Modifying Gelators for Sensing Applications and Developing Online Resources for Organic Courses

by

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Dedication

To my Mom, Dad, Aunt Bethann, and Brad

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Abstract

Part 1 of this thesis focuses on utilizing low molecular weight gels in sensing applications. Because low molecular weight gels are stimuli-responsive, they are ideal candidates for sensing. One challenge in the field is designing a gelator for a specific application, since gelators are often discovered serendipitously. In chapter 2, we review recent work understanding how structure and solvent affect gelation, which has helped streamline gelator discovery. In chapter 3, we describe an example of how one can design a gelator for sensing, specifically to detect nitrite. By modifying a known azosulfonate gelator scaffold, we synthesized five new gelators and selected the best candidate to successfully detect nitrite in dirty water. A limitation sometimes observed in gel-based sensors is poor sensitivity, especially when the analyte is not catalytic. In chapter 4, we describe our efforts to amplify the analyte signal in gel-based sensors using disassembling polymers. We describe modifying monomers of two polymer scaffolds and identified two gelators and one gelator-precursor to be used for analyte signal amplification.

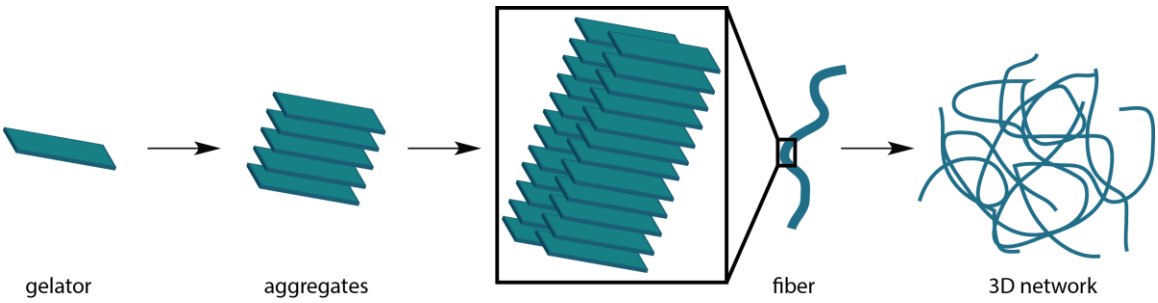
Part 2 of this thesis focuses on online homework in higher education with an emphasis on systems used in chemistry courses. One advantage of online homework is students receive immediate feedback, regardless of instructor time. While a number of organic chemistry homework platforms existed, we found that they did not contain the types of questions we use to assess our students learning, which are open-ended and literature-based. In chapter 5, we describe our efforts to create a feedback-driven online homework resource aligned with our course assessments. We describe a method with which undergraduate students were able to create usable questions with written feedback in an online platform. The questions were then released to incoming students as an optional resource. In chapter 6, we investigate whether our resource was effective in promoting student

learning. We observed low student participation due to resource cost and student time constraints, but some evidence of improved course performance in students who used the resource. We propose future research to assess student interactions with the resource and how these affect course performance.

Chapter 1
Introduction

Part 1: Low molecular weight gels

Low molecular weight gels are a biphasic material comprised of small molecules (i.e., gelators) that self-assemble to immobilize a liquid component.[1] Self-assembly occurs through non-covalent interactions such as π-stacking, hydrogen-bonding, metal coordination and van der Waals interactions to form fibers. These fibers self-aggregate to form 3D networks of fibers that physically entangle to entrap solvent (Scheme 1.1).[2] Because the gel network is formed through non-covalent interactions, these materials often undergo a reversible solution (sol) to gel transition in response to physical[3] (e.g., light) or chemical[4] (e.g., acid) stimuli that is useful in applications such as drug delivery,[5] environmental remediation,[6] tissue engineering,[7] and sensing.[8]

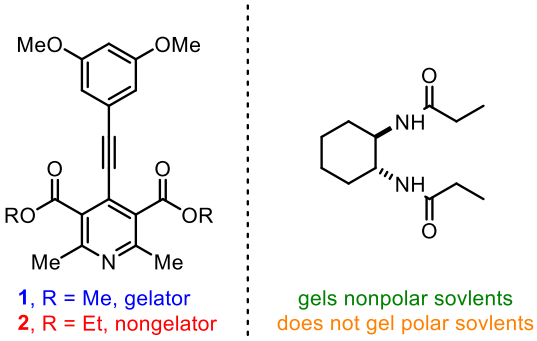


Scheme 1.1 Low molecular weight gel aggregation.

Designing low molecular weight gelators (LMWGs) for specific applications is challenging.[9] Small changes in structure can affect whether a compound is a gelator or a nongelator.[10] For instance, **1** is a gelator when the ester is a methyl-ester, but is not a gelator when the ester is an ethyl-ester (**2**) (Chart 1.1).[11] These poorly understood substituent effects necessitate extensive

derivative screening for gelator discovery. Solvent can also help promote or disrupt gelation.[12] Zweep and coworkers found that a bisamide gelator, which is proposed to self-assemble through intermolecular hydrogen bonds, gels nonpolar solvents but not polar solvents (Chart 1.1).[13] They hypothesize that polar solvents compete with the gelator for intermolecular hydrogen bonding sites. These solvent effects are important to keep in mind when designing gelators for applications where solvent choice is restricted, including biological and sensing applications.

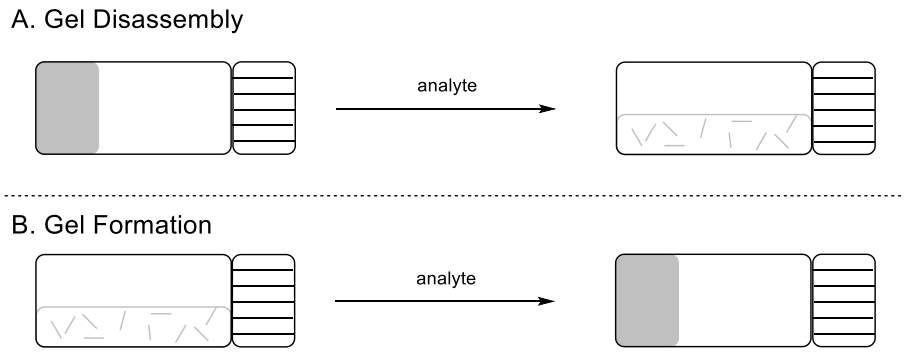
Chart 1.1



Because small changes in structure and solvent affect gel formation, new gelators are largely identified serendipitously or by derivatizing known gelators.[14] In Chapter 2, we detail recent advances in understanding the effects of structure and solvent on gel formation, as well as how these advances are leading to new *de novo* prediction methods.[15] These advances are streamlining the discovery of new gelators, which improve our ability to design gelators for applications.

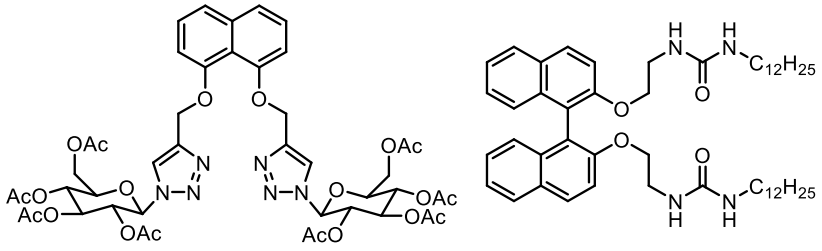
Sensors that are portable, inexpensive, and have an easily interpreted signal to identify harmful chemical compounds and enzymatic activity are needed. For example, in remote locations these types of sensors could be used to detect harmful chemicals in water that may cause sickness or death. LMWGs are appropriate for these sensing applications as their stimuli-responsive nature offers a clear yes/no signal of an analyte's presence, are portable and inexpensive.[4,8] In addition, gelation can occur in complex media and/or colored samples, which is an advantage over fluorescent and colorimetric sensors.

In low molecular weight gel-based sensors, analytes mediate a chemical process that either induces gel dissolution (Scheme 1.2A) or gel formation (Scheme 1.2B).[4] Acid, base, cations, anions, and enzymes have all facilitated gel transitions.[4,16] A sugar-triazole gelator (**3**, Chart 1.2) designed by Hemamalini and Das undergoes a gel-to-sol transition when Hg^{2+} is present.[17] In an example reported by Zhu and coworkers, a bisurea gelator (**4**, Chart 1.2) in cyclohexane disassembles when fluoride is added.[18] The disassembly is proposed to occur because fluoride binds to the urea moieties blocking the intermolecular hydrogen-bonding needed for gel formation. Gel-based sensors that disassemble have also been designed to detect nickel/zinc,[19] uric acid,[20] and other analytes.[21] However, this method could lead to false positives as disassembly can also occur through temperature change or mechanical stress.



Scheme 1.2 Gel-based sensors using (a) gel-to-sol or (b) sol-to-gel transitions.

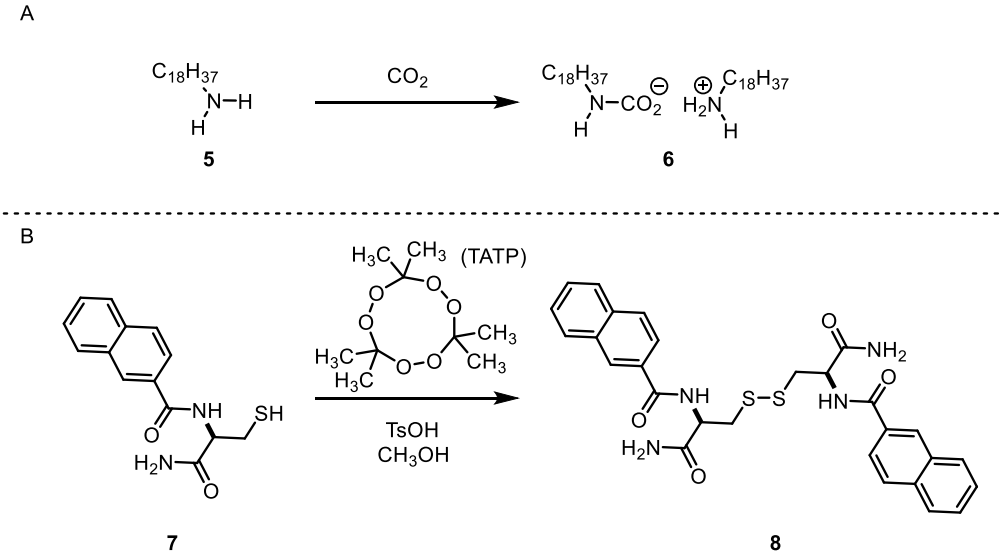
Chart 1.2



3 **4**

Because of this limitation, our group and others have developed gel-based sensors that undergo a sol-to-gel transition.[8,22,23] For example, George and

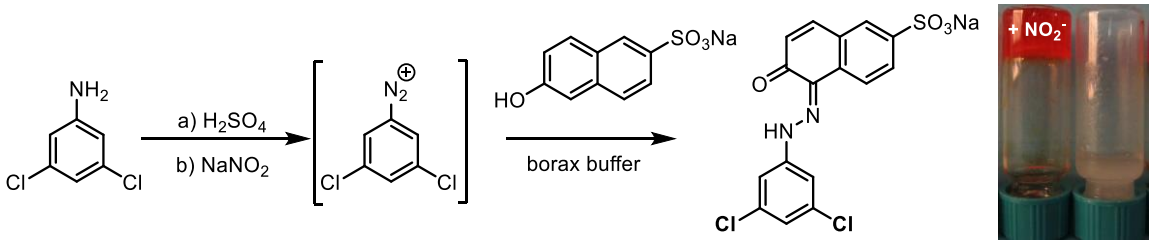
Weiss reported an ammonium carbamate gelator (**6**) that forms when long-chain alkylamine (**5**) reacts with CO_2 (Scheme 1.3A).[24] An example developed in our laboratory detected the peroxide-based explosive triacetone triperoxide (TATP) by oxidizing **7** to form a disulfide bond in gelator **8** (Scheme 1.3B). To develop these sensors we identify 1) a reaction that is mediated by the analyte, 2) a gelator that contains the functional group generated by the reaction, and 3) a non-gelling precursor.



Scheme 1.3 Reactions that produce gelators mediated by (a) carbon dioxide (b) TATP.

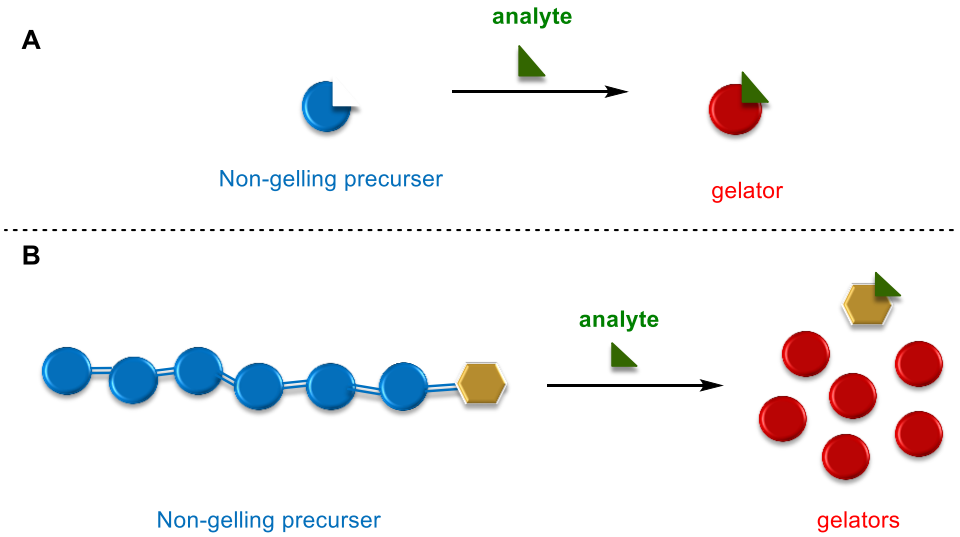
In Chapter 3, we develop a gel-based sensor for nitrite, which is linked to medical conditions such as blue baby syndrome.[25,26] Colorimetric,[27] electrochemical,[28] and other[29] nitrite-based sensors have been developed, but often require sample pre-treatment that could be eliminated with a gel-based sensor. To design our sensor, we identified that nitrite selectively reacts with amines to generate an azo-functional group.[30] Next, a class of known azo-sulfonate gelators were selected and derivatized.[31] Derivatization was necessary because the known azo-sulfonate gelators had high critical gelation concentrations (cgc). The cgc, which is the minimum gelator concentration required for a stable gel, is important because the detection limit in gel-based

sensors depend on the *in situ* yield of the reaction and cgc. Thus five new derivatives were synthesized, with the dichloro-derivative (Scheme 1.4) exhibiting the lowest cgc, as well as the highest intermediate stability and yield. Our gel-based sensor was able to detect nitrite at 90 ppm in water.



Scheme 1.4 Nitrite sensor (azo-hydrazone equilibrium, hydrazone is the dominant species in sensing conditions).

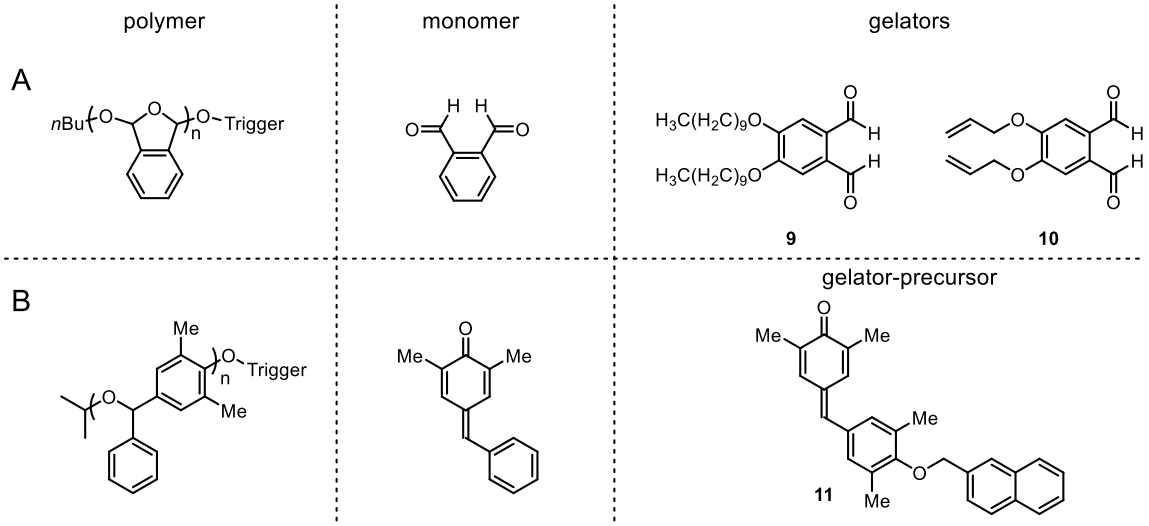
Unfortunately, the nitrite sensor did not meet the necessary Environmental Protection Agency detection limit (1 ppm).[32] This poor sensitivity has been observed in other gel-based sensors, notably when the analyte is not catalytic, in which case one equivalent of analyte is required to form one gelator (Scheme 1.5A).[15,33] In Chapter 4, we attempt to address the low sensitivity in gel-based sensors by developing a signal amplification system that utilizes disassembling polymers (Chapter 4, Scheme 1.5B) wherein an analyte cleaves a polymer end-group to release small molecule gelators, amplifying the analyte signal.



Scheme 1.5 (a) Current gel-based scaffold (b) Proposed amplification scaffold for gel-based sensors.

Four main depolymerizing scaffolds have been identified in the last 10 years including poly(carbonate)s,[34] poly(phthalaldehyde)s,[35] poly(ester amide)s,[36] and poly(benzyl ether)s.[37] For our gel-based sensor, we selected the poly(phthalaldehyde)s (Chart 1.3A) and poly(benzyl ether)s scaffolds (Chart 1.3B) because depolymerization times were reported to be less than 45 min. Our efforts then focused on modifying monomers of these scaffolds to be gelators or gelator-precursors. For the poly(phthalaldehyde) scaffold, two different gelators were synthesized (**9** and **10**). Unfortunately, **9** was insoluble under polymerization conditions. Current efforts are underway to access sufficient quantities of **10** for polymerization. For the poly(benzyl ether) scaffold, a gelator-precursor **11** was synthesized and successfully polymerized. To form the gelator, **11** undergoes hydration. Current efforts are underway to optimize polymerization, hydration, and depolymerization in response to a specific analyte. Both scaffolds have the potential to amplify analyte-signal in gel-based sensors.

Chart 1.3



In summary, part 1 of this dissertation details my work in the McNeil group developing LMWGs for sensing applications. We review state of the art tools used to predict gel formation, which facilitate LMWG identification. We demonstrate that known gelators can be modified for nitrite detection and

investigate methods to increase the sensitivity to non-catalytic analytes in gel-based sensors.

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Part 2: Online homework

Instructors provide homework to promote active engagement with course material, and improve learning and retention. Practice is particularly important to learning in courses such as general and organic chemistry which require students to develop problem-solving skills. In chemistry courses, a strong correlation has been found between course performance and time spent doing homework.[1] In the last two decades, online homework has begun to replace traditional paper-based homework in many large introductory courses, encouraging active learning, providing students with prompt feedback, and reducing faculty time spent on grading.[2–4] While not all homework systems are the same researchers have positively correlated performance a few different online homework systems to student course performance.[3,5] Additional studies have observed either no change or increased student performance when comparing online homework to traditional homework.[2,6,7] These learning advantages in online homework are hypothesized to be due to the students' ability to rework problems based on the immediate feedback they receive.

Feedback provided by most online homework systems offer students correct/incorrect responses and usually suggests ways students could fix an incorrect response. Feedback reduces "discrepancies between [students'] current understandings/performance and a desired goal."[8] However, feedback can negatively or positively impact learning depending on the type given.[8] For example, giving students information/hints to help them to the answer was better than telling students their response was correct/incorrect.[9] For feedback to be effective it must be timely, specific, understandable, and students must be willing to incorporate it.[10] Online homework can provide these types of effective feedback.

Students have favorable attitudes toward courses that utilize online homework with feedback. A study about online homework in organic chemistry reports >80% students perceived the system to be helpful for both mastering the material and preparing for exams.[2] In another study, students from two separate classes ranked online homework in the top three of "most useful" resources.[11]

Student behaviors in online homework have also been examined to determine whether students were learning from their mistakes (i.e., did immediate feedback help).[11] Richards and Babb found that 60% of students in their general chemistry class self-reported looking over their online homework assignment to learn from their mistakes.[3] The same study found students reworked the question (33.7%), sought help from print/online sources (68.6%) or other people (25.7%), guessed as a last resort (18.3%), immediately guessed (11.4%), or never guessed (1.7%). These findings indicate that guessing was limited and students used one or more problem-solving approaches to address their mistakes when interacting with the online system.

Even with the successes, online homework is still limited by the cost to students for a subscription and the need for a certain level of technical skills to use the system.[6,12] Furthermore, instructors are required to spend time and effort to learn the system, especially if the instructor needs to create their own questions and resolve technical issues such as problems with student access. Despite these costs, online homework is recommended in the literature because of the benefits to student learning described earlier (e.g., immediate feedback) and the time saved by the instructor (with respect to grading) is significant.

We felt students in our organic chemistry courses would benefit from the advantages associated with feedback-driven online homework. The introductory organic chemistry series at the University of Michigan (U-M) is taught over two semesters and has an enrollment for both courses of >1400 each semester. Course grades are based entirely on four examinations and students rely on a number of resources (e.g., lecture) to learn course content. However, existing online systems do not have literature-based, open-ended questions like we ask in our organic chemistry exams.[13]

In Chapter 5, we describe our design process to customize a feedback-driven online homework system by utilizing students to create the content. We used students because creating instructional material is proposed to give purpose to student work and challenge students to use higher order thinking skills.[14,15] We selected the online platform Sapling Learning[16] over Peerwise[17], a multiple

choice only platform where students have created content, because we could create questions with mechanistic and drawing capabilities.[18,19] Over 1100 questions were created with written feedback by students over four semesters and >80% of questions passed an internal review process. An external review of a random sub-set of questions revealed 27% needed no further edits, 55% contained technical and formatting problems and only 18% contained content errors (ranging from missing counter ions to wrong regioselectivity of a Diels Alder reaction). To address issues identified in the external review, questions are currently being edited in an honors section course as an assignment. After passing the internal review process, questions were released to students enrolled in the organic chemistry course as an optional homework resource. The details

In Chapter 6, we explore whether the optional feedback-driven online homework is effective in helping students learn course content. The system was released as an optional resource during the Fall 2014, Winter 2015, and Fall 2015 semesters for the first semester of organic chemistry (CHEM 210) and Fall 2015 for the second semester of organic chemistry (CHEM 215). During the semesters we observed low student participation but there is some evidence of improved course performance for students who used the resource. In addition, survey responses on specific questions found favorable student perceptions of resource content and provide feedback to improve the online resource. Lastly, student interactions with the resource are being investigated to determine how their use of the system correlates to course performance.

In summary, part 2 of this dissertation details my work with Dr. Anne McNeil and Dr. Brian Coppola in developing a feedback-driven online homework system. We designed a course, in which students generated over 1100 questions aligned with content in the organic series at U-M. Furthermore, students enrolled in the organic courses are utilizing the resource to learn course content.

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Part 1: Modifying gelators for sensing applications

Chapter 2*

Tools for identifying gelator scaffolds and solvents

The first small molecule gelator was serendipitously discovered in 1841 during a failed crystallization.[1] There was surprisingly little interest in these materials until the early 1990s.[2] We suspect that the Nobel Prize awarded to Cram, Lehn and Pedersen for their pioneering work in supramolecular chemistry led to an increased focus on supramolecular materials.[3] Molecular gels are now a widely studied class of soft materials with many applications, including drug delivery,[4] sensing,[5] remediation,[6] and tissue engineering.[7]

Gels form through the self-assembly of small molecules into supramolecular structures that immobilize the solvent via capillary forces and surface tension.[8] This self-aggregation is driven by non-covalent intermolecular interactions such as hydrogen bonding,[9] π-stacking,[10] van der Waals interactions,[11] and halogen bonding.[12] Because non-covalent interactions are involved, gel formation is responsive to changes in the local environment (e.g., temperature and pH). Physical interactions amongst the large aggregates (e.g., micelles, ribbons, fibers, sheets, and platelets) and with the solvent give rise to the macroscopic gel properties (e.g., resistance to flow).

Overall, gelation is both a complex and poorly understood process; understanding which molecules will form gels and under what conditions (e.g., concentration, solvent) remains a significant challenge.[13] As a consequence, many researchers have identified new gelators simply by modifying gelator scaffolds that were discovered serendipitously.[14] For example, Wu and co-workers[15] created a light-responsive gelator by appending an azobenzene group

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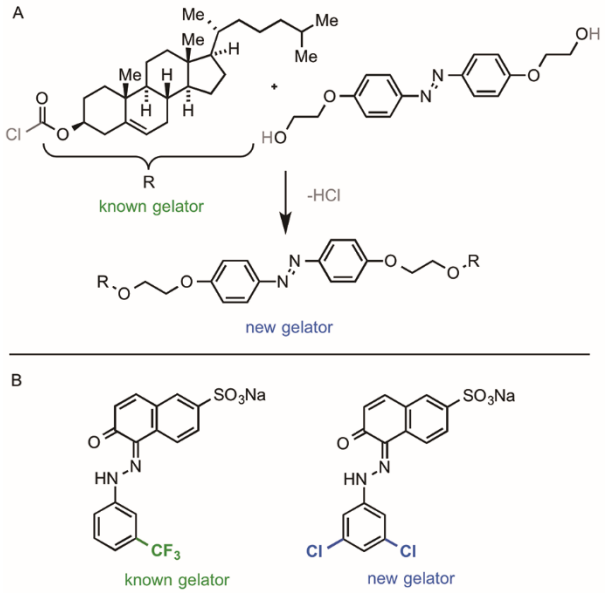
to cholesterol (a known gelator)[16] (Scheme 2.1A). This approach can be particularly useful for taking known gelators and tailoring them for a specific application. For example, we modified a known azo-sulfonate gelator[17] to create a new gelator that exhibits improved sensitivity to nitrite anions (Scheme 2.1B).[5d] Although successful, this approach is limited to existing gelator scaffolds and specific solvents, which may not be suitable for every application.

Scheme 2.1 Modifying Known Gelators



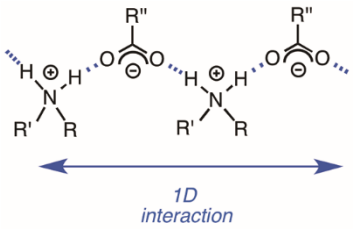
Over the last decade, several research groups have identified key structural features and molecular properties that correlate with gel formation. Additional efforts have focused on elucidating the relationship between solvent structure and gelation. This synopsis will describe the strategies that resulted from these studies. Each tool has been successfully implemented to generate novel gelator scaffolds or identify alternative solvents for gel formation.

1. The Importance of Unidirectional Interactions.

In a seminal paper, Hanabusa and co-workers hypothesized that gelation is promoted by molecules that exhibit “intermolecular interactions for building up macromolecular-like aggregates.”[18] An example of these so-called unidirectional (1D) interactions is depicted in Scheme 2.2.[19] The secondary amine forms two hydrogen bonds with the carboxylate to form a linear “macromolecular-like

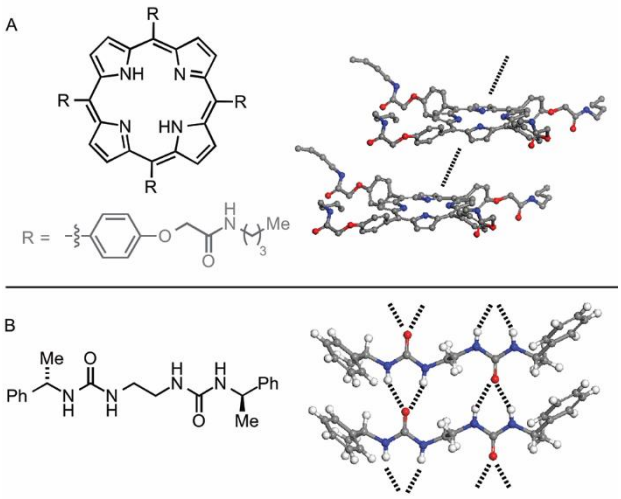
aggregate.” In contrast, if the amine is primary (R = H) or ammonium (R, R’ = H), then the intermolecular interactions can extend into the 2D and 3D.

Scheme 2.2 Representative Unidirectional (1D) Interactions



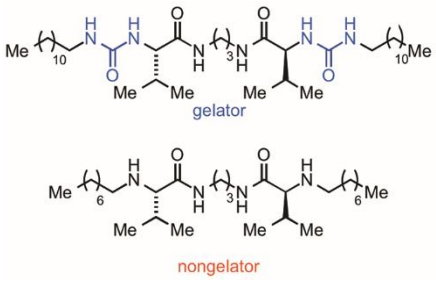
Solid-state analyses performed on a number of gelators has revealed the presence of 1D interactions in the gel state.[4a,20] To make this correlation, the authors identified obvious 1D interactions in the single-crystal X-ray structure and then demonstrated that a similar packing mode is observed in the gel (or xerogel) using powder X-ray diffraction (PXRD). Some recent and representative examples include: a porphyrin-based gelator that self-assembles into columns via a directional π-interaction (Scheme 2.3A),[21] and a urea-containing scaffold that promotes directional hydrogen bonding (Scheme 2.3B).[22] Although there appears to be a correlation between gel-forming scaffolds and the presence of 1D intermolecular interactions, many molecules exhibit these interactions but do not form gels.[23] In addition, it is also experimentally challenging to obtain high quality single crystals with a similar solid-state structure as the gel because the gel phase is often a kinetically trapped state[24] and not a thermodynamic minimum that is reached in crystallizations. Thus, few gelators have reported crystal structures and fewer still have crystal structures that match the gel form.[25] Nonetheless, targeting 1D interactions has proven to be one of the most successful strategies for identifying new gelator scaffolds.

Scheme 2.3 Unidirectional Interactions Observed in both Crystal Structures and Gels



Tool #1: Append Functional Groups with Directional Interactions. One approach to identify new gelators based on Hanabusa's hypothesis is to utilize functional groups that exhibit directional interactions. As an example, both the urea and amide functional groups, which exhibit directional hydrogen bonding, have been successfully utilized to create new gelators.[20a,26] Recently, Rubio and co-workers designed a new family of amphiphilic organogels by incorporating two urea groups into the molecular scaffold (Chart 2.1).[9] The resulting molecules formed gels in a wide range of solvents and exhibited remarkably high thermal stability. Infrared spectroscopic studies confirmed the presence of hydrogen bonding and molecular modeling supported a 1D aggregation mode. Notably, similar compounds without the urea group did not form stable gels, suggesting that the increase in hydrogen bonding interactions was important for gelation.[27]

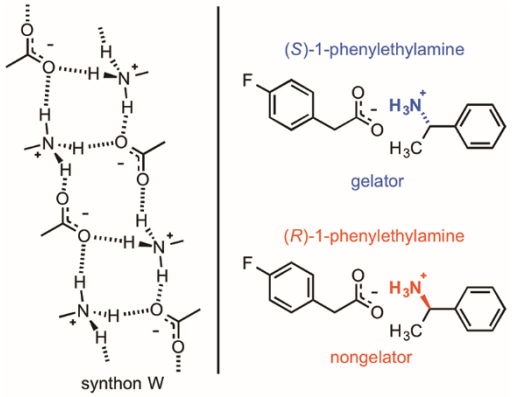
Chart 2.1



Tool #2: Search the Cambridge Structural Database for Scaffolds. Another approach based on Hanabusa's hypothesis is to specifically target molecular

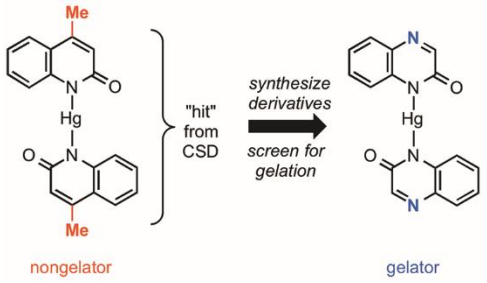
scaffolds that exhibit unidirectional interactions in the solid state. For example, Dastidar and coworkers used the Cambridge Structural Database (CSD) to identify 32 primary ammonium monocarboxylate salts that exhibit a 1D hydrogen-bonding network, which they called synthon W (Scheme 2.4).[23] They synthesized all 32 compounds and found that just nine were gelators. Single-crystal X-ray diffraction (SCXRD) and PXRD were used to confirm that all nine gelators exhibited synthon W packing within the fibers. Although successful, it is important to note that 23 compounds that exhibited the same packing motif did not form gels. A striking example is that one enantiomer of phenylethyl amine is a gelator when paired with 2-(4-fluorophenyl)acetic acid while the other enantiomer is not (Scheme 2.4).

Scheme 2.4 1D Hydrogen Bonding Networks in Gelators and Nongelators



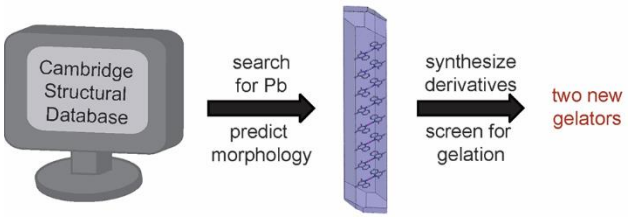
A slightly different approach is to mine the CSD for scaffolds that exhibit 1D interactions in the solid state and make derivatives. For example, we searched the CSD for molecules that contain a 1D Hg-π interaction.[28] We identified a quinoxalinone framework, synthesized several derivatives and screened them for gelation (Scheme 2.5). Although the original structure did not form gels, a structurally related derivative was a gelator. Unfortunately, the solid-state packing motif of the gel was not confirmed because crystal structures that matched the gel form were not accessible. Further derivatization created a new library of mercury containing complexes with 5 new gelators discovered amongst the 11 synthesized compounds.[6b]

Scheme 2.5 Gelator Inspired by CSD Search



Tool #3: Derivatize Scaffolds with High Aspect-Ratio Crystals. Although both CSD approaches described above led to new gelators, the process of selecting a promising scaffold was both time-consuming and qualitative. A better approach would be to select scaffolds based on the strength of the 1D intermolecular interactions in the solid state. We hypothesized that morphology prediction tools could provide this information because the relative growth rates of each crystal face is proportional to the strength of the intermolecular interactions in that direction (Scheme 2.6).[29] In other words, molecules exhibiting strong unidirectional interactions in a single direction will produce a high aspect-ratio morphology (e.g., a needle). We further hypothesized that these high aspect ratio-forming molecules represent potential gelator scaffolds. To test this hypothesis, we predicted the morphologies of 186 Pb-containing crystal structures. We selected two scaffolds from the highest 5% of predicted aspect ratios, synthesized derivatives, and screened for gelation. Remarkably, two new gelators were identified with minimal derivitization.[30]

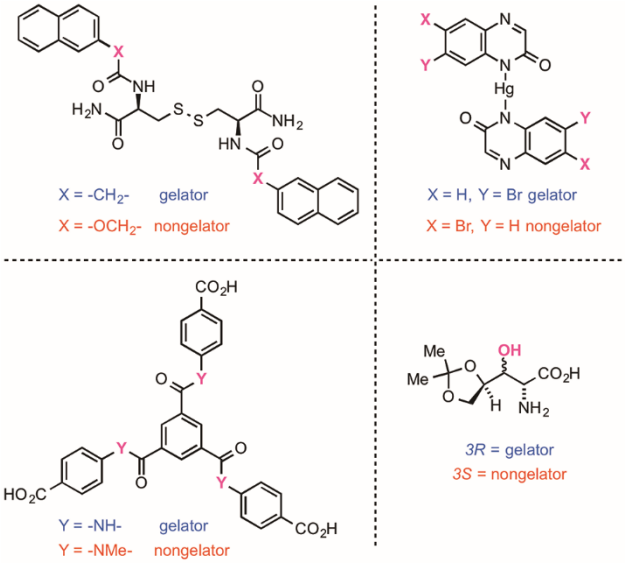
Scheme 2.6 New Gelators from High Aspect-Ratio Crystals



As noted above, the focus has largely been on molecular structure and unidirectional interactions. One significant remaining challenge is addressing the fact that subtle changes to a gelator structure can unpredictably disrupt gel formation; some representative examples can be found in Chart 2.2.[6b,31] In

addition, solvent structure plays an equally important, though often underappreciated, role in gel formation.

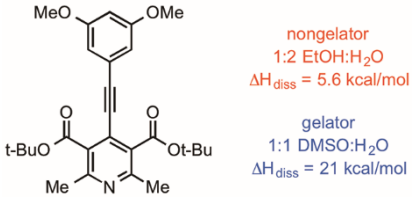
Chart 2.2



2. The Importance of Solvent.

Though the focus has largely been on gelator/gelator intermolecular interactions, solvent/gelator interactions also play a critical role. The adage has long been that gelators should not be too soluble or too insoluble.[14f,32] Focusing on bulk gelator solubility is an oversimplification, as we found no correlation between solubility and gelation ability amongst two different sets of gelators and three different solvent systems.[33] Instead, a more nuanced look at the competing gelator/gelator and gelator/solvent interactions is warranted. For example, the enthalpy of dissolution (i.e., solid gelator dissolving in the liquid solvent) captures both the enthalpic cost of disrupting the favorable gelator/gelator interactions and the enthalpic gain from the newly formed solvent/gelator interactions. Chart 2.3 highlights how a change in the solvent can lead to substantial changes in both dissolution enthalpy and gelation ability. Importantly, this large difference in enthalpy can only be attributed to changes in solvating the gelator, as the gelator/gelator interactions in both cases are identical. For this particular compound, there are weak solvent/gelator interactions in DMSO/H_2O and strong solvent/gelator interactions in EtOH/H_2O. Overall, these results highlight the important role of solvent in gel formation.

Chart 2.3



Because solvent plays such an important role, gel screening should be done in a variety of different solvents. Nevertheless, only a handful of solvents are often reported for each gelator, which ultimately limits its potential application. Recognizing the importance of solvent identity, many researchers have recently focused on the relationship between solvent parameters (e.g., dielectric constants,[34] Kamlet–Taft parameters,[35] Flory–Huggins parameter,[36] $E_T(30)$ parameters,[37] Teas parameters,[38] Hildebrand solubility parameter,[39] and Hansen solubility parameters[40] (HSPs)) and gel formation. Of these, the HSPs have been particularly successful in modeling gelation behavior for a diverse range of gelators.[41] As a consequence, examining the Hansen space of each gelator has led to a powerful new approach for identifying additional solvents for gel formation.

Tool #4. Using Hansen Solubility Parameters to Identify Alternative Solvents for Gelation.

Hansen solubility parameters describe the cohesive energy density of the solvent using three contributions, hydrogen bonding interactions (δ_h), van der Waals or dispersive interactions (δ_d), and dipole-dipole or polar interactions (δ_p). One can identify alternative solvents for gelation by fitting a large data set containing solvents that both promote and disrupt gelation. Such solvent clusters (i.e., spheres) become readily apparent in the 3D Hansen plots (c.f., Figure 2.1).[40] Solvents that are located within the gelation “spheres” are likely to be gelled by the particular molecule. Depending on solvent/gelator interactions two (or more) gelation spheres may be observed. Notably, gelators that gel mixed solvent systems can also be modeled (Figure 2.1).[42] The size of the observed spheres is

dependent on the concentration of gelator since gel formation itself depends on this variable.[43] A comprehensive study by Rogers and co-workers examined a variety of solubility parameters to rationalize the gelation behavior of 1,3:3,4-dibenzylidene sorbitol and found that the 3D Hansen model was amongst the most effective. [44]

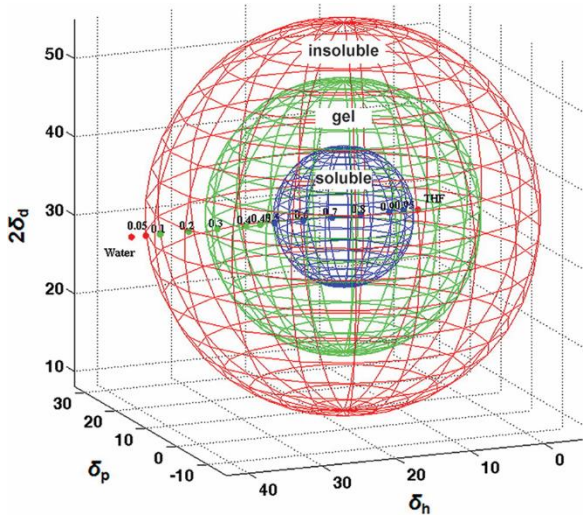


Figure 2.1 Plot of Hansen solubility data for a sugar-based gelator in THF/H_2O mixtures where δ_d is the dispersive interaction parameter, δ_p is the polar interaction parameter, and δ_h is the hydrogen bonding interaction parameter (blue/soluble; green/gel; red/insoluble). Reproduced with permission from ref 42.

The HSP model also provides some insight into the most important gelator/gelator and solvent/gelator interactions in the system. For example, Gao and co-workers fit the data for R-12-hydroxystearic acid and found that solvents with strong hydrogen-bonding capacity (larger δ_h) correlated with an increase in the critical gelation concentration (cgc).[45] This result suggests that the gelation relies on gelator/gelator hydrogen-bonding interactions, which are disrupted by hydrogen-bonding interactions with some solvents. Overall, the HSP approach can be a powerful tool to expand the scope of solvents that form gels, which should ultimately increase the utility of each gelator.

3. Future Outlook and Conclusions.

Considerable advances have been made over the past decade to make gelator discovery less serendipitous and more streamlined. As an example,

targeting compounds that exhibit 1D hydrogen bonding interactions in the solid-state led to the discovery of a cetirizine salt-based gelator designed to treat an allergic reaction.[46] In another example, the HSP solubility spheres of four gelator derivatives of (*R*)-12-hydroxystearic acid were analyzed, and as the alkyl group length increased, reducing the overall polarity, the gelation sphere shifted toward lower δ_h and δ_p values.[47] The authors proposed that rules to predict gelation domains of new gelators could be made by studying gel families using HSP parameters.

Despite these advances, truly predictive methods are still lacking. To achieve this goal, computational efforts to model gel formation (including both self-assembly and solvent) need to be developed further.[48] Importantly, these methods currently do not discriminate between gelators and nongelators, or gelling conditions versus non-gelling conditions and we believe this is an area that should be explored. Such models will benefit from recent efforts to elucidate the solid-state interactions involved in gelation using minimally invasive techniques, such as atomic force microscopy, cross polarization magic angle spinning nuclear magnetic resonance spectrometry (MAS NMR) and Raman spectroscopy.[49] We believe these efforts will lead to better prediction methods for molecular gels.

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Chapter 3*

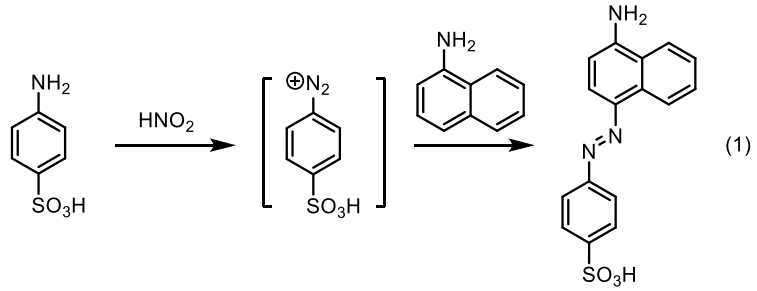
Modifying a Known Gelator Scaffold for Nitrite Detection

Small molecule-based gels are being explored for a variety of different applications.[1] Identifying an appropriate gelator for a specific application can be quite simple if the final gel state is all that matters. For example, different growth factors have been added to known peptide-based gelators and used as scaffolds in tissue engineering.[2] On the other hand, identifying an appropriate gelator can be quite challenging if the solution-to-gel phase transition is important to the application (e.g., sensing). In this case, one needs not only a gelator, but also a non-gelling, structurally related precursor. As a consequence, in our previous work, we found it easier to design a new gelator than to modify a known gelator for sensing applications.[3,4] Nevertheless, we were motivated to explore the alternative approach[5] given the inherent challenges in designing new gelators,[6] and the fact that there are over 1000 reported small molecule gelators.[7] Herein we demonstrate that modifying a known gelator for a new application can be successful. Specifically, we will highlight how a known gelator scaffold was first targeted and then modified to develop a gel-based sensor for detecting nitrite in aqueous solutions.

Nitrite (NO_2^-) contamination of water is a global concern because of its detrimental effects on human health.[8,9] Nitrite sensors based on electrochemical[10] and colorimetric methods,[11] among others,[12] have been developed, however, sample pre-treatment is often required. In contrast, sensors based on molecular gelation are portable and can operate in complex media

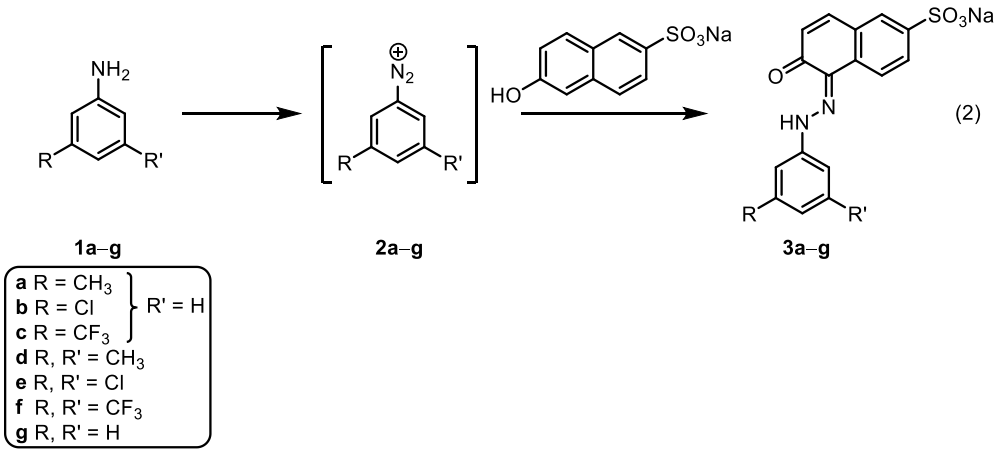
* Adapted from Zurcher, D. M.; Adhia, Y. J.; Romero, J. D.; McNeil, A. J. *Chem. Commun*. **2014**, *50*, 7813–7816 with permission from The Royal Society of Chemistry.

(e.g., opaque samples).[3,5,13] To develop a molecular gel-based sensor for nitrite, the first step involved identifying a chemical transformation that can be mediated by nitrite. Herein, the Griess reaction was chosen because of its high selectivity for nitrite, short reaction time, and high yield.[14] In the original Griess reaction, sulfanilic acid reacts with nitrous acid to form a diazonium ion, which is then reacted with α-naphthylamine to generate a red-violet azo dye (eq 1).[15]



(1)

The next step was to identify a gelator that can be formed via the Griess reaction. A search of the small molecule gel literature revealed a surprisingly large number of azo-containing organogelators[16–27] and a few hydrogelators.[28–31] In most cases, an azobenzene moiety was added to a known gelator scaffold to generate a light-responsive transition (via the *trans*-to-*cis* azobenzene isomerization). Because the non-azo-functionalized precursor is also a gelator, most of these scaffolds are unsuitable for sensing. We focused our attention solely on hydrogelators with scaffolds wherein the azo-functional group was part of the core structure (rather than an appendage). Only one promising scaffold fit these parameters: azo-sulfonates.[31] These azo-compounds can be accessed via the Griess reaction between an aniline derivative and sodium 6-hydroxynaphthalene-2-sulfonate, which are both non-gelling in aqueous solutions (eq 2). Azosulfonates **3c** and **3f** were reported to gel aqueous buffers, albeit at high concentrations.[31] Thus, we began our studies by modifying this scaffold to develop a gelation-based nitrite sensor for environmental samples.



We focused our efforts on meta-substituted derivatives because Hamada and co-workers previously reported that most para-substituted derivatives were nongelators under aqueous conditions.[31] In total, seven azosulfonates (**3a**–**3g**) were synthesized and screened for gelation (Table 3.1 and appendix 1).[32] All seven compounds formed gels in either borax buffer (65 mM, pH = 13) or EtOH/buffer (9/1 v/v).[33] Because the ultimate goal is to use aqueous samples from the environment, we focused on lowering the critical gel concentration (cgc) in neat borax buffer. The unsubstituted derivative (**3g**) was too soluble, so a single methyl- (**3a**), chloro- (**3b**) or trifluoromethyl- (**3c**) substituent was introduced to increase the hydrophobicity.[34] The most hydrophobic compound (**3c**) within this series gave the lowest cgc in borax buffer. Introducing a second, identical substituent (**3d**–**f**) had a large effect on cgc when R = Cl and a surprisingly small effect on cgc when R = CF_3. Overall, the dichloro-substituted derivative (**3e**) exhibited the lowest cgc, although **3b**, **3c** and **3f** were only slightly higher.

Table 3.1 Critical gel concentrations (cgc) in different conditions[a]

Azosulfonate	cgc (mM)	
	EtOH/borax buffer[b] (9/1, v/v)	borax buffer[b]
3a	23.5 ± 0.4	precipitate
3b	43 ± 3	29.4 ± 0.9[c]
3c	precipitate	24.2 ± 0.8
3d	35.5 ± 0.2	precipitate
3e	16.7 ± 0.6	21.3 ± 0.5
3f	precipitate	27 ± 1
3g	30.0 ± 0.5	soluble

[a] The error reported as a standard deviation is based on 3 samples. Each compound was screened for gelation at concentrations ≤ 2 wt%. The term "precipitate" was used when any amount of precipitate was observed. [b] Borax buffer (65 mM, pH = 13). [c] The solvent consisted of borax buffer (65 mM)/H_2SO_4 (4 M)/H_2O (7.6/2/0.4, v/v/v).

The mechanical strength and morphology of gels of **3a**–**g** were characterized using rheology and scanning electron microscopy, respectively.[35] Rheological testing of all gelators at 1.5 times the cgc revealed the expected 10-fold (or larger) storage modulus (*G'*) relative to the loss modulus (*G''*) in both the frequency and oscillating stress sweep experiments, confirming its gel-like nature (c.f., Figure 3.1A and appendix 1).[36] Optical and scanning electron microscopy was performed on each gel near or above its cgc to determine the morphology.[37] Consistent with most molecular gels, anisotropic fibers of varying widths were observed (c.f., Figure 3.1B and appendix 1).

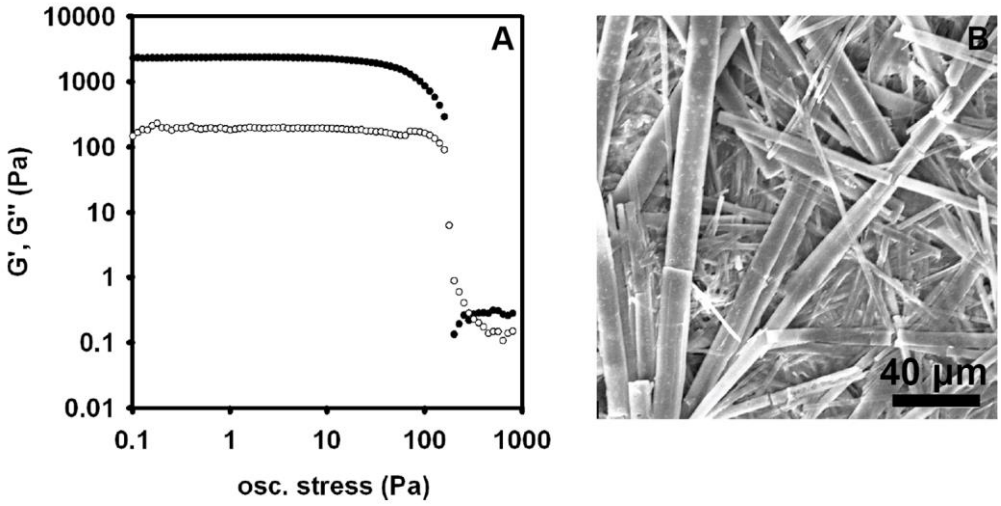


Figure 3.1 (A) Oscillating stress sweep for a gel of **3e** (32 mM in borax buffer, *G′* (•) and *G″* (◦)). (B) Scanning electron microscope image of a gel of **3e** (37 mM in EtOH/buffer (9/1, v/v)).

The Griess reaction is typically carried out at lower temperatures (e.g., 0 °C), presumably due to concerns about diazonium ion stability.[14] Nevertheless, a practical and portable sensor should operate at ambient temperatures. Thus, UV-vis spectroscopy was used to monitor the rate of diazonium ion formation (**2a**–**g**) and decomposition at room temperature. Gratifyingly, diazonium ions **2b** (Cl), **2c** (CF_3), **2e** (Cl/Cl) and **2f** (CF_3/CF_3) were stable at ambient temperatures for at least an hour (c.f., Figure 3.2A and appendix). ^{1}H NMR spectroscopy was used to confirm that a single, stable species was formed during the reaction (Figure 2B). In contrast, the CH_3-substituted derivatives (**2a**, **2d**) showed presumed loss of nitrogen after 2 min and the unsubstituted derivative (**2g**) decomposed after 30 min. Based on these results, our further studies focused solely on those gelators formed through stable diazonium intermediates (i.e., **3b**, **3c**, **3e** and **3f**).

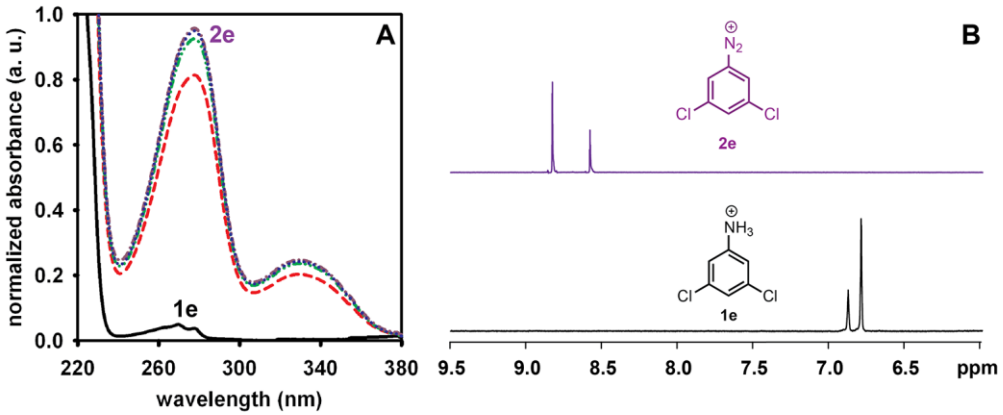


Figure 3.2 (A) Plot of the normalized absorbance versus wavelength for the reaction of **1e** (4.8 x 10^{-4} mmol) with $NaNO_2$ (4.8 x 10^{-4} mmol) at room temperature in 4 M aq. H_2SO_4 (0 min (black solid), 2 min (red dashed) 10 min (green dash dot dot), 30 min (blue dot), 60 min (purple dash dot)). (B) ^{1}H NMR spectra (in d_6-DMSO) acquired before (bottom) and 15 min after (top) adding $NaNO_2$ (0.03 mmol) to **1e** (0.03 mmol) in 4 M aq. H_2SO_4 at rt.

One concern that emerged from the syntheses of **3a**–**g** was the moderate-to-low isolated yields (e.g., 17% yield for **3e**, see appendix 1). The sensitivity of a gel-based sensor depends on both the critical gel concentration and the yield of the reaction used to generate the gelator. For example, although **3e** exhibited the lowest overall cgc, its low reaction yield could ultimately make it less suitable in the sensor platform. Because the low synthetic yields were presumably due to the extensive purification required to remove the excess salts, we used ^{1}H NMR spectroscopy to quantify the in situ reaction yield for **3b**, **3c**, **3e**, and **3f** using an internal standard (c.f., Figure 3.3 and appendix 1). Gratifyingly, all four reactions proceeded with yields exceeding 85% (ESI).

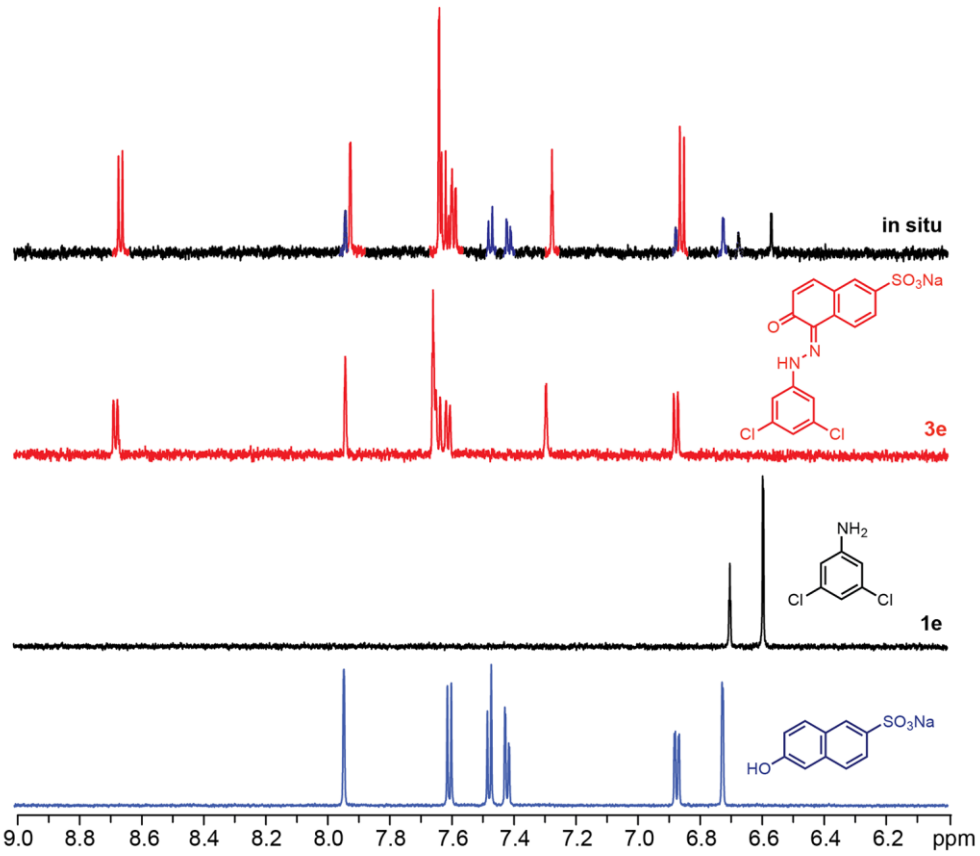


Figure 3.3 ^{1}H NMR spectra of the crude reaction mixture (without workup) for the reaction of **1e** (0.0078 mmol) with $NaNO_2$ (0.0071 mmol) and sodium 6-hydroxynaphthalene-2-sulfonate (0.0078 mmol) in deuterated borax buffer (top), and the corresponding starting materials and products under the same solvent conditions.

Gelator **3e** was ultimately selected for the sensor platform on the basis of its low cgc, stable diazonium ion intermediate, and high reaction conversion. We tested the nitrite sensor in different water sources by spiking each sample with $NaNO_2$ because the natural [NO_2^-] in non-polluted water is low. Vials containing **1e** (suspended in 4 M H_2SO_4) were treated with the spiked water samples for 10 min, followed by adding sodium 6-hydroxynaphthalene-2-sulfonate (in borax buffer). The resulting samples were heated to dissolve all solids and then allowed to cool to room temperature. The bright red/orange color is indicative of azosulfonate formation (Figure 3.4).

As evident in Figure 3.4, the gel-based nitrite sensor proved to be quite robust as it gelled tap water, river and pond water, as well as water drawn from a

muddy pond. The non-spiked water samples serve as a negative control. Surprisingly, the cgc determined under these reaction conditions was significantly lower (9.3 mM) than that observed with the isolated (and purified) compound (21.3 mM). We suspected that the change in pH from our screening conditions (pH = 13) to the reaction conditions (pH = 9) might play a role given the acidic hydrazine proton (pK_a ~ 11).[38] Indeed, a similar cgc was observed for isolated **3e** when the pH matched those of the reaction conditions (9.5 ± 0.3 mM, see appendix 1). Overall, the detection limit[39] in these studies was 500 ppm, which is above the EPA minimum set for safe drinking water (1 ppm).[9] We have previously demonstrated that using a smaller vial leads to a lower cgc, which can be attributed to an increase in the surface area between the container and the gel.[5] Herein, the detection limit dropped to 90 ppm using a 1.5 mL vial (instead of 4 mL, see appendix 1).[40] Further reducing this detection limit will require lowering the cgc, identifying a better gelator, or identifying a reaction that is catalytic in nitrite, wherein each nitrite produces more than one gelator molecule. Efforts to lower the cgc in other systems have been successful by either changing gelation solvent or adding additives.[41,42] In our system, phosphate buffer, which is compatible with the Griess reaction, could replace borate buffer and lead to a lower cgc. Alternatively, adding polymers can effect fiber growth, lowering the cgc of the gelator.[42]

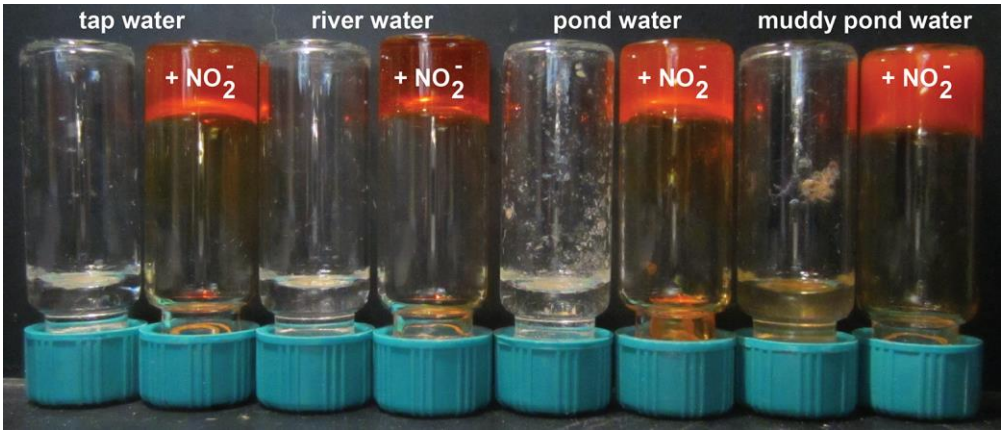


Figure 3.4 Gel formation is observed after a heat/cool cycle when tap water, river water, pond water, and muddy pond water containing $NaNO_2$ were reacted with **1e** for 10 min, followed by sodium 6-hydroxynaphthalene-2-sulfonate (see appendix 1 for experimental details).

In conclusion, these studies reveal that known gelators can be successfully modified and then utilized in targeted applications. Herein we demonstrated that by altering the substituents on the precursor aniline ring, we were able to develop a nitrite sensor that is operable under ambient temperatures in aqueous, environmental samples. Since the development of this gel-based nitrite sensor, other groups have employed a similar approach for designing application-specific molecular gels.[43] For example, Chen et. al. wanted to design a hydrogel that could undergo a solution-to-gel transition in neutral biological conditions, to be used as a 3D matrix for cell growth.[44] They modified a previously reported peptide scaffold to contain a phosphate-protected tyrosine moiety, which was soluble in neutral conditions but could undergo gel formation upon cleavage of phosphate. Similar to our design they were able to optimize the scaffold and reaction conditions to be compatible with their application. Applying these methods to the more than 1000 reported small molecule gelators[7] could be an important technique for developing other gelation-based applications.

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(37) Gels of **3c** were transparent within the limits of our optical microscope. In addition, the scanning electron microscope images only revealed salt crystals from the buffer solution.

(38)Oakes, J.; Gratton, P.; Clark, R.; Wilkes, I. *J. Chem. Soc., Perkin Trans. 2* **1998**, 2569–2575.

(39) The detection limit is based on the total volume of the gel sample and not the volume of nitrite-contaminated water.

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Chapter 4*

Amplification via Depolymerization in Gel-Based Sensors

Low-molecular weight gels have found application in drug delivery,[1] tissue engineering,[2] remediation,[3] and chemical sensing[4] in part because they exhibit stimuli-responsiveness (i.e., reversible sol-gel or gel-sol transition in response to external stimuli).[5] In chemical sensing, this responsiveness indicates a chemical's presence (i.e., analyte) by gel formation. Our research focuses on designing gel-based sensors as a potential on-site detection method for explosives, toxic metals in the environment, and diseases.[6]

A number of gel-based sensors have been designed, but poor sensitivity has been observed in cases where the analyte is not catalytic.[7] In those systems, an analyte reacts with one precursor to form one gelator (Figure 4.1A). To increase the sensitivity in these sensors, a signal amplification system is needed. Signal amplification of chemosensors has been accomplished using analyte-triggered disassembling polymers.[8] Disassembly of linear polymers and dendrimers can be initiated by an analyte cleaving an end group. Once cleavage occurs, the backbone of the polymer disassembles spontaneously, thus amplifying the initial analyte signal by a factor equivalent to the number of repeat units in the polymer.

We propose a similar amplification scaffold for our gel-based sensor, wherein disassembly of the polymer backbone will result in the release of small molecule gelators (Figure 4.1B). The sensitivity of the system will depend on the polymer length and critical gelation concentration (cgc), the minimum amount of

* D. M. Z. gratefully acknowledges the contributions of undergraduates Jessica Willison and Dylan Phillips for assisting with monomer synthesis as well as Dr. Cheryl Moy for her intellectual contributions.

gelator needed to form a stable gel of the gelator. In addition, analyte selectivity can be tuned by modifying the end group without affecting the polymer backbone or gelator (signal output). Thus, this analyte-triggered gelation amplification method has the potential to be used for a wide range of analytes.

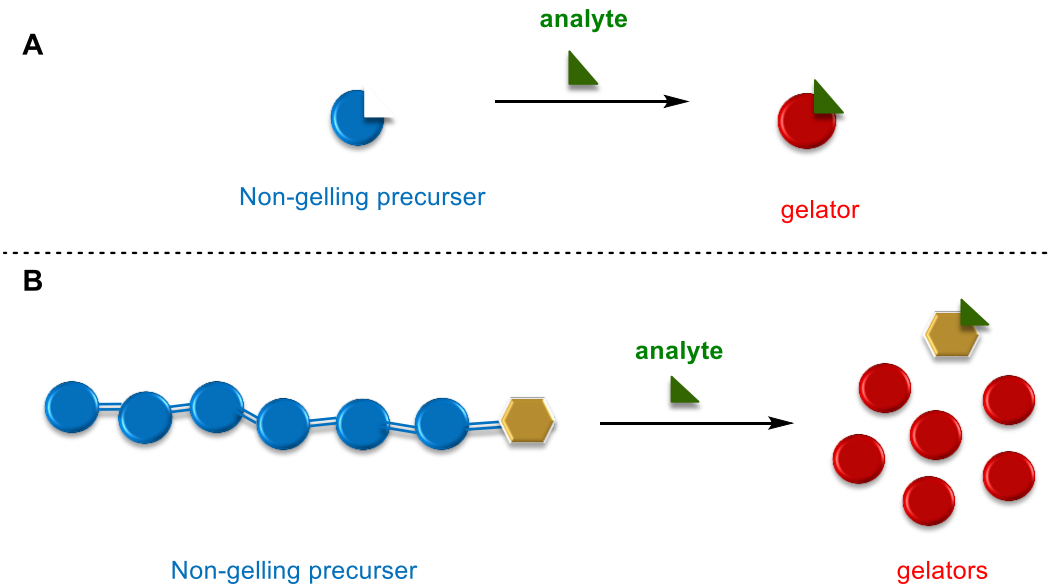


Figure 4.1 (A) Current gel-based scaffolds wherein one analyte reacts with a non-gelling precursor to form one gelator. (B) Proposed amplification scaffold wherein one analyte reacts to cleave an end group, the linear polymer then depolymerizes releasing gelators.

One other example of a signal amplification system in a gel-based sensor was recently reported by Hamachi and coworkers (Figure 4.2A).[9] Their dendritic signal amplification system was incorporated into the hydrogel (Figure 4.2B). When uric acid was present, H_2O_2 was produced which entered the signal amplification system to generate more H_2O_2 that led to gel fiber degradation. However, addition of the signal amplification system only increased their ability to detect uric acid by 3-fold. In contrast, our signal amplification system has the potential to further increase sensitivity of gel-based sensors. Two different linear polymers were examined – poly(phthalaldehyde)s and poly(benzyl ethers).

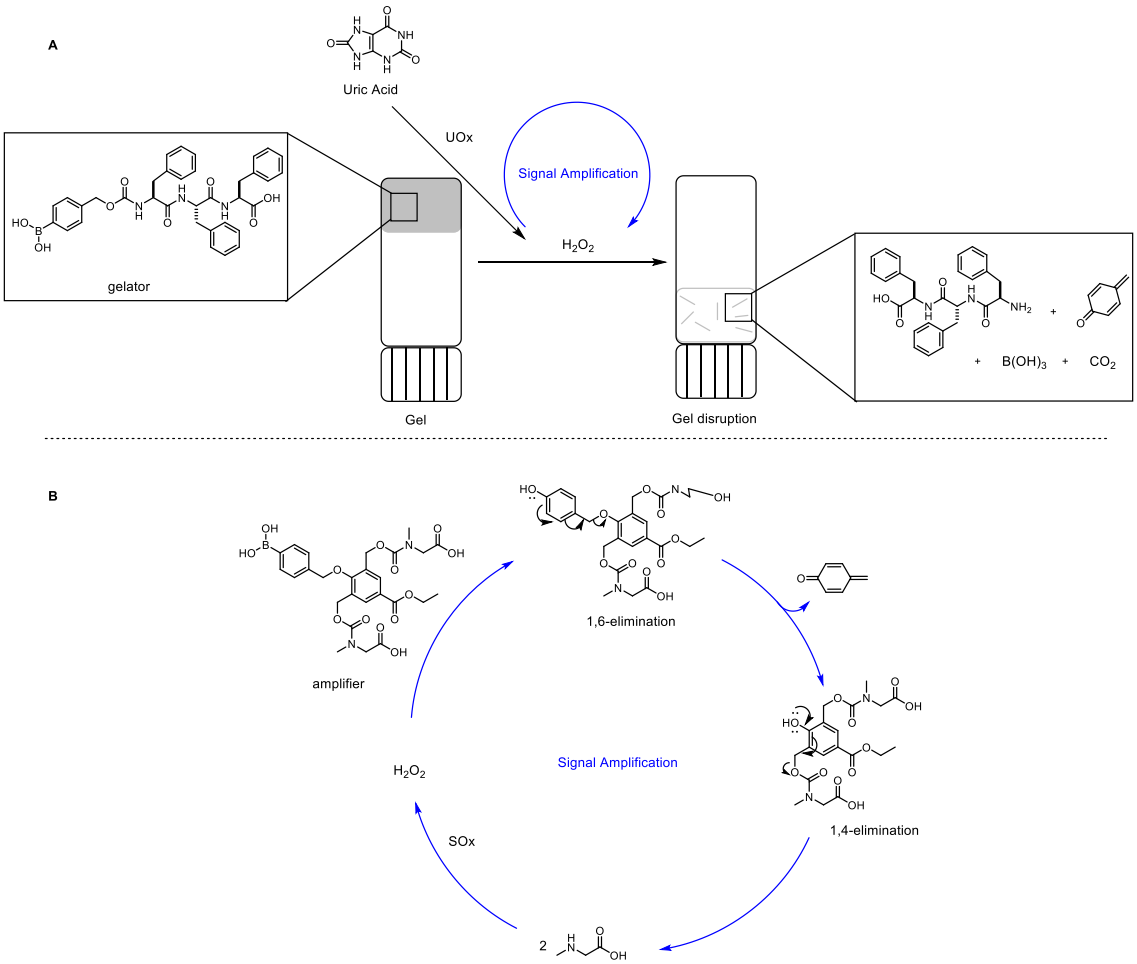
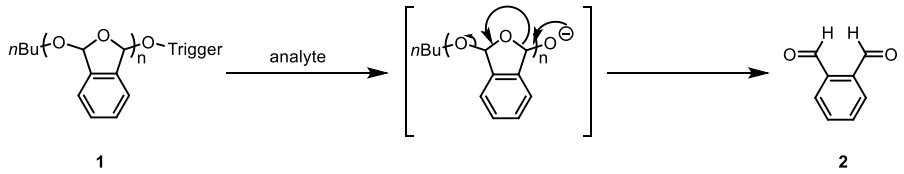


Figure 4.2 (A) Overall multi-component gel-based sensor to detect uric acid. (B) Signal amplification system in the gel-based sensor.

Poly(phthalaldehye) Scaffold

Our initial efforts to design a signal amplification system for gel-based sensors focused on poly(phthalaldehyde)s. Poly(phthalaldehyde)s and their disassembly were first reported in 1969 by Kunitake and coworkers.[10] However, it was not until 2010 that Phillips and coworkers used these polymers as a stimuli response system (Scheme 4.1).[11] They found that cleaving the end group on a poly(phthalaldehyde) polymer (**1**) led to depolymerization, generating phthalaldehdye (**2**). Complete depolymerization occurred within 15 min at room temperature because the polymer was above its ceiling temperature. Ceiling temperature is when the rate of polymerization and depolymerization are equal, and depends on monomer concentration. Because the ceiling temperature of **1** is

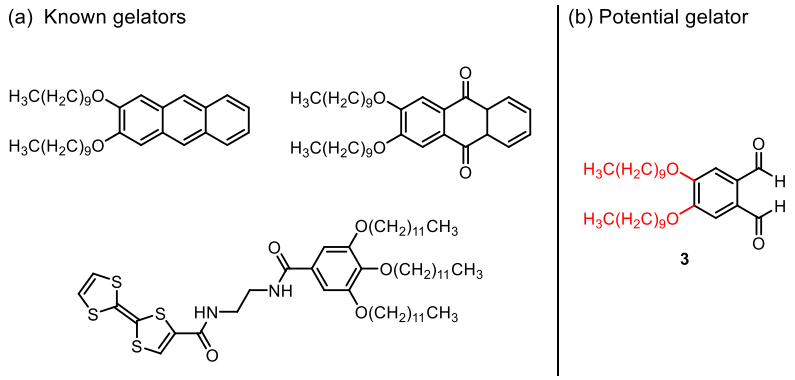
around -40 °C ([Monomer] = 0.75 M)[10], depolymerization is favored above this temperature (with polymerization favored below -40 °C). Excitingly, when the polymer is capped, depolymerization does not occur and the polymer is stable to 180 °C.



Scheme 4.1 Depolymerization mechanism of poly(phthalaldehdye).

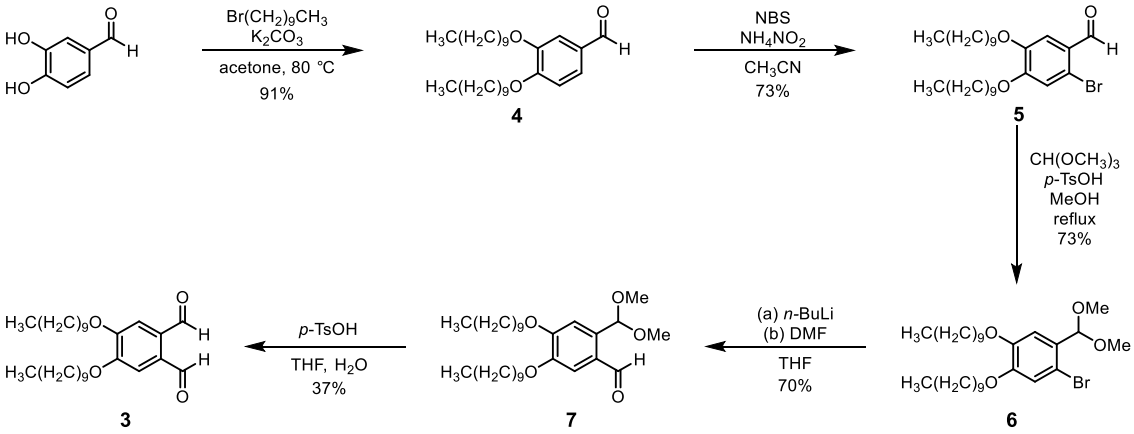
Having selected the poly(phthalaldehyde) backbone for our amplification scaffold, monomer **2** was found to be a nongelator and thus needed to be modified. Common motifs were identified from the literature to guide in **2**'s modification. One motif identified was the presence of long alkyl chains ortho to each other on aromatic rings (Chart 4.1a).[12] With this in mind we sought to modify **2** by adding two decyloxy chains to the 4 and 5 positions (Chart 4.1b).

Chart 4.1



A five-step synthesis was required to access 4,5-bis(decyloxy)phthalaldehyde (**3**). Scheme 4.2 outlines the synthesis of **3** starting with a Williamson ether alkylation to append the decyloxy side-chains, yielding **4**.[13] Compound **4** was brominated with *n*-bromosuccinimide (NBS) to give **5**. The aldehyde on **5** was protected with methyl orthoformate to give **6**. The protected aldehyde (**6**) then underwent sequential lithiation and acylation to append the

second aldehyde and yield **7**.[14] Finally, hydrolysis of **7** gave **3**, which was screened for gel formation.[14] Excitingly, after screening a variety of solvents, **3** was found to form a gel in 5:1 acetone:water (v:v) at 56 mM (Figure 4.2 and appendix 2).



Scheme 4.2 Synthetic route to 4,5-bis(decyloxy)phthalaldehyde (**3**).

Figure 4.3 Gelator **3** in acetone:water (5:1) (56 mM).

Having identified **3** as a gelator we investigated polymerization procedures. The commercial monomer (**2**) had been polymerized under both cationic[10,15] and anionic conditions.[11,16,17] Polymers synthesized under anionic conditions are better controlled than those prepared under cationic conditions. Therefore, we sought to polymerize **3** through an anionic route.

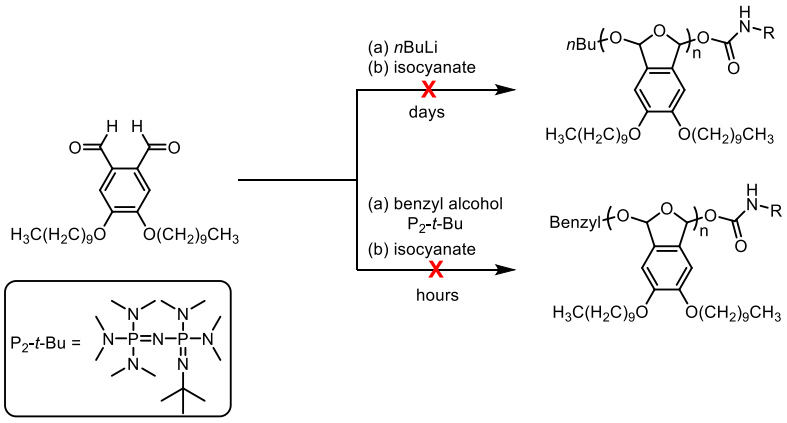
Polymerization of **3** was first attempted using *n*-butyllithium as the initiator at -70 °C in THF for a few days (Scheme 4.3).[11] The reaction is slow and long times are required to access long polymer lengths. Unfortunately, only monomer was recovered even after the reaction was run for days. An alternative procedure

was investigated that reported accessing poly(phthalaldehyde) in high molecular weights within hours rather than days using benzyl alcohol as the initiator and P_2-*t*-Bu phosphazene base† as a catalyst.[17,29] Gelator **3** was subjected to these conditions, however, only monomer was recovered.

During both reaction conditions a precipitate formed quickly upon cooling to -70 °C. Further investigation revealed that **3** precipitates readily at -70 °C within 5 min which is likely the reason for unsuccessful polymerization. To address this issue, polymerization was attempted at higher temperatures. We hypothesized that the ceiling temperature of gelator **3** would be close to -40 °C, the ceiling temperature **1**. Thus, attempts to polymerize gelator **3** with *n*-BuLi was carried out at temperatures as high as -50 °C, with consumption of **3** being monitored by *in situ* IR spectroscopy. During these reactions, monomer **3** was not consumed and precipitation still occurred.

Because **3** was still insoluble at higher temperatures, alternative solvents were investigated. Polymerizations were run in THF/cyclohexane and THF/1-methyl pyrrolidine, which had both showed moderate solubility of **3** at temperatures below -40 °C. Unfortunately, precipitation of **3** was still observed at a later time in the polymerization (after 20 min) and no polymer was obtained. Lastly, we investigated slow addition of gelator **3** to the reaction mixture. By adding **3** in slowly, we could start at lower concentrations. However, this approach was still unsuccessful at polymerizing **3**.

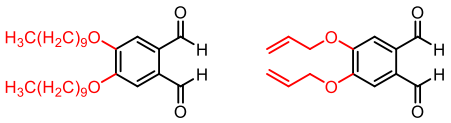
† 1-*tert*-butyl-2,2,4,4,4-pentakis(dimethylamino)-2Λ^5, 4Λ^5-catenadi(phosphazene)



Scheme 4.3 Polymerization attempts of monomer/gelator **3**.

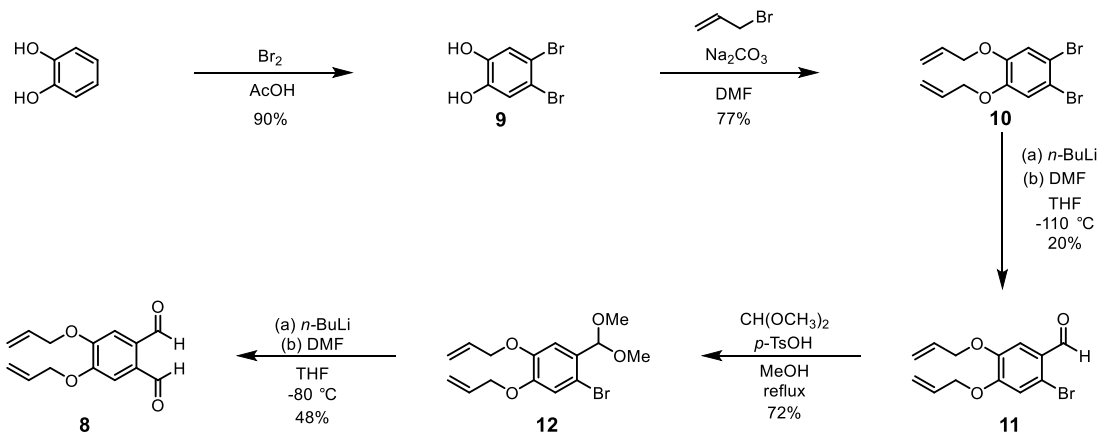
Given the solubility limitations associated with **3** and not **2**, we decreased the alkyl chain length to potentially increase solubility (Chart 4.2). Allyl chains were selected because they could promote π-stacking that could lead to gelation. Additionally, allyl chains could provide access to the original gelator **3** by two post-polymerization reactions.[18] We decided to synthesize a monomer containing allyl chains at the 4 and 5 positions and screen for gelation.

Chart 4.2



3 **8**

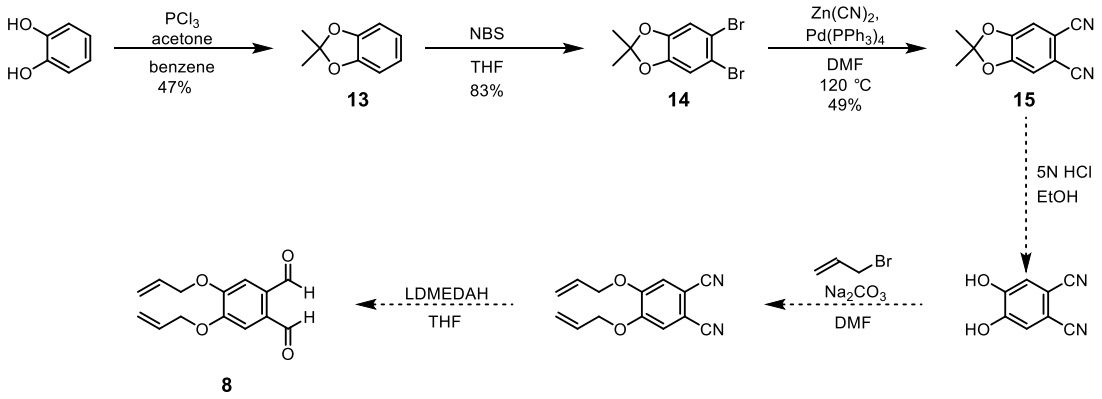
Scheme 4.4 details the five-step synthetic route to generate **8**. Dibromination of catachol to form **9** was followed by a Williamson ether alkylation to append allyl chains.[13,19] Lithation and acylation of **10** at -110 °C installed the first aldehyde, but only in 20% yield.[20] Subsequent protection of the aldehyde in **11** with methylorthoformate yielded **12**, which then underwent a second lithiation and acylation reaction to generate **8** after an acidic workup.[14] Solvents were then then screened for gel formation.



Scheme 4.4 Synthetic route to 4,5-bis(allyloxy)phthalaldehyde (**8**).

Figure 4.4 Gelator **8** in MeOH/H_2O (1:1).

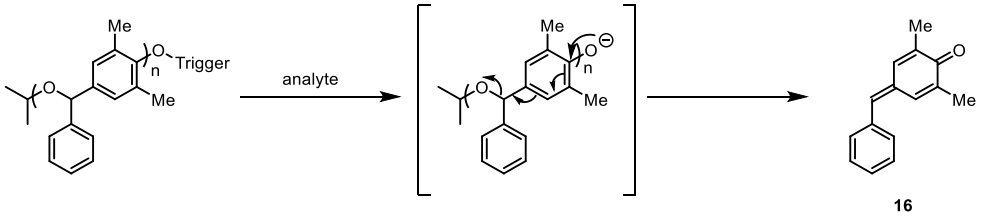
Excitingly, **8** formed a gel in MeOH/water (1:1) at 121 mM (Figure 4.3 and appendix 2). To test if **8** could be polymerized at low temperatures, sufficient quantities needed to be synthesized. Unfortunately, the first lithiation and acylation reaction proved challenging to repeat. Therefore an alternative synthetic route to access **8** was proposed (Scheme 4.5). In this route catechol was protected using acetone to form ketal **13**.[21] Dibromination of **13** at the 4 and 5 positions yielded **14** which subsequently underwent a tandem zinc-palladium catalyzed cyanation to generate **15**.[22,23] Hydrolysis of ketal **15** followed by base-catalyzed alkylation, and reduction of the aromatic nitriles will yield the target monomer/gelator **8**.[13, 24-25]



Scheme 4.5 Alternative synthetic route to **8**.

Poly(benzyl ether) Scaffold

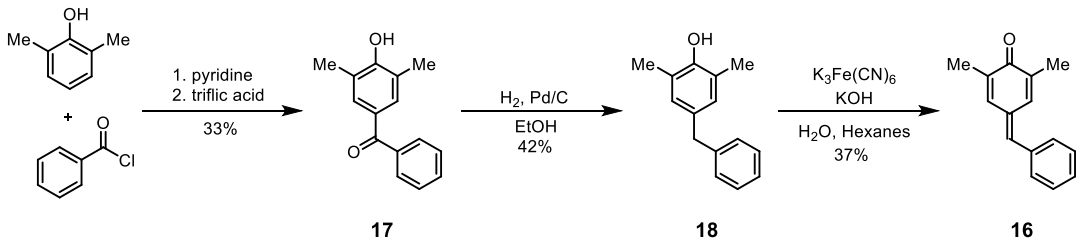
After extensive effort working on the poly(phthalaldehyde) scaffold a different polymer scaffold was examined. Poly(benzyl ether)s were reported by Phillips and coworkers to disassemble into monomers in response to specific stimuli.[26] Complete depolymerization occurred in polar solvents within 30 min and in nonpolar solvents within a week. Advantages of the poly(benzyl ether) over poly(phthalaldehyde) scaffold are increased acid/base stability and more favorable anionic polymerization conditions. Monomer **16** was shown to polymerize at temperatures as high as 20 °C, though recommended temperatures for polymerization are below -20 °C.



Scheme 4.6 Depolymerization mechanism of poly(benzyl ether).

Initial efforts focused on synthesizing monomer **16** because the extended conjugated system could potentially π-stack and promote gelation. A three-step synthesis to access **16** is detailed in Scheme 4.7.[26] Coupling of 2,6-dimethylphenol to benzyl chloride followed by rearomatization produced **17**.

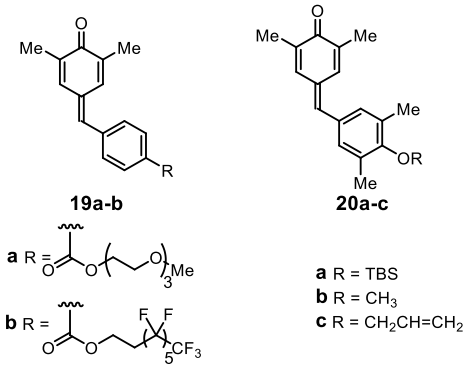
Hydrogenation and subsequent oxidation yielded **16**. Monomer **16** was screened for gel formation but found not to be a gelator in the solvents screened (appendix 2).

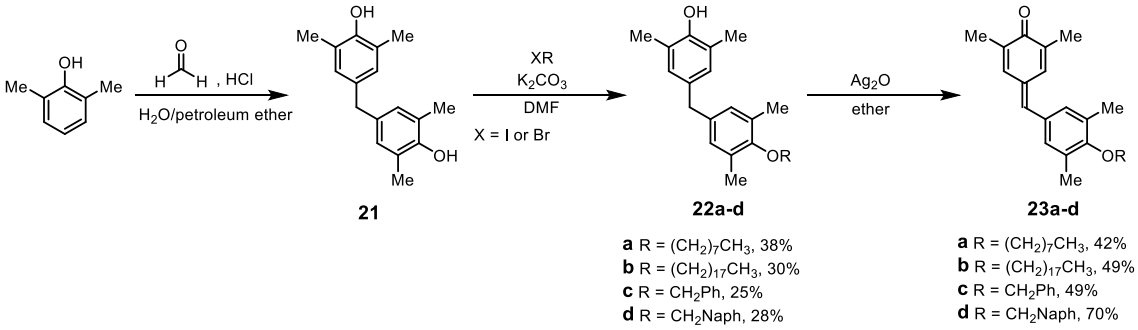


Scheme 4.7 Synthetic route to 4-benzylidene-2,6-dimethylcyclohexa-2,5-dien-1-one (**16**).

Derivatives of **16** were reported by Phillips and coworkers to polymerize (Chart 4.3).[27,28] Alternative synthetic routes were reported to access **19a–b** and **20a–c**. Monomers **20a–c** had the simplest synthetic route for accessing derivatives.[27] Two equivalents of 2,6-dimethylphenol were coupled with formaldehyde to afford **21**. Next, a base-catalyzed alkylation with corresponding bromo- or iodo-functionalized electrophiles yielded derivatives **22a–d**. Oxidizing each derivative afforded quinone methide monomers **23a–d,** which were then screened for gel formation.

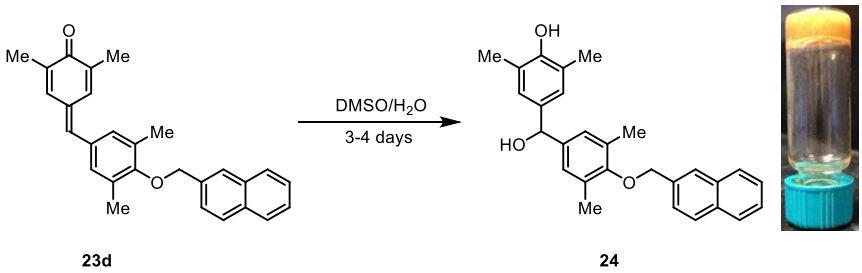
Chart 4.3



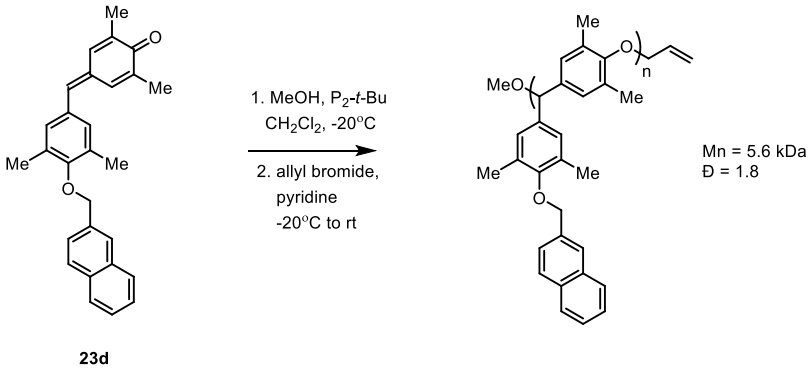


Scheme 4.8 Synthetic route to **23a–d**.

We focused on promoting gelation by appending large alkyl chains (**23a** and **23b**) to increase van der Waals interactions and aromatic groups, to increase π-stacking (**23c** and **23d**). All monomers (**23a–d**) were screened for gel formation in organic solvents but found to be highly soluble. Addition of water caused precipitation to occur, however no gelators were identified. Interestingly, we observed that **23d** in a DMSO/H_2O solution underwent hydration over a period of ~3–4 days to form a gel (Scheme 4.9). With **24** identified as a gel we set out to test whether **23d** polymerized under anionic conditions with the P_2-*t*-Bu base as a catalyst (Scheme 4.10). We targeted a polymer length of ~20 repeat units and obtained polymer after capping with allyl bromide (M_n = 5.6 kDa, Đ = 1.8, ~14 repeat units).



Scheme 4.9 Hydration of **23d** to **24** and subsequent gel formation.

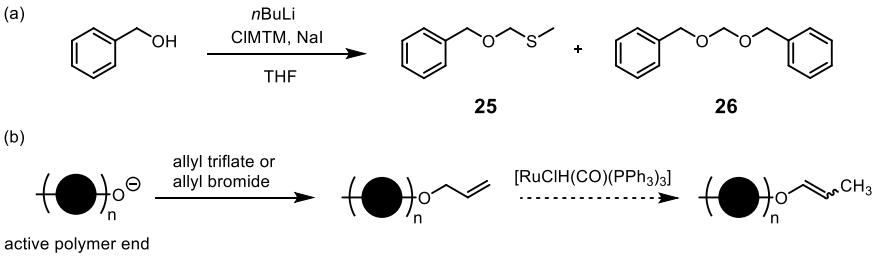


Scheme 4.10 Polymerization of **23d**.

Potential End Groups

A wide range of analytes can be detected with the use of different end groups. We were interested in detecting mercury because it is a powerful neurotoxin and an environmental pollutant that is found in drinking water.[29,30] The Environmental Protection Agency (EPA) has set the maximum level of inorganic mercury in drinking water at 2 ppb.[30] To detect inorganic mercury, an end group sensitive to mercury was needed. We initially proposed the use of methylthiomethyl (MTM) as the end group due to its ability to be selectively cleaved in the presence of Hg(II).[31]

A model system was designed to test if capping with MTM under polymerization conditions occurred (Scheme 4.10). Thus, benzyl alcohol was deprotonated with *n*-BuLi and reacted with ClMTM. Instead of obtaining only the desired product (**25**), **26** was observed as well. An alternative end group for mercury detection are vinyl ethers. Koide and co-workers showed that vinyl ethers are selectively cleaved by Hg(II).[32] To install this end group, we proposed first to allyl-cap the polymer and then convert it to a vinyl ether using a ruthenium catalyst (Scheme 4.11) because direct substitution with a vinyl group is not possible via an S_N2 mechanism.[33] Both poly(phthalaldehyde) and poly(benzyl ether)s have been capped with an allyl chain by reacting the active end of the polymer with allyl triflate or allyl bromide.



Scheme 4.11 (a) A model system to test capping the polymerization with MTM. (b) A proposed route to installing vinyl ether as a potential end group for mercury detection.

Conclusions and Future Directions

Two disassembling polymer scaffolds were investigated for amplifying analyte concentrations in gel-based sensors. While examining the poly(phthalaldehyde) scaffold, two monomers were synthesized and found to form gels in H_2O/acetone or H_2O/MeOH solutions. Unfortunately, monomer **3** was not successfully polymerized due to insolubility at low temperatures needed for polymerization. Alternatively, monomer **8** shows promise as its shorter chains may solve make it more soluble at low temperatures. While the first synthetic route to monomer **8** was problematic on scaling up, the route suggested in Scheme 4.5 gives moderate-to-high yields in the first three steps. Future work for the poly(phthalaldehyde) scaffold should focus on finishing the synthesis of **8**. After **8** is obtained in sufficient quantities, anionic polymerization with the P_2-*t*-Bu base should be tried.

While working on the poly(benzyl ether) scaffold, four different monomers (**23a–d**) were synthesized in three easy synthetic steps and screened for gel formation. The monomers themselves were found not to be gelators. However, **23d** was found to undergo hydration to **24**, which gelled DMSO/H_2O. Furthermore, we successfully polymerized **23d** under anionic conditions to obtain polymers with approximately 21 repeat units. These polymers were capped with allyl ethers, which can be converted to vinyl ethers by a post-polymerization reaction with a ruthenium catalyst outlined in Scheme 4.11b. Polymers capped with vinyl ethers will be useful for selectively detecting mercury. Upon cleavage of vinyl ether with mercury, depolymerization would release **23d**, which would undergo hydration (currently 3–4 days) to **24** and result in gelation. Overall, the

analyte signal would be amplified 21-fold. Future work on this scaffold should focus on four main areas: (i) enhancing hydration rate of **23d**, (ii) optimizing the polymerization of **23d** to access larger polymers, (iii) carrying out the conversion of allyl end groups to vinyl end groups, and (iv) optimizing depolymerization conditions to detect mercury.

To increase the hydration rate, catalytic acid (e.g., phosphoric acid) or base (e.g., NaOH) could be added. We propose testing base-catalyzed reactions first as basic conditions favor the anionic form promoting depolymerization.[26] It will be important to determine whether gelation still occurs under basic conditions. If gelation is disrupted, an acid catalyzed route could then be considered. As before, gelation and depolymerization should be checked in the presence of acid to determine whether it will affect either process.

While with our initial test we were able to access polymers with ~14 repeat units, longer polymers could be accessed by decreasing the molar equivalents of initiator added with respect to monomer. To date, polymers with ~2,300 repeat units have been reported using the quinone methide monomer **16**. By accessing longer polymers, we would be able to detect lower levels of analyte with our gel-based sensor.

In Scheme 4.10, the polymer was successfully capped with allyl bromide. The allyl ether should be converted to a vinyl ether to detect our analyte of interest, mercury. A model system that uses benzyl alcohol could be used to test the conditions described in Scheme 4.11b. After optimization, a short polymer should be capped with allyl bromide and converted to vinyl ether.

Lastly, depolymerization conditions need to be optimized. Conditions for depolymerization such as temperature and solvent should be considered. Room temperature is ideal for sensing purposes, though increased temperature could shorten the time required for complete depolymerization. In addition, solvent should be considered, as depolymerization of poly(benzyl ether)s has been experimentally observed to be faster in polar solvents than in nonpolar solvents.[26] Once each of these conditions are optimized, we will have achieved amplification of the analyte signal in our gel-based sensor.

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Part 2: Developing online resources for organic courses

Chapter 5*

Using Student-Generated Instructional Materials to Customize an Online e-Homework Platform

Online resources are increasingly prevalent in chemistry courses.[1] Online homework systems are particularly appealing because they engage students while providing feedback through hints, as well as links to texts, videos, etc.[2–5] These feedback-driven systems can help students identify areas of weakness without input from the instructor. Online homework systems have been studied by several research groups in organic chemistry. When courses have used online homework, comparable scores[4] or improved scores[6] on exams or course grades have been reported when compared with written homework. In addition, positive correlations between student online homework scores and grades[4,7] or exam scores[2,6,8–10] have been observed. Qualitative findings from these studies report positive student perceptions of online homework and high perceived helpfulness in learning course content.[4,6,7] Nevertheless, one disadvantage is that the questions may not be aligned with course assessments. Indeed, identifying an online resource for the introductory organic chemistry courses at the University of Michigan (U-M) proved difficult as our exams require students to answer open-ended questions to new and unfamiliar literature-based examples (Figure 5.1).[11,12] By using literature-based examples, students are provided motivation to learn organic chemistry by connecting what they learn in class to real world examples.[13] In addition, these type of questions require students to transfer knowledge gained in class to solve new unfamiliar examples forcing them to focus less on rote memorization and more on developing their reasoning skills.[14,15]

* Zurcher, D. M.; Coppola, B. P.; McNeil, A. J. *J. Chem. Educ.* **2015,** in revision.

For this reason, we decided to customize a feedback-driven online homework system (Sapling Learning), using students to generate the content.[16] While most questions in online homework systems are created by publishers or instructors, which undoubtedly help students learn course content, they do not provide the material from a student's perspective. Thus, we turned to student-generated instructional materials, which lend purpose to student work, encourages student engagement with course content, and can generate a significant quantity of material in a short period of time.[17,18] Furthermore, the questions created by students will be provided to future students as a supplemental instruction resource. At the outset, we wondered whether students could generate high quality questions, with structural drawing and mechanistic functionality, in an online homework system. The answer is a resounding "yes." Herein, we describe our course model, including platform selection, course design, and question review process for engaging students in generating content aligned with U-M course assessments.

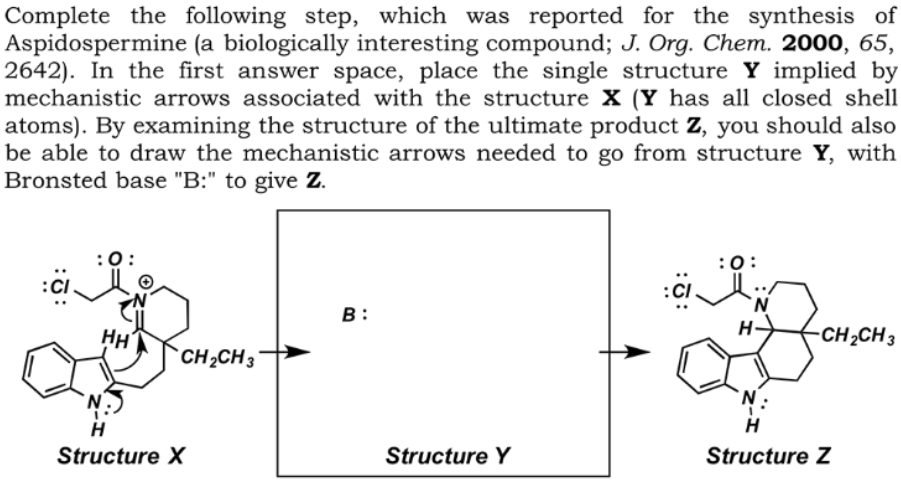


Figure 5.1 A representative exam question.

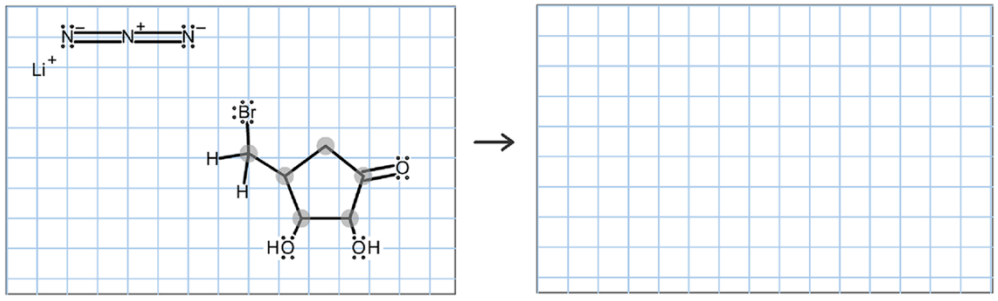
Approach

We first evaluated several online homework software platforms. PeerWise has been a successful platform for students to generate questions in but is limited to multiple choice questions.[19,20] We eventually selected Sapling Learning because the interface includes structural drawing and mechanistic functionality, as well as traditional formats (e.g., multiple choice and fill-in-the-blank questions).[16]

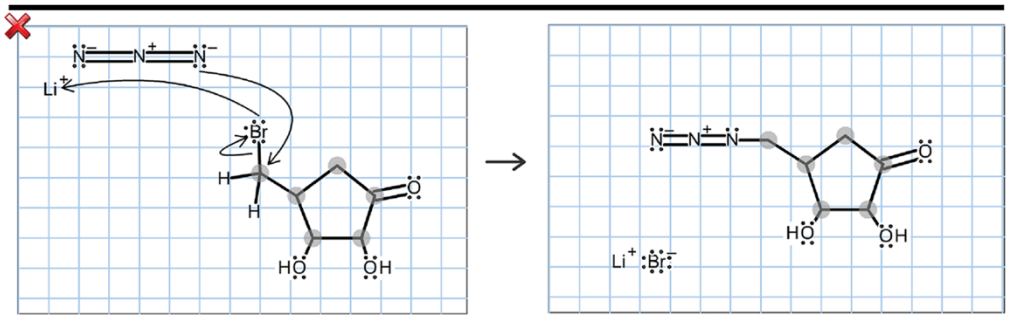
Moreover, the authoring interface is user-friendly, which should facilitate training of a number of students. In addition, multiple forms of feedback (e.g., specific, default, and solution) can be integrated into each question. Specific feedback provides hints associated with an incorrect answer, while default feedback gives a general response to any other incorrect answer. An example of specific and default feedback from a student-generated question is given in Figure 5.2. Solution feedback provides an explanation of the solution to students when they view the correct answer (Figure 5.3). All questions created by our students included these three types of feedback.

Question

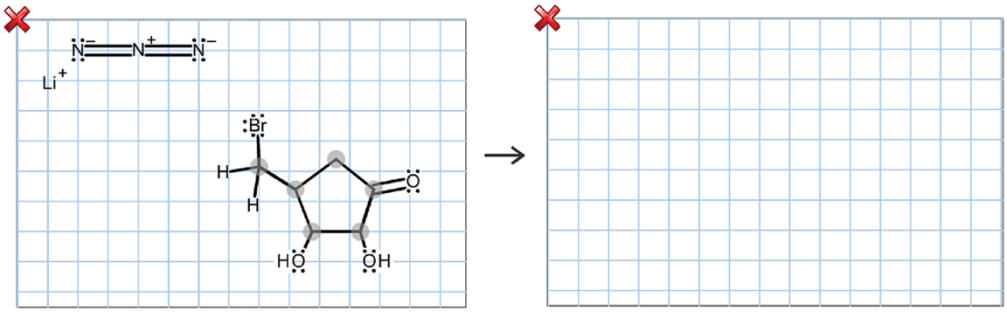
This reaction is part of an eight-step process to produce 5-amino-5-deoxy-aldonolactams from a monosaccharide (*Tetrahedron Lett.* **1997**, *38*, 7733–7736). This step involves a simple substitution at an sp^3 hybridized carbon. The bond between the carbon and bromine will break. A single bond will form between that carbon and a terminal nitrogen on the azide ion (N_3^-). Complete the reaction by adding curved arrows and drawing the products of the reaction step. Show all lone-pairs of electrons and formal charges.



Incorrect Answers



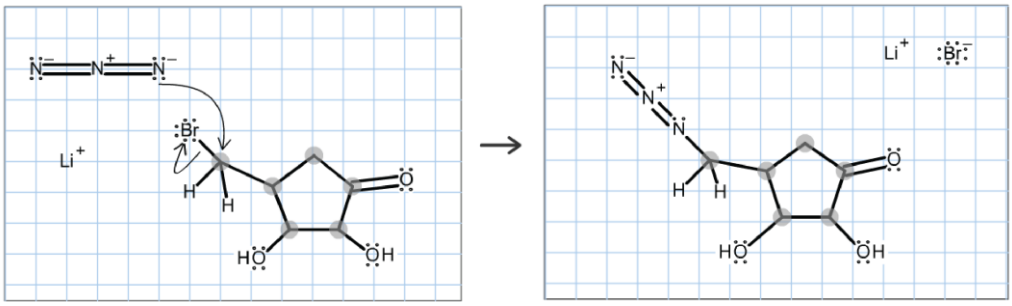
Specific Feedback: Incorrect. You have a curved arrow going to the wrong place. Arrows indicate either the formation or breaking of a covalent bond. What type of bond would form between a bromine and lithium ion?



Default Feedback: Incorrect. Read the directions carefully, as it indicates which bonds are formed and broken in this reaction. Remember curved arrows represent the movement of electrons and start with electrons from a lone pair or a bond. Check for formal charges and nonbonding electrons. Only the atoms shown in the starting materials should appear in the products.

Figure 5.2 A student-generated question and examples of specific and default feedback.

Correct Answer



Solution Feedback: As indicated in the problem instructions the reaction occurs in one mechanistic step. The terminal nitrogen (nucleophile), which has a negative charge, attacks the carbon (electrophile) that has a bromide attached forming a new bond. Upon attacking the carbon the bromide leaves in the same step with both electrons from the C-Br bond giving a negatively charged Br^-. The reaction is known as a nucleophilic substitution reaction.

Figure 5.3 The correct answer to the student-generated question in Figure 5.2.

For our pilot project, we targeted students in the Structured Study Group (SSG) program, a supplemental instruction option for students enrolled in first-semester organic chemistry.[21] The SSG program is led by junior- and senior-level undergraduate students. SSG classes meet two hours per week for 15 weeks. Most students who participated in SSG during our pilot were freshmen and sophomores (N = 142, Fall 2013). During the pilot project students-generated questions as just one assignment in the SSG curriculum, because of this there was insufficient time for multiple rounds of review and refinement. We subsequently decided to take a different approach and created a one-credit course focused solely on authoring questions. We invited students who generated high quality questions in the pilot project to enroll in this course (Winter 2014, N = 31; Fall 2014, N = 12; Winter 2015, N = 16). These students met once a week for one hour and each class was led by junior- and senior-level undergraduates. Students received credit for constructing questions, incorrect answers, and feedback. In addition, each student earned $250 if they programmed their questions, answers and feedback into Sapling Learning.

Question topics were identified by instructors of the course who defined a set of organic chemistry “skills” for which students would benefit from having additional practice with. A quintessential example is the curved-arrow convention used in

organic chemistry mechanisms. We assume students achieve literacy in curved arrows after it is introduced, however, some students struggle throughout the course.[22] These students may achieve proficiency in a feedback-driven environment such as Sapling Learning. The skill-based topics we identified for the first semester course were: curved-arrow notation, resonance, acid-base chemistry, individual stereochemistry relationships, comparative stereochemistry relationships, electrophilic addition, elimination, substitution, transition states, electrophilic aromatic substitution, reaction mechanisms, and aromaticity. For the second semester, during which many more reactions are presented, skill-based topics included: epoxide chemistry, aldehyde/ketone chemistry, acyl transfer reactions, enolate chemistry, Diels-Alder chemistry, peptide chemistry, and carbohydrate chemistry.

The training period for the pilot project (in the SSG course) took five weeks and is outlined in Figure 5.3. Students were first trained to create usable questions, answers and feedback. Then they learned how to program the questions into Sapling Learning. To try and instill purpose in their work, the students were informed that their questions would be used to instruct the next generation of students. Next, the training focused on how to create a question. Students were divided into groups (with 2–3 members) and given an example question to solve on the skill-based topic of curved arrow notation (Appendix 3). They were instructed to create an array of reasonable, but incorrect answers with feedback, and a general feedback response that hinted at key concepts. Each group then shared their incorrect answers and feedback with the class, and common incorrect answers were grouped into a master list. Students then authored the example question in Sapling Learning, peer reviewed the question, and addressed suggested edits. After the initial training period, the students were tasked with generating new questions using literature sources for inspiration. Overall, 172 questions were generated and subjected to an internal review process. First, classmates reviewed questions guided by a rubric (Appendix 3). Once the edits were complete, the questions were reviewed by the class leader and finally by the graduate student overseeing the project, who evaluated them on a pass/fail scale.

We evaluated each question for grammar, clarity, programming, accuracy of written feedback, and functionality in the interface. Unfortunately, only 64 (37%) of the 172 questions passed this internal review (Table 5.1). The majority of questions did not pass the graduate review due to incorrect chemistry, which we hypothesized stemmed from the students' inexperience in creating a question from the literature (e.g., unable to distinguish whether a reaction occurred under acidic or basic conditions, or if the mechanism was concerted or step-wise). We concluded that having the students use the primary literature as an inspiration for questions was not a viable approach.

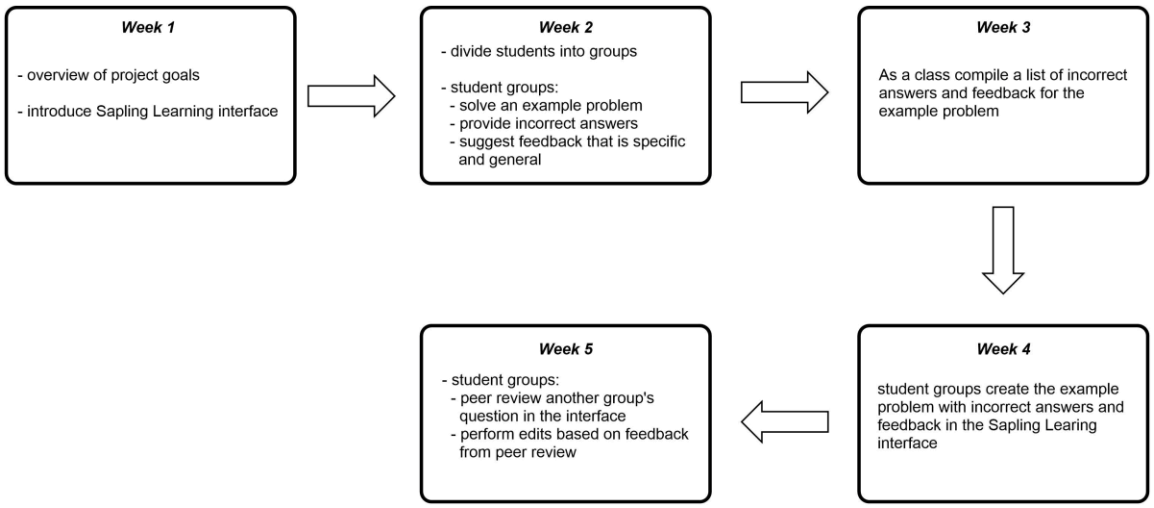


Figure 5.4 Timeline for training students to generate questions in Sapling Learning.

Table 5.1 Number of questions generated and publishable after the internal review process

	Pilot (Fall 2013)	*1-credit course (Winter 2014)*	*1-credit course (Fall 2014)*	*1-credit course (Winter 2015)*	*Total*
questions generated	172	639	192	290	1,293
publishable questions	64	627	167	256	1,114
% passed	37	98	87	88	86

We made several changes to address the shortfalls of the pilot project. First, we replaced the primary literature with old exams, which contain questions derived from the literature, as the source material. For example, an exam question focused on hydrogen-bonding can be transformed into an acid-base question (Figure 5.4). This approach enables students to generate an original question, but with chemistry that was previously vetted for the course. The second key change was moving from the SSG format to a stand-alone 1-credit course (Table 5.2). Students who participated in the first stand-alone course met 1h/week and were previously trained in the pilot project and began generating content immediately. Each student was responsible for generating two questions per week, where a different skill-based topic was selected for each week. Students also spent three weeks reviewing and editing questions. This accelerated timeline generated 639 questions over a single semester with 98% of the questions created deemed usable after internal review (Table 5.1). As a result, two subsequent 1-credit courses were implemented. These courses focused on creating content for the second semester of organic chemistry. A similar timeline was implemented and 87% (Fall 2014) and 88% (Winter 2015) of questions passed the internal review.

Table 5.2 Differences between each iteration of the project

	pilot (Fall 2013)	*1-credit course (Winter 2014)*	*1-credit course (Fall 2014)*	*1-credit course (Winter 2015)*
source material	literature journal	old test questions	old test questions	old test questions
course	organic chemistry I	organic chemistry I	organic chemistry II	organic chemistry II
# of participants	142	31	12	16
# of questions generated per student or group	3	20	16	18

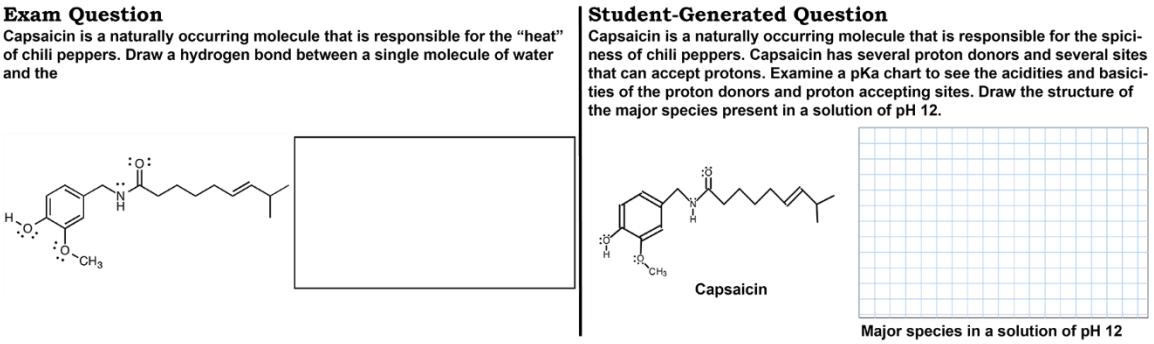


Figure 5.5 The original exam question (left) and student-generated question (right).

A randomly chosen subset of questions that had passed the internal review were submitted to a Sapling Learning technician to further assess the content quality. A total of 703 questions were examined, with 677 (96%) passing their review based on functionality in the interface (Table 5.3). A more in-depth review was carried out by a Sapling Learning technician on a randomly-selected set of 113 questions. While 31 (27%) needed no further edits, 62 (55%) contained technical and formatting problems and 20 (18%) contained content errors. Technical and format issues included insufficient programming with respect to benzene rings and stereocenters, improper bond angles, unclear feedback, and inefficient question layout.[23] Looking more closely at the content errors, 4 questions (3.5%) had wrong chemistry such as incorrect selectivity in a Diels-Alder reaction. The other 16 questions contained content errors such as missing counterions and missing lone pairs, which can quickly be corrected through editing. The issues identified by the external review will be addressed by updating the peer review criteria, students follow when reviewing questions, and the authoring manual. By making these changes we will negate the need for an external review in future iterations of the project.

Table 5.3 Quality of questions determined by the external review

	# of questions submitted	# of questions with formatting/technical issues	# of questions with content errors	# of questions passed
external technical review (% passed)	703	--	--	677 (96%)
external in-depth review (% of questions)	113	62 (55%)	20 (18%)	31 (27%)

Questions that passed the internal review (1,114 of the 1,293 questions) were released to students enrolled in the corresponding organic chemistry courses. Student users have reported several common errors, including missing or extra lone pairs and charges, extra carbons in side chains, and misspellings. In addition, some students had difficulty triggering specific feedback, which only occurs when the question is answered exactly the way it was programmed. Any additional mistake (e.g., forgetting a lone pair of electrons) triggers the default feedback. To improve the question quality, students currently enrolled in the SSG program are continuing to edit/revise the questions instead of generating more content. For example, they are asked to generate additional specific feedback responses and address formatting issues. Furthermore, studies suggest the type of feedback plays an important role in student learning.[24–26] Future effort should evaluate whether we can improve the feedback quality by incorporating animations, mechanistic drawings and additional types besides written.

We surveyed students who participated in the 1-credit course to assess their perceptions with respect to the efficacy of the project.[27] Students were asked about their experience in using the Sapling Learning interface to author questions. Students reported that programming in questions was mostly straightforward, but reported lower favorability with respect to specific interface qualities such as ease of use, utility (i.e., ability to perform several functions), and ability to allow for creativity (Appendix 3). Nevertheless, most students reported spending less than one hour programming each question into the interface (Appendix 3).

Because our resource content was generated by students, which is different from the previously studied online homework systems, we are currently assessing the effectiveness of the resource on students who used the online system during the organic chemistry course (not students who created the questions). We are evaluating the resource by collecting item-analysis data from exams to compare the performance of students who did or did not use Sapling Learning. A subset of this study will focus on how students are interacting with the online resource (see chapter 6).

Summary

We engaged students in generating questions for an online resource that were aligned with specific organic chemistry course assessments. Over 1,100 questions that passed the internal review process were generated over four semesters, and these questions are now being utilized by our currently enrolled students. We found that modifying old exam questions coupled with several rounds of peer review led to higher quality content, as judged by an internal and external review process. We generated a successful framework for the course design, which can be implemented by other instructors to generate online resources aligned with their own course assessments.

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Chapter 6*

Analyzing a Student-Generated Organic Chemistry e-Homework Platform

Online homework has increased steadily in popularity since the early 2000's, in part because it is an effective way to distribute and grade a large number questions, as well as provide immediate feedback to students.[1,2] When comparing online to "traditional" paper-based homework, reports are divided on whether one is more beneficial to student learning.[3–5] Numerous homework platforms have been investigated and positive correlations have been found between online homework use and course performance or online homework assignment grades and course performance.[6,7] The positive correlations are thought to be due to the immediate feedback that gives students the opportunity to identify weaknesses in their understanding. Online homework systems now include many types of feedback, including hints after incorrect responses. In addition, qualitative findings from these studies and others have reported students' attitudes and perceptions towards online homework to be favorable.[4,8,9]

Because of the advantages associated with online homework, we hypothesized students in the organic chemistry series at the University of Michigan (U-M) would benefit from a similar online system. Thus, we customized an online platform (Sapling Learning) using undergraduate students to generate questions tailored to the content in U-M organic courses.[10] For additional details related to generating questions for the customized online platform, see Chapter 5: "Using Student-Generated Instructional Materials to Customized an Online e-Homework Platform." Three types of feedback were programmed into each question: 1) specific incorrect feedback (which gave an explanation of why a specific answer was incorrect), 2) general incorrect feedback (that hinted at the

* D. M. Z. gratefully acknowledges the contributions of Swee Chiah for her statistical analyses.

concept needed to answer the question), and 3) solution feedback (that explained the correct answer).

Having created the feedback-driven online homework system, we initiated an exploratory study to determine whether it affected student learning measured by course exam scores and overall grade. We examine student perceptions of our platform, question quality, and the usefulness of feedback. We investigate whether student course performance improves upon using the platform and we explore how students interact with the platform to learn course content. Lastly, questions for future evaluation are proposed.[11]

Results

Students enrolled in either Organic Chemistry I (CHEM 210) or Organic Chemistry II (CHEM 215) had access to the online questions associated with their course. Because student's final grade in both courses are determined by four exams the online questions served as an optional resource. Students enrolled in these courses (CHEM 210: Fall 2014, Winter 2015, Fall 2015; CHEM 215: Fall 2015) received free access to the resource for 1-month at the beginning of the semester. After the trial period, a one-time fee of $28 was required for continued use. The 1-month free trial for CHEM 210 included 100 questions on three topics covered for the first exam: curved arrow notation, resonance, and acid-base chemistry. For CHEM 215, 50 questions were offered covering reactions with ketones/aldehydes, imines, and acetals/ketals. The rest of the content required students to pay the fee to access and (~550 questions for CHEM 210 and ~400 questions for CHEM 215) covered topics associated with the remaining exams. The resource was advertised using flyers and e-mail (Appendix 4). In addition, we met with two supplemental instruction groups to promote the resource: Science Learning Center (SLC) study group leaders, an optional study session for students, and structured study group (SSG) leaders, an optional honors credit class.

We found that students were more willing to use the resource during the free trial than when they had to pay for it. We observed low participation (<50%)

even during the free trial (Table 6.1a). To investigate the reasons for the low participation rate, we surveyed students from CHEM 210 (Fall 2014) during the free trial period, and found that 62% of respondents (N = 316) had used the resource to answer at least one question. Their top reasons for doing so were that they (1) wanted extra practice with the material, (2) wanted to master the topics and (3) were curious if the resource would be helpful (Figure 6.1a). However, some of these students decided to stop using it because they (1) thought the interface was cumbersome, (2) would eventually need to pay for it and (3) had no time (Figure 6.1b). The 38% of students who did not use the resource mentioned their top reasons for not doing so were that they (1) had no time, (2) eventually needed to pay for it and (3) were unaware of the resource (Figure 6.1c). Unfortunately, we were not able to provide the resource to all students for free after the 1-month trial period.

During the subsequent semesters of CHEM 210, participation decreased by 24% and then 7% during the free trial and 3% and then 2% during the paid period. This decrease could be due to ineffective advertising. Parker and Loudon also observed low participation when online homework was optional and found that grade incentives increased participation.[4]

Table 6.1 CHEM 210 and CHEM 215 class size and number of students who used the resource.

	CHEM 210			***CHEM 215***
	Fall 2014	*Winter 2015*	*Fall 2015*	*Fall 2015*
Students enrolled	1359	500	1278	367
Students who used the free trial	565 (42%)	90 (18%)	135 (11%)	37 (10%)
Students who purchased a subscription	114 (8%)	24 (5%)	44 (3%)	11 (3%)

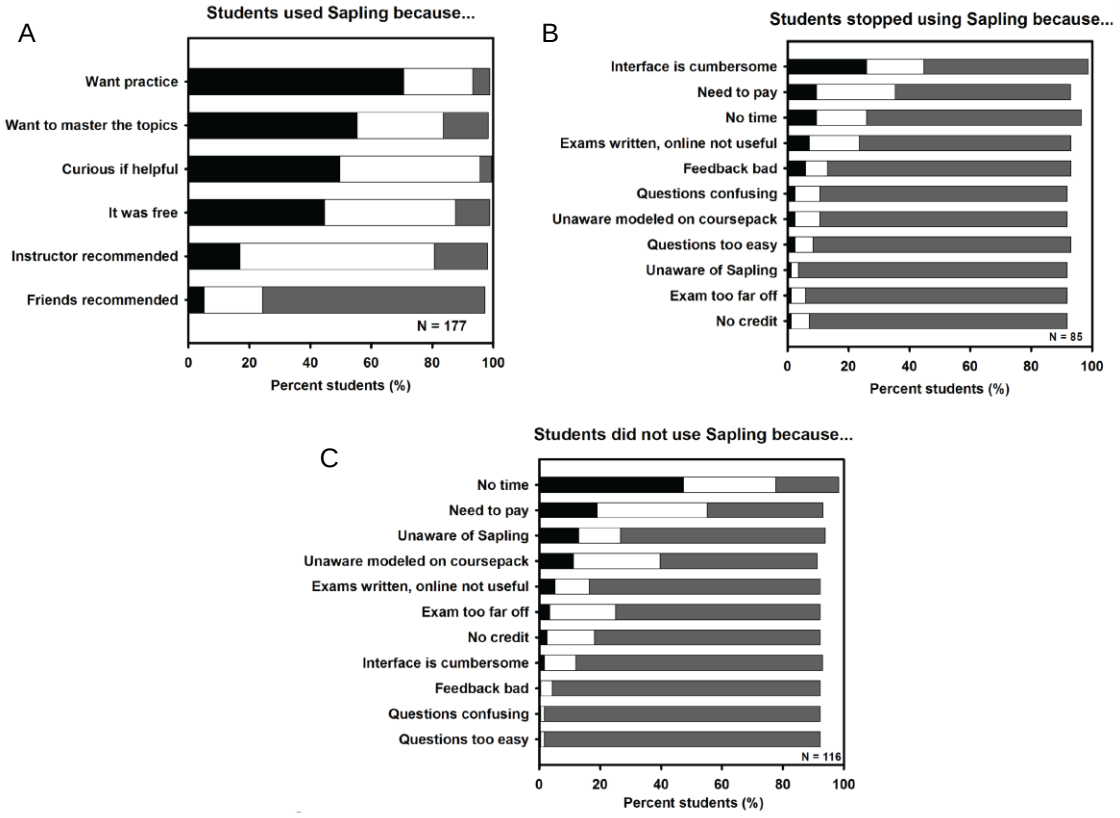

Figure 6.1 Survey data collected for participants who indicated reasons why they (a) were using Sapling Learning (b) stopped using Sapling Learning and (c) never used Sapling Learning. Black indicates that the reason was critical to them, white indicates the reason was important to them and grey indicates that the reason does not apply to them.

Students who used the resource for CHEM 210 and 215 were asked to give feedback on ease of use, clarity of question instructions and feedback, and the educational value of a question (i.e., how much can students learn). Responses were collected for 253 questions over all semesters the resource was offered. Students reported that questions were clearly written and provided helpful incorrect feedback as well as solution explanations (Figure 6.2a, b, and c). For nearly 75% of the questions, the educational value was rated high (≥4 on a scale of 1 to 5, 5 being the highest). Suggested improvements to questions included correcting grammar and providing more specific feedback. (Appendix 4). These questions are currently being improved through an editing assignment in SSG (Appendix 4).[12]

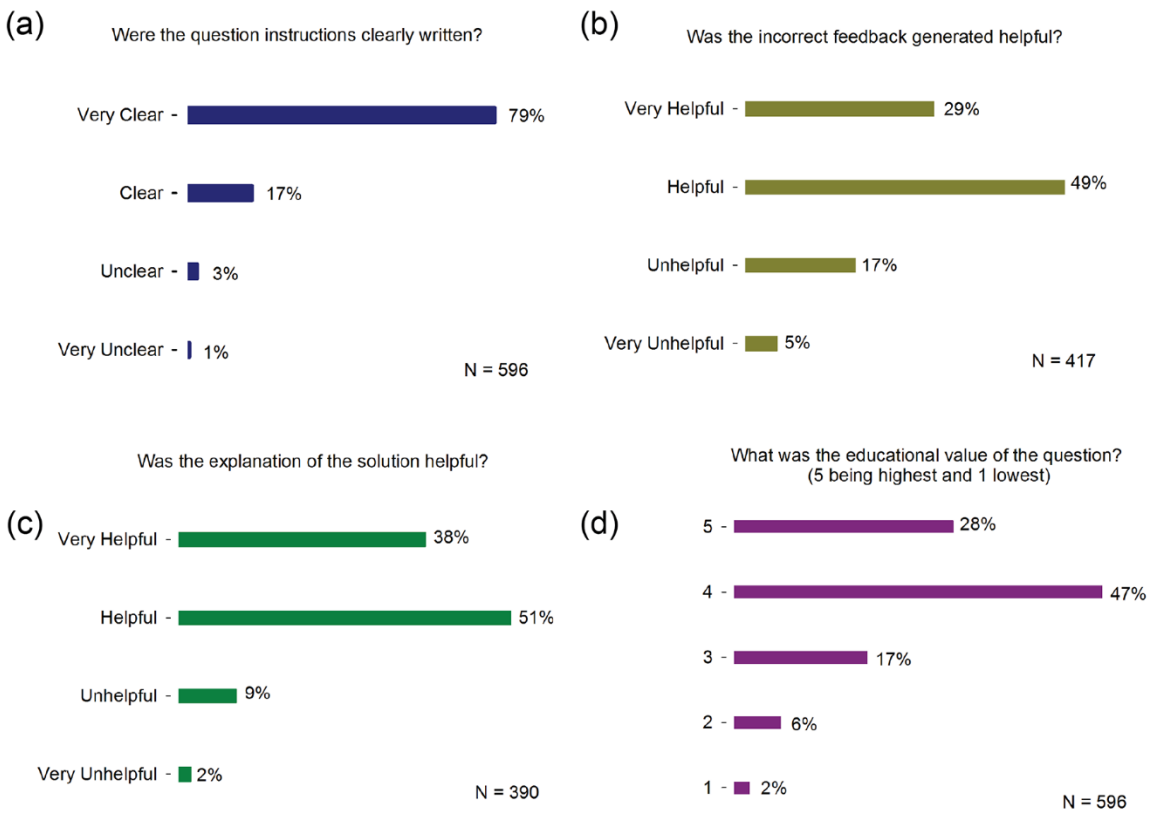

Figure 6.2 Survey data collected for 253 questions in response to (a) “Were the instructions to this questions clearly written?” (b) “Was the incorrect feedback generated helpful?” (c) “Was the explanation of the solution helpful?” (d) “On a scale of 5 to 1 with 5 being the highest, what is the educational value of this question (how much can students learn from this question)?” N indicates the total number of responses collected.

An advantage of Sapling Learning is that information on student interactions with each question is collected. Instructors can determine how many questions a student interacts with, the number of attempts a student takes to answer a specific question, and whether the student viewed the solution after an incorrect response (Figure 6.3). Using this information, we analyzed how the resource affected students’ course performance by evaluating student exam scores and question interactions. For initial analyses we delineated two populations, “users” and “non-users,” for the Fall 2014 CHEM 210 class and compared their exam scores by performing a Welch two sample t-test.[13] Users were defined as any student who interacted with at least one question on a topic

corresponding to that exam. The users performed better ($p < 0.05$) than non-users for exams 1 and 3 (Table 6.2).

Of note, a self-selection bias could influence the data because the resource was optional.[14] Self-selection is a phenomenon in which students sort themselves into two populations, in our case users and non-users, and these populations may have differences in intelligence, motivation, and interests. Thus, we must determine whether our observed increase in student performance is a result of our resource. Kochenour *et al*. addressed the issue of self-selection bias (in evaluating the effect of supplementary instruction on student performance) by using student high school grade point averages (HSGPA) and ACT/SAT scores.[15] We propose using a combination of HSGPA, ACT/SAT scores, and student performance on the chemistry entrance exam to determine whether self-selection influences our analyses. We suggest a combination because ACT/SAT scores are found to measure general ability, HSGPA is a measure of intelligence, motivation, and effort by the student, and the entrance sores will identify their level of chemical knowledge.[16] Together these measures will help us determine if a self-selection bias is present in our analysis. In addition, because it is unlikely that interacting with a single question strongly influenced exam performance, we compared exam scores for each test to the total number of questions students interacted with, but found no correlation after performing a Pearson's product-moment correlation (Appendix 4).

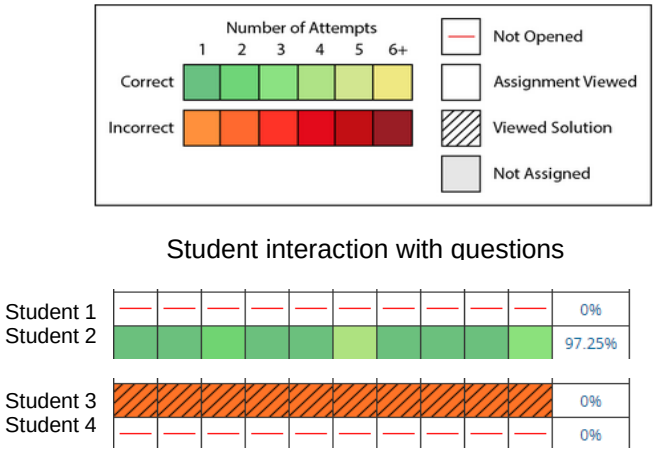

Figure 6.3 Example information collected by Sapling Learning on student interacts with questions. Each box indicates one question.

Table 6.2 Summary of Welch Two Sample t-test results. Bold results are significant ($p<0.05$).

Exam	Non-Sapling users average exam score points (# of students)	Sapling users average exam score (# of students)	p-value
Exam 1 (100 points possible)	**75.66 (794)**	**81.66 (565)**	**2.84e-13**
Exam 2 (120 points possible)	85.02 (1223)	88.18 (114)	0.1055
Exam 3 (140 points possible)	**81.80 (1224)**	**89.03 (90)**	**0.02299**
Final (240 points possible)	157.43 (1257)	155.96 (51)	0.8116
Overall course grade	403.73 (1194)	413.27 (113)	0.3120

While evaluating student interaction, we observed some students would simply click “view the solution” without inputting their answer. By not inputting the answer, students lose access to specific incorrect feedback but still receive general and solution feedback. Students who exhibited this behavior with >50% of the questions they interacted with were classified as “answer-clickers”. Surveying the answer-clickers (7 out of 75 responded) revealed that they worked through the problem on paper before viewing the solution. Three students also indicated at times they instead solved the questions in their head or read the question and immediately viewed the solution.

Students using paper to solve questions before interacting with an online homework platform has been reported in other studies.[8,8] However, because the online homework was required in those cases, they did not observe students completely bypassing the system to view the solution as we did. In particular, Pinhas and Smithrud found through a survey that out of 206 students, 128 (62%) reported solving the question on paper before recording the answer.[17] They showed that students who reported using paper performed better (mean exam score = 57) than students who reported only using the interface (mean exam

score = 51), although they did not quantify how often paper was used to solve a problem. Their hypothesis for this difference in populations is that handwriting causes motor-memory, which appears to be important for organic chemistry, while typing alone does not.

To investigate whether the behavior type and frequency affects course performance, we began a study to observe how students interact with the interface. A pilot study was carried out in Fall 2015 with four students in preparation for a larger study to be carried out in the Winter 2016 semester. All participants were female, with three freshman and one sophomore. At the time of the study, all participants were enrolled in CHEM 210 and had completed the first exam. Student participants were asked to engage with Sapling Learning for 25–30 min, during which time they were videotaped and the computer screen was captured. The screen-capture recorded students using interface tools in real time while the videotape captured other behaviors such as using paper. The participant's prior activity in Sapling Learning was noted to determine whether videotaping influenced their behavior.[18] Prior to the study we determined that three students had fully utilized the interface, while one student had some tendency towards answer-clicking. After the students used the interface, students were asked 10 questions about their opinions of the resource, their study habits for the class, and their computer-based learning experiences (Table 6.3).[2]

Preliminary analysis found that all four participants regularly input their answers into the interface. In addition, three students used material other than the computer to help answer questions. One used notes, one used paper to carry out pK_a calculations, and one used paper to draw structures. Interestingly, students used additional materials for less than 5 minutes of the 25–30 minute experiment. Furthermore, three students failed a question and then moved on without viewing the solution, even though there is no penalty associated with viewing the answer (Appendix 4).

The interview questions were taken as is or modified from a study that probed the role of online homework in a general chemistry course.[2] Questions focused on participant study habits, perception of online homework and

prior/current experience with web-based instruction in other classes (Table 6.3). Preliminary analysis found students use lecture and practice problems to study for the class. Practice problems included a variety of different resources: the textbook, SLC study group leader worksheets (paper-based problems), the course pack (a booklet of old exams without answers) and Sapling Learning. Participants found the explanations in the online resource to be useful but two mentioned that the feedback was at times (unspecified frequency) too generic. Lastly, all participants either had previous experience with or were currently using online homework in a different classes.

Our pilot study was successful at observing the subtle behaviors students exhibit when interacting with online homework. The full study performed in the Winter 2016 semester should focus on expanding the observational study to a larger population, especially answer-clickers. If possible, the study should be performed with each student three different times during the semester to make students more comfortable with the study environment and monitor changes over time. The study could also be run with pairs of students to see how communication between students impacts what we observe. Interview questions could be asked throughout the three sessions. Additional questions that could be asked are: (1) which materials do you use when answering questions online at home? (2) why did you choose not to view the solution for the question? and (3) did other people help you in your learning? (if so, who and how have they helped?) The interview data for both the pilot study and full study should be analyzed and then coded.[15]**Error! Bookmark not defined.** These observation studies should help delineate the *types* of behaviors, which could play a role in course performance.

Table 6.3 Interview questions and themes from the video study

Questions
1. What is your preferred learning style? (Do you learn best by reading, hearing, doing, etc?)
2. Which course tools have helped you learn the most?
3. Which course tools helped you learn the least?
4. What role does homework play in your learning process?
5. What role have computers played in your learning process?
6. How do you study for this course? Describe a typical week.
7. How do you know when you understand the material?
8. What is your opinion about the feedback that you receive using Sapling Learning?
9. During this study what materials did you use and why?
10. What have been your experiences with computer and web-based instruction in other classes?

Conclusions and Future directions

In evaluating our online homework resource we found low student participation, favorable student perception of resource content, some evidence of improved course performance, and that some students forwent inputting the answer into the interface. Collected survey data indicates low student participation is due to student time constraints and resource cost. Yet students who interacted with the resource content found it helpful and showed some improvement in performance. Future work should continue to analyze the data obtained during Fall 2014 with respect to exam performance and online homework use, specifically rerunning the Welch two sample t-test, with the user population excluding students that interacted with fewer than 25 questions. Similar tests should be run with data collected during Fall 2015 to determine reproducibility.

The Pinhas and Smithrud results suggest student behavior with the interface may influence student course performance.[17] We found that a population of students forwent the interface tools in favor of just viewing the solution and its associated feedback. Early evidence indicates they chose to work through problems with paper instead, using the interface as a solution manual. Video and interview data from a pilot study found that students 1) used additional material when answering questions online, 2) would not always view the solution, and 3) had some interaction with computer-based instruction in other classes.

Future research questions that could be addressed with the proposed Winter 2016 study include (1) whether certain behaviors influence exam performance (specifically, do “answer-clickers” that receive less feedback perform differently), (2) whether the behaviors correlate with a specific type of question or specific content, and (3) whether student study habits or prior experience with computer-based instruction influence the behaviors. Combined with the data already collected, these studies will yield a more complete picture of how students use the resource to learn course material and how that correlates to course performance. These studies will help address outstanding questions as to the effectiveness of feedback-driven resources in student learning.

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Appendix 1*

Supporting Information for Chapter 3:
Modifying a Known Gelator Scaffold for Nitrite Detection

I. Materials

All reagent grade materials and solvents were purchased from Sigma-Aldrich, Acros, or TCI. Anilines were distilled under vacuum before each use. Compounds **3a-g** were prepared from modified literature procedures.[1] Deionized water was used unless otherwise specified. Thermogravimetric analysis of the sodium 2-naphthol-6-sulfonate hydrate revealed 2.024 H_2O molecules on average. For the synthetic procedures, an average of 2 H_2O molecules was used.

II. General Experimental

NMR Spectroscopy – ^1H and ^{13}C NMR spectra for all compounds were acquired in d_6-DMSO or D_2O on a Varian vnmr 700 operating at 700 and 176 MHz, or a Varian Inova 500 operating at 500 and 126 MHz. The chemical shift data are reported in units of δ (ppm) relative to tetramethylsilane and referenced by residual protic solvent. An asterisk was used to indicate residual H_2O in all spectra while double bars are used to indicate peaks that have been truncated. The abbreviations s, d, t, at, dd, q, and m were used to signify singlet, doublet, triplet, apparent triplet, doublet of doublets, quartet, and multiplet, respectively.

High Resolution Mass Spectrometry (HRMS) – HRMS data were obtained on a Micromass AutoSpec Ultima Magnetic Sector mass spectrometer via electrospray ionization in negative ion mode.

UV-vis Spectroscopy – UV-vis spectra were taken on a Perkin-Elmer Lambda 850 UV-visible spectrometer. Calibration curves were measured at the λ_{max} for each compound. All experiments were run in triplicate at rt.

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Preparation of 65 mM Borax Buffer – $Na_2B_4O_7 \cdot H_2O$ (5.2 mmol) and NaOH (170 mmol) were dissolved in 80 mL of H_2O. The solution pH was determined to be 13 using a Beckman Coulter 3-in-1 pH Electrode.

Rheology - Rheological measurements were taken on an AR2000ex rheometer (TA Instruments) with a 25 mm serrated parallel plate. A gel (1.5x cgc) was loaded onto a serrated plate. The gap was then fixed at 300 μm. A solvent trap was used to limit solvent evaporation. The sample was pre-sheared under a stress of 0.1 Pa for 1 min before conducting the frequency sweep and oscillating stress sweep experiments. All measurements were repeated an average of 3 times to verify reproducibility. The frequency sweep experiment was performed under 0.1 Pa stress with a frequency range from 0.1 to 100 rad/s. The oscillating stress sweep experiment was performed at 1 Hz, with a stress range from 0.06 to 800 Pa (note that representative plots are shown in section VII).

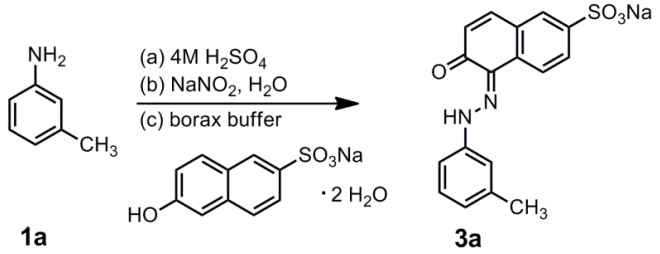
Optical Microscopy (OM) – OM was performed using a Nikon Eclipse 80i microscope under the transmission mode. The images were captured using a QICAM Fast 1394 Color digital camera mounted on the microscope and processed using the QCapture Pro v6.0 software. Gel samples were placed on a glass slide and covered with another glass slide to prevent solvent evaporation.

Scanning Electron Microscopy (SEM) – Wet gel samples were loaded onto a stainless steel SEM holder covered with copper tape and allowed to air dry overnight. Samples were then sputter-coated with Au for 2 min to reduce charge build-up during imaging. All gels were imaged using the high vacuum mode on a Hitachi S3200N SEM using a 15-KV accelerating voltage. The images were digitally recorded and processed using Adobe Photoshop.

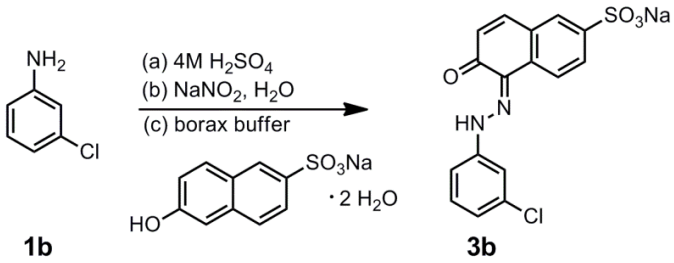
Thermogravimetric Analysis (TGA) - TGA was performed on a TA instruments TGA Q50. Data were analyzed with TA Universal Analysis software Version 4.3 A. Thermal behavior of the samples were studied under a nitrogen purge at 10 °C/min heating rate. The temperature range was 25 – 400 °C/min.

Elemental Analysis – Elemental samples were analyzed for carbon, hydrogen and nitrogen by Atlantic Microlabs. The water content calculation was based on deviation from expected C, H, and N values.

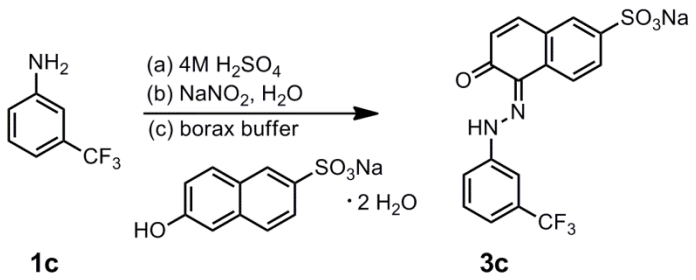
III. Synthetic Procedures



3a: In a round-bottom flask equipped with a stir bar, *m*-toluidine (0.34 mL, 3.1 mmol) was dissolved in 4M H_2SO_4 (10 mL). In a separate 4 mL vial, $NaNO_2$ (0.210 g, 3.05 mmol) was dissolved in H_2O (2 mL). The solution of $NaNO_2$ was then added to the aniline solution and stirred for 2 min at rt. Then sodium 2-naphthol-6-sulfonate dihydrate (0.504 g, 1.79 mmol) dissolved in borax buffer (38 mL) was added to the reaction solution. Within 1 h a red-orange precipitate was observed and collected by filtration. Purification of the precipitate was carried out by Soxhlet extraction with acetone (7 d). The resulting solid percipitate was collected by filtration to give a red-orange solid (0.28 g, 43% yield). HRMS (ESI): Cald for $C_{17}H_{13}N_2O_4S$, 341.0602; found 341.0607. Elemental Analysis: Cald for $C_{17}H_{13}N_2O_4SNa$ with water content = 2.4%, C, 54.69; H, 3.78; N, 7.50; Found C, 54.66; H, 3.70; N, 7.39.

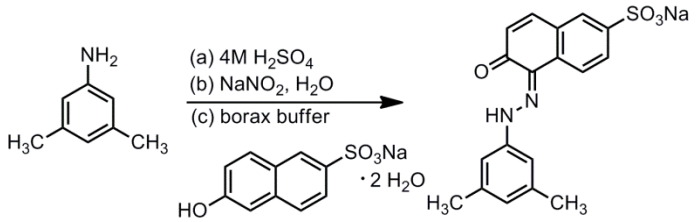


3b: In a round-bottom flask equipped with a stir bar, 3-chloroaniline (0.32 mL, 3.0 mmol) was dissolved in 4M H_2SO_4 (10 mL). In a separate 4 mL vial, $NaNO_2$ (0.211 g, 3.05 mmol) was dissolved in H_2O (2 mL). The solution of $NaNO_2$ was then added to the aniline solution and stirred for 2 min at rt. Then sodium 2-naphthol-6-sulfonate dihydrate (0.501 g, 1.78 mmol) dissolved in borax buffer (38 mL) was added to the reaction solution. Within 1 h a red-orange precipitate was observed and collected by filtration. Purification of the precipitate was carried out by Soxhlet extraction with acetone (2 d). The solid percipitate collected was then further purified by Soxhlet extraction with acetonitrile (5 d). The resulting solid percipitate was collected by filtration to give a red-orange solid (0.153 g, 22% yield). HRMS (ESI): $C_{16}H_{10}ClN_2O_4S$, 361.0055; found 361.0061. Elemental Analysis: Cald for $C_{16}H_{10}ClN_2O_4SNa$ with water content = 6.6%, C, 46.67; H, 3.18; N, 6.80; Found C, 46.74; H, 3.21; N, 6.68.



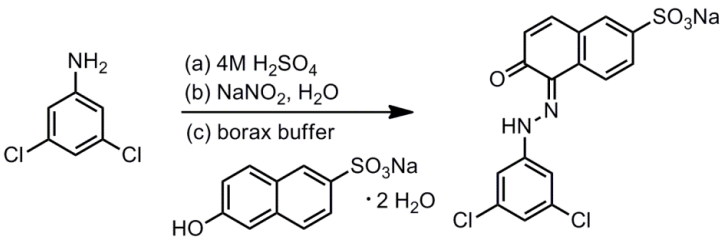
1c 3c

3c: In a round-bottom flask equipped with a stir bar, 3-(trifluoromethyl)aniline (0.38 mL, 3.0 mmol) was dissolved in 4M H_2SO_4 (10 mL). In a separate 4 mL vial, $NaNO_2$ (0.211 g, 3.06 mmol) was dissolved in H_2O (2 mL). The solution of $NaNO_2$ was then added to the aniline solution and stirred for 2 min at rt. Then sodium 2-naphthol-6-sulfonate dihydrate (0.502 g, 1.78 mmol) dissolved in borax buffer (38 mL) was added to the reaction solution. Within 1 h a red-orange precipitate was observed and collected by filtration. Purification of the precipitate was carried out by Soxhlet extraction with acetone (3 d). The solid percipitate collected was then further purified by Soxhlet extraction with acetonitrile (2 d). The resulting solid percipitate was collected by filtration to give a red-orange solid (0.191 g, 25% yield). HRMS (ESI): Cald for $C_{17}H_{10}F_3N_2O_4S$, 395.0319; found 395.0324. Elemental Analysis: Cald for $C_{17}H_{10}F_3N_2O_4SNa$ with water content = 2.1%, C, 47.78; H, 2.59; N, 6.56; Found C, 47.55; H, 2.50; N, 6.48.



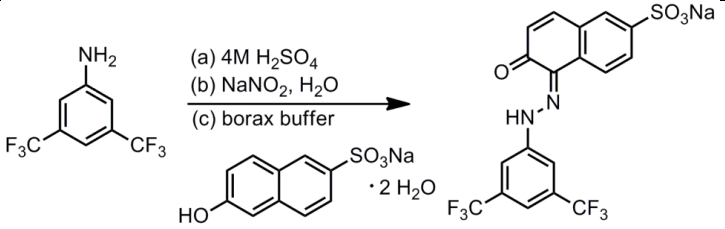
1d 3d

3d: In a round-bottom flask equipped with a stir bar, 3,5-dimethylaniline (0.38 mL, 3.1 mmol) was dissolved in 4M H_2SO_4 (10 mL). In a separate 4 mL vial, $NaNO_2$ (0.212 g, 3.06 mmol) was dissolved in H_2O (2 mL). The solution of $NaNO_2$ was then added to the aniline solution and stirred for 2 min at rt. Then sodium 2-naphthol-6-sulfonate dihydrate (0.504 g, 1.79 mmol) dissolved in borax buffer (38 mL) was added to the reaction solution. Within 1 h a red-orange precipitate was observed and collected by filtration. Purification of the precipitate was carried out by Soxhlet extraction with acetone (9 d). The resulting solid percipitate was collected by filtration to give a red-orange solid (0.273 g, 40% yield). HRMS (ESI): Cald for $C_{18}H_{15}N_2O_4S$, 355.0758; found 355.0763. Elemental Analysis: Cald for $C_{18}H_{15}N_2O_4SNa$ with water content = 2.3%, C, 55.81; H, 4.16; N, 7.23; Found C, 56.04; H, 4.16; N, 7.11.



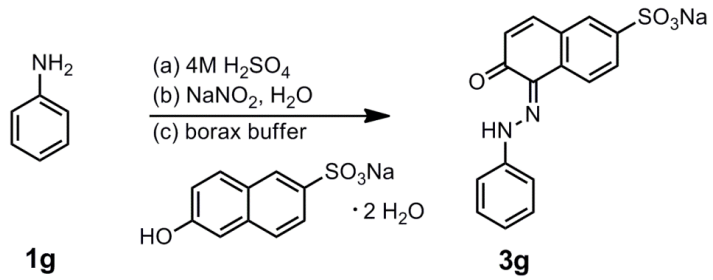
1e **3e**

3e: In a round-bottom flask equipped with a stir bar, 3,5-dichloroaniline (0.334 g, 2.04 mmol) was dissolved in 4M H_2SO_4 (10 mL). In a separate 4 mL vial, $NaNO_2$ (0.141 g, 2.03 mmol) was dissolved in H_2O (2 mL). The solution of $NaNO_2$ was then added to the aniline solution and stirred for 2 min at rt. Then sodium 2-naphthol-6-sulfonate dihydrate (0.500 g, 1.77 mmol) dissolved in borax buffer (38 mL) was added to the reaction solution. Within 1 h a red-orange precipitate was observed and collected by filtration. Purification of the precipitate was carried out by Soxhlet extraction with acetone/20% EtOH (2 d). The solid percipitate collected was then further purified by Soxhlet extraction with acetonitrile (4 d). The resulting solid percipitate was collected by filtration to give a red-orange solid (0.115 g, 15% yield). HRMS (ESI): Cald for $C_{16}H_9Cl_2N_2O_4S$, 394.9666; found 394.9670. Elemental Analysis: Cald for $C_{16}H_9Cl_2N_2O_4SNa$ with water content = 3.3%, C, 44.32; H, 2.46; N, 6.46; Found C, 44.15; H, 2.14; N, 6.16.



1f **3f**

3f: In a round-bottom flask equipped with a stir bar, 3,5-bis(trifluoromethyl)aniline (0.48 mL, 3.1 mmol) was dissolved in 4M H_2SO_4 (10 mL). In a separate 4 mL vial, $NaNO_2$ (0.212 g, 3.08 mmol) was dissolved in H_2O (2 mL). The solution of $NaNO_2$ was then added to the aniline solution and stirred for 2 min at rt. Then sodium 2-naphthol-6-sulfonate dihydrate (0.501 g, 1.77 mmol) dissolved in borax buffer (38 mL) was added to the reaction solution. Within 1 h a red-orange precipitate was observed and collected by filtration. Purification of the precipitate was carried out by Soxhlet extraction with acetone (2 d). The solid percipitate collected was then further purified by Soxhlet extraction with acetonitrile (3 d). The resulting solid percipitate was collected by filtration to give a red-orange solid (0.350 g, 40% yield). HRMS (ESI): Cald for $C_{18}H_9F_6N_2O_4S$, 463.0193; found 463.0198. Elemental Analysis: Cald for $C_{18}H_9F_6N_2O_4SNa$ with water content = 1.8%, C, 43.65; H, 2.03; N, 5.66; Found C, 43.40; H, 1.95; N, 5.59.



1g **3g**

3g: In a round-bottom flask equipped with a stir bar, aniline (0.28 mL, 3.1 mmol) was dissolved in 4M H_2SO_4 (10 mL). In a separate 4 mL vial, $NaNO_2$ (0.21 g, 3.1 mmol) was dissolved in H_2O (2 mL). The solution of $NaNO_2$ was then added to the aniline solution and stirred for 2 min at rt. Then sodium 2-naphthol-6-sulfonate dihydrate (0.51 g, 1.8 mmol) dissolved in borax buffer (38 mL) was added to the reaction solution. After 30 min NaCl (2 equiv.) was added to help precipitate the product. Within 1 h a red-orange precipitate was observed and collected by filtration. Purification of the precipitate was carried out by Soxhlet extraction with acetone (2 d). The solid percipitate collected was then further purified by Soxhlet extraction with acetonitrile (6 d). The resulting solid percipitate was collected by filtration to give a red-orange solid (0.133 g, 21% yield). HRMS (ESI): Cald for $C_{16}H_{11}N_2O_4S$, 327.0445; found 327.0449. Elemental Analysis: Cald for $C_{16}H_{11}N_2O_4Na$, C, 54.86; H, 3.16; N, 8.00; Found C, 54.66; H, 3.27; N, 7.99.

IV. ^{1}H and ^{13}C NMR Spectroscopic Data

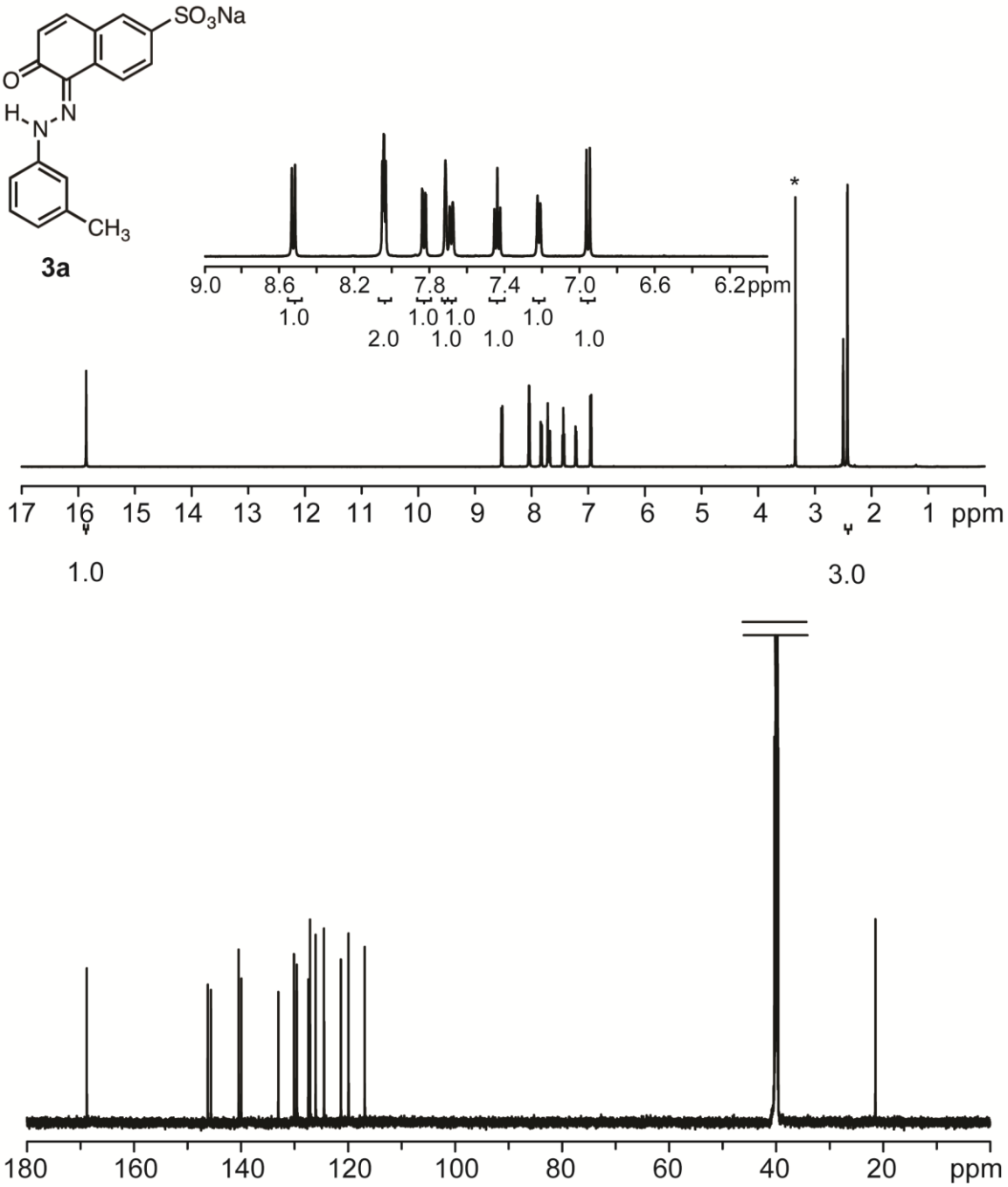


Figure S1.1 ^{1}H and ^{13}C NMR spectra of **3a**. ^{1}H NMR (500 MHz, DMSO-d_6) δ 15.86 (s, 1H), 8.53 (d, J = 8.7 Hz, 1H), 8.05 (m, 2 H), 7.84 (dd, J = 8.5, 1.6 Hz, 1H), 7.71 (s, 1H), 7.69 (d, J = 8.1 Hz, 1H), 7.45 (t, J = 7.8 Hz, 1H), 7.22 (d, J = 7.4 Hz, 1H), 6.96 (d, J = 9.5 Hz, 1H), 2.42 (s, 3H). ^{13}C NMR (176 MHz, DMSO-d_6) δ 168.81, 146.21, 145.61, 140.45, 139.94, 133.03, 130.10, 129.61, 129.56, 127.44, 127.09, 126.06, 124.49, 121.33, 119.91, 116.88, 21.44.

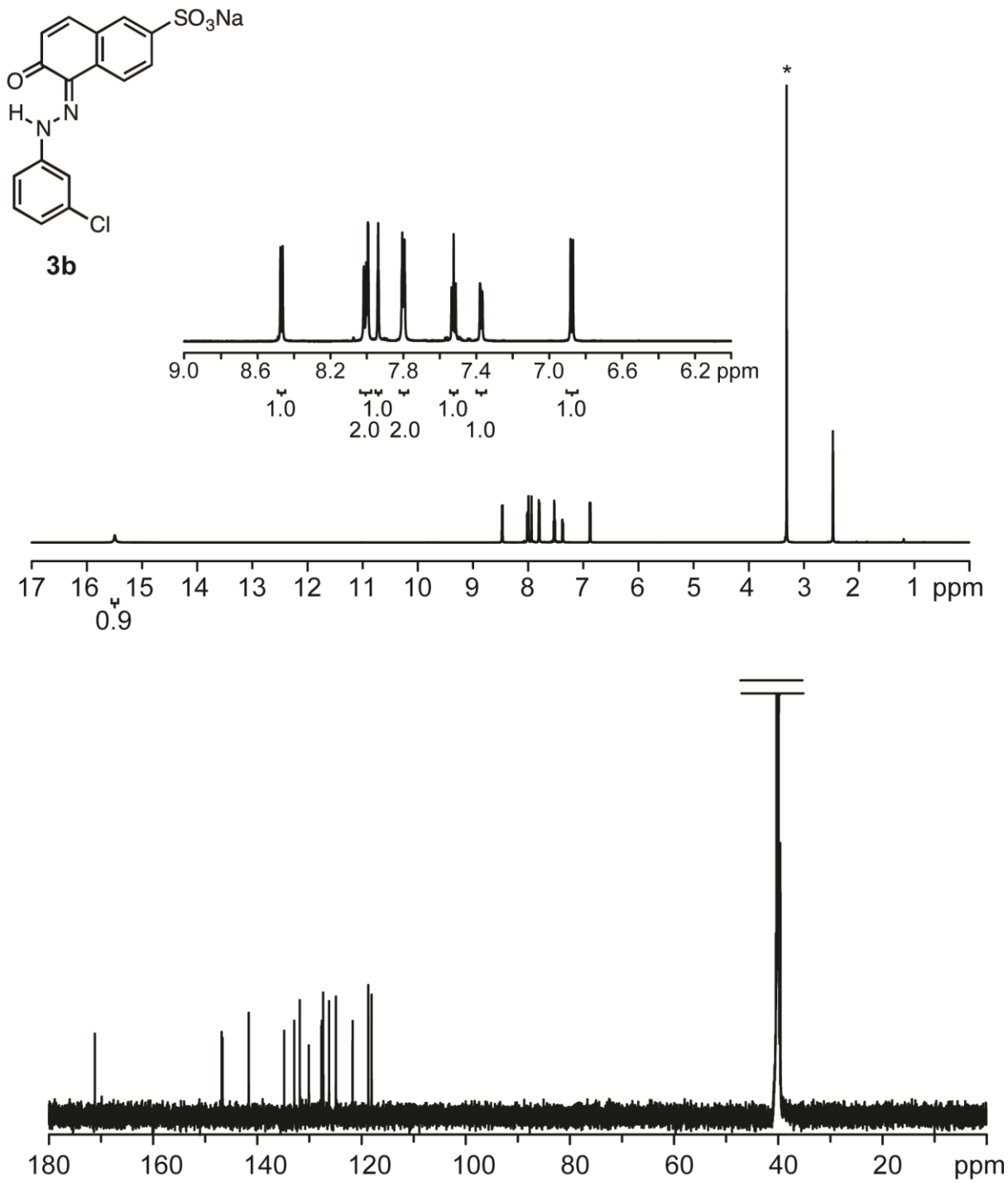


Figure S1.2 ^{1}H and ^{13}C NMR spectra of **3b**. ^{1}H NMR (700 MHz, DMSO-d_6) δ 15.52 (s, 1H), 8.48 (d, J = 8.9 Hz, 1H), 8.02 (m, 2H), 7.94 (t, J = 2.0 Hz, 1H), 7.81 (d, J = 8.5 Hz, 2H), 7.54 (t, J = 8.2 Hz, 1H), 7.38 (dd, J = 7.8, 1.4 Hz, 1H), 6.88 (d, J = 9.6 Hz, 1H). ^{13}C NMR (176 MHz, DMSO-d_6) δ 171.18, 146.83, 146.66, 141.65, 134.83, 132.91, 131.83, 130.09, 127.69, 127.62, 127.34, 126.20, 124.90, 121.70, 118.68, 118.04.

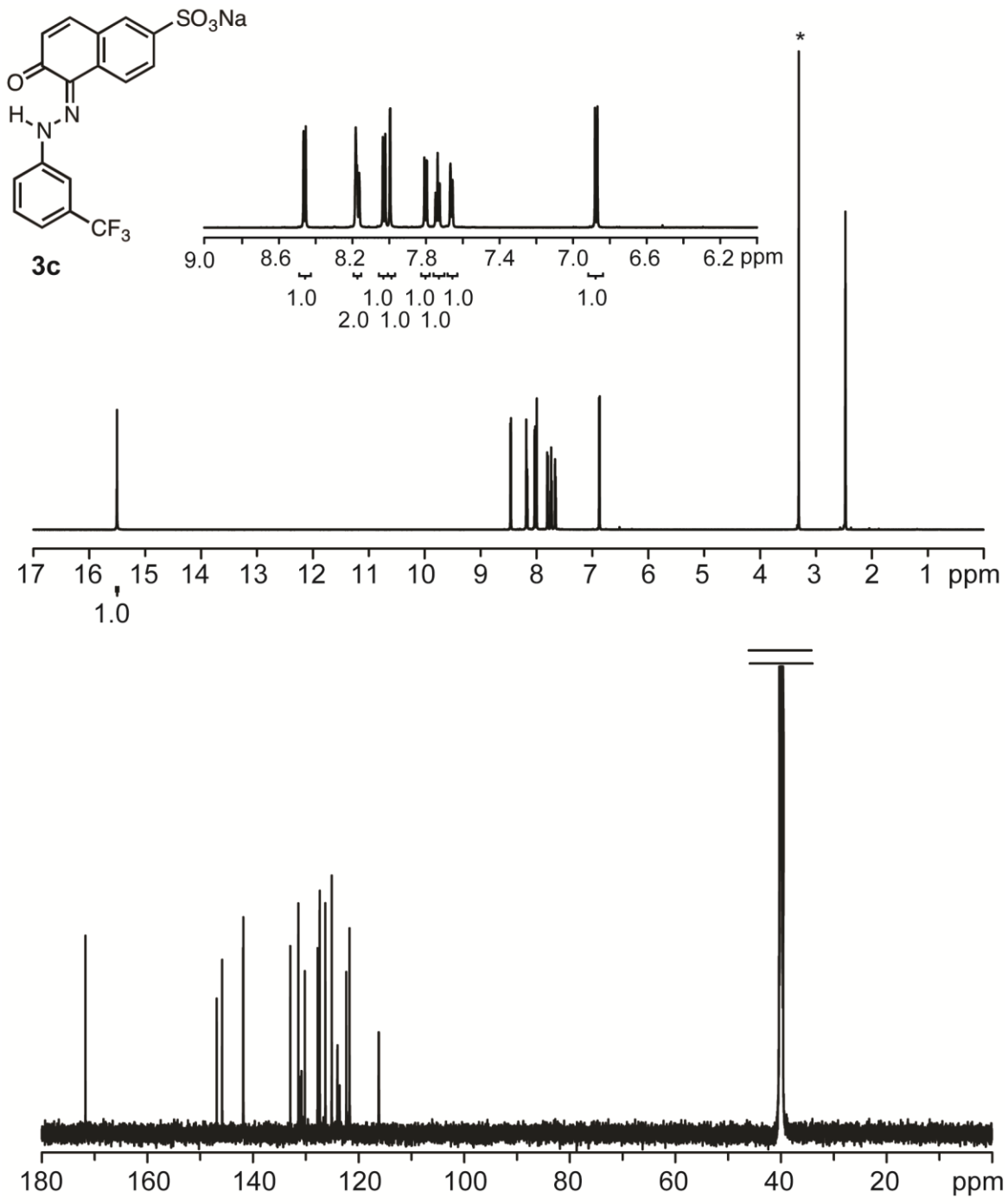


Figure S1.3 ^{1}H and ^{13}C NMR spectra of **3c**. ^{1}H NMR (500 MHz, DMSO-d_6) δ 15.50 (s, 1H), 8.47 (d, J = 8.5 Hz, 1H), 8.18 (m, 2H), 8.04 (d, J = 9.3 Hz, 1H), 8.00 (d, J = 1.7 Hz, 1H), 7.81 (dd, J = 8.4, 1.8 Hz, 1H), 7.75 (t, J = 8.1 Hz, 1H), 7.67 (d, J = 7.6 Hz, 1H) 6.88 (d, J = 9.4 Hz, 1H). ^{13}C NMR (176 MHz, DMSO-d_6) δ 171.52, 146.87, 145.84, 141.84, 132.95, 131.42, 131.17 (q, $J_{C\text{-}F}$ = 32.5 Hz), 130.24, 127.78, 127.38, 126.67 (q, $J_{C\text{-}F}$ = 271.5 Hz), 126.28, 125.00, 124.02 (q, $J_{C\text{-}F}$ = 3.8 Hz), 122.38, 121.68, 116.17 (q, $J_{C\text{-}F}$ = 3.4 Hz).

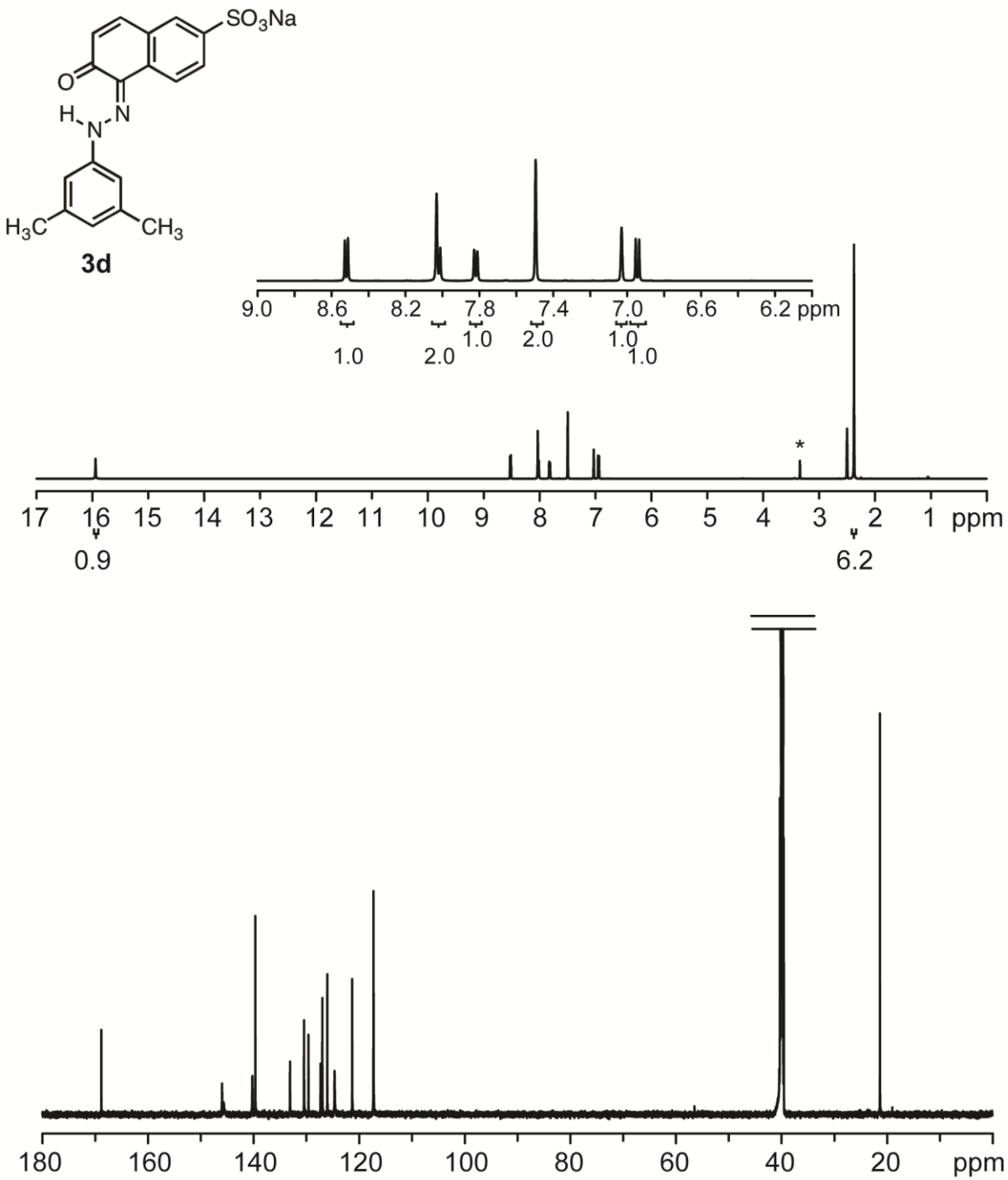


Figure S1.4 ^{1}H and ^{13}C NMR spectra of **3d**. ^{1}H NMR (500 MHz, DMSO-d_6) δ 15.94 (s, 1H), 8.53 (d, J = 8.7 Hz, 1H), 8.03 (m, 2H), 7.83 (d, J = 8.5 Hz, 1H), 7.50 (s, 2H), 7.03 (s, 1H), 6.95 (d, J = 9.6 Hz, 1H). ^{13}C NMR (176 MHz, DMSO-d_6) δ 168.83, 145.97, 145.67, 140.22, 139.66, 133.09, 130.43, 129.60, 127.31, 126.98, 126.04, 124.65, 121.31, 117.28, 21.35.

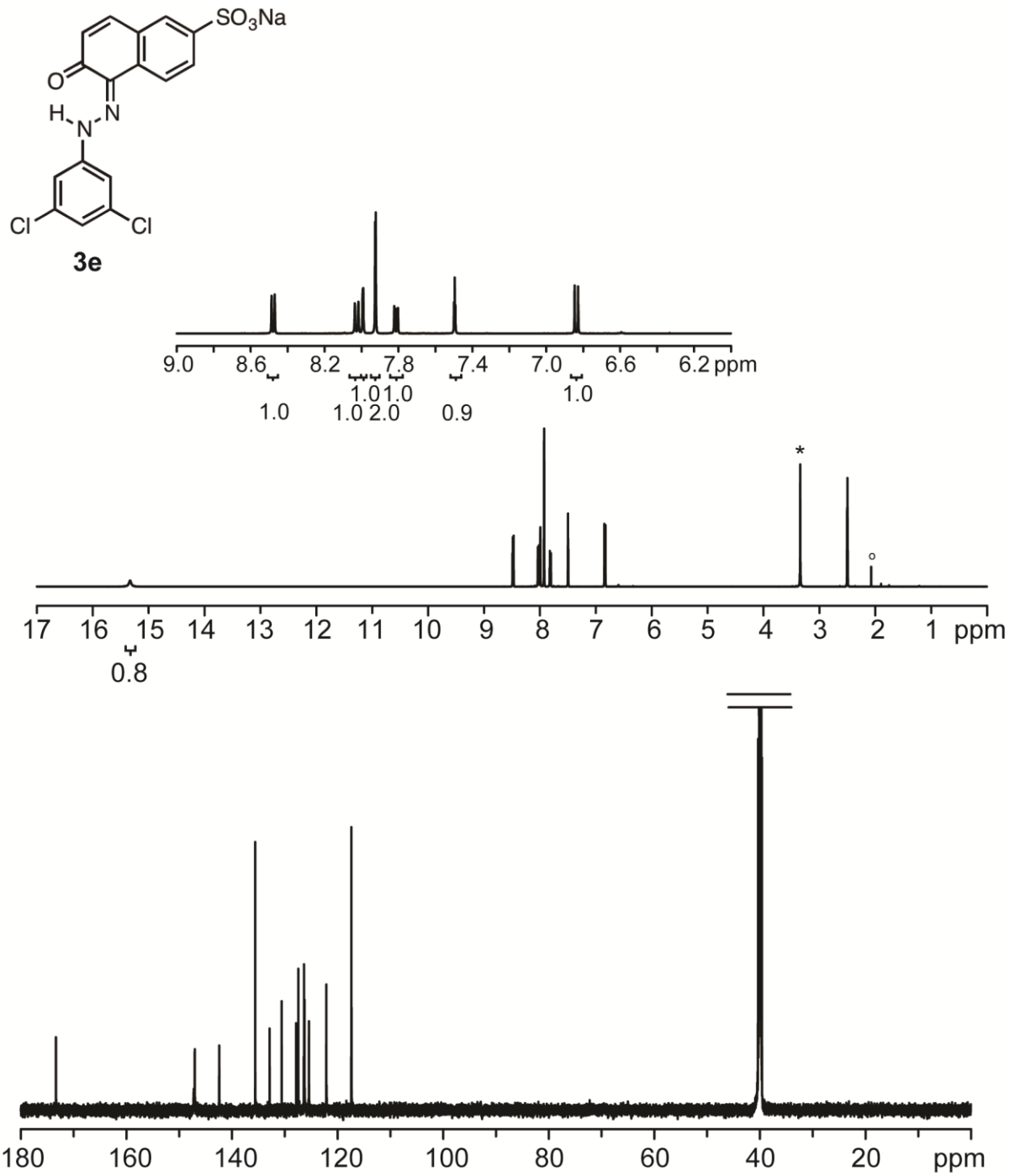


Figure S1.5 ^{1}H and ^{13}C NMR spectra of **3e**. ^{1}H NMR (500 MHz, DMSO-d_6) δ 15.49 (s, 1H), 8.49 (d, J = 9.2 Hz, 1H), 8.04 (d, J = 1.4 Hz, 1H), 7.93 (d, J = 2.0 Hz, 2H), 7.82 (dd, J = 8.4, 1.8 Hz, 1H), 7.50 (at, J = 2.0 Hz, 1H), 6.85 (d, J = 9.6 Hz, 1H). ^{13}C NMR (176 MHz, DMSO-d_6) δ 173.33, 147.23, 147.04, 142.41, 135.60, 132.86, 130.57, 127.85, 127.43, 126.36, 126.25, 125.42, 122.12, 117.37. Note: ^{O} indicates residual acetonitrile.

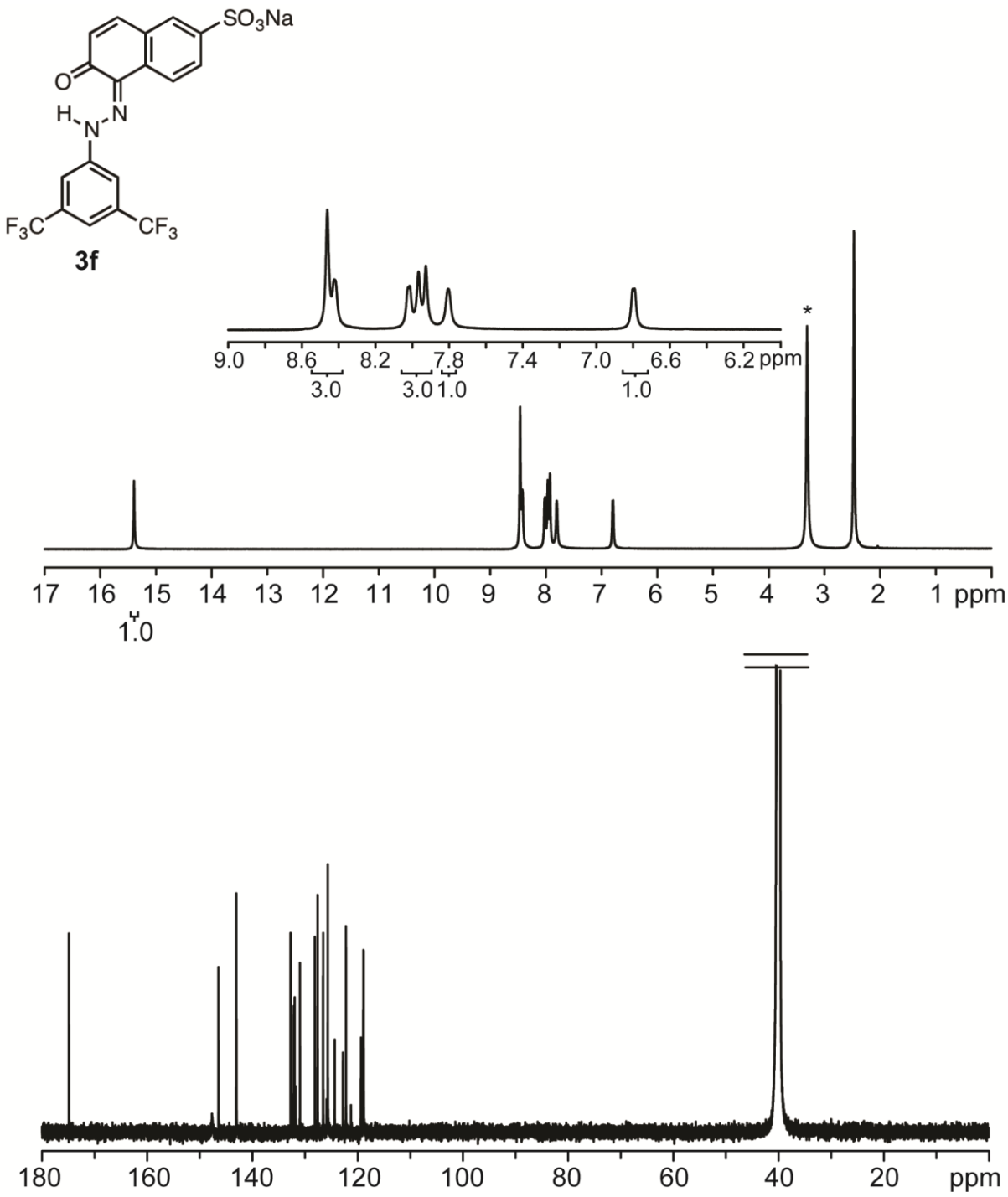


Figure S1.6 ^{1}H and ^{13}C NMR spectra of **3f**. ^{1}H NMR (700 MHz, DMSO-d_6) δ 15.39 (s, 1H), 8.46 (m, 3H), 8.02 (m, 3H), 7.81 (s, 1H), 6.80 (d, J = 7.7 Hz, 1H). ^{13}C NMR (176 MHz, DMSO-d_6) δ 174.87, 147.76, 146.44, 143.05, 132.73, 132.34 (q, $J_{C\text{-}F}$ = 33.1 Hz), 130.97, 128.12, 127.62, 126.55, 125.90 (q, $J_{C\text{-}F}$ = 274.1 Hz), 125.66, 122.22, 119.35, 118.89.

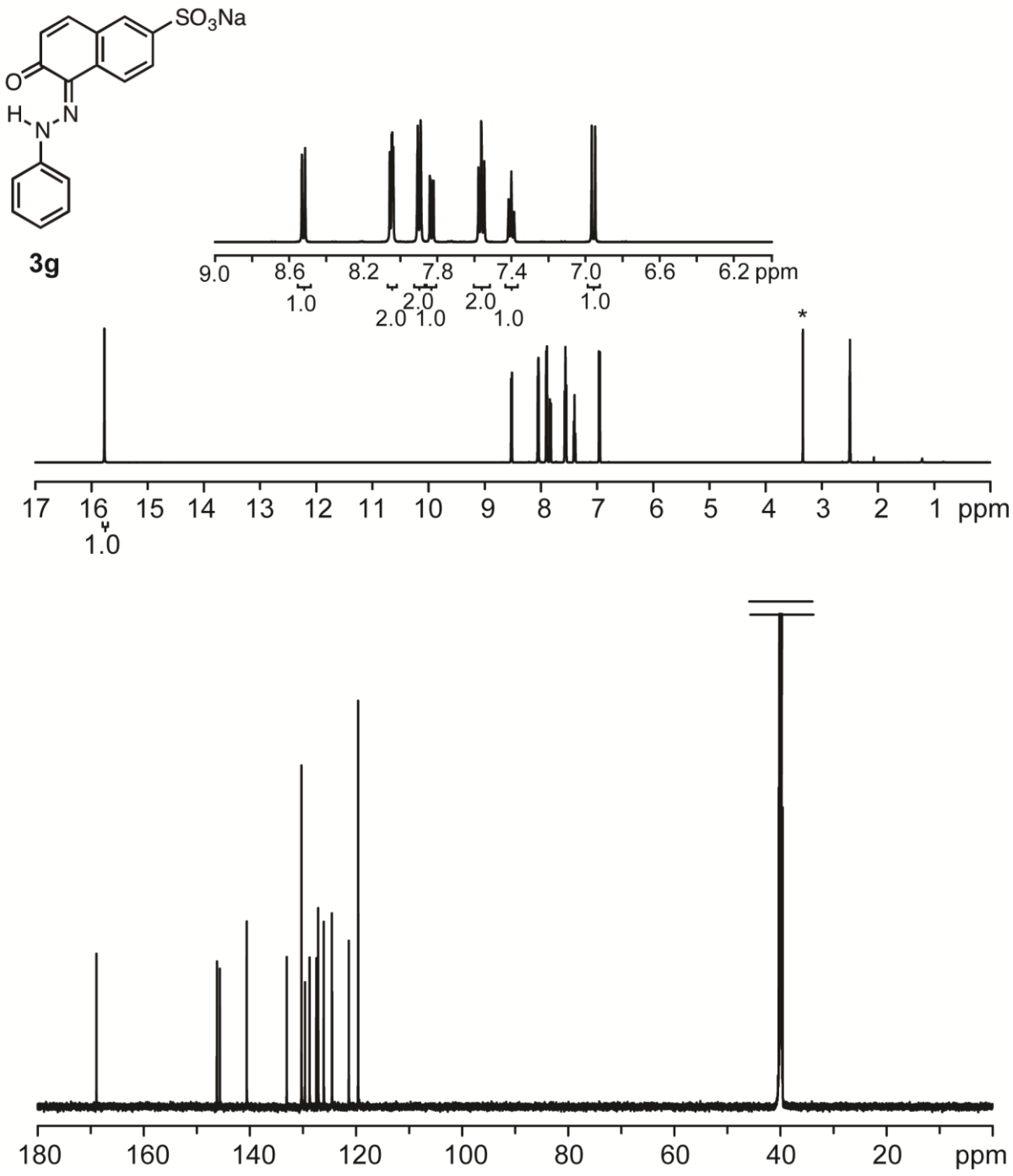


Figure S1.7 ^{1}H and ^{13}C NMR spectra of **3g**. ^{1}H NMR (500 MHz, DMSO-d_6) δ 15.78 (s, 1H), 8.53 (d, J = 8.6 Hz, 1H), 8.06 (m, 2H), 7.91 (d, J = 8.6 Hz, 2H), 7.84 (dd, J = 6.5, 1.7 Hz, 1H), 7.59 (at, J = 7.7 Hz, 2H), 7.42 (at, J = 7.2 Hz, 1H), 6.97 (d, J = 9.3 Hz, 1H). ^{13}C NMR (176 MHz, DMSO-d_6) δ 168.92, 146.21, 145.64, 140.59, 133.05, 130.28, 129.61, 128.73, 127.47, 127.12, 126.06, 124.51, 121.35, 119.60.

V. Determination of water in sodium 2-naphthol-6-sulfonate hydrate

Sodium 2-naphthol-6-sulfonate hydrate was purchased from TCI America as an unknown hydrate. TGA was performed to determine the average amount of water.

Sample Preparation Procedure **-** A sample of sodium 2-napthol-6-sulfonate hydrate was anaylzed by loading a small amount (2.809 mg) onto a platinum TGA pan and held under a nitrogen purge until dry, which was indicated by stabilization of the sample weight.

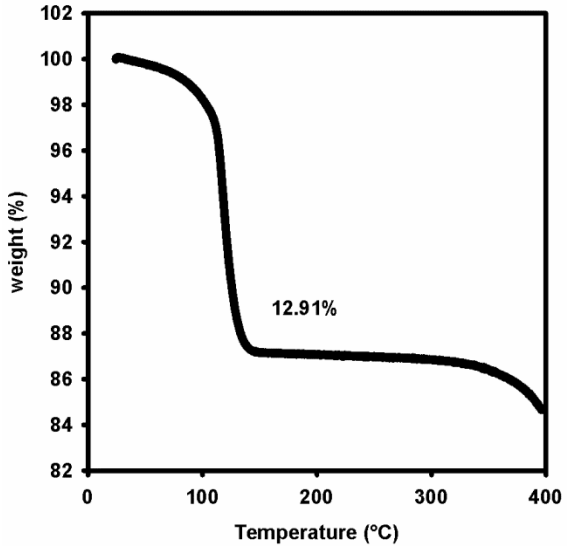


Figure S1.8 TGA of sodium 2-napthol-6-sulfonate hydrate.

Analysis of the above results indicated that sodium 2-napthol-6-sulfonate hydrate had an average of 2.024 H_2O per molecule of sodium 2-napthol-6-sulfonate hydrate. For the synthetic procedures, an average of 2 H_2O molecules was used.

VI. Gel Screening

Gel Screening and Critical Gel Concentration (cgc) Procedure – The cgc was determined by adding a known amount of gelator **3a–3g** (approximately 7-16 mg) into a 4 mL vial containing 1 mL of solvent. The vial was capped, heated to dissolve the solid, and allowed to cool with approximately 10 s of sonication in a rt water bath. If the resulting gel was stable-to-inversion, then 0.1 mL of solvent was added and the procedure was repeated until the gel was no longer stable-to-inversion. Sonication was not performed with **3d** as it disrupted gel formation.

Table S1.1 Summary of cgc data.[a]

	cgc (mM)	
compound	borax buffer	EtOH/borax buffer (9/1 v/v)
3a	Precipitate	23.5 ± 0.4
3b	29.4 ± 0.9[b]	43 ± 3
3c	24.2 ± 0.8	Precipitate
3d	Precipitate	35.5 ± 0.2
3e	21.3 ± 0.5	16.7 ± 0.6
3f	27 ± 1	Precipitate
3g	Soluble	30.0 ± 0.5

[a] Standard deviation was determined by an average of 3 runs. Gelation of each compound was tested up to 2 wt%. Precipitate in the above table refers to the observation of any amount of precipitate in the gelation media. The Cgc assumes the nonhydrated molecular weight of the product.
[b] Solution was 65 mM borax buffer:4M H_2SO_4:H_2O (7.6:2:0.4) (v/v/v)

Representative procedure for in situ detection of NO_2^- – In a 4 mL vial, **1e** (2.0 mg, 0.012 mmol, 1.1 equiv) was suspended in H_2SO_4 (0.2 mL, 4M). Then H_2O (40 µL) containing $NaNO_2$ (0.76 mg, 0.011 mmol, 1.0 equiv) was added. The vial was shaken for 30 s and let stand to react. After 10 min, sodium 2-napthol-6-sulfonate dihydrate (3.5 mg, 0.012 mmol, 1.1 equiv) dissolved in borax buffer (0.76 mL) was added and a color change from slight yellow to red-orange was observed. The vial was heated with a heat gun until all gelator was dissolved and then allowed to cool to rt.

*Determination of cgc at different pH for **3e*** – 65 mM borax buffer and sulfuric acid (18 M) were used to make solutions at a pH of 13, 9, and 6. A Beckman Coulter 3-in-1 pH Electrode was used to determine the pH. At each pH the cgc of **3e** was determined using the gel screening and cgc procedure.

Table S1.2 Summary of cgc data for **3e** at different pH.[a]

	cgc of **3e** (mM)
pH	
13	21.3 ± 0.5
9	9.6 ± 0.3
6	9.8 ± 0.3
Insitu (9)	9.3[b]

[a] The standard deviation was determined by an average of 3 runs. The cgc assumes the nonhydrated molecular weight of the product.
[b] See representative procedure for in situ detection of NO_2^-. The cgc was calculated based on a conversion of 85% (see section X)

VII. Gel Rheological Data

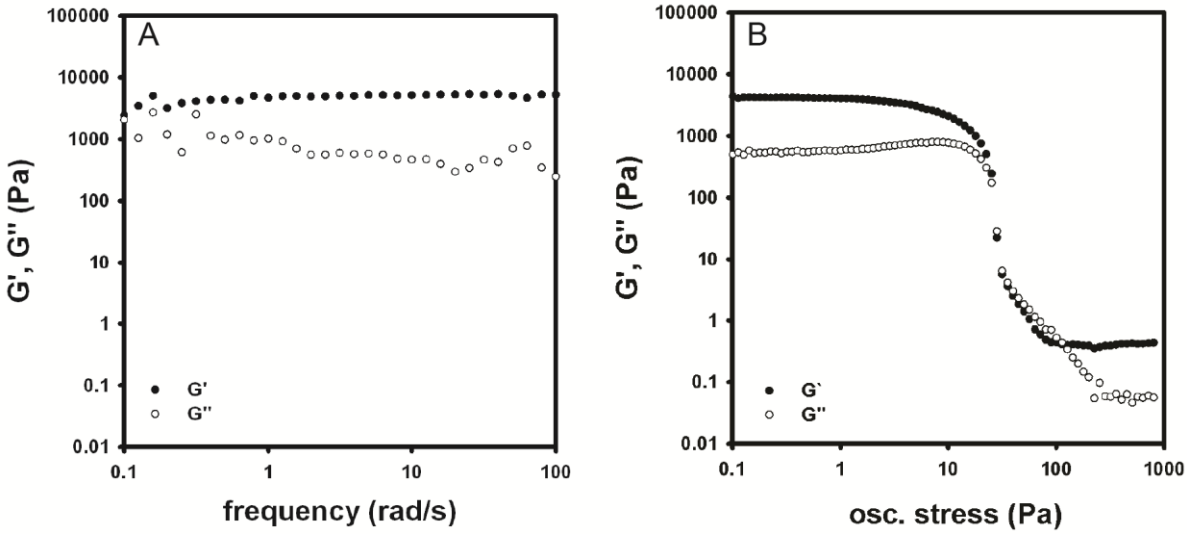


Figure S1.9 (A) Frequency sweep and (B) oscillating stress sweep of a gel of **3a** (50 mM in EtOH/borax buffer 9/1 (v/v)).

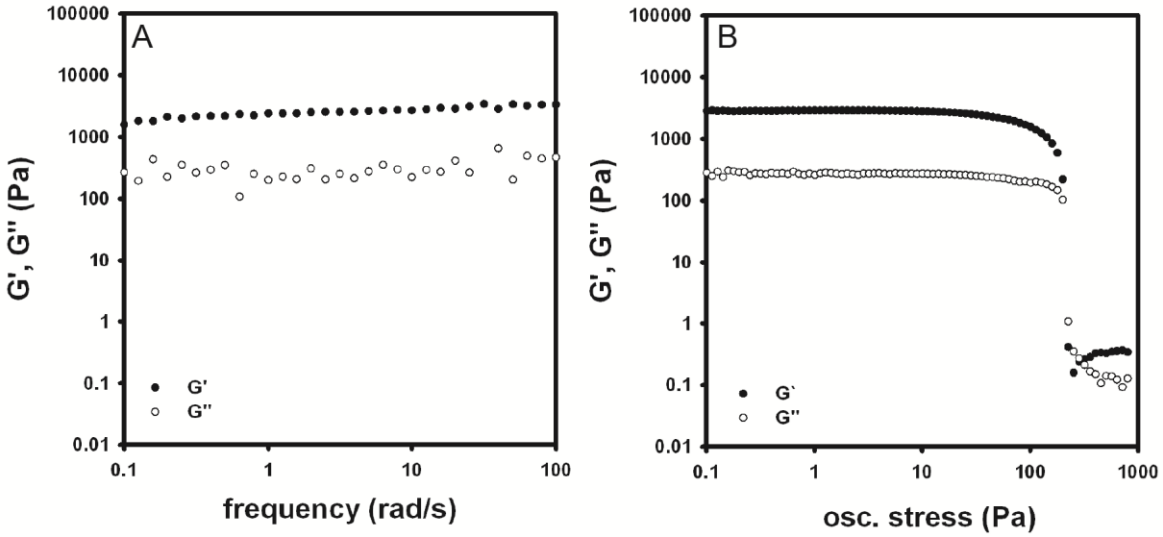


Figure S1.10 (A) Frequency sweep and (B) oscillating stress sweep of a gel of **3c** (36 mM in borax buffer).

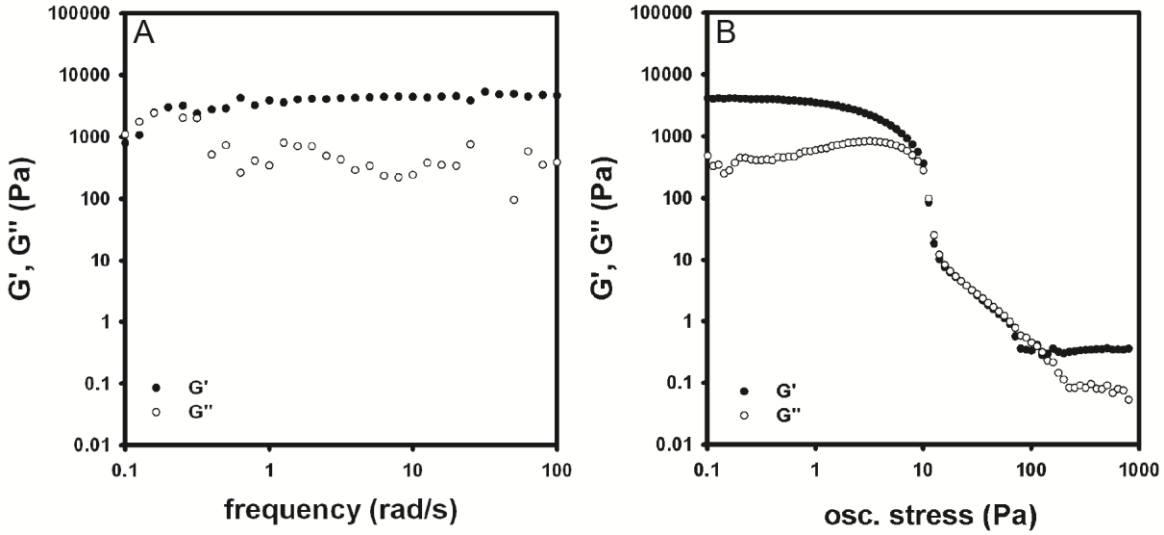


Figure S1.11 (A) Frequency sweep and (B) oscillating stress sweep of a gel of **3d** (53 mM in EtOH/borax buffer 9/1 (v/v)).

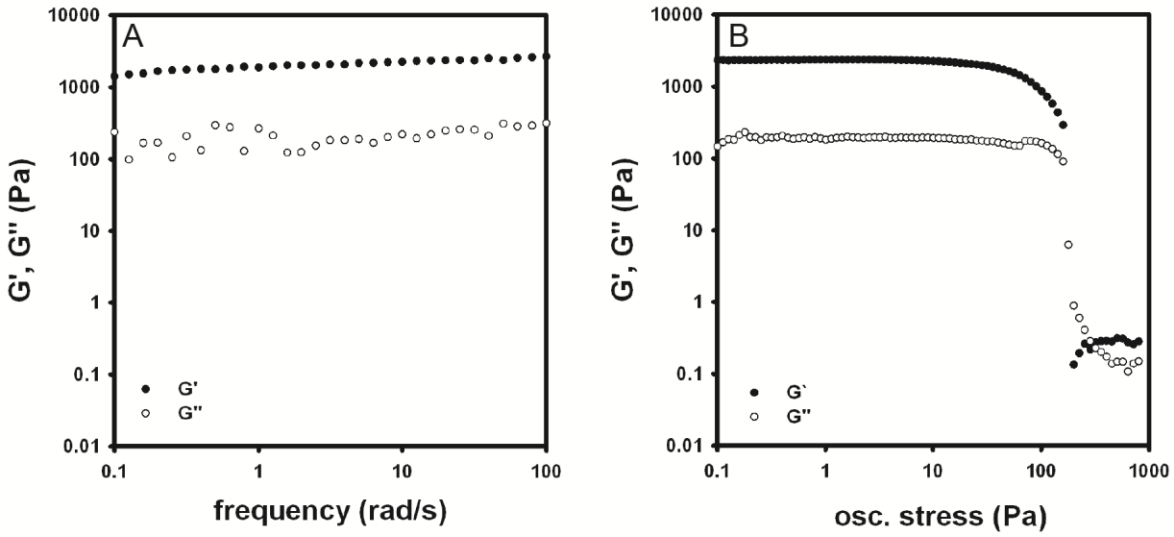


Figure S1.12 (A) Frequency sweep and (B) oscillating stress sweep of a gel of **3e** (32 mM in borax buffer).

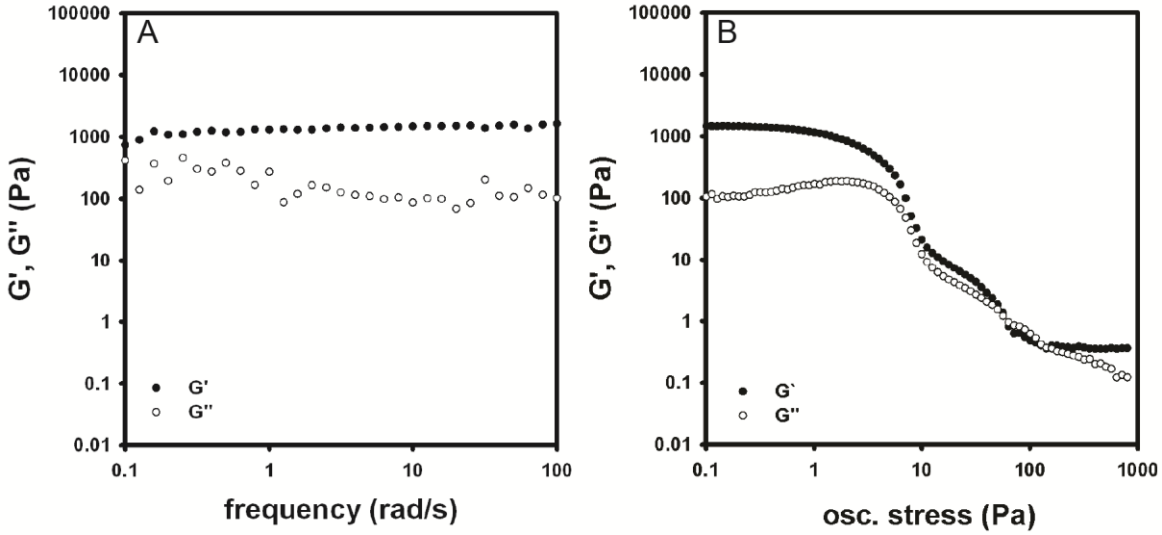


Figure S1.13 (A) Frequency sweep and (B) oscillating stress sweep of a gel of **3f** (42 mM in borax buffer).

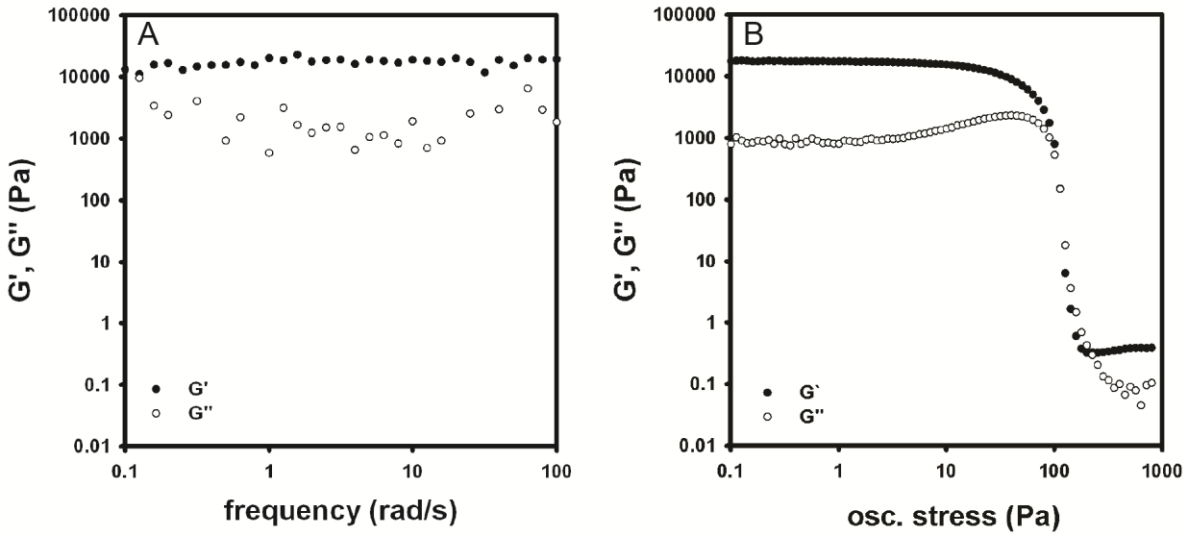


Figure S1.14 (A) Frequency sweep and (B) oscillating stress sweep of a gel of **3g** (45 mM in EtOH/borax buffer 9/1 (v/v)).

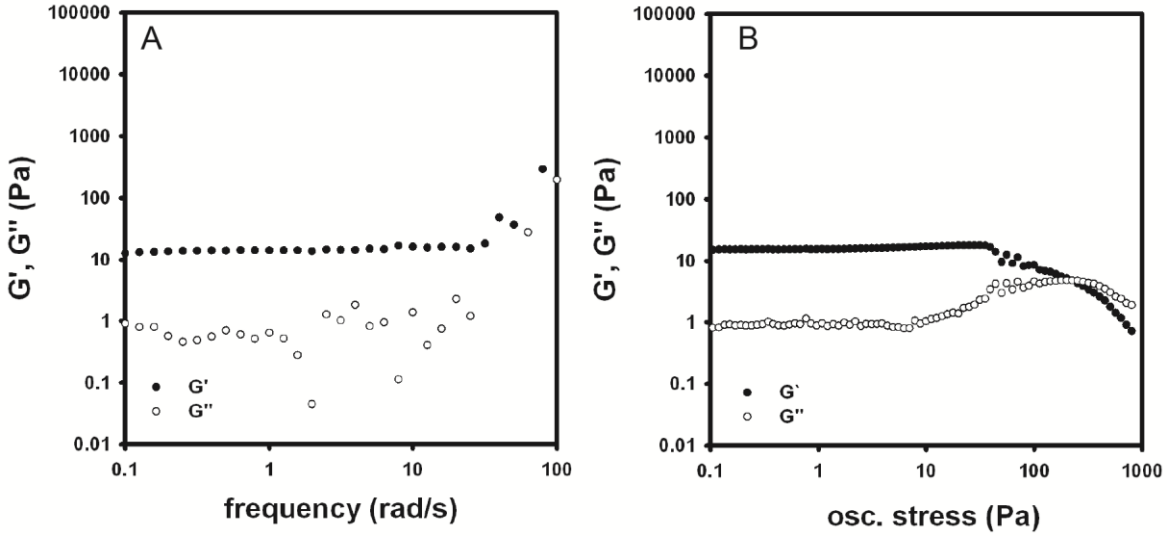


Figure S1.15 (A) Frequency sweep and (B) oscillating stress sweep of a gel of **3b** formed under in situ conditions at cgc (in borax buffer). See section VI for the in situ procedure.

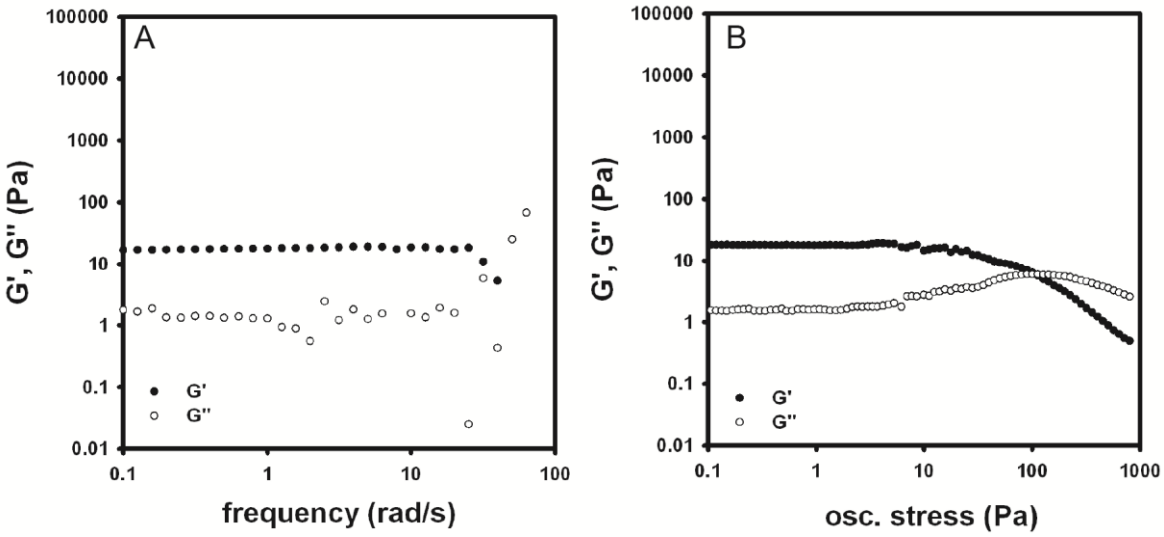


Figure S1.16 (A) Frequency sweep and (B) oscillating stress sweep of a gel of **3c** formed under in situ conditions at cgc (in borax buffer). See section VI for the in situ procedure.

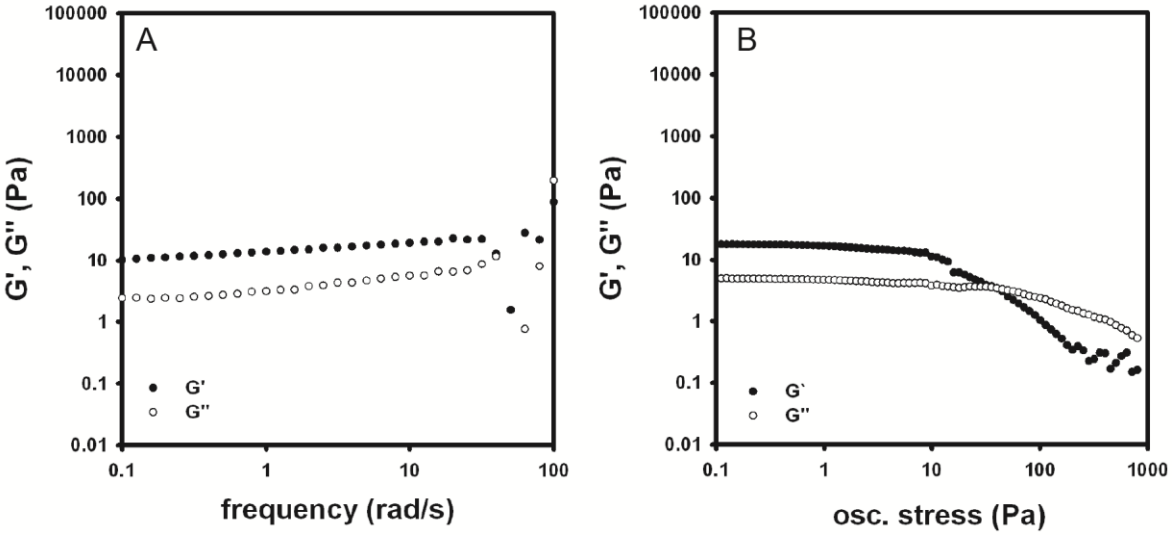


Figure S1.17 (A) Frequency sweep and (B) oscillating stress sweep of a gel of **3e** formed under in situ conditions at cgc (in borax buffer). See section VI for the in situ procedure.

Rheology of **3e** in situ gels with 1, 2, and 3 equiv of NO_2^-

Representative procedure of gel formation at 1 equiv of NO_2^-

Preparation of stock solutions

1e *solution (80.2 mM)* – **1e** (26.0 mg, 0.160 mmol) was dissolved in H_2SO_4 (2.0 mL, 4 M).

Sodium nitrite solution (405 mM) – $NaNO_2$ (12.3 mg, 0.178 mmol) was dissolved in H_2O (0.44 mL).

Sodium 2-naphthol-6-sulfonate dihydrate (21.4 mM) – Sodium 2-naphthol-6-sulfonate dihydrate (46.1 mg, 0.163 mmol) was dissolved in borax buffer (7.6 mL, 65 mM).

Representative procedure for in situ detection of NO_2^- - In a 4 mL vial, $NaNO_2$ solution (40 µL, 405 mM) was reacted with the **1e** solution (0.2 mL, 80.2 mM). The vial was shaken for 30 s and let stand to react for 10 min. Then the sodium 2-naphthol-6-sulfonate dihydrate solution (0.76 mL, 21.4 mM) was added and a color change from slight yellow to red-orange was observed. The vial was heated with a heat gun until all compounds were dissolved and then allowed to cool to rt. The vial was inverted to confirm stable gel formation.

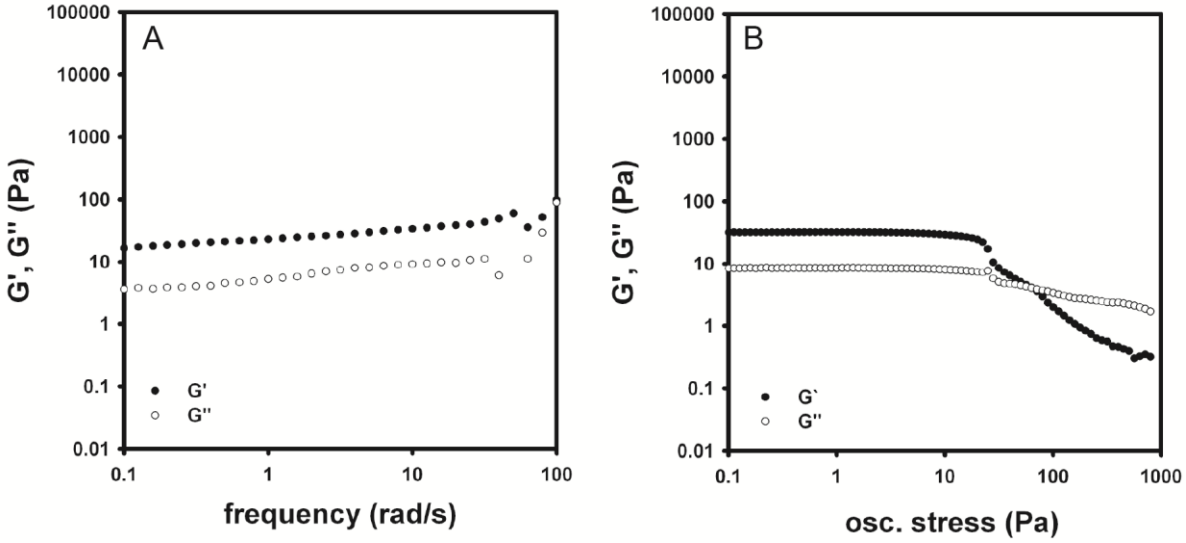


Figure S1.18 (A) Frequency sweep and (B) oscillating stress sweep of a gel of **3e** formed under in situ conditions at 1.5x cgc (in borax buffer) with 1 equiv of sodium nitrite.

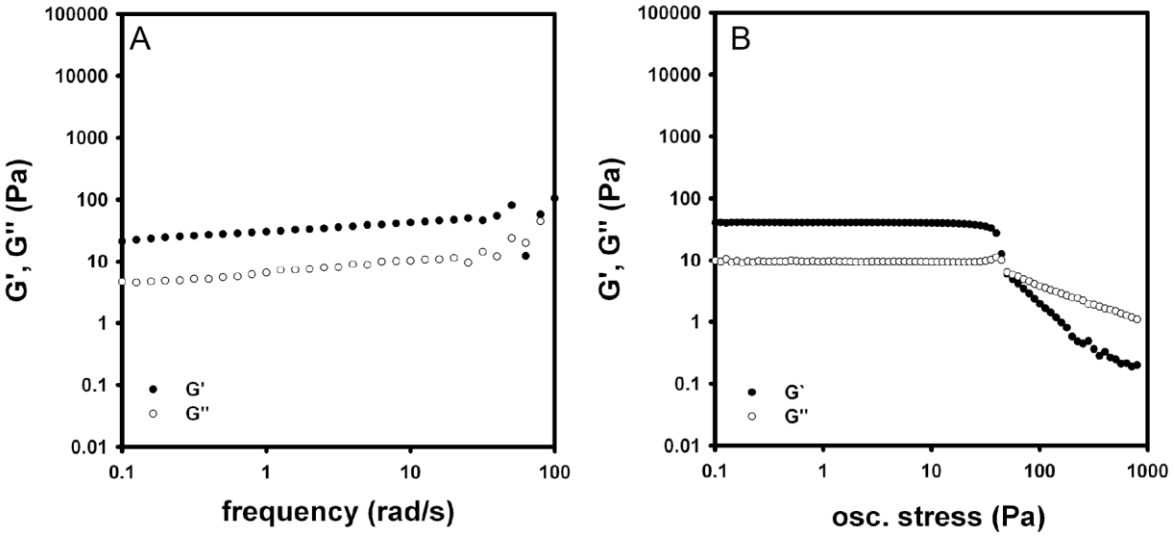


Figure S1.19 (A) Frequency sweep and (B) oscillating stress sweep of a gel of **3e** formed under in situ conditions at 1.5x cgc (in borax buffer) with 2 equiv of sodium nitrite.

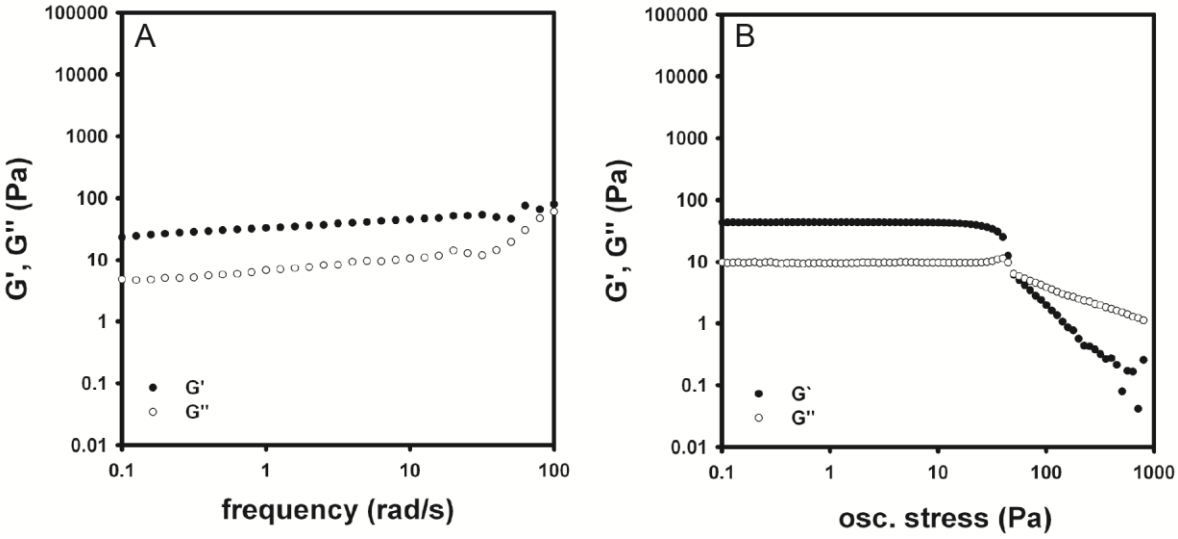


Figure S1.20 (A) Frequency sweep and (B) oscillating stress sweep of a gel of **3e** formed under in situ conditions at 1.5x cgc (in borax buffer) with 3 equiv of sodium nitrite.

VIII. Scanning Electron and Optical Microscopy Images

*SEM and OM of **3c*** - Gel fibers for **3c** were not observable within the range of the OM. SEM of gel **3c** only showed salt under conditions used (see section II).

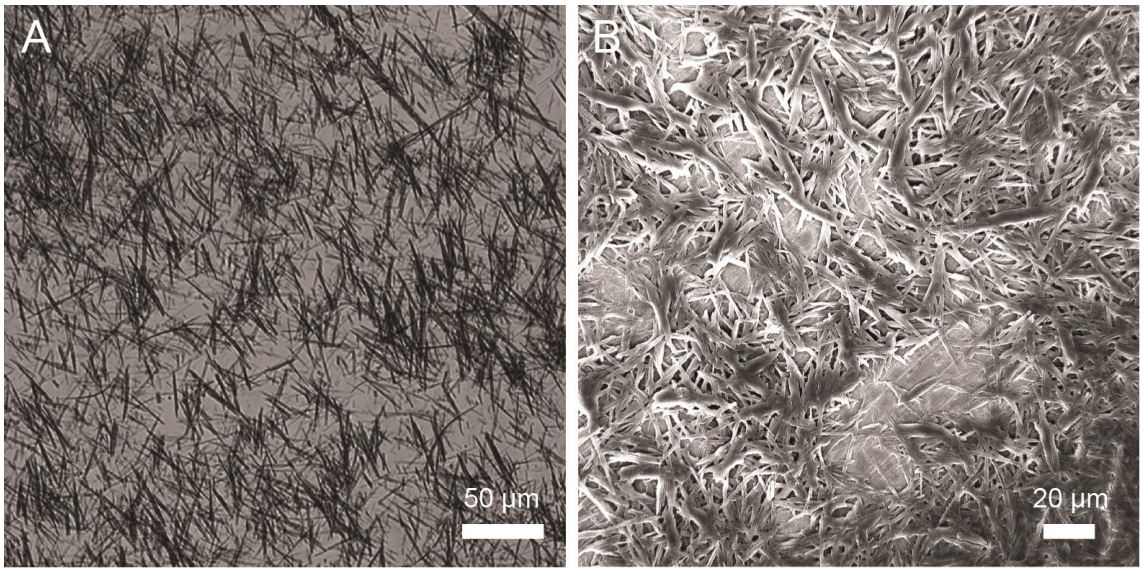


Figure S1.21 (A) OM and (B) SEM image of a gel of **3a** formed from purified material (44 mM in EtOH/borax buffer (9/1, v/v)).

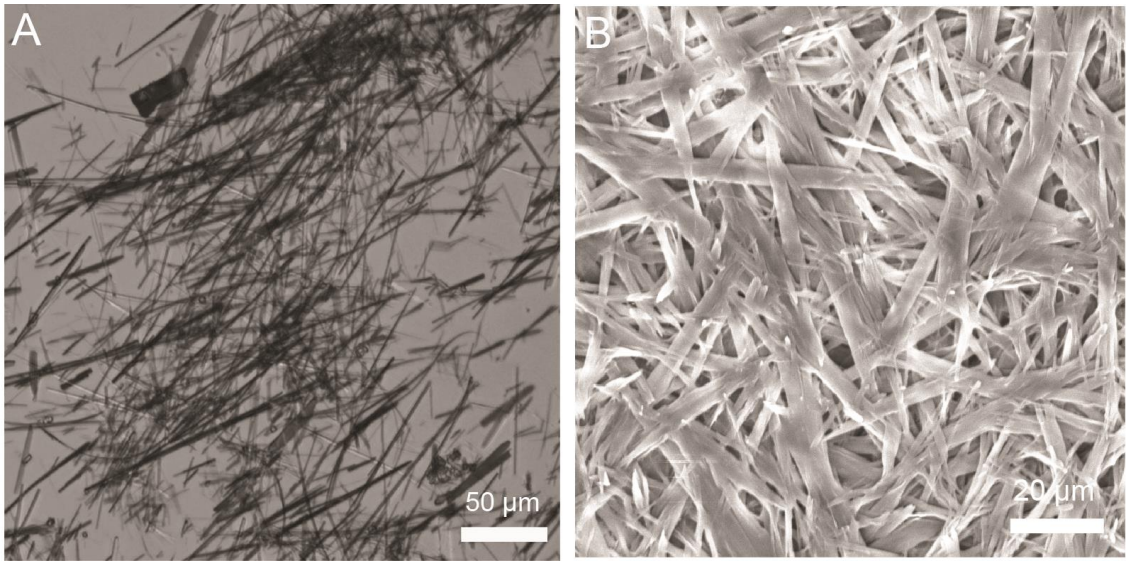


Figure S1.22 (A) OM and (B) SEM image of a gel of **3b** formed from purified material (38 mM in EtOH/borax buffer (9/1, v/v)).

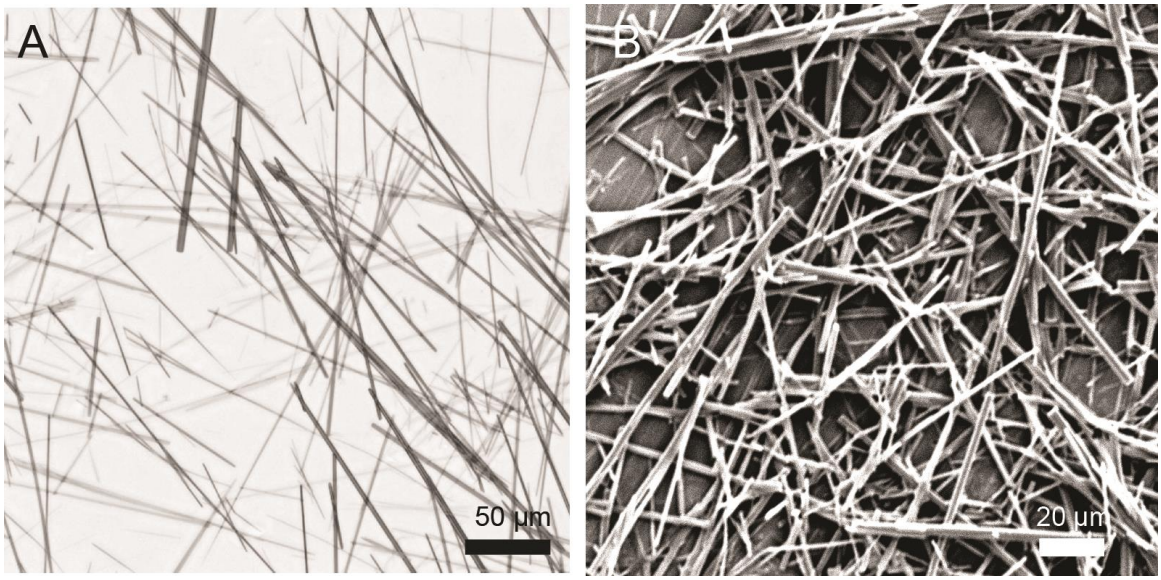


Figure S1.23 A) OM and B) SEM image of a gel of **3d** formed from purified material (48 mM in EtOH/borax buffer (9/1, v/v)).

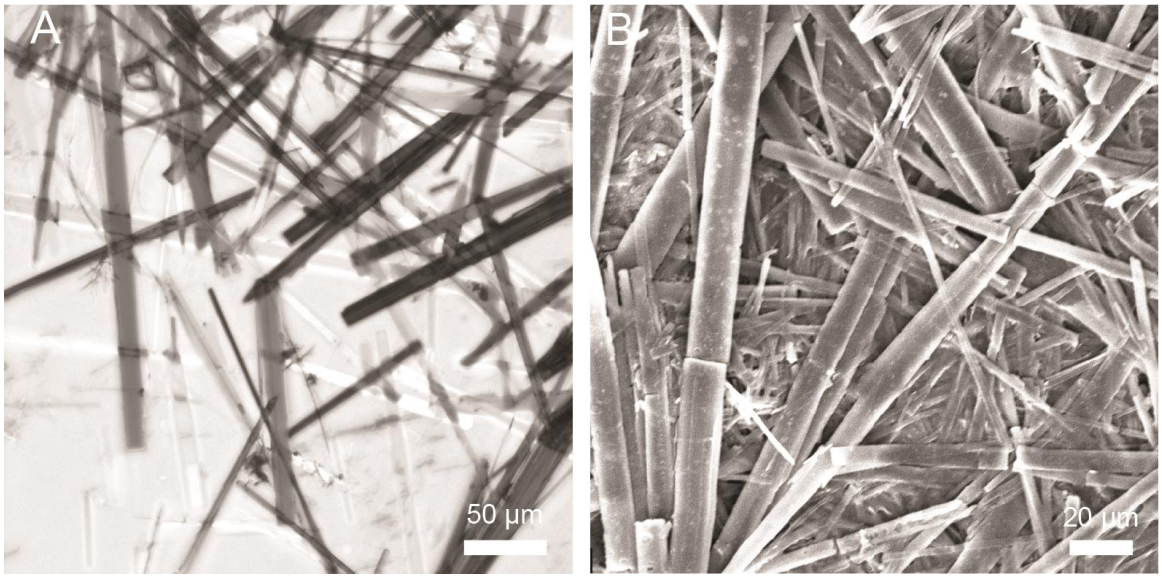


Figure S1.24 A) OM and B) SEM image of a gel of **3e** formed from purified material (37 mM in EtOH/borax buffer (9/1, v/v)).

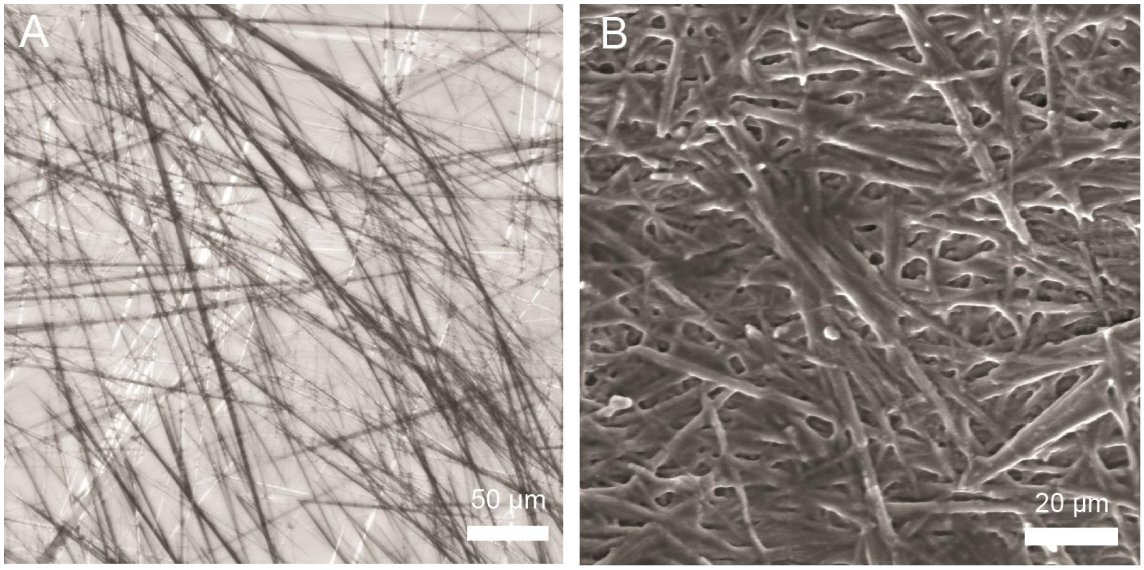


Figure S1.25 A) OM and B) SEM image of a gel of **3f** formed from purified material (30 mM in borax buffer).

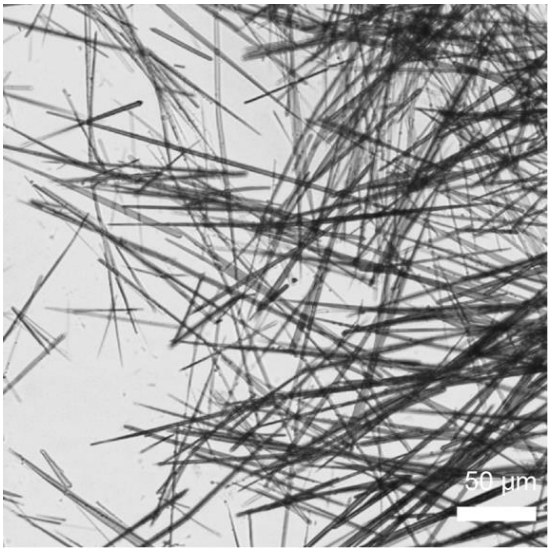
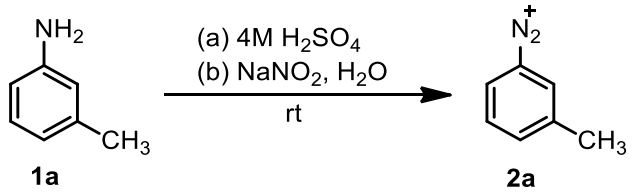


Figure S1.26 OM image of a gel of **3g** formed from purified material (49 mM in EtOH/borax buffer (9/1, v/v)).

IX. Diazonium Ion Formation by UV-vis and ^{1}H NMR Spectroscopy



1a **2a**

Preparation of stock solutions

Aniline Stock Solution – **1a** (0.025 mL, 0.20 mmol) was dissolved in aq. H_2SO_4 (10 mL, 4 M). Then 0.1 mL of this solution was diluted with aq. H_2SO_4 (0.9 mL, 4 M) to achieve a final concentration of 2.0 mM.

Nitrite Stock Solution - $NaNO_2$ (0.014 g, 0.20 mmol) was dissolved in H_2O (10 mL). Then 0.1 mL of this solution was diluted with H_2O (0.9 mL) to achieve a final concentration of 2.0 mM.

Procedure for forming the diazonium ion - In a 4 mL quartz cuvette, the aniline stock solution (0.1 mL, 2.0 mM) was diluted with aq. H_2SO_4 (3.8 mL, 4 M). The UV-vis spectrum of **1a** was then acquired. To the cuvette, the nitrite stock solution (0.1 mL, 2.0 mM) was added. The cuvette was inverted to mix the solution. Spectra were acquired at various time points over 60 min.

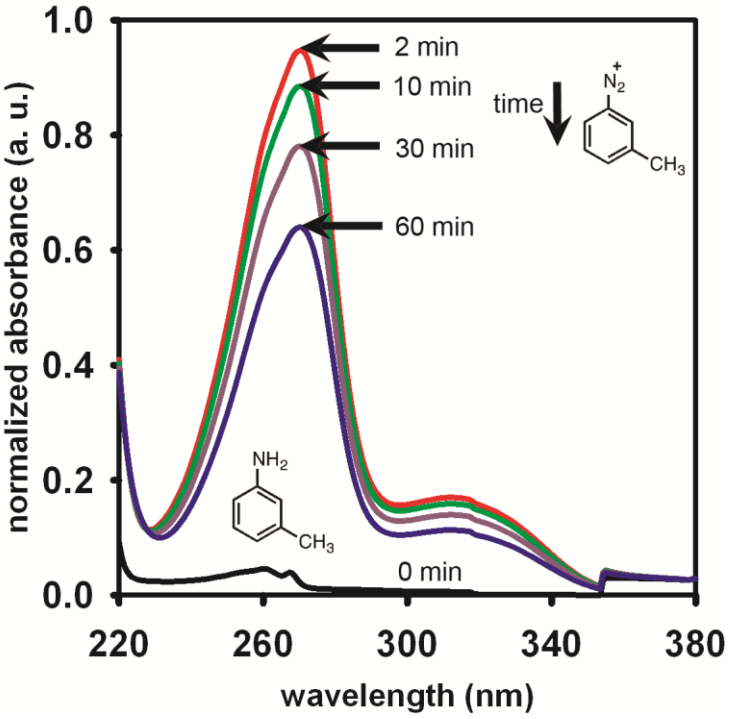
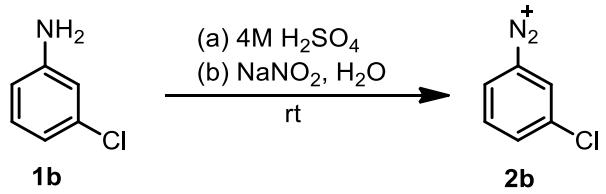


Figure S1.27 UV-vis spectra of **1a** (λ_{max}, 260.5 nm) to **2a** (λ_{max}, 270.25 nm).



1b **2b**

Preparation of stock solutions

Aniline Stock Solution – **1b** (0.030 mL, 0.28 mmol) was dissolved in aq. H_2SO_4 (10 mL, 4 M). Then 0.1 mL of this solution was diluted with aq. H_2SO_4 (0.9 mL, 4 M) to achieve a final concentration of 2.8 mM.

Nitrite Stock Solution - $NaNO_2$ (0.019 g, 0.28 mmol) was dissolved in H_2O (10 mL). Then 0.1 mL of this solution was diluted with H_2O (0.9 mL) to achieve a final concentration of 2.8 mM

Procedure for forming the diazonium ion - In a 4 mL quartz cuvette, the aniline stock solution (0.3 mL, 2.8 mM) was diluted with aq. H_2SO_4 (3.4 mL, 4 M). The UV-vis spectrum of **1b** was then acquired. To the cuvette, the nitrite stock solution (0.3 mL, 2.8 mM) was added. The cuvette was inverted to mix the solution. Spectra were acquired at various time points over 60 min.

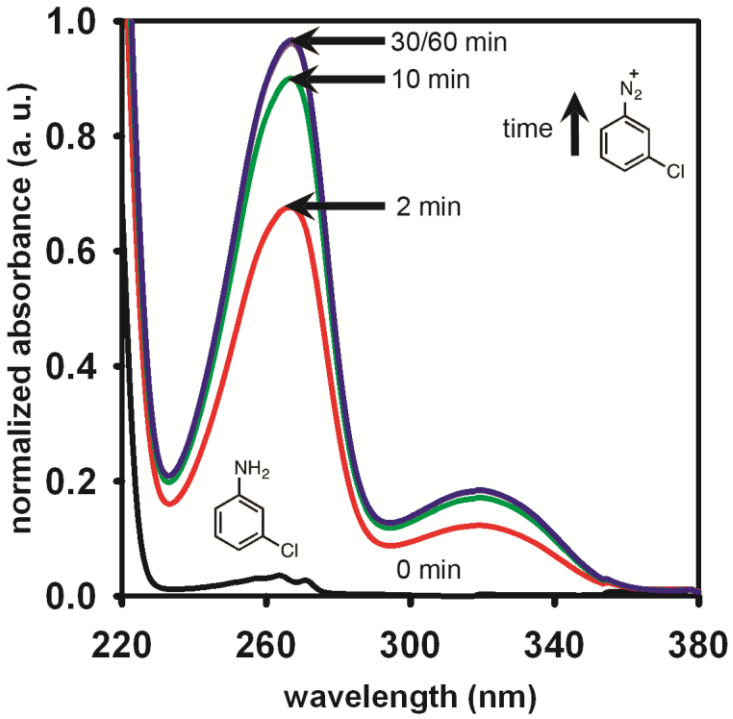
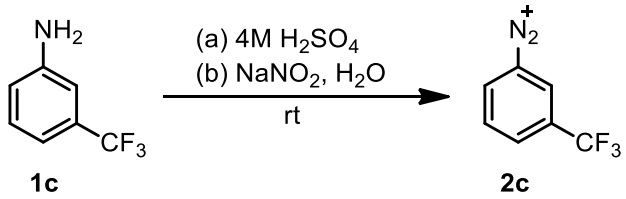


Figure S1.28 UV-vis spectra of **1b** (λ_{max}, 263.50 nm) to **2b** (λ_{max}, 266.50 nm).



1c **2c**

Preparation of stock solutions

Aniline Stock Solution – **1c** (0.035 mL, 0.28 mmol) was dissolved in aq. H_2SO_4 (10 mL, 4 M). Then 0.1 mL of this solution was diluted with aq. H_2SO_4 (0.9 mL, 4 M) to achieve a final concentration of 2.8 mM.

Nitrite Stock Solution - $NaNO_2$ (0.019 g, 0.28 mmol) was dissolved in H_2O (10 mL). Then 0.1 mL of this solution was diluted with H_2O (0.9 mL) to achieve a final concentration of 2.8 mM.

Procedure for forming the diazonium ion - In a 4 mL quartz cuvette, the aniline stock solution (0.2 mL, 2.8 mM) was diluted with aq. H_2SO_4 (3.6 mL, 4 M). The UV-vis spectrum of **1c** was then acquired. To the cuvette, the nitrite stock solution (0.2 mL, 2.8 mM) was added. The cuvette was inverted to mix the solution. Spectra were acquired at various time points.

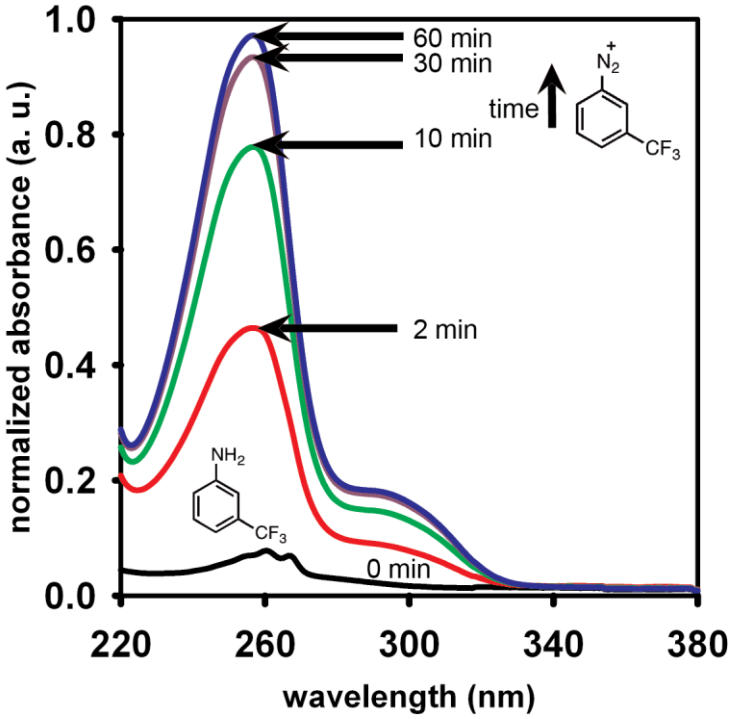
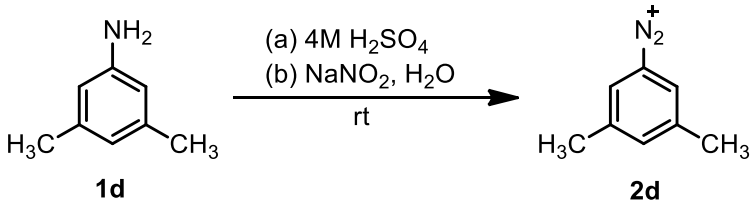


Figure S1.29 UV-vis spectra of **1c** (λ_{max}, 260 nm) to **2c** (λ_{max}, 256 nm).



1d **2d**

Preparation of Stock Solutions

Aniline Stock Solution – **1d** (0.025 mL, 0.20 mmol) was dissolved in aq. H_2SO_4 (10 mL, 4 M). Then 0.1 mL of this solution was diluted with aq. H_2SO_4 (0.9 mL, 4 M) to achieve a final concentration of 2.0 mM.

Nitrite Stock Solution - $NaNO_2$ (0.014 g, 0.20 mmol) was dissolved in H_2O (10 mL). Then 0.1 mL of this solution was diluted with H_2O (0.9 mL) to achieve a final concentration of 2.0 mM

Procedure for forming the diazonium ion - In a 4 mL quartz cuvette, the aniline stock solution (0.04 mL, 2.0 mM) was diluted with aq. H_2SO_4 (3.92 mL, 4M). The UV-vis spectrum of **1d** was then acquired. To the cuvette, the nitrite stock solution (0.04 mL, 2.0 mM) was added. The cuvette was inverted to mix the solution. Spectra were acquired at various time points over 60 min.

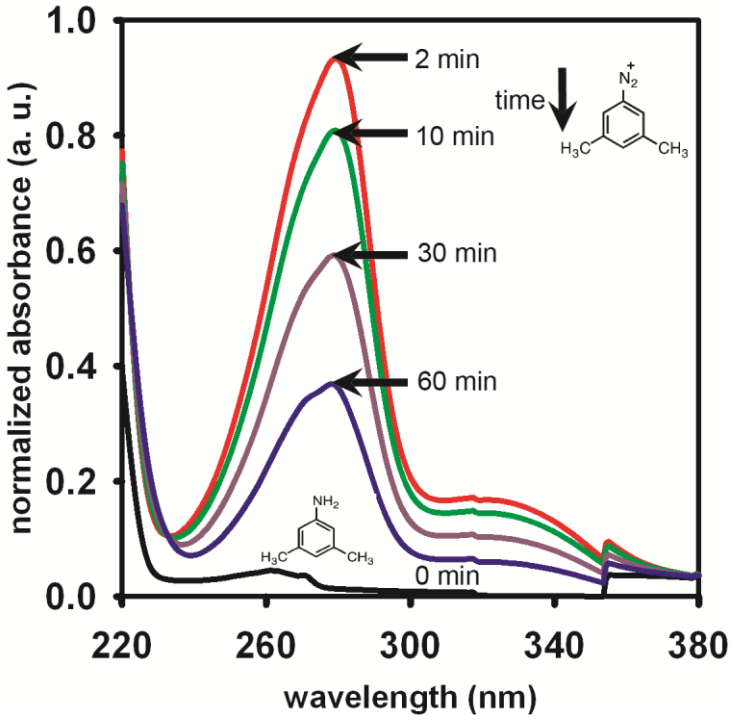
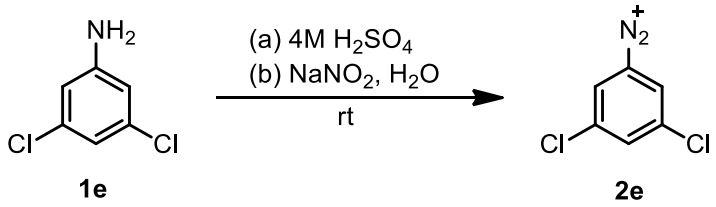


Figure S1.30 UV-vis spectra of **1d** (λ_{max}, 261.25 nm) to **2d** (λ_{max}, 278.5 nm).



1e **2e**

Preparation of stock solutions

Aniline Stock Solution – **1e** (0.026 g, 0.16 mmol) was dissolved in aq. H_2SO_4 (10 mL, 4 M). Then 0.1 mL of this solution was diluted with aq. H_2SO_4 (0.9 mL, 4 M) to achieve a final concentration of 1.6 mM.

Nitrite Stock Solution - $NaNO_2$ (0.011 g, 0.16 mmol) was dissolved in H_2O (10 mL). Then 0.1 mL of this solution was diluted with H_2O (0.9 mL) to achieve a final concentration of 1.6 mM

Procedure for forming the diazonium ion - In a 4 mL quartz cuvette, the aniline stock solution (0.3 mL, 1.6 mM) was diluted with aq. H_2SO_4 (3.4 mL, 4 M). The UV-vis spectrum of **1e** was then acquired. To the cuvette, the nitrite stock solution (0.3 mL, 1.6 mM) was added. The cuvette was inverted to mix the solution. Spectra were acquired at various time points over 60 min.

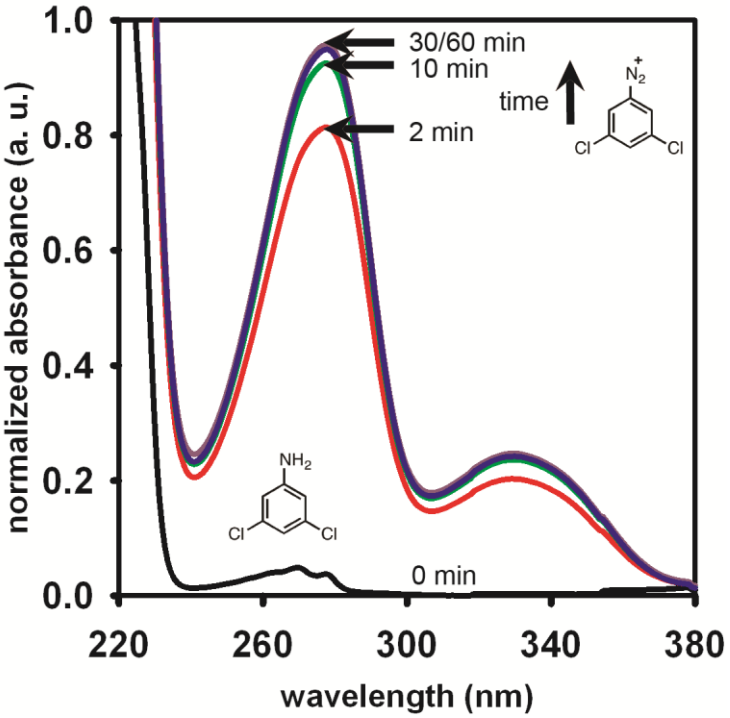
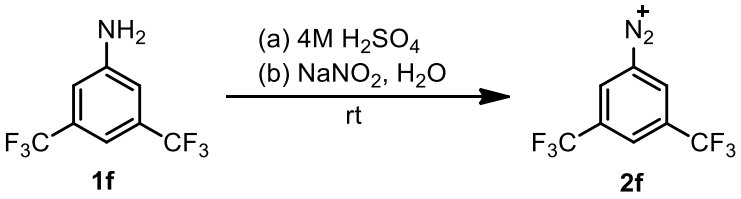


Figure S1.31 UV-vis spectra of **1e** (λ_{max}, 269.50 nm) to **2e** (λ_{max}, 277.75 nm).



1f **2f**

Preparation of stock solutions

Aniline Stock Solution – **1f** (0.040 mL, 0.32 mmol) was dissolved in aq. H_2SO_4 (10 mL, 4 M). Then 0.1 mL of this solution was diluted with aq. H_2SO_4 (0.9 mL, 4 M) to achieve a final concentration of 3.2 mM.

Nitrite Stock Solution - $NaNO_2$ (0.023 g, 0.33 mmol) was dissolved in H_2O (10 mL). Then 0.1 mL of this solution was diluted with H_2O (0.9 mL) to achieve a final concentration of 3.3 mM

Procedure for forming the diazonium ion - In a 4 mL quartz cuvette, the aniline stock solution (0.2 mL, 3.2 mM) was diluted with aq. H_2SO_4 (3.6 mL, 4M). The UV-vis spectrum of **1f** was then acquired. To the cuvette, the nitrite stock solution (0.2 mL, 3.3 mM) was added. The cuvette was inverted to mix the solution. Spectra were acquired at various time points over 60 min.

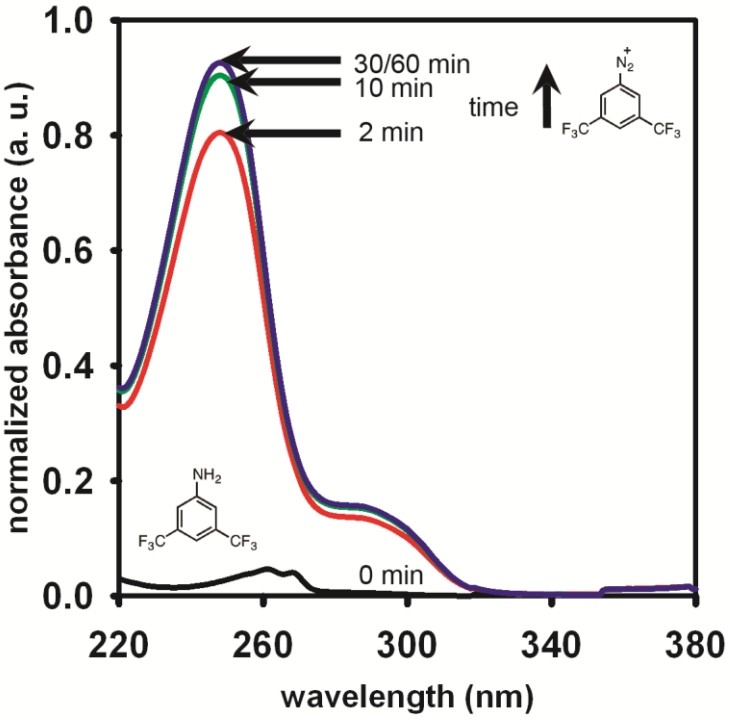
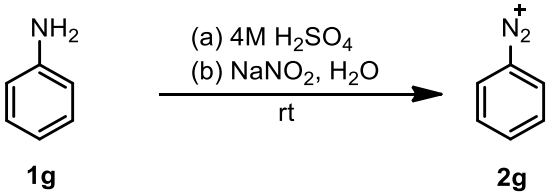


Figure S1.32 UV-vis spectra of **1f** (λ_{max}, 261.25 nm) to **2f** (λ_{max}, 247.25 nm).



Preparation of stock solutions

Aniline Stock Solution – **1g** (0.018 mL, 0.20 mmol) was dissolved in aq. H_2SO_4 (10 mL, 4 M). Then 0.1 mL of this solution was diluted with aq. H_2SO_4 (0.9 mL, 4 M) to achieve a final concentration of 2.0 mM.

Nitrite Stock Solution - $NaNO_2$ (0.015 g, 0.20 mmol) was dissolved in H_2O (10 mL). Then 0.1 mL of this solution was diluted with H_2O (0.9 mL) to achieve a final concentration of 2.0 mM.

Procedure for forming the diazonium ion - In a 4 mL quartz cuvette, the aniline stock solution (0.06 mL, 2.0 mM) was diluted with aq. H_2SO_4 (3.88 mL, 4 M). The UV-vis spectrum of **1g** was then acquired. To the cuvette, the nitrite stock solution (0.06 mL, 2.0 mM) was added. The cuvette was inverted to mix the solution. Spectra were acquired at various time points over 60 min.

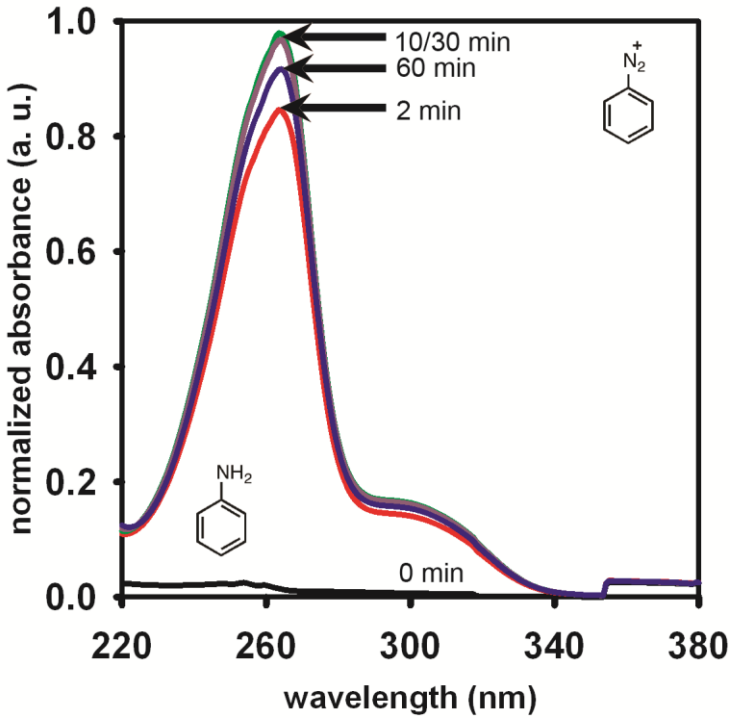


Figure S1.33 UV-vis spectra of **1g** (λ_{max}, 253.75 nm) to **2g** (λ_{max}, 264.25 nm).

[1]H NMR spectroscopic study of diazonium ion formation

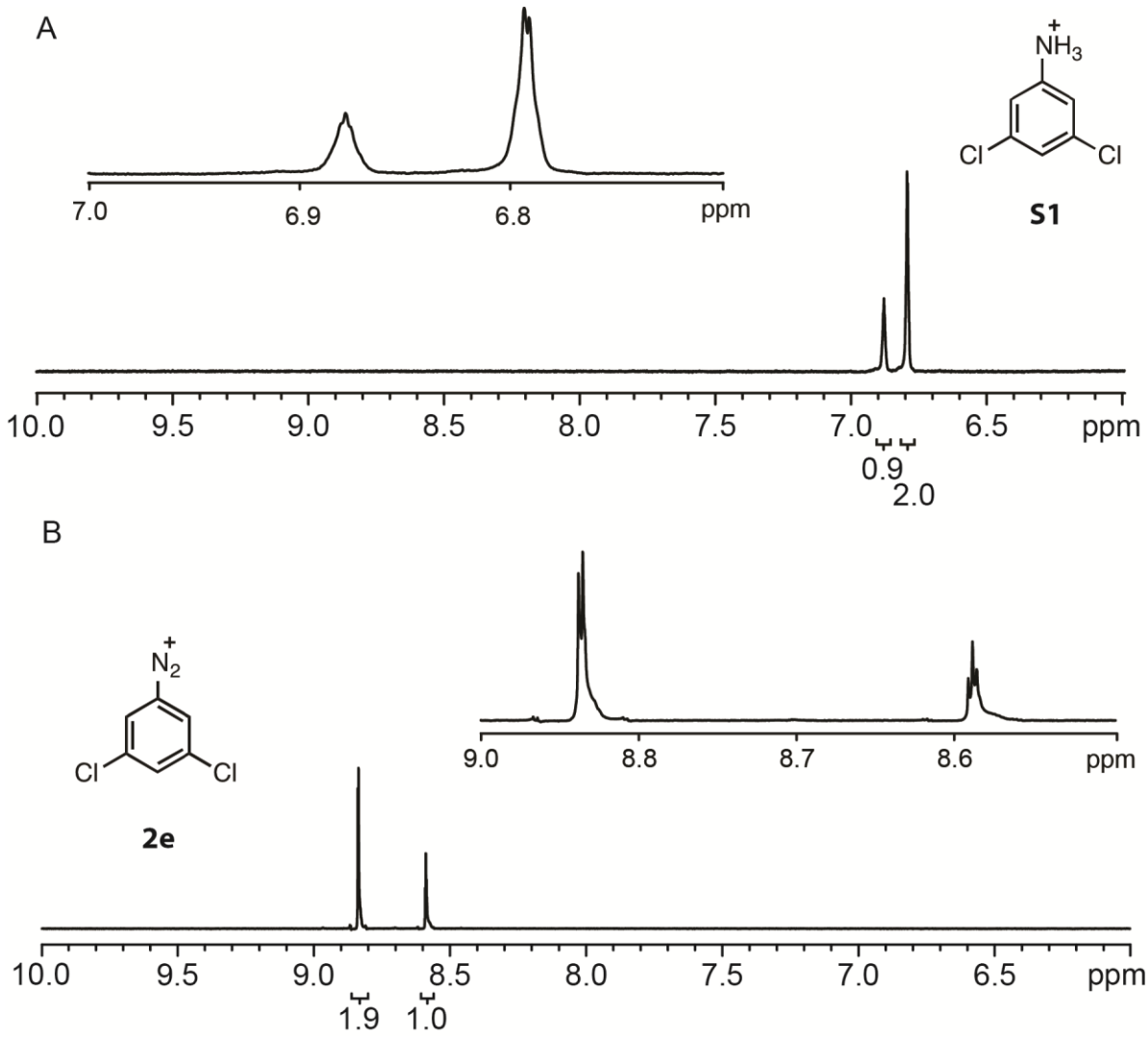
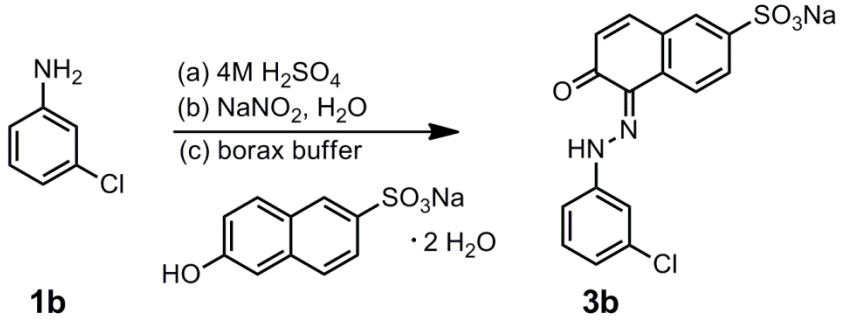


Figure S1.34 (A) [1]H NMR spectrum of **S1** in H_2SO_4 (4 M). [1]H NMR (700 MHz, DMSO-d_6) δ 6.88 (t, J = 1.8 Hz, 1H), 6.79 (d, J = 1.8 Hz, 2H), (B) [1]H NMR spectrum of **2e** H_2SO_4 (4 M). [1]H NMR (700 MHz, DMSO-d_6) δ 8.84 (d, J = 1.9 Hz, 2H), 8.59 (t, J = 1.9, 1H).

X. Product Formation of 3b, 3c, 3e, and 3f by ^{1}H NMR Spectroscopy



1b **3b**

Preparation of stock solutions

D_2O borax buffer (65 mM) – $Na_2B_4O_7{\cdot}H_2O$ (0.25 g, 5.2 mmol) and NaOH (0.85 g, 170 mmol) were dissolved in D_2O (10 mL).

D_2O H_2SO_4 (4 M) – H_2SO_4 (2.0 mL, 18 M) was added to D_2O (7.2 mL).

Sodium nitrite stock solution (175 mM) – In a 4 mL vial, $NaNO_2$ (11.9 mg, 0.172 mmol) was dissolved in D_2O (0.99 mL).

DMSO Stock (704 mM) – DMSO (0.05 mL) was added to D_2O borax buffer (0.95 mL).

Sodium 2-naphthol-6-sulfonate dihydrate/DMSO stock solution (10 mM) – In a 20 mL vial, sodium 2-naphthol-6-sulfonate dihydrate (22.7 mg, 0.0804 mmol) was dissolved in D_2O borax buffer (7.9 mL, 65 mM). To this, DMSO stock was added (0.1 mL, 704 mM) for use as an internal standard.

*Procedure to determine in situ formation of **3b*** – In a 4 mL vial, **1b** (8.1 µL, 0.077 mmol) was dissolved in D_2O H_2SO_4 (2.0 mL, 4 M). To the solution, sodium nitrite (0.4 mL, 175 mM) was added. Then, an aliquot of this reaction mixture (0.24 mL) was taken at 2, 10, 30 and 60 min and reacted with the sodium 2-naphthol-6-sulfonate dihydrate/DMSO (0.76 mL, 10 mM). After 2 min, D_2O borax buffer (0.3 mL, 65 mM) was added to completely dissolve all starting material and product. Each vial contained $NaNO_2$ (0.0070 mmol, 1.0 equiv), sodium 2-naphthol-6-sulfonate dihydrate (0.0077 mmol, 1.1 equiv), and **1b** (0.0077 mmol, 1.1 equiv). All samples were analyzed by ^{1}H NMR spectroscopy for percent yield calculations.

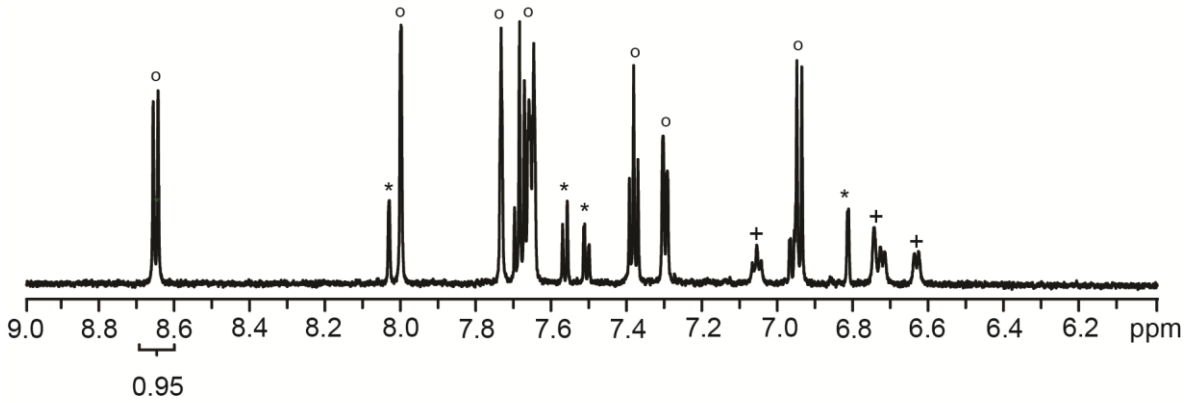
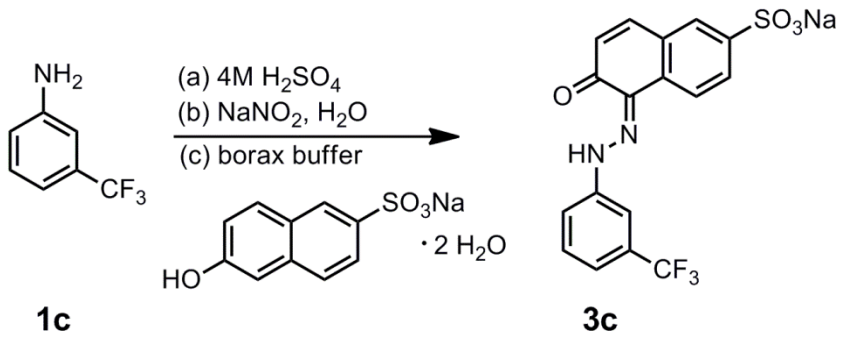


Figure S1.35 ^{1}H NMR (700 MHz, D_2O) spectrum of **3b** (^{O}) at 60 min. DMSO δ 2.61 (s, 6H). Unreacted sodium 2-naphthol-6-sulfonate dihydrate (*) and **1b** ($^{+}$) are indicated. The peak integrated was used for calculation of the percent yield.

Table S1.3 Percent yield of **3b** at different time points.

Time (min)	**3b** (mmol)[a]	Yield (%)[b]
2	0.0064	91 ± 1
10	0.0063	90 ± 2
30	0.0065	92 ± 2
60	0.0063	90 ± 1

[a] determined using an internal standard (DMSO)
[b] Percent yield is based on $NaNO_2$ (0.007 mmol). Standard deviation was determined by an average of 2 runs.



1c **3c**

Preparation of stock solutions

D_2O borax buffer (65 mM) – $Na_2B_4O_7{\cdot}H_2O$ (0.25 g, 5.2 mmol) and NaOH (0.85 g, 170 mmol) were dissolved in D_2O (10 mL).

D_2O H_2SO_4 (4 M) – H_2SO_4 (2.0 mL, 18 M) was added to D_2O (7.2 mL).

Sodium nitrite stock solution (175 mM) – In a 4 mL vial, $NaNO_2$ (11.2 mg, 0.163 mmol) was dissolved in D_2O (0.93 mL).

DMSO Stock (704 mM) – DMSO (0.10 mL) was added to D_2O borax buffer (1.90 mL).

Sodium 2-naphthol-6-sulfonate dihydrate/DMSO stock solution (10 mM) – In a 20 mL vial, sodium 2-naphthol-6-sulfonate dihydrate (21.7 mg, 0.0768 mmol) was dissolved in D_2O borax buffer (7.5 mL, 65 mM). To this, DMSO stock was added (0.1 mL, 704 mM) for use as an internal standard.

*Procedure to determine in situ formation of **3c*** – In a 4 mL vial, **1c** (9.6 µL, 0.077 mmol) was dissolved in D_2O H_2SO_4 (2.0 mL, 4 M). To the solution, sodium nitrite (0.4 mL, 175 mM) was added. Then, an aliquot of this reaction mixture (0.24 mL) was taken at 2, 10, 30 and 60 min and reacted with the sodium 2-naphthol-6-sulfonate dihydrate/DMSO (0.76 mL, 10 mM). After 2 min, D_2O borax buffer (0.3 mL, 65 mM) was added to completely dissolve all starting material and product. Each vial contained $NaNO_2$ (0.0070 mmol, 1.0 equiv), sodium 2-naphthol-6-sulfonate dihydrate (0.0077 mmol, 1.1 equiv), and **1c** (0.0077 mmol, 1.1 equiv). All samples were analyzed by ^1H NMR spectroscopy for percent yield calculations.

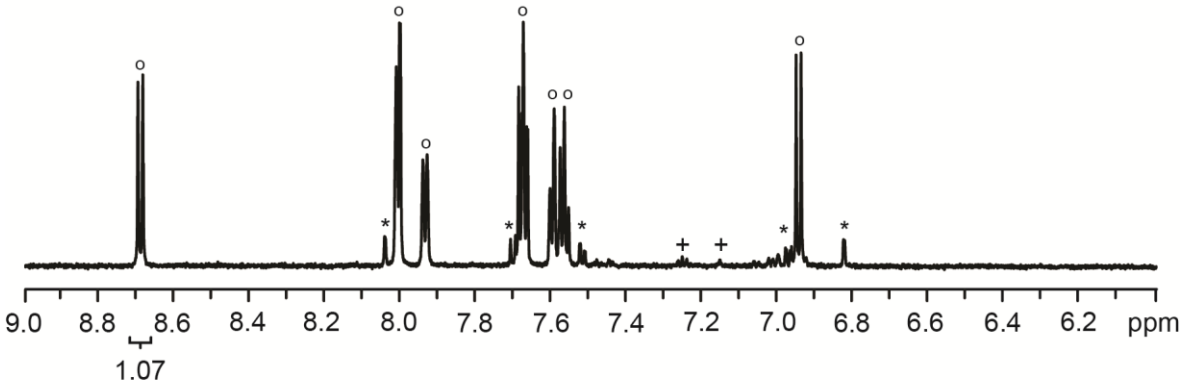


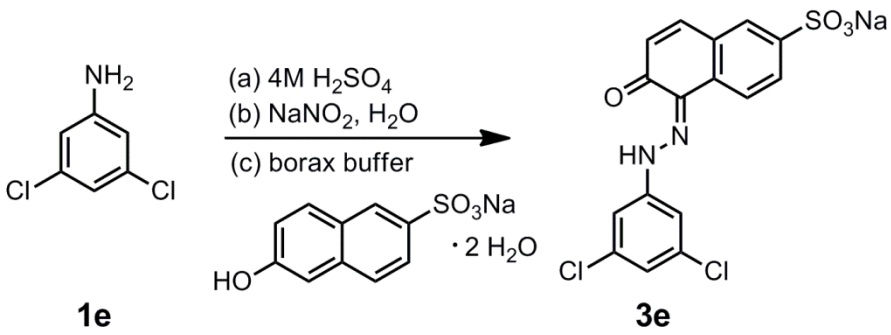
Figure S1.36 ^{1}H NMR (700 MHz, D_2O) spectrum of **3c** (^{O}) at 60 min. DMSO δ 2.62 (s, 6H). Unreacted sodium 2-naphthol-6-sulfonate dihydrate (*) and **1c** ($^{+}$) are indicated. The peak integrated was used for calculation of the percent yield.

Table S1.4 Percent yield of **3c** at different time points.

Time (min)	**3c** (mmol)[a]	Yield (%)[b]
2	0.0075	107 ± 2
10	0.0075	107 ± 2
30	0.0077	110 ± 2
60	0.0077	107 ± 2

[a] determined using an internal standard (DMSO)

[b] The relative integrations apparently overestimate the product formation. We believe this overestimation is due to the low concentrations needed to ensure complete solubility of all material. Percent yield is based on $NaNO_2$ (0.007 mmol). Standard deviation was determined by an average of 2 runs.



1e **3e**

Preparation of stock solutions

D_2O borax buffer (65 mM) – $Na_2B_4O_7{\cdot}H_2O$ (0.25 g, 5.2 mmol) and NaOH (0.85 g, 170 mmol) were dissolved in D_2O (10 mL).

D_2O H_2SO_4 (4 M) – H_2SO_4 (2.0 mL, 18 M) was added to D_2O (7.2 mL).

Sodium nitrite stock solution (175 mM) – In a 4 mL vial, $NaNO_2$ (5.84 mg, 0.0847 mmol) was dissolved in D_2O (0.48 mL).

DMSO Stock (704 mM) – DMSO (0.05 mL) was added to D_2O borax buffer (0.95 mL).

Sodium 2-naphthol-6-sulfonate dihydrate/DMSO stock solution (10 mM) – In a 20 mL vial, sodium 2-naphthol-6-sulfonate dihydrate (11.5 mg, 0.0409 mmol) was dissolved in D_2O borax buffer (3.9 mL, 65 mM). To this, DMSO stock was added (0.1 mL, 704 mM) for use as an internal standard.

*Procedure to determine in situ formation of **3e*** – In a 4 mL vial, **1e** (12.6 mg, 0.0772 mmol) was dissolved in D_2O H_2SO_4 (2.0 mL, 4 M). To the solution, sodium nitrite (0.4 mL, 175 mM) was added. Then, an aliquot of this reaction mixture (0.24 mL) was taken at 2, 10, 30 and 60 min and reacted with the sodium 2-naphthol-6-sulfonate dihydrate/DMSO (0.76 mL, 10 mM). After 2 min, D_2O borax buffer (3.0 mL, 65 mM) was added to completely dissolve all starting material and product. Then an aliquot of the mixture (0.1 mL) was added to an NMR tube and diluted with D_2O (0.5 mL). Each vial contained $NaNO_2$ (0.0071 mmol, 1.0 equiv), sodium 2-naphthol-6-sulfonate dihydrate (0.0078 mmol, 1.1 equiv), and **1e** (0.0078 mmol, 1.1 equiv). All samples were analyzed by ^1H NMR spectroscopy for percent yield calculations.

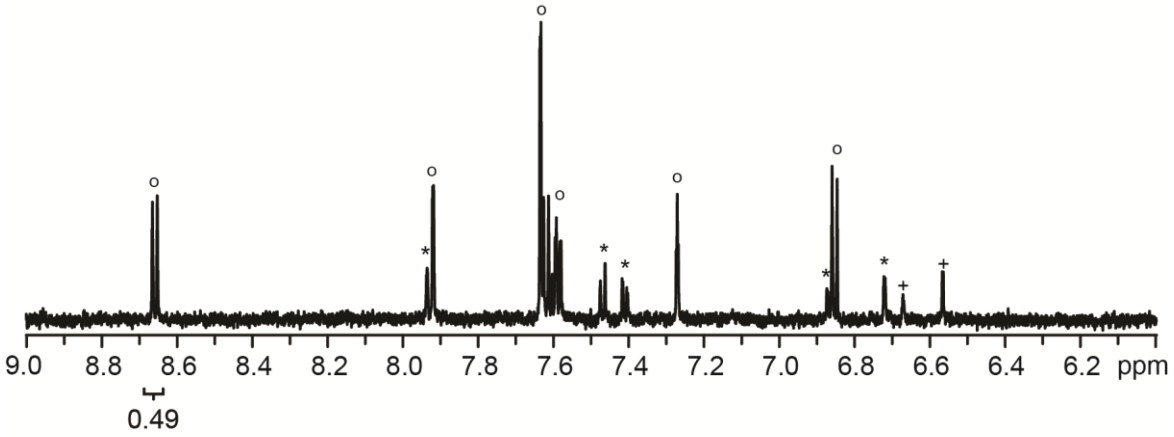
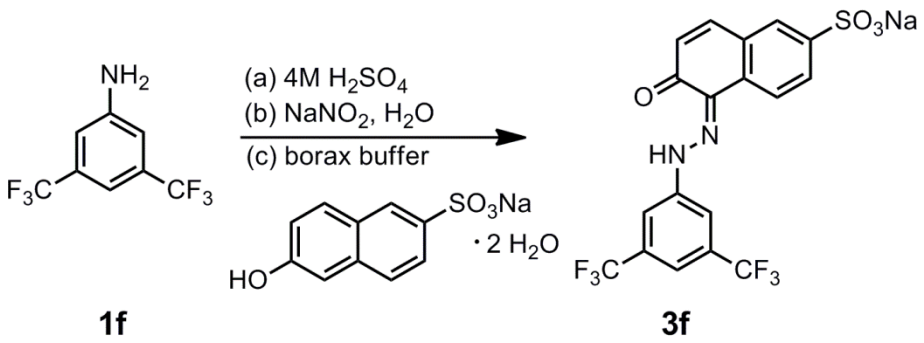


Figure S1.37 ^{1}H NMR (700 MHz, D_2O) spectrum of **3e** (^{O}) at 60 min. DMSO δ 2.52 (s, 6H). Unreacted sodium 2-naphthol-6-sulfonate dihydrate (*) and **1e** ($^{+}$) are indicated. The peak integrated was used for calculation of the percent yield.

Table S1.5 Percent yield of **3e** at different time points.

Time (min)	**3e** (mmol)[a]	Yield (%)[b]
2	0.0058	82 ± 1
10	0.0063	89 ± 3
30	0.0063	89 ± 9
60	0.0066	93 ± 8

[a] determined using an internal standard (DMSO)
[b] Percent yield is based on $NaNO_2$ (0.0071 mmol). Standard deviation was determined by an average of 2 runs.



1f **3f**

Preparation of stock solutions

D_2O borax buffer (65 mM) – $Na_2B_4O_7{\cdot}H_2O$ (5.2 mmol) and NaOH (170 mmol) were dissolved in D_2O (10 mL).

D_2O H_2SO_4 (4 M) – H_2SO_4 (2.0 mL, 18 M) was added to D_2O (7.2 mL).

Sodium nitrite stock solution (175 mM) – In a 4 mL vial, $NaNO_2$ (11.235 mg, 0.163 mmol) was dissolved in D_2O (0.93 mL).

DMSO Stock (704 mM) – DMSO (0.10 mL) was added to D_2O borax buffer (1.90 mL).

Sodium 2-naphthol-6-sulfonate dihydrate/DMSO stock solution (10 mM) – In a 20 mL vial, sodium 2-naphthol-6-sulfonate dihydrate (21.7 mg, 0.0768 mmol) was dissolved in D_2O borax buffer (7.5 mL, 65 mM). To this, DMSO stock was added (0.10 mL, 704 mM) for use as an internal standard.

*Procedure to determine in situ formation of **3f*** – In a 4 mL vial, **1f** (12 µL, 0.077 mmol) was dissolved in D_2O H_2SO_4 (2.0 mL, 4 M). To the solution, sodium nitrite (0.4 mL, 175 mM) was added. Then, an aliquot of this reaction mixture (0.24 mL) was taken at 2, 10, 30 and 60 min and reacted with the sodium 2-naphthol-6-sulfonate dihydrate/DMSO (0.76 mL, 10 mM). After 2 min, D_2O borax buffer (0.3 mL, 65 mM) was added to completely dissolve all starting material and product. Each vial contained $NaNO_2$ (0.0070 mmol, 1.0 equiv), sodium 2-naphthol-6-sulfonate dihydrate (0.0077 mmol, 1.1 equiv), and **1f** (0.0077 mmol, 1.1 equiv). All samples was analyzed by ^1H NMR spectroscopy for percent yield calculations.

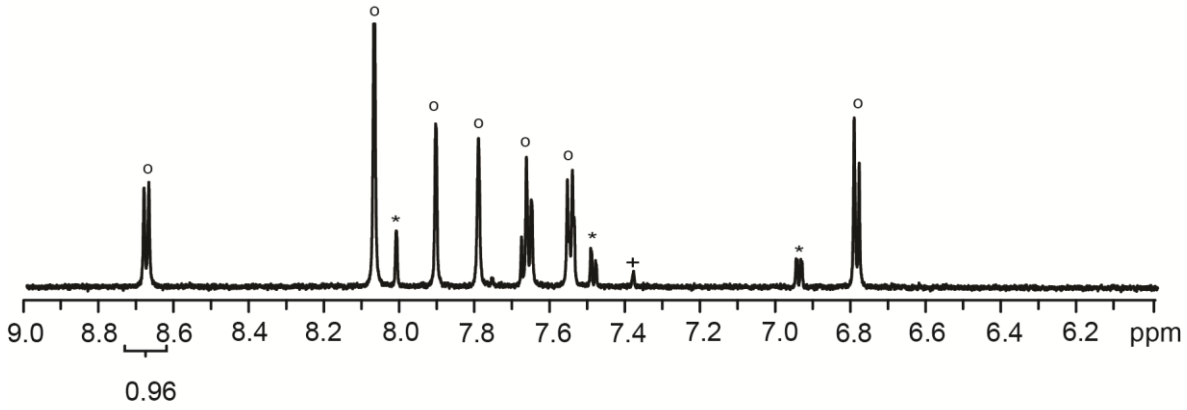


Figure S1.38 ^{1}H NMR (700 MHz, D_2O) spectrum of **3f** (^{O}) at 60 min. DMSO δ 2.60 (s, 6H). Unreacted sodium 2-naphthol-6-sulfonate dihydrate (*) and **1f** ($^{+}$) are indicated. The peak integrated was used for calculation of the percent yield.

Table S1.6 Percent yield of **3f** at different time points.

Time (min)	**3f** (mmol)[a]	Yield (%)[b]
2	0.0070	100 ± 1
10	0.0068	97 ± 2
30	0.0068	97 ± 3
60	0.0068	97 ± 3

[a] determined using an internal standard (DMSO)
[b] Percent yield is based on $NaNO_2$ (0.007 mmol). Standard deviation was determined by an average of 2 runs.

[1]H NMR spectroscopic study of **3e** formation in situ

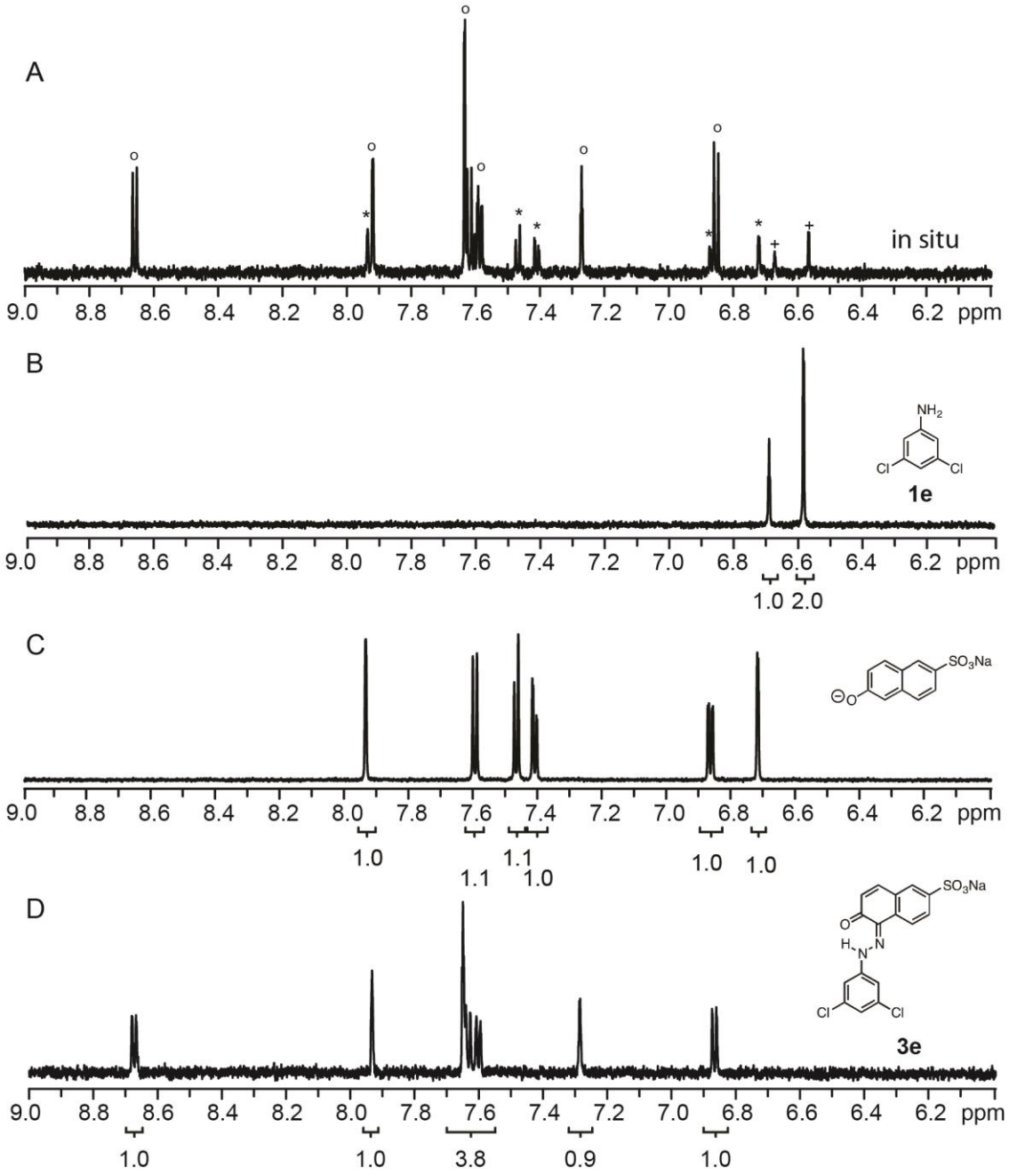


Figure S1.39 [1]H NMR spectra of (A) **3e** in in situ conditions (700 MHz, D_2O borax buffer) where [+]**1e**, *sodium 2-naphthol-6-sulfonate dehydrate, and [o]**3e**. (B) **1e** (700 MHz, D_2O borax buffer) δ 6.90 (t, *J* = 1.7 Hz, 1H), 6.58 (d, *J* = 1.7 Hz, 2H), (C) sodium 2-naphthol-6-sulfonate dihydrate (700 MHz, D_2O borax buffer) δ 7.93 (s, 1H), 7.60 (d, *J* = 9.1 Hz, 1H) 7.47 (d, *J* = 8.6 Hz, 1H), 7.42 (dd, *J* = 8.8, 1.7 Hz, 1H) 6.87 (dd, *J* = 9.3, 2.8 Hz, 1H), 6.72 (d, *J* = 2.3 Hz, 1H). (D) **3e** (700 MHz, D_2O borax buffer) δ 8.68 (d, *J* = 9.0 Hz, 1H), 7.93 (s, 1H) 7.65 (m, 4H), 7.29 (d, *J* = 2.08 Hz, 1H), 6.88 (d, *J* = 9.4 Hz, 1H).

XI. In Situ Gelation and In Situ Gelation in Environmental Conditions

In situ detection of NO_2^- in a 4 mL vial

Preparation of stock solutions

1e *solution (62.0 mM)* – **1e** (21.1 mg, 0.130 mmol) was dissolved in H_2SO_4 (2.1 mL, 4 M).

Sodium nitrite solution (276 mM) – $NaNO_2$ (32.4 mg, 0.470 mmol) was dissolved in H_2O (1.7 mL).

Sodium 2-naphthol-6-sulfonate dihydrate (16.2 mM) – Sodium 2-naphthol-6-sulfonate dihydrate (34.7 mg, 0.123 mmol) was dissolved in borax buffer (7.6 mL, 65 mM).

Representative procedure for in situ detection of NO_2^- - In a 4 mL vial, $NaNO_2$ solution (40 µL, 276 mM) was reacted with the **1e** solution (0.2 mL, 62.0 mM). The vial was shaken for 30 s and let stand to react for 10 min. Then the sodium 2-naphthol-6-sulfonate dihydrate solution (0.76 mL, 16.2 mM) was added and a color change from slight yellow to red-orange was observed. The vial was heated with a heat gun until all compounds were dissolved and then allowed to cool to rt.

Table S1.7 Concentration of NO_2^-

In Situ Generated Gelator	$NaNO_2$ (mmol)	Final NO_2^- (ppm)
3b	0.033	1500
3c	0.028	1300
3e	0.011	500

In situ detection of NO_2^- in a 1.5 mL vial

Preparation of stock solutions

1e *solution (11.0 mM)* – **1e** (5.53 mg, 0.0341 mmol) was dissolved in H_2SO_4 (3.1 mL, 4 M).

Sodium nitrite solution (49.0 mM) – $NaNO_2$ (3.08 mg, 0.0446 mmol) was dissolved in H_2O (0.91 mL).

Sodium 2-naphthol-6-sulfonate dihydrate (2.87 mM) – Sodium 2-naphthol-6-sulfonate dihydrate (3.23 mg, 0.0115 mmol) was dissolved in borax buffer (4.0 mL, 65 mM).

Procedure for in situ detection of NO_2^- - In a 1.5 mL vial, $NaNO_2$ solution (20 µL, 49.0 mM) was reacted with the **1e** solution (0.1 mL, 11.0 mM). The vial was shaken for 30 s and let stand to react for 10 min. Then sodium 2-naphthol-6-sulfonate dihydrate solution (0.38 mL, 2.87 mM) was added and a color change from slight yellow to red-orange was observed. The vial was shaken for 5 s, sonicated for 10 s and then allowed to stand at rt for 5 min.

Table S1.8 Concentration of NO_2^-

In Situ Generated Gelator	$NaNO_2$ (mmol)	Final NO_2^- (ppm)
3e	0.00098	90

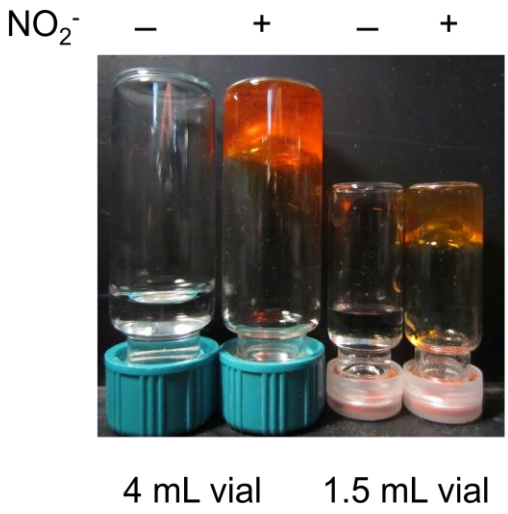


Figure S1.40 In situ gels of **3e** at 500 ppm of NO_2^- in a 4 mL vial and 90 ppm of NO_2^- in a 1.5 mL vial with negative controls.

Gelation in environmental conditions procedure – In situ gels of **3e** were formed via the representative procedure for in situ detection for NO_2^- (pg. S43). However, water from four different sources (lab tap water, Huron River water, pond water and muddy pond water) were spiked with $NaNO_2$ (0.76 mg, 0.011 mmol) and used in place of the sodium nitrite stock solution to determine if gelation occurred in environmental conditions. Additionally, a negative control with no $NaNO_2$ added was performed for each water source. Results are shown in Figure S38.

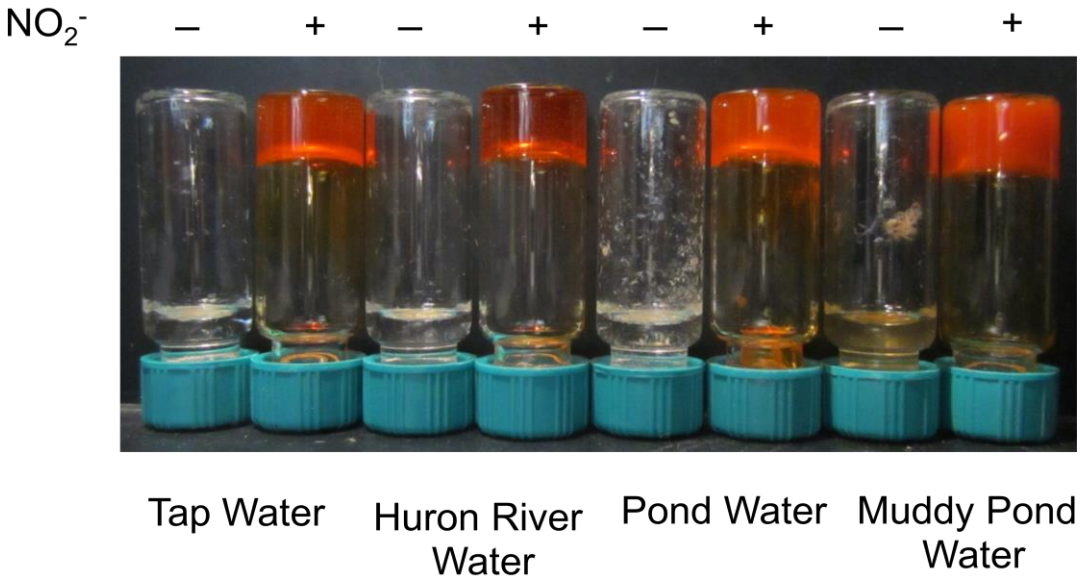


Figure S1.41 In situ gels of **3e** at 500 ppm of NO_2^- in various sources.

In situ detection of NO_2^- from a NO_2^- standard in a 1.5 mL vial

Preparation of stock solutions

1e *solution (12.1 mM)* – **1e** (1.94 mg, 0.0120 mmol) was dissolved in H_2SO_4 (0.99 mL, 4 M).

Sodium 2-naphthol-6-sulfonate dihydrate (2.95 mM) – Sodium 2-naphthol-6-sulfonate dihydrate (3.06 mg, 0.0109 mmol) was dissolved in borax buffer (3.65 mL, 65 mM).

Procedure for in situ detection of NO_2^- - In a 1.5 mL vial, SPEX Certiprep nitrite-nitrogen standard (45 µL, 1000 ppm) was reacted with the **1e** solution (0.09 mL, 12.1 mM). The vial was shaken for 30 s and let stand to react for 10 min. Then sodium 2-naphthol-6-sulfonate dihydrate solution (0.365 mL, 2.95 mM) was added and a color change from slight yellow to red-orange was observed. The vial was shaken for 5 s, sonicated for 5 s and then allowed to stand at rt for 10 min.

Table S1.9. Concentration of NO_2^-

In Situ Generated Gelator	Final NO_2^- (ppm)
3e	90

XII. Reference

(1) Kalatzis, E. *J. Chem. Soc. B.* **1967**, 273-277.

Appendix 2[1]

Supporting Information for Chapter 4:
Amplification via Depolymerization in Gel-Based Sensors

I. Materials

All reagent grade materials and solvents were purchased from Sigma-Aldrich, Acros, or TCI. Acetone, DMF, MeOH and pyridine were dried and distilled before being used.[1] THF was dried and deoxygenated using an Innovative Technology (IT) solvent purification system composed of activated alumina, copper catalyst and molecular sieves. *N*-Bromosuccinimide was recrystallized from hot water and dried over P_2O_5. Deionized water was used unless otherwise specified.

II. General Experimental

NMR Spectroscopy – ^{1}H and ^{13}C NMR spectra for all compounds were acquired in d-$CDCl_3$ on a Varian Inova 500 operating at 500 and 126 MHz, Varian vnmrs 500 operating at 500 and 126 MHz, Varian vnmrs 700 operating at 700 and 176 MHz, or a Varian MR400 operating at 400 MHz. The chemical shift data are reported in units of δ (ppm) relative to tetramethylsilane and referenced by residual protic solvent. An asterisk was used to indicate residual H_2O in all spectra while double bars are used to indicate peaks that have been truncated. The abbreviations s, d, t, at, dd, ddt, adq, adt and m were used to signify singlet, doublet, triplet, apparent triplet, doublet of doublets, doublet of doublets of triplets, and multiplet respectively.

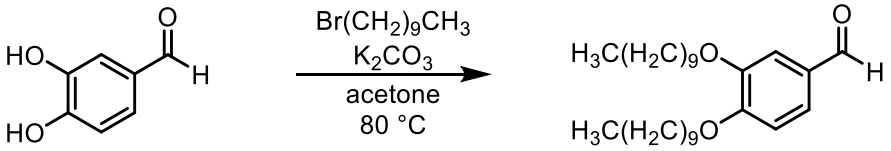
High Resolution Mass Spectrometry (HRMS) – HRMS data were obtained on a Micromass AutoSpec Ultima Magnetic Sector mass spectrometer via electron impact ionization or via electrospray ionization in positive ion mode.

Gel-Permeation Chromatography: Polymer molecular weights were determined by comparison with polystyrene standards (Varian, EasiCal PS-2 MW 580-377,400) on a Waters 1515 HPLC instrument equipped with column guard and three Phenogel columns (4.6 x 30 cm, 10^2 Å, 10^3 Å, 10^4 Å) in sequence and analyzed with Waters 2487 dual absorbance detector (254 nm). Samples were dissolved in THF (with mild heating) and passed through a 0.2 µm PTFE filter prior to analysis.

[1] D. M. Z. gratefully acknowledges the contributions of Jessi Willison and Dylan Phillips for assisting with monomer synthesis as well as Dr. Cheryl Moy for her intellectual contributions.

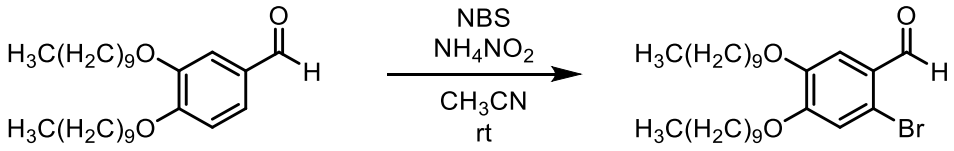
III. Poly(phthalaldehyde) Scaffold

(a) Synthetic Procedures



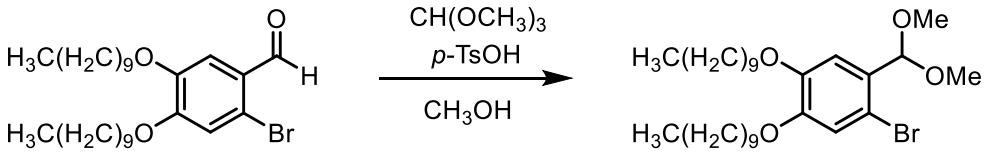
S1 **4**

4.[2] In a 100 mL round bottom flask equipped with a stir bar, **S1** (600 mg, 4.34 mmol, 1.0 equiv), potassium carbonate (2.40 g, 17.4 mmol, 4.0 equiv) and 1-bromodecane (3.63 mL, 17.5 mmol, 4.0 equiv) was suspended in acetone (30 mL). The reaction was then refluxed at 80 °C for 16 h. Potassium carbonate was filtered off and the filtrate was dried over $MgSO_4$ and concentrated. The crude solid was purified by column chromatography (10% EtOAc/hexanes) and afforded compound **4** (1.65 g, 91%).



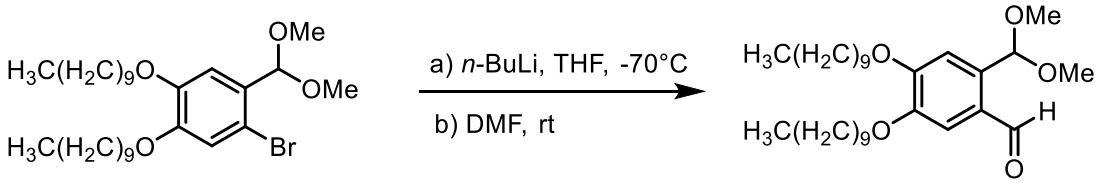
4 **5**

5. In a 50 mL round bottom flask equipped with a stir bar, **4** (2.04 g, 4.87 mmol, 1.0 equiv), *N*-bromosuccinimide (0.950 g, 5.34 mmol, 1.1 equiv), and ammonium nitrate (85.0 mg, 1.06 mmol, 0.2 equiv), were suspended in acetonitrile (30 mL) and stirred for 6 h. The reaction was quenched by addition of H_2O (20 mL) and then extracted with diethyl ether (3 x 10 mL). The combined organic layers were dried over $MgSO_4$ and concentrated. The residue was purified by column chromatography (2% EtOAc/hexanes) to afford **5** (1.78 g, 73%).



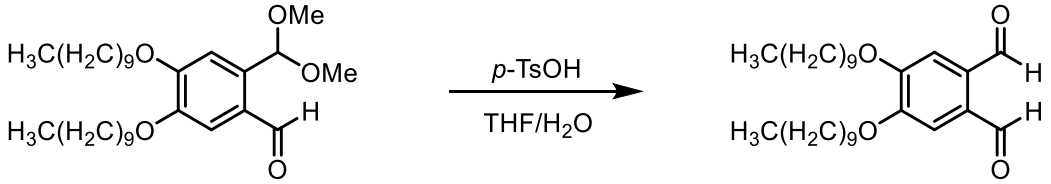
5 **6**

6.[3] In an oven dried 50 mL round bottom flask equipped with a stir bar, **5** (1.77 g, 3.56 mmol, 1.0 equiv) and *p*-toluenesulfonic acid monohydrate (0.013 g, 0.068 mmol, 0.02 equiv) was dissolved in dry MeOH (15 mL). To the reaction mixture methyl orthoformate (0.45 mL, 4.11 mmol, 1.2 equiv) was added dropwise and the reaction was refluxed at 60 °C for 36 h. The reaction was then quenched with $NaHCO_3$ (10 mL) and extracted with DCM (2 x 15 mL). The organic layer was then washed with H_2O (10 mL). It was then dried with $MgSO_4$ and concentrated. The yellow oil (1.41g, 73%) was used in the next reaction without purification.



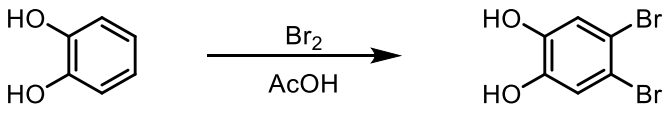
6 **7**

7.[3] In an oven dried 25 mL Schlenck flask equipped with a stir bar **6** (366 mg, 0.673 mmol, 1.0 equiv) was dissolved in THF (8.0 mL). The reaction flask was then cooled to -70 °C under N_2. To the cooled solution 1.6 M *n*-butyllithium (0.55 mL, 0.88 mmol, 1.3 equiv) was added dropwise. The reaction was stirred for 1h. Then DMF (0.1 mL, 1.3 mmol, 1.9 equiv) was added and the solution warmed up to rt over 2 h. The reaction was quenched by addition of H_2O (5 mL) and then extracted with DCM (3 x 10 mL). The combined organic layers were then dried over $MgSO_4$ and concentrated. The residue was not further purified (**7**) but used as collected in the next reaction (231 mg, 70%).



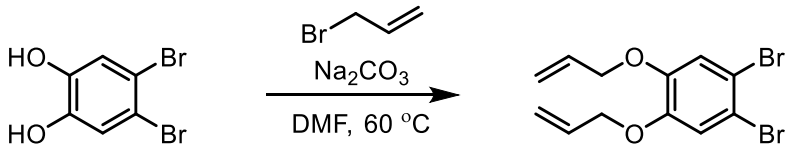
7 **3**

3.[3] In an oven dried 25 mL round bottom flask equipped with a stir bar **7** (920 mg, 1.87 mmol, 1.0 equiv) was dissolved in THF (6 mL). To the solution *p*-toluenesulfonic acid monohydrate (3.6 mg, 0.019 mmol, 0.01 equiv) dissolved in H_2O (3 mL) was added. The reaction was then refluxed overnight at 80°C. The reaction was washed with sat. $NaHCO_3$ (30 mL) and extracted with DCM (3 x 20 mL). The combined organic layers were then dried with $MgSO_4$ and concentrated. The residue was purified by column chromatography (20-40% EtOAc/hexanes) to give **3** (0.31 g, 37%).



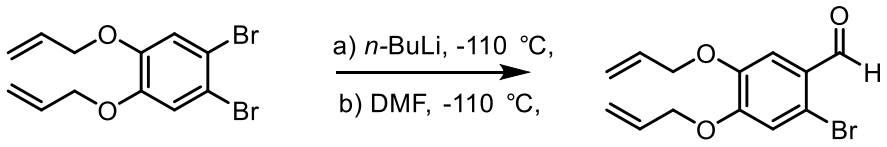
S2 **9**

9.[4] In an oven dried 50 mL round bottom flask equipped with a stir bar **S2** (1.96 g, 17.8 mmol, 1.0 equiv) was dissolved in acetic acid (7.0 mL). The solution was then cooled to 0°C and put under nitrogen. Bromine (1.92 mL, 37.4 mmol, 2.1 equiv) was added dropwise to the solution and stirred overnight. Upon completion the mixture was poured into ice water (20 mL) and the precipitate was filtered off. The crude solid was then recrystallized from $CHCl_3$. An off-white solid was collected (4.28 g, 90%).



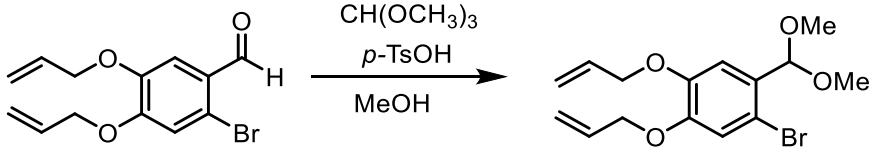
9 **10**

10. In an oven dried 100 mL bomb flask equipped with a stir bar **9** (3.09 g, 11.5 mmol, 1.0 equiv) was dissolved in DMF (18 mL). Then Na_2CO_3 (5.59 g, 52.7 mmol, 4.6 equiv) was added slowly while stirring vigorously to prevent clumping. Then allyl bromide (3.0 mL, 34.7 mmol, 3.0 equiv) was added and the reaction was heated to 60 °C and let stir for 2 d. The reaction was washed with H_2O (40 mL) extracted with Et_2O (2 x 20 mL) and EtOAc (2 x 20 mL). The combined organic layers were dried with $MgSO_4$ and concentrated. The residue was purified by column chromatography (2-40% EtOAc/hexanes) to give **10** (3.09 g, 77%).



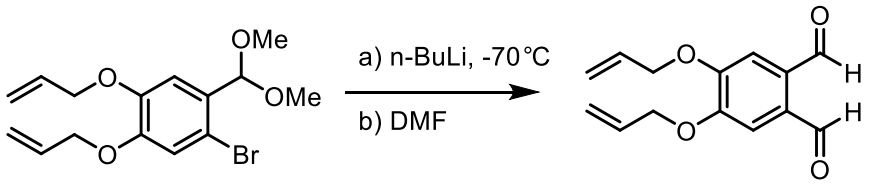
10 **11**

11.[5] In an oven dried 50 mL Schlenck flask equipped with a stir bar **10** (267 mg, 0.767 mmol, 1.0 equiv) was dissolved in THF (19 mL) and Et_2O (19 mL). The solution was then cooled to -110 °C and a 1.15 M *n*-BuLi (0.66 mL, 0.76 mmol, 1.0 equiv) was added dropwise along the side of the cooled flask. After 30 min DMF (0.22 mL, 2.84 mmol, 3.7 equiv) was added dropwise and let stir for 1 h as the solution warmed up to rt. The reaction was quenched with 3 M HCl in EtOH (10 mL) and then poured into a solution of 2 M HCl (10 mL). The organic layer was dried over $MgSO_4$ and concentrated. The residue was purified by column chromatography (10% EtOAc/hexanes) to give **11** (45 mg, 20%).



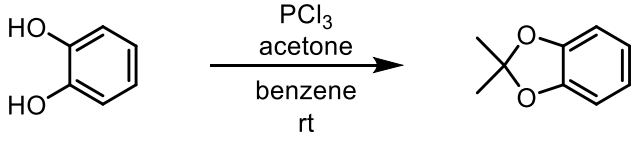
11 **12**

12.[3] In an oven dried 10 mL round-bottom flask equipped with a stir bar **11** (145 mg, 0.488 mmol, 1.0 equiv), methyl orthoformate (0.06 mL, 0.5 mmol, 1.0 equiv), *p*-toluenesulfonic acid monohydrate (2.0 mg, 0.01 mmol, 0.02 equiv) was dissolved in MeOH (5 mL). The reaction was refluxed for 24 h. The reaction was quenched with $NaHCO_3$ (1 mL) and extracted with DCM (2 x 10 mL). The combined organic layers were dried over $MgSO_4$ and concentrated. The product (121 mg, 72%) was used in the next reaction without further purification.



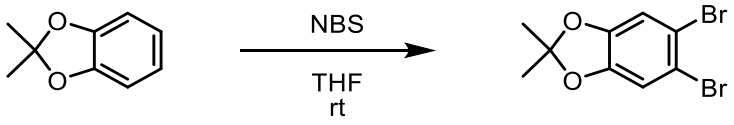
12 **8**

8.[3] In an oven dried 25 mL round bottom flask equipped with a stir bar **12** (121 mg, 0.348 mmol, 1.0 equiv) was dissolved in THF (6 mL). The reaction was then cooled to -70 °C and 1.15 M *n*-BuLi (0.45 mL, 0.52 mmol, 1.5 equiv) was added dropwise. The reaction was stirred for 30 min and then DMF (0.10 mL, 1.3 mmol, 3.7 equiv). After stirring for 1 h the reaction was warmed up to rt before being quenched with 3M HCl in EtOH (10 mL). After 3 M HCl (10 mL) was added and the extracted with DCM (2 x 10 mL). The combined organic layers were dried over $MgSO_4$ and concentrated. The residue was purified by column chromatography (10% EtOAc/hexanes) to give **8** with some ethyl acetate (41 mg, 48%).



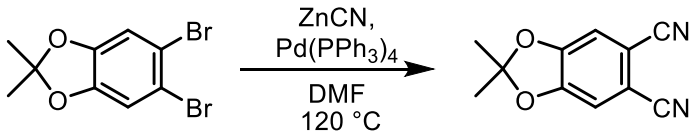
S2 **13**

13.[6] In a 10 mL round bottom flask equipped with a stir bar phosphorus trichloride (0.42 mL, 4.8 mmol, 0.5 equiv) was added dropwise to a stirred solution of **S2** (1.10 g, 9.99 mmol, 1.0 equiv) and acetone (0.7 mL, 9.53 mmol, 1.0 equiv) in benzene (3.6 mL).The reaction mixture was stirred for 24 h (white cloudy solution) and then poured onto K_2CO_3 (3.04 g). The organic layer was filtered and the precipitate was washed with benzene (10 mL). The filtrate was first washed with 10% NaOH (10 mL) and then extracted with additional benzene (2 x 10 mL). The combined organic layers were dried with $MgSO_4$ and benzene (b.p. 80 °C) was distilled off. A clear liquid product (b.p. 189°C) was obtained (0.71 g, 47%).



13 **14**

14.[7] In a 25 mL round bottom flask equipped with a stir bar, **13** (607 mg, 4.04 mmol, 1.0 equiv) and *N*-bromosuccinimide (1.67 g, 9.34 mmol, 2.3 equiv) was dissolved in dried THF (6.0 mL). The vial was then put under nitrogen and reacted overnight. Silica was then added to the reaction and the solvent was evaporated off. The silica was then dry loaded onto a column and 100% hexanes was used to elute the product. After concentrating the collected fractions, a white solid was obtained (1.03 g, 83%).



14 **15**

15.[8] In a 25 mL oven-dried Schlenck flask equipped with a stir bar **14** (204 mg, 0.662 mmol, 1.0 equiv) and zinc cyanide (234 mg, 1.99 mmol, 3.0 equiv) was suspended in DMF (2.6 mL) under N_2. The reaction flask was then sparged with N_2 for 15 min. Then tetrakis(triphenylphosphine) palladium(0) (78.6 mg, 0.068 mmol, 0.1 equiv) was taken from the glovebox and added quickly under N_2. The reaction was then heated to 120 °C and let stir overnight. The next morning the solution had turned deep red-orange. The resulting solution was filtered and rinsed with a small amount of acetone. The solution was then stirred rapidly while H_2O (16 mL) was added to precipitate the product. The solid was collected by filtration and rinsed with water before being dissolved in DCM (20 mL). Any solid that did not go into solution was then filtered off and the filtrate was dried with $MgSO_4$ and concentrated. Column chromatography (10–20% EtOAc/hexanes gradient) was carried out and a white solid was obtained (64.5 mg, 49%)

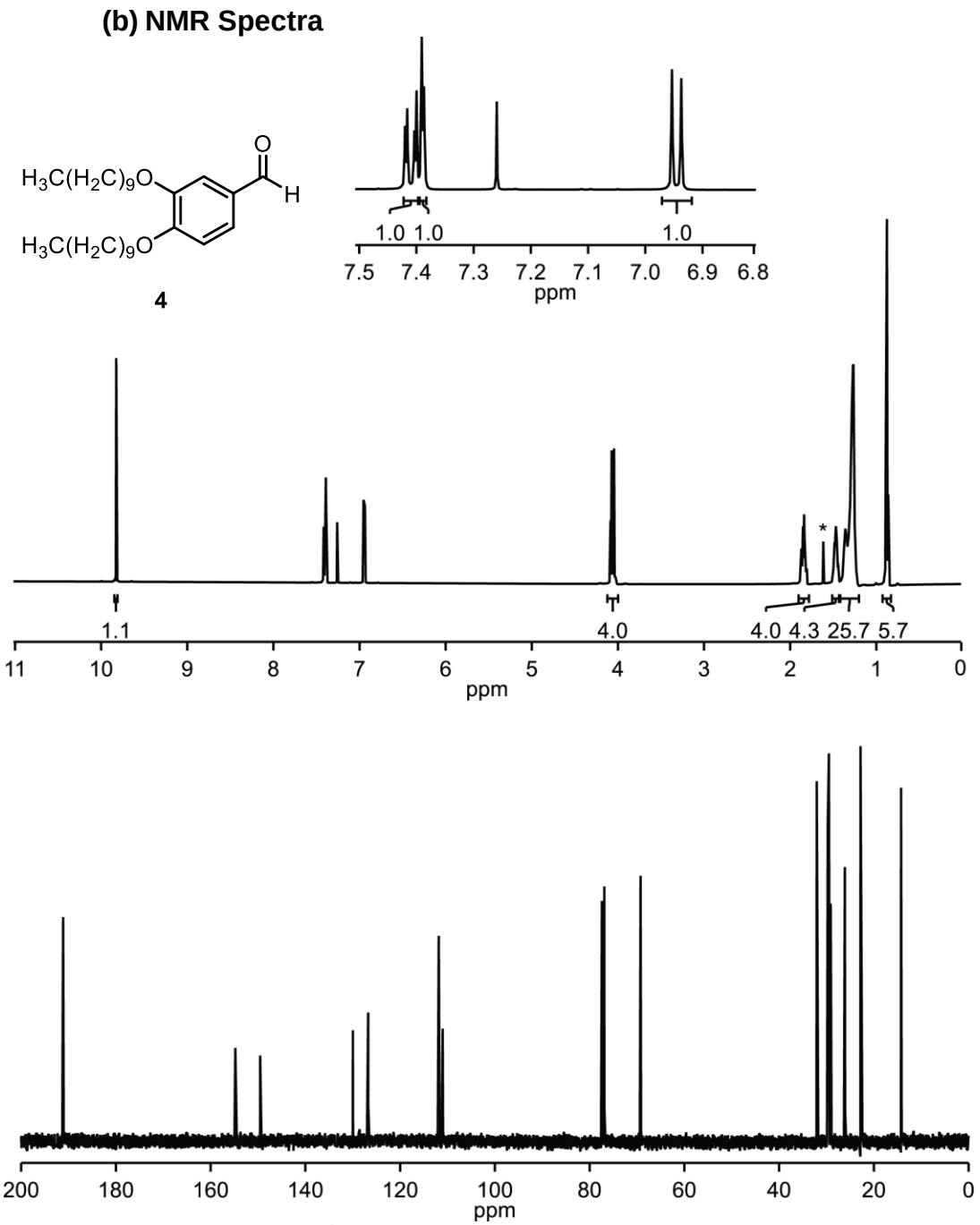


Figure S2.1 ^{1}H NMR and ^{13}C NMR spectra for **4**. ^{1}H NMR (500 MHz, $CDCl_3$) δ 9.82 (s, 1H), 7.41 (dd, *J* = 8.1, 1.9 Hz, 1H), 7.39 (d, *J* = 1.9 Hz, 1H), 6.95 (d, *J* = 8.1 Hz, 1H), 4.07 (t, *J* = 6.8 Hz, 2H), 4.04 (t, *J* = 6.8 Hz, 2H), 1.89–1.80 (m, 4H), 1.53–1.42 (m, 4H), 1.39–1.21 (m, 24H), 0.88 (t, *J* = 6.9 Hz, 6H). ^{13}C NMR (126 MHz, $CDCl_3$) δ 191.14, 154.79, 149.55, 129.98, 126.74, 111.85, 111.02, 69.25, 69.24, 32.05, 29.76, 29.73, 29.71, 29.70, 29.52, 29.49, 29.49, 29.20, 29.12, 26.13, 26.09, 22.83, 14.26. * indicates residual H_2O.

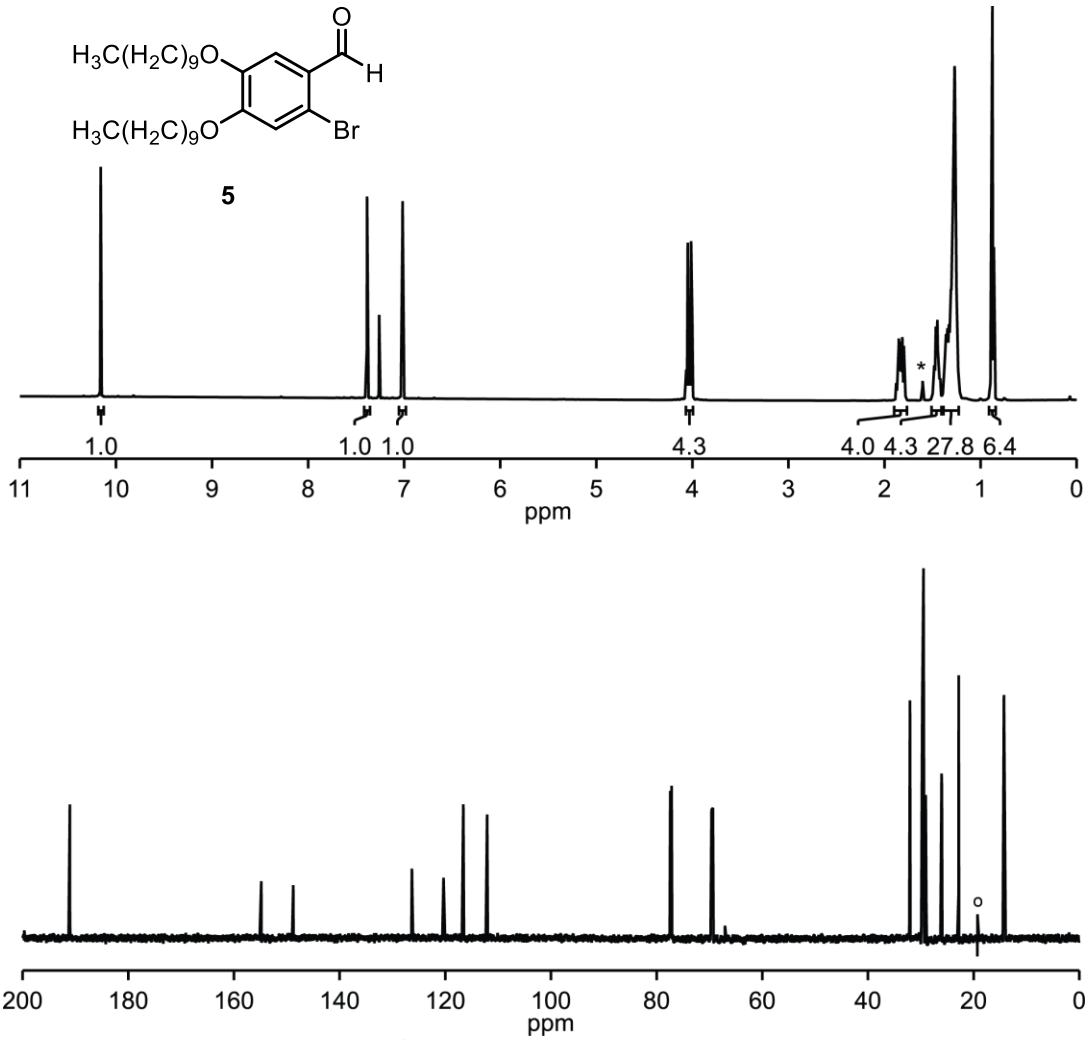


Figure S2.2 ^{1}H NMR and ^{13}C NMR spectra for **5**. ^{1}H NMR (500 MHz, $CDCl_3$) δ 10.16 (s, 1H), 7.39 (s, 1H), 7.02 (s, 1H), 4.05 (t, *J* = 6.6 Hz, 2H), 4.01 (t, *J* = 6.6 Hz, 2H), 1.8–1.78 (m, 4H), 1.52–1.41 (m, 4H), 1.39–1.21 (m, 24H), 0.88 (t, *J* = 6.8 Hz, 6H). ^{13}C NMR (126 MHz, $CDCl_3$) δ 191.06, 154.82, 148.77, 126.32, 120.33, 116.59, 112.08, 69.60, 69.35, 32.05, 29.74, 29.71, 29.70, 29.69, 29.49, 29.44, 29.08, 28.97, 26.07, 26.01, 22.83, 14.27. * indicates residual H_2O; ° indicates a ghost peak from the NMR instrument.

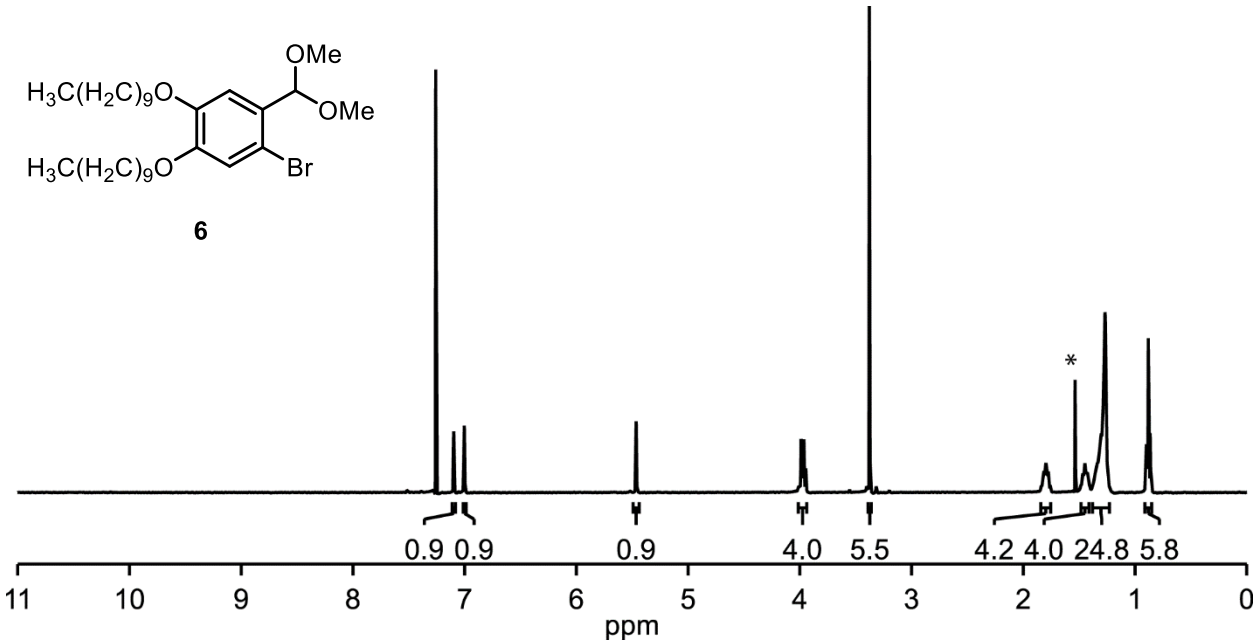


Figure S2.3 ^{1}H NMR spectrum for **6**. ^{1}H NMR (400 MHz, $CDCl_3$) δ 7.10 (s, 1H), 7.00 (s, 1H), 5.46 (s, 1H), 3.99 (d, *J* = 6.6 Hz, 2H), 3.96 (t, *J* = 6.7 Hz, 2H), 3.38 (s, 6H), 1.85–1.74 (m, 4H), 1.49–1.40 (m, 4H), 1.38–1.20 (m, 24H), 0.88 (t, *J* = 7.2 Hz, 6H). * indicates residual H_2O.

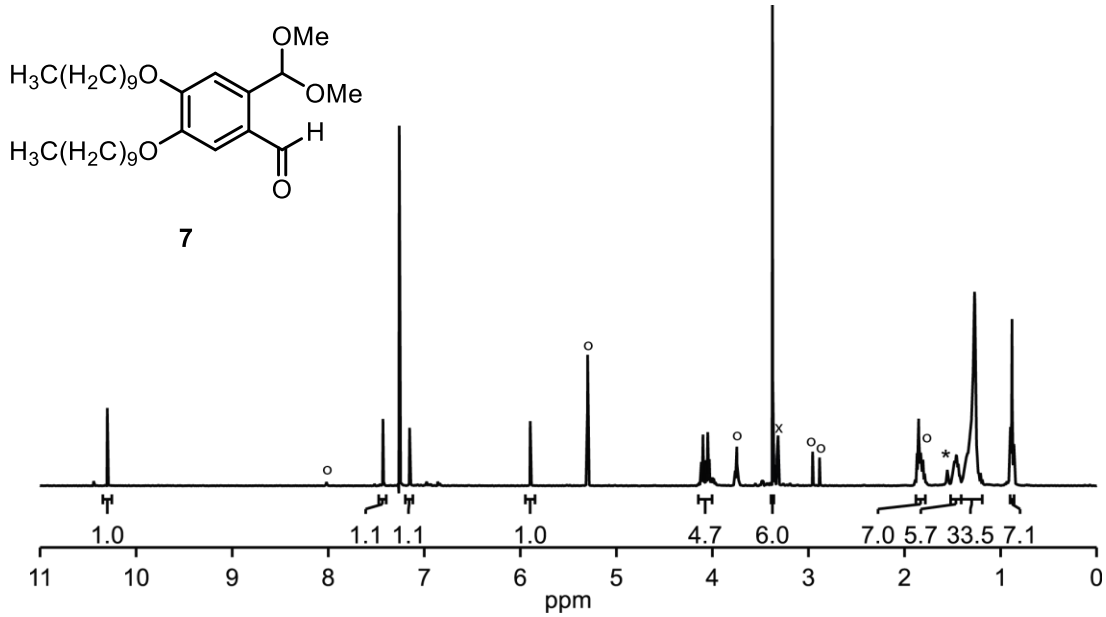


Figure S2.4 ^{1}H NMR spectrum for **7**. ^{1}H NMR (400 MHz, $CDCl_3$) δ 10.30 (s, 1H), 7.43 (s, 1H), 7.15 (s, 1H), 5.90 (s, 1H), 4.10 (t, *J* = 6.6 Hz, 2H), 4.05 (t, *J* = 6.7 Hz, 2H), 3.37 (s, 6H), 1.88–1.78 (m, 4H), 1.53–1.41 (m, 4H), 1.28 (d, *J* = 11.3 Hz, 24H), 0.89 (t, *J* = 7.1 Hz, 6H). * indicates residual H_2O; ^{o} indicates residual DMF, DCM, and THF; ^{x} indicates an impurity.

.

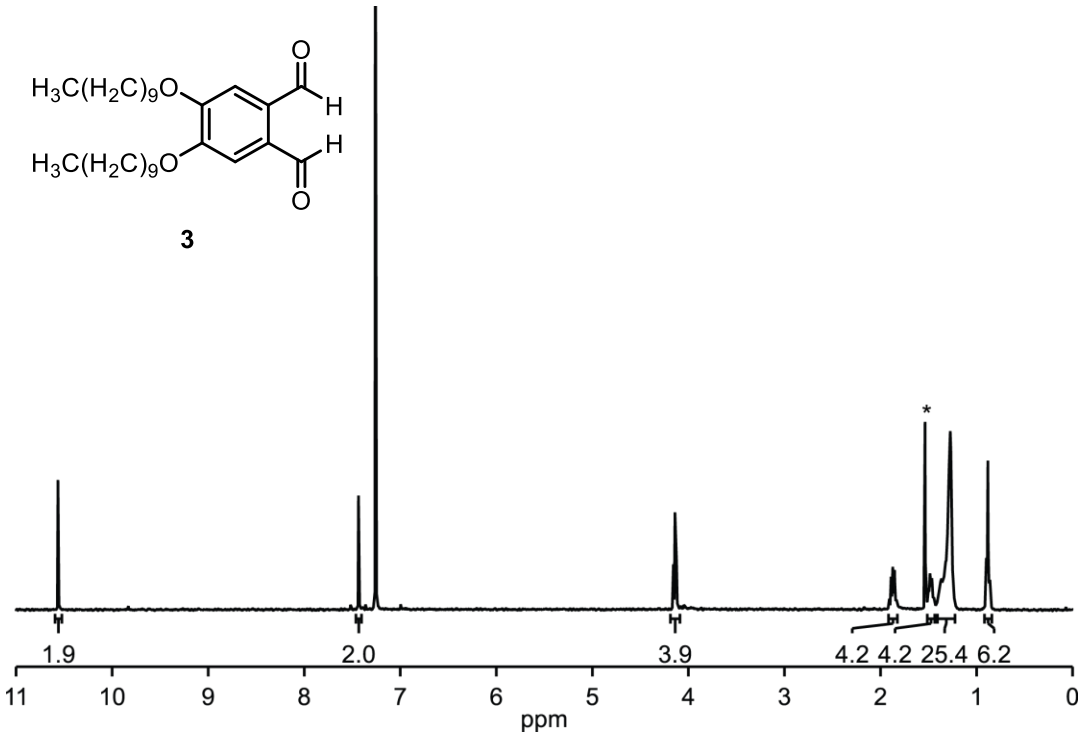


Figure S2.5 ^{1}H NMR spectrum for **3**. ^{1}H NMR (400 MHz, $CDCl_3$) δ 10.56 (s, 2H), 7.44 (s, 2H), 4.14 (t, *J* = 6.6 Hz, 4H), 1.87 (tt, *J* = 6.8 Hz, 4H), 1.52 – 1.43 (m, 4H), 1.41–1.05 (m, 24H), 0.88 (t, *J* = 6.9 Hz, 6H). * indicates residual H_2O.

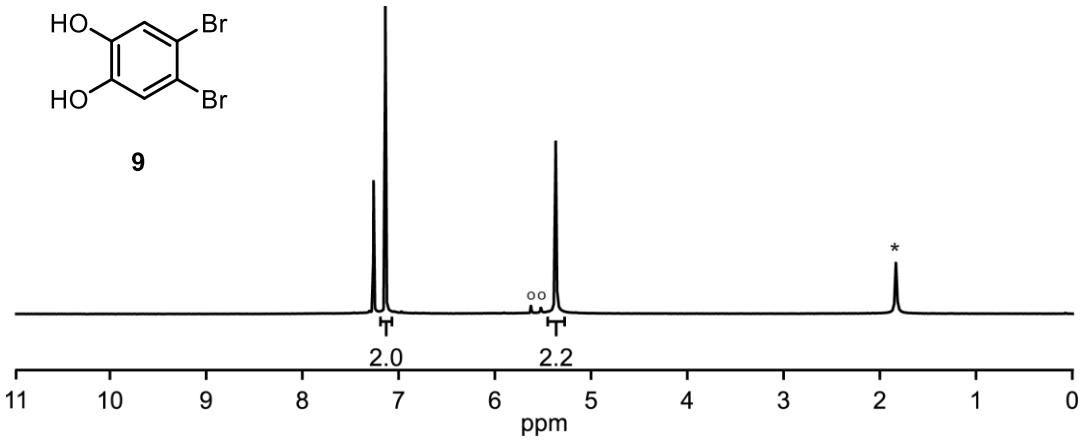


Figure S2.6 ^{1}H NMR spectrum for **9**. ^{1}H NMR (500 MHz, $CDCl_3$) δ 7.14 (s, 2H), 5.37 (s, 2H). * indicates residual H_2O; ^{o} indicates unidentified impurity.

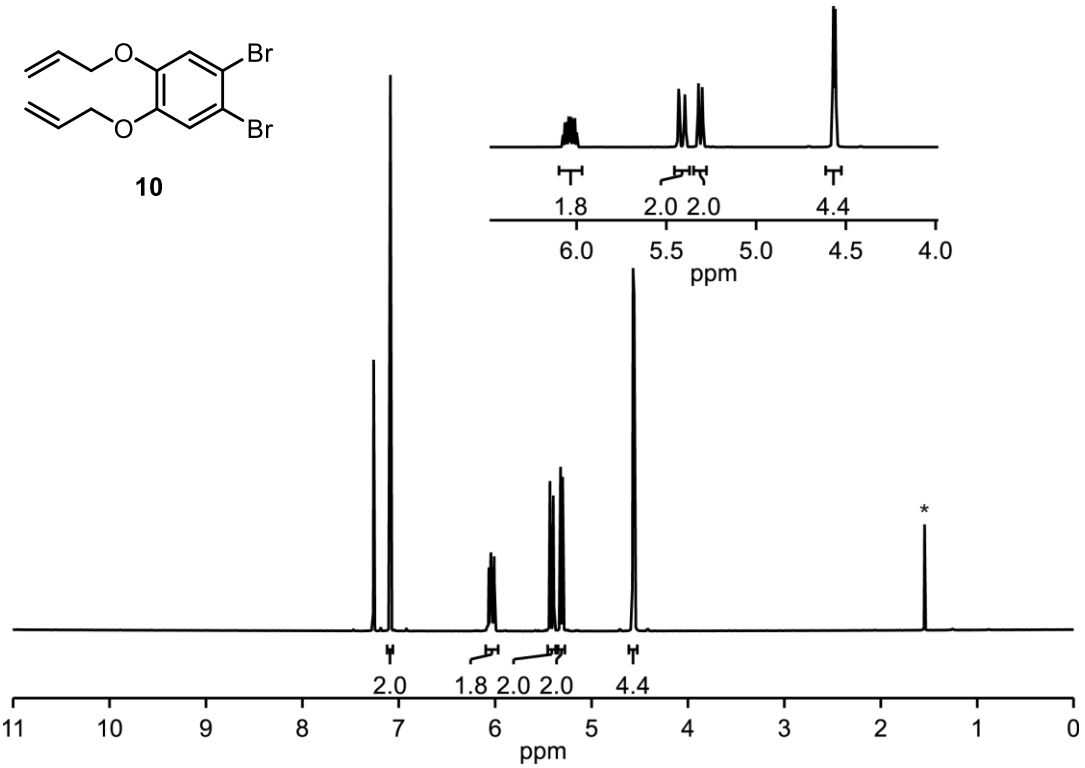


Figure S2.7 ^{1}H NMR spectrum for **10**. ^{1}H NMR (500 MHz, $CDCl_3$) δ 7.09 (s, 2H), 6.03 (ddt, *J* = 17.1, 10.6, 5.3 Hz, 2H), 5.48–5.37 (m, 2H), 5.36–5.28 (m, 2H), 4.56 (d, *J* = 5.3 Hz, 4H). * indicates residual H_2O.

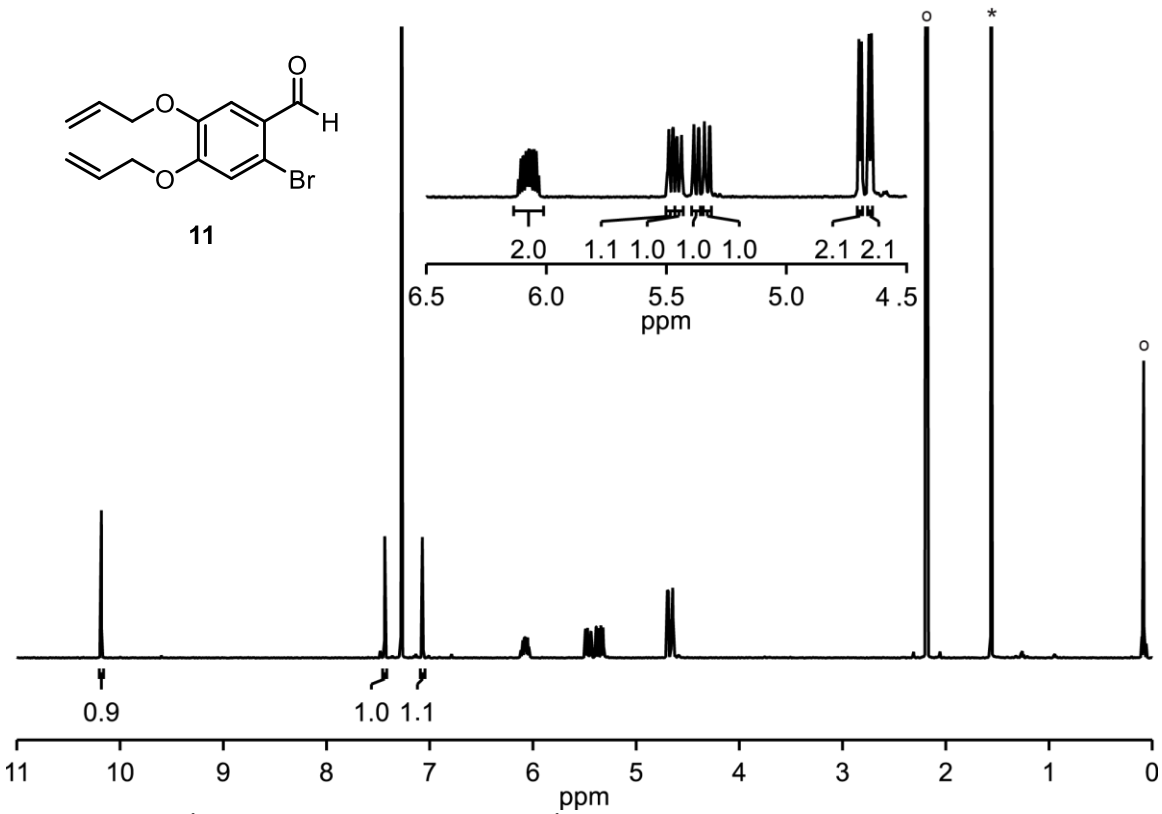


Figure S2.8 ^{1}H NMR spectrum for **11.** ^{1}H NMR (500 MHz, $CDCl_3$) δ 10.18 (s, 1H), 7.44 (s, 1H), 7.07 (s, 1H), 6.14–5.96 (m, 2H), 5.50–5.47 (m, 1H), 5.46–5.43 (m, 1H), 5.39–5.36 (m, 1H), 5.35–5.31 (m, 1H), 4.71–4.68 (m, 2H), 4.66–4.63 (m, 2H). ^{o} indicates grease and acetone; * indicates residual H_2O.

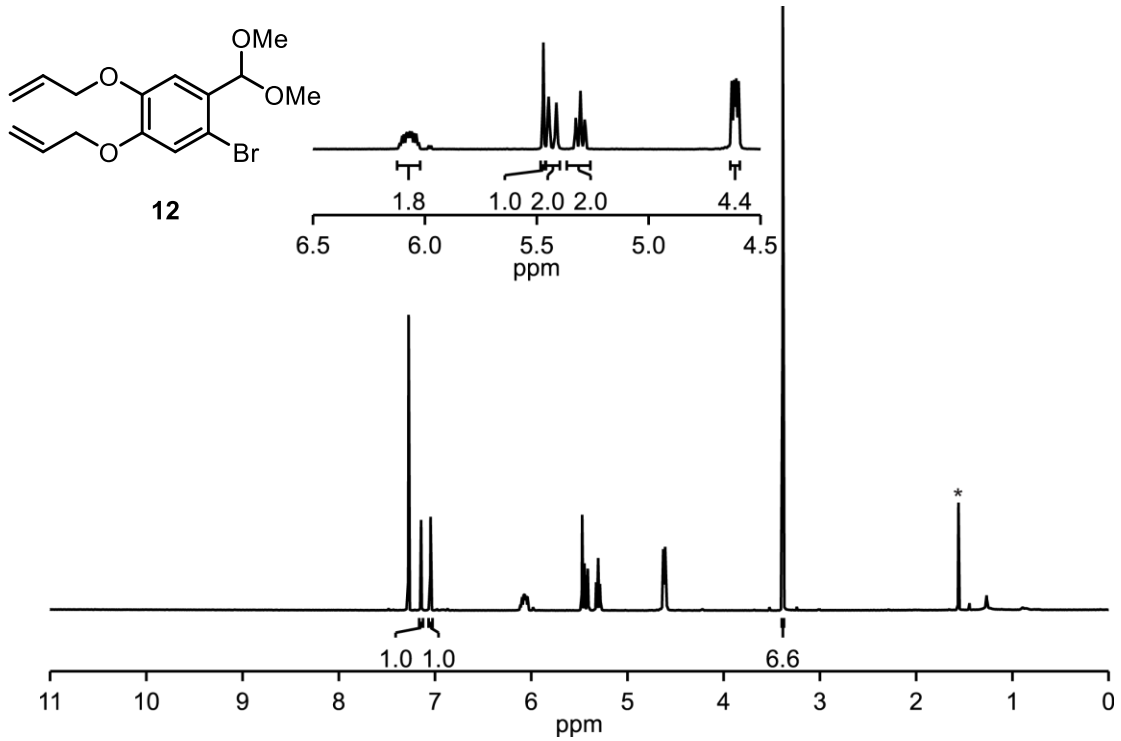


Figure S2.9 ^{1}H NMR spectrum for **12**. ^{1}H NMR (500 MHz, $CDCl_3$) δ 7.14 (s, 1H), 7.05 (s, 1H), 6.13–6.00 (m, 2H), 5.47 (s, 1H), 5.46–5.40 (m, 2H), 5.34–5.27 (m, 2H), 4.64–4.59 (m, 4H), 3.39 (s, 6H). * indicates residual H_2O.

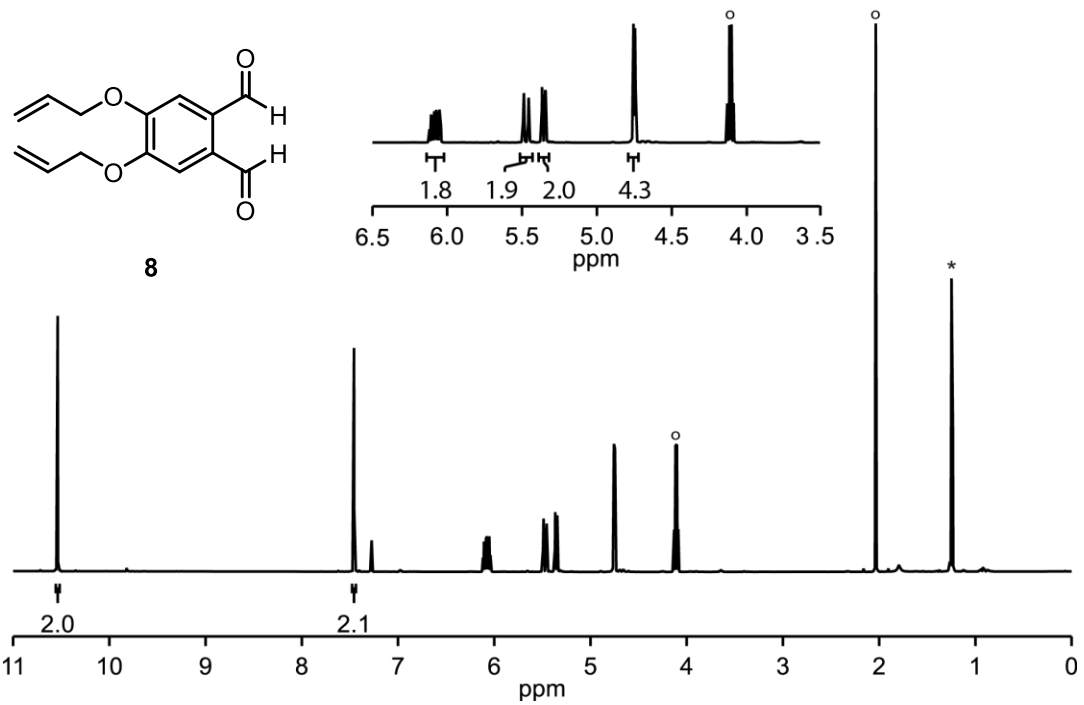


Figure S2.10 ^{1}H NMR spectrum for **8**. ^{1}H NMR (500 MHz, $CDCl_3$) δ 10.54 (s, 2H), 7.46 (s, 2H), 6.08 (ddt, *J* = 17.2, 10.5, 5.2 Hz, 2H), 5.50–5.44 (m, 2H), 5.38–5.33 (m, 2H), 4.77–4.71 (m, 4H). ° indicates ethyl acetate; * indicates residual H_2O.

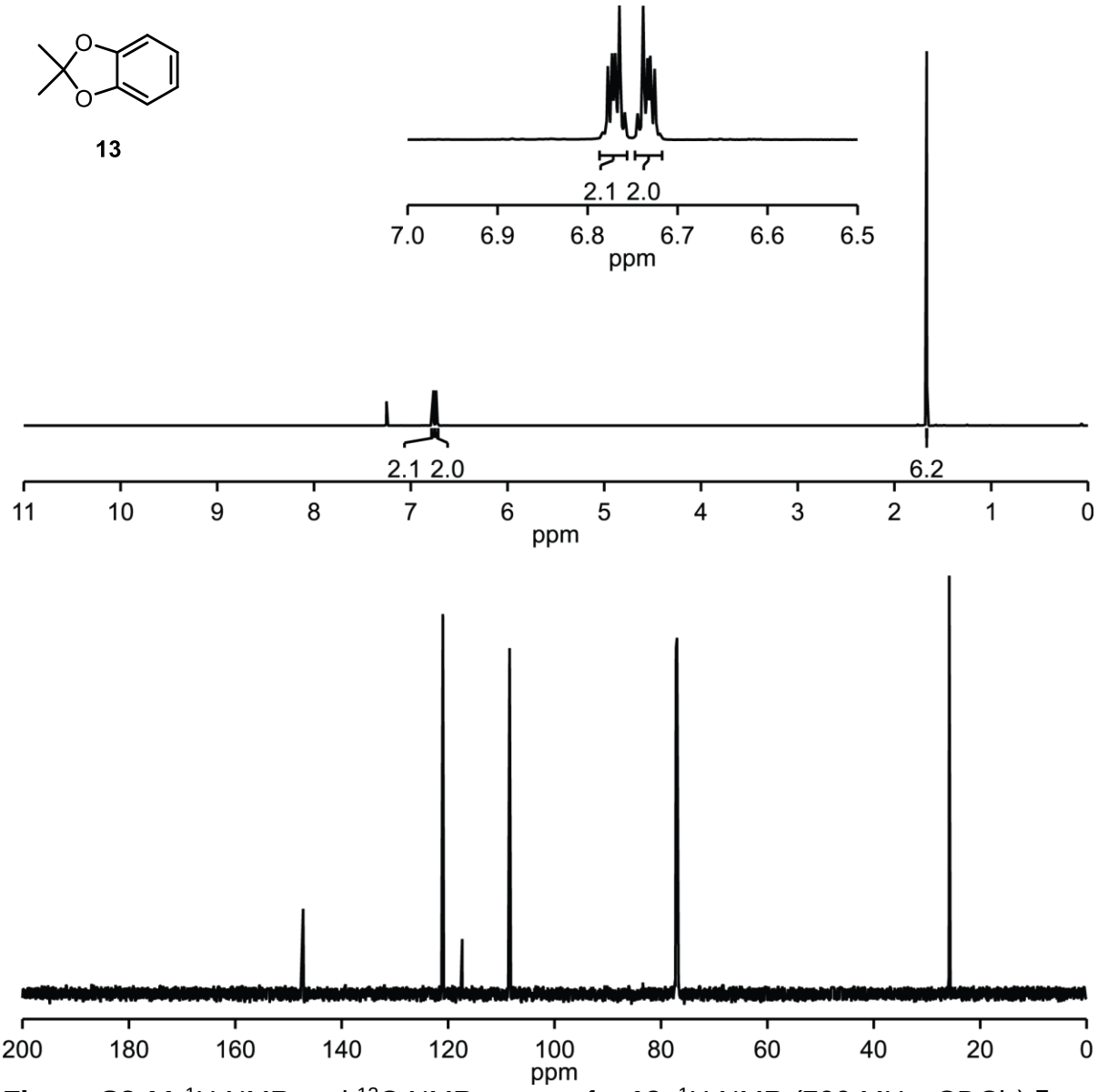


Figure S2.11 ^{1}H NMR and ^{13}C NMR spectra for **13**. ^{1}H NMR (700 MHz, $CDCl_3$) δ 6.78–6.75 (m, 2H), 6.75–6.72 (m, 2H), 1.67 (s, 6H). ^{13}C NMR (176 MHz, $CDCl_3$) δ 147.25, 120.99, 117.35, 108.44, 25.82. * indicates residual H_2O.

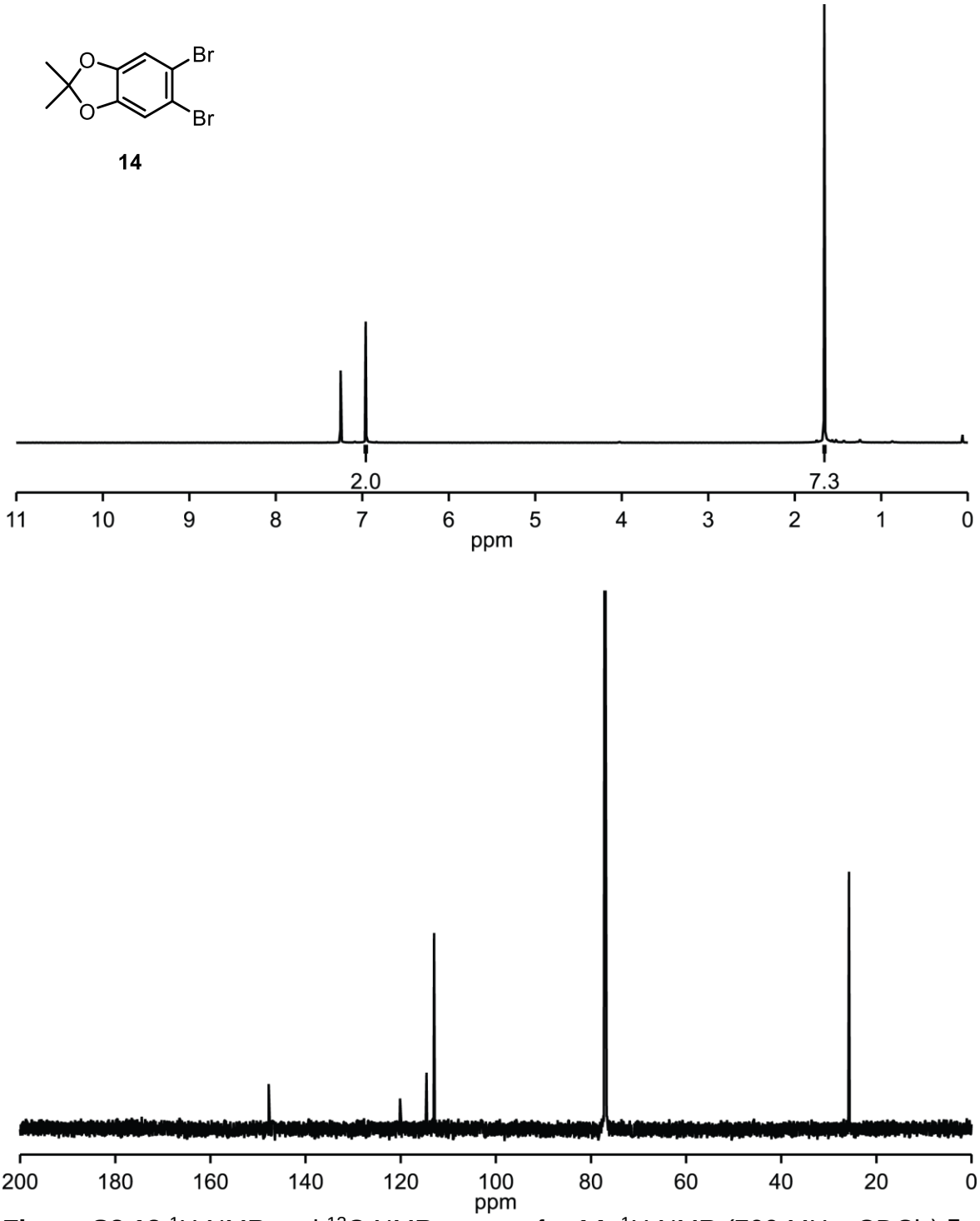


Figure S2.12 ^{1}H NMR and ^{13}C NMR spectra for **14**. ^{1}H NMR (700 MHz, $CDCl_3$) δ 6.96 (s, 2H), 1.66 (s, 6H). ^{13}C NMR (176 MHz, $CDCl_3$) δ 147.75, 120.13, 114.57, 112.98, 25.76. * indicates residual H_2O.

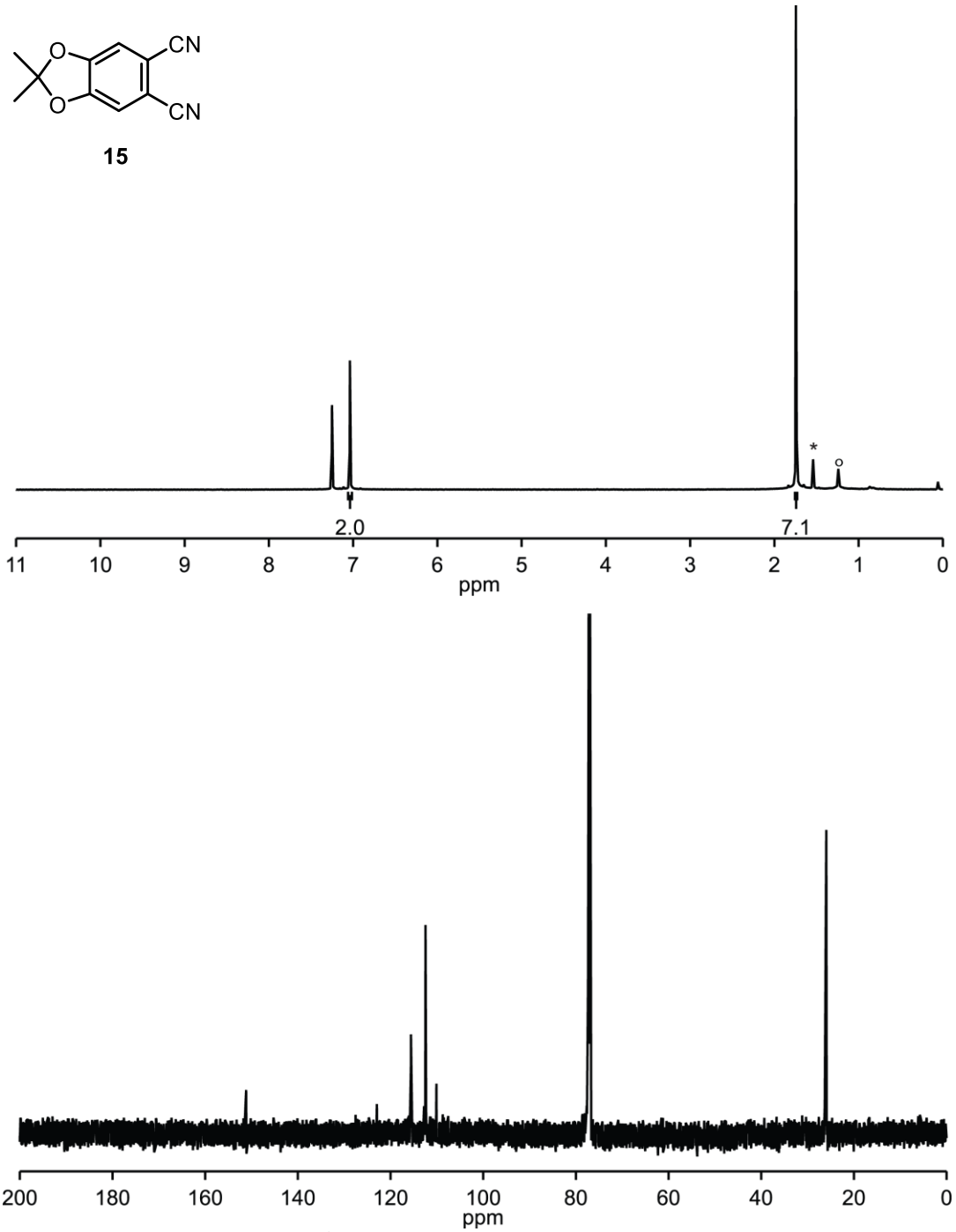


Figure S2.13 ^{1}H NMR and ^{13}C NMR spectra for **15**. ^{1}H NMR (700 MHz, $CDCl_3$) δ 7.04 (s, 2H), 1.74 (s, 6H). ^{13}C NMR (176 MHz, $CDCl_3$) δ 151.16, 122.95, 115.59, 112.45, 110.09, 25.96. * indicates residual H_2O.

(c) Gel Screening

Gel Screening Procedure - In a 4 mL vial a known amount of gelator **3** or **8** and a known amount of organic solvent was added. The vial was capped, heated to dissolve the solid and cooled to rt over 10 min. If the resulting gel was stable-to-inversion, then 0.1 mL of the organic solvent was added the procedure was repeated until the gel was no longer stable-to-inversion. If a gel did not form, the steps listed below were followed depending on what was observed.

1. If a precipitate formed the mixture was heated to dissolve, sonicated for 5-20 s and then cooled over 10 min to see if a gel formed. If a gel still did not form then 0.1 mL solvent was added and the procedure was repeated from the beginning.
2. If a precipitate did not form then a "bad" solvent (a solvent that the compound is not soluble in) was added and the procedure was repeated from the beginning.

Table S2.1 Summary of Gel Screening[a]

Solvent	3	8
acetone	P	S
acetone/H_2O	G (56 mM)[b,d]	P
MeOH	S	S
MeOH/H_2O	P	G (121 mM)[c,d]
EtOH	S	--
EtOH/H_2O	P	--
THF	S	--
EtOH	S	--
EtOH/H_2O	P	--
isopropanol	S	--
iPrOH/H_2O	S	--

[a] G: gel; S: solution; P: precipitate
[b] acetone: H_2O (5:1)
[c] MeOH: H_2O (1:1)
[d] concentration it gelled at (≥cgc)

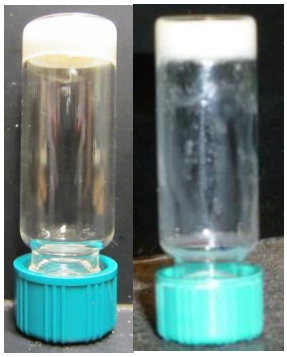
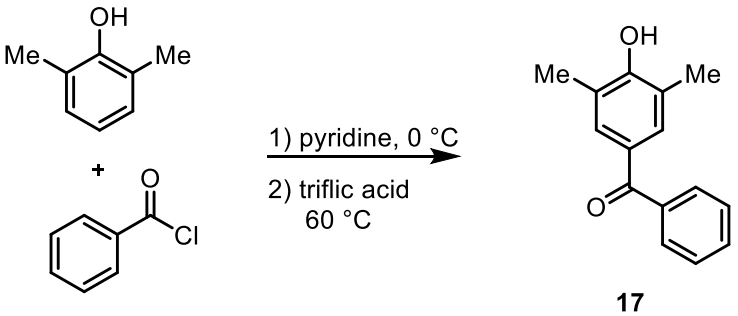


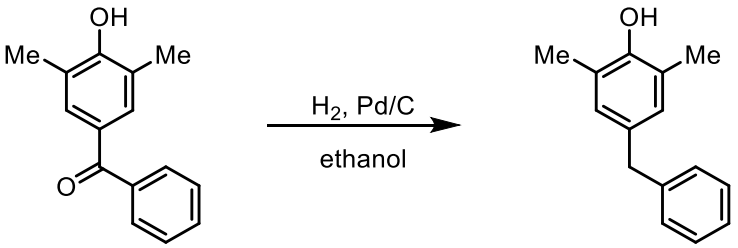
Figure S2.14 Gelators in a 4 mL vial (a) **3** in acetone/H_2O (5:1) (b) **8** in MeOH/H_2O (1:1).

IV. Poly(benzyl ether) Scaffold
(a) Synthetic Procedures



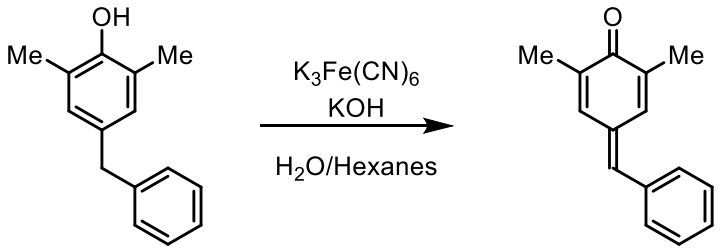
17

17.[9] Benzoyl chloride (0.29 mL, 2.50 mmol, 1.0 equiv) was added dropwise to a solution of 2,6–dimethylphenol (302 mg, 2.47 mmol, 1.0 equiv) in pyridine (0.9 mL) at 0 °C. The reaction mixture was warmed up and stirred at rt for 16 h. Ethyl acetate (15 mL) was added to the reaction mixture and the organic layer was washed with H_2O (2 x 15 mL). The organic layer was dried over $MgSO_4$ and concentrated. Trifluoromethanesulfonic acid (0.75 mL, 8.50 mmol, 3.4 equiv) was added in one portion to the resulting solid at 0 °C under N_2. The reaction was heated to 60 °C and stirred for 16 h. The reaction was cooled to rt and then poured into ice water (10 mL). The resulting solution was extracted with EtOAc (2 x 10 mL) and the combined organic layers were dried over $MgSO_4$ and concentrated. The crude residue was purified by column chromatography (2-20% EtOAc/hexanes) and afforded **17** as a solid with some solvent present (0.250 g, 33%).



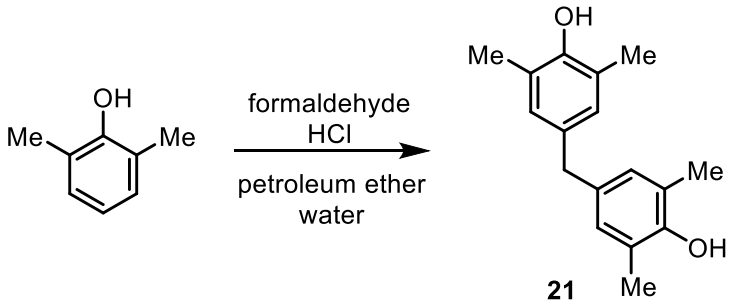
17 **18**

18.[9] Palladium (20% by weight on carbon powder) (27.3 mg, 11% by weight of compound **17**) was added in one portion to a solution of **17** (250 mg, 1.1 mmol, 1.0 equiv) in EtOH (3.6 mL) under N_2. The flask was evacuated and purged three times with H_2 gas. The reaction mixture was stirred vigorously for 2 d at rt under H_2 (balloon). The flask was evacuated, purged with N_2, and the reaction mixture was filtered through a pad of celite and the filtrate concentrated. The crude solid was purified via column chromatography (2-20% EtOAc/hexanes) to afford compound **18** as a white solid (98.3 mg, 42%). ^{1}H NMR indicates some solvent present.



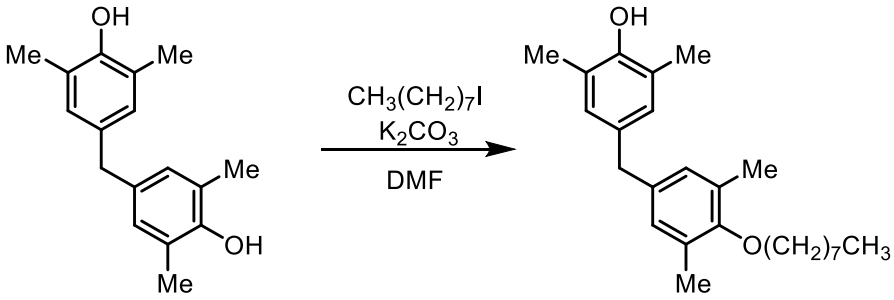
18 **16**

16.[9] In a 25 mL round bottom flask equipped with a stir bar **18** (98 mg, 0.462 mmol, 1.0 equiv) was dissolved in hexanes (12.5 mL) and put under N_2. In a separate 20 mL vial potassium ferricyanide (613 mg, 1.86 mmol, 4.0 equiv) and potassium hydroxide (110 mg, 1.96 mmol, 4.2 equiv) was dissolved in H_2O (2.5 mL) and the solution was added in one portion to the solution containing compound **18**. The reaction mixture was then stirred vigorously for 1h at rt. The aqueous layer was separated and extracted with hexanes (20 mL). The combined organic layers were washed with brine (20 mL), dried over $MgSO_4$, and concentrated. The crude oil was dissolved in pentane and any solid left over was filtered off. The filtrate was concentrated and recrystallized from cyclohexane. A solid was collected (36.4 mg, 37%). ^{1}H NMR indicates some solvent present.



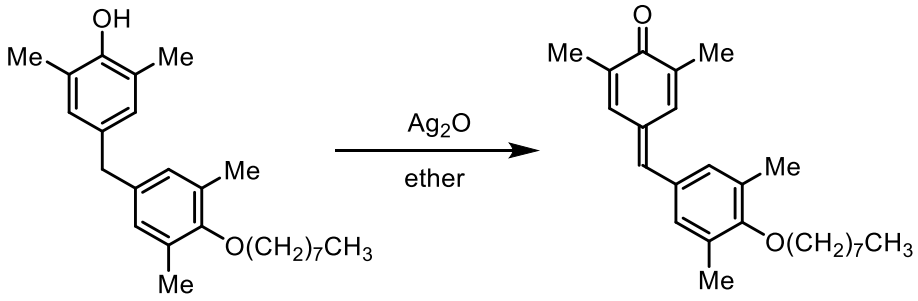
21

21.[10] In a 25 mL round bottom flask equipped with a stir bar 2,6-dimethylphenol (6.00 g, 49.1 mmol, 1.0 equiv.) was combined with formaldehyde (9.0 mL, 37% formalin solution in water, 111 mmol, 2.3 equiv) and dissolved in petroleum ether (25 mL). Then conc. hydrochloric acid (8.4 mL) was added dropwise to the solution over 5 min. The reaction was allowed to stir for 2 h at rt. Water (200 mL) was then added and the reaction mixture was stirred an additional 30 min. The white precipitate was collected by filtration washed further with H_2O (~20 mL) and dried overnight on the high vacuum. The white solid was then recrystallized in DCM (170 mL). White crystals were collected (4.48 g, 71%). HRMS (EI): Cald for $C_{17}H_{20}O_2$, 256.1463; found 256.1462.



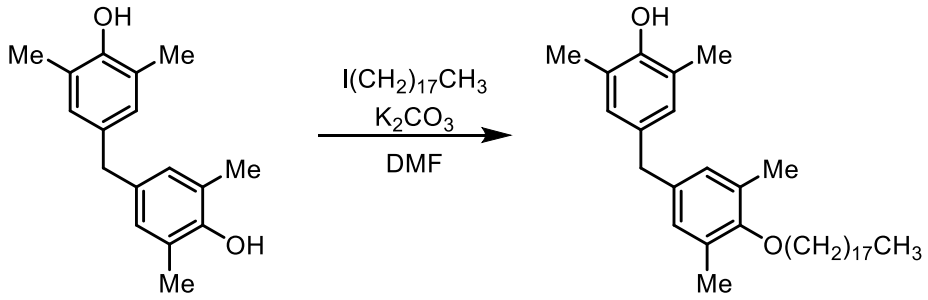
21 **22a**

22a.[10] In a 15 mL bomb flask equipped with a stir bar **21** (501 mg, 1.95 mmol, 1.0 equiv) was dissolved in DMF (5.4 mL). To the stirring solution K_2CO_3 (297 mg, 2.15 mmol, 1.1 equiv) was added. Next, 1-iodooctane (0.28 mL, 1.55 mmol, 0.8 equiv.) was added dropwise to the purple solution. A GC standard (n-docosane) was added to follow conversion of the reaction. The reaction was then heated to 30 ºC and let stir. After 18 h saturated NH_4Cl added (10 mL) to quench the reaction. The aqueous layer was extracted with EtOAc (4 x 10 mL) and the combined organic layers was washed with brine (15 mL). The organic layers were dried over $MgSO_4$, filtered, and concentrated down to a yellow oil. The yellow oil was purified by column chromatography (2-20% EtOAc/hexanes). A pale yellow oil was collect (216 mg, 38%). HRMS (ESI): Cald for $[M+NH_4]^+$: $C_{25}H_{36}O_2$, 386.3054; found 386.3053.



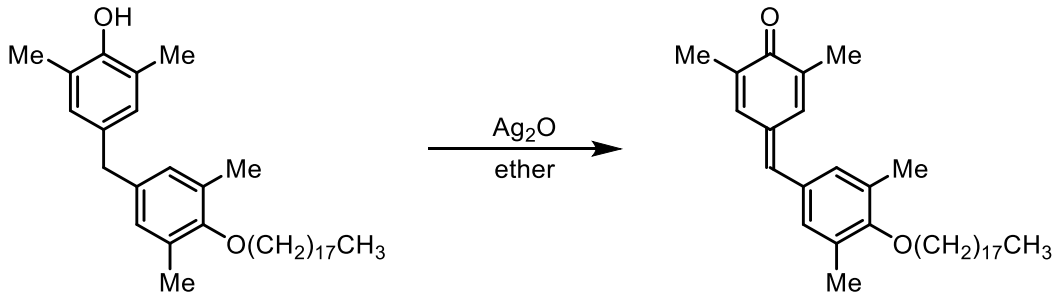
22a **23a**

23a.[10] In a 50 mL round bottom flask equipped with a stir bar compound **22a** (216 mg, 0.586 mmol, 1.0 equiv), was dissolved in diethyl ether (7.0 mL). To the solution silver oxide (272 mg, 1.17 mmol, 2.0 equiv) was added and the reaction was let stir overnight at rt. The mixture was filtered through celite to remove silver oxide. The yellow filtrate was concentrated and the yellow solid was purified by recrystallization in hexanes. A yellow solid was collected (90.8 mg, 42%). HRMS (ESI) $[M+H]^+$: Cald for $C_{25}H_{34}O_2$, 367.2632; found 367.2632.



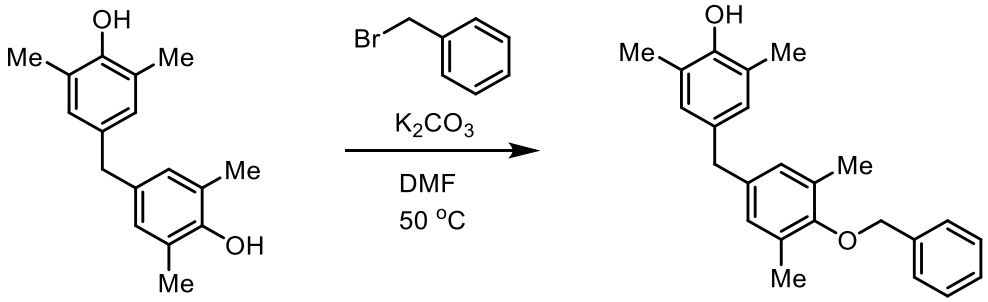
21 **22b**

22b.[10] In a 25 mL bomb flask equipped with a stir bar **21** (587 mg, 2.29 mmol, 1.0 equiv) was dissolved in DMF (7.4 mL). To the stirring solution K_2CO_3 (345 mg, 2.49 mmol, 1.1 equiv) was added. Next, 1-iodooctadecane (689 mg, 1.81 mmol, 0.8 equiv.) was added dropwise to the purple solution. A GC standard (n-docosane) was added to follow conversion of the reaction. The reaction was then stirred at rt overnight. The reaction was quenched with saturated NH_4Cl (10 mL). The aqueous layer was extracted with EtOAc (4 x 10 mL), DCM (2 x 10 mL) and the combined organic layers were washed with brine (2 x 20 mL). The organic layers were dried over $MgSO_4$, filtered, and concentrated to a yellow oil. The yellow oil was purified by column chromatography (10-80% CH_2Cl_2/hexanes). A pale yellow oil was collected (345 mg, 38%). HRMS (EI): Cald for $C_{35}H_{56}O_2$, 508.4280; found 508.4278.



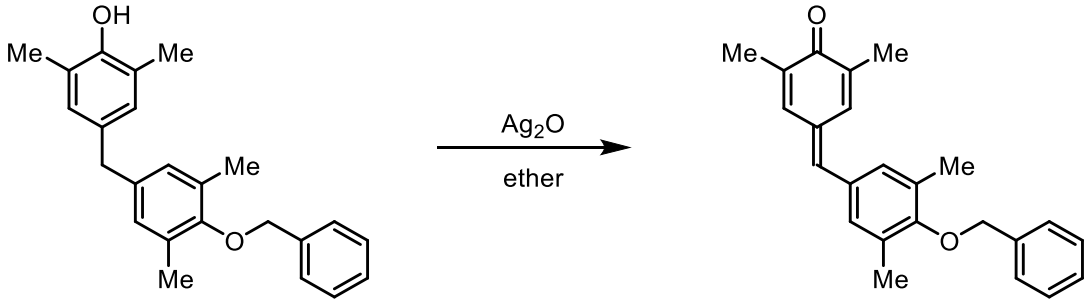
22b **23b**

23b.[10] In a 50 mL round bottom flask equipped with a stir bar compound **22b** (199 mg, 0.391 mmol, 1.0 equiv), was dissolved in Et_2O (6.3 mL). To the solution silver oxide (0.348 g, 1.50 mmol, 3.8 equiv) was added and the reaction was stirred overnight at rt. Upon completion of the reaction the mixture was filtered through celite to remove silver oxide. The yellow filtrate was concentrated the solid was purified by recrystallization in hexanes. A yellow solid was collected (92.8 g, 49%). HRMS (ESI) $[M+H]^+$: Cald for $C_{35}H_{54}O_2$, 507.4197; found 507.4196.



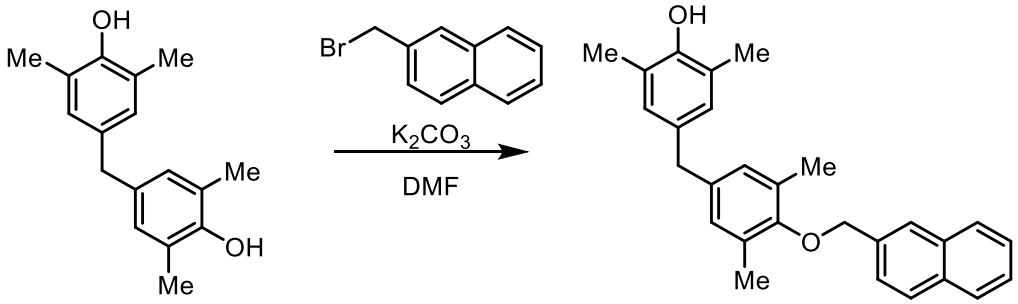
21 **22c**

22c.[10] In a 15 mL bomb flask equipped with a stir bar **21** (401 mg, 1.56 mmol, 1.0 equiv) was dissolved in DMF (4.4 mL). To the stirring solution K_2CO_3 (237 mg, 1.71 mmol, 1.1 equiv) was added. Next, benzyl bromide (0.15 mL, 1.3 mmol, 0.8 equiv) was added dropwise to the purple solution. The reaction was then heated to 50 ºC. After 2 h saturated NH_4Cl was added (10 mL) to quench the reaction. The aqueous layer was extracted with EtOAc (4 x 10 mL) and the combined organic layers were washed with brine (10 mL). The organic layers were dried over $MgSO_4$, filtered, and concentrated down to a yellow oil. The oil was purified by column chromatography (5% EtOAc/hexanes). A white solid was collect (137 mg, 32%). HRMS (EI): Cald for $C_{24}H_{26}O_2$, 346.1933; found 346.1945.



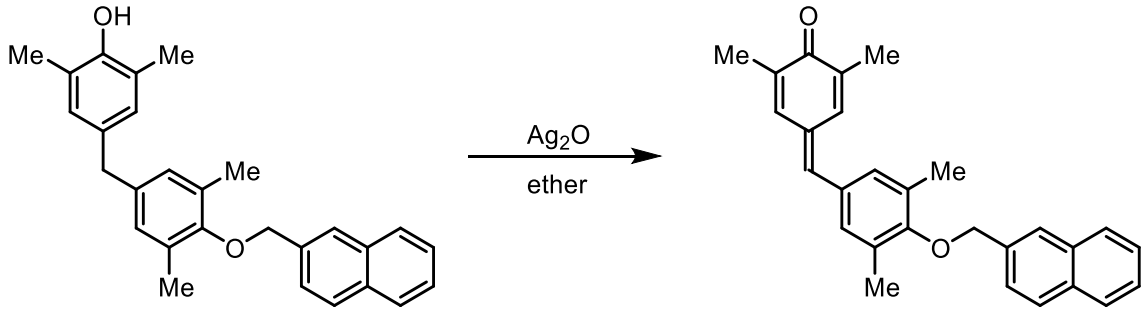
22c **23c**

23c.[10] In a 50 mL round bottom flask equipped with a stir bar compound **22c** (593 mg, 1.71 mmol, 1.0 equiv), was dissolved in Et_2O (20 mL). To the solution silver oxide (797 mg, 3.44 mmol, 2.0 equiv) was added and the reaction was let stir overnight at rt. Upon completion of the reaction the mixture was filtered through celite to remove silver oxide. The yellow filtrate was concentration by rotary evaporation to a bright yellow solid. The yellow solid was purified by recrystallization in hexanes. A yellow solid was collected (289 mg, 49%). HRMS (EI): Cald for $C_{25}H_{24}O_2$, 344.1776; found 344.1772.



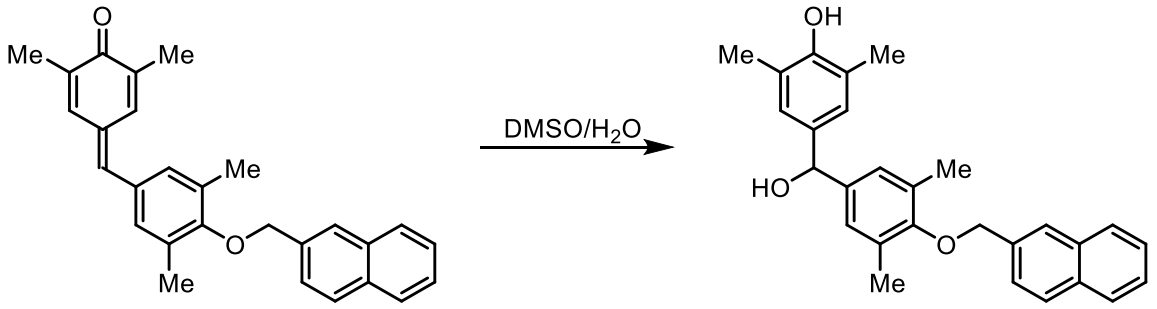
21 **22d**

22d.[10] In a 15 mL bomb flask equipped with a stir bar **21** (991 mg, 3.86 mmol, 1.0 equiv) was dissolved in DMF (12.5 mL). To the stirring solution K_2CO_3 (580 mg, 4.20 mmol, 1.1 equiv) was added. Next, 2-(bromomethyl)naphthalene (651 mg, 2.94 mmol, 0.76 equiv) was added dropwise to the purple solution. After 6 h saturated NH_4Cl was added (25 mL) to quench the reaction. The aqueous layer was extracted with DCM (3 x 20 mL) and the combined organic layers was washed with brine (15 mL). The organic layers were dried over $MgSO_4$, filtered, and concentrated down to a yellow oil. Purification of the yellow solid was carried out by column chromatography (5-60% EtOAc/Hexanes). A white solid was collect (546 mg, 47%). HRMS (EI): Cald for $C_{28}H_{28}O_2$, 396.2089; found 396.2090.



22d **23d**

23d.[10] In a 50 mL round bottom flask equipped with a stir bar compound **22d** (117 mg, 0.30 mmol, 1.0 equiv), was dissolved in Et_2O (3.8 mL). To the solution silver oxide (231 mg, 1.00 mmol, 3.3 equiv) was added and the reaction was let stir overnight at rt. Upon completion of the reaction the mixture was filtered through celite to remove silver oxide. The yellow filtrate was concentrated and the solid was purified by recrystallization by dissolving in DCM and layer hexanes on top. A yellow solid was collected (82.7 mg, 70%). HRMS (ESI) $[M+H]^+$: Cald for $C_{28}H_{26}O_2$, 394.1933; found 394.1942.



23d **24**

24. In a 20 mL vial equipped with a stir bar **23d** (20.0 mg, 0.05 mmol, 1 equiv) was suspended in water (0.5 mL) and DMSO (0.5 mL). The reaction was heated to 85 °C and let stir for 24 hrs. The vial was taken off the heating block as the cap seal had come loose and evaporation was occurring. The reaction was put on the lab bench for 12 days before being concentrated down first on the rotovap and then on the high vac. An oil was then purified material via column chromatography with a 15-100% EtOAc/hexanes gradient. A precipitate was obtained (57.8 mg, 59%). HRMS (EI): Cald for $C_{28}H_{28}O_3$, 412.2038; found 412.2021. ^{1}H NMR indicates some solvent present.

(b) NMR Spectra

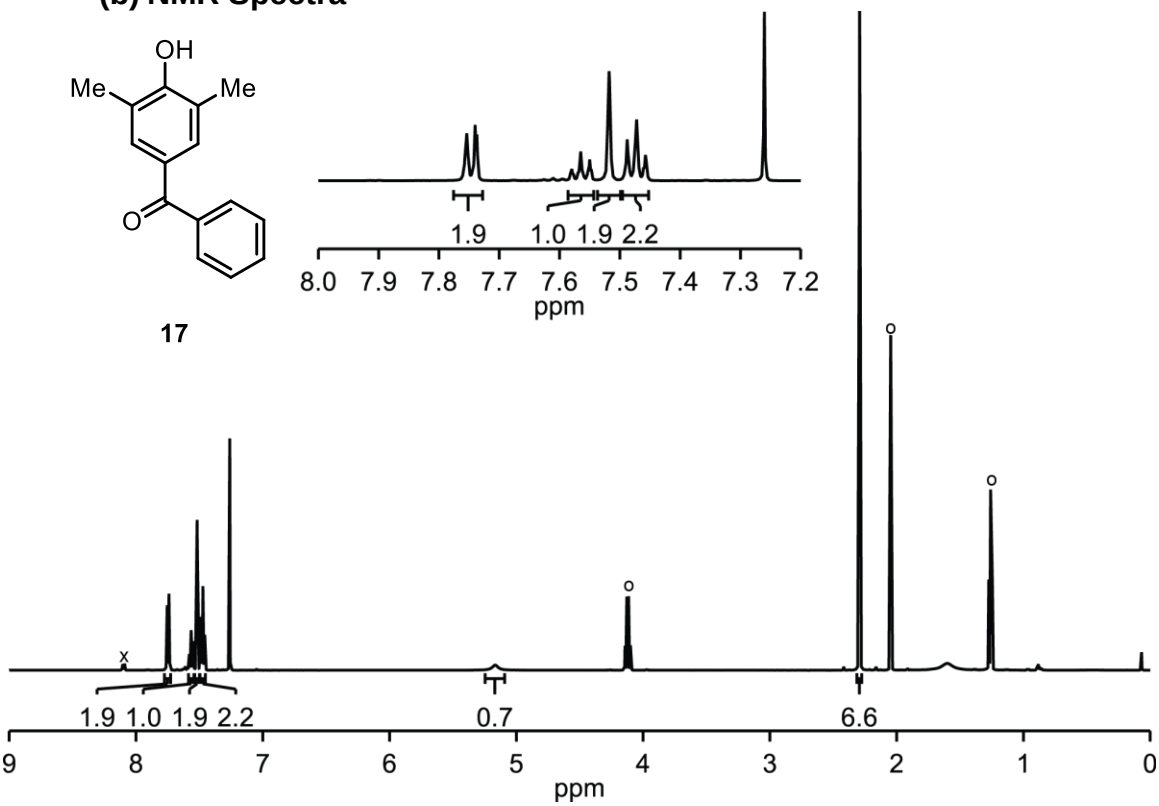


Figure S2.15 ^{1}H NMR spectrum for **17**. ^{1}H NMR (500 MHz, $CDCl_3$) δ 7.77–7.72 (m, 2H), 7.59–7.54 (m, 1H), 7.52 (s, 2H), 7.50–7.42 (m, 2H), 5.17 (s, 1H), 2.29 (s, 6H). ^{o} indicates residual ethyl acetate, ^{x} indicates starting material

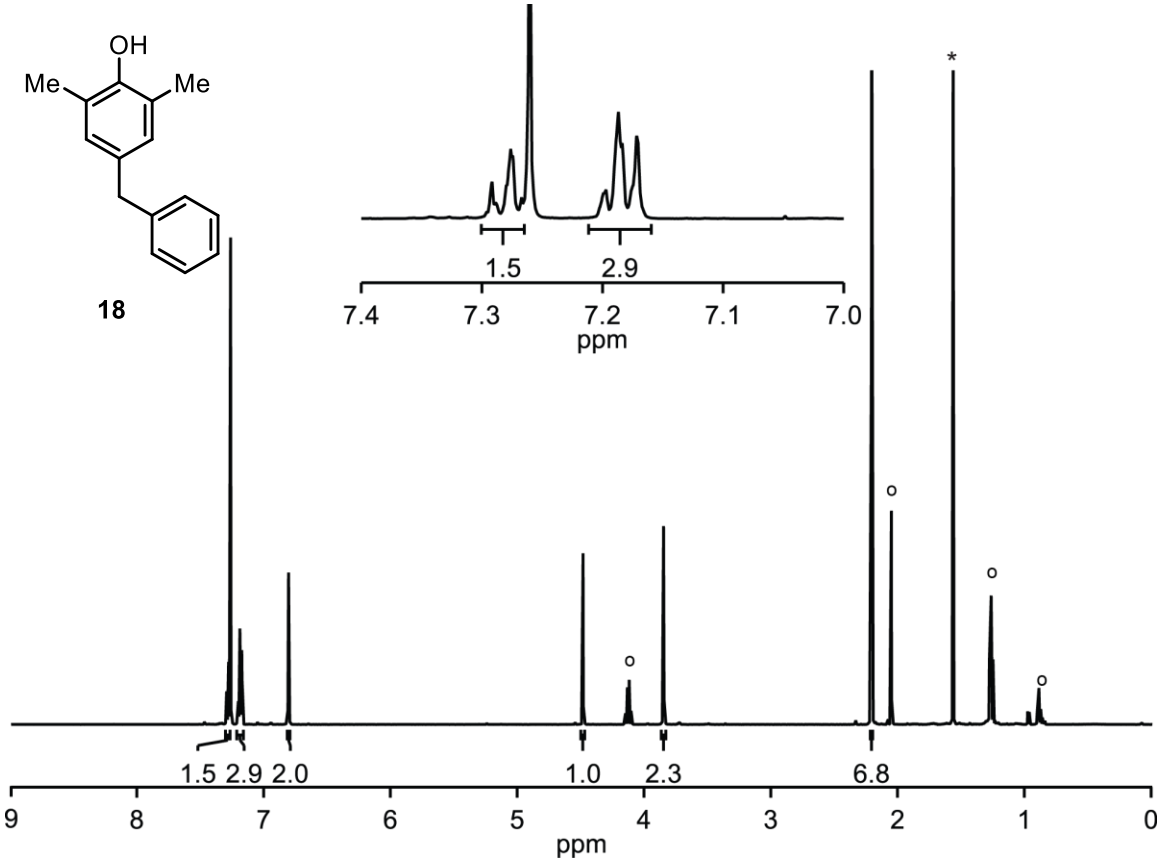


Figure S2.16 ^{1}H NMR spectrum for **18**. ^{1}H NMR (500 MHz, $CDCl_3$) δ 7.31–7.27 (m, 2H), 7.21–7.15 (m, 3H), 6.80 (s, 2H), 4.48 (s, 1H), 3.85 (s, 2H), 2.20 (s, 6H). * indicates residual H_2O, º indicates residual ethyl acetate and hexanes.

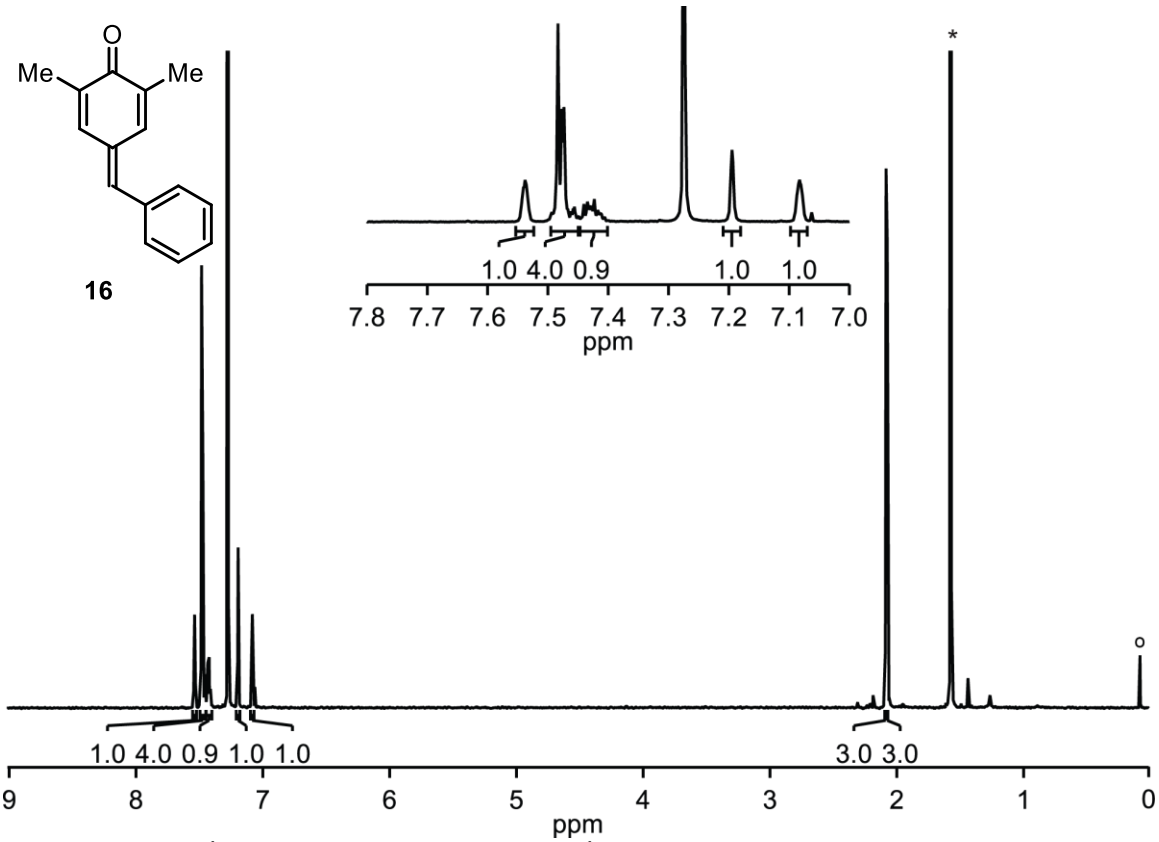


Figure S2.17 ^{1}H NMR spectrum for **16**. ^{1}H NMR (500 MHz, $CDCl_3$) δ 7.55–7.53 (m, 1H), 7.50–7.45 (m, 4H), 7.45–7.40 (m, 1H), 7.19 (s, 1H), 7.09–7.07 (m, 1H), 2.09 (d, *J* = 1.3 Hz, 3H), 2.08 (d, *J* = 1.1 Hz, 3H). * indicates residual H_2O, ^{o} indicates grease.

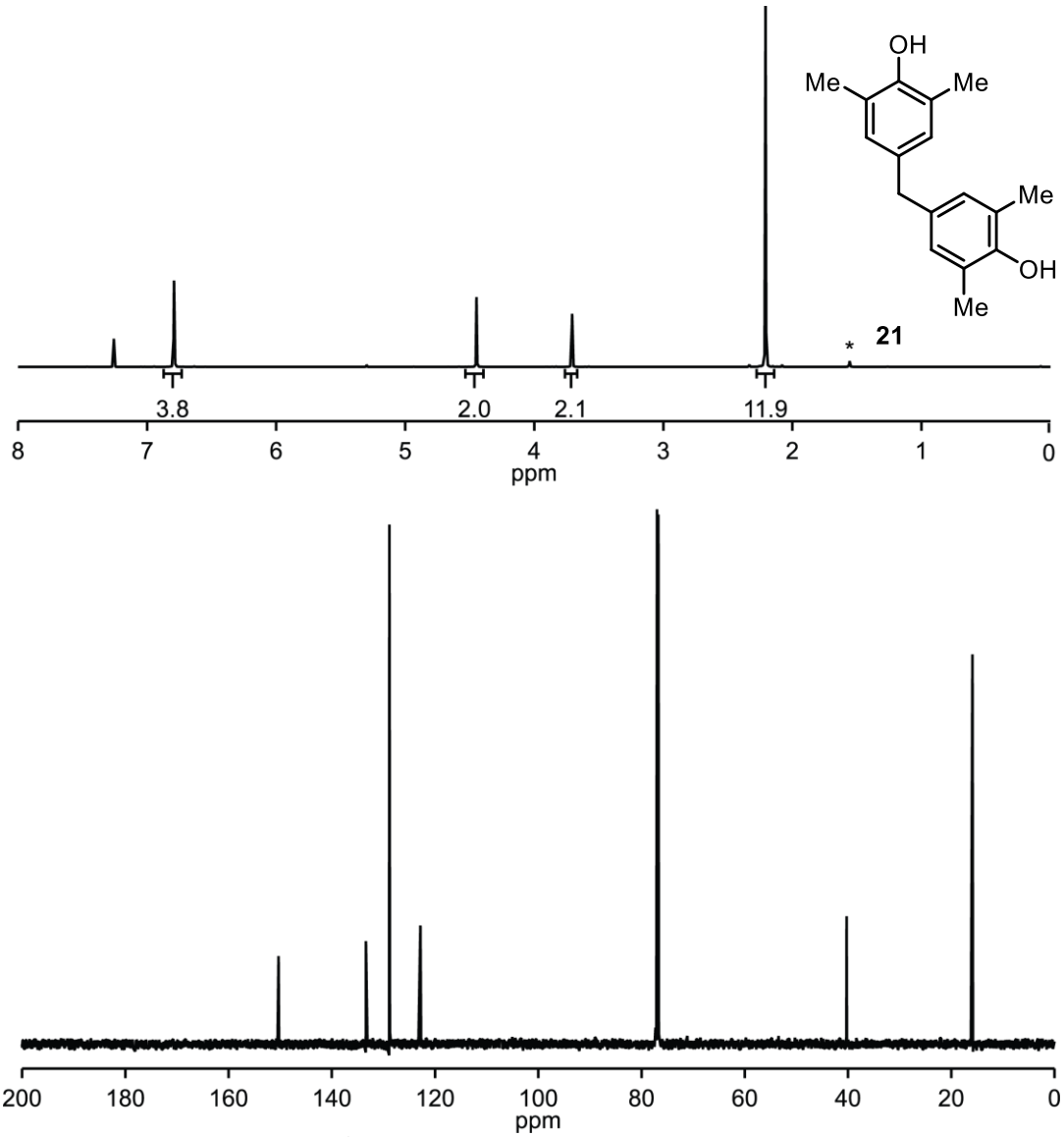


Figure S2.18 ^{1}H NMR and ^{13}C NMR spectra for **21**. ^{1}H NMR (500 MHz, $CDCl_3$) δ 6.79 (s, 4H), 4.45 (s, 2H), 3.71 (s, 2H), 2.21 (s, 12H). ^{13}C NMR (126 MHz, $CDCl_3$) δ 150.32, 133.39, 128.84, 122.84, 40.27, 15.90. * indicates residual H_2O.

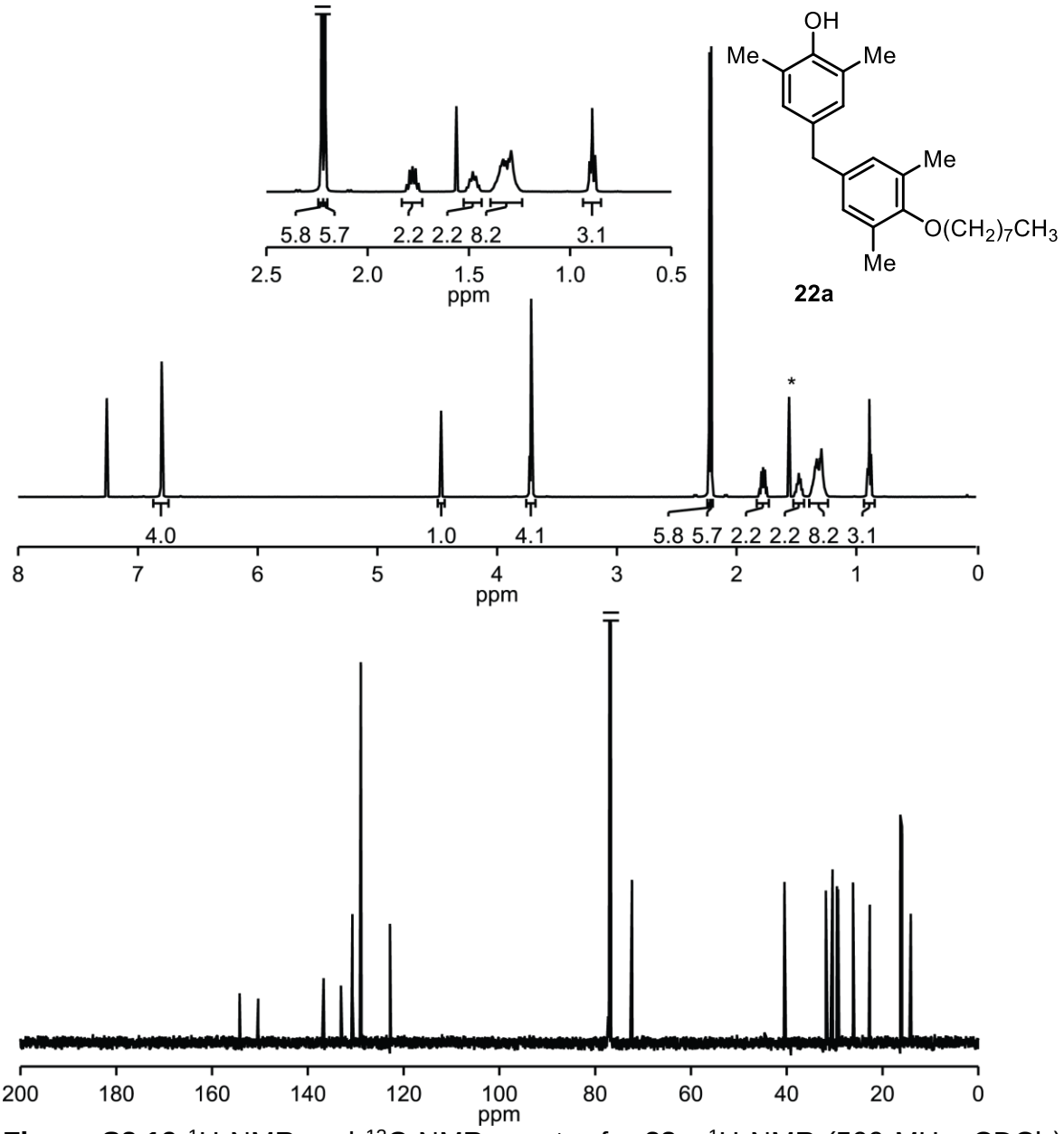


Figure S2.19 ^{1}H NMR and ^{13}C NMR spectra for **22a**. ^{1}H NMR (500 MHz, $CDCl_3$) δ 6.80 (s, 4H), 4.47 (s, 1H), 3.74–3.69 (m, 4H), 2.23 (s, 6H), 2.21 (s, 6H), 1.78 (tt, *J* = 6.7 Hz, 2H), 1.48 (tt, *J* = 7.4 Hz, 2H), 1.40–1.23 (m, 8H), 0.89 (t, *J* = 7.1 Hz, 3H). ^{13}C NMR (126 MHz, $CDCl_3$) δ 154.24, 150.36, 136.70, 133.08, 130.69, 128.94, 122.84, 72.31, 40.48, 31.83, 30.43, 29.52, 29.28, 26.16, 22.65, 16.29, 15.92, 14.10. * indicates residual H_2O.

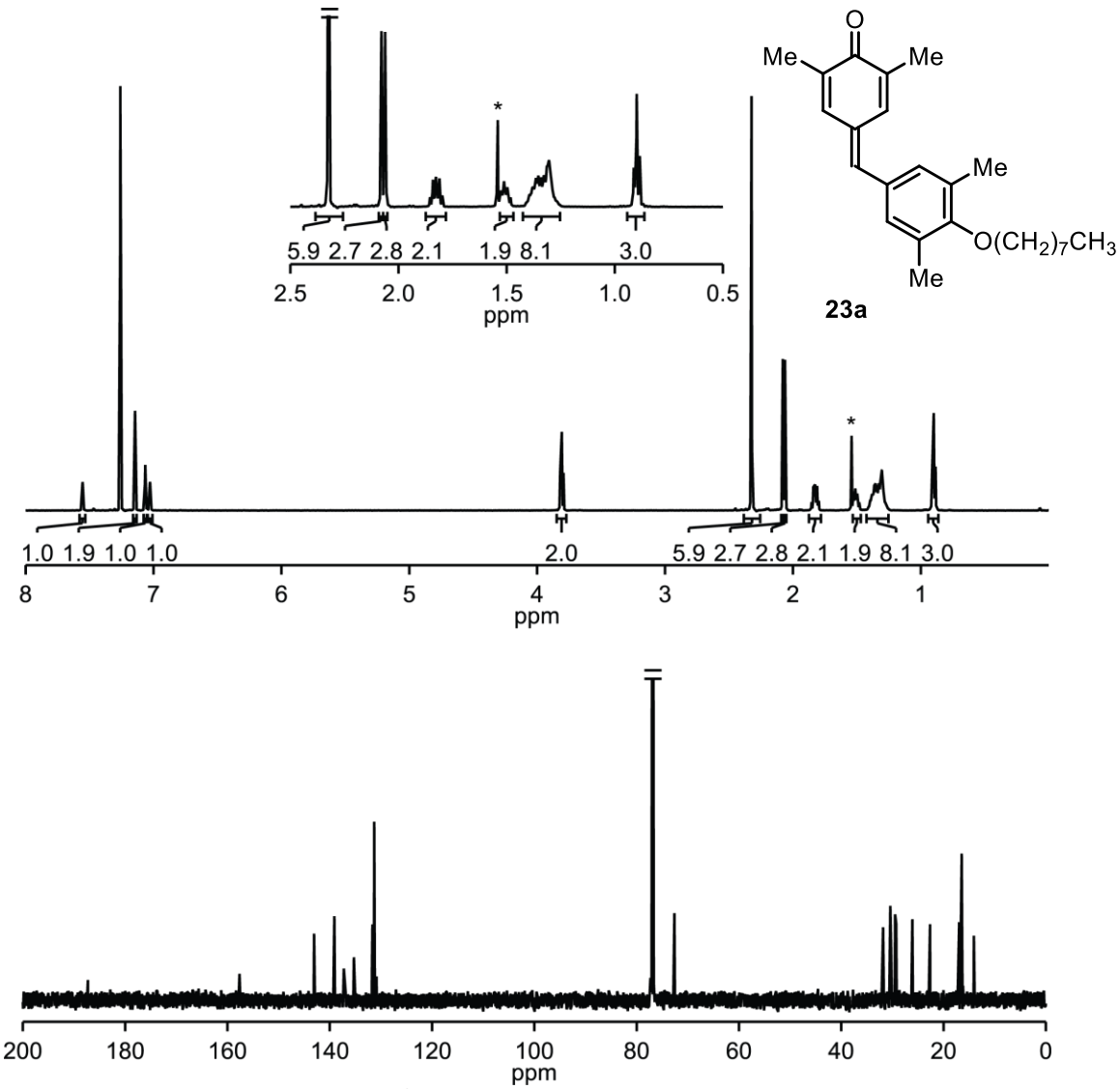


Figure S2.20 ^{1}H NMR and ^{13}C NMR spectra for **23a**. ^{1}H NMR (500 MHz, $CDCl_3$) δ 7.55 (s, 1H), 7.14 (s, 2 H), 7.06 (s, 1H), 7.03 (s, 1H), 3.81 (t, *J* = 6.6 Hz, 2H), 2.32 (s, 6H), 2.08 (s, 3H). 2.06 (s, 3H), 1.87–1.78 (m, 2H), 1.53–1.47 (m, 2H), 1.42–1.20 (m, 8H), 0.9 (t, *J* = 7.1 Hz, 3H). ^{13}C NMR (126 MHz, $CDCl_3$) δ 187.27, 157.64, 143.06, 139.10, 137.25, 135.28, 131.65, 131.48, 131.30, 131.07, 130.86, 72.62, 31.82, 30.41, 29.48, 29.26, 26.10, 22.64, 16.94, 16.46, 16.22, 14.08 * indicates residual H_2O.

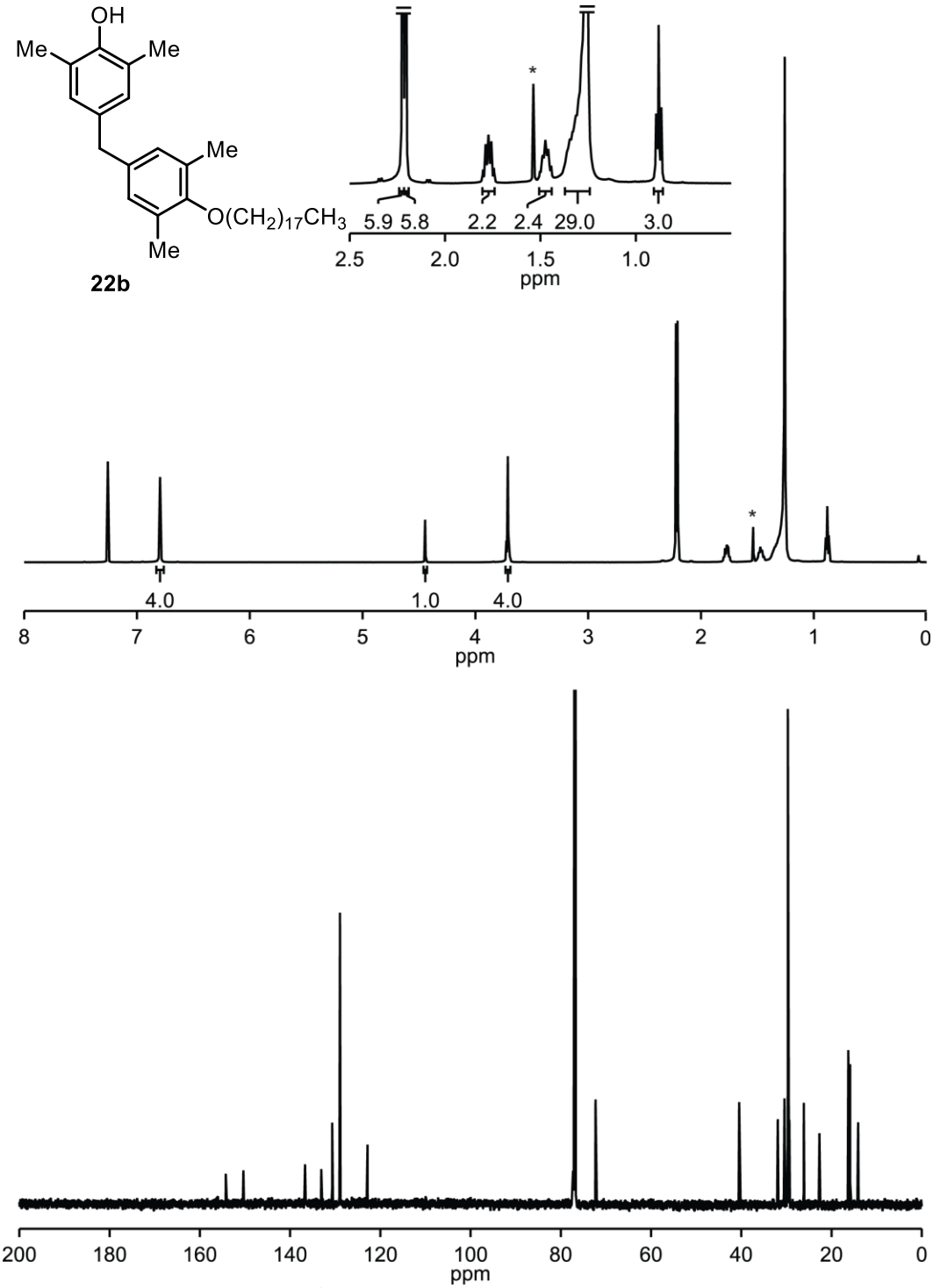


Figure S2.21 ^{1}H NMR and ^{13}C NMR spectra for **22b**. ^{1}H NMR (500 MHz, $CDCl_3$) δ 6.80 (s, 4H), 4.45 (s, 1H), 3.73–3.69 (m, 4H), 2.22 (s, 6H), 2.21 (s, 6H), 1.77 (tt, *J* = 7.4 Hz, 2H), 1.47 (tt, *J* = 7.4 Hz, 2H), 1.39–1.19 (m, 28H), 0.88 (t, *J* = 6.8 Hz, 3H). ^{13}C NMR (126 MHz, $CDCl_3$) δ 154.26, 150.35, 136.69, 133.09, 130.67, 128.94, 122.83, 72.31, 40.48, 31.91, 30.43, 29.68, 29.66, 29.65, 29.61, 29.56, 29.35, 26.15, 22.68, 16.29, 15.89, 14.10.* indicates residual H_2O.

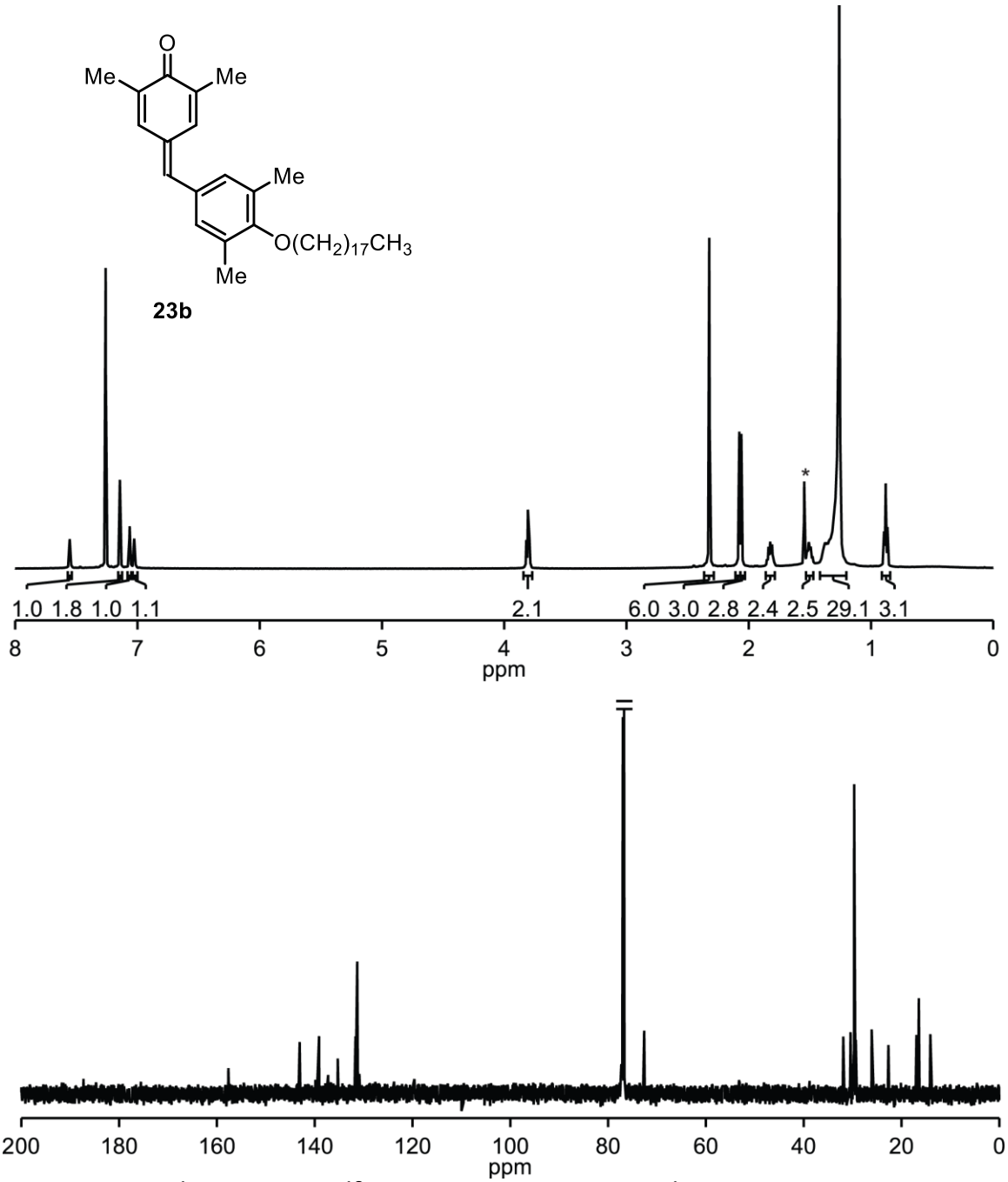


Figure S2.22 ^{1}H NMR and ^{13}C NMR spectra for **23b**. ^{1}H NMR (500 MHz, $CDCl_3$) δ 7.55 (s, 1H), 7.14 (s, 2H), 7.06 (s, 1H), 7.03 (s, 1H), 3.80 (t, *J* = 6.7 Hz, 2H), 2.32 (s, 6H), 2.08 (s, 3H), 2.06 (s, 3H), 1.87–1.78 (m, 2H), 1.53–1.47 (m, 2H), 1.42–1.19 (m, 28H), 0.88 (t, *J* = 7.2 Hz, 3H). ^{13}C NMR (126 MHz, $CDCl_3$) δ 157.65, 143.07, 139.10, 137.25, 135.28, 131.65, 131.48, 131.31, 131.07, 130.86, 72.62, 31.91, 30.42, 29.69, 29.66, 29.65, 29.60, 29.52, 29.35, 26.10, 22.68, 16.94, 16.46, 16.22, 14.10.

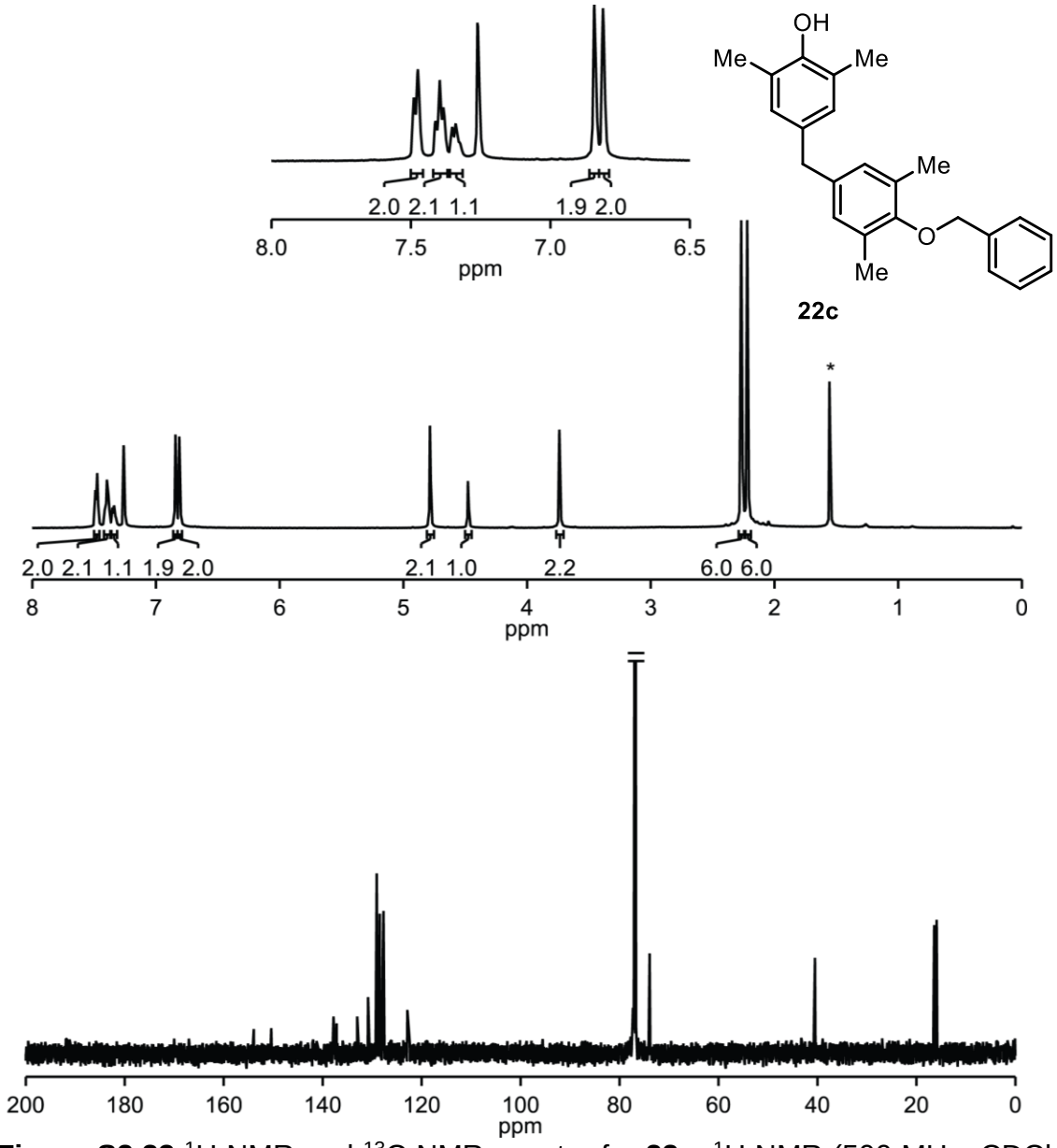


Figure S2.23 ^{1}H NMR and ^{13}C NMR spectra for **22c**. ^{1}H NMR (500 MHz, $CDCl_3$) δ 7.48 (dd, *J* = 69.5, 7.5 Hz, 2H), 7.40 (at, *J* = 6.3 Hz, 2H), 7.36–7.31 (m, 1H), 6.84 (s, 2H), 6.81 (s, 2H), 4.78 (s, 2H), 4.48 (s, 1H), 3.74 (s, 2H), 2.27 (s, 6H), 2.22 (s, 6H). ^{13}C NMR (126 MHz, $CDCl_3$) δ 153.93, 150.39, 137.81, 137.17, 133.01, 130.83, 129.07, 128.95, 128.46, 127.86, 127.70, 122.88, 73.92, 40.50, 16.41, 15.91. * indicates residual H_2O.

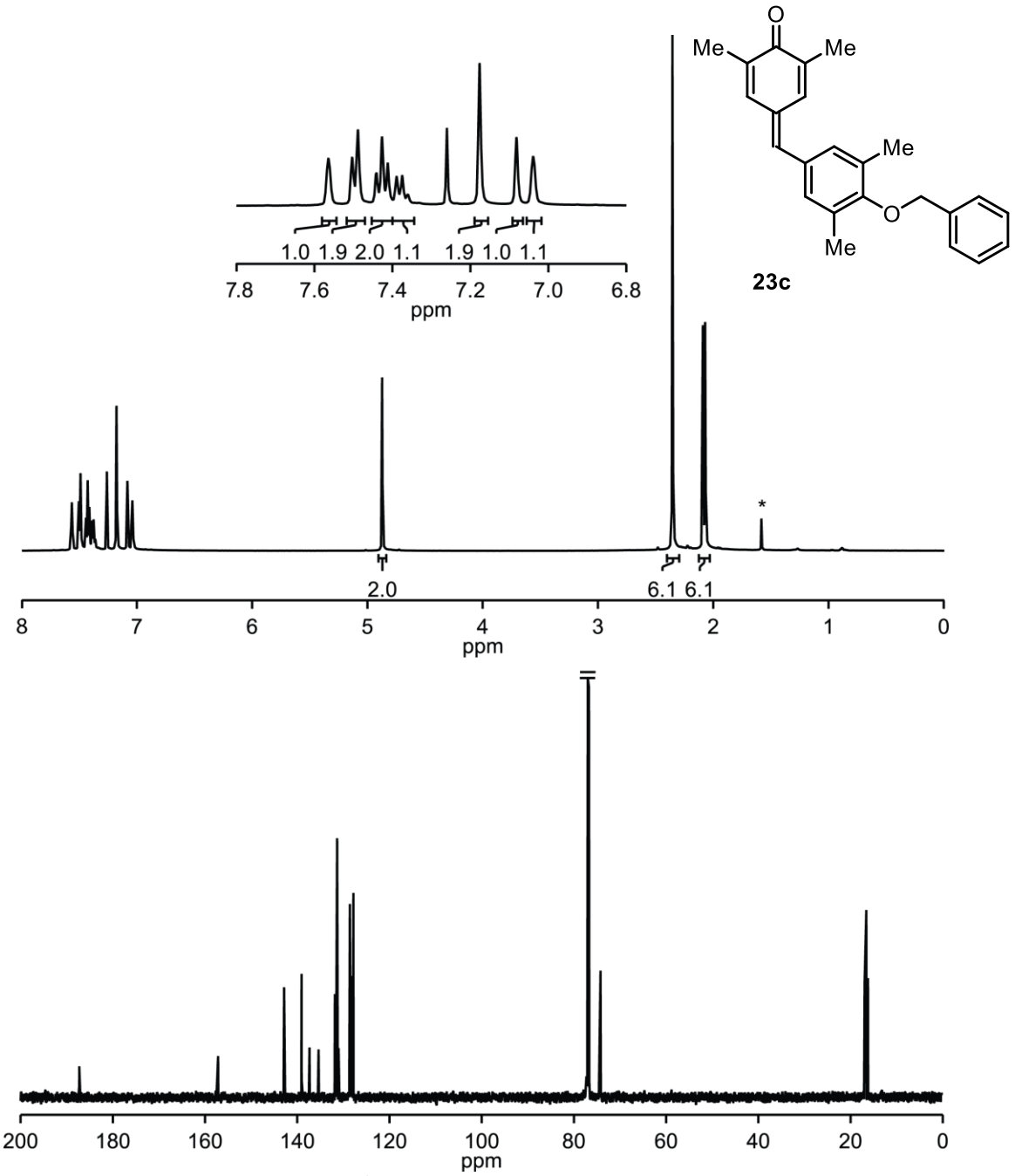


Figure S2.24 ^{1}H NMR and ^{13}C NMR spectra for **23c**. ^{1}H NMR (500 MHz, $CDCl_3$) δ 7.56 (s, 1H), 7.50 (d, *J* = 6.9 Hz, 2H), 7.43 (at, 2H), 7.40–7.34 (m, 1H), 7.18 (s, 2H), 7.08 (s, 1H), 7.04 (s, 1H), 4.87 (s, 2H), 2.35 (s, 6H), 2.09 (s, 3H), 2.07 (s, 3H). ^{13}C NMR (126 MHz, $CDCl_3$) δ 187.28, 157.16, 142.86, 139.06, 137.34, 137.18, 135.38, 131.83, 131.49, 131.42, 131.36, 131.04, 128.59, 128.19, 127.82, 74.23, 16.96, 16.59, 16.23. * indicates residual H_2O.

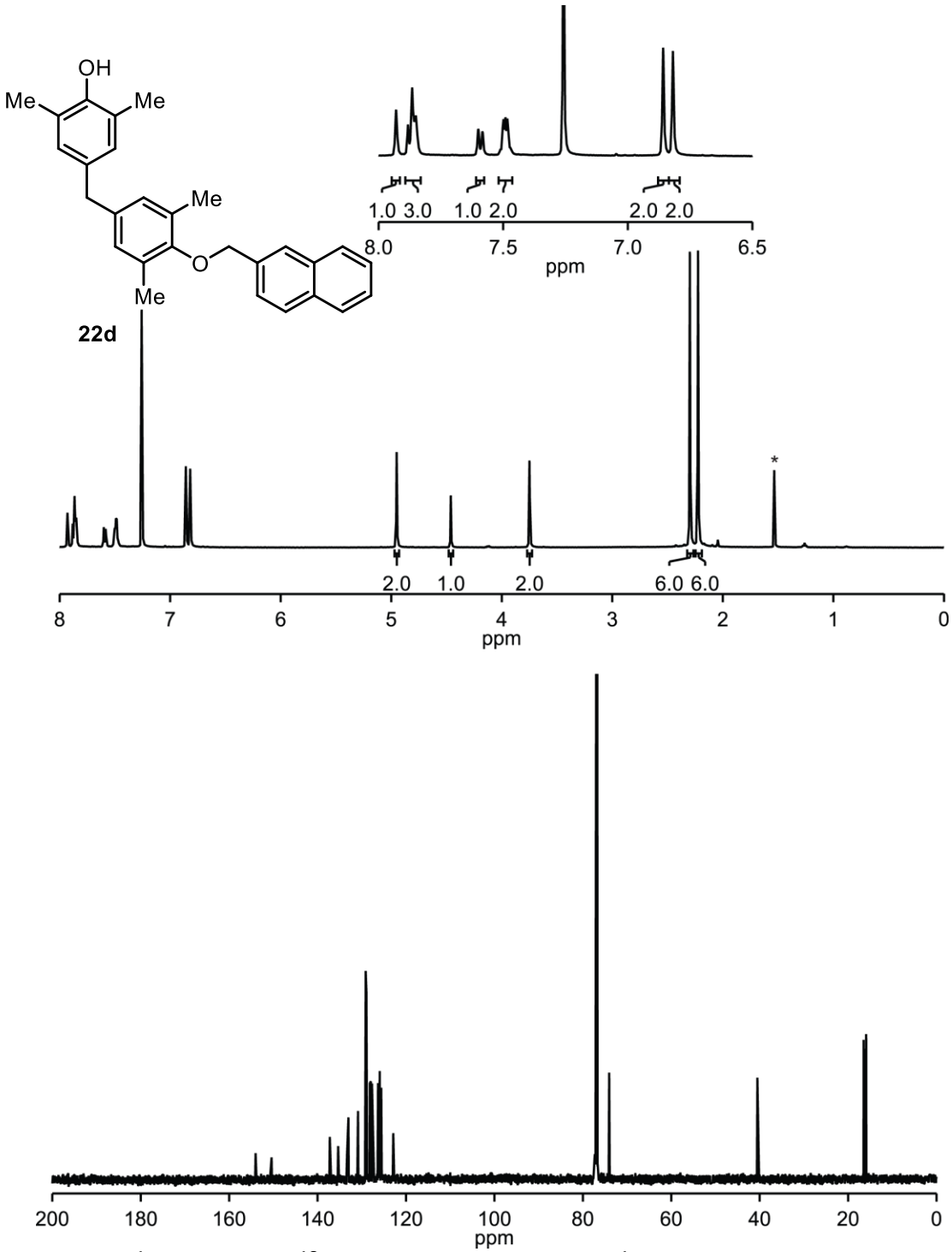


Figure S2.25 ^{1}H NMR and ^{13}C NMR spectra for **22d**. ^{1}H NMR (500 MHz, $CDCl_3$) δ 7.93 (s, 1H), 7.87 (t, *J* = 8.3 Hz, 3H), 7.59 (d, *J* = 8.5 Hz, 1H), 7.49 (dd, *J* = 6.4, 2.9 Hz, 2H), 6.86 (s, 2H), 6.82 (s, 2H), 4.95 (s, 2H), 4.46 (s, 1H), 3.75 (s, 2H), 2.30 (s, 6H), 2.22 (s, 6H). ^{13}C NMR (126 MHz, $CDCl_3$) δ 154.02, 150.40, 137.23, 135.34, 133.33, 133.03, 130.85, 129.12, 128.96, 128.16, 127.96, 127.70, 126.33, 126.12, 125.94, 125.61, 122.89, 74.04, 40.52, 16.49, 15.92. * indicates residual H_2O.

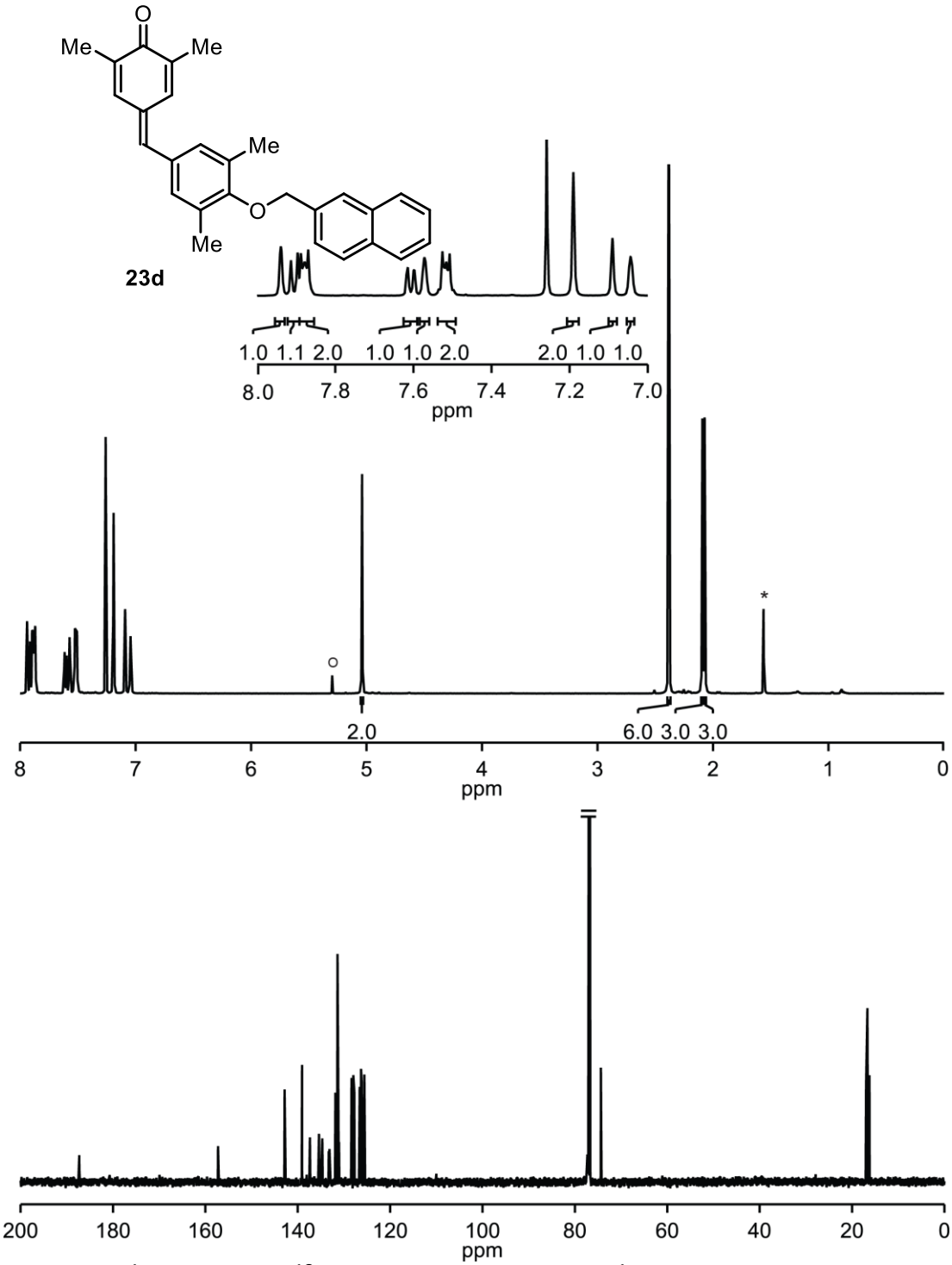


Figure S2.26 ^{1}H NMR and ^{13}C NMR spectra for **23d**. ^{1}H NMR (500 MHz, $CDCl_3$) δ 7.94 (s, 1H), 7.90 (d, *J* = 8.5 Hz, 1H), 7.89 – 7.86 (m, 2H), 7.61 (dd, *J* = 8.4, 1.7 Hz, 1H), 7.57 (s, 1H), 7.54–7.49 (m, 2H), 7.19 (s, 2H), 7.09 (s, 1H), 7.04 (s, 1H), 5.04 (s, 2H), 2.38 (s, 6H), 2.09 (s, 3H), 2.07 (s, 3H). ^{13}C NMR (126 MHz, $CDCl_3$) δ 187.29, 157.26, 142.85, 139.07, 137.36, 135.39, 134.68, 133.29, 133.13, 131.85, 131.54, 131.43, 131.39, 131.06, 128.36, 127.97, 127.75, 126.59, 126.29, 126.18, 125.57, 74.37, 16.97, 16.67, 16.23. ^{o} indicates residual DCM, * indicates residual H_2O.

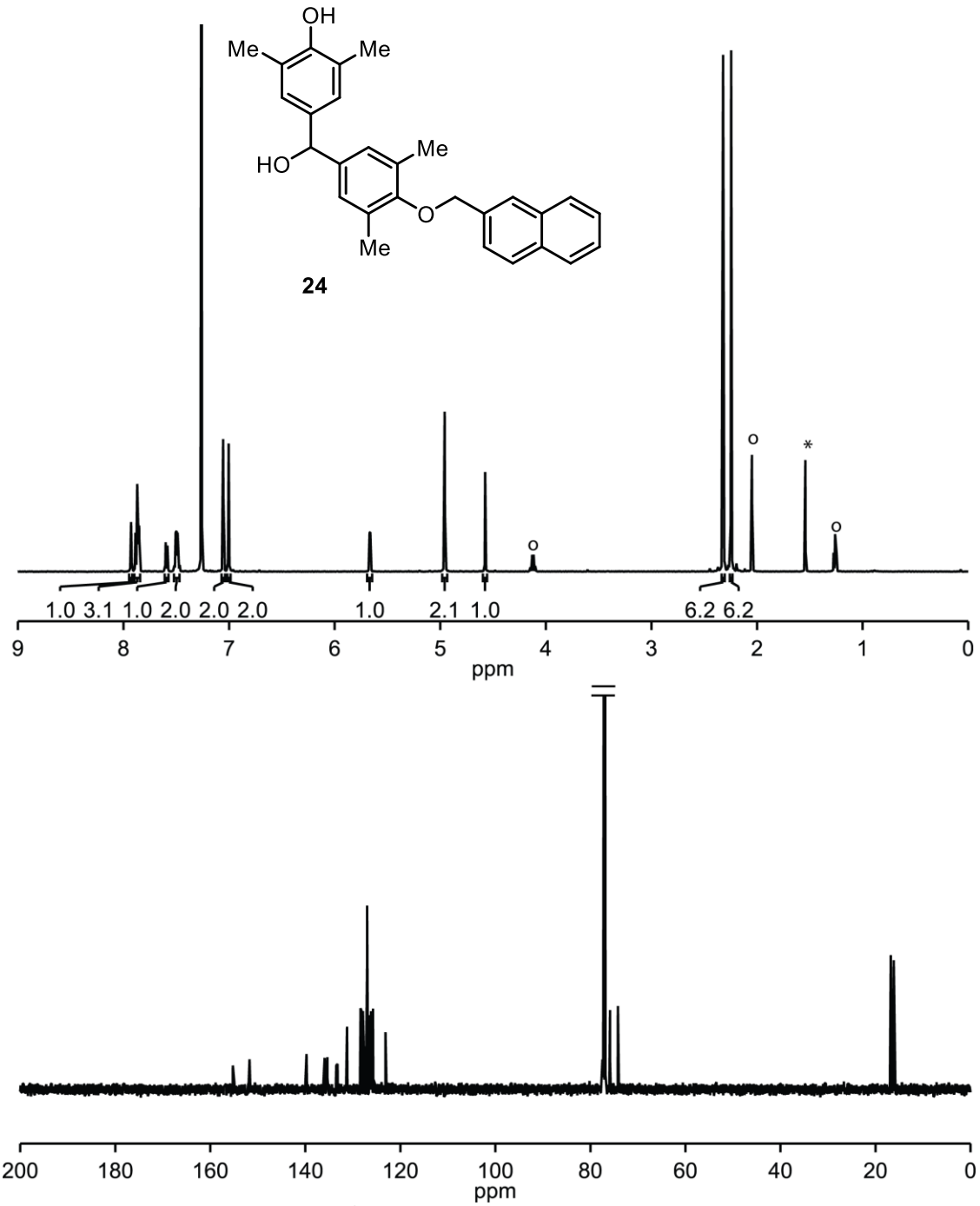


Figure S2.27 ^{1}H NMR and ^{13}C NMR spectra for **24.** ^{1}H NMR (500 MHz, $CDCl_3$) δ 7.93 (s, 1H), 7.89–7.84 (m, 3H), 7.59 (d, *J* = 8.4 Hz, 1H), 7.52 – 7.47 (m, 2H), 7.06 (s, 2H), 7.00 (s, 2H), 5.67 (d, *J* = 3.4 Hz, 1H), 4.96 (s, 2H), 4.57 (s, 1H), 2.32 (s, 6H), 2.24 (s, 6H). ^{13}C NMR (126 MHz, $CDCl_3$) δ 155.25, 151.74, 139.75, 135.93, 135.36, 133.49, 133.21, 131.22, 128.37, 128.13, 127.88, 126.99, 126.97, 126.55, 126.32, 126.16, 125.76, 123.13, 75.87, 74.21, 16.79, 16.17. ^{o} indicates residual EtOAc, * indicates residual H_2O.

(c) Gel Screening

Gel Screening Procedure - In a 4 mL vial a known amount of gelator **16, 23a–d** and a known amount of organic solvent was added. The vial was capped, heated to dissolve the solid and cooled to rt over 10 min. If the resulting gel was stable-to-inversion, then 0.1 mL of the organic solvent was added the procedure was repeated until the gel was no longer stable-to-inversion. If a gel did not form, the steps listed below were followed depending on what was observed.

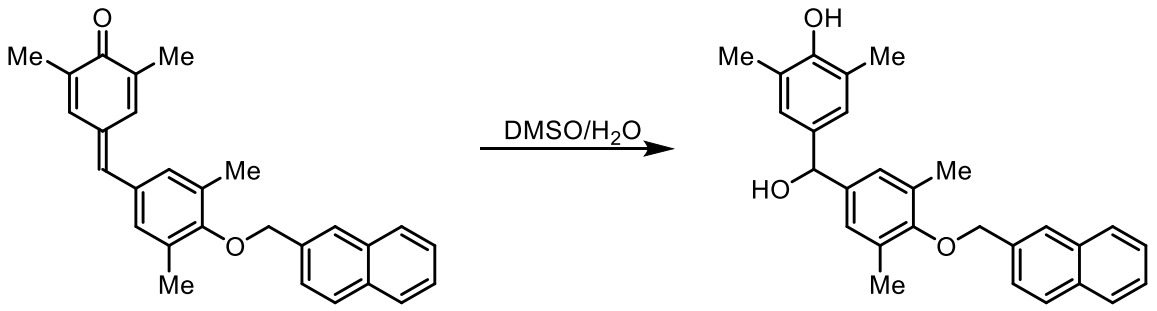
3. If a precipitate formed the mixture was heated to dissolve, sonicated for 5-20 s and then cooled over 10 min to see if a gel formed. If a gel still did not form then 0.1 mL solvent was added and the procedure was repeated from the beginning.
4. If a precipitate did not form then a "bad" solvent (a solvent that the compound is not soluble in) was added and the procedure was repeated from the beginning.

Table S2.2 Summary of Gel Screening[a]

Solvent	16	23a	23b	23c	23d
acetone	S	S	S	--	S
acetone/H_2O	P	P	P	--	P
EtOAc	S	S	S	--	S
DMSO	--	P	P	S	S
DMSO/H_2O	--	P	P	P[b]	P[b]
MeCN	--	P	P	--	--
MeCN/H_2O	--	P	--	--	--
2-methoxyEtOH	--	P	--	P	--
2-methoxyEtOH/ H_2O	--	P	--	P	--
EtOH	--	--	P	S	S
EtOH/H_2O	--	--	--	P	P
hexanes	--	--	S	P	P
isopropanol	S	--	S	--	--
iPrOH/H_2O	P	--	--	--	--
MeOH	S	--	P	--	S
MeOH/H_2O	P	--	--	--	P
DMF	--	--	--	--	S
DMF/H_2O	--	--	--	--	p

[a] S: solution; P: precipitate

[b] With heat and time (~3-4 d) hydration occurs



23d **24**

In Situ Gelation Procedure – In a 4 mL vial compound **23d** (13.8 mg) was dissolved in DMSO (0.4 mL) and precipitated out with water (0.3 mL). The vial was capped, heated to dissolve the solid and allowed to cool to rt. Over 3–4 d at neutral pH **23d** is hydrated to **24** which forms a gel.

Table S2.3 Summary of gel screening for **24**[a]

Solvent	24
DMSO/H_2O	G (48 mM)[b]

[a] G: gel; S: solution; P: precipitate
[b] concentration it gelled at (≥cgc)

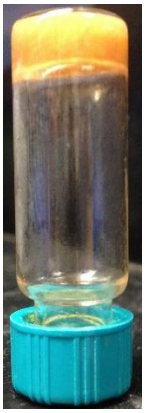
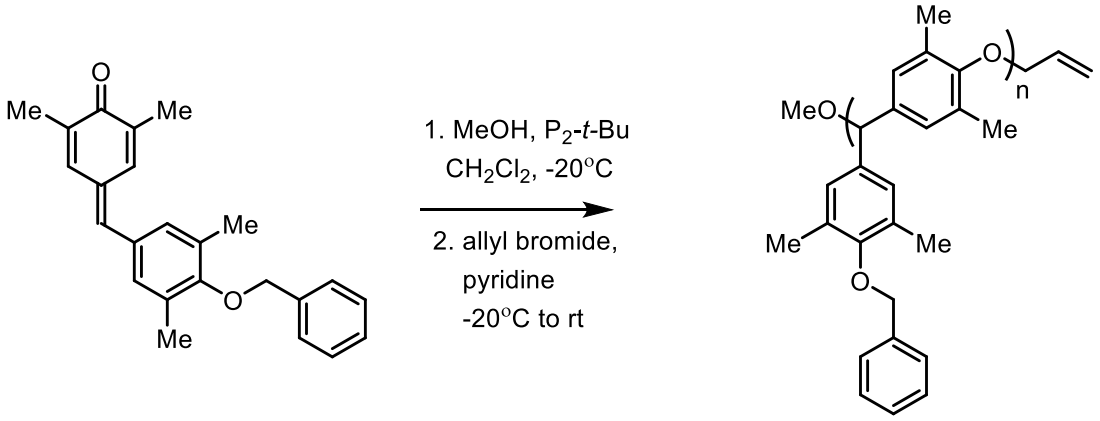


Figure S2.28 Gelator **24** in DMSO/H_2O.

(d) Polymerizations



23c **P1**

Preparation: The night before carrying out the polymerization **23c** (0.25 g, 0.73 mmol) was dried on the high vacuum overnight.

MeOH stock solution (0.54 M) - In the glovebox, distilled MeOH (110 µL, 2.7 mmol) was dissolved in anhydrous THF (5.0 mL).

P1.[10] In an oven dried 25 mL Schlenk flask equipped with a stir bar, **23c** (0.25 g, 0.73 mmol, 1.0 equiv) was added. The flask was evacuated and backfilled with N_2 3x. Anhydrous DCM (0.97 mL) was added and the resulting solution was degassed by freeze-pump-thawing 3x. The solution was then cooled to -20 °C. MEtOH (0.54 M, 67 µL, 0.036 mmol, 0.05 equiv) and P_2-t-Bu in THF (2.0 M, 18.1 µL, 0.036 mmol, 0.05 equiv) was added to the reaction quickly. The reaction was stirred for 2 h before adding pyridine (70 µL, 0.87 mmol, 1.2 equiv) and allyl bromide (69 µL, 0.79 mmol, 1.1 equiv). The reaction was stirred for 1 h at -20 °C and at rt for18 h. The polymer was precipitated by adding MeOH at 0 °C. The yellow crystalline solid was collected (95%, 0.2379 g). GPC showed some monomer still present. Polymer M_n = 7.3 kDa, Đ = 1.81.

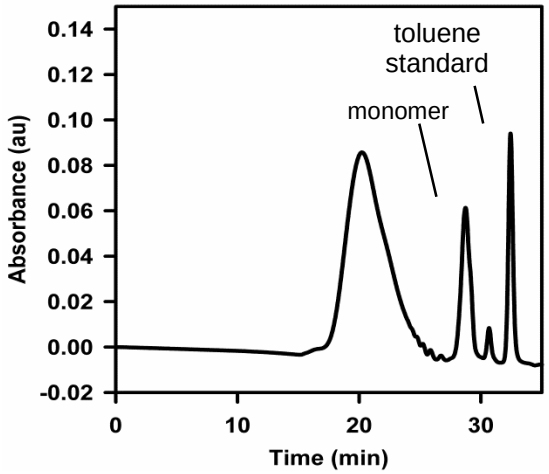
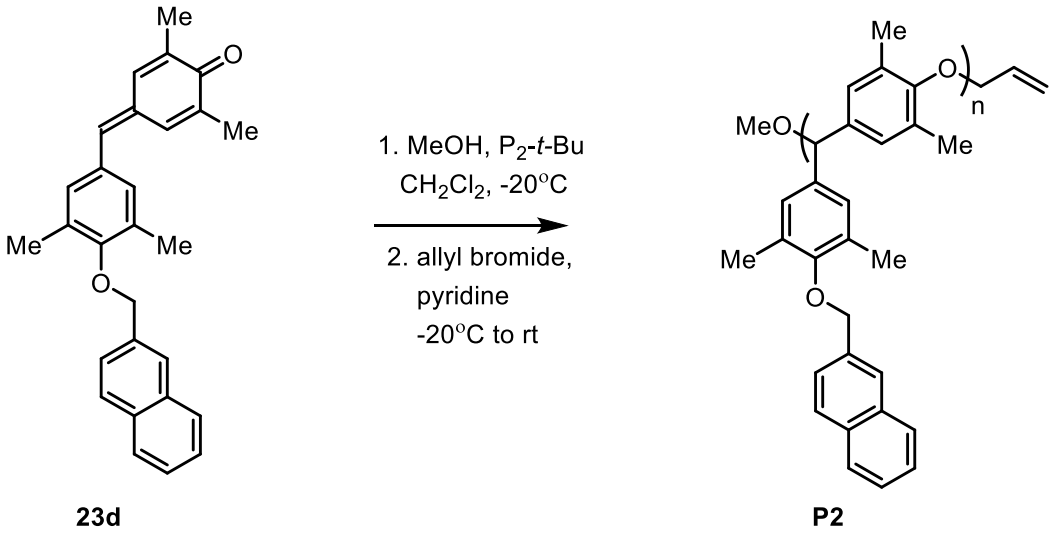


Figure S2.29 Representative GPC trace of **P1**.



23d **P2**

Preparation: The night before carrying out the polymerization **23d** (0.25 g, 0.63 mmol) was dried on the high vacuum overnight.

MEOH stock solution (0.54 M) - In the glovebox, distilled MeOH (110 µL, 2.7 mmol) was dissolved in anhydrous THF (5.0 mL).

P2.[10] In an oven dried 25 mL Schlenk flask equipped with a stir bar **23d** (0.25 g, 0.63 mmol, 1.0 equiv) was added. The flask was evacuated and backfilled with N_2 3x. Anhydrous DCM (0.95 mL) was added and the resulting solution was degassed by freeze-pump-thawing 3x. The solution was then cooled to -20 °C. However, when doing so precipitation occurred. Warmed the reaction back up to rt and added MeOH (0.54 M, 58 µL, 0.032 mmol, 0.05 equiv) and P_2-t-Bu in THF (2.0 M, 16 µL, 0.032 mmol, 0.05 equiv) to the reaction quickly. The reaction was stirred for 2 h before adding pyridine (61 µL, 0.76 mmol, 1.2 equiv) and allyl bromide (60 µL, 0.70 mmol, 1.1 equiv). The reaction was let stir for 1 h at -20 °C and at rt for18 h. The polymer was precipitated by addition of MeOH at 0 °C. The yellow crystalline solid was collected. GPC showed some monomer still present. Polymer M_n = 5.6 kDa, Đ = 1.81.

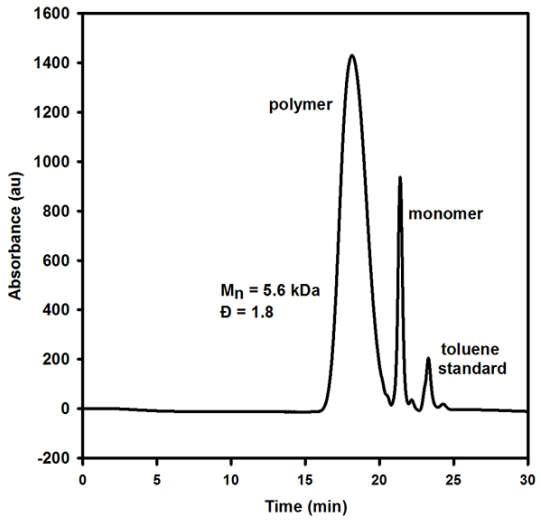


Figure S2.30 Representative GPC trace of **P2**

References

(1) Armarego, W. L. F.; Chai, C. L. L. *Purification of Laboratory Chemicals (Fifth edition),* Butterworth-Heinemann: Burlington, MA 2003.

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(4) Kalashnikova, I. P.; Zhukov, I. V.; Tomilova, L. G.; Zefirov, N. S. *Russ. Chem. Bull., Int. Ed.* **2003**, *52*,1709–1714.

(5) Chen, L. S.; Chen, G. J. *J. Organomet. Chem.* **1980**,*193*, 283–292.

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(7) Bryan, Z. J.; Smith, M. L.; McNeil, A. J. *Macromol. Rapid Commun.* **2012**, *33*, 842–847.

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(9) Olah, M. G.; Robbins, J. S.; Baker, M. S.; Phillips, S. T. *Macromolecules,* **2013**, *46*, 5924–5928.

(10) Yeung, K.; Kim, H.; Mohapatra, H.; Phillips, S. T. *J. Am. Chem. Soc*. **2015**, *137*, 5324–5327.

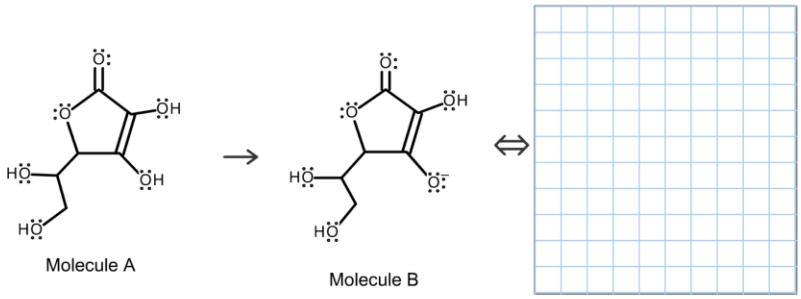
Appendix 3

Supporting Information for Chapter 5:
Using Student-Generated Instructional Materials to Customize an Online e-Homework Platform

I. Examples of Student-Generated Questions

Question

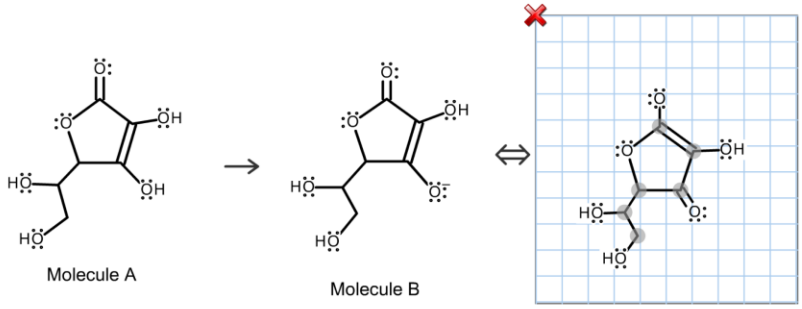
Molecule A is Vitamin C shown below. At pH 7, the most acidic site on Vitamin C mono-deprotonates in your bloodstream. Molecule B is the conjugate base of Vitamin C. **Draw the other possible resonance structure for molecule B.** Make sure that your molecule (1) has all closed shell atoms and (2) maintains a charge of -1/0/+1 on the atoms.



Molecule A Molecule B

Specific Feedback

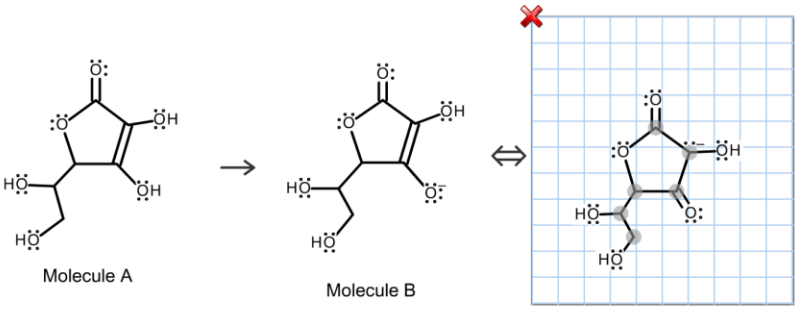
Molecule A is Vitamin C shown below. At pH 7, the most acidic site on Vitamin C mono-deprotonates in your bloodstream. Molecule B is the conjugate base of Vitamin C. **Draw the other possible resonance structure for molecule B.** Make sure that your molecule (1) has all closed shell atoms and (2) maintains a charge of -1/0/+1 on the atoms.



Molecule A Molecule B

Incorrect. Formal charge is an important concept in chemistry. Don't forget to include them.

Molecule A is Vitamin C shown below. At pH 7, the most acidic site on Vitamin C mono-deprotonates in your bloodstream. Molecule B is the conjugate base of Vitamin C. **Draw the other possible resonance structure for molecule B.** Make sure that your molecule (1) has all closed shell atoms and (2) maintains a charge of -1/0/+1 on the atoms.



Molecule A Molecule B

Incorrect.
While this is technically a valid resonance structure you've put a negative formal charge on carbon which is not very stable.

Consider the other more electronegative atom in this molecule that avoids formal charges on carbon atoms.

Figure S3.1 Question and two examples of specific feedback for a student-generated question on resonance.

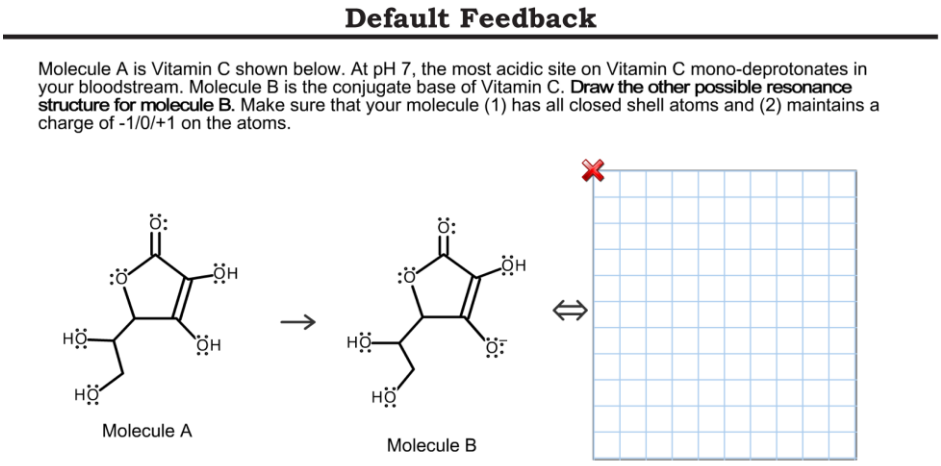


Figure S3.2 Default and solution feedback for a student-generated question on resonance.

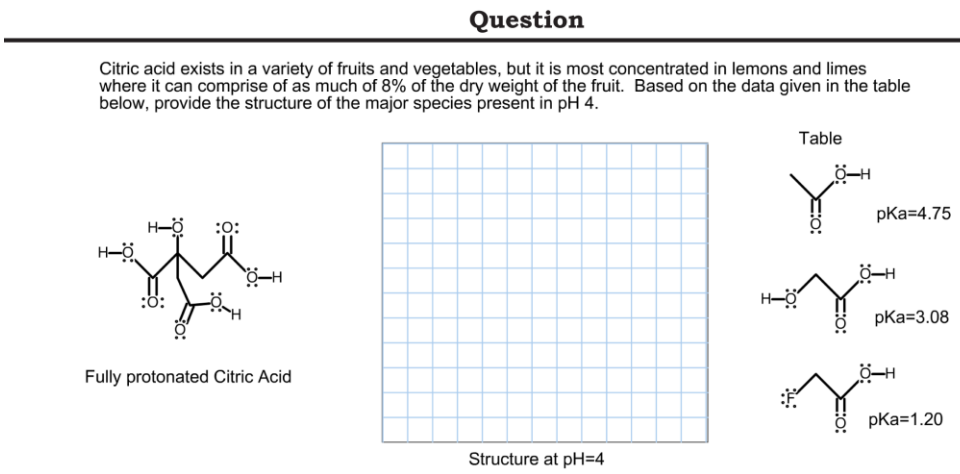
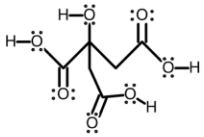


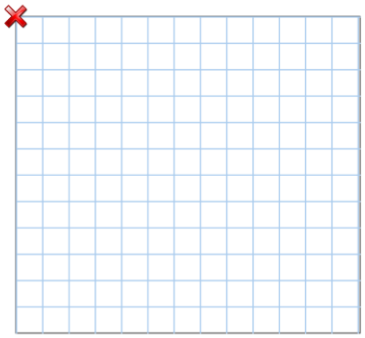
Figure S3.3 Question and two examples of specific feedback for a student-generated question on acid-base chemistry.

Default Feedback

Citric acid exists in a variety of fruits and vegetables, but it is most concentrated in lemons and limes where it can comprise of as much of 8% of the dry weight of the fruit. Based on the data given in the table below, provide the structure of the major species present in pH 4.

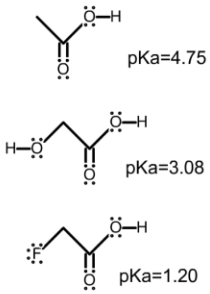


Fully protonated Citric Acid



Structure at pH=4

Table



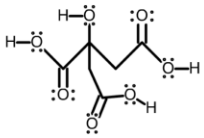
1. Assign pKa values to each hydrogen. There are 3 and they are unique in a way.

2. You will need to use the table in this problem to determine the effect the OH group has on each respective carboxylic acid.

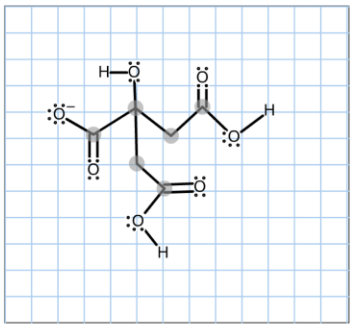
3. The OH group is also slightly acidic, but not as acidic as carboxylic acids.

Solution Feedback

Citric acid exists in a variety of fruits and vegetables, but it is most concentrated in lemons and limes where it can comprise of as much of 8% of the dry weight of the fruit. Based on the data given in the table below, provide the structure of the major species present in pH 4.

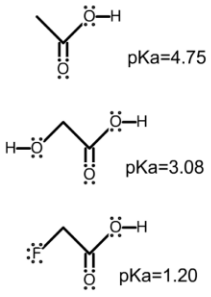


Fully protonated Citric Acid



Structure at pH=4

Table



Looking at the table, you can assign relative pKa's to each acidic proton.

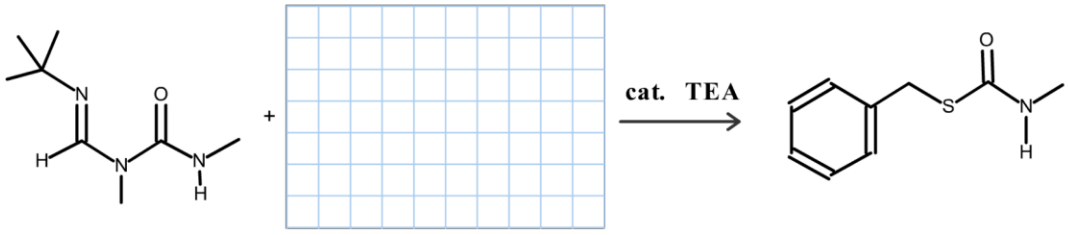
The far left carboxylic acid is about 3.08, the other two carboxylic acid's are above 4.75.

Thus, at a pKa of 4, only the most acidic proton will be deprotonated which is the far left carboxylic acid.

Figure S3.4 Default and solution feedback for a student-generated question on acid-base chemistry.

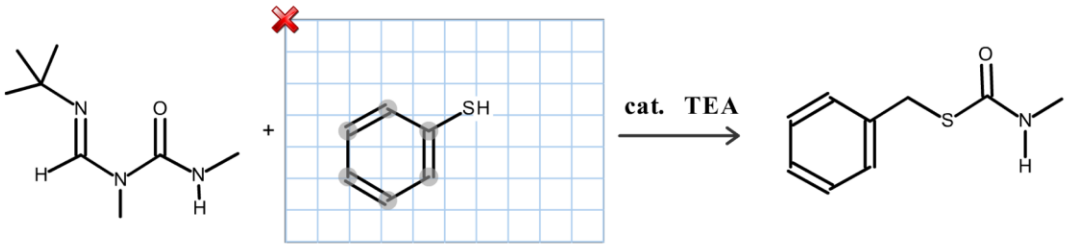
Question

For the following acyl transfer reaction (*Org. Lett.* **2004**, *6*, 43-46.), draw the second reactant given the following information:



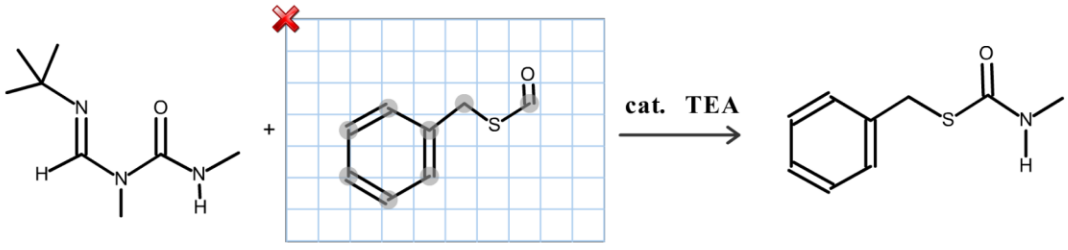
Specific Feedback

For the following acyl transfer reaction (*Org. Lett.* **2004**, *6*, 43-46.), draw the second reactant given the following information:



Incorrect.
You have the right concept but have missed a methylene group somewhere.

For the following acyl transfer reaction (*Org. Lett.* **2004**, *6*, 43-46.), draw the second reactant given the following information:

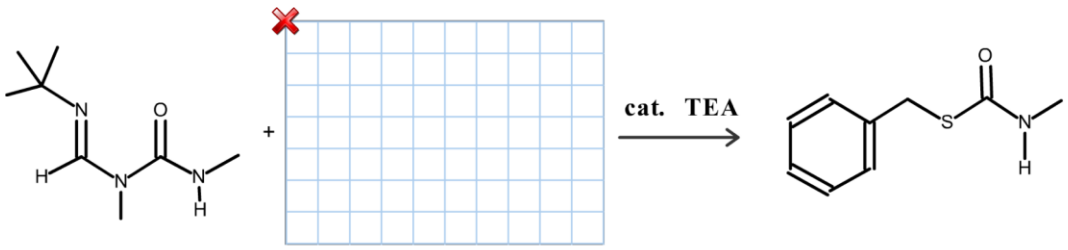


Incorrect.
The acyl group is present in the first reagent, not the second. Otherwise there would not be an acyl transfer reaction going on (as is drawn)

Figure S3.5 Question and two examples of specific feedback for a student-generated question on predicting starting material.

Default Feedback

For the following acyl transfer reaction (*Org. Lett.* **2004**, *6*, 43-46.), draw the second reactant given the following information:

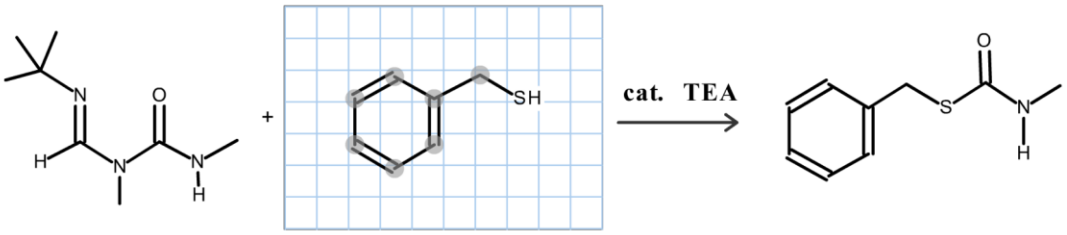


Incorrect. Compare the product to the reactant given, and determine where the acyl group came from.

Based on that, try figuring out a key property of the other reactant (Hint: TEA is a base).

Solution Feedback

For the following acyl transfer reaction (*Org. Lett.* **2004**, *6*, 43-46.), draw the second reactant given the following information:



The product is a thioamide and the first reagent given is a urea. Since the methyl amide portion comes from the first reagent, the other reagent must contain the sulfur and the benzyl group. Triethylamine is a strong base, which will deprotonate the thiol, making it a good nucleophile.

This will react with the urea carbonyl, forming a tetrahedral intermediate and kicking off the amidine leaving group. Note, the amidine can delocalize the electrons from the broken bond between both amines, increasing its leaving group ability.

Figure S3.6 Default and solution feedback for a student-generated question on predicting starting material.

II. Course Survey

The questions below were asked in an online survey to all students who participated in the 1-credit course. The term “coursepack” refers to a booklet of old test questions that were distributed to students and “CHEM 219/220” are the course numbers for the 1-credit course.

1. What was your experience authoring in the Sapling Learning user space?

Straightforward	Somewhat straightforward	Neutral	Somewhat complicated	Complicated

2. When authoring in Sapling Learning please rate your experience with the interface features (i.e. modules, different tabs).

(a) ease of use	Straightforward	Somewhat straightforward	Neutral	Somewhat complicated	Complicated
(b) utility (able to perform several functions)	Strongly agree	Agree	Neutral	Disagree	Strongly disagree
(c) flexibility (allows for creativity)	Strongly agree	Agree	Neutral	Disagree	Strongly disagree

3. By authoring questions in Sapling Learning my understanding of organic chemistry _____.

Improved	Slightly improved	Stayed the same	Slightly worsened	Worsened

4. In participating in CHEM 219/220 my ability to *(a)-(d)* in organic chemistry _____.

	Improved	Slightly improved	Stayed the same	Slightly worsened	Worsened
(a) explain a concept	5	4	3	2	1
(b) identify common areas of misconception	5	4	3	2	1
(c) receive feedback related to my work	5	4	3	2	1
(d) teach others	5	4	3	2	1

5A. In CHEM 219/220 how challenging was each part of the authoring process?

	Extremely	Significantly	Neutral	Not significantly	Not at all
(a) creating a problem	5	4	3	2	1
(b) creating possible responses and feedback	5	4	3	2	1
(c) inputting the question in the Sapling Learning interface	5	4	3	2	1
(d) reviewing my own work	5	4	3	2	1
(e) reviewing others work	5	4	3	2	1
(f) editing and revising my work	5	4	3	2	1

5B. Now, rank each part of the authoring process according to how challenging each task was.

	RANK (1 = most challenging; 6 = least challenging; no ties allowed!)					
(a) creating a problem	1	2	3	4	5	6
(b) creating possible responses and feedback	1	2	3	4	5	6
(c) inputting the question in the Sapling Learning interface	1	2	3	4	5	6
(d) reviewing my own work	1	2	3	4	5	6
(e) reviewing others work	1	2	3	4	5	6
(f) editing and revising my work	1	2	3	4	5	6

6. In CHEM 219/220 how much time on average did each step in the authoring process take to create one question.

(a) creating a problem	< ½ h	½ - 1 h	1 ½-2 h	2-2 ½ h	2 ½-3 h	>3 h
(b) creating possible responses and feedback	< ½ h	½ - 1 h	1 ½-2 h	2-2 ½ h	2 ½-3 h	>3 h
(c) inputting the question in the Sapling Learning interface	< ½ h	½ - 1 h	1 ½-2 h	2-2 ½ h	2 ½-3 h	>3 h
(d) reviewing my own work	< ½ h	½ - 1 h	1 ½-2 h	2-2 ½ h	2 ½-3 h	>3 h
(e) reviewing others work	< ½ h	½ - 1 h	1 ½-2 h	2-2 ½ h	2 ½-3 h	>3 h
(f) editing and revising my work	< ½ h	½ - 1 h	1 ½-2 h	2-2 ½ h	2 ½-3 h	>3 h

7. How effective was each part of the CHEM 219/220 class structure?

	Effective	Somewhat effective	Neutral	Somewhat ineffective	Ineffective
(a) coursepack as question inspiration	5	4	3	2	1
(b) thinking of possible responses and feedback	5	4	3	2	1
(c) reviewing your own work	5	4	3	2	1
(d) reviewing others work	5	4	3	2	1
(e) editing and revising your work based on comments from others	5	4	3	2	1

III. Course Survey Results

Students who participated in the Winter 2014 and Fall 2014 1-credit courses responded to the survey at least 3 months after taking the class. A total of 12 out of 34 students responded. Students who participated in the Winter 2015 1-credit course responded to the survey at the end of the class. A total of 16 out of 16 students responded. Both groups results are shown below.

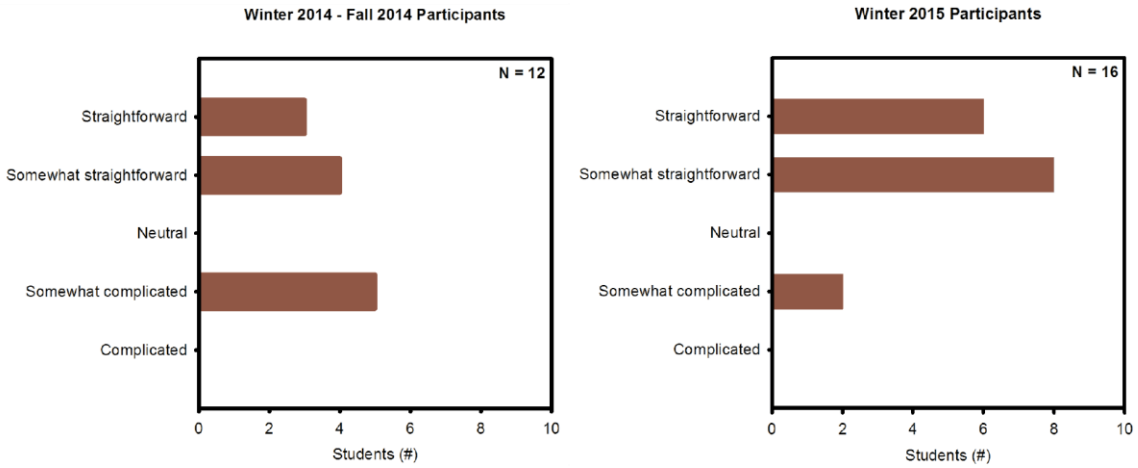


Figure S3.7 Survey results from the question "What was your experience in the Sapling Learning user space?"

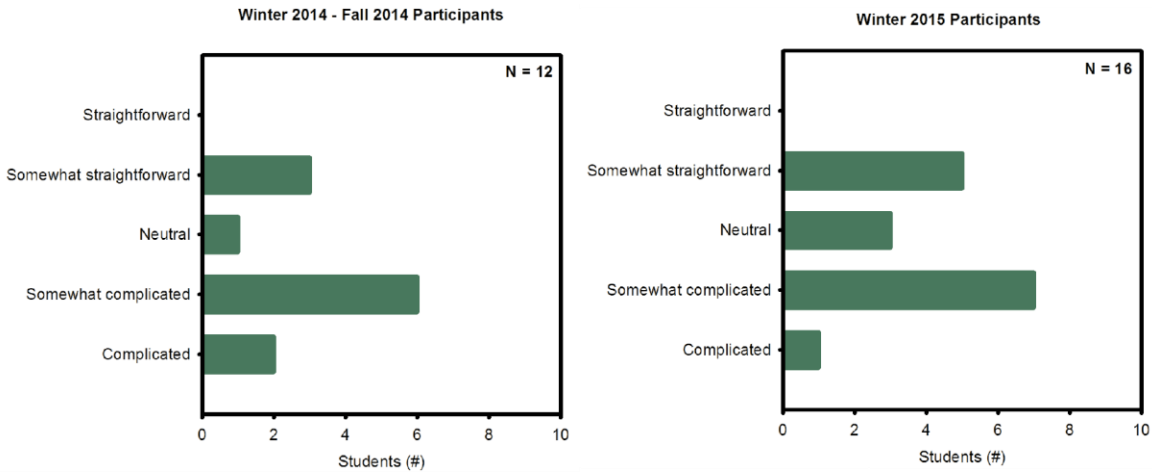


Figure S3.8 Survey results from the question "When authoring in Sapling Learning please rate your experience with the interface features (e.g., modules, different tabs) with respect to the interfaces ease of use."

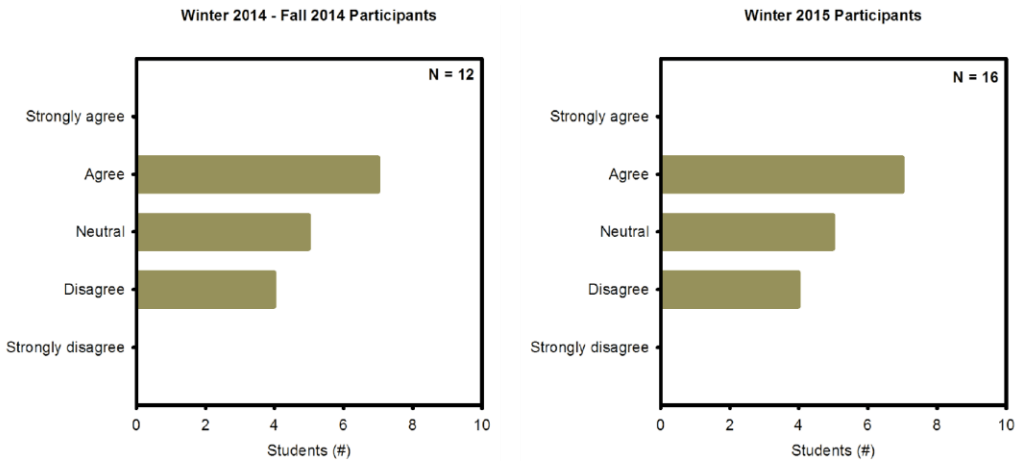


Figure S3.9 Survey results from the question "When authoring in Sapling Learning please rate your experience with the interface features (e.g., modules, different tabs) with respect to the interfaces utility (i.e., ability to perform several functions)."

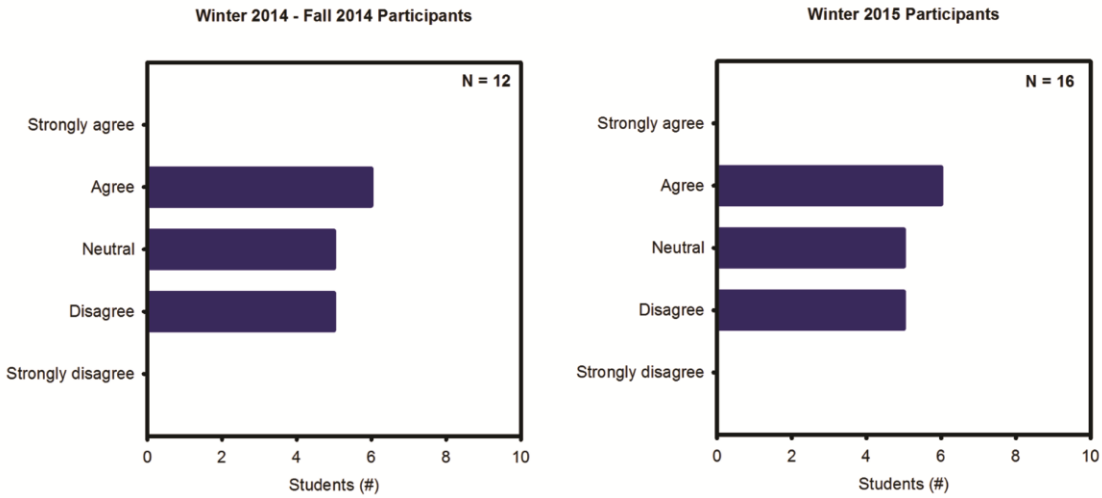


Figure S3.10 Survey results from the question "When authoring in Sapling Learning please rate your experience with the interface features (e.g., modules, different tabs) with respect to the interfaces flexibility (i.e., ability to allow for creativity)."

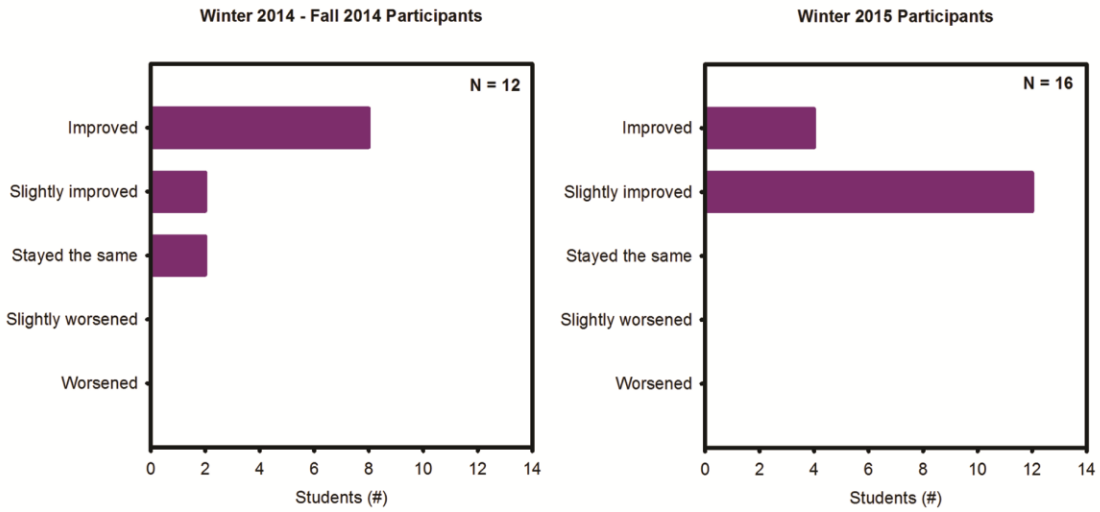


Figure S3.11 Survey results from the question "By authoring questions in Sapling Learning my understanding of organic chemistry…"

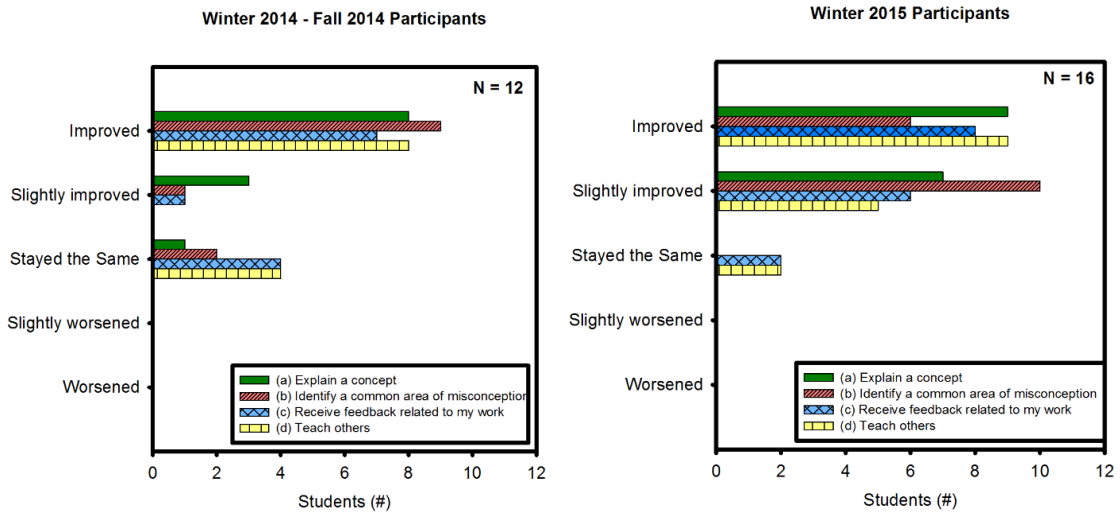


Figure S3.12 Survey results from the question "In participating in CHEM 219/220 my ability to (a)-(d) in organic chemistry____."

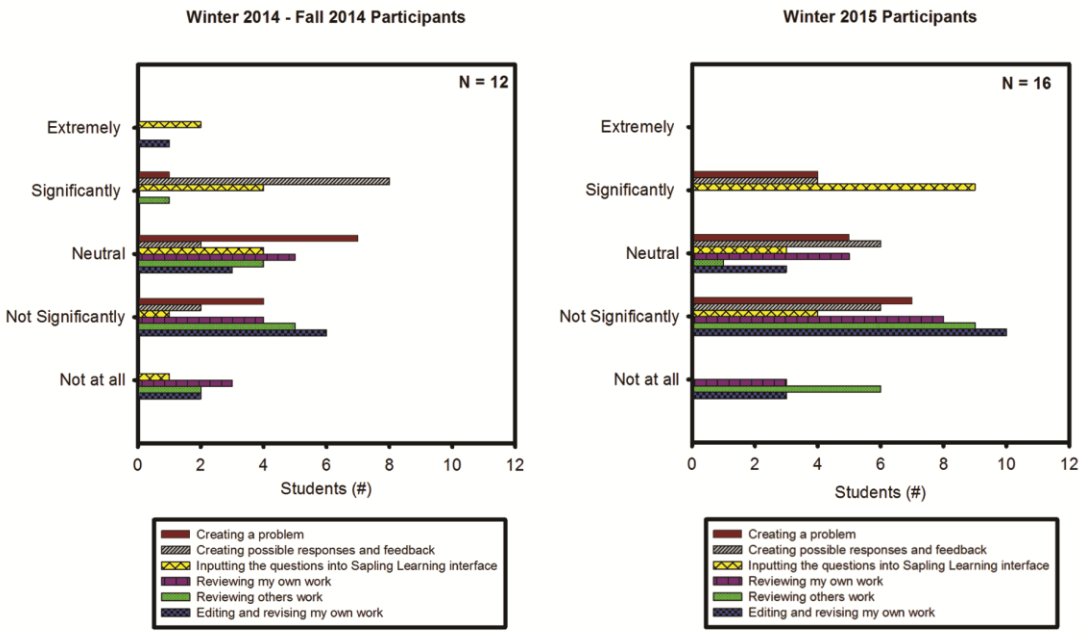


Figure S3.13 Survey results from the question “In Chem 219/220 how challenging was each part of the authoring process?”

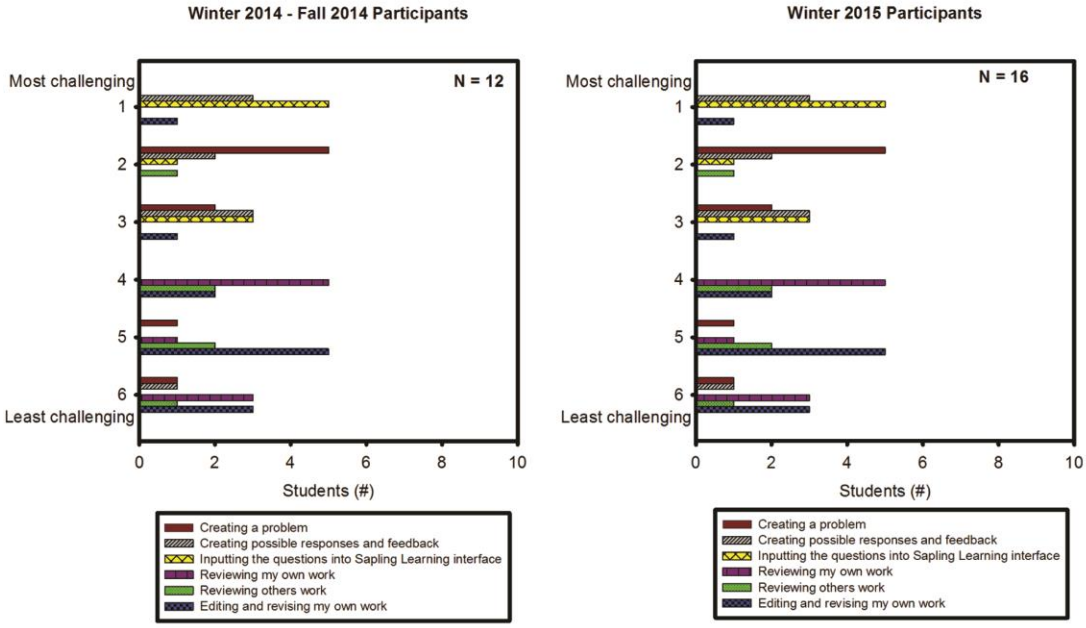


Figure S3.14 Survey results from the question “Now, rank each part of the authoring process according to how challenging each task was.”

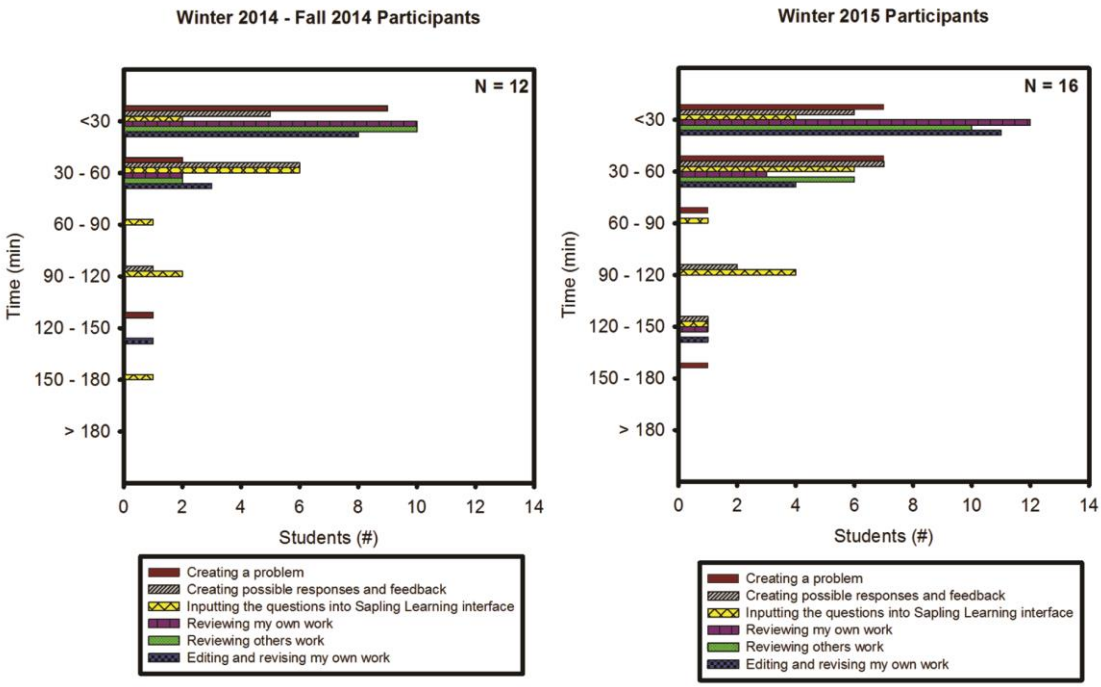


Figure S3.15 Survey results from the question “In CHEM 219/220 how much time on average did each step in the authoring process take to create one question?”

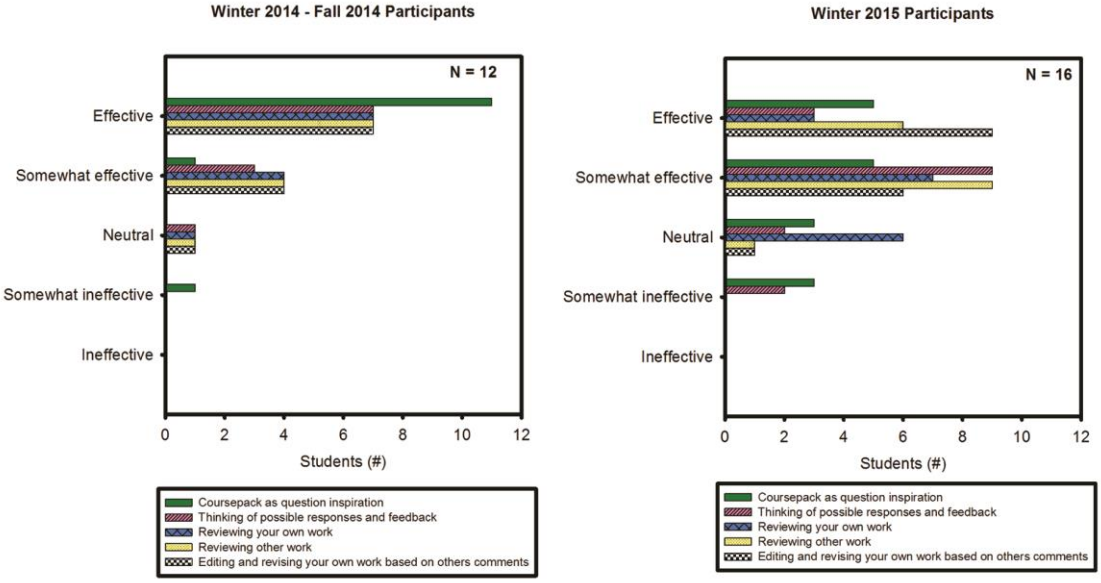


Figure S3.16 Survey results from the question “How effective was each part of the CHEM 219/220 class structure?”

IV. Instructor Responsibilities

Student-generated questions: Pilot Project

Below is a brief list of tasks performed by the instructor (e.g., graduate student) implementing the authoring assignment. The syllabus and handouts that were used during the assignment are provided on the indicated pages.

Timeline	Responsibilities	Page
Prior to the semester	Structured study group (SSG) leaders, a graduate student, and the instructor met with a Sapling Learning technician to learn how to author. Authoring instructions were created from this meeting.	196
	SSG leaders were tasked with generating one question in the interface. The graduate student oversaw the three week process.	200
	Created the pilot project syllabus with timeline.	202
During the semester	Created a handout to guide students in peer review	208
End of the semester	A graduate student reviewed all authored questions and suggested edits using the handout as a guide.	208

Student-generated questions: 1-credit course

Below is a brief list of tasks performed by the instructor implementing the 1-credit authoring class. Student author training was skipped due to their familiarity with the interface. The syllabus and handouts that were used during the class are provided on the indicated pages.

Timeline	Responsibilities	Page
Before the start of the semester	Created the 1-credit class syllabus with timeline.	Winter 2014 (CHEM 219) syllabus 210
		Fall 2014 (CHEM 220) syllabus 223
During the semester	Created handouts for each topic students generated questions on.	Winter 2014 handouts 235
		Fall 2014 handouts 250
	Created a handout to guide students in peer review	208
	A graduate student reviewed all authored questions and suggested edits using the handout as a guide.	208

The current instructions on how to author questions in Sapling Learning can be found at:
http://www2.saplinglearning.com/help/high-school-teachers-admins/authoring

Students were provided with an instruction sheet containing the information from the website on how to author. A brief introduction to the main parts of authoring in Sapling Learning are provided below.

AUTHORING HOMEWORK QUESTIONS IN SAPLING

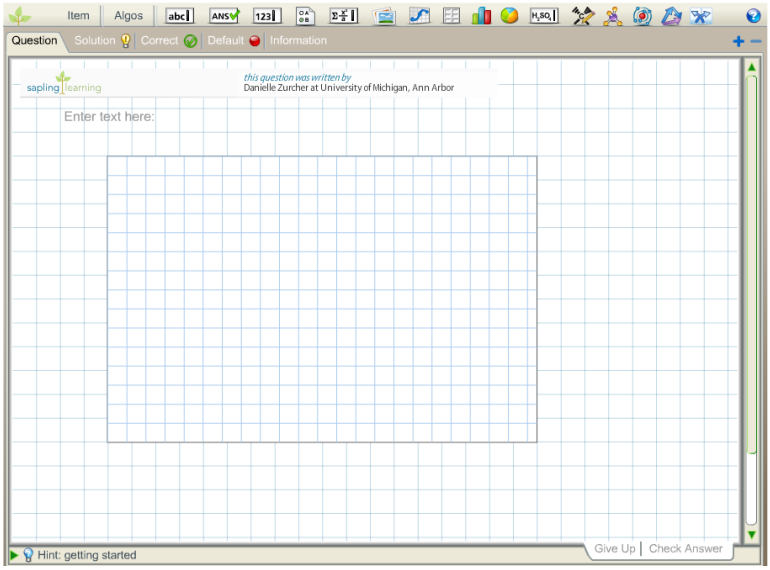
LEARNING TYPES OF TEMPLATES

To select the appropriate template, read through the following descriptions of the types of templates available. Select the one that best fits your question.

Chemical Equation – This module supports special formatting and symbols used in chemical equations, such as multi-level subscripts and stacked superscripts and subscripts for nuclear chemistry.

Mathematical Equation – This module recognizes a wide range of mathematical symbols and functions. The system uses standard order-of-operations and recognizes alternative forms of mathematical expressions.

Molecule Drawing (Organic) – This module provides tools for drawing different atoms, bonds, nonbonding electrons, charges, and reaction symbols (including electron-pushing arrows). In this version of the module, carbon atoms only display when hydrogen atoms are added. Hydrogen atoms and electrons are not graded. **THIS TEMPLATE WAS USED FOR MOST OF OUR QUESTIONS**



Multiple Choice – This module is used to create questions in which students can choose one of a group of options.

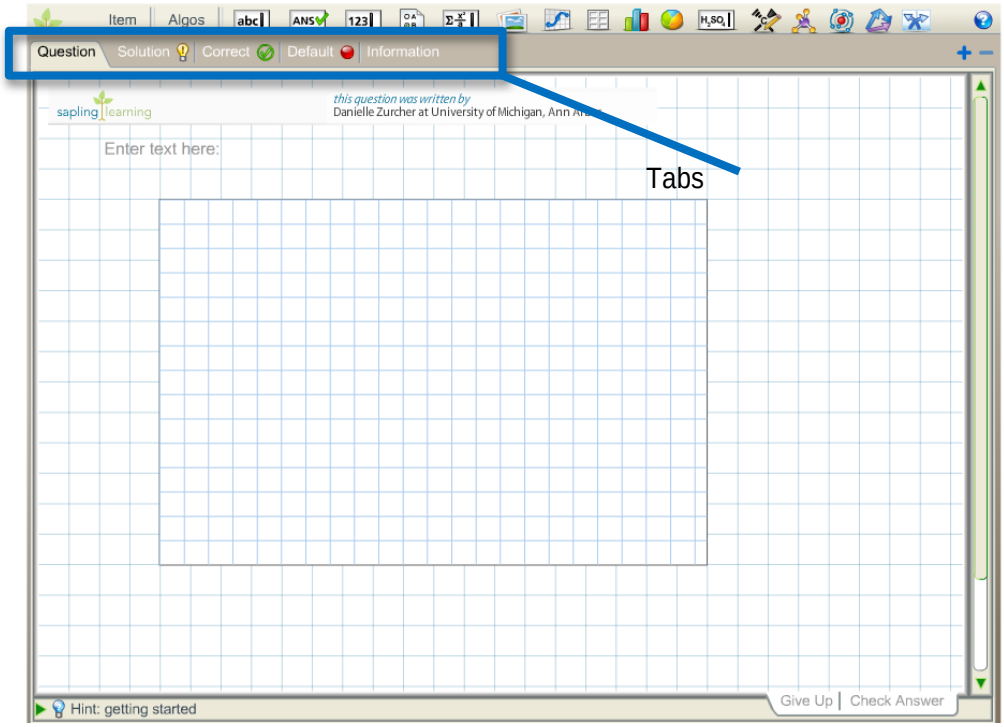
Multiple Select – This module is a variant of the Multiple Choice module in which students can choose more than one correct answer.

Numeric Entry – This module provides an entry space for numeric values. The module contains two potentially gradable fields: the numeric entry field and the units field.

Short Answer – This module provides an answer space for simple text entries. It is ideal for single- word answers, such as vocabulary questions.

DIFFERNCE BETWEEN DIFFERENT TABS FOR EACH QUESTION

After selecting the template your page will look like the page below:



There are five different tabs on every template.

Question tab – In this tab you place the question that the students will see.

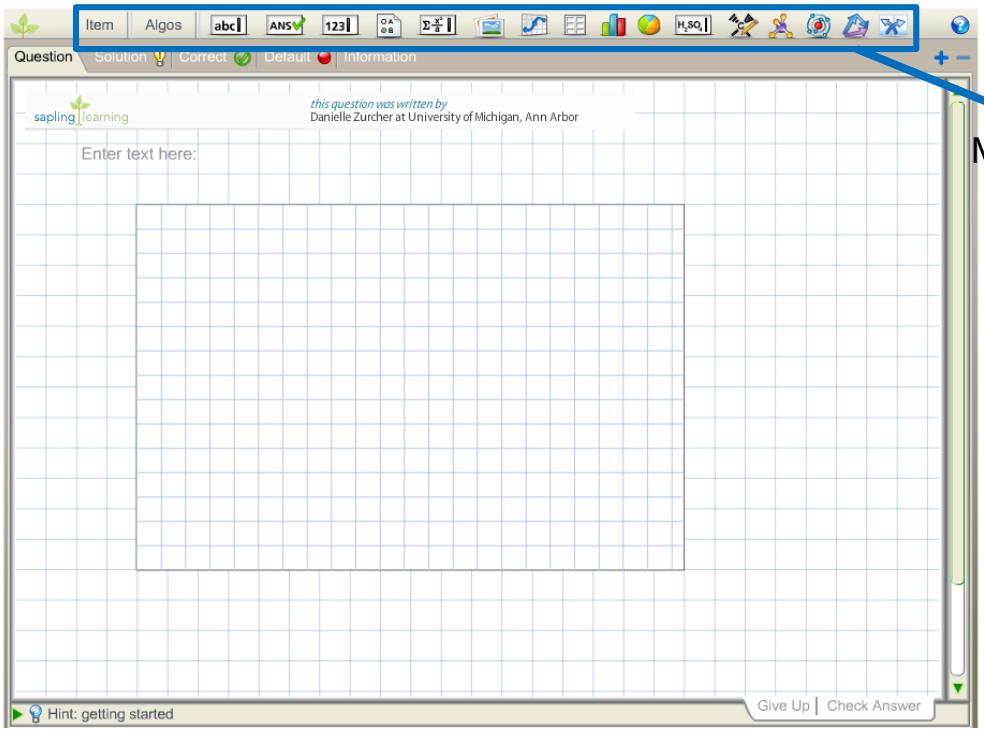
Solution tab – In this tab you will place the answer. This tab is what the student sees when they give up on the question.

Correct tab – In this tab you will place the answer. This tab is what the system uses to grade the actual question.

Default incorrect tab – In this tab you will place feedback that your students will receive if they get the wrong answer. (You may need multiple incorrect tabs in your question if you want to point out specific mistakes).

Information tab – This tab is where you will name and save your question.

THE DIFFERENT TYPES OF MODULES



Static text area  – This is an ungraded module used for question and feedback text. The module editor contains text formatting tools and common symbols. **You will use this module to type the text of the question you are authoring.**

Graded short text  – This module provides an answer space for simple text entries. It is ideal for single-word answers, such as vocabulary questions.

Graded numeric entry  – This module provides an entry space for numeric values and two gradable fields, the numeric entry field and the units field.

Graded multiple choice  – This module is used to create multiple-choice questions. The text area provides text formatting tools and common symbols and the order of choices can be randomized.

Graded or static symbolic equation  – This module supports a wide range of mathematical symbols and functions. The equation editor can evaluate up to 4 variables.

Graded or static animation or static image  – This module can be used to upload images and display them. Supported files are JPEG and SWF image formats.

Graded or static graph  – This module allows you to create graphs.

Static table – This module is an ungraded module and is used to display data in table form.

Static bar graph  – This module is an ungraded module and is used to display data in bar graph form.

Static pie chart  – This module is an ungraded module and is used to display data in pie chart form.

Graded or static chemical equation  – This module supports special formatting and symbols used in chemical equations, such as multi-level subscripts and stacked superscripts and subscripts for nuclear chemistry. **This module will be used to draw arrows from one 2-D molecule box to the next.**

Graded or static 2-D molecule  – This module is used to draw molecules. The molecule editor provides tool for drawing different atoms, bonds, nonbonding electrons, charges, and reaction symbols. **This module is the main module you will be using to author your question.**

Graded or static 3-D molecule  – This module can be used to upload PDB files (e.g. from ChemDraw).

Graded or static orbital diagram  – This module gives you the ability to grade drawn atomic orbitals.

Graded or static vector diagram  – This module give you the ability to grade drawn vector diagrams.

Sorting module  - This module allows you to create matching questions in which you can drag and sort items into categories.

For Fall 2013, “curved arrow notation” was the only topic for which problems were generated by SSG students. SSG leaders were tasked with authoring an example problem in Sapling Learning over three weeks to become familiar with the project and interface.

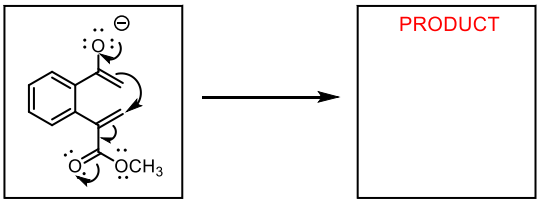
Timeline

Week 1	1. The four example problems (type I, II, III, or IV) were divided up among the eight SSG leaders (1 example problem/2 SSG leaders) 2. Each SSG leader in Sapling Learning: a. Solves their example problem b. Creates two reasonable incorrect answers c. Creates suggestions for what response should be associated with each incorrect answer d. Creates a generically useful response for incorrect answers that are not anticipated.
Week 2	Assignment: a. Peer review of another leaders authored problem. b. Leaders edit their questions based on feedback.
Week 3	Graduate student reviews questions and gives final feedback to each SSG leader.

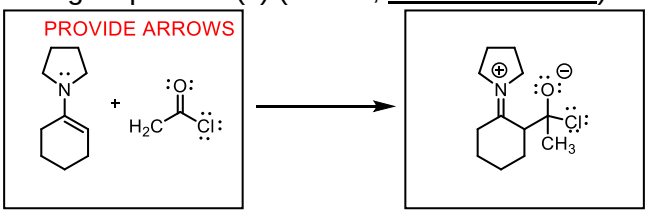
Question Types

Four question types each with a different format were used and are shown below.

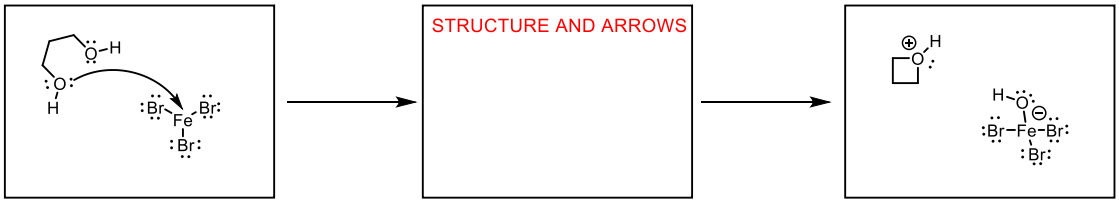
Type I: Follow the arrows from a starting material (A + arrows → *draw the product*)



Type II: Insert arrows to give product (s) (A → B, *draw the arrows*)

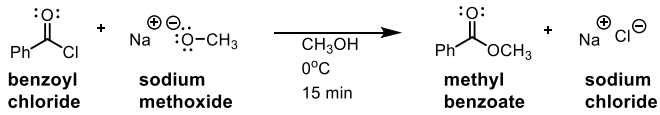


Type III: Problems that combine Type I and II
(A + arrows → *draw the intermediate and arrows* → B)



Type IV: Given A → B → C, etc. (verbal descriptions are used, *draw structures and arrows*)

The reaction depicted below is observed to take place quite rapidly under mild conditions.
The mechanism of the reaction is thought to occur in a two-step sequence.



benzoyl chloride + **sodium methoxide** → **methyl benzoate** + **sodium chloride**

In the spaces below, provide the structures and the curved arrrow mechanism, as described.

(a) In the first step, the oxygen atom of **sodium methoxide** forms a new single bond with the carbon atom of the carbon-oxygen double bond in **benzoyl chloride**. At the same time, the C-O pi bond breaks, resulting in a new oxygen anion. The sodium cation is a spectator ion, balancing the charges on the oxygen atoms, but not participating in the reaction.

provide: starting materials, arrows and balanced equation

(b) In the second step, the new oxygen anion formed in the first step reforms the C-O pi bond that was broken, and simultaneously, the C-Cl single bond is broken, resulting in the formation of **methyl benzoate** and a **chloride ion**. The sodium ion is once again a spectator ion.

provide: redraw the result from the balanced equation in part (a), then add the arrows that show the formation of the observed products, all of which should be included

INTRODUCTION TO THE PROJECT

Instructors in the organic chemistry program have been generally uninterested in the standard electronic homework systems because the underlying assumptions in these systems are at odds with a number of our most important pedagogical goals. In particular, we have not been interested in activities that would not reinforce our idea that students should be working to discuss and explain things to one another, face-to-face or in small groups, with tasks and problems for which there are not discrete answers.

On the other hand, we see great potential value in using the rigor of Sapling Learning's structural drawing interface to target a set of skill-based topics. Skill-based topics are core curriculum goals that are commonly and recurrently used to construct and provide explanations. These are the sorts of basic communication skills that we want students to have to be able to work effectively with one another.

Skill-based topics are the ones were we would like students to have 100% mastery of, and this mastery is achieved through having enough diverse – and yet rigorously monitored – problems to work on. You can read about how to drive and you can attend lessons, but none of this matters until you get behind the wheel. And we know that everyone comes to their mastery at different rates, with different amounts of practice that is nonetheless highly repetitive.

At the moment, there is a perceived gap between the skill level that can be achieved from the exercises in the textbook and the skills that are necessary for working on the coursepack (old exam) problems. This gap is not true for everyone because for many students, the book is enough. And for some students, the work they do with other students makes up the difference. But we know that there are still students who fail to master the basic skills, and this is one of the reasons they have trouble in the course.

Skill-based topics, by definition, are also ones that retain their value as the course goes on, and so they can be productively revisited to affirm mastery of these topics. As mentioned above, we think these are the skills for which we would like 100% of students to achieve mastery.

SKILL-BASED TOPICS FROM CHAPTERS 1-3

TOPIC: Curved Arrow Notation TYPES OF EXERCISES:

(i) follow the arrows from a starting material (A + arrows -•-> *draw the product*)
(ii) insert arrows for a given (A -•-> B, *draw the arrows*)
(iii) problems that combine both (A + arrows -•-> *draw intermediate, and arrows* -•-> B)
(iv) given A -•-> B -•-> C, etc. (verbal descriptions are used, *draw structures and arrows*)

TOPIC: Drawing Resonance Contributors TYPES OF EXERCISES:

(i) Drawing the resonance contributors (closed shell, limits on charges; evaluation)
(ii) Drawing a contributor as directed by some property
(iii) Drawing the most significant contributor starting from a minor contributor

TOPIC: ACID-BASE CHEMISTRY TYPES OF EXERCISES:

(i) Using pKa for predicting reaction equilibria
(ii) Predicting pKa from pKa table precedents
(iii) What is/are the form(s) at a given pH

We think that it will be an incredibly useful project for SSG students to learn how to generate, test, and critique problems using the Sapling Learning framework. Fall 2013, "curved arrow notation" will be the only topic for which problems will be generated by SSG students. By the end of the term, every student will have been responsible for leading the generation of one problem.

Fall Term 2013 Plan for the Project

Week 01	Sep 02: Sign-up (09/06/13)	
Week 02	Sep 09: First meeting and assignment	SAP-A: overview
Week 03	Sep 16:	SAP-A: assign problem; draft response
Week 04	Sep 23:	SAP-A: review response; finalize plan
Week 05	Sep 30: E1	SAP-A: learn to author; author
Week 06	Oct 07:	SAP-A: review draft; finalize
Week 07	Oct 14:	SAP-B: create problem; draft response
Week 08	Oct 21	SAP-B: review response; review
Week 09	Oct 28: E2	SAP-B: review; finalize
Week 10	Nov 04:	SAP-C: create problem; draft response
Week 11	Nov 11:	SAP-C: review response; review
Week 12	Nov 18:	SAP-C: review; finalize
Week 13	Nov 25: Break	
Week 14	Dec 02: E3	
Week 15	Dec 09: no meeting (FE 12/13/13)	

SAP-A: Training period – 4 curved arrow problems are distributed among the 8 groups

SAP-B: There are ca. 60-70 pairs of SSG students, so 60-70 problems get done in the SAP-B round. These are broken down as roughly 15-17 of each type. One student in each working pair takes the lead for the work of the pair.

SAP-C: Another 60-70 problems get done in the SAP-C round. The other member of the pair takes the lead in SAP-C. The problem is based on the same content as the SAP-B problem, but transformed into one of the other types.

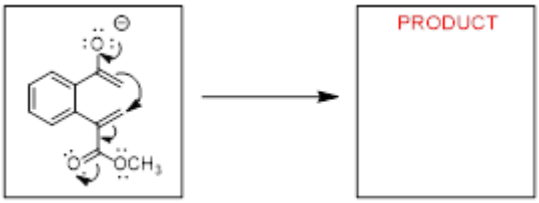
Once they are complete, and reviewed, the SAP-B problems will be opened up to CHEM 210 students, in general, for a hard trial (if we can work out the logistics for this).

There will be guidance for incorrect answers. However, it is anticipated that a set of STANDARDIZED pedagogical responses will emerge for a given type of problem, rather than giving specific hints for specific problems (i.e., for the Curved Arrow exercises, a response that delivered a mini-lesson reminder about the ground rules of curved arrows might be delivered, and this could be used repeatedly, instead of a reply customized to the specific structure; note that the errors might well be categorized, with the advice tailored to that type of error, e.g., “reminder: arrows need to start from the source of electrons”).

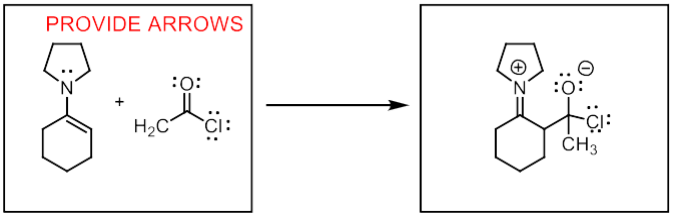
SAPLING-A

TOPIC: Curved Arrow Notation

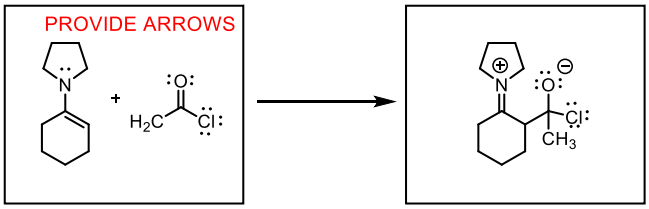
PROBLEM 01: TYPE 01: follow the arrows from a starting material (A + arrows -> *draw the product*)



PROBLEM 02: TYPE 02: insert arrows for a given (A -> B, *draw the arrows*)

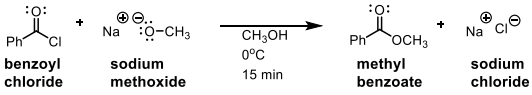


PROBLEM 03: TYPE 03: problems that combine both (A + arrows -> *draw intermediate, and arrows* -> B)



PROBLEM 04: TYPE 04: given A -> B -> C, etc. (verbal descriptions are used, *draw structures and arrows*)

The reaction depicted below is observed to take place quite rapidly under mild conditions.
The mechanism of the reaction is thought to occur in a two-step sequence.



benzoyl chloride | **sodium methoxide** | **methyl benzoate** | **sodium chloride**

In the spaces below, provide the structures and the curved arrrow mechanism, as described.

(a) In the first step, the oxygen atom of **sodium methoxide** forms a new single bond with the carbon atom of the carbon-oxygen double bond in **benzoyl chloride**. At the same time, the C-O pi bond breaks, resulting in a new oxygen anion. The sodium cation is a spectator ion, balancing the charges on the oxygen atoms, but not participating in the reaction.

provide: starting materials, arrows and balanced equation

(b) In the second step, the new oxygen anion formed in the first step reforms the C-O pi bond that was broken, and simultaneously, the C-Cl single bond is broken, resulting in the formation of **methyl benzoate** and a **chloride ion**. The sodium ion is once again a spectator ion.

provide: redraw the result from the balanced equation in part (a), then add the arrows that show the formation of the observed products, all of which should be included

Week 01 SSG Sign-Up

Week 02 Sep 09: First meeting, First assignment SAP-A: overview

SSG leaders review the intent of this project with the students in their groups, and possibly introduce the Sapling Learning system if there is adequate time to do so.

Week 03 Sep 16: SAP-A: assign problem; draft response

(a) SSG leaders will have divided up among the 4 problems (Type 01, 02, 03, or 04) at staff meeting
(b) SSGs will sub-divide into teams of 2 (with a group of 3 in the case of an odd number)
(c) Each group/problem will get a unique 6 digit Sapling Learning ID code (e.g. 34572)
(d) Assignment (done in ChemDraw):
    (i) Each SSG team solves their problem
    (ii) Each SSG team creates an array of reasonable, incorrect answers
    (iii) Each SSG team analyzes their array of incorrect answers for recurring themes for the errors, and creates suggestions for what response should be associated with each error
    (iv) There will be incorrect answers that are not anticipated, what should be the most generically useful response for incorrect answers that are not anticipated?

DUE: (a) The correct answer
(b) a set of incorrect answers along with the responses to go with each
(c) A suggestion for a generic response for unanticipated incorrect answers

Week 04 Sep 23: SAP-A: review response; finalize plan

1) The entire SSG shares its incorrect answers and the responses
2) The entire SSG compiles incorrect answers, considers others, reaches consensus on responses
3) Demonstration of Sapling Learning system
4) Assignment:
    (i) Each SSG gets the compiled responses from its section, and its partner section; starting from the compiled information, generate one more incorrect answer/reply

Week 05 Sep 30: E1 SAP-A: learn to author; author

(a) In-class authoring session on a sample problem (not one of the 4 from SAP-A)
(b) Assignment:

(i) Teams generate problems in Sapling Learning (yes, duplication) by midnight, Monday
(ii) Leaders review work for their sections before the SSG meetings

Week 06 Oct 07: SAP-A: review draft; finalize

(a) Leaders provide feedback to students from their review
(b) Peer Review: A team reviews work of another team
(c) Each SSG selects its best example, creates to-do list for those authors to publish final version
(d) Assignment:
(i) Final version of SSG's problem created by that one team
(ii) Each team selects a journal/year, uses a literature example to construct a curved arrow problem of the type they worked on in SAP-A (in ChemDraw, not Sapling)
(iii) Bring the suggested problem and a set of suggested incorrect responses, along with which of the standardized feedbacks would be used in reply, cleanly formatted so that it can be reviewed in next week's SSG meeting

Week 07 Oct 14: SAP-B: create problem; draft response

(a) Review drafted problems/incorrect answers/reply choices; gather feedback
(b) Assignment:
(i) Construct problem in Sapling Learning, due by midnight, Monday
(ii) Leaders carry out first review before SSGs meet

Week 08 Oct 21 SAP-B: review response; review

(a) Peer Review problems in Sapling; gather feedback
(b) Assignment: modify problem based on feedback

Week 09 Oct 28: E2 SAP-B: review; finalize

(a) review and finalize problems based on feedback
(b) Assignment:
(i) Finalize problem
(ii) Each team is assigned another genre of arrow problem and revises their SAP-B problem, accordingly: format the problem, suggest incorrect responses, attach feedback (reference to the work of other SSGs that perfected that genre will be needed)

Week 10 Nov 04: SAP-C: create problem; draft response

(a) Peer Review drafted problems/incorrect answers/reply choices; gather feedback
(b) Assignment:
    (i) Construct problem in Sapling, due by midnight, Monday
    (ii) Leaders carry out first review before SSGs meet

Week 11 Nov 11: SAP-C: review response; review

(a) Review problems in Sapling; gather feedback, esp. alternative answers
(b) Assignment: modify problem based on feedback

Week 12 Nov 25: SAP-C: review; finalize

(a) Review and finalize problems based on feedback
(b) Assignment:
    (i) Finalize problem
    (ii) Final review by leaders

Week 13 Nov 18:Break

Week 14 Dec 02: E3

Week 15 Dec 09: no meeting (Final Exam 12/13/13)

Name of the author:			
Name of the reviewer:			
Sapling ID of the question being reviewed:			
	Reviewer: Yes/No	**Reviewer: Comments**	**Author: Response - Edits made?**
General Questions			
Is the chemistry in the reaction correct?			
Is the question balanced (are all reagents accounted for)?			
Are the appropriate modules being used for the type of reaction?			
Does the question work in student mode (do you get the correct answer)?			
In the Question Tab:			
If nothing is to be graded in the box is it in static box mode?			
Do they have an appropriate number of boxes for the question?			
Is there a reaction arrow associated with the problem?			
Are all mechanistic arrows visible and correct (they don't overlap bonds)?			
Are all charges visible and correct?			
Do the structures look presentable?			
Is everything spelled correctly?			
Are there any fishhook arrows?			
Is the question balanced (are all reagents accounted for)?			
Do all carbons have hydrogens IF hydrogens are graded for? (If hydrogens are not graded for, skip this question)			

	Reviewer: Yes/No	Reviewer: Comments	Author: Response - Edits made?
In the Solution Tab			
Does it have the correct answer in the box?			
Are all arrows visible and correct (don't overlap bonds)?			
Are all charges visible and correct?			
Is there a thorough explanation of how to solve the problem?			
Do the structures look presentable?			
Is everything spelled correctly?			
In the Correct Tab			
Does at least one tab look the same as the solution tab?			
Does the question need multiple correct tabs? If so, are they present? (i.e. most benzene rings need multiple correct tabs)			
In the Incorrect Tabs (overall) - If one tab needs one of the following please indicate which tab in your response			
Does the problem have at least five incorrect tabs?			
Is the feedback relevant to the incorrect answer?			
Are there any spelling errors in the incorrect answer feedback?			
In the Default Tab			
Is there a default tab?			
Is it the last tab before the information tab?			
Is the answer box left blank?			
Is there general feedback written and does it make sense?			
In the Information Tab			
Is it labeled correctly?			
Is "focus" checked?			

CHEM 219
WINTER 2014
CREATING SKILL-BASED TEACHING MATERIALS

MEETINGS: 1 hour per week (arranged)

We are interested in using Sapling Learning's structural drawing interface to target a set of skill-based topics from CHEM 210. Skill-based topics are core curriculum goals that are commonly and recurrently used to construct and provide explanations. These are the sorts of basic communication skills that we want students to have to be able to work effectively with one another.

Skill-based topics are the ones where we would like students to have 100% mastery of, and this mastery is achieved through having enough diverse – and yet rigorously monitored – problems to work on. You can read about how to drive and you can attend lessons, but none of this matters until you get behind the wheel. And we know that everyone comes to their mastery at different rates, with different amounts of practice that is nonetheless highly repetitive.

At the moment, there is a perceived gap between the skill level that can be achieved from the exercises in the textbook and the skills that are necessary for working on the coursepack (old exam) problems. This gap is not true for everyone, because for many students, the book is enough. And for some students, the work they do with other students makes up the difference. But we know that there are still students who fail to master the basic skills, and this is one of the reasons they have trouble in the course.

Skill-based topics, by definition, are also ones that retain their value as the course goes on, and so they can be productively revisited to affirm mastery of these topics. As mentioned above, we think these are the skills for which we would like 100% of students to achieve mastery.

In your CHEM 219 session, we will take 10 skill-based topics and, prior to each session, you will generate 2 problems and their associated feedback that would be appropriate for use in the Sapling Learning system. During these sessions you will engage in peer review and discussion to revise and refine the subject matter issues.

As a supplemental activity, you can participate in the actual coding of the problems and their associated feedback into the Sapling Learning system, in order see what is necessary to create publication-quality content.

SKILL-BASED TOPICS FROM CHAPTERS 1-10 (CHEM 210)

TOPICS FROM CH 1-3 (Exam 1 Material)

SAP-I: Curved Arrow Notation

(i) Follow the arrows from a starting material
(ii) Insert arrows for a given reaction
(iii) Transformation problems that combine both

SAP-IIA: Drawing Resonance Contributors

Drawing the resonance contributors (closed shell, limits on charges; evaluation)

SAP-IIB: Drawing Resonance Contributors

(i) Drawing a contributor as directed by some property
(ii) Drawing the least to most significant resonance contributors

SAP-III: Acid-Base Chemistry

(i) Using pKa for predicting reactions
(ii) Predicting pKa from pKa table precedents
(iii) What is/are the form(s) at a given pH

TOPICS FROM CH 4-6 (Exam 2 Material)

SAP-IV: Transition State Drawings

SAP-V: Electrophilic Addition Reaction Mechanisms

SAP-VI: Structural Relationships (individual)

(i) Conformations
(ii) Stereoisomers

SAP-VII: Structural Relationships (comparative)

TOPICS FROM CH 7-9 (Exam 3 Material)

SAP-VIII: Reactions: Identification and classification

SAP-IX: Reactions: Application of general mechanistic type to specific examples

TOPICS FROM CH 10

SAP-X: Aromaticity And EAS

(i) Identification of aromatic compounds
(ii) EAS reactions

Winter Term 2014 Schedule

Jan 06: Recruiting and Scheduling

Jan 13: Introduction to Chem 219; standard weekly schedule Review Sapling authoring
Go through SAP-IIA example and claiming process
Select, claim and approve SAP-IIA problems Go through SAP-IIA module
Go through SAP-IIB and SAP-III examples
Assignment: *Author SAP-IIA problems*
Select and claim SAP-IIB problems

Jan 20: Peer review SAP-IIA
Approve SAP-IIB problems Go through SAP-IIB module
Assignment: *Author SAP-IIB problems*
Select and claim SAP-III problems

Jan 27: Peer review SAP-IIB
Approve SAP-III problems Go through SAP-III module
Assignment: *Author SAP-III problems*
Edit SAP-IIA and SAP-IIB problems

Feb 03: Peer review SAP-III
Go through SAP-IV and SAP-V examples
Assignment: *Edit SAP-III*
Turn in final versions of SAP-IIA, SAP-IIB, and SAP-III
Select and claim SAP-IV problems

Feb 10: Approve SAP-IV problems
Go through SAP-IV module
Go through SAP-VI and SAP-VII examples
Assignment: *Author SAP-IV problems*
Select and claim SAP-V problems

Feb 17: Peer review SAP-IV
Approve SAP-V problems Go through SAP-V

module

Assignment: *Author SAP-V problems*
Select and claim SAP-VI problems

Feb 24: Peer review SAP-V
Approve SAP-VI problems

Go through SAP-VI module

Assignment *Author SAP-VI problems*
Select and claim SAP-VII problems Edit SAP-IV problems

Mar 03: Spring Break

Mar 10: Peer review SAP-VI
Approve SAP-VII problems Go through SAP-VII module

Assignment: *Author SAP-VII problems*
Edit SAP-V and SAP-VI problems

Mar 17: Peer review SAP-VII
Go through SAP-VIII and SAP-IX examples

Assignment: *Edit SAP-VII problems*
Turn in final versions of SAP-IV, SAP-V, SAP-VI, and SAP-VII
Select and claim SAP-VIII problems

Mar 24: Approve SAP-VIII problems
Go through SAP-VIII module Go through SAP-X examples

Assignment: *Author SAP-VIII problems*
Select and claim SAP-IX problems

Mar 31: Peer review SAP-VIII
Approve SAP-IX problems Go through SAP-IX module

Assignment: *Author SAP-IX problems*
Select and claim SAP-X problems

Apr 07: Peer review SAP-IX
Approve SAP-X

problems Go
through SAP-X
module

Assignment: *Author SAP-X problems*
Edit SAP-VIII and SAP-IX problems

Apr 14: Peer review SAP-X
Answer last minute questions

Assignment: *Edit SAP-X problems*
Turn in final versions of SAP-VIII, SAP-IX, and SAP-X

Apr 21: Final versions due

Week 01 Jan 13: Review Sapling & Prepare SAP-IIA
In Class:

1) Introduction to CHEM 219

Throughout the semester, each student will be responsible for authoring 20 Sapling Learning problems, 2 per Skill-Based Topic. For each problem, the following process is expected:

a) Go through example problem (in class)
b) Select and claim problems (assigned)
c) Approve problems (in class)
d) Go through module (in class)
e) Author problems (assigned)
f) Peer review problems (in class)
g) Edit problems (assigned)
h) Turn in final versions (assigned)

2) Review experience with authoring problems in Sapling Learning. Discuss common problems with authoring in Sapling and how to avoid them in the future, based on both the students' experiences and the administrative review:

A. Always write down your 5-digit number identifying your authored question.
B. Be aware of the reagents used in the reaction you are authoring (i.e. is it acidic or basic conditions?).
C. If you are authoring a mechanism question, is the reaction really concerted?
D. Make sure you consider aesthetics of the problem, especially with the snap-to-grid function.
E. Make sure you take into account the limitations of Sapling, such as in ortho-substituted aromatic rings.

3) Go through SAP-IIA example and claiming process. Go through an example and discuss to consensus regarding the problem format for the SAP-IIA. Note, specifically, how this would appear in Sapling. Discuss claiming process. See handout(s) for examples.

4) Select, claim and approve SAP-IIA problems. Each student selects and claims 2 problems for SAP-IIA, approved by the instructor.

5) Review SAP-IIA module. Discuss specific skills necessary for authoring the SAP-IIA problems in Sapling Learning.

6) Go through SAP-IIB example. Go through an example and discuss to

consensus regarding the problem format for the SAP-IIB. Note, specifically, how this would appear in Sapling. See handout(s) for examples.

Assignment: Each student must complete the following during the week:

a) Author both SAP-IIA problems in their entirety in Sapling Learning, complete with a minimum of 5 incorrect answers (although this is to the discretion of the instructor).

b) Select and claim both SAP-IIB problems. Bring these problems printed out in ChemDraw format.

Week 02 Jan 20: Review SAP-IIA & Prepare SAP-IIB

In Class:

1) Peer review SAP-IIA problems. Review and provide feedback on all problems. Be sure to record this feedback carefully in order to edit/add/complete the revisions that will be necessary.

2) Each student gets each of their SAP-IIB problems approved by the instructor.

3) Review SAP-IIB module. Discuss specific skills necessary for authoring the SAP-IIB problems in Sapling Learning.

4) Go through SAP-III example. Go through an example and discuss to consensus regarding the problem format for the SAP-III. Note, specifically, how this would appear in Sapling. See handout(s) for examples.

Assignment: Each student must complete the following during the week:

a) Author both SAP-IIB problems in their entirety in Sapling Learning, complete with a minimum of 5 incorrect answers (although this is to the discretion of the instructor).

b) Select and claim both SAP-III problems. Bring these problems printed out in ChemDraw format.

Week 03 Jan 27: Review SAP-IIB & Prepare SAP-III

In Class:

1) Peer review SAP-IIB problems. Review and provide feedback on all problems. Be sure to record this feedback carefully in order to edit/add/complete the revisions that will be necessary.

2) Each student gets each of their SAP-III problems approved by the instructor.

3) Review SAP-III module. Discuss specific skills necessary for authoring the SAP-IIB problems in Sapling Learning.

Assignment: Each student must complete the following during the week:

a) Author both SAP-III problems in their entirety in Sapling Learning, complete with a minimum of 5 incorrect answers (although this is to the discretion of the instructor).

b) Begin to edit SAP-IIA and SAP-IIB problems based on feedback and discussion.

Week 04 Feb 03: Review SAP-III & Revise II-III

In Class:

1) Peer review SAP-III problems. Review and provide feedback on all problems. Be sure to record this feedback carefully in order to edit/add/complete the revisions that will be necessary.

2) Go through SAP-IV example. Go through an example and discuss to consensus regarding the problem format for the SAP-IV. Note, specifically, how this would appear in Sapling. See handout(s) for examples.

3) Go through SAP-V example. Go through an example and discuss to consensus regarding the problem format for the SAP-V. Note, specifically, how this would appear in Sapling. See handout(s) for examples.

Assignment: Each student must complete the following during the week:

a) Complete all edits on all SAP-IIA, SAP-IIB, and SAP-III problems.

b) Select and claim both SAP-IV problems. Bring these problems printed out in ChemDraw format.

Week 05 Feb 10: Introduce IV-VII & Prepare SAP-IV

In Class:

1) Each student gets each of their SAP-IV problems approved by the instructor.

2) Review SAP-IV module. Discuss specific skills necessary for authoring the SAP-IIB problems in Sapling Learning.

3) Go through SAP-VI example. Go through an example and discuss to consensus regarding the problem format for the SAP-VI. Note, specifically, how this would appear in Sapling. See handout(s) for examples.

4) Go through SAP-VII example. Go through an example and discuss to consensus regarding the problem format for the SAP-VII. Note, specifically, how this would appear in Sapling. See handout(s) for examples.

Assignment: Each student must complete the following during the week:

a) Author both SAP-IV problems in their entirety in Sapling Learning, complete with a minimum of 5 incorrect answers (although this is to the discretion of the instructor).

b) Select and claim both SAP-V problems. Bring these problems printed out in ChemDraw format.

Week 06 Feb 17: Review SAP-IV & Prepare SAP-V

In Class:

1) Peer review SAP-IV problems. Review and provide feedback on all problems. Be sure to record this feedback carefully in order to edit/add/complete the revisions that will be necessary.

2) Each student gets each of their SAP-V problems approved by the instructor.

3) Review SAP-V module. Discuss specific skills necessary for authoring the SAP-IIB problems in Sapling Learning.

Assignment: Each student must complete the following during the week:

a) Author both SAP-V problems in their entirety in Sapling Learning, complete with a minimum of 5 incorrect answers (although this is to the discretion of the instructor).

b) Select and claim both SAP-VI problems. Bring these problems printed out in ChemDraw format.

Week 07 Feb 24: Review SAP-V & Prepare SAP-VI

In Class:

1) Peer review SAP-V problems. Review and provide feedback on all problems. Be sure to record this feedback carefully in order to edit/add/complete the revisions that will be necessary.

2) Each student gets each of their SAP-VI problems approved by the instructor.

3) Review SAP-VI module. Discuss specific skills necessary for authoring the SAP-IIB problems in Sapling Learning.

Assignment: Each student must complete the following during the week:

a) Author both SAP-VI problems in their entirety in Sapling Learning, complete with a minimum of 5 incorrect answers (although this is to the discretion of the instructor).

b) Select and claim both SAP-VII problems. Bring these problems printed out in ChemDraw format.

c) Begin to edit SAP-IV and SAP-V.

Week 00 Mar 03: Spring Break

Week 08 Mar 10: Review SAP-VI & Prepare SAP-VII

Week 12

In Class:

1) Peer review SAP-VI problems. Review and provide feedback on all problems. Be sure to record this feedback carefully in order to edit/add/complete the revisions that will be necessary

2) Each student gets each of their SAP-VII problems approved by the instructor.

3) Review SAP-VII module. Discuss specific skills necessary for authoring the SAP-IIB problems in Sapling Learning.

Assignment: Each student must complete the following during the week:

a) Author both SAP-VII problems in their entirety in Sapling Learning, complete with a minimum of 5 incorrect answers (although this is to the discretion of the instructor).

b) Continue to edit SAP-IV and SAP-V. Begin to edit SAP-VI.

Week 09 Mar 17: Review SAP-VII & Revise IV-VII

In Class:

1) Peer review SAP-VII problems. Review and provide feedback on all problems. Be sure to record this feedback carefully in order to edit/add/complete the revisions that will be necessary.

2) Go through SAP-VIII example. Go through an example and discuss to consensus regarding the problem format for the SAP-VIII. Note, specifically, how this would appear in Sapling. See handout(s) for examples.

3) Go through SAP-IX example. Go through an example and discuss to consensus regarding the problem format for the SAP-IX. Note, specifically, how this would appear in Sapling. See handout(s) for examples.

Assignment: Each student must complete the following during the week:

a) Complete all edits on all SAP-IV, SAP-V, SAP-VI, and SAP-VII problems.

Week 12

c) Select and claim both SAP-VIII problems. Bring these problems printed out in ChemDraw format.

Week 10 Mar 24: Introduce VIII-X & Prepare SAP-VIII

In Class:

1) Each student gets each of their SAP-VIII problems approved by the instructor.

2) Review SAP-VIII module. Discuss specific skills necessary for authoring the SAP-IIB problems in Sapling Learning.

3) Go through SAP-X example. Go through an example and discuss to consensus regarding the problem format for the SAP-VI. Note, specifically, how this would appear in Sapling. See handout(s) for examples.

Assignment: Each student must complete the following during the week:

a) Author both SAP-VIII problems in their entirety in Sapling Learning, complete with a minimum of 5 incorrect answers (although this is to the discretion of the instructor).

b) Select and claim both SAP-IX problems. Bring these problems printed out in ChemDraw format.

Week 11 Mar 31: Review SAP-VIII & Prepare SAP-IX

In Class:

1) Peer review SAP-VIII problems. Review and provide feedback on all problems. Be sure to record this feedback carefully in order to edit/add/complete the revisions that will be necessary.

2) Each student gets each of their SAP-IX problems approved by the instructor.

3) Review SAP-IX module. Discuss specific skills necessary for authoring the SAP-IIB problems in Sapling Learning.

Assignment: Each student must complete the following during the week:

Week 12

a) Author both SAP-IX problems in their entirety in Sapling Learning, complete with a minimum of 5 incorrect answers (although this is to the discretion of the instructor).

b) Select and claim both SAP-X problems. Bring these problems printed out in ChemDraw format.

In Class:

1) Peer review SAP-IX problems. Review and provide feedback on all problems. Be sure to record this feedback carefully in order to edit/add/complete the revisions that will be necessary.

2) Each student gets each of their SAP-X problems approved by the instructor.

3) Review SAP-X module. Discuss specific skills necessary for authoring the SAP-IIB problems in Sapling Learning.

Assignment: Each student must complete the following during the week:

a) Author both SAP-X problems in their entirety in Sapling Learning, complete with a minimum of 5 incorrect answers (although this is to the discretion of the instructor).

b) Begin to edit SAP-VIII and SAP-IX.

Week 13 Apr 14: Review SAP-IX & Revise VIII-IX

In Class:

1) Peer review SAP-X problems. Review and provide feedback on all problems. Be sure to record this feedback carefully in order to edit/add/complete the revisions that will be necessary.

2) Discuss any last-minute questions and reactions.

Week 14 Apr 21: Final Versions Due

CHEM 220
FALL 2014
CREATING SKILL-BASED TEACHING MATERIALS

MEETINGS: 1 hour per week (arranged)

We are interested in using Sapling Learning's structural drawing interface to target a set of skill-based topics from CHEM 215. Skill-based topics are core curriculum goals that are commonly and recurrently used to construct and provide explanations. These are the sorts of basic communication skills that we want students to have to be able to work effectively with one another.

Skill-based topics are the ones where we would like students to have 100% mastery of, and this mastery is achieved through having enough diverse - and yet rigorously monitored - problems to work on. You can read about how to drive and you can attend lessons, but none of this matters until you get behind the wheel. And we know that everyone comes to their mastery at different rates, with different amounts of practice that is nonetheless highly repetitive.

At the moment, there is a perceived gap between the skill level that can be achieved from the exercises in the textbook and the skills that are necessary for working on the coursepack (old exam) problems. This gap is not true for everyone, because for many students, the book is enough. And for some students, the work they do with other students makes up the difference. But we know that there are still students who fail to master the basic skills, and this is one of the reasons they have trouble in the course.

Skill-based topics, by definition, are also ones that retain their value as the course goes on, and so they can be productively revisited to affirm mastery of these topics. As mentioned above, we think these are the skills for which we would like 100% of students to achieve mastery.

In your CHEM 220 session, we will take 10 skill-based topics and, prior to each session, you will generate 2 problems and their associated feedback that would be appropriate for use in the Sapling Learning system. During these sessions you will engage in peer review and discussion to revise and refine the subject matter issues.

As a supplemental activity, you can participate in the actual coding of the problems and their associated feedback into the Sapling Learning system, in order see what is necessary to create publication-quality content.

Sapling Learning topics for CHEM 215

CHEM 215 is a different sort of challenge than CHEM 210, because the content is more about applying the fundamental concepts developed in CHEM 210 rather than it is about developing a new suite of concepts. Thus, the idea of “skill-based” problems looks a bit different.

Thematically, however, a few patterns for working with reactions might be

useful. First, every simple chemical reaction A+B->C can be thought of in

three distinct ways:

I. predict the products: A+B-> ?
II. transformation: A -?-> C or B -?-> C
III. synthesis: ? -?-> C

So one thing we can do is take (nearly) any problem and transform it into the other two forms (most of the time). It might take hints or other information to make this work, particularly in Sapling Learning, but it is a source of problems that makes a point about not getting locked into one format.

Second, some of the topics in carbonyl chemistry benefit from clearly differentiating big picture thinking from mid-level thinking, from mechanism details. For example, it is easy to get buried in the details of acid-catalyzed mechanisms for ketal/acetal, acylation, and enol condensation, when blocking them off as overall mechanistic steps with clear descriptions can be useful.

Big Pictures:

(a) Aldehyde + 2 alcohols -> acetal + water
(b) Ester-A + alcohol-B -> ester-B + alcohol-A
(c) Ketone + Aldehyde -> Aldol condensation + water

Mid-Level Pictures:

(a) Ketone (undergoes acid-catalyzed addition of alcohols) -> hemi-ketal
Hemi-ketal (undergoes acid-catalyzed Sn1 of the OH, with a second alcohol) -> ketal

(b) Aldehyde 1 (undergoes acid-catalyzed tautomerization) -> enol
Aldehyde 2 (undergoes acid-catalyzed addition by enol) -> aldol reaction product Aldol Reaction product (undergoes E1cb) -> aldol condensation product + water

Detailed Pictures:

Ketone + Alcohol (protonation of carbonyl oxygen; nucleophilic addition of alcohol to protonated carbonyl; deprotonation of oxonium ion) -> hemi-ketal

SKILL-BASED TOPICS FROM CHAPTERS 13-17 + Special Topics (CHEM 215)

TOPICS FROM CH 13-14 (Exam 1 Material)

SAP-I: REFORMATTING REACTIONS

(a) oxidation of alcohols and aldehydes
(b) substitution of alcohols to give halides
(c) reactions that give ethers
(d) ring opening of oxiranes
(e) organometallic (HM & RM) additions to ald/ket
(f) big picture ald/ket to (thio)acetal/(thio)ketal/imine(et al) SAP-II: MID-LEVEL PICTURE RELATIONSHIPS
(a) ald/ket to [hemi](thio)acetal/(thio)ketal/imine(et al)
(b) deconstructing alcohols into (up to) 3 carbonyl addition pathways
(c) deconstructing alcohols into alkene addition & oxirane opening pathways
(d) sequencing step-wise transformations with carbonyl addition/ox/addition SAP-III: DETAILED PICTURE
(a) acid versus base oxirane opening
(b) any mid-level step mechanism (from Topic II)

TOPICS FROM CH 15-17, 21.3-5 (Exam 2 Material)

SAP-IV: REFORMATTING REACTIONS

(a) acyl transfer reactions (heteroatom nucleophiles)
(b) acyl transfer reactions (organometallic HM and RM nucleophiles)
(c) inter/intra enol/ate substitution reactions
(d) inter/intra enol/ate addition reactions (aldol)
(e) inter/intra enol/ate acylation reactions (hydrolysis/decarboxylation)
(f) inter/intra conjugate addition reactions (heteratom, enol/ate, RM) SAP-V: MID-LEVEL PICTURE RELATIONSHIPS
(a) acylation reactions via tetrahedral intermediate
(b) aldol reaction versus aldol condensation
(c) pre- versus post-hydrolysis/decarboxylation with active methylenes
(d) sequenced reactions (conjugate addition + intramol aldol, cf Robinson) SAP-VI: DETAILED PICTURE
(a) acid versus base acylation mechanisms
(b) any mid-level step mechanism (from Topic V)

TOPICS FROM CH Special Topics (Exam 3 Material)

SAP-VII: REFORMATTING REACTIONS

(a) Diels-Alder (regio- & stereochemistry)
(b) Carbohydrate anomeric
(c) Carbohydrate alcohol reactions
(d) Protection, deprotection, coupling of amino acids SAP-VIII: DETAILED PICTURE
(a) acid versus base acylation mechanisms
(b) any mid-level step mechanism

Fall Term 2014 Schedule

Sept 15: Recruiting and Scheduling

Sept 22: Introduction to Chem 220; standard weekly schedule Review Sapling authoring
Go through SAP-I example and claiming process
Select, claim and approve SAP-I problems Go through SAP-I module
Go through SAP-II and SAP-III examples
Assignment: Author SAP-I problems
Select and claim SAP-II problems

Sept 29: Peer review SAP-I
Approve SAP-II problems Go through SAP-II module
Assignment: Author SAP-II problems
Select and claim SAP-III problems

Oct 06: Peer review SAP-II
Approve SAP-III problems
Go through SAP-III module
Go through SAP-IV examples
Assignment: Author SAP-III problems
Select and claim SAP-IV problems Edit SAP-I and SAP-II problems

Oct 13: Peer review SAP-III
Approve SAP-IV problems Go through SAP-IV module

Assignment: Author SAP-IV
Edit SAP-III problems

Oct 20: Peer review SAP-IV
Go through SAP-V examples
Assignment: Edit SAP-IV problems
Turn in final versions of SAP-I, SAP-II, SAP-III, and SAP-IV Select and claim SAP-V problems

Oct 27: Approve SAP-V problems
Go through SAP-VI and SAP-VII examples
Assignment: Author SAP-V problems
Select and claim SAP-VI problems

Nov 03: Peer review SAP-V
Approve SAP-VI problems
Go through SAP-VI module
Assignment Author SAP-VI problems
Select and claim SAP-VII problems Edit SAP-V problems

Nov 10: Peer review SAP-VI
Approve SAP-VII problems Go through SAP-VII module
Go through SAP-VIII examples
Assignment: Author SAP-VII problems
Select and claim SAP-VIII problems Edit SAP-VI problems

Nov 17: Peer review SAP-VII
Approve SAP-VIII problems Go through SAP-VIII module
Assignment: Author SAP-VIII problems
Edit SAP-VII problems
Turn in final versions of SAP-V, SAP-VI, and SAP-VII

Nov 24: Thanksgiving Break

Dec 01: Peer review SAP-VIII
Answer last minute questions

Assignment: Edit SAP-VIII
Turn in final versions of SAP-VIII

Dec 08: Final versions of all problems due

Week 01 Sept 22: Review Sapling & Prepare SAP-I

In Class:

1) Introduction to CHEM 220
Throughout the semester, each student will be responsible for authoring 16 Sapling Learning problems, 2 per Skill-Based Topic. For each problem, the following process is expected:

a) Go through example problem (in class)
b) Select and claim problems (assigned)
c) Approve problems (in class)
d) Go through module (in class)
e) Author problems (assigned)
f) Peer review problems (in class)
g) Edit problems (assigned)
h) Turn in final versions (assigned)

2) Review experience with authoring problems in Sapling Learning. Discuss common problems with authoring Sapling and how to avoid them in the future, based on both the students' experiences and the administrative review:

A. Always write down your 5-digit number identifying your authored question.
B. Be aware of the reagents used in the reaction you are authoring (i.e. is it acidic or basic conditions?).
C. If you are authoring a mechanism question, is the reaction really concerted?
D. Make sure you consider aesthetics of the problem, especially with the snap-to-grid function.
E. Make sure you take into account the limitations of Sapling, such as in ortho-substituted aromatic rings.

3) Go through SAP-I example and claiming process. Go through an example and discuss to consensus regarding the problem format for the SAP-I. Note, specifically, how this would appear in Sapling. Discuss claiming process. See handout(s) for examples.

4) Select, claim and approve SAP-I problems. Each student selects and claims 2 problems for SAP-I, approved by the instructor.

5) Review SAP-I module. Discuss specific skills necessary for authoring the SAP-I problems in Sapling Learning.

6) Go through SAP-II example. Go through an example and discuss to consensus regarding the problem format for the SAP-II. Note, specifically, how this would appear in Sapling. See handout(s) for examples.

Assignment: Each student must complete the following during the week:

a) Author both SAP-I problems in their entirety in Sapling Learning, complete with a *minimum* of 5 incorrect answers (although this is to the discretion of the instructor).

b) Select and claim both SAP-II problems. Bring these problems printed out in ChemDraw format.

Week 02 Sept 29: Review SAP-I & Prepare SAP-II

In Class:

1) Peer review SAP-I problems. Review and provide feedback on all problems. Be sure to record this feedback carefully in order to edit/add/complete the revisions that will be necessary.

2) Each student will have both of his or her SAP-II problems approved by the instructor.

3) Review SAP-II module. Discuss specific skills necessary for authoring the SAP-II problems in Sapling Learning.

4) Go through SAP-III example. Go through an example and come to a consensus regarding the problem format for SAP-III. Note, specifically, how this would appear in Sapling. See handout(s) for examples.

Assignment: Each student must complete the following during the week:

a) Author both SAP-II problems in their entirety in Sapling Learning, complete with a

minimum of 5 incorrect answers (although this is to the discretion of the instructor).

b) Select and claim both SAP-III problems. Bring these problems printed out in ChemDraw format.

Week 03 Oct 06: Review SAP-II & Prepare SAP-III

In Class:

1) Peer review SAP-II problems. Review and provide feedback on all problems. Be sure to record this feedback carefully in order to edit/add/complete the revisions that will be necessary.

2) Each student will have both of his or her SAP-III problems approved by the instructor.

3) Review SAP-III module. Discuss specific skills necessary for authoring the SAP-III problems in Sapling Learning.

Assignment: Each student must complete the following during the week:

a) Author both SAP-III problems in their entirety in Sapling Learning, complete with a
minimum of 5 incorrect answers (although this is to the discretion of the instructor).

b) Select and claim both SAP-IV problems. Bring these problems printed out in ChemDraw format.

c) Begin to edit SAP-I and SAP-II problems based on feedback and discussion.

Week 04 Oct 13: Review SAP-III & Prepare SAP-IV

In Class:

1) Peer review SAP-III problems. Review and provide feedback on all problems. Be sure to record this feedback carefully in order to edit/add/complete the revisions that will be necessary.

2) Each student will have both of his or her SAP-IV problems approved by the instructor.

3) Review SAP-IV module. Discuss specific skills necessary for authoring the SAP-IV problems in Sapling Learning.

Assignment: Each student must complete the following during the week:

a) Author both SAP-IV problems in their entirety in Sapling Learning, complete with a minimum of 5 incorrect answers (although this is to the discretion of the instructor).

b) Begin to edit SAP-III problems based on feedback and discussion.

Week 05 Oct 20: Review SAP-IV & Introduce SAP-V

In Class:

1) Peer review SAP-IV problems. Review and provide feedback on all problems. Be sure to record this feedback carefully in order to edit/add/complete the revisions that will be necessary.

2) Go through SAP-V example. Go through an example and discuss to consensus regarding the problem format for the SAP-V. Note, specifically, how this would appear in Sapling. See handout(s) for examples.

Assignment: Each student must complete the following during the week:

a) Begin to edit SAP-IV problems based on feedback and discussion.

b) Complete all edits on all SAP-I, SAP-II, SAP-III, and SAP-IV problems.

c) Select and claim both SAP-V problems. Bring these problems printed out in ChemDraw format.

Week 06 Oct 27: Prepare SAP-V & Introduce SAP-VI and SAP-VII

In Class:

1) Each student will have both of his or her SAP-V problems approved by the

instructor.

2) Go through SAP-VI example. Go through an example and discuss to consensus regarding the problem format for the SAP-VI. Note, specifically, how this would appear in Sapling. See handout(s) for examples.

3) Go through SAP-VII example. Go through an example and discuss to consensus regarding the problem format for the SAP-VII. Note, specifically, how this would appear in Sapling. See handout(s) for examples.

Assignment: Each student must complete the following during the week:

a) Author both SAP-V problems in their entirety in Sapling Learning, complete with a *minimum* of 5 incorrect answers (although this is to the discretion of the instructor).

b) Select and claim both SAP-VI problems. Bring these problems printed out in ChemDraw format.

Week 07 Nov 03: Review SAP-V & Prepare SAP-VI

In Class:

1) Peer review SAP-V problems. Review and provide feedback on all problems. Be sure to record this feedback carefully in order to edit/add/complete the revisions that will be necessary.

2) Each student will have both of his or her SAP-VI problems approved by the instructor.

3) Review SAP-VI module. Discuss specific skills necessary for authoring the SAP-VI problems in Sapling Learning.

Assignment: Each student must complete the following during the week:

a) Author both SAP-VI problems in their entirety in Sapling Learning, complete with a
minimum of 5 incorrect answers (although this is to the discretion of the instructor).

b) Select and claim both SAP-VII problems. Bring these problems printed out in ChemDraw format.

c) Begin to edit SAP-V problems based on feedback and discussion.

Week 08 Nov 10: Review SAP-VI & Prepare SAP-VII

In Class:

1) Peer review SAP-VI problems. Review and provide feedback on all problems. Be sure to record this feedback carefully in order to edit/add/complete the revisions that will be necessary.

2) Each student will have both of his or her SAP-VII problems approved by the instructor.

3) Review SAP-VII module. Discuss specific skills necessary for authoring the SAP-VII problems in Sapling Learning.

4) Go through SAP-VIII example. Go through an example and discuss to consensus regarding the problem format for the SAP-VIII. Note, specifically, how this would appear in Sapling. See handout(s) for examples.

Assignment: Each student must complete the following during the week:

a) Author both SAP-VII problems in their entirety in Sapling Learning, complete with a
minimum of 5 incorrect answers (although this is to the discretion of the instructor).

b) Select and claim both SAP-VIII problems. Bring these problems printed out in ChemDraw format.

c) Begin to edit SAP-VI problems based on feedback and discussion.

Week 09 Nov 17: Review SAP-VII & Prepare SAP-VIII

In Class:

1) Peer review SAP-VII problems. Review and provide feedback on all problems. Be sure to record this feedback carefully in order to edit/add/complete the revisions that will be necessary.

2) Each student will have both of his or her SAP-VIII problems approved by the instructor.

3) Review SAP-VIII module. Discuss specific skills necessary for authoring the SAP-VIII problems in Sapling Learning.

Assignment: Each student must complete the following during the week:

a) Author both SAP-VIII problems in their entirety in Sapling Learning, complete with a
minimum of 5 incorrect answers (although this is to the discretion of the instructor).

b) Begin to edit SAP-VII problems based on feedback and discussion.

Week 10 Nov 24: Thanksgiving Break

Week 11 Dec 01: Review SAP-VIII & Conclusions

In Class:

1) Peer review SAP-VIII problems. Review and provide feedback on all problems. Be sure to record this feedback carefully in order to edit/add/complete the revisions that will be necessary.

2) Discuss the final review process & address any questions/concerns.

Assignment: Each student must complete the following during the week:

a) Begin to edit SAP-VIII problems based on feedback and discussion.

b) Complete all edits on all SAP-V, SAP-VI, SAP-VII, and SAP-VIII problems.

Week 12 Dec 08: Final Versions Due

SAP-IIA: Drawing Resonance Contributors

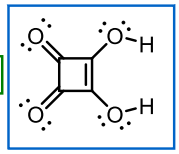
Format 1: Draw a resonance contributor

Squaric acid (Compound D) has been used to treat warts in children who have a skin infection caused by human papillomavius (*J Am Acad Dermatol*. **2000**, *42*, 803). The doubly deprotonated form of squaric acid (Compound E) is a di-anion that has a set of 3 other significant resonance contributors that (i) have all closed shell atoms, (ii) maintain charges of -1/0/+1 on the atoms, and (iii) keep negative charges located on the oxygen atoms.

Draw one of these other resonance contributors. Be sure to show all electron pairs and formal charges.

Module - Static Text

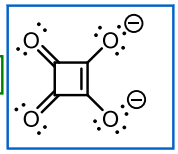
Compound **D**



Module - 2D molecule

Module - Static Text

Compound **E**



Module - 2D molecule

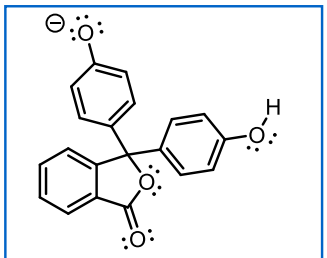
For the answer use:

Module - 2D molecule

Format 2: Draw the set of curved arrows connecting two resonance contributors

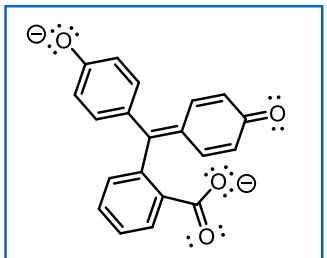
Phenolphthalien is a common acid-base indicator. The acidic (colorless) and basic (red-colored) forms are shown below. The basic (red-colored) form has a number of other significant resonance contributors. Provide the set of curved arrows on basic form **I** that can be used to explicitly show the relationship between the two basic forms (I and II) shown here.

Module - Chemical Equation



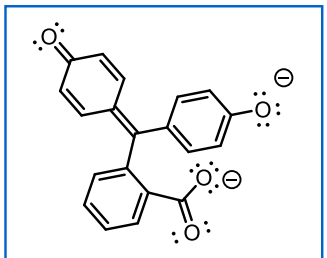
Acidic (colorless) form

Module - 2D molecule



Basic (red-color) form **I**

Module - 2D molecule



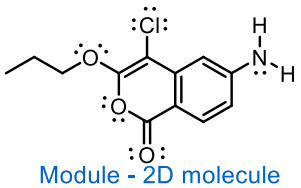
Basic (red-color) form II

Module - 2D molecule

Format 3: Draw the most significant resonance contributor

Toxoplasmosis is an infection that can be passed from cats to humans, and which results in flu-like symptoms. Molecules like the Compound **A** are observed to enhance the ability of toxoplasmosis to invade its host cells (not a good thing). This was reported in *Nature Chem. Bio. 2013, 9, 651*. Answer the following questions about Compound **A**.

There is a single significant resonance contributor (all closed shell atoms, all formal charges -1/0/+1) where the nitrogen atom's electrons have been delocalized to an oxygen atom. Draw this resonance contributor.



Module - 2D molecule

Module - Static Text Compound **A**

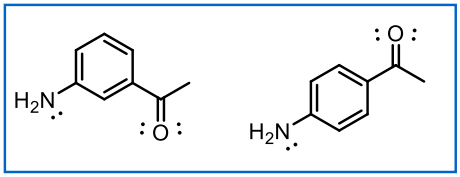
For the answer use:

Module - 2D molecule

SAP-IIB: Drawing Resonance Contributors

Format 1: Drawing a contributor as directed by some property

The length of the carbon-nitrogen bond in molecule **6** is different than the length of the carbon-nitrogen bond in molecule **7**. *Indicate which of these two molecules has the shorter carbon-nitrogen bond, and draw the **single** Lewis structure (with all atoms closed shell) that best **explains** your answer. Be sure to include all formal charges and draw in non-bonded electrons.*



Module - 2D molecule

Molecule **6**

Molecule **7**

Module - Static Text

The molecule with the shortest carbon-nitrogen bond is? Module - Multiple Choice

Molecule **6**
Molecule **7**

Lewis structure that explains your answer.

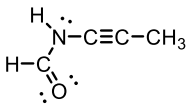
Module - 2D molecule

Format 2: Drawing the least to most significant resonance contributors

Ynamides (e.g. Molecule **2**) are useful building blocks for organic synthesis and have found applications in the construction of many significant biologically active molecules and natural products. One resonance form (A) of Molecule **2** is drawn below.

(a) Draw the other two resonance forms (B and C) of Molecule **2** that have all closed-shell atoms and formal charges of -1, 0, or +1 on all atoms. Be sure to include all non-zero formal charges and draw in all non-bonded electrons.

Module - 2D molecule



Molecule **2**
Resonance form A

Module - Static Text

Module - Chemical Equation

Module - 2D molecule

Molecule **2**
Resonance form B

Module - Static Text

Module - Chemical Equation

Module - 2D molecule

Molecule **2**
Resonance form C

Module - Static Text

(b) Which of the three resonance forms of Molecule **2** is the ***most*** significant contributor to the structure of Molecule **2**?

Module - Multiple Choice

Form A
Form B
Form C

(c) Which of the three resonance forms of Molecule **2** is the ***least*** significant contributor to the structure of Molecule **2**?

Module - Multiple Choice

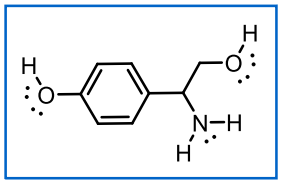
Form A
Form B
Form C

SAP-III: ACID-BASE CHEMISTRY

Format 1: Using pKa for predicting reactions

The amino alcohol **2** shown below can be obtained through reduction of tyrosine (a naturally occurring amino acid). Derivatives of **2** have been examined as potential anticancer agents. Which of the following bases can completely deprotonate ($K_{eq} > 10^3$) the most acidic proton in amino alcohol **2**.

Module - 2D molecule



Amino Alcohol **2**

Module - Static Text

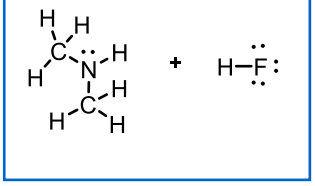
Module - Multiple Choice

NaBr
$CsOCH_2CH_3$
NaH
$NaNH_2$
NH_3

Format 2: Predicting pKa from pKa table precedents

Amines (like dimethylamine) are very versatile reagents in organic reactions. Predict any proton transfer that is likely to occur and evaluate the K_{eq} by filling in the appropriate exponent. Also, draw complete structures for all products and be sure to balance your equations.

Module - 2D molecule



Module - Chemical Equation

Module - 2D molecule

Module - Static Text

$K_{eq} = 10^X$

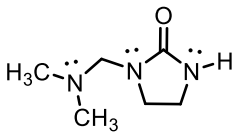
X =

Module - Graded Short Text

Format 3: What is/are the form(s) at a given pH

Many important biologically active molecules contain imidazolidin-2-one subunits. For example, molecule 8 has been investigated as a potentially useful antidepressant. The pKa of the most acidic proton in molecule 8 is 17, whereas the conjugate acid formed by protonation of the most basic atom in molecule 8 has a pKa of 11.

Module - 2D molecule



Module - Static Text

Molecule **8** pKa = 17
pKa of Conjugate Acid = 11

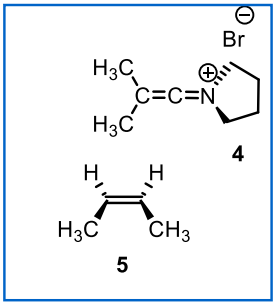
Provide the structure of the major species present in a pH 9 solution of molecule **8**.

Module - 2D molecule

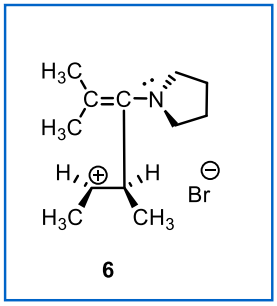
SAP-IV: Transition State Drawings

Kereniminium ions (e.g. **4**) undergo cycloaddition reactions with alkenes such as **5** to provide cyclobutane products (e.g. **7**). Experiments indicate this reaction proceeds via a two-step mechanism. First, the nucleophilic alkene attacks the electrophilic iminium ion to afford a carbocation intermediate (**6**). This intermediate then undergoes an intramolecular reaction to form a carbon-carbon bond and close the four-membered ring.

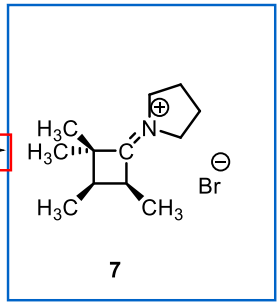
Module - 2D molecule



Module - 2D molecule



Module - 2D molecule

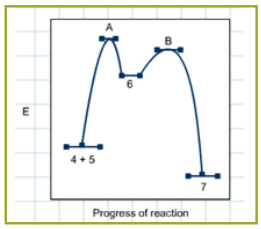


Module - Chemical Equation

Module - Chemical Equation

An energy diagram for the conversion of **4**+**5** to **7** is shown below. Given this energy diagram, answer the following questions.

Module - Graded or Static Graph



(a) The rate-determining step of the conversion of **4** + **5** to **7** is?

Module - Multiple Choice

Step one
Step two
Both occur at equal rates

(b) Which letter or number on the energy diagram represents the lowest energy transition state?

Module - Graded Short Text

(c) Is the conversion of **4** + **5** to **7** thermodynamically favorable?

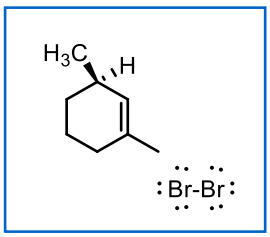
Module - Graded Short Text

SAP-V: Electrophilic Addition Reactions

Format 1: Predict intermediate or product reactions

Draw the product of the reaction that has only one R stereocenter.

Module - 2D molecule



Module - Chemical Equation

Module - 2D molecule

Format 2: Predict the starting material

Provide the starting material.

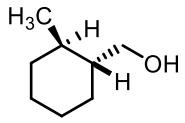
Module - 2D molecule

Module - Static Text

1) BH_3
2) $NaOH, H_2O_2$

Module - Chemical Equation

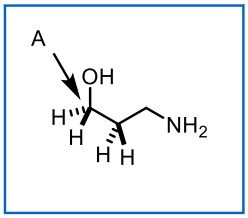
Module - 2D molecule



SAP-VI: Structural Relationships (individual)

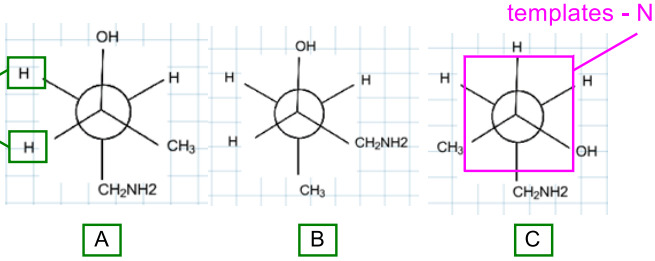
Format 1: Conformations

Module - 2D molecule



Module - Graded or Static Images
To find the image go to - upload image - templates - Newman staggered

Module - Static Text



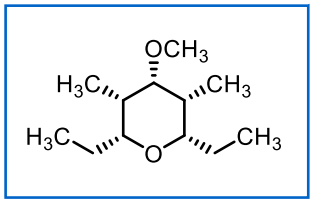
A B C

Module - Static Text

Which Newman projection of the above molecule viewed from Bond A is the most stable? Type in the letter below.

Module - Graded Short Text

Format 2: Stereoisomers



Module - 2D molecule

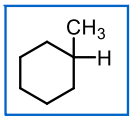
For the above molecule select each description that applies.

Module - Multiple Choice

- is not optically active
- has an enantiomer
- has at least one chiral diastereomer
- contains at least one R stereocenter
- has an achiral (meso) diastereomer

Format 3: Least and most stable chair conformations

Draw the two possible chair conformations of the molecule below and indicate which one is more stable.



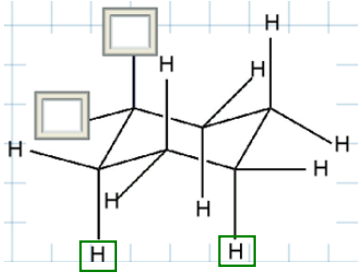
Module - 2D molecule

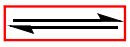
There are two ways of asking for students to fill in the chair

1) They just have to fill in the substituents on one carbon (chair on the left below)

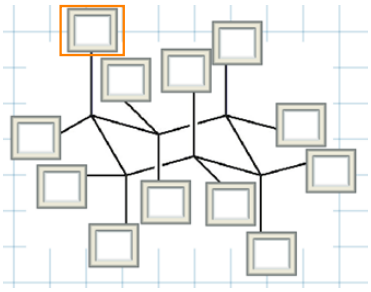
2) The have to fill in all the substituents (chair on the right below)

Module - Graded Short Text





Module - Chemical Equation



Module - Static Text

A

B

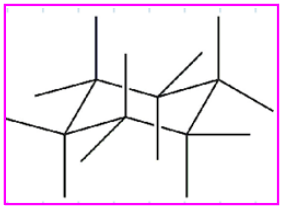
Which chair is more stable?

A
B

Module - Multiple Choice

To get the chair image add the module -graded or static images

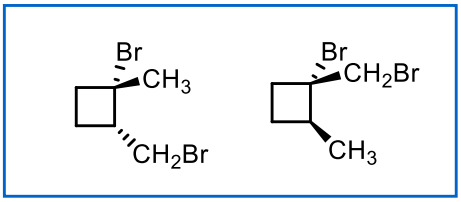
- To find the image got to upload image templates
- Click on Chair1 for the chair on the left above and Chair_2 for the flipped version (chair on the right above).



Module - Graded or Static Images

SAP-VII: Structural Relationships (comparative)

Module - 2D molecule



For the above molecules select each description that applies

Module - Static Text

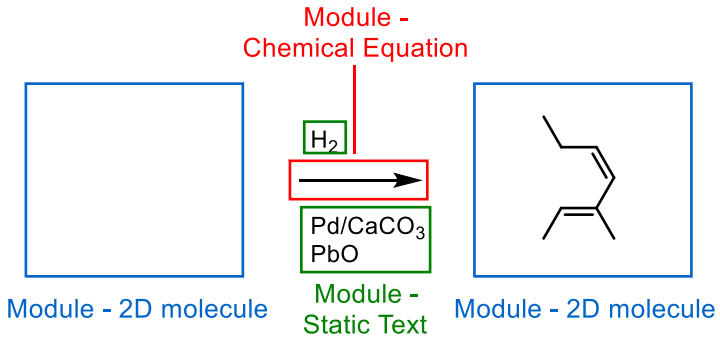
Module - Multiple Choice

They are structural isomers
They are enantiomers
They are diastereomers
They are conformational isomers
They are different molecules
Both are optically active

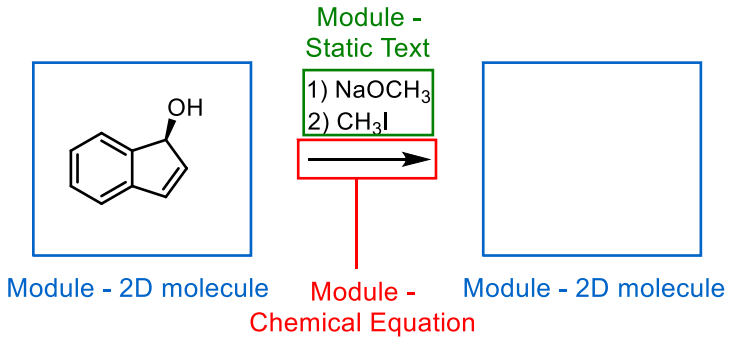
SAP-VIII: Reactions – identification and classification

Types – Electrophilic addition reactions, hydrogenation, ozonolysis, SN1, SN2, E1, E2, Epoxidation

Format 1: Predict the starting material



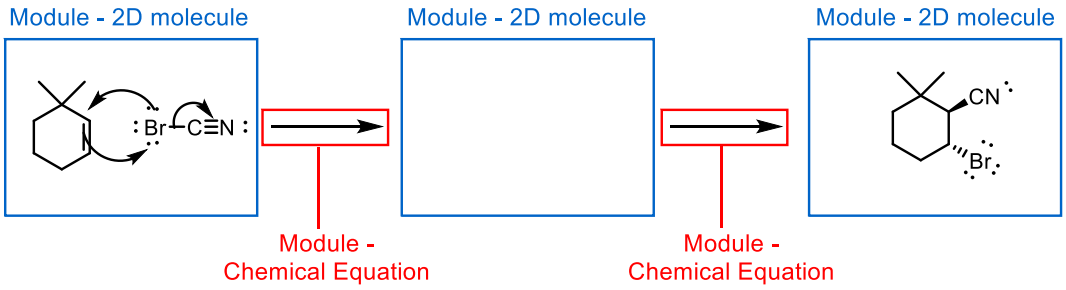
Format 1: Predict the product



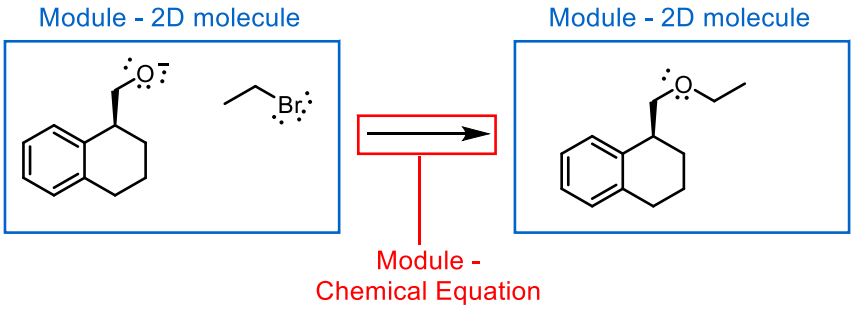
SAP-IX: Reactions – applications of general mechanistic type

Types – Electrophilic addition reactions, SN1, SN2, E1, E2, Epoxidation

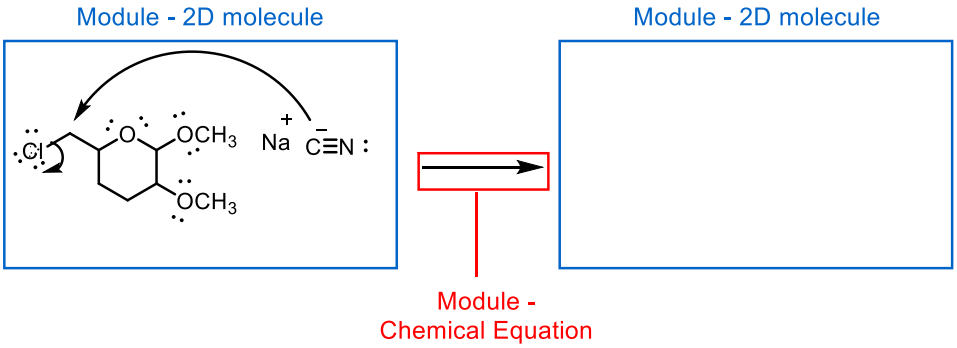
Format 1: Predict the intermediate and provide the arrows to the product



Format 2: Provide arrows to make the product



Format 3: Follow the arrows to predict the starting material

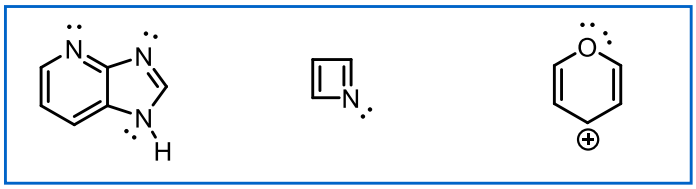


SAP-X: Aromaticity and EAS

Format 1: Identification of aromatic compounds

Predict which compounds below are aromatic.

Module - 2D molecule



A B C

Module - Multiple Choice

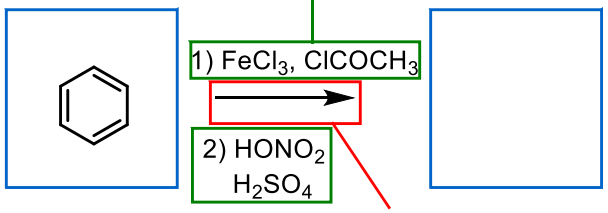
A
B
C

Format 2: EAS reactions provide the product

Module - Static Text

Module - 2D molecule

Module - 2D molecule

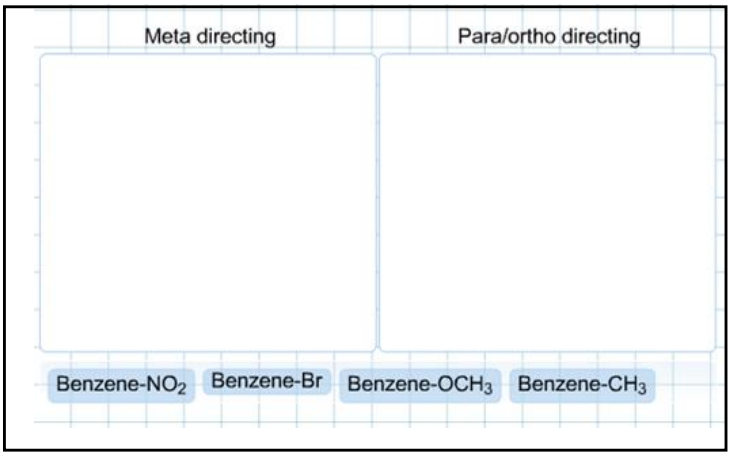


Module - Chemical Equation

Format 3: Understanding directing groups

Can ask meta vs para/ortho directing or inductive vs resonance

Sorting bin module



SAP-I: Reformatting reactions

Directions: Choose **ONE** type of exercise and **ONE** format

TYPES OF EXERCISES:

(a) oxidation of alcohols and aldehydes (Reagents: PCC, wet CrO3, swern reagents, or equivalent)

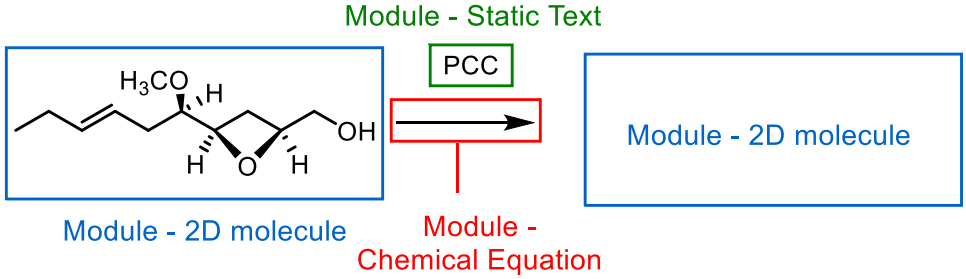
(b) substitution of alcohols to give halides (Reagents: PCl5, HX (X = Cl, Br, I), PCl3, SOCl2)

(c) ring opening of oxiranes (acid vs base conditions)

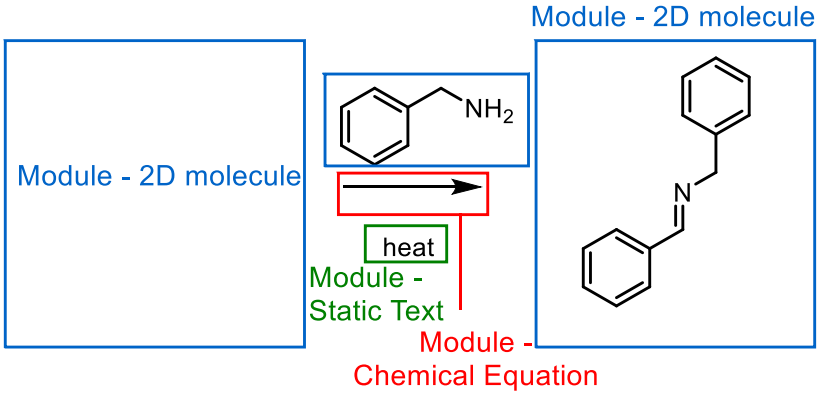
(d) organometallic (Hydrides and alkyl anions) additions to aldehyde/ketone

(e) big picture ald/ket to (thio)acetal/(thio)ketal/imine

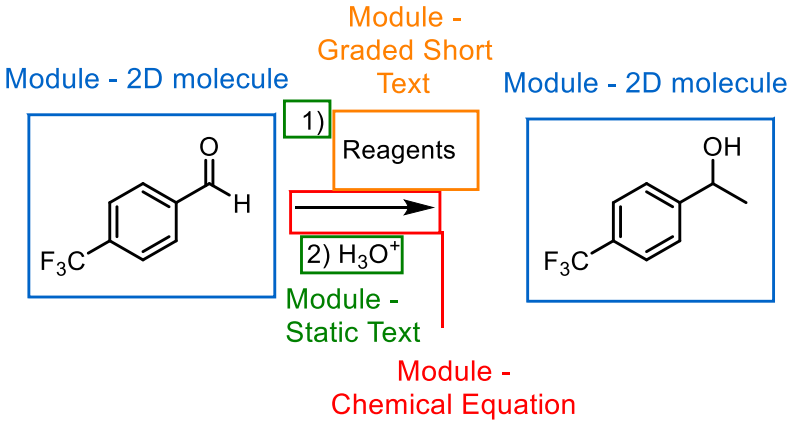
Format 1: Predict the product (example of type (a))



Format 2: Predict the starting material (example of type (e))



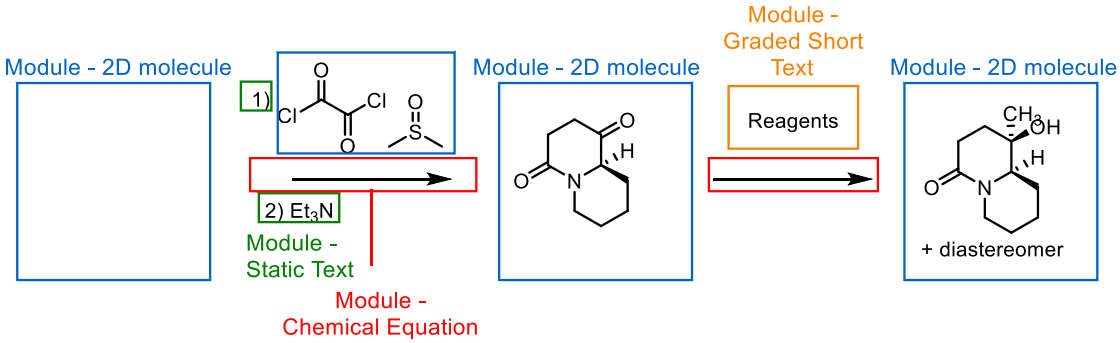
Format 3: Give the reagents (example of type (d))



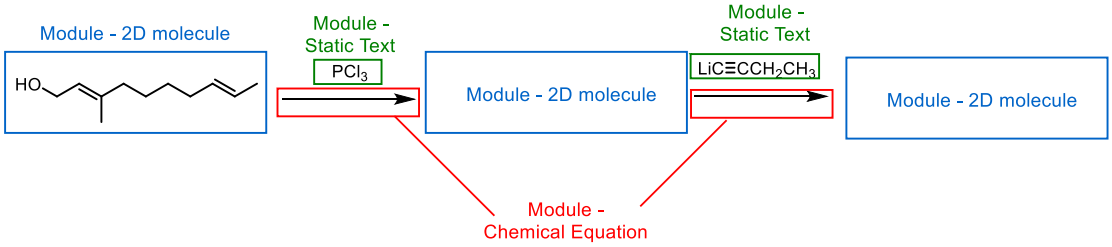
Format 4: Combinations of the above formats

For these combinations you can use a 210 reaction for one step out of the two steps if you want

Ex. 1- Predict starting material and give reagents (example of type (a) and (d))



Ex. 2 – Predict the product x2 (example of type (b) and 210 SN2)



SAP-II: Mid-level picture relationships

Directions: Choose **ONE** type of exercise and **ONE** format

TYPES OF EXERCISES:

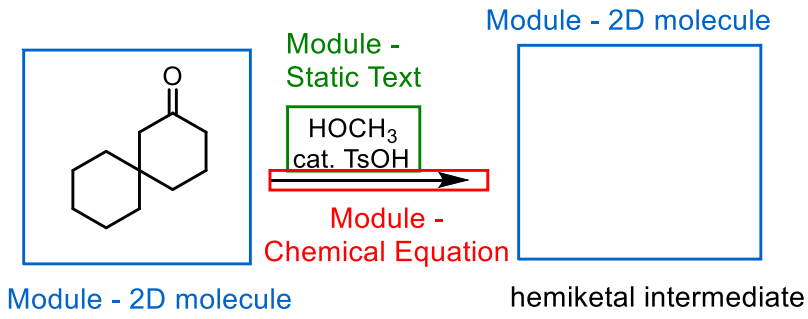
(a) Aldehyde/ketone to [hemi](thio)acetal/(thio)ketal/imine

(b) Deconstructing (retrosynthesis) alcohols into (up to) 3 carbonyl addition pathways

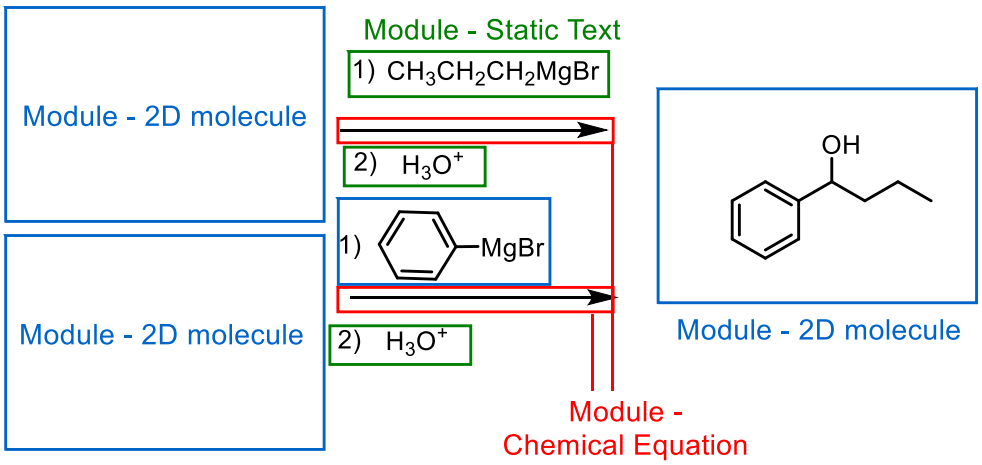
(c) Deconstructing (retrosynthesis) alcohols into alkene addition & oxirane opening pathways

(d) Sequencing step-wise transformations with carbonyl addition/ox/addition

Format 1: Predict the product (example of type (a))

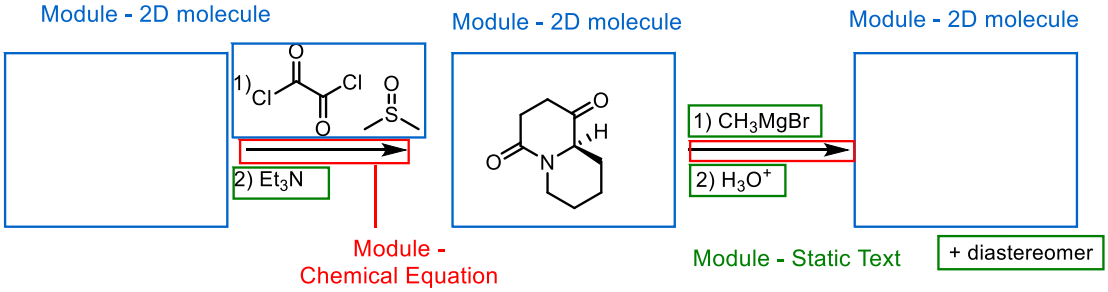


Format 2: Predict the SM (example of type (b))



Format 3: Combinations of the above formats

Ex. 1- Predict starting material and give reagents (example of type (d))



SAP-III: Detailed Picture

Directions: Choose **ONE** type of exercise and **ONE** format

TYPES OF EXERCISES:

(a) aldehyde/ketone to [hemi](thio)acetal/(thio)ketal/imine

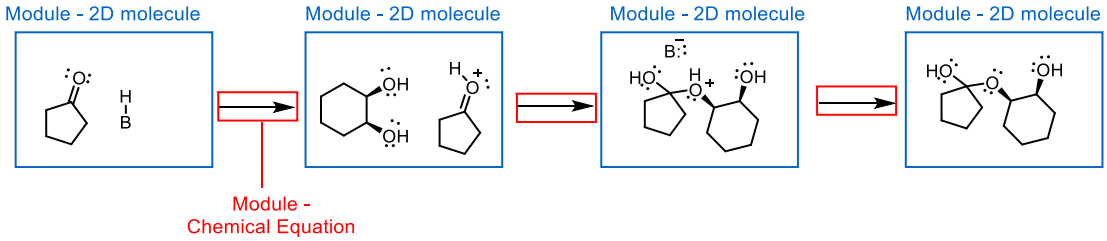
(b) acid vs. base oxirane opening

(c) oxidation to alcohols and aldehydes

(d) substitution of alcohols to give halides

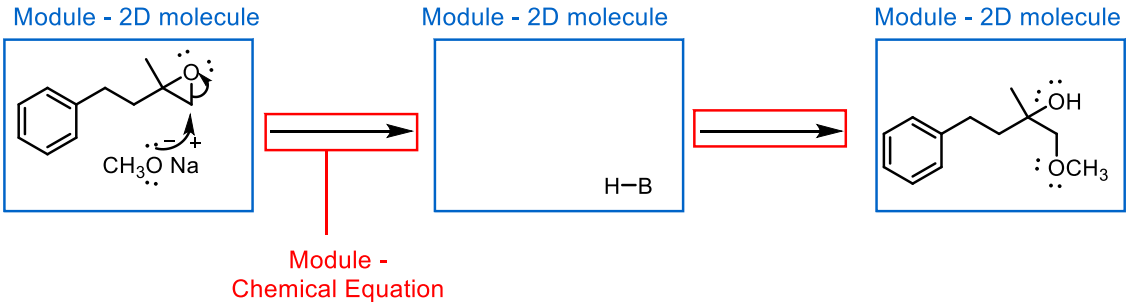
(e) organometallic additions to ald/ket

Format 1: Provide the arrows for all steps to the product (example of type (a))

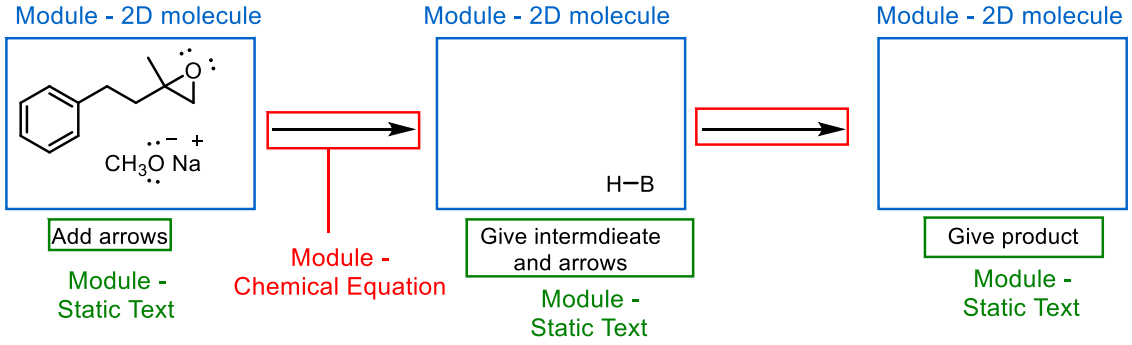


Format 2: Predict the intermediate and provide arrows to the product (example of type (b))

(a) Easier mechanistic option



(b) A more complicated problem using the same reaction



SAP-IV: Reformatting reactions

Directions: Choose **ONE** type of exercise and **ONE** format

TYPES OF EXERCISES:

(a) acyl transfer reactions (heteroatom nucleophiles)

(b) acyl transfer reactions (organometallic HM and RM nucleophiles)

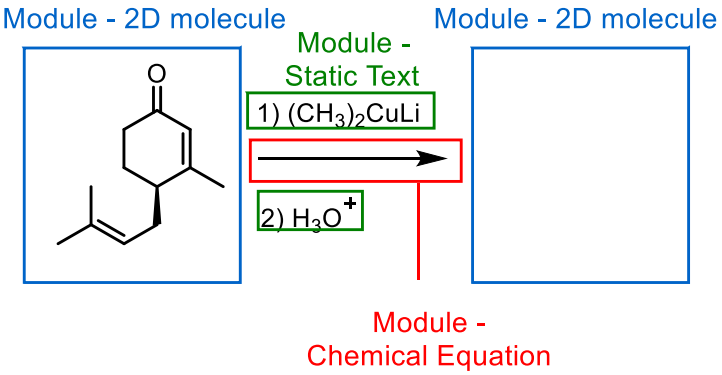
(c) inter/intra enol/ate substitution reactions

(d) inter/intra addition reactions (aldol/claisen)

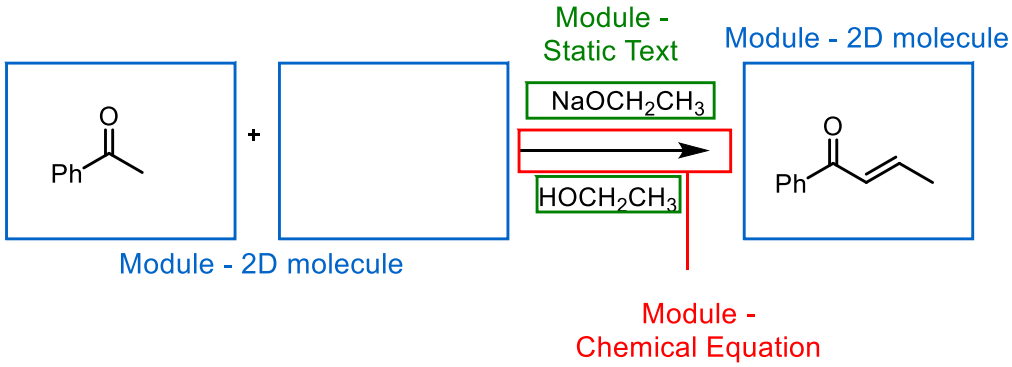
(e) decarboxylation reaction

(f) inter/intra conjugate addition reactions (heteratom, enol/ate, TM, i.e. things like Michael addition)

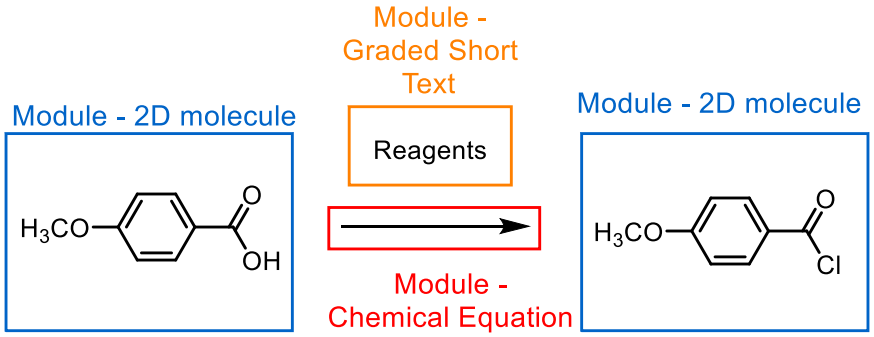
Format 1: Predict the product (example of type (f))



Format 2: Predict the starting material (example of type (d))



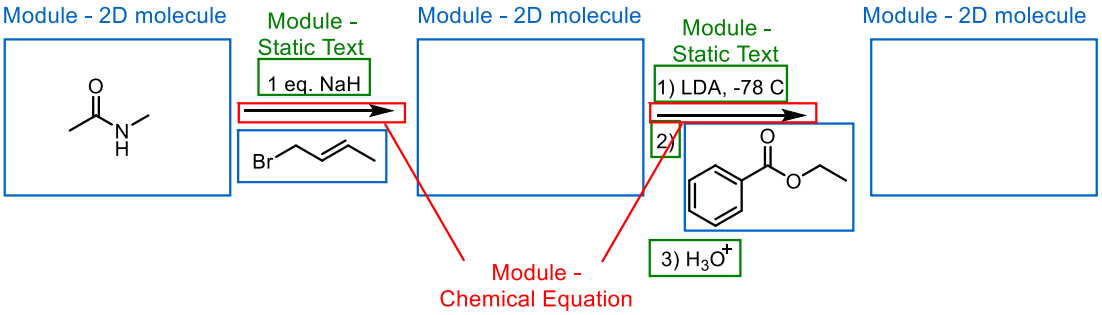
Format 3: Give the reagents (example of type (a))



Format 4: Combinations of the above formats

For these combinations you can use a 210 reaction for one step out of the two steps if you want

Ex. 1 – Predict the product x2 (example of type (d))



SAP-V: Mid-level picture relationships

Directions: Choose **ONE** type of exercise and **ONE** format

TYPES OF EXERCISES:

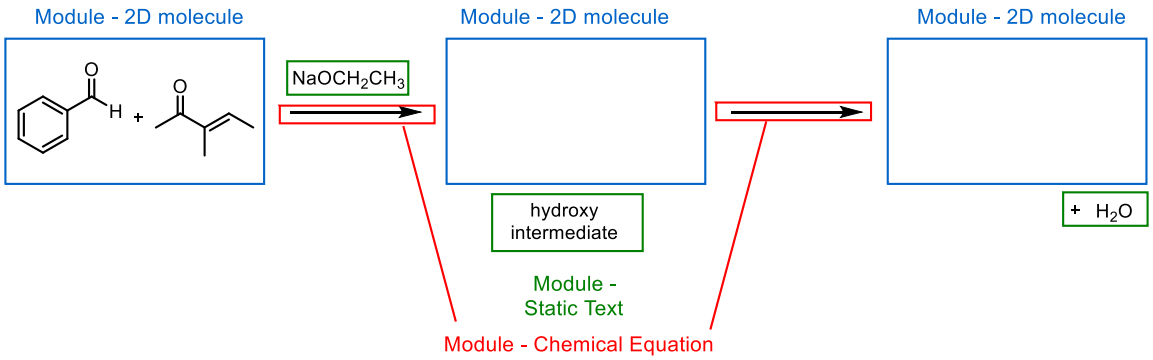
(a) acylation reactions via tetrahedral intermediate

(b) aldol reaction versus aldol condensation

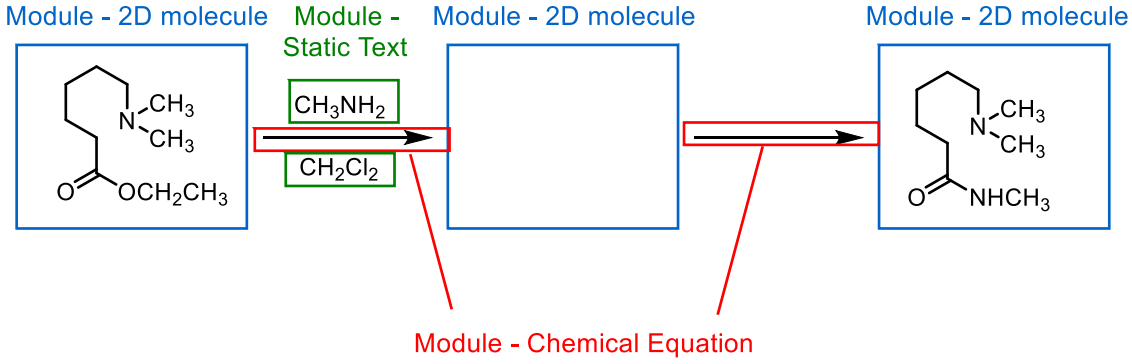
(c) pre-versus post-hydrolysis/decarboxylation with active methylenes

(d) sequenced reactions (conjugate addition + intramol aldol, cf Robinson)

Format 1: Predict the product (example of type (b))



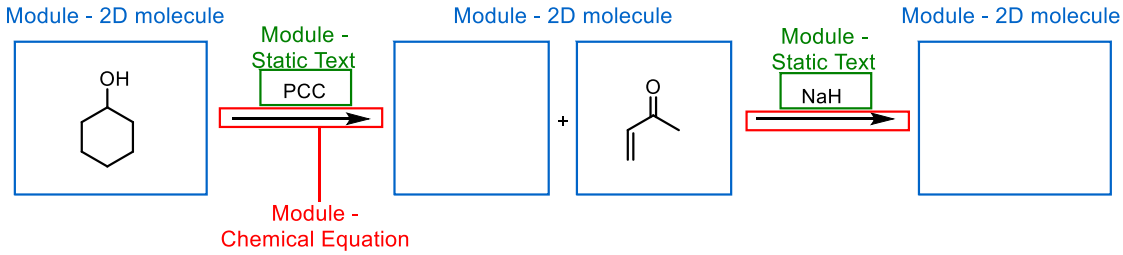
Format 2: Predict the intermediate (example of type (a))



Format 3: Combinations of the above formats

For these combinations you can use a 210 reaction for one step or material from Exam 1 material out of the two steps if you want

Ex. 1 – Predict the product x2 (example of Exam 1 material and type (d-Robinson))



SAP-VI: Detailed Picture

Directions: Choose **ONE** type of exercise and **ONE** format

TYPES OF EXERCISES:

(a) acid versus base acylation mechanisms

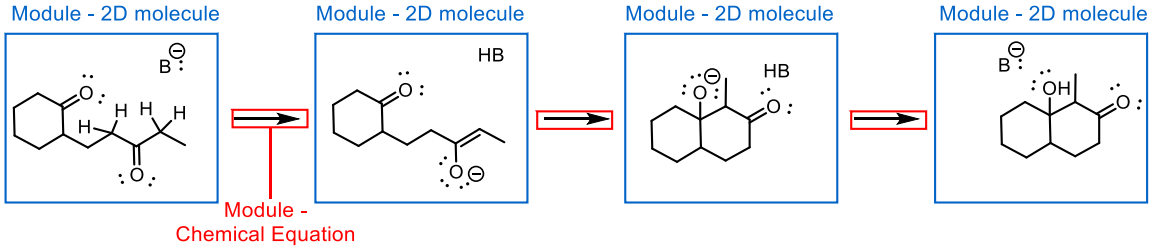
(b) acylation reactions

(c) aldol reaction versus aldol condensation

(d) pre-versus post-hydrolysis/decarboxylation with active methylenes

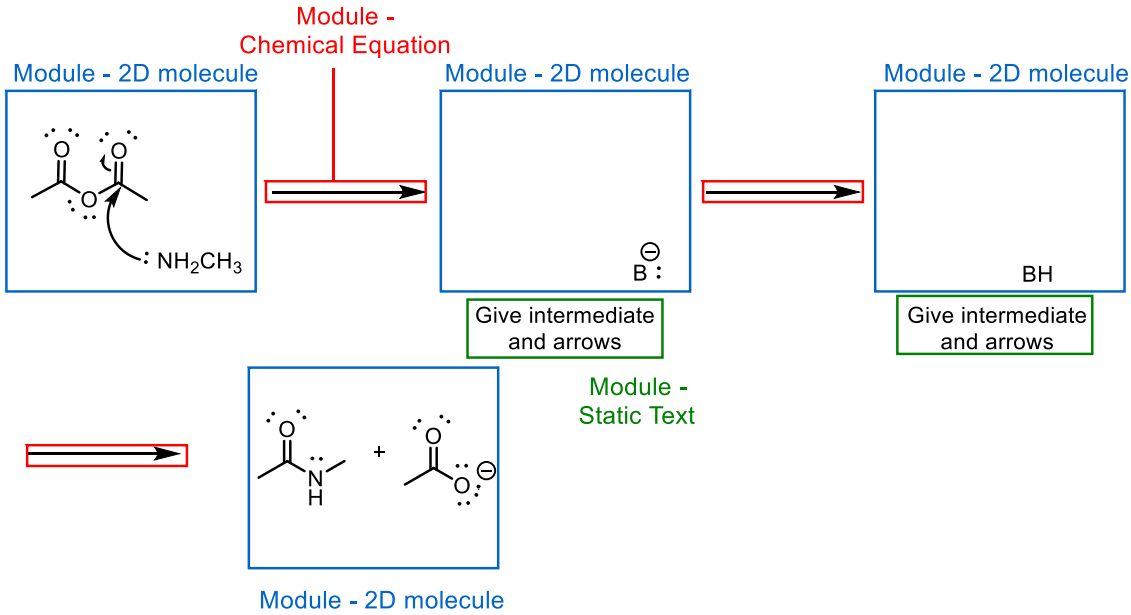
(e) sequenced reactions (conjugate addition + intramol aldol, cf Robinson)

Format 1: Provide the arrows for all steps to the product (example of type (c))



Format 2:Predict the intermediate and provide arrows to the product (example of type (a))

In the directions of this reaction I would state that the amine is in excess



SAP-VII: Reformatting reactions

Directions: Choose **ONE** type of exercise and **ONE** format

TYPES OF EXERCISES:

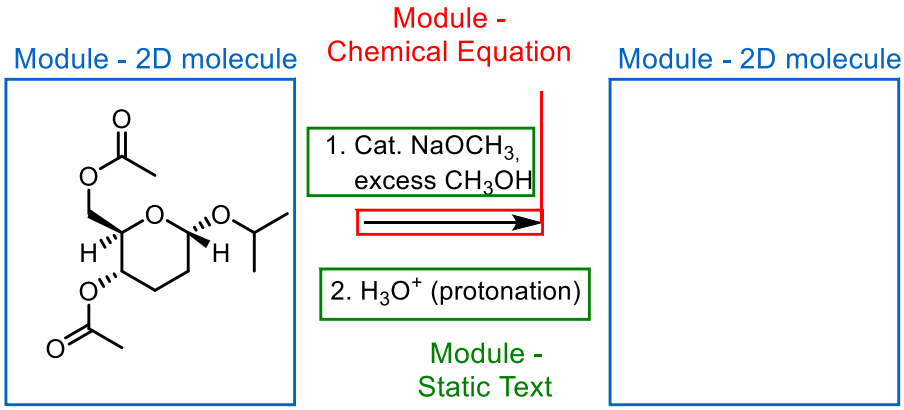
(a) Diels-Alder (region- & stereochemistry)

(b) Carbohydrate anomeric

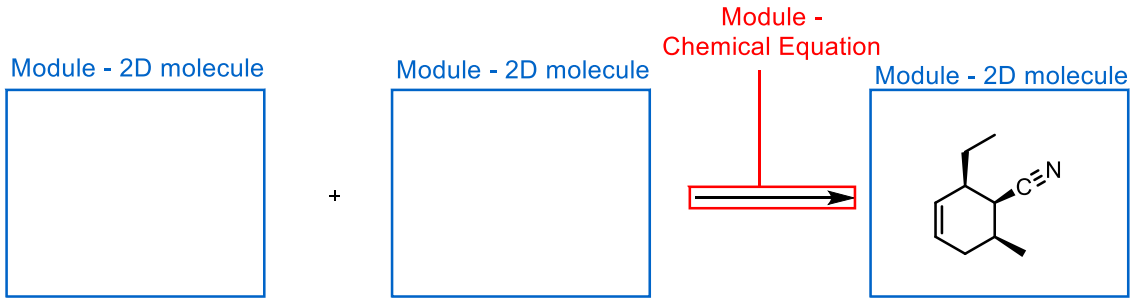
(c) Carbohydrate alcohol reactions

(d) Protection, deprotection, coupling of amino acids

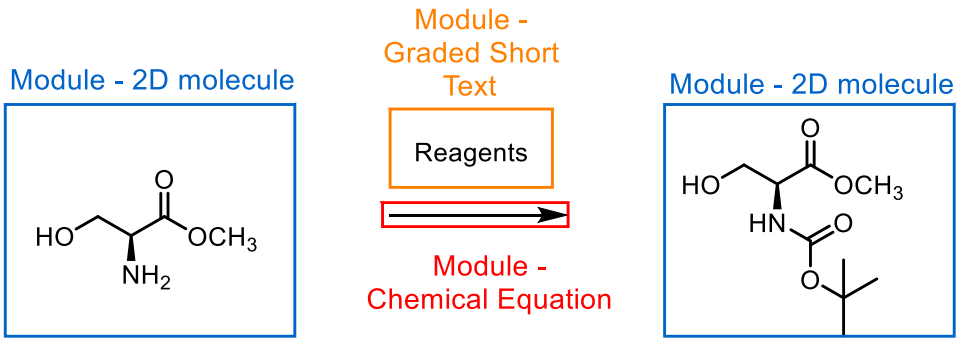
Format 1: Predict the product (example of type (c))



Format 2: Predict the starting material (example of type (a))



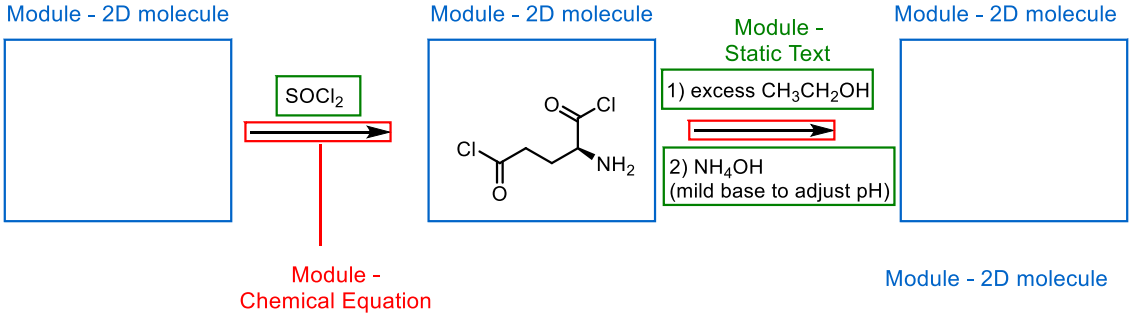
Format 3: Give the reagents (example of type (d))



Format 4: Combinations of the above formats

For these combinations you can use a 210 reaction for one step out of the two steps if you want

Ex. 1 – Predict the starting material and then the product (example of type (c) from this material and the other reaction is from exam 2 material)



SAP-VIII: Detailed Picture

Directions: Choose **ONE** type of exercise and **ONE** format

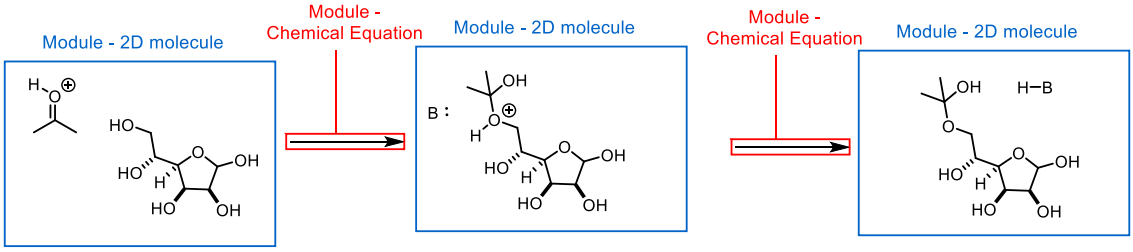
TYPES OF EXERCISES:

(a) carbohydrate alcohol reactions (these are all reactions that have been used previously but are now occurring with carbohydrates)

(b) carbohydrate hydrolysis

(c) protection, deprotection, and coupling of amino acids

Format 1: Provide the arrows for all steps to the product (example of type (a))
Reaction occurs under acidic conditions –For these reactions you do not have to do the entire mechanism but certain steps



Format and Topic of your choice from any of the material covered in 215!!

Appendix 4*

Supporting Information for Chapter 6:
Analyzing an Optional Student-Generated Organic Chemistry e-Homework Platform

I. Survey: Student perceptions on using Sapling Learning

(a) Survey questions

Greetings. This is a brief survey about your use or non-use, to date, of the new Sapling Learning resource in CHEM 210. As a reminder, there has been an open subscription for all UM students to try 100 sample questions geared towards three CHEM 210 skills: use of curved arrows, acid/base, and drawing resource contributors. A link to the site will be provided at the end of the survey. We are really interested in one question: why have you used, or not used, this resource? Question 2 is for those who are using Sapling. Question 3 is for those who tried it and stopped, or who never tried it.

1. I have created a user account and tried the Sapling problems at least once.
    a. Yes
    b. No

2. For those who have used Sapling.
    a. I am using Sapling because I want all the practice I can get
        i. Most critical reason to me
        ii. Important reason to me
        iii. Does not apply to me
    b. I am using Sapling because my instructors recommended it
        i. Most critical reason to me
        ii. Important reason to me
        iii. Does not apply to me
    c. I am using Sapling because my friends signed up and liked it
        i. Most critical reason to me
        ii. Important reason to me
        iii. Does not apply to me
    d. I am using Sapling because it was free
        i. Most critical reason to me

* D. M. Z. gratefully acknowledges the contributions of UM undergraduate Swee Chiah for her statistical analysis.

ii. Important reason to me
iii. Does not apply to me

e. I am using Sapling because I wanted to see if it was helpful
    i. Most critical reason to me
    ii. Important reason to me
    iii. Does not apply to me
f. I am using Sapling because I wanted to master these topics before doing the course pack
    i. Most critical reason to me
    ii. Important reason to me
    iii. Does not apply to me

3. This questions is for those who have tried Sapling and stopped, or who never tried it.
    a. I am not using Sapling because the interface is complicated and cumbersome
        i. Most critical reason to me
        ii. Important reason to me
        iii. Does not apply to me
    b. I am not using Sapling because I have not had the time to do so
        i. Most critical reason to me
        ii. Important reason to me
        iii. Does not apply to me
    c. I am not using Sapling because I did not hear about it. What is it?
        i. Most critical reason to me
        ii. Important reason to me
        iii. Does not apply to me
    d. I am not using Sapling because the feedback is not helpful enough
        i. Most critical reason to me
        ii. Important reason to me
        iii. Does not apply to me
    e. I am not using Sapling because the questions were confusing/poorly worded
        i. Most critical reason to me
        ii. Important reason to me
        iii. Does not apply to me
    f. I am not using Sapling because the exam was too far off and I was not worried yet
        i. Most critical reason to me
        ii. Important reason to me
        iii. Does not apply to me
    g. I am not using Sapling because the exam is pencil/paper, so online practice is not helpful
        i. Most critical reason to me
        ii. Important reason to me
        iii. Does not apply to me

h. I am not using Sapling because I did not know the problems were modeled after the course pack
    i. Most critical reason to me
    ii. Important reason to me
    iii. Does not apply to me
i. I am not using Sapling because the questions were not difficult enough
    i. Most critical reason to me
    ii. Important reason to me
    iii. Does not apply to me
j. I am not using Sapling because there is no credit associated with it
    i. Most critical reason to me
    ii. Important reason to me
    iii. Does not apply to me
k. I am not using Sapling because eventually I would need to pay for it
    i. Most critical reason to me
    ii. Important reason to me
    iii. Does not apply to me

(b) Overall results of the survey

The entire class received the survey N = 1359. The number of responses to each question is indicated on each graph.

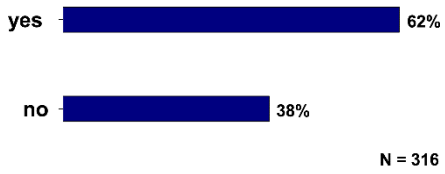


Figure S4.1 Survey data collected for “I have created a user account and tried the Sapling problems at least once.”

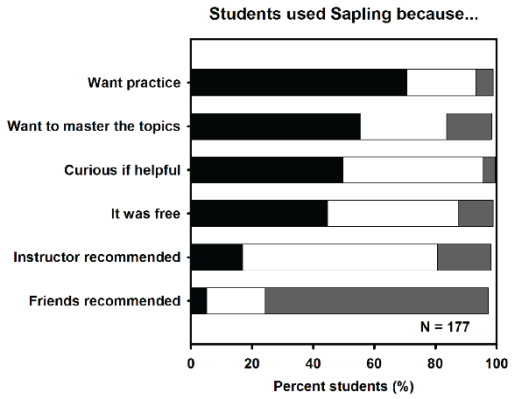


Figure S4.2 Survey data collected for participants who indicated reasons why they were using Sapling Learning Black indicates that the reason was critical to them, white indicates the reason was important to them and grey indicates that the reason does not apply to them.

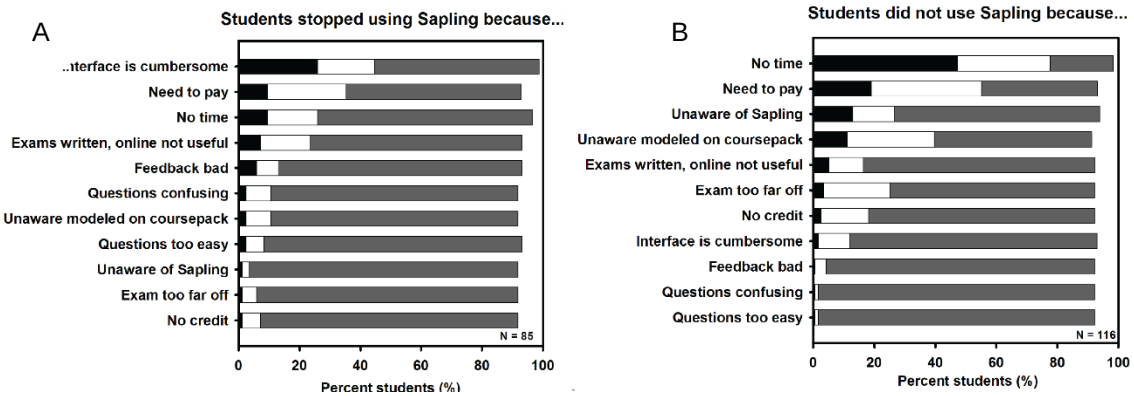


Figure S4.3 Survey data collected for participants who indicated reasons why they (a) stopped using Sapling Learning and (b) never used Sapling Learning. Black indicates that the reason was critical to them, white indicates the reason was important to them and grey indicates that the reason does not apply to them.

II. Students perceptions of specific questions

(a) Survey questions

Students were asked to fill out the following survey online for each question they interacted with in the Sapling Learning authoring interface.

1. Were the instructions to this questions clearly written?
    a. Very clear (No confusion on what was being asked)
    b. Clear (Understood what was being asked but has typos and other grammar errors)
    c. Unclear (Could not figure out easily what was being asked)
    d. Very unclear (Did not understand what was being asked)

2. Was the interface (e.g., drawing arrows, typing text) in this question easy to use?
    a. Very easy
    b. Easy
    c. Difficult
    d. Very difficult

3. If you got the question incorrect, was the feedback generated helpful?
    a. Very helpful
    b. Helpful
    c. Unhelpful
    d. Very unhelpful

4. If you vied the solution tab, please rank how helpful the explanation of the answer was?

5. On a scale of 5 to 1 with 5 being the highest, what is the educational value of this question (how much can students learn from this question)?
    a. 5
    b. 4
    c. 3
    d. 2
    e. 1

6. List any suggestions you have to improve the problem.

(b) Examples of question and associated student responses

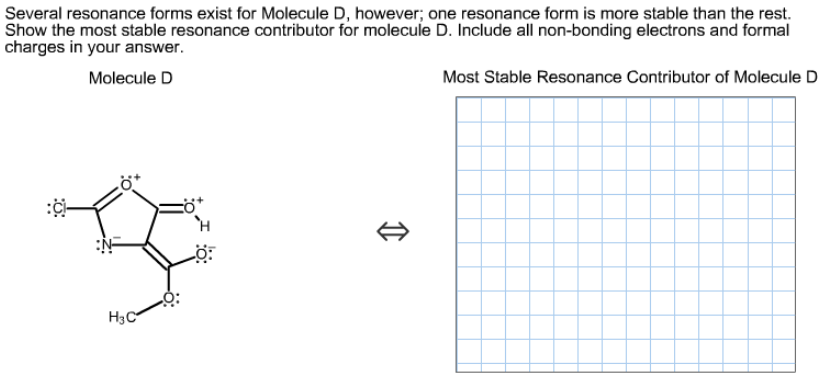


Figure S4.4 Screenshot of a student-generated question on resonance.

Table S4.1 Student responses to questions about the student-generated question in Figure S4.2.

Were the instructions to this question clearly written?	Was the interface (e.g., drawing arrows, typing text) in this question easy to use ?	If you got the question incorrect, was the feedback generated helpful?	If you viewed the solution tab, please rank how helpful the explanation of the answer was?	On a scale of 5 to 1 with 5 being the highest, what is the educational value of this question (how much can students learn from this question)?	List any suggestions you have to improve the problem.
Very Clear (No confusion on what was being asked)	Very easy	Helpful	Helpful	5	Express the importance of the stability rule to avoid charges.
Clear (Understood what was being asked but has typos and other grammar errors)	Easy	Unhelpful	Helpful	4	There are a few typos in the question statement. On the whole it is a very good problem, although the feedback for incorrect responses was generic and not very helpful.
Very Clear (No confusion on what was being asked)	Easy	Very helpful	Unhelpful	4	I think the solution could have been slightly more in-depth and described the exact changes that occur in electron distribution to create the new resonance contributor.
Very Clear (No confusion on what was being asked)	Very easy	question answered correctly		4	Question applies resonance structure knowledge as well as most significant resonance contributor, however, it eliminates the on page arrow pushing to show the process.
Very Clear (No confusion on what was being asked)	Easy			5	If students initially get the question incorrect, hint in the suggestion box that the most stable resonance contributor may involve pushing more than one electron pair.

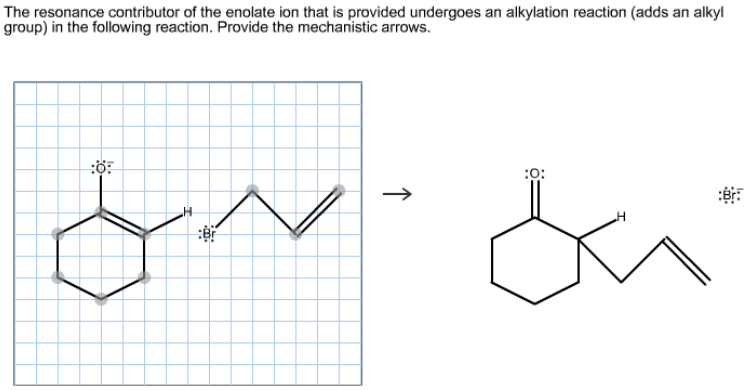


Figure S4.5 Screenshot of a student-generated question on curved arrow notation.

Table S4.2 Student responses to questions about the student-generated question in Figure S4.3.

Were the instructions to this question clearly written?	Was the interface (e.g., drawing arrows, typing text) in this question easy to use ?	If you got the question incorrect, was the feedback generated helpful?	If you viewed the solution tab, please rank how helpful the explanation of the answer was?	On a scale of 5 to 1 with 5 being the highest, what is the educational value of this question (how much can students learn from this question)?	List any suggestions you have to improve the problem.
Very Clear (No confusion on what was being asked)	Easy	helpful	Helpful	4	The problem might be able to suggest that in an incorrect response whether the starting points or end points of the transfer arrows are correct or not.
Clear (Understood what was being asked but has typos and other grammar errors)	Easy	Helpful	Helpful	5	The tools that are necessary to correctly answer the problem should be stated so the student does not try using everything available to them, potentially causing frustration.
Very Clear (No confusion on what was being asked)	Easy	Helpful	Helpful	4	The question might be able to provide how exactly some of the arrows are wrong. Perhaps maybe confirm if the starting points and end points of the arrows are wrong enough as opposed to an entire blanket wrong statement.

(c) Overall results of survey

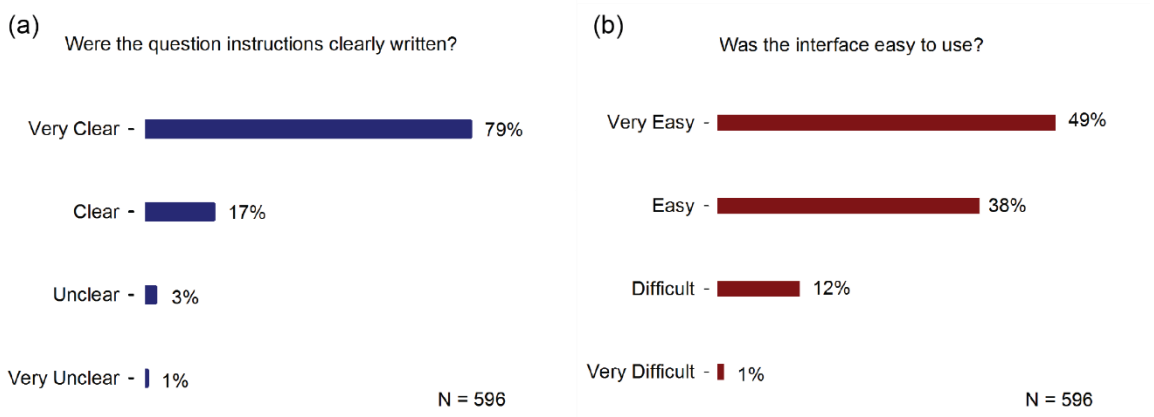


Figure S4.6 Survey data collected for 253 questions in response to (a) “Were the instructions to this questions clearly written?” and (b) “Was the interface (e.g., drawing arrows, typing text) in this question easy to use?” N indicates the total number of responses collected

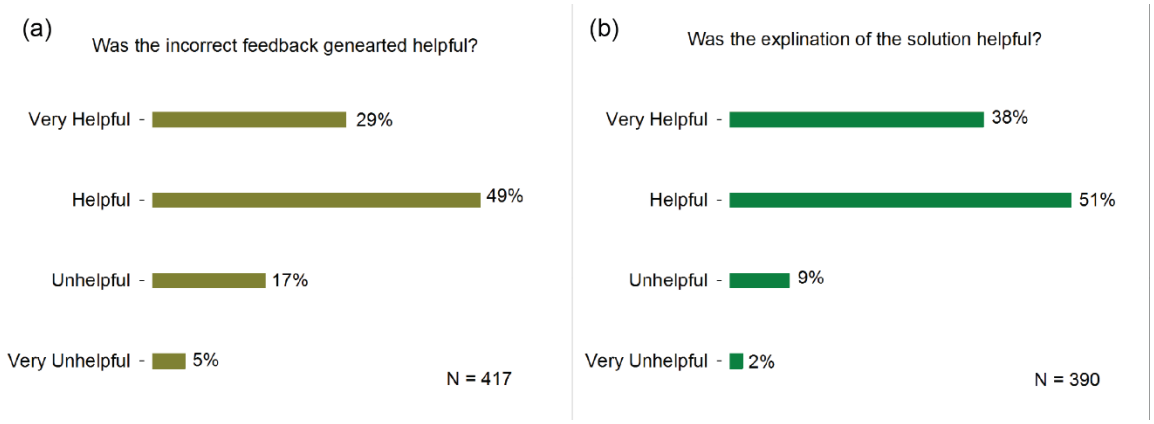


Figure S4.7 Survey data collected for 253 questions in response to (a) “If you got the question incorrect, was the feedback generated helpful?” and (b) “If you vied the solution tab, please rank how helpful the explanation of the answer was?” N indicates the total number of responses collected

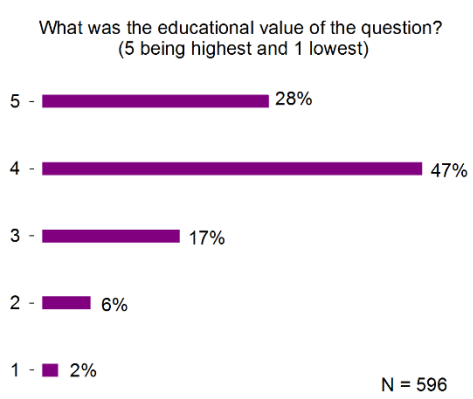


Figure S4.8 Survey data collected for 253 questions in response to “On a scale of 5 to 1 with 5 being the highest, what is the educational value of this question (how much can students learn from this question)?” N indicates the total number of responses collected

III. Brief survey of student answer-clickers

In the Fall 2014 semester students who were enrolled in CHEM 210, tried Sapling Learning and were identified to view the solution prior to imputing the answer in the interface and were asked the following question. 75 students were sent the survey.

We noticed that when students interacted with the Sapling Learning Resource, the interface was not used in some cases. Instead, when attempting a question, the solution was viewed prior to imputing the answer. We are interested in how you were using the resource. Please check all that apply.

- I read the problem and answered the question in my head before viewing the solution.
- I read the problem and immediately viewed the solution, after which I analyzed the answer.
- I read the problem and then worked out the solution on paper before viewing the solution.
- Other (please specify)

Table S4.3 Results from the survey of student answer clickers. Students were able to select all options that applied.

	# of students who selected (N = 7)
wrote it out	7
immediately viewed solution	2
did in head	1

IV. Statistical analysis of the Fall 2014 CHEM 210 course

Statistics were run using R which can be downloaded at https://www.r-project.org/. Only data collected from the Fall 2014 semester were analyzed. Tests that were carried out on the data were Welch two sample t-test, Pearson's product-moment correlation and linear regressions.

Table S4.4 Summary of Welch two sample t-test results.

exam	*non-Sapling users average exam score points (# of students)*	*Sapling users average exam score (# of students)*	*p-value*
exam 1 (100 points possible)	75.66 (794)	81.66 (565)	2.84e-13
exam 2 (120 points possible)	85.02 (1223)	88.18 (114)	0.1055
exam 3 (140 points possible)	81.80 (1224)	89.03 (90)	0.02299
final (240 points possible)	157.43 (1257)	155.96 (51)	0.8116
overall course grade	403.73 (1194)	413.27 (113)	0.3120

Table S4.5 Summary of Pearson's product-moment correlation for each exam when comparing exam score versus # of questions interacted with.

exam	*correlation (# of students)*	*p-value*
exam 1	0.091 (565)	0.0297
exam 2	-0.151 (114)	0.1072
exam 3	0.0496 (90)	0.640
final exam	0.0009 (51)	0.9949
overall course grade	0.034 (113)	0.7162

Table S4.6 Summary of Pearson's product-moment correlation for each exam when comparing exam score vs. percent score on assignments interacted with.

exam	*correlation (# of students)*	*p-value*
exam 1	0.1662 (565)	7.105e-5
exam 2	0.0547 (114)	0.5612
exam 3	0.1384 (90)	0.1909
final exam	0.2727 (51)	0.0505
overall course grade	0.0059 (113)	0.9505

Table S4.7 Summary of linear regressions for each exam after exam 1. Exam 1 was used as a measure of prior intelligence when comparing exam score vs. percent score on assignments interacted with.

exam	*linear regression*	*p-value*
exam 2	-0.06189	0.0215
exam 3	0.0509	0.3502
final exam	0.02201	0.8435

V. Video and interview protocols

Students who used the resource during the Fall 2015 free trial period were invited to partake in a follow up study. Out of the 135 students invited 4 were selected for a pilot study based on availability. Video equipment was rented from the ISS Media Center Loan office in the modern language building (MLB). The screenshot of the computer screen and audio recording were done on a Mac using Quicktime.

Protocol for video recording students using Sapling Learning
Interviewer will explain the reason for the interview. He/she will also ask permission to videotape the student working and will have students sign the consent form. He/she will ask for the students mailing address for payment purposes. He/she will then have the student log on to their Sapling Learning account and inform the student that he/she can use any of the material on the table (paper, pencils, book were provided) or that he/she has brought with them (e.g. lecture notes). He/she will inform the student that the study is looking at how they would normally use the online system to study and that they are free to interact with any of the questions on the interface.

He/she will inform the student that this part of the study will occur for 25 min and that at any point the student can ask to turn off the video camera. He/she will inform the student that he/she will be outside the door if any problems arise. Ask students if they have any questions. He/she will then turn on the screen capture tool on the Mac (Quicktime) and then turn on the video camera. Walk out of the room.

After 25 min the camera and screenshot was turned off and all data was saved and labeled as student 1, 2, 3, etc.

Interview protocol (Subjects who used the online resource)
The interviewer will explain the reason for the interview. He/She will also ask permission to audiotape the interview (Quicktime on Mac) and will remind students about the consent form. He/she will remind the interviewee that if he/she does not want to answer a question he/she can ask to skip the question. He/She will ask the student if he/she has any questions before the interview begins.

1. What is your preferred learning style? (Do you learn best by reading, hearing, doing, etc?)
2. Which course tools have helped you learn the most?
3. Which course tools helped you learn the least?
4. What role does homework play in your learning process?
5. What role have computers played in your learning process?
6. How do you study for this course? Describe a typical weak.
7. How do you know when you understand the material?
8. What is your opinion about the feedback that you receive using Sapling Learning?
9. During this study what materials did you use and why?
10. What have been your experiences with computer and web-based instruction in other classes?

Thank the student for his/her time and how helpful he/she has been to the study. Ask the student if he/she has any questions. Remind the student that he/she can withdraw from the study at any time and point out the contact information. After ~10 min the audio taping was turned off and all data was saved and labeled as Student 1, 2, 3, etc.

Audio transcriptions

The interviews with all four students were transcribed for each question. When "…" is present it indicates a pause by the student.

Table S4.8. Student responses to "What is your preferred learning style? (Do you learn best by reading, hearing, doing, etc?)."

Student 1	generally just lecture style where I go to lecture and I write things down and then I and then I take it and I do practice problems ummm like on Sapling Learning which is why I like it so much umm the course guide makes me really uncomfortable because there's no answers and I like to the see the answers and correct myself as part of how i learn so..
Student 2	doing practicing
Student 3	umm I like going to lectures and taking notes and basically reviewing my notes and that's the way I learn best
Student 4	like in this class or in general? (umm in this class) so I like to read the text book before going to lecture like the (cant understand the word) learning so i usually do that like I'll sit down one weekend and just like read the entire chapter before we are suppose to do it so the lecture is more like review and like the course is like the more important parts of the chapter as well and then I take notes on it by hand

Table S4.9. Student responses to “Which course tools have helped you learn the most?”

Student 1	umm I mean the lecture is up there ummm Khan academy helped a lot Sapling Learning as well that was a really good tool umm I don’t really use course guide .... I go to discussion sometimes and ummm that’s about it and I mean I have study group that’s another thing I go to study group and that’s really helpful they give me old test problems with answers which is helps me out
Student 2	ummm the back part of the course pack that actually has the answers the front part you don’t know the answers so you can do them but you actually don’t know if they are right and then I’ve gone to tutors they've helped me understand some concepts I know so ... the study groups SLC they’re called they helped a lot
Student 3	ah definitely the course pack because it gives me a lot of practice problems I can go over and also in study group I get practice exams and those help me as well
Student 4	ahhh probably textbook, lecture, course pack, and that I've used this like on and off so

Table S4.10. Student responses to “Which course tools helped you learn the least?”

Student 1	the textbook, the textbook was the least helpful resource most definitely I bought it and disregarded it .... yeah
Student 2	the textbook sometimes because it it just tries to explain in a complicated way that ends up confusing me more yeah
Student 3	ah the textbook because I don’t find the way it explains everything umm very clear so I find the lectures more helpful for me
Student 4	like I haven’t used really SLC resources at all so I guess like if you can answer it like that what I use is pretty helpful

Table S4.11. Student responses to “What role does homework play in your learning process?”

Student 1	ummm well they do’t really give homework which I find a little frustrating because I like to have that sorta thing so... I try I try and give myself homework like watch Khan academy videos that are related to what the lecture is on to make sure I understand that and then do the Sapling Learning that applies to the topic and that sorta thing yeah
Student 2	homework helps because you actually get to practice what you learn so it you have to do the homework you have to understand what you worked on that day and then if you practice it that same day I feel like its easier when you actually have to study for the exam
Student 3	ah very important role since I do a lot of practice to get the concepts
Student 4	like the SSG homework sometimes it’s annoying but sometimes it’s helpful so it depends on the week (Interviewer: and the assignment?) yeah and the assignment

Table S4.12. Student responses to “What role have computers played in your learning process?”

Student 1	yeah a lot of the resources I use are online ummm I.. its much easier for me to work off my computer than it is for me to work with a book .... I don't know
Student 2	I wouldn’t say that they play a huge role maybe for videos I watch videos but with the program sometimes it’s just so frustrating that I can get the thing right to work and I feel like I ...I spends so much time with problems that I can do faster if I don't like just writing them but then when you have the answers on the computer you at least it’s easier because you have the answers there and you know what you are doing wrong and you don't have the answers when you’re doing paper I mean its ups and downs
Student 3	ah I go on my computer a lot to look at notes that umm professors post and also Sapling
Student 4	probably minimal actually considering Sapling Learning is really the only thing I've used so far

Table S4.13. Student responses to “How do you study for this course? Describe a typical week.”

Student 1	How I study for this course ummm I attend lecture if I don't understand things in lecture or if I miss lecture I go to Khan academy or I go to the online notes from professor or the other professor ... I don’t remember and I umm I use their notes to kind of make sure I understand the material and then when it comes around to exam time and then I ummm then I go to study group and in study group they actually give me problems to work on and if I don't understand those problems umm then I take to Sapling Learning and I do those problems I understand or the problems I didn't really get and had trouble with until they showed me how and I do them online until I understand how to do them
Student 2	ahhh I'll study by myself and try to understand what we were taught in lecture and then I’ll go over course pack problems that my GSI assigns I’ll try to do them and then most of the time when i actually study for an exam I just get to the people and we just teach each other
Student 3	umm typically I go over like my lecture notes everyday like every time I go to lecture and then two weeks before I go over the course pack
Student 4	ok I already did that with the textbook stuff.... the textbook stuff I'd try to do course pack problems but usually that doesn’t work until the week before the test

Table S4.14. Student responses to “How do you know when you understand the material?”

Student 1	when I start getting 100% on the problems umm pretty much ... I mean I always feel like I understand the lecture when I attend Prof lecture but the problems are a little trickier for me definitely
Student 2	that’s a complicated question because I feel like I understand it and I go over it and I know it but then I look up problems and I try to apply what I think I know but it turns out to be wrong so it’s complicated there I guess that I know that I actually learn the material when the practice problems are correct
Student 3	umm when I start getting the questions right and like when I umm feel confident in my answers
Student 4	if I can like go into the course pack problem and like confidently answer it like you can still be wrong but like I’m able to understand my mistake as well

Table S4.15. Student responses to “What is your opinion about the feedback that you receive using Sapling Learning?”

Student 1	ummm its very useful ummm I find it difficult to go without answers like they want me to because I don't have other people I’m not a freshman I’m not in the dorms I don't have other people on organic chemistry around me that I can sorta recruit to talk about the course guide so... the getting feedback from sapling learning definitely helps me correct myself when I'm wrong and figure out my mistakes and I'll write them down in here so I permanently understand it so it’s really helpful
Student 2	can you explain the question "sometimes there are written responses in Sapling Learning so what did you ... what’s your opinion on that" Oh sometimes they help if .. if when I have no idea what I am doing they help you guide you through but when I know what I'm doing and there’s a technical mistake I read the things and it’s just telling me what I already know it’s like a general thing so if your lost it helps a lot but if you know what you’re doing and you don’t know why you’re getting it wrong it doesn’t help that much
Student 3	I find it very helpful because it gives the explanation and like what I did wrong and how I can like improve
Student 4	sometimes it’s like really good but other times it’s a little bit too cryptic or like vague as to what I am doing like it’ll suggest all these thing but like the problem may just be I forgot part of the structure that wasn’t really relevant to the problem like that I was stuck on one early because I forgot like 2 bonds that were like off to the side but everything else was right

Table S4.16. Student responses to “During this study what materials did you use and why?”

Student 1	umm I mean just this computer ... in this study right here? ...(me yes)... Actually no... I use them very sparingly normally but I always have them around just in case like if chair conformations are tripping me up right now and I'll check the diagram of what a chair conformation looks like where up down left right should go and that helps but i don't really use I don't really use umm other materials too much when IL going through Sapling.
Student 2	I use the paper to do some calculations like math and the pKa table that is all I used
Student 3	umm I looked I looked briefly through my notes because I forgot a certain concept
Student 4	so I .. used basically just the software, and my memory I didn’t really go back to my notes even though I had them I use the pencil and paper sometimes just drawing out the structure on paper it’s a little bit easier to do it on paper than it is to do it in the site itself like when you are trying to figure out mechanisms and stuff

Table S4.17. Student responses to “What have been your experiences with computer and web-based instruction in other classes?”

Student 1	ummm well right now I am in calculus and they have their web homework program which is much better than the web homework program I used in high school In high school they were launching all these web homeworks and they were not very good and they were not very intelligent and umm the software I've been using at Mi has been really smart and really responsive and it understands it understand like this program understands when you put a double bond on the other side of the ring that its still a ring that its still the same thing just flipped which is something my high school learning programs didn't understand at all so I really appreciate that umm and the web homework is similarly it understands if you plug in a whole function instead of a numerical answer it'll understand that it out puts an number and accept it so that's truly that really cool
Student 2	I haven’t been a lot of them ...but stuff like this?... (yeah sorta like computer instruction in other classes) for my math homework I have to like the math homework and its you don’t need to interact with the computer you just plug in the answers so this is more interactive computer
Student 3	ummm I’ve taken umm chemistry umm master in chemistry thing in high school on a computer and it was basically a homework based thing where we did our homework online and I found it helpful because it like gives you feedback
Student 4	I don’t prefer it to actual like person to person learning like in a normal classroom setting I took AP statistics online last yeahr and that was not a good experience at all

Summary of screen capture results

Each screen capture video was 25-30 min and was reviewed by one graduate student. Below is a summary of the types of questions the student interacted with in the online resource, (Sapling Learning) during the length of the study. In addition, the number of attempts for each question a student interacted with was recoded and the outcome of that final attempt.

Table S4.18. The number and variety of topics students interacted with in the online interface.

Student	Curved Arrows	Resonance	Acid/base	Chairs	Transition state	Electrophilic addition (no stereochem)	Stereo-chemistry	Total
1	--	--	--	3	--	3	--	6
2	2	2	1	--	--	--	--	5
3	--	--	--	1	10	2	1	14
4	--	--	--	5	--	3	--	8

Table S4.19. The number of attempts made by student 1 on each questions they interacted with.

Topic	# of attempts	Results after the final attempt
Chairs	2	Correct
	1	Viewed solution
	1	Correct
Electrophilic addition (w/o stereochemistry)	2	Correct
	2	Correct
	2	Correct

Table S4.20. The number of attempts made by student 2 on each questions they interacted with.

Topic	# of attempts	Results after the final attempt
Curved arrow	2	Moved on w/o viewing solution
	1	Correct
Resonance	1	2/3 correct then moved on w/o viewing solution
	2	Correct
Acid/base chemistry	1	Correct

Table S4.21. The number of attempts made by student 3 on each questions they interacted with.

Topic	# of attempts	Results after the final attempt
Transition state (10 questions)	1	Correct
Stereochemistry	1	Moved on w/o viewing solution
Electrophilic addition (w/o stereochemistry)	1	Viewed solution
	2	Correct
Chair	2	Correct

Table S4.22. The number of attempts made by student 4 on each questions they interacted with.

Topic	# of attempts	Results after the final attempt
Electrophilic addition (w/o stereochemistry)	2	Correct
	2	Moved on w/o viewing solution
	3	Correct
Chairs (4 problems)	1	Correct
	2	Correct

VI. Instructor materials for the assignment of editing

During the Fall 2014 semester students who enrolled in the SSG elective were tasked with editing previously authored student-generated questions. The following table lists the material used for this assignment.

Timeline	Material	Page
Prior to the semester	Editing syllabus and timeline	288
During the semester	Example of how to edit handout	292

VII. Material for advertising the Sapling Learning resource

Two flyers were created to advertise the Sapling learning interface. These flyers were sent out to students through e-mail and given to Science Learning Center and Structured Study Group leaders for distribution.

Timeline	Material	Page
Prior to the semester	Flyer for CHEM 210	295
	Flyer for CHEM 215	296

INTRODUCTION TO THE PROJECT

Instructors in the organic chemistry program have been generally uninterested in the standard electronic homework systems because the underlying assumptions in these systems are at odds with a number of our most important pedagogical goals. In particular, we have not been interested in activities that would not reinforce our idea that students should be working to discuss and explain things to one another, face-to-face, in small groups, with tasks and problems for which there are not discrete answers.

On the other hand, we see great potential value in using the rigor of Sapling Learning's structural drawing interface to target a set of skill-based topics. Skill-based topics are core curriculum goals that are commonly and recurrently used to construct and provide explanations. These are the sorts of basic communication skills that we want students to have to be able to work effectively with one another.

Skill-based topics are the ones were we would like students to have 100% mastery of, and this mastery is achieved through having enough diverse – and yet rigorously monitored – problems to work on. You can read about how to drive and you can attend lessons, but none of this matters until you get behind the wheel. And we know that everyone comes to their mastery at different rates, with different amounts of practice that is nonetheless highly repetitive.

We perceived a gap between the skill level that can be achieved from the exercises in the textbook and the skills that are necessary for working on the coursepack (old exam) problems. This gap is not true for everyone, because for many students, the book is enough. And for some students, the work they do with other students makes up the difference. But we know that there are still students who fail to master the basic skills, and this limitation is one of the reasons they have trouble in the course.

Skill-based topics, by definition, are also ones that retain their value as the course goes on, and so they can be productively revisited to affirm mastery of these topics. As mentioned above, we think these are the skills for which we would like 100% of students to achieve mastery.

FOR EXAMPLE: SKILL-BASED TOPICS FROM CHAPTERS 1-3

TOPIC: Curved Arrow Notation
TYPES OF EXERCISES:

(i) follow the arrows from a starting material (A + arrows -> *draw the product*)
(ii) insert arrows for a given (A -> B, *draw the arrows*)
(iii) problems that combine both (A + arrows -> *draw intermediate, and arrows* -> B)
(iv) given A -> B -> C, etc. (verbal descriptions are used, *draw structures and arrows*)

TOPIC: Drawing Resonance Contributors
TYPES OF EXERCISES:

(i) Drawing the resonance contributors (closed shell, limits on charges; evaluation)
(ii) Drawing a contributor as directed by some property
(iii) Drawing the most significant contributor starting from a minor contributor

TOPIC: ACID-BASE CHEMISTRY
TYPES OF EXERCISES:

(i) Using pKa for predicting reaction equilibria
(ii) Predicting pKa from pKa table precedents
(iii) What is/are the form(s) at a given pH

In 2013-14, SSG students generated almost 700 problems to be used by CHEM 210 students. While they were all deemed to be "publication ready" by the experts at Sapling Learning, we think that everything can be improved!

Fall Term 2014 Plan for the Project

All students in CHEM 210 now have access, if they wish, to the UM problems in Sapling Learning. Starting this year, SSG students will:

(a) learn how to navigate the Sapling Learning system as users;

(b) work in groups, at the start of the term, to first characterize the features of what makes a well-formatted problem a well-formatted problem, in the first place, by studying the old examination problems in the coursepack, and then apply these criteria to the comparable problems in Sapling Learning;

(c) work in groups, over the duration of the term, to improve the content and presentation of some of the UM problems in Sapling Learning

The overall sequence will be:

(a) to become familiar with the user interface on a set of about 60 problems that are open for general use for about one month

(b) to study the format of faculty-generated print problems (coursepack) and student-generated problems (Sapling Learning), to identify criteria for what makes a well-formatted problem

(c) to review, in detail, some of the existing CHEM 210 problems in Sapling Learning for both content and format, and to arrive at a consensus for how to improve the problem – each student, over the course of the term, will be responsible for editing one problem. A team of three will work together. The teams will alternate which member has responsibility for authoring the edits in the Sapling Environment.

Weeks 1-4:	learning Sapling as a user, analysis criteria formats & content
Weeks 5-7	Each team of 3 works on a problem from exam 1
Weeks 8-10	Each team of 3 works on a problem from exam 2
Weeks 11-13	Each team of 3 works on a problem from exam 3

Week 01 SSG Sign-Up

Week 02 Sep 08:
Leaders provide introduction to using Sapling Learning (access to ca. 60 problems from the Exam 1 topics, available for 1 month).

Assignment: practice with Sapling Learning (curved arrows & resonance, OK to wait until after ~ next Monday when this is all introduced in class)

Week 03 Sep 15:
Leaders debrief SSG students on using Sapling.

Assignment: find curved arrow & resonance problems in the coursepack and compare the formatting relative to Sapling problems. Pairs of students are assigned to one of the ~60 problems in the open-access set and does three things: (1) fill out the formal feedback sheet; (2) write a short description, including drawings, of whether anything about the presentation/format of the problem can be improved; (3) make at least three reasonable errors and evaluate the feedback provided by the problem.

Note for (3): Students must make the mistakes first before getting the answer correct in Sapling. Once they get it correct the system does not let them go back and try it again. I can reset the problem for them but I would have to go in manually to do that. I could teach the leaders how to reset problems as well.

Week 04 Sep 22:
Come to a consensus about the criteria for evaluating format and feedback on Sapling Learning problems.

Leaders introduce SSG students to authoring in Sapling Learning. Everyone gets the same sample problem, containing deliberate areas to improve, to edit, according to a list of guidelines/recommendations.

Assignment: Edit the sample problem.

Week 05 Sep 29: E1
In teams of 3, each team gets behind the scenes with one of the Exam 1 problems: (a) recommend any changes to the format
(b) recommend edits and/or additions to the feedback

Assignment: using images of the actual problem, draft a list of specific recommendations for how to improve the format and/or feedback. Provide images as needed.

Week 06 Oct 06:
A member from each group present, review, and discuss recommendations for edits.

Gather final recommendations based on discussion.

Assignment: groups edit their problem according to the discussion.

Week 07 Oct 13:
Groups present their edited problems. Gather a second round of feedback.

Assignment: groups edit their problem according to the discussion.

Week 08 Oct 20
In teams of 3, each team gets behind the scenes with one of the Exam 2 problems: (a) recommend any changes to the format
(b) recommend edits and/or additions to the feedback

Assignment: using images of the actual problem, draft a list of specific recommendations for how to improve the format and/or feedback. Provide images as needed.

Week 09 Oct 27: E2
A member from each group present, review, and discuss recommendations for edits.

Gather final recommendations based on discussion.

Assignment: groups edit their problem according to the discussion.

Week 10 Nov 03:
Groups present their edited problems. Gather a second round of feedback.

Assignment: groups edit their problem according to the discussion.

Week 11 Nov 10:
In teams of 3, each team gets behind the scenes with one of the Exam 2 problems: (a) recommend any changes to the format
(b) recommend edits and/or additions to the feedback

Assignment: using images of the actual problem, draft a list of specific recommendations for how to improve the format and/or feedback. Provide images as needed.

Week 12 Nov 17:
A member from each group present, review, and discuss recommendations for edits.

Gather final recommendations based on discussion.
Assignment: groups edit their problem according to the discussion.

Week 13 Nov 24: BREAK

Week 14 Dec 01:E3
Final edits due .

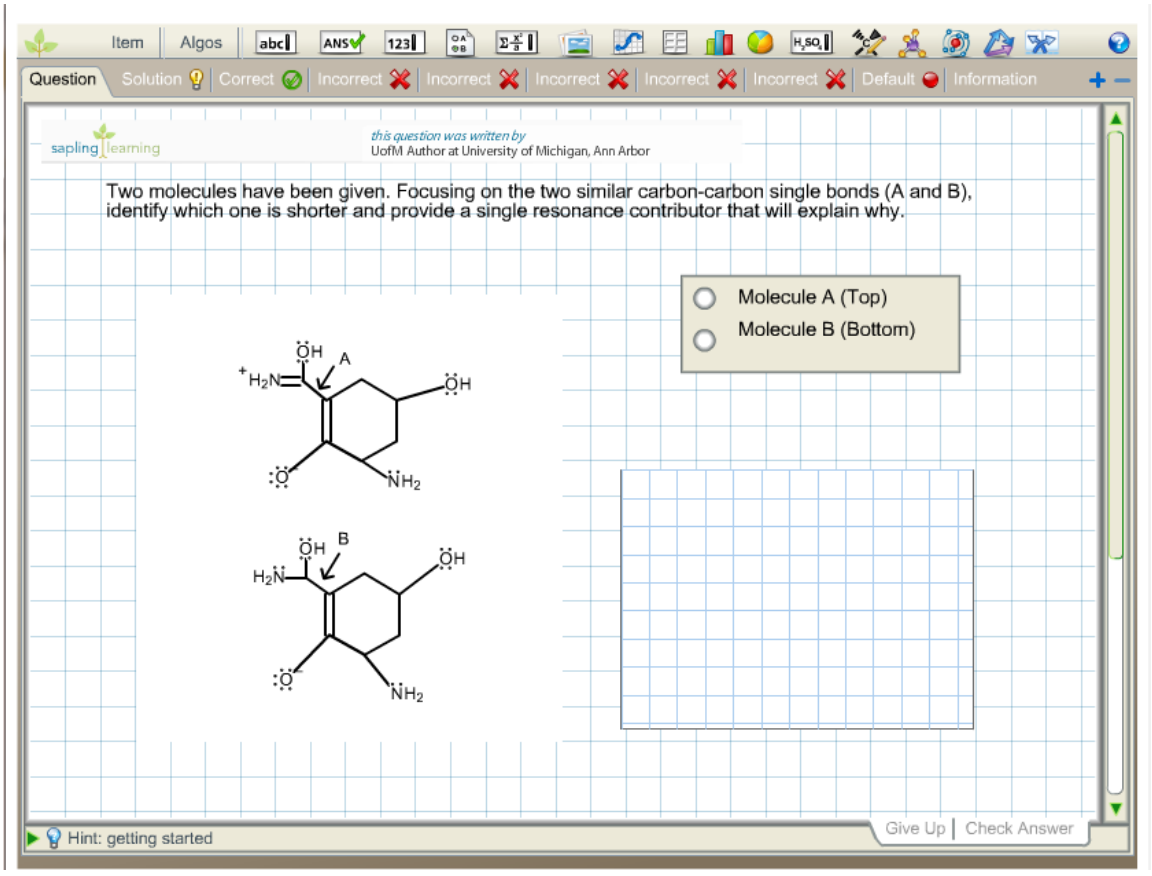
Week 15 Dec 05: no meeting (Final Exam 12/15/14)

Example Question for Editing in Sapling

Potential Edits (general)

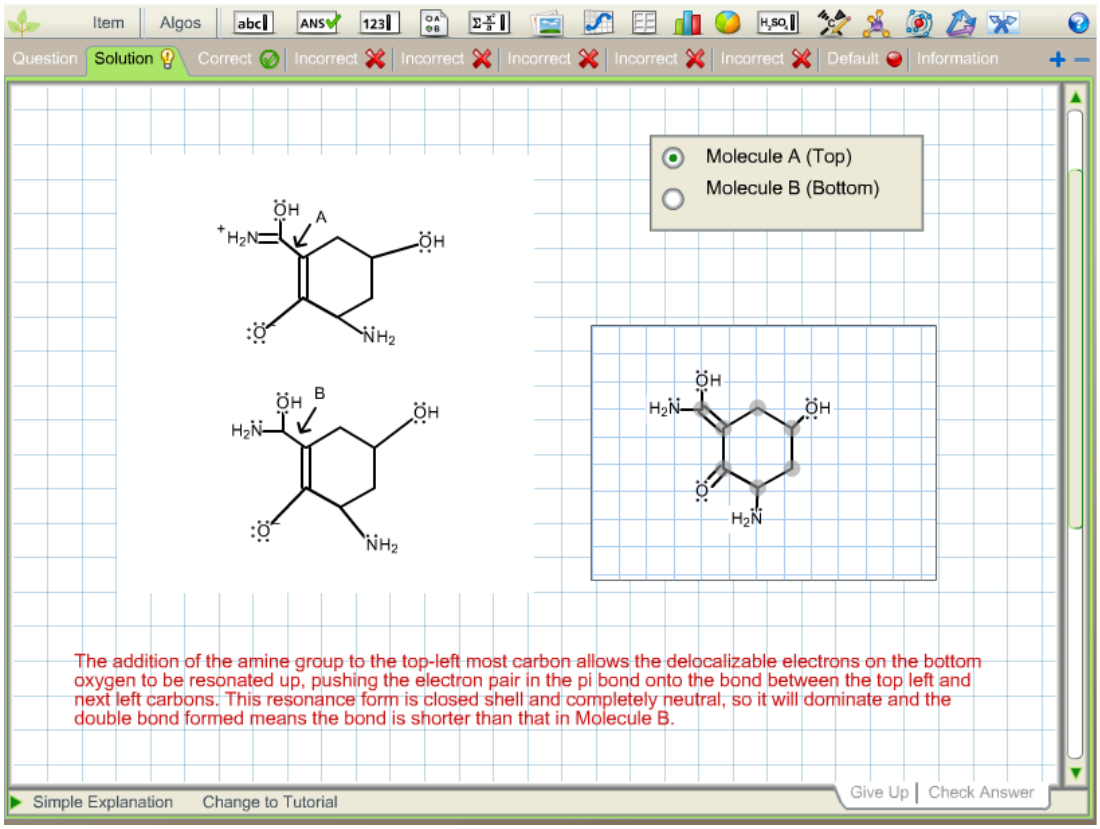
1. Rewording the question to make it more clear
2. Make structures aesthetically pleasing
3. If possible they need to come up with another potential incorrect answer for the question and add another incorrect tab
4. Simplifying explanations on incorrect tabs and solution tabs
    - For solution tabs potentially adding a new “2D module box”

Example - Resonance Question 83093



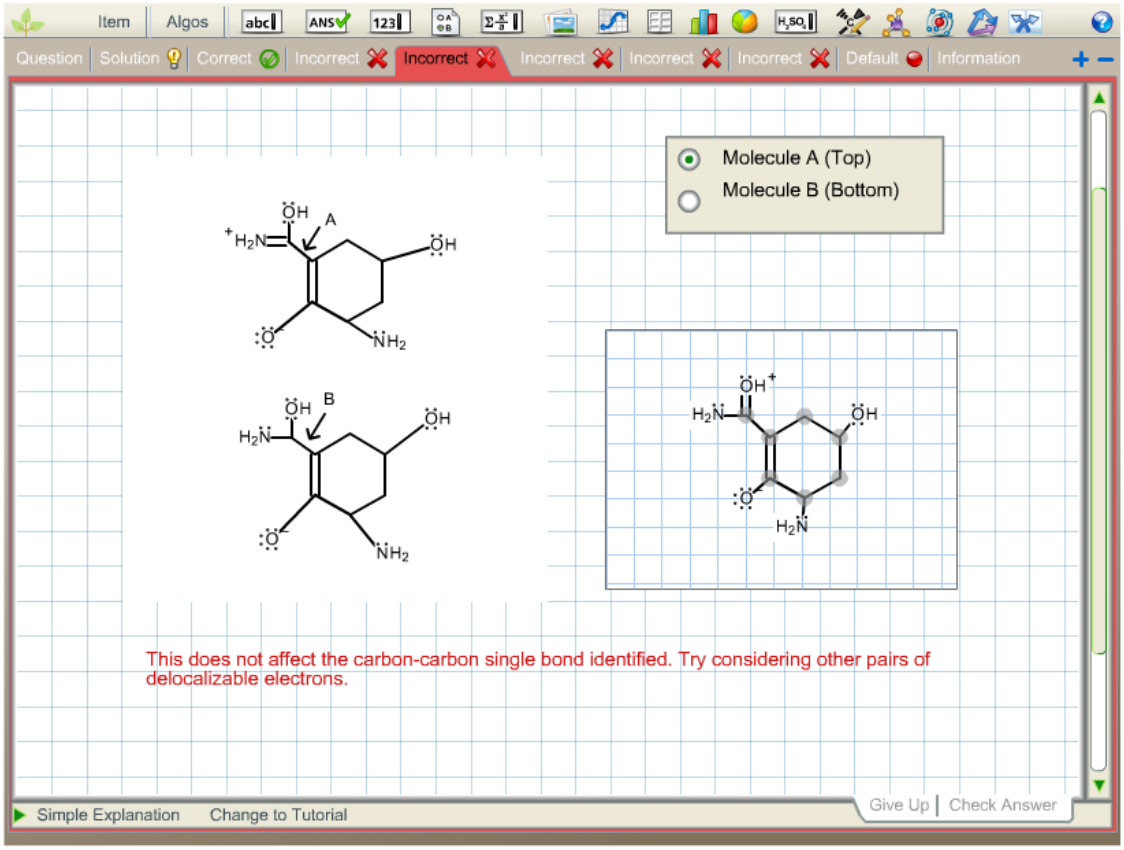
Question Tab Potential Edits:

- Make the bonds attached to the ring more aesthetically pleasing (snap to the grid option)
- Make negative charge more visible (if possible)



<u>Solution Tab Potential Edits:</u>

- Simplify explanation
    - Potentially reduce the amount of words and add another box that shows the arrows that are described in the explanation



Incorrect Tab Potential Edits:

- Because this is a two part question some people who got the first question right but the second were confused by the explanation. They stated " the feedback and hint made it seem like I got the 1st answer wrong when I didn't"
    - Maybe specify what step the feedback is for?

- Other edits on incorrect tabs maybe to simplify the wordy explanations (not so much a problem here)

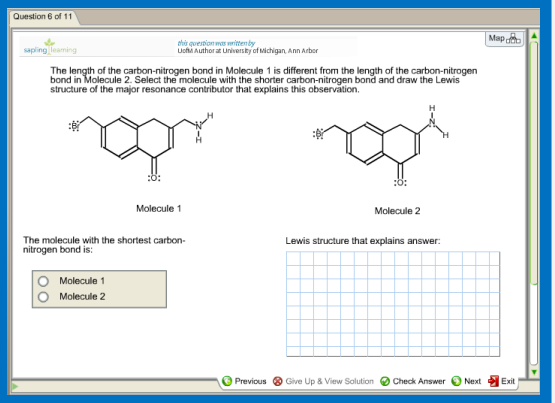
- **If possible they need to come up with another potential incorrect answer for the question and add another incorrect tab**

Important things to remember

1. Additional modules can be added to the solution tab, as this tab is not used by the interface to check the answer, the correct tab should have only the correct answer on it!

New

Resource: Sapling Learning



What is it?

Sapling Learning is a new online "homework" system – with a UM twist! Over the last year, students enrolled in 210 or a special course (CHEM 219) generated ~600 "homework" questions and answers (with feedback) centered on what we call a "skill-based topics" – skills that we want students to have 100% mastery of in the course. This mastery is achieved through practice, practice, and more practice, which requires there to be enough diverse problems to work on. These questions were modeled after the typical coursepack/exam questions and give you feedback when you answer incorrectly, as a result, these questions should provide an excellent format for you to practice your skills!

Two ways to access this resource!

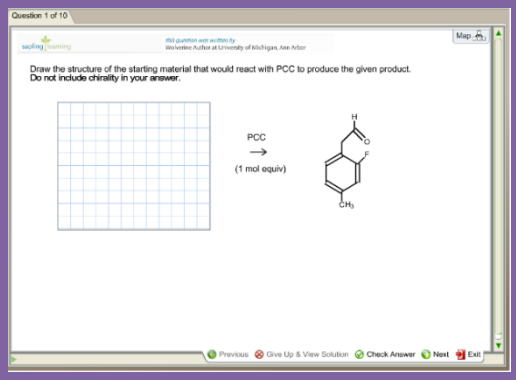
Free Trial

Access 100 questions on three topics for the first exam for free! Topics that will be available are resonance, curved arrows, and acid-base chemistry. To get your free trial follow instructions to sign up at http://bit.ly/saplinginstructions and enroll in University of Michigan – Ann Arbor – CHEM 210 – Fall15 – COPPOLA - **LIMITED ACCESS**.

Access an additional ~500 questions for just $28

Purchasing a subscription to Sapling Learning for the semester will give you access to an additional ~500 questions. Along with MORE resonance, curved arrow, and acid-base questions you will get access to question on topics dealing with transition states, electrophilic addition reactions, stereochemistry, aromaticity, SN1, SN2, E1, E2, and electrophilic aromatic substitution reactions. To sign up to access all ~500 questions enroll in University of Michigan – Ann Arbor – CHEM 210 – Fall15 – COPPOLA. Any questions about the resource contact zurcherd@umich.edu.

215 Resource: Sapling Learning



What is it?

Sapling Learning is a new online "homework" system – with a UM twist!

Over the last year, students enrolled in a special course (CHEM 220) generated >400 "homework" questions and answers (with feedback) centered on what we call a "skill-based topics" – skills that we want students to have 100% mastery of in the course. This mastery is achieved through practice, practice, and more practice, which requires there to be enough diverse problems to work on. These questions were modeled after the typical coursepack/exam questions and give you feedback when you answer incorrectly, as a result, these questions should provide an excellent format for you to practice your skills!

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Access an additional >350 questions for just $28

Purchasing a subscription to Sapling Learning for the semester will give you access to an additional >350 questions. Along with MORE oxidation reactions, acetal/ketal chemsitry, and imine chemistry questions you will get access to question on topics of acyl transfer reactions, enolate chemistry, peptide chemistry and more. To sign up to access all >400 questions enroll in University of Michigan – Ann Arbor – CHEM 215 – Fall15 – COPPOLA. Any questions about the resource contact zurcherd@umich.edu.