

A STUDY OF NUCLEOPHILICITY IN SELECTED SYSTEMS

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Kinetic studies have been carried out of the reactions of 15 nucleophiles with 2,4-dinitrophenyl acetate and 14 nucleophiles with 2,4-dinitrofluorobenzene in 52% (w/w) methanol at 25°C. The rate constant values obtained and literature data have been treated by the factor analysis. It has been found that the description of nucleophilicity at least needs two factors. The nucleophiles studied are divided into two groups (ionic and nitrogen-containing ones). In each group, the nucleophilic properties are affected by linear combination of both factors.

Nucleophilicity is defined as the ability of a nucleophile to use its free electron pair for formation of a new covalent bond¹. In contrast to the similarly defined basicity concept according to Lewis, the term "nucleophilicity" is used for description of the kinetic behaviour of the reagent. Therefore, the nucleophilicity is related to rate constants which form a basis for the parametrization in terms of extrathermodynamic relations². Out of the best known are the Brønsted relation³, the Swain-Scott equation⁴ and the relation derived therefrom⁵, the Edwards equation⁶, and the Ritchie relation⁷. The Brønsted relation³ correlates the reactivity of nucleophiles with their respective basicities by means of the pK_a values. The Swain-Scott equation⁴ is based on the empirical nucleophilicity scale obtained from the rate constants of the reactions of the nucleophiles with methyl bromide. The relations derived later from the Swain-Scott equation make use of methyl iodide or dichlorodipyridineplatinum(II) complex as the standard substrate⁵. The Edwards equation⁶ correlates the reactivity of nucleophiles with their basicity and polarizability. The Ritchie relation⁷ is a simple equation, the respective nucleophilicity scale being based on the reaction of the nucleophiles with *p*-nitromalachite green.

These papers and other communications have the drawback in that they only deal with nucleophilic reactions on a single substrate or on structurally similar substrates. In addition, these studies were carried out at different conditions, which makes mutual comparisons difficult.

The aim of our work, therefore, was to study the reactions of a series of nucleophiles at two different reaction centres (a carbonyl carbon and an aromatic carbon atoms) at the same reaction conditions and evaluate the results statistically.

EXPERIMENTAL

2,4-Dinitrophenyl acetate was prepared by the reaction of 2,4-dinitrophenol with acethanhydride⁸. The product was recrystallized from heptane, m.p. 70.5—71.5°C (ref.⁸ gives m.p. 72°C). 2,4-Dinitrofluorobenzene (International Enzymes Ltd., U.K.) was used without purification. Table I lists the nucleophiles studied. Sodium nitrite, sodium sulphite, sodium thiosulphate, potassium iodide, sodium azide, hydroxylamine hydrochloride, and phenol were commercial products and were used without further purification. Aniline, piperidine, morpholine, butylamine, thiophenol, and pyridine were redistilled before use. The concentrations of hydrogen peroxide solutions were determined manganometrically, those of hydrazine bromatometrically, and those of ammonia acidimetrically with hydrochloric acid.

The kinetic measurements (except for the reaction of 2,4-dinitrofluorobenzene with pyridine) were carried out spectrophotometrically with a Specord UV VIS apparatus (Zeiss) in 52% (w/w) aqueous methanol at pH 8.00 to 10.00 at ionic strength of 0.1 mol l⁻¹ (adjusted by addition of KCl). In the case of 2,4-dinitrophenyl acetate we followed the absorbance increases of 2,4-dinitrophenoxide, in the case of 2,4-dinitrofluorobenzene we followed the absorbance increases of the substitution products formed. From the data obtained we calculated the pseudo-first-order

TABLE I

The rate constants k (in l mol⁻¹ s⁻¹) with the standard deviations s_k and the relative reactivities for 2,4-dinitrophenylacetate (a_{DNFA}) and 2,4-dinitrofluorobenzene (a_{FDNB})

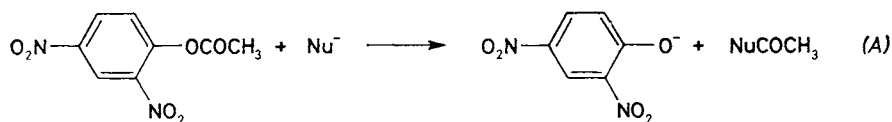
No.	Nucleophile	2,4-Dinitrophenylacetate			2,4-Dinitrofluorobenzene		
		$k \cdot 10^3$	$s_k \cdot 10^4$	a_{DNFA}	$k \cdot 10^3$	$s_k \cdot 10^4$	a_{FDNB}
1	Thiosulphate	3.97	5.44	0.000	—	—	—
2	Nitrite	9.79	9.02	0.076	0.591	0.506	0.000
3	Aniline	45.6	12.0	0.206	43.8	10.1	0.319
4	Iodide	79.0	71.5	0.253	—	—	—
5	Pyridine	201.0	48.3	0.332	1.43	1.25	0.066
6	Sulphite	278.0	542.0	0.359	675.0	171.0	0.521
7	Azide	546	400	0.416	107	42.4	0.385
8	Piperidine	2 840	443	0.459	80.0	20.8	0.346
9	Morpholine	10 400	2 180	0.666	509	136	0.500
10	Hydrazine	11 200	3 620	0.672	401	67.0	0.482
11	Thiophenolate	11 400	3 505	0.674	433 000	46 300	1.000
12	Hydroxylamine	16 400	5 150	0.704	21.2	13.9	0.265
13	Phenoxide	49 900	29 000	0.798	103	94.3	0.382
14	Anion of hydrogen peroxide	541 000	21 500	1.000	4 980	1 510	0.669
15	Ammonia	—	—	—	2.62	2.22	0.110
16	Methoxide ^a	—	—	—	14 500	—	0.748

^a The rate constant value for the reaction of methoxide with 2,4-dinitrofluorobenzene was assessed from ref.⁸.

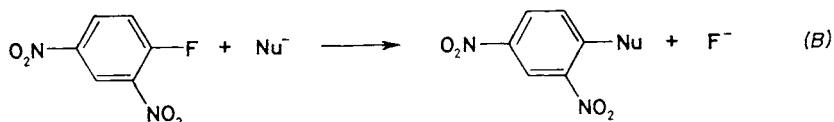
rate constant including the second-order rate constant of the nucleophilic substitution and the solvolysis rate constant of the given substrate. For each reaction of a nucleophile with substrate, we carried out 3—10 kinetic experiments with various concentrations of the nucleophile (the nucleophile to substrate concentration ratio was always at least 20 : 1) in the phosphate buffers whose pH was adjusted at the same value by means of an RTS 822 (Radiometer) pH-stabilizer. The rate of the reaction of pyridine with 2,4-dinitrofluorobenzene was carried out conductometrically by following the concentration increase of the fluoride ions released. In this case neither the ionic strength nor the pH value of the solutions used was adjusted.

RESULTS AND DISCUSSION

The nucleophilic substitution at carbonyl carbon atom of 2,4-dinitrophenyl acetate can be described by Eq. (A)



where Nu represents the nucleophilic agent. From the spectra of the products formed it was found that no observable attack of the nucleophile at aromatic carbon atoms took place. With 2,4-dinitrofluorobenzene the nucleophilic substitution is represented by Eq. (B).



The course of the reaction was verified by synthesis of the reaction products under conditions close to those of the measurements (see Table II).

According to ref.⁹, the reaction of 2,4-dinitrofluorobenzene with sodium azide is connected with the cyclization of the 2,4-dinitroazidobenzene formed to 5-nitrobenzofuroxane. Comparison of spectra of the latter compound prepared by thermal decomposition of 2,4-dinitroazidobenzene¹⁰ and of the reaction product from 2,4-dinitrofluorobenzene and sodium azide showed that this product does not undergo any observable decomposition to 5-nitrobenzofuroxane under the conditions of kinetic measurements. The reaction of 2,4-dinitrofluorobenzene with sodium nitrite gives 2,4-dinitrophenol, hence the reaction centre is at the oxygen atom in accordance with ref.¹¹. No reaction of the same substrate with iodide or thiosulphate was observed. In the reaction of 2,4-dinitrophenyl acetate with ammonia, the decomposition rate of this substrate only corresponds to its solvolysis rate in the given medium.

On the whole, the kinetic study concerns reactions of 15 nucleophiles with 2,4-dinitrophenyl acetate and 14 nucleophiles with 2,4-dinitrofluorobenzene. The dependence of the pseudo-first-order rate constants observed on the nucleophile concentration was treated by means of linear regression to obtain the slope whose value represents the second-order rate constant of the reaction between the nucleophile and substrate (Table I). These constants were used for calculation of relative nucleophilicity scales of the two substrates according to Eq. (1)

$$a = (\log k - \log k_{\min}) / (\log k_{\max} - \log k_{\min}), \quad (1)$$

TABLE II

The characteristics of products of the reactions of 2,4-dinitrofluorobenzene with nucleophiles

Nucleophile	Product	M.p., °C (lit.)	λ_{\max} nm	Ref.
Aniline	N-phenyl-2,4-dinitroaniline	155–156.5 (156–157)	360	17
Pyridine	N-(2,4-dinitrophenyl)pyridinium chloride	190–191 (191)	235	18
Azide	2,4-dinitroazidobenzene	64–66 (67–68)	305	19
Piperidine	N-(2,4-dinitrophenyl)piperidine	93–94 (93)	400	20
Morpholine	N-(2,4-dinitrophenyl)morpholine	118–119 (118–119)	375	21
Hydrazine	2,4-dinitrophenylhydrazine	199–201 (199–200)	360	22
Thiophenolate	2,4-dinitrodiphenyl sulphide	120–120.5 (117)	334	23
Hydroxylamine	2,4-dinitrophenylhydroxylamine	78–80 (80)	360	24
Phenoxide	2,4-dinitrodiphenyl ether	69–70 (70)	302	25
Ammonia	2,4-dinitroaniline	179–180 (180)	300	26
Ammonia	5-nitrobenzofuroxane	68–70 (71)	260, 390 ^a	27

^a The substance prepared by decomposition of 2,4-dinitroazidobenzene. The wavelength values of the maxima given in ref.²⁷ agree with the values mesured by us.

where a is the nucleophilicity value in the relative scale for the given nucleophile, k means the reaction rate constant of this nucleophile, and k_{\min} and k_{\max} are the rate constant values for the least and the most reactive nucleophiles, respectively. These relative nucleophilicity values obtained from Eq. (1) are given in Table I along with those for the reaction of methoxide with 2,4-dinitrofluorobenzene derived from literature data^{1,2}.

Hydrogen peroxide anion and thiophenolate anion were the most reactive reagents in the cases of 2,4-dinitrophenyl acetate and 2,4-dinitrofluorobenzene, respectively (Table I). This finding can be interpreted in terms of the concept of hard and soft acid and bases (HSAB)¹³. The carbonyl carbon atom of 2,4-dinitrophenyl acetate represents a harder centre than the aromatic carbon atom in 2,4-dinitrofluorobenzene. Therefore, 2,4-dinitrophenyl acetate tends to react better with HOO^- which is a harder nucleophile than thiophenolate anion.

The kinetic data obtained and those taken from literature were treated by means of factor analysis and principal component analysis^{14,15}. Out of the literature data (Table III) the following were selected for the treatment: the nucleophilicity scales from the Swain–Scott equation for methyl iodide (n_{MeI}) and dichlorodipyridineplatinum(II) complex (n_{Pt}) as standard substrates⁵, the polarizability scale E_n from the

TABLE III
The data used in the factor analysis

Nucleophile	$\log k_{\text{DNFA}}^a$	N_+^b	n_{Pt}^c	n_{MeI}^c	E_n^d
Thiosulphate	—	—	7.34	8.95	2.52
Nitrite	-0.275	3.04	3.22	5.35	1.73
Aniline	1.15	4.10	3.16	5.70	1.20
Iodide	—	—	5.46	7.42	2.06
Pyridine	2.17	5.00	3.19	5.23	1.20
Sulphite	—	7.90	5.79	8.53	2.57
Azide	1.76	7.60	3.58	5.78	1.58
Piperidine	4.58	6.11	3.13	7.30	—
Morpholine	3.68	5.25	—	—	—
Hydrazine	4.25	5.66	3.86	6.61	—
Thiophenolate	—	10.51	7.17	9.92	2.90
Hydroxylamine	3.45	5.05	3.85	6.60	—
Phenoxide	2.86	5.60	—	5.75	1.46
Anion of hydrogen peroxide	5.99	8.08	—	7.80	—
Ammonia	—	—	3.07	5.50	1.36
Methoxide	—	7.28	2.40	6.29	1.65

^a Ref. 16; ^b ref. 7; ^c ref. 5; ^d ref. 6.

Edwards equation⁶, the nucleophilicity scale N_+ from the Ritchie equation⁷, and logarithm of the rate constants of the reactions of 2,4-dinitrophenyl acetate with nucleophiles ($\log k_{\text{DNFA}}$) in aqueous medium¹⁶. From the correlation matrix (Table IV) it is obvious that the best correlation exists between the Ritchie's scale N_+ and our nucleophilicity scale for the reactions of 2,4-dinitrofluorobenzene in aqueous methanol, between the n_{Pt} and n_{MeI} scales (constructed at the same conditions and by means of the same methods), and between the kinetic data for the reactions of 2,4-dinitrophenyl acetate with nucleophiles in aqueous medium and our data about the corresponding reactions in aqueous methanol.

From position of the minimum at the Malinowski's IND function¹⁵ in the factor analysis of the source data (Table III) for all the nucleophiles it follows that at least two factors are necessary for the description of nucleophilicity. From the dislocation of the nucleophilicity scales in the space of these two factors (Fig. 1) it is obvious that the scales denoted as a_{DNFA} , $\log k_{\text{DNFA}}$, a_{FDNB} , N_+ , and n_{MeI} lie on a straight line. The scales E_n and n_{Pt} deviate from this straight line, since the two factors are projected into them in a different way. The factor analysis of the nucleophilicity scales of ionic nucleophiles (nitrite, azide, phenoxide, methoxide, iodide, sulphite, thiosulphate, thiophenolate, hydrogen peroxide anion) showed that the values of both scores lie on a straight line for these nucleophiles (Fig. 2), and their nucleophilic properties can be expressed by a single quantity. Similar conclusions were also made for uncharged nucleophiles with nitrogen atom as the reaction centre (pyridine, piperidine, morpholine, aniline, hydroxylamine, hydrazine, ammonia) (Fig. 3), as well as for all the nucleophiles with nitrogen atom as the reaction centre (extended by nitrite and azide) (Fig. 4).

The above results allow the conclusion that the nucleophiles studied can be divided into two groups (ionic and nitrogen-containing nucleophiles), the nucleophilic properties being affected by linear combination of both factors in each group.

TABLE IV

The correlation matrix of the nucleophilicity scales

Parameter	$\log k_{\text{DNFA}}$	N_+	a_{DNFA}	n_{Pt}	n_{MeI}	a_{FDNB}
N_+	0.667					
a_{DNFA}	0.900	0.824				
n_{Pt}	0.319	0.688	0.522			
n_{MeI}	0.559	0.843	0.720	0.917		
a_{FDNB}	0.632	0.945	0.806	0.627	0.780	
E_n	0.142	0.662	0.433	0.887	0.847	0.617

Therefore, it is possible to construct two nucleophilicity scales, one valid for the nucleophiles with the reaction centre at the nitrogen atom and the other for ionic nucleophiles. From Fig. 2 it follows that the value of the parameters for the negatively charged nucleophiles depends on the type of the atom of the reaction centre

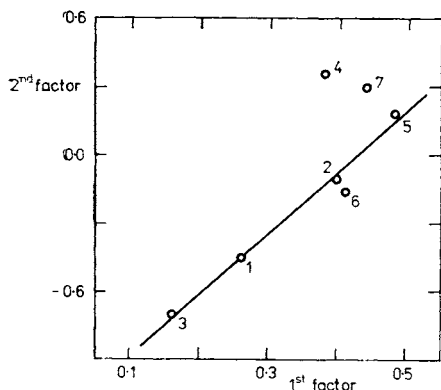


FIG. 1

The dislocation of nucleophilicity scales in the factor space 1 $\log k_{\text{DNFA}}$, 2 N_+ , 3 a_{DNFA} , 4 n_{Pt} , 5 n_{MeI} , 6 a_{FDNB} , 7 E_n

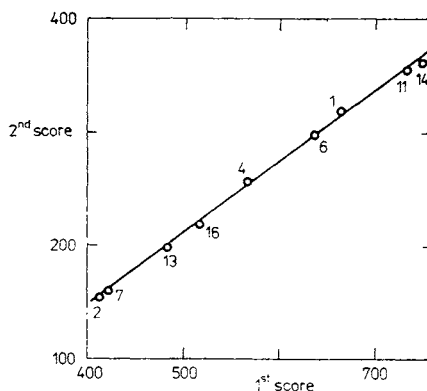


FIG. 2

The dislocation of negatively charged nucleophiles in the score space. For numbers of nucleophiles see Table I

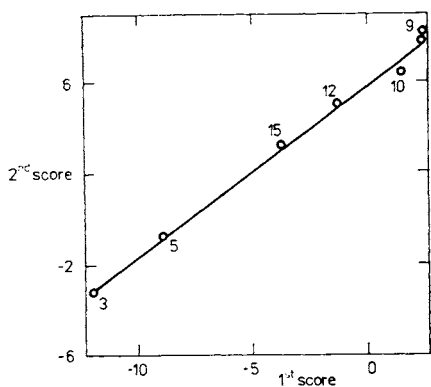


FIG. 3

The dislocation of uncharged nitrogen-containing nucleophiles in the score space. For numbers of nucleophiles see Table I

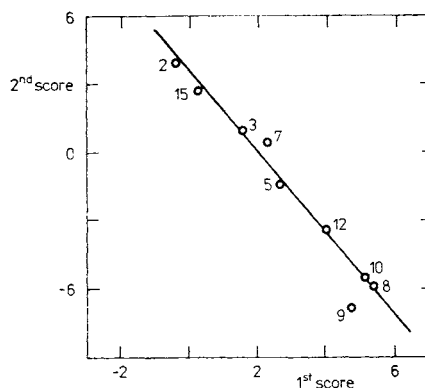


FIG. 4

The dislocation of the nucleophiles with nitrogen atom in the reaction centre in the score space. For numbers of nucleophiles see Table I

and on the α effect (if present). At the beginning of this scale is the hydrogen peroxide ion with its considerable α effect, and the other nucleophiles follow in the order given by decreasing softness of the reaction centre¹³. For the uncharged nucleophiles with nitrogen atom in the reaction centre, the order in the scale is given by the electron density at the central atom and by the α effect (if present). In Fig. 3 the lowest position belongs to aniline due to electron delocalization from the nitrogen atom to aromatic ring, whereas in pyridine the electron density lowering at nitrogen atom (due to the conjugated system) is smaller, and in ammonia no lowering is possible at all. Next nucleophiles of this series are hydroxylamine and hydrazine, in which the α effect makes itself felt, the nucleophilic properties of hydroxylamine being affected, in addition, by the $-I$ effect of adjacent hydroxyl group. The last nucleophiles of this scale are piperidine and morpholine: the $+I$ effect of methylene groups causes the highest electron density at nitrogen atom.

REFERENCES

1. Ibne-Rasa K. M.: *J. Chem. Educ.* **44**, 89 (1967).
2. Duboc C. in the book: *Correlation Analysis in Chemistry* (N. B. Chapman and J. Shorter, Eds), p. 313. Plenum Publishing Corporation, New York 1978.
3. Smith G. F.: *J. Chem. Soc.* **1943**, 521.
4. Swain C. G., Scott C. B.: *J. Am. Chem. Soc.* **75**, 141 (1953).
5. Pearson R. G., Sobel H., Songstad J.: *J. Am. Chem. Soc.* **90**, 319 (1968).
6. Edwards J. O.: *J. Am. Chem. Soc.* **76**, 1540 (1954).
7. Ritchie C. D., Virtanen P. O. I.: *J. Am. Chem. Soc.* **94**, 4966 (1972).
8. Blanksma J. J.: *Chem. Zentralbl.* **1909**, 1220.
9. Ritchie C. D., Sawada M.: *J. Am. Chem. Soc.* **99**, 3754 (1977).
10. Drost P.: *Liebigs Ann. Chem.* **307**, 49 (1899).
11. Broxton T. J., Muir D., Parker A. J.: *J. Org. Chem.* **40**, 2037 (1975).
12. Murto J.: *Acta Chem. Scand.*, **B 18**, 1029 (1964).
13. Ho T.L.: *Hard and Soft Acids and Bases Principle in Organic Chemistry*, p. 6. Academic Press, New York 1977.
14. Überla K.: *Faktorenanalyse*. Springer, Berlin 1971.
15. Malinowski E. R., Howery P. G.: *Factor Analysis in Chemistry*. Wiley, New York 1980.
16. Jencks W. P., Gilchrist M.: *J. Am. Chem. Soc.* **90**, 2622 (1968).
17. Reisert A., Goll G.: *Chem. Ber.* **38**, 93 (1905).
18. Compe A. F., Turicina V. F.: *Zh. Obshch. Khim.* **27**, 3282 (1957).
19. Powell G.: *J. Am. Chem. Soc.* **51**, 2438 (1929).
20. Spiegel L., Kaufman H.: *Chem. Ber.* **41**, 681 (1908).
21. Nishino J., Nishiura A., Kuroki N., Kinishi K.: *Kogyo Kagaku Zasshi* **62**, 119 (1959).
22. Brady O. L.: *J. Chem. Soc.* **1931**, 757.
23. Bost R. W., Turner J. O., Norton R. D.: *J. Am. Chem. Soc.* **54**, 1985 (1932).
24. Borsche W.: *Chem. Ber.* **56**, 1496 (1923).
25. Raiford L. C., Colbert J. C.: *J. Am. Chem. Soc.* **48**, 2652 (1926).
26. Engelhard L., Latschinow K.: *Z. Chem.* **1870**, 233.
27. Bailey A. S., Case J. R.: *Tetrahedron* **3**, 113 (1958).

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