

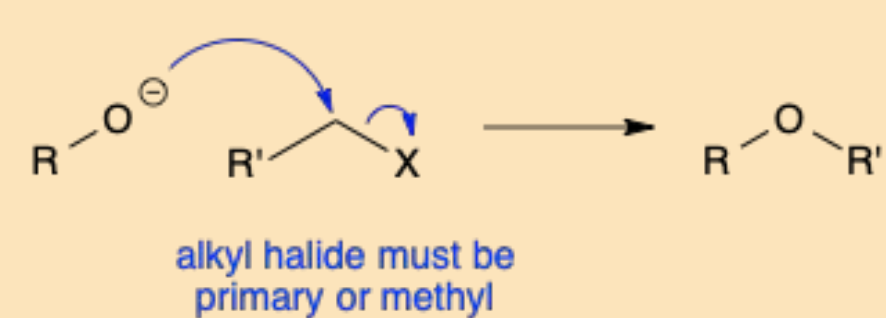
Abstract

Currently, the most useful synthetic tool for ether synthesis is the Williamson Ether Synthesis Method. However, the limitation of this method is that only primary or methyl groups can be used, which limits you to the creation of small Ethers. The Purpose of this project is to develop a new method for synthesizing bulky Ethers and Amines using novel ionic liquid solvents. In alcohol:ionic liquid dual solvent systems, solvolysis of 1-adamantyl mesylate forms a carbocation through a k_c reaction mechanism. The stabilizing effects of the ionic liquid solvent allows the carbocation to be primed for nucleophilic attack. The subsequent carbocation is trapped by the alcohol cosolvent, thus forming an Ether. The advantage of this method is that the solvent is not a competing factor for nucleophilic attack because Ionic Liquids are completely non-reactive as solvents. This means that a single product is guaranteed. Since proof of concept, the purpose has been to optimize reaction conditions and product yield so that this method can be seen as a useful tool for synthesizing naturally occurring and complex versions of these molecules. Various steps toward optimization have been made including: reaction temperature, reaction time, concentration of starting materials, and purification methods. Multiple ethers have been successfully synthesized using this technique.

Background

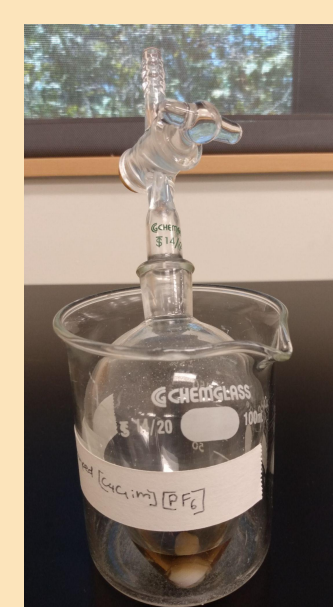
❖ Williamson Ether Synthesis

The Williamson Ether Synthesis is extensively used for ether formation. In this reaction an organohalide reacts with a deprotonated alcohol via an S_N2 reaction mechanism. Since this is an S_N2 mechanism, bulky reactants hinder the backside attack, rendering the reaction ineffective and causing elimination to be favored instead. This is the setback of this reaction: the halide must be attached to a primary or methyl group in order for it to work. Therefore it is impossible to synthesize big bulky ethers that are found in nature or the human body for medicinal purposes.



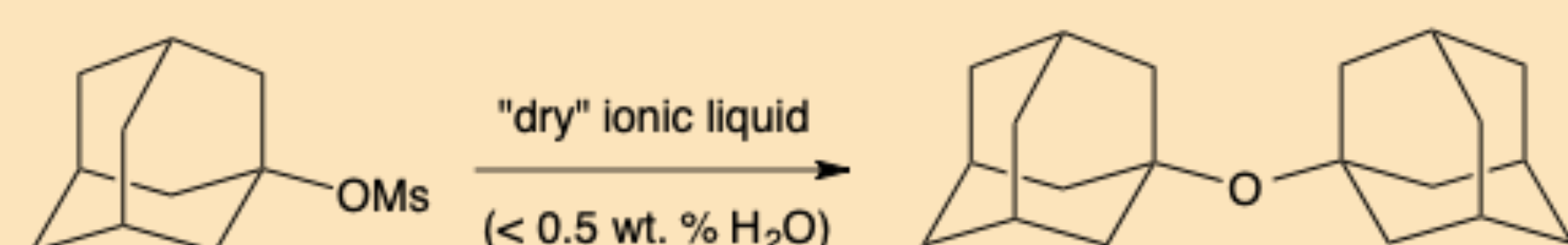
❖ Ionic Liquids: What are they?

Ionic Liquids (ILs) are poorly coordinated salts that are liquid at room temperature. They are hindered, delocalized blobs with a negative and positive component that will not interact with anything but each other. These characteristics make them ideal solvents in synthesis, because they provide a stable environment in which to carry out reactions involving unstable intermediates.



❖ Previous Work (Ether Synthesis Surprise)

A study conducted in 2005 demonstrated the viability of carbocation formation in ionic liquid solvents. In this study, it was discovered that the resulting carbocations react with trace amounts of water in the IL to form alcohol solvents. Furthermore, if the ionic liquid solvent is carefully dried (i.e. contains minimal amounts of water), the carbocation can be trapped by already-formed alcohol product, creating an ether.

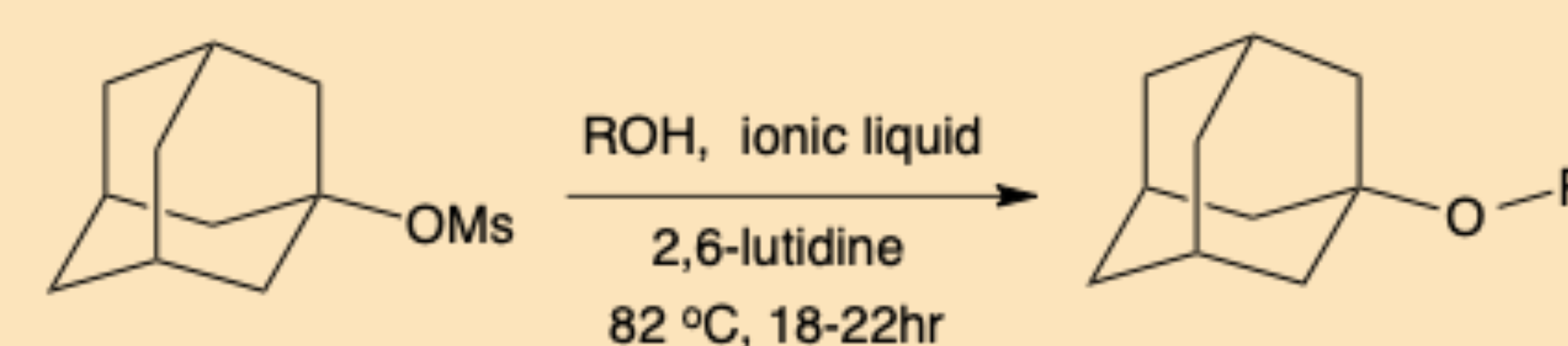


Goal

To use solvolysis in the development of a new synthetic method to synthesize bulky ethers and amines using Ionic liquids as the solvent, to figure out which ILs are the best fit for these reactions, and to test the hypothesis that the bulkier the product the less yield you will get.

Methods

1-Adamantyl mesylate was prepared from 1-Adamantanol, and solvolyzed in a series of ionic liquid:alcohol and ionic liquid:amine dual solvent systems. The Adamantyl Mesylate underwent a k_c solvolysis to form a carbocation. The cosolvent (alcohol or amine) reacted with the carbocation, acting as a trapping agent. 2,6-lutidine was added to the reaction solution to absorb the methanesulfonic acid that is produced as a byproduct during the solvolysis.



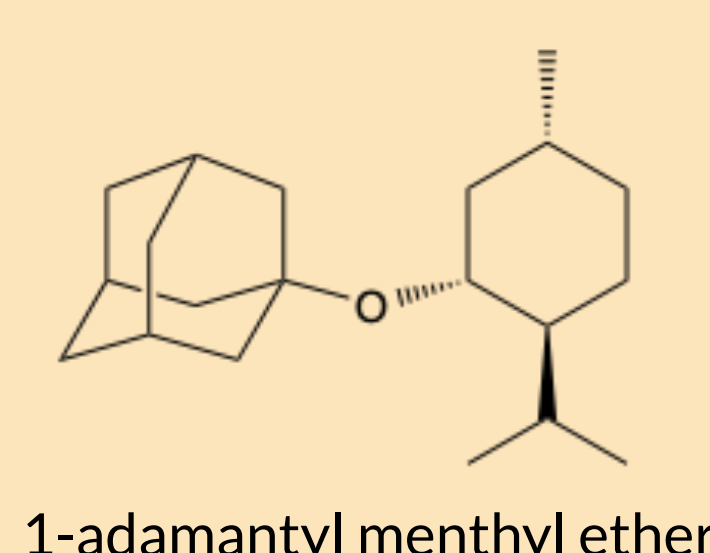
Previous work had shown that optimal reaction temperatures are 82°, and optimal reaction times are 18-22 hours depending on the trapping agent. In addition, it was determined that using 10 equivalents of alcohol or amine afforded the optimum yield. For this project, we used the ionic liquids $[C_4C_1im][NTf_2]$ and $[C_4C_1im][PF_6]$. Cosolvents included Menthol, Adamantanol L-borneol, and Diphenylamine.



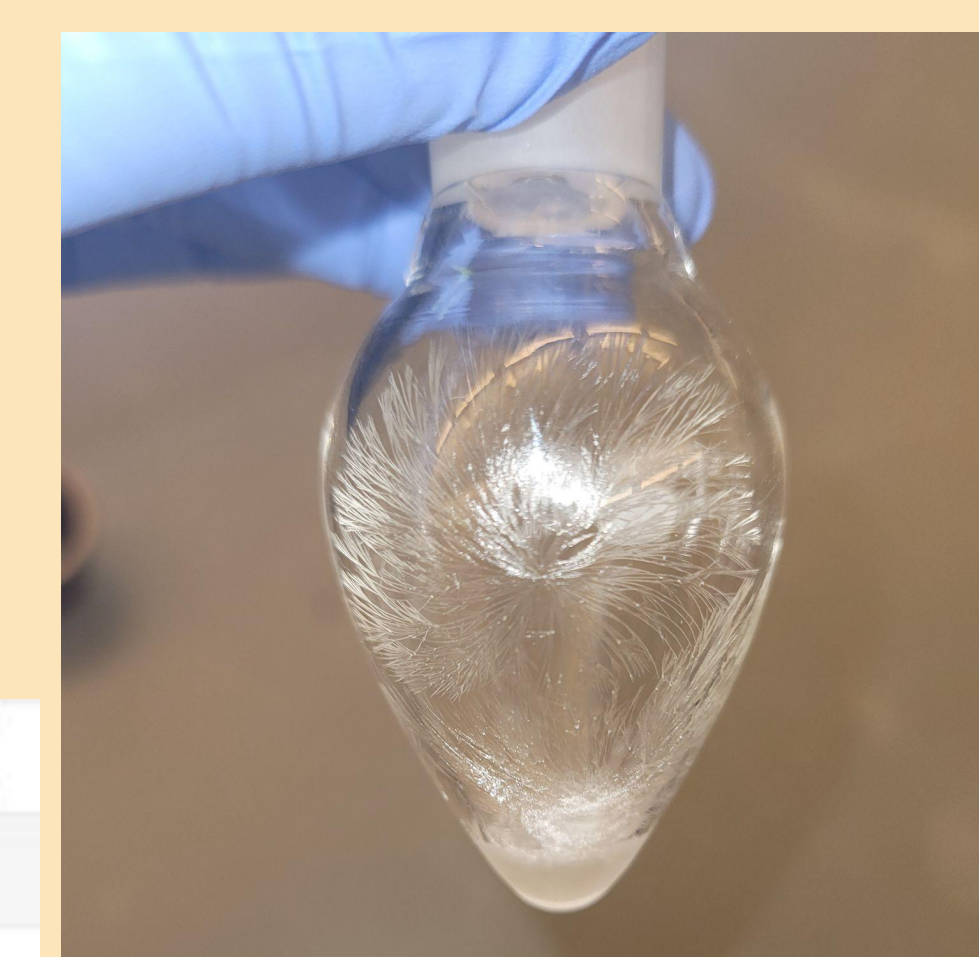
Crude products were extracted into hexanes and purified via column chromatography.

Results

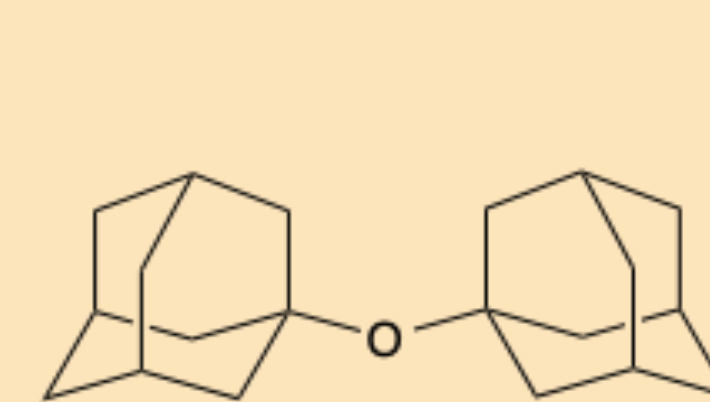
Yields were determined for the synthesis of 1-adamantyl menthyl ether in both $[C_4C_1im][NTf_2]$ and $[C_4C_1im][PF_6]$ with added menthol. The crude products were purified using column chromatography and the final product was weighed to determine yield. In comparing the yields of ether product between these two ILs, preliminary results have shown that $[C_4C_1im][NTf_2]$ has more potential as a solvent for this ether synthesis.



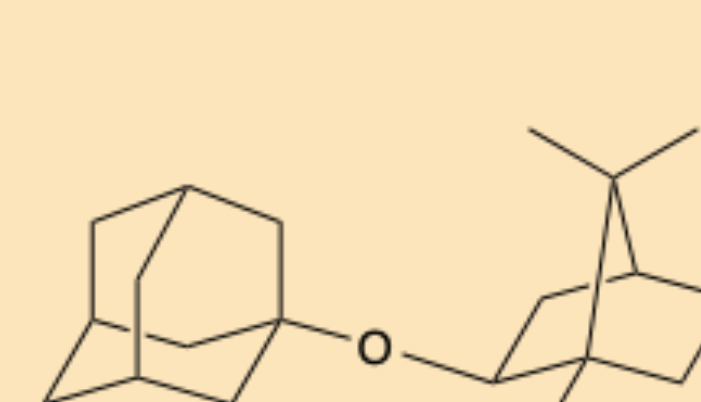
Ionic Liquid	[C4C1im][NTf2]	Ionic Liquid	[C4C1im][PF6]
Crude Yield	0.131g	Crude Yield	0.153g
Purified Yield	0.022g (36.7%)	Purified Yield	0.005g (8.3%)



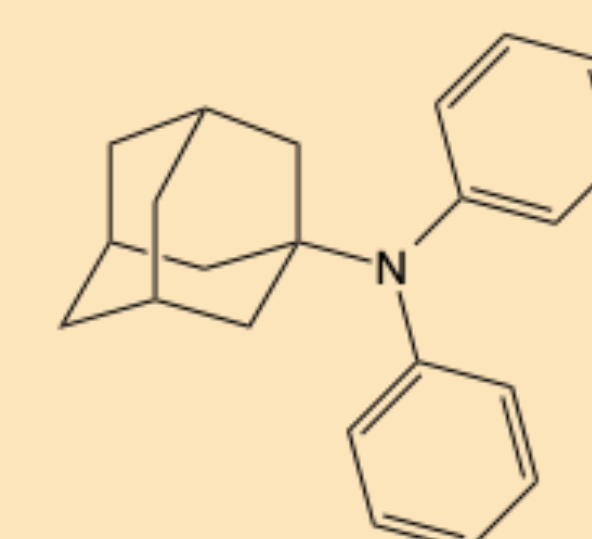
Other products that were also synthesized in the $[C_4C_1im][PF_6]$ solvent include di-1-adamantyl ether, adamantyl borneol ether, and adamantyl diphenyl amine.



di-1-adamantyl ether



1-adamantyl borneol ether



1-adamantyl diphenyl amine

Conclusions

While results are still preliminary for the ionic liquid that will produce the greatest yield margins, this project has demonstrated proof of concept for this novel ether synthesis. This method has been proven highly effective in ability and versatility of producing bulky ethers and amines.

Future studies will focus on comparison between these and additional ionic liquids to determine the optimal ionic liquid solvent for these reactions. We also intend to expand the breadth of trapping agents that can be used for this reaction.

References

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