REACTIVITY OF NUCLEOPHILES IN DIMETHYL SULFOXIDE AND ITS COMPARISON WITH NUCLEOPHLIC REACTIVITY IN PROTIC MEDIUM

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Reactions of 2,4-dinitrophenyl acetate and 2,4-dinitrofluorobenzene as model substrates with 12 nucleophiles have been studied in dimethyl sulfoxide. The rate constants obtained have been discussed with regard to the nucleophilic reactivity differences in dimethyl sulfoxide and protic solvents inclusive of the different manifestations of the charge of nucleophiles. The applicability of an earlier-suggested correlation equation to the data obtained has been verified. The reaction medium markedly affects the reactivity of nucleophiles, the effect of charge being substantially greater in aprotic solvents (electrostatic interaction) than in protic ones (solvation). In spite of these differences the correlation with application of an empirical nucleophilicity scale suggested earlier is satisfactory, the regression coefficients obtained reflect changes in the nature of medium.

The reactivity of nucleophiles is strongly affected by the solvent used[1]. A particularly significant change of medium is connected with a transition from protic to dipolar aprotic solvents[2]. The dipolar aprotic solvents in which nucleophilicity was most frequently studied include dimethylformamide (the reactions on aromatic[3] and aliphatic carbon atom[4]) and dimethyl sulfoxide (the reactions on aliphatic[5], carbonyl[6], and aromatic carbon atoms[7,8], and those with organic cations[9]). Most of the studies carried out, however, do not allow comparisons because the results were not obtained with the same substrates, sets of nucleophiles, and methods.

The aim of this present communication is to investigate the reactivity of nucleophiles in a dipolar aprotic solvent (dimethyl sulfoxide was used) using the same substrates and, predominantly, the same nucleophiles as in the previous work[10] dealing with the nucleophilicity in protic media. The main attention was focused on possible comparison of nucleophilic reactivity from the standpoint of solvent change, operation of charge, and quantitative description of the data obtained.

EXPERIMENTAL

The preparation and purification of substrates and some of the nucleophilic agents are described in the previous communication[10]. The other nucleophiles used were purified as follows: potas-

sium rhodanide, sodium acetate, and thiourea were recrystallized from water, imidazole was recrystallized from benzene, and 1-butylamine was redistilled before use. The ammonia solution was obtained by introducing dry gaseous ammonia into dimethyl sulfoxide. Its concentration was determined acidimetrically. Commercial dimethyl sulfoxide (pre-dried, p.a., Merck, F.R.G.) was purified in a known way[11] and kept over a molecular sieve A4.

The kinetic measurements were carried out spectrophotometrically using a Specord UV VIS and a Durrum D-150 apparatus. In the case of 2,4-dinitrofluorobenzene we monitored the absorbance increase of the products formed (the experimental wavelengths are given in Table I), in the case of 2,4-dinitrophenyl acetate the absorbance increase of the 2,4-dinitrophenoxide formed was measured at 440 nm. The kinetic measurements were repeated with different (4—11) concentrations of nucleophiles. Our own programs[12] were used to calculate the observed pseudo-first-order rate coefficients from the absorbance–time dependences. Its variance (the ratio of standard deviation to the value of pseudo-first-order rate coefficient) was less than 3% in all the cases. The dependence of this rate coefficient on the concentration of nucleophile was treated by linear regression to obtain the second-order rate constant (as the slope of this dependence). The identity of the reaction products from 2,4-dinitrofluorobenzene and nucleophiles was confirmed by comparison of their electronic spectra with the spectra of the authentic substances prepared synthetically (Table I).

RESULTS AND DISCUSSION

The values of calculated second-order rate constants of the reactions of the respective nucleophiles and substrates are given in Table II. The dependence of logarithms of rate constants of the reactions of nucleophiles with 2,4-dinitrophenyl acetate in dimethyl sulfoxide on the basicity $(pK_a$ in water[13]) of the nucleophiles (Fig. 1) shows that the points form three separate groups. The first linearly arranged group includes uncharged nitrogen nucleophiles. The second straight line with a smaller slope includes predominantly charged (except thiourea) nucleophiles with various nucleophilic atoms. The smaller slope can be explained by the decrease in hardness of the

TABLE I

Melting points and wavelenths of absorption maxima of products of reactions of 2,4-dinitrofluorobenzene with nucleophiles

| Nucleophile | Product | M.p., °C | | λ_{max}, nm | Ref. |
		literature	experiment		
Aniline	N-phenyl-2,4-dinitroaniline	156—157	161—161·5	380	16
Ammonia	2,4-dinitroaniline	180	178·5—179·5	356	17
Azide	2,4-dinitroazidobenzene	67—68	64—66	400	18
Morpholine	2,4-dinitrophenylmorpholine	118—119	118—119	395	19
Piperidine	2,4-dinitrophenylpiperidine	93	93—94	405	20
Imidazole	2,4-dinitrophenylimidazole	146—148	151—151·5	335	21

nucleophiles due to the presence of charge. To a certain extent this would also explain the involvement of thiourea. Generally anions are more reactive, which indicates a more distinct manifestation of charge in aprotic solvents as compared with protic ones[10]. The position od iodide ion can be explained either by the anomalous behaviour of halides observed as early as in the general parametrization of nucleophilicity[14] or by inappropriateness of the pK_a value determined in water[13]

TABLE II

Second-order rate constants $(k, 1 \, mol^{-1} \, s^{-1})$ and their standard deviations (s) for reactions of substrates with nucleophiles

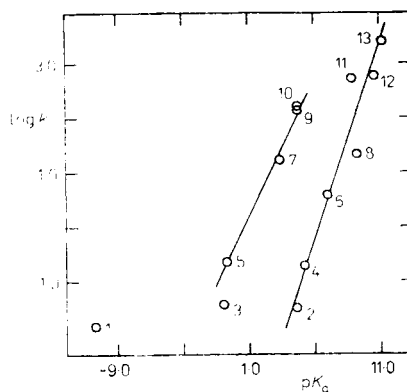| No.	Nucleophile	2,4-Dinitrophenyl acetate		2,4-Dinitrofluorobenzene	
		k	s_k	k	s_k
1	iodide	$1\cdot50 \cdot 10^{-2}$	$3\cdot01 \cdot 10^{-4}$	—	—
2	aniline	$3\cdot24 \cdot 10^{-2}$	$3\cdot89 \cdot 10^{-4}$	$1\cdot91 \cdot 10^{-2}$	$5\cdot40 \cdot 10^{-4}$
3	thiourea	$3\cdot77 \cdot 10^{-2}$	$2\cdot84 \cdot 10^{-3}$	—	—
4	pyridine	$1\cdot92 \cdot 10^{-1}$	$2\cdot26 \cdot 10^{-3}$	—	—
5	rhodanide	$2\cdot27 \cdot 10^{-1}$	$2\cdot10 \cdot 10^{-2}$	$8\cdot11 \cdot 10^{-2}$	$1\cdot88 \cdot 10^{-3}$
6	imidazole	$3\cdot72$	$7\cdot36 \cdot 10^{-2}$	$1\cdot74 \cdot 10^{-1}$	$8\cdot70 \cdot 10^{-3}$
7	nitrite	$1\cdot68 \cdot 10^{1}$	$8\cdot60 \cdot 10^{-1}$	$1\cdot14 \cdot 10^{-1}$	$2\cdot29 \cdot 10^{-3}$
8	ammonia	$2\cdot10 \cdot 10^{1}$	$6\cdot63 \cdot 10^{-1}$	$2\cdot60$	$4\cdot80 \cdot 10^{-2}$
9	acetate	$1\cdot36 \cdot 10^{2}$	$1\cdot89$	$3\cdot92 \cdot 10^{1}$	$2\cdot52$
10	azide	$1\cdot62 \cdot 10^{2}$	$4\cdot99$	$1\cdot52 \cdot 10^{3}$	$1\cdot83 \cdot 10^{2}$
11	morpholine	$5\cdot17 \cdot 10^{2}$	$8\cdot03$	$2\cdot02 \cdot 10^{1}$	$7\cdot75 \cdot 10^{-1}$
12	1-butylamine	$5\cdot81 \cdot 10^{2}$	$1\cdot10 \cdot 10^{1}$	$9\cdot16 \cdot 10^{1}$	$2\cdot00$
13	piperidine	$2\cdot51 \cdot 01^{3}$	$1\cdot67 \cdot 10^{1}$	$6\cdot26 \cdot 10^{2}$	$2\cdot02 \cdot 10^{1}$

FIG. 1

Dependence of reactivities of nucleophiles $(\log k)$ in their reactions with 2,4-dinitrophenyl acetate in dimethyl sulfoxide on basicity (pK_a) of the nucleophiles. For numbers of the nucleophiles see Table II

(the levelling effect), which is more likely. Formally identical is also the dependence for 2,4-dinitrofluorobenzene, which indicates certain generality of the conclusions made.

The correlation between the reactivities of nucleophiles in dimethyl sulfoxide and in aqueus methanol is very low. The correlation coefficient between the nucleophilic reactivities (represented as the logarithm of rate constant) for the reactions of 2,4-dinitrophenyl acetate in dimethyl sulfoxide (DNFA/DMSO) and in aqueous methanol (DNFA/MeOH) is 0·72, that for the reactions of 2,4-dinitrofluorobenzene in dimethyl sulfoxide (FDNB/DMSO) and in aqueous methanol (FDNB/MeOH) being 0·65. This phenomenon indicates different solvation of the reactants in the reactions studied. Generally, the reactivity of nucleophiles in dimethyl sulfoxide, as compared with their reactivity in aqueous methanol, is in average by about one order of magnitude higher for 2,4-dinitrophenyl acetate and by two orders higher for 2,4-dinitrofluorobenzene. In dimethyl sulfoxide the reactivity of ionic nucleophiles is markedly increased, the reactivity order of uncharged nucleophiles being the same in the two media (except for ammonia in the reaction with 2,4-dinitrofluorobenzene − it is distinctly more reactive in dimethyl sulfoxide). The reactivity increase of both ionic nucleophiles and ammonia on going from aqueous methanol to dimethyl sulfoxide is caused by decreased solvation of these nucleophiles. In contrast to the reactions in aqueous methanol[10], there exists a roughly linear relation between the behaviour of nucleophiles to 2,4-dinitrophenyl acetate and to 2,4-dinitrofluorobenzene in dimethyl sulfoxide with a slope near to one $(0·98 \pm 0·21)$ and the correlation coefficient $r = 0·87$. The non-linearity of this dependence in aqueous methanol is due to different solvation of the transition states as compared with the solvation of reactants in the reaction of 2,4-dinitrophenyl acetate and 2,4-dinitrofluorobenzene with nucleophiles. The different nucleophilicities of reagents in the reactions with the two substrates represent the observed consequence.

On the basis of the data obtained and with the use of multiple linear regression we tried to verify the validity of the empirical equation (*1*) suggested in the previous report[14].

$$\log k = a_0 + a_1 \cdot ND + a_2 \cdot PD + a_3 \cdot Z \qquad (1)$$

In Eq. (*1*) k represents the rate constant of the given reaction, ND is a parameter expressing the affinity to a general nucleus, PD expresses the affinity of nucleophile to the proton, and Z is the charge of nucleophile. Table III gives the statistically significant values of regression parameters for Eq. (*1*). The values of coefficients of multiple correlation are comparable with those obtained for other processes involving nucleophiles[14]. The determination coefficient R^2 explains the variability of $\log k$ up to $82-92\%$ in the individual systems. The experimental error variability of $\log k$ determined from a long-term monitoring is about 5%. Hence the regression according to Eq. (*1*) does not reflect all non-error variability but it definitely reflects

its substantial part due to general behaviour of nucleophiles[14]. Hence the regression coefficients obtained can become a basis for interpretation of the experiments carried out.

Table III shows that the effect of charge in the reactions of 2,4-dinitrophenyl acetate is changed on going from aqueous methanol to dimethyl sulfoxide. The positive value of a_3 parameter (the effect of charge) for the reactions of nucleophiles with 2,4-dinitrophenyl acetate (DNFA) in aqueous methanol indicates an increased solvation of negatively charged nucleophiles and, hence, their lower reactivity. The negative value of this parameter in the reactions with 2,4-dinitrophenyl acetate in DMSO indicates a predominance of the positive interaction of the charge of anionic nucleophiles with the substrate dipole in this medium. A similar conclusion can be made also for the effect of charge on the reactions of 2,4-dinitrofluorobenzene (FDNB) in aqueous methanol and in DMSO. In aqueous methanol the parameter ND of Eq. (1) makes itself felt with this substrate, which reflects the predominance of the softness of nucleophiles. Its significance can be explained on the basis of the HSAB theory. The increased reactivity of soft nucleophiles is attained by a combination of hard solvent (methanol, which interacts less with softer nucleophiles) and soft substrate (FDNB, which is a softer substrate than DNFA and reacts more easily with softer nucleophiles).

The above discussion not only indicates a good quantitative description of experiments by means of Eq. (1), but also shows the ability of this equation to reflect the factors affecting nucleophilicity under certain reaction conditions. In comparison with the other correlations of experimental values of logarithms of rate constants (Table III), the correlation for the reactions of FDNB in DMSO is less close, the multiple correlation coefficient being $R = 0.76$. The low R value is due to the considerable difference between experimental and calculated rate constants for nitrite.

TABLE III
Values of statistically significant regression coefficients (a_i) and their standard deviations (a_{ai}) for Eq. (1) (n number of points, R selection coefficient of multiple correlation, s residual standard deviation; for the meaning of other symbols see the text)

System	a_1	s_{a1}	a_2	s_{a2}	a_3	s_{a3}	n	R	s
DNFA/MeOH[a]	—	—	8.93	1.32	0.846	0.262	13	0.920	0.680
DNFA/DMSO	—	—	11.0	1.7	−3.00	0.68	12	0.906	0.843
FDNB/MeOH	13.6	1.30	—	—	0.637	0.251	13	0.961	0.500
FDNB/DMSO[b]	—	—	12.9	1.9	−4.77	0.86	9	0.939	0.745

[a] The iodide anion was excluded from the regression; [b] the nitrite anion was excluded from the regression.

This deviation can be caused by its ambident character. Nitrite reacts with FDNB by its oxygen atom[15], whereas in the empirical equation (*1*) the values of parameters were derived predominantly from the systems involving the nitrogen atom as the reaction centre of nitrite[14]. When excluding the values for nitrite from the correlation we can increase the multiple corelation coefficient up to 0·939 (see Table III).

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