SYNTHESIS AND APPLICATIONS

OF

ROOM TEMPERATURE IONIC LIQUIDS

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ABSTRACT

SYNTHESIS AND APPLICATIONS OF ROOM TEMPERATURE IONIC LIQUIDS

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A variety of room temperature ionic liquids have been synthesized and applied to various reactions. Four of these ionic liquids were prepared in a chiral manner: [1-butyl-3-methylimidazolium][L-lactate], [1-butyl-3-methylimidazolium][D-lactate], [1-butyl-3-methylimidazolium][(1S)(+)-10-camphorsulfonate], and [1-butyl-3-methylimidazolium][(1R)(-)-10-camphorsulfonate]. These chiral ionic liquids were used as solvents in asymmetric spiroacetal cyclizations and Truce-Smiles rearrangements to induce chirality to the reactions.

Additionally, four other ionic liquids were synthesized for use in electrochemical experiments: [1-butyl-3-methylimidazolium][BF_4], [1-butyl-3-methylimidazolium][PF_6], [1-butyl-3-methylimidazolium][SCN] and [1-butyl-3-methylimidazolium][Tau]. These ionic liquids were used as an additive during electrochemical nickel deposition and dissolution to improve the effect of the Watts solution.

ACKNOWLEDGEMENTS

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LIST OF ABBREVIATIONS

[α]	optical rotation / specific rotation
[bmim]	1-butyl-3-methylimidazole
[bmim][(1R)(-)CSA]	1-butyl-3-methylimidazolium (1R)-camphor-10-sulfonate
[bmim][(1S)(+)CSA]	1-butyl-3-methylimidazolium (1S)-camphor-10-sulfonate
[C_4py]	*N*-butylpyridinium
[$C_n$mim]	3-methylimidazole with a varying chain in the 1-position
$CDCl_3$	deuterated chloroform
CIL	chiral ionic liquid
DMSO	dimethylsulfoxide
EDS	electron diffraction spectroscopy
ee	enantiomeric excess
er	enantiomeric ratio
FID	flame ionization detector
FTIR	Fourier transform infrared
GC	gas chromatography
GCMS	gas chromatography mass spectrometry
GLC	gas-liquid chromatography

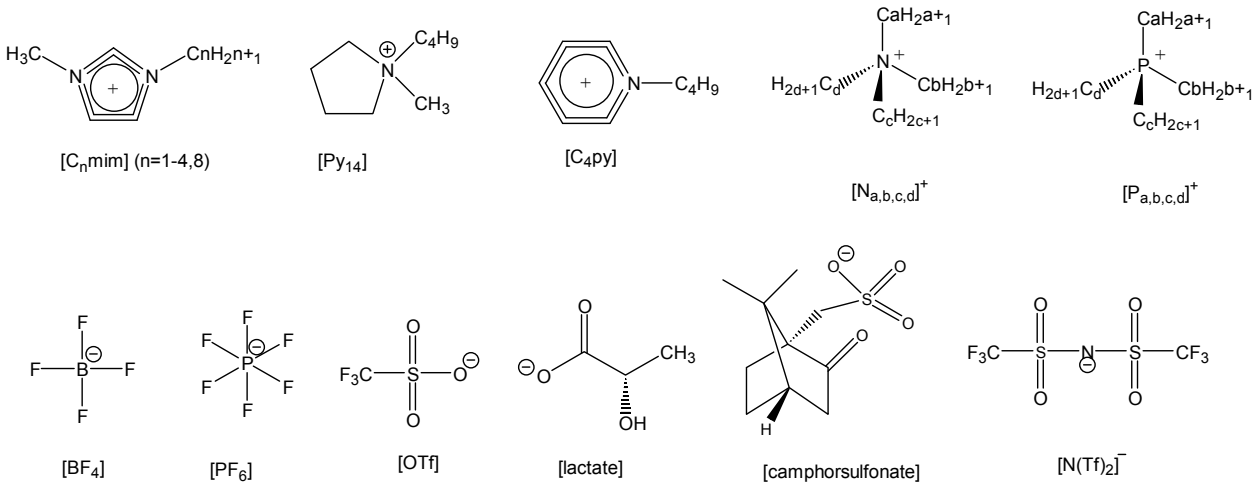
HPLC	high performance liquid chromatography
IL	ionic liquid
IR	infrared
MOPAC	molecular orbital package
MS	mass spectrum
NMR	nuclear magnetic resonance
[NTf]	trifylazide
[OTf]	triflate
[Py_{14}]	*N*-butyl-*N*-methylpyrrolidinium
Rac	racemic
RTIL	room temperature ionic liquid
SEM	scanning electron microscopy
[Tau]	taurinate
THF	tetrahydrofuran
TLC	thin layer chromatography
TMS	tetramethylsilane
UV	ultraviolet
XRD	X-ray diffraction

Chapter One: A Synthetic and Applied Review of Room Temperature Ionic Liquids

1.1 Introduction

Room temperature ionic liquids (RTIL) exist in the liquid state around 298K and are composed entirely of ions. They are typically comprised of a bulky organic cation (eg. imidazolium, pyrrolidinium, or pyridinium), as well as a weakly coordinating anion (eg. tetrafluoroborate, hexafluorophosphate, triflate). [1] According to Comptom and Silvester, RTILs can be loosely grouped into three main classes. The first generation are based upon aluminum halide anions such as $[AlCl_4]^-$, but are highly sensitive to moisture, making them difficult to handle, requiring them to be stored and manipulated in a glove box under inert atmospheric conditions.[1,2] The second generation of RTILs include anions such as $[BF_4]^-$ and $[PF_6]^-$ which are less reactive towards water, however they still adsorb moisture which alters their physical and chemical properties. [1,3] The third generation is comprised of "task-specific" RTILs which contain functional groups designed specifically to influence certain chemical reactions of interest.[1,4] The classification system is still very new and continues to undergo improvements. A large number of room temperature ionic liquids do not currently fall into these three categories. [1]

Figure 1. Common cations and anions in RTIL[1]



Room temperature ionic liquids have been gaining increased attention over the years due to their unique properties and applications in “green” chemistry. Due to their low volatility and high thermal stability, RTILs have become desired solvents in industry and academia. The insignificant vapour pressure greatly reduces the risk of accidental exposure compared to traditional organic solvents; furthermore, they have no damaging atmospheric photochemistry.[5]

In addition to the environmental benefits arising from the physical properties of RTILs, the ability to vary the cation and anion composition allows for extensive tuneability for tailor-made solvents to accommodate a wide variety of reactions.[5] For example, the melting point of a quaternary ammonium based ionic liquid can be lowered by introducing asymmetry on the cation through one or two moderately long chains (eg. octyl) with two or three shorter chains (eg. butyl). Additionally, branching on the longer chains, with two or more bonds separating the branch points, will also reduce the melting point. [5,6] The hydrophobicity can also be custom tailored to suit a variety of reaction conditions by altering the chain length on the cation or the identity of the anion. For instance, it has been found that $[C_n mim][PF_6]$ where n = 4, 6, or 8 forms two layers with water; however, $[C_n mim]Cl$ where n = 4, 6, or 8 does not. Additionally, miscibility of the $[C_n mim][PF_6]$ ionic liquids with water decreased as the alkyl chain length increased.[5,7] This is also evident in the case of $[C_n mim][BF_4]$ where n =2-5 is fully miscible with water and where n = 6-10 forms two layers.[5,8]

Furthermore, when utilized as a solvent in electrochemical experiments, RTILs possess wider potential windows compared to traditional solvents which often have windows of 1-3 V. Although impurities can narrow the potential window, it is typical for pure RTILs to have a potential window of 4.5-6V.The anodic and cathodic limits observed in ionic liquids are due to the oxidation and reduction of their anionic and cationic components, respectively. [9] As a result of the wider cathodic window, electrodeposition of various metals can be achieved at potentials that are not accessible in aqueous solvents.[1] Additionally, the increased viscosity of RTILs (1-2

orders of magnitude) compared to traditional solvents slows diffusion of the electroactive species. The viscosity can be greatly varied with anion identity and increasing the temperature can lower the viscosity as much as 20% over 5K. Because ionic liquids are made up purely of ions, they have an abundance of charge carriers, thus being naturally conductive. Together, the high viscosity and high conductivity offset each other, bringing the overall conductivity levels to values comparable to traditional organic solvent electrolyte solutions; however, the used of RTILs simplifies the setup and the overall waste is reduced.[1]

Table 1. Viscosity and Conductivity of common solvents and RTILs[1]

Solvent	Viscosity* / mPa s	Conductivity/ $m\Omega^{-1}$ cm^{-1}
N,N-dimethylformamide	0.80	4.0[+]
Acetonitrile	0.34	7.6[+]
Ethanol	1.07	0.6[+]
Dimethylsulfoxide	1.99	2.7[+]
$[C_2mim][N(Tf)_2]$	28	8.4
$[C_4mim][N(Tf)_2]$	44	3.9
$[C_8mim][N(Tf)_2]$	74	
$[C_{10}mim][N(Tf)_2]$	128	
$[C_2mim][BF_4]$	43	13
$[C_4mim][PF_6]$	275	5.2
$[P_{6,6,6,14}][N(Tf)_2]$	401	
$[N_{6,2,2,2}][N(Tf)_2]$	167	

* $T = 25$ °C, [+] solvent containing 0.1 M TBAP

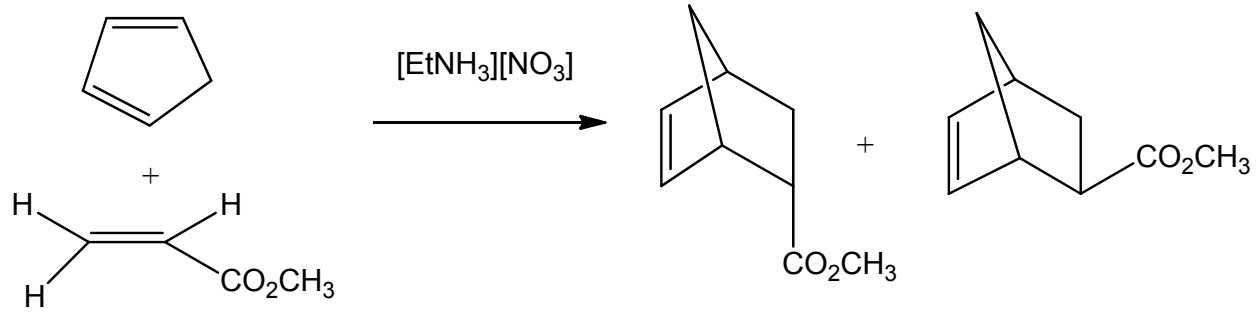
RTILs have also been used as a supporting electrolyte. Compton *et al.* discovered that by using a tris(perfluoroalkyl)trifluorophosphatebased ionic liquid in addition to acetonitrile, the anodic component of the electrochemical window was significantly widened, allowing for the study of oxidation waves of compounds that would have otherwise been reduced due to decomposition of background electrolytes.[1,9]

1.2 Synthetic Applications of RTILs

One of the first synthetic reactions to be explored in ionic liquids was the Diels-Alder reaction.[2] The ionic liquid ethylammonium nitrate was used as a substitute for water in the reaction of cyclopentadiene with methyl acrylate and methyl vinyl ketone(Scheme 1).[10] The reaction was shown to prefer the endo-product and have increased reaction rates compared to reactions done in nonpolar solvents. Although the increased rate and selectivity was not as great as when performed in water, this opened the doors to using moisture sensitive reagents in the future.[2]

The influence of hydrogen bonding on the selectivity and the rate of reaction in ionic liquids is very significant. In fact, further research conducted by Aggarwal *et al*. went on to show

Scheme 1. IL Diels-Alder Reaction[10]



that hydrogen bonding from the cation of the ionic liquid to the dienophile increased the endo selectivity of the reaction, while more hydrogen bond accepting anions decreased the endo selectivity of the reaction.[11]

Additionally, ionic liquids have been used in nucleophilic aromatic substitutions. These reactions are important for the formation of many pharmaceuticals and dyes; however, they often lead to a mixture of products that can be difficult to separate. Since ionic liquids have the ability to enhance the nucleophilicity of amines, they have been investigated as potentially useful solvents.[5] The substitution reactions of 2-substituted 5-nitrothiophenes with secondary amines pyrrolidine, piperidine, and morpholine in [bmim][PF_6], and [bmim][BF_4] have been extensively investigated kinetically. This revealed that the reactions were faster in all of the ionic liquids than the same reactions in either methanol or benzene. This result was attributed to a combination of the stabilization of the activated complex by generalized polarity effects coupled with less inhibition of the reactivity of the amine by hydrogen bond donation from the solvent. It was also noted that the ionic liquid with the more basic anion, [bmim][BF_4], gave faster reactions than that with the less basic anion, [bmim][PF_6].[5]

Another reaction to make use of ionic liquids includes 1,4-conjugate additions.[5] 1,4-conjugate additions are reactions in which a nucleophile adds to a Michael acceptor, which is activated by the presence of an electron-withdrawing group. However, they usually require the use of catalysts and unfavourable solvents, such as DMSO, to achieve the reaction. The first reported conjugate addition in an ionic liquid used tetraalkylammonium bromide as the solvent for the reaction of β-oxosulfides of benzothiazole with a variety of Michael acceptors. This allowed the stereoselective synthesis of spirocyclopropanes with a weaker base than usually required (i.e. sodium bicarbonate). [5]

Conjugate additions of a range of amine and thiol nucleophiles to various Michael acceptors in ethylammonium acetate have also been reported.[5] The interaction of the cation with the electron withdrawing group of the Michael acceptor was proposed to explain the enhanced reactivities observed.[5] However, it should also be noted that the ionic liquid increased the rates of the reactions of the thiols and the primary and secondary amines used, but not of the imidazoles, suggesting that activation of the nucleophile is also an important contributor. Thus, the cation effect and the anion effect on these reactions are acting synergistically.[5]

In spite of the fact that ionic liquids favor nucleophilic substitution over base-induced elimination, it is possible to favor elimination by choosing an appropriate substrate. [5] 1,1,1-tribromo-2,2-bis(dimethoxyphenyl)ethanes have a very strong preference for elimination, and therefore, their reactions with a variety of amines in [bmim][BF_4], and [bmim][PF_6], have been investigated. Only secondary cyclic amines were found to promote the reaction. Consequently, the importance of amine geometry, flexibility, and steric hindrance in determining the outcomes of these reactions was emphasized. This, together with additional kinetics data, led the authors to propose a shift in mechanism from E1 in methanol to E2 in the ionic liquids, i.e., from more charge separation during the reaction to less. This suggests that the ionic liquids are not specially ionizing solvents under these conditions. [5]

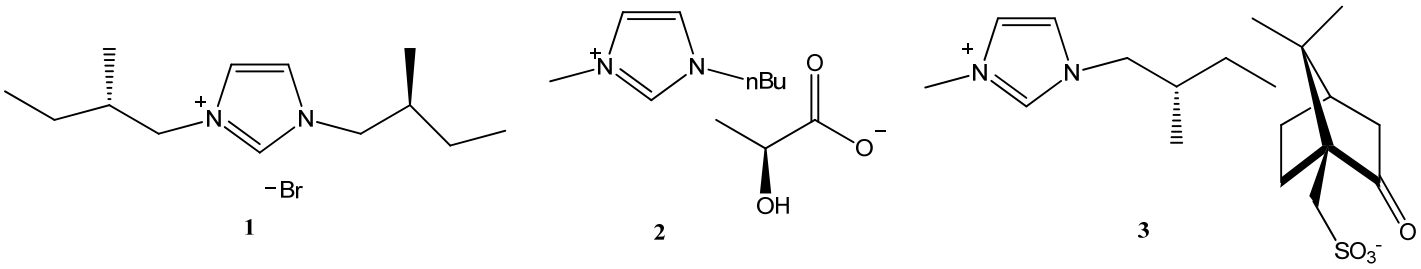
Ionic liquids have also been used in metal catalyzed hydrogenation reactions to introduce a biphasic system. The use of ionic liquids allows the incorporation of water sensitive catalysts and reagents. Additionally, this provides the advantages of homogenous catalysis, higher efficiency, and minimizes the disadvantages of separation difficulties.[12] For example, $RhCl(PPh_3)_3$ and [Rh(cyclooctadiene)$_2$][BF_4]have been used for the hydrogenation of cyclohexene in [bmim][BF_4]. Although $RhCl(PPh_3)_3$ gave higher turnover rates, the use of[Rh(cyclooctadiene)$_2$][BF_4] lead to higher overall conversion of cyclohexene to cyclohexane. It

is also notable that [Rh(cyclooctadiene)$_2$][BF_4] showed greater solubility in the ionic liquid than $RhCl(PPh_3)_3$ which allows for better separation of the product and catalyst when the reaction is complete.[12]

1.3 Chiral Room Temperature Ionic Liquids

One of the first chiral ionic liquids (CILs) ever reported was N,N-bis[(2S)-2-methylbutyl]imidazolium bromide, by Howarth *et al.*, in 1997.[13,14] In this case, the chirality was found on the cation; however, presently many CILs contain a variety of chiral cations, anions, or occasionally both (Figure 2).[13,15]

Figure 2. Chiral Ionic Liquids where the Chirality Location Varies[13]



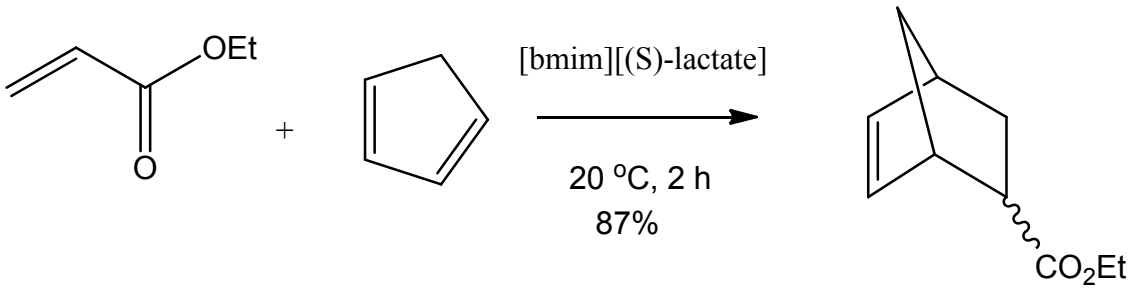
The field of chiral ionic liquids is ever growing and is now considered in a wide variety of applications. Gaertner *et al.* proposed that these applications can be divided into three groups: chiral ionic liquids in asymmetric synthesis, spectroscopic applications of chiral ionic liquids, chromatographic applications of chiral ionic liquids.[13]

1.3.1 Asymmetric Synthesis

1.3.1.1 Chiral Ionic Liquids as Solvents

The chiral ionic liquid 1-butyl-3-methylimidazolium -(S)-lactate was found to be a viable alternative to lithium perchlorate/diethyl ether mixtures for various Diels-Alder reactions. [16] The results of the Diels-Alder reaction with the CIL was compared to other nonchiral ionic liquids: 1-butyl-3-methylimidazolium trifluoromethansulfonate [bmim-OTf], 1-butyl-3-methylimidazolium hexafluorophosphate [bmim-PF_6] and 1-butyl-3-methylimidazolium tetrafluoroborate [bmim-BF_4]. It was discovered that the reaction rate was considerably higher in the CIL and a yield of 87% was obtained after 2 hours. Although no enantioselectivity was observed, a diastereoselectivity of 4.4:1 was reported (Scheme 2). [13,16]

Scheme 2. Diels-Alder Reaction Using 1-butyl-3-methylimidazolium -(S)-lactate[16]



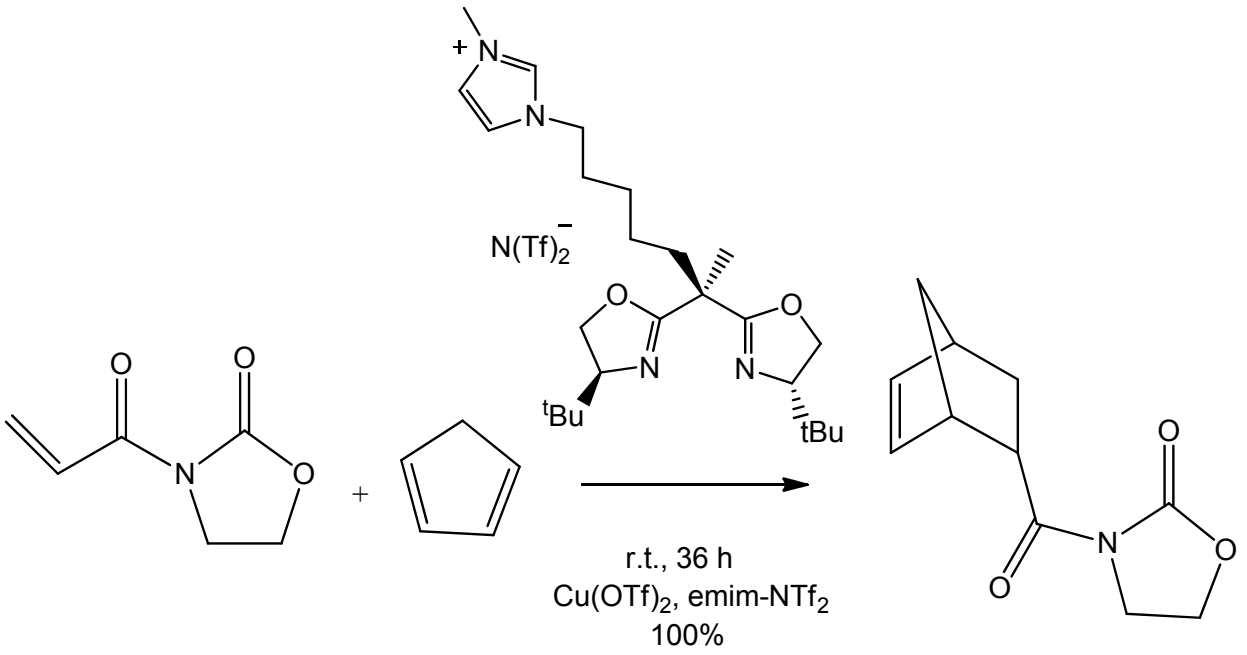
endo/exo = 4.4:1

The same Diels-Alder reaction was performed using 1-butyl-3-methylimidazolium (1S)-camphor-10-sulfonate or [bmim-(1S)-CSA] to investigate the effect the anion has on the diastereoselectivity.[17] The CIL was incorporated in solution with [bmim-BF_4] (15:100mol/mol) and due to the bulkiness of the camphorsulfonate, an increase in free imidazolium cations was observed. This resulted in a relatively high endo/exo ratio of 10.3:1. [17,13]

1.3.1.2 CILs as Catalysts

In 2007, Doherty *et al.* reported a highly stereoselective Diels-Alder reaction with the use of a CIL as a catalyst (Scheme 3).[18] Imidazolium-tagged bis(oxazolines) were used as chiral ligands in the copper(II)-catalysed cycloaddition of N-acryloyloxazolidinone and cyclopentadiene. A significant increase in reaction rate and enantioselectivity was observed compared to dichloromethane when 10 mol% of the IL-supported chiral ligand was used with the ionic liquid 1-ethyl-3-methylimidazolium bis(trifluoromethylsulfonyl)amide as a solvent. The reaction proceeded to give complete conversion, a modest endo/exo ratio of 7.3:1 and an enantioselectivity of 95% *ee* was achieved. Additionally, the catalyst was recycled ten times without loss of activity.[13,18]

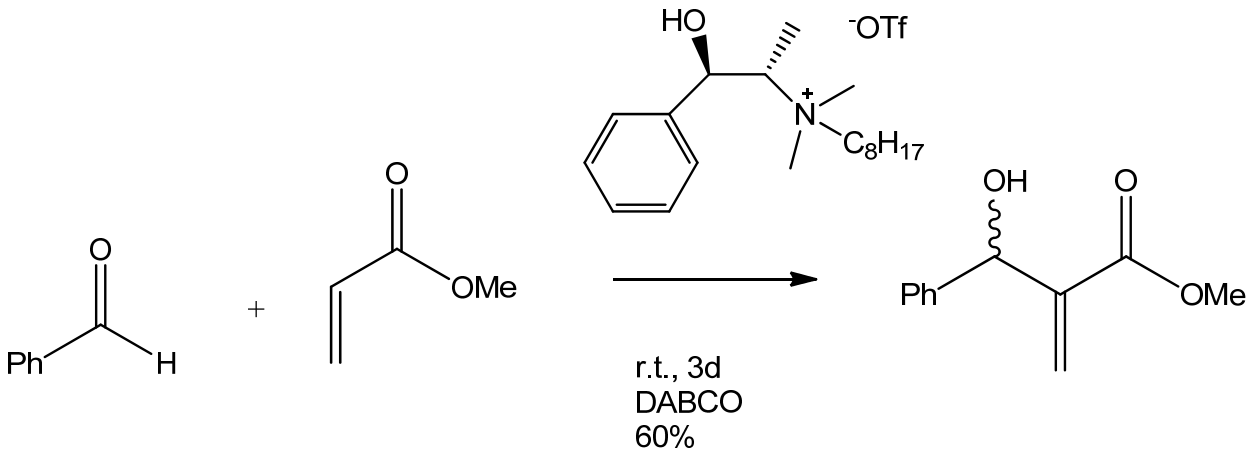
Scheme 3. Stereoselective Diels-Alder reaction Using CIL as a Catalyst[13]



endo/exo = 7.3:1, *ee* = 95%

Asymmetric induction using CILs is not only found in the Diels-Alder reaction. In fact, there are many additional examples to date. One such example involves the asymmetric Baylis–Hillman reaction of benzaldehyde and methyl acrylate (Scheme 4).[19] The reaction was performed using 1,4-diazabicyclo[2.2.2]octane) as a Lewis base in the presence of 0.5–3 equiv. of an ephedrinium based chiral ionic liquid. The product was isolated in 60% yield with an *ee* of 44%. Additionally, it was found that the enantioselectivity was dependant on the hydroxyl group, as when reactions proceeded with N-methylephedrine, the *ee* dropped to 9% but gave a higher yield of 75%. [13,19]

Scheme 4. Asymmetric Baylis–Hillman Reaction of Benzaldehyde and Methyl Acrylate[19]

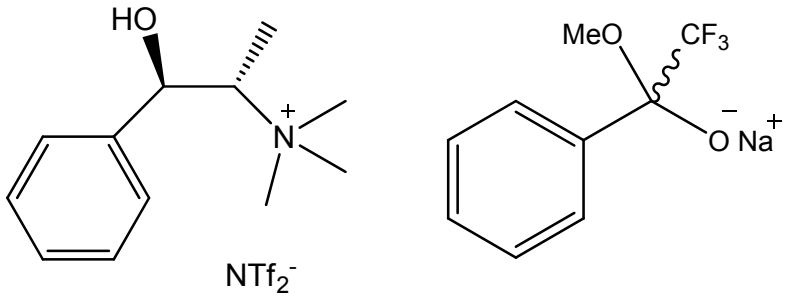


1.3.2 Chromatographic Applications

One of the first examples of the spectroscopic application of CILs was reported by Wasserscheid *et al.* in 2003 and it demonstrated that CILs can be used for the determination of enantiomeric excess of samples by NMR integration.[20] In this study, the authors analyzed a mixture of racemic Mosher's acid sodium salt and an ephedrine based CIL (Figure 3) using ^{19}F NMR spectroscopy. Depending on the ratio of CIL applied, splitting of the ^{19}F signal of the

CF_3group was detected, indicating a chiral environment. Furthermore, the chemical shift difference made it possible to determine the amount of CIL indicating a minimum concentration of 0.3 mmol/mL in order to achieve sufficient resolution.[13, 20] To date, there are many additional examples of splitting observed in ^{19}F NMR and additionally a handful that also show chiral recognition in ^{1}H NMR, although this is much more difficult to observe.[13]

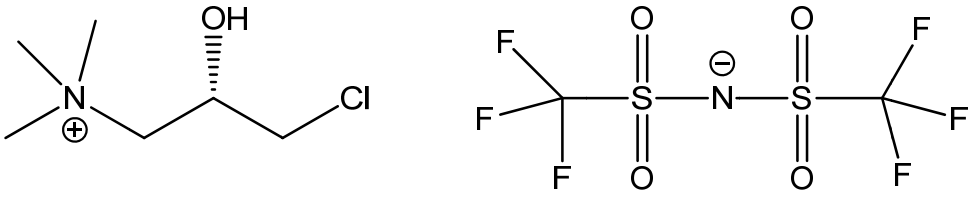
Figure 3. Mosher's Acid Sodium Salt and an Ephedrine Based CIL[13]



Chiral ionic liquids can also be used for chiral recognition in near-IR spectroscopy and as a chiral selector and solvent for the determination of the enantiomeric excess of common pharmaceutical drugs.[13] C. D. Tran *et al.* illustrated that their method of using fluorescence techniques followed by partial least squares analysis was superior to other techniques (HPLC, GC, NMR, FTIR) in terms of sensitivity and accuracy when determining enantiomeric composition. The group uses the S-[(3-chloro-2-hydroxypropyl) trimethylammonium] [bis((trifluoromethyl)sulfonyl)amide] (Figure 4) as it was found to have virtually no background absorption and fluorescence signal in the long wavelength UV and visible region.[21]

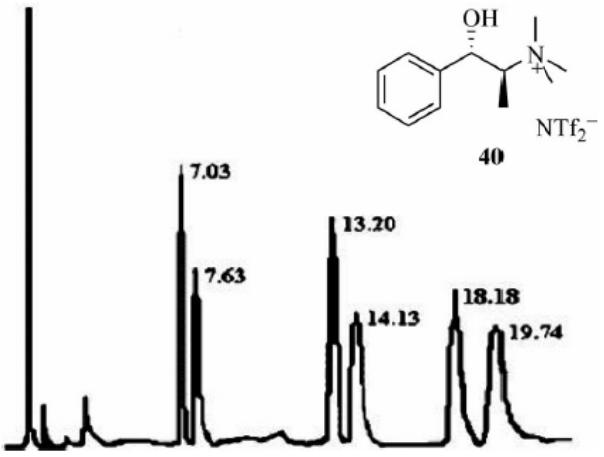
Figure 4. S-[(3-chloro-2-hydroxypropyl) trimethylammonium]

[bis((trifluoromethyl)sulfonyl)amide][21]



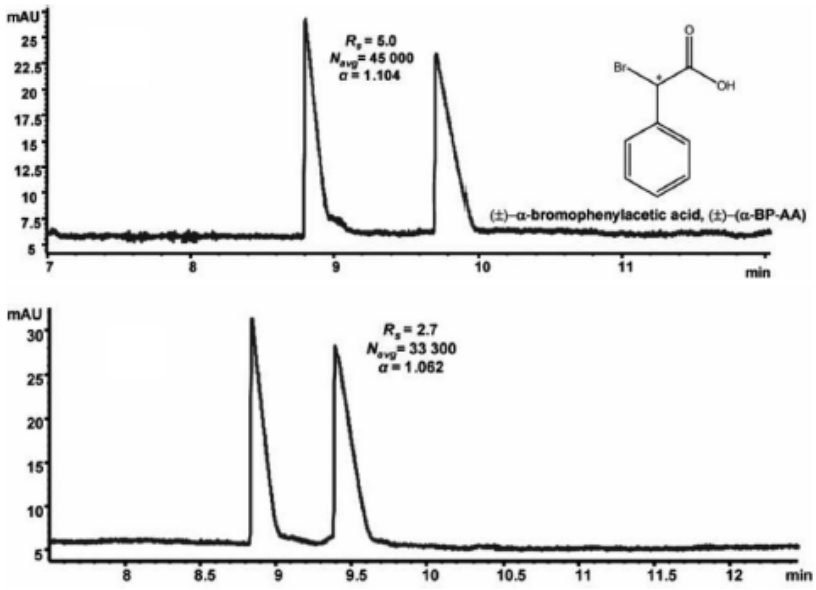
Alkylimidazolium-based ILs have already been successful as stable stationary phases for gas chromatography that have the ability to separate both polar and non-polar compounds.[13,22] In 2004, D.W. Armstrong *et al.* published one of the first examples of direct enantiomeric separation of different compounds using chiral ionic liquid stationary phases in gas chromatography.[23] The same ephedrine based CIL introduced by Wassercheid was coated on a fused-silica capillary column and a variety of chiral alcohols, epoxides and acetamides were successfully separated (Figure 5). The elution order can also conveniently be reversed by using the other naturally occurring enantiomer.[23]

Figure 5. GC Chromatogram Showing Separation of a Variety of Chiral Alcohols, Epoxides and Acetamides[23]



Additionally, CILs were found to enhance chiral separation of acidic analytes in micellar electrokinetic chromatography.[13] In 2006, Shamsi and Rizvi reported that two acidic analytes (rac)-α-bromophenylacetic acid and (rac)-2-(2-chlorophenoxy)propanoic acid could be separated with two amino acid-derived CILs as well as their polymers at 25 mM surfactant concentration (Figure 6).[13,24] However, chiral separation was found to be strongly dependant on the presence of opposite charge and structural compatibility between chiral selector and analyte.[24]

Figure 6. Enantioseparation of (rac)-α-bromophenylacetic acid with CIL[24]



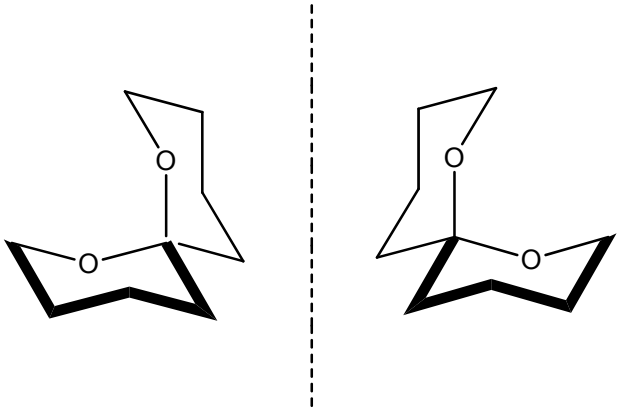
From this literature review, it can be seen that chirality can be imparted on various chemical reactions through the use of chiral ionic liquids as solvents and/or catalysts. Of particular interest are spiroacetal cyclizations which will be discussed in Chapter Two and chiral Truce-Smiles rearrangements in Chapter Three. Additionally, in Chapter Four, the unique electrochemical properties of ionic liquids make them of particular interest when researching electrochemical deposition of nickel.

Chapter Two: Asymmetric Spiroacetal Cyclization

2.1 Introduction

Acetals are bicyclic molecules that contain two oxygen-carbon single bonds on the same carbon atom, usually resulting from the reaction of a carbonyl with two moles of an alcohol.They are found naturally in cells and are used to construct a variety of other molecules including carbohydrates.[25] Acetals joining two rings are known as spiroacetals which are found in a wide range of biologically active compounds, including insect pheromones, plants and bacterial and marine sources.[25] According to Ley, the spiroacetal subunit of these compounds is not only essential for the bioactivity, but is also a valuable pharmacophore in drug discovery.[25,26] Therefore, controlling the relative and absolute configuration of the spiroacetal subunit is extremely important, especially in drug design. For example, the major female-produced sex pheromone of the olive fruit fly, olean, is found as a racemic mixture in nature; however, the stereoisomers display the remarkable property that the (R)-isomer is active on males while the (S)-isomer is active on females. Previous studies have introduced methods of attempting to control the stereoselective formation of (R) and (S)-olean as well as other similar spiroacetal compounds. [25]

Figure 7. Olean Stereoisomers[25]

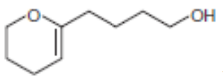
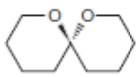
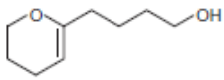
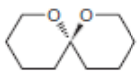
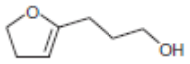
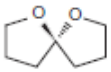
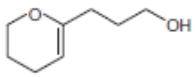
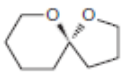
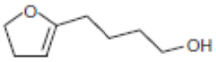
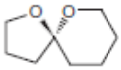
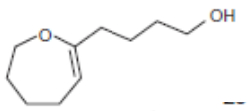
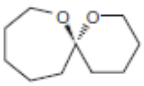
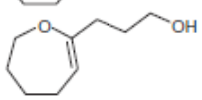
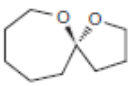


(*R*)-Olean
active on males

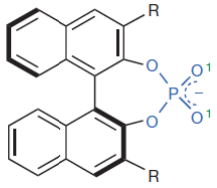
(*S*)-Olean
active on females

List and Ćorić targeted chiral Brønsted acid catalysed spiroacetalizations of readily available hydroxyenol ethers (Table 2). Their goal was to have direct access to spiroacetal motifs in a catalytic enantioselective manner. The main focus of their paper was the synthesis of a specialized Brønsted acid catalyst (6a) that would be able to impart its chirality into the cyclization via a sterically constrained active site.[25] They hypothesized that a confined space could increase selectivity by limiting the freedom of the molecule which would accommodate various transition state geometries thereby leading to different isomers.

Table 2: Catalytic Asymmetric Spiroacetalization[25]

Entry	Substrate	Reaction details	Product	Yield	e.r. or d.r.
1		**6a** (5 mol%), –25 °C, MTBE		77%	e.r. 98:2
2		*ent*-**6a** (5 mol%), –25 °C, MTBE		70%	e.r. 97.5:2.5
3		**6a** (0.1 mol%), –55 °C, CH_2Cl_2		62%	e.r. 96:4
4		**6a** (1 mol%), –35 °C, DCE		81%	e.r. 95.5:4.5
5		**6a** (1 mol%), –35 °C, MTBE		69%	e.r. 96:4
6		**6a** (1 mol%), –25 °C, MTBE		78%	e.r. 96:4
7		**6a** (1 mol%), –35 °C, MTBE		88%	e.r. 98.5:1.5

Where 6a represents the specialized Brønsted acid catalyst:



2.2 Results and Discussion

2.2.1 Spiroacetal Cyclization

Directly based on their results, the substrates from entries 1, 3, 4 and 5 (Table 2) from List and Ćorić's study were chosen to be cyclized in various room temperature ionic liquids and the products were labelled compounds **1**, **2**, **3** and **4** for the purpose of our study (Scheme 5). These compounds were chosen for their relative ease of synthesis and the availability of the starting materials. Each reaction begins with either an unsaturated furan or pyran ring system. Hydroxyl chains, varying in length from three to four carbons, are attached to the ring systems to obtain the product that will undergo the spiroacetal cyclization. Using four reactions the resulting [5, 5], [6, 5], [5, 6], [6, 6] ring combinations can be formed. As far as synthesis goes, the reactions were relatively simple to perform. The temperature was maintained at -78°C during the addition of the carbon chains to minimize unwanted by-products prior to cyclization. Column chromatography was performed to assure purity of the compounds to be cyclized and spectral data obtained on the purified compounds confirmed that the desired products were obtained.[25] The cyclization was performed using an organic acid and mixing at room temperature. For the cyclization, *p*-toluene sulphonic acid was chosen in hopes that it would not disrupt the structure and characteristics of the ionic liquids being used. The only difficulties arose when trying to adequately mix the compounds in the ionic liquids without applying heat. The ionic liquids are very viscous and since heat would compromise the chirality of them, the reactions had to be mixed much longer and thoroughly. Similar to List's work, the aim was to fit use the chirality of the reaction environment provided by the chiral RTIL to impart chirality on the cyclization products.

Each reaction was conducted in four different chiral room temperature ionic liquids: [bmim][L-lactate], [bmim][D-lactate], [bmim][(1S)(+)CSA] and [bmim][(1R)(-)CSA]. The optical

rotation was measured and compared to a non-chiral version of the reactions performed in THF instead of RTIL. The resulting specific rotations were obtained and can be found in Table 2. Only the enantiomeric ratios for 1,7-dioxaspiro[5.5]undecane could be calculated based on the literature value provided by Mori[26]. Since there are no literature values available for the other three products, the enantiomeric excess could not be calculated. In List's work the catalytic Bronsted acids gave predominantly the S-(+) products as determined by the measured optical rotations. As our measured rotations were negative values, the reactions tend to favour the R(-) products. As a result it was not possible to extrapolate a value for the R-(-) enantiomers, based on List's published values. With the exception of one outlier, changing the counter ion from L to D or R to S had little effect on the preferred enantiomer. The reaction resulting in smallest cyclized product (**1**) seems to result in the largest change in the specific rotation of the products while the largest product (**4**) sees the largest change with the larger ionic liquid. This is agreeable because the smaller ionic liquid wouldn't be able to impart it's chirality as well to the larger products due to a chiral mismatch, whereas the smaller product would be better accommodated.

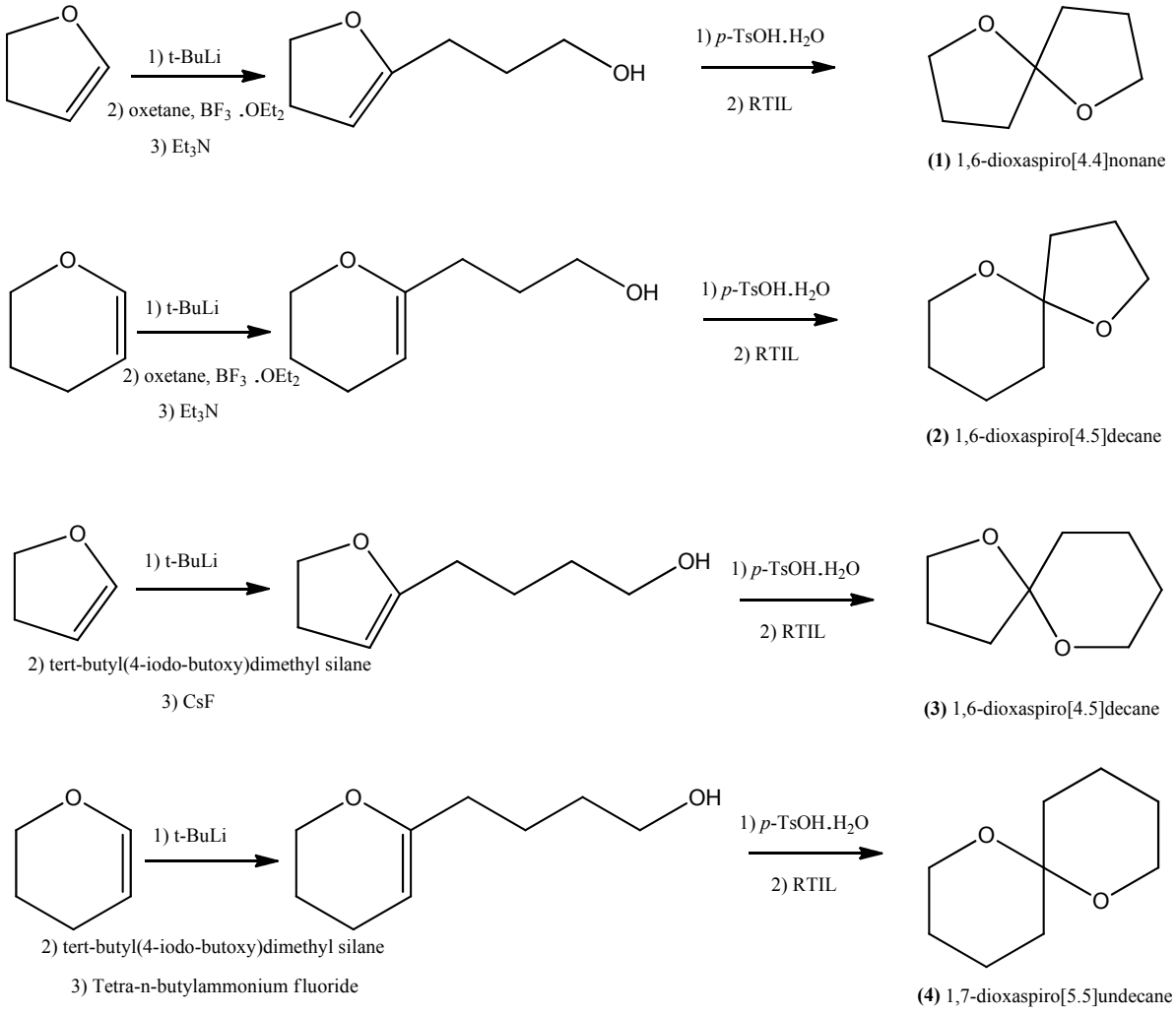
Table 3: Specific Rotation of Chiral Products Synthesized in Various Ionic Liquids

Cyclized Product	Ionic Liquid				
	No Ionic liquid	[1-butyl-3-methylimidazolium]		[1-butyl-3-methylimidazolium]	
		[L-lactate]	[D-lactate]	[(1S)(+)-10-camphorsulphonate]	[(1R)(-)-10-camphorsulphonate]
(1)	+0.93	-5.47	-6.38	-0.78	-1.20
(2)	-1.49	-5.10	-1.60	-2.25	-1.43
(3)	-2.40	-2.28	+0.49	-3.50	-3.09
(4)	-0.82	-1.32	-3.66	-6.25	-2.88

Table 4: Enantiomeric Ratios of 1,7-dioxaspiro[5.5]undecane in Various CILs

Ionic Liquid	*er*
[bmim][L-lactate]	51:49
[bmim][D-lactate]	53:47
[bmim][(1S)(+)CSA]	55:45
[bmim][(1R)(-)CSA]	52:48

Scheme 5



Although both products **2** and **3** are identical they are generated from different starting materials with different transition states, resulting in the formation of a five-membered versus the formation of a six-membered ring. If the size of the cyclizing ring in the transition state was most influenced by the chiral pocket, then the strongest relationship should be between compounds **1** and **2**, and between compounds **3** and **4**. While there is a relationship when (L)-lactate is used as the anion in the chiral ionic liquid for the formation of compounds **1** and **2**, the other cyclizations do not follow a pattern to support this hypothesis.

2.2.2 Future Work

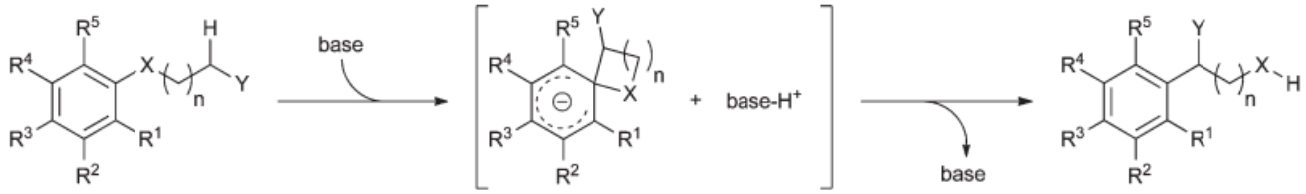
Future work would include optimizing the chirality of the ionic liquids being synthesized. This would involve varying the temperature and reaction time as well as potential solvents during the synthesis of the chiral room temperature ionic liquids. Since the reactions are being heated, some of the chirality is inevitably lost in the process. By optimizing the temperature and reaction time of the synthesis of the ionic liquids, it might be possible to maximize the chirality that can be imparted on the spiroacetal cyclizations. Additionally, increasing the scope of the ionic liquids involved would perhaps yield a better match for the size of the molecules and the size of the chiral pocket in the ionic liquids. A better fit would improve the chiral influence on the reactions. Enantiomeric ratios could not be calculated for all compounds as there was no literature data on the optical rotation of the pure enantiomeric products. A chiral column could be used to determine the enantiomeric ratio as well.

Chapter Three: Truce-Smiles Rearrangement

3.1 Introduction

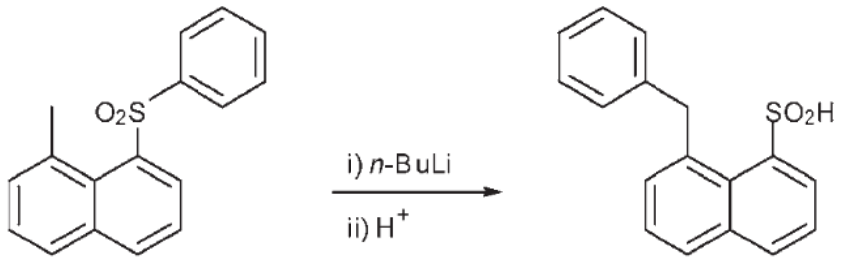
The Truce-Smiles rearrangement is an intramolecular nucleophilic substitution reaction that forms an aryl carbon-carbon sp^3 bond while simultaneously breaking a carbon-heteroatom bond.[27] The Truce-Smiles rearrangement was first developed by Truce in the 1950's and incorporates specific variations from the original Smiles rearrangement. In the Truce-Smiles rearrangement a carbanion is the nucleophile instead of the heteroatom. Additionally, the Smiles rearrangement requires an activating substituent in the migrating aryl ring unit that is not required in the Truce-Smiles rearrangement. [28] The carbanion is generated by deprotonation, which requires the inclusion of a functional group to lower the pK_a of the adjacent protons. The rearrangement is proposed to proceed through a bicyclic intermediate which is a delocalized anionic cyclohexadienyl σ-adduct which is typical of the S_NAr mechanism (Scheme 6).[27] The nature of the rearrangement allows access to structures of a more complex nature from easier to synthesize precursors and therefore a variety of different reactions have been explored.

Scheme 6: General Truce-Smiles Rearrangement



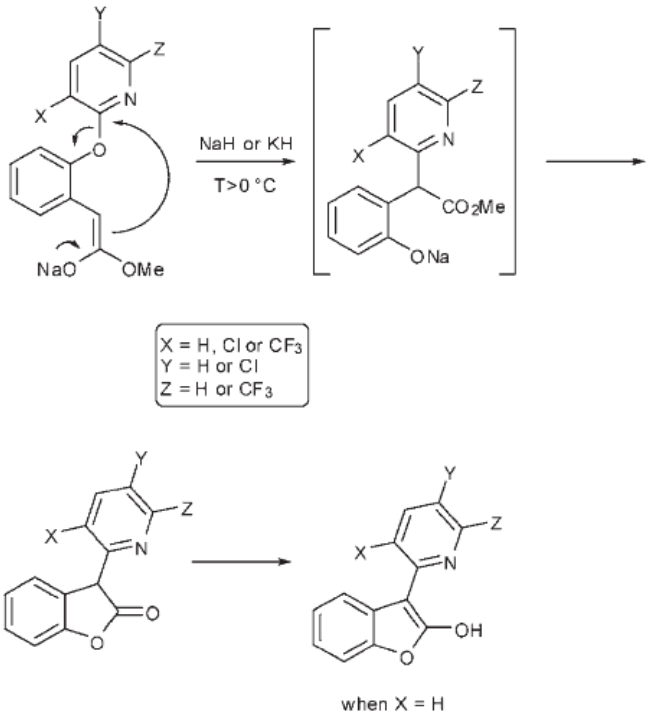
The majority of Truce's work involved a variety of rearrangements incorporating different sulphones. For example, the rearrangement has been demonstrated in methylnaphthyl phenyl sulphones (Scheme 7). The starting compound is deprotonated resulting in phenyl migration from sulfur to carbon to produce benzyl napththalenesulfinic acid. [28, 29]

Scheme 7: Rearrangement of methylnaphthyl phenyl sulfones



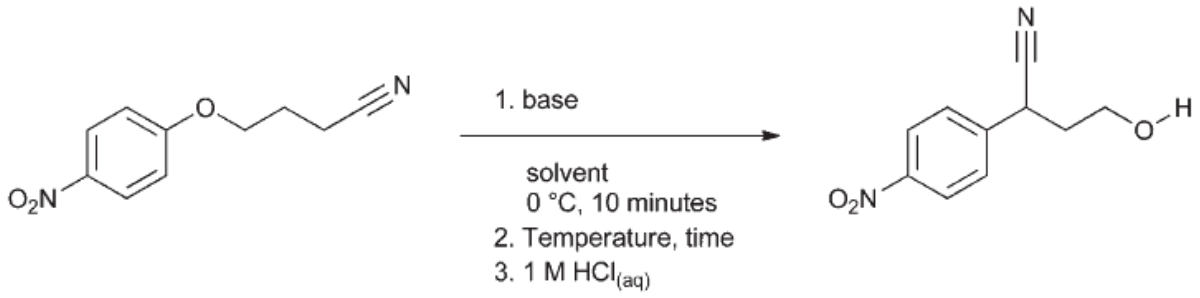
Additional reaction conditions were developed by Truce in the coming years [28]; however, in 1982, Itô's discovery of a unique Truce-Smiles rearrangement of substituted anilide intermediate upon exposure to LDA would be the last example of the Truce-Smiles rearrangement for nearly 20 years. Even so, the discovery in 2000 by Erickson and McKennon was an unexpected observation.[28] They observed interesting results when they attempted to formylate an ester enolate followed by O-methylation (Scheme 8). Instead of the expected formylation product, they observed enolate attack onto the pyridine ring. The authors rationalised the results as the product of a Truce-Smiles rearrangement and went on to reveal this, initially undesired transformation, as a new method for the preparation of 3-pyridyl-2-benzofuranones.[28]

Scheme 8.



One of the more recent examples of the Truce-Smiles rearrangement comes from Tabitha Wood *et. al.* in 2015.[27] The authors examined the requirement of aryl ring activation by strong-electron withdrawing substituents in substrates involved in the Truce-Smiles rearrangement. The results indicated that using strong electron withdrawing substituents, such as nitro-, cyano-, and benzoyl- functional groups was successful as expected, but also for multiple, weakly electron withdrawing substituents, such as chloro- and bromo-functional groups (Scheme 9).[27]

Scheme 9.



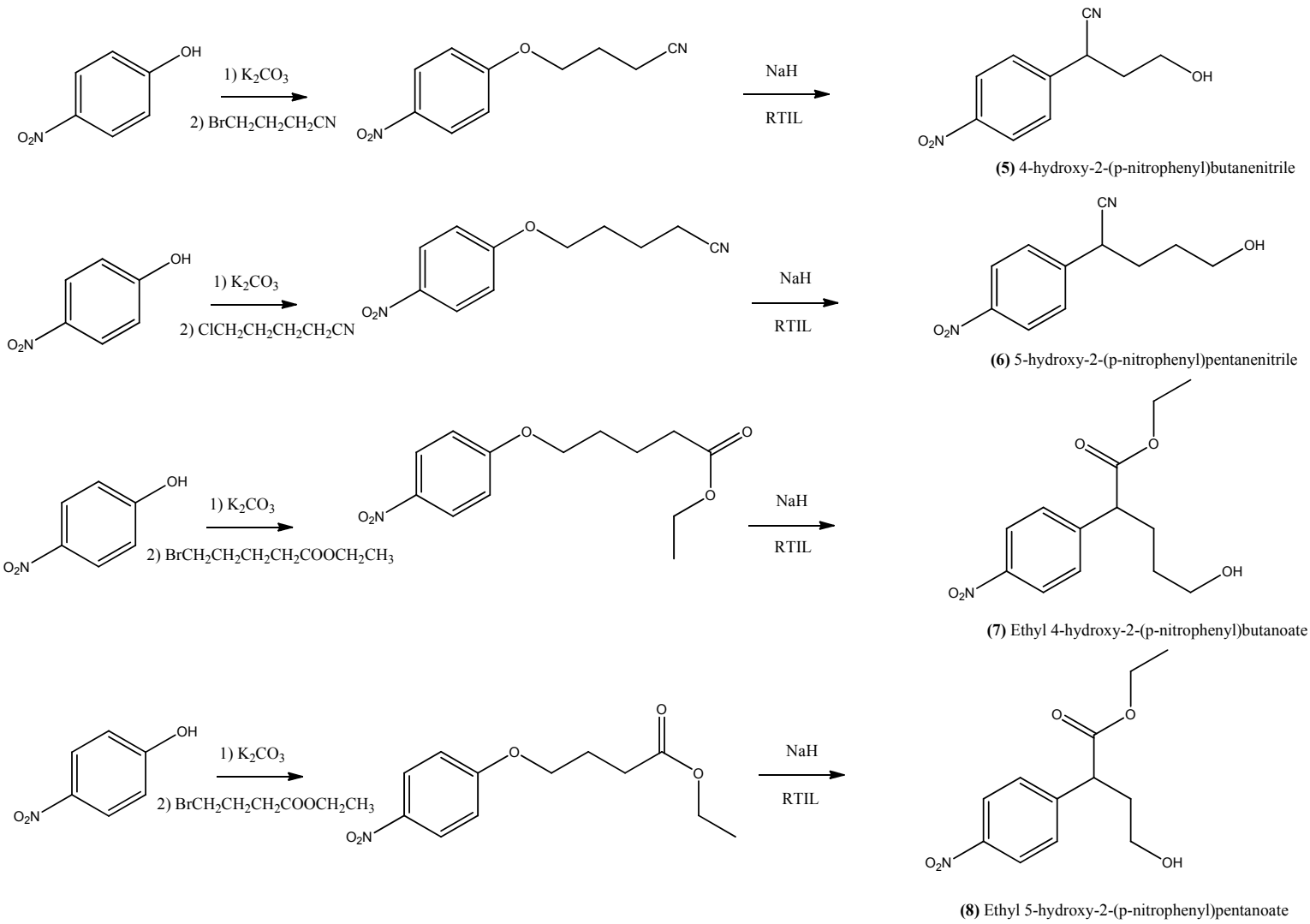
Although there is now a large amount of information on the substrate scope of the Truce-Smiles rearrangement, only one of these reactions has gone on to produce a chiral center. Furthermore, the enantioselectivity of such a reaction has never been explored until now.

3.2 Results and Discussion

3.2.1 Chiral Truce-Smiles Rearrangement

Four similar reactions were chosen for this study (Scheme 10). Each reaction begins with the same substituted aromatic compound, 4-nitrophenol. This starting material was chosen as it has been shown that ether derived from this starting material successfully undergo the Truce-Smiles reaction.[27] A Williamson ether synthesis is conducted using potassium carbonate and either an alkyl nitrile or an alkyl ester is attached to the ring. Sodium hydride is then added to the product to promote the Truce-Smiles rearrangement. In each reaction a chiral center is formed after the rearrangement occurs. Normally, a racemic mixture of each enantiomer would be expected; however, with the use of chiral room temperature ionic liquids (RTIL), it was anticipated that the enantiomeric selectivity could be manipulated. Each reaction was conducted in four different chiral room temperature ionic liquids: [bmim][L-lactate], [bmim][D-lactate], [bmim][(1S)(+)CSA] and [bmim][(1R)(-)CSA]. The optical activity was measured and compared to a non-chiral version of the reactions (taken place in THF instead of RTIL) (Table 5). The enantiomeric ratio cannot be calculated as there is no known literature value of the optical rotation of either pure enantiomer. However, looking at the optical rotations of the products it is clearly evident that the chiral ionic liquid in which the reaction takes place influences the chirality of the product.

Scheme 10



(5) 4-hydroxy-2-(p-nitrophenyl)butanenitrile

(6) 5-hydroxy-2-(p-nitrophenyl)pentanenitrile

(7) Ethyl 4-hydroxy-2-(p-nitrophenyl)butanoate

(8) Ethyl 5-hydroxy-2-(p-nitrophenyl)pentanoate

Table 5: Specific Rotation of Chiral Products Synthesized in Various Ionic Liquids

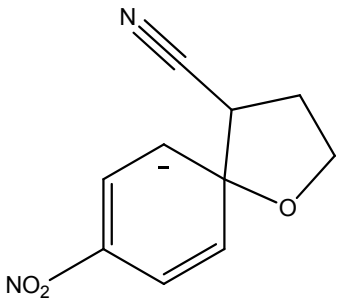
Rearranged Product	Ionic Liquid				
	No Ionic liquid	[1-butyl-3-methylimidazolium]		[1-butyl-3-methylimidazolium]	
		[L-lactate]	[D-lactate]	[(1S)(+)-10-camphorsulphonate]	[(1R)(-)-10-camphorsulphonate]
(5)	-0.56	-7.84	+1.09	-5.43	-3.75
(6)	-1.54	+1.49	+1.54	+4.55	-2.50
(7)	-2.24	+1.64	-1.39	+2.42	-0.71
(8)	-0.65	+3.23	-2.99	+5.00	-0.59

Unlike the study in Chapter Two of this thesis in which some literature values were known for the optical rotation of the pure enantiomers, the compounds synthesized in this study have only been reported as racemic mixtures.[27] As a result, the success of the chiral induction is difficult to measure. The literature was reviewed in an attempt to find a discussion of the size and shape of the chiral pockets for each of the ionic liquids as with that information in hand it would be possible to describe the fit of the intermediate into the chiral site to compare the magnitude of the chiral induction to that site. While studies have been performed on the influence of ion size on the properties of the ionic liquids, such as viscosity and electrical conductivity,[30] and reviews on the physical properties of ionic appear,[31] there is little reported on the size of the repeat units or ionic pockets which are formed. One computational study[32]determined the structure and the cation-anion interactions for [bmim][lactate]. In that study, energy minima were determined for five conformers of the ion pairs in which the hydrogen bond distances and strengths were determined. The interactions of only one anion and one cation were taken into account giving a two-dimensional picture when the structure of the chiral ionic pocket is required to determine a fit or match to the structure of the intermediate. Another approach to analyzing the success of the reaction is to look at the intermediates for all of the reactions and determine if there is indeed a pattern consistent with the size/volume of the intermediate, the two chiral ionic liquids and the change in the relative product mixture of enantiomers.

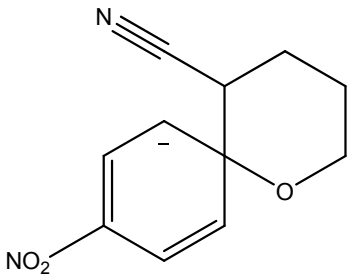
In Figure 8 the proposed intermediates for each of the Truce-Smiles products are illustrated. It is important to note that two of the products rely upon a 5-membered ring intermediate while the other two reactions proceed through a 6-membered ring intermediate. Using a low level MOPAC calculation (CS MOPAC Pro) a representative volume for each of the intermediates was calculated (Table 6). Two volumes are given, one of the entire molecule, and one of the cyclic intermediate portion in which the aromatic ring is excluded. The volume of the

intermediate ring only would be representative of an intermediate in which the aromatic ring is not being inserted or influenced by the chiral pocket of the RTIL. In Figure 9 the dimensions of the molecule are defined; height of the molecule would relate to the Z-axis.

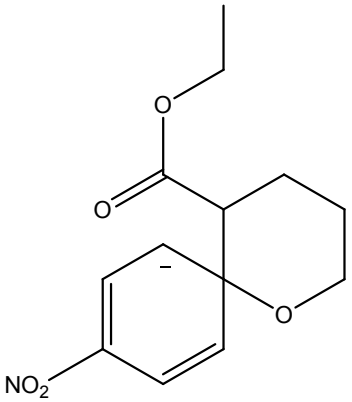
Figure 8: Proposed Intermediates for the Truce-Smiles Reactions



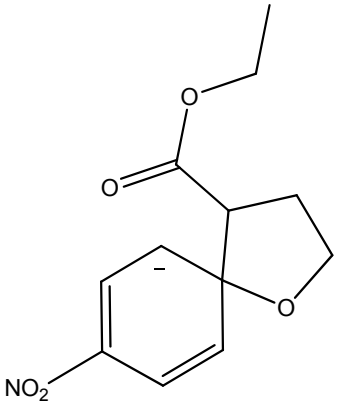
(5)-intermediate



(6)-intermediate



(7)-intermediate



(8)-intermediate

Figure 9: Illustration of the Dimensions Used for the Molecular Volume Calculation

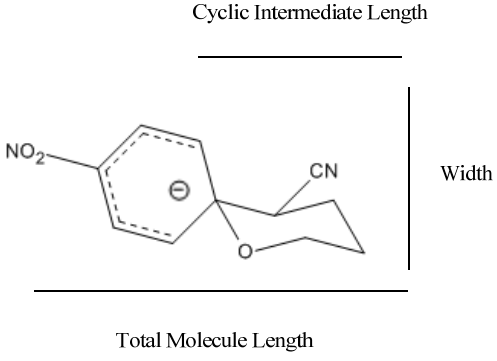


Table 6: Molecular Dimensions for the Intermediates in the Truce-Smiles Reactions

Compound	Length (Å)	Width (Å)	Height (Å)	Volume ($Å^3$)
5	Total molecule 9.51 Cyclic Intermediate 4.23	5.012	3.201	Total molecule 153 Cyclic Intermediate 67.8
6	Total molecule 9.23 Cyclic Intermediate 3.92	5.018	6.085	Total molecule 282 Cyclic Intermediate 120
7	Total molecule 9.12 Cyclic Intermediate 3.93	5.016	8.110	Total molecule 371 Cyclic Intermediate 160
8	Total molecule 11.8 Cyclic Intermediate 6.49	4.708	3.228	Total molecule 179 Cyclic Intermediate 98.7

It is interesting to note in Table 5 that in the Truce-Smiles reactions that were performed in THF, in an achiral environment, compound **7** exhibits a significant non-zero optical rotation. This compound also has the largest volume for both the total molecule and for the cyclic intermediate portion of the molecule. When looking for an overall pattern the smallest volumes are associated with compound **5** and this compound shows the largest optical rotations for all ionic liquids but [bmim][D-lactate]. In general, compounds **5** and **8** appear to show the greatest enantiomeric enhancement and have the smallest volumes. These limited results do suggest that with the appropriate combination of chiral ionic liquid and intermediate size chiral induction from the solvent can be obtained.

3.2.2 Future Work

Future work would involve obtaining further information on the size and shape of the chiral pockets of each ionic liquid and comparing that to the size of the molecules. The relationship of the size of the chiral pockets based on the size of the transition state or intermediate would have the potential to greatly influence the ability to induce chirality in these reactions. Calculating the size of the chiral pockets in the ionic liquids is beyond the scope of this study; however, having this knowledge would be of utmost importance when optimizing the capabilities of imparting chirality to the reactions. It is possible that there would be a more optimal ionic liquid that would better suit these reactions and provide even greater enantiomeric ratios. Additionally, the enantiomeric ratios may be calculated upon receiving data on the optical rotation of the pure enantiomeric products.

Chapter Four: Electrodeposition/dissolution of Nickel in RTILs

4.1 Introduction

The original purpose of introducing ionic liquids for electrodeposition was to obtain high concentrations of aluminum in a highly conducting aprotic medium for aluminum deposition.[33,34] As the number of published reports on various ionic liquids began to increase, several key advantages of RTIL have been discovered: wider potential windows, high solubility of metal salts, avoidance of water and water/metal chemistry, high conductivity compared to non-aqueous solvents. Additionally, due to their low vapour pressures, ionic liquids can be used to perform depositions at an elevated temperature which lowers the concerns about viscosity and conductivity and accelerates surface diffusion, nucleation and crystallization associated with metal deposition.[33]

Cationic structure and size affect the viscosity and conductivity of the liquid and thus can control mass transport of metal ions to the electrode surface (Table 7). Cations are also be adsorbed at the electrode surface at the deposition potential and therefore the structure of the double layer is cation dependant.[33] As a result, many cations have been investigated such as phosphonium[35] and sulfonium[36]; however, imidazolium based cations have been favoured due to their superior fluidity and conductivity. Furthermore, 1-butyl-3-methyl-imidazolium is most preferred due to its high conductivity.[33,37] Additional studies are required to investigate the effect of the cation on the Helmholtz layer thickness; although, according to Endres[38], the cation also appears to control the morphology of aluminum deposited from various triflimide based ionic liquids.[33]

Table 7: Physical Properties of Various Ionic Liquids[33]

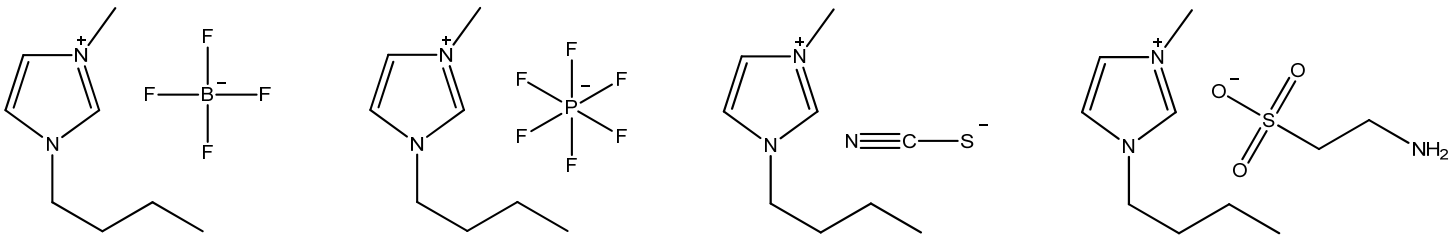
Salt	γ/mN m^{-1}	R_+/Å	R_-/Å	$P(r > R)$	$\eta/10^3$ Pa s	T/K
EMIm BF_4	46.7	3.31	2.50		38	298
EMIm TfO	39.2	3.31	2.97		45	293
EMIm Tf_2N	39.6	3.31	3.62		34	293
EMIm $(CN)_2$	42.6	3.31	2.66		16	298
BMIm BF_4	46.6	3.55	2.50	3.06×10^{-5}	219	298
BMIm PF_6	48.8	3.55	2.78	7.85×10^{-5}	450	298
BMIm Tf_2N	37.5	3.55	3.62	1.20×10^{-4}	69	298
HMIm PF_6	43.4	3.81	2.78	1.06×10^{-4}	585	298
OMIm PF_6	36.5	4.03	2.78	3.20×10^{-3}	682	303
Acetylcholine Tf_2N	38.6	3.70	3.62	4.85×10^{-5}	240	298
$BzCOOC_2H_4N(CH_3)_3$ Tf_2N	37.71	3.96	3.62	1.76×10^{-5}	6570	298
$Me_2N(Bz)(C_2H_4OH)$ Tf_2N	39.51	3.72	3.62	3.28×10^{-5}	762	298
$Me_2N(C_2H_4Br)(C_2H_4OH)$ Tf_2N	40.02	3.59	3.62	4.52×10^{-5}	626	298
$(C_4H_9)_4N$ picrate	26.4	4.13	3.66	5.29×10^{-3}	51	364
$PhCH_2mim$ Tf_2N	40.8	3.73	3.62	1.99×10^{-5}	110	298
NaCl	98	1.02	1.81	0.836	0.7	1273
Water	71.8	1.87		2.74×10^{-2}	1.00	298
CH_2Cl_2	26.54	2.62		0.141	0.39	303

While it is generally accepted that the cation is more important in controlling the physical properties of the ionic liquid, the anion has a greater effect on the stability and chemical reactivity.[33] Ionic liquids can be divided into two major classes: those based on discrete anions and those with anionic complexes. The anion can affect the coordination geometry around the metal ion, which in turn may affect the reduction potential, reduction current and nucleation; however, aside from Katayama's [39] work, this area is largely unstudied.[33] Anions such as BF_4^- and PF_6^- were initially used extensively because of their wide potential windows; however, slow hydrolysis by water yielding HF has led to an increase in the use of water stable anions such as $(CF_3SO_2)_2N^-$ which was found to have even larger potential windows, higher conductivities and lower viscosities.[33,40]

4.2 Results

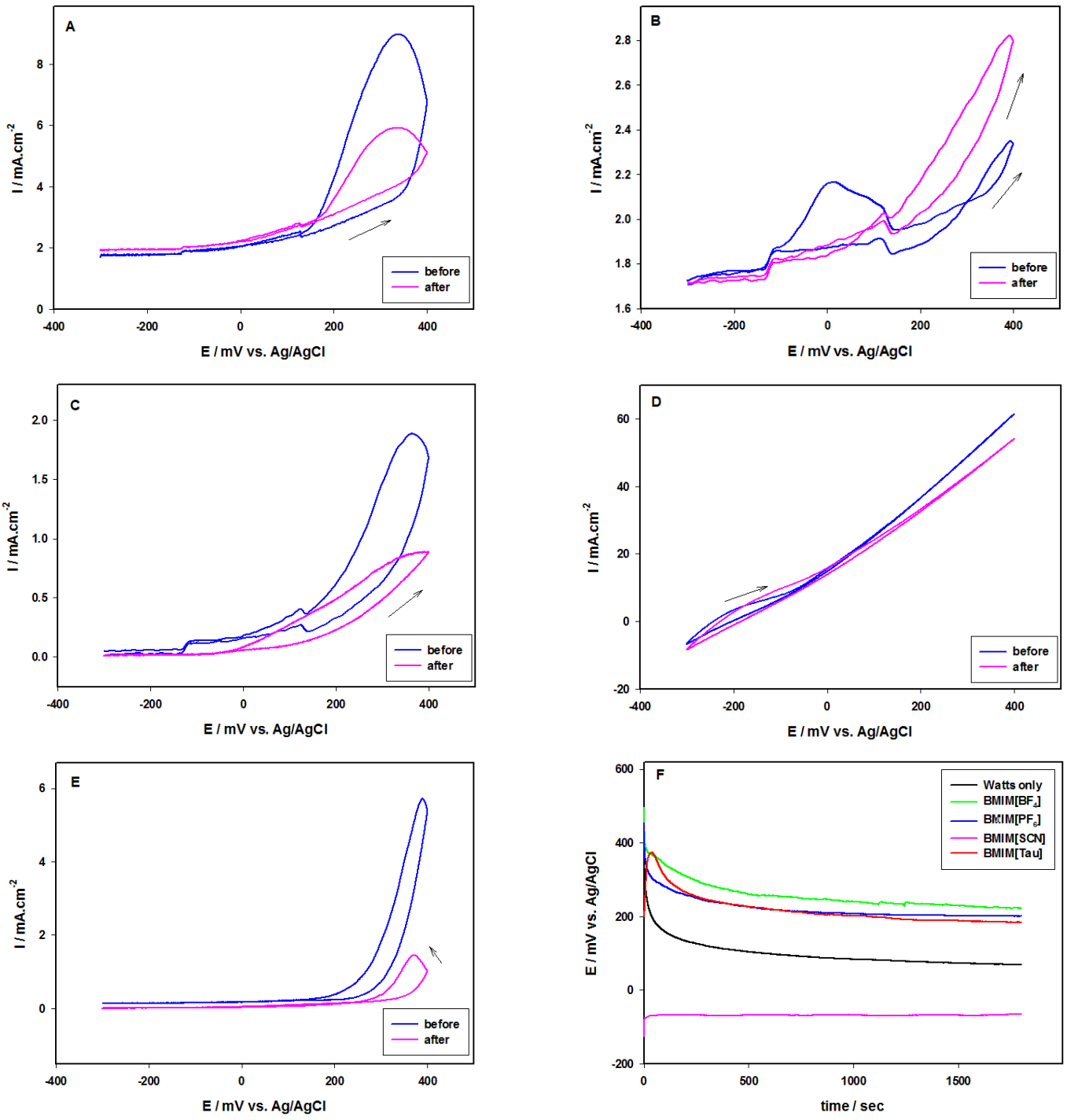
Nickel dissolution/deposition was investigated using Watts solution and a variety of RTILs. The solution contained 30mL of Watts solution which was stirred with 1 mL of an added ionic liquid: [bmim][BF_4], [bmim][PF_6], [bmim][SCN] or [bmim][Tau] (Figure 10). The working electrode was a 1mm thick sheet of nickel, the counter electrode was titanium which was etched for 2-5 mins and the reference electrode was silver/silver chloride. Each solution was stirred for30 mins before the experiment and maintained at a temperature of 55°C. Each individual solution underwent the experiment beginning with 10 cycles of cyclic voltammetry (SR= 20mV/s, -0.3 to 0.4V) (Figure 11), cyclic potentiometry at 8.0 mA/cm^2 (Figure 11F) followed by an additional 10 cycles of cyclic voltammetry using the same conditions as before (Figure 11). Based on the increased current response after the chronopotentiometry compared to that of the before one, it is obvious that the dissolution in the mixture of Watts solution and [bmim][BF_4] resulted in more activated sites. The highest current response was for the mixture of Watts solution and [bmim][SCN], followed by Watts solution only. Chronopotentiometry results demonstrated thatthe mixture with [bmim][SCN]had the lowest potential and [bmim][BF_4] the highest potential for dissolution. Only the solution with the addition of [bmim][SCN] improved the dissolution and further vulnerability of nickel compared to the Watts only solution.

Figure 10: Ionic Liquids Used for Electrodeposition-dissolution



[bmim][BF_4] [bmim][PF_6] [bmim][SCN] [bmim][Tau]

Figure 11: Cyclic Voltammetry of Nickel in A) Watts only; B) Watts + [bmim][BF_4]; C) Watts + [bmim][PF_6]; D) Watts + [bmim][SCN]; E) Watts + [bmim][tau]; and Chronopotentiometry of Nickel in these solutions for 30 min

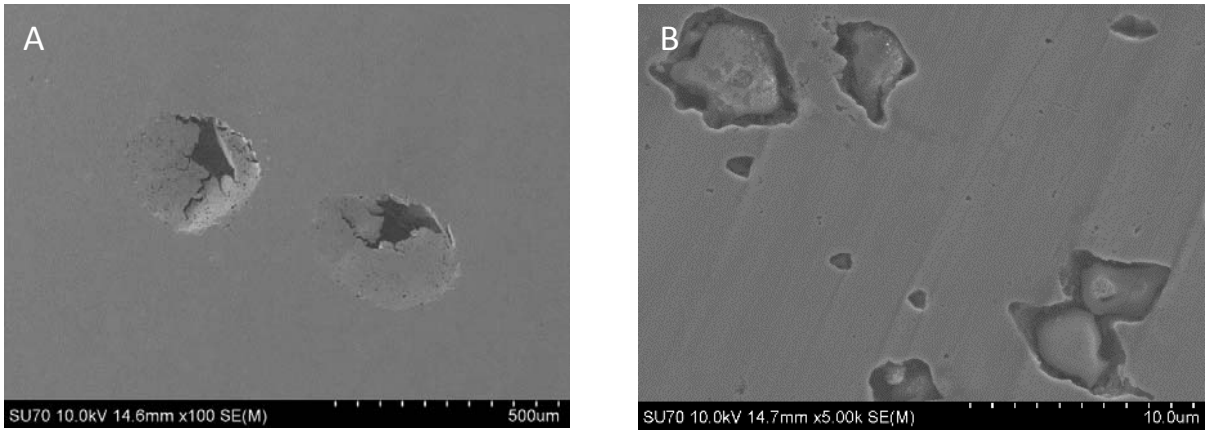


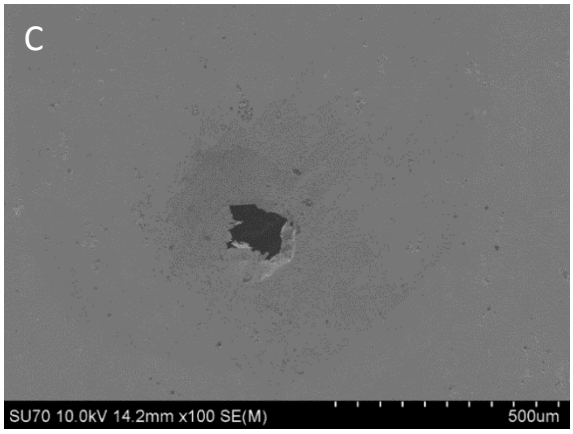
The solutions containing the ionic liquids all had dissolution efficiencies of greater than 90% (Table 8).The SEM images of the nickel electrodes after dissolution (Figure 12) show more uniform dissolution for some, compared to more localized dissolution for others. Also, while it seemed that it was more of a pitting like dissolution for Watts only solution or [bmim][BF_4] or [bmim][PF_6] with closed surface lace-like pits, [bmim][SCN] had dissolution on the grain boundary-like regions.

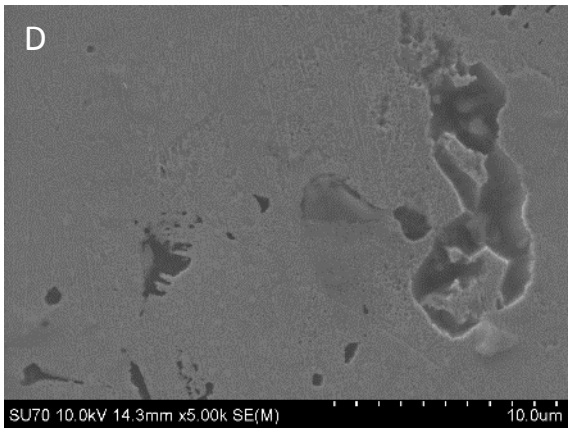
Table 8: Weight Changes and Anodic Efficiencies of Chronopotentiometry Process

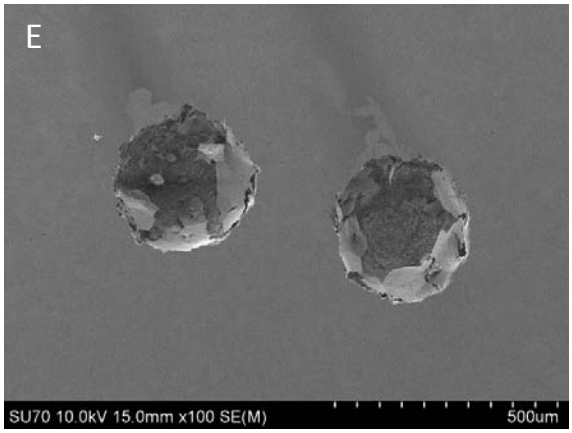
Solution	**ΔW_{anode}/ gr**	**η_{anode}/%**
Watts only	-0.0089	96.7
Watts + [bmim] [BF_4]	-0.0092	96.8
Watts + [bmim][PF_6]	-0.0087	96.7
Watts + [bmim][SCN]	-0.0089	92.7
Watts + [bmim][tau]	-0.0092	94.8

Figure 12: SEM images of two different magnifications of nickel electrodes after dissolution in A,B) Watts only; C,D) Watts + [bmim][BF_4]; E,F) Watts + [bmim][PF_6]; G,H) Watts + [bmim][SCN]; I,J) Watts + [bmim][tau]

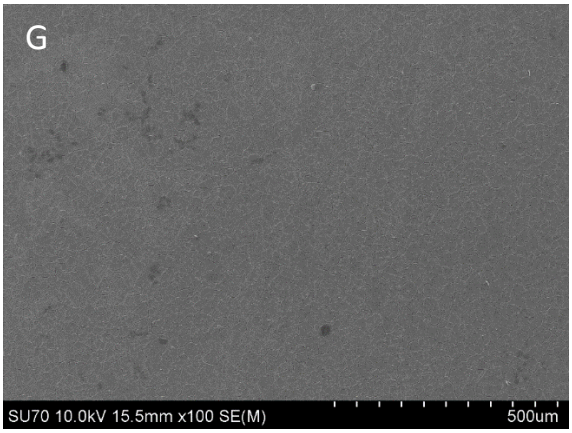


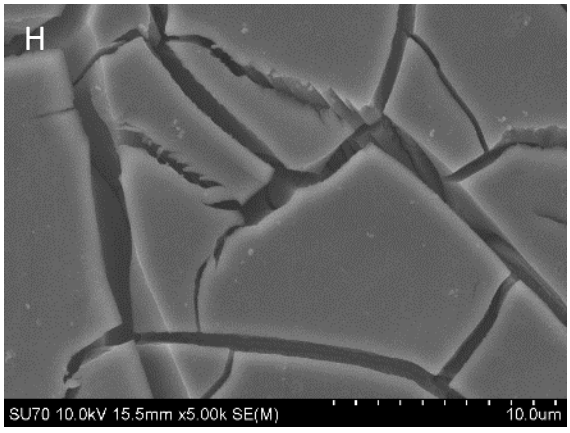

C
SU70 10.0kV 14.2mm x100 SE(M)
500um

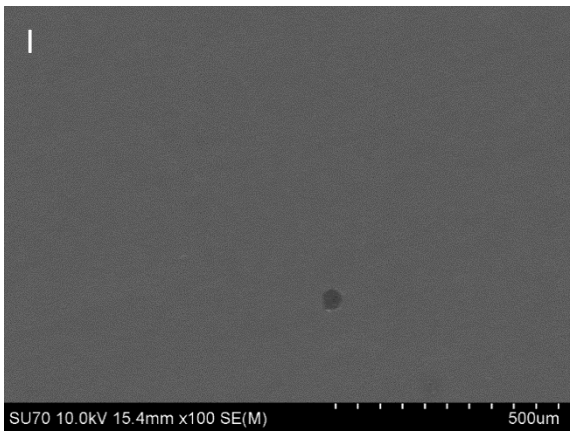

D
SU70 10.0kV 14.3mm x5.00k SE(M)
10.0um

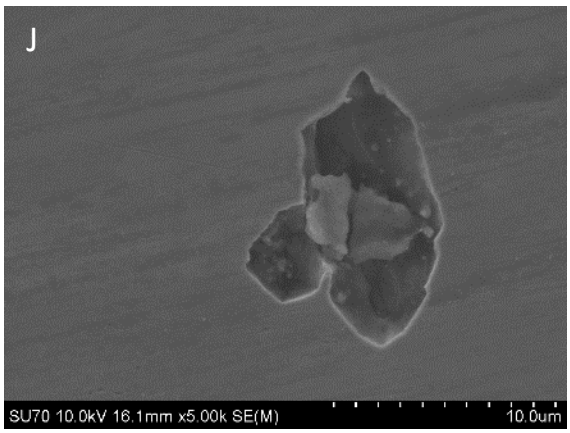

E
SU70 10.0kV 15.0mm x100 SE(M)
500um


F
SU70 10.0kV 15.0mm x5.00k SE(M)
10.0um


G
SU70 10.0kV 15.5mm x100 SE(M)
500um


H
SU70 10.0kV 15.5mm x5.00k SE(M)
10.0um


I
SU70 10.0kV 15.4mm x100 SE(M)
500um


J
SU70 10.0kV 16.1mm x5.00k SE(M)
10.0um

The energy-dispersive X-ray spectroscopy (Figure 13A) confirms that Ni has been deposited in all the solutions. However, the nickel crystal peaks deposited on titanium only showed up in Watts only solutions and the Watts-[bmim][SCN] solution using X-ray diffraction (Figure 13B). It shows that the coverage of the titanium electrode with nickel is comparable between the Watts only solution and the solution containing [bmim][SCN]. It is worth mentioning that nickel peaks of the coat formed in Watts-[bmim][SCN] solution were broad, which could be due to finer crystalline or amorphous-like structure. This means that the amount of deposited nickel for equal applied charge is lower in case of the rest of the solutions. Based on the SEM images of deposited nickel (Figure 14), the solutions containing [bmim][PF_6] and [bmim][tau] resulted in more localized deposition.

Figure 13: A) EDS , and B) XRD characterization of titanium electrodes after deposition of nickel in Watts only, Watts + [bmim][BF_4], Watts + [bmim][PF_6], Watts + [bmim][SCN], and Watts + [bmim][tau] solutions.

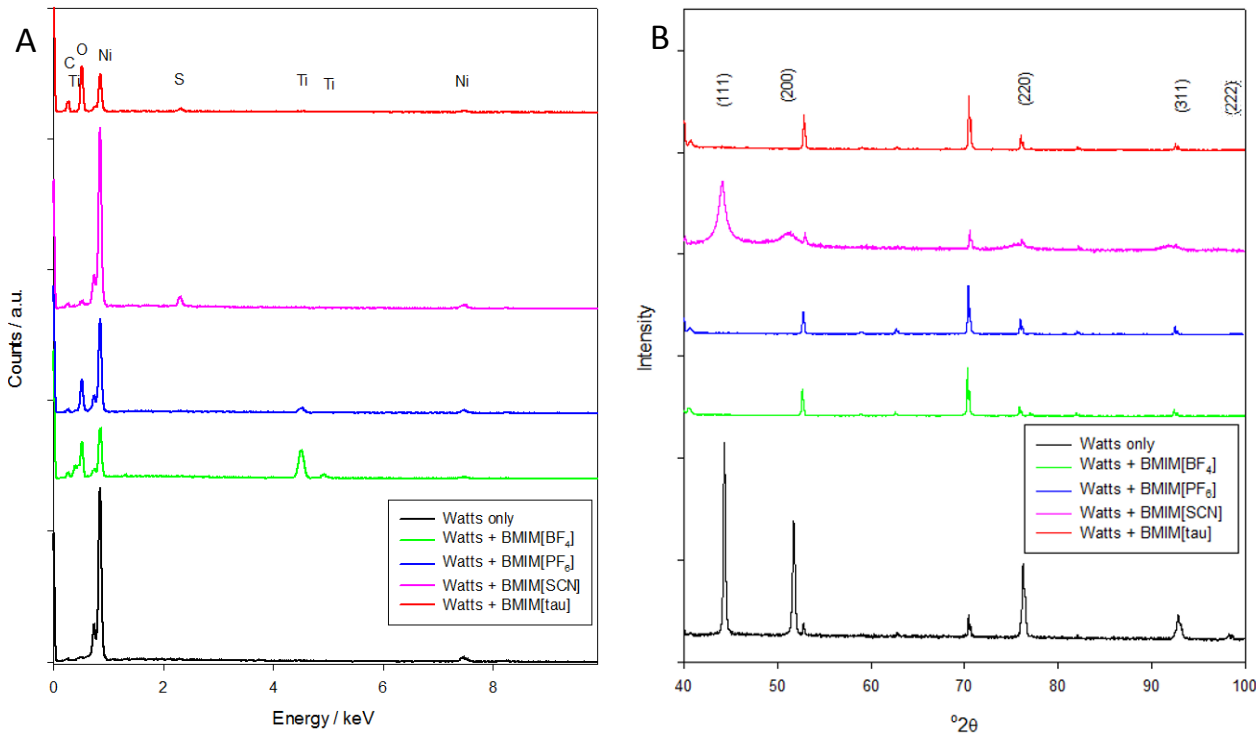
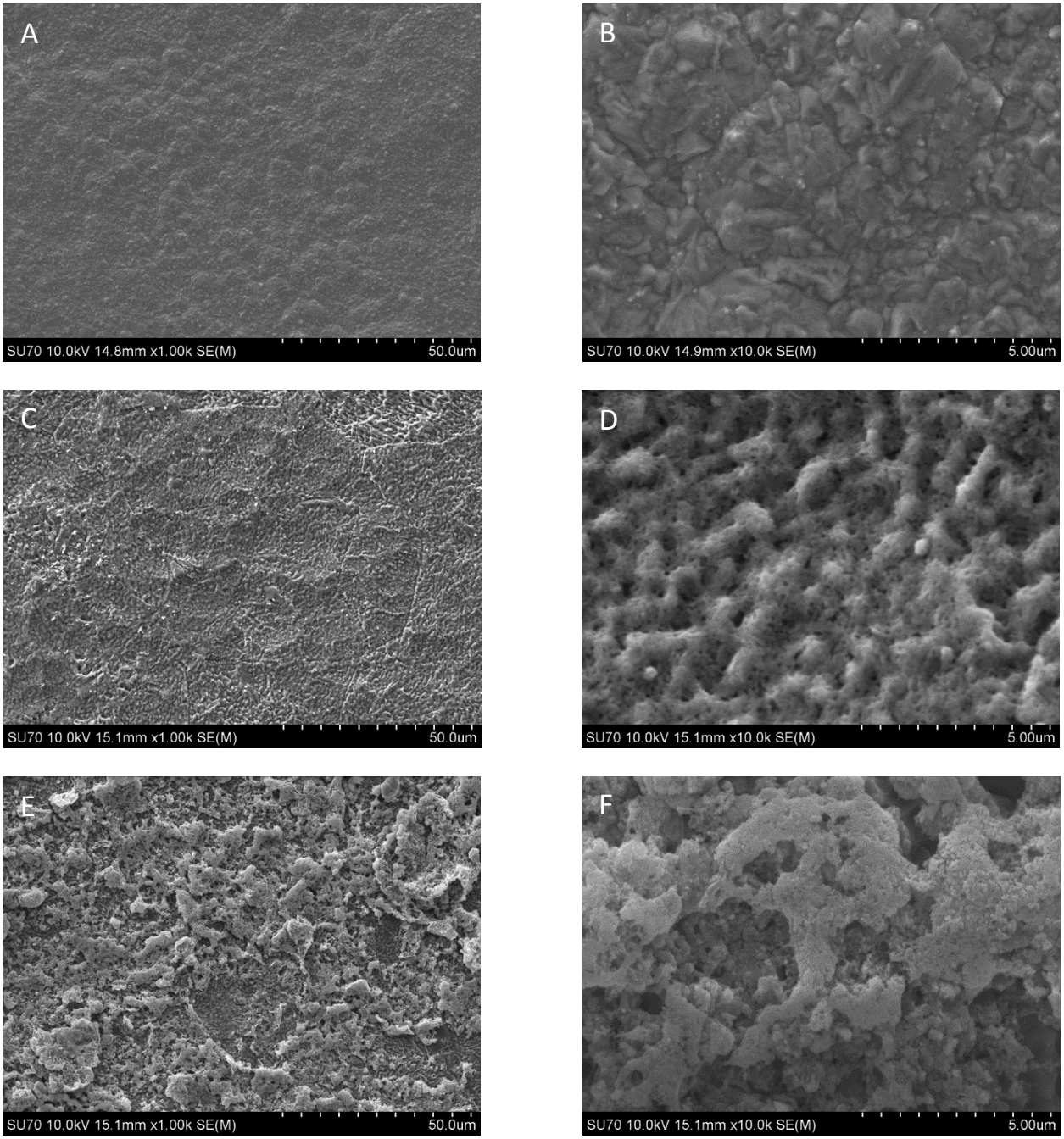
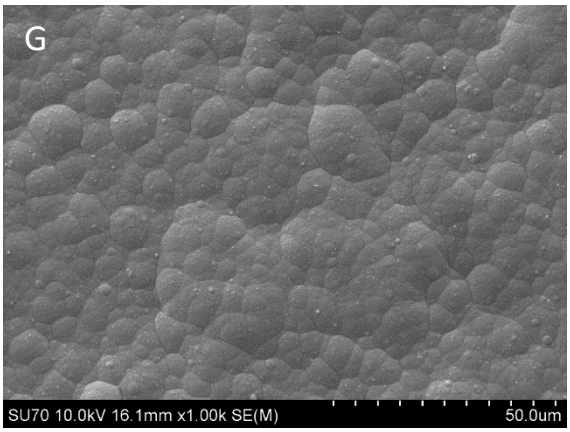
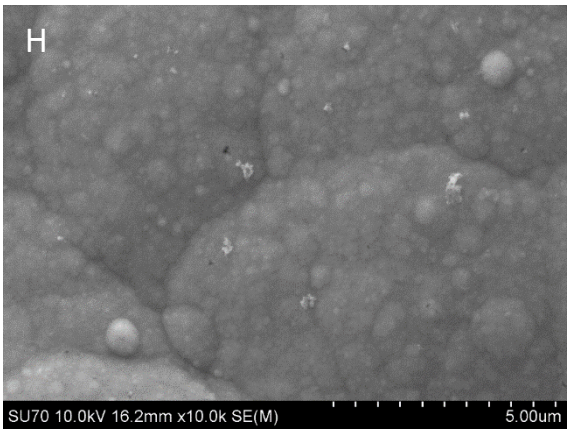
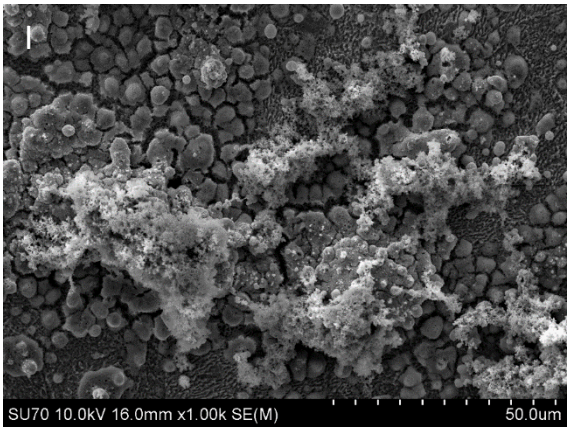


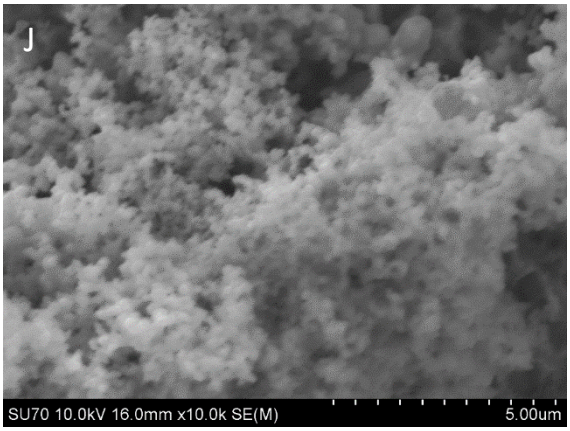
Figure 14: SEM images of two different magnifications of deposited nickel on titanium electrodes after the deposition process in A,B) Watts only; C,D) Watts + [bmim][BF_4]; E,F) Watts + [bmim][PF_6]; G,H) Watts + [bmim][SCN]; I,J) Watts + [bmim][tau]











4.3 Conclusions and Future Work

Overall the [bmim][SCN] additive resulted in the highest nickel deposition. However, all solutions provided successful dissolution. Future work would be to include additional ionic liquids to test with the Watt's solution as well as tuning the volume of ionic liquid to Watt's solution to find the optimal ratio to provide the best dissolution and deposition.

Chapter Five: Experimental

5.1 Experimental

5.1.1 General Experimental Techniques, Instrumentation and Materials

Analytical gas chromatography (GLC) was performed on a Hewlett Packard 5890 equipped with a flame ionization detector (FID) using a 30 m by 0.25 mm DB-5HT capillary column of (5% phenyl)methylpolysiloxane. The carrier gas was nitrogen with a flow rate of 2.0 mL/min and a column head pressure of 21 psi. The temperature program used was the following: initial temperature = 80°C, initial time = 5 minutes, rate = 10°C/minute, final temperature = 280°C, final time = 10 minutes. Gas chromatography-mass spectrometry (GCMS) was performed on a Hewlett Packard 5890 Series II gas chromatograph equipped with a 30 m by 0.25 mm Supelco SPB-5 capillary column. The carrier gas was helium with a linear velocity of 35cm/s at 80°C and a column head pressure of 15 psi. The temperature program used was the following: initial temperature = 80°C, initial time = 2 minutes, rate = 10°C/minute, final temperature = 280°C, final time = 15 minutes. The gas chromatograph was connected to a Micromass VG Autospec which measured the mass of samples between 52 and 510 mass units with a resolution of 3000 and an ionizing potential of 70 eV at 260°C and accelerating voltage of 7600 V. Mass spectral data are reported in the following fashion: parent ion (relative intensity), *m/e*of significant fragments.

Proton nuclear magnetic resonance (^{1}H NMR) spectra were measured on a Varian AS500 using the UNITYINOVA NMR spectrometer system, VNMR 6.1C software at room temperature unless otherwise stated. The solvent used was $CDCl_3$ unless otherwise stated. Chemical shifts are reported in parts per million (ppm) from an internal standard of tetramethylsilane (TMS). ^{13}C NMR spectra were also recorded using $CDCl_3$ as the solvent unless otherwise stated and TMS as the internal standard on the same spectrometer. The NMR

data are reported as follows: chemical shift (for ^{1}H NMR signals: multiplicity, coupling constant in Hertz, integration).

Infrared (IR) spectra were measured on a Perkin Elmer 1320 IR spectrometer with a resolution of 4 cm^{-1}. All spectra were determined without solvent (neat) unless otherwise noted, in the transmission mode using KBr plates and are reported as wavenumbers.

Optical rotations were measured on a Perkin Elmer Model 343 polarimeter with a sodium spectral lamp 93 122E. All measurements were taken at room temperature in a 1dm cell. Before each measurement, the polarimeter was zeroed with the solvent used to dilute the sample (dichloromethane).

All experiments were run under a positive pressure of nitrogen in flasks that were either flame or oven dried. Air and moisture sensitive reagents were transferred by syringe and introduced to the reaction flasks through rubber septa. Excess solvents were removed *in vacuo* at pressures obtained by a water aspirator drawing on a Buchi rotary evaporator. All compounds were stored at room temperature under atmospheric conditions unless noted otherwise. Tetrahydrofuran (THF) was rendered anhydrous by storing over 4Å molecular sieves. All other solvents were used as received.

Analytical thin layer chromatography (TLC) was performed on silica gel of 5-17 μm particle size, 60Å pore size, with a thickness of 250 μm, containing a 254 nm fluorescent indicator. The solvents used for chromatography are indicated in parentheses in the procedures and the relative concentrations are calculated by volume. Spots were viewed using ultraviolet light. Column chromatography was used to purify the reaction mixtures and was accomplished using 230-400 mesh silica gel unless otherwise stated and the solvent systems were determined by GC.

The SEM and EDS were carried out using a Hitachi SU-70. XRD spectra were recorded with PanAnalyticalXpert Pro Diffractometer with Ni filtered monochromatic Cu Kα (1.5406 Å, 2.2 KW Max.). Electrochemical experiments were done using VoltaLab 40 (PGZ301 &VoltaMaster 4) using a conventional one-compartment three- electrode cell.

All chemicals for which procedures are not listed were purchased from Aldrich. Compounds **1, 2, 3** and **4** and their monocyclic precursors were compared to previously reported literature values.[25] Compounds **5** and **6** were compared to previously reported literature values. [41] Compound **7** was compared to previously reported literature values. [42] Compound **8** was compared to recently reported literature values. [43]

5.2 Preparations

5.2.1 Experimental for Chapter Two

General Procedure for [1-butyl-3-methylimidazolium][L/D-Lactate]

Equimolar amounts of sodium L/D-lactate and 1-butyl-3-methylimidazolium chloride were combined in a heavy wall reaction flask with acetone and degassed by bubbling nitrogen through the solution for 30 seconds. The flask was sealed and heated to 50°C and allowed to stir for 24 hours. The product was filtered to remove sodium chloride and excess solvent was removed *in vacuo* to give a clear and colourless liquid.

General Procedure for [1-butyl-3-methylimidazolium][(1S/R)(+/-)-10-camphorsulfonate]

Equimolar amounts of (1S/R)(+/-)-10-camphorsulfonic acid and 1-butyl-3-methylimidazolium chloride were combined in a heavy wall reaction flask with acetone and degassed for 30 seconds. The flask was sealed and heated to 50°C and allowed to stir for 24 hours. Excess solvent was removed *in vacuo* to give a brown liquid.

1,6-dioxaspiro[4.4]nonane via 3-(4,5-dihydrofuran-2-yl)propan-1-ol

In a two-step reaction, dihydrofuran (378 µL, 5 mmol) in THF (2.0 mL) was cooled to -78°C under nitrogen atmosphere. Tert-butyl lithium in pentane (1.7 M, 3.0 mL, 5 mmol) was added dropwise. The mixture was allowed to warm to 0°C and stir for 30 minutes. Afterwards, the mixture was cooled again to -78°C and THF (3.0 mL),oxetane (650 µL, 10 mmol) and boron trifluoride diethyl etherate (634 µL, 5 mmol) were added dropwise. After the mixture stirred for 15 minutes at -78°C, triethylamine (2.0 mL) was added dropwise and the mixture was allowed to warm to room temperature. The mixture was filtered through aluminum oxide (activity 3, preconditioned with diethyl ether, 5% methanol/diethyl). Excess solvent was removed *in vacuo* to give a pale yellow liquid which was immediately used in the next step. No yield determined. Spectral data matched the literature report.[25]

General Method

p-Toluenesulphonic acid (0.0751 g, 0.4 mmol) was dissolved in THF (2.0 mL) and 3-(4,5-dihydrofuran-2-yl)propan-1-ol (0.0123 g, 0.1 mmol) was added. The mixture was allowed to stir at room temperature for 10 minutes. The mixture was then poured into saturated sodium bicarbonate, extracted with diethyl ether, washed with brine and dried over magnesium sulphate. Excess solvent was removed *in vacuo* to give 5.4 mg (43.9%) of **1** as a pale yellow liquid.

^{1}H NMR($CDCl_3$): δ 3.97-3.87 (m, 2H), 3.76-3.67 (m, 2H), 2.02-1.82 (m, 4H), 1.69-1.63 (m, 2H), 1.57-1.51 (m, 2H).

^{13}C NMR($CDCl_3$): δ 110.1, 67.4, 36.5, 19.5.

MS: 128.2, 71.1, 55.1, 43.1, exact mass calcd for $C_7H_{12}O_2$ *m/z* 128.1698, obsd *m/z* 128.2.

[α]: 0.93°

Ionic Liquid Method

Compound **1** was synthesized by adding3-(4,5-dihydrofuran-2-yl)propan-1-ol (0.0536 g, 0.4 mmol) to *p*-toluenesulphonic acid (0.1524 g, 0.8 mmol) dissolved in [1-butyl-3-methylimidazolium][L-lactate] (2.0 mL). The mixture was allowed to stir for 3 hours at room temperature. The mixture was then poured into saturated sodium bicarbonate, extracted with diethyl ether, washed with brine and dried over magnesium sulphate. Excess solvent was removed *in vacuo* to give 6.2 mg (12%) of **1** as a pale yellow liquid.

[α]: -5.47°

Compound **1** was synthesized by adding3-(4,5-dihydrofuran-2-yl)propan-1-ol (0.0573 g, 0.45 mmol)to *p*-toluenesulphonic acid (0.1731 g, 0.9 mmol) dissolved in [1-butyl-3-methylimidazolium][D-lactate] (2.0 mL). The mixture was allowed to stir for 3 hours at room temperature. The mixture was then poured into saturated sodium bicarbonate, extracted with diethyl ether, washed with brine and dried over magnesium sulphate. Excess solvent was removed *in vacuo* to give 4.7 mg (8.2%) of **1** as a pale yellow liquid.

[α]: -6.38°

Compound **1** was synthesized by adding 3-(4,5-dihydrofuran-2-yl)propan-1-ol (0.0550 g, 0.4 mmol)to *p*-toluenesulphonic acid (0.1584 g, 0.8 mmol) dissolved in [1-butyl-3-methylimidazolium][(1S)(+)-10-camphorsulphonate] (2.0 mL). The mixture was allowed to stir for 3 hours at room temperature. The mixture was then poured into saturated sodium bicarbonate, extracted with diethyl ether, washed with brine and dried over magnesium sulphate. Excess solvent was removed *in vacuo* to give 19.3 mg (35%) of **1** as a pale yellow liquid.

[α]: -0.78°

Compound **1** was synthesized by adding3-(4,5-dihydrofuran-2-yl)propan-1-ol (0.0537 g, 0.4 mmol) to *p*-toluenesulphonic acid (0.1550 g, 0.8 mmol) dissolved in [1-butyl-3-methylimidazolium][(1R)(-)-10-camphorsulphonate] (2.0 mL). The mixture was allowed to stir for 3 hours at room temperature. The mixture was then poured into saturated sodium bicarbonate, extracted with diethyl ether, washed with brine and dried over magnesium sulphate. Excess solvent was removed *in vacuo* to give 8.3 mg (15%) of **1** as a pale yellow liquid.

[α]: -1.20°

1,6-dioxaspiro[4.5]decane via 4-(3,4-dihydro-2H-pyran-6-yl)propan-1-ol

In a two-step reaction, 3,4-dihydro-2H-pyran (456 µL, 5 mmol) in THF (2.0 mL) was cooled to -78°C under nitrogen atmosphere. Tert-butyl lithium in pentane (1.7 M, 3.0 mL, 5 mmol) was added dropwise. The mixture was allowed to warm to 0°C and stir for 30 minutes. Afterwards, the mixture was cooled again to -78°C and THF (3.0 mL),oxetane (650 µL, 10 mmol) and boron trifluoride diethyl etherate (634 µL, 5 mmol) were added dropwise. After the mixture stirred for 15 minutes at -78°C, triethylamine (2.0 mL) was added dropwise and the mixture was allowed to warm to room temperature. The mixture was filtered through aluminum oxide (activity 3, preconditioned with diethyl ether, 5% methanol/diethyl ether). Excess solvent was removed *in vacuo* to give a pale yellow liquid which was purified by column chromatography (aluminum oxide column, activity 3, 20% ethyl acetate/hexanes) and then immediately used in the next step. No yield determined. Spectral data matched the literature report.[25]

General Method

p-Toluenesulphonic acid (0.1584 g, 0.8 mmol) was dissolved in THF (2.0 mL) and 4-(3,4-dihydro-2H-pyran-6-yl)propan-1-ol (0.0608 g, 0.4 mmol) was added. The mixture was allowed to stir at room temperature for 10 minutes. The mixture was then poured into saturated sodium bicarbonate, extracted with diethyl ether, washed with brine and dried over magnesium

sulphate. Excess solvent was removed *in vacuo* to give 10.1 mg (17%) of **2** as a pale yellow liquid.

^{1}H NMR($CDCl_3$): δ 3.97-3.91 (m, 1H), 3.88-3.85 (m, 1H), 3.78-3.73 (m, 1H), 3.62-3.58 (m, 1H), 2.02-1.82 (m, 3H), 1.68-1.58 (m, 2H), 1.56-1.38 (m, 4H), 1.30-1.22 (m, 1H).

^{13}C NMR($CDCl_3$): δ 103.8, 66.9, 61.7, 38.7, 34.3, 25.8, 23.8, 23.6.

MS: 142.2, 95.1, 71.1, 55.1, 43.1, exact mass calcd for $C_8H_{14}O_2$ *m/z* 142.1966, obsd *m/z* 142.2.

[α]: -1.49°

Ionic Liquid Method

Compound **2** was synthesized by adding 4-(3,4-dihydro-2H-pyran-6-yl)propan-1-ol (0.0523 g, 0.37 mmol) to *p*-toluenesulphonic acid (0.1354 g, 0.7 mmol) dissolved in [1-butyl-3-methylimidazolium][L-lactate] (2.0 mL). The mixture was allowed to stir for 3 hours. The mixture was then poured into saturated sodium bicarbonate, extracted with diethyl ether, washed with brine and dried over magnesium sulphate. Excess solvent was removed *in vacuo* to give 8.5 mg (16%) of **2** as a pale yellow liquid.

[α]: -5.10°

Compound **2** was synthesized by adding 4-(3,4-dihydro-2H-pyran-6-yl)propan-1-ol (0.0703 g, 0.5 mmol) to *p*-toluenesulphonic acid (0.1590 g, 0.8 mmol) dissolved in [1-butyl-3-methylimidazolium][D-lactate] (2.0 mL). The mixture was allowed to stir for 3 hours. The mixture was then poured into saturated sodium bicarbonate, extracted with diethyl ether, washed with brine and dried over magnesium sulphate. Excess solvent was removed *in vacuo* to give 9.4 mg (13%) of **2** as a pale yellow liquid.

[α]: -1.60°

Compound **2** was synthesized by adding 4-(3,4-dihydro-2H-pyran-6-yl)propan-1-ol (0.0609 g, 0.4 mmol) to *p*-toluenesulphonic acid (0.1415 g, 0.7 mmol) dissolved in [1-butyl-3-methylimidazolium][(1S)(+)-10-camphorsulphonate] (2.0 mL). The mixture was allowed to stir for 3 hours. The mixture was then poured into saturated sodium bicarbonate, extracted with diethyl ether, washed with brine and dried over magnesium sulphate. Excess solvent was removed *in vacuo* to give 20 mg (33%) of **2** as a pale yellow liquid.

[α]:-2.25°

Compound **2** was synthesized by adding 4-(3,4-dihydro-2H-pyran-6-yl)propan-1-ol (0.0563 g, 4 mmol) to *p*-toluenesulphonic acid (0.7 mmol) dissolved in [1-butyl-3-methylimidazolium][(1R)(-)-10-camphorsulphonate] (2.0 mL). The mixture was allowed to stir for 3 hours. The mixture was then poured into saturated sodium bicarbonate, extracted with diethyl ether, washed with brine and dried over magnesium sulphate. Excess solvent was removed *in vacuo* to give 14 mg (25%) of **2** as a pale yellow liquid.

[α]:-1.43°

<u>1,6-dioxaspiro[4.5]decane via 3-(4,5-dihydrofuran-2-yl)butan-1-ol</u>

In a two-step reaction, dihydrofuran (378 µL, 5 mmol) in THF (2.0 mL) was cooled to -78°C under nitrogen atmosphere. Tert-butyl lithium in pentane (1.7 M, 3.0 mL, 5 mmol) was added dropwise. The mixture was allowed to warm to 0°C and stir for 30 minutes. Afterwards, the mixture was cooled again to -78°C and tert-butyl(4-iodo-butoxy)dimethylsilane (1.29 mL, 5 mmol) in THF (2.0 mL) was added dropwise. After the mixture stirred for 15 minutes at -78°C, distilled water (10.0 mL) was added dropwise and the mixture was allowed to warm to room temperature. The mixture was extracted with hexanes, washed with distilled water and brine and dried over magnesium sulphate. The product was filtered and excess solvent was removed *in vacuo* to give a pale yellow liquid which was purified by column chromatography (aluminum

oxide column, activity 3, 20% ethyl acetate/hexanes). Cesium fluoride (1.1550 g, 7.5 mmol) in THF (7.5 mL) was added and allowed to stir overnight. The product was then extracted with diethyl ether, washed with brine and filtered through celite (100% diethyl ether). Excess solvent was removed *in vacuo* and the product was immediately used in the next step. No yield determined. Spectral data matched the literature report.[25]

General Method

p-Toluenesulphonic acid (0.1507 g, 0.8 mmol) was dissolved in THF (2.0 mL) and 3-(4,5-dihydrofuran-2-yl)butan-1-ol (0.0637 g, 0.4 mmol) was added. The mixture was allowed to stir at room temperature for 10 minutes. The mixture was then poured into saturated sodium bicarbonate, extracted with diethyl ether, washed with brine and dried over magnesium sulphate. Excess solvent was removed *in vacuo* to give 32.7 mg (51%) of **3** as a pale yellow liquid.

^{1}H NMR($CDCl_3$): δ 3.97-3.91 (m, 1H), 3.88-3.85 (m, 1H), 3.78-3.73 (m, 1H), 3.62-3.58 (m, 1H), 2.02-1.82 (m, 3H), 1.68-1.58 (m, 2H), 1.56-1.38 (m, 4H), 1.30-1.22 (m, 1H).

^{13}C NMR($CDCl_3$): δ 103.8, 66.9, 61.7, 38.7, 34.3, 25.8, 23.8, 23.6.

MS: 143.2, 101.1, 71.1, 55.1, 43.1, exact mass calcd for $C_8H_{14}O_2$ *m/z* 142.1966, obsd *m/z* 143.2.

[α]:-2.40°

Ionic Liquid Method

Compound **3** was synthesized by adding 3-(4,5-dihydrofuran-2-yl)butan-1-ol (0.0520 g, 0.4 mmol) to *p*-toluenesulphonic acid (0.1271 g, 0.7 mmol) dissolved in [1-butyl-3-methylimidazolium][L-lactate] (2.0 mL). The mixture was allowed to stir for 3 hours. The mixture

was then poured into saturated sodium bicarbonate, extracted with diethyl ether, washed with brine and dried over magnesium sulphate. Excess solvent was removed *in vacuo* to give 5.7 mg (11%) of **3** as a pale yellow liquid.

[α]:-2.28°

Compound **3** was synthesized by adding 3-(4,5-dihydrofuran-2-yl)butan-1-ol (0.0620 g, 0.4 mmol) to *p*-toluenesulphonic acid (0.1434 g, 0.8 mmol) dissolved in [1-butyl-3-methylimidazolium][D-lactate] (2.0 mL). The mixture was allowed to stir for 3 hours. The mixture was then poured into saturated sodium bicarbonate, extracted with diethyl ether, washed with brine and dried over magnesium sulphate. Excess solvent was removed *in vacuo* to give 20.6 mg (33%) of **3** as a pale yellow liquid.

[α]:+0.49°

Compound **3** was synthesized by adding 3-(4,5-dihydrofuran-2-yl)butan-1-ol (0.0635 g, 0.4 mmol) to *p*-toluenesulphonic acid (0.1554 g, 8.0 mmol) dissolved in [1-butyl-3-methylimidazolium][(1S)(+)-10-camphorsulphonate] (2.0 mL). The mixture was allowed to stir for 3 hours. The mixture was then poured into saturated sodium bicarbonate, extracted with diethyl ether, washed with brine and dried over magnesium sulphate. Excess solvent was removed *in vacuo* to give 14.3 mg (23%) of **3** as a pale yellow liquid.

[α]:-3.50°

Compound **3** was synthesized by adding 3-(4,5-dihydrofuran-2-yl)butan-1-ol (0.0614 g, 0.4 mmol) to *p*-toluenesulphonic acid (0.1504 g, 0.8 mmol) dissolved in [1-butyl-3-methylimidazolium][(1R)(-)-10-camphorsulphonate] (2.0 mL). The mixture was allowed to stir for 3 hours. The mixture was then poured into saturated sodium bicarbonate, extracted with diethyl

ether, washed with brine and dried over magnesium sulphate. Excess solvent was removed *in vacuo* to give 9.7 mg (16%) of **3** as a pale yellow liquid.

[α]:-3.09°

1,7-dioxaspiro[5.5]undecane via 4-(3,4-dihydro-2H-pyran-6-yl)butan-1-ol

In a two-step reaction, 3,4-dihydro-2H-pyran (456 µL, 5 mmol) in THF (2.0 mL) was cooled to -78°C under nitrogen atmosphere. Tert-butyl lithium in pentane (1.7 M, 3.0 mL, 5 mmol) was added dropwise. The mixture was allowed to warm to 0°C and stir for 30 minutes. Afterwards, the mixture was cooled again to -78°C and tert-butyl(4-iodo-butoxy)dimethylsilane (1.29 mL, 5 mmol) in THF (2.0 mL) was added dropwise. After the mixture stirred for 15 minutes at -78°C, distilled water (10.0 mL) was added dropwise and the mixture was allowed to warm to room temperature. The mixture was extracted with hexanes, washed with distilled water and brine and dried over magnesium sulphate. The product was filtered and excess solvent was removed *in vacuo* to give a pale yellow liquid which was purified by column chromatography (aluminum oxide column, activity 3, 20% ethyl acetate/hexanes). Tetra-n-butylammonium fluoride (1.8152 g, 7 mmol) in THF (7.5 mL) was added and allowed to stir overnight. The product was then extracted with diethyl ether, washed with brine and filtered through celite (100% diethyl ether). Excess solvent was removed *in vacuo* and the product was immediately used in the next step. No yield determined. Spectral data matched the literature report.[25]

General Method

p-Toluenesulphonic acid (0.1497 g, 0.8 mmol) was dissolved in THF (2.0 mL) and 4-(3,4-dihydro-2H-pyran-6-yl)butan-1-ol (0.0581 g, 0.4 mmol) was added. The mixture was allowed to stir at room temperature for 10 minutes. The mixture was then poured into saturated sodium bicarbonate, extracted with diethyl ether, washed with brine and dried over magnesium

sulphate. Excess solvent was removed *in vacuo* to give 18.2 mg (31%) of **4** as a pale yellow liquid.

^{1}H NMR($CDCl_3$): δ 3.69-3.66 (m, 2H), 3.60-3.53 (m, 2H), 2.05-1.91 (m, 2H), 1.68-1.60 (m, 2H), 1.51-1.30 (m, 6H), 1.26-1.23 (m, 2H).

^{13}C NMR($CDCl_3$): δ 94.9, 60.3, 35.7, 25.6, 18.5.

MS: 156.2, 111.1, 101.1, 83.1, 55.1, 41.1, exact mass calcd for $C_9H_{16}O_2$ *m/z* 156.2234, obsd *m/z* 156.2.

[α]:-0.82°

Ionic Liquid Method

Compound **4** was synthesized by adding 4-(3,4-dihydro-2H-pyran-6-yl)butan-1-ol (0.0583 g, 0.4 mmol) to *p*-toluenesulphonic acid (0.1747 g, 0.9 mmol) dissolved in [1-butyl-3-methylimidazolium][L-lactate] (2.0 mL). The mixture was allowed to stir for 3 hours. The mixture was then poured into saturated sodium bicarbonate, extracted with diethyl ether, washed with brine and dried over magnesium sulphate. Excess solvent was removed *in vacuo* to give 18.9 mg (32%) of **4** as a pale yellow liquid.

[α]:-1.32°

Compound **4** was synthesized by adding 4-(3,4-dihydro-2H-pyran-6-yl)butan-1-ol (0.0587 g, 0.4 mmol) to *p*-toluenesulphonic acid (0.1515 g, 0.8 mmol) dissolved in [1-butyl-3-methylimidazolium][D-lactate] (2.0 mL). The mixture was allowed to stir for 3 hours. The mixture was then poured into saturated sodium bicarbonate, extracted with diethyl ether, washed with brine and dried over magnesium sulphate. Excess solvent was removed *in vacuo* to give 4.1mg (7%) of **4** as a pale yellow liquid.

[α]:-3.66°

Compound **4** was synthesized by adding 4-(3,4-dihydro-2H-pyran-6-yl)butan-1-ol (0.0604 g, 0.4 mmol) to *p*-toluenesulphonic acid (0.1650 g, 0.8 mmol) dissolved in [1-butyl-3-methylimidazolium][(1S)(+)-10-camphorsulphonate] (2.0 mL). The mixture was allowed to stir for 3 hours. The mixture was then poured into saturated sodium bicarbonate, extracted with diethyl ether, washed with brine and dried over magnesium sulphate. Excess solvent was removed *in vacuo* to give 23.3 mg (38%) of **4** as a pale yellow liquid.

[α]:-6.25°

Compound **4**was synthesized by adding 4-(3,4-dihydro-2H-pyran-6-yl)butan-1-ol (0.0587 g, 0.4 mmol) to *p*-toluenesulphonic acid (0.1570 g, 0.8 mmol) dissolved in [1-butyl-3-methylimidazolium][(1R)(-)-10-camphorsulphonate] (2.0 mL). The mixture was allowed to stir for 3 hours. The mixture was then poured into saturated sodium bicarbonate, extracted with diethyl ether, washed with brine and dried over magnesium sulphate. Excess solvent was removed *in vacuo* to give 10.4 mg (18%) of **4** as a pale yellow liquid.

[α]:-2.88°

5.2.2 Experimental for Chapter Three

4-hydroxy-2-(*p*-nitrophenyl)butanenitrile

In a two-step reaction, 4-nitrophenol (0.2807 g, 2 mmol), bromobutyronitrile (0.199 mL, 0.296 g, 2 mmol) and potassium carbonate (0.3050 g, 2.2 mmol) were combined in acetone (3 mL). The mixture was allowed to stir and reflux at 65°C for 24 h. TLC was used to determine complete reaction of the phenol. Distilled water (5 mL) was added and the mixture was extracted with

ether, washed with sodium hydroxide and dried over magnesium sulphate. Excess solvent was removed *in vacuo* to give a pale yellow liquid which was immediately used in the next step. No yield was determined.

General Method

3-butyronitrile (4-nitro)phenol ether (0.2095 g, 1.0 mmol) in THF (1.0 mL) was added to a suspension of sodium hydride (1.1 mmol) in THF (3.0 mL). The mixture was allowed to stir at -5°C for 30 minutes and then allowed to warm up to room temperature. The reaction was quenched with distilled water (3.0 mL), extracted with ether, washed with saturated sodium bicarbonate and dried over magnesium sulphate. Excess solvent was removed *in vacuo* to give 165.8 mg (80%) of **5** as a pale yellow liquid.

IR(neat): 3424.45, 2220, 1593.50, 1512, 1343.

^{1}H NMR($CDCl_3$): δ 8.22 (d, J= 5.6 Hz, 2H), 6.96 (d, J= 5.6 Hz, 2H), 4.19 (t, J= 4.4 Hz, 2H), 2.63 (t, J= 5.2 Hz, 2H), 2.2 (m, 2H).

^{13}C NMR($CDCl_3$): δ 163.2, 141.0, 126.0, 118.7, 114.4, 66.0, 25.2, 14.2.

MS: 206.2, 139.1, 109.1, 93.1, 65.1, 41.1, exact mass calcd for $C_{10}H_{10}N_2O_3$ *m/z* 206.0212, obsd *m/z* 206.2.

[α]: -0.56°

Ionic Liquid Method

Compound **5** was synthesized by adding the phenol ether (0.2415g, 1.1 mmol) to sodium hydride (1.1 mmol) dissolved in [1-butyl-3-methylimidazolium][L-lactate] (2.0 mL). The mixture was allowed to stir for 1 hour before warming up to room temperature. The reaction was quenched with distilled water (3.0 mL), extracted with ether, washed with saturated sodium

bicarbonate and dried over magnesium sulphate. Excess solvent was removed *in vacuo* to give 0.1289 g (53%) of **5** as a pale yellow liquid.

[α]:-7.84°

Compound **5** was synthesized by adding the phenol ether (0.2115 g, 1.0 mmol) to sodium hydride (1.1 mmol) dissolved in [1-butyl-3-methylimidazolium][D-lactate] (2.0 mL). The mixture was allowed to stir for 1 hour before warming up to room temperature. The reaction was quenched with distilled water (3.0 mL), extracted with ether, washed with saturated sodium bicarbonate and dried over magnesium sulphate. Excess solvent was removed *in vacuo* to give 27.2 mg (13%) of **5** as a pale yellow liquid.

[α]:+1.09°

Compound **5** was synthesized by adding the phenol ether (0.2714 g, 1.3 mmol) to sodium hydride (1.1 mmol) dissolved in [1-butyl-3-methylimidazolium][(1S)(+)-10-camphorsulphonate] (2.0 mL). The mixture was allowed to stir for 1 hour before warming up to room temperature. The reaction was quenched with distilled water (3.0 mL), extracted with ether, washed with saturated sodium bicarbonate and dried over magnesium sulphate. Excess solvent was removed *in vacuo* to give 28.2 mg (10%) of **5** as a pale yellow liquid.

[α]:-5.43°

Compound **5** was synthesized by adding the phenol ether (0.2768, 1.3 mmol) to sodium hydride (1.1 mmol) dissolved in [1-butyl-3-methylimidazolium][(1R)(-)-10-camphorsulphonate] (2.0 mL). The mixture was allowed to stir for 1 hour before warming up to room temperature. The reaction was quenched with distilled water (3.0 mL), extracted with ether, washed with saturated sodium bicarbonate and dried over magnesium sulphate. Excess solvent was removed *in vacuo* to give 32.4 mg (12%) of **5** as a pale yellow liquid.

[α]:-3.75°

5-hydroxy-2-(*p*-nitrophenyl)pentanenitrile

In a two-step reaction, 4-nitrophenol (0.2796 g, 2 mmol), 5-chlorovaleronitrile (0.225 mL, 0.2351 g, 2 mmol) and potassium carbonate (0.3080 g, 2.2 mmol) were combined in acetone (3 mL). The mixture was allowed to stir and reflux at 65°C for 24 h. TLC was used to determine complete reaction of the phenol. Distilled water (5 mL) was added and the mixture was extracted with ether, washed with sodium hydroxide and dried over magnesium sulphate. Excess solvent was removed *in vacuo* to give a pale yellow liquid which was immediately used in the next step.

General Method

The phenol ether (0.2703 g, 1.2 mmol) in THF (1.0 mL) was added to a suspension of sodium hydride (1.1 mmol) in THF (3.0 mL). The mixture was allowed to stir at -5°C for 30 minutes and then allowed to warm up to room temperature. The reaction was quenched with distilled water (3.0 mL), extracted with ether, washed with saturated sodium bicarbonate and dried over magnesium sulphate. Excess solvent was removed *in vacuo* to give 180 mg (67%) of **6** as a pale yellow liquid.

IR(neat): 3423.91, 1639, 1512, 1340.

^{1}H NMR($CDCl_3$): δ 8.21 (d, J= 7.6 Hz, 2H), 6.95 (d, J= 7.6 Hz, 2H), 4.19 (t, J=4.5 Hz, 2H), 2.47 (t, J= 5.6 Hz, 1H), 1.89 (m, 5H).

^{13}C NMR($CDCl_3$): δ 125.9, 119.2, 114.4, 67.5, 43.7, 31.0, 22.7, 16.6.

MS: 219.01, 139.1, 109.1, 82.2, 55.1, exact mass calcd for $C_{11}H_{12}N_2O_3$ *m/z* 219.029, obsd *m/z* 219.01.

[α]:-1.54°

Ionic Liquid Method

Compound **6** was synthesized by adding the phenol ether (0.2276 g, 1.0 mmol) to sodium hydride (1.1 mmol) dissolved in [1-butyl-3-methylimidazolium][L-lactate] (2.0 mL). The mixture was allowed to stir for 1 hour before warming up to room temperature. The reaction was quenched with distilled water (3.0 mL), extracted with ether, washed with saturated sodium bicarbonate and dried over magnesium sulphate. Excess solvent was removed *in vacuo* to give 97.5 mg (43%) of **6** as a pale yellow liquid.

[α]:+1.49°

Compound **6** was synthesized by adding the phenol ether (0.2298 g, 1.0 mmol) to sodium hydride (1.1 mmol) dissolved in [1-butyl-3-methylimidazolium][D-lactate] (2.0 mL). The mixture was allowed to stir for 1 hour before warming up to room temperature. The reaction was quenched with distilled water (3.0 mL), extracted with ether, washed with saturated sodium bicarbonate and dried over magnesium sulphate. Excess solvent was removed *in vacuo* to give 13.5 mg (6%) of **6** as a pale yellow liquid.

[α]:+1.54°

Compound **6** was synthesized by adding the phenol ether (0.2520 g, 1.2 mmol) to sodium hydride (1.1 mmol) dissolved in [1-butyl-3-methylimidazolium][(1S)(+)-10-camphorsulphonate] (2.0 mL). The mixture was allowed to stir for 1 hour before warming up to room temperature. The reaction was quenched with distilled water (3.0 mL), extracted with ether, washed with saturated sodium bicarbonate and dried over magnesium sulphate. Excess solvent was removed *in vacuo* to give 19.2 mg (8%) of **6** as a pale yellow liquid.

[α]:+4.55°

Compound **6** was synthesized by adding the phenol ether (0.2275 g, 1.0 mmol) to sodium hydride (1.1 mmol) dissolved in [1-butyl-3-methylimidazolium][(1R)(-)-10-camphorsulphonate] (2.0 mL). The mixture was allowed to stir for 1 hour before warming up to room temperature. The reaction was quenched with distilled water (3.0 mL), extracted with ether, washed with saturated sodium bicarbonate and dried over magnesium sulphate. Excess solvent was removed *in vacuo* to give 12.0 mg (5%) of **6** as a pale yellow liquid.

[α]:-2.50°

Ethyl 4-hydroxy-2-(*p*-nitrophenyl)butanoate

In a two-step reaction, 4-nitrophenol (0.3545 g, 2.5 mmol), ethyl 5-bromovalerate (0.400 mL, 0.5284 g, 2.5 mmol) and potassium carbonate (0.3814 g, 2.8 mmol) were combined in acetone (3 mL). The mixture was allowed to stir and reflux at 65°C for 24 h. TLC was used to determine complete reaction of the phenol. Distilled water (5 mL) was added and the mixture was extracted with ether, washed with sodium hydroxide and dried over magnesium sulphate. Excess solvent was removed *in vacuo* to give a pale yellow liquid which was immediately used in the next step.

General Method

The phenol ether (0.2680 g, 1.1 mmol) in THF (1.0 mL) was added to a suspension of sodium hydride (1.1 mmol) in THF (3.0 mL). The mixture was allowed to stir at -5°C for 30 minutes and then allowed to warm up to room temperature. The reaction was quenched with distilled water (3.0 mL), extracted with ether, washed with saturated sodium bicarbonate and dried over magnesium sulphate. Excess solvent was removed *in vacuo* to give 229.2 mg (86%) of **7** as a pale yellow liquid.

IR(neat): 3424.02, 3056.45, 2986.80, 1727.65, 1609.33, 1594.63, 1514.95, 1342.19.

^{1}H NMR($CDCl_3$): δ 8.20 (d, J= 8.3 Hz, 2H), 6.94 (d, J= 8.4 Hz, 2H), 4.15 (q, J=5.6 Hz, 2H), 4.11 (t, J= 4.8 Hz, 2H), 2.53 (t, J= 5.6 Hz, 1H), 2.16 (m, 2H), 1.27 (t, J= 5.2 Hz, 3H).

^{13}C NMR($CDCl_3$): δ 172.9, 163.8, 141.5, 125.9, 114.4, 67.6, 60.6, 30.5, 24.3, 14.2.

MS: 253.0, 208.2, 115.1, 87.1, 69.2, 45.1, 43.1, exact mass calcd for $C_{12}H_{15}NO_5$ *m/z* 253.095, obsd *m/z* 253.0.

[α]:-2.24°

Ionic Liquid Method

Compound **7** was synthesized by adding the phenol ether (0.2711 g, 1.1 mmol) to sodium hydride (1.1 mmol) dissolved in [1-butyl-3-methylimidazolium][L-lactate] (2.0 mL). The mixture was allowed to stir for 1 hour before warming up to room temperature. The reaction was quenched with distilled water (3.0 mL), extracted with ether, washed with saturated sodium bicarbonate and dried over magnesium sulphate. Excess solvent was removed *in vacuo* to give 0.1407 g (52%) of **7** as a pale yellow liquid.

[α]:+1.64°

Compound **7** was synthesized by adding the phenol ether (0.2695 g, 1.1 mmol) to sodium hydride (1.1 mmol) dissolved in [1-butyl-3-methylimidazolium][D-lactate] (2.0 mL). The mixture was allowed to stir for 1 hour before warming up to room temperature. The reaction was quenched with distilled water (3.0 mL), extracted with ether, washed with saturated sodium bicarbonate and dried over magnesium sulphate. Excess solvent was removed *in vacuo* to give 98.9 mg (37%) of **7** as a pale yellow liquid.

[α]:-1.39°

Compound **7** was synthesized by adding the phenol ether (0.2767 g, 1.1 mmol) to sodium hydride (1.1 mmol) dissolved in [1-butyl-3-methylimidazolium][(1S)(+)-10-camphorsulphonate] (2.0 mL). The mixture was allowed to stir for 1 hour before warming up to room temperature. The reaction was quenched with distilled water (3.0 mL), extracted with ether, washed with saturated sodium bicarbonate and dried over magnesium sulphate. Excess solvent was removed *in vacuo* to give 6.2 mg (2%) of **7** as a pale yellow liquid.

[α]:+2.42°

Compound **7** was synthesized by adding the phenol ether (0.2773 g, 1.1 mmol) to sodium hydride (1.1 mmol) dissolved in [1-butyl-3-methylimidazolium][(1R)(-)-10-camphorsulphonate] (2.0 mL). The mixture was allowed to stir for 1 hour before warming up to room temperature. The reaction was quenched with distilled water (3.0 mL), extracted with ether, washed with saturated sodium bicarbonate and dried over magnesium sulphate. Excess solvent was removed *in vacuo* to give 17.0 mg (6%) of **7** as a pale yellow liquid.

[α]:-0.71°

Ethyl 5-hydroxy-2-(*p*-nitrophenyl)pentanoate

In a two-step reaction, 4-nitrophenol (0.2817 g, 2 mmol), ethyl 4-bromobutyrate (0.286 mL, 0.3898 g, 2 mmol) and potassium carbonate (0.3113 g, 2.2 mmol) were combined in acetone (3 mL). The mixture was allowed to stir and reflux at 65°C for 24 h. TLC was used to determine complete reaction of the phenol. Distilled water (5 mL) was added and the mixture was extracted with ether, washed with sodium hydroxide and dried over magnesium sulphate. Excess solvent was removed *in vacuo* to give a pale yellow liquid which was immediately used in the next step.

General Method

The phenol ether (0.2552 g, 1 mmol) in THF (1.0 mL) was added to a suspension of sodium hydride (1.1 mmol) in THF (3.0 mL). The mixture was allowed to stir at -5°C for 30 minutes and then allowed to warm up to room temperature. The reaction was quenched with distilled water (3.0 mL), extracted with ether, washed with saturated sodium bicarbonate and dried over magnesium sulphate. Excess solvent was removed *in vacuo* to give 174.8 mg (68%) of **8** as a pale yellow liquid.

IR(neat): 3424.02, 3056.45, 2986.80, 1727.65, 1609.33, 1594.63, 1514.95, 1342.19.

^{1}H NMR($CDCl_3$): δ 8.14 (d, J= 8.3 Hz, 2H), 6.94 (d, J= 8.4 Hz, 2H), 4.14 (q, J=5.6 Hz, 2H), 4.07 (t, J= 4.8 Hz, 2H), 2.40 (t, J= 5.2 Hz, 2H), 1.85 (m, 4H), 1.26 (t, J= 6.0 Hz, 3H).

^{13}C NMR($CDCl_3$): δ 173.3, 164.0, 141.8, 125.9, 114.4, 68.3, 60.5, 33.8, 28.4, 21.5, 14.3.

MS: 267.0, 222.2, 129.2, 101.1, 83.3, 59.1, 55.1, exact mass calcd for $C_{13}H_{17}NO_5$ *m/z* 267.029907, obsd *m/z* 267.0.

[α]:-0.65°

Ionic Liquid Method

Compound **8** was synthesized by adding the phenol ether (0.2356 g, 0.9 mmol) to sodium hydride (1.1 mmol) dissolved in [1-butyl-3-methylimidazolium][L-lactate] (2.0 mL). The mixture was allowed to stir for 1 hour before warming up to room temperature. The reaction was quenched with distilled water (3.0 mL), extracted with ether, washed with saturated sodium bicarbonate and dried over magnesium sulphate. Excess solvent was removed *in vacuo* to give 61.2 mg (26%) of **8** as a pale yellow liquid.

[α]:+3.23°

Compound **8** was synthesized by adding the phenol ether (0.2038 g, 7.6 mmol) to sodium hydride (1.1 mmol) dissolved in [1-butyl-3-methylimidazolium][D-lactate] (2.0 mL). The mixture was allowed to stir for 1 hour before warming up to room temperature. The reaction was quenched with distilled water (3.0 mL), extracted with ether, washed with saturated sodium bicarbonate and dried over magnesium sulphate. Excess solvent was removed *in vacuo* to give 81.9 mg (40%) of **8** as a pale yellow liquid.

[α]:-2.99°

Compound **8** was synthesized by adding the phenol ether (0.2700 g, 1.0 mmol) to sodium hydride (1.1 mmol) dissolved in [1-butyl-3-methylimidazolium][(1S)(+)-10-camphorsulphonate] (2.0 mL). The mixture was allowed to stir for 1 hour before warming up to room temperature. The reaction was quenched with distilled water (3.0 mL), extracted with ether, washed with saturated sodium bicarbonate and dried over magnesium sulphate. Excess solvent was removed *in vacuo* to give 60.0 mg (22%) of **8** as a pale yellow liquid.

[α]:+5.00°

Compound **8** was synthesized by adding the phenol ether (0.2688 g, 1.0 mmol) to sodium hydride (1.1 mmol) dissolved in [1-butyl-3-methylimidazolium][(1R)(-)-10-camphorsulphonate] (2.0 mL). The mixture was allowed to stir for 1 hour before warming up to room temperature. The reaction was quenched with distilled water (3.0 mL), extracted with ether, washed with saturated sodium bicarbonate and dried over magnesium sulphate. Excess solvent was removed *in vacuo* to give 55.2 mg (21%) of **8** as a pale yellow liquid.

[α]:-0.59°

5.2.3 Experimental for Chapter Four

[1-butyl-3-methylimidazolium][tetrafluoroborate]

1-butyl-3-methylimidazolium chloride (1.7980 g, 10 mmol) was combined with sodium tetrafluoroborate (1.1116 g, 10 mmol) and acetone (2 mL) in a heavy wall reaction vial. The vial was degassed and heated at 100°C and allowed to stir for 24 h. The product was filtered and excess solvent was removed *in vacuo* to give 2.16g (93%) of the product as a viscous pale yellow liquid.

^{1}H NMR($CDCl_3$): δ 9.36 (s, 1H), 7.44 (s, 1H), 7.39 (s, 1H), 4.34 (t, J= 3.2 Hz, 2H), 4.12 (s, 3H), 1.89 (m, 2H), 1.31 (m, 2H), 0.98 (t, J= 2.4 Hz, 3H).

[1-butyl-3-methylimidazolium][hexafluorophosphate]

1-butyl-3-methylimidazolium chloride (1.7793 g, 10 mmol) was combined with potassium hexafluorophosphate (1.8713 g, 10 mmol) and acetone (2 mL) in a heavy wall reaction vial. The vial was degassed and heated at 100°C and allowed to stir for 24 h. The product was filtered and excess solvent was removed *in vacuo* to give 2.765 g (96%) of the product as a viscous pale yellow liquid.

^{1}H NMR($CDCl_3$): δ 9.36 (s, 1H), 7.44 (s, 1H), 7.39 (s, 1H), 4.34 (t, J= 3.2 Hz, 2H), 4.12 (s, 3H), 1.89 (m, 2H), 1.31 (m, 2H), 0.98 (t, J= 2.4 Hz, 3H).

[1-butyl-3-methylimidazolium][thiocyanate]

1-butyl-3-methylimidazolium chloride (1.8760 g, 10.5 mmol) was combined with sodium thiocyanate (0.8576 g, 10.5 mmol) and acetone (2 mL) in a heavy wall reaction vial. The vial was degassed and heated at 100°C and allowed to stir for 24 h. The product was filtered and

excess solvent was removed *in vacuo* to give 2.020g (97%) of the ionic liquid as a viscous pale yellow liquid.

^{1}H NMR($CDCl_3$): δ 9.36 (s, 1H), 7.44 (s, 1H), 7.39 (s, 1H), 4.34 (t, J= 3.2 Hz, 2H), 4.12 (s, 3H), 1.89 (m, 2H), 1.31 (m, 2H), 0.98 (t, J= 2.4 Hz, 3H).

[1-butyl-3-methylimidazolium][taurinate]

1-butyl-3-methylimidazolium chloride (1.7585 g, 10 mmol) was combined with sodium taurinate

(1.5810 g, 10.5 mmol) and acetone (2 mL) in a heavy wall reaction vial. The vial was degassed and heated at 100°C and allowed to stir for 24 h. The product was filtered and excess solvent was removed *in vacuo* to give the ionic liquid as a viscous pale yellow liquid. No yield determined.

^{1}H NMR($CDCl_3$): δ 10.2 (s, 1H), 7.45 (d, J= 5.2 Hz, 1H), 7.34 (d, J= 5.2 Hz, 1H), 4.35 (t, J= 7.3 Hz, 2H), 4.13 (s, 3H), 3.15 (m, 2H), 2.96 (m, 2H), 1.82 (bs, 2H), 1.65 (m, 2H), 1.41 (m, 2H), 0.93 (t, J= 10 Hz, 3H)

General Procedure for Nickel Dissolution

Watts solution was prepared by combining nickel(II) sulphate hexahydrate (31.20 g, 0.1 mol) with nickel(II) chloride hexahydrate (4.50 g, 0.2 mol) and boric acid (3.75 g, 0.06 mol) and distilled water in a 100 mL volumetric flask. The solution was stirred and heated to 55°C and the ionic liquid (1 mL) was added to 30 mL of Watts solution. The working electrode was a nickel sheet (1 mm thick, Alfa Aesan-99.5%), the counter electrode was titanium and the reference electrode was silver/silver chloride.

The electrodes in solution underwent ten cyclic voltammetry cycles (SR of 20 mV/s) and

chronopotentiometry scans (8 mA/cm^2, 30 minutes) followed by ten additional cyclic voltammetry cycles (SR of 20 mV/s).

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