

Thermocatalytic Hydrolysis of Tri-6-bromo-2,4-dichlorophenyl Phosphate by Kinetic Methods

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The hydrolysis of tri-6-bromo-2,4-dichlorophenyl orthophosphate by kinetic studies is reported here in the acid range (0.01–4.5 M HCl) in 50% aqueous dioxane at 90°C to highlight some characteristic features like: (i) involvement of only one reactive form, the conjugate acid species, in the entire acid range examined, as shown by neutral electrolyte effect data and also by concordance between the observed and the calculated rates, (ii) demonstration of an ill-defined maximum, at the normal value of 4 M, (iii) higher rates due to solvation by dioxane in spite of decrease in ϵ with rise in percentage of dioxane in the mixed solvent, (iv) indirect hydrolysis *via* the formation of the corresponding diester, as derived by mirror method calculations, and (v) effect of mixed-halogen substituents (both electronic as well as steric) in over-simplification of its hydrolysis. The overall hydrolysis is bimolecular and proceeds with P—O bond fission.

INTRODUCTION

Kinetic study of the hydrolysis of tri-6-bromo-2,4-dichlorophenyl orthophosphate has been pursued to highlight combined electronic and ortho effects of mixed-halogen substituents¹ present in the aryl matrix. The study is done in mineral acid, HCl (0.01–4.5 M) in 50% dioxane-water mixture at 90°C, to notify the influence of structural features, in the most complex ester in the series, in over simplification of its hydrolysis. This leads to reduction in the total number of reactive forms, due to the absence of any free ionisable —OH group in the phosphate residue. The mixed-halogen substituents can act by their two-way perturbation depending upon the positions in which they are placed.

EXPERIMENTAL

The parent phenol, 6-bromo-2,4-dichlorophenol, was prepared by the method of Fox and Turner². Its phosphorylation was successfully done, when ratio of phenol to phosphorus oxychloride was fixed as 3:1 by weight, and the stirring of the two continued together in dry benzene for 6 h. On passing steam through this reaction mixture, a white solid mass was left behind in the flask. Treatment of the mass with 5% NaOH made it free from the unreacted phenol and other

related esters (formed if any) and it was washed to free it from excess of alkali. On recrystallisation with glacial AcOH, the pure substance melted at 190°C. % Analysis, Found (Calcd.) C = 27.93 (28.06), H = 1.02 (0.78) and P = 4.02 (4.02).

RESULTS AND DISCUSSION

Kinetic study of the hydrolytic degradation of the triester has been carried out at length in acid region, 0.01–4.5 M HCl, in 50% aqueous 1,4-dioxane at 90°C. Throughout the study, the concentration used within the limits of Beer's law was as low as 5.0×10^{-4} M, except for the effect of concentration changes. The end product of hydrolysis, the free inorganic phosphate, was quantitatively estimated using Allen's modified method³, by generating the coloured complex, phosphomolybdenum blue.

First-order rate coefficients have been obtained (Table-1) and the data plotted as presented in Fig. 1. Gradual increase in acid molarity brings about enhancement in rates up to 4 M HCl. Between 2 to 4 M HCl, the rates rise rather sluggishly, so that a well-defined maximum is lacking in acid-rate profile. However, the magnitude of rates at 4 M corresponds to the maximum, so that the presence and contribution of some characteristic form, the monoprotonated form, is obvious. However, this can be an impure or incompletely protonated form of the triester under observation, and it thus differs from maximum protonation observed in amides.

TABLE-1
RATES OF HYDROLYSIS OF TRI-6-BROMO-2,4-DICHLOROPHENYL
PHOSPHATE AT DIFFERENT ACID MOLARITIES IN 50%
DIOXANE-WATER MIXTURE AT 90°C

HCl (M)	$10^3 K_e$ calcd. (min^{-1})	$10^3 K_e$ obsd. (min^{-1})
0.1	0.49	0.48
0.2	0.95	0.97
0.3	1.39	1.39
0.4	1.80	1.86
0.5	2.19	2.18
1.0	3.84	3.74
1.5	5.04	4.94
2.0	5.89	5.69
2.5	6.43	6.33
3.0	6.76	6.68
3.5	6.90	6.83
4.0	6.90	6.95
4.5	3.21*	3.23

*n = 2.5

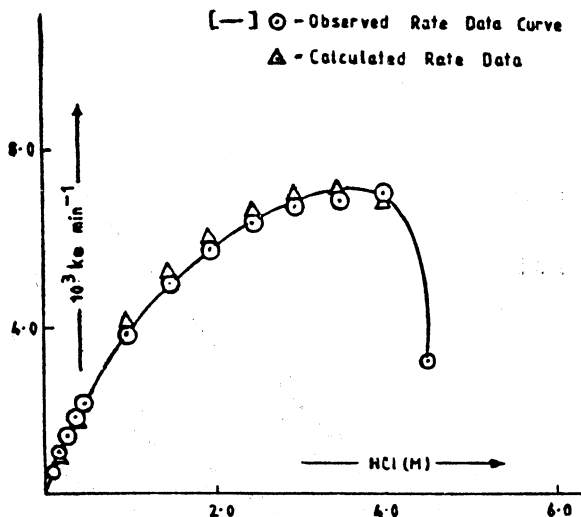


Fig. 1. Acid-rate profile for the hydrolysis of tri-6-bromo-2,4-dichlorophenyl phosphate in 50% dioxan-water (v/v) at 90°C.

Effect of study of constant ionic strengths⁴ (HCl + NaCl) is used to gain deeper insight into the contributory reactive forms of the ester under examination. Figure 2 based on rate data available at three values of μ corresponds to three linear curves meeting at the origin. This clearly indicates the participation of only one reactive species and that is the monoprotonated form possible in this condition. Since the slopes are found to decrease with the increase in μ , a negative ionic strength effect on the acid-catalysed rates is the result of this study. Absence of contribution by the neutral form is also confirmed by a study conducted in the pH range. At pH 4.17, where only neutral form of the triester is anticipated, $k_{e\text{Obsd.}} = 0.000037 \text{ min}^{-1}$, which is nearly zero, so that neutral form is almost non-contributory. The simpler, tri-2,4-dichlorophenyl phosphate⁵ also behaves in an analogous manner, so that introduction of a third chloro group in the *ortho* position does not vary much the electronic disposition from the aryl matrix towards the phosphorus atom.

The linear curves at each ionic strength may be represented by the following equation:

$$k_e = k_{H^+} \cdot C_{H^+} \quad (i)$$

Based on second empirical term of Debye-Hückel equation⁶, the rates *via* conjugate acid form alone may be expressed as under:

$$k_{H^+} = k_{H_0^+} \cdot \exp b_{H^+} \mu \quad (ii)$$

where k_{H^+} , $k_{H_0^+}$ and b_{H^+} respectively correspond to the specific acid-catalysed rates, specific acid-catalysed rate at zero ionic strength and a constant. The undissociated form being non-contributory, the total rates are calculated on the basis of Eq. (i), which lacks the inclusion of the corresponding rate factor for the neutral

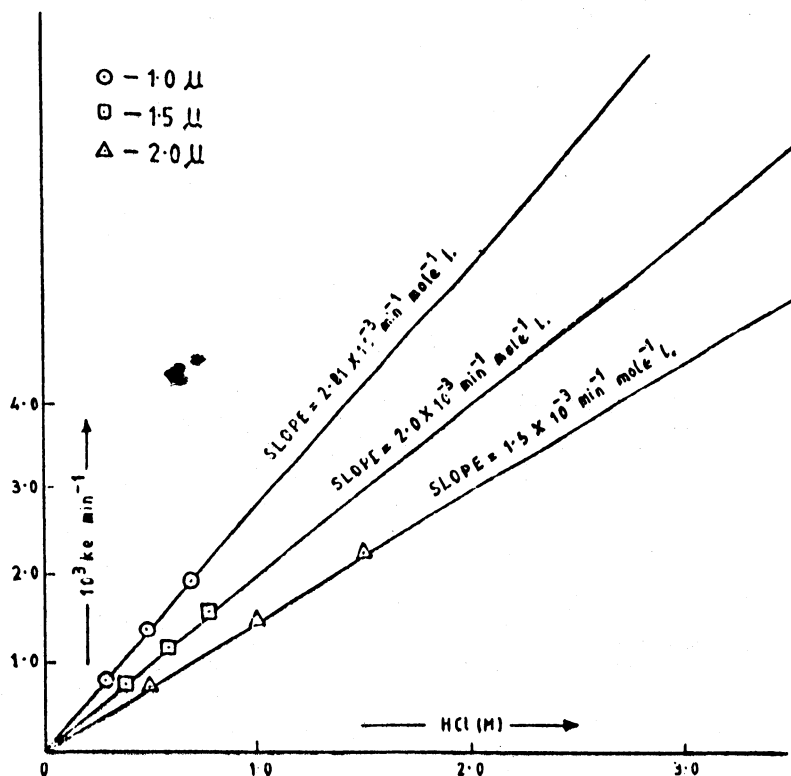


Fig. 2. Acid hydrolysis of tri-6-bromo-2,4-dichloro-phenyl phosphate at constant ionic strengths at 90°C.

form. In this respect, the present triester differs from the mono- and di-esters of the corresponding type. This may be in accordance with the higher degree of halogen substitution because of three tri-halo aryl nuclei present in each molecule of the triester. Eq. (i), may, therefore, be modified to calculate the theoretical rates from salt effect data, via the conjugate acid form alone, at different acid molarities used for study. Thus, we have:

$$k_e \text{ calcd.} = k_{H^+} C_{H^+} = K_{H_0^+} \cdot C_{H^+} \cdot \exp b_{H^+} \mu \quad (\text{iii})$$

$$\text{or,} \quad \log k_e = \log k_{H^+} \cdot C_{H^+} = \log k_{H_0^+} + \log C_{H^+} + b_{H^+} \mu \quad (\text{iv})$$

Further, the equation (iv) requires amendment, to include the trend of negative slopes with rise in μ so that:

$$\log k_e = \log k_{H_0^+} + \log C_{H^+} - b_{H^+} \mu \quad (\text{v})$$

Equation (v) may now be suitably applied to arrive at the theoretical rates via the sole contributory monoprotonated form. Table-1 summarises this rate data and also compares it with the experimentally observed rates. A close agreement between the two formulates the participation of the conjugate acid species in the entire acid range examined and also explains the rise in rates upto 4 M HCl with the increase in contribution of the species mentioned herein.

Negative ionic strength effect data is, however, in itself incapable of explaining the disparity in rates beyond 4 M at least. So, this requires a modification in the form of Brönsted-Bjerrum equation⁷, which includes another important aspect, the water activity term, which becomes significant in the higher acid (> 4 M) media. This may be cited as below:

$$k_e \text{ Calcd.} = k_{H_0} \cdot C_{H^+} \cdot \exp b_{H^+} \mu (a_{H_2O})_n \quad (\text{vi})$$

where a_{H_2O} represents water activity and 'n' corresponds to an integral value, 1, 2, 3 etc. For the present triester, it equals 2.5, indicating thereby the participation of a cluster of 2 to 3 water molecules for its conversion into the corresponding activated complex form. Thus, both negative ionic strength effect and water activity account for the decrease beyond 4 M.

Ionic strength data here also indicates specific⁸ acid catalysis, which could have been established by studies in solvent-isotope. However, in absence of this data, changes in solvent polarity were made to ascertain this aspect. A changeover to an amphiprotic solvent, acetic acid^{1,9} ($pK_a = 4.76$ and $\epsilon = 6.15$), lowered the rates of hydrolysis, so that the protonation of the triester is also decreased as compared to 50% aqueous dioxan¹⁰ ($D = 35.6$), the normal medium of dissolution used here. Rate data is given in Table 2. The increase, with rise in percentage of dioxane (> 50%), in rates is attributed to increased solvation of the products and also to intrinsic proton-donating ability of dioxane, known for quite some time now.

TABLE-2
EFFECT OF CHANGE IN DIOXANE CONTENT ON THE RATES OF HYDROLYSIS
OF TRI-6-BROMO-2,4-DICHLOROPHENYL PHOSPHATE AT 90°C

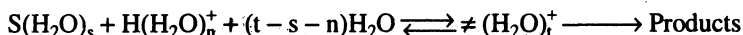
S.No.	HCl (M)	Percentage of dioxane (v/v)	D ¹⁰	10 ³ k _e obsd. (min ⁻¹)
1.	0.1	38.0*	6.15†	0.21
2.	0.1	50.0	35.6	0.48
3.	0.1	82.5	27.0	0.98
4.	3.0	50.0	35.0	6.68
5.	3.0	66.0	27.0	8.38

† At 20°C, Ref. 8.

* In glacial CH₃COOH-water mixture.

Various correlations may now be considered to examine the role of proton transferring media in a more accurate way. In higher acid media, H₀ is regarded as a better suited value for acidity (C_{H⁺}) and the Hammett¹¹ plot based on these values (data left out) gives a slope of 0.21, so that the involvement of a second reaction partner, water, is sought for the present hydrolysis. On the other hand, the modified Zücker-Hammett¹² plot (slope = 0.44) disregards the above require-

ment, as the slope here is far away from unity. Such exceptions are not uncommon *e.g.*, methyl mesitoate¹³ also shows such a disparity. Further, Bunnett's suggestion¹⁴ of a plot of $(\log k + H_0)$ vs. $\log a_{H_2O}$ if linear, or approximately so, indicates deviation of Hammett's plot ($\log k_{\psi}$ vs. $-H_0$) from slope unity, as a function of $\log a_{H_2O}$, and it gives a slope 'W'. Another parameter, W^* , based on Bunnett's plot¹⁴ data, is used to indicate the response of the hydrolytic reaction to catalysis by strong acid. These values, $W = 11.25$ and $W^* = 3.60$ both recommend attack of water on the protonated form of the triester, in the acid range examined. These criteria require hydration, at all the stages like the following, of the general type:



Bunnett in collaboration with Olsen¹⁵ further developed a correlation showing dependence of rates on both H_0 as well as C_H^+ . Here the slope, ϕ , being 1.55 ($> +1.00$) suggests that water here acts as a proton-transferring agent too, *i.e.* via the formation of hydronium ion type entity. In other words, the conversion of the neutral form of the triester is brought about by oxonium ions, H_3O^+ , into the corresponding monoprotinated form.

Arrhenius parameters¹⁶ based on three parallel linear curves at two different acid molarities are summarised in Table-3. This parallelism also supports the lacking of a well-defined maximum, so that incomplete protonation of the substrate, triester, is also justified. Above all, these parameters like energy of activation etc. postulate a bimolecular mode for the present hydrolysis. The decrease (Table-3) in the number of effective collisions with the rise in acid molarity is noticed clearly from the data computed, while the entropy is more negative as we go from 1.0 to 4.0 M HCl. This data is purely for acid catalysis, so the trend as above is not surprising. Free energy of activation (ΔG^\ddagger) for the present endergonic reaction is mainly governed by the entropy factor and its positive value is not of much practical utility.

TABLE-3
ARRHENIUS PARAMETERS FOR THE HYDROLYSIS OF TRI-6-BROMO-
2,4-DICHLOROPHENYL ORTHOPHOSPHATE

Condition	E (kcal/mole)	A (sec^{-1})	$-\Delta S^\ddagger$ (e.u.)	ΔG^\ddagger (kcal/mole)
1.0 M	22.89	4.38×10^7	17.10	29.09
4.0 M	18.93	1.79×10^5	26.77	28.65

Effect of concentration changes (Table 4) determined by isolation method shows constancy in rates. Thus, the rates are dependent on the concentration of the substrate, triester only. However, the overall results are referred to as pseudo-first order rate coefficients, because of the excess of the medium used here. The latter is 50% aqueous-dioxane and order with respect to this is difficult to determine.

TABLE-4
EFFECT OF CHANGES IN SUBSTRATE CONCENTRATIONS OF
THE TRIESTER AT 90°C

S.No.	Acid	Substrate concentration 10^3 M	$10^3 k_e$ obsd. (min^{-1})
1.	0.1 M	0.25	0.51
2.	0.1 M	0.50	0.48
3.	4.0 M	0.25	6.74
4.	4.0 M	0.50	6.95

In case of the present bimolecular hydrolysis *via* the conjugate acid form, the transition state with dispersal of charge is expected to form. According to the qualitative theory¹⁶ of Hughes and Ingold, rates may not be affected largely by increase in polarity of the solvents used. However, experimental data (Table-2) shows that the rates are raised with the decrease in ϵ . This indicates that the endothermic hydrolysis involves a transition state that largely resembles the products, so that the increase may be assigned to an increased solvation of transition state or products. Also, the initial protonation is significantly increased due to this lowering in dielectric constant of the media used.

Hydrolysis of the triester may proceed to form one of the end products, the free inorganic phosphate, either directly, or it may involve some stable intermediates like the corresponding di- and mono-esters, which may finally break down to liberate the free phosphate. In order to differentiate between these routes, theoretical rates were determined with the help of mirror method⁷ calculations. The experimentally observed rates ($6.95 \times 10^{-3} \text{ min}^{-1}$) are different from those computed ($11.83 \times 10^{-3} \text{ min}^{-1}$) at 4 M by the above method. Rather, they resemble those of the corresponding diester ($13.37 \times 10^{-3} \text{ min}^{-1}$) under almost similar conditions. This indirectly shows that the triester is converted somewhat rapidly into the corresponding diester, which then indirectly governs the hydrolysis of the reaction under observation. Product analysis was not possible at this stage because the diester remains completely dissolved even in low percentage of dioxane-water mixture.

Nature of bond fission, whether P—O or C—O, could not be decided by an experimental technique directly. However, a compilation of comparative data, of some triesters, with characteristic parameters, supports a similar P—O bond cleavage for this triester too. Formation of the free phenol from the singly protonated form of the triester is possible due to stability reasons and justifies P—O bond rupture, while in the latter formation of a carbonium ion type species is required, the chances of which are far remote.

The following order of acid catalysis in the triesters studied so far, indicates that phosphate esters containing one or more bromo groups (*ortho* or *para*) bring about noticeable increase in acid catalysis, while those with chloro groups (two or more in number) are less effective. This is possible due to the larger magnitude of +M effect of the O—Br group than the -I effect of O—Cl group, so that the conjugate acid form is easily formed in the ester containing the former halo-substituent.

Triester	6-Br-2,4-di-Cl	≈	S-tri-Br	>	2,4-di-Cl	>	S-tri-Cl
$10^5 k_{H_0}^+$ (sec ⁻¹)	8.35 (90°C)		15.92 (98°C)		13.87 (98°C)		5.27 (90°C)
Ref.	Present work		17		5		18

Charts 1 and 2 depict the routes of hydrolysis of the triester via the sole reactive species, the conjugate acid form, in different acid conditions.

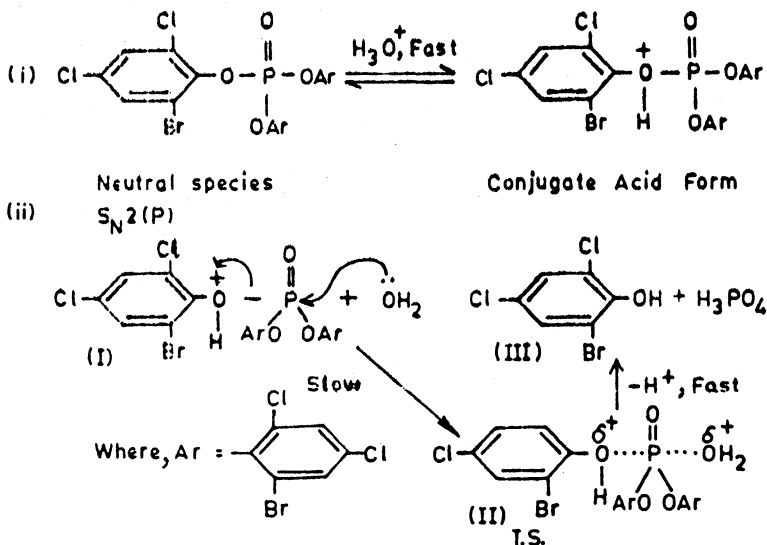


Chart 1. Hydrolysis of the triester in the low acid range via the protonated form with P—O bond cleavage.

(ii) $S_N2(P)$

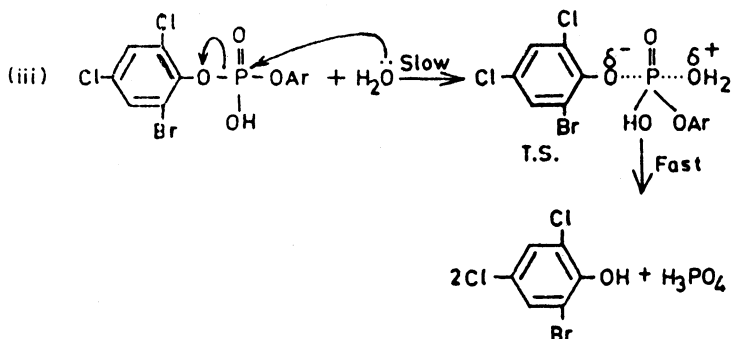
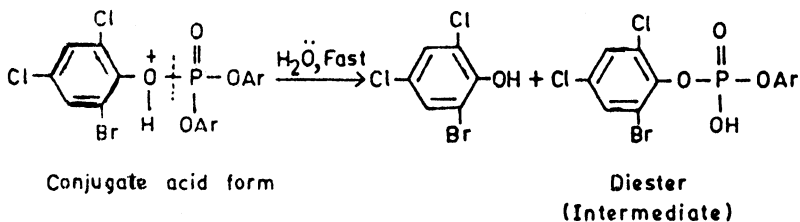


Chart 2. Bimolecular hydrolysis via conjugate acid form involving the diester as an intermediate in higher acid region.

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