The Stabilities of Meisenheimer Complexes. Part V.[1] Association with Barium and Calcium Ions in Methanol

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The stoicheiometric equilibrium constants for methoxide ion addition to 2-methoxycarbonyl-4,6-dinitroanisole, 4-methoxycarbonyl-2,6-dinitroanisole, and 2-chloro-4,6-dinitroanisole are greatly increased by the presence of small concentrations of barium and calcium ions. This is attributed to the stabilisation of the Meisenheimer complexes by association with these cations. In the case of the methoxide adduct from 2,4,6-trinitroanisole ion association is demonstrated by changes in the visible spectrum in the presence of various cations. However the methoxide adduct from 1,3,5-trinitrobenzene shows little tendency to associate with cations. It is suggested that when ion pairs are formed the cation is held by a cage effect by the two oxygen atoms of the methoxy-groups at the position of addition and by the electronegative substituent at the *ortho*-position.

THERE is considerable current interest in the Meisenheimer complexes [2-5] formed by methoxide ion addition to activated aromatic anisoles. Particular attention has centred on the relative stabilities of these adducts, most measurements having been made in methanol solutions using sodium methoxide.

We showed recently [6] that for several anisoles the measured stoicheiometric equilibrium constants K_C (= [Complex]/[Parent][NaOMe]) increased markedly with increasing sodium methoxide concentration even in dilute solutions. This is in contrast with the behaviour of anilines (used to measure the H_M acidity function [7] in this medium) where little variation in

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[1] Part IV, M. R. Crampton and H. A. Khan, *J.C.S. Perkin II*, 1973, 710.

[2] For recent reviews see M. R. Crampton, *Adv. Phys. Org. Chem.*, 1969, **7**, 211; M. J. Strauss, *Chem. Rev.*, 1970, **70**, 667; C. A. Fyfe, ' The Chemistry of the Hydroxyl Group,' ed. S. Patai, Interscience, New York, 1971, vol. 1, p. 51.

[3] C. F. Bernasconi, *J. Amer. Chem. Soc.*, 1971, **93**, 6975.

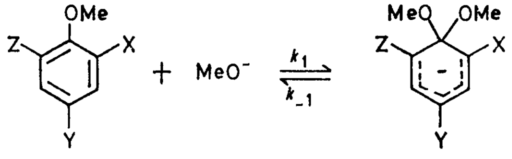
[4] M. P. Simmonin, M. J. Lecourt, F. Terrier, and C. A. Dearing, *Canad. J. Chem.*, 1972, **50**, 3558.

[5] J. H. Fendler and J. W. Larsen, *J. Org. Chem.*, 1972, **37**, 2608.

[6] M. R. Crampton and H. A. Khan, *J.C.S. Perkin II*, 1972, 1173.

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

ionisation constant is observed[8] at base concentrations below 0·1M. We attributed this effect to the stabilisation of the Meisenheimer complexes by association with sodium ions.[6] The results obtained with several different parent anisoles indicated that the magnitude of this effect varied with the nature of the substituents X, Y, and Z and the following approximate values for association with sodium ions were found: X = CO_2Me, Y = Z = NO_2, 90 l mol^{-1}; Y = CO_2Me, X = Z = NO_2, 50 l mol^{-1}; X = Cl, Y = Z = NO_2, 25 l mol^{-1}. Similar results were obtained using potassium as the counter-ion.[9] However with tetra-n-butylammonium ions a small non-specific stabilising effect was observed while lithium ions gave no evidence for association.[9]



(I)

We now report the dramatically large effects produced in the presence of the bivalent barium and calcium ions.

EXPERIMENTAL

Nitro-compounds and base solutions were prepared and purified as before.[6,9] AnalaR barium and calcium salts were dried under vacuum before use. Visible spectral measurements were made at 25° using Unicam SP 500 and SP 8000 instruments. Solutions containing the required concentrations of reagents were prepared immediately before use by suitable dilution of stock solutions. Kinetic measurements were made using previously described techniques.[6,9]

RESULTS AND DISCUSSION

2-Methoxycarbonyl-4,6-dinitroanisole.—In the presence of methoxide ions this anisole has been shown[6] to give a coloured adduct, $\lambda_{max.}$ 472 nm, of structure (I). The thermodynamic equilibrium constant for adduct formation, K_1, obtained[9] by extrapolation to zero base concentration has the value 8·3 l mol^{-1}. The results in Table 1 show the enormous increase in stoicheiometric equilibrium constant K_C (= [Complex]/[Parent][NaOMe]) produced on the addition of small concentrations of barium salts.

Several points are of interest. (i) Similar effects are observed on the addition of either barium chloride or barium perchlorate. (ii) The K_C value at a given concentration of barium salt decreases slightly as the sodium methoxide concentration is increased; this may be attributed to loss of barium ions by association with methoxide ions. (iii) The measured K_C values approach a limiting value at high concentration of added salt. Full analysis of the data is complicated and we shall attempt only a semi-quantative treatment. The cations present will associate with Meisenheimer complexes, equilibrium constant K_2, and with methoxide ions, equilibrium constant K_3, as in the Scheme.

TABLE 1

The effect of barium ions on the reaction of 2-methoxycarbonyl-4,6-dinitroanisole with sodium methoxide at 25°

[NaOMe]/mM	[$BaCl_2$]/mM	[$Ba(ClO_4)_2$]/mM	Optical density[a] at equilibrium (472 nm)	K_C/l mol^{-1}	10^2 k_{obs}/s^{-1}	k_1/l mol^{-1} s^{-1}	10^3 k_{-1}/s^{-1}
9·6			0·117	20	1·47	0·24	12·5
9·6	1·0		0·313	93	2·5	1·2	12·5
9·6	1·9		0·39	150	3·4	2·1	14
9·6	3·8		0·46	240	4·8	3·5	14
9·6	6·7		0·51	350	6·4	5·0	14·5
9·6	17		0·55	520			
9·6		3·8	0·47	260	4·5	3·3	13
9·6		6·7	0·51	350	6·0	4·8	13·5
9·6		30	0·58	750			
9·6		60	0·60	*ca.* 1000			
9·6		90	0·61	*ca.* 1200			
4·8			0·043	13	1·85	0·23	17·5
4·8	1·0		0·23	95	2·3	1·6	16
4·8	1·9		0·31	185	2·9	2·8	15
4·8	3·8		0·39	300	3·5	4·3	14
4·8	8·0		0·45	440	4·1	5·8	13
4·8		90	0·57	*ca.* 1300			
19		60	0·63				
19		90	0·63				
38		90	0·65				
500			0·73				

[a] The concentration of parent anisole is 3·84 × 10^{-5}M. The extinction coefficient of the complex is decreased by association with barium ions so that the optical density for complete conversion to ion-paired complex is 0·66.

$$\begin{tikzcd}
P + OMe^- + M^{n+} \arrow[r, shift left, "K_1"] \arrow[d, shift left, "K_3"] & P{\cdot}OMe^- + M^{n+} \arrow[l, shift left] \arrow[r, shift left, "K_2"] & P{\cdot}OMe^-, M^{n+} \arrow[l, shift left] \\
M^{n+}, OMe^- \arrow[u, shift left] & &
\end{tikzcd}$$

SCHEME

In the presence of both sodium and barium ions the stoicheiometric equilibrium constant K_C will be related to the thermodynamic constant K_1 by equation (1).

$$K_C = K_1 \frac{(1 + K_2^{Na}[Na^+] + K_2^{Ba}[Ba^{2+}])}{(1 + K_3^{Na}[Na^+] + K_3^{Ba}[Ba^{2+}])} \quad (1)$$

If it is assumed that for a given cation the value of K_3 is small compared with K_2, *i.e.* association of cations with

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[8] R. Schaal and G. Lambert, *J. Chim. Phys.*, 1962, 1151.

[9] M. R. Crampton and H. A. Khan, *J.C.S. Perkin II*, 1972, 2286.

methoxide ions is considerably weaker than with the Meisenheimer complex, then the denominator may be neglected. Then at constant sodium ion concentration a plot of K_C *versus* barium ion concentration should be linear with slope $K_1 . K_2^{Ba}$. From the limiting slopes of such plots at low barium ion concentrations we may estimate a value of *ca.* 10^4 l mol^{-1} for K_2^{Ba}. However this procedure gives only a minimum value for K_2^{Ba} since account should also be taken of the association of barium and methoxide ions. This will introduce a term in the denominator of equation (1) and will reduce the concentration of free barium ions. We have been unable to find a value in the literature for the ion-pair association constant of barium methoxide. However the association constants of bivalent cations with hydroxide ions in water [10] have values of *ca.* 10 l mol^{-1} and it seems likely that in methanol values will be larger. If we assume a value of 10^2 l mol^{-1} for K_3^{Ba} then in the presence of 10^{-2}M-methoxide ions considerable amounts of the ion pair Ba^{2+},OMe^- will be formed so that the concentration of free barium ions will be considerably reduced from the stoicheiometric concentration of added barium salt. Taking a value of 10^2 l mol^{-1} for K_3^{Ba} results in a value of 1·6 × 10^4 l mol^{-1} for K_2^{Ba}. We note that equation (1) predicts that at high barium ion concentrations the value of K_C should approach a limit of $K_1 . K_2^{Ba}/K_3^{Ba}$. The experimentally obtained limiting value of *ca.* 1200 is in reasonable agreement with that predicted from values of K_2^{Ba} *ca.* 1·6 × 10^4 and K_3^{Ba} *ca.* 1 × 10^2 l mol^{-1}. These are of course only very approximate values but demonstrate the very strong association of barium ions with this Meisenheimer complex. In a more quantitative treatment it would be necessary to consider association of barium ions with chloride or perchlorate ions and also variations in the activity coefficient of barium ions with concentration.

Measurement of the rate of attainment of equilibrium as described previously [6,9] allows the determination of the individual rate coefficients for complex formation ($k_{obs} = k_1[NaOMe] + k_{-1}$). The results in Table 1 show that the major effect of added barium ions is to increase the value of k_1 indicating that the interaction of cation with substrate is present to a considerable extent in the transition state for complex formation.

TABLE 2

The effect of barium ions on the complex formation of 4-methoxycarbonyl-2,6-dinitroanisole [a] with sodium methoxide at 25°

[NaOMe]/mM	[BaCl$_2$]/mM	Optical density at equilibrium (525 nm)	K_C/l mol^{-1}
9·6		0·064	9
9·6	1·0	0·141	23
9·6	1·9	0·196	34
9·6	3·8	0·26	50
9·6	5·8	0·30	63
9·6	11·0	0·36	86
1000		0·80	

[a] Concentration is 3·84 × 10^{-5}M.

In the presence of added calcium ions results following a similar general pattern to those described with barium ions were obtained and give a value for K_2^{Ca} of *ca.* 8 × 10^3M^{-1}.

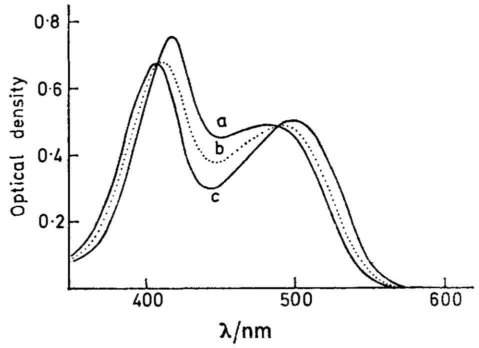
4-*Methoxycarbonyl*-2,6-*dinitroanisole*.—Previous results [6,9] show that in the presence of sodium methoxide a complex of structure (I) is formed with absorption maximum at 525 nm and with equilibrium constant K_1 = 5·5 l mol^{-1}. The results in Table 2 show that the presence of small concentrations of barium ions results in increased complex formation. By use of equation (1), taking K_3^{Ba} as 10^2 l mol^{-1} we calculate a value of *ca.* 5 × 10^3 for the ion-pair association constant of the Meisenheimer complex with barium ions.

TABLE 3

The effect of barium ions on complex formation of 2-chloro-4,6-dinitroanisole (3·84 × 10^{-5}M) with sodium methoxide at 25°

[NaOMe]/ mM	[BaCl$_2$]/ mM	[Ba(ClO$_4$)$_2$]/ mM	Optical density (500 nm)	K_C/ l mol^{-1}
9·6			0·034	4·0
9·6	1·9		0·056	6·8
9·6	3·8		0·072	8·9
9·6	5·8		0·084	10·6
9·6	17		0·115	15
19			0·075	4·6
19		4·8	0·12	8·0
19		9·6	0·15	10·2
19		19	0·19	13·2
19		29	0·21	16
1000			0·92	

2-*Chloro*-4,6-*dinitroanisole*.—The results in Table 3 indicate that for this anisole methoxide addition is enhanced in the presence of barium ions. They yield a value of *ca.* 1 × 10^3 l mol^{-1} for the ion-pair association constant of the complex with barium ions.



The effect of barium ions on the visible spectrum of the Meisenheimer complex from 2,4,6-trinitroanisole. Each sample was made up with 2·94 × 10^{-5}M-2,4,6-trinitroanisole and 1 × 10^{-2}M-tetra-n-butylammonium methoxide. The barium chloride concentrations are: a, 0; b, 2 × 10^{-3}M; c, 1·4 × 10^{-2}M

2,4,6-*Trinitroanisole*.—Sodium methoxide addition to 2,4,6-trinitroanisole to give a Meisenheimer complex of structure (I) has been studied by several groups of workers.[11-13] The value of the equilibrium constant K_1 is high (17,000 l mol^{-1}) [11] so that in solutions containing 1 × 10^{-2}M-methoxide conversion of the anisole to complex is virtually complete. The visible spectrum in the presence of 1 × 10^{-2}M-tetra-n-butylammonium methoxide is shown in the Figure. By analogy with previous results [9] the tetra-n-butylammonium cation would not be expected to associate strongly with the trinitrocyclohexadienide anion so that this spectrum will correspond to the unassociated anion. The changes in visible spectrum produced in the

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[10] R. P. Bell and J. E. Prue, *J. Chem. Soc.*, 1949, 362.

[11] J. H. Fendler, E. J. Fendler, and C. E. Griffin, *J. Org. Chem.*, 1969, **34**, 689.

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

[13] P. Bemporad, G. Illuminati, and F. Stegel, *J. Amer. Chem. Soc.*, 1969, **91**, 6742.

presence of barium ions are shown in the Figure. On increasing the barium chloride concentration to $1{\cdot}4 \times 10^{-2}$M the short wavelength maximum shifts from 418 to 405 nm and decreases in intensity while the long wavelength band shifts from 480 to 500 nm with little change in intensity. We interpret these changes as showing the formation of an ion associate of the methoxide adduct with barium ions [equilibrium (2)]. The change in spectral shape results no

$$\mathrm{P{\cdot}OMe^-} + \mathrm{Ba^{2+}} \overset{K_2}{\rightleftharpoons} \mathrm{P{\cdot}OMe^-Ba^{2+}} \qquad (2)$$

doubt from changes in charge distribution on ion association. Similarly the addition of calcium chloride or sodium chloride produced marked changes in visible spectrum of the adduct, details in Table 4. However the addition of lithium chloride in concentrations up to 0·2M produced no spectral change indicating little association of the adduct with lithium ions.

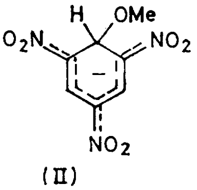
TABLE 4

The effect of the counter-ion on the visible spectrum of 2,4,6-trinitro-1,1-dimethoxycyclohexadienide ion in methanol

Cation	$\lambda_{\max.}$/nm	$10^{-4}\varepsilon$/ l mol^{-1} cm^{-1}	$\lambda_{\max.}$/nm	$10^{-4}\varepsilon$/ l mol^{-1} cm^{-1}
$(\mathrm{Bu^n})_4\mathrm{N^+}$	418	2·55	480	1·67
$\mathrm{Na^+}$	412	2·42	490	1·67
$\mathrm{Ba^{2+}}$	405	2·20	500	1·66
$\mathrm{Ca^{2+}}$	404	2·05	490	1·62

Using the variation in visible spectrum with cation concentration it was possible to calculate very approximate values for the ion-pair association constants K_2. Values are collected in Table 6 and should be regarded as giving the order of magnitude of the association constants rather than precise values. The value of *ca.* 70 l mol^{-1} for association with sodium ions indicates that in methanolic sodium methoxide solutions the effect of ion pairing will be small at base concentrations below 10^{-3}M. Hence the variation of measured equilibrium constant with base concentration observed by Illuminati and his co-workers [13] is unlikely to result from this source.

1,3,5-*Trinitrobenzene*.—As an example of a compound where methoxide addition occurs at a ring carbon atom carrying hydrogen we chose 1,3,5-trinitrobenzene, where (II) is formed. Using methanolic sodium methoxide Gold and Rochester [14] determined a value of 15·4 l mol^{-1} for the equilibrium constant K_1, while Bernasconi [15] found a value of 23 l mol^{-1} in solutions made up to constant ionic strength (0·2M) with sodium perchlorate. Our results indicate (Table 5) that with sodium methoxide there is a very slight increase in measured equilibrium constant K_C with increasing base concentration. However the addition of small concentrations of barium or calcium ions causes a reduction in optical density without changing the general spectral shape. This indicates that there is no strong association between the adduct (II) and calcium or barium ions. The decrease in absorption results from a reduction of the methoxide ion concentration by ion association with the bivalent cations. In this case, in terms of equation (1), the values of the association constants of bivalent cations with methoxide ions K_3 are larger than those for association with the adduct K_2.



(II)

TABLE 5

The effects of cations on the interaction of 1,3,5-trinitrobenzene (4×10^{-5}M) with sodium methoxide at 25°

[NaOMe]/mM		Optical density [a] (425 nm)	K_C/l mol^{-1}
10		0·160	18·1
20		0·282	18·5
40		0·45	19·0
60		0·57	20·2
80		0·65	21
	[BaCl$_2$]/mM		
10	1	0·155	17·6
10	2	0·153	17·4
10	8	0·147	16·5
	[CaCl$_2$]/mM		
10	1	0·150	17·0
10	2	0·140	15·5
10	4	0·123	13·4

[a] The value for complete conversion to complex is 1·04 as determined from the intercept of a linear Benesi–Hildebrand plot in solutions containing constant sodium ion concentration (0·10M).

Conclusions.—Our results clearly demonstrate the presence of ion association of Meisenheimer complexes with cations in methanol. The results with 2,4,6-trisubstituted anisoles show that the stoicheiometric equilibrium constants for complex formation are greatly increased by the presence of small concentrations of barium or calcium cations. Previously the stabilising effects of cationic micelles on Meisenheimer complexes have been noted; [16] our results show that simple cations may also be very effective in this respect.

The values for ion-pair association constants of several Meisenheimer complexes with various cations are summarised in Table 6. It should however be noted that the values K_2^{Ba} and K_2^{Ca} for association with barium and calcium ions are dependent on the values used for the ion-pair association constants of the metal methoxides. Hence they should be regarded as giving the orders of magnitude of the association rather than precise values. This uncertainty will not however affect the *relative* magnitudes of K_2 for the various Meisenheimer complexes.

TABLE 6

Association constants of Meisenheimer complexes with cations

Parent	K_1/ l mol^{-1}	K_2^{Na}/ l mol^{-1}	K_2^{Ba}/ l mol^{-1}	K_2^{Ca}/ l mol^{-1}
2-Methoxycarbonyl-4,6-dinitroanisole	8·3 [a]	90	$1{\cdot}6 \times 10^4$	8×10^3
4-Methoxycarbonyl-2,6-dinitroanisole	5·5 [a]	50	5×10^3	
2,4,6-Trinitroanisole	17,000 [b]	70	2×10^3	10^3
2-Chloro-4,6-dinitroanisole	3·4 [a]	25	1×10^3	
1,3,5-Trinitrobenzene	17	<10	$<10^2$	$<10^2$

[a] Ref. 9. [b] Ref. 11.

The extent of the association varies with the nature of the

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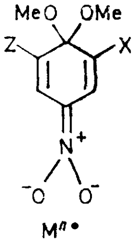
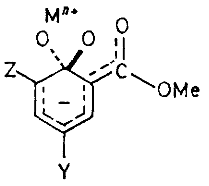
[14] V. Gold and C. H. Rochester, *J. Chem. Soc.*, 1964, 1692.

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

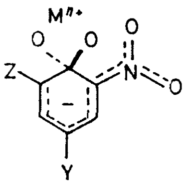
[16] J. A. Fendler, E. J. Fendler, and M. V. Merritt, *J. Org. Chem.*, 1971, **36**, 2172.



(III)



(IVa)



(IVb)

cation. From this and previous work [9] we find that association decreases in the order $\mathrm{Ba}^{2+} > \mathrm{Ca}^{2+} \gg \mathrm{Na}^{+} \sim \mathrm{K}^{+} > \mathrm{Li}^{+}$. There is apparently little tendency for lithium ions to associate with the Meisenheimer complexes studied possibly due to their strong solvation. The tendency to associate also varies widely with the structure of the parent nitro-compound being greatest with the adduct from 2-methoxycarbonyl-4,6-dinitroanisole. It is of interest to speculate on the structure of the ion associates produced. One possibility would be (III) where a metal ion associates strongly with a nitro-group, or other electronegative substituent such as CO_2Me, at the positions *para* or *ortho* to addition. Recent evidence [2,4] suggests that more negative charge resides at the *para*- than the *ortho*-position so that this form, as shown in (III), would be favoured. Indeed Meisenheimer in his original formulation [17] seventy years ago specifically associated the metal cation with the *para*-nitro-group. However the large variation in association constant K_2 with structure, and in particular the small tendency of the 1,3,5-trinitrobenzene adduct to associate, is difficult to rationalise on this basis. We think it more probable that an ion associate is formed whereby the cation is held by a cage effect by the oxygen atoms around the position of addition as shown in (IV). The two methoxy-groups at C-1 are orthogonal to the plane of the benzene ring while the *ortho*-substituents will be planar, or nearly planar, so that a favourable site for the cation is produced. Our data suggest that the *ortho*-CO_2Me group (IVa) provides somewhat better stabilisation than on *ortho*-NO_2 group (IVb). The necessity for two methoxy-groups at C-1 for strong ion association is demonstrated by the small association in the case of the adduct from 1,3,5-trinitrobenzene.

[3/136 *Received*, 22*nd January*, 1973]

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[17] J. Meisenheimer, *Annalen*, 1902, **323**, 205.