Solvolytic Fragmentation of 2-Halogenoalkylphosphonic Acids

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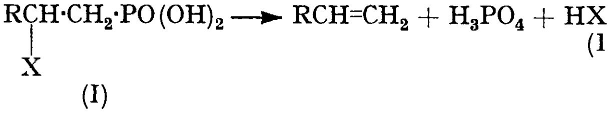
The fragmentations of 2-halogenoalkylphosphonic acid dianions have been studied at various pH values and temperatures, and in the presence of added salts. The data obtained, together with the lack of a deuterium solvent isotope effect and the effect of alkyl substitution at the β-carbon atoms, suggest that the reaction involves a transition state resembling a dipolar ion.

THE solvolytic fragmentation of a 2-halogenoethylphosphonic acid (I) in aqueous solution yields the corresponding alkene, phosphoric acid, and halide ion [equation (1)].[1,2] In non-aqueous solution, the reaction can be used to phosphorylate alcohols.[2] The mechanism of these fragmentation reactions has not been studied in detail, although it is thought that breakdown of the phosphonate dianion is involved.[3] Furthermore, Kenyon and Westheimer[4] have concluded that the fragmentation of some 2-halogenoalkylphosphonic acid occurs *via trans* elimination.



$$\underset{\displaystyle X}{RCH}\cdot CH_2\cdot PO(OH)_2 \longrightarrow RCH{=}CH_2 + H_3PO_4 + HX \qquad (1)$$

(I)

EXPERIMENTAL

Materials.—2-Chloroethylphosphonic acid (CEPA), m.p. 72—74° (lit.,[5] 74—75°), was obtained by recrystallization of a commercial sample from benzene. Dimethylsulphonioethylphosphonic acid bromide, m.p. 133°, was donated by Dr. A. J. Davidson, Plant Protection Limited.

2-*Iodoethylphosphonic acid.* A solution of 2-chloroethylphosphonic acid (5 g) and sodium iodide (20 g) in acetone (100 ml) was heated under reflux for 24 h, then filtered and distilled to dryness. The solid residue was extracted with hot chloroform (120 ml) and the solution was cooled and filtered. Petroleum (b.p. 60—80°) was added to the reheated solution until it became cloudy. On cooling, the *phosphonic acid* (3·2 g), m.p. 102—104°, was obtained as pale yellow leaflets (Found: C, 10·0; H, 2·4; I, 54·6; P, 13·7. $C_2H_6IO_3P$ requires C, 10·2; H, 2·5; I, 53·9; P, 13·2%).

2-*Chloropropylphosphonic acid.* Propene was passed into a suspension of phosphorus pentachloride (50 g) in benzene (50 ml) for 8 h at 0—5°. The mixture was left overnight, phosphorus pentoxide (11 g) was added, and the mixture was heated at 50° for 4 h. The solution was filtered and distilled to give crude 2-chloropropylphosphonic dichloride (14·2 g, 60%), b.p. 88—92° at 12 mmHg. A portion of the crude dichloride (2·0 g) was added dropwise to water (50 ml). The solution was evaporated to dryness to yield a solid (1·80 g) which afforded 2-*chloropropylphosphonic acid* (1·2 g, 74%), m.p. 85—87° (from toluene) (Found: C, 22·9; H, 5·2; Cl, 22·2; P, 20·6. $C_3H_8ClO_3P$ requires C, 22·7; H, 5·05; Cl, 21·9; P, 19·9%), τ 4·53 (m, CHCl), 2·32 (m, CH_2P), and 1·73 (d, J 6·5 Hz, CH_3).

2-*Chlorohexylphosphonic acid.* A mixture of hex-1-ene (20 g) and phosphorus pentachloride (98·4 g) in benzene (100 ml) was stirred at room temperature for 8 h. The suspension was poured on ice (100 g) and stirred thoroughly. The benzene layer was separated, dried ($MgSO_4$), and distilled, leaving a brown oil. The oil crystallized from petroleum to yield the phosphonic acid (4·4 g), m.p. 84—86° (lit.,[6] 81—82°) (Found: C, 36·2; H, 7·1; Cl, 17·8; P, 15·4. Calc. for $C_6H_{14}ClO_3P$: C, 36·0; H, 7·0; Cl, 17·7; P, 15·5%).

Kinetic Technique.—Reactions were followed by using a Radiometer TTT11 autotitrator; solutions were maintained at the required pH by the addition of 0·01M-potassium hydroxide in the required solvent. When aqueous methanol mixtures were used, the ' pH ' used was that obtained when the phosphonic acid was neutralized with 2 equiv. of base. First-order rate constants were obtained in the usual way, by using the titre as a measure of the extent of reaction. For some slow reactions the infinity titre used was the theoretical one. Activation energies were determined from runs at four temperatures between 26·5 and 50°.

Phosphate Analyses.—The presence of methyl phosphate in the products of the solvolysis of CEPA dianion in 50% aqueous methanol was shown by t.l.c. on Polymin P. In 0·24M-LiCl–0·01M-HCl, methyl dihydrogen phosphate had R_F 0·5. Inorganic phosphate was determined by the method of Lowry and Lopez,[7] and the yield of methyl dihydrogen phosphate was taken as the difference between the theoretical and determined yields of phosphate.

RESULTS

The solvolytic fragmentations of 2-halogenoalkylphosphonic acids were followed by measurement of liberated acid, using an autotitrator. At 50° the disappearance of 2-chloroethylphosphonic acid (CEPA) (I; R = H, X = Cl) at a given pH followed good first-order kinetics to four or more half-lives. The apparent first-order rate constant (k_{obs}) was found to be directly proportional to the fraction of the CEPA present as its dianion (see Figure). This result confirms the finding of Warner and Leopold[3] on the evolution of ethylene from CEPA. 2-Chlorohexylphosphonic acid (CHPA) and 2-chloropropylphosphonic acid reacted much more rapidly than CEPA and the fragmentation of these compounds could not be followed at pH values above 6 at 26·5°. However, it could be shown that the fragmentation rate was proportional to the fraction of the acid existing as the dianion. This large difference in rates of fragmentation of CEPA and higher 2-chloroalkylphosphonic acids was noted by Maynard and Swan,[2] but they drew no conclusions. Our data suggest that higher

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[1] J. B. Conant and A. A. Cook, *J. Amer. Chem. Soc.*, 1920, **42**, 830.

[2] J. A. Maynard and J. M. Swan, *Austral. J. Chem.*, 1963, **16**, 596.

[3] H. L. Warner and A. C. Leopold, *Plant Physiol.*, 1969, **44**, 156.

[4] G. L. Kenyon and F. H. Westheimer, *J. Amer. Chem. Soc.*, 1966, **88**, 3561.

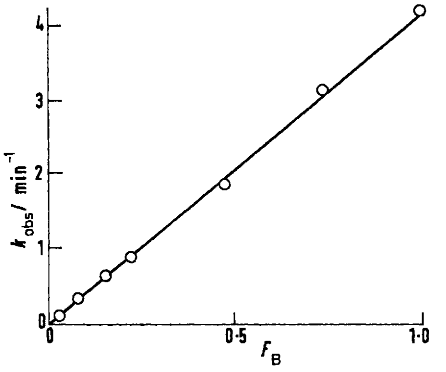
[5] M. I. Kabachnik and P. A. Rossiiskaya, *Izvest. Akad. Nauk. S.S.S.R. Otdel. khim. Nauk*, 1946, 403.

[6] G. K. Fedorova, R. N. Ruban, A. V. Kirsanov, *Zhur. obshchei. Khim.*, 1969, **39**, 1471.

[7] O. H. Lowry and J. A. Lopez, *J. Biol. Chem.*, 1946, **162**, 421.

2-chloroalkylphosphonic acids react *ca.* 10^4 times faster than CEPA at 25° (runs 13—15).

The activation energy for the fragmentation of CEPA dianion was found to be 120 ∓ 5 kJ mol^{-1}, and the entropy of activation to be -9 ∓ 15 J mol^{-1} K^{-1} at 50°.



Variation of k_{obs} with the fraction (F_B) of CEPA existing as its dianion in water at 50°

Rate constants from the fragmentation of 2-substituted alkylphosphonate dianions [$RCH(X)\cdot CH_2\cdot PO_3^{2-}$] at 50°

Run	R	X	Solvent	10^2k_{obs}/ min^{-1}
1	H	Cl	1M-KCl	4·0
2	H	Cl	1M-NaN_3	4·0
3	H	Cl	1M-KF	4·5
4	H	Cl	0·2M-KCl	4·4
5	H	Cl	0·4M-KCl	4·2
6	H	Cl	0·6M-KCl	4·2
7	H	Cl	0·8M-KCl	4·1
8	H	Cl	1M-KCl, 25% MeOH	3·5
9	H	Cl	1M-KCl, 50% MeOH	3·2
10	H	Cl	D_2O, 1M-KCl	4·3
11	H	I	1M-KCl	48
12	H	$\mathrm{Me_2\overset{+}{S}\overset{-}{Br}}$	1M-KCl	$<3 \times 10^{-3}$
13	H	Cl	1M-KCl	0·13 [a]
14	Bu^n	Cl	1M-KCl	920 [a,b]
15	Me	Cl	1M-KCl	1460 [a,b]

[a] At 26·5°. [b] Estimated from k_{obs} at lower pH values, assuming pK_a 7·0 for the second dissociation.

Reactions of CEPA dianion were carried out in 1M-azide and 1M-fluoride solutions. In neither case was the rate significantly affected, and in the latter instance a titre equivalent to the theoretical yield of phosphoric acid was obtained, showing that fluorophosphonic acid was not a major product (Table, runs 2 and 3).

The effect on the rate of varying the ionic strength is also shown in the Table (runs 4—7). There is a slight decrease in rate with increasing potassium chloride concentration.

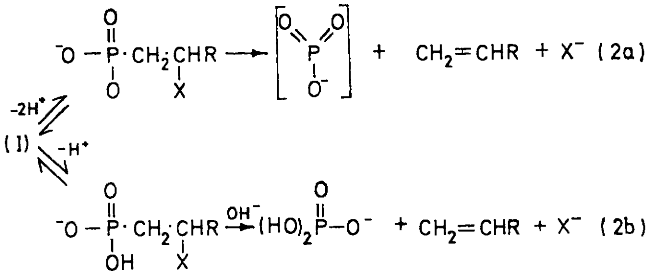
Reactions carried out in methanol–water (runs 8 and 9) were slightly slower than reactions carried out in water, but as the proportion of methanol in the solution increased the yield of phosphate decreased, being replaced by methyl dihydrogen phosphate. The yield of the latter was directly related to the mole fraction of methanol present in the solution; this showed that the fraction of CEPA reacting to give the ester was equal to the mole fraction of methanol present. The phosphorylating agent is thus indiscriminate towards the solvent species derived from water and from methanol.

The rate of the reaction was essentially the same in water and in 98% deuterium oxide (run 10).

The effect of various leaving groups on the rate is shown in the Table. 2-Iodoethylphosphonic acid (I; R = H, X = I) reacts *ca.* 12 times faster than CEPA, whereas 2-dimethylsulphonioethylphosphonic acid bromide (I; R = H, X = $\mathrm{Me_2\overset{+}{S}\overset{-}{Br}}$) does not appear to react at all.

DISCUSSION

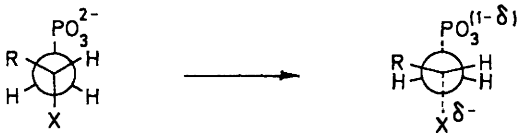
The results could be reconciled with a mechanism for the fragmentation of 2-halogenoalkylphosphonic acids which involved the unimolecular fragmentation of the acid dianion (2a) or alternatively a concerted bimolecular reaction, *e.g.* (2b).



The lack of catalysis by nucleophiles such as fluoride and azide ion, the lack of solvent effects on rates of reaction, and the general lack of specificity in the competitive phosphorylation of water and methanol favour the unimolecular mechanism (2a).

The effects of constitutional changes on the rates of fragmentation of these phosphonate dianions are marked. Whereas replacement of chlorine by iodine increases the rate of fragmentation by a factor of 12, 2-sulphonioethylphosphonate dianions do not appear to undergo fragmentation (run 12). However, the most dramatic changes in rate are observed when the β-carbon atom carries an alkyl group; the rates are then increased by 10^4 relative to CEPA.

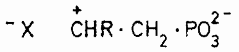
The acceleration by β-alkyl substitution could be due to relief of steric interactions in the transition state; for example, the interaction between R and the phosphonate group would be relieved in a concerted fragmentation such as that shown in (3). However, molecular models of these acids suggest that the interaction between alkyl and phosphonate groups in the *gauche* conformation shown is no bigger than a similar interaction between two chlorine atoms, which is estimated to be about 6 kJ mol^{-1}, whereas the change in free energy of activation is 23 kJ mol^{-1}. Furthermore, the rate differs little when R = Bu^n from when R = Me. Thus although steric repulsions may account partly for the



(3)

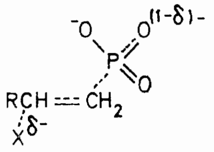
rate increases noted, these interactions would only account for no more than a 10-fold change in rate.

The magnitude of the rate increase on β-substitution is the same as that suggested by Ingold [8] for the increase in the rate of S_N1 reactions caused by substitution of methyl for hydrogen at the α-carbon atom. This raises



$^{-}X \quad \overset{+}{C}HR\cdot CH_2\cdot PO_3^{2-}$

(II)



(III)

the possibility that fragmentation of the phosphonate dianions proceeds *via* a transition state bearing a substantial positive change on the β-carbon atom. This would imply that C–X bond heterolysis is much more advanced in the transition state than is π-bond formation, leading in an extreme situation to a transition state resembling a carbonium ion (II). The extent of π-bonding due to C–P fission cannot be unequivocally assessed, but is thought to be small on the following grounds. Any release of electrons from the C–P bond to form a partial π-bond would decrease the positive change on the β-carbon atom, and would be expected to lower the sensitivity of the rate to β-substitution. As the rate enhancement due to methyl substitution is that given by Ingold for the effect of methyl substitution on the rates of S_N1 processes, it is plausible that the β-carbon bears a positive charge which approximates to that on a carbonium ion, even when the β-carbon atom is primary.

The above analysis, of necessity crude, suggests that the transition state of these fragmentations resembles more closely the dipolar ion species (II), than the charge-dispersed species (III). Similar transition states have been proposed [9] for the fragmentation and hydrolysis of a number of 2-halogenoethanecarboxylate ions, which bear a marked resemblance to the phosphonate dianions under consideration. In the former cases, it has been proposed that electrostatic interactions between the anionic group and the incipient carbonium ion centre assist the heterolysis of the C–X bond. Such an explanation would also accommodate the relatively easy formation of a dipolar ion from CEPA.

The main factor which appears to be inconsistent with a dipolar ion transition state is the effect of solvent composition on the rate of reaction. The rate decreases slightly with increasing methanol content (runs **8** and **9**), whereas the rate of solvolysis of t-butyl chloride decreases markedly. On the other hand if reaction occurred *via* species (III), the rate might be expected to increase slightly with increasing methanol content. A lack of sensitivity to solvent changes has also been found for the rates of solvolysis of 1- and 2-bromoalkanecarboxylate ions. A possible explanation is that molecular rotations of the solvent in the vicinity of the reacting molecule are restricted by the field of the anionic group leading to a region of low dielectric constant in the vicinity of the reaction centre, irrespective of the solvent composition. This condition would not be found in, for example, t-butyl chloride.

Thus, on the evidence available, the transition state for the fragmentation of 2-halogenoalkylphosphonate dianions probably resembles a dipolar ion (II), which is stabilized either by electrostatic interactions between the phosphonate dianion group and the incipient carbonium ion or by a small amount of partial π-bond formation. Whether an intermediate carbonium ion is formed subsequently, or whether the reaction is a one-step process cannot be determined, but in either case metaphosphate anion is thought to be produced as an intermediate.

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