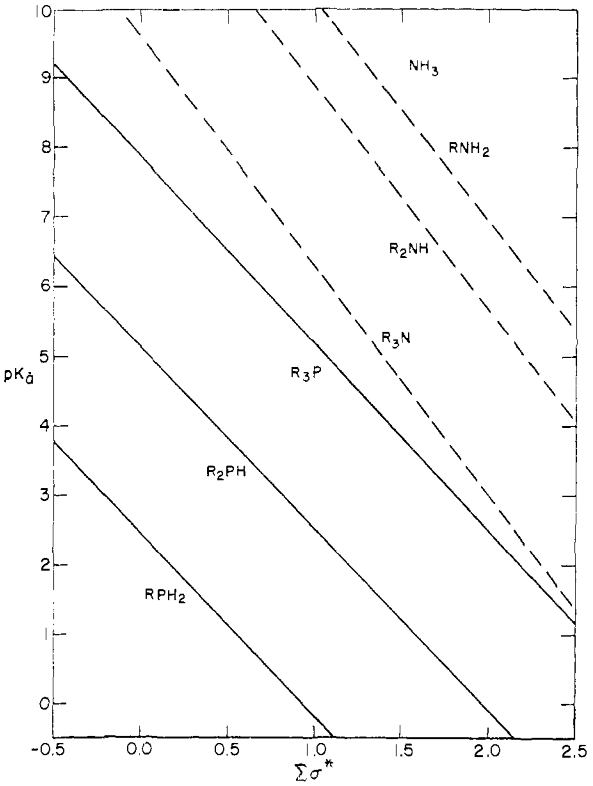

Fig. 2.—Plot of pK_a *versus* $\Sigma\sigma^*$ for phosphines and amines.

phine series and also by the points for secondary and primary phosphines.

The persistence of steric effects in the secondary and primary phosphines suggest the mode of operation of this effect. Since B-strain cannot occur in these phosphines, Brown's conclusion that B-strain is of no importance in the phosphines[2] must be accepted here also. Steric hindrance to attack by a solvated proton is unlikely, especially for secondary and primary phosphines, in view of the large size of the phosphorus atom and carbon–phosphorus bond. The existence of a steric effect is, therefore, ascribed to the varying amount of hindrance to solvation of the product phosphonium ion. Unlike the case for amines, where the solvation effect is important only in the primary and secondary series and invariant or negligible in the tertiary series,[4] the effect is still operative in the tertiary phosphines.

Figure 1 shows that the phenyl phosphines fall below the line by small but persistent amounts of the order of $^1/_2$ pK unit. While this may reflect a greater steric requirement of phenyl- than alkyl- or cyanoethyl-, it may also be a result of π-bond formation between the phosphorus atom and the benzene ring. The resulting electron delocalization would effect a lowering of the basicity of phenyl phosphines. The similar lowering of basicity of phosphines toward trimethylboron by vinyl groups was ascribed by Kaesz and Stone to operation of the same effect.[13]

The situation is quite different in the case of amines. The basicities of aniline, three N-alkylanilines and two N,N-dialkylanilines are lower than the values predicted by Hall's equations for alkylamines (Table II) by 2.4–4.0 pK units. This much larger decrease in basicity demonstrates the considerably greater importance of π-bonding in amines than phosphines and is part of the more general problem of weak double bond formation by the third row elements with carbon. While in the case of phosphorus, the lesser amount of double bond formation may to a first approximation be ascribed to a decrease in π-bond overlap occasioned by the greater length of the carbon-to-phosphorus σ-bond, final solution of the problem awaits exact calculation of the overlap integrals involved.

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[13] H. D. Kaesz and F. G. A. Stone, Abstracts of Papers, 135th Meeting, American Chemical Society, April 5, 1959.

[Contribution from the Chemical Research Department, Central Research Division, American Cyanamid Company, Stamford, Connecticut]

The Nucleophilicity of Phosphines

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The nucleophilicity of phosphines has been investigated by following the kinetics of the reaction of phosphines with alkyl halides. The effect of substituents on the nucleophilicity of the phosphine is interpreted in terms of inductive, steric and bond hybridization effects. The effect of varying the alky halide, solvent and temperatures are reported. An anomalous reactivity has been found for methyl phosphines.

Within the last few decades, there has been published a huge volume of synthetic work dealing with phosphines and other trivalent phosphorus compounds, and incident to this work have appeared many speculations as to the mechanisms of the reactions involved. There have been, however, no definitive publications concerning the effect of structure on the reactivity of the free electron pair of those compounds, a knowledge of which is vitally necessary to intelligent discussion of mechanism. To the authors' knowledge there are no more than three relevant papers of limited scope in the literature, only one of which is quantitative in nature.[1] None of these treats nucleophilicity from a theoretical point of view.

Therefore, we have conducted a broad investigation of the nucleophilicity of phosphines as reflected by the rate of S_N2 attack on alkyl halides

$$R_1R_2R_3P + R_4X \longrightarrow R_1R_2R_3R_4P^{\oplus} + X^{\ominus} \quad (1)$$

The effects of varying the phosphine, the alkyl

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[1] W. C. Davies and W. P. G. Lewis, *J. Chem. Soc.*, 1599 (1934).

group of the halide, the leaving group, the solvent and the temperature are reported here.

Method.—Phosphines were prepared by various methods as reported in the Experimental section, and their purity checked by boiling point, melting point, nuclear magnetic resonance and vapor phase chromatography. Phosphonium salts were prepared by standard methods and characterized by melting point. Satisfactory purity was demonstrated by Volhard titration. Solvents were reagent grade compounds used without further purification.

The first method used for following the kinetics of the quaternization was a titrimetric one. Solutions of less than 0.1 *N* concentration of the two reactants were mixed in a vessel in a constant temperature bath. Oxygen was excluded at all times. At appropriate intervals, aliquots were removed and titrated by the Volhard method for halide. It was necessary to extract unreacted alkyl halide from the aliquot with ether. Otherwise, spurious results were obtained on titration. The accuracy of the titration was demonstrated by satisfactory analysis of the pure standard phosphonium salts. Satisfactory retention of the salt during the extraction step was shown by 100% recovery of standard salt after extraction as shown by titration. The reaction was followed from 20 to 80% of completion and the data interpreted by the standard second order kinetic equation

$$k_2t = \frac{1}{b - a}\ln\left[\frac{a(b - x)}{b(a - x)}\right] \qquad (2)$$

derived from the rate expression

$$\frac{dx}{dt} = k_2(a - x)(b - x) \qquad (3)$$

where a is the initial concentration of phosphine, b is the initial concentration of alkyl halide and x is the instantaneous concentration of phosphonium salt at time t. Ten or more points were obtained from the titration data and a plot made by least squares of the quantity log $\frac{b-x}{a-x}$ *versus* time. Deviation of a single point from the line was less than 1.5%. Three or more runs were made for a given combination of phosphine, halide, solvent and concentration and second order rate constants calculated. Deviations from the average value were less than 2%.

The second method of following the quaternization was a conductometric one, which measures the production of phosphonium and halide ions as a function of time. Solutions made up as for the titrimetric runs were mixed and placed in a conductivity cell, oxygen being excluded at all times. The resistance was measured at appropriate intervals by means of a conductivity bridge. A standardization curve for converting conductivity to concentration was constructed for each phosphonium salt from data obtained by measuring the resistance of solutions of known concentration. Six or more points were plotted for each standardization curve. The individual points deviated from a straight line by less than 2%. The reaction was followed to not more than 0.4% completion and the data interpreted by the equation

$$kt = \frac{x}{ab} \qquad (4)$$

derived from the rate expression 3 under the condition that x is small enough that a and b may be considered invariant. Ten points were obtained from the conductometric data and a plot made by least squares of x *versus* time. The deviation of a single point from the line was less than 1%. No less than three runs were made for a given set of conditions and second order rate constants calculated. Deviation of one run from the average was usually less than 2%, and agreement with values obtained by the titration method was satisfactory.

Results

That with tertiary phosphines the reaction under investigation goes substantially to completion as written (Equation 1) is shown by the 100% yield of phosphonium salts obtained in synthesizing the standard compounds.

The situation is more complicated in the case of secondary phosphines since further reaction with a second mole of halide is possible.

$$\mathrm{R_2PH + R'X \xrightarrow{k_2} R_2R'\overset{+}{P}H + \overset{-}{X}} \qquad (5)$$

$$\mathrm{R_2R'\overset{+}{P}H + \overset{-}{X} \rightleftarrows R_2R'P + \overset{+}{H} + \overset{-}{X}} \qquad (6)$$

$$\mathrm{R_2R'P + R'X \longrightarrow R_2R'_2\overset{+}{P} + \overset{-}{X}} \qquad (7)$$

That the reaction stops at the first stage in the cases for which kinetic data are given is shown by the isolation and characterization of the hydroiodides after approximately 100% completion of reaction under the reaction conditions. No quaternary phosphonium salt could be detected. With diphenylphosphine in acetone, however, further reaction occurred; hence, no kinetic data could be obtained.

The assumption was made that Reaction 1 is second order; first order in phosphine and first order in halide. The assumption is validated by the good fit of the titrimetric experimental data to the second-order rate equation and by the invariance of the second-order rate constant as the initial concentrations of phosphine and halide are changed.

The results of the kinetic runs made in this investigation are given in Tables I–IV.

Discussion

The effect of substituents in the phosphine on the rate of the quaternization reaction is best discussed in terms of a Taft plot following the equation log $k/k_0 = \sigma^* \rho^*$.[2] Hence, the data in Table I following the equation

$$\mathrm{RR'R''P + EtI \xrightarrow[\text{acetone, }35°]{k_2} RR'R''EtP^{\oplus} + I^{\ominus}} \qquad (8)$$

have been plotted in Fig. 1 as log (10^5k_2) *versus* the sum of the σ^* values for the substituent groups. It can be seen that the reaction is very sensitive to changes in the phosphine, the rate of reaction varying from 6×10^{-6} to 8×10^{-3}, or more than three powers of ten.

The Taft σ^* value is a quantitative measure of the inductive effect alone of the substituent group.[2] Experimentally, it has been found that the Taft

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[2] This equation and its applications are described by R. W. Taft, Jr., in "Steric Effects in Organic Chemistry," M. S. Newman, ed., John Wiley and Sons, Inc., New York, N. Y., 1956.

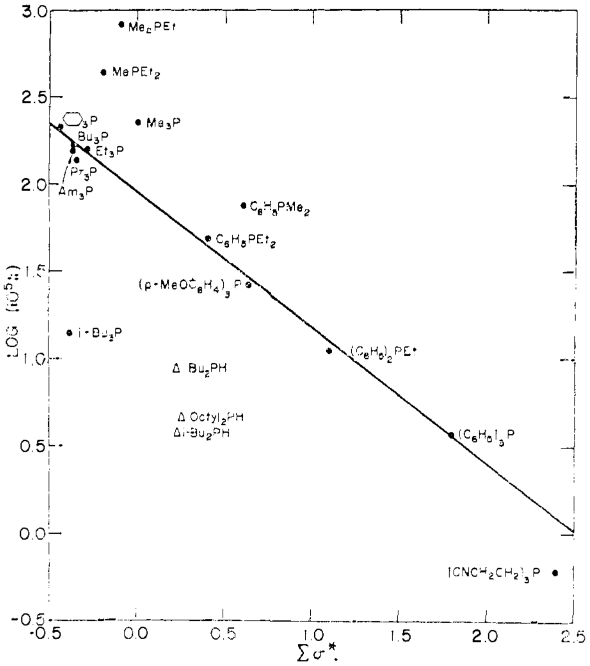

Fig. 1.—Plot of log 10^5k *versus* $\Sigma\sigma^*$ for the reaction of secondary and tertiary phosphines with ethyl iodide in acetone at 35°.

equation holds, *i.e.* a plot of log k *versus* σ^* is linear, *provided that* the substituents have only very small or constant effects of other types. Thus, any deviation from a straight line may be interpreted in terms of one or more other variables such as steric or resonance effects or changes in hybridization.

By visual inspection, the tertiary phosphines were divided into four categories. The main group, called the "normal" phosphines, was used to calculate by the method of least squares the line shown in Fig. 1. The equation of the line is

$$\log 10^5 k = 1.939 - 0.767\sigma^* \qquad (9)$$

The standard deviation of the slope is 0.020 and the standard deviation of a single "normal" phosphine from the line is 0.045 in log 10^5k. Equation 9 is equivalent to the Taft equation with $\rho^* = -0.767$ and $\log k_0 = -3.061$.

The second group of phosphines is composed of all those containing one or more methyl groups. These all fall above the line by more than six times the standard deviation; hence statistically there is less than one chance in one hundred that any one of them belongs to the "normal" group of phosphines.

TABLE I

$$RR'R''P + C_2H_5I \xrightarrow[(CH_3)_2CO \quad 34.97°]{k_2} RR'R''C_2H_5\overset{+}{P} + \overset{-}{I}$$

Phosphine	Sum σ^{*a}	Number of runs	k_2 (l. mole^{-1} sec.$^{-1}$)^b
$(CH_3)_3P$	0.000	3	$2.24 \pm 1.86 \times 10^{-3}$
$C_2H_5P(CH_3)_2$	− .100	3	$8.05 \pm 0.30 \times 10^{-3}$
$(C_2H_5)_2PCH_3$	− .200	3	$4.29 \pm .04 \times 10^{-3}$
$(C_2H_5)_3P$	− .300	4	$1.54 \pm .05 \times 10^{-3}$
$(n\text{-}C_3H_7)_3P$	− .345	4	$1.36 \pm .04 \times 10^{-3}$
$(n\text{-}C_4H_9)_3P$	− .390	4	$1.62 \pm .05 \times 10^{-3}$
		4	$1.89 \pm .03 \times 10^{-3d}$
$(i\text{-}C_4H_9)_3P$	−0 375	3	$1.38 \pm .01 \times 10^{-4}$
$(n\text{-}C_5H_{11})_3P$	−0.390^c	3	$1.58 \pm .04 \times 10^{-3}$
$(CNCH_2CH_2)_3P$	+2.400	4	$6.37 \pm .05 \times 10^{-6}$
$(cyclo\text{-}C_6H_{11})_3P$	−0.450	3	$2.07 \pm .02 \times 10^{-3}$
$C_6H_5P(CH_3)_2$	+ .600	3	$7.60 \pm .11 \times 10^{-4}$
$C_6H_5P(C_2H_5)_2$	+ .400	3	$4.75 \pm .05 \times 10^{-4e}$
$(C_6H_5)_2PC_2H_5$	+1.100	3	$1.12 \pm .01 \times 10^{-4}$
$(C_6H_5)_3P$	+1.800	4	$3.78 \pm .02 \times 10^{-5}$
		3	$4.15 \pm .05 \times 10^{-5d}$
$(p\text{-}CH_3OC_6H_4)_3P$	+0.630	3	$2.71 \pm .07 \times 10^{-4}$
$(n\text{-}C_4H_9)_2PH$	+ .230	3	$8.75 \pm .08 \times 10^{-5}$
$(n\text{-}C_8H_{17})_2PH$	+ .260	3	$4.53 \pm .07 \times 10^{-5}$
$(i\text{-}C_4H_9)_2PH$	+ .240	3	$3.83 \pm .07 \times 10^{-5}$

[a] Taken from ref. 2, p. 619. [b] Unless otherwise stated, kinetics followed by conductance. [c] Value of σ^* taken as same as for $n\text{-}C_4H_9$. [d] Kinetics followed by titration. [e] From Davies and Lewis.[1]

TABLE II

$$(n\text{-}C_4H_9)_3P + RX \xrightarrow[(CH_3)_2CO \quad 34.97°]{k_2} (n\text{-}C_4H_9)_3P\overset{+}{R} + \overset{-}{X}$$

Halide	σ^{*a}	Number of runs	k_2 (l. mole^{-1} sec.$^{-1}$)^b
CH_3I	0.000	3	$2.60 \pm 0.40 \times 10^{-1}$
C_2H_5I	−0.300	4	$1.54 \pm .05 \times 10^{-3}$
$n\text{-}C_3H_7Cl$	.....	3	$2.39 \pm .05 \times 10^{-7}$
$n\text{-}C_3H_7Br$	.....	3	$5.95 \pm .03 \times 10^{-5}$
$n\text{-}C_3H_7I$	−0.115	3	$6.37 \pm .11 \times 10^{-4}$
$n\text{-}C_4H_9I$	− .130	3	$5.68 \pm .04 \times 10^{-4}$
$i\text{-}C_4H_9I$	− .125	3	$4.94 \pm .02 \times 10^{-5}$
$neo\text{-}C_5H_{11}I$	− .165	..	................^{c}

[a] Taken from ref. 2, p. 619. [b] Kinetics followed by conductance. [c] Rate too slow to measure.

TABLE III

$$R_3P + C_2H_5I \xrightarrow[\text{Solvent} \quad 34.97°]{k_2} R_3PC_2H_5^+ + I^-$$

Phosphine	Solvent	Number of runs	k_2 (l. mole^{-1} sec.$^{-1}$)^b
$(n\text{-}C_4H_9)_3P$	$(CH_3)_2CO$	4	$1.54 \pm 0.05 \times 10^{-3}$
$(n\text{-}C_4H_9)_3P$	100% C_2H_5OH	2	$3.49 \pm .02 \times 10^{-4}$
$(n\text{-}C_4H_9)_3P$	95% C_2H_5OH	3	$5.94 \pm .04 \times 10^{-4}$
$(n\text{-}C_4H_9)_3P$	95% C_2H_5OH	2	$6.22 \pm .05 \times 10^{-4b}$
$(n\text{-}C_4H_9)_3P$	90% C_2H_5OH	2	$8.10 \pm .13 \times 10^{-4}$
$(n\text{-}C_4H_9)_3P$	CH_3OH	2	$1.31 \pm .18 \times 10^{-3}$
$(n\text{-}C_4H_9)_3P$	CH_3NO_2	2	$1.10 \pm .03 \times 10^{-2}$
$(C_6H_5)_3P$	$(CH_3)_2CO$	4	$3.78 \pm .02 \times 10^{-5}$
$(C_6H_5)_3P$	100% C_2H_5OH	2	$2.05 \pm .15 \times 10^{-5}$
$(C_6H_5)_3P$	95% C_2H_5OH	3	$4.00 \pm .07 \times 10^{-5}$
$(C_6H_5)_3P$	95% C_2H_5OH	2	$4.11 \pm .04 \times 10^{-5b}$
$(C_6H_5)_3P$	90% C_2H_5OH	2	$5.59 \pm .05 \times 10^{-5}$
$(C_6H_5)_3P$	CH_3OH	2	$4.92 \pm .06 \times 10^{-5}$
$(C_6H_5)_3P$	CH_3NO_2	2	$1.66 \pm .02 \times 10^{-4}$

[a] Unless otherwise stated, kinetics followed by conductance. [b] Kinetics followed by titration.

TABLE IV

$$R_3P + C_2H_5I \xrightarrow[(CH_3)_2CO,\ \text{Temp. °C.}]{k_2} R_3PC_2H_5^+ + I^-$$

Phosphine	Temp., °C.	Number of runs	k_2 (l. mole^{-1} sec.$^{-1}$)^a
$(n\text{-}C_4H_9)_3P$	34.97	4	$1.54 \pm 0.05 \times 10^{-3}$
$(n\text{-}C_4H_9)_3P$	15.81	3	$3.89 \pm .07 \times 10^{-4}$
$(n\text{-}C_4H_9)_3P$	0.18	3	$1.07 \pm .05 \times 10^{-4}$
$(C_6H_5)_3P$	34.97	4	$3.78 \pm .02 \times 10^{-5}$
$(C_6H_5)_3P$	15.78	3	$7.73 \pm .04 \times 10^{-6}$
$(C_6H_5)_3P$	0.20	3	$1.76 \pm .01 \times 10^{-6}$

[a] Kinetics followed by conductance.

The same criterion establishes the third and fourth categories consisting of triisobutyl- and tris-(2-cyanoethyl)-phosphine, respectively. Both of these fall below the line.

It can be seen that the rates of reaction of "normal" phosphines, *i.e.* alkyl and aryl phosphines of moderate steric requirements, may be predicted quantitatively by means of Equation 9. It may be assumed, therefore, that the operation of other factors such as resonance or steric hindrance has only a small or constant effect on the rate of reaction of these phosphines. The negative sign of ρ^* indicates that the energy of the activated complex in the reaction is lowered relative to the ground state by the presence of electron-supplying groups on the phosphorus. This is not surprising in view of the fact that the buildup of negative charge on phosphorus should increase the nucleophilicity of the free electron pair. The magnitude of ρ^*, 0.767, shows that this inductive effect is only a moderate one.

Davies[1] reported rates of reaction for a limited number of *p*-substituted diethylphenylphosphines with ethyl iodide in acetone. A Hammett plot of these values has been made and a value for ρ of -1.11 obtained. This indicates a roughly comparable value of the inductive effect as measured by the Hammett equation but yields no information about the relative importance of other effects.

The second group, containing the methyl phosphines, is not so easily explained. It is obvious that substitution of methyl for other groups substantially increases the nucleophilicity of the phosphines. It would appear that methyl substitution has a profound influence through operation of some type of steric effect but little more than this can be said with certainty.

A similar effect has been noted by Kaesz and Stone[3] who report the qualitative reactivity series $EtMe_2P > Me_3P \gg Et_3P$ toward trimethylborane. Steric effects are also of importance in the nucleophilicity of tertiary amines,[1,4] the basicity of amines[5,6] and the basicity of phosphines.[7]

It might be supposed that hyperconjugation would lower the activation energy by increasing the electron density on the electron-deficient phosphorus atom in the transition state. Evidence for such d-orbital resonance in phosphonium salts has been presented by Doering and Hoffmann,[8] who report deuterium exchange of tetramethyl phosphonium iodide and deuteroxide. But hyperconjugation would, provided the Taft equation and methyl σ^* value are valid, predict that the methyl ethyl phosphines would fall vertically off the line by amounts in the order $Et_3P < Et_2PMe < EtPMe_2 < Me_3P$. Experimentally this is not verified; trimethylphosphine is anomalous, the methyl ethyl phosphines falling off the line in the order $Et_3P < Me_3P < Et_2PMe < EtPMe_2$. In addition, it would be predicted that tricyclohexylphosphine, with fewer α-hydrogen atoms than the "normal" phosphines, would be abnormally unreactive. Such a difference in reactivity is not found. Hence, it is believed that hyperconjugation does not explain the enhanced reactivity of the methyl phosphines. Trimethylphosphine also occupies an anomalous position in the reactivity series of Kaesz and Stone.[3] Whether this effect is peculiar to phosphorus is not known since the requisite experimental data is lacking for amines.

Nor can the effect be a simple steric one since on the basis of steric hindrance it would also be predicted that the methyl ethyl phosphines would fall off the line in the order $Et_3P < MePEt_2 < Me_2PEt < Me_3P$. Certainly no single factor will explain the reactivity series encountered in the methyl ethyl phosphines. The explanation must lie in some complex combination of effects.

The third category comprising the single compound triisobutylphosphine is probably the result of a steric effect. Normally, it would not be expected that the methyl ethyl phosphines and triisobutylphosphine would show hindrance effects while the "normal" phosphines do not. Increments in steric hindrance have diminishing effects on reaction rates, and under conditions of high steric hindrance a saturation point is reached.[9] Also the degree of hindrance present in the isobutyl group as measured by E_s value[10] is only slightly more than that of the more hindered phosphines of the "normal" group and small compared to differences within the "normal" group. However, molecular models show that triisobutylphosphine is anomalous in one very important respect. While many of the "normal" phosphines have groups which may at times shield the free electron pair of phosphorus, the geometry of triisobutylphosphine alone is such that one methyl group is compelled at all times to effectively cover the electron pair. We suggest that for this reason triisobutylphosphine is exceedingly unreactive and believe that even more hindered phosphines would behave in the same manner.

The last tertiary phosphine, tris-(2-cyanoethyl)-phosphine, is believed to be less reactive than would be predicted as a result of interaction of the nitrile group and the phosphorus atom. There is the possibility, however, that the discrepancy is a result of experimental error at the very low reaction rate.

It has been pointed out by Gibbs[11] that the very large change in basicity in going from phosphine to trimethylphosphine may be related to changes in bond angle. The lesser bond angle of the hydride reflects a hybridization closer to p^3 than is the case with trimethyl phosphine. If this is true, then the rehybridization energy of the hydride in going to sp^3 hybridization during quaternization would be greater and the basicity of the hydride should be less.

Similar effects may very well be operative in the case of tertiary phosphines. Increasing the size of the alkyl groups attached to phosphorus would tend to spread the bond angle from p^3–sp^3 toward more nearly sp^3 hybridization. This would result in a lowering of the rehybridization energy and an

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[3] H. D. Kaesz and F. G. A. Stone, Abstracts of Papers, 135th Meeting American Chemical Society, Boston, Mass., 1959.

[4] R. P. Larsen and C. A. Kraus, *Proc. Natl. Acad. Sci. U. S.*, **40**, 70 (1954).

[5] H. K. Hall, Jr., THIS JOURNAL, **79**, 5441 (1957).

[6] H. C. Brown and M. Gerstein, *ibid.*, **72**, 2926 (1950).

[7] Wm. A. Henderson, Jr., and C. A. Streuli, *ibid.*, **82**, 5791 (1960).

[8] W. von E. Doering and A. K. Hoffmann, *ibid.*, **77**, 521 (1955).

[9] Ref. 2, p. 602.

[10] R. W. Taft, Jr., THIS JOURNAL, **74**, 3120 (1952).

[11] J. H. Gibbs, *J. Chem. Phys.*, **22**, 1460 (1954).

increase in reactivity. The same increase in size, however, would produce a decrease in reactivity through steric hindrance to the attacking group.

These two competing effects might explain the abnormal reactivity of the methyl phosphines, where hybridization changes would be the greatest and the hindrance of the attacking group small and perhaps also the apparent constancy of the steric effect in the "normal" series. An attempt was made to test this hypothesis by investigating the nuclear magnetic resonance shifts of the phosphines in the hope that these would reflect the type of hybridization of the phosphorus atom. The shifts (see Table VI) indicate that those of compounds with methyl groups are abnormally high. This may indicate more p character in the hybridization of phosphorus in methyl phosphines and a consequent lesser shielding, but the results are by no means conclusive.

The literature affords bond angle data only on phosphine and trimethylphosphine and this data is, to some extent, contradictory. It is indeed unfortunate that accurate values of bond angles are not available for a greater number of phosphines in order to further test the above hypothesis.

Also included in Fig. 1 are three points for secondary phosphines. It might be expected that a line similar to that for the "normal" tertiary phosphines could be drawn. Such a line might be parallel to the "normal" line through similar inductive effects but of different intercept through the difference in rehybridization energy. In actual fact, the three secondary phosphines for which the rates of reaction were measured fall on an almost vertical line.

Attempts to establish a point for diphenylphosphine, a secondary phosphine of significantly different σ^*, and hence to obtain the approximate slope of the line for secondary phosphines failed. It was found that in acetone diphenylethylphosphine hydroiodide is not sufficiently basic to retain a proton. The hydroiodide was thus not the final product and the methods used for following the kinetics could not be applied.

The three points obtained for secondary phosphines, although they all have approximately the same σ^* value, are still significant in that they demonstrate a high susceptibility to steric effects, falling off the hypothetical line in the order of their steric hindrance. Also, it may be pointed out that the phosphines of low degree of hindrance (tertiary phosphines containing methyl groups and secondary phosphines) are most affected by the steric factor. This lends weight to the argument that for these phosphines hybridization changes are of importance.

No work was done on primary phosphines since the basicity of the product secondary phosphines was too low to permit use of the conductivity method.

The effect of substituents in alkyl iodides was examined using tributylphosphine as the reference phosphine.

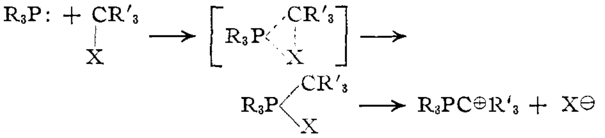
$$(n\text{-}C_4H_9)_3P + RI \longrightarrow (n\text{-}C_4H_9)_3\overset{+}{P}R + \overset{-}{I} \quad (10)$$

The results are recorded in Table II. The relative rates observed are

Me 5250, Et 31.2, *n*-Pr 12.9, *n*-Bu 11.5, *i*-Bu 1.0

These relative reactivities are quite similar to those found on varying the alkyl substituent in other S_N2 reactions,[12] the largest change occurring in going from methyl to ethyl. It is generally agreed that these differences in reactivity are due to both steric and electronic factors.

While the attack of a phosphine on an alkyl halide is without doubt S_N2, there is as yet no proof that the reaction proceeds by attack from the rear with inversion. It may be pointed out that for nucleophiles of higher atomic number and thus capable of expanding their valence shells there exists the possibility of attack on the carbon-to-halide bond with retention of configuration.



Results of the usual type for neopentyl iodide, which should hinder the conventional attack from the rear much more than attack on the carbon-to-iodine bond, tend to rule out the above mechanism.

The *n*-propyl halides gave the relative rates of reaction with tri-*n*-butylphosphine I:Br:Cl = 2660:248:1. While the corresponding series for the *n*-propyl halides and tri-*n*-propylamine is 2700:1370:1,[5] the usual range for S_N2 reactions involving alkyl halides is 40–150:20–60:1.[13,14] Thus, it may be seen that phosphines and also amines are more greatly influenced in their reactivity by the nature of the leaving group.

An investigation was made of the effect of solvent on the rate of reaction of two phosphines, tri-*n*-butyl- and triphenylphosphine. The rates of reaction, given in Table III, cannot be correlated quantitatively with dielectric constant, nor can they be correlated with Y-values[15] or Z-values[16] except for the very restricted series of aqueous ethanol mixtures. From this series, however, it is apparent that the reaction goes faster in more polar solvents. The change in reactivity is a reflection of the decrease in activation energy occasioned by the greater solvation of the relatively polar transition state.

This effect has been noted previously by Davies and Lewis who found that the rate of combination of aryldiethylphosphines with ethyl iodide in solvent acetone is increased by adding 10% water to the medium. It is not surprising that the analogous amines act in the same way. Thus, Menschutkin[17] showed that the combination of triethylamine with ethyl iodide proceeds more rapidly in alcohols than in hydrocarbons. This has been confirmed by other workers[18] for a number of amines and primary alkyl halides.

In connection with the effect of solvent on reactivity, it should be pointed out that the titration

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(12) C. K. Ingold, "Structure and Mechanism in Organic Chemistry," Cornell Univ. Press, Ithaca, N. Y., 1953, p. 323.

(13) Ref. 12, p. 339.

(14) A. Streitwieser, Jr., *Chem. Revs.*, **56**, 601 (1956).

(15) S. Winstein, *et al.*, THIS JOURNAL, **70**, 846 (1948); **73**, 2700 (1951); **78**, 2770 (1956); **79**, 1597, 1602, 1608 (1957).

(16) E. M. Kosower, *ibid.*, **80**, 3253, 3267 (1958).

(17) N. Menschutkin, *Z. physik. Chem.*, **5**, 589 (1890).

(18) H. E. Cox, *J. Chem. Soc.*, 142 (1942); J. A. Hawkins, *ibid.*, **121**, 1170 (1922); H. Essex and O. Gelormini, THIS JOURNAL, **48**, 882 (1926).

method of following the kinetics of the quaternization gave results only slightly but consistently higher than the conductometric method. Since the former was applied over the range 20–80% of completion while the latter was applied at less than 0.4%, the difference noted is most easily ascribed to a salt effect of the product phosphonium salt.

Activation quantities were obtained for tri-*n*-butyl- and triphenylphosphine. The results for their reaction with ethyl iodide in acetone as calculated from the appropriate data in Table IV are given in Table V.

TABLE V

Phosphine	ΔH^*, kcal./mole	ΔS^*, e.u.[a]
$(n\text{-}C_4H_9)_3P$	12.5 ± 0.1	-31 ± 1
$(C_6H_5)_3P$	14.2 ± 0.1	-33 ± 1

[a] Calculated for $T = 290°$K.

These values are of the correct magnitude for bimolecular nucleophilic reactions. For the corresponding reaction of triethylamine, the enthalpy and entropy of activation are 12.19 kcal./mole and −38.8 e.u., respectively.[19] The higher value of the entropy reflects the greater steric requirements of the amine, despite the presence on the amine of sterically less demanding substituents.

This comparison of entropies is highly significant in the larger sense, since it indicates that tertiary phosphines are more nucleophilic than tertiary amines predominantly as a result of steric effects in the amines. No comparative data is available for primary or secondary amines or phosphines, but it is believed that steric effects would be of lesser importance.

Experimental

Materials. Phosphines.—All phosphines were stored and handled under nitrogen with rigorous exclusion of air. Transferrals were made using nitrogen flushed pipet or syringes. Vapor-phase chromatographic and nuclear magnetic resonance analyses were run after the completion of all kinetic runs in order to insure that oxide formation through air contamination would be detected. A summary of the data is given in Table VI.

TABLE VI

Phosphine	Method purification	B.p., °C.[a]	M.p., °C.[a]	Maximum %, impurity by V.P.C.	Phosphorus n.m.r. shifts, p.p.m.[b]
$(CH_3)_3P$[c]	AgI complex[l]	40–41[m]	143–144[x]	3	+62
$(C_2H_5)_3P$[c]	Distillation	128–129[n]		2	+19
$(n\text{-}C_3H_7)_3P$[c]	Distillation	187–189[o]		2	+33
$(n\text{-}C_4H_9)_3P$[d]	Distillation	237–238		1	+33
$(n\text{-}C_5H_{11})_3P$[c]	Distillation	104–107 (0.5 mm.)[p]		3	+34
$(CNCH_2CH_2)_3P$[e]	Recrystallization	.....	97–98	..	+23
$(C_6H_5)_3P$[f]	Recrystallization	.....	80–81	..	+ 7
$C_6H_5P(C_2H_5)_2$[g]	Distillation	220[q]		4	+16
$(C_6H_5)_2PC_2H_5$[h]	Distillation	104–110 (0.3 mm.)[r]		3	+12
$(i\text{-}C_4H_9)_3P$[i]	Distillation	51–60 (0.1 mm.)		5	+40
$(p\text{-}CH_3OC_6H_4)_3P$[c]	Recrystallization	.....	128–130[y]	..	..
$(cyclo\text{-}C_6H_{11})_3P$[c]	Recrystallization	.....	73–75[z]	..	− 7
$C_6H_5P(CH_3)_2$[g]	Distillation	190–193[s]		3	+46
$(C_2H_5)_2PCH_3$[j]	AgI complex[l]	113[t]	171–173[x]	1	+34
$C_2H_5P(CH_3)_2$[j]	AgI complex[l]	80–81[u]	106–107[x]	..	+51
$(n\text{-}C_4H_9)_2PH$[k]	Distillation	184–185[v]		1	+64, 75
$(n\text{-}C_8H_{17})_2PH$[i]	Distillation	137–145 (0.1 mm.)[w]		3	+67, 76
$(i\text{-}C_4H_9)_2PH$[i]	Distillation			2	+77, 89

[a] All boiling points and melting points are uncorrected. [b] Shifts relative to 85% H_3PO_4; no peaks indicative of impurity were observed for any of the phosphines. [c] Synthesized from $PCl_3 + RMgX$. [d] Food Machinery and Chemical Corporation. [e] Synthesized by base-catalyzed reaction of $CH_2{=}CHCN$ and PH_3. [f] Eastman Kodak Company. [g] Synthesized by reaction of $C_6H_5PCl_2$ and RMgX. [h] Synthesized by reaction of $(C_6H_5)_2PCl$ and RMgX. [i] Synthesized by the radical-catalyzed reaction of an olefin and PH_3. [j] Synthesized by the method of Grayson, Keough and Johnson[20] from tris-(2-cyanoethyl)-phosphine. [k] Westvaco Corporation, b.p. 65–67° (12 mm.). [l] AgI complex recrystallized from acetone and the free phosphine regenerated by heating *in vacuo* by the method of Rosenbaum and Sandberg.[21] [m] Reported 37.8°.[21] [n] Reported 127°,[22] 127.5°.[23] [o] Reported 187.5°.[24] [p] Reported 165° (19 mm.).[25] [q] Reported 221.9°.[26] [r] Reported 184° (22 mm.).[27] [s] Reported 192°,[26] 190°.[27] [t] Reported 110–112°.[28] [u] Reported 78–80°.[28] [v] Reported 180–186°.[29] [w] Reported 137° (0.3 mm.).[30] [x] M.p. of AgI complex. [y] Reported 131°.[31] [z] Reported 76–78°.[32]

Halides.—Methyl-, ethyl-, propyl-, *n*-butyl- and isobutyl-iodide and propyl chloride and bromide obtained from Eastman Kodak were dried over anhydrous magnesium sulfate and distilled, a 50% middle cut being taken. Indexes of refraction were checked against the literature values. The iodides were stored under nitrogen over mercury in brown glass bottles.

Neopentyl iodide, b.p. 60° (30 mm.), was prepared in 60% yield by the method of Whitmore, *et al.*,[33] and stored as above.

Phosphonium Salts.—Slowly formed salts were prepared by adding the phosphine to a four-fold excess of the halide under nitrogen and allowing the solution to stand at room temperature until product precipitated. Faster reactions were run as above but with ethanol or diethyl ether added as

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(19) E. Tommila and P. Kavranen, *Acta Chem. Scand.*, **8**, 1152 (1954).

(20) M. Grayson, P. Keough and G. A. Johnson, THIS JOURNAL, **81**, 4803 (1959).

(21) E. J. Rosenbaum and C. R. Sandberg, *ibid.*, **62**, 1622 (1940).

(22) F. A. Letts and N. Collie, *Phil. Mag.*, (5), **22**, 183 (1886).

(23) F. G. Mann and D. Purdie, *J. Chem. Soc.*, 1549 (1935).

(24) W. C. Davies, *et al.*, *ibid.*, 1262 (1929).

(25) F. G. Mann and W. Purdie, *ibid.*, 873 (1936).

(26) A. Michaelis, *Ann.*, **181**, 265 (1876).

(27) J. Meisenheimer, *et al.*, *ibid.*, **449**, 213 (1906).

(28) N. Collie, *Trans. Chem. Soc.*, **53**, 636 (1888).

(29) Walling, U. S. Patent 2,437,795 (1948, to E. I. duPont Company).

(30) M. M. Rauhut, H. Currier, A. Semsel and V. P. Wystrach, *J. Org. Chem.*, **25**, in press (1960).

(31) F. G. Mann and E. J. Chaplin, *J. Chem. Soc.*, 527 (1937).

(32) K. Issleib and A. Brack, *Z. anorg. und. allgem. Chem.*, **277**, 258 (1954).

(33) F. C. Whitmore, E. L. Wittle and B. R. Harriman, THIS JOURNAL, **61**, 1585 (1939).

TABLE VII

Salt	M.p., °C.	Salt	M.p., °C.
$(CH_3)_3P(C_2H_5)I$	350–370	$(n\text{-}C_4H_9)_4PI$	99–100 (98)[37]
$(CH_3)_2P(C_2H_5)_2I$	340–343	$(n\text{-}C_4H_9)_3P(i\text{-}C_4H_9)I$	70–71
$(CH_3)P(C_2H_5)_3I$	317–319	$(i\text{-}C_4H_9)_3P(C_2H_5)I$	118–120
$(C_2H_5)_4PI$	297–298 (270–278)[34]	$(n\text{-}C_5H_{11})_3P(C_2H_5)I$	73–75
$(n\text{-}C_3H_7)_3P(C_2H_5)I$	272–275 (124–125)[35]	$(cyclo\text{-}C_6H_{11})_3PI$	195–196
$(n\text{-}C_4H_9)_3P(CH_3)I$	131–132 (133)[36]	$(CNCH_2CH_2)_3P(C_2H_5)I$	292–294
$(n\text{-}C_4H_9)_3P(C_2H_5)I$	147–152 (153)[36]	$(C_6H_5)P(CH_3)_2(C_2H_5)I$	143–145 (137)[38]
$(n\text{-}C_4H_9)_3P(n\text{-}C_8H^{17})Cl$	111–112	$(C_6H_5)P(C_2H_5)_3I$	140–141 (139)[1]
$(n\text{-}C_4H_9)_3P(n\text{-}C_8H^{17})Br$	98–100	$(C_6H_5)_2P(C_2H_5)_2I$	204–205 (207–208)[39]
$(n\text{-}C_4H_9)_3P(n\text{-}C_3H_7)I$	121–122	$(C_6H_5)_3P(C_2H_5)I$	168–169 (164–165)[40]
		$(p\text{-}MeOC_6H_4)_3P(C_2H_5)I$	170–172

solvent. Essentially pure products were obtained in 100% yield. Those phosphonium salts which were crystalline were recrystallized two or three times from ethanol–ether or acetone–ether. The salts containing higher alkyl groups than ethyl came down as oils which crystallized only when the last traces of solvent were removed. These were purified by repeated dissolution in ethanol and precipitation with ether followed by drying at 80° (1 mm.) for 1 hr. The solid cake was then ground and redried as above.

The purity of the salts was checked by Volhard titration of approximately 0.2 meq. of the salt in 20 ml. of acetone with 0.1 N silver nitrate and potassium thiocyanate. All analyses were within 0.3% of the theoretical value for halide with the exception of the higher alkyl salts which were as much as 0.5% below the theoretical. The phosphonium salts and their melting points are listed in Table VII.

Phosphine Hydroiodides.—These salts were extremely hygroscopic and accordingly were handled under nitrogen in the absence of air and water. Di-*n*-butylethylphosphine hydroiodide was synthesized by allowing equimolar quantities of dibutylphosphine and ethyl iodide to stand for 72 hr. The resultant crystalline mass was dissolved in absolute ethanol and precipitated as an oil with ether. The process was repeated and the resulting oil dried 12 hr. at 80° (1 mm.). The resultant crystalline cake was ground and redried as above to yield waxy crystals, m.p. 51–53°.

Ethyldiisobutylphosphine hydroiodide, m.p. 72–75°, was prepared in the same way as the di-*n*-butylethyl compound.

Ethyldi-*n*-octylphosphine hydroiodide, m.p. 65–67°, was prepared in the same way as the di-*n*-butylethyl compound.

Tri-*n*-butylphosphine hydroiodide was prepared from tri-*n*-butylphosphine in absolute ethanol by the addition of concentrated aqueous hydrogen iodide. The solution was dried over magnesium sulfate and the hydroiodide precipitated as an oil with ether. Drying at 80° (1 mm.) for 12 hr. yielded waxy crystals, m.p. 57–59°.

The compound was also prepared by the addition of a 50% excess of *n*-butyl iodide to di-*n*-butylphosphine in absolute ethanol. Purification as in the di-*n*-butylethyl case yielded crystals, m.p. 55–57°, and mixed m.p. 55–57°. Addition of mercuric chloride to the compound in ethanol afforded crystals which were recrystallized from glacial acetic acid; m.p. 134–136°, mixed m.p. 135–136° with the mercuric chloride adduct of authentic tributylphosphine, m.p. 134–136°.

Ethyldiphenylphosphine hydroiodide, m.p. 75–77°, was prepared by refluxing a 100% excess of ethyl iodide with diphenylphosphine in absolute ethanol for 20 hr. The mercuric chloride adduct had m.p. 203–206°, mixed m.p. 203–206° with the mercuric chloride of authentic ethyldiphenylphosphine, m.p. 203–205°.

Solvents.—Acetone and methanol were "Baker Analyzed" Reagent grade. Both were used without further purification. Ethanol solutions were prepared by mixing the required volumes of absolute ethanol and water. Nitromethane was Eastman Spectro Grade.

Kinetic Runs.—Titrimetric runs were made as follows. A solution 0.1 N or less in the phosphine was made by carefully weighing the phosphine into a nitrogen-filled 50 ml. volumetric flask. The flask was then filled to the mark with solvent at room temperature. A similar solution of the halide was made up in the same way. The two solutions were then placed in a large thermostatted water bath maintained within the limits ± 0.01° of the desired temperature. After a minimum of 30 minutes, 20 ml. aliquots of each solution were withdrawn with thermostatted volumetric pipets and transferred to a nitrogen-flushed, thermostatted two-neck, 100 ml. round-bottomed flask, one neck of which was closed with a rubber septum and the other with a stopcock. The flask was shaken for 30 seconds and returned to the bath. At appropriate intervals, approximately 4 ml. samples of the reaction mixture were withdrawn from the flask by means of a long hypodermic needle inserted through the septum. While samples were being withdrawn, a positive pressure of nitrogen was maintained through the stopcock to prevent the entry of air. An exact 3 ml. aliquot of the removed sample was immediately quenched in 10 ml. of acetone and 10 ml. of water. The time was measured from the beginning of shaking to the instant of quenching. The aqueous acetone solution was extracted three times with 10-ml. portions of ether and then titrated by the Volhard method as were the standard phosphonium salts.

Conductometric runs were made as follows: The solutions of reactants were prepared and mixed just as for the titrimetric runs. By means of a thermostatted pipet, the solution was transferred to a 25 ml. conductivity cell with unplatinized platinum electrodes of cell constant 0.4925. The cell was pre-flushed with nitrogen and suspended in the constant temperature bath. At appropriate intervals, the time was noted and the resistance measured at 60 c.p.s. with an Industrial Instruments, Incorporated Model RC 16 B 1 conductivity bridge.

Standard solutions of the phosphonium salts were made up by weighing appropriate amounts of the salts, transferring them to 100 ml. volumetric flasks and diluting to the mark with solvent. Less concentrated solutions were made by careful dilution. The conductivity was measured as above.

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(34) D. D. Coffman and C. S. Marvel, THIS JOURNAL, **51**, 3496 (1929).

(35) G. W. Fenton and C. K. Ingold, *J. Chem. Soc.*, 2342 (1929).

(36) W. C. Davies and W. J. Jones, *ibid.*, 33 (1929).

(37) E. R. Kline and C. A. Kraus, THIS JOURNAL, **69**, 814 (1947).

(38) H. Köhler and A. Michaelis, *Ber.*, **10**, 807 (1877).

(39) A. E. Arbusov, *J. Russ. Phys. Chem. Soc.*, **42**, 549 (1910).

(40) A. Michaelis and H. Soden, *Ann.*, **229**, 295 (1885).