The Stabilities of Meisenheimer Complexes. Part II.[1] Equilibrium Constants for the Formation of Methoxide Adducts of Low Stability and the J_M Acidity Function in Methanol–Dimethyl Sulphoxide

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A J_M acidity function has been measured for methanol–dimethyl sulphoxide mixtures containing 0·1M-sodium methoxide in respect of methoxide addition to substituted anisoles. This allows the determination of the thermodynamic equilibrium constants for sodium methoxide addition in methanol to 1,5-dimethoxy-2,4-dinitrobenzene ($3{\cdot}8 \times 10^{-6}$ l mol^{-1}), 2,4-dinitroanisole ($4{\cdot}6 \times 10^{-5}$ l mol^{-1}), 2,6-dinitroanisole ($9{\cdot}0 \times 10^{-5}$ l mol^{-1}), 4-chloro-2,6-dinitroanisole ($4{\cdot}3 \times 10^{-3}$ l mol^{-1}) and 2-fluoro-4,6-dinitroanisole (0·3 l mol^{-1}).

In Part I[1] we reported values for the equilibrium constants for formation of several relatively stable adducts from activated anisoles with sodium methoxide in methanol. In those cases conversion into complex was achieved in dilute sodium methoxide solutions. Here we are concerned with adducts of lower stability where appreciable conversion into complex occurs only in more basic media. Rochester[2,3] and Terrier,[4] using similar equilibria, have defined a J_M acidity function for concentrated methanolic solutions of alkali metal methoxides as in equation (1) where K_{MeOH} is the autoprotolysis constant for methanol ($pK_{MeOH} = 16{\cdot}92$).[3] These measurements lead to values of the thermodynamic equilibrium constants for adduct formation (K_1) referred to pure methanol as solvent.

$$J_M = p(K_1 K_{MeOH}) + \log_{10}[\text{Complex}]/[\text{Parent}] \quad (1)$$

Rochester[2] used the successive equilibria, some involving the formation of di- and tri-negatively charged anions, of 2,4-dinitroanisole, 2,4,6-trinitroanisole, the picrate ion, and the conjugate base of 2,4-dinitroaniline. Terrier's measurements[4] involved the formation of 1 : 1 adducts from substituted anisoles but lacked an indicator of intermediate stability between 2-fluoro-4,6-dinitroanisole and 2,6-dinitroanisole.

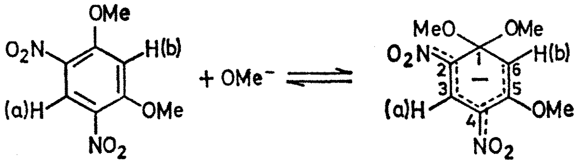
We have used the alternative approach of increasing the basicity of the medium by addition of dimethyl sulphoxide to methanol solutions containing a fixed concentration (0·1M) of sodium methoxide. Previously acidity functions in similar media have been determined by use of the ionisations of substituted anilines[5] (proton loss) and α-cyanostilbenes[6] (base addition). In view of our previous measurements[1] where divergent behaviour was found, even in dilute sodium methoxide solutions, for the variation of equilibrium constants with base concentration our first object was to test whether the compounds used would give a unique J_M acidity function for this medium, and if so to use the function to determine the stability constants for less reactive anisoles.

EXPERIMENTAL

2-Fluoro-4,6-dinitroanisole was prepared as a yellow oil by the nitration of 2-fluoroanisole.[7] 1,5-Dimethoxy-2,4-dinitrobenzene, m.p. 154 °C (lit.,[8] 154—157 °C), 4-chloro-2,6-dinitroanisole, m.p. 66 °C (lit.,[8] 66 °C), and 2,6-dinitroanisole, m.p. 118 °C (lit.,[4] 118 °C) were prepared from the respective chloro-compounds by reaction with methanolic sodium methoxide. Other compounds and solvents were prepared and purified as before.[1]

RESULTS

Structural Studies.—Solutions in methanol or dimethyl sulphoxide–methanol mixtures of each of the compounds studied are colourless. In the presence of sodium methoxide coloured species are produced whose structures were determined previously by use of ^{1}H n.m.r. spectroscopy. Thus in the cases of 2,4-dinitroanisole[9,10] and 2,6-dinitroanisole[10] these measurements show that methoxide addition occurs at the methoxy-substituted ring position. In the presence of sodium methoxide, 4-chloro-2,6-dinitroanisole gives initially an adduct by base addition at the unsubstituted 3-carbon atom though this quickly rearranges to give the thermodynamically more stable C(1) adduct.[11,12] Methoxide addition to 1,5-dimethoxy-2,4-dinitrobenzene has been studied by Foster and his co-workers,[10] but our results are not in agreement with their data and are therefore given in some detail.



(I) (II)

The spectrum of the parent compound in dimethyl sulphoxide shows in addition to solvent bands three singlets of relative intensity 1 : 1 : 6 at δ 8·66 p.p.m. (H_a), 7·05 p.p.m. (H_b), and 4·10 p.p.m. (OMe). All chemical shifts were measured from internal tetramethylsilane. On the addition of methanolic sodium methoxide a red colour was produced and the n.m.r. spectrum showed the presence of a new set of bands in addition to those of the parent com-

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[1] Part I, M. R. Crampton and H. A. Khan, preceding paper.

[2] C. H. Rochester, *J. Chem. Soc.*, 1965, 2404.

[3] C. H. Rochester, 'Acidity Functions,' Academic Press, New York, 1970.

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[5] R. Stewart, J. P. O'Donnell, J. P. Cram, and B. Rickborn, *Tetrahedron*, 1962, **18**, 917.

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[8] A. F. Holleman and A. J. den Hollander, *Rec. Trav. chim.*, 1920, **39**, 435.

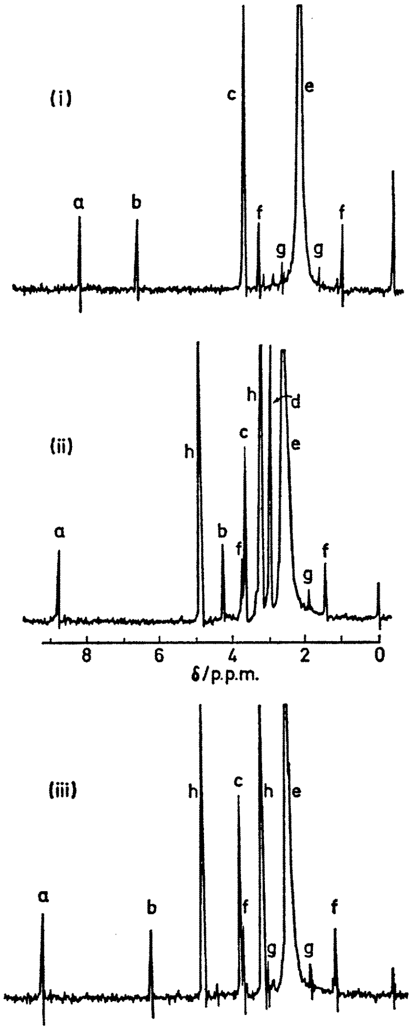
[9] M. R. Crampton and V. Gold, *J. Chem. Soc.* (*B*), 1966, 893.

[10] R. Foster, C. A. Fyfe, P. H. Emslie, and M. I. Foreman, *Tetrahedron*, 1967, **23**, 227.

[11] M. R. Crampton, M. A. El Ghariani, and H. A. Kahn, *Chem. Comm.*, 1971, 834.

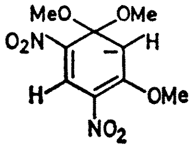
[12] F. Terrier and F. Millot, *Bull. Soc. chim. France*, 1970, 1743.

pound. As the ratio of methoxide to parent was increased the new bands grew at the expense of those due to the parent compound until by a mol ratio of 1 : 1 conversion into complex was complete. The spectrum of the complex shows four singlets with intensity ratio 1 : 1 : 3 : 6 at δ 8·85 (H$_a$), 4·27 (H$_b$), 3·68 [methoxy-protons at C(5)], and 2·97 p.p.m. [methoxy-protons at C(1)]. This spectrum is consistent only with structure (II). The large upfield shift of the resonance due to H$_b$ indicates an increase in negative charge at this position on complex formation and resonance form (III) may have some importance in the stabilisation of the adduct.

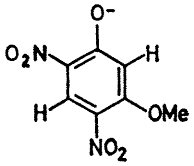


N.m.r. spectra of 1,5-dimethoxy-2,4-dinitrobenzene; (i) in dimethyl sulphoxide, (ii) after the addition of 1·3 equivalents of methanolic sodium methoxide, (iii) same spectrum after 1 h. Bands a and b are assigned to ring protons, c to methoxy-protons attached to *sp*^{2}-hybridised carbon and d to methoxy-protons at *sp*^{3}-hybridised carbon in the complex. Band e is the large solvent peak and bands f and g are respectively ^{13}C satellites and spinning side-bands. Bands labelled **h** are due to the hydroxy and methyl protons of methanol in the solvent

We find that the spectrum changes slowly with time so that the bands due to complex decrease in intensity and new bands at δ 8·75, 6·02, and 3·80 p.p.m. increase in intensity. The latter bands have intensity ratio 1 : 1 : 3 and are attributed to the slow production of 5-methoxy-2,4-dinitrophenol which will be present in basic media as the phenoxide ion (IV). This may be formed *via* traces of water in the solvent or possibly by demethylation of the parent compound by methoxide ions.[13] The bands observed by Foster *et al.*[10] at δ 8·70 and 6·00 p.p.m. which they attributed to the addition complex are in fact due to the phenoxide ion.



(III)



(IV)

Measurement of Indicator Ratios.—The experimental determination of indicator ratios (log$_{10}$[Complex]/[Parent]) required the knowledge of the extinction coefficients of the coloured species, in this case complex. By increasing the proportion of dimethyl sulphoxide in the solvent it was possible for each indicator to obtain virtually complete conversion into complex and hence obtain a value for the extinction coefficient in that medium. In order to check whether extinction coefficients varied appreciably with solvent composition we carried out a test experiment with 2,4,6-trinitroanisole. It is known that for this compound conversion into 1 : 1 complex is complete in methanol containing 10^{-2}M-sodium methoxide.[14] The measurements shown in Table 1, which correspond to methoxide addition at the C(1) position, were made in mixed solvents containing this concentration of base.

TABLE 1

Dimethyl sulphoxide (% v/v)	$\lambda_{max.}$/nm	Optical density
0	412	0·747
10	414	0·767
20	415	0·788
30	416	0·805
40	417	0·812
50	418	0·816
60	420	0·855
70	421	0·855
80	421	0·859

There is clearly a bathochromic shift as the proportion of dimethyl sulphoxide is increased and this is associated with an increase in extinction coefficient. Examination of the data indicates a linear correlation of extinction coefficient (proportional to optical density since conversion into complex is complete) with absorption maximum. Similar linear correlations were observed for other adducts studied. It was therefore assumed that for other adducts where conversion into complex was complete only in media rich in dimethyl sulphoxide a linear correlation would exist between the extinction coefficient and wavelength of maximum absorption, so that indicator ratios could be accurately determined. The measurements shown in Table 2 were all made in solutions containing 0·1M-sodium methoxide and at 25 °C.

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[13] G. Illuminati, P. Bemporad, and F. Stegel, *J. Amer. Chem. Soc.*, 1969, **91**, 6746.

[14] V. Gold and C. H. Rochester, *J. Chem. Soc.*, 1964, 1687.

TABLE 2

2-Chloro-4,6-dinitroanisole

Dimethyl sulphoxide (% v/v)	$\lambda_{max.}$/nm	Optical density [a]	$\log_{10}$ (Indicator ratio)
0	492	0·41	−0·11
5	492	0·54	+0·14
10	492	0·68	0·41
15	492	0·77	0·65
20	492	0·85	
25	493	0·90	
30	493	0·92	
40	494	0·95	
50	494	0·96	
60	495	0·97	
70	495	0·98	
80	496	0·99	

[a] With 4×10^{-5}M-indicator. Measurements [1] in methanolic sodium methoxide give an optical density of 0·93 for complete conversion.

4-Trifluoromethyl-2,6-dinitroanisole

Dimethyl sulphoxide (% v/v)	$\lambda_{max.}$/nm	Optical density [a]	$\log_{10}$ (Indicator ratio)
0	540	0·40	−0·18
5	540	0·522	+0·04
10	540	0·66	0·28
15	540	0·774	0·51
20	540	0·872	0·79
25	540	0·94	
30	541	0·99	
40	541	1·03	
50	542	1·08	
60	542	1·08	
70	543	1·10	
80	543	1·11	

[a] With 4×10^{-5}-indicator. Measurements [1] in methanolic sodium methoxide give a value of 1·00 for complete conversion.

2-Fluoro-4,6-dinitroanisole

Dimethyl sulphoxide (% v/v)	$\lambda_{max.}$/nm	Optical density [a]	$\log_{10}$ (Indicator ratio)
5	493	0·139	−0·81
10	493	0·206	−0·61
15	494	0·327	−0·35
20	494	0·470	−0·10
25	494	0·653	+0·18
30	494	0·821	0·46
40	495	1·05	
50	496	1·10	
60	497	1·14	

[a] With 4×10^{-5}M-indicator. Terrier [4] gives $\lambda_{max.}$ (methanol) 492 nm; $\varepsilon_{max.}$ 25,300 l mol^{-1} cm^{-1}.

4-Chloro-2,6-dinitroanisole

Dimethyl sulphoxide (% v/v)	$\lambda_{max.}$/nm	Optical density	$\log_{10}$ (Indicator ratio)
15	601	0·0061 [a]	−2·14
20	601	0·0103 [a]	−1·91
25	602	0·0177 [a]	−1·67
30	602	0·0313 [a]	−1·41
35	603	0·064	−1·11
40	603	0·117	−0·80
45	604	0·210	−0·49
50	604	0·37	−0·15
55	605	0·575	+0·23
60	606	0·74	0·58
65	607	0·89	
70	608	0·93	
75	608	0·94	

[a] Measured with indicator concentration ×10.

TABLE 2 (*Continued*)

2,6-Dinitroanisole

Dimethyl sulphoxide (% v/v)	$\lambda_{max.}$/nm	Optical density	$\log_{10}$ (Indicator ratio)
50	588	0·014 [a]	−1·81
55	588	0·031 [a]	−1·46
60	588	0·074	−1·07
65	588	0·159	−0·69
70	588	0·341	−0·25
75	589	0·600	+0·24
80	589	0·84	0·85
85	590	0·94	
90	591	0·97	

[a] Measured with indicator concentration ×10.

2,4-Dinitroanisole

Dimethyl sulphoxide (% v/v)	$\lambda_{max.}$/nm	Optical density	$\log_{10}$ (Indicator ratio)
50	498	0·0053 [a]	−2·14
55	498	0·0117 [a]	−1·79
60	499	0·029 [a]	−1·41
65	499	0·073	−0·99
70	499	0·19	−0·49
75	499	0·39	0·00
80	499	0·62	0·56
85	500	0·75	
90	500	0·80	

[a] Measured with indicator concentration ×10.

With solutions of 4-chloro-2,6-dinitroanisole in media rich in dimethyl sulphoxide the optical density at the absorption maximum initially increases to a maximum value (owing to rearrangement of the 1,3-complex to the thermodynamically more stable 1,1-complex) [11] and then gradually decreases. Extrapolation to zero time of the optical densities measured during the fading process gave the optical densities reported in Table 2 which correspond to formation of the 1,1-complex.

Measurements were also made with 2,4-dinitroanisole in 4 : 1 dimethyl sulphoxide–methanol with various sodium methoxide concentrations, allowing the determination of values of K_c {=[Complex]/([Parent][NaOMe])}. The observed value of K_c increased with base concentration but extrapolation to zero base concentration gave a value of 15 l mol^{-1}.

1,5-*Dimethoxy*-2,4-*dinitrobenzene*.—The red colour initially produced fades very slowly with time, owing to formation of 3-methoxy-4,6-dinitrophenol. Measurements were made at one-minute intervals and extrapolated to zero time.

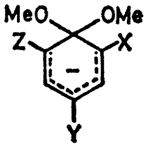
Dimethyl sulphoxide (% v/v)	Optical density [a] (490 nm)	$\log_{10}$ (Indicator ratio)
65	0·0066 [b]	−2·02
70	0·018 [b]	−1·58
75	0·054 [b]	−1·08
80	0·155	−0·55
85	0·370	+0·05
90	0·625	+0·90
95	0·703	
95 [c]	0·70	

[a] For indicator 3×10^{-5}M. [b] Measured with indicator concentration ×10. [c] With 0·2M-sodium methoxide.

Measurements in 4 : 1 dimethyl sulphoxide–methanol give a value of K_c extrapolated to zero base concentration of 1·5 l mol^{-1}.

DISCUSSION

For each compound studied methoxide addition occurs to give coloured adducts of structure (V).



(V)

Measurements of optical density were made in methanol–dimethyl sulphoxide mixtures containing 0·1M-sodium methoxide and indicator ratios calculated taking account of the variations of extinction coefficient with solvent composition. Examination of the results shows that indicator ratios for the different compounds studied vary in parallel fashion with solvent composition. For example, on changing the proportion of dimethyl sulphoxide from 65 to 80% (v/v) the indicator ratios for 2,4-dinitroanisole, 2,6-dinitroanisole, and 1,5-dimethoxy-2,4-dinitrobenzene increase respectively by 1·55, 1·54, and 1·47 logarithmic units. These results indicate that a single J_{M} acidity function can adequately describe the behaviour of these particular compounds in these media. This can only be the case if the activity coefficient ratios $f_{\mathrm{Parent}}/f_{\mathrm{Complex^-}}$ vary with solvent composition in similar fashion for the anisoles studied. In addition if, as suggested previously,[1] ion-pair formation in the complex is important then the affects of dimethyl sulphoxide on the ion-pair equilibria of all the adducts must be similar. The construction of a J_{M} acidity scale was carried out by use of the usual stepwise technique.[3] The question arises as to the value of J_{M} to take for 0·1M-sodium methoxide in methanol, the starting point of the scale. It was shown previously [1] that for the four compounds studied there were differences in the variation of equilibrium constant with sodium methoxide concentration below 0·1M. From the results for 2-chloro-4,6-dinitroanisole and 4-trifluoromethyl-2,6-dinitroanisole, indicators used in the present study, we calculate J_{M} values of 16·34 and 16·45 respectively for 0·1M-sodium methoxide. The average of these 16·40 is in reasonable agreement with the value of 16·45 found by Terrier.[4]

TABLE 3

Dimethyl sulphoxide (% v/v)	J_{M}	Dimethyl sulphoxide (% v/v)	J_{M}
0	16·40	55	19·51
5	16·63	60	19·89
10	16·87	65	20·29
15	17·11	70	20·75
20	17·36	75	21·24
25	17·62	80	21·80
30	17·89	85	22·40
35	18·19	90	23·25
40	18·50		
45	18·81		
50	19·51		

Three acidity scales have now been determined in methanol–dimethyl sulphoxide mixtures containing sodium methoxide (Table 3). The present scale which increases by 6·85 units on going from methanol to 90% (v/v) dimethyl sulphoxide is intermediate in behaviour between that involving proton loss from anilines [5] which increases by 5·80 units for a similar solvent change and that involving methoxide addition to α-cyanostilbenes [6] which increases by 7·85 units. The rather similar general behaviour of these acidity scales may result from the fact that the major source of increase in basicity in dimethyl sulphoxide is probably the desolvation of the base. This effect will of course be independent of the particular indicator used. It does not necessarily follow that methoxide addition to other aromatic nitro-compounds will comply with the J_{M} acidity function defined here, and preliminary measurements [15] with compounds such as 1,3,5-trinitrobenzene where methoxide addition occurs at an unsubstituted ring position indicate a slightly steeper increase of J_{M} with dimethyl sulphoxide proportion than observed here.

The equilibrium constants for complex formation calculated by use of the J_{M} acidity function are given in Table 4. Owing to the unavoidable inaccuracies resulting from use of an acidity function these values are probably accurate only within a factor of two. Our value for 2,4-dinitroanisole can be compared with values of $5·0 \times 10^{-5}$ found by Bernasconi [16] and $6·8 \times 10^{-5}$ by Terrier.[4]

TABLE 4

	K_1/l mol^{-1}
2-Fluoro-4,6-dinitroanisole	0·3
4-Chloro-2,6-dinitroanisole	$4·3 \times 10^{-3}$
2,6-Dinitroanisole	$9·0 \times 10^{-5}$
2,4-Dinitroanisole	$4·6 \times 10^{-5}$
1,5-Dimethoxy-2,4-dinitrobenzene	$3·8 \times 10^{-6}$

It is of interest that the complex formed from 1,5-dimethoxy-2,4-dinitrobenzene has a stability roughly ten times smaller than that from 2,4-dinitroanisole. This is evident both from the thermodynamic values in methanol determined *via* the acidity function and also applies to the equilibrium constants in 4 : 1 dimethyl sulphoxide–methanol where the values are 1·5 and 15 l mol^{-1} respectively. On statistical grounds the complex from 1,5-dimethoxy-2,4-dinitrobenzene should be favoured since there are two equivalent positions where methoxide addition can occur. Steric factors at the position of addition should be similar for the two complexes. However the smaller stability of the adduct from the dimethoxy-compound may result from steric interaction in the complex between the methoxy-group at C(5) and the nitro-group at C(4) [structure (II)]. This will cause the nitro-group to bend from the plane of the aromatic ring and so be less effective in accommodating the negative charge. The large upfield shift of the resonance of the hydrogen at C(6) indicates that some of the negative charge resides at this carbon atom in the complex. Bernasconi [17] has argued recently that resonance interaction of the form (2) may stabilise the parent anisoles. Comparison of 2,4-dinitroanisole with 1,5-dimethoxy-2,4-dinitrobenzene indicates that the former compound will lose two such resonance forms on

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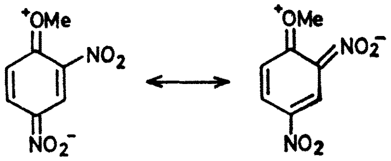
[15] M. R. Crampton and H. A. Khan, unpublished observations.

[16] C. F. Bernasconi, *J. Amer. Chem.*, 1968, **90**, 4982.

[17] C. F. Bernasconi, *J. Amer. Chem. Soc.*, 1970, **92**, 4682.

complex formation while the latter will lose four. This may also be a factor to account for the smaller stability



(2)

of the adduct from the latter compound, but is probably less important than the steric effects previously mentioned.

Also of interest is the greater stability of the adduct from 2,6-dinitroanisole than that from 2,4-dinitroanisole. It has frequently been argued that the presence of a strongly electron-withdrawing group *para* to the position of addition is of considerable importance in determining the stabilities of Meisenheimer complexes. Evidence for this comes from the present study in that the equilibrium constant for complex formation from 2-chloro-4,6-dinitroanisole[1] (3 l mol^{-1}) is roughtly 1000 times greater than that from 4-chloro-2,6-dinitroanisole. However the results for the isomeric dinitroanisoles indicate that this factor is not always of over-riding importance, and that steric requirements at the position of addition may be important.

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