KINETICS AND MECHANISM OF HYDROLYSIS OF MONO-p-IODO BENZYL PHOSPHATE (MONO AMMONIUM SALT)

M. M. MHALA AND A. V. KILLEDAR*

School of Post-Graduate Studies and Research in Chemistry, Jiwaji University, Gwalior

ABSTRACT

Hydrolysis of mono-p-iodobenzyl phosphate has been investigated in buffer solutions ranging from pH 1·00 to 8·04 at 80° C. Both neutral and mononegative species have been discovered as reactive species whose zones are demarkated in pH-log rate profile. Unlike monoaryl phosphates, mono-p-iodo benzyl phosphate does not show distinct maximum at ~ pH 4. Reactivity of the ester in buffer solutions decreases considerably than in acidic medium. Theoretical rates estimated from presumed pK values have been found to be in close agreement with the experimental rates. pK values have also been used to isolate rates of different species by determining their fractions. Arrhenius parameters, isokinetic relationship and comparative kinetic rate data have been used to propose the probable mechanism of the reaction.

THE importance of phosphoric acid derivatives and the role of phosphate linkages in Biochemistry are well understood. Consistently the kinetics of reactions of simple organic phosphates provides an insight into more complicated reactions occurring during their metabolism. Monoaryl phosphates hydrolyse rapidly at about pH 4 involving P–O fission of monoanions. Dianions of dinitrophenyl and o-carboxyl phenyl phosphates have been shown to be more reactive than their monoanions[1]. Very little is known about the behaviour of benzyl phosphates[2]. There is almost no record about the synthesis and kinetic study of hydrolysis of mono-p-iodo benzyl phosphate. Due to structural differences mono-p-iodo benzyl phosphate is expected to exhibit entirely different reaction paths than those envisaged for mono alkyl and aryl phosphates.

MATERIALS AND METHODS

Mono-p-iodo benzyl phosphate (mono ammonium salt) was prepared[3,4] by the step-wise degradation of Tri-p-iodo benzyl ester (Found : P = 9·28%, N = 4·41%, C = 24·82% and H = 3·28%, $C_7H_{11}PO_4NI$ requires : 9·36%, 4·23%, 25·40% and 3·35% respectively). The hydrolysis of mono-p-iodo benzyl phosphate (mono ammonium salt) (0·0005 M) was followed by colorimetric estimation of inorganic phosphate by the method of Allens[5]. Interpolated values of buffers at 80° determined from the work of Stenc[6] were used. All the chemicals used were of B.D.H. (A.R.) quality.

RESULTS AND DISCUSSION

Hydrolysis via neutral species.—The rate of hydrolysis of mono-p-iodo benzyl phosphate in the region pH 1·0 to 2·0 (Fig. 1) is represented by

$$k_e = k_{N_0} \cdot \frac{N}{N+M} + k_{M_0} \cdot \frac{M}{N+M} \qquad (1)$$

where k_e, k_{N_0} and k_{M_0} are total rate, specific neutral rate and specific mononegative rate respectively ; N/N+M and M/N+M are the fractions of neutral and mononegative species respectively. The calculated k_{N_0} value is $6·25 \times 10^{-4}$ min.$^{-1}$, which is different from the mononegative rate ($k_{M_0} = 1·33 \times 10^{-4}$ min.$^{-1}$) and the specific acid catalysed rate ($k_{H_0}^+ = 39·8 \times 10^{-4}$ min.$^{-1}$).
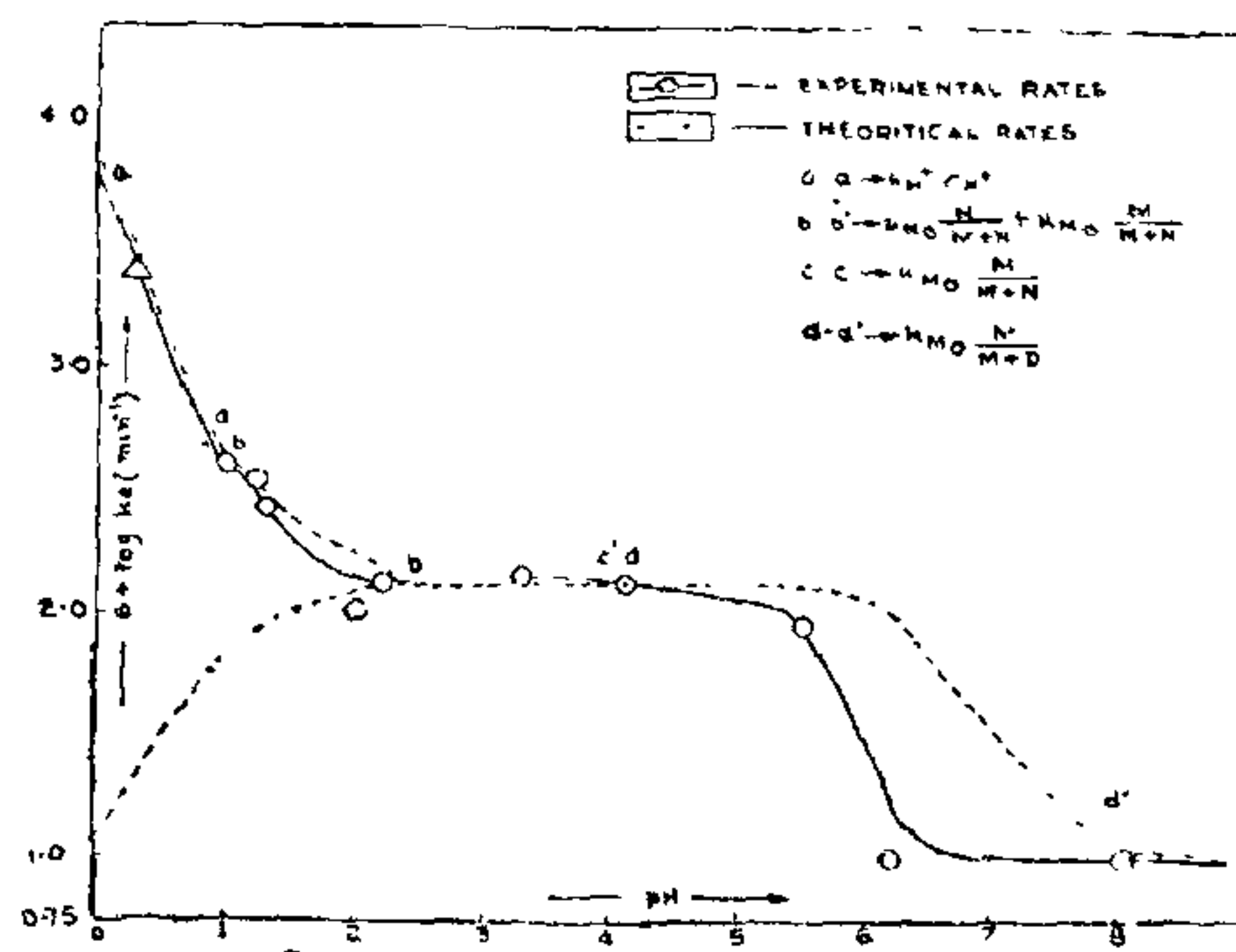

FIG. 1. pH log rate profile for the hydrolysis of mono-p-iodo benzyl phosphate at 80° C (Δ rate at 0·5 M HCl acid).

Table I shows the agreement between the estimated and observed rates. The slope of the linear plot in this region is almost unity indicating that monoprotonated form of the bulk mononegative species (Neutral) are reactive[7].

Effects of factors such as temperature solvent, etc., on the rate of reaction via neutral species could not be determined due to the concomitant hydrolysis of mononegative species in this region and due to negligible contribution of this reaction in acid region, because of the masking of this reaction by acid catalysis[8]. The neutral species

---

* Lecturer in Chemistry, Government College, Dholpur (Raj.).

TABLE I

Calculated and observed rates for the hydrolysis of mono-p-iodo benzyl phosphate at 80° C (From pK_1)

pH	$\dfrac{M}{N+M}$	$\dfrac{10^4 k_M}{(min.^{-1})}$	$\dfrac{N}{N+M}$	$\dfrac{10^4 k_N}{(min.^{-1})}$	$6 + \log k_e$ Calcd.	$6 + \log k_e$ Obsd.
1·00	0·500	0·67	0·500	3·12	2·58	2·59
1·23	0·629	0·84	0·371	2·32	2·50	2·54
1·30	0·666	0·89	0·334	2·09	2·47	2·42
2·00	0·909	1·21	0·091	0·56	2·25	2·00
2·29	0·941	1·26	0·059	0·37	2·21	2·11
3·30	0·961	1·28	0·039	0·24	2·18	2·15
4·00	0·999	1·33	0·001	..	2·12	2·11

of the ester is more likely to be cleaved at C–O linkage rather than P–O bond, as the *p*-iodo benzyl cation formed subsequently as the reaction intermediate would be greatly stabilised by the +M (electron releasing) effect of the iodosubstituent. This view is substantiated from the comparative kinetic data of other related monoesters (Table II). Mechanism of the hydrolysis of monoester via neutral species may therefore be represented as shown in Chart 1.
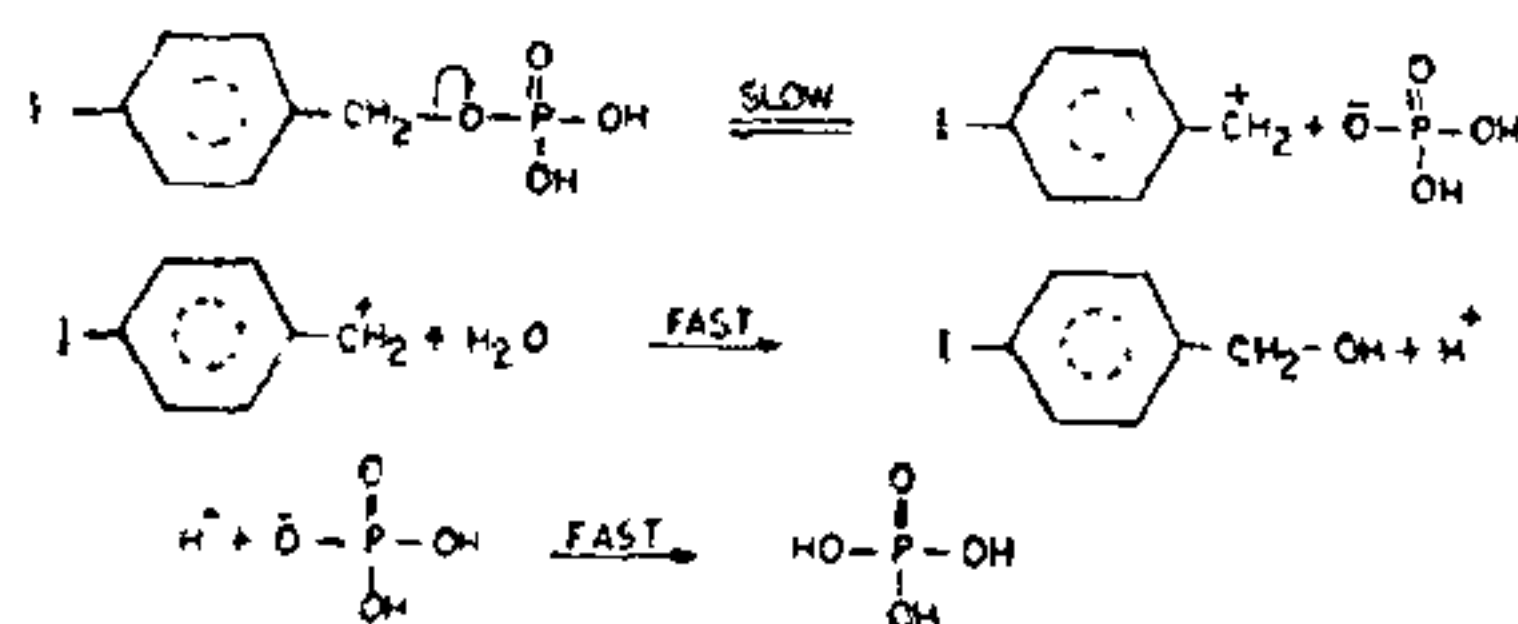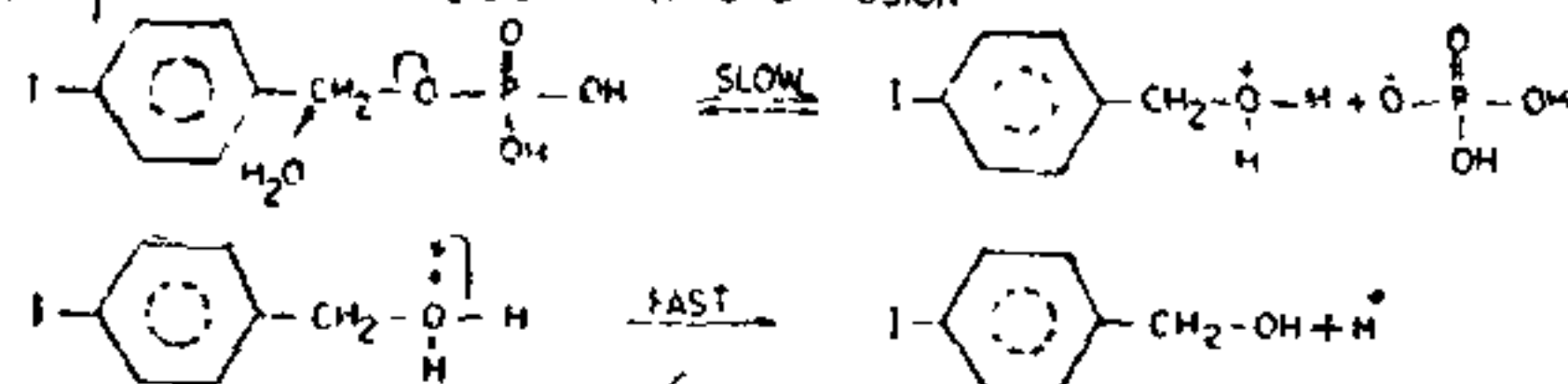

CHART 1. Probable reaction paths for the hydrolysis of mono-*p*-iodo benzyl phosphate *via* neutral species.

TABLE II

Comparative rate data for the hydrolysis of monophosphate esters via neutral species
Solvent—Water

Phosphate ester	$k_{N_0} \times 10^4$ (min.$^{-1}$)	Temp. °C	pK_1 value	Bond Fission
Methyl[9]	0·30	100·1	1·6	C–O
Benzyl[2]	0·60	75·6	..	C–O*
p-Iodo benzyl	6·25	80·0	1·00	C–O*
Allyl[10]	6·20	80·0	1·00	C–O*

* Fission presumed.

Hydrolysis via mononegative species.—The ester differs from aryl phosphates in not showing a distinct maximum at ~ pH 4. The dissociation constant value ($pK_1 = 1·00$) of the ester has been calculated by considering the following equilibrium and presuming the hydrolysis of monoester to be exclusively *via* monoanion at pH 4 :

Neutral species $\rightleftharpoons$ Mononegative species + H$^+$

$$\frac{K_1}{K_1 + H^+} = \frac{M}{M + N} \cdot \tag{2}$$

Theoretical rates *via* neutral and mononegative species are estimated as follows :

$$k_N = k_{N_0} \cdot \frac{N}{N + M} \qquad k_M = k_{M_0} \cdot \frac{M}{N + M} \cdot \tag{3}$$

Table I summarises the estimated and observed rates. Unlike aryl phosphates, the monoanion of this ester is considerably less reactive than its conjugate acid species ($k_{M_0} = 1·33 \times 10^{-4}$ min.$^{-1}$ while $k_{B_0}^+ = 39·8 \times 10^{-4}$ min.$^{-1}$).

In the region pH 4 to 8, the presumption of dissociation of monoanion into dianion and a proton ($pK_2 = 7·00$) permits estimation of the rates of mono and dinegative species. Results (Table III) show that the reaction is exclusively governed by mononegative species.

TABLE III

Calculated and observed rates for the hydrolysis of mono-p-iodo benzyl phosphate (From pK_2)

pH	$\dfrac{M}{M+D}$	$\dfrac{D}{M+D}$	$\dfrac{10^4 k_M}{(min.^{-1})}$	$6 + \log k_e$ (Calcd.)	$6 + \log k_e$ (Obsd.)
4·12	0·999	0·001	1·33	2·12	2·11
5·51	0·969	0·031	1·29	2·11	1·98
6·20	0·863	0·137	1·15	2·06	1·04
8·04	0·084	0·916	0·11	1·04	1·04

Arrhenius parameters (Fig. 2) for the hydrolysis at pH 4·12 have been found to be $\triangle$ S‡ = — 17·37
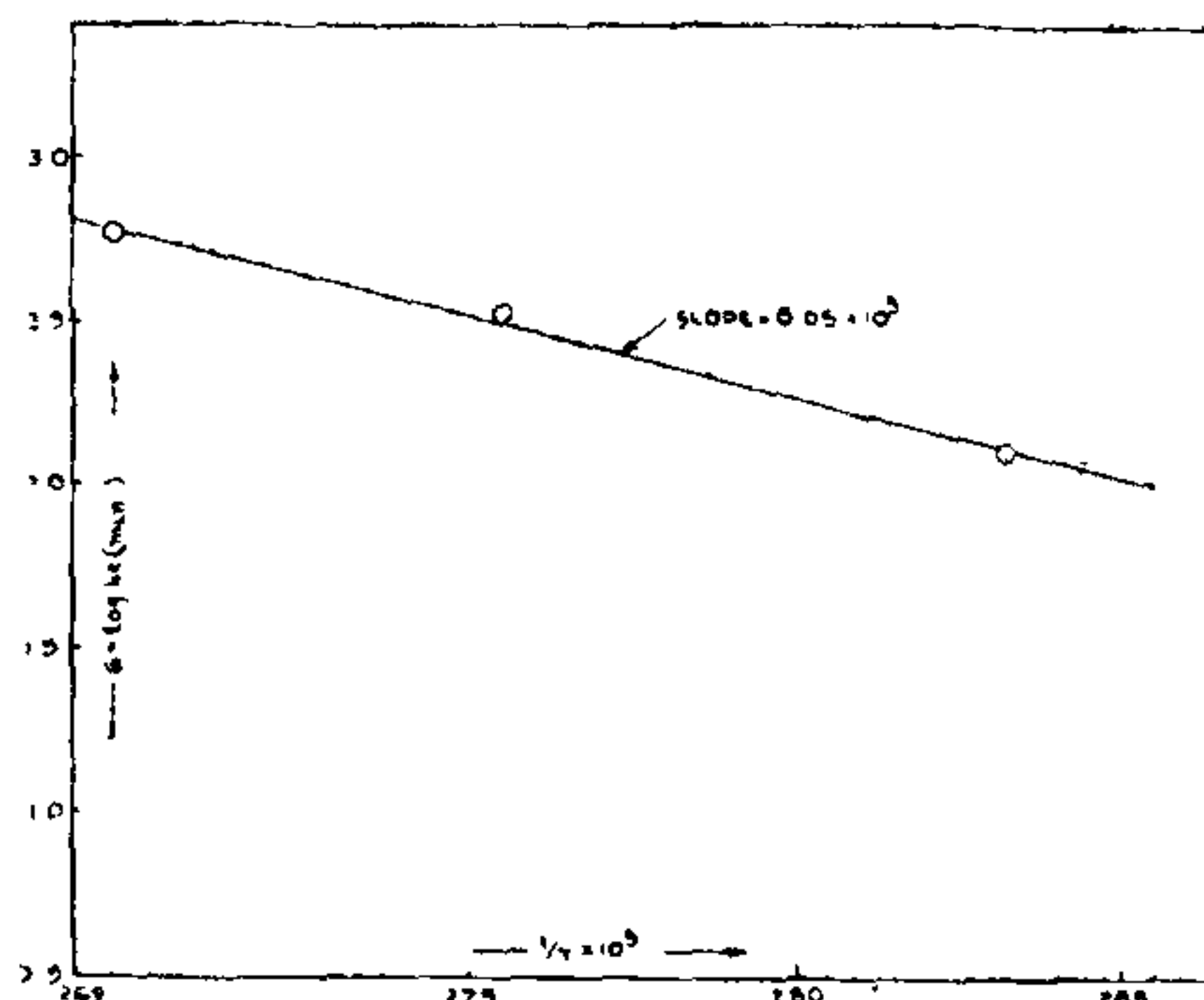

FIG. 2. Arrhenius plot for the hydrolysis of mono-*p*-iodo benzyl phosphate at 4·12 pH.

e.u., $E = 22.89$ K.cal/mole and frequency factor $= 3.20 \times 10^9$ sec.$^{-1}$. These results are consistent with bimolecular[11] nature of the reaction. The monoanions of both alkyl and aryl phosphates have been shown to hydrolyse exclusively *via* phosphorus-oxygen bond fission[12,13]. Isokinetic relationship (Fig. 3) shows a linear plot suggesting
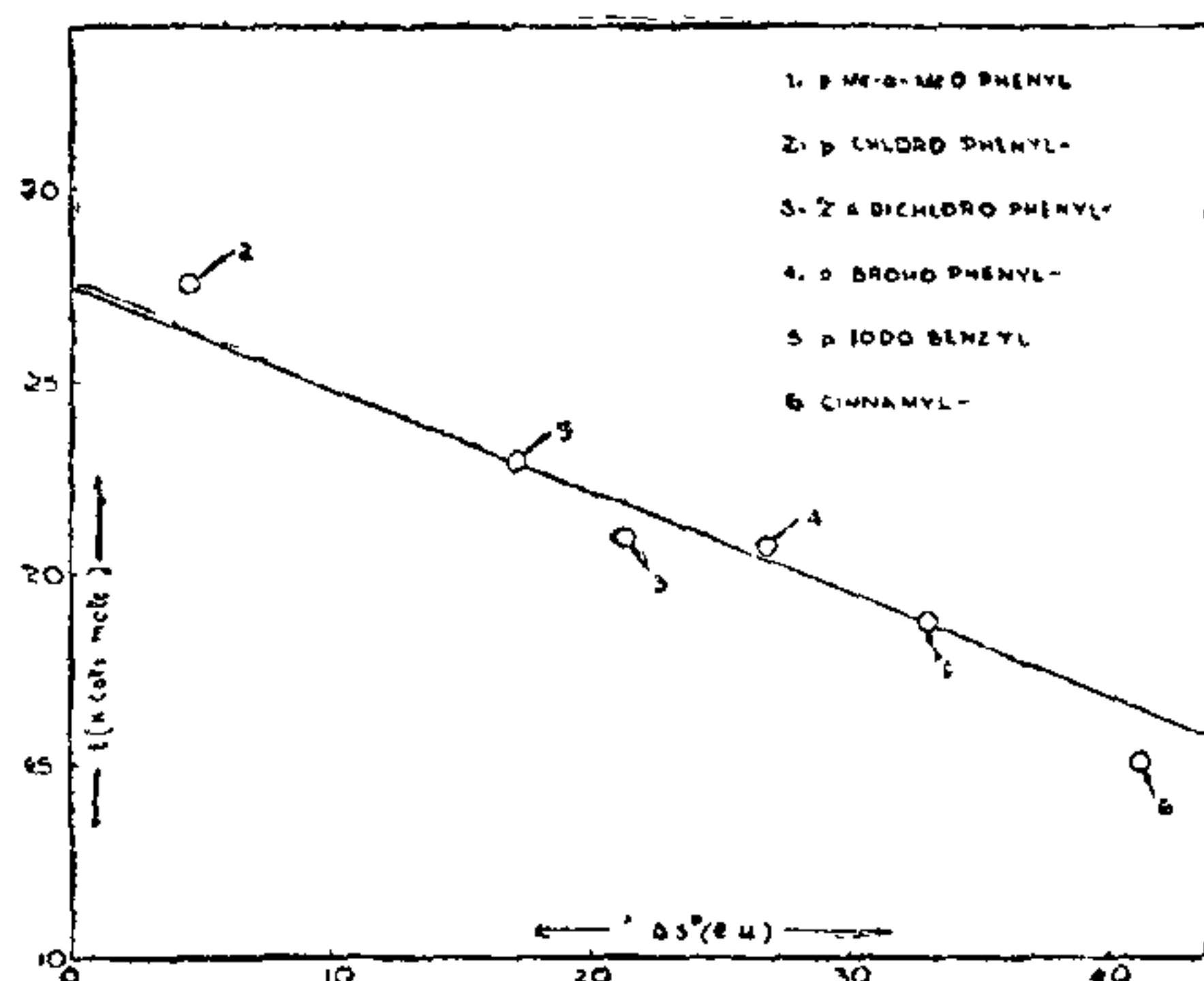

FIG. 3. Isokinetic relationship for the hydrolysis of phosphate monoesters *via* mononegative species.

similarity of mechanism for the hydrolysis of this ester and other related phosphates. Based on the results gathered, the probable reaction paths may, therefore, be formulated as shown in Chart 2.
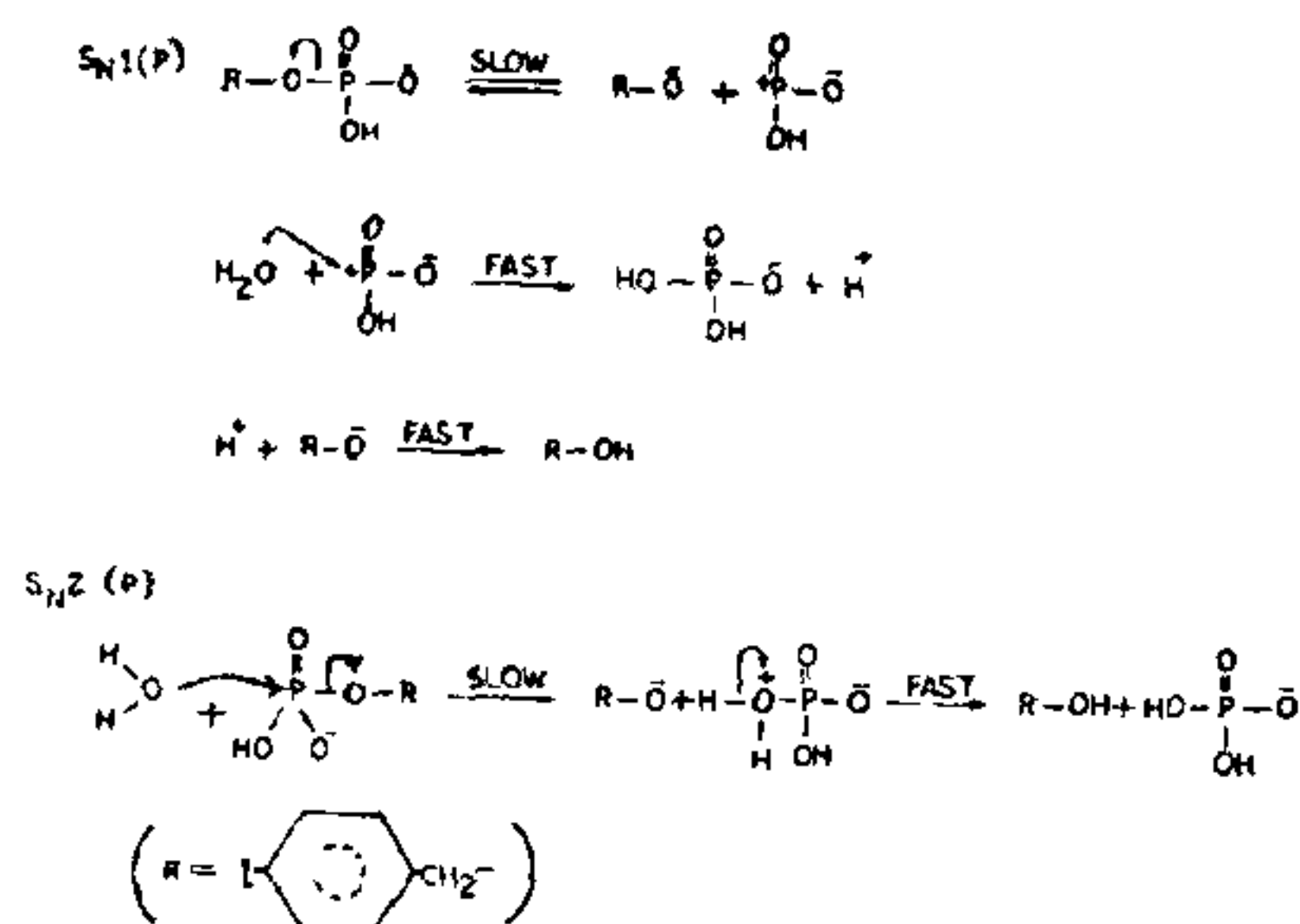

CHART 2. Mechanism of the hydrolysis of mono-*p*-iodo benzyl phosphate *via* monoanion.

The reaction paths *via* mononegative species may also be represented by rapid formation of the hydrogen bonded complexes (I) and (II) with water, which readily decompose with Phosphorus-Oxygen bond fission. (II) is preferred over (I) since the rate of hydrolysis increases with electron

attracting power of the substituent[13], which will not favour hydrogen bonding as shown in (I).

(I)   (II)

$(R = p - I - C_6H_5 - CH_2 -)$
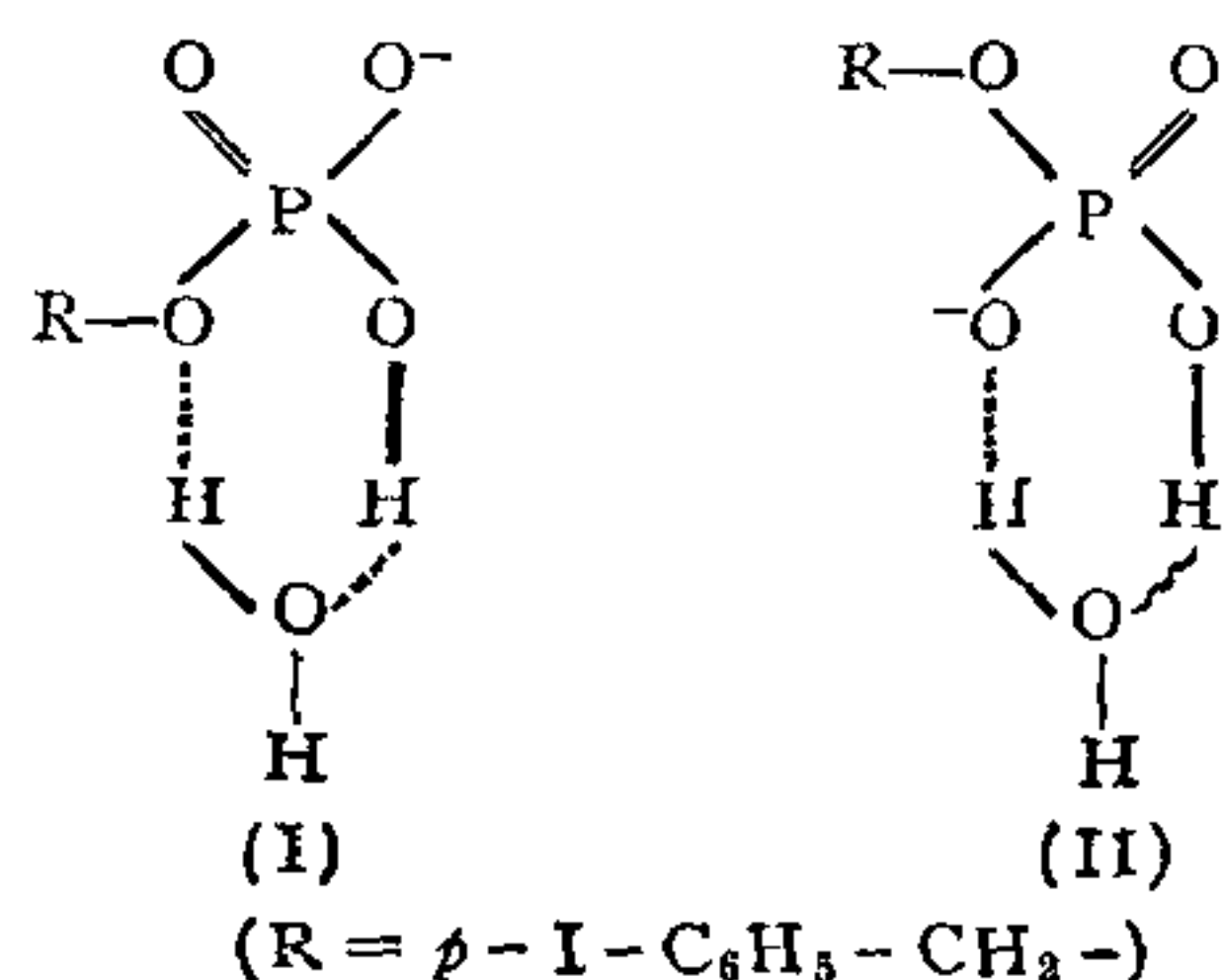
As the rate of hydrolysis increases by a change-over from water to deuterium oxide as a solvent, $(k_{D_2O}/k_{H_2O} = 2.36)$, following mechanism may also be suggested :

(Meta phosphate anion)
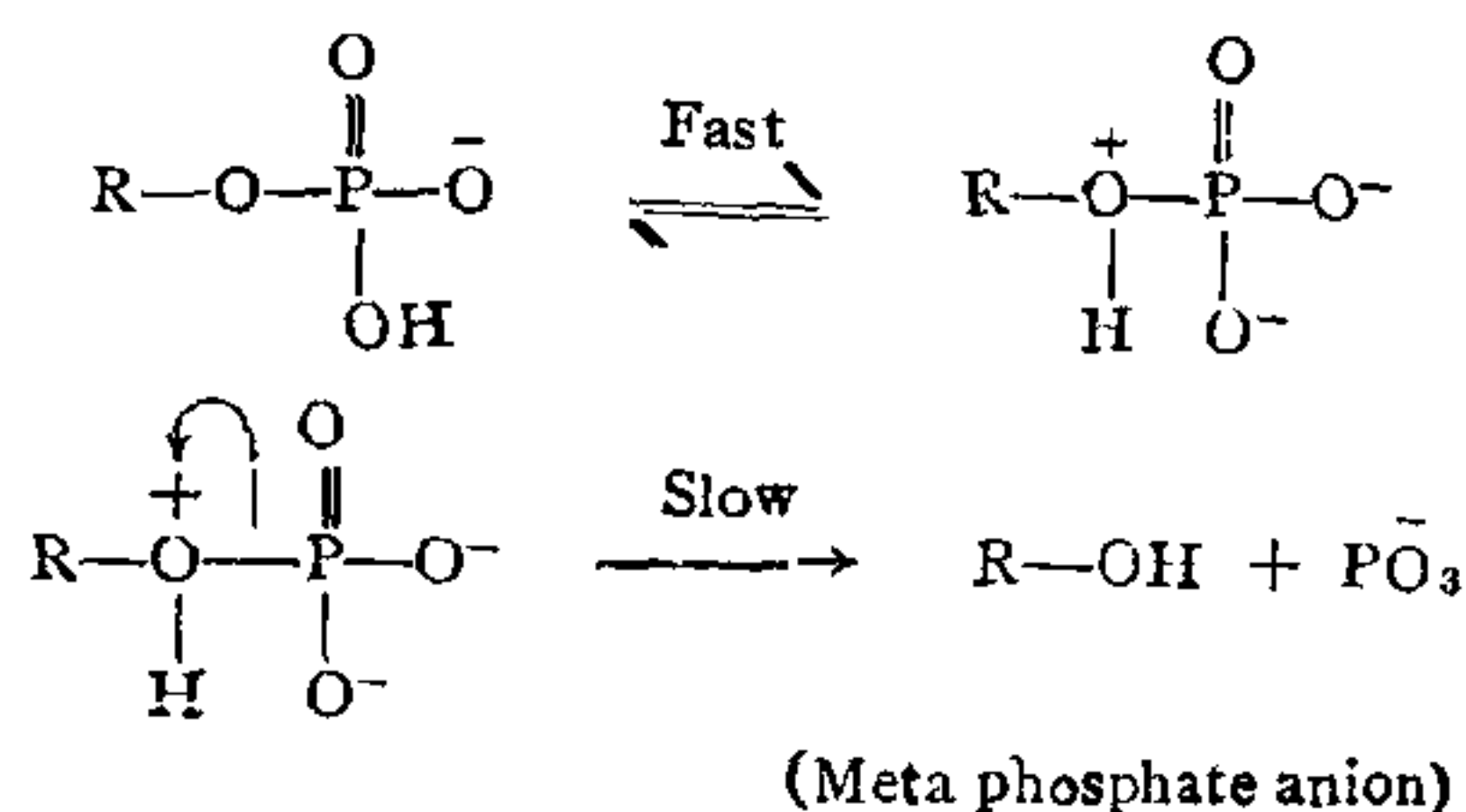
1. Bunton, C. A., Fendler, E. J. and Fendler, F. H., *J. Am. Chem. Soc.*, 1967, 89, 1221.
2. Kumamoto, J. and Westhimer, F. H., *Ibid.*, 1955, 77, 2515.
3. Zervas, L. and Dilaris, I., "Univ. of Athens, Greece," *Ibid.*, 1955, 77, 5354.
4. Masateru Miyano and Saburo Funahashi, "Nagoya University," *Ibid.*, 1955, 77, 3522.
5. Allens, R. J. L., *Biochem. J.*, 1940, 34, 858.
6. Stene, S., *Recl. Trav. Chim. Pays-Bas Belg.*, 1930, 49, 1133.
7. Frost, A. A. and Pearson, R. G., *Kinetics and Mechanism*, John Wiley, New York, 1953, p. 40.
8. Killedar, A. V., "Mechanism of the hydrolysis of nuclear substituted benzyl ortho phosphates," *Ph.D. Thesis*, Jiwaji University, Gwalior, 1972.
9. Barnard. Bunton, Llewellyn, Oldham, Silver and Verson, *Chem. and Ind.*, 1955. p. 760.
10. Mhala, M. M. and Saxena, S. B., *Indian J. Chem.*, 1971, 9, 127.
11. Schalger, L. L. and Long, F. A., *Advances in Physical Organic Chemistry*, Vol. I, Edited by V. Gold, Academic Press, Inc., New York, 1963, p. 26.
12. Cox, J. R. (Jr.) and Ramsay, O. B., *Chem. Rev.*, 1964, 64, 317.
13. Barnard, P. W. C., Bunton, C. A., Kellerman, D., Mhala, M. M., Silver, B. L., Vernon, C. A. and Welch, V. A., *J. Chem. Soc.*, *Sec. B*, 1966, p. 227.