George Gibson, Mark Olson, and William Macarthur offered invaluable computational assistance. Acknowledgment is made to the donors of the Petroleum Research Fund, administered by the American Chemical Society, for the support of this research. A generous grant of computer time by the SUNY at Binghamton Computer Center is also gratefully acknowledged.

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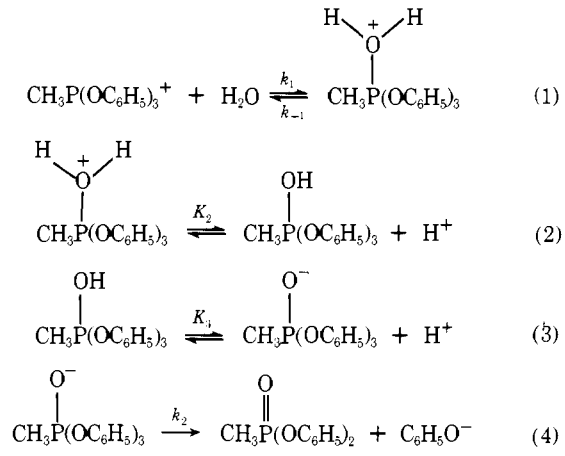
Kinetics and Mechanism of Hydrolysis of Aryloxyphosphonium Salts

Sir:

The hydrolysis of aryloxyphosphonium salts[1] such as $CH_3P(OC_6H_5)_3^+CF_3SO_3^-$ (A) may serve to model that of protonated aryl esters of phosphonic acids. The mechanism shown in Scheme I for the hydrolysis of methyltriphenoxyphosphonium triflate is supported by the kinetic data here reported.

The kinetics of hydrolysis can be followed spectrophotometrically in aqueous acetonitrile[1] by methods parallel to those previously published.[2] The rate of hydrolysis of $CH_3P(OC_6H_5)_3^+$ is too large to measure in pure water; the limit of our stopped-flow apparatus was reached with 8% water in acetonitrile.[3] The rate of the hydrolysis of the sterically hindered salt (B) methyltri(2,6-dimethylphenoxy)-phosphonium triflate can, however,[4] be measured in aqueous acetonitrile solution to more than 50% water, and then extrapolated to pure water. Since the two salts show parallel behavior in acetonitrile solutions with low water content,

Scheme I



the data (shown in Figure 1 and 2) allow a reasonable extrapolation of the rate of hydrolysis of A to pure water; note that the resulting rate constant of 0.6×10^4 s^{-1} exceeds by a power of ten any that can be measured for irreversible reactions in solution. We have as yet no explanation for the 10^6-fold increase in rate between 0.11 M and pure water.

If the mechanism presented in Scheme I is correct, k_1 should control the rate-limiting addition of water in dilute acid solutions, whereas in more concentrated acid, k_2 should control the rate-limiting loss of phenoxide ion from the phosphorane anion. The mechanism predicts that, at high acidity, the rate of hydrolysis will be inversely as the second power of h_0; Figures 3 and 4 show the rate constants of hydrolysis as a function of acid concentration at two concentrations of water in acetonitrile. Although the h_0 function for these solvent mixtures is not yet known,[5] the data qualitatively support the mechanism here advanced; the predicted inhibition of the reaction by acid is observed.

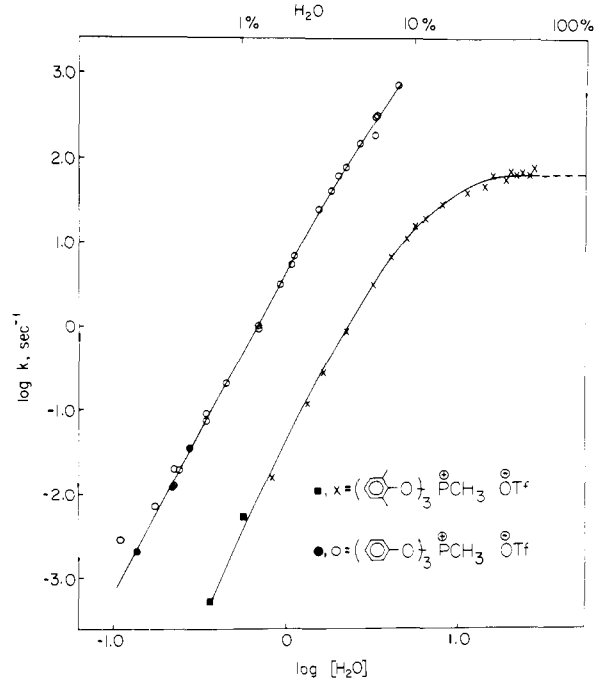


Figure 1. Rate constants in inverse seconds for the hydrolysis of methyltriphenoxyphosphonium triflate and of methyltri(2,6-dimethylphenoxy)phosphonium triflate, at 25°, plotted as a function of the concentration of water in acetonitrile as solvent. Open circles and ×'s: measurements with a Durham-Gibson stopped-flow apparatus; filled circles and squares: measurements with a Cary 15 spectrophotometer.

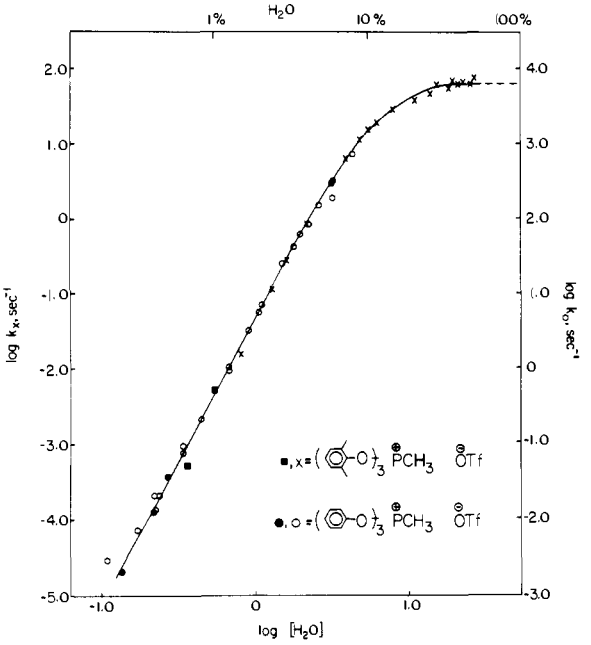


Figure 2. Rate constants in inverse seconds for the hydrolysis of methyltriphenoxyphosphonium triflate (right-hand scale) and for the hydrolysis of methyltri(2,6-dimethylphenoxy)phosphonium triflate (left-hand scale), at 25°, plotted as a function of the concentration of water in acetonitrile as solvent. The rate scale for the hydrolysis of the sterically hindered salt has been raised by 2.0 log units, as compared to that for the hydrolysis of the unhindered salt. Open circles and ×'s: measurements with a Durham-Gibson stopped-flow apparatus; filled circles and squares: measurements with a Cary 15 spectrophotometer.

The acid-catalyzed hydrolyses of aryl (but not of alkyl) esters of phosphoric acid show maximum rates of acid hydrolysis in 1–6 M acid, with a large decrease in rate at high acidity.[6-10] These acidity-rate profiles have been interpreted[6-9] as the result of a decrease in the activity of water in concentrated acid solution, although the fugacity of water, as measured by its vapor pressure,[11] is 0.7 in 4.3 M $HClO_4$, and correspondingly higher in more dilute solutions. An alternative explanation for the rate maximum could be based on a mechanism parallel to Scheme I, beginning, of course, with the protonation of the ester, e.g., eq 5.

$$CH_3P(OC_6H_5)_2 + H^+ \underset{}{\overset{K_1^{-1}}{\rightleftharpoons}} CH_3\overset{+}{P}(OH)(OC_6H_5)_2 \qquad (5)$$

C

This mechanism would predict an increase in rate with increase in the concentration of hydrogen ion at low acidity, since the rate of addition of water would depend on the concentration of the product, C, of reaction 5; at higher acidity, on the other hand, the loss of phenoxide ion would be rate limiting, and the overall process inhibited by acid. Solution of the kinetic equations for the mechanisms here advanced leads to the conclusion that, in those regions where $(H^+) \ll K_1$, and to the extent that the salt is a good model for the protonated ester, $k_{obsd}^{ester} = k_{obsd}^{salt}(H^+)/K_1$. The mechanisms qualitatively account for a maximum in the acidity-rate curve for the hydrolysis of aryl phosphates and phosphonates, and are consistent with a decrease in rate at high acidity even in solutions where the fugacity of water is nearly unity.

The quantitative comparisons, however, are unsatisfactory. The rate-acidity curve we predict for hydrolysis of B in 34% water–66% acetonitrile has its maximum at about 0.5 M acid, whereas that for triphenyl phosphate in 40% water–60% dioxane shows a maximum[6] at about 1.5 M acid. The

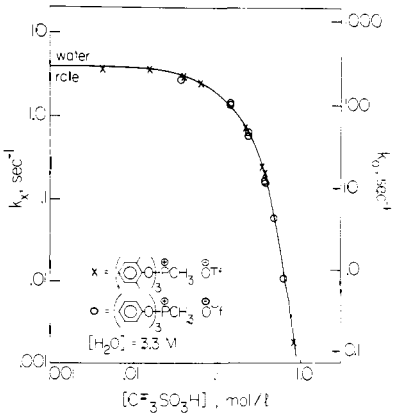


Figure 3. Rate constants in inverse seconds for the hydrolysis of methyltriphenoxyphosphonium triflate (right-hand scale) and for the hydrolysis of methyltri(2,6-dimethylphenoxy)phosphonium triflate (left-hand scale) in 6% aqueous acetonitrile at 25°, as a function of hydrogen ion concentration. The rate scale for the hydrolysis of the sterically hindered salt has been raised by 1.9 log units as compared to that for the unhindered salt.

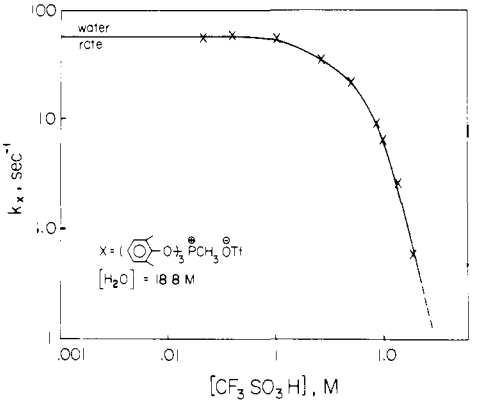


Figure 4. Rate constants in inverse seconds for the hydrolysis of methyltri(2,6-dimethylphenoxy)phosphonium triflate, in 34% aqueous acetonitrile as solvent, as a function of the hydrogen ion concentration.

absolute rate predicted for the ester depends upon pK_1; if this constant[11,12] is around −5, then the rate for the hydrolysis of the phosphonate at 25° in 1.5 M acid in pure water is calculated to be around 10^{-3} s^{-1}; the actual rate of hydrolysis of triphenyl phosphate[13] in 1.5 M acid extrapolated to pure water and 25° is around 10^{-6} s^{-1}. The discrepancy in the quantitative comparison of absolute rate is unacceptably large, even allowing for the problems introduced by modeling one salt with another and modeling the protonated ester by a salt; it is the subject of continuing investigation.

Acknowledgment. This work was supported by the National Science Foundation under Grant No. MPS-74-17595. One of us (S.J.K.) wishes to thank E.I. duPont deNemours for a graduate fellowship.

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Stereospecific Conversion of Diosgenin to α-Ecdysone

Sir:

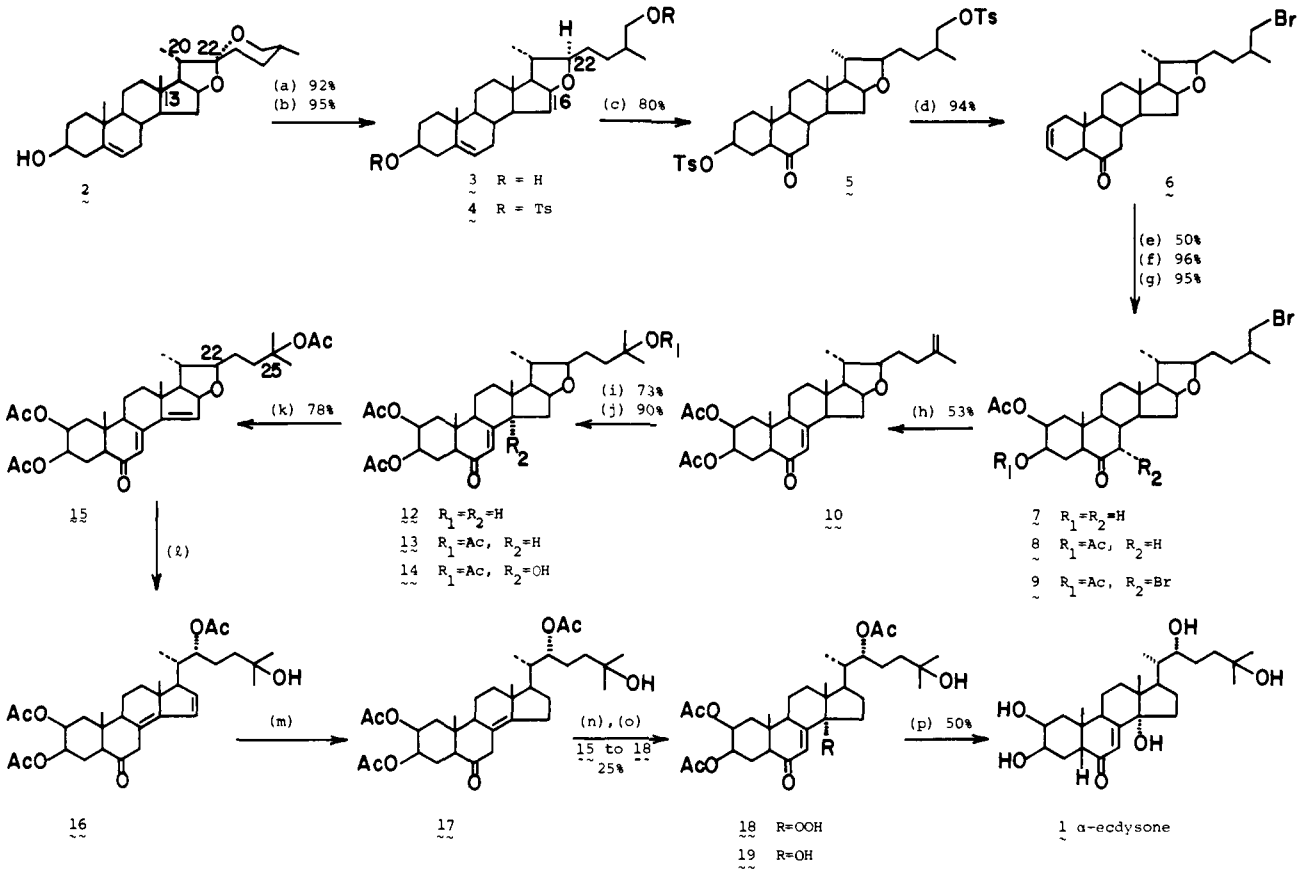
α-Ecdysone (**1**) was the first insect moulting hormone to be isolated,[1] characterized,[2] and synthesized.[3-6] In the following we report its synthesis from diosgenin (**2**), in which the correct configuration at C-22 is generated by stereospecific reduction of the diosgenin spiro-ketal group.

Okauchi et al.[7] reported that the cocoon spinning of a silk-worm colony can be synchronized when ecdysones are added to the diet (15 mg per 20 000 larvae) at a particular stage during the fifth instar. Extensive field tests carried out since have verified this, and further have shown that simultaneous application of lauryl alcohol repels larvae, automatically moving them towards the nesting area where spinning of high-quality cocoon is assured.[8] As far as we are aware, this is the first usage of ecdysones in insect control (in a positive sense).

The mixed hydride (LAH-$AlCl_3$) reduction of diosgenin is known to give dihydrodiosgenin (**3**) in excellent yield.[9] Examination of molecular models revealed that since the 13-Me would impose a greater steric hindrance than the 20-Me to a group approaching C-22, the dihydro-derivative **3** should possess the 22*R* configuration as shown.[10] A reductive cleavage of the C-16-O bond would then lead to a 22-OH having the same absolute configuration as that of the ecdysones,[2,11] a step which was achieved in transformation **15** → **16** (Scheme I).

Hydroboration-oxidation of dihydrodiosgenin ditosylate (**4**), mp 119.5-120.5 °C, gave 6-keto ditosylate (**5**), mp 133-134 °C, which when heated in DMF with LiBr produced **6**:[12] NMR δ 5.63, br s, 2-H, 3-H; 3.37, d, J = 5 Hz, 26-H; 0.83, s, 19-H; 0.73, s, 18-H. Prevost-Woodward hydroxylation[13] of **6** gave the 2-acetoxy-3-hydroxy derivative (**7**), mp 154-154.5 °C, which was acetylated to **8**, mp 147.5-148 °C. When crystalline **8** was treated with bromine under equilibrating conditions, 7α-bromo 6-ketone (**9**) was obtained in high yield as reported earlier for an analogous system.[13] Dehydrobromination of **9** in boiling DMF with Li_2CO_3 provided the 7,25-diene-6-one (**10**), mp 195.5-197 °C (NMR δ 5.72, distorted t, 7-H; 1.03, s, 19-H; 0.74, s, 18-H) in fair yield along with 4,25-dien-6-one (**11**),

Scheme I



[a] $LiAlH_4$, $AlCl_3$, ether, 0°/H^+. [b] TsCl, pyr, room temp. [c] B_2H_6, THF, room temp./H_2O_2, OH^-–CrO_3, H^+. [d] LiBr, DMF, 120°, 45 min. [e] Ag-OAc, I_2, HOAc, H_2O (trace), room temp. [f] Ac_2O, pyr, room temp. [g] Br_2, HOAc, HBr (trace), 70°, 90 min. [h] Li_2CO_3, DMF, Δ. [i] $Hg(OAc)_2$, THF, room temp./$NaBH_4$, OH^-, 0°/Ac_2O, CaH_2, 120°, 2 h. [j] SeO_2, dioxane, 80°, 30 min. [k] $(CF_3CO)_2O$, pyr, 0°, 20 min. [l] Zn, AcOH, Δ. [m] H_2, Pd(C), EtOAc, room temp. [n] O_2, rose bengal, MeOH, *hν*, room temp. [o] NaI, AcOH, MeOH, room temp. [p] K_2CO_3, MeOH, Δ.