

SOLVENT EFFECT ON GROUND-STATE VERSUS TRANSITION-STATE STABILIZATION
BY METAL IONS. CONTRASTING METAL ION BEHAVIOUR IN TETRAGLYME AND
ETHANOL FOR NUCLEOPHILIC DISPLACEMENT AT A PHOSPHORUS CENTRE

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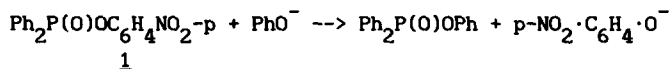
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Summary: The rate of reaction of p-nitrophenyl diphenylphosphinate with alkali metal phenoxide follows the order LiOPh > KOPh in ethanol as solvent but in tetraglyme the reactivity order is KOPh >> LiOPh and the reaction rate is much faster, which is accounted for on the basis of differing stabilization of the ground-state through hydrogen-bonding and of the transition-state by interaction with M⁺ in the two solvents.

We have reported that the reaction of p-nitrophenyl diphenylphosphinate, Ph₂P(O)OC₆H₄NO₂-p (**1**), with ethoxide ion in ethanol is subject to electrophilic catalysis by alkali metal cations (Li⁺ > K⁺) and that crown ethers and cryptands have a marked retarding effect on the rate of reaction.^{1a,b} We now report on the contrasting kinetic behaviour in the reaction of **1** with alkali-metal phenoxides in the solvents ethanol and tetraethylene glycol dimethyl ether (tetraglyme). The study affords insight on differential metal ion interactions with the ground-state and transition-state (catalysis or inhibition) and the role of solvent in stabilizing anions and cations through hydrogen-bonding and complexation.

The kinetic results for the reactions of lithium and potassium phenoxide with **1**,



in the solvents ethanol and tetraglyme at 25°C are displayed in Figures 1 and 2. The rates were measured by standard spectrophotometric methods for the slower reactions in ethanol, while stopped-flow techniques were used in the case of the faster reactions in tetraglyme, by following the appearance of the spectral absorption due to p-nitrophenoxide anion. The reactions proceeded quantitatively and in all cases clean first order kinetics were followed (phenoxide in large excess). Further notable results pertain to the effect of addition of crown ethers and cryptands; the effect of added salts (LiX, KX), and the effect of added water and phenol, as described below.

The key observations made are the following. For the reaction in ethanol: (1) k(LiOPh) > k(KOPh); (2) added Li⁺ and K⁺ salts (e.g. as MClO₄) accelerate the reaction (Li⁺ > K⁺); (3) added crown ethers and cryptands have a rate-retarding effect, and k(KOPh + 2,2,2-cryptand) =

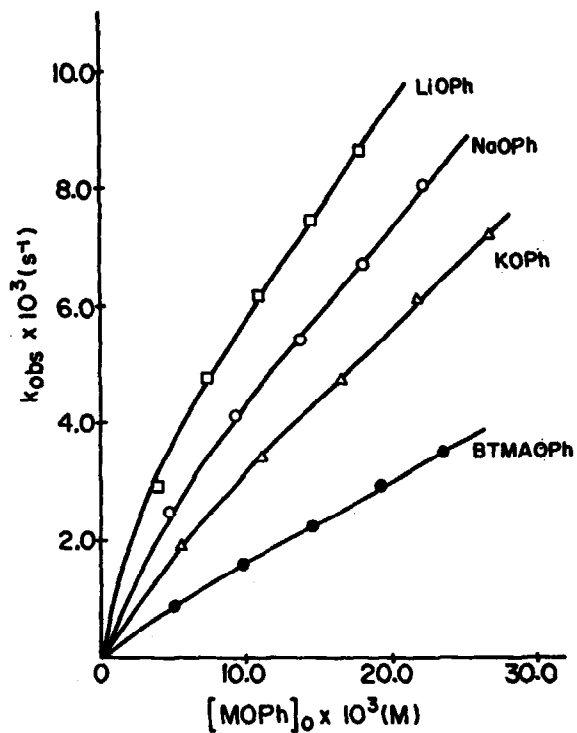


Figure 1. Kinetic data for reaction of p-nitrophenyl diphenylphosphinate (**1**) with alkali metal phenoxides and benzyltrimethylammonium phenoxide (BTMAOPh) in ethanol at 25°C.

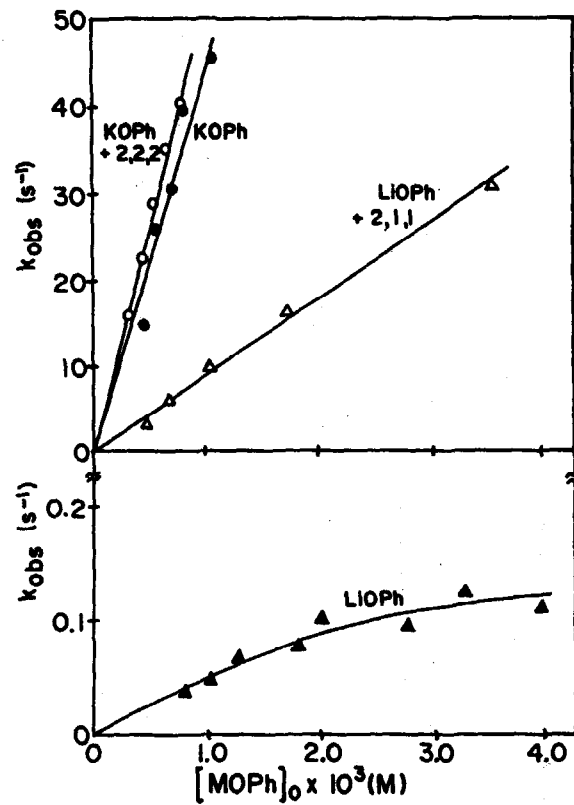


Figure 2. Kinetic data for reaction of **1** with lithium and potassium phenoxide in absence and presence of cryptand complexing agents in tetraglyme at 25°C.

$k(\text{LiOPh} + 2,1,1\text{-cryptand})$; (4) added water and phenol in small concentrations have little or no effect on the rate.^{1c}

For the reaction in tetraglyme: (1) $k(\text{LiOPh}) \ll k(\text{KOPh})$; (2) added Li^+ and K^+ have a small retarding effect ($\text{Li}^+ > \text{K}^+$); (3) added crown ethers and cryptands accelerate the reaction, with 2,1,1-cryptand having a much greater effect on the LiOPh reaction than 2,2,2-cryptand on the KOPh reaction; (4) added water and phenol have marked rate-inhibiting effects.

Importantly, the overall reactivity in tetraglyme is much greater compared to ethanol. On the assumptions that the KOPh + 2,2,2-cryptand system reflects the reactivity of free or dissociated phenoxide ion in tetraglyme (TG), and that the benzyltrimethylammonium phenoxide (BTMAOPh) correspondingly represents free phenoxide reactivity in ethanol, one obtains $k_{\text{PhO}^-}^{\text{TG}}/k_{\text{PhO}^-}^{\text{EtOH}} \sim 10^5$. The following reactivity relationships thus hold for the two solvents. For EtOH, $k(\text{Li}^+\text{PhO}^-) > k(\text{K}^+\text{PhO}^-) > k(\text{PhO}^-)$; and for tetraglyme, $k(\text{PhO}^-) \approx k(\text{K}^+\text{PhO}^-) \gg k(\text{Li}^+\text{PhO}^-)$, where $k(\text{Li}^+\text{PhO}^-)$ and $k(\text{K}^+\text{PhO}^-)$ represent the rate constants due to ion paired species while $k(\text{PhO}^-)$ is the rate constant for free phenoxide.

The very small reactivity of lithium phenoxide coupled with the large accelerating effect of 2,1,1-cryptand in tetraglyme suggests that LiOPh exists largely as unreactive aggregates in this solvent. On the other hand the smaller reactivity of the LiOPh + 2,1,1-cryptand system compared to KOPh + 2,2,2-cryptand suggests that there is appreciable ion pairing between the cryptated Li^+ and PhO^- in tetraglyme and that the $\text{Li}(211)^+\text{PhO}^-$ species has a lower reactivity than free phenoxide ion.

We conclude that the much smaller reactivity of PhO^- in ethanol compared to tetraglyme is mainly due to stabilization of the nucleophile by hydrogen-bonding in the hydroxylic solvent.² In tetraglyme, the powerful retarding effect of added water or phenol would similarly result from hydrogen-bonding interactions of PhO^- with these H-bond donors. The inhibition infers that this type of interaction is much weaker in the transition-state, i.e. the ground-state stabilization effect is predominant.

It is evident from the results that alkali-metal ions have a marked effect on the kinetic behaviour, which can arise from interactions of M^+ with the ground-state, transition-state or both, differentially. A rate acceleration (catalysis) would result if M^+ interacts more strongly with the transition-state and, conversely, a stronger interaction with the ground-state would lead to a rate retardation (inhibition).³ It is reasonable to assume that the ground-state interaction would involve primarily M^+ with phenoxide ion rather than with the neutral substrate (there is no direct evidence for significant association of alkali-metal ions with the substrate).

Thus the interaction of M^+ with PhO^- should be much weaker in ethanol than in tetraglyme, because of the competing H-bonding interaction in the former case ($\text{PhO}^- \text{---} \text{HOEt}$), although the more effective solvation of K^+ by TG would moderate the ground-state interaction in that

case.⁴ The rate acceleration by M^+ in ethanol can hence be accounted for by a stronger interaction with the transition-state relative to the ground-state. Conversely, in tetraglyme, M^+ will interact more strongly with PhO^- (ground-state effect) than with the transition-state, because PhO^- is no longer stabilized by the solvent, and this will lead to a rate retardation by added M^+ . The absolute effects are expected to be larger for Li^+ than for K^+ due to the higher charge density in the former,⁵ and hence the differences will also be larger for Li^+ than for K^+ .

Our results bring into focus the relative advantages of tetraglyme as a potential solvent for nucleophilic displacement processes, compared to ethanol, and the powerful role of hydrogen-bonding interactions. The absolute rates of reaction are much larger (comparable to DMSO⁶) in the former solvent, though reactivity is greatly retarded by added phenol and water which stabilize the nucleophile. On the other hand, metal ion catalysis is observed in ethanol but not in tetraglyme as a result of the change in balance between transition-state and ground-state stabilization by M^+ . Thus tetraglyme as a solvent not only alters dramatically the absolute reaction rates, but alters both qualitatively and quantitatively the influence of metal cations on these processes. Our demonstration of the solvent dependence of metal ion catalysis will have bearing on other processes where different types of metal ion effects have been observed.⁷

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