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Studies of Azo Colors. VIII.[1] The Azo-coupling Reactions of Active Methylene Compounds

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The kinetics of the azo-coupling reactions of various active methylene compounds with diazobenzene-4-sulfonic acid have been studied spectrophotometrically. In the reactions of all the active methylene compounds used, it was found that the reaction rate was proportional to both the concentration of the diazonium salt and the carbanion (or enolate ion) of the azo component. In the reactions of a series of β-dicarbonyl compounds, a plot of the logarithms of the rate constants against the pK_a values of active methylene compounds gave a straight line. However, the correlation between the reactivity and pK_a was found unsatisfactory in the case of active methylene compounds with such electron-withdrawing substituents as NO_2, CN, COR, SO_2R, and Cl. These results are discussed in terms of the nucleophilicity of these carbanions.

The reaction of aromatic diazo compounds with aromatic amines or phenols is well known to be a diazo-coupling reaction, and the kinetics of the reaction has been extensively studied in connection with the reaction mechanism and the effects of the substituents on the reactivity.[2]

On the other hand, aliphatic compounds containing an activated methylene or methyl group are known to react also with aromatic diazonium salts to form azo compounds or their tautomers. Although many active methylene compounds are known,[3,4] no systematic quantitative studies of their coupling reactions have yet been made. Therefore, little is known concerning the reaction mechanism and the relationship between the reactivity and the structure.

This paper will report the kinetics of the coupling reaction of various active methylene compounds with diazobenzene-4-sulfonic acid, and the structural effect of the active methylene compound on the reactivity.

Experimental

Materials. Bis(methylsulfonyl)methane and bis(ethylsulfonyl)methane were prepared by the method of Fromm.[5] Ethyl nitroacetate was prepared by the method of Arndt[6] from ethyl acetoacetate and nitric acid. *p*-Nitroacetoacetanilide was prepared according to the method of Fierz-David.[7] The other active methylene compounds and sulfanilic acid were of commercial origin and were used after purification by recrystallization or distillation. Their purities were confirmed by their physical constants and by thin-layer chromatography or gas chromatography.

*p*K$_a$ *Measurement.* The pK_a value of the azo component was measured spectrophotometrically at a appropriate wavelength in water (ionic strength, μ; 0.25) at 20±0.1°C. In the case of ethyl cyanoacetate, due to the decomposition in an alkaline solution, the extinction of carbanion was taken as a function of the time and was extrapolated back to zero time. The decomposition of ethyl cyanoacetate, however, was negligibly small in the pH range where kinetic measurements were performed. The results are given in Table 2 and Table 3.

Kinetic Measurements. The general experimental techniques are quite similar to those used in an earlier experiment.[8] The kinetic measurements were carried out when the azo component was present in at least a twenty-five-fold excess as compared to the diazonium salt. The apparent rate constant (k') was calculated using Eq. (1) by measuring the concentration of the product spectrophotometrically in a buffered aqueous solution at 20±0.1°C:

$$k't = 2.303 \log \frac{a}{a-x} = 2.303 \log \frac{E_\infty}{E_\infty - E_t} \qquad (1)$$

a: concentration of the dyestuff at an infinite time (a is proportional to the E_∞ extinction)

x: concentration of the dyestuff at time t (x is proportional to the E_∞ extinction)

The bimolecular rate constant (k_2) was obtained from Eq. (2):

$$k_2 = k'/[A^-] = k'[H^+]/K_a{}^{AH}[AH] \qquad (2)$$

where $[A^-]$, $[AH]$, and $K_a{}^{AH}$ represent the concentration of the carbanion, the undissociated form of the azo component, and the dissociation constant of AH respectively. The results are tabulated in Table 2 and Table 3. The initial concentration of the diazonium salt was 4×10^{-5} mol/l in all of the kinetic runs. The components of the buffer solutions used were as follows:

pH	Component			
2.0	0.066 mol	CH_3COONa	+0.084 mol	HCl/l
2.8	0.063 mol	CH_3COONa	+0.063 mol	HCl/l
3.7	0.066 mol	CH_3COONa	+0.059 mol	HCl/l
4.3	0.040 mol	CH_3COONa	+0.080 mol	CH_3COOH/l
4.7	0.063 mol	CH_3COONa	+0.047 mol	CH_3COOH/l
5.2	0.063 mol	CH_3COONa	+0.031 mol	CH_3COOH/l
5.8	0.040 mol	CH_3COONa	+0.003 mol	CH_3COOH/l
6.2	0.013 mol	Na_2HPO_4	+0.038 mol	KH_2PO_4/l
6.8	0.011 mol	Na_2HPO_4	+0.009 mol	KH_2PO_4/l
7.2	0.015 mol	Na_2HPO_4	+0.005 mol	KH_2PO_4/l

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[1] Part VII: Y. Hashida, S. Sekiguchi, and K. Matsui, *Kogyo Kagaku Zasshi*, **74**, 240 (1971).

[2] H. Zollinger, "Azo and Diazo Chemistry," Interscience Publishers, New York, N. Y. (1961), p. 221.

[3] S. M. Parmerter, "Organic Reaction," Vol. 10, ed. by R. Adams, John Wiley & Sons, Inc., New York, N. Y., (1959), p. 1.

[4] E. Enders, "Methoden der Organischen Chemie (Houben-Weyl)," Band X/3 (Stickstoffverbindungen 1), George Thieme Verlag., Stuttgart (1965), p. 471.

[5] E. Fromm, *Ann.*, **253**, 155 (1889).

[6] F. Arndt and J. P. Rose, *J. Chem. Soc.*, **1935**, 1.

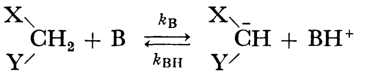
[7] H. E. Fierz-David and F. Ziegler, *Helv. Chim. Acta*, **2**, 779 (1928).

[8] Y. Hashida, K. Nakajima, S. Sekiguchi, and K. Matsui, *Kogyo Kagaku Zasshi*, **72**, 1132 (1969).

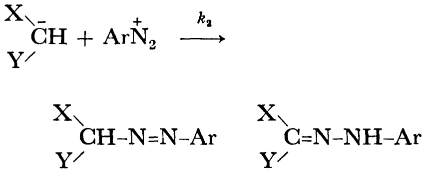
The ionic strength of the buffer solution was adjusted to 0.25, by the addition of potassium chloride.

Results and Discussion

Kinetic Equation. The mechanism expressed by the following equations is suggested as the most probable for the coupling of an active methylene compound:[9]



$$\genfrac{}{}{0pt}{}{X}{Y}\!>\!CH_2 + B \underset{k_{BH}}{\overset{k_B}{\rightleftharpoons}} \genfrac{}{}{0pt}{}{X}{Y}\!>\!\overset{-}{C}H + BH^+ \qquad (3)$$



$$\genfrac{}{}{0pt}{}{X}{Y}\!>\!\overset{-}{C}H + Ar\overset{+}{N}_2 \xrightarrow{k_2} \genfrac{}{}{0pt}{}{X}{Y}\!>\!CH\text{-}N{=}N\text{-}Ar \quad \genfrac{}{}{0pt}{}{X}{Y}\!>\!C{=}N\text{-}NH\text{-}Ar \qquad (4)$$

For instance, in the reactions of acetoacetanilide[10] and pyrazolones,[11,12] the ionization of the methylene group occurs first, followed by the rate-controlling step of the reaction; the rate of the coupling has been expressed by Eq. (5):

$$v = k_2[Ar\overset{+}{N}_2][X\text{-}\overset{-}{C}H\text{-}Y] \qquad (5)$$

The kinetic equation is similar to that for the coupling to phenols.[1]

On the other hand, in the case of nitroethane, the ionization of the C–H bond occurs slower than the second step, and a kinetic expression (6) has been presented:[13]

$$v = k_B[B][X\text{-}CH_2\text{-}Y] \qquad (6)$$

Equation (6) is similar to the one that applies to the base catalyzed halogenation of aliphatic compounds containing an activated methylene group. Thus, at present, two types of kinetic equations are known for the coupling reactions of active methylene compounds. Therefore, the reactions of other aliphatic compounds with diazonium salts are of interest with respect to the kinetic equation. In this paper, the active methylene compounds shown in Table 2 and Table 3 have been examined from the above point of view.

As is shown in Table 1, the first-order dependence with the diazonium salt was confirmed in the reaction of malononitrile according to Eq. (1) by using an excess of the azo component; the reaction also shows a first-order dependence on the concentration of malononitrile, judging from the results using different concentrations at a constant pH.

The dependence of log k' on pH was linear, as is shown in Fig. 1, with a unit slope over the pH range where the concentration of the dissociated form of malononitrile is much lower than that of the undissociated form. This result is consistent with a presumption that the rate determining step is the reaction of a carbanion with a diazonium salt.[10–12,14] Therefore, a second-order rate constant (k_2) was determined from Eq. (2). The k_2 values thus obtained are independent of the acidity of the medium, as is shown in Table 1.

TABLE 1. COUPLING RATE CONSTANT OF DIAZOBENZENE-4-SULFONIC ACID WITH MALONONITRILE (20°C, μ: 0.25)

pH	Concentration of malononitrile (mol/l) × 10^3	k' (min^{-1})	k_2 (l/mol·min) × 10^{-8}
4.37	1.00	0.0965	4.21
4.38	4.00	0.356	3.80
4.38	2.00	0.205	4.37
2.88	2.00	0.00623	4.19
3.74	2.00	0.0417	3.90
4.74	2.00	0.498	4.65

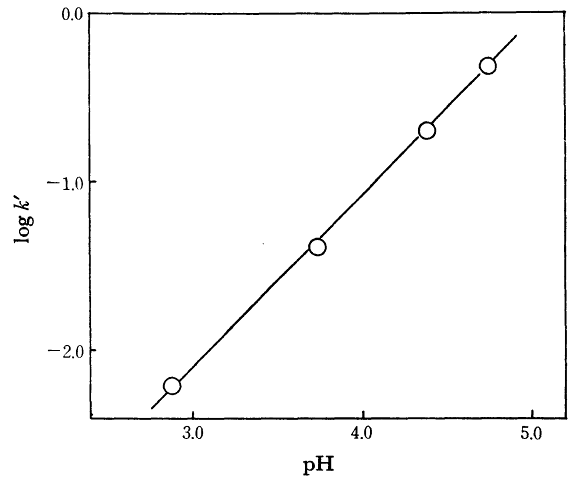


Fig. 1. Dependence of the rate constant (k') for the coupling reaction of diazobenzene-4-sulfonic acid with malononitrile on pH. (Concentration of malononitrile: 2×10^{-3} mol/l)

In all the active methylene compounds studied, it was found that the rate of coupling was expressed by Eq. (5) under the given set of conditions (Table 2 and Table 3) in a manner similar to that described above. Thus, in the present work we have found that the kinetic expression differs from that used for the reaction of nitroethane. It is assumed that a difference in the relative rates of the stages (3) and (4) is responsible for the difference in their kinetic expressions (5 and 6). In the active methylene compounds used, not only the reaction circumstances, such as the component of the buffer solution, which affect the velocity of stage (3) as a base, but also the magnitude of k_2, are not same as in the case of nitroethane. However, it is assumed that the slow ionization of nitroethane is at least partly responsible for the kinetic equation, Eq. (6), which differs from those of the other active methylene compounds. It is well known that the ionization of nitro-

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9) Ref. 2, p. 199.

10) V. Macháček, J. Panchartek, V. Štěrba, and M. Večeřa, *Collect. Czech. Chem. Commun.*, **35**, 844 (1970).

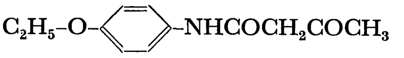
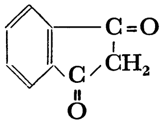
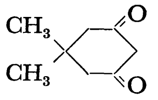
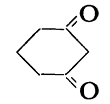
11) I. Dobáš, V. Štěrba, and M. Večeřa, *ibid.*, **34**, 3905 (1969).

12) I. Dobáš, V. Štěrba, and M. Večeřa, *ibid.*, **34**, 3895 (1969).

13) V. Macháček, J. Panchartek, V. Štěrba, and M. Večeřa, *ibid.*, **33**, 3154 (1968).

14) C. Wittwer and H. Zollinger, *Helv. Chim. Acta*, **37**, 1954 (1954).

TABLE 2. RATE CONSTANTS OF THE COUPLING REACTION OF DIAZOBENZENE-4-SULFONIC ACID WITH β-DICARBONYL COMPOUNDS (20°C, μ: 0.25)

Exp. No.	β-Dicarbonyl compounds	pK_a	k_2 (l/mol·min)	pH[a]
1		9.65	1.22×10^7	4.3—5.2
2		10.25	3.27×10^7	4.3—5.2
3		10.46	4.84×10^7	4.3—5.2
4		10.55	5.66×10^7	4.3—5.2
5		10.62	5.70×10^7	4.7—5.2
6		9.71	1.50×10^7	3.7—4.7
7		10.26	3.05×10^7	4.3—4.7
8	$CH_2(COOC_2H_5)_2$	13.3[b]	$4.8\ \times10^8$	6.2—7.2
9	$CH_3COCH_2COOC_2H_5$	10.79[c]	3.10×10^7	4.7—5.8
10	$CH_3COCH_2COOCH_3$	10.57	1.34×10^7	4.7—5.8
11	$CH_3COCH_2COCH_3$	9.01[c]	1.92×10^6	3.7—4.7
12	$C_6H_5COCH_2COCH_3$	8.77[d]	1.20×10^6	3.7—4.7
13	$CH_3COCH_2COCF_3$	6.40 (6.3[e])	4.31×10^2	4.3—6.2
14		6.38[f]	6.67×10^2	4.3—6.2
15		7.12	9.60×10^5	3.7—4.7
16		5.22[g]	1.99×10^4	2.0—2.8
17		5.07	6.06×10^3	2.8—3.7

a) pH range in which the reaction rate was measured
b) R. G. Pearson and J. M. Mills, *J. Amer. Chem. Soc.*, **72**, 1692 (1950).
c) W. S Walisch and H. A. Ruppersberg. *Chem. Ber.*, **92**, 2622 (1959).
d) M. Laloi and M. Rubinstein, *Bull. Soc. Chim. Fr.*, **1965**, 310.
e) J. C. Reid and M. Calvin, *J. Amer. Chem. Soc.*, **72**, 2948 (1950).
f) E. H. Cook and R. F. Taft, Jr., *ibid.*, **74**, 6103 (1952).
g) R. P. Bell and R. R. Robinson, *Trans. Farady Soc.*, **57**, 965 (1961).

ethane occurs substantially more slowly than those of the other active methylene compounds of the same acid strength.[15]

Effect of the Structure of the Azo Component on the Reactivity. Although many investigations concerning carbanion have been reported in the literature, there have been only fragmentary reports about the structural effect of the carbanion on the reactivity. Therefore, it seemed that is would be of interest to compare the reactivities of various carbanions towards the diazonium salt.

It may be seen in Table 2 that the effects of substituents in the benzene ring, including *ortho*-substituents, on the reactivity are small in acetoacetanilide (No. 1—7), and that the reaction is accelerated by an electron-donating substituent (No. 4 and 5). This result may be

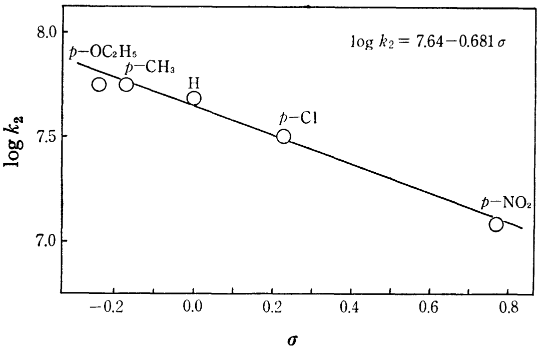


Fig. 2. Hammett plot for the reaction of diazobenzene-4-sulfonic acid with substituted acetoacetanilides.

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[15] R. G. Pearson and R. L. Dillon, *J. Amer. Chem. Soc.*, **75**, 2439 (1953).

interpreted on the basis of the increase in the nucleophilic character of the enolate ion, as will be described later. Figure 2 represents the linear dependence of log k_2 on the substituent constnat (σ). The small ρ value (0.681) can be explained in terms of the insulating effect of the NH–CO group for the transmission of the electronic effect of the substituent.

In β-dicarbonyl compounds (No. 1—17), the k_2 value varies considerably with the nature of the neighboring group. In Table 2, it may be seen that in general, the higher the pK_a value of a β-dicarbonyl compound, the more readily does the reaction occucr. The correlation between the reactivity and the pK_a value of an azo component is represented graphically in Fig. 3 by plotting the logarithms of the rate constants against the pK_a values.

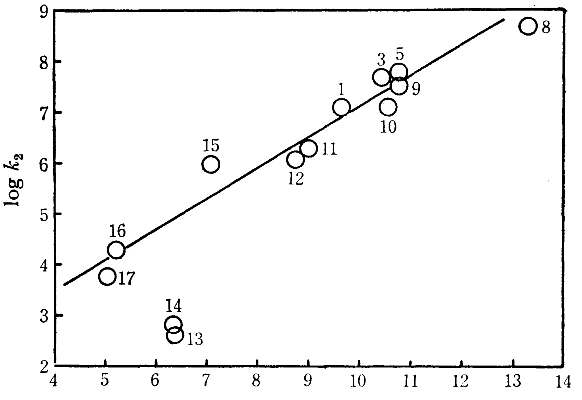
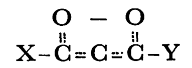


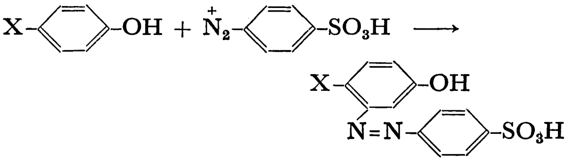
Fig. 3. Relation between pK_a values and rate constants (k_2) for the reaction of diazobenzene-4-sulfonic acid with β-dicar bonyl compounds. (The numbers refer to the β-dicarbonyl compounds as listed in Table 2.)

It is apparent from Fig. 3 that the plots of all the β-dicarbonyl compounds including alicyclic derivatives (No. 15—17), except for trifluoro-derivatives (No. 13 and 14), are on a straight line. These results indicate that the reactivity of an enolate ion (7), that is, the nucleophilicity of an enolate ion towards the diazonium cation, is closely related to its pK_a value.



$$\mathrm{X{-}\overset{O}{\overset{\|}{C}}{=}C{=}\overset{-\,O}{\overset{\|}{C}}{-}Y} \qquad (7)$$

A similar relationship between the reactivity and the pK_a of phenols has been found in the coupling reaction (8) of p-substituted phenols with diazobenzene-4-sulfonic acid.[16)]

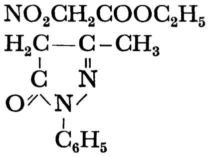
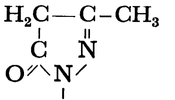
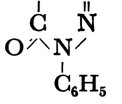


(8)

A similar parallelism between reactivity and pK_a has been observed for various active methylene compounds which include such activating substituents as CN, NO$_2$, COR, and Cl, as is shown in Table 3.

However, it is clear from Fig. 4 that, in contrast to the case of the β-dicarbonyl compound, a simple correlation was not observed. These results shown that the pK_a value is not a decisive measure of the nucleophilic reactivity of a carbanion in the coupling reaction.

TABLE 3. RATE CONSTANTS OF THE COUPLING REACTION OF DIAZOBENZENE-4-SULFONIC ACID WITH VARIOUS ACTIVE METHYLENE COMPOUNDS (20°C, μ: 0.25)

Exp. No.	Active methylene compound	pK_a	k_2 (l/mol·min)	pH
18	$ClCH_2COCH_3$	13.57$^{a)}$	8.82×10^7	6.2—7.2
19	$CNCH_2CONH_2$	13.45	2.06×10^9	5.2—6.2
20	$ClCH_2COCH_2Cl$	12.88$^{a)}$	2.43×10^8	5.8—6.8
21	$CH_3SO_2CH_2SO_2CH_3$	12.32 (12.50$^{b)}$)	3.10×10^7	6.2—7.2
22	$C_2H_5SO_2CH_2SO_2C_2H_5$	11.97	1.97×10^6	6.2—7.2
23	$CNCH_2COOC_2H_5$	11.4	1.6×10^8	4.3—5.2
24	$CNCH_2CN$	11.01 (11.16$^{a)}$)	4.09×10^8	2.8—4.7
25	$NO_2CH_2COOC_2H_5$	5.62 (5.82$^{c)}$)	1.29×10^3	3.7—4.7
26		7.15$^{d)}$	3.99×10^6	2.0—2.9
27		6.65$^{e)}$	1.15×10^6	2.0—2.9
28		4.49	8.21×10^3	2.9—3.7

a) F. Hashimoto, G. Tanaka, and S. Nagakura, *J. Mol. Spectrosc.*, **10**, 401 (1963).
b) W. Walter and H. L. Wiedemann, *Ann. Chem.*, **685**, 29 (1965).
c) Ref. 15. d) Ref. 11. e) Ref. 12.

[16)] Y. Hashida, I. Shimoda, S. Sekiguchi, and K. Matsui, *Kogyo Kagaku Zasshi*, **74**, 73 (1971).

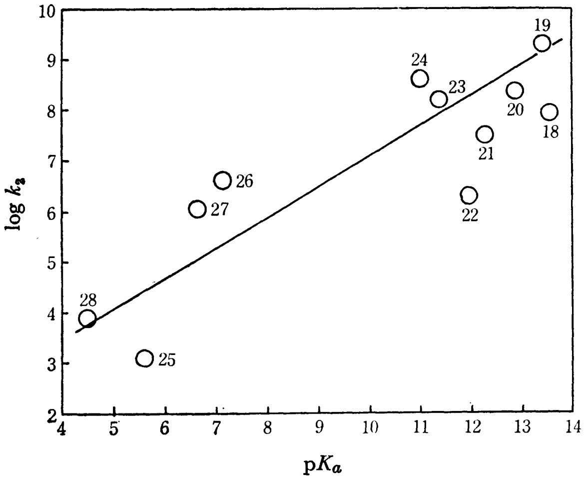


Fig. 4. Relation between pK_a values and rate constants (k_2) for the reaction of diazobenzene-4-sulfonic acid with various active methylene compounds. (The numbers refer to the compounds as listed in Table 3. The line here is drawn to same as that in Fig. 3.)

In general, there is no theoretical reason to expect a close parallelism between the nucleophilicity and the basicity,[17-9] since the nucleophilicity reflects a kinetic phenomenon, while the basicity is concerned with an equilibrium phenomenon. Nevertheless, it may be pointed out that the nucleophilicity is fairly well correlated with the basicity, and good correlations have been obtained by restricting nucleophilic reagents with a similar limited structure, such as substituted anilines or phenols.[2] However, with nucleophilic reagents with different structures, a close parallelism between basicity and nucleophilicity has not been found to hold;[21] the deviations from the line are usually explained by such factors as the polalizability, the steric effect, and the α-effect[22]

The above generalization fits our results. Within β-dicarbonyl compounds or p-substituted phenols, the reactivity was found to correlate well to the pK_a scale, whereas only an unsatisfactory linear relation has been observed over the wide range of active methylene compounds examined, as is shown in Table 3. These results can be explained by assuming that, in the former, the influencing factors on reactivity other than the pK_a value are the same, while in the latter cofactors exert different effects on the reaction rate. It is not easy to account for the deviation from the pK_a-log k_2 relationship. Unfortunately, there are not sufficient data available on the reactivities of a series of carbanions. Therefore, it is not apparent that the order of reactivity of carbanions illustrated in Figs. 3 and 4 is applicable to other reactions. This problem is now under investigation.

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17) J. Miller, "Aromatic Nucleophilic Substitution," Elsevier Publishing Company, Amsterdam (1968), p. 180.

18) C. K. Ingold, "Structure and Mechanism in Organic Chemistry," Cornell University Press., Ithaca and London (1969), p. 448.

19) J. E. Leffler and E. Grunwald, "Rates and Equilibria of Organic Reaction," translated ed., by Y. Tsuno, M. Sawada, N. Shimizu, and T. Fujii, Hirokawa Shoten, Tokyo (1968), p. 227.

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

21) R. G. Pearson, H. Sobel, and J. Songstad, *J. Amer. Chem. Soc.*, **90**, 319 (1968).

22) J. O. Edward and R. G. Pearson *ibid.*, **84**, 16 (1962).