Carbonate based ionic liquids and beyond

Alvise Perosa

Today’s outline

1. Synthesis of carbonate ionic liquids
2. Organocatalysis
   2.1 Carbon-Carbon bond
   2.2 Transesterification
3. Multiphase systems
4. Luminiescent ionic liquids
5. ...and beyond
1. Syntheses of ionic liquids

Ionic liquids synthesis, our toolbox

1. QUATERNARISATION REACTION:
Amines/Phosphines → Amonium/Phosphonium

1. DIMETHYLCARBONATE as methylating reagent:

DMC

100% NON-TOXIC
Why use dimethylcarbonate?

100% NON-TOXIC

Dimethylcarbonate (DMC)

Dimethylsulfate (DMS)

Methyl iodide

Dimethylcarbonate, its syntheses
Dimethylcarbonate, methylation reactivity

Dimethylcarbonate

\[
\text{NuH} + \text{CH}_3\text{O} = \text{O} \rightarrow \text{NuCH}_3 \rightarrow \text{CH}_3\text{OH} + \text{CO}_2
\]

Dimethylsulfate

\[
2\text{NuH} + \text{O}_\text{Si}=\text{O} \rightarrow 2\text{NuCH}_3 \rightarrow 2\text{H}_2\text{SO}_4
\]

For more on dimethylcarbonate

You might have visited poster no. 56!

Jess Stanley

... or poster no. 57!

Marco Noe’
**“Parent” Ionic liquids:**
Amines/phosphines + dimethylcarbonate

\[
\begin{align*}
R-N^+\text{CH}_3 + \text{HOCOCOCH}_3 & \rightarrow R-N^+\text{CH}_3\text{OOCOCOCH}_3 \\
R-P^+\text{CH}_3 + \text{HOCOCOCH}_3 & \rightarrow R-P^+\text{CH}_3\text{OOCOCOCH}_3
\end{align*}
\]

\[\text{Conditions: } 140 \, ^\circ\text{C}, 20 \, \text{h, some methanol}\]
\[\text{Workup: remove volatiles}\]

Pereza et al., Chem. Eur. J. 2005, 11, 12273;

---

**“Offspring” Ionic liquids:**
by anion exchange

\[
\begin{align*}
R-P^+\text{CH}_3 + \text{H}_2\text{O} & \rightarrow R-P^+\text{CH}_3\text{O} + \text{CH}_3\text{OH} \\
R-P^+\text{CH}_3 + \text{H-X} & \rightarrow R-P^+\text{CH}_3X^- + \text{CO}_2 + \text{CH}_3\text{OH}
\end{align*}
\]

\[\text{Conditions: } \text{RT}, 5 - 60 \, \text{minutes, no solvent}\]
\[\text{Workup: remove methanol}\]

Pereza et al., Chem. Eur. J. 2005, 11, 12273;
With MW irradiation as well...

Methylation to methylcarbonate salt

Neutralisation with acid to ionic species

[Rogers et al. Green Chem. 2010, 12, 407;]

Imidazolium methylcarbonate

Some recent examples:

\[
\begin{align*}
[N_{8,8,8,1}] & \quad \text{SO}_3^- & \quad \text{NH}_2 \\
[P_{8,8,8,1}] & \quad \text{O} & \quad \text{O} \\
[P_{8,8,8,1}] & \quad \text{O} & \quad \text{CF}_3 \\
[P_{8,8,8,1}] & \quad \text{O} & \quad \text{O}
\end{align*}
\]

Manuela Facchin

In summary:

<table>
<thead>
<tr>
<th>Compound</th>
<th>P_{16,6,6,1}</th>
<th>P_{24,8,8}</th>
<th>P_{16,6,6}</th>
<th>P_{8,8,8}</th>
<th>N_{16,6,6,1}</th>
<th>N_{8,8,8,1}</th>
<th>N_{6,6,6,1}</th>
</tr>
</thead>
<tbody>
<tr>
<td>CH_3COO</td>
<td>✓</td>
<td></td>
<td>✓</td>
<td>✓</td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>CF_3COO</td>
<td></td>
<td>✓</td>
<td></td>
<td>✓</td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>CH_2COO</td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td>✓</td>
</tr>
<tr>
<td>Ph_COO</td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td>✓</td>
</tr>
<tr>
<td>Anthranilate</td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td>✓</td>
</tr>
<tr>
<td>HPO_3</td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td>✓</td>
</tr>
<tr>
<td>Dicyanomethanide</td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td>✓</td>
</tr>
<tr>
<td>4-nitrobenzoate</td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td>✓</td>
</tr>
<tr>
<td>4-methylbenzoate</td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td>✓</td>
</tr>
<tr>
<td>Ph_COO</td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td>✓</td>
</tr>
<tr>
<td>Dibenzoylmethanate</td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td>✓</td>
</tr>
<tr>
<td>TTA</td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td>✓</td>
</tr>
</tbody>
</table>
Chiral ionic liquids:

<table>
<thead>
<tr>
<th>Anion</th>
<th>(\text{Ph}^+)</th>
<th>(\text{N}_{\text{Ph}}^-)</th>
</tr>
</thead>
<tbody>
<tr>
<td>(-)-Menthylcarbonate</td>
<td>✔</td>
<td></td>
</tr>
<tr>
<td>L-Phenylethyl carbonate</td>
<td>✔</td>
<td>✔</td>
</tr>
<tr>
<td>(-)-Methoxycacetate</td>
<td>✔</td>
<td>✓</td>
</tr>
<tr>
<td>(+)-Camphor-10-sulfate</td>
<td>✔</td>
<td>✓</td>
</tr>
<tr>
<td>L-Phenylalaninate</td>
<td></td>
<td>✓</td>
</tr>
<tr>
<td>L-Valinate</td>
<td></td>
<td>✓</td>
</tr>
</tbody>
</table>

*not isolated

Truly green synthesis...

“SIMPLE, EFFICIENT, & SAFE”

- Clean
  - 100% yields, 100% purity, 100% atom economy
  - one step
  - halide-free
  - some methanol as solvent
  - use of green reagents
  - no workup
  - no by-products
- Modular
  - not limited to one target product
  - make whole classes of compounds
  - tune properties
- Clear and robust materials
- (Relatively) large volumes
**Dibenzoylmethanate**

\[ \text{H-NMR} \]

Neat, 60 °C

\[ [\text{Para}] \text{H}_2\text{CO} \rightleftharpoons [\text{Para}] \text{CO}_2 + \text{CH}_3\text{OH} \]

**2-Thenoyl trifluoroacetonate**

\[ \text{H-NMR} \]

Neat, 60 °C

\[ [\text{Para}] \text{H}_2\text{CO} \rightleftharpoons [\text{Para}] \text{CO}_2 + \text{CH}_3\text{OH} \]
Nitromethane disappears

WHAT WE OBSERVED:

- the methylcarbonate anion slowly disappeared;
- nitroethane was converted 100%;
- no other proton signals appeared.
We hypothesised an α-elimination-rearrangement of nitroethane to yield the nitrite anion and ethylene:

\[
\begin{align*}
\text{NO}_2 + \text{CH}_2\text{CH}_2\text{O} & \rightarrow \text{H}_2\text{O} + \text{CO}_2 + \text{CH}_3\text{OH} \\
\text{H}_2\text{C} = \text{NO}_2 & \rightarrow \text{H}_2\text{C} = \text{C} - \text{NO}_2 \rightarrow \text{CH}_2\text{CH}_2\text{O} + \text{NO}_2^-
\end{align*}
\]


Further observations:

- Griess test was certainly positive for nitrite: NO₂
- Conflicting evidence for the presence of ethylene (GC-MS, GC-FID, GC-TCD)
... so we read the literature:

\[
\begin{align*}
\text{H}_3\text{C} & \text{NO}_2 \\
& \xrightarrow{\text{OH}} \\
& \text{H}_3\text{C} \text{N}_2\text{O} \\
& \xrightarrow{\text{OH}} \\
& \text{H}_3\text{C} \text{N}_2\text{O}_2 \\
& \xrightarrow{\text{OH}} \\
& \text{H}_3\text{C} \text{H} + \text{NO}_2 \\
& \xrightarrow{\text{OH}} \\
& \text{H}_3\text{C} \text{N}_2\text{O}_2
\end{align*}
\]


... still wondering what happens.

...but, it appears we have a route to nitrite ILs

\[
\begin{align*}
\text{F}_{6}\text{a}_{6}\text{a}_{3} & \text{H}_3\text{CO} \text{O}^+ \text{H} \text{NO}_2 \\
& \xrightarrow{} \\
& \text{F}_{6}\text{a}_{6}\text{a}_{3} \text{NO}_2
\end{align*}
\]
2. Organocatalysis

2.1 Carbon-Carbon Bond

IL organo-catalyst

\[ P_{8,8,8,1} \text{ MC} \]
The first hint

Michael reaction

Conditions: room temperature, no solvent, 0.4% P_{8,8,8,1} MC

A second hint: Henry Reaction

0.5 M in CDCl₃, Nitroethane 5 equiv., 25°C
Catalyst:aldehyde ratio = 5%

A second hint: Henry Reaction

$$R^\equiv + \text{NO}_2^{\text{P}}_{8,8,8,1}[\text{CH}_3\text{COO}] \rightarrow R^{-}\text{NO}_2$$

<table>
<thead>
<tr>
<th>Aldehyde R</th>
<th>time (h)</th>
<th>Nitroaldol product (%)</th>
<th>Y (%)b</th>
</tr>
</thead>
<tbody>
<tr>
<td>CH$_2$CH$_2$Ph</td>
<td>2</td>
<td>96</td>
<td>88</td>
</tr>
<tr>
<td>CH(CH$_3$)Ph</td>
<td>2</td>
<td>96</td>
<td>93</td>
</tr>
<tr>
<td>C$_2$H$_5$</td>
<td>2</td>
<td>93</td>
<td>90</td>
</tr>
<tr>
<td>C$<em>{10}$H$</em>{21}$</td>
<td>2</td>
<td>99</td>
<td>97</td>
</tr>
<tr>
<td>4-NO$_2$C$_6$H$_4$</td>
<td>2</td>
<td>95</td>
<td>91</td>
</tr>
<tr>
<td>4-ClC$_6$H$_4$</td>
<td>3</td>
<td>82</td>
<td>71</td>
</tr>
<tr>
<td>C$_6$H$_5$</td>
<td>2</td>
<td>35</td>
<td>35</td>
</tr>
</tbody>
</table>

T = 25°C


The third hint

Baylis-Hillman-type reaction

Conditions: 60 °C, no solvent, 1.0% P$_{8,8,8,1}$ MC
Accepted Baylis-Hillman reaction mechanism

So, why does $P_{8,8,8,1}$MC behave as a strong base/nucleophile?

Initial rates of conversion of cyclohexenone to the dimer in the presence of different nucleophilic $N$ and electrophilic catalyst $E$.

<table>
<thead>
<tr>
<th>$N$ (Anion)</th>
<th>pKa</th>
<th>$E$ (Cation)</th>
<th>rate $h^{-1}$</th>
</tr>
</thead>
<tbody>
<tr>
<td>MeOCO$_2$</td>
<td>5.51</td>
<td>$P_{8,8,8,1}$</td>
<td>12.60</td>
</tr>
<tr>
<td>Br</td>
<td>-4.8</td>
<td>$P_{8,8,8,1}$</td>
<td>0.00</td>
</tr>
<tr>
<td>$P_1$-Bu</td>
<td>26.98</td>
<td>-</td>
<td>9.37</td>
</tr>
<tr>
<td>DBU</td>
<td>24.34</td>
<td>-</td>
<td>1.48</td>
</tr>
</tbody>
</table>

Probably not just due to the pKa of the anion!
There must be something else going on …

Maybe activation by the cation?

Initial rates of conversion of cyclohexenone to the dimer in the presence of different nucleophilic $N$ and electrophilic catalyst $E$:

<table>
<thead>
<tr>
<th>$N$ (Anion)</th>
<th>$pK_a$</th>
<th>$E$ (Cation)</th>
<th>rate $h^{-1}$</th>
</tr>
</thead>
<tbody>
<tr>
<td>MeOCCO$_2$</td>
<td>5.51</td>
<td>$P_{8,8,8,1}$</td>
<td>12.60</td>
</tr>
<tr>
<td>Br$^-$</td>
<td>-4.9</td>
<td>$P_{8,8,8,1}$</td>
<td>0.00</td>
</tr>
<tr>
<td>$P_{1,8}lu$</td>
<td>26.98</td>
<td>-</td>
<td>9.37</td>
</tr>
<tr>
<td>DBU</td>
<td>24.34</td>
<td>-</td>
<td>1.48</td>
</tr>
</tbody>
</table>

To look at this we decided to “separate” the effect of the anion ($N$) from the effect of the cation ($E$):

we used DBU as the nucleophile ($N$)…

... and added increasing amounts of $P_{8,8,8,1}Br^-$

Added amounts of $P_{8,8,8,1}Br^-$

<table>
<thead>
<tr>
<th>$N$ (Anion)</th>
<th>$E$ (Cation)</th>
<th>$[E] /[N]$</th>
<th>rate $h^{-1}$</th>
</tr>
</thead>
<tbody>
<tr>
<td>Br$^-$</td>
<td>$P_{8,8,8,1}$</td>
<td>0.015</td>
<td>0.00</td>
</tr>
<tr>
<td></td>
<td>$P_{1,8}lu$</td>
<td>0.015</td>
<td>1.00</td>
</tr>
<tr>
<td>DBU</td>
<td>0.042</td>
<td>1.00</td>
<td>0.00</td>
</tr>
<tr>
<td></td>
<td>$P_{8,8,8,1}$</td>
<td>0.007</td>
<td>0.37</td>
</tr>
<tr>
<td></td>
<td>$P_{8,8,8,1}$</td>
<td>0.013</td>
<td>0.40</td>
</tr>
<tr>
<td></td>
<td>$P_{8,8,8,1}$</td>
<td>0.020</td>
<td>0.48</td>
</tr>
<tr>
<td></td>
<td>$P_{8,8,8,1}$</td>
<td>0.039</td>
<td>0.94</td>
</tr>
<tr>
<td></td>
<td>$P_{8,8,8,1}$</td>
<td>0.057</td>
<td>1.35</td>
</tr>
</tbody>
</table>

DBU by itself
Ambiphilic activation?

Electrophile

Nucleophile

Deconvolution of selected $^{13}$C resonances.
**Precedents...**

... hypotheses without experimental proof.


---

**Interesting application...**

Methylation using dimethyl carbonate catalysed by ionic liquids under continuous flow conditions

Toma N. Gnanov,*, John D. Hulbrey,† C. Oliver Kappe,** Kenneth R. Seddon* and Ting Yue†

Green Chemistry 2012 accepted article
2. Organocatalysis

2.2 Transesterification

Transesterification of organic carbonates.

\[
\text{H}_3\text{C}\text{O}_2\text{C}_2\text{H}_3 + \text{R-OH} \xrightarrow{\text{ILs cat \ 90-240 °C}} \text{H}_3\text{C}\text{O}_2\text{C}_2\text{H}_3 + \text{CH}_2\text{OH} \\
\text{R-OH} = \text{HO-CH=CHC_6H_4-CH}_2\text{CH(OH)CH(OH)CH(OH)CH}_2\text{CH}_2\text{CH}_2\text{CH}_2\text{CH}_3
\]

No decarboxylation of dimethylcarbonate is observed!
Transesterification of organic carbonates.

\[
\text{H}_2\text{C}_\text{O} \text{O} \text{CCH}_3 + \text{HO} \xrightarrow{\text{IL 1\% 200 °C}} \text{H}_2\text{C}_\text{O} \text{O} \text{CCH}_3 + \text{C}_3\text{H}_7\text{OH}
\]

Catalyst | Conversion (%) | Selectivity (%)
--- | --- | ---
[P₈₈₈₁][CH₃COO] | 52 |
[P₈₈₈₁][HOCOO] | 68 | >99
[P₈₈₈₁][AcO] | 93 |
[P₈₈₈₁][PhO] | 78 |


Transesterification of organic carbonates.

Transesterification of organic carbonates.


Transesterification of diols

M. Selva's work:
Transesterification of diols

<table>
<thead>
<tr>
<th>1,2 diols</th>
<th>1,3 diols</th>
<th>1,4 diols</th>
<th>1,6 diols</th>
</tr>
</thead>
<tbody>
<tr>
<td>1,1</td>
<td>1,1</td>
<td>1,4</td>
<td>1,6</td>
</tr>
<tr>
<td>1,2</td>
<td>1,2</td>
<td></td>
<td></td>
</tr>
<tr>
<td>2,2</td>
<td>2,2</td>
<td>1,4</td>
<td></td>
</tr>
<tr>
<td>2,3</td>
<td></td>
<td></td>
<td></td>
</tr>
</tbody>
</table>

Transesterification of diols

DMC : diol = 20 : 1
DMC : diol = 5 : 1
DMC : diol = 2 : 1
### Transesterification of diols

<table>
<thead>
<tr>
<th>Main Product</th>
<th>Isolation</th>
<th>Purity %</th>
<th>Yield %</th>
</tr>
</thead>
<tbody>
<tr>
<td>Distillation</td>
<td>&gt; 99%</td>
<td>70%</td>
<td></td>
</tr>
<tr>
<td>Sublimation</td>
<td>&gt; 99%</td>
<td>90%</td>
<td></td>
</tr>
<tr>
<td>Distillation</td>
<td>&gt; 99%</td>
<td>68%</td>
<td></td>
</tr>
<tr>
<td>mixture</td>
<td>-</td>
<td>-</td>
<td>-</td>
</tr>
<tr>
<td>Distillation</td>
<td>&gt; 99%</td>
<td>73%</td>
<td></td>
</tr>
</tbody>
</table>

**Steric hindrance effect**

**Chain length effect**

**Cyclic carbonate**

**Linear carbonate**
3. Multiphase systems based on ionic liquids

Marina Gottardo

Multiphase systems based on ILs

Multiphase systems based on ILs

no IL

IL = [N_{8,8,8,1}]Cl

Multiphase systems based on ILs applied to the upgrade of bio-based molecules

Catalyst: Ru/C 5%
**Strategy for multiphase system design**

1. Choose organic solvent
2. Choose ionic liquid

**Multiphase system design: Organic solvent choice**

<table>
<thead>
<tr>
<th>Solvent</th>
<th>LA solubility</th>
<th>GVL solubility</th>
<th>Solubility in water @ 20°C</th>
</tr>
</thead>
<tbody>
<tr>
<td>Iso-octane</td>
<td>no</td>
<td>no</td>
<td>immiscible</td>
</tr>
<tr>
<td>Cyclohexane</td>
<td>no</td>
<td>no</td>
<td>immiscible</td>
</tr>
<tr>
<td>Toluene</td>
<td>yes</td>
<td>yes</td>
<td>0.52 g/L</td>
</tr>
<tr>
<td>Ethyl acetate</td>
<td>yes</td>
<td>yes</td>
<td>0.83 g/L</td>
</tr>
<tr>
<td>Ethyl lactate</td>
<td>yes</td>
<td>yes</td>
<td>miscible</td>
</tr>
<tr>
<td>Acetonitrile</td>
<td>yes</td>
<td>yes</td>
<td>miscible</td>
</tr>
<tr>
<td>Water</td>
<td>yes</td>
<td>yes</td>
<td>miscible</td>
</tr>
</tbody>
</table>

IL = [N\(_{8,8,8,1}\)][Cl]
"Inverse" multiphase system

But... $[N_{8,8,8,1}]\text{Cl}$ is partially soluble in water....

Multiphase system design: Choice of IL

<table>
<thead>
<tr>
<th>IL</th>
<th>LA Conversion</th>
<th>IL in H$_2$O (%)</th>
</tr>
</thead>
<tbody>
<tr>
<td>$[N_{8,8,8,1}]\text{Cl}$</td>
<td>32</td>
<td>2.3</td>
</tr>
<tr>
<td>$[N_{8,8,8,1}]\text{NTf}_2$</td>
<td>100</td>
<td>not measurable</td>
</tr>
<tr>
<td>$[P_{8,8,8,1}]\text{NTf}_2$</td>
<td>100</td>
<td>not measurable</td>
</tr>
<tr>
<td>$[N_{8,8,8,1}]\text{TFA}$</td>
<td>100</td>
<td>41</td>
</tr>
<tr>
<td>$[P_{8,8,8,1}]\text{NO}_3$</td>
<td>100</td>
<td>17</td>
</tr>
</tbody>
</table>
Conversion of LA to GVL in the multiphase system with 5% Ru/C as a function of temperature after 30 min: (△) without the IL third phase; (□) with a third phase made by [P8,8,8,1][NTf2]. p[H2] = 35 bar, Ru 0.15 mol%.

Conversion of LA to GVL: recycling of the Ru/C catalyst system.
Same thing with homegenous RuCl₃

Conversion of LA to GVL: recycling of the RuCl₃ catalyst system (Conditions: 16 h, 150 °C, p[H₂] = 35 bar, RuCl₃ (20 mg, 0.0765 mmol; Ru = 1.0 mol%)
4. Luminescent ionic liquids

Manuela Facchin

Dibenzoylmethanate

\[
\text{[P}_{8,8,8,1}\text{]H}_2\text{CO} \rightarrow \text{[P}_{8,8,8,1}\text{]} + \text{CO}_2 + \text{CH}_3\text{OH}
\]

\(^1\text{H-NMR}

Neat 60 °C
2-Thenoyltrifluoroacetonate

$\text{H-NMR}$

Neat, 60 °C

UV irradiation

Luminescent ionic liquids
5. ongoing….

Zwitterionic liquids

\[ \text{Zwitterionic Liquid Structure} \]
Thank you!

and...

- Ministero Istruzione Universita’ Ricerca “PRIN”
- “Cooperlink”
- Regione Veneto (ESF)

- Maurizio Selva
- Thomas Maschmeyer (University of Sydney)
- Roberto Ballini (Universita’ di Camerino)
- Vittorio Lucchini (Universita’ Ca’ Foscari)