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Novel Synthesis of Carbamic Ester from Carbon Dioxide, Amine, and Ortho Ester

Shigeru Ishii, Hidenobu Nakayama, Yasuhiko Yoshida,* and Tadataka Yamashita
Department of Applied Chemistry, Faculty of Engineering, Toyo University, Kujirai, Kawagoe, Saitama 350
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Carbon dioxide reacted with aliphatic amines and ortho esters to form carbamic esters in good yields. The influence of different ortho esters on the carbamate synthetic reaction is described. In the case of orthocarbonates, carbamic esters were obtained in high yields. The reaction of carbon dioxide, amines, and ortho esters may involve a competitive reaction between the esterification of carbamic acid produced by a reaction of carbon dioxide with amine, and the alkylation of amine.

In recent years, great efforts have been made to find alternative raw materials for organic syntheses, instead of using diminishing fossil fuel. Carbon dioxide is hoped to be made available as a potential carbon source for future use since it is an almost inexhaustible resource. However, it has a great disadvantage due to its inertness in chemical reactions.

A large number of the fixation reactions of carbon dioxide has so far been studied. Especially, recent interest in the fixation of carbon dioxide has been leading to a starting material for the direct synthetic reactions of carbamic esters.[1-9] The usual synthetic methods for carbamic esters[10] are the reaction of alcohol with isocyanate or carbamoyl chloride, and the reaction of amine with chloroformate. However, a new process for preparing carbamic esters without these compounds should be developed, since these reagents are very toxic. Carbamic esters have not been obtained by a direct esterification of carbamic acid, since carbamic acid has been known only as a transient intermediate in the reaction of isocyanate with water, or the hydrolysis of carbamic ester,[11] and is not isolable.

Carbamic acid can also be obtained by a reaction of carbon dioxide with aliphatic amine (Eq. 1). However, carbon dioxide is not fixed by only the reaction with amine, because of an easy dissociation to carbon dioxide and amine.[12]

$$R_2NH + CO_2 \rightleftarrows R_2NCOOH \quad (1)$$

We reported previously the following reactions using carbamic acid as the reaction intermediate: the reaction of carbon dioxide and amines with epoxides to obtain 2-hydroxyalkyl carbamates in high yields,[3] the reaction with vinyl ethers to form 1-alkoxyalkyl carbamates selectively,[2] and the reaction with alkyl halides to yield the corresponding alkyl carbamates.[5] In the course of our studies concerning the fixation of carbon dioxide, a direct esterification of carbamic acid using ortho esters was found.

In this paper we describe this reaction of carbon dioxide, aliphatic amines, and ortho esters to afford directly carbamic esters.

Results and Discussion

Carbon dioxide reacted with amines and ortho esters to give carbamic esters in good yields, depending on the reactivities of amines and ortho esters, and the reaction conditions.

$$CO_2 + R_2NH + R'C(OR'')_3 \longrightarrow R_2NCOOR'' \quad (2)$$

Figure 1 suggests a dependence of the carbamate

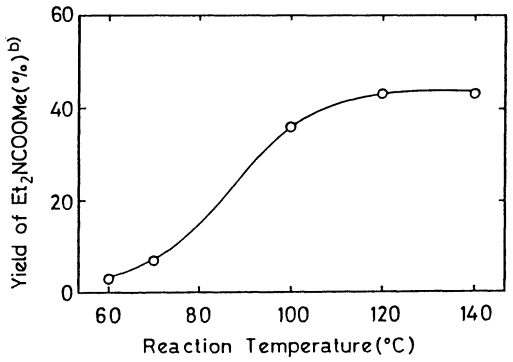

Fig. 1. The dependence of methyl diethylcarbamate yield on the reaction temperature.[a]
a) Et_2NH; 0.2 mol, $HC(OMe)_3$; 0.1 mol, CO_2; 40 atm, for 45 h.
b) Yield based on $HC(OMe)_3$.

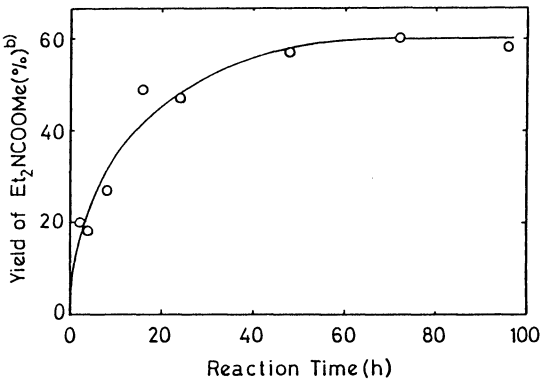

Fig. 2. The dependence of methyl diethylcarbamate yield on the reaction time.[a]
a) Et_2NH; 0.2 mol, $HC(OMe)_3$; 0.1 mol, CO_2; 40 atm, at 120 °C.
b) Yield based on $HC(OMe)_3$.

Table 1. Reaction of CO_2, Amines, and Ortho Esters[a]

No.	Amine	Ortho ester	Yield of products (%)[b]			
			Carbamate	Yield	Amide	Yield
1	Et_2NH	$CH_3C(OMe)_3$	$Et_2NCOOMe$	60	Et_2NCOCH_3	100
2	Et_2NH	$HC(OMe)_3$	$Et_2NCOOMe$	43	Et_2NCHO	88
3	Et_2NH	$HC(OEt)_3$	$Et_2NCOOEt$	83	Et_2NCHO	93
4	Et_2NH	$C(OMe)_4$	$Et_2NCOOMe$	127	—	—
5	Et_2NH	$C(OEt)_4$	$Et_2NCOOEt$	156	—	—
6		$HC(OMe)_3$		27		100
7		$HC(OEt)_3$		76		100
8		$HC(OMe)_3$		23		100
9		$HC(OEt)_3$		70		99
10	n-$PrNH_2$	$HC(OMe)_3$	n-PrNHCOOMe	67	n-PrNHCHO	13
11	PhMeNH	$HC(OEt)_3$	—	0	—	0

a) Amine; 0.2 mol, ortho ester; 0.1 mol, CO_2; 40 atm, 120 °C, 45 h. b) Yield based on ortho ester by GLC.

yield upon the reaction temperature in a reaction of diethylamine, carbon dioxide, and trimethyl orthoformate for 45 h. The yield of methyl diethylcarbamate was 3% at 60 °C, though the yield increased with the reaction temperature. The yield of methyl diethylcarbamate was 43% at 120 °C.

The relation between the reaction time and the yield of methyl diethylcarbamate is shown in Fig. 2. In this case, a longer reaction time enhanced the carbamate yield to 60% after 72 h.

The results for the reaction of carbon dioxide, various amines, and ortho esters at 120 °C for 45 h are summarized in Table 1. While aliphatic amines gave the carbamic esters in good yields (Table 1, Nos. 1—10), aromatic amine, such as *N*-methylaniline, did not give the carbamic ester (Table 1, No. 11). It appeared that aromatic amine does not react with carbon dioxide, since the basicities of aromatic amines are lower than those of aliphatic amines.

A reaction using orthoacetate gave a carbamic ester in higher yield than that of orthoformate (Nos. 1 and 2.). With orthocarbonates, the yields of methyl and ethyl carbamates were 127 and 156%, respectively (Nos. 4 and 5)

The reaction with ethyl ortho esters gave the corresponding carbamic esters in higher yields than those of methyl ortho esters (Nos. 2—9), even in the case of using any of the aliphatic secondary amines. The primary aliphatic amine reacted with methyl ortho ester to give the corresponding carbamic ester in a good yield (No. 10).

In order to obtain more details concerning the reaction mechanism, the by-products of the reaction with amines, carbon dioxide, and ortho esters at 120 °C for 45 h were studied in greater detail. The results are summarized in Table 2. The reaction of diethylamine, carbon dioxide, and triethyl orthoformate gave ethyl diethylcarbamate in 83% yield with *N*,*N*-diethylformamide, ethyl alcohol, and triethylamine as by-products in 93, 186, and 6%, respectively (Table 2, No. 1). From these results, the reaction mechanism is considered to be as follows. At first, carbamic acid, formed from a reaction of carbon dioxide with amine (Eq. 1), reacted with ortho ester to form carbamic ester, alcohol, and

Table 2. Reaction Mixture Obtained by the Reaction of CO_2, Amines, and Ortho Esters[a]

No.	Amine	Ortho ester	Reaction mixture	Yield (%)[b]
1	Et_2NH	$HC(OEt)_3$	Et_2NH	20
			Et_3N	6
			EtOH	186
			$HC(OEt)_3$	5
			$Et_2NCOOEt$	83
			Et_2NCHO	93
2		$HC(OMe)_3$		64
				23
				100
3		$HC(OEt)_3$		30
				70
				99
4	Et_2NH	$C(OEt)_4$	Et_2NH	21
			Et_3N	0
			EtOH	151
			$C(OEt)_4$	13
			$Et_2NCOOEt$	156
			$(EtO)_2CO$	31

a) Amine; 0.2 mol, ortho ester; 0.1 mol, CO_2; 40 atm, 120 °C, 45 h. b) Yield based on ortho ester by GLC.

carboxylic ester corresponding to ortho ester (Eq. 3). Then, the formed carboxylic ester reacted with amine (being present in large excess into the reaction system) to give the corresponding amide and alcohol (Eq. 4). The alkylation of amine by ortho ester also occurred to form tertiary amine (Eq. 5).

$$R_2NCOOH + R'C(OR'')_3 \longrightarrow R_2NCOOR'' + R''OH + R'COOR'' \quad (3)$$

$$R'COOR'' + R_2NH \longrightarrow R_2NCOR' + R''OH \quad (4)$$

$$R_2NH + R'C(OR'')_3 \longrightarrow R_2NR'' + R''OH + R'COOR'' \quad (5)$$

Using methyl orthoformate, the alkylation of morpholine was preferred to the esterification of carbamic acid to give *N*-methylmorpholine in good yield (No. 2). The reaction with ethyl orthoformate gave the carbamic ester in higher yield (No. 3).

When tetraethyl orthocarbonate was used in the synthetic reaction of the carbamic ester, ethyl diethylcarbamate was formed in a yield over 100%, based on the amount of ortho ester. The reaction of carbamic ester with tetraethyl orthocarbonate is considered to give ethyl diethylcarbamate, diethyl carbonate and ethyl alcohol in equimolar amounts (Eq. 6). Diethyl carbonate easily reacted with the amine to form carbamic ester (Eq. 7),[13-15] which corresponded to the amide obtained by reactions with orthoformate or orthoacetate.

$$R_2NCOOH + C(OR')_4 \longrightarrow R_2NCOOR' + (R'O)_2CO + R'OH \quad (6)$$

$$(R'O)_2CO + R_2NH \longrightarrow R_2NCOOR' + R'OH \quad (7)$$

The reaction of amines, carbon dioxide, and ortho esters is considered to involve competitive reactions between the esterification of carbamic acid and the alkylation of amine,[16,17] depending on the reactivities of the amines and ortho esters.

In conclusion, aliphatic amines react with carbon dioxide and ortho esters to give carbamic esters in good yields, though aromatic amines give no products at all. The reactions of carbon dioxide and amines with ethyl ortho esters give the carbamic esters selectively in high yields.

Experimental

Material. Commercially available amines and ortho esters were purified by employing the usual procedures and stored under a nitrogen atmosphere. Commercially high-purity carbon dioxide gas was introduced into an autoclave directly from a gas cylinder without further purification.

Measurements. IR spectra were recorded on Hitachi EPG-G3 and 260-50 equipment. NMR spectra on a Hitachi 24B spectrometer operating at 60 MHz and JEOL FX90Q at 90 MHz, using hexamethyldisiloxane (HMDS) as an internal standard. The GC-MS spectra were recorded on a Shimadzu QP1000 GC-MS spectrometer. Gas liquid chromatography (GLC) analyses were performed on a Shimadzu GC-4C apparatus with a thermal conductor, using a 3 mm×5 m column packed with Silicon OV-17 with helium as the carrier gas.

Syntheses of Carbamic Esters. Ethyl Diethylcarbamate: The typical reaction of amines and carbon dioxide with ortho esters is noted as follows. The mixture of diethylamine (0.2 mol; 20.7 cm^3) and triethyl orthoformate (0.1 mol; 16.6 cm^3) was added into a 100 cm^3 stainless autoclave, and carbon dioxide gas was introduced directly from a gas cylinder until the pressure reached 40 atm (4.05×10^6 Pa). After the autoclave was allowed to stand in an oil bath controlled at 120 °C for 45 h, an excess of carbon dioxide gas was released. The reaction mixture was subjected to fractional distillation under reduced pressure in order to isolate the product, ethyl diethylcarbamate (bp 60.8—61.2 °C/13 mmHg, (1 mmHg≈133.322 Pa) 11.0 g, 76%).

Preparations of other carbamic esters were carried out by a similar manner.

Identification of the Carbamic Ester. Methyl Diethylcarbamate: Bp 155—156 °C (lit,[18] bp 154—155 °C); IR (neat) 1695 cm^{-1} (C=O); ^1H NMR ($CDCl_3$) δ=0.99 (6H, t, $(C\underline{H}_3CH_2)_2N$), 2.88 (4H, q, $(CH_3C\underline{H}_2)_2N$), 3.21 (3H, s, CH_3O).

Ethyl Diethylcarbamate: Bp 60.8—61.2 °C/13 mmHg (lit,[19]; Bp 62—63 °C/14 mmHg); IR (neat) 1700 cm^{-1} ((C=O), ^1H NMR ($CDCl_3$) δ=1.1 (9H, t, CH_3), 3.24 (4H, q, $(CH_3C\underline{H}_2)_2N$), 4.12 (2H, q, $OC\underline{H}_2CH_3$).

***N*-Methoxycarbonylpiperidine:** Bp 101.0—101.5 °C/30 mmHg (lit,[20] bp 100 °C/30 mmHg); IR (neat) 1700 cm^{-1} (C=O); ^1H NMR ($CDCl_3$) δ=1.4 (6H, m, methylenes of piperidine ring), 3.2 (4H, m, CH_2N), 3.46 (3H, s, CH_3O).

***N*-Ethoxycarbonylpiperidine:** Bp 57.7—58.0 °C/1.5 mmHg (lit,[20] bp 55—56 °C/0.9 mmHg); IR (neat) 1705 cm^{-1} (C=O); ^1H NMR ($CDCl_3$) δ=0.97 (3H, t, $C\underline{H}_3CH_2O$), 1.3 (6H, m, methylene of piperidine ring), 3.2 (4H, m, CH_2N), 3.75 (2H, q, $CH_3C\underline{H}_2O$).

Methyl Propylcarbamate: Bp 79.0—80.0 °C/21 mmHg (lit,[22] bp 76 °C/20 mmHg); IR (neat) 1710 cm^{-1} (C=O); ^1H NMR ($CDCl_3$) δ=0.82 (3H, t, $C\underline{H}_3CH_2CH_2N$), 1.45 (2H, m, $CH_3C\underline{H}_2CH_2N$), 3.08 (2H, q, $CH_2C\underline{H}_2N$), 3.48 (3H, s, CH_3O), 5.1 (1H, s, NH).

***N*-Methoxycarbonylmorpholine:** Bp 59.7 °C/1.5 mmHg; IR (neat) 1700 cm^{-1} (C=O); ^1H NMR ($CDCl_3$) δ=3.3 (8H, m, methylene of morpholine ring), 3.57 (3H, s, CH_3O); Found: C, 49.42, H, 7.87; N, 9.46%. Calcd for $C_6H_{11}NO_3$: C, 49.46; H, 7.64; N, 9.64%.

***N*-Ethoxycarbonylmorpholine:** Bp 72.6—72.8 °C/2.3 mmHg. IR (neat) 1705 cm^{-1} (C=O); ^1H NMR ($CDCl_3$) δ= 1.13 (3H, t, $C\underline{H}_3CH_2O$), 3.4 (8H, m, methylene of morpholine ring), 4.01 (2H, q, $CH_3C\underline{H}_2O$); Found: C, 52.68; H, 8.36; N, 8.76%. Calcd for $C_7H_{13}NO_3$; C, 52.82; H, 8.23; N, 8.80%.

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