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Carbamate synthesis via transfunctionalization of substituted ureas and carbonates

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Abstract

Synthesis of carbamates from substituted ureas and organic carbonates has been demonstrated using di-*n*-butyltin oxide (DBTO) as a catalyst. Reactivity pattern of ureas indicated that substituents on ureas have no significant effect on the carbamate yields. While, the carbonate reactivity pattern seems to be following the rule that is expected based on the leaving group ability of alkoxides and phenoxide to form carbamate observed in aminolysis of carbonates, it has been shown that basicity of reacting urea plays a vital role in the catalytic activity of this reaction. The effect of reaction parameters such as temperature, catalyst loading, solvent, concentration of reactants, etc. were investigated for synthesis of methyl methyl carbamate (MMC). The Arrhenius activation energy for the reaction between dimethyl urea (DMU) and dimethyl carbonate (DMC) was found to be 7.57 kcal/mol. A reaction mechanism has been postulated explaining the role of DBTO in the synthesis of carbamate from urea and carbonate.

Keywords: Carbamates; Ureas; Carbonates; Transfunctionalization

1. Introduction

Carbamates are useful compounds having wide range of applications in chemical industry such as in the production of commodity chemicals like polyurethanes, herbicides and pesticides [1]. On the other hand, carbamates are also required in lower volumes but high-cost category segment, in specialty chemical industry for the production of drug intermediates in pharmaceutical industry [2]. Recently, due to the development of combinatorial techniques in the field of drug discovery and due to their medicinal and biological properties, carbamates have gained considerable importance in the preparation of small molecule libraries [3]. In organic synthesis, carbamates are often used as protecting groups for amine functionality [4]. The conventional process for the carbamate synthesis is based on phosgenation of amines [5]; this process besides being highly energy intensive uses highly corrosive and toxic phosgene and produces hydrochloric acid as a side product. Efforts are continuously being made for the replacement of phosgene-based technology with environmentally benign routes such as carbonylation of nitro compounds [6], oxidative carbonylation of amines [7], carboxylation of amines using organic carbonates [8] or carbon dioxide [9] and alcoholysis of substituted urea [10]. Synthesis of carbamate using carbonate or urea as reagents results in poor atom economy and in each case alcohol or amine is produced as a by-product reducing the functional group efficiency of the reagent (Scheme 1). One way of improving the atom economy in reactions (i) and (ii) is to eliminate the use of alcohol and amine by reacting substituted urea and carbonate in the presence of a catalyst. We reported recently, carbamate synthesis by reacting substituted urea and carbonate in the presence of a solid base catalyst [11]. In the present work, the effect of various homogeneous catalysts and the role of catalysis in carbamate production as well as the effect of process parameters on the synthesis of methyl methyl carbamate from dimethyl urea and dimethyl carbonate are reported.

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$$R^1NH_2 + R^2OCOOR^2 \xrightarrow[\text{Catalyst}]{\text{Carboxylation}} R^1NHCOOR^2 + R^2OH \quad \text{(i)}$$

$$R^1NHCONHR^1 + R^2OH \xrightarrow[\text{Catalyst}]{\text{Alcoholysis}} R^1NHCOOR^2 + R^1NH_2 \quad \text{(ii)}$$

Scheme 1.

2. Experimental

Substituted ureas and unsymmetrical phenyl methyl carbonate as reactants were synthesized by standard procedures and used after purification [12,13]. Diphenyl, dimethyl and diethyl carbonates were purchased from M/s. S.D. Fine chemicals, India, and were used as such. Catalyst precursors $Ti(IV)(O)(acac)_2$, $Cu(acac)_2$, $FeCl_3$, $AlCl_3$, $SnCl_4(H_2O)_6$ and Bu_2SnO (DBTO) were purchased from Aldrich, USA, and used as received. $Bu_2Sn(OPh)_2$ was prepared according to literature procedure [14]. In a typical experimental procedure, substituted urea (3.16 mmol), carbonate (15.6 mmol) and DBTO catalyst (0.89 mmol) were charged to a nitrogen flushed and dry glass reaction vessel (50 cm^3) equipped with temperature controller, a stirrer and reflux condenser. The contents were heated under stirring up to 150 °C and kept for 4 h under an inert atmosphere. After cooling to room temperature, the carbamate derivative was separated by column chromatography using silica gel and ethyl acetate: chloroform mixture in proportion 0.2:9.8 as an eluent. A 50-cm^3 autoclave was used while working with low boiling alkyl carbonates as substrates. Typically, in the synthesis of methyl methyl carbamate, catalyst DBTO (1.81 mmol), dimethyl urea (15.34 mmol) and 17 ml of dimethyl carbonate (169.2 mmol) were employed as reactant serving the purpose of a solvent as well. Reactions were carried out at 150 °C for 4 h at 500 psig of nitrogen pressure. For investigations on the effect of reaction conditions in MMC synthesis, toluene was used as a solvent. For determining the material balance and concentration–time profiles of liquid-phase reactants and products, samples were withdrawn at regular intervals and analyzed using GC for carbamates and carbonates while LC was used for substituted urea analysis. Initial rates of MMC formation at various temperatures were calculated by running the experiments with short reaction time (∼30 min) and analyzing the samples at the end of reactions for MMC formation.

2.1. Identification

All the carbamates reported herein were fully characterized by elemental analysis, ^{1}H NMR, ^{13}C NMR, IR, GC–MS (EI, 70 eV) and compared with authentic samples whenever possible. The ^{1}H NMR and ^{13}C NMR spectra in $CDCl_3$ were recorded on a 200 and 500 MHz Brucker instrument, respectively. Some carbamates were unstable towards injection temperature employed for GC–MS analysis and were analyzed as corresponding isocyanate and phenol derivatives by GC–MS (Table 2, entries 2–6 and 13). The analytical data for various carbamate derivatives are given bellow.

2.1.1. *N*-3-Cl phenyl phenyl carbamate (Table 2, entry 2)

IR (KBr) ν_{CO}: 1764 cm^{-1}. ^{1}H NMR: δ 7.57–7.07 (m, 9H); 6.97 (s, 1H). ^{13}C NMR: δ 116.84, 118.96, 121.52, 125.8, 126.27, 129.54, 130.01, 138.62, 150.43, 151.01, 151.51. *N*-3-Cl phenyl isocyanate (*m*/*z*): 153, 125, 90, 63, 50; phenol (*m*/*z*): 94, 66, 39. Microanalysis for $C_{13}H_{10}NO_2Cl$: Calc.: 63.03% C, 4.04% H, 5.65% N, 14.34% Cl; Found: 63.4% C, 4.02% H, 5.56% N, 13.97% Cl.

2.1.2. *N*-4-Cl phenyl phenyl carbamate (Table 2, entry 3)

IR (KBr) ν_{CO}: 1716 cm^{-1}. ^{1}H NMR: δ 7.45–7.17 (m, 9H); 6.98 (s, 1H). ^{13}C NMR: δ 120.30, 121.55, 125.83, 129.02, 129.15, 129.43, 135.98, 150.46, 151.41. *N*-4-Cl phenyl isocyanate (*m*/*z*): 153, 125, 90, 63, 50; phenol (*m*/*z*): 94, 66, 39. Microanalysis for $C_{13}H_{10}NO_2Cl$: Calc.: 63.03% C, 4.04% H, 5.65% N, 14.34%.

2.1.3. *N*-3-NO_2 phenyl phenyl carbamate (Table 2, entry 4)

IR (KBr) ν_{CO}: 1712 cm^{-1}. ^{1}H NMR: δ 8.31(t, $1H_{ortho,NO_2}$, J = 2 Hz), 7.92 (dd, $1H_{ortho,NO_2}$, J = 1.6, 7.9 Hz), 7.7 (d, $1H_{para,NO_2}$, J = 7.9 Hz), 7.45 (t, $1H_{meta,NO_2}$, J = 8.2 Hz), 7.37 (dd, 2H, J = 1.6, 7.5 Hz) 7.3 (bs, 1H), 7.22 (dd, 1H, J = 1.6, 7.6 Hz), 7.16 (dd, 2H, J = 7.5 Hz). ^{13}C NMR: δ 113.66, 118.42, 121.45, 124.42, 126.01, 129.46, 129.86, 138.69, 148.66, 150.22, 151.7. *N*-3-NO_2 phenyl isocyanate (*m*/*z*): 164, 118, 90, 63, 50; phenol (*m*/*z*): 94, 66, 39. Microanalysis for $C_{13}H_{10}N_2O_4$: Calc.: 60.46% C, 3.87% H, 10.85% N; Found: 61.45% C, 3.94% H, 10.52% N.

2.1.4. *N*-4-CH_3 phenyl phenyl carbamate (Table 2, entry 5)

IR (KBr) ν_{CO}: 1719 cm^{-1}. ^{1}H NMR: δ 7.43–7.11 (m, 9H), 6.95 (s, 1H), 2.32 (s, 3H). ^{13}C NMR: δ 20.69, 118.88, 121.67, 125.55, 126.25, 129.32, 129.6, 134.79, 150.68, 151.01. *N*-4-CH_3 phenyl isocyanate (*m*/*z*): 133, 104, 91, 63, 51; phenol (*m*/*z*): 94, 66, 39. Microanalysis for $C_{14}H_{13}NO_2$: Calc.: 74% C, 5.72% H, 6.16% N; Found: 73.75% C, 5.55% H, 6.38% N.

2.1.5. *N*-Phenyl phenyl carbamate (Table 2, entry 6)

IR (KBr) ν_{CO}: 1717 cm^{-1}. ^{1}H NMR: δ 7.46–7.09 (m, 10H), 6.95 (s, 1H). ^{13}C NMR: δ 118.84, 121.61,123.9, 125.66, 129.11, 129.37, 137.38, 150.6, 151.64. Phenyl isocyanate (*m*/*z*): 119, 91, 64, 51; phenol (*m*/*z*): 94, 66, 39. Microanalysis for $C_{13}H_{11}NO_2$: Calc.: 73.23% C, 5.16% H, 6.57% N; Found: 72.85% C, 5.27% H, 6.35% N.

2.1.6. *N*-Phenyl methyl carbamate (Table 2, entry 7)

IR (KBr) ν_{CO}: 1708 cm^{-1}. ^{1}H NMR: δ 7.4–7.02 (m, 5H), 6.69 (s, 1H), 3.77 (s, 3H). ^{13}C NMR: δ 52.21, 118.74, 123.38, 128.94, 137.84, 154.11. GC/MS (*m*/*z*): 151, 135, 119, 106, 92,

77, 65, 51, 39. Microanalysis for $C_8H_9NO_2$: Calc.: 63.57% C, 5.96% H, 9.27% N; Found: 63.05% C, 5.71% H, 8.98% N.

2.1.7. N-Phenyl ethyl carbamate (Table 2, entry 8)

IR (KBr) ν_{CO}: 1703 cm^{-1}; ^1H NMR: δ 7.42–7.03 (m, 5H), 6.66 (s, 1H), 4.22 (q, 3H, J = 7.32 Hz), 1.32 (t, 3H, J = 7.32 Hz). ^{13}C NMR: δ 14.45, 61.1, 118.71, 123.25, 128.91, 137.99, 153.7. GC/MS (*m*/*z*): 165, 137, 119, 93, 77, 65, 51, 39. Microanalysis for $C_8H_9NO_2$: Calc.: 65.45% C, 6.66% H, 8.48% N; Found: 65.69% C, 6.73% H, 8.46% N.

2.1.8. N-Phenyl butyl carbamate (Table 2, entry 9)

IR (KBr) ν_{CO}: 1702 cm^{-1}. ^1H NMR: δ 7.42–7.04 (m, 5H), 6.67 (s, 1H), 4.19 (t, 2H, J = 6.35 Hz), 1.69 (qu, 2H, J = 6.35, 6.83 Hz), 1.45 (m, 2H, J = 6.84, 7.33 Hz), 0.97 (t, 3H, J = 7.33 Hz). ^{13}C NMR: δ 13.66, 19.03, 30.95, 65.08, 118.67, 123.28, 128.97, 138.01, 153.76. GC/MS (*m*/*z*): 193, 137, 119, 93, 77, 65, 41. Microanalysis for $C_{11}H_{15}NO_2$: Calc.: 68.39% C, 7.77% H, 7.72% N; Found: 67.85% C, 7.78% H, 7.35% N.

2.1.9. N-Methyl methyl carbamate (Table 2, entry10)

IR (KBr) ν_{CO}: 1711 cm^{-1}. ^1H NMR: δ 4.93 (s, 1H), 3.67 (s, 3H), 2.78 (d, 3H, J = 4.88 Hz). ^{13}C NMR: δ 27.36, 51.91, 157.77. GC/MS (*m*/*z*): 89, 74, 58, 44.

2.1.10. N-Methyl ethyl carbamate (Table 2, entry11)

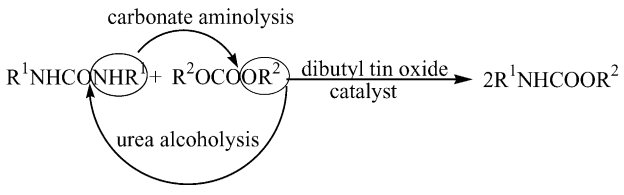
IR (KBr) ν_{CO}: 1704 cm^{-1}. ^1H NMR: δ 4.95 (s, 1H), 4.01 (q, 2H, J = 6.84, 7.32 Hz), 2.7 (d, 3H, J = 4.88 Hz), 1.16 (t, 3H, J = 6.83, 7.33 Hz). ^{13}C NMR: δ 14.42, 27.17, 60.47, 157.33. GC/MS (*m*/*z*): 103, 88, 74, 58, 44.

2.1.11. N-Methyl phenyl carbamate (Table 2, entry13)

GC/MS, methyl isocyanate (*m*/*z*): 57, 28, 15; phenol (*m*/*z*): 94, 66, 39.

3. Results and discussion

In this work, reaction between substituted urea and carbonate derivatives has been investigated using homogeneous catalysts (see Scheme 2). This reaction is also a case of ester aminolysis of carbonate and alcoholysis of urea operating in tandem.



Scheme 2.

Table 1
Catalyst screening for *N*-phenyl phenyl carbamate synthesis[a]

Entry	Catalyst	Time (h)	Yield[b] (%)
1	None	24	Traces
2	$Ti(IV)(O)(acac)_2$	15	34
3	$Cu(acac)_2$	4	71
4	NaOH	4	32
5	PhONa	4	56
6	$(C_2H_5)_4NBr$	4	81
7	$FeCl_3$	4	16
8	$AlCl_3$	4	22
9	$SnCl_4(H_2O)_6$	4	11
10	$Bu_2Sn(OPh)_2$	4	20
11	Bu_2SnO	4	93

[a] Reaction conditions: *N*,*N*′-diphenyl urea (3.16 mmol), diphenyl carbonate (15.6 mmol), catalyst (0.89 mmol), temperature (423 K), reaction volume 4 cm^3.
[b] Isolated carbamate yields based on urea.

3.1. Preliminary experiments for catalyst screening

Preliminary experiments were carried out for screening of the homogeneous catalysts targeting for industrially important carbamate such as *N*-phenyl phenyl carbamate (PPC) as a model. For this purpose, reactions were carried out employing diphenyl urea (DPU) and diphenyl carbonate (DPC) as substrates. The results on screening of catalysts for PPC synthesis are presented in Table 1.

These results indicated that a non-catalytic reaction between DPU and DPC produces only traces of PPC after 24 h indicating that catalyst is essential for formation of PPC (see Table 1, entry 1). Urea alcoholysis catalysts such as titanium and copper acetylacetonate complexes [10] were also screened (see entries 2 and 3) in which copper catalyst was found to show good activity. Further, classical acid catalysts such as $FeCl_3$, $AlCl_3$, $SnCl_4$ (see Table 1, entries 7–9) showed poor activity compared to the basic catalysts such NaOH, phenolate ion, onium salts (see Table 1, entries 4–6). Encouraged by these results, we explored organotin complexes, which are known to be excellent transesterification catalysts for carbonates and esters. Several organotin complexes were tested for synthesis of carbamate from DPU and DPC in which acidity of catalyst was varied to highly acidic to mild basic tin catalysts. The results of these experiments showed that basic tin complexes such as dibutyl tin oxides give excellent carbamate yield ∼93% (see Table 1, entry 11) compared to acidic tin compounds such as $SnCl_4{\cdot}6H_2O$ ∼11% (see Table 1, entry 9), while, $Bu_2Sn(OPh)_2$ having intermediate acidity showed moderate yields of PPC ∼20% (see Table 1, entry 10). Therefore, further reactions with various ureas and carbonates were carried out using DBTO as a catalyst.

3.2. Reactivity of substituted urea and carbonate towards carbamate formation

The reaction between substituted urea and carbonate to form carbamate is not well explored and practically very little is known about the reactivity pattern of ureas and carbonate

towards carbamate formation. However, considerable amount of work on similar systems viz. ester aminolysis of carbonate and alcoholysis of substituted ureas (see Scheme 1) has been reported in the literature (and discussed later) which will be useful in understanding the reactivity behavior observed for carbamate synthesis from substituted urea and carbonate.

It is well known that in ester aminolysis of substituted carbonates, the reaction depends upon the basicity of attacking amine [15,16]. It is generally believed that aminolysis proceeds smoothly when the pK_a values of attacking amine are about 4–5 units higher than that of the leaving group (e.g. alkoxide or aryloxide) [17]. The reactivity of carbonate depends upon the electrophilicity of carbonyl carbon; the factors that help increase in the electrophilicity of carbonyl carbon may therefore increase the rate of reaction. An electron-withdrawing substituents on phenoxide or alkoxide will facilitate nucleophilic attack (retarded by electron-donating substituents) [18]. However, the final reactivity will depend on the pK_a of attacking amine as noted earlier. Similarly, alcoholysis of substituted urea is accelerated by electron-donating group on alcohol and slowed by electron-withdrawing groups, provided that hindrance factor is not coming into play [10]. On the other hand, electron-donating substituents on phenyl urea increase reactivity of urea, while decreased by electron-attracting substituents on aryl group [19].

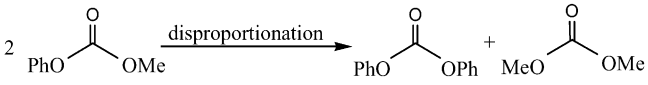
Several substituted ureas were subjected to reaction with diphenyl carbonate using DBTO as a catalyst and these results are summarized in Table 2. The yield of carbamate does not follow simple reactivity pattern expected due to electronic effect caused by substituents (discussed above). For example, substituted diphenyl urea having electron-withdrawing (entries 1–4) and -donating (entry 5) groups seem to react with equal ease with DPC (see, e.g. reaction with DPU, entry 6 for comparison), except that for sterically hindered *N*,*N*′-bis(2-chlorophenyl) urea which shows substantially low carbamate yields (see Table 2, entry 1). While carbonate reactivity towards diphenyl urea seems to be following the rule that carbonate reactivity increases with leaving group ability of methoxide and phenoxides (see entries 6 and 7), which is consistent with the trend observed in aminolysis of carbonates [15]. The reactivity of alkyl carbonates towards ureas was found to decrease in the order dimethyl carbonate > diethyl carbonate > dibutyl carbonate (entries 7–11). The observed reactivity of carbonate suggests that the carbonyl carbon of dimethyl carbonate is the most electrophilic center and that of dibutyl carbonate is least in the three carbonates investigated. A similar kind of reactivity was earlier observed for alcohols in transesterification of DMC and was attributed to the steric factors rather than electronic effect of various alcohols [20,21].

When unsymmetrical carbonate such as phenyl methyl carbonate (PhMC) was reacted with DPU, *N*-phenyl phenyl carbamate and *N*-phenyl methyl carbamate is formed in 62 and 10% yields, respectively (see Table 2, entry 12). However, as per the stoichiometry of reaction (see Scheme 1) equal amount of carbamates should have been formed. It is well known that, under the catalytic conditions employed in this work, disproportionation of PhMC to DPC and DMC is also likely to occur (see Scheme 3) [22]. Analysis of reaction crude has also confirmed the formation of symmetrical carbonates from PhMC. The symmetrical carbonates thus formed react independently with DPU to form corresponding carbamates and yields of carbamates depend upon the reactivity of carbonates viz. DPC and DMC. Since, the reactivity of DPC is higher than that of DMC, higher yield of *N*-phenyl phenyl carbamate is obtained. The reactivity pattern study shows a general behavior in that excellent carbamate yields are obtained when an aromatic (or aliphatic) urea is reacted with aromatic (or aliphatic) carbonate but poor yields are obtained when aromatic urea is reacted with aliphatic carbonate and vice versa. In fact in the reaction between *N*,*N*′-dimethyl urea and DPC at 150 °C, carbamate was not detected. However, when the reaction was carried out at 100 °C formation of *N*-methyl phenyl carbamate in the reaction sample could be detected by GC–MS (Table 2, entry 13).

Table 2
Synthesis of carbamates using dibutyl tin oxide catalyst[a]

Entry	R^1 (urea)	R^2 (carbonate)	Time (h)	ν_{CO}, carbamate (cm^{-1})	Yield[b] (%)
1	2-ClC_6H_4	C_6H_5	4	–	~25[c]
2	3-ClC_6H_4	C_6H_5	4	1764	92
3	4-ClC_6H_4	C_6H_5	4	1716	90
4	3-$NO_2C_6H_4$	C_6H_5	4	1712	89
5	4-$CH_3C_6H_5$	C_6H_5	4	1719	90
6	C_6H_5	C_6H_5	4	1717	93
7	C_6H_5	CH_3	4	1708	77
8	C_6H_5	C_2H_5	4	1703	61
9	C_6H_5	*n*-C_4H_9	4	1702	50
10	CH_3	CH_3	4	1711	91
11	CH_3	C_2H_5	4	1704	64
12	C_6H_5	PhMC[d]	15	–	72[e]
13[f]	CH_3	C_6H_5	4	–	25[g]

[a] Reaction conditions: same as Table 1, except that for reactions involving methyl, ethyl and butyl carbonates (DBTO = 1.81 mmol, DMU = 15.34 mmol, DMC = 169.2 mmol, temperature = 423 K, contact time = 4 h, P_{N_2} = 500 psig, reaction volume = 17 cm^3, stirrer speed = 800 rpm, reactor = 50 cm^3 S.S. autoclave).
[b] Isolated carbamate yields.
[c] Carbamate is unstable.
[d] PhMC = unsymmetrical phenyl methyl carbonate.
[e] Combined yield of *N*-phenyl phenyl carbamate (62% yield) and *N*-phenyl methyl carbamate (10% yield).
[f] Reaction temperature 100 °C.
[g] *N*-methyl phenyl carbamate is unstable towards silica gel column chromatography and therefore GC yields are reported.



Scheme 3.

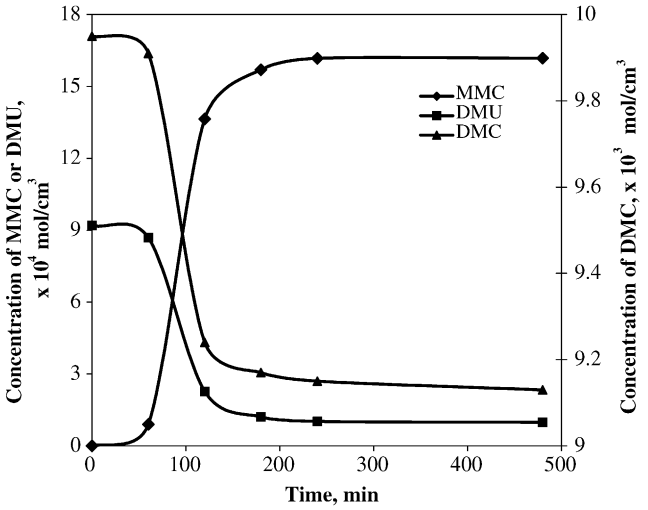


Fig. 1. Typical time profile of DMC, DMU and MMC. Conditions: DBTO = 1.81 mmol; DMC (solvent) = 169.2 mmol; DMU = 15.34 mmol; temperature 423 K; contact time = 4 h; P_{N_2} = 500 psig; reaction volume = 17 cm^3; stirrer speed = 800 rpm; reactor = 50 cm^3 autoclave.

3.3. Synthesis of methyl methyl carbamate

Methyl methyl carbamate an industrially important carbamate was synthesized by reacting dimethyl urea with dimethyl carbonate. For this purpose, a few initial experiments were carried out to examine the material balance (for side product formation, etc.) as well as the contribution of non-catalytic reactions in the formation of methyl methyl carbamate from dimethyl urea and dimethyl carbonate. Fig. 1 shows a typical concentration–time profile in a high-pressure batch reactor. Since DMC is acting as a solvent as well as one of the reactants, DMU is considered as the limiting reactant and on the basis of moles of DMU-reacted carbamate formation and DMC consumed were tallied. Almost complete conversion of DMU was achieved and correspondingly DMC was also consumed with concurrent formation of MMC, indicating no formation of side products and material balance was in complete agreement with the stoichiometry. A DMU conversion of 89.3% with almost 100% selectivity of MMC formation on the basis of DMU and DMC converted was observed at the end of eight hours of reaction time, this also shows that the reaction is thermodynamically favorable under the experimental conditions. It may be noted that Fig. 1 shows an induction period of about 45 min at this temperature and indicates the formation of an active catalytic species from catalyst precursor DBTO that is responsible for the catalytic reaction. Fu and Ono have also reported similar observation earlier for PbO-catalyzed methoxycarbonylation of aniline with dimethyl carbonate to carbamate [23].

3.3.1. Effect of reaction conditions on MMC synthesis

Reaction conditions such as temperature, catalyst and reactant concentrations, solvents, etc. were evaluated for the synthesis of MMC using dibutyl tin oxide as a catalyst and toluene as a solvent.

Table 3
Effect of catalytic conditions on MMC synthesis[a]

Entry	Conditions	MMC yield due to DBTO[b] (%)	Yields[c] of MMC (%)	Pressure (psig)
1	Non-catalytic	–	37	Autogenous
2	Non-catalytic	–	65	500 N_2
3	DBTO	54 (91-37)	91	Autogenous
4	Non-catalytic	–	9	500 CO_2
5	DBTO	53 (62-9)	62	500 CO_2

[a] Reaction conditions: DBTO = 1.81 mmol, DMU = 15.34 mmol, DMC = 169.2 mmol, temperature = 423 K, contact time = 4 h, reaction volume 17 cm^3.
[b] For details, see text.
[c] GC yields.

3.3.1.1. Effectiveness of DBTO as catalyst. Since, a base can effectively catalyzes the reaction between urea and carbonate, we were interested in exploring the possibility of a non-catalytic reaction between aliphatic urea (which is a mild base) and aliphatic carbonate. For this purpose non-catalytic reaction between *N*,*N*′-dimethyl urea and dimethyl carbonate was investigated and these results are presented in Table 3. The results of non-catalytic reaction between urea and carbonate shows that, basic urea such as *N*,*N*′-dimethyl urea can itself activate carbonates like dimethyl carbonate, giving *N*-methyl methyl carbamate in good yields even in the absence of any catalyst (MMC yields 37%; see Table 3, entry 1). On the other hand, less basic urea like *N*,*N*′-diphenyl urea needs catalyst for carbamate formation, for example, from diphenyl carbonate (Table 1, entry 1). Thus, catalysis is also dependent on acidity and basicity of catalyst as well as substrates. In order to further confirm that DMU having basic property itself catalyzes carbamate synthesis from DMU and carbonate, an experiment was performed with carbon dioxide with the aim to neutralize the basic sites of DMU and thus hampering its activity (if indeed it is due to basicity). Interestingly, in this experiment very poor yields of MMC were obtained (MMC yields 9%, see Table 3, entry 4). Thus, carbon dioxide deactivates DMU and thereby decreasing its ability to activate dimethyl carbonate, confirming our reasoning that DMU basicity is playing a key role in non-catalytic reaction between DMU and DMC and that DMU is both acting as a reactant as well as a catalyst in this case. The results obtained on the effect of pressure of inert gas such as nitrogen on non-catalytic reaction between DMU and DMC was however, most unexpected. Under 500 psig pressure of nitrogen, the MMC yield increased to about 65% (see entry 2). We do not have a definite reason at this stage as to why N_2 is enhancing the yields of MMC, but it is likely that N_2 could be modifying the reactivity of DMU and DMC towards carbamate formation.

Experiments were also undertaken to understand the effect of CO_2 on DBTO activity, and these results are also shown in Table 3. Since MMC is also formed via a non-catalytic route (Table 3, entries 1 and 2) activity due to DBTO alone

can be calculated by accounting for the contribution due to non-catalytic reaction. Entry 3 in Table 3 shows that overall yield of MMC obtained under DBTO-catalyzed reaction conditions is 91%, which includes 37% yield of MMC due to non-catalytic reaction (entry 1, yields in the absence of DBTO) and the rest 54% yields is thus due to DBTO. While, in the presence of CO_2, DBTO-catalyzed reaction shows 62% of MMC yield (entry 5) and under CO_2 atmosphere only 9% MMC is formed due to non-catalytic reaction (entry 4) it follows that even in the presence of CO_2, MMC yield due to DBTO is not affected (compare entries 3 and 5 for MMC yields due to DBTO). Therefore, it is clear that CO_2 interacts with DMU more strongly than DBTO and hence most of the catalytic activity of DBTO is retained even under CO_2 atmosphere.

3.3.1.2. Effect of DBTO concentration. Effect of DBTO concentration on conversion and selectivity behaviors in MMC synthesis was investigated in the range 0.27–1.6 × 10^{-4} mol/cm^3. A plot of MMC yields versus catalyst concentration shows that with increase in catalyst concentration MMC yield increases, showing first-order dependence normally observed for catalyst concentration effect, except at high DBTO catalyst loading the rates seems to be tapering off with catalyst loading (see Fig. 2). In the present case, both the reactants (urea and carbonate) are infinitely soluble in toluene under reaction conditions offering a homogeneous liquid phase and therefore no liquid side mass transfer resistance is expected. The catalyst was found to be completely soluble except at high loadings as precipitation was observed while withdrawing the sample (loading > 1.07 × 10^{-4} mol/cm^3) due to poor solubility of catalyst. However, it may be noted that in the absence of catalyst, appreciable

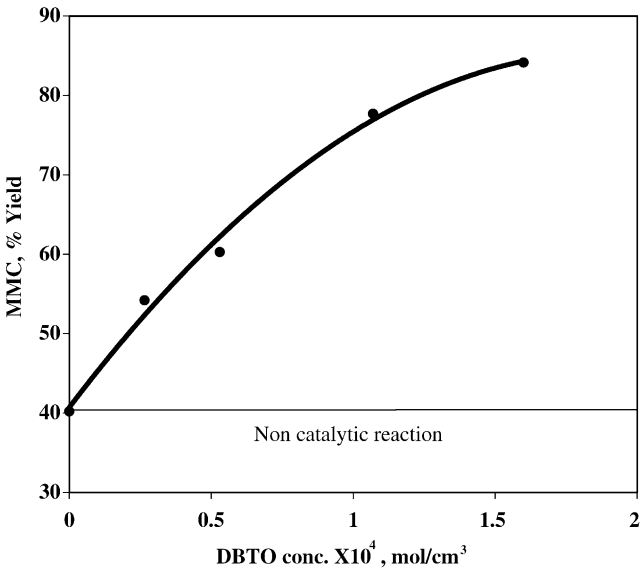


Fig. 2. Catalyst loading effect on MMC yield. Conditions: DMC = 55.56 mmol; DMU = 15.3 mmol; temperature = 423 K; contact time = 4 h; solvent = toluene; P_{N_2} = 500 psig; reaction volume = 17 cm^3.

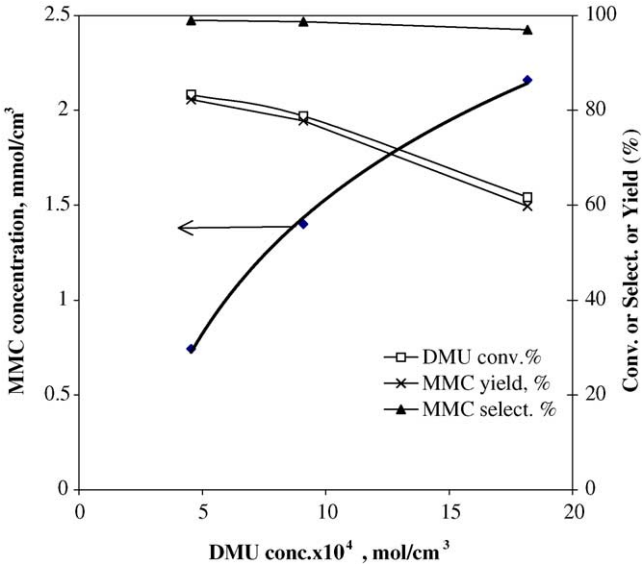


Fig. 3. Effect of DMU concentration on MMC production. Conditions: DBTO = 1.81 mmol; DMC = 55.56 mmol; temperature = 423 K; contact time = 4 h; solvent = toluene; P_{N_2} = 500 psig; reaction volume = 17 cm^3.

amount of non-catalytic reaction is also contributing to MMC yield, indicating that contribution of catalysis is not very significant for the reaction. Thus catalyst loading effect shows a first-order dependence on rate up to 1.07 × 10^{-4} mol/cm^3 DBTO concentration and beyond that showing less than first-order dependence with increase in catalyst concentration.

3.3.1.3. Effect of DMU concentration on MMC synthesis. The effect of DMU concentration on yield of MMC was investigated in the concentration range 4.5–18.2 × 10^{-4} mol/cm^3 and the results are presented in Fig. 3. The DMU concentration effect shows that increasing the concentration of DMU increases the MMC production showing a positive effect of DMU concentration. While, MMC yield and conversion of DMU decreases with increase in DMU concentration and a maximum of ∼82% of both MMC yield and DMU conversion is obtained when a lower DMU concentration is employed (∼4.5 × 10^{-4} mol/cm^3). However, selectivity for MMC is not affected with increase in DMU concentration and remains close to ∼98% in the concentration range of DMU investigated. The decrease in the yield of MMC as well as conversion of DMC is expected since with increase in the urea concentration, ratio of urea to catalyst increases (at constant catalyst concentration) and under such conditions yields and conversions are expected to decrease for a fix reaction time and is not due to deactivation of catalyst. Experiments with longer reaction times gave complete conversion with close to 100% yield of MMC, such is not the case when catalyst is deactivating. This observation has significance from the point of view of achieving higher output of MMC production, since our earlier work on synthesis of MMC via alkoxy oxidative carbonylation of methyl amine in the presence of methanol indicated that an equilibrium

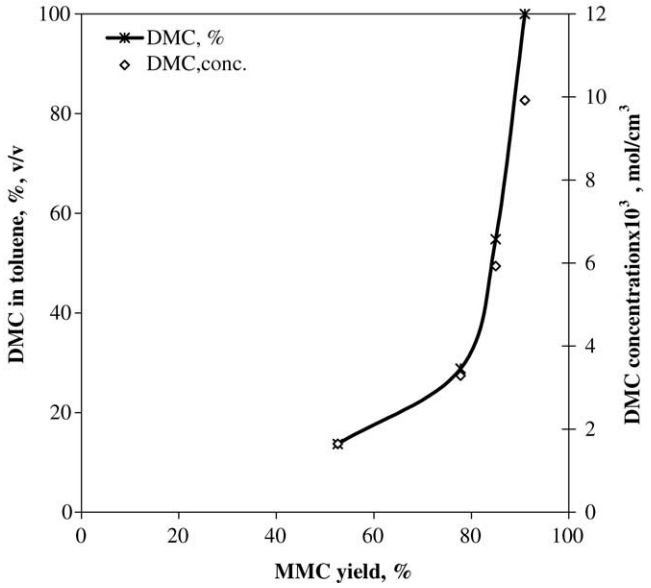


Fig. 4. Effect of DMC concentration on MMC yield. Conditions: DBTO = 1.81 mmol; DMU = 15.34 mmol; temperature = 423 K; contact time = 4 h; solvent = toluene; P_{N_2} = 500 psig; reaction volume = 17 cm^3.

exist for methanolysis of dimethyl urea reaction to MMC, and a maximum of only ~7.5% MMC concentration could be achieved and further increase in methyl amine concentration has no effect on MMC production [24].

3.3.1.4. Effect of DMC concentration on MMC synthesis. The concentration of DMC on effect of MMC yield was investigated in DMC concentration range 1.65–9.92 × 10^{-3} mol/cm^3, reactions were carried out at constant DMU concentration and the results are presented in Fig. 4. The yield of MMC increases sharply as DMC concentration is increased and in extreme case when pure DMC is employed as reactant maximum yield of 91% of MMC is obtained.

3.3.1.5. Effect of solvent on MMC synthesis. The effect of various solvents such as o-dichlorobenzene (ODCB), toluene, dimethyl formamide (DMF), diphenyl ether (DPE) and DMC was investigated and the results are presented in Fig. 5. It can be seen from this figure that polar solvents such as DMF, DMC and ODCB have no significant advantage over non-polar solvent like toluene. The highest yield obtained is with DMC as a solvent and it is due to a combined effect of DMC acting as a reactant as well as solvent.

3.3.1.6. Effect of temperature on MMC synthesis. The effect of temperature on MMC formation rate was investigated in the range 140–160 °C. For this purpose catalyst DBTO was pretreated at 150 °C with DMC under 500 psig of N_2 for 1 h in a pressure reactor and a fix amount of this pretreated catalyst solution (stored under N_2) was later used for temperature effect study. The pretreatment of catalyst avoids the complexities arising from the effect of temperature on induction period and gives more consistent and realistic initial rates

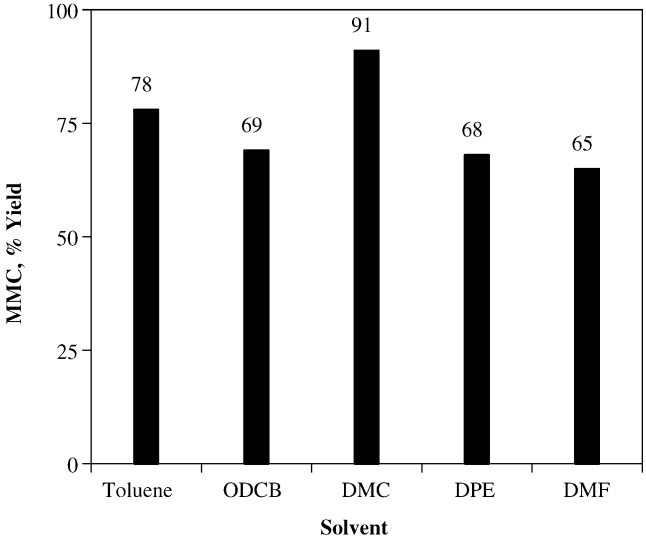


Fig. 5. Effect of solvent on MMC yield. Conditions: DBTO = 1.81 mmol; DMC = 55.56 mmol, DMU = 15.34 mmol; temperature = 423 K; contact time = 4 h; P_{N_2} = 500 psig; reaction volume = 17 cm^3.

for temperature parameter effect. Fig. 6 shows the effect of temperature on the reaction for MMC synthesis using DBTO as catalyst. From this figure the apparent activation energy obtained from Arrhenius law is found to be 7.57 kcal/mol. The low value of activation energy reflects the secondary role played by catalyst DBTO, which is expected for the reaction as in the absence of catalyst appreciable yields of MMC is obtained (see Section 3.3.1 on effectiveness of DBTO catalyst).

3.3.2. Plausible reaction mechanism

Basic tin complexes such as DBTO are known to interact with organic carbonate [14] indicating that interaction of carbonate with DBTO is more likely to be the first step towards

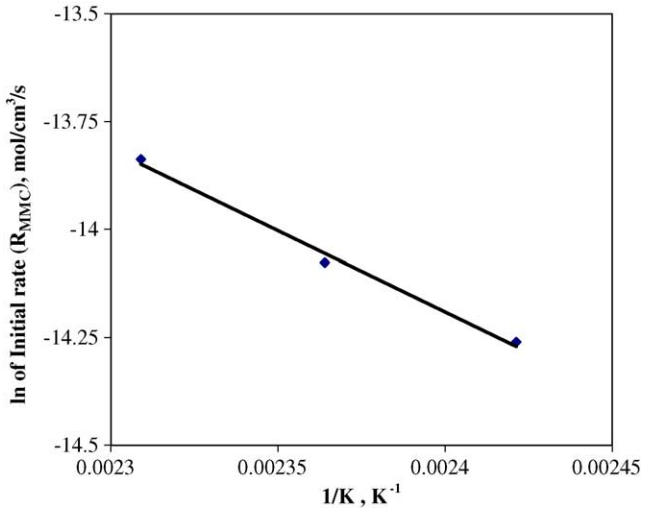
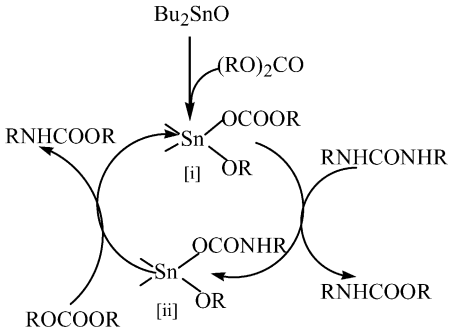


Fig. 6. Arrhenius plot. Conditions: DBTO = 1.81 mmol; DMC = 169.2 mmol; DMU = 15.34 mmol; contact time = 30 min; P_{N_2} = 500 psig; reaction volume = 17 cm^3.



Scheme 4.

activation of substrates in our case. Based on the reactivity of DBTO in the synthesis of dialkyl carbonates from alkyl carbamates and alcohol [25] and from the present investigation a plausible pathway for the formation of N-substituted carbamates from substituted ureas and carbonates is depicted in Scheme 4. The basic DBTO is believed to play a key role as a nucleophile attacking carbonyl carbon of carbonate forming catalytically active species, dibutyl alkoxy carbonato tin (**i**) [21]. Species **i** interacts with substituted urea to eliminate one molecule of carbamate forming dibutyl alkoxy carbamato tin (**ii**) [25]. A further reaction of species **ii** with carbonate results in the formation of one more molecule of carbamate with regeneration of active species **i**. The key step here is the formation of species **i**, which presumably does not get converted into $Bu_2Sn(OR)_2$ because of the presence of urea. However, further work in this area is necessary to arrive at a definitive mechanism for carbamate formation from substituted urea and carbonate catalyzed by tin complexes.

4. Conclusions

Synthesis of carbamates from substituted ureas and carbonates has been investigated. The catalyst screening study showed that basic homogeneous catalysts such as basic tin complexes and in particular dibutyl tin oxide show excellent activity towards carbamate synthesis. Aliphatic ureas show higher reactivity compared to aromatic ureas due to their higher basicity. Various substituents (e.g. Cl, CH_3 and NO_2) on aromatic urea do not show any significant effect on urea reactivity compared to non-substituted aromatic urea that is diphenyl urea, while aliphatic carbonates shows reactivity in accordance with the leaving group ability of alkoxy groups of carbonates. Reaction parameter effects on the synthesis of industrially important methyl methyl carbamate showed that maximum of ∼20% concentration could be obtained under experimental conditions employed in this investigation, which is a vast improvement (∼7 times) over MMC synthesis by oxidative carbonylation of methyl amine [24].

Acknowledgment

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