examine the reactions of nitriles in order to find an explanation for the high reactivity of both sulfhydryl ion and peroxide anion. Current work is directed toward a more detailed investigation of these points.

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The Effect of Halogen Atoms on the Reactivity of Other Halogen Atoms in the Same Molecule. III. The S_N2 Reactivity of Ethylene Halides[1]

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The interpretations of earlier data as showing that the replacement of β-hydrogen atoms in alkyl halides by halogen atoms causes increased S_N2 reactivity are shown to be unreliable. The kinetics of the bimolecular substitution reaction of sodium thiophenolate with ethyl bromide and five of its β-substituted derivatives have been studied. For the various β-substituents, the rates vary thus: $H > C_2H_5 \sim CH_3 > Cl \sim Br \sim F$. The heats of activation are found to increase with electron-withdrawing power of the substituents studied, while the entropies of activation decrease with increasing size.

The substitution of a β-hydrogen atom in an alkyl group by a halogen atom is commonly said[2] to increase the reactivity by the S_N2 or one-step bimolecular displacement mechanism.[3] The evidence quoted includes the data of Tronov and Gershevich,[4] who reported rate constants for the reaction of sodium methoxide with *n*-propyl bromide, isopropyl bromide, propylene bromide, trimethylene bromide, 1,2,3-tribromopropane and other halides of propane. From what is known of the chemistry of polyhalides of this type it might be expected that a major reaction with the strongly basic reagent sodium methoxide would be dehydrohalogenation.[5] Thus, the fractions of the rate constants obtained by these workers which are due to substitution reactions are not definitely known. The data of Slator, who studied the reactions of sodium thiosulfate with a number of halogen compounds,[6] have also been quoted in this connection. Slator indeed found that the second-order rate constant for the reaction with ethylene iodide is considerably greater than that for reaction with ethyl iodide, but no attention appears to have been called to his observation that ethylene bromide was considerably less reactive than ethyl bromide. Since we have now found that the reaction of ethylene iodide with sodium thiosulfate yields largely ethylene, it is clear that these data may not be used as the basis for generalizations concerning *displacement on carbon.*

It should also be noted that although Slator obtained reasonably steady first-order rate constants for the reaction of ethylene chlorobromide and chloroiodide with excess sodium thiosulfate, these are not the rate constants for first-order solvolysis, as has been suggested.[7] This follows from the fact that the rate constants for the solvolysis of these compounds are smaller by factors of more than one thousand than the constants reported by Slator,[8] as well as from inspection of some of Slator's data.[9] Although a second-order reaction in which rate "constants" climb (due to some replacement of the second halogen atom) could give reasonable first-order rate constants, we cannot be sure that this is being observed in the present case, since another side reaction, hydrolysis of the Bunte salt to a mercaptan and acid, was shown by Slator to be present and other reactions such as dehalogenation may also have been occurring.

From the data of Taylor[10] the rate of the second-order substitution reaction of ethanolic alkali with ethylene bromide may be calculated to be two or three times that for reaction with ethyl bromide, but this calculation depends on a difficult and not altogether satisfying analysis of the products of the former reaction.[11]

We have not been able to devise a method for determining accurately the effect of β-iodine atoms on S_N2 reactivity, since the nucleophilic reagents which have been studied attack the β-iodine atom

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[1] Papers I and II of this series: J. Hine and D. E. Lee, THIS JOURNAL, **73**, 22 (1951); **74**, 3182 (1952).

[2] E. R. Alexander, "Principles of Ionic Organic Reactions," John Wiley and Sons, Inc., New York, N. Y., 1950, p. 89; M. J. S. Dewar, "The Electronic Theory of Organic Chemistry," Oxford University Press, London, 1949, p. 71; A. E. Remick, "Electronic Interpretations of Organic Chemistry," 2nd Ed., John Wiley and Sons, Inc., New York, N. Y., 1949, p. 394. E. D. Hughes and C. K. Ingold [*J. Chem. Soc.*, 244 (1935)], have also made a statement of this type, but in an article which has come to our attention since this investigation began [E. D. Hughes, *Quart. Revs.*, (*London*), **5**, 254 (1951)], it is recognized that none of the existent data unambiguously describe the rate of a substitution (in contrast to elimination) process and stated ". . . investigations of suitable systems are being undertaken."

[3] For the significance of the term S_N2, see I. Dostrovsky, E. D. Hughes and C. K. Ingold, *J. Chem. Soc.*, 173 (1946), and earlier papers.

[4] B. V. Tronov and A. I. Gershevich, *J. Russ. Phys. Chem. Soc.*, **59**, 727 (1927); *C. A.*, **22**, 3389^9 (1928).

[5] Sodium hydroxide and 1,2,3-tribromopropane give 2,3-dibromopropene in more than 80% yield (R. Lespieau and M. Bourguel, "Organic Syntheses," Coll. Vol. I, 2nd Ed., John Wiley and Sons, Inc., New York, N. Y., 1941, p. 209). Ethylene bromide with sodium hydroxide in homogeneous aqueous dioxane solution gives more than 90% elimination (J. Hine and W. H. Brader, unpublished work).

[6] A. Slator, *J. Chem. Soc.*, **85**, 1286 (1904).

[7] L. P. Hammett, "Physical-Organic Chemistry," McGraw-Hill Book Co., Inc., New York, N. Y., 1940, p. 208. See also E. A. Moelwyn-Hughes, *Nature*, **133**, 294 (1934).

[8] J. Hine and W. H. Brader, unpublished work.

[9] The rate constants calculated as first order in ethylene chlorobromide increase with increasing thiosulfate concentration. The order of a reaction in which an excess of ethylene chloroiodide was used was reported to be about 1.85.

[10] W. Taylor, *J. Chem. Soc.*, 1514 (1935).

[11] The work of B. V. Tronov and L. V. Laduigina [*J. Russ. Phys. Chem. Soc.*, **62**, 2165 (1930); *C. A.*, **25**, 3957 (1931)], P. Petrenko-Kritchenko and V. Opotsky [*Ber.*, **59B**, 2131 (1926)] and many other data on reactions of nucleophilic reagents with 1,2-dihalides, also probably include large amounts of elimination as well as substitution reactions.

of β-iodoalkyl halides rather than solely the α-carbon atom.[12]

In order to learn the effect of β-bromine, chlorine and fluorine atoms on S_N2 reactivity, we have studied the kinetics of the reaction of suitably substituted alkyl bromides with the relatively weakly basic, but highly nucleophilic[13] reagent, sodium thiophenolate,[14] in absolute methanol solution. It was found that gas evolution occurred in none of the reactions, but to ensure that the reaction being studied was substitution, a substitution product, 1,2-bis-(phenylmercapto)-ethane, was isolated in 96% yield from the reaction with ethylene bromide, the halide thought most likely to give side reactions.[15]

Experimental

Apparatus.—Temperature was measured by a thermometer calibrated by the Bureau of Standards and is believed accurate within 0.03°. Kinetics at 20 and 34.6° were run in a Sargent constant temperature bath (Cat. No. S-84805) mounted in an insulated box with cooling water circulated through the coil when necessary. The bath temperature was observed to remain constant within 0.05°. Kinetics at 0° were run in a large dewar flask maintained full of a slurry of water and crushed ice covered with asbestos insulation and kept in a refrigerator at about 4° except when samples were being added or withdrawn. The temperature was found to remain within the range 0.0–0.1°.

Materials.—All of the alkyl bromides were fractionated through a $^1/_2$ inch column, 30 inches in length and packed with glass helices. Measurements of the refractive indices all agreed satisfactorily with values in the literature and were as follows: ethyl bromide, $n^{20}\mathrm{D}$ 1.4239; *n*-propyl bromide, $n^{15}\mathrm{D}$ 1.4370; *n*-butyl bromide, $n^{24.8}\mathrm{D}$ 1.4390; β-fluoroethyl bromide,[16] $n^{25}\mathrm{D}$ 1.4226; β-chloroethyl bromide, $n^{20.5}\mathrm{D}$ 1.4899; ethylene bromide, $n^{21.5}\mathrm{D}$ 1.5379. Methanol was dried by the method described by Fieser.[17] The thiophenol was found by iodometric titration to be 99.4% pure. Iodine solutions were standardized against arsenious oxide.

Kinetic Runs.—Standard solutions of sodium thiophenolate were prepared by weighing thiophenol into a volumetric flask under nitrogen, adding about a 2% excess of a standard solution of sodium methoxide and diluting to the mark with methanol. This assured that all of the thiophenol was present as the thiophenolate anion. The competing reaction of sodium methoxide with the alkyl halides was negligible because of its relatively small concentration and because it is much less reactive[18] than thiophenolate toward the halides used. Standard solutions of the alkyl bromides were also made up by weighing under nitrogen. The reactions were carried out in 100-ml. volumetric flasks whose necks and stoppers had been painted black. These flasks were immersed to about the middle of their necks in the constant temperature water-bath to which several bottles of black ink had been added to prevent any light-catalyzed reactions. The following procedure was used for the reactions studied at 20 and 34.6°. Into a nitrogen-filled reaction flask in the thermostatic bath were pipetted successive 15-ml. samples of the standard alkyl bromide and sodium thiophenolate solutions (both thermally equilibrated). The zero-time for the reaction was taken at the half-emptying of the thiophenolate pipet. The reaction was stopped at a given time by adding 2 ml. of glacial acetic acid to transform the thiophenolate ions into unreactive thiophenol.[19] The thiophenol concentration was then determined by titrating with a standard iodine solution until the yellow color of the iodine persisted.[20]

In the kinetic runs at 0°, the alkyl bromide was weighed into the 100-ml. volumetric flask and 50 ml. of methanol was added. When this solution had reached thermal equilibrium, 50 ml. of standard sodium thiophenolate solution and enough methanol (both at 0°) were added to bring the volume to exactly 100 ml. At various time intervals, 10-ml. samples were removed by pipet (while a slow stream of nitrogen was directed at the top of the reaction flask to prevent oxygen from entering), added to a flask containing 2 ml. of glacial acetic acid and titrated with standard iodine solution.

Reaction of Ethylene Iodide with Sodium Thiosulfate.—In a one-liter three-necked flask attached through a reflux condenser to a gas collection apparatus, 5.2 g. (0.0184 mole) of ethylene iodide, 250 ml. of absolute ethanol and 250 ml. of an aqueous solution of 20 g. (0.08 mole) of sodium thiosulfate pentahydrate were heated for five hours. The total volume of gas evolved (corrected for that displaced by the refluxing solvent) was 250 ml. (S.T.P.), a 60% yield. The collected gas was transformed to ethylene bromide (b.p. 130–134°) which was characterized by reaction with sodium thiophenolate to give 1,2-bis-(phenylmercapto)-ethane, m.p. 68–69°.[21]

Reaction of Ethylene Iodide with Sodium Thiophenolate.—The reaction of sodium thiophenolate with ethylene iodide in methanol also yielded considerable quantities of a gas which was assumed to be ethylene by analogy with the reaction of sodium thiosulfate.

Reaction of Ethylene Bromide with Sodium Thiophenolate.—Four hundred ninety ml. of a solution of 21.383 g. (0.1139 mole) of ethylene bromide, 39.354 g. (0.3572 mole) of thiophenol and 0.364 mole of sodium methoxide in methanol was kept at 35° for three days, diluted with aqueous sodium hydroxide solution, and the resultant precipitate filtered, washed with aqueous alkali and then with water (all under nitrogen). The resultant 1,2-bis-(phenylmercapto)-ethane melted at 68.5°,[21] and weighed 26.91 g. (96% yield). Oxidation of some of this material with hydrogen peroxide in glacial acetic acid yielded 1,2-bis-(phenylsulfonyl)-ethane, m.p. 180–181°, reported 179.5–180°.[22]

Results

Calculations.—For all of the compounds except ethylene bromide, rate constants were calculated from the integrated form of the second-order rate equation

$$k = \frac{2.303}{t(a - b)} \log \frac{b(a - x)}{a(b - x)}$$

where k is the rate constant, t the time in seconds, a

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(12) In addition to the data on reaction with thiosulfate ions, it is known that the reaction of ethylene iodide with sodium ethoxide or ammonium thiocyanate yields considerable ethylene [V. V. Korshak, K. K. Samplavskaya and N. M. Dovol'skaya, *J. Gen. Chem. U.S.S.R.*, **20**, 2153 (1950), (English translation)]. The reaction with iodide ion is well known to give ethylene [A. Slator, *J. Chem. Soc.*, **85**, 1697 (1904)] and we have found the reaction with sodium thiophenolate to give a similar result.

(13) O. R. Quayle and E. E. Royals, THIS JOURNAL, **64**, 1226 (1942); J. Hine, *ibid.*, **72**, 2438 (1950).

(14) This reagent has several advantages over the commonly used sodium thiosulfate. The latter yields Bunte salts which are rather susceptible to hydrolysis to sulfuric acid and mercaptans which interfere with the analytical method. The thiosulfate ion may also yield oxygen substitution products [P. M. Dunbar and L. P. Hammett, *ibid.*, **72**, 109 (1950)]. The divalent anion probably has greater tendencies to form ion-pairs.

(15) For the dibromides of olefins other than ethylene, some dehalogenation might occur, since B. G. Gavrilov and V. E. Tishchenko [*J. Gen. Chem. U.S.S.R.*, **18**, 1687 (1948); *C. A.*, **43**, 2569h (1949)], found that isobutylene dibromide gave 19.2% and 2,3-dibromobutane 8.6% olefin on reaction with sodium thiosulfate, although ethylene and propylene bromides gave none.

(16) Prepared by the method of F. W. Hoffmann, *J. Org. Chem.*, **14**, 105 (1949).

(17) L. F. Fieser, "Experiments in Organic Chemistry," 2nd Ed., D. C. Heath and Co., Inc., Boston, Mass., 1941, p. 359.

(18) The rate constant for the reaction of ethylene bromide with sodium thiophenolate at 30° is more than 25 times as large as that for sodium methoxide (J. Hine and W. H. Brader, unpublished work.)

(19) A spectrophotometric determination of pK_a for thiophenol in methanol solution, using the indicator brom cresol purple [pK_a in methanol 11.3, according to I. M. Kolthoff and L. S. Guss, THIS JOURNAL, **60**, 2516 (1938)], gave with 0.0242 N C_6H_5SNa and 0.0151 N C_6H_5SH the value 11.62 and with 0.0121 N C_6H_5SNa and 0.0492 N C_6H_5SH the value 11.61. From these data it may be shown that this addition of acetic acid reduces the concentration of the thiophenolate ion to a negligible value.

(20) P. Klason and T. Carlson, *Ber.*, **39**, 738 (1906).

(21) E. V. Bell and G. M. Bennett [*J. Chem. Soc.*, 3189 (1928)], report a melting point of 69° for this compound.

(22) R. Otto, *Ber.*, **13**, 1272 (1880).

and *b* the initial concentrations of the reactants and *x* the change in their concentration at time *t*. Initial concentrations ranged from 0.015 to 0.041 *M* for sodium thiophenolate and from 0.017 to 0.091 *M* for the alkyl bromides. Within these ranges no effect of concentration on the rate constants was detected. Since pertinent volumes were measured at the temperature at which the rates were studied and calculations made accordingly, no correction for solvent expansion is necessary for the rate constants recorded. For each compound, at each temperature, at least two independent runs with a total of at least nine points were made. Rate constants used are the average of those calculated from each of the individual points. Data on a typical run are shown in Table I. Most of the alkyl bromides were found to give satisfactory rate constants for at least 85% of the reaction. With ethylene chlorobromide a slight upward drift in the rate constants was noted when approximately equal concentrations of the reagents were used, but this could be avoided by use of a considerable excess of the halide. This drift, undoubtedly due to replacement of the second halogen atom, was so pronounced with ethylene bromide that the rate constants for this compound were obtained by plotting $\log b(a - x)/a(b - x)$ *versus* time on a large piece of graph paper and estimating the initial slope of the line by use of a tangent meter. The rate constants and average deviations for the six reactions studied are shown in Table II. The total rate constant for ethylene bromide is divided by two to give the rate constant *per bromine*.

TABLE I

REACTION OF ETHYLENE FLUOROBROMIDE WITH SODIUM THIOPHENOLATE IN METHANOL AT 0°

$[C_6H_5SNa]_0 = 0.03771$; $[FC_2H_4Br]_0 = 0.06360$

Time, sec.	0.02140 N I_2, ml.	$k \times 10^4$, sec.$^{-1}$ mole^{-1} l.
0	17.62	
75,420	14.68	0.401
167,160	11.91	.412
285,960	9.63	.393
344,460	8.47	.409
609,060	5.50	.406
	Av.	0.404 ± 0.006

TABLE II

RATE CONSTANTS FOR REACTION OF ALKYL BROMIDES WITH SODIUM THIOPHENOLATE IN METHANOL

	k (sec.$^{-1}$ mole^{-1} l.) $\times 10^4$			$\Delta H^{\ddagger}$,	$\Delta S^{\ddagger}$,
Alkyl	0°	20°	34.6°	kcal./mole	e.u./mole
HCH_2CH_2	3.79 ± 0.06	39.1 ± 0.6	182 ± 3	18.1	− 7.7
$CH_3CH_2CH_2$	2.56 ± .03	25.6 ± .3	112 ± 2	17.7	−10.0
$C_2H_5CH_2CH_2$	2.77 ± .03	26.9 ± .3	121 ± 1	17.7	−10.0
FCH_2CH_2	0.403 ± .006	4.95 ± .04	25.5 ± .2	19.4	− 7.3
$ClCH_2CH_2$	.486 ± .006	5.61 ± .03	28.5 ± .5	19.1	− 8.3
$BrCH_2CH_2$	.446 ± .010[a]	4.99 ± .15[a]	24.3 ± 1[a]	18.7	− 9.7

[a] This is the rate constant *per* bromine and is half of the total rate constant for ethylene bromide.

Heats and entropies of activation were calculated from the absolute rate equation[23]

$$k = \frac{\mathbf{k}T}{h} e^{-\Delta H^{\ddagger}/RT} e^{\Delta S^{\ddagger}/R}$$

by the method of least squares and are listed in Table II.

Except for ethylene bromide the average deviations of rate constants from the mean was in the vicinity of 1%. The corresponding values of $\Delta H^{\ddagger}$ are considered accurate within 0.3 kcal./mole and the values of $\Delta S^{\ddagger}$ within 0.7 e.u./mole. For ethylene bromide the corresponding errors are 3%, 0.7 kcal./mole and 1.5 e.u./mole.

Discussion.—From Table II it may be seen that β-fluorine, chlorine and bromine all cause a decrease (relative to hydrogen) in reactivity and that the magnitude of this decrease is very similar for the three halogens. The cause of the decrease varies, however, being entirely due to an increase in heat of activation for β-fluorine, while a less favorable activation entropy is important for β-bromine. It should be noted that the activation entropy decreases as the size of the β-group increases,[24] probably because of increased interference in rotation around the Cα–Cβ bond in the transition state. The heat of activation increases with the electron-withdrawing character of the β-group. These effects will be discussed in more detail in conjunction with experimental data on other types of substituted alkyl halides in a subsequent article.

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[23] S. Glasstone, K. J. Laidler and H. Eyring, "The Theory of Rate Processes," McGraw-Hill Book Co., Inc., New York, N. Y., 1941, p. 14.

[24] The deviation by β-fluorine is hardly beyond the experimental error.