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ORIGINAL PAPER

An easy base-assisted synthesis of unsymmetrical carbonates from alcohols with dimethyl carbonate

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Abstract A simple and convenient base-mediated synthesis of asymmetrical carbonates from alcohols with dimethyl carbonate is described. The reaction is remarkably influenced by the strength of the base employed and potassium *t*-butoxide was found to be best promoter for this reaction. Almost in all cases, the reaction is selective and afforded the corresponding unsymmetrical methyl carbonates in excellent yields (80–90 %).

Keywords Transesterification · Dimethyl carbonate · Organic carbonates · Base · Alcohol

Introduction

Alkyl organic carbonates have been recognized as extremely valuable synthetic intermediates in the chemical industry [1]. Owing to their higher stability than esters, organic carbonates have been widely used as protecting groups during the synthesis of complex molecules of biological importance. In addition, they also have numerous applications as monomers for organic glasses, as solvents in the manufacture of lithium batteries, and as intermediates in the synthesis of bioactive chemicals [2, 3]. The conventional synthesis of organic carbonates involves the reaction of hydroxyl compounds (aliphatic, aromatic) with excess pyridine and phosgene at or below room temperature. Another common method of their synthesis comprises the reaction of halo compounds with alcohols and phenols. Most symmetrical and unsymmetrical carbonates are formed by these two conventional approaches [4, 5]. However, both methods are associated with the limitations of using of toxic and hazardous materials and producing copious amounts of undesirable chloride salts. From the standpoint of green chemistry, the development of reaction systems which do not require hazardous reagents or volatile organic solvents is of tremendous interest [6]. In the last two decades, dimethyl carbonate (DMC) has gained prominence as a green reagent in base-catalyzed methylation or methoxy-carbonylation of anilines, phenols, active methylene compounds, and carboxylic acids. DMC is considered to be green as it is nontoxic and produces only CO_2 and MeOH that can easily be removed by distillation [7–9]. Owing to these aspects, the reaction of alcohols with DMC to give organic carbonates is considered to be an eco-friendly "carbonylation" route. In this context, a number of catalysts namely $ZnCl_2/Et_3N$ [10], $p\text{-}CH_3C_6H_4SO_3H$ [11], $YbCl_3$ [12], and ytterbium(III) triflate [13] have been used. However, in most cases, symmetrical carbonates were formed predominantly with a poor yield of the unsymmetrical carbonates at high temperature. Furthermore the higher cost of the catalysts and slow reaction rates make these methods less advantageous. Recently, a liquid-phase synthesis of alkyl carbonates by coupling of an alcohol, CO_2, and alkyl halide in the presence of Cs_2CO_3 at ambient temperature [14] and a solid-phase reaction involving an alcohol or amine, ligated to a resin through a CO_2 linker, in the presence of Cs_2CO_3 and tetrabutylammonium iodide (TBAI) [15] to produce the corresponding carbonates or carbamates were reported. The use of more than stoichiometric amounts of base, longer reaction times, and

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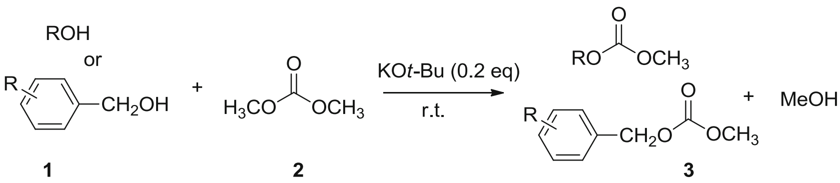
Scheme 1



moderate product yields make these procedures unattractive. Furthermore, the synthesis of unsymmetrical organic carbonates is achieved by the reaction of various alcohols with diethyl carbonate in the presence of a catalytic amount of MCM-41-TBD (1,5,7-triazabicyclo[4.4.0]dec-5-ene anchored on mesoporous MCM-41 silica) at ca. 338 K [16]. Since organically modified silicas are difficult to regenerate, the development a simple and facile alternative methodology is desirable. Consequently Kantam et al. [17] reported the use of nanocrystalline MgO and Zhou et al. [18] described the use of metal organic frameworks (MOFs) as heterogeneous catalysts for the synthesis of organic carbonates by the reaction of diethyl carbonate with alcohols. MOFs are difficult to synthesize and require expensive chemicals. Most recently, Veldurthy et al. [19] reported an efficient and green approach for the synthesis of unsymmetrical carbonates by using alcohols and diethyl carbonate in the presence of the heterogeneous base catalyst CsF/Al_2O_3. In this procedure the reactions were carried out at 130 °C and under a nitrogen atmosphere. Song et al. [20] reported the synthesis of unsymmetrical organic carbonates catalyzed by a sulfonic acid-functionalized zirconium phosphonate. Recently Tundo et al. [21] reported the methylation of primary alcohols with DMC for the synthesis of methyl ethers in the presence of basic alumina or hydrotalcite as catalyst at 200 °C. The methyl carbonates formed in the first step decarboxylate in the second step to yield the corresponding methyl ethers. In another report, Tundo et al. [22] studied the reaction of dialkyl carbonates with alcohols to investigate the behavior of preferential leaving and entering groups for the newly synthesized carbonates. Very recently Mutlu et al. [23] reported the use of TBD as an organocatalyst for the synthesis of unsymmetrical carbonates. However the reactions were carried out at 80 °C and afforded symmetrical carbonates as the by-products.

In view the aforementioned limitations of the existing methods, there is still a need to develop a simple and cost-effective methodology for the synthesis of unsymmetrical carbonates. In the present paper we report an easy base-assisted (such as potassium *t*-butoxide, KO*t*-Bu) methodology for the synthesis of unsymmetrical carbonates from the reaction of alcohols with DMC at room temperature (Scheme 1). A remarkable outcome of the present work is the high yield of products (90–95 %) in most cases with very high purity (>98 %) after a simple workup.

Table 1 Optimization experiments using 1-butanol as substrate

Entry	Base	Base amount[a]	Time/min	Conversion/ selectivity/%[b]
1	–	–	60	–
2	NaOH	0.2	30	68/98
3	KOH	0.2	15	90/100
4	K_2CO_3	0.2	35	48/95
5	Et_3N	0.2	40	52/98
6	KO*t*-Bu	0.2	10	92/100
7	KO*t*-Bu	0.1	15	90/100
8	KO*t*-Bu	0.3	8	94/100
9	KO*t*-Bu	0.5	5	97/100

1-Butanol/DMC (1:5) at room temperature

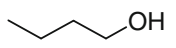
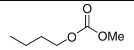
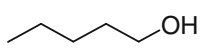
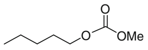
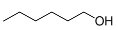
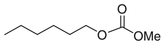
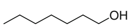
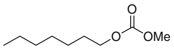
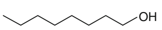
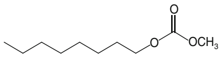
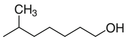
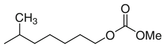
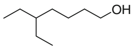
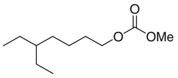
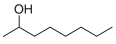
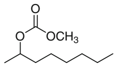
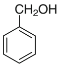
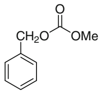
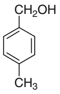
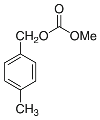
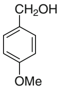
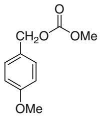
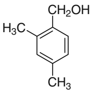
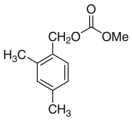
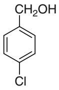
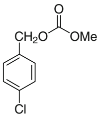
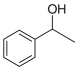
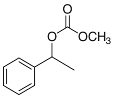
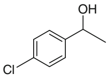
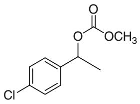
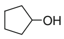
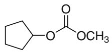
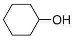
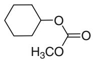
[a] Equiv. with respect to alcohol

[b] Determined by GC

Results and discussion

Initially we studied the effect of various bases such as KOH, K_2CO_3, and KO*t*-Bu for the reaction of 1-butanol (**1a**) with DMC (**2**) in a molar ratio of 1:5 in the presence of base (0.2 eq) at room temperature. The results of these experiments are summarized in Table 1 (entries 2–6). In a controlled blank experiment, no reaction occurred in the absence of base (Table 1, entry 1). Among the various bases KO*t*-Bu and KOH were found to be the catalysts of choice. Other selected bases such as NaOH, K_2CO_3, and Et_3N were also found to be quite effective but required longer reaction times. If we compare the time required for complete reaction and the strength of the bases, it can be concluded that the reaction is faster with stronger bases. We used excess DMC (fivefold more than alcohol) and this can easily be recovered by distillation after the reaction. We also performed the reaction of 1-butanol with DMC (molar ratio 1:5) by varying the amount of catalyst KO*t*-Bu from 0.1 to 0.5 eq under otherwise similar experimental conditions. The results are summarized in Table 1 (entries 7–9). Higher loadings of the

Table 2 KO*t*-Bu-catalyzed synthesis of unsymmetrical carbonates

Entry	Substrate	Product	Time/min	Conv/select /%	Yield /%[b]
1	 **1a**	 **3a**	10	92/100	90
2	 **1b**	 **3b**	10	92/100	90
3	 **1c**	 **3c**	12	96/100	93
4	 **1d**	 **3d**	15	94/100	92
5	 octan-1-ol **1e**	 methyl octyl carbonate **3e**	15	89/100	86
6	 **1f**	 **3f**	10	86/100	85
7	 **1g**	 **3g**	15	84/100	82
8	 **1h**	 **3h**	20	87/98	85[c]
9	 **1i**	 **3i**	20	90/100	88
10	 **1j**	 **3j**	15	94/100	93
11	 **1k**	 **3k**	15	96/100	95
12	 **1l**	 **3l**	20	90/100	88
13	 **1m**	 **3m**	30	86/100	82
14	 **1n**	 **3n**	25	92/97	90[d]
15	 **1o**	 **3o**	35	90/89	87[d]
16	 **1p**	 **3p**	30	91/100	89
17	 **1q**	 **3q**	30	92/100	90

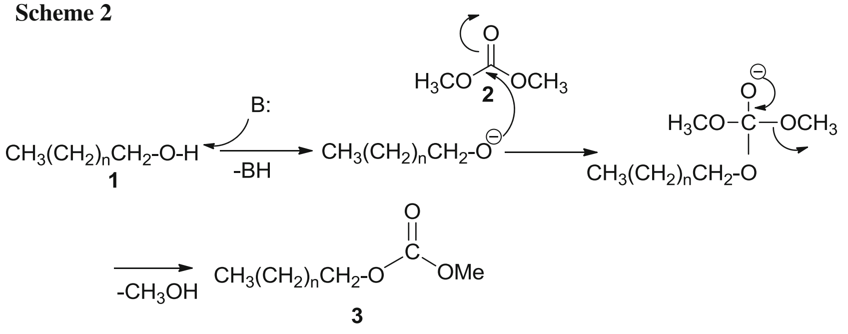
[a] Reaction conditions: alcohol/ DMC (1:5), KO*t*-Bu (0.2 eq) at room temperature; [b] Isolated yields;

[c] Symmetrical carbonate remained; [d] Corresponding styrenes wereobtained as by-products.

Table 3 Comparison of different catalysts with the present methodology

Entry	Catalyst	Reaction conditions	Conversion/selectivity/%	Advantage	Disadvantage
1	MCM-41-TBD	125 °C, 8 h, 0.1 g catalyst	96/99	Facile recovery and recycling of the catalyst	Multi-step synthesis, difficult to regenerate and high cost of the precursors
2	Mg/La metal oxide	125 °C, 3.5 h, 0.1 g catalyst	98	Higher product yield, easily recyclable catalyst system	Multi-step synthesis and expensive metal oxides
3	CsF/Al_2O_3	130 °C, 0.5 h, 0.1 g catalyst	98/100	Faster reaction, high product yield, recyclable catalyst	High cost of the catalyst
4	TBD	80 °C, 1 h, 0.1 mol% catalyst	99/97	Faster rates, high product yield	High cost and limited accessibility of the catalyst
5	Bu_2SnMoO_4	130 °C, 8 h	90/95	–	High cost and multi-step synthesis of the catalyst
6	*t*-BuOK			Comparatively low cost and high reactivity and mild experimental conditions	High catalyst loading
7	KOH			Inexpensive, easily available, highly reactive	

Scheme 2



catalyst reduced the reaction time, whereas lower amounts of base increased the reaction time but not to a great extent.

We explored the general scope of the reaction by using different aliphatic, aromatic, and cyclic alcohols with DMC under the optimized reaction conditions, e.g., alcohol **1** (1 eq.), KO*t*-Bu (0.2 eq), and DMC (5 eq) at room temperature. All the substrates were selectively transformed to the corresponding unsymmetrical carbonates **3** in high yields within 10–30 min as summarized in Table 2. The reaction of various aliphatic alcohols such as 1-butanol (**1a**), 1-pentanol (**1b**), 1-hexanol (**1c**), 1-heptanol (**1d**), and 1-octanol (**1e**) with DMC (**2**) afforded the corresponding alkyl methyl carbonates selectively, i.e., 1-butyl methylcarbonate (**3a**), 1-pentyl methylcarbonate (**3b**), 1-hexyl methylcarbonate (**3c**), 1-heptyl methylcarbonate (**3d**), and 1-octyl methylcarbonate (**3e**) in 90, 90, 93, 92, and 86 % yields, respectively (entries 1–5). Branched alcohols such as 6-methyl-1-heptanol (**1f**) and 5-ethyl-1-heptanol (**1g**) afforded the corresponding unsymmetrical alkyl methyl carbonates **3f** and **3g** in 85 and 82 % yields, respectively (entries 6, 7). Among all the alcohols studied, the activity of the primary alkyl alcohols was found to be highest and they were all transformed into the corresponding unsymmetrical carbonates selectively (Table 2, entries 1–7). The activity order of alkyl alcohols was primary alcohol > secondary alcohol (Table 2, entry 8), which could result mainly from steric hindrance. Tertiary alcohols such as *tert*-amyl alcohol did not undergo any reaction under the described experimental conditions. Benzylic and aromatic substituted alcohols (Table 2, entries 9–15) had lower activity than the alkyl alcohols because of the delocalization of electrons in the benzene ring, which reduces the nucleophilicity of the generated alkoxide ion. In the case of cyclic aliphatic alcohols (Table 2, entries 16, 17), the lower activity was due to the steric hindrance of the ring. In all cases except 2-hydroxyoctanol (Table 2, entry 8), benzhydrol (entry 14), and 4-chlorobenzhydrol (entry 15), the reaction was selective and afforded unsymmetrical carbonates in high to excellent yields.

The present methodology is advantageous as it uses an inexpensive base catalyst, mild reaction conditions, and allows the selective formation of unsymmetrical carbonates in high yields. To establish the superiority of the developed methodology, a comparison of different catalysts with the present methodology is shown in Table 3.

Although the exact mechanism of the reaction is not clear at this stage, a possible mechanistic pathway is shown in Scheme 2. We assume that the first step is the generation of an alkoxide ion (RO^-) through proton abstraction from the alcohol by the base. Then the alkoxide ion attacks the carbonyl carbon of DMC and forms a tetrahedral intermediate ion, which then generates a methyl ester molecule ($ROCO_2Me$) and methanol as shown in Scheme 2. Strong bases may facilitate the abstraction of the proton from the alcohol to give an alkoxide ion and therefore enhance the reaction rates.

Conclusion

We have described a simple and convenient base-promoted synthesis of unsymmetrical organic carbonates. The main advantages of the developed methodology are (a) use of environmentally benign DMC, (b) inexpensive and easily accessible catalyst, (c) elimination of toxic and hazardous materials, and (d) facile recovery of unreacted DMC and MeOH. Furthermore simple experimental conditions and fast reaction rates make this a convenient and practical approach for the synthesis of alkyl/aryl methyl carbonates.

Experimental

All the reagents and substrates are commercially available and used as received. Anhydrous K_2CO_3 and KOH flakes were used as received from Merck Chemicals. Potassium *t*-butoxide was obtained from Acros Organics and used as received. ^1H and ^{13}C NMR spectra were recorded for $CDCl_3$ solutions at 500 and 125 MHz, respectively. GC–MS (HP 5890, series II) analyses were carried out by using a mass-selective detecter (MSD) (30 m × 0.30 mm; 50–250 °C, 8 °C/min) and GC (GC, Agilent 6820) analysis was carried out using a silicon OV-17 column (50 m × 0.26; 50–250 °C; 5 min isothermal, 8 °C/min; FID 250 °C).

General experimental procedure

To a mixture of alcohol **1** (1 mmol) and DMC (5 mmol) was added potassium *t*-butoxide (0.2 mmol) and the resulting mixture was stirred at room temperature. Progress of the reaction was monitored by TLC (SiO_2). After completion, the unreacted DMC and methanol were isolated by distillation and the residue was taken in ethyl acetate and washed several times with water. The organic layer was dried over sodium sulfate and concentrated in vacuo. Purification by silica gel column chromatography with hexane/ethyl acetate (90:10, v/v) gave the corresponding methyl carbonates in the yields mentioned in Table 2. The conversion and purity of the product were determined by GC–MS and identity was confirmed by comparing the spectral data with those reported [9, 24]. Copies of the spectra and GC–MS chromatograms of the products are given in the Supplementary Material.

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