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Reactivity of a Trivalent Phosphorus Radical Cation as an Electrophile toward Pyridine Derivatives

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ABSTRACT: *The reaction of methylviologen (MV^{2+}) with tributylphosphine (**1p**) and diethylphenylphosphine (**1q**) in the presence of an alkyl-substituted pyridine (**2**) was found to take place through a single-electron transfer (SET) from **1** to MV^{2+} followed by nucleophilic attack by **2** on the resulting phosphine radical cation $\mathbf{1}^{\cdot+}$. Kinetic examination showed that, in the transition state for the reaction of $\mathbf{1}^{\cdot+}$ with **2**, an unpaired electron is largely delocalized to the pyridine moiety.* © 2000 John Wiley & Sons, Inc. Heteroatom Chem 11:152–157, 2000

INTRODUCTION

Trivalent phosphorus radical cations $Z_3P^{\cdot+}$, which are generated from the parent phosphorus compounds Z_3P upon the reactions with electron-deficient compounds [1,2], have a potential in synthetic use [3]. This point of view, as well as a mechanistic interest, has prompted us to study the reactivity of $Z_3P^{\cdot+}$. It has been shown that $Z_3P^{\cdot+}$ exhibits a cationic character rather than a free-radical character, undergoing easily an ionic reaction with a nucleophile [1].

Phosphoranyl free radicals are stabilized by an aromatic ligand attached to the central phosphorus atom [4,5], the stabilization resulting from delocalization of an unpaired electron to the aromatic ring. Such an effect of an aromatic ligand could be operative to stabilize trivalent phosphorus radical cations as well. That is, trivalent phosphorus radical cations, with and without an aromatic ligand, would exert different reactivity in their ionic reactions with a nucleophile. In this connection, we anticipate that an aromatic compound as a nucleophile would result in similar stabilization at the transition state if the nucleophile interacts strongly with the trivalent phosphorus radical cation.

Recently, we found that 1,1′-dimethyl-4,4′-bipyridinium dication (methylviologen; MV^{2+}) is reduced to its one-electron reduced form, MV^{+}, upon reaction with tributylphosphine (**1p**) in the presence of alcohol or thiol (RXH) [6]. Kinetic analysis of the reaction, together with other evidence, has shown that the reaction proceeds through initial single-electron transfer (SET) from **1p** to MV^{2+}, followed by an ionic reaction of the resulting phosphine radical cation $\mathbf{1p}^{\cdot+}$ with a nucleophile RXH. Importantly, a relative rate constant k_2^{rel} for the ionic reaction of $\mathbf{1p}^{\cdot+}$ with RXH has been given in this analysis, thus allowing us to estimate the relative reactivity of $\mathbf{1p}^{\cdot+}$ toward RXH.

We here take this reaction system to elucidate reactivity of a trivalent phosphorus radical cation in a reaction with an aromatic compound as a nucleophile. Thus, we performed kinetic examination on

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the reaction of tributylphosphine (**1p**) and diethylphenylphosphine (**1q**), phosphines without and with a phenyl ligand, respectively, with MV^{2+} in the presence of methyl-substituted pyridines (**2**). The results showed that **2** attacks nucleophilically the phosphine radical cation $\mathbf{1}^{\cdot+}$, and **2** exerts a specific effect to stabilize the transition state of this reaction.

RESULTS

Reaction of Phosphine 1 with MV^{2+} in the Presence of a Pyridine Nucleophile 2

Phosphine (**1**) was reacted with MV^{2+} (tetrafluoroborate salt) in the presence of a large excess of pyridine (**2**) in acetonitrile at 50°C under an argon atmosphere in the dark. Observed on a spectrophotometer was a gradual increase in the absorption at 398 and 605 nm, the wavelengths that are characteristic of the one-electron reduced form of MV^{2+}, MV^{+} [7–9]. The formation of MV^{+} in a nearly theoretical amount was confirmed based on its extinction coefficient at 605 nm [7], showing that MV^{2+} undergoes one-electron reduction to MV^{+} without further reduction to its two-electron reduced form, MV^{0}. No reduction of MV^{2+} took place in the absence of **2** within the period examined. Neither was there observed a reaction between MV^{2+} and **2** without **1**.

Kinetics

A kinetics investigation was carried out under conditions where the amounts of **1** and **2** were in large excess, and an increase in the absorbance at 605 nm due to MV^{+} was followed spectrophotometrically. Figure 1 shows the plot of $-\log\{(A_\infty - A_t)/A_\infty\}$ against time for the selected reactions, where A_∞ is the final absorption at 605 nm and A_t is the absorption at a given time t. Clearly, each reaction does not obey simple first-order kinetics, and instead, downward deviation of the plot is apparent in a later stage of the reaction.

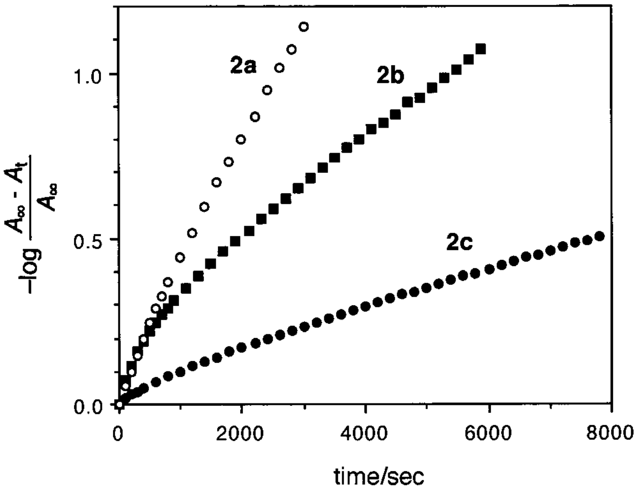


FIGURE 1 Logarithmic plot of increase in the absorption of MV^{+} at 605 nm against time. $[\mathbf{1}]_0 = 1.50 \times 10^{-1}$ mol dm^{-3}; $[MV^{2+}]_0 = 2.00 \times 10^{-4}$ mol dm^{-3}; $[\mathbf{2}]_0 = 1.50$ mol dm^{-3}. In acetonitrile at 50°C under an argon atmosphere in the dark.

DISCUSSION

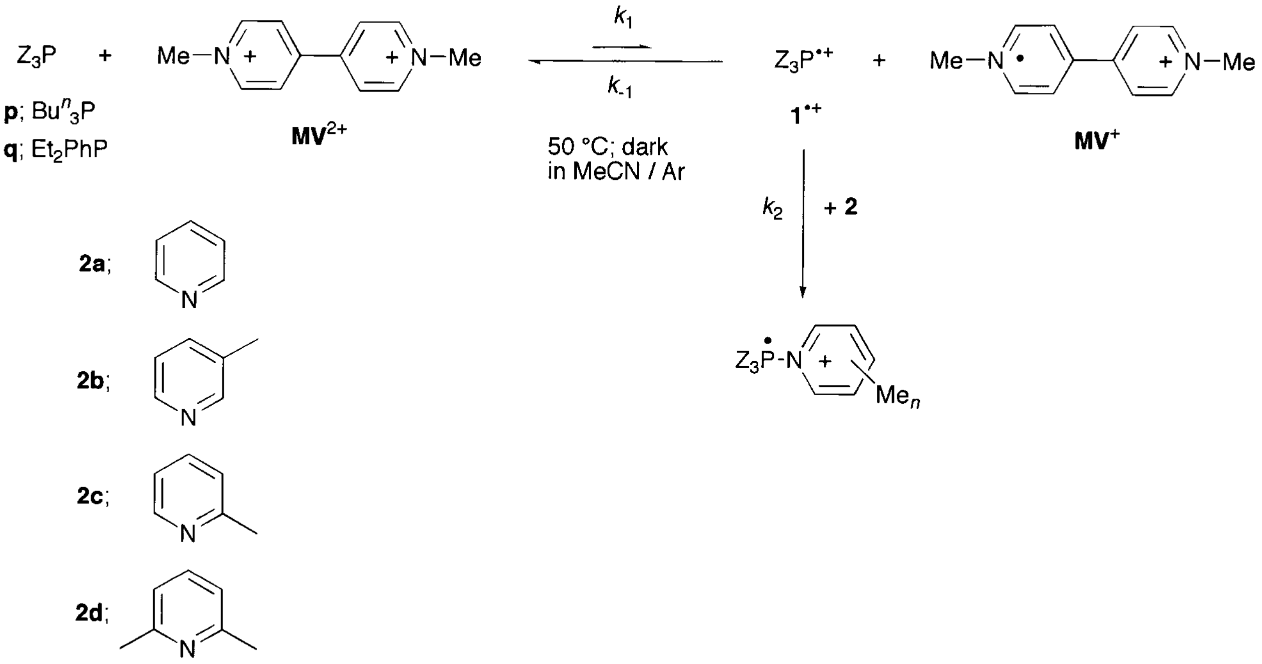
Methylviologen MV^{2+} is reduced to its one-electron reduction form MV^{+} upon the reaction with **1**, which is clear evidence for single-electron transfer (SET) occurring from **1** to MV^{2+}. On the other hand, a difference in redox potentials of **1** [10] and MV^{2+} [7] predicts that the SET step is highly endothermic so that MV^{+} is not accumulated in a practical amount. This enigma can be solved by taking into account a follow-up reaction of the radical cation $\mathbf{1}^{\cdot+}$. If $\mathbf{1}^{\cdot+}$, a product of the SET reaction, undergoes an irreversible chemical reaction to escape from the equilibrium of the SET step, the equilibrium would be shifted to the right side, resulting in an accumulation of MV^{+}. We have found that MV^{+} is formed in a practical amount in the reaction of **1** with MV^{2+} in the presence of alcohol or thiol (RXH) [6]. In the present reaction, **2** most likely assumes the role of RXH, undergoing an ionic reaction with $\mathbf{1}^{\cdot+}$ (Scheme 1). In support for this mechanism, no formation of MV^{+} was observed in the absence of **2**.

By a steady-state approximation with respect to the concentration of $\mathbf{1}^{\cdot+}$ in Scheme 1, an increase in the concentration of MV^{+} is expressed by Equation 1 [11].

$$d[MV^{+}]/dt = k_1k_2[\mathbf{1}][\mathbf{2}][MV^{2+}]/(k_{-1}[MV^{+}] + k_2[\mathbf{2}]) \quad (1)$$

This equation predicts the observed "bent" kinetics (Figure 1) when $k_{-1}[MV^{+}] \approx k_2[\mathbf{2}]$ [12,13]. In other words, the observation shows that the radical cation intermediate $\mathbf{1}^{\cdot+}$ undergoes the back-electron transfer to MV^{+} (k_{-1}) and an ionic reaction with **2** (k_2) with a comparable efficiency. In fact, an iterative calculation based on Equation 1 finally affords a theoretical line that fits excellently to the observed data, as seen in Figure 2 at certain values of constants k_1 and k_{-1}/k_2. These values are summarized in Table 1, together with relative rate constants of k_2, k_2^{rel}, which are estimated based on an assumption that the k_{-1} value is the same for all of the reactions.

The k_2^{rel} value represents the reactivity of the phosphine radical cation $\mathbf{1}^{\cdot+}$ toward the pyridine nucleophile **2**. Comparison of these values shows that an ionic reaction of $\mathbf{1p}^{\cdot+}$ with **2** is controlled mainly



SCHEME 1

by a steric factor, with little influence from an electronic factor; the reaction becomes less favorable with increasing steric hindrance of **2**, whereas the order of k_2^{rel} is opposite to that expected from the basicity of **2** represented by p*K*a. This finding suggests that both reactants are in proximity at the transition state (TS). A TS of such a structure would be expected to undergo stabilization by **2**; an unpaired electron would be delocalized into the pyridine moiety through resonance.

To test stabilization of the TS by an aromatic ring, we carried out the reaction of **1q**, a phosphine that has a phenyl ligand on the phosphorus, with MV^{2+} in the presence of **2** or methanol (MeOH). Results listed in Tables 1 and 2 show that attachment of a phenyl ring on the phosphorus results in retardation of the reaction, showing that stabilization by the phenyl ligand is more significant at the ground state than at the TS [14]. This is reasonable because the positive charge on the phosphorus is partly neutralized by a nucleophile, **2** or MeOH, at the TS. Importantly, the degree of the retardation is larger when the nucleophile is **2** than when the nucleophile is MeOH; the rate ratio $k_2^{\mathrm{rel}}(\mathbf{1p}^{\cdot+})/k_2^{\mathrm{rel}}(\mathbf{1q}^{\cdot+})$ is >11, >9.4, and >5.0, for the reactions with **2a**, **2b**, and **2c**, respectively, whereas the ratio is 1.4 for the reaction with MeOH. The difference in the rate retardation between the reactions with **2** and MeOH is accounted for because of specific stabilization of the TS by **2**. Pyridine **2** exerts an additional effect to stabilize the TS; the unpaired electron is delocalized into **2**. This effect of **2** is larger in the reaction of $\mathbf{1p}^{\cdot+}$ than in the reaction of $\mathbf{1q}^{\cdot+}$ because the TS for the latter reaction is already stabilized by the phenyl ligand [15]. As a result, the TSs for the reactions of $\mathbf{1p}^{\cdot+}$ and $\mathbf{1q}^{\cdot+}$ in the presence of **2** are close in energy to each other, resulting in a larger ratio in k_2^{rel} than that in the presence of MeOH. Energy diagrams of these reactions depicted in Figure 3 visualize our discussion here.

In conclusion, we have demonstrated clearly that an aromatic moiety stabilizes the TS for the reaction of a trivalent phosphorus radical cation with a nucleophile irrespective of whether it is a ligand on the phosphorus or the nucleophile itself. The stabilization results from delocalization of an unpaired electron, which is originally generated on the phosphorus atom, into the aromatic moiety.

Finally, we refer to the inconsistency in k_1 values. The k_1 values should be the same irrespective of the **2** present in the reaction system, because **2** is not one of the reactants in the k_1 step. Probably, pyridine **2** stabilizes both the ground state ($\mathbf{1} + \mathrm{MV}^{2+}$) and the TS by acting as a Lewis base, and the degree of such stabilization depends on **2**. Thus, both states are stabilized to a higher degree when the steric hindrance around the nitrogen of **2** is smaller. If one admits that the stabilization is more significant in the ground state than in the TS, taking into account that the positive charge is more localized in the former, the

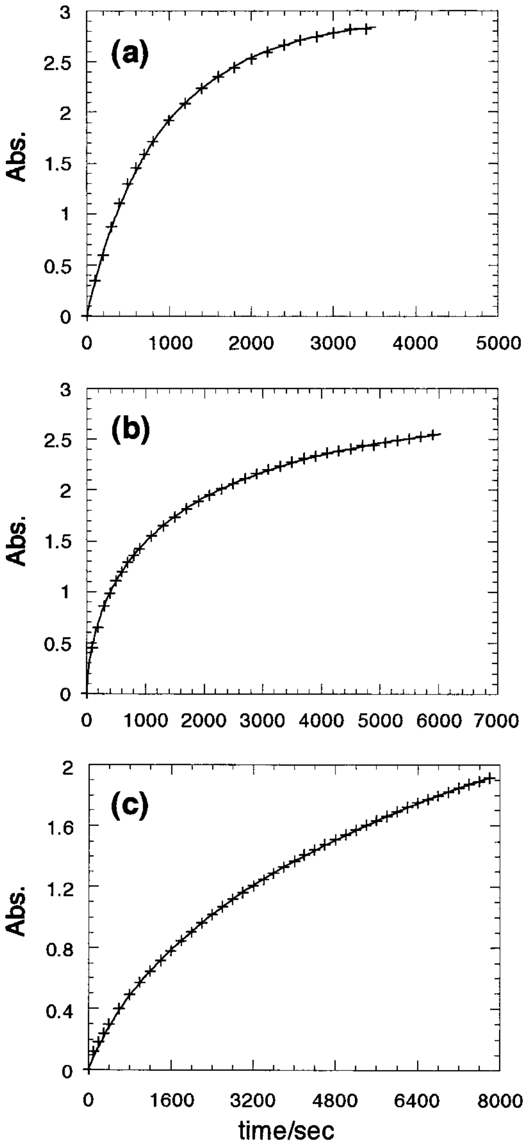


FIGURE 2 Time-course of increase in the absorption of MV^{+} at 605 nm for the reactions with **2a** (a), **2b** (b), and **2c** (c). The crosses (+) represent experimental points. The lines represent the best fit curve based on Equation 1.

TABLE 1 Reaction of Z_3P (1) with MV^{2+} in the Presence of Pyridine Derivatives (**2**)[a]

Z_3P	(**1**)	**2**	$10^3k_1/s^{-1}$ dm^3mol^{-1} [b]	$10^{-3}k_{-1}/k_2$ [b]	k_2^{rel} [c]	pK_a of **2**
Bu_3^nP	(**1p**)	**2a**	0.44	9.4	1	5.19
		2b	0.86	11	0.85	5.79
		2c	4.7	21	0.45	5.97
		2d	2.7	76	0.12	6.75
Et_2PhP	(**1q**)	**2a**	0.42	>100	<0.09	5.19
		2b	0.86	>100	<0.09	5.79
		2c	0.86	>100	<0.09	5.97

[a] $[\mathbf{1}]_0 = 1.50 \times 10^{-1}$ mol dm^{-3}; $[MV^{2+}]_0 = 2.00 \times 10^{-4}$ mol dm^{-3}; $[\mathbf{2}]_0 = 1.50$ mol dm^{-3}. In acetonitrile at 50°C under an argon atmosphere in the dark.
[b] Errors are within 3%.
[c] Relative value of rate constant k_2.

TABLE 2 Reaction of Z_3P (**1**) with MV^{2+} in the Presence of Methanol[a]

Z_3P	(**1**)	$10^3k_1/s^{-1}$ dm^3mol^{-1} [b]	$10^{-3}k_{-1}/k_2$ [b]	k_2^{rel} [c]	*Ref.*
Bu_3^nP	(**1p**)	0.33	4.0	0.50	[d]
Et_2PhP	(**1q**)	0.77	5.6	0.36	[e]

[a] $[1]_0 = 1.50 \times 10^{-1}$ mol dm^{-3}; $[MV^{2+}]_0 = 2.00 \times 10^{-4}$ mol dm^{-3}; $[MeOH]_0 = 1.50$ mol dm^{-3}. In acetonitrile at 50°C under an argon atmosphere in the dark.
[b] Errors are within 3%.
[c] Relative value of rate constant k_2.
[d] Previous work. Ref. [6].
[e] This work.

sterically less-hindered pyridine **2** results in a higher energy gap between the ground state and the TS to make the k_1 value smaller. The observation seems to be in accordance with this trend, but the situation may be more complicated because the basicity of **2** is also responsible for the stabilization of the ground state and the TS.

EXPERIMENTAL

Instruments

UV-visible spectra were recorded on a Shimadzu UV-2200A UV-vis recording spectrophotometer. GC analysis was done with a Shimadzu GC-14A gas chromatograph. Mass spectra were obtained on a Shimadzu GCMS-QP2000A gas chromatograph-mass spectrometer equipped with a Shimadzu GC-MSPAC 200S data processor. ^1H and ^{31}P NMR spectra were obtained on a Varian XL 200 NMR spectrometer operating at 200 and 81 MHz, respectively.

Materials

1,1′-Dimethyl-4,4′-bipyridinium (methylviologen; MV^{2+}) tetrafluoroborate was obtained according to the procedure described previously [6]. Tributylphosphine (**1p**) and pyridine derivatives (**2a–d**) were commercially available (Tokyo Chemical Industry) and distilled before use. Diethylphenylphosphine (**1q**) was prepared as described elsewhere [16,17], and summarized here. To a solution of two equivalents of ethylmagnesium bromide in tetrahydrofuran (THF), cooled by an ice bath, was added slowly a solution of dichlorophenylphosphine in THF, and

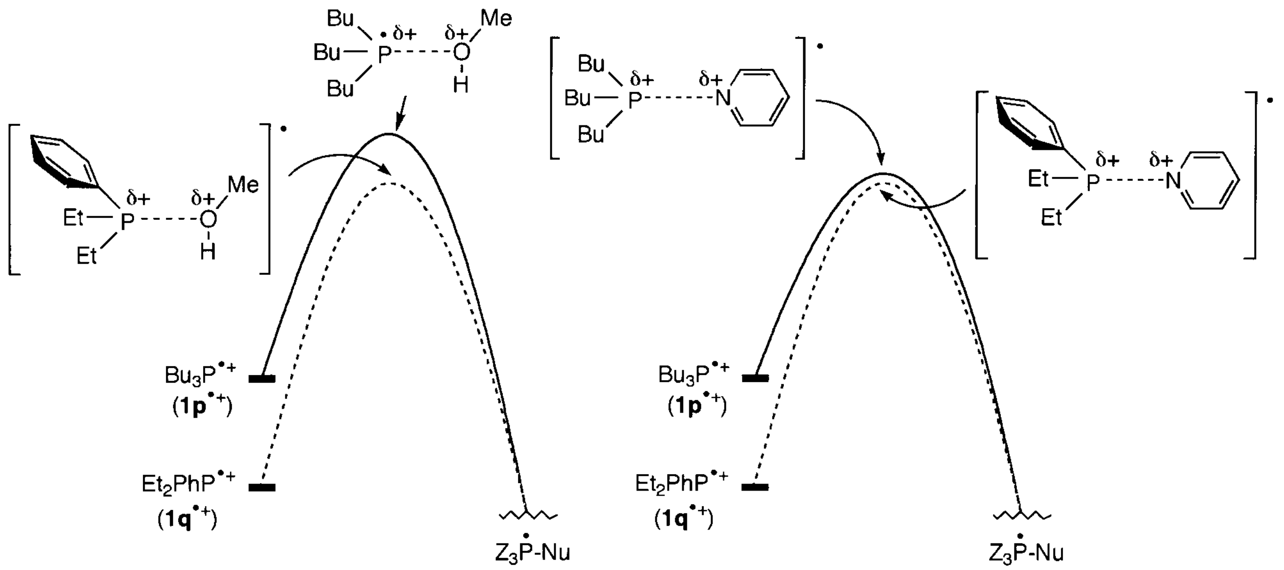


FIGURE 3 Energy diagrams for the reactions of trivalent phosphorus radical cations with MeOH (left) and with **2** (right). Solid and dashed lines denote the reactions of $\mathbf{1p}^{\cdot+}$ and $\mathbf{1q}^{\cdot+}$, respectively.

the mixture was left to react for an additional two hours at room temperature. Pyridine was added to the mixture to liberate the phosphine from the magnesium complex, and the magnesium salt that precipitated was removed by filtration. The filtrate was concentrated under reduced pressure, and the resulting crude material was purified by distillation (b.p. 53°C, 0.1 mmHg).

Kinetics

Kinetics experiments were carried out according to the procedure described before [6]. Kinetics data obtained was analyzed as in the previous works to calculate the rate constants [6,12,13].

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[11] As has been discussed in Ref. [6], a step represented by k_1/k_{-1} in Scheme 1 is a composite of several steps including a formation step of an encounter complex. Accordingly, constants k_1 and k_{-1} in Equation 1, respectively, are products of rate constants of these several steps. Even with this simplification, however, it is guaranteed that k_2 in Equation 1 is the rate constant for the ionic reaction of $1^{\cdot+}$ with a nucleophile.

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[14] Replacement of butyl groups in **1p** by ethyl groups is also responsible for the observed retardation of the rate, but the effect is hardly of significance, if any.
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