2011

Routes to Acylated Sydnone Esters

Amanda Marie Balaguer

Wright State University

Follow this and additional works at: http://corescholar.libraries.wright.edu/etd_all
Part of the Chemistry Commons

Repository Citation

This Thesis is brought to you for free and open access by the Theses and Dissertations at CORE Scholar. It has been accepted for inclusion in Browse all Theses and Dissertations by an authorized administrator of CORE Scholar. For more information, please contact corescholar@www.libraries.wright.edu.
A thesis submitted in partial fulfillment
of the requirements for the degree of
Master of Science

By

AMANDA MARIE BALAGUER
B.S., Wright State University, 2008

2011
Wright State University
I HEREBY RECOMMEND THAT THE THESIS PREPARED UNDER MY SUPERVISION BY Amanda Marie Balaguer ENTITLED Routes to Acylated Sydnone Esters BE ACCEPTED IN PARTIAL FULFILLMENT OF THE REQUIREMENTS FOR THE DEGREE OF Master of Science.

Kenneth Turnbull, Ph.D.
Thesis Director

Kenneth Turnbull, Ph.D.
Chair
Department of Chemistry
College of Math and Science

Committee on Final Examination

Kenneth Turnbull, Ph.D.

Eric Fossum, Ph.D.

Daniel M. Ketcha, Ph.D.

Andrew T. Hsu, Ph.D.
Dean, Graduate School
Abstract

Balaguer, Amanda Marie., M.S., Department of Chemistry, Wright State University, 2011. Routes to Acylated Sydnone Esters

Various 4-acyl-3-[2’-(carboalkoxy)phenyl]sydnones were synthesized by reaction of the parent sydnone with the corresponding anhydrides and Montmorillonite K-10. In the Q-tube, the acylation using acetic anhydride, which normally took 1.5 days for complete conversion thermally, was complete in 8.5 hours. Use of bismuth triflate as catalyst reduced the reaction time to 5 hours and, in the microwave, reactions were complete in 30 minutes and provided comparable yields. New sydnones were synthesized with acetic, propionic, butyric, and isobutyric anhydrides. Extension to various homogeneous metal triflates (lanthanum, yttrium, scandium, hafnium, gadolinium, and indium) was explored. Reactions were performed with 3-phenylsydnone as reactant, initially under thermal conditions overnight, individually with the six chosen catalysts. When optimal conditions were achieved, these predetermined parameters were employed for further optimization, performed under microwave irradiation. After multiple reactions, the best catalysts were determined to be the gadolinium and indium triflates.
# TABLE OF CONTENTS

<table>
<thead>
<tr>
<th>Section</th>
<th>Page</th>
</tr>
</thead>
<tbody>
<tr>
<td>Introduction</td>
<td>1</td>
</tr>
<tr>
<td>The Friedel-Crafts Reaction</td>
<td>1</td>
</tr>
<tr>
<td>I. The History of the Friedel-Crafts Reaction</td>
<td>1</td>
</tr>
<tr>
<td>II. Scope</td>
<td>5</td>
</tr>
<tr>
<td>III. Friedel-Crafts Acylation</td>
<td>8</td>
</tr>
<tr>
<td>A. Ketone Synthesis</td>
<td>8</td>
</tr>
<tr>
<td>B. Introduction of Formyl Groups</td>
<td>16</td>
</tr>
<tr>
<td>C. Introduction of Carboxyl Groups</td>
<td>17</td>
</tr>
<tr>
<td>IV. Homogenous Catalyst</td>
<td>19</td>
</tr>
<tr>
<td>V. Heterogenous Catalyst</td>
<td>24</td>
</tr>
<tr>
<td>Sydnones</td>
<td>26</td>
</tr>
<tr>
<td>I. Reactions of Sydnones</td>
<td>28</td>
</tr>
<tr>
<td>A. Electrophilic Aromatic Substitution Reactions</td>
<td>29</td>
</tr>
<tr>
<td>1. Direct Acylation</td>
<td>29</td>
</tr>
<tr>
<td>2. Halogenation</td>
<td>30</td>
</tr>
<tr>
<td>B. Lithiation</td>
<td>32</td>
</tr>
<tr>
<td>C. Cycloaddition</td>
<td>35</td>
</tr>
<tr>
<td>Aims of the Present Work</td>
<td>39</td>
</tr>
<tr>
<td>Results and Discussion</td>
<td>44</td>
</tr>
<tr>
<td>Experimental</td>
<td>86</td>
</tr>
<tr>
<td>References</td>
<td>158</td>
</tr>
</tbody>
</table>
# LIST OF TABLES

<table>
<thead>
<tr>
<th>Table</th>
<th>Page</th>
</tr>
</thead>
<tbody>
<tr>
<td>1. Molar Ratio of Sydnone to Acetic Anhydride</td>
<td>47</td>
</tr>
<tr>
<td>2. Thermal vs. Q-Tube Yields and Reaction Times for the Montmorillonite K-10 Catalyzed Syntheses of 3-(2’-Carbomethoxyphenyl)-4-acyl sydnones</td>
<td>52</td>
</tr>
<tr>
<td>3. Q-Tube Yields and Reaction Times for the Montmorillonite K-10 and Bismuth Triflate Catalyzed Syntheses of 4-Acyl-3-[2’-(carboalkoxy)phenyl] sydnones</td>
<td>54</td>
</tr>
<tr>
<td>4. MWI Yields for the Bismuth Triflate Catalyzed Syntheses of 4-Acyl-3-[2’-(carboalkoxy)phenyl] sydnones 68-71 and 75-78</td>
<td>58</td>
</tr>
<tr>
<td>5. Cost of Metal Triflate catalysts</td>
<td>62</td>
</tr>
<tr>
<td>6. Acylation of 3-Phenylsydnone with Lanthanum Triflate</td>
<td>64</td>
</tr>
<tr>
<td>7. Acylation of 3-Phenylsydnone with Yttrium Triflate</td>
<td>65</td>
</tr>
<tr>
<td>8. Acylation of 3-Phenylsydnone with Hafnium Triflate</td>
<td>66</td>
</tr>
<tr>
<td>9. Acylation of 3-Phenylsydnone with Scandium Triflate</td>
<td>67</td>
</tr>
<tr>
<td>10. Acylation of 3-Phenylsydnone with Gadolinium Triflate</td>
<td>68</td>
</tr>
<tr>
<td>11. Acylation of 3-Phenylsydnone with Indium Triflate</td>
<td>69</td>
</tr>
<tr>
<td>12. Microwave Optimization of the Acylation of 3-Phenylsydnone (33) with Lanthanum Triflate and Acetic Anhydride</td>
<td>72</td>
</tr>
<tr>
<td>13. Microwave Optimization of the Acylation of 3-Phenylsydnone (33) with Yttrium Triflate and Acetic Anhydride</td>
<td>73</td>
</tr>
<tr>
<td>14. Microwave Optimization of the Acylation of 3-Phenylsydnone (33) with Scandium Triflate and Acetic Anhydride</td>
<td>74</td>
</tr>
</tbody>
</table>
15. Microwave Optimization of the Acylation of 3-Phenylsydnone (33) with Hafnium Triflate and Acetic Anhydride .................................................................75

16. Microwave Optimization of the Acylation of 3-Phenylsydnone (33) with Gadolinium Triflate and Acetic Anhydride .................................................................76

17. Microwave Optimization of the Acylation of 3-Phenylsydnone (33) with Indium Triflate and Acetic Anhydride .................................................................76

18. Comparison of Optimal Microwave Reactions for the Acylation of 3-Phenylsydnone (33) in ACN or Ac₂O .................................................................78

19. Reduction of 3-[2’-(Carbomethoxy)phenyl] sydnone (67) with DIBAL ...........80
Acknowledgements

First and foremost, I would like to thank Dr. Turnbull for enduring the struggle of me writing my thesis. You have helped mold me into the chemist I am today, helping me to achieve my educational goals. You have aided me both inside in the lab and in my personal life, and for that I am grateful. I would like to express thanks to Dr. Fossum for his guidance in chemistry and our Monday morning football talks. I tip my cup of coffee to you. Last, I would like to thank Dr. Ketcha for helping me realize that answers to questions in organic chemistry can be “Nobody knows”.

Thank you to all of the current and past graduate and undergraduate chemistry students. You have helped me keep my sanity through reactions not working, no clean glassware, and rabblerousing students who do not understand labs. I have enjoyed our time together both working inside the lab and our escapades outside of the lab. I would also like to extend my gratitude to others in the Sydnone Institute, especially Ryan Selhorst for his work on optimization of metal triflate catalysts.

Lastly, I would like to thank my parents for supporting me on my decision to go to grad school. You make sure I have a roof over my head and food on the table. There is nothing more I can ask for. I would also like to thank my sister, Emilie, for keeping me grounded and highly caffeinated.
Introduction

The Friedel-Crafts Reaction

I. The History of the Friedel-Crafts Reaction

The Friedel-Crafts reaction is one of the fundamental chemical reactions taught in basic organic chemistry courses. In this reaction, an aromatic compound can undergo either an alkylation or acylation with assistance from a metal catalyst. Though it is named after Charles Friedel and James Mason Craft, there were prior publications\(^1\) that led them to their discovery. The first publication formally observed as an alkylation reaction that used a metal catalyst was from Zincke in 1869.\(^1\) In this reaction, Zincke was attempting to synthesize an aromatic acid, \(\beta\)-phenyl propionic acid (3), from benzyl chloride (1) and chloroacetic acid (2) in benzene (Scheme 1).\(^1\)

Scheme 1

\[
\begin{align*}
\text{(1)} & \quad \text{Cl} \quad \text{OH} \\
\text{(2) } & \quad \text{Cl} \quad \text{O} \\
\text{Zn} & \quad \text{OH}_2 \quad \text{Cl}_2
\end{align*}
\]

He used zinc powder to react with the liberated chlorine to make zinc chloride. Instead of \(\beta\)-phenyl propionic acid, diphenylmethane (4) was produced from reaction with the benzene solvent (Scheme 2).\(^1\)
Zincke furthered his investigation of this new transformation by reacting benzyl chloride (1) with just benzene, toluene, or xylene and using iron or silver as the metal catalysts. He stated that “the reaction is of such a peculiar nature that even now it is possible that a sufficient explanation has not been given.”

In other work preceding Friedel and Craft, Radzianovskii found in 1874 the general reaction of halides with aromatic compounds in the presence of zinc. In 1876, Doebner and Stackman used zinc oxide to alkylate phenol with chloroform to produce 2-hydroxy benzaldehyde (Scheme 5). It was reported that zinc chloride was formed as an intermediate but the authors did not understand its purpose. Later, Friedel and Craft would show that zinc chloride was the active condensing agent in all of the alkylation reactions.

The first acylation to be reported was in 1873 by Grucarevic and Merz. Here, again, zinc dust was used to catalyze the reaction. In these reactions, the aromatic compounds were acylated by acid halides. Zincke had also performed an acylation reaction by reacting benzoyl chloride (5) in benzene with either copper, zinc, or silver in an attempt to make benzil (6) (Scheme 3).
Scheme 3

The metal again was used to react with the liberated chlorine. The reaction did not take place as expected and benzophenone (7) resulted (Scheme 4).^6

Scheme 4

During all of these reactions prior to Friedel and Craft’s studies, there was no mention of a metal halide remaining in the final reaction mixture. The first mention of the development of a metal halide in the reaction mixture was in a paper by Doebner and Stackman in 1876.^4 They added zinc oxide before the start of the reaction and, after filtration, it was observed that zinc chloride was present at the end (Scheme 5).^4 Though it was noted in their paper that zinc chloride was produced, they did not fully understand the nature of the reaction taking place. In fact, none of the previously stated chemists entirely understood the true nature of the reaction. It was left to Friedel and Craft to show the importance of, and the necessity for, the metal chloride in the reaction.
In 1877, Charles Friedel and James Craft performed their first alkylation reaction. In this reaction, amyl chloride (8) was mixed with strips of aluminum in the presence of benzene and this resulted in the formation of a long chain alkyl halide, confirmed by melting point (Scheme 6).{7,8}

Their explanation for this result was that the hydrogen from one amyl chloride reacted with the halogen from the other to give hydrogen chloride as a byproduct. Their first reported case of the Friedel-Craft’s reaction was performed with an alkyl halide but it was thought for years that this reaction could only take place with aromatic species. In this and later reactions, Friedel and Craft found that the catalyst for this reaction was the formation of aluminum chloride. Many of their discoveries, conclusions, and limitations of this reaction were reported in three papers constructed over a six week time period. Since Friedel and Crafts development of the foundation for their new reaction, there has been built an enormous development and refinement in the process.
II. Scope

With Friedel and Craft’s discovery, it was now possible to prepare many different compounds. The common reactants that were used to produce alkyl benzenes were benzene, a short or long chain alkyl halide, and aluminum chloride (as shown below).

\[
\text{C}_6\text{H}_6 + \text{R'}\text{Cl} \xrightarrow{\text{AlCl}_3} \text{C}_6\text{H}_5\text{R'} + \text{HCl}
\]

\(\text{R'} = \text{alkyl chain}\)

In a similar manner, Friedel and Craft were able to synthesize keto-containing compounds using aluminum chloride as the catalyst.

\[
\text{R'COCl} + \text{C}_6\text{H}_6 \xrightarrow{\text{AlCl}_3} \text{C}_6\text{H}_5\text{COR'} + \text{HCl}
\]

\(\text{R'} = \text{alkyl chain}\)

They expanded their work by examining the nature of the alkyl halides they were using. They first exchanged the halide to determine whether or not any differences would result from using bromine or iodine. Accordingly, they reacted either ethyl iodide or methyl bromide with benzene to yield ethyl benzene or toluene, respectively. The reaction using ethyl iodide was less clean, giving large portions of high boiling by-products, than was that from using methyl bromide, however, from these reactions, Friedel and Craft concluded that this reaction was general and could be used with a variety of different alkyl halides.

Friedel and Craft studied also the ability to add multiple alkyl chains onto benzene. Thus, using the same procedure as stated above, viz. methyl chloride, benzene, and aluminum chloride, resulted in a mixture of toluene, xylene, mesitylene and durene.

Continuing with their work, they also found other limitations with the reaction. They performed extensive studies on the metal halide catalyst and it was found that the
aluminum could be exchanged with either zinc or iron but not with magnesium, cobalt, copper, mercury, or antimony. They mentioned Zincke’s work while discussing this discovery and they proved that the success of Zincke’s reaction was due to the presence of zinc chloride in the reaction vessel. They also postulated that an intermediate was formed between the metal halide and the aromatic compound.

As stated previously, the Friedel Crafts acylation is a general procedure where there is an addition of an acyl group onto an aromatic or aliphatic system by catalyzed addition of an acylating agent such as an acyl halide, acid anhydride, ester or carboxylic acid. As shown below, in each of the reactions, the main product will remain the same while the by-product will differ.

There are three main procedures used to determine the sequence of addition of reagents. The first and most widely used procedure is the Friedel-Crafts, Elbs procedure.
In this procedure, the catalyst is simply added last.\textsuperscript{11, 12} The second procedure is called the Bouveault procedure. In this method, the aromatic compound is mixed with the catalyst and the acylating agent is added last.\textsuperscript{13, 14} This is not ideal because of the potential formation of the hydrogen halide (acid), which may cause isomerization or disproportionation and result in two or more final products. The last method is the Perrier procedure. In this process, the catalyst and acylating agent are mixed prior to the addition of the aromatic substrate.\textsuperscript{15, 16} The reaction is normally carried out in a mixed solvent consisting of carbon disulfide, dichloromethane and ethylene chloride, where the $\text{RCOCl} \cdot \text{AlCl}_3$ complex is soluble but $\text{AlCl}_3$ is not. Excess $\text{AlCl}_3$ is not desirable since it might affect isomerization. The main advantage is that the acylated product will still be complexed with the catalyst, which then becomes insoluble. The complex can be separated by hydrolysis and finally the acylated product can be converted to the ketone.

There are many analogous reactions that mimic the Friedel-Crafts reaction and are considered to be subsets of the reaction. Thus, the Gatterman reaction is a reaction of hydrocyanic acid with an aromatic compound, which is catalyzed by aluminum chloride. After hydrolysis, an aldehyde containing compound is formed.\textsuperscript{17} The Houben-Hoesch reaction uses hydrochloric acid as the Lewis acid catalyst and a nitrile compound reacts with an arene compound to form an aryl ketone upon hydrolytic workup.\textsuperscript{18, 19} Similarly, the Fries reaction rearranges a phenolic ester to a hydroxyl aryl ketone with the use of a Lewis acid catalyst\textsuperscript{20} and the Scholl reaction is a coupling reaction that forms a single carbon bond between two arene compounds with the aid of a Lewis acid and protic acid.\textsuperscript{21}
III. Friedel-Crafts Acylation

Acylation reactions involve the introduction of an acyl group to a substrate where the product synthesized is dependent on the various reagents. The different types of group that can be introduced include keto, formyl, sulfonyl, nitro, and various other carbonyl containing species. The greatest amount of research compiled about the Friedel-Craft reaction, much from industry, concerns acylations, especially the introduction of a keto group. The reason for the reaction’s popularity is that acylations are generally simple reactions that yield stable, monoacylated products in good yields.

There are numerous variations that can be made to this reaction to yield unique organic products. The substrates that may be used can include aromatic, aliphatic, or heterocyclic species. Aromatic compounds that can be acylated include benzenoid compounds such as toluene, phenols, halobenzenes, thiols, and aromatic ethers. Likewise, heterocyclic compounds like furans, thiophenes, pyrroles, and indoles are prone to acylations. Lastly, aliphatic substrates may include alkanes, alkenes, alkynes, cycloalkanes and cycloalkenes.

A. Ketone Synthesis

The keto group can be introduced onto a variety of different substrates with the use of different acyl containing compounds. The most popular of the latter are acyl halides. It has been shown that the reactivity of acid halides decreases with increasing electronegativity of the halogen. Thus, reactivity is shown as RCOI > RCOBr > RCOCl > RCOF. This was determined experimentally based on yields produced and not from the kinetics. In most cases, the maximum reactivity is observed with the chloro or bromo acid halide.
It was observed early that through Friedel-Craft synthesis both alkylations and acylations can be achieved by using a metal halide as a catalyst. It was also noted the result of adding different acyl halides to the general benzene reaction. Using propionyl, butyryl and hexanoyl halides, ketone products resulted with the alkyl portion duplicating the corresponding alkyl chain attached to the carbonyl. For example, isobutyryl chloride reacts with benzene to yield isopropyl phenyl ketone. Likewise, cyclic acid halides behave in a similar manner. This observation made acylation an attractive new avenue to the production of an alkyl product by reduction of the initially produced ketone. This helped solve problems with compounds that would not alkylate or to avoid multiple alkylations from occurring.

The same synthetic methods can be applied to unsaturated acid halides though, sometimes, such species give complicated products due to the unsaturation. For example, when benzene reacts with 2-propenoyl chloride (9) it yields hydrindone (10) and not the expected vinyl phenyl ketone (Scheme 7).

**Scheme 7**

![Scheme 7](image)

To overcome this problem, longer or more complex unsaturated acid halides can be used to yield the expected ketone product and this can be seen in the reaction of benzene with 3,3-dimethyl acryloyl chloride (11) to give 3,3-dimethyl vinyl phenyl ketone (12) (Scheme 8).
Other early work that was performed by Friedel, Craft, and Ador\textsuperscript{32,33} was the synthesis of benzoyl chloride and benzophenone (Scheme 9). The original reaction was between benzene and phosgene (13) in the presence of aluminum chloride and it was shown that a variety of factors affected the proportions of products being produced, such as time, temperature, etc.\textsuperscript{34} This discovery led to a whole new avenue for the production of diaryl ketones using phosgene.

The use of oxalyl chloride (14) gives a much more complicated series of results, presumably since it decays rapidly to carbon monoxide and phosgene. With highly reactive species, such as anisole, the reaction takes place as expected to give the corresponding benzil derivative (Scheme 10).\textsuperscript{35,36}
With less reactive species, a myriad of different compounds, most of them simple ketones, can result due to the decomposition of oxalyl chloride. Uniquely, with polycyclic substrates, a bridged ketone can be formed with oxalyl chloride (Scheme 11).

Alkylated benzenes can be acylated in good yields with metal halide catalysts. In general, these reactions with mono-alkylated benzenes provide only one isomer as the main product but other isomers will result as byproducts in low yields (<10%).

Thus, acylations with toluene yield predominantly $p$-isomers. For example, in work by Brown, reaction of either acetyl chloride or benzoyl chloride with toluene in the presence of aluminum chloride provided the $p$-isomer in 97.6% yield with acetyl chloride and 91.7% yield with benzoyl chloride. Both $o$- and $p$-xylenes give only a single
isomeric product, thus, acylation takes place at the 4-position with $o$-xylene and at the 3-position with $p$-xylene (Figure 12). In contrast, $m$-xylene has been shown to give multiple isomers as well as diacylation on the ring.$^{40}$

**Figure 12**

![Diagram](https://via.placeholder.com/150)

In 1908, Fries and Fink reported that the ester of a phenol, when reacted with aluminum chloride, would rearrange to form a hydroxyaryl ketone (Scheme 13).$^{20}$

**Scheme 13**

![Diagram](https://via.placeholder.com/150)

Under Friedel-Crafts conditions, anhydrides react with the aromatic nucleus to yield one equivalent of ketone for each mole of anhydride used (Scheme 14).$^{41-43}$ In some circumstances, the remaining part of the anhydride may acylate the ring further and increase the yield.$^{44}$ Symmetric aliphatic anhydrides give alkyl aryl ketones where there is no reordering of the alkyl chain.$^{41}$
The most valuable aromatic anhydride to industry is phthalic anhydride (15). o-Aroylbenzoic acid has many uses but it is used primarily to synthesize various quinone products which are used in the formation of dyes (Scheme 15). The discovery of this reaction revolutionized the dye industry. Previously, to obtain anthraquinone (17) involved oxidization of anthracene by chromic acid. This new method resulted in a cleaner product that was less expensive to make with excellent yields (97%). There are numerous aromatic compounds that will give the corresponding o-aroylbenzoic acid. They range from benzene and toluene to halogenobenzenes, aromatic ethers, and anthracene. However, aromatic molecules containing electron-withdrawing groups, such as benzaldehyde, benzoic acid, and nitrobenzene, do not react.

The phthalic anhydride component may also be substituted with little to no effect on the overall reaction and the final product is always a substituted o-benzoylbenzoic acid (16). Some possible substituents on the phthalic anhydride are sulfur, bromine,
chlorine, and iodine, usually at the 3- or 4-positions. Tetrahalogeno phthalic anhydrides have been employed also.

Highly unsaturated ketenes, when reacted with aromatic compounds and the metal halide catalyst, will yield a ketone (Scheme 16). The reaction mechanism is not known, though, it is speculated that a direct addition to the ethylenic linkage may occur and that an organoaluminum intermediate is formed. However, the most plausible conjecture is that an acetyl chloride intermediate is involved. Benzene, naphthalene, and anisole are able to be acylated by a ketene, however, again strong electron-withdrawing groups on the aryl ring do not permit acylation.

\textbf{Scheme 16}

\begin{center}
\includegraphics[width=0.5\textwidth]{scheme16.png}
\end{center}

It is possible to introduce a ketone to an aromatic substrate by condensation with a carboxylic acid. The substrate is not directly acylated by the acid but by an intermediate that forms between the acid and metal halide, an acid halide. From there, the reaction proceeds as expected. An excess of metal halide is needed for the reaction to take place and, though the reaction requires a minimum of three times the quantity of metal halide, it still proves valuable in commercial work when inexpensive aluminum chloride is used. Similarly, aromatic acids react under these conditions. Polycarboxylic acids, such as pyromellitic acid (18), react to yield keto acids (Scheme 17).
Esters can acylate aromatic compounds and this may occur concurrently with an alkylation. This reaction has not been as comprehensively studied as other Friedel Crafts reactions, however, the acylations proceed with better yields when a bulky R group is attached to the ester. For example, phenyl acetate, aspirin, and ethyl acetate were reacted separately with benzene and aluminum chloride to yield acetophenone. Aspirin gave the highest yield at 70%.

The Hoesch-Houben reaction involves the use of a nitrile as the acylating agent to form a ketamine as an intermediate, which is then hydrolyzed to afford the appropriate ketone (Scheme 18). The nitrile is condensed with an aromatic species with either zinc chloride, aluminum chloride, or other anhydrous metal halides as catalyst.
B. Introduction of Formyl Groups

A formyl group here is regarded as a keto group in which the R group is instead hydrogen. The formyl group is normally introduced by formic acid and its derivative acids using a metal halide as a catalyst, though there are other methods to achieve this acylation, including the use of carbon monoxide.

The Gattermann reaction is a well-known reaction that introduces an aldehyde group to an aromatic system. In this reaction, a formimine is formed by reacting hydrogen cyanide with hydrochloric acid. This intermediate then reacts with aluminum chloride and the aromatic substrate to form the aldimine in good yields. Lastly, through a simple hydrolysis, the aldehyde is formed (Scheme 19). This reaction gives better yields when a phenol or aromatic ether is used as the substrate at low temperatures. Formylating benzene or alkyl benzenes is more difficult and requires high temperatures or pressure.

Scheme 18

Scheme 19
In a similar reaction, the Gattermann-Koch reaction, carbon monoxide, the hydrogen cyanide replacement, is reacted with hydrochloric acid to yield formyl chloride as the intermediate.\(^{57}\) The formyl chloride is then reacted with the aromatic substrate and aluminum chloride to yield directly the aromatic formyl compound (Scheme 20).

**Scheme 20**

\[
\text{CO} + \text{HCl} \rightarrow \begin{array}{c}
\text{H} \\
\text{O} \\
\text{C} \\
\text{Cl}
\end{array}
\]

As stated previously, a formyl group can be introduced directly with formic acid. Formyl chloride is formed by reacting formic acid with aluminum chloride.\(^{52}\) From there, the reaction takes place as seen in the Gatterman-Koch reaction to form the aromatic formyl compound (Scheme 21).

**Scheme 21**

\[
\text{H} \\
\text{C} \\
\text{O} \\
\text{O}
\]

C. Introduction of Carboxyl Groups

Carboxyl groups can be introduced to substrates by using derivatives of carbonic acid including urea chloride, carbonyl chloride, and carbon dioxide. When carbonyl chloride reacts with an aromatic compound, it produces an acid chloride which upon hydrolysis will yield an acid.\(^{8, 48, 59, 60}\) However, certain conditions must be used that favor...
acid formation and not ketone formation, such as low temperature, short reaction periods, and a low concentration of the hydrocarbon. Urea chloride will react with an aromatic substrate to form an amide which is hydrolyzed to yield the corresponding acid.$^{51, 62}$

Carbon dioxide alone can introduce a carboxyl group using a Friedel Craft reaction. Thus, under high pressure, an active aromatic compound, such as a hydroxy- or amino-benzene, will yield a mixture of a ketone and an acid in the presence of aluminum, zinc, or ferric chlorides.$^{63}$ A general example of this process is phenol reacting with carbon dioxide to yield both salicylaldehyde (19) and 4,4’-dihydroxybenzophenone (20) (Scheme 22). These reactions normally take place at temperatures between 100°C-150°C with pressures ranging from 70 to 120 atmospheres. The reactions with carbon dioxide warrant further experimentation because they produce acids and ketones inexpensively.

Scheme 22
IV. Homogeneous Catalysts

Much of what has been discussed in the introduction with respect to catalysts has included aluminum chloride or some variation of a metal halide. However, metal halide shortcomings include the necessary use of a more than stoichiometric amount of catalyst because of a strong complex that forms between the ketone product and the metal halide. Further, the workup includes hydrolysis to dissociate the complex, which leads to a corrosive waste stream. The catalysts are moisture sensitive, are prone to decomposition or deactivation in the presence of water and cannot be recycled. For these reasons, new catalysts have been developed to evolve the reaction to be more economic and environmentally friendly. The main goal of the “green revolution” is to make catalysts that are nontoxic, recyclable and, possibly, effective without a solvent. These homogeneous catalysts include trifluoroacetic acid, triflic acid and metal triflates. Metal triflates can be prepared from metal halides or metal oxides and triflic acid at -78ºC.\(^6\) In early work by Olah, boron-, aluminum-, and gallium triflates were tested as effective Friedel-Craft catalysts.\(^5\) In two different acylation experiments, the reactivity of the catalyst was found to be boron > gallium > aluminum, which corresponds with relative acidity strength determined by titration. In other studies, bismuth triflate has shown to be the superior metal triflate. Bismuth triflate can acylate both activated and deactivated aromatic compounds with anhydrides and acid chlorides in good yields (78%-95%).\(^5\) Bismuth triflate appears to have a higher catalytic activity when compared to aluminum, gallium, lanthanide, and scandium triflates. Previously mentioned metal triflates only acylate activated aromatic compounds with acyl chlorides.
Additional compounds can be added to the reaction to assist the catalyst. Thus, silver or lithium perchlorate in combination with a Lewis acid can greatly improve yields. For example, activated aromatic substrates react with an anhydride or acid chloride in the presence of gallium trichloride (10% mole) and silver perchlorate to afford aryl ketones in 80%-100% yield at room temperature. The mechanism for this reaction (Scheme 26) starts with the metal perchlorate catalyst reacting with the anhydride. The resulting intermediate reacts with the aromatic substrate to give the desired ketone product and perchloric acid as a by-product. The perchloric acid reacts with the alkyl metal salt to regenerate the catalyst. In comparative studies, it has been shown that anhydrides give better yields when using this experimental method than do the corresponding acid chlorides.

Scheme 26

Triflic acid has been shown to increase yields when used in combination with titanium (IV) monochlorotriflate and hafnium triflate. In work done by Kobayashi, a
study was performed to analyze the effects of triflic acid with hafnium triflate. Low yields were obtained when benzene was reacted with benzoyl chloride (5) in the presence of hafnium triflate (10% yield) or triflic acid (34% yield) at 5 mole percent (Scheme 27). When the catalysts were combined, both still at 5 mole %, the yield was increased to 77%. Raising the mole % to 10 mole % gave an 82% yield, however, further increase of catalyst did not affect the yields.

Scheme 27

Kobayashi also developed lanthanide triflates [Ln(OTf)₃] as catalysts for Friedel-Craft acylations. Lanthanide triflates act as strong Lewis acids because of their strong affinity with the oxygen in carbonyl groups. Moreover, these catalysts are slow to hydrolyze and can even be prepared in aqueous solutions. The efficiency of the rare-earth metal triflates varies from reaction to reaction but, in general, Sc(OTf)₃ has been shown to be higher in catalytic activity in comparison to Ln(OTf)₃ and Y(OTf)₃. This was determined by testing the acidity based on their competitive ligand dissociation from complexes using mass spectrometry. Ytterbium triflate is effective in acylating anisole with acetic anhydride at the para position (Scheme 28). Even when low amounts of the catalyst are used (5% mole), a 79% yield is still obtained. The catalyst can be recovered simply by extracting it from the aqueous layer and it can be used up to two more times with almost the same yields being achieved.
The amount of catalyst used in the reaction can change regioselectivity. Thus, in the acylation of 2-methoxynaphthalene (25) (Scheme 29), two products were formed, resulting in an acetyl group at the 1- or 6- position. When either Yb(OTf)₃ or Sc(OTf)₃ was used in low mole % (<20%), the major product was 1-acetyl-2-methoxynaphthalene (26). When 100 mole % was used with either catalyst, primarily 6-acetyl-2-methoxynaphthalene (27) was obtained.

### Scheme 29

<table>
<thead>
<tr>
<th>Ln(OTf)₃ (mole%)</th>
<th>Yield / %</th>
<th>1-Ac / 6-Ac (26) / (27)</th>
</tr>
</thead>
<tbody>
<tr>
<td>Yb(OTf)₃ (20%)</td>
<td>76%</td>
<td>88% / 12%</td>
</tr>
<tr>
<td>Yb(OTf)₃ (50%)</td>
<td>78%</td>
<td>85% / 15%</td>
</tr>
<tr>
<td>Yb(OTf)₃ (100%)</td>
<td>51%</td>
<td>8% / 92%</td>
</tr>
<tr>
<td>Sc(OTf)₃ (20%)</td>
<td>86%</td>
<td>85% / 15%</td>
</tr>
<tr>
<td>Sc(OTf)₃ (100%)</td>
<td>77%</td>
<td>5% / 95%</td>
</tr>
</tbody>
</table>
Ionic liquids are ideal media for reactions that include reactive ionic intermediates because of their ability to stabilize the charged intermediates. Advantages have been seen when using ionic liquids with metal triflates in place of conventional solvents. In benzoylation reactions with anisole, ionic liquids in the presence of metal triflates gave 100% conversion to a mixture of both ortho and para products. Ionic liquid metal triflate solution can be recycled for a minimum of three uses and, though the efficiency of the transformation may decrease, the product ratios are normally constant.

Though metal triflates are the largest class of homogeneous catalysts studied, individual metals have been utilized occasionally in Friedel-Craft acylations. Thus, indium, zinc, and iron metals have been shown to be effective catalysts for the acylation of aromatic compounds with benzoyl chloride and acyl chloride. Deactivated benzenes still show no activity with these catalysts under thermal conditions, however, zinc can acetylate and benzoylate both activated and deactivated compounds in high to moderate yields in solventless conditions under microwave irradiation.
V. Heterogeneous Catalysts

Heterogeneous catalysts have been shown to be effective solid acid catalysts in Friedel-Craft acylations. Heterogeneous catalysts include zeolites, clays, metal oxides, Nafion, and others. Perhaps because the catalysts are heterogeneous, there are conflicting reports about strength and active sites of the catalysts and these differences may result from the different approaches used for catalyst preparation or the different reaction conditions employed. The result is that it is still difficult to obtain uniform results from the use of heterogeneous catalysts.

Clays have been used for their catalytic ability due to their abundance in nature, high surface area, and sorptive and ion-exchange properties. Clays can be used as catalytic solid acids, bifunctional supports, and fillers to give solid catalysts with the required physical properties.

Clays are crystalline materials made of layered silicates ranging in size from less than 1µ to 150µm. The clay material is built from tetrahedral and octahedral layers. The tetrahedral layers consist of sheets of silica tetrahedrally linked to form a hexagonal mesh. The octahedral layers consist of flat layers containing cations in the center and anions at the apex. Different clays have varying arrangements of tetrahedral and octahedral layers. The kaolinite group has alternating tetrahedral sheets or an OT structure. The smectite clay, which includes montmorillonite, is a sandwich of two tetrahedral sheets with an octahedral sheet in the middle, or a TOT structure. The chlorite group is three TOT units alternating with a brucite layer. Of these three groups, the most abundant is the smectite group.
Smectites are divided into subclasses depending on the type of octahedral layer and predominant location of layer charge sites. Bentonite is the most abundant smectite; hence it is the most commercially available. Bentonite is largely made of montmorillonite (80%-90%) with mineral impurities as filler. The fillers are specific to the region of geological origin and may include quartz, cristobalite, feldspar, and other assorted clays.\(^6^7\)

Montmorillonite has a broad array of active catalytic forms due to a high cation exchange capacity. High catalytic activity is related to its acid strength. The acid site strength depends on the cations present in the inner layer. The exchangeable cations are \(\text{H}_3\text{O}^+, \text{Al}^{3+}, \text{Ca}^{2+},\) and \(\text{Na}^+\) where \(\text{H}_3\text{O}^+\) has the highest acidic strength and \(\text{Na}^+\) has the least acidic strength. A disadvantage to having a high acid strength is poor product selectivity.\(^6^7\)

Montmorillonite clays are advantageous to green chemistry. Such clays can be utilized in microwave synthesis, under solventless conditions, and can be recycled for further use.
Sydnones

Sydnones were first synthesized in 1935 by Earl and Mackney in Sydney, Australia.\(^8^4\) Earl and Mackney reported that treatment of N-nitroso-N-phenyl glycine (28) (R`=Ph) with acetic anhydride afford a light tan solid, which they named a sydnone (Scheme 30).\(^8^4\) Since their discovery, sydnones have received increasing interest stemming from their biological activity. Sydnones have shown utility as antibacterial\(^8^5\), antitumor\(^8^6\), antimalarial\(^8^7\), anti-inflammatory\(^8^8\), and antihypertensive agents\(^8^9\). Sydnones have also been used as precursors for MAOI, a type of antidepressant.\(^9^0, 9^1\)

Scheme 30

Earl and Mackney assigned a bicyclic structure to the sydnone (29), however, as sydnones were studied more in depth, it became clear that the chemical and physical properties were not consistent with a strained bicyclic ring. In the 1940s, Baker, Ollis, and Poole determined, through a series of experiments, that sydnones were monocyclic, dipolar oxadiazolone derivatives.\(^9^1\) They found that sydnones had a greater polarity, lower reactivity to acids and bases, and were more stable when heated than would be characteristic for a strained, bicyclic structure.
Baker, Ollis, and Poole coined the term mesoionic (from mesomeric and ionic) to characterize the unique sydnone ring system and, since their use of the term, many more ring structures have been added to this class. In 1953, they listed general criteria for a compound to be considered mesoionic. The qualifications for a mesoionic compound are: 1) contain fully delocalized positive and negative charges; 2) be a planar, 5-member heterocyclic ring with an exocyclic atom or functional group capable of bearing a considerable negative charge; and 3) possess a considerable resonance energy. These characteristics allow mesoionic compounds to be distinguished from other seemingly analogous compounds such as zwitterions and ylides. Since charge distribution is delocalized with mesoionic compounds, no single “true” resonance form can exist for sydnones, however (30a as shown) is the most commonly employed representation.

The sydnone ring has unique spectral characteristics that distinguish it from other similar compounds due to its dipolar structure. The infrared spectra displays two
distinctive features of the sydnone ring: a C-H stretch at the C-4 position, when present, is found at 3150 cm\(^{-1}\) with medium intensity and the strong carbonyl stretch (C-5) at 1750 cm\(^{-1}\), which is similar to a γ-lactone. Furthermore, the former is different than what would normally be expected with an alkyl or aryl C-H stretch, which would absorb near 2900-3050 cm\(^{-1}\). In the NMR spectra, the proton at the C-4 position, when present, is deshielded from where a typical vinyl proton would be found, appearing at 6.8 ppm. The sydnone has two distinctive peaks appearing in the carbon NMR at 165 ppm for the C-5 carbon and at about 95 ppm for the unsubstituted C-4 carbon.

Many sydnones are stable crystalline solids that can be recrystallized from ethanol. Sydnones can be degraded by concentrated acids to yield hydrazine derivatives and carbon dioxide.\(^93\) Some sydnones can be degraded by sunlight and extreme heat can break down the ring also. In general, sydnones are somewhat more stable to bases, however, treatment of a brominated sydnone with piperidine will result in ring cleavage to form the corresponding glycyl amide.\(^94\)

I. Reactions of Sydnones

A majority of the reactions performed on the sydnone ring take place at the C-4 position. The hydrogen at the C-4 position is acidic with a pKa at about 18-20. The C-4 position is also considered to be nucleophilic. This allows two main reactions to take place at the 4-position: 1) electrophilic aromatic substitution or 2) deprotonation followed by electrophilic addition.\(^95\) Further, other major transformations that can take place with the sydnone ring are treatment with an acid to form a hydrazine and 1,3-dipolar cycloaddition.
A. Electrophilic Aromatic Substitution Reactions

1. Direct Acylation

The classic Friedel-Crafts reaction can acylate the sydnone ring at the C-4 position, however, the “normal” Friedel-Crafts conditions are apparently not ideal. Thus, treatment of sydnones with anhydrides in the presence of aluminum chloride gives poor yields, if any, of the desired product. Presumptively, the Lewis acid coordinates with the exocyclic oxygen of the ring and inhibits the reaction from taking place. Because of this aspect, alternative methods have been developed. As reported by Tien, acylation can be achieved by sonicating sydnones with perchloric acid and acetic anhydride and Turnbull developed a method using Montmorillonite K-10 and acetic anhydride to yield the corresponding product (Scheme 31). The addition of an amide group onto the C-4 position of the ring can be performed with chlorosulfonyl isocyanate (Scheme 32).

**Scheme 31**

![Scheme 31](image)

**Scheme 32**

![Scheme 32](image)
2. Halogenation

A number of techniques have been developed for halogenation of the sydnone ring at the C-4 position. Currently, chloro, bromo, and iodo analogues have been synthesized using an assortment of electrophilic halogenating reagents and halogenation can take place with N-alkyl and N-aryl substituted sydnones in good yields. The N-aryl group may be functionalized to contain esters, ethers, halogens, and carboxylic acids and still yield the expected products.99

Bromination is the most studied halogenation method.100-105 A general procedure for bromination is illustrated by the treatment of 3-phenyl sydnone (33) with bromine and sodium bicarbonate to give the target compound (34) (78% yield) [Scheme 32].105 Work done by Turnbull et al.104 explored the possibility of competing bromination on the functionalized 3-aryl ring.

Scheme 32

Thus, activated 3-arylsydnones were treated with an excess of bromine and, remarkably, even a dimethoxyphenyl sydnone showed bromination at the C-4 position prior to any reaction on the 3-aryl ring. Conversely, 3-(2-aminophenyl) sydnone (35) gave a tribromo product (36), amongst other products, under similar conditions (Scheme 33). This result is justified by comparing Hammett values (p-MeO=-0.268, p- NH2=-0.660).106
Essentially, these studies support the strong electron withdrawing characteristic of the nitrogen atom (N-3) in the sydnone ring and the electron-rich nature of the C-4 position.

**Scheme 33**

![Scheme 33](image)

Several different methods have been developed to remove bromine from the sydnone ring and the overall process of bromination and the subsequent removal of the bromine has been employed as a protecting method. Originally, Kato and Ohta\(^{105}\) found that by heating 3-phenyl-4-bromosydnone with magnesium and quenching with water resulted in the unsubstituted parent sydnone via a Grignard intermediate. Other methods they discovered included the use of hydrazine monohydrate, sodium hydrosulfide, sodium sulfide, and sodium thiocresolate. Uniquely, Tien developed a method of removing the bromine by sonicating the sydnone in methanol in the presence of zinc.\(^{107}\) This method has been successful for a variety of different parent sydnones, some of which contain bromine on the 3-aryl ring. Lastly, the Turnbull group has shown that sodium borohydride, sodium dithionite or sodium sulfite can remove the bromine from the C-4 position.\(^{108, 109, 110}\)

There are a number of reactions that can take place with the halogen at the C-4 position, the most typical being metal-mediated cross-coupling reactions. Sonogashira coupling via a palladium catalyst takes place with the bromo-sydnone (34) when both the
alkyne and catalyst were added in small portions over time (Scheme 34).\textsuperscript{111} Browne has studied the Suzuki-Miyaura coupling with C-4 bromo-N-phenyl sydnone.\textsuperscript{112} It was found that aromatic boronic acids could be coupled successfully to form the corresponding 4-aryl species (37) in the presence of a variety of different palladium catalysts; such as palladium chloride trifphenylphosphene, palladium (II) acetate and palladium (IV) triphenylphosphene, where good yields (56%-93%) were obtained both thermally and by microwave synthesis (Scheme 35).

**Scheme 34**

![Scheme 34 diagram](image)

B. Lithiation

Lithiation reactions are favorable for the addition of functional groups by either deprotonation followed by quenching with an electrophile or lithiation followed by
transmetalation. Sydnone lithiations can be performed readily at the C-4 position with n-butyllithium and using this method, selenide, phosphide, and arsenide sydnone analogues were synthesized while tin, antimony, and tellurium were unsuccessful.\textsuperscript{113} Tien et al.\textsuperscript{107} introduced carbonyl compounds to the C-4 position via a lithiation approach (Scheme 36).

**Scheme 36**

\[
\begin{align*}
\text{R} & \quad \overset{^3\text{BuLi}}{\text{-50°C}} & \overset{\text{Electrophile}}{\text{-50°C}} & \overset{\text{HCl dil.}}{\text{-50°C}} \\
\text{(30)} & \quad & \text{R} & \quad \text{E} \\
\end{align*}
\]

Electrophiles

\[
\begin{align*}
\text{H} & \quad \text{NMe}_2 & \quad \text{NMe}_2 & \quad \text{H} \\
\text{CHO} & \quad \text{COMe} & \quad \text{C(OH)Me} \\
\end{align*}
\]

R = Ar or Cy 
E = CHO, COMe, C(OH)Me

Lithiations have also been used to synthesize fused ring sydnones. In this process, developed by Turnbull et al., a dilitiation takes place in the presence of TMEDA and the dilitio intermediate (38) is quenched by an ester to bind the biaryl rings (39) (Scheme 37).\textsuperscript{102} In extensions of this work, it was shown that non-tethering electrophiles could be used and this method opened the door to the synthesis of dihalogenated, diformyl, dithioester, dialkyl, dihydroxyalkyl, and disilylphenyl sydnones (Scheme 38).\textsuperscript{114}
Interesting results were found from an attempted synthesis of \emph{o}\-substituted aryl sydnones by a lithiation approach. Thus, 3-(2-bromophenyl) sydnone (41) was reacted with LDA to abstract the proton on the C-4 position of the sydnone ring followed by the addition of the protective silyl group. It was anticipated that lithium / halogen exchange to add an electrophile to the ortho position, followed by removal of the silyl group with fluoride ion would lead to the desired \emph{o}\-arylsydnone. However, this was not the case and
the isolated products were $\alpha$-silylsydnones (44). Apparently, after metal / halogen exchange, the intermediate $\alpha$-anion reacts with the 4-silyl group to effect migration to the ortho position, leaving a more stable sydnone anion (Scheme 39). The size of the silyl group had little to no effect on the migration process or yield.

**Scheme 39**

C. Cycloaddition

Sydnones are precursors for pyrazoles via a [4+2] cycloaddition with alkynes (and sometimes alkenes). Huisgen was the first to discover this reaction in 1962 and he reported successful cycloadditions with substituted alkynes which contained hydrocarbon, alcohol, acetal, acyl and ester groups. More recently, there has been increasing interest in pyrazoles because they are biologically active molecules.

Cycloaddition reactions can take place with either symmetric or asymmetric electron deficient alkynes or alkenes. For the purpose of this introduction, only alkynes will be discussed. In an example, dimethyl acetylenedicarboxylate (47) reacts smoothly
with C-4 iodo substituted sydnones (45) (Scheme 40) to form the corresponding pyrazoles (46) in good yield (70%-85%). Unsymmetrical alkynyl esters are more commonly used because they can be further functionalized once the pyrazole product has been formed and they are useful in studying the regioselectivity of the cycloaddition. Padwa et al. examined the regioselectivity of cycloadditions with various C-4 substituted sydnones (Scheme 41). While these reactions resulted in the moderate yields and low regiocontrol, when the substituted sydnones were reacted with methyl propiolate (49), the corresponding 3,5-disubstituted pyrazole (48) was the major product. A further study was performed on a proline derived sydnone (50) with methyl propiolate (49) and this resulted in an equal mixture of isomers (51-52) (Scheme 42).

Scheme 40

![Scheme 40 Diagram]
Scheme 41

![Reaction Scheme](image)

<table>
<thead>
<tr>
<th>R₁</th>
<th>R₂</th>
<th>Yield (%)</th>
</tr>
</thead>
<tbody>
<tr>
<td>Me</td>
<td>Bn</td>
<td>62% (7:2)</td>
</tr>
<tr>
<td>Ph</td>
<td>Me</td>
<td>42% (3:2)</td>
</tr>
<tr>
<td>Bn</td>
<td>Me</td>
<td>44% (9:2)</td>
</tr>
</tbody>
</table>

Scheme 42

![Reaction Scheme](image)

Alkynylborates have been studied also as an additional class of dienophiles since their reactions with sydnones provide a direct method for the production of pyrazoleboronic esters.\textsuperscript{119-121} Moderate to high regiocontrol was observed with 4-unsubstituted sydnones where the alkyne was terminal or contained alkyl or silyl groups. Conversely, all 4-substituted sydnones gave high levels of regiocontrol regardless of the alkyl borate used. Similarly, alkynyl silanes have been studied as a substitute for alkynyl borates with some success in regiocontrol.\textsuperscript{122} The best results were found with terminal silylacetylenes, which yielded 3-silylpyrazoles (54) (Scheme 44). As bulkier groups were added to the silyl group, the yields decreased but complete regioselectivity for the 4-silylpyrazole (53) continued to be observed. When unsymmetric, bulky silyl groups
were employed, crude yields were high (97%) but regioselectivity was found to be moderate (2:1).

**Scheme 44**

<table>
<thead>
<tr>
<th>R</th>
<th>Yield (%)</th>
</tr>
</thead>
<tbody>
<tr>
<td>SiMe₃</td>
<td>95% (100:0)</td>
</tr>
<tr>
<td>SiMe₂Ph</td>
<td>75% (100:0)</td>
</tr>
<tr>
<td>SiPh₂Bu¹</td>
<td>15% (100:0)</td>
</tr>
</tbody>
</table>
Aims of Current Work

The aims of the present work relate to the synthesis of a variety of fused ring sydnones, which are of interest because of the resultant electronic effects upon the ring and the prospect that such compounds might have anti-hypertensive properties, based on previous findings. For the latter, in 1977, Preston and Turnbull synthesized sydnobenzotriazine 55, a fused ring sydnone (Scheme 45). When treated with aqueous acid or base, the sydnone ring was cleaved to produce benzotriazine carboxylic acid 56 and a by-product proposed to be nitric oxide (NO) or some variant of NO. This was a unique cleavage of the sydnone ring since, under acidic conditions, the “average” sydnone is cleaved to form a hydrazine and under basic conditions, the corresponding N-nitroso compound is produced. The driving force for the observed cleavage mode was presumed to be the formation of an aromatic ring that would result. Thus, the conjecture is that fused ring sydnones have the capability to be NO prodrugs, which could be used as vasodilators. 123
The Friedel Crafts acylation has been explored exhaustively as a route to synthesize acylated sydnones and, specifically for this project, it was anticipated that Friedel Crafts acylations of ortho-aldehyde 59 or ortho-ester sydnones 57 would lead to dicarbonyl containing sydnones 60, which, after reduction of the ester function, would undergo pinacol coupling reactions to generate the corresponding fused ring sydnones 61 or McMurry coupling to afford the resulting sydnoquinolines 62 (Scheme 46).

Scheme 46
To generate the acylated sydnone products, to date, different methods and catalysts have been investigated. Under the normal conditions for Friedel Crafts acylations, viz. aluminum chloride and acid chloride, the sydnone decomposes, presumably due to the acidic environment, however, other successful methods have been established for acylation of the sydnone ring. Thus, Greco et al.\textsuperscript{124} were successful in acylating the sydnone with organic acids and phosphorus pentoxide (Scheme 47, Reagent 1), unfortunately with low yields. Yashunkii\textsuperscript{125} reported reasonable yields of the acylated product using boron trifluoride etherate and acetic anhydride (Scheme 47, Reagent 2), but these results could not be reproduced in this laboratory. As previously stated, Tien’s\textsuperscript{97} best procedure consisted of treatment of the sydnone with acetic anhydride and a catalytic amount of perchloric acid under ultrasonication (Scheme 47, Reagent 3).

**Scheme 47**
As possible approaches to fused-ring sydnones, the Turnbull group developed several different methods to acylate the sydnone ring at the C-4 position. Thus, Jones George\textsuperscript{96} acylated the sydnone ring via treatment of the sydnone with acetic anhydride and Montmorillonite K-10 overnight at 120{\degree}C (Scheme 47, Reagent 4). Longer reaction times were needed when electron withdrawing groups were present at the ortho position of the phenyl ring and, indeed, decomposition of the sydnone ring to an indazole occurred with 3-(2-acetylphenyl)sydnone, rendering this approach useless for fused-ring sydnone synthesis. In an attempt to develop milder, catalytic conditions, Jennifer Fisher\textsuperscript{126} utilized freshly made bismuth triflate as catalyst for sydnone acylations (Scheme 47, Reagent 5). As stated in the introduction, metal triflates are environmentally cleaner catalysts because only a catalytic amount is needed (20-25 mole \%). Fisher also used a variety of different anhydrides for acylation and observed that as the anhydride became more complex, the reaction time increased and the yields decreased. Accordingly, it was the first aim of the present work to extend the work that George and Fisher had initiated to examine the effects of different anhydrides with a variety of catalysts with the expectation that milder conditions and higher yields could be realized.

In both methods developed in the Turnbull group, the reaction times are between hours and days with varying product yields depending on the anhydride. To improve the reaction times, Amber Rumple\textsuperscript{127} optimized acylation reactions via microwave irradiation. Rumple duplicated much of Fisher’s work with bismuth triflate and reduced reaction times to minutes. Accordingly, the second aim of the present work was to extrapolate Rumple’s work to ortho substituted sydnones and, since the synthesis of
bismuth triflate is costly and time consuming, the last aim was to find other commercially available metal triflate catalysts that would afford similar or better results.
Results and Discussion

As mentioned in the Aims section, it was anticipated that acylation of 3-2′-(carbomethoxy)phenyl] sydnone (67) with an anhydride in the presence of a catalyst would yield the corresponding acylated sydnone 58. Accordingly, the first step of the present research was to prepare the parent sydnone 67 using the protocol developed in the Turnbull lab, with some modification in solvents employed. Thus, treatment of methyl anthranilate (64) with anhydrous sodium acetate and bromoacetic acid in water resulted in the formation of N-[2′-(carbomethoxy)-phenyl] glycine (65). The glycine then was subjected to nitrosation with isoamyl nitrite in dimethoxyethane (DME) or ethylene glycol diethyl ether to afford the corresponding N-nitroso glycine 66, which, with little purification, was cyclized with trifluoroacetic anhydride (TFAA) in dichloromethane (DCM) to yield the parent sydnone 67 in 54-77% yield (Scheme 48). The overall yield for this reaction was between 35-55%, achieved via a 65-72% yield to produce the glycine and a 54-77% yield to cyclize to the sydnone. At first, low yields were attained when the general procedure was carried out and, to improve yields, different solvents were employed with success. Thus, originally, to synthesize the nitroso species 66, DME was used as solvent in the reaction and diethyl ether was applied in the trituration process. In the present work, it was found that the use of ethylene glycol diethyl ether as solvent in place of DME and petroleum ether for the trituration process instead of diethyl ether returned a purer product in better yields. The ultimate sydnone product 67 was
digested with warm ether to afford a tan solid and it was identified as the target molecule by comparison (m.p., TLC, IR) with a known sample previously synthesized in this lab. Thus, the IR spectrum of the desired sydnone showed the trademark peak for the C-H stretch of the sydnone ring at 3146 cm\(^{-1}\) and two carbonyl peaks at 1731 cm\(^{-1}\) (ester carbonyl) and 1747 cm\(^{-1}\) (sydnone carbonyl). The \(^1H\) NMR spectrum exhibited a singlet for the C-4 proton at 6.6 ppm and a singlet at 3.85 ppm for the methyl of the methoxy group. The \(^13C\) NMR spectrum also showed classic characteristics of a sydnone, giving peaks at 97 ppm for the unsubstituted C-4 carbon and 163 ppm for the C-5 carbonyl carbon. The methyl from the methoxy group was found at 53 ppm and the carbonyl from the ester appeared at 168 ppm.

**Scheme 48**

Since George had synthesized 4-acetyl-3-[2’- (carbomethoxy)phenyl] sydnone (68) from the parent sydnone 67 using Montmorillonite K-10 (6 gram equivalents) and
acetic anhydride, but had not extended his work to other anhydrides, the next objective of this research was to generalize his findings to a series of anhydrides (Scheme 49).

Scheme 49

To provide a baseline comparison with George’s findings, the reaction was first performed with acetic anhydride. Surprisingly, the workup process was hampered by the presence of a substantial emulsion and, accordingly, to ease this procedure, different concentrations of the anhydride were used and the results were evaluated (Table 1).

Using the molar ratios 1:1, 1:2, 1:3, 1:4, and 1:5 (sydnone: anhydride), it was noted that the more acetic anhydride used, excluding Entry 1, which may be an artifact, the greater the amount of emulsion and the more difficult the separation. Entries 4 and 5 also showed more decomposed product on the thin layer chromatography (TLC) plate. Accordingly, it was chosen to use 4 molar equivalents of acetic anhydride to the sydnone for future experiments.
Table 1. Molar Ratio of Sydnone to Acetic Anhydride

<table>
<thead>
<tr>
<th>Entry</th>
<th>Molar Ratio</th>
<th>% Yield of 68</th>
</tr>
</thead>
<tbody>
<tr>
<td>1</td>
<td>1:1</td>
<td>7%</td>
</tr>
<tr>
<td>2</td>
<td>1:2</td>
<td>41%</td>
</tr>
<tr>
<td>3</td>
<td>1:3</td>
<td>50%</td>
</tr>
<tr>
<td>4</td>
<td>1:4</td>
<td>40%</td>
</tr>
<tr>
<td>5</td>
<td>1:5</td>
<td>34%</td>
</tr>
</tbody>
</table>

Reactions were then attempted with propionic, butyric, isobutyric, benzoic, and trifluoroacetic anhydrides. The general procedure given by George\(^6\), using Montmorillonite K-10, was employed for the first set of reactions and each was monitored for completion by TLC. It was observed that as the alkyl chain of the anhydride increased, the reaction time also increased. George had reported that the synthesis of 4-acetyl-3-[2’-(carbomethoxy)phenyl] sydnone (68) was achieved in 85% yield with reflux overnight at 110ºC. In the present work, an 80% yield of the same compound 68 was obtained under the same conditions, however, only after a 36 hour reaction.

The identity of the product, 4-acetyl-3-[2’-(carbomethoxy)phenyl] sydnone (68), was confirmed by comparison to an authentic sample (m.p., IR, TLC, NMR). Thus, the IR spectrum contained three carbonyl peaks observed at 1766 cm\(^{-1}\) (sydnone carbonyl), 1721 cm\(^{-1}\) (ester carbonyl), and 1671 cm\(^{-1}\) (acetyl carbonyl) and the 3150 cm\(^{-1}\) peak corresponding to the C-H stretch at the C-4 position of the sydnone ring was absent. The \(^1\)H NMR spectrum showed an absence of the C-4 proton normally found at 6.8 ppm, a singlet at 2.4 ppm for the methyl of the acetyl group, and another singlet at 3.8 ppm for the methyl in the methoxy group. The \(^13\)C NMR spectrum displayed the methyl carbon of the acetyl group at 27 ppm, the methoxy carbon at 52 ppm, the sydnone C-4 carbon at
107 ppm, the carbonyl of the ester at 163 ppm, the C-5 carbon of the sydnone at 165 ppm and the carbonyl of the acetyl group at 184 ppm.

Similarly, 3-[2’-(carbomethoxy)phenyl]-4-propionoyl sydnone (69) was synthesized in 29% yield from the reaction of 67 and propionic anhydride after 5 days of heating under reflux. The melting point was 107°C-108°C and the IR spectrum showed the absence of the 3150 cm\(^{-1}\) peak (indicative of reaction at the sydnone C-4 position) and three distinct carbonyl peaks: 1786 cm\(^{-1}\) (sydnone carbonyl), 1736 cm\(^{-1}\) (ester carbonyl), and 1675 cm\(^{-1}\) (propionyl carbonyl). The \(^1\)H NMR spectrum of the product showed an absence of the C-H proton at the C-4 position (no signal around 6.8 ppm), the presence of a triplet at 1.1 ppm, a quartet at 3.8 ppm (for the alkyl chain), and a singlet for the methoxy group at 3.8 ppm. As expected, the \(^{13}\)C NMR spectrum showed a total of 13 carbon peaks and, of these, the sydnone C-4 carbon was found at 107 ppm, which is characteristic of a substituted sydnone ring. The alkyl chain carbons were found at 7 ppm and 33 ppm, and the methoxy carbon was present at 52 ppm. The three carbonyl carbons were at 163 ppm (ester carbonyl), 165 ppm (sydnone carbonyl), and 188 ppm (propionyl carbonyl).

4-Butyryl-3-[2’-(carbomethoxy)phenyl] sydnone (70) was synthesized from 67 and butyric anhydride in 36% yield after 10 days of reflux under the same conditions, however, the product was isolated as a semisolid and no melting point could be performed. The IR spectrum showed the absence of the 3150 cm\(^{-1}\) peak, indicating the addition of the butyryl group. There were three carbonyl peaks observed at 1668 cm\(^{-1}\) (butyryl carbonyl), 1731 cm\(^{-1}\) (ester carbonyl), and 1770 cm\(^{-1}\) (sydnone carbonyl). The \(^1\)H NMR spectrum displayed peaks at 0.9, 1.6, and 2.9 ppm and \(^{13}\)C NMR peaks at 13, 16
and 41 ppm were in evidence for the alkyl chain in the butyryl group. The $^1$H NMR spectrum also showed a singlet at 3.8 ppm for the methoxy hydrogens. The $^{13}$C NMR spectrum displayed three carbonyl carbons at 163 ppm (ester carbonyl), 165 ppm (sydnone carbonyl), and 187 ppm (butyryl carbonyl) and the methyl of the methoxy group was found at 52 ppm.

3-[2’-(Carbomethoxy)phenyl]-4-isobutyryl sydnone (71) was synthesized in 21% yield from the reaction of 67 and isobutyric anhydride after 21 days (monitored by TLC) of reflux under the previously stated conditions and was obtained as a light yellow, crystalline solid with a melting point range of 120-121°C. The IR spectrum showed the absence of the C-H stretch at the C-4 position on the sydnone ring and three carbonyl peaks at 1669 cm$^{-1}$ (isobutyryl carbonyl), 1724 cm$^{-1}$ (ester carbonyl), and 1776 cm$^{-1}$ (sydnone carbonyl). The $^1$H NMR spectrum displayed a singlet at 3.8 ppm for the methoxy carbon and a septet at 3.5 ppm and a doublet at 1.1 ppm for the isobutyryl group. The $^{13}$C NMR spectrum consisted of three carbonyl peaks at 163 ppm (ester carbonyl), 165 ppm (sydnone carbonyl), and 191 ppm (butyryl carbonyl). The isobutyryl alkyl chain gave peaks at 17 ppm and 36 ppm, the methyl of the methoxy group was found at 52 ppm, and the C-4 carbon was observed at 106 ppm.

Some degradation of the product was observed in all of these reactions but was predominant in the reaction of 3-[2’-(carbomethoxy)phenyl] sydnone (67) with trifluoroacetic anhydride (to give 73) and the reaction with benzoic anhydride (to give 72), neither of which occurred. The reaction with trifluoroacetic anhydride was performed initially at 110°C with the expectation that the more reactive anhydride would react more quickly, however, only degradation products were observed by TLC. The
reaction was then attempted at both room temperature and 0°C, unfortunately, with similar results. The reaction with benzoic anhydride was allowed to heat for 21 days but, even after this time, workup and column gave only starting material, presumably due to the stability of the benzoic anhydride. The reactions using isobutyric anhydride did not always yield the expected product 71 and a majority of the product was found to be baseline material (TLC). Sporadically, though, low yields of the desired product 71 were achieved, so isobutyric anhydride was still included for further studies whereas the trifluoroacetic and benzoic anhydrides were not.

A problem that arose during the first set of experiments was the loss of solvent during multiple day reactions and, to address this, it was elected to use a sealed pressure tube, specifically a Q-tube. A Q-tube is a specialized pressure tube that releases the pressure that may build up during high temperature reactions. The manufacturer claims that the results are comparable to a microwave but that the Q-tube is cheaper and should provide better, cleaner, and more reproducible results.

For comparison purposes, the reactions conducted in the Q-tube were the same as the experiments performed thermally except, for the former, the temperature was raised to 140°C (Scheme 49). As seen in Table 2, a decrease in reaction time was definitely noticeable with use
of the Q-tube, and, with the exception of Entry 3, the yields were similar to the analogous thermal reactions. For Q-tube Entry 3, a noticeable amount of baseline material was observed by TLC examination, suggesting degradation of the sydnone ring. The Q-tube reactions with 3-(2’-carbomethoxyphenyl) sydnone (67) and the previously mentioned anhydrides were heated at 140°C and were monitored by TLC for completion. The reaction with acetic anhydride showed full conversion after 8.5 hours in the Q-tube in comparison to 36 hours thermally. As had been seen with thermal heating, the bulkier alkyl anhydrides took longer to react, presumably due to steric hindrance. Nonetheless, the advantages to using the Q-tube, in comparison to thermal heating, are clear. However, as will be discussed later, the results using the Q-tube pale by comparison with those obtained with microwave irradiation (MWI). All products synthesized were confirmed by comparison (TLC, m.p., IR) to authentic products previously synthesized in our lab.
Table 2. Thermal vs. Q-Tube Yields and Reaction Times for the Montmorillonite K-10 Catalyzed Syntheses of 4-Acyl-3-[2’-(carbomethoxy)phenyl] sydnones

<table>
<thead>
<tr>
<th>Entry</th>
<th>Anhydride</th>
<th>Product</th>
<th>Thermal Yield (%)</th>
<th>Time (days)</th>
<th>Q-tube Yield (%)</th>
<th>Time (days)</th>
</tr>
</thead>
<tbody>
<tr>
<td>1</td>
<td>Acetic</td>
<td>68</td>
<td>80</td>
<td>1.5</td>
<td>68</td>
<td>0.3</td>
</tr>
<tr>
<td>2</td>
<td>Propionic</td>
<td>69</td>
<td>29</td>
<td>5</td>
<td>25</td>
<td>2</td>
</tr>
<tr>
<td>3</td>
<td>n-Butyric</td>
<td>70</td>
<td>36</td>
<td>10</td>
<td>7</td>
<td>3</td>
</tr>
<tr>
<td>4</td>
<td>i-Butyric</td>
<td>71</td>
<td>14</td>
<td>21</td>
<td>20</td>
<td>5</td>
</tr>
</tbody>
</table>

Since the product yields from the K-10 catalyzed reactions were modest at best, it was elected to attempt acylation of 67 and its ethyl analog 74 using a different catalyst, bismuth triflate and lithium perchlorate (25 mole %, 25 mole %), under the same reaction conditions in the Q-tube (Scheme 50). Bismuth triflate, which had been used successfully in our lab previously for acylation of 3-phenylsydnone, was synthesized from commercially available triphenylbismuth and triflic anhydride in good to moderate yields (60%-80%) using a standard procedure\(^{128}\) (Scheme 51). In work performed by Fisher and Rumple, it was established that the bismuth triflate must be made fresh and used within a 3 to 4 day period to avoid substantial decreases in reaction yields. In the present work, this proved to be true also, and in instances where the product yields seemed to be unusually low, this could be correlated on every occasion to the age of the catalyst.
When comparing the acylation results using Montmorillonite K-10 to those with bismuth triflate, the main observable difference is the reaction time. As seen in Table 3, the longest reaction time required using bismuth triflate was overnight while the longest Montmorillonite K-10 catalyzed reaction took 120 hours (5 days). The amount of catalyst employed for each of these processes is another obvious differentiating factor, since six gram equivalents of Montmorillonite K-10 were required for reaction to precede, hardly a catalytic or ‘green’ amount, whereas bismuth triflate was employed in
catalytic amounts (25 mole %) with a simpler work-up, as previously determined by Jen Fisher. 126

Table 3. Q-Tube Yields and Reaction Times for the Montmorillonite K-10 and Bismuth Triflate Catalyzed Syntheses of 3-(2’-Carboxyalkoxyphenyl)-4-acyl sydnones

<table>
<thead>
<tr>
<th>o-carbomethoxyphenyl-4-acyl sydnones 68-71</th>
<th></th>
<th></th>
<th></th>
<th></th>
<th></th>
</tr>
</thead>
<tbody>
<tr>
<td>Entry</td>
<td>Anhydride</td>
<td>Product</td>
<td>Catalyst</td>
<td>Temperature</td>
<td>Time (hours)</td>
</tr>
<tr>
<td>1</td>
<td>Acetic</td>
<td>68</td>
<td>Montmorillonite K-10</td>
<td>140°C</td>
<td>68%</td>
</tr>
<tr>
<td>2</td>
<td>Propionic</td>
<td>69</td>
<td>Montmorillonite K-10</td>
<td>140°C</td>
<td>25%</td>
</tr>
<tr>
<td>3</td>
<td>n-Butyric</td>
<td>70</td>
<td>Montmorillonite K-10</td>
<td>140°C</td>
<td>7%</td>
</tr>
<tr>
<td>4</td>
<td>i-Butyric</td>
<td>71</td>
<td>Montmorillonite K-10</td>
<td>140°C</td>
<td>20%</td>
</tr>
</tbody>
</table>

<table>
<thead>
<tr>
<th>o-carbomethoxyphenyl-4-acyl sydnones 68-71</th>
<th></th>
<th></th>
<th></th>
<th></th>
<th></th>
</tr>
</thead>
<tbody>
<tr>
<td>Entry</td>
<td>Anhydride</td>
<td>Product</td>
<td>Catalyst</td>
<td>Temperature</td>
<td>Time (hours)</td>
</tr>
<tr>
<td>5</td>
<td>Acetic</td>
<td>68</td>
<td>Bi(OTf)₃ / LiClO₄</td>
<td>140°C</td>
<td>49%</td>
</tr>
<tr>
<td>6</td>
<td>Propionic</td>
<td>69</td>
<td>Bi(OTf)₃ / LiClO₄</td>
<td>140°C</td>
<td>31%</td>
</tr>
<tr>
<td>7</td>
<td>n-Butyric</td>
<td>70</td>
<td>Bi(OTf)₃ / LiClO₄</td>
<td>overnight</td>
<td>17%</td>
</tr>
<tr>
<td>8</td>
<td>i-Butyric</td>
<td>71</td>
<td>Bi(OTf)₃ / LiClO₄</td>
<td>overnight</td>
<td>3%</td>
</tr>
</tbody>
</table>

<table>
<thead>
<tr>
<th>o-carboethoxyphenyl-4-acyl sydnones 75-78</th>
<th></th>
<th></th>
<th></th>
<th></th>
<th></th>
</tr>
</thead>
<tbody>
<tr>
<td>Entry</td>
<td>Anhydride</td>
<td>Product</td>
<td>Catalyst</td>
<td>Temperature</td>
<td>Time (hours)</td>
</tr>
<tr>
<td>9</td>
<td>Acetic</td>
<td>75</td>
<td>Bi(OTf)₃ / LiClO₄</td>
<td>140°C</td>
<td>47%</td>
</tr>
<tr>
<td>10</td>
<td>Propionic</td>
<td>76</td>
<td>Bi(OTf)₃ / LiClO₄</td>
<td>140°C</td>
<td>30%</td>
</tr>
<tr>
<td>11</td>
<td>n-Butyric</td>
<td>77</td>
<td>Bi(OTf)₃ / LiClO₄</td>
<td>140°C</td>
<td>41%</td>
</tr>
<tr>
<td>12</td>
<td>i-Butyric</td>
<td>78</td>
<td>Bi(OTf)₃ / LiClO₄</td>
<td>overnight</td>
<td>---</td>
</tr>
</tbody>
</table>

The yields obtained did not overwhelmingly favor one catalyst over another and, although the Montmorillonite K-10 had disadvantages, it still produced better yields for products 68 and 71 (Entries 1 and 4), in comparison to those obtained using bismuth triflate as catalyst (Entries 5 and 8). This may be an artificial “victory”, however, in that the low yields reported in Entries 7 and 8, for example, may be due to the age of the bismuth triflate because the reactions were performed on the third and fourth days after
making the catalyst. The reactions performed with bismuth triflate, overall, gave moderate to poor yields in the Q-tube but were consistent with those achieved in the thermal trials with the Montmorillonite K-10 catalyst, in much less time (Table 2).

3-[2’-(Carboethoxy)phenyl] sydnone (74) was used in these experiments to observe whether any steric hindrance would occur by having a bulkier group on the phenyl ring. This sydnone was synthesized previously in this lab but was not resynthesized in this work. Surprisingly, from the experimental data, the 4-acyl-3-[2’-(carboethoxy)phenyl] sydnone products (75-77) were obtained in similar or better yields compared to their methoxy analogues (68-71), though, it should be noted that attempted preparation of 3-[2’-(carboethoxy)phenyl]-4-isobutyryl sydnone (78) was not successful and only decomposed baseline material (TLC) was observed. The explanation for these results is unclear but the purity and freshness of the bismuth triflate was difficult to assess visually and, accordingly, variations in product yield were common.

From these reactions, three new compounds were synthesized. The synthesis of 4-acetyl-3-[2’-(carboethoxy)phenyl] sydnone (75) was achieved in 47% yield by heating 74 and acetic anhydride in the Q-tube for 5 hours at 140ºC. The melting point was 114ºC-116ºC, which is comparable to that for 4-acetyl-3-[2’-(carbomethoxy)phenyl] sydnone (68) [viz. 116ºC-118 ºC], and the IR spectrum showed three carbonyl peaks at 1770 cm\(^{-1}\) (sydnone carbonyl), 1717 cm\(^{-1}\) (ester carbonyl), and 1674 cm\(^{-1}\) (acetyl carbonyl). The 3150 cm\(^{-1}\) peak corresponding to the C-H stretch at the C-4 position of the sydnone ring was absent (consistent with substitution at that position) and this was confirmed in the \(^1\)H NMR spectrum by the absence of the C-4 proton normally found at 6.8 ppm. A singlet at 2.5 ppm indicated the methyl of the acetyl group and there was a
triplet at 1.3 ppm and a quartet at 4.3 ppm for the ethoxy group. The $^{13}$C NMR spectrum showed the methyl carbon of the acetyl group at 27 ppm, the ethoxy carbons at 30 ppm and 62 ppm, and the sydnone C-4 carbon at 108 ppm. There were three carbonyl carbons present in the $^{13}$C NMR spectrum, at 163 ppm for the ester carbonyl, 166 ppm for the carbon at the C-5 position on the sydnone ring, and 184 ppm for the carbon of the acetyl group, in line with expectation.

3-[2’-(Carboethoxy)phenyl]-4-propionyl sydnone (76) was synthesized from the reaction of 74 with propionic anhydride in 29% yield after 5 days of heating in the Q-tube at 140 ºC. The melting point was 58ºC – 61ºC. The IR spectrum showed the absence of the 3150 cm$^{-1}$ peak, again indicating substitution at the sydnone C-4 position, and three distinct carbonyl peaks: 1774 cm$^{-1}$ (sydnone carbonyl), 1723 cm$^{-1}$ (ester carbonyl), and 1673 cm$^{-1}$ (propionyl carbonyl). The $^1$H NMR spectrum confirmed the absence of the C-H proton at the C-4 position, showed a triplet at 1.1 ppm and a quartet at 2.9 ppm for the alkyl chain and displayed a quartet at 4.3 ppm and a triplet at 1.3 ppm for the ethoxy group. The $^{13}$C NMR spectrum exhibited the sydnone C-4 signal at 107 ppm, which is characteristic of a substituted sydnone ring. The alkyl chain carbons were found at 7 ppm and 33 ppm and the ethoxy carbons were found at 13 ppm and 52 ppm. The three carbonyl carbons were at 162 ppm (ester carbonyl), 165 ppm (sydnone carbonyl), and 188 ppm (propionyl carbonyl).

4-Butyryl-3-[2’-(carboethoxy)phenyl] sydnone (77) was synthesized in the Q-tube from the reaction of 74 and butyric anhydride in a 41% yield after 7 days of heating at 140 ºC. The melting point was 55ºC-57ºC. The IR spectrum showed the absence of the 3150 cm$^{-1}$ peak, indicating the addition of the butyryl group, and there were three
carbonyl peaks observed at 1667 cm\(^{-1}\) (butyryl carbonyl), 1731 cm\(^{-1}\) (ester carbonyl), and 1770 cm\(^{-1}\) (sydnone carbonyl). The \(^1\)H NMR spectrum showed peaks at 0.92 ppm, 1.3 ppm, and 2.85 ppm and \(^{13}\)C NMR peaks at 13 ppm, 16 ppm and 41 ppm for the alkyl chain of the butyryl group. The \(^1\)H NMR spectrum also displayed a triplet at 1.3 ppm and a quartet at 4.25 ppm and the \(^{13}\)C NMR spectrum gave peaks at 14 ppm and 62 ppm for the ethoxy group. The \(^{13}\)C NMR displayed three carbonyl carbons at 162 ppm (ester carbonyl), 165 ppm (sydnone carbonyl), and 187 ppm (butyryl carbonyl).

The next obvious step was to perform these reactions \textit{via} microwave irradiation (MWI). In work done in this lab by Rumple\(^{127}\), the optimized reaction temperatures and times for the microwave-enhanced acylation of 3-phenylsydnone (33), with the aforementioned anhydrides and bismuth triflate (25 mole \%) / lithium perchlorate (25 mole \%) as catalyst were developed. It was determined that the optimal reaction conditions for such microwave syntheses were at 125°C for 30 minutes and, accordingly, the reactions reported here were performed using these parameters with both ortho-carboalkoxy sydnones 67 and 74 (Scheme 50). The results are tabulated in Table 4.

\textbf{Scheme 50}
Table 4. MWI Yields for the Bismuth Triflate Catalyzed Syntheses of 4-Acyl-3-[2’-(carboalkoxy)phenyl] sydnones 68-71 and 75-78

<table>
<thead>
<tr>
<th>4-acyl-3-[2’-(carboalkoxy)phenyl] sydnones 68-71</th>
<th>Entry</th>
<th>Anhydride</th>
<th>Product</th>
<th>Catalyst</th>
<th>Temperature</th>
<th>Time (min)</th>
<th>% Yield</th>
</tr>
</thead>
<tbody>
<tr>
<td>1</td>
<td>Acetic</td>
<td>68</td>
<td>Bi(OTf)_3/LiClO_4</td>
<td>125°C</td>
<td>30</td>
<td>54%</td>
<td></td>
</tr>
<tr>
<td>2</td>
<td>Propionic</td>
<td>69</td>
<td>Bi(OTf)_3/LiClO_4</td>
<td>125°C</td>
<td>30</td>
<td>58%</td>
<td></td>
</tr>
<tr>
<td>3</td>
<td>n-Butyric</td>
<td>70</td>
<td>Bi(OTf)_3/LiClO_4</td>
<td>125°C</td>
<td>30</td>
<td>36%</td>
<td></td>
</tr>
<tr>
<td>4</td>
<td>i-Butyric</td>
<td>71</td>
<td>Bi(OTf)_3/LiClO_4</td>
<td>125°C</td>
<td>30</td>
<td>21%</td>
<td></td>
</tr>
</tbody>
</table>

<table>
<thead>
<tr>
<th>4-acyl-3-[2’-(carboethoxy)phenyl] sydnones 75-78</th>
<th>Entry</th>
<th>Anhydride</th>
<th>Product</th>
<th>Catalyst</th>
<th>Temperature</th>
<th>Time (min)</th>
<th>% Yield</th>
</tr>
</thead>
<tbody>
<tr>
<td>5</td>
<td>Acetic</td>
<td>75</td>
<td>Bi(OTf)_3/LiClO_4</td>
<td>125°C</td>
<td>30</td>
<td>22%</td>
<td></td>
</tr>
<tr>
<td>6</td>
<td>Propionic</td>
<td>76</td>
<td>Bi(OTf)_3/LiClO_4</td>
<td>125°C</td>
<td>30</td>
<td>26%</td>
<td></td>
</tr>
<tr>
<td>7</td>
<td>n-Butyric</td>
<td>77</td>
<td>Bi(OTf)_3/LiClO_4</td>
<td>125°C</td>
<td>40</td>
<td>27%</td>
<td></td>
</tr>
<tr>
<td>8</td>
<td>i-Butyric</td>
<td>78</td>
<td>Bi(OTf)_3/LiClO_4</td>
<td>125°C</td>
<td>40</td>
<td>11%</td>
<td></td>
</tr>
</tbody>
</table>

Overall from Table 4, yields ranged from moderate to poor depending on the anhydride employed. Since bulkier anhydrides took longer to react in the thermal reactions, Entries 7 and 8 were run for 40 minutes instead of 30 minutes to see if the yields of the desired products would increase, but, unfortunately, that did not appear to be the result. Contrary to what was observed with the Q-tube, consistently better yields were obtained with 67 compared to 74, though it is unclear why. This observation is evident by comparison of Entries 3 and 4 to Entries 7 and 8, where yields of the methoxy-containing products are higher than those of the ethoxy products when bulkier anhydrides were employed. It is possible that these results reflect the use of freshly prepared bismuth triflate on each occasion, since this aspect was not rigorously maintained. All compounds were identical (TLC, m.p., IR, \(^1\)H NMR, and \(^13\)C NMR) to authentic samples previously synthesized in this work.
From this set of experiments, a new compound, 3-[2’-(carboethoxy)phenyl]-4-isobutyryl sydnone (78), was synthesized in an 11% yield in 40 minutes via MWI. The product was a light yellow solid with a melting point range of 80°C-83°C. The IR spectrum showed an absence of the C-H stretch at the C-4 position on the sydnone ring and three sharp carbonyl peaks were present at 1668 cm\(^{-1}\) (isobutyryl carbonyl), 1720 cm\(^{-1}\) (ester carbonyl), and 1761 cm\(^{-1}\) (sydnone carbonyl). The C-4 proton was absent from the \(^1\)H NMR spectrum (no signal at 6.8 ppm) and a doublet at 1.1 ppm for the two terminal methyl groups and a sextet at 3.5 ppm for the tertiary carbon of the isobutyryl group were evident. The ethoxy group showed two peaks; a triplet at 1.3 ppm and a quartet at 4.2 ppm. The \(^{13}\)C NMR spectrum displayed three carbonyl peaks at 162 ppm (ester carbonyl), 165 ppm (sydnone carbonyl), and 191 ppm (isobutyryl carbonyl) and the peaks for the alkyl chain of the isobutyryl group were found at 17 ppm for the terminal carbon and 36 ppm for the tertiary carbon. The ethoxy carbons were found at 14 ppm and 62 ppm and, lastly, the C-4 carbon was observable at 108 ppm.

In conclusion from this series of reactions, seven new compounds were synthesized using three different reaction protocols, with two different types of catalysts. Yields achieved from thermal reactions were on par, if not higher, to those achieved using the Q-tube or by MWI but took a considerably greater amount of time. With respect to reaction time, the MWI-catalyzed reactions were superlative since they took only minutes in comparison to the days required for the thermal reactions or hours for the Q-tube reactions. Accordingly, given the rapid reaction time that resulted with MWI, a slight decrease in yield could be tolerated. Another unfavorable feature of the thermal reactions, as stated earlier, was the loss of solvent, which was not an issue with the Q-
tube or MWI reactions. This project demonstrated the convenience of using MWI for reactions and has laid the ground work for future studies.

Evaluating the catalysts used, the Montmorillonite K-10 process did yield comparable results to bismuth triflate, if not better, but involved a lengthy, and sometimes complicated, work up and longer reaction time. Work up of the product with the Montmorillonite K-10 clay included the initial filtering of the clay, washing of the clay with dichloromethane and acetone and, on many occasions, sonication of the clay and re-filtering. From there, the filtrate was neutralized with sodium bicarbonate and the product was extracted with dichloromethane. Conversely, the bismuth triflate reactions proceeded smoothly in less time than their counterparts and had a simpler work up, which included only neutralization and extraction. The shortcoming of bismuth triflate was that it did not usually afford high product yields and the catalyst needed to be prepared just prior to use to ensure consistent results. There was no definitive visual test or indicator to check for the loss of activity of the bismuth triflate over time except for possible discoloration, so it is likely that partially-expired catalyst was used in some of the previously reported experiments. Overall, the bismuth triflate catalyst is a costly and time consuming catalyst because if it was not used in a short period of time, it had to be disposed of and remade. Because of these disadvantages for both bismuth triflate and Montmorillonite K-10, other commercially available metal catalysts were explored in the hope that a more attractive replacement could be found.

Previous research performed by Fisher included a brief, model study of various metal triflates as catalysts for sydnone acylation. This study included bismuth triflate and the latter had emerged as the best candidate from the initial examination. For the
evaluation, Fisher had used the Labmate shaker, a parallel synthesizer, for initial studies and analyzed results solely by TLC. From her preliminary experiments, only bismuth triflate in the presence of lithium perchlorate gave any indication of product formation. Ideally, it is better to just use one catalyst, due to cost, so the reactions were performed with and without lithium perchlorate to determine whether it would help or hinder the reaction.

For this research, six metal triflate catalysts were chosen, based on cost, availability and potential reactivity. Lanthanum (La) and gadolinium (Gd) triflates were chosen because the lanthanide series metal triflates are more water stable and may not degrade at as rapid a rate as the bismuth triflate. Other rare earth metal triflates, scandium (Sc) and yttrium (Y) triflate, were also selected. Indium (In) triflate had been used in another laboratory with much success, so a small amount was commandeered and used in preliminary experiments and, lastly, hafnium (Hf) triflate was selected because of its unique tetravalent structure (and its reported catalysis of acylations). Table 5 gives the costs per amount of catalyst available commercially from Sigma Aldrich. Hafnium and scandium triflates were purchased in 1g increments because of their higher cost / g. The estimated price to synthesize bismuth triflate was calculated assuming a 60% yield, which was the average yield for that reaction, then determining the amount of starting material needed, and adjusting the unit cost accordingly.
Table 5. Cost of Metal Triflate Catalysts

<table>
<thead>
<tr>
<th>Catalyst</th>
<th>Size</th>
<th>Price</th>
</tr>
</thead>
<tbody>
<tr>
<td>La(OTf)$_3$</td>
<td>5G</td>
<td>$67.90</td>
</tr>
<tr>
<td>Y(OTf)$_3$</td>
<td>5G</td>
<td>$46.90</td>
</tr>
<tr>
<td>Sc(OTf)$_3$</td>
<td>1G</td>
<td>$48.20</td>
</tr>
<tr>
<td>Hf(OTf)$_4$</td>
<td>1G</td>
<td>$48.00</td>
</tr>
<tr>
<td>Gd(OTf)$_3$</td>
<td>5G</td>
<td>$47.20</td>
</tr>
<tr>
<td>In(OTf)$_3$</td>
<td>5G</td>
<td>$76.50</td>
</tr>
<tr>
<td>Bi(OTf)$_3$</td>
<td>5G</td>
<td>$58.30</td>
</tr>
<tr>
<td>Bi(OTf)$_3$</td>
<td>5G</td>
<td>$72.47</td>
</tr>
</tbody>
</table>

The acylation reactions were performed with the simplest sydnone, 3-phenylsydnone (33), thermally overnight to assess the reactivity of the catalyst. The reactions were first conducted at 50°C, employing acetonitrile as solvent and 5 mole % of catalyst to see if any reaction would take place at lower temperatures and, since little to no reaction took place, the temperature was raised to 80°C or 100°C and the co-catalyst was employed at 20 mole %. Variables for these experiments were temperature, mole percent of catalyst, presence or absence of a solvent [acetonitrile (ACN)], concentration of acetic anhydride, and the addition, or otherwise, of a co-catalyst (lithium perchlorate) to determine optimal reaction conditions (Scheme 52). To establish these conditions, some reactions were run in duplicate with minor changes, for example, Entries 5 and 6 just change solvents. 3-Phenylsydnone was synthesized in two steps from commercially available N-phenylglycine, in yields of 60-74% for the two steps. The acylation reactions were checked in the morning by TLC, worked up, dried, and then separated by column chromatography to determine the amount of product, 4-acetyl-3-phenylsydnone (79) and starting material that remained. After determining the amount of starting material and final product, the converted yield was calculated. To find the converted yield, the amount
of recovered starting material was subtracted from the original amount of starting material. With the difference, the converted percent yield was calculated. This calculation was the same to determine regular percent yield (mole product / mole reactant) x 100%. Though the converted yields were established for the following reactions, there will be more emphasis on the actual yields from the reactions. Overall, eight reactions were performed thermally with each catalyst.

Scheme 52

\[
\begin{align*}
\text{N} & \text{N} \\
\text{O} & \text{O} \\
\text{N} & \text{N} \\
\text{O} & \text{O} \\
\text{Ac}_2\text{O} & \\
\text{M(OTf)}_x & \\
\text{LiClO}_4 & \text{overnight}
\end{align*}
\]

The first catalyst employed was lanthanum triflate [La(OTf)_3] and, overall, it gave poor results, except for under the conditions outlined in Entry 4 (Table 6). There was no reaction (TLC) at 50°C or 80°C when acetonitrile (ACN) was used as solvent (Entries 1 and 2), so the temperature was increased to 100°C such that the reaction went to completion, giving a 67% isolated yield of 79 (Entry 4). When lithium perchlorate was incorporated into the experiment, the yields dropped drastically, regardless of whether or not a solvent was used (Entries 5-8). Similar yields were achieved when employing acetic anhydride as solvent and reactant, regardless of other reaction conditions. From this series of experiments, the optimal reaction conditions were found to be at 100°C with 20 mole % of lanthanum triflate and ACN as solvent.
Table 6. Acylation of 3-Phenylsydnone with Lanthanum Triflate

<table>
<thead>
<tr>
<th>Entry</th>
<th>Temperature</th>
<th>Catalyst</th>
<th>mol%</th>
<th>Ac₂O solvent</th>
<th>% Converted</th>
</tr>
</thead>
<tbody>
<tr>
<td>1</td>
<td>50°C</td>
<td>La(OTf)₃</td>
<td>5%</td>
<td>4.5eq ACN</td>
<td>0</td>
</tr>
<tr>
<td>2</td>
<td>80°C</td>
<td>La(OTf)₃</td>
<td>20%</td>
<td>4.5eq ACN</td>
<td>91</td>
</tr>
<tr>
<td>3</td>
<td>80°C</td>
<td>La(OTf)₃</td>
<td>16 eq</td>
<td>AC₂O</td>
<td>30</td>
</tr>
<tr>
<td>4</td>
<td>100°C</td>
<td>La(OTf)₃</td>
<td>4.5 eq</td>
<td>ACN</td>
<td>67</td>
</tr>
<tr>
<td>5</td>
<td>100°C</td>
<td>La(OTf)₃</td>
<td>4.5 eq</td>
<td>ACN</td>
<td>14</td>
</tr>
<tr>
<td>6</td>
<td>100°C</td>
<td>La(OTf)₃</td>
<td>16 eq</td>
<td>Ac₂O</td>
<td>24</td>
</tr>
<tr>
<td>7</td>
<td>100°C</td>
<td>La(OTf)₃</td>
<td>4.5 eq</td>
<td>ACN</td>
<td>8</td>
</tr>
<tr>
<td>8</td>
<td>100°C</td>
<td>La(OTf)₃</td>
<td>16 eq</td>
<td>Ac₂O</td>
<td>27</td>
</tr>
</tbody>
</table>

The next catalyst that was analyzed was yttrium triflate [Y(OTf)₃], which, again, gave poor yields of the expected product (79) [Table 7]. Similarly to lanthanum triflate, there was no product seen in the first two reactions where ACN was used as solvent and a large percent of the starting material was recovered (Entries 1 and 2). The best result was seen at 100°C, producing 57% of product 79 (Entry 4). Similarly to what was observed above, when lithium perchlorate was added to the reaction mixture, the yields dropped dramatically. This may have been due to some formation of perchloric acid which would break down the sydnone ring. There was also no substantial difference between using acetonitrile or acetic anhydride as a solvent as low yields were achieved for all reactions containing lithium perchlorate (Entries 5-8). The ideal conditions for this catalyst were, again, at 100°C with 20 mole % of yttrium triflate and using ACN as solvent.
## Table 7. Acylation of 3-Phenylsydnone with Yttrium Triflate

<table>
<thead>
<tr>
<th>Entry</th>
<th>Temperature</th>
<th>Catalyst</th>
<th>mol%</th>
<th>Ac₂O solvent</th>
<th>% 79</th>
<th>% 33</th>
<th>% Converted</th>
</tr>
</thead>
<tbody>
<tr>
<td>1</td>
<td>50°C</td>
<td>Y(OTf)₃</td>
<td>5%</td>
<td>4.5 eq ACN</td>
<td>0</td>
<td>86</td>
<td>0</td>
</tr>
<tr>
<td>2</td>
<td>80°C</td>
<td>Y(OTf)₃</td>
<td>20%</td>
<td>4.5 eq ACN</td>
<td>0</td>
<td>77</td>
<td>0</td>
</tr>
<tr>
<td>3</td>
<td>80°C</td>
<td>Y(OTf)₃</td>
<td>20%</td>
<td>16 eq Ac₂O</td>
<td>44</td>
<td>52</td>
<td>90</td>
</tr>
<tr>
<td>4</td>
<td>100°C</td>
<td>Y(OTf)₃</td>
<td>20%</td>
<td>4.5 eq ACN</td>
<td>57</td>
<td>6</td>
<td>60</td>
</tr>
<tr>
<td>5</td>
<td>100°C</td>
<td>Y(OTf)₃ / LiClO₄</td>
<td>20%</td>
<td>4.5 eq ACN</td>
<td>13</td>
<td>28</td>
<td>19</td>
</tr>
<tr>
<td>6</td>
<td>100°C</td>
<td>Y(OTf)₃ / LiClO₄</td>
<td>20%</td>
<td>16 eq Ac₂O</td>
<td>18</td>
<td>0</td>
<td>18</td>
</tr>
<tr>
<td>7</td>
<td>100°C</td>
<td>Y(OTf)₃ / LiClO₄</td>
<td>20%</td>
<td>4.5 eq ACN</td>
<td>10</td>
<td>22</td>
<td>13</td>
</tr>
<tr>
<td>8</td>
<td>100°C</td>
<td>Y(OTf)₃ / LiClO₄</td>
<td>20%</td>
<td>16 eq Ac₂O</td>
<td>8</td>
<td>18</td>
<td>13</td>
</tr>
</tbody>
</table>

Hafnium triflate [Hf(OTf)₄] was tested next and the results are shown in Table 8.

In general, the yields were modest but, in contrast to the previous catalysts, some product was obtained with even the lowest temperatures and lowest amounts of catalysts (Entry 1). The best yield of product 79 was obtained in ACN as solvent at 100 °C with both hafnium triflate and lithium perchlorate catalysis (Entry 7), apparently similar to the situation with bismuth triflate (where the co-catalyst is required) rather than those with lanthanum and yttrium triflates. Accordingly, this catalyst seemed worthy of further study though, noticeably, a lower amount of starting material was recovered from the higher temperature experiments, which led to lower converted yields. Again, this may have been caused by the formation of perchloric acid or some amount of acetic acid as a byproduct.
Table 8. Acylation of 3-Phenylsydnone with Hafnium Triflate

<table>
<thead>
<tr>
<th>Entry</th>
<th>Temperature</th>
<th>Catalyst</th>
<th>mol%</th>
<th>Ac₂O</th>
<th>solvent</th>
<th>% 79</th>
<th>% 33</th>
<th>% Converted</th>
</tr>
</thead>
<tbody>
<tr>
<td>1</td>
<td>50°C</td>
<td>Hf(OTf)₄</td>
<td>5%</td>
<td>4.5eq</td>
<td>ACN</td>
<td>34</td>
<td>26</td>
<td>45</td>
</tr>
<tr>
<td>2</td>
<td>80°C</td>
<td>Hf(OTf)₄</td>
<td>20%</td>
<td>4.5eq</td>
<td>ACN</td>
<td>33</td>
<td>41</td>
<td>57</td>
</tr>
<tr>
<td>3</td>
<td>80°C</td>
<td>Hf(OTf)₄</td>
<td>20%</td>
<td>16eq</td>
<td>Ac₂O</td>
<td>9</td>
<td>18</td>
<td>11</td>
</tr>
<tr>
<td>4</td>
<td>100°C</td>
<td>Hf(OTf)₄</td>
<td>20%</td>
<td>4.5eq</td>
<td>ACN</td>
<td>51</td>
<td>28</td>
<td>70</td>
</tr>
<tr>
<td>5</td>
<td>100°C</td>
<td>Hf(OTf)₄</td>
<td>20% /</td>
<td>4.5eq</td>
<td>ACN</td>
<td>27</td>
<td>9</td>
<td>30</td>
</tr>
<tr>
<td></td>
<td></td>
<td>LiClO₄</td>
<td>5%</td>
<td></td>
<td>ACN</td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>6</td>
<td>100°C</td>
<td>Hf(OTf)₄</td>
<td>20%</td>
<td>16eq</td>
<td>Ac₂O</td>
<td>8</td>
<td>4</td>
<td>8</td>
</tr>
<tr>
<td>7</td>
<td>100°C</td>
<td>Hf(OTf)₄</td>
<td>20% /</td>
<td>4.5eq</td>
<td>ACN</td>
<td>61</td>
<td>0</td>
<td>61</td>
</tr>
<tr>
<td></td>
<td></td>
<td>LiClO₄</td>
<td>5%</td>
<td></td>
<td>ACN</td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>8</td>
<td>100°C</td>
<td>Hf(OTf)₄</td>
<td>20%</td>
<td>16eq</td>
<td>Ac₂O</td>
<td>9</td>
<td>0</td>
<td>9</td>
</tr>
<tr>
<td></td>
<td></td>
<td>LiClO₄</td>
<td>20%</td>
<td></td>
<td>ACN</td>
<td></td>
<td></td>
<td></td>
</tr>
</tbody>
</table>

The reactions involving scandium triflate [Sc(OTf)₃] were performed next and the results are shown in Table 9. For the lower temperature reactions in acetonitrile (Entries 1-3), little to no reaction took place, as expected, and a large amount of starting material was recovered. When acetic anhydride was used as both the solvent and the reactant (at 80°C), the acylated product 79 was isolated in poor yield and very little of the starting material was recovered (Entry 3). For the reactions run at 100°C, moderate yields of the acylated product 79 were obtained when ACN was used as solvent (Entry 4) and when the co-catalyst was employed (Entries 5 and 7), conversely, poorer yields were acquired when acetic anhydride was used as the reactant and solvent (Entries 6 and 8). In this reaction, it appears that the incorporation of the lithium perchlorate facilitates the reaction to form more of the desired product, as seen with hafnium triflate. The best yield achieved was 58% (Entry 5), conveying that the ultimate conditions for this catalyst are the addition of the catalyst at 20 mole % and the co-catalyst at 5 mole % with a reaction temperature of 100 °C and using ACN as solvent.
Table 9. Acylation of 3-Phenylsydnone with Scandium Triflate

<table>
<thead>
<tr>
<th>Entry</th>
<th>Temperature</th>
<th>Catalyst</th>
<th>mol%</th>
<th>Ac₂O</th>
<th>solvent</th>
<th>% 79</th>
<th>% 33</th>
<th>% Converted</th>
</tr>
</thead>
<tbody>
<tr>
<td>1</td>
<td>50°C</td>
<td>Sc(OTf)₃</td>
<td>5%</td>
<td>4.5eq</td>
<td>ACN</td>
<td>3</td>
<td>69</td>
<td>11</td>
</tr>
<tr>
<td>2</td>
<td>80°C</td>
<td>Sc(OTf)₃</td>
<td>20%</td>
<td>4.5eq</td>
<td>ACN</td>
<td>0</td>
<td>80</td>
<td>0</td>
</tr>
<tr>
<td>3</td>
<td>80°C</td>
<td>Sc(OTf)₃</td>
<td>20%</td>
<td>16eq</td>
<td>Ac₂O</td>
<td>27</td>
<td>9</td>
<td>30</td>
</tr>
<tr>
<td>4</td>
<td>100°C</td>
<td>Sc(OTf)₃</td>
<td>20%</td>
<td>4.5eq</td>
<td>ACN</td>
<td>47</td>
<td>29</td>
<td>67</td>
</tr>
<tr>
<td>5</td>
<td>100°C</td>
<td>Sc(OTf)₃ / LiClO₄</td>
<td>20% / 5%</td>
<td>4.5eq</td>
<td>ACN</td>
<td>58</td>
<td>18</td>
<td>70</td>
</tr>
<tr>
<td>6</td>
<td>100°C</td>
<td>Sc(OTf)₃ / LiClO₄</td>
<td>20% / 5%</td>
<td>16eq</td>
<td>Ac₂O</td>
<td>21</td>
<td>73</td>
<td>80</td>
</tr>
<tr>
<td>7</td>
<td>100°C</td>
<td>Sc(OTf)₃ / LiClO₄</td>
<td>20% / 20%</td>
<td>16eq</td>
<td>Ac₂O</td>
<td>51</td>
<td>10</td>
<td>56</td>
</tr>
<tr>
<td>8</td>
<td>100°C</td>
<td>Sc(OTf)₃ / LiClO₄</td>
<td>20% / 20%</td>
<td>16eq</td>
<td>Ac₂O</td>
<td>16</td>
<td>6</td>
<td>17</td>
</tr>
</tbody>
</table>

Gadolinium triflate [Gd(OTf)₃] was next used in this series of reactions. Table 10 illustrates that the products obtained in the first two experiments, as was common previously, were simply starting material (Entries 1 and 2). The reactions performed at 100 °C showed slight improvements in yield, with the best yields obtained being 45% and 48% (Entries 4 and 7) and employing ACN as solvent. It was noted that very small amounts of starting material were recovered when using acetic anhydride as solvent, possibly due to cleavage of the sydnone ring by the resulting acetic acid. Lastly, it was not apparent whether the lithium perchlorate helped or hindered the reaction since the best yields were obtained with either no co-catalyst or 20 mole % co-catalyst. Overall, however, none of the yields was high enough to give confidence that this catalyst would be worthy of further pursuit.
Table 10. Acylation of 3-Phenylsydnone with Gadolinium Triflate

<table>
<thead>
<tr>
<th>Entry</th>
<th>Temperature</th>
<th>Catalyst</th>
<th>mol%</th>
<th>Ac₂O</th>
<th>solvent</th>
<th>% 79</th>
<th>% 33</th>
<th>% Converted</th>
</tr>
</thead>
<tbody>
<tr>
<td>1</td>
<td>50°C</td>
<td>Gd(OTf)₃</td>
<td>5%</td>
<td>4.5eq</td>
<td>ACN</td>
<td>0</td>
<td>93</td>
<td>0</td>
</tr>
<tr>
<td>2</td>
<td>80°C</td>
<td>Gd(OTf)₃</td>
<td>20%</td>
<td>ACN</td>
<td>0</td>
<td>94</td>
<td>0</td>
<td>0</td>
</tr>
<tr>
<td>3</td>
<td>80°C</td>
<td>Gd(OTf)₃</td>
<td>16eq</td>
<td>Ac₂O</td>
<td>24</td>
<td>5</td>
<td>25</td>
<td></td>
</tr>
<tr>
<td>4</td>
<td>100°C</td>
<td>Gd(OTf)₃</td>
<td>20%</td>
<td>ACN</td>
<td>45</td>
<td>22</td>
<td>57</td>
<td></td>
</tr>
<tr>
<td>5</td>
<td>100°C</td>
<td>Gd(OTf)₃</td>
<td>20%</td>
<td>ACN</td>
<td>17</td>
<td>53</td>
<td>37</td>
<td></td>
</tr>
<tr>
<td>6</td>
<td>100°C</td>
<td>Gd(OTf)₃</td>
<td>20/5</td>
<td>Ac₂O</td>
<td>18</td>
<td>0</td>
<td>18</td>
<td></td>
</tr>
<tr>
<td>7</td>
<td>100°C</td>
<td>Gd(OTf)₃</td>
<td>20/5</td>
<td>ACN</td>
<td>48</td>
<td>16</td>
<td>58</td>
<td></td>
</tr>
<tr>
<td>8</td>
<td>100°C</td>
<td>Gd(OTf)₃</td>
<td>20/5</td>
<td>Ac₂O</td>
<td>20</td>
<td>1</td>
<td>20</td>
<td></td>
</tr>
</tbody>
</table>

The reactions employing indium triflate [In(OTf)₃] gave the best yields overall of all of the thermal acylation reactions studied and the results are shown in Table 11.

Contrary to what was observed in most previous examples, the reaction at 50°C gave the desired product with a 48% yield (Entry 1). When the temperature was increased to 80°C, the reaction using ACN as solvent (Entry 2) gave the best yield for the entire series of thermal reactions with a 77% yield. This is ideal because the sydnone ring decomposes faster at higher temperatures. There was a distinct difference in yields depending on which solvent was used, with Table 11 demonstrating that better yields were obtained when ACN (Entries 2, 4, 5, and 7) was employed in the reaction.
Table 11. Acylation of 3-Phenylsydnone with Indium Triflate

<table>
<thead>
<tr>
<th>Entry</th>
<th>Temperature</th>
<th>Catalyst</th>
<th>mol%</th>
<th>Ac₂O</th>
<th>solvent</th>
<th>% 79</th>
<th>% 33</th>
<th>% Converted</th>
</tr>
</thead>
<tbody>
<tr>
<td>1</td>
<td>50°C</td>
<td>In(OTf)₃</td>
<td>5%</td>
<td>4.5eq</td>
<td>ACN</td>
<td>48</td>
<td>11</td>
<td>52</td>
</tr>
<tr>
<td>2</td>
<td>80°C</td>
<td>In(OTf)₃</td>
<td>20%</td>
<td>4.5eq</td>
<td>ACN</td>
<td>77</td>
<td>5</td>
<td>81</td>
</tr>
<tr>
<td>3</td>
<td>80°C</td>
<td>In(OTf)₃</td>
<td>20%</td>
<td>16eq</td>
<td>Ac₂O</td>
<td>39</td>
<td>0</td>
<td>39</td>
</tr>
<tr>
<td>4</td>
<td>100°C</td>
<td>In(OTf)₃</td>
<td>20%</td>
<td>4.5eq</td>
<td>ACN</td>
<td>53</td>
<td>16</td>
<td>64</td>
</tr>
<tr>
<td>5</td>
<td>100°C</td>
<td>In(OTf)₃</td>
<td>20%</td>
<td>4.5eq</td>
<td>ACN</td>
<td>70</td>
<td>0</td>
<td>70</td>
</tr>
<tr>
<td>6</td>
<td>100°C</td>
<td>In(OTf)₃</td>
<td>20%</td>
<td>16eq</td>
<td>Ac₂O</td>
<td>33</td>
<td>2</td>
<td>34</td>
</tr>
<tr>
<td>7</td>
<td>100°C</td>
<td>In(OTf)₃</td>
<td>20%</td>
<td>4.5eq</td>
<td>ACN</td>
<td>59</td>
<td>6</td>
<td>62</td>
</tr>
<tr>
<td>8</td>
<td>100°C</td>
<td>In(OTf)₃</td>
<td>20%</td>
<td>16eq</td>
<td>Ac₂O</td>
<td>29</td>
<td>14</td>
<td>33</td>
</tr>
</tbody>
</table>

From these reactions, the desired product, 4-acetyl-3-phenylsydnone (79), was best achieved in 77% yield using the indium triflate catalyst at 80°C (Table 11, Entry 2). The product was confirmed by melting point (136°C-138°C, Fisher126: 134°C-135°C), IR [two carbonyl peaks at 1777 cm⁻¹ (sydnone) and 1666 cm⁻¹ (acetyl); lack of C-H stretch at 3150 cm⁻¹], ¹H NMR [methyl H at 2.5 ppm], and ¹³C NMR [methyl C at 28 ppm, acetyl carbonyl at 184 ppm, C-4 carbon at 106 ppm, and sydnone carbonyl at 166 ppm].

Overall, general trends were recognized in this series of experiments, the foremost being that, more often than not, an increase in temperature led to an increase in the amount of the desired product, 4-acetyl-3-phenylsydnone (79). Understandably, when the catalyst was employed at 5 mole % at 50°C, little to no reaction took place except for in the reaction using hafnium triflate as the catalyst. Further, when acetic anhydride was utilized in ACN, similar or better yields of the desired product were obtained, most likely due to the lessened acidic conditions in the reaction vessel and the easier work-up mode.

In conclusion, the best results obtained by thermal heating were completed with the indium triflate catalyst. Based upon all of the thermal trials, the optimal conditions for
the reactions were at 100°C, with ACN as solvent and utilizing only 20 mole % of the metal triflate catalyst.

Simultaneously to the above studies, reactions were performed via MWI where all six catalysts were investigated with and without the co-catalyst, lithium perchlorate (Scheme 52). The variables in these studies were temperature, time, and mole % of lithium perchlorate added. The mole % of the catalyst employed and the concentration of acetic anhydride added were kept constant at 20 mole % and 1mL, respectively. In work done by Rumple127, the best yield achieved for the microwave reactions using bismuth triflate and lithium perchlorate as catalysts was 94% but the normal range of yields was 55%-80%. The working model was that the ideal replacement catalyst for bismuth triflate should be able to generate similar or better results than this range. The reactions in this study were performed at three different temperatures (100°C, 125°C, and 150°C) to determine the optimal reaction conditions for the microwave synthesis. The reactions performed at the higher temperature (150 °C) in the microwave were run for 15 minutes instead of 30 minutes in hopes of achieving less breakdown product. Work up of these reactions included neutralization of the acid with sodium bicarbonate, extraction with dichloromethane, and drying of the resulting organic layer. If the reaction mixture displayed multiple products by TLC, the acylated product was isolated via flash column chromatography. The results from the experiments are shown in the following tables and discussed in the associated text.
The reactions using lanthanum triflate produced moderate to poor yields, as seen in Table 12. The best yield achieved was at 150°C for 15 minutes in the microwave, which resulted in a 66% yield (Entry 5), attaining close to what was achieved thermally (67%, Table 6, Entry 4). It was observed that as the temperature increased, the amount of starting material recovered decreased, most likely due to greater conversion. With respect to the converted yields, the poorest yields were obtained when the lithium perchlorate was added to the reaction as the co-catalyst. By comparing the reactions performed at 125 °C and 150 °C (Entries 2-6), the yield of the acylated product decreased by half or more when the co-catalyst was added, corresponding to what was observed thermally. The yields achieved from MWI were similar to those obtained thermally (Table 6) but were obtained in much less time, which was as anticipated.
Table 12. Microwave Optimization of the Acylation of 3-Phenylsydnone (33) with Lanthanum Triflate and Acetic Anhydride

<table>
<thead>
<tr>
<th>Entry</th>
<th>Catalyst</th>
<th>Mole %</th>
<th>Temperature</th>
<th>Time (min)</th>
<th>% 79</th>
<th>% 33</th>
<th>% Converted</th>
</tr>
</thead>
<tbody>
<tr>
<td>1</td>
<td>La(OTf)₃</td>
<td>20%</td>
<td>100°C</td>
<td>30</td>
<td>18</td>
<td>71</td>
<td>63</td>
</tr>
<tr>
<td>2</td>
<td>La(OTf)₃</td>
<td>20%</td>
<td>125°C</td>
<td>30</td>
<td>46</td>
<td>26</td>
<td>61</td>
</tr>
<tr>
<td>3</td>
<td>La(OTf)₃</td>
<td>20%</td>
<td>125°C</td>
<td>30</td>
<td>23</td>
<td>18</td>
<td>28</td>
</tr>
<tr>
<td>4</td>
<td>La(OTf)₃</td>
<td>20% / 5%</td>
<td>125°C</td>
<td>30</td>
<td>21</td>
<td>0</td>
<td>21</td>
</tr>
<tr>
<td>5</td>
<td>La(OTf)₃</td>
<td>20%</td>
<td>150°C</td>
<td>15</td>
<td>66</td>
<td>0</td>
<td>66</td>
</tr>
<tr>
<td>6</td>
<td>La(OTf)₃</td>
<td>20% / 20%</td>
<td>150°C</td>
<td>15</td>
<td>30</td>
<td>10</td>
<td>33</td>
</tr>
</tbody>
</table>

The acylation reactions of 3-phenylsydnone (33) with yttrium triflate catalysis under microwave conditions were studied next and the results are shown in Table 13. The yields obtained from these reactions, much as seen previously in Table 7, were mainly very poor (generally ranging from 34-23%), though the highest yield achieved was 57% (Entry 5), similar to what was obtained thermally. Parallel trends were detected, as with the lanthanum triflate, where the amount of starting material recovered diminished as the temperature increased or lithium perchlorate was present (Entries 3-6). Though the reactions at 125°C (Entries 2-4) afforded similar yields, the converted yields determined for those experiments decreased by 10% as the mole % of lithium perchlorate increased. This trend was apparent also when the reactions were performed at 150°C (Entries 5-6), yielding 57% of 79 without lithium perchlorate and a 28% yield with the addition of the co-catalyst.
Table 13. Microwave Optimization of the Acylation of 3-Phenylsydnone (33) with Yttrium Triflate and Acetic Anhydride

<table>
<thead>
<tr>
<th>Entry</th>
<th>Catalyst</th>
<th>Mole %</th>
<th>Temperature</th>
<th>Time (min)</th>
<th>% 79</th>
<th>% 33</th>
<th>% Converted</th>
</tr>
</thead>
<tbody>
<tr>
<td>1</td>
<td>Y(OTf)$_3$</td>
<td>20%</td>
<td>100°C</td>
<td>30</td>
<td>23</td>
<td>61</td>
<td>58</td>
</tr>
<tr>
<td>2</td>
<td>Y(OTf)$_3$</td>
<td>20%</td>
<td>125°C</td>
<td>30</td>
<td>30</td>
<td>36</td>
<td>47</td>
</tr>
<tr>
<td>3</td>
<td>Y(OTf)$_3$</td>
<td>20% / 20%</td>
<td>125°C</td>
<td>30</td>
<td>34</td>
<td>11</td>
<td>38</td>
</tr>
<tr>
<td>4</td>
<td>Y(OTf)$_3$</td>
<td>20% / 20%</td>
<td>125°C</td>
<td>30</td>
<td>27</td>
<td>4</td>
<td>28</td>
</tr>
<tr>
<td>5</td>
<td>Y(OTf)$_3$</td>
<td>20%</td>
<td>150°C</td>
<td>15</td>
<td>57</td>
<td>0</td>
<td>57</td>
</tr>
<tr>
<td>6</td>
<td>Y(OTf)$_3$</td>
<td>20% / 20%</td>
<td>150°C</td>
<td>15</td>
<td>28</td>
<td>0</td>
<td>28</td>
</tr>
</tbody>
</table>

The acylation reactions of 3-phenylsydnone (33) with scandium triflate catalysis under microwave conditions proceeded smoothly, but, notably, little to no starting material was recovered for any of these reactions. Since this was a reoccurrence, it was speculated that a low recovery of starting material was due to the large amount of acid byproduct. The best yields achieved were seen at Entries 2 and 5 with yields of 49% and 47%, respectively. Again, lower yields were achieved when lithium perchlorate was employed as the co-catalyst. Unfortunately, the yields obtained from the microwave reactions using scandium triflate were lower than those obtained thermally (as shown in Table 9), where the best yields obtained were in the 50% range. Because of this, it was determined that scandium triflate would not be advantageous to use as a replacement for bismuth triflate.
Table 14. Microwave Optimization of the Acylation of 3-Phenylsydnone (33) with Scandium Triflate and Acetic Anhydride

<table>
<thead>
<tr>
<th>Entry</th>
<th>Catalyst</th>
<th>Mole %</th>
<th>Temperature</th>
<th>Time (min)</th>
<th>% 79</th>
<th>% 33</th>
<th>% Converted</th>
</tr>
</thead>
<tbody>
<tr>
<td>1</td>
<td>Sc(OTf)(_3)</td>
<td>20%</td>
<td>100°C</td>
<td>30</td>
<td>32</td>
<td>28</td>
<td>44</td>
</tr>
<tr>
<td>2</td>
<td>Sc(OTf)(_3)</td>
<td>20%</td>
<td>125°C</td>
<td>30</td>
<td>49</td>
<td>0</td>
<td>49</td>
</tr>
<tr>
<td>3</td>
<td>Sc(OTf)(_3)</td>
<td>20% / 5%</td>
<td>125°C</td>
<td>30</td>
<td>37</td>
<td>0</td>
<td>37</td>
</tr>
<tr>
<td>4</td>
<td>Sc(OTf)(_3) / LiClO(_4)</td>
<td>20% / 20%</td>
<td>125°C</td>
<td>30</td>
<td>19</td>
<td>0</td>
<td>19</td>
</tr>
<tr>
<td>5</td>
<td>Sc(OTf)(_3)</td>
<td>20%</td>
<td>150°C</td>
<td>15</td>
<td>47</td>
<td>0</td>
<td>47</td>
</tr>
<tr>
<td>6</td>
<td>Sc(OTf)(_3) / LiClO(_4)</td>
<td>20%</td>
<td>150°C</td>
<td>15</td>
<td>25</td>
<td>0</td>
<td>25</td>
</tr>
</tbody>
</table>

The acylation reactions of 3-phenylsydnone (33) performed in the microwave with hafnium triflate as catalyst produced lower yields (Table 15) than those obtained thermally. The best yield achieved thermally was 61% (Table 8, Entry 7), while the best yield obtained from microwave synthesis was 43% (Table 15, Entry 3). The large difference in yields between Entries 2-4 was peculiar because, as previously documented, the co-catalyst had been shown to decrease or maintain the yield of the expected product in the microwave while, here, when the mole % of the lithium perchlorate was increased, the yield increased then drastically decreased. From those specific reactions, it seems most likely that there has been an experimental error, which will need reassessment. Nonetheless, since such poor yields were achieved overall, hafnium triflate was not pursued further as a replacement for bismuth triflate.
Table 15. Microwave Optimization of the Acylation of 3-Phenylsydnone (33) with Hafnium Triflate and Acetic Anhydride

<table>
<thead>
<tr>
<th>Entry</th>
<th>Catalyst</th>
<th>Mole %</th>
<th>Temperature</th>
<th>Time (min)</th>
<th>% 79</th>
<th>% 33</th>
<th>% Converted</th>
</tr>
</thead>
<tbody>
<tr>
<td>1</td>
<td>Hf(OTf)$_4$</td>
<td>20%</td>
<td>100°C</td>
<td>30</td>
<td>36</td>
<td>7</td>
<td>39</td>
</tr>
<tr>
<td>2</td>
<td>Hf(OTf)$_4$</td>
<td>20%</td>
<td>125°C</td>
<td>30</td>
<td>26</td>
<td>10</td>
<td>29</td>
</tr>
<tr>
<td>3</td>
<td>Hf(OTf)$_4$</td>
<td>20%</td>
<td>125°C</td>
<td>30</td>
<td>43</td>
<td>0</td>
<td>43</td>
</tr>
<tr>
<td>4</td>
<td>Hf(OTf)$_4$ / LiClO$_4$</td>
<td>20% / 5%</td>
<td>125°C</td>
<td>30</td>
<td>9</td>
<td>0</td>
<td>9</td>
</tr>
<tr>
<td>5</td>
<td>Hf(OTf)$_4$</td>
<td>20%</td>
<td>150°C</td>
<td>15</td>
<td>25</td>
<td>0</td>
<td>25</td>
</tr>
<tr>
<td>6</td>
<td>Hf(OTf)$_4$</td>
<td>20%</td>
<td>150°C</td>
<td>15</td>
<td>10</td>
<td>0</td>
<td>10</td>
</tr>
</tbody>
</table>

For the acylation reactions of 3-phenylsydnone (33) under microwave conditions, somewhat surprisingly, gadolinium triflate performed better at lower temperatures to yield moderate yields of the desired product 79 in the absence of lithium perchlorate (Entry 1, Table 16). This is ideal because, as previously stated, the sydnone ring begins to breakdown at higher temperatures and, accordingly, produces less of the desired product. The best yield achieved was 60% (Entry 1), with a converted yield of 90%. For the remainder of the reactions, while no starting material was recovered in any case, the yields were lower, or considerably lower, than those obtained at 100°C. The addition of the lithium perchlorate hindered the reaction and gave less of the acylated product. Overall, this catalyst performed better under microwave conditions compared to thermal, producing moderate yields at lower temperatures, which is a quintessential requirement for the replacement catalyst.
Table 16. Microwave Optimization of the Acylation of 3-Phenylsydnone (33) with Gadolinium Triflate and Acetic Anhydride

<table>
<thead>
<tr>
<th>Entry</th>
<th>Catalyst</th>
<th>Mole %</th>
<th>Temperature</th>
<th>Time (min)</th>
<th>% 79</th>
<th>% 33</th>
<th>% Converted</th>
</tr>
</thead>
<tbody>
<tr>
<td>1</td>
<td>Gd(OTf)₃</td>
<td>20%</td>
<td>100°C</td>
<td>30</td>
<td>60</td>
<td>33</td>
<td>90</td>
</tr>
<tr>
<td>2</td>
<td>Gd(OTf)₃</td>
<td>20%</td>
<td>125°C</td>
<td>30</td>
<td>51</td>
<td>0</td>
<td>51</td>
</tr>
<tr>
<td>3</td>
<td>Gd(OTf)₃</td>
<td>5%</td>
<td>125°C</td>
<td>30</td>
<td>36</td>
<td>0</td>
<td>36</td>
</tr>
<tr>
<td>4</td>
<td>Gd(OTf)₃</td>
<td>20% / 20%</td>
<td>125°C</td>
<td>30</td>
<td>15</td>
<td>0</td>
<td>15</td>
</tr>
<tr>
<td>5</td>
<td>Gd(OTf)₃</td>
<td>20% / 20%</td>
<td>150°C</td>
<td>15</td>
<td>47</td>
<td>0</td>
<td>47</td>
</tr>
<tr>
<td>6</td>
<td>Gd(OTf)₃</td>
<td>20% / 20%</td>
<td>150°C</td>
<td>15</td>
<td>35</td>
<td>0</td>
<td>35</td>
</tr>
</tbody>
</table>

Lastly, the acylation reactions of 3-phenylsydnone (33) with indium triflate as catalyst were examined under microwave conditions and gave, on average, poor yields (Table 17). The ideal condition for the reaction with indium triflate was at 125°C for 30 minutes, which gave a 57% yield (Entry 2). This was discouraging considering how well this catalyst performed in the thermal trials (Table 11). At low (100°C) [Entry 1] and high temperatures (150°C) [Entries 5 and 6], the reaction did not go to completion and gave poor yields of the desired product 79. Again, as the amount of lithium perchlorate was increased, the yield of 79 also decreased.

Table 17. Microwave Optimization of the Acylation of 3-Phenylsydnone (33) with Indium Triflate and Acetic Anhydride

<table>
<thead>
<tr>
<th>Entry</th>
<th>Catalyst</th>
<th>Mole %</th>
<th>Temperature</th>
<th>Time (min)</th>
<th>% 79</th>
<th>% 33</th>
<th>% Converted</th>
</tr>
</thead>
<tbody>
<tr>
<td>1</td>
<td>In(OTf)₃</td>
<td>20%</td>
<td>100°C</td>
<td>30</td>
<td>24</td>
<td>14</td>
<td>28</td>
</tr>
<tr>
<td>2</td>
<td>In(OTf)₃</td>
<td>20%</td>
<td>125°C</td>
<td>30</td>
<td>57</td>
<td>5</td>
<td>60</td>
</tr>
<tr>
<td>3</td>
<td>In(OTf)₃</td>
<td>20% / 5%</td>
<td>125°C</td>
<td>30</td>
<td>33</td>
<td>10</td>
<td>37</td>
</tr>
<tr>
<td>4</td>
<td>In(OTf)₃</td>
<td>20% / 20%</td>
<td>125°C</td>
<td>30</td>
<td>25</td>
<td>8</td>
<td>27</td>
</tr>
<tr>
<td>5</td>
<td>In(OTf)₃</td>
<td>20% / 20%</td>
<td>150°C</td>
<td>15</td>
<td>22</td>
<td>9</td>
<td>31</td>
</tr>
<tr>
<td>6</td>
<td>In(OTf)₃</td>
<td>20% / 20%</td>
<td>150°C</td>
<td>15</td>
<td>34</td>
<td>10</td>
<td>37</td>
</tr>
</tbody>
</table>
Overall, the use of the microwave synthesizer decreased reaction times considerably while maintaining similar yields to those obtained thermally for the desired product 79. Analyzing the microwave data, there is no one temperature that produces the best yields for the different catalysts. It was determined, though, that the lithium perchlorate was generally detrimental to the success of the acylation reactions, and reactions that included it almost always led to lower yields when compared to the benchmark reaction at the same temperature. On the whole, the best yield achieved for the microwave reactions was observed with lanthanum triflate, producing a 66% yield of 79 (Table 12, Entry 5). Subpar yields were obtained with hafnium and scandium triflates, so they were both rejected as potential replacements for bismuth triflate. Since the microwave reactions were only performed with acetic anhydride as both reagent and solvent, the next step was to perform the same reactions with ACN as solvent. The reactions were performed only under the optimal conditions that were determined from the previous set of microwave reactions and Table 18 illustrates that the addition of ACN gives mixed results, affording a better yield of the acyl product 79 with scandium and hafnium triflates (Entries 3 and 4) but a considerably lower yield with lanthanum and yttrium triflates as catalyst (Entry 1 and 2). Paramount yields were achieved with gadolinium and indium triflate as the catalysts, yielding 74% and 67% of the product (Entries 5 and 6), and, as such, these catalysts should be further studied and employed in future acylations as a replacement for bismuth triflate.
### Table 18. Comparison of Optimal Microwave Reactions for the Acylation of 3-Phenylsydnone (33) in ACN or Ac$_2$O

<table>
<thead>
<tr>
<th>Entry</th>
<th>Catalyst</th>
<th>Time (min)</th>
<th>Temperature</th>
<th>% 79 with ACN</th>
<th>% 79 with Ac$_2$O</th>
</tr>
</thead>
<tbody>
<tr>
<td>1</td>
<td>La(OTf)$_3$</td>
<td>15</td>
<td>150°C</td>
<td>34</td>
<td>66</td>
</tr>
<tr>
<td>2</td>
<td>Y(OTf)$_3$</td>
<td>15</td>
<td>150°C</td>
<td>44</td>
<td>57</td>
</tr>
<tr>
<td>3</td>
<td>Sc(OTf)$_3$</td>
<td>30</td>
<td>125°C</td>
<td>53</td>
<td>49</td>
</tr>
<tr>
<td>4</td>
<td>Hf(OTf)$_4$</td>
<td>30</td>
<td>100°C</td>
<td>54</td>
<td>36</td>
</tr>
<tr>
<td>5</td>
<td>Gd(OTf)$_3$</td>
<td>30</td>
<td>100°C</td>
<td>74</td>
<td>60</td>
</tr>
<tr>
<td>6</td>
<td>In(OTf)$_3$</td>
<td>30</td>
<td>125°C</td>
<td>67</td>
<td>57</td>
</tr>
</tbody>
</table>

With the pinacol coupling reaction in mind (as outlined previously in Scheme 53), the last portion of this project was to yield a pinacol precursor, e.g. 79, by reduction of the ester substituent on the phenyl ring to an aldehyde, either prior to acylation or after. This was attempted via two different avenues with 3-[2’-(carbomethoxy)phenyl]sydnone; by reducing the ester to an aldehyde then acylating the sydnone ring or by acylating the sydnone ring then reducing the ester substituent (Scheme 53). The reduction of 3-[2’-(carbomethoxy)phenyl] sydnone (67) was performed from a standard procedure$^{129}$ with diisobutyl aluminum hydride (DIBAL) at -78°C using DCM as solvent to yield 3-(2’-formylphenyl) sydnone (59). In the first attempts, the experiment was followed exactly as the previous protocol dictated, employing only 1.1eq of DIBAL slowly and allowing the mixture to stir for one hour. This reaction was attempted multiple times under the stated conditions, but full conversion to the $o$-formyl product 59 was never achieved, resulting in a mixed product mainly consisting of starting material (TLC). To remedy this problem, optimization experiments were examined where the amount of DIBAL was increased in 0.5eq increments ranging from 1.5 to 3eq and, in some instances, by allowing the reaction to cool for
longer periods of time than one hour (Table 19), in which the reaction was monitored by TLC for completion. When the amount of DIBAL added to the reaction was increased, the yields increased, however, they plateaued eventually at 2-2.5eq for 1.3-1.5 hours, yielding at best 73% (Entries 7 and 9) of the desired product 59. While a longer reaction time period was necessary to guarantee the reduction of ester, in some cases, increased sydnone degradation, along with an over-reduction to the alcohol. 3-[2’-(hydroxymethyl)phenyl] sydnone (80) as a minor byproduct was observed (Scheme 54). The alcohol byproduct was also detected when 2 or more equivalents of DIBAL were employed in the reaction (Entries 8 and 11) and the highest yield of 80 obtained throughout the reduction experiments was 16% when 3eq of DIBAL was employed (Entry 11). No trend was noticed whether the amount of starting material affected the percent yield of desired product afforded from the experiment.
Table 19. Reduction of 3-[2′-(Carbomethoxy)phenyl] sydnone (67) with DIBAL

<table>
<thead>
<tr>
<th>Entry</th>
<th>DIBAL (eq)</th>
<th>Time (hrs)</th>
<th>% 59</th>
</tr>
</thead>
<tbody>
<tr>
<td>1</td>
<td>56.3 mg</td>
<td>1.1</td>
<td>33</td>
</tr>
<tr>
<td>2</td>
<td>55 mg</td>
<td>1.1</td>
<td>19</td>
</tr>
<tr>
<td>3</td>
<td>171 mg</td>
<td>1.5</td>
<td>38</td>
</tr>
<tr>
<td>4</td>
<td>35.3 mg</td>
<td>1.5</td>
<td>57</td>
</tr>
<tr>
<td>5</td>
<td>502.2 mg</td>
<td>1.5</td>
<td>47</td>
</tr>
<tr>
<td>6</td>
<td>200 mg</td>
<td>2</td>
<td>63</td>
</tr>
<tr>
<td>7</td>
<td>619 mg</td>
<td>2</td>
<td>73</td>
</tr>
<tr>
<td>8</td>
<td>1.447 mg</td>
<td>2</td>
<td>49</td>
</tr>
<tr>
<td>9</td>
<td>1.008 g</td>
<td>2.6</td>
<td>73</td>
</tr>
<tr>
<td>10</td>
<td>190.4 mg</td>
<td>3</td>
<td>65</td>
</tr>
<tr>
<td>11</td>
<td>516.5 mg</td>
<td>3</td>
<td>15</td>
</tr>
</tbody>
</table>

The identity of the product, 3-[2’-(formyl)phenyl] sydnone (59), was confirmed by comparison to an authentic sample (m.p., IR, TLC, NMR). The melting point was 88-90°C (Literature: 93-94°C)\(^{129}\). The IR displayed two carbonyl peaks at 1754 cm\(^{-1}\) (sydnone carbonyl) and 1694 cm\(^{-1}\) (aldehyde carbonyl) and the C-H stretch for the C-4 sydnone carbon was found at 3129 cm\(^{-1}\). The \(^1\)H NMR spectrum exhibited the C-4 proton at 6.7 ppm and the aldehyde proton at 9.9 ppm. The \(^{13}\)C NMR spectrum revealed the C-4 carbon at 98 ppm, the C-5 carbon at 168 ppm, and the aldehyde carbon at 186 ppm.
The identity of the byproduct, 3-[2’-(hydroxymethyl)phenyl] sydnone (80), which had resulted in light yellow crystals and was not further purified after column, was determined by m.p., IR, and NMR. The melting point was 53-56°C, which was much lower than literature (73-75°C)\textsuperscript{129}, but is undoubtedly due to impurities still in the product. The IR spectrum displayed a large, broad peak at 3419 cm\(^{-1}\) for the –OH stretch, a peak at 3156 cm\(^{-1}\) for the C-H stretch at the C-4 position, and a peak at 1747 cm\(^{-1}\) for the sydnone carbonyl. The \(^1\)H NMR spectrum exhibited the C-4 proton at 6.7 ppm, the alcohol at 3.5 ppm, and the alkyl proton at 4.6 ppm. The \(^{13}\)C NMR spectrum revealed the C-4 carbon at 97 ppm, the C-5 carbon at 169 ppm, and the alkyl carbon at 60 ppm.

To obtain more of the 3-[2’-(formyl)phenyl] sydnone (59), the by-product, 3-[2’-(hydroxymethyl)phenyl] sydnone (80), could be oxidized to 59 by dissolving 3-[2’-(hydroxymethyl)phenyl] sydnone (80) in DCM, adding 1.5 molar equivalents of pyridinium dichromate (PDC), and allowing the mixture to stir overnight at room temperature (Scheme 55). The PDC was simply removed by filtration and, if a mixed product resulted (TLC) due to degradation, column chromatography was straightforward and allowed isolation of the desired sydnone 59 in up to 48% yield.

Scheme 55
To simplify the protocol, where two products were obviously produced from the DIBAL reduction (TLC evidence), to save time, the reduction of 57 with DIBAL was followed immediately by the oxidation with PDC of the mixed sample without performing a column to separate the desired product from the alcohol byproduct 80. Thus, the 3-[2’(carbomethoxy)-phenyl] sydnone was reduced by 2.5eq of DIBAL to produce a mixed product determined to be a 70:30 mixture of 59:80 (approximated by TLC) with a ~75% crude yield. The oxidation of the mixed product was then performed with PDC under the conditions stated previously and was allowed to react until there were no signs of 3-[2’-(hydroxymethyl)phenyl] sydnone (80) by TLC examination. The reaction mixture was filtered to remove PDC and then columned. The yield from the second reaction was 49%, which gave a 37% yield overall yield for the reaction. Though this saved time, it was not ideal since a lower overall yield of the desired product was obtained by this protocol compared to that obtained using two separate processes. The desired product was identified as 59 by TLC, m.p., and IR.

With a substantial amount of 3-[2’-(formyl)phenyl] sydnone (57) synthesized, the Friedel Crafts acylation reaction was then attempted on the material with all of the aforementioned catalysts (Scheme 53). The reaction was first attempted with Montmorillonite K-10 thermally at 110°C and in the Q-tube at 120°C, but only resulted in baseline material, as indicated by TLC. Next, it was elected to try the reaction employing bismuth triflate as the catalyst. After the catalyst had been synthesized, the reaction was attempted multiple times in the Q-tube at 110°C and was monitored by TLC, with reaction times ranging from 9 hours to overnight. A less polar compound (higher Rf) was detected by TLC to be the main product from the reactions and it was
isolated by column chromatography as a light yellow solid (26% yield), which was determined to be 1H-indazole (81) by NMR, GCMS analysis and melting point (Scheme 56). The melting point was 145-147°C which almost matched the literature range of 147-149°C. The $^1$H NMR spectra displayed a signal at 10.9 ppm for the N-H stretch and the C-H proton from the pyrazole was at 8.2 ppm. The $^{13}$C NMR spectra exhibited seven carbons; six of which were aromatic and the pyrazole carbon was at 134 ppm, which corresponds to the known spectral data. GCMS gave the M$^+$ to be 118. This result was abnormal but was in agreement to what had been observed in some previous studies, especially that of George\textsuperscript{96}, when he attempted acylation of an ortho-substituted arylsydnone with Montmorillonite K-10 as catalyst. The proposed mechanism for this occurrence is initial protonation of the carbonyl of the aldehyde followed by an attack on the C=O carbon by the N-2 nitrogen of the sydnone ring, followed by hydrolysis and release of carbon dioxide. It was concluded that degradation to the indazole did not transpire in the acylations of the 3-[2’-(carboalkoxy)phenyl] sydnones 67 and 74 because the ester moiety contains a less nucleophilic carbonyl oxygen atom, preventing initial protonation.

Scheme 56
Accordingly, since neither of the previous methods or catalysts produced the desired product 79, the other six metal catalysts were employed in the reaction of 59 with acetic anhydride using MWI. The optimal reaction conditions that had been predetermined in this work (Table 18) were chosen for this reaction, employing ACN as solvent for all reactions. Unfortunately, in all cases, the reactions (Scheme 57) produced a yellow oil that was determined to be 1-acetyl-1H-indazole (82). The IR spectra displayed only one carbonyl, present at 1720 cm$^{-1}$, which corresponded well with the $^{13}$C NMR, which presented the carbonyl at 171 ppm, established as the ketone, and the methyl group at 23 ppm. The $^1$H NMR spectrum showed a signal at 2.8 ppm for the methyl group and the aromatic region displayed two doublets (8.4 ppm and 7.8 ppm) and two triplets (7.6 ppm and 7.4 ppm), which indicated an ortho-substituted ring. The GCMS gave the M$^+$ to be 160.

**Scheme 57**

Since the first avenue to the dicarbonyl sydnone 79 was unsuccessful, the other projected path was attempted where 4-acetyl-3-[2’-(carboalkoxy)phenyl] sydnone (68 and 75) [synthesized in this work] was reacted with DIBAL. The reaction was performed initially at -78°C, employing 2eq of DIBAL with 68, for one hour and resulted in starting material (TLC, m.p., IR). The reaction was attempted at higher temperatures (0 °C and -40 °C) in an effort to increase the reactivity possibilities. Next, 75 was used under the
same conditions and, unfortunately, both of these experiments failed, resulting only in starting material (TLC, m.p., IR), thus ending the quest to synthesize the dicarbonyl sydnone \textit{79}.

Keeping in mind the work completed within this project, there are many avenues for future work to be performed. First, indium and gadolinium triflate should be employed with other parent sydnones to test for their effectiveness and reactivity, especially other ortho-substituted sydnones since the latter can lead to fused ring sydnones. Also, the recovery and reusability of the catalyst should be explored as a greener avenue for these experiments. Next, since more rapid reaction times were achieved with microwave synthesis, more reactions should be explored and optimized through this reaction medium. Other useful anhydrides should be investigated to synthesize novel sydnones that could lead to the synthesis of fused ring sydnones. Lastly, since the acylation of 3-[2’-(formyl)phenyl] sydnone (\textit{59}) was attempted only with acetic anhydride, it is imperative that other bulkier anhydrides be explored in order to exhaust (or otherwise) that reaction route.
Experimental

General Notes

All starting materials and catalysts were purchased commercially without purification unless otherwise noted. Melting points were determined on a Mel-Temp melting point device and were uncorrected. The infrared spectra were taken on a Nicolet 6700 FTIR. NMR spectra were obtained on a Bruker Avance 300 MHz NMR in CDCl3 and are reported relative to tetramethylsilane as an internal standard. Microwave reactions were performed in a CEM Discover 300W Monomode commercial microwave. Pressure tube reactions were performed in a Q-Tube™. Column chromatography was performed either manually or on a CombiFlash Separator System 100c. GC/MS measurements were performed using Hewless-Packard 6890 Series GC with auto injection and mass fragments were reported as mass per charge, m/z. The GC was couples with a mass spectrometer with a Hewlett-Packard 5973 mass selective detector/quadrupole system. Elemental analyses were performed by Midwest Microlab LLC, Indianapolis, Indiana.

Synthesis of 3-Phenylsydnone

3-Phenylsydnone was synthesized from commercially available N-phenylglycine according to the reported procedure.130

Synthesis of N-[(2’-carbomethoxy) phenyl] glycine (65) from methyl anthranilate (64)
To a stirred solution of methyl anthranilate (64) [25.02 g, 151.6 mmol] in water (30 mL) was added a solution of bromoacetic acid (21.18 g, 152.4 mmol) and sodium acetate (12.41 g, 151.2 mmol) in water (25 mL). The solution was heated at 60°C for 14 hours. After the allotted time, the tan powder-like product was filtered off and washed with water (200 mL). The solid was then digested in warm ether and filtered to yield 19.24 g (92.1 mmol, 61%) of 65 as an off white powder. The product was characterized by IR, TLC, and melting point (184-185°C) [literature m.p. (185-186°C)] and matched known values.

**IR (KBr):** 3346 (N-H), 1722 (C=O), 1684 (C=O), 1601, 1510, 1432, 1325, 1253, 1193, 1127, 1081, 756 cm⁻¹

**Nitrosation of the glycine 65 to form N-(2-carbomethoxy) phenyl-N-nitrosoglycine (66)**

To N-[2’-(carbomethoxy)phenyl] glycine (65) [3.5828 g, 17.1 mmol] in ethylene glycol diethyl ether (10 mL) was added isoamyl nitrite (3.0 mL, 22.2 mmol) at 50°C. The solution was allowed to stir under reflux for 1.25 hours, after which time the solvent and excess isoamyl nitrite were evaporated off in a fume hood overnight. A dark red oil resulted, which was triturated with hexane: petroleum ether (2:1) and the liquid layer was decanted off to leave the nitroso compound, which was used for the next step without further purification. No characterization was performed due to the potential health risks associated with the target N-(2-carbomethoxy) phenyl-N-nitrosoglycine (66).

**Cyclization of 66 to yield 3-[2’-(carbomethoxy) phenyl] sydnone (67)**

Due to the potential health risk of 66, the masses used are based on the assumption of its complete conversion. To a solution of 66 (4.08 g, 171 mmol) in dichloromethane (15
mL) at approximately 0°C, trifluoroacetic anhydride (4 mL, 28.32 mmol) was added. The mixture was allowed to stir for 1 hour under nitrogen gas, after which time complete conversion of starting material had occurred by TLC. The solution was neutralized with aqueous sodium bicarbonate solution (5% w:v) and extracted with dichloromethane (3 x 50 mL). The combined organic layers were dried and evaporated \textit{in vacuo} to yield an orange solid. The latter was then digested with warm ether to give a light tan solid. The compound was alike to known\textsuperscript{129} \textit{67} by IR, TLC, \textsuperscript{1}H NMR, and \textsuperscript{13}C NMR. The melting point was 98-101°C [literature m.p. (104-106°C)].\textsuperscript{129}

\textbf{IR (KBr)}: 3151 (sydnone C-H), 1747 (sydnone C=O), 1731 (C=O), 1469, 1284, 1103, 1080, 940, 764 cm\textsuperscript{-1}

\textbf{\textsuperscript{1}H NMR (CDCl\textsubscript{3})}: 3.85 (s, 3H), 6.6 (s, 1H, sydnone C-4), 7.6 (m, 1H), 7.8 (m, 2H), 8.15 (m, 1H) ppm

\textbf{\textsuperscript{13}C NMR (CDCl\textsubscript{3})}: 168.71 (C=O), 163.73 (sydnone C=O), 133.63, 133.46, 132.55, 132.11, 127.02, 126.45, 97.75 (sydnone C-4), 53.07 ppm

\textit{General procedure for acylations of 3-[2'--(carbomethoxy) phenyl] sydnone (67) with Montmorillonite K-10}

To a round bottom flask was added 3-[2'--(carbomethoxy) phenyl] sydnone (67) [-100 mg], dioxane (~5 mL), the appropriate anhydride, and Montmorillonite K-10 (6 gram equivalents). The mixture was stirred in an oil bath at 110°C under reflux until complete conversion was achieved, as seen by TLC. The mixture was filtered and the clay was washed and sonicated with dichloromethane and acetone. The combined organic layers were neutralized with aqueous sodium bicarbonate solution and extracted
with dichloromethane (3 x 50 mL). The combined organic layers were dried (MgSO$_4$), filtered and then evaporated in vacuo. The crude material was then columned (if necessary) and recrystallized from hot ethanol.

**Synthesis of 4-acetyl-3-[2’-(carbomethoxy) phenyl] sydnone (68) with Montmorillonite K-10**

Using the general procedure, 3-[2’-(carbomethoxy) phenyl] sydnone (67) [66.7 mg, 0.303 mmol], Montmorillonite K-10 (400.1 mg), dioxane (5 mL) and acetic anhydride (0.12 mL, 1.27 mmol) were stirred under reflux for 24 hours. The resulting oily solid was recrystallized from ethanol to give light yellow crystals of 68 (63.3 mg, 80%), m.p. 110-113°C (George 96 118-119°C).

**IR (KBr):** 2956, 2924, 1766 (sydnone C=O), 1721 (C=O), 1671 (C=O), 1435, 1384, 1288, 1132, 1093, 1051, 771, 614 cm$^{-1}$

**$^1$H NMR (CDCl$_3$):** 2.4 (s, 3H), 3.8 (s, 3H), 7.3 (m, 1H), 7.7 (m, 2H), 8.2 (m, 1H) ppm

**$^{13}$C NMR (CDCl$_3$):** 184.63 (C=O), 165.87 (sydnone C=O), 163.12 (C=O), 134.88, 133.45, 132.19, 131.78, 126.92, 126.43, 107.54 (sydnone C-4), 52.83, 27.50 ppm

**Synthesis of 4-acetyl-3-[2’-(carbomethoxy) phenyl] sydnone (68) with Montmorillonite K-10 using a 1:1 ratio of sydnone to acetic anhydride**

Using the general procedure, 3-[2’-(carbomethoxy) phenyl] sydnone (67) [92.6 mg, 0.421 mmol], Montmorillonite K-10 (594 mg), dioxane (5 mL) and acetic anhydride (0.046 mL, 0.421 mmol) were stirred under reflux for 24 hours. The resulting oily solid was recrystallized from ethanol to give light yellow crystals of 68 (8.2 mg, 7%).
Synthesis of 4-acetyl-3-[2’-(carbomethoxy) phenyl] sydnone (68) with Montmorillonite K-10 using a 1:2 ratio of sydnone to acetic anhydride

Using the general procedure, 3-[2’-(carbomethoxy) phenyl] sydnone (67) [102.0 mg, 0.463 mmol], Montmorillonite K-10 (612.4 mg), dioxane (5 mL) and acetic anhydride (0.12 mL, 1.09 mmol) were stirred under reflux for 24 hours. The resulting oily solid was recrystallized from ethanol to give light yellow crystals of 68 (49.9 mg, 41%).

Synthesis of 4-acetyl-3-[2’-(carbomethoxy) phenyl] sydnone (68) with Montmorillonite K-10 using a 1:3 ratio of sydnone to acetic anhydride

Using the general procedure, 3-[2’-(carbomethoxy) phenyl] sydnone (67) [107.5 mg, 0.489 mmol], Montmorillonite K-10 (621.6 mg), dioxane (5 mL) and acetic anhydride (0.15 mL, 1.36 mmol) were stirred under reflux for 24 hours. The resulting oily solid was recrystallized from ethanol to give light yellow crystals of 68 (64.1 mg, 50%).

Synthesis of 4-acetyl-3-[2’-(carbomethoxy) phenyl] sydnone (68) with Montmorillonite K-10 using a 1:4 ratio of sydnone to acetic anhydride

Using the general procedure, 3-[2’-(carbomethoxy) phenyl] sydnone (67) [202.3 mg, 0.919 mmol], Montmorillonite K-10 (1.21 g), dioxane (5 mL) and acetic anhydride (0.37 mL, 3.35 mmol) were stirred under reflux for 24 hours. The resulting oily solid was recrystallized from ethanol to give light yellow crystals of 68 (96.3 mg, 40%).
Synthesis of 4-acetyl-3-[2’-(carbomethoxy) phenyl] sydnone (68) with Montmorillonite K-10 using a 1:5 ratio of sydnone to acetic anhydride

Using the general procedure, 3-[2’-(carbomethoxy) phenyl] sydnone (67) [106.2 mg, 0.482 mmol], Montmorillonite K-10 (623.5 mg), dioxane (5 mL) and acetic anhydride (0.27 mL, 2.44 mmol) were stirred under reflux for 24 hours. The resulting oily solid was recrystallized from ethanol to give light yellow crystals of 68 (43.2 mg, 34%).

Synthesis of 3-[2’-(carbomethoxy) phenyl]-4-propionoyl sydnone (69) with Montmorillonite K-10

Using the general procedure, 3-[2’-(carbomethoxy) phenyl] sydnone (67) [127.1 mg, 0.578 mmol], Montmorillonite K-10 (706.0 mg), dioxane (5 mL) and propionic anhydride (0.3 mL, 2.28 mmol) were stirred under reflux for 5 days. The resulting dark brown oil was columned and recrystallized from ethanol to give 69 as a yellow solid (43.2 mg, 34%), m.p. 107-108°C.

IR (KBr): 2946, 1778 (sydnone C=O), 1722 (C=O), 1667 (C=O), 1434, 1380, 1180, 1093, 758, 600 cm\(^{-1}\)

\(^1H\) NMR (CDCl\(_3\)): 1.1 (t, 3H), 2.9 (q, 2H), 3.8 (s, 3H), 7.4 (m, 1H), 7.7 (m, 2H), 8.25 (m, 1H)

\(^13C\) NMR (CDCl\(_3\)): 188.24 (C=O), 165.71 (sydnone C=O), 163.13 (C=O), 134.96, 133.47, 132.14, 131.77, 126.93, 126.39, 107.33 (sydnone C-4), 52.79, 33.32, 7.09 ppm
**Elemental Analysis:** \( \text{C}_13\text{H}_{12}\text{N}_2\text{O}_5 \) (MW: 276.24): Calculated: C: 56.52; N: 10.14; H: 4.38; Found: C 56.81; N: 10.10; H: 4.64

**Synthesis of 4-Butyryl-3-[2’-(carbomethoxy) phenyl] sydnone (70) with Montmorillonite K-10**

Using the general procedure, 3-[2’-(carbomethoxy) phenyl] sydnone (67) [138.1 mg, 0.628 mmol], Montmorillonite K-10 (820.2 mg), dioxane (5 mL) and butyric anhydride (0.43 mL, 2.81 mmol) were stirred under reflux for 10 days. The resulting dark, brown oil was columned to give 70 as a semisolid. The semisolid was then recrystallized in hot ethanol to yield a light yellow solid (65.0 mg, 36%), m.p. 85-87 ºC.

**IR (KBr):** 2962, 2934, 1770 (sydnone C=O), 1731 (C=O), 1668 (C=O), 1606, 1434, 1285, 1139, 1039, 1014, 771, 698 cm\(^{-1}\)

**\(^1\)H NMR (CDCl\(_3\)):** 0.93 (t, 3H), 1.60 (m, 2H), 2.86 (s, 3H), 3.82 (s, 3H), 7.41 (m, 1H), 7.78 (m, 2H), 8.25 (m, 1H) ppm

**\(^13\)C NMR (CDCl\(_3\)):** 187.77 (C=O), 165.68 (sydnone C=O), 163.11 (C=O), 135.00, 133.45, 132.12, 131.77, 126.90, 126.43, 107.47 (sydnone C-4), 52.78, 41.58, 16.86, 13.52 ppm

**Elemental Analysis:** \( \text{C}_{14}\text{H}_{14}\text{N}_2\text{O}_5 \) (MW: 290.27): Calculated: C: 57.93; N: 9.65; H: 4.86; Found: C: 57.91; N: 9.44; H: 4.92

**Synthesis of 3-[2’-(Carbomethoxy) phenyl]-4-isobutyryl sydnone (71) with Montmorillonite K-10**
Using the general procedure, 3-2’-(carbomethoxy)phenyl] sydnone (67) [122.5 mg, 0.557 mmol], Montmorillonite K-10 (730.5 mg), dioxane (5 mL) and isobutryric anhydride (0.4 mL, 2.65 mmol) were stirred under reflux for 21 days. The resulting dark, brown oil was columned to give 71 as a colorless solid (22.1 mg, 14%), m.p. 121-122°C.

**IR (KBr):** 2972, 1776 (sydnone C=O), 1724 (C=O), 1669 (C=O), 1604, 1428, 1286, 1179, 996, 761 cm⁻¹

**¹H NMR (CDCl₃):** 1.1 (d, 3H), 1.2 (d, 3H), 3.5 (sept, 1H), 3.8 (s, 3H), 7.4 (m, 1H), 7.8 (m, 2H), 8.2 (m, 1H) ppm

**¹³C NMR (CDCl₃):** 191.98 (C=O), 165.24 (sydnone C=O), 163.13 (C=O), 135.08, 133.47, 132.07, 131.75, 126.86, 126.34, 106.99 (sydnone C-4), 52.74, 35.60, 17.66 ppm

**Elemental Analysis:** C₁₄H₁₆N₂O₅ (MW: 290.27): Calculated: C: 57.53; N: 9.58; H: 5.52; Found: C: 57.45; N: 9.64; H: 5.25

** Attempted synthesis of 3-2’-(Carbomethoxy)phenyl]-4-trifluoroacetyl sydnone (73) with Montmorillonite K-10**

Using the general procedure, 3-2’-(carbomethoxy)phenyl] sydnone (67) [98.2 mg, 0.446 mmol], Montmorillonite K-10 (678.2 mg), dioxane (5 mL) and trifluoroacetic anhydride (0.2 mL, 0.634 mmol) were stirred at room temperature for 2 days with no signs of the reaction taking place (TLC), so the temperature was raised to 50 °C. After 6 days there were no signs of the reaction occurring, despite the addition of an additional 1mL of trifluoroacetic anhydride, at which point it was decided not to pursue the reaction further.
Attempted synthesis of 4-Benzoyl-3-[2’-(carbomethoxy) phenyl] sydnone (72) with Montmorillonite K-10

Using the general procedure, 3-[2’-(carbomethoxy)phenyl] sydnone (67) [92.0 mg, 0.418 mmol], Montmorillonite K-10 (555.2 mg), dioxane (5 mL) and benzoic anhydride (457 mg, 2.022 mmol) were stirred under reflux for 21 days with no signs of the reaction taking place. Accordingly, this anhydride was not pursued further.

General procedure for acylations of 3-[2’-(carbomethoxy)phenyl] sydnone (67) with Montmorillonite K-10 in the Q-tube

To a Q-tube vessel was added 3-[2’-(carbomethoxy) phenyl] sydnone (67) [~100 mg], dioxane (~2 mL), the appropriate anhydride (4 eq.), Montmorillonite K-10 (approximately 6 gram equivalents), and a stir bar. The Q-tube was sealed and the mixture was stirred in an oil bath at 140°C until complete conversion was achieved, as seen by TLC. The mixture was filtered and the clay was washed and sonicated with dichloromethane and acetone. The combined organic layers were neutralized with aqueous sodium bicarbonate solution and extracted with dichloromethane (3 x 50 mL). The combined organic layers were dried (MgSO₄), filtered, and then evaporated in vacuo. The crude material was then columned on the CombiFlash instrument (12 g silica gel column, gradient of hexanes to dichloromethane to ethyl acetate) to yield the desired material.

Synthesis of 4-acetyl-3-[2’-(carbomethoxy)phenyl] sydnone (68) with Montmorillonite K-10 in the Q-tube
Using the general procedure, 3-[2’-(carbomethoxy) phenyl] sydnone (67) [106.0 mg, 0.482 mmol], Montmorillonite K-10 (594 mg), acetic anhydride (0.2 mL, 1.81 mmol), and dioxane (2 mL) were stirred in the Q-tube for 8.5 hours at 140°C. TLC analysis showed full conversion with baseline material. Column chromatography of the crude product yielded 85.3 mg (68%) of 68, identical (TLC, mp, IR) to an authentic sample.

Synthesis of 3-[2’-(carbomethoxy)phenyl]-4-propionoyl sydnone (69) with Montmorillonite K-10 in the Q-tube

Using the general procedure, 3-[2’-(carbomethoxy) phenyl] sydnone (67) [107.2 mg, 0.487 mmol], Montmorillonite K-10 (564 mg), propionic anhydride (1 mL, 7.57 mmol), and dioxane (2 mL) were stirred in the Q-tube for 2 days at 140°C. TLC analysis showed full conversion with baseline material. Column chromatography of the crude product yielded 33.2 mg (25%) of 69, identical (TLC, mp, IR) to an authentic sample.

Synthesis of 4-Butyryl-3-[2’-(carbomethoxy)phenyl] sydnone (70) with Montmorillonite K-10

Using the general procedure, 3-[2’-(carbomethoxy) phenyl] sydnone (67) [91.5 mg, 0.416 mmol], Montmorillonite K-10 (575 mg), butyric anhydride (1 mL, 6.54 mmol), and dioxane (2 mL) were stirred in the Q-tube for 3 days at 140°C. TLC analysis showed full conversion with a great deal of baseline material. Column chromatography of the crude product yielded 8.3 mg (7%) of 70, m.p. 86-88°C, identical (TLC, mp, IR) to an authentic sample.
Synthesis of 3-(2′-Carbomethoxyphenyl)-4-isobutyryl (71) sydnone with Montmorillonite K-10

Using the general procedure, 3-[2′-(carbomethoxy)phenyl] sydnone (67) [50.4 mg, .229 mmol], Montmorillonite K-10 (302 mg), isobutyric anhydride (1 mL, 6.63 mmol), and dioxane (2 mL) were stirred in the Q-tube for 5 days at 140°C. TLC analysis showed full conversion with baseline material. Column chromatography of the crude product yielded 13.4 mg (20%) of 71, identical (TLC, mp, IR) to an authentic sample.

Synthesis of Bismuth Triflate

To an oven dried 3-neck round bottom flask was added triphenylbismuth (2.005 g, 4.556 mol) dissolved in anhydrous dichloromethane (~20 mL) and filled with argon gas for 5 minutes. The solution was cooled in a liquid nitrogen and ethyl acetate slush bath (~84°C). After the solution had cooled, triflic anhydride was added (2.5 mL, 5.28 mmol). After 10 minutes of cooling, the solution was allowed to mix at room temperature overnight. The desired product was collected by filtration with a frit funnel without further purification to yield a white powder (1.96 g, 68%).

General procedure for acylations of 3-[2′-(carbomethoxy)phenyl] sydnone (67) with Bismuth Triflate in the Q-tube

To a Q-tube vessel was added 3-[2′-(carbomethoxy)phenyl] sydnone (67) (~100 mg), acetonitrile (~2 mL), the appropriate anhydride (~4 eq.), bismuth triflate (25 mole %), lithium perchlorate (25 mole %), and a stir bar. The Q-tube was sealed and the mixture was stirred in an oil bath at 140°C until complete conversion was achieved, as seen by TLC. The reaction mixture was neutralized with sodium bicarbonate solution
and extracted with dichloromethane (3 x 50 mL). The combined organic layers were
dried (MgSO$_4$), filtered, and then evaporated in vacuo. The crude material was then
columned on the CombiFlash instrument (12 g silica gel column, gradient of hexanes to
dichloromethane to ethyl acetate) to yield the desired material.

**Synthesis of 4-acetyl-3-[2’-(carbomethoxy)phenyl] sydnone (68) with Bismuth Triflate in the Q-tube**

Using the general procedure, 3-[2’-(carbomethoxy)phenyl] sydnone (67) [104.7 mg, 0.476 mmol], bismuth triflate (80 mg), lithium perchlorate (13 mg), acetic anhydride (0.25 mL, 2.265 mmol), and acetonitrile (2 mL) were stirred in the Q-tube for 5 hours at 140°C. TLC analysis showed full conversion with baseline material. Column chromatography of the crude product yielded 60.8 mg (49%) of 68, identical (TLC, mp, IR) to an authentic sample.

**Synthesis of 3-[2’-(carbomethoxy)phenyl]-4-propionoyl sydnone (69) with Bismuth Triflate in the Q-tube**

Using the general procedure, 3-[2’-(carbomethoxy)phenyl] sydnone (67) [98.1 mg, 0.446 mmol], bismuth triflate (75 mg), lithium perchlorate (12 mg), propionic anhydride (0.25 mL, 1.89 mmol), and acetonitrile (2 mL) were stirred in the Q-tube for 5 hours at 140°C. TLC analysis showed full conversion with baseline material. Column chromatography of the crude product yielded 37.8 mg (31%) of 69, identical (TLC, mp, IR) to an authentic sample.

**Synthesis of 4-Butyryl-3-[2’-(carbomethoxy)phenyl] sydnone (70) with Bismuth Triflate in the Q-tube**
Using the general procedure, 3-[2’-(carbomethoxy)phenyl] sydnone (67) [97.5 mg, 0.443 mmol], bismuth triflate (74 mg), lithium perchlorate (12 mg), butyric anhydride (0.3 mL, 1.964 mmol), and acetonitrile (2 mL) were stirred in the Q-tube overnight at 140°C. TLC analysis showed full conversion with a large amount of baseline material. Column chromatography of the crude product yielded 21.8 mg (17%) of 70, identical (TLC, mp, IR) to an authentic sample.

**Synthesis of 3-[2’-(Carbomethoxy)phenyl]-4-isobutyryl sydnone (71) with Bismuth Triflate in the Q-tube**

Using the general procedure, 3-[2’-(carbomethoxy)phenyl] sydnone (67) [94.3 mg, 0.429 mmol], bismuth triflate (72 mg), lithium perchlorate (11 mg), isobutyric anhydride (0.3 mL, 1.990 mmol), and acetonitrile (2 mL) were stirred in the Q-tube overnight at 140°C. TLC analysis showed full conversion with a large amount of baseline material. Column chromatography of the crude product yielded 3.4 mg (3%) of 71, identical (TLC, mp, IR) to an authentic sample.

**General procedure for acylations of 3-[2’-(carboethoxy)phenyl] sydnone (74) with bismuth triflate in the Q-tube**

To a Q-tube vessel was added 3-[2’-(carboethoxy) phenyl] sydnone (74) [~100 mg], acetonitrile (~2 mL), the appropriate anhydride (~4 eq.), bismuth triflate (25 mole %), lithium perchlorate (25 mole %), and a stir bar. The Q-tube was sealed and the mixture was stirred in an oil bath at 140°C until complete conversion was achieved, as seen by TLC. The reaction mixture was neutralized with sodium bicarbonate solution and extracted with dichloromethane (3 x 50 mL). The combined organic extracts were
dried (MgSO₄), filtered, and then evaporated in vacuo. The crude material was then columned on the CombiFlash instrument (12 g silica gel column, gradient of hexanes to dichloromethane to ethyl acetate) to yield the desired material.

**Synthesis of 4-acetyl-3-[2’-(carboethoxy)phenyl] sydnone (75) with Bismuth Triflate**

Using the general procedure, 3-[2’-(carboethoxy)phenyl] sydnone (74) [99.0 mg, 0.423 mmol], bismuth triflate (76 mg), lithium perchlorate (12 mg), acetic anhydride (0.25 mL, 2.265 mmol), and acetonitrile (2 mL) were stirred in the Q-tube for 5 hours at 140°C. TLC analysis showed full conversion with baseline material. Column chromatography of the crude product yielded 54.8 mg (47%) of 75, m.p. 111-113°C.

**IR (KBr):** 1770 (sydnone C=O), 1717 (C=O), 1674 (C=O), 1434, 1278, 767, 614 cm⁻¹

**¹H NMR (CDCl₃):** 1.28 (t, 3H), 2.48 (s, 3H), 4.26 (q, 2H), 7.40 (m, 1H), 7.77 (m, 2H), 8.27 (m, 1H) ppm

**¹³C NMR (CDCl₃):** 184.50 (C=O), 165.87 (sydnone C=O), 162.69 (C=O), 134.73, 133.29, 132.15, 131.93, 126.84, 126.80, 108.05 (C-4), 62.05, 29.67, 27.49 ppm

**Elemental Analysis:** C₁₃N₂O₅H₁₂ (MW: 276.24): Calculated: C: 56.52; H: 4.38; N: 10.14; Found: C: 56.64; H: 4.40; N: 10.08

**Synthesis of 3-[2’-(carboethoxy) phenyl]-4-propionoyl sydnone (76) with Bismuth Triflate**

Using the general procedure, 3-[2’-(carboethoxy)phenyl] sydnone (74) [93.2 mg, 0.398 mmol], bismuth triflate (67 mg), lithium perchlorate (10.5 mg), propionic anhydride (0.25 mL, 1.895 mmol), and acetonitrile (2 mL) were stirred in the Q-tube for
6 hours at 140°C. TLC analysis showed full conversion with baseline material. Column chromatography of the crude product yielded 34.3 mg (30%) of **76**, m.p. 58-61°C.

**IR (KBr):** 2982, 1774 (sydnone C=O), 1723 (C=O), 1673 (C=O), 1605, 1430, 1293, 1183, 1022, 961, 767 cm\(^{-1}\)

**\(^{1}\)H NMR (CDCl\(_3\)):** 1.06 (t, 3H), 1.28 (t, 3H), 2.49 (q, 2H), 4.26 (q, 2H), 7.41 (m, 1H), 7.77 (m, 2H), 8.27 (m, 1H) ppm

**\(^{13}\)C NMR (CDCl\(_3\)):** 188.09 (C=O), 165.70 (sydnone C=O), 162.69 (C=O), 134.80, 133.30, 132.09, 131.89, 129.83, 126.81, 107.40 (C-4), 62.02, 33.32, 13.89, 7.07 ppm

**Elemental Analysis:** C\(_{14}\)N\(_2\)O\(_5\)H\(_{14}\) \(* \frac{1}{3}\) H\(_2\)O (MW: 209.27): Calculated: C: 56.75; H: 4.99; N: 9.46; Found: C: 56.88; H: 4.89; N: 9.07

**Synthesis of 4-Butyryl-3-[2’-(carboethoxy) phenyl] sydnone (77) with Bismuth Triflate**

Using the general procedure, 3-[2’-(carboethoxy)phenyl] sydnone (74) [97.3 mg, 0.416 mmol], bismuth triflate (70 mg), lithium perchlorate (11 mg), butyric anhydride (0.3 mL, 1.964 mmol), and acetonitrile (2 mL) were stirred in the Q-tube for 7 hours at 140°C. TLC analysis showed full conversion with baseline material. Column chromatography of the crude product yielded 51.1 mg (41%) of **77**, m.p. 59-60°C.

**IR (KBr):** 2966, 2935, 2876, 1770 (sydnone C=O), 1731 (C=O), 1667 (C=O), 1605, 1343, 1367, 1275 cm\(^{-1}\)

**\(^{1}\)H NMR (CDCl\(_3\)):** 0.92 (t, 3H), 1.27 (t, 3H), 1.60 (sextet, 2H), 2.85 (t, 2H), 4.25 (q, 2H), 7.40 (m, 1H), 7.77 (m, 2H), 8.27 (m, 1H) ppm
$^{13}$C NMR (CDCl$_3$): 187.64 (C=O), 165.69 (sydnone C=O), 162.71 (C=O), 134.85, 133.30, 132.08, 131.92, 126.83, 126.80, 107.54 (C-4), 62.02, 41.59, 16.80, 13.91, 13.54 ppm

**Elemental Analysis:** C$_{15}$N$_2$O$_3$H$_{16}$ * 1¼ H$_2$O (MW: 304.30): Calculated: C: 55.13; H: 5.71; N: 8.37 Found: C: 55.28; H: 5.71; N: 8.02

**Attempted synthesis of 3-[2’-(Carboethoxy) phenyl]-4-isobutyryl sydnone (78) with Bismuth Triflate**

Using the general procedure, 3-[2’-(carboethoxy)phenyl] sydnone (74) [97.8 mg, 0.418 mmol], bismuth triflate (70 mg), lithium perchlorate (11 mg), isobutyric anhydride (0.3 mL, 1.990 mmol), and acetonitrile (2 mL) were stirred in the Q-tube overnight at 140°C. TLC analysis showed only baseline material.

**General procedure for acylations of 3-[2’-(carbomethoxy) phenyl] sydnone (67) with Bismuth Triflate under Microwave Irradiation (MWI)**

To a microwave vessel was added 3-[2’-(carbomethoxy) phenyl] sydnone (67) [~100 mg], acetonitrile (~2 mL), the appropriate anhydride (~4 eq.), bismuth triflate (25 mole %), lithium perchlorate (25 mole %), and a stir bar. The reaction vessel was sealed with a crimp cap and placed in a 300W Monomode CEM Discover. The reaction mixture was microwaved at 125°C for 30 minutes. The reaction mixture was neutralized with sodium bicarbonate solution and extracted with dichloromethane (3 x 50 mL). The combined organic extracts were dried (MgSO$_4$) filtered, and then evaporated *in vacuo*. The crude material was then columned on the CombiFlash instrument (12 g silica gel.
column, gradient of hexanes to dichloromethane to ethyl acetate) to yield the desired material.

**Synthesis of 4-acetyl-3-[2’-(carbomethoxy) phenyl] sydnone (68) with Bismuth Triflate under MWI**

Using the general procedure, 3-[2’-(carbomethoxy)phenyl] sydnone (67) [101.1 mg, 0.459 mmol], bismuth triflate (77 mg), lithium perchlorate (12 mg), acetic anhydride (0.25 mL, 2.265 mmol), and acetonitrile (2 mL) were stirred under MWI for 30 minutes at 125°C. TLC analysis showed full conversion with baseline material. Column chromatography of the crude product yielded 64.8 mg (54%) of 68, identical (TLC, mp, IR) to an authentic sample.

**Synthesis of 3-[2’-(carbomethoxy) phenyl]-4-propionoyl sydnone (69) with Bismuth Triflate under MWI**

Using the general procedure, 3-[2’-(carbomethoxy)phenyl] sydnone (67) [98.4 mg, 0.447 mmol], bismuth triflate (75 mg), lithium perchlorate (12 mg), propionic anhydride (0.25 mL, 1.895 mmol), and acetonitrile (2 mL) were stirred under MWI for 30 minutes at 125°C. TLC analysis showed full conversion with baseline material. Column chromatography of the crude product yielded 71.4 mg (58%) of 69, identical (TLC, mp, IR) to an authentic sample.

**Synthesis of 4-Butyryl-3-[2’-(carbomethoxy) phenyl] sydnone (70) with Bismuth Triflate under MWI**
Using the general procedure, 3-[2’-(carbomethoxy)phenyl] sydnone (67) [99.7 mg, 0.453 mmol], bismuth triflate (76 mg), lithium perchlorate (12 mg), butyric anhydride (0.3 mL, 1.964 mmol), and acetonitrile (2 mL) were stirred under MWI for 30 minutes at 125°C. TLC analysis showed full conversion with baseline material. Column chromatography of the crude product yielded 47.7 mg (36%) of 70, identical (TLC, mp, IR) to an authentic sample.

Synthesis of 3-[2’-(Carbomethoxy) phenyl]-4-isobutyryl sydnone (71) with Bismuth Triflate under MWI

Using the general procedure, 3-[2’-(carbomethoxy)phenyl] sydnone (67) [102.3 mg, 0.465 mmol], bismuth triflate (78 mg), lithium perchlorate (12 mg), isobutyric anhydride (0.3 mL, 1.990 mmol), and acetonitrile (2 mL) were stirred under MWI for 30 minutes at 125°C. TLC analysis showed full conversion with a good portion of baseline material. Column chromatography of the crude product yielded 28.7 mg (21%) of 71, identical (TLC, mp, IR) to an authentic sample.

General procedure for acylations of 3-[2’-(carboethoxy) phenyl] sydnone (74) with bismuth triflate under MWI

To a microwave vessel was added 3-[2’-(carboethoxy) phenyl] sydnone (74) [-100 mg], acetonitrile (~2 mL), the appropriate anhydride (~4 eq.), bismuth triflate (25 mole %), lithium perchlorate (25 mole %), and a stir bar. The microwave vessel was sealed with a crimp cap and the mixture was placed in a 300W Monomode CEM Discover. The reaction was microwaved at 125°C for 30 minutes. The reaction mixture was neutralized with sodium bicarbonate solution and extracted with dichloromethane (3
x 50 mL). The combined organic extracts were dried (MgSO₄), filtered, and then evaporated in vacuo. The crude material was then columned on the CombiFlash instrument (12 g silica gel column, gradient of hexanes to dichloromethane to ethyl acetate) to yield the desired material.

Synthesis of 4-acetyl-3-[2’-(carboethoxy) phenyl] sydnone (75) with Bismuth Triflate under MWI

Using the general procedure, 3-[2’-(carboethoxy)phenyl] sydnone (74) [90.8 mg, 0.388 mmol], bismuth triflate (65 mg), lithium perchlorate (10 mg), acetic anhydride (0.2 mL, 1.812 mmol), and acetonitrile (2 mL) were stirred under MWI for 30 minutes at 125°C. TLC analysis showed full conversion with baseline material. Column chromatography of the crude product yielded 23.5 mg (22%) of 75, identical (TLC, mp, IR) to an authentic sample.

Synthesis of 3-[2’-(carboethoxy) phenyl]-4-propionoyl sydnone (76) with Bismuth Triflate under MWI

Using the general procedure, 3-[2’-(carboethoxy)phenyl] sydnone (74) [93.4 mg, 0.399 mmol], bismuth triflate (67 mg), lithium perchlorate (10 mg), propionic anhydride (0.25 mL, 1.895 mmol), and acetonitrile (2 mL) were stirred under MWI for 30 minutes at 125°C. TLC analysis showed full conversion with baseline material. Column chromatography of the crude product yielded 30.4 mg (26%) of 76, identical (TLC, mp, IR) to an authentic sample.

Synthesis of 4-Butyryl-3-[2’-(carboethoxy) phenyl] sydnone (77) with Bismuth Triflate under MWI
Using the general procedure, 3-[2’-(carboethoxy)phenyl] sydnone (74) [98.7 mg, 0.422 mmol], bismuth triflate (71 mg), lithium perchlorate (11 mg), butyric anhydride (0.3 mL, 1.964 mmol), and acetonitrile (2 mL) were stirred under MWI for 40 minutes at 125°C. TLC analysis showed full conversion with baseline material. Column chromatography of the crude product yielded 34.5 mg (27%) of 77, identical (TLC, mp, IR) to an authentic sample.

Synthesis of 3-[2’-(Carboethoxy)phenyl]-4-isobutyryl sydnone (78) with Bismuth Triflate under MWI

Using the general procedure, 3-[2’-(carboethoxy)phenyl] sydnone (74) [99.8 mg, 0.426 mmol], bismuth triflate (72 mg), lithium perchlorate (11 mg), isobutyric anhydride (0.3 mL, 1.990 mmol), and acetonitrile (2 mL) were stirred under MWI for 40 minutes at 125°C. TLC analysis showed full conversion with baseline material. Column chromatography of the crude product yielded 14.1 mg (11%) of 78, m.p. 80-83°C.

IR (KBr): 1761 (sydnone C=O), 1720 (C=O), 1668 (C=O), 1279, 1139, 1096, 1019, 996, 760, 643, 615 cm⁻¹

¹H NMR (CDCl₃): 1.10 (d, 6H), 1.28 (t, 3H), 3.51 (septet, 1H), 4.25 (q, 2H), 7.41 (m, 1H), 7.77 (m, 2H), 8.23 (m, 1H) ppm

¹³C NMR (CDCl₃): 191.94 (C=O), 165.26 (sydnone C=O), 162.70 (C=O), 134.99, 133.31, 132.03, 131.91, 126.76, 108.05 (sydnone C-4), 62.01, 36.70, 17.69, 13.93 ppm

Elemental Analysis: C₁₅N₂O₅H₁₆ (MW: 304.30): Calculated: C: 59.21; H: 5.30; N: 9.21; Found: C: 59.22; H: 5.34; N: 9.11
General procedure for the synthesis of 4-acetyl-3-phenylsydnone (79) using metal triflate catalysts

To a round bottom flask was added 3-phenylsydnone (33) (~100 mg), metal triflate catalyst (20 mole %), acetonitrile (5 mL), and acetic anhydride (0.28 mL, 2.537 mmol). The reaction was heated to 100°C or the otherwise stated temperature under reflux with stirring overnight and was evaluated by TLC in the morning. The mixture was transferred to a separatory funnel using a portion of dichloromethane, neutralized with saturated sodium bicarbonate and then extracted with dichloromethane (3 x 20 mL). The combined organic layers were dried with magnesium sulfate, filtered, and evaporated in vacuo. The crude material was then columned via CombiFlash (12 g silica gel column, gradient of hexanes to dichloromethane to ethyl acetate) to yield the desired material.

Attempted synthesis of 79 using lanthanum triflate at 50°C

Using the general procedure, 3-phenylsydnone (102.1 mg, 0.630 mmol), lanthanum triflate (18 mg, 5 mole %), acetonitrile (5 mL), and acetic anhydride (0.28 mL) were stirred at 50°C overnight. TLC only showed starting material and returned 46.3 mg (45%) of 33.

Attempted synthesis of 79 using yttrium triflate at 50°C

Using the general procedure, 3-phenylsydnone (101.1 mg, 0.624 mmol), lanthanum triflate (16.5 mg, 5 mole %), acetonitrile (5 mL), and acetic anhydride (0.28 mL) were stirred at 50°C overnight. TLC showed only starting material and returned 85.7 mg (86%) of 33 after recrystallization.
Synthesis of 79 using scandium triflate at 50°C

Using the general procedure, 3-phenylsydnone (97.5 mg, 0.602 mmol), scandium triflate (15 mg, 5 mole %), acetonitrile (5 mL), and acetic anhydride (0.28 mL) were stirred at 50°C overnight. TLC showed a majority of starting material and a small amount of the desired product yielding 4.2 mg (3%) of 79, m.p. 141-143°C (literature126 141-142°C), and 69.3 mg (69%) of 33 after column chromatography.

IR (KBr): 1774 (sydnone C=O), 1665 (C=O), 1425, 1090, 768, 692, 617 cm⁻¹

¹H NMR (CDCl₃): 2.55 (s, 3H), 7.5 (d, 2H), 7.6 (t, 2H), 7.75 (t, 1H) ppm

¹³C NMR (CDCl₃): 184.19 (C=O), 166.23 (sydnone C=O), 134.97, 132.33, 130.16, 129.41, 124.96, 124.85, 106.10 (sydnone C-4), 28.06 ppm

Synthesis of 79 using hafnium triflate at 50°C

Using the general procedure, 3-phenylsydnone (102.3 mg, 0.631 mmol), hafnium triflate (24 mg, 5 mole %), acetonitrile (5 mL), and acetic anhydride (0.28 mL) were stirred at 50°C overnight. TLC showed a partial conversion to the desired product yielding 42.6 mg (34%) of 79, identical (TLC, m.p, IR) to an authentic sample, and 25.8 mg (26%) of 33 after column chromatography.

Attempted synthesis of 79 using gadolinium triflate at 50°C

Using the general procedure, 3-phenylsydnone (100.5 mg, 0.620 mmol), gadolinium triflate (19 mg, 5 mole %), acetonitrile (5 mL), and acetic anhydride (0.28 mL) were stirred at 50°C overnight. TLC showed only starting material and 93.2 mg (93%) of 33 was recovered.
Synthesis of 79 using indium triflate at 50 °C

Using the general procedure, 3-phenylsydnone (99.9 mg, 0.617 mmol), indium triflate (18.7 mg, 5 mole %), acetonitrile (5 mL), and acetic anhydride (0.28 mL) were stirred at 50 °C overnight. TLC showed partial conversion to the desired product and a small amount of starting material. Column chromatography of the crude material yielded 59.9 mg (48%) of 79 and 11.3 mg (11%) of 33.

Attempted synthesis of 79 using lanthanum triflate at 80°C with ACN as solvent

Using the general procedure, 3-phenylsydnone (103.1 mg, 0.636 mmol), lanthanum triflate (72 mg, 20 mole %), acetonitrile (5 mL), and acetic anhydride (0.28 mL) were stirred at 80°C overnight. TLC showed only starting material and returned 80.6 mg (81%) of 33 after recrystallization.

Attempted synthesis of 79 using yttrium triflate at 80°C with ACN as solvent

Using the general procedure, 3-phenylsydnone (98.5 mg, 0.608 mmol), yttrium triflate (66 mg, 20 mole %), acetonitrile (5 mL), and acetic anhydride (0.28 mL) were stirred at 80°C overnight. TLC showed only starting material and returned 76.6 mg (77%) of 33 after recrystallization.

Attempted synthesis of 79 using scandium triflate at 80°C with ACN as solvent

Using the general procedure, 3-phenylsydnone (96.8 mg, 0.597 mmol), scandium triflate (61 mg, 20 mole %), acetonitrile (5 mL), and acetic anhydride (0.28 mL) were stirred at 80°C overnight. TLC showed only starting material and returned 80.4 mg (80%) of 33 after recrystallization.
Synthesis of 79 using hafnium triflate at 80°C with ACN as solvent

Using the general procedure, 3-phenylsydnone (99.8 mg, 0.161 mmol), hafnium triflate (96 mg, 20 mole %), acetonitrile (5 mL), and acetic anhydride (0.28 mL) were stirred at 80°C overnight. TLC showed a partial conversion to the desired product yielding 42.0 mg (33%) of 79, identical (TLC, m.p, IR) to an authentic sample, and 41.0 mg (41%) of 33 after column chromatography.

Attempted synthesis of 79 using gadolinium triflate at 80°C with ACN as solvent

Using the general procedure, 3-phenylsydnone (100.7 mg, 0.622 mmol), gadolinium triflate (75 mg, 20 mole %), acetonitrile (5 mL), and acetic anhydride (0.28 mL) were stirred at 80°C overnight. TLC showed only starting material, recovering 94.3 mg (94%) of 33 after recrystallization.

Synthesis of 79 using indium triflate at 80°C with ACN as solvent

Using the general procedure, 3-phenylsydnone (100.5 mg, 0.620 mmol), indium triflate (70.7 mg, 20 mole %), acetonitrile (5 mL), and acetic anhydride (0.28 mL) were stirred at 80 °C overnight. TLC showed an almost full conversion to the desired product and a small amount of starting material. Column chromatography of the crude product yielded 95.9 mg (77%) of 79, identical (TLC, m.p, IR) to an authentic sample, and 4.5 mg (5%) of 33.

Synthesis of 79 using lanthanum triflate at 80°C with Ac₂O as solvent

Using the general procedure, 3-phenylsydnone (102.1 mg, 0.630 mmol), lanthanum triflate (72 mg, 20 mole %), and acetic anhydride (1 mL, 9.061 mmol) were
stirred at 80°C overnight. TLC showed a partial conversion to the desired product yielding 32.9 mg (26%) of 79, identical (TLC, m.p, IR) to an authentic sample, and 30.4 mg (30%) of 33 after column chromatography.

Synthesis of 79 using yttrium triflate at 80°C with Ac₂O as solvent

Using the general procedure, 3-phenylsydnone (101.9 mg, 0.629 mmol), yttrium triflate (66 mg, 20 mole %), and acetic anhydride (1 mL, 9.061 mmol) were stirred at 80°C overnight. TLC showed a partial conversion to the desired product yielding 55.2 mg (44%) of 79, identical (TLC, m.p, IR) to an authentic sample, and 51.6 mg (52%) of 33 after column chromatography.

Synthesis of 79 using scandium triflate at 80°C with Ac₂O as solvent

Using the general procedure, 3-phenylsydnone (102.1 mg, 0.630 mmol), scandium triflate (61 mg, 20 mole %), and acetic anhydride (1 mL, 9.061 mmol) were stirred at 80°C overnight. TLC showed baseline material and the desired product, yielding 34.3 mg (27%) of 79, identical (TLC, m.p, IR) to an authentic sample, after column chromatography.

Synthesis of 79 using hafnium triflate at 80°C with Ac₂O as solvent

Using the general procedure, 3-phenylsydnone (103.4 mg, 0.638 mmol), hafnium triflate (96 mg, 20 mole %), and acetic anhydride (1 mL, 9.061 mmol) were stirred at 80°C overnight. TLC showed a partial conversion to the desired product and a large amount of baseline material. Column chromatography of the crude product yielded 42.0
mg (33%) of 79, identical (TLC, m.p, IR) to an authentic sample, and 41.0 mg (41%) of 33.

**Synthesis of 79 using gadolinium triflate at 80°C with Ac₂O as solvent**

Using the general procedure, 3-phenylsydnone (97.3 mg, 0.601 mmol), gadolinium triflate (75 mg, 5 mole %), and acetic anhydride (1 mL, 9.061 mmol) were stirred at 80°C overnight. TLC showed a partial conversion to the desired product and a large amount of baseline material. Column chromatography of the crude product yielded 30.3 mg (24%) of 79, identical (TLC, m.p, IR) to an authentic sample, and 4.6 mg (5%) of 33.

**Synthesis of 79 using indium triflate at 80 °C with Ac₂O as solvent**

Using the general procedure, 3-phenylsydnone (100.4 mg, 0.620 mmol), indium triflate (69.1 mg, 20 mole %), and acetic anhydride (1 mL, 9.061 mmol) were stirred at 80 °C overnight. TLC showed full conversion to the desired product with a small amount of baseline material. Column chromatography of the crude product yielded 48.4 mg (39%) of 79.

**Synthesis of 79 using lanthanum triflate at 100°C with ACN as solvent**

Using the general procedure, 3-phenylsydnone (100.9 mg, 0.623 mmol), lanthanum triflate (72 mg, 20 mole %), acetonitrile (5 mL), and acetic anhydride (0.28 mL, 2.537 mmol) were stirred at 100°C overnight. TLC showed full conversion to the desired product. Column chromatography of the crude product yielded 83.8 mg (67%) of 79, identical (TLC, m.p, IR) to an authentic sample.
Synthesis of 79 using yttrium triflate at 100°C with ACN as solvent

Using the general procedure, 3-phenylsydnone (100.7 mg, 0.622 mmol), yttrium triflate (66 mg, 20 mole %), acetonitrile (5 mL), and acetic anhydride (0.28 mL, 2.537 mmol) were stirred at 100°C overnight. TLC showed a partial conversion to the desired product and a small amount of starting material. Column chromatography of the crude product yielded 71.2 mg (57%) of 79, identical (TLC, m.p, IR) to an authentic sample, and 5.7 mg (6%) of 33.

Synthesis of 79 using scandium triflate at 100°C with ACN as solvent

Using the general procedure, 3-phenylsydnone (101.5 mg, 0.627 mmol), scandium triflate (61 mg, 20 mole %), acetonitrile (5 mL), and acetic anhydride (0.28 mL, 2.537 mmol) were stirred at 100°C overnight. TLC showed a partial conversion to the desired product and a considerable amount of starting material. Column chromatography of the crude product yielded 58.1 mg (47%) of 79, identical (TLC, m.p, IR) to an authentic sample, and 29.0 mg (29%) of 33.

Synthesis of 79 using hafnium triflate at 100°C with ACN as solvent

Using the general procedure, 3-phenylsydnone (99.4 mg, 0.614 mmol), hafnium triflate (96 mg, 20 mole %), acetonitrile (5 mL), and acetic anhydride (0.28 mL, 2.537 mmol) were stirred at 100°C overnight. TLC showed a partial conversion to the desired product and a considerable amount of starting material. Column chromatography of the crude product yielded 63.6 mg (51%) of 79, identical (TLC, m.p, IR) to an authentic sample, and 28.3 mg (28%) of 33.
Synthesis of 79 using gadolinium triflate at 100°C with ACN as solvent

Using the general procedure, 3-phenylsydnone (100.3 mg, 0.619 mmol), gadolinium triflate (75 mg, 5 mole %), acetonitrile (5 mL), and acetic anhydride (0.28 mL, 2.537 mmol) were stirred at 100°C overnight. TLC showed a partial conversion to the desired product and a considerable amount of starting material. Column chromatography of the crude product yielded 56.3 mg (45%) of 79, identical (TLC, m.p, IR) to an authentic sample, and 21.9 mg (22%) of 33.

Synthesis of 79 using indium triflate at 100°C with ACN as solvent

Using the general procedure, 3-phenylsydnone (100.9 mg, 0.623 mmol), indium triflate (19 mg, 5 mole %), acetonitrile (5 mL), and acetic anhydride (0.28 mL, 2.537 mmol) were stirred at 100°C overnight. TLC showed a partial conversion to the desired product and a small amount of starting material. Column chromatography of the crude product yielded 67.3 mg (53%) of 79, identical (TLC, m.p, IR) to an authentic sample, and 16.2 mg (16%) of 33.

General procedure for the synthesis of 4-acetyl-3-phenylsydnone (79) using metal triflate catalysts and lithium perchlorate

To a round bottom flask was added 3-phenylsydnone (33) [~100 mg], metal triflate catalyst (20 mole %), lithium perchlorate (5 or 20 mole %), acetonitrile (1 mL), and acetic anhydride (0.28 mL, 2.537 mmol). The reaction was heated to 100°C under reflux with stirring overnight and was evaluated by TLC in the morning. The mixture was transferred to a separatory funnel using a portion of dichloromethane, neutralized with saturated sodium bicarbonate and then extracted with dichloromethane (3 x 20 mL).
The combined organic layers were dried with magnesium sulfate, filtered, and evaporated in vacuo. The crude material was then columned via CombiFlash (12 g silica gel column, gradient of hexanes to dichloromethane to ethyl acetate) to yield the desired material.

Synthesis of 79 using yttrium triflate and lithium perchlorate (5 mole %) at 100 °C with ACN as solvent

Using the general procedure, 3-phenylsydnone (100.4 mg, 0.620 mmol), yttrium triflate (65.8 mg, 20 mole %), lithium perchlorate (3.1 mg, 5 mole %), acetonitrile (1 mL), and acetic anhydride (0.28 mL, 2.537 mmol) were stirred at 100 °C overnight. TLC showed a partial conversion to the desired product, small amount of starting material, and a large amount of baseline material. Column chromatography of the crude product yielded 17.2 mg (13%) of 79, identical (TLC, m.p, IR) to an authentic sample, and 27.6 mg (28%) of 33.

Synthesis of 79 using yttrium triflate and lithium perchlorate (5 mole %) at 100 °C with ACN as solvent

Using the general procedure, 3-phenylsydnone (100.4 mg, 0.620 mmol), yttrium triflate (65.8 mg, 20 mole %), lithium perchlorate (3.1 mg, 5 mole %), acetonitrile (1 mL), and acetic anhydride (0.28 mL, 2.537 mmol) were stirred at 100 °C overnight. TLC showed a partial conversion to the desired product, a small amount of starting material, and a large amount of baseline material. Column chromatography of the crude product yielded 17.2 mg (13%) of 79, identical (TLC, m.p, IR) to an authentic sample, and 27.6 mg (28%) of 33.
Synthesis of 79 using scandium triflate and lithium perchlorate (5 mole %) at 100 °C with ACN as solvent

Using the general procedure, 3-phenylsydnone (100.7 mg, 0.622 mmol), scandium triflate (61.8 mg, 20 mole %), lithium perchlorate (3.2 mg, 5 mole %), acetonitrile (1 mL), and acetic anhydride (0.28 mL, 2.537 mmol) were stirred at 100 °C overnight. TLC showed a partial conversion to the desired product and some starting material. Column chromatography of the crude product yielded 72.6 mg (58%) of 79, identical (TLC, m.p, IR) to an authentic sample, and 18.2 mg (18%) of 33.

Synthesis of 79 using hafnium triflate and lithium perchlorate (5 mole %) at 100 °C with ACN as solvent

Using the general procedure, 3-phenylsydnone (100.5 mg, 0.620 mmol), hafnium triflate (95.4 mg, 20 mole %), lithium perchlorate (3.2 mg, 5 mole %), acetonitrile (1 mL), and acetic anhydride (0.28 mL, 2.537 mmol) were stirred at 100 °C overnight. TLC showed an incomplete conversion to the desired product and a small amount of starting material. Column chromatography of the crude product yielded 35.0 mg (27%) of 79, identical (TLC, m.p, IR) to an authentic sample, and 8.7 mg (9%) of 33.

Synthesis of 79 using gadolinium triflate and lithium perchlorate (5 mole %) at 100 °C with ACN as solvent

Using the general procedure, 3-phenylsydnone (99.4 mg, 0.614 mmol), gadolinium triflate (74.2 mg, 20 mole %), lithium perchlorate (3.6 mg, 5 mole %), acetonitrile (1 mL), and acetic anhydride (0.28 mL, 2.537 mmol) were stirred at 100 °C overnight. TLC showed slight conversion to the desired product and a considerable
amount of starting material. Column chromatography of the crude product yielded 21.9 mg (17%) of \(79\), identical (TLC, m.p, IR) to an authentic sample, and 53.0 mg (53%) of \(33\).

Synthesis of \(79\) using indium triflate and lithium perchlorate (5 mole %) at 100 °C with ACN as solvent

Using the general procedure, 3-phenylsydnone (100.7 mg, 0.622 mmol), indium triflate (69 mg, 20 mole %), lithium perchlorate (3.2 mg, 5 mole %), acetonitrile (1 mL), and acetic anhydride (0.28 mL, 2.537 mmol) were stirred at 100 °C overnight. TLC showed full conversion to the desired product. Column chromatography of the crude product yielded 86.9 mg (70%) of \(79\), identical (TLC, m.p, IR) to an authentic sample.

Synthesis of \(79\) using lanthanum triflate and lithium perchlorate (5 mole %) at 100 °C with \(\text{Ac}_2\text{O}\) as solvent

Using the general procedure, 3-phenylsydnone (100.4 mg, 0.620 mmol), lanthanum triflate (74.2 mg, 20 mole %), lithium perchlorate (3.0 mg, 5 mole %), and acetic anhydride (1 mL, 9.061 mmol) were stirred at 100 °C overnight. TLC showed partial conversion to the desired product and a significant amount of starting material. Column chromatography of the crude product yielded 29.6 mg (24%) of \(79\), identical (TLC, m.p, IR) to an authentic sample, and 23.7 mg (24%) of \(33\).

Synthesis of \(79\) using yttrium triflate and lithium perchlorate (5 mole %) at 100 °C with \(\text{Ac}_2\text{O}\) as solvent
Using the general procedure, 3-phenylsydnone (101.4 mg, 0.620 mmol), yttrium triflate (66 mg, 20 mole %), acetonitrile (5 mL), and acetic anhydride (1 mL, 9.061 mmol) were stirred at 100 °C overnight. TLC showed a partial conversion to the desired product and a large amount of baseline material. Column chromatography of the crude product yielded 23.5 mg (18%) of 79, identical (TLC, m.p, IR) to an authentic sample.

**Synthesis of 79 using scandium triflate and lithium perchlorate (5 mole %) at 100 °C with Ac₂O as solvent**

Using the general procedure, 3-phenylsydnone (99.3 mg, 0.613 mmol), scandium triflate (60.3 mg, 20 mole %), lithium perchlorate (4.7 mg, 5 mole %), and acetic anhydride (1 mL, 9.061 mmol) were stirred at 100 °C overnight. TLC showed slight conversion to the desired product and a considerable amount of starting material. Column chromatography of the crude product yielded 26.6 mg (21%) of 79, identical (TLC, m.p, IR) to an authentic sample, and 73.8 mg (74%) of 33.

**Synthesis of 79 using hafnium triflate and lithium perchlorate (5 mole %) at 100 °C with Ac₂O as solvent**

Using the general procedure, 3-phenylsydnone (98.7 mg, 0.609 mmol), hafnium triflate (96 mg, 20 mole %), lithium perchlorate (4.7 mg, 5 mole %), and acetic anhydride (1 mL, 9.061 mmol) were stirred at 100 °C overnight. TLC showed weak spots for both the final product and starting material and a large spot for baseline material. Column chromatography of the crude product yielded 9.6 mg (8%) of 79, identical (TLC, m.p, IR) to an authentic sample, and 3.4 mg (3%) of 33.
Synthesis of 79 using gadolinium triflate and lithium perchlorate (5 mole %) at 100 °C with Ac₂O as solvent

Using the general procedure, 3-phenylsydnone (100.2 mg, 0.619 mmol), gadolinium triflate (74.6 mg, 20 mole %), lithium perchlorate (2.9 mg, 5 mole %), and acetic anhydride (1 mL, 9.061 mmol) were stirred at 100°C overnight. TLC showed full conversion to the desired product and a considerable amount of baseline material. Column chromatography of the crude product yielded 22.5 mg (18%) of 79, identical (TLC, m.p, IR) to an authentic sample.

Synthesis of 79 using indium triflate and lithium perchlorate (5 mole %) at 100 °C with Ac₂O as solvent

Using the general procedure, 3-phenylsydnone (99.7 mg, 0.615 mmol), indium triflate (69 mg, 20 mole %), lithium perchlorate (3 mg, 5 mole %), and acetic anhydride (1 mL, 9.061 mmol) were stirred at 100°C overnight. TLC showed a partial conversion to the desired product and a small amount of starting material. Column chromatography of the crude product yielded 40.9 mg (33%) of 79, identical (TLC, m.p, IR) to an authentic sample, and 1.5 mg (2%) of 33.

Synthesis of 79 using lanthanum triflate and lithium perchlorate (20 mole %) at 100 °C with ACN as solvent

Using the general procedure, 3-phenylsydnone (100.1 mg, 0.618 mmol), lanthanum triflate (72 mg, 20 mole %), acetonitrile (5 mL), and acetic anhydride (0.28 mL, 2.537 mmol) were stirred at 100 °C overnight. TLC showed partial conversion to the desired product and starting material. Column chromatography of the crude product
yielded 10.1 mg (8%) of 79, identical (TLC, m.p, IR) to an authentic sample, and 58.0 mg (58%) of 33.

Synthesis of 79 using yttrium triflate and lithium perchlorate (20 mole %) at 100 °C with ACN as solvent

Using the general procedure, 3-phenylsydnone (99.8 mg, 0.616 mmol), yttrium triflate (65.6 mg, 20 mole %), lithium perchlorate (12.6 mg, 20 mole %), acetonitrile (1mL), and acetic anhydride (0.28 mL, 2.537 mmol) were stirred at 100 °C overnight. TLC showed a partial conversion to the desired product, a sizeable amount of starting material, and a large amount of baseline material. Column chromatography of the crude product yielded 12.5 mg (10%) of 79, identical (TLC, m.p, IR) to an authentic sample, and 22.0 mg (22%) of 33.

Synthesis of 79 using scandium triflate and lithium perchlorate (20 mole %) at 100 °C with ACN as solvent

Using the general procedure, 3-phenylsydnone (99.1  mg, 0.612 mmol), scandium triflate (62.1 mg, 20 mole %), lithium perchlorate (13.4 mg, 20 mole %), acetonitrile (1 mL), and acetic anhydride (0.28 mL, 2.537 mmol) were stirred at 100 °C overnight. TLC showed a partial conversion to the desired product and a small amount of starting material. Column chromatography of the crude product yielded 63.9 mg (51%) of 79, identical (TLC, m.p, IR) to an authentic sample, and 10.2 mg (10%) of 33.

Synthesis of 79 using hafnium triflate and lithium perchlorate (20 mole %) at 100 °C with ACN as solvent
Using the general procedure, 3-phenylsydnone (100.6 mg, 0.621 mmol), hafnium triflate (96.2 mg, 20 mole %), lithium perchlorate (12.5 mg, 20 mole %), acetonitrile (1 mL), and acetic anhydride (0.28 mL, 2.537 mmol) were stirred at 100 °C overnight. TLC showed full conversion to the desired product. Column chromatography of the crude product yielded 78.0 mg (61%) of 79, identical (TLC, m.p, IR) to an authentic sample.

Synthesis of 79 using gadolinium triflate and lithium perchlorate (20 mole %) at 100 °C with ACN as solvent

Using the general procedure, 3-phenylsydnone (101.2 mg, 0.625 mmol), gadolinium triflate (76.7 mg, 20 mole %), lithium perchlorate (14.3 mg, 20 mole %), acetonitrile (1 mL), and acetic anhydride (0.28 mL, 2.537 mmol) were stirred at 100°C overnight. TLC showed a partial conversion to the desired product and a moderate amount of starting material. Column chromatography of the crude product yielded 61.3 mg (48%) of 79, identical (TLC, m.p, IR) to an authentic sample, and 16.0 mg (16%) of 33.

Synthesis of 79 using indium triflate and lithium perchlorate (20 mole %) at 100 °C with ACN as solvent

Using the general procedure, 3-phenylsydnone (100.3 mg, 0.619 mmol), indium triflate (70 mg, 20 mole %), lithium perchlorate (13.4 mg, 20 mole %), acetonitrile (1 mL), and acetic anhydride (0.28 mL, 2.537 mmol) were stirred at 100 °C overnight. TLC showed a partial conversion to the desired product and a small amount of starting material. Column chromatography of the crude product yielded 73.3 mg (59%) of 79, identical (TLC, m.p, IR) to an authentic sample, and 6.2 mg (6%) of 33.
Synthesis of 79 using lanthanum triflate and lithium perchlorate (20 mole %) at 100 °C with Ac₂O as solvent

Using the general procedure, 3-phenylsydnone (101.0 mg, 0.623 mmol), lanthanum triflate (72.7 mg, 20 mole %), lithium perchlorate (12.7 mg, 20 mole %), and acetic anhydride (1 mL, 9.061 mmol) were stirred at 100 °C overnight. TLC showed partial conversion to the desired product and a large amount of starting material. Column chromatography of the crude product yielded 34.5 mg (27%) of 79, identical (TLC, m.p, IR) to an authentic sample, and 42.7 mg (43%) of 33.

Synthesis of 79 using yttrium triflate and lithium perchlorate (20 mole %) at 100 °C with Ac₂O as solvent

Using the general procedure, 3-phenylsydnone (100.3 mg, 0.619 mmol), yttrium triflate (67.2 mg, 20 mole %), lithium perchlorate (12.5 mg, 20 mole %), and acetic anhydride (1 mL, 9.061 mmol) were stirred at 100 °C overnight. TLC showed a partial conversion to the desired product, a small amount of starting material, and a large amount of baseline material. Column chromatography of the crude product yielded 10.3 mg (8%) of 79, identical (TLC, m.p, IR) to an authentic sample, and 17.7 mg (18%) of 33.

Synthesis of 79 using scandium triflate and lithium perchlorate (20 mole %) at 100 °C with Ac₂O as solvent

Using the general procedure, 3-phenylsydnone (99.8 mg, 0.616 mmol), scandium triflate (65.2 mg, 20 mole %), lithium perchlorate (13.5 mg, 20 mole %), and acetic anhydride (1 mL, 9.061 mmol) were stirred at 100 °C overnight. TLC showed a partial conversion to the desired product, a small amount of starting material, and a large amount
of baseline material. Column chromatography of the crude product yielded 20.0 mg (16%) of 79, identical (TLC, m.p, IR) to an authentic sample, and 5.5 mg (6%) of 33.

Synthesis of 79 using hafnium triflate and lithium perchlorate (20 mole %) at 100 °C with Ac$_2$O as solvent

Using the general procedure, 3-phenylsydnone (100.2 mg, 0.619 mmol), hafnium triflate (95.6 mg, 20 mole %), lithium perchlorate (13.0 mg, 20 mole %), and acetic anhydride (1 mL, 9.061 mmol) were stirred at 100 °C overnight. TLC showed full conversion to the desired product and a considerable amount of baseline material. Column chromatography of the crude product yielded 12.0 mg (9%) of 79, identical (TLC, m.p, IR) to an authentic sample.

Synthesis of 79 using gadolinium triflate and lithium perchlorate (20 mole %) at 100 °C with Ac$_2$O as solvent

Using the general procedure, 3-phenylsydnone (100.3 mg, 0.619 mmol), gadolinium triflate (76.5 mg, 20 mole %), lithium perchlorate (13.1 mg, 20 mole %), and acetic anhydride (1 mL, 9.061 mmol) were stirred at 100 °C overnight. TLC showed almost full conversion to the desired product, a small amount of starting material, and a considerable amount of baseline material. Column chromatography of the crude product yielded 24.1 mg (19%) of 79, identical (TLC, m.p, IR) to an authentic sample, and 1.1 mg (1%) of 33.

Synthesis of 79 using indium triflate and lithium perchlorate (20 mole %) at 100 °C with Ac$_2$O as solvent
Using the general procedure, 3-phenylsydnone (100.3 mg, 0.619 mmol), indium triflate (70 mg, 20 mole %), lithium perchlorate (12.7 mg, 20 mole %), and acetic anhydride (1 mL, 9.061 mmol) were stirred at 100 °C overnight. TLC showed a partial conversion to the desired product, a small amount of starting material, and a noticeable amount of baseline material. Column chromatography of the crude product yielded 35.9 mg (29%) of 79, identical (TLC, m.p, IR) to an authentic sample, and 14.0 mg (14%) of 33.

General procedure for the synthesis of 4-acetyl-3-phenylsydnone (79) using metal triflate catalysts and lithium perchlorate under MWI with Ac₂O as solvent

To a microwave vessel was added 3-phenylsydnone (33) [~100 mg], metal triflate catalyst (20 mole %), lithium perchlorate (5 or 20 mole %), and acetic anhydride (0.5 mL, 4.530 mmol). The reaction vessel was sealed with a crimp cap and placed in a 300 W Monomode CEM Discover. The reaction mixture was microwaved at 125°C or the temperature otherwise stated for 30 minutes and was evaluated by TLC. The mixture was transferred to a separatory funnel using a portion of dichloromethane, neutralized with saturated sodium bicarbonate, and then extracted with dichloromethane (3 x 20 mL). The combined organic layers were dried with magnesium sulfate, filtered, and evaporated in vacuo. The crude material was then columned via CombiFlash (12 g silica gel column, gradient of hexanes to dichloromethane to ethyl acetate) to yield the desired material.

Synthesis of 79 using lanthanum triflate and MWI for 30 minutes at 100°C

Using the general procedure, 3-phenylsydnone (100.3 mg, 0.619 mmol), lanthanum triflate (72 mg, 20 mole %), and acetic anhydride (0.5 mL, 4.530 mmol) were
stirred under MWI at 100°C for 30 minutes. TLC showed little conversion to the desired product and much of the starting material remained. Column chromatography of the crude product yielded 23.3 mg (18%) of 79, identical (TLC, m.p, IR) to an authentic sample, and 71.1 mg (71%) of 33.

Synthesis of 79 using yttrium triflate and MWI for 30 minutes at 100°C

Using the general procedure, 3-phenylsydnone (98.2 mg, 0.606 mmol), yttrium triflate (66 mg, 20 mole %), and acetic anhydride (0.5 mL, 4.530 mmol) were stirred under MWI at 100°C for 30 minutes. TLC showed a partial conversion to the desired product and a large amount of starting material. Column chromatography of the crude product yielded 28.7 mg (23%) of 79, identical (TLC, m.p, IR) to an authentic sample, and 60.7 mg (61%) of 33.

Synthesis of 79 using scandium triflate and MWI for 30 minutes at 100°C

Using the general procedure, 3-phenylsydnone (102.5 mg, 0.633 mmol), scandium triflate (61 mg, 20 mole %), and acetic anhydride (0.5 mL, 4.530 mmol) were stirred under MWI at 100°C for 30 minutes. TLC showed a partial conversion to the desired product, a significant amount of starting material, and a considerable amount of baseline material. Column chromatography of the crude product yielded 40.0 mg (32%) of 79, identical (TLC, m.p, IR) to an authentic sample, and 28.4 mg (28%) of 33.

Synthesis of 79 using hafnium triflate and MWI for 30 minutes at 100°C

Using the general procedure, 3-phenylsydnone (97.9 mg, 0.604 mmol), hafnium triflate (96 mg, 20 mole %), and acetic anhydride (0.5 mL, 4.530 mmol) were stirred
under MWI at 100°C for 30 minutes. TLC showed a partial conversion to the desired product, a small amount of starting material, and baseline material. Column chromatography of the crude product yielded 45.7 mg (36%) of 79, identical (TLC, m.p, IR) to an authentic sample, and 7.1 mg (7%) of 33.

Synthesis of 79 using gadolinium triflate and MWI for 30 minutes at 100°C

Using the general procedure, 3-phenylsydnone (103.1 mg, 0.636 mmol), gadolinium triflate (75 mg, 20 mole %), and acetic anhydride (0.5 mL, 4.530 mmol) were stirred under MWI at 100°C for 30 minutes. TLC showed a partial conversion to the desired product and a considerable amount of starting material. Column chromatography of the crude product yielded 76.6 mg (60%) of 79, identical (TLC, m.p, IR) to an authentic sample, and 32.8 mg (33%) of 33.

Synthesis of 79 using indium triflate and MWI for 30 minutes at 100°C

Using the general procedure, 3-phenylsydnone (101.2 mg, 0.625 mmol), indium triflate (19 mg, 20 mole %), and acetic anhydride (0.5 mL, 4.530 mmol) were stirred under MWI at 100°C for 30 minutes. TLC showed a partial conversion to the desired product, a small amount of starting material, and baseline material. Column chromatography of the crude product yielded 29.8 mg (24%) of 79, identical (TLC, m.p, IR) to an authentic sample, and 14.4 mg (14%) of 33.

Synthesis of 79 using lanthanum triflate and MWI for 30 minutes at 125°C

Using the general procedure, 3-phenylsydnone (100.9 mg, 0.623 mmol), lanthanum triflate (72 mg, 20 mole %), and acetic anhydride (0.5 mL, 4.530 mmol) were
stirred under MWI at 125°C for 30 minutes. TLC showed incomplete conversion to the desired product and starting material remained. Column chromatography of the crude product yielded 58.5 mg (46%) of 79, identical (TLC, m.p, IR) to an authentic sample, and 23.3 mg (23%) of 33.

**Synthesis of 79 using yttrium triflate and MWI for 30 minutes at 125°C**

Using the general procedure, 3-phenylsydnone (99.6 mg, 0.615 mmol), yttrium triflate (66 mg, 20 mole %), and acetic anhydride (0.5 mL, 4.530 mmol) were stirred under MWI at 125°C for 30 minutes. TLC showed a partial conversion to the desired product and a significant amount of starting material. Column chromatography of the crude product yielded 38.1 mg (30%) of 79, identical (TLC, m.p, IR) to an authentic sample, and 36 mg (36%) of 33.

**Synthesis of 79 using scandium triflate and MWI for 30 minutes at 125°C**

Using the general procedure, 3-phenylsydnone (100.3 mg, 0.619 mmol), scandium triflate (61 mg, 20 mole %), and acetic anhydride (0.5 mL, 4.530 mmol) were stirred under MWI at 125°C for 30 minutes. TLC showed full conversion to the desired product with baseline material. Column chromatography of the crude product yielded 61.4 mg (49%) of 79, identical (TLC, m.p, IR) to an authentic sample.

**Synthesis of 79 using hafnium triflate and MWI for 30 minutes at 125°C**

Using the general procedure, 3-phenylsydnone (102.0 mg, 0.630 mmol), hafnium triflate (96 mg, 20 mole %), and acetic anhydride (0.5 mL, 4.530 mmol) were stirred under MWI at 125°C for 30 minutes. TLC showed a partial conversion to the desired product and starting material remained.
product, a small amount of starting material, and considerable amount of baseline material. Column chromatography of the crude product yielded 32.7 mg (26%) of 79, identical (TLC, m.p, IR) to an authentic sample, and 10.0 mg (10%) of 33.

**Synthesis of 79 using gadolinium triflate and MWI for 30 minutes at 125°C**

Using the general procedure, 3-phenylsydnone (97.8 mg, 0.604 mmol), gadolinium triflate (75 mg, 20 mole %), and acetic anhydride (0.5 mL, 4.530 mmol) were stirred under MWI at 125°C for 30 minutes. TLC showed a full conversion to the desired product and some baseline material. Column chromatography of the crude product yielded 64.5 mg (51%) of 79, identical (TLC, m.p, IR) to an authentic sample.

**Synthesis of 79 using indium triflate and MWI for 30 minutes at 125°C**

Using the general procedure, 3-phenylsydnone (98.3 mg, 0.607 mmol), indium triflate (60 mg, 20 mole %), and acetic anhydride (0.5 mL, 4.530 mmol) were stirred under MWI at 125°C for 30 minutes. TLC showed an almost full conversion to the desired product and a small amount of starting material. Column chromatography of the crude product yielded 71.7 mg (57%) of 79, identical (TLC, m.p, IR) to an authentic sample, and 4.8 mg (5%) of 33.

**Synthesis of 79 using lanthanum triflate, lithium perchlorate (5 mole %), and MWI for 30 minutes at 125°C**

Using the general procedure, 3-phenylsydnone (102.0 mg, 0.630 mmol), lanthanum triflate (72 mg, 20 mole %), lithium perchlorate (4 mg, 5 mole %), and acetic anhydride (0.5 mL, 4.530 mmol) were stirred under MWI at 125°C for 30 minutes. TLC
showed incomplete conversion to the desired product, starting material, and baseline material. Column chromatography of the crude product yielded 58.5 mg (46%) of 79, identical (TLC, m.p, IR) to an authentic sample, and 23.3 mg (23%) of 33.

**Synthesis of 79 using yttrium triflate, lithium perchlorate (5 mole %), and MWI for 30 minutes at 125°C**

Using the general procedure, 3-phenylsydnone (100.2 mg, 0.619 mmol), yttrium triflate (66 mg, 20 mole %), lithium perchlorate (3mg, 5 mole %), and acetic anhydride (0.5 mL, 4.530 mmol) were stirred under MWI at 125°C for 30 minutes. TLC showed a partial conversion to the desired product and a small amount of starting material. Column chromatography of the crude product yielded 53.3 mg (42%) of 79, identical (TLC, m.p, IR) to an authentic sample, and 16.7 mg (17%) of 33.

**Synthesis of 79 using scandium triflate, lithium perchlorate (5 mole %), and MWI for 30 minutes at 125°C**

Using the general procedure, 3-phenylsydnone (100.7 mg, 0.622 mmol), scandium triflate (61 mg, 20 mole %), lithium perchlorate (3mg, 5 mole %), and acetic anhydride (0.5mL, 4.530 mmol) were stirred under MWI at 125°C for 30 minutes. TLC showed full conversion to the desired product with a large amount of baseline material. Column chromatography of the crude product yielded 46.1 mg (37%) of 79, identical (TLC, m.p, IR) to an authentic sample.

**Synthesis of 79 using hafnium triflate, lithium perchlorate (5 mole %), and MWI for 30 minutes at 125°C**
Using the general procedure, 3-phenylsydnone (101.5 mg, 0.627 mmol), hafnium triflate (96 mg, 20 mole %), lithium perchlorate (3 mg, 5 mole %), and acetic anhydride (0.5 mL, 4.530 mmol) were stirred under MWI at 125°C for 30 minutes. TLC showed full conversion to the desired product and a considerable amount of baseline material. Column chromatography of the crude product yielded 53.6 mg (43%) of 79, identical (TLC, m.p, IR) to an authentic sample.

**Synthesis of 79 using gadolinium triflate, lithium perchlorate (5 mole %), and MWI for 30 minutes at 125°C**

Using the general procedure, 3-phenylsydnone (101.7 mg, 0.628 mmol), gadolinium triflate (75 mg, 20 mole %), lithium perchlorate (3 mg, 5 mole %), and acetic anhydride (0.5 mL, 4.530 mmol) were stirred under MWI at 125°C for 30 minutes. TLC showed essentially full conversion to the desired product, a very small amount of starting material, and some baseline material. Column chromatography of the crude product yielded 45.0 mg (36%) of 79, identical (TLC, m.p, IR) to an authentic sample, and 1.2 mg (1%) of 33.

**Synthesis of 79 using indium triflate, lithium perchlorate (5 mole %), and MWI for 30 minutes at 125°C**

Using the general procedure, 3-phenylsydnone (98.6 mg, 0.609 mmol), indium triflate (60 mg, 20 mole %), lithium perchlorate (3 mg, 5 mole %), and acetic anhydride (0.5 mL, 4.530 mmol) were stirred under MWI at 125°C for 30 minutes. TLC showed partial conversion to the desired product, a small amount of starting material, and a large amount of baseline material. Column chromatography of the crude product yielded 41.6
mg (33%) of \textbf{79}, identical (TLC, m.p, IR) to an authentic sample, and 9.8 mg (10%) of \textbf{33}.

**Synthesis of \textbf{79} using lanthanum triflate, lithium perchlorate (20 mole %), and MWI for 30 minutes at 125°C**

Using the general procedure, 3-phenylsydnone (99.7 mg, 0.615 mmol), lanthanum triflate (72 mg, 20 mole %), lithium perchlorate (13 mg, 20 mole %), and acetic anhydride (0.5 mL, 4.530 mmol) were stirred under MWI at 125°C for 30 minutes. TLC showed complete conversion to the desired product and baseline material. Column chromatography of the crude product yielded 26.9 mg (21%) of \textbf{79}, identical (TLC, m.p, IR) to an authentic sample.

**Synthesis of \textbf{79} using yttrium triflate, lithium perchlorate (20 mole %), and MWI for 30 minutes at 125°C**

Using the general procedure, 3-phenylsydnone (98.1 mg, 0.606 mmol), yttrium triflate (66 mg, 20 mole %), lithium perchlorate (13 mg, 20 mole %), and acetic anhydride (0.5 mL, 4.530 mmol) were stirred under MWI at 125°C for 30 minutes. TLC showed almost complete conversion to the desired product, a small amount of starting material, and a large amount of baseline material. Column chromatography of the crude product yielded 34.2 mg (27%) of \textbf{79}, identical (TLC, m.p, IR) to an authentic sample, and 3.5 mg (4%) of \textbf{33}.

**Synthesis of \textbf{79} using scandium triflate, lithium perchlorate (20 mole %), and MWI for 30 minutes at 125°C**
Using the general procedure, 3-phenylsydnone (103.4 mg, 0.638 mmol), scandium triflate (61 mg, 20 mole %), lithium perchlorate (13 mg, 20 mole %), and acetic anhydride (0.5mL, 4.530 mmol) were stirred under MWI at 125°C for 30 minutes. TLC showed full conversion to the desired product and a large amount of baseline material. Column chromatography of the crude product yielded 23.5 mg (19%) of 79, identical (TLC, m.p, IR) to an authentic sample.

Synthesis of 79 using hafnium triflate, lithium perchlorate (20 mole %), and MWI for 30 minutes at 125°C

Using the general procedure, 3-phenylsydnone (100.7 mg, 0.622 mmol), hafnium triflate (96 mg, 20 mole %), lithium perchlorate (13 mg, 20 mole %), and acetic anhydride (0.5 mL, 4.530 mmol) were stirred under MWI at 125°C for 30 minutes. TLC showed full conversion to the desired product and a considerable amount of baseline material. Column chromatography of the crude product yielded 10.8 mg (9%) of 79, identical (TLC, m.p, IR) to an authentic sample.

Synthesis of 79 using gadolinium triflate, lithium perchlorate (20 mole %), and MWI for 30 minutes at 125°C

Using the general procedure, 3-phenylsydnone (100.1 mg, 0.618 mmol), gadolinium triflate (75 mg, 20 mole %), lithium perchlorate (13 mg, 20 mole %), and acetic anhydride (0.5 mL, 4.530 mmol) were stirred under MWI at 125°C for 30 minutes. TLC showed a full conversion to the desired product and a substantial amount of baseline material. Column chromatography of the crude product yielded 18.6 mg (15%) of 79, identical (TLC, m.p, IR) to an authentic sample.
Synthesis of 79 using indium triflate, lithium perchlorate (20 mole %), and MWI for 30 minutes at 125°C

Using the general procedure, 3-phenylsydnone (99.2 mg, 0.612 mmol), indium triflate (60 mg, 20 mole %), lithium perchlorate (13 mg, 20 mole %), and acetic anhydride (0.5 mL, 4.530 mmol) were stirred under MWI at 125°C for 30 minutes. TLC showed partial conversion to the desired product and a large amount of baseline material. Column chromatography of the crude product yielded 31.9 mg (25%) of 79, identical (TLC, m.p, IR) to an authentic sample, and 8.0 mg (8%) of 33.

Synthesis of 79 using lanthanum triflate and MWI for 15 minutes at 150°C

Using the general procedure, 3-phenylsydnone (102.7 mg, 0.634 mmol), lanthanum triflate (72 mg, 20 mole %), and acetic anhydride (0.5 mL, 4.530 mmol) were stirred under MWI at 150°C for 15 minutes. TLC showed full conversion to the desired product. Column chromatography of the crude product yielded 83.6 mg (66%) of 79, identical (TLC, m.p, IR) to an authentic sample.

Synthesis of 79 using yttrium triflate and MWI for 15 minutes at 150°C

Using the general procedure, 3-phenylsydnone (103.9 mg, 0.641 mmol), yttrium triflate (66 mg, 20 mole %), and acetic anhydride (0.5 mL, 4.530 mmol) were stirred under MWI at 150°C for 15 minutes. TLC showed full conversion to the desired product. Column chromatography of the crude product yielded 72.1 mg (57%) of 79, identical (TLC, m.p, IR) to an authentic sample.

Synthesis of 79 using scandium triflate and MWI for 15 minutes at 150°C
Using the general procedure, 3-phenylsydnone (98.5 mg, 0.608 mmol), scandium triflate (61 mg, 20 mole %), and acetic anhydride (0.5 mL, 4.530 mmol) were stirred under MWI at 150°C for 15 minutes. TLC showed full conversion to the desired product and a small amount of baseline material. Column chromatography of the crude product yielded 59.7 mg (47%) of 79, identical (TLC, m.p, IR) to an authentic sample.

**Synthesis of 79 using hafnium triflate and MWI for 15 minutes at 150°C**

Using the general procedure, 3-phenylsydnone (100.3 mg, 0.619 mmol), hafnium triflate (96 mg, 20 mole %), and acetic anhydride (0.5 mL, 4.530 mmol) were stirred under MWI at 150°C for 15 minutes. TLC showed full conversion to the desired product and a large amount of baseline material. Column chromatography of the crude product yielded 31.8 mg (25%) of 79, identical (TLC, m.p, IR) to an authentic sample.

**Synthesis of 79 using gadolinium triflate and MWI for 15 minutes at 150°C**

Using the general procedure, 3-phenylsydnone (101.5 mg, 0.627 mmol), gadolinium triflate (75 mg, 20 mole %), and acetic anhydride (0.5 mL, 4.530 mmol) were stirred under MWI at 150°C for 15 minutes. TLC showed full conversion to the desired product and a small amount of baseline material. Column chromatography of the crude product yielded 59.5 mg (47%) of 79, identical (TLC, m.p, IR) to an authentic sample.

**Synthesis of 79 using indium triflate and MWI for 30 minutes at 100°C**

Using the general procedure, 3-phenylsydnone (100.8 mg, 0.622 mmol), indium triflate (19 mg, 20 mole %), and acetic anhydride (0.5 mL, 4.530 mmol) were stirred under MWI at 150°C for 15 minutes. TLC showed a partial conversion to the desired
product, a small amount of starting material, and substantial amount of baseline material.

Column chromatography of the crude product yielded 28.2 mg (22%) of 79, identical (TLC, m.p, IR) to an authentic sample, and 9.4 mg (9%) of 33.

Synthesis of 79 using lanthanum triflate, lithium perchlorate (20 mole %), and MWI for 15 minutes at 150°C

Using the general procedure, 3-phenylsydnone (97.8 mg, 0.604 mmol), lanthanum triflate (72 mg, 20 mole %), lithium perchlorate (13 mg, 20 mole %), and acetic anhydride (0.5 mL, 4.530 mmol) were stirred under MWI at 150°C for 15 minutes. TLC showed incomplete conversion to the desired product, a small amount of starting material, and baseline material. Column chromatography of the crude product yielded 37.3 mg (30%) of 79, identical (TLC, m.p, IR) to an authentic sample, and 10.0 mg (10%) of 33.

Synthesis of 79 using yttrium triflate, lithium perchlorate (20 mole %), and MWI for 15 minutes at 150°C

Using the general procedure, 3-phenylsydnone (102.4 mg, 0.632 mmol), yttrium triflate (66 mg, 20 mole %), lithium perchlorate (13 mg, 20 mole %), and acetic anhydride (0.5 mL, 4.530 mmol) were stirred under MWI at 150°C for 15 minutes. TLC showed almost complete conversion to the desired product and a large amount of baseline material. Column chromatography of the crude product yielded 35.5 mg (28%) of 79, identical (TLC, m.p, IR) to an authentic sample.

Synthesis of 79 using scandium triflate, lithium perchlorate (20 mole %), and MWI for 15 minutes at 150°C
Using the general procedure, 3-phenylsydnone (100.4 mg, 0.620 mmol), scandium triflate (61 mg, 20 mole %), lithium perchlorate (13 mg, 20 mole %), and acetic anhydride (0.5mL, 4.530 mmol) were stirred under MWI at 150°C for 15 minutes. TLC showed full conversion to the desired product and a large amount of baseline material. Column chromatography of the crude product yielded 32.0 mg (25%) of 79, identical (TLC, m.p, IR) to an authentic sample.

**Synthesis of 79 using hafnium triflate, lithium perchlorate (20 mole %), and MWI for 15 minutes at 150°C**

Using the general procedure, 3-phenylsydnone (96.8 mg, 0.598 mmol), hafnium triflate (96 mg, 20 mole %), lithium perchlorate (13 mg, 20 mole %), and acetic anhydride (0.5 mL, 4.530 mmol) were stirred under MWI at 150°C for 15 minutes. TLC showed full conversion to the desired product and a considerable amount of baseline material. Column chromatography of the crude product yielded 12.4 mg (10%) of 79, identical (TLC, m.p, IR) to an authentic sample.

**Synthesis of 79 using gadolinium triflate, lithium perchlorate (20 mole %), and MWI for 15 minutes at 150°C**

Using the general procedure, 3-phenylsydnone (97.2 mg, 0.600 mmol), gadolinium triflate (75 mg, 20 mole %), lithium perchlorate (13 mg, 20 mole %), and acetic anhydride (0.5 mL, 4.530 mmol) were stirred under MWI at 150°C for 15 minutes. TLC showed full conversion to the desired product and a small amount of baseline material. Column chromatography of the crude product yielded 43.5 mg (35%) of 79, identical (TLC, m.p, IR) to an authentic sample.
Synthesis of 79 using indium triflate, lithium perchlorate (20 mole %), and MWI for 15 minutes at 150°C

Using the general procedure, 3-phenylsydnone (101.4 mg, 0.626 mmol), indium triflate (60 mg, 20 mole %), lithium perchlorate (13 mg, 20 mole %), and acetic anhydride (0.5 mL, 4.530 mmol) were stirred under MWI at 150°C for 15 minutes. TLC showed partial conversion to the desired product, a small amount of starting material, and baseline material. Column chromatography of the crude product yielded 42.5 mg (34%) of 79, identical (TLC, m.p, IR) to an authentic sample, and 9.8 mg (10%) of 33.

General procedure for the synthesis of 4-acetyl-3-phenylsydnone (79) using metal triflate catalysts under MWI with ACN as solvent

To a microwave vessel was added 3-phenylsydnone (33) (~100 mg), metal triflate catalyst (20 mole %), acetonitrile (1 mL), and acetic anhydride (0.28 mL, 2.537 mmol). The reaction vessel was sealed with a crimp cap and placed in a 300 W Monomode CEM Discover. The reaction mixture was microwaved at 125°C or the temperature otherwise stated for 30 minutes and was evaluated by TLC. The mixture was transferred to a separatory funnel by a portion of dichloromethane, neutralized with saturated sodium bicarbonate, and then extracted with dichloromethane (3 x 20 mL). The combined organic layers were dried with magnesium sulfate, filtered, and evaporated in vacuo. The crude material was then columned via CombiFlash (12 g silica gel column, gradient of hexanes to dichloromethane to ethyl acetate) to yield the desired material.

Synthesis of 79 using lanthanum triflate and MWI for 15 minutes at 150°C
Using the general procedure, 3-phenylsydnone (100.0 mg, 0.617 mmol), lanthanum triflate (72.5 mg, 20 mole %), acetonitrile (1 mL) and acetic anhydride (0.28 mL, 2.537 mmol) were stirred under MWI at 150°C for 15 minutes. TLC showed partial conversion to the desired product and starting material. Column chromatography of the crude product yielded 43.2 mg (34%) of 79, identical (TLC, m.p, IR) to an authentic sample, and 42.6 mg (43%) of 33.

**Synthesis of 79 using yttrium triflate and MWI for 15 minutes at 150°C**

Using the general procedure, 3-phenylsydnone (98.8 mg, 0.610 mmol), yttrium triflate (61.8 mg, 20 mole %), acetonitrile (1 mL), and acetic anhydride (0.28 mL, 2.537 mmol) were stirred under MWI at 150°C for 15 minutes. TLC showed incomplete conversion to the desired product and a considerable amount of starting material. Column chromatography of the crude product yielded 56.0 mg (45%) of 79, identical (TLC, m.p, IR) to an authentic sample, 38.6 mg (39%) of 33.

**Synthesis of 79 using scandium triflate and MWI for 30 minutes at 125°C**

Using the general procedure, 3-phenylsydnone (101.1 mg, 0.624 mmol), scandium triflate (65.9 mg, 20 mole %), acetonitrile (1 mL), and acetic anhydride (0.28 mL, 2.537 mmol) were stirred under MWI at 125°C for 30 minutes. TLC showed partial conversion to the desired product and a small amount of starting material, and baseline material. Column chromatography of the crude product yielded 67.0 mg (53%) of 79, identical (TLC, m.p, IR) to an authentic sample, and 5.0 mg (5%) of 33.

**Synthesis of 79 using hafnium triflate and MWI for 30 minutes at 125°C**
Using the general procedure, 3-phenylsydnone (102.8 mg, 0.635 mmol), hafnium triflate (98.9 mg, 20 mole %), acetonitrile (1 mL), and acetic anhydride (0.28 mL, 2.537 mmol) were stirred under MWI at 125°C for 30 minutes. TLC showed a partial conversion to the desired product and a small amount of starting material. Column chromatography of the crude product yielded 68.1 mg (54%) of 79, identical (TLC, m.p, IR) to an authentic sample, and 15.7 mg (16%) of 33.

Synthesis of 79 using gadolinium triflate and MWI for 30 minutes at 125°C

Using the general procedure, 3-phenylsydnone (102.3 mg, 0.631 mmol), gadolinium triflate (75 mg, 20 mole %), acetonitrile (1 mL), and acetic anhydride (0.28 mL, 2.537 mmol) were stirred under MWI at 125°C for 30 minutes. TLC showed full conversion to the desired product. Column chromatography of the crude product yielded 93.3 mg (74%) of 79, identical (TLC, m.p, IR) to an authentic sample.

Synthesis of 79 using indium triflate and MWI for 30 minutes at 125°C

Using the general procedure, 3-phenylsydnone (100.6 mg, 0.621 mmol), indium triflate (60 mg, 20 mole %), acetonitrile (1 mL), and acetic anhydride (0.28 mL, 2.537 mmol) were stirred under MWI at 125°C for 30 minutes. TLC showed full conversion to the desired product. Column chromatography of the crude product yielded 84.8 mg (67%) of 79, identical (TLC, m.p, IR) to an authentic sample.

General procedure for the synthesis of 3-(2’-[formyl] phenyl) sydnone (59) from 67

To an oven dried 3-neck round bottom flask was added 3-(2’-[carbomethoxy] phenyl) sydnone (67) in anhydrous dichloromethane (~10 mL) at -78°C (dry ice: acetone)
under nitrogen. After the solution was allowed to cool, DIBALH (1.0 M solution in dichloromethane) was added with slow stirring. After 1 hour, the reaction was quenched while still at -78°C by the slow addition of 10% HCl (5 mL). The mixture was allowed to warm to room temperature and was then poured into distilled water. The aqueous layer was extracted with dichloromethane (3 x 20 mL) and the organic layers were combined, dried with magnesium sulfate, and reduced in vacuo to yield an orange oil. The crude oil was then columned via CombiFlash (12 g silica gel column, gradient of hexanes to dichloromethane to ethyl acetate), and all fractions containing only 3-(2’-[formyl] phenyl) sydnone (59) were reduced in vacuo to a yellow solid, m.p. 88-90°C, identical (m.p., TLC, IR, ¹H NMR, and ¹³C NMR) to an authentic sample.¹²⁹

Synthesis of 3-(2’-[formyl] phenyl) sydnone (59) with DIBALH (1.1 eq)

Following the general procedure, 3-(2’-[carbomethoxy] phenyl) sydnone (67) [56.3 mg, 0.254 mmol) was dissolved in dichloromethane (5 mL) at -78°C (dry ice: acetone) under nitrogen. After the solution was allowed to cool, DIBALH (0.4 mL, 0.4 mmol) [1.0 M solution in dichloromethane] was added with slow stirring. After 1 hour, the reaction was quenched while still at -78°C by the slow addition of 10% HCl (5 mL). TLC showed only partial conversion to the formyl product with starting material remaining. Column chromatography of the crude product yielded 15.9 mg (33%) of 59, identical (TLC, m.p, IR) to an authentic sample.

Synthesis of 3-(2’-[formyl] phenyl) sydnone (59) with DIBALH (1.5 eq) for 1 hour

Following the general procedure, 3-(2’-[carbomethoxy] phenyl) sydnone (67) [35.3 mg, 0.160 mmol) was dissolved in dichloromethane (5 mL) at -78°C (dry ice:
acetone) under nitrogen. After the solution was allowed to cool, DIBALH (0.25 mL, 0.25 mmol) [1.0 M solution in dichloromethane] was added slowly with stirring. After 1 hour, the reaction was quenched while still at -78°C by the slow addition of 10% HCl (5 mL). TLC showed only partial conversion to the formyl product with starting material remaining. Column chromatography of the crude product yielded 17.9 mg (57%) of 59, identical (TLC, m.p, IR) to an authentic sample.

Synthesis of 3-(2’-[formyl] phenyl) sydnone (59) with DIBALH (1.5 eq) for 2 hours

Following the general procedure, 3-(2’-[carboxmethoxy] phenyl) sydnone (67) [502.2 mg, 2.28 mmol] was dissolved in dichloromethane (10 mL) at -78°C (dry ice: acetone) under nitrogen. After the solution was allowed to cool, DIBALH (3.5 mL, 3.5 mmol) [1.0 M solution in dichloromethane] was added slowly with stirring. After 2 hours, the reaction was quenched while still at -78°C by the slow addition of 10% HCl (5 mL). TLC showed only partial conversion to the formyl product. Column chromatography of the crude product yielded 205.4 mg (47%) of 59, identical (TLC, m.p, IR) to an authentic sample.

Synthesis of 3-(2’-[formyl] phenyl) sydnone (59) with DIBALH (2 eq) for 1 hour

Following the general procedure, 3-(2’-[carboxmethoxy] phenyl) sydnone (67) [200.4 mg, 0.856 mmol] was dissolved in dichloromethane (5 mL) at -78°C (dry ice: acetone) under nitrogen. After the solution was allowed to cool, DIBALH (1.8 mL, 1.8 mmol) [1.0 M solution in dichloromethane] was added slowly with stirring. After 1 hour, the reaction was quenched while still at -78°C by the slow addition of 10% HCl (5 mL). TLC showed only partial conversion to the formyl product with starting material
remaining. Column chromatography of the crude product yielded 102.2 mg (63%) of 59, identical (TLC, m.p, IR) to an authentic sample.

**Synthesis of 3-(2’-[formyl] phenyl) sydnone (59) with DIBALH (2 eq) for 1.5 hours**

Following the general procedure, 3-(2’-[carbomethoxy] phenyl) sydnone (67) (619.0 mg, 2.81 mmol) was dissolved in dichloromethane (10 mL) at -78°C (dry ice: acetone) under nitrogen. After the solution was allowed to cool, DIBALH (5.6 mL, 5.6 mmol) [1.0 M solution in dichloromethane] was added slowly with stirring. After 1.5 hours, the reaction was quenched while still at -78°C by the slow addition of 10% HCl (5 mL). TLC showed full conversion to the formyl product. Column chromatography of the crude product yielded 319.0 mg (73%) of 59, identical (TLC, m.p, IR) to an authentic sample.

**Synthesis of 3-(2’-[formyl] phenyl) sydnone (59) with DIBALH (2 eq) for 2 hours**

Following the general procedure, 3-(2’-[carbomethoxy] phenyl) sydnone (67) (1.447 g, 6.57 mmol) was dissolved in dichloromethane (15 mL) at -78°C (dry ice: acetone) under nitrogen. After the solution was allowed to cool, DIBALH (13.1 mL, 13.1 mmol) [1.0 M solution in dichloromethane] was added slowly with stirring. After 2 hours, the reaction was quenched while still at -78°C by the slow addition of 10% HCl (5 mL). TLC showed full conversion to the formyl and hydroxymethyl (over-reduction) products. Column chromatography of the crude product mixture yielded 611.6 mg (49%) of 59, identical (TLC, m.p, IR) to an authentic sample.

**Synthesis of 3-(2’-[formyl] phenyl) sydnone (59) with DIBALH (2.6 eq) for 1.3 hours**
Following the general procedure, 3-(2’-[carbomethoxy] phenyl) sydnone (67) [1.008 g, 4.581 mmol) was dissolved in dichloromethane (10 mL) at -78°C (dry ice: acetone) under nitrogen. After the solution was allowed to cool, DIBALH (12 mL, 12 mmol) [1.0 M solution in dichloromethane] was added slowly with stirring in two increments (7 mL initially, 5 mL 45 minutes later). After 1.3 hours, the reaction was quenched while still at -78°C by the slow addition of 10% HCl (5 mL). TLC only showed conversion to the formyl and hydroxymethyl products. Column chromatography of the crude product mixture yielded 15.9 mg (33%) of 59, identical (TLC, m.p, IR) to an authentic sample.

Synthesis of 3-(2’-[formyl] phenyl) sydnone (59) with DIBALH (3 eq) for 1 hour

Following the general procedure, 3-(2’-[carbomethoxy] phenyl) sydnone (67) [190.4 mg, .814 mmol) was dissolved in dichloromethane (5 mL) at -78°C (dry ice: acetone) under nitrogen. After the solution was allowed to cool, DIBALH (2.5 mL, 2.5 mmol) [1.0 M solution in dichloromethane] was added slowly with stirring. After 1 hour, the reaction was quenched while still at -78°C by the slow addition of 10% HCl (5 mL). TLC showed partial conversion to the formyl product and formation of the hydroxymethyl product. Column chromatography of the crude product yielded 100.0 mg (65%) of 59, identical (TLC, m.p, IR) to an authentic sample.

Synthesis of 3-(2’-[formyl] phenyl) sydnone (59) by oxidation of 80 with PDC

The title compound was prepared in 48% yield from 3-[2’-(hydroxymethyl)phenyl] sydnone (80) by a literature method (pyridinium dichromate / dichloromethane)129.
Attempted synthesis of 3-[2’-(formyl) phenyl]-4-acetyl sydnone (79) with
Montmorillonite K-10

To a round bottom flask was added 3-(2’-[formyl] phenyl) sydnone (59) [79.0 mg, 0.415 mmol], acetic anhydride (1.8 mL, 16.3 mmol), Montmorillonite K-10 (474 mg), and dioxane (1 mL). The reaction was heated to 110°C under reflux and monitored by TLC. After stirring for 3 days, the solution was filtered to remove the clay, neutralized with saturated sodium bicarbonate solution and extracted with dichloromethane (3 x 25 mL). The organic layers were combined, dried with magnesium sulfate, and reduced in vacuo to afford a red oil. By TLC examination, only baseline material was detected and, accordingly, the reaction was not pursued further with Montmorillonite K-10.

Attempted synthesis of 3-[2’-(formyl) phenyl]-4-acetyl sydnone (79) with Bismuth Triflate in the Q-tube

To a Q-tube vessel was added 3-(2’-[formyl] phenyl) sydnone (59) [391 mg, 2.05 mmol], acetic anhydride (4 mL, 36.243 mmol), bismuth triflate (294 mg, 25 mole %), lithium perchlorate (46 mg, 25 mole %), and acetonitrile (2.5 mL). The reaction mixture was heated at 110°C with stirring and monitored by TLC, which showed full conversion to an upper running compound after 9 hours. The solution was neutralized with saturated sodium bicarbonate solution and extracted with dichloromethane (3 x 25 mL). The organic layers were combined, dried with magnesium sulfate, and reduced in vacuo to afford a red oil. The oil was then columned via CombiFlash (12 g silica gel column, gradient of hexanes to dichloromethane to ethyl acetate). The material was isolated and
confirmed to be 1H- indazole (64.3 mg, 26%), m.p.145-147°C [literature 145-146.5°C].

\(^1\)H NMR (CDCl\(_3\)):  7.18 (t, 1H), 7.38 (t, 1H), 7.5 (d, 1H), 7.7 (d, 1H), 8.12 (s, 1H), 10.99 (s, 1H) ppm

\(^{13}\)C NMR (CDCl\(_3\)): 140.14 (C-N), 134.77 (C=N), 126.83, 123.22, 121.00, 120.90, 109.80 ppm

Attempted synthesis of 3-[2’-(formyl) phenyl]-4-acetyl sydnone (79) with Lanthanum Triflate via MWI

In a microwave vessel, 3-(2’-[formyl] phenyl) sydnone (59) [64.7 mg, 0.341 mmol], lanthanum triflate (40.3 mg, 20 mole %), acetic anhydride (0.5 mL, 4.530 mmol), and acetonitrile (1 mL) were stirred under MWI at 150°C for 15 minutes. TLC examination showed full conversion to an upper running compound and baseline material. The solution was neutralized with saturated sodium bicarbonate solution and extracted with dichloromethane (3 x 15 mL). The organic layers were combined, dried with magnesium sulfate, and reduced in vacuo to afford a red oil. The oil was then columned via CombiFlash (12 g silica gel column, gradient of hexanes to dichloromethane to ethyl acetate). The material was isolated as a clear oil and, with no further purification, confirmed to be 1-acetyl-1H-indazole (82) [36.3 mg, 67%].

IR (KBr): 1720 (C=O), 1610, 1503, 1383, 1196, 1146, 938, 752, 688 cm\(^{-1}\)

\(^1\)H NMR (CDCl\(_3\)):  2.79 (s, 3H), 7.36 (t, 1H), 7.56 (t, 1H), 7.74 (d, 1H), 8.13 (s, 1H), 8.46 (d, 1H) ppm
\[ ^{13}\text{C NMR (CDCl}_3\text{): 171.10 (C=O), 139.72 (C-N), 139.04 (C=N), 129.44, 126.31, 124.46, 120.85, 115.58, 23.03 \text{ ppm}} \]

**Attempted synthesis of 3-[2’-(formyl) phenyl]-4-acetyl sydnone (79) with Yttrium Triflate via MWI**

To a microwave vessel, 3-(2’-[formyl] phenyl) sydnone (59) [52.3 mg, 0.275 mmol], yttrium triflate (29.5 mg, 20 mole %), acetic anhydride (0.5 mL, 4.530 mmol), and acetonitrile (1 mL) were stirred under MWI at 150°C for 15 minutes. TLC examination showed full conversion to an upper running compound and baseline material. The solution was neutralized with saturated sodium bicarbonate solution and extracted with dichloromethane (3 x 15 mL). The organic layers were combined, dried with magnesium sulfate, and reduced in vacuo to afford a red oil. The oil was then columned via CombiFlash (12 g silica gel column, gradient of hexanes to dichloromethane to ethyl acetate). The product was isolated as a clear oil and confirmed to be 1-acetyl-1H-indazole (82) [22.9 mg, 52%], identical (TLC, IR, \(^1\text{H NMR, }^{13}\text{C NMR}) to an authentic sample.

**Attempted synthesis of 3-[2’-(formyl) phenyl]-4-acetyl sydnone (79) with Hafnium Triflate via MWI**

To a microwave vessel, 3-(2’-[formyl] phenyl) sydnone (59) [50.3 mg, 0.265 mmol], hafnium triflate (41.5 mg, 20 mole %), acetic anhydride (0.5 mL, 4.530 mmol), and acetonitrile (1 mL) were stirred under MWI at 125°C for 30 minutes. TLC examination showed full conversion to an upper running compound and baseline material. The solution was neutralized with saturated sodium bicarbonate solution and
extracted with dichloromethane (3 x 15 mL). The organic layers were combined, dried with magnesium sulfate, and reduced in vacuo to afford a red oil. The oil was then columned via CombiFlash (12 g silica gel column, gradient of hexanes to dichloromethane to ethyl acetate). The product was isolated as a clear oil and confirmed to be 1-acetyl-1H-indazole (82) [15.2 mg, 36%], identical (TLC, IR, $^1$H NMR, $^{13}$C NMR) to an authentic sample.

Attempted synthesis of 3-[2’-(formyl) phenyl]-4-acetyl sydnone (79) with Scandium Triflate via MWI

To a microwave vessel, 3-(2’-[formyl] phenyl) sydnone (59) [50.5 mg, 0.266 mmol], scandium triflate (26.4 mg, 20 mole %), acetic anhydride (0.5 mL, 4.530 mmol), and acetonitrile (1 mL) were stirred under MWI at 125°C for 30 minutes. TLC examination showed full conversion to an upper running compound and baseline material. The solution was neutralized with saturated sodium bicarbonate solution and extracted with dichloromethane (3 x 15 mL). The organic layers were combined, dried with magnesium sulfate, and reduced in vacuo to afford a red oil. The oil was then columned via CombiFlash (12 g silica gel column, gradient of hexanes to dichloromethane to ethyl acetate). The product was isolated as a clear oil and confirmed to be 1-acetyl-1H-indazole (82) [12.6 mg, 30%], identical (TLC, IR, $^1$H NMR, $^{13}$C NMR) to an authentic sample.

Attempted synthesis of 3-[2’-(formyl) phenyl]-4-acetyl sydnone (79) with Gadolinium Triflate via MWI
To a microwave vessel, 3-(2'-[formyl] phenyl) sydnone (59) [48.5 mg, 0.255 mmol], gadolinium triflate (31.3 mg, 20 mole %), acetic anhydride (0.5 mL, 4.530 mmol), and acetonitrile (1 mL) were stirred under MWI at 100°C for 30 minutes. TLC examination showed full conversion to an upper running compound and baseline material. The solution was neutralized with saturated sodium bicarbonate solution and extracted with dichloromethane (3 x 15 mL). The organic layers were combined, dried with magnesium sulfate, and reduced *in vacuo* to afford a red oil. The oil was then columned *via* CombiFlash (12 g silica gel column, gradient of hexanes to dichloromethane to ethyl acetate). The product was isolated as a clear oil and confirmed to be 1-acetyl-1H-indazole (82) [31.3 mg, 77%], identical (TLC, IR, $^1$H NMR, $^{13}$C NMR) to an authentic sample.

**Attempted synthesis of 3-[2'-(formyl) phenyl]-4-acetyl sydnone (79) with Indium Triflate *via* MWI**

To a microwave vessel, 3-(2'-[formyl] phenyl) sydnone (59) [51.6 mg, 0.272 mmol], indium triflate (31.4 mg, 20 mole %), acetic anhydride (0.5 mL, 4.530 mmol), and acetonitrile (1 mL) were stirred under MWI at 125°C for 30 minutes. TLC examination showed full conversion to an upper running compound and baseline material. The solution was neutralized with saturated sodium bicarbonate solution and extracted with dichloromethane (3 x 15 mL). The organic layers were combined, dried with magnesium sulfate, and reduced *in vacuo* to afford a red oil. The oil was then columned *via* CombiFlash (12 g silica gel column, gradient of hexanes to dichloromethane to ethyl acetate). The product was isolated as a clear oil and confirmed
to be 1-acetyl-1H-indazole (82) [34.4 mg, 67%], identical (TLC, IR, $^1$H NMR, $^{13}$C NMR) to an authentic sample.

**Attempted synthesis of 3-(2’-[formyl] phenyl)-4-acetyl sydnone (79) with DIBALH (2 eq) for 1 hour**

In an oven dried three neck round bottom flask under nitrogen was added 3-(2’-[carbomethoxy] phenyl)-4-acetyl sydnone (68) [48.0 mg, 0.182 mmol) dissolved in dichloromethane (5 mL). After the solution was allowed to cool to -78°C (dry ice: acetone), DIBALH (0.4 mL, 0.4 mmol) [ 1.0 M solution in dichloromethane] was added slowly with stirring. After 1 hour, the reaction was quenched while still at -78°C by the slow addition of 5% HCl (5 mL). TLC examination indicated the presence of starting material and baseline material. The aqueous layer was extracted with dichloromethane (3 x 15 mL) and the organic layers were combined, dried with magnesium sulfate, and reduced *in vacuo* to yield an orange semisolid. The mixture was then columned *via* CombiFlash (12 g silica gel column, gradient of hexanes to dichloromethane to ethyl acetate). The columned material yielded 42.1 mg (88%) of the starting material 68, identical (TLC, m.p, IR) to an authentic sample.

**Attempted synthesis of 3-(2’-[formyl] phenyl)-4-acetyl sydnone (79) with DIBALH (2 eq) overnight at -40°C**

In an oven dried three neck round bottom flask was added 3-(2’-[carbomethoxy] phenyl)-4-acetyl sydnone (68) [54.0 mg, 0.205 mmol), which was dissolved in dichloromethane (5 mL) at -40°C (ethylene glycol: water, 60:40, in dry ice) under nitrogen. After the solution was allowed to cool, DIBALH (0.4 mL, 0.4 mmol) [1.0 M
solution in dichloromethane] as added slowly with stirring. Overnight, the reaction was allowed to warm to room temperature, whereupon, the reaction was quenched at room temperature by the slow addition of 5% HCl (5 mL). TLC examination indicated the presence of starting material and baseline material. The aqueous layer was extracted with dichloromethane (3 x 15 mL) and the organic layers were combined, dried with magnesium sulfate, and reduced \textit{in vacuo} to yield an orange semisolid. The mixture was then columned via CombiFlash (12 g silica gel column, gradient of hexanes to dichloromethane to ethyl acetate). The columned material yielded 46.1 mg (86%) of the starting material 68, identical (TLC, m.p, IR) to an authentic sample.

\textbf{Attempted synthesis of 3-(2’-[formyl] phenyl)-4-acetyl sydnone (79) with DIBALH (2 eq) overnight at 0°C}

In an oven dried three neck round bottom flask was added 3-(2’-[carbomethoxy]phenyl)-4-acetyl sydnone (68) [52.0 mg, 0.198 mmol), which was dissolved in dichloromethane (5 mL) at 0°C (ice) under nitrogen. After the solution was allowed to cool, DIBALH (0.4 mL, 0.4 mmol) [1.0 M solution in dichloromethane] was added slowly with stirring. Overnight, the reaction was allowed to warm to room temperature, whereupon, the reaction was quenched at room temperature by the slow addition of 5% HCl (5 mL). TLC examination indicated the presence of only starting material. The aqueous layer was extracted with dichloromethane (3 x 15 mL) and the organic layers were combined, dried with magnesium sulfate, and reduced \textit{in vacuo} to yield an orange solid, 51.6 mg (99%), identified as the starting material 68, identical (TLC, m.p, IR) to an authentic sample.
Attempted synthesis of 3-(2’-[formyl] phenyl)-4-acetyl sydnone (79) with DIBALH (2 eq) for 2 hours

In an oven dried three neck round bottom flask was added 3-(2’-[carboethoxy] phenyl)-4-acetyl sydnone (75) [65.0 mg, 0.235 mmol), which was dissolved in dichloromethane (5 mL) at -78°C (dry ice: acetone) under nitrogen. After the solution was allowed to cool, DIBALH (0.35 mL, 0.35 mmol) [1.0 M solution in dichloromethane] was added slowly with stirring. After 2 hours, the reaction was quenched while still at -78°C by the slow addition of 5% HCl (5 mL). TLC examination showed the presence of starting material and baseline material. The aqueous layer was extracted with dichloromethane (3 x 15 mL) and the organic layers were combined, dried with magnesium sulfate, and reduced in vacuo to yield an orange semisolid. The mixture was then columned via CombiFlash (12 g silica gel column, gradient of hexanes to dichloromethane to ethyl acetate). The columned material yielded 50.7 mg (78%) of the starting material 75, identical (TLC, m.p, IR) to an authentic sample.
References

(1) Zincke, T. Ber. **1869**, 2, 737.


(3) Radzivanovski, C. Ber. **1874**, 7, 141.

(4) Doebner, O.; Stackman, W. Ber. **1876**, 9, 1918.


(6) Zincke, T. Ber. **1873**, 6, 137.


(15) Perrier, G. Ber. **1900**, 33, 815.


152


(44) Groggins, P. H.; Nagel, R. H. Ind. Eng. Chem. 1934, 26, 1313.


(47) Heller, G.; Schulke, K. Ber. 1908, 41, 3627.

(48) Ador, E.; Rilliet, A. Ber. 1878, 11, 399.

(49) Calloway, N. O. Iowa State Coll. J. Sci. 1934, 9, 141.


(53) Phillipi, R. Monatsh 1911, 136, 125.

(54) Cryer, J. Phil. Trans. 1925, 3, 29.

(55) Krollpeiffer, F. Ber. 1923, 56, 2360.

(56) Gattermann, L. Ann. 1909, 357, 313.

(57) Gattermann, L.; Koch, J. Ber. 1897, 30, 1622.

(58) Hinkel British patent 397,124, 1934.

(60) Michler, W. *Ber.* **1876**, 9, 400.


(92) Baker, W.; Ollis, W. D.; Poole, V. D. *Chem. Ind.* **1955**.


(126) Fisher, J. Bismuth Triflate Catalyzed Friedel-Crafts Acylations of Sydnones, Wright State University, 2005.

(127) Rumple, A. Routes to acylated sydnones utilizing microwave chemistry, Wright State University, 2010.

