

A Convenient and General Synthesis of Alkylcarbamates from Tertiary Isocyanates and Alcohols

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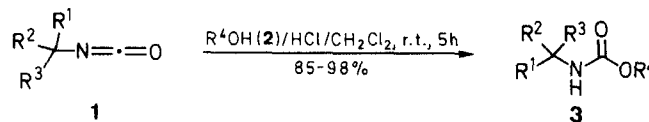
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Reaction of primary, secondary and tertiary alkyl isocyanates with benzyl alcohol, *tert*-butyl alcohol or 1-adamantanol in the presence of 5% hydrogen chloride provides a mild and convenient method for alkyl alkylcarbamate synthesis.

Alkyl isocyanates react slowly at room temperature with secondary and tertiary alcohols and, under thermal conditions, often give low yields of expected carbamates and variable amounts of elimination products.^{1,2} Therefore, catalysis of alcohol/isocyanate reactions is a topic which has received a great deal of interest³ resulting in the use of several effective catalysts including organolead⁴ and organotin⁵ compounds, lithium alkoxide,² carboxylic acids,⁶ tertiary amines⁷ and light.⁸ Recently, Duggan et al.⁹ recommended the activation of alkyl isocyanates with copper(I) chloride in the presence of one equivalent of primary, secondary or tertiary alcohols in dimethylformamide at room temperature. Moderate to good results were obtained with 1-adamantanol whereas with *tert*-butyl alcohol, it was necessary to use five equivalents of alcohol to ensure good yields.

We report here a very simple high yield method for the formation of alkyl alkylcarbamates **3** via hydrogen chloride activation of alkyl isocyanates **1** in the presence of alcohols according to the Scheme.

In a typical procedure, the alcohol (1.5 equiv) was added to a mixture of the isocyanate (1 equiv) and HCl (0.05 equiv) in dichloromethane at room temperature. After 5 hours, the reaction was complete leading to carbamates **3** which were isolated in excellent yields (Table).



1-3	R ¹	R ²	R ³	R ⁴
a	Et	H	H	Bn
b	Et	H	H	<i>t</i> -Bu
c	Et	H	H	1-adamantyl
d	Me	Me	H	Bn
e	Me	Me	H	<i>t</i> -Bu
f	Me	Me	H	1-adamantyl
g	Me	Me	Me	Bn
h	Me	Me	Me	<i>t</i> -Bu
i	Me	Me	Me	1-adamantyl
k	Ph	Me	H	<i>t</i> -Bu

In the absence of catalyst, the reaction was observed to be sluggish as it is demonstrated by the following observations. The reaction of benzyl alcohol and propyl isocyanate proceeded only to about 20% completion at room temperature in two days, but was complete after 23 hours in refluxing benzene. With *tert*-butyl alcohol and 1-adamantanol, no reaction was observed after 48 hours at ambient temperature. In refluxing benzene, the isocyanate was completely consumed after 70 and 88 hours, respectively.

The hydrogen chloride catalyzed addition¹⁰ of alcohols to isocyanates proceeds quite efficiently at room tempera-

Table. Alkylcarbamates **3** Prepared

Product	Yield ^a (%)	mp (°C) ^b [bp (°C)/mbar]	Molecular Formula ^c	IR (Nujol or film) ν _{NH} , ν _{C=O} , (cm ⁻¹)	¹ H-NMR (CDCl ₃ /TMS) δ, J (Hz)
3a	92	34 [74/0.001]	C ₁₁ H ₁₅ NO ₂	3330, 1705	0.87 (t, 3H, J = 7.2), 1.47 (sext, 2H, J = 7.2), 3.12 (q, 2H, J = 6.6), 5.0 (br s, 1H), 5.10 (s, 2H), 7.0-7.30 (m, 5H)
3b	94	[40/0.001]	C ₈ H ₁₇ NO ₂	3340, 1690	0.87 (t, 3H, J = 7.2), 1.40 (s, 9H), 1.47 (sext, 2H, J = 7.2), 3.03 (q, 2H, J = 6.6), 4.6 (br s, 1H)
3c	86 ^d	68	C ₁₄ H ₂₃ NO ₂	3340, 1680	0.93 (t, 3H, J = 7.2), 1.50 (sext, 2H, J = 7.2), 1.6-1.8 (m, 6H), 2.0-2.3 (m, 9H), 3.08 (q, 2H, J = 6.6), 4.55 (br s, 1H)
3d	98	57 [60/0.001]	C ₁₁ H ₁₅ NO ₂	3330, 1690	1.10 (d, 6H, J = 6.5), 3.80 (oct, 1H, J = 6.5), 4.85 (br s, 1H), 5.05 (s, 2H), 7.1-7.4 (m, 5H)
3e	96	74 [42/0.001]	C ₈ H ₁₇ NO ₂	3340, 1700	1.15 (d, 6H, J = 6.5), 1.47 (s, 9H), 3.75 (oct, 1H, J = 6.5), 4.5 (br s, 1H)
3f	89 ^d	100	C ₁₄ H ₂₃ NO ₂	3320, 1670	1.15 (d, 6H, J = 6.5), 1.5-1.8 (m, 6H), 2.0-2.3 (m, 9H), 3.75 (oct, 1H, J = 6.5), 4.37 (br s, 1H)
3g	90	[64/0.001]	C ₁₂ H ₁₇ NO ₂	3340, 1710	1.33 (s, 9H), 4.7 (br s, 1H), 5.05 (s, 2H), 7.1-7.4 (m, 5H)
3h	85	50 [34/0.001]	C ₉ H ₁₉ NO ₂	3300, 1700	1.30 (s, 9H), 1.45 (s, 9H), 1.45 (s, 9H), 4.5 (br s, 1H)
3i	96 ^d	120	C ₁₅ H ₂₅ NO ₂	3350, 1675	1.33 (s, 9H), 1.5-1.8 (m, 6H), 2.0-2.2 (m, 9H), 4.5 (br s, 1H)
3j	96	88 [58/0.001]	C ₁₃ H ₁₉ NO ₂	3380, 1675	1.42 (s, 9H), 1.45 (d, 3H, J = 6.9), 5.1-4.5 (m, 2H), 7.1-7.4 (m, 5H)

^a Yield of isolated pure product based on **1**.

^b Uncorrected.

^c Satisfactory microanalyses obtained: C ± 0.40, H ± 0.26, N ± 0.32.

^d Purified by column chromatography (eluent hexane/Et₂O, 80 : 20: **3c** R_f 0.44; **3i** R_f 0.46).

