# 614. *Organic Carbonates. Part V.*[1] *The Mechanism of Hydrolysis of Cyclic Carbonates: Tracer Studies.*

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Acid- and base-catalysed hydrolysis of carbonates of 2,2-dialkylpropane-1,3-diol in $H_2{}^{18}O$ proceeds with CO–O bond-fission at both stages. Under both conditions oxygen exchange occurs during the hydrolysis, in all the cases studied, between the exocyclic oxygen atom and the solvent. These facts are interpreted in terms of a possibly non-cyclic intermediate in which the carbonyl-oxygen atom participates in a reversible fashion.

WE have tried to establish the positions of bond fission in the acid- and base-catalysed hydrolysis of cyclic carbonates, by using $^{18}O$ as tracer. Garner and Lucas [2] have shown that the formation, followed by acid- and alkali-catalysed hydrolysis, of the optically active 1,2-dimethylethylene carbonate proceeded with retention of configuration and concluded that these hydrolyses involved carbonyl–oxygen bond fission in both stages of the reaction. In conformity, the reactions of cyclic carbonates with nucleophilic reagents such as ammonia,[3] amines,[4] hydrazine,[5] alcohols,[6] thiols,[6] and polyols,[7] at temperatures below 100°, lead to the respective derivatives of carbonic acid. At temperatures above 100°, however, the reactions of carbonates of vicinal diols with a variety of nucleophiles containing active hydrogen can lead to the formation of 2-hydroxyethyl derivatives such as would be obtained similarly by employing ethylene oxide. These reactions proceed with alcohols, thiols, phenols, thiophenols, amines, and carboxylic acids at temperatures between 100° and 200°, with or without a catalyst, with loss of carbon dioxide.[8] Carbonates of αβ- and αγ-diols also react with potassium thiocyanate at temperatures above 100°, to give fair yields of cyclic sulphides with loss of carbon dioxide and liberation of potassium cyanate.[9] These reactions require the conclusion that, in certain conditions, cyclic carbonates may be cleaved, at least partially, at the carbon–oxygen bond.

A preliminary account of our work has been given.[10]

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[1] Part IV, Sarel, Pohoryles, and Ben-Shoshan, *J. Org. Chem.*, 1959, **24**, 1873.

[2] Garner and Lucas, *J. Amer. Chem. Soc.*, 1950, **72**, 5497.

[3] Baizer, Clark, and Swirdinsky, *J. Org. Chem.*, 1957, **22**, 1595; Ludwig and Piech, *J. Amer. Chem. Soc.*, 1951, **73**, 5779; ref. 1.

[4] Baizer, Clark, and Smith, *J. Org. Chem.*, 1957, **22**, 1706; Delaby, Chabrier, and Najer, *Compt. rend.*, 1952, **234**, 2374.

[5] Delaby, Sekera, Chabrier, and Piganiol, *Bull. Soc. chim. France*, 1951, 392.

[6] Pauly, Schubel, and Lockemann, *Annalen*, 1911, **383**, 230, 288.

[7] Pattison, *J. Amer. Chem. Soc.*, 1957, **79**, 3455; Bruson and Riener, *ibid.*, 1952, **74**, 2100.

[8] Morgan and Cretcher, *J. Amer. Chem. Soc.*, 1946, **68**, 781; Carlson and Cretcher, *ibid.*, 1947, **69**, 1952; Carlson, *Chem. Abs.*, 1949, **43**, 673; U.S.P., 2,448,767.

[9] Searles and Lutz, *J. Amer. Chem. Soc.*, 1958, **80**, 3168.

[10] Levin, Pohoryles, and Sarel, *Bull. Res. Council Israel*, 1958, **7*A***, 221.

## EXPERIMENTAL

The materials have been described in Part IV. Enriched water, containing 1·5% of $H_2{}^{18}O$, was supplied by The Isotope Department, The Weizmann Institute of Science, Rehovot.

*Location of Bond-fission.*—(a) *Hydrolysis in alkaline solution.* 2,2-Dimethylpropane-1,3-diol carbonate (0·13 g.) was added to enriched water (50 ml.) containing two equivalents of sodium hydroxide. The mixture was heated to 50° for 5 hr. to effect complete reaction. The diol was recovered by ether-extraction, drying ($Na_2SO_4$), and removal of solvent. Two recrystallisations from carbon tetrachloride afforded the pure glycol, m. p. 126°, which was used for isotopic analysis. Hydrolysis of the carbonate was complete in 5 min. at room temperature.

(b) *Hydrolysis in acid solution.* A mixture of the carbonate (130 mg.) and enriched water (50 ml.) containing 0·1N-hydrochloric acid was heated under reflux for 24 hr. The diol was recovered and purified as described above.

*Isotopic Analysis.*—The diol was analysed for the content of $^{18}O$ as described by Anbar *et al.*[11]

*Isotopic Analysis of Recovered Cyclic Carbonates after Partial Hydrolysis.*—2,2-Dimethylpropane-1,3-diol carbonate (158 mg.) was allowed to react with enriched water (50 ml.) containing 1·5 equivalents of potassium carbonate at 0°. At time intervals, corresponding to 10%, 17%, 31%, 42%, and 50% hydrolysis, determined independently by parallel in ordinary water, the reactions were stopped by adding aqueous perchloric acid to the reaction mixture so as to give pH 7. The unchanged ester was recovered by ether.

Recovered carbonate was dried ($P_2O_5$; high vacuum) before being analysed for the content of $^{18}O$. In a similar fashion, 2,2-diethylpropane-1,3-diol carbonate (316 mg.) was partially hydrolysed in enriched water (25 ml.) containing perchloric acid (0·14N) at 50° (thermostat). The reaction was stopped by cooling and then neutralising samples at time intervals corresponding to 5% and 50% hydrolysis. The unchanged carbonate was recovered and analysed for the content of $^{18}O$ as described above. Similar experiments were carried out at different acid concentrations.

*Isotopic Analysis of Recovered Cyclic Carbonate.*—The content of $^{18}O$ in the recovered ester was determined by isotopic analysis of the carbon dioxide liberated in its acid-hydrolysis in a sealed system. In a typical experiment, recovered ester (29 mg.), trifluoroacetic acid (48·6 mg.), and distilled water (13 mg.) were placed in an ampoule and cooled to liquid-air temperature before being sealed under a high vacuum. The whole was then heated at 50° for 30 hr., at which time the ester hydrolysis and the $^{18}O$ exchange between all components in the system were complete. The isotopic analysis of liberated carbon dioxide was carried out after the ampoule had been broken in the inlet system of the mass spectrometer. Since the atom-fraction excess of $^{18}O$ in the ester-carbonyl group presumably decreases upon its conversion into carbon dioxide, the true isotopic composition of the recovered carbonate was then computed by use of the ordinary isotopic dilution formula, as follows:

$$2N_A - N_0 = N$$

$$N_A = \tfrac{1}{2}[(2n_1 + 2n_2 + n_3)N_B - (2n_2 + n_3)N_0]/n_1$$

where $N$ is the atom fraction of $^{18}O$ in the ester-carbonyl group, $N_B$ and $N_A$ are the isotopic compositions of carbon dioxide before and after correction, respectively, $n_1$, $n_2$, and $n_3$ are the corresponding mmol. of recovered carbonate, trifluoroacetic acid, and water. The natural $^{18}O$-abundance ($N_0$) of carbon dioxide was 0·20. The results of these isotopic analyses are given in Table 1.

TABLE 1. *Isotopic analysis of* 2,2-*diethylpropan*-1,3-*diol carbonate recovered after partial hydrolysis in* 1·5% $H_2{}^{18}O$.

| Time (min.) | Hydrolysis (%) | $N - N_0$ $^{18}O$ atom % excess on exocyclic oxygen | Time (min.) | Hydrolysis (%) | $N - N_0$ $^{18}O$ atom % excess on exocyclic oxygen |
|---|---|---|---|---|---|
| | *Acidic*[a] | | | *Alkaline*[d] | |
| 5[b] | 5 | 0·128 | 0·5 | 10 | 0 |
| 30[b] | 34·5 | 0·520 | 1 | 17 | 0 |
| 240[c] | — | 0 | 3 | 31 | 0 |
| | | | 8 | 42 | 0·10 |
| | *Neutral* | | 12 | 50 | 0·15 |
| 15 | 0 | 0 | | | |
| 30[a] | 0 | 0 | | | |

[a] At 50°. [b] With 0·1M-$HClO_4$. [c] With 3·16 × $10^{-4}$M-$HClO_4$. [d] With 0·03M-$K_2CO_3$ at 0°.

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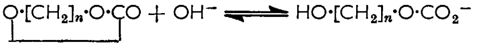
[11] Anbar, Dostrovsky, Klein, and Samuel, *J.*, 1955, 155.

## DISCUSSION

In the base- and acid-catalysed hydrolysis of cyclic αβ- and αγ-carbonates in $H_2{}^{18}O$, the diol produced was isotopically normal, proving that cleavage of cyclic carbonates had occurred with carbonyl–oxygen bond-fission in both stages of the hydrolysis.

Miller and Case [12] have shown that the hydrolysis of diethyl carbonate in alkali is a two-stage process. The first stage, which follows second-order kinetics, is followed by a slow first-order reaction. Faurholt and his associates,[13] who studied the first-order decomposition of alkyl hydrogen carbonates, revealed that this reaction is accompanied by the reverse process (esterification) * which is also a first-order reaction. Thus, he was able to calculate the rates and equilibrium constants of hydrolysis for a series of alkyl and hydroxyalkyl hydrogen carbonates in alkali. In view of this, the opening-stage in the base-catalysed hydrolysis of cyclic carbonates, which has been shown to proceed rapidly by second-order kinetics,[15] can be depicted as occurring reversibly and may be labelled $B_{AC}2$.

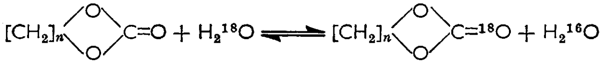
On the other hand, the second-stage in these hydrolyses probably proceeds by a unimolecular mechanism and can be tentatively labelled either $B_{AC}1$ or $S_E1$. The latter illustrates a unimolecular *O*-decarboxylation (reaction 2).[16]



$$O{\cdot}[CH_2]_n{\cdot}O{\cdot}CO + OH^- \rightleftharpoons HO{\cdot}[CH_2]_n{\cdot}O{\cdot}CO_2^- \quad . \; . \; B_{AC}2 \; . \; . \; . \; (1)$$

$$HO{\cdot}[CH_2]_n{\cdot}O{\cdot}CO_2^- \rightleftharpoons HO{\cdot}[CH_2]_n{\cdot}O^- + CO_2 \quad . \; . \; B_{AC}1 \text{ or } S_E1 \; . \; (2)$$

The exchange reaction of the type (3) seems to occur in significant competition with the acid- or base-hydrolysis of cyclic 1,3-carbonates.



. . . . . (3)

In every case the exchange between the solvent and the cyclic ester took place *only* during the hydrolysis (Table 1). Conceivably, these findings can be explained in terms of the formation, during alkaline hydrolysis, of an intermediate in which the carbonyl-oxygen atom of the ester participates reversibly, by analogy with the mechanism proposed by Bender for alkaline hydrolysis of carboxylic esters.[17]

Our results require that during alkaline hydrolysis the reversible interconversion between ionised ester hydrate intermediates (I, III) by way of the un-ionised form (II) should be rapid. Scheme (4) illustrates an alternative proposal; this requires that the breakage of the cyclic C–O bond in (I) occurs in significant competition with its conversion into (II) and that the resulting acyclic ionised intermediate (IV) can undergo both ready exchange and, at least partially, ring-closure into (I) or (III). If the atom fraction of $^{18}O$ in recovered ester is expressed in terms of percent, from the equation $1{\cdot}5x + (1 - x)0{\cdot}2 = 0{\cdot}35$ [where $x$ is the fraction of recovered ester having the same isotopic composition on the carbonyl-oxygen atom as that of the solvent ($1{\cdot}5\%$ of $H_2O^{18}$) and

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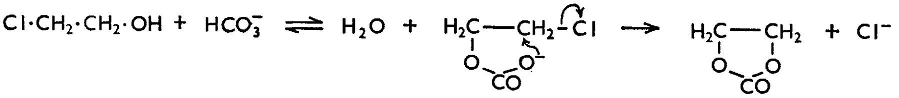
* The formation of ethylene carbonate by reaction of ethylene chlorohydrin and concentrated aqueous bicarbonate [14] presumably involves the reaction sequence:



and illustrates the type of esterification (reversal of hydrolysis) discussed here.

[12] Miller and Case, *J. Amer. Chem. Soc.*, 1935, **57**, 810.

[13] Noring, Jensen, and Faurholt, *Acta Chem. Scand.*, 1952, **6**, 404 and previous papers cited there.

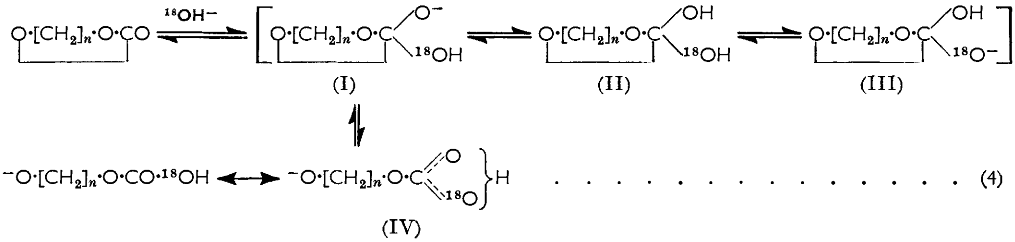
[14] Steimmig and Wittmer, German Patent 516,281.

[15] Pohoryles and Sarel, *Compt. rend.*, 1957, **245**, 2321; Pohoryles, Levin, and Sarel, *Bull. Res. Council Israel*, 1958, **7***A*, 221; Kempa and Lee, *J.*, 1959, 1576.

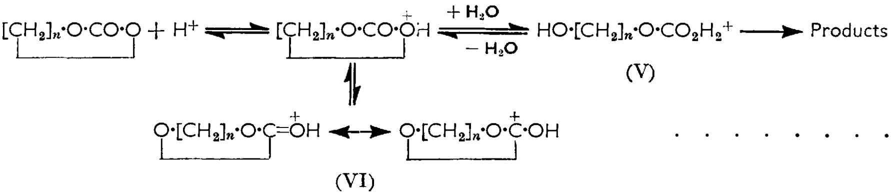
[16] Brown, *Quart. Rev.*, 1951, **5**, 131.

[17] Bender, *J. Amer. Chem. Soc.*, 1951 ,**73**, 1626.

$(1 - x)$ is the fraction containing the natural abundance of $O^{18}$ (0·2%)], it can be calculated that with 50% hydrolysis the re-formation of the cyclic ester from the assumed intermediate amounts to only 11·5%.



. . . . . . . . . . . . . . . (4)



. . . . . . . . . (5)

Evidently, the exchange process expressed in equation (4) provides a reasonable explanation of our results but it should be regarded as tentative.

The acid-hydrolysis can be written as a multi-stage process of the type shown in equation (5). The initial step, a pre-equilibrium proton-transfer, is followed by a slow bimolecular acyl–oxygen bond-fission[18] ($A_{AC}2$) and then by a fast unimolecular acyl–oxygen bond-fission ($A_{AC}1$). Since oxygen exchange under acidic conditions occurs in significant competition with hydrolysis (see above), positively charged ester hydrates such as (V) and (VI) may contribute to the structures of intermediates capable of exchange.

We are indebted to The Isotopic Department, The Weizmann Institute of Science, Rehovot, for a generous gift of enriched water and for the isotopic analysis, and to Dr. F. Klein of that Department for help and useful discussions.

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[*Received, June 17th,* 1959.]

[18] Ingold, " Structure and Mechanism in Organic Chemistry," Bell, London, 1953, p. 769; Levin, Pohoryles, Sarel, and Usieli, *Bull. Res. Council Israel*, 1958, *7A*, 220.