Methylcarbonate and Bicarbonate Phosphonium Salts as Catalysts for the Nitroaldol (Henry) Reaction

Massimo Fabris,[†] Marco Noè,[†] Alvise Perosa,[†] Maurizio Selva,[†,*] and Roberto Ballini[‡]

[†]Dipartimento di Scienze Molecolari e Nanosistemi dell'Università Ca' Foscari Venezia, calle Larga S. Marta, 2137-30123 Venezia, Italy

[‡]School of Science and Technology, Chemistry Division, University of Camerino, Via S. Agostino 1, 62032 Camerino, Italy

Ⓢ Supporting Information

ABSTRACT: Phosphonium ionic liquids exchanged with bicarbonate and methylcarbonate anions (CILs) exhibit catalytic performances comparable to those of sterically hindered (non nucleophilic) organo-superbases such as DBU. At 25−50 °C, under solventless conditions, CILs efficiently catalyze the Henry addition of different aldehydes and ketones to nitroalkanes: not only they allow the selective formation of nitroaldols but they unlock a novel high-yielding access to dinitromethyl derivatives of ketones.
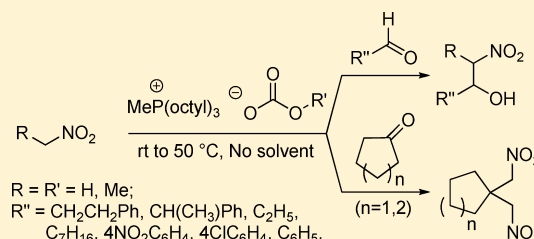
INTRODUCTION

Catalysis by ionic liquids (ILs) is gaining a preeminent position.[1] Modern literature reports a number of transformations including esterifications, nitrations, aldol condensations, Friedel−Crafts substitutions, acetalysations, etc., where ILs as such or binary/ternary IL-based systems act as efficient catalysts.[2] A peculiar field is represented by C−C bond-forming reactions,[3] where catalysis by ILs is effective on both the kinetic and the chemoselectivity of such processes. Among several examples, a remarkable one is the Henry reaction of nitroalkanes with carbonyl derivatives.[4] Different ILs of either acid or basic character including chloroaluminate systems, tetramethylguanidinium and quinolinium salts, (supported) basic 1,2-dimethylimidazolium hydroxides and acetates, as well as commercially available phosphonium-based ILs are reported as catalysts for such a process (Scheme 1).[5]

Scheme 1
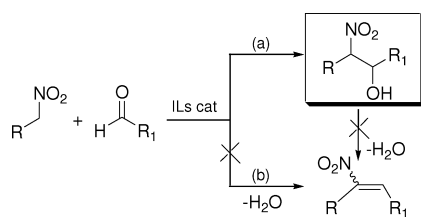
The mechanisms of activation of both nitroalkanes and aldehydes depend on the nature of the organocatalysts, nonetheless both acidic and basic ILs steer the Henry addition selectively to the formation of nitroaldols (Scheme 1, top), while the competitive dehydration to conjugated nitroalkenes (Scheme 1, bottom) is not observed.

As a part of our current research program on green methods for C−C bond-forming reactions,[6] we were interested to test the catalytic behavior of new ionic liquids recently synthesized by us,[7] namely methyl carbonate and bicarbonate phosphonium salts (CILs, Scheme 2: **1a** and **1b**).

Scheme 2
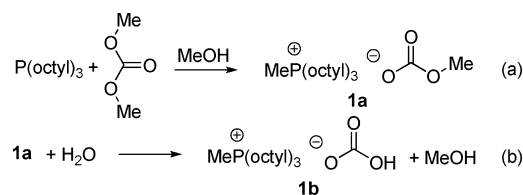
These compounds possess peculiarities which make them attractive in the context of this work: (i) they are unexpectedly strong base catalysts, as indicated by their performance in model Michael additions;[7] (ii) they are halide-free and stable for months on the shelf; (iii) they are prepared through a simple green method based on the methylation of an alkyl phosphine with nontoxic dimethyl carbonate (DMC/MeO-CO₂Me),[8] followed by a hydrolysis reaction in the case of **1b**; (iv) they can be used straight out from the reaction vessel since they are obtained in a high purity with no byproduct. In addition, a promoting effect by the phosphonium cation was foreseen, as hypothesized previously.[5f]

This paper reports an unprecedented application of methylcarbonate and bicarbonate salts **1a** and **1b**. Both CILs, particularly **1b**, exhibit an excellent activity as catalysts for the Henry reaction. The condensation of aldehydes with nitroalkanes takes place under very mild solventless conditions: for example, at 25 °C, the addition of nitroethane to 3-phenylpropionaldehyde catalyzed by **1a** or **1b** is complete in

80−100 min, at rates comparable to those achieved with powerful organic bases such as DBU. Although more demanding conditions (50 °C, 20 h) are required for ketones, the use of CILs catalysts provides a novel approach for the double addition of nitromethane to rather hindered carbonyls of cyclohexanone and cyclopentanone.

RESULTS AND DISCUSSION

Different Catalysts. Onium salts **1a** and **1b** and four conventional bases including 1,8-diazabicyclo[5.4.0]undec-7-ene (DBU), phenyltetramethylguanidine (PhTMG), triethylamine, and dimethylaminopyridine (DMAP) were used. The rationale for the choice of these bases was to operate under homogeneous conditions (as with ILs) and to cover a relatively wide p*K* range, approximately from 24 to 18. DBU, Et$_3$N, and DMAP were commercially available, while PhTMG was prepared from 1,1,3,3-tetramethylurea and aniline, using a reported procedure.[9]

The addition of nitroethane to 3-phenylpropionaldehyde (PPA, **2a**) was chosen as a model reaction (Scheme 3).[10]

Scheme 3
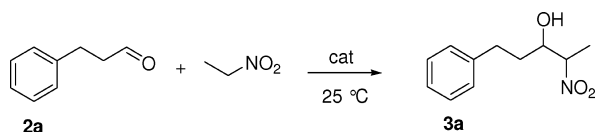
Initial experiments were carried out in an NMR tube charged with PPA (67 mg, 0.50 mmol) and CDCl$_3$ (1 mL). This mixture was set to react with a solution (0.18 mL) of the selected base catalyst (see above: 0.025 mmol, 0.05 molar equiv with respect to PPA) in nitroethane (188 mg, 2.5 mmol, molar ratio nitroethane/PPA = 5). Once the tube was inserted in the NMR spectrometer, spectra of the reacting mixture were recorded at defined time intervals for a total time of 190 min.

This analysis showed that at 25 °C, the Henry condensation proceeded smoothly and PPA produced the corresponding aldol derivative (**3a**) with total selectivity. In all experiments, both nitroaldol diastereoisomers were observed and the corresponding syn to anti ratio ranged from 50:50 to 69:31.

The integration of distinctive diagnostic signals of **2a** and **3a** allowed to collect kinetic profiles of the reactions automatically. Figure 1 illustrates the reaction PPA and nitroethane catalyzed by salt **1b**. Profiles are shown until 88 min; after that time, the composition of the reaction mixture did not vary appreciably.

No appreciable interferences by the catalyst were observed, due to its very low concentration.

The comparison among different base catalysts are summarized in Figure 2 where the amount of nitroaldol **3a** (sum of two diastereoisomers) is plotted against time.

The behavior of the different catalysts emerged quite clearly from these results. CILs, especially the bicarbonate salt **1b**, allowed a reaction outcome comparable to that obtained with DBU: after 25 min, the conversion of PPA into aldol **3a** was 80, 89, and 94% in the presence of **1a**, **1b**, and DBU, respectively (blue, red, and black profiles). By contrast, the reaction turned out to be extremely sluggish using both PhTMG and Et$_3$N. The corresponding conversions were 27 and 6%, respectively, after 180 min (teal and fuchsia profiles). Finally, even after 20 h, no appreciable formation of nitroaldol **3a** was observed in the presence of DMAP (olive profile). The overall trend suggested a very good parallel between the catalytic activity and the
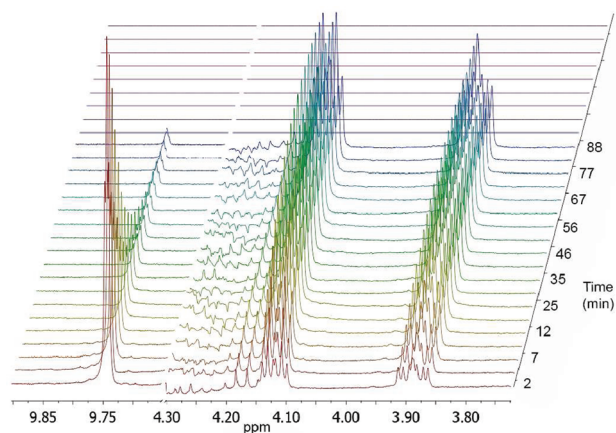

Figure 1. Henry condensation of 3-phenylpropionaldehyde with nitroethane carried out at 25 °C in the presence of **1b** as catalyst and CDCl$_3$ as solvent. ^{1}H NMR spectra highlight signals of the aldehydic proton and of two nitroaldol diastereoisomers.
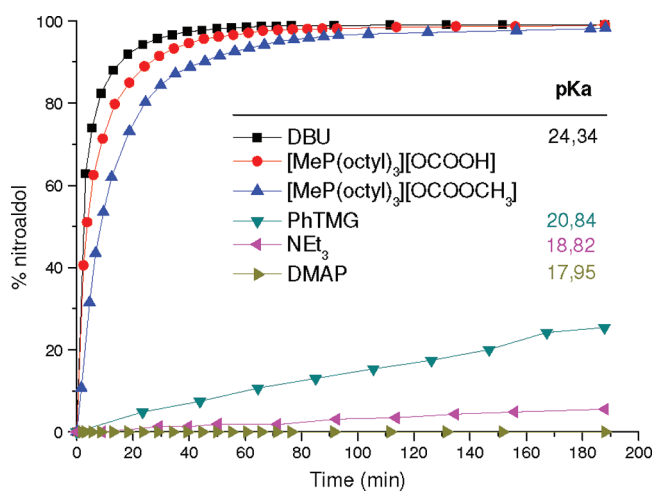

Figure 2. Comparison of different base catalysts (**1a**, **1b**, DBU, PhTMG, ET$_3$N, and DMAP) in the Henry condensation of 3-phenylpropionaldehyde with nitroethane carried out at 25 °C, in the presence of CDCl$_3$ as solvent.

dissociation constants (pK_a) of catalysts. The higher the pK_a (24.34, 20.84, 18.82, 17.95 for DBU, PhTMG, Et$_3$N and DMAP, respectively, in acetonitrile solvent[11]), the stronger the base, the better its performance. In particular, the activity of compounds **1a** and **1b** placed them in the range of organosuperbases (pK_a ~24) which appeared remarkable considering that both salts were exchanged with very poorly basic anions such as methylcarbonate and carbonate ones. Several factors, including solvation, ion pair strength, cation size, etc., offered an intriguing basis for discussion. At this stage, however, this was beyond the scope of the paper.

Henry Reaction of Different Aldehydes with Nitroethane. Salts **1a** and **1b** were further investigated as catalysts for the Henry condensation of different aldehydes with nitroethane. Optimization of the reaction of nitroethane with PPA and 4-nitrobenzaldehyde allowed to intensify the reaction conditions. With respect to Figure 1: (i) the CIL-to-aldehyde molar ratio was decreased to 0.01,[12] (ii) nitroethane was used in only 1.2 molar excess over aldehydes; (iii) no additional solvents were used. Five aliphatic and three aromatic aldehydes were considered (**2a**, PhCH$_2$CH$_2$CHO; **2b**, PhCH(CH$_3$)CHO;

2c, C₂H₅CHO; 2d, *n*-C₁₀H₂₁CHO; 2e, (CH₃)₃CHO; 2f, 4-NO₂C₆H₄CHO; 2g, 4-ClC₆H₄CHO; 2h, C₆H₅CHO; Scheme

Scheme 4

R = CH₂CH₂Ph, CH(CH₃)Ph, C₂H₅, C₇H₁₆, (CH₃)₃C
4NO₂C₆H₄, 4ClC₆H₄, C₆H₅,
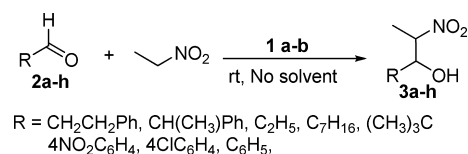
4). Accordingly, experiments were carried out at 25 °C, starting from 1.5 mmol of aldehyde (87−255 mg), 1.8 mmol of nitroethane (135 mg), and 0.015 mmol of 1a and 1b (7.4 and 6.7 mg, respectively). Final reaction mixtures were quenched by adding a 1% HCl aqueous solution (1.0 mL) (further details are in the Experimental Section). All reactions were highly selective toward the formation of nitroaldols: neither nitroolefins (Scheme 1) nor self-condensation products of enolizable aldehydes or other byproduct were observed by NMR. The nitroaldol derivatives were obtained as a mixture of diastereoisomers and purified by filtration over silica gel (2.0 g). Table 1 shows the amount (%) of nitrolaldol products as

Table 1. Reaction of Different Aldehydes with Nitroethane in the Presence of Catalyst 1a[a]

| no. | RC(O)H, R | time (h) | nitroaldol product, 3 | | syn/anti[c] |
			(%, by NMR)	yield[b] (%)	
1	2a: CH₂CH₂Ph	2	96	88	51:49
2	2b: CH(CH₃)Ph	2	96	93	10:55 25:10[d]
3	2c: C₂H₅	2	93	90	53:47
4	2d: *n*-C₁₀H₂₁	2	99	97	50:50
5	2e: (CH₃)₃C	2	47	48	30:70
6	2f: 4-NO₂C₆H₄	2	95	91	40:60
7	2g: 4-ClC₆H₄	3	82	71	64:36
8	2h: C₆H₅	2	35	35	69:31
		24	34	nd	

[a]All reactions were carried out at 25 °C under solventless conditions. The molar ratio nitroethane/aldehyde and catalyst/aldehyde were of 1.2 and 0.01, respectively. [b]Isolated yield of nitroaldols after purification through silica gel. [c]Determined by ¹H NMR.[13] [d]2b generated 4 diastereoisomers.

determined by NMR, the isolated yield of such products after FFC purification on silica, and the diasteroselectivity of the reaction.

Results for catalyst 1a are summarized in Table 1.

Equilibrium conditions of all Henry additions were achieved rapidly in the chosen experiment time. Aliphatic aldehydes 2a−d were readily converted into the corresponding aldol derivatives 3a−d which were isolated as highly pure (>95%) products in excellent yields (88−97%, entries 1−4). Pivalaldehyde (2e) however, gave product 3e in a 48% yield only: a result plausibly due to the steric hindrance of *tert*-butyl group.

The behavior of aromatic aldehydes was greatly affected by the nature of the aryl substituents. Compounds 2f−g, activated by EW groups (*p*-Cl or *p*-NO₂), offered results comparable to aliphatic substrates 2a−d (entries 5−6). This held true especially for *p*-nitrobenzaldehyde (2f), whose nitroadol was isolated in 91% yield (entry 5). By contrast, the reaction of benzaldehyde reached a less favorable equilibrium position at which the conversion did not exceed 35%, as confirmed also at prolonged reaction times (up to 24 h, entry 6). Other investigations on the reversibility of the nitroaldol addition of benzaldehyde reported a similar behavior.[10] Even more generally, recent studies confirmed that equilibrium constants of nucleophilic additions on aromatic aldehydes were altered by changing aryl substituents.[14]
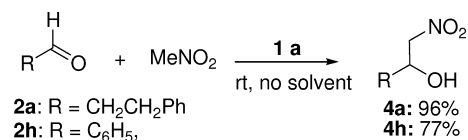
Reactions of substrates 2c and 2d with nitroethane were carried out on a larger scale starting from 30 mmol of aldehyde (1.74 and 4.68 g of 2c and 2d, respectively), methyl carbonate phosphonium salt (1a, 0.3 mmol), and nitroethane (36 mmol). After 2 h, both products 3c and 3d were isolated in 92% (3.67 g) and 97% (6.73 g) yields, respectively.

Finally, under the conditions of Table 1, hydrogen carbonate salt 1b did not show appreciable differences from methylcarbonate 1a. The reactions of aliphatic aldehydes catalyzed by 1b, were as fast as with 1a, and no other practical advantages were observed during the isolation of the aldol products.

Henry Reaction of Different Aldehydes with Nitromethane. 3-Phenylpropanal and benzaldehyde (2a and 2h) were chosen as models for aliphatic and aromatic aldehydes, respectively. They were set to react with nitromethane in the presence of salt 1a as the catalyst (conditions of Table 2: 1.5 mmol of aldehyde, 2a: 201 mg, 2h: 159 mg; the molar ratio nitromethane/aldehyde and catalyst/aldehyde were of 1.2 and 0.01, respectively). Also in this case, the reaction was selective toward nitroaldols, and no other byproducts (nitroolefins, self-condensation, or Cannizzaro products) were observed by NMR (Scheme 5).

At 25 °C, after 2 h, 3-phenylpropanal and benzaldehyde gave the corresponding nitroaldols in 96 and 77% isolated yields, respectively. In particular, benzaldehyde derivative 4h from nitromethane was obtained in a better yield than the analogue product from nitroethane (3h: 34%, Table 2). The relative

Table 2. Henry Reaction of Cyclic Ketones (5a and 5b) with Nitromethane Catalyzed by 1a

| entry | ketone | 1a:5[a] (mol/mol) | MeNO₂:5[b] (mol/mol) | T (°C) | conv (%, by NMR) | products (%, by NMR) | | yield[c] (%) | |
						7	8	7	8
1	5a	0.1	1.2	25	63	61	2	58	
2	5a	0.2	5.0	50	74	22	52		
3	5a	0.5	5.0	50	88	8	80		81
4	5b	0.1	1.2	25	39	27	12	25	
5	5b	0.2	5.0	50	74	3	71		
6	5b	0.5	5.0	50	93	1	92		91

[a]All reactions were carried out under solventless conditions and for 20 h. The molar ratio catalyst/ketone. [b]The molar ratio nitromethane/ketone. [c]Isolated yields of nitroaldols 7a and 7b or dinitromethylderivative 8a and 8b, after purification through silica gel.

Scheme 5

2a: R = CH₂CH₂Ph   **4a**: 96%
**2h**: R = C₆H₅,   **4h**: 77%

stabilities of compounds **3h** and **4h** plausibly accounted for such a result.

Henry Reaction of Different Ketones with Nitro-alkanes. In the literature, several examples reported that Henry additions of ketones were quite less effective than those of aldehydes.[15] Both electronic and steric effects were claimed to account for this difference, and in most cases, C_5–C_6 cyclic ketones were good model substrates to investigate such an aspect. These observations prompted us to explore the reactions of cyclohexanone and cyclopentanone (**5a** and **5b**, respectively) with nitroethane and nitromethane, respectively, in the presence of salt **1a** as the catalyst.

Nitroethane. Experiments were carried out at 25 °C for 20 h. Nitroethane (0.45–1.88 g) and the ketone (**5a**: 490 mg; **5b**: 420 mg) were mixed in a 1.2:5 molar ratio, while the salt **1a** was used in 0.1–0.5 molar equiv with respect to the ketone (**1a**: 246–1230 mg) (Scheme 6; for further details, see the

Scheme 6

5a: n = 2   **6a**
5b: n = 1   **6b**
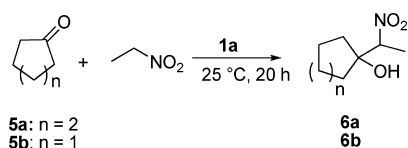
Experimental Section). ^{1}H NMR analysis showed that the Henry condensation proceeded selectively to the expected nitroaldol derivatives (**6a,b**). However, under the conditions used for aldehydes (Table 1), conversions of both cyclo-hexanone and cyclopentanone were of only 23% and 10%, respectively, even after a prolonged reaction time (20 h).

The increase of the catalyst loading (**1a**/**5** from 0.1 to 0.5) favored the formation of nitroaldols **6a** and **6b**: the corresponding isolated yields were of 57% and 17%. Larger amounts of both the salt **1a** and nitroethane (up to 1 and 5 molar equiv, respectively) did not further improve the reaction outcome.[16] For comparison, it should be noted that different procedures for the synthesis of **6a** claimed yields in the range of 22–82%,[17] while the isolation (or yield) of nitroaldol **6b** was never reported.

Nitromethane. Experiments were carried out at two different temperatures of 25 and 50 °C and for 20 h. The Henry reactants were mixed in a 1.2:5 molar ratio (nitro-methane: 366–1525 mg; 490 mg; **5b**: 420 mg), while the catalyst **1a** (246–1230 mg) was used in 0.1–0.5 molar equiv with respect to the ketone (for further details, see the Experimental Section). Under such conditions, ^{1}H NMR analysis showed the formation of nitroaldols (**7a,b**) and dinitromethyl derivatives **8a,b**. (Scheme 7).

Results are summarized in Table 2.

Since the (methylene)nitronate was a powerful nucleophile, conversions of ketones **5a** and **5b** were generally higher than those observed with nitroethane (entries 1 and 4). However, the most significant effect was the dramatic change of the product distribution induced by the combined increases of both

Scheme 7

5a: n = 2   **7a**   **8a**
5b: n = 1   **7b**   **8b**
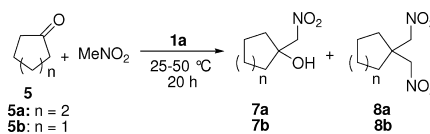
the catalyst and nitroalkane amounts, as well as by the temperature.

At 25 °C, in the presence of 10 mol % of **1a**, conversions were in the range of 39–63% and nitroaldols were the major products: the reaction of cyclohexanone proceeded with a good selectivity (up to 97%) toward **7a**, while cyclopentanone yielded derivatives **7b** and **8b** in a 2:1 ratio, respectively (entries 1 and 4).

When the temperature was increased to 50 °C and additional amounts of both nitromethane and catalyst **1a** were used (nitromethane/ketone and catalyst/ketone molar ratios of 5 and 0.2–0.5, respectively), the reactions proceeded further and afforded the products of double addition of nitromethane **8a** and **8b** on an almost exclusive basis. Conversions of cyclohexanone and cyclopentanone increased up to 88% and 93%, and the corresponding dinitromethyl derivatives **8a** and **8b** were isolated in excellent yields (81 and 91%, respectively, entries 3 and 6). For comparison, in the representative work of Kisanga et al.,[17c] the formation of products **8a** and **8b** from the reaction of ketones and nitromethane was observed only when a very strong neutral base (proazaphosphatrane, 30% mol) was used. However, yields did not exceed 21% even in the presence of overstoichiometric amounts of $MgSO_4$ as a carbonyl group activator and a rigorously inert atmosphere.

Overall, the results of Scheme 6 and Table 2 confirmed the efficiency of CILs as base catalysts also for the Henry addition to ketones. In the case of nitromethane, although the reaction hardly stopped to nitroaldol derivatives, the procedure unlocked the potential of CILs to access dinitromethyl derivatives **8** hitherto difficult to prepare.

Mechanism and Role of the Catalyst. The reaction of cyclic ketones with nitromethane yielding both nitroaldols **7** and dinitromethyl derivatives **8** was chosen as a model for a mechanistic hypothesis (Scheme 8).

An initial acid–base reaction between the salt **1a** and nitromethane generated the active nucleophile, i.e. the nitronate onium salt ($Q^+CH_2NO_2^-$), along with the rather unstable methyl carbonic acid ($MeOCO_2H$)[18] that readily decomposed to CO_2 and methanol (top cycle). 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 only recently reported,[19] the reversible trapping of CO_2 by simple alkoxide anions was a well-known process.[20] (Scheme 9).

In our case, this explained the restoration of catalyst **1a** (Scheme 8, top cycle, left).

The reaction could stop at this stage or, if an excess of nitromethane and a higher temperature (50 °C) were used, it could proceed further via the nucleophilic displacement of the nitronate salt ($Q^+CH_2NO_2^-$) on nitroaldol **7**. Although OH^- is not a good leaving group, the great affinity between phosphorus (of Q^+ cation) and oxygen atoms may assist the simultaneous formation of hydroxide salt (Q^+OH^-) and dinitromethyl product **8** (bottom).[21] In analogy to Scheme 8, the CO_2

Scheme 8

$Q^+ = MeP(Octyl)_3^+$

$n = 1, 2$

Scheme 9

$$MeO^- + CO_2 \rightleftharpoons MeOCO_2^-$$
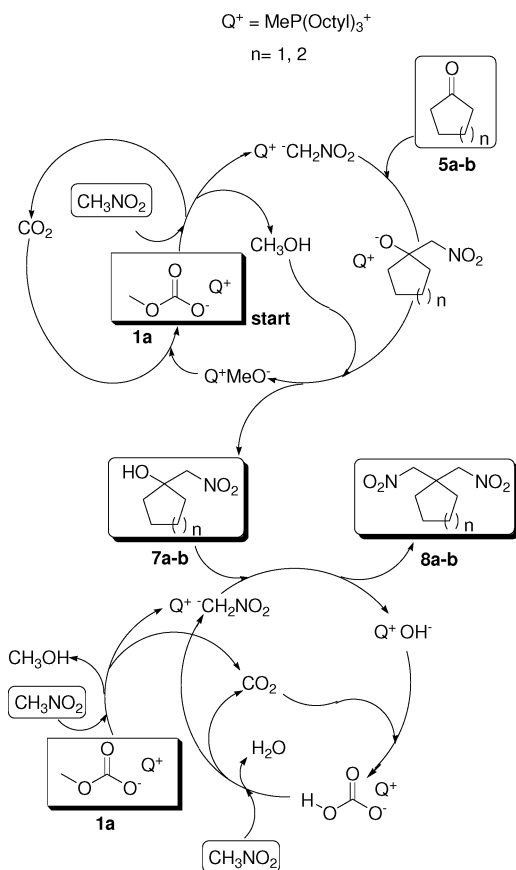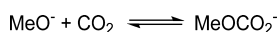
uptake by hydroxide produced $Q^+HOCO_2^-$ which became the actual catalyst.[22]

The easy elimination of water from nitroaldols **7** might also be considered (Scheme 1): however, under the investigated conditions, this pathway was ruled out since not even traces of the expected products (nitroolefins) were 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 corroborated by the fact that under the conditions of Table 2, also compound **1b** was able to catalyze the formation of both products **8a** and **8b**.

CONCLUSIONS

With a view to develop new superbase organocatalysts by using ILs properties, trioctyl methyl phosphonium methylcarbonate and bicarbonate salts (CILs **1a** and **1b**) offers a promising and unexplored starting tool.

In the Henry reaction of both aldehydes and ketones, compounds **1a** and **1b** act as powerful task specific (basic) catalysts with performances comparable to those of sterically hindered (non-nucleophilic) strong bases such as DBU. Aldehydes allow the selective formation of the corresponding nitroaldols. For ketones, reaction conditions can be tuned to

produce dinitromethyl compounds in excellent yields (80–90%). To our knowledge, the procedure here described offers some of the best ever reported results for the synthesis of such dinitromethyl ketone derivatives.

In both cases, a modest excess of nitroalkanes was used with no additional solvent.

The reaction mechanism plausibly involves the transformation of the initial catalytic species $[MeP(Octyl)_3^+ \ ROCO_2^-;\ R= Me,\ H]$ through reversible loss and uptake of CO_2.

EXPERIMENTAL SECTION

General Methods. All reagents used were ACS grade and were used as received, except for liquid aldehydes that were distilled prior to their use.

Phenyltetramethylguanidine (PhTMG) was prepared from 1,1,3,3-tetramethylurea and aniline using a reported procedure.[23] Starting from 1.16 g of 1,1,3,3-tetramethylguanidine (10.0 mmol), 1.63 g of crude product was obtained. The product was purified by distillation (85−100 °C; 0.06 atm) to yield 1.35 g of pure PhTMG (71%).

Methylcarbonate and bicarbonate phosphonium salts (CILs, **1a** and **1b**) were obtained according to a methodology previously reported by our group.[24] Starting from 20.8 g of trioctylphosphine (56.1 mmol), 30 mL of DMC, 30 mL of MeOH, and 27.5 g of trioctylmethylphosphonium methylcarbonate (55.8 mmol; 99%) was obtained **1a**. Product **1a** (3.00 g; 6.09 mmol) was reacted with water (1.00 g; 55.6 mmol) yielding 2.72 g (6.09 mmol; 100%) of **1b**.

^{1}H NMR and ^{13}C NMR spectra were collected in CDCl$_3$ solution at 25 °C at 400 and 100 MHz, respectively. Chemical shifts (δ) are reported in parts per million (ppm) downfield from TMS.

General Procedures. *Addition of Nitroethane to 3-Phenyl-propionaldehyde Catalyzed by Different Base Catalysts (Figure 1).* An NMR tube was charged with PPA (67 mg; 0.5 mmol) in CDCl$_3$ (1 mL) and set to react with a preformed solution of the selected base catalyst (0.025 mmol; triethylamine, 2.5 mg; DBU, 3.8 mg; DMAP, 3.1 mg; PhTMG, 4.8 mg; **1a**, 11.5 mg; **1b**, 11.2 mg; 0.05 molar equiv with respect to PPA) in nitroethane (188 mg; 2.5 mmol; molar ratio nitroethane/PPA = 5). Once the tube was inserted in the NMR spectrometer, it was thermostated at 25 °C. Then, spectra of the reacting mixture were recorded at time intervals. Experiments were carried out for 190 min. ^{1}H NMR analyses of the reaction mixture showed that PPA produced the corresponding aldol derivative (**3a**) with no other side products.

Reaction of Different Aldehydes with Nitroethane in the Presence of CILs as Catalysts (Table 1). A 7-mL glass reactor shaped as a test tube was charged with the aldehyde (1.5 mmol; **2a**: 201 mg; **2b**: 201 mg; **2c**: 87 mg; **2d**: 243 mg; **2e**: 226 mg; **2f**: 210 mg; **2g**: 159 mg) and a 0.116 M solution of methylcarbonate phosphonium salt (0.13 mL; **1a**: 7.4 mg; 1.5×10^{-2} mmol) in nitroethane. Under these conditions, the molar ratio nitroethane/**2** and catalyst/**2** were 1.2 and 0.01, respectively.

The reactor was kept at room temperature (25 °C), and the mixture was kept under magnetic stirring throughout the reaction. After the desired time, usually 2 h (see Table 1 for details), the reaction mixture was quenched by adding a 1% HCl aqueous solution (1.0 mL). A sample of the organic phase was then analyzed by ^{1}H NMR: the amount of nitroaldol products (**3**) were reported in Table 1. Diethylether (2 mL) was added to the reaction mixture, and the extracted organic phase was filtrated on silica gel (2 g, eluant diethylether, 25 mL) to remove the catalyst **1a**. Finally, the resulting solution was rotary evaporated (40 °C, 150 mbar). The products 4-nitro-1-phenylpentan-3-ol (**3a**: 276 mg, yield = 88%), 2-nitro-4-phenylpentan-3-ol (**3b**: 291 mg, yield = 93%), 2-nitropentan-3-ol (**3c**: 180 mg, yield = 90%), 2-nitrododecan-3-ol (**3d**: 336 mg, yield = 97%), 2-nitro-1-(4-nitrophenyl)propan-1-ol (**3e**: 308 mg, yield = 91%), 1-(4-chlorophenyl)-2-nitropropan-1-ol (**3f**: 229 mg, yield = 71%), and 2-nitro-1-phenylpropan-1-ol (**3g**: 95 mg, yield = 35%) were obtained as a mixture of diastereoisomers and characterized by ^{1}H and ^{13}C NMR.

The above-described procedure was adapted for the following experiments [(i) and (ii)]: *(i) Reactions Using Bicarbonate Phosphonium Salt (1b) as the Catalyst.* With all the other conditions unaltered, catalyst **1b** (6.7 mg; 1.5×10^{-2} mmol) was used in place of **1a**. The results, not reported here, did not showed appreciable differences between the two catalytic systems. *(ii) Reactions on Larger Scale Carried out Using Substrates 2c and 2d.* A 25-mL glass flask was charged with the aldehyde (30 mmol; **2c**: 1.74 g; **2d**: 4.68 g), methyl carbonate phosphonium salt (**1a**, 0.3 mmol, 148 mg) and nitroethane (36 mmol; 2.7 g). Under these conditions, the molar ratio nitroethane:**2** and catalyst:**2** were 1.2 and 0.01, respectively. The reactions were carried out at 25 °C for 2 h, then a 1% HCl aqueous solution was added (10 mL). Once the aqueous phase was removed, the nitroaldol products were purified through a filtration on silica gel (5 g of silica gel, 200 mL of diethylether). Products were obtained with high purity (95%): **3c** (3.67 g) and **3d** (6.72 g) were isolated in 92 and 97% yields, respectively.

Addition of Nitroethane to Cyclic Ketones in the Presence of CILs as Catalyst. A 7-mL glass reactor shaped as a test tube was charged with the ketone (**5**: 5.0 mmol; **5a**: 490 mg; **5b**: 420 mg), phosphonium salt (**1a**: 246, 492, 1230 mg; 0.5, 1, 2.5 mmol), and nitroethane (450 mg and 1875 mg; 6.0 and 25.0 mmol). Molar ratios nitroethane/ketone and **1a**/ketones were in the range of 1.2–5.0 and 0.1–0.5, respectively. The mixture was kept under magnetic stirring at room temperature for 20 h. Then, the reaction was quenched by adding a 5% HCl aqueous solution (3.0 mL). The resulting mixture was extracted with diethylether (2.0 mL) from which products **6a** and **6b** were isolated. These compounds were purified by column chromatography (eluant: ethylacetate/petroleum ether mixture, 30/70 v/v) yielding pure 1-(1-nitroethyl)cyclohexanol (**6a**, 248 mg, yield = 57%) and 1-(1-nitroethyl)cyclopentanol (**6b**, 69 mg, yield = 17%).

Addition of Nitromethane to Cyclic Ketones in the Presence of CILs as Catalyst. Reactions of Table 2 were carried out according to the following procedure. A 7-mL glass reactor shaped as a test tube, was charged with the ketone (**5**: 5.0 mmol; **5a**: 490 mg; **5b**: 420 mg), phosphonium salt (**1a**: 246, 492, 1230 mg; 0.5, 1, 2.5 mmol) and nitromethane (366 mg and 1525 mg; 6.0, 25.0 mmol). Molar ratios nitroethane/ketone and **1a**/ketones were in the range of 1.2–5.0 and 0.1–1.0, respectively.

The reactor was heated at the desired temperature (25–50 °C, see Table 2 for details), and the mixture was kept under magnetic stirring throughout the reaction. After 20 h, the reaction was quenched by adding a 5% HCl aqueous solution (3.0 mL).

At the end of reactions of entries 1, 3, 4, and 6 of Table 2, diethyl ether (3 mL) was added to the reaction mixtures and the aqueous phase was separated. Products were purified by column chromatography (eluant: ethyl acetate/petroleum ether mixture, 30/70 v/v) yielding 1-(nitromethyl)cyclohexanol (**7a**, 461 mg, yield = 58%), 1-(nitromethyl)cyclopentanol (**7b**, 200 mg, yield =25%), 1,1-bis-(nitromethyl)cyclohexane (**8a**, 410 mg, yield = 81%), 1,1-bis-(nitromethyl)cyclopentane (**8b**, 426 mg, yield = 91%). The structures of all products were confirmed by ^{1}H and ^{13}C NMR.

ASSOCIATED CONTENT

Ⓢ Supporting Information

Characterization data and NMR spectra of compound **6b**. This material is available free of charge via the Internet at http://pubs.acs.org.

AUTHOR INFORMATION

Corresponding Author

*E-mail: selva@unive.it.

Notes

The authors declare no competing financial interest.

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