The Hydrolysis of three Alkoxy-diethyl-phosphine Oxides

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The rate constants of the alkaline hydrolysis of ethoxy-, 2-methoxyethoxy-, and 2-hydroxyethoxy-diethyl-phosphine oxide have been determined. From kinetic and IR-data, the facilitation of the hydrolysis by a neighbouring hydroxyl group has been interpreted as an internal catalysis caused by an intramolecular hydrogen bond to the phosphoryl group.

In an earlier paper one of the present authors postulated that the remarkably high rate of the hydrolysis of dimethylaminoethoxy-methyl-phosphoryl fluoride would depend upon the formation of an intramolecular hydrogen bond in the protonized species, which should facilitate the attack of a hydroxyl ion on the phosphorus atom.[1] This hypothesis has been supported by the results found by Hansen in his study of the hydrolysis of aminoalkylesters of carboxylic acids.[2] The purpose of the present investigation has been to study the effect of a neighbouring hydroxyl group on the hydrolysis of an organo-phosphorus compound. Similar investigations of the catalytic effect of a neighbouring hydroxyl group in cyclic esters of acetic acid have been performed earlier.[3,4]

EXPERIMENTAL

Materials. Ethoxy-diethyl-phosphine oxide. Diethoxy-ethyl-phosphine was synthesized from ethyl-dichlorophosphine[5] according to Schreiber[6] and isomerized by an Arbuzov rearrangement[7] giving ethoxy-diethyl-phosphine oxide in a yield of 90 %.

2-Hydroxyethoxy-diethyl-phosphine oxide. 42.0 g of diethyl-chloro-phosphine oxide, obtained by chlorination of ethoxy-diethyl-phosphine oxide with carbonyl chloride,[8] was dissolved in 100 ml of toluene and added dropwise to a stirred suspension of 20.7 g of sodium ethylene glycolate in 200 ml of toluene. During the addition the reaction mixture was kept at 40−50°C. Afterwards the temperature was raised to 90°C and the mixture stirred for about one hour. After cooling, the sodium chloride formed was filtered off on a sintered glass funnel and was washed thoroughly with toluene. The filtrate was concentrated by distillation in vacuum. The residue was purified by repeated distillation. Yield 41 %.

2-Methoxyethoxy-diethyl-phosphine oxide. 42.0 g of diethyl-chloro-phosphine oxide in 100 ml of ether was added to a stirred suspension of 24.6 g of sodium methoxyethoxide in 50 ml of ether at such a rate that the mixture boiled gently towards the end of the addition. Afterwards the reaction mixture was refluxed for about one hour and treated

Table 1. Analytical data of the three alkoxy-diethyl-phosphine oxides,

$$C_2H_5-\underset{\underset{R'}{|}}{\overset{\overset{C_2H_5}{|}}{P}}=O$$
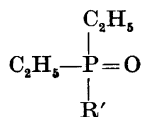
Compounds	R'	C in %		H in %		n_D^{25}	B.p. °C/mm Hg
		calc.	found	calc.	found		
Ethoxy-diethyl-phosphine oxide	C_2H_5O-	48.0	47.1	10.1	10.3	1.4301*	84/10*
2-Hydroxyethoxy-diethyl-phosphine oxide	HOC_2H_4O-	43.4	42.7	9.1	9.0	1.4582	90—94/0.1
2-Methoxyethoxy-diethyl-phosphine oxide	$CH_3OC_2H_4O$-	46.7	46.7	9.6	9.6	1.4431	70—75/0.05

* According to Ref. 7, n_D^{20} = 1.4301 and b.p. 91—92°C/14 mm Hg.

analogously to that described above. After evaporation of ether the residue was purified by two distillations. Yield 74 %.

The analytical data of the compounds synthesized are given in Table 1.

Kinetic measurements. The hydrolysis was followed by an acid-base titration method. All measurements were made in a water-bath maintained at 25.0 ± 0.1°C. The reaction was started by dissolving about 10 mmoles of the ester in 100.0 ml of approximately 0.15 or 0.45 M thermally equilibrated sodium hydroxide. To terminate the hydrolysis, aliquots (4 ml) were neutralized with hydrochloric acid (4 ml) of about the same concentration as the sodium hydroxide. The excess of acid was titrated with 0.0995 M sodium hydroxide to pH 7.0 using an automatic titrator, Radiometer Typ TTT 1a.

Because of small amounts of acid impurities in the esters, corrections of the initial concentration of the sodium hydroxide had to be made by extrapolation to zero time from a plot of time *versus* consumption of titrator. The actual concentration of ester was determined by titration at infinite time. The rate constants were calculated according to conventional second order kinetics. An example of a run is given in Table 2.

Infrared spectrophotometric measurements. The infrared spectra were recorded between 2 and 12 μm on a Perkin-Elmer spectrophotometer, Model 21, equipped with a rock salt prism. The thickness of the cell was 0.105 mm. The compounds were dissolved in carbon-tetrachloride in a concentration of 0.20 M. In addition, a 0.05 M solution of the hydroxyethoxy-derivative was recorded.

RESULTS AND DISCUSSION

The infrared spectrum of the 2-hydroxyethoxy derivative shows a sharp absorption band at 3300 cm^{-1} (3.03 μm) indicating a hydrogen bonded hydroxyl group. Evidence for intramolecular hydrogen bonding was obtained from the fact that fourfold dilution caused no frequency shift. Such a bond to the phosphoryl group is expected to be accompanied by a displacement of the

Table 2. The hydrolysis of ethoxy-diethyl-phosphine oxide at 25.0°C ($a-x$ and $b-x$ denote molarity of sodium hydroxide and ester, respectively).

t in min	$a-x$	$b-x$	$k \times 10^4$ l mole^{-1} sec^{-1}
0	0.1815	0.0849	—
50	0.1790	0.0824	0.565
130	0.1750	0.0784	0.580
180	0.1725	0.0759	0.592
235	0.1698	0.0732	0.604
300	0.1677	0.0711	0.569
1385	0.1380	0.0414	0.554
1440	0.1369	0.0403	0.556
1620	0.1328	0.0362	0.576
1670	0.1326	0.0360	0.563
1730	0.1313	0.0347	0.570
1790	0.1305	0.0339	0.567
2850	0.1191	0.0225	0.549
3000	0.1174	0.0208	0.559
3210	0.1155	0.0189	0.565

$$0.569 \pm 0.015$$

P=O band to lower frequencies. This was confirmed in the spectra; the P=O band at 1206 cm^{-1} (8.29 μm) in the ethoxy- and methoxyethoxy-derivatives shifted to 1188 cm^{-1} (8.42 μm) in the hydroxyethoxy compound.

From the data of Tables 2 and 3 it can be seen that the hydrolysis of the compounds follows second order kinetics. By substituting a 2-methoxyethoxy group for the ethoxy group, a more than fourfold increase of the rate of hydrolysis is obtained. This is consistent with what can be expected from the inductive effect of a methoxy group.[4] Concerning the 2-hydroxyethoxy derivative, it has been shown that an intramolecular hydrogen bond exists, and that its hydrolysis is more rapid than an inductive effect might explain. These two arguments support the hypothesis that such a hydrogen bond would act

Table 3. The rate constants at 25.0°C for the alkaline hydrolysis of the three esters.

Ester	C_{NaOH} mole/l	C_{ester} mole/l	$k \times 10^4$	l mole^{-1} sec^{-1}
Ethoxy-diethyl-phosphine oxide	0.1815	0.0849	0.569	
	0.4856	0.0885	0.577	0.573
2-Hydroxyethoxy-diethyl-phosphine oxide	0.1473	0.0708	4.50	
	0.1475	0.0710	4.39	4.42
	0.4204	0.0715	4.36	
2-Methoxyethoxy-diethyl-phosphine oxide	0.1856	0.0955	2.55	
	0.1849	0.0950	2.58	2.55
	0.4565	0.0950	2.53	

as an internal catalyst in making the phosphorus atom more positive, thereby facilitating a nucleophilic attack of a hydroxyl ion. By replacing the hydroxy group with the protonized species of an amino group the reactivity is considerably increased,[1,2] which is quite in accordance with the theory of internal catalysis; a hydrogen atom bonded to a positively charged atom will make a much stronger hydrogen bond.

Based upon some studies of the hydrolysis of acetates of cyclic alcohols, Bruice and Fife [4] have concluded that in this type of compounds the catalytic effect of a hydroxy group would involve an intramolecular hydrogen bond in the transition state, rather than in the ground state. The alkaline hydrolysis of organophosphorus esters is, however, considered as simple one-stage displacement reactions [1] as distinguished from that of the esters of carboxylic acids. Bruice and Fife's arguments are thus not directly relevant to organophosphorus esters and do not contradict that the internal catalysis depends upon a hydrogen bond in the ground state. From the data obtained in the present study it is, however, not possible to exclude a contribution to the increased reactivity from a hydrogen bond in the transition state, and the following mechanism is suggested for the hydrolysis of an organophosphorus ester containing a neighbouring hydroxyl group:
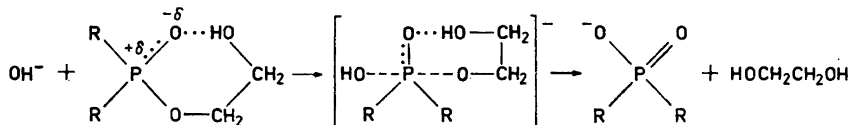
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