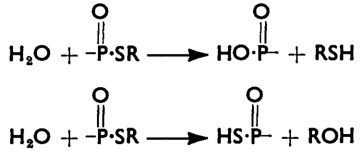
634. *The Hydrolysis of Di*iso*propyl Methylphosphonodithiolate.*

By R. F. HUDSON and L. KEAY.

Measurements of the rate of hydrolysis of di*iso*propyl methylphosphonodithiolate by estimation of acid and thio-compound produced show that P–S fission occurs both in acid and alkaline solution, which may be attributed to the low bond strength. This is reflected in the high reactivity in alkaline solution (*ca.* 10^4 times as reactive as di*iso*propyl methylphosphonate). The rate in acid solution is about 5 times less than that of the oxygen-ester, although in this case also a considerable decrease in activation energy is observed.

THE position of bond fission in the hydrolysis of thiol esters may be determined by direct observations on the nature of the reaction products.[1] An elegant method for determining



$$H_2O + -\overset{\overset{\displaystyle O}{\|}}{P}\cdot SR \longrightarrow HO\cdot\overset{\overset{\displaystyle O}{\|}}{P}- + RSH$$

$$H_2O + -\overset{\overset{\displaystyle O}{\|}}{P}\cdot SR \longrightarrow HS\cdot\overset{\overset{\displaystyle O}{\|}}{P}- + ROH$$

the end products quantitatively, described by Bohme and Schran [2] in the hydrolysis of thiolacetates, consists of oxidising thiols and thio-acids with iodine to the corresponding disulphide and hydrogen iodide, and titrating this acid with alkali. Dialkyl phosphonothiolates are readily oxidised electrolytically and by halogens,[3] and other phosphoro- and phosphono-thiolates are oxidised similarly [4] by halogens :

$$2(RO)_2PO\cdot SH + I_2 = (RO)_2PO\cdot S\cdot S\cdot PO(OR)_2 + 2HI$$

Considering the two possible reaction mechanisms :

$$\begin{aligned} &(a)\ P\cdot SR + H_2O = P\cdot SH + ROH \\ &\quad\ 2\,P\cdot SH + I_2 = P\cdot S\cdot S\cdot P + 2HI \\ &(b)\ P\cdot SR + H_2O = P\cdot OH + RSH \\ &\quad\ 2RSH + I_2 = R\cdot S\cdot S\cdot R + 2HI \end{aligned}$$

It follows that one equivalent of acid is produced for each equivalent of iodine reduced if mechanism (*a*) is correct, but two equivalents of acid per equivalent of iodine if mechanism (*b*) is correct.

The results shown in Table 1 show clearly that the thiol and not the alcohol is produced in the reaction with hydroxyl ions, so that reaction proceeds at the phosphorus atom. Whereas methyl thiolacetate is slightly less reactive than methyl acetate,[5] di*iso*propyl methylphosphonodithiolate reacts $2{\cdot}5 \times 10^4$ times faster in alkali than the corresponding oxygen-ester (Table 3) with a corresponding decrease in activation energy. The decreased rate and increased activation energy of the reaction of methyl thiolacetate may be attributed to the reduced electronegativity of the sulphur atom, thus reducing the electrostatic attraction of the hydroxide ion :

$$R\cdot CO\cdot SR + OH^- \rightleftharpoons R\cdot C(OH)(SR)\cdot O^- \longrightarrow R\cdot CO_2H + RS^-$$

This decrease in reactivity is opposed by the decrease in C–S bond strength (54 kcal. mole^{-1}) compared with the C–C bond energy (75 kcal. mole^{-1}).[6] For phosphonates the

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[1] Morse and Tarbell, *J. Amer. Chem. Soc.*, 1952, **74**, 416; Stevens and Tarbell, *J. Org. Chem.*, 1954, **19**, 1996; Schaefgen, *J. Amer. Chem. Soc.*, 1948, **70**, 1308.

[2] Bohme and Schran, *Chem. Ber.*, 1949, **82**, 456.

[3] Foss, *Acta Chem. Scand.*, 1947, **1**, 8; *Kgl. norske Videnskab. Selskabs, Forhandl.*, 1942, **15**, 119.

[4] Malatesta and Pizzotti, *Chimica e Industria*, 1945, **27**, 6; *Gazzetta*, 1946, **76**, 167, 182.

[5] Rylander and Tarbell, *J. Amer. Chem. Soc.*, 1950, **72**, 3021.

[6] Neale and Williams, personal communication.

decrease in bond strength (95—100 to 45—50 kcal. mole^{-1})[7] is so great as to cause a considerable increase in reactivity. The increase in the collision factor (PZ) accompanying the decrease in activation energy (Table 3) is interesting since the two Arrhenius parameters frequently increase together,[8] as, for example, in the reaction of the corresponding carboxylic esters. The increased collision factor may be due to the greater covalent radius of the sulphur atom compared with the oxygen atom, which removes the bulky *iso*propyl groups further from the centre of substitution.

TABLE 1. *The hydrolysis of di*iso*propyl methylphosphonodithiolate in* 0·2N-NaOH *at* 0°.

The reaction mixture (5 ml.) was quenched in potassium hydrogen phthalate (5 ml. ≡ 5·20 ml. of 0·178N-sodium hydroxide), oxidised by 10 ml. of iodine solution, and titrated against 0·1N-sodium thiosulphate.

Time (min.)	Titre of $Na_2S_2O_3$ (ml.)	Change in $Na_2S_2O_3$ titre, ΔT_1 (ml.)	Titre of NaOH (ml.)	Change in NaOH (0·1N) titre, ΔT_2 (ml.)	$\frac{\Delta T_2}{\Delta T_1}$
1	6·80	—	1·81	—	—
1·75	6·47	0·33	2·30	0·87	2·63
3·0	5·67	1·13	3·05	2·22	1·97
4·75	5·24	1·56	3·60	3·20	2·05
6·50	4·83	1·97	4·02	3·95	2·00
8·0	4·50	2·30	4·35	4·54	1·97
10·0	4·26	2·54	4·62	5·02	1·98
12·0	3·91	2·89	4·90	5·52	1·91
∞	2·40	4·40	6·40	8·20	1·87

TABLE 2. *The reactivity in acid solution of esters and thiolesters.*

	k	E (kcal. mole^{-1})	log PZ
Bu^t acetate	8·00 (30°)	23·2	13·6
Bu^t thiolacetate	0·82 (30°)	20·7	10·8
Pr$^i_2$ methylphosphonate	2·00 (110°)	25·6	11·4
Pr$^i_2$ methylphosphonodithiolate	0·46 (110°)	15·1	4·85

TABLE 3. *The reactivity in alkaline solution of esters and thiolesters.*

	k (l. mole^{-1} min.$^{-1}$)	E (kcal. mole^{-1})	log PZ
Me acetate	3·96 (20°)	12·2	9·7
Me thiolacetate	2·41 (20°)	13·1	10·2
Pr$^i_2$ methylphosphonate	0·55 (80°)	14·9	5·4
Pr$^i_2$ methylphosphonodithiolate	2·41 (25°)	11·4	7·3

Measurements in acid solution showed that similarly the thiol and not the alcohol is produced (Table 4), so that substitution proceeds at the phosphorus atom, and not at the carbon atom as is probably the case in the reaction of the corresponding oxygen-ester. The activation energy of the reaction of the thiol-ester (15·1 kcal. mole^{-1}) is much less than that of the oxygen ester (25·6 kcal. mole^{-1}) and the PZ factor is also reduced considerably (Table 2). This is consistent with a change in mechanism from an S_N1 ionisation mechanism in the acid hydrolysis of the oxygen-ester, to a bimolecular substitution at the phosphorus atom. This change in mechanism is understandable since the P–S bond is very much weaker than the P–O bond and even weaker than the C–S bond. A similar change in mechanism has also been observed in the case of the acetates and thiolacetates of tertiary alcohols (Table 2). *tert.*-Butyl acetate hydrolyses, with alkyl–oxygen fission, by the S_N1 mechanism in acid solution,[9] whereas the thiol-ester is hydrolysed only one-tenth as fast with a reduced activation energy and PZ factor with acyl–sulphur fission.[5]

EXPERIMENTAL

*Preparation of Di*iso*propyl Methylphosphonodithiolate.*—Methylphosphonic dichloride (66 g.) in ether (200 ml.) was added dropwise with stirring and ice-cooling to propane-2-thiol (76 g.)

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[7] Pauling " Nature of the Chemical Bond," Cornell Univ. Press, New York, 1940.

[8] Fairclough and Hinshelwood, *J.*, 1937, 538, 1573.

[9] Bunton, *Research*, 1951, **4**, 383; Stimson, *J.*, 1955, 2010.

and triethylamine (135 ml.) in ether (1 l.). Then the mixture was set aside at room temperature overnight. The precipitate was filtered off and washed with ether. The ether was removed from the combined filtrate and washings and the *ester* was distilled *in vacuo* (yield 72%; b. p. 94°/0·2 mm.) (Found : C, 39·8; H, 8·2. $C_7H_7POS_2$ requires C, 39·6; H, 8·1%).

Products of Hydrolysis.—Aliquot parts (5 ml.) of the reaction mixture were pipetted into flasks containing known volumes of standard iodine and hydrochloric acid. The excess of iodine was titrated with 0·1N-sodium thiosulphate solution with starch as indicator. When the blue colour just disappeared, phenolphthalein was added and the acid content determined by titration with standard sodium hydroxide. From these measurements the ratio of the equivalents of acid to iodine titrated was calculated for various stages of the reaction (Table 1).

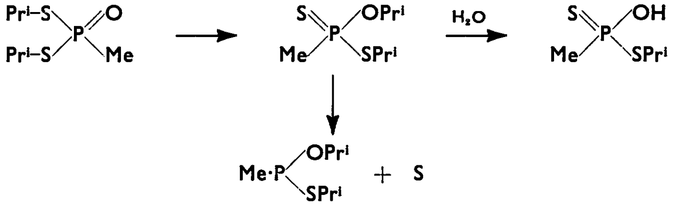
In order to determine the amount of thiol produced on acid hydrolysis, 2·477 g. of the ester were refluxed for 40 hr. with 50 ml. of N-hydrochloric acid. The solvent was distilled off and the remainder made up to 100 ml. with distilled water. An aliquot part (5 ml.) of this solution was added to excess of iodine and back-titrated with 0·1N-thiosulphate. The 5 ml. aliquot part was equivalent to 5·79 ml. of iodine solution, therefore 1 mole of ester produces 0·99 mole of thiol. The kinetic results are given in Table 4. From the initial reading it would appear that thiol alone is released in the first stage, but the increasing ratio suggests that some further decomposition occurs as the reaction progresses. Although the ratio of acid to iodine reduced is greater than 2, the rates of reaction determined from the two series of estimations are very similar. This indicates that the increased ratio is caused by a side reaction in which sulphur is produced in a non-oxidisable form. Thiol-esters are known to be thermally labile, and sulphur was gradually precipitated on prolonged storage of the phosphonodithiolate. Since isomerisation also readily occurs in these systems the side reaction may proceed by a series of processes of the following kind :

TABLE 4. *The hydrolysis of diisopropyl methylphosphonodithiolate in N-benzenesulphonic acid at* 111·3°.

Time (min.)	Titre of $Na_2S_2O_3$ (ml.)	Change in $Na_2S_2O_3$ titre, ΔT_1 (ml.)	Titre of NaOH (ml.)	Change in 0·1N-NaOH titre, ΔT_2 (ml.)	$\frac{\Delta T_2}{\Delta T_1}$	Reaction (%) from NaOH	Reaction (%) from $Na_2S_2O_3$
0	9·02	—	25·20	—	—	0	0
10	8·65	0·37	25·60	0·80	2·16	5·13	6·2
35	8·01	1·01	26·45	2·50	2·47	16·0	17·1
60	7·39	1·63	27·28	4·16	2·55	26·7	27·6
120	6·36	2·11	28·70	7·00	2·63	44·9	45·1
180	5·55	3·47	29·75	8·90	2·57	58·3	58·8
300	5·10	3·92	30·70	11·00	2·81	70·5	66·4
∞	3·12	5·90	33·0	15·60	2·65	—	—

TABLE 5. *Rate of hydrolysis of diisopropyl methylphosphonodithiolate.*

	0·20N-NaOH			1·0N-Ph·SO_3H	
Temp.	[Ester]	k (l. mole^{-1} hr.$^{-1}$)	Temp.	[Ester]	k (hr.$^{-1}$)
0·0	0·11	42·7	92·5°	0·20	0·200
5·0	0·08	59·6	100·1	0·25	0·338
10·0	0·08	80·5	109·4	0·20	0·464
14·0	0·09	110	113·3	0·25	0·556
25·0	0·08	241			



QUEEN MARY COLLEGE,
MILE END ROAD, LONDON, E.1.

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