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Publication Date
2012

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New Methods for the Deoxygenation of 1,2-diols and Epoxides

by

Peter Charles Marsden

A thesis submitted in partial satisfaction of the

requirements for the degree of

Doctor of Philosophy

in

Chemistry

in the

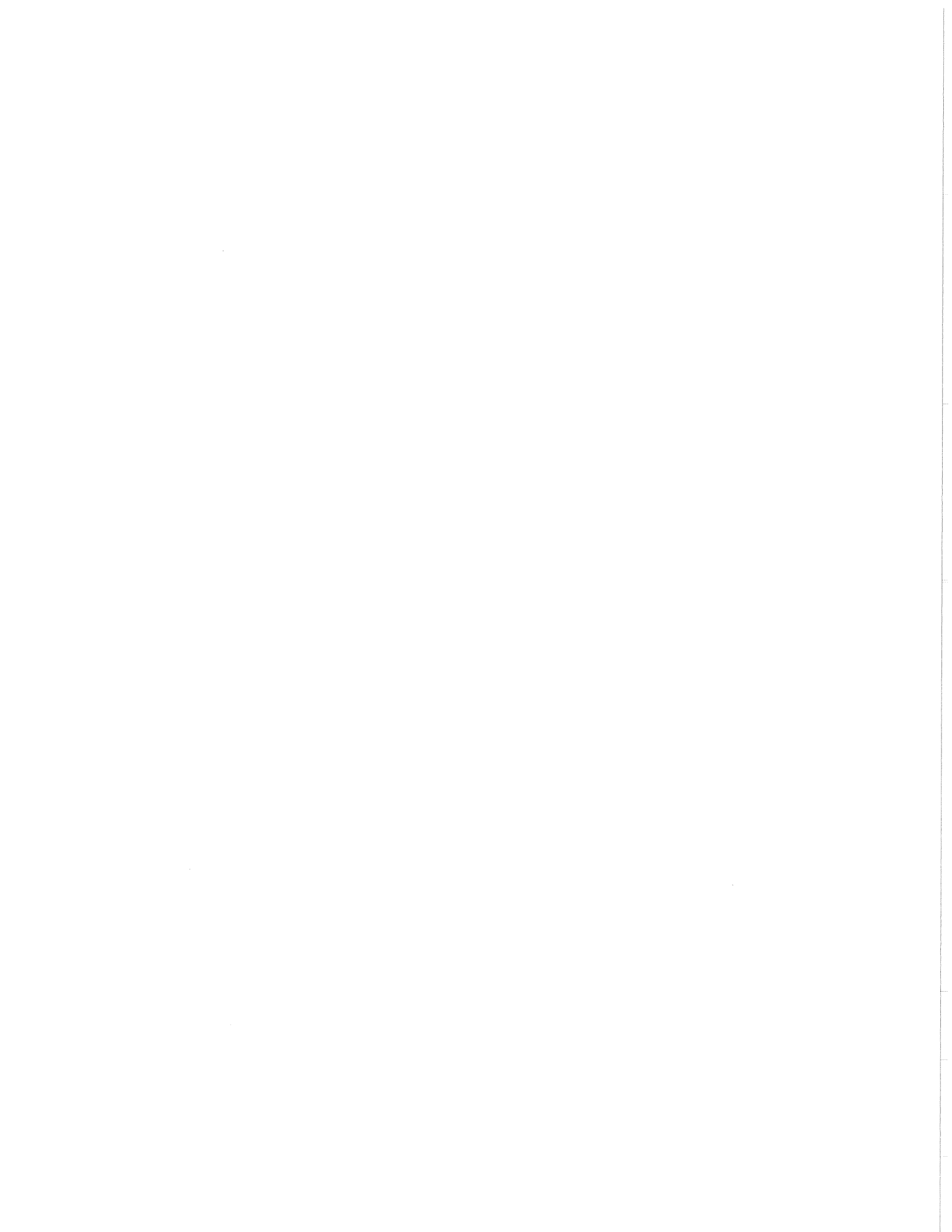Graduate Division

of the

University of California, Berkeley

Committee in charge:

Professor Robert Bergman, Chair

Professor F. Dean Toste

Professor Seung-Wuk Lee

Spring 2012

Abstracts

Chapter 1 : Introduction.

Our chemical industry is currently capable of converting fossil fuel feedstocks (unsaturated hydrocarbons) into useful polymers and chemicals. Replacing those feedstocks with renewable sources is an important goal for sustainability. Our research focuses on the defunctionalization of heavily oxygenated biomass materials so they can be used in the chemical industry's current factories. Of particular interest are three and four carbon monomers which would be obtained from the defunctionalization of the simple alditols glycerol and erythritol.

Chapter 2 : Formic Acid-Mediated Didehydroxylation of Vicinal Diols: Reaction Development and Mechanistic Studies

We developed a simple formic acid-mediated didehydroxylation of diols. Our substrate scope was limited to simple polyols. Isotope labeling studies suggested the intermediacy of a carbocation as well as an orthoformate ester. Attempts at isolating the carbocation intermediate were unsuccessful.

Chapter 3 : CO$_2$ Reduction – *In situ* Formation of Formic Acid with Concomitant Didehydroxylation of Vicinal Diols

We successfully reduced carbon dioxide with a heterogeneous rhodium catalyst to form a mixture of formic acid and amine. Attempts at didehydroxylation using the synthesized mixture were successful, though low yielding. Concomitant reduction of carbon dioxide and didehydroxylation was not achieved.

Chapter 4 : Rhenium-Catalyzed Deoxygenation of Diols and Epoxides

Many oxo-rhenium catalysts were synthesized and used for the deoxygenation of diols and epoxides. We were unable to obtain conclusive spectroscopic data of the reaction's progress, limiting our ability to propose a mechanism.

Dedicated to my family and friends.

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1. Introduction

1.1 Biomass

Biomass is an abundant and readily available feedstock that has great potential as a renewable source of energy and chemical intermediates.[1] Many chemicals used by the chemical industry can be derived from biomass, potentially reducing the industry's reliance on petroleum.[1] The processing technology for fossil fuel-derived raw materials is well known and developed, but it differs radically from the technology in place for bio-feedstocks.[1c] Petroleum feeds contain a complex mixture of hydrocarbons of various molecular weights and usually have few functional groups, which makes these feeds suitable for catalytic processing (**Figure 1.1**).
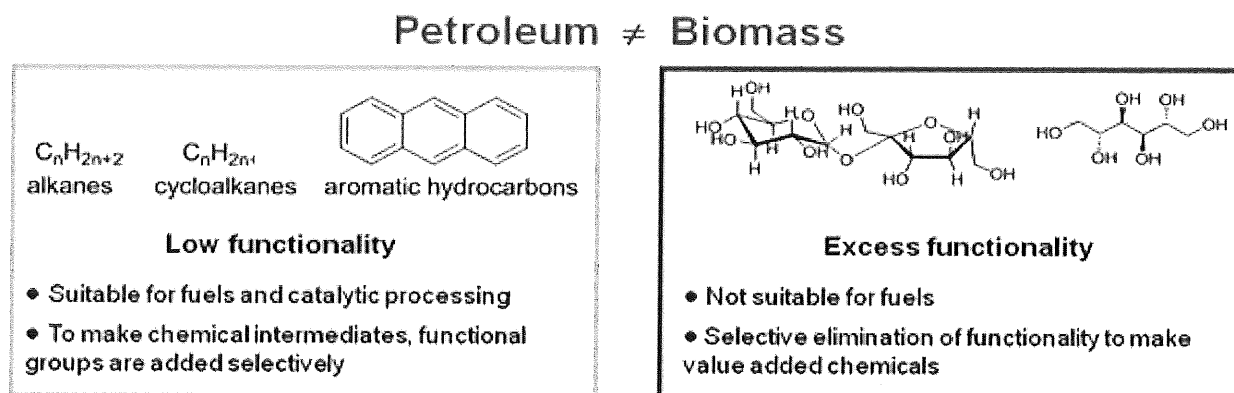
Figure 1.1 Comparison of petroleum and biomass

Biomass feeds contain excess functionality, which complicates their use as fuels and chemicals. In order to develop a biorefinery that can effectively be an alternative to the current industry, efficient methods need to be developed for the transformation of compounds normally found in biomass to value-added chemicals. The conversion of biomass to useful chemicals commonly requires the *removal* of oxygen atoms from the natural precursors. In this context, the deoxygenation of polyhydroxy compounds is an important target.[2] Such reactions are known, but widespread opportunity exists for the development of new deoxygenation processes and for improvement in selectivity and efficiency of the ones that exist. In addition, even for transformations that have so far been developed, little is known about their mechanisms.

We are interested in three-carbon and four-carbon value-added chemicals. We envision the feedstocks for these chemicals to come from the simple polyols glycerol and erythritol instead of the currently used feedstocks of propene and syngas (H_2/CO).

1.2 Glycerol

Glycerol (1,2,3-propanetriol) (**1.1**) is the main byproduct in the triglyceride transesterification process for biodiesel manufacture (**Figure 1.2**).[3] The recent market expansion of biomass-derived fuels has resulted in an increase in glycerol production with a subsequent drop in price, rendering it extremely attractive as a starting material for the synthesis of more valuable chemicals.[4]

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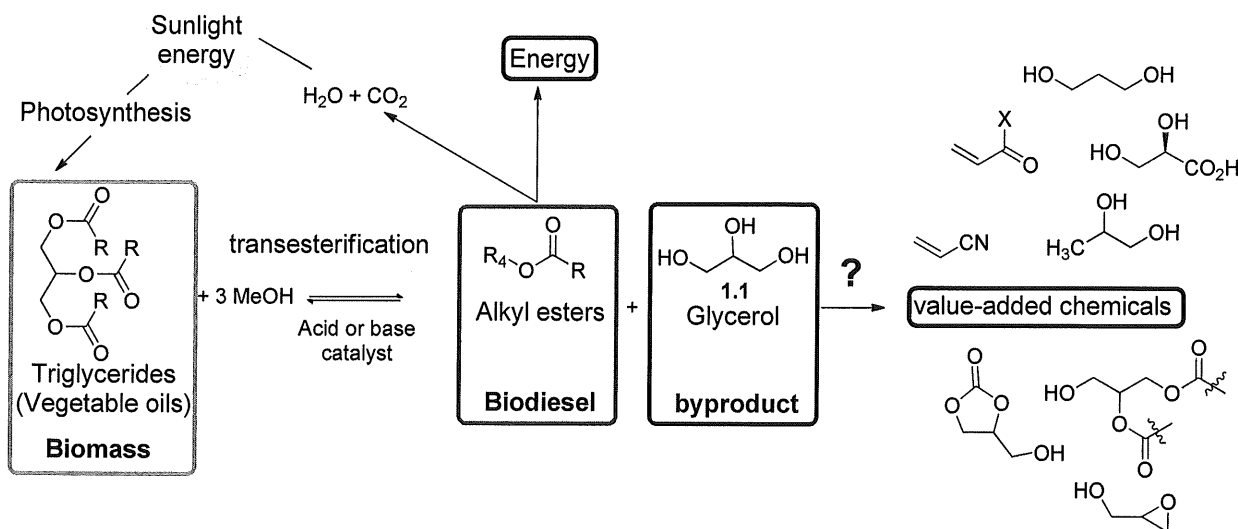
Figure 1.2 Glycerol as a byproduct in the biodiesel manufacture and potential source of value-added chemicals

This triol could be a useful feedstock for some of the chemical industry's most important monomers: acrolein (**1.2**), epichlorohydrin (**1.3**), 1,3-propanediol (**1.4**) and allyl alcohol (**1.5**) (**Figure 1.3**).
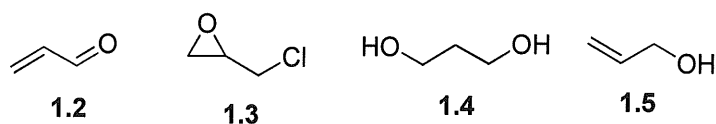
Figure 1.3 Three-carbon value-added chemicals

1.2.1 Acrolein

Glycerol is known to undergo proton-catalyzed dehydration reactions in the presence of solid acid catalysts[5] to afford the unsaturated aldehyde acrolein (**1.2**) (**Scheme 1.1**). Acrolein can be used as an intermediate for making acrylic acid and a variety of other useful industrial compounds.[6] According to *Organic Syntheses*, dehydration of glycerol at 200 °C in the presence of potassium bisulfate and potassium sulfate forms acrolein in 45% yield.[7] Dehydration of glycerol to acrolein has also been accomplished in supercritical water with selectivity as high as 75%.[8a,b] Though these processes convert glycerol to acrolein, the mechanism of reaction is difficult to study.[8c] One of the goals of our project is to develop a method of deoxygenation amenable to mechanistic probing.
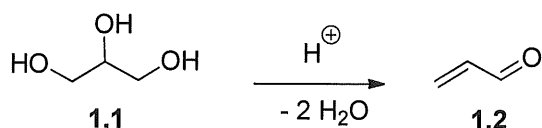
Scheme 1.1 Acid-catalyzed dehydration of glycerol

1.2.2 Epichlorohydrin

Epichlorohydrin (**1.3**) is a reactive compound commonly used for the synthesis of diglycidyl ethers of bisphenol A (DGEBA) (**Scheme 1.2**).[9] These DGEBA polymers are used for coatings, castings, tooling, flooring, adhesives and composites.[9] Before 2006, epichlorohydrin was produced using two major synthetic schemes starting from the petroleum derived 3-carbon compound, propene (**Scheme 1.3**).[9,10] In 2006, the Solvay process was developed which employed glycerol (**1.1**) as the starting material for the synthesis of **1.3** (**Scheme 1.4**).[11]
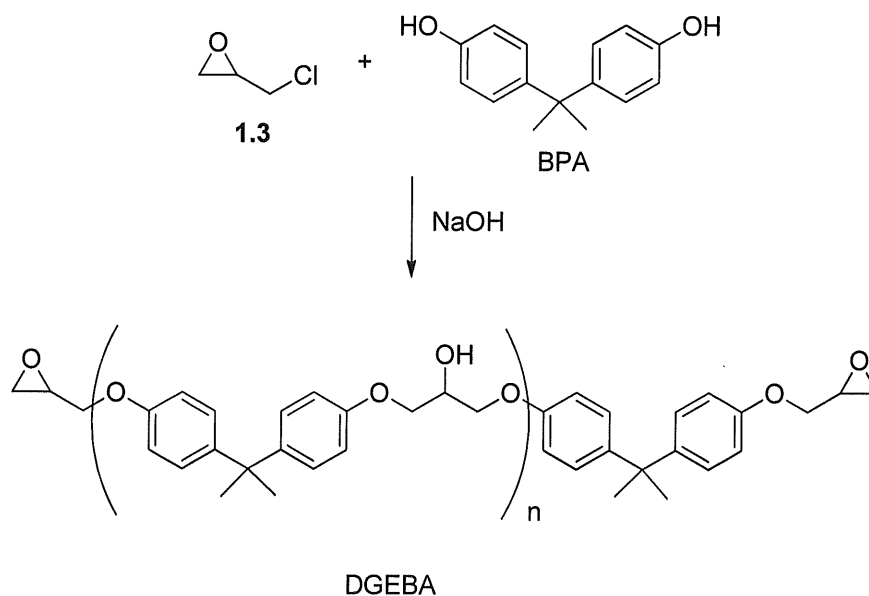
Scheme 1.2 Incorporation of **1.3** into the polymer DGEBA

(a) DOW process
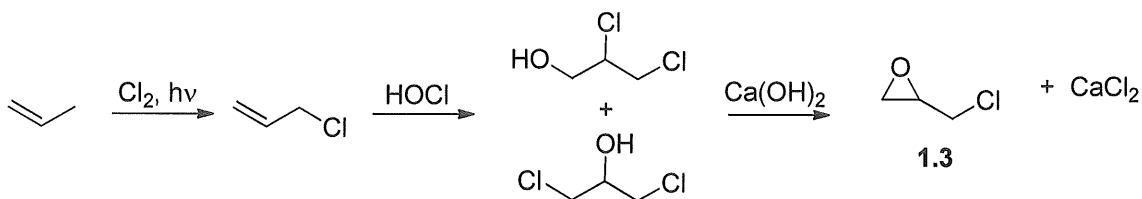
(b) Showa Denko K.K. process
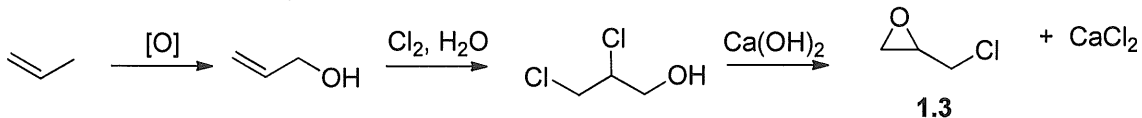
Scheme 1.3 Synthesis of **1.3** from propylene

3
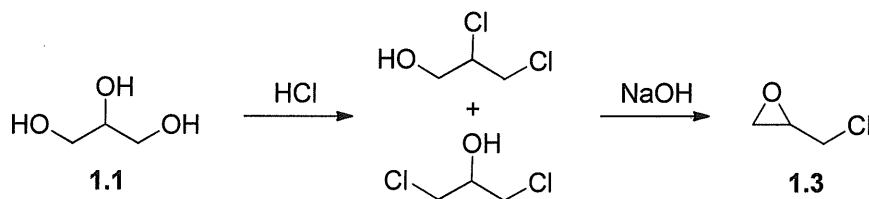
Scheme 1.4 Synthesis of **1.3** from glycerol (Solvay process)

1.2.3 1,3-Propanediol

1,3-Propanediol (**1.4**) is prevalent in the polymer industry as a chain extender for urethane based polymers, sealer and primer.[12] The auto industry also utilizes **1.4** as an additive to diesel engines to limit unburned fuel as well as an additive to coolant systems to increase efficiency.[12] This use of this chemical has increased over the past two decades due to lower production costs.[12]

There are currently three major production processes for **1.4** (**Scheme 1.5**). The Shell Chemical Company utilizes hydroformylation of ethylene oxide (*a*, **Scheme 1.5**),[13a] Dupont hydrates acrolein and hydrogenates the aldehyde product (*b*, **Scheme 1.5**),[13b] and a new fermentation of glycerol by *Clostridium butyricum* (*c*, **Scheme 1.5**).[13c] The Shell process proceeds in 80% yield based on the starting ethylene oxide and produced 45,000 tons of **1.4** in 1999.[13a] The Dupont process proceeds in 65% yield based on acrolein (**1.2**) and produced 9,000 tons of **1.4** in 1999.[13b] The fermentation process has not been widely adopted for production of 1,3-propanediol due to the production rate of 55 g of product per liter of media per hour.[13c]

(a) Shell Chemical Company process
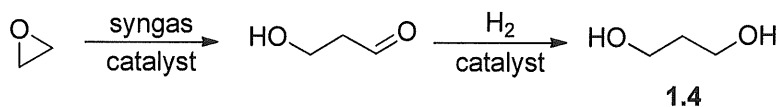
(b) Dupont process
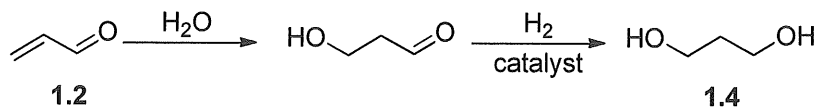
(c) Fermentation process
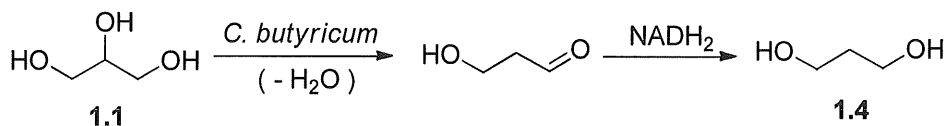
Scheme 1.5 Industrial processes for the production of **1.4**

1.2.4 Allyl alcohol

Allyl alcohol (**1.5**) has been a versatile molecule in the chemical industry for the past 60 years. Before 1985, **1.5** was used as the starting chemical for glycerol production (Daicel Chemical Company) and as a monomer for diethylene glycol bis(allyl

4

carbonate), a plastic used in optical lenses.[14] Early in 1985, Showa Denko K.K. began production of epichlorohydrin (**1.3**) from allyl alcohol.[10,14] In the 1990s, ARCO Chemical Company began production of 1,4-butanediol using **1.5** as the feedstock; the process produces 35 thousand tons of 1,4-butanediol per year, consuming tens of thousands of tons of **1.5**.[14]

There have been 4 major processes responsible for industrial production of **1.5** (**Scheme 1.6**). In the early 1950s, two competing processes were used: hydrolysis of allyl chloride (*a,* **Scheme 1.6**)[15] and acrolein reduction (*b,* **Scheme 1.6**).[16] These two processes were supplanted in 1973 by the lithium phosphate-promoted isomerization of propylene oxide (*c,* **Scheme 1.6**).[16] Since 1985, the major process for allyl alcohol production has been the hydrolysis of allyl acetate (Showa Denko K.K., *d,* **Scheme 1.6**).[17]

(a) Allyl Chloride hydrolysis
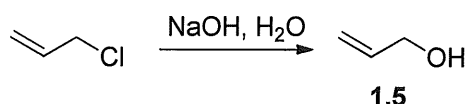
(b) Propylene oxidation
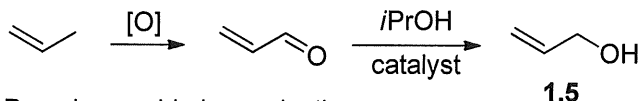
(c) Propylene oxide isomerization
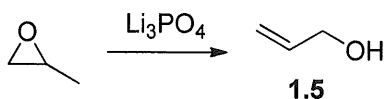
(d) Showa Denko K.K. process
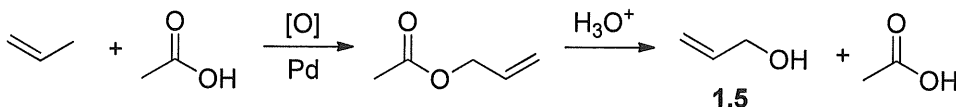
Scheme 1.6 Industrial processes for the production of **1.5**

These four industrially relevant 3-carbon products could all be produced from the defunctionalization of glycerol instead of the functionalization of propylene. In subsequent chapters, our research results will show that allyl alcohol can be obtained from the didehydroxylation of glycerol in two different processes: (1) reaction with formic acid and (2) reaction with catalytic rhenium complexes.

1.3 Erythritol

Erythritol (**1.6, Figure 1.4**) is a 4-carbon tetritol currently used in Japan as a low-calorie sweetener.[18] The main source of this molecule is via biological fermentation. The two organisms used to biosynthesize **1.6** are *Torula utilis* and *Aspergillus niger*.[19] *T. utilis* converts 6.5% glucose feed into **1.6** while *A. niger* converts sodium acetate into erythritol in 8% yield but with very low selectivity.[19b]

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Figure 1.4 Erythritol (**1.6**), tetrahydrofuran (**1.7**) and 2,5-dihydrofuran (**1.8**)

This highly oxygenated carbon source could be a useful feedstock for some of the chemical industry's most important cyclic ethers, tetrahydrofuran (THF, **1.7**) and 2,5-dihydrofuran (**1.8**) (**Figure 1.4**).

1.3.1 Tetrahydrofuran

Cyclic ether functionalities are prone to acid-catalyzed ring opening. The industrial process for the fabrication of Spandex utilizes the acid-catalyzed ring opening of THF (**1.7**) to form poly(tetramethylene ether) glycol, PTMEG (**1.9**, **Scheme 1.7**), a large component of the polymer.[20] The consumption of THF as a solvent in experimental research accounts for less than 1% of the worldwide supply.[21]

Scheme 1.7 Acid-catalyzed ring opening and polymerization of **1.7**

The most prevalent synthesis of **1.7** is the acid-catalyzed dehydrative cyclization of 1,4-butanediol (**1.10**) (**a, Scheme 1.8**).[20] Dupont produces THF via hydrogenation of maleic anhydride (**b, Scheme 1.8**).[21] It was shown in 1943 that furan could be hydrogenated to THF at high temperatures and pressures, though this process has not been employed industrially (**c, Scheme 1.8**).[22] Furan is an attractive feedstock for THF because it can be synthesized from biologically produced pentoses.[20]

6

(a) Dehydrative cyclization

1.10

catalyst

1.7

(b) Dupont process

[O] catalyst

[H] catalyst

1.7

(c) Furan reduction

[H] catalyst

1.7

Scheme 1.8 Syntheses of THF

1.3.2 **2,5-Dihydrofuran**

2,5-Dihydrofuran and its analogues are building blocks for the pharmaceutical and commodity chemical industries.[23-26] 2,5-Dihydrofuran (**1.8**) is used as a polymerization chain transfer agent in the production of copolymer latex.[23] It can also be hydrogenated to yield **1.7**, the previously discussed commodity chemical THF.[24]

Ring closing metathesis of diallyl ether has been shown to give high yields of **1.8** (*a*, **Scheme 1.9**).[25] Industrially, the catalytic rearrangement of vinyl oxirane is used to produce **1.8** (*b*, **Scheme 1.9**).[26] Our research will show that **1.8** can be synthesized directly from erythritol via formic acid-mediated cyclization and didehydroxylation.

(a) Ring closing metathesis (RCM)

[Ru]

1.8
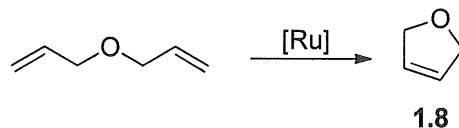
(b) Isomerization of vinyl oxirane

catalyst

1.8
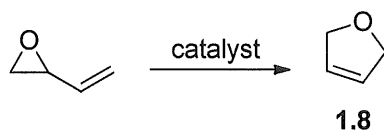
Scheme 1.9 Syntheses of DHF (**1.8**)

1.4 Synthetic stoichiometric defunctionalization of diols

The easiest compounds to isolate from natural sources are carbohydrates, compounds with numerous vicinal diol moieties. There are relatively few synthetic methods capable of removing this functionality (**Scheme 1.10**).[27] The Corey-Winter reaction (*a*, **Scheme 1.10**)[27e] defunctionalizes a diol by first converting the starting material into a xanthate, followed by phosphine-promoted reduction of the xanthate to yield an alkene, CO_2, and a phosphinesulfide. The first didehydroxylation of a vicinal diol was accomplished with titanium metal in THF solution (*b*, **Scheme 1.10**).[27f]

(a) Corey-Winter olefination
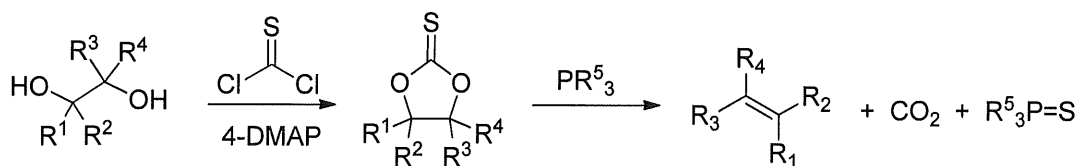
(b) Titanium promoted olefination
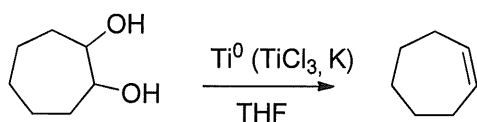
Scheme 1.10 Literature examples of methods for the didehydroxylation of vicinal diols to olefins[27e,f]

1.5 Rhenium-catalyzed defunctionalization of diols

There are three literature reports of catalytic conversion of vicinal diols to alkenes using rhenium catalysts.[28] The first rhenium-catalyzed defunctionalization of a diol was reported in 1996.[28a] In the presence of catalytic Cp*ReO_3 and stoichiometric PPh_3, a variety of diols were reduced to alkenes (**Figure 1.5**). The authors proposed a mechanism involving condensation of the diol onto the rhenium center to form a diolate, followed by thermal decomposition of the diolate to an alkene and an oxidized rhenium center. Their rhenium catalyst was then reduced to its active form by PPh_3.
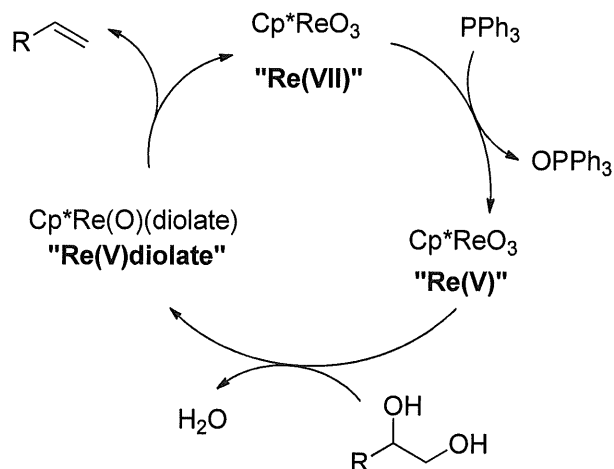
Figure 1.5 Cp*ReO$_3$ catalyzed didehydroxylation of vicinal diols[28a]

More recently, MeReO$_3$ has been shown to deoxygenate epoxides and diols in the presence of H$_2$ gas (**Figure 1.6**).[28b,c] This process is synthetically preferable to the Cp*ReO$_3$ catalyzed process because there is no high molecular weight waste product. The problem with this method is the over reduction of the substrates to alkanes. The rhenium center was competent at reducing alkenes to alkanes under the reducing conditions.
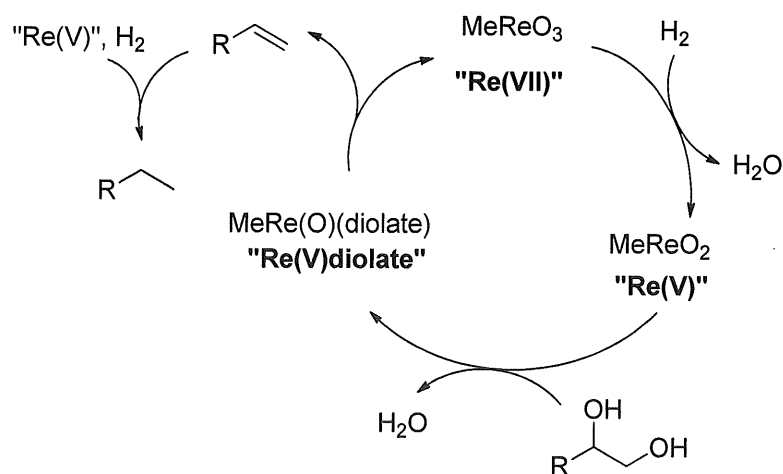
Figure 1.6 MeReO$_3$ catalyzed didehydroxylation of vicinal diols[28b,c]

Upon reaction with air at high temperatures, Re$_2$CO$_{10}$ has been shown to reduce vicinal diols to alkenes with a large aliphatic alcohol as the terminal reductant.[28d] A wide variety of biologically relevant polyols were converted to alkenes, including shikimic acid (**1.11**) to benzoic acid (**1.12**) (**Table 1.1**). One of our research goals was to expand upon this method and identify a catalytic system that could be studied mechanistically.
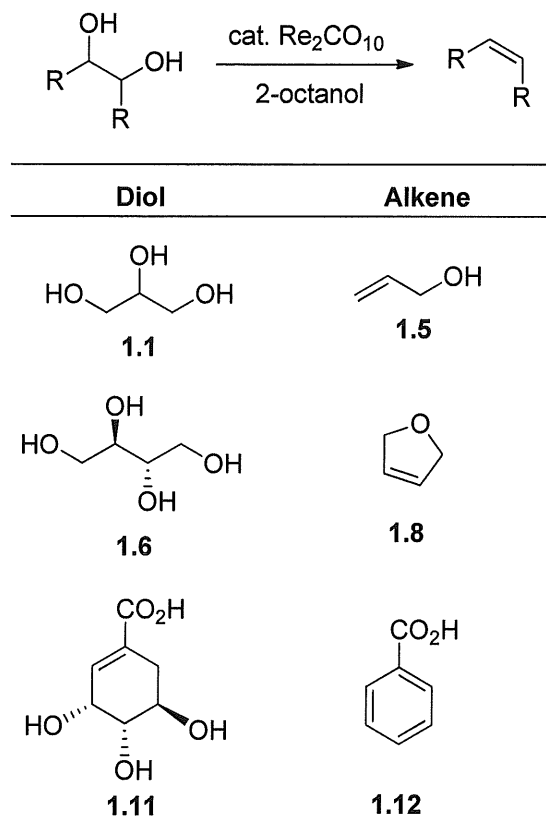
Table 1.1 Re_2CO_{10} catalyzed conversion of biologically relevant diols to alkenes[28d]

Our overall goal in this project is to further develop the body of reactions capable of defunctionalizing highly oxygenated molecules, with a focus on application towards biologically relevant substrates. In the following chapters we will discuss the results of our work in formic acid-mediated didehydroxylations and our efforts to develop a spectroscopically observable oxo rhenium-catalyzed defunctionalization of diols and epoxides.

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2. Formic Acid-Mediated Deoxygenation of Vicinal Diols : Reaction Development and Mechanistic Studies

2.1 Background – Development of formic acid-mediated didehydroxylation of vicinal diols (Dr. Elena Arceo)[1]

In the course of our investigation of the acid-catalyzed dehydration of glycerol (**2.1**), we developed a practical process for the production of allyl alcohol (**2.3**). Allyl alcohol is currently made from propylene; it is used as a starting material in the manufacture of various polymers, pharmaceuticals, pesticides and as a chemical intermediate in the preparation of 1,4-butanediol, 2-methyl-1,3-propanediol, allyl diglycol carbonate, allyl glycidyl ether, allyl methacrylate or triallyl cyanurate.[2]

Currently there is no industrial process for the large-scale preparation of allyl alcohol from glycerol. Earlier studies[3] reported substantial charring during the treatment of glycerol with formic acid (**2.2**). We have now found that running the reaction in an inert atmosphere provided a much more tractable process. Specifically, treatment of glycerol with formic acid while directing a stream of nitrogen through the reaction mixture completely eliminated charring. The method thus substantially improved the yield and selectivity of the process (**Figure 2.1**).

$$HO\!\!-\!\!CH_2\!\!-\!\!CH(OH)\!\!-\!\!CH_2\!\!-\!\!OH \quad \xrightarrow[230\text{-}240^{\circ}C]{\substack{HCO_2H \\ \textbf{2.2}}} \quad CO_2 \;/\; CH_2\!\!=\!\!CH\!\!-\!\!CH_2\!\!-\!\!OR$$

2.1

2.3 R: H
2.4 R: (CO)H

50 mmol (4.6 g)

Three additions of **2.2**:
1) 29.6 mmol
2) 21.1 mmol
3) 21.1 mmol
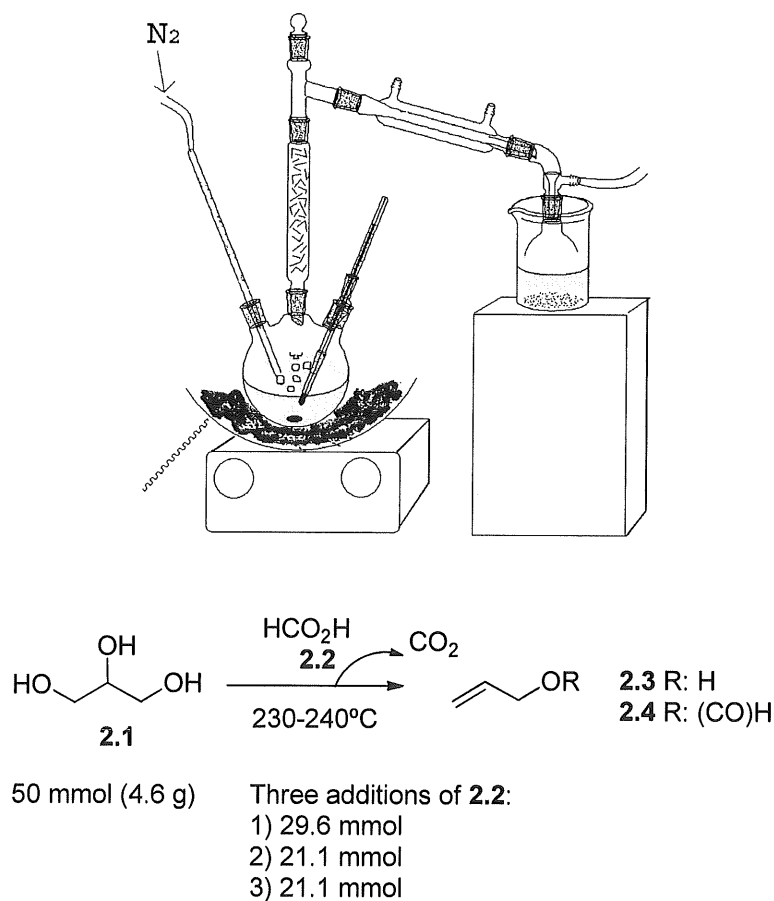
Figure 2.1 Experimental setup for the formic acid-mediated didehydroxylation of glycerol.

By continuously removing the sensitive alcohol product (the most volatile component of the reaction mixture) by distillation, the high temperature was maintained while the reaction proceeded nearly to completion, resulting in a yield of 80% after purification by distillation over K_2CO_3. In addition to protecting the product from atmospheric oxidation, sparging the reaction with nitrogen facilitated distillation of the alcohol.

The reaction of glycerol and formic acid following this procedure gave a very clean distillate that contained allyl alcohol, allyl formate, formic acid and water (**Figure 2.2**). No other products were detected. The reaction was carried out starting with different amounts of glycerol (10, 50, 150 mmol) and using the same procedure in order to prove scalability. The yields were 80-90% after purification by distillation. Even at a relatively large scale (0.5 kg; 5.4 mol) the reaction provided the allyl alcohol product in high yield (86%).
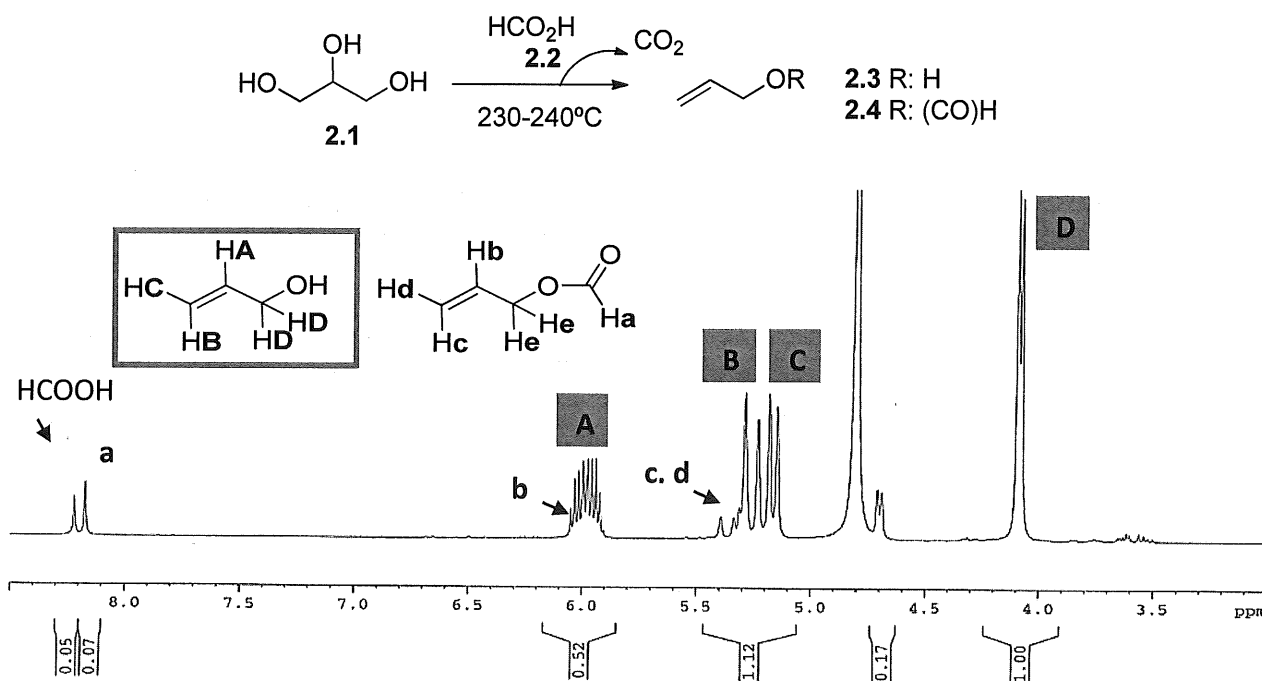
Figure 2.2. ^1H NMR spectrum of the distillate obtained in the formic acid-mediated didehydroxylation of glycerol

With respect to the mechanism of this reaction, our first hypothesis (**Figure 2.3**) proposed initial acid-induced dehydration of glycerol to acrolein via a 1,2-hydride shift pathway, followed by reduction of the aldehyde carbonyl group by formic acid. This reduction step is consistent with the well-documented role of formic acid as a hydride donor.[4]
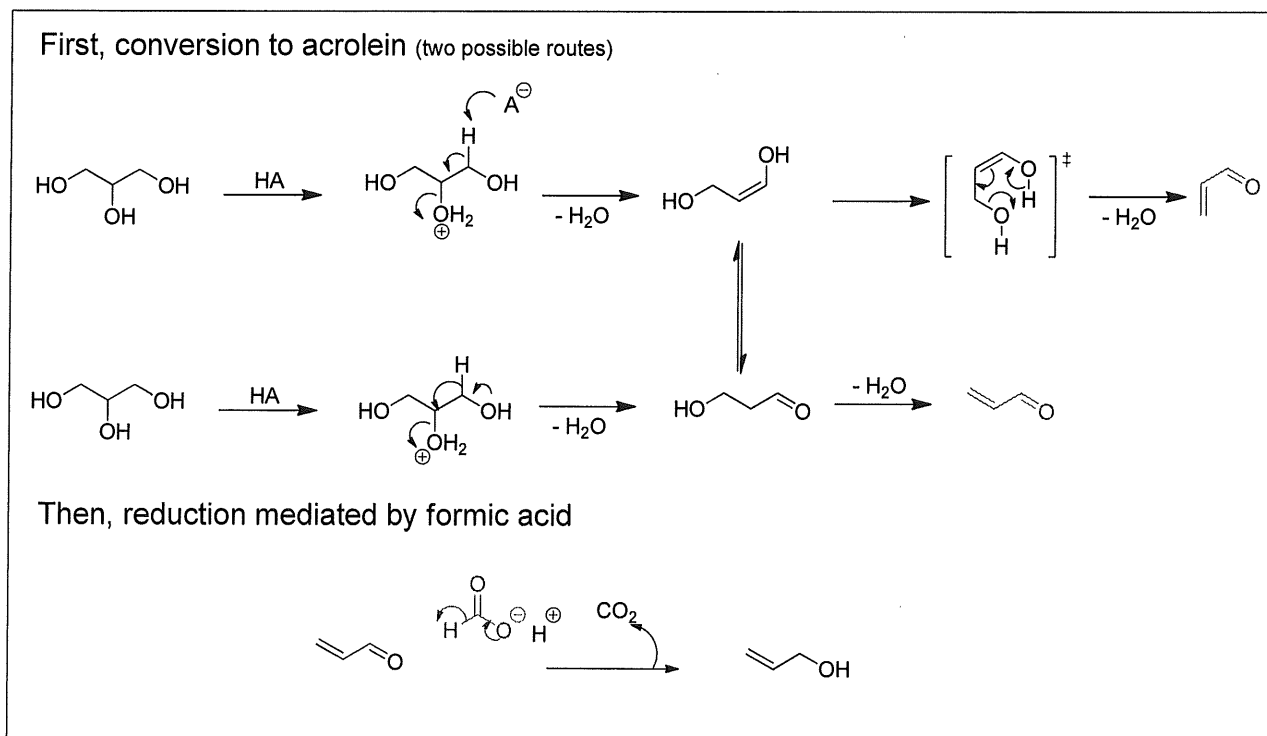
Figure 2.3 First hypothesis about the mechanism

In order to test this hypothesis, we carried out isotopic labeling experiments using deuterated glycerol ([1,1,2,3,3-^{2}H$_5$]glycerol) (**2.1.d$_5$**) or deuterated formic acid ([^{2}H$_2$]-formic acid) (**2.2.d$_2$**) (**Figure 2.4**). The incorporation of deuterium in the final product was monitored by ^{2}H-Nuclear Magnetic Resonance (NMR) spectroscopy.

First, **2.1.d$_5$** was treated with **2.2** and, surprisingly, *no* protons were incorporated from the supposed reducing agent formic acid into the product alcohol. Instead, the allyl alcohol product was completely deuterated at all carbon positions (**2.3.d$_5$**) (**Figure 2.4, a'**). Similarly, when **2.2.d$_2$** was employed in the reaction with non-labeled **2.1**, no deuterium was incorporated in the final product (**2.3**), except for the exchange of deuterium into the hydroxyl group (**2.3.d$_1$**) and the formyl proton of the minor allyl ester **2.4.d$_1$** (**Figure 2.4, b'**). This isotopic labeling study revealed that there was no hydride transfer from formic acid and disproved our proposed mechanism.

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Predicted from initially proposed mechanism

a)

2.1.d$_5$

2.2
────────
230-240 °C

R: H, (CO)H

b)

2.1

2.2.d$_2$
────────
230-240 °C

R: H, (CO)D

Experimental outcome

a')

2.1.d$_5$

2.2
────────
230-240 °C

2.3.d$_5$ R: H

2.4.d$_5$ R: (CO)H

b')

2.1

2.2.d$_2$
────────
230-240 °C

2.3 R': H
2.3.d$_1$ R': D

+

2.4.d$_1$
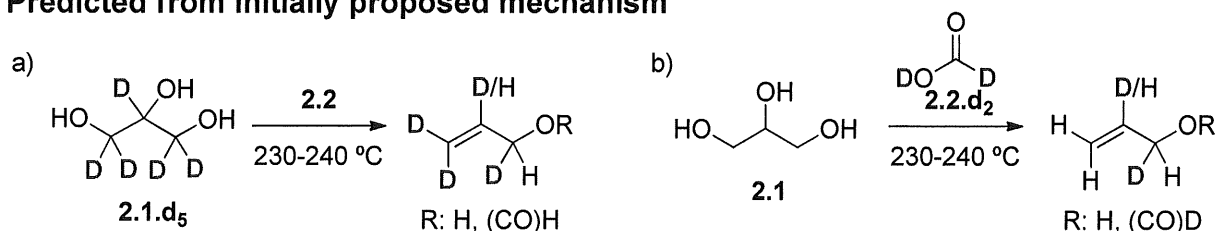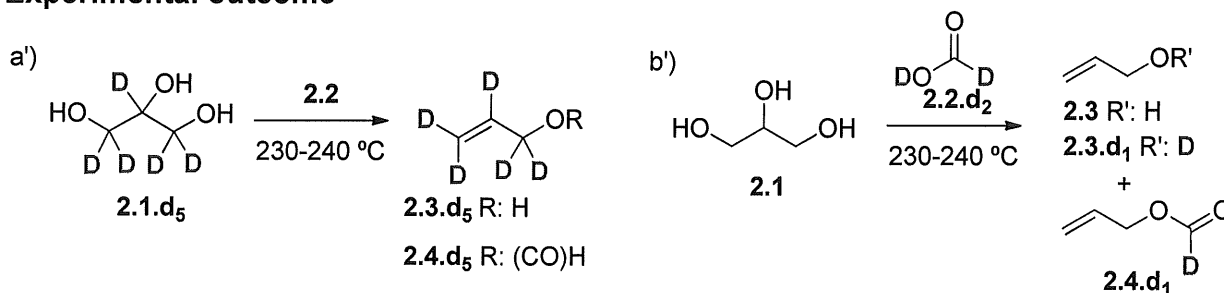
Figure 2.4 Isotopic labeling experiments

We concluded from the above labeling experiments that formic acid was somehow inducing a direct removal of two hydroxy groups (a didehydroxylation reaction) from glycerol. To examine the generality of this deoxygenation process, we investigated the reaction of several simple diols following the procedure discussed above.

The reaction was found applicable in the case of 1,2-diols such as 1,2-octanediol (**2.5**) and 1,2-decanediol (**2.6**) which smoothly underwent conversion to the corresponding alkenes in yields over 90%. Cyclic diols including cis-1,2-cyclopentanediol (**2.7**), cis-1,2-hexanediol (**2.8**) and cis-1,2-cyclooctanediol (**2.9**) afforded the corresponding cyclic olefins in high yields. Treatment of trihydroxy compounds (1,2,3-hexanetriol (**2.10**) and 1,2,6-trihydroxyhexane (**2.11**) with formic acid at elevated temperatures also led to the corresponding alkenes **2.17** and **2.18** (**Scheme 2.1**).

2.5 n=5
2.6 n=7

2.12 n=5 (91%)
2.13 n=7 (93%)

HCO$_2$H
────────
230 °C

2.7 n=1
2.8 n=2
2.9 n=4

2.14 n=1 (86%)
2.15 n=2 (78%)
2.16 n=4 (96%)

2.10

2.11

HCO$_2$H
────────
230 °C

2.17 (56%)

2.18 (84%)
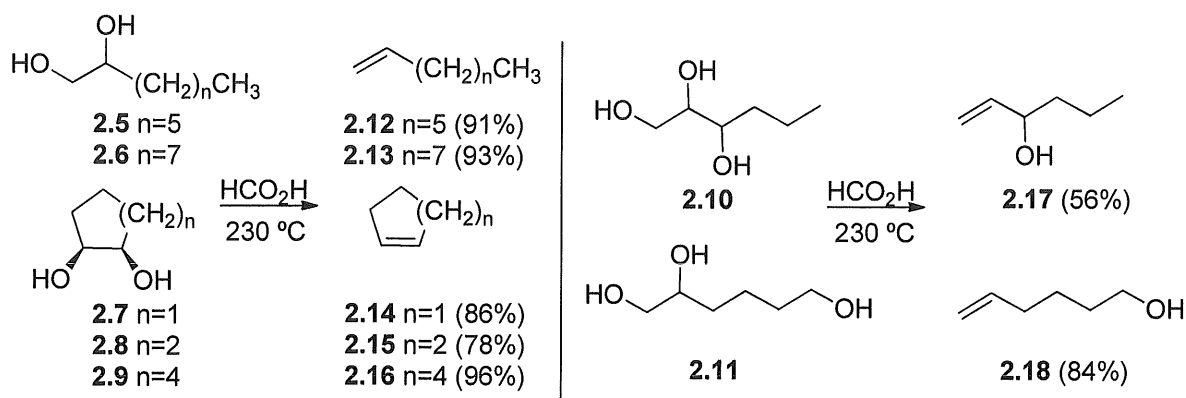
Scheme 2.1 Formic acid-mediated didehydroxylation of diols and triols

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The reaction was also found applicable to those diols (i.e. **2.19** and **2.20**, **Scheme 2.2**) for which the alkene products are high boiling compounds (**2.21** and **2.22**). In such cases, the alkene did not distill (just water and formic acid would distill) and the product was obtained by extraction from the reaction mixture. In the last example in **Scheme 2.2**, the sensitive olefin styrene (**2.24**) was synthesized in good yield from the corresponding diol (**2.23**).

a)

HO
OH
$(CH_2)_9CH_3$
2.19

$\xrightarrow[230\ ^\circ C]{HCO_2H}$

$(CH_2)_9CH_3$
2.21

bp 214°C

HO
OH
$(CH_2)_{11}CH_3$
2.20

$\xrightarrow[230\ ^\circ C]{HCO_2H}$

$(CH_2)_{11}CH_3$
2.22

bp 251°C

b)

OH
OH
2.23

$\xrightarrow[230\ ^\circ C]{HCO_2H}$

2.24
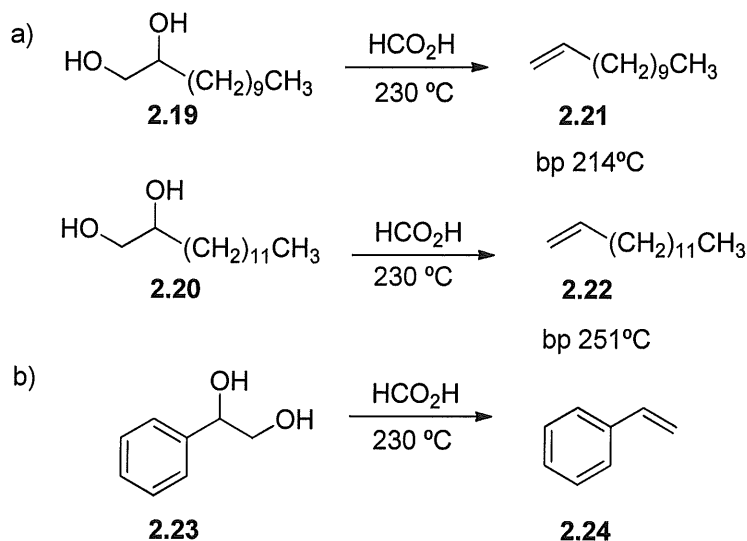
Scheme 2.2. Formation of products with high boiling points

Deoxygenation of diols to produce olefins is a useful synthetic transformation. There are several methods for the generation of unsaturated compounds from simple vicinal diols.[5] Most of these procedures first require transformation of the vicinal diol into an activated group, which is subsequently converted into an olefin in a further step (**Figure 2.5**). The formic acid-mediated didehydroxylation provides a one-step and simple procedure that directly affords the alkenes in high yield and purity.

(a) Corey-Winter olefination

HO
R^3 R^4
R^1 R^2
OH

$\xrightarrow[\text{4-DMAP}]{}$

$\underset{S}{\overset{\|}{C}}$
Cl   Cl

O   O
R^1 R^4
R^2 R^3

$\xrightarrow{PR^5_3}$

R_4
R_3 R_2
R_1

$+ CO_2 + R^5_3P{=}S$

(b) Titanium promoted olefination

OH
OH

$\xrightarrow[\text{THF}]{Ti^0\ (TiCl_3,\ K)}$
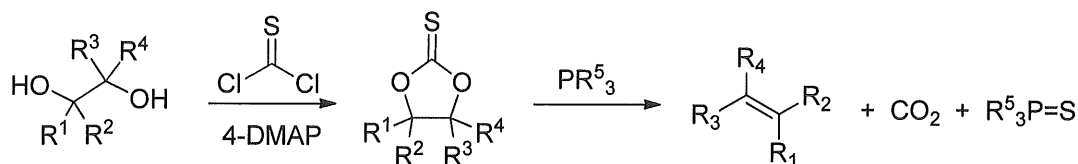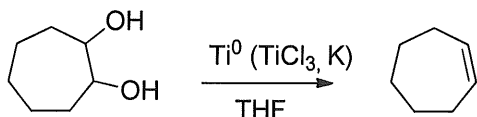
Figure 2.5 Literature examples of methods for the didehydroxylation of diols to olefins[6]

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We believe that the formic acid-mediated didehydroxylation proceeds through an orthoester-type intermediate, a hypothesis inspired by Eastwood's procedure for the conversion of vicinal diols to olefins using triethyl orthoformate and acetic anhydride[7] and by the thermal decomposition observed for 2-acetoxy-1,3-dioxolanes.[8] A potential mechanism for the formic acid-mediated didehydroxylation of glycerol is given in **Figure 2.6**.

Figure 2.6 Mechanism proposed for the formic acid-mediated didehydroxylation

In the proposed mechanism, the reaction of formic acid and a vicinal diol at high temperature involves the transient formation of a cyclic carbocation intermediate (**c**, **Figure 2.6**) which is resonance-stabilized by the two oxygen atoms vicinal to the cationic center. The preparation and characterization of 1,3-dioxolan-2-ylium ions from *alpha* glycols has been previously described. The most plausible route from the 1,3-dioxolan-2-ylium carbocation to the observed product involves attack of the carbonyl oxygen of formic acid to provide a 2-formyloxy-1,3-dioxolane (**d**, **Figure 2.6**), which then undergoes thermal carbon dioxide elimination and proton transfer to give an olefin and formic acid.

The fact that *cis*-1,2-cyclopentanediol (**2. 7**) reacted cleanly with formic acid at high temperature to yield cyclopentene (**2. 14**), while *trans*-1,2-cyclopentanediol (**2.7'**) did not form the olefin, (**Scheme 2.3**) suggested that the formic acid mediated didehydroxylation is a highly stereospecific reaction based on a *syn* elimination, which is in accordance with the pathway proposed above.

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Scheme 2.3 Stereochemical restriction of starting diol for *cis* orientation

In order to confirm this supposition, we subjected two stereoisomeric internal acyclic 1,2-diols to the reaction. In these experiments we observed that the olefins were formed stereospecifically. Thus, treatment of ($3R^*$, $4R^*$)-decane-3,4-diol (**2.27**) and ($3S^*$, $4R^*$)-decane-3,4-diol (**2.28**) with formic acid proceeded readily and generated the *trans* (**2.29**) and *cis* (**2.30**) isomers of 3-decene respectively (**Scheme 2.4**). Both reactions were stereospecific as observed by ^{1}H NMR spectroscopy of the crude distillates, in which no signals (< 1 %) due to the alkene with the opposite stereochemistry were detected.
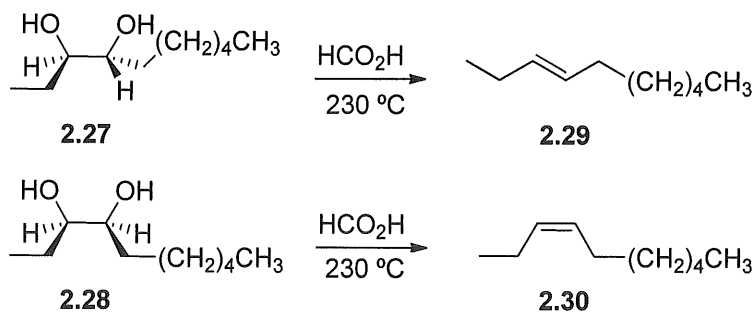

Scheme 2.4 Stereospecific didehydroxylation of diols **2.27** and **2.28**

2.2 Current Results – Didehydroxylation of polyols and biomass derivatives

Our research activity then focused on the application of the didehydroxylation methodology to biomass-related substrates. The experimental results with glycerol and simple diols suggested that the formic acid-mediated didehydroxylation might be extendable to carbohydrates, an economically and environmentally important target. Preliminary results with sugar polyols were very promising. Erythritol (**2. 31**) is a naturally occurring four-carbon tetra-alcohol that is used as a low calorie bulk sweetener

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in the food industry and is accessible through yeast or fungal fermentation of glucose from corn starch[9][16]. The reaction of **2.31** with formic acid at 210-220 °C, following the procedure described above for glycerol, gave a distillate that contained 2,5-dihydrofuran (**2.26**) along with water and formic acid. A 39% yield of the pure dihydrofuran **2.26** was isolated after purification by fractional distillation (**Figure 2.7**).
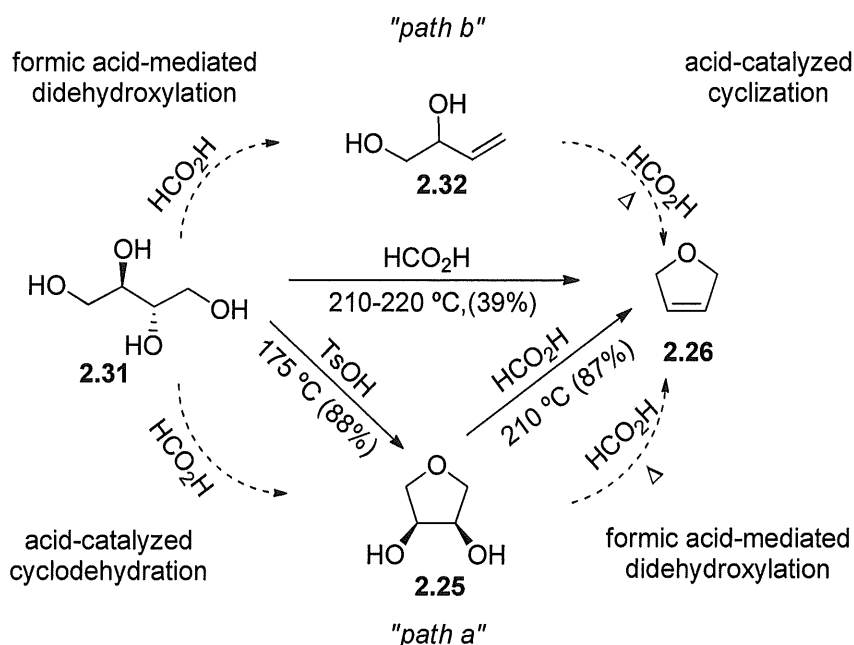
Figure 2.7 Synthesis of 2,5-dihydrofuran (**2.26**) from erythritol (**2.31**) and possible intermediates **2.25** and **2.32** (pathways *a* and *b* respectively)
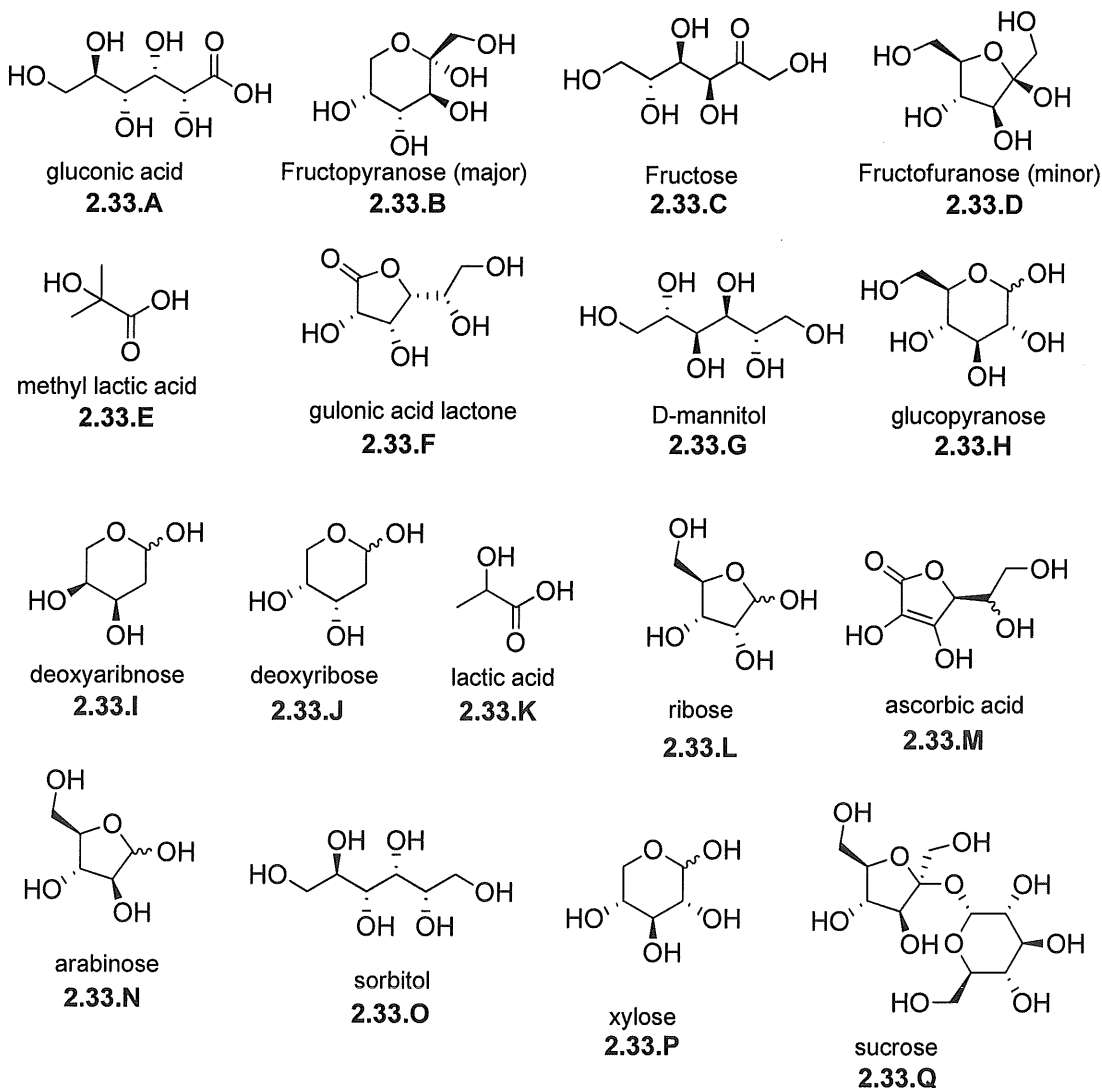
In the presence of an acid catalyst, the initial ring closure condensation of erythritol to 1,4-anhydroerythritol (**2.25**) is highly favored.[10] A conceivable reaction pathway for the conversion to **2.31** involves the formic acid-mediated didehydroxylation of **2.25** in a second step (**Figure 2.7**, *path a*), through an orthoester-type intermediate.

To investigate the course of this reaction, *cis*-1,4-anhydroerythritol (**2.25**) was prepared by acid-catalyzed cyclodehydration of erythritol with *p*-toluenesulfonic acid monohydrate[11] in 88% yield . Formic acid-mediated didehydroxylation of the cyclic product **2.25** afforded the corresponding olefin **2.26** in 87% yield after purification by redistillation. The reaction of 3,4-dihydroxybutene (**2.32**) with formic acid was also investigated, as it is a reasonable potential intermediate in the conversion of erythritol to 2,5-dihydrofuran. If deoxygenation of the vicinal primary and secondary hydroxy groups (through an orthoester-type intermediate) occurred, the diol **2.32** could possibly provide the product **2.26** by acid-catalyzed cyclodehydration (**Figure 2.7**, *path b*). However, as shown in **Figure 2.7**, 3,4-dihydroxybutene did not yield 2,5-dihydrofuran when submitted to our standard formic acid-mediated didehydroxylation conditions, pointing to *path a* as the most plausible reaction pathway.

The transformation of erythritol (**2. 31**) to 2,5-dihydrofuran (**2.26**) is an example of how this reaction could offer an efficient approach to the conversion of biomass to value-added chemicals. 2,5-Dihydrofurans are building blocks for the pharmaceutical

and commodity chemical industry. 2,5-Dihydrofuran (**2.26**) is presently prepared by ring closing metathesis[12] or by catalytic rearrangement of vinyl oxirane[13] and can be used as a polymerization chain transfer agent in the production of copolymer latex[14] and for the preparation of tetrahydrofuran,[15] which is a high volume chemical in the U.S.

A large amount of effort was expended in making this method applicable to higher polyols and sugars, such as sorbitol or glucose. However, these larger polyhydroxy compounds (**2.33.A-Q**) presented serious difficulties regarding the thermal stabilities of the starting materials and possible alkene products (**Figure 2.8**). Each compound present in the figure failed to yield alkene product when submitted to our formic acid-mediated deoxygenation conditions. Below is a representative analysis of the possible reactions of sorbitol (**2.polyhydroxy.O**) under our conditions (**Figure 2.9**)


gluconic acid
2.33.A

Fructopyranose (major)
2.33.B

Fructose
2.33.C

Fructofuranose (minor)
2.33.D

methyl lactic acid
2.33.E

gulonic acid lactone
2.33.F

D-mannitol
2.33.G

glucopyranose
2.33.H

deoxyaribnose
2.33.I

deoxyribose
2.33.J

lactic acid
2.33.K

ribose
2.33.L

ascorbic acid
2.33.M

arabinose
2.33.N

sorbitol
2.33.O

xylose
2.33.P

sucrose
2.33.Q

Figure 2.8. Polyoxygenated bio-molecules incompatible with formic acid-mediated didehydroxylation chemistry

Acid-catalyzed cyclization of **2.33.O** can afford four different products (**Figure 2.9**). Compounds **2.34.A-2.34.C** were purchased and submitted to our formic acid-

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mediated didehydroxylation conditions, with similar results. The starting polyols quickly decomposed, presumably via oligomerization, at 150 °C (60 °C below the necessary temperature for deoxygenation) in the presence or absence of formic acid. Further reaction of the decomposed materials did not lead to alkene products.
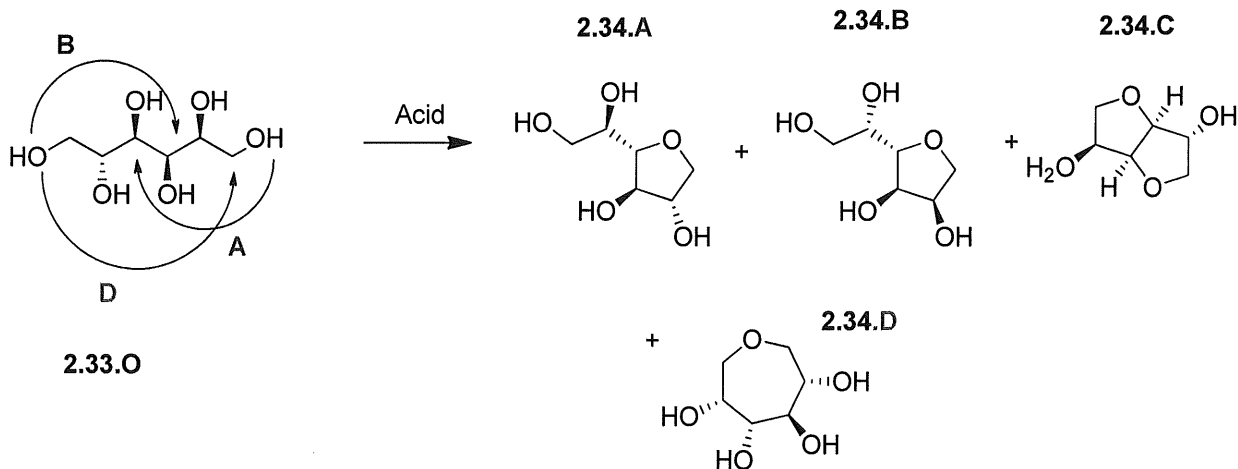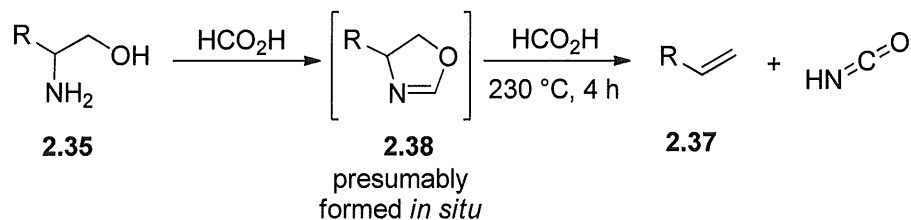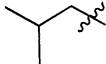

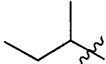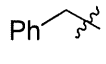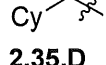**Figure 2.9** Possible cyclic ethers derived from **2.33.O**

We also investigated the reduction of amino acid derivatives to form alkenes. If amino alcohols (**2.35**) derived from amino acids (**2.36**) could undergo dehydroxyamination to alkenes, a wide variety of terminal alkenes (**2.37**) could be synthesized for use in the polymerization industry (**Scheme 2.5**).
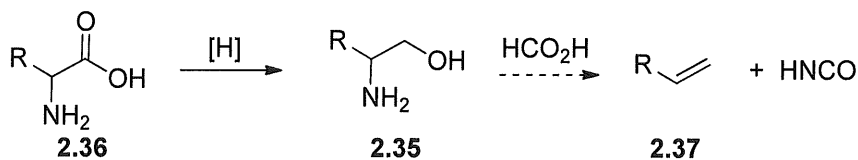
Scheme 2.5 Proposed dehydroxyamination of aminoalcohols derived from amino acids

Four amino alcohols (**2.35.A-D**) were mixed with formic acid, followed by heating to 230 °C under distillation conditions and a nitrogen atmosphere (**Scheme 2.6**). Condensation of amino alcohols with formic acid is known to result in oxazoline products (**2.38**).[16] When amino alcohols (**Table 2.1**) or their corresponding oxazolines (**Table 2.2**) were heated in the presence of formic acid, starting material was consumed but was converted to intractable mixtures rather than to the desired alkene products. We hypothesize that the lack of desired reactivity of these compounds was due to the difficulty in forming isocyanic acid. As a result, the dehydroxyamination approach to alkene generation was concluded at this point.

Scheme: R-CH(NH$_2$)-CH$_2$-OH (**2.35**) + HCO$_2$H → [oxazoline **2.38**, presumably formed *in situ*] → (HCO$_2$H, 230 °C, 4 h) → R-CH=CH$_2$ (**2.37**) + HN=C=O

Entry[a]	R	Conversion[b]	2.37 Yield	Result
1	**2.35.A**	100%	0%	no **2.38.A** observed during reaction or at the end of the reaction
2	**2.35.B**	100%	0%	no **2.38.B** observed during reaction or at the end of the reaction
3	Ph **2.35.C**	100%	0%	no **2.38.C** observed during reaction or at the end of the reaction
4	Cy **2.35.D**	100%	0%	no **2.38.D** observed during reaction or at the end of the reaction

[a] The reactions were run under distillation conditions where N$_2$ gas was bubbled through the reaction mixture. Each reaction contained 15 mmol of substrate. Formic acid was added to the reaction in four 12 mmol additions, one each hour. [b] The conversions were etermined by ^{1}H NMR spectroscopy using 1,3,5-trimethoxybenzene as an internal standard.

Table 2.1 Reactions between amino alcohols **2.35.A-D** and formic acid

	R⟍⟍⟍O		R⟍⟍ + HN=C=O
	N=⟍	HCO₂H / 230 °C, 4 h	
	2.38		**2.37**

Entry[a]	Oxazoline	Conversion[b]	2.37 Yield	Result
1	**2.38.A**	100%	0%	**2.38.A** consumed after first addition of HCO₂H.
2	**2.38.B**	100%	0%	**2.38.B** consumed after first addition of HCO₂H.
3	**2.38.C**	100%	0%	**2.38.C** consumed once reaction temperature reached 130 °C, before first addition of HCO₂H.
4	**2.38.D**	100%	0%	**2.38.D** consumed after first addition of HCO₂H.

[a] The reactions were run under distillation conditions where N_2 gas was bubbled through the reaction mixture. Each reaction contained 15 mmol of substrate. Formic acid was added to the reaction in four 12 mmol additions, one each hour. [b] The conversions were determined by ^1H NMR spectroscopy using 1,3,5-trimethoxy benzene as an internal standard.

Table 2.2 Reactions between oxazolines **2.38.A-D** and formic acid.

2.3 Background – Experiments and calculations of the didehydroxylation of vicinal diols (Dr. Elena Arceo and Dr. Jamin Krinsky)

Figure 2.6 Proposed mechanism for the formic acid-mediated didehydroxylation of glycerol

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In order to demonstrate the capability of the thermal transformation of cyclic orthoesters of type **d** (**Figure 2.6**) to generate a double bond, the synthesis of a 2-acyloxy-1,3-dioxolane from a 2-alkyloxy-1,3-dioxolane was carried out. 1,2-Decanediol (**2.6**) was used as a model diol for this study. The 2-ethoxy-1,3-dioxolane derivative **2.39** of 1,2-decanediol was prepared and subsequently converted to the 2-acetoxy-1,3-dioxolane **2.40** as shown in **Scheme 2.6**.[8] When a mixture of dioxolanes **2.39** and **2.40** was carefully heated, the 2-acetoxy-1,3-dioxolane **2.40** was transformed into the olefin **2.13** at 40-48 °C, while compound **2.39** was unaffected.
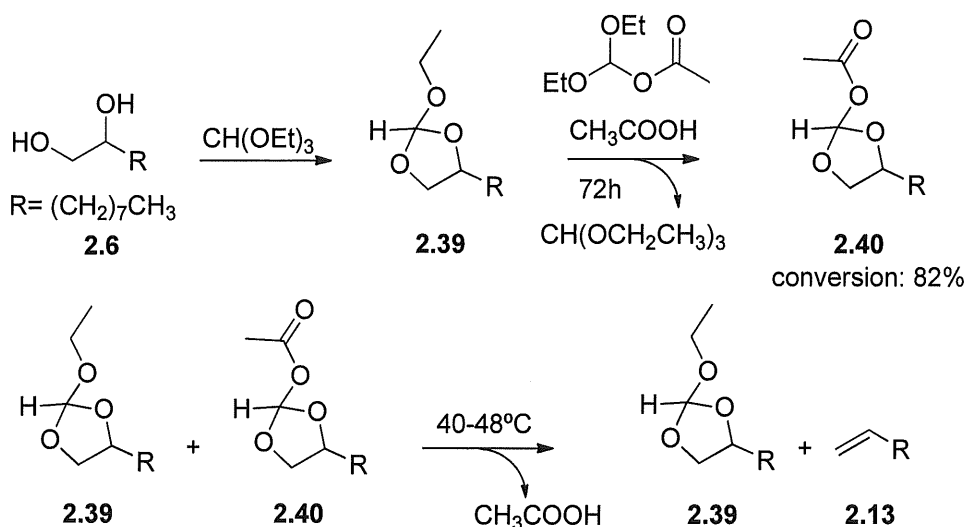
Scheme 2.6 Synthesis and thermal transformation of 2-acetoxy-1,3-dioxolane **2.40**

New insights into the reaction mechanism were provided in computations performed by Dr. Jamin L. Krinsky. DFT calculations were performed on the model compound ethylene glycol. Geometries and frequencies were calculated in the gas phase with B3LYP/6-31+G(d,p) (BS1). Electronic energies were calculated using the PCM (Polarizable Continuum Model) methanol model with B3LYP/6-311++(2df,2p) (BS2, $H_{0K} = E_{elec}(BS2/PCM) + E_{ZPE}(BS1/G.P.)$). Similar results were obtained using the M05-2X functional. A summary of those results are presented in **Figure 2.7**.
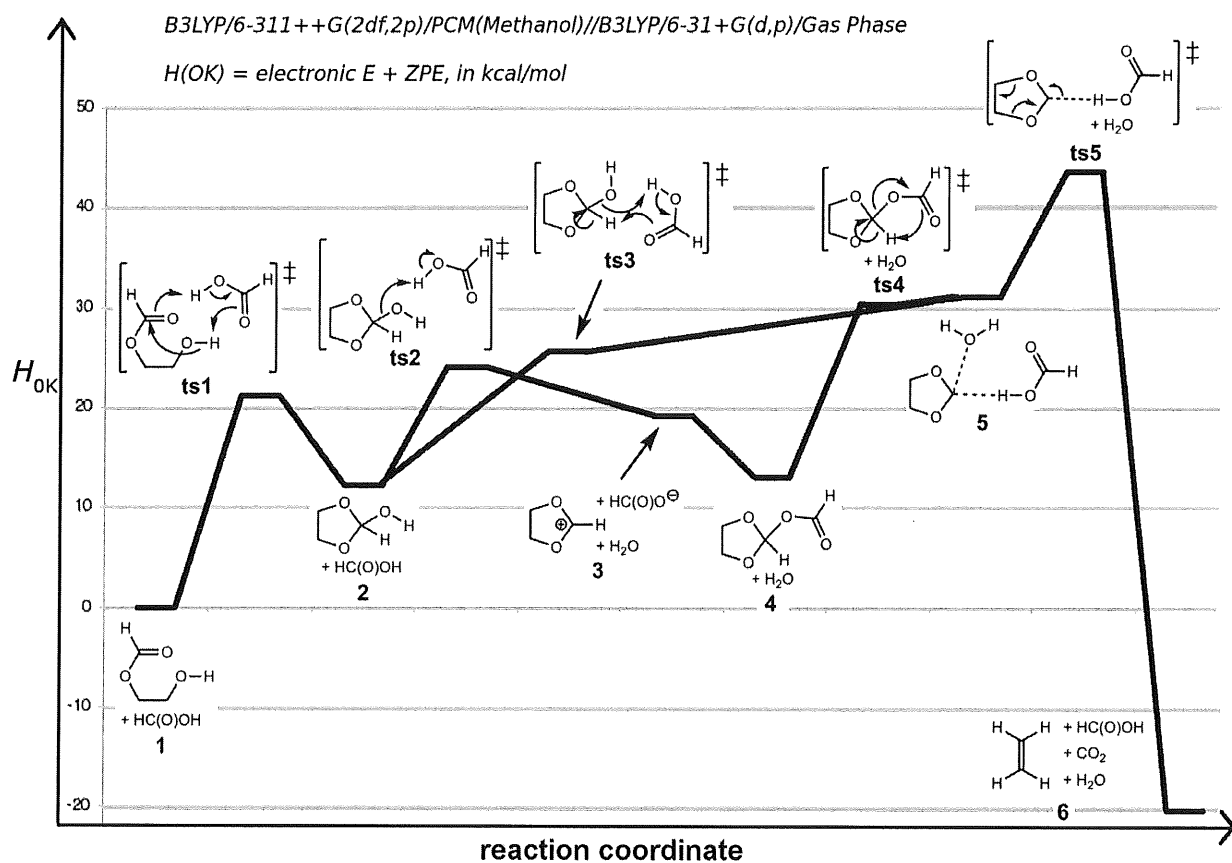
Figure 2.7 Proposed mechanism based on DFT calculations (courtesy Dr. Jamin Krinsky)

The critical difference between the mechanism suggested by the DFT study (**Figure 2.7**) and the previously proposed mechanism (**Figure 2.6**), is that the reaction proceeds through thermolysis of a solvated carbene intermediate species (**5, Figure 2.7**) with extrusion of CO_2 and alkene, instead of through a concerted fragmentation of a 2-formyloxy-1,3-dioxolane species.

There is literature precedent for dioxocarbene thermolysis. Mechanistic studies on the Corey-Winter reaction[17] (1,3-dioxolane-2-thione desulfurization for the synthesis of olefins) suggested the involvement of a carbene and subsequent fragmentation to an olefin. In another example, the halide-catalyzed reaction of carbonyl metal complexes with ethylene oxide gave dioxocarbene complexes[18] and in the case of $Fe(CO)_4$(carbene), the complex decomposed to ethylene and carbon dioxide when heated in methylene chloride.

Another unexpected feature of this new proposed mechanism is the role played by formic acid as a proton shuttle in the transition state **ts1** (**Figure 2.8**), greatly reducing the activation barrier for formation of **2** from **Figure 2.7**. After that step (from **1** to **2**, **Figure 2.7**), the pathway through transition state **ts3** (direct from **2** to **5**) seems to be competitive with the carbocation **3** pathway. All steps in the mechanism, except for the last, are predicted to be reversible unless water is removed. That the intramolecular

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carbene fragmentation appears to be the rate-limiting step suggests that the reaction may not be amenable to further catalysis.
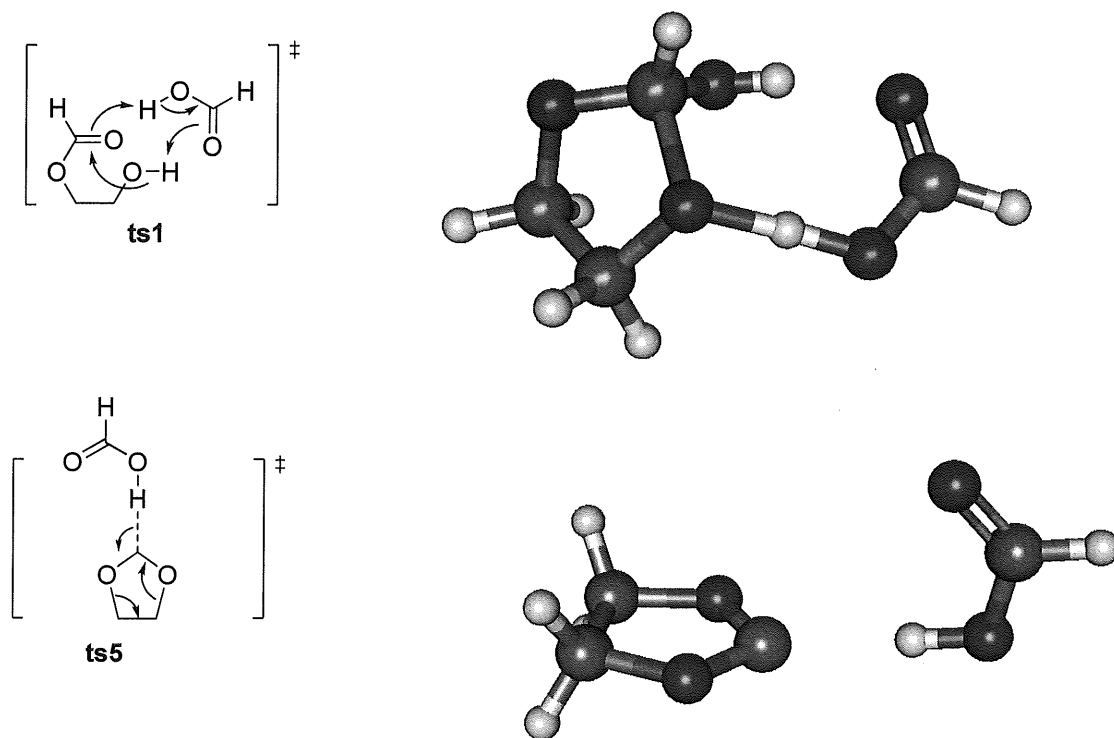

Figure 2.8 Key transition states

2.4 Background - Generation and preliminary studies on a 1,3-dioxolan-2-ylium carbocation (Dr. Elena Arceo)

During the course of our investigation on the mechanism of the formic acid-mediated didehydroxylation, we became interested in studying the independent generation of the proposed carbocation intermediate from a vicinal diol or the corresponding formate esters. There are a few methods for the generation of 1,3-dioxolan-2-ylium carbocations[19][32] (**2.41**, **Figure 2.9**) and other related cations such as 1,3-dioxan-2-ylium, 1,3-oxathiolan- 2-ylium, 1,3-dithiolan-2-ylium, 1,3-dithian-2-ylium and 1,3-oxathian-2-ylium cations. However, the 1,3-dioxolan-2-ylium carbocations in which R=H (**Figure 2.9**) have not been isolated and characterized previously and was therefore an interesting species for us to study, considering our proposed mechanism.
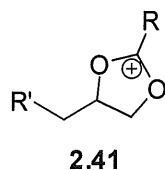
Figure 2.9 1,3-dioxolan-2-ylium cation **2.41**

By using a very strong acid (TfOH: trifluoromethanesulfonic acid), the desired carbocation (**2.42**) from the diformate ester of 1,2-decanediol (**2.43**) was formed (**Scheme 2.9**) . The expected chemical shifts were observed by ^{1}H NMR spectroscopy in experiments conducted at room temperature, neat or in CH_2Cl_2 (**Figure 2.9**).
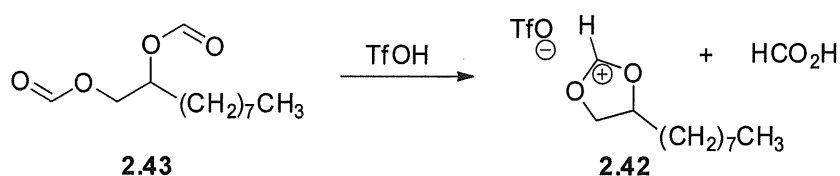

**Scheme 2.9** Formation of 1,3-dioxolan-2-ylium cation (**2.42**) of 1,2-decanediformate (**2.43**)
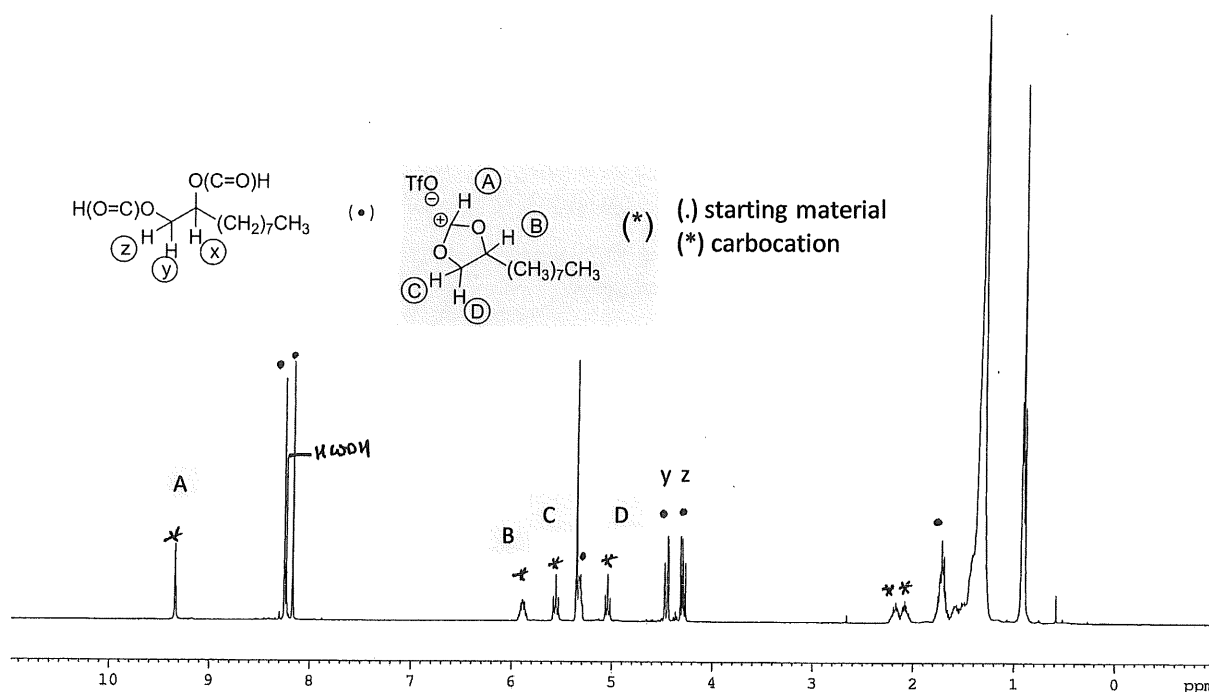
Figure 2.9 ^{1}H NMR (CD_2Cl_2) of an aliquot from the reaction between **2.43** and TfOH, at intermediate conversion to **2.42**

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Several attempts to precipitate the carbocation as its triflate salt were performed, in order to obtain a crystal structure for further characterization and to isolate the compound for additional studies. However, precipitation in different solvents (such as pentane and CCl_4) did not occur, even at low temperatures. Efforts to exchange the triflate anion with BF_4^-, ClO_4^- or $BArF_{24}^-$ were unproductive. Also, **2.42.Sb** could be generated with $SbCl_5$ in CH_2Cl_2 (**Scheme 2.7**) from **2.43** (**Figure 2.10**). However, none of these approaches afforded the desired solid.
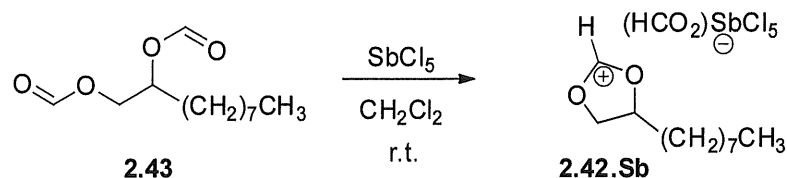
**Scheme 2.7** Formation of **2.42.Sb** from **2.43** using $SbCl_5$
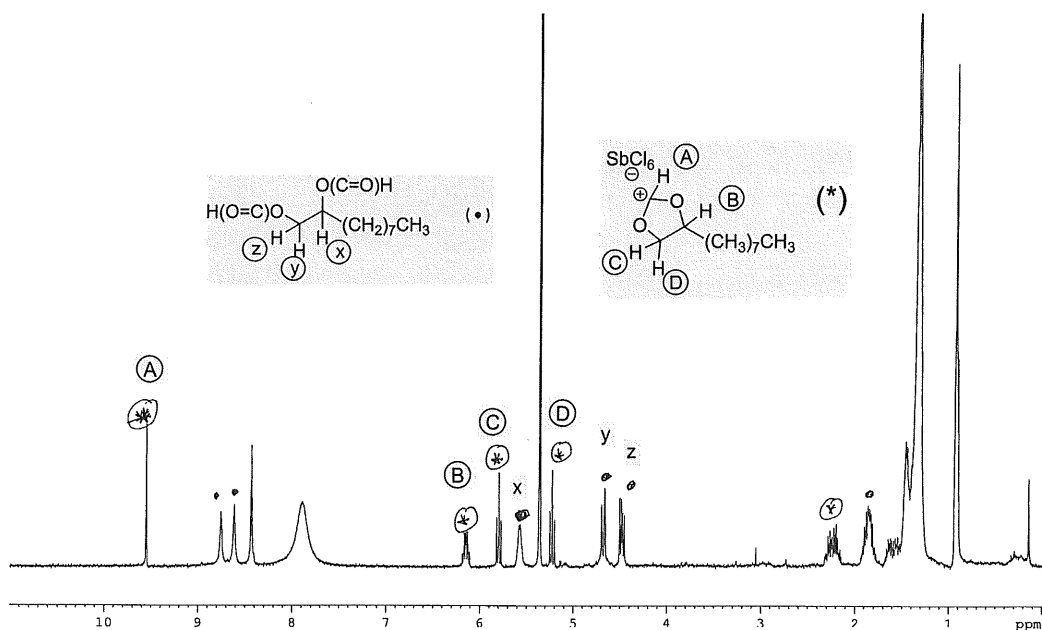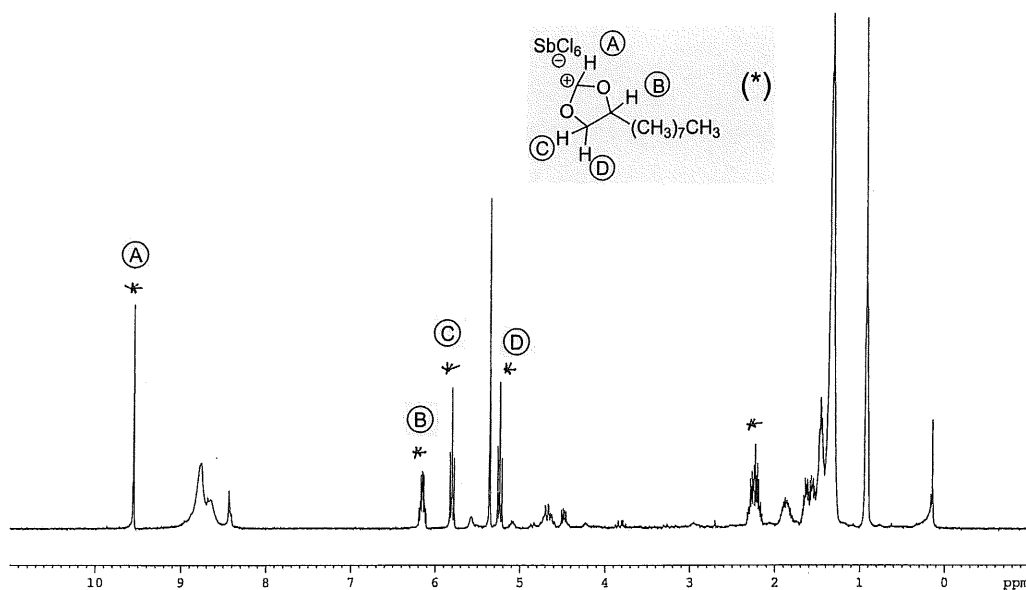
Figure 2.10 ^{1}H NMR (CD$_2$Cl$_2$) of an aliquot from the reaction mixture of **2.43** and SbCl$_5$ (in CD$_2$Cl$_2$ at 23 °C) at intermediate (top) and complete (bottom) conversion

2.5 Current Results – Generation of a 1,3-dioxolan-2-ylium carbocation and crystallization attempts

Isolation of 1,3-dioxolan-2-ylium carbocations (**2.41**) has been accomplished by Meerwein (**Scheme 2.8**).[20] They combined 3 equivalents of an orthoester (**2.43**) with 4 equivalents of BF$_3$ etherate in CH$_2$Cl$_2$ for 2 hours at 50 °C and isolated a solid compound, presumably **2.44**. Neither X-ray analysis nor NMR analysis were performed on the solid, but a melting point was obtained.[20]
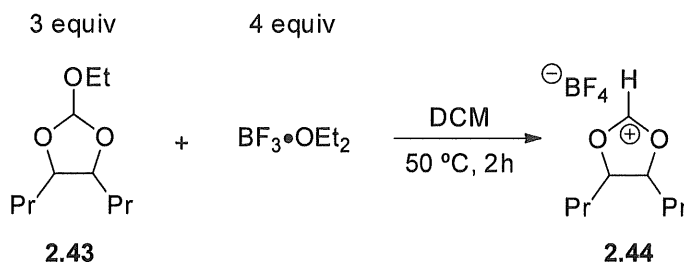

Scheme 2.8 Formation of 1,3-dioxolan-2-ylium cation **2.44** with BF$_4^-$ counterion[20]

When we attempted to reproduce the synthesis, full conversion of **2.43** to the 1,3-dioxolan-2-ylium salt **2.44** did not occur. The maximum conversion to the salt was 50% as observed by ^{1}H NMR (**Figure 2.12**) and no solids were ever obtained. However, heartened by the appearance of a carbocation, we pursued other methods of forming the carbocation from 4,5-octanediformate (**2.45**).

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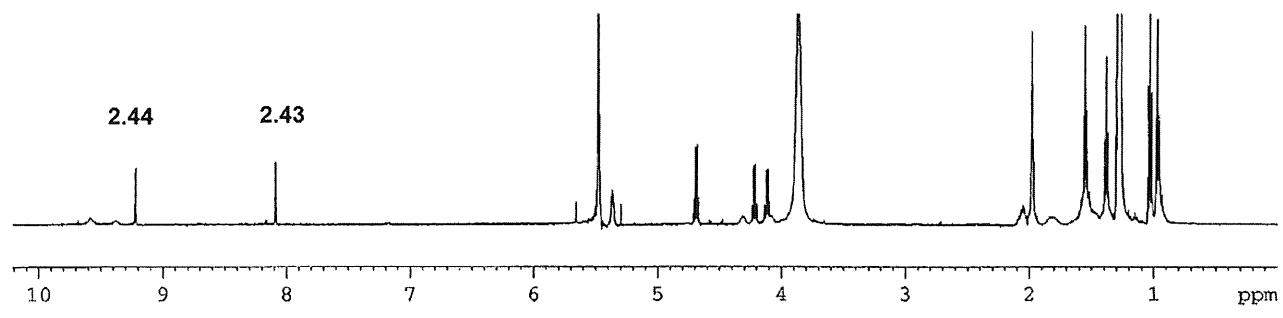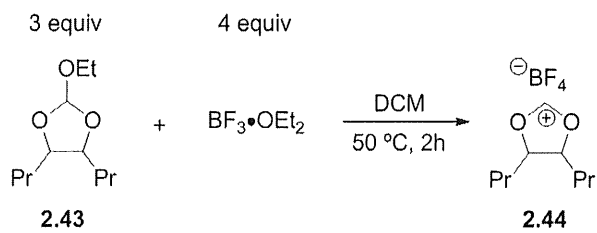
Figure 2.11 ^{1}H NMR (CD$_2$Cl$_2$) spectrum of the mixture formed on reaction between **2.43** and BF$_3$ etherate

Dr. Arceo has shown that reaction of a diformate with TfOH in anhydrous CH$_2$Cl$_2$ results in the formation of a carbocation in solution (*vide supra*). When **2.45** was submitted to these reaction conditions, full conversion of the diformate to a carbocation (**2.46**) occurred in 6 hours (**Figure 2.12**). The proton at the 2 position of the 1,3-dioxolan-2-ylium cation appeared at 9.4 ppm in the ^{1}H NMR. Removal of the solvent *in vacuo* resulted in a red oil. Attempts to precipitate the carbocation via trituration with diethyl ether or hydrocarbon solvents were unproductive, as was cooling the oil to -78 °C for several weeks.
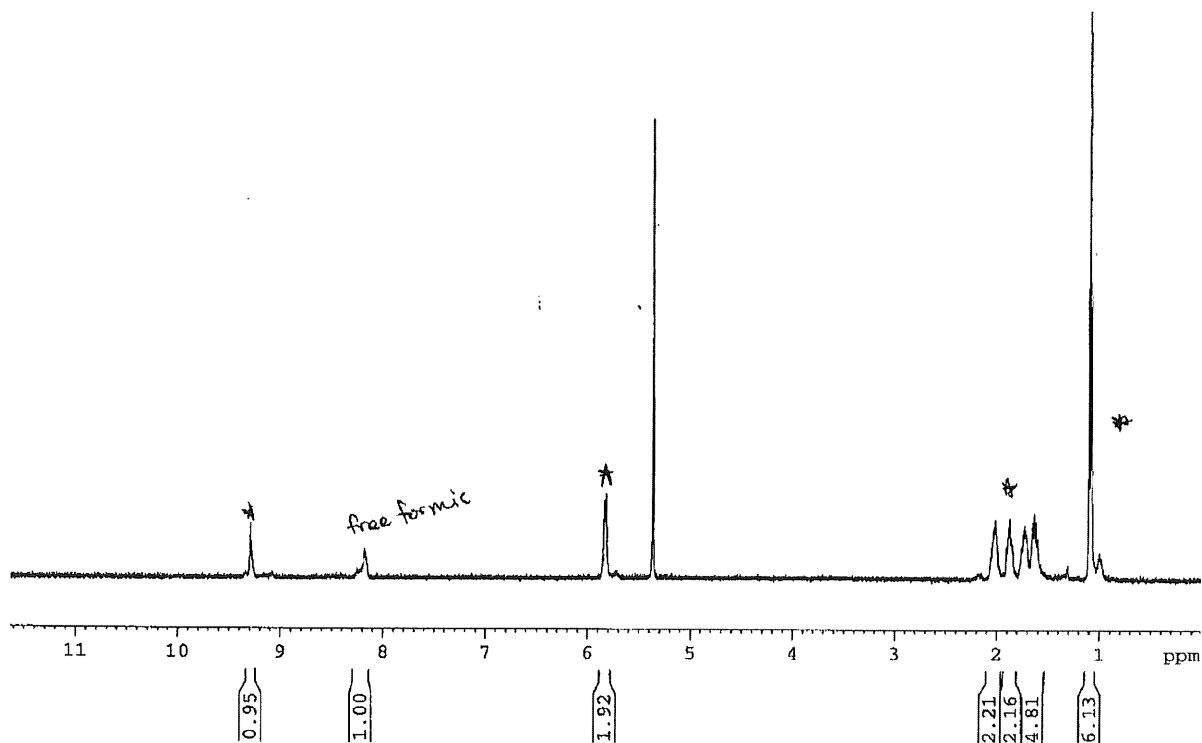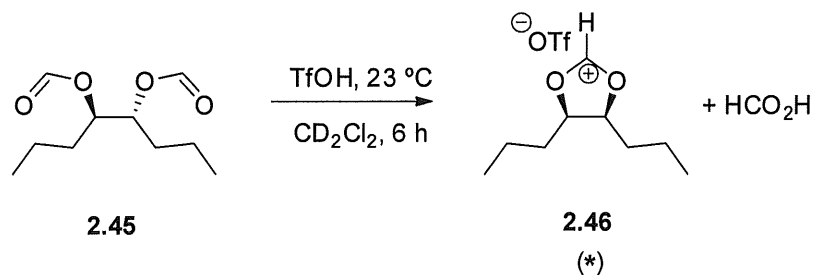
Figure 2.12 ^{1}H NMR spectrum of **2.46** in CD_2Cl_2

Other diformate compounds were obtained and treated with TfOH in dichloromethane to form various analogs of the 1,3-dioxolan-2-ylium cation (**Figure 2.13**). We were interested in the 2,3-butanediformate compounds (**2.47.A-C**) because of their small hydrophobic side chains. We explored the reactions of compounds **2.48**, **2.49** and **2.50** because we thought the aromatic rings would aid in precipitation of a solid once the carbocation was formed in solution. Unfortunately, the compounds did not cleanly form carbocations under our TfOH conditions.
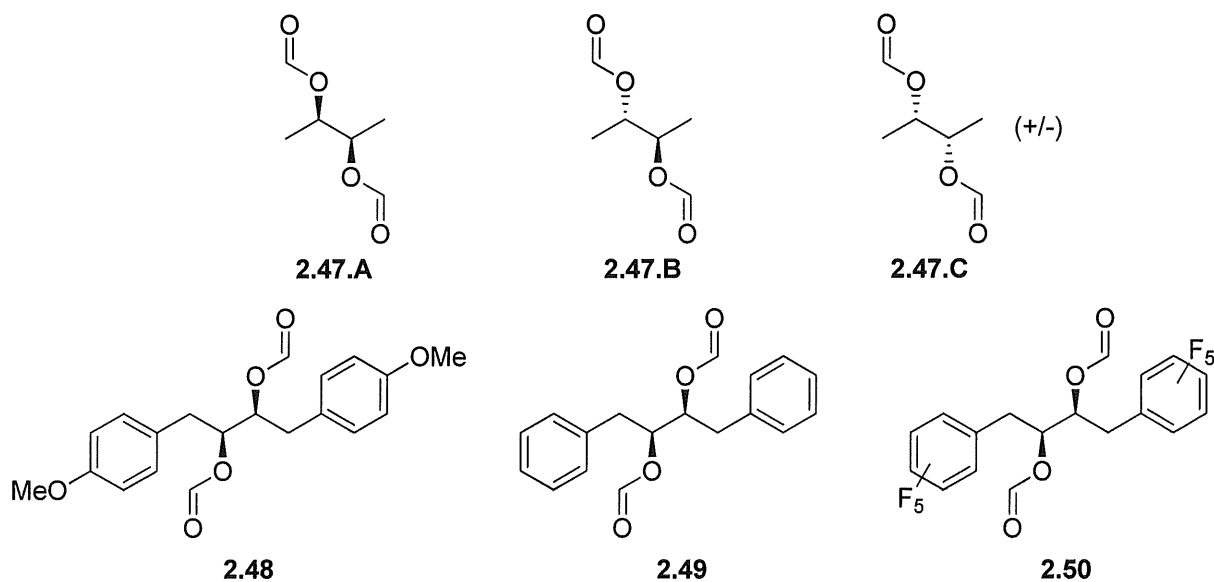
**Figure 2.13** Diformates that did not fully convert to 1,3-dioxolan-2-ylium caions when treated with TfOH

Since our efforts at changing the identity of the diformate starting material were unproductive, we investigated anion exchange of the triflate with other compounds. The anions we were interested in were [SbF$_6$]$^-$, [BF$_4$]$^-$, [PF$_6$]$^-$ and hexabromocarborane (**Figure 2.14**). The silver (**2.51.Ag**) and cesium (**2.51.Cs**) salts of hexabromocarborane were obtained from the Reed research group (UC Riverside).
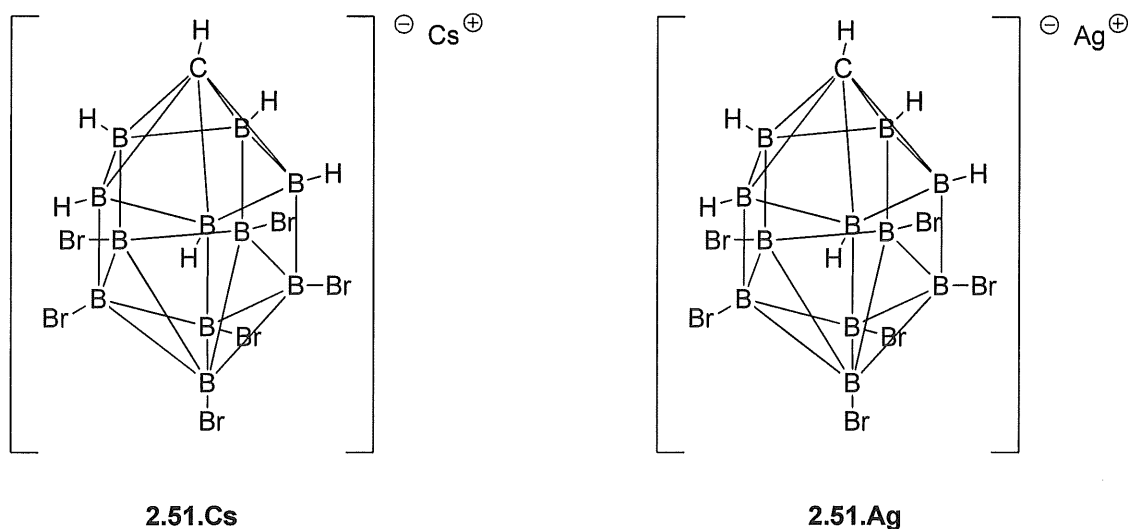
Figure 2.14 Structures of the cesium and silver salts of hexabromocarborane (**2.51.Ag** and **2.51.Cs**) courtesy of the Reed research group (UC Riverside)

The carbocation **2.46** was generated *in situ* and then the appropriate anion salt was added to the reaction mixture. An example of the process is shown in **Table 2.3** where Et$_2$O was the solvent. Similar screens were accomplished with C$_5$H$_{12}$, C$_6$H$_{14}$, C$_7$H$_{16}$, CD$_2$Cl$_2$ and CH$_3$CN as the solvent, leading to similar results. Despite the many

solvent systems and anion sources, crystals of our desired 1,3-dioxolan-2-yilum compound were never obtained. We therefore decided to pursue a different synthetic route for the formation of **2.46**.
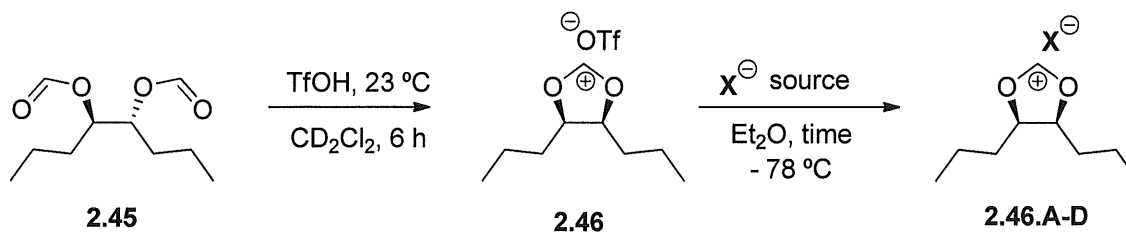
Entry[a]	X[−] source	Time	Result
1	2.51.Ag	1 h	no pcpt
2		5 h	no pcpt
3		24 h	no pcpt
4		1 wk	no pcpt
5		3 wk	no pcpt
6	2.51.Cs	1 h	no pcpt
7		5 h	no pcpt
8		24 h	no pcpt
9		1 wk	no pcpt
10		3 wk	no pcpt
11	AgSbF$_6$	1 h	no pcpt
12		5 h	no pcpt
13		24 h	no pcpt
14		1 wk	no pcpt
15		3 wk	no pcpt

Entry[a]	X[−] source	Time	Result
16	AgBF$_4$	1 h	no pcpt
17		5 h	no pcpt
18		24 h	no pcpt
19		1 wk	no pcpt
20		3 wk	no pcpt
21	AgPF$_6$	1 h	no pcpt
22		5 h	no pcpt
23		24 h	no pcpt
24		1 wk	no pcpt
25		3 wk	no pcpt

X[−]	Cation
Carborane	2.46.A
SbF$_6$	2.46.B
BF$_4$	2.46.C
PF$_6$	2.46.D

[a] Each reaction was run with 1 mmol **2.45**, 1 mmol TfOH and 2 mL CD$_2$Cl$_2$ in an atmosphere of N$_2$ for 6 h. The presence of **2.46** was determined by ^{1}H NMR. The CD$_2$Cl$_2$ solvent was removed, 2 mL Et$_2$O was added along with the X[−] source. The reaction mixture was then cooled to -78 °C and monitored over time for precipitate (pcpt) formation.

**Table 2.3** Example of a crystallization screen where Et$_2$O was the solvent.

We hypothesized that a halo-formate starting material (**2.52**) would react with a silver salt to result in our desired cation **2.46** (**Table 2.4**). Unfortunately, upon treatment with silver salts, **2.52** formed an intractable oligomer. We were unable to characterize the oligomers formed and unable to dissolve them.
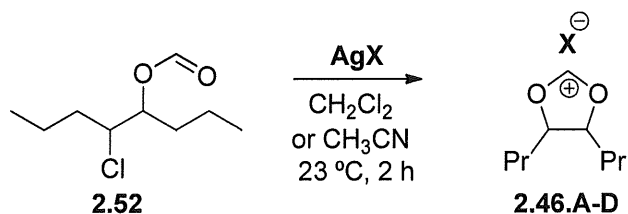
Table 2.4 Reactions between **2.52** and silver salts

Entry	AgX	Results
1	**2.51.Ag**	intractable mixture
2	$AgPF_6$	intractable mixture
3	$AgBF_4$	intractable mixture
4	$AgSbF_6$	intractable mixture

Our final efforts for the synthesis of the desired **2.46** involved the use of $SbCl_5$ to abstract a chloride from 4-chloro-5-octaneformate (**2.52**) and directly form the salt without the need for anion exchange. Unfortunately, **2.52** quickly decomposed upon treatment with $SbCl_5$ at 23 °C or at -78 °C (**Table 2.5**).
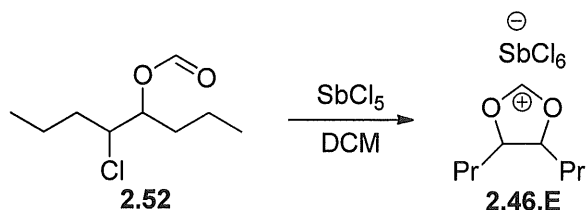
Table 2.5 Reactions between **2.52** and $SbCl_5$

Entry	Sb Source	Temperature	Result
1	$SbCl_5$ (neat)	23 °C	fast decomposition of **2.52**
2	$SbCl_5$ (1.0M in DCM)	23 °C	fast decomposition of **2.52**
3	$SbCl_5$ (1.0M in DCM)	-78 °C	slow decomposition of **2.52**

2.6 Conclusion

We have developed a stereospecific, formic-acid mediated process for the didehydroxylation of vicinal diols in excellent yield. Glycerol and erythritol, biologically derived polyols, underwent didehydroxylation to yield allyl alcohol and 2,5-dihydrofuran, respectively. Though these simple polyhydroxylated compounds were amenable to our

method, more complex compounds such as sorbitol and glucose were incompatible, yielding intractable mixtures when submitted to the formic acid-mediated conditions.

We carried out isotope labeling studies to clarify the possible mechanistic pathways of our didehydroxylation reaction. We also performed DFT calculations to analyze the possible transition states of the process which alluded to the presence of both a carbocation intermediate as well as a carbene intermediate. Extensive synthetic work was done on the synthesis and isolation of the proposed 1,3-dioxolan-2-ylium carbocation species which we observed in solution with ^{1}H NMR spectroscopy. However, attempts at crystallizing the species were unsuccessful.

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2. Appendix : Experimental : Formic Acid Reduction and Carbocation Formation

General procedure for the formic acid-mediated didehydroxylation of vicinal diols

The diol and formic acid (**2.2**) (0.60 equivalents) were first mixed in a flask fitted with a Vigreaux column, distillation head and a collection flask. The temperature was monitored by a thermometer immersed in the reaction mixture. Nitrogen was bubbled through the mixture using a perforated tube immersed in the solution for 20 minutes at room temperature or, if the starting material was a solid, at a temperature slightly over its melting point. The reaction was performed by heating the mixture to 230-240 °C using a preheated sand bath with continuation of the nitrogen bubbling. Under these conditions distillation of the product took place. Heating was continued until no more distillate appeared. This procedure was repeated in the same manner as described above, by making two more additions of formic acid (0.42 equivalents each). When all the starting material was consumed, potassium carbonate was added to the distillate and water was removed by decantation; the resulting product was the pure alkene. The final products were identified by ^{1}H and ^{13}C NMR spectroscopy, in agreement with literature data.

Formic acid-mediated didehydroxylation of erythritol (2.31)

A 500 mL three neck round-bottomed flask was charged with *meso*-erythritol (**2.31**) (36.6 g, 300 mmol) and 99% formic acid (**2.2**) (7.54 mL, 240 mmol). The flask was fitted with a distillation apparatus, a thermometer for internal temperature monitoring and an inlet to bubble nitrogen gas through the solution. The collecting flask was cooled to -78 °C with a dry ice and acetone bath. The reaction mixture was slowly heated to 240 °C over one hour. After that, the mixture was heated and stirred for 12 h at an internal temperature of 210 °C and the distillate collected in the collection flask. The mixture was then cooled to room temperature and another portion of formic acid (6.8 mL, 180 mmol) was added. The solution was heated again to 210 °C for 9 hours with concomitant distillation of product and formic acid. The mixture was allowed to cool to room temperature and a final portion of formic acid (180 mmol) was added. The mixture was then slowly reheated to 210 °C and held at that temperature for 9 hours. The distillate was then redistilled affording 39.8 g (117 mmol) of pure 2,5-dihydrofuran (**2.26**) in 39.3% yield. bp 65-67 °C. ^{1}H NMR (CD$_3$CN) δ 4.59 (d, 4H, J=1Hz), 5.91 (s, 2H).^{13}C NMR (CD$_3$CN) δ 74.8, 125.7.

Acid-catalyzed cyclization of erythritol

meso-Erythritol (**2.31**) (122 g, 1 mol) and *para*-toluenesulfonic acid mono-hydrate (9.51 g, 50 mmol) were mixed in a round-bottomed flask with a stir bar. The reaction flask was fitted with a Vigreaux column, distillation head and collection flask. The system was heated to 175 °C under reduced pressure (0.5 torr) for 4 hours. After that time, the collection flask contained 91.5 g (880 mmol) of 1,4-anhydroerythritol (**2.25**) (Yield 88%). bp 110-112 °C at 0.5 torr (lit : 111-113 °C at 0.5 torr)[1a] ^{1}H NMR: (CD$_3$CN) δ 3.54 (m, 2H), 3.62 (broad s, 2H), 3.81 (m, 2H), 4.13 (m, 2H); ^{13}C NMR (CD$_3$CN) δ 69.12, 71.93.[1b]

## Formic acid-mediated didehydroxylation of 1,4-anhydroerythritol

The general method described above for the formic acid-mediated didehydroxylation of 1,2-diols was followed. 1.56 g (15 mmol) of *cis*-1,4-anhydroerythritol (**2.25**) yielded 0.914 g of 2,5-dihydrofuran (**2.26**) (87%). bp 65-67 °C (lit 66-67 °C).[2] ^{1}H NMR (CD$_3$CN) δ 4.59 (d, 4H, *J*=1 Hz), 5.91 (s, 2H), ^{13}C NMR (CD$_3$CN) δ 74.81, 125.73.[2]

General procedure for the formic acid-mediated dehydroxyamination of vicinal aminoalcohols

A three neck round-bottomed flask was charged with amino alcohol (15 mmol), formic acid (0.4 mL, 12 mmol) and a magnetic stir bar. The flask was fitted with a distillation apparatus and a perforated tube to allow nitrogen gas to bubble through the solution. The reaction mixture was heated to 230 °C for 1 hour and then cooled to room temperature. Another 12 mmol portion of formic acid was added to the reaction mixture; the mixture heated to 230 °C for an hour and then cooled to room temperature. This process was repeated until a total of 4 additions of formic acid were completed. The reaction flask and collection flask were monitored via ^{1}H NMR spectroscopy after each addition of formic acid. For each amino alcohol studied (**2.35.A-D**), the starting material was fully consumed, but was converted into an intractable mixture after 2 additions of formic acid.

Formation of 1,3-dioxolan-2-ylium salt 2.46

Under anhydrous, air-free conditions, a 10 mL round-bottomed flask was charged with **2.45** (202 mg, 1.0 mmol), TfOH (0.09 mL, 1 mmol), 2 mL CD$_2$Cl$_2$ and a magnetic stir bar. The reaction mixture was stirred at room temperature for 6 hours. After 6 hours, an aliquot of the red reaction mixture was analyzed via ^{1}H NMR spectroscopy, revealing >90% conversion of the diformate **2.45** to the cation salt **2.46**. ^{1}H NMR : (CD$_2$Cl$_2$) δ 1.15 (6H, t, J=3 Hz), 1.63 (2H, m), 1.72 (2H, m), 1.85 (2H, m), 2.01 (2H, m), 5.85 (2H, m), 9.23 (1H, s).
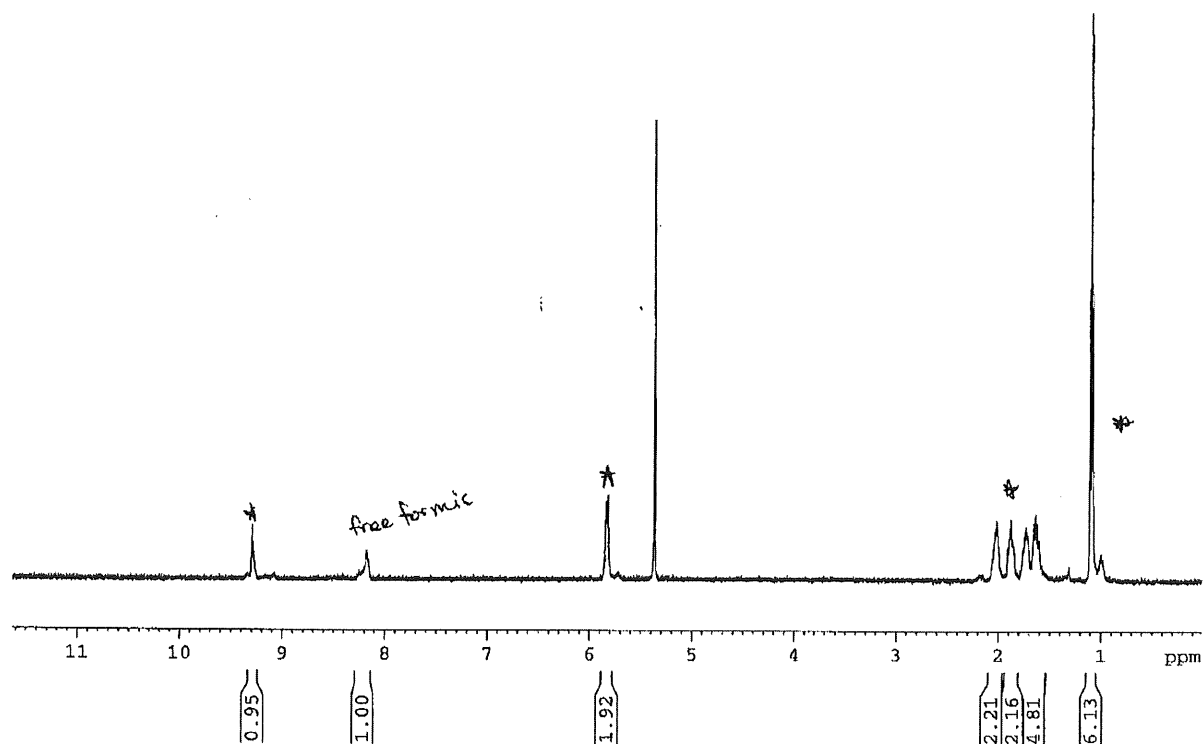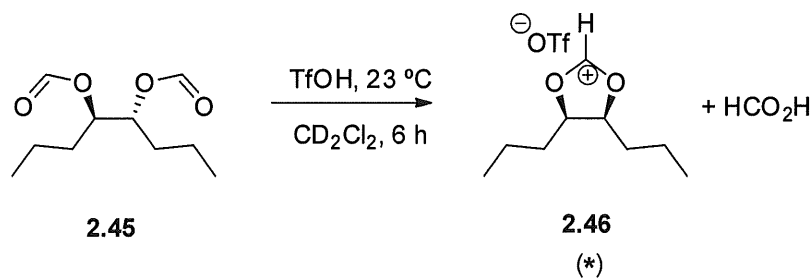
Figure 2.12 ^{1}H NMR spectrum of **2.46** in CD_2Cl_2

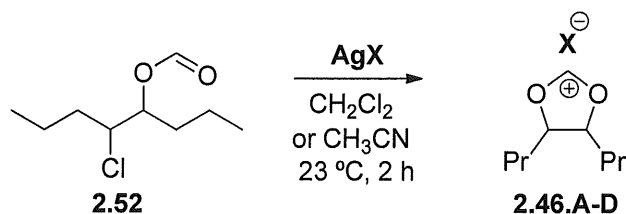## General procedure for the anion exchange of 2.46

Under anhydrous, air-free conditions, a 10 mL round-bottomed flask was charged with **2.45** (202 mg, 1.0 mmol), TfOH (0.09 mL, 1 mmol), 1 mL CD_2Cl_2 and a magnetic stir bar. The reaction mixture was stirred at room temperature for 6 hours. After 6 hours, an aliquot of the red reaction mixture was analyzed via ^{1}H NMR spectroscopy, revealing >90% conversion of the diformate **2.45** to the cation salt **2.46**. Once the presence of the cation was confirmed, the CD_2Cl_2 solvent was removed *in vacuo*. A new solvent (2 mL) was then added to the reaction flask along with an anion source (1 mmol). The reaction mixture was then cooled to -78 °C and monitored over the course of three weeks.

Exchange of the triflate anion of 2.46 with tetrafluoroborate

A solution of **2.46** was obtained by following the general procedure. Once the presence of the cation was confirmed, the CD_2Cl_2 solvent was removed *in vacuo*. Diethyl ether (2 mL) was then added to the reaction flask along with silver tetrafluoroborate (195 mg, 1 mmol). The reaction mixture was then cooled to -78 °C and monitored over the course of three weeks, yielding no crystal growth.

General procedure for the formation of 1,3-dioxolan-2-ylium salts 2.46.A-D from 4-chloro-5-formyl-octane (2.52)

Under anhydrous, air-free conditions, a 10 mL round-bottomed flask was charged with **2.52** (193 mg, 1 mmol), 2 mL solvent and a silver salt (1 mmol). The reaction mixture was allowed to stir at room temperature for 2 hours, and then aliquots of the reaction mixture were monitored via ^{1}H NMR spectroscopy to determine the conversion of **2.52**. There were no discernible species in the spectra of the reaction mixtures.


Entry	AgX	Results
1	**2.51.Ag**	intractable mixture
2	$AgPF_6$	intractable mixture
3	$AgBF_4$	intractable mixture
4	$AgSbF_6$	intractable mixture

Table 2.4 Reactions between **2.52** and silver salts

General procedure for the formation of 1,3-dioxolan-2-ylium salt 2.46.E from 2.52

Under anhydrous, air-free conditions, a 10 mL round-bottomed flask was charged with **2.52** (193 mg, 1 mmol), 1 mL CH_2Cl_2 and $SbCl_5$ (0.13 mL, 1 mmol). The reaction mixture was allowed to stir for 2 hours at a constant temperature, and then an aliquot of the reaction mixture was monitored via ^{1}H NMR spectroscopy. Rapid degradation of the ^{1}H NMR resonances was observed, indicative of decomposition of the starting material.
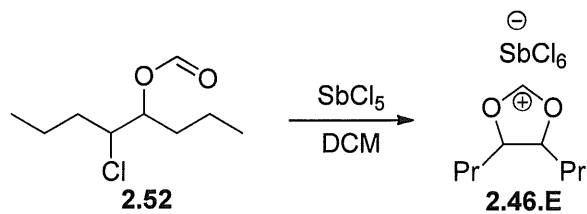
Entry	Sb Source	Temperature	Result
1	$SbCl_5$ (neat)	23 °C	fast decomposition of **2.52**
2	$SbCl_5$ (1.0M in DCM)	23 °C	fast decomposition of **2.52**
3	$SbCl_5$ (1.0M in DCM)	-78 °C	slow decomposition of **2.52**

**Table 2.5** Reactions between **2.52** and $SbCl_5$

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3. CO$_2$ Reduction : *In situ* formation of formic acid with concomitant didehydroxylation of vicinal diols

3.1 Introduction

In the previous chapter, we described the process of didehydroxylation of vicinal diols with formic acid. The success of this method led us to the current research of using CO$_2$ as a shuttle for the reducing agent, dihydrogen.[1] Our overall plan for this project was to use carbon dioxide gas, hydrogen gas, a transition metal-based catalyst and vicinal diols to directly create alkanes (**Scheme 3.1**).
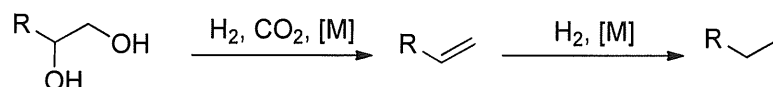
Scheme 3.1 Planned process for vicinal diol didehydroxylation with formic acid produced *in situ*

Our approach to solving this process involved three stages. The first stage was to determine the efficacy of formic acid and amine mixtures in the didehydroxylation of vicinal diols. These experiments would determine a minimum ratio of formic acid to amine that is capable of performing our desired reaction (**Scheme 3.2**, *a*). Our second stage was the investigation of carbon dioxide reduction conditions that yield the appropriate ratio of formic acid and amine (**Scheme 3.2**, *b*). The final stage of this project was to combine carbon dioxide reduction with concomitant didehydroxylation of vicinal diols (**Scheme 3.2**, *c*).
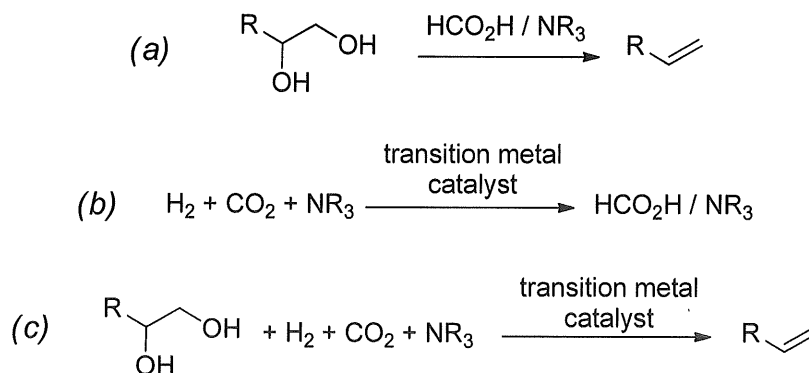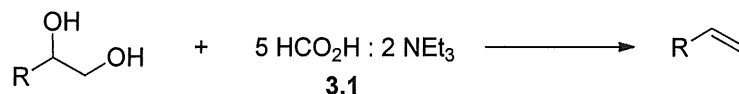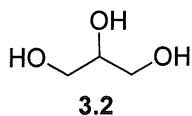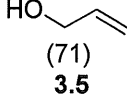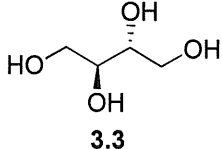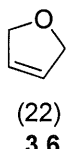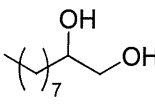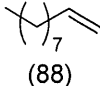

Scheme 3.2 Three stage plan for vicinal diol didehydroxylation with formic acid produced *in situ*

3.2 Reduction of vicinal diols via mixtures of formic acid and amines

The majority of carbon dioxide reduction schemes reported in the literature utilize an amine base to drive the formation of formic acid.[2] These procedures reliably produce a 5:2 mixture of formic acid to amine. Our first goal was to determine the efficacy of an amine-acid mixture in the didehydroxylation of diol moieties. We began with a homogeneous 5:2 mixture of formic acid and triethylamine (TEA) (**3.1**) (**Table 3.1**). In

analogy to the formic acid mediated didehydroxylation chemistry,[3] glycerol (**3.2**), *meso*-erythritol (**3.3**), and 1,2-decanediol (**3.4**) were converted to their corresponding alkenes in yields corresponding to those reported earlier.

$$\text{R}\!\!\underset{\text{OH}}{\overset{\text{OH}}{\diagup}}\!\!\text{OH} \quad + \quad 5\,\text{HCO}_2\text{H}:2\,\text{NEt}_3 \quad \longrightarrow \quad \text{R}\diagup\!\!\diagdown$$

3.1

Entry[a]	Substrate	Temp (°C)	Time (h)	Product (% yield)[b]	Previous Yield[c]
1	HO⤴OH⤴OH **3.2**	220	3	HO⤴ (71) **3.5**	82%
2	HO⤴OH⤴OH⤴OH **3.3**	220	4	⬡O (22) **3.6**	39%
3	⤴OH⤴OH₇ **3.4**	220	3	⤴₇ (88) **3.7**	93%

[a] The reactions were run under distillation conditions where N_2 gas was bubbled through the reaction mixture. Each reaction contained 15 mmol of substrate and 10 equivalents of formic acid (2 equivalents of a premixed solution of **3.1**). [b] Determined by ^{1}H NMR using 1,3,5-trimethoxybenzene as internal standard. [c] These yields were obtained using 10 equivalents of formic acid in the absence of amine.[3]

Table 3.1 Control didehydroxylations of vicinal diols using a mixture of formic acid and triethylamine as the reductant

The largest difference between these two didehydroxylation methods is that the amine additive distills with the alkene, requiring further purification to obtain the pure alkene product. A high boiling amine, such as tri-*n*-octylamine (**3.8**), would remain in the reaction flask during the didehydroxylation chemistry, thus circumventing problems with separation. A biphasic 5:2 mixture of formic acid and tri-*n*-octylamine (**3.9**) was tested in polyol didehydroxylation (**Table 3.2**). Lower yields of alkene were observed compared to those observed when triethylamine was used. The reaction flask contained polyformates incapable of undergoing the didehydroxylation chemistry.

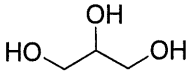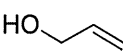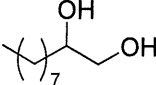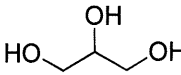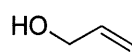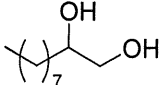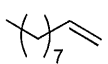| Entry[a]	Substrate	Time (h)	Product	Yield (%)[b]
1	**3.2**	3	**3.5**	68
2	**3.4**	4	**3.7**	71

[a] The reactions were run under distillation conditions where N_2 gas was bubbled through the reaction mixture. Each reaction contained 15 mmol of substrate and 10 equivalents of formic acid (2 equivalents of a premixed solution of **3.9**). [b] Determined by ^{1}H NMR using 1,3,5-trimethoxybenzene as internal standard.

Table 3.2 Didehydroxylation of diols using **3.9** as the acid / amine mixture

In an attempt to decrease the amount of polyformates formed in the reaction flask, the formic acid (**3.10**) was added incrementally to the polyol and tri-*n*-octylamine (**3.8**) reaction mixture (**Table 3.3**). Though these new conditions did not affect the outcome of the reaction, the homogeneity of the reactants made the experiment easier to accomplish.

Reaction scheme:

R−CH(OH)−CH2OH + N(n-octyl)3 (3.8) + HCO2H (3.10) → (230 °C, 4 h) → R−CH=CH2
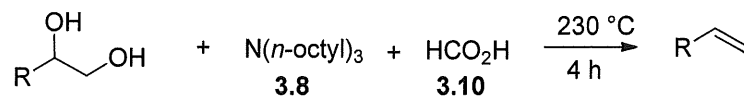
Entry[a]	Substrate	Product	Yield (%)[b]
1	HO⌒CH(OH)⌒CH2OH **3.2**	HO⌒CH=CH2 **3.5**	67
2	substrate **3.4**	product **3.7**	74

[a] The reactions were run under distillation conditions where N_2 gas was bubbled through the reaction mixture. Each reaction contained 15 mmol of substrate and 4.8 mmol amine. Formic acid was added to the reaction in four 12 mmol additions, one each hour. [b] The yields area an average over two separate runs. The yields were determined by ^{1}H NMR using 1,3,5-trimethoxybenzene as internal standard.

Table 3.3 Didehydroxylation of diols in which formic acid and amine were added separately to the reaction mixture

We also hypothesized that adding a solvent to the reaction mixture would decrease the presence of unreactive polyformates (**Table 3.4**). The solvents we tested were dimethylsulfoxide (DMSO), a common solvent used in the metal-mediated conversion of CO_2 to formic acid,[2] and sulfolane (**3.11**), a high boiling cyclic sulfone. DMSO reacted with formic acid, leading to decomposition of the starting materials and the solvent. Reactions performed in sulfolane were higher yielding than reactions run in the absence of sulfolane, but still slightly lower than reactions run with triethylamine instead of tri-n-octylamine. The lower yield was acceptable since amine was no longer present in the distillate containing the alkene product.

Reaction scheme:

$$\text{R-CH(OH)-CH}_2\text{OH} \quad + \quad \text{N}(n\text{-octyl})_3 \quad + \quad \text{HCO}_2\text{H} \xrightarrow[\text{230 °C, 4 h}]{\text{solvent}} \text{R-CH=CH}_2$$

3.8   **3.10**
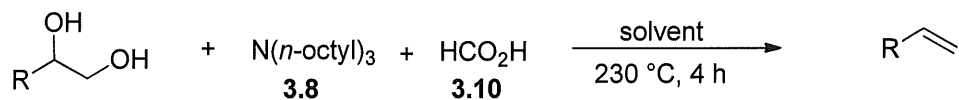
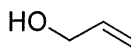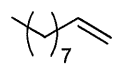| Entry[a]	Substrate	3.8 (mmol)	Solvent (mL)	Product	Yield (%)[b]
1	3.2	4.8	DMSO (2)	HO⌒⌒ **3.5**	5
2	3.4	4.8	DMSO (2)	⌇₇⌒ **3.7**	9
3	3.3	4.8	DMSO (2)	(O-ring) **3.6**	0
4	3.2	0	sulfolane (2)	**3.5**	83
5	3.2	4.8	none	**3.5**	79
6	3.2	4.8	sulfolane (2)	**3.5**	81
7	3.4	0	sulfolane (2)	**3.7**	85
8	3.4	4.8	none	**3.7**	86
9	3.4	4.8	sulfolane (2)	**3.7**	88
10	3.3	0	sulfolane (2)	**3.6**	31
11	3.3	4.8	none	**3.6**	33
12	3.3	4.8	sulfolane (2)	**3.6**	29

[a] The reactions were run under distillation conditions where N_2 gas was bubbled through the reaction mixture. Each reaction contained 15 mmol of substrate. Formic acid was added to the reaction in four 12 mmol additions, one each hour. [b] The yields are an average over two separate runs. The yields were determined by ^{1}H NMR using 1,3,5-trimethoxybenzene as internal standard.

Table 3.4 Effect of solvent on the didehydroxylation of diols with amine and formic acid mixtures

3.3 Carbon dioxide reduction via homogeneous catalysis

The control reactions with mixtures of amine and formic acid convinced us to pursue metal-catalyzed carbon dioxide reduction. We decided to investigate rhodium and ruthenium catalysts known to convert hydrogen and carbon dioxide gas into formate salts. Leitner and coworkers showed modest formate conversion using mixtures of the commercially available rhodium catalyst $[Rh(COD)Cl]_2$, bis-(diphenyl-phosphino)butane (dppb), and TEA with DMSO as the solvent.[4] In our experiments, the solvent was changed to sulfolane due to the incompatibility of DMSO with the didehydroxylation reaction. Ruthenium catalysts are effective at carbon dioxide reduction in ethanol and DMSO solutions with TEA as the base.[5] Control reactions using these literature procedures confirmed our hypothesis that sulfolane and DMSO are comparable solvents for the rhodium-mediated chemistry (**Table 3.5**). Unfortunately, the ruthenium systems did not work without ethanol as a solvent. Due to this limitation, we decided to pursue the rhodium-mediated method.

$$H_2 \ + \ CO_2 \ + \ NEt_3 \ \xrightarrow[\text{sulfolane}]{\text{catalyst}} \ HCO_2H : NEt_3$$
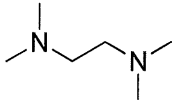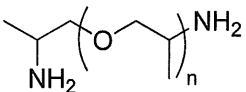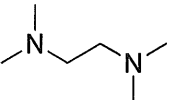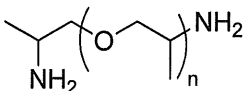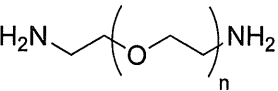
Entry[a]	Catalyst	$HCO_2H : NEt_3$ ratio[b]
1	$[Rh(cod)Cl]_2$	3 : 2
2[c]	$[Rh(cod)Cl]_2$	3 : 2
3	$Ru(H)_2(PPh_3)_4$	no reaction
4	$Ru(H)_2(CO)(PPh_3)_3$	no reaction

[a] The reactions were run at 6.0mM in transition metal in the presence of 1.2 mmol NEt_3, a 1:1 preformed mixture of H_2 and CO_2 at 600 psi for 24 hours at room temperature. [b] The ratio of formic acid to amine was determined via ^1H NMR with 1,3,5-trimethoxy benzene as an internal standard. [c] Phosphine ligand was added (1 equivalent dppb per rhodium atom).

Table 3.5 Control reactions of CO_2 reduction.

Upon identification of a viable catalytic system, we attempted to optimize the amine base (**Table 3.6**). Polymeric amines, triethanolamine, trioctylamine and tri-(ethylamino)amine showed no conversion of H_2 and CO_2 to formate. Tetramethyl-ethylenediamine (TMEDA) was competent in the reaction, but did not yield as much formate as TEA.

$$H_2 + CO_2 + Amine \xrightarrow[\text{sulfolane}]{[Rh(COD)Cl]_2,\ dppb} HCO_2H : Amine$$
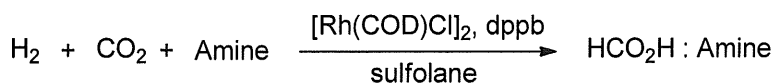
Entry[a]	Amine	HCO$_2$H : Amine ratio[b]	Entry[a]	Amine	HCO$_2$H : Amine ratio[b]
1	NEt$_3$ (TEA)	3 : 2	6	(TMEDA)	1 : 2
2	(diamine–PEG structure) MW ~400	no reaction	7[c]	(TMEDA)	no reaction
3	(diamine–PEG structure) MW ~2300	no reaction	8	N(CH$_2$CH$_2$NH$_2$)$_3$	no reaction
4	H$_2$N–(O)$_n$–NH$_2$ MW ~2000	no reaction	9	N(octyl)$_3$ **3.8**	no reaction
5	N(EtOH)$_3$	1 : 25			

[a] The reactions were run at 6.0mM in transition metal in the presence of 1 equivalent of dppb, 1.2 mmol amine, a 1:1 preformed mixture of H$_2$ and CO$_2$ at 600 psi for 24 hours at room temperature. [b] The ratio of formic acid to amine was determined via ^{1}H NMR with 1,3,5-trimethoxy benzene as an internal standard. [c] This reaction was run without sulfolane.

Table 3.6 Effects of amine identity on the rhodium-mediated reduction of carbon dioxide.

Next, we investigated the possibility of concomitant didehydroxylation of diols and production of formic acid. Unfortunately, upon heating the reaction mixture to the temperatures necessary for didehydroxylation, the pressure reached 3000 psi, exceeding the maximum holding capacity for the reaction vessel. Due to this limitation, we decided to attempt this process in two steps. First, we reduced carbon dioxide using the rhodium-mediated process, then used the resulting mixture for the didehydroxylation chemistry using a distillation apparatus (**Table 3.7**). Upon heating, whether in the presence or absence of a diol reactant, the formic acid decomposed. When the temperature was reduced, the formic acid completely decomposed after 12 hours of stirring. These results confirm that the carbon dioxide reduction chemistry is reversible, and that when high pressure is removed, formic acid is converted to carbon dioxide and hydrogen gas by the rhodium catalyst.

$$H_2 + CO_2 + NEt_3 \xrightarrow[\text{sulfolane}]{[Rh(COD)Cl]_2, \text{dppb}} HCO_2H : NEt_3 \xrightarrow[\text{temperature}]{\text{diol}} \text{Alkene}$$
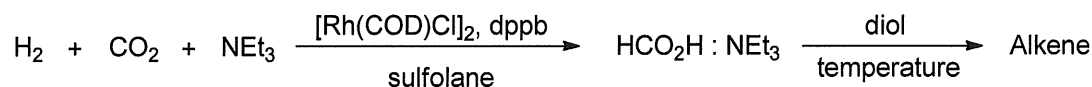
Entry[a]	HCO$_2$H : NEt$_3$ ratio[b]	Diol[c,d]	Temp °C	Alkene	Result[b]
1	3 : 2	3.2	230	3.5	no alkene, no more formic acid
2	3 : 2	3.2	22	3.5	no alkene, no more formic acid
3	5 : 4	3.4	230	3.7	no alkene, no more formic acid
4	3 : 2	3.4	22	3.7	no alkene, no more formic acid
5	6 : 5	3.3	230	3.6	no alkene, no more formic acid
6	5 : 4	3.3	22	3.6	no alkene, no more formic acid
7	3 : 2	none	230	none	no more formic acid
8	3 : 2	none	22	none	no more formic acid

[a] The reactions were run at 6.0mM in transition metal in the presence of 1 equivalent of dppb, 1.2 mmol NEt$_3$, a 1:1 preformed mixture of H$_2$ and CO$_2$ at 600 psi for 24 hours at room temp. [b] The ratio of formic acid to amine was determined via ^{1}H NMR with 1,3,5-trimethoxy benzene as an internal standard. [c] The reaction mixture was transferred from the high-pressure vessel to a round bottom flask equipped with a distillation apparatus. [d] 0.5 mmol of diol was added to the flask and the mixture heated for 4 hours.

Table 3.7 Didehydroxylation chemistry with freshly formed formic acid

To minimize the decomposition of formic acid, we considered the possibility of deactivating the catalyst in the presence of excess phosphine ligand (Table 3.8). A solution of formic acid and TEA was prepared using the rhodium system and then analyzed via ^{1}H NMR to determine the ratio of acid to amine. To this solution, 8 equivalents of phosphine were added. The mixture was stirred at room temperature for 12 hours and then analyzed. The small, bidentate phosphine, dppm, showed an appreciable decrease in the decomposition of formic acid. When the solution was heated to 100 °C, the formic acid completely decomposed, which conclusively showed that a different method of catalyst deactivation was necessary.

$$H_2 + CO_2 + NEt_3 \xrightarrow[\text{sulfolane}]{[Rh(COD)Cl]_2,\ dppb} HCO_2H : NEt_3 \xrightarrow[\text{23 °C, 12 h}]{\text{phosphine}} HCO_2H : NEt_3$$
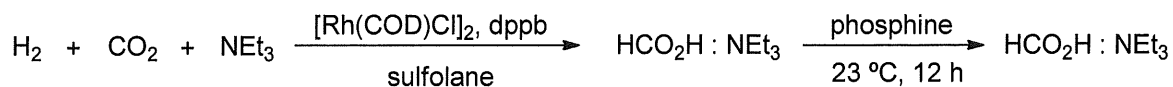
Entry[a]	init. $HCO_2H : NEt_3$ ratio[b]	Phosphine[c]	end $HCO_2H : NEt_3$ ratio[b]
1	3 : 2	none	1 : 10
2	3 : 2	PPh₃	1 : 20
3	3 : 2	dppb	1 : 3
4	5 : 4	dppm	1 : 2
5[d]	5 : 4	dppm	no formic acid

[a] The reactions were run at 6.0mM in transition metal in the presence of 1 equivalent of dppb, 1.2 mmol NEt_3, a 1:1 preformed mixture of H_2 and CO_2 at 600 psi for 24 hours at room temp. [b] The ratio of formic acid to amine was determined via ^{1}H NMR with 1,3,5-trimethoxybenzene as an internal standard. [c] 8 equivalents of phosphine were added to the reaction vessel and the mixture stirred at room temperature for 12 hours. [d] After stirring at room temperature for 12 hours, the reaction mixture was heated to 100 °C and stirred for 4 more hours.

Table 3.8 Deactivation of rhodium with excess phosphine ligand

We also attempted to deactivate the rhodium catalyst by oxidizing the metal by sparging the reaction mixture with air (**Table 3.9**). The reaction mixtures were monitored every 2 hours for 12 hours to follow the loss of formic acid. Two hours of sparging the mixture with air did not deactivate the rhodium catalyst. Our efforts at using homogeneous catalyst systems ended with these experiments, and we began an investigation of heterogeneous systems which would allow for facile removal of the active catalyst.

$$H_2 + CO_2 + NEt_3 \xrightarrow[\text{sulfolane}]{[Rh(COD)Cl]_2,\ dppb} HCO_2H : NEt_3\ \mathbf{3.11.A} \xrightarrow[\text{time}]{\text{air}} HCO_2H : NEt_3\ \mathbf{3.11.B} \xrightarrow[\substack{23\ ^{\circ}C \\ 12\ h}]{\text{stir}} HCO_2H : NEt_3\ \mathbf{3.11.C}$$
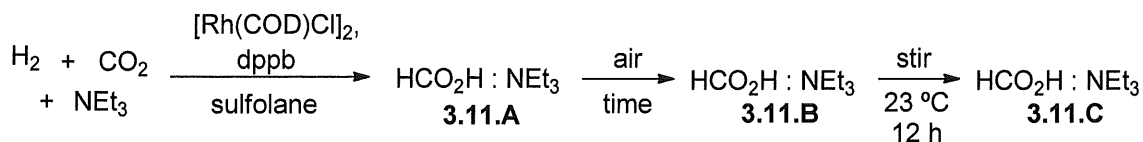
Entry[a]	3.11.A[b]	Sparge time (min)[c]	3.11.B[b]	3.11.C[b]
1	3 : 2	0	3 : 2	1 : 10
2	5 : 4	5	1 : 1	1 : 10
3	3 : 2	30	1 : 1	1 : 10
4	5 : 4	60	1 : 1	1 : 10
5	3 : 2	120	3 : 2	1 : 10

[a] The reactions were run at 6.0mM in transition metal in the presence of 1 equivalent of dppb, 1.2 mmol NEt_3, a 1:1 preformed mixture of H_2 and CO_2 at 600 psi for 24 hours at room temp.
[b] The ratio of formic acid to amine was determined via ^1H NMR with 1,3,5-trimethoxy benzene as an internal standard. [c] The reaction mixture was sparged with air using a glass pipette.

Table 3.9 Attempted deactivation of rhodium via air oxidation

3.4 Carbon dioxide reduction via heterogeneous catalysis

We investigated the viability of two different heterogeneous rhodium sources for the reduction of carbon dioxide (**Table 3.10**). The solid rhodium catalysts were removed from the reaction mixture via centrifugation prior to ^1H NMR analysis. Rhodium supported on carbon provided very low yields of formic acid compared to rhodium supported on alumina. Reduction of carbon dioxide did not proceed in the absence of solvent or in the absence of phosphine. The optimal reaction conditions are seen in entry 8 of **Table 3.10**. The heterogeneous process is not as effective at producing formic acid as the homogeneous process (entry 19).

$$\text{H}_2 \ + \ \text{CO}_2 \ + \ \text{NEt}_3 \ \xrightarrow[\text{sulfolane, 24 h}]{\text{Rh source, additive}} \ \underset{\textbf{3.12}}{\text{HCO}_2\text{H : NEt}_3}$$
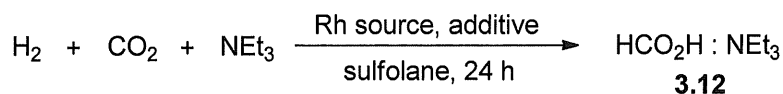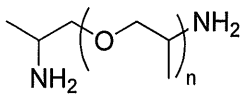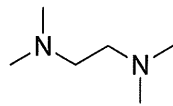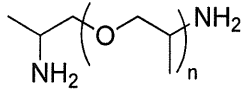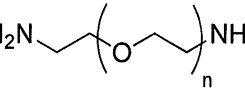
Entry[a]	Rh source	Additive (mmol)	Temp °C	3.12[b]
1	5% Rh/Al$_2$O$_3$	none	23	no formic acid
2	5% Rh/Al$_2$O$_3$	none	60	no formic acid
3	5% Rh/Al$_2$O$_3$	none	110	no formic acid
4[c]	5% Rh/Al$_2$O$_3$	none	23	no formic acid
5[c]	5% Rh/Al$_2$O$_3$	none	60	no formic acid
6[c]	5% Rh/Al$_2$O$_3$	none	110	no formic acid
7	5% Rh/Al$_2$O$_3$	dppb (0.13)	23	1 : 5
8	5% Rh/Al$_2$O$_3$	dppb (0.13)	60	3 : 4
9	5% Rh/Al$_2$O$_3$	dppb (0.13)	110	2 : 5
10	5% Rh/C	none	23	no formic acid
11	5% Rh/C	none	60	no formic acid
12	5% Rh/C	none	110	no formic acid
13[c]	5% Rh/C	none	23	no formic acid
14[c]	5% Rh/C	none	60	no formic acid
15[c]	5% Rh/C	none	110	no formic acid
16	5% Rh/C	dppb (0.13)	23	1 : 20
17	5% Rh/C	dppb (0.13)	60	1 : 10
18	5% Rh/C	dppb (0.13)	110	1 : 15
19[d]	[Rh(COD)Cl]$_2$	dppb (0.13)	23	3 : 2

[a] The reactions were run with 108 µmol of rhodium, 21 mmol NEt$_3$, 18 mL sulfolane, and under 600 psi of a premixed 1:1 mixture of H$_2$ and CO$_2$ gas. [b] The ratio of formic acid to amine was determined via ^{1}H NMR with 1,3,5-trimethoxy benzene as an internal standard after the solid catalyst was removed via centrifugation. [c] These reactions were run in the absence of sulfolane. [d] This entry is to allow comparison between heterogeneous and homogeneous methods.

Table 3.10 Reduction of carbon dioxide with heterogeneous rhodium sources

A screen of various amines (**Table 3.11**) revealed that triethylamine is the most effective amine in the heterogeneous chemistry. We also optimized the concentration of the reaction as well as the catalyst loading.

$$H_2 + CO_2 + Amine \xrightarrow[\text{sulfolane}]{\text{5% Rh/Al}_2\text{O}_3,\ \text{dppb}} HCO_2H : Amine$$
3.13

Entry[a]	Amine	3.13[b]	Entry[a]	Amine	3.13[b]
1	NEt₃ (TEA)	3 : 4	5	N(EtOH)₃	no reaction
2	MW ~400	no reaction	6	(TMEDA)	1 : 9
3	MW ~2300	no reaction	7	N(CH₂CH₂NH₂)₃	no reaction
4	MW ~2000	no reaction	8	N(octyl)₃ **3.8**	no reaction

[a] The reactions were run with 108 μmol rhodium, 120 μmol dppb, 21 mmol amine, 18 mL sulfolane, and under 600 psi of a premixed 1:1 mixture of H_2 and CO_2 gas at 60 °C for 24 h. [b] The ratio of formic acid to amine was determined via ^1H NMR with 1,3,5-trimethoxybenzene as an internal standard after the solid catalyst was removed via centrifugation.

Table 3.11 Effects of amine identity on the heterogeneous rhodium-mediated reduction of carbon dioxide.

We changed the total volume of sulfolane for the heterogeneous reduction chemistry, varying the concentration of the reaction (**Table 3.12**). The ratio of formic acid to amine remained steady when the concentration was increased threefold. Further increase in concentration resulted in a drop of formic acid production. Our next experiments determined the effect of concentration on the removal of the catalyst from the solution. The heterogeneous catalyst was difficult to remove from the concentrated solutions, as evidenced by the decrease in formic acid upon multiple cycles of centrifugation. The results of these two experiments led us to a new optimal concentration of the heterogeneous reaction, 1.75 M with respect to TEA or 0.01 M with respect to rhodium.

$$H_2 + CO_2 + NEt_3 \xrightarrow[\substack{\text{sulfolane (mL)} \\ 60\ ^\circ C,\ 24\ h}]{\text{Rh/Al}_2\text{O}_3,\ \text{dppb}} HCO_2H : NEt_3 \xrightarrow{\text{centrifuge}} HCO_2H : NEt_3 \xrightarrow{\text{centrifuge}} HCO_2H : NEt_3$$
$$\textbf{3.14.A} \qquad\qquad \textbf{3.14.B} \qquad\qquad \textbf{3.14.C}$$
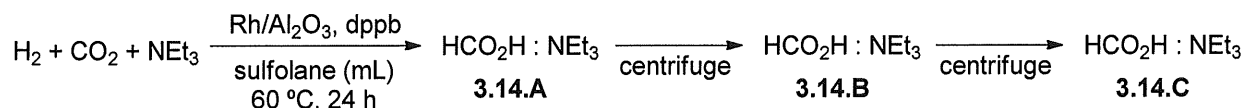
Entry[a]	Sulfolane (mL)	3.14.A[b]	3.14.B[b]	3.14.C[b]
1	18	2 : 3	2 : 3	2 : 3
2	12	2 : 3	2 : 3	2 : 3
3	9	2 : 3	1 : 3	1 : 10
4	6	2 : 3	1 : 5	1 : 25
5	4	2 : 5	2 : 25	no formate
6	2	2 : 5	1 : 25	no formate

[a] The reactions were run with 108 μmol rhodium, 120 μmol dppb, 21 mmol TEA, varied volumes of sulfolane, and under 600 psi of a premixed 1:1 mixture of H_2 and CO_2 gas at 60 °C for 24 h.
[b] The ratio of formic acid to amine was determined via ^{1}H NMR with 1,3,5-trimethoxybenzene as an internal standard after the solid catalyst was removed via centrifugation.

Table 3.12 Concentration effects on heterogeneous reduction of carbon dioxide

An exploration of catalyst loading revealed a maximum ratio of formic acid to TEA of approximately 1 : 1 (**Table 3.13**). When 2% rhodium was used, removal of the heterogeneous catalyst via centrifugation resulted in modest decomposition of formic acid. When 1% rhodium catalyst was employed, centrifugation did not result in a loss of formic acid product.

$$H_2 + CO_2 + NEt_3 \xrightarrow[\substack{\text{sulfolane (12 mL)} \\ 60\ ^\circ C,\ 24\ h}]{\text{Rh/Al}_2\text{O}_3,\ \text{dppb}} HCO_2H : NEt_3$$
$$\textbf{3.15}$$
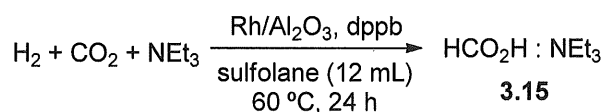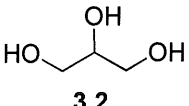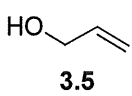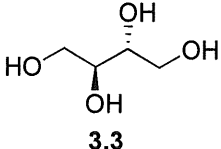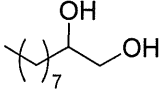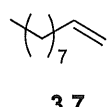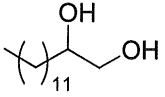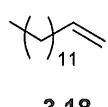
Entry[a]	Rh (mol%)[b]	3.15[c]
1	0.5	3 : 4
2	1.0	4 : 5
3	2.0	1 : 1
4	5.0	1 : 1

[a] The reactions were performed with 21 mmol TEA, 12 mL sulfolane, and under 600 psi of a premixed 1:1 mixture of H_2 and CO_2 gas at 60 °C for 24 h. [b] The mol% of rhodium is expressed with respect to TEA. 1.2 equivalents of dppb were also added. [c] The ratio of formic acid to amine was determined via ^{1}H NMR with 1,3,5-trimethoxy benzene as an internal standard after the solid catalyst was removed via centrifugation.

Table 3.13 Catalyst loading effects on reduction of carbon dioxide

Didehydroxylation of diols using the ratio of formic acid to TEA obtained from the heterogeneous CO_2 reduction was shown to be possible, but at least 8 additions (approximately 6 equivalents of formic acid) of the mixture were necessary to obtain a reasonable yield of alkene and full conversion of the substrate diol (**Table 3.14**). In these experiments, only the acid and amine mixture was added, but the heterogeneous carbon dioxide reduction reactions were run in 12 mL of sulfolane. The repeated addition of the carbon dioxide reduction mixtures to the didehydroxylation diluted the reaction and decreased its efficacy. To avoid this dilemma, isolation of the formic acid from the sulfolane solution was explored.
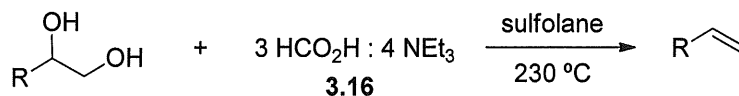
Entry[a]	Substrate	Additions	Alkene	Alkene Yield (%)[b]
1	**3.2**	12	**3.5**	48
2	**3.3**	15	**3.6**	8
3	**3.4**	8	**3.7**	44
4[c]	**3.17**	10	**3.18**	50

[a] The reactions were run under distillation conditions where N_2 gas was bubbled through the reaction mixture. Each reaction contained 15 mmol substrate and 15 mL sulfolane. Portions of 12 mmol formic acid as a premixed solution of **3.16** were added to the solution and the reaction allowed to stir at 230 °C for 3 hours.
[b] Determined by ^1H NMR using 1,3,5-trimethoxybenzene as internal standard. [c] Tetradecene did not distill into the collection flask, but remained in the reaction flask.

Table 3.14 Acid and amine ratio obtained from heterogeneous CO_2 reduction used for diol didehydroxylation

Vacuum transfer was the most efficient technique for the isolation of formic acid and TEA from the carbon dioxide reduction mixture. Centrifugation of the crude reaction was necessary in order to remove the majority of the rhodium catalyst. Traditional

distillation proved difficult due to the small volume of desired distillate. Recycling the used rhodium catalyst was our next goal to improve the overall efficacy of this process.

Optimal conditions for the reduction chemistry resulted from approximately 150 turnovers of the rhodium catalyst. We wanted to see if 150 turnovers was a result of equilibrium or inactivation of the catalyst. To do this, we ran a series of carbon dioxide reduction reactions using the same rhodium catalyst (**Table 3.15**). The second reduction showed a large decrease in formic acid yield, and the third reaction failed.

$$H_2 + CO_2 + NEt_3 \xrightarrow[\substack{\text{sulfolane (12 mL)}\\60\ ^\circ C,\ 24\ h}]{\text{Rh/Al}_2O_3,\ \text{dppb}} HCO_2H : NEt_3$$

3.19

Entry[a]	Run[b]	3.19[c]
1	1	3 : 4
2	2	1 : 20
3	3	no formic acid

[a] The reactions were performed with 216 μmol rhodium, 240 μmol dppb, 21 mmol TEA, 12 mL sulfolane, and under 600 psi of a premixed 1:1 mixture of H_2 and CO_2 gas at 60 °C for 24 h. [b] The solid catalyst pellet obtained following centrifugation was reused for runs 2 and 3. [c] The ratio of formic acid to amine was determined via ^{1}H NMR with 1,3,5-trimethoxy benzene as an internal standard after the solid catalyst was removed via centrifugation.

Table 3.15 Efficacy of recycled rhodium catalyst

3.5 Conclusions

The use of a mixture of formic acid and triethylamine as a reagent for the didehydroxylation of diols was explored. Control reactions revealed that approximately 6 equivalents of formic acid, in the presence of triethylamine in various ratios, were needed for diol didehydroxylation. Reduction of carbon dioxide with both homogeneous and heterogeneous rhodium catalysts was accomplished with triethylamine as a base and sulfolane as the solvent. The homogeneous system was more effective at the reduction chemistry, but was not applicable to further use in didehydroxylation chemistry. The heterogeneous catalytic system produced solutions of formic acid and triethylamine that were competent at didehydroxylation of diols, but only if the mixture was isolated from the sulfolane solvent. Our rhodium catalyst deactivated after 150 turnovers, and attempts at recycling the solid catalyst were ineffective.

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3. Appendix : Experimental Section : Carbon dioxide reduction

General Procedure for didehydroxylation of vicinal diols using miscible amine / formic acid mixtures

A stock solution of a mixture of formic acid and triethylamine (**3.1**) was prepared (3.8 mL HCO_2H (100 mmol) and 5.6 mL NEt_3 (40 mmol)). A 3-necked round-bottom flask was charged with 15 mmol diol substrate, 1 mL **3.1** (10 mmol HCO_2H and 4 mmol NEt_3) and a magnetic stir bar. The flask was fitted with a short-path distillation apparatus and a nitrogen inlet for sparging the solution. The reaction mixture was heated to 220 °C for 1 hour and alkene product, formic acid and triethylamine were recovered in the collection flask. The reaction mixture was cooled to room temperature, and another 1 mL portion of **3.1** was added to the mixture. The mixture was then heated to 220 °C for 1 hour, and more alkene, formic acid and triethylamine were collected. Aliquots of the contents of the reaction flask and the collection flask were monitored via proton NMR spectroscopy with 1,3,5-trimethoxybenzene as an internal standard.

Example of didehydroxylation of glycerol with the 5:2 mixture of formic acid and triethylamine

A stock solution of a mixture of formic acid and triethylamine (**3.1**) was prepared (3.8 mL HCO_2H (100 mmol) and 5.6 mL NEt_3 (40 mmol)). A 3-necked round-bottom flask was charged with glycerol (1.28 g, 15 mmol), 1 mL **3.1** (10 mmol HCO_2H and 4 mmol NEt_3) and a magnetic stir bar. The flask was fitted with a short-path distillation apparatus and a nitrogen inlet for sparging the solution. The reaction mixture was heated to 220 °C for 1 hour and allyl alcohol, formic acid and triethylamine were recovered in the collection flask. The reaction mixture was cooled to room temperature, and another 1 mL portion of **3.1** was added to the mixture. The mixture was then heated to 220 °C for 1 hour, and more allyl alcohol, formic acid and triethylamine were collected. Aliquots of the contents of the reaction flask and the collection flask were monitored via proton NMR spectroscopy with 1,3,5-trimethoxybenzene as an internal standard. 71% yield allyl alcohol.

General Procedure for didehydroxylation of vicinal diols using immiscible amine / formic acid mixtures

A 3-necked round-bottom flask was charged with 15 mmol diol substrate, 4.8 mmol amine, 2 mL solvent and a magnetic stir bar. The flask was fitted with a short-path distillation apparatus and a nitrogen inlet for sparging the solution. A 0.45 mL portion (12 mmol) of formic acid was then added to the reaction flask, and the mixture was heated to 220 °C for one hour. Alkene product and formic acid were recovered in the collection flask, the reaction mixture was cooled to room temperature, and another 0.45 mL portion of formic acid was added to the reaction flask. This process was repeated until a total of four 0.45 mL portions of formic acid were added. Aliquots of the contents of the reaction flask and the collection flask were monitored via proton NMR spectroscopy with 1,3,5-trimethoxybenzene as an internal standard.

Example of didehydroxylation of decanediol using trioctylamine and formic acid

A 3-necked round-bottom flask was charged with 1,2-decanediol (2.61 g, 15 mmol), trioctylamine (2.3 mL, 4.8 mmol), 2 mL sulfolane and a magnetic stir bar. The flask was fitted with a short-path distillation apparatus and a nitrogen inlet for sparging the solution. A 0.45 mL portion (12 mmol) of formic acid was then added to the reaction flask, and the mixture was heated to 220 °C for one hour. 1-Decene and formic acid were recovered in the collection flask, the reaction mixture was cooled to room temperature, and another 0.45 mL portion of formic acid was added to the reaction flask. This process was repeated until a total of four 0.45 mL portions of formic acid were added. Aliquots of the contents of the reaction flask and the collection flask were monitored via proton NMR spectroscopy with 1,3,5-trimethoxybenzene as an internal standard. 74% yield of 1-decene.

General Procedure for the reduction of CO_2 under homogeneous conditions

A 100 mL Parr Reactor pressure vessel was charged with 1.2 mmol amine, 6.0 µmol transition metal catalyst, 1 mL sulfolane and a magnetic stir bar. The vessel was then sealed, flushed with nitrogen gas, evacuated, then charged to 600 psi with a 1:1 mixture of hydrogen gas and carbon dioxide gas. The reaction mixture was then stirred at room temperature for 24 hours. After 24 hours, the reaction vessel was degassed and the reaction mixture was monitored via proton NMR spectroscopy to determine the ratio of formic acid to amine.

Example of CO_2 reduction with [Rh(COD)Cl]$_2$ as a homogeneous catalyst

A 100 mL Parr Reactor pressure vessel was charged with triethylamine (0.17 mL, 1.2 mmol), [Rh(COD)Cl]$_2$ (3.0 mg, 6.0 µmol), dppb (2.6 mg, 6.0 µmol), 1 mL sulfolane and a magnetic stir bar. The vessel was then sealed, flushed with nitrogen gas, evacuated, then charged to 600 psi with a 1:1 mixture of hydrogen gas and carbon dioxide gas. The reaction mixture was then stirred at room temperature for 24 hours. After 24 hours, the reaction vessel was degassed and the reaction mixture was monitored via proton NMR spectroscopy to determine the ratio of formic acid to amine. Final ratio formic acid to triethylamine was 3 to 2 which corresponded to 1.8 mmol formic acid, 300 turnovers of the rhodium catalyst.

General Procedure for the reduction of CO_2 under heterogeneous conditions

A 100 mL Parr Reactor pressure vessel was charged with 21 mmol amine, 18 mL sulfolane, 108 µmol rhodium, 130 µmol dppb and a magnetic stir bar in an inert atmosphere glove box. The reaction vessel was sealed, removed from the glove box, and charged to 600 psi with a 1:1 mixture of hydrogen gas and carbon dioxide gas. The reaction mixture was then stirred at a constant temperature for 24 hours. After 24 hours, the reaction vessel was opened, the reaction mixture transferred to a centrifuge vial and spun in a centrifuge at 10000 rpm for 3 hours. Aliquots of the reaction mixture before and after centrifugation were analyzed via proton NMR spectroscopy.

Example of CO$_2$ reduction with Rh/Al$_2$O$_3$ as a heterogeneous catalyst

A 100 mL Parr Reactor pressure vessel was charged with triethylamine (2.8 mL, 21 mmol), 18 mL sulfolane, 5 wt% Rh/Al$_2$O$_3$ (222 mg, 108 μmol rhodium), dppb (55.4 mg, 130 μmol) and a magnetic stir bar in an inert atmosphere glove box. The reaction vessel was sealed, removed from the glove box, and charged to 600 psi with a 1:1 mixture of hydrogen gas and carbon dioxide gas. The reaction mixture was then warmed to 60 °C and stirred for 24 hours. After 24 hours, the reaction vessel was opened, the reaction mixture transferred to a centrifuge vial and spun in a centrifuge at 10000 rpm for 3 hours. Aliquots of the reaction mixture before and after centrifugation were analyzed via proton NMR spectroscopy. Before centrifugation, the ratio of formic acid to triethylamine was 3 to 4 which corresponds to 15.8 mmol formic acid and approximately 150 turnovers of the catalyst. The ratio remained the same after centrifugation.

4. Rhenium-catalyzed deoxygenation of diols and epoxides

4.1 Background – Rhenium-catalyzed didehydroxylation of vicinal diols (Dr. Elena Arceo)

Deoxygenation of vicinal diols, such as 1,2-tetradecanediol (**4.1**), has recently been achieved in our group with Re_2CO_{10} (**4.2**) as the catalyst and 3-octanol (**4.3**) as the reductant and solvent.[1] The reduction proceeded most readily in the presence of acid and air, giving high yields of 1-tetradecene (**4.4**) after approximately 2 hours (**Table 4.1**).
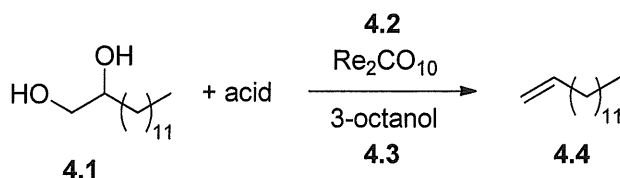
Entry	4.2 (mol %)[a]	4.3 (mL)	acid (mol %)[b]	temp. (° C)	time (h)	conv. (%)	yield 4.4 (%)[c]
1	2.5	4	--	155	5	0	0
2	2.5	4	T (5)	155	2.5	100	74 (76)
3	1	3	--	170	16	80	46
4	1	3	T (2)	155	1.5	100	77
5	1	5	T (2)	155	1.8	100	87 (83)
6	2.5	5	S (2)	155	2	100	82 (85)
7	1.25	5	S (2)	155	2	100	79

[a]Reactions conducted at 2.5 mmol scale, under air. [b] T is *para*-toluene sulfonic acid and S is sulfuric acid. [c]Determined by ^{1}H NMR using 1,3,5-trimethoxybenzene as internal standard. Isolated yield in parentheses.

Table 4.1 Didehydroxylation data previously reported from the Bergman and Ellman groups[1]

4.2 Optimization of the Re_2CO_{10} catalytic system

We were interested in discovering the mechanism of the rhenium-mediated deoxygenation of vicinal diols. Based on the previous work in the group, we hypothesized that a rhenium-oxo compound may be responsible for the observed reduction chemistry. Rhenium-oxo compounds have been known in the literature to oxidize alkenes to epoxides,[2] but have rarely been shown to catalyze the reverse

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reaction. As our chemistry involved the reduction of diols, we were interested in exploring rhenium-oxo chemistry further.

To begin, control deoxygenation reactions were run with 1,2-decanediol (**4.5**) and 1,2-tetradecanediol (**4.1**) under neutral and acidic conditions using Re_2CO_{10} (**4.2**) as the catalyst. ^{1}H NMR spectroscopy was employed to ascertain the conversion of starting material as well as the yield of alkene product (**Table 4.2**). These long chain diols were used as model compounds for sugar polyols due to their chemical simplicity and low volatility of the desired product alkenes, facilitating analysis. The chemistry proceeded at lower temperatures when acid was present with no detriment to the yield of alkene as compared to the reactions run at higher temperatures without an acid additive.
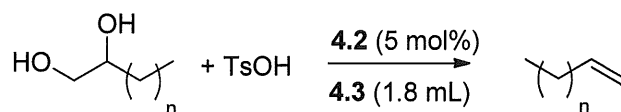
Entry[a]	n	Acid (%)	Temp (° C)	Time (h)	Conv. (%)	Yield alkene (%)[b]
1	11	0	180	4	100	71
2	11	2	155	3	100	75
3	7	0	180	3	100	72
4	7	2	155	2	100	78

[a]Reactions conducted at 1 mmol scale, in 1.8 mL **4.3**, under air. [b] Determined by ^{1}H NMR using 1,3,5-trimethoxybenzene as internal standard.

Table 4.2 Control didehydroxylation reactions of **4.1** and **4.5**

For the purpose of finding a system that could operate at temperatures below 150 °C, additional additives were employed (**Table 4.3**). Phosphines were used to probe the effect of a different reducing agent present in the reaction along with the 3-octanol solvent. Unfortunately, triphenylphosphine (PPh₃) and bis(diphenylphosphino)ferrocene (dppf) were ineffective at increasing the reactivity of the system at lower temperatures. Sodium borohydride was used to facilitate dissociation of carbonyl ligands from the rhenium center, in analogy to the procedure developed in earlier work.[3] Reactivity similar to that observed in the control reactions was only observed when the temperature was increased to 155 °C in the presence of 2 mol% acid. Increased reactivity was not observed with any of these additives.

$$\text{4.5} + \text{Additive} + \text{TsOH} \xrightarrow[\text{4.3 (1.8 mL)}]{\text{4.2 (5 mol\%)}} \text{4.6}$$
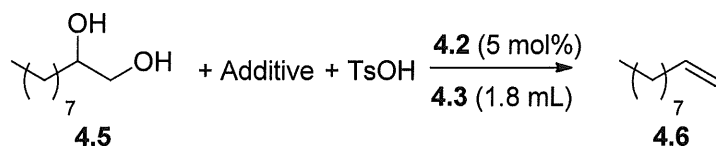
Entry[a]	Additive (%)	Acid (%)	Temp. (°C)	Time (h)	Conv (%)	Yield 4.6 (%)[b]
1	PPh$_3$ (7.5)	0	130	1 5	0 0	0 0
2	PPh$_3$ (7.5)	2	130	1 5	0 0	0 0
3	dppf (3)	0	130	1 5	0 0	0 0
4	NaBH$_4$ (5)	0	130	1 2 3	0 0 0	0 0 0
5	NaBH$_4$ (5)	2	130	1 2 3	0 0 0	0 0 0
6	PPh$_3$ (7.5)	0	155	1 2 3	0 0 0	0 0 0
7	PPh$_3$ (7.5)	2	155	1 5	0 0	0 0
8	dppf (3)	0	155	1 2 3	0 0 5	0 0 <5
9	NaBH$_4$ (5)	0	155	1 2 3	0 0 0	0 0 0
10	NaBH$_4$ (5)	2	155	1 2 3	0 25 45	0 15 25

[a]Reactions conducted at 1 mmol scale, in 1.8 mL **4.3**, under air. [b] Determined by ^{1}H NMR using 1,3,5-trimethoxybenzene as internal standard.

Table 4.3 Effects of additives on the didehydroxylation of diols

4.3 Experimental investigation of Re(I) catalysts

Because additives alone were not enough to increase the reactivity of the system, we decided to synthesize related rhenium complexes and study their effectiveness at deoxygenating diols. We specifically targeted ligands that could render the resting state of the catalysts potentially observable by NMR spectroscopy. A survey of the literature brought to our attention Re(I) carbonyl complexes with pyridyl benzimidazole (**4.7**) and pyridyl benzoxazole (**4.8**) ligands.[4] After preparation of these compounds following literature procedures, they were tested in the deoxygenation of **4.5** (**Table 4.4**). These Re(I) compounds did not deoxygenate the starting material until the temperature was raised to 180 °C. At this temperature, the rhenium complexes were no longer observable by NMR spectroscopy and the solution became extremely dark and heterogeneous.
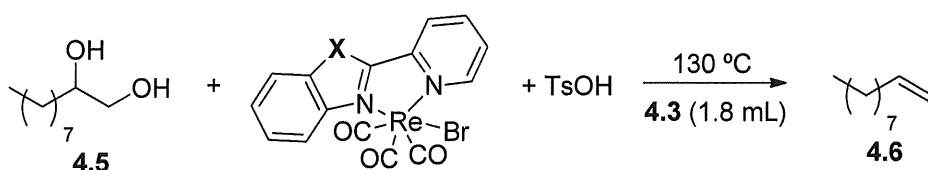
Entry	X	Acid (%)	Time (h)	Conv (%)[b]
1	NH **4.7**	2	1	0
			2	0
			12	0
2	NH **4.7**	0	1	0
			2	0
			12	0
3	O **4.8**	2	1	0
			2	0
			12	0
4	O **4.8**	0	1	0
			2	0
			12	0

[a]Reactions conducted at 1 mmol scale, in 1.8 mL **4.3**, under air with 5 mol% Re.

[b] Determined by ^{1}H NMR using 1,3,5-trimethoxybenzene as internal standard.

Table 4.4 Synthesized Re(I) compounds and their inactivity towards didehydroxylations

The pyridyl benzazole rhenium complexes **4.7** and **4.8** suffered from decomposition at high temperatures under aerobic conditions. In an effort to minimize catalyst decomposition, complexes were synthesized using ligands that were resistant to oxidation. Of particular note were hydroxamic acids, glyoximes and diazafluorenone (**Figure 4.1**).[5] These hydroxamic acid complexes were synthesized by adapting the procedure used to create the glyoxime compounds.[5a]
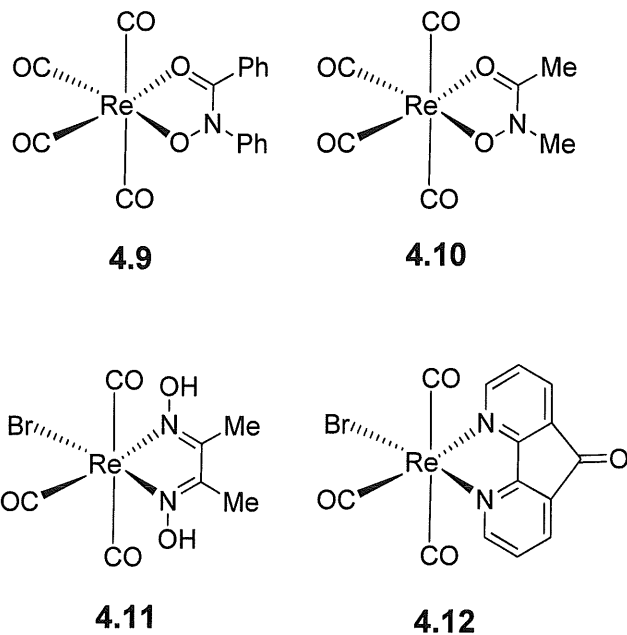
Figure 4.1 Re(I) compounds bearing oxidation resistant ligands

Rhenium(I) complexes **4.9** – **4.12** were tested as catalysts for the deoxygenation of 1,2-decanediol at 170 °C to ascertain whether they could perform the chemistry in a manner comparable to that of the original Re_2CO_{10} catalyst. Compounds **4.9** and **4.10** showed results comparable to those seen with Re_2CO_{10} (**Table 4.5**) under neutral and acidic conditions. Compound **4.11** decomposed very quickly, leading to no discernible alkene product and a heterogeneous, dark mixture after 1 hour. Compound **4.12** was unreactive under these conditions, showing no change in either the starting diol or the catalyst. When the reaction time was extended to 24 hours, the starting diol began to decompose, but the rhenium complex remained untouched.
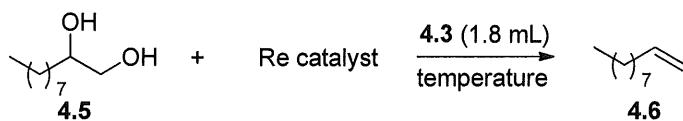
Entry[a]	Catalyst	Additive[b]	Time (h)	Conv (%)[c]	Yield 4.6 (%)[c]
1	4.9		1 3	75 100	55 80
2	4.9	TsOH	1 3	80 100	60 75
3	4.10		1 3	55 90	40 60
4	4.10	TsOH	1 3	60 90	40 60
5	4.11		1 3	0 0	0 0
6	4.11	TsOH	1 3	0 0	0 0
7	4.12		1 3	0 0	0 0
8	4.12	TsOH	1 3	0 0	0 0

[a] Reactions conducted at 1 mmol scale, in 1.8 mL **4.3**, under air with 5 mol% Re.
[b] 2 mol% acid was used. [c] Determined by ^{1}H NMR using 1,3,5-trimethoxybenzene as internal standard.

Table 4.5 Initial didehydroxylation reactions run with Re(I) synthetic compounds

Complexes **4.9** and **4.10** were then used in a temperature screen to ascertain the minimum temperature required to observe desired alkene formation (**Table 4.6**). Unfortunately, only minimal reactivity was observed at 150 °C after 24 h of reaction time for complex **4.9**, accompanied by considerable decomposition of the catalyst. Complex **4.10** remained unreactive until the temperature was increased to 170 °C. Reactions using this complex were difficult to monitor by ^{1}H NMR due to signal overlap of the catalyst's ligand methyl resonances with the 1,2-decanediol alkyl resonances. However, since there was no observable reactivity until the temperature was very high, the complex most likely decomposed into a compound that was active, in analogy to what we believe occurs when Re_2CO_{10} is used as a catalyst.

Table reaction scheme: Compound **4.5** (OH, OH) + Re catalyst → 4.3 (1.8 mL) / temperature → **4.6**

Entry[a]	Catalyst	Additive[b]	Temp (°C)	Time (h)[c]	Conv (%)[d]	Yield 4.6 (%)[d]
1	4.9	none	115	4	0	0
			135	8	5	0
			150	12	55	25
2	4.9	TsOH	115	4	0	0
			135	8	10	0
			150	12	65	25
3	4.10	none	115	4	0	0
			135	8	5	0
			150	12	25	0
4	4.10	TsOH	115	4	0	0
			135	8	15	0
			150	12	35	0

[a] Reactions conducted at 1 mmol scale, in 1.8 mL **4.3**, under air with 5 mol% Re. [b] 2 mol% acid was used. [c] The total reaction time is shown in this column. The reaction was held at each temperature for a total of 4 hours, and then increased. [d] Determined by ^{1}H NMR using 1,3,5-trimethoxybenzene as internal standard.

Table 4.6 Low temperature screen of Re(I) complexes **4.9** and **4.10**

4.4 Experimental investigations of Re(V) catalysts

After the Re(I) compounds failed to show catalytic activity at low temperatures, complexes with higher oxidation states were explored, specifically those with at least one oxo ligand. We had hypothesized that an oxo ligand was responsible for the desired reactivity during catalysis by $Re_2(CO)_{10}$, so activity observed with isolable higher oxidation state Re complexes would corroborate this assumption. A wide variety of Re(V) species were obtained via commercial sources or literature synthetic methods (**Figure 4.2**).[6a-d] Compounds **4.13f**, **4.13g**, **4.13j**, and **4.13m** were synthesized by adapting synthetic methods used to create **4.13b** except that the hydroxymethyl-benzimidazole ligand was replaced with hydroxamic acid ligands.[5c] Compound **4.13m** is a zwitterionic complex which resulted from the reduction of the hydroxamic acid ligand via PPh₃. X-ray analysis of the crystals can be found in the experimental data.
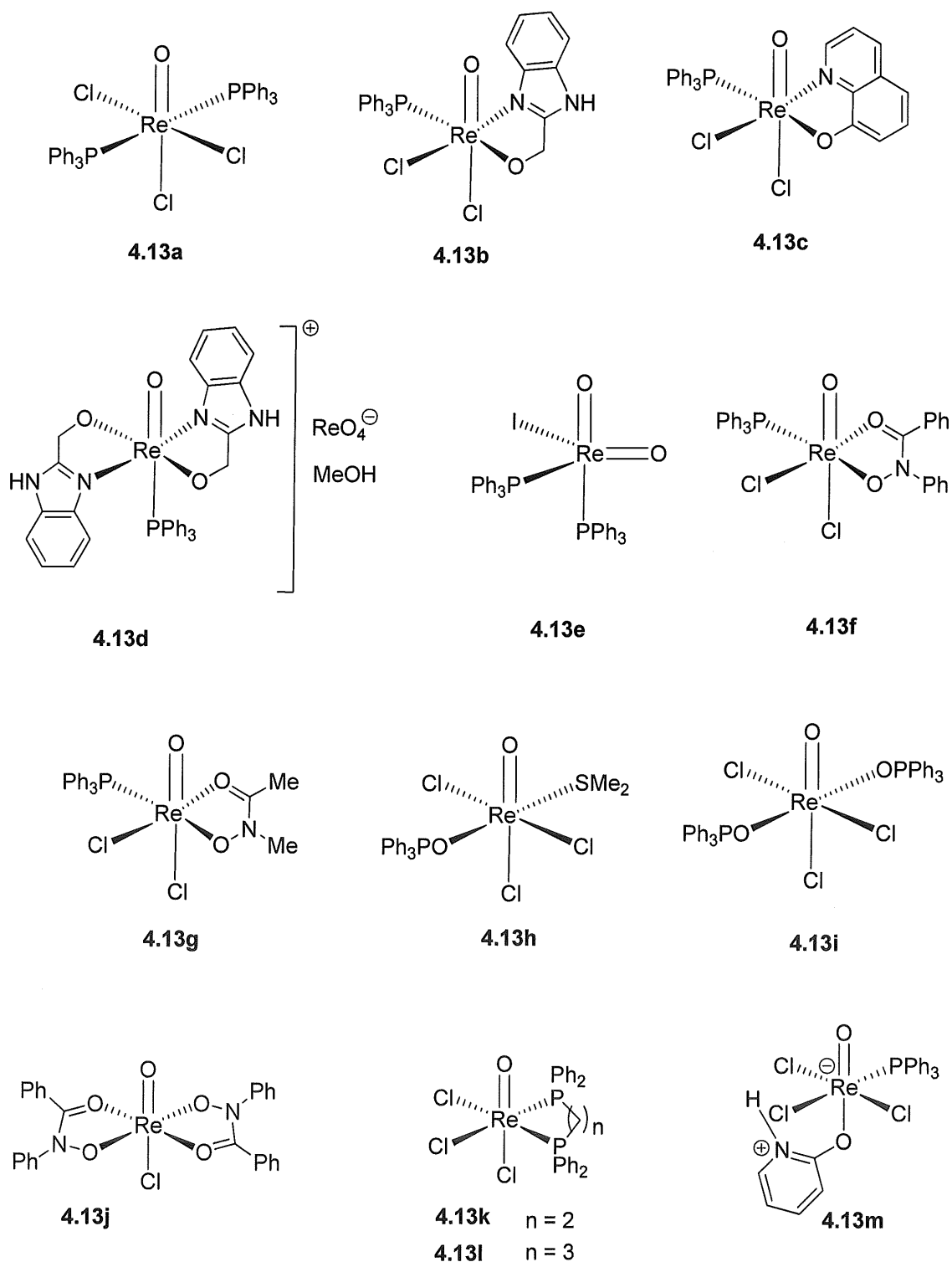
Figure 4.2 Re(V) compounds prepared and purchased for deoxygenation catalysis

The Re(V) oxo complexes were then screened as catalysts for the didehydroxylation of 1,2-decanediol at 170 °C (**Table 4.7**). Acid additives were left out of these reactions due to their limited effect on the reactions seen previously. Successful

didehydroxylation was achieved with catalysts **4.13a, 4.13e, 4.13f, 4.13h, 4.13i** and **4.13m**.

Entry	Catalyst	Time (h)	Conv (%)[b]	Yield 4.6 (%)[b]
1	4.13a	1	100	75
2	4.13b	1 3	0 15	0 0
3	4.13c	1 3	0 10	0 0
4	4.13d	1 3	0 15	0 0
5	4.13e	1 3	85 100	75 85
6	4.13f	1 3	55 95	40 65
7	4.13g	1 3	0 15	0 0
8	4.13h	1 3	90 100	75 85
9	4.13i	1 3	85 100	70 90
10	4.13j	1 3	0 10	0 0
11	4.13k	1 3	0 15	0 0
12	4.13l	1 3	0 10	0 0
13	4.13m	1 3	30 52	25 35

[a]Reactions conducted at 1 mmol scale, in 1.8 mL **4.3**, under air with 5 mol% Re.
[b] Determined by ^{1}H NMR using 1,3,5-trimethoxybenzene as internal standard.

Table 4.7 Re(V) high temperature catalyst screen

To further test the hypothesis that a higher oxidation state of rhenium was necessary for reactivity, two of the successful Re(V) catalysts and Re(CO)$_5$Br were tested under a nitrogen atmosphere (**Table 4.8**). Gratifyingly, the oxidized compounds were capable of performing catalysis while the Re(I) compound failed to react, even at elevated temperatures, presumably due to the lack of oxygen.
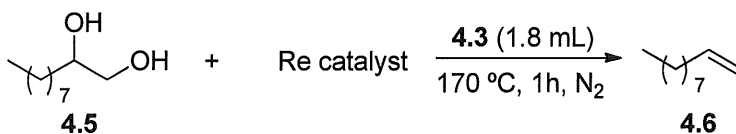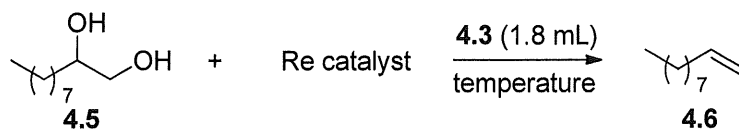
Entry[a]	Catalyst	Yield 4.6 (%)[b]
1	**4.13a**	65
2	**4.13f**	73
3	Re(CO)$_5$Br	0

[a]Reactions conducted at 1 mmol scale, in 1.8 mL **4.3**, under N$_2$ atmosphere with 5 mol% Re. [b] Determined by ^{1}H NMR using 1,3,5-trimethoxybenzene as internal standard.

Table 4.8 Air free didehydroxylation catalysis

A temperature screen was run to explore the reactivity of the competent Re(V) catalysts between 115 °C and 170 °C (**Table 4.9**). Most of the catalysts showed little to no reactivity until the temperature was raised to 150 °C. Long reaction times at this temperature led to decomposition of 1,2-decanediol. Catalysts **4.13a** and **4.13h** gave the highest yield of alkene after 4 hours of reaction at 150 °C and full conversion of the starting diol. Unfortunately, neither of these catalysts contains a moiety easily tracked by either ^{1}H NMR or ^{31}P NMR. The triphenylphosphine ligands of **4.13a** oxidize within the first 15 minutes of the reaction.
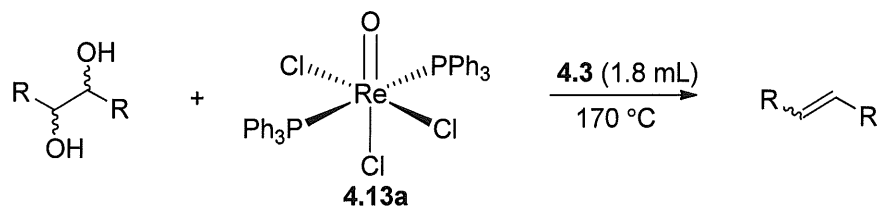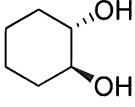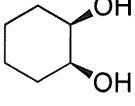
$$\text{OH}$$

4.5 — diol structure + Re catalyst →(4.3 (1.8 mL), temperature) 4.6 — alkene structure
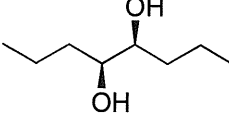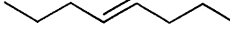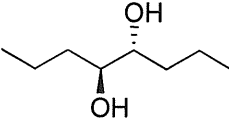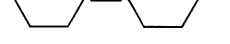
Entry[a]	Catalyst	Temp (°C)	Time (h)[b]	Conv (%)[c]	Yield 4.6 (%)[c]
1	4.13a	115	4	0	0
		135	8	10	0
		150	12	75	60
2	4.13e	115	4	0	0
		135	8	10	0
		150	12	60	38
3	4.13f	115	4	0	0
		135	8	5	0
		150	12	43	15
4	4.13h	115	4	0	0
		135	8	15	0
		150	12	88	60
5	4.13i	115	4	0	0
		135	8	5	0
		150	12	69	43
6	4.13m	115	4	0	0
		135	8	10	0
		150	12	35	12

[a] Reactions conducted at 1 mmol scale, in 1.8 mL 4.3, under air with 5 mol% Re. [b] The total reaction time is shown in this column. The reaction was held at each temperature for a total of 4 hours, and then increased. [c] Determined by ^{1}H NMR using 1,3,5-trimethoxybenzene as internal standard.

Table 4.9 Temperature screen for didehdroxylation with Re(V) catalysts

We next carried out experiments designed to examine the stereospecificity of the oxo-rhenium-mediated didehydroxylation. In analogy to the Re_2CO_{10} system, the didehydroxylation occurred stereospecifically (**Table 4.10**). *trans*-Cyclohexane-1,2-diol (**4.14**) yielded no alkene product after 24 hours at 170 °C, while *cis*-cyclohexane-1,2-diol (**4.15**) was converted to cyclohexene in 71% yield after 2 hours. Similarly, *meso*-octane-4,5-diol (**4.16**) was converted to *cis*-4-octene and *racemic*-octane-4,5-diol (**4.17**) was converted to *trans*-4-octene. These results indicate that removal of oxygen from the substrates occurs either *via* a concerted mechanism or a stepwise process via intermediates in which bond cleavage occurs more quickly than bond rotation.

| Entry[a]	Diol	Time (h)	Product[b]
1	(+/-) *trans*-cyclohexane-1,2-diol	24	none
2	*cis*-cyclohexane-1,2-diol	2	cyclohexene, 71% yield
3	(+/-) octane-4,5-diol	2	(E)-4-octene, 74% yield
4	octane-4,5-diol	2	(Z)-4-octene, 68% yield

[a] Reactions conducted at 1 mmol scale, in 1.8 mL **4.3**, under air with 5 mol% Re.
[b] Determined by ^{1}H NMR using 1,3,5-trimethoxybenzene as internal standard.

Table 4.10 Stereospecificity probes for didehydroxylation via Re(V) oxo complexes

4.5 Experimental investigations of the deoxygenation of epoxides with Re(V)

Our efforts were unable to provide a system in which the course of the reaction could be monitored by NMR spectroscopy. To continue our search, we considered changing our substrate from a diol to an epoxide. Though epoxides are much less similar to biomass sugars and poly-oxygenated compounds, they could serve to help us understand the reactivity of our rhenium catalysts. To this end, the Re(V) catalysts were tested for the deoxygenation of 1-decene oxide (**4.18**) at 170 °C (**Table 4.11**). The acid additive was universally detrimental to the reaction, causing swift decomposition of the starting material. In the absence of additives, complexes **4.13a**, **4.13e**, **4.13h**, **4.13i**, and **4.13m** successfully reduced **4.18** to decene (**4.6**) with moderate yields.
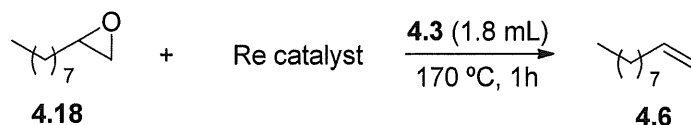
Entry[a]	Catalyst	Conv (%)[b]	Yield 4.6 (%)[b]
1	4.13a	100	65
2	4.13b	65	0
3	4.13c	60	0
4	4.13d	15	0
5	4.13e	100	60
6	4.13f	85	0
7	4.13g	90	0
8	4.13h	100	60
9	4.13i	100	65
10	4.13j	25	0
11	4.13k	65	0
12	4.13l	75	0
13	4.13m	75	60

[a]Reactions conducted at 1 mmol scale, in 1.8 mL 4.3, under air with 5 mol% Re.
[b] Determined by ^{1}H NMR using 1,3,5-trimethoxybenzene as internal standard.

Table 4.11 Re(V) catalyst screen for the deoxygenation of epoxides

A lower temperature screen was run with **4.13a**, a commercially available catalyst, to ascertain the minimum temperature required for reduction of the epoxide (**Table 4.12**). The chemistry proceeded in modest yield at 70 °C after 4 hours. The reduction of the epoxide, even at low temperatures, does not proceed as cleanly as the reduction of the diols. This can most likely be attributed to the higher reactivity of the epoxides, and their propensity to polymerize under acidic conditions. When catalyst loading was reduced, the yield was greatly reduced even at full conversion of the starting epoxide.
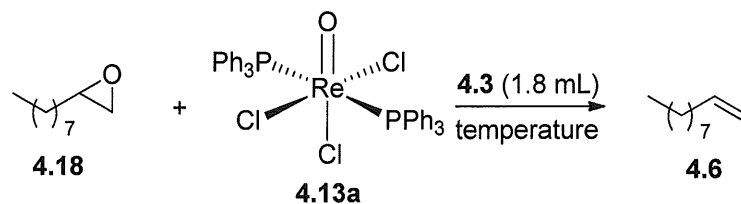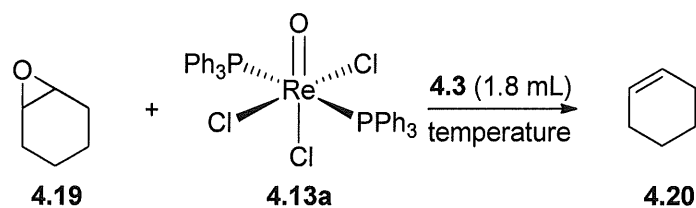
Entry[a]	4.13a mol%	Temp (°C)	Time (h)	Yield 4.6 (%)[b]
1	5	170	1	65%
2	5	160	1	63%
3	5	150	2	68%
4	5	140	2	64%
5	5	130	3	59%
6	5	70	4	46%
7	0.5	70	8	42%

[a] Reactions conducted at 1 mmol scale, in 1.8 mL **4.3**, under air to full conversion.
[b] Determined by ^{1}H NMR using 1,3,5-trimethoxybenzene as internal standard.

Table 4.12 Temperature screen for deoxygenation of **4.18** with catalyst **4.13a**

We hypothesized that a more strained epoxide would deoxygenate more quickly than octene oxide. Unfortunately, cyclohexene oxide (**4.19**) showed reactivity similar to that of octene oxide (**Table 4.13**). Epoxides more reactive than cyclohexene oxide were not stable under the deoxygenation reaction conditions. cis-Stilbene oxide and trans-stilbene oxide decomposed completely after 1 hour at 70 °C as did styrene oxide. Glycidol was converted to allyl alcohol in 22% yield after 4 hours of reaction time at 100 °C. This epoxy alcohol decomposed less quickly than the other reactive epoxides, but was still too unstable under the reaction conditions to be a viable substrate for studying the mechanism of the reaction.

O

O
+ Ph$_3$P$_{\prime\prime\prime\prime}$$\underset{Cl}{\overset{\|}{Re}}$$_{\prime\prime\prime\prime}$Cl
Cl$\swarrow$ $\searrow$PPh$_3$
Cl

$\xrightarrow{\quad \textbf{4.3} \text{ (1.8 mL)} \quad}$
temperature

4.19 **4.13a** **4.20**

| Entry[a]	4.13a mol %	Temp (°C)	Time (h)	Yield 4.20 (%)[b]
1	5	170	1	61%
2	5	160	1	65%
3	5	150	2	52%
4	5	140	2	57%
5	5	130	3	51%
6	5	70	4	38%
7	0.5	70	8	29%

[a] Reactions conducted at 1 mmol scale, in 1.8 mL **4.3**, under air to full conversion.
[b] Determined by ^{1}H NMR using 1,3,5-trimethoxybenzene as internal standard.

Table 4.13 Deoxygenation of **4.19** with catalyst **4.13a** at various temperatures

4.6 Investigation of solvent effects

A lingering question from our earlier studies with Re$_2$CO$_{10}$ was the effect of *iso*propanol (**4.21**) on the reaction. The small alcohol was not only inefficient in the deoxygenation reaction, it actively inhibited reactivity.[1] We explored the effect of **4.21** on the Re(V) catalyzed deoxygenation reactions of diols (**Table 4.14**). When **4.3** was replaced with **4.21** as the solvent and reductant, diols **4.5** and **4.15** could not be deoxygenated. When the reactions were run in a sealed vessel to allow increase in the temperature, conversion was very low after several days. The presence of 1,2-cyclohexanedione was detected by ^{1}H NMR as well as GC/MS after the pressurized reaction of **4.15** which indicated the starting material acted as the reductant instead of *iso*propanol. Unfortunately, we still cannot provide an explanation for this unusual observation.
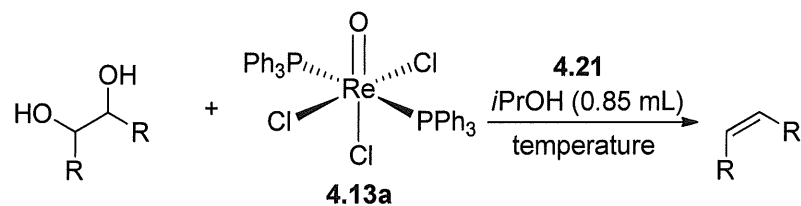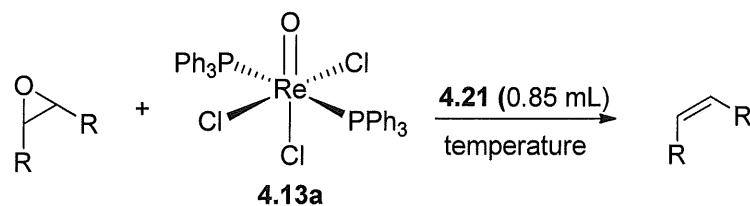
Entry[a]	Diol	Temp (°C)	Alkene	Yield (%)
1	**4.5**	110	**4.6**	0
2[c]	**4.5**	170	**4.6**	11
3	**4.15**	110	**4.20**	0
4[c]	**4.15**	170	**4.20**	15

[a] Reactions conducted at 1 mmol scale, in 0.85 mL **4.21**, under air for 48 h and 5 mol% **4.13a**. [b] Determined by ^{1}H NMR using 1,3,5-trimethoxybenzene as internal standard. [c] Run in a sealed reaction vessel.

Table 4.14 Vicinal diol reactivity with *iso*propanol as the reductant

The deoxygenation of epoxides was also investigated using **4.21** as the reductant (**Table 4.15**). The epoxides were reduced at lower temperatures than their diol analogues. However, the yield of alkene, at full conversion, was attenuated when compared to that observed using 2-octanol as the reductant. n-Decane was used as an additive to increase the hydrophobicity of the reaction system, but produced no change in the overall reactivity observed (entry 5).

$$\text{epoxide} + \textbf{4.13a} \xrightarrow[\text{temperature}]{\textbf{4.21 (0.85 mL)}} \text{alkene}$$

4.13a (Ph$_3$P, O=Re, Cl, Cl, Cl, PPh$_3$ complex)

Entry[a]	Epoxide	Temp (°C)	Time (h)	Alkene	Yield (%)[b]
1	**4.18**	70	4	**4.6**	28
2	**4.18**	110	2	**4.6**	30
3	**4.19**	70	4	**4.20**	24
4	**4.19**	110	2	**4.20**	34
5[c]	**4.19**	110	2	**4.20**	33

[a] Reactions conducted at 1 mmol scale, in 0.85 mL **4.21**, with 5 mol% **4.13a** under air.
[b] Determined by ^{1}H NMR using 1,3,5-trimethoxybenzene as internal standard.
[c] 2 mL of decane added to increase the hydrophobicity of the solution.

Table 4.15 Epoxide reactivity with **4.21** as the reductant

4.7 Conclusion

In conclusion, rhenium-oxo complexes are competent catalysts for the deoxygenation of vicinal diols and epoxides when 2-octanol is used as a reductant. Under optimal conditions, a vicinal diol was reduced to an alkene in 85% yield after 2 hours at 170 °C. Cyclohexene oxide and 1,2-decene oxide were also reduced to alkenes by **4.13a** in good yield at relatively low temperatures. Though we were unable to obtain concrete spectroscopic information about the mechanism of the rhenium-oxo complex-catalyzed deoxygenations, we believe that an active rhenium center is created following ligand dissociation. The active rhenium species then undergoes association with the substrate, leading to a presumed diolate intermediate. This intermediate then decomposes, releasing an alkene product and an oxidized form of the rhenium complex. The rhenium complex is then presumably reduced by the alcohol solvent.

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(6)   (a) Sigouin, O.; Beauchamp, A. L. *Can. J. Chem.*, **2005**, *83*, 460. (b) Lebuis, A.; Beauchamp, A. *Can. J. Chem.*, **1993**, *71*, 441. (c) Machura, B.; Wolff, M.; Kusz, J. *Polyhedron*, **2010**, *29*, 1619. (d) Dinda, S.; Drew, M. G. B.; Bhattacharyya, R. *Catalysis Communications*, **2009**, *10*, 720.

4. Appendix : Experimental Section : Rhenium Deoxygenation Chemistry

General Experimental. Unless otherwise noted, all reagents were obtained from commercial suppliers and used without further purification. Tetrahydrofuran, methylene chloride, and toluene were passed through a column of activated alumina under nitrogen. All glassware was dried at 150 °C overnight or flame-dried under vacuum immediately prior to use. Unless otherwise noted, all solvent was removed under reduced pressure with a rotary evaporator. Chromatography was performed on Merck 60 230-240 mesh silica gel or using a Biotage SP1 Flash Purification System. Unless otherwise noted, all NMR spectra were obtained on an AVQ-400 ,DRX-500 or AV-500 spectrometer. NMR chemical shifts are reported in ppm relative to either the residual solvent peak (^{1}H, ^{13}C) or TMS (^{1}H). X-Ray crystallographic data were obtained by David Tatum in the CheXray facility at the University of California, Berkeley on an Apex II Quazar instrument. Many of the syntheses were exploratory, and full characterization of compounds was only carried out with catalytically active species.

Synthesis of Re(I) Compounds

4.7   **4.8**
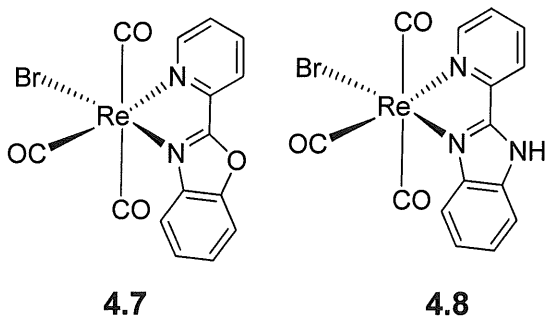
Compounds 4.7 and 4.8. The pyridyl benzoxazole (**4.7**) and pyridyl benzimidazole (**4.8**) Re(I) compounds were synthesized according to literature procedures.[1] A 25 mL round-bottom flask was charged with 406 mg (1 mmol) ReBr(CO)$_5$, 1 mmol pyridyl benzazol, 11 mL toluene and a magnetic stir bar. The flask was fitted with a reflux condenser, put under an atmosphere of nitrogen, and lowered into an oil bath heated to 120 °C. After 4 hours, the flask was removed and the yellow complexes that had precipitated were isolated via vacuum filtration. Their ^{1}H NMR spectra were consistent with literature values.[1] Yield **4.7**, 508 mg (92%). Yield **4.8**, 420 mg (76%).


4.9   **4.10**
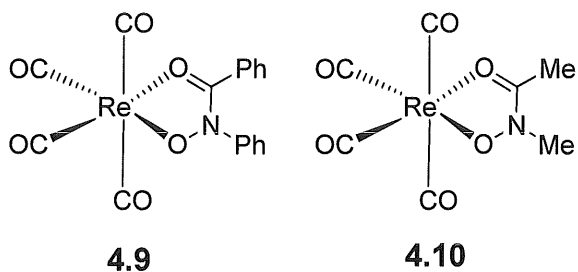
Compounds 4.9 and 4.10. Hydroxamato Re(I) complexes **4.9** and **4.10** were synthesized using an adaptation of the synthesis of **4.7** and **4.8** wherein the pyridyl benzazole substrate was replaced with the corresponding hydroxamic acid substrate.

Yield **4.9**, 231 mg (45%); ^{1}H NMR (500 MHz, CD_2Cl_2): δ 7.47 (3H, m), 7.37 (7H, m).
Yield **4.10**, 137 mg (35%); ^{1}H NMR (500 MHz, D_2O): δ 1.66 (3H, s), 1.62 (3H, s).
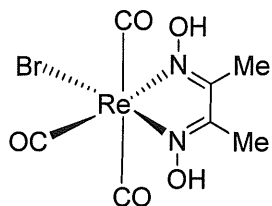

4.11

Compound 4.11. The glyoxime complex was synthesized according to literature procedure.[2] A 25 mL round-bottom flask was charged with 101 mg (0.25 mmol) $ReBr(CO)_5$, 29.0 mg (0.25 mmol) dimethylglyoxime, 15 mL water and a magnetic stir bar. The flask was fitted with a reflux condenser and placed in an oil bath heated to 120 °C. The reaction mixture was heated at reflux for 30 minutes yielding an orange solution. Upon cooling, the water was removed and an orange solid was obtained. Yield **4.11**, 94.7 mg (83%). The ^{1}H NMR spectrum was consistent with literature values.[2]
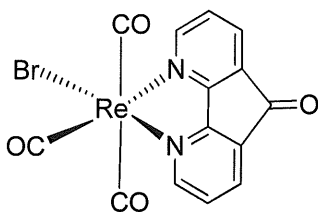

4.12

Compound 4.12. The 4,5-diazafluorenone complex was synthesized according to literature procedure.[3] A 25 mL round bottom flask was charged with 183 mg (0.45 mmol) $ReBr(CO)_5$, 91.1 mg (0.5 mmol) 4,5-diazafluorenone, 10 mL toluene and a magnetic stir bar. The flask was fitted with a reflux condenser, the reaction put under a nitrogen atmosphere, and the flask placed in an oil bath heated to 110 °C. The reaction mixture was heated at reflux for 4 hours, resulting in a bright orange solution and bright orange solid. The solid was obtained via vacuum filtration. Yield **4.12**, 127 mg (51%). The ^{1}H NMR spectrum was consistent with literature values.[3]
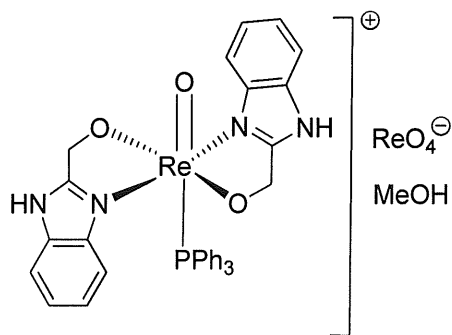
Synthesis of Re(V) Compounds
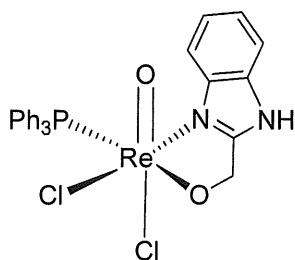
4.13b

Compound 4.13b. 4.13b was synthesized according to literature procedure.[4] A 100 mL round-bottom flask was charged with 98.8 mg (0.67 mmol) hydroxymethyl-benzimidazole, 500 mg (0.60 mmol) Re(O)Cl$_3$(PPh$_3$)$_2$, 60 mL THF and a magnetic stir bar. The reaction flask was equipped with a reflux condenser, put under an atmosphere of nitrogen and placed in an oil bath heated to 75 °C. The reaction mixture was heated at reflux for 4 hours. Upon cooling to room temperature, a blue powder precipitated from solution and was obtained via vacuum filtration. Yield **4.13b**, 255 mg (72%). The ^{1}H and ^{31}P NMR spectra were consistent with literature values.[4]
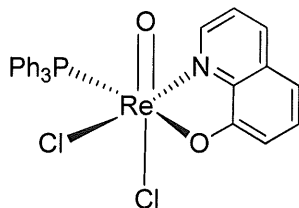

4.13c

Compound 4.13c. 4.13c was synthesized according to literature procedure.[5] A 100 mL round-bottom flask was charged with 17.5 mg (0.12 mmol) 8-hydroxyquinoline, 100 mg (0.12 mmol) Re(O)Cl$_3$(PPh$_3$)$_2$, 10 mL THF and a magnetic stir bar. The flask was equipped with a reflux condenser, the reaction mixture placed under an atmosphere of nitrogen and the flask lowered into an oil bath heated to 75 °C. The reaction mixture was heated at reflux for 19 h. Upon cooling to room temperature, the brown precipitate was isolated via vacuum filtration. Yield **4.13c**, 41.6 mg (49%). The ^{1}H and ^{31}P NMR spectra were consistent with literature values.[5]

4.13d

Compound 4.13d. 4.13d was synthesized according to literature procedure.[4] A 25 mL round-bottom flask was charged with 118 mg (0.20 mmol) **4.13b**, 10 mL MeOH and a magnetic stir bar. The flask was equipped with a reflux condenser and lowered into an oil bath heated to 75 °C. The reaction mixture was heated at reflux for 1 hour. Upon cooling, blue crystals precipitated from solution. The crystals were obtained via vacuum filtration. Yield **4.13d**, 67.7 mg (65%). The ^{1}H NMR spectrum was consistent with literature values.[4]
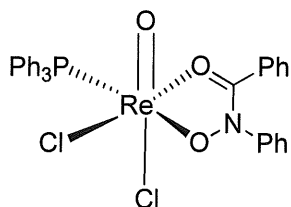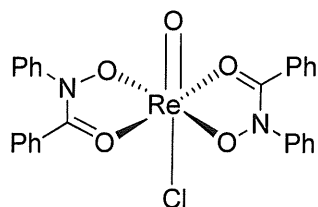

4.13f

Compound 4.13f. A 100 mL round-bottom flask was charged with 142 mg (0.67 mmol) diphenyl hydroxamic acid, 500 mg (0.6 mmol) Re(O)Cl$_3$(PPh$_3$)$_2$, 60 mL THF and a magnetic stir bar. The reaction flask was fitted with a reflux condenser, placed under a nitrogen atmosphere and lowered into an oil bath heated to 75 °C. The reaction mixture was heated at reflux for 4 hours. The mixture was then cooled to room temperature and the THF removed via rotary evaporation. The resulting green paste was recrystallized from 10 mL dichloromethane and 3 mL hexanes. Yield **4.13f**, 292 mg (65%). ^{1}H NMR (500 MHz, CD$_2$Cl$_2$): δ 7.78 (1H, m), 7.67-7.30 (24H, m). ^{31}P NMR (CD$_2$Cl$_2$): δ -14.8. Anal. calc. for C$_{31}$H$_{25}$Cl$_2$NO$_3$PRe (%) : C 49.80, H 3.37, N 1.87; found: C 49.89, H 3.21, N 1.87.
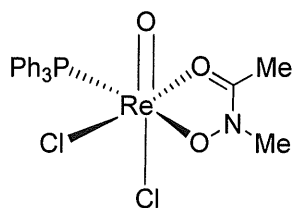
4.13g

Compound 4.13g. A 100 mL round-bottom flask was charged with 59.4 mg (0.67 mmol) dimethyl hydroxamic acid, 500 mg (0.6 mmol) Re(O)Cl$_3$(PPh$_3$)$_2$, 60 mL THF and a magnetic stir bar. The reaction flask was fitted with a reflux condenser, placed under a nitrogen atmosphere and lowered into an oil bath heated to 75 °C. The reaction mixture was heated at reflux for 4 hours. The mixture was then cooled to room temperature and the THF removed via rotary evaporation. The resulting green paste was recrystallized from 10 mL dichloromethane and 3 mL hexanes. Yield **4.13g**, 161mg (43%). ^{1}H NMR (500 MHz, CD$_3$CN): δ 7.38-7.34 (18H, m), 7.31-7.28 (12H, m), 1.85 (6H, s). ^{31}P NMR (CD$_3$CN): δ -12.5. Anal. calc. for C$_{21}$H$_{21}$Cl$_2$NO$_3$PRe (%) : C 40.45, H 3.39, N 2.25; found: C 40.51, H 3.42, N 2.24.


4.13j

Compound 4.13j. A 100 mL round-bottom flask was charged with 284 mg (1.33 mmol) diphenyl hydroxamic acid, 500 mg (0.6 mmol) Re(O)Cl$_3$(PPh$_3$)$_2$, 60 mL THF and a magnetic stir bar. The reaction flask was fitted with a reflux condenser, placed under a nitrogen atmosphere and lowered into an oil bath heated to 75 °C. The reaction mixture was heated at reflux for 4 hours. The mixture was then cooled to room temperature and the THF removed via rotary evaporation. The resulting brown paste was recrystallized from 10 mL acetone and 3 mL hexanes. Yield **4.13j**, 212 mg (32%). ^{1}H NMR (500 MHz, CD$_2$Cl$_2$): δ 7.59 (6H, m), 7.48 (14H, m). ^{31}P NMR (CD$_2$Cl$_2$) : No signal found.
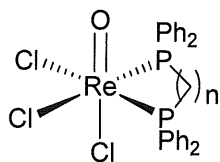
4.13k   n = 2
4.13l   n = 3

Compounds 4.13k and 4.13l. These bis-diphenylphosphino Re(V) compounds were synthesized following a literature procedure.[6] A 50 mL round-bottom flask was charged with 0.3 mmol of the appropriate phosphine ligand, 240 mg (0.3 mmol) $Re(O)Cl_3(PPh_3)_2$, 10 mL acetonitrile, 10 mL acetone and a magnetic stir bar. The reaction flask was equipped with a reflux condenser, placed under a nitrogen atmosphere and lowered into an oil bath heated to 90 °C. The reaction mixture was heated at reflux for 90 minutes and then allowed to cool. The precipitate was collected via vacuum filtration. Yield **4.13k**, 122 mg (61%). Yield **4.13l**, 95.2 mg (44%). The ^{1}H and ^{31}P NMR spectra were consistent with literature values for both compounds.[6]
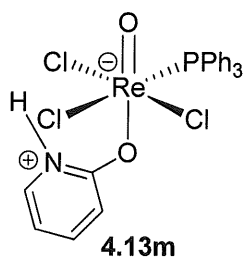
Compound 4.13m. A 1000 mL round-bottom flask was charged with 61.1 mg (0.55 mmol) 2-hydroxy-pyridine-N-oxide, 416.5 mg (0.50 mmol) $Re(O)Cl_3(PPh_3)_2$, 50 mL dichloromethane and a magnetic stir bar. The reaction flask was fitted with a reflux condenser, the reaction placed under a nitrogen atmosphere, and the flask placed in an oil bath heated to 55 °C. The reaction mixture was heated at reflux for 2 hours. The mixture was then cooled to room temperature and large, green, X-ray quality crystals crystallized out of solution. Yield **4.13m**, 165 mg (22%). ^{31}P NMR (CD_2Cl_2) : δ -19.01.
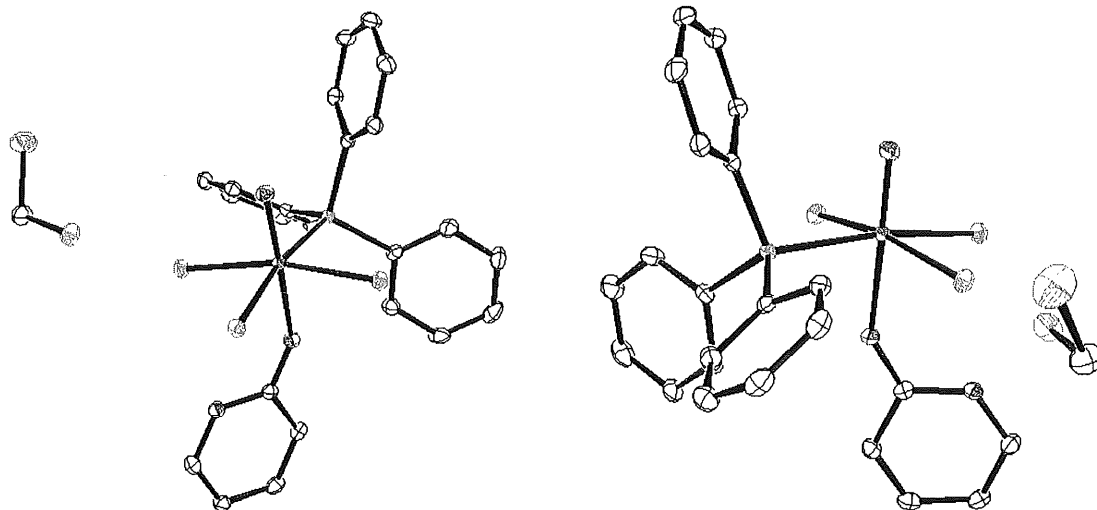
Crystal Structure Data for 4.13m

Table 1. Crystal data and structure refinement for **4.13m**.

Identification code	PCM-VI-4.13m
Empirical formula	C24 H22 Cl5 N1 O2 P Re
Formula weight	750.88
Temperature	100(2) K
Wavelength	0.71073 Å
Crystal system	Triclinic
Space group	P1
Unit cell dimensions	a = 9.156 Å α= 91.56°.
	b = 11.022 Å β= 98.77°.
	c = 13.385 Å γ = 99.01°.
Volume	1316.7 Å^3
Z	2
Density (calculated)	2.101 Mg/m^3
Absorption coefficient	5.076 mm^{-1}
F(000)	820
Crystal size	1.1 x 0.41 x 0.35 mm^3
Theta range for data collection	1.54 to 25.44°.
Index ranges	-11<=h<=11, -13<=k<=13, -16<=l<=15
Reflections collected	26953
Independent reflections	4831 [R(int) = 0.0230]
Completeness to theta = 25.44°	99.3 %
Absorption correction	None

Refinement method	Full-matrix least-squares on F^2
Data / restraints / parameters	4831 / 0 / 307
Goodness-of-fit on F^2	1.022
Final R indices [I>2sigma(I)]	R1 = 0.0135, wR2 = 0.0310
R indices (all data)	R1 = 0.0141, wR2 = 0.0313
Largest diff. peak and hole	0.696 and -0.615 e.Å^{-3}

General Reaction conditions for rhenium-mediated deoxygenation. A 10 mL round-bottom flask was charged with 1 equivalent of substrate, 11 equivalents of 3-octanol, 0.05 equivalents of rhenium complex and a magnetic stir bar. The flask was then fitted with a reflux condenser and the reaction temperature was raised. The reaction was held at the specified temperature with aliquots being removed for NMR analysis every hour. Trimethoxybenzene was added to the aliquots as an external standard.

Representative Deoxygenation Reaction of a diol: 1,2-decanediol and Re(O)Cl₃(PPh₃)₂. A 10 mL round-bottom flask was charged with 174 mg (1 mmol) 1,2-decanediol, 1.8 mL 3-octanol (11 mmol), 41.7 mg (0.05 mmol) Re(O)Cl₃(PPh₃)₂ and a magnetic stir bar. The flask was then fitted with a reflux condenser and the flask lowered into an oil bath heated to 170 °C. After 3 hours, the flask was removed from the oil bath, the reaction mixture allowed to cool to room temperature, and the reaction mixture was analyzed via ^{1}H NMR spectroscopy. Yield 1-decene, 75%.

Representative Deoxygenation Reaction of an epoxide : Cyclohexene oxide and Re(O)Cl₃(PPh₃)₂. A 10 mL round-bottom flask was charged with 0.10 mL (1 mmol) cyclohexene-oxide, 1.8 mL 3-octanol (11 mmol), 41.7 mg (0.05 mmol) Re(O)Cl₃(PPh₃)₂ and a magnetic stir bar. The flask was then fitted with a reflux condenser and the flask lowered into an oil bath heated to 160 °C. After 1 hour, the flask was removed from the oil bath, the reaction mixture allowed to cool to room temperature and analyzed via ^{1}H NMR spectroscopy. Yield cyclohexene, 65%

References

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