# THE EFFECT OF PRESSURE ON THE SPONTANEOUS HYDROLYSIS OF ACETYL PHOSPHATE MONO-ANION AND DI-ANION AND OF ACETYL PHENYL PHOSPHATE MONO-ANION

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# THE EFFECT OF PRESSURE ON THE SPONTANEOUS HYDROLYSIS OF ACETYL PHOSPHATE MONO-ANION AND DI-ANION AND OF ACETYL PHENYL PHOSPHATE MONO-ANION[1]

G. Di Sabato,[2] W. P. Jencks,[2] and E. Whalley[3]

The spontaneous hydrolysis of acetyl phosphate mono-anion and di-anion and of acetyl phenyl phosphate has been studied in a number of ways in order to determine the mechanisms (1). The effect of pressure on the rates of reactions in solution has been used

to help determine mechanisms (2). In this note the effect of pressure up to about 2.5 kilobars on the rates of hydrolysis of acetyl phosphate mono-anion and di-anion and of acetyl phenyl phosphate is described and the results are discussed in relation to the mechanisms.

## EXPERIMENTAL METHODS AND RESULTS

The analytical and high-pressure techniques have been described in previous papers (1, 3). The buffer solutions were as described by Di Sabato and Jencks (1); the effect of pressures up to 2.5 kilobars on the pH of the buffers is not enough to change significantly the relative concentrations of the ions of the substituted phosphates. The first-order rate constants are listed in Table I, and shown graphically in Fig. 1. The accuracy is about 5%.
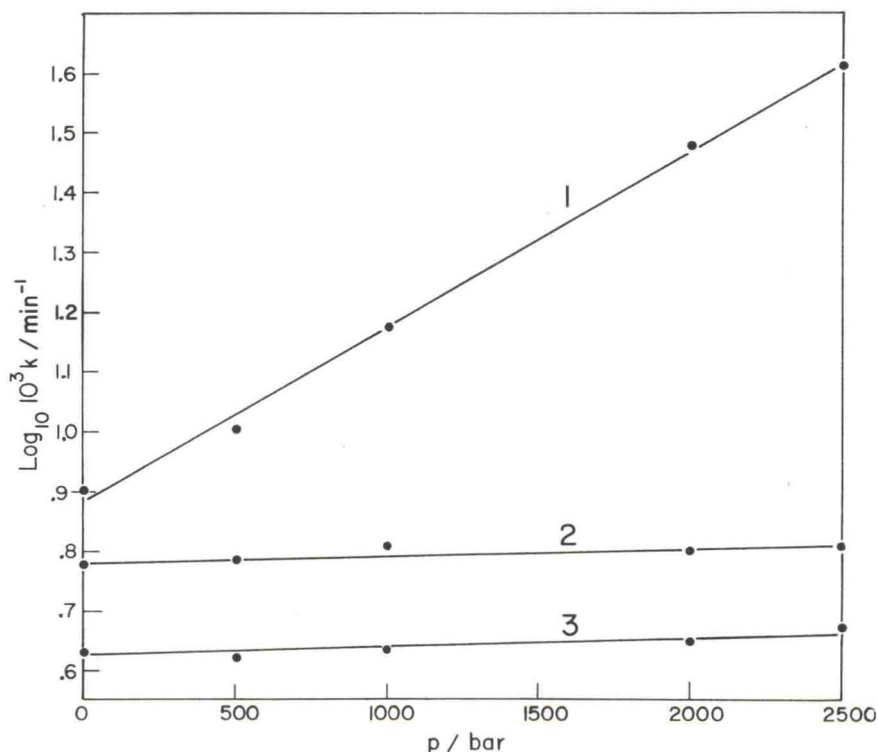


FIG. 1. Effect of pressure on the spontaneous hydrolysis of: curve 1, acetyl phenyl phosphate mono-anion at 60° C, ordinate increased 0.9 units; curve 2, acetyl phosphate mono-anion at 39° C, ordinate decreased 0.4 units; curve 3, acetyl phosphate di-anion at 39° C.

The volumes of activation $\Delta V\ddagger$ at zero pressure calculated from the usual relation $\partial \ln k/\partial p = -\Delta V\ddagger/RT$ are as follows:

| | |
|---|---|
| acetyl phosphate mono-anion | $-0.6\pm\sim1.0$ cm³ mole⁻¹ at 39° C |
| acetyl phosphate di-anion | $-1.0\pm\sim1.0$ cm³ mole⁻¹ at 39° C |
| acetyl phenyl phosphate mono-anion | $-19\pm\sim2$ cm³ mole⁻¹ at 60° C |

## DISCUSSION

The main mechanisms of hydrolysis to be considered appear to be a unimolecular decomposition of the anion, a bimolecular reaction of water with the anion, and a bimolecular reaction of hydroxide ion with the conjugate acid of the anion.

TABLE I

Spontaneous hydrolysis of acetyl phosphate mono-anion and di-anion
and of acetyl phenyl phosphate

| Substrate | Temperature/°C | $p$/kilobar | $10^3 k$/min$^{-1}$ |
|---|---|---|---|
| Acetyl phosphate di-anion*† | 39.0 | 0 | 4.20, 4.39 |
| | | 0.5 | 4.19, 4.15 |
| | | 1.0 | 4.32, 4.26 |
| | | 2.0 | 4.41, 4.47 |
| | | 2.5 | 4.59, 4.35 |
| Acetyl phosphate mono-anion†‡ | 39.0 | 0 | 15.3, 15.0 |
| | | 0.5 | 15.5, 15.0 |
| | | 1.0 | 15.9, 16.5 |
| | | 2.0 | 15.6, 16.0 |
| | | 2.5 | 15.9, 15.6 |
| Acetyl phenyl phosphate mono-anion†§ | 60.0 | 0 | 1.00, 1.01 |
| | | 0.5 | 1.33, 1.19 |
| | | 1.0 | 1.87 |
| | | 2.0 | 3.82, 3.71 |
| | | 2.5 | 5.43, 5.30 |

*Potassium phosphate buffer, 0.1 $M$, pH 6.7 at 1 atm.
†Ionic strength brought to 0.6 with KCl.
‡Potassium formate buffer, 0.2 $M$, pH 2.9 at 1 atm.
§Potassium phenyl phosphate buffer, 0.1 $M$, pH 4.8 at 1 atm. Control experiments showed no hydrolysis of the buffer under the experimental conditions employed.

The spontaneous hydrolyses of acetyl phosphate mono-anion and di-anion occur with P—O bond cleavage (4, 5). The volumes of activation are $-0.6 \pm \sim 1.0$ cm$^3$ mole$^{-1}$ for the mono-anion and $-1.0 \pm \sim 1.0$ cm$^3$ mole$^{-1}$ for the di-anion. If the mechanisms involved the attack of water on the phosphorus atom, then the volumes of activation should be considerably more negative because volume would be lost due to the formation of a partial valence bond and to a possible increased polarity. If the mechanism involved a reaction of hydroxide ion with the conjugate acid of the phosphate ion then, from arguments similar to those developed below for acetyl phenyl phosphate mono-anion, a large negative volume of activation would also be expected. For the di-anion, therefore, the mechanism is probably a unimolecular decomposition to give metaphosphate ion (1):

$$CH_3CO_2PO_3{}^{2-} \xrightarrow{\text{slow}} CH_3CO_2{}^- + PO_3{}^- \xrightarrow[\text{fast}]{H_2O} H_2PO_4{}^-, \qquad [1]$$
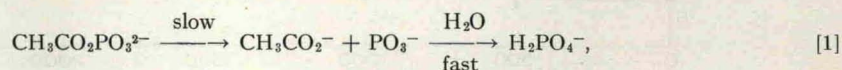
as is suggested (6–8) for the hydrolysis of phosphate monoester mono-anions. For the mono-anion, both a similar mechanism,

$$CH_3CO_2PO_3H^- \xrightarrow{\text{slow}} CH_3CO_2{}^- + HPO_3 \xrightarrow[\text{fast}]{H_2O} H_2PO_4{}^- + H^+, \qquad [2]$$
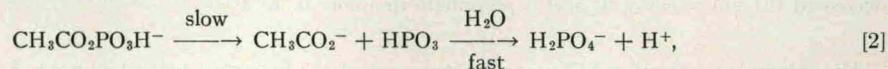
and one in which a proton has been transferred to the leaving acetate group and the transition state is close to acetic acid and metaphosphate ion are consistent with the volume of activation.

The hydrolysis of acetyl phenyl phosphate mono-anion in 90% aqueous methanol occurs with C—O bond cleavage (1) and we shall assume that this also occurs in aqueous solution. The rate is decreased 2.5-fold in deuterium oxide solution (1) and the entropy and volume of activation are, respectively, $-28.8$ cal deg$^{-1}$ mole$^{-1}$ (1) and $-19$ cm$^3$ mole$^{-1}$. The volume of activation does not allow us to distinguish between the possible

mechanisms, as the following considerations show. A unimolecular decomposition to give acylium ion:

$$CH_3COOPO_3C_6H_5^- \rightarrow CH_3CO^+ + C_6H_5OPO_3^{2-}, \tag{3}$$

is consistent with the volume and entropy of activation, because the polarity is greatly increased in the transition state. However, the relatively large effect of solvent deuterium oxide, which seems to require that at least one O—H (O—D in deuterium oxide) bond be strongly modified in the transition state, and the great stability of benzoyl phenyl phosphate (9) are difficult to explain by this mechanism. A bimolecular reaction involving solvent could proceed through transition states I, II, III, or IV, which differ in the position

$$
\begin{array}{cc}
& \text{O} \quad\quad \text{O}^- \\
\delta+ & \| \quad \delta- \quad | \\
H_2O...\text{C}...\text{O}-\text{P}-OC_6H_5 \\
& | \quad\quad \| \\
& \text{CH}_3 \quad\quad \text{O} \\
& \text{I}
\end{array}
\qquad
\begin{array}{cc}
& \text{OH}^+ \quad\quad \text{O}- \\
\delta- & \| \quad (1-\delta)- \quad | \\
HO...\text{C}...\text{O}\!-\!\!-\!\!-\text{P}-OC_6H_5 \\
& | \quad\quad\quad \| \\
& \text{CH}_3 \quad\quad\quad \text{O} \\
& \text{II}
\end{array}
$$

$$
\begin{array}{cc}
& \text{O} \quad\quad \text{O}- \\
\delta- & \| \quad \delta+ \quad | \\
HO...\text{C}...\text{OH}-\text{P}-OC_6H_5 \\
& | \quad\quad \| \\
& \text{CH}_3 \quad\quad \text{O} \\
& \text{III}
\end{array}
\qquad
\begin{array}{cc}
& \text{O} \quad\quad \text{OH} \\
\delta- & \| \quad (1-\delta)- \quad | \\
HO...\text{C}...\text{O}\!-\!\!-\!\!-\text{P}-OC_6H_5 \\
& | \quad\quad\quad \| \\
& \text{CH}_3 \quad\quad\quad \text{O} \\
& \text{IV}
\end{array}
$$
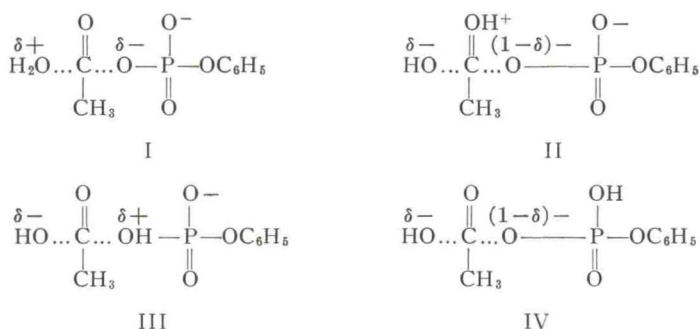
of a proton. Each has, of course, resonating forms. The structures might be further modified if the incoming group adds rather than substitutes, as has been suggested (10) for some carboxyl reactions, and if several water molecules are incorporated into the transition state to aid in proton transfer (1, 11). All of these mechanisms appear to be consistent with the volume of activation and other (1) data. It is interesting to compare the experimental data with calculated values for a special case of mechanism IV, according to reactions [4] and [5]:

$$CH_3COOPO_3C_6H_5^- + H_2O \underset{}{\overset{fast}{\rightleftharpoons}} CH_3COOPO_3HC_6H_5 + OH^- \tag{4}$$

$$CH_3COOPO_3HC_6H_5 + OH^- \overset{slow}{\longrightarrow} CH_3COOH + C_6H_5PO_4H^-. \tag{5}$$

It seems likely that the volume and entropy change and the deuterium isotope effect of reaction [4] will be similar to those for the reaction

$$H_2PO_4^- + H_2O \rightleftharpoons H_3PO_4 + OH^-, \tag{6}$$
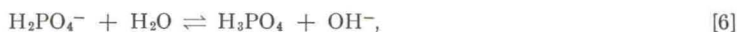
and those for reaction [5] will be similar to those for the alkaline hydrolysis of esters, in which a hydroxide ion also attacks an acetate group:

$$CH_3COOR + OH^- \rightarrow CH_3COOH + OR^-. \tag{7}$$

The thermodynamic parameters for reaction [6] can be obtained from those for the reactions

$$H_3PO_4 \rightleftharpoons H_2PO_4^- + H^+ \tag{8}$$

and

$$H_2O \rightleftharpoons H^+ + OH^-. \tag{9}$$

The data are given in Table II. They are mostly for temperatures near 25° C but this should not affect the conclusions in any important way. It is clear that the volume and entropy of activation and the deuterium isotope effect are quantitatively consistent with the mechanism given in reactions [4] and [5].

TABLE II

| Reaction No. | $\Delta V$/cm³ mole⁻¹ | | $\Delta S$/cal deg⁻¹ mole⁻¹ | | $K_H/K_D$ or $k_H/k_D$ | |
|---|---|---|---|---|---|---|
| 8 equil. | −15.1 | (12) | −15.6 | (15, p. 758) | 1.61 | (17) |
| 9 equil. | −23.4 | (13) | −18.7 | (15, p. 667) | 5.43 | (17–19) |
| 6 equil. | −7.9 | | −3.0 | | 3.37 | |
| 7 rate | −9 | (14) | −27 | (16) | 0.75 | (20) |
| 4 and 5 rate, expected value | −17 | | −30 | | 2.53 | |
| Exptl. value | −19± ∼2 | (this work) | −28.8 | (1) | 2.5 | (1) |

NOTE: $K_H/K_D$ and $k_H/k_D$ are the ratio of equilibrium and rate constants in $H_2O$ and $D_2O$.

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