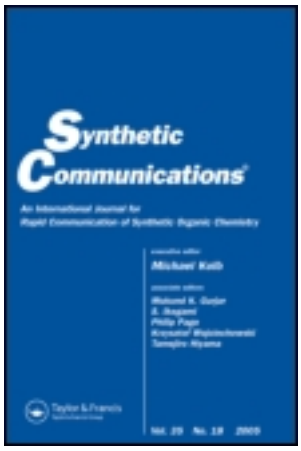

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AN EFFICIENT ONE POT SYNTHESIS OF CARBAMATE ESTERS THROUGH ALCOHOLIC TOSYLATES*

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AN EFFICIENT ONE POT SYNTHESIS OF CARBAMATE ESTERS THROUGH ALCOHOLIC TOSYLATES*

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ABSTRACT

An efficient *O*-alkylation of alcoholic tosylates with amines in a K_2CO_3/CO_2 system in the presence of tetrabutyl ammonium iodide (TBAI) provides exclusive formation of carbamates.

Key Words: *O*-Alkylation of tosylates; Tetrabutylammonium-iodide (TBAI); Carbamates

Organic carbamates represent an important class of compounds having various properties. They have largely found use as agrochemicals[1] (pesticides, fungicides, herbicides), pharmaceuticals,[2] as intermediates in organic synthesis,[3] protecting groups in peptide synthesis[4] and as linkers in combinatorial chemistry.[5] Hence considerable interest has generated in the recent past for development of an effecient and safe methodology for carbamate synthesis. Classical syntheses of carbamates involve direct alcoholysis of phosgene or its derivatives,[6] aminolysis of chloroformates[7] and

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alcoholysis of isocyanates,[8] thus utilizing phosgene, a harmful chemical, directly or indirectly.

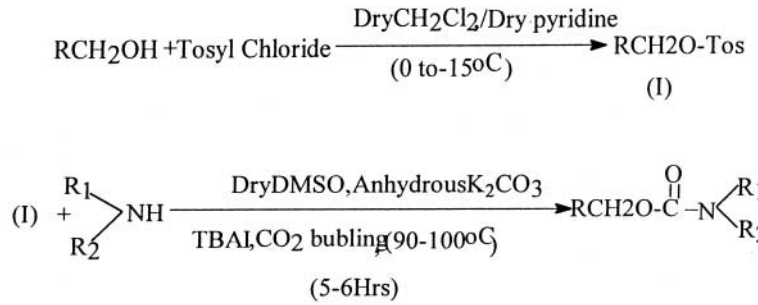
Recently carbondioxide, a cheap and safe reagent, has been tapped as an alternative to phosgene for the introduction of a CO group. Preparation of carbamates has been reported using CO_2 electrochemically,[9] super critically[10] and in combination of metal and non-metal species.[11] CO_2 alone has low reactivity with nucleophiles. With amines it gives unstable carbamic acid (1). However, with 2 molar equivalence of amine, monoalkylammonium alkyl carbamate ion (2) is formed.

$$\underset{(1)}{RNHCOOH}. \quad \underset{(2)}{[RNH_3]^+ \ ^-[OOCNHR]}$$

The alkylammonium carbamate thus formed reacts with alkyl halide to give rise to *N*- or *O*-alkylation (carbamate) products. Formation of O-alkylation product has been reported in the reaction of primary or secondary amines, CO_2 and alkyl halides in the presence of strong proton acceptors e.g., DBU,[12] transition metal complexes and crown ether.[13]

It was observed,[14,15,16] that presence of a phase transfer catalyst in the alkylation of secondary amines with various alkyl halides led to the formation of carbamates.

Based on the concept of formation of the ionic species 2, we investigated the carbamate synthesis from alcoholic tosylates. The carbonium ion generated from the tosyl esters would undergo nucleophilic attack by 2 leading to the formation of carbamate esters (Scheme 1). Thus, tosyl ester of an alcohol which is easily synthesized[17] by reacting alcohol with *p*-toluene sulphonyl chloride was used as a substrate for the preparation of carbamates. Different alcoholic tosylates were reacted with the aliphatic/aromatic amines in dry DMSO in the presence of CO_2/K_2CO_3 and a phase transfer catalyst,



Scheme 1.

Table 1.

Entry No.	R	R_1	R_2	Time (h)	Yields %
1	*n*-C_3H_7	C_8H_{17}	H	5–6	90.5
2	$(H_3C)_2 \cdot CH \cdot CH_2$	C_8H_{17}	H	5–6	73.16
3	$H_3C(CH_2)_3$	C_4H_9	H	5–6	75.1
4	$H_3C(CH_2)_4$	Cyclohexyl	H	5–6	88.25
5	$H_3C(CH_2)_4$	C_3H_7	H	5–6	72.26
6	$H_3C(CH_2)_6$	3-$MePhCH_2$	H	5–6	90.03
7	$H_3C(CH_2)_8$	C_6H_{13}	H	5–6	82.60
8	$PhCH_2$	C_4H_9	H	5–6	88.65
9	$PhCH_2CH_2$	C_6H_{13}	H	5–6	80.06
10	$PhCH_2$	C_3H_7	C_3H_7	5–6	71.13

tetrabutyl ammonium iodide, to furnish desired carbamate esters in high yields. The order of yield of carbamates formed from amines was found to be as follows: $RNH_2 > R_2NH > Ar\text{-}NH_2$. In the case of aromatic amines, use of benzyl triethyl ammonium hydroxide (Triton B) as phase transfer catalyst and dry HMPA as a solvent gave better results. The yields of various carbamates prepared by using different amines and alcoholic tosylates is given in the Table 1.

TYPICAL METHOD OF PREPARATION

***n*-Butyl *n*-octylcarbamate (1):** A mixture of anhydrous K_2CO_3 (5 gm), dry DMSO (30 mL), *n*-octylamine (0.72 mL, 4 mmole), was taken in a 50 mL two neck flask. The temperature of the reaction was maintained at 90–100°C and purified CO_2 gas was bubbled through it. Reaction was continued for 1 h, tetrabutylammonium iodide (0.20 gm, 5 mmole) was added to it. The reaction was further continued for 1/2 h, *n*-butyltosyl ester (0.5 gm, 2.19 mmole) was added to it and reaction continued for another 3–4 h. The completion of the reaction was checked by TLC. Reaction mixture was poured in to distilled water (50 mL) and extracted with ethylacetate thrice. The organic layer was dried over anhydrous Na_2SO_4 and concentrated to get pure oily compound (Yield 0.43 gm, 90.52%, oil) IR = 1787 cm^{-1} (O-CO-NH). ^1H NMR ($CDCl_3$) $\delta = 0.77$–0.87 (t, 6H, CH_3), 0.89–0.99 (m, 4H, CH_2), 1.02–1.21 (m, 4H, CH_2), 1.25–1.34 (m, 4H, CH_2), 1.35–1.39 (m, 2H, CH_2), 1.52–1.54 (m, 2H, CH_2), 3.87–3.92 (t, 2H, CH_2), 4.02–4.06 (t, 2H, CH_2O), 4.67–4.71 (bs, H, NH).

Isoamyl *n*-Octylcarbamate (2): IR (Neat) = 1702 cm^{-1} (-O-CO-NH). ^{1}H NMR ($CDCl_3$) δ = 0.67–0.75 (d, 6H, CH_3), 0.85–0.93 (t, 3H, CH_3), 0.95–1.34 (m, 12H, CH_2), 1.35–1.37 (m, H, CH), 1.7–1.9 (m, 2H, CH_2), 4.02–4.04 (t, 2H, CH_2), 4.73–4.75 (bs, H, NH). (Yield 0.36 g, oil).

***n*-Pentyl *n*-butylcarbamate (3):** IR (Neat) = 1789 cm^{-1} (O-CO-NH). ^{1}H NMR ($CDCl_3$) δ = 0.87–0.95 (t, 6H, CH_3), 1.02–1.66 (m, 12H, CH_2), 4.05–4.21 (t, 2H, OCH_2), 4.65–4.73 (bs, H, NH), (Yield, 0.29 g, oil).

***n*-Hexyl cyclohexylcarbamate (4):** IR (KBr) = 1698 cm^{-1} (O-CO-NH), ^{1}H NMR ($CDCl_3$) δ = 0.85–0.91 (t, 3H, CH_3), 0.95–1.71 (m, 6H, CH_2), 4.02–4.06 (t, 2H, CH_2-O), 4.75–4.78 (bs, H, NH), 1.99–2.10 (m, 10H, cyclohexyl-CH_2), 1.91–2.1 (m, CH of cyclohexyl ring) (Yield 0.43 g, m.p. 139–140°C).

***n*-Hexyl *n*-propylcarbamate (5):** IR (Neat) = 1693 cm^{-1} (O-CO-NH), ^{1}H NMR ($CDCl_3$) δ = 0.85–0.93 (m, 3H, CH_3), 1.22–1.66 (m, 12H, CH_2), 2.3–2.7 (s, 2H, CH_2), 3.7–3.7 (s, 3H, OCH_3), 4.73–4.77 (bs, H, NH), 7.12–7.77 (m, 4H, Ar-H) (Yield, 0.26 g, oil).

***n*-Octyl *m*-methoxybenzylcarbamate (6):** IR (KBr) = 1705 cm^{-1} (O-CO-NH) ^{1}H NMR ($CDCl_3$) δ = 0.87–0.93 (t, 6H, CH_3), 1.02–1.77 (m, 10H, CH_2), 3.22–3.55 (m, 2H, $\underline{CH_2}$-NH), 4.05–4.12 (t, 2H, CH_2) (Yield 0.45 g, m.p. 137°C).

***n*-Decyl *n*-hexylcarbamate (7):** IR (Neat): 1693 cm^{-1}.^{1}H NMR ($CDCl_3$) δ = 0.89–0.93 (m, 12H, CH_2), 1.55–1.67 (m, 8H, CH_2), 2.96–2.99 (t, 2H, CH_2), 4.10–4.32 (t, 2H, CH_2-O), (Yield 0.38 g, oil).

2-Phenylethyl *n*-butylcarbamate (8):[18] IR(neat): 1692 cm^{-1} (O-CO-NH). ^{1}H NMR ($CDCl_3$) δ = 0.87–0.94 (3H, m, CH_3), 1.25–1.35 (2H, m, CH_2), 1.38–1.44 (2H, m, CH_2), 2.13–2.20 (2H, m, $\underline{CH_2}$NH), 2.3–2.7 (2H, m, $\underline{CH_2}$Ar), 3.5–3.8 (2H, t, $\underline{CH_2}$O), 7.12–7.77 (5H, m, $\underline{Ar}$-H) (Yield 0.37 g, oil).

3-Phenylpropyl *n*-hexylcarbamate (9): IR (Neat) = 1697 cm^{-1} (O-CO-NH). ^{1}H NMR ($CDCl_3$) δ = 0.92–0.97 (t, 3H, CH_3), 1.29–1.32 (m, 10H, CH_2), 2.93–2.85 (t, 2H, $\underline{CH_2}$-N), 2.87–2.95 (t, 2H, $\underline{CH_2}$-Ar), 4.22–4.32 (t, 2H, CH_2), 7.12–7.77 (m, 5H, Ar-H) (Yield 0.38 g, oil).

2-Phenylethyl di-isopropylcarbamate (10): IR (Neat) = 1695 cm^{-1} (-O-CO-NH). ^{1}H NMR ($CDCl_3$) δ = 0.89–0.94 (t, 6H, CH_3), 1.23–1.44 (m, 8H, CH_2), 2.83–2.86 (t, 4H, CH_2), 2.87–2.95 (t, 2H, $\underline{CH_2}$-Ar), 4.21–4.32 (t, 2H, CH_2-O), 7.13–7.77 (m, 5H, Ar-H) (Yield, 0.38 g, oil).

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