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Solvent Effects in Diazo-coupling Reactions

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The kinetics of the diazo-coupling reactions of benzenediazonium fluoroborates with 1,3,5-trimethoxybenzene and 2-naphthol have been studied in non-aqueous media including both protic and dipolar aprotic solvents. In the case of the reaction with 1,3,5-trimethoxybenzene, no significant solvent effect on the reaction rate was observed. However, in the case of the reaction with 2-naphthol, the reaction rate was affected markedly by the solvent; in dipolar aprotic solvents, the reaction proceeded much faster than in protic solvents. The observed results are interpreted in terms of the difference in solvation toward the naphtholate ion.

Generally, diazo-coupling reactions are carried out in an aqueous medium. The mechanisms of these reactions and the reactivities of the reactants have been extensively studied kinetically.[1] However, little is known about the solvent effects on the reaction rate. Recently, a kinetic study of the coupling reactions of *N,N*-dimethylaniline in several dipolar aprotic solvents (nitromethane, acetonitrile, and sulfolane) has been reported by Penton *et al.*,[2] who showed that no significant solvent effect was observed.

In this paper, we wish to report the solvent effects on the reactions of diazonium salts with 1,3,5-trimethoxybenzene and 2-naphthol.

Experimental

Reagents. Commerical 1,3,5-trimethoxybenzene and 2-naphthol were recrystallized from ethanol and water respectively. *m*-Nitrobenzenediazonium fluoroborate and benzenediazonium fluoroborate were prepared by the usual method[3] and dried under a vacuum over phosphorus pentoxide in the dark.

Solvents. The methanol was dried with calcium oxide and fractionally distilled. The formic acid was twice fractionally distilled. The acetic acid was purified according to the method of MacInnes *et al.*[4] The propionic acid was dried over anhydrous sodium sulfate and fractionally distilled. The nitromethane and acetonitrile were purified by drying over phosphorus pentoxide and fractionally distilled. The dimethyl sulfoxide was purified by distillation on sodium hydroxide. The dimethylformamide was purified according to the method of Clare.[5]

Kinetic Measurements. The rates were measured by following the increase in the optical density of the azo compound formed with the lapse of time using a Hitachi 124-type spectrophotometer thermostated at 20 °C. As a large excess of the substrate was always present, the reactions followed a pseudo-first-order relationship (1):

$$k't = \ln \frac{E_\infty}{E_\infty - E_t} \tag{1}$$

where E_∞ and E_t denote the optical densities at an infinite time and at time t respectively. The rate constants thus obtained were constant up to more than 80% of the reaction.

Reaction with 1,3,5-Trimethoxybenzeme: To 100 ml of a solution of 1,3,5-trimethoxybenzene (2×10^{-3}M), was added 1 ml of a solution of *m*-nitrobenzenediazonium salt (4×10^{-3}M). Aliquots of the reaction mixture were pipetted into a thermostated spectrophotometric cell at 20 °C, and the optical density was measured at the absorption maximum of the azo compound.

Reaction with 2-Naphthol: Because of the dependence of the apparent rate constant (k') on the solvent acidity, all the kinetic measurements were carried out in appropriate buffer solutions. A reaction mixture containing 2-naphthol ($1—5 \times 10^{-3}$M) and appropriate buffer reagents was divided into two parts. One of the parts was used for the kinetic measurement in a manner similar to that described in the reaction of 1,3,5-trimethoxybenzene. The 475 mμ wavelength was monitored for an increase in the optical density of the azo compound. The other part was used for the measurement of the acidity function (H_-) using Eq. (2), by adding an appropriate indicator; the ionization ratio of an indicator was measured spectrophotometrically.

$$H_- = \mathrm{p}K_a + \log \mathrm{R} \tag{2}$$

$\mathrm{p}K_a$: Ionization constant of an indicator in a given solvent
R: Ionization ratio for an indicator in a given solvent

Table 1 lists the indicators employed and their $\mathrm{p}K_a$ values. The kinetic results are summarized in Tables 2, 3, 4, and 5.

In an aqueous medium, the rates were measured as follows: bacause of the low solubility of the azo compound, 10 ml portions of the sample solution were withdrawn from the reaction mixture at definite time intervals and added to 5 ml of a 2 M HCl solution in order to stop the reaction. The solution was then diluted to 25 ml with methanol, and the extinction was measured.

$\mathrm{p}K_a$ *Measurements.* The $\mathrm{p}K_a$ values of 2-naphthol in organic solvent were determined by the indicator method using Eq. (3);[6] the ratio of the acidic to the basic form of an indicator and 2-naphthol was determined spectrophotometrically.

$$\mathrm{p}K_a = \mathrm{p}K_I + \log \frac{C_{Ib} \times C_{Na}}{C_{Ia} \times C_{Nb}} \tag{3}$$

$\mathrm{p}K_a$: $\mathrm{p}K_a$ value of 2-naphthol

Table 1. $\mathrm{p}K_a$ values of indicators

Indicator	Neutral red	Brom cresol green	Brom cresol green	Brom phenol blue
Solvent	Acetonitrile	Dimethyl sulfoxide	Dimethylformamide	Methanol
$\mathrm{p}K_a$	15.6[a]	7.4[b]	8.3[c]	8.9[d]

a) I. M. Kolthoff, M. K. Chantoni, Jr., and S. Bhowmik, *Anal. Chem.*, **39**, 315(1967). b) I. M. Kolthoff and T. B. Reddy, *Inorg. Chem.*, **1**, 189 (1962). c) Ref. (5). d) I. M. Kolthoff, *J. Amer. Chem. Soc.*, **60**, 2516 (1938).

TABLE 2. APPARENT RATE CONSTANTS FOR THE REACTION OF BENZENEDIAZONIUM FLUOROBORATE WITH 2-NAPHTHOL IN METHANOL AT 20 °C
(Ar–$\overset{+}{N}_2$: 3×10^{-5} M, Ar–OH: 2.5×10^{-3} M)

Buffer	AA(0.007M)– AAS(0.007M)[a]	AA(0.02M)– AAS(0.01M)	NBA(0.01M)– NBAS(0.01M)[b]
H_-	9.24	8.79	8.43
k'(min^{-1})	3.48	1.58	0.708

a) AA and AAS denote acetic acid and its sodium slat respectively. b) NBA and NBAS denote *p*-nitrobenzoic acid and its sodium salt respectively.

TABLE 3. APPARENT RATE CONSTANTS FOR THE REACTION OF BENZENEDIAZONIUM FLUOROBORATE WITH 2-NAPHTHOL IN DIMETHYLFORMAMIDE AT 20 °C
(Ar–$\overset{+}{N}_2$: 3×10^{-5} M, Ar–OH: 3.2×10^{-3} M)

Buffer	NB(0.004M)– NBS(0.001M)[a]	NB(0.008M)– NBS(0.002M)	DNB(0.002M)– DNBS(0.002M)[b]	DNB(0.004M)– DNBS(0.002M)
H_-	9.02	8.72	8.07	7.80
k'(min^{-1})	1.71	0.781	0.178	0.0762

a) NB and NBS denote *p*-nitrobenzoic acid and its sodium salt respectively. b) DNB and DNBS denote 3,5-dinitrobenzoic acid and its sodium salt respectively.

TABLE 4. APPARENT RATE CONSTANTS FOR THE REACTION OF BENZENEDIAZONIUM FLUOROBORATE WITH 2-NAPHTHOL IN DIMETHYL SULFOXIDE AT 20 °C
(Ar–$\overset{+}{N}_2$: 3×10^{-5} M Ar–OH: 2.5×10^{-3} M)

Buffer	DNB(0.004M)– DNBS(0.01M)[a]	DNB(0.01M)– DNBS(0.01M)	DNB(0.01M)– DNBS(0.005M)	DMB(0.01M)– DMBS(0.004M)	DNB(0.01M)– DNBS(0.002M)
H^-	8.20	7.63	7.26	7.15	6.77
k'(min^{-1})	0.117	0.0495	0.0247	0.0194	0.0109

a) DNB and DNBS denote 3,5-dinitrobenzoic acid and its sodium salt respectively.

TABLE 5. APPARENT RATE CONSTANTS FOR THE REACTION OF BENZENEDIAZONIUM FLUOROBÒRATE WITH 2-NAPHTHOL IN ACETONITRILE AT 20 °C (Ar–$\overset{+}{N}_2$: 3×10^{-5} M Ar–OH: 1.25×10^{-3} M)

Buffer	DNB(0.003M)– DNBT(0.002M)[a]	DNB(0.0035M)– DNBT(0.002M)	DNB(0.005M)– DNBT(0.002M)	DNB(0.007M)– DNBT(0.002M)
H_-	16.06	15.67	15.29	15.04
k'(min^{-1})	0.928	0.331	0.154	0.0795

a) DNB and DNBT denote 3,5-dinitrobenzoic acid and its tetrabutylammonium salt respectively.

TABLE 6. pK_a VALUES FOR PHENOL AND 2-NAPHTHOL AT 20 °C

Acid	pK_a(H_2O)	pK_a(MeOH)	pK_a(DMF)	pK_a(DMSO)	pK_a(MeCN)
Phenol	—	14.3 (14.2)[a]	—	16.4 (16.4)[b]	(27.2)[b]
2-Naphthol	9.51	13.8	14.5	16.2	27.0
Indicator	—	14.0[c] (Thymol blue)	13.85[d] (*m*-Nitrophenol)	15.3[b] (Thymol blue)	27.2[b] (Thymol blue)

a) B. D. England and D. A. House, *J. Chem. Soc.*, **1962**, 4421. b) I. M. Kolthoff and M. K. Chantonni, *J. Amer. Chem. Soc.*, **90**, 23 (1968). c) I. M. Kolthoff, *ibid.*, **60**, 2516 (1938). d) S. M. Petrov and Yu. I. Umanskii, *Zh. Fiz. Khim.*, **41**, 1374 (1967).

pK_I: pK_a value of an indicator

C_{Ia}, C_{Ib}: Concentrations of the acidic and basic forms of an indicator respectively.

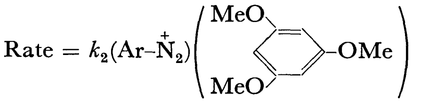
C_{Na}, C_{Nb}: Concentrations of the acidic and dissociated forms of naphthol respectively

The results obtained are summarized in Table 6.

As a check of the method described above, the pK_a value of phenol was also measured. As is evident from Table 6, there is no disagreement between the pK_a values of phenol in the present work and the reference.

Results and Discussion

Reaction with 1,3,5-Trimethoxybenzene. The first-order dependence of the reaction rate on the concentration of a diazonium salt may be apparent from the applicability of Eq. (1) to this reaction; the reaction rate (k') also showed a first-order dependence on the substrate concentration. Thus, the reaction rate can be expressed by Eq. (6), showing that this is a reaction between a cation and an uncharged molecule:



$$\text{Rate} = k_2(\text{Ar-}\overset{+}{\text{N}}_2)(\text{(MeO)}_3\text{C}_6\text{H}_3) \qquad (6)$$

The reaction rates in the presence of a base (pyridine, 0.2 M) were also measured in aqueous media. However, no base catalysis was observed, suggesting that the rate-determining step involves a bond formation between the diazonium ion and the substrate, followed by a fast deprotonation to give the final product.[1)]

The second-order rate constants (k_2) can be obtained by dividing the k' values by the stoichiometric concentrations of the substrate. Table 7 lists the k_2 values thus obtained for the reactions of 1,3,5-trimethoxybenzene with *m*-nitrobenzenediazonium fluoroborate in seven solvents.

TABLE 7. RATE CONSTANTS FOR THE REACTION OF *m*-NITROBENZENEDIAZONIUM FLUOROBORATE WITH 1,3,5-TRIMETHOXYBENZENE AT 20 °C

No.	Solvent	k_2(l·mol^{-1}·min^{-1})
1	H_2O	11.7
2	CH_3OH	7.0
3	HCOOH	29.7
4	CH_3COOH	20.6
5	CH_3CH_2COOH	1.2
6	CH_3NO_2	7.7
7	CH_3CN	4.9

It is known that protic and dipolar aprotic solvents differ in their ability to solvate a cation,[7)] and that the reactions between cations and neutral molecules are considerably affected by the solvent employed.[8)] The results in Table 7 show, however, that the rate was affected slightly not only by protic solvents (No. 1—5), but also by dipolar aprotic solvents (No. 6—7). In addition, there is no significant correlation between the reaction rates and any common physical property of the solvents, such as the dielectric constant or the dipole moment. On the other hand, within a series of protic solvents of similar structures, the rate was faster in a more polar solvent in this order; $H_2O > CH_3OH$ or $HCOOH > CH_3COOH > CH_3CH_2COOH$. These results are similar to those of the coupling with aromatic amine.[2)] Thus, it may be concluded that the rate of the coupling of diazonium salt with an uncharged molecule is practically independent of the solvent, regardless of the kind of substrate. These results may be interpreted by assuming that neither the diazonium ion nor the substrate is strongly solvated and that the transition state would not involve a significant solvent reorganization, as has been postulated by Penton *et al.*[2)]

Reaction with 2-Naphthol. It is well known that, in the coupling reaction with naphthol in an aqueous solution, the reactive species of the substrate is the naphtolate anion;[1)] however, the reactive form in non-aqueous media has not been investigated. Therefore, it is necessary at first to decide the kinetic equation for the reactions in non-aqueous media.

In all the solvents employed, the rate (k') showed a good first-order dependence on the substrate concentration at a given solvent acidity. Tables 2, 3, 4, and 5 (see Experimental Section) list the dependences of the apparent rate constant (k') on the solvent acidity function (H_-) with methanol, dimethylformamide, dimethyl sulfoxide, and acetonitrile respectively. When the logarithms of the rate constants (k') are plotted against the acidity functions (H_-) of the solvents, a straight line with a slope of unit[9)] is obtained in every case, suggesting that the naphtholate ion is the reactive species in the reactions in these solvents.

Table 8 lists the dependences of the rate constant (k_2 in Eq. (7)) on the ionic strength of the medium.

TABLE 8. DEPENDENCE OF RATE CONSTANT FOR THE REACTION OF BENZENEDIAZONIUM FLUOROBORATE WITH 2-NAPHTHOL IN DIMETHYL SULFOXIDE ON IONIC STRENGTH (20 °C)

Ionic strength	k_2(l·mol^{-1}·min^{-1})
0.01	7.7×10^9
0.05[a)]	4.4×10^9
0.10[a)]	4.0×10^9
0.25[a)]	3.3×10^9
0.50[a)]	3.0×10^9

a) Ionic strength was adjusted by the addition of potassium nitrate.

As is evident from Table 8, a negative salt effect was observed, confirming that these reactions are cation-anion combination reactions.[10,11)] Thus, the kinetic expression for the coupling reactions in non-aqueous media is given by Eq. (7), which is consistent with that in an aqueous solution;[1)]

$$\text{Rate} = k_2(\text{Ar-}\overset{+}{\text{N}}_2)(\text{Ar}'\text{-O}^-) \qquad (7)$$

Table 9 lists the second-order rate constants (k_2) which were calculated using Eq. (7) by dividing the first-order rate constant (k') by the concentration of the naphtholate ion under the given kinetic conditions. The k_2 values thus obtained were practically independent of the solvent acidity.

TABLE 9. RATE CONSTANTS FOR THE REACTION OF BENZENEDIAZONIUM FLUOROBORATE WITH 2-NAPHTHOL AT 20 °C

No.	Solvent	k_2(l·mol^{-1}·min^{-1})
8	H_2O	4.7×10^5
9	MeOH	6.0×10^7
10	Me_2NCOH	1.6×10^8
11	$(Me)_2SO$	7.7×10^9
12	MeCN	3.1×10^{13}

The results in Table 9 lead to the following conclusions: in contrast to the coupling reaction with 1,3,5-trimethoxybenzene, in the reaction with the naphtholate ion the solvent effects are significant and the reaction is very fast in dipolar aprotic solvents. These results are understandable in light of the following considerations.

The results in Table 6 indicate that there is no need to consider the different solvation of the diazonium ion. Furthermore, the solvation in the transition state must be small, because this reaction is a cation-anion combination reaction and in the transition state the charge is considered to have almost disappeared.[1] Therefore, the rate change shown in Table 9 is considered to depend mainly on the difference in solvation energy toward the naphtholate ion.

It is well known that an anion is solvated in protic solvents by the general hydrogen-bonding interaction;[7] consequently, the substrate is stabilized and the rate is slow in the hydroxylic solvents, as can be seen in Table 9. The increase in the rate on transfer from water to methanol may be understood from the difference in the hydrogen-bonding capacity of these solvents.[12] On the other hand, the fact that anions are poorly solvated in dipolar aprotic solvents[7] is considered to be responsible for the rapid reactions in these solvents.

It is interesting that, despite the similar physical properties of dimethyl sulfoxide and acetonitrile, a large difference was observed between the rate constants of the reactions in these solvents; the reactivity sequence in Table 9 is in accord with the order of the pK_a values of naphthol (Table 6) in these solvents. The results suggest that a naphthol generates a reactive naphtholate ion in a solvent in which it indicates a high pK_a value. However, a detailed discussion of these results must wait until later.

References

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4) D. A. MacInnes and T. Schedlovsky, *J. Amer. Chem. Soc.*, **54**, 1429 (1932).

5) B. W. Clare, D. Cook, E. C. F. Ko, Y. C. Mac, and A. J. Parker, *ibid.*, **88**, 1911 (1966).

6) In a given solvent, the acidity functions are expressed by Eqs. (4) and (5):

$$H_- = \mathrm{p}K_\mathrm{I} + \log \frac{C_\mathrm{Ib}}{C_\mathrm{Ia}} \tag{4}$$

$$H_- = \mathrm{p}K_\mathrm{a} + \log \frac{C_\mathrm{Nb}}{C_\mathrm{Na}} \tag{5}$$

Eq. (3) is obtained by taking Eqs. (4) and (5) as equal.

7) For recent reviews, see, a) A. J. Parker, *Quart. Rev.* (London), **1962** 163 b) A. J. Parker, *Chem. Rev.*, **69**, 1 (1969); c) A. J. Parker, "Advances in Physical Organic Chemistry," Vol. 5, ed. by V. Gold, Academic Press, New York (1967), p. 173. d) C. D. Ritchie, *Accounts Chem. Res.* **5**, 348 (1972).

8) E. D. Hughes and D. J. Whitingham, *J. Chem. Soc.*, **1960**, 806

9) In the case of dimethyl sulfoxide, the slope of the line is 0.85. This small deviation from unit, however, may be ascribed to the change of the ionic strength of the reaction medium.

10) H. Zollinger, *Helv. Chim. Acta.*, **36**, 1723 (1953).

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