2003

Application of the Chan-Evans diaryl ether synthesis to the formation of Bis(bibenzyls)

Eric Rosenthal
Colby College

Follow this and additional works at: https://digitalcommons.colby.edu/honorstheses

Part of the Chemistry Commons

Colby College theses are protected by copyright. They may be viewed or downloaded from this site for the purposes of research and scholarship. Reproduction or distribution for commercial purposes is prohibited without written permission of the author.

Recommended Citation
https://digitalcommons.colby.edu/honorstheses/214
Application of the Chan-Evans Diaryl Ether Synthesis to the Formation of Bis(bibenzyls)

Eric Rosenthal
Application of the Chan-Evans Diaryl Ether Synthesis to the Formation of Bis(bibenzyls)

A thesis submitted as a requirement for graduation with Honors in Chemistry

[Signatures]

Jeffrey Katz, Advisor
Dasan Thamattoor, Reader
Table of Contents

<table>
<thead>
<tr>
<th>Section</th>
<th>Page</th>
</tr>
</thead>
<tbody>
<tr>
<td>Acceptance</td>
<td>2</td>
</tr>
<tr>
<td>List of Figures</td>
<td>4</td>
</tr>
<tr>
<td>Introduction</td>
<td>5</td>
</tr>
<tr>
<td>Discussion and Results</td>
<td>12</td>
</tr>
<tr>
<td>Conclusion</td>
<td>20</td>
</tr>
<tr>
<td>Experimental</td>
<td>21</td>
</tr>
<tr>
<td>References</td>
<td>26</td>
</tr>
<tr>
<td>List of Spectra</td>
<td>27</td>
</tr>
<tr>
<td>Appendix: Spectra</td>
<td>28</td>
</tr>
<tr>
<td>Acknowledgements</td>
<td>41</td>
</tr>
</tbody>
</table>
List of Figures

Figure 1: Structure of marchantin-A

Figure 2: Kodama's application of an Ullman ether synthesis to forming marchantin-A synthetic intermediates

Figure 3: Sawyer's example of a Diels-Alder diaryl ether formation

Figure 4: Chan-Evans ether synthesis from arylboronic acid and phenol

Figure 5: Evans' application of Copper (II)-mediated formation of diaryl ether from arylboronic acid and phenol

Figure 6: Decicco's example of intramolecular diaryl ether formation from an arylboronic acid mediated by copper

Figure 7: Structure of Target Compound

Figure 8: Preliminary retrosynthesis of target compound

Figure 9: Initial synthetic plan, TBS protecting group, TBAF

Figure 10: Formation of silylated alcohol

Figure 11: Conversion of the bis(silylated) product to the desired silylated alcohol

Figure 12: Formation of silylated bromide

Figure 13: Formation of the silylated phosphonium salt

Figure 14: Attempted preparation of alkene

Figure 15: Formation of tosylate

Figure 16: New partial retrosynthesis

Figure 17: Formation of silylated aldehyde

Figure 18: Formation of phosphonium salt

Figure 19: Attempted preparation of alkane

Figure 20: Attempted preparation of the boronic acid

Figure 21: Planned preparation of target bis(bibenzyl)
Introduction

Marchantin-A is a macrocyclic bis(bibenzyl) (Figure 1) isolated from liverwort.\(^1\) Bis(bibenzyls) are compounds containing two diaryl ether functionalities linked by alkyl bridges. Many bis(bibenzyls) are also macrocyclic. Several of these compounds have been isolated from the liverwort *Marchantia polymorpha* and related species.

Figure 1: Structure of marchantin-A (15)

Liverwort extracts are commonly used in oriental medicine, and the isolation of Marchantin-A along with other bis(bibenzyls) from these extracts has attracted research attention.\(^2\)

Since their isolation, researchers have attributed cytotoxic, antifungal, antibacterial, 5-lipoxygenase, calmodulin inhibitory, and other activities to this class of molecules. This broad range of biological activity has sparked considerable interest in these compounds. Marchantin-A was found to possess all of the activities listed above, and we have selected to study synthetic methods that could be applied to it.\(^2\)

Marchantin-A has been previously synthesized by Kodama in twelve steps utilizing an Ullman ether synthesis to form the diaryl ethers and an intramolecular Wittig
reaction to form the product macrocycle (figure 2). While the Ullman ether synthesis does work well for many systems, it requires the use of base at high temperatures and can result in variable yields. Kodama’s synthesis required the Ullman ether synthesis to be applied twice resulting in one-step yields of 68%, and 42%.

Figure 2: Kodama’s application of an Ullman ether synthesis to forming marchantin-A synthetic intermediates

Any reaction that can be used to form diaryl ethers is of interest as this functionality is present in bis(bibenzyls) as well as many other natural products. Therefore, it is not surprising that a great amount of research effort has been focused on
the development and improvement of methods used to form diaryl ethers. An older method for forming diaryl ethers is the use of $S_NAr$ addition reactions. This involves the direct nucleophilic coupling of a phenol to an electron deficient aromatic system. $S_NAr$ addition methods have recently found use in the synthesis of vancomycin and other natural products.\textsuperscript{5,6} Methods have also been developed using cycloadditions such as the Diels-Alder reaction to form the second ring of a diaryl ether (figure 3).\textsuperscript{7}

\begin{center}
\begin{tikzpicture}
\node (a) at (0,0) {\includegraphics[width=\textwidth]{figure3.png}};
\node at (0.5,0.5) {1. COOMe toluene, sealed tube};
\node at (0.5,0) {2. DDQ, benzene 64\%};
\end{tikzpicture}
\end{center}

**Figure 3:** Sawyer's example of a Diels-Alder diaryl ether formation

More recently, it has been shown by Chan and Evans that diaryl ethers can be formed at room temperature in high yield using a copper (II) species to mediate ether formation from a phenol and an arylboronic acid.\textsuperscript{8,9,10}

\begin{center}
\begin{tikzpicture}
\node (a) at (0,0) {\includegraphics[width=\textwidth]{figure4.png}};
\node at (0.5,0.5) {Base, Cu(II)};
\end{tikzpicture}
\end{center}

**Figure 4:** Chan-Evans ether synthesis from arylboronic acid and phenol

The Chan-Evans ether synthesis results in better synthetic yields than previous methods for many systems. One situation that has caused problems for other methods of forming diaryl ethers is the presence of electron donating groups ortho to the phenol. Evans has shown through a formal synthesis of thyroxine that the Chan-Evans ether synthesis is tolerant of such functional groups.\textsuperscript{10} Since this reaction is also run at room
temperature, the racemization problems that are often seen with the Ullman ether synthesis are also avoided.

![Figure 5](image)

**Figure 5: Evans’ application of Copper (II)-mediated formation of diaryl ether from arylboronic acid and phenol**

We intend to achieve a novel synthesis of a macrocyclic bis(bibenzyl) product through the use of the Chan-Evans copper-mediated arylation of phenols to form the diaryl ethers. This reaction allows us to bypass the Ullman ether synthesis and pursue a more convergent synthesis by permitting ether formation from groups of bridged aromatic rings instead of adding each aromatic group through a stepwise pathway. Kodama’s synthesis added each ring in sequence requiring more functionalities to be carried through a greater number of steps resulting in a decreased cumulative yield. Decicco has shown that the Chan-Evans diaryl ether synthesis can be applied to intramolecular systems in the formation of macrocyclic rings (Figure 6). A convergent approach would allow for the two sides of the macrocycle, separated by the ether, to be created separately and joined at the end of the synthesis.
Figure 6: Decicco's example of intramolecular diaryl ether formation from an arylboronic acid mediated by copper.

Figure 7: Structure of Target Compound

We designed a simplified analog of marchantin-A as a target compound (figure 7). The target compound lacks the hydroxyl functionalities present in marchantin-A, and is symmetrical. All of the aromatic rings in the target compound are meta-substituted whereas the marchantins also contain ortho-substituted and para-substituted rings. However, the target retains the two ethyl bridges, and two diaryl ethers, which are the key features of the marchantins.
We developed a retrosynthetic plan (Figure 8) for our target molecule. We planned to construct the target from two identical halves, joined using the Chan-Evans ether synthesis. Each half could be formed using a Wittig reaction to bridge the ring systems.

![Figure 8: Preliminary retrosynthesis of target compound (14)](image)

We designed a synthetic plan based on our retrosynthesis in the hope of achieving an efficient, convergent, synthesis of our target (figure 9).
Figure 9: Initial synthetic plan (main), TBS protecting group (B), TBAF (C)
**Discussion and Results**

Studies were exclusively directed towards the total synthesis of our target compound. We allowed for substantial flexibility within the synthetic plan but maintained the requirement that the target molecule should be formed using the copper-mediated ether synthesis.

The synthesis was started with the commercially available compound 3-hydroxybenzyl alcohol (1), which was reacted with tert-butyldimethylsilyl chloride (TBS-Cl) and imidizole in DMF to form the silylated alcohol (2) (figure 10).

![Figure 10: Formation of silylated alcohol (2)](image)

Through the first few attempts at this reaction, none of the desired product was produced. Studies were conducted using increased amounts of imidizole and TBS-Cl and yielded no improvement. The reaction was also tested on the alternative substrate 3-hydroxybenzaldehyde which also did not produce the silylated product. It was decided that the likely source of problems was our solvent supply. Upon using new, dry DMF, (2) was formed in good yield. However, as we had drastically increased the amounts of imidzole and DMF being used, we were also producing substantial quantities of the bis(silylated) product (2a). It was found that the bis(silylated) product could be converted easily to the desired silylated alcohol (2) through reaction with HCl in EtOH (Figure 10).
However, we found it more efficient to decrease the amounts of TBS-Cl and imidizole and selectively silate the phenol only. This is accomplished as the phenol is more acidic than the alcohol so deprotonation of the phenolic site is more favorable. The resultant negatively charged oxygen can attack the silicon through a nucleophilic mechanism.

The silylated alcohol (2) was reacted with phosphorus tribromide and pyridine in ethyl ether in an effort to form the silylated bromide (4). However, upon addition of the bromide a white precipitate was immediately formed and the reaction did not proceed. We were unable to readily determine the cause so we decided to try carbon tetrabromide. We then reacted the silylated alcohol (2) with carbon tetrabromide and triphenylphosphine in methylene chloride to successfully form the silylated bromide (3) (figure 12). In the same flask, additional triphenylphosphine was added to form the phosphonium salt (4) (figure 12) in 89% yield.
Figure 13: Formation of the silylated phosphonium salt

Phosphonium salt (4) was formed and reacted directly in a Wittig reaction with 3-bromobenzaldehyde (5) and sodium hydride in an effort to form the alkene (6), but none of the desired product was formed.

Figure 14: Attempted preparation of alkene (6)

Although attempts were made, we were unable to reproduce the pure phosphonium salt (4) through the scheme above. So we hypothesized that one possible problem with the Wittig reaction (Figure 14) was contamination of the phosphonium salt with silylated alcohol (2). This presented a problem, as the phosphonium salt and the preceding bromide were difficult to produce and purify. It was speculated that the efficiency of the reaction to produce the bromide might be increased if we produced it from a tosylate instead of directly from the alcohol. We moved toward examining this possibility by reacting the silylated alcohol (2) with tosyl chloride to form tosylate (7).
Tosylate (7) was reacted with tetra-n-propylammonium bromide in an attempt to form bromide (3), but the reaction did not produce the bromide.

At this point it was decided that examining a new approach was warranted. We determined that the alkene product (6) might be more easily formed from different precursors.

3-Hydroxybenzaldehyde (8) was reacted with TBS-Cl and imidazole in DMF to form silylated aldehyde (9) (figure 17).
Figure 17: Formation of silylated aldehyde (9)

The product was formed in 88% yield following flash chromatography. The required phosphonium salt (11) was then formed by reacting 3-bromobenzyl bromide (10) with triphenyl phosphine (figure 17).

Figure 18: Formation of phosphonium salt (11)

The phosphonium salt product (11) was then used in the Wittig reaction. The ylide was formed by reacting the phosphonium salt with phenyl lithium. The ylide was then reacted with the silylated aldehyde (9) to form alkene (6). Low yields were obtained through this method. It was later found that better yields could be obtained by using sodium bis(trimethylsilyl)amide instead of phenyl lithium. However, results with the amide base were also more variable with some reactions failing to produce any of the desired product. Although we continued to have problems running an efficient Wittig reaction, we were still able to isolate enough of the desired alkene to continue to the next
step. The isolated alkene was left as a cis/trans mixture as the cis and trans products could not readily be resolved using column chromatography. However, we were able to isolate a small fraction of the exclusively trans product. $^1$HNMR data suggested that the alkene was produced in approximately equal amounts of cis and trans which is curious as this reaction would be expected to produce mostly the cis product. At this point our inability to separate the isomers was inconsequential as we planned to reduce the double bond in the next step.

![Figure 19: Attempted preparation of alkane (12)](image)

Alkene (6) was then reduced through reaction with hydrogen catalyzed by palladium on carbon (figure 19). Unfortunately, it was found that this reaction also removed an unknown percentage of the bromine that is required to continue to the next step. Initial mass spectrometry examination suggested that the bromine was still in place. However, when we attempted to borolate alkane (12) to form boronic acid (13), we observed no reaction by TLC. The compound was reisolated by column chromatography.
and analyzed using mass spectrometry. The observed compound, which appeared identical to the starting material by TLC was shown by mass spectrometry to not have the bromine. The hydrogenation was conducted again for a shorter time period, and the reaction was monitored by TLC, but the same results were obtained.

It was decided that we would attempt to borolate alkene (6) directly before hydrogenating the double bond. The alkene was reacted with tert-butyl lithium and then trimethyl borate in efforts to form boronic acid (12).

![Reaction diagram](image)

**Figure 20: Attempted preparation of the boronic acid (12)**

However, this reaction did not yield detectable amounts of the boronic acid. Analysis of the products by $^1$HNMR showed the formation of multiple products containing only one aromatic ring. One of these products also contained the TBS protecting group suggesting that the reaction conditions induced a cleavage reaction. There are still a few options remaining that have not yet been explored.

Alternative methods of hydrogenating alkene (6) that would not remove the bromine should be explored. This would allow for the boronic acid to be carried through fewer synthetic steps. Alternative methods of forming the boronic acid also need to be
examined to find a method which works on our substrate (either alkene (6) or alkane (12)).

Figure 21: Planned preparation of target bis(bibenzyl) (14)

Hopefully, this would allow for the production of the desired boronic acid (13) and target bis(bibenzyl) (14).
Conclusion

Alkene (6) was produced in three steps from 3-hydroxybenzaldehyde (8), and 3-bromobenzyl bromide (10). A variety of strategies were employed to synthesize the desired boronic acid (13), but as of this time none have been successful. The synthesis of this boronic acid is necessary to study the feasibility of applying the Chan-Evans copper mediated formation of diaryl ethers to a bis(bibenzyl) synthesis (Figure 19).

In seeking to exploit the advantages of the Chan-Evans ether synthesis over the Ullman ether synthesis, we have encountered some of the associated difficulties. The utilization of an arylboronic acid to produce a diaryl ether first requires the production of the appropriate boronic acid. This has been shown to be no trivial task. As our boronic acid (14) is to be derived from a bromide, the copper mediated reaction requires an additional step (conversion of the bromide to the boronic acid), which would not be necessary if the Ullman ether synthesis were employed.

Future work in this group should be directed towards the use of alternative methods of hydrogenating alkene (6). Also, methods need to be further developed to allow for the efficient conversion of the bromide to the boronic acid for this type of system.

Further work is required to determine the feasibility of using the Chan-Evans ether synthesis to form bis(bibenzyls).
Experimental

Preparation of silylated alcohol (2) from 3-hydroxybenzyl alcohol (1):

In a round bottom flask at 0°C under argon, 1.00g (8.06mmol) of (1) was combined with 1.04g (15.3mmol) of imidizole. Approximately 15 mL of DMF was added as solvent. 1.15g (7.65mmol) of TBS-Cl was added to the stirring solution. The reaction was allowed to stir for 30 min and progress was monitored by TLC. The reaction was extracted in approximately 100mL of EtOAc. The base and TBS-Cl were quenched with 40 mL washes of 1M HCl, and sat. CuSO₄, respectively. The organic layer was washed with 40 mL of brine and dried over sodium sulfate. Following filtration, the solvent was removed with a rotary evaporator. The product was isolated by flash column chromatography on silica gel in 10:90 EtOAc/Hexanes, yielding 1.34g (5.6mmol) of (2) as a clear oil (74% yield).

Preparation of phosphonium salt (4) from silylated alcohol (2):

In a roundbottom flask with a condenser at room temperature (RT) under argon, 105mg (.441mmol) of (2) in methylene chloride was combined with 162mg (.618mmol) of triphenyl phosphine and 205mg (.618mmol) of carbon tetrabromide. The solution was stirred for 3 hours to form intermediate bromide (3). An additional 127mg (.4851mmol) of triphenyl phosphine was added and the reaction was heated at reflux for 18 hours under argon. The solvent was removed with a rotary evaporator. The phosphonium salt was isolated by column chromatography on silica gel in 5:95 ethanol/methylene chloride to yield 218mg (.39mmol) of a white solid (89% yield).
Attempted preparation of alkene (6) from phosphonium salt (4) and 3-bromobenzaldehyde (5):

In a round-bottom flask at RT under argon, 218mg (.39mmol) of (4) was combined in THF with 72mg (.39mmol) of (5), and 56.16mg (2.34mmol) of NaH. The reaction was stirred under argon 48 hours. The reaction was quenched with water. The aqueous layer was extracted with methylene chloride and the combined organic layers were washed with brine. The organic layer was dried over sodium sulfate and the filtered solvent was removed by rotary evaporator. The resulting products were isolated by flash column chromatography.

Preparation of tosylate (7) from silylated alcohol (2):

In a round-bottom flask at RT under argon, 52mg (.2184mmol) of (2) was combined in methylene chloride with 33mg (.328mmol) of triethylamine and 50mg (.262mmol) of tosyl chloride. The reaction was stirred 4 hours under argon. The reaction was quenched with 1M HCl, and washed with brine. The organic layer was dried over sodium sulfate and the filtered solvent was removed using a rotary evaporator. The product was isolated using flash column chromatography on silica gel in 5:95 EtOAc/Hexanes, yielding 53mg (.135mmol) of (7) (62% yield).

Attempted preparation of bromide (3) from tosylate (7):

In a round-bottom flask with condenser under argon, 53mg (.135mmol) of (7) were combined in THF with 43mg (.1624mmol) of tetra-n-propylammonium bromide. The reaction was heated at reflux overnight under argon. The reaction was extracted with
methylene chloride and washed with brine. The organic layer was dried over sodium sulfate and the filtered solvent was removed with a rotary evaporator.

Preparation of silylated aldehyde (9):

In a roundbottom flask at 0°C under argon, 500 mg (4.09 mmol) of 3-hydroxybenzaldehyde was combined with 670 mg (9.8 mmol) of imidazole in approximately 20 mL of DMF. 737.4 mg (4.9 mmol) of TBS-Cl were added to the stirring solution. The reaction was stirred for 3 hours and was followed by TLC. The reaction was extracted in EtOAc then washed with 1M HCl, sat. CuSO4, and brine in sequence. The organic layer was dried over sodium sulfate and the filtered solvent was removed with a rotary evaporator. The product was isolated by flash column chromatography on silica gel in 10:90 EtOAc/Hexanes, yielding 826.7 mg (3.5 mmol) of (9) (86% yield): 1H NMR δ 9.94 (1H, s, CHO), 7.46 (1H, d, J=7.5 Hz, para to O), 7.38 (1H, t, J=7.8 Hz, meta to O), 7.32 (1H, t, J=1.5 Hz, ortho to O and carboxyl), 7.09 (1H, ddd, J= 8.0, 2.4, 0.9 Hz, para to carboxyl), 0.98 (9H, s, t-Bu), 0.21 (6H, s, 2Me).

Preparation of Phosphonium salt (11):

In a roundbottom flask with a condenser under argon, 500 mg (2.0 mmol) of 3-bromobenzyl bromide (10) were combined in methylene chloride with 629 mg (2.4 mmol) of triphenyl phosphine. The solution was heated at reflux under argon for 18 hours and the reaction was monitored by TLC. The solvent was removed with a rotary evaporator to yield a white solid. The product was purified by trituration with hexanes. The resulting phosphonium salt was dried with a dean stark trap with benzene: 1H NMR
δ 7.80(9H, m, phenyl), 7.64(6H, m, phenyl), 7.37(1H, d, J=7.7 Hz, para to CH₂),
7.32(1H, d, J=7.9. para to Br), 7.02(1H, t, J= 7.9, meta to Br), 6.93(1H, d, J=1.9 Hz, ortho to Br and CH₂) 5.58(2H, d, J=14.69 Hz, CH₂).

Preparation of alkene (6):

To a roundbottom flask at -15°C under argon containing 422mg (.825mmol) of the phosphonium salt (11) in THF, 1.6 mL of 1M (1.6mmol) of sodium bis(trimethylsilyl)amide was added dropwise. The reaction was allowed to stir for 2 hours and warm to 5°C. The reaction was then cooled to -78°C and 195mg (8.25mmol) of the silylated aldehyde (9) in THF was added slowly via cannula. The reaction was then stirred 20 minutes at -78°C before being allowed to warm to room temperature. The reaction was extracted in EtOAc and washed with 1M HCl and Brine in sequence. The organic layer was dried over sodium sulfate and the solvent was removed with a rotary evaporator. The product was isolated by flash column chromatography on silica gel in 8:92 ether/pentane, yielding 141mg (.378mmol) of alkene (46% yield). ¹H NMR δ 7.36(1H, s, ortho to Br and CH), 7.31(1H, d, J=7.9 Hz, ortho to Br), 7.16(3H, m), 6.81(1H, d, J=7.6 Hz, para to O), 6.70(1H, dd, J=8.0, 2.2 Hz, meta to O), 6.66(1H, s, ortho to O and CH), 6.60(1H, d, J=12.2 Hz, CH), 6.50(1H, d, J=12.2 Hz, CH), 0.93(9H, s, t-Bu), 0.08(6H, s, 2Me).

Attempted preparation of alkane (12):

In a roundbottom flask at RT under argon, 40mg (.0378mmol) of 10% Pd/C was added to 141mg (.3782mmol) of the alkene (6) in EtOAc. The suspension was stirred.
and flushed with hydrogen atmosphere. The reaction was allowed to stir under hydrogen atmosphere for 1 hour and the reaction was monitored by TLC. The flask was then flushed with argon. The resulting suspension was filtered through celite and the solvent was removed with a rotary evaporator.

Attempted Preparation of Boronic Acid (12):

In a round-bottom flask at -78°C under argon containing 110mg (0.282mmol) of the alkene (6), 0.75 mL (1.128mmol) of 1.5M tert-butyl lithium was added dropwise. After the solution was allowed to stir for 5 min, 0.161 mL (1.41 mmol) of B(OMe)3, freshly distilled from Naº, was added dropwise. The reaction was allowed to stir for an additional 5 minutes before being allowed to warm to RT. The reaction was quenched with 1M HCl and extracted in EtOAc. The organic layer was washed with brine and dried over sodium sulfate. The solvent was removed with a rotary evaporator and products were isolated by flash column chromatography on silica gel in 10:90 EtOAc/Hexanes.
References


<table>
<thead>
<tr>
<th>Page</th>
<th>Heading</th>
<th>Description</th>
</tr>
</thead>
<tbody>
<tr>
<td>28</td>
<td>protected aldehyde er</td>
<td>$^{1}$H NMR of silylated aldehyde (9) full spectra</td>
</tr>
<tr>
<td>29</td>
<td>protected aldehyde er</td>
<td>$^{1}$H NMR of silylated aldehyde (9) aromatic region</td>
</tr>
<tr>
<td>30</td>
<td>protected aldehyde er</td>
<td>$^{13}$C NMR of silylated aldehyde (9) full spectra</td>
</tr>
<tr>
<td>31</td>
<td>phosphonium salt er</td>
<td>$^{1}$H NMR of phosphonium salt (11) full spectra</td>
</tr>
<tr>
<td>32</td>
<td>phosphonium salt er</td>
<td>$^{1}$H NMR of phosphonium salt (11) aromatic region</td>
</tr>
<tr>
<td>33</td>
<td>2nd eluent column</td>
<td>$^{1}$H NMR of trans alkene (6) full spectra</td>
</tr>
<tr>
<td>34</td>
<td>2nd eluent column</td>
<td>$^{1}$H NMR of trans alkene (6) aromatic region</td>
</tr>
<tr>
<td>35</td>
<td>scan 162...</td>
<td>MS of alkene (6)</td>
</tr>
<tr>
<td>36</td>
<td>scan 52...</td>
<td>MS of attempted hydrogenation reaction product</td>
</tr>
<tr>
<td>37</td>
<td>scan 127...</td>
<td>MS of attempted borotation reaction product</td>
</tr>
<tr>
<td>38</td>
<td>monoprotected</td>
<td>$^{1}$H NMR of silylated alcohol (2) full spectra</td>
</tr>
<tr>
<td>39</td>
<td>ER 1/8/03</td>
<td>$^{1}$H NMR of tosylate (7) full spectra</td>
</tr>
<tr>
<td>40</td>
<td>ER 1/8/03</td>
<td>$^{1}$H NMR of tosylate (7) aromatic region</td>
</tr>
</tbody>
</table>
Acknowledgements

I would like to thank all of the people who have helped me in the preparation of this thesis and throughout my academic career. I would like to specifically thank Prof. Jeff Katz, my research advisor; Prof. Julie Millard, my academic advisor; Prof. Brad Mundy; and Prof. Das Thamattoor. I would also like to thank the entirety of the Colby Chemistry Department, students, faculty and staff.