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Carbonate based ionic liquids and beyond

Alvise Perosa

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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

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1. Syntheses of ionic liquids

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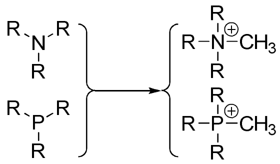
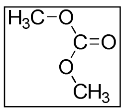
Ionic liquids synthesis, our toolbox

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



1. **DIMETHYLCARBONATE as methylating reagent:**

DMC 100% NON-TOXIC



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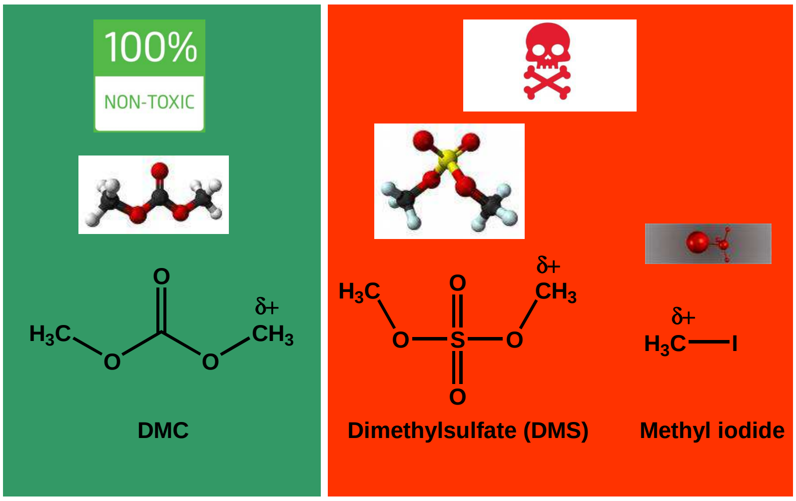
Why use dimethylcarbonate?



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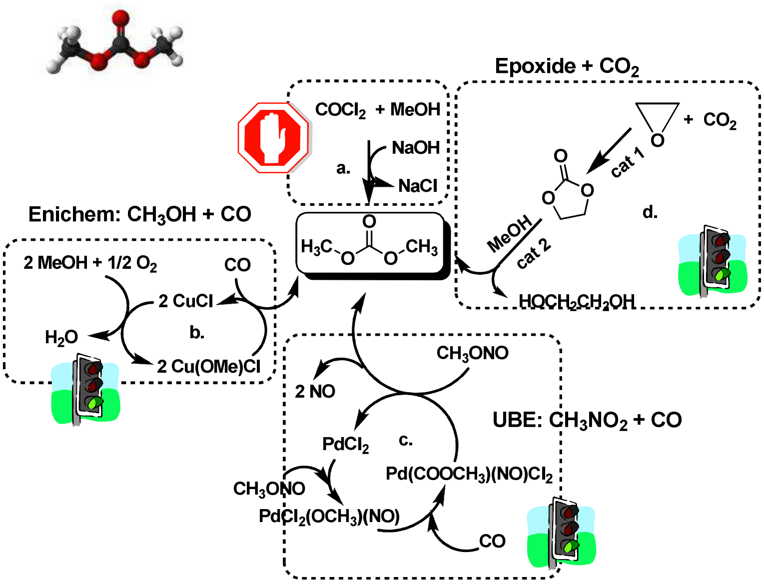
Dimethylcarbonate, its syntheses



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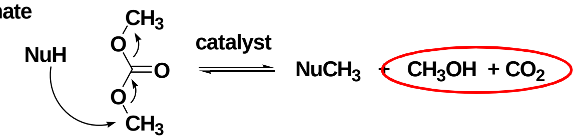
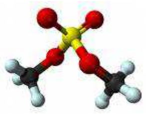
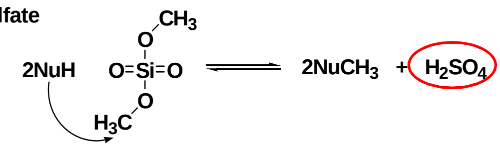
Dimethylcarbonate, methylation reactivity

Dimethylcarbonate



Dimethylsulfate





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For more on dimethylcarbonate

Jess Stanley

You might have visisted poster no. 56!

… or poster no. 57!

Marco Noe'

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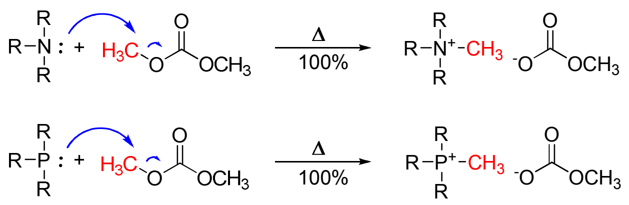
"Parent" Ionic liquids: Amines/phosphines + dimethylcarbonate



R = octyl, hexyl, *n*-butyl, *i*-butyl
$P_{8,8,8,1}$, $P_{6,6,6,1}$, $P_{4,4,4,1}$, $P_{i4,i4,i4,1}$
$N_{8,8,8,1}$, $N_{6,6,6,1}$, $N_{4,4,4,1}$

Conditions: 140 °C, 20 h, some methanol
Workup: remove volatiles

Perosa et al. *Chem. Eur. J.* **2009**, *15*, 12273;

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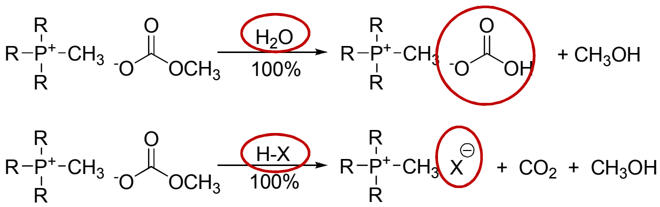
"Offspring" ionic liquids: by anion exchange



X = Cl, Br, I, TosO, CF_3CO_2, CH_3COO, NTf_2, NO_3, amino acids, …

Conditions: RT, 5 - 60 minutes, no solvent
Workup: remove methanol

Perosa et al. *Chem. Eur. J.* **2009**, *15*, 12273;

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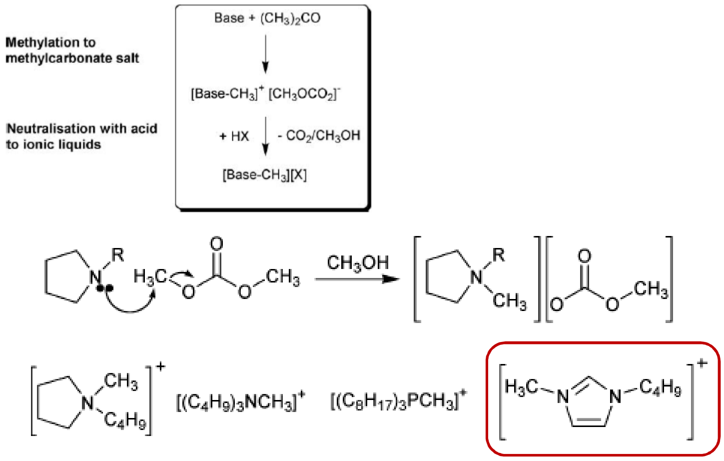
With MW irradiation as well…



Rogers et al. *Green Chem.* **2010**, *12*, 407;

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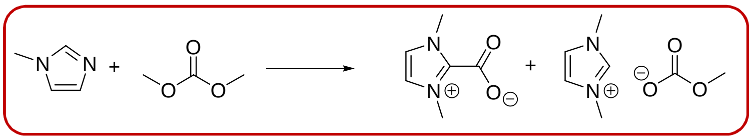
Imidazolium methylcarbonate



J. D. Holbrey, W. M. Reichert, I. Tkatchenko, E. Bouajila, O. Walter, I. Tommasi and R. D. Rogers, Chem. Commun., 2003, 28

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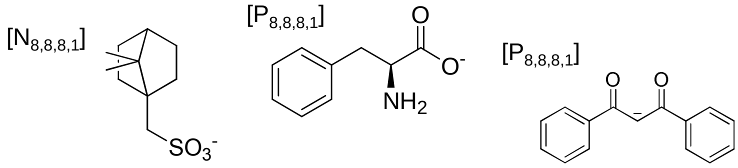
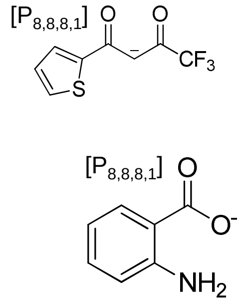
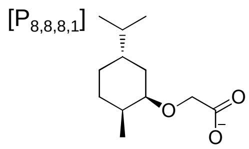
Some recent examples:







Manuela Facchin

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In summary:

	$P_{i4,i4,i4,1}$	$P_{4,4,4,1}$	$P_{6,6,6,1}$	$P_{8,8,8,1}$	$N_{6,6,6,1}$	$N_{8,8,8,1}$	$N_{8,1,1,1}$
$OCOOCH_3$	✓	✓	✓	✓	✓	✓	✓*
HOCOO				✓		✓	
NO_3				✓		✓	
Halides	✓		✓	✓		✓	
TosO		✓	✓	✓			
PhO				✓			
CF_3COO				✓		✓	
CH_3COO				✓			
NTf_2				✓		✓	
Anthranilate				✓			
HPO_3				✓			
Dicyanomethanide				✓			
4-nitrobenzoate				✓			
4-methylbenzoate				✓			
PhCOO				✓			
Dibenzoylmethanate				✓			
TTA				✓			

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Chiral ionic liquids:

	Cation	
Anion	$[P_{8,8,8,1}]$	$[N_{8,8,8,1}]$
(-)Menthylcarbonate*	✓	
1-Phenyl ethyl carbonate*	✓	✓
(-)-Menthyloxyacetate	✓	
(+)Camphor-10-sulfonate	✓	✓
L-Phenylalaninate	✓	
L-Valinate	✓	

*not isolated

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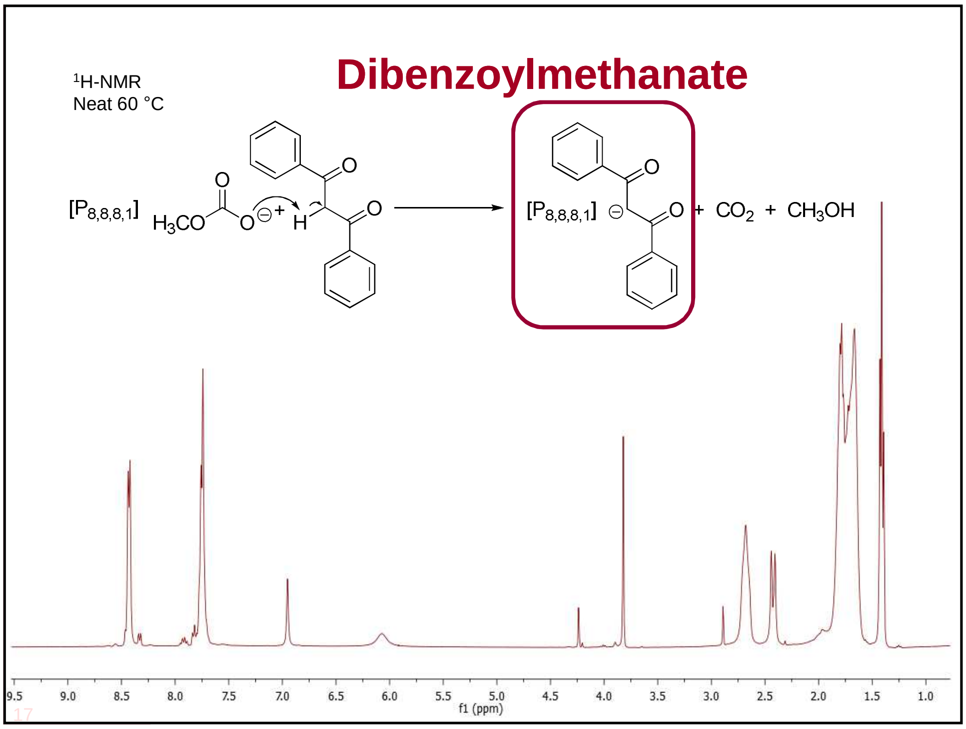
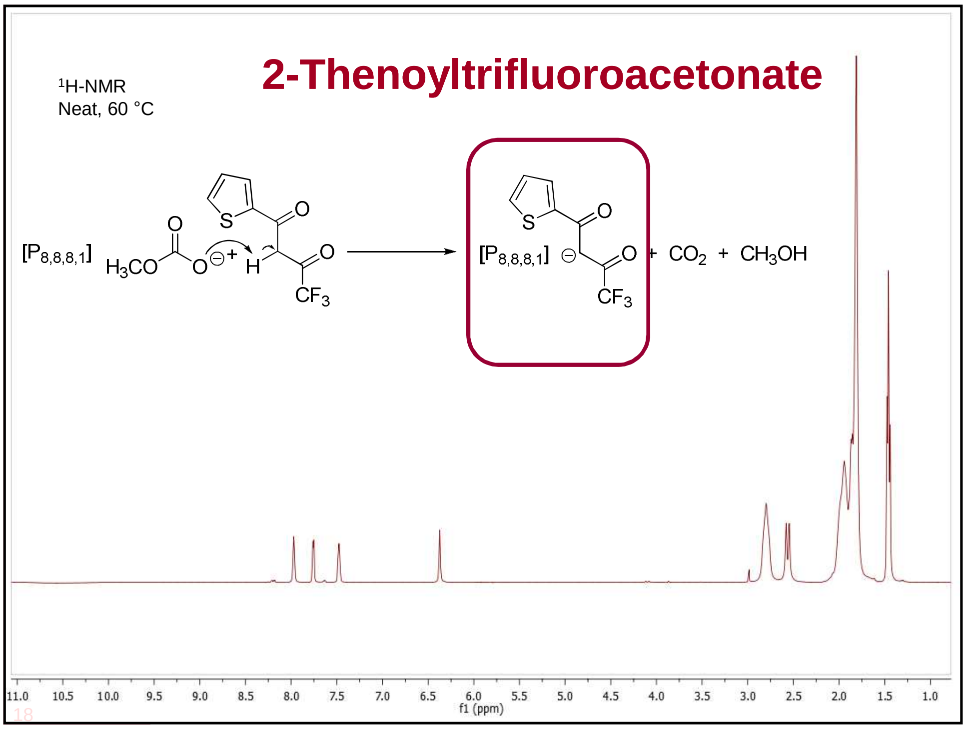
Truly green synthesis…

“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
1H-NMR
Neat 60 °C
[P8,8,8,1]
H3CO
O
H
CO2 + CH3OH
f1 (ppm)


2-Thenoyltrifluoroacetonate
1H-NMR
Neat, 60 °C
[P8,8,8,1]
H3CO
S
CF3
CO2 + CH3OH
f1 (ppm)

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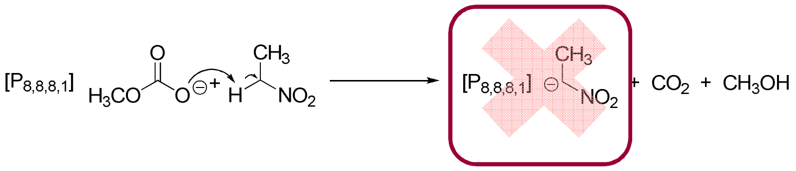
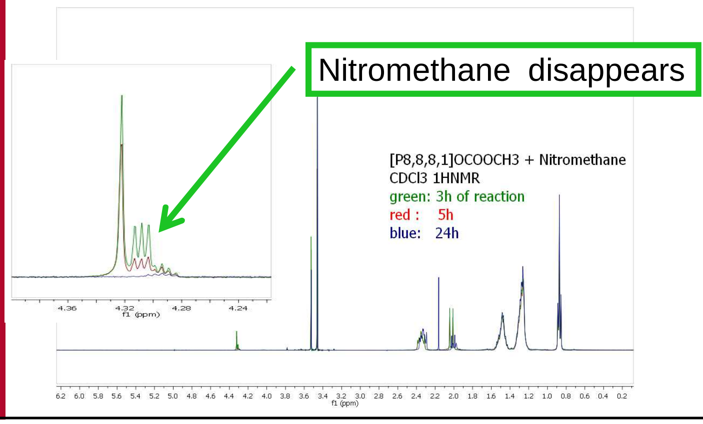
Nitroethanoate IL





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WHAT WE OBSERVED:

- the methylcarbonate anion slowly disappeared;
- nitroethane was converted 100%;
- no other proton signals appeared.

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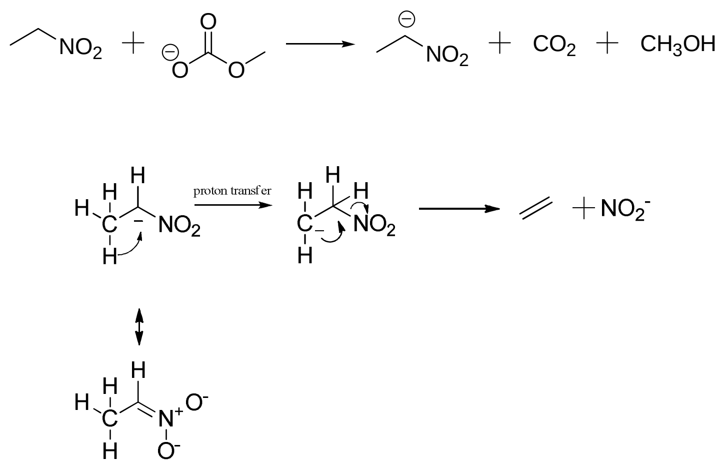
We hypothesised an α-elimation-rearrangement of nitroethane to yield the nitrite anion and ethylene:



Zimmerman, H. E.; Munch, J. H.,. *Journal of the American Chemical Society* 1968, *90* (1), 187-196.

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Further observations:

- Griess test was certainly positive for nitrite: NO_2
- conflicting evidence for the presence of ethylene (GC-MS, GC-FID, GC-TCD)

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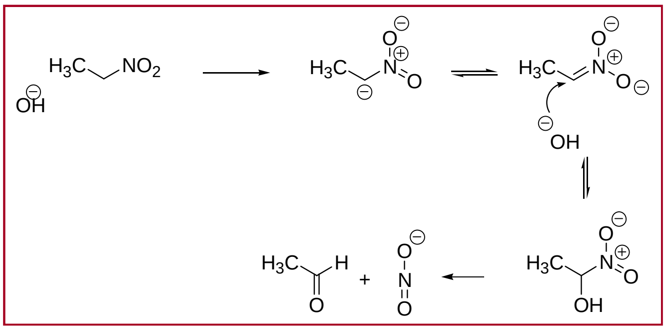
… so we read the literature:



Can. J. Chem. **1969**, *47*, 3107; *J. Am. Chem. Soc.* **1940**, *62*, 2604; *J. Chem. Soc.* **1900**, *77*, 1262; *J. Chem. Soc.* **1891**, *59*, 410

… still wondering what happens.

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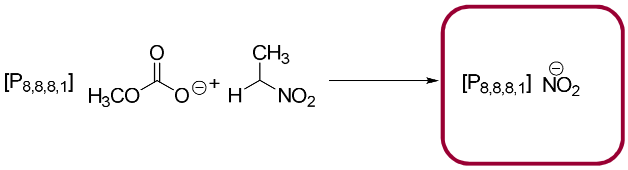
…but, it appears we have a route to nitrite ILs



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2. Organocatalysis

2.1 Carbon-Carbon Bond

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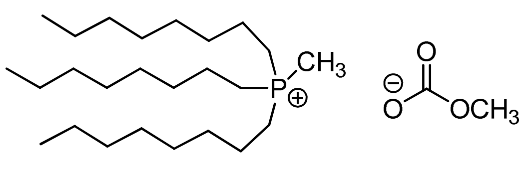
IL organo-catalyst



$P_{8,8,8,1}$ MC

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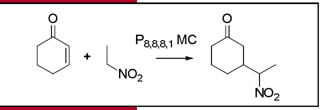
The first hint



Michael reaction

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

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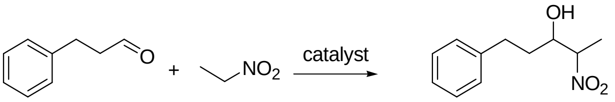
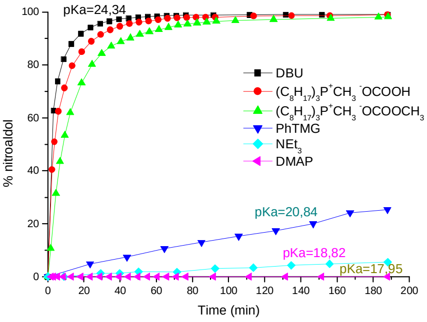
A second hint: Henry Reaction



0,5 M in $CDCl_3$, Nitroethane 5 equiv., 25°C
Catalyst:aldehyde ratio = 5%



M. Fabris, **M. Noè**, A. Perosa, M. Selva, R. Ballini *J. Org. Chem.* **2012**, *77*, 1805

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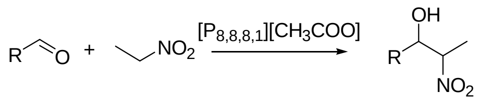
A second hint: Henry Reaction



Aldehyde R	time (h)	Nitroaldol product	
		(%, by NMR)	Y (%)[b]
CH_2CH_2Ph	2	96	88
$CH(CH_3)Ph$	2	96	93
C_2H_5	2	93	*90*
$C_{10}H_{21}$	2	99	97
4-$NO_2C_6H_4$	2	95	91
4-ClC_6H_4	3	82	71
C_6H_5	2	35	35

T = 25 °C

M. Fabris, M. Noè, A. Perosa, M. Selva, R. Ballini *J. Org. Chem.* **2012**, *77*, 1805

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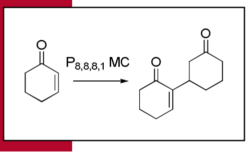
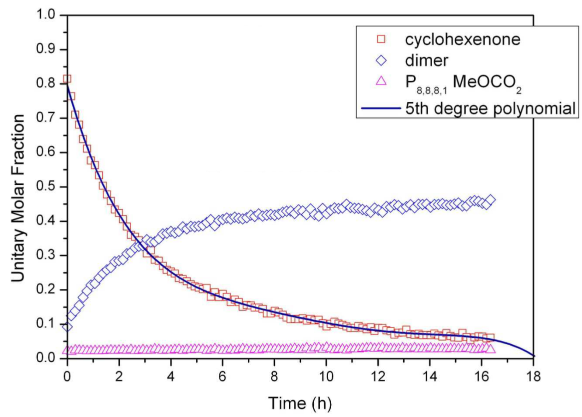
The third hint



Baylis-Hillman-type reaction



Conditions: 60 °C, no solvent, 1.0% $P_{8,8,8,1}$ MC

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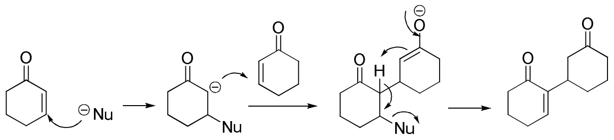
Accepted Baylis-Hillman reaction mechanism



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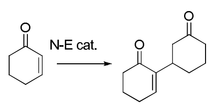
So, why does $P_{8,8,8,1}$MC behave as a strong base/nucleophile?



Baylis-Hillman-type reaction

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

N (Anion)	pKa	**E** (Cation)	rate h^{-1}
$MeOCO_2^-$	**5.51**	**$P_{8,8,8,1}$**	**12.60**
Br^-	-4.9	$P_{8,8,8,1}$	0.00
P_1-*t*Bu	26.98	-	9.37
DBU	24.34	-	1.48

Probably not just due to the pKa of the anion!

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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**.

N (Anion)	pKa	**E** (Cation)	rate h^{-1}
$MeOCO_2^-$	5.51	$P_{8,8,8,1}$	12.60
Br^-	-4.9	$P_{8,8,8,1}$	0.00
P_1-*t*Bu	26.98	-	9.37
DBU	**24.34**	**-**	**1.48**

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^-

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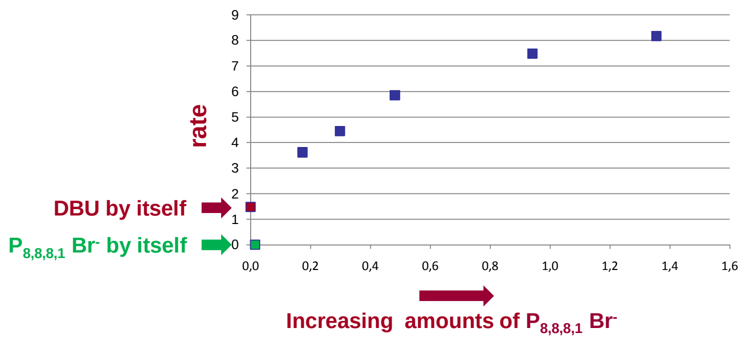
Added amounts of $P_{8,8,8,1}$ Br^-



N		E		{E}/{N}	rate h^{-1}
	{N}		{E}		
Br^-	0.015	$P_{8,8,8,1}$	0.015	1.00	0.00
DBU	0.042	–	–	0.00	1.48
		$P_{8,8,8,1}$	0.007	0.17	3.62
		$P_{8,8,8,1}$	0.013	0.30	4.46
		$P_{8,8,8,1}$	0.020	0.48	5.86
		$P_{8,8,8,1}$	0.039	0.94	7.48
		$P_{8,8,8,1}$	0.057	1.35	8.17

DBU by itself

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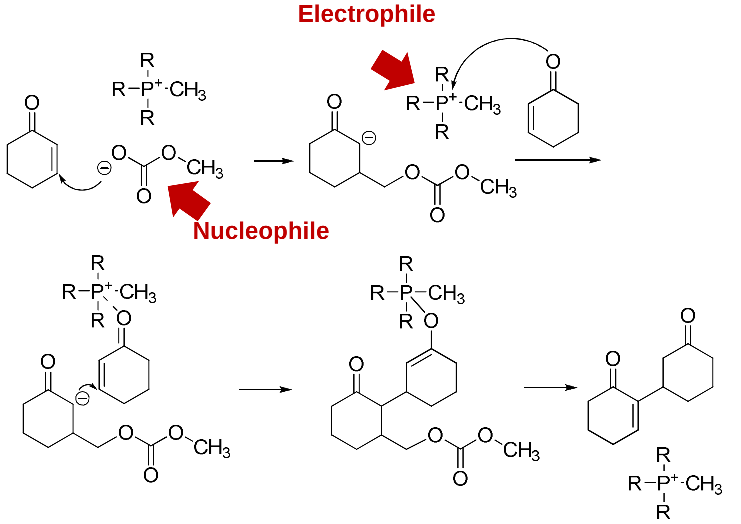
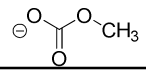
Ambiphilic activation?



V.Lucchini, M. Noe` , M. Selva, M. Fabris A. Perosa Chem. Commun., 2012, **48, 5178**



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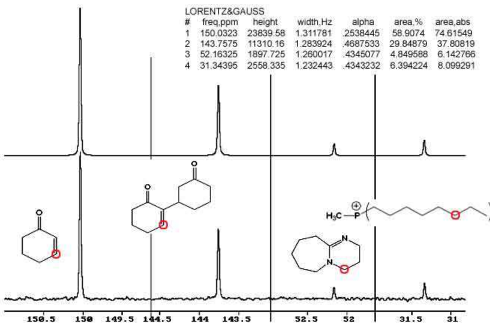
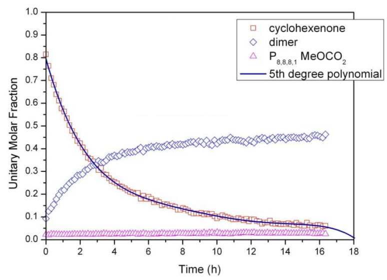
Deconvolution of selected ^{13}C resonances.



LORENTZ&GAUSS

#	freq,ppm	height	width,Hz	alpha	area,%	area,abs
1	150.0323	23839.58	1.311781	.2538445	58.9074	74.61549
2	143.7575	11310.16	1.283924	.4687533	29.84879	37.80819
3	52.16325	1897.725	1.260017	.4345077	4.849588	6.142766
4	31.34395	2558.335	1.232443	.4343232	6.394224	8.099291



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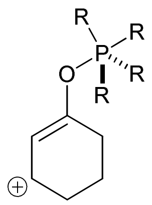
Precedents...



... hypotheses without experimental proof.

H. Schmidbaur, W. Buchner, F. H. Köhler, *J. Am. Chem. Soc.,* 1974, **96**, 6208-6210
J. McNulty, J. Dick, V. Larichev, A. Capretta, A. J. Robertson, *Lett. Org. Chem.*, 2004, **1**, 137-139

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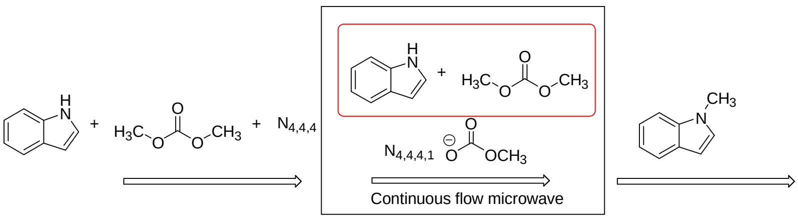
Interesting application...

Methylation using dimethylcarbonate catalysed by ionic liquids under continuous flow conditions

Toma N. Glasnov,[a] John D. Holbrey,*[b] C. Oliver Kappe,*[a] Kenneth R. Seddon[b] and Ting Yan[b]



Green Chemistry 2012 accepted article

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Jess Stanley

2. Organocatalysis

2.2 Transesterification

Alessio Caretto

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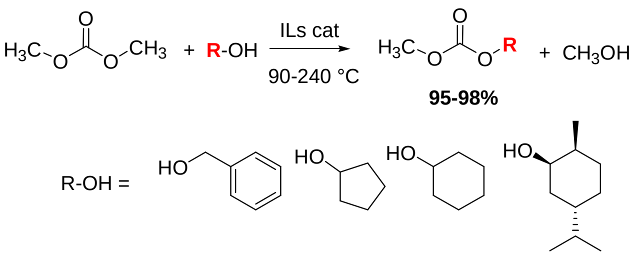
Transesterification of organic carbonates.



No decarboxylation of dimethylcarbonate is observed!

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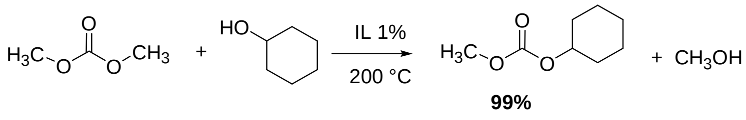
Transesterification of organic carbonates.



Catalyst	Conversion (%)	Selectivity (%)
[P_{8881}][CH_3OCOO]	52	>99
[P_{8881}][HOCOO]	68	
[P_{8881}][AcO]	93	
[P_{8881}][PhO]	78	

M. Selva, M. Noè, A.Perosa, M. Gottardo *Org. Biomol. Chem.*, **2012**, *10*, 6569

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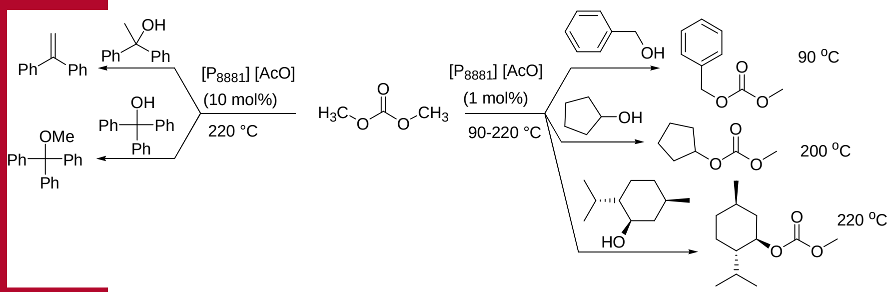
Transesterification of organic carbonates.



M. Selva, M. Noè, A.Perosa, M. Gottardo *Org. Biomol. Chem.*, **2012**, *10*, 6569

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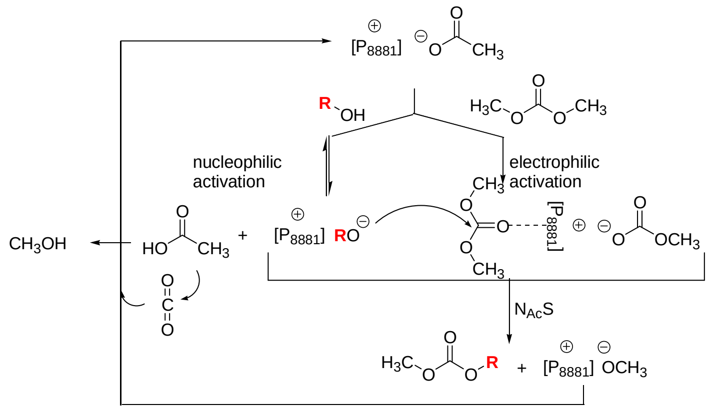
Transesterification of organic carbonates.



M. Selva, M. Noè, A.Perosa, M. Gottardo *Org. Biomol. Chem.*, **2012**, *10*, 6569

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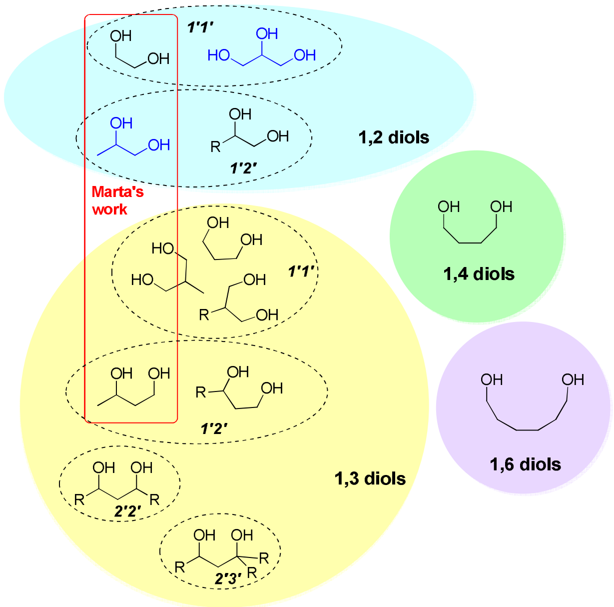
Transesterification of diols



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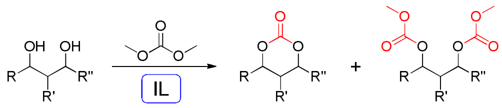
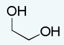
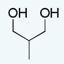
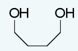
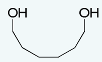
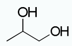
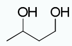
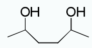
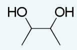
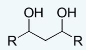
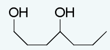
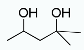
Transesterification of diols



	1,2 diols	1,3 diols	1,4 diols	1,6 diols
1,1				1h 
1,2				-
2,2				-
2,3	-		-	-

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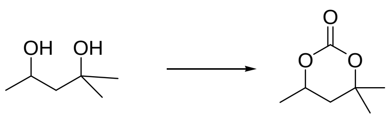
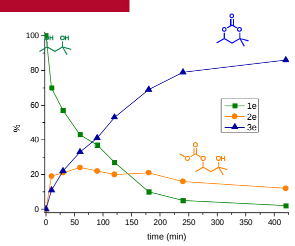
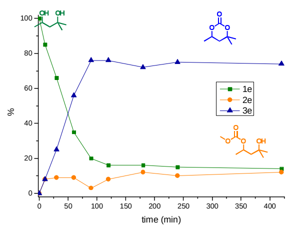
Transesterification of diols

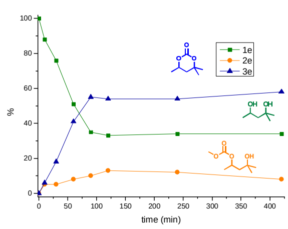




DMC : diol = 20 : 1



DMC : diol = 5 : 1



DMC : diol = 2 : 1

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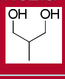
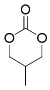
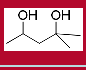
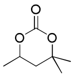
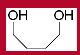
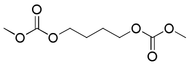
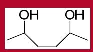
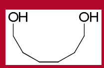
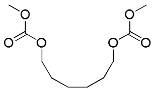
Transesterification of diols

	Main Product	Isolation	Purity %	Yield %
		Distillation	> 99%	70%
		Sublimation	> 99%	90%
		Distillation	> 99%	68%
	mixture	-	-	-
		Distillation	> 99%	73%

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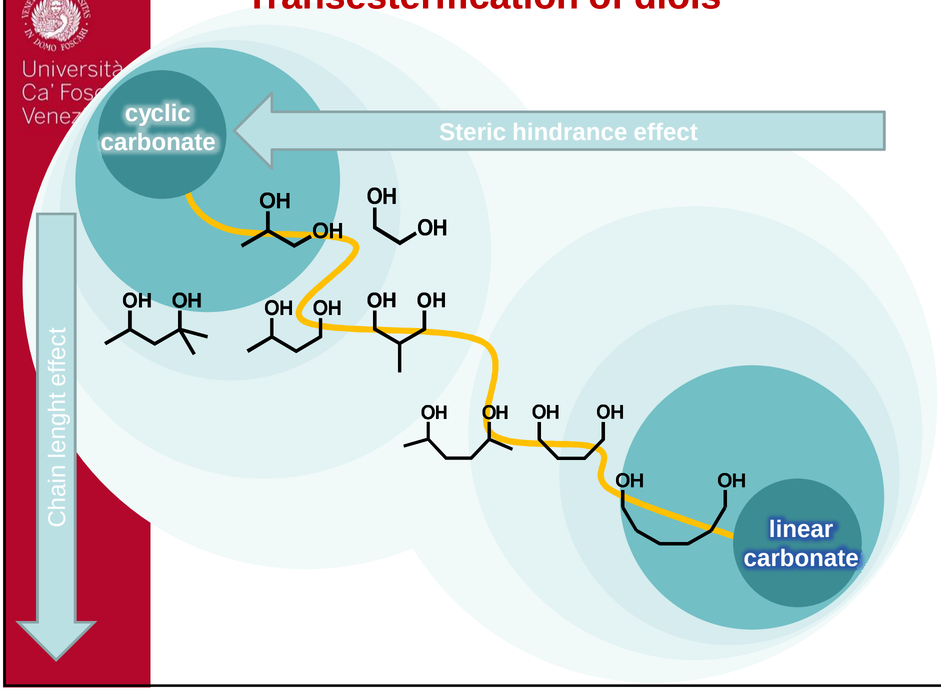
Transesterification of diols



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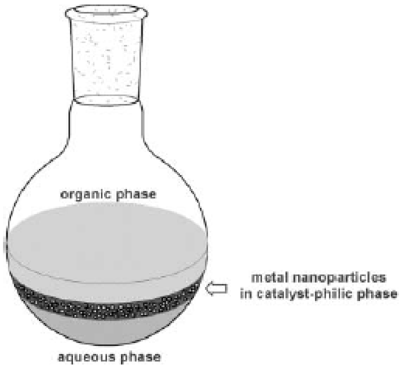
3. Multiphase systems based on ionic liquids

Marina Gottardo

Università Ca' Foscari Venezia

Multiphase systems based on ILs



Chem. Commun., 2006, 4480–4482
Adv. Synth. Catal. 2007, 349, 1858 – 1862
Chem. Soc. Rev., 2007, 36, 532–550

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Multiphase systems based on ILs

no IL

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

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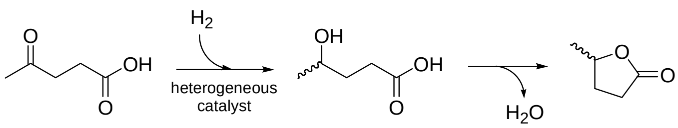
Multiphase systems based on ILs applied to the upgrade of bio-based molecules



Levulinic Acid — γ-Hydroxyvaleric acid — γ-Valerolactone (GVL)

Catalyst: Ru/C 5%

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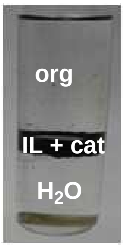
Strategy for multiphase system design



1. Choose organic solvent
2. Choose ionic liquid

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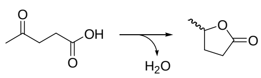
Multiphase system design: Organic solvent choice

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

Solvent	LA solubility	GVL solubility	Solubility in water @ 20°C
Iso-octane	no	no	immiscible
Cyclohexane	no	no	immiscible
Toluene	yes	yes	0.52 g/L
Ethyl acetate	yes	yes	0.83 g/L
Ethyl lactate	yes	yes	miscible
Acetonitrile	yes	yes	miscible
water	yes	yes	miscible



Levulinic Acid

γ-Valerolactone (GVL)

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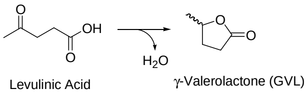
"Inverse" multiphase system

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

Levulinic acid and GVL



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

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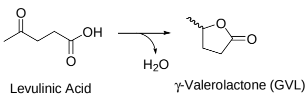
Multiphase system design: Choice of IL

IL	LA Conversion	IL in H_2O (%, wt)
$[N_{8,8,8,1}][Cl]$	32	2-3
$[N_{8,8,8,1}][NTf_2]$	100	not measurable
$[P_{8,8,8,1}][NTf_2]$	100	not measurable
$[N_{8,8,8,1}][TFA]$	100	41
$[P_{8,8,8,1}][NO_3]$	100	17



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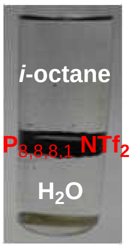
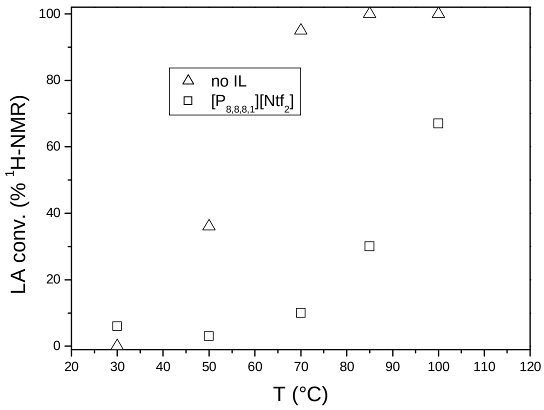
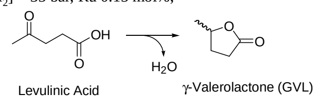
Multiphase system





Conversion of LA to GVL in the multiphase system with 5% Ru/C as a function of temperature after 30 min: (Δ) without the IL third phase; (□) with a third phase made by $[P_{8,8,8,1}][NTf_2]$. $p[H_2]$ = 35 bar, Ru 0.15 mol%,



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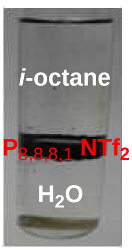
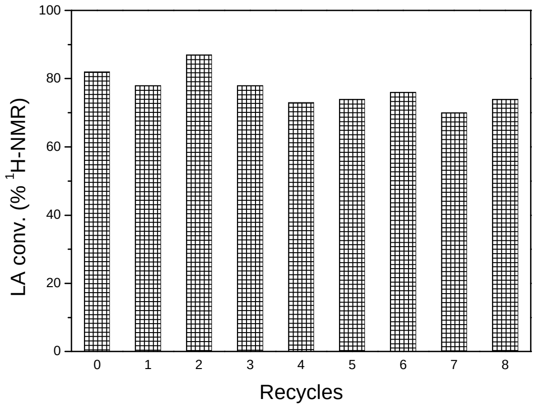
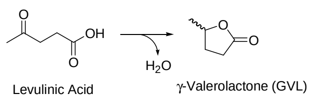
Multiphase system





Conversion of LA to GVL: recycling of the Ru/C catalyst system.



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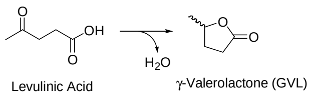
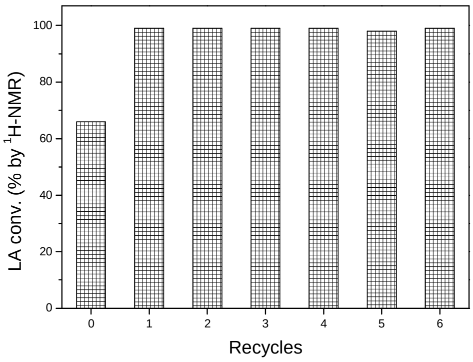
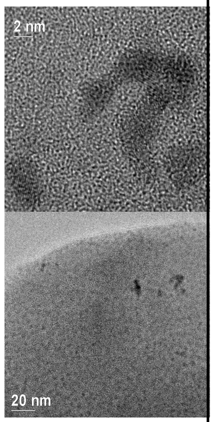
Same thing with homegenous $RuCl_3$







Conversion of LA to GVL: recycling of the $RuCl_3$ catalyst system {Conditions: 16 h, 150 °C, p[H_2] = 35 bar, $RuCl_3$ (20 mg, 0.0765 mmol; Ru = 1.0 mol%)

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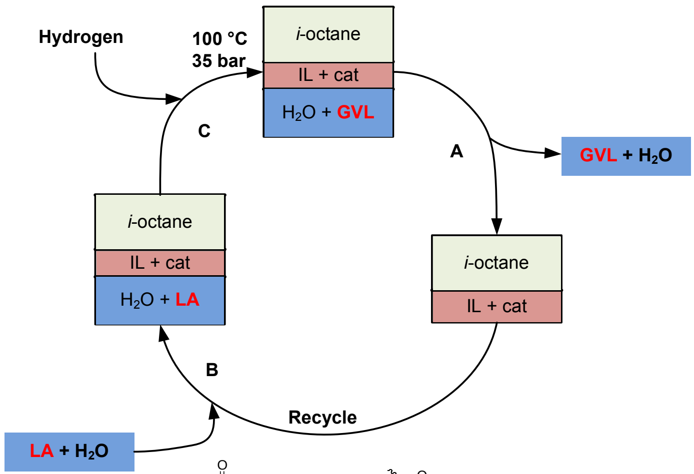
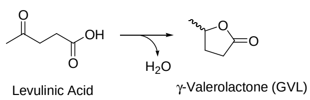
Multiphase system





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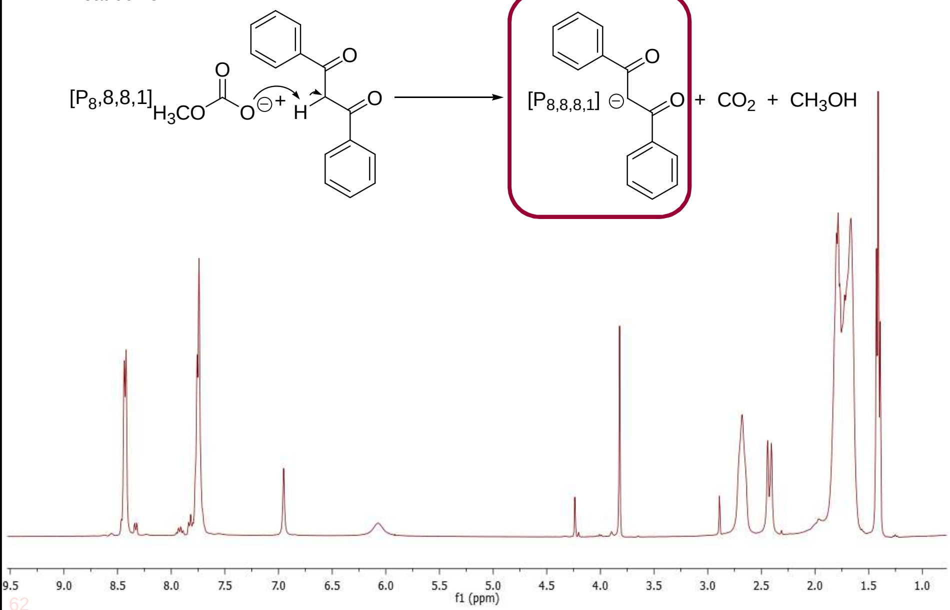
Chandrashekhar Malba

4. Luminescent ionic liquids

Manuela Facchin

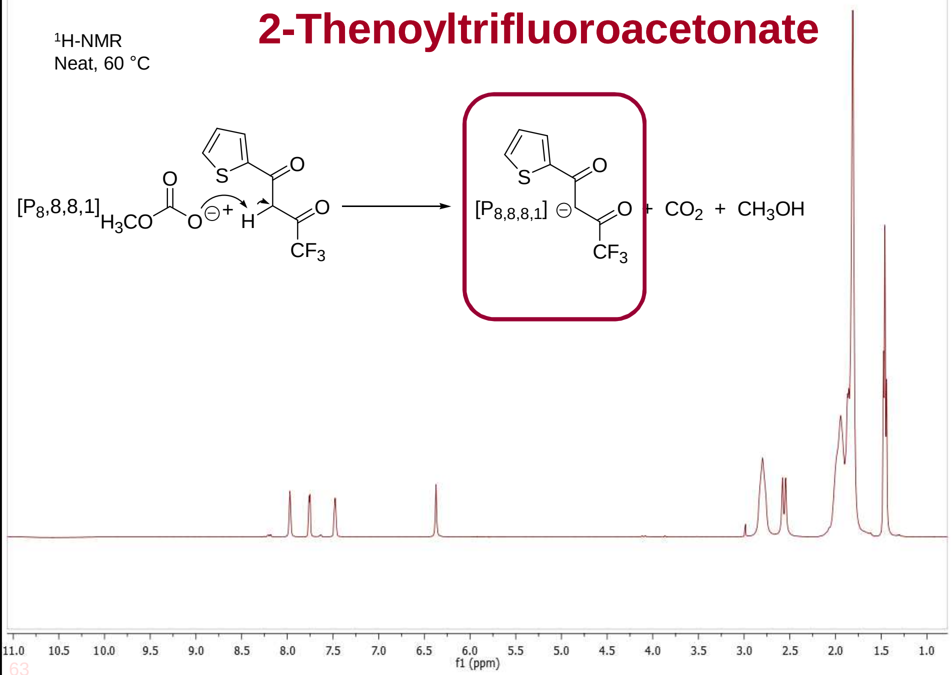
Dibenzoylmethanate

^{1}H-NMR
Neat 60 °C



2-Thenoyltrifluoroacetonate

^{1}H-NMR
Neat, 60 °C



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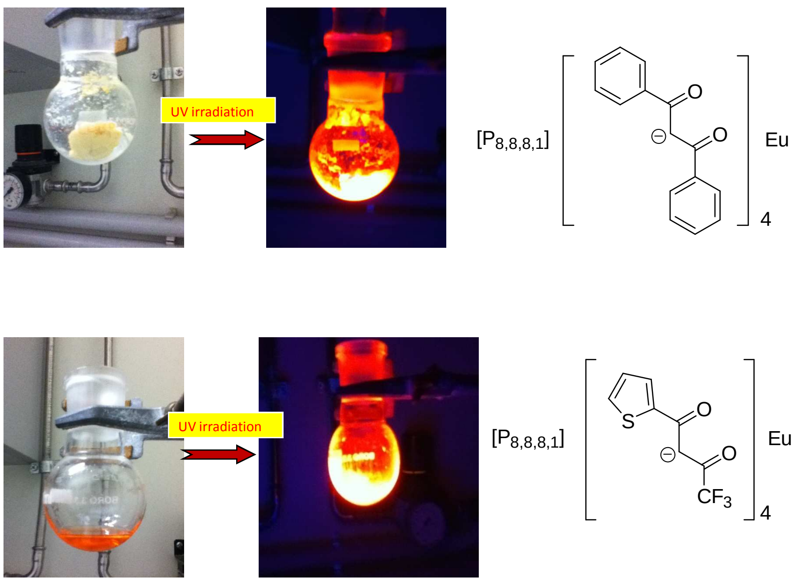
Luminescent ionic liquids



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5. ongoing….

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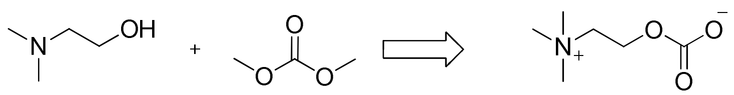
Zwitterionic liquids



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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)