Ionic Liquids in Organic Synthesis

Adam M. Azman
15 November 2006
What is an Ionic Liquid?

- Any salt above its melting point
- Technically, all molten salts, such as NaCl (mp = 800°C), are ionic liquids
- Obviously not practical for organic synthesis
What is an Ionic Liquid?

- **Definitions from Literature**
  - “The term ionic liquid implies a material that is fluid at (or close to) ambient temperature, is colorless, has a low viscosity and is easily handled.” (Sheldon)
  - “Room temperature ionic liquids are generally salts of organic cations, e.g. tetraalkylammonium, tetraalkylphosphonium, N-alkylpyridinium, 1,3-dialkylimidazolium and trialkylsulfonium cations.” (Sheldon)
  - “Most basic definition of a room temperature ionic liquid is a salt that has a melting point at or near room temperature.” (Handy)
  - “Organic salts with melting points below ambient or reaction temperature.” (Maio)
  - “Ionic liquid is a salt with a melting temperature below the boiling point of water.” (Wilkes)

- **Salt of organic cation which has a melting point near ambient temperature (up to ~100°C)**

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Synonyms for Ionic Liquids

- Ionic Liquid (IL)
- Room temperature ionic liquid (RTIL)
- Molten salt
- Room temperature molten salt
- Ambient temperature molten salt/ionic liquid
- Task specific ionic liquid (TSIL)
- Liquid organic salt
- Fused salt
- Neoteric solvent
A (very) Brief History of Ionic Liquids

- **1800s** – So called “red oil” formed during Friedel-Crafts reactions
  - Identified as long presumed intermediate called sigma complex
- **Early 1900s** - Alkylammonium nitrates found to be liquids at room temperature
  - Ethylammonium nitrate (1914) has melting temperature of 12°C
  - Used as liquid propellants for naval guns
- **1960s-Present** – Air Force Academy has continuous research effort for ionic liquids for thermal batteries
  - Thermal batteries have molten salt electrolyte (LiCl-KCl)
  - Reaches temperatures between 375-550°C
- **Start of modern era of ionic liquids** began with discovery of 1-butylpyridinium chloride-aluminum chloride mixture
  - Melting point = 40°C, butylpyridinium cation easily reduced
- It was noticed that large anions with many degrees of freedom inhibited crystalization until lower temperature
  - Large, asymmetric anions should lower melting point, as should large, asymmetric cations
- **1970s** – Fast computer method (1 week) for predicting electrochemical properties of ammonium salts
  - Imidazolium theorized to be excellent candidate (experimentally true)
  - Imidazolium cation more stable to reduction, melting point below room temperature
- **Chloroaluminate salts** are reactive to water – not a problem for batteries
  - Early 1990s – Ethylmethylimidazolium halides prepared, then anion metathesis with various silver salts provided a small library of room temperature ionic liquids
- **Late 1990s-Present (and beyond)** – Envelope (as always) being pushed
  - Exotic anions, functionalized cations, functionalized anions, chiral cations/anions, …
  - Limitless possibilities of new ionic salts to fill every niche of chemistry
Properties

- Non-flammable
- Negligible vapor pressure
- High thermal/chemical/electrochemical stability
- Solvating ability
- Large liquidus range (span of temperatures between melting and boiling point of a liquid)
- Easy recyclability
- Highly polar
- Non-coordinating
- Tunable miscibility with water or organic solvents
- Generally do not coordinate with metals, enzymes
- Able to be stored for long time without decomposition
- Chiral ionic liquids may control stereoselectivity

“Pure imidazolium ionic liquids can be described as polymeric hydrogen-bonded supramolecules and in some cases when mixed with other molecules, they should better be regarded as nonstructured materials with polar and non-polar regions rather than homogeneous solvent.” (Dupont)
Properties

• **Stability/Thermal decomposition**
  - Imidazolium cation stable above 300°C
  - Decomposition: cleavage of C-N bond between imidazole nitrogen and alkyl chain
  - Anion plays a role
    - Less nucleophilic – higher stability

• **Density**
  - Least effected by temperature variation or impurity
  - All greater than 1 for imidazolium cation
  - Lengthening alkyl chain – lower density
  - Increasing halogen content – higher density

• **Viscosity**
  - Even least viscous room temperature ionic liquids are quite viscous compared to conventional solvents
  - Highly sensitive to temperature and impurities
  - Short alkyl chain/functionalized alkyl chain – lower viscosity
    - Longer alkyl chain – increased van der Waals forces – increased energy required for molecular motion
  - BF$_4^-$ anion causes lower viscosity than PF$_6^-$ anion

• **Conductivity**
  - Inversely parallels viscosity
The Cation

- Infinite in number
- Most common:
  - Dialkylimidazolium
  - Alkylpyridinium
  - Tetraalkylammonium
  - Tetraalkylphosphonium
- Can be tuned to properties needed
- For liquid at room temperature, should be unsymmetrical
  - Functionalizing side chain on cation can change melting point of straight-chain relative
  - Presence of C2-methyl group generally increases melting point of unsubstituted relative
  - Substituting at C4 has little effect on melting point
The Anion

- Much diversity
  - Common:
    - Tetrafluoroborate
    - Hexafluorophosphate
    - Bis(trifluoromethanesulfonyl)imide
    - Halogen
    - Mesylate/tosylate/triflate
  - Larger, more weakly coordinating anion
    - lower melting temperature
Melting Point Variation

Melting point for R Methyl Imidazolium Cation with Varying Anion

Length of Alkyl Chain (# Carbon Atoms)

Melting Points for Symmetrical Ionic Liquids (PF6 Anion)

# Carbon atoms (per side)
Other Ionic Liquid Cations

- **Pyridinium**
  - Possibly unstable in presence of nucleophiles
  - Alkyl chain length effect on melting point mirrors imidazolium

- **Tetraalkylammonium**
  - Known for much longer than imidazolium
  - Highly viscous/difficult to handle
  - Long alkyl chain/decreased symmetry – lower melting point

- **Others**
  - Triazolium, pyrazolium, thiazolium, benzimidazolium
  - Guanidinium, phosphonium, sulfonium
“Synthesis”

<table>
<thead>
<tr>
<th>Products</th>
<th>Related Information</th>
<th>Take a Tour</th>
</tr>
</thead>
</table>

- **Ionic Liquids**

  1. 1-Butyl-3-methylimidazolium chloride 0.98% 25 GR 356601020 71
  2. 1-Octyl-3-methylimidazolium chloride 0.98% 10 GR 356601100 12
  3. 1-Octaethyl-3-methylimidazolium chloride 0.98% 10 GR 356601120 12
  4. 1-Octyl-3-methylimidazolium hexafluorophosphate 99% 10 GR 356601120 12
  5. 1-Octyl-3-methylimidazolium tetrafluoroborate 99% 10 GR 356601120 12
  6. 1-Octyl-3-methylimidazolium hexafluorophosphate 99% 25 GR 356601120 12
  7. 1-Octyl-3-methylimidazolium tetrafluoroborate 99% 5 GR 356601120 12
  8. 1-Octyl-3-methylimidazolium tetrafluoroborate 99% 25 GR 356601120 12
  9. 1-Octyl-3-methylimidazolium hexafluorophosphate 99% 5 GR 356601120 12
  10. 1-Octyl-3-methylimidazolium chloride 0.98% 25 GR 356601120 12
  11. 1-Octyl-3-methylimidazolium chloride 0.98% 10 GR 356601120 12
  12. 1-Octyl-3-methylimidazolium chloride 0.98% 5 GR 356601120 12
  13. 1-Octyl-3-methylimidazolium chloride 0.98% 25 GR 356601120 12
  14. 1-Octyl-3-methylimidazolium chloride 0.98% 5 GR 356601120 12
  15. 1-Octyl-3-methylimidazolium chloride 0.98% 25 GR 356601120 12
  16. 1-Octyl-3-methylimidazolium chloride 0.98% 5 GR 356601120 12
  17. 1-Octyl-3-methylimidazolium chloride 0.98% 25 GR 356601120 12

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Ionic Liquids

AMA 13
Why do I care?

“Problems” with molecular solvents:
- Grant money becoming more competitive
- Chemical “bunker” a real inconvenience
- Toxic/hazardous properties of solvents, notably chlorinated hydrocarbons
- Expensive catalysts
- Strong acids
- High temperatures
- Long reaction times
- Possible cumbersome isolation procedures
- Other drives to anchor catalyst for recovery/reuse require additional catalyst/enzyme modification
  - Steric hindrance causes decrease in efficiency of reaction

“Solutions” with ionic liquids:
- Combine best advantages of molten salts and avoid worst disadvantages caused by high temperatures
- Two phase system allows product in one phase, everything else in other phase
- Ionic liquid immobilizes catalyst/reagent for recycling and reuse
- Ionic liquids can act as solvent and catalyst in some systems without need for additional catalyst or ligand
- Rate acceleration effect on some catalytic reactions
Limitations

- A “dearth” of information on biodegradability and toxicity
- Cannot be purified by distillation
- Trace impurities can have significant impact on physical properties—must be initially produced in high purity
- Some ionic liquids are prone to hydrolysis – especially in reactions involving metals
- C2 hydrogen relatively acidic ($pK_a = 21-23$)
  - Deprotonation generates N-heterocyclic carbene
  - Good ligand for metal complexes
- Oxidative addition to electron-rich Ni$^0$ or Pd$^0$ to generate (carbene)metal hydride compounds
- Decomposition possible under sonochemical conditions
  - Creates hot spots in solvent
  - May limit ultrasound- and microwave-assisted processes
Applications

- Storage media for toxic gases
- Lubricants
- Performance additives in pigments
- Propellants
- Organic chemistry:
  - Hydrogenation
  - Hydroformylation
  - Alkoxycarbonylation
  - Cross coupling (Heck, Suzuki, Negishi, Stille)
  - Allylic substitution
  - Friedel-Crafts alkylation
  - Diels-Alder
  - Diol/carbonyl protection
  - Epoxidation/Epoxide opening
  - Cyanosilylation of aldehydes
  - Esterification
  - Ring closing metathesis
  - Knoevenagel condensation
  - Baylis-Hillman
  - Wittig
  - Robinson annulation
  - Dihydroxylation
  - Alcohol oxidation
  - Friedlander reaction
  - Nitration of phenols
  - Bromination of aromatics/alkynes
  - Cyclopropanation
  - Synthesis of 2,4,5-triaryl imidazoles
  - Synthesis of 3,4-dihydropyrimidin-2(1H)-ones
  - Dimer-/Oligomer-/Polymerization
  - Chiral solvent for asymmetric synthesis
  - Kinetic resolution
  - Biocatalysis
Diol/Carbonyl Protection

- In molecular solvents – large excess of reagents
- Monosubstituted imidazolium ionic liquids serve as Brønsted acids
- Acidic ionic liquids afford protected product with:
  - No added catalyst
  - 1:1 ratio of carbonyl to diol
  - No refluxing/Dean-Stark trap
  - No molecular solvent
  - Recyclable catalyst
- Acetals immiscible with ionic liquid – no need to remove water

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Diol/Carbonyl Protection

\[
\begin{array}{c}
\text{Carbonyl Alcohol Molar Ratio Time (h) Selectivity (%) Conversion (%)}
\end{array}
\]

<table>
<thead>
<tr>
<th>Carbonyl</th>
<th>Alcohol</th>
<th>Molar Ratio</th>
<th>Time (h)</th>
<th>Selectivity (%)</th>
<th>Conversion (%)</th>
</tr>
</thead>
<tbody>
<tr>
<td>(n\text{hex})</td>
<td>(\text{H})</td>
<td>1:1</td>
<td>3</td>
<td>100</td>
<td>98</td>
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<tr>
<td>(\text{CH}_3)</td>
<td>(\text{CH}_3)</td>
<td>1:1</td>
<td>3.5</td>
<td>100</td>
<td>100</td>
</tr>
<tr>
<td>(\text{Ph})</td>
<td>(\text{H})</td>
<td>1:1</td>
<td>6</td>
<td>100</td>
<td>93</td>
</tr>
<tr>
<td>(\text{Ph}^+)</td>
<td>(\text{O})</td>
<td>1:1</td>
<td>6</td>
<td>100</td>
<td>76</td>
</tr>
<tr>
<td>(\text{Ph}^+)</td>
<td>(\text{NO}_2)</td>
<td>1:1</td>
<td>6</td>
<td>100</td>
<td>93</td>
</tr>
</tbody>
</table>

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Friedlander Synthesis

- Common additives: HCl, H$_2$SO$_4$, PTSA, microwave, ZnCl$_2$/NEt$_3$, ruthenium or palladium complexes
- Can be run in ionic liquid with no additive
- Efficacy correlated to basicity of anions of ionic liquid
- Ionic liquid can be recovered almost completely and recycled at least twice

<table>
<thead>
<tr>
<th>Ionic Liquid</th>
<th>$pK_a$ of Acid of Anion, HX</th>
<th>Yield (%)</th>
</tr>
</thead>
<tbody>
<tr>
<td>[bbim][ClO$_4$]</td>
<td>-11</td>
<td>37</td>
</tr>
<tr>
<td>[bbim][Br]</td>
<td>-9</td>
<td>50</td>
</tr>
<tr>
<td>[bbim][Cl]</td>
<td>-7</td>
<td>50</td>
</tr>
<tr>
<td>[bbim][PF$_6$]</td>
<td>0.5</td>
<td>70</td>
</tr>
<tr>
<td>[bbim][BF$_4$]</td>
<td>0.5</td>
<td>75</td>
</tr>
<tr>
<td>[Hbim][ClO$_4$]</td>
<td>-11</td>
<td>50</td>
</tr>
<tr>
<td>[Hbim][Br]</td>
<td>-9</td>
<td>75</td>
</tr>
<tr>
<td>[Hbim][Cl]</td>
<td>-7</td>
<td>73.8</td>
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<td>[Hbim][PF$_6$]</td>
<td>0.5</td>
<td>90</td>
</tr>
<tr>
<td>[Hbim][BF$_4$]</td>
<td>0.5</td>
<td>96</td>
</tr>
</tbody>
</table>

Friedlander Synthesis

### Friedlander Synthesis

![Chemical Structures and Reactions](image)

<table>
<thead>
<tr>
<th>Compound 1</th>
<th>Compound 2</th>
<th>Product</th>
<th>Time (h)</th>
<th>Yield (%)</th>
</tr>
</thead>
<tbody>
<tr>
<td>R1 Me O</td>
<td>R2 OEt</td>
<td>[Hbim][BF₄]</td>
<td>3</td>
<td>A 94 93 93</td>
</tr>
<tr>
<td>R1 Me O</td>
<td>R2 OEt</td>
<td>[Hbim][BF₄]</td>
<td>3.3</td>
<td>A 94 93 93</td>
</tr>
<tr>
<td>R1 Me O</td>
<td>R2 OEt</td>
<td>[Hbim][BF₄]</td>
<td>3</td>
<td>A 94 93 93</td>
</tr>
<tr>
<td>R1 Me O</td>
<td>R2 OEt</td>
<td>[Hbim][BF₄]</td>
<td>3</td>
<td>A 94 93 93</td>
</tr>
<tr>
<td>R1 Me O</td>
<td>R2 OEt</td>
<td>[Hbim][BF₄]</td>
<td>4</td>
<td>A 94 93 93</td>
</tr>
<tr>
<td>R1 Me O</td>
<td>R2 OEt</td>
<td>[Hbim][BF₄]</td>
<td>6</td>
<td>A 93 92 90</td>
</tr>
</tbody>
</table>

Knoevenagel Condensation/Robinson Annulation

- Reactions performed in air without rigorous drying of ionic liquid
- Product extracted with toluene
- Ionic liquid washed with toluene and reused without further purification

Knoevenagel Condensation/Robinson Annulation

\[
\text{EWG} \_ \text{EWG} \xrightarrow{\text{glycine (0.2 eq.)}} \text{MWG} \_ \text{MWG}
\]

<table>
<thead>
<tr>
<th>Malonate Derivative</th>
<th>Carbonyl Derivative</th>
<th>Product</th>
<th>Yield (%) (unoptimized)</th>
</tr>
</thead>
<tbody>
<tr>
<td>NC _NC</td>
<td>Cl H O</td>
<td>Cl _CN</td>
<td>86</td>
</tr>
<tr>
<td>NC _NC</td>
<td>O₂N H O</td>
<td>O₂N _CN</td>
<td>74</td>
</tr>
<tr>
<td>NC _NC</td>
<td>MeO H O</td>
<td>MeO _CN</td>
<td>77</td>
</tr>
<tr>
<td>NC _NC</td>
<td>Ph H O</td>
<td>Ph _CN</td>
<td>62</td>
</tr>
<tr>
<td>NC _NC</td>
<td>O₂H O</td>
<td>O₂H _CN</td>
<td>32</td>
</tr>
<tr>
<td>EtO _CO Me</td>
<td>Ph _CO-Ch</td>
<td>Ph _CO-Ch</td>
<td>48</td>
</tr>
</tbody>
</table>

"10 cycles performed without dropping below 90% conversion."

Hydrogenation

- First example by Chauvin, 1995
- Dupont showed RuCl₂(Ph₃P)₃ in [bmim][BF₄] has turnover number = 540 h⁻¹
  - Metal complex recyclable

```
\[
\text{CO}_2 \xrightarrow{H_2} \text{CO}_2
\]
```

<table>
<thead>
<tr>
<th>Catalyst</th>
<th>Substrate</th>
<th>Product</th>
<th>Solvent System</th>
<th>Conversion (%)</th>
<th>% ee</th>
</tr>
</thead>
<tbody>
<tr>
<td><em>in situ</em> Ru-(S)-BINAP</td>
<td>Ph</td>
<td>(S) CO₂</td>
<td>MeOH</td>
<td>100</td>
<td>62 (S)</td>
</tr>
<tr>
<td>[RuCl₂(S)-BINAP₂⁺NEt₃]</td>
<td>Ph</td>
<td>(S) CO₂</td>
<td>MeOH</td>
<td>100</td>
<td>63 (S)</td>
</tr>
<tr>
<td><em>in situ</em> Ru-(R)-BINAP</td>
<td>Ph</td>
<td>(R) CO₂</td>
<td>i-PrOH</td>
<td>100</td>
<td>72 (R)</td>
</tr>
<tr>
<td><em>in situ</em> Ru-(R)-BINAP</td>
<td>Ph</td>
<td>(R) CO₂</td>
<td>[bmim][BF₄]/i-PrOH</td>
<td>99</td>
<td>69 (R)</td>
</tr>
<tr>
<td>1st recycle</td>
<td>Ph</td>
<td>(R) CO₂</td>
<td>[bmim][BF₄]/i-PrOH</td>
<td>99</td>
<td>72 (R)</td>
</tr>
<tr>
<td>2nd recycle</td>
<td>Ph</td>
<td>(R) CO₂</td>
<td>[bmim][BF₄]/i-PrOH</td>
<td>99</td>
<td>77 (R)</td>
</tr>
<tr>
<td>3rd recycle</td>
<td>Ph</td>
<td>(R) CO₂</td>
<td>[bmim][BF₄]/i-PrOH</td>
<td>99</td>
<td>70 (R)</td>
</tr>
<tr>
<td>[RuCl₂(S)-BINAP₂⁺NEt₃]</td>
<td>Ph</td>
<td>(S) CO₂</td>
<td>[bmim][BF₄]/i-PrOH</td>
<td>100</td>
<td>78 (S)</td>
</tr>
<tr>
<td>1st recycle</td>
<td>Ph</td>
<td>(S) CO₂</td>
<td>[bmim][BF₄]/i-PrOH</td>
<td>100</td>
<td>84 (S)</td>
</tr>
<tr>
<td>2nd recycle</td>
<td>Ph</td>
<td>(S) CO₂</td>
<td>[bmim][BF₄]/i-PrOH</td>
<td>90</td>
<td>79 (S)</td>
</tr>
<tr>
<td>3rd recycle</td>
<td>Ph</td>
<td>(S) CO₂</td>
<td>[bmim][BF₄]/i-PrOH</td>
<td>95</td>
<td>67 (S)</td>
</tr>
<tr>
<td>[Ru-(S)-BINAP]</td>
<td>MeO</td>
<td>(S)-Naproxen</td>
<td>[bmim][BF₄]/i-PrOH</td>
<td>100</td>
<td>80 (S)</td>
</tr>
</tbody>
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Ionic Liquids

Diels–Alder

- Ionic liquid allows for catalyst recovery, rate acceleration, selectivity enhancement

\[
\begin{array}{c}
\text{benzene} \quad \text{allyl} \\
\text{Sc(OTf)}_3 (0.2 \text{ mol%}) \\
solvent, \text{rt}, 2h
\end{array}
\rightarrow
\begin{array}{c}
\text{diene} \\
\text{product}
\end{array}
\]

<table>
<thead>
<tr>
<th>Solvent</th>
<th>Yield (%)</th>
</tr>
</thead>
<tbody>
<tr>
<td>CD$_2$Cl$_2$</td>
<td>22</td>
</tr>
<tr>
<td>[bmim][PF$_6$] (1 eq.) + CD$_2$Cl$_2$</td>
<td>46</td>
</tr>
<tr>
<td>[bmim][PF$_6$]</td>
<td>&gt;99</td>
</tr>
</tbody>
</table>

<table>
<thead>
<tr>
<th>Dienophile</th>
<th>Diene</th>
<th>Product</th>
<th>Endo:exo</th>
<th>Yield (%)</th>
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</table>

Me\[\text{N}^+\text{N}^+\text{Bu}\]PF$_6^-$

Olefin Epoxidation

- (R,R)-Jacobsen’s catalyst immobilized in ionic liquid
- Rate enhancement noticed over molecular solvents
- Enantioselectivity and activity decrease upon reuse – possible catalyst degradation over time
- Co-solvent used for reactions below room temperature, because ionic liquid solid at reaction temperature
Olefin Epoxidation

(R, R)-Jacobsen’s Catalyst

NaOCl

[bmim][PF₆]-CH₂Cl₂

0°C

<table>
<thead>
<tr>
<th>Substrate</th>
<th>Product</th>
<th>Time (h)</th>
<th>Yield (%)</th>
<th>% ee</th>
</tr>
</thead>
<tbody>
<tr>
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</table>

Me-N⁺ Bu⁻ PF₆⁻

[bmim][PF₆]−

O

O

Ph Me

NC

O

O

O

O

Product

Heck Reaction

- 1996 – First example in ionic liquid by Kaufmann
  - Used ammonium and phosphonium salts
- Under basic conditions, deprotonation and formation of palladium complexes of imidazolium carbenes facile
- Competition of cationic and neutral pathways for enol ethers nonexistent in ionic liquids – α-arylation (cationic) regiospecific

  - Allows catalyst to be recovered and reused
- Similar results for Suzuki, Stille, and Negishi (although yield decreases on recycle experiments for Negishi)
Heck Reaction

\[ \text{DPPP (2 eq.)} \quad \text{NEt3 (1.2 eq.)} \quad \text{Pd(OAc)}_2 (2.5 \text{ mol%}) \]
\[ \text{[bmim][BF}_4\text{]} \quad 100^\circ \text{C, 18h} \]

<table>
<thead>
<tr>
<th>Substrate</th>
<th>Temperature (°C)</th>
<th>Time (h)</th>
<th>Conversion (%)</th>
<th>α/β</th>
<th>Yield (%)</th>
</tr>
</thead>
<tbody>
<tr>
<td>1-Br</td>
<td>100</td>
<td>24</td>
<td>100</td>
<td>&gt;99/1</td>
<td>95</td>
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<tr>
<td>1-I</td>
<td>80</td>
<td>24</td>
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<td>&gt;99/1</td>
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<tr>
<td>2,4-BrNC</td>
<td>110</td>
<td>36</td>
<td>100</td>
<td>&gt;99/1</td>
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<tr>
<td>2,4-BrMeO</td>
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<td>36</td>
<td>100</td>
<td>&gt;99/1</td>
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<td>2,4-BrMe</td>
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<td>36</td>
<td>100</td>
<td>&gt;99/1</td>
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<tr>
<td>2,4-BrH</td>
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<td>24</td>
<td>100</td>
<td>&gt;99/1</td>
<td>93</td>
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<td>&gt;99/1</td>
<td>95</td>
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<tr>
<td>2,4-BrMe</td>
<td>120</td>
<td>36</td>
<td>100</td>
<td>&gt;99/1</td>
<td>88</td>
</tr>
</tbody>
</table>

Swern Oxidation

• Ionic liquid tethered “dimethyl sulfoxide” can be prepared with no chromatography and no volatile (read: smelly) organosulfur reagents
• Products separated from ionic liquid by phase extraction with ether
• Reduced sulfide may be reoxidized and reused for at least 4 recycles with small loss of activity
• Also able to tether TEMPO catalyst

He, X.; Chan, T. H. *Tetrahedron*, 2006, 62, 3389-3394
Swern Oxidation

\[ \text{Substrate} \xrightarrow{H_2O_6} \text{Product} \]

<table>
<thead>
<tr>
<th>Substrate</th>
<th>Product</th>
<th>Yield(%)</th>
</tr>
</thead>
<tbody>
<tr>
<td>( \text{BnO} )</td>
<td>( \text{Me} )</td>
<td>90 87 86 81</td>
</tr>
<tr>
<td>( \text{Me} )</td>
<td>( \text{Me} )</td>
<td>88</td>
</tr>
<tr>
<td>( \text{OH} )</td>
<td>( \text{OH} )</td>
<td>82</td>
</tr>
<tr>
<td>( \text{Me} )</td>
<td>( \text{Me} )</td>
<td>90</td>
</tr>
<tr>
<td>( \text{Me} )</td>
<td>( \text{Me} )</td>
<td>90</td>
</tr>
</tbody>
</table>

He, X.; Chan, T. H. *Tetrahedron*, 2006, 62, 3389-3394
• Simple dissolution of catalyst not effective – catalyst soluble in organic solvents & decomposes

Ring Closing Metathesis

![Reaction scheme]

<table>
<thead>
<tr>
<th>R</th>
<th>Substrate</th>
<th>Product</th>
<th>Conversion(%)</th>
</tr>
</thead>
<tbody>
<tr>
<td>PCy₃</td>
<td></td>
<td></td>
<td>&gt;98 &gt;98 &gt;98 &gt;98 &gt;98</td>
</tr>
<tr>
<td>PCy₃</td>
<td></td>
<td></td>
<td>&gt;98 &gt;98 &gt;98 96   93  91  80</td>
</tr>
<tr>
<td>sIMes</td>
<td></td>
<td></td>
<td>&gt;98 &gt;98 &gt;98 &gt;98 &gt;98 &gt;98 95  95</td>
</tr>
<tr>
<td>sIMes (25°C)</td>
<td></td>
<td></td>
<td>&gt;98 &gt;98 &gt;98 &gt;98 &gt;98 &gt;98 83   33</td>
</tr>
<tr>
<td>PCy₃</td>
<td></td>
<td></td>
<td>94    78    48</td>
</tr>
</tbody>
</table>

In some cases, the reactions are performed in a biphasic system with toluene (25:75, [bmim][PF₆] : toluene).

The Future

- **Chiral functionalized ionic liquid**
  - Side chain or anion incorporates chirality
  - Asymmetric induction
  - Kinetic resolution
- **Task-specific ionic liquids**
  - Incorporate reagent or catalyst or substrate into cation or anion
  - If substrate – can carry substrate on several steps, immobilized in ionic liquid – allows for easy separation/recovery
- **Supercritical CO$_2$**
  - Used to extract product from ionic liquid phase without using “molecular solvents”
Summary

• Ionic liquids viable alternative to molecular solvents in many reaction types
• Ionic liquids allow for potential recovery/reuse of catalyst (it may be the catalyst itself)
• Rate enhancement, ease of product isolation, recyclability of catalyst – ionic liquids could become widely popular in near future
References

• Properties:

• Reactions: