

## A New Synthesis of Carbamic Esters from Carbon Dioxide, Epoxides, and Amines

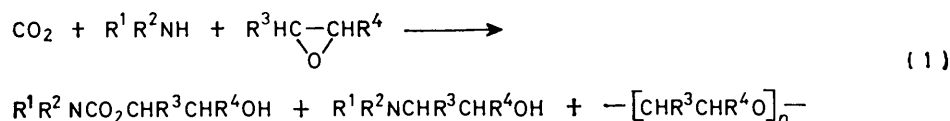
By Yasuhiko Yoshida and Shohei Inoue,\* Department of Synthetic Chemistry, Faculty of Engineering, The University of Tokyo, Bunkyo-ku, Hongo, Tokyo 113

Carbamic esters may be prepared directly by the reaction of carbon dioxide, epoxides, and primary or secondary aliphatic amines. For example, the monocarbamic ester of the 1,2-diol derived from epoxycyclohexane was obtained in good yield when epoxycyclohexane was reacted with amine in an atmosphere of carbon dioxide. The reaction between an epoxide and a carbamic acid or its ammonium salt, formed from carbon dioxide and amine, is proposed as a reasonable mechanism for the formation of the carbamic ester.

CARBON dioxide is well known to react rapidly with amines to form carbamic acids.<sup>1</sup> In this respect, an amine can be considered as a good reagent for the fixation of carbon dioxide. However, synthetic reactions involving carbon dioxide and amines are very limited, except for the industrial process of urea synthesis, because the formation of carbamic acid is reversible, though very rapid, and the fixation of carbon dioxide may not be accomplished by this reaction alone. Further reaction of carbamic acid or the ammonium salt usually requires either vigorous conditions (high temperature and high pressure) as in the industrial synthesis of urea, or a strong dehydrating agent such as diphenyl phosphite, as in the formation of urea under mild conditions.<sup>2</sup> The formation of a formamide from carbon dioxide, an amine, and hydrogen with a transition-metal catalyst is a different class of reaction, *i.e.* the reduction of carbon

amate), amino-alcohol, and/or an oligomer of the epoxide, depending upon the nature of amine and epoxide, and reaction conditions.

As shown in Table 1, hydroxycarbamate was obtained selectively in good yield by the reaction of carbon dioxide, epoxycyclohexane and diethylamine (Et<sub>2</sub>NH) or propylamine (PrNH<sub>2</sub>) (runs 2 and 3). In the case of dimethylamine (Me<sub>2</sub>NH), however, the reaction was accompanied by the formation of a considerable amount of amino-alcohol (run 1). Using epoxypropane instead of epoxycyclohexane, the main product was amino-alcohol, and the yield of hydroxycarbamate was low (runs 4—6). The reaction of epoxyethane, carbon dioxide, and amine gave a large amount of epoxyethane oligomer and the yield of hydroxycarbamate was low (runs 7—9). In the reaction of carbon dioxide and an epoxide with an amine of low basicity [*e.g.* diphenyl-



dioxide to formic acid (salt), followed by the reaction with amine.<sup>3</sup>

In the course of our studies on the reaction of carbon dioxide and epoxides with organometallic catalyst systems,<sup>4</sup> we have found that the reaction of tetrakis-(dimethylamido)titanium(IV), carbon dioxide, and an epoxide gives the monocarbamic ester of the 1,2-diol corresponding to the epoxide in a quantitative yield.<sup>5</sup> In the course of further studies, we have found recently a novel and simple fixation of carbon dioxide with amine and epoxide to form the monocarbamic ester of the 1,2-diol corresponding to the epoxide.<sup>6</sup> In this reaction, the high reactivity of epoxide is considered to be of importance for the fixation of carbamic acid formed reversibly from carbon dioxide and amine. In this paper we describe further details of the reaction including the mechanistic aspects.

### RESULTS AND DISCUSSION

*The reaction of Carbon Dioxide, Amine, and Epoxide.*—Carbon dioxide reacted with amine and epoxide to give the monocarbamic ester of a 1,2-diol (hydroxycarb-

amate) hydroxycarbamate and other products were not obtained at all (runs 10—13).

In the reaction of carbon dioxide, diethylamine, and epoxycyclohexane, the yield of hydroxycarbamate

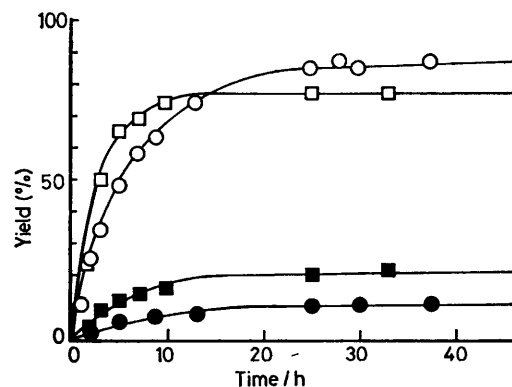


FIGURE 1 Reaction of carbon dioxide, diethylamine, epoxy-cyclohexane; 80 °C, ○, carbamate, ●, amino-alcohol; 100 °C, □, carbamate, ■, amino-alcohol

TABLE 1  
Reaction between CO<sub>2</sub>, amine, and epoxide <sup>a</sup>

Run	Epoxide <sup>b</sup>	Amine	Products <sup>c</sup> (%)		
			Carbamate	Amino-alcohol	Others
1 <sup>d</sup>	cho	Me <sub>2</sub> NH	42	40	
2	cho	Et <sub>2</sub> NH	62	5	
3	cho	PrNH <sub>2</sub>	54	5	
4	po	Me <sub>2</sub> NH	16	2	
5	po	Et <sub>2</sub> NH	24	42	<i>e</i>
6	po	PrNH <sub>2</sub>	20	21 <sup>f</sup>	<i>g</i>
7	eo	Me <sub>2</sub> NH	6	15	<i>g</i>
8	eo	Et <sub>2</sub> NH	21	15	<i>g</i>
9	eo	PrNH <sub>2</sub>	15	6	<i>g</i>
10	cho	Ph <sub>2</sub> NH	0	0	
11 <sup>h</sup>	cho	PhNH <sub>2</sub>	0		
12	po	Ph <sub>2</sub> NH	0	0	
13	eo	Ph <sub>2</sub> NH	0	0	

<sup>a</sup> Conditions; 80 °C, 22 h, CO<sub>2</sub> at 50 atm; amine and epoxide, 0.2 mol, respectively, except for run 1. <sup>b</sup> Epoxycyclohexane (cyclohexene oxide; cho), epoxypropane (propylene oxide; po) and epoxyethane (ethylene oxide; eo). <sup>c</sup> Yields are based on epoxide. <sup>d</sup> 80 °C, 22 h, CO<sub>2</sub> at 50 atm; amine and epoxide, 0.3 and 0.38 mol, respectively. <sup>e</sup> The existence of a trace amount of cyclic carbonate was detected from the i.r. spectrum. <sup>f</sup> PrN(CH<sub>2</sub>CHMeOH)<sub>2</sub>. <sup>g</sup> Epoxide oligomer was obtained. <sup>h</sup> 70 h.

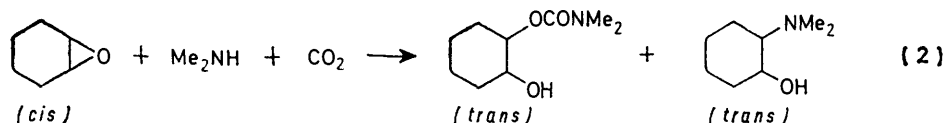
increased with temperature up to 80–90 °C.<sup>6</sup> In view of the fact that the yield of amino-alcohol also increased with temperature, 80 °C is the optimum temperature

hexane and diethylamine reacted within *ca.* 20 h to give hydroxycarbamate (90% yield) and amino-alcohol (10% yield).

**Mechanism.**—In order to obtain information about the mechanism of the formation of hydroxycarbamate, the stereochemistry of the ring opening of the epoxide was studied. Since the reaction of *cis*-epoxycyclohexane, dimethylamine, and carbon dioxide gave *trans*-2-hydroxycyclohexyl dimethylcarbamate and *trans*-2-dimethylaminocyclohexanol, it appears that the configuration of the carbon atom at which ring cleavage takes place is inverted during the ring-opening of the epoxide.

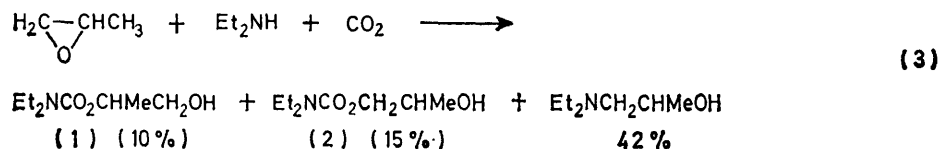
In the reaction of an amine with carbon dioxide and a monosubstituted epoxyethane, there are two reaction pathways because there are two kinds of carbon-oxygen bond which may be cleaved. In fact, epoxypropane, diethylamine, and carbon dioxide yielded 10% of 1-methyl-2-hydroxyethyl diethylcarbamate (1), 15% of 2-hydroxypropyl diethylcarbamate (2) and 42% of 1-diethylaminopropan-2-ol.

Product (1) arose from methine-oxygen bond scission, whilst product (2) resulted from methylene-oxygen bond scission. It is known that monosubstituted epoxides, which give entirely the product resulting from ring cleavage at the methylene-oxygen linkage under basic



for the synthesis of hydroxycarbamate under the other reaction conditions examined.

Figure 1 shows the relation between the reaction time



and the yields of hydroxycarbamate and amino-alcohol in the reaction of carbon dioxide, diethylamine, and epoxycyclohexane. At *e.g.* 80 °C all the epoxycyclo-

conditions, produce a mixture of products *via* scission of the methylene- and methine-oxygen bonds under acidic conditions.<sup>7</sup> Therefore, the present results indi-

cate that the formation of hydroxycarbamate does not proceed by simple nucleophilic attack of carbamate anion on the epoxide, but is aided by the addition of a

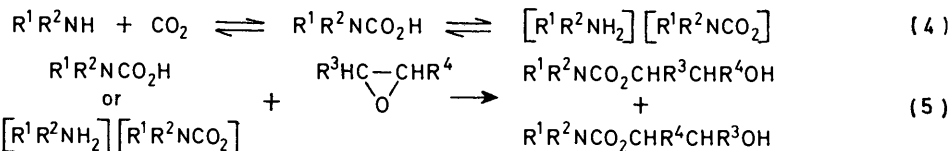
TABLE 2  
New hydroxycarbamates

Run	Hydroxycarbamate <sup>a</sup>				M.p. (°C)	B.p. (°C)	Formula	Analysis (%)		
	R <sup>1</sup>	R <sup>2</sup>	R <sup>3</sup>	R <sup>4</sup>				Found	(Calc.)	Nitrogen
1	Me	Me	[CH <sub>2</sub> ] <sub>4</sub>		52–53 <sup>b</sup>	<i>ca.</i> 90/1 mmHg	C <sub>9</sub> H <sub>17</sub> NO <sub>3</sub>	57.75 (57.73)	9.3 (9.15)	7.5 (7.48)
2	Et	Et	[CH <sub>2</sub> ] <sub>4</sub>		34–35 <sup>b</sup>	<i>ca.</i> 105/1 mmHg	C <sub>11</sub> H <sub>21</sub> NO <sub>3</sub>	61.25 (61.37)	10.55 (9.83)	6.50 (6.51)
3	Pr	H	[CH <sub>2</sub> ] <sub>4</sub>		84–85 <sup>c</sup>		C <sub>10</sub> H <sub>19</sub> NO <sub>3</sub>	59.6 (59.68)	9.85 (9.51)	6.95 (6.96)
4	Et	Et	Me H	H Me		<i>ca.</i> 83/1 mmHg	C <sub>8</sub> H <sub>17</sub> NO <sub>3</sub>	54.2 (54.83)	9.55 (9.78)	7.85 (8.00)
5	Pr	H	Me H	H Me		113–116/2 mmHg	C <sub>7</sub> H <sub>15</sub> NO <sub>3</sub>	53.05 (52.15)	9.7 (9.38)	8.4 (8.69)

<sup>a</sup> R<sup>1</sup>R<sup>2</sup>NCO<sub>2</sub>CHR<sup>3</sup>CHR<sup>4</sup>OH. <sup>b</sup> Recrystallized from light petroleum. <sup>c</sup> Recrystallized from acetone-light petroleum (1 : 8 v/v).

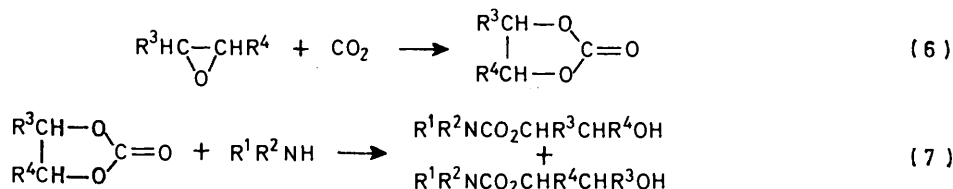
proton from carbamic acid or its ammonium salt, formed by the reaction of carbon dioxide and amine.

An alternative mechanism for the formation of carbamic ester would be the reaction between amine and



cyclic carbonate, formed from carbon dioxide and epoxide.

It is known that ethylene carbonate is obtained from the reaction of epoxyethane and carbon dioxide using as the catalyst a quaternary ammonium or Group 2A salt at 200 °C,<sup>8</sup> or tertiary amine-alcohol system at 100 °C. The reaction of epoxypropane and carbon dioxide is



known to give propylene carbonate in the presence of hydrazine or a hydrazinium salt at 200 °C. However, the reaction between carbon dioxide and epoxide (epoxyethane, epoxypropane, or epoxy cyclohexane) at 80 °C in the presence of triethylamine did not lead to the formation of cyclic carbonate.\* Thus cyclic carbonate is not considered to be the intermediate giving hydroxycarbamate in the reaction. Furthermore, the distribution of the isomeric products in the reaction between amine and cyclic carbonate, if it were formed, would be different from that in the reaction between carbamic acid or its ammonium salt and epoxide.

When diethylamine was interacted with propylene carbonate at 60 °C for 22 h, the isomeric hydroxycarbamates, (1) and (2), were obtained in 66% and 34% yield, respectively.

It was reported also that, in the reaction of propylene carbonate with butylamine at 60 °C, a mixture of the isomeric hydroxycarbamates rich in the product corresponding to (1) was obtained.<sup>9</sup>

As the ratio of isomers [(1) : (2) = 2 : 1] formed by the reaction between propylene carbonate and diethylamine [equation (8)] differed from that [(1) : (2) = 2 : 3] obtained by the reaction of carbon dioxide, diethylamine, and epoxypropane [equation (3)], it is concluded that the reaction of carbon dioxide, amine, and epoxide does not proceed through a cyclic carbonate as the intermediate.

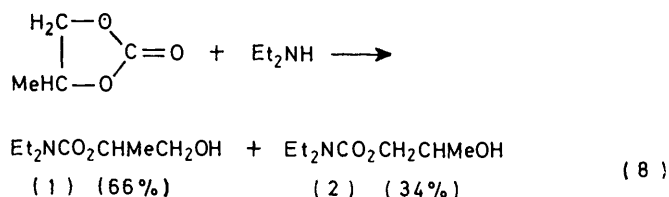
\* The existence of a trace amount of propylene carbonate was detected (from the i.r. spectrum) in the reaction of carbon dioxide, diethylamine, and epoxypropane (Table 1, run 5). However, it is considered that this trace of propylene carbonate was formed by the thermal decomposition of hydroxycarbamate during the distillation for the product separation.

The formation as by-products of amino-alcohol and the epoxide oligomer is considered to proceed by nucleophilic attack of an amine on an epoxide, and of the amino-alcohol on further molecules of epoxide. In

accordance with this, only the amino-alcohol resulting from methylene-oxygen cleavage was obtained in the reaction involving epoxypropane [equation (3)]. The higher reactivity of terminal over internal epoxide towards amine or alcohol,<sup>10</sup> as well as the higher reactivity of epoxyethane over epoxypropane towards alcohol,<sup>11</sup> is the cause of the remarkable formation of

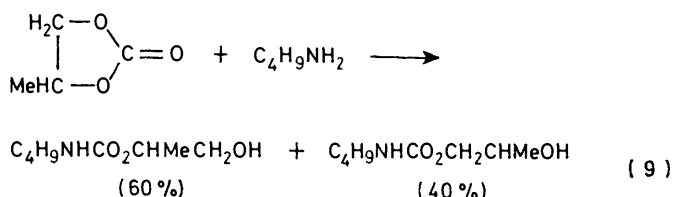
amino-alcohol in the case of epoxypropane, and the formation of oligomer in the case of epoxyethane.

In conclusion, the reaction of carbon dioxide, amine, and epoxide is considered to proceed through carbamic



acid or its ammonium salt, formed from carbon dioxide and amine.

Toda and his co-workers recently reported, independently of our work, the reaction of primary amines,



carbon dioxide, and styrene oxide or epichlorohydrin in methanol to form carbamic ester, and suggested a mechanism involving the reaction between the ammonium salt of carbamic acid and epoxide.<sup>12</sup>

The studies based on our proposed mechanism have been successfully extended to the development of a novel synthesis of a carbamic ester from carbon dioxide,

amine, and vinyl ether,<sup>13</sup> where the reaction is considered to involve the carbamic acid rather than its ammonium salt.

#### EXPERIMENTAL

**Materials.**—Commercially available epoxides and amines were purified employing the usual procedures and stored in a nitrogen atmosphere. Epoxyethane was kindly supplied by Nippon Shokubai Kagaku Kogyo Co. Commercial high-purity carbon dioxide gas was introduced into an autoclave directly from a gas cylinder without further purification.

**Measurements.**—I.r. spectra were recorded on a Hitachi EPI-G3 apparatus, and n.m.r. spectra on a JEOL-100 spectrometer operating at 100 MHz, using hexamethyl-disiloxane (HMDS) as internal standard. Gas-liquid chromatography (g.l.c.) was performed on a Shimadzu GC-4B apparatus with a thermal-conductivity detector.

**Identification of the Products.**—N.m.r. and i.r. spectra and the g.l.c.  $R_t$  of amino-alcohols were identical with those of authentic samples.\* Hydroxycarbamates obtained from the reaction of carbon dioxide, epoxyethane, and dimethylamine, diethylamine, or propylamine were confirmed to be 2-hydroxyethyl dimethylcarbamate, diethylcarbamate, or propylcarbamate, respectively, by comparison with authentic samples prepared by the reaction of ethylene carbonate with dimethylamine, diethylamine, or propylamine.<sup>18,19</sup> The other hydroxycarbamates prepared are summarized in Table 2.

**Preparation of Hydroxycarbamate.**—(a) *Reaction of carbon dioxide, dimethylamine, and epoxy cyclohexane.* A mixture of 1,2-epoxycyclohexane (30 ml; 0.3 mol) and dimethylamine (25 ml; 0.38 mol) was placed in a 200-ml autoclave fitted with a magnetic stirrer under a pressure of carbon dioxide (50 atm) † at 80 °C for 22 h. The reaction mixture was subjected to fractional distillation under reduced pressure to isolate the products, *trans*-2-dimethylaminocyclohexanol (17.5 g, 40%), b.p. 82 °C at 9 mmHg (lit.,<sup>15</sup> 88 °C at 14 mmHg), and *trans*-2-hydroxycyclohexyl dimethylcarbamate, b.p. ca. 90 °C at 1 mmHg (23.5 g, 42%).

This hydroxycarbamate was confirmed as the *trans*-isomer by comparison with an authentic sample prepared by a reaction of *trans*-cyclohexane-1,2-diol with dimethylcarbamoyl chloride in the presence of pyridine.

Preparations of other hydroxycarbamates were carried out by a similar procedure.

(b) *Relation between reaction time and yields.* A mixture of epoxy cyclohexane (50.5 ml; 0.5 mol), diethylamine (52 ml; 0.5 mol), and hexadecane (5.80 g) as an

\*  $R^1R^2N(CH_2)_2OH$  ( $R^1 = R^2 = Me$ ;  $R^1 = R^2 = Et$ ;  $R^1 = Pr$ ,  $R^2 = H$ ) and  $R^1R^2NCH_2CHMeOH$  ( $R^1 = R^2 = Me$ ;  $R^1 = R^2 = Et$ ) were commercially available.  $PrN(CH_2CHMeOH)_2$ <sup>14</sup> and  $R^1R^2NCHR^3CHR^4OH$  ( $R^1 = R^2 = Me$ ;  $R^3 = R^4 = Et$ ;  $R^1 = Pr$ ,  $R^2 = H$ ;  $R^3, R^4 = [CH_2]_2$ )<sup>15-17</sup> were synthesized.

† 1 atm. = 101 325 Pa.

‡  $Et_2NCO_2CHMeCH_2Cl$  was prepared by the reaction between diethylcarbamoyl chloride and 1-chloropropan-2-ol (obtained by the reduction of chloroacetone with lithium aluminium hydride); n.m.r. of  $Et_2NCO_2CHMeCH_2Cl$ ;  $\delta$  1.16 (6 H, t,  $NCH_2CH_3$ ), 1.36 (3 H, d,  $CHCH_3$ ), 3.30 (4 H, q,  $NCH_2CH_2$ ), 3.66 (2 H, d,  $CH_2Cl$ ), and 5.04 (1 H, m,  $OCHMeCH_2Cl$ ).

$Et_2NCO_2CH_2CHMeCl$  was obtained by the reaction of diethylcarbamoyl chloride and 2-chloropropan-1-ol (prepared by the reaction of  $\alpha$ -chloropropionic acid and lithium aluminium hydride<sup>20</sup>); n.m.r. of  $Et_2NCO_2CH_2CHMeCl$ ;  $\delta$  1.16 (6 H, t,  $NCH_2CH_3$ ), 1.52 (3 H, d,  $CHClCH_3$ ), 3.30 (4 H, q,  $NCH_2CH_2$ ) and 4.20 (3 H, m,  $OCH_2CHMeCl$ ).

internal standard was placed in a 500-ml autoclave fitted with a magnetic stirrer under a pressure of carbon dioxide (50 atm) at 80 °C, and an aliquot was removed every 30 min. By use of gas chromatography, the products (hydroxycarbamate and amino-alcohol) were identified and the yields were determined (Figure 1).

(c) *Reaction of propylene carbonate with diethylamine.* After a mixture of propylene carbonate (21.9 g; 0.3 mol) and diethylamine (30.6 g; 0.3 mol) had been heated at 60 °C for 22 h, distillation of the reaction mixture under reduced pressure gave 45 g (86%) of the monocarbamic ester of propane-1,2-diol [a mixture of (1) and (2), b.p. ca. 100 °C at 5 mmHg].

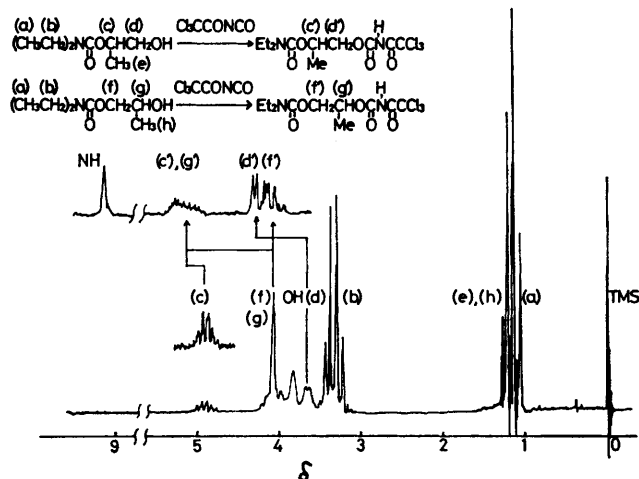


FIGURE 2

(d) *Determination of the ratio of the isomeric hydroxycarbamates (1) and (2).* N.m.r. spectra of a mixture of (1) and (2) (obtained from the reaction of carbon dioxide, diethylamine, and epoxypropane) were measured in  $CDCl_3$  solution (*c* 150 mg per 0.5 ml), using HMDS as internal standard (Figure 2). The chemical shifts could be assigned from spectra of 2-chloro-1-methylethyl diethylcarbamate ( $Et_2NCO_2CHMeCH_2Cl$ ) and 2-chloropropyl diethylcarbamate ( $Et_2NCO_2CH_2CHMeCl$ ).<sup>‡</sup> These assignments were confirmed by use of trichloroacetyl isocyanate.<sup>§</sup> The isomer ratio (1) : (2) of the hydroxycarbamate was calculated from Figure 2.

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§ It is reported that when trichloroacetyl isocyanate reacted with primary or secondary hydroxy-groups, shifts of ca. 0.5–0.9 p.p.m. occurred for  $\alpha$ -hydrogens to primary hydroxy-groups compared with shifts of ca. 1.0–1.5 p.p.m. for  $\alpha$ -hydrogens to secondary hydroxy groups (V. W. Goodlett, *Analyt. Chem.*, 1965, **37**, 431). In the present case of the mixture of isomeric hydroxycarbamates (1) and (2), shifts of ca. 0.8 p.p.m. occurred for the peak (d) at  $\delta$  3.60. For the peak (f + g) at  $\delta$  4.10, a part shifted by ca. 1.1 p.p.m. [g; multiplet overlapping (c)], whilst the residual part shifted by ca. 0.1 p.p.m. (f; doublet)

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