxide[10] using an AB_3 dendron with two choline molecules, which react with choline oxidase when cleaved to generate additional H_2O_2 that react with the phenylboronic acid trigger (Figure 4-3).
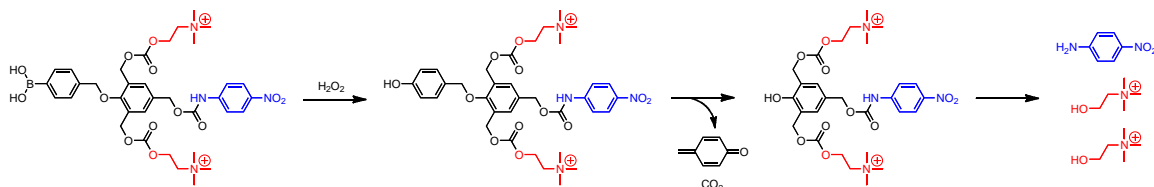
Figure 4-3. AB_3 disassembling dendron end-capped with hydrogen peroxide sensitive phenylboronic acid (blue, *p*-nitroaniline reporter; red, choline units that can further initiate dendron disassembly.

In the presence of hydrogen peroxide, the phenylboronic acid undergoes a hydroboronation and subsequent hydrolysis to release the trigger, which initiates the spontaneous 1,4- and 1,6-elimination reactions that release the fluorescent reporter molecule and two choline molecules. The choline units are then oxidized by choline oxidase to generate more hydrogen peroxide, illustrating a system that self-generates the analyte of interest to improve the detection limit. The possibility of appending releasable or cleavable units in both the 1,4 and 1,6 position of the quinone-methide substrate could also have potential in our system. That is each dendrimer generation requires a multi-step synthetic process and it is difficult to verify that all tail-ends have been functionalized. Also, the 1,4 elimination is much slower than the 1,6 elimination. Therefore, we initially focused on the linear polymer. Starting with the linear poly(carbamate) scaffold we attempted to modify **1** to convert it into a gelator.

There are a few examples where non-gelator drug molecules or amino saccharides have been converted to gelators by appending molecules with strong preferences for

hydrogen-bonding to initiate the 1D aggregation attributed to gel fiber formation. Because these systems are used in the biomedical applications,[11] these gelators are normally hydrogelators, forming gels in water to aid with biocompatibility. Therefore, carrying out similar modifications to the carbamate monomer could lead to the development of hydrogelators that could be used in aqueous systems and be developed as a sensor for contaminants in water. Amino acids have strong 1D hydrogen-bonding intermolecular interactions and have been shown to convert non-gelators like ibuprofen and gluosamine into gelators.[12] We initially focused on appending **2** to the carbamate repeat unit **3** through a Heck cross-coupling, and methyl ester deprotection to synthesize our target **5** for gel screening (Figure 4-4).[12, 13, 28]
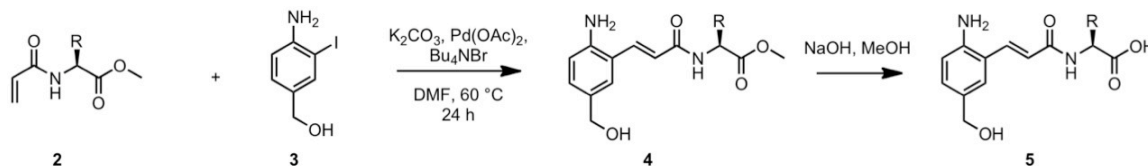
Figure 4-4. Synthesis of target **5**

To guide our modifications and the type of amino acid derivatives we should couple, we initially investigated the solubility of 4-aminobenzylalcohol **7** and the solubility of Shabat's disassembled monomer **8**[18] in various polar solvents. Although the interactions that ultimately lead to gelation over precipitation or crystallization are not understood, it has been hypothesized that gelators require a delicate balance between hydrophobicity and hydrophilicity.[14,15,16] Hydrophilicity is necessary to obtain a supersaturated solution, and hydrophobicity promotes self-assembly and fiber formation necessary for gelation.

7   8
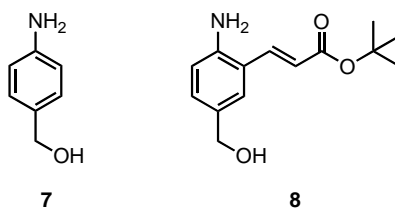
Acrylamide derivatives **2a-i** were synthesized by the addition of acryloyl chloride to various amino acids.[17]   4-Amino-3-iodophenylmethanol (**3**) was synthesized by iodoinating ethyl-4-aminobenzoate (**6**), followed by a followed by a DIBAL-H reduction of the ester.[18] The acylamides (**2a-i**) were then reacted with **3** using the Heck reaction (Figure 4-5). The resulting products (**4a-i**) were hydrolyzed to yield the target compounds (**5a-i**) for gel screening (Figure 4-5).[10]
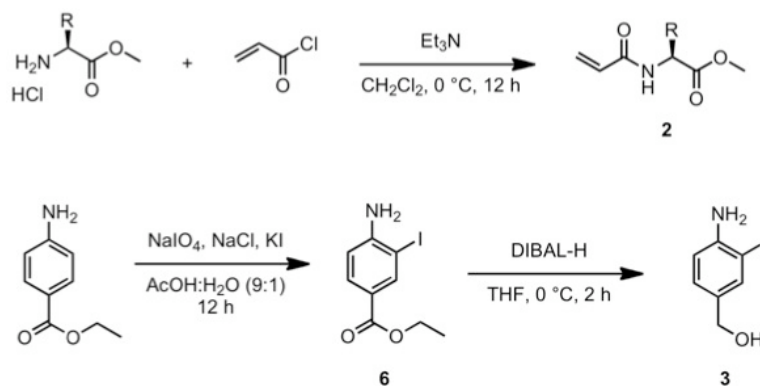
Figure 4-5. Synthesis of **2** and **3**.

Figure 4-6 shows the amino acid derivatives synthesized. In order to confidently assign the connectivity of the methyl ester, COSY was done on (**4f**) to determine that we successfully coupled the acrylamide.
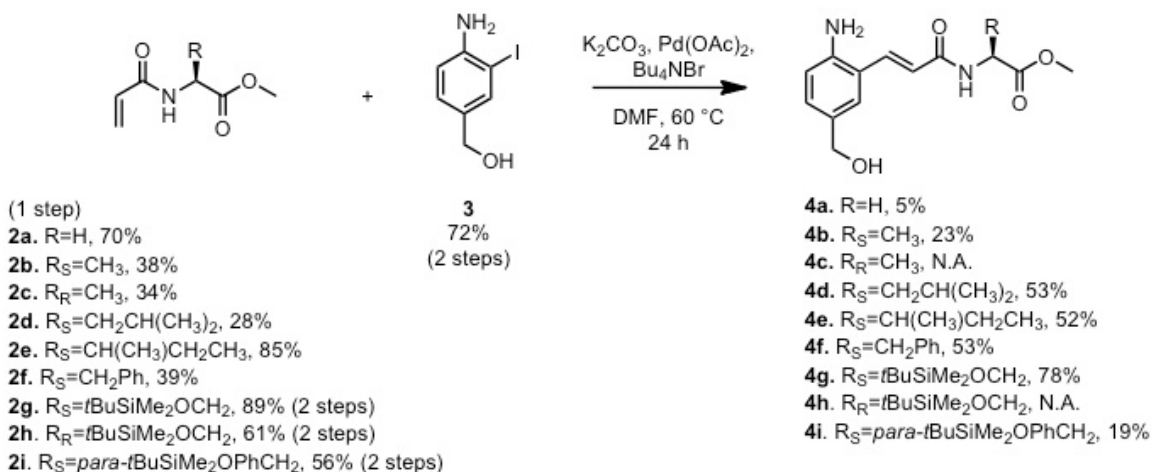
Figure 4-6. Synthetic yields

(1 step)
2a. R=H, 70%
2b. R_S=CH₃, 38%
2c. R_R=CH₃, 34%
2d. R_S=CH₂CH(CH₃)₂, 28%
2e. R_S=CH(CH₃)CH₂CH₃, 85%
2f. R_S=CH₂Ph, 39%
2g. R_S=tBuSiMe₂OCH₂, 89% (2 steps)
2h. R_R=tBuSiMe₂OCH₂, 61% (2 steps)
2i. R_S=para-tBuSiMe₂OPhCH₂, 56% (2 steps)

3
72%
(2 steps)

4a. R=H, 5%
4b. R_S=CH₃, 23%
4c. R_R=CH₃, N.A.
4d. R_S=CH₂CH(CH₃)₂, 53%
4e. R_S=CH(CH₃)CH₂CH₃, 52%
4f. R_S=CH₂Ph, 53%
4g. R_S=tBuSiMe₂OCH₂, 78%
4h. R_R=tBuSiMe₂OCH₂, N.A.
4i. R_S=para-tBuSiMe₂OPhCH₂, 19%

	Solvent System			
	H_2O	DMSO	EtOH	iPrOH
7	S	S	S	S
8	I	I	I	I
3	I	I	I	I

Table 4-1. Preliminary solubility data. I=insoluble, S=solubleafter cooling to rt

Through these results (Table 4-1), we anticipated that adding substituents to the 4-aminobenzylalcohol core structure might favor gelation as it would likely decrease **7**'s high solubility in water. In addition, guided by hypotheses that hydrogen bonding plays a large a role in gelation, we anticipated that appending amino acid side chains may increase the hydrogen bonding capabilities of the substrate. In addition, the carboxylic acid moiety may decrease the insolubility of **8** in protic solvents. However, in general the modifications to direct gel formation are weakly guided hypotheses.[19]

The solubility and potential gelation ability of **4a-i** were tested in a variety of polar, nonpolar, aprotic, and protic solvents. Although our target substrate is the amino acid, we screened the methyl ester derivatives for gelation because Zinić reported dipeptides gelators in water, water/DMSO and water/DMF with ester protecting groups[:20,]

[21] However, in our case, the methyl ester protecting group did not form gels in any of the solvents, and the molecules were extremely insoluble in water and other protic solvents. Therefore hydrolysis conditions were investigated to increase hydrophilicity. However, the methyl group will be necessary for the protection of the acid during polymerization, therefore a post polymerization hydrolysis will be needed to yield the appropriate gelling monomer after depolymerization.

Hydrolysis of the methyl esters and isolation of the resulting acids proved to be challenging due to similar pka of the aryl amine. A number of basic conditions in a variety of solvents were explored and it was discovered that a 5% NaOH solution in MeOH followed by quenching with 1 M AcOH after 24 h and purification by reverse phase chromatography with a C18 column were the best conditions. An alternative workup procedure that eliminates the chromatography step is to bubble with $HCl_{(g)}$ to quench the excess NaOH.
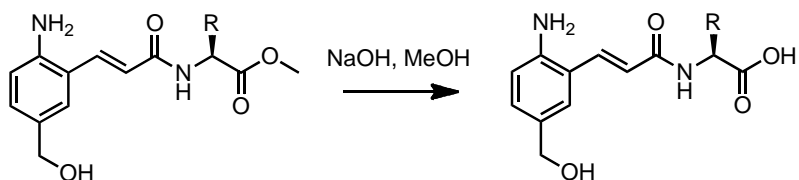
5a. R=H, N.A.
5b. R_S=CH$_3$, 23%
5c. R_R=CH$_3$, N.A.
5d. R_S=CH$_2$CH(CH$_3$)$_2$, 53%
5e. R_S=CH(CH$_3$)CH$_2$CH$_3$, 60%
5f. R_S=CH$_2$Ph, 53%
5g. R_S=*t*BuSiMe$_2$OCH$_2$, N.A.
5h. R_R=*t*BuSiMe$_2$OCH$_2$, N.A.
5i. R_S=*para-t*BuSiMe$_2$OPhCH$_2$, 72%

We initially screened for solvents in which the amino acid derivatives **5b, 5d, 5e, 5f**, and **5i** were highly soluble (i.e., a good solvent) or largely insoluble (i.e., a bad solvent, even when heated). Good solvents were methanol, nanopure water, and dimethyl

sulfoxide.   Bad solvents were isopropyl alcohol, chloroform, methylene chloride, benzene, and acetone. Different solvent ratios and mixtures of the solvents listed above were then screened and none of the combinations lead to gel formation. We made an effort to focused on finding gelation conditions for substrates **5f**, and **5i**, because many gelators have aromatic moieties to increase the number of the π–stacking interactions.[22] These interactions are hypothesized to promote 1D aggregation, which can lead to fiber formation. We then considered varying the pH and cation/anion concentrations, and returned to the starting the methyl-ester protected substrates (**4a-i**) and when we screened **4f** for gelation, we were able to form a 2.7 M gel in 0.1 mL by adding 5.6 M NaOH allowing the solution to react for 5 min then adding 1.4 M of HCl. From this initial hit, we systematically reduced the mass of the starting **4f** ester and increased the total volume of methanol and water.   We were eventually able to lower the cgc to 0.4 M in 3:1 MeOH:H_2O by adding 0.8 M NaOH, allowing the solution to react for 5 min then adding 0.6 M HCl. We anticipated that the initial addition of NaOH deprotected the ester and subsequent addition of HCl formed the carboxylic acid derivative. However, when we directly synthesized the carboxylic acid derivative, we were unable to find conditions that could form gels. Unfortunately these *in situ* deprotection gelation conditions were irreproducible from batch to batch and we were concerned about the unexplained color change during the heating process to produce the gels.   After considering the high concentration at which these molecules formed gels (0.4 M), eventually we realized that these gelators would require DP $= 4 \times 10^7$ to detect nM concentrations of an analyte, which is impractical from a synthetic standpoint.

C. Poly(phthalaldehydes) as the Disassembling Backbone

After extensive efforts at modifying the carbamate monomer into a gelator, we decided to explore an alternative disassembling backbone. Although poly(phthaladehydes) were originally developed and their disassembly studied by Tunitake and coworkers in 1969, Philips and coworkers recently used these polymers to illustrate a smart responsive system.[23] Poly(phthaladehydes) depolymerize into dialdehyde monomers within 15 min, significantly faster than the poly(carbamate)s discussed above. The driving force for depolymerization is due to the property known as ceiling temperature. The ceiling temperature of a polymer is when the rate of polymerization is equal to the rate of depolymerization at a certain concentration.[24] This equilibrium condition is dependent on the concentrations of both the monomer and polymer, and the ceiling temperature is often reported as the maximum temperature at which no polymerization occurs. When the polymer is end-functionalized with an oxygen anion, and is above its ceiling temperature, the rate of depolymerization is faster than the rate of polymerization. Both the temperature of the reaction and the equilibrium between the monomer concentration and the polymer concentration drives polymerization. The equilibrium concentration shifts towards polymer when the reaction is below the ceiling temperature, and above the ceiling temperature the equilibrium shifts, increasing monomer concentration. The ceiling temperature of poly(phthaladehydes) is -43 °C.[24] The next step was to modify the monomer structure to convert it into a gelator. The dialdehyde functional groups of the monomer react during polymerization, therefore we started with a known gelator and functionalized it with dialdehydes, then screened for gelation. The gelator that was chosen, in collaboration with my colleague Danielle

Zurcher, was 2,3-di-*n*-decyloxyanthracene (DDOA) (**9**), which forms gels in a variety of solvents, such as alcohols and alkanes, and the cgc is particularly low in methanol, 0.6 mM.[25] There have been extensive studies to better understand the driving force behind DDOA gel formation, such as elucidating the role of chain length. Alkoxy chain lengths lower than seven saturated carbons did not form gels and the researchers hypothesized that the shorter chains are able to closely aggregate and form crystals rather than gels. Through fluorescence spectroscopy, Bouas-Laurent were able to observe a red-shift during gel formation, indicative of aggregation of the π-moieties. We anticipated that adding aldehyde groups might not drastically affect these driving forces and attempted to synthesize **11** and screen for gelation.[26] A potential synthetic route for 6, 7-bis(decyloxy)anthracene-2,3-dicarbaldehyde (**11**) is the Wittig coupling of 4,5-bis(decyloxy)phthalaldehyde to yield a succinic acid diester that in the presence of base undergoes a Knoevenagel condensation to yield a napthalene-diester derivative.[27] Subsequent reduction and Swern oxidation gives a dialdehyde product that can then again be subjected to 2-(trialkyl-5-phosphanylid-ene)-succinic acid diester, catalytic base and then a reduction and oxidation to give the desired di-*n*-decyloxyanthracene dialdehyde derivative **11** (Figure 4-7).
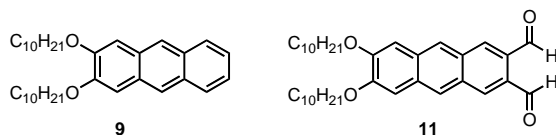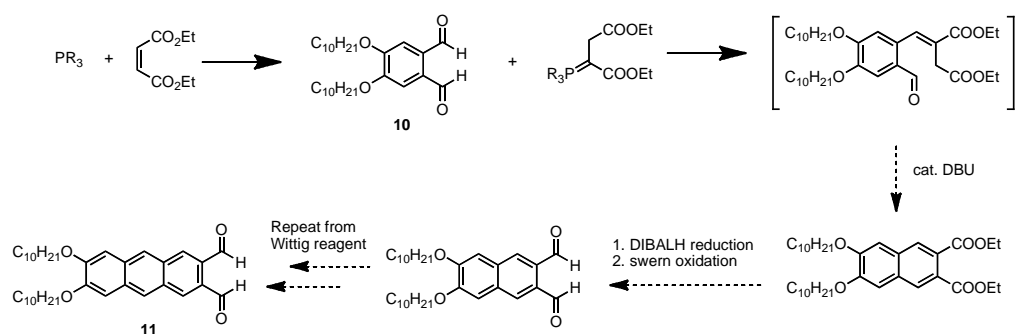
Figure 4-7. Synthesis of target monomer **11**

However this synthesis requires the 5-step synthesis of 4,5-bis(decyloxy)phthaldehyde (**10**) prior to the Wittig reaction. After synthesizing 4,5-bis(decyloxy)phthaldehyde, and screening for gel conditions, Danielle found that the phthaldehyde derivative (**10**) is a gelator at 54 mM in 5:1 acetone:water (v:v). This finding was exciting given our previous challenges in modifying the carbamate monomer; however 54 mM is a high cgc, because we anticipate that it would require a polymer with a DP $= 5 \times 10^6$ to detect nM concentrations of analytes. Therefore, as Danielle worked on developing polymerization conditions, I focused on the synthesis of the napthalene and anthracene derivatives that should enhance the $\pi-\pi$ interactions and potentially decrease the cgc.

D. Exploring Synthetic Routes for 2,3-di-*n*-decyloxyanthracene dialdehyde

Our original synthetic route (Figure 4-7) for **11** through the homo-elongation route required 11 steps, therefore we sought alternative pathways to decrease the potential for material loss, expedite the synthesis, and focus on screening for gelation. Figure 4-8 outlines the proposed synthesis of **11** starting with a Diels-Alder reaction with commercial benzoquinone and 2,3-dimethoxy-1,3-butadiene under toluene at reflux.[28]

Then demethylation of **13** with HBr and acetic acid would yield **14** that could undergo
Williamson ether alkylation conditions to append the alkoxy side-chains.
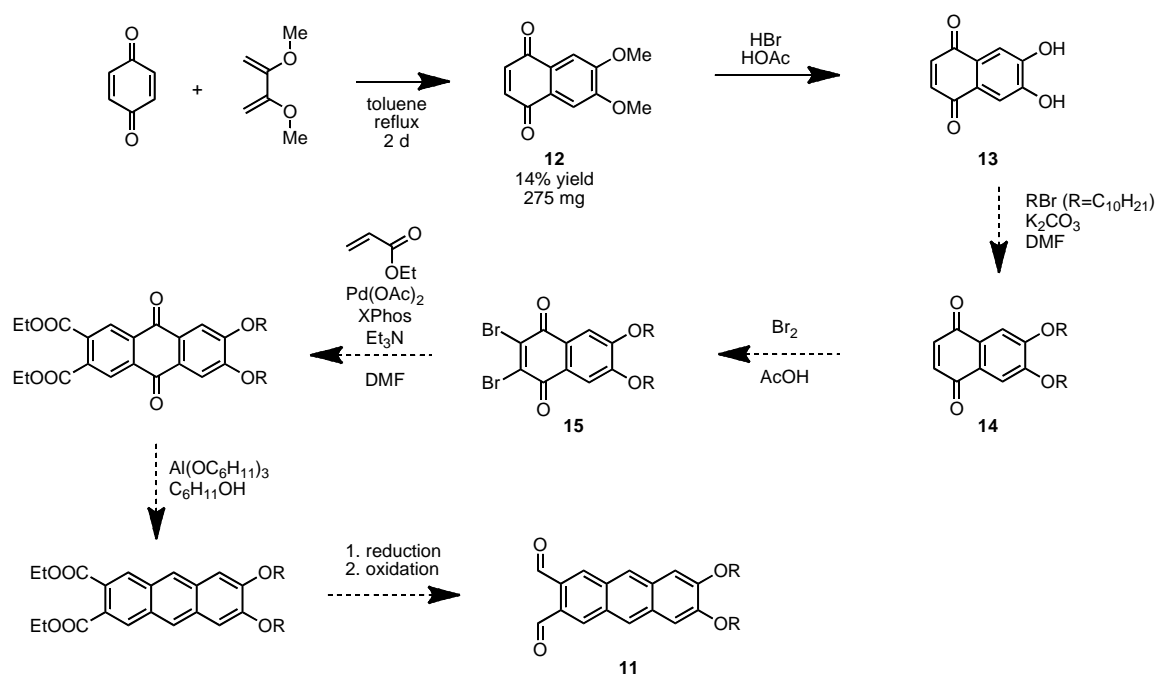
Figure 4-8. Alternative synthesis to **11**

Then bromination of **14** would be necessary to carry out the following Heck-6π-electrocyclization reaction with ethyl acrylate to append the third ring system to generate the anthracene core.[29] Then subsequent Meerwein-Pondorff-Verley[28] reduction of the ketones on the central ring, and reduction and oxidation of the ethyl esters to dialdehydes would provide **11**. The Diels-Alder reaction was successful, although with 14% yield, but subsequent cleavage of the methyl ethers were challenging. Therefore we alternatively tried to directly synthesize **15a** by brominating **12** in the 2 and 3 positions, carry out the Heck-6π-electrocyclization and alkylate at a later stage (Figure 4-9).
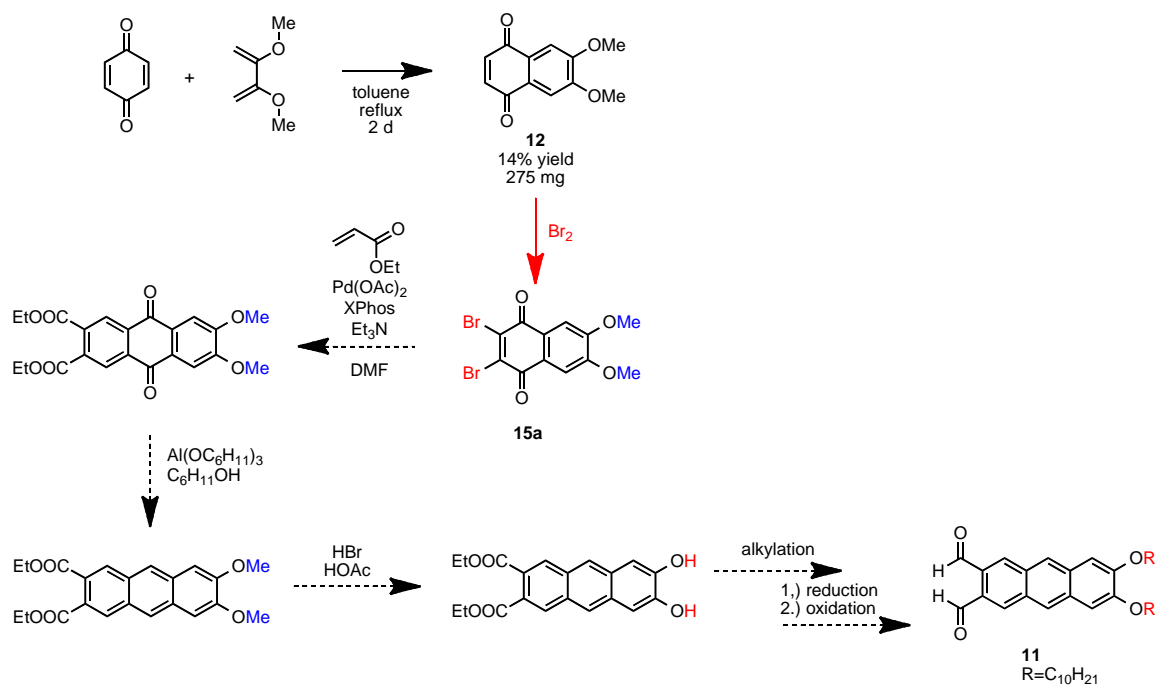
Figure 4-9. Modification of Synthesis of **11**

One advantage of this alternative pathway is that the alkoxy side-chains could be appended later in the synthesis to easily alter this aspect to improve solubility or gelation ability. Although it is expected that the bromination would occur at the 5 and 8 positions on the naphthalene substrate (**12**), we found literature precedent that milder conditions such as *n*-bromosuccinimide in water would preferentially brominate at the 2 and 3 positions.[30]   However, as confirmed by ^{13}C NMR, we only saw products **15b** (Figure 4-10).
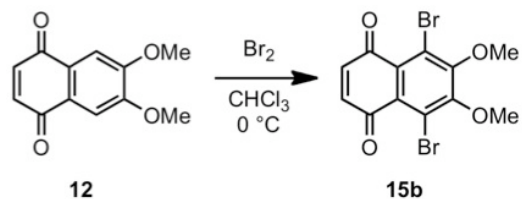
Figure 4-10. Synthesis of **15b**

Therefore our next steps were to dibrominate in the 2 and 3 positions of the starting benzoquinone then undergo the subsequent Diels-Alder reaction. Unfortunately we were only able to synthesize the other regioisomer where the bromines are in the 2 and 6 positions. We alternatively pursued a different retrosynthetic pathway towards **11**.

Figure 4-11 is our alternative synthetic pathway starting with the naphthalene diol. Bromination at the 6 and 7 positions[31] yields **17**, which can then undergo sequential lithiation and acylation to append the aldehyde and yield **19**.
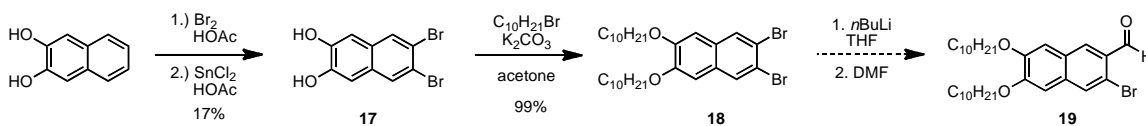
Figure 4-11. Synthetic pathway #2 to **11**

This synthesis would also be two fewer steps than the original Wittig synthetic pathway (Figure 4-7) to reach the naphthalene derivative. Initially we worked with commercial dibromobenzene to find suitable lithiation and acylation conditions. However, after forming a number of biphenyl derivatives using different metalation reagents (*n*BuLi, iPrMgCl*LiCl, Mg(0)), we learned that the anion generated is unstable above -90 °C. The conditions we found for the acylation of dibromobenzene were to add *n*-BuLi to a solution of dibromobenzene in 1:1 THF/toluene (v:v) at -110 °C, stir for 15 min, then added dry DMF at -110 °C. However, we were unable to use these conditions to synthesize **19** because **18** was insoluble at temperatures below -70 °C in a number of THF/ethers/toluene solvent mixtures.

The challenges to install the dialdehydes to the naphthalene derivative lead us to propose an alternative synthetic pathway that could install the dialdehydes through a

convergent synthesis. The following procedure is a future direction for the synthesis of the anthracene derivatives. This new procedure begins with a previous synthetic pathway outlined earlier in Figure 4-8. There are literature examples where after installation of the alkoxy side chains, **14** could undergo a second Diels-Alder reaction with dimethyl 2,3-dimethylenesuccinate (**20**) to afford **21**[32] (Figure 4-12). Then subsequent reduction and oxidation of **21** will yield the target monomer/gelator **11**. There is a literature precedent for the synthesis of dimethyl 2,3-dimethylenesuccinate (**20**) by reacting methyl α-bromoacrylate with Ni(COD)$_2$ in DMF at -78 °C to afford the symmetrical 1,3-diene.[33]
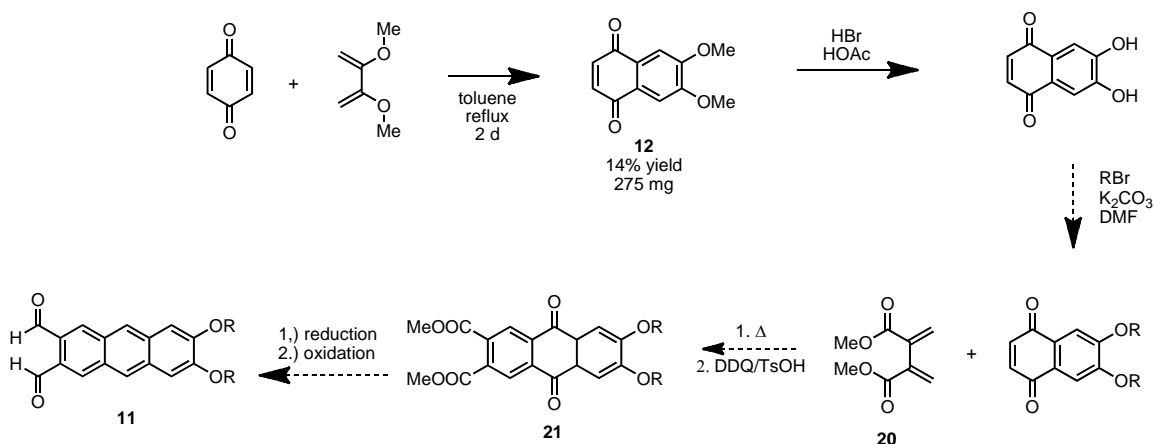
Figure 4-12. Future work: alternative pathway for the synthesis **11**

E. Potential Triggers to Explore

Depolymerizing systems are able to amplify the signal of the trigger release event, but another advantage of the system is that the trigger can be easily exchangeable to develop a sensor array with minimal modification to the entire system. The analyte of interest to us initially while exploring the poly(carbamate) backbone was hydrogen peroxide H$_2$O$_2$ because it is both a byproduct of the improvised explosive triacetone

triperoxide (TATP) and a reagent for the synthesis of the explosive.[34] The use of this explosive by criminals and terrorist groups is rapidly increasing because of its ease in synthesis from commercially available reagents. In the presence of acid, TATP decomposes to generate H_2O_2 and acetone. We hypothesized that a trigger that is sensitive to hydrogen peroxide could be used to initiate depolymerization. In the presence of hydrogen peroxide, aryl borate esters generates an intermediate that upon hydrolysis generates a phenol that then carries out 1,6-elimination and decarboxylation reactions for the cascade-release of gelators. The deprotection followed by the cascade release that we envision is illustrated in Figure 4-13. Shabat and coworkers developed a similar system where an aryl borate ester is cleaved in the presence of hydrogen peroxide and initiates the disassembly and release of the dendrimer's building blocks.[35]
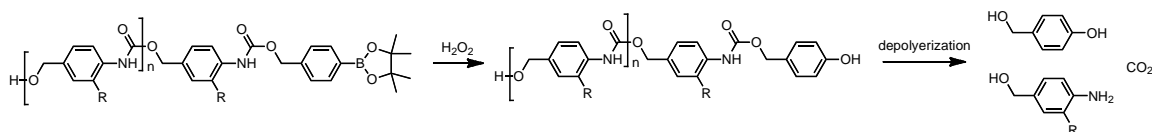
Figure 4-13. Deprotection of aryl borate esters by H_2O_2 to initiate depolymerization

Although we have transitioned from the poly(carbamate) disassembling backbone to poly(phthalaldehydes) as the disassembling backbone, we anticipate that capping the polymer with aryl borate ester to detect H_2O_2 would still be possible (Figure 4-14). These depolymerizing systems have the potential to quickly design indicators for a wide range of analytes by simply replacing the trigger.
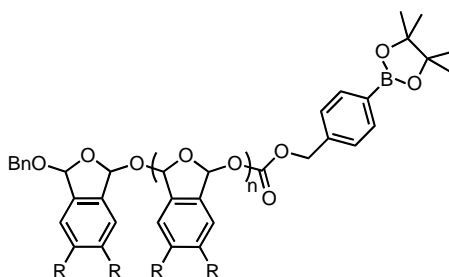
Figure 4-14. Poly(phthalaldehyde) functionalized with H_2O_2 sensitive trigger.

F. Conclusions

Although we were unable to find a gelator for the initial poly(aryl)carbamate backbone, we are excited for the potential to use poly(phthalaldehydes) to demonstrate our analyte-triggered depolymerization and amplification system. The unique aspect of this system is that the positive signal or analyte-detection method would be the formation of a stable gel. After finding a gelator that is polymerizable, there are several next steps to fully develop the system. First is to synthesize the polymer and my colleague, Danielle Zurcher is making significant progress on that aspect. Second is to decrease the cgc of the monomer, this proved to be a very difficult task due to the limited solubility of the scaffold; however, we have presented several potential synthetic methods to attempt to work around the solubility issue. To complete the system, we would append an analyte-sensitive triggers and illustrate depolymerization and subsequent gelation when the trigger is released. A significant advantage of this system over other analyte-triggered gelations is that it is flexible in the type of analyte it can detect. For a new analyte, the entire system can essentially be kept consistent and the trigger would only need to be exchanged.

G. Experimental Section

G.1. Materials

Flash chromatography was performed on SiliCycle silica gel (40-63 μm) and thin layer chromatography was performed on Merck TLC plates pre-coated with silica gel 60 F254. Diisobutylaluminum hydride (1.0 M in hexanes) was purchased in 100 mL quantities from Aldrich. Pd(OAc)$_2$ was purchased from Strem. Dibutyltin dilaurate was purchased from TCI America. All reagent grade materials and solvents were purchased from Aldrich, Acros, EMD, or Fisher and used without further purification unless otherwise noted. THF was dried using a solvent purification system in which pressurized nitrogen gas circulates solvent through a series of filter columns to remove moisture. All glassware was oven-dried at 120 °C for at least 1 h before use.

G.2. Representative Procedure for Gel Screening

In a typical gelation experiment, a small amount of material, approximately 10 mg was added to a 4 mL vial, 0.5 mL of bad solvent was added, capped, heated to the solvent's boiling point to dissolve the compound, and then allowed to cool to room temperature. When the solution was turbid and viscous but the solvent did not gel as indicated by the invert-vial test, more material was added (approximately 10 mg) and the heat/cool process was repeated. If upon cooling to room temperature, the compound precipitated out of solution, 0.1 mL of good solvent was added as a means of slowing the

process of crystallization and potentially induce high-aspect ratio fiber formation and gelation, and again the heat/cool process was repeated.

G.3. Synthetic Procedures

G.3.1 Ethyl-4-amino-3-iodobenzoate (**6**)[18]

A 100 mL round-bottom flask was equipped with a stir bar, ethyl-4-aminobenzoate (5.0 g, 0.03 mol, 1.0 equiv) and AcOH (58.5 mL) and H_2O (6.5 mL). $NaIO_4$ (6.4 g, 0.03 mol, 1.0 equiv), NaCl (5.6 g, 0.06 mol, 2.0 equiv), and KI (5.1 g, 0.03 mol, 1.0 equiv) were then added. The reaction mixture was stirred for 12 h at rt. The deep brown solution was diluted with EtOAc (60 mL), washed with brine (3 x 75 mL), sat. $Na_2S_2O_3$ (3 x 75 mL) and sat. Na_2CO_3 (3 x 75 mL). The combined organic layers were dried over $MgSO_4$, filtered, and concentrated in vacuo. The crude product was purified by column chromatography using 70/30 hexanes/EtOAc as the eluent to give 6.9 g of product as a white solid (78% yield). Figure 4-15, page 84.

G.3.2 (4-amino-3-iodophenyl)methanol (**3**)

An oven-dried 25 mL Schlenk flask was equipped with stir bar and septum, evacuated, and cooled to rt under vacuum, and filled with N_2. Ethyl-4-amino-3-iodobenzoate (**6**) (0.7 g, 2.0 mmol, 1.0 equiv) and anhydrous THF (7 mL) were added to the flask. The solution was then cooled to 0 °C and DIBAL-H (7.0 mL, 1.0 M, 3.0 equiv) was added via syringe over 30 min. The reaction was allowed to warm to rt and stirred at

rt for 2 h. Additional THF was added to keep reaction as a solution. The thick yellow solution was quenched dropwise with H_2O (8 mL). The mixture was diluted with THF and celite was added to complex with the aluminum byproducts and stirred for 45 min. The reaction was filtered, the solid rinsed with THF, and concentrated in vacuo. The crude product was purified by column chromatography using 75/25 ether/hexanes as the eluent to give 0.4 g as a yellow solid (70% yield). Figure 4-16, page 85.

G.3.3 (*E*)-*tert*-butyl 3-(2-amino-5-(hydroxymethyl)phenyl)acrylate (**8**)

A 25 mL round-bottom flask was flushed with N_2 and (4-amino-3-iodophenyl)methanol (**3**) (0.1 g, 0.5 mmol, 1.0 equiv) was dissolved in anhydrous DMF (1 mL). $Pd(OAc)_2$ (5.0 mg, 0.02 mmol, 0.05 equiv), Bu_4NBr (0.19 g, 0.59 mmol, 1.3 equiv), K_2CO_3 (0.3 g, 2.0 mmol, 5.0 equiv) and tertbutyl acrylate (0.11 mL, 0.72 mmol, 1.5 equiv) was added to the flask and the reaction mixture was stirred for 12 h at 60 °C under N_2. The reaction was cooled to rt and diluted with EtOAc (15 mL) and washed with brine (2 x 10 mL), dried with $MgSO_4$, filtered and concentrated in vacuo. The crude product was purified by column chromatography using an eluent gradient from hexanes to 30/70 EtOAc/hexanes as the eluent to give 125 mg of a white solid (84% yield).Figure 4-17, page 86.

G.3.4 (*E*)-*tert*-butyl-3-(5-(hydroxymethyl)-2-((phenoxycarbonyl)amino)phenyl)acrylate.

In a 100 mL round-bottom flask, distilled triethylamine (0.33 mL, 2.3 mmol, 1.5 equiv) was added via syringe to a solution of (*E*)-*tert*-butyl 3-(2-amino-5-

(hydroxymethyl)phenyl)acrylate (0.4 g, 2.0 mmol, 1.0 equiv) in THF (40 mL). Then phenylchloroformate (0.32 mL, 1.7 mmol, 1.1 equiv) was added via syringe. The reaction mixture was stirred for 12 h at rt. The cloudy, pale yellow solution was diluted with EtOAc (25 mL) and washed with sat. NH_2Cl (3 x 50 mL), and the combined organic layers were dried over $MgSO_4$, filtered, and concentrated in vacuo. The crude product was purified by column chromatography using 75/25 ether/hexanes as the eluent to give 172 mg as a clear film (30% yield).

G.3.5 General Procedure for Polycarbamate

An oven-dried 4 mL conical vial was equipped with stir bar and septum, cooled to rt under vacuum, and filled with N_2. (*E*)-*tert*-butyl 3-(5-(hydroxymethyl)-2-((phenoxycarbonyl)amino)phenyl)acrylate (0.2 mg, 0.5 mmol, 1.0 equiv) was transferred as a solution in anhydrous toluene (1.0 mL) and equilibrated at 110 °C under N_2 for 10 min. Tin catalyst (28 μL, 0.05 mmol, 0.1 equiv) was added and stirred for 15 min. Then 4-hydroxy-2-butanone (40 μL, 0.47 mmol, 1.0 equiv) was added and allowed reaction to cool to rt. Reaction was added dropwise to a solution MeOH (50 mL), solution turns a cloudy white but precipitates were not large enough to collect by centrifuge. Concentrated the supernatant. Crude product verified by NMR.

G.3.6 Methyl 2-acrylamidoacetate. (**2a**)

An oven-dried 100 mL round-bottom flask equipped with stir bar and septum, cooled to rt under vacuum, and filled with N_2. Glycene methyl ester hydrochloride (5 g,

0.03 mol, 1 equiv), anhydrous CH_2Cl_2 (50 mL) and triethylamine (10 mL, 0.08 mol, 2 equiv) were added to the flask. The solution was then cooled to 0 °C and acryloyl chloride (3.4 ml, 0.045 mmol, 1.1 equiv) was added as a solution in CH_2Cl_2 (10 mL) dropwise via syringe. The reaction was stirred vigorously and allowed to warm to rt over 12 h. The crude reaction mixture was concentrated in vacuo, diluted with EtOAc (50 mL) and the resulting precipitate was filtered and washed with EtOAc. Combined organic layers were washed with 0.5 M $NaHSO_4$ (2 x 50 mL), 5% $NaHCO_3$ (2 x 50 mL), brine (1 x 50 mL), dried with $MgSO_4$, filtered and concentrated in vacuo. Extract from aqueous layer excess with CH_2Cl_2, and methyl 2-acrylamidoacetate was obtained after column chromatography using EtOAc as the eluent to give a yellow liquid (3 g, 70% yield).

G.3.7 (*S*)-methyl 2-acrylamidopropanoate (**2b**)

An oven-dried 100 mL round-bottom flask equipped with stir bar and septum, cooled to rt under vacuum, and filled with N_2. L-alanine methyl ester hydrochloride (3 g, 2 mmol, 1 equiv), anhydrous CH_2Cl_2 (20 mL) and triethylamine (6.3 mL, 4.5 mmol, 2.1 equiv) were added to the flask. The solution was then cooled to 0 °C and acryloyl chloride (1.8 ml, 2.3 mmol, 1.1 equiv) was added as a solution in CH_2Cl_2 (10 mL) dropwise via syringe. The reaction was stirred vigorously and allowed to warm to rt over 12 h. The crude reaction mixture was concentrated in vacuo, diluted with EtOAc (50 mL) and the resulting precipitate was filtered and washed with EtOAc. Combined organic layers were washed with 0.5 M $NaHSO_4$ (2 x 50 mL), 5% $NaHCO_3$ (2 x 50 mL), brine (1 x 50 mL), dried with $MgSO_4$, filtered and concentrated in vacuo. The crude product was purified by column chromatography using 50/50 EtOAc/hexanes, thin layer

chromatography plates were visualized using potassium permanganate stain, to give 1.3 g as a pale yellow solid (38% yield). Figure 4-19, page 88

G.3.8 (*R*)-ethyl 2-acrylamidopropanoate (**2c**)

An oven-dried 100 mL round-bottom flask equipped with stir bar and septum, cooled to rt under vacuum, and filled with N_2. D-alanine ethyl ester hydrochloride (0.5 g, 2 mmol, 1 equiv), anhydrous CH_2Cl_2 (5 mL) and triethylamine (1 mL, 9 mmol, 2 equiv) were added to the flask. The solution was then cooled to 0 °C and acryloyl chloride (0.3 ml, 3 mmol, 1 equiv) was added as a solution in CH_2Cl_2 (3 mL) dropwise via syringe. The reaction was stirred vigorously and allowed to warm to rt over 12 h. The crude reaction mixture was concentrated in vacuo, diluted with EtOAc (50 mL) and the resulting precipitate was filtered and washed with EtOAc. Combined organic layers were washed with 0.5 M $NaHSO_4$ (2 x 50 mL), 5% $NaHCO_3$ (2 x 50 mL), brine (1 x 50 mL), dried with $MgSO_4$, filtered and concentrated in vacuo. (*R*)-ethyl 2-acrylamidopropanoate was obtained after column chromatography using 50/50 EtOAc/hexanes (560 mg, 34% yield). Figure 4-20, page 89.

G.3.9 (S)-methyl 2-acrylamido-4-methylpentanoate (**2d**) [17]

An oven-dried 25 mL Schlenk flask was equipped with stir bar and septum, cooled to rt under vacuum, and filled with N_2. L-lucine methyl ester hydrochloride (0.5 g, 3.0 mmol, 1.0 equiv), anhydrous CH_2Cl_2 (2 mL) and triethylamine (0.8 mL, 6.0 mmol, 2.0 equiv) were added to the flask. The solution was then cooled to 0 °C and acryloyl chloride (0.30 ml, 2.9 mmol, 1.1 equiv) was added as a solution in CH_2Cl_2 (3 mL)

dropwise via syringe. The reaction was stirred vigorously and allowed to warm to rt over 12 h. The crude reaction mixture was concentrated in vacuo, diluted with EtOAc (20 mL) and the resulting precipitate was filtered and washed with EtOAc. Combined organic layers were washed with 0.5 M $NaHSO_4$ (2 x 20 mL), 5% $NaHCO_3$ (2 x 20 mL), brine (1 x 20 mL), dried with $MgSO_4$, filtered and concentrated in vacuo. The crude product was purified by column chromatography using 50/50 EtOAc/hexanes, thin layer chromatography plates were visualized using potassium permanganate stain, to give 150 mg as a slightly yellow solid (28% yield). Figure 4-21, page 90.

G.3.10 (2*S*,3*R*)-methyl 2-acrylamido-3-methylpentanoate (**2e**)

An oven-dried 50 mL Schlenk flask was equipped with stir bar and septum, cooled to rt under vacuum, and filled with N_2. L-isolucine methyl ester hydrochloride (0.2 g, 3 mmol, 1 equiv), anhydrous CH_2Cl_2 (10 mL) and triethylamine (3.2 mL, 0.023 mol, 2.1 equiv) were added to the flask. The solution was then cooled to 0 °C and acryloyl chloride (0.96 ml, 0.012 mol, 1.1 equiv) was added as a solution in CH_2Cl_2 (10 mL) dropwise via syringe. The reaction was stirred vigorously and allowed to warm to rt over 12 h. The crude reaction mixture was concentrated in vacuo, diluted with EtOAc (20 mL) and the resulting precipitate was filtered and washed with EtOAc. Combined organic layers were washed with 0.5 M $NaHSO_4$ (2 x 20 mL), 5% $NaHCO_3$ (2 x 20 mL), brine (1 x 20 mL), dried with $MgSO_4$, filtered and concentrated in vacuo. (2*S*,3*R*)-methyl 2-acrylamido-3-methylpentanoate was obtained after column chromatography using 50/50 EtOAc/hexanes as a yellow solid (1.7 g, 85% yield). Figure 4-22, page 91.

G.3.11 (*S*)-methyl 2-acrylamido-3-phenylpropanoate (**2f**)

An oven-dried 100 mL round-bottom flask equipped with stir bar and septum, cooled to rt under vacuum, and filled with N_2. L-phenylalanine methyl ester hydrochloride (1.0 g, 5.0 mmol, 1.0 equiv), anhydrous CH_2Cl_2 (8 mL) and triethylamine (1.2 mL, 9.7 mmol, 2.1 equiv) were added to the flask. The solution was then cooled to 0 °C and acryloyl chloride (0.41 ml, 4.8 mmol, 1.1 equiv) was added as a solution in CH_2Cl_2 (2 mL) dropwise via syringe. The reaction was stirred vigorously and allowed to warm to rt over 12 h. The reaction mixture was diluted with CH_2Cl_2, washed concentration HCl (2 x 40 mL), sat. $NaHCO_3$ (2 x 40 mL), brine (2 x 40 mL), the combined organic layers dried with $MgSO_4$ and concentrated in vacuo. The crude product was purified by column chromatography using 50/50 EtOAc/hexanes, thin layer chromatography plates were visualized using potassium permanganate stain, to give 430 mg as a pale yellow solid (39% yield). Figure 4-23, page 92.

G.3.12 (*S*)-methyl 2-acrylamido-3-((*tert*-butyldimethylsilyl)oxy)propanoate (**2g**)

Prior to synthesizing (*S*)-methyl 2-acrylamido-3-((*tert*-butyldimethylsilyl)oxy)propanoate, (*S*)-methyl 2-amino-3-hydroxypropanoate hydrochloride will need to be protected by *tert*-butyldimethylsilyl protecting group[36], this is done by combining imidazole (220 mg, 3.2 mmol, 2.5 equiv), DMF (1 mL), (*S*)-methyl 2-amino-3-hydroxypropanoate hydrochloride (200 mg, 1 mmol, 1 equiv) and *tert*-butyldimethylsilyl chloride (230 mg, 1.5 mmol, 1.2 equiv) into a 5 mL pear flask and stir

over night at rt. The reaction mixture was diluted with EtOAc (10 mL), washed with H_2O (2 x 10 mL), washed with brine (2 x 10 mL), the combined organic layers were dried with $MgSO_4$, filtered, and concentrated in vacuo. The crude product, (*S*)-methyl 2-amino-3-hydroxypropanoate hydrochloride was purified by column chromatography using 75/2 EtOAc/hexanes, thin layer chromatography plates were visualized using a potassium permanganate stain to give 74 mg of a yellow liquid (25% yield). Then this product was carried to the synthesis of (*S*)-methyl 2-acrylamido-3-((*tert*-butyldimethylsilyl)oxy)propanoate. In an oven-dried 25 mL round-bottom flask equipped with stir bar and septum, cooled to rt under vacuum, and filled with N_2. (*S*)-methyl 2-amino-3-hydroxypropanoate (70 mg, 3 mmol, 1 equiv), anhydrous CH_2Cl_2 (1 mL) and triethylamine (90 μL, 6 mmol, 2 equiv) were added to the flask. The solution was then cooled to 0 °C and acryloyl chloride (30 μl, 3 mmol, 1 equiv) was added as a solution in CH_2Cl_2 (1 mL) dropwise via syringe. The reaction was stirred vigorously and allowed to warm to rt over 12 h. The crude reaction mixture was concentrated in vacuo, diluted with EtOAc (50 mL) and the resulting precipitate was filtered and washed with EtOAc. Combined organic layers were washed with 0.5 M $NaHSO_4$ (2 x 10 mL), 5% $NaHCO_3$ (2 x 10 mL), brine (1 x 10 mL), dried with $MgSO_4$, filtered and concentrated in vacuo. The crude product was purified by column chromatography using 25/75 EtOAc/hexanes, thin layer chromatography plates were visualized using potassium permanganate stain, to give 77 mg (83% yield).

G.3.13 (*S*)-methyl-2-acrylamido-3-(4-(*tert*-butyldimethylsilyl)phenoxy)propanoate (**2h**)

Prior to synthesizing (*S*)-methyl-2-acrylamido-3-(4-(*tert*-butyldimethylsilyl)phenoxy)propanoate, (*S*)-methyl 2-amino-3-(4-hydroxyphenyl)propanoate hydrochloride will need to be protected by *tert*-butyldimethylsilyl protecting group[37], this is done by combining imidazole (1.5 g, 0.21 mol, 2.5 equiv), CH_3CN (8 mL), (*S*)-methyl 2-amino-3-(4-hydroxyphenyl)propanoate hydrochloride (2 g, 9 mmol, 1 equiv) and *tert*-butyldimethylsilyl chloride (1.6 g, 0.010 mol, 1.2 equiv) dropwise into a 25 mL round-bottom flask and stir vigorously for 12 h at 45 °C. The reaction mixture was diluted with EtOAc (20 mL), washed with H_2O (2 x 20 mL), washed with brine (2 x 20 mL), the combined organic layers were dried with $MgSO_4$, filtered, and concentrated in vacuo. The crude product, (*S*)-methyl 2-amino-3-(4-hydroxyphenyl)propanoate hydrochloride was purified by column chromatography using 75/2 EtOAc/hexanes, thin layer chromatography plates were visualized using a potassium permanganate stain to give 2.7 g (86% yield). Then this product was carried to the synthesis of (*S*)-methyl-2-acrylamido-3-(4-(*tert*-butyldimethylsilyl)phenoxy)propanoate. In an oven-dried 25 mL round-bottom flask equipped with stir bar and septum, cooled to rt under vacuum, and filled with N_2. (*S*)-methyl 2-amino-3-(4-hydroxyphenyl)propanoate hydrochloride (300 mg, 1 mmol, 1 equiv), anhydrous CH_2Cl_2 (3 mL) and triethylamine (0.3 mL, 2 mmol, 2 equiv) were added to the flask. The solution was then cooled to 0 °C and acryloyl chloride (90 μl, 1 mmol, 1 equiv) was added as a solution in CH_2Cl_2 (2 mL) dropwise via syringe. The reaction was stirred vigorously and allowed to warm to rt over 12 h. The crude reaction mixture was concentrated in vacuo, diluted with EtOAc (50 mL) and the resulting precipitate was filtered and washed with EtOAc. Combined organic layers were washed with 0.5 M $NaHSO_4$ (2 x 10 mL), 5% $NaHCO_3$ (2 x 10 mL), brine (1

x 10 mL), dried with MgSO$_4$, filtered and concentrated in vacuo. The crude product was purified by column chromatography using 50/50 EtOAc/hexanes, thin layer chromatography plates were visualized using potassium permanganate stain, to give 330 mg (85% yield).

G.3.14 (*E*)-methyl 2-(3-(2-amino-5-(hydroxymethyl)phenyl)acrylamido)acetate (**4a**)

An oven-dried 25 mL Schneck flask was cooled to rt under vacuum and flushed with N$_2$ and (4-amino-3-iodophenyl)methanol (0.5 g, 2 mmol, 1.0 equiv) was dissolved in anhydrous DMF (10 mL). Pd(OAc)$_2$ (50 mg, 0.2 mmol, 0.1 equiv), Bu$_4$NBr (0.84 g, 2.5 mmol, 1.3 equiv), K$_2$CO$_3$ (1.4 g, 10.0 mol, 5.1 equiv) and methyl 2-acrylamidoacetate (0.43 g, 3.1 mmol, 1.5 equiv) was added to the flask and the reaction mixture was stirred for 12 h at 60 °C under N$_2$. The reaction was cooled to rt and diluted with EtOAc (15 mL) and washed with brine (2 x 10 mL), dried with MgSO$_4$, filtered and concentrated in vacuo. However, we hypothesize that much of the product was lost due to its high volatility, 20 mg (5% yield).

G.3.15 (*S*,*E*)-methyl-2-(3-(2-amino-5-(hydroxymethyl)phenyl)acrylamido)propanoate (**4b**)

A 25 mL Schneck flask was flushed with N$_2$ and (4-amino-3-iodophenyl)methanol (0.1 g, 0.04 mmol, 1.0 equiv) was dissolved in anhydrous DMF (1 mL). Pd(OAc)$_2$ (5.0 mg, 0.02 mmol, 0.05 equiv), Bu$_4$NBr (0.18 g, 0.59 mmol, 1.3 equiv), K$_2$CO$_3$ (0.3 g, 2.0 mmol, 5.0 equiv) and (*S*)-methyl 2-acrylamidopropanoate (0.11

g, 0.59 mmol, 1.5 equiv) was added to the flask and the reaction mixture was stirred for 12 h at 60 °C under N_2. The reaction was cooled to rt and diluted with EtOAc (15 mL) and washed with brine (2 x 10 mL), dried with $MgSO_4$, filtered and concentrated in vacuo. The crude product was purified by column chromatography using an eluent gradient from hexanes to 30/70 EtOAc/hexanes as the eluent to give 30 mg of a golden yellow solid (23% yield). Figure 4-24, page 93.

G.3.16 (*S*,*E*)-methyl-2-(3-(2-amino-5-(hydroxymethyl)phenyl)acrylamido)-4-methylpentanoate (**4d**)

A 25 mL Schneck flask was flushed with N_2 and (4-amino-3-iodophenyl)methanol (130 mg, 0.52 mmol, 1.0 equiv) was dissolved in anhydrous DMF (1 mL). $Pd(OAc)_2$ (5.9 mg, 0.03 mmol, 0.05 equiv), Bu_4NBr (216 mg, 0.65 mmol, 1.25 equiv), K_2CO_3 (359 mg, 2.6 mmol, 5.0 equiv) and (S)-methyl 2-acrylamido-4-methylpentanoate (155 g, 0.78 mmol, 1.5 equiv) was added to the flask and the reaction mixture was stirred for 36 h at 60 °C under N_2. The reaction was cooled to rt and diluted with EtOAc (15 mL) and washed with brine (2 x 10 mL), dried with $MgSO_4$, filtered and concentrated in vacuo. The crude product was purified by column chromatography using 25/75 EtOAc/hexanes as the eluent to give 167 mg of a yellow solid (53% yield). Figure 4-25, page 94.

G.3.17 (2*S*,3*R*)-methyl 2-((*E*)-3-(2-amino-5-(hydroxymethyl)phenyl)acrylamido)-3-methylpentanoate (**4e**)

An oven-dried 25 mL Schneck flask cooled to rt under vacuum and flushed with N$_2$, and (4-amino-3-iodophenyl)methanol (0.1 g, 0.4 mmol, 1.0 equiv) was dissolved in anhydrous DMF (1 mL). Pd(OAc)$_2$ (9 mg, 0.04 mmol, 0.05 equiv), Bu$_4$NBr (200 mg, 0.49 mmol, 1.3 equiv), K$_2$CO$_3$ (300 mg, 10 mmol, 5.0 equiv) and (2S,3R)-methyl 2-acrylamido-3-methylpentanoate (120 mg, 0.59 mmol, 1.5 equiv) was added to the flask and the reaction mixture was stirred for 12 h at 60 °C under N$_2$. The reaction was cooled to rt and diluted with EtOAc (15 mL) and washed with brine (2 x 10 mL), dried with MgSO$_4$, filtered and concentrated in vacuo. The crude product was purified by column chromatography using 75/25 EtOAc/hexanes as the eluent to give 67 mg of a yellow solid (52% yield). Figure 4-26, page 95.

G.3.18 (S,E)-methyl-2-(3-(2-amino-5-(hydroxymethyl)phenyl)acrylamido)-3-phenylpropanoate (**4f**)

In a 25 mL Schneck flask was flushed with N$_2$ (4-amino-3-iodophenyl)methanol (0.5 g, 2.0 mmol, 1.0 equiv) was dissolved in anhydrous DMF (1 mL). Pd(OAc)$_2$ (0.05 g, 0.2 mmol, 0.05 equiv), Bu$_4$NBr (0.85 g, 2.5 mmol, 1.3 equiv), K$_2$CO$_3$ (1.3 g, 10 mmol, 5.0 equiv) and (S)-methyl 2-acrylamido-3-phenylpropanoate (0.7X g, 3.0 mmol, 1.5 equiv) was added to the flask and the reaction mixture was stirred for 12 h at 60 °C under N$_2$. The reaction was cooled to rt and diluted with EtOAc (15 mL) and washed with brine (2 x 10 mL), dried with MgSO$_4$, filtered and concentrated in vacuo. The crude product was purified by column chromatography using a gradient from 50/50 to 75/25 EtOAc/hexanes as the eluent to give 380 mg of a yellow solid (53% yield). Figure 4-27, page 96.

78

G.3.19 (*S,E*)-methyl   2-(3-(2-amino-5-(hydroxymethyl)phenyl)acrylamido)-3-((*tert*-butyldimethylsilyl)oxy)propanoate (**4g**)

In an oven-dried 25 mL Schneck flask cooled to rt under vacuum and flushed with N$_2$, (4-amino-3-iodophenyl)methanol (0.3 g, 1 mmol, 1.0 equiv) was dissolved in anhydrous DMF (6 mL). Pd(OAc)$_2$ (30 mg, 0.1 mmol, 0.1 equiv), Bu$_4$NBr (500 mg, 2 mmol, 2 equiv), K$_2$CO$_3$ (900 mg, 6 mmol, 5 equiv) and (*S*)-methyl 2-acrylamido-3-((*tert*-butyldimethylsilyl)oxy)propanoate (550 mg, 1.9 mmol, 1.5 equiv) was added to the flask and the reaction mixture was stirred for 12 h at 60 °C under N$_2$.   The reaction was cooled to rt and diluted with EtOAc (20 mL) and washed with brine (2 x 20 mL), dried with MgSO$_4$, filtered and concentrated in vacuo. The crude product was purified by column chromatography using 75/25 EtOAc/hexanes as the eluent to give 54 mg of a yellow solid (78% yield). Figure 4-28, page 97.

G.3.20 (*S,E*)-methyl   2-(3-(2-amino-5-(hydroxymethyl)phenyl)acrylamido)-3-(4-((*tert*-butyldimethylsilyl)oxy)phenyl)propanoate (**4h**)

In an oven-dried 25 mL Schneck flask, cooled to rt under vacuum, and flushed with N$_2$, (4-amino-3-iodophenyl)methanol (0.5 g, 2 mmol, 1.0 equiv) was dissolved in anhydrous DMF (10 mL). Pd(OAc)$_2$ (50 mg, 0.2 mmol, 0.1 equiv), Bu$_4$NBr (0.84 g, 2.5 mmol, 1.3 equiv), K$_2$CO$_3$ (1.4 g, 10.0 mol, 5.1 equiv) and (*S*)-methyl 2-acrylamido-3-(4-((*tert*-butyldimethylsilyl)oxy)phenyl)propanoate (1.01 g, 3.02 mmol, 1.51 equiv) was added to the flask and the reaction mixture was stirred for 12 h at 60 °C under N$_2$.   The reaction was cooled to rt and diluted with EtOAc (50 mL), washed with water (50 mL),

and washed with brine (2 x 50 mL), dried with MgSO$_4$, filtered, mixed with decolorizing carbon, filtered with celite, washed with EtOAc and concentrated in vacuo. The crude product was purified by column chromatography using a gradient from 40/60 to 75/25 EtOAc/hexanes as the eluent to give 40 mg of the silyl protected product (5% yield), and 140 mg of the desilylated product (19% yield). Figure 4-29, page 98.

G.3.21 (2*S*,3*R*)-2-((*E*)-3-(2-amino-5-(hydroxymethyl)phenyl)acrylamido)-3-methylpentanoic acid (**5e**)

In a 20 mL vial with (2*S*,3*R*)-methyl 2-((*E*)-3-(2-amino-5-(hydroxymethyl)phenyl)acrylamido)-3-methylpentanoate (0.1 mg, 0.3 mmol, 1.0 equiv), 1.1 equiv of 5% NaOH (0.5 mL) in MeOH was added and stirred for 4 h. After, 0.5 mL of 1 M AcOH was added dropwise until solution turned cloudy, pH = 4/5, filtered and concentrated filtrate. The product was precipitated and washed with CH$_2$Cl$_2$, filtered again, and the solid dissolved with MeOH. The product was dried in vacuo yielding 50 mg (60% yield).

G.3.22 (*S*,*E*)-2-(3-(2-amino-5-(hydroxymethyl)phenyl)acrylamido)-3-phenylpropanoic acid (**5f**)

In a 20 mL vial with (*S*,*E*)-methyl-2-(3-(2-amino-5-(hydroxymethyl)phenyl)acrylamido)-3-phenylpropanoate (0.1 mg, 0.3 mmol, 1.0 equiv), 1.1 equiv of 5% NaOH (0.5 mL) in MeOH was added and stirred for 4 h. After, 0.5 mL of 1 M AcOH was added dropwise until solution turned cloudy, pH = 4/5. The product

was precipitated and washed with CH_2Cl_2, filtered again, and the solid dissolved with MeOH. The product was dried in vacuo yielding 80 mg (80% yield).

G.3.23 (*S*,*E*)-2-(3-(2-amino-5-(hydroxymethyl)phenyl)acrylamido)-3-(4-hydroxyphenyl)propanoic acid (**5i**)

In a 20 mL vial with (*S*,*E*)-methyl 2-(3-(2-amino-5-(hydroxymethyl)phenyl)acrylamido)-3-(4-hydroxyphenyl)propanoate (0.5 mg, 0.1 mmol, 1 equiv), 1.1 equiv of 5% NaOH (0.5 mL) in MeOH was added and stirred for 4 h. After, 0.5 mL of 1 M AcOH was added dropwise until precipitate formed, pH=4/5. The product was filtered and washed with CH_2Cl_2 and dried in vacuo yielding 30 mg (72% yield).

G.3.24 6,7-dimethoxynaphthalene-1,4-dione (**12**)[28]

A 10 mL pear flask with condenser was purged with N_2 and benzoquinone (1.01 g, 9.25 mmol, 1 equiv.) and dry toluene (2 mL) was added to the flask and heated to 140 °C. Then, 2,3-dimethoxybutadine (370 µL, 2.3 mmol, 0.25 equiv.) was added dropwise. After stirring for 40 h under N_2 atmosphere at 140 °C, the reaction was cooled to rt, rinsed with hexanes (30 mL), and filtered, rinsed with hot H_2O (30 mL), acetone (40 mL), and dried. The crude product was purified by column chromatography with 20/80 EtOAc/hexanes as the eluent to 280 mg of a dark orange product (14% yield).

G.3.25 5,8-dibromo-6,7-dimethoxynaphthalene-1,4-dione (**15b**)[38]

In a 10 mL round-bottom flask, bromine (25 μL, 0.46 mmol, 1 equiv) was added dropwise to a cooled to 0 °C solution of dimethoxynapthaquinone (0.1 mg, 0.5 mmol, 1 equiv) in 1.6 mL CHCl₃. The solution was stirred at 0 °C for 60 min, then Et₃N (70 μL, 0.5 mmol, 1 equiv) was added quickly. The reaction was diluted with 30 mL CH₂Cl₂, washed with Na₂S₂O₃ (30 mL), washed with bring (30 mL), dried with MgSO₄, filtered and concentrated. The crude product was chromatographed with 20/80 EtOAc/Hex to yield at deep red product, by NMR, this did not provide the desired product (**15**), yield was not taken.

G.3.26 6,7-dibromonaphthalene-2,3-diol (**17**)[39]

In 25 mL round-bottom flask, 2,3-dihydroxynaphthalene (1.00 g, 6.24 mmol, 1 equiv) was added to AcOH (10.5 mL), then bromine (1.4 mL, 25.0 mmol, 4 equiv) was added dropwise. The reaction was then stirred at reflux for 1 hr, cooled to rt, poured into ice water (100 mL), and filtered. The precipitate was dissolved in ether (100 mL), washed with H₂O (2 x 50 mL) and brine (2 x 50 mL), and recrystallized in AcOH. The resulting crystals were then dissolved in AcOH, SnCl₂ (8.2 g, excess) and heated to reflux. Concentrated HCl (18.0 mL) was added and stirred at reflux for 40 min. The reaction was cooled to rt, and poured into a solution of H₂O and 10 % HCl. The precipitate was filtered and recrystallized with toluene to give 715 mg of a white solid (12% yield). Figure 4-33, page 102.

G.3.27 2,3-dibromo-6,7-bis(decyloxy)naphthalene (**18**)

In a 25 mL round-bottom flask, 2,3-dibromo-6,7-hydroxynaphthalene (0.1 mg, 0.3 mmol, 1 equiv), K_2CO_3 (0.2 mg, 2 mmol, 5 equiv), bromodecane (0.2 mL, 0.9 mmol, 3 equiv), and acetone (2.5 mL) were combined and purged with N_2 for 5 min. Then the reaction was refluxed for 2 d. The reaction was filtered over silica, the filtrate was washed with EtOAc (20 mL), H_2O (20 mL), dried with $MgSO_4$, filtered, and concentrated in vacuo. The crude product was chromatographed to give 190 mg of a white solid (99% yield). Figure 4-34, page 103.

G.4. NMR Spectra
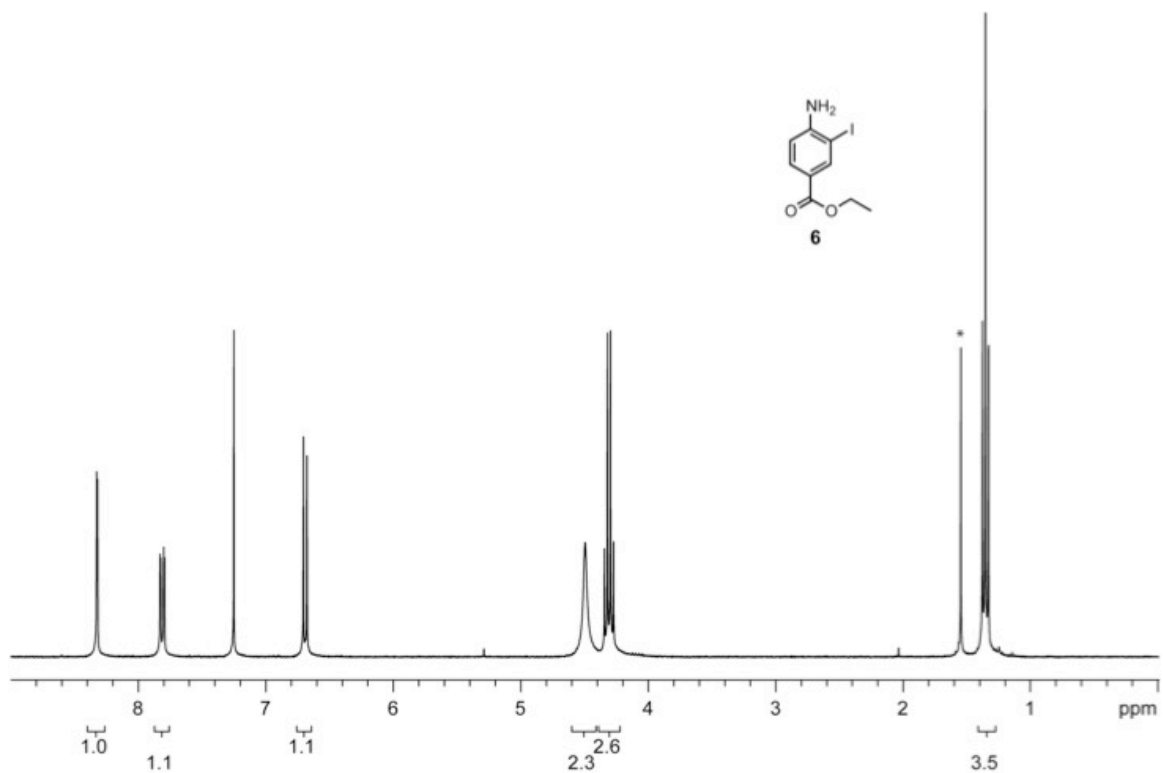
Figure 4-15. ^{1}H Spectrum of ethyl-4-amino-3-iodobenzoate (6).
1H NMR (300 MHz, CDCl3) δ 8.32 (d, 1h), 7.82 (dd, 1 h), 6.69 (d, 1h), 4.48 (br s, 2h), 4.31 (q, 2h), 1.34 (t, 3h). NMR spectra agrees well with previously reported values. *residual H2O.
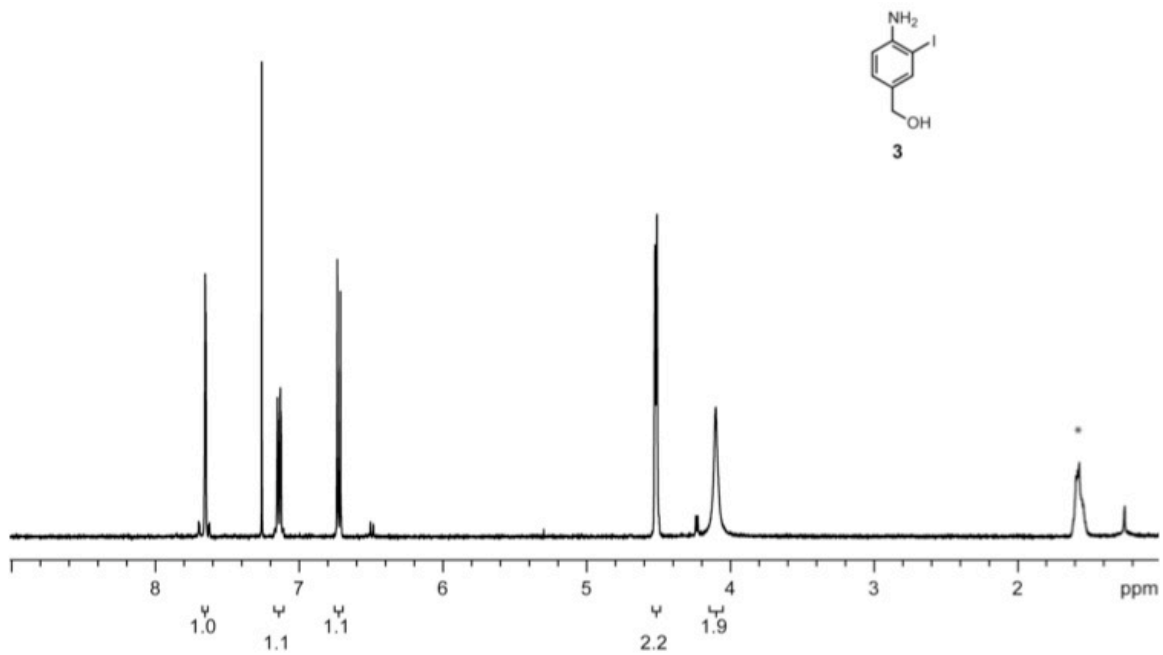
Figure 4-16. ^{1}H NMR Spectrum of (4-amino-3-iodophenyl)methanol. **(3)** ^{1}H NMR (400 MHz, CDCl$_3$) δ 7.63 (d, 1h), 7.13 (dd, 1 h), 6.69 (d, 1h), 4.50 (d, 2h), 4.08 (br s, 2h). NMR spectral data agrees well with previously reported values. *residual grease.
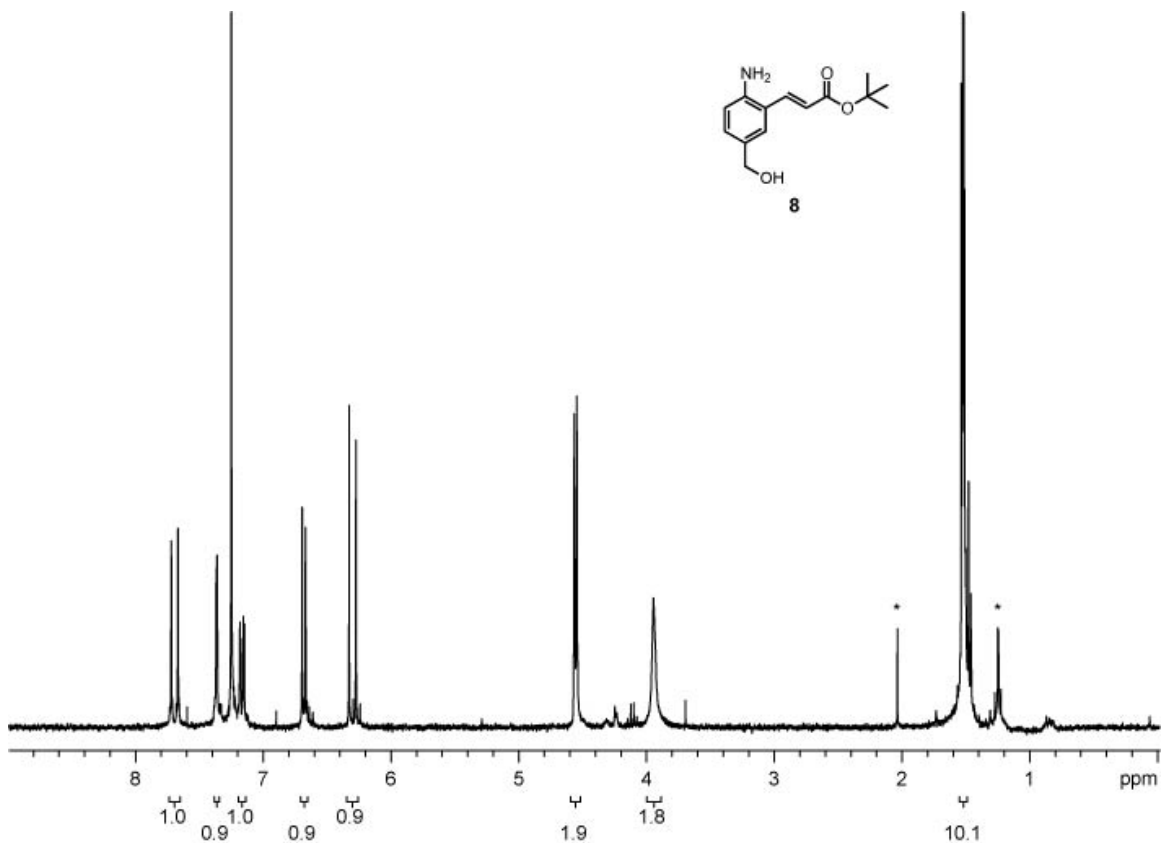
Figure 4-17. ^{1}H NMR Spectrum of (*E*)-*tert*-butyl 3-(2-amino-5-(hydroxymethyl)phenyl)acrylate. (8) 1H NMR (300 MHz, CDCl3) δ 7.71 (d, 1h), 7.35 (d, 1 h),, 7.17 (dd, 1h), 6.68 (d, 1h), 6.26 (d, 1h), 4.55 (d, 2h), 3.94 (br s, 2h), 1.50 (m, 9h). NMR spectral data agrees well with previously reported values. *residual H2O and hexanes.
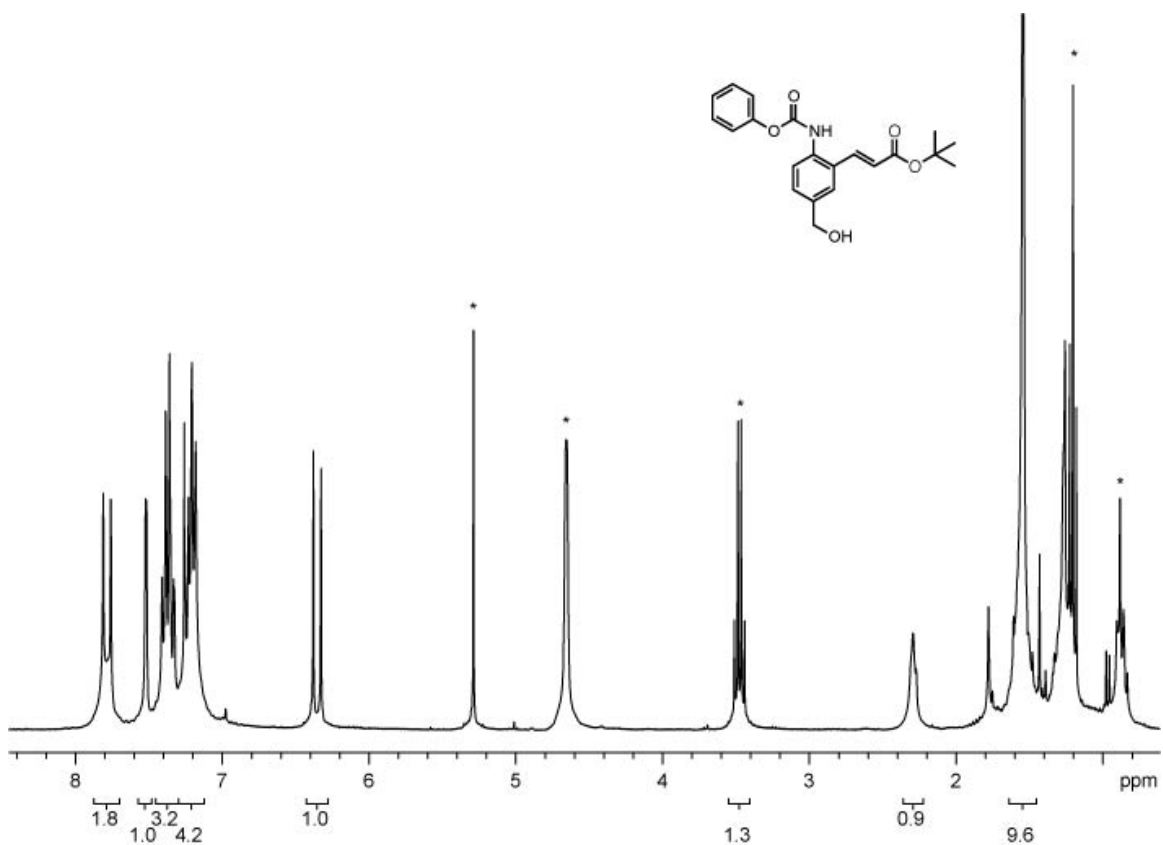
Figure 4-18. ¹H NMR Spectrum of (*E*)-*tert*-butyl 3-(5-(hydroxymethyl)-2-((phenoxycarbonyl)amino)phenyl)acrylate.
1H NMR (300 MHz, CDCl3) δ 7.80 (d, 2h), 7.52 (d, 1h), 7.39 (m, 2h), 7.20 (m, 3h), 6.32-6.38 (d, 1h), 4.66 (br s, 2h), 1.54(s, 9h). *residual hexanes, ethyl acetate and CH2Cl2.
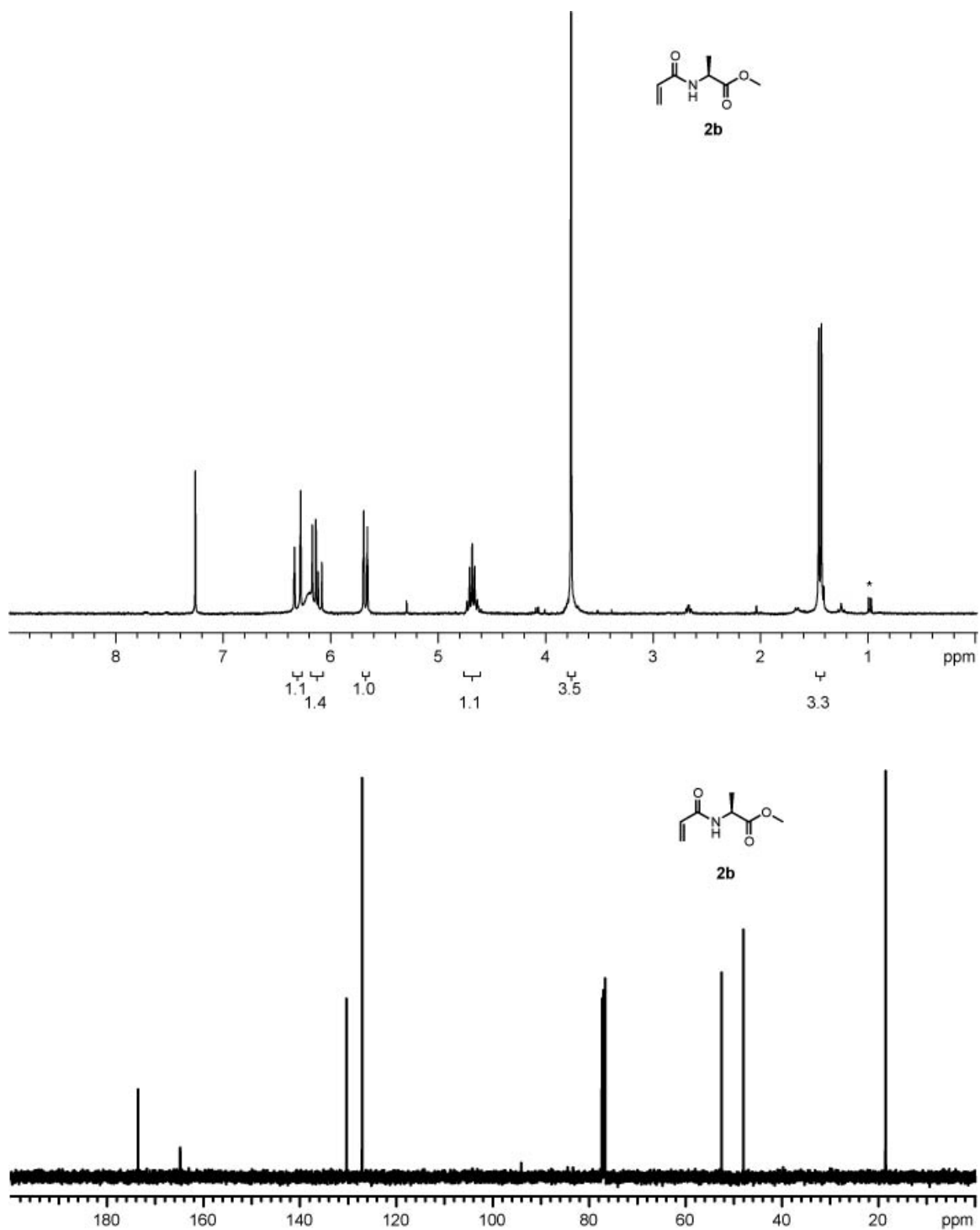
Figure 4-19. ^{1}H and ^{13}C NMR Spectra of (*S*)-methyl 2-acrylamidopropanoate (2b). ^{1}H NMR (300 MHz, CDCl$_3$) δ 6.34-6.27 (d, 1h), 6.17-6.08 (dd, 2h), 5.70-5.65 (m, 1h), 3.76 (s, 3h), 1.46-1.43 (d, 3h); ^{13}C NMR (100 MHz, CDCl$_3$) δ 173.5, 164.8, 130.3, 127.1, 52.5, 48.0, 18.5. *residual hexanes.
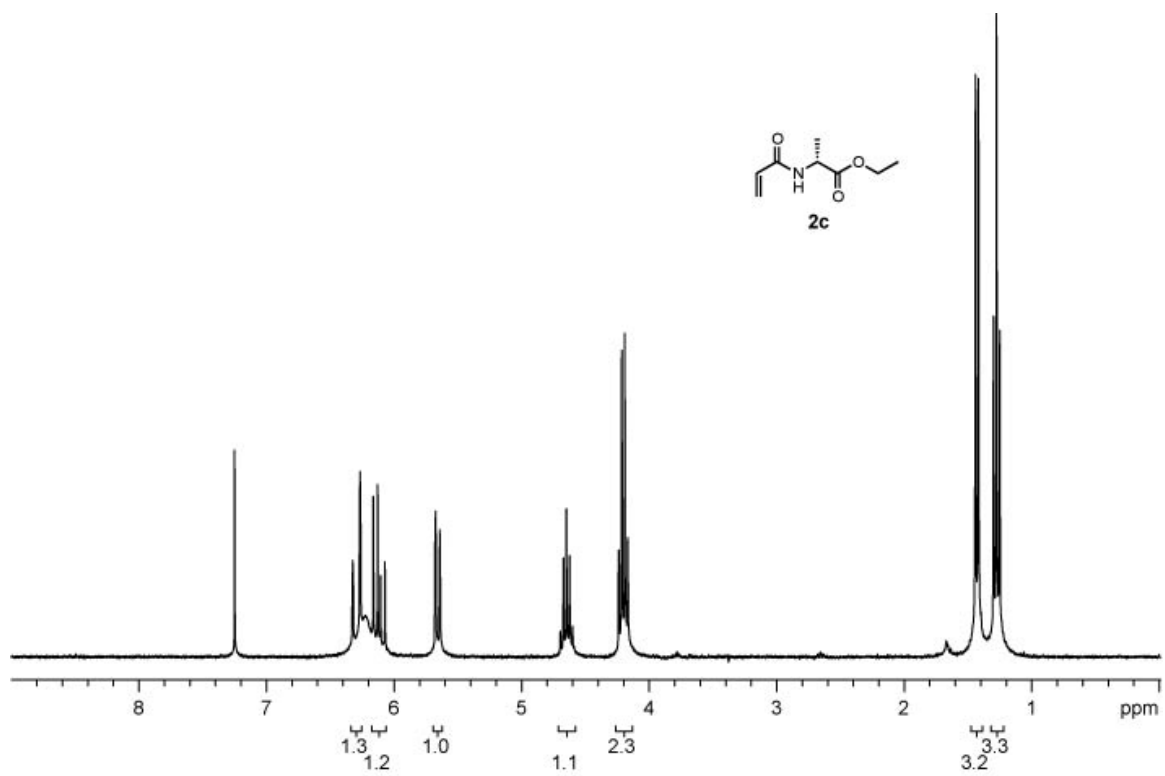
Figure 4-20. ^{1}H NMR Spectra of (*R*)-ethyl 2-acrylamidopropanoate. (**2c**). ^{1}H NMR (300 MHz, CDCl$_3$) δ 6.34-6.27 (d, 1h), 6.17-6.08 (dd, 2h), 5.70-5.65 (m, 1h), 4.23 (m, 3h), 1.46-1.43 (m, 2h), 1.23-1.25 (t, 3h).
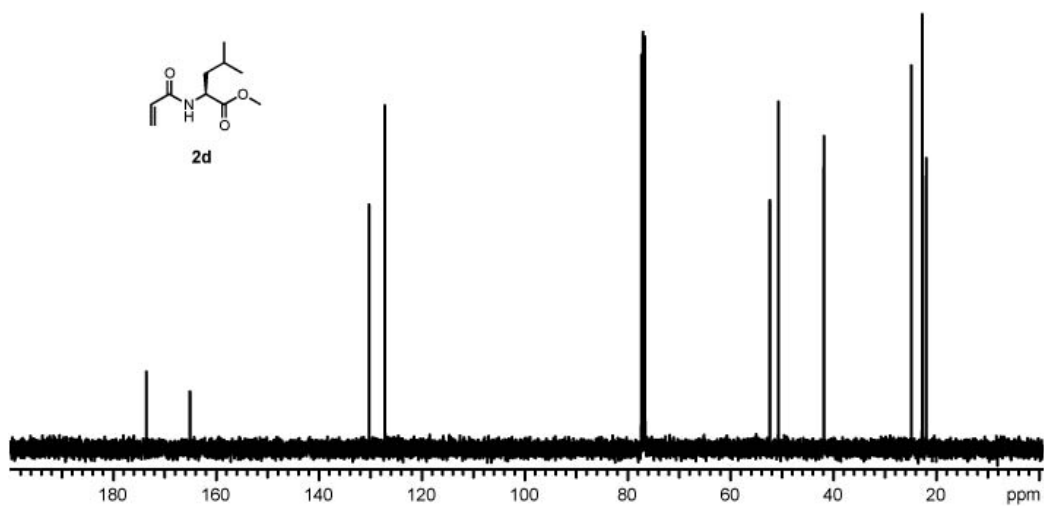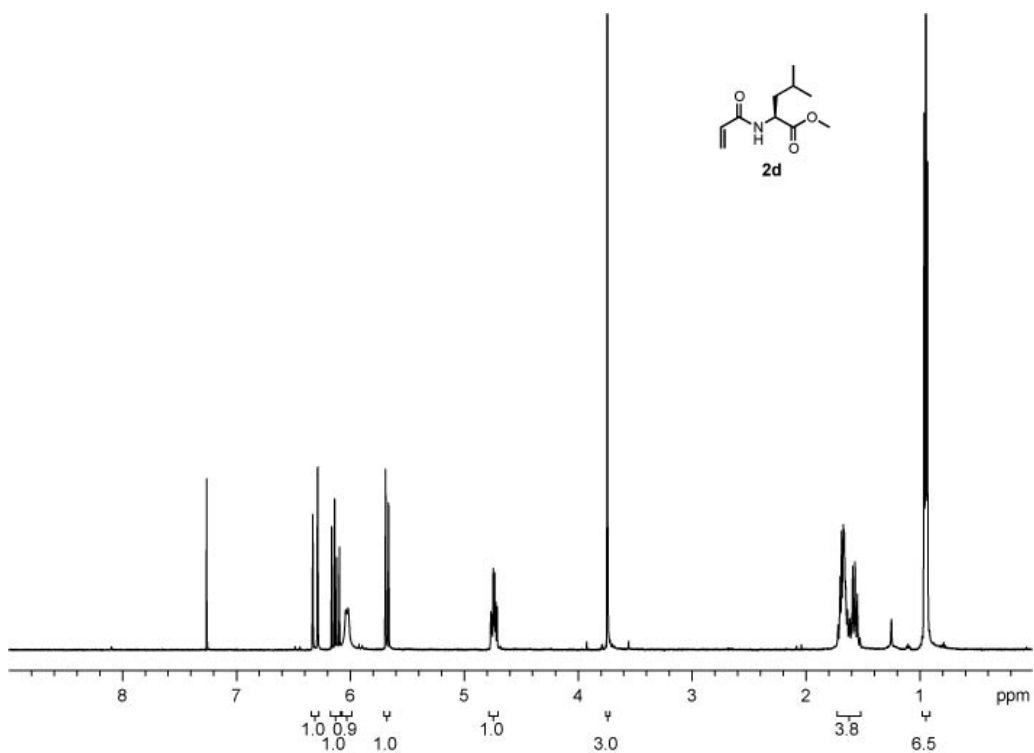
Figure 4-21. ^{1}H and ^{13}C NMR Spectra of (S)-methyl 2-acrylamido-4-methylpentanoate (**2d**). ^{1}H NMR (300 MHz, CDCl₃) δ 6.33-6.29 (dd, 1h), 6.16-6.10 (dd 1h), 6.03 (br, 1h), 5.69-5.66 (dd, 1h), 4.77-4.71 (m, 1h), 3.74 (s, 3 h), 1.72-1.54 (m, 3h), 0.95 (t, 6 h); ^{13}C NMR (100 MHz, CDCl₃) δ 173.6, 165.1, 130.3, 127.2, 52.3, 50.7, 41.9, 24.9, 22.8, 22.0.
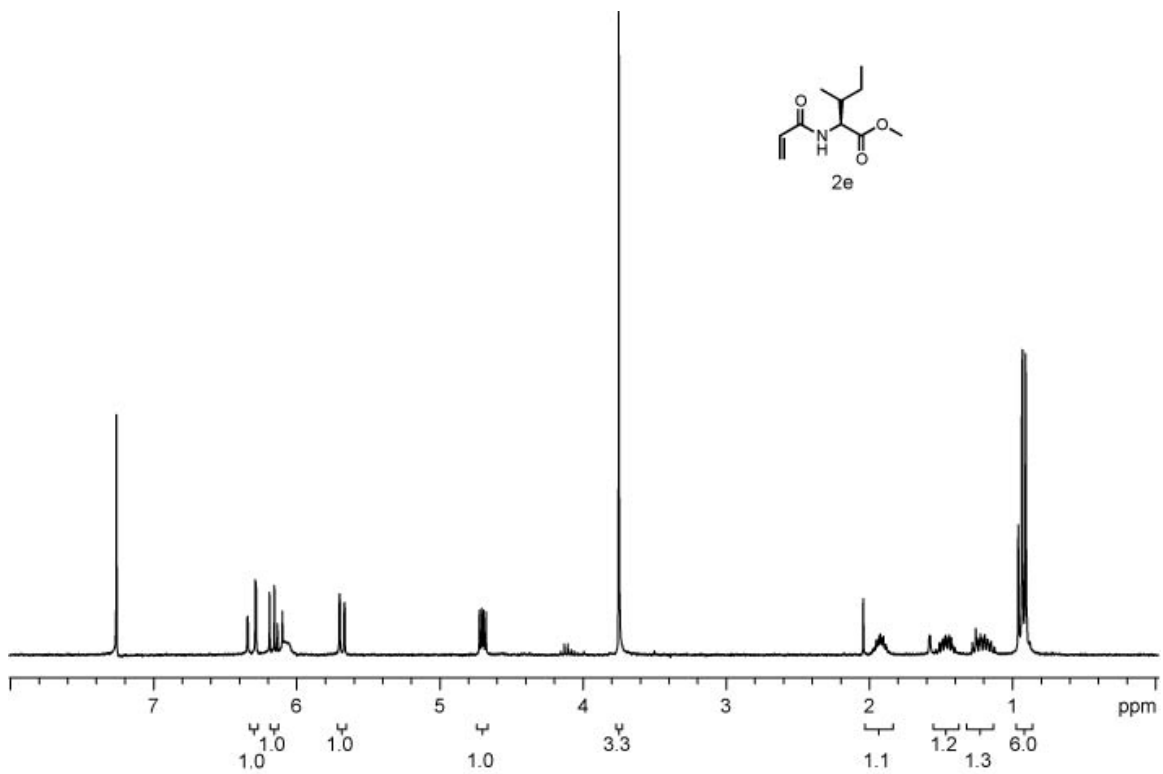
Figure 4-22. ^{1}H NMR Spectra of (2S,3R)-methyl 2-acrylamido-3-methylpentanoate (**2e**) ^{1}H NMR (300 MHz, CDCl$_3$) δ 6.3 (dd, 1h), 6.18-6.11 (dd 1h), 4.5 (m, 1h), 3.78 (s, 3 h), 1.95 (m, 1h), 1.5 (m, 1h), 1.2 (m, 1h), 0.95 (t, 6 h).

91
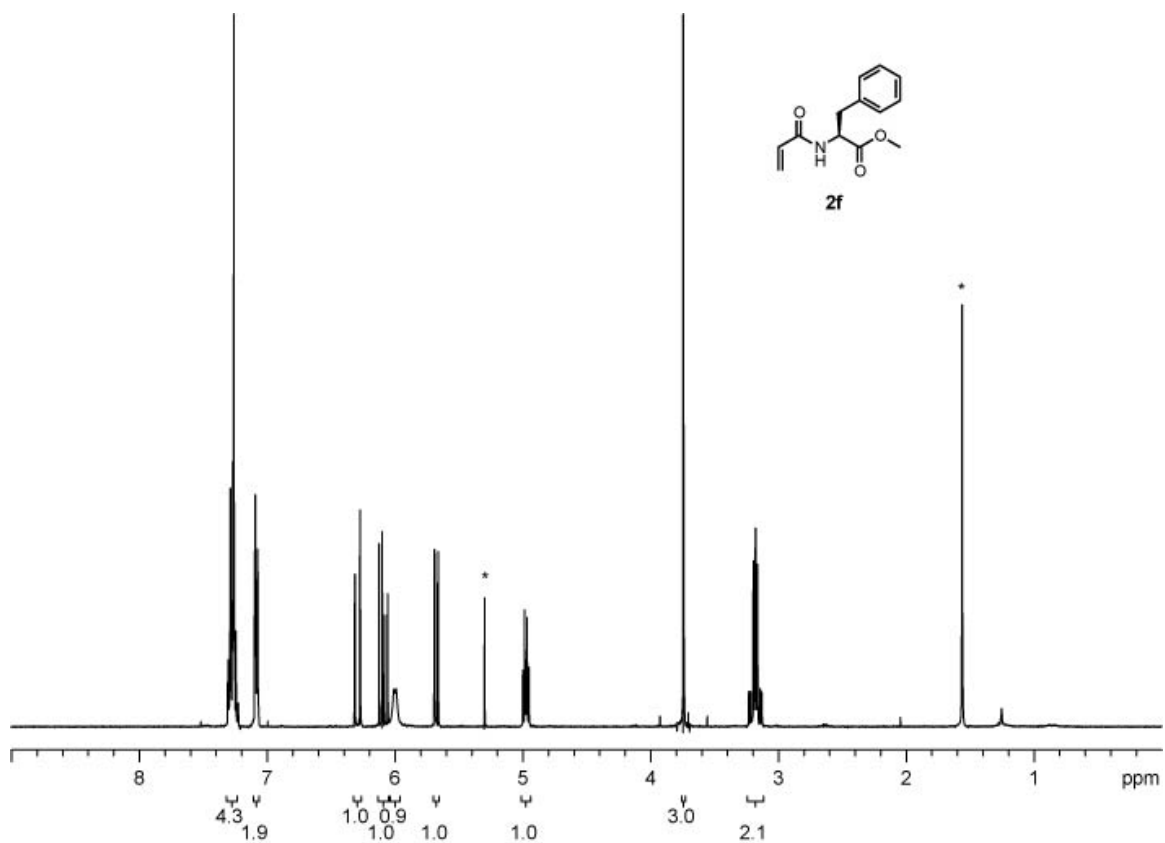
Figure 4-23. ^{1}H NMR Spectrum of (*S*)-methyl 2-acrylamido-3-phenylpropanoate (**2f**). ^{1}H NMR (400 MHz, CDCl$_3$) δ 7.31-7.24 (m, 4h), 7.10-7.08 (dd, 2h), 6.32-6.27 (dd, 1h), 6.13-5.99 (m and br(NH), 2h), 5.69-5.66 (dd, 1h), 4.98 (m, 1h), 3.74 (s, 3h), 3.2-3.1 (m, 2h). *residual H$_2$O at 2.6 ppm and CH$_2$Cl$_2$ at 5.3 ppm.
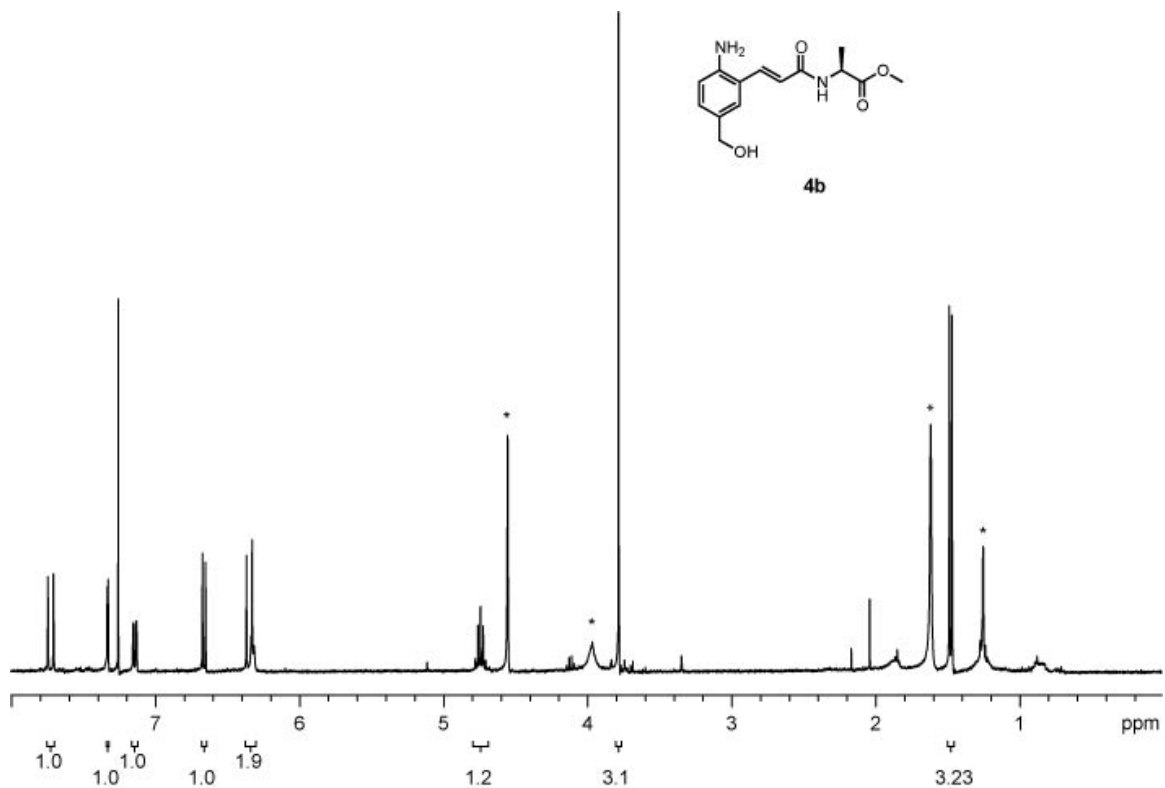
Figure 4-24. ^{1}H NMR Spectrum of (*S,E*)-methyl-2-(3-(2-amino-5-(hydroxymethyl)phenyl)acrylamido)propanoate (4b) ^{1}H NMR (400 MHz, CDCl$_3$) δ 7.75-7.71 (d, 1h), 7.33 (d, 1h), 7.15-7.13 (dd, 1h), 6.68-6.65 (d, 1h), 6.36-6.33 (d, 2h), 4.74 (quin., 1 h), 4.56 (s, 2h), 3.79 (s, 3h), 1.49-1.47 (d, 3h); ^{13}C NMR (100 MHz, CDCl$_3$) δ 166, 146, 137.2, 131.9, 130.5, 127.2, 120.6, 119.6, 117.05, 65.36, 52.90, 48.52, 18.89. *residual CH$_2$Cl$_2$ and hexanes
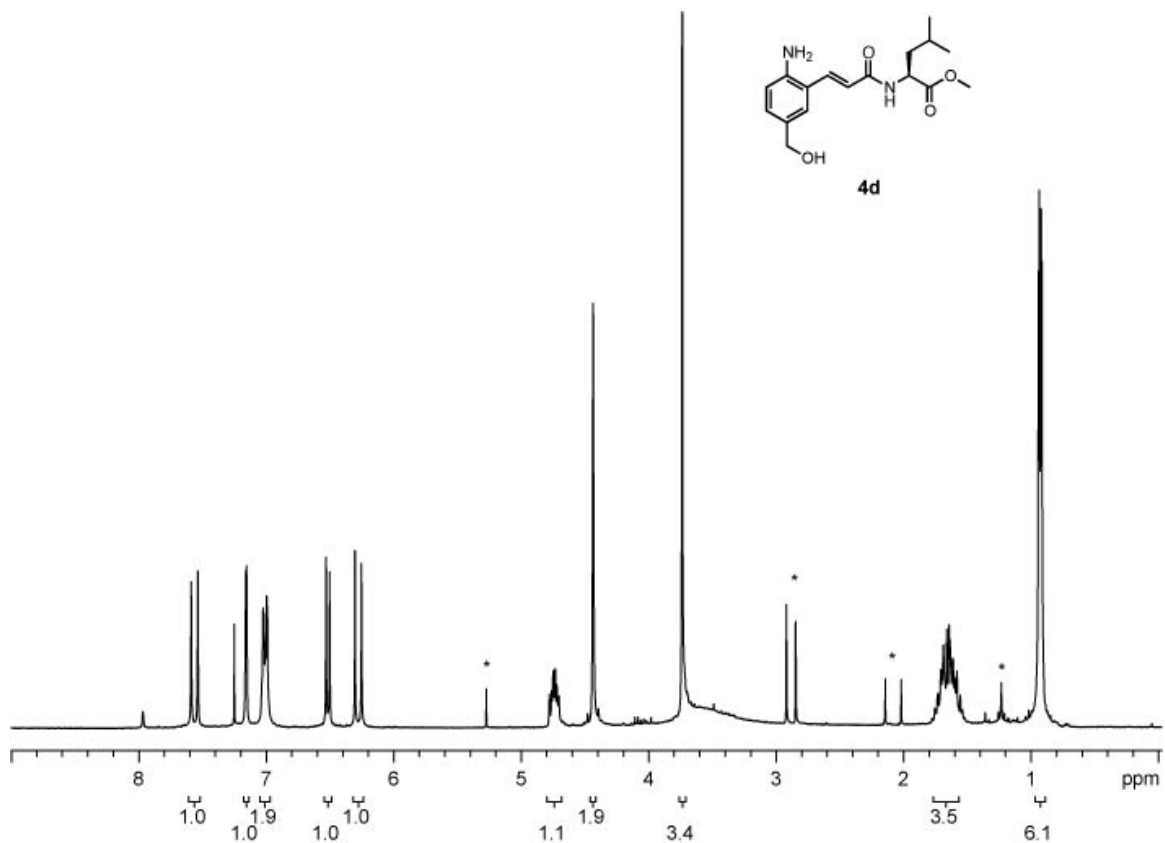
Figure 4-25. ^{1}H NMR Spectrum of (*S,E*)-methyl 2-(3-(2-amino-5-(hydroxymethyl)phenyl)acrylamido)-4-methylpentanoate (**4d**). ^{1}H NMR (300 MHz, CDCl$_3$) δ 7.59-7.55 (d, 1h), 7.17 (s, 1h), 7.03-7.00 (d, 2h), 6.54-6.51 (d, 1h), 6.31-6.26 (d, 1h), 4.76-4.74 (m, 1h), 4.44 (s, 2h), 3.75 (s, 3h), 1.63 (m, 3h), 0.93 (s, 6h). *residual hexanes, DMF, and CH$_2$Cl$_2$.
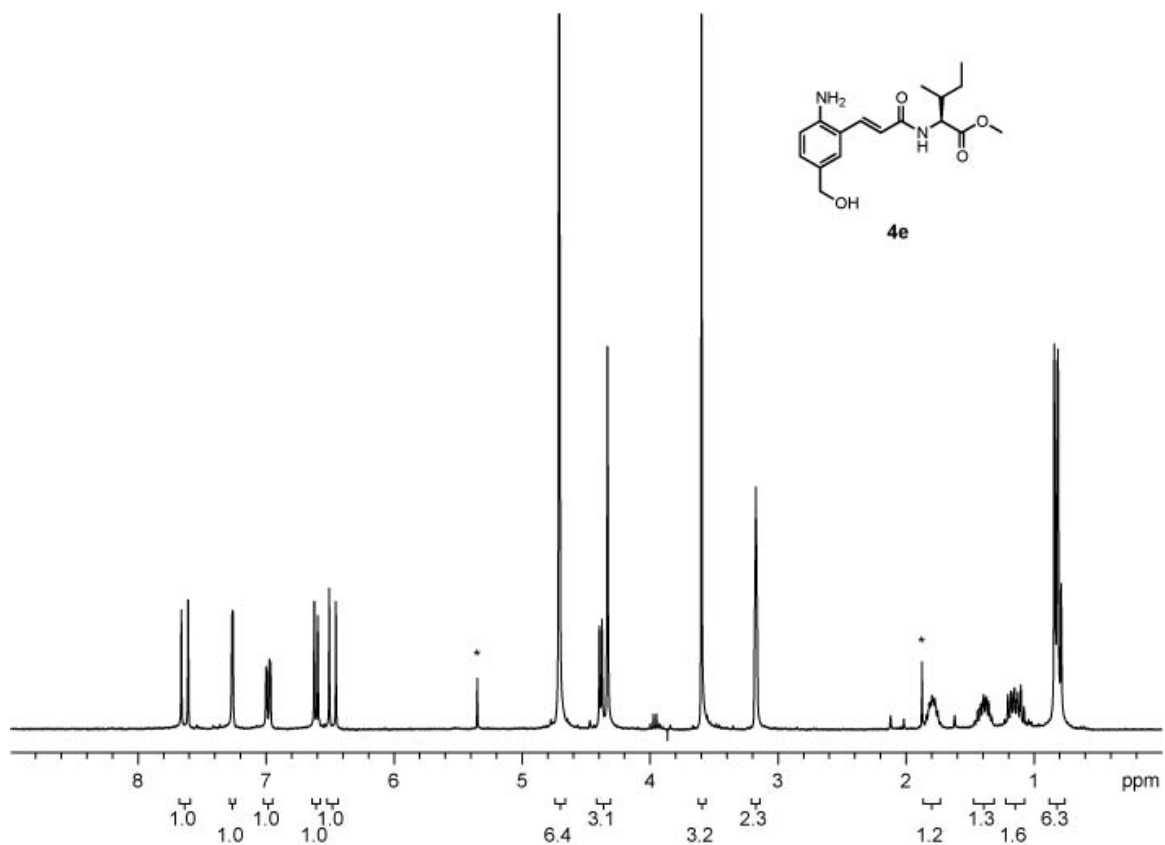
Figure 4-26. ¹H NMR spectrum of (2*S*,3*R*)-methyl 2-((*E*)-3-(2-amino-5-(hydroxymethyl)phenyl)acrylamido)-3-methylpentanoate (**4e**). ¹H NMR (300 MHz, CDCl₃) δ 7.56-7.51 (d, 1h), 7.16 (s, 1h), 6.90-6.87 (d, 1h), 6.52-6.49 (d, 1h), 6.41-6.36 (d, 1h), 4.28 (s, 3h), 1.78-1.68 (m, 1h), 1.30-1.26 (m, 1h), 1.08-1.00 (m, 2h), 0.72 (m, 6h) *residual H₂O and CH₂Cl₂.
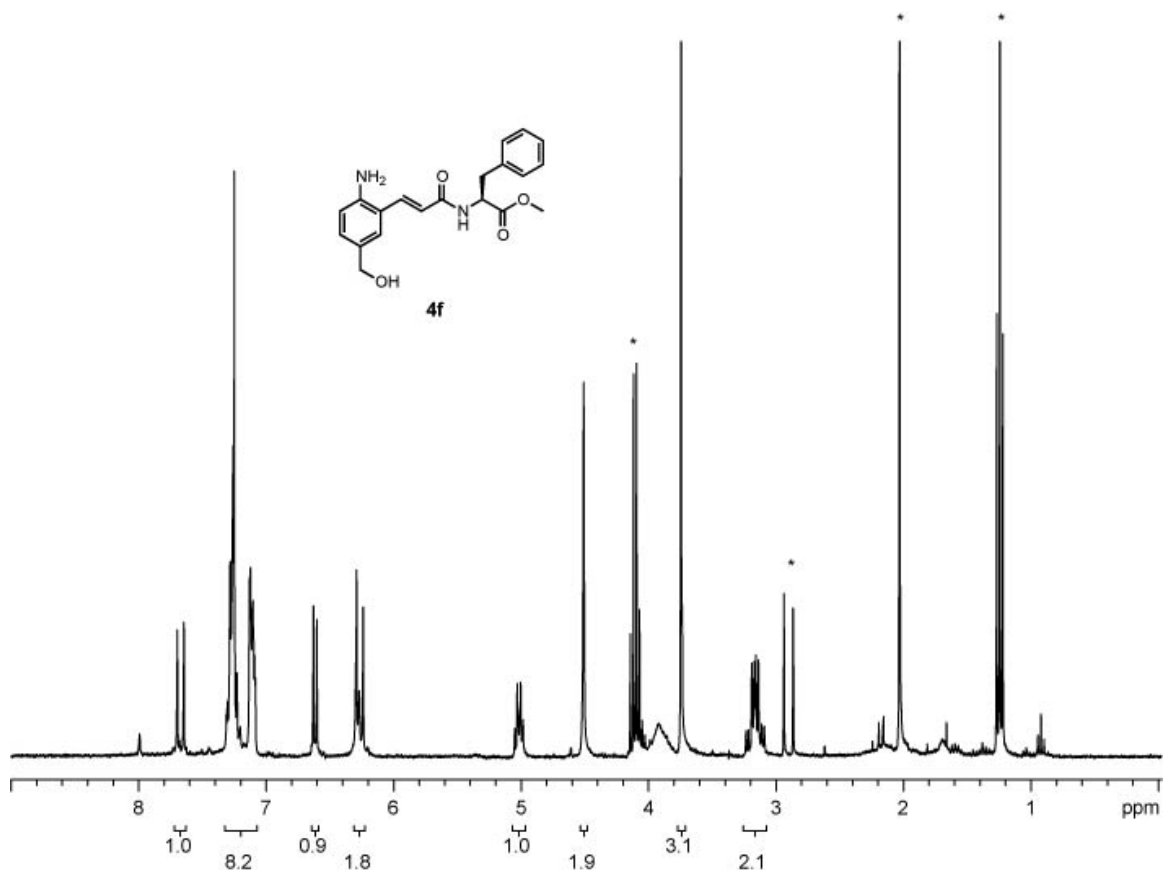
Figure 4-27. ^{1}H NMR Spectrum of (*S,E*)-methyl 2-(3-(2-amino-5-(hydroxymethyl)phenyl)acrylamido)-3-phenylpropanoate (**4f**). ^{1}H NMR (300 MHz, CDCl$_3$) δ 7.71-7.66 (d, 1h), 7.32 (m, 8h), 6.64-6.61 (d, 1h), 6.30-6.25 (m, 2h), 5.02 (m, 1h), 4.52 (s, 2h), 3.76 (s, 3h), 3.20-3.15 (m, 2h) *residual EtOAc and DMF.
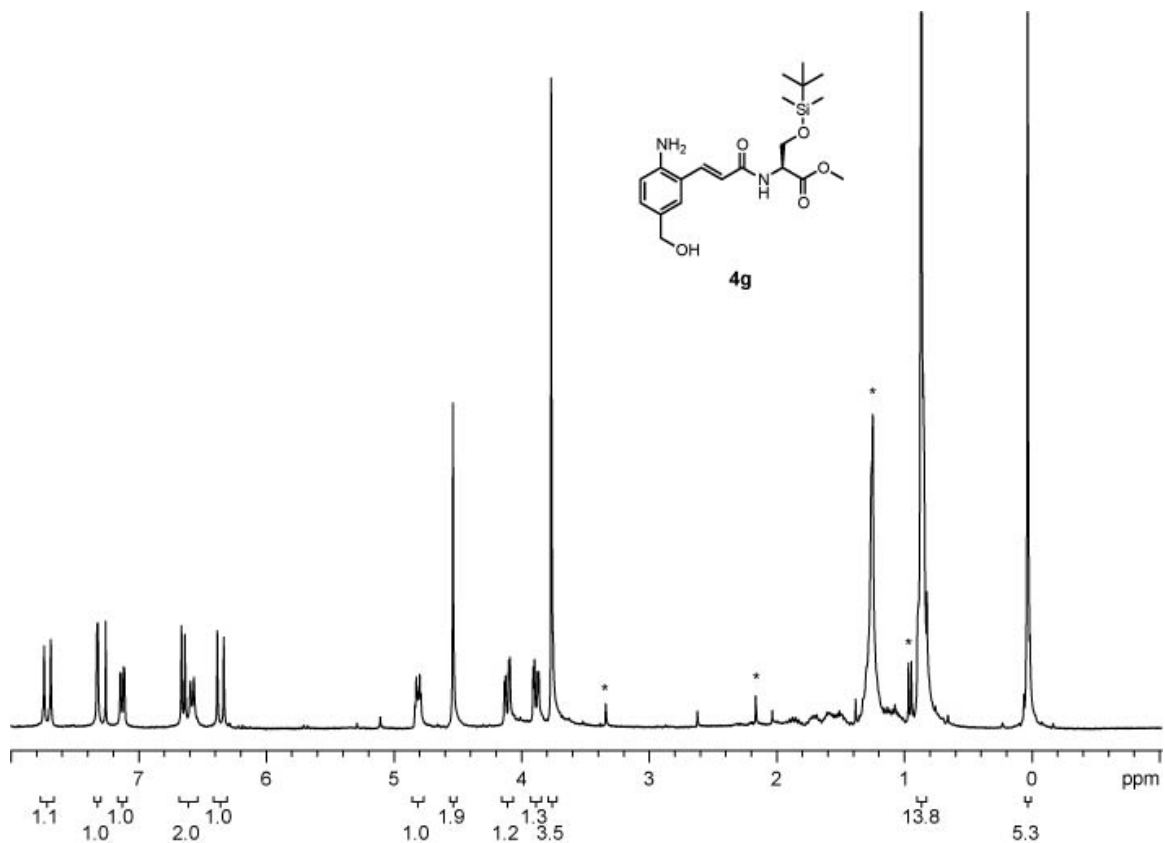
Figure 4-28. ^{1}H NMR Spectrum of (*S,E*)-methyl 2-(3-(2-amino-5-(hydroxymethyl)phenyl)acrylamido)-3-((*tert*-butyldimethylsilyl)oxy)propanoate (**4g**). ^{1}H NMR (300 MHz, CD$_3$OD) δ 7.74 (d, 1h), 7.32 (d, 1h), 7.14 (d, 1h), 6.66 (d, 1h), 6.57 (d, 1h), 6.38 (d, 1h), 4.80 (m, 1h), 4.54 (s, 2 h), 4.13-4.10 (m, 1h), 3.91-3.87 (m, 1h), 3.77 (s, 3h), 0.87 (br, 12h), 0.04 (br, 6 h). *residual H$_2$O and unknown byproduct.

97
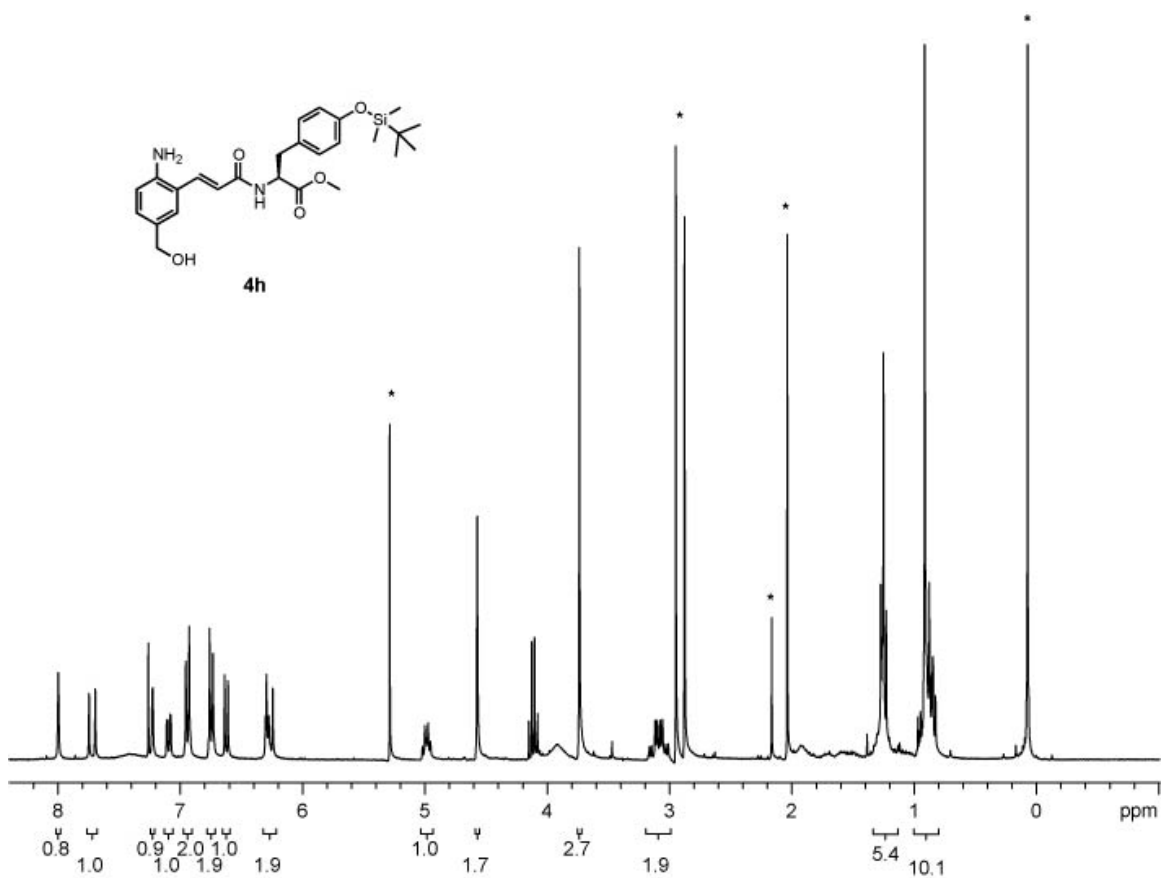
Figure 4-29. ^{1}H NMR Spectrum of (*S,E*)-methyl 2-(3-(2-amino-5-(hydroxymethyl)phenyl)acrylamido)-3-(4-((*tert*-butyldimethylsilyl)oxy)phenyl)propanoate (**4h**). 1H NMR (300 MHz, CD3OD) δ 8.21 (s, 1h), 7.96-7.90 (d, 1h), 7.47-7.44 (d, 1h), 7.32-7.31 (d, 1h), 7.16-7.14 (d, 2h), 6.97-6.94 (d, 2h), 6.85-6.82 (d, 1h), 6.50 (m, 2h), 5.20 (m, 1h), 4.78 (s, 2h), 3.95 (s, 3h), 3.33-3.27 (m, 2h), 1.48 (br, 5h), 1.13 (br, 10h). *residual CH2Cl2, DMF, hexanes.

98
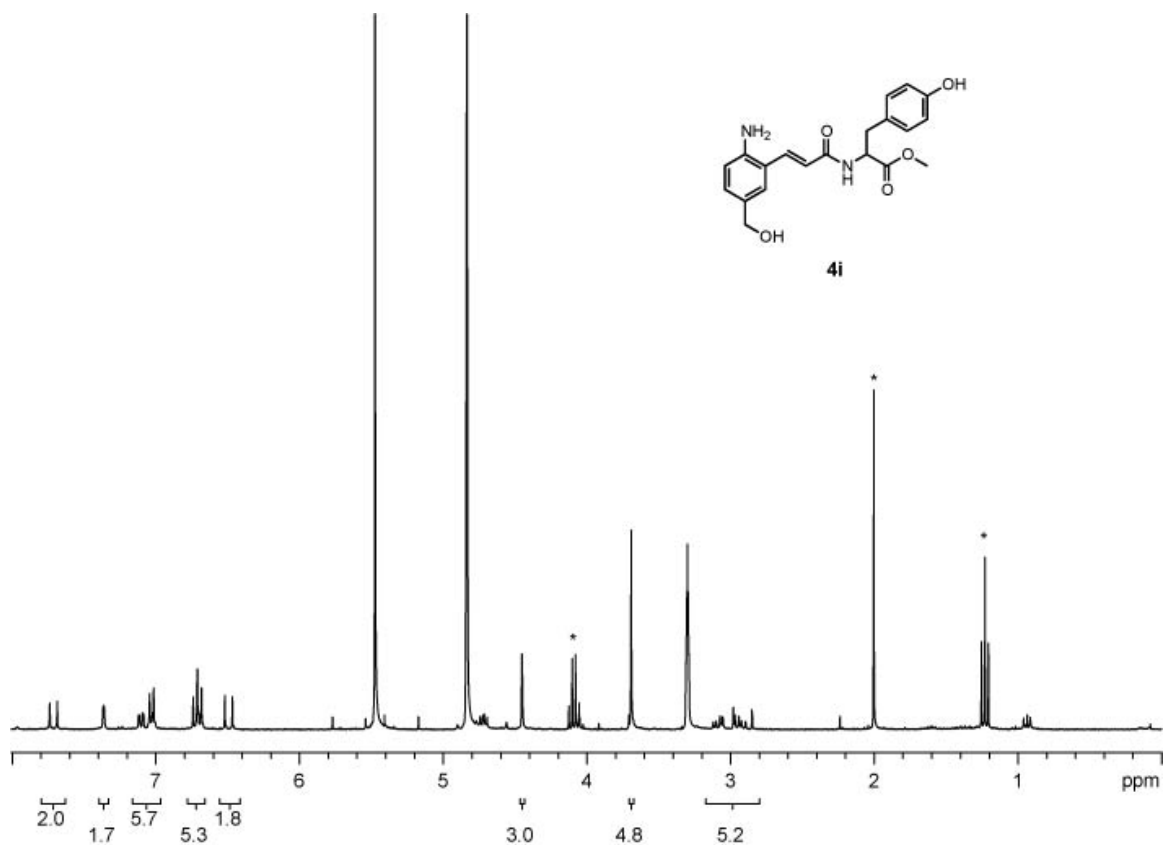
Figure 4-30. ^{1}H NMR Spectrum of (*E*)-methyl 2-(3-(2-amino-5-(hydroxymethyl)phenyl)acrylamido)-3-(4-hydroxyphenyl)propanoate (**4i**). ^{1}H NMR (300 MHz, CD$_3$OD) δ 7.68-7.63 (d, 2h), 7.31 (br, 2h), 7.06-6.96 (dd, 6h), 6.96 (m, 6h), 6.46-6.41 (d, 2h), 4.40 (s, 3h), 3.02-2.79 (m, 5h). *residual H$_2$O and ethyl acetate.
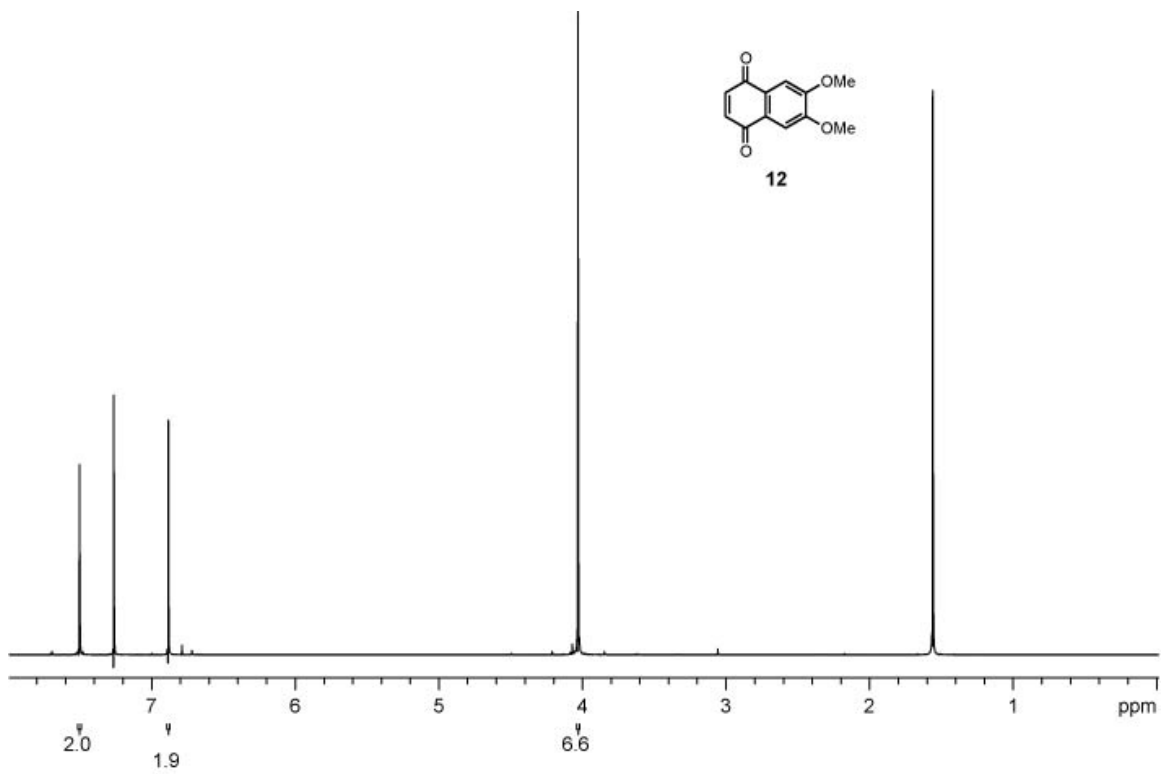
Figure 4-31. ¹H NMR Spectrum of 6,7-dimethoxynaphthalene-1,4-dione (**12**). ¹H NMR (400 Hz, CDCl₃) δ 7.26 (s, 2h), 6.88 (s, 2h), 4.03 (s, 6h). *residual H₂O.
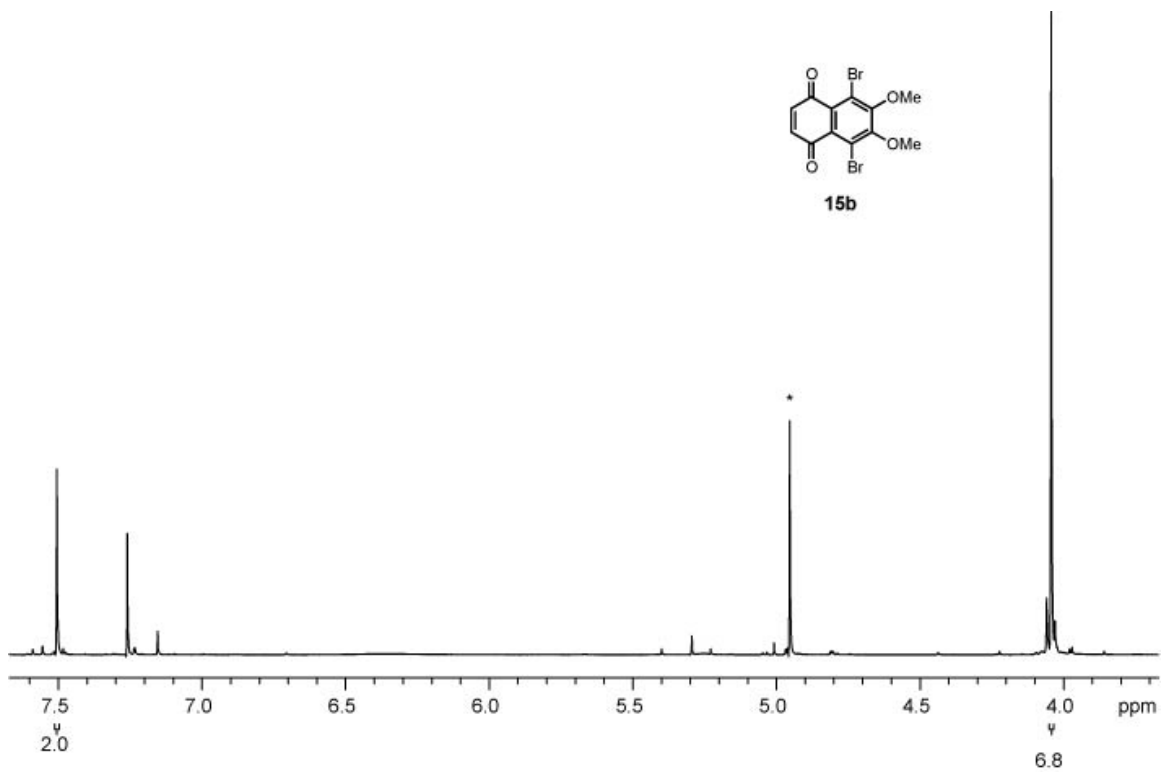
Figure 4-32. ^{1}H NMR Spectrum of 5,8-dibromo-6,7-dimethoxynaphthalene-1,4-dione (**15b**). ^{1}H NMR (400 Hz, CDCl$_3$) δ 7.51 (s, 2 h), 4.04 (s, 6 h). *residual CH$_2$Cl$_2$.
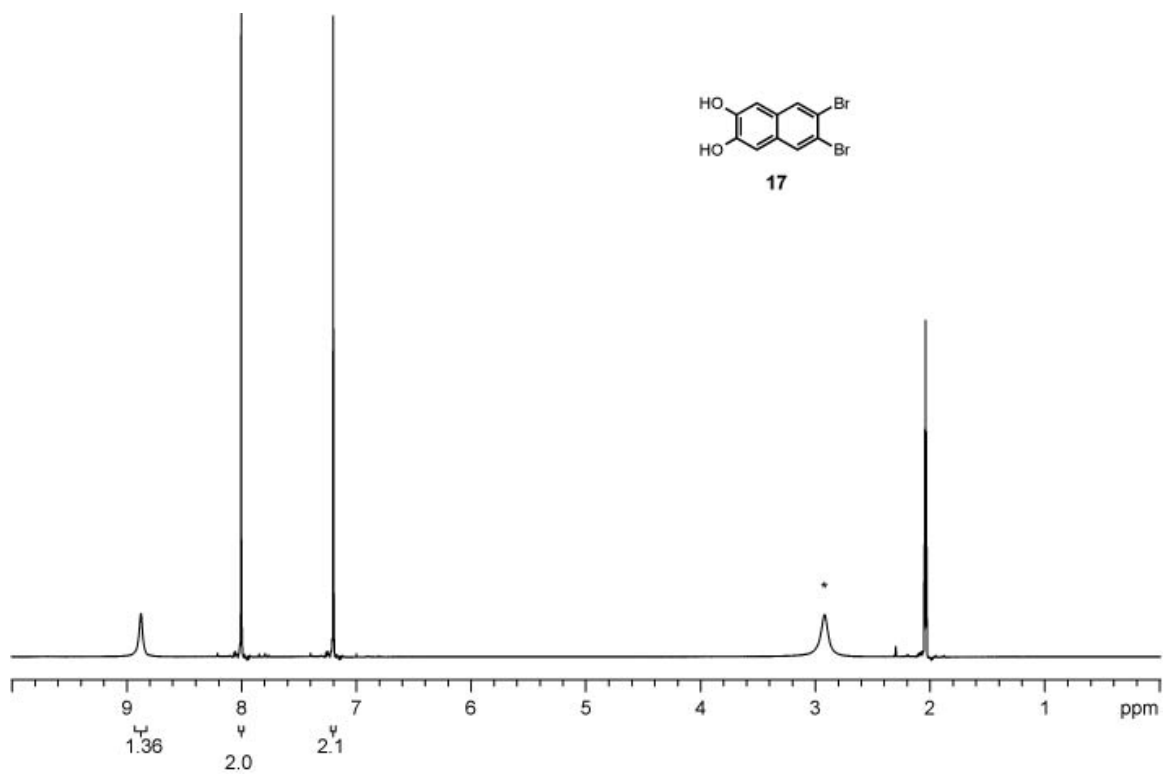
Figure 4-33. ^{1}H NMR Spectrum of 6,7-dibromonaphthalene-2,3-diol (**17**). ^{1}H NMR (400 Hz, D-Acetone) δ 8.89 (br, 2h), 8.01 (s, 2h), 7.211 (s, 2 h). matches with literature values. *residual H_2O.
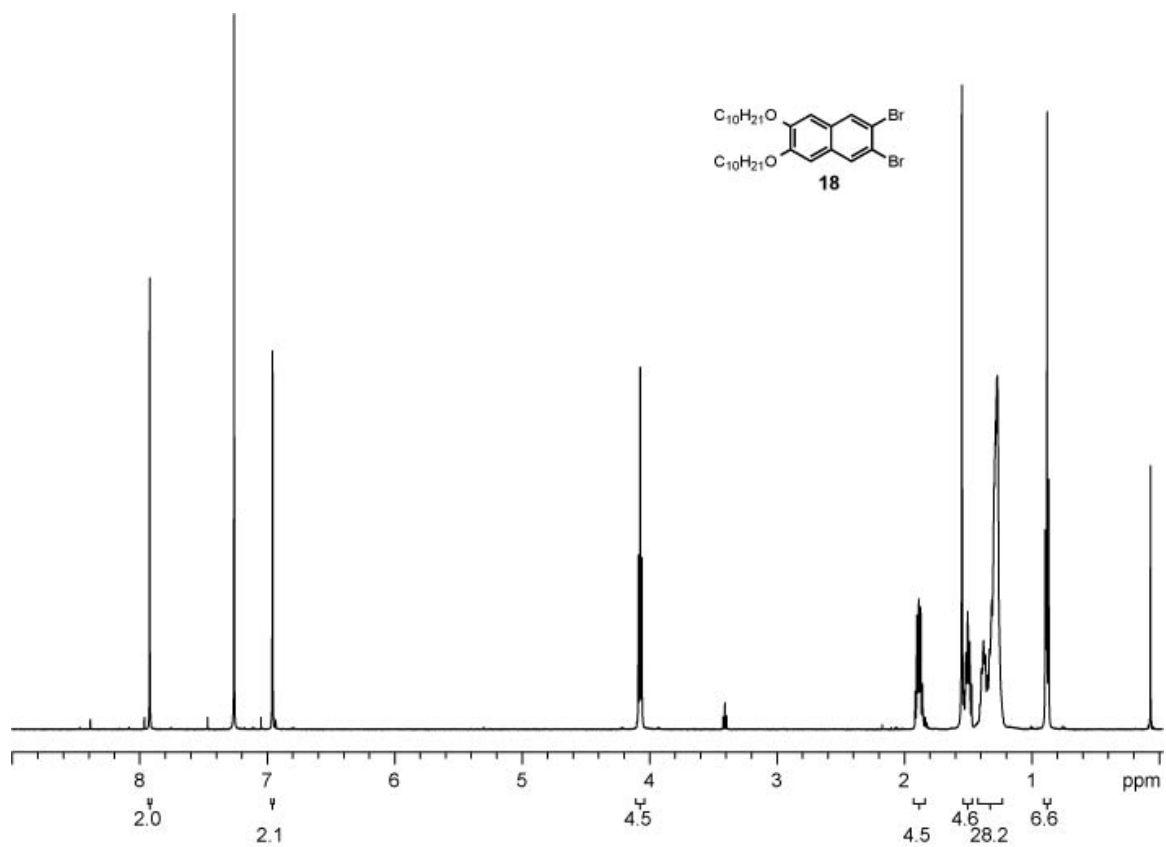
Figure 4-34. ^{1}H NMR Spectrum of 2,3-dibromo-6,7-bis(decyloxy)naphthalene (**18**). ^{1}H NMP (500 Hz CDCl$_3$) δ 7.92 (s, 2h), 6.96 (s, 2h), 4.07 (t, 5h), 1.89 (m, 4h), 1.55-1.49 (br, 4h), 1.39-1.28 (br, 28h), 0.88 (m, 6h).

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Chapter 5

Design and Implementation of a Graduate-Level Class Project Centered on Editing

Wikipedia[a]

A. Background

The need for the general public to have a fundamental understanding of science and technology to be informed and involved in the current political and social discourse is becoming more and more apparent.[1, 2, 3] However, graduate curricula rarely include training for future scientists on how to communicate advance concepts to a broad and diverse audience.[4] Learning to write well is an important part of scientific training[5], which is why science courses often include a writing assignment in addition to examinations to assess student understanding.[6] Through writing assignments, students are required to not only gather relevant information, but also to reconstruct and revise material so that it fits into their own understanding, leading to learning and deep conceptual understanding.[7] It has also been shown that when students are writing for their

peers or for an audience that is not their instructor, they retain the information longer.[6] Researchers hypothesize that when students write to a specific audience, they perceive the assignment as requiring them to understand the concept well enough to explain it to others, and this process can enhance student learning.[6] This hypothesis is very similar to research investigating the learning gained by students who perceive themselves in explanatory roles.[8] Students assuming teaching roles may also be responsible for the success of peer discussions in improving student performance. Recently, peer discussions have been incorporated in active learning environments by utilizing "clicker questions". For "clicker questions", students are presented with a multiple-choice question related to the topic being presented in class. Students submit their answers, providing a real-time distribution of student understanding. Then, students have the opportunity to convince their peers that their answer is the correct one before answering the question a second time; this is the key component of the "clicker question" method that affects student learning. Smith et al found that even when groups did not have a student who initially answered correctly, when presented with a related conceptual question, they were still able to correctly answer the question,[9] showing that social learning is an effective and valuable method for enhancing understanding. Although these students are not directly doing a writing project, they are using and learning collaborative learning and peer discussion skills that group writing projects can teach. Through these pedagogical exercises the students learn the concept presented, incorporate this concept into their own understanding, and then formulate a response to explain it to their peers. From these findings a writing project with components of collaboration, perceived teaching, and peer discussion has the potential to increase learning.

Therefore, we developed a group project centered on editing Wikipedia. The primary objective of the project was to learn advanced topics in chemistry, and we further hypothesized that working collaboratively and the nature of Wikipedia's large readership would contribute to the students' learning experience. In collaboration with my advisor, Professor Anne McNeil, and two colleagues, Professor Brian Coppola and Jonas Locke, we designed a graduate class project using Wikipedia.org, the free online encyclopedia that anyone can edit. This project provides students with both the opportunity and platform to communicate advanced topics in science to the general public.[10] We anticipate that the students will assess the material they add to the entry more critically compared to when they are simply studying for the class due to the prevalent use of Wikipedia. In general, this observation is consistent with Coleman's notion of student's developing a higher level of explanatory knowledge when they are explicitly aware of the need to engage in teaching.[11, 12] Although Coleman studied direct instruction, it is reasonable to think that editing a Wikipedia entry carries a comparable, if not higher, awareness about a future teaching event while learning is taking place.

One method of incorporating peer discussion in writing assignments is to include a formal peer-review component where classmates critique each other's work based on a set of criteria. Not only does this introduce students to peer review, a process familiar to the scientific community, but students have also reported in interviews for another study that they feel participation in the peer review process improves their own writing.[13]

Wikipedia is a highly visible, and open platform on the Internet for communicating information to both general and technical audiences.[14] Founded in 2001, Wikipedia is the sixth most-accessed site on the Internet,[15] with over 3 million articles in

108

the English language Wikipedia and over 280 different language Wikipedias. Wikipedia entries can be created or edited by anyone with minimal instructions, entries can be readily interconnected through links, and the edits for each entry are tracked, providing a history of all changes. Wikipedia's visibility has the potential to influence the students' perceptions of who will be viewing their work and therefore we anticipate that the students will be more critical of their own work and in turn promote learning.

When we started this project, there were only a handful of known projects incorporating Wikipedia editing in the classroom, and even fewer science courses.[16] We initially implemented the project in the Fall 2008 in a graduate-level Organic Principles course, the project is designed to be flexible, which enabled the extension of this project in a variety of graduate chemistry courses ranging in size, topic and professor. Since then, with the efforts of the Wikimedia Foundation's Global Education Program, the number of projects has grown significantly with over 100 school projects in Spring 2012.[17, 18] The large number of academic institutions willing to be involved in improving the content on Wikipedia illustrates the potential for Wikipedia to be an effective educational platform. This chapter will describe the design of the project, the modifications made each semester to improve student learning, and analysis of student learning as a results of participating in the project.

B. Description of the Project

We hypothesized that through this class project, students will explore advanced concepts in chemistry and learn how to communicate science to a diverse audience by

collaboratively editing an entry in Wikipedia. Although Wikipedia can be edited by anyone with minimal instruction, through the design of this project, we found that substantial edits from new editors are more prone to deletion by the underlying Wikipedia community of editors and editorial process.[19] Therefore, it was important to give the students specific assignments that not only increased the quality of their work, but also conveyed our commitment to the project, that enabled the students to also engage in the impact of their work. These resources resulted in the students' edits not being deleted by the Wikipedia community of editors.[20]

At the beginning of each semester, we provided the students with a description of the project that outlined the goal, how efforts were to be reported, and how they would be evaluated on the project (Figure 5-1), a timeline (Figure 5-2), group assignments, and criteria for peer review. Later sections in this chapter will elaborate on the various modifications we made to the timeline each semester and the criteria provided to the students for peer review. The project was a group assignment to include an aspect of the course that would enable students to learn a transferable skill, such as group-work.[21] There were 2 to 3 students in each group and the group members were assigned. The students in these courses came from a range of backgrounds and disciplines, from senior undergraduate students, to first/second year graduate students studying biochemistry, engineering, and chemistry. To vary the students' interactions with each other and other disciplines we assigned the groups. Students submitted three topic proposals, advocating the importance of that topic to the field of chemistry, identify the strengths and weaknesses, and what additions and improvements could be made to the entry. The

instructor finalized concepts or topics by considering the relevance of the topic to the course, and degree to which the students could make a substantial contribution.

Improving Science in Wikipedia

Goal: You and your partner must identify an important topic or person related to polymer chemistry and either create or substantially improve the Wikipedia site on that topic.

Report: The results of your efforts (additions to site) will be presented to the class in a 20-min presentation.

Groups: Each group will be assigned a sandbox so that we can track the changes made.

Peer Review: Each of you will be individually assigned another group to peer review their outline and sandbox versions of the site. You will be graded on the quality of your peer reviews (25 pts).

Grading: The Wiki site will be graded on five aspects:

(a) *Content*: A minimum of 3 sections must be added to the site, including an introductory paragraph aimed at the general public. The quantity and quality of the added content will be evaluated. (25 pts)

(b) *Figures*: A minimum of 3 figures or schemes must be added to the site. Again, both quantity and quality will be evaluated (20 pts)

(c) *References*: A minimum of 8 references must be added to the site. The quality and appropriateness of these references will be evaluated. Note that references should come from all sources, including textbooks, primary literature, review article, etc. (10 pts)

(d) *Presentation:* Each group member must participate in the presentation and present their <u>individual</u> contribution to the site. You will be graded <u>individually</u> on the clarity and content of your presentation. (10 pts)

(e) *Attendance:* You must attend all of the presentations to receive full credit. (10 pts)

Figure 5-1. Project description for Design 5.

Wiki-project Timeline	
January 14, 2011	Group assignments are given.
January 28, 2011	Each group will turn in a 1-page (total) description of their top three topic choices and their reasoning.
February 4, 2011	GSI B will give an in-class presentation on how to create a username and edit Wikipedia. Please bring your computer so you can follow along. Post a note on the discussion page about your intentions and link to your sandbox.
February 11, 2011	Each group will generate an outline of their site in their sandbox.
February 18, 2011	Peer reviews of the outline are due. Post the peer reviews in the *discussion* page associated with the reviewed sandbox.
March 18, 2011	The "sandbox" version of the site is due.
March 25, 2011	Peer reviews of the "sandbox" versions are due. Again, post your peer review in the discussion page associated with the reviewed sandbox.
April 8, 2011	GSI B will give and in-class presentation on how to properly move your sandbox into the live site. Please bring your computer so you can follow along. Each group will then put their newly revised site online.
April 11, 13, and 15	In-class presentations.

Figure 5-2. Wiki-project timeline for Design 5

The topics that were worked on by the students ranged from new entries (pages that did not exist), to entries that Wikipedia assigned as "stubs", and even some groups made additions to entries that were already substantial. Wikipedia defines stub pages as entries that have only a few sentences describing general information to convey its relevance to the encyclopedia but have incomplete information[22] (Figure 5-3).

Figure 5-3. Polyfluorene is an example of a stub article that the students expanded. At the top of the page is a box that reads "This article needs attention from an expert on the subject". Appendix D showcases the completed Polyfluorene page done by the students.

These pages are often created to encourage other editors with expertise in the topic or access to the appropriate resources to expand on the page. We felt that students who worked on pages that started with minimal information would not only add useful information to Wikipedia and but also enabled the students to engage their creativity.

The student were evaluated on the following criteria outlined in Figure 5-1, students were required to expand the reference list, add additional sections and figures, and ensure that their entry was adequately hyperlinked. The grades assigned were based both on completion of these criteria and the quality of the additions. The references needed to be appropriate, current, and cover a range of resources; meaning that the students needed to cite books and review articles in addition to primary literature. Broad resources are important because academic institutions purchase institutional licenses that provide the access to primary literature, but the average Wikipedia reader will most likely

113

not have access to the article cited if it requires a license to read it.[23] Just as we would like the students to think critically about what they read, we would like those who access the students' pages to do the same and be able to pull up the references that they students cite. The students were required to add three new sections and a section aimed at the general public. These sections were evaluated on the quality of the writing and coverage of the topic. In more recent iterations of the project, we added several rounds of peer review to assess the quality and completeness of the entries prior to assigning final evaluations. As previously mentioned, peer review enable students to improve on their own writing.[13] During the peer review process, each entry was assigned at least two classmates that were from different groups to critique the site. The criteria that the students followed in their peer review and questions they should consider addressing in their peer review are outlined in Figure 5-4.[24] This criteria was based on attributes we looked for when we graded the students' work in previous semesters. The students commented on the coverage of the topic, writing style, comprehensibility, formatting, and original figures of the entry assigned. The students were also required to familiarize themselves with the topic they were assigned to peer review by reading a review article on the topic so that they would be knowledgeable enough in the topic to make well-informed comments on the site. Each figure was evaluated on the quality of the image and the extent to which it clarified and enhanced the key concepts of the entry. Proper hyperlinking of their entries was important for keeping the entry focused on the topic rather than background information that is detailed on the respective Wikipedia page that can be hyperlinked. At the end of the semester, the students gave an in-class presentation on their topic, the modifications they made to the entry, and future additions. The

presentation was evaluated on individual contribution to the Wikipedia page and clarity

of the presentation.

Guidelines for Peer Review

Read the current site on the topic (if there is one).

Read the outline prepared by the students.

Read at least one review or reference article on the topic.

Provide feedback to the assigned group by writing a 1-page "comment" on their outline (font size Ariel 10, spacing 1.5, margins 1" on all sides). You should address each section of the outline.

Section 1
Are the objectives original, clear, and appropriate for Wikipedia. Check to see if any other sites duplicate this information. Suggest possible sites that they could link to. Is the length feasible and appropriate?

Section 2
Is the length appropriate? Should sections be merged? Split? Are any important concepts missing? Is there continuity and coherence to the site (i.e., new additions complement the current site)? Does it meet the stated objectives?

Images
Are the images clear and understandable without reading the text? Is there a take-home message for each image? Are they informative? Do they look nice? Are the appropriate Chemdraw settings used?

Section 3
Are the references diverse (including textbooks, review articles, original research articles)? Are they complete? Do a quick literature search yourself to make sure they aren't missing any key papers or review articles or chapters from books.

Overall comments
Provide a short summary of your critique, highlighting both what the groups did well and as well as what can be improved.

Figure 5-4. Peer review criteria for sandbox version implemented during Design 4

C. Wikipedia as an Editor

Many are familiar with Wikipedia as a reader, browsing Wikipedia for information, and clicking through the hyperlinks that connect related topics. As stated earlier, although there is technically no criteria or credentials needed to make an edit in Wikipedia, there is a large body of seasoned editors (Wikipedia Community), who are the "watchdogs" of Wikipedia that prevent copyright violations, vandalism, and potentially libelous edits. Because there are millions of users[15], and over 17 million people trying to edit[25], there are tools for seasoned editors to efficiently counter vandalism that place a large focus on anonymous[26] editors, and new editors or newly minted accounts.[19] Unfortunately, when students are editing Wikipedia for a class project, it is assumed that a majority of them do not have an existing account and have a history of zero contributions, and then have a higher chance of being immediately flagged by seasoned editors. Therefore, it is good to be aware of this community of seasoned editors when students are confused about their edits disappearing. If the students' edits are of quality, all edits are logged, saved within the history page, and can be restored. This editorial process within the Wikipedia community is potentially an additional layer of oversight to ensuring that the students' edits are well written and well cited.

Throughout this project, through conversations with the Wikipedia editing community, I learned that edits also have a higher likelihood of survival and were not

116

prone to deletion by seasoned editors if students were familiar with and interacted with the community of seasoned editors. In addition, there is a unique Wikipedia markup language is that is a simplified alternative to HTML. Therefore I organized and developed an editing tutorial session during the semester to familiarize the students with the tools and terminology of the Wikipedia editing interface. To better understand the aspects of editing used throughout this chapter, I will first outline common Wikipedia editing terminology. These tools within the Wikipedia interface are often overlooked by the typical Wikipedia user but were important for the students to be familiar with to be able to make contributions to Wikipedia. The following aspects are designated in Figure 5-5.

1. **Userpage:** after creating a username, this is the user's personal space for the user to use how he/she would like such as describing one's self or placing "hidden" sandboxes. "Hidden" means that when a topic is searched, the second level pages stored on the userpage will not be found. Everything that is posted on Wikipedia can be seen by anyone with the hyperlink to the sandbox.

2. **Sandbox**: a second level page within one's user space (first level) where pages can be kept "hidden" until the page is complete or ready to be live

3. **Talk tab:** where comments, suggestions, and inquiries about the entry are expressed. Here is where the editing community (editors who create pages and make edits) often discusses, debates, and attempts to reach a consensus as to what should be included, the validity of the information, and the importance of the information being added.

4. **Edit**: clicking this link brings one to the editing interface

5. View history: this is a record of when and whom made every edit to the page
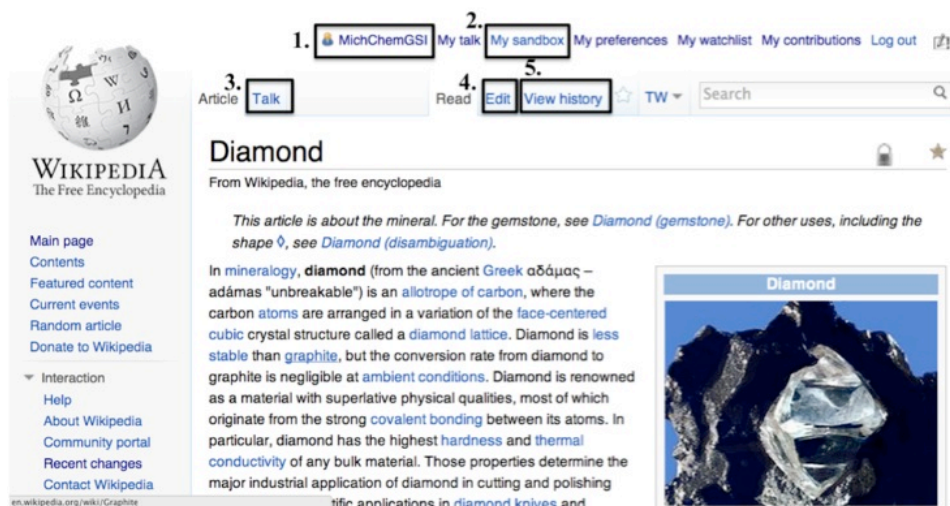
Figure 5-5. Editing Components of the Wikipedia Interface.

The in-class editing tutorial worked best when the students had their computer with them so that they could follow along. Again, Wikipedia has its own unique markup language that is not a common word processor and these tutorials were essential, as not all students would have programming background specifically in Wikitext.[27] The tutorial would outline the just described basic Anatomy of a Wikipedia page, walk the students through the creation of a username, inserting references and what the corresponding markup language would look like, how to upload images, and the a brief tutorial on copyright. It was important to relay to the students that the content in Wikipedia is under a Creative Commons CC-BY-SA license, which means that the images and text are free to copy and distribute as long as there is attribution.[28] We require that all of the students create their own images to best fit with the content on their page. Images cannot be copied or scanned directly from the journal articles and uploaded to Wikipedia. We developed these specific qualifications to prevent the students from violating copyright

118

laws and making mistakes that are common of new editors that would result in their work being removed by other Wikipedia editors. An example of the editing tutorial presented to the students can be found in Appendix D.

D. Wiki-project Timeline

At the time this thesis is being written, the Wikipedia project has seen five iterations in the graduate-level courses taught by Professor Anne McNeil, each designated as Design 1 through 5. This section will highlight each implementation, describing what we learned after each semester, what we modified, and why we made these modifications. Throughout this section, the use of "we" refers to Professor Anne McNeil, the primary instructor of the course, and I or in some cases noted, the graduate student instructor the semester in mention. The first semester we[29] had our students edit Wikipedia pages is noted as Design 1. We started the project mid-semester, had a brief editing demonstration, and there were no assignments in between the initial topic submission and the final presentation. Table 5-6 is an aggregation of the timelines we gave the students each semester; highlighted cells indicate alterations from the previous semester. In general, the student feedback at the end of the semester conveyed that there were not enough time allotted for the project and that various checkpoints would enable them to make progress on the project throughout the semester.

In Design 2, Professor McNeil and I assigned groups at the start of the semester and the project spanned 13 weeks. I developed the timeline for the project with guidance from Professor McNeil for the project to fit into the rest of the course syllabus, and we

added three additional milestones, a list of potential references to be submitted week 5 of the semester, an outline submitted in week 7, and in week 11 students submitted the "sandbox" version of their site for approval. We were also able to provide exemplary examples of sites and presentations from Design 1 to help guide the students with what was expected for the project. These handouts are detailed throughout this chapter. I suggested the list of references as a milestone to enable the students begin the research on their topic early and for the instructors to assess the reference coverage on their topic. However, after surveying the students with an open-response survey at the conclusion of the semester, and assessing the additional milestones from the previous semester, we decided to eliminate the reference list submission milestone. As one student noted when prompted to "*List two things that you would change to make the project better in the future*":

> "Personally I skimmed references to find ones that I thought would be relevant, and I turned those in for the checkpoint. But it wasn't until I actually started writing my portions of the text that I delved deeper in the references. At this point I realized that some of the references I had said I would use didn't fit well, and that I wanted to include other references that I hadn't turned in for the "checkpoint".

The reference list assignment was submitted before the students had started to write, and therefore was not as helpful as we had originally anticipated. We also did not want to convey that the students necessarily had to use only the references that we had "approved" of early in the semester, we do understand that through the writing process, some references can be more appropriate than others.

The next semester, Design 3, we eliminated the reference list submission and requested an outline of the students' entry in week 5 rather than week 7. We did not give

specific guidance in the outline, but found that we were able to provide much more substantial feedback to groups that were as detailed as possible in their site additions. For example, some groups had not only considered the sections that would be added but also what each subsection would cover, including potential references, and description of images. Therefore, for the following semester, we developed criteria for the outline submission. Figure 5-6 are the guidelines we provided for the outline submission during Design 4. Requiring these details enabled the students to begin working on the project in the semester and we anticipate prevent them from procrastinating until the end of the semester to begin working on the project. For the outline, the students were required to being to draft the figures they anticipate adding, indicate what would be the main points for each section, and list potential references.

Guidelines for Wikipedia Outline

Section 1
List your objectives for the site. What do you plan on additions and why are these additions going to enhance or improve the site.

Section 2
The format of the outlines should mimic the "Contents" box on the Wikipedia page. Add sections and section titles that you plan to create. Within each section, list (using bullets points) the main content you will add to site. Include all images you want to add to the site (see guidelines on how to make high quality images). The images should enhance understanding of the concept, not just display it.

Section 3
List any references you plan to add to the site. Limit citations to websites since they are fluxional.

Figure 5-6. Guidelines for Wikipedia outline

During Design 4 and Design 5 we also we added additional peer-review milestones[24] to the assignment to further engage the students in collaborative working environments. The specific aspects of the outline and sandbox version of the site that we required the students to comment on in their peer review were outlined earlier in the

chapter and are in Figure 5-4. We anticipated that incorporating peer-review aspects to the project should also contribute to improving the students' writing, resulting in higher quality entries, and reduce instructor workload.[30, 31] I suggested prior to Design 5 that these peer reviews be written on the discussion pages within the sandbox entry to further familiarize the students with Wikipedia editing. When the sandbox entry transfers to the "live" entry, these peer reviews are also transferred and the suggestions made by their peers are documented if further discussions were to arise from the editing community. The peer review suggestions maybe by the students online were implemented in Design 5.

In the first four design implementations, we assigned group login names and passwords in order to easily identify the specific edits made by our students. Because Wikipedia is an open platform we were concerned about the possibility for other members of the editing community working on the entries that the students were working on throughout the semester. Group accounts allowed us to accurately grade the contributions of our students and to differentiate from edits made by the community. Community interference was rare as our students generally edited within the sandbox space. However, the community felt that group accounts were neglected after the project or semester was completed and it was difficult to interact with the students at a later date if changes needed to be made. Therefore, we now require each student to create their own user account; and we internally keep track of the individual usernames for each student. Individual user accounts also enables us to resolve disputes about a team member not sufficiently contributing to the group project as all edits are logged.

E. Other Graduate Courses that Edited Wikipedia at Michigan

In addition to the five project designs described in previous sections, there have been an additional eight graduate courses over the span of five years that have created and/or edited Wikipedia entries at the University of Michigan. These courses have ranged in class sizes of 10-40 students in a variety of departments such as Astronomy, Environmental Engineering, and other courses in Chemistry not taught by Professor Anne McNeil. The number of courses and range of disciplines illustrates the flexibility, ease of implementation, and interest in the pedagogical potential of this project.[32] Each of these additional courses created their own timelines and requirements, but based their timelines on the designs outlined previously. In each course I provided expertise on how to best fit the project timeline within the course, presented the in-class editing demonstration, developed handouts for the students, and was available by email or online through Wikipedia's chat client, IRC (Internet relay chat), during the semester to troubleshoot editing challenges. For the courses that I have been the Graduate Student Instructor for, I have also been responsible for helping with topic selection, providing feedback for the students on their pages, and assessing the final project.

F. Other Professors' Motivation for Implementing the Project

It was exciting that other instructors were willing to incorporate the Wikipedia editing project in their courses after hearing about our successes with the project. I surveyed these instructors to better understand their motivation for implementing the

project. The first question asked was: "What drew you to this project?" and a representative quote is given below:

> *"There is substantial work in the analysis of learning effectiveness that student driven work is an excellent approach to increasing both quality and quantity of learning and retention. I had used student driven work for years but had not made the results available to the broader community, ie via Wikipedia. This was a great idea and one I was happy to adopt."*

From this representative quote, we observe that these instructors had similar hypotheses that the project, due to Wikipedia's visible nature, would expand student learning. A few of these professors also continued to implement the project for subsequent semesters and indicated that they did so because:

> *"The student's produce very worthwhile mini reviews of chemistry that should be shared with the broader scientific community. The student's like that their work has greater worth than a grade in a course.*"

These comments about the project were encouraging and supported our hypothesis that the project would provide greater learning than a traditional literature review assignment. However, improvements to the project that were suggested were to consider how to best support the students in the project – both in terms of scientific writing and in terms of the technical aspects of working with Wikipedia. Another professor also indicated a similar need for technical support because "*a lot of students complained too much time was spent on learning coding techniques and text and figures they put on were often immediately taken off by other Wikipedia editors*". The next section in this chapter describes the development of materials to ease the training of new editors for classroom activities. However, even with well designed materials and resources, the students will need to be made aware that this project will require the commitment to learning a new markup

language. The use of Wikis is becoming more prevalent in many organizations from federal agencies[33, 34] to regulatory agencies.[35] Wikis are an efficient platform to share updated information within the organization and to rapidly incorporate new research findings. With these examples of Wiki usage in organizations outside of academia and Wikipedia, it is possible that Wikitext markup language skills will be a valuable asset for these students in their future work.

G. Development of Resources

I created a handbook entitled *Editing Wikipedia as a Class Project* to facilitate incorporation of this project into other courses at our institution and beyond. This handbook provided detailed and streamlined instructions for both the instructor and the students. Although the handbook has not been updated since its publication[36], many of the in-class editing tutorials have been updated to accommodate the new editing interface. In 2011, the Wikimedia Foundation modified the editing interface to incorporate templates to simplify many of the attributes of the editing process such as adding references and images. The instructions in the handbook are generally still relevant as the Wikitext markup language, which is presented in the handbook for these editing attributes, has not changed. The changes to the interface that simplify these actions are in the form of button shortcuts in the editing interface are not included in the manual. An example of an in-class Powerpoint presentation used to guide the students through the new Wikitext editing interface is provided in Appendix D. A majority of the

guidelines for topic section, project timeline, and navigating the Wikipedia community that were originally in the handbook have been updated and included throughout this chapter.

H. Evaluation of the Project

H.1. Open-Response Feedback

Through an informal survey at the completion of the semester, the students indicated that they were generally very excited to do the project and were motivated by the visibility of their efforts. This informal survey was an open-response written survey was given to the students taught by Professor Anne McNeil, to gage the students' perspectives of the project and their input on how to improve the project. Open-ended questions are the most effective at gathering authentic information about a person's experience.[37] In general the feedback from the students in the Design 1 implementation, indicated that the students had gained a greater understanding of their topic and had learned how to communicate advanced concepts in science to the general public. The students were asked to list the benefits of doing this project; some representative responses follow:

- "Teaches us how to present theories in a manner that people who don't have prior knowledge can understand it."
- "It was good having the scientific responsibility to create/fix a Web site in which millions of people can access."
- "It encourages collaborative learning and betters the quality of scientific information available to the public"

126

- "Learned in depth about a particular topic in physical organic chemistry and to explore this topic for applications that I found most interesting."
- "It helped improve Wikipedia!"

For a more thorough analysis of the student responses, after Design 1 and Design 2, the survey asked the following questions:

1. List two benefits of doing the class project
2. List two things you would change to make the project better in the future
3. On a scale of 1 to 10 (with 10 being strongly agree) – did doing the class project enhance your learning experience in [course name]?
4. Do you think the timing for each stage was appropriate? Or is there too much or too little time between milestones? Please be specific!
5. Were you given enough guidelines or would more be helpful? If you say more, suggest exactly what other guidelines you would have liked?
6. Any other comments you would like to make about the project?

The responses from the students can be divided into the following categories in Table 5-1 to illustrate the range of the feedback.[37] For each student, if there was a comment about the category of "project timing" for example, we decided if the comment was favorable or unfavorable for that category, and counted the number of favorable and unfavorable comments in each category. To have a better idea how responses were categorized, an example of positive comment for the category of timing would be if comment said that the length of time for the project was sufficient, and a comment categorized as negative would be if the respondent suggested starting the project earlier in the semester.[38]

Category		Design 1	Design 2
Project timing	Positive	35%	78%
	Negative	65%	22%
Amount of Wikitext editing guidance	Positive	71%	25%
	Negative	29%	75%
Amount of guidance on what was expected	Positive	54%	70%
	Negative	45%	30%
Benefited from group work	Positive	66%	100%
	Negative	33%	0%
Benefited from learning gained	Positive	94%	100%
	Negative	6%	0%

Table 5-1. Categorized student responses from informal open-response survey

The categorization of the students' responses can illustrate that the transition to the project encompassing the entire semester between Design 1 to Design 2 might have been a favorable change as in Design 1 there were 65% responses that indicated unfavorable project timing to only 22% of the students in Design 2. Several students also indicated that they benefited from learning the Wikipedia markup language. However, there were also comments from the students that learning the Wikipedia markup language was difficult and time consuming. It is also because of these comments that we decided to develop a more detailed manual specifically geared towards editing Wikipedia in a classroom setting. And in later implementations of the project, we had students bring their computers to the editing tutorial session to follow along. Almost half of the students in Design 1 felt that there was not enough guidance throughout the project, and this decreased slightly to 30% during Design 2. During the second semester (Design 2) we were able to provide the students with example sites and presentations from the students who participated in Design 1, which we believe, attributed to the Design 2 students

having felt they received adequate guidance. A majority of the students also felt that the

project was a positive experience on their learning in the course. Table 5-2 also tabulates

the responses to question 3: "*On a scale of 1 to 10 (with 10 being strongly agree) – did*

doing the class project enhance your learning experience in Michigan X?" In this

informal questioning, over 70% of the students' response are a rating of 8 or higher,

supporting that the students overall did feel that the project enhanced their learning

experience in the course.

Rating	Number of responses from Design 1	Number of responses from Design 2
3	1	0
5	4	0
6	0	0
7	6	2
8	9	2
9	2	2
10	2	3

Table 5-2. Student responses to question 3: "*On a scale of 1 to 10 (with 10 being strongly agree) – did doing the class project enhance your learning experience in Michigan X?"* of an informal open-response survey about Wikipedia project

The above survey was not given after Design 3, Design 4, and Design 5, but

instead Professor Anne McNeil requested that when submitting their teaching evaluations

for the entire course, that the students specifically evaluate the Wikipedia project in the

"additional comments" section of the evaluation. I divided these responses into key

phrases that the students used to provide the feedback range of the project in during

Design 3, 4, and 5 (Table 5-3).

Keyword or phrase	Percentages of responses using key phrase
fun, good, great, enjoyed, liked	46%
a lot of work	38%
presentations were unnecessary	23%

Table 5-3. Summary of student responses categorized by keywords or phrases used. Sample size = 26 responses.

In these responses, the students were generally interested and excited in the project and being able to contribute to a resource that is prevalently used. The words "fun", "good", "great", "enjoyed" or "liked" in a positive manner was used to describe the project as a whole in 46% of the responses. However, in these semesters, students also expressed that the project was a significant amount of work in both the balancing of schedules to meet with group members and ultimately coding their pages. The phase "a lot of work" – or a variation of this phrase describing the challenges of the project and that the challenges were not sufficiently weighted in their final grade – was written by the 38% of the respondents. 23% of the students also mentioned that the class time spent on presentations were not worth their time and would have rather had lecture be used to present more case studies. This dissatisfaction in the information presented by their classmate's may indicate that the students needed more guidance on what should be covered in the presentations. One student felt that they did not learn a lot from the project, especially because Wikipedia generally presents cursory information.

> "The Wikipedia project is good, but a paper would allow us to look at topics of interest in more depth, whereas Wikipedia encourages superficiality"

However, this comment is an isolated case, as there were a few comments like the one above (8%) and we cannot find substantial data that supports this student's claim about

130

Wikipedia. Research groups who study online communities and the quality of open resources do think that Wikipedia is of sufficient quality.[39] Some of the students (12%) did want to eliminate the project completely but a majority of their reasons were not for lack of learning, but that to them the project required a significant amount of work to collaboratively create a well-written, well-researched page and that they in general disliked group work. Through the project a majority the students were able to go in depth into their topic and provide information that would be useful for both the general public and academics who may access the entry to quickly gain detailed information about a particular topic in chemistry. As the main goal of the project was for the students to learn more details about a particular topic that cannot be taught in lecture due to time constraints, 15% of the responses specifically used the phrase "I learned a lot about my topic" through the project.

I also surveyed the students in the courses where I was only facilitating in the Wikipedia project and Professor Anne McNeil was not teaching the main course material. This feedback was important for gaining insight into the effectiveness of the manual and if relevant information was being passed on when we were not the primary instructor for the course.

On the basis of the feedback from the students in the other course in chemistry in which Professor Anne McNeil was not the primary instructor, the students reported that the in-class editing demonstration[40] was most helpful in teaching them how to edit Wikipedia and navigate with the Wikipedia community of editors. Only a few students

indicated that they referred back to the editing manual provided as a means of reminding them what was presented in the demonstration. Therefore it was important to stay informed about Wikipedia's constantly changing interface and to modify the demonstration after every semester to improve the editing tutorials.

From the feedback we also learned that the students would have preferred to know more about how they were going to be evaluated. Student felt that project expectations were not conveyed and a point distribution rubric would have been helpful for the students to gauge their progress. This feedback helps to recognize that each instructor and each course should develop a rubric that is appropriate for the individual course.

H.2. Retrospective Survey

In Design 2 and Design 3 in which Professor Anne McNeil was the lead instructor and I was the Graduate Student Instructor, a retrospective survey using student panels was implemented to evaluate whether the Wikipedia project significantly contributed to the learning objectives of the course namely:

1. Learning advanced concepts in chemistry

2. Communicating science to a diverse and general audience

3. Identifying appropriate references and other resources for building an argument

4. Working collaboratively

5. Understanding how a well-researched explanation is constructed

We identified seven learning resources for the course: classroom lecture, the textbook, problem sets, literature papers, Wikipedia project, working alone, and working in groups.

In order to put the Wikipedia project in context, we implemented a survey that asked students two questions about all seven of the resources as they applied to the five learning goals. The questions and statements that students were asked to respond to are in Figure 5-7.

A. The [*first*] learning goal for Chem 540 was to [*explore and learn advanced concepts in chemistry*]. To what degree do you think that each of the following resources contributed to this goal?

B. Now, rank these seven resources according to their significance in getting you to [*explore and learn advanced concepts in chemistry*].

Figure 5-7. Retrospective survey questions

For Question A, respondents used a 7-point scale to rate how the resources contributed to achieving the goal, from 7-1 in which 7 indicated "extremely", 4 indicated "neutral", and 1 indicated "not at all". For Question B, respondents ranked each of the seven resources using a 7-point scale, from 1-7, in which 1 indicated "most significant", and 7 indicated "least significant", with no ties allowed. Note that the scale in Question B was inverted from Question A to intentionally differentiate the rating questions from ranking question.

133

We used student panels rather than individual student responses. Using student panels that discuss and come to consensus is the recommended strategy to overcome the intrinsic unreliability of retrospective self-assessment of learning gains.[41, 42]

There were 30 students in the course during Design 3 and 26 students in the course during Design 4. In both cases the students were divided into 6 panels in order to have the same number of panels between the two sets of data. The panels worked on their responses for an average of 45 min. Responses were anonymous. The results for organic principles were compiled and analyzed by someone external to the class and the analysis was performed after grades were assigned and submitted.

The primary purpose of Question B, which asked for an absolute ranking of the usefulness of the resources, was to check the reliability of the responses to Question A. The inverted numerical scales make it particularly difficult for respondents to simply translate the rating responses from Question A to the rankings of Question B. We plotted the average score given by the panels across the range of resources with respect to each learning goal, predicting that the higher the rating score that a resources received from Question A, the more significant its ranking should be from Question B. We carried out a least-squares regression on the data from each of the five learning goals and observed r^2 correlation coefficients of 0.91-0.96 for the responses from Design 3, and r^2 correlation coefficients of 0.96-0.97 for the responses from Design 4, from which we conclude that the ratings given to Question A are highly reliable.

To evaluate whether or not a given resource was being deemed by the students to contribute significantly to the learning goal, intra-resource comparisons are not useful. We wished to understand how far from "neutral" the students were rating the contribution

of a resource to their learning for any given instructional goal. Consequently, the ratings

for each resource were compared for their statistical difference from a hypothetical

response set of all 4's (i.e., perfectly neutral), using a two-tailed type-2 *t*-test. Table 5-4

provides the results of this analysis for Design 3, and Table 5-5 is for Design 4, expressed

as the average rating from the six student panels along with the *p*-value derived from

comparing the student data set with the hypothetical response set.

Resource	Learning Objectives and Ratings: Average Scores (*p*-Values)				
	1. Learn Advanced Concepts	2. Communicate Science to a General Audience	3. Identify Resources for Building an Argument	4. Work Collaboratively	5. Construct Well-Researched Explanations
Lecture	**6.33** (0.000)	4.83 (0.318)	**5.67** (0.000)	2.17 (0.012)	**6.67** (0.000)
Textbook	4.17 (0.599)	3.67 (0.651)	4.00 (1.000)	**1.33** (0.000)	3.83 (0.828)
Problem Sets	**6.00** (0.000)	4.33 (0.145)	4.50 (0.270)	*5.33* (0.003)	**5.50** (0.000)
Literature papers	4.33 (0.515)	3.33 (0.373)	**5.67** (0.000)	*2.67* (0.038)	**6.17** (0.000)
Wikipedia	3.33 (0.207)	**5.83** (0.000)	**6.50** (0.000)	**6.00** (0.000)	4.67 (0.304)
Working alone	**6.17** (0.000)	3.83 (0.845)	2.83 (0.128)	**1.33** (0.000)	3.67 (0.628)
Working in Groups	*5.33* (0.003)	5.33 (0.038)	3.17 (0.318)	*5.50* (0.006)	3.83 (0.734)

Table 5-4. Design 3 retrospective survey results.

Resource	Learning Objectives and Ratings: Average Scores (*p*-Values)				
	1. Learn Advanced Concepts	2. Communicate Science to a General Audience	3. Identify Resources for Building an Argument	4. Work Collaboratively	5. Construct Well-Researched Explanations
Lecture	**6.67** (0.000)	5.00 (0.270)	5.33 (0.010)	2.17 (0.019)	**6.67** (0.000)
Textbook	3.67 (0.447)	3.50 (0.527)	3.64 (0.341)	**1.33** (0.000)	4.33 (0.341)
Problem Sets	**5.67** (0.000)	2.67 (0.073)	3.50 (0.549)	4.17 (0.734)	5.00 (0.201)
Literature papers	3.50 (0.270)	2.50 (0.078)	4.67 (0.303)	**1.50** (0.000)	**5.17** (0.000)
Wikipedia	3.83 (0.599)	**6.67** (0.000)	**6.33** (0.000)	**6.67** (0.000)	*5.33* (0.002)
Working alone	**6.33** (0.000)	*1.83* (0.008)	2.00 (0.010)	**1.00** (0.000)	2.83 (0.081)
Working in Groups	4.20 (0.770)	4.00 (1.000)	2.20 (0.070)	*6.00* (0.007)	4.00 (1.000)

Table 5-5. Design 4 retrospective survey results.

We have used relatively conservative criteria to evaluate our results. We deemed $p \leq 0.0005$ as a statistical threshold for resources that the students report to contribute most significantly to their learning of a particular goal; *p*-values between 0.001 and 0.01 as marginally significant; and values of $p \geq 0.01$ as insignificant. The two sets of data from Design 3 and Design 4 are very similar. The validity of the student responses is reflected, we believe, in their responses to the learning goal of "working collaboratively". The Wikipedia project was deemed to be the most useful, working on problem sets and studying with others were deemed useful, and using the textbook and studying alone were not useful.

Specifically focusing on how students evaluated the Wikipedia project, it was the only resource with a significant contribution to "communicating science to a diverse and general audience", and it was the most significant resource for "identifying appropriate

136

references and other resources for building an argument" and "working collaboratively" for both classes. While no resource should or can carry the entire burden for the learning goals of any class, we do note that the Wikipedia project received the best ratings out of the seven resources (this project contributed significantly to three of the five learning goals), just above lecture, which also contributed to three of the five learning goals.

H.3. Survey Inquiring if Students Continued to Edit Post-semester

Recent studies have suggested that Wikipedia is experiencing a decline in active editors.[43, 44] This decline is concerning as Wikipedia is a successful resource of information because of the community of volunteers that work together to form this online encyclopedia. Without this community contributing and vetting the entries, there is a great potential for Wikipedia to fall into the hands of those who only want to spread false and inaccurate information to advance their own personal causes.[45] Although vandalism might not as big of a concern to science-related pages, with the exception to politically topics such as climate change, if the encyclopedia becomes out-of-date, incomplete, or inaccurate, it will be a poor starting resource for gathering background information.[46] To gauge if these types of classroom projects would be beneficial for the retention of active editors or increase the survival time of new editor, we carried out a survey to inquire if any of the students continued to edit after the end of the semester.

In Fall 2010, we did an informal survey of all of the students that had participated in the project to see how many students have continued to edit Wikipedia. A total of six courses had implemented the project, totaling over 120 students. There were 51 students

who voluntarily responded to our survey, 17.5% of them made at least 1 edit once the semester was completed, and were motivated to do so by their desire to fix the mistake. All of these contributions were small changes, grammatical and spelling errors, estimating that they had done less than 25 edits. This information is potentially helpful for the Wikimedia Foundation as they investigate opportunities for scientific experts to be involved in contributing to Wikipedia.[47, 48] The Wikipedia Foundation would like to increase the number of experts who contribute to improve the quality of the entries, cover more scholarly and encyclopedic content, and increase the diversity of participants.[49] Although this is only a small sample set, classroom projects may not be a means to gain new prolific or highly active editors. The number of active editors that we gained through the project is similar to those that the Wikimedia Foundation has found through their survey of expert participation,[50] which is about 10%. Wikipedia research has shown that regardless of lack of time or unfamiliarity with the editing syntax, in general, academics do not contribute because through the platform they cannot be identified as experts, their well-researched contributions have a high potential of being over-written, and they are not rewarded for their contributions because in academia advancement is measured by grants received and publications awarded. However, these responses are potentially only capturing reasons attributed to professors rather than students in the academic environment. Other than the speculation that students are not editing due to time constraints we unfortunately cannot address the underlying reason why students have not continued to edit after the end of the project. Because the Wikipedia Foundation has found that a majority of the editors are males with advanced degrees, students would be a great means for harnessing expert opinions and research into how to motivate them to

edit would be advantageous for Wikipedia. As the breath of editorship increases, we anticipate that the information presented on Wikipedia will also include a wider subject body and improve the well used resource.[51]

I. Wikipedia Editing Community Involvement

We would like to take this opportunity to express our appreciation for the Wikipedia editing community throughout this project, especially the editors involved in WikiProject Chemistry.[52] Because Wikipedia is the work of dedicated volunteers, the lack of an intuitive infrastructure makes it difficult for new editors to navigate. For example, we initially did not recognize that there were discussion pages where disputes are settled. But along the development of this project we have met some very helpful editors who overall have been very helpful in providing our students with feedback and suggestions on the content of their pages. They have also been very helpful in bringing to our attention that Wikipedia has certain style guidelines that students should be introduced to at the start of the project.[53] An example of their suggestions was previously described in the change from group names to requiring the students to create individual accounts. They were also significantly helpful when I was outlining the directions for the development of animations described in Chapter 6 for the undergraduate project. When we initially started the project, there were a few editors, who, on principle, objected to students editing entries for course credit. But these editors were overwhelmingly out-voted by the majority of editors in the community. As other instructors in other

disciplines consider implementing this project in their own course, it is good to be aware that brand new editing accounts are easily identified by Wikipedia's "watchdogs" and depending on the active editors in that field, some editors do make edits that are discouraging to both the instructor and the students. This frustration felt by new editors is a common characteristic of Wikipedia and its prolific editors.[54] However, many are trying to dispel this characteristic of Wikipedia in order to encourage more experts to contribute and edit.[55] We very much appreciated the editors who supported our efforts, and took an interest in our student's work.

J. Future Work

Through the implementation and student learning analysis of the Wikipedia project over a number of semesters, we have shown that the project can encourage students to learn advanced topics in chemistry, and that working in groups and Wikipedia's visibility, would further contribute to the students' learning. Often times writing assignments are assigned to enable students go in depth into a topic that can only briefly be introduced in lecture and for students to gain valuable research skills.[7,5,56] Therefore, the Wikipedia project was developed to replace a traditional writing assignment and due to Wikipedia's visibility and the general public as its natural audience, we hypothesized that students would gain a greater degree of learning as they would be assessing the material more critically because their work could be read by anyone accessing their page. The next steps for the project would be to directly compare the learning gained in participating in the Wikipedia project against learning gained in

140

writing a traditional literature review. We have compared the Wikipedia project and its contribution to learning for undergraduate students in the context of a number of different projects and the analysis is described in Chapter 6. However, the assignment as a whole for the Wikipedia project at the undergraduate-level was significantly different than the assignment at the graduate-level. Therefore, we would like to compare the learning gained for graduate students in replacing a traditional literature review with the Wikipedia project. Traditional literature reviews are often done individually and the students' completed work are not usually published for others to read.[56] To focus on the hypothesis that students learn more in publishing a Wikipedia page because they are developing explanatory knowledge skills, we can assign the Wikipedia project as an assignment to be done individually. Some professors have expressed potentially giving students the option of either doing a traditional writing assignment or a Wikipedia page, and this potentially can be a means for comparing the learning gained in the two assignments.[57] Both assignments would have the same milestones for peer review as outlined previously in this chapter. This can potentially address the degree of learning gained by the students in publishing work for the broader community as oppose to only the professor. Another option is to assign both the Wikipedia assignment and a traditional review assignment. A colleague previously assigned both assignments, to be worked on in groups, and although the feedback from the students were that having both assignments was overwhelming, their primary concern was the lack of guidance as to what was expected for each assignment (student responses are aggregated in Appendix D). If both projects' expectations were clearly defined, there is the potential for the students to gain different skills in each assignment. To analyze the learning gained by the

141

Wikipedia assignment relative to a traditional literature review, we will have the students complete a pre- and post-semester survey similar to one given to the undergraduate students described in Chapter 6. Student satisfaction with the course is usually measured through course evaluations after the end of the semester; however surveying the students' expectations at the start of the semester and perceptions at the end of the semester can provide the degree to which students felt the course and its components were in lines with their own goals for the course.[58] Surveying the students' expectations at the start of the semester and perceptions at the end of the semester can provide information about student learning. The learning objectives or goals for the course would remain as they were in the retrospective survey: 1.) Learning advanced concepts, 2.) Communicating science to a general audience, 3.) Identify resources for building an argument, 4.) Work collaboratively, and 5.) Construct a well-researched explanation. There would be an additional resource for the course, the traditional literature review assignment done in groups. There would be eight learning resources for the course: classroom lecture, the textbook, problem sets, literature papers assigned to read, Wikipedia project, literature review, working alone, and working in groups. I hypothesized that the Wikipedia project would continue to be rated high for the learning goal of "communicating science to a general audience" due to its inherent audience that the students will need to consider for the project, but in the other learning objectives that scored high in the retrospective survey previously mentioned, "identifying appropriate references and other resources for building an argument" and "working collaboratively", both the literature review and Wikipedia project would score an equally high rating. If both assignments are shown to be generally equivalent in the learning the students expect to gain and perceived to gain

at the end of the semester, I would argue for the implementation of the Wikipedia project over a traditional review because of the current shift for scientists to participate in the political and social discourse.[59] Encouraging students to contribute to a resource that the general public has access to, like Wikipedia, may encourage their participation in these important discussions about the direction of research as well as be a means for solidifying concepts they are learning.

As mentioned previously, the modifications that we have made to the project have been in response to both student and Wikipedia community feedback. A common critique that we have received from the community is that because our students edit in a sandbox, they are unable to offer suggestions or review the page before the students complete the project at the end of the semester. We initially had the students edit within the sandbox to encourage a collaborative effort between the group member and enable students to comment on group members' contributions prior to publication. The next time we implement the project we will have the groups upload the individual sections as they complete the section rather than the entire page at the end of the semester. We are excited that this change will bring possibility of the students being able receive feedback from the community. Although we attempted to solicit feedback from the community on the sandboxes by providing links to the students' sandboxes on the Wikiproject Chemistry page, very few in the community commented. We anticipate that uploading to the "live" page will be a more direct way of soliciting feedback. To facilitate this collaborative process we anticipate developing guidelines for the community to comment on, in the hopes that the suggestions address both structural (wiki formatting) and flow and content. In addition, we may need to develop some means of calling on experts as some topics are

143

more actively edited than others and some groups' pages may get more feedback. A potential avenue for garnering expert contribution is to involve the professional societies. We are excited to see the beginnings of an initiative at the Association for Psychological Sciences[60] that calls on its members to participate in improving pages related to psychology either by editing or having their students edit. If the American Chemical Society would be willing to develop a similar initiative, we can encourage participation in peer reviewing our students' pages.

K. Conclusions

We have implemented a graduate-level project centered on editing Wikipedia in a number of graduate courses at the University of Michigan. Through open-response written feedback and a retrospective student panel survey, we illustrated that teaching with Wikipedia has the potential to be an exciting and encouraging means for students to explore advanced topics in chemistry and learn how to communicate science to a diverse audience. In addition, through this platform students learn important skills such as copyright, collaboration, and Wiki editing[61].

	Design 1	**Design 2**	**Design 3**	**Design 4**	**Design 5**
Week 1		Group assignments are given	Group assignments are given	Group assignments are given	Group assignments are given
Week 3		Groups submit three topic choices	Groups submit three topic choices	Groups submit three topic choices	Groups submit three topic choices
Week 4					Editing tutorial
Week 5	Group assignments are given	Reference list due	MS word outline of groups' site	MS word outline of groups' site	Outline submitted online in sandbox
Week 6	Groups submit three topic choices		Editing tutorial	Peer review of outline	Peer review of outline done online
Week 7	Editing tutorial	Editing tutorial		Editing tutorial	
Week 10			Groups turn in "sandbox" version of site	Groups turn in "sandbox" version of site	Groups turn in "sandbox" version of site
Week 11	In-class presentations	Groups turn in "sandbox" version of site		Peer review of "sandbox"	Peer review of "sandbox" also done online
Week 13		In-class presentation	In-class presentation	In-class presentation	In-class presentation

Table 5-6. Timelines for each design implementation, highlighted are alterations from the previous design.

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Chapter 6

Development of an Undergraduate-Level Class Project and Student-Run Organization

Centered on Editing Wikipedia

A. Introduction

In the Spring 2010, the Wikimedia Foundation (WMF) invited Professor Anne McNeil and I to a conference at their headquarters called "Using Wikipedia as a Teaching Tool" to learn more about our experience with developing class projects that required students to edit a Wikipedia entry.[1] At the time the WMF was developing the Public Policy Initiative (PPI), a national program that encouraged instructors of public policy classes to incorporate a project on editing Wikipedia in their courses. The questions they had in anticipation to the launch of the program for the Fall 2010 paralleled questions we had to expand the project: 1.) How can we expand the project so it can be adapted for a number of programs? (ie undergraduate students) and 2.) How can we best develop a self-sustaining mentoring system? To answer these questions specifically at the University of Michigan, we reasoned that adjusting the scope and depth of expectations would make the project more manageable for undergraduate students and I proposed that the development of a student club would be a means for transitioning and passing along editing knowledge as students complete their degree requirements and graduate.

B. Undergraduate Students Editing Wikipedia

B.1. Wikipedia in Education

A recent large-scale survey of university students looked closely at students' research habits and in particular, how they used Wikipedia.[2] They found that a majority of students (70% of respondents) reported using Wikipedia at the beginning of the research process, and very few reported using it at the end (2% of respondents). The authors credit the broad, current, and in some cases, comprehensive coverage of Wikipedia to its use as a tool in pre-research. Yet, despite its prominent prevalent use to initially gather information, students do recognize Wikipedia's limitation. The academic research community has recognized that there is a need for pre-research resources like Wikipedia, and has even gone to encourage its role in educational settings.[3] Therefore, to understand the relationship of Wikipedia and its role in education and student learning, we developed the class project centered on editing Wikipedia. To measure the students' perceptions of the project and their learning in doing the project, we focused on comparing the students' learning expectations at the start of the semester and the learning the students felt they gained at the end of the semester. This type of analysis is similar to gap analysis done in quality management to identify areas of improvement.[4] Meeting expectations can be one measurement of quality and can potentially add valuable information on how to improve teaching methods and assignments.[5] In one particular

study, third and fourth year university students were asked to list the five things that they believe everyone should learn at college, and then to explain and rank how effective the courses and faculty at the institution helped in learning the items they listed.[5] The students' responses could be categorized into three categories: content, career/academic skills, and life skills. In the areas that were identified, the students were mostly positive (either very effective or somewhat effective) in the assessment of the university's faculty and courses' effectiveness in helping their learning of those areas. However, in their explanations of the scaled responses the students identified themselves as the source of their learning rather than the faculty.[5]

Another study compared students' perception of an ideal college-learning environment to the anticipation of the college-learning environment they would most likely experience. In their study the authors found that although students would prefer not to have group assignments, students expect these assignments and understand that they are necessary for achieving learning objectives. The authors go on to hypothesize that learning may be improved if students were engaged and involved with the materials being taught rather than only being engaged with their peers.[4] We anticipate that engaging in teaching roles could potentially be a means for students to be involved in the material and incorporate group work necessary for satisfying the learning objective of increasing team-building skills.[6]

B.2. Motivation for the Undergraduate-level Wikipedia Project

A logical extension of the graduate-level Wikipedia project was to implement the project in undergraduate-level courses. In collaboration with Professor Brian Coppola and the leaders of a unique honors-credit option for students at the University of Michigan, called structured study groups (SSG),[7] we adapted the Wikipedia project for a second-semester honors undergraduate organic chemistry course. Adapting assignments like the Wikipedia project for undergraduate-level courses is challenging because these students are often learning introductory concepts and have less experience navigating scientific literature. In contrast to graduate students, who are familiarized with the conventions of scientific writing, we anticipated that the undergraduate students would find writing a well-researched explanation more challenging due to their minimal experience. In the graduate courses, the students were assumed to have the necessary research skills to gather relevant information, revise and reconstruct the material into a format appropriate for an encyclopedia entry. The graduate-level projects contributed, in total, over 100,000 bites of information in detailed analysis of applications, properties, and synthetic challenges to either existing pages or entirely new topics.[8] Adequate instruction is further complicated by the increased class size of most undergraduate classes. Therefore we anticipated that several adaptations to the project designed for graduate-level courses in chemistry (Chapter 5) would be necessary for undergraduate courses.

Similar to the graduate-level project, the undergraduate-level project would be done in groups. We tested the project with a small subset of second semester organic students who opted into participating in a "Structured Study Group" (SSG).[7, 9] SSG is a unique opportunity for Michigan undergraduate organic students to receive Honors credit

153

by meeting outside of the required lecture for an additional 2 h session per week. Each SSG section is comprised of between 15-32 students and is lead by an upper-class undergraduate student. In implementing the project in this context, it was comparable to the total number of students in a graduate-level class and allowed for suitable comparisons. Design U1 and Design U2 are assigned to identify the two semesters that this project was implemented at the undergraduate-level; the 'U' differentiates these from the graduate-level implementations and modifications. In Design U1 there were 61 students enrolled in the SSG option, and in Design U2 there were 27 students enrolled. Each 15-32 students large SSG section then divided itself into even smaller groups of 4-8 students to work on the Wikipedia page assignments.

The Wikipedia assignment was one of five different projects in SSG. The four other projects were a spectroscopy study, an aspartame study[10], constructing problems for an online database, and the discussion of ethical case studies. Therefore, the scope of the Wikipedia project was condensed to be in balance with the other projects in the course.

Specifically, we divided the Wikipedia Project into weekly assignments, and were mindful of scaling the project relative to the four other projects. The students were given a limited set of named reactions to choose from, rather than a call for potential topics, as was the case for the graduate students. We specified the sections that would be added to the page, which included a history section, an animation of the mechanism, and key spectroscopic features for the transformation. The third major modification was that edits were made during weekly SSG section meeting times where a designated leader was present to guide the students in what content was appropriate to upload. In the graduate-level project, the students were responsible for planning when they would meet and the

154

content that they added. Although these changes were made, the objective of the undergraduate-level project remained similar to the graduate-level project; students were to learn topics in chemistry and that a collaborative environment and Wikipedia's prominent use as a resource would motivate the students' efforts to learn.

B.3. Project Structure

We implemented the project over two semesters, designated as Design U1 and Design U2, and the Wikipedia assignment was one of five different projects that was the focus of the SSG the entire semester. All five projects were worked on throughout the entire semester. Although all of these projects were worked on and the analysis below includes all of the projects, the particular focus of this chapter are the benefits of the Wikipedia project and how to appropriately modify the project for the most learning gained by undergraduate chemistry students. Therefore, the execution of other projects will not be outlined in detail for this thesis. However, this analysis does place the Wikipedia project and the learning gained from the project in the context of other traditional assignments, which is an aspect that is missing from the graduate-level analysis. The Wikipedia assignment had each SSG section focus on a different named reaction entry. For each entry, there were four distinct tasks:

1. clean up the entry, in terms of text and/or images
2. create a rational animation for an exemplar mechanism

3. overview the history of the reaction

4. identify the key spectroscopic features that characterize the reaction

As mentioned above, the scope of the project was condensed and divided into weekly tasks to make the project more manageable for the students and guide them through what needed to be done. An example of the weekly tasks for the Wikipedia assignment can be seen in Figure 6-1 for Week 1. Assignments for Weeks 2-13 are detailed in Appendix E. Each week there would be tasks for the various groups involved: Wikipedia assistant, SSG leader, and what the students are working on for the Wikipedia project during the SSG session.

Wikipedia Project on Named Organic Reactions
Assistants:

Leader tasks: Familarize yourself with Wikipedia language: userpages, discussion pages, help line through IRC. Look over Wikipedia Manual of Style for Chemistry: http://en.wikipedia.org/wiki/Wikipedia:Manual_of_Style_(chemistry)
Assistant tasks: Help SSG leaders with simple editing tasks
In class: Introduce some of the features of Wikipedia from our wiki-assistants
                  Learn how to create a username

Wikipedia Assignment #1

<u>Goal</u>: To think of yourselves as Wikipedia editors

1. Create a username
   Do not use your real name or your umich unique name, nothing that could connect your username to you, but still would be unique to you. (e.g.: my friend pj plays the piano, so he is pjthepiano). Try not to have something relating to chemistry, you don't want to seem precocious.

   Include your email when you sign up, this way your SSG leaders can contact you about your pages through the Wiki interface.
2. Email your SSG leader your username
3. Begin to look at the Wikipedia pages for the various named reactions
   http://en.wikipedia.org/wiki/List_of_organic_reactions

The SSG leaders have already screened these reactions and helped to narrow down these choices. You are not responsible for selecting one these (yet!), but it will be useful for you to see the type of entries on which you will be working this semester. If one of these begins to appeal to you as a work target, start to think about your argument for it should be the one that your SSG section ends up selecting.

Appel	Baeyer-Villiger Oxidation
Baeyer's Reagent	Baker-Venkatarman rearrangement
Dakin-West Reaction	Edman degredation
Jones Oxidation	Fischer glycosidation
Hammick Reaction	Halohydrin formation
Japp-Maitland condensation	Kornblum Oxidation
Leuckart Reaction	Pellizzari Reaction
Perkin Reaction	Ritter Reaction
Robinson-Gabriel Synthesis	Swern oxidation

Figure 6-1. Example weekly assignment for Wikipedia project

B.4. Evaluation of the Project

We analyzed if the undergraduate students felt that the Wikipedia project contributed to their learning goals. Student satisfaction usually is measured through

course evaluations after the end of the semester; however surveying the students' expectations at the start of the semester and perceptions at the end of the semester can provide the degree to which students felt the course was satisfactory or unsatisfactory. Both a pre-semester and post-semester survey was given to the students to evaluate if the Wikipedia project significantly contributed to the learning objectives of the course in the following ways:

1. Depth of understanding of the subject matter

2. Connecting of chemistry to other areas

3. Communicating science to peers

4. Changing one mind through debate

5. Communicating science to a broad audience

6. Doing academic research on a scientific topic

7. Improving academic skills - working alone

8. Improving academic skills - working in teams

The students were surveyed within the first two weeks of the semester and then surveyed again in the last weeks of a 14-week semester. The Wikipedia project was one of five major projects or tasks for the SSG to accomplish but through those five projects there were, in total, nine different learning methods that the students could engage in to satisfy the learning objectives outlined above. To summarize, the learning methods that we observed were the following:

1. Peer review

2. Work in teams

3. Study spectroscopy

4. Study aspartame

5. Construct ACE problems (or construct a podcast in Design U2)

6. Analysis of a case study

7. Writing a case study

8. Wikipedia project

9. Problem sets

The survey had two key parts. In the first part, students were asked to self-assess their personal skill level on the nine learning objectives for the course. The students would indicate their personal assessment of that skill level on a Likert-like[4] scale:

5.) high (I have a lot of these skills, could teach others)

4.) average-high (I have a bit more skills, I think, than others)

3.) average (I have about the skills that others have)

2.) average-low (I have some skills, but I think most others have more)

1.) low (I have a lot to learn).

In the second part, the students were asked to assess how each of the nine learning aspects (above) contributed to their attainment of that skill (ex: Skill 1: My depth of understanding of the subject matter in Organic Chemistry), indicating again on a Likert scale: "I anticipate that the following methods/learning aspects will contribute to increasing this skill":

5.) substantially and unavoidably

159

4.) in a noteworthy way

3.) in general, and rather normally, not substantially

2.) to a degree, but not as the major thing

1.) not at all.

The pre-test would indicated the students' anticipation in how much learning would be gained for a given learning aspects of the class. The post-test would report on how the students felt the skill was affected. We hypothesized that the student's perspective of what he/she can obtain (pre-test) and did obtain (post-test) from the learning aspect can be an indicator for its effect on a learning objective.[11]

B.5. Results and Discussion

In Table 6-1 and Table 6-2 are the post-test averages for Design U1 and Design U2 respectively. The differences in the pre-test average greater than ± 0.20 are delineated in parenthesis. A two-tailed paired *t*-test was done for both semesters and the asterisks indicate values that were statistically significant. The first row of values that are italicized are the post-test averages of how the students assessed their personal skill level. A majority of the responses are greater than a value of 3.75; potentially further supporting Walker's finding that students attribute their learning to their own efforts.[5] From these values we can gather that the students were very confident in their knowledge of the material.

We are specifically interested in how the students evaluated the Wikipedia project compared to the other classroom resources in achieving the indicated learning goals. Seeing the other learning methods provides a context for the Wikipedia project, how it fits into the entire course, and its contribution to the students' learning overall. Focusing initially on the Design U1 results (Table 6-1), using an arbitrary cut-off value of 3.75, and reading across the row for the Wikipedia project, the project had a strong influence in five learning objectives: connecting chemistry with other areas, communicating science to peers, communicating science to a broad audience, doing research on an academic topic and improving academic skills by working in teams. The skill with the greatest gain (highest positive difference from the pre-test rating and post-test rating) from the Wikipedia project was in improving academic skills by working in teams. The Wikipedia project was also granted the highest rating of all the other resources for the learning objective: communicating science to a broad audience.

The greatest gain in improving academics skills through working in teams indicates that initially the students underestimated the affect or gain of the Wikipedia project on improving their teamwork skills. Each student's pre-course response for each resource were compared for their statistical difference from their post-course response, which enabled us to carried out a two-tailed paired (type-1) *t*-test analysis.

In the second iteration of this project, Design U2 (Table 6-2), the project had a strong influence in communicating science to peers, communicating science to a broad audience, academic research on a science topic, and improving academic skills by working in teams. Overall, the values for the second iteration (Design U2) of the Wikipedia project are slightly lower than the previous the results (Design U1). It is

161

important to note that the sample size was significantly smaller, n=27 for Design U2 as oppose to n=61 for Design U1. In addition, we eliminated the construction of ACE problems and replaced it with the construction of a podcast. The Wikipedia project in Design U2 also shows the largest losses between the pre-test average and post-test average in two learning objectives. The students in the pre-test overestimated the gain or effect of the Wikipedia project in increasing the depth of understanding in the subject of chemistry and communicating science to a broad audience.

At the time that this thesis is being written, we were only able to implement the project for two semesters at the undergraduate-level. From these two sets of data, we can conclude that the Wikipedia project does provide students with the opportunity to communicate science to their peers, communicate science to a broad audience, and improve their academic skills of working in teams. However, the largest losses between the students' expectation of the project (pre-test) and perception of learning (post-test) were for two learning objectives; depth of understanding of the subject matter and communicating science to a broad audience.

From conversations with the SSG leaders, we can speculate that in Design U2 the students might have been frustrated by the difficulty of coding in Wikitext and their frustrations with the coding outweighed the focused of learning chemistry for the project. Ancedotal evidence[12] may indicate that the students failed to recognize the relevancy of the project to the rest of course thereby ranking the Wikipedia lower than their classmates in Design U1 in contributing to the learning objectives outlined. Unfortunately in the open-response feedback, the students were not specific in what about the Wikipedia project they thought was unhelpful to their learning other than its lack of relevancy to the

162

course. The following is an example of a student's open-response feedback from Design U2:

- The Wikipedia project was interesting, but it didn't teach us as much about the subject material of organic chemistry as some of the other things we learned, such as IR/NMR. Studying spectroscopy in depth made learning it in [course name/lecture] very easy, so I would recommend spending less time on the Wikipedia project and more time on spectroscopy.

As was the case in the graduate-level project, editing a Wikipedia entry should contribute to the undergraduate students' learning as by doing this we hypothesize that they are actively engaging in explanatory roles.[6] Knowing that the scope of the graduate-level project would be too broad, we modified the project to potentially accommodate the difference in research skills between graduate students and undergraduate students. The response highlighted above suggests that the undergraduate student did not recognize that in editing Wikipedia they would be in teaching roles or that learning about named reactions would help them in the course. We suspect that unless the topics are directly connected to the course or if concepts were seen on exams (as was the case of spectroscopy), the students might not recognize the contribution of the project to their learning. In the next iteration of the project, it might be advantageous to encourage the SSG leaders to tell the student that in editing a Wikipedia page, they will be providing this information for other undergraduate students at other universities taking organic chemistry. We assumed that the prominence of Wikipedia would naturally convey to the undergraduate students that they were creating a resource for other students and would encourage their efforts to learn, however considering the lack of a strong research base that first- and second-year undergraduate students have in comparison to first-year

163

graduate students or even third- and four-year undergraduate students, this assumption was incorrect. For the undergraduate-level project, these aspects of engaging in teaching by editing and that Wikipedia is a widely used resource for pre-research[2] may need to be stated more explicitly or that the project scope again needs to be more specific.

B.6. Conclusion

The receptiveness of the Wikipedia project in the graduate-level course encouraged us to modify the project for an undergraduate-level course. The primary objective for the project remained similar to the graduate-level project; through the project the students would learn topics in chemistry, and working collaboratively through the popular Wikipedia platform would contribute to their learning experience. After two designs of the undergraduate project the students recognized that the Wikipedia project contributes to improving their science communication skills to both their peers as well as a broad audience and the collaborative nature of the project improves the academic skill of working in teams. However, the lower post-test average values overall for the Wikipedia project in Design U2 than Design U1 indicates that modifications are still needed to meet the students' expectations of learning for the project. Our next adaptation is to focus the project on a single aspect of the Wikipedia page for the students to improve. For example the students would add a well designed and thought out animation of the mechanism for a named reaction. We anticipate that focusing the discussion to arrow pushing conventions and key experiments will enable the student to clearly recognize the learning gained and the connection of the project to course.

C. Michigan Wikipedians

C.1. Background

Even without a centralized bureaucracy, Wikipedia has still managed to become an extensive resource. However, it is this lack of an intuitive infrastructure in Wikipedia that makes it difficult for new editors to understand the various layers of Wikipedia and to find their roles before they become too frustrated to continue to edit.[13] I hypothesized that through a campus organization such as a student club, new editors can be introduced to Wikipedia and learn to navigate the layers of the online community. The idea for the student club came out of discussions during the previously mentioned conference[1] with the Wikimedia Foundation. In addition to adapting the Wikipedia project for a broad range of courses, the Wikimedia Foundation (WMF) solicited ideas to help sustain and encourage the student editors that were trained through classroom projects or participated as Campus Ambassadors.

Campus Ambassadors is a program developed by the WMF that officially trained students to serve as mentors for first-time Wikipedians in the classroom.[14] In the Fall 2010 the Public Policy Initiative (PPI) had 13 faculty members at various universities implementing the project, and were supported by 12 campus ambassadors. The program grew significantly in Spring 2011 expanding to 32 faculty members and 54 campus ambassadors at 22 universities as well as 91 online ambassadors that supported the courses virtually.[15] All of the Campus Ambassadors were required to attend a 2-day training session in their region which not only outlined the basics of Wikipedia editing but also incorporated opportunities for the volunteers to practice teaching in the

165

classroom, and case studies of potential problems that might arise between students and the Wikipedia community. Recent analysis by the Foundation indicates that this type of support system is very valuable for the students.[16] They found that the interactions with students who could provide resources on campus and access to online resources helped students to quickly overcome many of the challenges attributed to learning the Wikipedia markup language and navigating Wikipedia.[17] Campus Ambassadors are trained to provide students with the knowledge and skills to navigate Wikipedia in order to aid museums, libraries, or other professors to start projects that edit articles on Wikipedia. However, as this program expands, in the Spring 2012 there were 59 US Campus Ambassadors, the WMF cannot sustain training new students semester after semester. Therefore, an internal organization at each school participating in the Global Education Program (previously called the PPI) has the potential to be a means for training future Campus Ambassadors. In addition, the student club can be an avenue for transitioning new editors into long-time Wikipedians as it provides support for learning the non-intuitive infrastructure of Wikipedia. Recent research has suggested that there is a decline in active editors on Wikipedia.[18] One hypothesis for the decline in editorship is that edits contributed by newcomers are often quickly reverted and are therefore demotivating to newcomers who feel that their contributions are not valued.[19] This decline in strong editorship is a concern because Wikipedia's success in being a resource of information, whether it is obscure, important, or common, is attributed to the work of hundreds and thousands of volunteers. Without the contributions and oversight of this community, the encyclopedia can lose its value and enable vandalizing edits to persist.[20]

In June 2010, I established the first student-led organization (in the US) centered on improving Wikipedia.[21] The only other group at the time was at McGill University (Canada), established earlier that year in February, called Students Supporting Wikipedia.[22] The Michigan Wikipedians (formerly, the Wikipedians of the University of Michigan) was founded to investigate if student organizations would be a viable means of sustaining the Campus Ambassador program and to teach students how to edit Wikipedia and encourage them to edit. This program not only has the potential to be an effective path for the Global Education Program to continue to grow but also to solve Wikipedia's problem of newcomer retention. I will present some preliminary results that suggest that a student club has the potential to help new editors find their roles and ease the transition from new editor to Wikipedian and lower the known activation barrier for new editors.[18, 23]

C.2. Retaining Membership

One of the challenges for a new organization that makes it difficult to recruit members is that students do not have a natural inclination to be identified with the group. Many scholastic organizations such as the American Chemical Society Student Affiliates or Greek organizations are developed and stemmed out of their parent organization. Although the Wikimedia Foundation knew of our efforts, and were very supportive and encouraging, they did not have the resources to help initiate a national effort, therefore the development of this organization was truly a grassroots movement. Presented in this

work is a case study on this a particular student club at the University of Michigan and how it alters from the general pattern of new editors.

At the end of two years, 97 undergraduate students showed an interest by their willingness to be on our listserv and receive regular emails from the group, of those 97 students; 32 students self-identified with our organization by posting their username on our namespace, and 10 members are considered active members (regularly coming to meetings, making at least one edit during the meeting). Participating in the campus-wide student organization fairs at the start of the academic year was the most successful recruiting strategy. In addition, we found that immediate involvement or active editing during the first several meetings, and meeting weekly in a computer space greatly increased the success of retaining membership.

The group met on a weekly basis during the academic school year. The organization is modeled after other decentralized groups where each member can have a leadership role, learn leadership skills, and have a stake in the direction of the organization.[24] Each meeting would start with a volunteer who would present the work they had done the previous week. The types of accomplishments that the students would normally present were along the lines of having started a new page, uploaded a new category of images, or participated in the various activities that are hosted by the Wikipedia community. But the opportunity to encourage each other and an avenue for teaching another student something you had figured out during the week was exciting. Many of the students started with small edits, such as fixing "dead links", which are website links that when clicked on lead to a non-existent webpage.

C.3. Preliminary Results

As mentioned previously, Wikipedia editorship is currently declining and we would like to know if student clubs or classroom projects would be a feasible avenue for retaining new student editors. We will analyze the contributions of students involved in classroom projects, the student club, and a random sample of 1000 new editors to understand if in these situations, when students are being formally guided through Wikipedia's vast policies, they more likely to continue to edit. In collaboration with Aaron Halfaker, a computer science PhD student at the University of Minnesota, we looked at the average number of edits per month from the point of username registration for each of the category of users mentioned above (Figure 6-2). We specifically focused within the first year of having an account for each user. The random sample of new editors represents the general population of people that create an account and make at least one edit in the first month of creating their account. Then this set of editors is compared to two other samples of users that have participated in some type of formal training to edit Wikipedia, in one set are students who are required to edit for a class project, and the second set are the students who participated in the student club. The analyzed club members do not include students who created accounts prior to joining the club, assuming that these students were active editors and or did not need the formal training we thought the organization could provide.
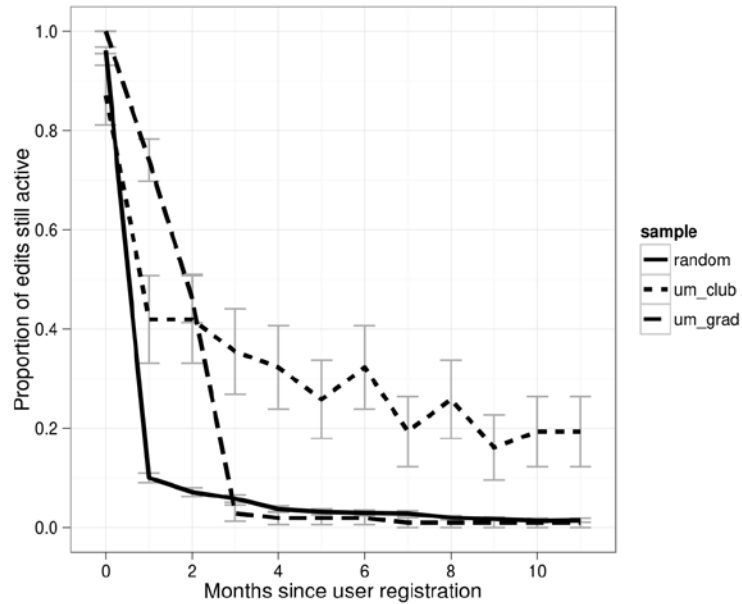
Figure 6-2. Comparing percentage of editors still active from the three sample sets: random new users, students involved in the student club, and students who edited for the class project.

Figure 6-2 illustrates that the graduate students involved in the class project are very similar to the general population. There is a burst of activity within the first four months of creating an account, and then these users tend to leave or do significantly less editing.[25] However, the students who enter the Wikipedia community through the student club have a different editing contribution pattern than the general population and the students who enter through a class project. These editors still remain active after a year from creating the account. Although they start at a lower editing efficiency, they peak later in the year and have a more gradual decline in active editing activity. This preliminary data prompts further investigation into the question if the student club creates a situated learning environment thereby guiding the students through small low-risk edits that would make them more likely to stick with the community.[25] There is the possibility that these student who are part of the club have somehow self-selected themselves to

have been more inclined to have continued to edit even without the formal socialization the organization provided. To account for this, we can design experiments that compare student editors invited to a club and student editors that are not invited to a club, or to compare students who are getting help through an online resource such as Wikipedia's newly developed Teahouse.[26] These comparisons would investigate if the editing habits of student club members were a cause and effect relationship.

C.4. Conclusion

Michigan Wikipedia is still a very new organization, but it has a lot of potential to both to help in classroom projects and encourage students to continue to edit. Even after three years of working with students on their Wikipedia pages for classes, I am learning something new about the editing community each time I make an edit. Wikipedia is a very complicated community to navigate because there is so much to do and so many different pockets of people trying to grow the encyclopedia. But adding a social aspect to those who are new to editing, such as the involvement in a student organization, can alleviate some of the overwhelmingness of finding one's role in a community such as Wikipedia.

	Learning Objective and Post-test average (difference from pre-test if applicable)							
	Depth of understanding in subject	**connecting chemistry to other areas**	**communicating science to peers**	**change mind through debate**	**communicating science broad audience**	**academic research on science topic**	**improve academic skills - work alone**	**improve academic skills - work teams**
	3.90 (+0.23)	*3.70 (+0.42)*	*4.07 (+0.27)*	*3.72*	*3.75 (+0.35)*	*3.80 (+0.43)*	*4.08*	*3.95 (+0.30)*
Method								
peer review	3.93	3.52	4.40 (-0.28)	4.12	3.95	3.19 (-0.29)	3.02	4.72
work in teams	3.97	3.75	**4.5**	**4.22**	4.07 (-0.37)*	3.51	2.53	**4.75**
study spectroscopy	**4.45 (+0.30)**	3.68	3.27 (+0.39)*	2.93	2.86	3.34 (-0.47)*	3.85	3.33 (+0.43)*
study Aspartame	3.95	**4.48 (+0.33)***	3.80 (+0.57)**	3.76 (+1.02)**	3.75 (+0.39)	**4.24**	3.47	3.40 (+0.60)**
construct ACE probs	2.58 (-0.72)**	2.86 (-0.44)	2.80 (-0.53)*	2.41 (-0.51)*	2.85 (-0.51)	2.42 (-0.46)	3.03	2.88 (-0.38)
analy case ethics	3.07	3.97	3.33	3.47	3.59	3.29 (-0.44)*	3.11	3.1
write case ethics	2.86	3.83	3.3	3.15	3.54	3.22 (-0.63)**	3.27	2.85
Wiki project	3.53	4.07	3.92	3.1	**4.24**	4.07	3.1	4.13 (+0.68)**

			3.59		3.32		3.82
problem sets	4.37	3.52	3.63	(+0.61)*	2.98	(-0.58)**	**4.22**	(+0.37)

Table 6-1. Design U1 results: n=61, the main entry values are the post-test averages, in parentheses is the difference from the pre-test average when relevant. Bold type indicates the highest resource for that learning objective. ** $p \leq 0.001$, * $p \leq 0.01$. The Wikipedia project is shaded to bring attention to the focus of this chapter.

	Learning Objective and Post-test average (difference from pre-test if applicable)							
	Depth of understanding in subject	**connecting chemistry to other areas**	**communicating science to peers**	**change mind through debate**	**communicating science broad audience**	**academic research on science topic**	**improve academic skills - work alone**	**improve academic skills - work teams**
	3.96	*3.81 (+0.37)**	*3.93*	*3.81 (+0.30)*	*3.74 (+0.52)*	*3.78 (+0.44)*	*4.15*	*4.19 (+0.41)*
Method								
peer review	3.92	3.56	**4.62**	**4.30 (-0.22)**	3.96	3.48 (-0.30)	3.07 (+0.22)	**4.52 (-0.30)***
work in teams	4.19 (+0.38)	3.56	**4.62**	4.26 (-0.22)	**4.04**	3.56 (-0.56)*	2.89 (+0.37)	**4.52 (-0.26)***
study spectroscopy	**4.35 (+0.38)**	3.72 (+0.31)	3.54 (+0.46)	3.33 (+0.52)	3.19	3.70	**4.22 (+0.81)****	3.63 (+0.78)*
study Aspartame	3.80	**4.20**	3.42 (+0.38)	3.19 (+0.34)	3.56 (-0.41)*	3.96 (-0.20)	3.74 (+0.47)	3.63 (+0.78)*
construct podcast	3.46	3.04 (-0.29)	4.19	3.30 (+0.37)	3.74	3.41 (+0.29)	3.35	3.96
analy case ethics	3.38 (+0.53)	4.08 (+0.52)	3.62 (+0.69)*	3.67	3.41	3.81	3.52 (+0.52)	3.67 (+0.48)
write case ethics	3.32 (+0.51)	3.92 (+0.40)	3.62 (+0.69)*	3.48	3.35	**4.00**	3.81 (+0.70)*	3.26 (+0.48)*
Wiki project	3.15 (-0.51)	3.32 (-0.27)	3.85	3.15 (-0.26)	3.78 (-0.59)	3.78	3.33	3.81 (-0.26)

| problem sets | 4.27 | 3.64 (+0.23) | 3.81 (+0.55)* | 3.78 (+0.63)* | 3.41 (+0.52) | 3.74 | 4.11 (-0.44) | 3.70 |

Table 6-2. Design U2 results: n=27, the main entry values are the post-test averages, in parentheses is the difference from the pre-test average when relevant. Bold type indicates the highest resource for that learning objective. ** $p \leq 0.005$, * $p \leq 0.05$ The Wikipedia project is shaded to bring attention to the focus of this chapter.

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Chapter 7

Conclusions and Future Directions

A. Part I: Molecular Gels

Molecular gels have been studied for 160 years, but in just the last twenty years, a number of applications for these materials have emerged such as environmental remediation,[1] drug delivery,[2] regenerative medicine,[3] catalysis,[4] and as reversible liquid crystalline materials.[5] Our research group, along with others, is interested in molecule gels for chemical sensing[6] applications because of the easily distinguishable solution-to-gel phase transition. Inducing this evident phase transition (liquid-to-gel) when an analyte of interest is added can be a portable, inexpensive, stimuli-responsive system for on-site detection of explosives[7], toxic metals[8], and to diagnose disease.[9] However, chemoresponsive molecular gels that are not enzyme-based systems are plagued by low sensitivity because they require one analyte molecule for each precursor to be transformed into a gelator. To improve the sensitivity of gel systems for chemical sensing, we targeted a polymer that depolymerizes when an analyte-sensitive trigger is released to generate a large number of gelators relative to the analyte signal (Chapter 4). Poly(carbamates)[10] and poly(phthalaldehydes)[11] are two common disassembling backbones explored, and through appending common gelator motifs to the monomeric units, we attempted to convert the monomer scaffold into a gelator. Despite significant

attempts, no carbamate monomers were found to be gelators, but we were able to identify a phthalaldehyde gelator. A number of different synthetic pathways were explored to synthesize modified phthaladehyde complexes that would decrease the minimum gelation concentration to increase the sensitivity of the system. However, ultimately the solubility of intermediate synthetic complexes and regioselectivity prevented the complete synthesis of the target substrates. Overall, these studies revealed that designing gelators for a specific application continues to be a significant challenge and suggests that efforts towards developing a method for predicting if a molecular scaffold can form gels be done in the future.

The difficulty in developing application-specific gelators is attributed to the unclear relationship between molecular structure and gel formation. To help elucidate the structural features that influence gel formation, we investigated a class of aryl trihydroxyborate salt gelators (Chapter 2). Prior to this work, there were no examples of aryl trihydroxyborate salt gelators. The aryl trihydroxyborate salt scaffold was modified through extending the length of the alkoxy chains and the addition of a halide substiuent. These modifications enabled us to discover an unusual dependence of gelation on alkoxy chain length, highlighting that there are a number of unknown interactions that drive gel formation. Additionally, because these gelators were able to form gels in a variety of organic solvents, in the future, free-radical polymerization of a styrene- or divinylbenzene-based solvent could lead to porous materials after removal of the aryl trihydroxyborate salt.

A second methodology towards developing means for the facile design of new gelators is to find an attribute common for gelators. In another class of gelators and

nongelators, pyridine-based scaffold and dipeptide-based scaffold, structure-property relationship investigations found that dissolution enthalpies correlated with gelation ability.[12] If general, this parameter can help distinguish gelators from nongelators and, as a result, has the potential to predict if a specific molecular structure will form a gel. Therefore, we targeted molecular mechanics simulations to model dissolution enthalpies (Chapter 3). We developed models that represented the solid-solvent interactions and solid-solid interactions, extracted the enthalpies of these interactions, and subtracted the solid-solid interactions from the solid-solvent interactions to solve for the dissolution enthalpies for each molecule. Although the experimental observations of higher dissolution enthalpies for gelators were not reproduced through the models, these preliminary results suggest that the model developed underestimates the solid-state interactions important in gelation. Molecular modeling techniques to design new gelators have the potential to greatly expand the structural scope and applications of molecular gelators. Future direction of this work will focus on developing simulation strategies that better represent the solid-state interactions by starting with known crystal structures. Additionally, future work will couple traditional synthetic methods to design new gelator scaffolds and elucidate the complex structural features that determine gel formation. A model for predicting gel formation will increase the ability to design gelators for specific applications. For example, a specific chemical reaction between the precursor and analyte could be designed to improve the selectivity of gelation-based sensors.

B. Part 2: Teaching With Wikipedia

Students are often assigned a traditional writing assignment to both enable them to go in depth into a topic not explored in class due to the time constraints of lecture, and to gain important research and writing skills.[13] Additionally, graduate curricula rarely include training for future scientists to communicate advanced concepts to a broad and diverse audience.[14] Therefore we developed a class project centered on editing Wikipedia, to take advantage of Wikipedia's broad audience and ease of contributing to enable students to explore advanced concepts in chemistry and learn to communicate science to a diverse audience. When we started this project, there were only a handful of known projects incorporating Wikipedia editing as a class assignment, and even fewer science courses.[15] We implemented this project over five semesters and each semester improved the project to maximize the learning that the students gained through the project. Through informal open-response surveys and retrospective panel surveys, the students' responses indicated that teaching with Wikipedia is an effective method for students to explore advanced topics and learn how to communicate science to a diverse audience. The project has been adapted for chemistry undergraduate courses as well as influenced the development of a student organization to foster the online collaboration skills and media literacy skills that the students gain in editing Wikipedia.

To further improve the student learning gained through this project, future directions should focus three different avenues: (1) Developing assignments and guidance in the project to best support the students in evolving their scientific writing skills and

learning the technical aspects of Wikipedia. An example of an assignment would be for the students to rewrite a technical paragraph for a general audience, and to provide the students with specific criteria for addressing a general audience. (2) Directly comparing the Wikipedia project with a traditional writing assignment will shed light on the benefits and pitfalls in replacing a writing assignment with the Wikipedia project. (3) Developing a mechanism for involving experts and academics to review the students' work and entries on Wikipedia would expand the feedback the students received and help the students to develop a broader understanding of their topic.

Since this project's initial implementation in Fall 2008, it has greatly expanded to include the participation of other chemistry courses as well as courses in other departments. Additionally, our design was instrumental in the development of a national program headed by the Wikimedia Foundation.[16] The broad interest in this project has shown to be an exciting means for students to both learn and contribute to the access of information to the broader community, and indicates its potential to be a valuable classroom exercise to be further developed.

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Appendix A

For Chapter 2: Aryl Trihydroxyborate Salts: Thermally Unstable Species with Unusual

Gelation Abilities

A. Materials

Flash chromatography was performed on silica gel (40-63 μm) and thin layer chromatography was performed on TLC plates pre-coated with silica gel 60 F254. *N*-bromosuccinimide (NBS) was recrystallized from boiling water and dried over P_2O_5. All reagent grade materials and solvents were purchased and used without further purification unless otherwise noted. THF was dried using a solvent purification system in which pressurized nitrogen gas circulates solvent through a series of filter columns to remove moisture. All glassware was oven-dried at 120 °C for at least 1 h before use.

B. General Experimental

NMR Spectroscopy: ^{1}H, ^{13}C, and ^{11}B NMR spectra for all compounds were acquired in $CDCl_3$, CD_3OD, or C_6D_6 on spectrometers operating at 400, 100 and 128 MHz, respectively. ^{13}C NMR spectra of **1a-e** and **2a-e** were acquired in CD_3OD on a spectrometer operating at 125 MHz. For ^{1}H, ^{13}C and ^{11}B NMR spectra the chemical shift data are reported in units of δ (ppm) relative to tetramethylsilane (TMS) and referenced to residual solvent. Multiplicities are reported as follows: singlet (s), doublet (d), doublet of doublet (dd), triplet (t), multiplet (m), and broad resonance (br). All NMR spectra were recorded at rt unless otherwise noted. Note that integrations for protons on the alkyl chains of some compounds are high due to insufficient relaxation time.

High Performance Liquid Chromatography: HPLC was performed with a 3.9 x 300 mm 10 μm silica column. Samples were run using 99/1 hexanes/EtOAc as the eluent at 1 mL/min. An internal standard (nitrobenzene) was used for quantitative measurements. The retention time for the nitrobenzene standard is 7.19 min.

Atomic Force Microscopy: AFM images were taken on an AFM under 1 atm. Gel samples were added to a freshly cleaved mica surface on a 14" AFM puck and allowed to dry for 1 h. Tapping mode with silicon cantilevers was used. (Tip radius <10 nm, force constant 40 N/m, resonance frequency 300 kHz). Most samples were taken at cgc unless they were weak gels, then they were taken slightly above cgc.

Rheology: Rheological measurements were taken on a rheometer with a 20 mm top-serrated parallel plate, with the gap fixed at 500 μm. A preformed gel at 2 x cgc (with the exception of **1e**, which was at cgc, and **2b-c**, as noted), allowed to stand for 24 h in the vial, was loaded on the Peltier plate at 20 °C with solvent trap. All samples were initially subjected to a frequency sweep, followed by an oscillating stress sweep. All measurements were performed at 20 °C and repeated 2x with a new preformed gel sample. Frequency sweep was performed under a constant stress of 0.1 Pa with a frequency range from 0.628 rad/s to 62.8 rad/s (i.e., 0.1 Hz-10 Hz). Oscillating stress sweep was performed at 1 Hz, with a stress ranging from 0.03 Pa to 200 Pa. Under both runs, the gels were well within the linear viscoelastic regime.

Powder X-ray Diffraction: Powder X-ray diffraction (PXRD) patterns were collected at ambient temperature using a diffractometer with a detector using graphite monochromated Cu-Kα radiation (1.5406 Å). Gels at 10% above cgc were flash dried and loaded onto glass microscope slides.

T_{gel}: The T_{gel} was determined by the falling ball method.[1] A copper-coated steel ball (4.5 mm, 0.177 cal) was placed gently on top of the gel at 2 x cgc and the vial was sealed. The vial was placed in a stirred water bath and heated at a rate of 5 °C/min. The gel-to-solution transition temperature was recorded as the temperature at which the steel ball

reached the bottom of the vial.

Thermal Gravimetric Analysis: Bulk solid of aryl trihydroxyborate salts was placed on a tared aluminum pan and the temperature was ramped from 30 °C to 400 °C at 10 °C/min under a flow of N_2 gas.

Scanning Electron Microscopy: Wet gel samples were loaded onto a stainless steel SEM holder and mounted with copper tape. The gels were observed using the low-vacuum mode with a 15kV accelerating voltage.

Representative Procedure for Gel Formation: An aliquot (0.50 mL) of a NaOH solution (0.10 M in CH_3OH) was added to a 4 mL vial. The CH_3OH was removed in vacuo and the resulting solid NaOH was held under vacuum overnight. Subsequently, (2,5-bis(hexyloxy)phenyl)boronic acid (**S6**, 1 mL, 0.06 M in benzene) was added to the vial. The heterogeneous mixture was sonicated for 5 min to create a homogenous solution of **1c**. Gel formation occurred if the solution was left undisturbed for approximately 5 min.

C. Synthetic Procedures
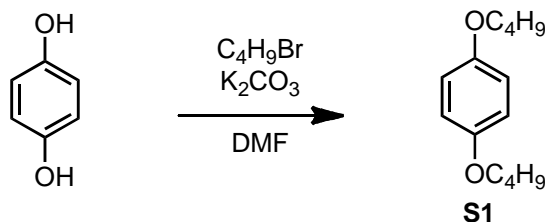
1,4-dibutoxybenzene (S1): Hydroquinone (20.02 g, 0.1818 mol, 1.0 equiv), 1-bromobutane (48.0 mL, 0.454 mol, 2.5 equiv), and DMF (120 mL) were added under N_2 to a 500 mL flask and heated to 80 °C with vigorous stirring. Then, K_2CO_3 (62.77 g, 0.4542 mol, 2.5 equiv) was added and the reaction mixture was stirred for 3 d. The reaction was cooled to rt, filtered and washed with hexanes. The filtrate was washed with water (2 x 200 mL) and brine (2 x 200 mL), dried over anhydrous $MgSO_4$, filtered and concentrated in vacuo. The crude product was recrystallized from hot CH_3OH to give 24.10 g of **S1** as a white crystalline solid (60% yield). HRMS (ESI) Calcd. for $C_{14}H_{22}O_2$, 223.1698 $[M + H]^+$; Found 223.1696.
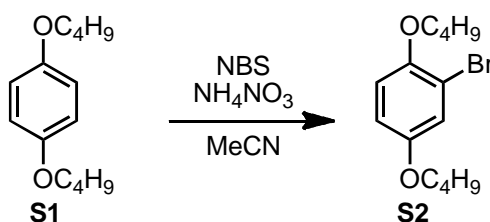
2-bromo-1,4-dibutoxybenzene (S2): Sequentially, **S1** (5.039 g, 0.0226 mol, 1.0 equiv), acetonitrile (38.5 mL), NH_4NO_3 (0.180 g, 0.0022 mol, 0.1 equiv) and *N*-bromosuccinimide (4.029 g, 0.0226 mol, 1.0 equiv) were added to a 100 mL round-bottom flask with a stir bar. The reaction was stirred at rt for 2 h, then quenched with water (50 mL). The aqueous mixture was extracted with EtOAc (2 x 50 mL). The combined organic layers were washed with water (2 x 50 mL) and brine (2 x 50 mL), dried over anhydrous $MgSO_4$, filtered and concentrated in vacuo. The crude product was

purified by column chromatography using 14.95/85.00/0.05 toluene/hexanes/EtOAc as the eluent to give 3.96 g of **S2** as a clear colorless oil (58% yield). HRMS (ESI) Calcd. for $C_{14}H_{21}BrO_2$, 300.0725 $[M]^+$; Found 300.0722.
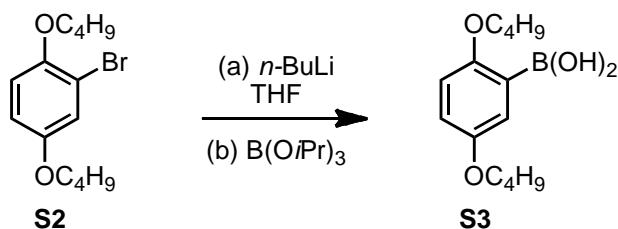
(2,5-dibutoxyphenyl)boronic acid (S3): An oven-dried 50 mL Schlenk flask was equipped with a stir bar and septum, cooled to rt under vacuum and filled with N_2. **S2** (1.002 g, 0.0033 mol, 1.0 equiv) and THF (32 mL) were added to the flask. The solution was then cooled to -78 °C. Then *n*-BuLi (2.3 mL, 1.6 M, 1.1 equiv) was added via syringe. After 20 min, triisopropyl borate (2.3 mL, 1.0 mmol, 3.0 equiv) was added. The reaction was gradually warmed to rt and stirred for 24 h. The mixture was cooled to 0 °C and aqueous HCl (5 mL, 2 M) was added and stirred for 20 min. The aqueous mixture was extracted with ether (2 x 50 mL). The combined organic layers were washed with brine (1 x 50 mL). The organic layer was dried over anhydrous $MgSO_4$, filtered and concentrated in vacuo. The crude product was purified by column chromatography using 5/15/80 EtOAc/CH_2Cl_2/hexanes as the eluent to give 477 mg of **S3** as a white solid (53% yield). HRMS (ESI): Calcd. for $C_{14}H_{23}BO_4$, 266.1689 $[M]^+$; Found 266.1697. ^{11}B NMR (128 MHz, $CDCl_3$) δ 29.24.
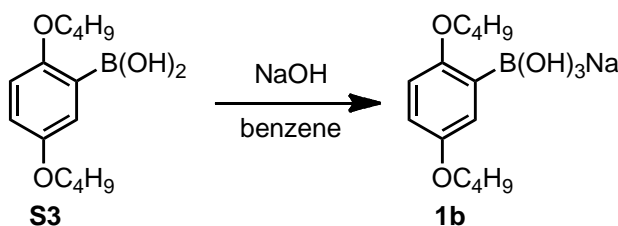
1b: S3 (357 mg, 1.34 mmol, 1.0 equiv) was dissolved in benzene (10.0 mL), then NaOH (57.4 mg, 1.44 mmol, 1.1 equiv) was added. The reaction was stirred for 20 h at rt and the

solution turned into a white suspension. The mixture was concentrated in vacuo isolating 405 mg of a white solid (99% yield). ^{11}B NMR (128 MHz, CD$_3$OD) δ 4.76.
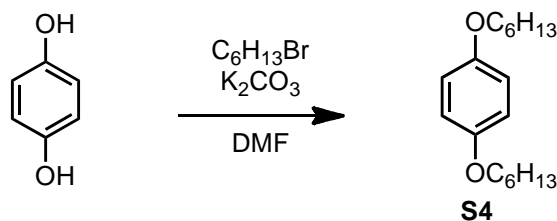
1,4-bis(hexyloxy)benzene (S4): Hydroquinone (10.02 g, 0.0909 mol, 1.0 equiv), 1-bromohexane (32.0 mL, 0.227 mol, 2.5 equiv), and DMF (60 mL) were added under N$_2$ to a 500 mL flask and heated to 80 °C with vigorous stirring. Then, K$_2$CO$_3$ (31.36 g, 0.2269 mol, 2.5 equiv) was added and the reaction mixture was stirred for 3 d. The reaction was cooled to rt, filtered and washed with hexanes. The filtrate was washed with water (2 x 200 mL) and brine (2 x 200 mL), dried over anhydrous MgSO$_4$, filtered and concentrated in vacuo. The crude product was recrystallized twice from hot EtOH to give 16.06 g of **S4** as a white crystalline solid (63% yield). HRMS (ESI) Calcd. for C$_{18}$H$_{30}$O$_2$, 279.2324 [M + H]$^+$; Found 279.2328.
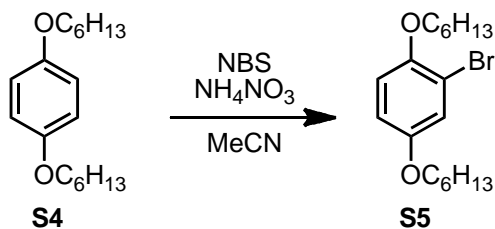
2-bromo-1,4-bis(hexyloxy)benzene (S5): Sequentially, **S4** (3.002 g, 0.0108 mol, 1.0 equiv), acetonitrile (17 mL), NH$_4$NO$_3$ (0.089 g, 0.0011 mol, 0.1 equiv) and *N*-bromosuccinimide (1.923 g, 0.0108 mol, 1.0 equiv) were added to a 100 mL round-bottom flask with a stir bar. The reaction was stirred at rt for 2 h, then quenched with water (50 mL). The aqueous mixture was extracted with EtOAc (2 x 50 mL). The combined organic layers were washed with water (2 x 50 mL) and brine (2 x 50 mL),

dried over anhydrous MgSO$_4$, filtered and concentrated in vacuo. The crude product was purified by column chromatography using 14.95/85.00/0.05 toluene/hexanes/EtOAc as the eluent to give 2.808 g of **S5** as a clear colorless oil (35% yield). HRMS (ESI) Calcd. for C$_{18}$H$_{29}$BrO$_2$, 356.1351 [M]$^+$; Found 356.1336.
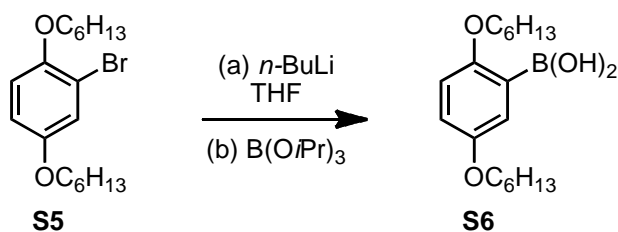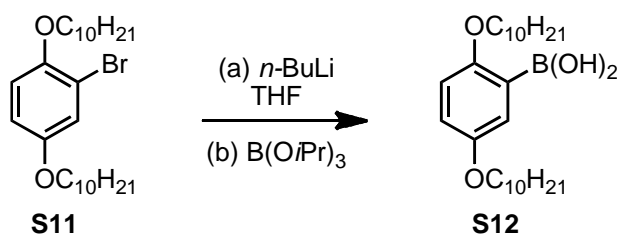

(2,5-bis(hexyloxy)phenyl)boronic acid (S6): An oven-dried 50 mL Schlenk flask was equipped with a stir bar and septum, cooled to rt under vacuum and filled with N$_2$. **S5** (0.983 g, 0.0027 mol, 1.0 equiv) and THF (27.0 mL) were added to the flask. The solution was then cooled to -78 °C. Then *n*-BuLi (1.90 mL, 1.6 M, 1.1 equiv) was added via syringe. After 20 min, triisopropyl borate (1.90 mL, 0.008 mol, 3.0 equiv) was added. The reaction was gradually warmed to rt and stirred for 24 h. The mixture was cooled to 0 °C and aqueous HCl (5 mL, 2 M) was added and stirred for 20 min. The aqueous mixture was extracted with ether (2 x 30 mL). The combined organic layers were washed with water (1 x 30 mL) and brine (1 x 30 mL). The organic layer was dried over anhydrous MgSO$_4$, filtered and concentrated in vacuo. The crude product was purified by column chromatography using 5/15/80 EtOAc/CH$_2$Cl$_2$/hexanes as the eluent to give 400 mg of **S6** as a white solid (26% yield). HRMS (ESI): Calcd. for C$_{18}$H$_{31}$BO$_4$ [M + Na]$^+$ 345.2213; Found 345.2222. ^{11}B NMR (128 MHz, CD$_3$OD) δ 29.67.
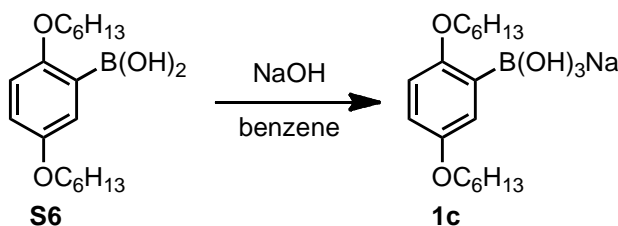
1c: S6 (400 mg, 1.24 mmol, 1.0 equiv) was dissolved in benzene (12.0 mL), then NaOH (50.4 mg, 1.26 mmol, 1.0 equiv) was added. The reaction was stirred for 21 h at rt and the solution turned into a thick suspension/unstable gel. The mixture was concentrated in vacuo isolating 450 mg of **1c** as a white solid (100% yield). ^{11}B NMR (128 MHz, CD$_3$OD) δ 4.51.
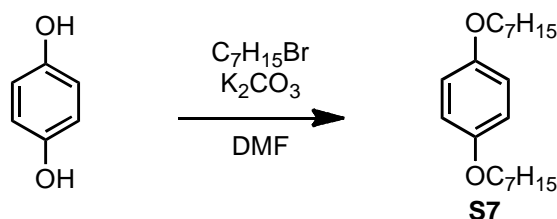
1,4-bis(heptyloxy)benzene (S7): Hydroquinone (10.01 g, 0.0909 mol, 1.0 equiv), 1-bromoheptane (37.6 mL, 0.239 mol, 2.5 equiv), and DMF (61 mL) were added under N$_2$ to a 500 mL flask and heated to 80 °C with vigorous stirring. Then, K$_2$CO$_3$ (31.34 g, 0.2267 mol, 2.5 equiv) was added and the reaction mixture was stirred for 3 d. The reaction was cooled to rt, filtered and washed with hexanes. The filtrate was washed with water (2 x 200 mL) and brine (2 x 200 mL), dried over anhydrous MgSO$_4$, filtered and concentrated in vacuo. The crude product was recrystallized twice from hot EtOH to give 11.59 g of **S7** as a white crystalline solid (42% yield). HRMS (ESI) Calcd. for C$_{20}$H$_{34}$O$_2$, 307.2637 [M + H]$^+$; Found 307.2634.
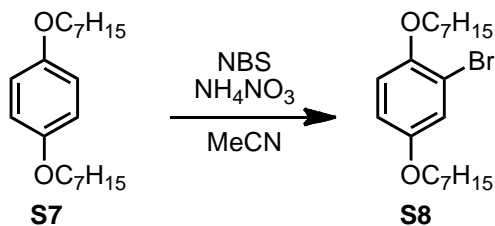
2-bromo-1,4-bis(heptyloxy)benzene (S8): Sequentially, **S7** (3.014 g, 0.0098 mol, 1.0 equiv), acetonitrile (15 mL), NH$_4$NO$_3$ (0.079 g, 0.0010 mol, 0.1 equiv) and *N*-bromosuccinimide (1.760 g, 0.0098 mol, 1.0 equiv) were added to a 100 mL round-bottom flask with a stir bar. The reaction was heated slightly at 35 °C to dissolve all

reagents and then stirred at rt for 12 h, then quenched with water (50 mL). The aqueous mixture was extracted with EtOAc (2 x 50 mL). The combined organic layers were washed with water (2 x 50 mL) and brine (2 x 50 mL), dried over anhydrous MgSO$_4$, filtered and concentrated in vacuo. The crude product was purified by column chromatography using 14.95/85.00/0.05 toluene/hexanes/EtOAc as the eluent to give 2.964 g of **S8** as a clear colorless oil (34% yield). HRMS (ESI) Calcd. for C$_{20}$H$_{33}$BrO$_2$, 384.1664 [M]$^+$; Found 384.1677.
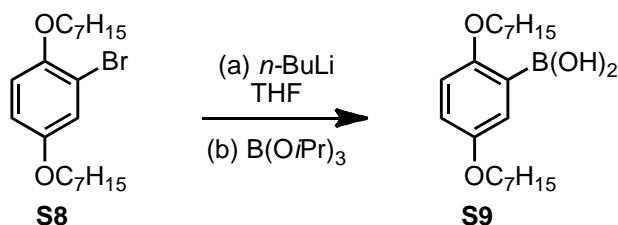
(2,5-bis(heptyloxy)phenyl)boronic acid (S9): An oven-dried 50 mL Schlenk flask was equipped with a stir bar and septum, cooled to rt under vacuum and filled with N$_2$. **S8** (1.025 g, 0.0027 mol, 1.0 equiv) and THF (27.0 mL) were added to the flask. The solution was then cooled to -78 °C. Then *n*-BuLi (1.80 mL, 1.6 M, 1.1 equiv) was added via syringe. After 20 min, triisopropyl borate (1.80 mL, 0.008 mol, 2.9 equiv) was added. The reaction was gradually warmed to rt and stirred for 24 h. The mixture was cooled to 0 °C and aqueous HCl (5 mL, 2 M) was added and stirred for 20 min. The aqueous mixture was extracted with ether (50 mL). The combined organic layers were washed with brine (1 x 20 mL). The organic layer was dried over anhydrous MgSO$_4$, filtered and concentrated in vacuo. The crude product was purified by column chromatography using 5/15/80 EtOAc/CH$_2$Cl$_2$/hexanes as the eluent to give 713 mg of **S9** as a white solid (62% yield). HRMS (ESI) Calcd. for C$_{20}$H$_{35}$BO$_4$, 350.2628 [M]$^+$; Found 350.2635. ^{11}B NMR (128 MHz, CDCl$_3$) δ 28.87.
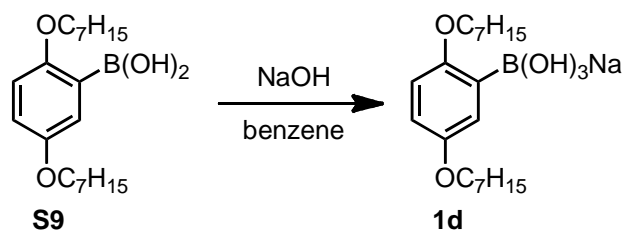
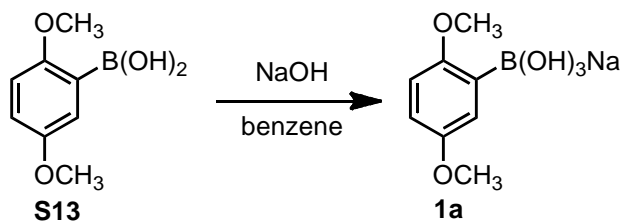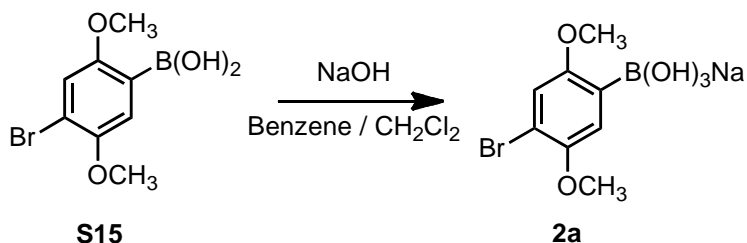**1d: S9** (545 mg, 1.55 mmol, 1.0 equiv) was dissolved in benzene (15.5 mL), then NaOH (60.6 mg, 1.51 mmol, 0.97 equiv) was added. The reaction was stirred for 21 h at rt. The mixture was concentrated in vacuo isolating 488 mg of **1d** as a white solid (80% yield). ^{11}B NMR (128 MHz, CD$_3$OD) δ 4.65.
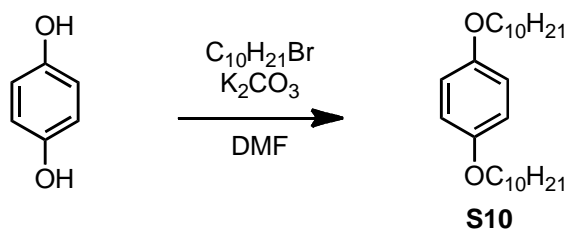
1,4-bis(decyloxy)benzene (S10): Hydroquinone (10.00 g, 0.0908 mol, 1.0 equiv), 1-bromodecane (48.0 mL, 0.231 mol, 2.6 equiv), and DMF (62 mL) were added under N$_2$ to a 500 mL flask and heated to 80 °C with vigorous stirring. Then, K$_2$CO$_3$ (31.82 g, 0.230 mol, 2.5 equiv) was added and the reaction mixture was stirred for 3 d. The reaction was cooled to rt, filtered and washed with hexanes. The filtrate was washed with water (2 x 200 mL) and brine (2 x 200 mL), dried over anhydrous MgSO$_4$, filtered and concentrated in vacuo. The crude product was recrystallized three times from hot EtOH to give 27.034 g of **S10** as a white crystalline solid (76% yield). HRMS (ESI) Calcd. for C$_{26}$H$_{46}$O$_2$, 390.3498 [M]$^+$; Found 390.3500.
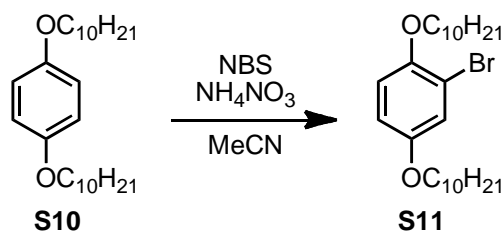
2-bromo-1,4-bis(decyloxy)benzene (S11): Sequentially, **S10** (3.011 g, 0.0077 mol, 1.0 equiv), acetonitrile (20 mL), NH$_4$NO$_3$ (0.063 g, 0.0008 mol, 0.1000 equiv) and *N*-bromosuccinimide (1.365 g, 0.0008 mol, 1.0 equiv) were added to a 100 mL round-bottom flask with a stir bar. The reaction was stirred and heated 35 °C for 24 h, then quenched with water (50 mL). The aqueous mixture was extracted with EtOAc (2 x 50 mL). The combined organic layers were washed with water (2 x 50 mL) and brine (2 x 50 mL), dried over anhydrous MgSO$_4$, filtered and concentrated in vacuo. The crude product was purified by column chromatography using 20/80/0.05 toluene/hexanes/EtOAc as the eluent to give 1.43 g of **S11** as a clear crystalline solid (40% yield). HRMS (ESI) Calcd. for C$_{26}$H$_{45}$BrO$_2$, 468.2603 [M]$^+$; Found 468.2598.
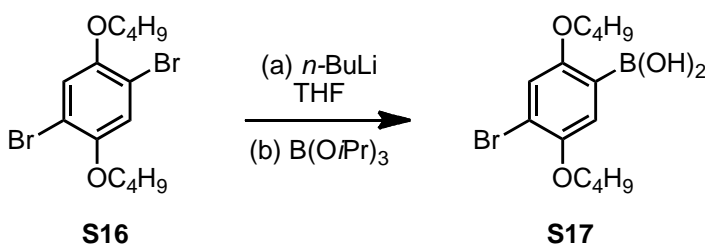

(2,5-bis(decyloxy)phenyl)boronic acid (S12): An oven-dried 50 mL Schlenk flask was equipped with a stir bar and septum, cooled to rt under vacuum and filled with N$_2$. **S11** (1.016 g, 0.0022 mol, 1.0 equiv) and THF (22.0 mL) were added to the flask. The solution was then cooled to -78 °C. Then *n*-BuLi (1.50 mL, 1.6 M, 1.1 equiv) was added via syringe. After 20 min, triisopropyl borate (1.50 mL, 0.007 mol, 3.0 equiv) was added. The reaction was gradually warmed to rt and stirred for 24 h. The mixture was cooled to 0 °C and aqueous HCl (5 mL, 2 M) was added and stirred for 20 min. The aqueous

mixture was extracted with ether (50 mL). The combined organic layers were washed with brine (1 x 20 mL). The organic layer was dried over anhydrous $MgSO_4$, filtered and concentrated in vacuo. The crude product was purified by column chromatography using 5/15/80 EtOAc/CH_2Cl_2/hexanes as the eluent to give 404 mg of **S12** as a white solid (43% yield). HRMS (ESI) Calcd. for $C_{26}H_{47}BO_4$, 457.3465 [M + Na]$^+$; Found 457.3460. ^{11}B NMR (128 MHz, CDCl$_3$) δ 29.13.
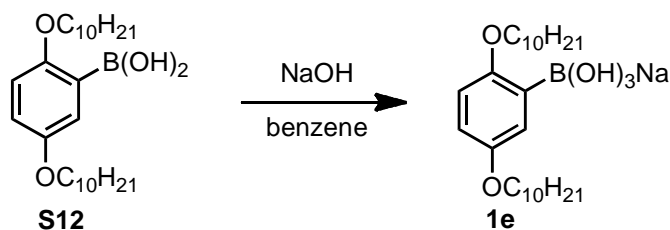
1e: S12 (404 mg, 0.93 mmol, 1.0 equiv) was dissolved in benzene (10.0 mL), then NaOH (35.7 mg, 0.89 mmol, 0.96 equiv) was added. The reaction was stirred for 11 h at rt. The mixture was concentrated in vacuo isolating 429 mg of **1e** as a clear viscous oil (97% yield). ^{11}B NMR (128 MHz, CD$_3$OD) δ 4.41.
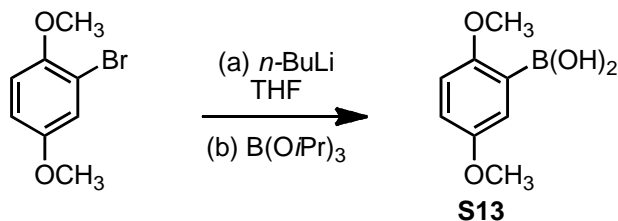

(2,5-dimethoxyphenyl)boronic acid (S13): An oven-dried 50 mL Schlenk flask was equipped with a stir bar and septum, cooled to rt under vacuum and filled with N_2. Bromodimethoxybenzene (1.012 g, 0.0047 mol, 1.0 equiv) and THF (46.0 mL) were added to the flask. The solution was then cooled to -78 °C. Then *n*-BuLi (3.2 mL, 1.6 M, 1.1 equiv) was added via syringe. After 20 min, triisopropyl borate (3.2 mL, 0.014 mol, 2.9 equiv) was added. The reaction was gradually warmed to rt and stirred for 24 h. The mixture was cooled to 0 °C and aqueous HCl (5 mL, 2 M) was added and stirred for 20 min. The aqueous mixture was extracted with ether (2 x 50 mL). The combined organic

layers were washed with brine (1 x 50 mL). The organic layer was dried over anhydrous MgSO₄, filtered and concentrated in vacuo. The crude product was purified by column chromatography using 20/80 EtOAc/hexanes as the eluent to give 490 mg of **S13** as a white solid (58% yield). HRMS (ESI): Calcd. for $C_8H_{11}BO_4$, 182.0750 $[M]^+$; Found 182.0757. ^{11}B NMR (128 MHz, CDCl₃) δ 29.22.

1a: S13 (359 mg, 1.97 mmol, 1.0 equiv) was dissolved in benzene (10.0 mL), then NaOH (77.2 mg, 1.93 mmol, 0.98 equiv) was added. The reaction was stirred for 20 h at rt and the solution turned into a white suspension. The mixture was concentrated in vacuo isolating 390 mg of a white solid (89% yield). ^{11}B NMR (128 MHz, CD₃OD) δ 4.63.
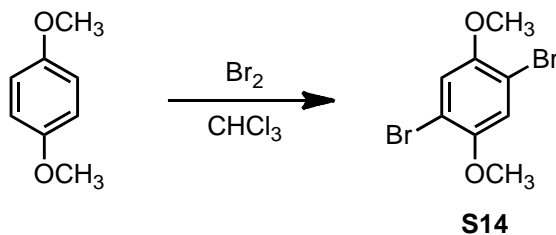
1,4-dibromo-2,5-dimethoxybenzene (S14): Dimethoxybenzene (2.009 g, 0.0146 mol, 1.0 equiv) was dissolved in CHCl₃, cooled to 0 °C under N₂ and the pressure was vented through a 10% aq Na₂SO₃ solution (~100 mL). Bromine (1.9 mL, 0.04 mol, 2.5 equiv) was added dropwise via syringe. The ice bath was then removed and the reaction continued to stir at rt for 3 h. The reaction was quenched with 10% aq Na₂SO₃ (50 mL) and extracted with CH₂Cl₂ (2 x 50 mL). The organic layer was washed with brine (2 x 50 mL), dried over anhydrous MgSO₄, filtered and concentrated in vacuo. The crude product was recrystallized from CH₂Cl₂/MeOH to give 2.894 g of **S14** as white crystals (67% yield). HRMS (ESI) Calcd. for $C_8H_8Br_2O_2$, 293.8891 $[M]^+$; Found 293.8882.
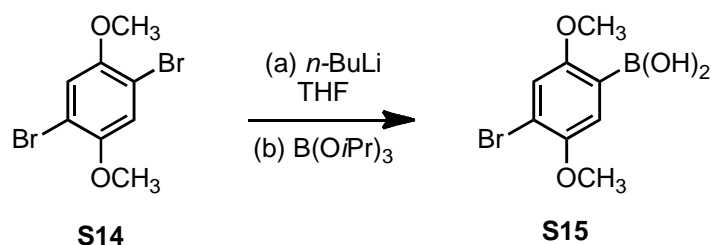
(4-bromo-2,5-dimethoxyphenyl)boronic acid (S15): An oven-dried 50 mL Schlenk flask was equipped with a stir bar and septum, cooled to rt under vacuum and filled with N_2. **S14** (1.002 g, 0.0034 mol, 1.0 equiv) and THF (34.0 mL) were added to the flask. The solution was then cooled to -78 °C. Then *n*-BuLi (2.3 mL, 1.6 M, 1.1 equiv) was added via syringe. After 20 min, triisopropyl borate (2.30 mL, 0.010 mol, 2.9 equiv) was added. The reaction was gradually warmed to rt and stirred for 24 h. The mixture was cooled to 0 °C and aqueous HCl (5 mL, 2 M) was added and stirred for 20 min. The aqueous mixture was extracted with ether (2 x 50 mL). The combined organic layers were washed with brine (1 x 50 mL). The organic layer was dried over anhydrous $MgSO_4$, filtered and concentrated in vacuo. The crude product was purified by column chromatography using 20/80 EtOAc/hexanes as the eluent to give 556 mg of **S15** as a white solid (63% yield). HRMS (ESI) Calcd. for $C_8H_{10}BBrO_4$, 259.9856 [M]$^+$; Found 259.9862. ^{11}B NMR (128 MHz, CDCl$_3$) δ 28.96.

2a: S15 (414 mg, 1.59 mmol, 1.0 equiv) was dissolved in benzene (10.0 mL), and CH_2Cl_2 (5.0 mL). Then NaOH (64.4 mg, 1.61 mmol, 1.0 equiv) was added. The reaction was stirred for 11 h at rt. The mixture was concentrated in vacuo isolating 437 mg of **2a** as a white solid (92% yield). ^{11}B NMR (128 MHz, CD$_3$OD) δ 4.88.
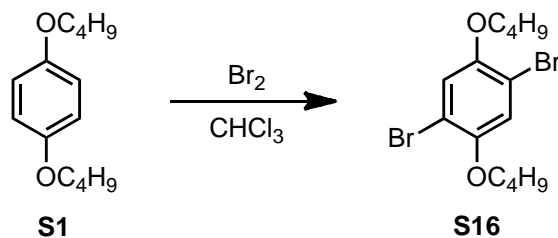
1,4-dibromo-2,5-dibutoxybenzene (S16): S1 (2.015 g, 0.0091 mol, 1.0 equiv) was dissolved in CHCl$_3$, cooled to 0 °C under N$_2$ and the pressure was vented through a 10% aq Na$_2$SO$_3$ solution (~100 mL). Bromine (1.15 mL, 0.02 mol, 2.5 equiv) was added dropwise via syringe. The ice bath was then removed and the reaction continued to stir at rt for 3 h. The reaction was quenched with 10% aq Na$_2$SO$_3$ (50 mL) and extracted with CH$_2$Cl$_2$ (40 mL). The organic layer was washed with brine (20 mL), dried over anhydrous MgSO$_4$, filtered and concentrated in vacuo. The crude product was recrystallized from CH$_2$Cl$_2$/MeOH to give 2.804 g of **S16** as white crystals (81% yield). HRMS (ESI) Calcd. for C$_{14}$H$_{20}$Br$_2$O$_2$, 377.9830 [M]$^+$; Found 377.9829.

(4-bromo-2,5-dibutoxyphenyl)boronic acid (S17): An oven-dried 50 mL Schlenk flask was equipped with a stir bar and septum, cooled to rt under vacuum and filled with N$_2$. **S11** (1.009 g, 0.0026 mol, 1.0 equiv) and THF (26.0 mL) were added to the flask. The solution was then cooled to -78 °C. Then *n*-BuLi (1.80 mL, 1.6 M, 1.1 equiv) was added via syringe. After 20 min, triisopropyl borate (1.80 mL, 0.008 mol, 2.9 equiv) was added. The reaction was gradually warmed to rt and stirred for 24 h. The mixture was cooled to 0 °C and aqueous HCl (5 mL, 2 M) was added and stirred for 20 min. The aqueous mixture was extracted with ether (2 x 50 mL). The combined organic layers were washed with brine (1 x 50 mL). The organic layer was dried over anhydrous MgSO$_4$, filtered and concentrated in vacuo. The crude product was purified by column chromatography using

5/15/80 EtOAc/CH$_2$Cl$_2$/hexanes as the eluent to give 420 mg of **S17** as a white solid (46% yield). HRMS (ESI) Calcd. for C$_{14}$H$_{22}$BBrO$_4$, 344.0795 [M]$^+$; Found 344.0796. ^{11}B NMR (128 MHz, CDCl$_3$) δ 29.05.

S17   **2b**
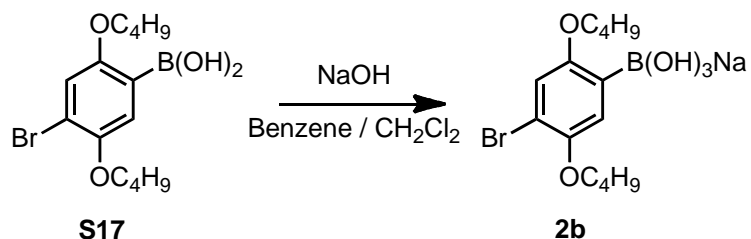
2b: S17 (303 mg, 0.0009 mol, 1.0 equiv) was dissolved in benzene (5.0 mL) and CH$_2$Cl$_2$ (5.0 mL), then NaOH (36.3 mg, 0.0009 mol, 1.0 equiv) was added. The reaction was stirred for 24 h at rt and the solution turned into a white suspension. The mixture was concentrated in vacuo isolating 337 mg of a white solid (99% yield). ^{11}B NMR (128 MHz, CD$_3$OD) δ 4.57.

S4   **S18**
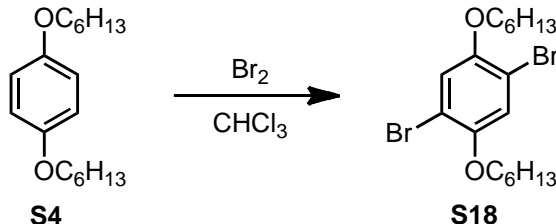
1,4-dibromo-2,5-bis(hexyloxy)benzene (S18): In a 100 mL round bottom flask, **S4** (2.007 g, 0.0072 mol, 1.0 equiv) was dissolved in CHCl$_3$, cooled to 0 °C under N$_2$ and the pressure was vented through a 10% aq Na$_2$SO$_3$ solution (~100 mL). Bromine (0.925 mL, 0.018 mol, 2.5 equiv) was added dropwise via syringe. The ice bath was then removed and the reaction continued to stir at rt for 3 h. The reaction was quenched with 10% aq Na$_2$SO$_3$ (50 mL) and extracted with CH$_2$Cl$_2$ (40 mL). The organic layer was washed with brine (20 mL), dried over anhydrous MgSO$_4$, filtered and concentrated in vacuo. The crude product was recrystallized from CH$_2$Cl$_2$/MeOH to give 2.758 g of **S18** as white crystals (88% yield). HRMS (ESI) Calcd. for C$_{18}$H$_{28}$Br$_2$O$_2$, 434.0456 [M]$^+$; Found 434.0448.
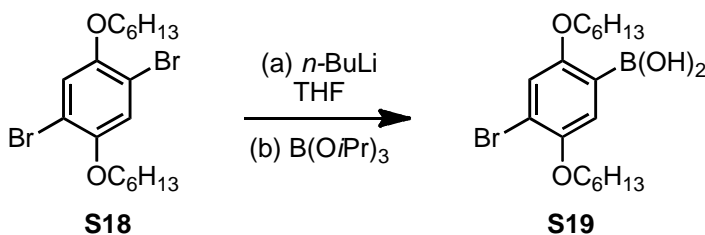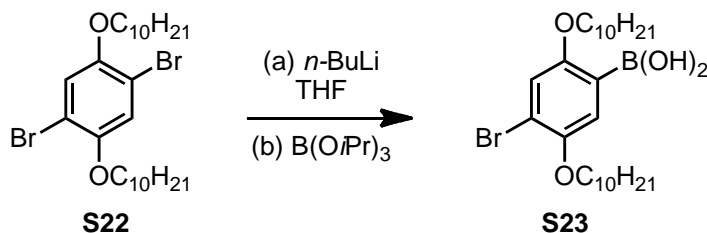
(4-bromo-2,5-bis(hexyloxy)phenyl)boronic acid (S19): An oven-dried 50 mL Schlenk flask was equipped with a stir bar and septum, cooled to rt under vacuum and filled with N$_2$. **S19** (1.006 g, 0.0023 mol, 1.0 equiv) and THF (23 mL) were added to the flask. The solution was then cooled to -78 °C. Then *n*-BuLi (2.49 mL, 1.0 M, 1.1 equiv) was added via syringe. After 20 min, triisopropyl borate (2.50 mL, 0.011 mol, 4.7 equiv) was added. The reaction was gradually warmed to rt and stirred for 24 h. The mixture was cooled to 0 °C and aqueous HCl (5 mL, 2 M) was added and stirred for 20 min. The aqueous mixture was extracted with ether (2 x 20 mL). The combined organic layers were washed with water (1 x 20 mL) and brine (1 x 20 mL). The organic layer was dried over anhydrous MgSO$_4$, filtered and concentrated in vacuo. The crude product was purified by column chromatography using 5/15/80 EtOAc/CH$_2$Cl$_2$/hexanes as the eluent to give 525 mg of **S19** as a white solid (57% yield). HRMS (ESI) Calcd. for C$_{18}$H$_{30}$BBrO$_4$, 400.1421 [M]$^+$; Found 400.1434. ^{11}B NMR (128 MHz, CDCl$_3$) δ 28.78.
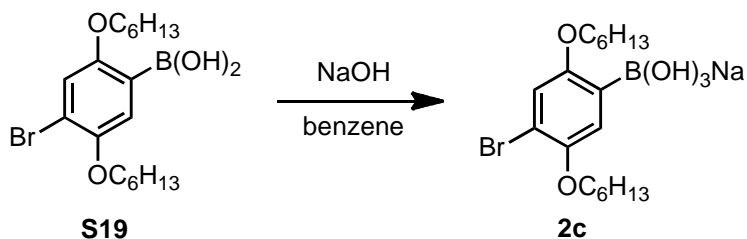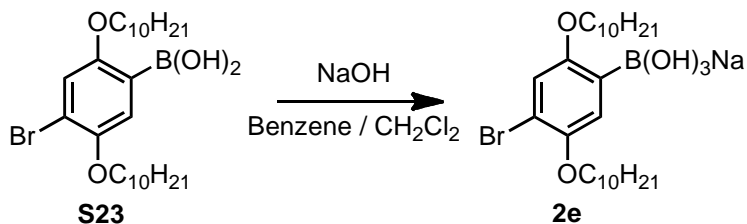

2c: S19 (425 mg, 0.001 mol, 1.0 equiv) was dissolved in benzene (10.0 mL), then NaOH (41.7 mg, 0.001 mol, 0.98 equiv) was added. The reaction was stirred for 17 h at rt and the solution turned into a white suspension. The mixture was concentrated in vacuo isolating 438 mg of a white solid (94% yield). ^{11}B NMR (128 MHz, CD$_3$OD) δ 4.53.
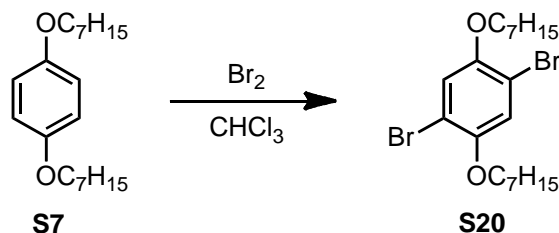
1,4-dibromo-2,5-bis(heptyloxy)benzene (S20): In a 100 mL round bottom flask, **S7** (2.009 g, 0.0066 mol, 1.0 equiv) was dissolved in CHCl$_3$, cooled to 0 °C under N$_2$ and the pressure was vented through a 10% aq Na$_2$SO$_3$ solution (~100 mL). Bromine (0.845 mL, 0.016 mol, 2.5 equiv) was added dropwise via syringe. The ice bath was then removed and the reaction continued to stir at rt for 3 h. The reaction was quenched with 10% aq Na$_2$SO$_3$ (50 mL) and extracted with CH$_2$Cl$_2$ (40 mL). The organic layer was washed with brine (20 mL), dried over anhydrous MgSO$_4$, filtered and concentrated in vacuo. The crude product was recrystallized from CH$_2$Cl$_2$/MeOH to give 2.835 g of **S20** as white crystals (93% yield). HRMS (ESI) Calcd. for C$_{20}$H$_{32}$Br$_2$O$_2$, 462.0769 [M]$^+$; Found 462.0779.
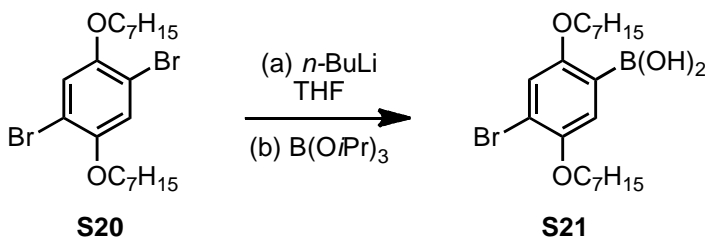
(4-bromo-2,5-bis(heptyloxy)phenyl)boronic acid (S21): An oven-dried 50 mL Schlenk flask was equipped with a stir bar and septum, cooled to rt under vacuum and filled with N$_2$. **S20** (1.003 g, 0.0021 mol, 1.0 equiv) and THF (23 mL) were added to the flask. The solution was then cooled to -78 °C. Then *n*-BuLi (2.40 mL, 1.0 M, 1.1 equiv) was added via syringe. After 20 min, triisopropyl borate (2.41 mL, 0.011 mol, 5.0 equiv) was added. The reaction was gradually warmed to rt and stirred for 24 h. The mixture was cooled to 0 °C and aqueous HCl (5 mL, 2 M) was added and stirred for 20 min. The aqueous mixture was extracted with ether (2 x 20 mL). The combined organic layers were washed with water (1 x 20 mL) and brine (1 x 20 mL). The organic layer was dried over anhydrous MgSO$_4$, filtered and concentrated in vacuo. The crude product was purified by

column chromatography using 5/15/80 EtOAc/CH$_2$Cl$_2$/hexanes as the eluent to give 315 mg of **S21** as a white solid (34% yield). HRMS (ESI): Calcd. for C$_{20}$H$_{34}$BBrO$_4$ [M + Na]$^+$ 451.1626; Found 451.1640. ^{11}B NMR (128 MHz, CDCl$_3$) δ 29.04.

S21   **2d**
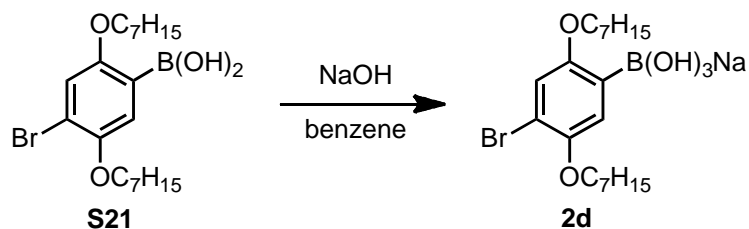
2d: S17 (315 mg, 0.73 mmol, 1.0 equiv) was dissolved in benzene (8.0 mL), then NaOH (29.8 mg, 0.75 mmol, 1.0 equiv) was added. The reaction was stirred for 17 h at rt and the solution turned into a white suspension. The mixture was concentrated in vacuo isolating 310 mg of a white solid (90% yield). ^{11}B NMR (128 MHz, CD$_3$OD) δ 4.49.

S10   **S22**
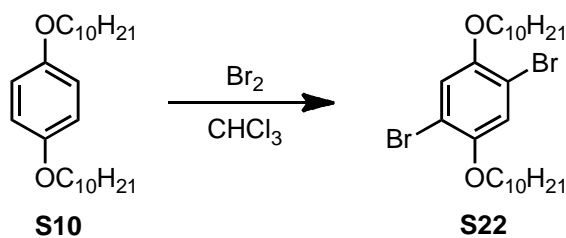
1,4-dibromo-2,5-bis(decyloxy)benzene (S22): In a 100 mL round bottom flask, **S10** (2.002 g, 0.0051 mol, 1.0 equiv) was dissolved in CHCl$_3$, cooled to 0 °C under N$_2$ and the pressure was vented through a 10% aq Na$_2$SO$_3$ solution (~100 mL). Bromine (0.70 mL, 0.01 mol, 2.7 equiv) was added dropwise via syringe. The ice bath was then removed and the reaction continued to stir at rt for 3 h. The reaction was quenched with 10% aq Na$_2$SO$_3$ (50 mL) and extracted with CH$_2$Cl$_2$ (2 x 50 mL). The organic layer was washed with brine (2 x 50 mL), dried over anhydrous MgSO$_4$, filtered and concentrated in vacuo. The crude product was recrystallized from CH$_2$Cl$_2$/MeOH to give 2.557 g of **S22** as white crystals (91% yield). HRMS (ESI) Calcd. for C$_{26}$H$_{44}$Br$_2$O$_2$, 546.1708 [M]$^+$; Found 546.1707.

(4-bromo-2,5-bis(decyloxy)phenyl)boronic acid (S23): An oven-dried 50 mL Schlenk flask was equipped with a stir bar and septum, cooled to rt under vacuum and filled with N_2. **S22** (1.009 g, 0.0018 mol, 1.0 equiv) and THF (20.0 mL) were added to the flask. The solution was then cooled to -78 °C. Then *n*-BuLi (1.30 mL, 1.6 M, 1.1 equiv) was added via syringe. After 20 min, triisopropyl borate (1.30 mL, 0.005 mol, 3.1 equiv) was added. The reaction was gradually warmed to rt and stirred for 24 h. The mixture was cooled to 0 °C and aqueous HCl (5 mL, 2 M) was added and stirred for 20 min. The aqueous mixture was extracted with ether (2 x 50 mL). The combined organic layers were washed with brine (1 x 50 mL). The organic layer was dried over anhydrous $MgSO_4$, filtered and concentrated in vacuo. The crude product was purified by column chromatography using 5/15/80 EtOAc/CH_2Cl_2/hexanes as the eluent to give 193 mg of **S23** as a white solid (20% yield). HRMS (ESI): Calcd. for $C_{26}H_{46}BBrO_4$ [M]$^+$ 512.2672; Found 512.2665. ^{11}B NMR (128 MHz, $CDCl_3$) δ 26.44.

2e: S23 (188 mg, 0.366 mmol, 1.0 equiv) was dissolved in benzene (10.0 mL) and CH_2Cl_2 (5 mL). Then NaOH (14.6 mg, 0.365 mol, 1.0 equiv) was added. The reaction was stirred for 24 h at rt and the solution turned into a white suspension. The mixture was concentrated in vacuo isolating 193 mg of a white solid (95% yield). ^{11}B NMR (128 MHz, CD_3OD) δ 4.35.

D. NMR Spectra
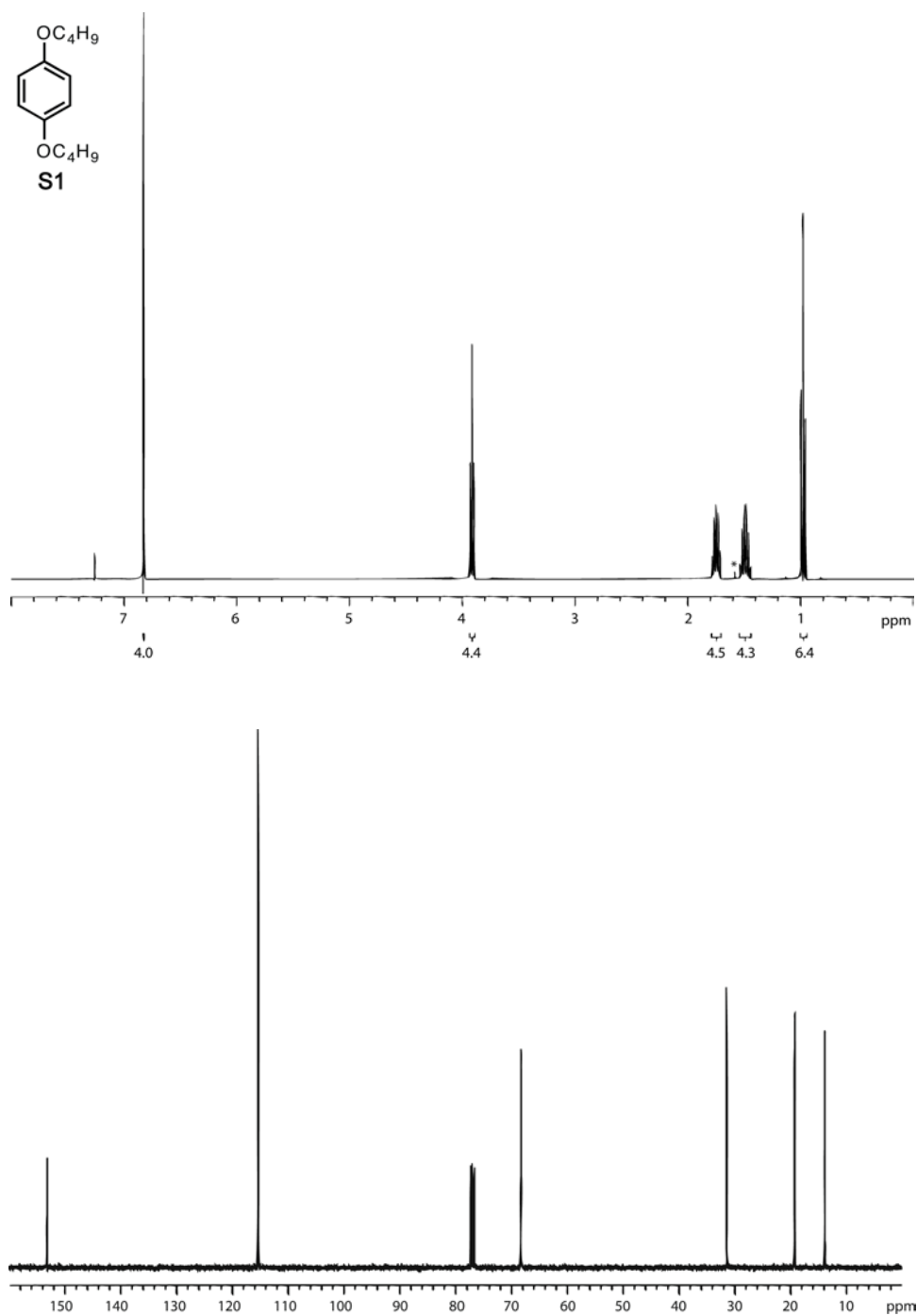
Figure S1. ^1H and ^{13}C NMR spectra of **S1**. ^1H NMR (400 MHz, CDCl$_3$) δ 6.83 (s, 4H), 3.91 (t, *J* = 6.4 Hz, 4H), 1.75 (m, 4H), 1.49 (m, 4H), 0.98 (m, 6H). *residual H$_2$O. ^{13}C NMR (100 MHz, CDCl$_3$) δ 153.18, 115.36, 68.30, 31.45, 19.24, 13.85.
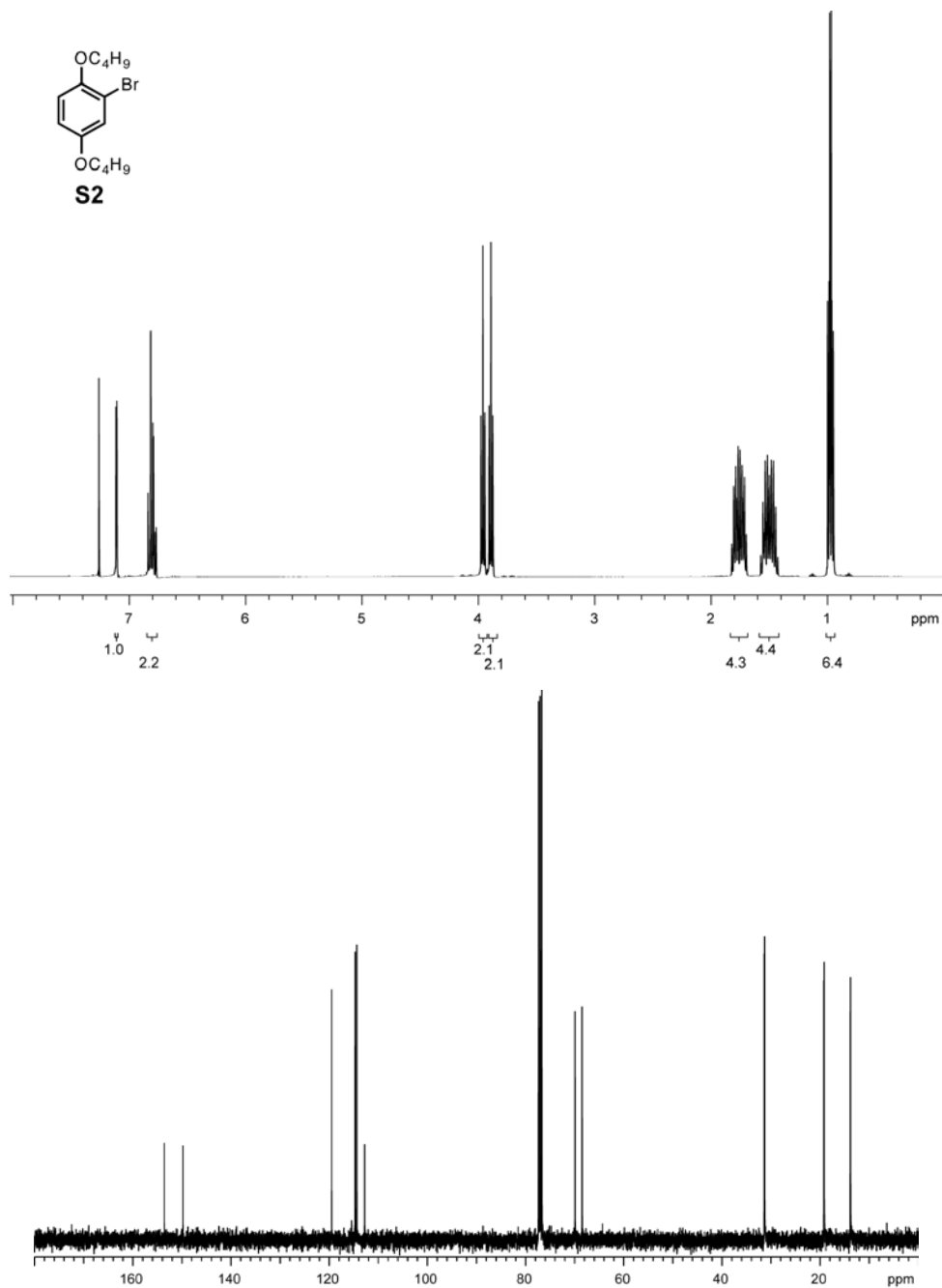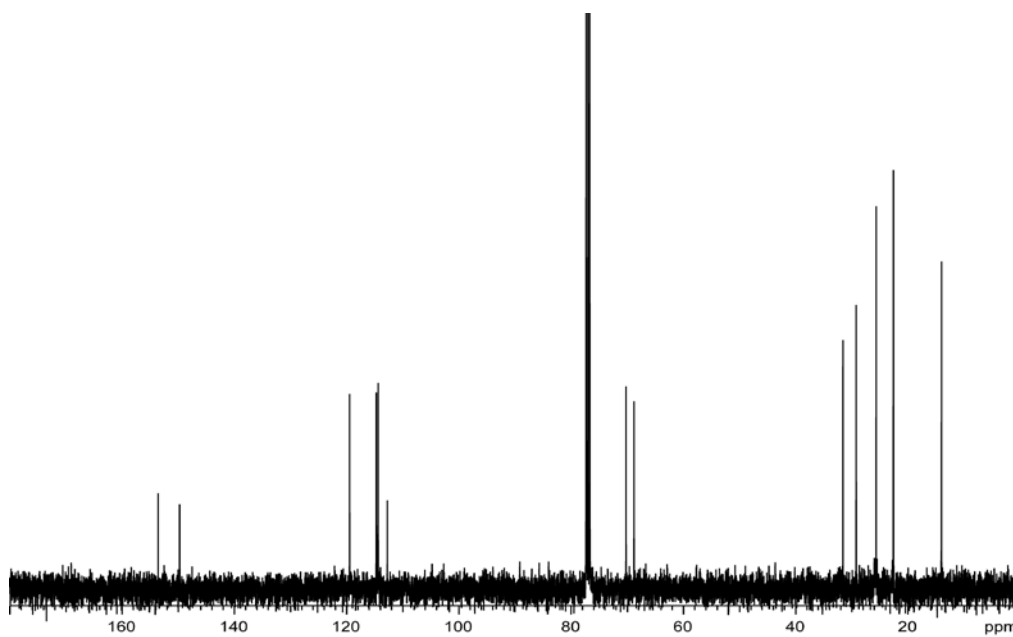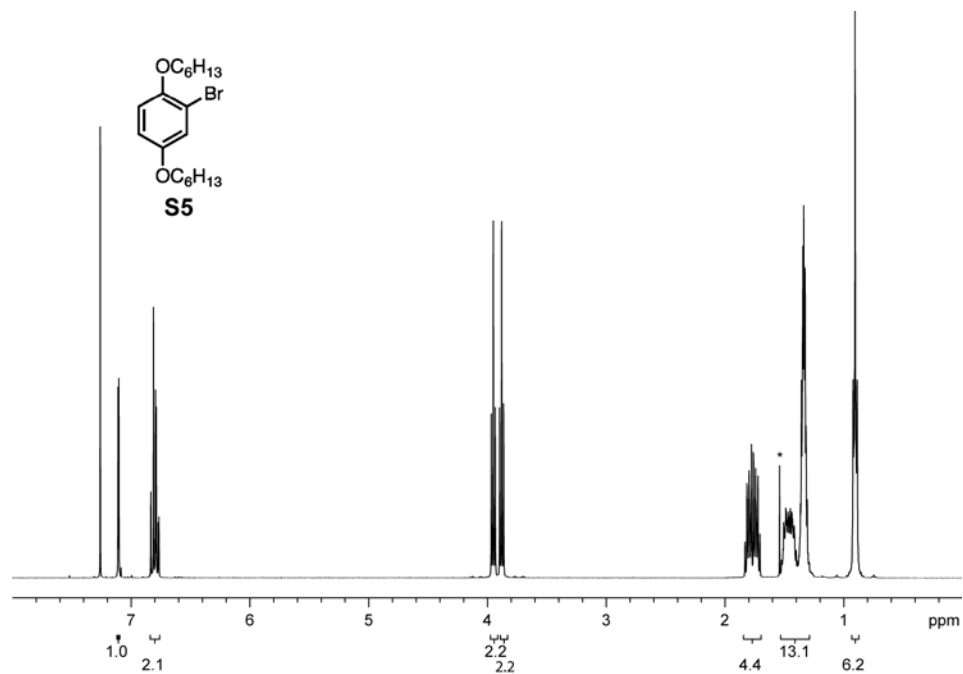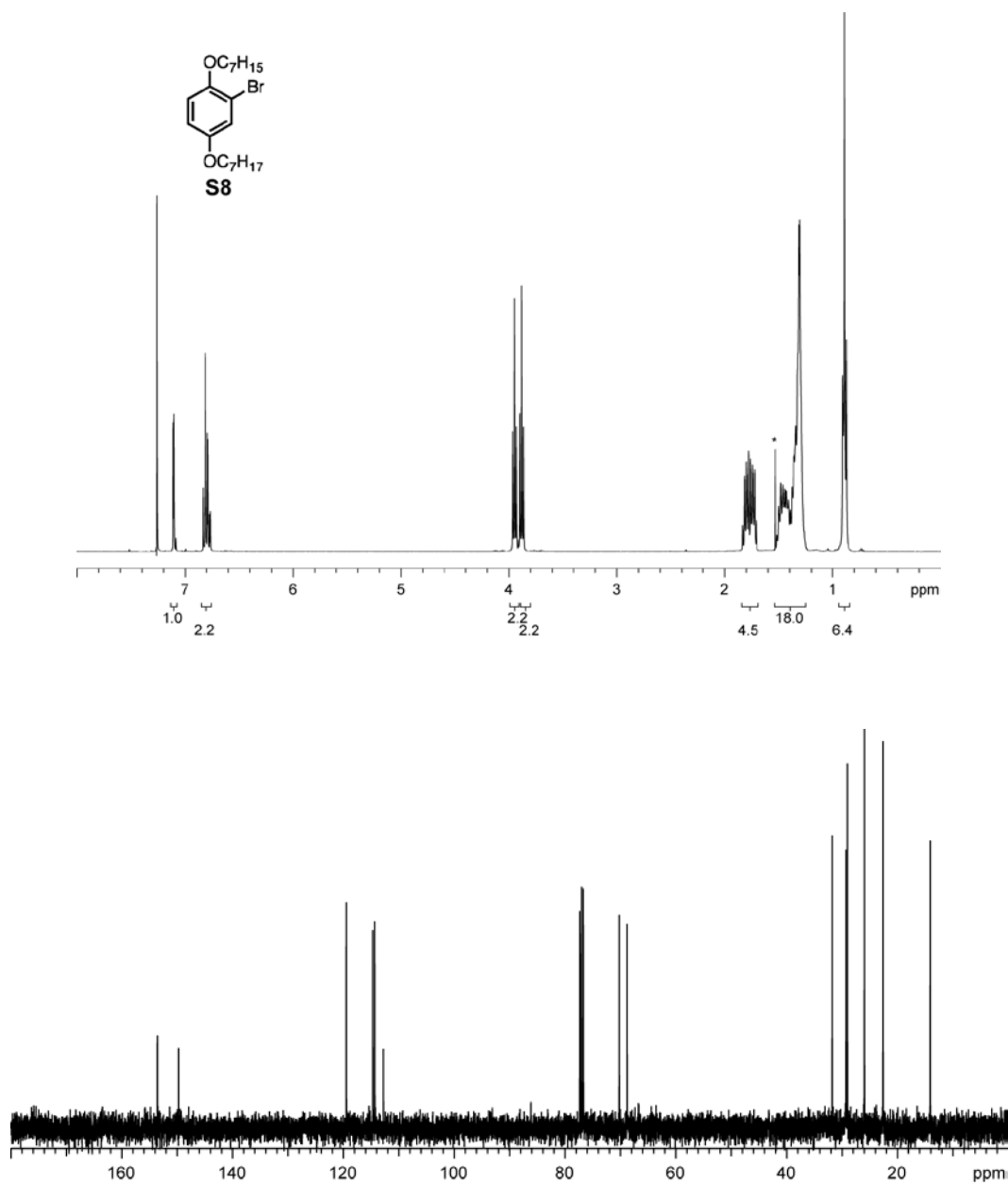
Figure S2. ¹H and ¹³C NMR spectra of **S2**. ¹H NMR (400 MHz, CDCl₃) δ 7.11 (d, *J* = 2.4 Hz, 1H), 6.82 (m, 2H), 3.96 (t, *J* = 6.4 Hz, 2H), 3.89 (t, *J* = 6.4 Hz, 2H), 1.76 (m, 4H), 1.50 (m, 4H), 0.97 (m, 6H) ¹³C NMR (100 MHz, CDCl₃) δ 153.58, 149.76, 119.48, 114.70, 114.38, 112.77. 69.89, 68.49, 31.35, 31.30, 19.24, 19.19. 13.85, 13.81.

Figure S3. ¹H and ¹³C NMR spectra of **S3**. ¹H NMR (400 MHz, CDCl₃) δ 7.39 (d, *J* = 3.2 Hz, 1H), 6.97 (dd, *J* = 8.8, 3.2 Hz, 1H), 6.84 (d, *J* = 8.8 Hz, 1H), 6.49 (s, 2H), 4.03 (t, *J* = 6.8 Hz, 2H), 3.96 (t, *J* = 6.8 Hz, 2H), 1.77 (m, 4H), 1.48 (m, 4H), 0.98 (m, 6H). ¹³C NMR (100 MHz, CDCl₃) δ 158.18, 153.25, 121.29, 119.32, 112.11, 68.67, 68.26, 31.43, 31.35, 19.25, 19.21, 13.97, 13.79. C *ipso* to B is not observed.
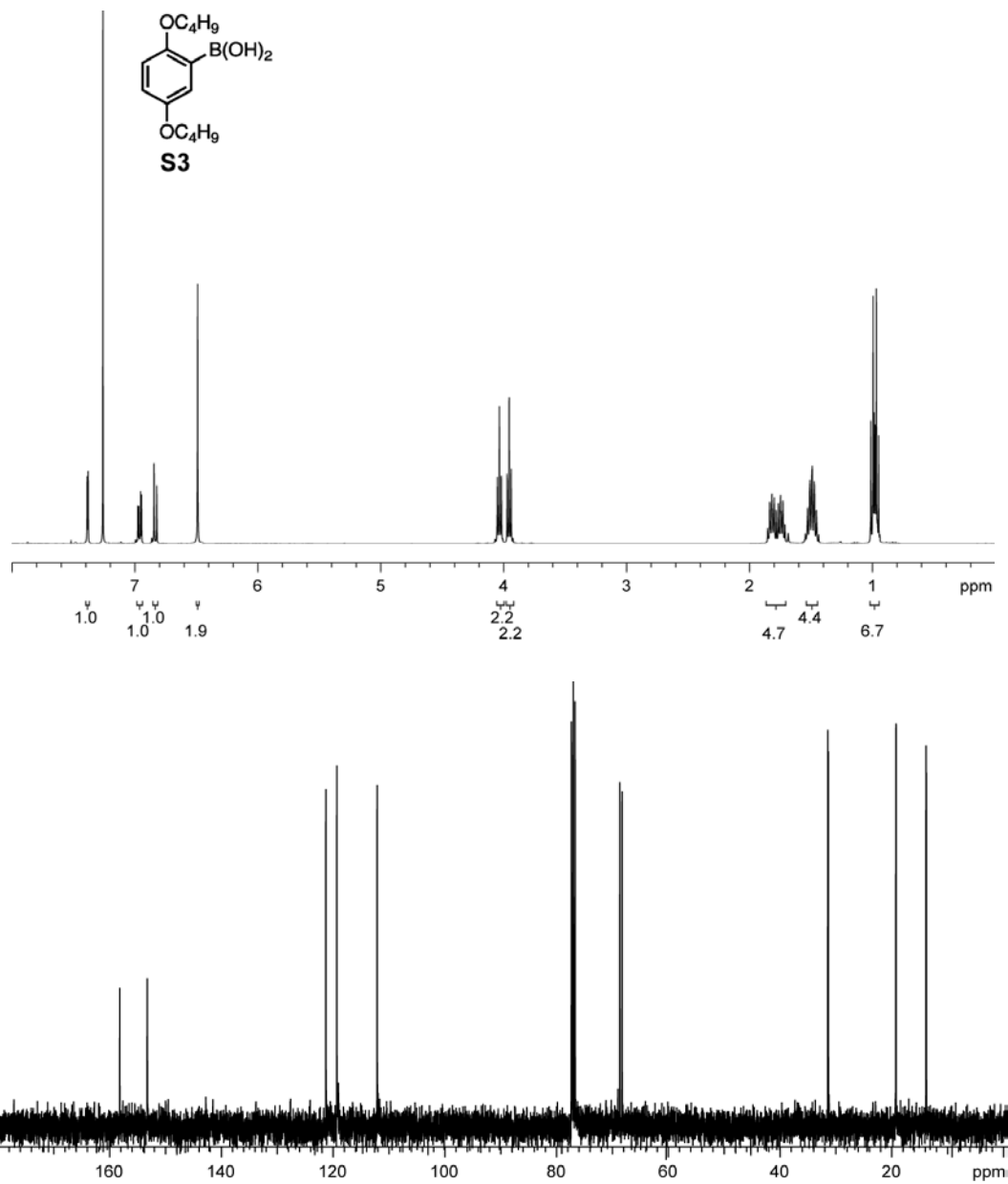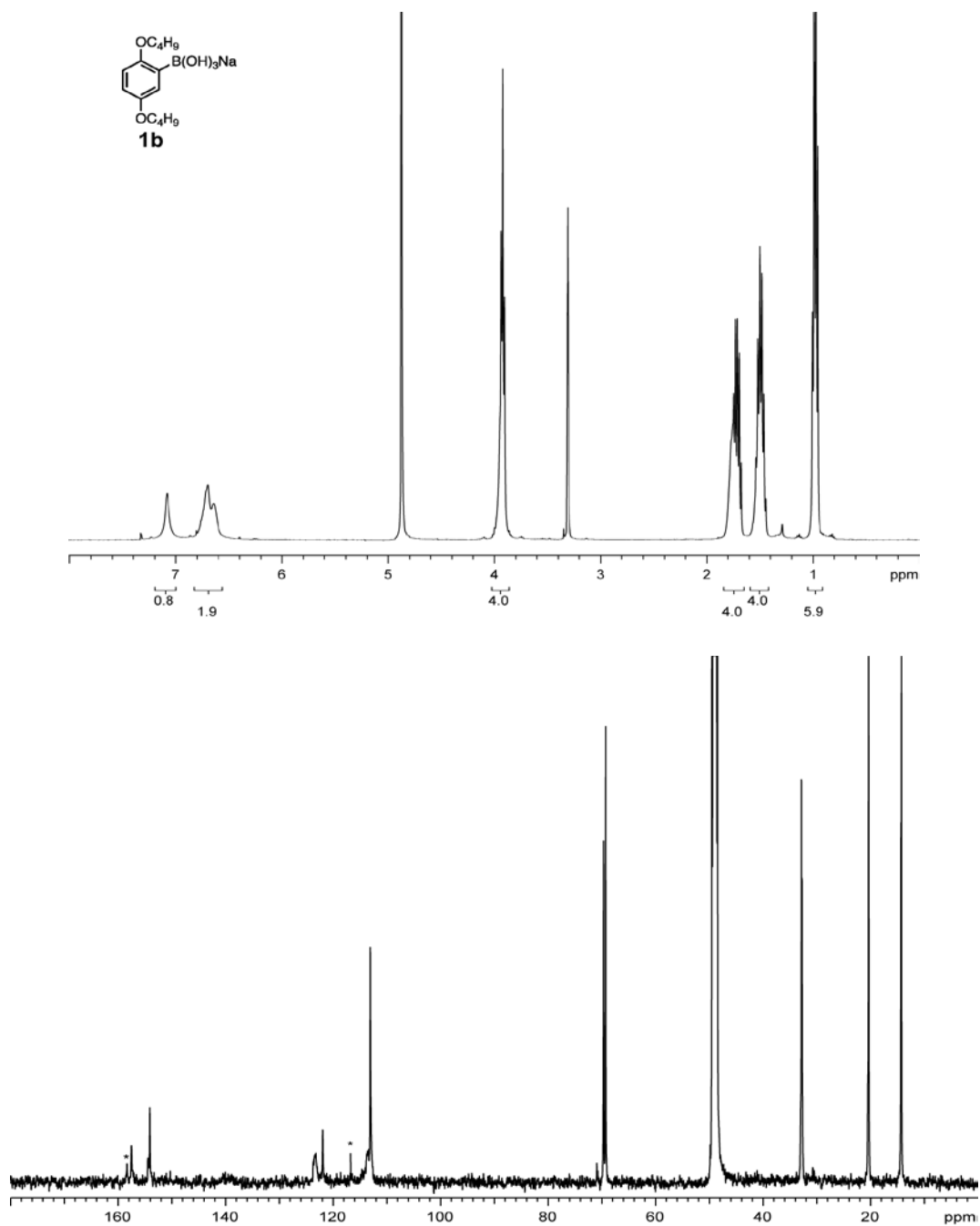
Figure S4. ^1H and ^{13}C NMR spectra of **1b**. ^1H NMR (400 MHz, CD$_3$OD) δ 7.08 (br, 1H), 6.70 (br, 2H), 3.92 (t, $J = 6.4$ Hz, 4H), 1.7 (m, 4H), 1.5 (m, 4H), 0.99 (m, 6H). ^{13}C NMR (125 MHz, CDCl$_3$) δ 157.51, 154.09, 123.19, 121.92, 113.60, 113.08, 69.67, 69.28, 32.86, 32.74, 20.36, 14.35, 14.25. *trace decomposition product as verified by HPLC, one carbon in the butyl chains is unresolved.

207
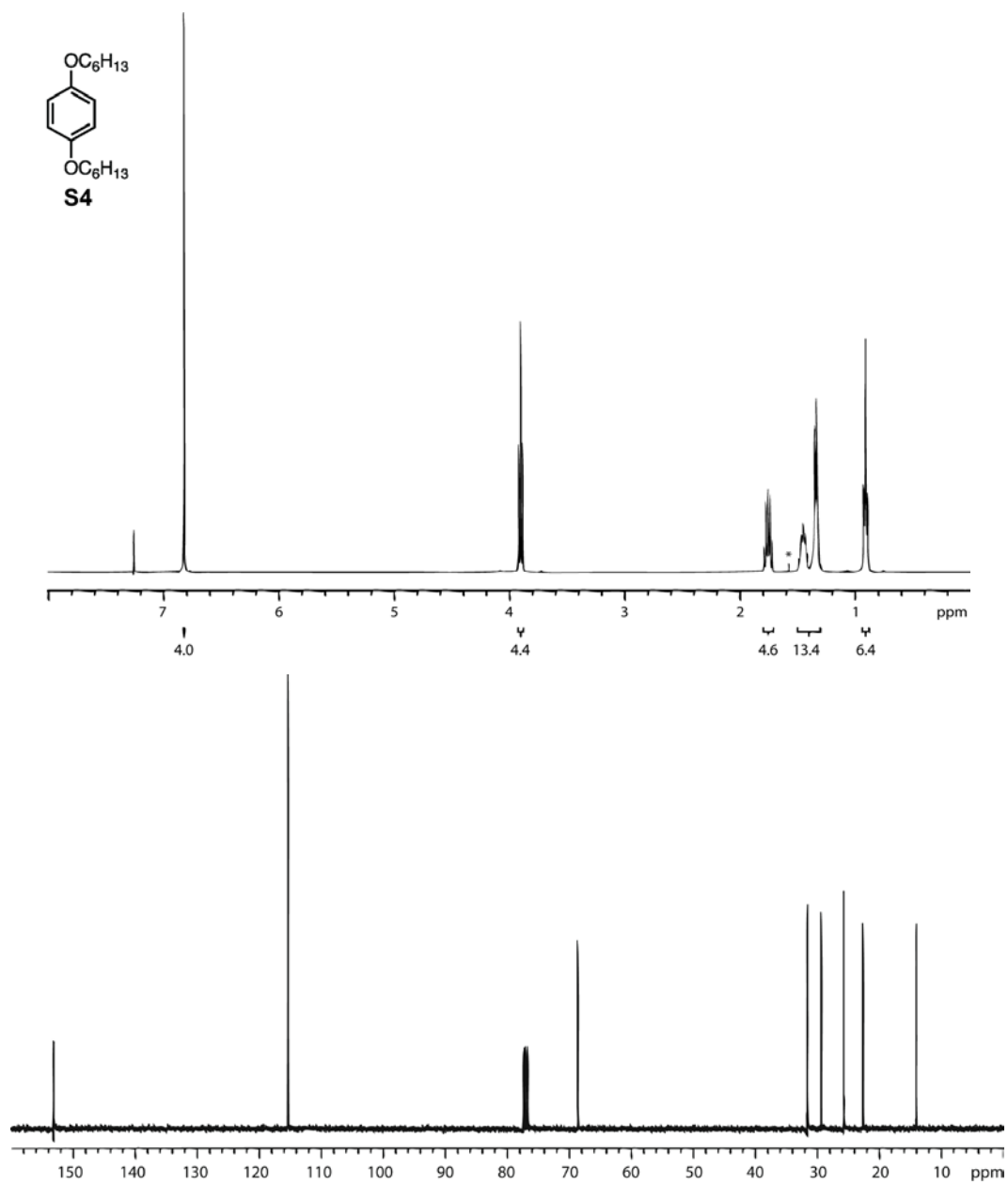
Figure S5. ^{1}H and ^{13}C NMR spectra of **S4**. ^{1}H NMR (400 MHz, CDCl$_3$) δ 6.83 (s, 4H), 3.90 (t, *J* = 6.8 Hz, 4H), 1.76 (m, 4H), 1.47-1.32 (br, 12H), 0.91 (m, 6H). *residual H$_2$O. ^{13}C NMR (100 MHz, CDCl$_3$) δ 153.17, 115.35, 68.62, 31.61, 29.36, 25.73, 22.60, 14.03.

Figure S6. ^{1}H and ^{13}C NMR spectra of **S5**. ^{1}H NMR (400 MHz, CDCl$_3$) δ 7.11 (d, J = 2.8 Hz, 1H), 6.79 (m, 2H), 3.95 (t, J = 6.8 Hz, 2H), 3.88 (t, J = 6.8 Hz, 2H), 1.77 (m, 4H), 1.83-1.31 (br, 12H), 0.91 (m, 6H). *residual H$_2$O ^{13}C NMR (100 MHz, CDCl$_3$) δ 153.56, 149.75, 119.45, 114.70, 114.38, 112.77. 70.22, 68.81, 31.55, 29.22, 29.23, 25.67, 22.59, 14.03. Some carbons on the hexyl chains are unresolved.
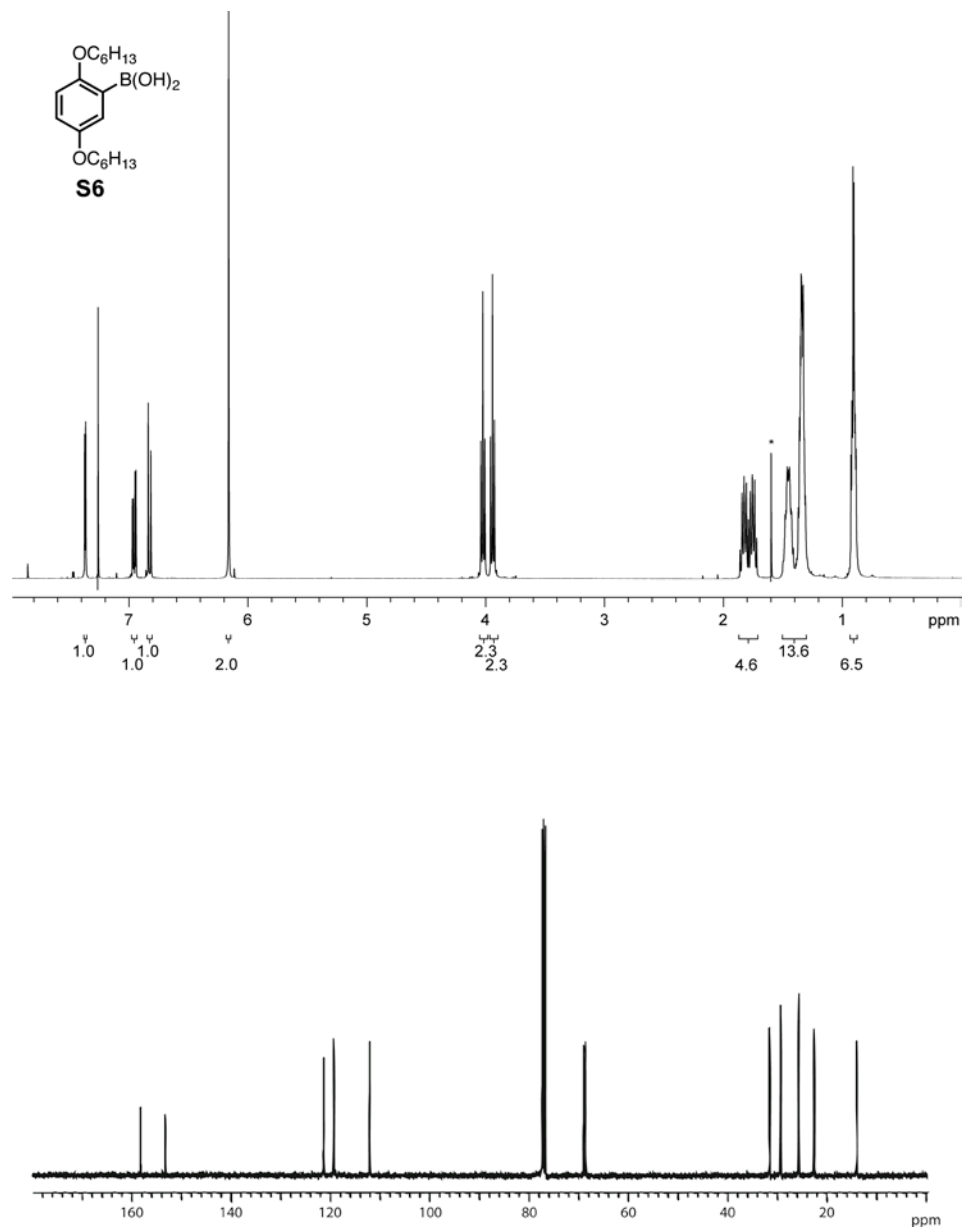
Figure S7. ^{1}H and ^{13}C NMR spectra of **S6**. ^{1}H NMR (400 MHz, CDCl$_3$) δ 7.37 (d, *J* = 3.2 Hz, 1H), 6.96 (dd, *J* = 8.8, 3.2 Hz, 1H), 6.84 (d, *J* = 8.8 Hz, 1H), 6.16 (s, 2H), 4.02 (t, *J* = 6.4 Hz, 2H), 3.94 (t, *J* = 6.8 Hz, 2H), 1.79 (m, 4H), 1.48-1.31 (br, 12H), 0.91 (m, 6H). *residual H$_2$O. ^{13}C NMR (100 MHz, CDCl$_3$) δ 158.22, 153.26, 121.36, 119.29, 112.12, 68.99, 68.61, 31.59, 31.48, 29.26, 29.29, 25.71, 25.69, 22.60, 22.51, 14.03, 13.97. C *ipso* to B is not observed.

210
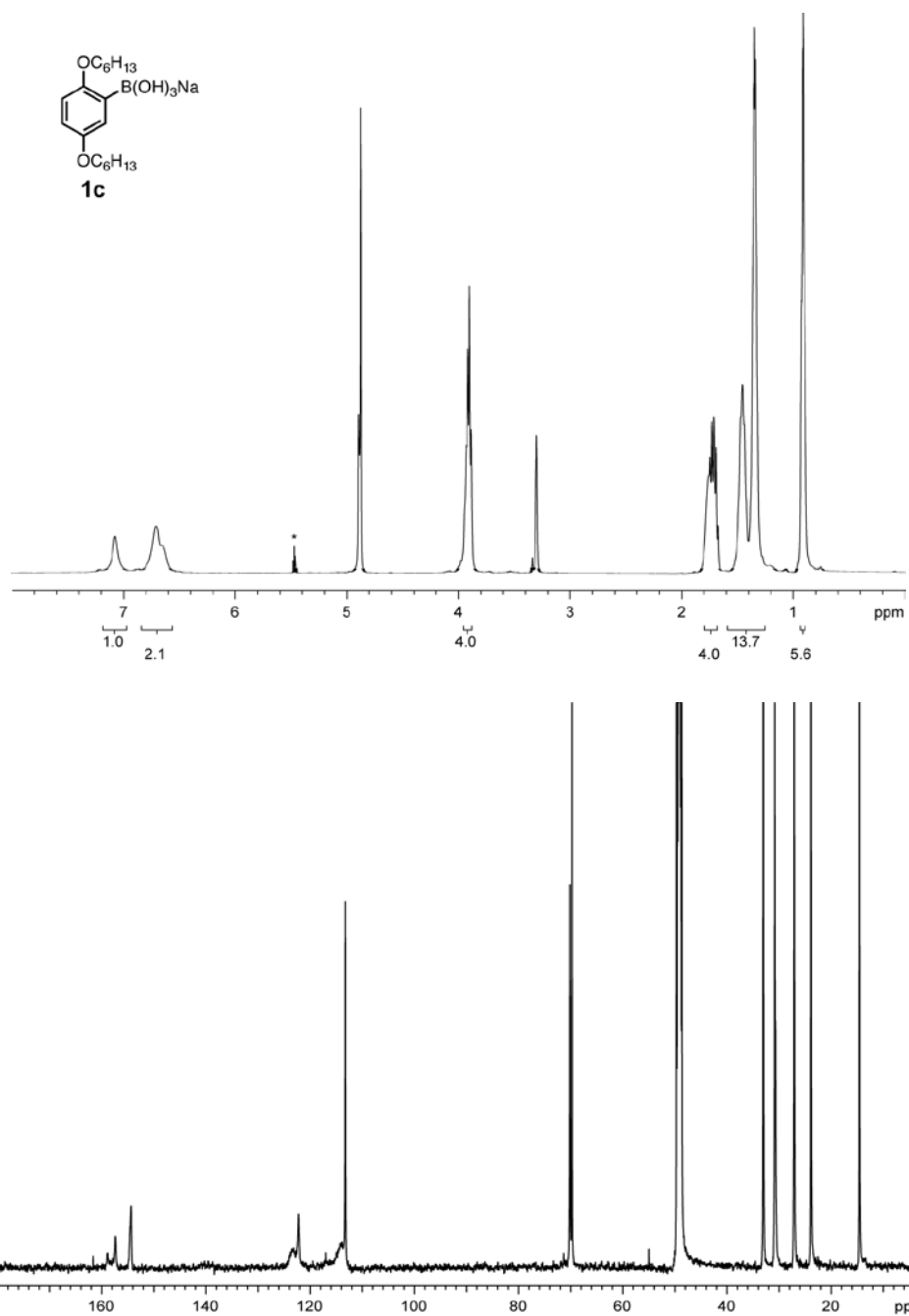
Figure S8. ^{1}H and ^{13}C NMR spectra of **1c.** ^{1}H NMR (400 MHz, CD$_3$OD) δ 7.08 (br, 1H), 6.71-6.65 (br, 2H), 3.90 (m, 2H), 1.71 (m, 4H), 1.47-1.34 (br, 12H), 0.91 (m, 6H). *residual CH$_2$Cl$_2$ ^{13}C NMR (125 MHz, CD$_3$OD) δ 157.42, 154.35, 123.16, 122.21, 113.95, 113.23, 70.13, 69.73, 33.05, 33.00, 30.82, 27.09, 23.87, 14.58. Some carbons on the hexyl chains are unresolved.

Figure S9. ^{1}H and ^{13}C NMR spectra of **S7**. ^{1}H NMR (400 MHz, CDCl$_3$) δ 6.82 (s, 4H), 3.90 (t, J = 6.8 Hz, 4H), 1.75 (m, 4H), 1.46-1.28 (br, 16H), 0.90 (m, 6H). *residual H$_2$O ^{13}C NMR (100 MHz, CDCl$_3$) δ 153.19, 115.37, 68.64, 31.79, 29.40, 29.08. 26.02, 22.60, 14.08.
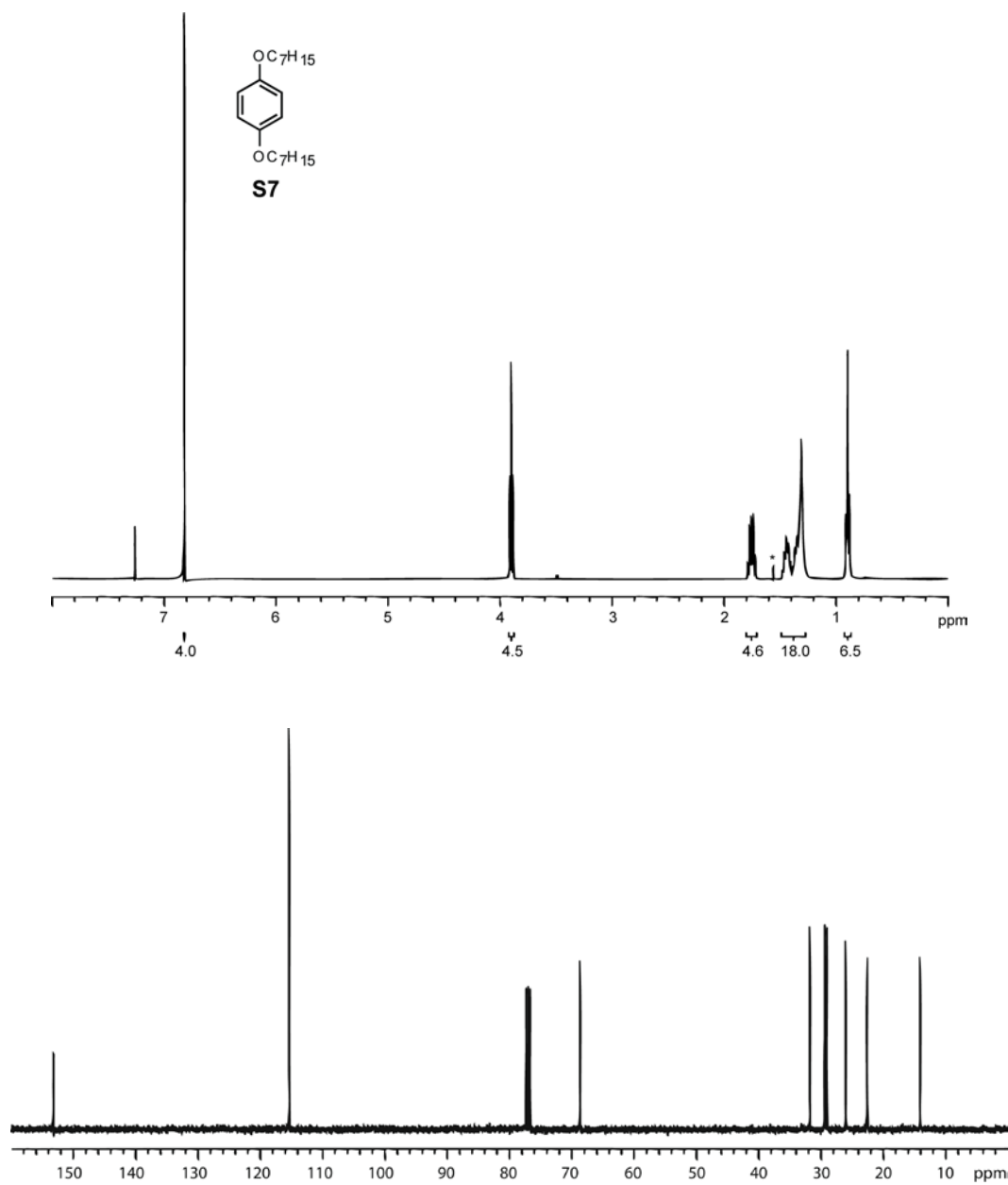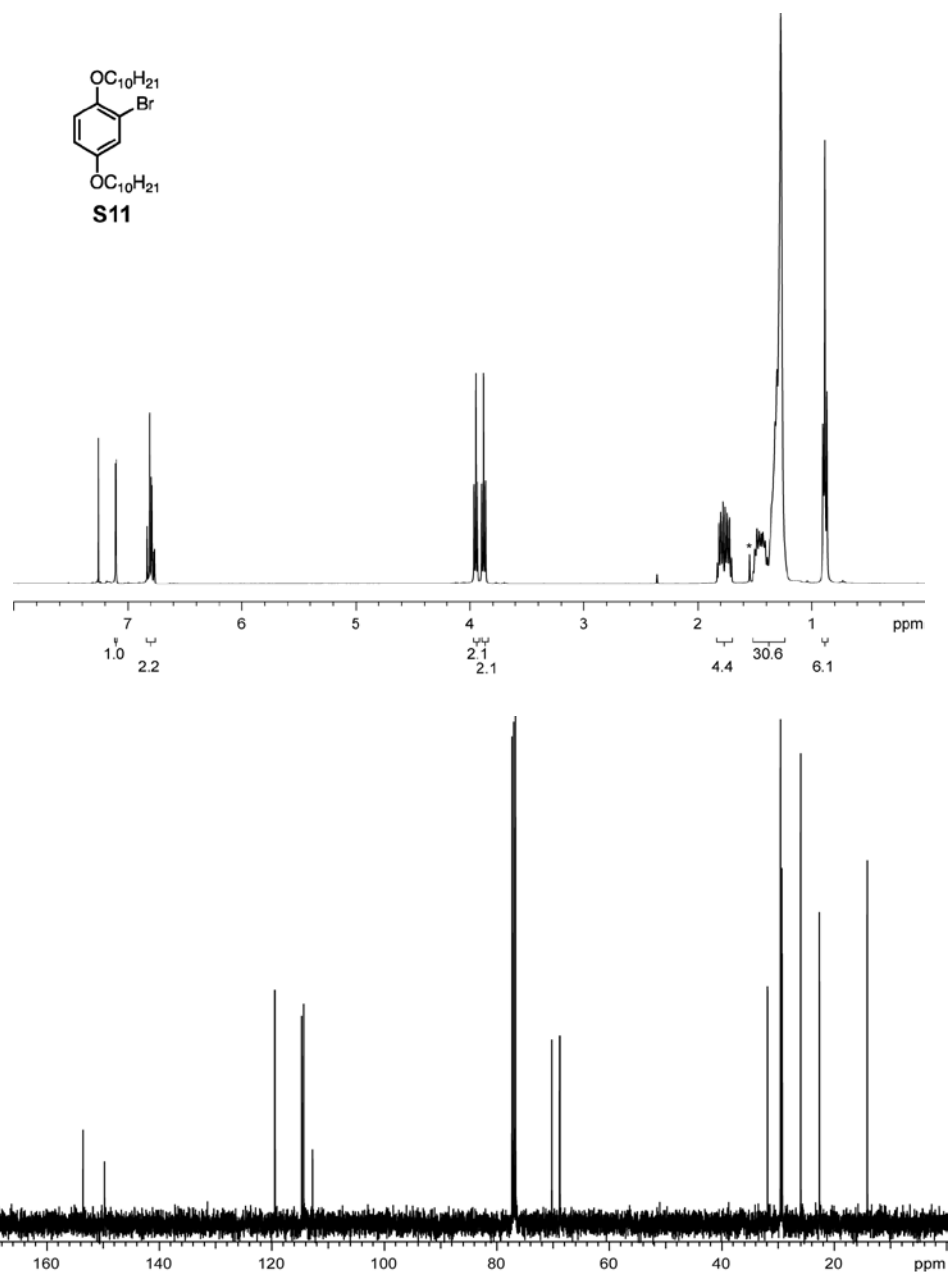
Figure S10. ^{1}H and ^{13}C NMR spectra of **S8**. ^{1}H NMR (400 MHz, CDCl$_3$) δ 7.11 (d, J = 2.8 Hz, 1H), 6.79 (m, 2H), 3.95 (t, J = 6.4 Hz, 2H), 3.88 (t, J = 6.4 Hz, 2H), 1.76 (m, 4H), 1.49-1.30 (br, 16H), 0.91 (m, 6H) *residual H$_2$O. ^{13}C NMR (100 MHz, CDCl$_3$) δ 153.56, 149.75, 119.45, 114.69, 114.35, 112.77. 70.20, 68.79, 31.77, 31.76, 29.27, 29.25, 29.03. 25.96, 22.59, 14.07, 14.06. Some carbons on the heptyl chains are unresolved.
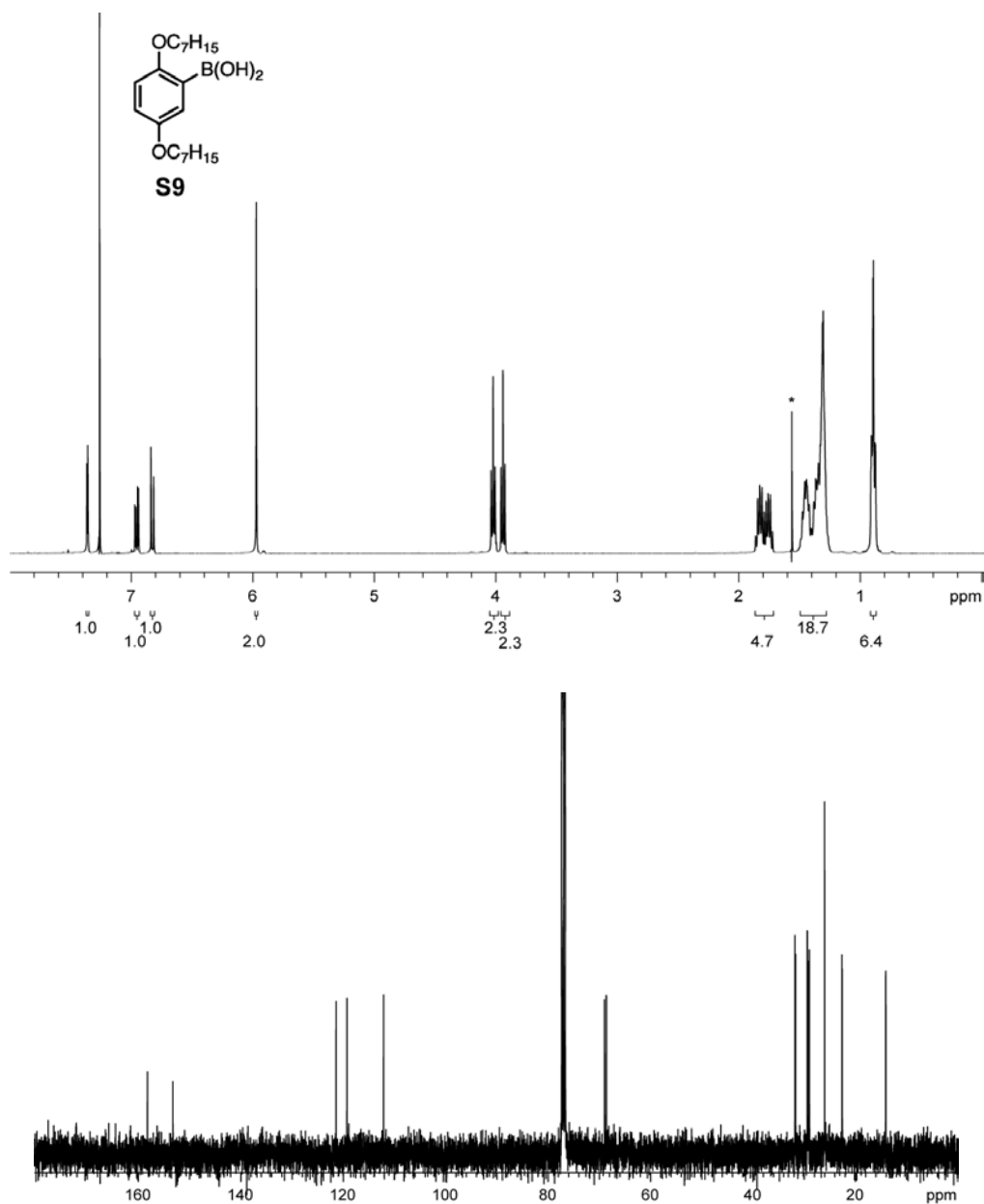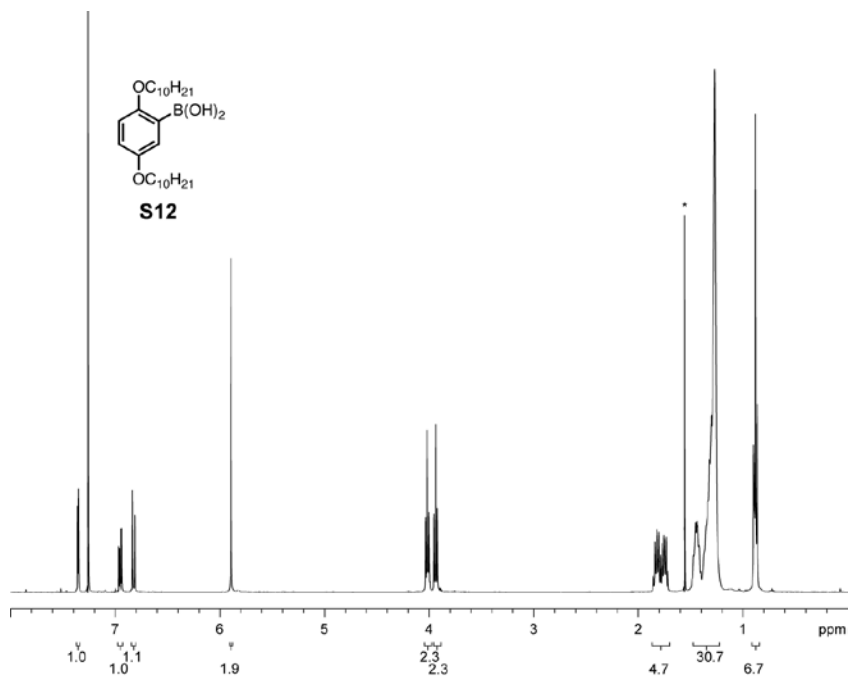
Figure S11. ^{1}H and ^{13}C NMR spectra of **S9**. ^{1}H NMR (400 MHz, CDCl$_3$) δ 7.36 (d, J = 3.2 Hz, 1H), 6.96 (dd, J = 8.8, 3.2 Hz, 1H), 6.84 (d, J = 8.8 Hz, 1H), 5.97 (s, 2H), 4.02 (t, J = 6.8 Hz, 2H), 3.94 (t, J = 6.8 Hz, 2H), 1.77 (m, 4H), 1.48-1.30 (br, 16H), 0.89 (m, 6H). *residual H$_2$O. ^{13}C NMR (100 MHz, CDCl$_3$) δ 158.24, 153.26, 121.39, 119.28, 112.13, 68.99, 68.62, 31.79, 31.68, 29.35, 29.07, 28.99, 26.00, 22.61, 22.56, 14.08, 14.05. C *ipso* to B is not observed, some carbons on the heptyl chains are unresolved.

214
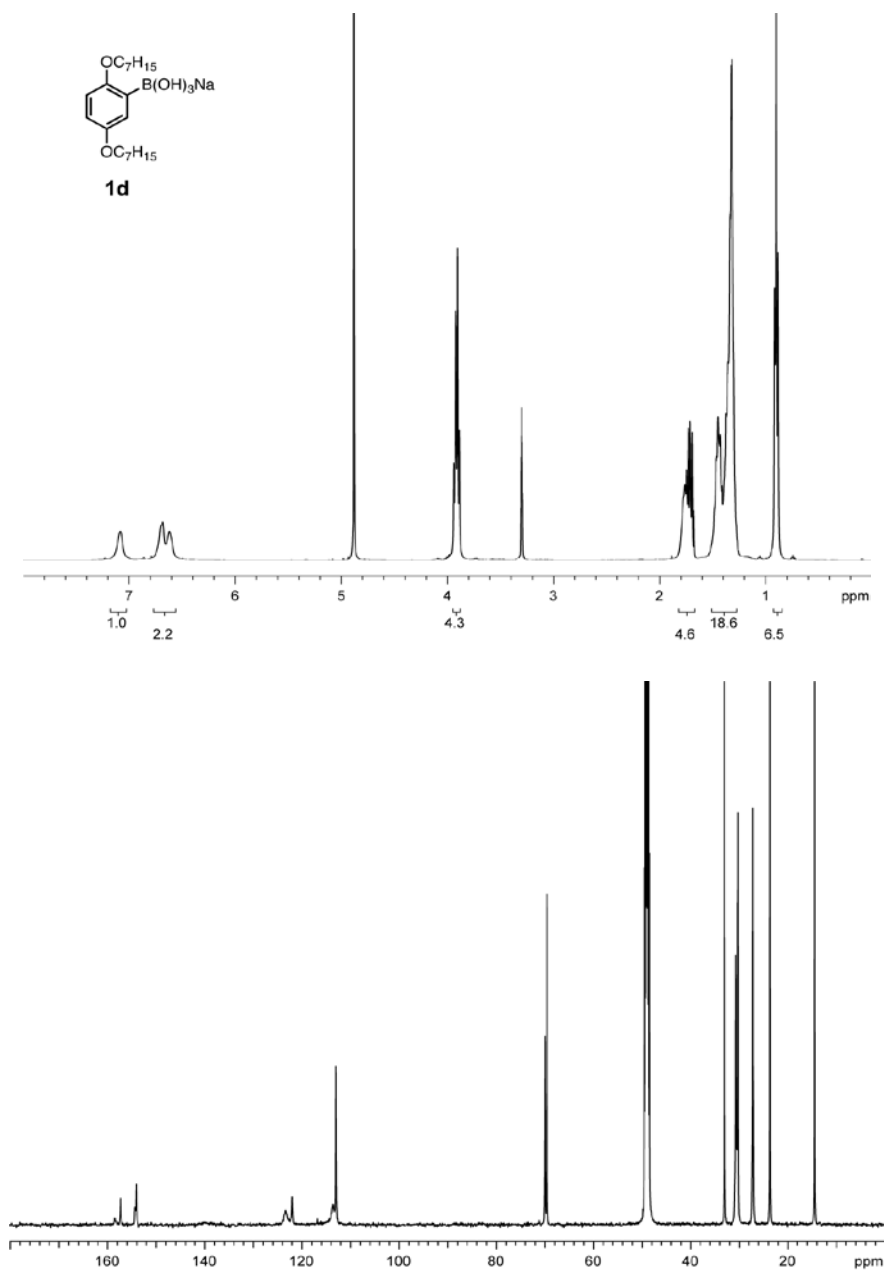
Figure S12. ^1H and ^{13}C NMR spectra of **1d**. ^1H NMR (400 MHz, CD$_3$OD) δ 7.08 (br, 1H), 6.69-6.62 (br, 2H), 3.94 (m, 4H), 1.71 (m, 4H), 1.47-1.27 (br, 16H), 0.90 (m, 6H). ^{13}C NMR (125 MHz, CD$_3$OD) δ 157.33, 154.09, 123.36, 121.97, 113.60, 113.02, 69.96, 69.55, 33.02, 30.71, 30.52, 30.35, 30.27, 27.21, 23.69, 14.44. Some carbons on the heptyl chains are unresolved.
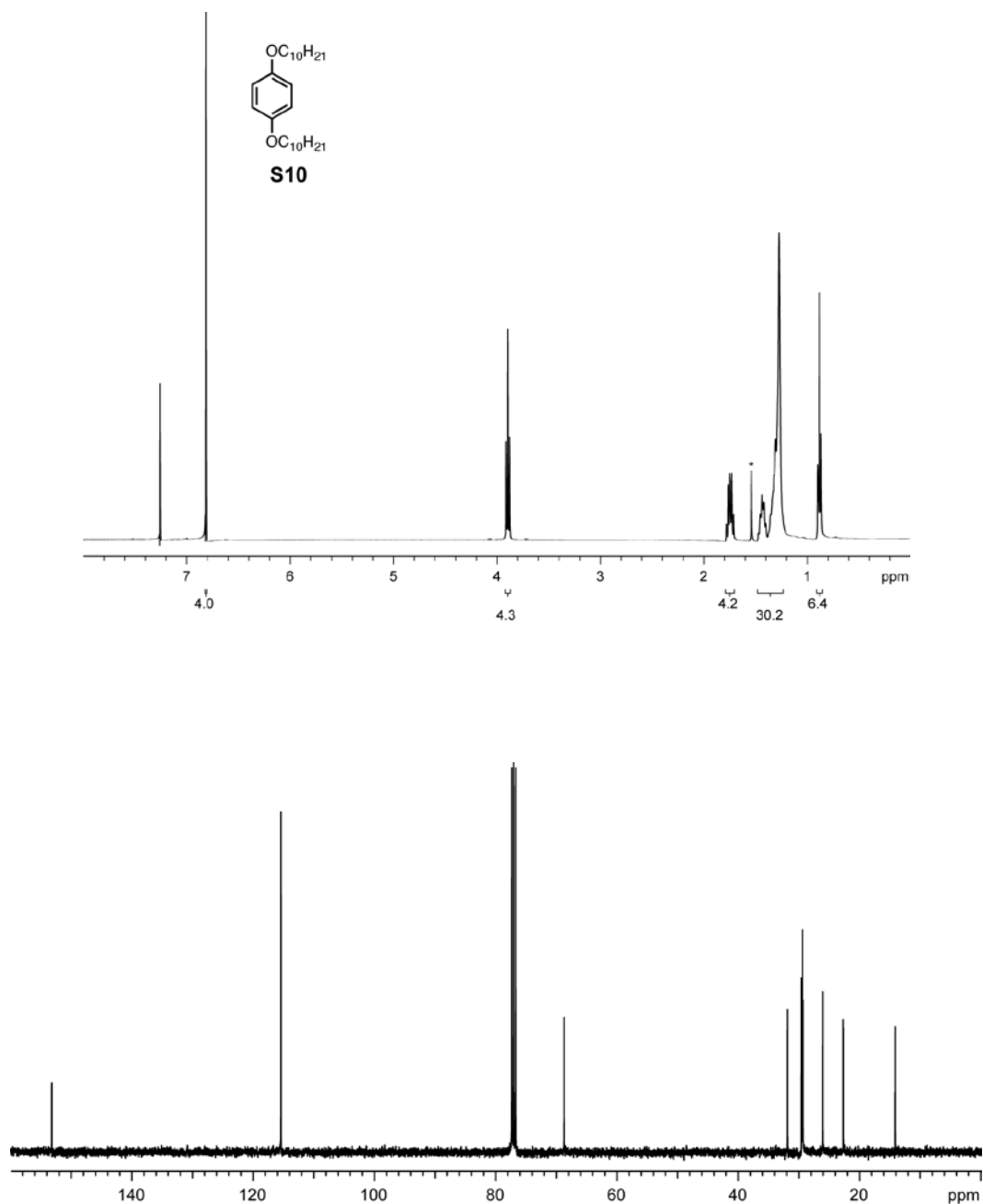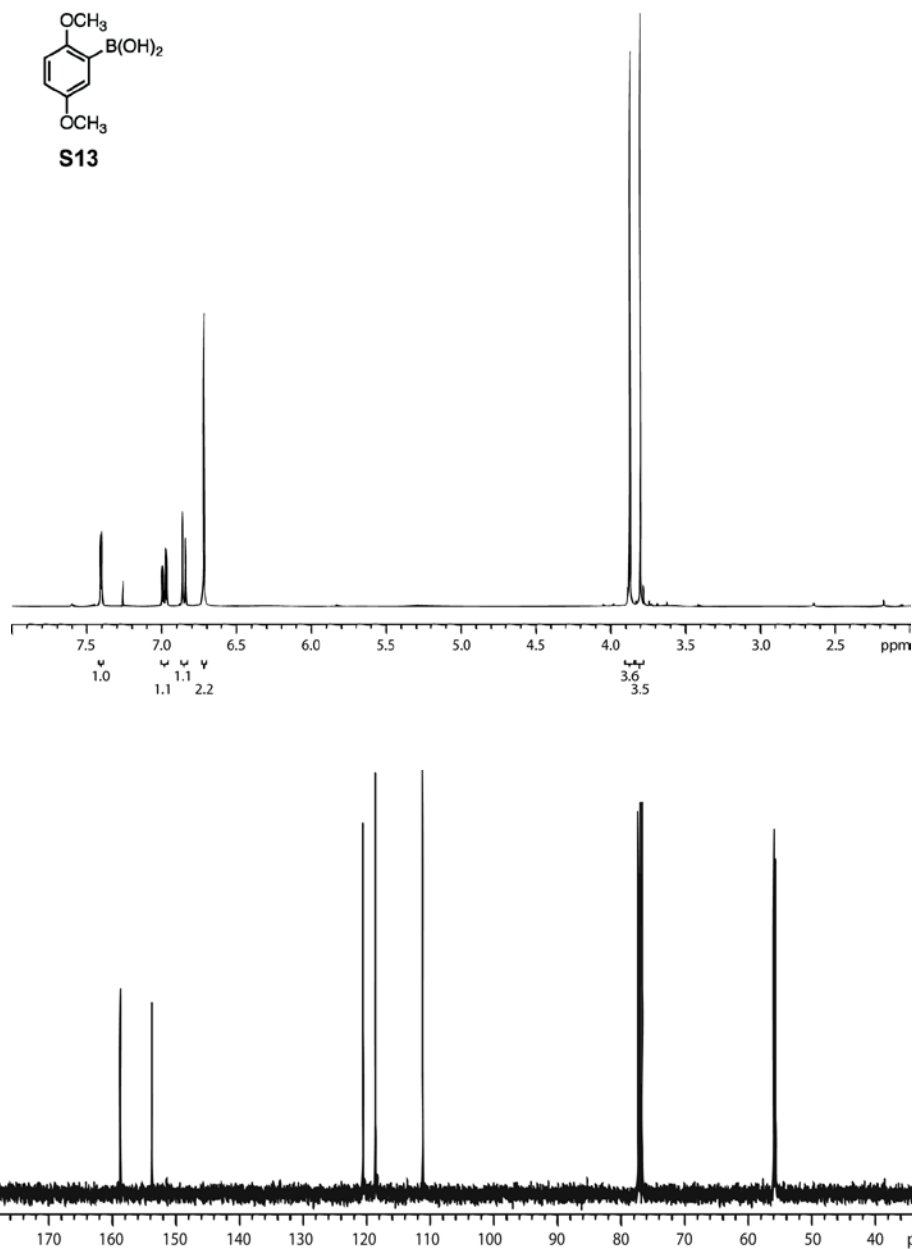
Figure S13. ¹H and ¹³C NMR spectra of **S10**. ¹H NMR (400 MHz, CDCl₃) δ 6.82 (s, 4H), 3.90 (t, *J* = 6.8 Hz, 4H), 1.73 (m, 4H), 1.46-1.27 (m, 28H), 0.88 (t, *J* = 6.4 Hz, 6H). *residual H₂O. ¹³C NMR (100 MHz, CDCl₃) δ 153.21, 115.40, 68.68, 31.89, 29.57, 29.55, 29.41, 29.31, 26.06, 22.67, 14.09. Some carbons on the decyl chains are unresolved.

Figure S14. ^{1}H and ^{13}C NMR spectra of **S11**. ^{1}H NMR (400 MHz, CDCl$_3$) δ 7.11 (d, J = 2.8 Hz, 1H), 6.81 (m, 2H), 3.95 (t, J = 6.4 Hz, 2H), 3.88 (t, J = 6.4 Hz, 2H), 1.76 (m, 4H), 1.49-1.27 (br, 28H), 0.88 (m, 6H). *residual H$_2$O ^{13}C NMR (100 MHz, CDCl$_3$) δ 153.56, 149.75, 119.45, 114.69, 114.36, 112.76, 70.21, 68.81, 31.90, 29.56, 29.54, 29.35, 29.32, 29.26, 29.25, 25.98, 22.68, 14.11. Some carbons on the decyl chains are unresolved.
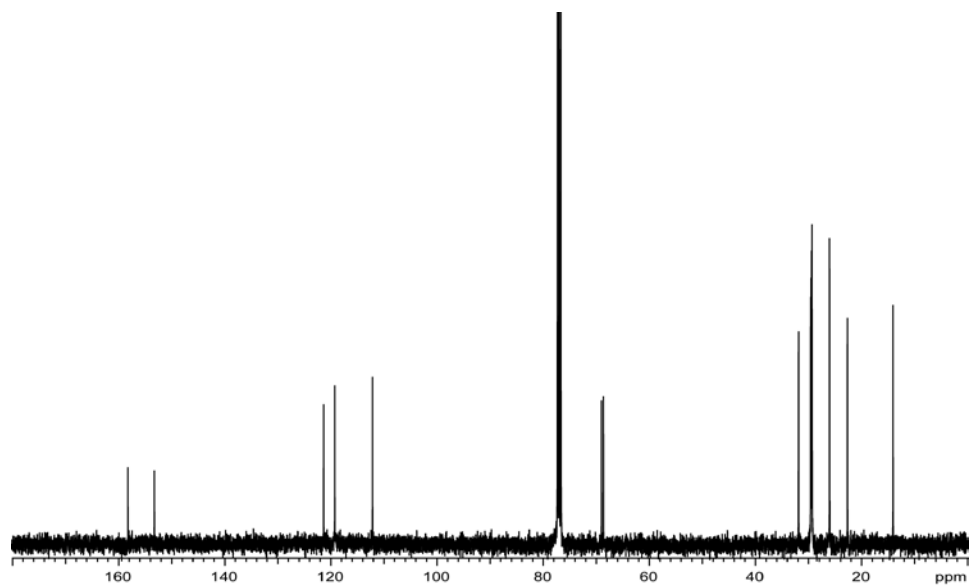
Figure S15. ^{1}H and ^{13}C NMR spectra of **S12**. ^{1}H NMR (400 MHz, CDCl$_3$) δ 7.36 (d, J = 3.2 Hz, 1H), 6.97 (dd, J = 8.8, 3.2 Hz, 1H), 6.84 (d, J = 8.8 Hz, 1H), 5.90 (s, 2H), 4.02 (t, J = 6.8 Hz, 2H), 3.94 (t, J = 6.8 Hz, 2H), 1.78 (m, 4H), 1.45-1.27 (br, 28H), 0.88 (m, 6H). *residual H$_2$O ^{13}C NMR (100 MHz, CDCl$_3$) δ 158.22, 153.25, 121.38, 119.26, 112.11, 68.98, 68.61, 31.89, 31.87, 29.55, 29.50, 29.40, 29.34, 29.32, 29.28, 26.04, 22.67, 14.10. C *ipso* to B is not observed, some carbons on the decyl chains are unresolved.
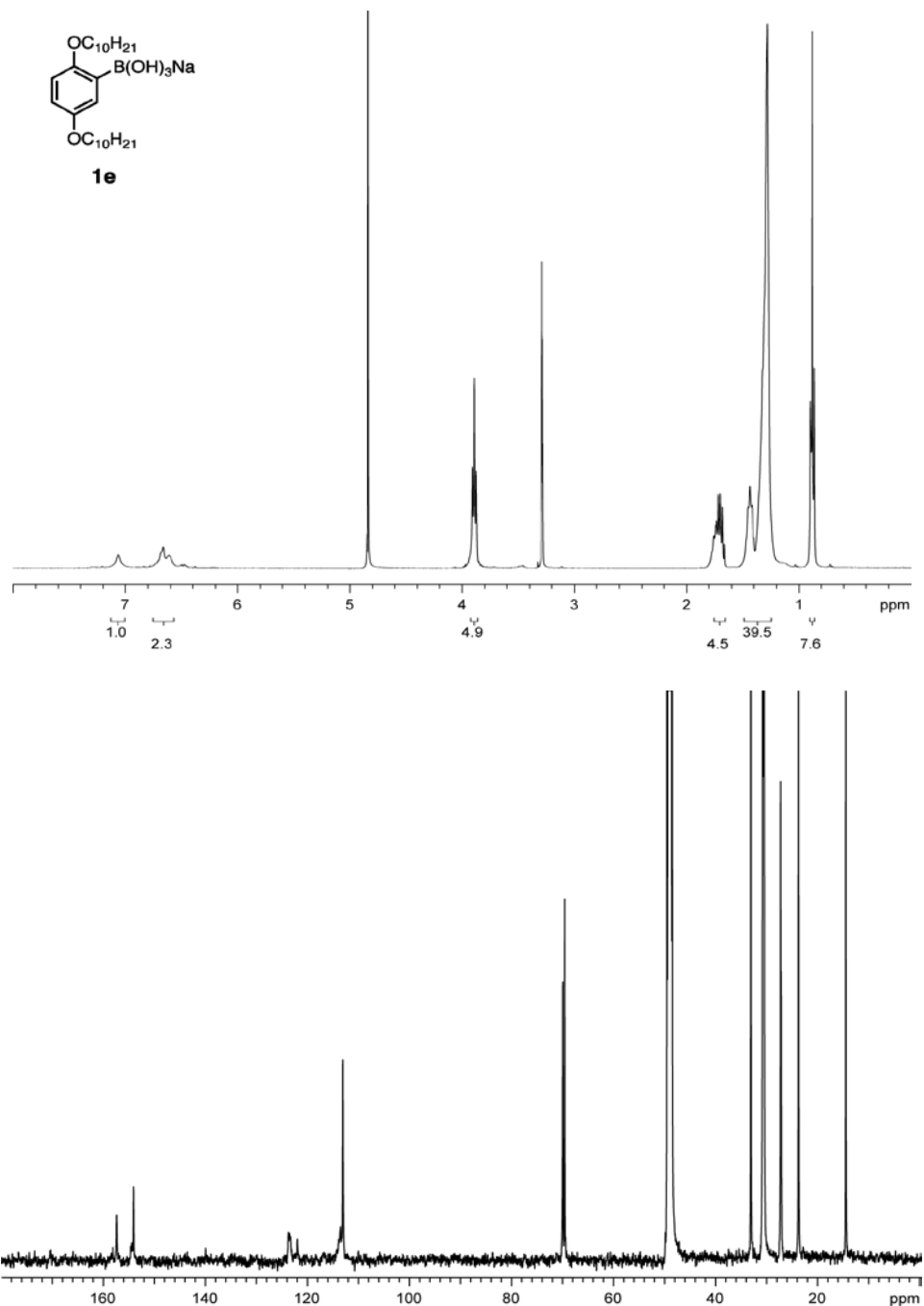
Figure S16. ^{1}H and ^{13}C NMR spectra of **1e**. ^{1}H NMR (400 MHz, CDCl$_3$) δ 7.08 (br, 1H), 6.98-6.63 (br, 2H), 3.91 (t, J = 6.4 Hz, 4H), 1.73 (m, 4H), 1.46-1.29 (br, 28H), 0.89 (m, 6H). ^{13}C NMR (125 MHz, CDCl$_3$) δ 157.39, 154.07, 123.72, 121.96, 113.51, 113.05, 69.94, 69.56, 33.07, 30.71, 30.58, 30.48, 27.24, 27.14, 23.74, 14.45. Some carbons on the decyl chains are unresolved.

Figure S17. ^{1}H and ^{13}C NMR spectra of **S13**. ^{1}H NMR (400 MHz, CDCl$_3$) δ 7.41 (d, J = 3.2 Hz, 1H), 7.00-6.97 (dd, J = 8.8, 3.2 Hz, 1H), 6.86 (d, J = 8.8 Hz, 1H), 6.72 (s, 2H), 3.87 (s, 3H), 3.81 (s, 3H). ^{13}C NMR (100 MHz, CDCl$_3$) δ 158.76, 153.78, 120.58, 118.61, 111.21, 55.97, 55.70.*C *ipso* to B not observed.
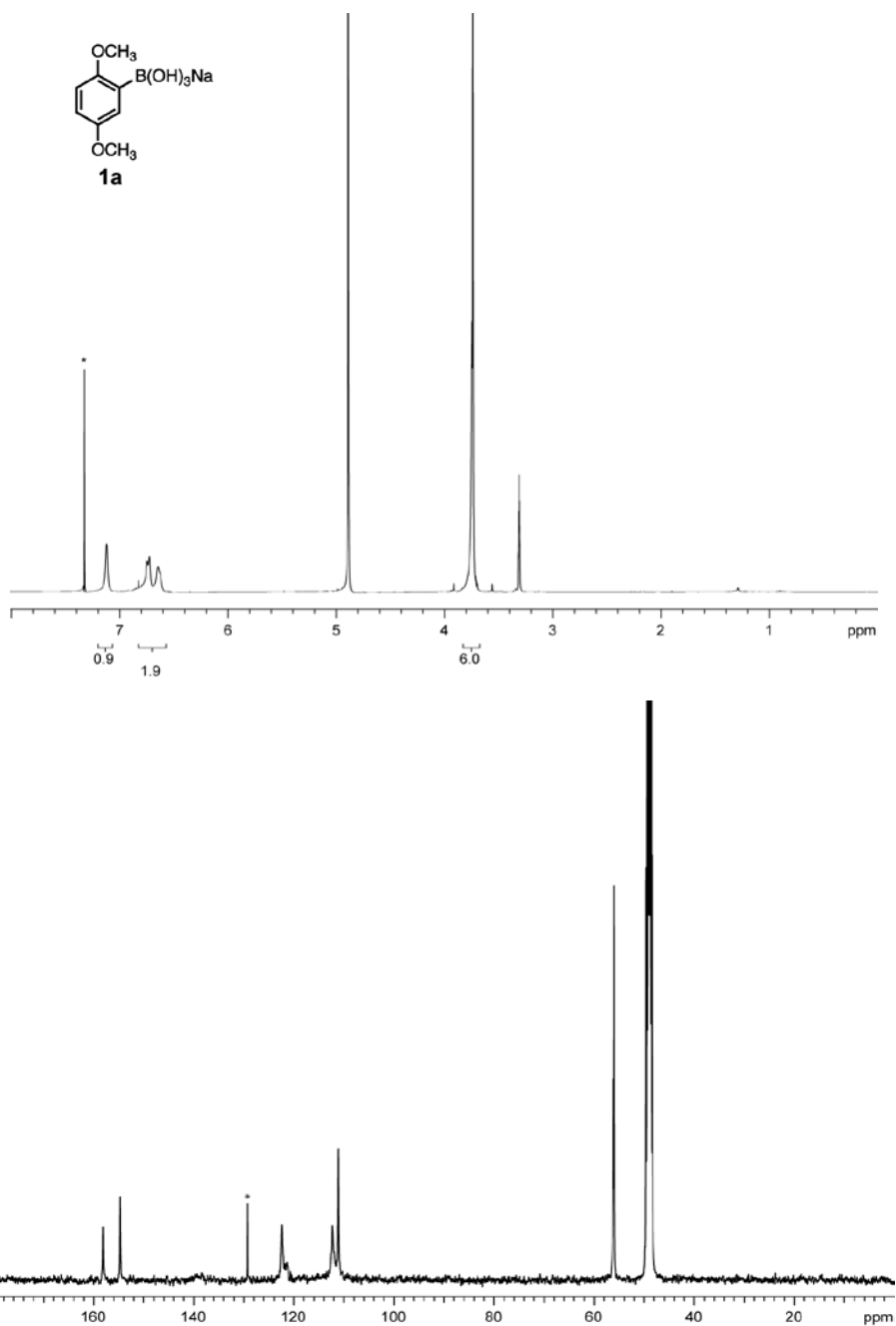
Figure S18. ^{1}H and ^{13}C NMR spectra of **1a**. ^{1}H NMR (400 MHz, CD$_3$OD) δ 7.12 (br, 1H), 6.74-6.65 (br, 2H) 3.74 (br, 6H) ^{13}C NMR (125 MHz, CD$_3$OD) δ 158.07, 154.71, 122.38, 112.27, 111.14, 56.14, 55.97. *residual benzene, C *ipso* to B is not observed.
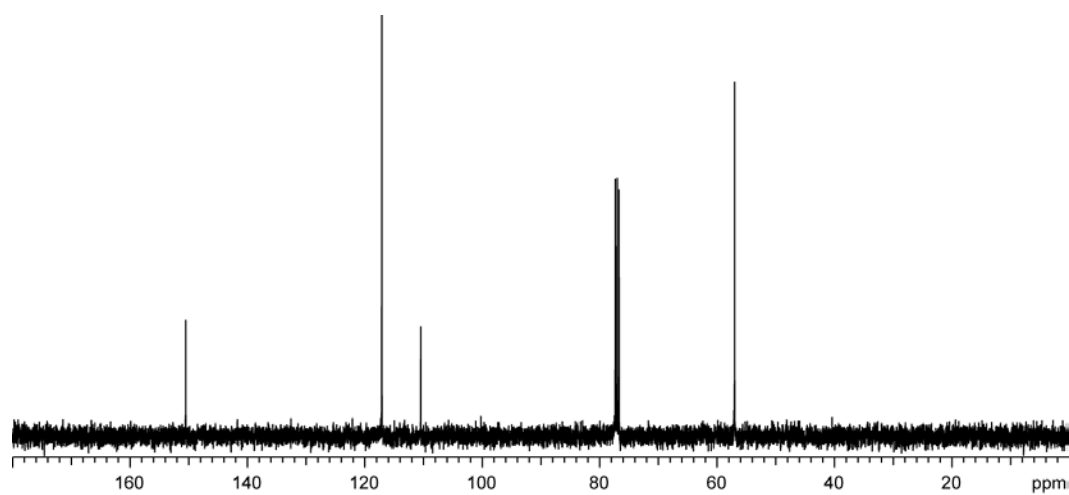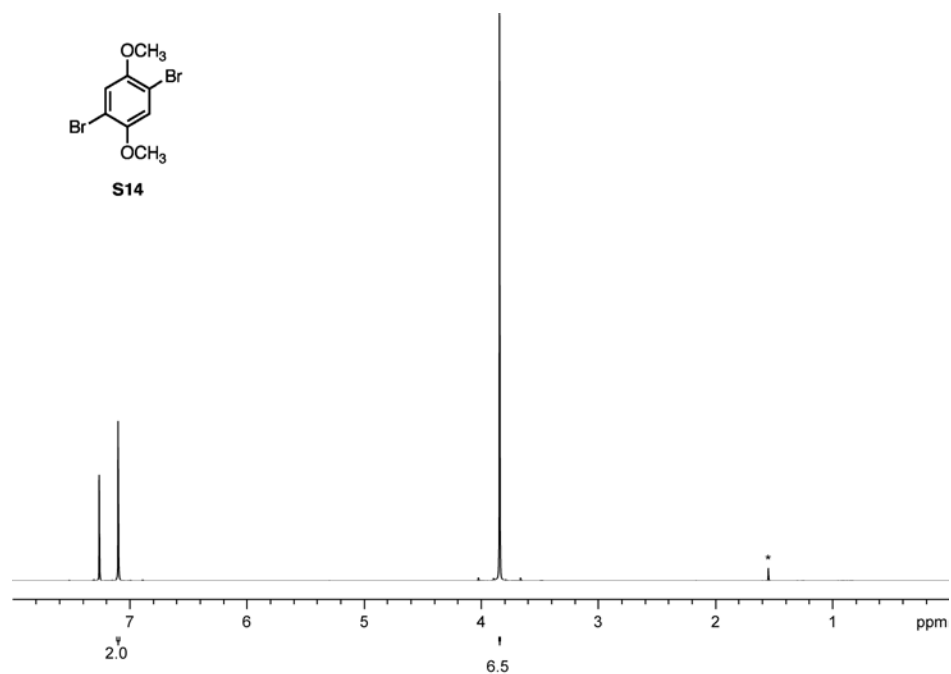
Figure S19. ¹H and ¹³C NMR spectra of **S14**. ¹H NMR (400 MHz, CDCl₃) δ 7.10 (s, 2H), 3.84 (s, 6H). *residual H₂O ¹³C NMR (100 MHz, CDCl₃) δ 150.50, 117.11, 110.47, 57.00.
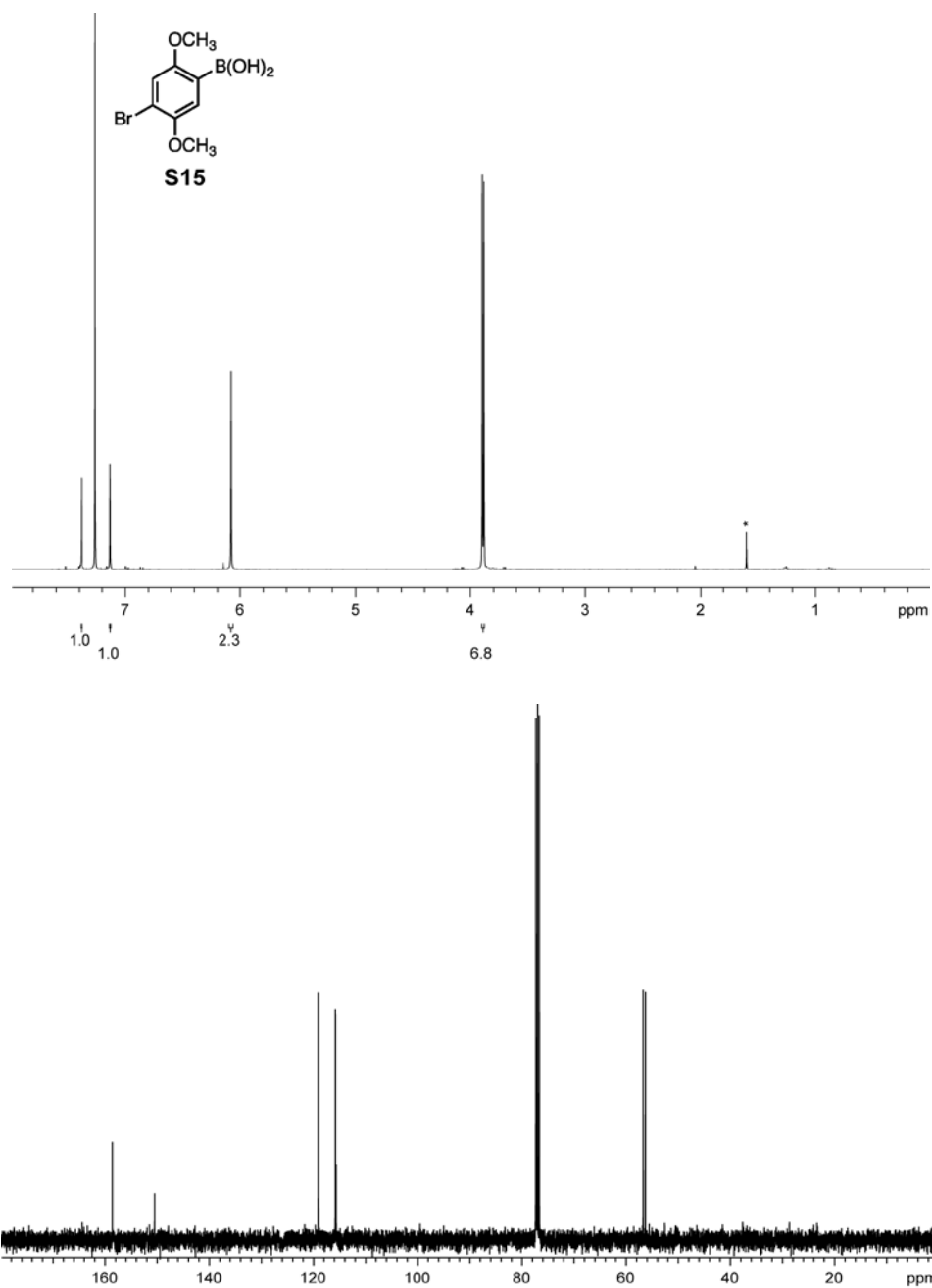
Figure S20. ^{1}H and ^{13}C NMR spectra of **S15**. ^{1}H NMR (400 MHz, CDCl$_3$) δ 7.38 (s, 1H), 7.13 (s, 1H), 6.08 (s, 2H), 3.89 (s, 3H), 3.88 (s, 3H). *residual H$_2$O. ^{13}C NMR (100 MHz, CDCl$_3$) δ 158.59, 150.49, 119.07, 115.97, 115.65, 56.72, 56.28. C *ipso* to B is not observed.
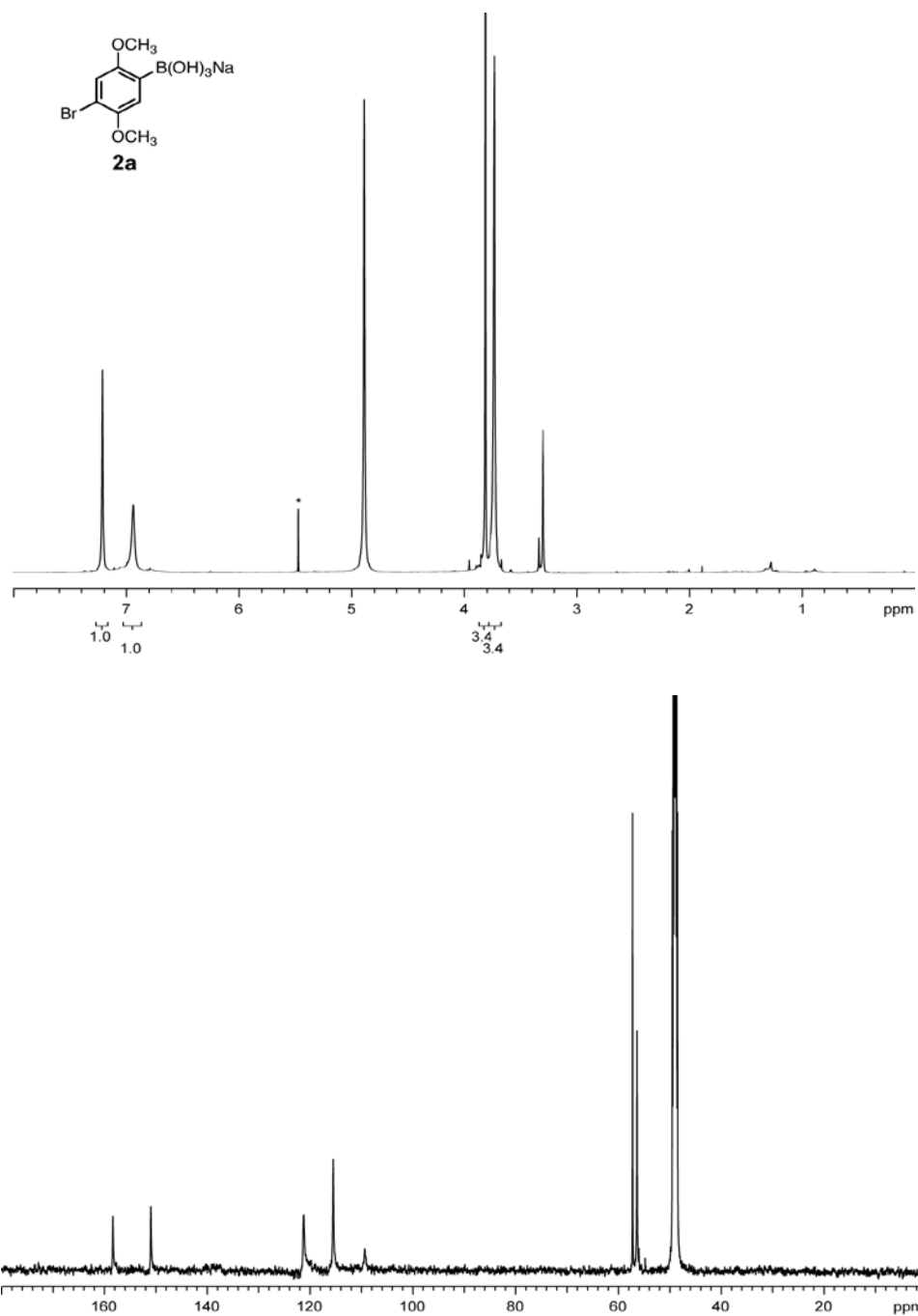
Figure S21. ^{1}H and ^{13}C NMR spectra of **2a**. ^{1}H NMR (500 MHz, CD$_3$OD) δ 7.22 (br, 1H), 6.94 (br, 1H) 3.81 (br, 3H), 3.73 (br, 3H). *residual CH$_2$Cl$_2$. ^{13}C NMR (125 MHz, CD$_3$OD) δ 159.34, 150.96, 121.23, 115.49, 109.35, 57.25, 56.38. C *ipso* to B is not observed.
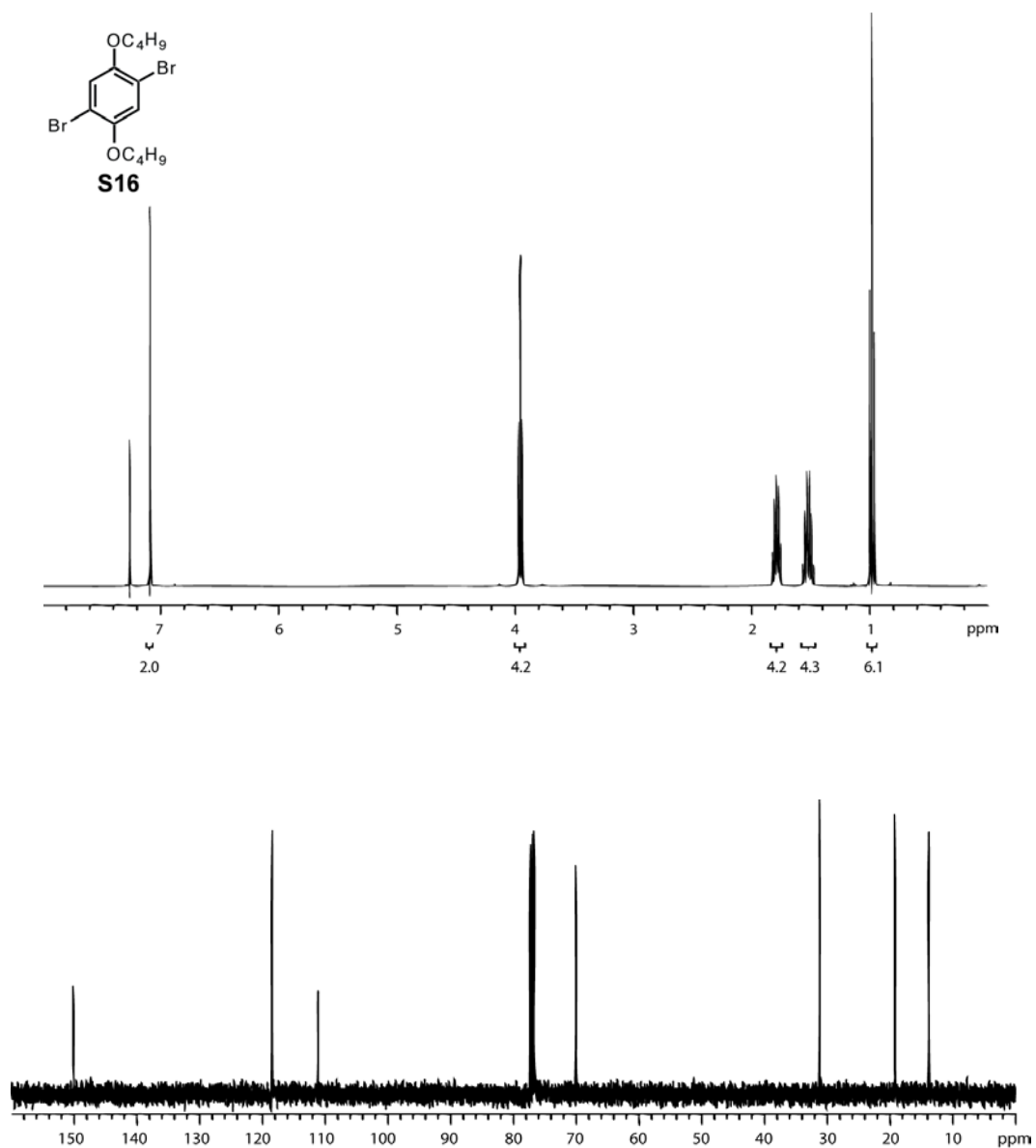
Figure S22. ^{1}H and ^{13}C NMR spectra of **S16**. ^{1}H NMR (400 MHz, CDCl$_3$) δ 7.08 (s, 2H), 3.96 (t, J = 6.8 Hz, 4H), 1.80 (m, 4H), 1.53 (m, 4H), 0.98 (m, 6H). ^{13}C NMR (100 MHz, CDCl$_3$) δ 150.09, 118.47, 111.13, 70.00, 31.19, 19.19, 13.81.
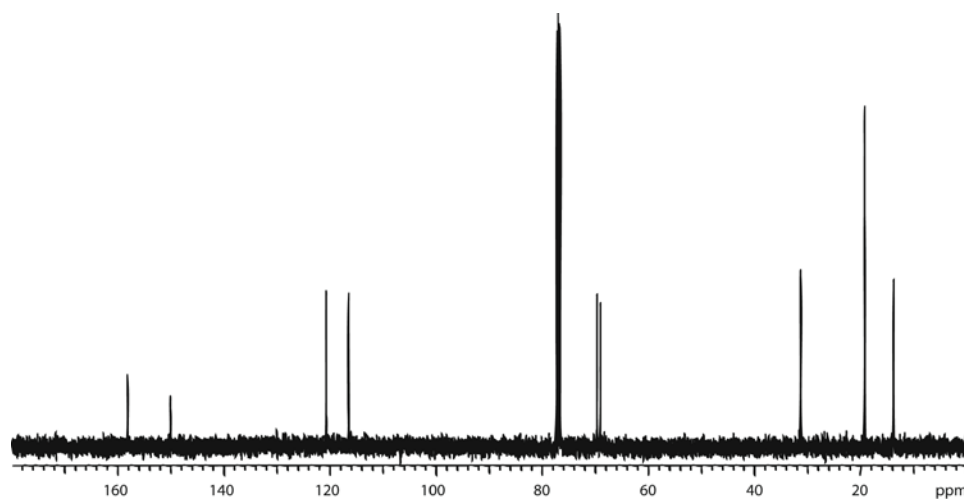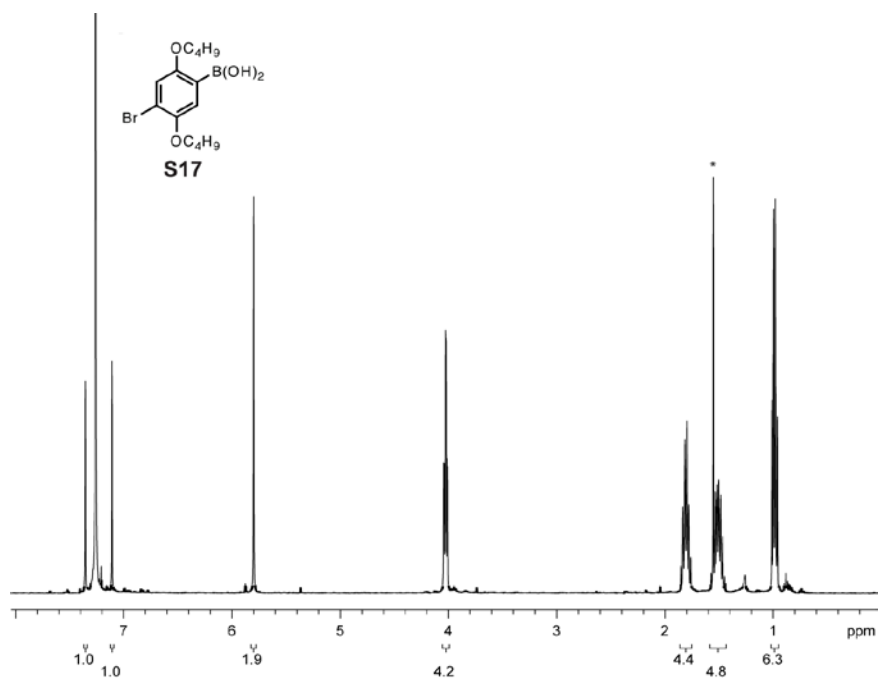
Figure S23. ^{1}H and ^{13}C NMR spectra of **S17**. ^{1}H NMR (400 MHz, CDCl$_3$) δ 7.37 (s,1H), 7.10 (s, 1H), 5.80 (s, 2H), 4.02 (m, 4H), 1.80 (m, 4H), 1.0 (m, 4H), 0.98 (m, 6H). * residual H$_2$O ^{13}C NMR (100 MHz, CDCl$_3$) δ 158.10, 150.06, 120.70, 116.56, 116.45, 69.67, 69.04, 31.34, 31.23, 19.22, 13.85, 13.76. C *ipso* to B is not observed, some carbons on the butyl chains are unresolved.
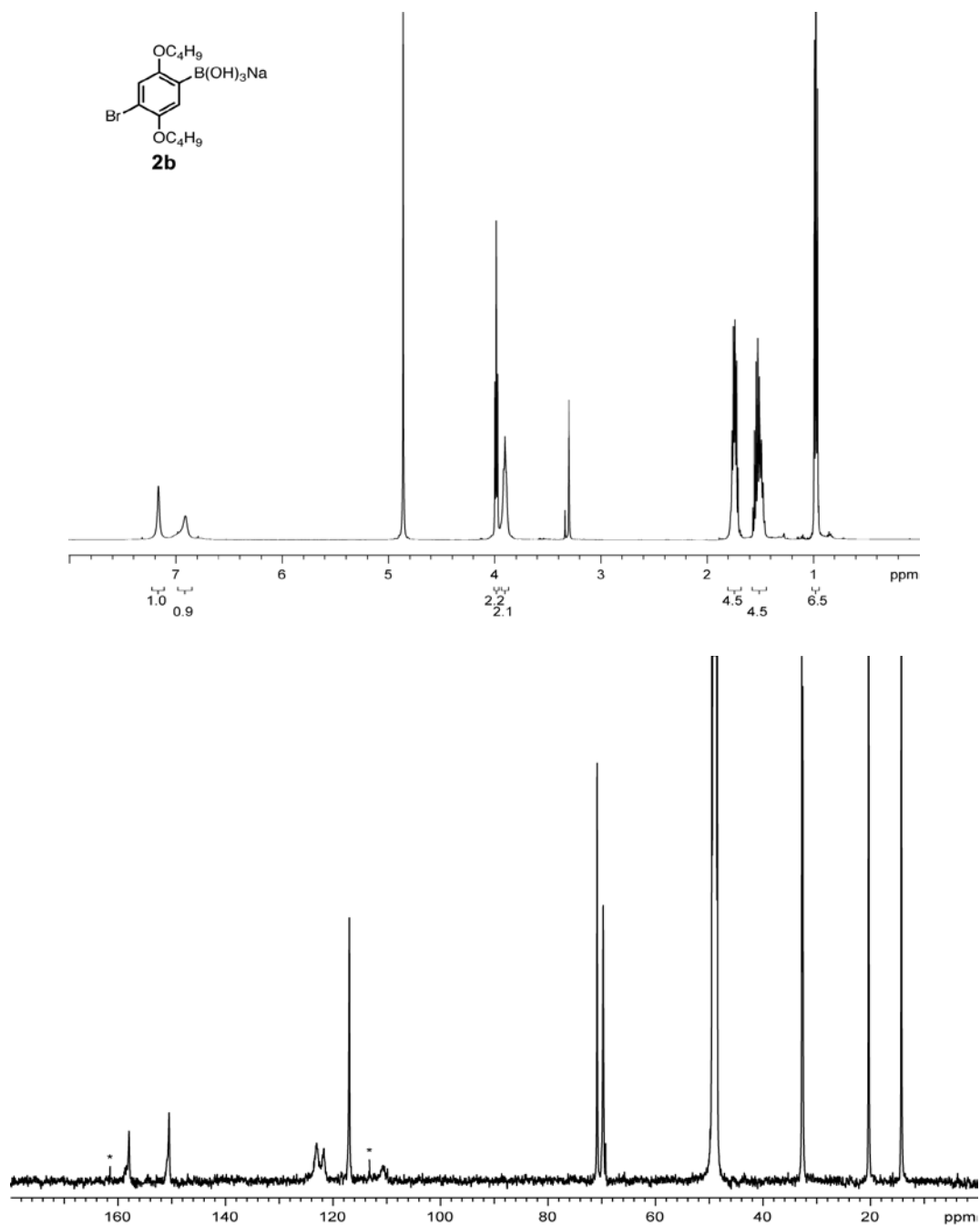
Figure S24. ^{1}H and ^{13}C NMR spectra of **2b.** ^{1}H NMR (400 MHz, CD$_3$OD) δ 7.17 (br, 1H), 6.91 (br, 1H), 3.99 (m, 2H), 3.92-3.89 (br, 2H), 1.74 (m, 4H), 1.52 (m, 4H), 0.98 (m, 6H). ^{13}C NMR (125 MHz, CD$_3$OD) δ 157.95, 150.49, 123.04, 121.67, 116.96, 110.68, 70.85, 69.73, 32.78, 32.59, 20.37, 14.28, 14.23. *trace decomposition product, verified by HPLC. Some carbons on the butyl chains are unresolved.
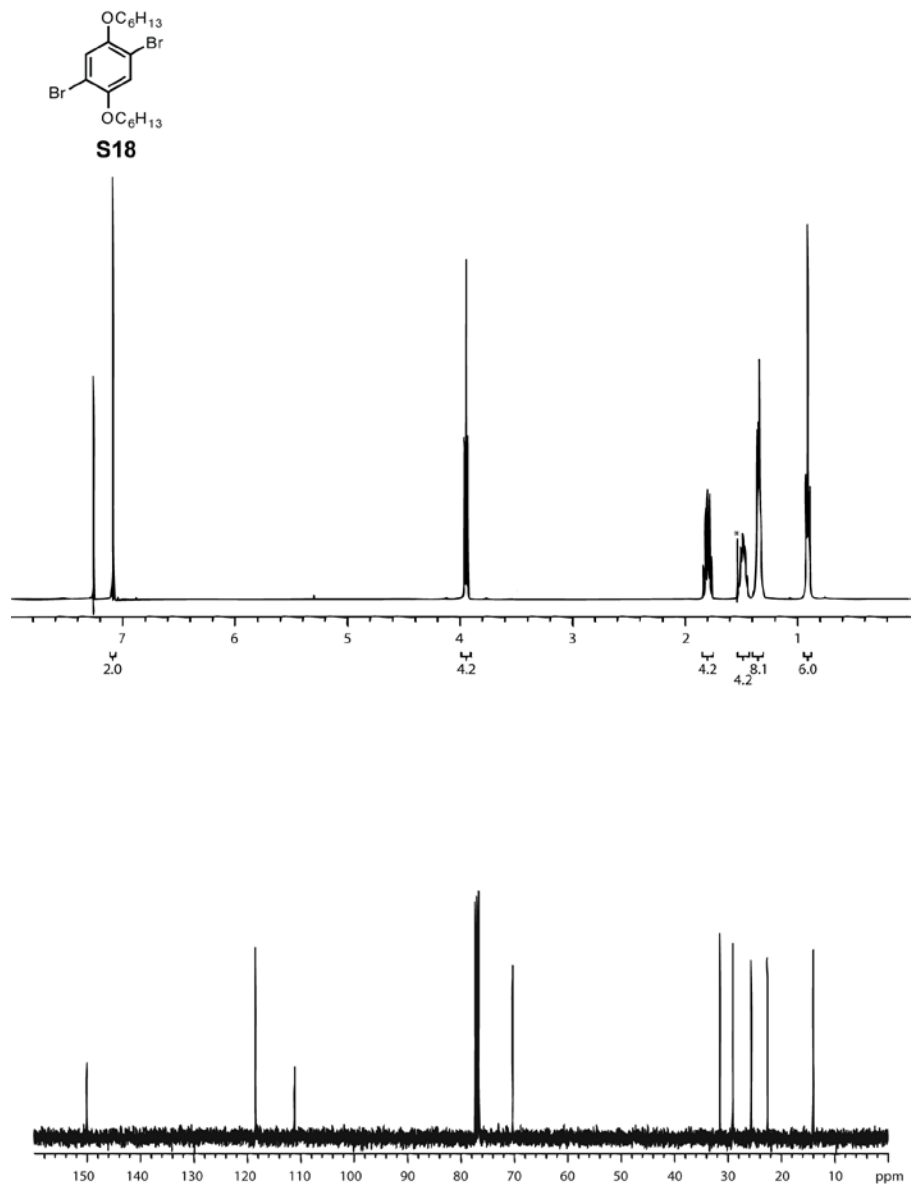
Figure S25. ^{1}H and ^{13}C NMR spectra of **S18**. ^{1}H NMR (400 MHz, CDCl$_3$) δ 7.09 (s, 2H), 3.95 (t, *J* = 6.4 Hz, 4H), 1.80 (m, 4H), 1.49 (m, 4H), 1.35 (m, 8H), 0.91 (m, 6H). *residual H$_2$O. ^{13}C NMR (100 MHz, CDCl$_3$) δ 150.09, 118.49, 111.14, 70.32, 31.47, 29.08, 25.60, 22.56, 14.00.
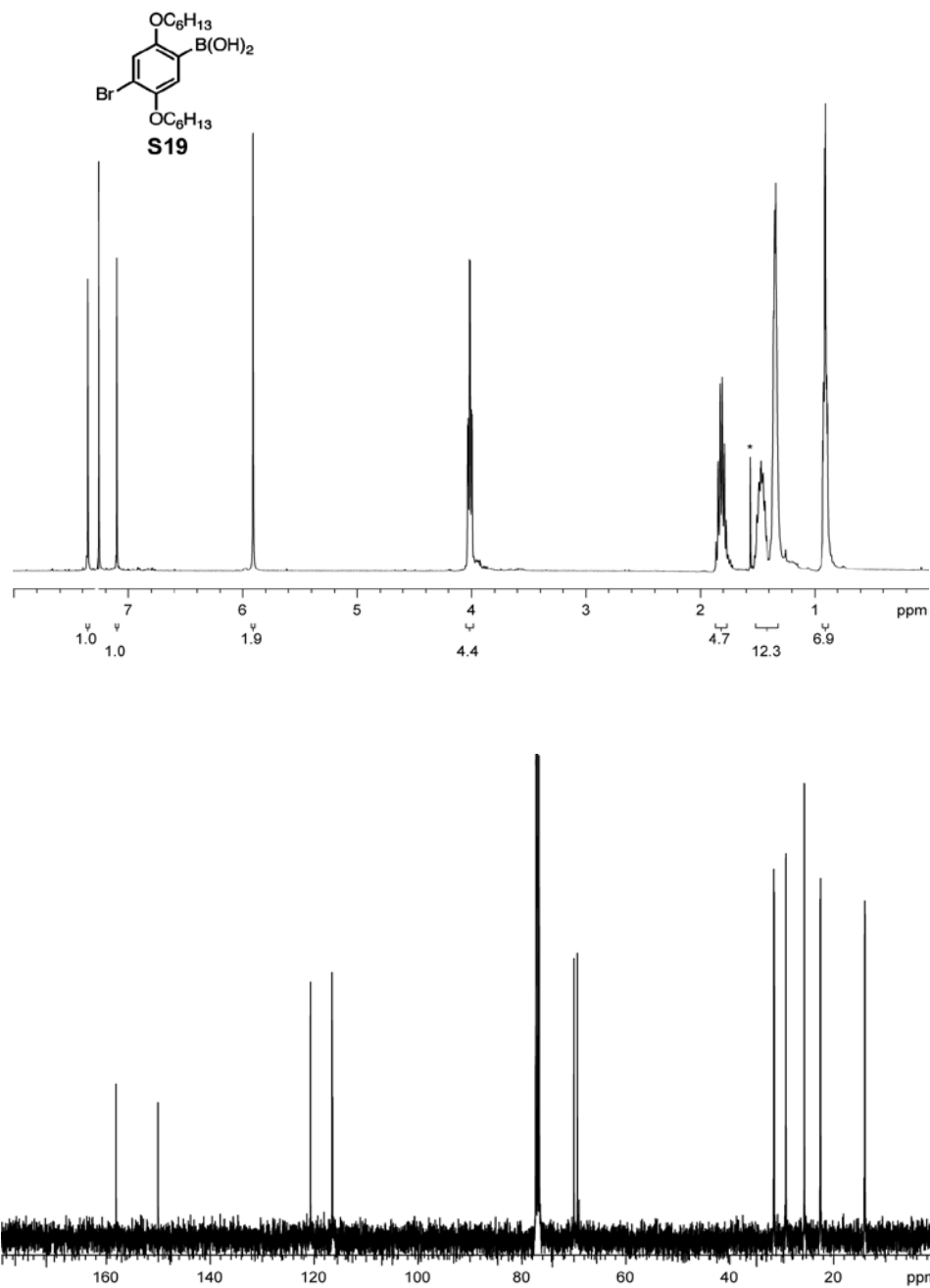
Figure S26. ^{1}H and ^{13}C NMR spectra of **S19**. ^{1}H NMR (400 MHz, CDCl$_3$) δ 7.35 (s, 1H), 7.10 (s, 1H), 5.91 (s, 1H), 4.02 (m, 4H), 1.81 (m, 4H), 1.50-1.34 (br, 12H), 0.91 (m, 6H). *residual H$_2$O ^{13}C NMR (100 MHz, CDCl$_3$) δ 158.11, 150.03, 120.69, 116.54, 69.98, 69.32, 31.52, 31.42, 29.20, 29.17, 25.64, 25.63, 22.58, 22.50, 14.02, 13.95. C *ipso* to B is not observed.
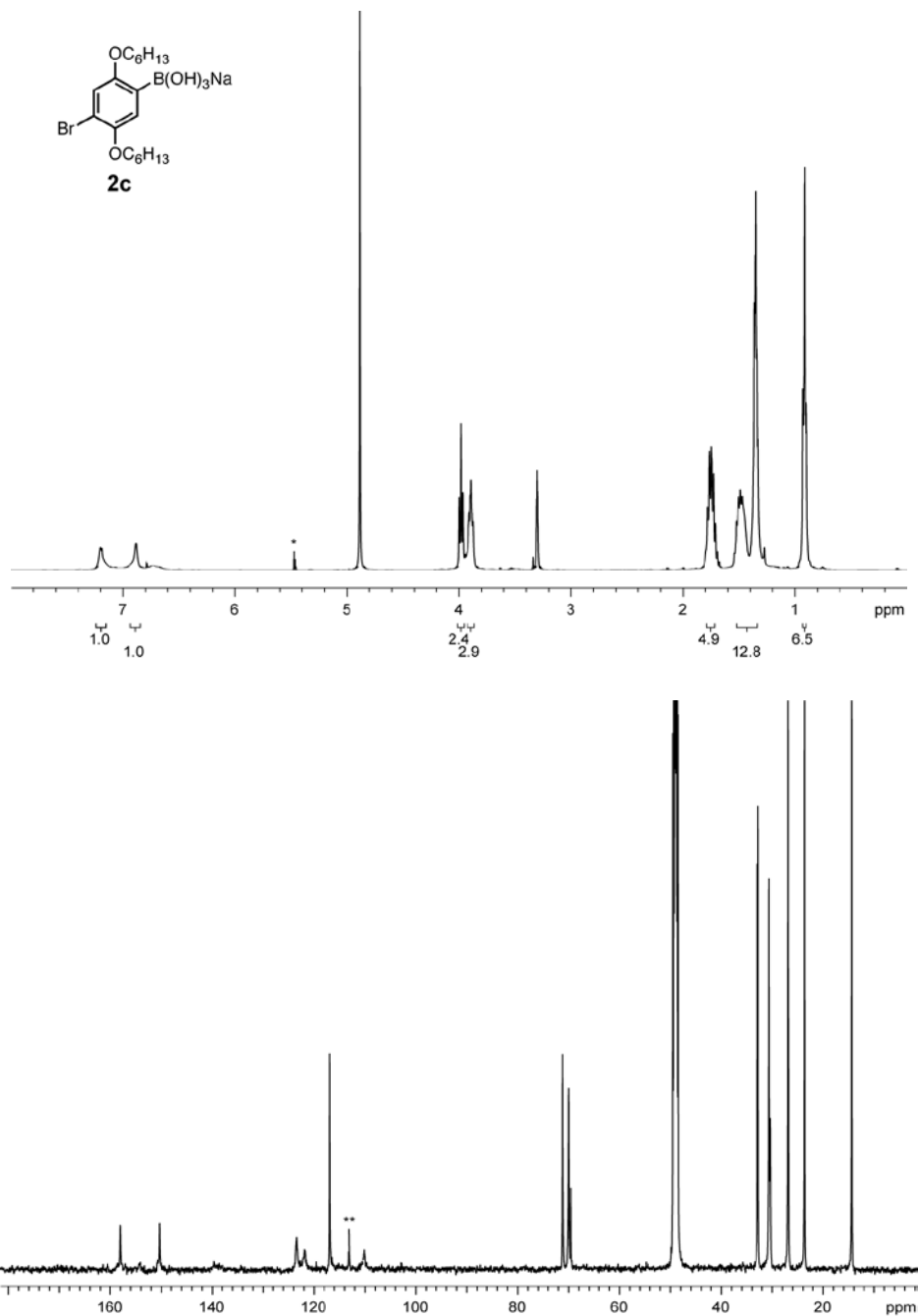
Figure S27. ^{1}H and ^{13}C NMR spectra of **2c**. ^{1}H NMR (400 MHz, CD$_3$OD) δ 7.19 (br, 1H), 6.88 (br, 1H), 3.98 (t, J = 6.4 Hz, 2H), 3.89 (m, 2H), 1.75 (m, 4H), 1.54-1.33 (br, 12H), 0.92 (m, 6H). *residual CH$_2$Cl$_2$. ^{13}C NMR (125 MHz, CD$_3$OD) δ 158.00, 150.36, 123.40, 121.86, 116.86, 110.15, 71.16, 69.98, 32.88, 32.76, 30.61, 30.36, 26.91, 23.70, 14.41. **Trace decomposition product, verified by HPLC. Some carbons on the hexyl chains are unresolved.
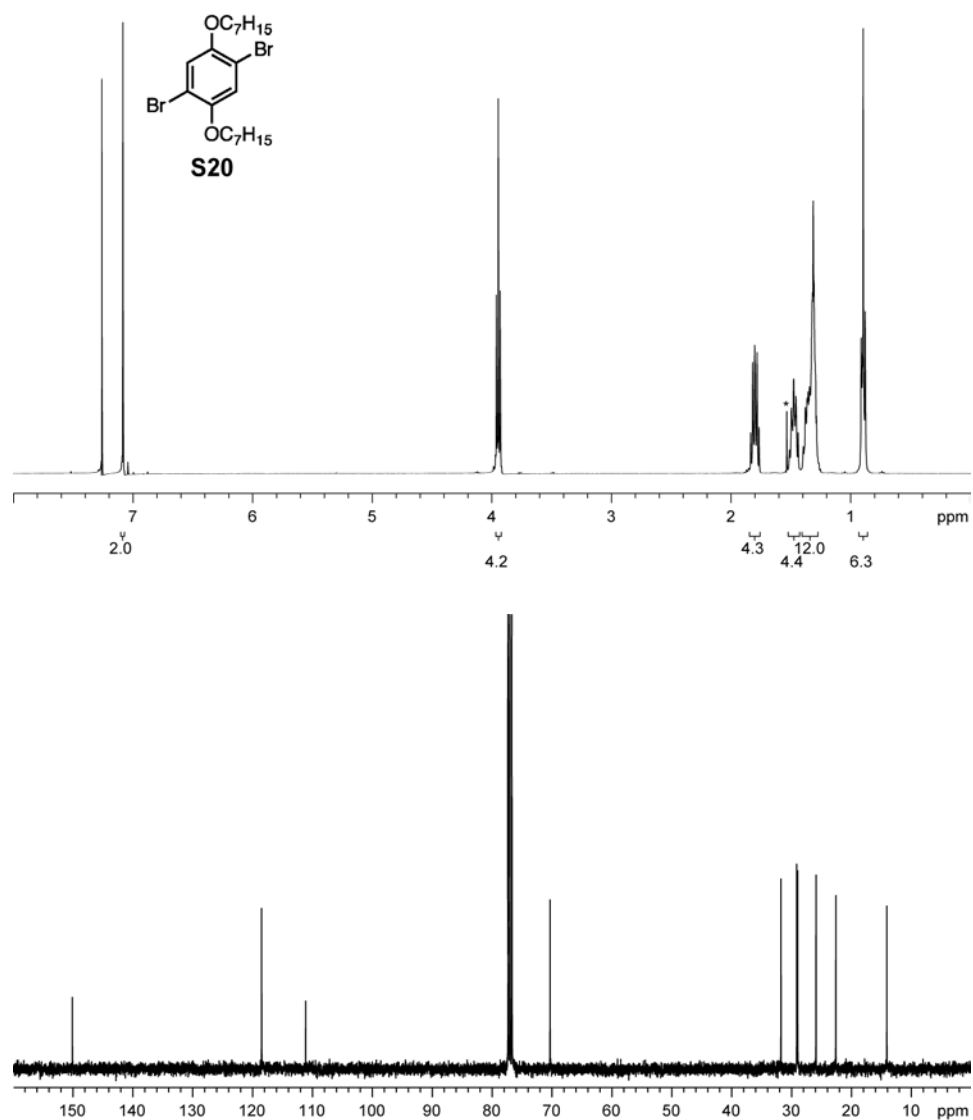
Figure S28. ¹H and ¹³C NMR spectra of **S20**. ¹H NMR (400 MHz, CDCl₃) δ 7.08 (s, 2H), 3.95 (t, *J* = 6.8 Hz, 4H), 1.79 (m, 4H), 1.48 (m, 4H), 1.38-1.31 (br, 12H), 0.90 (m, 6H). *residual H₂O. ¹³C NMR (100 MHz, CDCl₃) δ 150.09, 118.48, 111.13, 70.32, 31.57, 29.12, 28.97, 25.90, 22.59, 14.08.
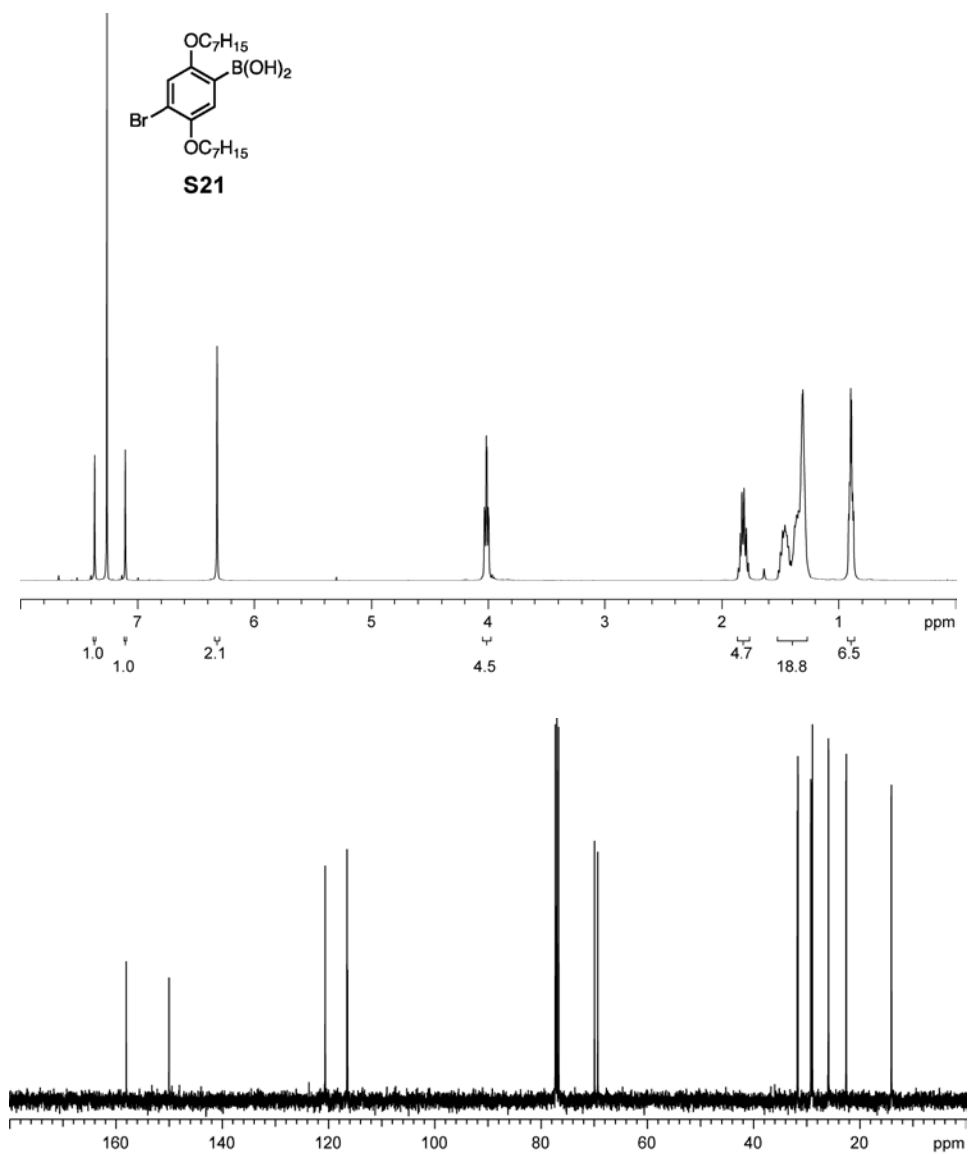
Figure S29. ^{1}H and ^{13}C NMR spectra of **S21**. ^{1}H NMR (400 MHz, CDCl$_3$) δ 7.36 (s, 1H), 7.10 (s, 1H), 6.32 (s, 1H), 4.01 (m, 4H), 1.81 (m, 4H), 1.48-1.31 (br, 16H), 0.89 (m, 6H). ^{13}C NMR (100 MHz, CDCl$_3$) δ 158.06, 150.02, 120.63, 116.52, 116.40, 69.94, 69.32, 31.77, 31.65, 29.23, 29.19, 29.01, 28.92, 25.92, 25.90, 22.60, 22.55, 14.09, 14.04. C *ipso* to B is not observed.
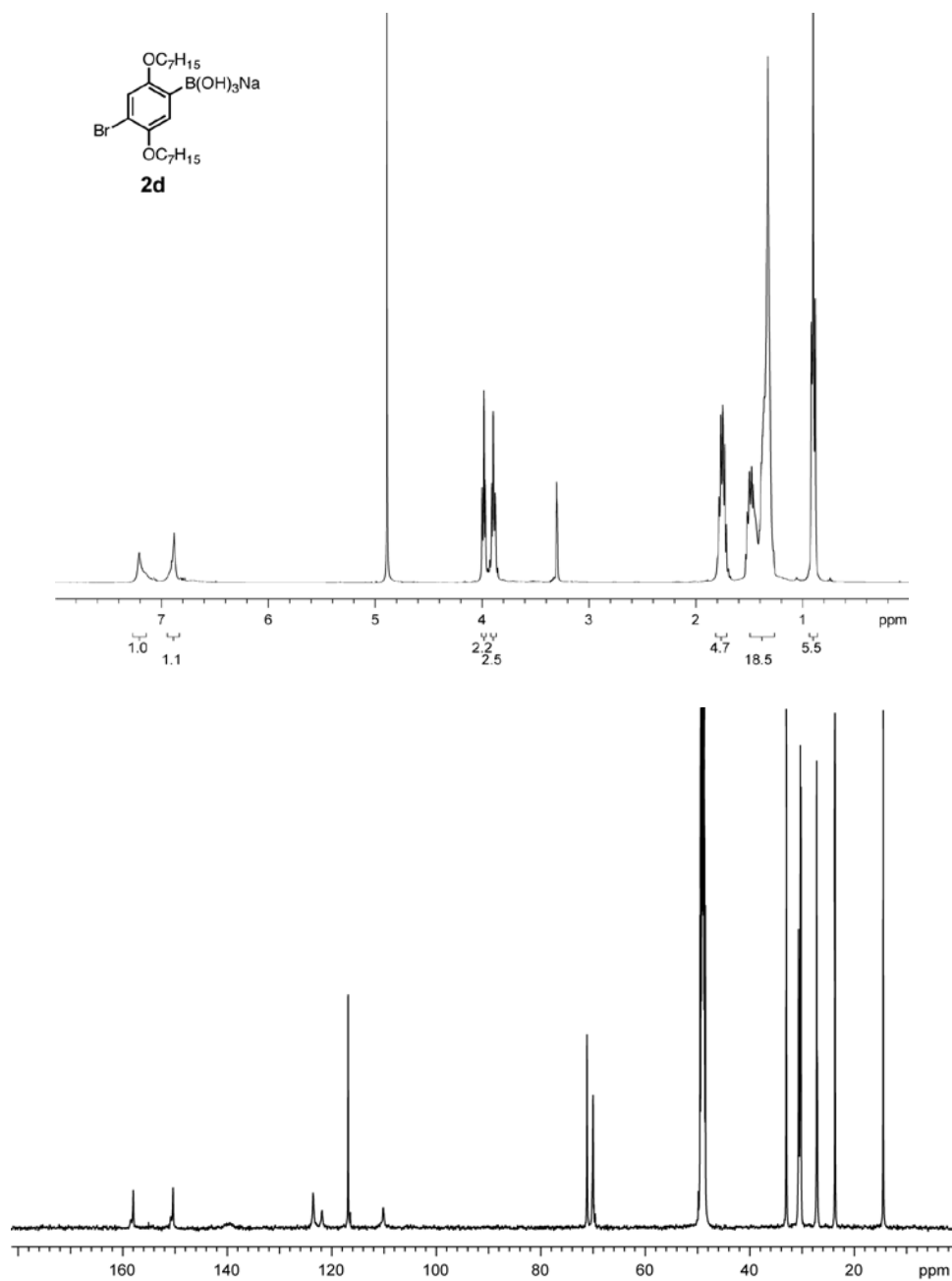
Figure S30. ^{1}H and ^{13}C NMR spectra of **2d.** ^{1}H NMR (400 MHz, CD$_3$OD) δ 7.21 (br, 1H), 6.88 (br, 1H), 3.98 (t, J = 6.8 Hz, 2H), 3.91 (t, J = 6.8 Hz, 2H), 1.75 (m, 4H), 1.53-1.27 (br, 16H), 0.90 (m, 6H). ^{13}C NMR (125 MHz, CD$_3$OD) δ 157.96, 150.35, 123.56, 121.84, 116.85, 110.11, 71.14, 69.98, 33.01, 30.66, 30.32, 30.19, 27.19, 27.09, 23.69, 14.46. Some carbons on the heptyl chains are unresolved.
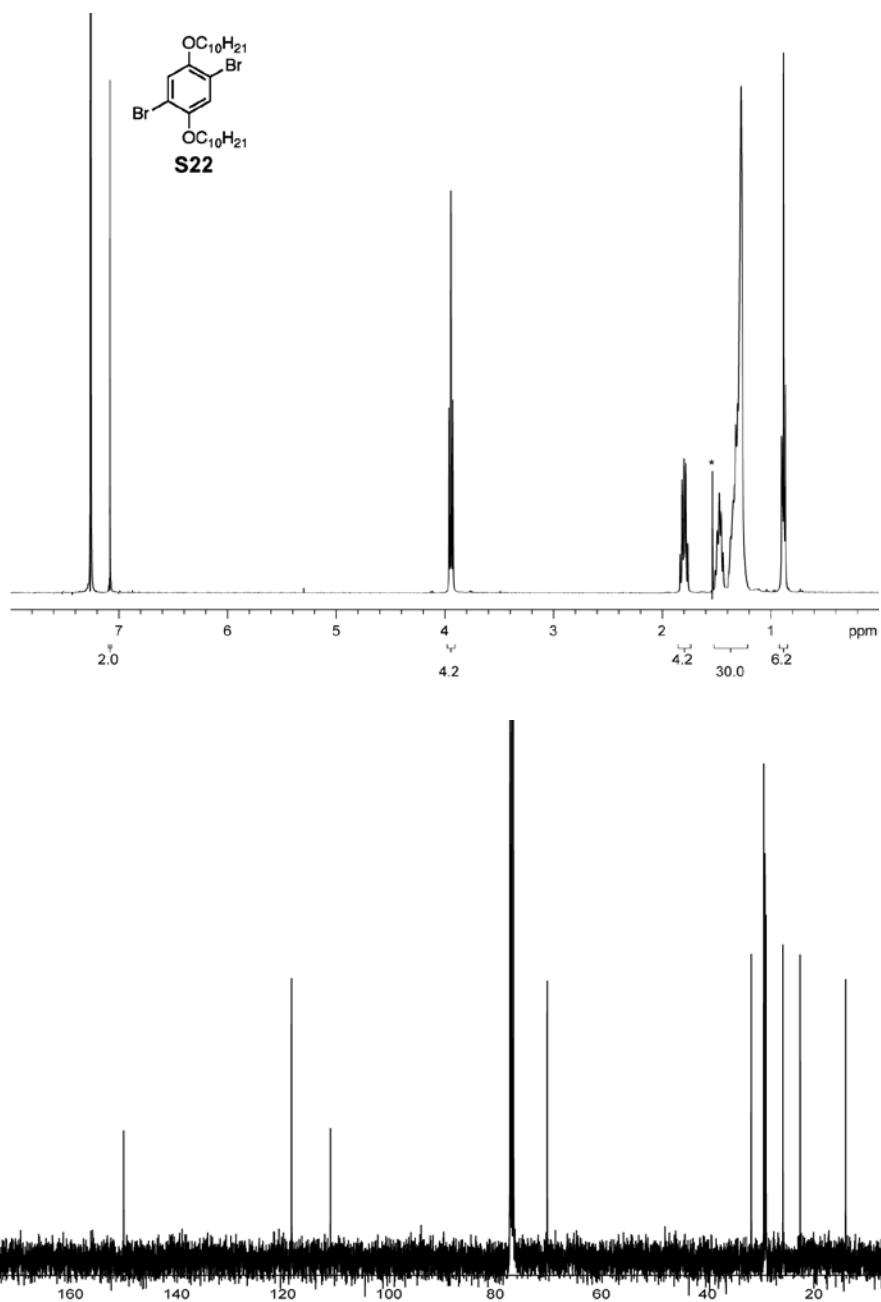
Figure S31. ^{1}H and ^{13}C NMR spectra of **S22**. ^{1}H NMR (400 MHz, CDCl$_3$) δ 7.08 (s, 2H), 3.94 (t, J = 6.4 Hz, 4H), 1.80 (m, 4H), 1.54-1.27 (br, 28H), 0.90 (m, 6H). *residual H$_2$O. ^{13}C NMR (100 MHz, CDCl$_3$) δ 150.07, 118.46, 111.12, 70.31, 31.89, 29.53, 29.31, 29.29, 29.10, 25.92, 22.68, 14.12. Some carbons on the decyl chains are unresolved.
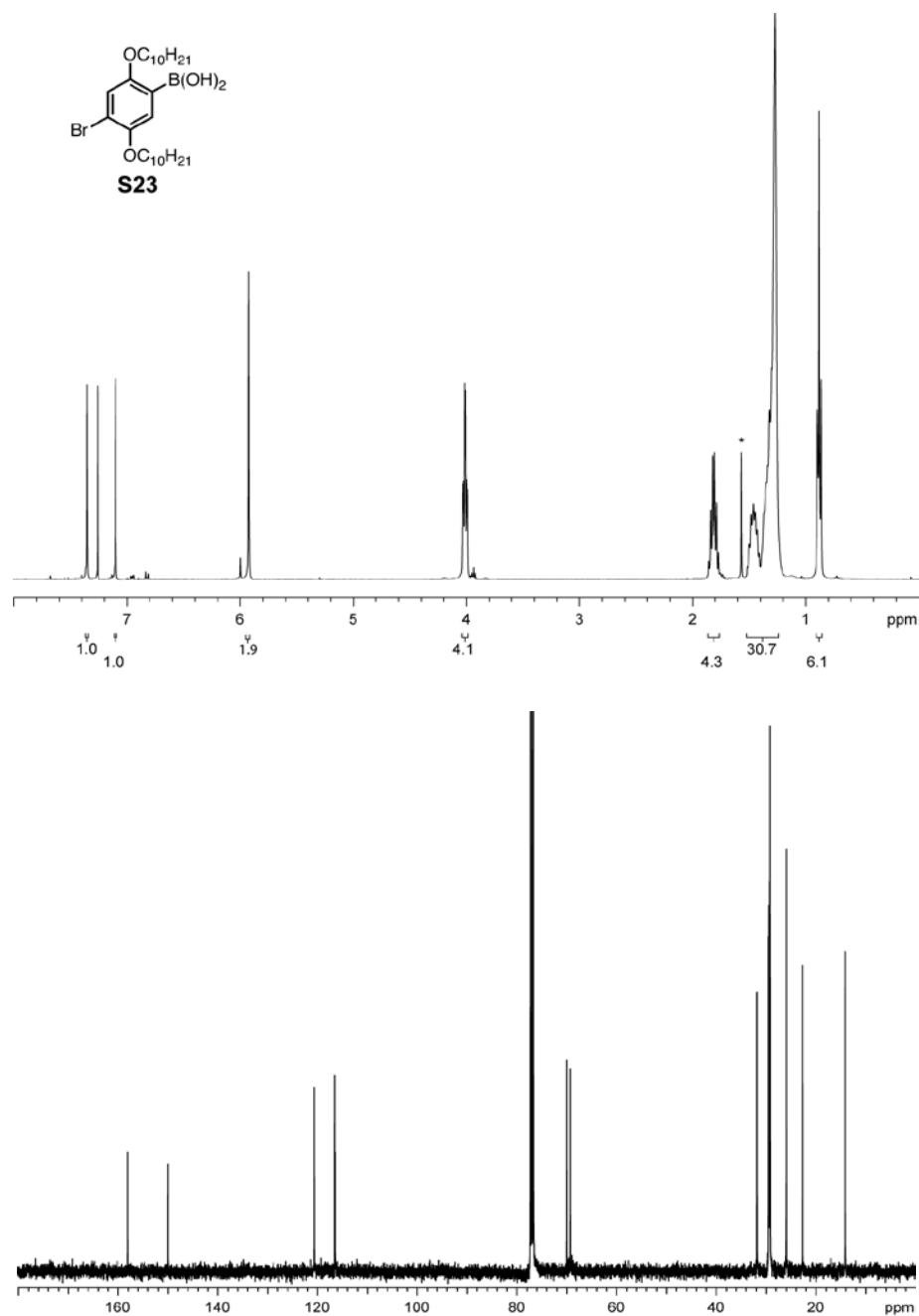
Figure S32. ¹H and ¹³C NMR spectra of **S23**. ¹H NMR (400 MHz, CDCl₃) δ 7.35 (s, 1H), 7.10 (s, 1H), 5.93 (s, 2H), 4.01 (m, 4H), 1.81 (m, 4H), 1.57-1.27 (br, 28H), 0.88 (m, 6H). ¹³C NMR (100 MHz, CDCl₃) δ 158.12, 150.04, 120.71, 116.55, 116.45, 69.99, 69.33, 31.90, 31.86, 29.56, 29.55, 29.49, 29.48, 29.40, 29.34, 29.32, 29.27, 29.25, 29.21, 25.97, 22.68, 22.67, 14.10. C *ipso* to B is not observed, some carbons on the decyl chains are unresolved.
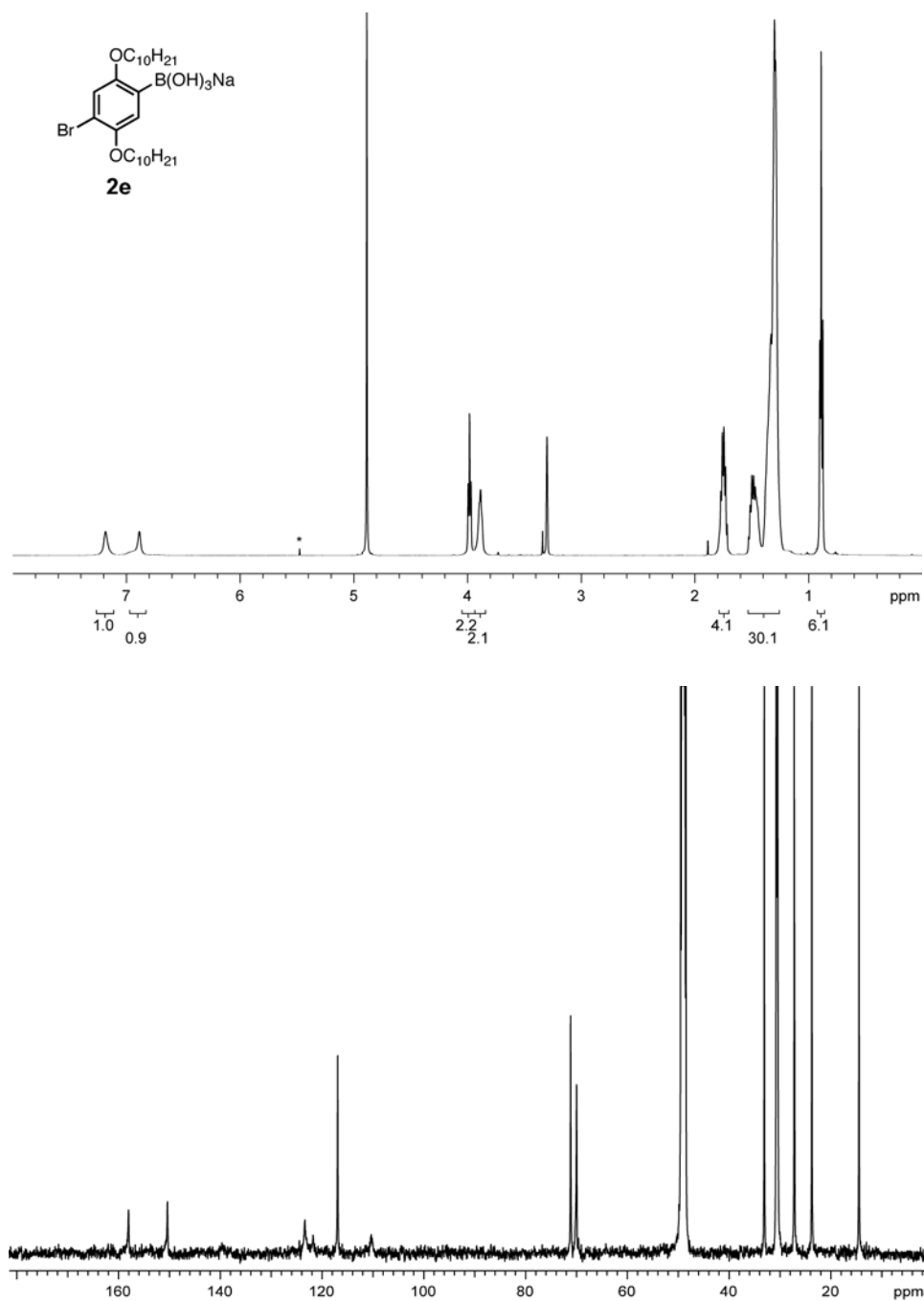
Figure S33. ^{1}H and ^{13}C NMR spectra of **2e**. ^{1}H NMR (500 MHz, CDCl$_3$) δ 7.18 (br, 1H), 6.89 (br, 1H), 3.98 (m, 2H), 3.89 (br, 2H), 1.75 (m, 4H), 1.52-1.29 (br, 28H), 0.89 (m, 6H). *residual CH$_2$Cl$_2$. ^{13}C NMR (125 MHz, CDCl$_3$) δ 158.03, 150.38, 123.37, 121.77, 116.92, 110.33, 71.14, 69.96, 33.07, 30.73, 30.68, 30.62, 30.47, 27.20, 23.74, 14.46. Some carbons on the decyl chains are unresolved.

E. Calibration Curves

Solutions containing a constant concentration of nitrobenzene (0.01 M) and varying concentrations of **S1** and **S2** were prepared in benzene. Each was analyzed by HPLC and the response factor (**F**) was determined by fitting the data to the following equation:

$$\frac{\text{analyte area}}{[\text{analyte}]} = F \, \frac{\text{nitrobenzene area}}{[\text{nitrobenzene}]}$$
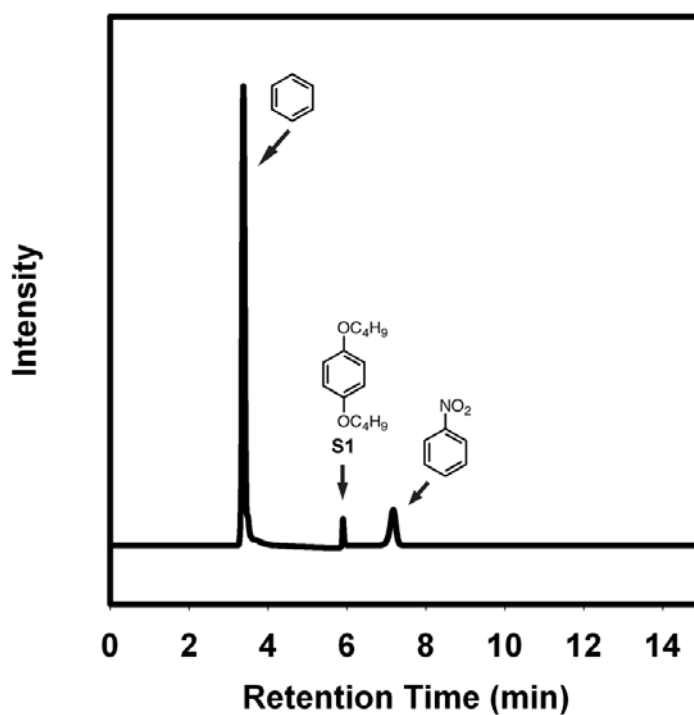

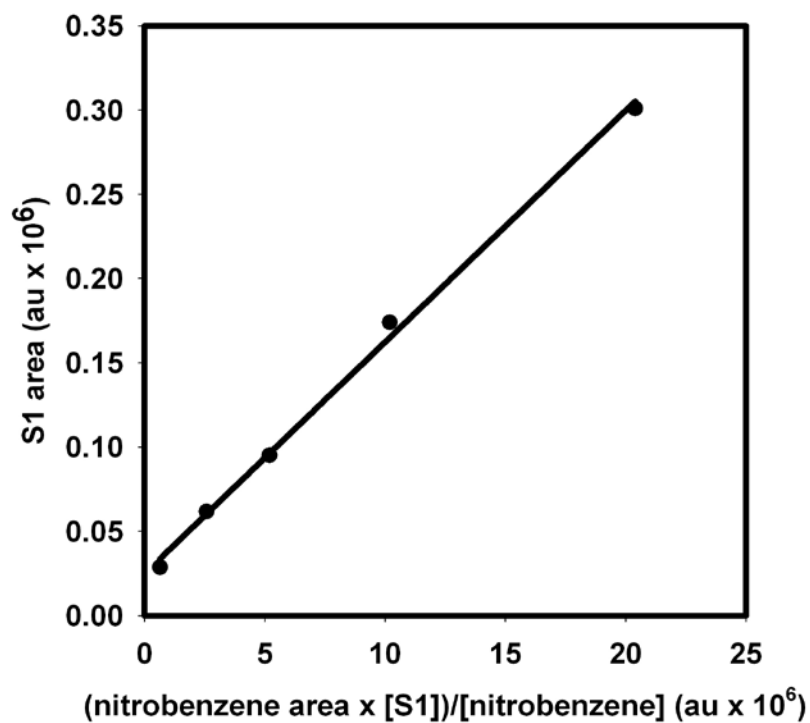**Figure S34.** Representative HPLC chromatogram showing the retention time for **S1**.

Figure S35. Plot of **S1** area versus (nitrobenzene area x [**S1**])/[nitrobenzene] fitted to y = mx + b where $m = 0.0139 \pm 0.0002$ $b = 0.0207 \pm 0.0006$ x 10^7

Table S1. Data for plot in Figure S35.

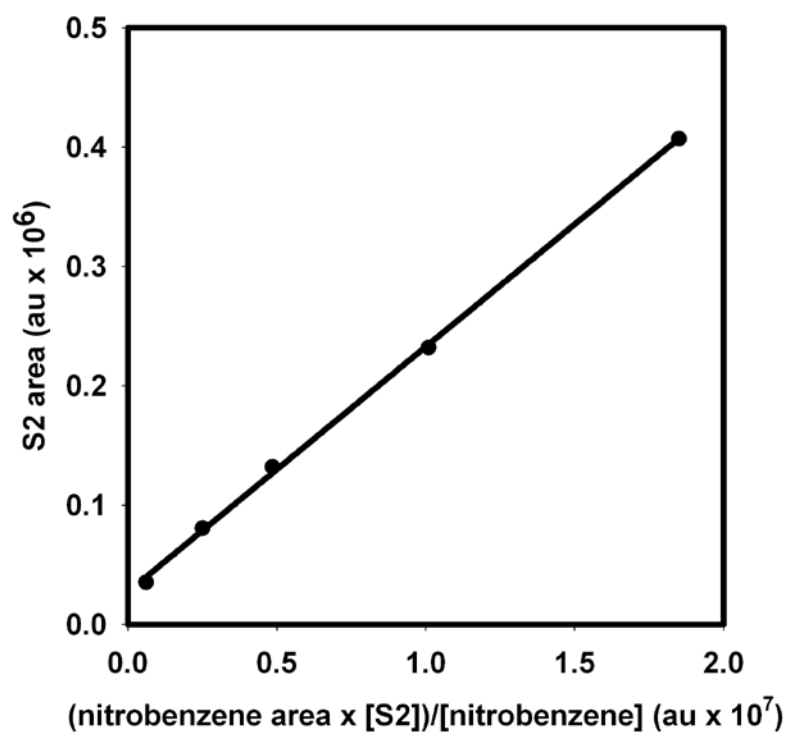| [**S1**] (M)	Area **S1** (au x 10^6)	area nitrobenzene (au x 10^6)	(nitrobenzene area x [**S1**])/[nitrobenzene] (au x 10^6)
0.16	0.3010	1.280	20.40
0.08	0.1740	1.280	10.20
0.04	0.0950	1.290	5.190
0.02	0.0620	1.290	2.580
5.0 x 10^{-3}	0.0290	1.290	0.6430

Figure S36. Plot of **S2** area versus (nitrobenzene area x [**S2**])/[nitrobenzene] fitted to y = mx + b where $m = 0.0205 \pm 0.0008$ $b = 0.003 \pm 0.002$ x 10^7

Table S2. Data for plot in Figure S36.

[**S2**] (M)	Area **S2** (au x 10^6)	area nitrobenzene (au x 10^6)	(nitrobenzene area x [**S2**])/[nitrobenzene] (au x 10^7)
0.16	0.4070	1.160	1.850
0.08	0.2320	1.270	1.010
0.04	0.1320	1.210	0.4860
0.02	0.0800	1.250	0.2510
5.0 x 10^{-3}	0.0350	1.230	0.0610

F. Conversion Plots

Solutions of **1b** and **2b** in benzene, were heated at 100 °C and 60 °C respectively. Aliquots were taken at various time points, diluted with CH_2Cl_2, analyzed by HPLC and the percent conversion was calculated.
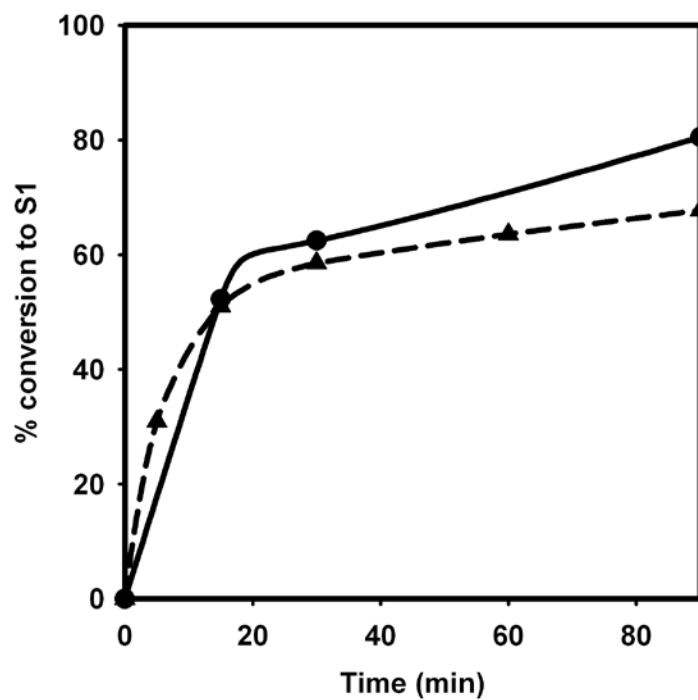

Figure S37. Conversion of **1b** to **S1** at 100 °C in benzene ([**1b**] = 0.05 M; run 1 (●), run 2 (▲)).
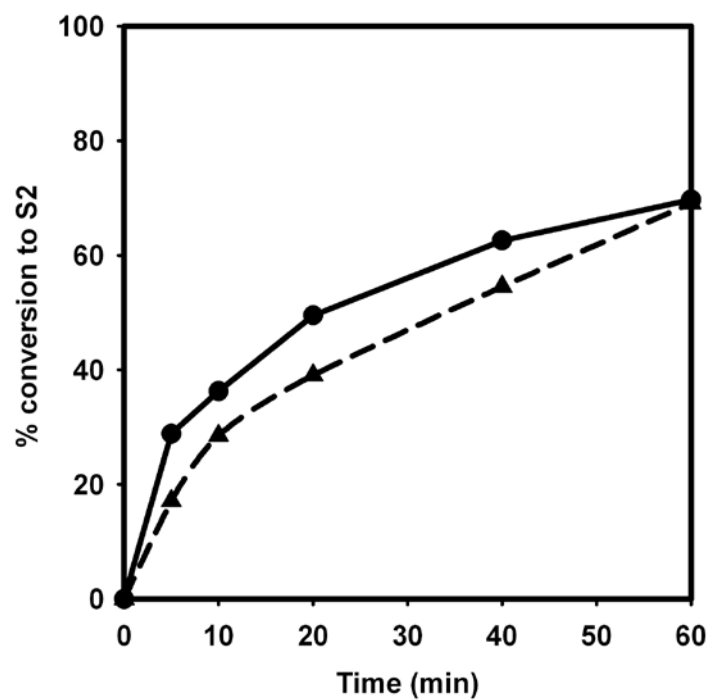
Figure S38. Conversion of **2b** to **S2** at 60 °C in benzene ([**2b**] = 0.08 M; run 1 (●), run 2

(▲)).

Quantitative Conversion of 1c to S1

Solid **1c** was heated at 200 °C for 30 min in a bomb flask.
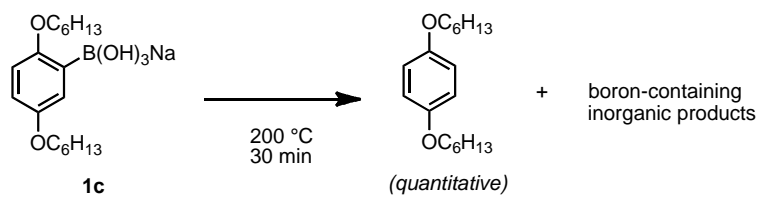
a.
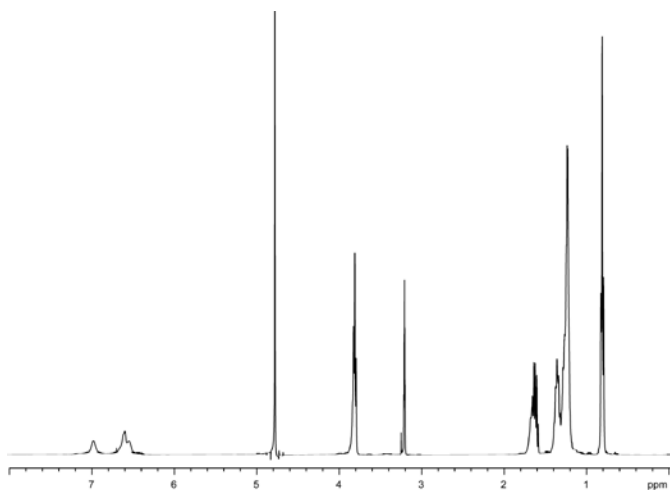
b.
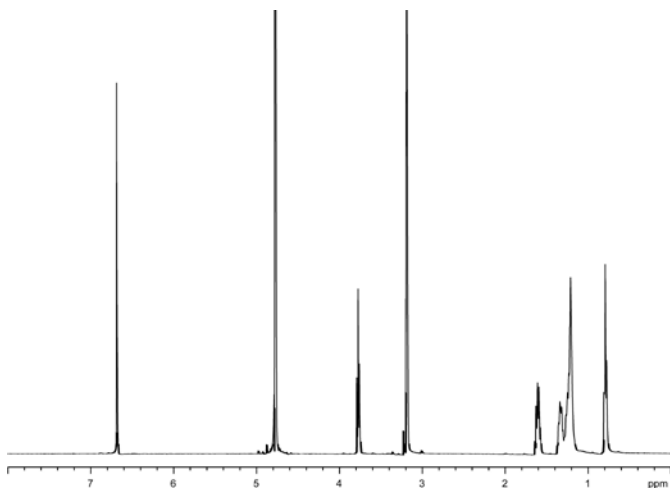
Figure S39. ^{1}H NMR spectra of the same sample before (a) and after (b) heating **1c** to 200 °C for 30 min.

AFM Images

a.
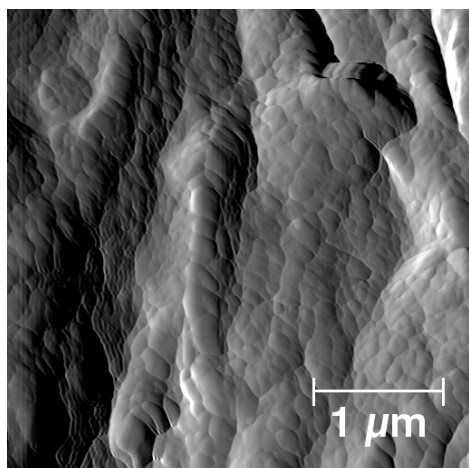
b.
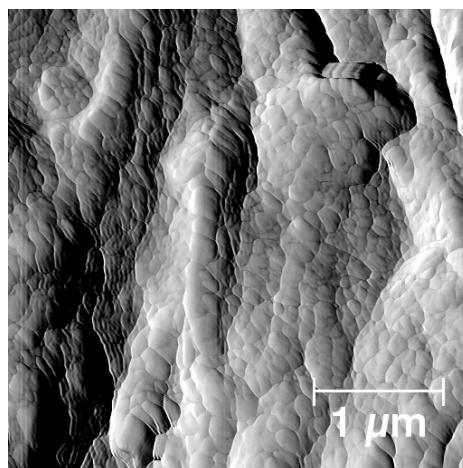
Figure S40. (a.) Amplitude and (b.) Phase mode images of gels of **1a** (22 mg/mL).

a.
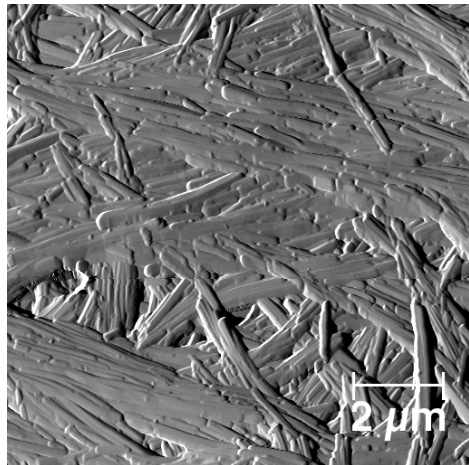
b.
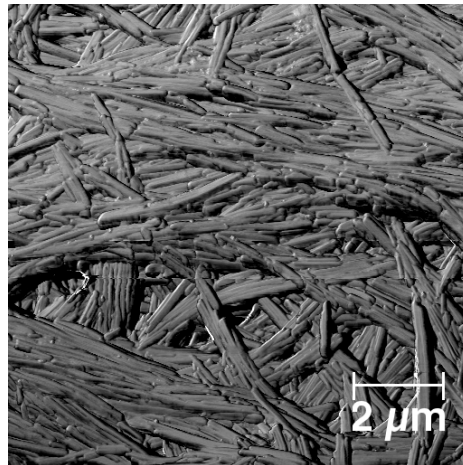
Figure S41. (a.) Amplitude and (b.) Phase mode images of gels of **1b** (17 mg/mL).
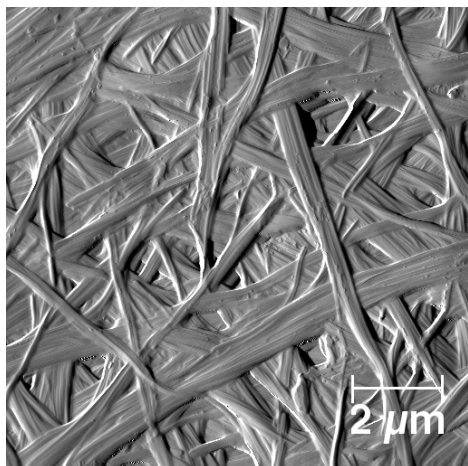
a.
b.
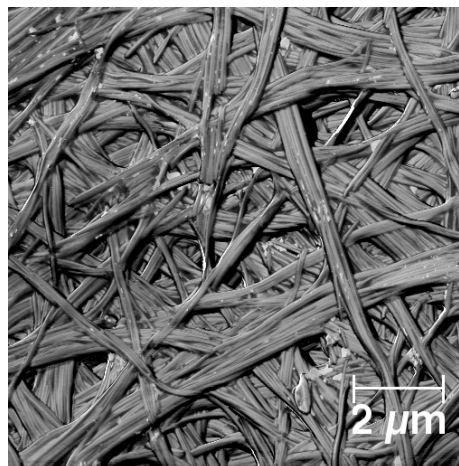
Figure S42. Amplitude and Phase mode images of gels of **1c** (12 mg/mL).
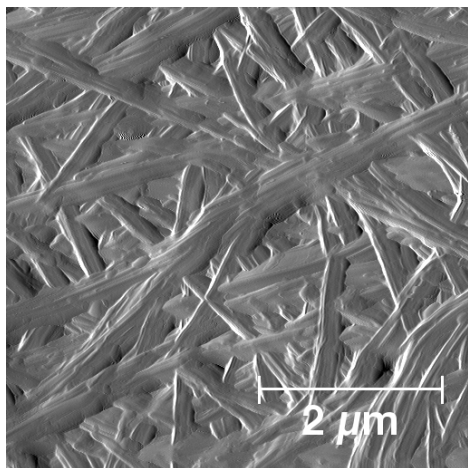
a.
b.
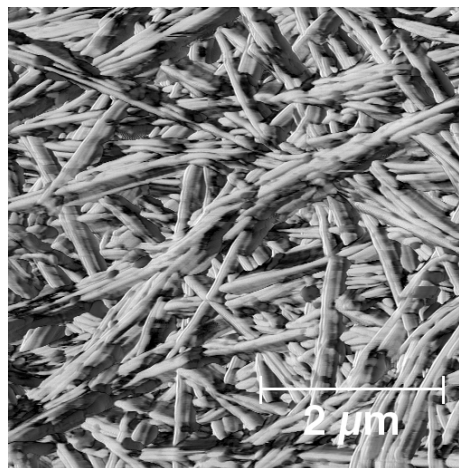
Figure S43. Amplitude and Phase mode images of gels of **1d** (26 mg/mL).

a.
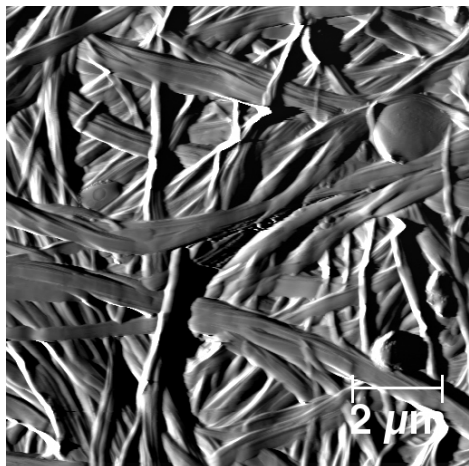
b.
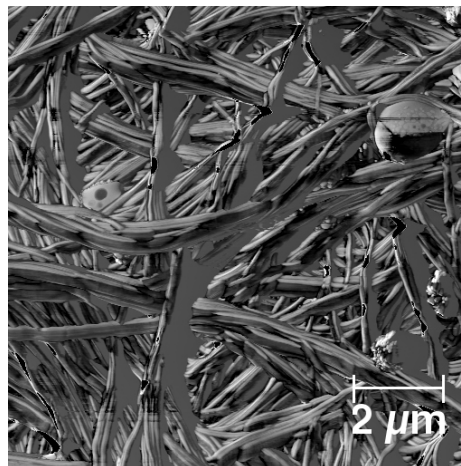
Figure S44. Amplitude and Phase mode images of gel of **1e** (44 mg/mL).

a.
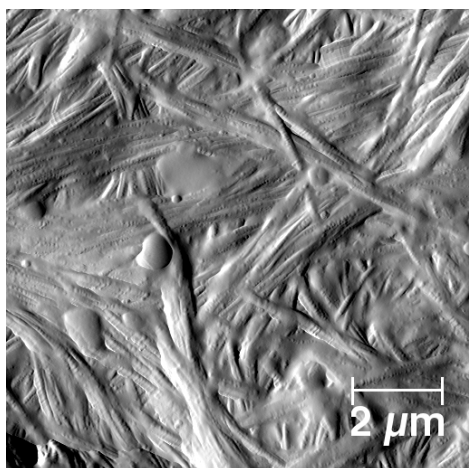
b.
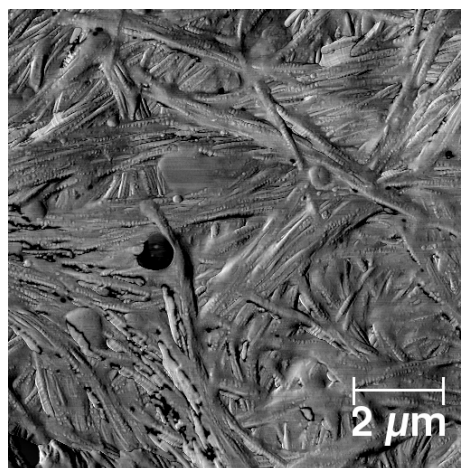
Figure S45. (a.) Amplitude and (b.) Phase mode images of gel of **2b** (28 mg/mL).

a.
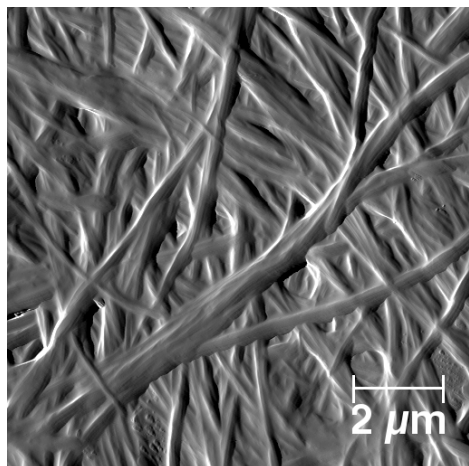
b.
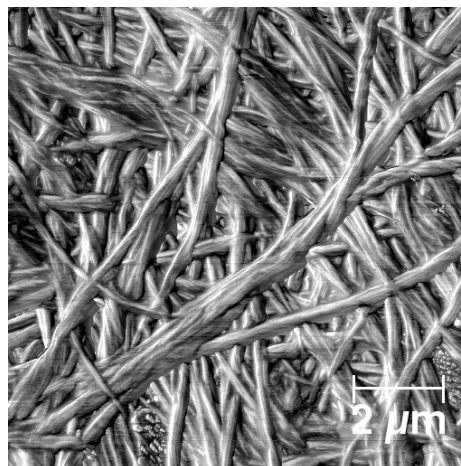
Figure S46. (a.) Amplitude and (b.) Phase mode images of gel of **2c** (32 mg/mL).

a.
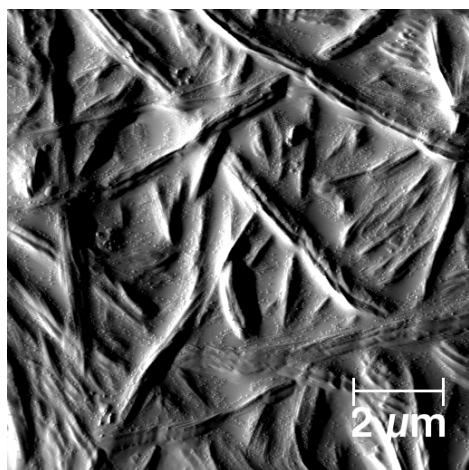
b.
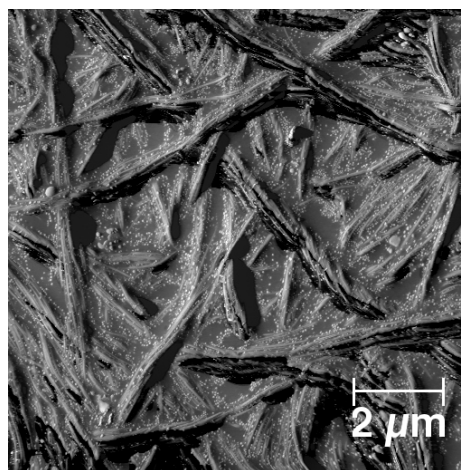
Figure S47. (a.) Amplitude and (b.) Phase mode images of gels of **2d** (32 mg/mL).

G. Rheological Properties of Gels in Benzene

a.
                                      b.
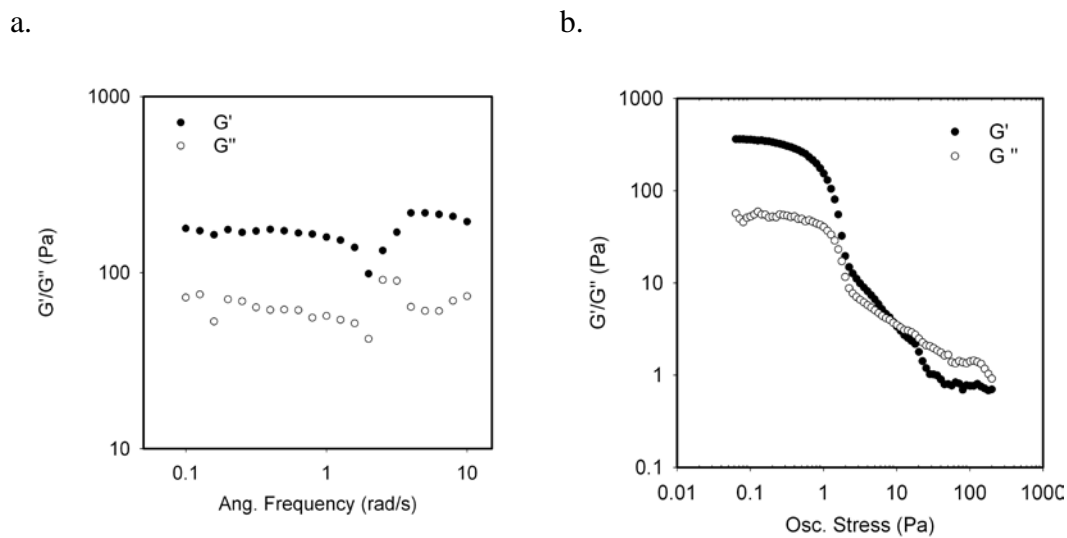
Figure S48. (a.) Frequency and (b.) oscillating stress sweep of preformed gel of **1a** (44 mg/mL).

a.
                                        b.
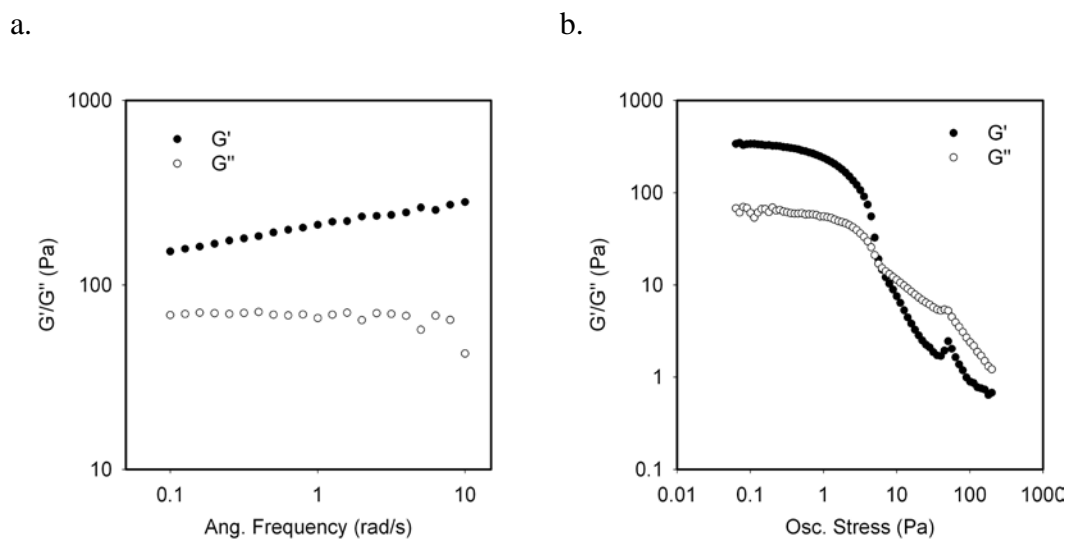
Figure S49. (a.) Frequency and (b.) oscillating stress sweep of preformed gel of **1b** (30 mg/mL).

a.   b.
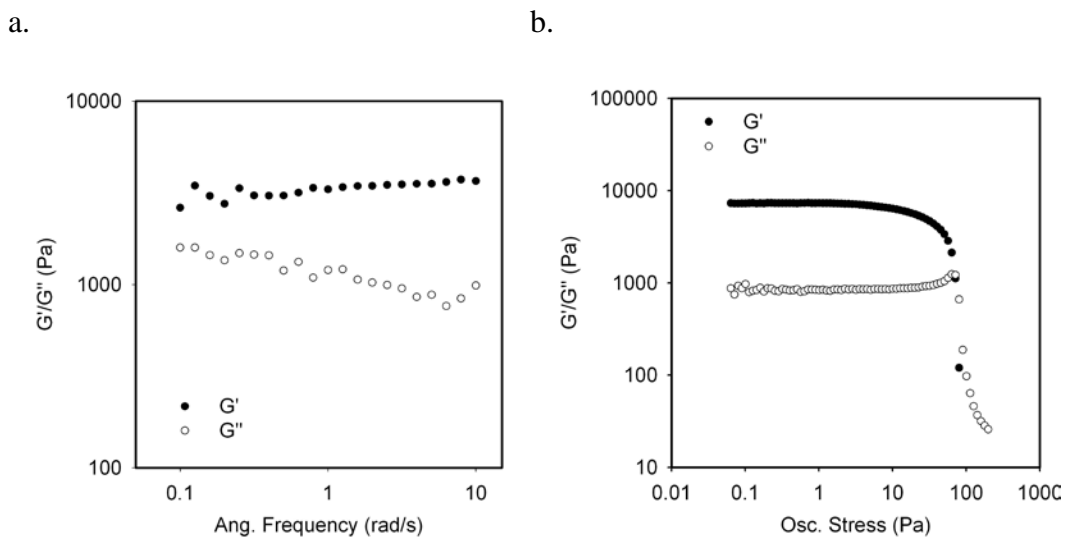
Figure S50. (a.) Frequency and (b.) oscillating stress sweep of preformed gel of **1c** (20 mg/mL).

a.   b.
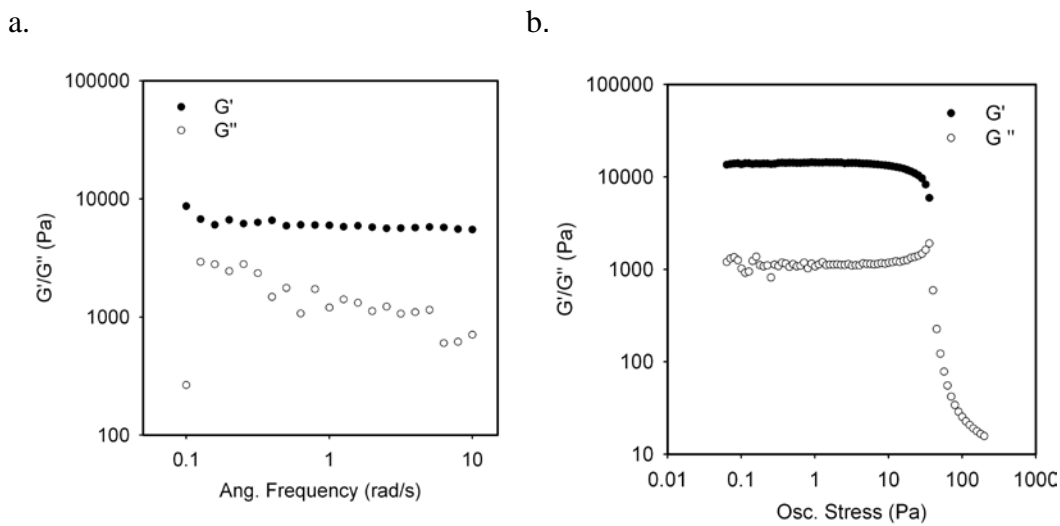
Figure S51. (a.) Frequency and (b.) oscillating stress sweep of preformed gel of **1d** (54 mg/mL).

a.
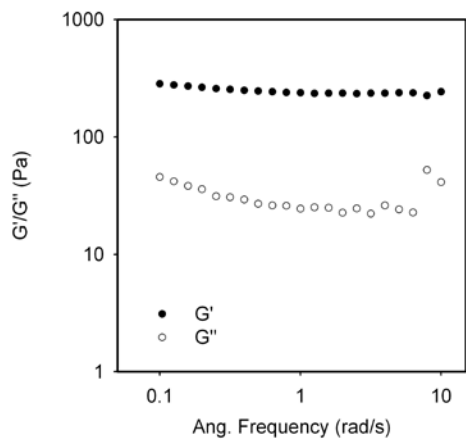
b.
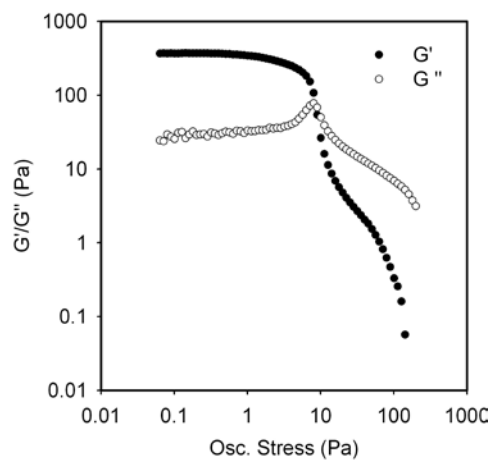
Figure S52. (a.) Frequency and (b.) oscillating stress sweep of preformed gel of **1e** (44 mg/mL).

a.
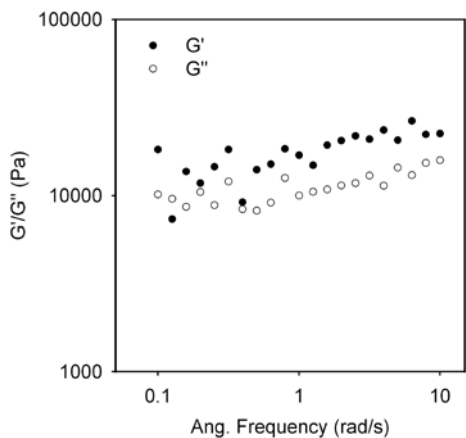
b.
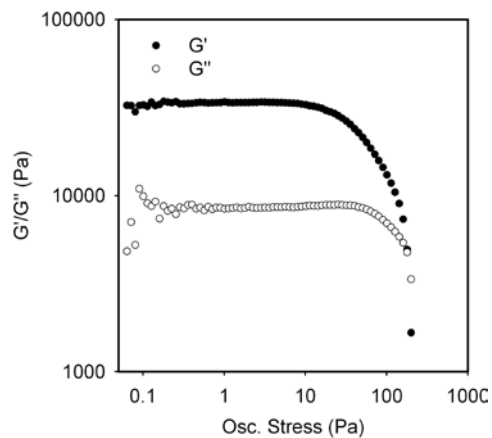
Figure S53. (a.) Frequency and (b.) oscillating stress sweep of preformed gel of **2b** (52 mg/mL).
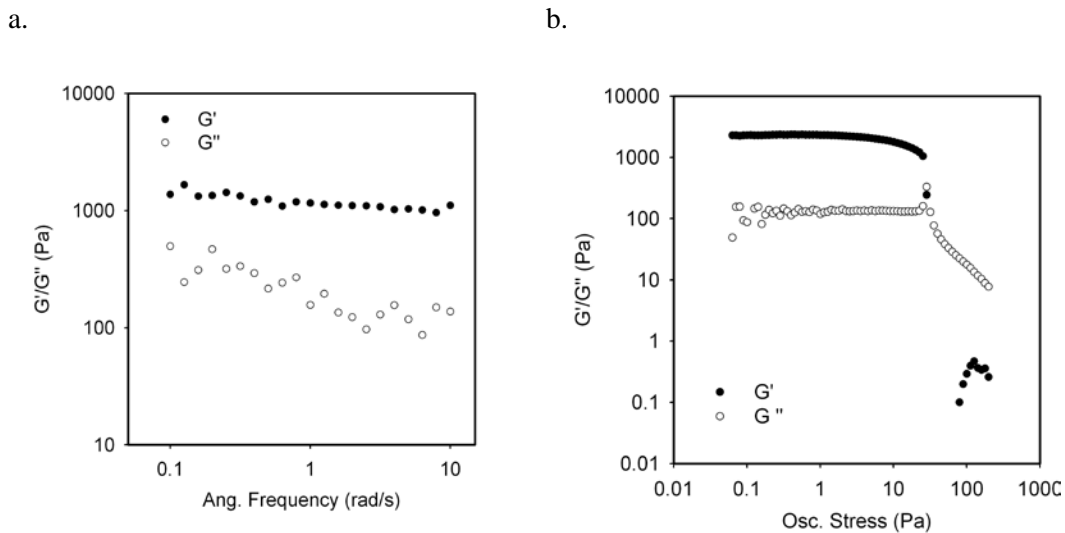
Figure S54. (a.) Frequency and (b.) oscillating stress sweep of preformed gel of **2c** (48 mg/mL).
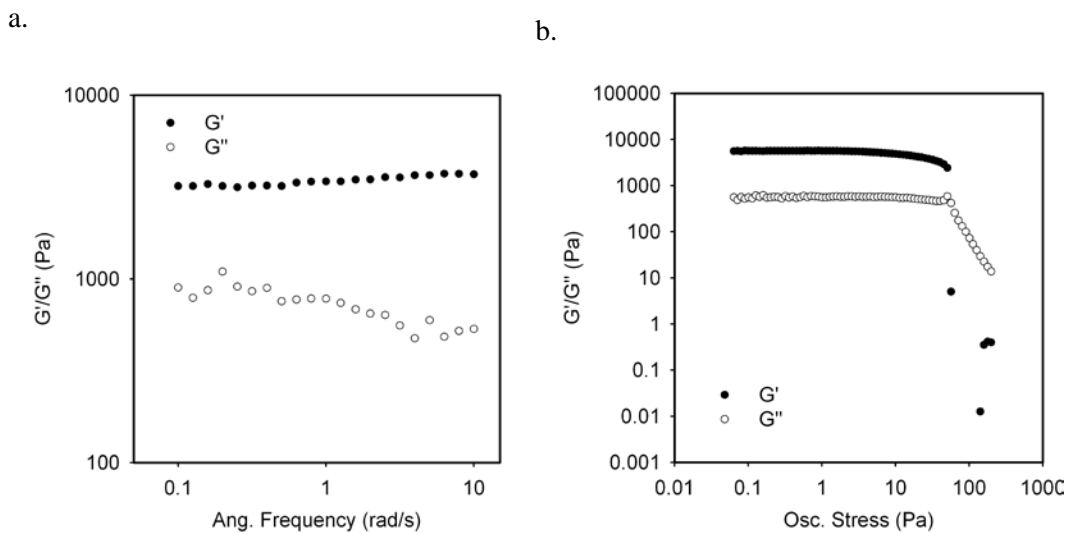
Figure S55. (a.) Frequency and (b.) oscillating stress sweep of preformed gel of **2d** (64 mg/mL).

Powder X-ray Diffraction Data
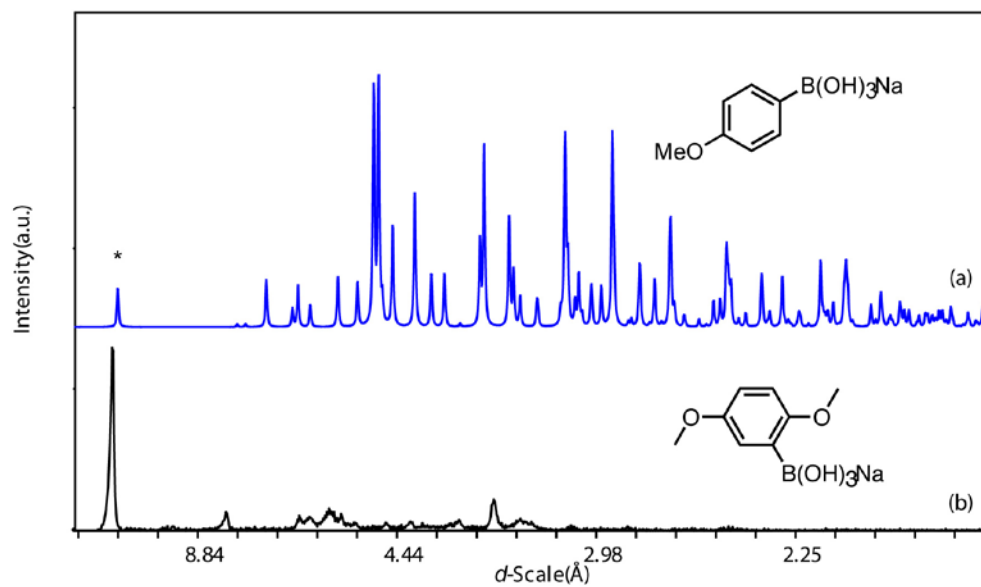
Figure S56. Powder X-ray diffraction patterns for (a) simulated (*p*-MeOC$_6$H$_4$B(OH)$_3$Na)^2 (b) xerogel of **1a** (25 mg/mL). *Both have similar *d*-spacing corresponding to a distance of 15.6 Å.

TGA Data
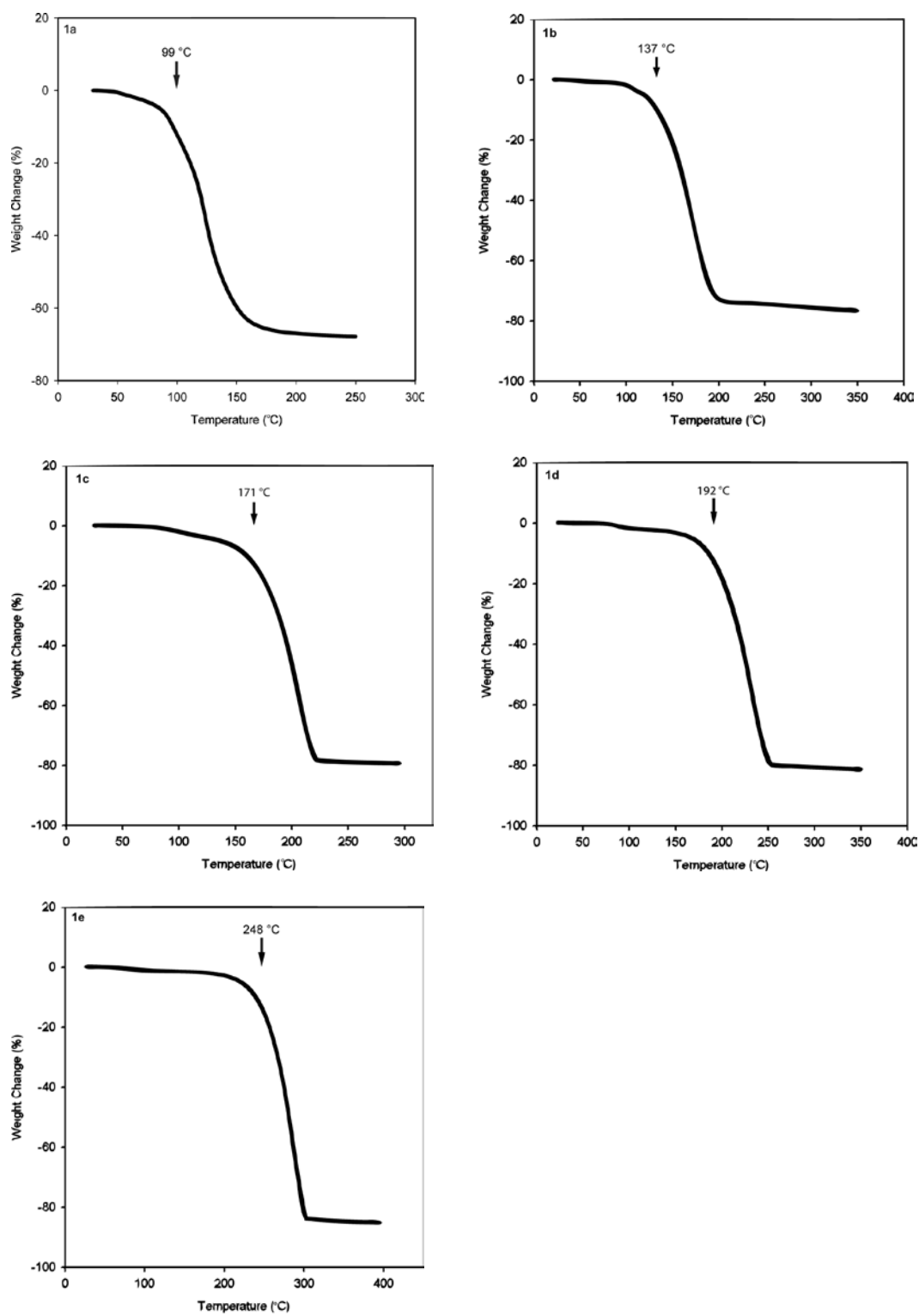
Figure S57. TGA curves for compounds **1a-e.**
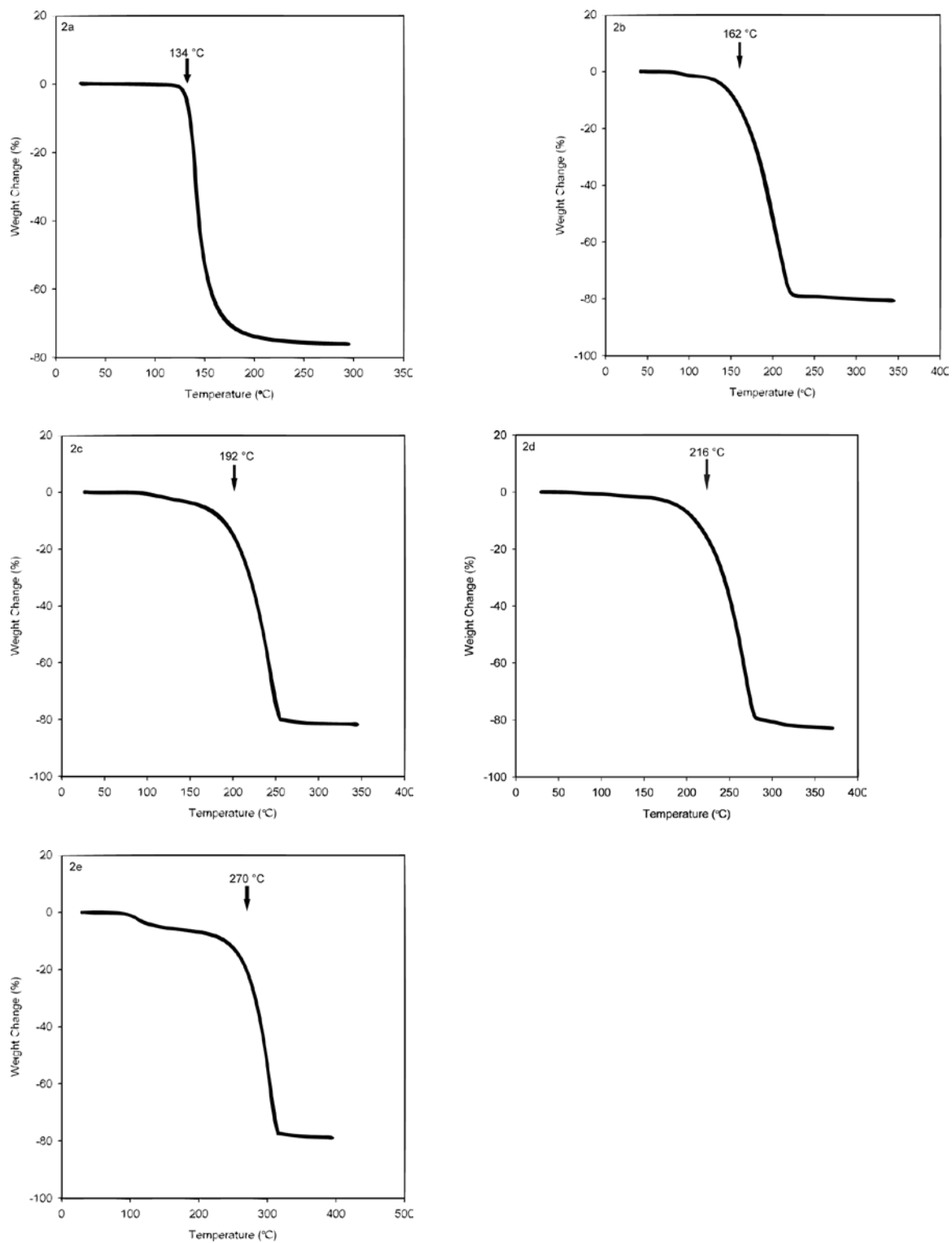
Figure S58. TGA curves for compounds **2a-e.**

SEM Image
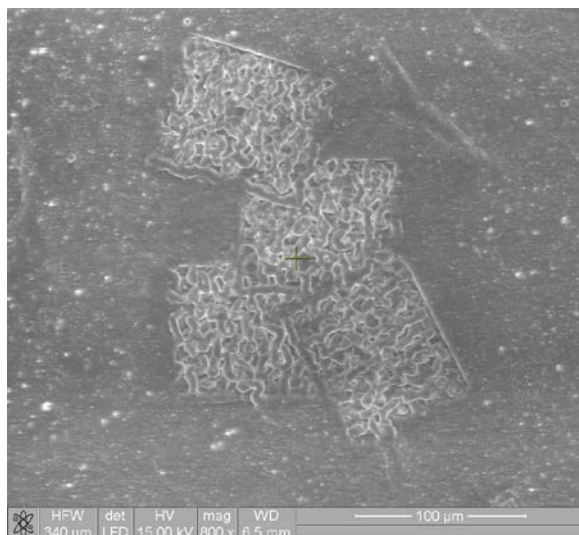
Figure S59. SEM image of gel **1c**.

H. T_{gel} Data

Gelator	T_{gel} (°C)
1a	> 80
1b	52
1c	50
1d	48
1e	25*
2b	60
2c	30
2d	38

* Gel could not support the weight of the ball at room temperature.

I. References

[1] Van Esch, J.; Schoonbeek, F.; de Loos, M.; Kooijman, H.; Spek, A. L.; Kellogg, R. M.; Feringa, B. L. *Chem. Eur. J.* **1999**, 937-950.

[2] Cammidge, A.N.; Goddard, V. H. M.; Gopee, H.; Harrison, N. L.; Hughes, D. L.; Schubert, C. J.; Sutton, B. M.; Watts, G. L.; Whitehead, A. J. *Org. Lett.* **2006**, *8,* 4071-4074.

Appendix B

For Chapter 3 Molecular Dynamic Simulations of Gelator and Nongelator Dissolution

Enthalpies

A. $H_{\text{pure liquid}}$

Example CHARMM input script for calculating $H_{\text{pure liquid}}$ for **1a** (Figure 3-5)

```
* 1a
*

! Usage: The plan is to start with "small" molecules by scaling the bond lengths and
! molecular volumes (L-J radii) to enable the fluid phase to develop. We run a
! relatively short higher temperature MD to randomize this system, then we move
! through various phases of increasing the size of the molecules and starting dynamics
! from the end of the previous run. Thus, a scheme for running would be:
!
! 1) Initialize system with scaling of 0.5:
! $CHARMMEXEC scale=0.5 < 1a_chrm_liquid.inp > out_0.5
!
! This produces the following files:
!        1a_chrm_liquid_min.psf <= psf for cubic box
!        1a_chrm_liquid_min.pdb <= minimized coordinates for cubic box
!        cube.psf, cube.pdb <= cube "shape" and psf for display in vmd
!        1a_liquid_0.5.dcd, 1a_liquid_0.5.pdb <= dcd and pdb files from 500K MD
!
! 2) Expand the molecules from oldscale (0.5 above) to scale, minimize cubic volume
! and do 500 K MD:
! $CHARMMEXEC oldscale=0.5 scale=0.65 size=<last boxsize from previous run>
! mingrow=1 < 1a_chrm_liquid.inp > out_0.65
!
! This step scales-up the system from oldscale to scale and runs MD. It is important to set
! the boxsize with the size variable to that from the end of the previous run. This stage
```

! may need to be repeated several times with more intermediates until one reaches a scale
! of 1 (i.e., no scaling). Values of 0.5, 0.65, 0.8, 0.95 and 1 seem to work.
!
! **3) Do final expansion from <oldscale> to 1 as above but using the following**
! **command:**
! **$CHARMMEXEC oldscale=0.95 size=<*last boxsize from previous run*> mingrow=1**
! **< 1a_chrm_liquid.inp > out_1.0**
!
! This sets by default scale to 1.0, but otherwise works as step 2) above.
!
! **4) Finally, we run MD to equilibrate the fluid and calculate the average energy per**
! **molecule with the scale at 1.**
! **$charmmexec dynamics=1 restart=1 oldscale=1 size=<*last boxsize from previous***
! *run*> **< 1a_chrm_liquid.inp > out_dynam**
!
! **5) Analyze results from trajectory**
! **$CHARMMEXEC size=<last boxsize from previous run> analysis=1 <**
! **1a_chrm_liquid.inp > out_anal**
!
! This produces a file 1a_liquid_1.0.enr which is the time series for the total energy of the
! system. From this one can compute the running average of this total, and would like to
! see this running average converge with time. The energy (or enthalpy) per molecule
! then becomes the total average energy / # molecules. (units kcal/mol)
!

if @?thigh eq 0 set thigh = 500
if @?nsthigh eq 0 set nsthigh = 2000
if @?tlow eq 0 set tlow = 350
if @?nstlow eq 0 set nstlow = 10000
if @?cube ne 0 goto makecube

read rtf card name 1a_chrm_1a.rtf
if @?scale eq 0 then
    read param card name 1a_chrm_1a.prm
else
    system "awk -f scaleparam.awk -v scale=@SCALE 1a_chrm_1a.prm > tmp.prm"
    read param card name tmp.prm
endif

if @?analysis ne 0 goto analysis

read sequ 1a 1
generate est

read coor pdb name 1a_chrm_1a-new.pdb resi
rename segid 1a select segid est end

```
scalar mass stat
set Mass = ?stot  !g/mol
set dens = 1300 !kg/m^3 - average density of many organics

Calc dens = @dens * 1000 * 6.022e-7 / @Mass
if @?size eq 0 Calc size = ( 125 / @dens ) ** ( 1 / 3 ) * 1.0

if @?box ne 0 then
   ! construct box for visualiztion
   system "$CHARMMEXEC cube=@SIZE < 1a_chrm_liquid.inp > outtmp"
   system "rm outtmp"
endif

if @?dynamics ne 0 goto dynamics
if @?mingrow ne 0 then
    if @?oldscale eq 0 stop
    if @?scale eq 0 set scale = 1.0
    delete atom select all end
    read psf card name 1a_chrm_liquid.psf
    read coor pdb name 1a_liquid_@oldscale.pdb resid
    goto domini
endif

mini sd nstep 1000


write coor pdb name 1asmall.pdb
write psf card name 1asmall.psf

coor orie !Puts molecule with longest axis along x

Calc xdis =  @size / 5 ! spacing between particles placed on lattice

set nrep = 125
set ydis = @xdis
set zdis = @xdis
set lxo2 = 2
set lyo2 = 2
set lzo2 = 2

replica n nreplica @nrep
delete atom select segid 1a end

replica reset
```

```
set ires = 1
set x = -@lxo2
label dox

    set y = -@lyo2
    label doy

        set z = -@lzo2
        label doz

            Calc phi = ?rand * 180
            coor rotate xdir ?rand ydir ?rand zdir ?rand phi @phi select ires @ires end
            Calc xd = @x * @xdis
            Calc yd = @y * @ydis
            Calc zd = @z * @zdis
            coor translate xdir @xd ydir @yd zdir @zd -
                select segid n@ires end

            if @ires eq 1  then
                rename segid 1a select segid n@ires end
            else
                join 1a n@ires renumber
            endif

            incr ires by 1
            incr z by 1
        if z le @lzo2 goto doz
        incr y by 1
    if y le @lyo2 goto doy
    incr x by 1
if x le @lxo2 goto dox


coor stat
write psf card name 1a_chrm_liquid.psf
write coor pdb name 1a_chrm_liquid.pdb

label domini

    crystal defi cubic  @size @size @size 90 90 90
    crystal build cutoff 15 noper 0
    image byres xcen 0 ycen 0 zcen 0 select all end

    Energy -
        inbfrq -1 imgfrq -1  -
        eps 1.0 cutnb 12 cutim 12 ctofnb 10 ctonnb 8.5 vswi bycb -
```

```
        ewald kappa 0.33 kmax 4 pmewald order 4 fftx 48 ffty 48 fftz 48

    mini abnr nstep 400 tolgrd 0.5
    mini abnr nstep 200
    write coor pdb name 1a_chrm_liquid_min.pdb

    coor stat

if @?minonly ne 0 stop

label dynamics

    if @?dynamics ne 0 then
        if @?scale eq 0 set scale = 1.0
        delete atom select all end
        read psf card name 1a_chrm_liquid.psf
        read coor pdb name 1a_liquid_@oldscale.pdb resid
    endif

    coor stat
    echo @size

    crystal defi cubic  @size @size @size 90 90 90
    crystal build cutoff 15 noper 0
    image byres xcen 0 ycen 0 zcen 0 select all end

    Energy -
        inbfrq -1 imgfrq -1  -
        eps 1.0 cutnb 12 cutim 12 ctofnb 10 ctonnb 8.5 vswi bycb -
        ewald kappa 0.33 kmax 4 pmewald order 4 fftx 48 ffty 48 fftz 48

    if @?restart ne 0 goto restart

    system "date +%H%M%S | awk '{seed=$0*2+1;print "* Title"; print "*"; print "set
seed = "seed}' > seed.stream"
    stream seed.stream
    system "rm seed.stream"
!    set seed = 3245949

    open unit 2 write form name 1a_liquid.res
    open unit 1 write unform name 1a_liquid_@scale.dcd
    dynamics cpt leap start timestep 0.001 nstep @nsthigh nprint @thigh iprfrq 1000 - !
@nsthigh MD steps at @thigh K
            firstt @thigh finalt @thigh twindl -5 twindh 5 -
            ichew 0 ihtfrq 0 ieqfrq 0 iseed @seed -
            iunwri 2 iuncrd 1 nsavc 100 -
```

```
            iasors 1 iasvel 1 iscvel 0 -
            inbfrq -1 imgfrq -1 echeck -1 -
            ntrfq 2000 -
            pconstant pmass 500 pref 1 pgamma 25  - !  Constant pressure
            Hoover tmass 1000 refT @thigh

     write coor pdb name 1a_liquid_@scale.pdb
     stop


    label restart
    system "date +%H%M%S | awk '{seed=$0*2+1;print "* Title"; print "*"; print "set
seed = "seed}' > seed.stream"
    stream seed.stream
    system "rm seed.stream"
!    set seed = 32423411
    open unit 2 write form name 1a_liquid.res
    open unit 1 write unform name 1a_liquid_@scale.dcd
    dynamics cpt leap restart timestep 0.002 nstep @nstlow nprint 1000 iprfrq 1000 - !
@nstlow MD steps at @tlow K
           firstt @tlow finalt @tlow twindl -5 twindh 5 -
           ichew 0 ihtfrq 0 ieqfrq 0 iseed @seed -
           iunwri 2 iunrea 2 iuncrd 1 nsavc 100 -
           iasors 1 iasvel 1 iscvel 0 -
           inbfrq -1 imgfrq -1 echeck -1 -
           ntrfq 2000 -
           pconstant pmass 500 pref 1 pgamma 25  - !  Constant pressure
           Hoover tmass 1000 refT @tlow


    open unit 2 write form name 1a_liquid.res
    open unit 1 write unform name 1a_liquid_@scale.dcd

    Calc nsteps = 5 * @nstlow
    dynamics cpt leap restart timestep 0.002 nstep @nsteps nprint 1000 iprfrq 1000 - !
@nsteps MD steps at @tlow K
           firstt @tlow finalt @tlow twindl -5 twindh 5 -
           ichew 0 ihtfrq 0 ieqfrq 0 iseed @seed -
           iunwri 2 iunrea 2 iuncrd 1 nsavc 100 -
           iasors 1 iasvel 1 iscvel 0 -
           inbfrq -1 imgfrq -1 echeck -1 -
           ntrfq 2000 -
           pconstant pmass 500 pref 1 pgamma 25  - !  Constant pressure
           Hoover tmass 1000 refT @tlow

     write coor pdb name 1a_liquid_@scale.pdb
stop
```

```
label analysis

    if @?scale eq 0 set scale = 1.0
    if @?size eq 0 then
       echo "Need to input size"
       stop
    endif

    read psf card name 1a_chrm_liquid.psf
    read coor pdb name 1a_liquid_@scale.pdb resid
    faster on
    crystal defi cubic  @size @size @size 90 90 90
    crystal build cutoff 15 noper 0
    image byres xcen 0 ycen 0 zcen 0 select all end

    Energy -
        inbfrq -1 imgfrq -1  -
        eps 1.0 cutnb 12 cutim 12 ctofnb 10 ctonnb 8.5 vswi bycb -
        ewald kappa 0.33 kmax 4 pmewald order 4 fftx 48 ffty 48 fftz 48

    open unit 1 read unform name 1a_liquid_@scale.dcd

    traj query unit 1
    traj firstu 1
    open unit 2 write form name 1a_liquid_@scale.enr
    echu 2
    set step = 1
    set sd = 0
    set avene = 0
    set avene2 = 0

    label enerdyn
        traj read
        energy

        echo @step ?ener
        Calc avene = @avene + ?ener
        Calc avene2 = @avene2 + ?ener * ?ener
        incr step by 1
    if step le ?nfile goto enerdyn

    Calc avene = @avene / ?nfile
    Calc avene2 = @avene2 / ?nfile
    Calc sd = sqrt ( @avene2 - @avene * @avene )
    echo "# Average: @AVENE +/- @SD"
```

```
stop
label makecube


read rtf card
* title
*
   33    1

mass 1 s 1

residue cube 0
atom t1 s 0
atom t2 s 0
atom t3 s 0
atom t4 s 0
atom t5 s 0
atom t6 s 0
atom t7 s 0
atom t8 s 0
bond t1 t2  t2 t4  t3 t4  t3 t1
bond t5 t6  t6 t8  t7 t8  t7 t5
bond t1 t5  t2 t6  t3 t7  t4 t8

end

read param card
* title
*
bond s s 1 @cube
nonbonded
s 0 0 -0.1 4

end

read sequ cube 1
generate cube

scalar x set 0
scalar y set 0
scalar z set 0

calc so2 = @cube / 2

set bn = 1
```

```
set x = -@so2
label makex
    set y = -@so2
    label makey
        set z = -@so2
        label makez

            coor translate xdir @x ydir @y zdir @z select bynu @bn end
            incr bn by 1

            incr z by @cube
        if z le @so2 goto makez
        incr y by @cube
    if y le @cube goto makey
    incr x by @cube
if x le @cube goto makex

write psf card name cube.psf
write coor pdb name cube.pdb

delete atom select all end

stop
```

B. H_{xtrl}

Example CHARMM input script for calculating H_{xtrl} of 1a

```
* 1a
*
read rtf card name 1a_chrm_1a.rtf
read param card name 1a_chrm_1a.prm

read sequ 1a 1
generate test

read coor pdb name 1a_chrm_1a-new.pdb resi
rename segid 1a select segid test end
print coor
```

```
coor copy compare

energy

crystal define monoclinic  9.6696  24.3088  11.4833  90.00 111.31  90.00
crystal build cutoff 30 noperations 3
 (-x, y+1/2, -z+1/2)
 (x, -y-1/2, z-1/2)
 (-x, -y, -z)

if @?dynam ne 0 goto dynam
if @?analysis ne 0 goto analysis

Energy cutnb 50 cutim 50 ctofnb 30 ctonnb 20 switch vswitch

mini abnr nstep 2500 nprint 100 tolgrd 0.01 inbfrq -1 imgfrq -1
write coor pdb name 1a_chrm_xtlmin.pdb

coor orie rms
stop
! Perform the minimisation.
Minimise Abnr Lattice Nstep 2500 Nprint 50 Tolgrd 0.1 Inbfrq 0 Imgfrq 0
coor orie rms
coor swap
cons harm clear
Minimise Abnr Lattice Nstep 2500 Nprint 50 Tolgrd 0.1 Inbfrq 0 Imgfrq 0

cons harm force 100
mini abnr nstep 10000
coor orie rms
cons harm force 0
mini abnr nstep 10000
coor orie rms
stop

write coor pdb name 1a_min.pdb

stop

label dynam

read coor pdb name 1a_chrm_xtlmin.pdb resi
!image byres xcen 0 ycen 0 zcen 0 select all end

Energy cutnb 20 cutim 20 ctofnb 15 ctonnb 10 switch vswitch bycb
```

```
faster on

shake bonh param tol 1e-7
set seed = 123734357

open unit 2 write form name 1a_chrm_xtl.res
dynamics cpt leap start timestep 0.0015 nstep 10000 nprint 1000 iprfrq 1000 -
     firstt 350 finalt 350 twindl -5 twindh 5 -
     ichew 0 ihtfrq 0 ieqfrq 0 iseed @seed -
     iunrea 2 iunwri 2 iuncrd 0 nsavc 0 -
     iasors 1 iasvel 1 iscvel 0 -
     inbfrq -1 imgfrq -1 echeck -1 -
     ntrfq 2000 -
     pconstant pmass 500 pref 1 pgamma 25  - !  Constant pressure
     Hoover tmass 1000 refT 350


open unit 1 write unform name 1a_chrm_xtl.dcd
open unit 2 write form name 1a_chrm_xtl.res
dynamics cpt leap restart timestep 0.0015 nstep 50000 nprint 1000 iprfrq 1000 -
     firstt 350 finalt 350 twindl -5 twindh 5 -
     ichew 0 ihtfrq 0 ieqfrq 0 iseed @seed -
     iunrea 2 iunwri 2 iuncrd 1 nsavc 100 -
     iasors 1 iasvel 1 iscvel 0 -
     inbfrq -1 imgfrq -1 echeck -1 -
     ntrfq 2000 -
     pconstant pmass 500 pref 1 pgamma 25  - !  Constant pressure
     Hoover tmass 1000 refT 350

write coor pdb name 1a_chrm_xtl_dyn.pdb
stop


label analysis

    faster on
    Energy cutnb 20 cutim 20 ctofnb 15 ctonnb 10 switch vswitch bycb

    open unit 1 read unform name 1a_chrm_xtl.dcd

    traj query unit 1
    traj firstu 1
    open unit 2 write form name 1a_chrm_xtl.enr
    echu 2
    set step = 1
    set sd = 0
```

```
    set avene = 0
    set avene2 = 0

    label enerdyn
        traj read
        energy

        echo @step ?ener
        Calc avene = @avene + ?ener
        Calc avene2 = @avene2 + ?ener * ?ener
        incr step by 1
    if step le ?nfile goto enerdyn

    Calc avene = @avene / ?nfile
    Calc avene2 = @avene2 / ?nfile
    Calc sd = sqrt ( @avene2 - @avene * @avene )
    echo "# Average: @AVENE +/- @SD"

stop

awk     '{cnt++;e+=$2;e2+=$2*$2;}END{print        e/cnt"+/-"sqrt(e2/cnt-e*e/cnt/cnt)}'
1a_chrm_xtl.enr
-187.959+/-10.181
```

C. $H_{solution}$

Example CHARMM input script for calculating $H_{solution}$ for **1a** in 1:1 DMSO:H_2O

v:v

```
* title
*

read rtf card name "/usr/local/charmm/c37a1dev/toppar/top_all22_prot.inp"
read rtf card name dmso.rtf append
read rtf card name 1a_chrm_dmso.rtf append
read param card name "/usr/local/charmm/c37a1dev/toppar/par_all22_prot.inp"
read param card name 1a_chrm_dmso.prm append
```

```
if @?analysis ne 0 goto analysis
if @?dynam ne 0 goto dodyn
read sequ 1a 1
generate test

read coor pdb name 1a_chrm_dmso-new.pdb resi
rename segid 1a select segid test end

coor orie select segid 1a end

read sequ tip3 1152
generate tip3 noangl nodihe
read sequ dmso 288
generate dmso

read coor pdb name ../solvent/big_h2o_+dmso_dyna.pdb resi

coor stat select segid 1a end
coor trans xdir -?xave ydir -?yave zdir -?zave select segid 1a end
coor stat select .not. segid 1a end
coor trans xdir -?xave ydir -?yave zdir -?zave select .not. segid 1a end


define solvent select .not. resname 1a .and. .not. type hydrogen end
define solute select resname 1a .and. .not. hydrogen end

delete atom sele .byres. ( solvent .and. -
            (( solute ) -
            .around. 2.8 )) end

write psf card name 1a+h2o+dmso.psf
write coor pdb name 1a_h2o+dmso.pdb resi

stop
label dodyn
if @?dynam ne 0 then
  read psf card name 1a+h2o+dmso.psf
  read coor pdb name 1a_h2o+dmso.pdb resi
endif

crystal defi cubic 45 45 45 90 90 90
crystal build cutoff 15 noper 0
image byres xcen 0 ycen 0 zcen 0 select all end

!Energy cutnb 50 cutim 50 ctofnb 30 ctonnb 20 switch vswitch
faster on
```

```
Energy -
    inbfrq -1 imgfrq -1  -
    eps 1.0 cutnb 12 cutim 12 ctofnb 10 ctonnb 8.5 vswi bycb -
    ewald kappa 0.33 kmax 4 pmewald order 4 fftx 48 ffty 48 fftz 48
    !Energy cutnb 50 cutim 50 ctofnb 30 ctonnb 20 switch vswitch

print coor
!stop

if @?restart eq 0 mini sd nstep 200

shake bonh param tol 1e-7
set seed = 3245949
if @?restart gt 0 goto restart

open unit 2 write form name 1a_h2o+dmso.res
dynamics cpt leap start timestep 0.0015 nstep 5000 nprint 1000 iprfrq 1000 -
    firstt 350 finalt 350 twindl -5 twindh 5 -
    ichew 0 ihtfrq 0 ieqfrq 0 iseed @seed -
    iunwri 2 -
    iasors 1 iasvel 1 iscvel 0 -
    inbfrq -1 imgfrq -1 echeck -1 -
    ntrfq 2000 -
    pconstant pmass 500 pref 1 pgamma 25  - !  Constant pressure
    Hoover tmass 1000 refT 350

write coor pdb name 1a_h2o+dmso_equil.pdb

label restart
system "date +%H%M%S | awk '{seed=$0*2+1;print "* Title"; print "*"; print "set seed
= "seed}' > seed.stream"
stream seed.stream
system "rm seed.stream"
!set seed = 12394599

open unit 2 write form name 1a_h2o+dmso.res
open unit 1 write unform name 1a_h2o+dmso.dcd
dynamics cpt leap restart timestep 0.0015 nstep 100000 nprint 1000 iprfrq 1000 -
    firstt 350 finalt 350 twindl -5 twindh 5 -
    ichew 0 ihtfrq 0 ieqfrq 0 iseed @seed -
    iunrea 2 iunwri 2 iuncrd 1 nsavc 100 -
    iasors 1 iasvel 1 iscvel 0 -
    inbfrq -1 imgfrq -1 echeck -1 -
    ntrfq 2000 -
    pconstant pmass 500 pref 1 pgamma 25  - !  Constant pressure
```

```
        Hoover tmass 1000 refT 350


write coor pdb name 1a_h2o+dmso_final.pdb

stop

label analysis
    read psf card name 1a+h2o+dmso.psf
    read coor pdb name 1a_h2o+dmso.pdb resi

    crystal defi cubic 43 43 43 90 90 90
    crystal build cutoff 15 noper 0
    image byres xcen 0 ycen 0 zcen 0 select all end

    energy -
        inbfrq -1 imgfrq -1  -
        eps 1.0 cutnb 14 cutim 14 ctofnb 12 ctonnb 10 vswi bycb

    open unit 1 read unform name 1a_h2o+dmso.dcd
    traj query unit 1
    traj firstu 1

    set cnt = 1
    open unit 2 write form name 1a_chrm_h2o+dmso.enr
    echu 2
    set eadmso = 0
    set ea2dmso = 0
    set eawat = 0
    set ea2wat = 0
    set ealig = 0
    set ea2lig = 0

    define dmso select segid dmso end
    set resi = ?selires
    set nadmso = ?nsel

    define dmso select ires @resi end
    Calc nmoldmso = @nadmso / ?nsel

    define wat select segid tip3 end
    set resi = ?selires
    set nawat = ?nsel

    define wat select ires @resi end
    Calc nmolwat = @nawat / ?nsel
```

```
label getener

    traj read
    energy
    set ligenr = ?ener
    inte select .not. segid 1a end select .not. segid 1a end
    Calc ligenr = @ligenr - ?ener
    set esolv = ?ener
    inte select segid dmso end select all end
    Calc edmso = ?ener / @nmoldmso
    inte select segid tip3 end select all end
    Calc ewat = ?ener / @nmolwat

    Calc ealig = @ealig + @ligenr
    Calc eadmso = @eadmso + @edmso
    Calc eawat = @eawat + @ewat
    Calc ea2lig = @ea2lig + @ligenr * @ligenr
    Calc ea2dmso = @ea2dmso + @edmso * @edmso
    Calc ea2wat = @ea2wat + @ewat * @ewat

    echo @cnt @ligenr @edmso @ewat

    incr cnt by 1
if cnt le ?nfile goto getener


Calc ealig = @ealig / ?nfile
Calc eadmso = @eadmso / ( ?nfile )
Calc eawat = @eawat / ( ?nfile )
Calc ea2lig = @ea2lig / ?nfile
Calc ea2dmso = @ea2dmso / ( ?nfile )
Calc ea2wat = @ea2wat / ( ?nfile )

Calc sdlig = sqrt ( @ea2lig - @ealig * @ealig )
Calc sddmso = sqrt ( @ea2dmso - @eadmso * @eadmso )
Calc sdwat = sqrt ( @ea2wat - @eawat * @eawat )

echo # E(ligand) = @ealig +/- @sdlig
echo # E(dmso) = @eadmso +/- @sddmso
echo # E(wat) = @eawat +/- @sdwat

stop

awk
'{e+=$2;e2+=$2*$2;ed+=$3;ed2+=$3*$3;ew+=$4;ew2+=$4*$4;cnt+=1;}END{print
```

e/cnt"+/-"sqrt(e2/cnt-e*e/cnt/cnt), ed/cnt"+/-"sqrt(ed2/cnt-ed*ed/cnt/cnt), ew/cnt"+/-"sqrt(ew2/cnt-ew*ew/cnt/cnt)}' *.enr

---

D. Creating the Solvent Box

CHARMM input script for creating the 1:1 DMSO:H_2O v:v box

big_h2o_+dmso_dyna.pdb used in $H_{solution}$ CHARMM input script

---

```
* title
*

read rtf card name top_dmso.rtf
read param card name "/usr/local/charmm/c37a1dev/toppar/par_all22_prot.inp"
read rtf card name dmso.rtf append
read param card name dmso.prm append
!read param card name "/usr/local/charmm/c37a1dev/toppar/par_all22_prot.inp"
!read param card name ../1a_solvent_1-1/1a_chrm_dmso.prm append

goto biganlys
!goto rundyn
goto bigbox
if @analysis ne 0 goto analysis
if @process ne 0 goto process

read sequ tip3 216

generate tip3 noangl nodihe

read coor card name "/usr/local/charmm/c37a1dev/test/data/tip216.crd"

set ndel 1
label next
define size select segid tip3 end
calc nres = ?nsel / 3
calc i = int ( ?rand * @nres )
define atmi select ires @i end
open unit 1 write form name tmp
```

```
coor mind unit 1 select atmi end select type oh2 .and. .not. atmi end
system "awk '{if(/TIP3/){print "set j = ",$10}}' tmp > str"
stream str
define atmj select atom tip3 @j oh2 end
coor stat select atmi .or. atmj end

read sequ dmso 1
generate dmso
read coor pdb name dmso.pdb resid

coor orie select segid dmso end
coor trans xdir ?xave ydir ?yave zdir ?zave select segid dmso end
coor stat select segid dmso end

if @ndel eq 1 then
   rename segid d select segid dmso end
else
   join d dmso renumber
endif

delete atom select .byres. ( atmi .or. atmj ) end


incr ndel by 1
if ndel le 36 goto next

mini sd nstep 1000

write psf card name h2o_dmso.psf
write coor pdb name h2o_dmso.pdb
write coor card name h2o_dmso.chr

!goto process
stop



echo ?selires

stop

read rtf card name "/usr/local/charmm/c37a1dev/toppar/top_all36_cgenff.rtf"
read param card name "/usr/local/charmm/c37a1dev/toppar/par_all36_cgenff.prm"
!stream "~/charmm/c36a5dev/toppar/stream/toppar_water_ions.str"

read sequ dmso 1
```

```
generate dmso setup
ic param
ic seed 1 o1 1 s2 1 c3
ic build
print coor

write coor pdb name dmso.pdb
write coor card name dmso.chr

stop

label process

read sequ tip3 144
generate tip3 noangl nodihe

read sequ dmso 36
generate dmso
delete bond select type h1 end select type h2 end
write psf card name h2o_dmso_nobond.psf
!stop
read coor card name h2o_dmso.chr

coor orie

coor stat

crystal defi cubit 20 20 20 90 90 90
crystal build cutoff 9 noper 0
image byres xcen 0 ycen 0 zcen 0 select all end

faster on

mini sd nstep 200

shake bonh param tol 1e-6

open unit 1 write unform name h2o_dmso.dcd
dynamics cpt leap start timestep 0.001 nstep 20000 iprfrq 1000 -
      firstt 298 finalt 298 twindl -5 twindh 5 -
      ichew 1 ihtfrq 0 ieqfrq 0 -
      iuncrd 1 nsavc 100 -
      iasors 1 iasvel 1 iscvel 0 -
      inbfrq -1 imgfrq -1 echeck -1 -
      eps 1.0 cutnb 11 cutim 11 ctofnb 9 ctonnb 7 vswi bycb -
      ewald kappa 0.320 pmEwald qcor 1 order 4 fftx 32 ffty 32 fftz 32 -
```

```
            ntrfq 2000 -
            pconstant pmass 100.0 pref 1.0 pgamma 20.0  - !  Constant pressure
            Hoover tmass 50  refT 298


stop

label analysis

read sequ tip3 144
generate tip3 noangl nodihe

read sequ dmso 36
generate dmso

read coor card name h2o_dmso.chr

crystal defi cubit 20 20 20 90 90 90
crystal build cutoff 9 noper 0
image byres xcen 0 ycen 0 zcen 0 select all end

open unit 1 read unform name h2o_dmso.dcd
traj query unit 1

traj firstu 1 begin 20000

traj read

write coor pdb name h2o+dmso_dynlast.pdb

stop

label bigbox

read sequ tip3 144
generate tip3 noangl nodihe

read sequ dmso 36
generate dmso
read coor pdb name h2o+dmso_dynlast.pdb resi

coor stat

replica s nrep 8 select all end

delete atom select segid dmso .or. segid tip3 end
```

```
Calc boxhalf = 23 / 2
set x = -@boxhalf
set i = 0
label x
    set y = -@boxhalf
    label y
        set z = -@boxhalf
        label z
            incr i by 1
            coor trans xdir @x ydir @y zdir @z select segid s@i end
            incr z by 23
        if z le 23 goto z
        incr y by 23
    if y le 23 goto y
    incr x by 23
if x le 23 goto x

coor stat

write coor pdb name big_h2o+dmso.pdb
system "convpdb.pl -nsel DMSO -segnames -renumber 1 big_h2o+dmso.pdb >
big_dmso.pdb"
system "convpdb.pl -nsel TIP3 -segnames -renumber 1 big_h2o+dmso.pdb >
big_h2o.pdb"
replica reset
delete atom select all end

label rundyn
read sequ tip3 1152
generate wt00 noangl nodihe
read coor pdb name big_h2o.pdb resid
read sequ dmso 288
generate pro0
read coor pdb name big_dmso.pdb resid
rename segid tip3 select segid wt00 end
rename segid dmso select segid pro0 end


crystal defi cubit 46 46 46 90 90 90
crystal build cutoff 9 noper 0
image byres xcen 0 ycen 0 zcen 0 select all end

faster on

mini sd nstep 200
```

```
shake bonh param tol 1e-7

open unit 1 write unform name big_h2o_dmso.dcd
open unit 2 write form name big_h2o_dmso.res
dynamics cpt leap start timestep 0.0015 nstep 50000 iprfrq 2000 -
      firstt 298 finalt 298 twindl -5 twindh 5 -
      ichew 1 ihtfrq 0 ieqfrq 0 -
      iunwri 2 iunrea 2 iuncrd 1 nsavc 100 nsavv 0 nprint 2000 -
      iasors 1 iasvel 1 iscvel 0 -
      inbfrq -1 imgfrq -1 echeck 200 -
      eps 1 cutnb 11 cutim 11 ctofnb 9 ctonnb 7 vswi bycb -
      ewald kappa 0.320 pmEwald order 4 fftx 32 ffty 32 fftz 32 -
      ntrfq 2000 -
      pconstant pmass 500 pref 1 pgamma 20  - !  Constant pressure
      Hoover tmass 1000  refT 298

write coor pdb name big_h2o_+dmso_dyna.pdb

stop

label biganlys

    read sequ tip3 1152
    generate tip3 noangl nodihe
    read sequ dmso 288
    generate dmso
    read coor pdb name big_h2o_+dmso_dyna.pdb resi

    crystal defi cubic 46 46 46 90 90 90
    crystal build cutoff 15 noper 0
    image byres xcen 0 ycen 0 zcen 0 select all end

    energy -
          inbfrq -1 imgfrq -1  -
          eps 1.0 cutnb 14 cutim 14 ctofnb 12 ctonnb 10 vswi bycb

    open unit 1 read unform name big_h2o_dmso.dcd
    traj query unit 1
    traj firstu 1

    set cnt = 1
    open unit 2 write form name 1a_h2o+dmso.enr
    echu 2

    define dmso select segid dmso end
```

```
set resi = ?selires
set nadmso = ?nsel

define dmso select ires @resi end
Calc nmoldmso = @nadmso / ?nsel

define wat select segid tip3 end
set resi = ?selires
set nawat = ?nsel

define wat select ires @resi end
Calc nmolwat = @nawat / ?nsel

label getener

    traj read
    inte select segid dmso end select all end
    Calc edmso = ?ener / @nmoldmso
    inte select segid tip3 end select all end
    Calc ewat = ?ener / @nmolwat

    echo @cnt @edmso @ewat

    incr cnt by 1
if cnt le ?nfile goto getener

stop


awk     '{ed+=$2;ed2+=$2*$2;ew+=$3;ew2+=$3*$3;cnt+=1;}END{print     ed/cnt"+/-
"sqrt(ed2/cnt-ed*ed/cnt/cnt), ew/cnt"+/-"sqrt(ew2/cnt-ew*ew/cnt/cnt)}' *.enr


-44.5787+/-0.355467 -16.0828+/-0.273378
```

Appendix C

For Chapter 5 Design and Implementation of a Graduate-Level Class Project Centered on

Editing Wikipedia

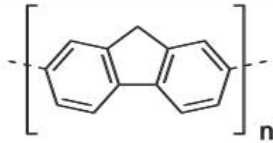A. Example Student Completed Entry – Polyfluorene

Polyfluorene

From Wikipedia, the free encyclopedia

> This is an old revision of this page, as edited by Aromaticmoleculessmell (talk | contribs) at 16:48, 11 April 2011. It may differ significantly from the current revision (//en.wikipedia.org /wiki/Polyfluorene).

(diff) ← Previous revision | Latest revision (diff) | Newer revision → (diff)

Polyfluorenes are an important class of polymeric materials. They are relevant to both academic and industrial research because of their optical and electrical properties. Furthermore they are a prototypical conjugated polymer which can be used to discuss property tuning; polyfluorenes are the only class of conjugated polymers which can be tuned to emit light throughout the entire visible region. They are not a naturally occurring material, but rather, they are designed and synthesized for their applications. Modern chemistry has enabled adaptable synthesis and control over polyfluorenes, which has facilitated use in many organic electronic applications. Polyfluorenes are primarily interesting because of the optoelectronic properties imbued by their chromophoric constituents and their extended conjugation. The design of polyfluorene derivatives relies on the character and properties of their monomers. Thus, the discovery and development of these polymeric repeat units has had a profound influence on the development of polyfluorenes.

Polyfluorene	
Identifiers	
CAS number	95270-88-5 ✓
Properties	
Molecular formula	$(C_{13}H_8)_n$
Molar mass	Variable
✓ (verify) (what is: ✓/✗?)	
Except where noted otherwise, data are given for materials in their standard state (at 25 °C, 100 kPa)	
Infobox references	

Fluorene-based polymers are of great interest to industrial researchers because of their ability to act as electro and photoactive materials. As with many conjugated polymers, researchers have always been interested in using polyfluorenes in light-emitting diodes, field-effect transistors (FET), and plastic solar cells. As stated previously polyfluorenes gave high photoluminescence quantum yields, this along with their excellent solubility and the ability to control their properties by substituting different groups at the 9,9 position of the fluorene monomer has motivated researchers to use polyfluorenes as blue light emitters in polymer light-emitting diodes.[1]

Contents

281

History of polyfluorenes

Fluorene, a principal repeat unit in polyfluorene derivatives, was isolated from coal tar and discovered by Marcellin Berthelot prior to 1883.[2][3][4] So-named due to its interesting fluorescence, fluorene became the subject of chemical-structure related color variation (visible rather than luminescent), among other things, throughout the early to mid-20th century. Since it was an interesting chromophore researchers wanted to understand which parts of the molecule were chemically reactive, and how substituting these sites influenced the color. For instance, by adding various electron donating or electron accepting moieties to fluorene, and by reacting with bases, researchers were able to change the color of the molecule.[2][5][6]

The physical properties of the fluorene molecule were recognizably desirable for polymers; as early as the 1970s researchers began incorporating this moiety into polymers. For instance, because of fluorene's rigid, planar shape a polymer containing fluorene was shown to exhibit enhanced thermo-mechanical stability.[7] Perhaps more interesting, however, was the promise of integrating the optoelectronic properties of fluorene into a polymer. Reports of the oxidative polymerization of fluorene (into a fully conjugated form) exist from at least 1972[8]. However, it was not until after the highly publicized high conductivity of doped polyacetylene, presented in 1977 by Heeger, MacDiarmid and Shirakawa, that substantial interest in the electronic properties of conjugated polymers was aroused.

As interest in conducting plastics grew, fluorene again found application. The aromatic nature of fluorene makes it an excellent candidate component of a conducting polymer because it can stabilize and conduct a charge; in the early 1980s fluorene was electropolymerized into conjugated polymer films with conductivities of 10^{-4} S cm^{-1}.[9][10] Additionally, the optical properties (such as variable luminescence and visible light absorption) that accompany the extended conjugation in polymers of fluorene have become increasingly attractive for device applications. Throughout the 1990s and into the 2000s, many devices such as OLEDs[11], organic solar cells.[12], organic thin film transistors[13], and biosensors[14][15] have all taken advantage of the luminescent, electronic and absorptive properties of polyfluorenes.
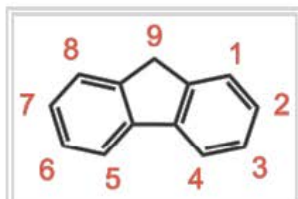
282

Properties of polyfluorenes

Figure 1. The fluorene molecule is most commonly linked at the 2 and 7 positions in polyfluorene derivatives. Also, the 9 position is typically where side chains are attached.

Polyfluorenes encompass an important class of polymers which have the potential to act as both electroactive and photoactive materials. This is partly due to the shape of fluorene. Fluorene is mostly planar[16][17]; p-orbital overlap at the linkage between its two benzene rings results in conjugation across the molecule. This in turn allows for a reduced band gap due to the delocalized excited state molecular orbitals.[18]

Figure 2. This is the photoluminescence of two very similarly structured polyfluorene derivatives. The one on the left has the structure in Figure 6, and the one on the right has the structure in Figure 3.

Furthermore, since the degree of delocalization and the spatial location of the orbitals on the molecule is influenced by the electron donating (or withdrawing) character of its substituents, the band gap energy can be varied. This chemical control over the band gap directly dictates the color of the molecule by limiting the energies of light which it absorbs.[1]

Interest in polyfluorene derivatives has increased because of their high photoluminescence quantum efficiency, high thermal stability, and also because of their facile color tunability, which can be obtained by introducing low-band-gap co-monomers. Research in this field has increased significantly due to potential application in organic light-emitting diodes (OLEDs). In this application, polyfluorenes are desirable because they are the only family of conjugated polymers that can emit colors spanning the entire visible range with high efficiency and low operating voltage. Furthermore, polyfluorenes are relatively soluble in most solvents, which makes them ideal for general applications.[19]

Figure 3. This polyfluorene derivative has a structure similar to that in Figure 6, except that the alcohol side chains can participate in ESIPT with the neighboring oxadiazole nitrogens causing a red-shifted emission. The meta-linkages in the backbone impart solubility in lieu of multiple side chains.

Another important quality of polyfluorenes is their thermotropic liquid crystallinity which allows the polymers to be used on rubbed polyimide layers. Thermotropic liquid crystallinity refers to the polymers ability to exhibit a phase transition into the liquid crystal phase as the temperature is changed. This is very important to the development of LCD's (liquid crystal display) because the synthesis of liquid crystal displays requires that the liquid-crystal molecules at the two glass surfaces of the cell be aligned parallel to the two polarizer foils.[20] This can only be done by coating the inner-surfaces of the cell with a thin, transparent

283

film of polyamide which is then rubbed with a velvet cloth. Microscopic grooves are then generated in the polyamide layer and the liquid crystal in contact with the polyamide, which is polyfluorene, can align in the rubbing direction. In addition to LCDs, polyfluorene can also be used to synthesize LEDs. By using polyfluorene, LEDs have been synthesized that can emit polarized light with polarization ratios of more than 20 and with brightness of 100 cd m^{-2}. Even though this is very impressive it is not sufficient for general applications. [21]

Challenges associated with polyfluorenes

Researchers have encountered several issues with polyfluorenes which inhibit their use in many general applications. Polyfluorenes often show both excimer and aggregate formation upon thermal annealing or when current is passed through them. Excimer formation involves the generation of dimerized units of the polymer which emit light at lower energies than the polymer itself. This hinders the use of polyfluorenes for most applications, including light-emitting diodes (LED). When excimer or aggregate formation occurs this lowers the efficiency of the LEDs by decreasing the efficiency of charge carrier recombination. Excimer formation also causes a red shift in the emission spectrum.[22]

In addition to excimer and aggregate formation, polyfluorenes can also undergo decomposition. There are two known ways in which decomposition can occur; the first involves the oxidation of the polymer which leads to the formation of an aromatic ketone. This carbonyl group that is formed quenches the fluorescence. The second process results in aggregation formation, which then leads to a red-shifted fluorescence and reduced intensity, be exciton migration and relaxation through excimers. [23]

Researchers have attempted to eliminate excimer formation and enhance the efficiency of polyfluorenes by copolymerizing polyfluorene with anthracene and end-capping polyfluorenes with bulky groups which could sterically hinder excimer formation. Additionally, researchers have tried adding large substituents at the ninth position of the fluorine in order to inhibit excimer and aggregate formation. Furthermore, researchers have tried to improve LEDs by synthesizing fluorene-triarylamine copolymers and other multilayer devices that are based on polyfluorenes that can be cross-linked. These have been found to have high brightness and reasonable efficiencies.[24]

Aggregation has also been combated through chemical structure variation. For example, when conjugated polymers aggregate (as they have a natural tendency to do in the solid state), their emission can be self-quenched, reducing luminescent quantum yields and reducing luminescent device performance. In opposition to this tendency, researchers have used tri-functional monomers to create highly branched polyfluorenes which resist aggregation due to their bulkiness. This design strategy has achieved luminescent quantum yields of 42% in the solid state.[25] Unfortunately, this solution reduces the ease of processability of the material because branched polymers have increased chain entanglement.

Another problem commonly encountered by polyfluorenes is a commonly observed broad green, parasitic emission which detracts from the color purity and efficiency needed for an OLED. [26] [19][1] Initially attributed to excimer emission, this green emission has been shown to be due to the formation of ketone defects along the fluorene polymer backbone (oxidation of the 9 position on the monomer in Figure 1) at incompletely substituted 9 positions of the fluorene monomer. [1] Routes to combat this

284

involve ensuring full substitution of the monomer's active site, or including aromatic substituents. [1] These solutions may present sub-optimal structures (in terms of bulkiness) or may be synthetically difficult.

Synthesis and design of polyfluorenes

One of the reasons that conjugated polymers, polyfluorene included, are such a versatile class of material is because of the variability of relevant properties that molecular design and synthesis afford. Polyfluorenes are designed and synthesized for their applications, usually requiring appropriate luminescent emission, appropriate absorption wavelengths and processability, among other properties. [19] As mentioned above, the color of conjugated molecules can be designed through control over the electron donating or withdrawing character of the substituents on fluorene or similarly, of the comonomers in polyfluorene (as in Figure 4). [27][28][20] Processability, on the other hand, is primarily the result of the solubility of the polymers because solution state processing is very common. Since conjugated polymers, with their planar structure, tend to aggregate bulky side chains are added (to the 9 position of fluorene) to prevent this and to instill solubility. With these concepts in mind, an understanding of the synthesis of polyfluorenes can be developed.
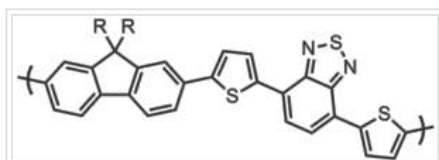
Figure 4. This is the structure of a common low band-gap polyflourene derivative.[12] It has electron donating fluorene (left) and electron withdrawing benzothiadiazole (mid right between two thiophenes) monomers which allow for a reduced band gap due to charge transfer absorption.

Oxidative polymerization

The earliest polymerizations of fluorene were oxidative polymerization with $AlCl_3$[8] or $FeCl_3$[29][30], and more commonly electropolymerization[9][10]. Electropolymerization is an easy route to obtain thin, insoluble conducting polymer films. Unfortunately it does not provide easy control over the site on the monomer from which chain growth occurs and since the polymer is insoluble, processing and characterization are difficult. Oxidative polymerization produces a similarly poor site-selectivity on the monomer for chain growth resulting in poor control over the regularity of the polymers structure, especially for asymmetric monomers. However, oxidative polymerization does produce soluble polymers (from side-chain containing monomers) which are more easily characterized with nuclear magnetic resonance (NMR).

285

Cross coupling polymerizations

The design of polymeric properties requires great control over the structure of the polymer. For instance, low band gap polymers require regularly alternating electron donating and electron accepting monomers (such as that in Figure 4 with fluorene on the left and benzothiadiazole on the mid-right). [12] [1] More recently, many popular cross-coupling chemistries have been applied to polyfluorenes and have enabled controlled polymerization; Palladium catalyzed cross couplings such as Suzuki coupling [31] [28] [32] [25], Heck coupling [33], etc., as well as nickel catalyzed[20] Yamamoto [27][11] and Grignard [34] coupling reactions have been applied to polymerization of fluorene derivatives. Such routes have enabled excellent control over the properties of polyfluorenes; the polymer in Figure 4, with a band gap of 1.78 eV when the side chains are alkoxy[12], appears blue because it is absorbing in the red wavelengths.
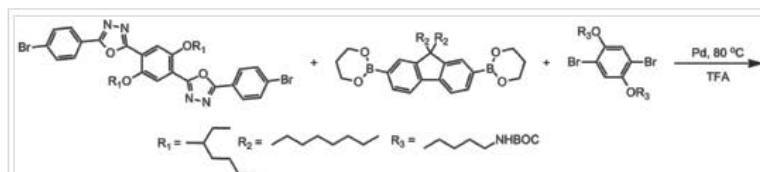
Figure 5. These are the monomers used to obtain the complex polyfluorene derivative in Figure 6. This Suzuki polymerization utilizes a palladium cross coupling between monomers with halogens and boronic esters.[35][14]

Design of polyfluorenes

Modern coupling chemistries allow other properties of polyfluorenes to be controlled through implementation of complex molecular designs. For instance, using Suzuki coupling (Figure 5) the complicated polymer in Figure 6 was produced. It has excellent (94%, solution in chloroform) photoluminescent quantum yields, partly due to its fluorene monomer, excellent stability, due to its oxadiazole comonomer, good solubility, due to its many and branched alkyl side chains, and has an amine functionalized side chain for tethering to other molecules or to a substrate.[14] The luminescent color of polyfluorenes can be changed, for example, (from blue to green-yellow in Figure 2) by adding functional groups which participate in excited state intramolecular proton transfer (ESIPT). Exchanging the alkoxy side chains for alcohol side groups (Figure 3) allows for energy dissipation (and a red-shift in emission) through reversible transfer of a proton from the alcohol to the nitrogen (on the oxadiazole). These complicated molecular structures were engineered to have these properties and were only able to be realized through careful control of their ordering and side group functionality through polymerization chemistry.

286

Figure 6. This is the structure of a complex polyflourene derivative. It contains multiple monomers, including fluorene on the far right, which give it desirable characteristics[14]

Industrial uses of polyfluorene

OLEDs

Main article: OLED

In recent years many industrial efforts have been focused on tuning color using polyfluorenes. It was found that by doping green or red emitting materials into polyfluorenes one could tune the color emitted by the polymers. Since polyf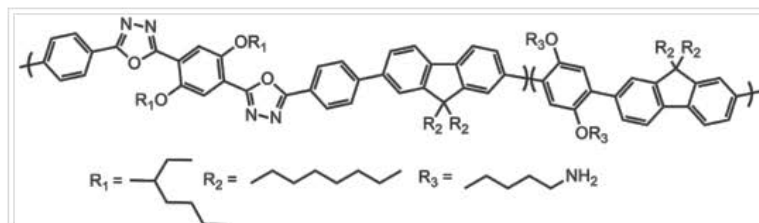luorene homopolymers emit higher energy blue light, they can transfer energy via FRET to lower energy emitters. In addition to doping, it was found that one could tune the color of polyfluorenes by copolymerizing the fluorene monomers with other low band gap monomers. Researchers at the Dow Chemical Company synthesized several fluorene-based copolymers by alternating copolymerization using 5,5-dibromo-2,2-bithiophene which showed yellow emission and 4,7-dibromo-2,1,3-benzothiadiazole, which showed green emission. Other copolymerizations are also suitable; researchers at IBM performed random copolymerization of fluorene with 3,9(10)-dibromoperylene,4,4-dibromo-R-cyanostilbene, and 1,4-bis(2-(4-bromophenyl)-1-cyanovinyl)-2-(2-ethylhexyl)-5-methoxybenzene. Only a small amount of the co-monomer, approximately 5%, was needed to tune the emission of the polyfluorene from blue to yellow. This example further illustrates that by introducing monomers that have a lower band gap than the fluorene monomer, one can tune the color that is emitted by the polymer. [20]

Substitution at the ninth position with various moieties has also been examined as a means to control the color emitted by polyfluorene. In the past researchers have tried putting alkyl substituents on the ninth position, however it has been found that by putting bulkier groups, such as alkoxyphenyl groups, the polymers had enhanced blue emission stability and superior polymer light-emitting diode performance (compared to polymers which have alkyl substituents at the ninth position).[21]

Polymer solar cells

Main article: Polymer solar cell

Polyfluorenes are also used in polymer solar cells (as in Figure 7) because of their affinity for property tuning. Copolymerization of fluorene with other monomers allows researchers to optimize the absorption

287

and electronic energy levels as a means to increase the photovoltaic performance. For instance, by lowering the band gap of polyfluorenes, the absorption spectrum of the polymer can be adjusted to coincide with the maximum photon flux region of the solar spectrum.[12] [36] This helps the solar cell absorb more of the suns energy and to increase its energy conversion efficiency; donor-acceptor structured copolymers of fluorene have achieved efficiencies above 4% when their absorption edge was pushed to 700 nm. [37]

The voltage of polymer solar cells has also been increased through the design of polyfluorenes. These devices are typically produced by blending electron accepting and electron donating molecules which help separate charge to produce power. In polymer blend solar cells, the voltage produced by the device is determined by the difference between the electron donating polymer's highest occupied

Figure 7. This is a laboratory scale polymer:PCBM blend solar cell. Polyfluorenes are utilized in similar devices.

molecular orbital (HOMO) energy level and the electron accepting molecules lowest unoccupied molecular orbital energy level. By adding electron withdrawing pendant molecules to conjugated polymers, their HOMO energy level can be lowered.[36] For instance by adding electronegative groups on the end of conjugated side chains, researchers lowered the HOMO of a polyfluorene copolymer to -5.30 eV and increased the voltage of a solar cell to 0.99 V.[37][36][38]

Typical polymer solar cells utilize fullerene molecules as electron acceptors because of their low LUMO energy level (high electron affinity). However the tunability of polyfluorenes allows their LUMO to be lowered to a level appropriate for use as an electron acceptor. Thus, polyfluorene copolymers have also been used in polymer:polymer blend solar cells, where their electron accepting, electron conducting and light absorbing properties enhance device performance. [39][40]

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290

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B. Slides for an Example Editing Tutorial Presentation

An editing-tutorial session was approximately 50 min long and was best when students were in a computer lab or brought with them a laptop computer to follow along with the instructions.

Basics of Editing Wikipedia

1
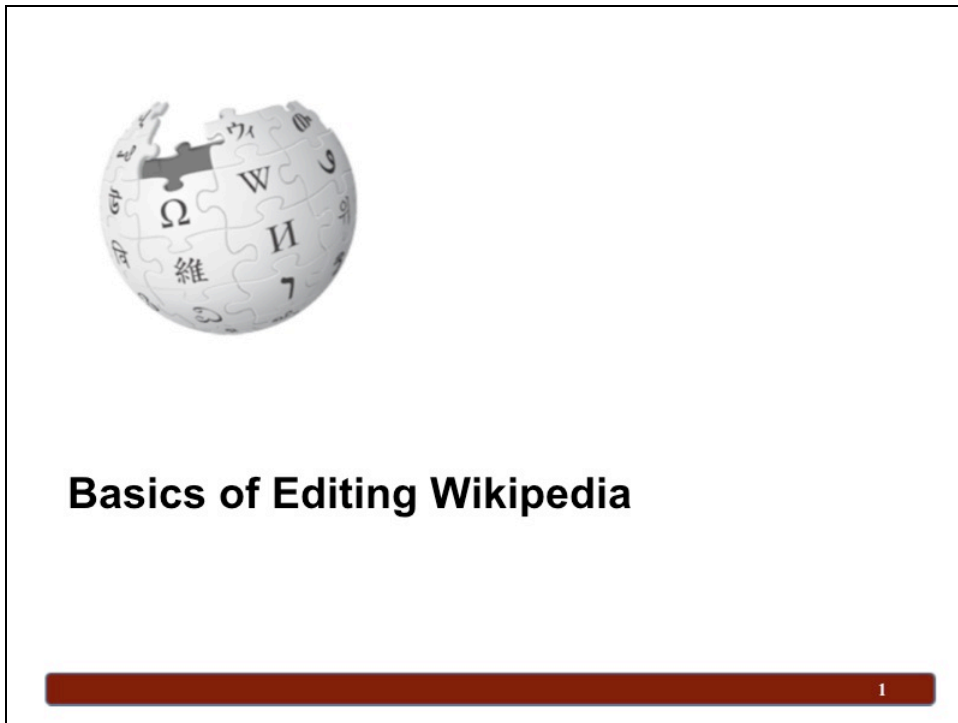
Objectives

- discuss what makes a good Wikipedia article
- create username and userpage
- know how to use article discussion pages and user talk pages
- know editing basics
- able to add references
- able to add images
- where to find help

2

What is Wikipedia? The 5 Pillars

1. Wikipedia is an encyclopedia.
2. Wikipedia has a neutral point of view.
3. Wikipedia is free content that anyone can edit and distribute.
4. Wikipedians should interact in a respectful and civil manner.
5. Wikipedia does not have firm rules besides the five general principles presented here.

3

What Wikipedia 'is not'…

- A paper encyclopedia or a dictionary.
- A publisher of original thought.
- An indiscriminate collection of information.
- A personal blog or social networking vehicle.
- A means of promotion.
- A repository of links, images, or media files.
- A directory, manual, textbook, or scientific journal.
- A democracy, bureaucracy, battleground or anarchy.
- A crystal ball.

4

What is a good Wikipedia Article?

- Thoughts on the Diamond site?
- What was good?
- What could be improved?

5

Setting up a User Account

1. go to en.wikipedia.org
2. click on Log in/create account, located in the top right hand corner.
3. click on "create one" next to "Don't have an account?..."
4. choose your username
   - you have the option to have anonymity
5. select your password
6. click create account

6

Creating a User Page

1. Click "Start the User:Username page"
2. Enter information about yourself into the empty text box
3. Click "Save page"
Note: You may be prompted to create a userpage and provide a short bio immediately after creating your account. The account creation process is being revamped, so if it differs from what's described here, just go with the flow!

7

Article vs Discussion/Talk Page

Article | Discussion | Read | Edit | View history

Public policy
From Wikipedia, the free encyclopedia

Where the article content is.
● Contains limited editorial markings
● No information about editors

Article | Discussion | Read | Edit | New section

Talk:Public policy
From Wikipedia, the free encyclopedia

Where editors talk about:
● Editing plans
● Potential problems
Also:
● You can list sources or build an outline here
● You will put peer review comments here
● Sign your comments (~~~~)
● Don't delete other people's comments

8

Practice

Once you have chosen your topic, leave a note on the talk page of that topic telling readers that you will be working on improving the page through out the semester.

click on discussion, then click on edit

don't forget to sign your note with your username by typing ~~~~

9

296

Editing

Editing (cont.)

Create a "Sandbox" to practice editing

- Let's create a sandbox in your **own userspace**
  - click on your username (top right)
  - click on edit
  - type [[/sandbox]] on your user page
  - save page at bottom
  - notice that the link is RED that is because that page has not been created yet.
  - click on it, type something, then scroll to the bottom and save the page.

12

Adding References

- will not see the code for references
  - recommend using "preview" button


```
B  I  ✇ ☒ 📄  ▸ Advanced  ▸ Special characters  ▸ Help

Different policy schools tackle policy analysis differently. The [[Harris School of Public Policy Studies]] at the
[[University of Chicago]] has a more quantitative and economics approach to policy, the [[Heinz College]] at [[Carnegie
Mellon]] uses [[computational science|computational]] and [[empirical]] methods, while the [[John F. Kennedy School of
Government]] at [[Harvard University]] and the [[Trent Lott Public Policy Leadership Institute]] at the [[University of
Mississippi]] have a more political science and leadership based approach. The [[Indiana University School of Public and
Environmental Affairs]] provides traditional public policy training with multidisciplinary concentrations available in the
environmental sciences and nonprofit management.{{Citation needed|date=July 2010||this is excellent material, but still needs
sourcing from the various departments}}

==See also==
* [[List of public administration schools]]
* [[Mandate (politics)]]
* [[Overton window]]

==References==
<references/>

==External links==
* [http://www.appam.org/home.asp Association for Public Policy Analysis and Management]
```

==References==

13

298

Adding References (cont.)

- there is now a very nice wizard for adding references
- anything between <ref> and </ref> are part of your reference

Editing Rock and roll
From Wikipedia, the free encyclopedia

B *I* ▸ Advanced ▸ Special characters ▸ Hel ▾ Cite

Templates ▾   amed references   Error check
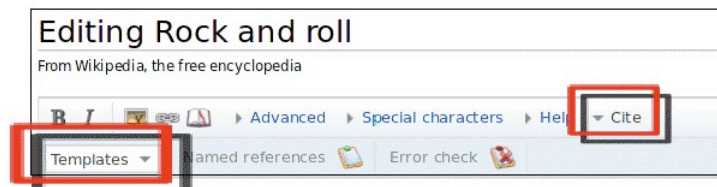
- Press "Cite", then select source type from "Templates"
- Type in information about the source into the appropriate boxes
- Recommended: add a reference name if using the citation multiple times throughout the article

14

Uploading Images to Wikimedia Commons
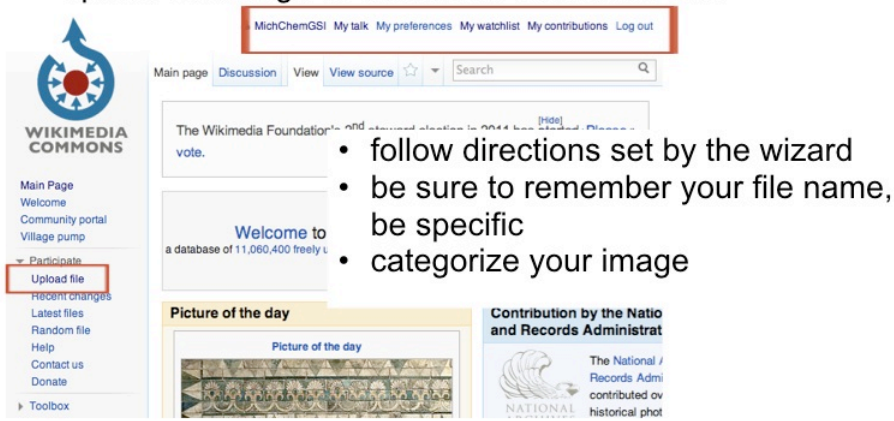
Things to keep in mind:

- you need to build/create your own images
  - you **cannot**, under any circumstance, upload an image you do not hold the copyright to as a "place holder"
- modify images from literature
  - remember your audience
  - no need to refer to fig.1 etc in text, place image near relevant text
- please refer to Chemistry Manual of Style for how chemical structures should be drawn

15

Uploading Images

- before you can use an image in Wikipedia, you need to upload the image to Wikimedia Commons first

MichChemGSI My talk My preferences My watchlist My contributions Log out

Main page Discussion   View View source   Search

The Wikimedia Foundation's 2nd steward election in 2011 has started. [Hide] Please vote.

WIKIMEDIA COMMONS

Main Page
Welcome
Community portal
Village pump
▾ Participate
Upload file
Recent changes
Latest files
Random file
Help
Contact us
Donate
▸ Toolbox

Welcome to
a database of 11,060,400 freely u

- follow directions set by the wizard
- be sure to remember your file name, be specific
- categorize your image

Picture of the day

Picture of the day

Contribution by the Natio and Records Administrat

The National /
Records Admi
contributed ov
historical phot

NATIONAL

16

Where to get help

- is there a page that is doing something you like?
  - just c/p the code and change the relevant information
- write message on my talkpage
  - user:MichChemGSI
  (http://en.wikipedia.org/wiki/User_talk:MichChemGSI)
- Michigan Wikipedians
  - Student organization centered around editing Wikipedia
- Internet Relay Chat (IRC) channel
  - To get instant help with editing problems
  - #wikipedia-en-classroom
  (http://webchat.freenode.net/?channels=wikipedia-en-classroom)
- Type WP: XXXX into the search box (example WP:infobox or WP:IRC)

17

300

C. Other Graduate Courses at Michigan, Student Open-Response Survey

Below are selected student responses to prompts about the Wikipedia project; the primary instructor for these courses was not Professor Anne McNeil. However, I did provide guidance for these courses in the Wikipedia project by developing the syllabus, giving the in-class editing tutorial, and providing editing help when needed. In one of the following courses, the primary instructor assigned both a traditional review and the Wikipedia project. Overall, the students felt that they were not given enough guidance on what was expected for each project and how the two were differentiated. However, similar to the results from assigning the Wikipedia project alone, the students who were required to do both assignments still expressed that they benefited from the opportunity to do an in depth investigation of a topic and to communicate science to the general public.

- "It was a little confusing in terms of the project paper vs. wikipedia entry. Could be more specific on what you would expect for each."
- "I think more guidelines about how specific we should be. How much in depth should we write. Also if wiki page and case study should be written different (which I think they should be) then you should explain how they should be different."

Appendix D

For Chapter 6 Development of an Undergraduate-Level Class Project and Student-Run

Organization Centered on Editing Wikipedia

A. Weekly Assignments for Wikipedia Project in SSG Design U1

Week 1   Brief overview of Wikipedia project

Although the Wikipedia is an open and editable resource, it is still governed by some stringent policies and a hierarchical editorial structure. On the other hand, if you are willing to learn the rules of the game, you can play, too. The Wikipedia and its users benefit when thoughtful people with particular expertise seek to improve this public resource. As a semester-long project, your SSG section is going to adopt and improve a Wikipedia entry related to organic chemistry. We will be pushing on the frontiers of Wiki entries by including types of items that are not yet typical, and we will be pushing on the frontiers of undergraduate education by exploring whether a large group of undergraduate students can make this contribution in the first place.

To date, members of the department have tested this idea out with graduate students in their graduate level classes, where students have edited some fairly high-level articles.

Now it is your turn! One of the classical ways of referring to common and usual organic reactions is by the name or names of the person who discovered and/or popularized it. The 2010 Nobel Prize in Chemistry went to Richard Heck, Ei-ichi Negishi, and Akira Suzuki. Not surprisingly, the reactions for which they were awarded the Nobel Prize are known as the Heck Reaction, the Negishi Coupling, and the Suzuki Coupling. These are examples of Named Organic Reactions.

Although it is not as common as it was a few years ago, the inversion of configuration that accompanies an S_N2 reaction was known for many years as a Walden Inversion. When you use alkaline potassium permanganate to oxidize a double bond, you are using Baeyer's Reagent. And one of the poisoned catalysts for hydrogenation of alkynes

(palladium on calcium carbonate, doped with various forms of lead) is know as the Lindlar catalyst. In the years before people understood about reaction mechanisms, using a person's name was the most convenient way to index and communicate about chemical transformations. You will encounter many of these named reactions. Today, although the practice is hardly necessary, it is still a matter of some pride among chemists to end up with a reaction named after you (and still a matter of pride for trivia buffs to prove you know these names).

During the first few weeks of the term, you are going to be learning about becoming responsible wiki editors, and you will be selecting the Wikipedia entry that your SSG section will be editing. For each entry, there will be 4 distinct tasks:

(1) to clean up the entry, in terms of text and/or images
(2) to create a rational animation for an exemplar mechanism
(3) to overview the history of the reaction
(4) to identify the key spectroscopic features that characterize the reaction

Wikipedia Project on Named Organic Reactions
Assistants:

Leader tasks: Familarize yourself with Wikipedia language: userpages, discussion pages, help line through IRC. Look over Wikipedia Manual of Style for Chemistry: http://en.wikipedia.org/wiki/Wikipedia:Manual_of_Style_(chemistry)
Assistant tasks: 		Help SSG leaders with simple editing tasks
In class: 	Introduce some of the features of Wikipedia from our wiki-assistants
Learn how to create a username

Wikipedia Assignment #1

<u>Goal</u>: To think of yourselves as Wikipedia editors

Create a username
Do not use your real name or your umich unique name, nothing that could connect your username to you, but still would be unique to you. (e.g.: my friend pj plays the piano, so he is pjthepiano). Try not to have something relating to chemistry, you don't want to seem precocious.

Include your email when you sign up, this way your SSG leaders can contact you about your pages through the Wiki interface.
Email your SSG leader your username
Begin to look at the Wikipedia pages for the various named reactions
<u>http://en.wikipedia.org/wiki/List_of_organic_reactions</u>

The SSG leaders have already screened these reactions and helped to narrow down these choices. You are not responsible for selecting one these (yet!), but it will be useful for you to see the type of entries on which you will be working this semester. If one of these begins to appeal to you as a work target, start to think about your argument for it should be the one that your SSG section ends up selecting.

Appel	Baeyer-Villiger Oxidation
Baeyer's Reagent	Baker-Venkatarman rearrangement
Dakin-West Reaction	Edman degredation
Jones Oxidation	Fischer glycosidation
Hammick Reaction	Halohydrin formation
Japp-Maitland condensation	Kornblum Oxidation
Leuckart Reaction	Pellizzari Reaction
Perkin Reaction	Ritter Reaction
Robinson-Gabriel Synthesis	Swern oxidation

Week 2

Leader tasks: Leaders make their userpages before SSG meetings
Assistant tasks: Be available to help leaders create userpages, walk through
demo for creating and editing userpages
In class: Continue presentation about wiki editing
                Finalize groups (3-4 people/group)
                Demo for students to "create" and "edit" userpages

Wikipedia Assignment #2

Goals: To think of yourselves as Wikipedia editors
                Creating links and simple editing
                Determine the mechanism that your SSG section will work on this
semester

WikiProject Chemistry assesses articles on a scale for which the top ranking is A-Class. Become familiar with the criteria that are used by this assessment; after all, wouldn't it be swell to end up with an A-Class article? Be prepared to briefly discuss the criteria, and provide an example or two of evidence to back up what you mean by any given criterion.

In your assigned groups, pick a reaction from the list (see Week #1) that you will work on this term. Be prepared to make an argument for why this would be an interesting article to work on.

familiarize yourself with "userpages"
example: SSG leader's page (now has all students' usernames)
in your userpage add links of the reaction that your group of 3-4 proposes to work on this semester
write a little bit in your userpage as to why you think this reaction's Wikipedia page would be interesting to work on this semester

Week 3

SSG Leader tasks: Review the additions to the userpages, note some examples
for class
                            Copy over the selected article into the leader's space
Assistant tasks: Show leaders page history tab and comparison feature.
In class: Discuss the criteria for an A-Class wiki article
                Leaders review noteworthy remarks made on userpages
                Groups spend a few minutes proposing which reaction the SSG ought to
work on
                Figure out a process for the group to select which reaction to work on, and
do it
"Page history"/"comparison of page"/"discussion page" demo (allows students to see
what changes have been made in the sandbox by each other in the SSG)
                Assign a member from each team to report out on the history research next
week
                Assign a member from each team to report out on analysis & possible
edits

Wikipedia Assignment #3

Goals: Begin to do research into historical aspects of the reaction
                Begin to list the sorts of edits, additions and changes to do on the article

(1) The team should spend some team-time doing some research (be creative) about the
scientist(s) and chemical background of the SSG's Named Reaction. Who was this
person? Where did they do their work? What were some of the exact reactions performed
(complete citations)? Use more than the internet for your searching! We have an
exceptionally competent chemistry librarian on campus; meet her! Although the final
product will not be a review, you should assemble as much information as you can about
a topic so that you know what to chose from – after all, Class-A articles don't grow on
trees!

(2) The team should sit with the actual Wiki article for the SSG's Named Reaction and
think about what aspects of the article are in good shape, what needs to be changed, and
what needs to be added (text and pictures).

Wiki Project Checklist:
                History: start doing research
                Animation: nothing
                Spectroscopy: nothing
                Editing: start doing analysis

Week 4

SSG Leader tasks: Review experimental sections of journal articles and how to get the supplementary information. Bring some examples of simple molecules to class, with references and the spectroscopic data, to analyze as a group.

Assistant tasks: Be familiar with the history/past edits of the mechanisms chosen

In class: Team member reports on historical research results

SSG as a whole begins to rank these in value AND archives them (somehow)

SSG decides what else might be needed for the history
Team member selected for historical report next week
Team member reports on lists of edits and changes to make
SSG as a whole begins to build a consensus on these
Team member selected for edits/changes report next week
Team member selected to report out on spectroscopy and mechanism

Wikipedia Assignment #4

Goals: Conclude research into historical aspects of the reaction
Refine the list the edits, additions and changes to do on the article

(1) Based on the SSG meeting, the team should conclude its research into the history of the reaction

(2) Based on the SSG meeting, the team should revisit the Wiki article and refine the list of changes, edits, etc, that they think are needed

(3) The team should start to do its research on the mechanism of the reaction, working on the traditional, static, curved arrow version. Pick at least 3 real examples of the reaction from the recent literature (citations needed). In these recent references, the authors will have reported on the structure of the product resulting from the reaction. Be sure to copy the experimental information and get a copy of the spectra from the supplementary information, if available, and think about what are the spectroscopic clues that allowed the experimentalist to determine that a reaction has taken place.

Wiki Project Checklist:
History: conclude doing research
Animation: start doing research
Spectroscopy: start identifying characteristics
Editing: refine list of suggestions

Week 5

SSG Leader tasks: Discuss and come up with a consensus for how to approach a PI for the spectroscopic information that is needed for the project. Think about what Plan B ought to be.

Assistant tasks: general oversight, keeping up with the process

In class: Team member reports on historical research results
          SSG comes to consensus on what materials will be used; how to distribute to all
          Team member selected for historical draft (decide format)
          Team member reports on final list of edits and changes to make
          SSG comes to a consensus on these; archive this
          Team member selected to incorporate draft edits to Wiki article (decide format)
          Team member reports out on spectroscopy and mechanism
          Select a set of 5 examples of actual reactions and spectra that are illustrative –
                    (this might take a second round of research to get it refined)
          Discuss strategy for contacting faculty members about getting good spectra
          Team member selected to draft memo to faculty members for spectra
          Come to consensus on mechanism, or identify what else is needed to get there

Wikipedia Assignment #5

Goals: Write a draft of the historical aspects of the reaction for the Wiki article (format?)
          First draft of edits to Wiki article (format?)
          Identify what else, if anything, is needed for understanding the mechanism
          Draft the memo to faculty members to get ahold of nice copies of needed spectra

(1) Based on the SSG meeting, the team should draft the history section

(2) Based on the SSG meeting, the team should draft revisions to the Article

(3) Based on the SSG meeting, the team should either affirm the final mechanism, or get what is needed to affirm it. Either way, each team should come with a "final" mechanism for this reaction, and they ought to converge on the same thing!

(4) Based on the SSG meeting, the team should draft a memo to get the spectra from the research advisor whose article will be used (note that this might be delayed if there are not the right examples with good characteristic appearances that have emerged from the research)

Wiki Project Checklist:
        History: first draft of the text
        Animation: continue doing research
        Spectroscopy: draft a request to an author for good copies of spectra and why needed
                (AND continue the research, as needed)
        Editing: first draft of edits

Week 6

SSG Leader tasks: The PIs for the spectra need to be coordinated so that they do not get more than one request. This is unlikely, but possible. Good to check.
Assistant tasks: general oversight, keeping up with the process
In class: Team members present historical drafts
                SSG comes to consensus on what goes into the common document
                Team member selected for second draft of historical part (decide format)
                Team members report on revision of the Article
                SSG comes to consensus on what goes into the common document
                Team member selected for second draft edits to Wiki article (decide format)
                SSG converges on curved arrow mechanism for the reaction
                SSG decides the final spectra that are potentially needed to illustrate the reaction
                SSG finalizes format of spectral data requests and who will send to whom

Wikipedia Assignment #6

Goals: Second draft of the historical aspects of the reaction for the Wiki article (format?)
                Second draft of edits to Wiki article (format?)
                Nothing new for the mechanism unless there is still an open question
Get ready to send the memos (coordinate across the entire class in case of duplicates)

(1) Based on the SSG meeting, the team should second draft the history section

(2) Based on the SSG meeting, the team should second draft revisions to the Article

(3) Based on the SSG meeting, the team sent out its memo to get the spectra from the research advisor whose article will be used

Wiki Project Checklist:
                History: second draft of the text
                Animation: nothing unless there is still an open question
                Spectroscopy: send the requests
                Editing: second draft of edits

Week 7

SSG Leader tasks:
Assistant tasks: Inserting images into the Wikipedia page/sandbox/space when editing
                    Introduction of gadgets for easy editing
Creating/editing in sandbox

In class: Team members present second historical drafts
               SSG comes to consensus on what goes into the final document
               Team member selected for final draft of historical part (decide format)
               Team members report on second revision of the Article
               SSG comes to consensus on what goes into the final document
               Team member selected for final draft edits to Wiki article in sandbox
               Overview of storyboarding and its features
               Update on spectra requests

Wikipedia Assignment #7

Goals: Final draft of the historical aspects of the reaction for the Wiki article (format?)
               Final draft of edits to Wiki article, in sandbox
               Storyboard the animation (individual assignment)

(1) Based on the SSG meeting, the team should final draft the history section

(2) Based on the SSG meeting, the team should start revising the Article

(3) Everyone in the section should storyboard the mechanism using a 5x6 grid, consider strongly: (a) placement, (b) use of annotations, (c) extent to which progress of bond changes and transition states are shown, (d) how arrows are depicted; the assignment will be of great value to the SSG as a whole if you work individually and bring your divergent ideas to the table for discussion

Wiki Project Checklist:
               History: final edit of the text
               Animation: first storyboard for animation
               Spectroscopy: nothing unless there is something to report back, already
               Editing: start to edit the Wikipedia article

SPRING BREAK

Week 8

SSG Leader tasks: How to do an animation
Assistant tasks: How to do an animation for Wikipedia
                           Look over edits being added to the sandbox, let SSG leaders know of any potential problems with community (neutral point of view)

In class: Team members present final historical draft
               SSG comes to consensus on what goes into the Article
               Team member selected for adding the history to the Article
               Team members report on edit of the Article
               SSG comes to consensus on what else might be needed
               Team member selected for edits to Wiki article
               Review storyboards and come to consensus on the features and format
               Update on spectra requests (decide if follow-up is needed)
               Come to consensus on the format of the spectroscopic features section (format?)

Wikipedia Assignment #8

Goals: Final draft of the historical aspects to the Wiki article
               Continue to edit Wiki article, in sandbox
               Produce the key frames for the animation
               Draft the portion of the Article related to spectroscopic features

(1) Based on the SSG meeting, the team should start to enter the history section into the Article

(2) Based on the SSG meeting, the team should edit the Article

(3) Based on the SSG meeting, the team should produce a set of 30 or so key frames for the animation that are illustrative of all desired features

(4) Based on the SSG meeting, the team should begin to draft the section of the Article that relates to the spectroscopic features

Wiki Project Checklist:
               History: start to edit the Wikipedia article
               Animation: produce the set of key frames for the animation
               Spectroscopy: draft the portion of the article related to key spectroscopic features
               Editing: continue to edit the Wikipedia article

Week 9

SSG Leader tasks:
Assistant tasks: How to format spectra for Wikipedia

In class: Team members present the first version of the history section
                SSG comes to consensus on what else is needed for the history section
                Team member selected to finalize the history section of the Article
                Team members report on any edits of the Article
                SSG comes to consensus on what else might be needed
                Team member selected for edits to Wiki article, if needed
Review key frames for the animation and decide on any changes prior to producing the set of animations from this SSG
                Team members present the first version of the spectroscopic features
section
                SSG comes to consensus about edits, format, and style of spectral section
                Team member selected for edits to spectral section

Wikipedia Assignment #9

Goals: Continue to edit the history section of the Wiki article, as needed
                Continue to edit Wiki article, as needed
                Produce part of the animation for review
                Edit the portion of the Article related to spectroscopic features

(1) Based on the SSG meeting, the team should continue to edit the Article, in general, and the history portion, in particular, as needed. Soon it will be time to decide which versions goes public.

(2) Based on the SSG meeting, the team should begin to produce the animation. It might be that different teams take different segments so that they can be combined after reformatting and editing, later.

(4) Based on the SSG meeting, the team should edit the section of the Article that relates to the spectroscopic features

Wiki Project Checklist:
                History: continue to edit the history section of the Wikipedia article, as
needed
                Animation: start producing the animation
                Spectroscopy: edit the key spectroscopic features section
                Editing: continue to edit the Wikipedia article, as needed

Week 10

SSG Leader tasks:
Assistant tasks: How to upload spectra onto CC (creative commons), insert into sandbox

In class: SSG reviews Article for edits
Review draft animations and decide on any changes prior to producing the set of final animations from this SSG
                Team members present second version of the spectroscopic features section
                SSG comes to consensus about final edits of spectral section
                Team member selected for moving spectral section to Article

Wikipedia Assignment #10

Goals: Continue to edit the history section of the Wiki article, as needed
                Continue to edit Wiki article, as needed
                Complete the animation
                Write the part of the Article related to spectroscopic features

(1) Based on the SSG meeting, the team should complete the animation.

(2) Based on the SSG meeting, the team should write the section of the Article that relates to the spectroscopic features

Wiki Project Checklist:
                History: continue to edit the history section of the Wikipedia article, as needed
                Animation: finish producing the animation
                Spectroscopy: final edit for the key spectroscopic features section
                Editing: continue to edit the Wikipedia article, as needed

Week 11

SSG Leader tasks:
Assistant tasks: How to upload animation on to commons, insert into sandbox

In class: SSG reviews Article for edits
Review final animations and decide on any changes
SSG comes to consensus on how to select final animation and format Article
Team members draft animation section of the Article
            Team members present final version of the spectroscopic features section
            SSG reviews spectral section of the Article for edits
            Team member selected for editing spectral section of the Article

Wikipedia Assignment #11

Goals: Continue to edit the history section of the Wiki article, as needed
            Continue to edit Wiki article, as needed
            Continue to edit the spectroscopic features section of the Wiki article, as needed
            Draft the animation section of the Article

(1) Based on the SSG meeting, the team should draft the animation section.

(2) Criteria for selecting the final posted versions should be prepared for discussion next week.

Wiki Project Checklist:
            History: continue to edit the history section of the Wikipedia article, as needed
            Animation: final edits to the animation, draft entry into Article
            Spectroscopy: final edits to the key spectroscopic features section
            Editing: continue to edit the Wikipedia article, as needed

Week 12

SSG Leader tasks: Formally "move" page
Assistant tasks: Last look at sandbox before they go live, check formatting,
for errors in coding
              How to request to formally "move" page

In class: SSG reviews Article for edits
Review animation article and decide on any changes
Team members finalize animation section of the Article
SSG comes to consensus on how to select the final version for posting

Wikipedia Assignment #12

Goals: Continue to edit the history section of the Wiki article, as needed
              Continue to edit Wiki article, as needed
              Continue to edit the spectroscopic features section of the Wiki article, as
needed
              Final draft the animation section of the Article

(1) Based on the SSG meeting, the team should finalize the animation section.

(2) Prepare for posting

Wiki Project Checklist:
              History: continue to edit the history section of the Wikipedia article, as
needed
              Animation: final edits to the animation section of the Article
              Spectroscopy: continue to edit the key spectroscopic features section
              Editing: continue to edit the Wikipedia article, as needed

Week 13

SSG Leader tasks: Oversee uploading/move and posting
Assistant tasks: Oversee uploading/move and posting

In class: Upload and posting