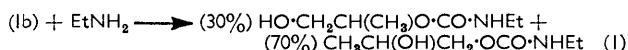


## Organic Carbonates. Part XIV.<sup>1</sup> Polar and Steric Effects of Substituents influencing the Modes of Ring-opening of Highly-branched Ethylene and Trimethylene Carbonates by Various Nucleophiles: A Nuclear Magnetic Resonance Study

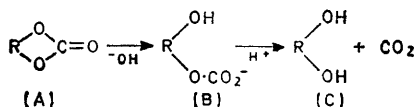
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The appearance of intermediates and the formation of isomeric products resulting from interactions of ten highly branched ethylene (Ib—k) and seven trimethylene carbonates (IIa—g) with nucleophiles such as hydroxide, n-butylamine, ethylenediamine, glycine, and imidazole, were monitored and quantitatively estimated by the n.m.r. technique. The nucleophilic ring-opening of the 1-monosubstituted (Ib, If—k, Iic—g) and 1,1-disubstituted series (Id, Iie—f) gave rise to isomeric hydroxyalkyl carbonates and/or hydroxyalkyl carbamates, the ratio of which varies with substituents and pH. In the 1-monosubstituted carbonates the preferred mode of O—CO bond cleavage is that which leads to the more acidic alcoholic species, whereas in the 1,1-disubstituted series the mode of ring-opening which leads to the more basic alcohol species is the preferred one. The product ratio in the 1-monosubstituted series is linearly dependent on the  $\sigma^*$  value of the substituent on the ring, and also yields a linear Brønsted correlation. The two modes of ring-opening in 1-monosubstituted carbonates is governed by the difference in the electronic effects of the leaving oxygens. In the case of 1,1-disubstituted carbonates the polar effect of the leaving group appears to be obliterated by steric factors (conformational and torsional effects) which become mode-determining for the breakdown of the tetrahedral intermediate.

ORGANIC carbonates are known to undergo nucleophilic attack by amines,<sup>2a-c</sup> alcohols,<sup>3</sup> and thiols.<sup>4</sup> With unsymmetrically substituted carbonates two modes of ring-opening can occur. Thus, in the reaction of propylene carbonate (Ib) with ethylamine the isomeric hydroxycarbamates were obtained, as in equation (1).<sup>5</sup>



In Parts XII<sup>6</sup> and XIII<sup>1</sup> we showed that basic hydrolysis of cyclic carbonates is a multi-stage process. The first step is a nucleophilic attack by hydroxide ion on the carbonyl carbon (A) to form an open chain hydroxyalkyl carbonate anion (B). It is then followed by extrusion of carbon dioxide from (B) to provide the corresponding diol (C).



Since the rate of formation and decomposition of (B)

<sup>1</sup> Part XIII, J. Katzhendler, L. A. Poles, and S. Sarel, *Israel J. Chem.*, 1972, **10**, 111.

<sup>2</sup> (a) M. M. Baizer, J. R. Clark, and J. Swidinsky, *J. Org. Chem.*, 1957, **22**, 1595; (b) B. R. Delaly, A. Sekera, P. Chabrier, and P. Piganiol, *Bull. Soc. chim. France*, 1951, 392; (c) C. R. M. Acheson, *Accounts Chem. Res.*, 1971, **4**, 177.

<sup>3</sup> E. I. Stout, W. M. Doane, and K. E. Kolb, *J. Org. Chem.*, 1971, **36**, 3126.

<sup>4</sup> H. Pauly, K. Schubel, and K. Lockermann, *Annalen*, 1911, **383**, 288.

<sup>5</sup> M. M. Baizer, J. R. Clark, and E. Smith, *J. Org. Chem.*, 1957, **22**, 1706.

<sup>6</sup> J. Katzhendler, L. A. Poles, and S. Sarel, *J. Chem. Soc. (B)*, 1971, 1847.

<sup>7</sup> (a) E. S. Hand and W. P. Jencks, *J. Amer. Chem. Soc.*, 1967, **84**, 3505; (b) W. P. Jencks and M. Gilchrist, *ibid.*, 1968, **90**, 2622; (c) G. M. Blackburn and W. P. Jencks, *ibid.*, p. 2638.

<sup>8</sup> (a) R. H. De Wolfe and F. B. Augustine, *J. Org. Chem.*, 1965, **30**, 699; (b) R. H. De Wolfe, *ibid.*, 1971, **36**, 162.

<sup>9</sup> (a) M. Kandel and E. H. Cordes, *J. Org. Chem.*, 1967, **32**, 3061; (b) T. Pletcher, S. Kochler, and E. H. Cordes, *J. Amer. Chem. Soc.*, 1968, **90**, 7072.

can be controlled by varying base concentration and temperature, it should then be possible to detect the appearance of such intermediates in the reaction by n.m.r. spectroscopy. This afforded a deeper insight into assessing factors governing the rates and modes of ring-opening of unsymmetrically substituted carbonates on reaction with amines and hydroxides. The study of the competition between different leaving groups in the same molecule could be of general interest. Such studies have been made of many solvolytic reactions, *e.g.*, of imidates,<sup>7-10</sup> thioimidates,<sup>11</sup> oxazolines,<sup>12,13</sup> thiazolines,<sup>14</sup> and epoxides,<sup>15</sup> in the reduction of acetals,<sup>16</sup> glutarimides and barbiturates,<sup>17</sup> 1,3-disubstituted imidazolium iodide<sup>18</sup> and in the chlorination of propylene sulphite.<sup>19</sup> Cyclic carbonates are a good model for these competitive studies since the complication of different heteroatoms is avoided.

We present here n.m.r. data on the product distribution from nucleophilic attack by the hydroxide ion, n-butylamine, ethylenediamine, glycine, and imidazole

<sup>10</sup> (a) R. K. Chaturvedi and G. L. Schmir, *J. Amer. Chem. Soc.*, 1968, **90**, 4413; (b) G. L. Schmir and B. A. Cunningham, *ibid.*, 1965, **87**, 5692; 1966, **88**, 551; 1967, **89**, 917.

<sup>11</sup> (a) P. K. Chaturvedi, A. E. McMahon, and G. L. Schmir, *J. Amer. Chem. Soc.*, 1967, **89**, 6984; (b) R. K. Chaturvedi and G. L. Schmir, *ibid.*, 1969, **91**, 737.

<sup>12</sup> (a) R. B. Martin and A. Parcell, *J. Amer. Chem. Soc.*, 1961, **83**, 4835; (b) R. B. Martin, R. I. Hedrick, and A. Parcell, *J. Org. Chem.*, 1964, **29**, 3197.

<sup>13</sup> R. Greenhalg, R. M. Heggie, and M. A. Weinberger, *Canad. J. Chem.*, 1963, **41**, 1662.

<sup>14</sup> (a) R. B. Martin and A. Parcell, *J. Amer. Chem. Soc.*, 1961, **83**, 4830; (b) R. E. Barnett and W. P. Jencks, *ibid.*, 1969, **91**, 2358.

<sup>15</sup> (a) J. Biggs, N. B. Chapman, A. F. Finch, and V. Wray, *J. Chem. Soc. (B)*, 1971, 55, 63, 66, 71; (b) R. E. Parker and N. S. Isaacs, *Chem. Rev.*, 1959, **59**, 737.

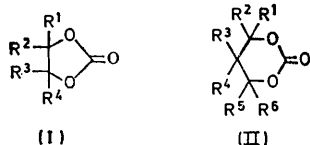
<sup>16</sup> E. L. Eliel, V. G. Badding, and M. N. Rerick, *J. Amer. Chem. Soc.*, 1962, **84**, 2371.

<sup>17</sup> Y. Kondo and B. Witkop, *J. Org. Chem.*, 1968, **33**, 206.

<sup>18</sup> E. F. Godefiori, *J. Org. Chem.*, 1968, **33**, 860.

<sup>19</sup> P. A. Bristow, R. G. Jones, and J. G. Tillett, 'Mechanism of Reaction of Sulfur Compounds,' Interscience, 1968, vol. 2, p. 163.

on unsymmetrically substituted five- (I) and six-membered ring carbonates (II).



## EXPERIMENTAL

The cyclic carbonates were prepared from the respective diols (Eastman Organic Chemicals) by the methods described in Part IV.<sup>20</sup> The following carbonates were prepared by transesterification of the appropriate diols: *methoxymethylethylene carbonate* (Ih), b.p. 105 °C at 0.2 mmHg,  $n_D^{20} = 1.4330$ ,  $\nu_{\max}$  1810  $\text{cm}^{-1}$  (C=O) (Found: C, 45.3; H, 5.9.  $\text{C}_5\text{H}_8\text{O}_4$  requires C, 45.4; H, 6.1%); *phenylethylene carbonate* (If) m.p. 54 °C (from  $\text{CCl}_4$ ) (lit.,<sup>21</sup> 53–55 °C),  $\nu_{\max}$  1785  $\text{cm}^{-1}$  (C=O) (Found: C, 66.2; H, 4.8. Calc. for  $\text{C}_9\text{H}_8\text{O}_3$ : C, 65.9; H, 4.9%); *dimethylamino-methylethylene carbonate* (Ij), b.p. 100 °C at 0.5 mmHg,  $n_D^{20} = 1.4990$ ,  $\nu_{\max}$  1800  $\text{cm}^{-1}$  (C=O) (Found: C, 49.6; H, 7.1; N, 9.8.  $\text{C}_6\text{H}_{11}\text{ON}$  requires C, 49.6; H, 6.9; N, 9.7%); *p-chlorophenoxy-methylethylene carbonate* (Ii), m.p.

TABLE 1

Chemical shifts ( $\delta$ /p.p.m.) for compounds (I)		
(Ia)	$\text{R}^1 = \text{R}^2 = \text{R}^3 = \text{R}^4 = \text{H}$	4.50 (s)
(Ib)	$\text{R}^1 = \text{Me}$	1.49 (d)
	$\text{R}^2 = \text{H}$	4.87 (m)
	$\text{R}^3 = \text{R}^4 = \text{H}$	4.57, 4.04 (dd, dd)
(Ic)	$\text{R}^1 = \text{R}^3 = \text{Me}$	1.35 (m)
	$\text{R}^2 = \text{R}^4 = \text{H}$	4.85 (m)
(Id)	$\text{R}^1 = \text{R}^2 = \text{Me}$	1.37, 1.50 (s, s)
	$\text{R}^3 = \text{Me}$	1.37 (d)
	$\text{R}^4 = \text{H}$	4.42 (q)
(Ie)	$\text{R}^1 = \text{R}^2 = \text{R}^3 = \text{R}^4 = \text{Me}$	1.40 (s)
(If)	$\text{R}^1 = \text{Ph}$	7.37 (s)
	$\text{R}^2 = \text{H}$	5.65 (dd)
	$\text{R}^3 = \text{R}^4 = \text{H}$	4.77, 4.30 (dd, dd)
(Ig)	$\text{R}^1 = \text{ClCH}_2$	3.83, 3.75 (dd, dd)
	$\text{R}^2 = \text{H}$	5.02 (m)
	$\text{R}^3 = \text{R}^4 = \text{H}$	4.60, 4.40 (dd, dd)
(Ih)	$\text{R}^1 = \text{MeOCH}_2$	a: 3.65, 3.65 (dd, dd) b: 3.41 (s)
	$\text{R}^2 = \text{H}$	4.84 (m)
	$\text{R}^3 = \text{R}^4 = \text{H}$	4.51, 4.36 (dd, dd)
(Ii)	$\text{R}^1 = p\text{-ClC}_6\text{H}_4\text{-OCH}_2$	4.19, 4.09 (dd, dd)
	$\text{R}^2 = \text{H}$	4.98 (m)
	$\text{R}^3 = \text{R}^4 = \text{H}$	4.57, 4.47 (dd, dd)
(Ij)	$\text{R}^2 = \text{Me}_2\text{NCH}_2$	a: 2.63 (d) b: 2.31 (s)
	$\text{R}^2 = \text{H}$	4.79 (m)
	$\text{R}^3 = \text{R}^4 = \text{H}$	4.53, 4.22 (dd, dd)
(Ik)	$\text{R}^1 = \text{Me}_3\text{NCH}_2$	a: 3.80 (d) b: 3.30 (s)
	$\text{R}^2 = \text{H}$	5.60 (m)
	$\text{R}^3 = \text{R}^4 = \text{H}$	5.00, 4.40 (d, d)

90 °C (from  $\text{C}_6\text{H}_6$ ),  $\nu_{\max}$  1795  $\text{cm}^{-1}$  (C=O) (Found: C, 52.5; H, 4.5; Cl, 15.1.  $\text{C}_{10}\text{H}_9\text{O}_4\text{Cl}$  requires C, 52.5; H, 3.9; Cl, 15.5%); *chloromethylethylene carbonate* (Ig), prepared by the phosgene method, b.p. 144 °C,  $n_D^{20} = 1.4680$ ,

<sup>20</sup> S. Sarel, L. A. Pohoryles, and R. Ben-Shoshan, *J. Org. Chem.*, 1959, **24**, 1873.

$\nu_{\max}$  1800  $\text{cm}^{-1}$  (C=O) (Found: C, 34.9; H, 4.5; Cl, 15.1.  $\text{C}_4\text{H}_5\text{O}_4\text{Cl}$  requires C, 35.2; H, 3.7; Cl, 15.5%); *2,3-carbonyldioxypropyltrimethylammonium iodide* (Ik). Compound (Ij) was dissolved in benzene. To this solution methyl iodide (0.12 mol) was slowly added, and the precipitate thus obtained was recrystallized from water, m.p. 163 °C,  $\nu_{\max}$  1777  $\text{cm}^{-1}$  (Found: C, 29.2; H, 5.1; N, 5.0; I, 45.0.  $\text{C}_7\text{H}_{14}\text{NO}_3\text{I}$  requires C, 29.5; H, 4.9; N, 4.9; I, 44.3%).

TABLE 2

Chemical shifts ( $\delta$ /p.p.m.) for compounds (II)		
(IIa)	$\text{R}^1 = \text{R}^2 = \text{R}^5 = \text{R}^6 = \text{H}$	4.13 (s)
	$\text{R}^3 = \text{R}^4 = \text{Me}$	1.10 (s)
(IIb)	$\text{R}^1 = \text{R}^2 = \text{R}^5 = \text{R}^6 = \text{H}$	4.10 (s)
	$\text{R}^3 = \text{R}^4 = \text{MeCH}_2$	a: 1.40 (q) b: 0.90 (t)
(IIc)	$\text{R}^1 = \text{Me}$	1.29 (d)
	$\text{R}^2 = \text{H}$	4.35 (q)
	$\text{R}^3 = \text{R}^4 = \text{Me}$	1.07, 0.98 (s, s)
	$\text{R}^5 = \text{R}^6 = \text{H}$	4.07, 3.98 (d, d)
(IId)	$\text{R}^1 = \text{Me}$	1.40 (d)
	$\text{R}^2 = \text{H}$	4.65 (m)
	$\text{R}^3 = \text{R}^4 = \text{H}$	2.08, 1.88 (m, m)
	$\text{R}^5 = \text{R}^6 = \text{H}$	4.46, 4.38 (m, m)
(IIE)	$\text{R}^1 = \text{R}^2 = \text{Me}$	1.48 (s)
	$\text{R}^3 = \text{R}^4 = \text{H}$	2.02 (t)
	$\text{R}^5 = \text{R}^6 = \text{H}$	4.43 (t)
(IIf)	$\text{R}^1 = \text{R}^2 = \text{Me}$	1.45 (s)
	$\text{R}^3 = \text{R}^4 = \text{H}$	2.07, 1.74 (m, m)
	$\text{R}^5 = \text{Me}$	1.39 (d)
	$\text{R}^6 = \text{H}$	4.67 (m)
(IIg)	$\text{R}^1 = \text{CHMe}_2$	a: 2.00 (m) b: 1.08 (d)
	$\text{R}^2 = \text{H}$	3.98 (d)
	$\text{R}^3 = \text{R}^4 = \text{Me}$	1.13, 1.05 (s, s)
	$\text{R}^5 = \text{R}^6 = \text{H}$	4.04, 3.85 (d, d)

*Reaction of Cyclic Carbonate with NaOD.*—The cyclic carbonate (0.001 mol) was mixed with an excess of 1N-NaOD in an n.m.r. tube at  $10 \pm 0.1$  °C and measurements were taken thereafter at 5 min intervals.

*Reaction of Cyclic Carbonates with Neat Amines.*—An excess of the amine (aniline, n-butylamine, or ethylenediamine) was mixed with the appropriate carbonate, and kept at  $60 \pm 0.1$  °C overnight. The excess of the amine was then removed in a rotary evaporator, and the product distribution was determined from the appropriate peaks in the spectrum. In the case of (If), the isomeric ratio was also assessed by means of preparative t.l.c. (silica, 50% cyclohexane-ethyl acetate).

*Reaction of Cyclic Carbonates with Imidazole, n-Butylamine, and Glycine in D<sub>2</sub>O and H<sub>2</sub>O.*—(a) Three solutions of equal amounts of imidazole in D<sub>2</sub>O were titrated with conc. DCl solution to 0.25, 0.5, and 0.75 neutralization. The pD values of the solutions, 7.28, 6.88, and 6.48, respectively, were determined with a glass electrode by using a Radiometer 26 pH meter with corrections made for the D<sup>+</sup> ion.<sup>22</sup> To each three n.m.r. tubes were added equal quantities of the carbonate and 0.6 ml of each of the above imidazole solutions of varying pH. The final concentrations of the substrate and of the imidazole were 0.327 and 2.61M, respectively. The solutions were heated to  $60 \pm 0.1$  °C, and the progress of the reaction was monitored by

<sup>21</sup> I. R. Morris and D. J. Hubbard, *J. Org. Chem.*, 1962, **27**, 1451.

<sup>22</sup> T. H. Fife and T. C. Bruice, *J. Phys. Chem.*, 1961, **65**, 1079.

n.m.r. measurements every 5 min. Measurements were carried out in this manner for carbonates (Ib), (IIa), and (IIf).

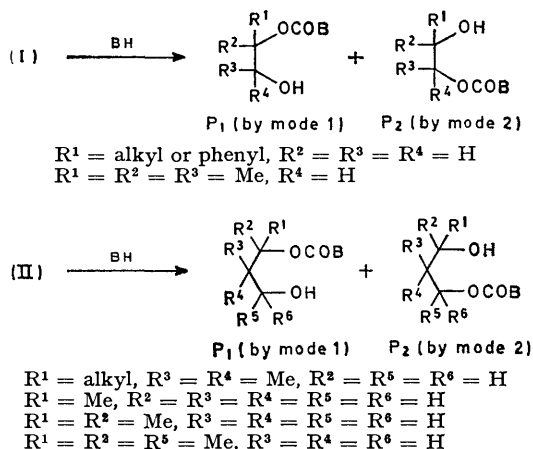
(b) Solutions of pD 9.06, 9.73, and 10.4 were prepared and placed in ampoules. To 1.0 ml of each of these solutions were added equal amounts of the carbonate and of glycine resulting in 0.29M-carbonate and 1.97M-glycine. The ampoules were sealed and placed in a constant temperature bath of  $60 \pm 0.1$  °C for 3 days. In this way the ring-opening of compounds (Ib), (IIa), and (IIf) were analysed by n.m.r. spectroscopy, using TSP as an internal reference. For comparison, solutions of the appropriate diols and glycine were similarly prepared.

(c) Three identical solutions of n-butylamine were titrated with acid to 0.25, 0.50, and 0.75 neutralization resulting in pH 9.42, 9.92, and 10.42, respectively. To 8.0 ml of these amine solutions (placed in test tubes) was added the carbonate (If), (IIa), or (IIf). The final concentrations of the carbonate and the amine were 0.15 and 5.85M, respectively. The tubes were heated to  $60 \pm 0.1$  °C and after a few hours the amine was removed by distillation. The residue was extracted with chloroform and dried ( $\text{MgSO}_4$ ). After removal of solvent the residues were subjected to n.m.r. analysis ( $\text{CDCl}_3$ ).

## RESULTS

Analysis of the product emerging from the aminolysis or the basic hydrolysis of the five- and six-membered ring carbonates (see Table 3) reveals the occurrence of two modes of ring cleavage of types 1 and 2. These modes lead to isomeric mixtures of products  $P_1$  and  $P_2$ , respectively, as depicted in Scheme 1.

For all the hydroxycarbonates and carbamates measured, the peak positions of the hydrogens adjacent to either the carbonate or carbamate group showed shifts up to 30 Hz in comparison to the chemical shifts of the same protons in the cyclic esters, while all the peaks of hydrogens adjacent to the hydroxy-group are diamagnetically shifted in a



SCHEME 1

range 54–96 Hz. These observed chemical shift differences for the two types of protons permit assignment of the relative amounts of the unstable hydroxycarbonate isomers formed as intermediates during the basic hydrolysis of cyclic carbonates. The 3 : 2 ratio for the two modes of ring-opening of (IIc) can easily be deduced from the relative areas of ( $\text{H}^1 + \text{H}^2$ ) and ( $\text{H}^{1'} + \text{H}^{2'}$ ) (Figure 1).

For hydroxycarbonates which result as stable compounds from aminolysis, the chemical shifts could be assigned from spectra of the pure compounds separated by p.l.c. The n.m.r. spectra of the separated open-chain carbamate

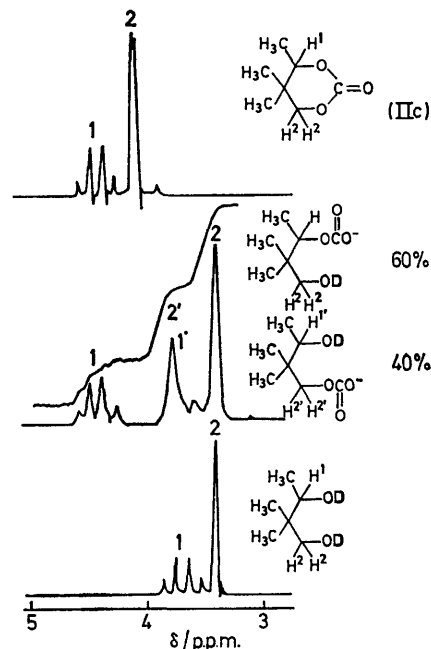


FIGURE 1 N.m.r. spectra of carbonate (IIc), the hydroxycarbonate isomers, and the corresponding diol

isomers and of the reaction mixture are shown in Figure 2. The relative amounts of isomers in the mixture (7 : 3) were calculated from the known chemical shifts of each isomer.

TABLE 3

Isomeric distribution of hydroxy-carbamates, and -carbonates, obtained by nucleophilic attack on unsymmetrical cyclic carbonates

Substrate	Isomer distribution (%)					
	n-Butylamine		Ethylenediamine		Hydroxide	
	Mode 1	Mode 2	Mode 1	Mode 2	Mode 1	Mode 2
(Ib)	60	40	60	40	60	40
(Id)						~100
(If)	30	70	30	70	30	70
(Ig)	20	80				
(Ih)	40	60	40	60		
(Ii)	18	82				
(Ij)					40	60
(Ik)					5	95
(IIc)	60	40	60	40	60	40
(IIId)	60	40	60	40	60	40
(IIe)	27	73			27	73
(IIIf)	20	80	20	80	20	80
(IIg)	85	15			85	15

The isomer distribution formed *via* the two modes of ring-opening for all unsymmetrical cyclic carbonates was calculated and is presented in Table 3.

The product ratio  $P_2/P_1$  for the 1-monosubstituted compounds (Ia), (Ib), (If–k), (IIc), (IIId), and (IIg) is linearly dependent on the  $\sigma^*$  value of the substituent. Equation (2) obtained by means of a least squares program represents such a Hammett-Taft correlation [ $\sigma^*$  values

were taken from ref. 23, except for compound (Ij) whose  $\sigma^*$  value was calculated from ref. 23c].

$$\log P_2/P_1 = 0.7436\sigma^* - 0.175 \quad (r = 0.965) \quad (2)$$

Since the polar effect of the substituent might influence both modes of ring-opening, the  $\rho^*$  value of 0.743 is only a relative criterion of the susceptibility of the ring-opening

Carbamates were not always the only products obtained in the aminolysis of cyclic carbonates. In the presence of glycine a competition between the formation of diol and open-chain carbamate was observed. The extent of either reaction was found to be pH dependent, such that an increase in the pH of the reacting system led to an increase in the relative amount of the carbamates (Table 5).

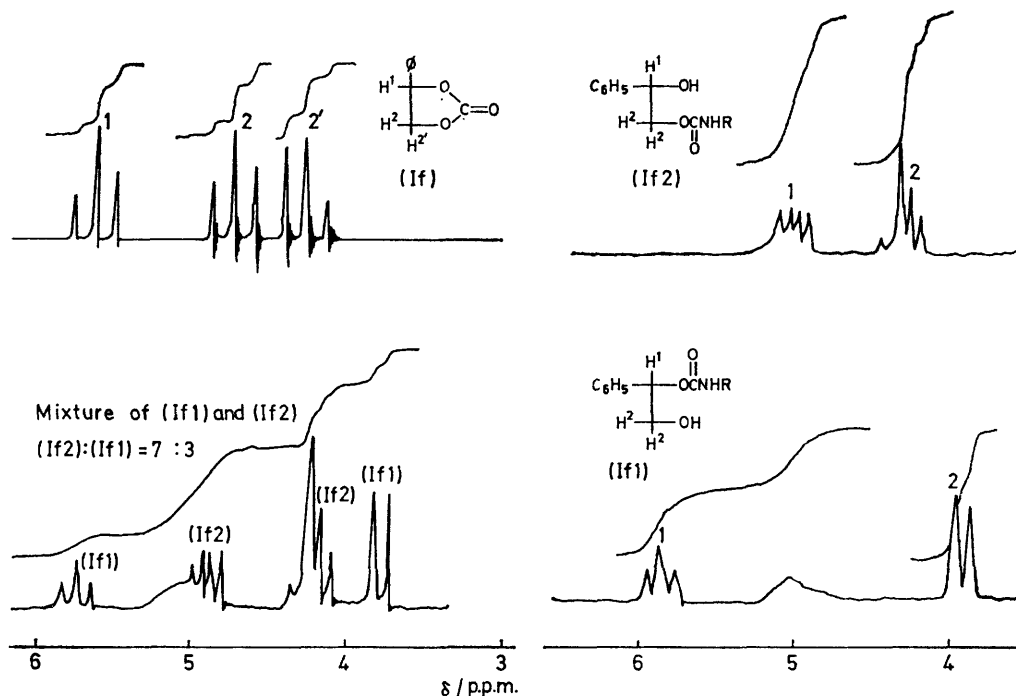


FIGURE 2 N.m.r. spectra of the separated (by t.l.c.) carbamates (If1) and (If2) and their relative ratio in the reaction mixture

stage to substituent inductive effects. To account for the effect of the substituent on one side of the ring, a fall-off factor of 2.8 was assumed for each intervening carbon atom. The corrected value  $\rho^*_{\text{corr.}}$ , 1.15, was deduced from equation (3).

$$\log P_2/P_1 = \sigma^*\rho^* = \sigma^*\rho^*_{\text{corr.}} - \sigma^*\rho^*_{\text{corr.}}/2.8 \quad (3)$$

$$\rho^*_{\text{corr.}} = 1.55 \times 0.743 = 1.15.$$

From the term  $\sigma^*\rho^*_{\text{corr.}}$ , a new product ratio  $(P_2/P_1)_{\text{corr.}}$  can be derived which is devoid of the polar effect component in  $P_1$ . The latter ratio exhibits a linear correlation with the  $pK_a$  value of the leaving group according to equation (4) which was calculated by a least squares method. ( $pK_a$  Values of alcohols were taken from refs. 23a and 24a, b.)

$$\log (P_2/P_1)_{\text{corr.}} = 0.865 pK_a + 13.77 \quad (r = 0.955) \quad (4)$$

The product ratios in Table 3 were obtained from neat reactions or from reactions carried out in  $D_2O$  at high pH. When the pH of the reaction solution was varied, the product distribution was also altered. From the data assembled in Table 4 it can be seen that as the pH of the reacting system decreases, the isomeric ratio approaches a value of unity.

<sup>23</sup> (a) P. Ballinger and F. A. Long, *J. Amer. Chem. Soc.*, 1960, **82**, 795; (b) R. W. Taft in 'Steric Effects in Organic Chemistry,' Chapman and Hall, London, 1956, pp. 595 and 619; (c) E. M. Kosower, 'Physical Organic Chemistry,' Wiley, New York, 1968, p. 49.

Measurements of the reactions between imidazole and cyclic carbonate were performed by the n.m.r. method at  $60 \pm 0.1^\circ C$ . First-order rate constants are given in

TABLE 4

pH Dependence of product ratio ( $P_2/P_1$ ) in the n-butanolysis of cyclic carbonates

	pH 9.42	9.92	10.42
Carbamates derived from			
(If)	1.12	1.38	1.63
(IId)	0.82	0.82	0.64
(IIf)	1.85	3.00	4.00

TABLE 5

Carbamate versus diol formation (%) in the presence of glycine at varying pH

	pH 9.06		9.73		10.40	
Cyclic carbonates	Diol	Carb-amate	Diol	Carb-amate	Diol	Carb-amate
(IIa)	68	32	27	73	24	76
(IIf)	100*	0	96	4	60	40
(Ib)	80	20	60	40	55	45

\* 23% Cyclic carbonate remains unchanged.

<sup>24</sup> (a) A. R. Fersht and W. P. Jencks, *J. Amer. Chem. Soc.*, 1970, **92**, 5442; (b) G. M. Blackburn and L. H. Dodds, *J. Chem. Soc. (B)*, 1971, 826.

Table 6. A plot of the rate constant *versus* the free amine gives a straight line, indicating a first-order dependence on the amine concentration. The second-order rates could be calculated from the plots. The only product obtained in the presence of imidazole was the diol.

TABLE 6

Rate constants of cyclic carbonates in the presence of imidazole in D<sub>2</sub>O,  $T = 60 \pm 0.1^\circ\text{C}$

Cyclic carbonates	pH 7.28			6.88			6.48		
	$10^5k/\text{min}^{-1} \pm 5\%$			$10^5k/\text{min}^{-1} \pm 5\%$			$10^5k/\text{min}^{-1} \pm 5\%$		
(IIa)	3730.0	2380.0	1310.0	3730.0	2380.0	1310.0	3730.0	2380.0	1310.0
(IIb)	18.4	12.1	7.7	18.4	12.1	7.7	18.4	12.1	7.7
(Ib)	284.0	161.0	102.0	284.0	161.0	102.0	284.0	161.0	102.0

## DISCUSSION

Analysis of data presented above (Table 3) reveals that the isomeric distribution  $P_2/P_1$  following the ring cleavage in the 1-monosubstituted series (Ib), (If—k), (IIc), (Id), and (IIg) and in the disubstituted series (Id), (IIe), (IIf) is governed by different chemical factors. For the 1-monosubstituted carbonates the preferred mode of O—CO bond cleavage is that which gives rise to the more acidic alcohol. The opposite is the case for the 1,1-disubstituted series where the mode of preferred ring-opening is that which leads to formation of the more basic alcohol. For the case in which the diol is branched at both 1- and 2-carbon sites, the product distribution following the two modes of ring-opening can be estimated quantitatively. For example, the product ratio  $P_1/P_2$  for (IIc) is 1.5, but is 0.37 in the case of (IIe). As a consequence, the approximate value for (IIc) can be calculated as  $0.37/1.5 = 0.24$ , which is in accord with the experimental value.

**1-Monosubstituted Carbonates.**—In the 1-monosubstituted carbonates the observed isomeric distribution can be attributed to the differences in the basicity of the two endocyclic oxygens; *i.e.*, as oxygen becomes a better leaving group, O—CO bond cleavage at this oxygen is preferred. Such a phenomenon is well known in acyl transfer reactions where the kinetic and the microscopic mechanisms exhibits dependence on the basicity of either the attacking nucleophile or the leaving group.<sup>7b, 24a</sup>

Since the hydroxy-group is known to participate in hydrolysis<sup>10b, 25</sup> by an intramolecular reaction, the possibility of thermodynamic equilibrium between the products was checked experimentally and ruled out. No equilibrium mixture was detected for the isolated isomers represented in Figure 2 when treated in solution under the usual conditions.

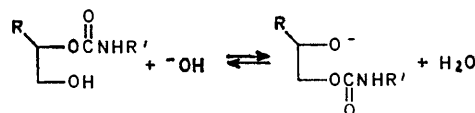
Other evidence also suggests that thermodynamic control in the product distribution can be excluded for

<sup>25</sup> T. C. Bruice and F. H. Marquardt, *J. Amer. Chem. Soc.*, 1962, **84**, 365.

<sup>26</sup> W. P. Jencks, B. Schaffhausen, K. Tornheim, and H. White, *J. Amer. Chem. Soc.*, 1971, **93**, 3917.

<sup>27</sup> (a) J. Gerstein and W. P. Jencks, *J. Amer. Chem. Soc.*, 1964, **86**, 4655; (b) S. L. Johnson, *Adv. Phys. Org. Chem.*, 1967, **5**, 237.

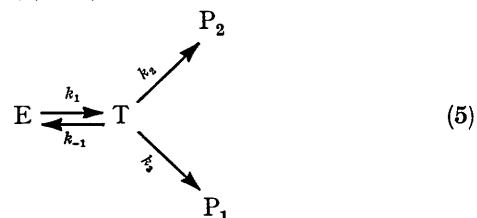
the following reasons. (a) Although the five- and the six-membered ring carbonates are different in their steric demand toward nucleophilic attack, their product distribution is almost identical for similar leaving group basicity. (b) The *gem*-1,1-dialkyl effect is expected to increase the tendency of the more substituted alkoxy-group to undergo nucleophilic attack, and as a result mode 1 of ring-opening would be preferred, which again is not the case. (c) In the hydrolyses of cyclic carbonates by alkali hydroxide the  $pK_a$  values of the attacking nucleophile and of the leaving group of 1-monosubstituted carbonates are in the same order of magnitude ( $pK_a$  of hydroxide and of ethanol are 15.75 and 15.9, respectively). An equilibrium mixture of open chain carbonate and cyclic carbonate would be expected. This was not detected experimentally. (d) From acyl transfer equilibrium not involving donation or abstraction of a proton an absolute  $\beta$  value greater than the observed 0.86 is expected. For alkoxy the value is 1.7<sup>26, 27a</sup> and for amine 1.5.<sup>26, 28b</sup> An equilibrium of the type in Scheme 2 might give a  $\beta$  value of 0.86. But an approach to such an equilibrium must be slow.<sup>28b</sup>



SCHEME 2

(e) The intramolecular catalysis of the hydroxy-group in 2-hydroxyphenyl carbonate<sup>29</sup> has been shown not to involve an attack on the carbonyl by an ionised hydroxy-group in the rate-determining step. The reaction was assumed to be general base catalysed with assistance from the phenoxide ion. A similar conclusion was deduced from the deuterium isotope effect  $k_H/k_D = 3$  noted in the study of the decarboxylative hydrolysis of 3-hydroxybutyl carbonate derived from (IIb).

Indeed, the data represented here can be best explained in terms of kinetic control involving the intermediacy of tetrahedral species (T) in the course of nucleophilic ring cleavage of cyclic carbonates, as shown in equations (5)—(7).



$$V(P_2) = [k_1 k_2 / (k_{-1} + k_2 + k_3)] \cdot E \quad (6)$$

$$V(P_1) = [k_1 k_3 / (k_{-1} + k_2 + k_3)] \cdot E \quad (7)$$

$$P_2/P_1 = k_2/k_3$$

<sup>28</sup> (a) A. R. Fersht and Y. Requena, *J. Amer. Chem. Soc.*, 1971, **93**, 3499; (b) *ibid.*, p. 3504.

<sup>29</sup> J. G. Tillett and D. E. Wiggins, *Tetrahedron Letters*, 1971, **911**.

The product ratio  $P_2/P_1$  is kinetically dependent only on the intermediate decomposition rates  $k_2$  and  $k_3$ , and not on its formation rate  $k_1$ . Since a common tetrahedral intermediate is formed for both products, the same product ratio is obtained either if the rate-determining step is a nucleophilic attack or an intermediate breakdown. If the products are formed *via* different transition states,  $k_1$  in equations (6) and (7) would not have the same value, and the product ratio would depend on the attacking nucleophile.

Comparison between polar effects influencing nucleophilic attack in ester solvolysis and product distribution in the cyclic carbonates indicates that the difference in the product distribution of the 1-monoalkyl carbonates is determined by the partition ( $k_2/k_3$ ) of the tetrahedral intermediate. In ester solvolysis nucleophilic attack of hydroxide ion and amine has different  $\rho$  values (for phenyl acetate  $\rho_{OH} = 1.1$ ;  $\rho_N = 2.1-2.9$ <sup>31</sup> compared with  $\rho$  of 1.7—2.1<sup>30</sup> for the dissociation of substituted phenols). In this work no such dependence on the electronic character of the attacking nucleophile was found. The same product distribution is observed for both the open-chain carbonate and carbamate in the strongly basic solution. The same is also true for the  $\beta$  Brönsted value where alkaline hydrolyses and nucleophilic aminolysis of esters have  $\beta$  values of 0.32<sup>32</sup> and 0.7—0.8,<sup>7b</sup> respectively. On similar grounds an  $S_N2$  reaction can be excluded.

Although the partition of the intermediate is very fast, it might still be sensitive to electronic substituent effects and proton transfer.<sup>33</sup> A large  $\beta$  value of -0.86 and a  $\rho^*_{corr}$  value of 1.15 (compared to  $\rho^*$  of 1.42 for the dissociation of alcohol,<sup>29a</sup> where the development of charge is complete) indicate that during the formation of the open-chain carbonate or carbamate considerable charge is either formed or lost.

From  $pK_a$  values of hydrated ketones given by Bell<sup>34</sup> a  $pK_a$  value of 10 was estimated for the exocyclic oxygen in the tetrahedral carbonate intermediate. Since the covalently bonded oxy-ion in the tetrahedral intermediate displaces the endocyclic oxygen in product formation, the charge development should resemble a 'late' transition state of bimolecular reaction with a Brönsted  $\beta$  value of 0.7—0.9 as observed in the aminolysis of esters.

A linear correlation between the product ratio  $(P_1/P_2)_{corr}$  of carbonates and the relative rates of *p*-nitrophenolate ion attack on esters for an identical leaving group is given in equation (8) where  $k_0$  was chosen for ethyl acetate. The rate determining step in these reactions is the breakdown of the tetrahedral intermediate.<sup>24a</sup>

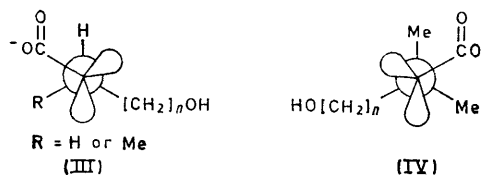
$$\log (P_2/P_1)_{corr} = 0.742 \log k/k_0 - 0.092 \quad (r = 0.973) \quad (8)$$

<sup>30</sup> T. C. Bruice and M. F. Mayahi, *J. Amer. Chem. Soc.*, 1960, **82**, 3067.

<sup>31</sup> T. C. Bruice and S. J. Benkovic, *J. Amer. Chem. Soc.*, 1964, **86**, 418.

<sup>32</sup> J. F. Kirsh and W. P. Jencks, *J. Amer. Chem. Soc.*, 1964, **86**, 837.

**1,1-Disubstituted Carbonates.**—The preference of cleavage at the more basic endocyclic oxygen in strongly basic solution cannot be explained in terms of the differences in protonation of the leaving group, since in a more acidic solution the amount of tertiary alcohol isomer expected should increase. The experimental results (Table 4), however, show a decrease in isomer ratio  $P_2/P_1$  with increasing acidity. It cannot be explained either on the basis of strain derived from the *gem*-dialkyl effect in the ground state of the molecule. In such a case the two modes of ring-opening are accompanied by the same relief of steric strain.



In contrast to the 1-mono-substituted carbonates where the product ratio is assumed to be controlled by the difference in the electronic effects of the two leaving oxygen atoms, the product ratio of the 1,1-disubstituted carbonates may be controlled by a steric factor in the product-like transition state. From the reduction of ketones it is known that eclipsing or dipolar factors play a role in the pathway of the mechanism, and may govern the product isomer ratio.<sup>35</sup> It seems likely that torsional strain can also affect the ring-opening of cyclic carbonate disubstituted on C-1, to yield the conformer with less torsional strain. It can be seen that isomer (III) is of lower energy than (IV). It thus seems likely that the steric effect controlling the formation of (III) may outweigh a value of  $\Delta\Delta F_{25} = 0.2$  kcal mol<sup>-1</sup> which was calculated for the difference in polar energy for the two modes of ring-opening.

It has been shown experimentally that the mode of ring-opening in cyclic carbonates and in cyclic acetals<sup>16</sup> are similar. Although the mechanism of the ring-opening in acetals is different from that in cyclic carbonates, this strong analogy points out that a similar product-like transition state may be obtained in both systems from the breakdown of the tetrahedral intermediate.

**Effect of pH.**—Table 4 reveals that product distribution in the aminolysis of cyclic carbonates is pH-dependent. As the pH of the solution decreases, the product ratio approaches unity. This phenomenon resembles the product distribution obtained in analogous systems such as imidates<sup>9a</sup> and cannot be explained only on the basis of equilibrium between anionic and neutral intermediates. The change in the rate-determining step from amine attack to the breakdown of tetrahedral intermediate also cannot be the reason for

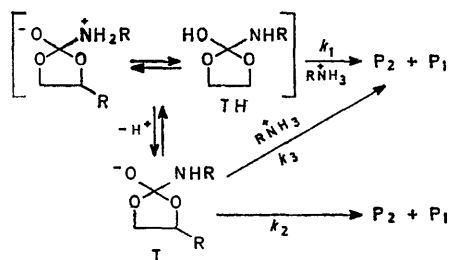
<sup>33</sup> M. L. Bender and R. J. Thomas, *J. Amer. Chem. Soc.*, 1961, **83**, 4189.

<sup>34</sup> R. P. Bell, *Adv. Phys. Org. Chem.*, 1966, **4**, 325.

<sup>35</sup> (a) E. L. Eliel and Y. Senda, *Tetrahedron*, 1970, **26**, 2411; (b) M. Cherest and H. Felkin, *Tetrahedron Letters*, 1968, 2205.

the decreasing product ratio  $P_2/P_1$  with increasing acidity (for ethyl *N*-methylacetimidate, and methoxyethyl *N*-methylacetimidate the  $pK_a$  values of the crossover product ratios are 9.8 and 9.4, respectively). It seems that general acid catalysis is involved in the breakdown step. Such catalysis might occur at the anionic intermediate or the equilibrating intermediate as was suggested by Jencks<sup>7c</sup> and Bruice.<sup>36</sup> It may also occur *via* a one-encounter mechanism in which the catalyst abstracts a proton from the neutral intermediate and donates it to the leaving group. Since in reactions involving acid catalysis the susceptibility to electronic effects decreases,<sup>36</sup> this might explain the decrease in the product ratio ( $P_2/P_1$ ) obtained in carbonate with increasing acidity.

The pathway of the formation of products from the tetrahedral intermediates is represented in Scheme 3.



SCHEME 3

*Aniline, Glycine.*—A very weak base such as aniline ( $pK_a = 4.6$ ) cannot displace an alkoxide ion by direct nucleophilic attack, but can *via* a general base catalysis reaction.<sup>37a</sup> This is in accord with our experimental results. No ring-opening of carbonate occurred when heated with aniline (neat) at 60 °C for four days.

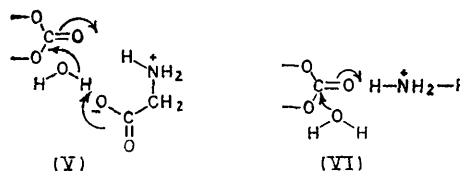
The reaction of the carbonates with glycine yielded, in addition to carbamate, a large amount of diol (see Table 5). It seems that the products are formed during the ring-opening reaction and not as a result of further hydrolysis of the open carbamate to diol and amine,<sup>38</sup> since (a) the ratio of carbamate to diol increases with an increasing basicity of the solution and (b) the rates of basic hydrolysis of (IIb), (Ib), and (IIf) shown in Part XIII<sup>1</sup> are in the order  $k_{OH}$  (IIb) >  $k_{OH}$  (Ib) >  $k_{OH}$  (IIf), and the ratios of carbamate to diol are also in accord with this order, showing (IIb) > (Ib) > (IIf). The large amount of diol formed in the presence of glycine as catalyst even at pH 10.40 indicates a strong competition between nucleophilic attack by hydroxide ion and amine. This was not found in the presence of *n*-butylamine as catalyst. Bruice<sup>36</sup> and Jencks<sup>37b</sup> have shown that in the aminolysis of phenyl acetate *n*-butylamine reacts with the substrate *via* (a) nucleophilic attack ( $k_n$ ), and (b) a general base catalysis assisted by

<sup>36</sup> T. C. Bruice, A. Donzel, R. W. Huffman, and A. R. Butler, *J. Amer. Chem. Soc.*, 1967, **89**, 2106.

<sup>37</sup> (a) W. P. Jencks and J. C. Carriulo, *J. Amer. Chem. Soc.*, 1961, **83**, 1743; (b) *ibid.*, 1960, **82**, 675.

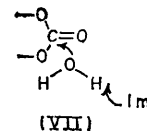
amine ( $k_N$ ) or by hydroxide ion ( $k_{OH}$ ).  $k_{OH}$  was shown to be 160–200 times greater than  $k_N$ . With glycine as catalyst only  $k_n$  and  $k_N$  terms were observed. Since in cyclic carbonates diol is formed *via* the  $k_n(\bar{O}H)$  pathway, the relative amount of diol should increase in the presence of glycine compared to *n*-butylamine as catalyst.

The change in the product ratio of carbamate to diol for (IIa) and (Ib) is greater in the region of pH between the  $pK_a$  value of glycine and 0.5 unit below it, than in the region between the  $pK_a$  value and 0.5 unit above it. This may indicate that  $\bar{O}H$  attack is responsible only partially for the diol formation and that the pathway might also be *via* general acid catalysis as in (V) or (VI).



*Imidazole.*—Imidazole by analogy with aniline cannot displace an alkoxy-group of high basicity in esters by direct nucleophilic attack, and the reaction proceeds *via* general base catalysis. A similar reaction of imidazole with carbonates would be anticipated. Imidazole in  $CDCl_3$  does not cause ring opening of carbonates, while in  $D_2O$  as solvent the product obtained is exclusively diol. This is in accord with kinetic data which show that the attack of 5-nitrocatechol carbonate by water is catalysed by imidazole.<sup>39</sup> The same mechanism seems to operate in compounds (IIb), (Ib), and (IIf).

In the hydrolysis of esters the ratio of the rate constants for the nucleophilic attack of hydroxide ion ( $k_{OH}$ ) *versus* imidazole catalysis ( $k_{Im}$ ) indicates whether the imidazole reacts *via* a nucleophilic or a general base catalysis mechanism.<sup>27b</sup> A ratio of  $k_{OH}/k_{Im}$  is the range  $10^5$ – $10^6$  is an indication of general base catalysis. Comparison of the second order rates for imidazole as given in Table 6 with the rates of nucleophilic hydroxide ion attack on cyclic carbonates as given in Part XII<sup>6</sup> revealed a ratio of  $k_{OH}/k_{Im} = 10^5$ – $10^6$ . This confirms a general base catalysis mechanism of type (VII).



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<sup>38</sup> M. L. Bender and R. B. Homer, *J. Org. Chem.*, 1965, **30**, 3975.

<sup>39</sup> T. H. Fife and D. M. McMahon, *J. Org. Chem.*, 1970, **35**, 3700.