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Kinetic Studies of Bimolecular Nucleophilic Substitution. III.*1 Rates of S_N2 and E2 Reactions of ω-Chloroalkylbenzenes with Sodium Acetate in 50 vol% Aqueous Acetone—Alternation Effects in Saturated Carbon Chains

Kunio OKAMOTO, Teruo KITA and Haruo SHINGU

Department of Hydrocarbon Chemistry, Faculty of Engineering, Kyoto University, Sakyo-ku, Kyoto

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The rate of the bimolecular reactions of a series of ω-chloroalkylbenzenes, $C_6H_5(CH_2)_nCl$ ($n=1-4$), with sodium acetate have been measured in 50 vol% aqueous acetone in the range from 100 to 130°C. The second-order rate constants, k_2, have been obtained by measuring the rate of chloride-ion liberation. From the k_2 values, *i. e.*, $k_{S_N2}+k_{E2}$, and the olefin percentage in the products, which was determined by measuring the rate of acetic acid formation, the S_N2 rate constant, k_{S_N2}, and the E2 rate constant, k_{E2}, for each chloride have been calculated. For purposes of comparison, the k_{S_N2} and k_{E2} values for n-alkyl chlorides, $C_nH_{2n+1}Cl$ ($n=1-4$), in the same solvent at 120°C have been calculated by a similar treatment of the rate in the bimolecular reactions of titled chlorides with sodium acetate. There is an alternation effect on the S_N2-rate sequence of the ω-chloroalkylbenzenes, whereas no alternation effect has been observed for the E2 reactions of ω-chloroalkylbenzenes or for the S_N2 and the E2 reactions of n-alkyl chlorides. From an examination of these data, together with the results previously reported in the literature, the zigzagging of the rate sequence in the S_N2 reactions of ω-substituted alkyl halides has been thought most probably to originate from steric effects. In contrast to the previous observation in the E2 reactions of alkyl bromides with sodium ethoxide, the rate sequence for alkyl chlorides with sodium acetate has been found to be governed by the Hofmann rule.

Within the last few decades, there have been several publications1-6) concerning alternation effects on the bimolecular nucleophilic substitutions of homologous series of ω-substituted alkyl halides. In these kinetic sutdies, the reaction of potassium iodide in acetone has been most commonly used because it offers the advantages of wide applicability and relative freedom from side reactions, *e. g.*, the E2 reaction. It was our purpose to examine some nucleophiles other than the iodide ion; we expected these to offer additional examples of the alternation effect, and also to make it possible to observe the reactivity in the concomittant E2 reactions. As one of those nucleophiles, we chose sodium acetate because of its relatively low basicity, *i. e.*, its low reactivity in the E2 reaction, and because of the simplicity with which both S_N2 and E2 reaction rates could be measured. ω-Chloroalkylbenzenes were used as the compounds typical of the substrates which show alternation phenomena in their S_N2 reactions.

Results and Discussion

The rate measurements of a series of ω-chloroalkylbenzenes, *i. e.*, $C_6H_5(CH_2)_nCl$ ($n=1$—4), were carried out in 50 vol% aqueous acetone in the range from 100 to 130°C by a sealed ampoule method. At appropriate intervals, aliquots, in removed ampoules, were first titrated with sodium hydroxide for the liberated acetic acid, and then by the Mohr method for chloride ions. The latter titration data were interpreted by the standard second-order kinetic equation:

$$k_2=\frac{1}{t(b-a)}\ln\frac{a(b-x)}{b(a-x)} \qquad (1)$$

where a is the initial concentration of the chlorides, b is the initial concentration of sodium acetate, and x is the instantaneous concentration of chloride ions at time t.

In these reaction conditions, the S_N2 and the E2 reactions compete with each other, and both the reactions should obey the second-order kinetics. Therefore, we can divide the observed second-order rate constant, k_2, into two parts, *i. e.*, k_{S_N2} and k_{E2} (see Eq. (2)):

$$k_2 = k_{S_N2} + k_{E2} \qquad (2)$$

Throughout the reaction, the ratio of the E2 reaction product, *i. e.*, an olefin, to the S_N2 reaction product, *i. e.*, an acetate, should be expressed by Eq. (3):

$$(k_{E2}/k_{S_N2}) = (\text{Olefin})/(\text{Acetate}) \qquad (3)$$

The amount of the olefin so formed can be measured by the amount of acetic acid liberated during the reaction, according to the following equation:

$$\text{R-CH}_2\text{-CH}_2\text{-Cl} + \text{NaOAc} \rightarrow$$
$$\text{R-CH=CH}_2 + \text{HOAc} + \text{NaCl}$$

Thus we can calculate the rate constants for each reaction by using Eqs. (4) and (2′):

$$k_{E2} = k_2 \times \frac{(\text{HOAc})}{(\text{Cl}^-)} \qquad (4)$$

$$k_{S_N2} = k_2 - k_{E2} \qquad (2')$$

For purposes of comparison, the rate measurements were conducted in 50 vol% aqueous acetone at 120°C for a series of alkyl chlorides, $C_nH_{2n+1}+Cl$ ($n=1$—4), with sodium acetate, and in a similar fashion,the k_{S_N2} and the k_{E2} values were obtained for each chloride.

During the reaction of benzyl chloride a concomittant hydrolysis of this chloride was found to proceed competitively with the S_N2 reaction of the acetate. In this case the rate data were treated according to the method of Hughes, Ingold and Shapiro[7] on the basis of the asumption that the total reaction is composed of competitive first- and second-order reactions.

The results of the rate measurements are tabulated in Table 2 for ω-chloroalkylbenzenes and in Table 3 for *n*-alkyl chlorides. A representative simple kinetic result is shown in Table 1.

As expected, the S_N2 rates of ω-chloroalkylbenzenes showed a "zigzagging" from the odd to

TABLE 1. SIMPLE KINETIC DATA OF S_N2 AND E2 REACTIONS OF 0.0369 M γ-CHLOROPROPYLBENZENE WITH 0.07535 N SODIUM ACETATE IN 50 vol%[a] AQUEOUS ACETONE AT 110±0.05°C

Time min	Titer[b] $AgNO_3$ cc	Titer[c] NaOH cc	E2%[d]	10^4k_2 $sec^{-1}\,M^{-1}$
0	0.260	0.150	—	—
83	0.523	0.230	28.2	2.18
120	0.591	0.260	30.8	1.92
160	0.675	0.285	30.1	1.79
200	0.770	0.310	29.1	1.86
247	0.870	0.340	28.9	1.89
280	0.928	0.356	28.6	1.81
320	1.010	0.380	28.4	1.81
∞	3.778	—	—	—
		Average:	29.2±0.3	1.89±0.03
			26.9±0.8[e]	1.91±0.02[e]

a) Composition based on volumes of pure components at 25°C before mixing.
b) Concentration of $AgNO_3$ was 0.04885 N.
c) Concentration of NaOH was 0.04526 N.
d) [(Titer NaOH)/(Titer $AgNO_3$)]×100.
e) For the duplicate run.

[*1] Part II: K. Okamoto, I. Nitta, T. Imoto and H. Shingu, This Bulletin, **40**, 1905 (1967).

1) J. B. Conant and W. R. Kirner, *J. Am. Chem. Soc.*, **46**, 232 (1924).

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TABLE 2. SECOND-ORDER RATE CONSTANTS AND ACTIVATION PARAMETERS FOR REACTION OF SODIUM ACETATE[a] WITH ω-CHLOROALKYLBENZENES IN 50 vol%[b] AQUEOUS ACETONE

Substrate $C_6H_5(CH_2)_nCl$ $n=$	Initial concentration, M	Reaction	10^4k_2[c] $\sec^{-1}$ M^{-1} 110°C	120°C	130°C	E_A kcal/mol	$\Delta S^{\ddagger}$ 120° e. u.
1	0.0530	S_N2	792[d]	1310		16.9	−26.7
2	0.0390	S_N2	0.681	1.37	3.02	22.9	−20.4
		E2	0.440	0.883	1.92	22.7	−21.7
		(E2 %)[e]	(39.2)	(39.1)	(38.9)		
3	0.0369	S_N2	1.37	2.68	4.52	18.4	−30.8
		E2	0.532	1.22	2.36	22.9	−20.8
		(E2 %)	(28.0)	(31.3)	(34.3)		
4	0.0270	S_N2	1.12	2.29	4.29	20.6	−25.4
		E2	0.748	1.87	3.54	23.9	−17.4
		(E2 %)	(40.0)	(45.0)	(45.2)		

a) Initial concentrations of sodium acetate were 0.0750—0.0754 N.
b) Composition based on volumes of pure components at 25°C before mixing.
c) The average values for the two runs.
d) The second-order rate constant of S_N2 reaction at 100°C was 4.13×10^{-3} ($\sec^{-1}$ M^{-1}).
e) See Table 1.

TABLE 3. SECOND-ORDER RATE CONSTANTS FOR REACTION OF SODIUM ACETATE[a] WITH n-ALKYL CHLORIDES IN 50 vol%[b] AQUEOUS ACETONE AT 120.0±0.05°C

Substrate	Initial concn. M	Reaction	10^4k_2[b] $\sec^{-1}$ M^{-1}	E2%[d]
MeCl	0.0220	S_N2	16.0	—
EtCl	0.0190	S_N2	3.77	48.0
		E2	3.48	
n-PrCl	0.0360	S_N2	2.35	55.4
		E2	2.92	
n-BuCl	0.0450	S_N2	1.68	53.6
		E2	1.94	

a) Initial concentration was 0.0760 N.
b) Composition based on volumes of pure components at 25°C before mixing.
c) The average values for the two runs.
d) See Table 1.

the even members of the series (see Fig. 1), whereas those of n-alkyl chlorides decreased continuously from methyl chloride to n-butyl chloride (Fig. 1).

These results reconfirm the qualitatively-known reactivity sequence of ω-chloroalkylbenzenes and of n-alkyl chlorides toward various nucleophiles. In Tables 4 and 5, the S_N2 rate constants of homologous series of halides are summarised; the S_N2 reactions with alternation effects[1-6] are indicated in the former, and those without alternation effects,[6,8-13] in the latter.

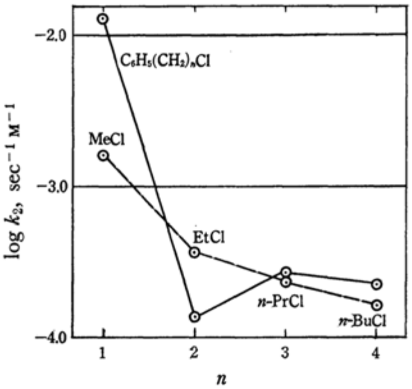

Fig. 1. Second-order rate constants for the S_N2 reaction of various alkyl chlorides with sodium acetate in 50 vol% aqueous acetone at 120°C.

In the activation energies for the S_N2 reactions of the ω-chloroalkylbenzenes with sodium acetate, there is also an alternation effect; this is reflected in a "zigzagging" of the rates. However, this does not simply mean that the alternation effect is electronic in origin, since, as Eliel[14] has pointed out, an electronic effect such as second-order hyperconjuation[15] can not be the basis of such an explanation in view of there being found no alternation in S_N1-type reactions such as the reaction of

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TABLE 4. ALTERNATION EFFECTS IN S_N2 REACTIONS OF HOMOLOGOUS SERIES OF HALIDES
(Relative rates to n-butyl halide as unity)

Substrate	Nucleophiles	$n=1$	2	3	4	5	6	7	Ref.
$C_6H_5C{\equiv}C(CH_2)_nCl$ (Acetone, 60.0°C)	KI	782	0.48	1.9	—	—	—	—	5
$C_6H_5(CH_2)_nCl$ (Acetone, 50.0°C)	KI	195	1.12	1.72	1.49	1.42	1.46	1.40	1
$CH_2{=}CH(CH_2)_nCl$ (Acetone, 15.0°C)	KI	68.1	3.35	3.49	—	—	—	—	4
$CH_2{=}CH(CH_2)_nBr$ (Acetone, 15.0°C)	KI	64	0.319	0.415	—	—	—	—	4
$EtOCO(CH_2)_nCl$ (Acetone, 50.0°C)	KI	2800	1.61	1.65	1.35	—	—	—	1
$C_6H_5O(CH_2)_nCl$ (Acetone, 50.0°C)	KI	—	0.30	1.67	1.37	—	—	—	3
$C_6H_5S(CH_2)_nCl$ (Acetone, 75.0°C)	KI	540	0.79	3.1	1.8	1.4	—	—	6
$C_6H_5COO(CH_2)_nCl$ (Acetone, 50.0°C)	KI	59.1	0.45	1.57	—	—	—	—	3
$CH_3COO(CH_2)_nCl$ (Acetone, 50.0°C)	KI	270	0.45	39.3	—	—	—	—	2
$NC(CH_2)_nCl$ (Acetone, 75.0°C)	KI	3000	2.8	3.7	2.8	—	—	—	6
$C_6H_5SO(CH_2)_nCl$ (Acetone, 75.0°C)	KI	0.25	2.7	2.6	3.3	2.6	—	—	6
$C_6H_5(CH_2)_nCl$ (50% aq. Acetone, 120.0°C)	NaOAc	79.2	0.82	1.65	1.31	—	—	—	This paper

TABLE 5. S_N2 RATE CONSTANTS OF HOMOLOGOUS SERIES OF HALIDES WITHOUT ALTERNATION EFFECTS
(Relative to n-butyl halide as unity)

Substrate	Nucleophiles	$n=1$	2	3	4	5	6	7	8	Ref.
$C_nH_{2n+1}Cl$ (Acetone, 50.0°C)	KI	—	2.52	1.08	1.00	1.35	1.30	1.25	1.35	8
$C_nH_{2n+1}Cl$ (50% aq. Acetone, 120°C)	NaOAc	9.53	2.24	1.40	1.00	—	—	—	—	This paper
$C_nH_{2n+1}Br$ (EtOH, 55°C)	NaOEt	87	4.35	1.38	1.00	0.90	—	—	—	9
$C_nH_{2n+1}Br$ (MeOH, 80.0°C)	NaOMe	24.2	2.70	1.00	1.00	—	—	—	—	10
$C_nH_{2n+1}Br$ (MeOH, 80.0°C)	NaOPh	9.20	2.00	0.92	1.00	—	—	—	—	10
$C_nH_{2n+1}Br$ (95% aq. EtOH, 25.0°C)	NaSCN	—	1.46	1.01	1.00	1.05	1.07	1.09	1.11	11
$C_nH_{2n+1}Br$ (MeOH, 80.0°C)	Di-Me-Aniline	42.6	1.96	0.96	1.00	—	—	—	—	11
$C_nH_{2n+1}I$ (EtOH, 42.5°C)	NaOPh	12.5	2.78	1.07	1.00	—	—	—	—	12
$C_nH_{2n+1}I$ (Acetone, 35°C)	$(n\text{-Bu})_3P$	456	3.71	1.12	1.00	—	—	—	—	13
$C_6H_5CO(CH_2)_nCl$ (Acetone, 75.0°C)	KI	32000	44.0	2.1	1.7	—	—	—	—	6
$CH_3CO(CH_2)_nCl$ (Acetone, 75.0°C)	KI	35000	7.0	1.4	—	—	—	—	—	6
$C_6H_5SO_2(CH_2)_nCl$ (Acetone, 75.0°C)	KI	0.02	0.38	3.6	3.8	—	—	—	—	6

ω-bromoalkylbenzenes with mercuric nitrate.[16]

As has been shown in Fig. 1, the S_N2 rate of β-phenylethyl chloride is substantially smaller than that of ethyl chloride in 50 vol% aqueous acetone at 120°C. This indicates that the steric retardation of the β-phenyl group outweighs its electronic acceleration, whereas this acceleration is predominant in the benzyl system, as is observed in the sequence: benzyl>methyl (Fig. 1).

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Although no complete explanation for a "zigzagging" in the S_N2-rate sequence has yet been advanced, the presence of such terminal groups in saturated carbon chains as phenylethinyl, phenyl, vinyl, carbethoxy, phenoxy, thiophenoxy, benzoxy, acetoxy, cyano and phenylsulfoxy groups (see Table 4) seems to be a necessary factor for the alternation phenomena. Furthermore, as has been pointed out by Eliel,[14] it is most likely that this effect is steric in origin. However, this seems to be specific for the individual functional group, since the similar functional groups[6] in the ω-position, such as benzoyl, acetyl and benzenesulfonyl groups (see Table 5), cause no alternation in S_N2 reactivity sequences.

In the rate sequence of the E2 elimination reaction of ω-chloroalkylbenzenes with sodium acetate, there is no alternation effect, but a "continuous" increase with the increase in the carbon numbers in the saturated carbon chains is observed (see Table 2). On the other hand, the E2-rate sequence under the same reaction conditions was found to be Et$>$$n$-Pr$>$$n$-Bu in the series of n-alkyl chlorides (Fig. 2), indicating that the elimination reactions proceeded according to the Hofmann rule.[17] This is in marked contrast to the previously-known sequence, n-Pr$>$$n$-Bu$>$Et, in the E2 reactions of n-alkyl bromides with sodium ethoxide in ethanol.[18]

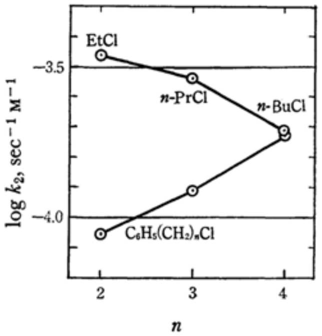

Fig. 2. Second-order rate constants for the E2 reaction of various alkyl chlorides with sodium acetate in 50 vol% aqueous acetone at 120°C.

The minimum for β-phenylethyl chloride in the E2-rate sequence may be explained by the steric retardation by the phenyl group in the β-position in view of the fact that the E2 rates of n-butyl chloride and δ-chlorobutylbenzene are almost the same (see Fig. 2). This minimum for β-phenylethyl chloride is also in contrast to the previous observation[18] that, in the reaction with sodium ethoxide in ethanol, β-phenylethyl bromide has a E2 reaction rate greater than any other n-alkyl bromide.

Although a complete explanation of these reaction sequence in the E2 elimination reactions must await further study, it is conceivable that the difference in base strength, *e. g.*, $EtO^- > AcO^-$, and also in the nature of a leaving group, *e. g.*, Br and Cl, may cause a subtle variation in the character of the E2 transition state and may result in such a reversal of the sequence in each E2 reaction series as has been mentioned above.[19]

Experimental

Materials. ω-Chloroalkylbenzenes, $C_6H_5(CH_2)_nCl$ (n=2—4), were prepared by the chlorination of the respective ω-phenylalkanols with thionyl chloride; β-chloroethylbenzene, bp 65.0—66.0°C/2 mmHg, n_D^{20} 1.5277 (lit. n_D^{20} 1.5294[20a]), d_4^{25} 1.0680 (lit. d_4^{25} 1.069[20a]); γ-chloropropylbenzene, bp 63.0—66.0°C/2—3 mmHg, n_D^{25} 1.5227 (lit. n_D^{25} 1.52030[20b]), d_4^{25} 1.0526 (lit. d_4^{25} 1.056[20b]); δ-chlorobutylbenzene, bp 90.0°C/4 mmHg, n_D^{25} 1.5166 (lit. n_D^{25} 1.5183[21]), d_4^{25} 1.0206 (lit. d_{25}^{25} 1.0295[21]). Benzyl chloride (bp 47.5—48.2°C/2 mmHg), ethyl chloride (bp 12.0°C), n-propyl chloride (bp 46.0—47.0°C), and n-butyl chloride (bp 78.0°C) were purified by the fractional distillation of reagent-grade chemicals. A stock solution of methyl chloride in 50 vol% aqueous acetone was prepared by leading methyl chloride gas from the bomb into the solvent; after appropriate dilution with the solvent, this was used for the kinetic runs. In a similar fashion, a stock solution of ethyl chloride was prepared. Sodium acetate was dried *in vacuo* at 110°C.

Kinetic Measurements. A sealed-ampoule technique was used; in each ampoule a 5-cc aliquot was placed. After a specified length of time, the ampoule was removed from the bath (maintained at an appropriate temperature (±0.05°C)), cooled in ice water, and opened. The contents were then poured into a 50-cc flask, titrated with standard sodium hydroxide (N/20), using phenolphthalein as an indicator, and finally titrated with standard silver nitrate (N/20), using potassium chromate as an indicator. The rate data were treated as has been described in the text. The solvolysis rates of benzyl chloride in 50 vol% aqueous acetone were measured as control runs; the following first-order rate constants were obtained: $10^4 k_1$ (sec^{-1}), 1.90 at 100°C, 3.88 at 110°C, 7.60 at 120°C.

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