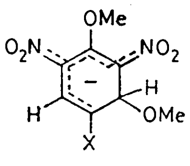
A Spectroscopic Study of the Formation of Isomeric Meisenheimer Complexes from 1-Methoxycarbonyl-3,5-Dinitrobenzene

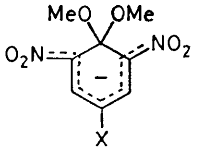
By **M. R. Crampton** * and **H. A. Khan**, Chemistry Department, The University, Durham

The covalent addition of methoxide, sulphite, and acetonate ions to 1-methoxycarbonyl-3,5-dinitrobenzene has been studied using ^{1}H n.m.r. and visible spectroscopy. With each nucleophile initial addition at the 4-position is followed by rearrangement to a mixture of the isomeric adducts. Surprisingly the methoxide ion shows little thermodynamic discrimination for the three hydrogen-bearing ring positions, although with sulphite or acetonate ions addition at the 2-position is thermodynamically favoured. Some corresponding measurements have been made with 3,5-dinitrobenzoic acid.

SEVERAL examples have been reported[1,2] of the initial formation under kinetic control of 1,3-Meisenheimer complexes (I) from substituted anisoles, and their subsequent rearrangement to the thermodynamically more stable 1,1-complexes (II).

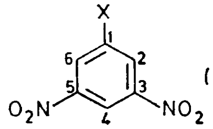


(I)



(II)

Similarly there is the possibility of isomeric addition to 1-X-3,5-dinitrobenzenes (III). Pollitt and Saunders[3] attempted to distinguish the possibilities of addition at C-2 (or C-6) from addition at C-4 from visible spectral data—addition at the 4-position was thought to give rise to absorption at longer wavelength than at the 2-position. However ^{1}H n.m.r. spectroscopy should give more conclusive results. Foreman and Foster[4] used this technique to examine the adducts formed from (III; X = CN or CF_3) with methoxide in wet dimethyl sulphoxide. Addition of base (hydroxide or methoxide) was found to occur exclusively at C-2. However in the presence of carbanions generated from ketones both possible adducts were initially produced although it is not clear from their work whether this is the situation at equilibrium.



(III)

In order to obtain more detailed information regarding isomeric addition we have examined the interactions of 3,5-dinitrobenzoic acid and its methyl ester with a series

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[1] For recent reviews on Meisenheimer complexes see: (*a*) M. R. Crampton, *Adv. Phys. Org. Chem.*, 1969, **211**; (*b*) M. J. Strauss, *Chem. Rev.*, 1970, 667.

[2] K. L. Servis, *J. Amer. Chem. Soc.*, 1967, 1508; M. R. Crampton and V. Gold, *J. Chem. Soc.* (*B*), 1966, 893; J. H. Fendler, E. J. Fendler, and C. E. Griffin, *J. Org. Chem.*, 1969, **34**, 689; F. Terrier and F. Millot, *Bull. Soc. chim. France*, 1969, 2692; F. Terrier and F. Millot, *Bull. Soc. chim. France*, 1970, 1743; M. P. Terrier and M. P. Simmonin, *Bull. Soc. chim. France*, 1971, 677.

[3] R. J. Pollitt and B. C. Saunders, *J. Chem. Soc.*, 1965, 4615.

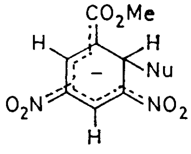
[4] M. I. Foreman and R. Foster, *Canad. J. Chem.*, 1969, 729.

of nucleophiles. In particular we were interested in the relative rates of addition at C-2 and C-4 and the relative thermodynamic stabilities of the adducts so produced. After the completion of our work Terrier *et al.*[5] published a communication in which they reported a reinvestigation of the reaction 1-cyano-3,5-dinitrobenzene with hydroxide and methoxide in dimethyl sulphoxide. Their conclusions that base addition occurs first at C-4 followed by rearrangement to the C-2-adduct which is thermodynamically more stable are in general agreement with our own although there are interesting differences between the methoxycarbonyl- and cyano-substituted compounds.

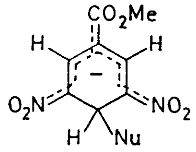
RESULTS AND DISCUSSION

1-*Methoxycarbonyl*-3,5-*dinitrobenzene and Sodium Methoxide*.—The ^{1}H n.m.r. spectrum produced on the addition of a concentrated solution of sodium methoxide in methanol to a solution of the substrate in dimethyl sulphoxide shows clearly that both isomeric adducts are produced (Figure 1). The ring protons of (IV; Nu = OMe) give three spin-coupled bands of equal intensity at δ 5·83, 8·51, and 8·09 p.p.m. (downfield from internal tetramethylsilane) while the ring protons of (V; Nu = OMe) give two sets of bands with intensity ratio 2 : 1 at δ 8·27 and 6·22 p.p.m. respectively. In each case the band due to the proton at the position of addition is shifted considerably to high field consistent with a change in hybridisation at this position. Measurements were taken between 5 and 60 min from the time of mixing and showed no change in the relative intensities of these bands. Thus under these conditions a thermodynamically stable mixture of adducts is produced. The intensities measured at 25° indicate that (IV) is favoured over (V) in the ratio 73 ± 3 : 27 ± 3.

FIGURE 1 ^{1}H N.m.r. spectrum produced on the addition of 1 equivalent of sodium methoxide in methanol to 1-methoxycarbonyl-3,5-dinitrobenzene in dimethyl sulphoxide



(IV)



(V)

Additional independent information is given by visible spectra recorded in more dilute solutions. In media rich in dimethyl sulphoxide a red-purple species ($\lambda_{max.}$ 378, 514, and 550 nm) is initially formed. However the spectrum changes quickly with time as shown in Figure 2. It seems likely in view of the n.m.r. data that at equilibrium both isomeric adducts will be present so that the time-stable spectrum will be comprised of two overlapping sets of bands. Analysis of this final spectrum indicates that at equilibrium 30 ± 5% of the initially formed species is present and 70 ± 5% of the isomer. This does not of itself indicate which is the kinetically preferred isomer, however comparison with the spectra of the adducts formed with sulphite ion shows that (V; Nu = OMe) is initially produced. The equilibrium ratio of (IV) : (V) = 7 : 3 obtained is in good agreement with that obtained independently from the n.m.r. data.

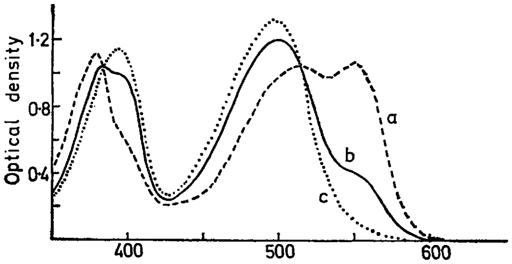


FIGURE 2 Visible spectra of 1-methoxycarbonyl-3,5-dinitrobenzene (6·0 × 10^{-5}M) and sodium methoxide (4·0 × 10^{-4}M) in dimethyl sulphoxide–methanol 97 : 3 (v/v): (a) initial spectrum corresponds to (V; Nu = OMe), (b) time-stable spectrum recorded after 20 min, corresponds to a mixture of (IV) and (V), (c) spectrum calculated for (IV; Nu = OMe)

These results were obtained in media containing only a small amount of methanol (3% v/v). However the shape of the time-stable spectrum measured in media containing from 3 to 50% methanol was independent of solvent. This indicates that there is no large change in the proportion of the two isomers present at equilibrium with change of solvent. However in the more methanolic solvents spectra recorded within 1 min of mixing corresponded to the equilibrium mixture of isomers, so that the rate of the conversion of (V) to (IV) is increased.

1-*Methoxycarbonyl*-3,5-*dinitrobenzene and Sodium Sulphite*.—In the presence of sodium sulphite (4 × 10^{-3}M) in dimethyl sulphoxide–water (19/1, v/v) a blue species is initially produced which rearranges slowly ($t_{\frac{1}{2}}$ = 15 h) to a red species. Visible spectra are in Figure 3. Increasing the proportion of water in the solvent causes an increase in the rate of the rearrangement; thus in a solvent containing 15% water $t_{\frac{1}{2}}$ is *ca.* 5 min while with 30% water the spectrum recorded within 1 min of mixing is that of the red species. N.m.r. spectra recorded in more concentrated solutions in the latter solvent system showed three bands of equal intensity at δ 5·50, 8·22, and 7·72 p.p.m., clearly indicating structure (IV; Nu = SO_3^-) for the thermodynamically more stable red species. It was not possible to obtain an n.m.r. spectrum of the blue species initially formed in media containing more dimethyl sulphoxide due to the insolubility of sodium sulphite in these media. However there can be little doubt that it has structure (V; Nu = SO_3^-).

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[5] F. Terrier, F. Millot, and M. P. Simmonin, *Tetrahedron Letters*, 1971, 2933.

1-Methoxycarbonyl-3,5-dinitrobenzene and Acetonate Ions.—Acetonate ions were generated from acetone in dimethyl sulphoxide using either triethylamine or sodium methoxide. In either case the n.m.r. spectrum showed initial addition at C-4 to give (V; Nu = CH_2COCH_3). Rearrangement occurred slowly with time ($t_{\frac{1}{2}} \sim$ several days) to give an equilibrium mixture of (IV) and (V) (Nu = CH_2COCH_3) in the ratio (IV) : (V) = 7 : 1. Visible spectra recorded in more dilute solutions indicated similar behaviour.

3,5-Dinitrobenzoic Acid.—The addition of one equivalent of sodium methoxide to the acid in dimethyl sulphoxide results in the formation of the carboxylate ion without the product of colour. Further addition of base gave a red colour, the visible spectrum showing a maximum at 530 nm with small shoulder at 600 nm. Unfortunately n.m.r. measurements were not successful probably due to the formation of small quantities of radical anions.[4,6]

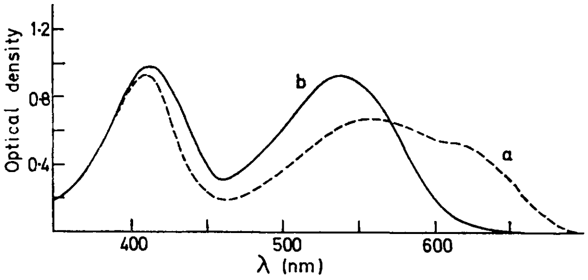
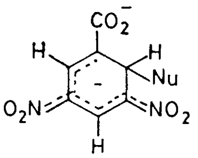
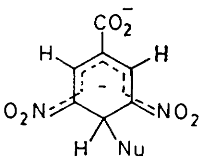


FIGURE 3 Visible spectra of 1-methoxycarbonyl-3,5-dinitrobenzene ($5·4 \times 10^{-5}$M) and sodium sulphite (4×10^{-3}M) in dimethyl sulphoxide–water (90/10 (v/v): (a) initial spectrum corresponds to (V; Nu = SO_3^-), (b) final spectrum recorded after 12 h corresponds to (IV; Nu = SO_3^-)

However the n.m.r. spectra produced in the presence of acetone show the initial formation of (VII) which rearranges quantitatively with time to (VI; Nu = CH_2COCH_3). A similar change is indicated from visible spectra which initially show two bands $\lambda_{max.}$ 580 and 680 nm [due to (VII)], while eventually a single band $\lambda_{max.}$ 555 nm is observed in this region of the spectrum [due to (VI)]. Chemical evidence for the formation of (VII) has previously been given by Akatsuka.[7]



(VI)



(VII)

The visible spectra produced from this compound with acetonate ion are, then, basically similar to those of the corresponding adducts produced from the methyl ester. Arguing on this basis the visible spectrum produced with methoxide as the attacking nucleophile indicates that both adducts (VI) and (VII) (Nu = OMe) are formed. If most of the absorption at 600 nm is due to (VII; Nu = OMe) then we estimate that between 10 and 20% of this isomer is present in the equilibrium mixture.

Equilibrium Constants.—The equilibrium constants for formation of Meisenheimer complexes from a number of compounds with sodium methoxide in methanol have been determined[1] and we sought to compare the value for 1-methoxycarbonyl-3,5-dinitrobenzene. Direct measurement in methanol was not possible due to the low value of the equilibrium constant. However measurements of optical density in mixed solvents containing 40—60 and 50—50 (v/v) dimethyl sulphoxide–methanol gave values for K_c of 2·9 and 19 l mol^{-1} respectively. The variation of equilibrium constant of 1,3,5-trinitrobenzene with sodium methoxide in mixed solvents has previously been measured,[8] when an enhancement of $1·0 \times 10^3$ was found on going from methanol to 40% dimethyl sulphoxide. Assuming that the equilibrium constants for the two compounds will vary in a similar way with solvent composition, a value of $2·9 \times 10^{-3}$ is obtained for the reaction of the methoxycarbonyl compound in methanol. This is roughly 5000 times smaller than the corresponding value for the 1,3,5-trinitrobenzene. However the observed value is is the sum of the values for the formation of (IV) and (V). Hence the equilibrium constants for the formation of (IV) and (V) have the values $2·0 \times 10^{-3}$ and $0·9 \times 10^{-3}$ respectively.

In addition we find that the equilibrium constant for complex formation with sodium thioethoxide in methanol has the value 2·0 ± 0·5 l mol^{-1} which is roughly 2000 times smaller than the corresponding value[8] for 1,3,5-trinitrobenzene ($3·5 \times 10^3$ l mol^{-1}).

CONCLUSIONS

With each nucleophile studied addition at the 4-position of 1-methoxycarbonyl-3,5-dinitrobenzene is a faster process than at the equivalent 2- or 6-positions. This result is similar to that previously obtained[6] with (III; X = CN). Our results show that the proportions of the isomers (IV) and (V) present at equilibrium depends on the attacking nucleophile. With methoxide (IV) is favoured over (V) in the approximate ratio 7 : 3. However it should be noted that there is a statistical factor of 2 : 1 favouring (IV) so that in fact methoxide shows very little discrimination for the three hydrogen-carrying ring positions. With acetonate ion (IV) is clearly favoured over (V) at equilibrium while with sulphite the amount of (V) present at equilibrium is below our detection limit. These differences may reflect differences in the steric requirements of the two types of adduct.

The argument has been frequently used[1] both by others and by one of us that one of the important factors governing the stabilities of Meisenheimer complexes is the presence of a strongly electron-withdrawing group *para* to the position of addition. Thus the stabilities of the

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[6] S. M. Shein, V. V. Brovko, and A. O. Khmelinskaya, *Zhur. org. Khim.*, 1970, **6**, 781.

[7] M. Akatsuka, *Yakugaku Zasshi*, 1960, **80**, 375, 378, 389.

[8] M. R. Crampton, *J. Chem. Soc.* (*B*), 1968, 1208.

adducts formed from anisoles containing nitro- and cyano-groups have been rationalised on this basis.[9] Accordingly (III; X = CN) gives with methoxide only 5% of the adduct formed by addition *para* to the cyano-group but 95% of the adduct with a *para*-nitro-group.[5] On the basis of σ or σ-values [10] the nitro-group and cyano-groups are considerably more electron-withdrawing than the methoxycarbonyl group. It is, then, surprising that the stabilities of (IV) and (V) (Nu = OMe) are so nearly equal. It would have been expected that (IV) where addition occurs *para* to a nitro-group would be thermodynamically favoured relative to (V) where there is a *para*-methoxycarbonyl group. In addition our results although less certain suggest that some of the adduct (VII; Nu = OMe) is present in the equilibrium mixture formed by addition to the 3,5-dinitrobenzoate ion. Clearly the electron-withdrawing ability of the group *para* to the position of addition is not of overriding importance in determining the relative stabilities of *these* complexes. More work is in progress with similar systems.

TABLE 1

Chemical shifts [a] (δ/p.p.m. downfield from internal tetramethylsilane) and coupling constants (J/Hz) [b]

	Ring protons							
	2-H	4-H	6-H	CO_2Me	OMe	J_{24}	J_{46}	J_{26}
(III; X = CO_2Me)	8·95	9·08	8·95	4·05		2·0	2·0	
(IV; Nu = OMe)	5·83	8·51	8·09	3·72	3·06	1·4	2·0	0·5
(IV; Nu = SO_3^-)	5·50	8·22	7·72	3·70		1·3	1·9	0·3
(IV; Nu = CH_2COCH_3)	4·61	8·31	7·82			1·0	2·0	0·3 [c]
(V; Nu = OMe)	8·27	6·22	8·27			1·2	1·2	
(V; Nu = CH_2COCH_3)	8·05	5·07	8·05			1·0	1·0	[c]
(VI; Nu = CH_2COCH_3)	4·68	8·35	7·58			1·0	2·0	0·3 [c]
(VII; Nu = CH_2COCH_3)	8·23	5·10	8·23			1·0	1·0	[c]

[a] Solvent is dimethyl sulphoxide containing a little methanol or water. [b] Accurate to ±0·2 Hz. [c] Coupling $J \sim 5{\cdot}5$ Hz is observed between the ring proton at high field and the methylene protons of the acetone.

EXPERIMENTAL

1-Methoxycarbonyl-3,5-dinitrobenzene (m.p. 112°) was prepared by esterification of the parent acid. Dimethyl sulphoxide was dried over calcium hydride and distilled under reduced pressure, the middle fraction being collected.

^1H N.m.r. spectra were recorded with a varian A56/60 instrument using solutions of concentration *ca.* 0·2M. Spectral analysis was carried out using standard methods.[11] Details of chemical shifts and coupling constants are in Table 1. The ring protons of the parent methoxycarbonyl compound give an AB_2 spectrum and a spectrum simulated with $J_{AB} = 2{\cdot}0$ Hz, $\nu_0(\delta_A - \delta_B) = 7{\cdot}7$ Hz gave good agreement with that observed. The ring protons of adducts of structure (IV) or (VI) give an AMX pattern. In each case the coupling constant J_{24} was found to be *ca.* 2·0 Hz as in the parent compound, while coupling across the methoxycarbonyl group, J_{26}, was small. The value of J_{46} was found to vary between 1·0 and 1·4 Hz depending on the attacking nucleophile. This variation accounts for the difference in appearance of the bands due to the proton at C-4 (triplet with methoxide, quartet with acetonate ion). When the attacking nucleophile is the acetonate ion, coupling $J \simeq 5{\cdot}5$ Hz is observed between the ring proton at the position of addition and the methylene protons of the acetone.

There was no evidence from n.m.r. spectra for non-equivalence of ring-protons resulting from restricted rotation of the CO_2Me group.

Visible spectral measurements were made with Unicam SP 800 and SP 500 instruments, with substrate concentrations of *ca.* 4 × 10^{-5}M. Details are in Table 2. Measurements of optical density at 500 nm were used to determine the overall equilibrium constant at 25° for complex formation of (III; X = CO_2Me) with sodium methoxide in methanol–dimethyl sulphoxide mixtures. The values of K_c increased slightly with sodium methoxide concentration. Extrapolation to zero base gave values of 2·9 l mol^{-1} and 19 l mol^{-1} in solvents containing respectively 40 and 50% (v/v) dimethyl sulphoxide.

TABLE 2

Visible spectral data for adducts from 1-methoxycarbonyl-3,5-dinitrobenzene in dimethyl sulphoxide

	$\lambda_{max.}$ (nm)	$10^{-4}\varepsilon$	$\lambda_{max.}$ (nm)	$10^{-4}\varepsilon$	$\lambda_{max.}$ (nm)	$10^{-4}\varepsilon$
(IV; Nu = OMe)	392	1·85	496	2·20		
(IV; Nu = SO_3^-	414	1·80	538	1·70		
(IV; Nu = CH_2COCH_3)	414		545			
(V; Nu = OMe)	378	1·80	514	1·75	550	1·75
(V; Nu = SO_3^-)	410	1·75	560	1·30	620sh	1·00
(V; Nu = CH_2COCH_3)	410		560		630sh	

[1/2046 *Received, 3rd November*, 1971]

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[9] E. J. Fendler, J. H. Fendler, C. E. Griffin, and J. W. Larsen, *J. Org. Chem.*, 1970, 287.

[10] H. Van Bekkum, P. E. Verkade, and P. M. Wepster, *Rec. Trav. chim.*, 1959, 815.

[11] J. A. Pople, W. G. Schneider, and H. J. Bernstein, 'High Resolution Nuclear Magnetic Resonance,' McGraw-Hill, New York, 1959.