BULLETIN OF THE CHEMICAL SOCIETY OF JAPAN VOL. 40 1905—1908 (1967)

Kinetic Studies of Bimolecular Nucleophilic Substitution. II.*1 Structural Effects of Alkyl Halides on the Rate of S_N2 Reactions —A Reinvestigation of the Linear Free-Energy Relationships for the Structural Variation of the Alkyl Groups

Kunio OKAMOTO, Issei NITTA, Tetsuo IMOTO and Haruo SHINGU

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

(Received November 14, 1966)

The linear free-energy relationships have been examined for 35 S_N2 reaction series, including 4 series of the S_N2 reactions of alkyl bromides which rates were measured in these laboratories. These results have then been treated using the equation, $\log(k/k_0)=r\alpha$, where α is a structural constant for methyl, ethyl, *n*-propyl, *n*-butyl, *i*-propyl, *i*-butyl, and neopentyl groups and where r is a reaction constant. The α values have been estimated as the arithmetic means of the $\log k_{S_N2}$ values of the reaction series examined for each alkyl. The correlation coefficients for r's are greater than 0.960 for all of the reaction series except two. The inapplicability of Taft's polar and steric substituent constants (σ^* and E_s) to the S_N2 reactivity of these alkyl groups has been discussed.

Although it is well established[1] that the order of S_N2 reactivity is fairly constant for different alkyl-substrates, to our knowledge there have been few relevant studies,[2] aimed at establishing the quantitative correlation of the relative reactivity of the alkyl group; Streitwieser[2] gave a semi-quatitative measure of the S_N2 reactivity for several alkyl derivatives, while Hine[3a] and Taft[3b] have proposed Eq. (1):

$$\log (k/k_0) = r\alpha \qquad (1)$$

to correlate the S_N2 reactivity, where α is a structural constant dependent on the nature of the alkyl group and where r is a reaction constant. However, the details of the data of the latter two authors have not yet been disclosed.

In this paper the applicability and accuracy of linear free-energy relationships have been evaluated for a series of alkyl-substrates, *i. e.*, methyl, ethyl, *n*-propyl, *n*-butyl, *i*-propyl, *i*-butyl, and neopentyl derivatives, using Eq. (1). As the structural constants, corresponding to α in Eq. (1), we chose the arithmetic means of the logarithms of the rates of the alkyl-substrates relative to ethyl, with the rate of the latter taken as unity.

TABLE 1. VALUES OF THE REACTION CONSTANT, r, IN THE LINEAR FREE-ENERGY RELATIONSHIPS FOR THE STRUCTURAL VARIATION OF ALKYL GROUPS

$(\log k_{RX}-\log k_{EtX})=r\times(\log k_{RX}-\log k_{EtX})_{av.}=r\times\alpha$

Range of r values	S_N2 reactions	Solvents	Temp., °C	r	Correlation coefficients	Number of measurements
$r\geq1.3$	RI+Et_3N	$C_6H_5NO_2$	25	1.521	0.998	3[a]
	RCl+LiCl	Acetone	25	1.410	—	2[b]
	RI+*n*-Bu_3P	Acetone	35	1.396	0.990	5[c]
$1.3>r\geq1.1$	RBr+$Na_2S_2O_3$	50% aq. acetone	12.5	1.291	0.987	5[d]
	RBr+LiI	Acetone	25.0	1.119	0.989	6[e]
	RBr+NaSCN	EtOH	25.0	1.172	0.981	4[f]
	RI+Me_3N	Benzene	100	1.286	0.996	3[g]
	RI+Quinuclidine	$C_6H_5NO_2$	25	1.154	1.000	3[a]
	RI+2-Me-Pyridine	$C_6H_5NO_2$	25	1.198	1.000	3[h]
	RBr+Di-Me-Aniline	MeOH	80	1.134	0.990	5[i]
	RBr+Pyridine	MeOH	80	1.102	0.990	4[i]

*1 Part I: K. Okamoto, H. Kushiro, I. Nitta and H. Shingu, This Bulletin, **40**, 1900 (1967).

1) L. P. Hammett, "Physical Organic Chemistry," McGraw-Hill Co., New York (1940), p. 154.

2) A. Streitwieser, Jr., *Chem. Revs.*, **56**, 571 (1956).

3) a) J. Hine, "Physical Organic Chemistry," McGraw-Hill Co., New York (1956), p. 158; b) R. W. Taft, Jr., cited in Ref. 2.

Table 1. (Contiuned)

Range of r values	S_N2 reactions	Solvents	Temp., °C	r	Correlation coefficients	Number of measurements
$1.1>r\geq0.9$	RCl+KI	Acetone	50.0	0.939	0.963	3[j]
	RBr+LiBr	Acetone	25.0	1.062	0.994	6[k]
	RBr+LiCl	Acetone	25.0	1.010	0.990	6[l]
	RI+NaI	Acetone	25.0	0.952	0.993	3[m]
	RI+NaI	EtOH	50.0	0.927	0.998	5[n]
	RI+LiCl	Acetone	25.0	0.969	0.998	6[o]
	RI+LiBr	Acetone	25.0	1.034	0.990	5[p]
	RBr+EtONa	EtOH	20.0	1.070	0.999	6[q]
	RI+Na 1-Phenyl-3-thiourazolate	50% aq. acetone	25.0	0.949	0.978	6[r]
	RI+EtONa	EtOH	30.0	0.909	0.997	3[s]
$1.1>r\geq0.9$	RI+*n*-PrONa	*n*-PrOH	30.0	0.968	0.995	3[s]
	RI+Et_3N	Acetone	100	0.922	0.960	5[t]
	RI+Di-Me-Aniline	EtOH	40	0.975	0.996	3[u]
$0.9>r\geq0.7$	RBr+MeONa	MeOH	80.0	0.781	0.997	5[i]
	RI+*i*-Pr_3N	EtOH	40.0	0.846	0.976	3[u]
	RI+Pyridine	$C_6H_5NO_2$	25.0	0.875	0.998	3[h]
	RI+Pyridine	Benzene	100	0.740	0.992	4[g]
$0.7>r$	RI+MeONa	MeOH	30.0	0.698	0.993	3[s]
	RBr+C_6H_5ONa	MeOH	80.0	0.646	0.991	5[i]
	RI+C_6H_5ONa	EtOH	42.5	0.449	0.911	6[v]
	RI+Na α-Naphthoxide	EtOH	40.0	0.500	0.990	3[w]
	RI+Na β-Naphthoxide	EtOH	40.0	0.540	0.989	4[u]
	RI+Na Eugenoxide	EtOH	50.0	0.553	0.985	4[x]
	RBr+$NaSC_6H_5$	MeOH	20.0	0.417	0.945	3[y]

a) H. C. Brown and N. R. Eldred, *J. Am. Chem. Soc.*, **71**, 445 (1949).
b) P. B. D. de la Mare, *J. Chem. Soc.*, **1955**, 3169.
c) W. A. Henderson, Jr., and S. A. Buckler, *J. Am. Chem. Soc.*, **82**, 5794 (1960).
d) T. I. Crowell and L. P. Hammett, *ibid.*, **70**, 3444 (1948); P. M. Dunbar and L. P. Hammett, *ibid.*, **72**, 109 (1950).
e) L. Fowden, E. D. Hughes and C. K. Ingold, *J. Chem. Soc.*, **1955**, 3187.
f) T. I. Crowell, *J. Am. Chem. Soc.*, **75**, 6046 (1953).
g) C. A. Winkler and C. N. Hinshelwood, *J. Chem. Soc.*, **1935**, 1147.
h) H. C. Brown and A. Cahn, *J. Am. Chem. Soc.*, **77**, 1715 (1955).
i) This paper.
j) J. B. Conant and R. E. Hussay, *J. Am. Chem. Soc.*, **47**, 476 (1925).
k) P. B. D. de la Mare, *J. Chem. Soc.*, **1955**, 3180.
l) E. D. Hughes, C. K. Ingold and J. D. H. Mackie, *ibid.*, **1955**, 3173.
m) P. B. D. de la Mare, *ibid.*, **1955**, 3196.
n) H. A. McKay, *J. Am. Chem. Soc.*, **65**, 702 (1943).
o) E. D. Hughes, C. K. Ingold and J. D. H. Mackie, *J. Chem. Soc.*, **1955**, 3177.
p) L. Fowden, E. D. Hughes and C. K. Ingold, *ibid.*, **1955**, 3193.
q) M. L. Dhar, E. D. Hughes, C. K. Ingold and S. Masterman, *ibid.*, **1948**, 2055; I. Dostrovsky and E. D. Hughes, *ibid.*, **1946**, 157.
r) S. F. Acree and G. H. Shadinger, *Am. Chem. J.*, **39**, 226 (1908).
s) W. Hecht, M. Conrad and C. Brückner, *Z. phys. Chem.*, **4**, 273 (1889).
t) N. Menschtkin, *ibid.*, **5**, 589 (1990).
u) R. W. Prestone and H. D. Jones, *J. Chem. Soc.*, **101**, 1930 (1912).
v) D. Segaller, *ibid.*, **105**, 106 (1914).
w) H. E. Cox, *ibid.*, **113**, 666 (1918).
x) S. S. Woolf, *ibid.*, **1937**, 1172.
y) J. Hine and W. H. Brader, *J. Am. Chem. Soc.*, **75**, 3964 (1953).

Linear Free-Energy Relationships for the Structural Variation of the Alkyl Groups. Table 1 presents the results of the estimation of r values for 35 S_N2 reaction series, along with the correlation coefficients.[4] Of the 35 reaction series, four reaction series of alkyl bromides, *i. e.*,

4) H. H. Jaffé, *Chem. Revs.*, **53**, 234, 253 (1953).

the S_N2 reactions with sodium methoxide, sodium phenoxide, dimethylaniline, and pyridine, have been measured in these laboratories. The results are tabulated in Table 3 (see Experimental Section). The r values listed in Table 1 vary over the range from 0.4 to 1.5; 23 reaction series among the 35 give r values greater than 0.9. The correlation coefficients have been used as a measure of the precision of these linear free-energy relationships. All of the reaction series except two have been found to have correlation coefficients greater than 0.960. These findings show that such a linear free-energy approximation gives a much more satisfactory agreement than had been expected.[3]

The structural constants, calculated using the 35 reaction series, are shown in Table 2 along with the average relative rates of the alkyl system, as calculated from 21 reaction series by Streitwieser.[2] The two series of structural constants show a fairly good parallelism.

The Separation of the Alkyl Reactivity Scale into Polar and Steric Parts. We examined the separation of the alkyl reactivity scale by applying Taft's treatment.[5] In Fig. 1 the alkyl reactivity constants, $(\log k_{RX} - \log k_{EtX})_{av}$. (Table 2), are plotted against Taft's polar substituent constant, σ^*;[5] the gap between the curved line so obtained and a tangent line, drawn at the point representing the methyl group, is treated as the steric retardation by these alkyl groups. The plot of this steric part, as estimated from the gap in Fig. 1, against Taft's steric substituent constant, E_s,[6] gives a curved line (the dotted line A in Fig. 2). This indicates that Taft's treatment is not satisfactory for the S_N2 reactivity scale of the alkyl groups. Even if most of the alkyl reactivity was only a reflection of the steric factor in S_N2 reactions, the E_s value approximation still agrees poorly with the observed average reactivity. This is shown by the curved line B in Fig. 2.

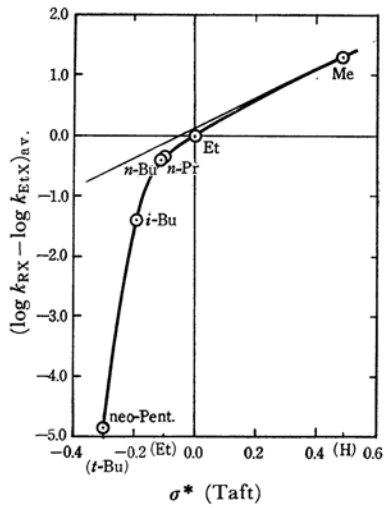

Fig. 1. Comparison of alkyl reactivity constants and Taft's σ^* values.

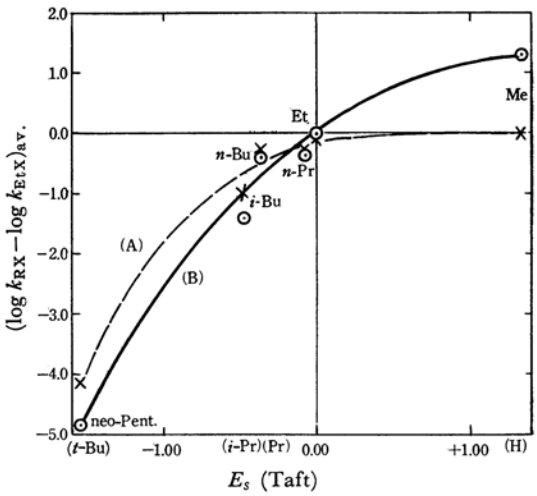

Fig. 2. Comparison of alkyl reactivity constants and Taft's E_s values.

TABLE 2. ALKYL REACTIVITY CONSTANTS* IN THE S_N2 REACTIONS

Methyl	+1.308	+1.5**
Ethyl	0.000	0.0**
n-Propyl	−0.359	−0.4**
n-Butyl	−0.371	−0.4**
i-Propyl	−1.615	−1.6**
i-Butyl	−1.387	−1.5**
Neopentyl	−4.875	−5.0**

* $(\log k_{RX} - \log k_{EtBr})_{av}$.
** A. Streitwieser, Jr.[2]

Thus, for bimolecular nucleophilic substitution on a saturated carbon atom, we have need of a polar and steric substituent other than Taft's σ^* and E_s scales, which were estimated from the reaction series of an unsaturated carbon system. Investigations are under way in search of new polar and steric substituent constants applicable to the S_N2 reactions on a saturated carbon.

Experimental

Materials. The reagent-grade alkyl bromides (methyl, ethyl, *n*-propyl, *n*-butyl, and *i*-butyl bromide), dimethylaniline, and pyridine were purified by fractional distillation. Methanolic sodium methoxide was prepared by dissolving metallic sodium into methanol, which had been purified by fractional distillation. Sodium phenoxide was prepared from sodium ethoxide and phenol. The ethanolic solution of the slight excess of phenol was mixed with the ethanolic sodium ethoxide.

5) R. W. Taft, Jr., *J. Am. Chem. Soc.*, **75**, 4231 (1953).
6) R. W. Taft, Jr., in "Steric Effects in Organic Chemistry," ed. by M. S. Newman, John Wiley and Sons, New York (1956), Chapter 13.

TABLE 3. SECOND-ORDER RATE CONSTANTS ($sec^{-1}M^{-1}$) OF S_N2 REACTIONS OF VARIOUS ALKYL BROMIDES WITH SODIUM METHOXIDE, SODIUM PHENOXIDE, DIMETHYLANILINE AND PYRIDINE IN METHANOL AT 80.0±0.1°C**

	MeBr	EtBr	*n*-PrBr	*n*-BuBr	*i*-BuBr
NaOMe	8.14×10^{-2}*	9.06×10^{-3}	3.35×10^{-3}	3.34×10^{-3}	6.75×10^{-4}
NaOPh	2.84×10^{-2}*	6.21×10^{-3}	2.89×10^{-3}	3.08×10^{-3}	5.12×10^{-4}
Di-Me-Aniline	2.78×10^{-5}	1.78×10^{-4}	8.67×10^{-5}	9.03×10^{-5}	3.10×10^{-6}
Pyridine	2.71×10^{-5}	1.52×10^{-4}	8.42×10^{-5}	—	2.54×10^{-6}

* Extrapolated from the data at lower temperatures 3.18×10^{-4} at 24.7°C, 4.69×10^{-3} at 50.05°C, and 2.03×10^{-2} at 65.0°C for sodium methoxide; 1.44×10^{-3} at 50.05°C and 1.76×10^{-2} at 75.0°C for sodium phenoxide.

** Initial concentrations were 0.100 M for alkyl bromides, sodium methoxide and sodium phenoxide. Initial concentrations for dimethylaniline and pyridine were 0.200 M, except the reactions with methyl bromide. In the latter cases the concentrations were 0.100 M.

The sodium phenoxide was filtered, washed with ether, and then dried *in vacuo* to a constant weight at 100—110°C.

Kinetic Measurements. All the kinetics were measured at 80.0±0.1°C, except for the reactions of methyl bromide with sodium methoxide and sodium phenoxide (see Table 3). The sealed ampoule technique was used. Each ampoule contained 1.000 cc of an aliquot of the reaction mixture. The reactions were followed by the titration of bromide ions, using the Volhard method. The rate data were treated graphically, and a smooth linear relationship was obtained for each run. The reactions were followed to at least 70% completion. Infinity titers, as determined at least ninety half-lives, gave reproducible results. The results are tabulated in Table 3.