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Kinetic Studies of Bimolecular Nucleophilic Substitution. IV.*[1] Rates of the S_N2 and E2 Reactions of β-Substituted Ethyl Chlorides with Sodium Acetate in Aqueous Solutions

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Rates in the S_N2 and E2 reactions of a series of β-substituted ethyl chloride (RCH_2CH_2Cl, R=Et, MeO, PhO, Cl, and H) in aqueous solutions have been measured at temperatures ranging from 90 to 150°C, using sodium acetate as a nucleophile. The mild rate-retarding effect of β-subtituents in the S_N2 reactions, observed in the rate order, H>Et>MeO>Cl>PhO, may be attributed to the steric effects. In a similar fashion, the retardation of E2 reaction rates by the β-substituents, which is in the rate sequence H>MeO>Et>PhO>Cl, may be ascribed to the steric effects, which outweigh the electronic effects. The β-substituent effects of several other substituents, which are known in the literature, have also been discussed.

In contrast to α-substituted alkyl halides, the S_N2 reactivities of β-substituted alkyl halides have been relatively little studied, particularly with repect to the substituent effects.[1-4] Similarly, although E2 reactions of alkyl halides have been extensively studied, the β-substituent effects on the E2 reactivity of ethyl halides have been subjected to little systematic scrutiny.[5-7]

We have measured the S_N2 and E2 reaction rates of several β-substituted ethyl chlorides in aqueous solutions in order to obtain additional data for systematic studies of β-substituent effects on the S_N2 and E2 reactivities. As a nucleophile, sodium acetate was chosen for the sake of simplicity in the measurement of the competitive S_N2 and E2 reactions, since, as has previously been reported,[8] the total rate for the competitive reactions can be followed by titrating the liberated chloride ions, whereas the rate of the E2 reaction can be estimated by titrating the hydrogen ions liberated in the course of the reactions.

Results and Discussion

The reaction of sodium acetate with a series of β-substituted ethyl chlorides, *i. e.*, RCH_2CH_2Cl (R=H, MeO, PhO, Cl, Et), was conducted in aqueous solutions, except for the reaction of β-phenoxyethyl chloride, which was carried out in 50 vol% aqueous ethanol. The total second-order rate constants, *i. e.*, $k_{S_N2}+k_{E2}$, have been calculated on the basis of the rate of chloride-ion liberation; the rate constants for the E2 reaction were obtained as the product of the total rate constant and the ratio of the concentration of the liberated hydrogen ions to that of the chloride ions.[8] The results of the rate measurements in the range between 90 and 150°C are tabulated in Table 1, together with the activation parameters derived.

β-Substituent Effect on the S_N2 Reactivity. The relative S_N2 rate constants of various β-substituted ethyl chlorides, summarized in Table 2, are useful for an examination of the β-substituent effects due to selected functional groups. The alkyl (Me, Et), phenyl, alkoxy (MeO, EtO), phenoxy and halogen (F, Cl, Br) groups were mildly rate-retarding (1/10 to 1/100), this being indicated in the rate order, H>Me>Et>Ph>MeO>Cl, F, Br>PhO.

The attachment of the alkyl substituent at the β-carbon atom is known to retard S_N2 reactions;[9] this deactivating effect is ascribed to either an electron-releasing inductive effect or a steric retardation effect. Although the precise description of the part played by each effect is still open to question,[9] conceivably the steric retardation is predominant in view of the fact that the inductive effect decreases rapidly through saturated carbon chains.

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*[1] Part III: K. Okamoto, T. Kita and H. Shingu, This Bulletin, **40**, 1908 (1967).

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[8] K. Okamoto, T. Kita and H. Shingu, This Bulletin, **40**, 1908 (1967).

[9] For a summary, see K. Okamoto, I. Nitta, T. Imoto and H. Shingu, *ibid.*, **40**, 1905 (1967).

TABLE 1. THE RATE CONSTANTS AND ACTIVATION PARAMETERS FOR S_N2 AND E2 REACTIONS OF 0.05 M β-SUBSTITUTED ETHYL CHLORIDE WITH 0.075 N SODIUM ACETATE IN AQUEOUS SOLUTION

RCH_2CH_2Cl R=		10^5k_2 (sec^{-1} M^{-1}) and E2 %					E_A kcal/mol	$\Delta S^{\neq}_{120°}$ e. u.
	Temp.	100°C	110°C	120°C	130°C	150°C		
H[a]	S_N2	48.4	121	235	—	—	20.9	−19.9
	E2	26.9	73.1	149	—	—	22.4	−16.2
	E2 %	35.8	37.7	38.7	—	—		
Et	S_N2	—	—	57.0	124	541	24.2	−14.2
	E2	—	—	15.0	30.3	119	22.9	−20.2
	E2 %	—	—	20.9	19.7	18.0		
Cl[b]	S_N2	2.35	—	9.80	—	—	20.8	−26.5
	E2	0.565	—	2.30	—	—	20.5	−25.8
	E2 %	19.4	—	19.0	—	—		
MeO	S_N2	3.07[d]	—	18.0	—	—	16.2	−36.0
	E2	1.73[d]	—	26.0	—	—	25.5	−13.3
	E2 %	36.1[d]	—	59.2	—	—		
PhO[c]	S_N2	—	—	5.62	—	33.3	19.5	−30.1
	E2	—	—	6.08	—	36.1	19.6	−30.5
	E2 %	—	—	52.0	—	52.0		

a) Initial concentrations of ethyl chloride were 0.026 M.
b) Rate constant per chlorine. See also experimental part.
c) The solvent was 50 vol% aqueous ethanol.
d) Rate constant measured at 90.0°C.

TABLE 2. S_N2 RATE CONSTANTS OF β-SUBSTITUTED ETHYL CHLORIDES (relative to ethyl derivatives as unity)

RCH_2CH_2X Nucleophile Solvent Temp.	X=Cl NaOAc H_2O 120°C	X=Cl[8] NaOAc 50% aq. Actone 120°C	X=Cl[1] KI Acetone 75°C	X=Br[2] NaSPh MeOH 20°C	X=Cl[3] H_2O aq. Dioxane (H_2O, 20 M) 100°C	X=OTs[4] EtOH EtOH 100°C
R=H	1.00	1.00	1.00[c]	1.00	1.00[c]	1.00
Me	—	0.63	—	0.66	0.48	—
Et	0.38	0.44	0.55	0.69	0.60	—
Ph	—	0.36	—	—	—	0.26[e]
MeO	0.12	—	—	—	—	—
EtO	—	—	—	—	0.48	0.18
PhO	0.038[a]	—	—	—	0.056	—
F	—	—	—	0.13	—	—
Cl	0.065[b]	—	—	0.14	—	—
Br	—	—	—	0.13[b]	—	—
MeCO	—	—	3.82	—	—	—
PhCO	—	—	24.0	—	—	—
EtOCO	—	—	0.88	—	—	—
EtS	—	—	—	—	1700[d]	—
EtSO	—	—	—	—	0.18	—
$EtSO_2$	—	—	—	—	0.54	—
PhS	—	—	0.43	—	55	—
PhSO	—	—	1.48	—	—	—
$PhSO_2$	—	—	0.21	—	0.84	—
NC	—	—	1.53	—	—	0.059

a) In 50% aqueous ethanol. b) Rate constant per halogen.
c) Estimated from the rate constant for *n*-butyl chloride.
d) Intramolecular S_N2 reaction. e) At 75°C.

On the other hand, the inductive effects of electron-withdrawing substituents with positive σ^* values,10) such as alkoxy, phenoxy and halogen, may be said to be rate-accelerating.11) However, the observed rate sequence shows a predominance of rate retardation by these substituents. This indicates that the inductive effects for electron-withdrawing are overshadowed by the presence of large steric retardation due to these substituents at the β-position of ethyl chloride. Thus plots of the relative rates (in a logrithmic scale) against the Taft σ^* value, *i. e.*, a measure of the inductive effects, give no linear correlation; this is illustrated in Fig. 1. A trial of Taft's E_s treatment10) for the correlation of the steric factor was not successful; this indicates that the steric factor in S_N2 reactions is substantially different in nature from that in carbonyl reactions, on which Taft's E_s values are based.

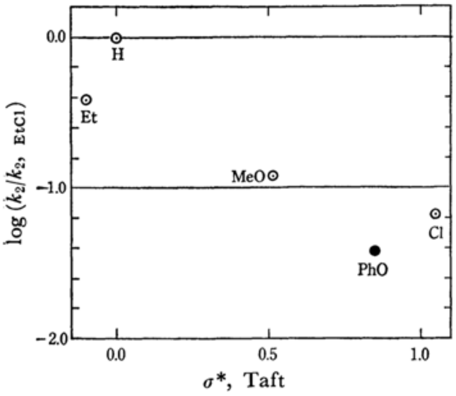

Fig. 1. S_N2 reactions of β-substituted ethyl chloride in aqueous solution at 120°C.
(solid circle: in 50% aqueous ethanol)

Concerning the β-substituent effects due to the substituents containing carbonyl (MeCO, PhCO, EtOCO), sulfur (EtS, EtSO, $EtSO_2$, PhS, PhSO, $PhSO_2$), and CN, all these groups have rate-enhancing electronic effects, as has been extensively studied by Bordwell and Brannen.1) The observed rate retardation by ErOCO, EtSO, $EtSO_2$, PhS, and $PhSO_2$ groups, therefore, may be ascribed to the steric origin of these substituents. The balance between the steric rate retardation and the electronic acceleration in thiophenoxy and cyano substituents seems to depend on the nature of the attacking nucleophile. In the case of a thiophenoxy substituent, an ionic nucleophile (*i. e.*, I^-) reacts slower than with ethyl chloride, while a dipolar nucleophile (*i. e.*, H_2O) reacts faster. For a β-cyano substituent, a reversal of this situation was observed (see Table 2).

The acceleration by a β-PhS substituent may be ascribed to the partial presence of the intramolecular S_N2 reaction, as has been suggested in the case of a β-EtS group.12) Although a complete interpretation of the acceleration by a β-cyano substituent must await future studies, it is conceivable that there exists a sort of field effect between the cyano group and an ionic nucleophile with a large polarizability, as has been suggested for the acceleration by an α-carbonyl substituent in the S_N2 reaction.1,13)

β-Substituent Effect on the E2 Reactivity. The E2 rate constants, relative to ethyl chloride as unity, for various β-substituted ethyl chlorides are summarized in Table 3.

TABLE 3. E2 RATE CONSTANTS OF β-SUBSTITUTED ETHYL CHLORIDE
(relative to ethyl derivatives as unity)

RCH_2CH_2X	$X=Cl$	$X=Cl$ 8)	$X=Br$ 6)	$X=Br$ 5)	$X=N^+Me_3$ 7)	$X=S^+Me_2$ 7)
Nucleophile	NaOAc	NaOAc	NaOEt	NaOH	OEt^-	OEt^-
Solvent	H_2O	50% aq. Acetone	EtOH	50% aq. Dioxane	EtOH	EtOH
Temp.	120°C	120°C	55°C	70°C	64°C	101°C
R=H	1.00	1.00	1.00	—	1.00	1.00
Me	—	0.84	3.31	—	0.07	0.38
Et	0.10	0.56	2.69	—	0.04	0.27
Ph	—	0.25	350	—	—	—
MeO	0.175	—	—	—	—	—
PhO	0.041a)	—	—	—	—	—
F	—	—	—	0.052c)	—	—
Cl	0.015b)	—	—	0.68c)	—	—
Br	—	—	—	1.00b,c)	—	—

a) In 50% aqueous ethanol.
b) Rate constant per halogen.
c) Relative to 1,2-dibromoethane as unity.

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10) R. W. Taft, Jr., in "Steric Effects in Organic Chemistry," ed. by M. S. Newman, John Wiley and Sons, New York (1956), Chap. 13.

11) E. D. Hughes, *Trans. Faraday Soc.*, **37**, 603 (1941).

12) For a summary, see A. Streitwieser, Jr., *Chem. Revs.*, **56**, 571 (1956).

13) For a summary, see C. A. Bunton, "Nucleophilic substitution at Saturated Carbon Atom," Elsevier, Amsterdam (1963), pp. 36—38.

In the E2 reactions with sodium acetate, the alkyl (Me, Et), phenyl, methoxy, phenoxy, and halogen substituents mildly (1/10 to 1/100) diminish the E2 reactivity of ethyl chloride. As has previously been pointed out,[8] this reactivity sequence for the alkyl and phenyl groups is in agreement with the Hofmann rule and is in marked contrast to the E2 reactivity of a series of alkyl bromides with sodium ethoxide,[6] which is controlled by the Saytzeff pattern of structural effects. This retardation by alkyl and phenyl groups may be ascribed to their steric effects, which traverse their electronic effects, such as inductive and electromeric effects.

In a similar fashion, the rate retardation by MeO, PhO, and Cl groups in the E2 reactions with sodium acetate may be explained by their steric effects, although their electromeric effects might partially deactivate the E2 reactivity of β-hydrogen in ethyl chloride. The retardation by a β-chloro substituent is also in contrast to the general view that β-halogen substituents increase the E2 reactivity, largely by their inductive effect.[14]

From these results it is clear that, in the E2 reactions of alkyl halides, the nature of the nucleophilic reagent can change the reactivity sequence, *e. g.*, from the Saytzeff to the Hofmann pattern of structural effects. This probably indicates that the nature of the transition state of the E2 reaction is not single but changeable, as has been pointed out by Bunnett,[15] or that the E2 reaction mechanism should be divided into subordinate mechanisms which afford a clear interpretation of the variation in the pattern of structural effects. This reconsideration of the E2 mechanism remains as a problem for future.

Experimental

Materials. β-Methoxyethyl chloride, bp 90.0—91.0°C (lit. bp 93°C[16]), was prepared from dimethylsulfate and ethylene chlorohydrin according to the method of Jones and Powers.[16] β-Phenoxyethyl chloride, bp 121—122°C/25 mmHg (lit. bp 122.3°C/26 mmHg[17]), was prepared by stirring a mixture of aqueous sodium phenoxide and an excess of 1, 2-dichloroethane for 10 hr at 90°C. Ethyl chloride (bp 12.0°C), *n*-butyl chloride (bp 78.0°C), 1, 2-dichloroethane (bp 83.0°C), and ethyl acetate (bp 77.0°C) were purified by fractional distillation of reagent-grade chemicals.

A stock solution of ethyl chloride in water was prepared by leading gaseous ethyl chloride from the ampoule into the solvent; after appropriate dilution with water, it was used for kinetic runs. Ethanol was purified according to the method of Fieser[18] by refluxing it over magnesium turnings. Sodium acetate was dried *in vacuo* to a constant weight at 110°C.

Kinetic Measurements. A sealed ampoule technique was employed; in each ampoule 5 cc of the reaction mixture was placed. At intervals the ampoule was removed from the bath (maintained at an appropriate temperature (±0.05°C)), and then cooled in ice water. From the ampoule two 2-cc aliquots were removed. The first aliquot was titrated with standard aqueous silver nitrate, using potassium chromate as an indicator; the second was titrated with standard aqueous potassium hydroxide, using bromothymol blue as an indicator. The rate data were treated as has been described above. The titrimetric rate constant was nicely second-order for each run. A simple kinetic data for a representative run is shown in Table 4. In order to estimate the rate of the hydrolysis of ethyl acetate (*i. e.*, a reaction product from ethyl chloride and sodium acetate) a control experiment was carried out in an aqueous solution at 120°C. It was found that the rate was negligibly small (*i. e.*, 1.2×10^{-5} (sec^{-1}), calculated as the first-order rate constant) compared to the total rate of the reaction of ethyl chloride with sodium acetate.

Table 4. Simple kinetic data for the S_N2 and E2 reactions of 0.0257 M ethyl chloride with 0.07157 N sodium acetate in aqueous solution at 110±0.05°C

Time min	Titer[a] $AgNO_3$ cc	Titer[b] KOH cc	E2%	10^3k_2 sec^{-1} M^{-1}
0	0.00	0.00	—	—
18	0.152	0.063	36.45	2.03
25	0.200	0.085	37.4	1.99
33	0.253	0.105	36.5	2.00
41	0.300	0.127	37.25	1.95
51	0.350	0.151	38.0	1.92
61	0.403	0.173	38.0	1.92
73	0.450	0.196	38.35	2.01
86	0.500	0.217	38.25	1.90
115	0.600	0.255	37.35	1.90
161	0.701	0.290	36.45	1.82
222	0.798	0.320	36.45	(1.77)
∞	1.082	—	—	—
		Average:	37.7	1.94±0.04

a) Concentration of $AgNO_3$ was 0.04709 N.
b) Concentration of KOH was 0.04131 N.
c) [(Titer KOH)/(Titer $AgNO_3$)]×100

In the case of the reaction of 1, 2-dichloroethane with sodium acetate, the total rate was treated as $k_{E2}+2k_{S_N2}$ instead of as $k_{E2}+k_{S_N2}$, on the assumption that 1, 2-dichloroethane produces two equivalents of chloride ions in its S_N2 reaction. The measurements of the k_{S_N2} and k_{E2} of this compound by another method gave almost the same values as were obtained by the treatment described above; this will be reported on in the succeeding paper.[19]

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