The extremely low intrinsic reactivity of the *P*-(formylmethyl)triphenylphosphonium cation: an artefact due to strong covalent hydration of the carbonyl group

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The title cation is found to exhibit the lowest Marcus intrinsic reactivity known so far for a carbon acid; this situation is shown to reflect a rate-limiting hydration/dehydration reaction of the aldehyde functionality.

It is well known that the intrinsic reactivity (k_0 in the Marcus sense) of a carbon acid is closely related to the degree of resonance stabilization of the conjugate carbanion.[1,2] The greater the importance of this stabilization, the greater the lag with which it develops relative to the extent of proton transfer along the reaction coordinate and the lower the intrinsic reactivity of the carbon acid.[1–4] In recent years, the use of the log k_0 scale has been very helpful in clarifying the electronic mode of action of some unusual activating structures, *e.g.* neutral or positively charged organometallic residues, in governing the reactivity of carbon acid sites.[5,6] In this communication we report our finding that the ionization of the *P*-(formylmethyl)triphenylphosphonium cation **1** is associated with the lowest intrinsic reactivity known to date for a carbon acid in aqueous solution. As will be shown, this result rules out classical carbon acid behaviour according to eqn. (1), being instead a spectacular manifestation of the high susceptibility of the carbonyl group of this Wittig reagent precursor to covalent hydration.

$$\mathrm{Ph_3\overset{+}{P}CH_2COR} \underset{k-\mathbf{p}^{\mathrm{BH^+}}[\mathrm{BH^+}]+k-\mathbf{p}^{\mathrm{H_2O}}}{\overset{k_\mathrm{p}{}^\mathrm{B}[\mathrm{B}]+k_\mathrm{p}{}^\mathrm{OH}[\mathrm{OH^-}]}{\rightleftharpoons}} \mathrm{Ph_3\overset{+}{P}\overset{-}{C}HCOR} \quad (1)$$

1 R = H — **C-1**
2 R = CH_3 — **C-2**
3 R = C_6H_5 — **C-3**

Based first on eqn. (1), all rate and equilibrium measurements pertaining to the ionization of **1** were carried out in a 70%H_2O–30%Me_2SO (v/v) mixture at 25 °C and constant ionic strength of 0.5 mol dm^{-3} KCl. The pK_a value of **1** was determined both by potentiometry and analysis of the observed absorbance variations at λ_{max} of **C-1** (266 nm) obtained at equilibrium as a function of pH using a set of carboxylic acid buffers: p$K_a{}^1 = 5.67 \pm 0.03$. Pseudo-first-order rate constants, k_{obsd}, for the interconversion of **1** and **C-1** were measured by monitoring the appearance of **C-1** at 266 nm in various primary and secondary amine buffers (B). In each buffer, the concentration of the amine reagent was varied in the range 5×10^{-3}–0.1 mol dm^{-3} at constant pH ([**1**] ≈ 5×10^{-5} mol dm^{-3}) and a direct dependence of k_{obsd} upon [B] according to the reduced eqn. (2) was observed. As shown in Fig. 1, the results obtained

$$k_{obsd} = k_p{}^B\,[B] + k_p{}^{OH}\,[OH^-] \qquad (2)$$

for the series of amines used describe a satisfactory Brønsted relationship ($\beta_B = 0.89$). From this plot, the log value of the intrinsic rate constant of **1** was readily determined as log k_0 = log ($k_p{}^B/q$) at p$K_a{}^1$ = p$K_a{}^B$ + log (p/q); log $k_0 = -3.30$. From the contribution of the hydroxide ion pathway to eqn. (2) which was appreciable at the highest pH studied, one obtains: $k_p{}^{OH} = 9.1 \times 10^4$ dm^3 mol^{-1} s^{-1}.

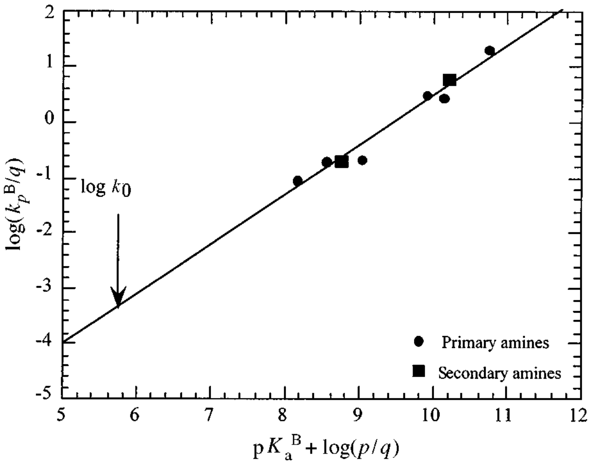
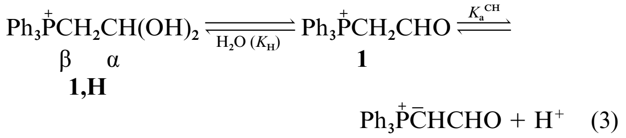


Fig. 1 Brønsted plot for ionization of **1** by primary and secondary amines in 70%H_2O–30%Me_2SO (v/v) at $I = 0.5$ mol dm^{-3} KCl and $T = 25$ °C.

The collected data call for five principal comments: (1) the intrinsic reactivity of **1** is by far the lowest which has ever been measured for a carbon acid;[7] (2) perhaps more importantly, this intrinsic reactivity is lower by more than 6 log units than those of the closely related *P*-acetonyl and *P*-phenacyltriphenylphosphonium cations **2** and **3** which behave as many carbonyl acids,[10] *i.e.* log $k_0 = 3.44$ for **2** (3.92 in 50/50 at 20 °C);[11] log $k_0 = 3.55$ for **3**, in 70%H_2O–30%Me_2SO; (3) the low reactivity of **1** is also reflected by the $k_p{}^{OH}$ value which is more than 1000-fold lower than those for **2** (p$K_a{}^2 = 7.40$, $k_p{}^{OH} = 1.7 \times 10^8$ dm^3 mol^{-1} s^{-1}) and **3** (p$K_a{}^3 = 6.55$, $k_p{}^{OH} = 2.1 \times 10^8$ dm^3 mol^{-1} s^{-1}) in the same solvent; (4) the β value is surprisingly high, being out of the range 0.5 ± 0.1 commonly found for carbon acids, including the two analogs **2** and **3**;[1] (5) the points for the six primary amines and the two secondary amines employed lie on the same Brønsted plot. This is in marked contrast with the general observation that because of differences in solvation requirements of the conjugated ammonium cations, secondary amines are more reactive than primary amines in proton transfers at carbon. Altogether, these results suggest that the ionization of **1** cannot proceed through the simple equilibrium approach of eqn. (1).

Although the characterization of the hydrated species **1,H** does not seem to have been reported previously,[9,12] a most reasonable way to account for the observed behaviour of **1** is in terms of a high susceptibility of the strongly activated aldehyde function to undergo covalent hydration.[13–16] Interestingly, the NMR evidence (^1H, ^{13}C, ^{31}P) is that a 0.1 mol dm^{-3} solution of **1** in 50%H_2O–50%Me_2SO mixture consists of only 20% of a mixture of the related *Z*- and *E*-enol tautomers but 80% of **1,H**

(^{31}P: $\delta_P = 20.4$; ^{1}H: $\delta_{H_\alpha} = 5.05$, $\delta_{H_\beta} = 3.60$, $^3J(H_\alpha H_\beta) = 5.6$, $^2J(PH_\beta) = 13$, $^3J(PH_\alpha) = 4.1$; ^{13}C: $\delta_{C_\alpha} = 87.6$, $\delta_{C_\beta} = 32$, $^1J(PC_\beta) = 53.3$)[17] with no trace at all of the parent aldehyde form. This makes it reasonable to assume that an essentially complete conversion of **1** to **1,H** occurs at the low substrate concentrations ($\approx 5 \times 10^{-5}$ mol dm^{-3}) involved in our kinetic measurements conducted in the 70%H$_2$O–30%Me$_2$SO mixture. It follows that the ionization of **1** is better depicted by eqn. (3) rather than



$$\underset{\beta\quad\alpha}{Ph_3\overset{+}{P}CH_2CH(OH)_2} \underset{H_2O\ (K_H)}{\rightleftharpoons} Ph_3\overset{+}{P}CH_2CHO \overset{K_a^{CH}}{\rightleftharpoons} Ph_3\overset{+}{P}\overset{-}{C}HCHO + H^+ \quad (3)$$

1,H **1** **C-1**

eqn. (1), implying that both the above measured pK_a and log k_0 values are apparent values that we will now refer to as pK_a^{obsd} and log k_0^{obsd}.

Based on the above evidence two different arguments can be used to obtain an estimate of the hydration constant $K_H = K_a^{CH}/K_a^{obsd}$. The first is based on previous findings that the relative acidifying effects of the CHO and COR′ (R′ = CH$_3$, C$_6$H$_5$) groups upon the carbon acidity of compounds of general structure RCH$_2$COR′ depend very little on the R′ substituent, *e.g.* $pK_a^{COC_6H_5} - pK_a^{CHO} \approx 3$.[14] Based on this difference, a pK_a^{CH} value of ≈3.50 can be calculated for **1** in 70%H$_2$O–30%Me$_2$SO. Combining with $pK_a^{obsd} = 5.67$ yields $K_H \approx 150$ ($pK_H = -2.17$) in this solvent. For comparison, a value of $K_H = 37$ has been reported for the hydration of chloroacetaldehyde.[13]

Providing that the ionization of the aldehyde form remains the rate-limiting step of the overall process of eqn. (3), another estimate of K_H can be obtained from the relationship (4).

$$\log k_0^{obsd} = \log k_0 + pK_H \qquad (4)$$

Should **1** actually behave as **2** and **3** and exhibit normal carbon acid behaviour, an intrinsic reactivity typical of a carbonyl compound should be found with $\log k_0 \approx 3$–3.5. From eqn. (4), one thus obtains: $pK_H \approx -6.5$, a value which combined with pK_a^{obsd} will imply that **1** is a very strong acid ($pK_a^{CH} \approx -1$). In view of the aforementioned relationship governing the carbon acidities of RCH$_2$COR′ (R′ = H, CH$_3$, C$_6$H$_5$) compounds,[14] such a conclusion is totally unreasonable. We therefore conclude that the set of pK_H and pK_a^{CH} values obtained in the first approach is more realistic and that the rate limiting step of eqn. (3) must be the hydration/dehydration pathway and not the ionization of **1**.

In summary, we have found that the ionization of **1** is formally associated with the lowest Marcus intrinsic reactivity which has ever been reported for a carbon acid.[18] However, it is clear that this behaviour is an artefact, being the reflection of the strong susceptibility of the aldehyde function to covalent hydration. Interestingly, the available evidence is that the approach to the **1,H**⇌**1** equilibrium is the rate-limiting step of the overall ionization process. In order to delineate all the mechanistic facets of the behaviour of this compound, we are currently focussing our efforts on the design of experimental conditions allowing a direct kinetic study of this step.

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