Phosphonium ionic liquids (PILs) as organocatalysts for green reactions: nucleophilic electrophilic cooperative catalysis

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Abstract: With the aim of developing a green synthesis of phosphonium ionic liquids (PILs), we prepared a series of methyltrialkylphosphonium methyl carbonates $[P_{n,n,n,1}]^+[O(CO)OCH_3]^-$ by the alkylation of trialkylphosphines with the non toxic dimethylcarbonate. These compounds proved to be active organocatalysts for a number of base-promoted organic reactions such as Michael, Henry, and Baylis-Hillman condensations, and transesterification reactions. In addition methyl carbonate salts were a convenient starting material to synthesise a large array of ionic liquids where the phosphonium cation was coupled to weakly basic anions such as bicarbonate, acetate, trifluoroacetate, phenate, chloride, bromide and many more. Mechanistic studies indicated that the anionic and the cationic partners of such ionic liquids acted cooperatively and independently as nucleophilic and electrophilic catalysts. The ambiphilic propensity of these salts was demonstrated by kinetically discriminating the contributions of the anion (nucleophilic catalyst) and of the cation (electrophilic catalyst) on the model solvent-free Baylis–Hillman dimerization of cyclohexenone.

Keywords: phosphonium ionic liquids, organocatalysis, green organic reactions, dimethylcarbonate

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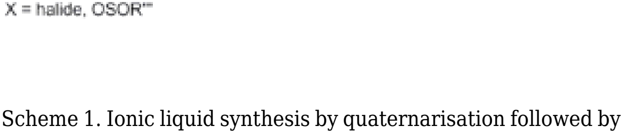
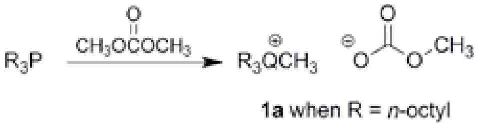
1. Introduction

Ionic liquids (ILs) have elicited phenomenal interest among chemists. Their applications for clean catalysis and for the development of green and innovative processes in chemical industry are well known [1,2]. However, considering ILs as ecosustainable solvents is somehow a gamble, although, being neoteric solvents, they have been used as reaction media to improve the sustainability of chemical reactions [3]. The reason why often the use of ionic liquids is considered poorly environmental compatible mainly lies in the manufacturing process of these materials. ILs synthesis, in fact, generally involves two potentially environmentally adverse steps [4]: quaternarisation of a nitrogen or phosphorous atom, usually by alkylation with hazardous alkyl halides, to obtain an halide salt, followed by an halide anion metathesis with formation of the desired IL and equimolar amounts of a salt by-product (Scheme 1) [5,6].Atom economy and mass index [7] of the overall process are quite poor, since only part of the alkylating agent ends up in the desired compound and by-products (*i.e.* inorganic salts) can be very difficult to separate from the desired IL, especially in the case of hydrophilic ionic liquids. Even if some halide-free ILs syntheses were optimised [8,9], those procedures still require the use hazardous and highly toxic reagents such as methanesulfonyl chloride [10] or dialkylsulfates [11], and generate unwanted by-products.



Scheme 1. Ionic liquid synthesis by quaternarisation followed by anion exchange.

To overcome such drawbacks, we have recently reported an innovative synthesis of a series of methyl carbonate phosphonium salts by methylation of trialkylphosphines with dimethyl carbonate (DMC) (Scheme 2) [12]. This procedure was genuinely green: it was not only simple and halide-free, but it also involved non toxic DMC as an alkylating agent, to obtain very pure ionic liquids that could be used straight out from the reaction vessel.



Scheme 2. Trialkylphosphine quaternarisation with DMC.

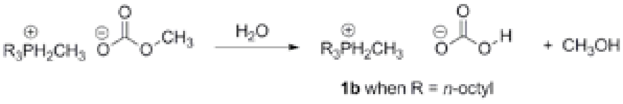
The resulting phosphonium methylcarbonate ILs, were stable for months on the shelf.

These methylcarbonate ILs react readily with Brønsted acids (H-A, Scheme 3) to yield the corresponding anion exchanged salts (Q^+A^-) along with methylhydrogencarbonate (i.e. the half-ester of carbonic acid). The latter compound is unstable above -36 °C [13], and immediately decomposed to form methanol and CO_2, thus providing its built-in removal (Scheme 3). This exchange procedure was tested for a number of acids.

Scheme 3. Reaction of -onium methylcarbonates with Brønsted acids: general route.

The combination of the simple quaternarisation of phosphines and the easy and free of additional solvents work up step for anion metathesis allowed us to prepare an offspring of different ionic liquids, more specifically, phosphonium based ionic liquids (PILs).

When water is used as the Brønsted acid the outcome is different and hydrogencarbonate salts are obtained (Scheme 4).



Scheme 4. Reaction of -onium methylcarbonates with Brønsted acids: synthesis of hydrogencarbonate PILs.

Methylcarbonate and hydrogencarbonate salts, $[P_{n,n,n,1}][O(CO)OCH_3]$ and $[P_{n,n,n,1}][O(CO)OH]$, were an interesting class of model compounds. The most intriguing peculiarity of such ILs was their exceptionally high activity for base-catalysed reactions [12], even though they both possessed intrinsically poor basic anions (methylcarbonate and bicarbonate). Phosphonium salts obtained from metathesis with similar anions such as acetate and phenolate, showed analogue organocatalytic performances. Therefore, we were prompted to investigate this class of PILs to develop new procedures for green catalytic reactions, possibly carried out under solventless conditions.

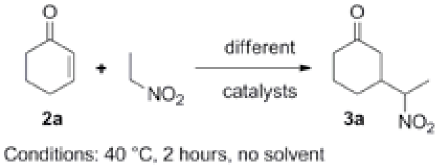
The most relevant results of this research are reported here and discussed to offer a rationale for the unexpected behaviour of PILs as organocatalysts.

2. Results and discussion

2.2. Basic PILs as catalysts

2.2.1. Michael type addition

Methylcarbonate and hydrogencarbonate PILs were expected to be somewhat basic, but in many instances, they actually exceeded our expectations. This was exemplified by the Michael addition of nitroethane to cyclohexenone which was chosen as a probe reaction (Scheme 5) [14].



Scheme 5. Michael reaction of nitroethane with cyclohexenone.

Trioctylmethyl phosphonium methylcarbonate, $[P_{8881}][O(CO)OCH_3]$ **1a** and bicarbonate $[P_{8881}][O(CO)OH]$ **1b** were so active as base catalysts at the point that they could be employed in amounts as low as 0.4% mol. A series of experiments was therefore carried out to compare salts **1a** and **1b** to conventional basic catalysts, such as sterically hindered tertiary organic amines (DBU = 1,8-diazabicyclo [5.4.0]undec-7-ene, DMAP = dimethylaminopyridine, DABCO = 1,4-diazabicyclo[2.2.2]octane, P_1-t-Bu = phosphazene base, sodium bicarbonate, and sodium hydroxide), as reported in Table 1. **1a** and **1b** (Entries 1 and 2, Table 1) were more efficient than any other organic bases tested for the investigated reaction. Of striking interest was the comparison of **1b** (Entry 2, Table 1) to $NaHCO_3$ (Entry 8, Table 1): notwithstanding both salts had the same anion, **1b** was among the best catalysts, while $NaHCO_3$ was not active at all. This suggested that properties of the [O(CO)OH] anion were tremendously affected by its coupling to the onium cation.

Table 1. Michael reaction of nitroethane with cyclohexenone using different bases.[a]

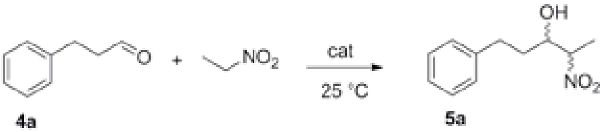
Catalyst	pKa	Conv. (% GC)	Selectivity[b]
$[P_{8,8,8,1}][OCOOCH_3]$ **1a**	-	87	100
$[P_{8,8,8,1}][OCOOH]$ **1b**	-	86	100
Phosphazene base P_1-*t*-Bu	27 [15,c]	82	100
DBU	24 [16,c]	77	92
DMAP	18[16,c]	0	-
NaOH	15.7 [d]	7	100
DABCO	8.5 [17,c]	0	-
$NaHCO_3$	6.4 [d]	0	-

[a] Conditions: 40 °C, 2 h, solventless, catalyst:cyclohexenone molar ratio = 0.004. [b] Selectivity towards 15. [c] pKa's of entries 3, 4, 5, 7 were measures in acetonitrile. [d] pKa's of entries 6, 8 were measured in aqueous solution

This procedure was generalised and a number of Michael adducts between donors such as nitrobutane, dibenzoylmethane and dimethylmalonate with ethyl vinyl ketone as the acceptor, were obtained in high yield via a green protocol [2,12]. Reactions were carried out successfully in the absence of any added solvent, with very low amount of catalyst, and with a remarkably simplified work up and product isolation.

2.2.2. Henry reaction

A different protocol for C-C bond formation was then investigated. In particular, Henry reaction between nitroalkanes and carbonyl derivatives was considered [18]. The addition of nitroethane to 3-phenyl propionaldehyde (PPA, **4a**) was chosen as the model reaction (Scheme 6) [19].



Scheme 6. Henry reaction of 3-phenylpropionaldehyde with nitroethane.

Methyl trioctyl phosphonium salts **1a** and **1b** were compared to four different conventional bases which were selected to operate under homogeneous conditions (as with ILs) and to cover a relatively wide pK_a range, approximately from 24 to 18 [20]. Non-ionic bases employed were DBU, DMAP, 1,1,3,3-tetramethylamino-2-phenylguanidine (PhTMG) and triethylamine (NEt_3).

A set of experiments was carried out at 25°C and using a 0.01:1 catalyst/aldehyde molar ratio. The reactions outcome was monitored in time by ^1H NMR. Figure 1 plots the amount of nitroaldol products (**5a**) against time obtained for each of the base catalysts used.

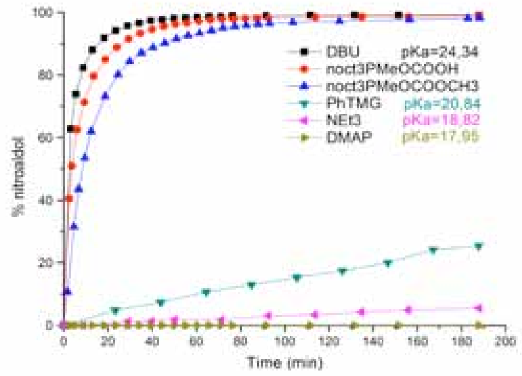
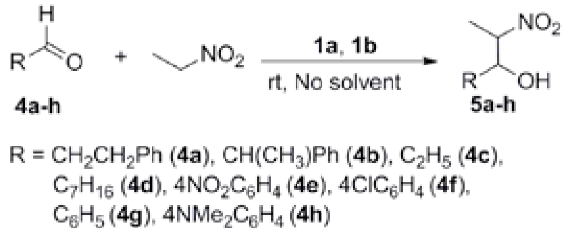


Fig. 1. Comparison of different base catalysts (**1a**, **1b**, DBU, PhTMG, Et_3N, and DMAP) in the Henry condensation of PPA with nitroethane (T =25 °C, solvent: $CDCl_3$) (pKa values in acetonitrile).

The behaviour of the different catalysts emerged quite clearly. Carbonate ionic liquids, especially the bicarbonate salt **1b**, lead to a reaction outcome comparable to that of DBU (blue, red, and black profiles). By contrast, the reaction turned out to be extremely sluggish using both PhTMG and Et_3N. Finally, when using DMAP as catalyst, no appreciable formation of nitroaldol **5a** was observed, even after 20 hours of reaction (olive profile).

The overall trend suggested a very good correlation between the catalytic activity and the dissociation constants (pK_a) of the basic catalysts. The higher the pK_a, the stronger the base, the better its performance. In particular, the activity of **1a** and **1b** salts places them in the range of organo-superbases (pK_a≈24).

In search for a synthetic application of salts **1a** and **1b**, a further investigation on carbonate ionic liquids as catalysts for the Henry condensation of different aldehydes with nitroethane was performed (Scheme 7).

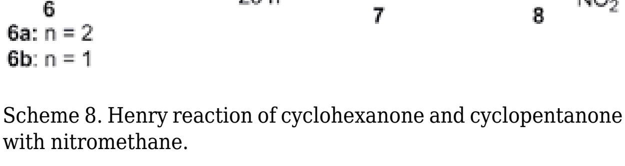


Scheme 7. Henry condensation of selected aldehydes with nitroethane under solvent free conditions.

In all cases, the expected nitroaldol derivatives were obtained in moderate to good yields (71-97%) requiring short reaction times (2-3 hours). Due to the low catalyst loading, work up and isolation of products was greatly simplified.

2.2.2.1. The Henry reaction of ketones with nitromethane

The catalytic performance of carbonate salts **1a** and **1b** for the Henry additions of aldehydes, prompted us to explore their efficiency in the same reactions with ketones. Both electronic and steric effects make ketones less reactive than aldehydes. For this reason, the reactions of cyclohexanone and cyclopentanone (**6a** and **6b**, respectively) with an activated nucleophile precursor, such as nitromethane, was investigated. Under the conditions summarised in Scheme 8, Henry reactants (nitromethane and ketone) were mixed in a 1:1.2 molar ratio, with 10% molar equivs. of **1a** or **1b**.



Scheme 8. Henry reaction of cyclohexanone and cyclopentanone with nitromethane.

Results are summarised in Table 2. The use of **1a** rather than **1b** as catalysts, did not appreciably affected the reaction outcome (compare Entries 1-2, 3-4, 5-6, and 7-8, Table 2). A temperature increase from 25 to 50 °C, however, induced a dramatic change of the product distribution. At 50 °C, dinitroderivatives **8** became major products (Entries 5-10, Table 2). In particular, selectivity for **8b** increased up to 93% (Entry 7, Table 2). Conversion of both ketones levelled off at moderate values (25-58%), because the formation of **8** extensively consumed nitromethane.

In order to selectively obtain products **8** we increased the nitromethane:ketone and the **1a**:ketone ratios. Accordingly, products **8a-b** could be obtained with very high selectivity (91 and 98 % by NMR, respectively) in very good isolated yields (81 and 91% respectively) (Entries 9 and 10, Table 2).

It should be noted that in the reaction of ketones and nitroalkanes, Kisanga et al. [21], observed the formation of compounds **8** only when using 30% molar equivalents of a very strong and air sensitive base (proazaphosphatrane) in combination with more than 2 equivalents of anhydrous $MgSO_4$, obtaining the derivatives **8** only in 20 % yield.

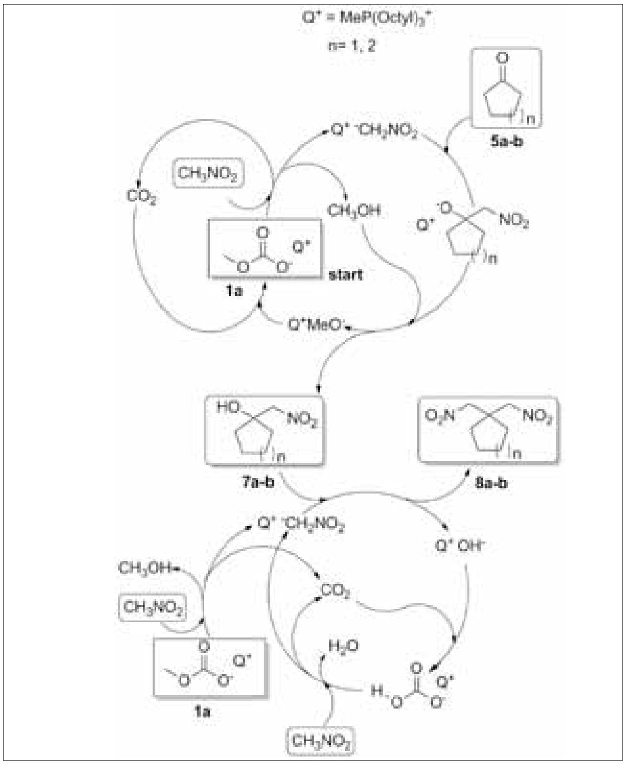
Table 2. Henry reaction of cyclic ketones with nitromethane catalysed by ILs **1a** and **1b.**[a]

Entry	Ketone	Cat.	T (°C)	Products (%, by NMR)		Isolated yield
				7a/b	**8a/b**	(%)[b]
1	**6a**	**1a**	25	61	2	58
2	**6a**	**1b**	25	57	11	
3	**6b**	**1a**	25	27	12	25
4	**6b**	**1b**	25	27	13	
5	**6a**	**1a**	50	24	29	
6	**6a**	**1b**	50	24	34	
7	**6a**	**1a**	50	4	50	
8	**6b**	**1b**	50	9	48	
9[c]	**6a**	**1a**	50	8	80	81
10[c]	**6b**	**1a**	50	1	92	91

[a]Nitromethane: ketone and catalyst: ketone molar ratio were of 1.2 and 0.10 respectively. [b]Isolated yield of the main product after purification through silica gel. [c]The molar ratio nitromethane:ketone and catalyst:ketone were of 5.0 and 0.50 respectively.

2.2.2.2. Mechanism proposal for PILs catalysed Henry additions

The proposed mechanism is summarized in Scheme 9.



Scheme 9. Proposed mechanism for the phopshonium carbonate salts catalysed Henry condensation.

The active nucleophile is generated by an initial acid-base reaction between the salt **1a** and nitromethane giving the nitronate onium salt ($Q^+CH_2NO_2^-$), along with the rather unstable methyl carbonic acid ($MeOCO_2H$) [13].The latter readily decomposed to CO_2 and methanol. Then, a nucleophilic addition of $Q^+CH_2NO_2^-$ to the ketone carbonyl followed by a second acid/base reaction with methanol produced the nitroaldol **7** and a methoxide onium salt (Q^+MeO^-). Although the existence of methoxide ionic liquids was reported only recently [22], the reversible trapping of CO_2 by simple alkoxide anions is a well-known process (Scheme 10) [23].

$$MeO^- + CO_2 \rightleftharpoons MeOCO_2^-$$

Scheme 10. Trapping of CO_2 by methoxyde anion.

In our case, this explained the restoration of catalyst **1a**.

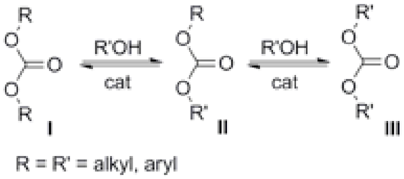
The reaction could stop at this stage or, in presence of an excess of nitromethane and at higher temperature (50°C), could proceed further via the nucleophilic displacement of the nitronate salt ($Q^+CH_2NO_2^-$) on nitroaldol **7**.

The easy dehydration of nitroaldols **7** to the corresponding nitroolefins might also be considered: however, under the investigated conditions, this pathway was ruled out since the expected by-products were not observed. As for aldehydes, products of self-condensation of ketones were not detected.

Overall, the double addition of nitromethane to cyclic ketones was a genuine catalytic process, but the initial methyl carbonate catalyst **1a** was plausibly transformed in the hydrogen carbonate analogue **1b**. This was confirmed by the formation of both products **8a** and **8b** also when compound **1b** was used as catalyst (Entry 8, Table 2).

2.2.3. Transesterifications

Catalytic transesterification reactions are among the most established protocols for the synthesis of both diaryl and dialkyl carbonates (Scheme 11) [24].



Scheme 11. Transesterification of organic carbonates.

These transformations, however, continue to fuel an extensive research activity because of the growing interest on eco-friendly carbonates as solvents and intermediates in pharmaceutical, lubricants and polymer industries [25].

With the aim to further explore the potential of compounds **1a-1b** as organocatalysts, we decided to use them to catalyze the transesterification of dialkyl carbonates (DAlCs) with model primary and secondary alcohols [26]. ILs derived from **1a**, were also considered in this study. Reaction conditions were optimised for the transesterification reaction between DMC and cyclohexanol (CyOH) in the presence of four different catalysts: the salt **1a** $[P_{8,8,8,1}][O(CO)OCH_3]$, and representative basic transesterification catalysts such as K_2CO_3, and the non-ionic organic bases DMAP and DBU [27].Results are summarised in Table 3.

Table 3. The transesterification of DMC with cyclohexanol over different catalysts.[a]

Entry	Cat:CyOH (mol:mol,%)[b]	Conversion of CyOH (%)[c]				CyMC (%)[d]
		K_2CO_3	DBU	DMAP	**1a**	Isolated yield
1	10	1	3	65	97	93
2	5	2	1	32	90	90
3	2	0	0	2	60	
4	1	0	0	0	32	
5	no cat.					no react.

[a] All reactions were carried for 3.5 h at 90 °C. [b] % Molar ratio catalyst:cyclohexanol. [c] Conversion of cyclohexanol determined by GC, using different catalysts. [d]CyMC: cyclohexyl methyl carbonate ($CyOCO_2CH_3$): % selectivity (Sel) and % isolated yield (crude compound). Y was determined after FCC purification of the reaction catalyzed by **1a**.

As reported in Table 3, DBU and K_2CO_3 were not efficient trasesterification catalysts. DMAP allowed the reaction to proceed to some extent in selected experimental conditions (Entries 1 and 2, Table 3). PIL **1a** however, was by far the most efficient system for the synthesis of the monotransesterification product, cyclohexyl methyl carbonate ($CyMCO_2CH_3$, CyMC) that was isolated in 93% yield. In particular, noteworthy aspects were: i) **1a** selectively catalyzed the formation of the monotransesterification product (selectivity > 99%) with quantitative conversions of CyOH (Entries 1 and 2, Table 3); ii) the reaction required low amounts (1-2 % mol) of **1a** (Entries 3 and 4, Table 3), while in the same experimental conditions DMAP was not an effective catalyst (Entries 3 and 4, Table 3).

Different PILs were employed as catalysts for the transesterification of DMC with cyclohexanol. In particular, methyltrioctylphosphonium bicarbonate (**1b**: $[P_{8,8,8,1}][O(CO)OH]$), methyltrioctylphosphonium acetate (**1c**: $[P_{8,8,8,1}][CH_3(CO)O]$), and methyltrioctylphosphonium phenolate (**1d**: $[P_{8881}][PhO]$), were considered. Results, compared to catalyst **1a**, are summarised in Table 4.

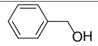
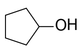
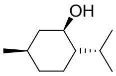
Table 4. The transesterification of DMC with cyclohexanol using catalysts **1a**, **1b**, **1c** and **1d**.[a]

Entry	Catalyst	Cat:CyOH (mol:mol,%)[b]	Conv. (%)[c]	Sel. (%)[c]
1	**1a**: $[P_{8881}][CH_3OCOO]$	1	52	>99
2	**1b**: $[P_{8881}][HOCOO]$	1	68	
3	**1c**: $[P_{8881}][AcO]$	1	93	
4	**1d**: $[P_{8881}][PhO]$	1	78	

[a] All reactions were carried for 3 h at 200 °C. [b] % Molar ratio catalyst:cyclohexanol. [c]Conv.: conversion of cyclohexanol determined by GC; Sel.: the selectivity towards cyclohexyl methyl carbonate (CyMC).

Salts **1b**, **1c** and **1d** were efficient and selective catalysts towards the formation of CyMC, observing, in all cases, an increased activity compared to **1a**. In particular, with catalyst **1c** quantitative formation of CyMC was observed in 1h 30’ (Entry 3, Table 4), with a catalyst loading of only 1 % mol. The excellent catalytic activity of **1c** was further exploited for the transesterification of DMC with different aliphatic alcohols. Results are reported in Table 5.

Table 5. The reaction of DMC with different alcohols catalysed by salt **1c.**[a]

Entry	Alcohol (ROH)	T (°C)	t (h)	Conv. (%)[b]	$ROCO_2Me$, (%)[c]	Y (%)[d]
1		90	6	100	97	95
2		150	6	29	29	
3		200	2	100	100	96
4		220	6	95	95	92

[a]% Molar ratio catalyst:alcohol was 1.0. [b]Conv.: conversion of alcohol (ROH) determined by GC. [c] Major reaction products detected by GC. [d] Y: Isolated yield of products of transesterification ($ROCO_2Me$).Products were purified by FCC on silica-gel.

In all cases, a quantitive and selective formation of the monotransesterification product was observed, even with sterically hindered alcohols such as menthol, isolating the corresponding alkylmethylcarbonate derivatives in quantitative yields.

2.2.3.1. PILs as transesterification catalysts

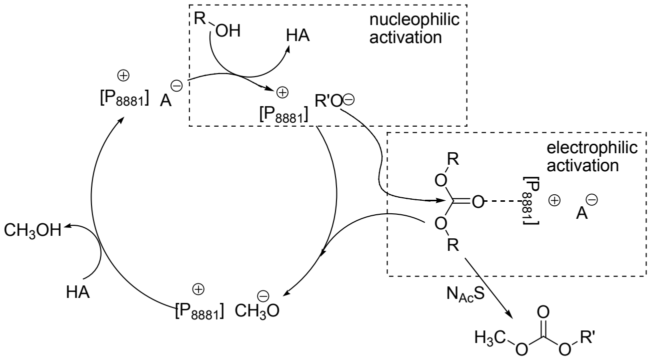
ILs **1a-1d** have shown an increased activity, in comparison to known organic and inorganic based transesterification catalysts, for the model transesterification of DMC with cyclohexanol. It is well known that, at T >180°C, both solid bases (K_2CO_3, MgO, Al_2O_3) and zeolites efficiently activate the reactions of dialkyl carbonates (DAlCs) with several nucleophiles [28]; these transformations however, often proceed along with extensive decarboxylations of DAlCs themselves to produce the corresponding ethers (ROR) and CO_2 [29]. PILs **1a-1d** were able to selectively catalyse the transesterification reaction, without formation of appreciable amounts of CO_2. Not only the investigated ILs are inactive to decarboxylation side processes, but they allow to improve the overall reaction sustainability since unconverted dialkyl carbonates (dimethrylcarbonate, DMC and diethylcarbonate, DEC) can be fully recovered by simple distillation and reused [30]. Salts **1a-1d** share the same cation structure and are all obtained by exchange of methyltrioctylphosphonium methylcarbonate with weakly basic anions (methylcarbonate, bicarbonate, acetate and phenolate, respectively).

The dissociation constants in water (pK_a) of the corresponding acids precursors are [31]:

4.76 (AcOH) < 5.6 (CH_3OCO_2H) < 6.4 (H_2CO_3) [32] < 9.89 (PhOH).

Comparing such values to the activity trend observed for the transesterification of DMC with cylohexanol (Table 3: **1a** $[P_{8881}][CH_3OCO_2]$ <**1b** $[P_{8881}][HOCO_2]$ <**1d** $[P_{8881}][PhO]$ <**1c** $[P_{8881}][CH_3CO_2]$), it is evident that no correlation can be inferred. In fact, acetate salt (**1c**) is the most active catalyst , as well as the weakest anionic base, followed by the phenolate salt (**1d**) which is the strongest anionic base. The overall trend is hardly affected by the anion basicity. A contribution by the counter-ion must be taken into account for an exhaustive description of the activation mechanism.

The catalytic activity of PILs is due to both their nucleophilicity and their electrophilicity, this ambiphilic nature [1, 33] leads to the selective generation of ion pairs with the nucleophiles and the electrophiles present in the reaction mixture: (i) the anion activates the alcohol moiety by formation of the corresponding alkoxide (nucleophilic activation); (ii) while the cation coordinates the carbonate (electrophilic) moieties, as summarised in Scheme 12, where the model example of catalyst **1c** is considered. The greater phosphorous/oxygen affinity favours the coordination of the P centre of the catalyst (as a Lewis acid) to the basic carboxylic oxygen of the dialkyl carbonate (top right, Scheme 12). Another acid-base reaction between the alcohol and **1c** likely accounts for the nucleophilic activation (top left, Scheme 12): an alcoholate exchanged IL, namely $[MeP(octyl)_3{}^+RO^-]$, forms. The existence of such salts has been recently proved [22].



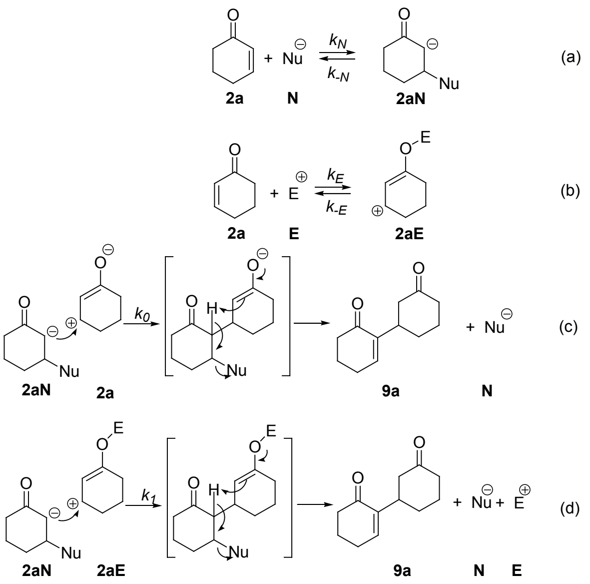
Scheme 12. Cooperative (ambiphilic) catalysis in the transesterification reaction by the anion and the cation of a generic phosphonium salt.

This cooperative PIL catalysed activation, allows DMC and the alcohol of choice to react according to the usual pattern of nucleophilic acyl substitutions ($N_{Ac}S$) to yield the transesterification product $ROCO_2R'$ and restore the initial ionic liquid **1c**. This cooperative anion/cation effect goes through a complex mix of charge-to-charge interactions. This explanation could justify also the lack of correlation between catalytic activity and anion basicity.

The cooperative catalytic effect can also be taken into account for the reaction selectivity. Mono transesterification products ($ROCO_2R'$) are more hindered than DMC therefore, cannot undergo efficient electrophilic and nucleophilic activation since the formation of corresponding acid-base adducts is sterically disfavoured (see Scheme 12). In our case, the progressive crowding at the OH-group, explains the observed reactivity of alcohols (BnOH>>CpOH>CyOH> menthol, Table 3 and Table 5), particularly of menthol, which requires more severe reaction conditions [34].

2.2.4.2. Experimental demonstration of nucleophilic-electrophilic cooperative catalysis

In all the previously described examples we have assumed that some kind of contribution to the catalytic activity should come from the cation. In this scenario basic/nucleophilic anion and electrophilic cation act simultaneously without interfering each other. To probe this kind of ambiphilic nucleophilic-electrophilic catalysis, we have investigated as a case study, the Baylis-Hillman (B-H) type dimerization of cyclohexenone **2a** to the dimer **9a** [35], in the presence of catalytic quantities of ionic liquids. In particular, salts **1a**, **1b**, methyltrioctylphosphonium bromide [$P_{8,8,8,1}$][Br] **1e**, and 1-butyl-3-methylimidazolium bromide [C_4mim][Br] **10**, were compared against phosphazene P_1-*t*-Bu and DBU (Scheme 13).



Scheme 13. Mechanicistic pathways for the Baylis-Hillman dimerization of cyclohexenone **2a**.

Reaction kinetics were performed solventless. Under these conditions, signals of reagent, product and catalyst can be adequately followed by ^{13}C NMR spectroscopy. The experimental procedure for sample preparation and the obtaining of kinetic data are described elsewhere [36], as well as details on the calculations [37].

The results for an exemplificative kinetic run are shown in Figure 2. It is well established that the mechanism of B-H type reactions requires nucleophilic catalysis [35], as shown in Scheme 13, step (a), where **N** is the nucleophilic catalyst (represented as an anionic species), and **2aN** is the activated nucleophilic complex. Electrophilic catalysis is also possible, as shown in Scheme 13, step (b), where **E** is the electrophilic catalyst (represented as a cationic species) and **2aE** is the activated electrophilic complex.

A Michael type attack of **2aN** follows, either on the non activated “free” cyclohexenone **2a** (represented in the convenient mesomeric structure), (Scheme 13, step (c)), with a kinetic constant k_0, or on the activated **2aE**, (Scheme 13, step (d)), with constant k_1. As representative kinetic parameter of this whole set of processes, we selected the normalized initial rate constant (-d{**2a**}$_0$/dt)/{**2a**}$_0$.

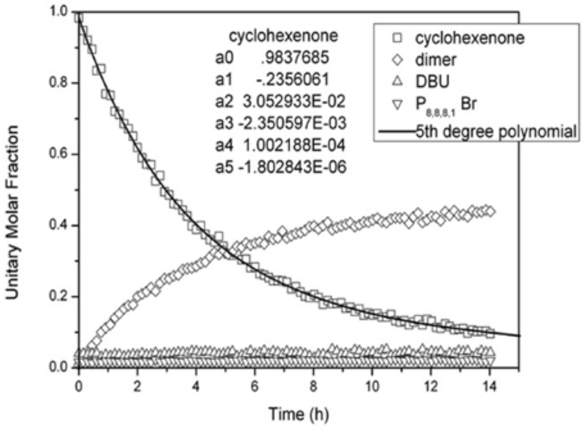


Fig. 2. Conversion (Entry 9, Table 6) of cyclohexenone 2a to dimer 9 in presence of [$P_{8,8,8,1}$][Br] 1e and DBU 12 as catalysts. The interpolation of the decrease of 2a with a 5th degree polynomial and the corresponding a0-a5 coefficients are also reported.

The NMR spectra revealed that the catalysts were regenerated (in agreement with the mechanisms in the scheme) and that they were also thermally stable.

The results for the B-H dimerization of **2a** with the described catalysts are collected in Table 6. The anions of ILs **1a**, **1b**, **1e**, [C_4mim][Br] and basic molecules like DBU and P_1-*t*-Bu were the nucleophilic catalysts **N**. The countercations [$P_{8,8,8,1}$] for **1a**, **1b**, **1e** and [C_4mim] were considered as the potential electrophilic catalysts **E**.

A rigorous comparison between rate constants would entail the use of a nucleophilicity scale. However, in the absence of nucleophilicity values for DBU [38], and since phosphazenes are only qualitatively described as poor nucleophiles [39], we referred to literature [40-43] pK$_a$ values (listed in Table 6).

The results summarised in Table 6 are characterized by two striking features: (i) even thought the basicities (and thus presumably the nucleophilicities) of hydrogencarbonate and of methylcarbonate anions are far lower than those of P_1-*t*-Bu and DBU, nevertheless, the dimerization of cyclohexenone catalyzed by **1a** and **1b** proceeded with similar or even greater rates compare to the organic noncharged nucleophiles, envisaging an electrophilic catalytic role to the [$P_{8,8,8,1}$] cationic counterpart; (ii) due to the neglectable basicity of the bromide anion, [$P_{8,8,8,1}$][Br] **1e** and [C_4mim][Br] **10** were totally inactive toward cyclohexenone dimerization, confirming that a strong nucleophile was necessary to trigger the B-H reaction, regardless of the role of the cation as a potential electrophile. This circumstance led to devise a strategy to discriminate between the contributions of the nucleophilic **N** and the electrophilic **E** catalysts. A series of five further experiments were carried out, at a constant amount of DBU as specific nucleophilic catalyst, and increasing amounts of [$P_{8,8,8,1}$][Br] as potential electrophilic co-catalyst. Entry 12, Table 6 describes a reaction carried out with DBU and [C_4mim]Br for comparison.

Table 6. Initial rates for the conversion of cyclohexenone **2a** to the dimer **9a**, at 60˚C under solvent-free conditions, in the presence of a series of nucleophilic catalysts N and of differing quantities of an electrophilic catalyst E. {X} means "unitary molar fraction" (see text).

#	**N**		**E**		$-\mathbf{a_1}^c$	$\mathbf{a_0}^c$	**{E}/{N}**	$-\mathbf{a_1}/(\mathbf{a_0}\{\mathbf{N}\})$
		{N}[b]		**{E}**[b]	h^{-1}			h^{-1}
1	$MeOCO_2^-$ [a]	0.027	$P_{8,8,8,1}$	0.027	0.27	0.79	1.00	12.60
2	$HOCO_2^-$ [a]	0.028	$P_{8,8,8,1}$	0.028	0.24	0.84	1.00	10.09
3	Br^- [a]	0.015	$P_{8,8,8,1}$	0.015	(0.0)	(1.0)	1.00	0.00
4	Br^- [a]	0.043	C_4mim	0.043	(0.0)	(1.0)	1.00	0.00
5	P_1-*t*Bu [a]	0.031	–	–	0.28	0.96	–	9.37
6	DBU [a]	0.045	–	–	0.07	0.99	0.00	1.48
7	DBU	0.041	$P_{8,8,8,1}$	0.007	0.14	0.95	0.17	3.62
8	DBU	0.044	$P_{8,8,8,1}$	0.013	0.19	0.96	0.30	4.46
9	DBU	0.041	$P_{8,8,8,1}$	0.020	0.24	0.98	0.48	5.86
10	DBU	0.041	$P_{8,8,8,1}$	0.039	0.29	0.93	0.94	7.48
11	DBU	0.042	$P_{8,8,8,1}$	0.057	0.32	0.95	1.35	8.17
12	DBU	0.053	C_4mim	0.043	0.50	0.90	0.81	10.48

[a]. Indicative pK_a from the literature: $MeOCO_2^-$ = 5.51[40], $HOCO_2^-$ = 6.37[41], Br^- = -4.9[42], P_1-*t*Bu = 26.98[43], DBU = 24.34[43]. [b]. Average of the values measured during the kinetic run. c. $\mathbf{a_0}$({**2a**}$_0$), $\mathbf{a_1}$ (d{**2a**}$_0$/dt): zero and first order coefficients of the 5th degree polynomial interpolation of the decrease of **2a** (except for Entries 3 and 4).

The results are listed in the table and plotted in Figure 3.

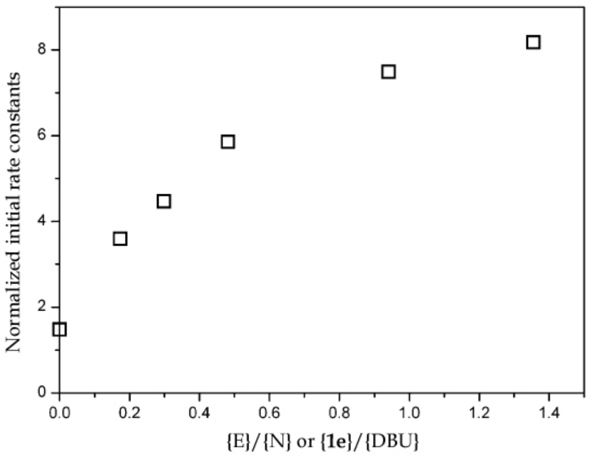
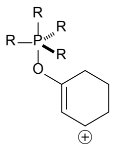


Fig. 3. The solvent free conversion of cyclohexenone **2a** into the dimer **9a**, cocatalyzed by [$P_{8,8,8,1}$][Br] **1e** and DBU (Entries 6-11, Table 6). Initial rate constants, normalized against {DBU}, are plotted vs. the ratio {1e}/{DBU}.

It was readily apparent that the rate of the dimerization reaction increased with increasing amounts of **1e**, indicating that an electrophilic catalysis on the –onium ion (Scheme 12, steps (b) and (d)). These considerations could be safely extended to the enhanced catalytic activity observed for PILs **1a** and **1b**, where the nucleophilic and the electrophilic catalysts were the anionic and cationic parts of the same entity.

The phosphorous atom can accommodate a high valence number and also possesses great affinity toward oxygen. The structure **10** can be proposed for the activated complex **2aE**, similar to that established for another tetralkylalkoxyphosphorane [44].



10

Fig. 4. Proposed structure for the activated complex 2aE.

Experimental results (Entry 4, Table 6) using [C_4mim][Br] alone confirmed that bromide was inactive as nucleophile. However, when [C_4mim][Br] was coupled with DBU (Entry 12, Table 6), the [C_4mim] cation was itself able to act as electrophilic catalyst. This kind of activation finds precedents for imidazolium ionic liquids [45], and lends further support to our conclusions.

3. Conclusions

A green synthetic procedure of a class of ionic liquids was developed through the alkylation of phosphines with dimethyl carbonate. The clear, colourless, halide free methylcarbonate PILs were isolated quantitatively as pure products simply by removing methanol (a co-solvent) and excess DMC under vacuum. These salts acted as precursors for the preparation of a plethora of different PILs which were obtained by simple anion-exchange reactions using acids or water (and no solvents).

The carbonate based PILs **1a** and **1b** showed striking organocatalytic properties: even when used in just 0.4 % mol with respect to the substrate, they were able to generate different carbonucleophiles that could act as Michael donors, or could be successfully used in Henry reactions of both aldehydes and ketones. In the latter case, compounds **1a** and **1b** allowed the tune the reaction selectivity towards the formation of nitroaldols from aldehydes, or dinitromethyl compounds from ketones. These products were obtained in excellent yields (80-90%). To our knowledge, the PILs-based procedure offered some of the best ever reported results for the synthesis of such dinitromethyl ketone derivatives.

In addition, PILs salts **1a-1d** with carbonate, acetate and phenolate anions, proved to be excellent organocatalysts for the transesterification of DMC with primary and secondary alcohols, obtaining the corresponding non symmetrical alkyl methyl carbonates with very good yields (>90%) and selectivity (>99%).

In all the reaction tested the catalytic performance of PILs is comparable to those of sterically hindered (non nucleophilic) strong bases such as DBU. This behaviour can not be explained on the concept of a superbase nature of the anion; rather, due to their ionic structures, PILs may display ambiphilic properties which operate synchronously without interfering with each other. Accordingly, both electrophilic and nucleophilic activations of the reactants can be invoked under a cooperative catalysis mechanism.

The investigation on the kinetic parameter for the condensation of cyclohexenone catalysed by different basic catalysts offered us the first clear-cut piece of evidence that ionic liquids or (more generally) organic salts can operate synchronously as nucleophilic and as electrophilic catalysts. The ability of other ionic liquids as catalysts has been already noted, but left totally unexplained [46]. In general, when the basicity or nucleophilicy of a catalyst goes beyond the usual scale, the action is attributed to the presence and the boost of another base or nucleophile [47]. This cannot account for the unusual high nucleophilicity of methyl carbonate in **1a** or of hydrogencarbonate in **1b** since no other nucleophile is present. Rather, the ambiphilic abilities of ionic liquids **1a** and **1b** must be considered: they operate cooperatively but independently, without interfering with each other.

Ambiphilic catalysis by ionic liquids rests upon a delicate equilibrium: the ILs must be a strong enough nucleophilic and electrophilic catalysts in order to operate, but not too strong in order to avoid reciprocal annihilation as in the case of the degradation of ammonium salts via Hofmann elimination [48].

4. Acknowledgements

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5. Notes and references

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