

## A Comparison between Hydrogen Bond Formation and the Acid Hydrolysis of Phosphoryl and Carbonyl Compounds

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The acid catalysed reactions of trialkylphosphites, diisopropyl fluorophosphate and acetamide are discussed in relation to their ability to form hydrogen bonds. Their special behaviour in acid hydrolysis, the decrease of the specific rate constant of the hydrogen ions with increasing concentration of acid, is assumed to be due to hydrogen bonding between the hydroxonium ions and the substrate.

In two previous papers<sup>1,2</sup> we have examined the very strong hydrogen bonds which are formed between phenol and the phosphoryl group in organophosphorus compounds and between phenol and the carbonyl group in N-diethylacetamide. In a third paper<sup>3</sup>, nucleophilic displacements on phosphorus are discussed. Evidence has been gathered that the chemical reactivity with regard to nucleophilic substitution on phosphorus depends strongly on both the polarity and the polarisability of the phosphorus compounds. The purpose of this paper is to examine the connection between the ability of hydrogen bond formation of some phosphoryl and carbonyl compounds and their chemical reactivity in acid catalysis.

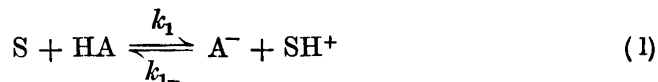
### PREVIOUS FINDINGS CONCERNING THE ACID HYDROLYSIS OF AMIDES AND ORGANOPHOSPHORUS COMPOUNDS

It has been known for a long time that the acid hydrolysis of amides and organophosphorus compounds show exceptional behaviour. Euler<sup>4</sup> showed that in the acid hydrolysis of acetamide the first order rate constant of the hydrogen ion catalysis increased less than directly proportional to the acid concentration. Later it was observed that this behaviour was a common feature of all amides<sup>5</sup>. Nylén<sup>6</sup> found that the acid catalysis of dialkylphosphites depended on the hydrogen ion concentration in the same way as

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for the amides. The same observation was made by Kilpatrick and Kilpatrick<sup>7</sup> in their study of the acid catalysis of diisopropylfluorophosphate.

Euler explained the results from his ionization theory of catalysis<sup>8</sup>. He considered the substrate (S) and the acid HA to be in equilibrium with the conjugated acid SH<sup>+</sup> of the substrate:



The rate of hydrolysis was then determined by the rate of splitting of SH<sup>+</sup>



He assumed that the base strength of S was of the same order as A<sup>-</sup>, i.e.  $k_1 \sim k_{1-}$ . If now  $k^* \ll k_{1-}$  it is easily found that the observed rate of hydrolysis ( $k_{\text{obs}}$ ) is satisfied by the following equation

$$k_{\text{obs}} = \frac{k^* \cdot H^+ \cdot K_B}{1 + H^+ \cdot K_B} \quad (3)$$

where  $k^*$  is the specific rate constant of the hydrogen ions. H<sup>+</sup> is the concentration of hydrogen ions.  $K_B$  is the base constant of the substrate defined as:  $K_B = K_1/K_w$ , where  $K_1$  is the ionization constant of the base referred to water solution, and  $K_w$  is the ion product of water.

When eqn. (3) above is rearranged we get:

$$\frac{k_{\text{obs}}^{\text{obs}}}{H^+} = -k_{\text{obs}} \cdot K_B + k^* \cdot K_B \quad (4)$$

We find therefore that  $k_{\text{obs}}/H^+$  shall vary linearly with  $k_{\text{obs}}$ . The slope of the line is equal to  $K_B$ .

The experimental data of Euler<sup>4</sup>, Nylén<sup>6</sup>, Kilpatrick and Kilpatrick<sup>7</sup> obey all a linear relation according to eqn. (4). In Table 1 are recorded the base constants of different substrates calculated according to eqn. (4).

Table 1.  $K_B$ -values calculated from reaction kinetic data (eqn. 4).

Compound	Constant ionic strength: 4.00			HCl, ionic strength: 0–0.3
	HCl + NaCl	HBr + NaBr	HClO <sub>4</sub> + NaClO <sub>4</sub>	
Dimethyl-phosphite	~0.5	0.3	0.5	~0.5
Diethylphosphite	1.1	1.3	1.3	~0.7
Di- <i>n</i> -propyl phosphite	1.6	1.7	1.7	~0.9
Diisopropyl-phosphite	1.9	1.8	1.8	~2.0
Diisopropyl-fluorophosphate	—	—	—	2.2
Acetamide	—	—	—	0.7

Table 2. Association constants between phenol and different compounds in  $\text{CCl}_4^{1,2}$ .

Compound	Association constant l/mole, 20°C
Dimethylphosphite	123
Diethylphosphite	167
Di- <i>n</i> -propylphosphite	200
Diisopropylphosphite	237
N-Diethylacetamide	170

## HYDROGEN BOND ASSOCIATION CONSTANTS

In Table 2 are recorded the association constants for the hydrogen bond association between phenol and dialkylphosphites and between phenol and N-diethylacetamide in carbon tetrachloride <sup>1,2</sup>.

From the presence of the stretching vibration band of the phosphoryl group and its displacement upon hydrogen bonding we conclude that the dialkylphosphites have phosphoryl structure and that it is the P=O bond which participates in hydrogen bonding <sup>3</sup>.

THE CONNECTION BETWEEN  $pK_B$  OF SOLVENTS AND THE FREQUENCY SHIFT OF THE O—D BAND IN THE SAME SOLVENTS

Gordy <sup>4</sup> has shown that there exist a simple relation between the basicity of solvents and their ability to form hydrogen bonds. He observed that the frequency shifts of the O—D stretching band of deuterium alcohol and deuterium oxide in different basic solvents are proportional to the  $pK_B$  of the solvents. In Fig. 1 are reproduced his observations of the frequency shift of the O—D stretching band of deuterium oxide in 19 different solvents. The equation of the line is according to Gordy <sup>4</sup>:

$$\Delta\mu = 0.0175 \log K_B + 0.297 \quad (5)$$

where  $\Delta\mu$  is the frequency shift of the O—D band.  $K_B$  is defined as:  $K_B = K_1/K_W$ , where  $K_1$  is the ionization constant of the base referred to water solution and  $K_W$  is the ion product of water.

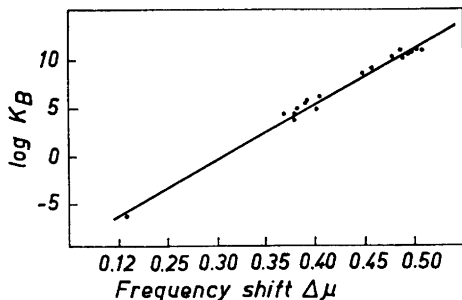


Fig. 1. Relation of basicity constants of solvent to their shifts of the vibrational band of  $\text{D}_2\text{O}$ . (Reproduced from the paper of Gordy <sup>4</sup>). Lowest point in fig.: acetophenone; middle points in fig.: pyridine and aniline derivatives; upper points in fig.: aliphatic and alicyclic amines.

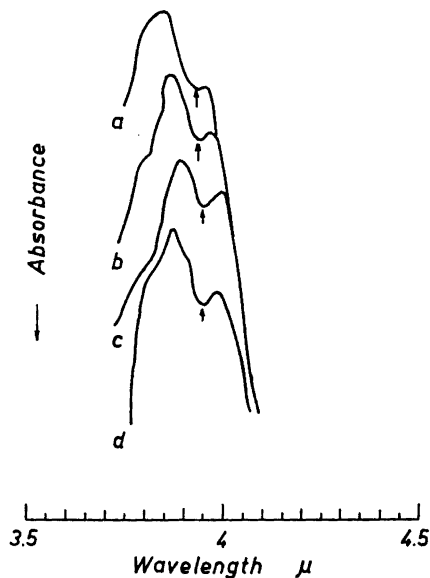


Fig. 2. The vibrational bands of  $D_2O$  in dialkylphosphites. a) Dimethylphosphite, b) diethylphosphite, c) dipropylphosphite, d) diisopropylphosphite.

We have used this equation to estimate the apparent basicity constants of the trialkylphosphites, diisopropylfluorophosphate and acetamide. In Fig. 2 are shown the absorption bands of the O—D stretching vibration of deuterium-oxide when it is dissolved in the different dialkylphosphites. Due to the broadness of the O—D band it is difficult to get a very accurate measure of the O—D displacement, but there is a distinct increase of  $\Delta\mu$  of the O—D band from dimethyl to diisopropylphosphite. The calculated basicity constants are recorded in Table 3.

#### DISCUSSION

If we compare the basicity constants calculated from eqn. (4) in Table 1 with the basicity constants of the compounds determined from the frequency shift of the O—D band in Table 3, we find in both cases  $K_B$  values of the same order of magnitude. The  $K_B$  values calculated from the kinetic data show the ordinary variation with ionic strength. None of the methods can be expected to give very accurate values of  $K_B$ . The  $K_B$  values of the dialkylphosphites calculated from the kinetic measurements indicate an increase in basicity of the dialkylphosphites from dimethyl- to diisopropylphosphite. This is in agreement with the determined association constants between phenol and dialkylphosphites in carbon tetrachloride recorded in Table 2. The same general tendency is shown by the  $K_B$ -values of the dialkylphosphites determined by the frequency shift method in Table 3.

The kinetic picture given by Euler<sup>4,8</sup> is apparently in good agreement with the above results. But there is a serious objection to the application of the theory of Euler. If there existed a proton transfer equilibrium between the

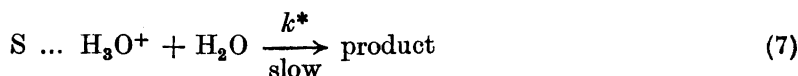
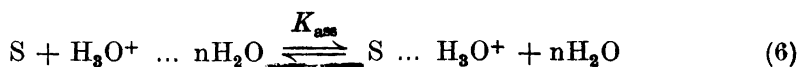
Table 3.  $K_B$ -values calculated from the frequency shift of the stretching band (eqn. 5).

Compound	$\Delta\mu$ of O—D band	Calculated $K_B$
Dimethylphosphite	0.282	0.2
Diethylphosphite	0.290	0.4
Di- <i>n</i> -propylphosphite	0.295	0.8
Diisopropylphosphite	0.300	1.5
Acetamide	0.285	0.3
Diisopropylfluoro-phosphate	0.300	1.5

hydrogen ions and the substrate we should expect a measurable change in the pH of the solution when the substrate is dissolved in water.

Nylén<sup>6</sup> was unable to find any significant change in the pH of water solutions of dialkylphosphites. We have repeated the pH-measurements not only for the dialkylphosphites but also for the extremely strong hydrogen bonding substrate trimethylphosphine oxide which, according to the relation found by Gordy<sup>9</sup>, should have a  $K_B$  value of approximately  $10^4$ . In none of the cases have we been able to demonstrate the expected changes in the pH of their water solutions.

We conclude therefore that the observed reaction kinetics do not deal with proton transfer equilibrium but with hydrogen bond equilibrium. The following kinetic scheme is postulated:



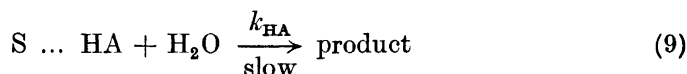
The reaction (6) shows that the substrate due to its tendency of hydrogen bond formation will compete with water in capturing hydroxonium ions. The kinetics of the reaction will be the same as in theory of Euler<sup>4</sup>. The difference lies in the meaning of the equilibrium constants.  $K_{ass}$  in eqn. (6) is not the base constant of the substrate but the hydrogen bond association constant between substrate and hydroxonium ions relative to that of water. But since the hydrogen ions are not lost from the water to the substrate through a proton transfer reaction but are only gathered in the neighbourhood of the substrate due to hydrogen bonding, we cannot expect the same influence on the acidity in the last case as compared with a proton transfer reaction. It seems more correct to speak about a small influence upon the activity of the hydrogen ions due to their hydrogen bonding with the substrate.

The hydrolysis of dialkylphosphites and diisopropylfluorophosphate shows general acid catalysis<sup>6,7,10</sup>. This observations are in complete agreement with

the postulated reaction scheme. In this case one will in addition to the equilibrium reaction (6) have to include an equilibrium reaction of the general type:

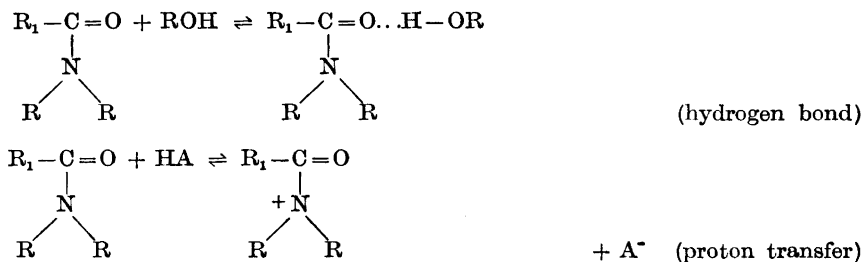


where HA means an undissociated acid, and



where  $k_{HA}$  is the rate constant of hydrolysis due to the undissociated acid.

The hydrolysis of amides gives also support to the hydrogen bond mechanism of hydrolysis. It was mentioned in a previous paper<sup>1</sup> that it is the C=O bond in amides which participates in hydrogen bonding, but when a sufficiently strong acid is used to produce a proton transfer reaction the proton is captured by the nitrogen:



Now it is known that the rate of acid hydrolysis of amides goes through a maximum at about 5–6 M acid<sup>5</sup>. The maximum in rate has been explained as caused by the drop of water concentration (or of its activity) at high acid concentrations<sup>5</sup>.

Lately it has been observed that the amides in nearly water-free strong acids are also hydrolysed at a relative high rate and that the rate decreases upon adding small amounts of water<sup>11</sup>.

The only reasonable explanation of this behaviour is that there exists two different mechanisms of hydrolysis of the amides. In water-free strong acids all of the amides will exist in the protonised form with the proton attached to the nitrogen. The splitting of the protonised form in concentrated acids will most likely be a unimolecular reaction which is retarded in the presence of too much water. The logical interpretation of the hydrolysis of amides in dilute water solution (which are the measurements referred to in this paper) is therefore that the reaction follows a bimolecular reaction scheme (A-2) according to eqns. (6) and (7) where the C=O group participates in a hydrogen bond equilibrium reaction with the hydroxonium ions.

The phosphoryl and carbonyl compounds discussed in this paper show a common feature in their strong ability of hydrogen bond formation. It seems unlikely that other carbonyl and phosphoryl compounds with less polar C=O or P=O bonds should behave in a different manner. But their hydrogen bond

association constants with hydroxonium ions should be expected to be so small that the measured rate constants will appear to be proportional to the acid concentration. From the paper of Gordy<sup>9</sup> we find that the O—D shift,  $\Delta\mu$ , of deuterium oxide in ethylacetate is 0.21, which corresponds to an apparent  $K_B$ -value of approximately  $10^{-5}$ . Such a low  $K_B$ -value inserted in eqn. (3) will not give observable deviation of  $k_{\text{obs}}$  from proportionality. A consequence of this view is that the acid catalysed reaction of compounds where the C=O or P=O bonds are attacked by the acid previous to the formation of the transition state should be expected to belong to the bimolecular reaction scheme (A-2). This follows from eqn. (7).

In a previous paper<sup>12</sup> where the acid hydrolysis of quaternary ammonium esters were studied, it was found that the carbonyl oxygen was attacked by the hydroxonium ions during the hydrolysis of the esters. There is now convincing evidence that the hydrolysis of aliphatic esters belong to a bimolecular mechanism (A-2)<sup>13</sup>. The hydrolysis of esters will therefore fit into the reaction scheme proposed in this paper.

Direct evidence for an acid catalysed ester hydrolysis by the unimolecular mechanism (A-1) was obtained in the hydrolysis of esters of mesoic acids<sup>14</sup> (2,4,6-trimethylbenzoic acid). These esters give with concentrated strong acids benzoylum ions. But this observation proves that the proton transfer reaction in this case must have occurred at the ether oxygen of the esters.

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Received February 8, 1960.