Table III

Reactions of 1-Substituted-2,4-dinitrobenzenes with Thiophenoxide and Methoxide Ions

	Reactions with thiophenoxide			Reactions with methoxide	
1-Substituent	k at 0.0°, l. mole^{-1} sec.$^{-1}$	ΔE, kcal.	ΔS^*, cal./deg.	k at 0.0°, l. mole^{-1} sec.$^{-1}$	$\frac{k_{\text{thiophenoxide}}}{k_{\text{methoxide}}}$
F	103.4			1.76[a]	59
Cl	3.89	10.3	−20.0	2.00×10^{-3}[b]	1950
Br	6.68	9.8	−20.6	1.38×10^{-3}[b]	4850
I	5.17	10.7	−17.9	3.08×10^{-4}[b]	16800
$-OC_6H_4NO_2$-*p*	1.56	12.1	−15.2		

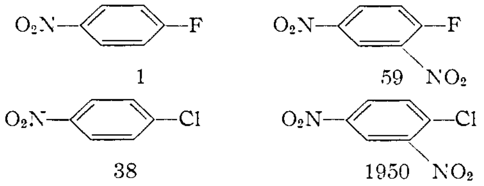
[a] From C. W. L. Bevan and G. C. Bye, *J. Chem. Soc.*, 3091 (1954). [b] From A. L. Beckwith, J. Miller and G. D. Leahy, *ibid.*, 3552 (1952).

F > I ~ Br > Cl. However, the thiophenoxide: methoxide ratio varies in a regular manner as shown in the far right-hand column of Table III. Thiophenoxide is relatively most effective in the displacement of iodine and relatively least effective in displacing fluorine; chlorine and bromine fall between in regular order. Of the two reagents thiophenoxide has the higher polarizability, and in the series of four halogens polarizability increases steadily from fluorine (least) to iodine (greatest).[17] The reagent of greater polarizability is relatively more effective in displacing a halogen substituent of greater polarizability. This is a general tendency in bimolecular nucleophilic substitution reactions, and it will be discussed more fully in another article.

The thiophenoxide:methoxide ratio also varies with the degree of activation of the substituent being replaced. This is shown in Chart I in which this ratio is set directly beneath the structure of each substrate.[18] Notice that thiophenoxide is not only relatively more reactive in the displacement of chlorine rather than fluorine in both the mononitro and dinitro series, but also that thiophenoxide is relatively more reactive in the displacement of a given halogen when it is activated by two nitro groups rather than by one. The latter implies that the Hammett ρ constant[19] for displacements initiated by thiophenoxide should be significantly higher than for displacements initiated by methoxide ion, and suggests that the provisional ρ value for the reactions of thiophenoxide with 4-substituted-2-nitrochlorobenzenes[5c] may be too low. Further data bearing on this question would be of interest.

Chart I

Thiophenoxide:Methoxide Rate Ratios



This investigation has thus shown that the thiophenoxide ion is in general a much stronger nucleophilic reagent than methoxide ion in reactions with aromatic substrates, but that its degree of dominance varies with the substituent being replaced and with the extent of activation by electron-withdrawing groups. With one substrate it is no stronger than methoxide, and it is likely that with yet other substrates, such as fluorobenzene itself, thiophenoxide ion may be much less reactive than methoxide ion.[20]

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mole^{-1} sec.$^{-1}$ $\times$ 10^4). These runs were followed by titration of unconsumed thiophenol (in acid-quenched solutions) with iodine with use of a polarized end-point detector.[16]

(16) C. N. Reilley, W. D. Cooke and N. H. Furman, *Anal. Chem.*, **23**, 1223 (1951).

(17) C. K. Ingold, "Structure and Mechanism in Organic Chemistry," Cornell University Press, Ithaca, N. Y., 1953, p. 124.

(18) The values given are derived from data in Table III, in footnote 15, and from ref. 14.

(19) L. P. Hammett, "Physical Organic Chemistry," McGraw-Hill Book Co., Inc., New York, N.Y., 1940, p. 186.

(20) Preliminary experiments in this Laboratory have indicated that unactivated aryl bromides are remarkably unreactive toward sodium thiophenoxide in alcoholic solvents at elevated temperatures.

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[Contribution from the Venable Chemical Laboratory, University of North Carolina]

A New Factor Affecting Reactivity in Bimolecular Nucleophilic Displacement Reactions[1]

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In several bimolecular nucleophilic substitution reaction series, reagents such as iodide and thiophenoxide ions are found to be, in respect to reagents such as methoxide ion, especially reactive with substrates having halogen substituents of larger size and weight at or near the site of substitution. For example, the thiophenoxide:methoxide rate ratio is higher for reaction with α-iodo than with α-bromo substrates. The special characteristics in both reagents and substrates responsible for this behavior are tentatively identified as polarizabilities, and their special interaction is thought to be of the nature of London forces.

In this article, attention is called to a heretofore unrecognized factor having an important influence on reactivity in bimolecular nucleophilic displacement reactions. This factor has escaped notice because, although significant, it is not a primary determinant of reactivity, and therefore its effect is not usually evident from examination of rate coefficients for a single reaction series. It becomes evi-

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(1) Financial assistance from the Office of Ordnance Research, U. S. Army, is gratefully acknowledged.

dent upon comparison of data for two or more appropriate reaction series, and only recently have sufficient data been accumulated for the effect to be recognized.

The new factor first came to my attention from examination of the data in Table I, concerning rates of some aromatic nucleophilic substitution reactions. In this set of data, there are three obvious features which have long been recognized in data of this type: thiophenoxide ion is much more reactive than either methoxide ion or piperidine with each of the four substrates, fluorine is by far the most rapidly replaced of the halogens in reaction with each of the three nucleophilic reagents, and iodine tends to be somewhat less mobile than the other halogens. These are major consequences of the primary factors determining reactivity in these reactions, but they are not the focus of our present interest. The new factor is more subtle in its manifestation; it is recognized by comparison of rate ratios as set forth in the two right-hand columns of Table I. Such comparison shows that thiophenoxide ion, relative to methoxide ion, is much more effective in displacing a halogen of larger size and weight. Piperidine and methoxide, on the other hand, are more nearly the same when such ratios are compared, although piperidine does show some favoritism for displacement of a larger and heavier halogen; the change is sufficient to actually invert the order of relative reactivity in the middle of the group of four halogens. Nevertheless, the tendency of thiophenoxide ion, relative to either methoxide ion or to piperidine, to favor displacement of halogens in order of their size and weight is the most striking new relationship in Table I.

TABLE I

REACTIONS OF THREE NUCLEOPHILIC REAGENTS WITH 1-HALO-2,4-DINITROBENZENES[a]

Halogen	Rate coefficient at 0°, l. mole^{-1} sec.$^{-1}$ NaOCH$_3$	Piperidine[b]	NaSC$_6$H$_5$[c]	$\frac{k_{C_6H_5S^-}}{k_{OCH_3^-}}$	$\frac{k_{piperidine}}{k_{OCH_3^-}}$
F	1.76[d]	1.5	103.4	59	0.85
Cl	2.00×10^{-3}[e]	1.95×10^{-3}	3.89	1950	0.98
Br	1.38×10^{-3}[e]	1.97×10^{-3}	6.68	4840	1.43
I	3.08×10^{-4}[e]	4.57×10^{-4}	5.17	16800	1.48

[a] The halogen is displaced by the nucleophilic reagent in each reaction. All reactions in methanol solvent. [b] Data from J. F. Bunnett, E. W. Garbisch, Jr., and K. M. Pruitt, THIS JOURNAL, **79**, 385 (1957). [c] Data of J. F. Bunnett and W. D. Merritt, Jr., *ibid.*, **79**, 5967 (1957). [d] From C. W. L. Bevan and G. C. Bye, *J. Chem. Soc.*, 3091 (1954). [e] From A. L. Beckwith, J. Miller and G. D. Leahy, *ibid.*, 3552 (1952).

Similar tendencies are discernible in a set of data shown in Table II, due to de la Mare, Hughes, Ingold and co-workers, concerning rates of nucleophilic halogen exchange in alkyl halides. Rates of reactions of several alkyl bromides and the corresponding alkyl iodides with chloride, bromide and iodide ions in acetone solution are summarized in this table. Obvious and familiar features in these data are that bromide ion is more reactive than chloride ion with all substrates and about the same as iodide ion in reactivity. Also, every alkyl iodide except methyl iodide is more reactive than the corresponding bromide with any halide ion reagent. The more subtle relationship which is our present concern is that bromide ion in respect to chloride ion and iodide ion in respect to bromide ion are especially reactive with alkyl iodides as compared to the corresponding alkyl bromides. This is shown by the rate ratios at the right side of the table. (The rate ratios at the bottom of the table will be discussed later.)

TABLE II

REACTIONS OF HALIDE IONS WITH ALKYL HALIDES IN ACETONE

Alkyl halide	Rate coefficient at 25°, l. mole^{-1} sec.$^{-1}$ $\times$ 10^5, for reacn. with LiCl[a]	LiBr[b]	NaI[c]	$\frac{k_{Br^-}}{k_{Cl^-}}$	$\frac{k_{I^-}}{k_{Br^-}}$
CH$_3$Br	600	13000		22	
CH$_3$I	468	27000		58	
C$_2$H$_5$Br	9.88	170	196	17	1.15
C$_2$H$_5$I	42.0	1490	6000	36	4.03
n-C$_3$H$_7$Br	6.45	110		17	
n-C$_3$H$_7$I	24.6	1050		43	
Iso-C$_3$H$_7$Br	0.13	1.8	1.3	14	0.72
Iso-C$_3$H$_7$I	1.33	37	53	28	1.43
Iso-C$_4$H$_9$Br	1.53	5.7	6.0		
Neo-C$_5$H$_{11}$Br	0.00026	0.0026	0.0020		0.77
Neo-C$_5$H$_{11}$I	0.00058		0.16		
	Rate ratios				
$\frac{k_{iso\text{-}C_4H_9Br}}{k_{C_2H_5Br}}$	0.16	0.034	0.031		
$\frac{k_{neo\text{-}C_5H_{11}Br}}{k_{C_2H_5Br}}$	2.6×10^{-5}	1.5×10^{-5}	1.0×10^{-5}		

[a] Data from E. D. Hughes, C. K. Ingold and J. D. H. Mackie, *J. Chem. Soc.*, 3173, 3177 (1955). [b] Data from P. B. D. de la Mare, *ibid.*, 3180 (1955), and from L. Fowden, E. D. Hughes and C. K. Ingold, *ibid.*, 3193 (1955). [c] Data from L. Fowden, E. D. Hughes and C. K. Ingold, *ibid.*, 3187 (1955), and from P. B. D. de la Mare, *ibid.*, 3196 (1955).

Relationships of similar type, though involving a new feature, were noted in data from Hine's laboratory, displayed in Table III, concerning reactions of α-substituted methyl halides with three nucleophilic reagents. In these data, the immediately apparent features are the following: (a) sodium thiophenoxide is much more reactive than sodium methoxide and somewhat more reactive than sodium iodide with all the substrates listed; (b) iodine is displaced by each reagent more rapidly than bromine similarly situated (compare BrCH$_2$I with BrCH$_2$Br and ClCH$_2$I with ClCH$_2$Br); and (c) of the four halogens acting as α-substituents, fluorine is the

TABLE III

REACTIONS OF THREE NUCLEOPHILIC REAGENTS WITH α-SUBSTITUTED METHYL HALIDES

Substrate	α-Substituent	Rate coefficient at 50°, l. mole^{-1} sec.$^{-1}$ $\times$ 10^5, for reacn. with NaI[a]	NaOCH$_3$[b]	NaSC$_6$H$_5$[c]	$\frac{k_{C_6H_5S^-}}{k_{OCH_3^-}}$	$\frac{k_{I^-}}{k_{OCH_3^-}}$
CH$_3$CH$_2$Br	CH$_3$	1700	47.2	4120	87	36
FCH$_2$Br[d]	F	1350	225	3800	17	6.0
ClCH$_2$Br[d]	Cl	218	2.36	678	288	92
BrCH$_2$Br[e]	Br	69	0.370	277	749	186
ClCH$_2$I[f]	Cl		4.41	3770	855	
BrCH$_2$I[f]	Br		1.02	2100	2060	
ICH$_2$I[e]	I		0.536	2800	5230	

[a] Acetone solvent; data from J. Hine, C. H. Thomas and S. J. Ehrenson, THIS JOURNAL, **77**, 3886 (1955). [b] Methanol solvent; data from J. Hine, *et al.*, preceding reference. [c] Methanol solvent; data extrapolated from J. Hine, S. J. Ehrenson and W. H. Brader, Jr., *ibid.*, **78**, 2282 (1956). [d] Bromine is undoubtedly the halogen displaced.[a] [e] The observed rate coefficients have been divided by a statistical factor of two. [f] Iodine is probably the halogen displaced.[a]

most favorable to reaction and iodine the least, with chlorine and bromine falling in order between. The more subtle tendencies with which this paper is concerned are discerned by comparisons of two types. First, thiophenoxide ion relative to methoxide ion is seen to be comparatively more effective in the displacement of iodine as compared to similarly situated bromine (compare the $k_{C_6H_5S^-}/k_{OCH_3^-}$ ratios for $BrCH_2I$ *vs.* $BrCH_2Br$ and for $ClCH_2I$ *vs.* $ClCH_2Br$); this is analogous to relationships in the data of Table I. Second, thiophenoxide ion and iodide ion are relatively more effective than methoxide ion in the displacement of a given halogen when the *α-substituent* is a halogen of larger size and weight. This new feature is seen by comparison of the rate ratios in the two right-hand columns of the Table.

Having examined these three sets of data, let us now pause and consider the new relationships which have been revealed. We have seen that certain nucleophilic reagents typified by thiophenoxide and iodide ions, when compared to other reagents typified by chloride and methoxide ions, are especially reactive in the displacement of halogens of greater size and weight and in reactions with substrates having α-halogen substituents of greater size and weight. There is evidently some characteristic in reagents such as thiophenoxide and iodide ions which causes them to act comparatively most effectively on substrates having larger halogens at the site of reaction, and conversely some characteristic in substrates having larger halogens at the site of reaction which causes them to react comparatively most rapidly with reagents such as the thiophenoxide and iodide ions. Our problem is to recognize, if possible, what these characteristics are.

The Special Substrate Characteristic.—This characteristic is plainly *not* fundamentally concerned with the breaking of the bond between the carbon atom which is the site of substitution and the α-halogen substituents which affect relative reactivity. To be sure, the halogen being displaced in a rate-determining step *can* affect relative reactivity, as is seen in all the comparisons in Table II and some of those in Table III, but α-halogen substituents which are not displaced in the rate-determining step (Table I)[2] or not displaced at all (many of the comparisons in Table III) have similar effects. Thus the substrate characteristic has to do with the presence of certain halogens at or near the site of substitution and not with their being displaced in a rate-determining step. In this connection, the data in Table IV are of interest. They concern the effects of *o*-, *m*- and *p*-bromine substituents on the relative reactivity of benzyl chlorides with potassium iodide in acetone and potassium hydroxide in 50% acetone, in reactions which are assuredly bimolecular in mechanism. The rate ratios show that the comparative reactivity of iodide ion is greatly increased by the introduction of an *o*-bromine substituent but that the effect dwindles as the bromine is moved to the *meta* and then to the *para* position. These data show that it is sufficient to have a large and heavy halogen *near*, and not necessarily *at*, the site of substitution and that the special reactivity with a reagent such as iodide ion diminishes as the large halogen is moved away from the site of substitution.[3]

TABLE IV

REACTIONS OF SUBSTITUTED BENZYL CHLORIDES WITH POTASSIUM IODIDE AND WITH POTASSIUM HYDROXIDE

Substituent	Rate coefficient at 30°, l. mole^{-1} sec.$^{-1}$ × 10^5, for reacn. with KI[a]	KOH[b]	$\frac{k_{I^-}}{k_{OH^-}}$
H	103	4.86	21
o-Br	401	3.43	117
m-Br	190	2.83	67
p-Br	250	5.27	47

[a] Acetone solvent; data extrapolated from G. M. Bennett and B. Jones, *J. Chem. Soc.*, 1817 (1935). [b] 50% acetone solvent; data from S. C. J. Olivier and A. P. Weber, *Rec. trav. chim.*, **53**, 873 (1934).

It might be suspected that the substrate characteristic is a simple steric effect, concerning hindrance of reagent approach to the reaction site, since the α-halogen substituents which especially enhance reactivity with reagents such as thiophenoxide ion are those of larger bulk. This seems unlikely for several reasons. One is that in the transition state for S_N2 substitution in a methyl halide,[4] the halogen atom cannot interact sterically with the substitution reagent and has the very minimum of interaction with the rest of the substrate structure, yet k_{Br^-}/k_{Cl^-} is typically higher for methyl iodide then for methyl bromide. Another is that in the data of Table IV, *m*- and *p*-bromine atoms rather far from the site of reaction have the typical influence, albeit in muted form. Still further evidence is the rate ratios at the bottom of Table II; these show that the reactivity of bromides with bulky α-alkyl substituents, relative to ethyl bromide as a standard, actually decreases somewhat as the halide ion reagent increases in size and weight.[5] Thus the special substrate characteristic conferred by α-halogen substituents of larger size and weight is not due simply to their larger bulk.

Other properties of the halogens which vary regularly with increasing size and weight must then be considered as possible causes of the special substrate characteristic. These include their inductive effects which decrease steadily from fluorine to iodine,[6] mesomeric effects which decrease in the same order[6] and polarizabilities which increase from fluorine steadily to iodine.[7] That mesomeric effects are responsible is unlikely because the amount of mesomeric interaction of the halogen with the rest of the substrate or transition state varies from none at all, as in the reactions of Table II, to less in

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(2) J. F. Bunnett, E. W. Garbisch, Jr., and K. M. Pruitt, THIS JOURNAL, **79**, 385 (1957).

(3) It would be desirable to further test such relationships with similar data concerning the effects of other halogens in various nuclear positions and concerning reactions with other reagents. Appropriate data could not be found in the literature, but experimental work on such reactions is planned.

(4) C. K. Ingold, *Quart. Revs.*, **11**, 1 (1957).

(5) From data of I. Dostrovsky and E. D. Hughes, *J. Chem. Soc.*, 157 (1946), $k_{iso\text{-}C_4H_9Br}/k_{C_2H_5Br} = 0.30$ and $k_{neo\text{-}C_5H_{11}Br}/k_{C_2H_5Br} = 4.2 \times 10^{-6}$ for reactions with sodium ethoxide in absolute ethanol, further indicating that rate ratios of this type do not change much as the reagent is changed.

(6) R. W. Taft, Jr., in M. S. Newman, "Steric Effects in Organic Chemistry," John Wiley and Sons, Inc., New York, N. Y., 1956, p. 595.

(7) C. K. Ingold, "Structure and Mechanism in Organic Chemistry," Cornell University Press, Ithaca, N. Y., 1953, pp. 119-137.

TABLE V

REACTIONS OF ETHYL AND *n*-PROPYL HALIDES WITH SEVERAL NUCLEOPHILIC REAGENTS[aa]

Reagent and conditions	$k_{C_2H_5I}$	$k_{C_2H_5Br}$	$\frac{k_{C_2H_5I}}{k_{C_2H_5Br}}$	$k_{n\text{-}C_3H_7I}$	$k_{n\text{-}C_3H_7Br}$	$\frac{k_{n\text{-}C_3H_7I}}{k_{n\text{-}C_3H_7Br}}$	Ref.
NaI, acetone							
25°	6000	195	30.8				a,b
$C_6H_5COCHC_2H_5^-$, ether							
30°	1.3	0.1	13				c
LiBr, acetone							
25°	1490	170	8.76	1050	110	9.55	d,e
16.5°	615	66.2	9.28				d,e
Pyridine, benzene							
99.7°	13.8	2.49	5.54	4.84	1.01	4.79	f
$C_6H_5S^-$, CH_3OH							
19.95°				1280	256	5.00	g
$(CH_3)_3N$, benzene							
99.7°				219	42.6	5.14	f
LiCl, acetone							
25°	42.0	9.88	4.25	24.6	6.45	3.82	h
35.36°	113	26.0	4.35				
45.72°	275	64.6	4.26				
54.04°	526	136	3.87				
NaSR,[m] 50% C_2H_5OH							
25°	600	195	3.08	333	127	2.62	i
$NaOC_2H_5$, C_2H_5OH							
25°	13.5	6.60	2.04				j
$Na_2S_2O_3$, water							
25°	83.3	51.6	1.61				k
H_2O in 60.72% dioxane							
50°	0.047	0.045	1.04				l

[aa] Rate coefficients in l. mole^{-1} sec.$^{-1}$ × 10^{-5}. [a] P. B. D. de la Mare, *J. Chem. Soc.*, 3196 (1955). [b] L. Fowden, E. D. Hughes and C. K. Ingold, *ibid.*, 3187 (1955). [c] H. D. Zook and W. L. Rellahan, THIS JOURNAL, **79**, 881 (1957). [d] L. Fowden, E. D. Hughes and C. K. Ingold, *J. Chem. Soc.*, 3193 (1955). [e] P. B. D. de la Mare, *ibid.*, 3180 (1955). [f] C. A. Winkler and C. N. Hinshelwood, *ibid.*, 1147 (1935). [g] J. Hine, S. J. Ehrenson and W. H. Brader, Jr., THIS JOURNAL, **78**, 2282 (1956). [h] E. D. Hughes, C. K. Ingold and J. D. H. Mackie, *J. Chem. Soc.*, 3173, 3177 (1955). [i] S. F. Acree and G. H. Shadinger, *Am. Chem. J.*, **39**, 226 (1908). [j] E. K. Marshall and S. F. Acree, *J. Phys. Chem.*, **19**, 589 (1915). [k] A. Slator and D. F. Twiss, *J. Chem. Soc.*, **95**, 93 (1909). [l] H. R. McCleary and L. P. Hammett, THIS JOURNAL, **63**, 2259 (1941). [m] NaSR stands for sodium 3-phenyl-1-thiourazolate.

the transition state than in the substrate, as in the reactions of Table I, to more in the transition state than in the substrate, as in the reactions of Table III. If mesomeric effects were responsible, such a constancy of the effects of α-halogen substituents as we have noted in the various types of reactions would not have been the result. Inductive effects also seem unlikely to be the essence of the special substrate characteristic since their variation from one halogen to another[6] is small while the variation in rate ratios in Tables I, II and III is large. Also, the rate ratios pertaining to ethyl bromide in Table II indicate that the contribution of an α-methyl substituent to the special substrate characteristic is between that of fluorine and of chlorine; the inductive effect of a methyl group certainly does not lie there.

The polarizabilities of the halogens do, on the other hand, vary substantially from one halogen to another.[8] Also the polarizability of a methyl group is between that of fluorine and that of chlorine, thus leading to a rational interpretation of the rate ratios for ethyl bromide in Table II. It is profitable to identify, at least tentatively, the special substrate characteristic with the polarizabilities of α-substituents.

The Special Reagent Characteristic.—We have seen that the reagents which are particularly reactive with substrates having α-substituents of high polarizability are typified by iodide ion and thiophenoxide ion. What is it about these reagents that is responsible for this special characteristic? What do these reagents have that chloride ion and methoxide ion lack? Two answers come to mind: high general nucleophilic reactivity and high polarizability.

Some guidance as to which is fundamentally responsible can be gained from Table V, in which data on reactions of several nucleophilic reagents with ethyl and *n*-propyl bromides and iodides are presented. The reagents are arranged in approximate order of decreasing k_{RI}/k_{RBr} ratio. Inspection of this table shows that there is little support for the idea that a high RI:RBr ratio is necessarily associated with high nucleophilic reactivity. For example, the enolate ion (second listing in Table V) is relatively unreactive but gives a high ratio while thiosulfate ion (second from the bottom) is quite reactive but gives a low ratio. Admittedly, some of the differences in reactivity are due to differences in the solvents used for the various reactions, but it does not appear that the application of suitable corrections for solvent effects would bring RI:RBr ra-

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(8) Atomic refraction constants (D-line) of the halogens are F, 1.09; Cl, 5.97; Br, 8.86; I, 13.90 (ref. 7).

tios into direct parallelism with general nucleophilic reactivity.

Edwards[9] has shown that the rates and equilibria of reactions of many nucleophilic reagents can be correlated satisfactorily by the equation

$$\log (k/k_0) = AP + BH \qquad (1)$$

in which k is the rate or equilibrium constant for reaction of a substrate with a nucleophilic reagent and k_0 is that for reaction of the same substrate with water, P and H are constants characteristic of the nucleophilic reagent, and A and B are constants characteristic of the substrate. H is a measure of the basicity of the reagent, being derived from its pK_a value, and P is a measure of its polarizability, being defined as equal to $\log (R/R_{H_2O})$ in which R and R_{H_2O} are molar refractions. A and B express the susceptibility of the substrate to the polarizability and basicity characteristics of the reagent, respectively.

In general the reagents high in Table V are those of high polarizability and those low in the table are low in this quality. This encourages one to identify the special reagent characteristic as polarizability. Accepting this identification for the moment, let us further assume that ethyl bromide and ethyl iodide are equally susceptible to the basicity of nucleophilic reagents (that is, that $B_{C_2H_5Br} = B_{C_2H_5I}$) and therefore that the difference in their reactivity toward nucleophilic reagents is due entirely to a difference in their A values. From equation 1 one can then easily derive the relationship

$$\log(k_{C_2H_5I}/k_{C_2H_5Br}) = (A_{C_2H_5I} - A_{C_2H_5Br})P + \log\left(\frac{k_{o,C_2H_5I}}{k_{o,C_2H_5Br}}\right) \qquad (2)$$

Since the A values and the k_0 values are constants, this equation implies that a plot of $\log(k_{C_2H_5I}/k_{C_2H_5Br})$ for various reagents against their P values should be linear with slope $(A_{C_2H_5I} - A_{C_2H_5Br})$ and intercept $\log (k_{o,C_2H_5J}/k_{o,C_2H_5Br})$. The data necessary for such a plot could be found for only four reagents; the resulting plot is shown in Fig. 1. The four points do indeed approximate a straight line, and this tends to support identification of the special reagent characteristic with polarizability as well as the assumption that the B values of ethyl bromide and ethyl iodide do not differ appreciably.

One difficulty in application of Edwards' treatment is that the evaluation of P values for many reagents is difficult. Though one may know the molar refraction of a polyatomic reagent, one does not know just how much of the molar refraction is due to that part of the molecule which contributes to its nucleophilic reactivity. The refractions of methoxide and ethoxide ions differ appreciably, but it is unlikely that their P values do. If equation 2 is valid, one should be able to read off the P value for a reagent from the point on the (least squares) line in Fig. 1 corresponding to $\log (k_{C_2H_5I}/k_{C_2H_5Br})$ for that reagent. In this way one obtains, using data in Table V, a P value of 0.179 for ethoxide ion; this compares with Edwards' P value of 0.143 for hydroxide ion. The agreement is encouraging, for one would expect the effective polarizability of ethoxide ion to be somewhat greater than that of hydroxide. This treatment also gives $P = 0.580$ for the enolate ion of butyrophenone; this is a not unreasonable value for a carbanion and would certainly be hard to determine by other methods.

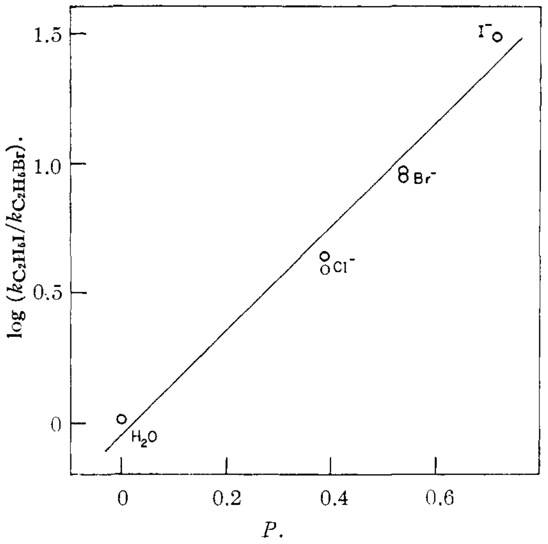

Fig. 1.—Relationship of ethyl iodide: ethyl bromide rate ratios to reagent polarizabilities. The plot is based on data in Table V and on these P values from ref. 9: H_2O, 0.00; Cl^-, 0.389; Br^-, 0.539; I^-, 0.718.

However, the ratios in Table V for the sulfur reagents are low. From Fig. 1 one would, for example, obtain a P value of 0.372 for thiophenoxide ion (using a ratio from n-propyl halides), less than 0.397 for pyridine. The sulfur atom in thiophenoxide ion certainly has a higher polarizability than the nitrogen atom in a tertiary amine, and therefore the P value of 0.372 for thiophenoxide must be false. Thus the evaluation of P values from Fig. 1 does not appear to be justified at this time. It is interesting to note, on the other hand, that the data in Tables I and III indicate thiophenoxide to far exceed piperidine and methoxide ion in polarizability, if indeed this is the special reagent characteristic, and to approximate iodide ion in this respect. This is more reasonable. Why the effective polarizability of sulfur reagents in reactions with alkyl halides, as revealed in RI:RBr rate ratios, is so low is an interesting question. One consideration that may be very important is that polarizability is not generally uniform in all directions.[7] The effective polarizability of a reagent (or of an α-substituent) may therefore vary with the geometry of the transition state. The S–C–X bond angle is close to 180° in the transition states of the SN2 displacements of Table V but in the region of 90–110° in the transition states relevant to Tables I and III.

The Nature of the Special Interaction between Reagents and Substrates.—We have seen that nucleophilic reagents such as thiophenoxide and iodide and substrates having large halogen substituents at or near the site of substitution are especially reactive with one another. We have tentatively identified both the special substrate characteristic responsible for this behavior and the special

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[9] (a) J. O. Edwards, This Journal, **76**, 1540 (1954); (b) **78**, 1819 (1956).

reagent characteristic as polarizability.[10] But we have not considered the physical nature of the special interaction of reagent with substrate.

Some of the most important forces of attraction between molecules not undergoing chemical reaction are those variously known as van der Waals or London or dispersion forces.[11] These forces are proportional to the product of the polarizabilities of the atoms concerned and inversely proportional to the seventh power of the distance between the atoms. London forces have an important influence on many physical properties. They are, for example, largely responsible for the greater solubility of iodine (I_2) and of stannic iodide in bromoalkane solvents than in corresponding chloroalkanes.[12,13]

One would expect London forces to contribute to the lowering of transition state energy and thus to an increase in reaction rate, when the transition state structure is such as to bring atoms of high polarizability close to one another. This would appear to be the nature of the effect with which this paper is concerned.[14]

It should be emphasized that the accelerative effect arising from the mutual interaction of substrate and reagent atoms of high polarizability does not mean that change from a substituent or reagent of low to one of high polarizability necessarily brings about an increase in reaction rate. The new substituent, for example, may have steric, inductive and/or mesomeric effects which depress the reaction rate. Examples can be found in Tables I, II and III. What it does mean is that after allowances have been made for these other factors, as we have done by considering suitable rate ratios, the change to a substituent of higher polarizability will have caused more acceleration, or less deceleration, the greater the effective polarizability of the nucleophilic reagent.

Assuming that the special characteristics in reagent and substrate are correctly identified as polarizabilities and that their special interaction is in the nature of London forces, we can expect that this factor exerts a significant influence in yet other classes of chemical reactions. It will be of interest to discover other manifestations of this effect.

It is a pleasure to acknowledge discussions with Drs. Herbert C. Brown and Will D. Merritt, Jr., which have been of great help in formulating the ideas set forth in this paper.

CHAPEL HILL, N. C.

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[10] For many years, polarizability in a nucleophilic reagent has been considered to contribute substantially to nucleophilic reactivity and polarizability in a group being displaced has been considered to contribute substantially to displaceability. *Cf.* E. D. Hughes, *Trans. Faraday Soc.*, **34**, 195 (1938); G. E. K. Branch and M. Calvin, "The Theory of Organic Chemistry," Prentice-Hall, Inc., New York, N. Y., 1941, p. 422; C. G. Swain and C. B. Scott, THIS JOURNAL, **75**, 141 (1953). These views appear to be sound, but they should be clearly differentiated from the proposition that has been arrived at in this paper, namely, that the *special increase* in reactivity which attends the reaction of a reagent such as the iodide ion with a substrate having a large and heavy halogen atom at or near the site of substitution is due to the high polarizabilities of both reagent and halogen substituent. The *general* contribution of polarizability to nucleophilic reactivity is allowed for, and the *special* reagent characteristic is revealed, by comparison of substrate ratios such as the k_{RI}/k_{RBr} ratios in Table V.

[11] O. K. Rice, "Electronic Structure and Chemical Binding," McGraw-Hill Book Co., Inc., New York, N. Y., 1940, p. 354; J. R. Partington, "An Advanced Treatise on Physical Chemistry," Vol. I, Longmans, Green and Co., London, 1949, p. 741.

[12] J. H. Hildebrand and R. L. Scott, "The Solubility of Nonelectrolytes," 3rd ed., Reinhold Publishing Corp., New York, N. Y., 1950, pp. 373 and 376.

[13] S. A. Shchukarev, L. S. Lilich and A. B. Sheinin, *Doklady Akad. Nauk S.S.S.R.*, **86**, 1333 (1952); *C. A.*, **47**, 383 (1953).

[14] There is one troublesome point concerning this interpretation. If the special interaction is indeed of the nature of London forces, it seems strange that bromine atoms in *m*- and *p*-bromobenzyl chlorides should still exert a significant influence on the iodide:hydroxide ratio (Table IV). London forces fall off extremely rapidly with distance. This point requires further consideration.

[CONTRIBUTION FROM THE DEPARTMENT OF RESEARCH IN CHEMICAL PHYSICS, MELLON INSTITUTE]

Spectral Evidence for Tautomerism in Diazo Ketones

BY FOIL A. MILLER AND WILLIAM B. WHITE

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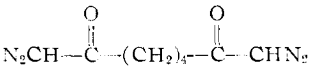
Ultraviolet absorption of the group $N_2CH-CO-CH_2-$ varies considerably with change in solvent. In cyclohexane and dioxane there is a single intense band near 247 mμ; in water and acetic acid this band is weaker, and another intense one appears near 275 mμ. Seven other solvents gave intermediate results. In mixtures of water and acetonitrile of varying composition there is a smooth transition from the one case to the other. The resulting family of curves goes through an approximate isosbestic point, which suggests an equilibrium between two forms. Two such equilibria were considered: a keto-enol tautomerism and a diazo-isodiazo tautomerism. Although the results are not conclusive, infrared measurements of the intensities of the diazo and the carbonyl bands support the latter. It may be represented as $\overset{-}{N}{=}\overset{+}{N}{=}CH{-}CO{-} \rightleftarrows HN{=}\overset{+}{N}{=}\overset{-}{C}{-}CO{-}$

Introduction

Ultraviolet absorption is useful in studying diazo ketones because the group $N_2-CH-CO-$ has a characteristic band at 245–250 mμ.[1] Although changing the solvent usually has only a minor effect on the absorption spectrum, Morgan, Renfrew and Moore[2] discovered that the electronic spectrum of 1,8-bisdiazo-2,7-octanedione (I) depends markedly



$$N_2CH-\overset{\overset{O}{\|}}{C}-(CH_2)_4-\overset{\overset{O}{\|}}{C}-CHN_2$$

I

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[1] (a) S. A. Fusari, *et al.*, THIS JOURNAL, **76**, 2878 (1954); (b) S. A. Fusari, T. H. Haskell, R. P. Frohardt and Q. R. Bartz, *ibid.*, **76**, 2881 (1954).

[2] M. S. Morgan, A. G. Renfrew and A. M. Moore, paper presented at 129th Meeting of Amer. Chem. Soc., Dallas, Tex., April, 1956.