energy due to steric hindrance, just as we have found. The entropy of activation values at 40° are −5 e.u. for the unhindered ring formation and +2 e.u. for the cyclization involving steric hindrance and the displacement of a substituent from a secondary carbon atom. Thus displacement of the substituent from the secondary carbon gives a slightly positive entropy of activation, as we have found, and the difference in entropy of activation involved in cyclization by attack at a secondary carbon compared to a primary is +7 e.u., which is in excellent agreement with our +6 e.u. difference for the cyclization of substituted alkylnitroguanidines.

The analogies between the thermodynamic quantities of activation for the cyclization of substituted alkylnitroguanidines and the cyclizations of both chloroalkyl phenyl sulfides and haloalkylamines, especially the latter, are evidence that the unimolecular S_N2 mechanism is common to all these reactions.

In general, it may be pointed out that the entropies of activation of the cyclizations of substituted alkylnitroguanidines do not differ much from zero, as is expected of a unimolecular reaction.

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[CONTRIBUTION FROM THE DEPARTMENT OF CHEMISTRY, PURDUE UNIVERSITY]

Rates of Reaction of Some Halogen-containing Esters with Potassium Iodide in Dry Acetone[1,2]

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The rates of reaction of ethyl bromoacetate, ethyl bromochloroacetate, ethyl bromofluoroacetate, ethyl α-bromopropanoate, ethyl chloroacetate and ethyl dibromoacetate at 20 and 0°, and of ethyl chlorofluoroacetate, ethyl dibromofluoroacetate and ethyl dichloroacetate at 40 and 20° with potassium iodide in dry acetone have been measured. The results show that inductive and steric effects are significant.

Alexander[3] and Royals[4] state that in S_N2 reactions, the effect of a second halogen atom on the reactivity of a halogen atom attached to the same carbon atom is twofold. First, due to the higher partial positive charge on the carbon atom, the approach of a negative ion is facilitated. Secondly, the size of the halogen atom itself would tend to shield the carbon atom from rearward attack. The higher partial positive charge on the carbon atom would tend to make a stronger carbon to halogen bond thus making it more difficult for this bond to be broken.[5] Since the van der Waals radii of fluorine and hydrogen are similar (1.35 Å. compared to 1.29 Å.[6]), it would be expected that polar effects become of greater relative importance when the second halogen is fluorine. There are, however, no data available in the literature for this type of reaction.[7]

In the present investigation, rates have been measured for the reaction of potassium iodide with a series of dihalo esters in which the second halogen was varied successively from fluorine to chlorine to bromine. The results (Table I) show that both inductive and steric effects are significant in the reaction. The great drop in reactivity from the bromo- to the bromofluoro ester and also of the dichloro- to the chlorofluoro ester must be explained almost entirely on the basis of an inductive effect. This observation shows that Reeve, McCaffery and Kaiser[8] probably understated inductive effects for this type of reaction when they claimed that polar effects are unimportant. The decreasing reactivity of ethyl bromochloro- and dibromoacetate indicate that steric effects are also important, since one would expect the reverse order of reactivities based on the inductive effect. It is also clearly shown that the steric effect of the methyl group in ethyl α-bromopropanoate greatly overshadows the inductive effect. If based on the inductive effect entirely, its rate would be faster than that of ethyl bromoacetate. To show that the measured rate of the reaction between ethyl bromofluoroacetate and

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(1) This paper represents part of a thesis submitted by D. L. Christman to the Graduate School of Purdue University in partial fulfillment of the requirements for the degree of Doctor of Philosophy. Ethyl Corporation Fellow, 1953–54.

(2) From a thesis submitted by R. W. Johnson, Jr., to the Graduate School, Purdue University in partial fulfillment of the requirements for the degree of Master of Science.

(3) E. R. Alexander, "Principles of Ionic Organic Reactions," John Wiley and Sons, Inc., New York, N. Y., 1950, pp. 88–89.

(4) E. E. Royals, "Advanced Organic Chemistry," Prentice-Hall, Inc., New York, N. Y., 1954, p. 291.

(5) Available data indicate that the steric effect is predominant. Thus, E. D. Hughes, *Trans. Faraday Soc.*, **37**, 625 (1941), found that methylene chloride reacts more slowly than methyl chloride with basic reagents, and H. A. C. McKay, THIS JOURNAL, **65**, 702 (1943), observed the same effect in a comparison of relative reactivities of methyl iodide and methylene iodide toward exchange with radioactive iodide ion. H. A. Smith and W. H. King, *ibid.*, **72**, 95 (1950), found from ethanolysis reactions that a chlorine atom on a double-bonded carbon in allyl chloride had little effect on the rate of reaction or energy of activation but that the rate decreased 100-fold, while the activation energy increased by nearly 6 kcal. per mole, when there was a second chlorine atom in the allylic position. P. Petrenko-Kritschenko and V. Okatzky, *Ber.*, **59B**, 2131 (1926), made similar observations regarding reactivities of a number of polyhalo methanes and ethanes compared with the monohalo compounds.

(6) L. Pauling, "The Nature of the Chemical Bond," Cornell University Press, Ithaca, N. Y., 1939, p. 189.

(7) The hydrolysis of benzodifluorochloride in 50% aqueous acetone studied by J. Hine and D. E. Lee, THIS JOURNAL, **74**, 3182 (1952), is an S_N1 reaction. J. Banus, H. J. Emeleus and R. N. Haszeldine, *J. Chem. Soc.*, 60 (1951), have shown that the exchange of radioactive iodide ion with the iodine atom of trifluoroiodomethane is first order with respect to organic iodide and zero order with respect to inorganic iodide and have explained this finding by an initial ionization of the trifluoromethyl iodide. J. E. Boggs, *Dissertation Abst.*, **14**, 591 (1954), recently determined the kinetics of exchange of isotopic chlorine between hydrogen chloride and methyl chloride, chlorofluoromethane, chlorodifluoromethane and chlorotrifluoromethane. However, these reactions are either first order or complex order in reactants.

(8) W. Reeve, E. L. McCaffery and T. E. Kaiser, THIS JOURNAL, **76**, 1858 (1954).

potassium iodide actually determines the replacement of bromine by iodine, an experiment was conducted in which the ethyl iodofluoroacetate was isolated in 72% yield.

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Experimental

Kinetic Measurements.—The titration method of Andrews[9] and Juvala[10] was used to follow the reactions of the halogen-containing esters with potassium iodide in acetone. The concentration of each ester with the exception of ethyl bromoacetate, ethyl dichloroacetate and ethyl chlorofluoroacetate was approximately 0.06 *M*. Due to the rapid rate of reaction of ethyl bromoacetate with potassium iodide, a concentration of approximately 0.006 *M* of this ester was used. On the other hand, a concentration of approximately 0.12 *M* ethyl dichloroacetate and 0.12 *M* ethyl chlorofluoroacetate was used due to their slow rate of reaction with potassium iodide. The concentration of potassium iodide was approximately 0.005 *M* for the reactions with ethyl bromoacetate, ethyl bromofluoroacetate and ethyl α-bromopropanoate at 20 and 0° and the reactions with ethyl bromochloroacetate at 20°. In the remainder of the experiments, the concentration of the potassium iodide was approximately 0.015 *M*. The temperatures were controlled to ±0.05°. The rates of reaction of potassium iodide with ethyl bromoacetate and ethyl α-bromopropanoate at 20 and 0° and with ethyl bromofluoroacetate and ethyl chloroacetate at 20° were followed by quenching the reaction mixtures at definite time periods. The remaining rates of reaction were followed by removing and quenching aliquot portions of the reaction mixture at desired periods. The data were plotted according to the form of the equation for a bimolecular reaction

$$kt = \frac{2.303}{(M - 1)b} \log_{10} \frac{M - Z}{M(1 - Z)}$$

where *M* is the initial molecular proportion of organic halide to inorganic halide, *b* is the initial concentration of potassium iodide and *Z* is the fraction of iodide which has reacted in time *t*. The values of the rate constants were obtained from linear plots of this equation using the method of least squares. The deviation from the mean value for each of the esters was never more than 4% and in nearly all cases was less than 2%. Due to the evident decomposition of the iodo ester formed, second-order kinetics were only followed to approximately 35% completion for each of the esters named: ethyl bromochloroacetate and ethyl α-bromopropanoate at 0°, ethyl dibromoacetate at 20 and 0°, ethyl dibromofluoroacetate and ethyl dichloroacetate at 40 and 20°. For the same reason, the rate with ethyl chlorofluoroacetate was only followed to 29% at 40° and 18% completion at 20°. All other rates were measured to at least 60% completion. Negative tests for fluoride ion were obtained in the hydrolyzed reaction mixtures of the fluorinated esters.

Table I

Rates of Reaction of Some Halogen-containing Esters with Potassium Iodide in Dry Acetone

Ester	Temp., °C.	k, l. mole^{-1} hr.$^{-1}$	E_a, kcal.
$CH_2BrCOOEt$	0	1920	11.5
$CH_2BrCOOEt$	20	8180	
$CHBrFCOOEt$	0	5.99	
$CHBrFCOOEt$	20	30.5	12.9
$CH_3CHBrCOOEt$	0	2.96	
$CH_3CHBrCOOEt$	20	27.8	17.8
$CH_2ClCOOEt$	0	1.36	
$CH_2ClCOOEt$	20	11.7[a]	17.1
$CHBrClCOOEt$	0	0.769	
$CHBrClCOOEt$	20	7.98	18.6
$CHBr_2COOEt$	0	0.332	
$CHBr_2COOEt$	20	4.02	19.8
$CBr_2FCOOEt$	20	0.230	
$CBr_2FCOOEt$	40	2.12	20.1
$CHCl_2COOEt$	20	0.068	
$CHCl_2COOEt$	40	.790	22.3
$CHClFCOOEt$	20	.011	
$CHClFCOOEt$	40	.227	27.5

[a] J. B. Conant and W. R. Kirner, This Journal, 46, 232 (1924), report a k value of 14.9 liter mole^{-1} hour^{-1} at 25°. The literature value was multiplied by 2.303.

Ethyl Bromofluoroacetate.—This ester was prepared by the series of reactions described by McBee, Pierce and Christman,[11] b.p. 68° (32 mm.), n^{20}_D 1.4275.

Ethyl Bromochloroacetate.—α,β-Dichlorovinyl ethyl ether, b.p. 123–126°, n^{20}_D 1.4540, was obtained in 71% yield by the method of Crompton and Vanderstichele.[12] Addition of bromine to the unsaturated ether, followed by hydrolysis of the resulting ether with water in the manner of Crompton and Triffitt,[13] gave a 64% yield of ethyl bromochloroacetate, b.p. 65° (12 mm.), n^{20}_D 1.4703.

Ethyl Iodofluoroacetate.—A solution of 27.8 g. (0.15 mole) of ethyl bromofluoroacetate in 20 ml. of dry acetone was added, with stirring, during 1 hr. to a solution of 49.8 g. (0.30 mole) of potassium iodide in 120 ml. of dry acetone at 25°. The flask was wrapped with aluminum foil, stirring was continued for 2 hr., and the mixture was allowed to stand at room temperature for 22 hr. The solution was filtered, concentrated *in vacuo* to 100 ml. and diluted with 60 ml. of benzene. The precipitate was filtered and washed with three 35-ml. portions of benzene. The combined benzene solutions were washed with two 30-ml. portions of water and dried over magnesium sulfate. The benzene was removed under reduced pressure and the residual liquid was distilled under reduced pressure to give 25 g. (72%) of ethyl iodofluoroacetate, b.p. 68–72° (14 mm.), n^{20}_D 1.4820 (lit.[14] b.p. 180° dec., 103° (30 mm.).

Anal. Calcd. for $C_4H_6FIO_2$: C, 20.70; H, 2.59; I, 54.72. Found: C, 21.00; H, 2.58; I, 54.39.

Ethyl dibromofluoroacetate was prepared by the method of Swarts[15] in 43% yield, b.p. 66–67° (10 mm.), n^{20}_D 1.4630, d^{20}_4 1.8860 (lit.[14] b.p. 171–173°).

Anal. Calcd. for $C_4H_5Br_2FO_2$: C, 18.20; H, 1.91; Br, 60.56; F, 7.20. Found: C, 18.35; H, 1.95; Br, 60.49; F, 7.23.

The physical constants of the esters used in these experiments are listed in Table II.

Table II

Physical Constants of Pure Compounds

Ester	B.p., °C.	Mm.	n^{20}_D
$CH_2BrCOOEt$	154	Atm.	1.4499
$CHBrFCOOEt$	68	32	1.4275
$CH_2ClCOOEt$	142	Atm.	1.4211
$CHBrClCOOEt$	66	12	1.4703
$CHBr_2COOEt$	65	5	1.4973
$CHCl_2COOEt$	73	30	1.4380
$CHClFCOOEt$	95.5	Atm.	1.3578
$CBr_2FCOOEt$	66–67	10	1.4630
$CH_3CHBrCOOEt$	52–53	12	1.4451

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(9) L. W. Andrews, This Journal, 25, 756 (1903).

(10) A. Juvala, *Ber.*, **63B**, 1989 (1930).

(11) E. T. McBee, O. R. Pierce and D. L. Christman, to be published.

(12) H. Crompton and P. L. Vanderstichele, *J. Chem. Soc.*, **117**, 691 (1920).

(13) H. Crompton and P. M. Triffitt, *ibid.*, **119**, 1874 (1921).

(14) F. Swarts, *Chem. Zentr.*, **74**, I, 13 (1903).

(15) F. Swarts, *Ber.*, **51**, 672 (1918).