[CONTRIBUTION FROM THE SCHOOL OF CHEMISTRY OF THE GEORGIA INSTITUTE OF TECHNOLOGY]

The Effect of Halogen Atoms on the Reactivity of Other Halogen Atoms in the Same Molecule. VII. The Reaction of β-Haloethyl Bromides with Sodium Hydroxide[1]

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The kinetics of the reactions of β-fluoroethyl bromide, β-chloroethyl bromide and β-bromoethyl bromide with sodium hydroxide in 50% aqueous dioxane have been investigated. Since the substitution reaction product (an ethylene halohydrin) is quite reactive toward alkali, while the elimination reaction product (a vinyl halide) is much less reactive, the relative extent to which the reaction of a given halide follows the two possible paths may be determined from the number of moles of base required to react with one mole of the β-haloethyl bromide. The β-bromo compound reacts about three times as fast as the β-chloro compound, both reactions being largely eliminations. The β-fluoro derivative reacts less than 4% as fast and its reaction is largely substitution. Heats and entropies of activation are calculated, and possible causes of the differing behavior of the β-halo substituents are discussed.

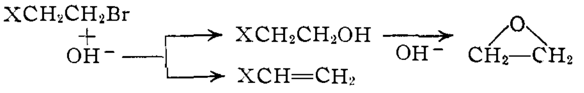
Introduction

A number of observations, including both product studies and kinetic data, show that β-chlorine and -bromine substituents increase the rate of alkaline dehydrohalogenation (E2) reactions.[2] Such data have led to generalizations that β-halogen substituents increase the E2 reactivity and that this increase in reactivity is largely due to the inductive effect of the β-halogen which makes the β-hydrogen atoms more acidic.[3]

Since there appeared to be no investigations reported that permit a direct comparison of the relative extents to which different β-halogen substituents affect E2 reactivity, we undertook to obtain such data. Since the completion of our experiments Goering and Espy have published a careful study of the dehydrohalogenation of some 1,1- and 1,2-dihalocyclohexanes.[4] They found that E2 reactivity was increased considerably by a β-chloro substituent and slightly more so by β-bromine. The α-chloro substituent, on the other hand, appeared to decrease the E2 reactivity and α-bromine definitely did so.

Results

We have compared only β-bromine, chlorine and fluorine substituents, since the β-iodo substituent is removed by nucleophilic attack at a rate comparable to that of β-hydrogen removal.[5] This comparison consisted of studying the kinetics of the reaction of the three β-haloethyl bromides with sodium hydroxide in aqueous dioxane solution. The reaction may follow either of two possible paths, substitution (SN2) or elimination.[2] By use



of the hydroxide ion it is relatively convenient to determine the extent to which the reaction has followed each of the two possible paths. This is because the substitution product, an ethylene halohydrin, is much more reactive toward hydroxide ion than is the starting ethylene halide while the elimination reaction product, a vinyl halide, is much less reactive. In fact, the data of Stevens, McCabe and Warner show that ethylene halohydrins may be treated as reactive intermediates whose concentrations never become comparable with those of the reactants and products under our reaction conditions.[6] Our own rough determinations of the rate constant for the reaction of vinyl bromide with base showed it to be much less reactive than any of the three β-haloethyl bromides. Vinyl chloride and vinyl fluoride should be considerably less reactive than vinyl bromide.

The over-all reaction rate will be

$$v = k_{E_2}[\mathrm{RBr}][\mathrm{OH^-}] + k_{S_{N_2}}[\mathrm{RBr}][\mathrm{OH^-}]$$

or if f is the fraction of the reaction which follows the SN2 path

$$\mathrm{d}x/\mathrm{d}t = k_2(a - x)[b - (1 + f)x] \qquad (1)$$

where $a = [\mathrm{RBr}]_0$, $b = [\mathrm{OH^-}]_0$, $x = \Delta\,[\mathrm{RX}]_t$, $k_2 f = k_{S_{N_2}}$, and $k_2(1 - f) = k_{E_2}$. Integration of equation 1 gives

$$k_2 = \frac{2.303}{t[b - (1 + f)a]} \log \frac{a[b - (1 + f)x]}{b(a - x)} \qquad (2)$$

The value of f could not be determined by permitting the reaction with excess alkali to go to completion, because of the slow reaction of the vinyl halide. Instead, f was calculated by a short extrapolation. The extrapolation was carried out by taking one point past 90% reaction (and yet early enough so that no appreciable reaction of vinyl halide should have occurred) and choosing, by suc-

TABLE I

KINETICS OF THE REACTION OF β-CHLOROETHYL BROMIDE WITH SODIUM HYDROXIDE IN 50% AQUEOUS DIOXANE AT 30°

$[\mathrm{NaOH}]_0 = 0.02503$; $[\mathrm{ClC_2H_4Br}]_0 = 0.01820$; $f = 0.028 \pm 0.028$

Time, sec.	Ml. 0.1090 N HCl/50 ml.	$10^4 k_2$, l. mole^{-1} sec.$^{-1}$
0	11.48	
72,360	8.90	2.258
108,780	8.02	2.291
159,180	7.15	2.276
209,580	6.50	2.262
271,080	5.90	2.250
447,300	4.78	2.271
	Av.	2.268 ± 0.011

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(1) For paper VI in this series see J. Hine, S. J. Ehrenson and W. H. Brader, Jr., THIS JOURNAL, **78**, 2282 (1956).

(2) For the significance of the terms E2 and SN2 see C. K. Ingold, "Structure and Mechanism in Organic Chemistry," Cornell University Press, Ithaca, N. Y., 1953, Chapters VIII and VII.

(3) *Cf.* Ingold, ref. 2, p. 446.

(4) H. L. Goering and H. H. Espy, THIS JOURNAL, **78**, 1454 (1956).

(5) J. Hine and W. H. Brader, Jr., *ibid.*, **75**, 3964 (1953), and references cited therein.

(6) J. E. Stevens, C. L. McCabe and J. C. Warner, *ibid.*, **70**, 2449 (1948); C. L. McCabe and J. C. Warner, *ibid.*, **70**, 4031 (1948).

TABLE II

KINETIC CONSTANTS FOR REACTION WITH SODIUM HYDROXIDE IN 50% AQUEOUS DIOXANE[a]

Compound		10^4k		$\Delta H^{\ddagger}$,	$\Delta S^{\ddagger}$,
		30.0°	70.0°	kcal.	e.u.
$BrCH_2CH_2Br$[b]	E2	3.17 ± 0.17	180 ± 10	20.2 ± 0.5	− 7.8 ± 1.7
	SN2	0.17 ± .17	10 ± 10	....	....
$ClCH_2CH_2Br$	E2	2.21 ± .06	122 ± 4	20.1 ± 0.3	− 9.0 ± 1.0
	SN2	0.06 ± .06	4 ± 4	....	....
FCH_2CH_2Br	E2	.050 ± .050[c]	0.94 ± 0.30	....	....
	SN2	.495 ± .050[c]	3.52 ± .35	21.1 ± 2.0	−13.2 ± 6.0
$CH_2{=}CHBr$		.0014 ± .0004	0.27 ± .05[d]	23.9 ± 3.0	−11.1 ± 10.0

[a] By volume. [b] The rate constants obtained have been divided by a statistical factor of two to give the rate constant *per bromine*. [c] At 50.1°. [d] At 75 ± 2°.

cessive approximation, the value of f that gives a value of k_2 for this point equal to the average of the values calculated from the earlier points. From k_2 and f, k_{SN2} and k_{E2} may be calculated. Data for a typical run are listed in Table I.

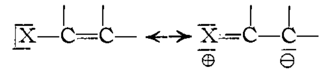
In Table II are listed all of the rate constants obtained and heats and entropies of activation calculated from the absolute rate equation[7]

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

Because of the generally observed greater reactivity of alkyl bromides compared to the corresponding chlorides and fluorides, it is assumed that the reactions of the compounds studied involve largely displacement of *bromine* in the rate-controlling step. It may be seen that β-bromoethyl bromide (1,2-dibromoethane) and β-chloroethyl bromide (1-bromo-2-chloroethane) reacted much faster than did β-fluoroethyl bromide (1-bromo-2-fluoroethane). The reactions of the former two compounds were so largely E2 that the value of k_{SN2} could not be determined with any reliability. The fluorobromide reacted largely by the SN2 mechanism. While it is clear that the β-bromine and -chlorine substituents encouraged E2 reactivity in comparison to β-fluorine, the evidence is insufficient to establish any differences in SN2 reactivity. It has been reported earlier that all three β-halogen substituents have about the same effect on SN2 reactivity toward the thiophenolate anion.[4]

Discussion

Ingold and co-workers have pointed out that the acidity of the β-hydrogen and the stability of the olefin being formed in the transition state are two important factors in determining reactivity in E2 reactions.[8] Schramm and Brown and co-workers have pointed out the importance of steric factors.[9] Our data seem explicable on the basis of the two factors suggested by Ingold. In our elimination reactions the nature of the halogen atom should, in two ways, affect the difference in stability between the starting saturated halide and the haloölefin produced. The olefin should be stabilized by the familiar resonance of the type



$$\overline{\underline{|X}}-\overset{|}{C}=\overset{|}{C}- \longleftrightarrow \underset{\oplus}{\overline{\underline{X}}}=\overset{|}{C}-\underset{\ominus}{\overset{|}{\underline{C}}}-$$

According to the usual estimate of the mesomeric effect, the extent of this stabilization should vary as follows[10]: F > Cl > Br > I. On the other hand, some of the stabilization of the reacting saturated halide, due to the electronegativity difference[11] between the β-carbon and β-halogen atoms, will be lost in the vinyl halide produced, since unsaturated carbon appears to be more electronegative than saturated carbon.[12] Since the extra energy of the bond between two atoms varies approximately with the *square* of the electronegativity difference,[13] the amount of stability lost will be greatest with a fluoride.[14] Thus the two principal factors that control olefin stabilization appear to operate in the opposite direction for halogen substituents. We are unable to estimate which factor should be more important *a priori* and are aware of no direct experimental data upon which such an estimate could be based. However, the observations of Goering and Espy,[4] that α-chloro and -bromo substituents do not have a large effect on the E2 reactivity of cyclohexyl halides, suggest that the two factors may be reasonably nearly balanced. It seems then that the strong activating influence of β-chlorine and -bromine must be due to their increasing the acidity of the β-hydrogen. Ingold has attributed this influence to the inductive effect of the halogens[3] and Goering and Espy agree with this appraisal, although they find β-bromine to activate slightly more than β-chlorine. They point out that chlorine and bromine have inductive effects of about the same size. Our observation that β-fluorine brings about a much lower level of E2 reactivity than β-chlorine or -bromine shows

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(7) 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.

(8) C. K. Ingold, ref. 2, sec. 31.

(9) C. H. Schramm, *Science*, **112**, 367 (1950); H. C. Brown and H. L. Berneis, THIS JOURNAL, **75**, 10 (1953); H. C. Brown and I. Moritani, *ibid.*, **75**, 4112 (1953); and earlier references cited therein.

(10) C. K. Ingold, ref. 2, p. 75.

(11) G. W. Wheland, "The Theory of Resonance and its Application to Organic Chemistry," 1st Ed., John Wiley and Sons, Inc., New York, N. Y., 1944, sec. 3–6.

(12) Reference 11, pp. 131, 176.

(13) Reference 11, equation on p. 84.

(14) To give an idea of how important this factor could be, it may be calculated[13] that if unsaturated carbon is 0.2 unit more electronegative than saturated carbon, a vinyl fluoride would lose 13 kcal./mole of resonance stabilization compared to the corresponding saturated fluoride, a vinyl chloride would lose 3.7 kcal., and a bromide 1.9 kcal. The fact that benzoquinuclidine is 2.86 *pK* units a weaker base than quinuclidine, at least largely because of the greater electronegativity of unsaturated carbon,[15] shows that 0.2 may not be an unreasonably large estimate of the added electronegativity of unsaturated carbon. Note that the *pK*'s of HOCl and HOBr and of HOBr and HOI differ by 1.4 and 1.8 *pK* units, respectively.

(15) B. M. Wepster, *Rec. trav. chim.*, **71**, 1171 (1952).

that the inductive effect is not controlling. While the data could be explained in other terms[16] it seems to us that the acidity of the β-hydrogen is indeed the important factor since the observed order of E2 activation, Br > Cl > F, is just that which has been found for the effect of the various halogens on the rates of the base-catalyzed deuterium exchange of haloforms.[18] Possible reasons why the various halogens have the observed effect on the acidity of hydrogen atoms attached to the same carbon will be discussed subsequently in connection with data on the deuterium exchange of haloforms.

Experimental

Apparatus and Materials.—The constant temperature baths used and the purification of the organic bromides employed have been described previously.[5] Dioxane was purified by the method described by Fieser.[19] The vinyl bromide was distilled before use and stabilized with diphenylamine.

Kinetic Runs.—In a typical run 50 ml. of a thermostated dioxane solution, 0.1800 M in β-chloroethyl bromide and 0.01 M in diphenylamine,[20] was added by pipet to a 500-ml. volumetric flask in which 200 ml. of dioxane and 250 ml. of a standard aqueous solution, 0.04950 N in carbonate-free sodium hydroxide, had been mixed and allowed to reach thermal equilibrium. The flask was immediately shaken and at various times 50-ml. samples were withdrawn and titrated immediately with standard hydrochloric acid to the phenolphthalein end-point. In the runs with ethylene bromide and β-chloroethyl bromide at 70°, the samples were added to excess acid to stop the reaction and the excess acid was then back-titrated. In the other runs the amount of reaction that took place between sample withdrawal and the completion of the titration was negligible. In the calculation of rate constants allowance was made for the deviation from strict volume additivity in mixtures of water and dioxane.

Experiments designed to check our determinations of f were not successful. Analysis for ethylene oxide was not satisfactory because ethylene oxide is hydrated to ethylene glycol at a rate comparable to our reaction rates.[21] Hydration of ethylene oxide to ethylene glycol and titration of ethylene glycol with periodic acid was found to be unsuccessful because of interference by bromide ion.

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[16] It seems unlikely, however, that the effect of β-halogens is due to differences in the relative stabilities of the rotational conformations. It must be the gauche conformation that undergoes the E2 reaction since only in this form is there a β-hydrogen atom *trans* to the bromine atom being displaced. Ethylene chloride has been shown to exist in the gauche form to a slightly larger extent than ethylene bromide under the same conditions.[17] From this fact we would expect the fractions of our halides in the reactive gauche form to vary in the order $FC_2H_4Br > ClC_2H_4Br > BrC_2H_4Br$ (the differences being small), the reverse of the observed order of E2 reactivities.

[17] S. Mizushima, Y. Morino, I. Watanabe, T. Simanouti and S. Yamaguchi, *J. Chem. Phys.*, **17**, 591 (1949).

[18] J. Hine, R. C. Peek, Jr., and B. D. Oakes, THIS JOURNAL, **76**, 827 (1954); J. Hine and N. W. Burske, *ibid.*, **78**, 3337 (1956); and unpublished data from this Laboratory.

[19] L. F. Fieser, "Experiments in Organic Chemistry," 2nd Ed., D. C. Heath and Co., Inc., New York, N. Y., 1941, part II, chap. III.

[20] In runs where no diphenylamine was used the rate constants climbed, apparently because of the dehydrohalogenation of polyvinyl halide.

[21] H. J. Lichtenstein and G. H. Twigg, *Trans. Faraday Soc.*, **44**, 905 (1948).

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[CONTRIBUTION FROM THE MCPHERSON CHEMICAL LABORATORY, THE OHIO STATE UNIVERSITY]

The Behavior of 3-Chlorophthalic Anhydride in Friedel–Crafts and Grignard Condensations

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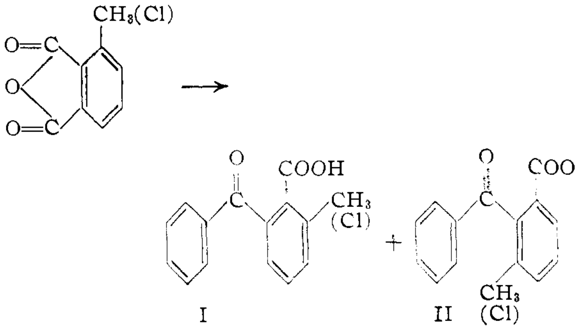
The reactions of 3-chlorophthalic anhydride with benzene, *m*-xylene and mesitylene (Friedel–Crafts) and with phenyl-, *m*-xylyl- and mesitylmagnesium bromides are summarized. Condensation at the internal (hindered) carbonyl group takes place exclusively with benzene and *m*-xylene and predominantly with mesitylene. However, in the Grignard reactions, condensation occurs mainly at the external (unhindered) carbonyl group. The results are contrasted to previous results obtained with 3-methylphthalic anhydride.

In previous studies on the behavior of 3-methylphthalic anhydride, the respective reactivity of the carbonyl groups in the 1- and 2-positions were evaluated in the Grignard and Friedel–Crafts reactions by estimation of the isomeric benzoylbenzoic acids formed.[2] Reactions were carried out with phenylmagnesium bromide, 2,4-dimethyl- and 2,4,6-trimethylphenyl-magnesium bromides and with benzene, *m*-xylene and mesitylene in the Friedel–Crafts reaction in order to see what effect on the ratio of isomers formed there would be when 0, 1 and 2 methyl groups were *ortho* to the position of condensation. Reaction at the unhindered carbonyl yields products of general structure I whereas reaction at the hindered carbonyl yields products of structure II. The results are summarized in Table I.



I II

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[1] Taken from the Ph.D. thesis of P.G.S., The Ohio State University, 1953.

[2] (a) M. S. Newman and C. D. McCleary, THIS JOURNAL, **63**, 1542 (1941); (b) M. S. Newman and C. W. Muth, *ibid.*, **72**, 5191 (1950).