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## Kinetic Studies of Bimolecular Nucleophilic Substitution. II.\*<sup>1</sup> Structural Effects of Alkyl Halides on the Rate of S<sub>N</sub>2 Reactions —A Reinvestigation of the Linear Free-Energy Relationships for the Structural Variation of the Alkyl Groups

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The linear free-energy relationships have been examined for  $35 \text{ S}_{\text{N}}2$  reaction series, including 4 series of the  $\text{S}_{\text{N}}2$  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  $\alpha$  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  $\alpha$  values have been estimated as the arithmetic means of the  $\log k_{\text{S}_{\text{N}}2}$  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 ( $\sigma^*$  and  $E_s$ ) to the  $S_{\text{N}}2$  reactivity of these alkyl groups has been discussed.

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

$$\log\left(k/k_0\right) = r\alpha \tag{1}$$

to correlate the  $S_N 2$  reactivity, where  $\alpha$  is a struc-

tural 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  $\alpha$  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	RE.	ACTION	CONST	ANT,	r, 1	N	THE	LINEAR	FREE-ENERGY	
	RELA	ATIONSHI	PS 1	FOR	THE	STRUCT	<b>FURAL</b>	VARI	ATIC	ON	OF	ALKYL	GROUPS	

$(\log k_{\rm RX} - \log k_{\rm EtX}) = r \times (\log k_{\rm RX} - \log k_{\rm EtX})_{\rm av.} = r \times$	α
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Range of $r$ values	$S_N 2$ reactions	Solvents Te	emp., °C	r	Correlation coefficients	Number of measurements
<u>r≥1.3</u>	RI+Et <sub>3</sub> N	C <sub>6</sub> H <sub>5</sub> NO <sub>2</sub>	25	1.521	0.998	<b>3</b> a)
	RCl+LiCl	Acetone	25	1.410		2b)
	RI+n-Bu <sub>3</sub> P	Acetone	35	1.396	0.990	5c)
$1.3 > r \ge 1.1$	$RBr + Na_2S_2O_3$	50% aq. aceton	e 12.5	1.291	0.987	5d)
	RBr+LiI	Acetone	25.0	1.119	0.989	6e)
	RBr+NaSCN	EtOH	25.0	1.172	0.981	<b>4</b> f)
	$RI + Me_3N$	Benzene	100	1.286	0.996	3g)
	RI+Quinuclidine	$C_6H_5NO_2$	25	1.154	1.000	<b>3</b> a)
	RI+2-Me-Pyridine	$C_6H_5NO_2$	25	1.198	1.000	3h)
	RBr+Di-Me-Aniline	MeOH	80	1.134	0.990	<b>5</b> i)
	RBr+Pyridine	MeOH	80	1.102	0.990	<b>4i</b> )

\*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.

$S_N 2$ reactions	Solvents T	°emp., °C	r	coefficients	Number of measurements
RCl+KI	Acetone	50.0	0.939	0.963	31)
RBr+LiBr	Acetone	25.0	1.062	0.994	6 <sup>k</sup> )
RBr+LiCl	Acetone	25.0	1.010	0.990	<b>6</b> <sup>1</sup> )
RI+NaI	Acetone	25.0	0.952	0.993	<b>3</b> m)
RI+NaI	EtOH	50.0	0.927	0.998	5 <sup>n</sup> )
RI+LiCl	Acetone	25.0	0.969	0.998	60>
RI+LiBr	Acetone	25.0	1.034	0.990	<b>5</b> p)
RBr+EtONa	EtOH	20.0	1.070	0.999	<b>6</b> 9)
RI+Na 1-Phenyl-3-thiourazolate	50% aq. acetor	ne 25.0	0.949	0.978	6 <sup>r</sup> )
RI+EtONa	EtOH	30.0	0.909	0.997	3s)
RI+n-PrONa	<i>n</i> -PrOH	30.0	0.968	0.995	3s)
$RI + Et_3N$	Acetone	100	0.922	0.960	5t)
RI+Di-Me-Aniline	EtOH	40	0.975	0.996	<b>3</b> u)
RBr+MeONa	MeOH	80.0	0.781	0.997	5i)
RI+i-Pr <sub>3</sub> N	EtOH	40.0	0.846	0.976	<b>3</b> u)
RI+Pyridine	$C_6H_5NO_2$	25.0	0.875	0.998	<b>3</b> h)
RI+Pyridine	Benzene	100	0.740	0.992	4g)
RI+MeONa	MeOH	30.0	0.698	0.993	3s)
$RBr + C_6H_5ONa$	MeOH	80.0	0.646	0.991	<b>5</b> <sup>i</sup> )
$RI + C_6 H_5 ONa$	EtOH	42.5	0.449	0.911	6 <sup>v</sup> )
RI+Na $\alpha$ -Naphthoxide	EtOH	40.0	0.500	0.990	3w)
RI+Na $\beta$ -Naphthoxide	EtOH	40.0	0.540	0.989	4u)
RI+Na Eugenoxide	EtOH	50.0	0.553	0.985	4x)
$ m RBr+NaSC_6H_5$	MeOH	20.0	0.417	0.945	33)
<ul> <li>I. C. Brown and N. R. Eldred, J.</li> <li>P. B. D. de la Mare, J. Chem. Soc.,</li> <li>V. A. Henderson, Jr., and S. A. B</li> <li>T. I. Crowell and L. P. Hammett,</li> <li>Hammett, <i>ibid.</i>, <b>72</b>, 109 (1950).</li> <li>Fowden, E. D. Hughes and C. J.</li> <li>Fowden, E. D. Hughes and C. J.</li> <li>T. Crowell, J. Am. Chem. Soc., <b>7</b></li> <li>C. A. Winkler and C. N. Hinshelw</li> <li>H. C. Brown and A. Cahn, J. Am.</li> <li>Chis paper.</li> <li>B. Conant and R. E. Hussay, J.</li> <li>B. D. de la Mare, J. Chem. Soc.,</li> <li>C. D. Hughes, C. K. Ingold and J.</li> <li>B. D. de la Mare, <i>ibid.</i>, <b>1955</b>, 33</li> <li>H. A. McKay, J. Am. Chem. Soc., <b>6</b></li> <li>D. Hughes, C. K. Ingold and J.</li> </ul>	<ul> <li>Am. Chem. Soc.,</li> <li>1955, 3169.</li> <li>uckler, J. Am. C</li> <li>ibid., 70, 3444</li> <li>K. Ingold, J. Cl.</li> <li>5, 6046 (1953).</li> <li>ood, J. Chem. Sc</li> <li>Chem. Soc., 77,</li> <li>Am. Chem. Soc.,</li> <li>1955, 3180.</li> <li>D. H. Mackie,</li> <li>196.</li> <li>15, 702 (1943).</li> <li>D. H. Mackie,</li> </ul>	<ul> <li>71, 445 (1)</li> <li>Chem. Soc., 4</li> <li>(1948); 1</li> <li>hem. Soc., 1</li> <li>oc., 1935, 1</li> <li>1715 (1955</li> <li>47, 476 (1</li> <li>ibid., 1955</li> <li>J. Chem.</li> </ul>	<ul> <li>(949).</li> <li>82, 5794</li> <li>P. M. 1</li> <li>955, 318</li> <li>147.</li> <li>).</li> <li>925).</li> <li>5, 3173.</li> <li>Soc., 195</li> </ul>	(1960). Dunbar and 7. <b>5</b> , 3177.	<b>L. P.</b>
	RCl+KI RBr+LiBr RBr+LiCl RI+NaI RI+NaI RI+NaI RI+LiCl RI+LiCl RI+LiBr RBr+EtONa RI+LiBr RBr+EtONa RI+EtaN RI+Di-Me-Aniline RBr+MeONa RI+Di-Me-Aniline RBr+MeONa RI+Pyridine RI+Pyridine RI+Pyridine RI+Pyridine RI+Pyridine RI+MeONa RI+C6H5ONa RI+C6H5ONa RI+C6H5ONa RI+Na $\alpha$ -Naphthoxide RI+Na $\beta$ -Naphthoxide RI+Na $\beta$ -Naphthoxide RI+Na $\beta$ -Naphthoxide RI+Na Eugenoxide RBr+NaSC6H5 H. C. Brown and N. R. Eldred, J. B. D. de la Mare, J. Chem. Soc., V. A. Henderson, Jr., and S. A. B C. I. Crowell and L. P. Hammett, Hammett, <i>ibid.</i> , <b>72</b> , 109 (1950). J. Crowell, J. Am. Chem. Soc., <b>72</b> A. Winkler and C. N. Hinshelw H. C. Brown and A. Cahn, J. Am. Chis paper. B. Conant and R. E. Hussay, J. B. D. de la Mare, <i>J. Chem. Soc.</i> , C. D. Hughes, C. K. Ingold and J. B. D. de la Mare, <i>ibid.</i> , <b>1955</b> , 3 I. A. McKay, J. Am. Chem. Soc., <b>5</b> D. Hughes, C. K. Ingold and J. B. D. de la Mare, <i>ibid.</i> , <b>1955</b> , 3 I. A. McKay, J. Am. Chem. Soc., <b>5</b> D. Hughes, C. K. Ingold and J. B. D. de la Mare, <i>ibid.</i> , <b>1955</b> , 3 I. A. McKay, J. Am. Chem. Soc., <b>6</b> D. Hughes, C. K. Ingold and J. B. D. de la Mare, <i>ibid.</i> , <b>1955</b> , 3 I. A. McKay, J. Am. Chem. Soc., <b>75</b> N. B. D. de la Mare, <i>ibid.</i> , <b>1955</b> , 3 I. A. McKay, J. Am. Chem. Soc., <b>75</b> N. B. D. de la Mare, <i>ibid.</i> , <b>1955</b> , 3 I. A. McKay, J. Am. Chem. Soc., <b>75</b> I. B. D. de la Mare, <i>ibid.</i> , <b>1955</b> , 3 I. A. McKay, J. Am. Chem. Soc., <b>75</b> I. B. D. de la Mare, <i>ibid.</i> , <b>1955</b> , 3 I. A. McKay, J. Am. Chem. Soc., <b>75</b> I. B. D. de la Mare, <i>ibid.</i> , <b>1955</b> , 3 I. A. McKay, J. Am. Chem. Soc., <b>75</b> I. A. McKay, J. Am. Chem. Soc., <b></b>	RCl+KIAcetoneRBr+LiBrAcetoneRBr+LiClAcetoneRI+NaIAcetoneRI+NaIEtOHRI+NaIEtOHRI+LiBrAcetoneRI+LiBrAcetoneRI+LiBrAcetoneRI+LiBrAcetoneRI+LiBrAcetoneRI+LiBrAcetoneRI+EtONaEtOHRI+Na 1-Phenyl-3-thiourazolate $50\%$ aq. acetorRI+EtONaRetOHRI+ParoNan-PrOHRI+EtasNAcetoneRI+Di-Me-AnilineEtOHRBr+MeONaMeOHRI+PyridineC6H5NO2RI+PyridineBenzeneRI+MeONaMeOHRI+C6H5ONaMeOHRI+Na $\alpha$ -NaphthoxideEtOHRI+Na $\alpha$ -NaphthoxideEtOHRI+Na $\alpha$ -NaphthoxideEtOHRI+Na $\beta$ -Na	RCl+KI         Acetone         50.0           RBr+LiBr         Acetone         25.0           RBr+LiCl         Acetone         25.0           RI+NaI         Acetone         25.0           RI+NaI         EtOH         50.0           RI+NaI         EtOH         50.0           RI+NaI         EtOH         50.0           RI+LiCl         Acetone         25.0           RI+LiBr         Acetone         25.0           RI+LiBr         Acetone         25.0           RI+An         1-Phenyl-3-thiourazolate         50% aq. acetone         25.0           RI+An         1-Phenyl-3-thiourazolate         50% aq. acetone         25.0           RI+ADNA         EtOH         30.0         30.0         30.0           RI+ParoNa         n-PrOH         30.0         30.0           RI+Pitone         EtOH         40         30.0           RI+Pyridine         Benzene         100         30.0           RI+Pyridine         Benzene         100         30.0           RI+CeH5ONa         MeOH         80.0         30.0           RI+Na $\alpha$ -Naphthoxide         EtOH         40.0         30.0           RI+Na $\beta$ -Naphthoxide	RCl+KI         Acetone         50.0         0.939           RBr+LiBr         Acetone         25.0         1.062           RBr+LiCl         Acetone         25.0         1.010           RI+NaI         Acetone         25.0         0.952           RI+NaI         EtOH         50.0         0.952           RI+NaI         EtOH         50.0         0.952           RI+LiBr         Acetone         25.0         0.969           RI+LiBr         Acetone         25.0         0.969           RI+AI         Phonyl-3-thiourazolate         50% aq. acetone         25.0         0.949           RI+A         1-Phenyl-3-thiourazolate         50% aq. acetone         25.0         0.949           RI+A         1-Phonyl-3-thiourazolate         50% aq. acetone         100         0.922           RI+AEONa         n-PrOH         30.0         0.968         RI++Et <sub>3</sub> N         Acetone         100         0.922           RI+PortoNa         n-PrOH         40.0         0.781         RI++i-Pra,N         EtOH         40.0         0.846           RI++Pyridine         Celsh_5NO2         25.0         0.875         RI+Po-Pyridine         Gelson         0.00         0.646	RCl+KI         Acetone         50.0         0.939         0.963           RBr+LiBr         Acetone         25.0         1.062         0.994           RBr+LiBr         Acetone         25.0         1.010         0.990           RH+NaI         Acetone         25.0         0.952         0.993           RI+NaI         EtOH         50.0         0.927         0.998           RI+LiCl         Acetone         25.0         0.969         0.998           RI+LiBr         Acetone         25.0         0.969         0.998           RI+LiBr         Acetone         25.0         0.969         0.999           RI+N01         Phenyl-3-thiourazolate         50% aq. acetone         25.0         0.949         0.977           RI+EtONa         EtOH         30.0         0.906         0.997         Ri+n-PrONa         n-PrOH         30.0         0.9668         0.995           RI++MeONa         MeOH         80.0         0.781         0.997         Ri+rhetaN           RI+PriMone         EtOH         40.0         0.846         0.992           RI++MeONa         MeOH         30.0         0.698         0.993           RI+Pyridine         CgH_sNO2 <td< td=""></td<>

TABLE 1. (Contiuned)

- 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).
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- 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 rvalues for 35 S<sub>N</sub>2 reaction series, along with the correlation coefficients.<sup>4)</sup> Of the 35 reaction series, four reaction series of alkyl bromides, *i. e.*,

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

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the  $S_N 2$  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.<sup>30</sup>

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.<sup>2)</sup> 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.<sup>5</sup>) In Fig. 1 the alkyl reactivity constants,  $(\log k_{\rm RX} - \log k_{\rm EtX})_{\rm av}$ . (Table 2), are plotted against Taft's polar substituent constant,  $\sigma^*$ ;<sup>5</sup>) 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,  $E_{s}$ ,<sup>6</sup>) gives a curved line (the dotted line A in



Fig. 1. Comparison of alkyl reactivity constants and Taft's  $\sigma^*$  values.

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 2. Alkyl reactivity constants\* in the  $$S_{\rm N}2$$  reactions

+1.308	+1.5**
0.000	0.0**
-0.359	-0.4**
-0.371	-0.4**
-1.615	-1.6**
-1.387	-1.5**
-4.875	-5.0**
	$\begin{array}{c} 0.000\\ -0.359\\ -0.371\\ -1.615\\ -1.387\\ -4.875\end{array}$

\*  $(\log k_{\rm RX} - \log k_{\rm EtBr})_{\rm av}$ 

\*\* A. Streitwieser, Jr.<sup>2)</sup>

Fig. 2). This indicates that Taft's treatment is not satisfactory for the  $S_N 2$  reactivity scale of the alkyl groups. Even if most of the alkyl reactivity was only a reflection of the steric factor in  $S_N 2$ 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.

Thus, for bimolecular nucleophilic substitution on a saturated carbon atom, we have need of a polar and steric substituent other than Taft's  $\sigma^*$  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.

TABLE 3.	Second-order rate constants (sec $^{-1}$ m $^{-1}$ ) of SN2 reactions of various alkyl bromides
	WITH SODIUM METHOXIDE, SODIUM PHENOXIDE, DIMETHYLANILINE AND PYRIDINE
	IN METHANOL AT $80.0+0.1^{\circ}C^{**}$

	MeBr	EtBr	<i>n</i> -PrBr	<i>n</i> -BuBr	<i>i</i> -BuBr
NaOMe	8.14×10 <sup>-2*</sup>	9.06×10-3	$3.35 \times 10^{-3}$	$3.34 \times 10^{-8}$	6.75×10-4
NaOPh	$2.84 \times 10^{-2*}$	6.21×10 <sup>-3</sup>	$2.89 \times 10^{-3}$	3.08×10 <sup>-3</sup>	5.12×10-4
Di-Me-Aniline	2.78×10-5	1.78×10-4	8.67×10 <sup>-5</sup>	9.03×10 <sup>-5</sup>	3.10×10 <sup>-6</sup>
Pyridine	$2.71 \times 10^{-5}$	$1.52 \times 10^{-4}$	$8.42 \times 10^{-5}$		$2.54 \times 10^{-6}$

\* Extrapolated from the data at lower temperatures  $3.18 \times 10^{-4}$  at  $24.7^{\circ}$ C,  $4.69 \times 10^{-3}$  at  $50.05^{\circ}$ C, and  $2.03 \times 10^{-2}$  at  $65.0^{\circ}$ C for sodium methoxide;  $1.44 \times 10^{-3}$  at  $50.05^{\circ}$ C and  $1.76 \times 10^{-2}$  at  $75.0^{\circ}$ 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  $80.0\pm0.1$  °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.