

## SYNTHESIS OF CAMPHOR USING IONIC LIQUIDS

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## Abstract

This investigation involved the synthesis of two ionic liquids, both used the 1-hexyl-3-methylimidazolium cation ([hmim]<sup>+</sup>) coupled to either trifluoroacetate ([CF<sub>3</sub>COO]<sup>-</sup>) or hexa fluorophosphate ([PF<sub>6</sub>]<sup>-</sup>) anions. These ionic liquids can be substituted for traditional organic solvents and used for the oxidation of isoborneol to produce camphor. Ionic liquids can stabilize charged intermediates better than traditional solvents and the product yields are typically much higher. As an example, the reported reaction gives a 17-26% increase in product yield when an ionic liquid was used as the reaction solvent.

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## Introduction

Volatile organic solvents are widely used in industry and commercial manufacturing.<sup>1</sup> These typically end up contaminating the air, land, and water because they are difficult to contain, recycle, or reclaim.<sup>1</sup> Researchers have been focusing on how to develop processes to reduce solvent use and establish more efficient methods.<sup>2</sup> One of these environmentally friendly alternatives is the use of ionic liquids, which has been garnering more attention due to the low vapor pressure and ability to replace volatile organic solvents.<sup>3</sup> Ionic liquids are being used as solvents in a wide range of reactions including cationic polymerizations,<sup>4-6</sup> Friedel-Crafts aromatic substitutions,<sup>7-10</sup> electrophilic aromatic nitration,<sup>11, 12</sup> benzoin condensation,<sup>13</sup> esterifications,<sup>14</sup> diazo coupling,<sup>15</sup> chiral ionic liquid synthesis,<sup>16, 17</sup> and, for this study, oxidation.<sup>18</sup> Ionic liquids are ideal for these types of reactions, as they stabilize intermediates such as carbocations, carbanions, or other charged species, allowing more product formation, while also lowering the activation energy of these reactions.<sup>19-22</sup>

In this study, the oxidation reaction of a secondary alcohol, isoborneol (*exo*-1, 7, 7-trimethylbicyclo [2.2.1] heptan-2-ol), to produce a ketone, camphor (1, 7, 7-trimethylbicyclo [2.2.1] heptan-2-one), was the focus.<sup>23, 24</sup> The goal in this work was to find an alternative oxidation method for this reaction. The top scheme in Figure 1 shows the camphor reaction<sup>26</sup> that could benefit from the use of ionic liquids to potentially increase yields, while replacing undesirable solvents or reactants.

One oxidation method currently used to produce camphor is the Jones' reagent (chromium trioxide and concentrated sulfuric acid, both dissolved in acetone).<sup>23, 24</sup> This method produces higher yields (65-75%), however, the use of chromium trioxide is not ideal since the hexavalent chromium systems has serious health and environmental effects.<sup>27</sup> The hexavalent chromium system is suspected of being a carcinogen displaying negative effects on the nasal passages, intestines, kidneys, and liver.<sup>27</sup> In an effort to replace the hazardous chromium oxidizer, a different method was introduced. This method, represented by the top scheme in Figure 1, used aqueous sodium hypochlorite dissolved in glacial acetic acid,<sup>26</sup> produced lower

yields (45-55%).

Camphor is an important product in the chemical industry due to its many uses.<sup>28</sup> Some of these uses include: plasticizer for cellulose nitrate, moth and insect repellent, antimicrobials, fireworks, anti-itch gels, organocatalytic, and nasal decongestants.<sup>25, 28, 29</sup> Therefore, it is imperative to find a method that produces higher yields in a safer way. The use of an ionic liquid replacement solvent (1-hexyl-3-methylimidazolium cation [hmim]<sup>+</sup> coupled to either trifluoroacetate ([CF<sub>3</sub>COO]<sup>-</sup>) or hexafluorophosphate ([PF<sub>6</sub>]<sup>-</sup>) anion, combined with a more environmentally friendly oxidizing agent (sodium hypochlorite), could potentially lead to a safer synthetic method. The work in our study would suggest this to be true. The bottom scheme in Figure 1 shows the use of ionic liquids produces comparable yields (70-79%) to the Jones' method.

## Method

## Preparation of the ionic liquid:

The 1-hexyl-3-methylimidazolium cation was prepared by combining equimolar quantities of 1-methylimidazole (60 mL) and 1-chlorohexane (104 mL).<sup>15</sup> Reagents were heated to 70°C, stirred and allowed to react for 48 hours. The resulting liquid was then cooled and washed with three 50 mL portions of ethyl acetate to remove unreacted starting material.<sup>15</sup> Re-

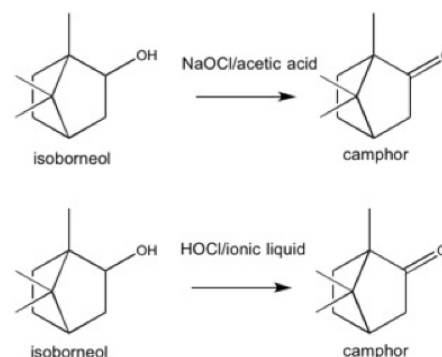


Figure 1: Synthesis of Camphor Reaction Scheme.

Top Literature Scheme<sup>26</sup>. Reaction Conditions. NaOCl/Acetic Acid (Camphor yield 45-55%)

Bottom Ionic Liquid Scheme. Reaction Conditions NaOCl/Ionic Liquid (Camphor yield 70-79%)

sidual ethyl acetate was removed by rotary evaporation.<sup>15</sup> The 1-hexyl-3-methylimidazolium chloride was combined with 125 mL of water then slowly reacted with 27.0 mL of trifluoroacetic acid or 50 mL of hexafluorophosphoric acid, while keeping the temperature below 30°C. After the addition was complete, each solution was stirred for 12 hours to allow the anion substitution to take place as represented by the formation of two layers. The lower ionic liquid (IL) layer was extracted using three 50 mL portions of methylene chloride. These methylene chloride extracts were washed with a series of three 50 mL portions of aqueous saturated sodium carbonate solutions to remove excess trifluoroacetic or hexafluorophosphoric acid. After rotary evaporation of the methylene chloride, the result was the desired product: 1-hexyl-3-methylimidazolium trifluoroacetate ([hmim]<sup>+</sup> [CF<sub>3</sub>COO]<sup>-</sup>) or 1-hexyl-3-methylimidazolium hexafluorophosphate ([hmim]<sup>+</sup> [PF<sub>6</sub>]<sup>-</sup>). The ionic liquid products were analyzed using a Perkin-Elmer Spectrum Two FT-IR to verify the existence of the acetate carbonyl (1600-1550 cm<sup>-1</sup>) and the acetate oxygen (1250-1230 cm<sup>-1</sup>) for the trifluoroacetate and the P-F bonds (850-980 cm<sup>-1</sup>) for the hexafluorophosphate.<sup>30</sup>

#### Synthesis of Camphor from Isoborneol:

Isoborneol (0.5 grams) was dissolved in 5.0 mL of the solvent (either glacial acetic acid or one of the ionic liquids). While on ice, 5.0 mL of 12.5% sodium hypochlorite was added dropwise with agitation, keeping the temperature between 25 and 30°C. After the addition of the sodium hypochlorite, the solution was stirred for twenty minutes then tested with potassium iodide starch paper to confirm the presence of excess chloride ion. When acetic acid was used as the solvent, deionized water (25 mL) was added to the flask to precipitate the impure camphor. After vacuum filtration, the impure camphor was purified by sublimation.<sup>23</sup> The camphor was extracted from the ionic liquids using three 50 mL portions of diethyl ether. The ether was evaporated from the extracts and the solid camphor was also purified by sublimation. In order to confirm the purity of each camphor product the melting point was determined (175-177°C).<sup>23</sup> Analysis of each camphor product using FT-IR (Perkin-Elmer Spectrum Two) and FT-NMR (Ana-sazi Instruments EFT 60) were compared with literature spectra.<sup>23</sup> After the camphor was extracted, each ionic liquid was washed with 150 mL of ethyl acetate to remove any unreacted reagents. Each ionic liquid was recycled and used in subsequent camphor reactions or for other future reactions.

## Discussion

In the oxidation reaction of isoborneol (secondary alcohol) to produce camphor (ketone), the solvent acid and sodium hypochlorite (NaOCl) react to produce hypochlorous acid (HOCl). The hypochlorous acid chlorinates the hydroxyl group

of the isoborneol (R-OH → R-O-Cl).<sup>31</sup> The elimination of HCl from the R-O-Cl intermediate by dehydrohalogenation facilitates the formation of the camphor carbonyl.<sup>31</sup> Alternatively, the use of ionic liquids provides a less acidic environment when compared to acetic acid, thus resulting in higher product yields. One explanation for this might suggest the hypochlorite ion was stabilized by the ionic liquid which allowed the hypochlorite ion to react by the same mechanism as the hypochlorous acid.

Our goal in this study was to use the less toxic sodium hypochlorite oxidizer and an ionic liquid solvent to establish safer conditions and produce higher yields for this classic reaction. Therefore, the use of two recyclable ionic liquids provided a less hazardous alternative with potentially more effectiveness.

## Conclusion

Overall, replacing acetic acid with each ionic liquid was more effective in the oxidation of camphor from isoborneol. Table 1 shows the comparison of percentage yields for three replicate trials of camphor run concurrently in acetic acid or in either ionic liquid using sodium hypochlorite as the oxidizing agent. The data suggests the acetic acid method produced lower yields (53.3 +/- 2.68%) than either of the ionic liquids (70.4 +/- 1.06% and 79.2 +/- 1.03%), as evidenced by the 17% increase using 1-hexyl-3-methylimidazolium trifluoroacetate and 26% increase using 1-hexyl-3-methylimidazolium hexafluorophosphate. Therefore, using either ionic liquid as the solvent and sodium hypochlorite as the oxidizing agent, proves that higher product yields can be obtained without resorting to the toxic chromic acid reagent.

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**Table 1.** Acetic Acid vs. Ionic Liquid. Product yield comparison using hypochlorite as the oxidizing agent.

Acetic Acid 1	54.6%	hmim TFA 1	70.5%	hmim PF <sub>6</sub> 1	79.4%
Acetic Acid 2	49.6%	hmim TFA 2	71.7%	hmim PF <sub>6</sub> 2	77.9%
Acetic Acid 3	55.8%	hmim TFA 3	69.1%	hmim PF <sub>6</sub> 3	80.3%
Mean	<b>53.3%</b>	Mean	<b>70.4%</b>	Mean	<b>79.2%</b>
STD	+/-2.68%	STD	+/-1.06%	STD	+/-1.03%

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