THE USE OF NEW TECHNOLOGIES TO DEVELOP ENVIRONMENTALLY
BENIGN PROCESSES: ACID-CATALYZED HYDROLYSIS OF PINENE IN
AQUEOUS MEDIA

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THE USE OF NEW TECHNOLOGIES TO DEVELOP ENVIRONMENTALLY BENIGN PROCESSES: ACID-CATALYZED HYDROLYSIS OF PINENE IN AQUEOUS MEDIA

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It's never too late... You only live once. Go for it!
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# TABLE OF CONTENTS

ACKNOWLEDGEMENTS  iv  
LIST OF TABLES  ix  
LIST OF FIGURES  x  
SUMMARY  xiv  

CHAPTER I. INTRODUCTION  1  

CHAPTER II. BACKGROUND: THE CHEMISTRY OF β-PINENE AND α-TERPINEOL  5  

CHAPTER III. ACID-CATALYZED HYDRATION OF PINENE IN SDS MICELLES  

<table>
<thead>
<tr>
<th>Section</th>
<th>Page</th>
</tr>
</thead>
<tbody>
<tr>
<td>Introduction</td>
<td>23</td>
</tr>
<tr>
<td>Results and Discussion</td>
<td>28</td>
</tr>
<tr>
<td>Conclusion</td>
<td>32</td>
</tr>
<tr>
<td>Experimental</td>
<td>33</td>
</tr>
<tr>
<td>Literature Cited</td>
<td>37</td>
</tr>
</tbody>
</table>

CHAPTER IV. ACID-CATALYZED HYDRATION OF β-PINENE IN HOT WATER 200 °C  

<table>
<thead>
<tr>
<th>Section</th>
<th>Page</th>
</tr>
</thead>
<tbody>
<tr>
<td>Introduction</td>
<td>38</td>
</tr>
<tr>
<td>Results and Discussion</td>
<td>42</td>
</tr>
<tr>
<td>Conclusion</td>
<td>50</td>
</tr>
<tr>
<td>Recommendations for Future Work</td>
<td>51</td>
</tr>
<tr>
<td>Experimental</td>
<td>53</td>
</tr>
<tr>
<td>Literature Cited</td>
<td>57</td>
</tr>
</tbody>
</table>

CHAPTER V. ACID-CATALYZED HYDRATION OF β-PINENE IN GAS EXPANDED LIQUID (GXL)  

<table>
<thead>
<tr>
<th>Section</th>
<th>Page</th>
</tr>
</thead>
<tbody>
<tr>
<td>Introduction</td>
<td>60</td>
</tr>
<tr>
<td>Results and Discussion</td>
<td>64</td>
</tr>
<tr>
<td>Conclusion</td>
<td>70</td>
</tr>
<tr>
<td>Recommendations for Future Work</td>
<td>71</td>
</tr>
<tr>
<td>Experimental</td>
<td>75</td>
</tr>
<tr>
<td>Literature Cited</td>
<td>79</td>
</tr>
</tbody>
</table>

CHAPTER VI. CONCLUSION  82  

vii
### LIST OF TABLES

| Table 2-1 | Percentage of optical isomers present in authentic samples of different citrus essential oils | 9 |
| Table 2-2 | Sample of pinene hydration literature (see full summary in Appendix A) | 11 |
| Table 2-3 | Summary from the literature for product composition for pinene solvolysis reactions (% of product mixture) | 15 |
| Table 2-4 | Summary of literature rate data for pinene hydration (from Reference 1) | 18 |
| Table 3-1 | Summary of kinetic data for pinene hydrolysis reactions | 29 |
| Table 3-2 | Summary of experimental conditions for pinene hydration experiments | 35 |
| Table 4-1 | Properties of water | 39 |
| Table 4-2 | Hot water reaction composition and relative rate data | 44 |
| Table 5-1 | pH and dielectric constant values for MeOH/H2O/CO2 GXL's | 63 |
| Table 5-2 | Summary of GXL composition and results | 69 |
| Table 5-3 | Possible factorial design for DOE investigation of GXL reactions | 73 |
| Table 5-4 | GXL composition summary | 77 |
| Table 6-1 | Product distribution comparison between the systems investigated in this study | 84 |
| Table A-1 | Literature summary of pinene hydrolysis and formation of α-terpineol | 87 |
| Table B-1 | Peak identification for GC chromatograms | 95 |
| Figure 2-1 | α-Terpineol and isomers | 5 |
| Figure 2-2 | Classical method for the manufacture of terpineol from pinene | 7 |
| Figure 2-3 | Predicted conformation of the pinene isomers | 7 |
| Figure 2-4 | Pinane-based versatile reagents (PVR) from reference 12 | 9 |
| Figure 2-5 | Mechanism for the acid-catalyzed rearrangement and hydrolysis of β-pinene | 13 |
| Figure 2-6 | Stereochemistry in the pinene reaction | 15 |
| Figure 3-1 | Common surfactants: SDS-anionic; CTAB-cationic; Tween 20-nonionic | 23 |
| Figure 3-2 | Graphical representation of surfactant concentration vs. some physical properties of a micelle-forming surfactant | 24 |
| Figure 3-3 | Graphical representation (2-D) of a spherical ionic micelle | 25 |
| Figure 3-4 | Solubilization of Orange OT dye in alkyl sulfate micelles | 26 |
| Figure 3-5 | Major products of the acid-catalyzed cyclization/hydration of citronellal | 27 |
| Figure 3-6 | Major products of terpene ester hydrolysis reactions | 28 |
| Figure 3-7 | Pseudo first order rate plot for α-pinene (4) in an aqueous SDS micelle at pH=2.3 | 29 |
| Figure 3-8 | Product distribution for pinene reactions: 1=α-pinene (4) in aqueous emulsion, 75 hr; 2= α-pinene (4) in Tween 80, 48 hr; 3 & 4= α-pinene (4) in SDS micelle, 24 hr; 5 & 6= β-pinene (5) in SDS micelle, 24 hr. | 30 |
| Figure 3-9 | Proposed mechanism for micellar selectivity in the pinene hydration reaction | 32 |
| Figure 4-1 | Hydrogen bond donating ability (α) of water as a function of temperature | 40 |
| Figure 4-2 | Ionization constant (pKₐ) of water as a function of temperature | 40 |
Figure 4.3  Major reaction products from pinene acid-catalyzed hydration

Figure 4.4  Product distribution and relative rates for ~90% conversion of β-pinene (2) in hot water (#1) vs. co-solvent systems: 75% / 25% H₂O/ETHOH (#2); 50% / 50% H₂O/acetone (#3); 50% / 50% H₂O/ETHOH (#4); 50% / 50% H₂O/THF (#5); 50% / 50% H₂O/IPA (#6) [IPA/water reaction stopped at 80% conversion]

Figure 4.5  Disappearance of β-pinene (2) and mass balance for 50% THF/50% H₂O (by volume) at 200°C over time

Figure 4.6  Product distribution over time for 50% THF/50% H₂O (by volume) over time

Figure 4.7  Formation of bicyclic alcohols in all solvent systems at 200°C

Figure 4.8  Formation of bicyclic alcohols from β-pinene (2) in 50/50 ethanol/water at 200°C

Figure 4.9  Formation of ether product in 50/50 ethanol/water at 200°C

Figure 4.10 Recovery of β-pinene (2) after 2 hours in control reactions

Figure 4.11 Diagram of the heated aluminum block and titantium reactor tube

Figure 4.12 Diagram of the variable-volume vessel apparatus

Figure 5.1  A pictorial view of the relationship of GXL’s to other common solvent systems

Figure 5.2  Formation of carbonic acids

Figure 5.3  Summary of pinene recovery from GXL control reactions

Figure 5.4  Product distribution reproducibility for 6 runs of the 1:1 pinene MeOH/water GXL

Figure 5.5  β-Pinene conversion and product distribution variations with different MeOH/water ratios (75°C, 24 hr)

Figure 5.6  Two equilibrium reactions contributing to “acid strength” of alkyl carboxylic acids in GXL’s
Figure 6-1  Pinene hydration product distribution comparison  84
Figure B-1  GC-FID chromatogram from a β-pinene MeOH/water/CO₂ (1:1) GXL after 24 hours at 75 °C  93
Figure B-2  GC-FID chromatogram from a β-pinene hot water/acetone (1:1) reaction (68 minutes)  94
Figure B-3  MS total ion chromatogram comparison of control reaction for β-pinene in acetone at 200 °C  98
Figure B-4  MS comparison of β-pinene (bottom) vs. the peak tentatively identified as the reaction product of acetone and β-pinene.  99
Figure C-1  Relationship of acidity and ethanol concentration for benzoic acid in mixed aqueous solvent  101
Figure C-2  Relationship of pKₐ for benzoic acid vs. 1/c for different solvents  102
Figure D-1  100 % water, 200 °C; β- pinene and mass balance  106
Figure D-2  100 % water, 200 °C; terpineol and hydrocarbons  106
Figure D-3  100 % water, 200 °C; bicyclic alcohols  107
Figure D-4  75 % water/ 25 % EtOH (volume), 200 °C; β- pinene and mass balance  108
Figure D-5  75 % water/ 25 % EtOH (volume), 200 °C; terpineol and hydrocarbons  108
Figure D-6  75 % water/ 25 % EtOH (volume), 200 °C; bicyclic alcohols and ether.  109
Figure D-7  50 % water/ 50 % EtOH (volume), 200 °C; β- pinene and mass balance  110
Figure D-8  50 % water/ 50 % EtOH (volume), 200 °C; terpineol and hydrocarbons  110
Figure D-9  50 % water/ 50 % EtOH (volume), 200 °C; terpineol and hydrocarbons  111
Figure D-10  50 % water/ 50 % acetone (volume), 200 °C; β-pinene and  112
<table>
<thead>
<tr>
<th>Figure</th>
<th>Description</th>
</tr>
</thead>
<tbody>
<tr>
<td>D-11</td>
<td>50% water/ 50% acetone (volume), 200°C: terpineol and hydrocarbons</td>
</tr>
<tr>
<td>D-12</td>
<td>50% water/ 50% acetone (volume), 200°C, bicyclic alcohols</td>
</tr>
<tr>
<td>D-13</td>
<td>50% water/ 50% THF (volume), 200°C, β-pinene and mass balance</td>
</tr>
<tr>
<td>D-14</td>
<td>50% water/ 50% THF (volume), 200°C, terpineol and hydrocarbons</td>
</tr>
<tr>
<td>D-15</td>
<td>50% water/ 50% THF (volume), 200°C, bicyclic alcohols</td>
</tr>
<tr>
<td>D-16</td>
<td>50% water/ 50% IPA (volume), 200°C, β-pinene and mass balance</td>
</tr>
<tr>
<td>D-17</td>
<td>50% water/ 50% IPA (volume), 200°C, terpineol and hydrocarbons</td>
</tr>
<tr>
<td>D-18</td>
<td>50% water/ 50% IPA (volume), 200°C, bicyclic alcohols</td>
</tr>
</tbody>
</table>
SUMMARY

The ultimate goal of the Green Chemistry initiative is to make the world a better place to live through prevention of pollution. This is a lofty and worthwhile goal which is currently being achieved through the investigation of alternative synthetic pathways, designing safer chemicals and development of alternative green processes to achieve desired chemical transformations. The work of this dissertation focuses on development of green reaction processes that can substitute for traditional, less environmentally friendly methods, in particular: acid catalyzed reactions.

This project investigated the effect of a variety of aqueous systems on the reaction of the terpene hydrocarbon, β-pinene; and, in the process demonstrated the utility of two in situ acid sources: hot water and gas expanded liquids. The acid-catalyzed hydration of β-pinene is a reaction of commercial significance, especially to the flavor and fragrance industry. The products of the reaction are alcohols (terpineol and bicyclic alcohols) and hydrocarbons. From a commercial standpoint, the alcohols are the desired products.

CO₂ gas-expanded liquids (GXL) and hot water (200 °C) are demonstrated as green substitutes for strong acid in the hydrolysis of β-pinene. Relatively mild CO₂ pressures (well below the critical pressure) can be used to create a GXL and provide the in situ catalysis. Additionally the ratio of desired hydrolysis products to hydrocarbon products was improved in the GXL over most conventional acid-catalyzed systems. Hot water, well below the critical point at 200 °C and with no added acid, is also a successful reaction media for β-pinene hydrolysis.
CHAPTER I
INTRODUCTION

The area of Green Chemistry is an excellent example of the benefits and achievements that are possible when academia and industry collaborate. Each year, since 1995, the Presidential Green Chemistry Challenge Awards are given to recognize innovative achievements that promote cleaner more environmentally friendly ways of doing chemistry. The list of past awardees is a mixture of industry and academic workers. Some of the achievements recognized last year include: a wastewater free process for synthesis of solid oxide catalysts (Süd-Chemie Inc.), microbial production of 1,3-propanediol (Dupont); new options for mild and selective polymerizations using lipases (Prof. Richard Gross, Polytechnic University) and development of an effective, environmentally friendly biofungicide (AgraQuest, Inc.).

The overall goal of Green Chemistry is to “develop creative strategies to prevent pollution...achieve cleaner water, land and skies...[and ultimately] leave our planet a much better place for our children and their children.” This is a lofty and worthwhile goal which is currently being achieved through the investigation of alternative synthetic pathways, designing safer chemicals and development of alternative green processes to achieve desired chemical transformations.

The work of this dissertation focuses on development of green reaction processes that can substitute for traditional, less environmentally friendly methods. Acid-base reactions are important parts of many chemical transformations. In fact acid catalysis is one of the most widespread methods of catalysis used in industry. The major
disadvantage of traditional methods of acid catalysis is the generation of waste during the required neutralization step. The accumulation of waste can be quite significant. In addition, neutralization processes can also introduce product separation challenges. Both of these problems, waste and product separation, add cost to the process.

This work presents two alternatives to traditional acid catalysis: hot water and gas expanded liquids (GXL). These two processes have several advantages. In both, the acid catalyst is generated in situ. This provides advantages on the front end of a process by potentially lowering ingredient and reaction set-up costs because an acid catalyst is not needed. The other advantage of in situ acid is elimination of waste. The in situ acids discussed here do not require neutralization. Product separation and recovery is also easier. Other benefits of the systems are less tangible, but no less important. The systems use non-toxic, non-flammable, naturally abundant materials (water and CO₂). These factors are appealing to an environmentally conscious society and can be used by industry and academia to promote public relations and improve the public image of chemistry.

The specific goals of this project are to demonstrate the utility of two in situ acid sources, hot water and gas expanded liquids, and in the process, gain understanding of the chemistry involved. The hydration reaction of β-pinene was chosen as a model system for this work. Pinene has widespread use as a raw material in synthetic organic chemistry for making flavor and perfume materials, resins, pharmaceuticals and many other organic compounds. Acid-catalyzed hydrolysis of pinene produces α-terpineol which is an important flavor and fragrance material. Chapter II provides a review of pinene chemistry. The hydration reactions of pinene have been of great interest to academics as
well as industrial chemists due to the unique ring opening and rearrangement reactions that occur.

Chapter III reports on investigations in our laboratory of pinene hydration, first with conventional acid catalysis using an aqueous emulsion and then using a less conventional system: an SDS micelle. Rate and product effects are presented as well as the advantages and disadvantages of the micelle reaction. Micellar catalysis and product selectivity were observed in the hydration reaction of α- and β-pinene.

Chapters IV and V discuss the in situ acid formation techniques: hot water (Chapter IV) and gas expanded liquid (GXL) (Chapter V). Each chapter starts with an introduction of the technique and background discussion. Full experimental details are listed, followed by the discussion of results and conclusions. Finally, recommendations for future work are given. Solvent effects, product distributions and relative rates of the reactions are discussed. This work presents an example of the successful application of these methods to a reaction of commercial significance and adds to our knowledge about the benefits and effects of co-solvents.

Finally, Chapter VI provides a conclusion which summarizes the advantages and disadvantages of each of the investigated methods and attempts to give perspective to the impact and contribution of this work. Several appendices are included which provide support and more detailed information pertaining to the topics covered.
Literature Cited


CHAPTER II

BACKGROUND: THE CHEMISTRY OF β-PINEENE AND α-TERPINEOL

Introduction

Many important fragrance and flavor compounds are members of the terpene class of compounds. Terpenes occur naturally in fruits, spices, flowers, leaves and other natural sources. The supply of natural compounds is inherently limited and therefore natural terpenes generally command a premium cost. Terpenes have been commercially produced from natural and synthetic sources for many years. α-Terpineol (1) is an important compound to both the flavor and fragrance industry and was chosen as a target molecule for our studies.

α-Terpineol (1) is a naturally occurring terpene alcohol that is used in both the flavor and fragrance industry. The term terpineol is commonly used for a mixture of terpene alcohol isomers with the α- isomer being the dominant compound. (Figure 2-1)

Figure 2-1. α-Terpineol and isomers
β-terpineol (2), γ-terpineol (3), terpinen-1-ol (4) and terpinen-4-ol (5)). Depending on the source of terpineol, and other compounds that are isolated with it, the aroma can range from a delicate lilac that is popular with perfumists to a harsher pine aroma that is common in cleaning materials. Terpineol is also known for its citrus character and it is an important constituent in distilled lime oil, typically at a level of ~10% by weight.\textsuperscript{1} α-Terpineol exists as two optical isomers. (4R(+)\textendash α-Terpineol has been described as having a heavy floral, lilac-like aroma, while the (4S(-)- isomer has a coniferous, tarry aroma.\textsuperscript{2} α-Terpineol (1) has been reported to occur in over 150 essential oils. However, the amounts are relatively small (with a few notable exceptions, e.g. 70% α-terpineol in yellow pine oil) and/or the oils are relatively uncommon and not available in large supply (e.g. cajeput and niaouli oils).\textsuperscript{3, 4} Therefore, the major source of terpineol is through chemical reaction of pinene. Commercial production of terpineol has been practiced since the late nineteenth century.\textsuperscript{5} The classical method for manufacture of terpineol uses α- and β-pinene (6, 7) from turpentine in a two-step procedure (see Figure 2-2). The reaction is performed in a solution of strong aqueous acid for long periods of time with low to moderate heating to produce the diol, 1,8-terpin (8). After isolation and purification, 1,8-terpin can be dehydrated to α-terpineol in dilute aqueous acid. Pure α-terpineol is a white, crystalline powder. The dil mixture has a boiling point of 218-219 °C and a melting point of 35 °C. Commercial terpineol, which is a mixture of several isomers, is a colorless, fairly viscous liquid at room temperature. Terpineol is slightly soluble in water and soluble at a ratio of 1:8 in a 50% alcohol mixture.\textsuperscript{10} The terpineols are tertiary alcohols and are susceptible to dehydration to form monoterpene hydrocarbons such as terpinolene (19) and limonene (21) (see Figure 2-5).
Pinene is a common starting material for the manufacture of terpenes, in particular α-terpinol (1). Pinene is a bicyclic unsaturated terpene that occurs in two forms, α- (6) with an endocyclic double bond and β- (7) with an exocyclic double bond. The double bond position results in slightly different conformation for the two bicyclic ring systems (Figure 2-3). α-Pinene (6) adopts a preferred “V-shaped” conformation in which C1-C2-C3-C2-C3 are planar and the cyclobutane dihedral angle is ~150°. β-Pinene (7) adopts a “bridged chair” conformation, such that C1-C2-C4-C5 and C2-C3-C4 form two planes with an angle of ~160°. These conformations are explained by a preferred equatorial position for C10 in 7. The two isomers also have different reactivities. For
example, acid-catalyzed hydrolysis of β-pinene (7) is approximately ten times faster than α-pinene (6) due to steric and electronic advantages of the β-pinene (7) structure. The exo-cyclic double bond is more accessible to proton attack. In addition, α-pinene (6) is considered to be a less strained molecule compared to β-pinene (7), making it less reactive and more stable.6,7 Both isomers are colorless liquids with boiling points at 155-156 °C for α-pinene (6) and 165-166 °C for β-pinene (7).8 Pinene is insoluble in water, slightly soluble in propylene glycol and soluble in alcohol and ether.

The two pinene isomers usually occur together and have been reported in over 400 essential oils. A significant source for pinene is pine trees, especially in turpentine. The pinene content of turpentine can be as much as 90% depending on the specific variety and α-pinene (6) is usually found in greater amounts than the β-isomer (7) (60% α-30% β-).9,10 Pinene is also found in many other plant materials such as sage, rosemary, thyme, lavender, neroli, lemon and ylang ylang.10 Both isomers of pinene are optically active and the distribution of the optical isomers varies from species to species. For example, (+)-β-pinene is the prevalent isomer in American and Russian pine trees while (-)-β-pinene is more dominant in French pine.9 Other sources of (+)-α-pinene (Figure 2-3) include sage, cumin and ylang ylang, while (-)-α-pinene can be obtained from thyme, lavender and rosemary.10 The distribution of optical isomers of pinene in citrus is very specific and this information is used to detect adulteration of citrus essential oils.11 For example, a summary of the chiral distribution of pinene in four citrus species is shown in Table 2-1.
Table 2-1. Percentage of optical isomers present in authentic samples of different citrus essential oils (average values from Ref. 11)

<table>
<thead>
<tr>
<th></th>
<th>lemon</th>
<th>mandarin</th>
<th>sweet orange</th>
<th>distilled lime</th>
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<tr>
<td>(+)</td>
<td>(-)</td>
<td>(+)</td>
<td>(-)</td>
<td>(+)</td>
</tr>
<tr>
<td>α-pinene (6)</td>
<td>30</td>
<td>70</td>
<td>60</td>
<td>40</td>
</tr>
<tr>
<td>β-pinene (7)</td>
<td>5</td>
<td>95</td>
<td>90</td>
<td>10</td>
</tr>
<tr>
<td>α-terpineol (1)</td>
<td>23</td>
<td>77</td>
<td></td>
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Pinene has widespread use as a reagent or raw material in synthetic organic chemistry for making flavor and perfume materials, resins, medicines and many other organic compounds. For example, a recent review article summarizes the utility of pinane-based reagents in modern asymmetric synthesis.12 (see Figure 2-4). Some notable examples of pinene use as a raw material include: the synthesis of menthol from β-

![Figure 2-4. Pinane-based Versatile Reagents (PVR) from Ref. 12](image-url)
the synthesis of pinene by hydrogenation of pinene,\textsuperscript{13, 15} the synthesis of the taxol C-ring precursor from α- pinene (6),\textsuperscript{16} the isomerisation of α- pinene (6) to form camphene\textsuperscript{17} and the microbial metabolism of pinenes to form flavors including α-terpineol (1).\textsuperscript{18}

Pinene chemistry in the gas phase has also been investigated. Significant terpene emissions have been found from forests throughout the world. Forests cover approximately one quarter of the earth’s surface and are estimated to contribute up to $1 \times 10^{14}$ g terpene VOC per year to the atmosphere.\textsuperscript{19} α- and β-Pinene (6, 7) can react with hydroxyl radicals and ozone in the troposphere; and, in the presence of NO, will form hydroxynitrates, dihydroxynitrates and dihydroxycarbonyls.\textsuperscript{20, 21} Further reaction of these compounds with water leads to formation of carboxylic acids which contribute to “acid rain.” Possible aerosol formation of these reaction products in the atmosphere is suspected and this has been implicated in climate modification. Therefore, industries with the potential to add terpene emissions to the atmosphere, such as lumber, paper and pulp production, are faced with regulations for limiting emissions. Consequently, they have become sources for terpene raw materials.\textsuperscript{22}

Of primary interest to our work is the acid-catalyzed hydration reaction of β-pinene (7). Commercial production of terpineol from pinene has been practiced since the late nineteenth century.\textsuperscript{1} Appendix A is a summary of most of the literature and patents published from 1879 to the present on pinene hydration reactions to form α-terpineol (1). Table 2-2 shows a sample of these methods. Early manufacturing processes usually
Table 2-2. Sample of pinene hydration literature (see full summary in Appendix A)

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<th>Reagents</th>
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<tbody>
<tr>
<td>1 kg turpentine, 2 kg glacial acetic acid, 100 g 50% H&lt;sub&gt;2&lt;/sub&gt;SO&lt;sub&gt;4&lt;/sub&gt;</td>
<td>~3 days</td>
<td>95% terpineol</td>
<td>23, 1892</td>
</tr>
<tr>
<td>500 parts turpentine, 2000 parts 25% H&lt;sub&gt;2&lt;/sub&gt;SO&lt;sub&gt;4&lt;/sub&gt;, 5-10 parts polyglycol emulsifier followed by: 7.5 parts phthalic anhydride, 3000 parts water</td>
<td>30-40 °C, 99-100 °C</td>
<td>24, 1942</td>
<td></td>
</tr>
<tr>
<td>β-pinene (7), 95% acetone/water, 0.73N H&lt;sub&gt;2&lt;/sub&gt;SO&lt;sub&gt;4&lt;/sub&gt;</td>
<td>1 hr, 75°C</td>
<td>42% terpineol</td>
<td>25, 1971</td>
</tr>
<tr>
<td>α-pinene (6), Dowex 50W-X8 (cation exchange resin), aqueous acetone (4% water)</td>
<td>10-17 hrs, 75 °C</td>
<td>30-40% terpineol</td>
<td>26, 1984</td>
</tr>
<tr>
<td>α- or β-pinene (6, 7), chloroacetic acid, Sc triflate</td>
<td>2 hrs, 60 °C</td>
<td>57% terpineol</td>
<td>27, 1996</td>
</tr>
</tbody>
</table>

involved two steps as previously described (Figure 2-2). Step 1 involved full hydration of pinene (or turpentine) with strong acid to form the diol, 1,8 terpin (8), followed by dehydration back to the alcohol α-terpineol (1). The procedure could take from 1 day to 2 months and was generally performed at elevated temperature. Yields of terpineol were often not reported in early work. Emulsifiers and co-solvents were introduced to the process in the late 1940's through 1960's to improve starting material solubility. Reaction time was decreased and yields of 40 to 70% terpineol were reported. Modifications to the process continued through the 1980's and 90's. A cation exchange resin was used and various different acids and catalysts were tried, but yields above 50% were unusual. One common feature of all the methods is extensive neutralization and/or product separation steps.
The hydration reactions of pinene were of great interest to academics as well as industrial chemists due to the unique ring opening and rearrangement reactions. These reactions were not well understood even up to the 1950's.\textsuperscript{28} About this time the pinenes became widely studied as model reactants during investigations of carbocation rearrangements; and, as a result, the mechanism of acid-catalyzed hydrolysis of pinene is now well understood. Clark and Chamblee provide a review of the current understanding of pinene hydration mechanisms and kinetics,\textsuperscript{1} and a summary will be included here.

The generally accepted pathway for the reaction is shown in Figure 2-5.\textsuperscript{25,29,30} Simple olefin protonation to form carbocation $\text{2}$ from $\beta$-pinene (7) is the initial and also rate determining step of the reaction. Carbocyclen rearrangement then occurs with either the C$_{1}$-C$_{8}$ bond moving to form $\text{10}$ or the C$_{1}$-C$_{7}$ bond to form $\text{11}$. Carbocations $\text{2}$ and $\text{10}$ can also be represented as nonclassical carbocation $\text{12}$; and, $\text{2}$ and $\text{11}$ by nonclassical carbocation $\text{13}$. Attack of water at C$_{1}$ of $\text{10}$ leads to borneol (14). Wagner-Meerwein rearrangement of $\text{10}$ followed by elimination of a proton leads to the bicyclic hydrocarbon, camphene (15). Likewise, attack of water at C$_{1}$ of $\text{11}$ leads to fenchol (16) and Wagner-Meerwein rearrangement of $\text{11}$ gives fenchene (17). The bicyclic products are relatively minor products representing typically 10% of the reaction mixture at room temperature and pH 2.2.\textsuperscript{1} The bicyclics however have relatively potent aromas/flavors\textsuperscript{11} and therefore can significantly impact the flavor profile of the fual reaction mixture. The major reaction product, $\alpha$-terpineol (1) (72% yield in a dilute solution at room temperature, pH =2.2, 73 hr$^\dagger$), is formed by breakage of bond C$_{1}$-C$_{8}$ to form $\text{18}$.
Figure 2-5. Mechanism for the acid-catalyzed rearrangement and hydrolysis of β-pinene (7)
followed by attack of water to give 1. Monocyclic hydrocarbons terpinolene (19) and limonene (20) can form through elimination of a proton from 18. Stereochemistry is preserved in this reaction. Thus, (+)-α-pinene has been shown to yield (+)-α-terpineol.32 (Figure 2-6). The same retention of configuration will occur with β-pinene (7).

A summary of the reported product composition for pinene solvolysis reactions is shown in Table 2-3. The results show an increase in hydrocarbon yield as temperature increases. Also, the product distribution is very similar between α- and β-pinene, with the rate being faster with β-pinene.

There are two types of catalysis used to help understand the mechanisms of acid-catalyzed reactions: specific acid catalysis and general acid catalysis.33,34 In specific acid catalysis the rate constant of the reaction is directly proportional to hydrogen ion concentration, specifically [H₂O⁺] in water, and not affected by the type of acid present. In this case the reaction can be represented by two steps: a fast equilibrium involving the formation of the conjugate acid of the reactant, followed by a slower, rate limiting step to form product.

\[
R + H_3O^+ \xrightarrow{\text{fast}} RH^+ + H_2O
\]

\[
RH^+ \xrightarrow{\text{slow}} \text{products}
\]

Therefore, \( \text{rate} = k[RH^+] \). Since the equilibrium constant of the first step is \( K = \frac{[RH^+][A^-]}{[R][HA]} \) and for acid HA is \( K_{\text{eq}} = \frac{[H^+][A^-]}{[HA]} \), \( \text{rate} = \frac{kK}{K_{\text{eq}}}[R][H^+] \); and,
(+)α-pinene

(+)-α-terpinol

Figure 2.6. Stereochemistry in the pinene reaction

<table>
<thead>
<tr>
<th>Conditions (Ref)</th>
<th>α-pinene (6), pH=2.2, buffered aqueous plant gum emulsion, 25 °C, 73 hr (f)</th>
<th>α-pinene (6), 0.073N H₂SO₄, 95% acetone/water, 75 °C, 4 hr (25)</th>
<th>β-pinene (7), 0.072N H₂SO₄, 95% acetone/water, 75 °C, 1 hr (25)</th>
<th>α-pinene (6), 0.06N H₂SO₄, 95% acetone/water, 75 °C, 7 hr (37)</th>
<th>β-pinene (7), 0.05M HClO₄, dioxane/water, 75 °C, 24 hr (30)</th>
<th>α-pinene (6), 0.05M HClO₄, dioxane/water, 75 °C, 3 hr (30)</th>
</tr>
</thead>
<tbody>
<tr>
<td></td>
<td>pinene remaining</td>
<td>hydrocarbons</td>
<td>terpineol</td>
<td>bicyclic alcohol</td>
<td>terpineol</td>
<td>bicyclic alcohol</td>
</tr>
<tr>
<td>α-pinene (6), pH=2.2, buffered aqueous plant gum emulsion, 25 °C, 73 hr (f)</td>
<td>6.3</td>
<td>12.4</td>
<td>71.7</td>
<td>10.4</td>
<td></td>
<td></td>
</tr>
<tr>
<td>α-pinene (6), 0.073N H₂SO₄, 95% acetone/water, 75 °C, 4 hr (25)</td>
<td>9</td>
<td>39</td>
<td>41</td>
<td>20</td>
<td></td>
<td></td>
</tr>
<tr>
<td>β-pinene (7), 0.072N H₂SO₄, 95% acetone/water, 75 °C, 1 hr (25)</td>
<td>12 (α-.)</td>
<td>38</td>
<td>42</td>
<td>19</td>
<td></td>
<td></td>
</tr>
<tr>
<td>α-pinene (6), 0.06N H₂SO₄, 95% acetone/water, 75 °C, 7 hr (37)</td>
<td>10</td>
<td>37.4</td>
<td>52</td>
<td>7</td>
<td></td>
<td></td>
</tr>
<tr>
<td>β-pinene (7), 0.05M HClO₄, dioxane/water, 75 °C, 24 hr (30)</td>
<td>17</td>
<td>33</td>
<td>55</td>
<td>12</td>
<td></td>
<td></td>
</tr>
<tr>
<td>α-pinene (6), 0.05M HClO₄, dioxane/water, 75 °C, 3 hr (30)</td>
<td>19</td>
<td>30</td>
<td>56</td>
<td>9</td>
<td></td>
<td></td>
</tr>
</tbody>
</table>

*a terpineol = α-terpineol (1) and terpinen-4-ol (5).  b This reaction also reports 5% 1,8-terpin (8).
rate is shown to be directly proportional to [H⁺] or pH. Also, since [H⁺] is a catalyst and is regenerated during the reaction, it is considered a constant and pseudo first order kinetics can be assumed. In specific acid catalysis the proton transfer step is not rate determining.

In general acid catalysis, the proton transfer step is rate determining. This type of catalysis can be represented by the following equations:

\[
\begin{align*}
R + HA & \xrightarrow{k_{1 \text{ slow}}} RH^+ + A^- \\
RH^+ & \xrightarrow{k_{1 \text{ fast}}} \text{products} \\
R + H_3O^+ & \xrightarrow{k_{1 \text{ fast}}} RH^+ + H_2O \\
RH^+ + A^- & \xrightarrow{k_{2 \text{ slow}}} \text{products} + HA
\end{align*}
\]

Here \( k_{1,2} \) and \( K_a = [HA] \times [A^-] / [H_3O^+] \) and since, \( \text{rate} = K_a \times k_{2} \times [R] \times [HA] \). Acids in general catalyze the reaction, not just H⁺.

Olefin hydration has been found to follow general acid catalysis. This is supported by work examining the effect of electron donating (rate is increased) and electron withdrawing (rate is decreased) substituents. The variation in rate with different substituents shows that the protonation step is rate determining. In addition, primary isotope effects in the range of 1-6 have been reported for various alkene and acid combinations. This indicates that the proton is involved with the rate determining
transition step. Numerous other studies supporting general acid catalysis for olefins are summarized in Reference 33.

Clark and Chamblee summarize the literature kinetic data for α- and β-pinene (6, 7) in mixed solvents (Table 2-4). Since pinene is virtually insoluble in water, few results are reported in 100% aqueous conditions. However, one experiment using an aqueous buffered α-pinene (6) emulsion at pH=2.2 and 25 °C reports a rate 200 times faster than the mixed solvents (after temperature adjustment). This appears to be a reasonable solvent effect. Rate constants for constant acid concentration decrease significantly as the percent of organic solvent is increased. (See also Appendix C) Kinetic isotope effects have been measured for both α- and β-pinene (6, 7). The $k_{H}/k_{D}$ is reported as 1.48 for α-pinene (6) and 1.60 for β-pinene (7). Both are consistent with a rate limiting protonation step and general acid catalysis.
Table 2-4. Summary of literature rate data for pinene hydration (from Reference 1).

<table>
<thead>
<tr>
<th>temp</th>
<th>k (hr⁻¹)</th>
<th>conditions</th>
<th>Reference</th>
</tr>
</thead>
<tbody>
<tr>
<td>25</td>
<td>0.04</td>
<td>α-pinene (6): pH 2.2 aqueous HCl/sodiumcitrate buffer</td>
<td>1</td>
</tr>
<tr>
<td>50</td>
<td>0.03</td>
<td>α-pinene (6): 0.05 M HClO₄, dioxane/water, 4:1</td>
<td>30</td>
</tr>
<tr>
<td>60</td>
<td>0.08</td>
<td>α-pinene (6): 0.05 M HClO₄, dioxane/water, 4:1</td>
<td>30</td>
</tr>
<tr>
<td>70</td>
<td>0.25</td>
<td>α-pinene (6): 0.05 M HClO₄, dioxane/water, 4:1</td>
<td>30</td>
</tr>
<tr>
<td>75</td>
<td>0.36</td>
<td>α-pinene (6): 0.06 N H₂SO₄, 95% acetone/water</td>
<td>37</td>
</tr>
<tr>
<td>75</td>
<td>0.59</td>
<td>α-pinene (6): 0.075 N H₂SO₄, 95% acetone/water</td>
<td>25</td>
</tr>
<tr>
<td>80</td>
<td>0.73</td>
<td>α-pinene (6): 0.05 M HClO₄, dioxane/water, 4:1</td>
<td>30</td>
</tr>
<tr>
<td>40</td>
<td>0.054</td>
<td>β-pinene (7): 0.05 M HClO₄, dioxane/water, 4:1</td>
<td>30</td>
</tr>
<tr>
<td>40</td>
<td>0.147</td>
<td>β-pinene (7): 0.097 M HClO₄, dioxane/water, 4:1</td>
<td>30</td>
</tr>
<tr>
<td>40</td>
<td>0.695</td>
<td>β-pinene (7): 0.28 M HClO₄, dioxane/water, 4:1</td>
<td>30</td>
</tr>
<tr>
<td>50</td>
<td>0.197</td>
<td>β-pinene (7): 0.05 M HClO₄, dioxane/water, 4:1</td>
<td>30</td>
</tr>
<tr>
<td>60</td>
<td>0.059</td>
<td>β-pinene (7): 0.05 M HClO₄, dioxane/water, 4:1</td>
<td>30</td>
</tr>
<tr>
<td>60</td>
<td>0.135</td>
<td>β-pinene (7): 0.097 M HClO₄, dioxane/water, 4:1</td>
<td>30</td>
</tr>
</tbody>
</table>

β-Pinene (7) reacts faster than α-pinene (6). This is due to steric and structural differences in the two compounds. The exo-cyclic double bond of β-pinene (7) is slightly less hindered than the endo-cyclic double bond of α-pinene (6). However, a more important factor is probably the overall stability of the molecules. α-Pinene (6) has been found to be more stable than β-pinene (7). This is consistent with the more substituted
double bond being more stable. The more stable α-pinene (6) molecule will therefore
have a lower ground state energy and thus greater energy of activation will be required to
form the carbocation intermediate. Both α- and β-pinene (6, 7) appear to react through
the same carbocation intermediate. Therefore the difference in activation energy is
apparently 10-fold, based on our kinetic measurements (Chapter III) and literature data.
Literature Cited


23) Bertram and Walshe, Ger. Pat, 67,255, April 12, 1892.


21


31) According to reference 1 borneol is described as having a dry-camphoraceous, woody-peppery odor; fenchol is described as earthy, musty, camphoraceous and sometimes citrus/lime-like. The taste recognition threshold is 100-400 ppb.


CHAPTER III

ACID-CATALYZED HYDRATION OF PINENE IN AQUEOUS SDS MICELLES

Introduction

Micelles are a type of organized structure that forms spontaneously in solutions of surfactant molecules. A surfactant is a molecule that has both hydrophobic (nonpolar) and hydrophilic (polar) properties within the same molecule. This causes the molecules to be surface active which means that they are attracted to air-water or oil-water interfaces. Surfactants can be nonionic, anionic or cationic. Examples of each type are shown in Figure 3-1. At low concentration, the properties of surfactants in solution are similar to other electrolytes with the exception of surface activity. Surface activity of surfactant solutions decreases rapidly. At higher concentrations, micelles will form.

\[
\text{CH}_3\text{(CH}_2\text{)}_9\text{S}^\odot \text{O}^- \text{Na}^\oplus \\
\text{SDB - sodium dodecyl sulfate}
\]

\[
\text{CH}_3\text{(CH}_2\text{)}_1\text{N}^\oplus \text{O}^- \text{(CH}_3\text{)}_2 \text{Br}^\ominus \\
\text{CTAB - cetyl trimethyl ammonium bromide}
\]

\[
\text{HO(CH}_2\text{CH}_2\text{O)}_w \text{HO(CH}_2\text{CH}_2\text{)}_x\text{OH} \\
\text{CH}_2\text{OH(CH}_2\text{CH}_2\text{O)}_2 \text{CH}_2\text{H}_2\text{O} \text{C} \text{C}_2 \text{H}_5\text{CH}_3\text{C}_2 \text{H}_5
\]

**Figure 3-1.** Common surfactants: SDS-anionic; CTAB-cationic; Tween 20-nonionic
The concentration at which micelles form is called the critical micelle concentration (CMC) and it varies from surfactant to surfactant. CMC is dependent on the structure of the surfactant.\(^1\) For example, longer chain surfactants generally have lower CMC’s. Addition of electrolytes will reduce the CMC of ionic surfactants. Formation of micelles in a surfactant solution results in dramatic changes in the physical properties of the solution (see Figure 3-2). This allows for accurate determination of the CMC.

![Graphical representation of surfactant concentration vs. some physical properties of a micelle-forming surfactant. (Redrawn from Reference 1, pg. 36)](image)

**Figure 3-2.** Graphical representation of surfactant concentration vs. some physical properties of a micelle-forming surfactant. (Redrawn from Reference 1, pg. 36)

The micelle is a dynamic structure that actually exists as a monomer-micelle equilibria. NMR studies have shown that the frequency for exchange of surfactant molecules between the micelle and the bulk solvent is \(10^3\) sec\(^{-1}\).\(^2\) Even so, it is useful to depict the micelle as a spherical structure as shown in Figure 3-3. In this example, the hydrophobic hydrocarbon chains of the surfactant molecules congregate together, placing the polar head groups on the outside towards the bulk aqueous phase. The resulting structure has a hydrocarbon core which is capable of solubilizing hydrophobic material.
Figure 3-3. Graphical representation (2-D) of a spherical ionic micelle. Redrawn from Reference 2, pg. 31.

The driving force for micelle formation in aqueous systems is the unfavorable interaction of the hydrophobic hydrocarbon chains and water.\(^1\) Hydrocarbons by themselves in water will phase separate to avoid this interaction. The surfactant contains a hydrophilic part which counteracts this tendency and causes aggregation or micelle formation instead. The formation of micelles has been referred to as an “invisible” phase transition. Another way to look at it focuses on the free energy decrease of the system which results from micelle formation.\(^2\) The free energy changes are primarily due to changes in the water structure and entropy. Surfactant monomers in water cause an entropy decrease due to increased structure of water molecules. As the monomers aggregate to form micelles, the hydrophobic parts of the molecule have less exposure to the water and there is a loss of order for water and a large entropy increase.

Micelle solutions are thermodynamically stable. This means that they will not separate over time like emulsions. The concentration of monomers in a surfactant

25
solution above the CMC is constant. In other words, as surfactant is added above the CMC, more micelles will be formed or the micelles will expand. The aggregation number of micelles is affected by the head group repulsion and is generally 60-100 monomers/micelle with a net charge of 50-70 for ionic micelles. The amount of water penetration into the micelle varies and can be considerable.

Two significant impacts of micelle formation in a solution are: 1) increased solubilization of hydrophobic compounds (solute); and, 2) micellar catalysis of certain reactions. Micelle solubilization in general has been found to be directly proportional to surfactant concentration over a relatively large range. In other words, as more surfactant is added above the CMC, and thus more micelles are formed, more solute can be solubilized. Figure 3-4 shows an example of solubilization of a dye, Orange OT, in C_{10} and C_{12} sodium alkyl sulfate micelles. A saturation point at which no more solute will dissolve in the micelle will eventually be reached. This is called the maximum additive concentration (MAC). Micellar solubilization is dependent on surfactant and solute.

Figure 3-4. Solubilization of Orange OT dye in alkyl sulfate micelles (Redrawn from Reference 1 pg. 222)
structure, temperature and other additives in the solution and the specifics for each system must be determined individually.\textsuperscript{2}

It is known that micelles can exhibit a catalytic effect for many reactions.\textsuperscript{2} Anionic micelles of sodium dodecyl sulfate (SDS) have been shown to affect the selectivity and rate of terpene rearrangements.\textsuperscript{3,4} Selectivity and rate were increased for the cyclization reaction of citronellal (1) in the SDS micelle (Figure 3-5). The rate of reaction increased 5-fold in SDS micelle vs. an aqueous buffered control and the product ratio of cis/trans diol was shifted from 2:1 in aqueous buffer to 5:1 in an SDS micelle.\textsuperscript{5} Similarly, the ester hydrolysis reactions of linalyl and geranyl acetate (2, 3) were studied. Both cyclic and acyclic alcohols are formed during this reaction (Figure 3-6). The SDS micelle was shown to favor formation of acyclic product and to promote a rate increase of 7-fold for the slower acyl-cleavage solvolysis of geranyl acetate. These examples of terpene reactions in aqueous micelles involve oxygenated compounds that have limited but measurable solubility in water. α- and β-Pinene (4, 5) are examples of non-polar terpenes that are virtually insoluble in water. The micelle will potentially affect the rate and selectivity of the reaction in a favorable way.

\begin{figure}[h]
\centering
\includegraphics[width=0.8\textwidth]{figure3-5.png}
\caption{Major products of the acid-catalyzed cyclization/hydration of citronellal}
\end{figure}
Results and Discussion

Pseudo first order rates were calculated for the pinene hydration reactions and the results are shown in Table 3-2. The pseudo first order rate plots for duplicate α-pinene/SDS reactions are shown as a sample of the data in Figure 3-7. The results show a modest micellar catalysis for the hydrolysis reaction of α-pinene (4) in both the SDS micelle and the nonionic Tween micelle vs. an aqueous emulsion (2/1.5/1). The SDS micelle increases the rate by approximately 2-fold. This is consistent with the carbocation intermediate mechanism described in Chapter II. The carbocation is stabilized by the anionic micelle compared to the nonionic and emulsion systems. Other factors contributing to micellar catalysis are increased solubilization in the micelle,
Table 3-1. Summary of kinetic data for pinene hydrolysis reactions

<table>
<thead>
<tr>
<th></th>
<th>α-pinene (4)</th>
<th>α-pinene (4) Tween (#2)</th>
<th>α-pinene, (4) SDS, #3</th>
<th>α-pinene (4), SDS, #4</th>
<th>β-pinene (5), SDS, #5</th>
<th>β-pinene (5), SDS, #6</th>
</tr>
</thead>
<tbody>
<tr>
<td>pH</td>
<td>2.2</td>
<td>2.3</td>
<td>2.3</td>
<td>2.3</td>
<td>3.0</td>
<td>3.1</td>
</tr>
<tr>
<td>k (hr⁻¹)</td>
<td>0.033</td>
<td>0.037</td>
<td>0.064</td>
<td>0.055</td>
<td>0.105</td>
<td>0.116</td>
</tr>
<tr>
<td>k₉⁻¹</td>
<td>4.63</td>
<td>7.16</td>
<td>10.16</td>
<td>10.40</td>
<td>105</td>
<td>92</td>
</tr>
<tr>
<td>r²</td>
<td>0.9987</td>
<td>0.9987</td>
<td>0.9973</td>
<td>0.9997</td>
<td>0.9999</td>
<td>0.9996</td>
</tr>
</tbody>
</table>

*See Table 3-1 for detailed experimental conditions

⁺k₉⁻¹ is the pH adjusted rate constant and is equal to k[H⁺]

Figure 3-7. Pseudo first order rate plot for α-pinene (4) in an aqueous SDS micelle at pH=2.3

and possible localized pH effects caused by the anionic micelle. The rate data also shows a 10-fold increase in β-pinene (5) rate vs. α-pinene (4). This is consistent with literature results as described in Chapter II.

Figure 3-8 shows a summary of the product distribution results for the emulsion and micelle reactions. The hydration reaction of pinene is described in detail in Chapter II. The major product is α-terpineol (6). Bicyclic alcohols are also formed such as borneol (7) and fenchol (8). Terpene hydrocarbons such as limonene (9) and terpinolene
will also be formed. The emulsion and Tween 80 reactions show low overall recoveries. These are typical recoveries for reactions in emulsions that are often difficult to extract. Also, these reactions were slower than the micelle reactions, and reactions of terpenes in aqueous solutions run for extended periods of time have been shown to yield low mass balances.\(^3\) Recoveries from the micelle reactions are close to 100%.

![Diagram of reactions](image)

**Figure 3-8.** Product distribution for pinene reactions: 1= α-pinene (4) in aqueous emulsion, 75 hr; 2= α-pinene (4) in Tween 80, 48 hr; 3 & 4= α-pinene (4) in SDS micelle, 24 hr; 5 & 6= β-pinene (5) in SDS micelle, 24 hr. (see Table 1 for more experimental details)

The product distribution achieved in the aqueous emulsion (42% α-terpineol (6), 3% bicyclic alcohol (7, 8) and 5% hydrocarbon) is consistent with literature reports.
(terpineol 30-55%; bicyclic-OH 5-20%; hydrocarbons 30-50%). One difference is the low levels of hydrocarbon product. This is probably because most experiments reported in the literature were conducted at temperatures significantly higher than room temperature, which increases hydrocarbon yield. The SDS micelle appears to yield higher levels of terpineol (70%) and bicyclic alcohols (10%) compared to the emulsion and Tween, but a variance was not fully assessed (relative standard deviation of terpineol for experiments 3 & 4 and 5 & 6 is 15%). Analysis of the monocyclic to bicyclic alcohol product ratios reveals that the micelle exhibits a selectivity effect as well. The terpineol to bicyclic-OH ratio changes from ~14:1 in aqueous emulsion to 7:1 in SDS micelle. This increase in bicyclic alcohols can significantly affect the flavor of the mixture as the bicyclic alcohols are strongly camphoraceous vs. the relatively mild α-terpineol (6). The product distribution achieved with β-pinene (5) in SDS micelle is very similar to α-pinene (4), as expected from the literature. While β-pinene (5) reacts faster, it is reacting through the same carbocation intermediate, therefore the product distribution is the same.

An explanation for the micellar ratio effects can be made similar to that proposed for the shift in cis/trans product ratio for the acid-catalyzed reaction of citronellal in the SDS micelle. When α-pinene (4) is protonated to form the carbocation intermediate it will most likely be positioned for maximum stabilization in the Stern layer of the micelle as depicted in Figure 3-9. Rearrangement to form carbocation A or B, which lead to bicyclic product, will also be stabilized in the Stern layer. Carbocation C, leading to monocyclic product, will be generated deeper in the hydrophobic part of the micelle and will be destabilized relative to A and B. In addition, water will not be as readily available
deeper in the micelle and the rate of α-terpineol (6) formation will be somewhat decreased.

![Chemical reaction diagram](image)

**Figure 3-9. Proposed mechanism for micellar selectivity in the pinene hydration reaction**

**Conclusion**

Pseudo first order reaction data was obtained from acid catalyzed reactions of α-pinene in an aqueous emulsion and SDS micelle. The reaction is relatively slow at room temperature with a half-life of ~ 1 day at pH 2.2. The rate is increased 2-fold by using an SDS micelle. The micelle also modified the product distribution by increasing the formation of bicyclic alcohols vs. monocyclic. This is demonstrated by a 2-fold increase in borneol (7) and fenchol (8) in the product mixture. We propose a mechanism which shows a stabilization of the carbocation intermediates in the micelle. Reactions with β-
pinene (5) in the micelle confirmed that the reaction is 10 times faster for the exo isomer, but the product distribution is the same.

The SDS micelle provides advantages for reaction rate and selectivity. While the rate increase is admittedly small in this case (~2-fold increase), this can be important and useful for very slow reactions like hydration of double bonds. For example, the reaction can be completed in days rather than weeks. This may be significant from a commercial perspective. In the case of the pinene reaction, the selectivity effect and shift in product profile from monocyclic to bicyclic has a flavor impact. The micelle provides a unique way, under mild conditions, to alter the product distribution in a way that may be difficult or even impossible to achieve with other methods.

The disadvantage of the micelle system lies in product separation and generation of waste. The SDS surfactant can be precipitated from the solution by addition of salts; however, the separation can be messy. In addition, traditional means of neutralization and separation are necessary to recover the products. For these reasons it is unlikely that SDS micelles will find widespread commercial use for pinene hydration. However, micelles still remain an interesting potential tool for achieving selectivity and rate effects in organic reactions.

**Experimental**

\( \alpha \)- and \( \beta \)-pinene (4, 5) (99 % by GC) from Aldrich Chemical Company were used as is. Purified water was obtained from a Solution 2000 water filtration system. Buffers were prepared using Fisher certified chemicals: citric acid monohydrate, sodium phosphate dibasic heptahydrate, hydrochloric acid. The sodium dodecyl sulfate (SDS) was obtained from Aldrich Chemical Company and recrystallized twice from ethanol or
from Bio Rad Laboratories and used as is. The SDS purity was checked by running a
ccontrol reaction with no pinene, followed by extraction and GC-MS analysis. No peaks
were found. As a further check of purity, the CMC using our sample of SDS was
determined by conductivity. The value was found to agree with the literature value of
0.008 M. Tetradecane internal standard (99 % by GC) was obtained from Fluka.

The reactions were carried out in aqueous buffer at pH = 2.2. Since α-pinene (4)
is practically insoluble in water, an emulsion was used to introduce 4 into the control
reaction. A simple gum acacia/ester gum emulsion was used. A mucilage consisting of
gum acacia and purified water was combined with a 40/60 (wt/wt) ester gum/α-pinene oil
blend. The emulsion was homogenized with a Vertis 45 homogenizer for 4 minutes at
speed 70. Emulsion (1.2 g) was added to 90 mL of HCl/NaCIT buffer to give a 7x(10⁻⁴)
M solution of α-pinene (4). The solution remained slightly cloudy.

α-Pinene (4) was added to the second "control" in a Tween 80 emulsion. Since
the start of this work it has been determined that the Tween 80 concentration of this
system is above the CMC for this surfactant which is 1.3 (10⁻⁵) g/100 mL, according to
reference 1. Therefore, this system may actually be an example of a nonionic micelle
rather than a "control." The reaction solution consisted of 12% Tween 80, 12% α-
pinene (4) and 76 % purified water. The solution was homogenized with the Vertis 45
homogenizer for 2 minutes at speed 70. A stock solution was prepared using a 1:10
dilution of water. The reaction consisted of 0.69 g stock solution in 90 mL of HCl/NaCIT
buffer. The solution was slightly cloudy at first but became clear after 24 hrs.

The SDS micelle reactions consisted of 1.1 g SDS added to 100 mL of aqueous
buffer. Using a calibrated syringe, α- or β-pinene (4, 5) at 20 °C was added to 90 mL of
SDS buffer to give 7 (10^{-4}) M pinene at pH= 2.3. Table 3-2 shows a summary of the reactions studied.

<table>
<thead>
<tr>
<th>#</th>
<th>Starting material</th>
<th>Reaction conditions</th>
<th>time</th>
</tr>
</thead>
<tbody>
<tr>
<td>1</td>
<td>α-pinene (4)</td>
<td>HCl/citrate buffer, pH=2.2, water gum acacia emulsion, 20 °C</td>
<td>73 hr</td>
</tr>
<tr>
<td>2</td>
<td>α-pinene (4)</td>
<td>HCl/citrate buffer, pH=2.2, water/Tween 80 micelle (8.9 (10^{-3}) g/mL Tween), 20 °C</td>
<td>48 hrs</td>
</tr>
<tr>
<td>3 &amp; 4</td>
<td>α-pinene (4)</td>
<td>Citrate/phosphate buffer, SDS micelle (0.038 M SDS), pH=2.3, 20 °C</td>
<td>73 hrs</td>
</tr>
<tr>
<td>5 &amp; 6</td>
<td>β-pinene (5)</td>
<td>Citrate/phosphate buffer, SDS micelle (0.038 M SDS), pH=2.8, 25 °C</td>
<td>24 hrs</td>
</tr>
</tbody>
</table>

*0.038 M is well above the critical micelle concentration of 0.008 M for SDS

All of the reactions were sonicated for 15 minutes after addition of pinene and then placed in a water bath at 20 °C or 25 °C. Aliquots were taken for extraction and analysis at various time intervals. The samples were extracted with either ethyl ether or methylene chloride after addition of internal standard, tetradecane. Each sample was extracted three times with solvent. The organic layer was then washed with saturated aqueous NaHCO₃, purified water and saturated NaCl (brine). The solvent was then concentrated to ~2 mL using a Kadema Danish evaporator and hot water bath (~75 °C). Previous work in our laboratory confirms that the KD evaporator is suitable for quantitative concentration of ether and methylene chloride samples.

An HP 5890 GC equipped with a 6890 series autosampler was used for GC-FID analysis with a DB-5 capillary column (30 M x 0.32 mm x 1.0 μm film). The oven temperature program was as follows: initial temperature 70 °C; initial hold 10 min.; 2 °C/min to 200 °C; final hold 50 min. Other settings of the GC were: injector temperature 200 °C; detector temperature 240 °C; carrier gas helium; column flow at initial
temperature 1.91 mL/min; carrier gas pressure (constant pressure) = 10 psi; split ratio = 20:1. 1μl injection. An Agilent GC Chemstation method was used for peak integration and data analysis. Response factors were calculated for all of the major compounds based on the internal standard tetradecane and the results were reported as absolute concentration values (mg/ml). These were converted to % of starting material for this report unless otherwise specified.

GC-MS analysis of the reaction mixtures were conducted on an HP 5972 MSD coupled with an HP 5890 GC. A DB-5 column (30 M x 0.32 mm x 1 μm film thickness) was used with temperature program (10 min. initial hold at 60 °C, 2 °C/min to 200 °C, 50 min. final hold at 200 °C). The GC injector temperature was 190 °C and MSD transfer line temperature was 280 °C. The GC was operated in constant flow mode at 1.2 mL/min with vacuum compensation. Peak identifications were made using our in house citrus.l library, the Wiley 6th edition MS library and retention time data found in the literature.9
Literature Cited


6) See Chapter II for more details.


CHAPTER IV

ACID-CATALYZED HYDRATION OF β-PINENE IN HOT WATER 200 °C

Introduction

The use of water as a reaction solvent has several advantages. First, water is plentiful. In fact, it is the abundant material on the earth’s surface, making up ~70 %. Water, even purified water, is also relatively cheap compared to typical organic solvents. For example, according to the 2003-2004 Aldrich catalog, the ingredient costs for 3 organic solvents, all HPLC grade, are as follows: acetone, $13.84/L; methanol, $10.76/L; hexane, $13.90/L. HPLC grade water is listed at $9.07/L. These prices do not include extra storage and handling costs that may be required due to hazard ratings. The following hazard warnings are listed for all three organic solvents in the 2000 Emergency Response Guidebook: highly flammable, toxic vapors, skin/eye irritation, explosive vapors, pollution run-off danger, and more. These properties require special handling and storage in order to prevent accidents and property damage. In contrast, water is not even listed in the Emergency Response Guidebook. In fact, water is often recommended as an antidote for skin or eye exposure to organic solvents. The elimination of special storage/handling conditions could result in significant savings in large scale production situations. Finally, organic solvent waste disposal is expensive and can be controversial. Waste disposal is also a potential risk factor as a source of costly litigation if not handled correctly. The use of water as a reaction solvent can significantly reduce the generation of reaction waste. In short, water is an ideal reaction media, except for one important
fact. Most organic compounds are virtually insoluble in water at room temperature. Superheated water can overcome this limitation.

Supercritical water (400 °C, 200 bar) and near-critical water (275 °C, 60 bar) are systems that have received attention as environmentally benign alternative solvent/reaction media. Superheated water is a useful medium for organic reactions due to the physical and chemical changes that occur to water at elevated temperature. For example, both density (1.0 to 0.7 g/cm³) and dielectric constant (ε=80 to 20) decrease as water approaches 275 °C (Table 4-1). Thus, water at near-critical conditions has some solvent properties similar to a polar organic solvent such as acetone (ε=21). As a result the solubility of organic compounds is greatly increased.

<table>
<thead>
<tr>
<th>Table 4-1. Properties of Water</th>
</tr>
</thead>
<tbody>
<tr>
<td>Temperature, °C</td>
</tr>
<tr>
<td>Pressure, bars</td>
</tr>
<tr>
<td>Density, g/cc</td>
</tr>
<tr>
<td>Dielectric constant</td>
</tr>
</tbody>
</table>

Other properties of water are affected as it is heated. The hydrogen bond (H-bond) donating ability (Kamlett-Taft α) of water decreases from ~1.18 to ~0.8 as water is heated from sub-ambient to 275 °C (Figure 4-1). This means that the H-bonding ability of water decreases as the temperature increases, such that water at 300 °C acts has similar properties to ethanol. Additionally, the ionization constant of water (Kw) is affected by temperature (Figure 4-2). Kw increases by three orders of magnitude from 10⁻¹⁴ at 25 °C to a maximum just below 10⁻¹¹ at 250-275 °C. Kw represents the ability of
Figure 4-1. Hydrogen bond donating ability (α) of water as a function of temperature (● Lu et al, Reference #10, □ Marcus et al, Reference #11).

Figure 4-2. Ionization constant (pKₐ) of water as a function of temperature (Marshall and Franck, Reference #12).
water to dissociate into $H^+$ and $OH^-$ ions. Thus, water at elevated temperatures has increased ability to perform acid and base catalyzed reactions.

Although superheated water as a reaction media is relatively new in synthetic organic chemistry, the use of hot water under pressure has existed for millions of years as the major reaction pathway for the formation of the earth’s petroleum resources. Organic chemists began to utilize the unique properties of supercritical water (sH$_2$O) approximately twenty five years ago. Supercritical H$_2$O (400 °C, 200 bar) has been found to be especially useful for breaking bonds. For example, the following transformations have been reported in the literature: 2,5-dimethylfuran cleavage (250 °C); acetel/ketal hydrolysis (205-250 °C), breakdown of cellulose to glucose (400 °C), hydrolysis of esters and nitriles (250 °C), decomposition of polymers (200-300 °C), ether cleavage (315 °C), dehydration of alcohols (250-300 °C). While it is not a surprise that the relatively harsh conditions of superheated water are useful for bond breaking, some bond forming transformations have also been accomplished: Diels-Alder reactions, aldol chemistry (250 °C), Friedel-Crafts reactions (275 °C), alklylation reactions (275 °C) and limited experiments on terpene rearrangements.

The reaction of pinene to form $\alpha$-terpinone has been known since the late nineteenth century. $\alpha$- and $\beta$-pinene (1, 2) will hydrolyze in aqueous acid to form a tertiary carbocation. The major product of the reaction is $\alpha$-terpinone (3); however, rearrangement of the carbocation also occurs to give isomers such as terpinen-4-ol (4) $\beta$- and $\gamma$-terpineol (5, 6). Together these monocyclic alcohols are known as “terpinols.” Smaller amounts of the bicyclic alcohols fenchol (7) and borneol (8) are formed through Wagner-Meerwein rearrangement. Ethers will also form when the reaction is performed.
in alcohol. Undesirable side reactions producing hydrocarbons (through elimination and dehydration) are also possible and difficult to eliminate completely.\(^{21}\) (see Chapter II for more detailed information on pinene chemistry).

![Figure 4-3. Major reaction products from pinene acid-catalyzed hydration](image)

**Results and Discussion**

Water would be an ideal choice as an environmentally benign solvent for chemical processes except for one fact: many organic compounds are virtually insoluble in water. This is certainly the case with hydrocarbons such as β-pinene (2). The use of superheated water can overcome this situation and also has the added advantage of an *in situ* acid effect. We have found that hot water at 200 °C (well below the critical point) also has modified solvent properties sufficient enough to make it a useful reaction media. Our work demonstrates that the solubility and *in situ* acid catalyst ability can be effective even under these milder conditions. We also show the effect of added co-solvents. The
acid-catalyzed hydrolysis reaction of β-pinene (2) to form terpineol is a reaction of commercial significance (see chapter II) that can be accomplished in a more environmentally friendly manner using the in situ acid formation capabilities of hot water. Despite the low solubility of β-pinene (2) in room temperature aqueous systems, good conversion of the starting material and good yields of the desired alcohol products are achieved in hot water at 200 °C.

Our initial experiments were performed in 100 % water at 200 °C. Conversion of β-pinene (2) was fast (100 % conversion in less than 20 min); however, the yield of terpineol was low (~10 %). The major products were monocyclic hydrocarbons through elimination and dehydration reactions (see Figure 4-4, #1). The yield of terpineol was even lower at 250 °C. In an attempt to improve the product distribution, several co-solvents were tried. The experimental conditions and relative rate results are summarized in Table 4-2.

Figure 4-4. Product distribution and relative rates for ~90% conversion of β-pinene (2) in hot water (#1) vs. co-solvent systems: 75%/25% H2O/EtOH (#2); 50%/50% H2O/acetone (#3); 50%/50% H2O/EtOH (#4); 50%/50% H2O/THF (#5); 50%/50% H2O/IPA (#6) [IPA/water reaction stopped at 80% conversion]
Table 4-2. Hot water reaction composition and relative rate data.

<table>
<thead>
<tr>
<th>Volume ratios</th>
<th>mMol water</th>
<th>Time for 90% conversion of β-pinene (2) (min)</th>
<th>Dielectric constant of co-solvent</th>
<th>Estimated dielectric constant a</th>
</tr>
</thead>
<tbody>
<tr>
<td>100 water</td>
<td>89</td>
<td>20</td>
<td>80</td>
<td>80</td>
</tr>
<tr>
<td>75/25 water/EtOH</td>
<td>67</td>
<td>20</td>
<td>24</td>
<td>66</td>
</tr>
<tr>
<td>50/50 water/acetone</td>
<td>44</td>
<td>30</td>
<td>21</td>
<td>50</td>
</tr>
<tr>
<td>50/50 water/EtOH</td>
<td>44</td>
<td>40</td>
<td>24</td>
<td>52</td>
</tr>
<tr>
<td>50/50 water/THF</td>
<td>44</td>
<td>90</td>
<td>7</td>
<td>43</td>
</tr>
<tr>
<td>50/50 water/isopropanol</td>
<td>44</td>
<td>150</td>
<td>18</td>
<td>49</td>
</tr>
</tbody>
</table>

a Estimated dielectric constant is based on \( \varepsilon_{eq} = f_a \varepsilon_a + f_b \varepsilon_b \), where \( f \) = volume fraction; \( \varepsilon_A \) and \( \varepsilon_B \) = solvent A and B respectively.

In general, the addition of co-solvent decreased the rate of β-pinene (2) conversion. This would be expected, as the moles of water (the source of in situ acid, \( [H^+] \)) is decreased. At the same time, the amount of hydrolysis product that was recovered was increased from 10% in 100% water to an overall yield of ~40% terpeneol in IPA/water.

The α-terpineol (3) is not stable at 200 °C. In Figure 4-5 and 4-6 (see Appendix D for detailed graphs for the other solvent systems), terpineol levels begin to decrease and hydrocarbons continue to increase when the β-pinene (2) is completely reacted.

Since excellent mass balance was achieved (>95%) and the GC analysis does not show any large unidentified peaks, this indicates that dehydration of the alcohol products occurs at this temperature. The rate of dehydration is apparently slower than hydrolysis of pinene, thus the product curve continues to rise as long as pinene is still available. This suggests that greater yields of terpineol could be achieved if it was possible to remove the alcohol from the system as it is formed.

44
Figure 4-5. Disappearance of β-pinen (2) and mass balance for 50 % THF/ 50 % H₂O (by volume) at 200 °C over time.

Figure 4-6. Product distribution over time for 50 % THF/50 % H₂O (by volume) over time.

The hydrolysis reaction of β-pinen (2) was slowest in the IPA/water system (20 % pinene remaining after 130 min.). At this point, the ratio of hydrolysis products to hydrocarbon products was ~1:1. By looking at the product distribution over time for the
other solvents, it was discovered that the same 1:1 ratio of hydrolysis/hydrocarbon products was also reached at the 20% pinene remaining mark for the other co-solvents as well. Since the hydrolysis reaction of β-pinene is pseudo first order in acid, the relative rate results suggest that the pH of the co-solvent systems follows the following order: IPA>THF>50:50 EtOH/water>acetone>75/25 EtOH/water. As Table 4-2 shows the co-solvent systems had less H₂O on a molar basis and thus less potential for “in situ” acid, which may account for why the co-solvent systems have slower rates than 100% water. However, no clear correlation could be found to explain the results between the co-solvents. The system is apparently more complex with competing effects of solubility, dielectric constant and acid dissociation behavior (see Appendix C for a discussion of solvent effect on acid dissociation).

The bicyclic alcohols, fenchol (7) and borneol (8), were stable under the hot water conditions. As Figure 4-7 shows, even though the relative rates of formation were

![bicyclic alcohol formation in hot water](image)

Figure 4-7. Formation of bicyclic alcohols in all solvent systems at 200 °C

46
slightly different in each solvent system, the levels of bicyclic alcohol product rose to a maximum at 3-4%, leveled off, and remained stable at 200 °C in all the solvent systems. Figure 4-8 shows the formation of the bicyclic alcohols in the 50:50 ethanol/water system alone and gives a better idea of the reproducibility for the formation of this product.

![Graph showing formation of bicyclic alcohols](image)

**Figure 4-8. Formation of bicyclic alcohols from β-pinene (2) in 50/50 ethanol/water at 200 °C**

An ether product was identified in the ethanol/water system (α-terpinyl ether (9)). As Figure 4-9 shows, the data for ether formation did not fit a curve as tightly as the other products. The ether product is apparently even less stable at 200 °C than α-terpineol (3). Up to ~5% is formed quickly and then slowly disappears, probably through elimination of ethanol.

47
Several control reactions were analyzed to confirm the "in situ acid" effect of the hot water. β-Pinene (2) plus 1) 100% hexane; 2) 100% acetone; and 3) 100% ethanol, were heated in sealed reactor tubes at 200 °C for 2 hrs. All the pinene was recovered unreacted using hexane and ethanol. Ten percent loss of pinene was observed with 100% acetone. (Figure 4-10) Analysis of the GC/MS plot for this reaction showed a late eluting peak which was tentatively identified as the reaction product of β-pinene (2) with acetone (10) (see Appendix B-3 and B-4 for chromatograms and MS). Only trace amounts (<1%) of hydrolysis product were found. These results confirm that the water is required to achieve the in situ acid effect; and, the protic solvent ethanol does not contribute appreciably to the in situ acid effect.

A check of solubility was conducted for three of the solvent systems studied using a variable volume cell equipped with an observation window. Phase behavior was observed for 100% water, 50/50 water/ethanol and 50/50 acetone/water. At the reaction conditions of 200 °C the 50/50 water/ethanol was observed to be one phase. The 100% water and 50/50 acetone/water were observed to have a very slight amount of oil droplets remaining under these same conditions. These results indicate that solubility is probably
Figure 4-9. Formation of ether product in 50/50 ethanol/water at 200 °C

Figure 4-10. Recovery of β-pinene (2) after 2 hours in control reactions.
not a major factor contributing to the rate effects since the 100 % water system would be expected to have the lowest solubility; yet, it has the fastest relative rate.

**Conclusion**

Hot water, well below the critical point at 200 °C, is a successful reaction media for β-pinene (2) hydrolysis. The increase in $K_w$ achieved in water at 200 °C was sufficient to affect the hydrolysis at a rate ~10 times faster than the conventional acid-catalyzed systems and the product distribution is maintained or improved. The hot water reaction system required no added acid and allows for simple neutralization by cooling, thus simplifying product recovery and waste disposal.

The reaction rate and ultimately the product distribution can be tuned to achieve greater hydrolysis over dehydration by the use of various organic co-solvents. The addition of co-solvents slowed the reaction. For example, with 50/50 isopropanol/water 80 % conversion of β-pinene was achieved after 2.2 hr vs. < 20 min. in 100 % water. The distribution of hydrocarbons/ hydrolysis products was ~1:1 with 40 % yield of terpineol in 50/50 IPA/water after 130 min. In fact, by sampling the reactions over several time intervals it was possible to see that a product ratio of ~1:1 (hydrolysis/hydrocarbons) is achieved with each of the co-solvents at the 80 % pinene conversion point. Allowing the reaction to continue to 90 % conversion resulted in dehydration of terpineol and an increase of hydrocarbon products. Therefore, the maximum % yield of terpineol was 40 %. Greater yields could potentially be achieved if it was possible to remove the alcohol product from the system as it is formed.
One possible explanation for the relative rate results is the simple effect of less water (the source of the acid catalyst) being present in the co-solvent systems, therefore, less acid strength (or higher pH). While the results in the EtOH/water systems were consistent with this, the data from other co-solvent mixtures were not (Table 4-2). For example, the acetone, THF and IPA systems each contain the same amount of water on a molar basis, yet the time to achieve 90% conversion of β-pinene (2) ranges from 30 min to 150 min. Apparently several competing properties are involved which are affecting the acid strength, reaction intermediate and product stability in the system.

**Recommendations for Future Work**

The results of our experiments indicate that the pH of the hot water/co-solvent systems can be adjusted across a range of values. Understanding of our results would be facilitated by accurate knowledge of the pH of the individual systems. pH measurement at high temperatures and pressures has been developed and used extensively, especially in the areas of geothermal research and the study of nuclear reactor cooling water solutions. For example, a yttria stabilized zirconia electrode with both aqueous internal junction and metal-metal oxide internal junction has been reported to be capable of measuring pH in the range of 3-8 at temperatures from 25-285 °C and at 1200 psi (~80 bar). 23,24,25 Several variations of this type of electrode have been reported. 23,24,25 The system has been used to measure pH in high temperature subcritical and supercritical aqueous solutions, 26 and may be suitable to measure pH in our systems. Generation of accurate pH vs. water/co-solvent composition could lead to correlation of pH with solvent
properties and development of a predictive model for pH vs. temperature and solution composition.

Our results indicate that removal of the alcohol product during the reaction would increase yield. While removal of a reaction component during a process is not unusual in systems operating at conventional temperatures and pressures (i.e. azeotropes etc.), this may be more challenging under subcritical aqueous conditions. It could possibly be accomplished through design of a novel solvent composition that would allow in vitro separation of the product away from the in situ acid in the reactor. While none of the solvents we looked at so far are capable of accomplishing this, it is not inconceivable that a system could be designed that would be biphasic at 200 °C (aqueous / nonaqueous) and be able to differentiate between hydrocarbon starting material and alcohol product.

Supercritical water (400 °C, 200 bar) and near-critical water (275 °C, 60 bar) are systems that have received attention as environmentally benign alternative solvent/reaction media.28 However, there are few industrial applications of this technology. This is due in part to the rather harsh conditions of these systems making specialized equipment necessary, especially on a large scale. This is why our results at 200 °C are potentially useful. We have shown that β-pinene (Ω) hydration can be achieved at relatively mild conditions. Work to investigate the viability of these conditions for other high-value fine chemicals may reveal lucrative industrial applications. In addition, even lower temperatures should be investigated. For example, in the case of the β-pinene reaction, a decrease of rate for 90 % conversion of starting material from ~24 hours using conventional systems to < 30 min. using hot water at 200 °C may represent a significant cost savings in labor and energy costs. If the reaction

52
could also be accomplished at 150 °C in 8 hours, with possibly less capital investment than would be required for supercritical chemistry coupled with waste disposal savings, this may be attractive to industry. Therefore, future work with hot water may involve cost analysis of the milder hot water conditions and if the results are favorable, investigation of other specific acid-catalyzed processes currently being commercialized as possible candidates for this technology.

**Experimental**

(15S)-(+)-β-Pinene (2) (99 % by GC) from Aldrich Chemical Company was used. HPLC grade solvents were obtained from Aldrich: water; acetone; tetrahydrofuran; isopropanol and reagent grade anhydrous ethanol. Tetradecane internal standard (99 % by GC) was obtained from Fluka.

Reactions were conducted in 3 mL sealed titanium reactor tubes. Titanium was required due to its low level of impurities and resistance to corrosion vs. other metals. The reactors were heated using a thermostated aluminum block with temperature control of +/- 1°C (Figure 4-11). The entire temperature block was mounted on a shaker platform (Eberbach Corporation) which afforded some agitation to the reactor tubes. Reproducibility was improved with shaking.
The temperature block was capable of heating to the reaction setpoint (200 °C) in 5 min or less. Rapid cooling of the reactor tubes was achieved using a cold water bath. Solvents and β-pinene were added to the reactor tubes using an Eppendorf pipet. The concentration of pinene in the reactors was ~2 % (0.16 M). Reaction work-up consisted of transferring the contents of the reactor tube after cooling with a glass pipet to a 10 mL volumetric flask. Tetradecane was added as an internal standard. The reactor tube was rinsed with acetone and the rinse solvent was added to the volumetric flask up to 10 mL. Samples were analyzed by GC-FID and GC-MS. Since the heated block contained up to 10 reactor slots, it was possible to sample the reaction at several time intervals and ensure that the reaction conditions were essentially the same. Each solvent mixture was typically sampled at 5 intervals from time zero to ~ 2 hours.

**GC and GC-MS.** An Agilent 5890 GC equipped with a 6890 series autosampler was used for GC-FID analysis with a DB-5 capillary column (30 M x 0.32 mm x 1.0 µm film). The oven temperature program was as follows: initial temperature= 70 °C; initial hold= 10 min; 2 %/min to 200 °C; final hold: 50 min. Other settings of the GC were: injector temperature: 200 °C; detector temperature: 240 °C; carrier gas: helium; column
flow at initial temperature: 1.91 mL/min; carrier gas pressure (constant pressure): 10 psi; split ratio: 20:1; 1µL injection. An Agilent GC Chemstation method was used for peak integration and data analysis. Response factors were calculated for all of the major compounds based on the internal standard tetradecane and the results were reported as absolute concentration values (mg/mL). These were converted to percent of starting material. The mass balance for the hot water reactions was 95-100 %.

Mass spectrometric (MS) analysis was conducted on an Agilent 5972 MSD coupled with an Agilent 5890 GC. A DB-5 column (30 M x 0.32 mm x 1µm film thickness) was used with temperature program (10 min initial hold at 60 °C, 2 °C/min to 200 °C, 50 min final hold at 200 °C). The GC injector temperature was 190 °C and MSD transfer line temperature was 280 °C. The GC was operated in constant flow mode at 1.2 mL/min with vacuum compensation. Peak identifications were made using an in house reference compound library, the Wiley 6th edition MS library and retention time data found in the literature.27

Solubility/phase behavior of β-pinene in hot water and a hot water/ethanol system was observed using a variable-volume windowed vessel (2.5 cm diameter sapphire window, maximum volume = 20 mL) (Figure 4-5).24 Temperature of the vessel was controlled by placing it in a GC oven (modified Varian 3400 GC, +/- 0.5 °C). Temperature was measured using a handheld Omega readout connected to an Omega Type K thermocouple which was inserted into the variable-volume cell. Volume and pressure in the cell were controlled with an Isco 110D syringe pump attached to the piston of the variable-volume cell. The pressure on the back side of the piston (read on the Isco pump) was found to be the same as the pressure of the aqueous mixtures in the
vessel by previous work in our laboratory. Solutions were stirred by a small magnetic stir bar in the vessel. Phase behavior was observed visually by watching an image projected on a video monitor by a CCD camera (Sony) mounted on a borescope (Olympus).

Figure 4-12. Diagram of the variable-volume vessel apparatus.


CHAPTER V
ACID-CATALYZED HYDRATION OF \( \beta \)-PINENE IN GAS EXPANDED LIQUID (GXL)

Introduction

A gas-expanded liquid (GXL) is formed from the dissolution of a gas in a liquid. Most commonly, \( \text{CO}_2 \) is the gas and organic solvents are the liquid. The resulting expanded liquid will have enhanced transport properties due to the addition of the gas and also modified solvent properties (see Figure 5-1). In fact, depending on the composition of the mixture, which can be controlled by the pressure of the gas, the solvent properties can be “tuned.” Tunable solvent properties have been described for supercritical fluids.\(^1\)

The same phenomenon has been observed in gas expanded liquids. For example, an effective range of polarity from diethyl ether to heptane was achieved in a dioxane/\( \text{CO}_2 \) system by adjusting the \( \text{CO}_2 \) pressure from 0 to 28 bar.\(^2\)

![Diagram](image)

Figure 5-1. A pictorial view of the relationship of GXL’s to other common solvent systems.
The use of gas-expanded liquids to improve transport properties and adjust solvent properties has been well demonstrated. Gas-expanded liquid mobile phases in liquid chromatography have achieved faster separations because of enhanced mass transfer and increased optimum linear velocities. The enhanced solvating power of GXL's compared to supercritical fluids has been utilized for extraction of high molecular weight solutes and extractions from difficult matrices such as sediment. The gas in a GXL has also been used as an antisolvent. By increasing or “tuning” the composition of the gas in a GXL mixture, precipitation of individual compounds can be achieved. This property can be used for catalyst recovery, reaction work-up or compound purifications. The same concept has been used for manufacture of nanoparticles.

GXL’s have also found use as a reaction solvent. Blanchard and Brennecke achieved improved yields for the esterification of acetic acid with ethanol under equilibrium conditions by incorporating 30 mol% CO₂ (333 K, 58.6 bar). Subramanian and co-workers demonstrated the unique and “green” benefits of CO₂ expanded solvents for performing homogeneous catalytic oxidations. By using up to 80 % CO₂ in acetonitrile, they achieved greater turn over frequency for oxidation reactions due to increased solubility of oxygen and the catalysts in the system. In addition, the GXL has advantages for reaction work-up and catalyst recovery.

Another unique and potentially useful property of CO₂/aqueous alcohol GXL’s is the generation of in situ acid. When CO₂ and water are combined, carbonic acid is formed (Figure 5-2). Two groups have investigated the pH affect in CO₂/aqueous systems. Towes et al measured pH values of 2.8-2.95 in supercritical CO₂/water systems by monitoring the spectrum of bromophenol blue. A decrease in pH can also occur in
Figure 5-2. Formation of carbonic acids

CO₂ expanded liquids. Wen and Olesik used several pH indicators and UV/visible spectrum measurements to determine pH in CO₂/water/MeOH gas expanded liquids (Table 5-1).¹⁰ The results show a decrease in pH as the CO₂ composition increases to 5.6 mol % ratio. However, pH then increases from 4.22 to 4.73 up to 19.2 mol % CO₂. This is apparently due to the competing affect of dielectric constant, which decreases with increasing CO₂ concentration. The authors speculate that dissociation of the carbonic acid is inhibited with lower dielectric constant, thus resulting in an increase of pH after 5.6 mol % of CO₂. They find from the literature that dielectric constants of alcohol mixtures to which nonpolar alkanes are added will decrease proportionally with the mole percent of nonpolar additive. This information was used to determine the dielectric constant for their CO₂ gas expanded mixtures by using ε values of methanol/H₂O mixtures from the literature¹¹ and the mole fraction of CO₂ in the mixture. They were then able to match each GXL with a corresponding MeOH/water mixture having the same dielectric constant (see Table 5-1). These mixtures were used to establish calibration curves for [H⁺] determination. This study also showed that the pH of CO₂/MeOH/water systems was not affected by pressure changes from 100 – 200 atm.
<table>
<thead>
<tr>
<th>MeOH/H₂O/CO₂ Molar ratio</th>
<th>pH</th>
<th>Dielectric constant</th>
<th>MeOH/water system w/ equiv. DE Molar ratio</th>
</tr>
</thead>
<tbody>
<tr>
<td>1</td>
<td>68.2:30.6:1.2</td>
<td>4.54</td>
<td>42</td>
</tr>
<tr>
<td>2</td>
<td>65.1:29.3:5.6</td>
<td>4.22</td>
<td>40</td>
</tr>
<tr>
<td>3</td>
<td>61.7:27.7:10.6</td>
<td>4.38</td>
<td>38</td>
</tr>
<tr>
<td>4</td>
<td>55.7:25.1:19.2</td>
<td>4.73</td>
<td>34</td>
</tr>
</tbody>
</table>

West et al reported that the in situ formation of acid found in water/CO₂ systems (carbonic acid) extends to alcohol/CO₂ systems as well (Figure 5-2). ¹² They demonstrated relative acid strengths in the order of CH₃-O-CO₂H > CH₃CH₂-O-CO₂H > H-O-CO₂H > iPr-O-CO₂H > iBu-O-CO₂H for a series of alcohol-CO₂ interactions using the protoration of the methyne carbon on diazodiphosphinylmethane as a probe. The presence of methyl carbonic acid in MeOH/CO₂ mixtures was further demonstrated by Feng et al in studies of acetal formation with cyclohexanone in CO₂/MeOH GXL’s (10-40 bar). ¹³

The acid-catalyzed hydrolysis reaction of β-pinene to form terpineol is a reaction of commercial significance (see chapter II). A favorable product distribution would consist of high alcohol vs. hydrocarbon products. This can be accomplished in a more environmentally friendly manner using the in situ acid formation capabilities of a MeOH/water/CO₂ gas expanded liquid. Despite the low solubility of β-pinene in aqueous systems and the subsequent heterogeneous nature of the reaction, good conversion of the starting material and good yields of the desired alcohol products are achieved.
Results and Discussion

In order to confirm the \textit{in situ} acid formation ability of the GXL, several control reactions were performed with either no CO$_2$ or no heat. A summary of the control reaction results is shown in Figure 5-3. When the reactor was run for 24 hrs at room temperature (25 °C) with MeOH/water (1:1), 0.013 M β-pinene and no CO$_2$, there was virtually no reaction, as expected. Recovery of the pinene starting material was 98%. In addition, when the reactor was run for 24 hrs at room temperature (25 °C) with MeOH/water (1:1), 0.128 M β-pinene and CO$_2$, there was still virtually no reaction with 97% of the pinene recovered. This demonstrated that some heat is required for the reaction to proceed at a reasonable rate. When the reactor was run for 24 hrs at 75 °C with MeOH/water (1:1) 0.128 M β-pinene and no CO$_2$, the recovery of pinene was only 82%, however virtually no hydrolysis products were found in the reaction mixture according to GC analysis. The full mass recovery for this system was 84%. This suggests that oligomerization, possible polymerization or other loss of pinene (such as condensation in the stirring mechanism) occurs at the higher temperature. Pinene is itself a relatively volatile compound. In fact, it is considered to be a flammable liquid in neat form with a flash point of 35 °C. Since it is virtually insoluble in water at room temperature it may evaporate.
Figure 5-3. Summary of pinene recovery from GXL control reactions.

The possibility of polymerization in this type of reaction also exists. To investigate the behavior of the molecule when heated, neat β-pinene (1 mL) was heated at 75 °C for 24 hrs in a sealed titanium tube with no stirring. Analysis of the contents of the tube after 24 hrs. showed a loss of 8 % of the pinene according to the GC analysis. Again no reaction products were detected by GC analysis, indicating possible polymerization of β-pinene. This phenomenon has been described in the literature for bicyclic unsaturated terpenes. For example, oxidation reactions of 3-carene and α-pinene were conducted at room temperature to avoid polymerization.14 Dimerization and polymerization products were reported in α-pinene reactions after “prolonged reaction times.”15 In addition, speculation of the formation of relatively nonvolatile triols or triterpene products was used as an explanation of low mass recoveries for the acid-catalyzed cyclization of farnesol and nerolidol.16 The GC chromatogram for the GXL reactions showed some late eluting unidentified peaks (see Appendix B-1 for a typical chromatogram), possibly triols, bis-ether compounds, hydroxy ethers or other relatively polar, nonvolatile compounds. The unidentified portion of the chromatogram represented 65
~ 2 % of the total chromatogram area. If the compounds are diols or triols, extraction efficiency from an aqueous mixture may be low, requiring an extra response factor to determine the actual amount. In summary, the control reactions showed that full recovery of pinene may be difficult from aqueous mixtures held at elevated temperatures for an extended period of time, yet, elevated temperatures are required to obtain reasonable rates of reaction.

When the reactor was charged with CO₂ and held at 75 °C for 24 hr, hydrolysis products were detected. A typical GC chromatogram with labeled peaks is shown in Appendix B-1 with peak identifications listed in Appendix B-3. At 24 hours, we achieved typically 50 % conversion of the β-pinene or greater. The most successful CO₂-GXL for hydrolysis of β-pinene from a yield and product distribution standpoint was a 1:1 mixture of MeOH/water containing ~3 mol % CO₂. This system achieved 71 % conversion of β-pinene in 24 hr and produced a favorable product distribution. Since the β-pinene was not soluble in the 50:50 MeOH/water mixture even at 75 °C, the reaction is not homogeneous, therefore a kinetic analysis was not done. However, a surprisingly reproducible product mixture is obtained from the reaction. Figure 5-4 shows the distribution of products after ~24 hr from 6 separate runs of the 1:1 MeOH/H₂O/CO₂ gas expanded liquid. The system gives a favorable ratio of terpineol vs. hydrocarbon products: ~3.5:1. As described previously, total recovery of pinene is difficult due to its volatility and lack of solubility in aqueous systems, however, when extra care was taken to eliminate leaks in the system and thoroughly rinse the reactor during workup, a consistent percent conversion of 71 % (±1 % for duplicate experiments) was achieved.
Figure 5-4. Product Distribution reproducibility for 6 runs of the 1:1 pinene MeOH/water GXL.

Figure 5-5. β-Pinene conversion and product distribution variations with different MeOH/water ratios (75 °C, 24 hr)
The mass recovery was 92% (+/- 4%). The product distribution was: 14% hydrocarbons, 58% terpineol, 7% bicyclic alcohols and 19% methyl ether (2% unknown GC volatile material). This product distribution is favorable compared to the literature which reports product distributions of 30-50% for hydrocarbons, 50-55% for terpineol and 6-20% for bicyclic alcohols.15,17,18 In addition, there are other advantages to the GXL system. The self-neutralizing capability of the system (the acid disappears when the CO₂ pressure is released) results in complete elimination of waste salt or acid separation steps. Additionally, product recovery is simplified because upon depressurization, the products are present in a simple aqueous mixture (water and co-solvent) which can be used as is or concentrated as needed.

The fastest conversion of β-pinene occurred at 1:1 methanol/water. A range of other mixtures, from almost pure methanol to pure water indicated that as the water content increased, the β-pinene conversion decreased from 70% to less than 50% (Figure 5-5 and Table 5-2). This was expected since carbonic acid (pKₐ=6.3719) is a weaker acid than methyl carbonic acid (pKₐ=5.6120). The product distribution was similar with increased water except for progressively less ether product being formed as alcohol was decreased. An increase in water was also accompanied by lower recovery of starting material from the reactor. Since β-pinene is virtually insoluble in water, recovery from the heated, pressurized reaction vessel was difficult when the water content was high. Therefore, the calculated conversion of pinene was at most 50% and likely lower due to expected pinene loss.

Interestingly, as the methanol to water ratio was increased to 100:1, the conversion dropped precipitously to 2%. This is likely due to the decrease in dielectric
<table>
<thead>
<tr>
<th>Volume (mL) (MeOH/water volume ratio)</th>
<th>Mole fraction %</th>
<th>% conversion of pinene after 24 h</th>
<th>Product distribution</th>
<th>Mass recovery</th>
</tr>
</thead>
<tbody>
<tr>
<td>MeOH/water/CO&lt;sub&gt;2&lt;/sub&gt;</td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>30/0.5/3 (100:1)</td>
<td>94/2/4</td>
<td>2.1</td>
<td>59.2</td>
<td>40.8</td>
</tr>
<tr>
<td>37/3/4 (3:1)</td>
<td>53/42/4</td>
<td>18.9</td>
<td>68.1</td>
<td>31.9</td>
</tr>
<tr>
<td>25/25/4 (1:1)</td>
<td>30/67/3</td>
<td>70.9</td>
<td>84.0</td>
<td>14.0</td>
</tr>
<tr>
<td>13/37/4 (1:3)</td>
<td>13/84/3</td>
<td>49.3</td>
<td>84.0</td>
<td>16.0</td>
</tr>
<tr>
<td>0/50/5 (100% H&lt;sub&gt;2&lt;/sub&gt;O)</td>
<td>0/97/3</td>
<td>47.6</td>
<td>80.9</td>
<td>19.1</td>
</tr>
</tbody>
</table>

| EOH/water/CO<sub>2</sub>             |                 |                                  |                     |              |
| 25/25/3                              | 23/74/3         | 48.6                             | 78.2                | 21.8         | 62.3         |

| Acetone/water/CO<sub>2</sub>         |                 |                                  |                     |              |
| 25/25/4                              | 19/77/4         | 10.4                             | 75.6                | 24.4         | 94.9         |

constant of the mixed solvent. Previous studies have shown an inverse linear relationship between pK<sub>a</sub> of a weak acid and dielectric constant of various water/organic mixed solvents. The lower the dielectric constant, the more difficult it is for the acidic proton to dissociate from the acid. Thus, as the mixed solvent becomes mostly methanol (c=32), the acid strength drops, which in turn slows conversion of pinene (see Appendix C for a discussion of solvent effects on pK<sub>a</sub>). When the mixed solvent is mostly water (c=80), one might expect increased acid strength. However, the acid is changing from methyl carbonic to carbonic acid, a weaker acid. The decrease in dielectric constant is competing with acid strength which explains a maximum conversion with varying solvent ratio.

Both acetone and ethanol were also used as co-solvents with water for the reaction. Since the dielectric constants of acetone (c=21) and ethanol (c=24) are both below that of methanol, one would expect lower conversion for these GXLs than methanol GXLs at any solvent ratio, which was observed. Ethanol, with only a slightly

69
higher dielectric constant than acetone, gave much higher conversion (49 \%) versus acetone (10 \%), which also is consistent with alkyl carbonic acid playing an important role in GXL catalysis. West et al also found faster rates with ethanol vs. water, indicating that ethyl carbonic acid is stronger than carbonic acid.\textsuperscript{12}

**Conclusion**

CO\textsubscript{2} gas expanded liquids were demonstrated as green substitutes for acid-catalyzed hydrolysis of β-pinene. Relatively mild CO\textsubscript{2} pressures (well below the critical pressure) can be used with a GXL to provide the *in situ* catalysis. Of the solvents investigated in this study, a 1:1 mixture (volume) of MeOH/water gave the best results with respect to rate of reaction and product distribution. Starting with a heterogeneous mixture of alcohol/water and β-pinene at 0.13 M concentration, up to 71 \% conversion of β-pinene was achieved at 75 °C after 24 hr. A ratio of hydrolysis to hydrocarbon products of 6:1 was obtained. Experiments with other solvents revealed the importance of balancing acid strength vs. solvent composition. For example, even though methyl carbonic acid is theoretically a stronger acid than carbonic acid, its acid strength (pK\textsubscript{A}) is apparently considerably decreased as the dielectric constant decreases with increased methanol. So, even though greater levels of methyl carbonic acid are probably formed with increased methanol content, the pK\textsubscript{A} is decreased. Thus, solvent mixtures with more than 50 \% methanol had less conversion of β-pinene. Further work to understand this relationship will be useful for predicting other systems to try for *in situ* acid formation.
Recommendation for Future Work

The current work demonstrates that in situ acid formation under relatively mild conditions in a gas expanded liquid (75 °C, 200 psi) is useful for performing acid-catalyzed hydration reactions. Work is underway in our group to show the usefulness of this technique for other commercially significant processes. A better understanding of the experimental parameters of this system such as pH, phase behavior and mass transfer, and their effect on reaction efficiency and yield will be necessary for industrial scale-up. This knowledge will also be useful for identifying other applications for this process.

Some of this information could be determined through optimization experiments using the pinene to terpineol reaction or other important reactions that are currently under investigation in the group. The GXL process seems to be a good candidate for Design of Experiment (DOE). DOE is a powerful statistical technique that can be used to help elucidate the important factors of complex processes with a minimum number of experiments. The GXL process has several counteracting phenomenon at work. For example, increasing CO₂ pressure will theoretically increase carboxylic acid formation; however, increased levels of CO₂ will decrease the dielectric constant of the solution which can result in less acid activity. Another example of competing processes in the pinene reaction is the dehydration of the alcohol product. Theoretically increased time or temperature will result in greater formation of alcohol product, yet these factors will also cause dehydration and loss of the alcohol as well. DOE may be especially helpful for determining the optimum conditions for the best yield in a reaction.

Implementation of DOE requires identification of the variables in the reaction. For the β-pinene hydration reaction, the following four quantitative variables would be
important: CO₂ pressure, amount of co-solvent, time and temperature. The measured response would be yield of terpineol. This set of variables could be investigated using a 2^4 factorial design resulting in a total of 16 experiments (see Table 5-3). Another important variable for this process is the type of co-solvent. So far, most of the work has been done with methanol. Other possible co-solvents are: ethanol and propanol. Each of these co-solvents could be optimized separately or the solvent type could be incorporated into the initial experimental design. After completion of the full matrix of experiments, regression of the data is possible. Plots of the results and generation of response surfaces can lead to better understanding of the mechanism of the reaction and optimum conditions to give a particular result.
Table 5.3. Possible factorial design for a DOE investigation on GXL reactions.

<table>
<thead>
<tr>
<th>Run</th>
<th>Time</th>
<th>Temp.</th>
<th>Amount of co-solvent</th>
<th>Amount of CO₂</th>
</tr>
</thead>
<tbody>
<tr>
<td>1</td>
<td>-</td>
<td>-</td>
<td>-</td>
<td>-</td>
</tr>
<tr>
<td>2</td>
<td>+</td>
<td>-</td>
<td>-</td>
<td>-</td>
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<tr>
<td>3</td>
<td>-</td>
<td>+</td>
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<tr>
<td>4</td>
<td>+</td>
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<tr>
<td>7</td>
<td>-</td>
<td>+</td>
<td>+</td>
<td>-</td>
</tr>
<tr>
<td>8</td>
<td>+</td>
<td>+</td>
<td>+</td>
<td>-</td>
</tr>
<tr>
<td>9</td>
<td>-</td>
<td>-</td>
<td>+</td>
<td>+</td>
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<td>10</td>
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<td>15</td>
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<td>+</td>
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</tr>
<tr>
<td>16</td>
<td>+</td>
<td>+</td>
<td>+</td>
<td>+</td>
</tr>
</tbody>
</table>

Variables:
Time = 15-45 hr
Temperature = 50-100 °C
Amount of co-solvent (mol %) = 25-75 %
Amount of CO₂ (mol %) = 2-8 %
The GXL system is complicated by several competing effects and processes: acid formation, changing dielectric constant, changing solubility of components, acid dissociation. The optimization experiments may provide insight into some of the competing effects and their relationship to each other but more fundamental data is also needed. Relative acid strengths of alkyl carbonic acids were determined by our group. However, these rates are affected by the equilibrium responsible for the initial formation of the carbonic acid and the acid strength of the acid itself as defined by its dissociation constant ($K_a$) (Figure 5-6). Measurement of the individual equilibrium constants would provide information useful for predicting acid strengths and ultimately rates of reaction in GXL’s. This would be best approached using a system with one acid present (i.e. methyl carbonic) rather than the dual acid systems used for the experiments in this dissertation. Measurement of solvent kinetic isotope effects can give information about rate determining steps and indicate whether general or specific acid catalysis is the dominating mechanism.
**Experimental**

(1S)-(−)-β-Pinene (99% by GC analysis) from Aldrich Chemical Company was used. HPLC grade solvents were obtained from the following suppliers: water (Aldrich); methanol (Aldrich, anhydrous 99.8 %); ethanol (Aldrich, reagent grade, anhydrous); acetone (Sigma Aldrich, 99.9+ %); methylene chloride (Fisher, certified ACS). The tetradecone internal standard (99% by GC analysis) was obtained from Fluka. Carbon dioxide (SFC/SFE grade) was obtained from AirGas.

The reactions were performed in a Model 4560, inconel, 100 mL Parr reactor fitted with an overhead magnetic stirrer controlled by a Model 4842 stirrer and heater controller. The temperature of the reactor was maintained within 1 °C of the setpoint. The stirrer was operated at its maximum speed of 725 rpm. The CO₂ was added to the reactor using an Isco 500 D syringe pump with a Series D controller. The pressure of the Parr reactor was monitored using an Ashcroft pressure gauge. The pressure of the reactor was typically 200-300 psi (14-21 bar). At the end of the reaction period the reactor was allowed to cool to room temperature (~1-1.5 hr) and the pressure was released into a 250 mL degassing flask fitted with a glass frit filter and ~ 200 mL of acetone. The degassing process continued for ~ 5 min.

At the end of the degassing period, the entire contents of the reactor was poured into a 200 mL separatory funnel. Tetradecone (0.05 mL) was added as an internal standard using an Eppendorf pipet. The reactor, and as much of the stirring mechanism as possible, were thoroughly rinsed with methylene chloride. The rinse solvent was added to the separatory funnel (~ 50 mL solvent) and the mixture was extracted and allowed to separate. The extraction was repeated two more times. The final organic
layer (~150 mL) was concentrated to ~15 mL using a Kuderna Danish evaporator and
hot water bath (~75 °C). Previous work in our laboratory confirms that the KD
evaporator is suitable for quantitative concentration of methylene chloride samples. The
efficiency of the work-up procedure was checked by taking a 50 mL solution of
MeOH/water containing 1 mL of β-pinene through the extraction and concentration step.
The percent recovery of β-pinene was 96 % as determined by GC-FID. Internal standard
(0.05 mL tetradecane) was also added to the acetone degassing solvent which was then
concentrated to ~15 mL using a rotovap set to relatively mild conditions (~ 40 °C, 20 in-
Hg). The degas solvent was found to contain usually less than 5 % of the mass balance,
however the levels rose to ~20 % in a few cases, probably due to degas flows that were
set too fast. The concentrated samples were analyzed by GC-FID and GC-MSD.

Phase equilibria studies were conducted with a 300 mL Parr equipped with an
observation window. The same temperature and stirring controller as previously
described was used. The reaction mixture (total volume = 100 mL in this case) and CO₂
were added to the Parr as previously described and the phase behavior of the system was
observed at the window as the reactor temperature was increased. All GXL solvent
mixtures used in this study were found to be monophasic at reaction conditions. Once
pinene was added, the mixture was biphasic since pinene was not fully soluble at these
centrations.

The following solvent mixtures were investigated as reaction media for β-pinene
(0.128 M) hydrolysis:
### Table 5-4. GXL composition summary

<table>
<thead>
<tr>
<th>Volume (mL) [MeOH/water volume ratio]</th>
<th>Mole fraction % MeOH/water/CO₂</th>
<th>Mass recovery (% of starting material)</th>
</tr>
</thead>
<tbody>
<tr>
<td>MeOH/water/CO₂</td>
<td></td>
<td></td>
</tr>
<tr>
<td>50/0.5 (100:1)</td>
<td>94/2/4</td>
<td>101.2</td>
</tr>
<tr>
<td>37/13/4 (3:1)</td>
<td>53/42/4</td>
<td>84.6</td>
</tr>
<tr>
<td>25/25/5 (1:1)*</td>
<td>30/67/3</td>
<td>94.2</td>
</tr>
<tr>
<td>13/37/4 (1:3)</td>
<td>13/84/3</td>
<td>68.9</td>
</tr>
<tr>
<td>0.5/5/5 (100% H₂O)</td>
<td>0/97/3</td>
<td>65.8</td>
</tr>
<tr>
<td>EtOH/water/CO₂</td>
<td></td>
<td></td>
</tr>
<tr>
<td>25/25/3</td>
<td>25/74/3</td>
<td>62.3</td>
</tr>
<tr>
<td>Acetone/water/CO₂</td>
<td></td>
<td></td>
</tr>
<tr>
<td>25/25/4</td>
<td>19/77/4</td>
<td>94.9</td>
</tr>
</tbody>
</table>

*Numerous experiments were conducted with 50/50 MeOH/water. The actual CO₂ volume ranged from 2-5 mL, thus MeOH/water/CO₂ mole fraction % ranged from 30/68/2 to 29/66/5

An HP 5890 GC equipped with a 6890 series autosampler was used for GC-FID analysis with a DB-5 capillary column (30 M x 0.32 mm x 1.0 μm film). The oven temperature program was as follows: initial temperature 70 °C; initial hold 10 min.; 2 °C/min to 200 °C; final hold 50 min. Other settings of the GC were: injector temperature 200 °C; detector temperature 240 °C; carrier gas helium; column flow at initial temperature 1.91 mL/min; carrier gas pressure (constant pressure) = 10 psi; split ratio = 20:1; 1μl injection. An Agilent GC Chemstation method was used for peak integration and data analysis. Response factors were calculated for all of the major compounds based on the internal standard tetradecane and the results were reported as absolute concentration values (mg/ml). These were converted to % of starting material for this report unless otherwise specified.

GC-MS analysis of the reaction mixtures were conducted on an HP 5972 MSD coupled with an HP 5890 GC. A DB-5 column (30 M x 0.32 mm x 1 μm film thickness)
was used with temperature program (10 min. initial hold at 60 °C, 2 °C/min to 200 °C, 50 min final hold at 200 °C). The GC injector temperature was 190 °C and MSD transfer line temperature was 280 °C. The GC was operated in constant flow mode at 1.2 mL/min with vacuum compensation. Peak identifications were made using our in house citrus1 library, the Wiley 6th edition MS library and retention time data found in the literature.23

2) Brown, J. S., et al. work in progress. Results based on the measurement of rates of azobenzene cis-trans isomerization.


80
19) CRC Handbook of Chemistry and Physics, 52nd edition.


CHAPTER VI
CONCLUSION

This project investigated the effect of a variety of aqueous systems on the reaction of the terpene hydrocarbon, β-pinene; and, in the process demonstrated the utility of two in situ acid sources: hot water and gas expanded liquids. The acid-catalyzed hydration of β-pinene is a reaction of commercial significance, especially to the flavor and fragrance industry. The products of the reaction are alcohols (terpeneol and bicyclic alcohols) and hydrocarbons. From a commercial standpoint, the alcohols are the desired products.

Table 6.1 and Figure 6-1 show a product distribution comparison between all the systems discussed in this study. The traditional methods used for pinene hydration use strong acids and heat. Under these conditions the typical product distribution is ~1:1 (alcohols:hydrocarbons). When the reaction is performed at room temperature in an aqueous emulsion, the alcohol/hydrocarbon ratio is improved, but the reaction is relatively slow. Using an SDS micelle improves the rate and also modifies the selectivity of the reaction, giving more bicyclic alcohols vs. terpeneol. This will have an impact on the flavor character of the mixture. While aqueous emulsions and SDS micelles give good product distributions, they have the disadvantages of waste generation and complicated product separation steps.

CO2 gas-expanded liquids and hot water (200 °C) were demonstrated as green substitutes for strong acid in the hydrolysis of β-pinene. Relatively mild CO2 pressures (well below the critical pressure) can be used to create a GXL and provide the in situ catalysis. Additionally the ratio of desired hydrolysis products to hydrocarbon products
was improved in the GXL over most conventional acid-catalyzed systems (3.5:1 GXL vs. 1:1 conventional). Hot water, well below the critical point at 200 °C, is also a successful reaction media for β-pinene hydrolysis. The reaction rate and product distribution can be tuned to achieve greater hydrolysis over dehydration by the use of various organic co-solvents. Although the product distribution for the hot water reaction is not as favorable as the GXL systems with respect to hydrocarbon production, the results are still comparable to conventional acid systems. The hot water system gives faster reaction times compared to the GXL’s and also provides the benefits of simplified product recovery over conventional systems due to elimination of acid separation steps. This system further offers a greater variety of co-solvent choices that show promising results. Both in situ acid reaction systems require no added acid and allow for simple neutralization by either depressurization and/or cooling, thus simplifying product recovery and waste disposal.

It is difficult to quantitatively compare rates of these systems due to the temperature variation and current lack of knowledge of the true pH/acid strength of some of the reactions. However, an approximate relative rate comparison of the systems as they were configured in this study at maximum yields (i.e. no temperature or pH adjustments) is as follows (slowest to fastest): traditional aqueous acid ("literature average")-GXL (75 °C)<aqueous emulsion (pH=2.2, 25 °C)<SDS micelle (pH=2.8, 25 °C)<hot water(200 °C). The approximate ratio is 12:12:5:3:1 (literature: GXL:emulsion:SDS micelle:hot water). The literature, emulsion and SDS micelle all require added acid and neutralization steps.
Table 6-1. Product distribution comparison between the systems investigated in this study

<table>
<thead>
<tr>
<th>System Description</th>
<th>% of product mixture recovered</th>
</tr>
</thead>
<tbody>
<tr>
<td></td>
<td>terpineol</td>
</tr>
<tr>
<td>Traditional aqueous acid, 60-75 °C, 1-24 hr, α-pinene (average from the literature)</td>
<td>40</td>
</tr>
<tr>
<td>Aqueous acidic emulsion, pH=2.2, 20 °C, 73 hr, α-pinene</td>
<td>87</td>
</tr>
<tr>
<td>SDS micelle, pH=3.1, 25 °C, 24 hr, β-pinene</td>
<td>66</td>
</tr>
<tr>
<td>Water/MeOH/CO₂ GXL, 75 °C, 24 hr, β-pinene</td>
<td>55</td>
</tr>
<tr>
<td>Hot water/co-solvent, 200 °C, β-pinene, time varies depending on co-solvent (0.5 hr-2 hr)</td>
<td>47</td>
</tr>
</tbody>
</table>

![Figure 6-1. Pinene hydration product distribution](image)

84
Commercial application of the *in situ* acid technologies will require two things. First, an economic analysis of the cost comparison of the new system vs. current systems would need to be done in order to decide if new capital investment was worth the cost. It is likely that the analysis would show favorable advantages for the *in situ* acid systems when all factors are taken into consideration such as: yield, time, ingredient cost, ingredient storage, waste storage, waste disposal costs, labor costs, other uses for the equipment, etc. If the economic analysis was favorable, optimization experiments would be necessary to ensure that the best conditions were employed. The results of optimization would likely improve the economics as well. Knowledge of fundamental parameters of the systems (rate constants, acid equilibrium constants, etc) would help with optimization; however, lack of this information should not prevent commercial application of the techniques.
APPENDIX A.

LITERATURE SUMMARY OF PINENE HYDROLYSIS
<table>
<thead>
<tr>
<th>Reagents</th>
<th>Time/temp</th>
<th>Yield</th>
<th>Reference</th>
</tr>
</thead>
<tbody>
<tr>
<td>Formation of terpineol from pinene or turpentine</td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>1 part 1-turpentine, 1.5 parts 90% alcohol, and 0.5 parts H₂SO₄</td>
<td>10 hr/ice</td>
<td>1-terpineol</td>
<td>Flavitsky, <em>Berichte</em>, 1879, 12, p. 2354; Godlevsky, <em>J. Russ. Phys. Chem. Soc.</em>, 1899, 31, p. 205; Kremenets, <em>Pharm. Rev.</em>, 1908, 26, p. 104</td>
</tr>
<tr>
<td>Turpentine and 1.5 vol glacial acetic acid</td>
<td>155-158 °C</td>
<td>1-terpineol</td>
<td>Bouchardat and Lafont, <em>Ann. Chem. Phys.</em>, [6], 1886, 9, p. 523</td>
</tr>
<tr>
<td>1 kg turpentine; 2 kg glacial acetic acid containing 100 g of 50% H₂SO₄; mixture is neutralized; steam distill ester; saponify</td>
<td></td>
<td></td>
<td>Bertram and Walbaum, Ger. Pat. 67,255, April 12, 1892</td>
</tr>
<tr>
<td>400 g 1-pinene, 400 g 95% alcohol, 300 g 50% nitrous acid</td>
<td>2 months</td>
<td>60% 1-terpineol</td>
<td>Genvrresse, <em>Compt. Rend.</em>, 1901, 132, p. 683</td>
</tr>
<tr>
<td>2000 g pinene, 1200 g 70% formic acid, 400 g 70% H₃PO₄</td>
<td>8 hr/35-45 °C</td>
<td>70% terpineol</td>
<td>French Pat. 800,457, 1936 (Hercules Powder Company)</td>
</tr>
<tr>
<td>Benzene-, toluene- or xylene-sulphuric acid or methyl-, ethyl-sulphuric acid with</td>
<td>&lt;60 °C</td>
<td>terpineol</td>
<td>U. S. Pat. 2,178,349, 1937 (Hercules Powder Co.)</td>
</tr>
</tbody>
</table>

87
<table>
<thead>
<tr>
<th>acetone or dioxane</th>
<th>100 parts α-pinene, 1080 parts 39% sulfuric acid, 420 parts acetone; separate oil from acid; washed; neutralized with 250 parts 10% NaCO₃; fractional distillation</th>
<th>6 hr/ 35-40 °C</th>
<th>Terpineol 43%</th>
<th>Sheffield, U. S. Pat. 2,178349, Oct. 31, 1939</th>
</tr>
</thead>
<tbody>
<tr>
<td>Part 1: 500 parts turpentine, 2000 parts H₂SO₄ (25 %), 5-10 parts polyglycol-mono-iso-octylphenyl ether; neutralize with NaCO₃</td>
<td>48 hr/30-40 °C</td>
<td>Terpin hydrate, 95%</td>
<td>Weissenborn, U. S. Pat. 2,295,705, Sept. 15 1942</td>
<td></td>
</tr>
<tr>
<td>Part 2: 7.5 parts phthalic anhydride, 3000 parts water, 500 parts terpin hydrate</td>
<td>15 hr/99-100 °C</td>
<td>99 % terpinol</td>
<td>Sheffield, U. S. Pat., 2,336,575, Jan. 22, 1941</td>
<td></td>
</tr>
<tr>
<td>1. 2000 parts β-pinene, 1600 parts water, 400 parts H₂NSO₃H and 1 g “Emulgar A”</td>
<td>15 hr/68-70 °C</td>
<td>72 % terpene alcohols</td>
<td>Borglin, J. N., U. S. Pat. 2,432,556, Dec. 16, 1947</td>
<td></td>
</tr>
<tr>
<td>2. 2000 parts β-pinene, 800 parts water, 200 parts H₂NSO₃H, 200 parts 9 % H₂SO₄ and 800 g acetone</td>
<td>17 hr/51-53 °C</td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>150 parts turpentine, 460 parts 25 % H₂SO₄, 40 parts 25 % toluene sulfonic acid</td>
<td>30 hr/34-37 °C</td>
<td>Terpin hydrate, 70%</td>
<td>King, R. G., U. S. Pat. 2,481,845, Sept. 13, 1949 (King Organic Chemicals)</td>
<td></td>
</tr>
<tr>
<td>α-pinene, 95% acetone/water, 0.06 N H₂SO₄</td>
<td>7 hr/75 °C</td>
<td>55 % terpinol</td>
<td>Valkanas, G. and Iconomou, N., “121. Reaktionen in der Terpen-Reihe I. Mittellung Hydratisierung von α-Pinen,” Helv. Chim. Acta, 46, 1963, 1089</td>
<td></td>
</tr>
<tr>
<td>100 g α-pinene, 100 g 50 % acetic or formic acid, 10 g 52 % BF₃, acetic acid complex</td>
<td>6 hr/65-70 °C</td>
<td>50 % terpinol, maximum</td>
<td>Arakawa, M.; Nakamura, Y., Uemura, Y. and Onori, T., U. S. Pat. 3,281,479, Oct. 25, 1966</td>
<td></td>
</tr>
<tr>
<td>Turpentine or pinene, 20-75 % H₂SO₄, non-ionic surfactants,</td>
<td>4-8 hr/S-55 °C</td>
<td>60-90 % terpinol</td>
<td>Swaminathan, M. S., Indian Pat., 113193, Nov. 16, 1967</td>
<td></td>
</tr>
<tr>
<td>β-pinene, 95 % acetone/water, 0.073N H₂SO₄</td>
<td>1 hr/75 °C</td>
<td>42 % terpinol</td>
<td>Williams, C. M., and Whittaker, D., “Rearrangements of Pinane Derivatives. Part 1. Products of Acid Catalyzed Hydration of α-Pinene and β-Pinene,” J. Chem. Soc. (B), 1971, 668-672</td>
<td></td>
</tr>
<tr>
<td>Component</td>
<td>Reaction Conditions</td>
<td>Product</td>
<td>Reference</td>
<td></td>
</tr>
<tr>
<td>-----------</td>
<td>---------------------</td>
<td>---------</td>
<td>-----------</td>
<td></td>
</tr>
<tr>
<td>α-pinene, aqueous H₂SO₄</td>
<td>75-200 °C</td>
<td>0-48% terpineol</td>
<td>Kerssen, R., “Acid catalyzed hydration and isomerization of α-pinene, The effect of temperature and acid concentration on the reaction rate and products,” Paperia ja puu, 61, 1979, 165-8, 170-1</td>
<td></td>
</tr>
<tr>
<td>1000 ml α- or β-pinene, 1000 ml 25 % H₃PO₄, 1.15 g emulsifier (C₁₄ fatty alc./ethylene oxide)</td>
<td>24 hr/70 °C</td>
<td>850 g crude α-terpineol as oil</td>
<td>Charwath, M., European Pat., 35, 703 (cl. C07C33/14), Sept. 16, 1981</td>
<td></td>
</tr>
<tr>
<td>α- or β-pinene, 1-30 % aq. H₃PO₄ or 0.2-2 % H₂SO₄</td>
<td>4 hr/100 °C (reflux)</td>
<td>37% terpineol</td>
<td>Moelenken, R. Ger. Offen. DE 4,111,900, April 12, 1991</td>
<td></td>
</tr>
<tr>
<td>α- or β-pinene, CICH₂CO₂H, H₂O and Sc triflate</td>
<td>2 hr/60 °C</td>
<td>57% terpineol</td>
<td>Tanaka, S.; Yamamoto, J.; Koshino, J., Japan. Pat. 96-95376, April 17, 1996</td>
<td></td>
</tr>
<tr>
<td>Step 1: α-pinene, 30 % H₂SO₄, 0.7 %</td>
<td>24 hr/28-31</td>
<td>73% terpin</td>
<td>Oui, X.; Chen, Y.; He, Y.; Li, X., Linchun Huaxue</td>
<td></td>
</tr>
<tr>
<td>Step 2: 0.3 % H₂SO₄</td>
<td>°C</td>
<td>hydrate 53 % terpineol</td>
<td>Yu Gongye, 1997, 17(4), 33-44.</td>
<td></td>
</tr>
<tr>
<td>------------------</td>
<td>----</td>
<td>------------------------</td>
<td>-------------------------------</td>
<td></td>
</tr>
<tr>
<td>β-pinene, MeOH/water/CO₂ GXL</td>
<td>24 hr, 75 °C</td>
<td>55 % terpineol</td>
<td></td>
<td></td>
</tr>
</tbody>
</table>

**Formation of terpineol from terpin hydrate**

Terpin hydrate, H₂SO₄ or H₃PO₄, acetic acid and KH₂SO₃

<table>
<thead>
<tr>
<th>dl-terpineol</th>
<th>Wallach, Annalen, 1885, 230, p 253</th>
</tr>
</thead>
<tbody>
<tr>
<td>50 kg terpin hydrate, 110 L 20 % H₃PO₄</td>
<td>15 min/ warmed</td>
</tr>
<tr>
<td>100 g purified terpin hydrate, 25 g 100 % H₂SO₄, 475 g water, 100 g benzene</td>
<td>4 hrs/73-75 °C</td>
</tr>
<tr>
<td>70-80 kg terpin hydrate, 3 % aqueous H₃PO₄</td>
<td>3-4 hrs/ 100 °C (boiling)</td>
</tr>
</tbody>
</table>

**Formation of terpineol from other terpenes**

| linalool with acetic anhydride | 150°-160 °C | d-terpineol | Stephan, J. prakt. Chem., 2, 1898, 58, p111 |
| linalool with glacial acetic acid | 122 °C | Bertram, German Pat. 80,711 |
| linalool with strong formic acid | 22 °C | |
| α-linalool, conc. formic acid | | | Stephan, J. prakt. Chem., 2, 1898, 58, p. 119 |
| α-linalool, HCl-activated bleaching earth (Floridin) | 1.5 hr/ 105 °C | l-terpineol | Pugilevsky, Kanetskaya and Platonova, J. Gen. Chem. U.S.S.R. 1937, 7, p. 873 |
| linalool and 30 % H₂SO₄ | 10 hr/ 100 °C | 12 % d-terpineol, 44 % hydrocarbons | Matsurra, J. Science Hiroshima Univ., Series A, 1938, 8, p. 303 |
| Geraniol and anhydrous formic acid or a | | | Stephan, J. prakt. Chem., 2, 1899, 60, p. 244. |
| mixture of glacial acetic and sulphuric acids | 7 hr/ 60 °C | $d$-terpineol | Kuvata, T., *J. Soc. Chem. Ind. Japan* (Suppl), 1933, 36, p. 583B |
| 50 g geraniol, 100 g acetone, 25 g acid clay | 1 hr | $l$-terpineol | Wallach, *Annalen*, 1900, 360, p. 88 |
| $l$-pinene hydrate, ether, 100 volumes 5% H$_2$SO$_4$ |  |  |  |
APPENDIX B

GC Chromatograms and peak assignments for reactions

Figure B-1. GC-FID for β-pinene MeOH/water/CO₂ (1:1) GXL

Figure B-2. GC-FID for β-pinene hot water/acetone (1:1)

Table B-1. Peak Identifications for GC-chromatograms

Figure B-3. MS TIC of control reaction of β-pinene in acetone at 200 °C

Figure B-4. MS for peak tentatively identified as the reaction product of acetone with β-pinene
Figure B-1: GC-FID chromatogram from a β-pinene MeOH/water/CO₂ (1:1) GXL after 24 hours at 75 °C (see Appendix A-4 for peak identifications.)
Figure B-2: GC-FID chromatogram from a β-pinene hot water/acetone (1:1) reaction (68 minutes) (see Appendix A-4 for peak identifications.)
<table>
<thead>
<tr>
<th>Peak No.</th>
<th>Name</th>
<th>Structure</th>
<th>Peak No.</th>
<th>Name</th>
<th>Structure</th>
</tr>
</thead>
<tbody>
<tr>
<td>1</td>
<td>α-pinene</td>
<td><img src="image1" alt="Structure" /></td>
<td>6</td>
<td>1,4-cineol</td>
<td><img src="image2" alt="Structure" /></td>
</tr>
<tr>
<td>2</td>
<td>fenchene</td>
<td><img src="image3" alt="Structure" /></td>
<td>7</td>
<td>α-terpinene</td>
<td><img src="image4" alt="Structure" /></td>
</tr>
<tr>
<td>3</td>
<td>camphene</td>
<td><img src="image5" alt="Structure" /></td>
<td>8</td>
<td>p-cymene</td>
<td><img src="image6" alt="Structure" /></td>
</tr>
<tr>
<td>4</td>
<td>β-pinene</td>
<td><img src="image7" alt="Structure" /></td>
<td>9</td>
<td>limonene</td>
<td><img src="image8" alt="Structure" /></td>
</tr>
<tr>
<td>5</td>
<td>myrcene</td>
<td><img src="image9" alt="Structure" /></td>
<td>10</td>
<td>1,8-cineol</td>
<td><img src="image10" alt="Structure" /></td>
</tr>
<tr>
<td>5a</td>
<td>α-phellandrene</td>
<td><img src="image11" alt="Structure" /></td>
<td>11</td>
<td>γ-terpinene</td>
<td><img src="image12" alt="Structure" /></td>
</tr>
<tr>
<td>Peak No.</td>
<td>Name</td>
<td>Structure</td>
<td>Peak No.</td>
<td>Name</td>
<td>Structure</td>
</tr>
<tr>
<td>---------</td>
<td>-----------------------</td>
<td>-----------</td>
<td>----------</td>
<td>-----------------</td>
<td>-----------</td>
</tr>
<tr>
<td>12</td>
<td>fenchyl methyl ether</td>
<td><img src="image1.png" alt="Structure" /></td>
<td>18</td>
<td>c-β-terpineol</td>
<td><img src="image2.png" alt="Structure" /></td>
</tr>
<tr>
<td>13</td>
<td>terpinolene</td>
<td><img src="image3.png" alt="Structure" /></td>
<td>19</td>
<td>isoborneol</td>
<td><img src="image4.png" alt="Structure" /></td>
</tr>
<tr>
<td>14</td>
<td>bornyl methyl ether</td>
<td><img src="image5.png" alt="Structure" /></td>
<td>20</td>
<td>r-β-terpineol</td>
<td><img src="image6.png" alt="Structure" /></td>
</tr>
<tr>
<td>15</td>
<td>α-fenchol</td>
<td><img src="image7.png" alt="Structure" /></td>
<td>21</td>
<td>borneol</td>
<td><img src="image8.png" alt="Structure" /></td>
</tr>
<tr>
<td>16</td>
<td>β-fenchol</td>
<td><img src="image9.png" alt="Structure" /></td>
<td>22</td>
<td>terpinen-4-ol</td>
<td><img src="image10.png" alt="Structure" /></td>
</tr>
<tr>
<td>17</td>
<td>terpinen-1-ol</td>
<td><img src="image11.png" alt="Structure" /></td>
<td>23</td>
<td>p-methyl acetophenone</td>
<td><img src="image12.png" alt="Structure" /></td>
</tr>
<tr>
<td>Peak No.</td>
<td>Name</td>
<td>Structure</td>
<td>Peak No.</td>
<td>Name</td>
<td>Structure</td>
</tr>
<tr>
<td>---------</td>
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<td>----------</td>
<td>-----------------------------</td>
<td>-----------</td>
</tr>
<tr>
<td>24</td>
<td>α-terpineol</td>
<td><img src="image1.png" alt="Structure" /></td>
<td>29</td>
<td>p-menth-1-ene-4,8-diol (I)</td>
<td><img src="image2.png" alt="Structure" /></td>
</tr>
<tr>
<td>25</td>
<td>γ-terpineol</td>
<td><img src="image3.png" alt="Structure" /></td>
<td>30</td>
<td>p-mentha-1,4-dien-7-ol (I)</td>
<td><img src="image4.png" alt="Structure" /></td>
</tr>
<tr>
<td>26</td>
<td>terpinyl methyl ether</td>
<td><img src="image5.png" alt="Structure" /></td>
<td>31</td>
<td>tridecane</td>
<td>Impurity from the internal standard</td>
</tr>
<tr>
<td>27</td>
<td>p-mentha 1(7), 8(10)-dien-9-ol (I)</td>
<td><img src="image6.png" alt="Structure" /></td>
<td>32</td>
<td>p-menthen-6,8-diol</td>
<td><img src="image7.png" alt="Structure" /></td>
</tr>
<tr>
<td>28</td>
<td><em>trans</em>-1,8-terpin</td>
<td><img src="image8.png" alt="Structure" /></td>
<td></td>
<td></td>
<td></td>
</tr>
</tbody>
</table>
Figure B-4. MS comparison of β-pinene (bottom) vs. the peak tentatively identified as the reaction product of acetone with β-pinene.
APPENDIX C

Background Discussion of Solvent Effects on Acid-Base Behavior

Considerable work has been done to study the effect of solvent on the ionization constants of acids and bases.\(^1\) We are interested in the effect of organic co-solvents on the pK\(_a\) of acid catalysts in aqueous mixtures. Although the solute-solvent interactions in these systems can be quite complex, a simplified interpretation breaks the influence of organic solvents into two effects: 1) electrostatic and 2) medium (or solute-solvent effects).

The electrostatic effects can be described by the Born approach which is derived from the following equation for free energy of transfer (\(\Delta G\)) of a solute from water (\(w\)) to a solvent\((s)\):\(^2\,^3\,^4\)

\[
\Delta G_{w\rightarrow s}^{\text{el}} = \frac{N\varepsilon^2 e^2}{2r} \left( \frac{1}{\varepsilon_s} - \frac{1}{\varepsilon_w} \right)
\]

where \(r\) = radius of the solute
\(\varepsilon\) = charge number of the solute
\(N\) = Avogadro’s number
\(\varepsilon\) = dielectric constant for water (\(w\)) \((78.3 \text{ @ } 25^\circ\text{C})\) and solvent \((s)\)

Using the case of a monovalent acid, you can assume that \(r^+ = r^-\) and \(\varepsilon = 1\). The equation is then reduced to

\[
\Delta G_{w\rightarrow s}^{\text{el}} = \frac{694}{\varepsilon} \left( \frac{1}{\varepsilon_s} - 0.0128 \right).
\]

100
Since $\Delta G^0 = -RT \ln K_c$, where $R$ is the gas constant and $T$=temperature, the shift in $pK_a$ for a particular solvent can then be described by $\Delta pK_a = \frac{A}{e^c} + B$, where $A$ and $B$ are constants. This indicates that $pK_a$ values are linearly and inversely dependent on the dielectric constant of the solvent. Therefore, as the dielectric constant decreases, $pK_a$ is increased. This increase can be dramatic. For example, the $pK_a$ of benzoic acid increases from 4.21 in water to 15.1 in $t$-butyl alcohol and 20.7 in acetonitrile. One explanation for this result is that as the dielectric constant of a solution decreases, there is less "charge shielding" and subsequent increased tendency for ion pairs to form. Thus, fewer free ions are available in a mixed solvent vs. water. The linear relationship between $pK_a$ and $1/e$ has been shown to hold true for water/alcohol mixtures up to ~80 % alcohol content (see Figure C-1), however, it is not necessarily a general phenomenon for all solvents. Figure C-2 shows the wide variation in effect of dielectric constant on $pK_a$ when different solvents are evaluated. In fact, Reichardt explains that this approach can only be used

![Figure C-1](image)

**Figure C-1. Relationship of acidity and ethanol concentration for benzoic acid in mixed aqueous solvent.**
for comparing solvents of equal acid and base strength since only the electrostatic effect is considered.\(^1\)

The Born approach considers the electrostatic effects only. The process is clearly more complicated. Therefore, the medium effect strives to incorporate the effect of individual solute-solvent interactions and varying solvent parameters. The solubility of the individual solutes generated in an acid-base equilibrium \((HA \leftrightarrow H^+ + A^-)\) is determined by many factors such as dipole interaction, hydrogen bonding and electron acceptor interactions. One theoretical measure of solvation is the Gibbs energy of transfer \((\Delta G^{\ddagger})\) which represents the energy required to transfer an ion from water\((w)\) to another solvent\(s)\).\(^1\)

\[
\Delta G^{\ddagger} = -RT \ln(\gamma_a / \gamma_w)
\]

Energy expressions using concentration are solvent dependent. The use of activity coefficients are necessary to obtain solvent independent relationships. Activity coefficients can be determined from vapor pressure, solubility, potentiometric and
distribution coefficients measurements. Sarmini et al refer to $\gamma_i$ as the "medium effect." It is also known as the transfer activity coefficient. The medium effect is $>0$ when the species is more stable in water and $<0$ when the species is more stable in solvent. For an acid/base equilibrium, the medium effect is applied to all the species involved in order to determine the shift in $pK_a$. Therefore,

$$\gamma_i = \frac{Y_i}{Y}$$

$$\Delta G^0 = -RT \ln \left( \frac{\gamma_{H^+} \cdot \gamma_{H^+}}{\gamma_{H^+} \cdot \gamma_{H^+}} \right)$$

$$\Delta pK_{a,HL} = pK_{a,HL} - pK_{a,HL} = \log \left[ \frac{\gamma_{H^+} \cdot \gamma_{H^+}}{\gamma_{H^+} \cdot \gamma_{H^+}} \right]$$

The $pK_a$ shift is determined by a solvent’s ability to solvate $[H^+]$ and anions. This is related to other solvent parameters such as H-bonding ability, dipole interactions and more. For neutral acids in aqueous alcohol systems, the predominant influence on $pK_a$ will be the dielectric constant because ionization involves the formation of ionic species. As the dielectric constant decreases the equilibrium is shifted more to the left towards the un-dissociated acid, resulting in lower acid strength. However, it is important to consider solute-solvent interactions as well especially with other solvents.

The ionization constants for many acidic organic compounds in aqueous solutions are available in the literature; however, less information is available for $pK_a$’s in non-aqueous solutions.
Literature Cited


APPENDIX D.
Graphs for β-pinene in superheated water

Figure D-1. 100 % water, 200 °C: pinene and mass balance
Figure D-2. 100 % water, 200 °C: terpinolene and hydrocarbons
Figure D-3. 100 % water, 200 °C: bicyclic alcohols
Figure D-4. 75 % water/ 25 % EtOH (volume), 200 °C: pinene and mass balance
Figure D-5. 75 % water/ 25 % EtOH (volume), 200 °C: terpinolene and hydrocarbons
Figure D-6. 75 % water/ 25 % EtOH (volume), 200 °C: bicyclic alcohols and ether
Figure D-7. 50 % water/ 50 % EtOH (volume), 200 °C: pinene and mass balance
Figure D-8. 50 % water/ 50 % EtOH (volume), 200 °C: terpinolene and hydrocarbons
Figure D-9. 50 % water/ 50 % EtOH (volume), 200 °C: bicyclic alcohols and ether
Figure D-10. 50 % water/ 50 % acetone (volume), 200 °C: pinene and mass balance
Figure D-11. 50 % water/ 50 % acetone (volume), 200 °C: terpinolene and hydrocarbons
Figure D-12. 50 % water/ 50 % acetone (volume), 200 °C, bicyclic alcohols
Figure D-13. 50 % water/ 50 % THF (volume), 200 °C, pinene and mass balance
Figure D-14. 50 % water/ 50 % THF (volume), 200 °C, terpinolene and hydrocarbons
Figure D-15. 50 % water/ 50 % THF (volume), 200 °C, bicyclic alcohols
Figure D-16. 50 % water/ 50 % IPA (volume), 200 °C, pinene and mass balance
Figure D-17. 50 % water/ 50 % IPA (volume), 200 °C, terpinolene and hydrocarbons
Figure D-18. 50 % water/ 50 % IPA (volume), 200 °C, bicyclic alcohols
$\beta$-Pinene in 100 % water at 200 °C

Figure D-1. 100 % water, 200 °C: $\beta$-pinene and mass balance

$\beta$-pinene in water

Figure D-2. 100 % water, 200 °C: terpineol and hydrocarbons
Figure D-3. 100 % water, 200 °C: bicyclic alcohols
$\beta$-Pine in 75 % water/25 % EtOH at 200 °C

Figure D-4. 75 % water / 25 % EtOH (volume), 200 °C: $\beta$-pinene and mass balance

Figure D-5. 75 % water / 25 % EtOH (volume), 200 °C: terpineol and hydrocarbons
Figure D-6. 75 % water/ 25 % EtOH (volume), 200 °C: bicyclic alcohols and ether.
**β-Pinene in 50% water/ 50% EtOH at 200 °C**

**Figure D-7.** 50 % water/ 50 % EtOH (volume), 200 °C: β- pinene and mass balance

**Figure D-8.** 50 % water/ 50 % EtOH (volume), 200 °C: terpineol and hydrocarbons

110
Figure D-9. 50 % water/ 50 % EtOH (volume), 200 °C: bicyclic alcohols and ether
**β-Pinene in 50 % water/50 % acetone at 200 °C**

![Graph showing β-pinene and mass balance over time](image1)

Figure D-10. 50 % water/50 % acetone (volume), 200 °C: β-pinene and mass balance

![Graph showing terpineol and hydrocarbons over time](image2)

Figure D-11. 50 % water/50 % acetone (volume), 200 °C: terpineol and hydrocarbons
Figure D-12. 50 % water/ 50 % acetone (volume), 200 °C, bicyclic alcohols
β-Pinene in 50 % water/ 50 % THF at 200 °C

Figure D-13. 50 % water/ 50 % THF (volume), 200 °C, β-pinene and mass balance

Figure D-14. 50 % water/ 50 % THF (volume), 200 °C, terpineol and hydrocarbons
Figure D-15. 50 % water/ 50 % THF (volume), 200 °C, bicyclic alcohols
\( \beta \)-Pinene in 50 % water/ 50 % isopropyl alcohol (IPA) at 200 °C

![Graph](image1.png)

Figure D-16. 50 % water/ 50 % IPA (volume), 200 °C, \( \beta \)-pinene and mass balance

![Graph](image2.png)

Figure D-17. 50 % water/ 50 % IPA (volume), 200 °C, terpineol and hydrocarbons

116
Figure D-18. 50 % water/50 % IPA (volume), 200 °C, bicyclic alcohols
Theresa S. Chamblee was born in Nantucket, Massachusetts, the first of three daughters of Albert and Connie Sullivan. She grew up and received early education in West Springfield, Mass., Charlotte, N.C. and Roswell, Ga. She graduated as valedictorian of her Crestwood High School class (Roswell, Ga). Theresa started her college career at Vanderbilt University Engineering School in Nashville, Tenn. During her freshman year she realized that chemistry and not engineering was her true calling and she transferred to Emory University in Atlanta Georgia where she received a BS/MS degree in analytical chemistry. Her masters thesis entitled “Acetylcholine Ion-Selective Micro-electrodes” was written under the direction of Dr. Joseph Justice at Emory.

Theresa began her career as a chemist at The Coca-Cola Company immediately after graduation from Emory. Theresa is currently beginning her 23rd year as a research chemist at Coca-Cola. Her current title is Principal Scientist and her areas of expertise are: flavor and beverage chemistry research including the analytical techniques used to characterize flavors/essential oils and understand their reactions in aqueous acid systems, chromatography (GC and HPLC), GC/MS, structure elucidation, computer data analysis, and beverage technology. In recent years she has also been involved in flavor/process development and cost optimization projects. With the encouragement and support of her mentor and supervisor at the time, Dr. Benjamin C. Clark, Jr., Theresa began taking graduate organic chemistry classes at Georgia Tech in the early 1990’s, “during her spare time.” This activity gradually developed into an official part-time enrollment in the graduate school at Georgia Tech and eventually lead to membership in the Liotta-Eckert...
joint research group. Dr. Charles L. Liotta is Regents' Professor in the School of
Chemistry and Biochemistry and Vice-Provost for Research and Dean of Graduate
Studies. Dr. Charles A. Eckert holds the J. Erskine Love, Jr. Institute Chair in
Engineering in the School of Chemical and Biochemical Engineering and is Director of
the Specialty Separations Center. Theresa is scheduled to complete her Ph.D. degree in
Organic Chemistry in April 2004. Theresa has one publication currently in press which
discusses the work she has done at Georgia Tech. She has numerous other publications
and presentations from her career at Coca-Cola (see attached list). Theresa has also been
active in local and national professional organizations over the years. She regularly
reviews articles for the Journal of Agriculture and Food Chemistry and The Journal of
Essential Oil Research.

Theresa is married to John C. Chamblee and has one daughter, Caroline, who will
be 3 three years old in August 2004.

Professional Affiliations

American Chemical Society (Agricultural and Food Chemistry Division), 1981-
present
Georg Section ACS - Treasurer, 1990-1991; Chair-Elect/Program Chairman,
1992; Chairman, 1993; Chemistry Olympiad Coordinator, 1993-1997; Operation
Journal of Essential Oil Research Editorial Board, 1997- present
Atlanta/Athens Mass Specrometry Discussion Group, 1992-1998
Kennesaw College, Science Department Advisory Board, 1994-present
Sigma Xi, Scientific Research Society, 1982-present
Toastmasters International (Coca-Cola chapter), 1987-present; served as
President, Vice President of Education, Vice President of Membership/Public
Relations and Treasurer

119


T. S. Chamblee, "Flavor Protection in Beverage by FD&C Colors," Seminar, Corporate Research and Development Department, 2/8/84.


T. S. Chamblee, "Recent Advances in Flavor Chemistry at The Coca-Cola Company," Emory Student Affiliate Chapter of the ACS, Emory University, 2/18/88.


T. S. Chamblee, “Chemistry of Lemon and Lime Essential Oils,” Seminar, Corporate Research and Development Department, 6/7/90.


T. S. Chamblee, “Chemistry and Organoleptic Analysis of Lemon Flavor,” Seminar, Corporate Research and Development Department, 3/31/93.


