DOI: 10.1002/adsc.200600525

An Efficient Synthesis of Organic Carbonates using Nanocrystalline Magnesium Oxide

M. Lakshmi Kantam,[a,*] Ujjwal Pal,[a] B. Sreedhar,[a] and B. M. Choudary[b]

[a] Inorganic and Physical Chemistry Division, Indian Institute of Chemical Technology, Hyderabad 500 007, India
Phone: (+91)-40-2719-3510; fax: (+91)-40-2716-0921; e-mail: mlakshmi@iict.res.in
[b] Ogene Systems (I) Pvt. Ltd., 11-6-56, GSR Estates, Moosapet, Hyderabad, India

Received: October 12, 2006; Revised: April 11, 2007

Supporting information for this article is available on the WWW under http://asc.wiley-vch.de/home/.

Abstract: An efficient and selective synthesis of organic carbonates using nanocrystalline magnesium oxide has been realized by the direct condensation of alcohols and diethyl carbonate. The catalyst is quantitatively recovered by simple centrifugation and can be reused for four cycles with almost consistent activity.

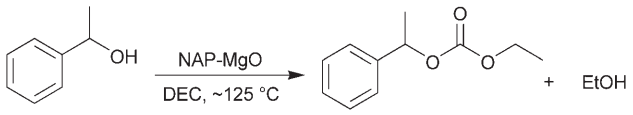
Keywords: chiral auxiliaries; direct condensation; nanocrystalline magnesium oxide; selectivity; solvent-free conditions; unsymmetrical organic carbonates

Organic carbonates are important intermediates for the synthesis of fine chemicals,[1,2] pharmaceuticals,[3] plasticizers, synthetic lubricants,[4] monomers for organic glasses, and solvents.[5,6] They are also used in the field of solid phase chemistry as linkers and tagging moieties.[7] Most of the catalytic systems for the synthesis of carbonates require the toxic and hazardous phosgene as reagent.[1,2,8] In order to address this problem, several groups have used dimethyl carbonate (DMC) as a substituent for phosgene.[9] The preparation of organic carbonates has been recently reviewed by Shaik and Sivaram.[9d] Jung et al. reported a mild and efficient preparation of alkyl carbonates on solid supports.[9e–g] Heterogeneous basic catalysts, MCM-41-TBD or Mg-La metal oxide afforded unsymmetrical alkyl carbonates from the reaction of diethyl carbonate (DEC) with various alcohols/amines at 125 °C.[10] Some of reactions are time consuming and the synthesized organics grafted on silica are not easily regenerated. Nanocrystalline metal oxides find excellent applications as active adsorbents for gases and destruction of hazardous chemicals and as catalysts for various organic transformations.[11,12]

We herein report an efficient method for the synthesis of unsymmetrical organic carbonates in quantitative yields *via* direct condensation of various alcohols with diethyl carbonate in the presence of nanocrystalline magnesium oxide (NAP-MgO).[12a,b]

Initially different nano metal oxides were screened for the synthesis of organic carbonates using 1-phenylethanol and DEC as a model reaction (Scheme 1). Among these metal oxides, NAP-MgO provided optimum results (Table 1).

Later, various magnesium oxide crystals[13] [commercial MgO, CM-MgO (SSA: 30 $m^2 g^{-1}$); conventionally prepared MgO, NA-MgO (SSA: 250 $m^2 g^{-1}$), and aerogel-prepared MgO, NAP-MgO (SSA: 590 $m^2 g^{-1}$)] were screened. NAP-MgO shows higher activity in terms of yields and selectivity compared to NA-MgO and CM-MgO (Figure 1). To understand the relationship between structure and reactivity in



Scheme 1. Synthesis of organic carbonates using nanocrystalline magnesium oxide.

Table 1. Comparative study of different nano metal oxides.[a]

Entry	Catalyst	Time [min]	Conversion [%][b]	Selectivity [%][b]
1	Nano-MgO	15	100	100
2	Nano-Al_2O_3	15	<1	—
3	Nano-ZnO	15	<1	—
4	Nano-TiO_2	15	20	100

[a] *Conditions:* 1-phenylethanol (2 mmol) and DEC (33 mmol, 4 mL) molar ratio (1: excess), catalyst (0.125 g) at *ca.* 125 °C.
[b] Determined by GC.

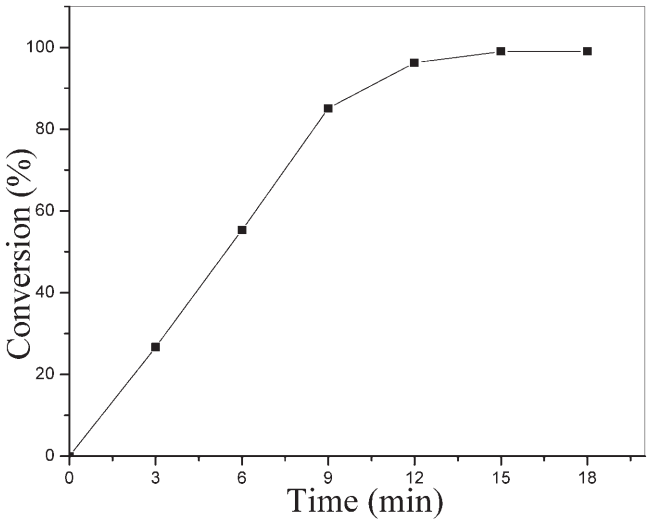


Figure 1. Direct condensation of 1-phenylethanol and DEC using NAP-MgO at *ca.* 125 °C, determined by GC analysis. *Conditions:* 1-phenylethanol (2 mmol), DEC (33 mmol, 4 mL) and catalyst (0.125 g).

the synthesis of organic carbonates, it is better to know the structure and nature of the reactive sites of NAP-MgO. The CM-MgO samples are generally large cubic crystals, the NA-MgO samples are thin hexagonal platelets, about 150 nm long and 10 nm thick having large exposed areas of the (100) crystal face. NAP-MgO has a three-dimensional polyhedral structure, having high surface concentrations of edge/corner sites and various exposed crystal planes (such as 002, 001, and 111), which leads to inherently high surface reactivity per unit area. Thus, NAP-MgO indeed displayed the highest activity and selectivity compared to those of NA-MgO and CM-MgO. Besides this, NAP-MgO has a Lewis acid site Mg^{2+}, Lewis basic sites O^{2-} and O^{-}, lattice bound and isolated Brønsted hydroxy groups, and anionic and cationic vacancies.[14] The direct condensation of various alcohols with DEC is known to be driven by base catalysts, and accordingly, the surface OH and O^{2-} functions of these oxide crystals are expected to trigger these reactions. To examine the role of OH groups, the Sil-NA-MgO and Sil-NAP-MgO[15] devoid of free OH groups, were tested in these reactions (Table 2). The silylated NAP-MgO and NA-MgO samples are prepared by the addition of MgO (500 mg) and methoxytrimethylsilane (300 mg) in dry toluene (20 mL) under reflux for 7 hours, after which the reaction mixture was allowed to cool and centrifuged to obtain silylated MgO, which was washed several times with *n*-pentane.[15] These results indicate that Brønsted hydroxy groups add to the activity in the reactions, which is largely driven by Lewis basic O^{2-} and O^{-} sites. A comparison of the different MgO samples (Table 2) shows that NAP-MgO reacts efficiently with a higher reaction rate, while NA-MgO affords undesirable by-products along with carbonate product and CM-MgO gives very low conversion. The results were checked by gas chromatography with a Shimadzu GC-2010 gas chromatograph equipped with a ZB5 capillary column (Figure 1). The activity of NAP-MgO in the direct condensation of 1-phenylethanol with DEC was compared with those of MCM-41-TBD,[10a] supported fluorides,[10b] and Mg/La mixed oxides[10c] and the results are presented in Table 3.

Table 2. Direct condensation of 1-phenylethanol and DEC by different crystallites of MgO at *ca.* 125 °C.[a]

Entry	Catalyst	Time [min]	Conversion [%][b]	Selectivity [%][b]
1	NAP-MgO	15	100	100
2	NA-MgO	15	86[c]	7
3	CM-MgO	15	<1	—
4	Sil-NAP-MgO	15	33	97
5	Sil-NA-MgO	15	15[c]	2

[a] *Conditions:* 1-phenylethanol (2 mmol), DEC (33 mmol, 4 mL) and catalyst (0.125 g).
[b] Determined by GC.
[c] The by-products were olefin, corresponding ether, diether and unidentified polymeric products.

The reaction works efficiently with a variety of alcohols including aromatic, cyclic, heterocyclic or aliphatic compounds (Table 4). Phenolic OH and amine groups remain inert under similar reaction conditions. The organic carbonates obtained as cholesteric liquid crystals from cholesterol (Table 4, entry 6) find application in electro-optics.

To widen the scope, NAP-MgO was tested in the tandem synthesis of the oxazolidine **1** moiety (Scheme 2) at *ca.* 125 °C.[16]

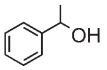
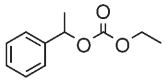
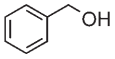
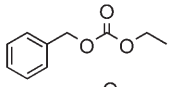
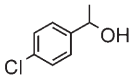
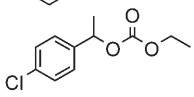
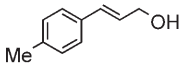
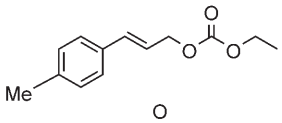
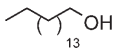
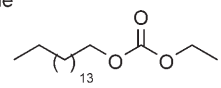
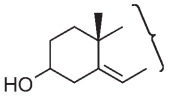
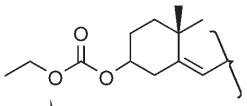
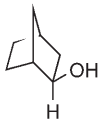
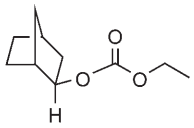
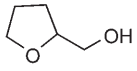
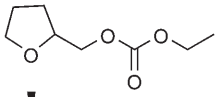
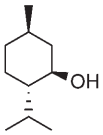
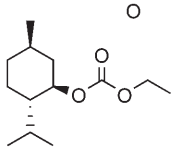
We have recently reported asymmetric epoxidation and Henry reactions using NAP-MgO.[12a,b] Herein a highly promising strategy for the syntheis of various

Table 3. Comparing the activity of NAP-MgO with other heterogeneous catalysts in direct condensation of 1-phenylethanol with DEC at *ca.* 125 °C.[a]

Entry	Catalyst	Time [h]	Yield [%][b]
1	NAP-MgO	0.25	99
2	MCM-41-TBD	8	93[c]
3	KF/Al_2O_3	5	99
4	MgLa-mixed oxides	4	99

[a] *Conditions:* 1-phenylethanol (2 mmol), DEC (33 mmol, 4 mL) and catalyst (entry 1, 0.125 g; entries 2–4, 0.100 g).
[b] Isolated yields.
[c] Benzyl alcohol (10 mmol), DEC (20 mL) and catalyst (0.100 g).

Table 4. Synthesis of organic carbonates using NAP-MgO as catalyst at *ca.* 125 °C in solvent-free system.[a]

Entry	Substrate	Time [min]	Product	Selectivity [%][b]	Yield [%][c]
1		15		100	99, 98[d]
2		240		99	97
3		120		100	98
4		300		98	96
5		15		100	99
6		90		96	88
7		30		100	98
8		180		100	99
9		30		100	99

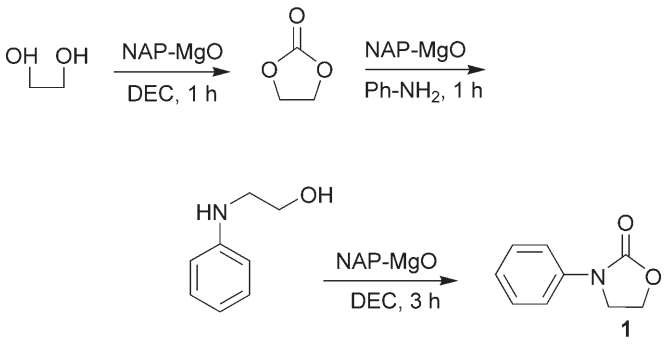
[a] *Conditions:* substrate and DEC molar ratio (1:excess), NAP-MgO (0.125 g).
[b] Determined by GC.
[c] Isolated yields.
[d] 4th recycle (i.e. fifth cycle).

chiral auxiliaries by NAP-MgO is described (Scheme 3).

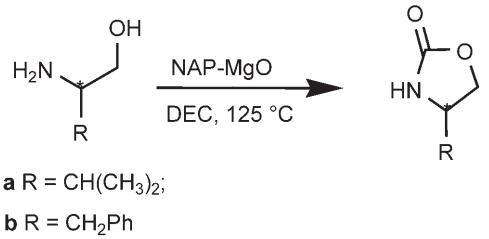
The $[\alpha]_D$ value of the carbonate obtained from the chiral auxiliaries (*R*)-(−)-2-amino-3-methyl-1-butanol (**a**) is found to be −18° ($c=6$, C_2H_5OH), and that from (*S*)-(−)-2-amino-3-phenyl-1-propanol (b) is found to be −62°, ($c=1$, $CHCl_3$), therefore it can be concluded that the amino alcohol is neither racemized nor inverted but retains its stereochemistry after the reaction.

The NAP-MgO was reused for four cycles with consistent activity after activating the used catalyst under a nitrogen atmosphere at 250 °C for 1 h (Table 4, entry 1).

We prepared surface transient organometallic intermediates by treating NAP-MgO with 1-phenylethanol and characterized them by XPS and TGA-MS. XPS high resolution narrow scan for Mg 2*p* in the fresh NAP-MgO exhibits one line at 48.7 eV (Figure 2). The XPS spectrum of the 1-phenylethanol-treated NAP-MgO for the Mg 2*p* exhibits two lines at 48.7 and 50.7 eV, which can be attributed to magnesium in NAP-MgO and Ph-CH(Me)-O-MgO, respectively (Figure 2). This provides evidence that in the proposed mechanism, O^{2-}/O^{-} of NAP-MgO abstracts an acidic proton of the 1-phenylethanol, giving a Ph-CH(Me)-O^{-}, which forms a complex with the unsaturated Mg^{+} site (Lewis acid-type) of NAP-MgO (Scheme 4). 1-Phenylethanol-treated NAP-MgO samples were subjected to TGA-DTA-MS to detect the evolved gas fragments as a function of temperature. The observed *m/z* values of the fragments for Ph-CH(Me)-O^{-}-NAP-MgO are 90, 91, 104 and 122 amu that correspond to C_7H_6, C_7H_7, C_8H_8 and $C_8H_{10}O$, re-



Scheme 2. Tandem synthesis of the oxazoldine moiety using NAP-MgO.



Scheme 3. Synthesis of chiral auxiliaries using NAP-MgO.

spectively. The major fragment, $m/z = 91$ amu observed corresponds to the benzyl radical cation of the surface transient organometallic intermediate (see Supporting Information, Fig. 3) further supports the proposed mechanism.

The synthesis of unsymmetrical organic carbonates proceeds *via* dual activation of both substrates (nucleophiles and electrophiles) by NAP-MgO. Thus, the Lewis base sites (O^{2-}/O^{-}) of the catalyst activate 1-phenylethanol, and the Lewis acid sites (Mg^{2+}/Mg^{+}) activate the carbonyls of DEC (Scheme 4).[18] Therefore, the DEC bound NAP-MgO directs the delivery of Ph-CH(Me)-O stereoselectively to the Mg^{+} (Lewis acid)-activated carbonyl of DEC *via* oxygen coordination to afford the desired product.

In conclusion, the synthesis of organic carbonates is achieved by using a recyclable heterogeneous catalyst, nanocrystalline magnesium oxide with excellent yields and selectivities.

Experimental Section

The activation of the solid catalyst (fresh catalyst) was carried out at 450 °C for 4 h.

General Procedure for the Synthesis of Unsymmetrical Organic Carbonates

DEC (33 mmol, 4 mL), alcohol (2 mmol) (the ratio of DEC/alcohol = 16.5:1) and catalyst (0.125 g) were charged into a oven-dried, nitrogen-flushed 25-mL flask, equipped with a magnetic stirring bar and a reflux condenser. The reaction mixture was stirred under a nitrogen atmosphere at 125 °C until the completion of the reaction. After completion of the reaction, (monitored by TLC, and GC), the reaction mixture was centrifuged to separate the catalyst and washed several times with ether. The combined organic layers were dried over Na_2SO_4 and the solvent was removed under reduced pressure. The crude product was purified by column chromatography (silica gel: 100–200 mesh) using a mixture

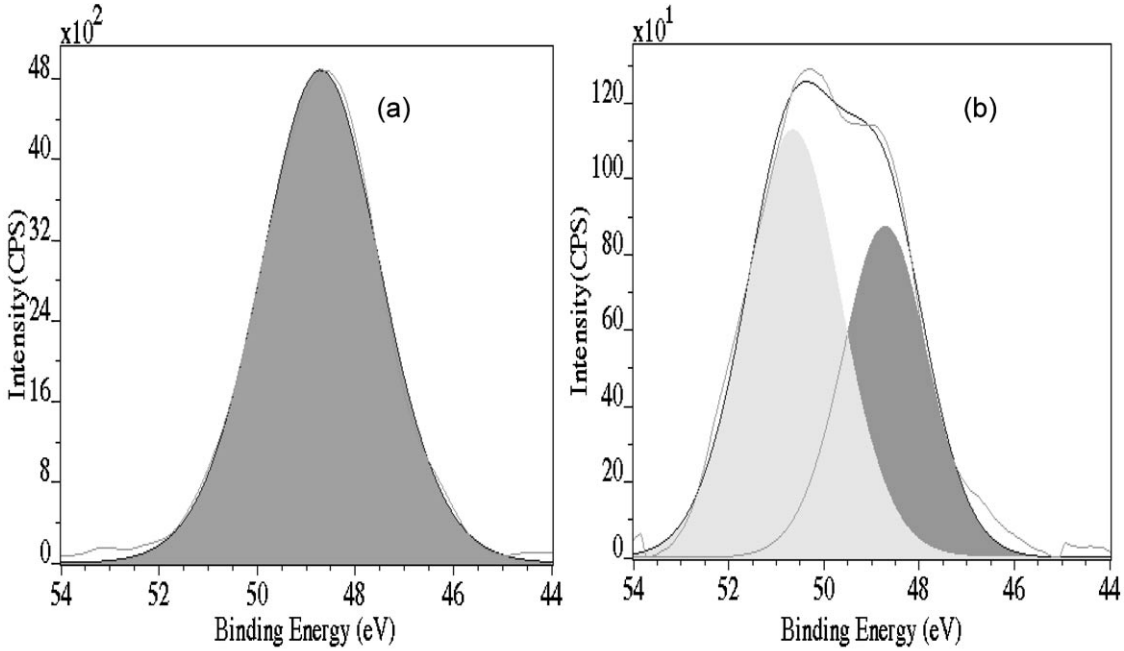
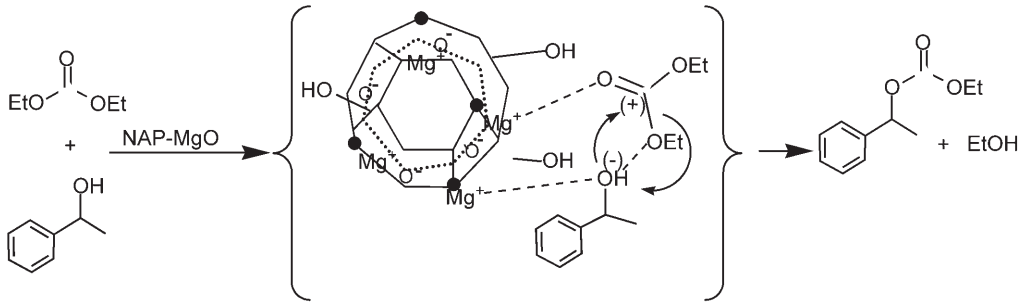


Figure 2. XPS high resolution narrow scans for Mg 2*p* of (**a**) NAP-MgO and of (**b**) 1-phenylethanol-treated NAP-MgO.



Scheme 4. Proposed mechanism for the synthesis of unsymmetrical organic carbonates.

of hexane:ethyl acetate, 80:20, as eluent to give the corresponding organic carbonate.

Reuse of the Catalysts

After completion of the reaction, the catalyst was recovered by centrifugation and activated under a nitrogen flow for 1 h at 250 °C for further reuse. NAP-MgO showed consistent activity for five cycles under the same reaction conditions. (Table 4, entry 1), The reusability of NAP-MgO catalyst is summarized in the Supporting Information (Fig. 4).

Supporting Information

^{1}H NMR and mass spectral data of all compounds as well as GC, XPS, TGA-DTA-MS results.

Acknowledgements

We wish to thank the CSIR for financial support under the Task Force Project CMM-0005. U. Pal thanks Council of Scientific and Industrial Research, India, for research fellowship. Nanocrystalline MgO catalysts were obtained from Nano-Scale Materials Inc., Manhattan, Kansas, USA.

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