The Anodic Oxidation of 1,1-Diphenyl Ketones in the Presence of Nucleophiles

By

Boris Sheludko

Faculty Advisor: Dr. Albert J. Fry

A Dissertation submitted to the Faculty of Wesleyan University in partial fulfillment of the requirements for the degree of Master of Arts

Middletown, Connecticut May 2012
ACKNOWLEDGEMENTS

First and foremost, I’d like to thank Professor Fry. Thank you for allowing me the opportunity to perform research in your laboratory and for being my mentor over the years. I have become a better scientist than before under your guidance, and your dedication to your field has instilled in me a passion that I hope to hold on to for the rest of my professional career. Thank you.

Rachel Merzel, thank you for keeping me company over this past year. From the very first time you explained your project to me until now, we’ve been in this together and you’ve been extremely helpful. Anthony Davis, thank you for all of your advice and support, even when it didn’t seem most convenient for you – I appreciate it immensely. I wish you both well in everything you do.

To the other Chemistry Professors at Wesleyan University and Andrea Roberts especially, thank you for your dedication to your work. You’ve made my time here more enjoyable and something I’ll never forget – Professor Roberts, I’ll miss your yelling at me to go home and rest when you saw me using the GC late at night.

To my family, much love and thank you for your support, both moral and financial. I apologize for how busy I’ve been these last few months – hopefully this makes that time worth it. To Gabby, I expect that you’ll read this one day. Twice.

To my friends who’ve kept me company over this last year – Shipra Kanjlia, Linda Kung and Stacy Chi – you’ve made some good times better and some bad times not so bad. And thank you for the birthday celebration; it was fun and only slightly embarrassing.

To Tim Fong, thank you for keeping me company, albeit not in person – hopefully that will change soon. Our conversations have kept me grounded when I needed it most.

To Lindsay Kenney, you’ve been there through the worst of it – the long nights, the early mornings and all the stress in between. I couldn’t thank you enough if I tried. Just know that you made this possible.
# TABLE OF CONTENTS

Acknowledgements ........................................................................................................................................ i

Table of Contents........................................................................................................................................ ii

Abstract ......................................................................................................................................................... iv

Introduction ..................................................................................................................................................... 1

Results ............................................................................................................................................................ 12

A. Synthesis of Starting Materials ................................................................................................................. 12
B. Cyclic Voltammetry ..................................................................................................................................... 15
C. Electrolyses ................................................................................................................................................ 19
  (i). Synthetic Studies ..................................................................................................................................... 19
     a. 1,1-Diphenylacetone (18) with Cyclohexanol at 100mA ................................................................. 19
     b. 1,1-Diphenylacetone (18) with Cyclohexanol at 25mA .................................................................... 23
     c. 1,1-Diphenylacetone (18) with Cyclohexanol and p-TsOH .............................................................. 30
     d. 1,1-Diphenylacetone (18) with Phenethyl alcohol ........................................................................... 31
     e. 1,1-Diphenylacetone (18) with Phenethyl alcohol and p-TsOH ....................................................... 40
     f. 1,1-Diphenylacetone (18) with Triethylcarbinol ................................................................................ 41
     g. 1,1-Diphenylacetone (18) with Methanol (10 mol eq.) ..................................................................... 48
     h. 1,1-Diphenylacetone (18) with Benzyl alcohol ................................................................................ 51
     i. 1,1-Diphenylacetone (18) with Ethyl vinyl ether ............................................................................... 54
     j. 1-Methyl-1,1-diphenylacetone (19a) with Phenethyl alcohol ............................................................ 57
     k. 6,6-Diphenyl-5-decanone (19b) with Phenethyl alcohol .................................................................... 64
     l. Benzopinacolone (19c) with Phenethyl alcohol .................................................................................. 73
     m. Benzopinacolone (19c) with Cyclohexanol ....................................................................................... 76
     n. Benzopinacolone (19c) with Cyclohexanol (Divided Cell) ............................................................... 79
     o. 1,1-Dimethylacetone (37) with Phenethyl alcohol ............................................................................. 80
  (ii). Mechanistic Studies .............................................................................................................................. 82
     a. 1,1-Diphenylacetone (18) with Oxygen-labeled Water ..................................................................... 82
     b. 1-Cyclohexoxy-1,1-diphenylacetone (21a) without Nucleophile ..................................................... 87
     c. 1-D-1,1-diphenyl-3-D_3-acetone (20) with Phenethyl alcohol ........................................................... 91
  (iii). Reductive Preparation of Ketones ....................................................................................................... 96
a. Reduction of 1-Cyclohexoxy-1,1-diphenylacetone (21a) without Nucleophile (Divided Cell) ........................................................................96

b. Reduction of Benzopinacolone (19c) without Nucleophile (Divided Cell) ..................................................................................97

D. Gaussian Modeling .................................................................................................................. 99
   (i). Electrostatic Potential Maps (Neutral Compounds): .............................. 100
   (ii). Electrostatic Potential Maps (Cation Radical Compounds): ............... 102
   (iii). HOMOs (Neutral Compounds): .............................................................. 104
   (iv). LUMOs (Neutral Compounds): ............................................................... 106

METHODS .................................................................................................................................. 108
   A. Instrumentation ........................................................................................ 108
   B. Electrolyses .............................................................................................. 109
   C. Syntheses ..................................................................................................... 112

DISCUSSION ............................................................................................................................... 128
   Overview ............................................................................................................. 128
   Enol Mechanism .............................................................................................. 130
   Effect of Added Acid ....................................................................................... 131
   Oxidation of the α-alkoxyketones .................................................................. 131
   A Novel Conjugation ....................................................................................... 133
   Preferred Pathway ......................................................................................... 136
   Oxidation of α-Substituted Ketones ............................................................... 137
   Conclusions ....................................................................................................... 139
   Scope .................................................................................................................. 140
   Other Nucleophiles ......................................................................................... 142
   Cathodic Generation of Ethers ...................................................................... 143
   Difficulties ........................................................................................................ 146
   Future Work ...................................................................................................... 148

REFERENCES ......................................................................................................................... 151
ABSTRACT

The anodic oxidation of 1,1-diphenylethylene has been previously shown to proceed via the intermediate 2,2-diphenylacetaldehyde. Subsequent anodic oxidation of this compound in a 99:1 acetonitrile:water solvent resulted in the isolation of benzophenone. Performing the electrolysis in the presence of alcoholic nucleophiles instead generated α-alkoxyaldehydes which were then oxidized further to form benzhydryl alkyl ethers. In this thesis, 1,1-diphenylacetone and several derivatives thereof were electrolytically oxidized in the presence of various nucleophiles in order to determine the course and mechanism of this reaction and the effect substitutions have on it.

It is shown that in the majority of cases, the reaction proceeds to the benzhydryl alkyl ether corresponding to the nucleophile used. The primary mechanism by which this reaction occurs is shown via electrolyses and computational modeling to proceed via a cation radical delocalized across the carbonyl oxygen and one phenyl ring of the benzhydryl moiety in a novel type of conjugation specific to α-benzhydryl ketones. This mechanism stands in contrast to that of anodic oxidation of 2,2-diphenylacetaldehyde, which was shown previously to be oxidized primarily via its enol.
INTRODUCTION

With the rising cost of chemicals in the current economy, the application of electrochemistry in the laboratory is a prudent one. The cost per mole of electrons is several orders of magnitude lower than even some of the most inexpensive chemicals available. In the field of redox chemistry specifically, it is true that electrochemistry is also much more environmentally friendly, foregoing the use of toxic transition metals such as osmium, chromium, and manganese in favor of a power source easily available in any modern laboratory. Electrochemistry thus partly eliminates the need for waste disposal, which is both hazardous and costly, and it is cost-effective.¹

Typical anodic oxidations involve the removal of either a π-bonding or non-bonding electron to generate the radical cation of the substrate. This reactive intermediate then undergoes stabilization by the reorganization of electrons to generate different products, oftentimes with different σ-bond backbones compared to the starting material. Several such single-electron processes can occur in a given electrochemical oxidation. On the other hand, an electrochemical reduction consists of the insertion of an electron into a substrate, followed by chemical reaction to generate products.²

Previous work investigating the anodic oxidation of trans-stilbene (1) in aqueous acetonitrile has shed light on the products generated in this reaction.³ A proposed mechanism is provided below.⁴
In the above mechanism, 1 loses an electron to generate a cation radical (2) which is captured by a molecule of water to form an alcohol. The remaining radical is then oxidized to a second cation which is captured by a second molecule of water to form a diol (3). A third oxidative step results in the loss of a nonbonding electron on one of the oxygen atoms, followed by the homolytic bond cleavage of a carbon-carbon bond to release one molecule of benzaldehyde (4). This produces another radical which is oxidized a final time to form a second molecule of 4.

In a related study performed by Matt Sagotsky in Professor Fry’s laboratory, the oxidation of 1,1-diphenylethylene (5) was shown to produce benzophenone (8). The proposed mechanism for this reaction follows.
Figure 2. Proposed mechanism for the anodic oxidation of 5 to 8.

In the above mechanism, a cation radical (6) is generated after the first oxidation which is captured by a molecule of water in a reaction similar to that seen in Figure 1. The remaining radical is then oxidized to form the second cation (7), which is rapidly captured by a second molecule of water. This step is followed by homolytic cleavage of a carbon-carbon bond to give 8.

Of note is that in the oxidation of 5, small amounts of 2,2-diphenylacetaldehyde (9) were formed by a competing mechanistic pathway. It was hypothesized to be an intermediate in the reaction, and it could arise through the mechanism shown in Figure 3, of which the first steps are identical to those shown in Figure 2.
In this mechanism, the cation 7 is formed from attack of water on 6 much like in the mechanism in Figure 2, but this intermediate loses a proton to form the enol 9b in a pathway that competes with capture of this cation by water (Figure 2). This enol can then tautomerize to give 9a. It is now also known in the literature that 1 can be anodically oxidized to afford 9 as well, in a mechanism which includes a migration of a phenyl group to generate the benzhydryl moiety in this product.7

The anodic oxidation of 9 was subsequently attempted by Rachel Merzel in Professor Fry’s laboratory to further investigate the conversion of 5 to 8.8 It was observed that varying amounts of current were required to take this reaction to completion from one electrolysis to the next. This suggested that a process separate from the electrochemical reaction was taking place. It was ultimately shown by

Figure 3. Proposed mechanism for the anodic oxidation of 5 to 9.
Merzel via reaction with doubly labeled oxygen that 9 does indeed react chemically to produce 8. This reaction has been known for many years, but the mechanism was never studied in detail. A proposed pathway is indicated below (Figure 4). In this mechanism, formic acid is presumably the second product.

\[
\begin{align*}
\text{9a} & \quad \text{9b} \\
\end{align*}
\]

**Figure 4.** Proposed mechanism for the reaction of 9 with oxygen.

This mechanism proceeds via reaction of the enol tautomer 9b. However, this reaction is slow and passing current showed an increase in reaction rate. It was hypothesized that the electrochemical oxidation of 9 to 8 proceeds via a mechanism in which 9b is oxidized, as seen in the following figure.
Figure 5. Proposed mechanism for anodic oxidation of 9 in the presence of water.

In the above mechanism, the enol tautomer 9b is oxidized to generate the cation radical (10). 10b is captured by a molecule of water, and the remaining radical is oxidized a second time to form 2-hydroxy-2,2-diphenylacetaldehyde (11). This compound is oxidized again to generate a cation radical on the aldehyde oxygen, which allows the homolytic cleavage of a carbon-carbon bond to release an acylium ion and the benzhydrol radical 12. This radical is oxidized a final time to generate 8.

To test the validity of this mechanism, various alcoholic nucleophiles were employed in an attempt to trap 10b and form a stable α-alkoxyaldehyde instead of 8. 
In an experiment using cyclohexanol as the nucleophile, the reaction was shown by Merzel to proceed first to an unstable hemiacetal (13) prior to decomposing to form the anticipated 1,1-diphenyl-1-cyclohexoxyaldehyde (14) over time. Upon passing more current, 14 reacted to give a final product shown to be benzhydryl cyclohexyl ether (16a), as seen in the following figure.\(^8\)

**Figure 6.** Reaction sequence for the electrochemical oxidation of 9 with cyclohexanol.
Compound 16a would arise via a mechanism seen below, paralleling that in Figure 5.

![Chemical structures](image)

**Figure 7.** Proposed mechanism for anodic oxidation of 9 in the presence of cyclohexanol.

In this mechanism, 9 is oxidized to give the cation radical 10. The resonance form 10a is captured by cyclohexanol to give a radical hemiacetal which is rapidly oxidized to a cation, followed by attack of cyclohexanol a second time to afford the α-alkoxyhemiacetal 13. If the electrolysis was left to sit with no current passing at this point, the slow conversion of 13 to 14 was witnessed, and it was thus shown that...
this conversion is a chemical step. 14 is then oxidized to a second cation radical, which goes on to homolytically cleave the carbon-carbonyl bond to release an acylium ion and afford the radical species 15. 15 then acquires a hydrogen atom from solvent to generate compound 16a.

The reaction shown in Figure 6 was performed with primary, secondary and tertiary alcohols and it followed the same pattern in all cases. It is important to note that there is no literature precedent for either the anodic conversion of aldehydes to α-alkoxyaldehydes or for the anodic decarbonylation of α-benzhydryl aldehydes.\textsuperscript{10} Literature on the anodic cleavage of aldehydes and ketones does exist,\textsuperscript{10,11} but the mechanism thereof has not been studied in detail.

Miller and colleagues performed the anodic oxidation of several benzylic aldehydes and ketones in acetonitrile previously, 9 included. In the anodic oxidation of 9 specifically, the products isolated were benzophenone (8) and benzhydryl acetamide (17) in a 5.4:1 ratio.\textsuperscript{11} 17 is formed presumably via reaction of the generated benzhydryl cation with solvent. Miller has also shown that when this same electrolysis is performed in the presence of excess methanol, 9 is oxidized at +1.71V vs. Ag/Ag\textsuperscript{+} to give benzhydryl methyl ether (16d), as seen in Figure 8.\textsuperscript{11} However, Miller and colleagues make no mention of an α-alkoxyaldehyde intermediate and also state that the yield of the ether obtained in this reaction should be invariably low because it is oxidized at the potentials used.\textsuperscript{12}
Upon close inspection, Miller’s work does not provide a reasonable mechanism for this transformation and the arguments therein have several gaps in the reasoning. Miller and colleagues speculate that the electron removed must come from one of the aromatic rings due to the oxidation potential observed in the reaction of 9, which is lower than what one would expect for the oxidation of a carbonyl.\textsuperscript{11} However, numerous sources\textsuperscript{13,14} disagree, placing the oxidation potential of benzene, the prototypical aromatic system, at values such as +2.08V and +2.382V vs. Ag/Ag\textsuperscript{+}. Substitutions of electron-donating groups on the aromatic ring bring this value down (Toluene has an oxidation potential of +1.98V\textsuperscript{13} vs. Ag/Ag\textsuperscript{+}) due to stabilization of the resulting cation radical, but a more complex rationale than that provided by the authors would be necessary to understand the remarkably low oxidation potential they have recorded.

Instead of the mechanism offered by Miller, the generation of an α-alkoxyaldehyde intermediate implies that the oxidation of 9 proceeds via the tautomeric enol 9b, which loses a π-electron to generate a radical cation. The fact that 9 displays unusually high enol content as a result of π-conjugation with the two
substituent phenyl rings would presumably accelerate this reaction. Merzel’s work has shown that acid catalysis results in a greater accumulation of 14 in the oxidation of 9 with cyclohexanol to support this claim. Furthermore, the oxidation potentials of enols, and olefins in a general sense, are closer to that reported by Miller and colleagues.

One approach available to clarify which of these several possibilities is correct, and to elucidate the mechanism in general, is to synthesize compounds with various substitutions on them and to see what effect these substitutions have on the reaction. Substitution of the aldehyde hydrogen of 9 for a methyl group to create 1,1-diphenylacetone (18) might result in a decreased reaction rate due the possibility of a nonproductive enol tautomer (18c) being formed. However, the oxidation might still occur by way of oxidation of the keto form (18a) due to the ease with which an electron in one of the two lone pairs of the oxygen can be removed.

![Tautomeric forms of 18](image)

**Figure 9.** Tautomeric forms of 18. Oxidation of 18b or 18c would presumably lead to the formation of α-alkoxyketones.

Therefore, in this thesis, the mechanism of anodic oxidation of 1,1-diphenylacetone (18) and several derivatives thereof in the presence of various alcohols and other nucleophiles was investigated.
RESULTS

As mentioned, the oxidation of 18 was investigated in this thesis. Several ketones with substitutions at the 1 position (19a-c) were also investigated to determine if compounds that could not enolize toward the benzhydryl position could still be cleaved.

A. Synthesis of Starting Materials

The known\textsuperscript{16,17} compounds 1-methyl-1,1-diphenylacetone (19a) and 6,6-diphenyl-5-decanone (19b) were synthesized via a pinacol reduction-\textit{cum}-rearrangement of the corresponding phenone in the presence of aluminum chloride and zinc powder.\textsuperscript{16} Benzopinacolone (18c) was obtained commercially from Sigma-Aldrich.

\begin{align*}
18: R &= H, R' = Me \\
19a: R &= R' = Me \\
19b: R &= R' = nBu \\
19c: R &= R' = Ph
\end{align*}

1-methyl-1,1-diphenylacetone (19a): 
\begin{itemize}
  \item $m/z$: [M]$^+$ = 224, 181, 165.
  \item $^1$H NMR (CD$_3$CN, 400MHz) $\delta$(ppm): 7.7-7.0 (m, 10H), 2.15 (s, 3H), 1.8 (s, 3H).
\end{itemize}
6,6-diphenyl-5-decanone (19b): \( m/z \): 307, 290, 279, 265, 251, 223, 193, 181, 167. 
ESI/APCI \( m/z \): \([MH]^+ = 309.2222\). \(^1\)H NMR (CDCl\(_3\), 400MHz) \( \delta \) (ppm): 7.4-7.0 (m, 10H), 2.375 (m, 2H), 1.4-0.8 (m, 16H).

1-D-1,1-diphenyl-3-D\(_3\)-acetone (20) was synthesized by stirring 18 with deuterated water and deuterated sulfuric acid.

1-D-1,1-diphenyl-3-D\(_3\)-acetone (20): \( m/z \): 214, 168. \(^1\)H NMR (CDCl\(_3\), 400MHz) \( \delta \) (ppm): 7.4-7.0 (m, 10H).

Figure 12. \(^1\)H NMR spectrum of 20.
The above spectrum shows the complete absence of benzhydryl and methyl protons. The peak at 1.97 ppm corresponds to trace acetonitrile.

The mass spectrum in Figure 13 shows a parent peak $m/z$: [M]$^+$ = 214, indicative of incorporation of four deuterium atoms. There is also a peak for $m/z$: [M]$^+$ = 213, which implies that the deuteration on the methyl group did not proceed to 100% completion and a small amount (Less than 1% based on the $^1$H NMR spectrum in Figure 12) of the compound only contains three deuterium atoms. The peak at $m/z$: 168 corresponds to diphenylmethyl cation with the benzhydryl proton exchanged for a deuterium atom.

Figure 13. Mass fragmentation pattern of 20.
B. Cyclic Voltammetry

In this section are presented the cyclic voltammograms and calculated oxidation potentials\textsuperscript{18} for the various ketones investigated in this thesis as well as 2,2-diphenylacetalddehyde (9). In all cases, a background scan was performed and subtracted from the cyclic voltammogram of the compound being tested, and the oxidation potential for each compound was the potential at the peak of the voltammetric wave, which initially scanned from right to left.

Anthony Davis in Professor Fry’s lab previously acquired the CV of 2,2-diphenylacetalddehyde (9), which shows an oxidation potential of +1.92V.\textsuperscript{6}

Figure 14. Cyclic voltammogram of 9.
1,1-diphenylacetone (18) produces the following cyclic voltammogram, which shows an oxidation potential of +2.09V.

![Cyclic voltammogram of 18](image1)

**Figure 15.** Cyclic voltammogram of 18. This oxidation is expected to be nonreversible and so the small peak in reverse scan is most likely an artifact arising from background subtraction.

1-methyl-1,1-diphenylacetone (19a) produces the following cyclic voltammogram, which shows an oxidation potential of +2.07V.

![Cyclic voltammogram of 19a](image2)

**Figure 16.** Cyclic voltammogram of 19a. As expected, this compound does not produce a corresponding reduction peak in the reverse scan.
6,6-diphenyl-5-decanone (19b) produces the following cyclic voltammogram, which shows an oxidation potential of +2.21V.

![Cyclic voltammogram of 19b](image)

**Figure 17.** Cyclic voltammogram of 19b. As expected, this compound does not produce a corresponding reduction peak in the reverse scan.

Compounds 21 were seen to arise in several of the electrolyses performed. Only the oxidation potentials of 21a-b was determined with cyclic voltammetry and is reported here.

1-phenethoxy-1,1-diphenylacetone (21b) produces the following cyclic voltammogram, which shows an oxidation potential of +2.14V.

![Cyclic voltammogram of 21b](image)

**Figure 18.** Cyclic voltammogram of 21b. As expected, this compound does not produce a corresponding reduction peak in the reverse scan.

21a, R = Cy
21b, R = PhEt
21c, R = Me
21d, R = Bz
1-cyclohexoxy-1,1-diphenylacetone (21a) produces the following cyclic voltammogram, which shows an oxidation potential of +2.18V.

![Cyclic Voltammogram](image)

**Figure 19.** Cyclic voltammogram of 21a. As expected, this compound does not produce a corresponding reduction peak in the reverse scan.¹⁸

The results from these cyclic voltammograms are summarized in the following table, alongside their calculated oxidation potentials.

<table>
<thead>
<tr>
<th>Compound Name</th>
<th>Oxidation Potential (Exp.)</th>
<th>Oxidation Potential (Comp.)</th>
</tr>
</thead>
<tbody>
<tr>
<td>2,2-diphenylacetaldehyde (9)</td>
<td>1.92V</td>
<td>N/A</td>
</tr>
<tr>
<td>1,1-diphenylacetone (18)</td>
<td>2.09V</td>
<td>2.19V</td>
</tr>
<tr>
<td>1-methyl-1,1-diphenylacetone (19a)</td>
<td>2.07V</td>
<td>2.10V</td>
</tr>
<tr>
<td>6,6-diphenyl-5-decanone (19b)</td>
<td>2.21V</td>
<td>1.95V</td>
</tr>
<tr>
<td>Benzopinacolone (19c)</td>
<td>N/A</td>
<td>1.94V</td>
</tr>
<tr>
<td>1-phenethoxy-1,1-diphenylacetone (21b)</td>
<td>2.14V</td>
<td>1.92V</td>
</tr>
<tr>
<td>1-cyclohexoxy-1,1-diphenylacetone (21a)</td>
<td>2.18V</td>
<td>N/A</td>
</tr>
</tbody>
</table>

**Figure 20.** Summary of the oxidation potentials of the several compounds tested as determined by CV.

Of note is the relatively high measured oxidation potential of 19b, which may be due to adsorption of the compound at the anode – a phenomenon known in the literature to occur with long chain alkanes.¹⁹
C. Electrolyses

(i). Synthetic Studies

a. Electrochemical Oxidation of 1,1-Diphenylacetone (18) in the Presence of Cyclohexanol at 100mA:

The oxidation of 18 with cyclohexanol was performed in order to compare the results to those from the oxidation of 9 with cyclohexanol, which Merzel performed previously and from which she managed to isolate 1-cyclohexoxy-2,2-diphenylacetaldehyde, the compound analogous to 21a. The reaction was seen to follow the progression shown.

To the undivided cell setup described in the experimental was added 15 mL dry acetonitrile containing 0.1 M supporting electrolyte, 0.236 g (1.12 x 10⁻³ mol) 18 and 0.113 g (1.131 x 10⁻³ mol, 0.118 mL) of cyclohexanol. After 408 coulombs (3.77 F/mol) of current had passed, analysis by GC-MS showed that all of the starting material had been consumed and several products were formed.
The workup yielded 0.243 g of a dark yellow oil, which was chromatographed over silica gel (93:7 hexanes:ethyl acetate) to yield 0.058 g (2.19 x 10^-4 mol) of nearly pure benzhydryl cyclohexyl ether (16a) as an off-white oil, identified by GC-MS, NMR and comparison to data on the known compound the chemical literature.\textsuperscript{20} GC yield = 62\%, isolated yield = 19.5\%. The following TIC represents the end of the reaction.

![Figure 21](image.png)

**Figure 21.** Total ion chromatogram (TIC) of electrolysis of 18 with cyclohexanol after 408 coulombs of current were passed.

Compound E (RT = \textbf{13.05 minutes}) was identified as 16a upon comparison of spectra to those of a sample Merzel prepared previously\textsuperscript{8} and to those in the literature.\textsuperscript{20} Its mass spectrum contained peaks at $m/z$: $[M]^+ = 266, 183, 167$. Its $^1$H NMR (CD$_3$CN, 400MHz) spectrum contained peaks at $\delta$(ppm) 7.45-7.2 (m, 10H), 5.630 (s, 1H), 3.364 (m, 1H), 1.936 (m, 2H), 1.735 (m, 2H), 1.6-1.2 (m, 6H). Its $^{13}$C NMR (CD$_3$CN, 400MHz) spectrum contained peaks at $\delta$(ppm) 144.00, 128.56, 127.42, 127.05, 79.85, 75.03, 32.41, 25.88, 24.03. These data confirm the correct structure.
Ethers 16 were recurring products in the following electrolyses and were seen with alkyl groups corresponding to the nucleophile used.

Compound A (RT = 3.1 minutes) was identified as cyclohexanol (remaining starting material).

Compound B (RT = 5.5 minutes) was identified as cyclohexyl acetate (22) based on comparison of its retention time and fragmentation pattern to those of a synthetic sample\(^{21}\), prepared from the reaction of cyclohexanol with acetic anhydride in the presence of catalytic p-toluenesulfonic acid.

\[
\begin{array}{c}
\text{OH} \\
\text{cat. p-TsOH} \\
90 ^\circ \text{C, 30 hrs.} \\
\text{O} \\
\text{O} \\
\text{H}
\end{array}
\]

\[22\]

Its mass spectrum contained the peaks \(m/z\): 127, 99, 82, 67, 55.

Compound C (RT = 10.6 minutes) was identified as benzophenone (8) upon comparison of the retention time and mass fragmentation pattern to those of an authentic sample obtained from Sigma-Aldrich. Its mass spectrum contained the peaks \(m/z\): \([M]^+ = 182, 105, 77, 51\). This was a recurring product in most of the reactions performed.

Compound D (RT = 11.1 minutes) was identified to be benzhydryl acetate (23) by comparison of its retention time and fragmentation pattern to those of a
synthetic sample and those in the literature\textsuperscript{22}, prepared by the reaction of benzhydryl chloride (24) with acetic acid.

![Reaction Diagram]

Its mass spectrum contained peaks including $m/z$: [M]$^+$ = 226, 184, 165. An accurate mass (ESI/APCI) spectrum of the sample isolated from electrolysis revealed the correct accurate mass and thus agreed with the proposed molecular formula of the compound, $m/z$: [MNH$_4^+$]$^+$ = 244.1341. This was a recurring product in most of the reactions performed, appearing every time the oxidation of 1,1-diphenylacetone (18) was attempted.

Compound D (RT = \textbf{16.2 minutes}) was identified to be dibenzhydryl ether (25) based on comparison of its fragmentation pattern and $^1$H NMR spectrum to those in the literature.\textsuperscript{23} Its mass spectrum contained peaks at $m/z$: 272, 183, 167, and an accurate mass spectrum (ESI/APCI) showed a peak representing the compound complexed with an ammonium ion, $m/z$: [MNH$_4^+$]$^+$ = 368. An accurate mass (LIFDI) spectrum supported its structure by providing the correct molecular weight, $m/z$: [M]$^+$ = 350. This was a recurring product in most of the reactions performed.
b. Electrochemical Oxidation of 1,1-Diphenylacetone (18) in the Presence of Cyclohexanol at 25mA:

The procedure was identical to the preceding oxidation of 18 with cyclohexanol at 100 mA. The results were not exceptionally different except for the appearance of a small peak in the TIC at RT = 14.1 minutes [GC Data not shown] which was identified as the new compound 1-cyclohexoxy-1,1-diphenylacetone (21a) based on comparison of its retention time and fragmentation pattern to those of a synthetic sample. This new compound was synthesized by the sequential bromination of 1,1-diphenylacetone (18) according to a literature procedure\textsuperscript{24} followed by reaction of the product from this reaction, 1-bromo-1,1-diphenylacetone (26), with cyclohexanol in the presence of silver tetrafluoroborate, a procedure also adapted from the literature.\textsuperscript{25}

\begin{center}
\begin{tikzpicture}
\node (18) at (0,0) {18};
\node (26) at (2,0) {26};
\node (21a) at (4,0) {21a};
\draw[->] (18) -- (26) node[midway,above] {Br$_2$} node[midway,below] {CH$_2$Cl$_2$};
\draw[->] (26) -- (21a) node[midway,above] {HO} node[midway,below] {THF, -78°C};
\end{tikzpicture}
\end{center}

The mass spectrum of this compound contained peaks at \(m/z\): 265, 209, 183, 165. An accurate mass (ESI/APCI) spectrum provided the correct molecular formula by showing a peak for the compound complexed with ammonium and another peak showing the compound complexed with sodium, \(m/z\): \([\text{MNH}_4]^+ = 326.2121\), \([\text{MNa}]^+ = 331.1665\). Its \(^1\text{H}(\text{CDCl}_3, 400\text{MHz})\) NMR spectrum contained peaks at \(\delta(\text{ppm})\):

- 7.29-7.49 (m, 10H)
- 3.4 (m, 1H)
- 2.19 (m, 3H)
- 1.61 (m, 2H)
- 1.39 (m, 2H)
- 1.21 (m,
3H) and 1.06 (m, 3H). Its $^{13}$C (CDCl$_3$, 400MHz) NMR spectrum contained peaks at δ(ppm): 209.241, 141.390, 129.305, 128.793, 128.243, 128.109, 73.870, 33.575, 26.360, 25.562, 24.102.

The next several figures provide spectral data for this compound. Its mass spectrum is seen in Figure 23.

![Mass spectrum of 21a](image)

**Figure 23.** Mass spectrum of 21a.

The above figure shows the mass spectrum obtained for this compound. Note that no molecular ion peak is visible in this spectrum. However, the peaks that are visible can be arrived at in a straightforward manner, as shown by the pathways in Figure 24.
It is interesting to note in the above fragmentation pathway that a 9-methylfluorene cation is generated. This is not unprecedented and occurs with many compounds analyzed in this thesis. This rearrangement has also been shown to occur with several other diphenyl species in the literature.²⁶

The following accurate mass spectrum was obtained to verify the proposed structure by generating a molecular ion peak.
Figure 25. ESI/APCI accurate mass spectrum of 21a showing the compound complexed separately with the ions NH4+ and with Na+. Both signals seen in the above spectrum correspond to a molecular formula of C_{21}H_{24}O_{2}, which is the predicted molecular formula of the compound.

NMR data was acquired to further characterize the compound as follows.
Visible in the above spectrum is the ether proton shifted further downfield from the remaining ten cyclohexyl protons, between 1.6 – 0.8 ppm. Also noted is the appearance of the methyl protons of the acetyl group at 2.21 ppm.

This spectrum, along with the following HSQC, can assist in making the carbon assignments for this compound.
The above gHSQC spectrum shows both the axial and equatorial protons attached to the four carbons J and K, along with the two protons found on carbon L, which is shifted further downfield from the other alkyl carbons. The cross-peak at (3.2 ppm, 58 ppm) is due to impurity in the sample which could not be removed.
Figure 28. $^{13}$C NMR spectrum of 21a, along with an expanded view of the aromatic region.

Visible are the carbon assignments of the compound, deduced based on the preceding gHSCQ spectrum. Two peaks in the aromatic region are shown to display accidental equivalence, and are tentatively labeled as carbons D and A.
c. Electrochemical Oxidation of 1,1-Diphenylacetone (18) in the Presence of Cyclohexanol and Catalytic p-Toluenesulfonic Acid (p-TsOH):

This experiment was performed to study whether acid catalysis has any effect on this reaction. The procedure was identical to that of the preceding reaction, except for the addition of 5 mol % p-TsOH. The reaction was monitored via GC-MS and it was qualitatively observed that less 21a was produced as an intermediate and that the final product ether benzhydryl cyclohexyl ether (16a) was formed more slowly.
d. Electrochemical Oxidation of 1,1-Diphenylacetone (18) in the Presence of Phenethyl Alcohol:

The oxidation of 18 was then attempted with phenethyl alcohol, a primary alcohol, to see if it would follow a similar progression. This was seen to be the case.

To the undivided cell setup described in the experimental was added 30 mL dry acetonitrile containing 0.1 M supporting electrolyte, 0.472 g (2.245 x 10⁻³ mol) of 18 and 0.295 g (2.414 x 10⁻³ mol, 0.29 mL) of phenethyl alcohol. After 402.6 coulombs (1.86 F/mol) of current had passed, analysis by GC-MS showed the appearance of one major product identified to be benzhydryl phenethyl ether (16b), along with several byproducts including benzhydryl acetate (23) and dibenzhydryl ether (25). At this point, the reaction was stopped. The workup yielded 0.642 g of crude yellow oil, which was chromatographed over silica gel (95:5 hexanes:ethyl acetate) to yield 0.123 g (4.26 x 10⁻⁴ mol) of a colorless oil which, from comparison of its ¹H NMR spectrum to that in the literature was identified to be mainly 16b.²⁷
GC yield = 50%, isolated yield = 19.0%. The following TIC indicates the endpoint of this reaction.

**Figure 29.** Total ion chromatogram (TIC) of electrolysis of 18 with phenethyl alcohol after 402.6 coulombs of current have passed.

Compound F (**RT = 14.3 minutes**) was identified as 16b based on comparison of its fragmentation pattern and NMR spectra to those in the literature. Its mass spectrum contained peaks at $m/z$: [M]$^+$ = 288, 183, 167. Its $^1$H NMR showed signals at $\delta$(ppm) of 7.1-7.4 (m, 15H), 5.43 (s, 1H), 3.67 (t, 2H), and 2.94 (t, 2H). The two triplets correspond to the methylene protons of the phenethyl moiety, the singlet corresponds to the benzhydryl proton, and the aromatic region integrates to the number of aromatic protons expected. Its $^{13}$C NMR contained peaks at $\delta$(ppm) 143.23, 139.92, 129.28, 128.63, 128.51, 127.58, 126.90, 126.35, 83.38, 69.82, 36.31. These peaks agree closely with those of the known compound.

Compound A (**RT = 6.4 minutes**) was identified as phenethyl alcohol (starting material). This compound came off as a very broad peak, as evidenced by Compound B.

Compound B (**RT = 7.9 minutes**) was found to represent a mixture of phenethyl alcohol, supporting electrolyte, and an unidentified compound with a peak
of 121 in its mass fragmentation pattern. Phenethyl acetate (27) was synthesized by the reaction of phenethyl alcohol and acetic anhydride in the presence of p-toluenesulfonic acid, and it was shown to match this peak in its retention time.

![Synthesis of Phenethyl Acetate](image)

The similar retention times and fragmentation patterns of the two samples make it reasonable to conclude that this is compound B. Its mass spectrum contained peaks at $m/z$: 121, 104.

Compound C (RT = 11.1 minutes) was identified as 23 using methods described previously (See Results, Section C.(i).a).

Compound D (RT = 11.2 minutes) was identified as 18 (starting material).

Compound E (RT = 13.9 minutes) was identified to be benzhydryl benzyl ether (16e) based on comparison of its GC-MS data to that of a synthetic sample, prepared via the reaction of benzhydryl chloride with benzyl alcohol in the presence of silver tetrafluoroborate.

![Synthesis of Benzhydryl Benzyl Ether](image)
Its mass spectrum contained the peaks \( m/z \): \([M]^+ = 260, 183, 165, 152 \).

Compound G (RT = 15.2 minutes) was identified as the new compound 1-phenethoxy-1,1-diphenylacetone (21b) based on comparison of its GC-MS data to that of a synthetic sample, prepared by the reaction of 1-bromo-1,1-diphenylacetone (26) with phenethyl alcohol in the presence of silver tetrafluoroborate.\(^{25}\)

![Reaction Scheme]

Its mass spectrum contained peaks at \( m/z \): 287, 183, 165, 105, 91. Since no molecular ion was seen, an accurate mass (ESI/APCI) spectrum was performed and showed peaks at \( m/z \): \([\text{MNH}_4]^+ = 348.1946, [\text{MNa}]^+ = 353.1517 \). Both of these peaks corresponded to the correct molecular formula. Its \(^1\text{H}\) (CD\(_3\)CN, 400MHz) NMR spectrum showed peaks at \( \delta (\text{ppm}) \) 7.2-7.5 (15H), 3.30 (t, 2H, J=6Hz), 2.89 (t, 2H, J=6Hz), 2.221 (s, 3H).

The next several figures provide the spectral data of 21b.

**Figure 30.** Mass fragmentation pattern of as 21b.
The above mass fragmentation pattern does not show a parent peak. However, all of the peaks present can be rationalized from the starting compound as follows.

![Diagram of chemical structures and mass values](image)

**Figure 31.** Series of fragments arising from 21b, and their corresponding m/z values.

It is interesting to note in the above fragmentation pathway that a 9-methylfluorene cation is generated, much as in the fragmentation pattern of 1-cyclohexoxy-1,1-diphenylacetone (21a). A parent peak is not seen in the above mass spectrum, so an accurate mass was obtained.
In the above ESI/APCI accurate mass spectrum of 21b, two peaks can be observed. One of the peaks corresponds to the complex of the molecular ion with a sodium atom, and the other corresponds to the complex of the molecular ion with ammonium. Both of these peaks are in agreement with the predicted molecular formula of the compound, C_{23}H_{22}O_{2}.

NMR data was acquired to further characterize the compound as follows.
Visible are the two methylene proton signals of the phenethyl moiety which have identical coupling constants, and the methyl group of the acetyl moiety. The peak at 2.09ppm is trace water. This spectrum, along with the following gHSQC, assisted in the carbon assignments for this molecule.

**Figure 33.** $^1$H NMR spectrum of 21b.

**Figure 34.** Overlay of two gHSQC spectra of 21b.
Several gHSQC spectra of this product were acquired, yet none had a good enough signal-to-noise ratio to clearly show all of the peaks. However, an overlay of two spectra produced the figure shown above, which contains all the peaks expected from this compound. In the above gHSQC overlay, the cross peaks for both groups of methylene protons are visible. A weak signal is observed for the methyl group. Broad signals are visible for the aromatic crosspeaks and the downfield methylene group due to non-ideal phasing of the spectra.
Figure 35. $^{13}$C NMR spectrum of 21b along with an expanded view of the aromatic region.

The $^{13}$C NMR spectrum shown above contains all of the peaks expected for this compound. The phenyl rings of the benzhydryl moiety are equivalent and thus, only eight aromatic signals are seen.
Compound H ($RT = 16.2 \text{ minutes}$) was identified as 25 using methods described previously. (See Results, Section C.(i).a)

Other peaks in the TIC could not be identified based on their fragmentation pattern and couldn’t be isolated in a large enough quantity to determine NMR spectra. These were not pursued further.

e. Electrochemical Oxidation of 1,1-Diphenylacetone (18) in the Presence of Phenethyl Alcohol and Catalytic p-Toluenesulfonic Acid (p-TsOH):

This experiment was performed to study whether acid catalysis has any effect on this reaction. The procedure was identical to that of the preceding reaction, except for the addition of 5 mol % p-TsOH. The reaction was monitored via GC-MS and it was qualitatively observed that the ether 16b was formed as in the previous reaction. However, far less 21b was produced throughout the course of the reaction.
f. Electrochemical Oxidation of 1,1-Diphenylacetone (18) in the Presence of Triethylcarbinol:

The oxidation of 18 was then attempted with triethylcarbinol, a tertiary alcohol, to see if it would follow a similar progression. In spite of the sterically hindered hydroxyl group of triethylcarbinol, this reaction still proceeded to give a product ether.

\[
\begin{align*}
\text{18} & \xrightarrow{[O]} \text{16c} + \text{23} + \text{25} \\
\end{align*}
\]

Into a three-necked round-bottom flask with two of the three necks sealed was distilled off phosphorus pentoxide 30 mL of acetonitrile solvent. The flask contained two electrodes, a stir bar, 0.473 g (2.25 x 10^{-3} mol) of 18 and 0.983 g (2.99 x 10^{-3} mol) of supporting electrolyte which was freshly dried using an Abderhalden drying pistol. The solid was dissolved by stirring and 0.32 mL (0.26 g, 2.26 x 10^{-3} mol) of triethylcarbinol was injected into the solution via syringe. At this point, current was applied and after 556.2 coulombs (2.56 F/mol) of current had passed, analysis by GC-MS showed the appearance of benzhydryl acetate (23), benzhydryl ether (25) and
what was identified to be benzhydryl triethylcarbinyl ether (16c). The reaction was stopped and worked up as described previously. Purification over silica gel (99:1 – 95:5 hexanes:diethyl ether) resulted in the isolation of 0.064 g (2.28 x 10^{-4} mol) of a colorless oil determined to be the new compound 16c. GC yield = 23%, isolated yield = 10.1%. The TIC for this reaction at its endpoint is seen below.

![Figure 36](image)

**Figure 36.** Total ion chromatogram (TIC) of electrolysis of 18 with triethylcarbinol after 556.2 coulombs of current were passed.

Compound C (RT = 12.5 minutes) was identified to be the new compound 16c based on analysis of its GC-MS and NMR spectra. The $^1$H NMR (CDCl$_3$, 300MHz) spectrum of this compound contained signals at $\delta$(ppm) 7.41 (d, 4H), 7.27 (t, 4H), 7.17 (t, 2H), 5.52 (s, 1H), 1.52 (q, 6H, J = 6Hz), 0.72 (t, 9H, J = 6Hz). The $^{13}$C NMR (CDCl$_3$, 300MHz) spectrum of this compound contained signals at $\delta$(ppm) 145.99, 128.29, 126.77, 126.73, 82.20, 74.81, 27.87, 8.21. Its gHQSC NMR (CDCl$_3$, 400MHz) spectrum contained crosspeaks at ($\delta_H$, $\delta_C$) (ppm) (7.42, 126.48), (7.28, 129.45), (7.17, 126.54), (5.53, 74.66), (1.52, 28.7), (0.72, 7.67).
Taking into account the symmetry of the molecule, the structure in the figure above contains labels for only one of the three equivalent ethyl groups in the triethylcarbinyl moiety. Visible in the above spectrum are the triplet and quartet in the alkyl region integrating the eight and six protons, respectively. These two peaks have the same coupling constant implying that they represent protons coupled to each other. There is one benzhydryl proton as expected, and the aromatic region integrates to a total of ten protons. The individual aromatic peaks can in this case be resolved.
Figure 38. gHSQC of 16c, along with an expanded view of the aromatic region in the same spectrum with altered phasing.

The above gHSQC spectrum shows well resolved, though not ideally phased, cross peaks in the aromatic region, helping to assign carbons in the $^{13}$C NMR spectrum shown in Figure 39 which would otherwise have been ambiguous.
Figure 39. $^{13}$C NMR of 16c and an expanded view of the aromatic region in the same spectrum.

The above spectrum shows all of the carbon assignments for the compound 16c. Four aromatic peaks are seen, two of which partially overlap at 126 ppm. Two peaks are visible for the carbons of the three ethyl groups, which are chemically equivalent. The two ether carbons are seen close to 80 ppm, which the benzhydryl carbon shifted further downfield by the two phenyl rings.
Several syntheses of this compound were attempted in order to acquire a sample with which to compare this data. However, attempts at synthesizing $16c$ in the same way$^{25}$ as other ethers of type $16$, by reaction with the nucleophile triethylcarbinol in the presence of silver tetrafluoroborate, resulted in reaction with trace water to produce $23$ and $25$ instead. This is a direct result of the fact that the nucleophile is very large and its reaction with a tertiary center such as the benzhydryl carbon in benzhydryl chloride (24) is sterically unfavorable.

![Chemical structures](image)

**Figure 40.** Attempted synthesis of $16c$, resulting instead in the formation of $23$ and $25$.

Attempts at performing the oxymercuration-reduction$^{28}$ of 3-ethyl-2-pentene (28) with benzhydrol (29) produced what appeared to be isomers of the desired product, based on similar but not identical retention times and fragmentation patterns.
in the GC-MS (Data not shown). These results were not reproducible and none of the products was isolated or analyzed with NMR.

![Chemical structure](image)

**Figure 41.** Attempted oxymercuration-reduction of 28 does not result in the desired ether being formed.

Thus, although the structure of the product ether could not be verified with an independent synthesis, the data collected on this compound fits with the conclusion that ether 16c is in fact formed. However, water is found to compete with triethylcarbinol to generate alternate products.

Compounds A (RT = 11.1 minutes) and D (RT = 16.1 minutes) were identified as 23 and 25, respectively, as described previously (See Results, Section C.(i).a).

Compound B (RT = 11.2 minutes) is 18, remaining starting material.

The electrolyses were then performed with several other nucleophiles in order to further establish the scope of this reaction.
g. Electrochemical Oxidation of 1,1-Diphenylacetone (18) in the Presence of Methanol (10 mol eq.):

This reaction was seen to follow the progression shown.

![Chemical Structure](image)

To the undivided cell setup described in the experimental was added 30 mL dry acetonitrile containing 0.1 M supporting electrolyte, 0.476 g (2.25 x 10^{-3} mol) of 17 and 0.721 g (2.25 x 10^{-2} mol, 0.91 mL) of methanol. Analysis by GC-MS showed the appearance of benzhydryl methyl ether (16d) as the major product and an unresolved peak with a mass spectrum indicative of 1-methoxy-1,1-diphenylacetone (21c). After 517.8 coulombs (2.38 F/mol) of current had passed, the reaction was stopped because analysis by GC-MS showed the formation of dibenzhydryl ether (25), indicative of reaction with water (See Results, Section C.(ii).a). The reaction was worked up in the usual way to yield 0.261 g of crude residue, which was then chromatographed over silica gel (70:30 hexanes:DCM) to yield 0.077 g (3.89 x 10^{-4} mol) of 16d as an off-white oil, identified by GC-MS, NMR and comparison to the chemical literature.\(^9\) GC yield = 50%, isolated yield = 17.3%.
Figure 42. Total ion chromatogram (TIC) of the oxidation of 18 in the presence of methanol after 517.8 coulombs of current had passed.

Compound A (RT = 10.1 minutes) was identified as 16d upon comparison of mass fragmentation pattern and $^1$H NMR spectrum with those in the literature.\textsuperscript{29} Its mass spectrum contained peaks at $m/z$: [M]$^+$ = 198, 183, 167, 152, 121, 105, and 91. Its $^1$H NMR (CD$_3$CN, 400MHz) contained peaks at $\delta$(ppm) 7.5-7.2 (m, 10H), 5.276 (s, 1H), 3.417 (s, 3H).

Compound C (RT = 11.5 minutes) showed a mass spectrum characteristic of 21c. This compound was then synthesized by the reaction of 1-bromo-1,1-diphenylacetone (26) with methanol in the presence of silver tetrafluoroborate in a procedure adapted from the literature\textsuperscript{25} to determine if it was indeed the compound being produced.
The mass spectrum of both compounds contained the peaks \( m/z \): 197, 183, 167. The \(^1\text{H} \text{ NMR} (\text{CD}_3\text{CN}, 400\text{MHz}) \) contained the peaks \( \delta \text{(ppm)}: 7.5 – 7.3 \) (m, 10H), 3.09 (s, 3H), 2.21 (s, 3H). The retention times of the two samples were in agreement with each other, and this data thus collectively showed that this peak corresponded to 21c.

Compound B (RT = 11.2 minutes) is 18 (starting material).

Compound D (RT = 16.2 minutes) was identified to be dibenzhydryl ether (25) as described previously (See Results, Section C.(i).a).
h. Electrochemical Oxidation of 1,1-Diphenylacetone (18) in the Presence of Benzyl Alcohol:

This reaction was seen to follow the progression shown.

\[
\begin{align*}
18 & \rightarrow 21d + 16e + 31 (\text{minor})
\end{align*}
\]

To the undivided cell setup described in the experimental was added 30 mL dry acetonitrile containing 0.1 M supporting electrolyte, 0.474 g (2.25 x 10^{-3} mol) of 18 and 0.240 g (2.22 x 10^{-3} mol, 0.23 mL) of benzyl alcohol. Analysis by GC-MS showed the appearance of benzhydryl benzyl ether (16e) as the major product. After 412.8 coulombs (1.90 F/mol) of current had passed, analysis by GC-MS showed no change in the relative intensities of the peaks, potentially due to the oxidation of benzyl alcohol as a side reaction, and the reaction was stopped. The solvent was removed \textit{in vacuo} and the organic residue was redissolved in diethyl ether. This was then washed three times with 10 mL deionized water and dried over sodium sulfate.
The solvent was again removed to yield 0.356 g of crude material. No ideal elution solvent was found for column chromatography, so most of the starting ketone was reacted using Girard’s Reagent T[^30] and washed out, and the residue was chromatographed (95:5 hexanes:ethyl acetate) to yield 0.028 g (1.018 x 10^-4 mol) of what was identified to be pure 16e via comparison of NMR and GC-MS spectra to those of a synthetic sample. GC yield = 44%, isolated yield = 4.5%.

**Figure 43.** Total ion chromatogram (TIC) of electrolysis of 18 with benzyl alcohol after 412.8 coulombs of current had passed.

In the above spectrum, it can be seen that there was a large amount of starting material remaining. This was shown not to react further after several coulombs of current were passed.

Compound E (RT = 13.9 minutes) was identified to be 16e as described previously (See Results, Section C.(i).d).

Compound F (RT = 14.9 minutes) was identified to be 1-benzyloxy-1,1-diphenylacetone (21d) based on comparison of retention time and mass fragmentation pattern to those of a synthetic sample, which was prepared in the same way[^25] as 21a-c.
In its mass spectrum were peaks at \( m/z \): 273, 183, 165, 105, 91, 77. Since no molecular ion peak was visible, an accurate mass (ESI/APCI) spectrum was obtained, which showed peaks at \( m/z \): \([\text{MNH}_4]^+ = 334.1795, [\text{MNa}]^+ = 339.1356\). Both of these peaks agreed with the proposed molecular formula.

Compounds B and G (RT = 11.1 and 16.2 minutes) are visible, corresponding to benzhydryl acetate (23) and dibenzhydryl ether (25), products arising due to contamination of the reaction with water (See Results, Section C.(ii).a).

Compound A (RT = 7.5 minutes) was identified to be benzyl acetate (30) based on comparison of its mass fragmentation pattern and retention time to those of a synthetic sample, generated from the reaction of benzyl alcohol with acetic anhydride in the presence of catalytic p-toluenesulfonic acid. Its mass spectrum contained peaks at \( m/z \): \([\text{M}]^+ = 150, 135, 108\).
Compound D (RT = 12.9 minutes) was identified to be triphenylmethane (31) based on accurate mass analysis, comparison of mass fragmentation pattern, retention time and $^1$H NMR spectrum to those of an authentic sample and those found in the literature.\textsuperscript{31} Its mass spectrum contains peaks at $m/z$: [M]$^+$ = 244, 167, 165. To confirm the molecular weight, an accurate mass (ESI/APCI) spectrum was obtained, and it contained peaks at $m/z$: [M – H]$^+$ = 243.1171, [M-C$_6$H$_5$]$^+$ = 165.0700. Its proton spectrum contained peaks at $\delta$(ppm): 7.5-7.0 (m, 15H), 5.63 (s, 1H).

i. Electrochemical Oxidation of 1,1-diphenylacetone (18) in the Presence of Ethyl Vinyl Ether:

This reaction was seen to proceed to the products shown below.

![Chemical Structures](image)

To the undivided cell setup described in the experimental was added 30 mL dry acetonitrile containing 0.1 M supporting electrolyte, 0.471 g (2.243 x 10$^{-3}$ mol) of 18 and 1.631 g (2.262 x 10$^{-3}$ mol, 2.16 mL) of ethyl vinyl ether. After 255 coulombs (1.18 F/mol) of current had passed, analysis by GC-MS showed the appearance of benzhydryl acetate (23), dibenzhydryl ether (25) and what was identified to be benzhydryl ethyl ether (16f) with numerous other minor products beginning to form. The reaction mixture was left to sit for roughly a week and the rest of the 18 was
shown to have been converted to 25 by a mechanism which is not fully understood; the amount of 16f, however, did not change. Purification over silica gel (95:5 hexanes:ethyl acetate) resulted in the isolation of 0.206 g (9.74 x 10^{-4} mol) of an offwhite oil identified to be 16f based on comparison to a synthetic sample and the literature.\textsuperscript{32} GC yield = 19\%, isolated yield = 43.3\%.

![Figure 44](chart.png)

**Figure 44.** Total ion chromatogram (TIC) of oxidation of 18 with ethyl vinyl ether after 255 coulombs of current were passed and the solution was left to sit for several days.

Compound A (RT = 10.4 minutes) was identified to be 16f based on comparison of GC-MS and NMR spectra to those of a synthetic sample, prepared by refluxing benzhydryl chloride with ethanol. The mass spectrum of this compound contained peaks at m/z: [M]^{+} = 212, 183, 167, 152, 135, 105, 77, 51. The parent peak was visible and the rest of the peaks matched those of the known compound. Its \textsuperscript{1}H NMR spectrum contained peaks at δ(ppm): 7.40 (d, 4H), 7.35 (t, 4H), 7.26 (t, 2H), 5.438 (s, 1H), 3.511 (q, 2H, J = 6.84Hz), 1.246 (t, 3H, J = 6.84Hz).
Compound B (RT = 11.1 minutes) was identified as 23 using methods described previously. (See Results, Section C.(i).a)

Compound C (RT = 11.2 minutes) is remaining starting material 18.

Compound D (RT = 16.2 minutes) was identified as 25 using methods described previously. (See Results, Section C.(ii).a)

When it was established that 1,1-diphenylacetone (18) is oxidized to form ethers in the presence of nucleophiles and that this reaction is facile, other ketones with substitutions on the benzhydryl carbon were tested to determine if the reaction would proceed.
j. Electrochemical Oxidation of 1-Methyl-1,1-diphenylacetone (19a) in the Presence of Phenethyl Alcohol:

This reaction was seen to produce a benzhydryl ether in the same way as reactions previously described.

To the undivided cell setup described in the experimental was added 15 mL dry acetonitrile containing 0.1 M supporting electrolyte, 0.208 g (9.272 x 10^-4 mol) of 19a and 0.109 g (8.930 x 10^-4 mol, 0.11 mL) of phenethyl alcohol. Analysis by GC-MS showed the conversion of the ketone to 1-phenethoxy-1,1-diphenylethane (32a). After 418.8 coulombs (4.68 F/mol) of current had passed, several other byproducts began to form and the reaction was stopped and worked up using the procedure described above. From this, 0.126 g of crude was isolated, which was then chromatographed over silica gel (98:2 – 80:20 hexanes:ethyl acetate) to yield 0.006 g
(2.053 \times 10^{-5} \text{ mol}) \text{ of the new compound } 32a, \text{ which was characterized via GC-MS and NMR. GC yield } = 34\%, \text{ isolated yield } = 2.2\%.

**Figure 45.** Total Ion Chromatogram (TIC) for the oxidation of 19a with phenethyl alcohol after 418.8 couloms of current had passed.

Compound E (RT = 14.5 minutes) was identified to be the new compound 32a and was characterized based on its spectroscopic data. Its mass spectrum contained peaks at \( m/z: [M]^+ = 302, 287, 181, 165, 105, 77 \). An accurate (EI) mass spectrum was obtained to confirm the molecular formula, and it showed a peak at \( m/z: [MNa]^+ = 325.1570 \), which agreed with the previous mass spectrum. Its \(^1\text{H} \text{ NMR (CD}_3\text{CN, 300MHz)} \text{ spectrum contained peaks at } \delta(\text{ppm}): 7.6-7.1 \text{ (m, 15H), 3.47 (t, 2H), 2.90 (t, 2H), 1.83 (s, 3H). Its } ^{13}\text{C NMR (CD}_3\text{CN, 400MHz) spectrum contained peaks at } \delta(\text{ppm}): 147.36, 140.19, 129.41, 128.44, 128.20, 126.90, 126.60, 126.29, 80.45, 63.69, 36.80, 24.88. \text{ The spectra containing this spectroscopic data are presented in the following figures.}
**Figure 46.** Mass fragmentation spectrum for 32a. \([M]^+ = 302, [M - CH_3]^+ = 287, [287 - PhCH_2CH_3]^+ = 181.\)

In the above mass spectrum, the molecular ion at \(m/z: 302\) is seen, along with several fragments which can be rationalized as follows.

**Figure 47.** Fragmentation pathways for 32a. The peak arising from the fluorene cation have been seen previously (See Results, Section C.(i).b).
Although the above mass spectrum shows a molecular ion peak, an exact mass spectrum was acquired to confirm the molecular formula.

**Figure 48.** Exact mass spectrum for 32a, showing the molecule complexed with a sodium atom.

The above accurate mass spectrum predicts a molecular formula of $C_{22}H_{22}ONa$ for the ion seen, which corresponds to the correct molecular formula of $C_{22}H_{22}O$ for the compound. The exact mass spectrum also contains a strong peak for 181 [Data not shown] which corresponds to the fragment of that $m/z$ seen in Figure 46.
Figure 49. $^1$H NMR spectrum of 32a, with proton assignments visible.

The $^1$H NMR spectrum above shows all the peaks expected for this molecule. A small peak at 1.96ppm corresponds to solvent acetonitrile. Two small peaks corresponding to hexanes are seen around 1.0ppm. The two small peaks at roughly 3.7ppm and 3.2ppm correspond to impurity which was not identified.

Unfortunately, the work-up performed yielded a very small amount of this compound, and an HSQC with a good signal-to-noise ratio could not be acquired in order to resolve all the peaks expected. The following $^{13}$C NMR spectrum thus contains only tentative assignments.
Figure 50. $^{13}$C NMR spectrum of 32a with an expanded view of the aromatic region.

In the above diagram, there are eight aromatic peaks visible, two of which are quaternary, as evidenced by their further downfield shift and lower intensity. The assignments for the six remaining aromatic peaks are ambiguous given the available data, and so were left unlabeled. However, the correct number of peaks is seen and the rest of the spectral data support the proposed structure for this compound.
Compound A (RT = 8.0 minutes) was found to contain a peak of 121 in its mass fragmentation pattern not present elsewhere in the TIC, which was characteristic of phenethyl acetate (27). A sample of 27 was synthesized as described previously (See Results, Section C.(i).d) and was shown to match this peak in its retention time.

![Figure 51](image)

**Figure 51.** Expanded view of the mass fragmentation pattern of the peak at RT = 8.0 minutes showing the signal with weak intensity at m/z: 121.

Compound B (RT = 9.6 minutes) was found to be 1,1-diphenylethane (33) based on comparison of its mass fragmentation pattern to that in the literature.\(^{33}\) [M]\(^+\) = 182, [M - CH\(_3\)]\(^+\) = 167.

Compound C (RT = 10.6 minutes) was found to be 1,1-diphenylethanol (34) based on comparison of its retention time and mass fragmentation pattern to those of an authentic sample. Its mass spectrum contained peaks at m/z: [M]\(^+\) = 198, 183, 165, 105, 77.

Compound D (RT = 11.6 minutes) was found to be leftover starting material 19a.
k. Electrochemical Oxidation of 6,6-diphenyl-5-decanone (19b) in the Presence of Phenethyl Alcohol:

\[
\begin{align*}
\text{19b} & \quad \text{[O]} \quad \text{32b} \\
\end{align*}
\]

To the undivided cell setup described in the experimental was added 30 mL dry acetonitrile with 0.1 M supporting electrolyte, 0.693 g (2.25 x 10^{-3} mol) of 19b and 0.275 g (2.25 x 10^{-3} mol, 0.27 mL) of phenethyl alcohol. After 882.6 coulombs (4.06 F/mol) of current had passed, analysis via GC-MS showed conversion to 1-phenethoxy-1,1-diphenylbutane (32b) along with several byproducts. At this point, the reaction was stopped to make separation of products simpler. The reaction was worked up to yield 0.603 g of crude material. The crude material was purified over silica gel (80:20-60:40 hexanes:DCM) to yield 0.101 g (2.93 x 10^{-4} mol) offwhite oil identified via NMR and GC-MS to be nearly pure 32b. Roughly half of this material was further purified via prep-TLC (60:40 hexanes:DCM) to yield 0.024 g (7.06 x 10^{-5} mol) of the new compound 32b uncontaminated by other substances. GC yield = 22%, isolated yield = 3.1%.
Figure 52. Total Ion Chromatogram (TIC) of the anodic oxidation of 19b after 882.6 coulombs of current had passed.

No other peak in the TIC save compound B (RT = 14.2 minutes) could be identified. This peak was identified to be the new compound 32b, based on analysis of retention time and fragmentation pattern. Its mass spectrum contained peaks at m/z: 287, 223, 195, 105, 91, 77, 65, 51. Since no molecular ion peak was seen, an accurate mass (ESI/APCI) spectrum was obtained, and it contained a peak at m/z: [MNH₄⁺] = 362.2477, which agreed with the predicted molecular formula. Its ¹H NMR (CDCl₃, 400MHz) spectrum contained peaks at δ(ppm): 7.4-7.0 (m, 15H), 3.354 (t, 2H, J = 8Hz), 2.915 (t, 2H, J = 8Hz), 2.277 (m, 2H), 1.265 (s, 2H, J = 8Hz), 1.041 (m, 2H), 0.838 (t, 3H, J = 8Hz). Its ¹³C NMR (CDCl₃, 400MHz) spectrum contained peaks at δ(ppm): 146.321, 139.859, 129.391, 128.422, 128.010, 127.071, 126.613, 126.278, 82.207, 63.217, 37.145, 35.497, 25.082, 23.266, 14.332. A gHQSC (CDCl₃, 400MHz) spectrum was acquired to further characterize the compound, and it contained cross peaks at (δ_H, δ_C) (ppm): (7.29, 128.85), (3.33, 63.69), (2.9, 37.24), (2.31, 34.79), (0.81, 14.71)
Figure 53. Mass fragmentation pattern of 32b. Rationalizations of the peaks seen are given in the following figure.

Figure 54. Fragments arising from 32b to explain the major peaks seen.

Smaller peaks have been explained previously (See Figure 31). The molecular ion peak is not seen in the above mass spectrum, so an exact mass spectrum was obtained to determine the molecular formula of the compound. This is given in the following figure.
Figure 55. In the above ESI/APCI mass spectrum, one can observe the $[\text{MNH}_4]^+$ peak corresponding to the predicted molecular formula of $32b$. Other anomalous peaks are due to potential impurity in the sample.

The $[\text{MNH}_4]^+$ peak is found to correspond to a molecular formula of $\text{C}_{25}\text{H}_{32}\text{ON}$. The uncomplexed compound would then have the molecular formula $\text{C}_{25}\text{H}_{28}\text{O}$, which matches the proposed structure.
Figure 56. gDQCOSY spectrum of 32b.

The above gDQCOSY spectrum shows coupling between peaks E and F, E and D, and C and D, along with the expected correlation between the two triplets of the phenethyl moiety, B and A. These couplings are represented schematically in the following figure.

Figure 57. COSY couplings for 32b represented schematically. Note that the single-headed arrows represent the path taken to “step along” the molecule and determine connectivity.

This information sheds light on the connectivity of the alkyl protons in the n-butyl group. Specifically, since the methyl group F is furthest upfield, it can be deduced that the methylene group directly connected to it is E. This group in turn
shows coupling to D, which ultimately shows coupling to C. The full proton assignments are shown in the following spectrum.

**Figure 58.** $^1$H NMR spectrum of 32b.

Visible in the above spectrum are the two peaks at 3.36 and 2.92 ppm characteristic of the phenethyl moiety and the four alkyl peaks characteristic of an n-butyl group. The H$_C$ protons are shifted further downfield due to their proximity to the benzhydryl and alkoxy moieties.

The following gHSQC allows the proton assignments to be correlated to carbon atoms and for these atoms to be assigned in the carbon spectrum.
The cross peaks at roughly (3.2 ppm, 60 ppm) and (1.0 ppm, 23 ppm) are due to impurity in the sample. Two cross peaks for protons of the butyl group are not visible in the above spectrum. However, it can be deduced which carbons they are assigned to based on the preceding proton assignments. Long-range coupling of the $H_C$ methylene protons to the quaternary aromatic carbons of the benzhydryl moiety can be observed at (2.3 ppm, 146.5 ppm), indicating that these atoms are in close through-bond proximity to each other, providing further support for the proposed structure of the compound. Full carbon assignments are given in the following spectrum.
Figure 60. $^{13}$C NMR spectrum and expanded aromatic region of $32b$.

The assignments in the above spectrum are determined from the HSQC spectrum immediately preceding it. The furthest upfield carbon is assigned to the terminal methyl carbon on the butyl group. Since the HSQC shows that the carbon peak at 35.50 ppm is due to the methylene carbon M attached to the quaternary benzhydryl carbon L, and that the two carbons O and N between P and M are
intermediate between them with respect to chemical shift, they are represented by the signals at 25.09 ppm and 23.27 ppm. If these carbon atoms are assumed to follow the same order in chemical shifts as their connected protons, then $C_N$ would be further upfield at 23.27 ppm and $C_O$ would be assigned the peak at 25.09 ppm.

Thus although this compound wasn’t compared to a synthetic sample, the spectral data agrees with the proposed structure.

Compound A ($RT = \textbf{13.0 minutes}$) is left over starting material, \textbf{19b}. 

1. **Electrochemical Oxidation of Benzopinacolone (19c) in the Presence of Phenethyl Alcohol:**

This reaction was seen to follow the progression shown.

![Reaction Progression](image)

To the undivided cell setup described in the experimental was added 30 mL dry acetonitrile with 0.1 M supporting electrolyte, 0.782 g (2.24 x 10^{-3} mol) of 19c, and 0.275 g (2.25 x 10^{-3} mol, 0.27 mL) of phenethyl alcohol. The sparingly soluble 19c necessitated that this reaction be run at an elevated temperature (60 °C), and solvent was refilled as it evaporated. After 894.6 coulombs (4.14 F/mol) of current had passed, analysis by GC-MS showed conversion to phenethyl trityl ether (32c), with triphenylmethane (31) and triphenylmethanol (35) as minor products. The mini-workup performed in this reaction consisted of simply diluting a reaction aliquot with dichloromethane, due to the poor solubility of 19c in acetonitrile. The reaction was worked up to yield 0.670 g of crude organics which were chromatographed over silica.
gel (90:10-75:25 hexanes:dichloromethane) to afford 0.178 g (5.44 x 10⁻¹ mol) of a colorless solid identified as 32c by comparison to the literature, GC yield = 30.6%, isolated yield = 24.3%.

![Figure 61. Total Ion Chromatogram (TIC) of the anodic oxidation of 19c with phenethyl alcohol after 894.6 coulombs of current had passed.](image)

Compound E (RT = **15.5 minutes**) was identified as 32c, based on comparison of its GC-MS and NMR spectra to those of a synthetic sample, which was synthesized by reacting trityl chloride (36) with phenethyl alcohol in the presence of silver tetrafluoroborate in a procedure adapted from the literature²⁵, as explained previously. \( m/z: [M]^+ = 364, 287, 243, 165, 105, 77 \). Its \(^1\)H NMR (CDCl₃, 400MHz) spectrum contained a multiplet in the aromatic region integrating to 15 protons and two triplets at 3.23 ppm and 2.89 ppm integrating to 2 protons each. This matched the literature data on this known compound.²⁴
Compound A (RT = 7.0 minutes) was identified as electrolyte that was not washed out during the mini workup of the GC-MS sample.

Compound B (RT = 12.2 minutes) was identified to be triphenylmethane (31) using methods described previously. (See Results, Section C.(i).h)

Compound C (RT = 12.9 minutes) was identified to be triphenylmethanol (35) based on comparison of its retention time and fragmentation pattern to those of an authentic sample. Its mass spectrum contained peaks at m/z: [M]\(^{+}\) = 260, 243, 183.

Compound D (RT = 15.4 minutes) was identified as 19c, starting material.
m. Electrochemical Oxidation of Benzopinacolone (19c) in the Presence of Cyclohexanol:

To the undivided cell setup described in the experimental was added 30 mL dry acetonitrile with 0.1 M supporting electrolyte, 0.786 g (2.25 x 10^{-3} mol) of 19c, and 0.226 g (2.26 x 10^{-3} mol, 0.24 mL) of cyclohexanol. The sparingly soluble 19c necessitated that this reaction be run at an elevated temperature (60 °C), and solvent was refilled as it was carried off by nitrogen gas. The mini-workup performed in this reaction, as in the previous one, consisted of simply diluting a reaction aliquot with dichloromethane, due to the poor solubility in acetonitrile of 19c. After 527.4 coulombs (2.43 F/mol) of current had passed, analysis by GC-MS showed conversion to triphenylmethane (31) and triphenylmethanol (35), with several other minor products. The reaction was left to sit for several days, after which time the slow conversion of cyclohexyl trityl ether (32d) to 35, presumably by hydrolysis, took place. The reaction was not worked up, since the anticipated 32d was a minor
product which would have made isolation impossible. GC yield = 7.8%, no isolated yield.

![Figure 62](image-url)  

**Figure 62.** Total ion chromatogram (TIC) of reduction of 19c with cyclohexanol after 527.4 coulombs of current were passed.

Compound C (RT = 14.5 minutes) was identified to be 32d based on comparison of its fragmentation pattern to that in the literature. Its mass spectrum, seen below, contains the peaks m/z: [M]+ = 342, 265, 259, 243, 183, 165.

![Figure 63](image-url)  

**Figure 63.** Mass fragmentation pattern of 32d.

In the above mass spectrum, the molecular ion peak is visible, giving a confirmation that the molecule has the molecular weight of 32d. Structural rationalizations for the peaks follow in the next figure.
A synthesis of this ether was attempted using trityl chloride and cyclohexanol in the presence of silver tetrafluoroborate as previously explained, but the major products of this reaction were instead triphenylmethanol and triphenylmethane. Triphenylmethanol arose from the reaction of the trityl chloride with water and triphenylmethane arose from hydride abstraction by the trityl cation from cyclohexanol, a process well-established in the literature.

Compound A (RT = 12.1 minutes) was identified as 31 using methods described previously. (See Results, Section C.(i).h)

Compound B (RT = 12.8 minutes) was identified as 35 using methods described previously. (See Results, Section C.(i).l)
No other peaks could be identified and were not produced in a large enough quantity to pursue further.

n. Electrochemical Oxidation of Benzopinacolone (19c) with Cyclohexanol:

The procedure was identical to the preceding oxidation and the results were similar. A similar amount of cyclohexyl trityl ether (32d) was produced as in the undivided cell. This result implies that the ether is not quickly oxidized after formation but that it is instead simply not forming due to competition of water as a nucleophile in solution. It is nevertheless the case that if the ether is left to sit in acidic medium as was done in the reaction previous to this, it is hydrolyzed on a longer timescale.
Electrochemical Oxidation of 1,1-Dimethylacetone (37) with Phenethyl:

This reaction was performed in order to determine the importance of the two phenyl groups of the benzhydryl moiety in the reaction mechanism.

\[
\begin{align*}
\text{37} & \quad \xrightarrow{[O]} \quad \left(\begin{array}{c}
\text{38} \\
\end{array}\right) + \ ?
\end{align*}
\]

To the undivided cell setup described in the experimental was added 30 mL acetonitrile containing 0.1 M supporting electrolyte, 0.192 g (2.23 x 10^{-3} mol, 0.24 mL) of 37 and 0.275 g (2.25 x 10^{-3} mol, 0.27 mL) of phenethyl alcohol. After 568.2 coulombs (2.62 F/mol) of current had passed, analysis by GC-MS showed the abundances of products remaining constant, from which it was inferred that the reaction was complete. The reaction was worked up in the usual way and purified over silica gel (96:4 hexanes:ethyl acetate) to yield a mixture of two of the three products formed which could not be separated further. The third product, which corresponds to the peak in the following TIC with the longest retention time, was found to decompose on silica gel. No pure isolated yield was recorded.
Figure 65. Total ion chromatogram (TIC) of oxidation of 37 with phenethyl alcohol after 568.2 coulombs of current were passed.

The first of two peaks at roughly RT = 12.8 minutes, compound C, was identified to be bis[2-phenylethyl] formaldehyde acetal (38), based on comparison of retention time, fragmentation pattern, and \(^1\)H NMR data to those of a synthetic sample of this acetal. This was prepared by reacting two equivalents of phenethyl alcohol with formaldehyde to generate the acetal.

\[
\begin{align*}
\text{H} & \quad \text{H} \\
\text{O} & \\
\text{O} & \\
\text{O} & \\
\text{CH}_2
\end{align*}
\]

38

The peaks in the mass spectrum included \(m/z\): 226, 135, 121, 105, 91, 77. The \(^1\)H NMR (CDCl\(_3\), 400MHz) had peaks at δ(ppm): 7.32 – 7.20 (m, 10H), 4.67 (s, 2H), 3.71 (t, 4H, J = 8Hz), 2.86 (t, 4H, J = 8Hz). This spectrum matched the compound obtained from the electrolysis exactly.\(^{37}\)

Compound A (RT = 8 minutes) was identified to be phenethyl alcohol, a starting material.

Compound B (RT = 12.2 minutes) corresponded to a product which could not be separated from 38 and could not be characterized further.
Compound D (RT = 12.9 minutes) decomposed on silica gel and could not be analyzed.

Compounds B and D produced fragmentation patterns similar to that of C, implying that the compounds were similar in structure.

(ii). Mechanistic Studies

In order to probe the mechanism of this reaction, several labeling experiments were done using deuterated solvents and oxygen-labeled water. These experiments further shed light on the mechanism.

a. Electrochemical Oxidation of 1,1-Diphenylacetone (18) in the Presence of Oxygen-labeled Water:

After showing that this oxidation proceeds to a product ether with various ketones in the presence of various nucleophiles (See Results, Section C.(i)), it was of interest to see what products are obtained from the reaction of 17 with water. In this experiment, labeled water (H$_2^{18}$O) was used to track incorporation of oxygen into the products seen via GC-MS. In the following reaction scheme, heavy oxygen is represented by a shaded circle.
To the undivided cell setup described in the experimental was added 10 mL dry acetonitrile containing 0.1 M supporting electrolyte, 0.157 g (7.48 x 10^-4 mol) of 18, and 100 μL of oxygen-labeled water (1% by volume). After 191.4 coulombs (2.65 F/mol) of current had passed, analysis by GC-MS showed the appearance of various major products showing incorporation of heavy oxygen.

Figure 66. Total ion chromatogram (TIC) of oxidation of 18 in the presence of labeled water after 191.4 coulombs of current had passed.
Compound A (RT = 7.2 minutes) was identified to be electrolyte not washed out in the mini-workup.

In the above TIC, there are two peaks present at RT = 10.6 minutes. The peak with a shorter retention time, compound B, was determined to be oxygen-labeled benzophenone (8), based on comparison of its fragmentation pattern (Figure 67) to that of an authentic sample of the unlabeled isomer. m/z: [M]+ = 184, 107, 77, 51.

Figure 67. Mass fragmentation pattern of oxygen-labeled 8. m/z: [M]+ = 184, [M - Ph]+ = 107.

The peak with a slightly longer retention time, compound C, was identified as oxygen-labeled benzhydrol (29) based on comparison of its fragmentation pattern (Figure 68) to that of an unlabeled sample in the literature.\textsuperscript{38} m/z: [M]+ = 186, 107, 77, 51.
Figure 68. Mass fragmentation pattern of oxygen-labeled 29. m/z: [M]$^+$ = 186, [PhC$^{18}$O]$^+$ = 107.

Compound D, the small shoulder in the TIC with RT = 11.1 minutes was identified as oxygen-labeled benzhydryl acetate (23), based on comparison of its fragmentation pattern (Figure 69) to that of a synthetic sample of the unlabeled isomer. m/z: [M]$^+$ = 228, 184, 165, 152, 77.

Figure 69. Mass fragmentation pattern of oxygen-labeled 23. [M]$^+$ = 228. All mass peaks heavier than 228 are background noise characteristic of the column used for gas chromatography.

Compound E (RT = 11.2 minutes) is 18, remaining starting material.

Compound F (RT = 16.1 minutes) was identified as oxygen-labeled dibenzhydryl ether (25), based on comparison of its fragmentation pattern (Figure 23) to that of the unlabeled isomer in the chemical literature and to spectroscopic
characteristics of a sample isolated from a separate electrolysis (See Results, Section C.(i).d).^2^3 \[ m/z: \] 274, 185, 167.

Figure 70. Mass fragmentation pattern of 25. \[ [M - C_6H_6]^+ = 274. \] All mass peaks heavier than 228 are background noise characteristic of the column used.

This experiment showed conclusively that when the electrolysis was performed in the presence of water, the water acts as a nucleophile and incorporates into the products seen: 8, 23, 25, and 29.
b. Electrochemical Oxidation of 1-Cyclohexoxy-1,1-diphenylacetone (21a) without Nucleophile in Deuterated Acetonitrile (CD$_3$CN):

This reaction was performed to determine the products when 21a is oxidized with no nucleophile and to see if the expected deuterated product ether benzhydryl cyclohexyl ether (16a) is among them. The starting material was synthesized as previously explained (See Results, Section A).

To a 25 mL round bottom flask with a stir bar was added 15 mL dry deuterated acetonitrile and 0.492 g (1.50 x 10$^{-3}$ mol, 0.1 M) of supporting electrolyte, and stored on molecular sieves overnight. To this solution in the morning was added 0.294 g (9.57 x 10$^{-4}$ mol) of 21a. GC-MS was used to monitor reaction progress. After 165 coulombs (1.79 F/mol) of current had passed, analysis by GC-MS showed
the appearance of numerous products, including those from reaction with water, and
the reaction was stopped to make for a simpler interpretation of the results.

![Figure 71. Total ion chromatogram (TIC) of oxidation of 19a in CD3CN after 165 coulombs of current had passed.](image)

Compound A \( \text{RT} = 5.5 \text{ minutes} \) was identified as a mixture of deuterated and undeuterated cyclohexanol (CyOD and CyOH, respectively), based on mass fragmentation pattern analysis.

Compound B \( \text{RT} = 10.8 \text{ minutes} \) was identified to be benzophenone (8), by comparison of the observed mass fragmentation to that of an authentic sample, as described previously. (See Results, Section C.(i).a)

Compound C \( \text{RT} = 11.1 \text{ minutes} \) was identified as a mixture of deuterated and undeuterated benzhydryl acetate (23), based on mass fragmentation pattern analysis. Species containing one through four deuterium atoms were observed.

Compound D \( \text{RT} = 13.1 \text{ minutes} \) was identified to be a mixture of deuterated and undeuterated benzhydryl cyclohexyl ether (16a), by mass fragmentation pattern analysis (Figure 72) and comparison to the spectroscopic data in the literature.\(^{20}\) \( m/z: [\text{M}]^+ = 267, 184, 168, 152. \)
In the above mass spectrum, the parent peak of 267 demonstrates one deuterium substitution since it is one greater than the expected molecular weight of the ether, 266. The fact that the base peak 168 is also one greater than the expected 167 strongly suggests that this substitution appears at the benzhydryl position, as seen in Figure 73.

**Figure 73.** A comparison of the structures and molecular weights of the protio (left) and deutero (right) isomers of benzhydryl carbocation.

**Compound E (RT = 14.0 minutes)** was identified as starting material **21a**.

**Compound F (RT = 16.1 minutes)** was shown to be deuterated dibenzhydryl ether (25), based on comparison of its retention time and fragmentation pattern to that of the unlabeled isomer in the chemical literature and to spectroscopic
characteristics of a sample isolated from a separate electrolysis (See page X). \( m/z: 273, 183, 168, 153. \)

![Mass fragmentation pattern](image)

**Figure 74.** Mass fragmentation pattern of deuterated 25.

The above spectrum does not provide information about the ratio of mixed-label deuteron isomers of 25, since \( m/z: 273 \) is not the parent peak, but instead a fragment which can contain only one deuterium label at most. Thus, it is possible that this peak is also a mixture of labeled deutero-isomers.

No remaining peaks could be identified from the data obtained.

This experiment demonstrated that the \( \alpha \)-alkoxyketone is indeed an intermediate in the pathway leading to the final ether product. When the carbon-carbon bond cleavage in the \( \alpha \)-alkoxyketone intermediate compounds occurs, the resulting radical acquires a proton from the solvent, acetonitrile. Although protio ether was formed, it had to have formed due to contamination with water since this is the most likely source of protons in solution. The presence of water is confirmed by the products 23 and 25.
c. **Electrochemical Oxidation of 1-D-1,1-diphenyl-3-D₃-acetone (20) in the Presence of Phenethyl alcohol:**

In this experiment, deuterated 1,1-diphenylacetone (20) was oxidized in order to determine what percentage of the product ether retains the deuterium at the benzhydryl position. Phenethyl alcohol was used in order to avoid the issue of sterics with more crowded nucleophiles.

![Chemical structures](image)

To the undivided cell setup described in the experimental was added 30 mL dry acetonitrile containing 0.1 M supporting electrolyte, 0.448 g (2.09 x 10⁻³ mol) of 20, which was synthesized as explained previously (See Results, Section A) and 0.25 g (2.05 x 10⁻³ mol, 0.25 mL) of phenethyl alcohol. After 556.2 coulombs (2.76 F/mol) of current had passed, the reaction was stopped. The reaction was worked up in the usual way to yield 0.639 g of crude organics. A ^1H NMR spectrum was acquired of this mixture in order to determine the ratio of protio to deutero ether product (Figure 78).
Figure 75. Total Ion Chromatogram (TIC) for the oxidation of 20 with phenethyl alcohol after 556.2 coulombs of current had passed.

Compound C (RT = 14.2 minutes) was identified to be deuterated benzhydryl phenethyl ether (16b) based on its retention time and fragmentation pattern. \(m/z\): [M]⁺ = 289, 183, 168, 153.

Figure 76. Mass fragmentation pattern of deuterated 16b.

Compound A (RT = 11.1 minutes) was identified to be a mixture of labeled deuterio isomers of benzhydryl acetate (23) based on its retention time and fragmentation pattern. \(m/z\): [M]⁺ = 230, 229, 186, 166, 165, 153.
Figure 77. Mass fragmentation pattern of deuterated 23.

Compound B (RT = 11.2 minutes) is starting material 20, which exhibits the mass fragmentation pattern shown in Figure 17. Different scans along this peak showed fragmentation patterns with different parent peaks ranging from m/z: 227 to 230, indicative of the loss of between one and four deuterium atoms presumably via exchange through the enol. [Data not shown]

Compound D (RT = 16.1 minutes) was identified as a mixture of deuterated and undeuterated dibenzhydryl ether (25), based on mass fragmentation pattern analysis, as described previously (See Results, Section C.(ii).a).

The ¹H NMR of the crude product isolated is seen in Figure 78.
Figure 78. $^1$H NMR spectrum of the crude organics obtained from the electrolysis of $19b$ in the presence of phenethyl alcohol. Shown also is an expanded view of the area of the spectrum containing the alkyl peaks belonging to deuterated $16b$.

The presence of numerous similarly sized peaks in the region containing the trace benzhydryl proton peak made the assignment ambiguous, but an overlay of this spectrum with that of the pure compound isolated from an electrolysis with undeuterated starting material revealed that the peak at 5.44 ppm is in fact the benzhydryl proton. This overlay appears in Figure 79.
Figure 79. An overlay of $^1$H spectra. The top spectrum was acquired from a pure sample of protio 16b obtained from a previous electrolysis and confirmed as previously explained (See Results, Section C.(i).d). The bottom spectrum is the crude material obtained from this reaction.

From the above overlay, the peak at 5.44 ppm is seen to correspond to trace protio 16b formed in the electrolysis. As seen in Figure 79, this peak integrates to 0.16 relative to a peak corresponding to the O-$\text{CH}_2$ in the phenethyl moiety of the ether with a known integration of 2.00. The other methylene peak was overlapped by proton signals from other compounds in the sample, and could not be used as a satisfactory reference. Thus, 16% of 20 lost the deuterium tag at its benzhydryl position and 84% did not.
(iii). Reductive Preparation of Ketones

a. Electrochemical Reduction of 1-Cyclohexoxy-1,1-diphenylacetone (21a) in the Cathode Chamber of a Divided Cell without Nucleophile:

To the cathode chamber of the divided cell setup described in the experimental was added 20 mL of acetonitrile and 0.096g (3.129 x 10^-4 mol) of 21a. After 124.8 coulombs (4.13 F/mol) of current had passed, the voltage was observed to spike dramatically. This was taken to indicate that the reaction was finished and the current was stopped. Analysis by GC-MS showed nearly complete conversion of the starting material to benzhydryl cyclohexyl ether (16a). No isolated yield.

![Figure 80. Total ion chromatogram (TIC) of reduction of 21a after 124.8 coulombs of current were passed.](image)

Compound A (RT = 10.5 minutes) was identified to be 8 using methods described previously. (See Results, Section C.(i).a)
Compound B (RT = 13.05 minutes) was identified to be 16a using methods described previously. (See Results, Section C.(i).a)

Compound C (RT = 14.0 minutes) is an impurity which was present prior to reaction.

1,1-Diphenylacetone (18) was not generated in this reaction. This mechanism nevertheless leads to the ether product 16a.

b. Electrochemical Reduction of Benzopinacolone (19c) in the Cathode Chamber of a Divided Cell without Nucleophile:

To the cathode chamber of the divided cell setup described in the experimental was added 20 mL of dichloromethane and 0.101 g (2.90 x 10^-4 mol) of 19c. After 133.2 coulombs (4.76 F/mol) of current had passed, analysis by GC-MS showed that the reaction was finished, and the current was stopped. GC-MS showed nearly complete conversion of the starting material to triphenylmethane (31). No isolated yield.
Figure 81. Total ion chromatogram (TIC) of reduction of 19c after 133.2 coulombs of current were passed.

Compound C (RT = 12.2 minutes) was identified as 31 as explained previously (See Results, Section C.(i).h).\textsuperscript{31}

Compound A (RT = 7.0 minutes) was identified as electrolyte not washed out in the workup. Compound B (RT = 8.4 minutes) was identified as a benzoyl derivative by comparison of its fragmentation pattern to that of benzoic acid, known in the literature.\textsuperscript{39} m/z: 123, 105, 77, 51.

No other peaks could be identified or were produced in a quantity large enough to isolate. These were not pursued further.
D. Gaussian Modeling

To probe the electronic properties of the ketones being studied, Gaussian geometry optimization computations were done. In these analyses, the electrostatic potential (ESP) maps of the surfaces of the neutral and cation radical species obtained from oxidation, along with their respective frontier orbitals (HOMO and LUMO), were visualized as follows. Red indicates a high electron density (local negative charge), green is neutral, and blue represents low electron density (local positive charge).

It is important to qualify the Gaussian results presented by saying that these results do not necessarily represent global energetic minima of the systems shown. These are local minima which have been calculated dependent on the starting geometries of the molecules, which were arbitrarily chosen. Only in the case of 21b were several structures tested, but the analysis was by no means exhaustive. In spite of this, from the pseudo-symmetry of the molecules analyzed, there should be a degree of conjugation between at least one of the phenyl groups and the carbonyl in every molecule regardless of what orientation it is in.
(i). Electrostatic Potential Maps (Neutral Compounds):

2,2-diphenylacetaldehyde (9)  1,1-diphenylacetone (18)

1-methyl-1,1-diphenylacetone (19a)  6,6-diphenyl-5-decanone (19b)
In 18 and 19a-b, the greatest electron density is seen to be shared by the carbonyl and one of the adjacent phenyl rings, but the situation is less so with 19c. Compound 21b has two areas of high electron density, with the phenethoxy phenyl ring developing a partial negative charge due to lack of conjugation and a large through-space distance from the rest of the molecule, inhibiting delocalization of electron density. The optimization for 21b was performed twice – once with the input structure containing the two oxygen atoms eclipsed as shown, and once with the oxygen atoms anti to each other. The structure shown was found to be of a lower energy, and so the other result is not reported here or in the following images. Of
note is that 9 exhibits far less delocalization of electron density onto the phenyl rings, as evidenced by the less negative electrostatic potential of the phenyl rings.

(ii). Electrostatic Potential Maps (Cation Radical Compounds):

2,2-diphenylacetaldehyde (9) 1,1-diphenylacetone (18)

1-methyl-1,1-diphenylacetone (19a) 6,6-diphenyl-5-decanone (19b)
Figure 83. ESP surfaces of the cation radicals of 9, 18, 19a-c, and 21b.

Of note is the localization of the charge to the benzhydryl carbon in 18 (The “underside” of the molecule). The compounds 19a and 19c show the charge delocalized across at least one of the phenyl rings of the benzhydryl moiety, while two of the three phenyl rings of the trityl moiety in 19c hold most of the charge in that compound. Compound 19b shows that the charge is localized chiefly to the benzhydryl carbon.

In the cation radical structure shown for 21b, the carbon-carbonyl bond was shown to extend in length past the typical length of a σ-bond, implying that this bond is dramatically weakened (but not necessarily broken) when an electron is removed from this compound. Furthermore, a partial π-bond is seen to be forming between the
benzhydryl carbon and the ether oxygen. Analysis of the structure indicates that the geometry around the benzhydryl carbon more closely resembles that of an sp\(^2\) rather than an sp\(^3\) hybridized carbon.

It is interesting to compare these results with the ESP map obtained for 9, which shows that the charge localizes to the aldehyde hydrogen more than to either the carbonyl or the phenyl rings, implying a different reaction mechanism.

(iii). HOMOs (Neutral Compounds):

2,2-diphenylacetaldehyde (9)  1,1-diphenylacetone (18)

1-methyl-1,1-diphenylacetone (19a)  6,6-diphenyl-5-decanone (19b)
Figure 84. The HOMOs of compounds 9, 17, 19a-c, and 21b.

The HOMOs of 18 and 19a-b encompass both phenyl rings and the carbonyl moiety – a lobe of this orbital can be seen in 18 and 19a extending from the π-system onto the carbonyl oxygen. 19b possesses a HOMO which has a node at the benzhydryl carbon and includes one of the phenyl rings and the carbonyl as well. In 19c, the HOMO is localized to two of the three trityl phenyl rings, with virtually nonexistent lobes on the carbonyl. This is similar to the situation in 9. 21b possesses a HOMO which includes both the carbonyl and the ether oxygen atoms, along with one of the phenyl rings. The other phenyl ring is obscured in the image, but it is not contained within the HOMO. Thus, this compound experiences a different sort of conjugation.
(iv). LUMOs (Neutral Compounds):

**2,2-diphenylacetaldehyde (9)**

**1-methyl-1,1-diphenylacetone (19a)**

**6,6-diphenyl-5-decanone (19b)**

**Benzopinacolone (19c)**

**1-phenethoxy-1,1-diphenylacetone (21b)**

*Figure 85.* The LUMOs of compounds 9, 17, 19a-b, and 21b.
The LUMOs of compounds 19a-c and 21b are seen to extend from the carbonyl onto one or more phenyl rings. The majority of the LUMO of 9 seems to lie well off the molecule in a deviation from the trend exhibited by the remaining compounds.
METHODS

A. Instrumentation

GC-MS spectra were acquired using an Agilent Technologies 5979 Network mass selective detector with 6890 network GC system. Two GC oven methods were used – method (1) for the oxidation of ketones 18 and 19a-b, and method (2) for ketone 19c. Method (1) consisted of a run starting at 50 °C where it was held for three minutes, after which time the temperature was ramped at 17 °C/min to a final temperature of 280 °C, where it was held for a further three minutes. Method (2) consisted of a run starting at 50°C, where it was also held for three minutes, after which time the temperature was ramped at 25 °C/min to a temperature of 100 °C, where it was held for one minute. The temperature was then ramped a second time at 20 °C/min to a temperature of 280 °C, where it was held for ten minutes. All spectra were performed in split-injection mode, with a 225 °C inlet temperature and an average gas velocity of 52cm/sec. A 2.5 minute solvent delay was employed in all cases unless otherwise stated.

All NMR spectra were obtained at Wesleyan University, on either the Varian Mercury Vx 300MHz or the Unity Plus 400MHz NMR spectrometer, as noted in the results. ChemDraw Ultra 8.0 NMR prediction software was used to predict spectra of postulated structures and closely matched the experimental spectra collected.

Melting points were obtained on an Electrothermal® Manual Mel-Temp melting point apparatus, Model #1001.
Cyclic voltammetry was performed on a CHI650A (Austin, TX, USA) computer-based electrochemistry system. The experiments were carried out in a solution of 0.1 M tetrabutylammonium tetrafluoroborate in acetonitrile at a scan rate of 0.1 V/s. Carbon and platinum wires were used as the anode and the cathode, respectively. A silver wire in 0.1 M silver nitrate acetonitrile solution was used as a reference electrode.

Exact mass spectra were obtained at the University of California, Riverside High Resolution Mass Spectrometry facility using either ESI/APCI or LIFDI capabilities, as noted in the results.\textsuperscript{40}

Neutral geometries were optimized to a minimum in Gaussian\textsuperscript{18} at the B3LYP/6-31G(d) level using Density Functional Theory (DFT), with the default solvation model using acetonitrile as solvent. The geometries of cation radicals were computed with the same parameters at the B3LYP/6-31G+(d) level.

**B. Electrolyses**

Electrolyses were performed in a 30 mL three-necked round-bottom flask. The counter electrode consisted of a 3 cm x 3 cm platinum mesh threaded through with a 10 cm platinum wire. The working electrode consisted of a 3 cm x 3 cm carbon cloth, also threaded through with a platinum wire of the same length. All solutions were made up ahead of time and all solutions/solvents were dried on molecular sieves for at least six hours prior to use. Molecular sieves were activated by heating to 225 °C for several hours and stored until use in a desiccator, as recommended in the literature.\textsuperscript{41} Dry acetonitrile was used as the solvent unless stated otherwise, and 0.1M tetrabutylammonium tetrafluoroborate was used as the
electrolyte. A current of 10 mA was used unless otherwise noted and the reaction was stirred continuously. Nitrogen gas was bubbled through a bubbler and the reaction solution connected in series to degas it for fifteen minutes prior to turning on the current, and also for the duration of the reaction. In the event that a reaction had to be paused for long periods of time, the solution was degassed again prior to turning on the current. Substrates showed no evidence of the rapid atmospheric degradation characteristic of 2,2-diphenylacetaldehyde (9) or any degradation relevant on the timescale of these experiments, so no extra precautions were taken.

In the reactions which necessitated a divided cell, a conducting gel was prepared using methylcellulose-saturated DMF 0.1 M electrolyte solution which was dripped onto the fritted disk membrane and allowed to cool and harden. In Figure 87 below, the dashed rectangle at the membrane between the two chambers represents this plug.

**Figure 86.** Typical undivided cell electrolysis setup.
The progress of reactions was monitored regularly in either one of two ways. Either (a) roughly 100 µL of solution was withdrawn, the solvent was removed *in vacuo*, and the residue was rinsed with an equivalent volume of n-pentane, or (b) roughly 100 µL of solution was withdrawn and partitioned between fifteen drops each of pentane and water. These two methods of extraction were observed to produce equivalent results. In both cases, 1-2 µL of the organic phase was injected into the GC-MS instrument for analysis.

The workup consisted of removing the solvent *in vacuo*, redissolving in 20 mL pentane, and washing three times with 5 mL deionized water. The water was then collected and washed with three times with 5 mL pentane. The pentane layers were combined and the solvent was removed *in vacuo*.
C. Syntheses

In this section are detailed the syntheses performed in this work. The compounds proceed in numerical order.

**Benzhydryl benzyl ether (16e):**

\[
\begin{align*}
\text{Cl} & \quad \text{O} \\
\text{AgBF}_4 & \quad \text{THF} \\
\text{24} & \quad 16e
\end{align*}
\]

To a 100 mL round-bottom flask containing 30 mL THF and a stir bar was added 0.195 g (1.00 x 10^{-3} mol) of silver tetrafluoroborate and 0.097 g (8.930 x 10^{-4} mol, 0.0925 mL) of benzyl alcohol. To this solution was added 0.182 g (9.00 x 10^{-4} mol, 0.160 mL) of benzhydryl chloride (24), with the solution rapidly turning an opaque white color. The reaction was allowed to stir for thirty minutes, after which time was added 0.094 g (1.075 x 10^{-3} mol) of sodium bicarbonate. The reaction was filtered through celite to remove particulates, and the solvent was removed *in vacuo*. The residue was redissolved in 25 mL diethyl ether and washed three times with 5 mL deionized water. The organic layers were combined and the solvent was again removed *in vacuo*. The product was isolated via column chromatography (96:4 hexanes:ethyl acetate) and solvent was removed *in vacuo*, to yield 0.131 g (4.77 x 10^{-4} mol) of (16e) as a clear oil, % Yield = 52.3%. Purity was determined by comparison of spectra to those in the literature.\(^{27}\) \(m/z\): \([M^+] = 260, 183, 165, 152. \) \(^1\)H
NMR (CD$_3$CN, 300MHz) $\delta$(ppm): 7.5-7.2 (m, 15H), 5.547 (s, 1H), 4.526 (s, 2H). $^{13}$C NMR (CD$_3$CN, 400MHz) $\delta$(ppm): 142.899, 138.848, 128.677, 128.578, 127.945, 127.777, 127.670, 126.968, 82.845, 70.630.

**Benzhydryl ethyl ether (16f):**

![Diagram of benzhydryl ethyl ether](image)

To a 30 mL round bottom flask was added 15 mL ethanol as a solvent and 0.239 g (1.18 x 10^{-3} mol, 0.210 mL) of benzhydryl chloride (24). The reaction was stirred at reflux for ten hours, and reaction progress was monitored by GC-MS. Upon completion, reaction was allowed to cool to near room temperature and the solvent was removed *in vacuo*. The residue was washed three times with 10 mL deionized water and dried over sodium sulfate to yield 0.237 g (1.11 x 10^{-3} mol) of 16f, identified via comparison to the literature, \(^{32}\) % Yield = 94.1%. *m/z*: [M]$^+$ = 212, 183, 167, 152, 135, 105, 77, 51. $^{1}H$ NMR (CD$_3$CN, 300MHz) $\delta$(ppm): 7.40 (d, 4H), 7.35 (t, 4H), 7.26 (t, 2H), 5.438 (s, 1H), 3.511 (q, 2H, J = 6.84Hz), 1.246 (t, 3H, J = 6.84Hz). $^{13}$C NMR (CD$_3$CN, 400MHz) $\delta$(ppm): 143.464, 128.655, 127.556, 126.900, 83.257, 64.411, 14.962.
1-Methyl-1,1-diphenylacetone (19a):

To a 100 mL three-necked-round bottom flask was added 3.002 g (2.25 x 10^{-2} mol) of anhydrous aluminum chloride and 1.506 g (2.30 x 10^{-2} mol) of zinc powder. The flask was flushed with nitrogen and 60 mL of solvent acetonitrile was added. To this mixture was added 1.347 g (1.121 x 10^{-2} mol, 1.310 mL) of acetophenone. The mixture was heated to 80 °C and refluxed for roughly ten hours. The reaction was left overnight, during which time the solvent evaporated. The residual solid was washed with cold water and extracted with dichloromethane to yield 1.344 g of crude. This was further purified via column chromatography (50:50 hexanes:dichloromethane), to yield 0.405 g (1.808 x 10^{-3} mol) of an off-white to yellow oil which was confirmed to be 19a spectroscopically and by comparison to the literature,^{17} % Yield = 32.3%. \( m/z: [M]^+ = 224, 181, 165, 103, 77. \) \(^1\text{H NMR (CD}_3\text{CN, 400MHz)} \) \( \delta(\text{ppm}): 7.7-7.0 \) (m, 10H), 2.15 (s, 3H), 1.8 (s, 3H). \(^{13}\text{C NMR (CD}_3\text{CN, 400MHz)} \) \( \delta(\text{ppm}): 209.99, 144.92, 129.31, 127.86, 27.88, 26.31. \)
6,6-Diphenyl-5-decanone (19b):

To a 100 mL three-necked-round bottom flask was added 3.178 g (2.38 x 10^{-2} mol) of anhydrous aluminum chloride and 1.543 g (2.36 x 10^{-2} mol) of zinc powder. The flask was flushed with nitrogen and 60 mL of solvent acetonitrile was added. To this mixture was added 1.927 g (1.189 x 10^{-2} mol, 1.95 mL) of valerophenone. The mixture was heated to 80 °C and refluxed for roughly eighteen hours. The reaction was left overnight, during which time the solvent boiled off. The residual solid was washed with cold water, extracted with dichloromethane and filtered with simple column chromatography (100% DCM) to yield 1.421 g (4.61 x 10^{-3} mol) of crude product. The product was purified further over silica gel (75:25 hexanes:DCM) to yield 0.913 g (2.96 x 10^{-3} mol) of pure 19b as a yellow oil, % Yield = 49.8%. Purity was confirmed via comparison of spectroscopic data to that in the literature.\(^\text{16}\) m/z: 307, 290, 279, 265, 251, 223, 193, 181, 167. \(^1\)H NMR (CDCl\(_3\), 400MHz) δ(ppm): 7.4-7.0 (m, 5H), 2.375 (m, 2H), 1.4-0.8 (m, 16H).
1-D-1,1-diphenyl-3-D₃-acetone (20):

To a 50 mL round-bottom flask containing 30 mL dry acetonitrile and a stir bar was added 0.601 g (2.86 x 10⁻³ mol) of 18, 0.47 g (2.61 x 10⁻² mol, 0.52 mL) of heavy water and 0.16 g (1.59 x 10⁻³ mol, 0.3 mL) of d₂-sulfuric acid. The reaction was allowed to stir for forty-eight hours. The reaction was then diluted with water and extracted with dichloromethane. The organics were dried over magnesium sulfate to yield partially deuterated starting material, as determined by ¹H NMR. This procedure was repeated six times to yield 0.537 g (2.51 x 10⁻³ mol) of 20, deuterated >99% at both the benzhydryl and the methyl positions as determined by ¹H NMR and GC-MS analysis, % Yield = 87.8%. m/z: [M]+ = 214, 168. ¹H NMR (CDCl₃, 400MHz) δ(ppm): 7.4-7.0 (m, 10H).
1-Cyclohexoxy-1,1-diphenylacetone (21a):

![Chemical Structure]

To a 100 mL round-bottom flask containing 50 mL THF and a stir bar was added 8.424 g (4.33 x 10^{-2} mol) of silver tetrafluoroborate and 1.741 g (1.74 x 10^{-2} mol, 1.81 mL) of cyclohexanol, and cooled to -78 °C. To this solution was added 4.996 g (1.73 x 10^{-2} mol) of 1-bromo-1,1-diphenylacetone (26), which was synthesized as previously described. The solution then rapidly turned opaque white. The reaction was allowed to stir for forty-five minutes, after which time was added 1.521 g (1.81 x 10^{-2} mol) of sodium bicarbonate. The reaction was filtered through celite to remove particulates, and the solvent was removed in vacuo. The residue was redissolved in 50 mL diethylether and washed three times with 15 mL deionized water. The washes were collected and washed with 15 mL of diethyl ether. The organic layers were combined and the solvent was again removed in vacuo. The product was isolated via gradient column chromatography (Pure hexanes to 90:10 hexanes:ethyl acetate) and solvent was removed in vacuo, to yield 2.002 g (6.51 x 10^{-3} mol) of the new compound 21a as a yellowish oil which crystallized upon standing, % Yield = 37.6%. m.p. 64-67°C. m/z: 265, 209, 183, 165, 105. ESI/APCI
m/z: [MNH₄]⁺ = 326.2121, [MNa]⁺ = 331.1665. ¹H NMR (CD₃CN, 400MHz)
δ(ppm): 7.29-7.49 (m, 10H), 3.4 (m, 1H), 2.19 (m, 3H), 1.61 (m, 2H), 1.39 (m, 2H), 1.21 (m, 3H), 1.06 (m, 3H). ¹³C NMR (CD₃CN, 400MHz) δ(ppm): 209.241, 141.390, 129.305, 128.793, 128.243, 128.109, 73.870, 33.575, 26.360, 25.562, 24.102. gHQSC (CD₃CN, 400MHz) (δ_H, δ_C) (ppm): (7.44, 129.2), (3.34, 73.57), (2.2, 26.28), (1.6, 23.58), (1.4, 33.11), (1.39, 25.11), (1.16, 25.11), (1.03, 23.58)

1-Phenethoxy-1,1-diphenylacetone (21b):

To a 250 mL round-bottom flask containing 100 mL THF and a stir bar was added 5.055 g (2.60 x 10⁻² mol) of silver tetrafluoroborate and 1.271 g (1.041 x 10⁻² mol, 1.25 mL) of phenethyl alcohol, and the flask was cooled to -78 °C. To this solution was added 2.998 g (1.037 x 10⁻² mol) of 1-bromo-1,1-diphenylacetone (26), with the solution rapidly turning opaque white. The reaction was allowed to stir for forty-five minutes, after which time was added 1.141 g (1.358 x 10⁻² mol) of sodium bicarbonate. The reaction was filtered through celite to remove particulates, and the solvent was removed in vacuo. The residue was redissolved in 50 mL diethylether and washed three times with 15 mL deionized water. The washes were collected and
washed with 15 mL diethyl ether. The organic layers were combined and the solvent was again removed in vacuo. The product was isolated via gradient column chromatography (Pure hexanes to 95:5 hexanes:ethyl acetate) and solvent was removed in vacuo, to yield 1.210 g (3.67 x 10^{-3} mol) of \(21b\) a colorless oil, % Yield = 35.4%. \(m/z\): 287, 183, 165, 105, 91, 77. ESI/APCI \(m/z\): \([\text{MNH}_4]^+ = 348.1946, [\text{MNa}]^+ = 353.1517. \ ^1\text{H NMR} (\text{CD}_3\text{CN}, 400\text{MHz}) \delta(\text{ppm}): 7.2-7.5 (15\text{H}), 3.30 (t, 2\text{H}, J=6\text{Hz}), 2.89 (t, 2\text{H}, J=6\text{Hz}), 2.221 (s, 3\text{H}). \ ^{13}\text{C NMR} (\text{CD}_3\text{CN}, 400\text{MHz}) \delta(\text{ppm}): 208.913, 139.937, 139.627, 129.469, 128.902, 128.831, 128.529, 128.168, 126.493, 90.920, 66.357, 36.354, 25.499. \ ^{1}\text{H QC} (\text{CD}_3\text{CN}, 400\text{MHz}) (\delta_H, \delta_C) (\text{ppm}): (7.3, 127.51), (3.32, 64.82), (2.9, 35.61), (2.04, 25.26).

1-Methoxy-diphenylacetone (21c):

\[\text{26} \xrightarrow{\text{AgBF}_4, \text{THF, -78°C}} \text{21c}\]

To a 100 mL round-bottom flask containing 30 mL THF and a stir bar was added 1.03 g (5.29 x 10^{-3} mol) of silver tetrafluoroborate and 90 µL (2.25 x 10^{-3} mol, 0.071 g) of methanol, and cooled to -78 °C. To this solution was added 0.62 g (2.14 x 10^{-3} mol) of 1-bromo-1,1-diphenylacetone (26), with the solution rapidly turning
opaque white. The reaction was allowed to stir for thirty minutes, after which time was added excess sodium bicarbonate. The reaction was filtered through celite to remove particulates, and the solvent was removed in vacuo. The residue was redissolved in 25 mL diethylether and washed three times with 10 mL deionized water. The organic layers were combined, passed through a chromatography column (100% DCM), and the solvent was removed in vacuo to yield 0.361 g crude. The product was isolated via gradient column chromatography (Pure hexanes to 96:4 hexanes:ethyl acetate) and solvent was removed in vacuo again to yield 0.259 g (1.08 x 10\(^{-3}\) mol) of 21c as a yellow oil, identified via \(^1\)H NMR comparison to the literature.\(^{43}\) % Yield = 59.9%. \(m/z\): 197, 105, 77. \(^1\)H NMR (CD\(_3\)CN, 400MHz) \(\delta(\text{ppm})\): 7.5 – 7.3 (m, 10H), 3.09 (s, 3H), 2.21 (s, 3H).

1-Benzylxyloxy-1,1-diphenylacetone (21d):

To a 100 mL round-bottom flask containing 50 mL THF and a stir bar was added 0.762 g (3.92 x 10\(^{-3}\) mol) of silver tetrafluoroborate and 0.167 g (1.54 x 10\(^{-3}\) mol, 0.16 mL) of benzyl alcohol, and cooled to -78 °C. To this solution was added 0.450 g (1.56 x 10\(^{-3}\) mol) of 1-bromo-1,1-diphenylacetone (26), with the solution
rapidly turning opaque white. The reaction was allowed to stir for sixty minutes, after which time was added 0.352 g (4.18 x 10^{-3} mol) of sodium bicarbonate. The reaction was filtered through celite to remove particulates, and the solvent was removed in vacuo. The residue was redissolved in 50 mL diethyl ether and washed three times with 15 mL deionized water. The washes were collected and washed with 15 mL diethyl ether. The organic layers were combined and the solvent was again removed in vacuo. The product was isolated via gradient column chromatography (Pure hexanes to 95:5 hexanes:ethyl acetate) and solvent was removed in vacuo, to yield 0.275 g (8.71 x 10^{-4} mol) of 21d as a colorless oil which solidified upon standing, identified via comparison to the literature. 44% Yield = 56%. m/z: 273, 183, 165, 105, 91, 77. ESI/APCI m/z: [MNH₄]⁺ = 334.1795, [MNa]⁺ = 339.1356. ¹H NMR (CD₃CN, 300MHz) δ(ppm): 7.6-7.2 (m, 10H), 4.232 (s, 2H), 2.280 (s, 3H). ¹³C NMR (CD₃CN, 400MHz) δ(ppm): 208.501, 139.786, 138.566, 128.983, 128.655, 128.456, 128.357, 127.800, 127.510, 91.229, 67.089, 25.850.

**Cyclohexyl acetate (22):**

![Cyclohexyl acetate reaction](image)

To a 25 mL three-necked round-bottom flask charged with a stir bar was added 10 mL of acetic anhydride, 180 µL (1.729 x 10^{-3} mol, 0.173 g) of
cyclohexanol, and a spatula tip of catalytic p-toluenesulfonic acid (p-TsOH). The reaction vessel was fitted with a reflux condenser and heated to 90 °C for thirty hours. Upon completion, the reaction solution was diluted with cold deionized water and the excess acetic anhydride was destroyed with sodium bicarbonate. This solution was extracted three times with 15 mL dichloromethane and dried over sodium sulfate. The organics were passed through a silica gel column (DCM), and the solvent was removed in vacuo to yield 0.130 g (9.162 x 10⁻⁴ mol) of 22. Purity was confirmed via comparison GC-MS and NMR spectra to those in the literature,²¹ % Yield = 53%. m/z: 127, 99, 82, 67, 55. ¹H NMR (CD₃CN, 400MHz) δ(ppm): 4.68 (m, 1H), 1.98 (s, 3H), 1.83 (m, 2H), 1.73 (m, 2H), 1.55 (m, 1H), 1.39 (m, 5H).

**Benzhydryl acetate (23):**

\[
\begin{align*}
\text{Cl} & \quad \text{Δ, 60 hrs.} \\
\text{O} & \quad \text{24} \\
\text{O} & \quad \text{23}
\end{align*}
\]

To a 30 mL round-bottom flask was added 15 mL of acetic acid and 1.000 g (4.93 x 10⁻³ mol, 0.877 mL) of benzhydryl chloride (24). The reaction was stirred at 70 °C for twenty-four hours. Analysis by GC showed the reaction to have proceeded halfway to completion. The temperature was increased to 115 °C and stirred for a
further four hours. [At this time, the power in the laboratory building was lost and the reaction stood idle for forty-eight hours.] The reaction was then stirred for a further thirty hours at 120 °C. At the end of this time, the solvent was removed in vacuo to yield 0.608 g (2.69 x 10⁻³ mol) of 23, the purity of which was established via comparison of spectroscopic properties to those in the literature, 22% Yield = 54.6%. m/z: 226, 184, 165, 152, 105, 77, 51. ¹H NMR (CD₃CN, 400MHz) δ(ppm): 7.5-7.3 (m, 10H), 6.829 (s, 1H), 2.155 (s, 3H).

1-Bromo-1,1-diphenylacetone (26):

To a 100 mL three-necked round-bottom flask containing 40 mL dichloromethane and a stir bar was added 4.994 g (2.38 x 10⁻² mol) of 18, and cooled to -15 °C using a dry ice bath (5:95 ethylene glycol:ethanol). In a separate 15 mL beaker, 3.836 g (2.40 x 10⁻² mol, 1.23 mL) of bromine was dissolved in 5 mL of dichloromethane. To the reaction flask was added 10% of this solution (0.5 mL) dropwise. Once the color of the solution faded, the rest of the bromine was added dropwise over five minutes, and the reaction was allowed to stir for fifty minutes. At the end of this time, excess bromine was destroyed with sodium thiosulfate. The
reaction solution was washed three times with 10 mL deionized water. The washes were collected and washed three times with 5 mL dichloromethane. The organic layers were combined and the solvent removed in vacuo to yield 8.170 g \( (2.83 \times 10^{-2} \text{ mol}) \) of an amber colored oil, 1-bromo-1,1-diphenylacetone (26). \(^1\text{H} \text{NMR} \) showed the product to be pure,\(^2\) with abundant residual dichloromethane which could not be removed by prolonged exposure to vacuum. \% Yield = 119\%. \(^1\text{H} \text{NMR} \) (CDCl\(_3\), 300MHz) \( \delta \text{ (ppm)}: 7.35 \text{ (m, 10H)}, 2.48 \text{ (s, 3H)}. \)

**Phenethyl acetate (27):**

![Diagram of Phenethyl acetate (27)]

To a 25 mL three-necked round-bottom flask charged with a stir bar was added 15 mL of acetic anhydride, 180 \( \mu \text{L} \) \( (1.449 \times 10^{-3} \text{ mol, 0.177 g}) \) of phenethyl alcohol, and a spatula tip of catalytic p-toluenesulfonic acid. The reaction vessel was fitted with a reflux condenser and heated to 80 °C for twenty-four hours. Upon completion, the reaction solution was diluted with cold deionized water and the excess acetic anhydride was destroyed with sodium bicarbonate. This solution was extracted three times with 15 mL with dichloromethane and dried over sodium sulfate. The organics were passed through a simple silica gel column (DCM), and most the solvent was removed in vacuo to yield 0.248 g \( (1.520 \times 10^{-3} \text{ mol}) \) of 27. \% Yield = 104.9\%. Purity was confirmed by GC-MS and NMR, along with comparison
to literature values.\textsuperscript{45} \textsuperscript{1}H NMR δ(ppm): 7.4-7.2 (m, 5H), 4.256 (t, 2H), 2.927 (t, 2H), 1.976 (s, 3H).

**Benzyl acetate (30):**

\[
\text{OH} \quad \text{cat. p-TsOH} \quad 80 ^\circ\text{C, 24 hrs.} \quad \text{O} \quad \text{O} \quad \text{30}
\]

To a 25 mL three-necked round-bottom flask charged with a stir bar was added 10 mL of acetic anhydride, 173 μL (1.670x10\textsuperscript{-3} mol, 0.181 g) of benzyl alcohol, and a spatula tip of catalytic p-toluenesulfonic acid (p-TsOH). The reaction vessel was fitted with a reflux condenser and heated to 80 °C for twenty-four hours. Upon completion, the reaction solution was diluted with cold deionized water and the excess acetic anhydride was destroyed with sodium bicarbonate. This solution was washed three times with 15 mL of dichloromethane and dried over sodium sulfate. The organics were passed through a simple silica gel column (DCM), and the solvent was removed \textit{in vacuo} to yield 0.397 g (2.644 x 10\textsuperscript{-3} mol) of 30, % Yield = 158.3%. Analysis by GC-MS showed minor byproducts, but the \textsuperscript{1}H NMR spectrum demonstrated the compound’s purity.\textsuperscript{46} \textit{m/z}: 150, 135, 108, 91, 79, 65, 51. \textsuperscript{1}H NMR (CD\textsubscript{3}CN, 300MHz) δ(ppm): 7.5-7.2 (m, 5H), 5.099 (s, 2H), 2.068 (s, 3H).
Phenethyl trityl ether (32c):

To a 100 mL round-bottom flask containing 30 mL of THF and a stir bar was added 0.142 g (7.556 x 10^{-4} mol) of silver tetrafluoroborate and 0.084 g (6.834 x 10^{-4} mol, 80 µL) of phenethyl alcohol. To this solution was added 0.197 g (7.059 x 10^{-4} mol) of trityl chloride (36), with the solution rapidly changing color to deep yellow. After a few moments, the color faded and a white precipitate formed. The reaction was allowed to stir for thirty minutes, after which time was added excess sodium bicarbonate. The reaction was filtered through celite to remove particulates, and the solvent was removed in vacuo. The residue was redissolved in 25 mL diethyl ether and washed three times with 5 mL deionized water. The organic layers were combined and the solvent was again removed in vacuo. The product was purified over silica gel (80:20 hexanes:dichloromethane) and solvent was removed in vacuo to yield 0.050 g (1.385 x 10^{-4} mol) of a clear glassy solid identified as 32c, with a yield of 19.6%. Purity was confirmed with GC-MS, NMR and comparison to literature sources.\textsuperscript{34} m.p. 77-80°C. (No lit.data). \textsuperscript{1}H NMR (CDCl\textsubscript{3}, 300MHz) δ(ppm): 7.5-7.3 (m, 15H), 3.23 (t, 2H), 2.89 (t, 2H). \textsuperscript{13}C NMR (CDCl\textsubscript{3}, 400MHz) δ(ppm): 144.54, 139.63, 129.49, 128.95, 128.52, 128.00, 127.14, 126.41, 86.89, 65.30, 37.03.
Bis[2-phenylethyl]formaldehyde acetal (38):

![Diagram of the chemical structure of Bis[2-phenylethyl]formaldehyde acetal (38).]

To a 50 mL round-bottom flask with a stir bar was added 25 mL n-heptane, a spatula tip of catalytic p-toluenesulfonic acid (p-TsOH), 0.94 mL (7.84 x 10^{-3} mol, 0.956 g) of phenethyl alcohol and 0.119 g (3.96 x 10^{-3} mol) of formaldehyde in the form of paraformaldehyde. The reaction was heated to 80 °C for twenty-four hours, at which point analysis by GC-MS showed nearly full conversion to 38. The reaction was washed three times with 10 mL DI H$_2$O and the solvent was removed in vacuo with heating to yield 0.882 g (3.44 x 10^{-3} mol) of crude material. This was then chromatographed over silica gel (95:5 hexanes:ethyl acetate) to yield 0.268 g (1.05 x 10^{-3} mol) of pure bis[2-phenylethyl]formaldehyde acetal (38), as determined by comparison of GC-MS and NMR spectra to the literature.\(^{37}\) % Yield = 26.5%.

m/z: 226, 135, 121, 105, 91, 77. \(^1\)H NMR (CDCl$_3$, 400MHz) \(\delta\) (ppm): 7.32 – 7.20 (m, 10H), 4.67 (s, 2H), 3.71 (t, 4H, J = 8Hz), 2.86 (t, 4H, J = 8Hz).
DISCUSSION

Overview

The reactions described in the results section and the products arising from them can be rationalized in terms of the comprehensive set of mechanistic pathways presented in Figure 88. A generic α-benzhydryl ketone (39) is represented as its keto (39a) and enol (39b) tautomers. Should 39a be oxidized, the cation radical formed (40) exhibits the resonance forms shown, with some charge present on both the carbonyl and the benzhydryl moiety. 40 then breaks down by α-cleavage to release an acylium ion and the benzhydryl radical (41). 41 can then be oxidized a second time to generate the benzhydryl carbocation 42, which can then form the ether (43) by attack of a nucleophilic alcohol.

The enol tautomer 39b can also be oxidized to generate the cation radical 44. The cation can be attacked by a molecule of alcohol to generate the radical 45, which is then oxidized to generate the α-alkoxyketone 46. Sequential oxidation of 46 results in the cation radical 47, which has resonance forms with the cation radical diffused across the carbonyl, the benzhydryl moiety and the ether oxygen. This compound can then break down by α-cleavage to release an acylium ion and the benzhydryl radical 48, which abstracts a proton, presumably from solvent acetonitrile, to generate the final product ether 49. Note that in the case of 1,1-diphenylacetone (39a, R = H and R’ = Me) the ethers 43 and 49 are equivalent.
Figure 88. Comprehensive mechanistic pathways in the oxidation of α-benzhydryl ketones.
Enol Mechanism

Merzel has previously shown that the anodic oxidation of 2,2-diphenylacetaldehyde (9) in the presence of various nucleophiles yields intermediate \( \alpha \)-alkoxyaldehydes of the type 46 \((R' = H)\)\(^8\). Merzel carried out mechanistic studies with 9 showing that there exists an enol mechanism by which this transformation occurs. The addition of strong acid to the oxidation of 9 in the presence of cyclohexanol increases rate of formation of this intermediate.

Similarly, the occurrence of an \( \alpha \)-alkoxyketone intermediate 46 \((R' = \text{Me})\) in the oxidation of 1,1-diphenylacetone (18) with primary and secondary alcohols demonstrates that, in these reactions as well, a carbocation can and does form on the benzhydryl carbon prior to carbon-carbonyl bond cleavage.

In order to determine whether 46 is indeed an intermediate in the reaction of 39 and that the radical leading to the ether (48) acquires a hydrogen atom from solution, the oxidation of 1-cyclohexoxy-1,1-diphenylacetone (46a, \(R' = \text{Me}, R'' = \text{Cy}\)) was attempted in deuterated solvent. It was found that the expected ether did form with incorporation of deuterium. It can be concluded from this result that 46 is indeed an intermediate.

Of note is that byproducts from this reaction included those arising from the oxidation of 18 in the presence of water. The generation of 18 from 46, which didn’t accumulate but had to have been produced, would be a reductive process. To prove that 18 was being reductively formed, the reduction of 46a in the cathode compartment of a divided cell was attempted. Surprisingly, complete conversion to benzhydryl cyclohexyl ether (49a, \(R'' = \text{Cy}\)) took place. This result, though not
relevant to a discussion of the mechanism of the reaction at hand, is interesting and unprecedented as a separate point and will be returned to later.

With 46 shown to be an intermediate, monitoring the reactions in which it appeared by gas chromatography revealed that it does not accumulate appreciably. This implied that 46 is oxidized at potentials close to that of the starting material 1,1-diphenylacetone (18). The CV data and Gaussian computations, which demonstrated very similar oxidation potentials for both 18 and the intermediate 1-phenethoxy-1,1-diphenylacetone (47b), support this hypothesis (See Results, Section B).

Effect of Added Acid

Interestingly, when the oxidation of 18 with either cyclohexanol or phenethyl alcohol was performed in the presence of catalytic acid, no increase in the amount of the α-alkoxyketone intermediates, 47a and 47b respectively, was seen. In fact, less of this intermediate was seen in the reactions attempted. This result shows that only a small amount of 18 reacts via the enol and that the addition of acid, which increases the rate of conversion between the keto and enol tautomers (39a and 39b), allows more of 18 to react via the α-cleavage pathway.

Oxidation of the α-alkoxyketones

Once 46 is formed, the cation radical resulting from another oxidation (47) is observed to be diffused across the molecule, including the carbonyl, one phenyl ring and the ether oxygen, as evidenced by the HOMO of 1-phenethoxy-1,1-diphenylacetone (46b, R’ = Me, R” = PhEt). This is taken to be representative of the
cation radicals 47 in general, although this was the only HOMO visualized with Gaussian.

![Molecular structure](image)

**Figure 89.** HOMO of 1-phenethoxy-1,1-diphenylacetone (46b) showing involvement of the carbonyl, a phenyl ring and the ether oxygen.

Thus, the electron removed from these species originates from a HOMO encompassing these groups. The fact that the compounds 1-cyclohexoxy-1,1-diphenylacetone (46a, R’ = Me, R” = Cy) and 47b have similar oxidation potentials to those of the starting ketones 18 and 19a-c seems to imply that the ether oxygen provides little to no added stabilization of the cation radical. The structure of the cation radical computed by Gaussian shows a very low bond order between the benzhydryl and carbonyl carbons, indicating a severe weakening of this bond. The majority of the charge in this species is seen to reside on the acyl moiety. Although this does indeed demonstrate that the charge is not primarily on the ether or benzhydryl moieties, the precise implications of this result, specifically the weakening of the carbon-carbonyl bond, require further analysis.

A question remains concerning why the benzhydryl radical 48 that abstracts a hydrogen from solvent acetonitrile to form the stable ether is not oxidized in the same
way as radicals 41 and 45. It could be argued that 48 is oxidized to a cation which then participates in hydride abstraction from the alcohol. However, this would result in the accumulation of ketones arising from the alcohols upon loss of hydride, which would be detected by GC. Furthermore, the GC yields from the reactions performed would be far lower if this were occurring stoichiometrically. The more likely explanation is that the alkoxy moiety results in enhanced stability of the radical compared to an alkyl group, making this intermediate long-lived enough to escape the electrode surface and abstract a hydrogen atom.

**A Novel Conjugation**

Miller and colleagues previously speculated that the oxidation of 2,2-diphenylacetaldehyde (9) proceeds via removal of an electron from an aromatic π-system instead of from the enol tautomer.\(^\text{11}\) Though this was shown fairly certainly to not be the case in the oxidation of 9, the reaction of which proceeds via the enol tautomer as described previously by Merzel,\(^\text{8}\) the evidence for 1,1-diphenylacetone (18) instead seems to partially agree with Miller’s conclusions. The measured oxidation potential of 18 is higher than what would be expected for oxidation of an olefin, and the computed value agrees (See Results, Section B). This, taken together with the fact that acid catalysis seems to have no positive effect on the amount of the 46 generated and instead seems to slow the reaction down, implies that the tautomer primarily involved in this reaction is the keto form, and that this is instead what is being oxidized. An explanation of why Miller’s reported oxidation potentials seem incorrect, however, is less clear.
Further evidence for the fact that the enol tautomer of 1,1-diphenylacetone (18) is not the one mainly involved in this oxidation was provided by Gaussian computations performed to determine the optimized geometry and electronic character of the various ketones examined. It was found that in the case of 18, as in the case of 46b, the highest occupied molecular orbital (HOMO) spans both the carbonyl and the benzhydryl moieties in the molecule. Since the electron removed is the one least strongly held (In other words, is located in the orbital with the highest energy), it is this orbital from which an electron will be removed. The resulting cation radical is thus shared by the phenyl groups and the oxygen of the carbonyl.

This delocalization, as seen in Figure 89, represents a form of conjugation similar to that in β-silyl compounds described previously by Chris Kaimakliotis in Professor Fry’s laboratory. Kaimakliotis showed that the experimental oxidation potentials of aryl species with silyl groups β- to the ring are lower than the analogous compounds without these silyl groups, presumably because the resulting cation radical is stabilized by partial orbital overlap with the back lobe of a σ-bonding orbital of the silyl moiety. It is possible that a similar effect is responsible for a decrease in the oxidation potential of β-carbonyl-substituted aromatic systems if the electron being removed indeed comes from the HOMO encompassing an aromatic ring and the carbonyl moiety instead of from the enol tautomer.
Figure 90. Clockwise from top: β-silyl effect as described by Chris Kaimaklioti; proposed orbital conjugation seen in 18; Gaussian computed HOMO of 18 showing the diffusion of this orbital across the benzhydryl and carbonyl moieties.

Interestingly, the Gaussian electrostatic potential maps of 18 and the various α-alkyl substituted ketones 19a-c seem to suggest that the carbonyl experiences this interaction with only one of the two phenyl rings. This is explained by the fact that the other ring is twisted out of the plane optimal for this interaction due to steric crowding effects around the benzhydryl carbon and is thus excluded from this interaction; it is known that the phenyl rings of the benzhydryl moiety are not coplanar.\textsuperscript{48} In the case of benzopinacolone (19c), the degree of this conjugation is far smaller, with the majority of the HOMO residing on two of the three phenyl rings of the trityl moiety, as seen in the results (See Results, Section D). Furthermore, the majority of the charge in the cation radical is seen to reside on the two phenyl rings mentioned, and there is no observed charge on the carbonyl. These data can be
similarly rationalized by the fact that none of the three phenyl rings of the trityl moiety can achieve the necessary conformation in order to interact with the carbonyl oxygen, due to the crowdedness around the trityl carbon they share. This affects the mechanism by which benzopinacolone (19c) is oxidized, as will be shown later.

**Preferred Pathway**

Of mechanistic importance was determining how much of the oxidation of 1,1-diphenylacetone (18) proceeds via oxidation of the enol, and thus via the intermediate 46, and how much proceeds via initial carbon-carbonyl bond cleavage to form 41. Gas chromatography cannot answer this question since, as mentioned, the intermediate 46 is oxidized at potentials similar to the starting materials and so is not expected to accumulate.

An important distinction between the two possibilities is that when 46 is formed, the benzhydryl proton, if $R' = H$, is necessarily lost. One can track this by labeling the benzhydryl position with deuterium and observing how much of the product retains the tag. This experiment was attempted with 18 and it was observed that 86% of the product retained the benzhydryl deuterium tag (See Results, Section C.(ii).c). This directly implies that the mechanism by which the oxidation of 18 mainly proceeds is initial carbon-carbonyl bond cleavage, and that in turn implies that the enol is minimally involved. However, this result applies only to 18, since different ketones are expected to behave differently depending on their varying electronic characteristics.
Oxidation of α-Substituted Ketones

Knowing that this reaction proceeds primarily via a mechanism involving the keto form instead of the enol, it was prudent to examine the outcome of the oxidation of ketones that are substituted at the benzhydryl position with alkyl groups (39, R ≠ H). These ketones cannot generate the α-alkoxyketones 46 since they cannot tautomerize to 39b. When the oxidation of the α-substituted ketones 19a-c was attempted in the presence of the primary phenethyl alcohol, the reaction proceeded to give the ether products 43 in all cases. Analyses of the ketones’ ESPs showed a hyperconjugation identical to that in the case of 18 in all cases except benzopinacolone (19c). The remaining alkyl-substituted ketones 19a-b proceed to the ether via a radical cation delocalized over the carbonyl oxygen and at least one of the phenyl rings, as illustrated by their HOMOs (See Results, Section D). In 19c, the HOMO includes two of the three phenyl rings and only barely overlaps the carbonyl group as shown in Figure 91.

Figure 91. HOMO of 19c, showing that it contains primarily the two phenyl rings.
This result implies that only in 19c is it true that the two phenyl rings of the HOMO carry most of the charge of the cation radical, and so the mechanism presented in Figure 92 has to be correct.

![Chemical structures](image)

**Figure 92.** Mechanism of anodic oxidation of 19c.

The presence of both 51 and 52 is supported by the appearance of byproducts in all of the reactions performed with benzopinacolone. Specifically, triphenylmethane (31) and triphenylmethanol (35) were observed as significant peaks in the GC spectrum. The compound 31 may arise either from radical hydrogen abstraction from solvent acetonitrile by 51 or by hydride abstraction from the alcohol used as a nucleophile by 52 in a mechanism that is well established. 32 may arise by attack of water on the trityl cation 52.
Conclusions

Thus, it has been shown based on evidence collected in silico and from reactions performed in this work that α-benzhydryl substituted ketone compounds exhibit a novel through-space conjugation involving one of the phenyl π-systems and the nonbonding oxygen electrons. This conjugation results in a stabilization of the keto form and, in the case of 1,1-diphenylacetone (18), results in such a small amount of enol content that the reaction is almost absent of oxidation products arising from it.

Based on this finding, the primary mechanism of the oxidation of the ketones studied here has been elucidated in detail. The first cation radical formed (40) is distributed across a phenyl group and the through-space conjugated carbonyl. The carbon-carbonyl bond is cleaved, followed by attack of nucleophile on the cation generated by sequential oxidation to form the ether 43.

In the case of α-alkyl substituted ketones (19a-c), the reaction has been shown to be more variable, depending on the specific ketone used. 1-Methyl-1,1-diphenylacetone (19a) was shown to have a HOMO containing both a phenyl group and the carbonyl in the same way as DPA. However, in the case of benzopinacolone (19c), the HOMO includes only two of the three phenyl rings in the trityl moiety and only slightly overlaps the carbonyl, implying that the reaction proceeds via oxidation of one of these π-systems, as shown in Figure 92.

It seems, though, that the ratio of charge on the carbonyl to the phenyl groups, and thus the percent value of the reaction proceeding one way or another, lies on a spectrum, and it is intuitive that this value may change from one ketone to the next.
In light of these findings, it seems that benzhydryl ketones are in a class of their own with regards to their mechanism of oxidation, and should be regarded as such in future work.

**Scope**

It is probable that a combination of steric and electronic effects operates in determining the outcome of these oxidations. In the reactions with 1,1-diphenylacetone (18), those involving a bulkier nucleophile such as triethylcarbinol resulted in competition with trace water for the benzhydryl carbocation produced.

This trend was also seen with benzopinacolone (19c). In spite of the fact that the trityl cation (52) is planar at the central carbon,\(^\text{49}\) sterics are known to play a role in its reactivity due to the three rings being twisted out of the plane.\(^\text{49}\) It has been shown previously in the reaction of benzhydryl and trityl cations with trialkylamines that reactivity falls off by an order of magnitude with the addition of the third phenyl group.\(^\text{50}\) Compounded with the steric bulk of the third phenyl ring is the delocalization of the positive charge, making this reaction less favorable. The reaction of benzopinacolone (19c), in which this is the reactive species, was relatively facile with phenethyl alcohol, while that with cyclohexanol produced cyclohexyl trityl ether (32d) as only a minor product (See Results, sections C.(i).m and C.(i).n). Its reaction with triethylcarbinol did not proceed in spite of a nine-fold excess of nucleophile, and it instead either reacted with trace water or proceeded via hydride abstraction of the
alcohol to generate triphenylmethane (31) as a major product. This reaction was thus not reported.

1-Methyl-1,1-diphenylacetone (19a) and 6,6-diphenyl-5-decanone (19b) are intermediate in steric bulk between 18 and 19c at the benzhydryl carbon and do not possess as much cation stabilization as benzopinacolone (19c). In light of this, it is speculated that they would react more readily with secondary alcohols than 19c, though this was not tested. Nevertheless, it is clear from the results of this work that tertiary or otherwise crowded nucleophiles would necessitate extremely dry conditions in order to avoid competition of water with the nucleophile.

From a mechanistic point of view, the fact that sterics of both the ketone and nucleophile used impact the rate of reaction seems to imply that attack of the nucleophile onto the carbocations generated in the course of this reaction (42 and 44) is rate-determining. This would imply that the cation radicals 42 and 44 have some degree of stability, which can be explained by the delocalization of charge due to the conjugation mentioned previously.

Ketones with long alkane chains result in messier reactions, as evidenced by the oxidation of 19b. The TIC of this reaction upon completion showed numerous products, none of which, save the ether, was isolated. Miller and colleagues have previously shown that long-chain alkyl ketones are prone to remote substitution of acetamide,40 and this is speculated to be involved in what occurs here on the two n-butyl chains.

In theory, one can imagine using various other groups of nucleophiles to arrive at alternate products – carboxylic acids might afford esters, for example. This
reaction may already have been shown to proceed by reaction with water, which generates either benzhydrol (29) or acetic acid in situ in the oxidation of 1,1-diphenylacetone (18), one or both of which go on to generate benzhydryl acetate (23) and dibenzhydryl ether (25) as explained in the results (See Results, Section C.(ii).a). Thus, the only stipulations in choosing the nucleophile are that it has to be fairly unhindered and that it has to be oxidized at a potential greater than that of the ketone.

Incidentally, allyltrimethylsilane proved to be too weak a nucleophile for any reaction to occur.

Other Nucleophiles

As already mentioned, the generation of several nucleophiles has been either directly observed or hypothesized to occur. Benzhydrol (29) has been observed to accumulate in the presence of water as a nucleophile (See Results, Section C.ii.a), and acetic acid is speculated to form by capture of produced acylium ion with water.

Of note also is the production of benzhydryl ethyl ether (16f) in the reaction of 18 with ethyl vinyl ether. The mechanism of this specific reaction has not been defined completely, but one possibility is that the ethyl vinyl ether is hydrolyzed in the presence of acid to afford ethanol, as shown in Figure 93 in a mechanism known in the literature. ⁵¹
This would fit the experimental data, which shows that this reaction proceeds far slower than the other primary nucleophiles used. If this is the correct mechanism, the reaction would be mediated by the concentration of water in solution, which is very low.

**Cathodic Generation of Ethers**

It was previously mentioned that the cathodic reduction of 1-cyclohexoxy-1,1-diphenylacetone (21a) in a divided cell resulted in complete conversion to benzhydryl cyclohexyl ether (16a). This result had to have occurred via a mechanism for which only a few possibilities seem reasonable. Cathodic generation of hydroxide and \( S_N2 \) attack by this strong base on the carbonyl was one possibility explored (Figure 94).
Figure 94. Possible base-mediated mechanism for reductive cleavage of 21a.

However, 21a was stirred with sodium hydroxide in an acetonitrile-water solution and no reaction was observed; adding electrolyte to replicate a typical electrolysis had no effect.

Another possibility known in the literature is generation of a superoxide anion which can participate in α-cleavage reactions of ketones. However, nitrogen gas was bubbled through this reaction in order to remove any traces of oxygen so this possibility is unlikely. Trace oxygen may have been present, though, since the absence thereof was never explicitly shown. Bubbling oxygen through the solution might accelerate this reaction, but this has not been attempted yet.

The elimination of these two possibilities leaves the possibility that the ketone is reduced directly by insertion of an electron into the carbonyl moiety followed by homolytic carbon bond cleavage. Previous work by Eastman and Leone has shown that the cathodic reduction of phenyl alkyl ketones occurs at potentials between 1.45 and 1.55V at pH = 9 depending on the alkyl substituent, with more electron-donating groups necessitating a higher potential due to the destabilization of the resulting negative charge, as expected. The reactions of acetophenone and propiophenone,
among other ketones, were observed to produce radical-coupled pinacol derivatives. However, these reactions were performed in solvents containing protons available from water and ethanol, and the conclusions drawn are thus limited only to reactions performed in aqueous media. Should the production of free radical carbinol species, which according to Eastman and Leone relies on the presence of protons in solution, be impeded as is the case in nonaqueous, nonacidic media, the reaction would presumably take a different path. Furthermore, none of the ketones examined in their work contained the benzhydryl moiety of the ketones in this thesis.

If this reductive mechanism is indeed the one responsible for this reaction, then compounds with other electron withdrawing groups substituted on the benzhydryl carbon would stabilize this reaction further. Indeed, when the divided-cell reduction of benzopinacolone (19c) was attempted, triphenylmethane (31) was formed. Further support for this mechanism is the shape of the LUMOs on the compounds tested (See Results, Section D). The LUMO of benzopinacolone (19c) contains the acetophenone moiety, and in the case of 1-phenethoxy-1,1-diphenylacetone (21b), it is diffused across one of the benzhydryl phenyl rings. These two results suggest that the inserted electron would have increased stabilization relative to the bare carbonyl. A mechanism can be seen in Figure 95.
Thus, although a rigorous proof of the ether bond breakage was not established, the reductive α-cleavage of benzhydryl ketones, an unprecedented reaction which results in ethers cleanly and is worth pursuing in future work was demonstrated instead. From the LUMOs of the remaining compounds visualized, it seems that the remaining ketones 19a-b can be reduced in the same way, while 1,1-diphenylacetone (9) would not accept an electron as readily.

**Difficulties**

A puzzling characteristic of all of the reactions attempted in this thesis was that water invariably managed to contaminate the system. Several precautions were taken to assure that this would not happen, and the fact that it occurred regardless means that the only way to completely avoid contamination by atmospheric water is to run these electrolyses in a glove box. The same precautions, however, including the use of a drying tube on the nitrogen line and the drying of solvents and solutions ahead of time, should still be continued.
Although the reactions have been shown both by GC yields and $^1$H NMR spectra of the crude product obtained from reaction to be fairly efficient, separation of the desired ether products via column chromatography over silica gel has proven challenging. First, all of the electrolyses save those in which the nucleophile was used in vast excess resulted in the isolation of a brown, thick sludge containing the product. This substance has not been characterized but is theorized to be a product from oxidation of the tetrabutylammonium tetrafluoroborate salt.

Once the organic products were isolated from the brown substance isolated in the crude material, it was discovered in the vast majority of cases that the Rf values of the several components of this crude mixture were similar across several different solvent systems and thus made separation using silica gel challenging.

Another difficulty encountered is that the product ethers, particularly the more crowded ones such as cyclohexyl trityl ether (32d), obtained from these reactions may have been hydrolyzed or otherwise decomposed on silica gel. The ether mentioned has been shown to hydrolyze slowly in acidic solution (See Results, Section C.ii.m), so this possibility is worth considering. In light of this, perhaps separation by another method such as preparatory gas chromatography, or column chromatography with a non-acidic solid phase in the future would prove beneficial. Once these practical difficulties are dealt with, these reactions would almost certainly produce higher yields and make for an easier crude separation.
Future Work

Future work should focus on the elucidation of the exact mechanism of oxidation of 1-alkyl substituted benzhydryl ketones such as 19a-c. It has been shown with every ketone except benzopinacolone (19c) that a cation radical is generated in a HOMO delocalized across the benzhydryl and carbonyl moieties. However, this was concluded from only one initial Gaussian input structure in each case, and the generated HOMO results should be verified by using various input rotamers that put the carbonyl at various orientations relative to the phenyl rings.

There is also uncertainty concerning the fate of the liberated acetyl moiety that appears in the mechanism of oxidation. It has been shown here that it goes on to react with nucleophiles such as water or the alcohol used to generated the acetylated analogues of the nucleophiles, but the exact ratios of these reactions, or any others which have not been observed, are unknown. This is partly due to the fact that, if this acetyl moiety is attacked by water to form an acid, the product would be washed out in the workup.

A second mechanistic pathway involving the acetyl moiety was evidenced in the reaction of 1,1-dimethylacetone (37) with phenethyl alcohol. This reaction produced three distinct products, all in low yield. One of these products decomposed on silica gel and could not be isolated, while the other two eluted simultaneously. Of these two latter products, one was identified spectroscopically to be bis[2-phenylethyl]formaldehyde acetal (38), as described in the results. This compound would have had to arise from the reaction of two equivalents of phenethyl alcohol and one equivalent of either solvent or 37. An electrolysis involving only phenethyl
alcohol and no 37 was performed and no reaction was observed. Therefore, this product has to correspond to attack of two molecules of phenethyl alcohol on the methyl group α to the carbonyl moiety followed by cleavage of the methyl carbonyl carbon bond.

This reaction path can be rationalized as follows. Since the two phenyl groups in 18 are missing in 37, this reaction would have a mechanism absent of any sort of hyperconjugation of the carbonyl moiety. It is likely that, in this case, the reaction may proceed via the enol (See Reaction 96).

Figure 96. Proposed mechanism of formation of 37.

Enolization in the direction of the isopropyl carbon would be less likely than in the direction of the methyl group since this would generate a more sterically crowded alkene, since there is no added stabilization due to the lack of the two phenyl rings. The presence of an oxygen on the methyl group would stabilize a radical formed at this carbon, but this stabilization is apparently not enough of a driving force to break the methyl carbon bond. Thus, the alcohol adds in a second iteration of the
reaction and only then is the cleavage of the carbon bond favored. This is reminiscent of the haloform reaction in which a halogen adds iteratively to the α-position of a ketone followed by the eventual cleavage and liberation of a trihalomethane.

In an attempt to deduce the precise fate of this molecular fragment in benzhydryl ketones directly, an oxidation using 2,2-diphenylcyclohexanone (53) with water was attempted. This would have allowed for the acetyl group to remain attached to the product ether isolated. However, the yield was very low and the several products formed could not be separated. The same oxidation performed with phenethyl alcohol resulted in the production of many products arising from what appeared to be iterative nucleophilic attack on the ketone – none of these products could be isolated in a sufficient yield to be characterized. These reactions have not resulted in any isolated products or data, and were thus not reported in the Results. There are several possible reasons underlying the relative complexity of this reaction, including possible remote substitution of acetamide on the cyclohexane ring as seen in the case of 6,6-diphenyl-5-decanone (19b). This reaction would have to be studied in more detail in the future.
REFERENCES


35. NSF grants CHE-0742001, CHE-0541848.


47. Kaimakliotis, C. Z., Production of *Umpolung*, Proposal of a Novel Anodic Silicon Effect and Electrochemical Desilylation of α-Silyl Esters. Wesleyan University, Middletown, CT., **2003**.


