Formation of Cyclic Urethanes from Amino Alcohols and Carbon Dioxide Using Phosphorus(III) Reagents and Halogenoalkanes

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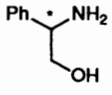
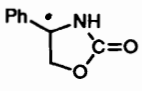
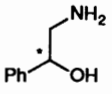
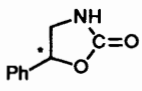
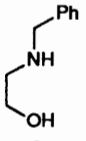
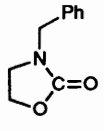
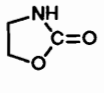
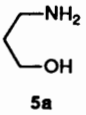
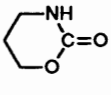
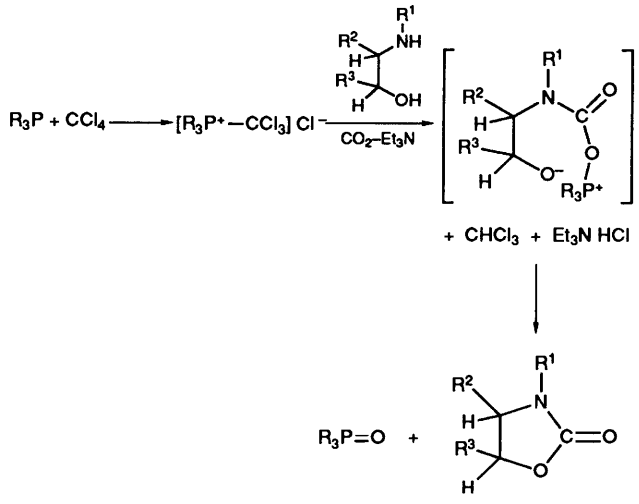
Cyclic urethanes are obtained in good yields under mild conditions from amino alcohols and carbon dioxide using phosphorus(III) reagents [Ph_3P, $(PhO)_3P$, *etc.*] and halogenoalkanes (CCl_4 and CCl_3CCl_3).

The reaction of β-amino alcohols with carbon dioxide to form 2-oxazolidone derivatives is an attractive process for the utilization of carbon dioxide into such useful chemical materials as anticonvulsants,[1] antibacterials,[2] auxiliaries,[3] *etc.*[4,5] The process has been successfully examined using tetraphenylpyrophosphate,[6] triphenylstibine,[7] and a redox reaction between phosphines and disulfides.[8–10] Appel and Kleinstück, on the other hand, reported that aziridines are obtained in a high yield from *N*-substituted β-amino alcohols, triphenylphosphine (TPP), CCl_4 and Et_3N.[11] This led us to presume that the addition of carbon dioxide to their reaction system should provide 2-oxazolidone derivatives according to Scheme 1. Here, we describe a successful study on the efficient formation of cyclic urethanes from carbon dioxide and amino alcohols. The structures of the amino alcohols used here **1a–5a** are shown in Table 1. Equimolar amounts of amino alcohol, TPP and Et_3N were dissolved in MeCN (5.0 cm^3). Under carbon dioxide at atmospheric pressure, the reaction was initiated by the addition of an equimolar amount of CCl_4, and was continued with stirring at room temperature. The reaction products were analysed by HPLC (ODS column; MeCN–H_2O = 70:30 v/v). At the same time, the products from **1a–3a** were isolated by thin layer chromatography on silica gel (hexane–EtOAc = 67:33 v/v) and those from **4a** and **5a** were isolated by column chromatography on silica gel ($CHCl_3$–EtOH = 85:15 v/v). Isolated products were purified by recrystallization and identified by IR, ^1H NMR (200 MHz, $CDCl_3$) and mass spectral analyses as well as melting point (m.p.) measurements. The

Table 1 Yields and characterization of cyclic urethanes[a]

Amino alcohol	Product	Yield[b] (%)	m.p.[d] (°C)	δ_H (Assignment)	ν/cm^{-1}
 *R*-**1a**	 **1b**	91	132–133	4.19 (t, 1 H, *J* 7.6, -CHPh), 4.74 (t, 1 H, *J* 8.6, $-CH_BO$), 4.96 (t, 1 H, *J* 7.8, $-CH_AO$), 5.73 (br s, 1 H, NH), 7.45–7.26 (m, 5-H, Ph)	3262 (NH) 1751 (C=O)
 Racemic **2a**	 **2b**	67	90–92 (88–90)	3.55 (t, 1 H, *J* 8.2, $-CH_BN$), 3.99 (t, 1 H, *J* 8.6, $-CH_AN$), 5.63 (t, 1 H, *J* 8.1, -CHPh), 6.38 (br s, 1 H, NH) 7.39 (s, 5 H, Ph)	3288 (NH) 1745 (C=O)
 **3a**	 **3b**	93	80–81 (78.3–79.2)	3.43 (t, 2 H, *J* 8.0, $-CH_2O$), 4.31 (t, 2 H, *J* 8.0, $-CH_2N$), 4.44 (s, 2 H, $-CH_2Ph$), 7.34–7.26 (m, 5 H, Ph)	1735 (C=O)
 **4a**	 **4b**	51[c]	90–91 (90–91)	3.65 (t, 2 H, *J* 8.0, $-CH_2O$), 4.47 (t, 2 H, *J* 8.0, $-CH_2N$), 5.86 (br, s, 1 H, NH)	3263 (NH) 1733 (C=O)
 **5a**	 **5b**	33	83–84 (79–80)	1.98 (m, 2 H, $-CH_2-$), 3.37 (m, 2 H, $-CH_2N$), 4.30 (t, 2 H, *J* 5.2, $-CH_2O$), 7.00 (br s, 1 H, NH)	3264 (NH) 1702 (C=O)

[a] [Amino alcohol] = [Ph_3P] = [Et_3N] = [CCl_4] = 0.12 mol dm^{-3} in MeCN, Reaction time; 20 h at room temperature. [b] HPLC yield. [c] Isolated yield (HPLC yield could not be obtained because of overlapping of peaks). [d] Uncorrected. Figures in parentheses denote literature values. Literature values of **2b**, **3b**, **4b** and **5b** are cited from refs. 1, 13, 14 and 6, respectively.



Scheme 1

spectral data and m.p., as well as yields, of the cyclic urethanes after 20 h are summarized in Table 1. The IR bands at 3260–3290 cm^{-1} (NH stretching) except for **3b** and at 1700–1750 cm^{-1} (C=O stretching) clearly supported the existence of cyclic urethane bonds. NMR signals at 5.7–7.0 ppm (NH proton) other than for **3b** also substantiated the urethane structure, and all other signals observed were compatible with the predicted structures. Furthermore, m.p. values agreed well with the literature values.[6,13,14] For compound **1b**, the structure was also supported by mass spectrometry.

The reaction proceeded smoothly and the final yield of 4-phenyl-2-oxazolidone **1b** reached more than 90%. It was further found that the yield of **1b** was almost proportional to the amount of TPP or CCl_4 employed and that urethane formation was hardly observed when TPP and CCl_4 were replaced with dichlorotriphenylphosphorane (Ph_3PCl_2). Two reaction mechanisms, A and B, are known to be involved in a three-component system composed of TPP, CCl_4 and a proton-active nucleophile.[12] In A, the active intermediate is $[Ph_3P–CCl_3]^+$ Cl^-, while in B it is Ph_3PCl_2. The above-mentioned results may suggest that path A, as shown in Scheme 1, is the predominant process under the present reaction conditions.

Although the cyclic urethanes were obtained in relatively good yields for **1a–5a**, the yields were low for 4-aminobutan-1-ol, 5-aminopentan-1-ol and 6-aminohexan-1-ol. For these larger amino alcohols, linear urea derivatives, $HO(CH_2)_n$-$NHCONH(CH_2)_nOH$ (n = 4, 5, 6), were primarily formed from two amino alcohols and one carbon dioxide instead of cyclic urethanes. The linear urea compound was also formed to some extent even in the case of 3-aminopropan-1-ol.

Interestingly, CCl_3CCl_3 was also applicable as an alternative organohalogen compound in the present reaction system; in fact, **3b** was obtained in 33% yield in a TPP–CCl_3CCl_3 system. Moreover, other phosphorus(III) compounds, Bu_3P, $(PhO)_3P$ and $(MeO)_3P$, showed activity, as well as TPP.

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