Role of Through Space 2p–3d Overlap in the Alkylation of (ω-*N*,*N*-Dimethylaminoalkyl)diphenylphosphines and in the Alkaline Decomposition of Related Quaternary Phosphonium Salts

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Abstract: A series of (ω-*N*,*N*-dimethylaminoalkyl)diphenylphosphines has been prepared and subjected to reaction with benzyl chloride in benzene–methanol (60:40 v/v) at 31.0 ± 0.1 °C. Each of the quaternization reactions was found to follow the second-order rate law, and the data indicated the operation of a modest degree of through space 2p–3d overlap between the amino nitrogen and the phosphorus atom in the transition state. A series of quaternary phosphonium bromides containing an ω-*N*,*N*-dimethylaminoalkyl group bonded to phosphorus was prepared and subjected to hydroxide-induced decomposition reactions in Me_2SO at 22.0 ± 0.1 °C. Each reaction was found to follow the third-order rate law, and the data indicated the operation of a pronounced through space 2p–3d overlap effect. Finally, a series of quaternary phosphonium iodides containing an ω-methoxyalkyl group bonded to phosphorus was prepared and subjected to hydroxide-induced decomposition reactions in dioxane–water (1:1) at 45.0 ± 0.1 °C. Each reaction was found to follow the third-order rate law, and the relative velocities of reaction were found to be influenced by the inductive, electron-withdrawing effect of the methoxy group bonded to a saturated carbon atom of sufficient magnitude to mask any possible 2p–3d overlap effect.

Introduction

Kinetics data for the S_N2 reactions of various triarylphosphines with benzyl chloride, benzyl bromide, and *n*-butyl chloride, and of aryldiethylphosphines with ethyl iodide, have been presented in previous publications.[1-4] Four particularly important effects were observed. (1) The presence of an *o*-methoxy substituent on an aryl group of the phosphine causes a significant increase in the rate of the reaction. (2) The ratio of the rates of reaction of a given triarylphosphine with benzyl chloride and with *n*-butyl chloride is about 20, probably the smallest such ratio ever reported for S_N2 reactions of these alkyl chlorides. (3) Rate and activation-parameter profiles for the reactions of the isomeric anisyldialkylphosphines and anisyldialkylamines, respectively, with alkyl halides are distinctly different. (4) Diphenyl(2,6-dimethoxyphenyl)phosphine undergoes the quaternization reaction with alkyl halides faster than any other phosphine we have used, including tris(*o*-anisyl)phosphine and bis(*o*-methoxyphenyl)phenylphosphine. A rationalization of these observations has been presented based partly on the concept of through-space overlap of a pair of 2p electrons of the oxygen atom of a 2-methoxyphenyl group with an empty 3d orbital (or hybrid orbital) of phosphorus in an early transition state, this phenomenon being modified by the effects of ortho substituents on CPC bond angles and by possible double overlap effects.

It has also been suggested[1-4] that, if a through space 2p–3d overlap effect exists in the transition state of an S_N2 reaction, it will also be apparent in the phosphonium cation which is the product of the reaction. Three lines of support for this concept have been offered. (1) An X-ray diffraction study of benzyl(2-methoxyphenyl)diphenylphosphonium bromide has revealed that the P–O distance is substantially shorter than the sum of the van der Waals radii of phosphorus and oxygen. Furthermore, the bond angles indicate that the *o*-methoxyphenyl group is actually leaning toward the phosphorus in order to facilitate a P–O bonding interaction, and energy minimization calculations, in which the total steric energy is made up primarily of bond stretching energies and van der Waals nonbonded interactions, also indicate that a weak P–O bonding interaction exists. (2) For reasons cited in the previous papers,[1-4] the chemical shift of the protons of the methylene group directly bonded to phosphorus in the phosphonium salt represents the best probe of the overlap effect in the NMR spectrum of each compound. An upfield shift of the methylene hydrogens is expected when the electron density at phosphorus is increased owing to the overlap effect, and this is observed. (3) The rates of alkaline cleavage of a series of benzyltriarylphosphonium chlorides in 50% v/v aqueous dioxane at 10.1 °C have been determined.[6] The salts containing *o*-methoxy groups have been found to undergo reaction much more slowly than those containing *p*-methoxy groups. For example, benzylbis(*o*-methoxyphenyl)phenylphosphonium chloride reacts but 2.6×10^{-3} times as fast as benzylbis(*p*-methoxyphenyl)phenylphosphonium chloride. Benzyl(2,6-dimethoxyphenyl)diphenylphosphonium chloride reacts about ten times slower than the bis(*o*-methoxyphenyl) compound. These are the results anticipated based on the operation of the through-space 2p–3d overlap effect of the ortho-substituted compounds.

It has also been found[4] that, in the attempted reaction of diphenyl(methoxymethyl)phosphine with benzyl chloride, the inductive, electron-withdrawing effect of a methoxy group bonded to a saturated carbon atom is so large that the rate of reaction with benzyl chloride in benzene–methanol at 31 °C is essentially zero. In the reaction of diphenyl(4-methoxybutyl)phosphine with benzyl chloride, the inductive effect is still being felt, even though four methylene groups intervene between the phosphorus atom and the methoxy group, as evidenced by the fact that the rate is slightly lower than that of the reaction of diphenyl-*n*-butylphosphine with benzyl chloride. In spite of what must be large rate-depressing inductive effects of the methoxy group in the reactions of diphenyl(2-methoxyethyl)phosphine and diphenyl(3-methoxypropyl)-phosphine with benzyl chloride, these reactions are faster than those of diphenylethylphosphine and diphenyl-*n*-propylphosphine, respectively. Thus, it was concluded[4] that the 2p–3d overlap must be significant in the cases of the 2-methoxyethyl and 3-methoxypropyl compounds, inasmuch as the overlap effects are still apparent even though masked by the counterbalancing inductive effects. Since these results have important implications with respect to hydrolysis and exchange reactions of biologically important phosphate esters, in which alkoxyl groups of carbohydrate moieties are almost always in close proximity to the phosphorus atom of the phosphate group, we decided to expand the study to include the effects of methoxyalkyl groups on the rates of alkaline cleavage of quaternary

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Table I. Rate Data for Reactions of (ω-*N*,*N*-Dimethylaminoalkyl)-diphenylphosphines with Benzyl Chloride in Benzene–Methanol (3:2) at 21.0 ± 0.1 °C

phosphine	$k_2 \times 10^2$, L mol^{-1} h^{-1} [a]
diphenyl(2,6-dimethoxyphenyl)-[4]	539 ± 32
tris(*o*-anisyl)-[1]	195 ± 4
bis(*o*-anisyl)phenyl-[1]	146 ± 3
diphenyl(*o*-anisyl)-[1]	53.6 ± 0.7
diphenylmethyl-[4]	35.5 ± 0.3
diphenyl(2-methoxyethyl)-[4]	33.8 ± 0.3
diphenyl(3-methoxypropyl)-[4]	31.2 ± 0.2
diphenylethyl-[4]	27.1 ± 0.1
(*N*,*N*-dimethylaminomethyl)diphenyl-	26.6 ± 0.2
(δ-*N*,*N*-dimethylaminobutyl)diphenyl-	26.5 ± 0.2
diphenyl-*n*-butyl-[4]	26.0 ± 0.1
diphenyl-*n*-propyl-[4]	25.9 ± 0.1
(β-*N*,*N*-dimethylaminoethyl)diphenyl-	18.9 ± 0.2
(γ-*N*,*N*-dimethylaminopropyl)diphenyl-	13.7 ±.2
triphenyl-[1]	7.22 ± 0.13
diphenyl(methoxymethyl)-[4]	0.00[b]

[a] Average deviation based on four to ten experimental results. [b] Too slow to measure under conditions cited.

phosphonium salts, and also to examine the effects of ω-*N*,*N*-dimethylaminoalkyl groups in both alkylation of phosphines and the alkaline cleavage of phosphonium salts.

Results

(*N*,*N*-Dimethylaminomethyl)diphenylphosphine and the homologous β-*N*,*N*-dimethylaminoethyl-, γ-*N*,*N*-dimethylamino-*n*-propyl-, and δ-*N*,*N*-dimethylamino-*n*-butylphosphines were prepared and subjected to reaction with benzyl chloride in benzene–methanol (60:40 v/v) at 31.0 ± 0.1 °C. All of the quaternization reactions were found to follow the second-order rate law, and the results are summarized in Table I, together with a few selected results from previous studies for purposes of comparison.

Four new quaternary phosphonium bromides containing an ω-dimethylaminoalkyl group bonded to phosphorus were prepared and subjected to hydroxide-induced decomposition reactions in Me_2SO at 22.0 ± 0.1 °C. For purposes of comparison, benzyltriphenylphosphonium bromide was subjected to the same reaction conditions. All of the reactions were found to follow the third-order rate law, and the results are summarized in Table II.

Four new quaternary phosphonium iodides containing an ω-methoxyalkyl group bonded to phosphorus were prepared and subjected to hydroxide-induced decomposition reactions in dioxane–water (1:1) at 45.0 ± 0.1 °C. For purposes of comparison, the corresponding methyl, ethyl, *n*-propyl, and *n*-butyl salts were also subjected to the same reaction conditions. All of the reactions were found to follow the third-order rate law, and the results are summarized in Table III.

Discussion

In general, as found in previous studies,[4] there is an inverse relationship between the rate of alkylation of a given phosphine and the rate of decomposition of the corresponding quaternary phosphonium hydroxide. For example, as shown in Table I, diphenyl(methoxymethyl)phosphine does not undergo reaction with benzyl chloride at a measurable rate in benzene–methanol (3:2) at 31.0 ± 0.1 °C. However, as shown in Table III, (methoxymethyl)diphenylbenzylphosphonium iodide undergoes the alkaline decomposition reaction in dioxane–water (1:1) at 45.0 ± 0.1 °C at a faster rate than any of the other phosphonium iodides listed. Clearly, it is the inductive, electron-withdrawing effect of a methoxyl group bonded to a saturated carbon atom[7] which is responsible for both results. This effect

Table II. Rate Data for the Decomposition of Phosphonium Hydroxides at 22.0 ± 0.1 °C in Me_2SO

phosphonium bromide	$k_3 \times 10$, L^2 mol^{-2} min^{-1}
benzyltriphenyl-[a]	2310 ± 1
(γ-*N*,*N*-dimethylaminopropyl)diphenylbenzyl-	31.7 ± 0.3
(β-*N*,*N*-dimethylaminoethyl)diphenylbenzyl-	16.2 ± 0.2
(δ-*N*,*N*-dimethylbutyl)diphenylbenzyl-	5.7 ± 0.7
(*N*,*N*-dimethylaminoethyl)diphenylbenzyl-	5.1 ± 0.5

[a] The decomposition reactions of simple alkyldiphenylbenzylphosphonium hydroxides (alkyl = methyl, ethyl, *n*-propyl, *n*-butyl) were too fast to be measured under these conditions.

Table III. Rate Data for the Decomposition of Phosphonium Hydroxides at 45.0 ± 0.1 °C in Dioxane–Water (1:1)

phosphonium iodide	$k_3 \times 10$, L mol^{-2} min^{-1}
(methoxymethyl)diphenylbenzyl-	1750 ± 80
(β-methoxyethyl)diphenylbenzyl-	94.3 ± 12.3
methyldiphenylbenzyl-	16.7 ± 0.3
(γ-methoxypropyl)diphenylbenzyl-	4.19 ± 0.10
ethyldiphenylbenzyl-	1.76 ± 0.06
(δ-methoxybutyl)diphenylbenzyl-	1.64 ± 0.02
n-propyldiphenylbenzyl-	1.38 ± 0.10
n-butyldiphenylbenzyl-	0.917 ± 0.050

decreases the nucleophilicity of the phosphine and causes a decrease in the rate of the S_N2 reaction with benzyl chloride, but it increases the electrophilic reactivity of the phosphorus atom in the phosphonium salt and, by causing an increase in the concentration of the intermediate hydroxyphosphorane,[8-19] brings about an overall increase in the rate of alkaline cleavage. There is no clear evidence of a 2p–3d overlap effect in either reaction.

It is also apparent from the data presented in Table III that there is no major influence on rates of alkaline cleavage of the other ω-methoxyalkylphosphonium salts caused by possible 2p–3d overlap effects. This can best be seen by means of a comparison of the rate ratios for each ω-methoxyalkylphosphonium hydroxide decomposition to the corresponding simple alkylphosphonium hydroxide decomposition. For example, the ratio of the third-order rate constants for the (methoxymethyl)diphenylbenzylphosphonium hydroxide and methyldiphenylbenzylphosphonium hydroxide decomposition reactions is 1750/16.7 = 105. The corresponding ratios for the remaining pairs of reactions are β-methoxyethyl/ethyl = 54, γ-methoxypropyl/*n*-propyl = 3, and δ-methoxybutyl/*n*-butyl = 1.8. These results would seem to reflect mainly a normal dampening of the inductive, electron-withdrawal effect of the methoxy group bonded to a saturated carbon atom as the number of methylene groups from the phosphorus atom is increased. At the very least, any possible 2p–3d overlap effect is being masked quite effectively by the inductive effect.[20]

The apparent effects of the presence of ω-*N*,*N*-dimethylamino groups on the rates of alkylation reactions, shown in Table I, are not impressive. However, the same type of argument as used in the corresponding (ω-methoxyalkyl)phosphine reactions[4] can be invoked for the occurrence of at least a weak 2p–3d overlap effect. The inductive, electron-withdrawing effect of a dimethylamino group bonded to a saturated carbon atom is not as large as that of a methoxy group,[7] but it is nevertheless appreciable.[21] Nevertheless, each (ω-*N*,*N*-dimethylaminoalkyl)phosphine undergoes reaction with benzyl chloride at about the same rate as the corresponding simple alkylphosphine. Specifically, the ratio of the rates of reaction of (*N*,*N*-dimethylaminomethyl)diphenylphosphine and methyldiphenylphosphine with benzyl chloride is 26.6/35.5 = 0.75. The corresponding ratios for the remaining pairs of

Table IV. NMR Absorption Data Taken in $CDCl_3$ or CD_3OD Solution for the Methylene Hydrogens of Phosphonium Bromides

phosphonium cation	δ, ppm (CH_2)
benzytriphenyl-[a]	5.32
o-anisylbenzyldiphenyl-[a]	5.10
bis(*o*-anisyl)benzyldiphenyl-[a]	4.82
tris(o-anisyl)benzyldiphenyl-[a]	4.67
(*N,N*-dimethylaminomethyl)benzyldiphenyl-[b]	4.01-4.22[c]
(β-*N,N*-dimethylaminoethyl)benzyldiphenyl-[b]	4.10-4.40[c]
(γ-*N,N*-dimethylaminopropyl)benzyldiphenyl-[b]	4.27-4.40[c]
(δ-*N,N*-dimethylaminobutyl)benzyldiphenyl-[b]	4.06-4.45[c]

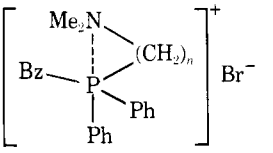
[a] $CDCl_3$ solution. [b] CD_3OD solution. [c] The presence of two 2H peaks, each with evidence of splitting, prohibited definitive assignment of *J* values.

reactions are β-*N,N*-dimethylaminoethyl/ethyl = 0.70, γ-*N,N*-dimethylaminopropyl/*n*-propyl = 0.53, and δ-*N,N*-dimethylaminobutyl/*n*-butyl = 1.02, Thus, in spite of what must be substantial rate-depressing inductive effects of the dimethylamino group, the compensating through space 2p-3d overlap effects are causing the ratios cited above to be close to unity.

The most convincing evidence for through space 2p-3d overlap involving the dimethylamino group as the donor is to be found by consideration of the rates of decomposition of phosphonium hydroxides containing the ω-*N,N*-dimethylaminoalkyl group. Whereas the simple alkyldiphenylbenzylphosphonium hydroxides (alkyl = methyl, ethyl, *n*-propyl, and *n*-butyl) undergo decomposition in Me_2SO at 22.0 ± 0.1 °C at too rapid a rate to permit convenient measurement,[22] the quaternary phosphonium hydroxides containing an ω-*N,N*-dimethylaminoalkyl group react at rates several orders of magnitude slower (Table II). This observation can be explained in a satisfactory manner by application of HSAB theory.[23] Tetrahedral phosphorus, with its high degree of positive charge and its empty d orbitals, resembles a proton in its reactivity. Thus, through space 2p-3d overlap is highly effective with a basic group as the donor; i.e., a dimethylamino group engages in more effective overlap than a methoxy group. The same would not apply to the S_N2 reactions of the phosphines, inasmuch as the transition state for this reaction is an early one,[2-4,24] and the degree of positive charge on the phosphorus in the transition state is very small. The data presented previously[4] and in Table I indicate that there is relatively little difference in the ability of nitrogen in the dimethylamino group and of oxygen in the methoxy group to act as the donor in the through space 2p-3d overlap effect as applied to the quaternization reactions.

It is reasonable to believe that steric effects should play some role in determining the relative rates of the quaternization reactions of the (ω-*N,N*-dimethylaminoalkyl)phosphines as against those of the analogous (ω-methoxyalkyl)phosphines. It is obvious that the dimethylamino group is larger than the methoxy group, but there seems to be no direct comparison of the steric requirements of these two substituent groups in the literature. However, an indirect comparison can be made. Taft[25] has listed the increasing order of steric hindrance of some common substituents to be OMe < F < Br ~ Me < *t*-Bu, while similar steric effects for the Me_2N and *t*-Bu groups have been reported by Eliel[26] on the basis of conformational studies of substituted cyclohexanes. Thus, in a comparison of the rate of reaction of (β-methoxyethyl)diphenylphosphine with benzyl chloride as against that of (β-*N,N*-dimethylaminoethyl)diphenylphosphine, for example, two mutually antagonistic factors would have to be taken into consideration in addition to 2p-3d overlap effects. The reaction of the (β-ethoxyethyl)phosphine should be faster than that of the (β-*N,N*-dimethylaminoethyl)phosphine on the basis of steric considerations, but, as mentioned previously,[7,21] slower on the basis of the operation of the inductive effect. Thus, the effect that the β-methoxyethyl compound is somewhat less than twice as reactive as the β-*N,N*-dimethylaminoethyl compound, while not predictable, is also not surprising. The small differences in reactivity between the quaternization reactions of the γ-methoxypropyl- and γ-*N,N*-dimethylaminopropylphosphines and between the reactions of the δ-methoxybutyl- and δ-*N,N*-dimethylaminobutylphosphines, respectively, can also be rationalized in the same manner. The only major difference in reactivity between pairs of analogous phosphines involves the methoxymethyl- and *N,N*-dimethylaminomethylphosphines. Here, as mentioned previously, the very strong inductive electron-withdrawing effect of the methoxy group bonded to a saturated carbon, and removed from the phosphorus atom by but one methylene group, is the dominant factor in controlling the relative lack of reactivity of the methoxymethylphosphine.

Examination of models indicates that the degree of steric interaction between the methyl and phenyl groups resulting from a binding interaction between the basic nitrogen and the positive phosphorus atoms in the phosphonium cations increases in the order $Me_2N(CH_2)_4P^+Ph_2Bz$ < $Me_2N(CH_2)_2P^+Ph_2Bz$ < $Me_2N(CH_2)_3P^+Ph_2Bz$. Thus, the somewhat weakened 2p-3d bonding interaction in the latter cation would lead to a greater concentration of hydroxyphosphorane in the reaction with hydroxide ion and a greater overall rate of alkaline decomposition, as observed (Table II). It is noteworthy that $Me_2NCH_2P^+Ph_2Bz$ undergoes alkaline cleavage at the slowest rate among the homologous compounds listed in Table II, and this indicates that there are no particular constraints on the operation of 2p-3d overlap involving a quasi-three-membered ring interaction, as depicted in **1**.



1, *n* = 1
2, *n* = 2
3, *n* = 3
4, *n* = 4

As mentioned in the Introduction, the chemical shifts of the protons of the methylene groups directly bonded to phosphorus in each phosphonium salt represent the best probe of the 2p-3d overlap effect in the NMR spectrum of each compound. An upfield shift of the methylene protons is expected when the electron density at phosphorus is increased owing to the overlap effect.[1-4] As shown in Table IV, which also includes data on a few additional phosphonium salts for purposes of comparison, this effect is observed in the NMR spectra of compounds **1-4.** It should also be mentioned that the NMR spectra of the salts **1-4** offer definitive proof that alkylation has occurred at phosphorus rather than nitrogen in the reactions of the ω-*N,N*-dimethylaminoalkylphosphines with benzyl bromide (see Experimental Section).

We have completed syntheses of the phosphines **5-8** by the methods outlined in Scheme I.

The chlorobenzylate salts of phosphines **5-8** could not be purified, and the use of benzyl iodide in reaction with the phosphines tended to produce bisiodobenzylates. The use of benzyl bromide in hexane proved to be satisfactory and gave the desired *P*-benzylphosphonium bromides **1-4** of the phosphines **5-8**.

The preparation of the phosphines which were the precursors of the iodobenzylate salts listed in Table III has been described elsewhere.[4]

Scheme I

$$(C_6H_5)_2P^-Li^{+27} + ClCH_2NMe_2^{28} \xrightarrow{THF} Me_2NCH_2P(C_6H_5)_2$$
5

$$(C_6H_5)_2P^-Li^{+27} + ClCH_2CH_2NMe_2^{29} \xrightarrow{C_6H_6} Me_2N(CH_2)_2P(C_6H_5)_2$$

$$(C_6H_5)_2P^-Li^{+27} + Cl(CH_2)_3NMe_2^{29} \xrightarrow{C_6H_6} Me_2N(CH_2)_3P(C_6H_5)_2$$

$$(C_6H_5)_2P^-Li^{+27} + Cl(CH_2)_3C{\equiv}N^{30} \xrightarrow[HMPA]{THF}$$

$$(C_6H_5)_2P(CH_2)_3CN \xrightarrow[ether]{LiAlH_4} (C_6H_5)P(CH_2)_4NH_2$$

$$\xrightarrow[CH_2O,\ MeOH]{HCO_2H} Me_2N(CH_2)_4P(C_6H_5)_2$$
8

Experimental Section

General. All chemicals and solvents used in this study were of reagent-grade quality. Solvents used in kinetics determinations were subjected to further treatment. For example, benzene was redistilled from phosphorus pentoxide and stored under argon gas. Methanol was refluxed over magnesium metal, distilled from the same, and stored over 3 Å molecular sieves. Dioxane was purified by the method of Wiberg;[31] it was then stored in a brown bottle over 3 Å molecular sieves under a positive argon pressure. This solvent was periodically checked for peroxide formation by use of acidic potassium iodide solution. The water used in kinetics measurements was distilled from alkaline potassium permanganate solution.

The phosphines used in this research program were prepared by normal addition of the appropriate alkyl halide to lithium diphenylphosphide. Phosphines and phosphonium halides used in kinetics experiments were crystallized to constant melting points or distilled to constant boiling points. Reagent-grade benzyl chloride (or benzyl bromide, or benzyl iodide) was redistilled before use. All melting points and boiling points are uncorrected. Proton magnetic resonance spectra were determined on a Varian Model A-60 spectrophotometer. All ^1H NMR spectral values are corrected for nonlinearity of the instrument used.

(*N,N*-Dimethylaminomethyl)diphenylphosphine (5). A solution of lithium diphenylphosphide[27] (made from 0.1 mol of triphenylphosphine and 0.2 mol of lithium metal) in 100 mL of dry tetrahydrofuran was added slowly to a tetrahydrofuran suspension of 0.1 mol of chloromethyldimethylamine.[28] An immediate, mildly exothermic reaction occurred with slow dissolution of the amine. The tetrahydrofuran was removed by use of a rotatory evaporator, and the residue was vacuum distilled, yielding 15.3 g (66%) of (*N,N*-dimethylaminomethyl)diphenylphosphine, bp 130.0 °C (0.2 mm). The NMR spectrum of this compound in deuteriochloroform solution showed a singlet at δ 2.00 ppm (6 H), a doublet at 7.00 ppm (2 H) (J = 3 Hz), and a multiplet at 6.60–7.26 ppm (10 H).

Anal. Calcd for $C_{15}H_{18}NP$: C, 74.05; H, 7.46. Found: C, 74.29; H, 7.47.

(β-*N,N*-Dimethylaminoethyl)diphenylphosphine (6). To a solution of lithium diphenylphosphide[27] (0.1 mol) in 120 mL of dry tetrahydrofuran at 65.0 °C was added a solution of 10.5 g (0.1 mol) of β-*N,N*-dimethylaminoethyl chloride[29] in 60 mL of dry benzene. After the addition had been completed, the mixture was refluxed overnight. The solution was cooled to room temperature, and 200 mL of saturated, degassed aqueous ammonium chloride was added. The organic layer was dried over magnesium sulfate for at least 3 h. Evaporation of the solvent left a yellow oil, which was distilled at 125–126 °C (0.05 mm).

The NMR spectrum of this compound in deuteriochloroform showed a singlet at δ 2.05 ppm (6 H), a multiplet at 2.00–2.45 ppm (4 H), and another multiplet at 7.05–7.55 ppm (10 H).

Anal. Calcd for $C_{16}H_{20}PN$: C, 74.68; H, 7.84; P, 12.04. Found: C, 75.06; H, 7.88; P, 11.92.

(γ-*N,N*-Dimethylaminopropyl)diphenylphosphine (7). To a solution of lithium diphenylphosphide[27] (0.1 mol) in 120 mL of dry tetrahydrofuran at 65.0 °C was added a solution of 11.7 g (0.1 mol) of γ-*N,N*-dimethylaminopropyl chloride[29] in 60 mL of dry benzene. After the addition had been completed, the mixture was refluxed overnight. The solution was cooled to room temperature, and 200 mL of degassed, saturated aqueous ammonium chloride was added. The organic layer was dried over magnesium sulfate for at least 3 h. Evaporation of the solvent left a light brown oil, which was distilled at 124 °C (0.05 mm).

The NMR spectrum of this compound in chloroform-*d* solution showed a singlet at δ 2.10 ppm (6 H), a multiplet at 1.20–1.85 ppm (2 H), a second multiplet at 1.90–2.50 ppm (4 H), and a third multiplet at 7.15–7.65 ppm (10 H).

Anal. Calcd for $C_{17}H_{22}NP$: C, 75.25; H, 8.17; N, 5.16; P, 11.42. Found: C, 75.40; H, 8.11; N, 4.84; P, 11.18.

(δ-*N,N*-Dimethylaminobutyl)diphenylphosphine (8). To a solution of lithium diphenylphosphide[27] (0.37 mol) in 500 mL of dry tetrahydrofuran at 65.0 °C (also containing 20 mL of hexamethylphosphoramide) was slowly added a solution of 0.37 mol of 4-chlorobutyronitrile[30] in 60 mL of dry tetrahydrofuran. After the addition had been completed, the mixture was refluxed for 2 days. The reaction mixture was cooled to room temperature, and 200 mL of saturated, degassed aqueous ammonium chloride was added. The organic layer was dried over magnesium sulfate. Evaporation of the solvent left a yellow oil which was heated at 100 °C under high vacuum (0.1 mm) to remove the unreacted 4-chlorobutyronitrile and the hexamethylphosphoramide. The light brown residue left in the flask was dissolved in 50 mL of anhydrous ether containing a small amount of dry tetrahydrofuran. The ether solution of the phosphine was added dropwise to a solution of 1 mol of $LiAlH_4$ in 300 mL of anhydrous ether under a nitrogen atmosphere. The slurry was agitated overnight and heated on a steam bath for 15 min. Water (10 mL), 7.6 mL of sodium hydroxide solution (20%), and 35.2 mL of water were cautiously added in succession. The solution was decanted from a white precipitate, which was then washed twice with 50 mL of ether. The ether layer was dried over magnesium sulfate. Evaporation of the ether left a yellow oil [impure (δ-aminobutyl)diphenylphosphine], which was dissolved in 300 mL of methanol. The methanol solution of the phosphine was added slowly to 1 mol of formic acid (99–100%), the mixture being maintained in a cold water bath. After addition of 0.6 mol of formalin (35–40%) had been completed, the reaction mixture was heated to 90–100 °C for 2–3 min in an oil bath and refluxed overnight. The solution was cooled to room temperature, and 35 mL of concentrated hydrochloric acid was added. Evaporation of the solvent left a green oil, which was treated with 40% sodium hydroxide solution until the solution became basic. The mixture was extracted with 100 mL of benzene, and the benzene solution was dried over anhydrous potassium carbonate. Evaporation of the solvent left a yellow oil which was distilled at 158 °C (0.1 mm).

The NMR spectrum of this compound in chloroform-*d* solution showed a singlet at 1.95 ppm (6 H), a multiplet at 1.05–1.70 ppm (4 H), a second multiplet at 1.70–2.20 ppm (4 H), and a third multiplet at 6.93–7.50 ppm (10 H).

Anal. Calcd for $C_{18}H_{24}PN$: C, 75.76; H, 8.48; N, 4.91. Found: C, 76.23; H, 8.39; N, 4.49.

(*N,N*-Dimethylaminomethyl)benzyldiphenylphosphonium Bromide (1). To a stirred solution of 0.023 mol of (*N,N*-dimethylaminomethyl)diphenylphosphine (**5**) in 200 mL of dry 30% benzene–hexane contained in a 300-mL three-necked round-bottomed flask and maintained under argon at room temperature was added a solution of an excess of benzyl bromide in 50.0 mL of dry benzene over a 1-h period. The reaction mixture was stirred overnight. Colorless crystals which had formed were separated from the solution and washed with benzene. The crystals were recrystallized from methanol–ether, mp 179–180 °C.

The NMR spectrum of this salt in methanol-d_4 consisted of a singlet at δ 2.70 ppm (6 H), a multiplet at 4.01–4.42 ppm (4 H), and a multiplet centered at 7.10 ppm (15 H).

Anal. Calcd for $C_{22}H_{25}PNBr$: C, 63.77; H, 6.08; N, 3.38; P, 7.48; Br, 19.29. Found: C, 63.82; H, 6.38; N, 3.35; P, 7.27; Br, 19.47.

(β-*N,N*-Dimethylaminoethyl)benzyldiphenylphosphonium Bromide (2). To a stirred solution of 10 g (0.04 mol) of (β-*N,N*-dimethylaminoethyl)diphenylphosphine (**6**) in 150 mL of hexane contained in a 300-mL three-necked flask and maintained under argon at room temperature was added a solution of 3.42 g (0.02 mol) of benzyl

Table V. Properties of Quaternary Phosphonium Iodides, $(R)(C_6H_5CH_2)(C_6H_5)_2P^+I^-$

R	mp, °C	anal., %	C	H	P	I	yield, %
CH_3	243–245	calcd	57.43	4.82	7.41	30.34	77[a]
		found	57.30	4.87	7.28	30.64	
CH_3CH_2	220–222 dec	calcd	58.35	5.13	7.17	29.36	71
		found	58.45	5.38	7.01	29.52	
$CH_3CH_2CH_2$	212–213.5	calcd	59.21	5.42	6.94	28.43	77
		found	59.09	5.48	6.79	28.68	
$CH_3CH_2CH_2CH_2$	184–186	calcd	60.01	5.69	6.73	27.57	80
		found	60.06	5.82	6.63	27.32	
CH_3OCH_2	183–185	calcd	56.27	4.95	6.91	28.31	70
		found	56.21	4.95	6.88	28.52	
$CH_3OCH_2CH_2$	128–130	calcd	57.16	5.23	6.70	27.45	49[b]
		found	57.30	5.09	6.79	27.75	
$CH_3O(CH_2)_3$	172–174	calcd	58.00	5.50	6.50	26.64	73
		found	57.71	5.72	6.28	26.77	
$CH_3O(CH_2)_4$	108–111	calcd	58.79	5.76	6.32	25.88	48
		found	58.79	5.91	6.19	26.19	

[a] Only slightly soluble in ethanol. [b] Tends to form oils. Can be recrystallized from 4/1 ethyl acetate–ethanol.

bromide in 75 mL of hexane over a 5-h period. The reaction mixture was stirred for 48 h. Then a solution of 1.71 g (0.01 mol) of benzyl bromide in 50 mL of hexane was added to the reaction mixture over a 1-h period, and the mixture was stirred for another 48 h. The white crystals which had formed were collected by filtration and washed with benzene. The solid was dried in a desiccator for a few hours. Then it was washed with 15 mL of distilled water and allowed to dry under high vacuum overnight. The decomposition point of this salt was 94.5–95.0 °C.

The NMR spectrum of this compound in methanol-d_4 consisted of a singlet at δ 2.75 ppm (6 H), a multiplet at 2.10–3.16 ppm (4 H), a multiplet at 4.10–4.40 ppm (4 H), and a singlet at 7.03 ppm (15 H).

Anal. Calcd for $C_{23}H_{27}NPBr\cdot H_2O$: C, 61.88; H, 6.55; N, 3.14; P, 6.94; Br, 17.90. Found: C, 61.88; H, 6.78; N, 3.01; P, 6.55; Br, 18.48.

The NMR spectrum of this compound in Me_2SO-d_6 showed a new singlet at δ 3.60 ppm (2 H) indicating a single water of hydration, and there was a very broad peak at 3430–3480 cm^{-1} in the IR spectrum.

(γ-*N*,*N*-Dimethylaminopropyl)diphenylbenzylphosphonium Bromide (3). To a stirred solution of 10 g (0.037 mol) of (γ-*N*,*N*-dimethylaminopropyl)diphenylphosphine (**7**) in hexane contained in a 300-mL three-necked flask and maintained under argon at 25.0 °C was added a solution of 5.74 g (0.0275 mol) of benzyl bromide in 100 mL of hexane over a 3-h period. The reaction mixture was stirred overnight. White crystals which had formed were collected and washed with benzene. The solid was dissolved in the limiting amount of acetonitrile, and an undissolved impurity was removed by filtration. The filtrate was transferred into a round-bottomed flask and the solvent was evaporated by use of a high-vacuum pump, fine crystals being formed. This solid could be recrystallized from isopropyl alcohol, mp 153 °C.

The NMR spectrum of this compound in methanol-d_4 consisted of a singlet at δ 2.75 ppm (6 H), a multiplet at 4.27–4.40 ppm, a multiplet at 1.75–2.00 ppm (2 H), a multiplet at 3.00–3.30 ppm (2 H), and a multiplet at 6.83–7.54 ppm (15 H).

Anal. Calcd for $C_{24}H_{29}NPBr$: C, 65.16; H, 6.61; N, 3.17; P, 7.00; Br, 18.07. Found: C, 64.94; H, 6.72; N, 3.07; P, 6.94; Br, 18.24.

(δ-*N*,*N*-Dimethylaminobutyl)diphenylbenzylphosphonium Bromide (4). To a solution of 10.0 g (0.035 mol) of (δ-*N*,*N*-dimethylaminobutyl)diphenylphosphine (**8**) in 200 mL of hexane contained in a 300-mL three-necked flask and maintained under argon at 25 °C was added a solution of 5.98 g (0.035 mol) of benzyl bromide in 50 mL of hexane over a 3-h period. The reaction mixture was stirred overnight. The white precipitate which had formed was collected and washed with pentane. The crystals were then washed with 20-mL portions of distilled water a few times. (The white crystals became a somewhat transparent oil by this treatment.) The oil was dissolved in methanol and filtered through a fritted glass funnel. The solvent was removed by evaporation, and the residue was dried under high vacuum to form a crystalline material (hygroscopic), mp 68 °C (under nitrogen).

The NMR spectrum of this salt in methanol-d_4 consisted of a singlet at δ 2.68 ppm (6 H), a multiplet at 0.91–2.10 ppm (6 H), a multiplet at 2.78–3.30 ppm (3 H), a multiplet at 4.06–4.45 ppm (4 H), and a multiplet at 6.56–7.75 ppm (15 H).

Anal. Calcd for $C_{25}H_{31}NPBr\cdot 1\frac{1}{2}H_2O$: C, 62.06; H, 7.07; N, 2.89; P, 6.41. Found: C, 62.56; H, 6.70; N, 2.49; P, 6.24.

Phosphonium Iodides. All of the phosphonium iodides were prepared by the reaction of the appropriate phosphine with benzyl iodide in acetone solution. To a mixture of 0.03 mol of the phosphine and 0.03 mol of benzyl iodide was added 50 mL of anhydrous acetone. The mixture was stirred, under argon, for 12 h, the flask being protected from light. The precipitate which had formed was collected by filtration and crystallized from absolute ethanol, these operations also being carried out in an argon atmosphere. Yields, analytical results, and physical properties of the phosphonium iodides are provided in Table V.

Kinetics Procedures. A. For Quaternization Reactions. A 60% benzene–methanol solution was prepared by pipetting the appropriate amounts of degassed (air removed by bubbling argon through the solvent for several hours) anhydrous benzene and degassed absolute methanol into a brown bottle and covering the mixture with a blanket of argon before agitation. After thorough mixing, the solution was stored under a positive argon pressure until it was used.

An accurately weighed sample of the phosphine was added to a 250-mL volumetric flask which was then filled to the mark with the 60% benzene–methanol solvent (≃0.02 N). The solution was briefly covered with a blanket of argon and subsequently mixed thoroughly. A 100-mL portion of freshly prepared 0.02 N phosphine solution was pipetted into a 100-mL three-necked round-bottomed flask, fitted with a ⅋ joint (14/20), a gas-inlet adapter, and a rubber stopper, and the solution was equilibrated at 31.0 ± 0.1 °C under a positive argon pressure for 2 h. After this period, the required volume (2–3 mL) of a 1.00 N solution of benzyl chloride in 60% benzene–methanol solution was added.

At various time intervals, a 10-mL aliquot of the reaction mixture was removed and added to 5.0 mL of water (distilled from alkaline potassium permanganate solution) by use of a syringe. This procedure served to quench the reaction. The resulting two-phase system was titrated with a standard solution of silver nitrate (0.01 N), a 5% potassium chromate solution being used as the indicator (Mohr method of chloride analysis).

B. For Hydroxide-Induced Decomposition of ω-*N*,*N*-Dimethylaminoalkylphosphonium Salts. Kinetics runs were carried out in a constant-temperature bath with distilled water as the bath liquid. The water was covered with small pieces of polystyrene foam, both to serve as insulation and to cut down on evaporation. The bath temperature was recorded by means of a Fisher 15-000B thermometer. The cooling necessary to achieve a temperature of 22.0 ± 0.1 °C was provided by a Lauda Model 1c-6 cooling unit.

An accurately weighed sample of each phosphonium salt was added to a 250-mL volumetric flask and filled to the mark with Me_2SO. Then 100 mL of phosphonium salt solution (≃0.01 N) was transferred to a 250-mL Erlenmeyer flask fitted with a 24/40 standard taper joint. The flask was stoppered with a ⅋ 24/40 stopper and placed in the

constant-temperature bath for at least 2 h prior to the beginning of a kinetics run. A quantity of Fisher 1.00 N aqueous sodium hydroxide exactly equivalent to the weighed quantity of phosphonium salt in the vial was also placed in the bath at least 2 h prior to the beginning of a kinetics run.

After the indicated temperature equilibration period, the required volume of 1.00 N sodium hydroxide (1–1.5 mL) was added to the phosphonium salt solution. At various time intervals, a 10-mL aliquot of the reaction mixture was transferred into a 2.0-mL aliquot of Fisher 0.100 10–0.099 95 N hydrochloric acid to quench the reaction. Then each mixture was diluted to 80 mL (to minimize drifting during the subsequent pH titration) and back-titrated with Fisher 0.1000 N aqueous sodium hydroxide dispensed from a class A 5-mL microburet. pH changes were followed by means of a Corning Model 12 Research pH meter, and, as a general procedure, the base solution was added in 0.040-mL increments in the vicinity of the end point (pH 6.90).

C. For Hydroxide-Induced Decomposition of Phosphonium Iodides. For the preparation of an 0.800 M potassium iodide solution, solid KI was weighed into a tared 50-mL beaker on the analytical balance. The bulk of this salt was then poured into a 500-mL volumetric flask through a funnel placed in the neck. The beaker and funnel were rinsed several times with water and the flask was then filled almost to the mark. The solution was then allowed to stand until it had returned to room temperature and then the volume was brought to the mark. The solution was stored in a brown glass bottle, but it became yellow over a period of weeks.

For the preparation of 50/50 dioxane–water solutions, equal volumes of dioxane and 0.800 M KI solution were added by volumetric pipet to a 1-L brown glass bottle. The bottle was swirled to ensure thorough mixing and allowed to return to room temperature before use. This solution was never stored for more than 48 h.

The phosphonium salts were weighed by difference from brown glass bottles into funnels placed in the necks of 250-mL volumetric flasks. It was important that salt crystals be broken up prior to weighing so that they would fit through the stem of the funnel. The salt was then rinsed into the flask using small quantities of dioxane/KI/H_2O. The funnel was thoroughly rinsed and removed. The flask was filled to the mark and, in most cases, a small stirring bar was added. Several hours of stirring were required to dissolve most of the salts in the presence of 0.4 M KI. Volumetric flasks were wrapped in Al foil to protect them from light at all times. Solutions were cooled to room temperature before use. Phosphonium salt concentrations ranged from 0.006 to 0.016 M.

The steps in each kinetics run were as follows.

1. Exactly 100 mL of phosphonium salt solution was pipetted into a 250-mL Erlenmeyer flask fitted with a ⅋ 24/40 joint. Two aliquots were taken from each 250-mL volumetric flask.

2. The Erlenmeyer flask was placed in a 45.0 °C constant-temperature bath and allowed to equilibrate for a minimum of 2 h.

3. A 5.0-mL aliquot of 0.10 N HCl was placed in a 150-mL beaker.

4. The amount of 1.0 N NaOH required to make the solution equimolar in OH^- and phosphonium salt was added to the solution by graduated pipet. The time at which the first NaOH entered the salt solution was taken as t_0. The Erlenmeyer flask was stoppered and swirled without removing it from the bath. The concentration of hydroxide ion in the 100+ mL of solution was calculated and used as $[OH^-]_0$. Only the OH^- concentration is measured in these studies.

5. A 10.0-mL aliquot was withdrawn from the kinetics solution and added to the 5-mL of 0.10 N HCl. This was first done immediately after mixing in the base.

6. Sample aliquots were diluted to 70–80 mL using distilled water and titrated to pH 7 using 0.10 N NaOH and following the titration with a pH meter.

7. Steps 3, 5, and 6 were repeated at appropriate time intervals.

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