of 2-hydroxymethyl-1-methylpyrrolidine (0.466 g, 4.05 mmol) was added *n*-butyllithium (6.75 mmol) at 0 °C. After 30 min, the reaction mixture was cooled to −123 °C. An ether (2 mL) solution of benzaldehyde (0.106 g, 1 mmol) was added and stirred for 1 h at −123 °C. The usual workup gave (*S*)-1-phenyl-1-pentanol (0.146 g, 89%): $[\alpha]^{24}_D$ −4.3° (*c* 2.99, benzene) (14%, optical purity).

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Oxyphosphorane and Monomeric Metaphosphate Ion Intermediates in Phosphoryl Transfer from 2,4-Dinitrophenyl Phosphate in Aprotic and Protic Solvents

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Abstract: The reactions of 2,4-dinitrophenyl dihydrogen phosphate, $ArPH_2$, and of salts of type $(ArPH)^-(R_4N)^+$, $(ArPH)^-(R_3NH)^+$, $(ArP)^{2-}(R_4N)^+(R_3NH)^+$, and $(ArP)^{2-}2(R_3NH)^+$, where R_4N^+ = $(n\text{-}C_4H_9)_4N^+$ and R_3N = $(i\text{-}C_3H_7)_2C_2H_5N$, have been studied in aprotic and protic solvents, in the absence and in the presence of alcohols or water, ROH, following the release of phenol and the fate of the phosphorus. The results are interpreted as follows. (1) The *acid* and the *monoanion* react via oxyphosphorane intermediates, P(5). (2) The *dianion* reacts via a monomeric metaphosphate ion intermediate, PO_3^-. In the absence of ROH, acid, monoanion, and dianion generate cyclic trimetaphosphoric acid or its salts, $(CP_3)^{3-}$ in aprotic solvents. Phosphoryl transfer to ROH by the P(5) mechanism proceeds at a relatively slow rate, the rate depends on alcohol size, and the reaction does not generate *tert*-butyl phosphate from *tert*-butyl alcohol. Rates are faster and independent of alcohol size, and *tert*-butyl phosphate is formed from *tert*-butyl alcohol by the PO_3^- mechanism. Formation of $(CP_3)^{3-}$ is not an indication of PO_3^- intermediacy in phosphorylation. The conclusions are limited to aminium salts of $ArPH_2$ where the amine is sterically hindered.

This work is concerned with the mechanisms by which phosphomonoesters transfer their phosphoryl group to nucleophiles in solutions:

$$XP(O)(OH)_2 + ROH \rightarrow ROP(O)(OH)_2 + XH \quad (1)$$

We have studied the behavior of anhydrous 2,4-dinitrophenyl phosphate[2] in aprotic and protic media, in the absence of bases and in the presence of one or more molar equivalents of the sterically hindered diisopropylethylamine, and have compared the results with those obtained utilizing the anhydrous monotetra-*n*-butylammonium salt of the acid, $(ArPH)^-(R_4N)^+$. From such studies, we have obtained compelling evidence for the participation of oxyphosphorane, P(5), and of monomeric metaphosphate ion, PO_3^-, intermediates in these reactions, depending on experimental conditions.

The participation of P(5) intermediates in reactions of phosphotriesters and phosphodiesters is widely accepted.[3-9] The intervention of PO_3^- intermediates in the hydrolysis of *alkyl* phosphates was proposed to account for a maximum reaction rate at the pH which corresponds to a maximum concentration of monoanion, $(RPH)^-$[10-13] (eq 2).[10-11]

Aryl phosphates, $XP(O)(OH)_2$, derived from phenols, XH,

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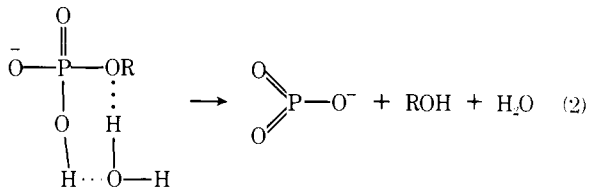
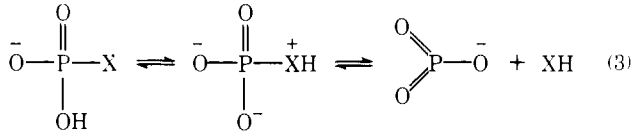


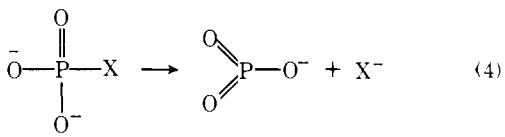
(2)

with pK_a >5.5 (in water) have pH-rate profiles similar to those of alkyl phosphates.[14-16] Kirby[15] concluded that, in the absence of nucleophilic amines, monoanions of this type undergo hydrolysis via PO_3^-, as shown in eq. 3.



(3)

Aryl phosphates derived from phenols with pK_a <5.5 show maximum reaction rate at the pH which corresponds to a maximum concentration of dianion.[15,16] Kirby proposed that this type of phosphate can undergo hydrolysis via PO_3^- from both the monoanion (eq 3), and the dianion (eq 4), with the



(4)

latter mechanism resulting in a faster reaction rate. The mechanism of eq 4 has also been invoked by other investigators.[17-26]

The PO_3^- intermediate hypothesis has been extensively discussed.[27-31] Monomeric alkyl metaphosphates, $ROPO_2$, have also been proposed as intermediates in certain pyrolyses,[32,33] and in mass spectrometry.[34] There is also a growing literature[35-40] dealing with transformations of structures XP(A)(Y)(ZH) into YP(=A)(=Z).

The biochemical literature[41-48] contains several studies involving the particular phosphomonoester, $ArPH_2$,[2] as a model for enzymatic phosphoryl transfer reactions.

Results

Acid-Base Equilibria in Reactions of $ArPH_2$.[1b] The acids relevant to the present study have the following pK_as in water: $ArPH_2$, ~1.0 and 4.6; RPH_2,[49] ~1.5 and 6.6; phosphoric acid, 2.1, 7.2, and 12.0; cyclic trimetaphosphoric acid, ~1.0; ArOH, 4.1; and the aminium cation, R_3NH^+, 11.0. Acids become much weaker in nonaqueous solvents than in water,[50-53] and a particularly large effect has been noted in acetonitrile, which is the main aprotic solvent used in this study.[54] We assume that the monoanion, although present in significant amounts, is in equilibrium with the acid, $ArPH_2$, when 1 molar equiv of R_3N is added to the latter in acetonitrile. Likewise, significant amounts of both $(ArPH)^-$ and $(ArP)^{2-}$ are expected in the mixed aprotic-protic media when $ArPH_2$ is treated with 2 molar equiv of R_3N.

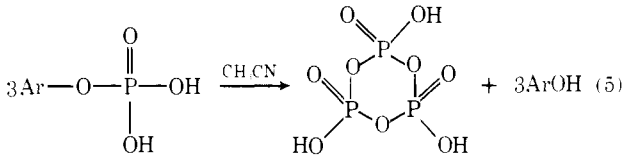
Reactions of the Free Acid, $ArPH_2$. The pure acid is reasonably stable in the crystalline state, but it is slowly transformed into trimetaphosphoric acid in acetonitrile (eq 5 and Table I). Phosphoryl transfer to 1 molar equiv of methanol occurs faster than cyclization in acetonitrile (eq 6). The rate of alkyl phosphate formation is sensitive to the size of the alcohol, and *tert*-butyl alcohol does not function as substrate in this reaction.

Alcoholysis of $ArPH_2$ is not significantly faster in the pure alcohol than in acetonitrile, in spite of the large increase in alcohol/acid ratio, which suggests a retardation of the reaction in the protic medium. This same effect is noted in the cyclization reaction. The behavior of $ArPH_2$ toward water[55] and alcohols is comparable, according to the representative data included in Table I. Independent experiments show that RPH_2 and H_3PO_4 are not produced from CP_3H_3 in these experiments.

Table I. Reactions of 2,4-Dinitrophenyl Phosphate, $ArPH_2$, in 1.0 M Solution at 35 °C, RPH_2 = Alkyl Phosphate, CP_3H_3 = Cyclic Trimetaphosphoric Acid

solvent	reagent (molar equiv)[a]	t_{obsd}[b]	results[c,d]
CD_3CN	none	5 days	CP_3H_3
CD_3CN	CH_3OH (1)	15 h	RPH_2
CD_3CN	$(CH_3)_2CHCH_2OH$ (1)	2 days	RPH_2
CD_3CN	$(CH_3)_2CHOH$ (1)	6 days	RPH_2
CD_3CN	$(CH_3)_3COH$ (1)	3 days[e]	CP_3H_3
CH_3OH	CH_3OH (25)	7 h	RPH_2
$(CH_3)_2CHOH$	$(CH_3)_2CHOH$ (13)	7 days	RPH_2
$(CH_3)_3COH$	$(CH_3)_3COH$ (10)	5 days[f]	no reaction
CD_3CN	H_2O (1)	10 h	H_3PO_4
H_2O	H_2O (55)	10 h	H_3PO_4

[a] Per mol of phosphate. [b] Values are approximate half-times of reaction. $[ArPH_2] \sim$ [product], unless otherwise noted. [c] Phosphate analyses by ^{31}P and ^1H NMR spectrometry, with reference to the authentic compounds. ArOH analyses by ^1H NMR. [d] The products indicated were those observed at t_∞. [e] $t_{obsd} \neq t_{1/2}$; there is evidence for side reactions of CP_3H_3, probably slow hydrolysis. [f] Observations discontinued owing to side reactions of $ArPH_2$.



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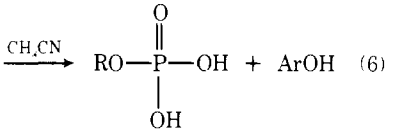
$\delta^{31}P$ −7.6 ppm $\delta^{31}P$ −22.4 ppm

$ArPH_2$ + ROH (1 molar equiv)



(6)

R = primary, secondary alkyl or H

Reactions of the Monoanion, $(ArPH)^-$. The salt $(ArPH)^-(R_4N)^+$ is transformed into $(CP_3)^{3-}$ in pure acetonitrile at a rate which is comparable to, or perhaps slightly higher than, the rate of cyclization of $ArPH_2$ (eq 7 and Table II). However, the salt does not transfer its phosphoryl group to 1 molar equiv of methanol in the aprotic solvent, as was observed with $ArPH_2$ (eq 8).

$$(ArPH)^-(R_4N)^+ \xrightarrow{CH_3CN} {}^1/_3(CP_3)^{3-} + ArOH \quad (7)$$

$(ArPH)^-$ + ROH (1 molar equiv)

$$\xrightarrow{CH_3CN} {}^1/_3(CP_3)^{3-} + ArOH \quad (8)$$

R = primary, secondary, tertiary alkyl or H

The phosphorylation of methanol by the monoanion occurs in the pure alcohol, although at a very slow rate. Analogous reactions carried out with higher primary and secondary alcohols generate both $(CP_3)^{3-}$ and $(RPH)^-$. In mixtures of acetonitrile and methanol, the monoanion produces both $(CP_3)^{3-}$ and $(RPH)^-$, with cyclization predominating over phosphorylation below certain methanol/phosphate ratios, and vice versa. It should be emphasized that an increase in the alcohol/phosphate ratio inevitably alters the nature of the me-

Table II. Reactions of 2,4-Dinitrophenyl Phosphate Monoanion, $(ArPH)^-$, at 35 °C

solvent	M	reagent (molar equiv)	t_{obsd}[a], days	results
		$(ArPH)^-[(n\text{-}C_4H_9)_4N]^+$		
CD_3CN	1.0	none	2[b]	$(CP_3)^{3-}$ + $(ArPH)^-$
CD_3CN	1.0	CH_3OH (1)	3[b]	$(CP_3)^{3-}$ + $(ArPH)^-$
CH_3OH	1.0	CH_3OH (25)	14[b]	$(RPH)^-$ + $(ArPH)^-$
CD_3CN-CH_3OH, 90:10[c]	0.2	CH_3OH (12)	13	$(CP_3)^{3-}$; traces of $(RPH)^-$
CD_3CN-CH_3OH, 50:50	0.2	CH_3OH (62)	13	$(CP_3)^{3-}$ + $(RPH)^-$ + $(ArPH)^-$; 1:2:2
CD_3CN-CH_3OH, 10:90	0.2	CH_3OH (112)	13	$(RPH)^-$ + $(ArPH)^-$; 1:1
CD_3CN-$(CH_3)_2CHOH$, 85:15	0.2	$(CH_3)_2CHOH$ (10)	7	$(CP_3)^{3-}$
CD_3CN-$(CH_3)_2CHOH$, 50:50	0.2	$(CH_3)_2CHOH$ (30)	14	$(CP_3)^{3-}$
$(CH_3)_2CHOH$	0.2	$(CH_3)_2CHOH$ (60)	14	$(CP_3)^{3-}$ + $(ArPH)^-$; 4:1
CD_3CN-$CH_3(CH_2)_2OH$, 85:15	0.2	$CH_3(CH_2)_2OH$ (10)	7	$(CP_3)^{3-}$
CD_3CN-$CH_3(CH_2)_2OH$, 50:50	0.2	$CH_3(CH_2)_2OH$ (30)	14	$(CP_3)^{3-}$ + $(ArPH)^-$; 4:1
$CH_3(CH_2)_2OH$	0.2	$CH_3(CH_2)_2OH$ (60)	14	$(CP_3)^{3-}$ + $(ArPH)^-$; 1:2
CD_3CN-$(CH_3)_3COH$, 80:20	0.2	$(CH_3)_3COH$ (10)	7	$(CP_3)^{3-}$
CD_3CN-$(CH_3)_3COH$, 45:55	0.2	$(CH_3)_3COH$ (30)	10	$(CP_3)^{3-}$ + $(ArPH)^-$; 2:1
CD_3CN	1.0	H_2O (1)	2[b]	$(CP_3)^{3-}$ + $(ArPH)^-$
H_2O	1.0	H_2O (55)	6[b,d]	$H_2PO_4^-$ + $(ArPH)^-$
CD_3CN-$(CH_3)_2CHOH$, 80:20	0.2[e]	$H_2PO_4^-(R_3NH)^+$, $(CH_3)_2CHOH$	10	$H_2P_2O_7^{2-}$[f]
		$ArPH_2$ + $(i\text{-}C_3H_7)_2C_2H_5N \rightleftharpoons (ArPH)^-[(i\text{-}C_3H_7)_2C_2H_5NH]^+$		
CD_3CN	1.0	none	6[b]	$(CP_3)^{3-}$ + $(ArPH)^-$
CD_3CN	1.0	CH_3OH (1)	8[b]	$(CP_3)^{3-}$ + $(ArPH)^-$
CH_3OH	1.0	CH_3Oh (25)	14[b]	$(RPH)^-$ + $(ArPH)^-$
CD_3CN	1.0	H_2O (1)	7[b]	$(CP_3)^{3-}$ + $(ArPH)^-$
CD_3CN	1.0	H_2O (10)	7	$(CP_3)^{3-}$ + $H_2PO_4^-$

[a] Time at which the product analyses were performed, unless otherwise noted. [b] Approximate half-time of reaction, $[(ArPH)^-] \sim$ [product]. Only the product indicated is observed at t_∞. [c] All mixed solvents are v/v. [d] $(CH_3)_4N^+$ salt employed for solubility reasons. [e] At 25 °C. [f] Small amounts of $(RPH)^-$ and $RHP_2O_7^{2-}$ and traces of $(CP_3)^{3-}$ also present.

dium, and this effect is quite significant even at the lowest phosphate concentrations permissible by our analytical methods, which follow the fate of the phosphorus, as well as that of the aryl group. This undoubtedly affects the extent of dissociation of the acids present.

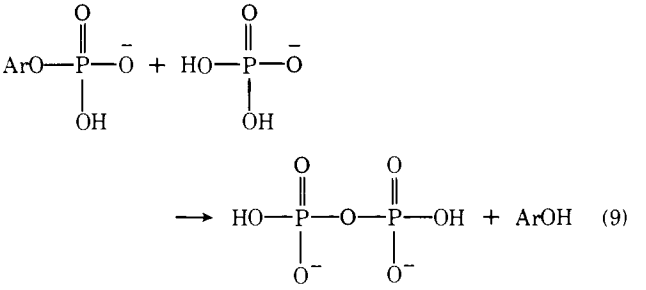
In mixtures of acetonitrile and alcohols, phosphorylation is not competitive with cyclization for alcohols larger than methanol. However, with the exception of *tert*-butyl alcohol, these alcohols can be phosphorylated at higher temperatures and in relatively dilute solutions of the salt in the pure alcohol. Independent experiments show that the alkyl phosphates are not generated from preformed $(CP_3)^{3-}$.

Two other trends are noted in these reactions. (1) The rate of cyclization decreases as the medium becomes poorer in acetonitrile and richer in alcohol. (2) The structure of the alcohols affects the cyclization rate; e.g., the cyclization is slower in 1-propanol than in 2-propanol, under comparable conditions. The behavior of the salt $(ArPH)^-(R_4N)^+$ toward water follows the same general trends as its behavior toward methanol.

Analogous studies have been carried out in solutions containing equimolar amounts of $ArPH_2$ and diisopropylethylamine, and it can be seen that they parallel the results obtained with the preformed alkylammonium salt, $(ArPH)^-(R_4N)^+$, although the latter reactions are slightly faster. We infer that the sterically hindered amine is acting simply as proton acceptor and is not exercising any catalytic effect.

In one of the experiments shown in Table II, the alkylammonium salt, $(ArPH)^-(R_4N)^+$, is allowed to react with the aminium salt derived from anhydrous orthophosphoric acid.[56] The major product of this reaction is inorganic pyrophosphate, while $(CP_3)^{3-}$ is obtained only in trace amounts. A comparable reaction, in the absence of orthophosphate, yields exclusively $(CP_3)^{3-}$. Evidently, the formation of $(CP_3)^{3-}$ from $(ArPH)^-$ is interdicted by orthophosphate, $(HPH)^-$ (eq 9).

Reactions of the Dianion, $(ArP)^{2-}$. Addition of 1 molar equiv of diisopropylethylamine to the salt $(ArPH)^-(R_4N)^+$ in acetonitrile results in an extraordinarily rapid formation of $(CP_3)^{3-}$; see eq 10 and Table III. This cyclization is much



(9)

faster than that of the monoanion, $(ArPH)^-$, which supports the conclusion that $(CP_3)^{3-}$ is indeed coming from $(ArP)^{2-}$. The rate-limiting step in the cyclization must have a large rate constant, since the concentration of $(ArP)^{2-}$ in pure acetonitrile cannot be very high under the conditions of the experiment.

$$(ArPH)^-(R_4N)^+ + R_3N \text{ or } ArPH_2 + 2R_3N \xrightarrow{CH_3CN} {}^1/_3(CP_3)^{3-} + ArO^- \quad (10)$$

Transfer of the phosphoryl group to 1 molar equiv of methanol is observed when 1 molar equiv of amine is added to $(ArPH)^-$ in acetonitrile. The rate of phosphorylation is comparable to that of the cyclization, and is insensitive to the structure of the alcohol. In fact, *tert*-butyl phosphate is the sole product observed in the presence of 1 molar equiv of *tert*-butyl alcohol (eq 11).

$$\begin{matrix}(ArPH)^- \\ \downarrow\uparrow \\ (ArP)^{2-}\end{matrix} + ROH\ (1\ \text{molar equiv}) \xrightarrow{CH_3CN} (RPH)^- + ArO^- \quad (11)$$

R = primary, secondary, tertiary alkyl or H

The system produced by addition of 2 molar equiv of the hindered amine, R_3N, to the acid, $ArPH_2$, is comparable to that produced when 1 molar equiv of R_3N is added to the salt

$(ArPH)^-(R_4N)^+$. Again, as in the monoanion case, the systems containing alkylammonium cations react at a faster rate than those which contain only aminium cations. This difference may reflect differences in degree of dissociation of the respective salts in the aprotic and mixed solvents.

From a number of experiments using $(ArP)^{2-}2(R_3NH)^+$ several trends are noted. (1) Phosphorylation of alcohols is slower in the pure alcohols than in acetonitrile, in spite of the increase in alcohol/phosphate ratio and the higher concentration of $(ArP)^{2-}$ expected in protic media. (2) In the pure aprotic solvents, the phosphorylation rate decreases as the solvent polarity decreases. (3) The behavior of the dianion toward water parallels its behavior toward alcohols.

Discussion

This investigation provides a reasonable basis for the following conclusions: (1) The free acid, $ArPH_2$, and the monoanion, $(ArPH)^-$, derived from alkylammonium or sterically hindered aminium cations react via P(5) intermediates in aprotic and protic media. (2) The dianion, $(ArP)^{2-}$, derived from the same types of cation reacts via a PO_3^- intermediate in comparable media.

These mechanistic pathways are associated with several characteristic experimental results, e.g.: (a) The reactions which proceed via P(5) generate their corresponding products at a much slower rate than the reactions which proceed via PO_3^-. (b) No *tert*-butyl phosphate is generated via P(5), but this hindered phosphomonoester is readily formed via PO_3^-.

It should be emphasized that these conclusions apply exclusively to the quaternary ammonium salts, and to the salts derived from the type of sterically hindered tertiary amine that is represented by diisopropylethylamine. Presumably, such amines are incapable of giving rise to nucleophilic catalysis in phosphorylation because they are unable to establish a P–N bond in the mandatory P(5) intermediate.

The first step in the formation of CP_3H_3 from $ArPH_2$ in acetonitrile is assumed to yield the P(5) intermediate shown in Scheme I. This step is probably acid catalyzed. The second step is the collapse of P(5) with loss of ArOH and formation of 2,4-dinitrophenyl pyrophosphate.

The aryl pyrophosphate should be more reactive than $ArPH_2$ owing to double activation of a phosphorus atom by electron-withdrawing groups. Therefore, the third step of the reaction is assumed to be relatively fast, and yields a P(5) intermediate which again collapses with loss of ArOH and formation of 2,4-dinitrophenyl tripolyphosphate (Scheme II). The latter is sterically well suited for an intramolecular step which yields a six-membered cyclic P(5), and finally the observed CP_3H_3.

Scheme III shows the P(5) intermediate suggested for the phosphorylation of alcohols and water by $ArPH_2$.

The mechanisms shown in these schemes accommodate the observed trend toward a decrease in rates of cyclization and phosphorylation of $ArPH_2$ in going from aprotic to protic solvents.[57,58] It is reasonable to expect a higher degree of polarity in the ground state than in the oxyphosphorane-like transition states for these reactions. Hence, preferential solvation,[59] and hence stabilization, of the more polar ground state by the protic solvent could lead to rate depression,[60] as observed.

The transformation of $(ArPH)^-$ into $(CP_3)^{3-}$ is assumed to proceed as shown in Scheme IV. Subsequent steps are analogous to those given in the cyclization of $ArPH_2$. The electrophile $(ArPH)^-$ should be less reactive than $ArPH_3^+$, but the former should be present in higher concentration than the latter in all the media employed.

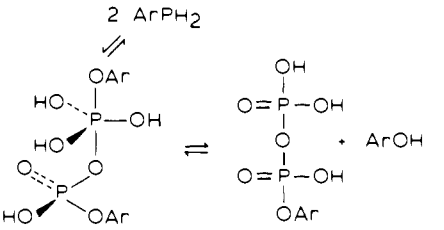
The decrease in rate of cyclization from $(ArPH)^-$ in protic vs. aprotic solvents seems to be another manifestation of the

Table III. Reactions of 2,4-Dinitrophenyl Phosphate Dianion, $(ArP)^{2-}$, in 1.0 M Solution at 35 °C, $R_3N = (i\text{-}C_3H_7)_2C_2H_5N$

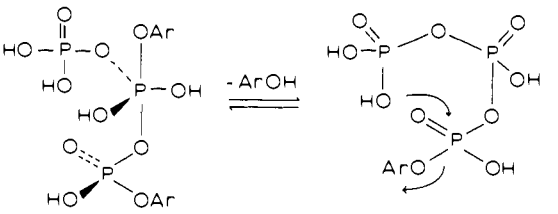
solvent	reagent (molar equiv)	t_{obsd}[a]	results
	$(ArPH)^-[(n\text{-}C_4H_9)_4N]^+ + R_3N \rightleftharpoons (ArP)^{2-}[(n\text{-}C_4H_9)_4N]^+(R_3NH)^+$		
CD_3CN	none	1 min	$(CP_3)^{3-}$
CD_3CN	CH_3OH (1)	1 min	$(RPH)^-$
CD_3CN	$(CH_3)_2CHOH$ (1)	1 min	$(RPH)^-$
CD_3CN	$(C_2H_5)_2CHOH$ (1)	1 min	$(RPH)^-$
CD_3CN	$(CH_3)_3COH$ (1)	1 min	$(RPH)^-$
CD_3CN	H_2O (1)	1 min	$H_2PO_4^-$
	$ArPH_2 + R_3N \rightleftharpoons (ArPH)^-(R_3NH)^+$; $(ArPH)^-(R_3NH^+) + R_3N \rightleftharpoons (ArP)^{2-}2(R_3NH)^+$		
CD_3CN	none	40 min	$(CP_3)^{3-}$
CD_3CN	CH_3OH (1)	30 min	$(RPH)^-$
CH_2Cl_2	CH_3OH (1)	4 h	$(RPH)^-$
CD_3CN	$(CH_3)_3COH$ (1)	35 min	$(RPH)^-$
$(CH_3)_2CO$	$(CH_3)_3COH$ (1)	2.5 h	$(RPH)^-$
CH_2Cl_2	$(CH_3)_3COH$ (1)	4 h	$(RPH)^-$
CH_3OH	CH_3OH (25)	3.5 h	$(RPH)^-$
$(CH_3)_2CHOH$	$(CH_3)_2CHOH$ (13)	3.5 h	$(RPH)^-$
$(CH_3)_3COH$	$(CH_3)_3OH$	*b*	$(RPH)^-$
CD_3CN	H_2O (1)	20 min	$H_2PO_4^-$ [c]
H_2O	H_2O (55)	2.5 h	$H_2PO_4^-$
H_2O	H_2O (55)[d]	2.5 h	$H_2PO_4^-$

[a] Values are approximate half-times of reaction. The products indicated are observed at t_∞. [b] Salt is only partially soluble. [c] After several half-lives, weak ^{31}P signal at −10.4 ppm observed (probably $H_2P_2O_7^{2-}$). [d] Two molar equivalents of $[(CH_3)_4N]^+OH^-$ (pentahydrate) added to $ArPH_2$, both in water.

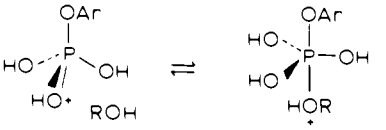
Scheme I



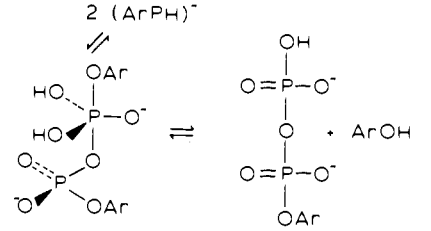
Scheme II



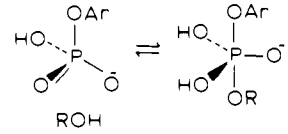
Scheme III



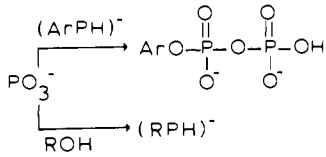
Scheme IV



Scheme V



Scheme VI

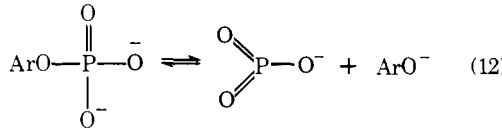


phenomenon of preferential solvation of ground state relative to transition state[60] in phosphate → oxyphosphorane transformations. The rate depression is significantly larger for a linear than for a branched alcohol, suggesting a more effective solvation of the ester by the former alcohol.

Support for the formation of a transient aryl pyrophosphate in the cyclization is provided by the effect of orthophosphate in this reaction. Orthophosphate, $(HPH)^-$, should be more nucleophilic than the monoanion, $(ArPH)^-$, and should replace the latter in the P(5) structure of Scheme IV. The result would be inorganic pyrophosphate, $H_2P_2O_7^{2-}$, as observed.

The P(5) intermediate postulated for the slow transfer of the phosphoryl group from $(ArPH)^-$ to alcohols is depicted in Scheme V. A comparison between Schemes III and V justifies the relatively faster rate of phosphorylation by $ArPH_2$ vs. $(ArPH)^-$.

The rate-limiting step in the reactions of the dianion is assumed to be the formation of the PO_3^- intermediate, as previously postulated[19-29] (eq 12).



(12)

The products formed from the dianion are rationalized according to Scheme VI.

The trend toward a decrease in rate of phosphorylation from $(ArP)^{2-}$ in protic vs. aprotic solvents is also in line with the preferential solvation of a more polar ground state relative to a less polar transition state.[60] In this case, the transition state of the rate-limiting step refers to the incipient three-coordinate phosphorus. The decrease in rate of phosphorylation from $(ArP)^{2-}$ in aprotic solvents, as the dielectric constant of the latter decreases, can be traced simply to a further decrease in the extent of dissociation of $(ArPH)^-$ to $(ArP)^{2-}$ as ϵ decreases.

Conclusions

Some of the conclusions reached in this work differ significantly from those found in the literature. Thus, Kirby[15] suggests that the monoanion, $(ArPH)^-$, undergoes hydrolysis via PO_3^- in the absence of nucleophilic amines. We propose, however, that this, and related phosphoryl transfers from $(ArPH)^-$, proceeds via P(5). The generation of PO_3^- by the mechanism of eq 3 is not operative, presumably because X is not sufficiently basic[61] in molecules $XP(O)(OH)_2$ when XH has pK_a below ~5.5. The mechanism of eq 3 could, however, be operative in monoanions derived from alkyl phosphates and from molecules where XH has pK_a above ~5.5.[10-16]

Other conclusions from our work are in agreement with those previously advanced. A number of investigators[14-29] have proposed that the dianion, $(ArP)^{2-}$, undergoes hydrolysis via a PO_3^- intermediate, in the absence of nucleophilic amines, which is entirely consistent with our data on phosphoryl transfer in media where significant amounts of $(ArP)^{2-}$ are likely to be present.

It should be evident that the duality of mechanisms operative in 2,4-dinitrophenyl phosphate as a function of the state of ionization of the molecule, and the sensitivity of both types of mechanisms to medium effects, must be taken into account in studies of enzymatic phosphoryl transfer reactions by means of this particular phosphomonoester as model.[41-48]

Experimental Section

^{31}P NMR spectra were measured on a Varian T-60A spectrometer at 24.3 MHz. Product analyses are accurate to ca. 5%. The ^{31}P NMR signals are given in parts per million vs. 85% H_3PO_4 = 0 (positive values are downfield from the reference). The ^1H NMR signals are given in parts per million vs. Me_4Si = 10 (τ).

Crystalline, Anhydrous 2,4-Dinitrophenyl Dihydrogen Phosphate ($ArPH_2$). This compound was prepared from dibenzyl phosphorochloridate[62] as described in the preceding communication.[1b]

Preparation of Tetra-*n*-butylammonium 2,4-Dinitrophenyl Hydrogen Phosphate. An aliquot of commercially available methanolic tetra-*n*-butylammonium hydroxide containing 0.43 mmol of the base was added to a solution of $ArPH_2$ (0.115 g, 0.43 mmol) in methanol (1 mL). The solution was *immediately* evaporated, and the residue was kept for 45 min at 25 °C (0.2 mm) and dissolved in CD_3CN. The ^1N NMR spectrum disclosed that the salt contained water. Evaporation of the solvent followed by evacuation at 0.2 mm for 2 h gave the anhydrous salt, δ ^{31}P −4.5 ppm (CD_3CN).

Reactions of Acid, $ArPH_2$, and of Salts, $(ArPH)^-$ and $(ArP)^{2-}$, Containing the Cations $(R_4N)^+$ and $(R_3NH)^+$. These reactions are described in Tables I-III.

Isolation and Characterization of Cyclic Trimetaphosphoric Acid, CP_3H_3, and Its Salts. These procedures have been described elsewhere.[1b]

Preparation of Anhydrous Crystalline Orthophosphoric Acid. Crystalline H_3PO_4 was prepared from commercially available 85% phosphoric acid by the method of Weber and King.[56] A sample (0.131 g, 1.3 mmol) was dissolved in D_2O (1 mL), and the solution was treated with acetonitrile (0.053 g, 1.3 mmol), used as internal reference for assay by ^1H NMR spectrometry. Integration of the CH_3CN vs. the HOD signals confirmed the absence of water in the samples of H_3PO_4 used in the present research.

Attempt to Isolate Bistetra-*n*-butylammonium 2,4-Dinitrophenyl Phosphate. Two molar equivalents of tetra-*n*-butylammonium hydroxide in methanol was added to an ice-cold solution of $ArPH_2$ (0.105 g, 0.4 mmol) in methanol (1 mL). The solution was *immediately* evaporated at −20 °C (0.1 mm), kept for 10 min under those conditions, and dissolved in CD_3CN (0.4 mL). The ^{31}P NMR spectrum revealed the presence of salts from methyl hydrogen phosphate (quartet) and dihydrogen phosphate (singlet) at ~+1.6 ppm. The ^1H NMR spectrum confirmed the presence of 2,4-dinitrophenoxide ion. There was no evidence for the presence of the desired ArP^{2-} salt.

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(1) (a) Research supported by Grants GM-20672 from the National Institutes of General Medical Sciences, and CHE76-16785 from the National Science Foundation. (b) Preliminary communication: F. Ramirez and J. F. Marecek, *Synthesis*, 601 (1978).

(2) The following abbreviations will be employed: $ArPH_2$ = 2,4-dinitrophenyl dihydrogen phosphate; R_3N = diisopropylethylamine; R_4N^+ = tetra-*n*-butylammonium; P(5) = oxyphosphorane; RPH_2 = alkyl dihydrogen phosphate; ArOH = 2,4-dinitrophenol; CP_3H_3 = cyclic trimethaphosphoric acid.

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A Mechanistic Study of the Reactions of Methylallyl Chlorides with Silver Nitrate in Acetonitrile[1]

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Abstract: The reactions of α-, β-, and γ-methylallyl chlorides with silver nitrate in acetonitrile approximate to a 2.5-order kinetic pattern, first order in the allyl chloride and 1.5 order in silver nitrate. At 45.1 °C the relative rates are allyl (1.0), β-methylallyl (2.2), α-methylallyl (5.3), *cis*-γ-methylallyl (15), and *trans*-γ-methylallyl (19). In contrast, the accompanying silver ion assisted allylic rearrangements and the slower reactions with silver perchlorate are faster for the α-methylallyl chloride than for the γ-methylallyl chlorides. In reaction with 0.20 M silver nitrate, 0.30 M *trans*-γ-methylallyl chloride gives 88% *trans*-γ-methylallyl nitrate and 12% α-methylallyl nitrate and, during reaction, there is negligible rearrangement to α-methylallyl chloride. The *cis*-γ-methylallyl chloride gives essentially identical product ratios, again without any geometric isomerization. The α-methylallyl chloride leads to 66% α-methylallyl nitrate and 34% γ-methylallyl nitrates but, during reaction, appreciable isomerization to γ-methylallyl chlorides occurs and correction for products formed after isomerization leads to a true product ratio for direct formation from α-methylallyl chloride of 79% α-methylallyl nitrate and 21% γ-methylallyl nitrates. Mechanistic implications of the above results are discussed.

Several alkyl halides[2-6] have been studied in their reactions with silver nitrate in acetonitrile. Comparison of reaction rates with those for silver perchlorate provides a semiquantitative measure of the extent of nucleophilic participation in the rate-determining step and application of this principle to allyl bromide[7] indicated considerable nucleophilic assistance.

Extension to methylallyl chlorides is of interest since the α- and γ-substituted compounds show intermediate (borderline) mechanisms in their solvolyses.[8,9] Allyl systems have been included among those for which the borderline behavior has been postulated to involve rate-determining attack upon a preformed ion-pair intermediate[10,11] and a search for additional evidence for a mechanism of this type is included within this study.

The study has some parallels with a previous one carried out in water.[12] It has, however, several practical and theoretical

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