

Reactions of Aromatic Nitro-compounds in Alkaline Media. Part XI.* Structural Investigations by Proton Magnetic Resonance Spectroscopy

By M. R. Crampton and V. Gold

The interactions of a series of di- and tri-nitrobenzene derivatives with base (mostly methoxide in a mixed solvent of equimolar amounts of methanol and dimethyl sulphoxide) have been investigated by proton magnetic resonance spectroscopy. Three types of interaction are recognised: (a) addition of base to a nuclear position carrying hydrogen (*e.g.*, 1,3,5-trinitrobenzene, *NN*-dimethylpicramide), (b) addition of base to a nuclear position carrying a substituent, usually a methoxyl group (*e.g.*, methyl picrate, 2,4-dinitroanisole), and (c) (primary or secondary amines) loss of a proton from an amino-group (*e.g.*, 2,4- and 2,6-dinitroaniline, 2,4-dinitrodiphenylamine). In picramide proton loss and methoxide addition of type (a) compete and their relative proportions can be changed by varying the base and solvent used. In several cases two equivalents of methoxide can react with one aromatic molecule: *e.g.*, *NN*-dimethylpicramide can add two methoxide ions in equivalent positions, whereas one molecule of *N*-methylpicramide can lose an amino-proton and add a methoxide ion to the aromatic ring.

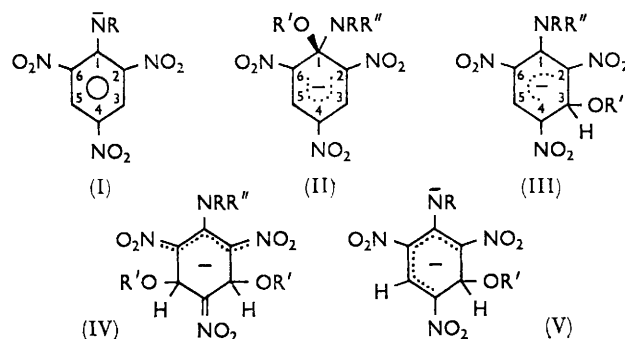
Addition of type (a) tends to be more rapid than type (b), but the latter process results in the thermodynamically more stable product.

THE use of nuclear magnetic spectroscopy in the establishment of the structure of covalent adducts of alkoxide ions with 1,3,5-trinitrobenzene and methyl picrate was described¹ in 1964. The same method has been applied to the coloured species produced from nitroaromatic amines in alkaline media² and a summary of further measurements on related systems has been published.³ We now fully report these experiments.

Our measurements and main conclusions have been confirmed in the course of other investigations,⁴⁻⁶ but there are some differences in detail. In our work most measurements relate to solutions in equimolar dimethyl sulphoxide-methanol mixture containing sodium methoxide, and some to mixtures of dimethyl sulphoxide with water or alcohols and the appropriate sodium lyate. The substrates now studied include 2,4- and 2,6-dinitroaniline, picramide, and its *N*-methyl and *NN*-dimethyl derivatives, 2,4-dinitro- and 2,4,6-trinitro-diphenylamine, 2,4-dinitroanisole, 2,4-dinitrophenol, and, less successfully, *m*-dinitrobenzene.

The structural problems existing for nitroaromatic ethers⁷ and nitroaromatic amines⁸ in relation to the evidence provided by electronic spectra have been discussed. For primary or secondary nitroaromatic amines the most probable alternative structural possibilities are (I), (II), and (III) (*R* = H, alkyl, phenyl; *R'* = H, alkyl; *R''* = H). Formula (II), the analogue of Meisenheimer's formula for adducts of ethers,⁹ was suggested by Busch and Kogel¹⁰ for solid compounds prepared by the action of alcoholic alkali on secondary amines and by Farmer¹¹ for the potassium methoxide adduct of picramide. Green and Rowe,¹² however, considered that alkali-metal analyses supported formula (I) in many nitroanilines, and it was also adopted by

Slough for nitrodiphenylamines.¹³ Formula (III) was suggested by Gold and Rochester⁸ who adduced evidence that, in solutions of picramide in methanolic sodium methoxide, both ions (III) and (I) were present, with



(III) predominating, whereas for tertiary amines (III) was the only important formula for the result of reversible 1:1 interaction. For 1:2 interactions structures (IV) and (V) are the corresponding possibilities if new covalencies are formed.

The mode of ionisation of the primary and secondary amines is also important in view of the use of these compounds as indicators for the establishment of acidity functions in alkaline media.²

EXPERIMENTAL

Picramide and its *N*-substituted derivatives were prepared by the addition of aqueous ammonia or the appropriate amine to methanolic picryl chloride,¹⁴ and recrystallised to constant m. p. The other substrates were recrystallised commercial specimens.

Solvents were purified as previously described.¹⁵ Nuclear magnetic resonance (n.m.r.) spectra were recorded at 31° with an instrument operating at 28 Mc./sec. (constructed

* Part X, M. R. Crampton and V. Gold, *J. Chem. Soc. (B)*, 1966, 498.

¹ M. R. Crampton and V. Gold, *J. Chem. Soc.*, 1964, 4293.

² M. R. Crampton and V. Gold, *Proc. Chem. Soc.*, 1964, 298.

³ M. R. Crampton and V. Gold, *Chem. Comm.*, 1965, 256.

⁴ R. Foster, C. A. Fyfe, and J. W. Morris, *Rec. Trav. chim.*, 1965, **84**, 516.

⁵ R. Foster and C. A. Fyfe, *Tetrahedron*, 1965, **21**, 3363.

⁶ K. L. Servis, *J. Amer. Chem. Soc.*, 1965, **87**, 5495.

⁷ V. Gold and C. H. Rochester, *J. Chem. Soc.*, 1964, 1687, 1710.

⁸ V. Gold and C. H. Rochester, *J. Chem. Soc.*, 1964, 1697, 1727.

⁹ J. Meisenheimer, *Annalen*, 1902, **323**, 205.

¹⁰ M. Busch and W. Kogel, *Ber.*, 1910, **43**, 1549.

¹¹ R. C. Farmer, *J. Chem. Soc.*, 1959, 3433.

¹² A. G. Green and F. M. Rowe, *J. Chem. Soc.*, 1913, 508.

¹³ W. Slough, *Trans. Faraday Soc.*, 1961, **57**, 366.

¹⁴ J. Glazer, E. D. Hughes, C. K. Ingold, A. T. James, G. T. Jones, and E. Roberts, *J. Chem. Soc.*, 1950, 2674.

¹⁵ M. R. Crampton and V. Gold, *J. Chem. Soc. (B)*, 1966, 498.

by Dr. J. Cartlidge and Dr. M. S. Blackie) except for the measurements on 2,4-dinitrophenol and some of those on *N*-methylpicramide, for which a Perkin-Elmer spectrometer (60 Mc./sec.) was used. Line separations from the major solvent peak were obtained to an accuracy of ± 1 c./sec. with the aid of a side-band oscillator. These separations were then related to the position of internal tetramethylsilane in the solvent system used. All chemical shifts are expressed in p.p.m. relative to internal tetramethylsilane.

Picramide-Sodium Methoxide Complex.—Sodium methoxide in methanol (0.75M, 1 equiv.) was added to a stirred solution of picramide (1.5 g.) in dry benzene (125 ml.). An orange-brown precipitate immediately formed and was quickly filtered off, washed with benzene, and dried *in vacuo*.

Interactions of Nitro-compounds with Base in Solution.—Solutions of various concentrations of sodium methoxide in methanol or sodium hydroxide in water were added to solutions of nitro-compound in dimethyl sulphoxide (1 M). The mole ratio of base to nitro-compound was thus varied without varying the overall solvent composition. Unless

These results are consistent only with a fast exchange between dinitroaniline and a negative ion formed by proton loss from the amino-group, since a single set of sharp bands due to ring protons is observed when both dinitroaniline and its anion are present in solution. Methoxide addition would produce a resonance at *ca.* -6.2 p.p.m., associated with the hydrogen atom at the site of addition, with a coupling constant of 1–2 c./sec. to the hydrogen nucleus at the position *meta* relative to this site, and is therefore ruled out. Also, in those cases where it has been observed, separate signals due to parent compound and complex are obtained.^{1,5}

Interaction of 2,4-Dinitrophenylamine with Sodium Methoxide.—The spectrum of the parent compound resembles that of 2,4-dinitroaniline (Table 1, *B*). The protons of the unsubstituted ring, *e*, give a single unresolved peak.

The resonances due to *a*, *b*, and *c* move systematically to high field with unchanged intensities and spin-coupling constants as the proportion of base to nitro-compound is increased. The amino-protons give a combined line with the hydroxylic protons of the solvent. The phenyl protons (*e*) now give a complex spectrum with two major lines.

TABLE 1
Spectra of 2,4-dinitroaniline derivatives in presence of sodium methoxide

| | Mole ratio [OMe ⁻]/[Amine] | Chemical shifts (p.p.m. from tetramethylsilane) * | | | | |
|--|---|---|--------------|--------------|--------------|--------|
| | | Proton <i>a</i> † | <i>b</i> †‡ | <i>c</i> † | <i>e</i> | Amino |
| <i>A</i> : 2,4-Dinitroaniline | 0 | –8.71 | –8.28, –7.93 | –7.21, –6.88 | — | –8.32 |
| | 0.4 | –8.71 | –8.04, –7.68 | –7.00, –6.68 | — | — |
| | 0.75 | –8.71 | –7.83, –7.47 | –6.84, –6.46 | — | — |
| | 1.15 | –8.71 | –7.73, –7.37 | –6.71, –6.36 | — | — |
| | 1.6 | –8.71 | –7.69, –7.33 | –6.68, –6.36 | — | — |
| | 0 | –8.90 | –8.40, –8.07 | –7.28, –6.96 | –7.50 | –10.25 |
| <i>B</i> : 2,4-Dinitrodiphenylamine... | 0.55 | –8.86 | –8.00, –7.63 | –6.88, –6.56 | –7.25 | — |
| | 0.67 | –8.82 | –7.86, –7.49 | –6.76, –6.44 | –7.15 | — |
| | 1.0 | –8.68 | –7.68, –7.32 | –6.53, –6.18 | –7.11, –6.93 | — |
| | 1.5 | –8.68 | –7.68, –7.32 | –6.53, –6.18 | –7.11, –6.93 | — |

* For identification of positions *a*, *b*, *c* see Table 4B; *e* refers to protons in unsubstituted phenyl group. † Mean values for doublets ($J \sim 2.5$ c./sec.). ‡ The two values given are positions at 28 Mc./sec. of the two components of a doublet due to spin coupling between *b* and *c*: the chemical shift is in every case the mean of these.

otherwise specified, the solvents contained 50 moles-% of dimethyl sulphoxide and 50 moles-% of the hydroxylic component. Spectra were generally recorded about 3–5 min. after the solutions had been mixed. Except for *m*-dinitrobenzene, addition of acid resulted in precipitation of the parent nitro-compound.

RESULTS AND SPECTRAL ASSIGNMENTS

Interaction of 2,4-Dinitroaniline with Sodium Methoxide.—The n.m.r. spectrum of 2,4-dinitroaniline shows a series of bands with shifts between -9 and -7 p.p.m. The amino-protons give a fairly broad resonance superimposed on the spectrum of the ring protons. The addition of a trace of methanolic methoxide to a solution of the nitro-compound in dimethyl sulphoxide caused exchange between the amino-protons and the hydroxyl protons of the methanol so that a clear spectrum of the ring protons, consistent with the parameters given in Table 1, *A* was observed. As the concentration of base was increased up to a mole ratio of 1:1 the resonances attributed to *b* and *c* moved smoothly to high field while there was no detectable change in the position of the doublet due to *a*, the spin coupling constants of these protons remaining constant. No new band was observed. Further increase of the proportion of base had no effect.

The change in the appearance of the spectrum of the C_6H_5 protons in this case is attributed to the different proportions of the negative charge carried by the different positions.

Again the unchanged coupling constants of the protons in the nitro-substituted ring, together with the fact that a combined resonance due to amino-protons and hydroxyl protons of the solvent is observed, indicates proton loss; and methoxide addition is excluded.

Interaction of 2,6-Dinitroaniline with Sodium Methoxide (Table 2).—The addition of a trace of base results in a single fairly broad combination line due to amino-protons and hydroxyl protons of the solvent. Increasing the amount of methoxide present causes the resonances due to ring protons to shift to high field, the spin-coupling remaining unaltered. In contrast to the behaviour of 2,4-dinitroaniline, the nuclear resonances do not remain sharp as the methoxide concentration is increased, but broaden until by a mole ratio methoxide:nitro-compound of 1:2 they are scarcely visible. The broadness of the lines beyond a mole ratio 1:2 renders the chemical shift doubtful in this concentration region. Again these spectral changes are interpreted as indicating proton loss from the amino-group in basic solution. In the concentration range where

the ring protons give clear spectra no change in the pattern of the spectra is observed, and this excludes addition of methoxide. The broadness of the resonances could be the result of a rate of exchange between parent compound and anion which is not sufficiently large to produce sharp time-averaged spectra. This exchange process is slower than in the case of 2,4-dinitroaniline, and it seems likely that here

TABLE 2
2,6-Dinitroaniline-Sodium methoxide

| Mole ratio [OMe ⁻] [Dinitroaniline] | Chemical shifts * | | |
|---|-------------------|----------|-------|
| | Protons <i>a</i> | <i>b</i> | Amino |
| 0 | -8.46 † | -6.82 † | -8.38 |
| 0.25 | -8.38 † | -6.64 † | |
| 0.4 | -8.30 † | -6.50 † | |
| 0.75 | Very broad | | |
| 1.0 | -7.89 † | -6.14 † | |

* *a* = 3,5-positions. *b* = 4-position. † Doublet, *J* = 8 c./sec. ‡ Triplet, *J* = 8 c./sec.

the two nitro-groups *ortho* to the amino-group have a steric effect which decreases the rate. Another possibility is that a small concentration of a radical is causing relaxation, to

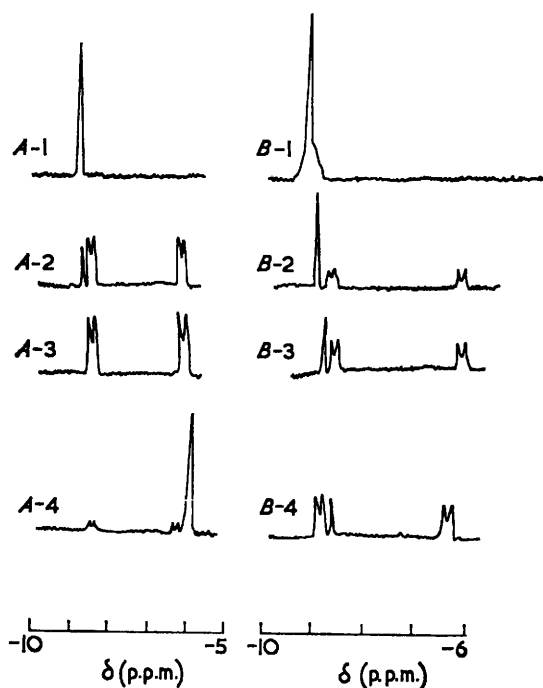
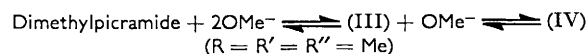


FIGURE 1 N.m.r. spectra (28 Mc/sec.) for (A) *NN*-dimethylpicramide (1, in equimolar dimethyl sulphoxide-methanol, with ratio [NaOMe]/[Amine] = 0; 2, same, ratio = 0.75; 3, same, ratio = 1.0; 4, same, ratio = 2.1) and (B) picramide (1, in dimethyl sulphoxide; 2, in equimolar dimethyl sulphoxide-methanol, with ratio [NaOMe]/[Amine] = 0.5; 3, same, ratio = 0.75; 4, same, ratio = 1.0)

the effect of which our failure to observe an n.m.r. spectrum of *m*-dinitrobenzene under similar conditions may be due.

Interaction of *NN*-Dimethylpicramide with Sodium Methoxide (Figure 1, A).—The sharp methyl proton resonance of the parent compound at -2.89 p.p.m. has an intensity three times that of the sharp resonance at -8.84 p.p.m. due to the ring protons. The addition of base causes the appearance of two doublets (*J* ~ 1.5 c./sec.), centred at -6.17 and -8.46 p.p.m., respectively, which have equal

intensity. As the methoxide concentration is increased up to that of the dimethylpicramide these new lines grow in intensity at the expense of the line at -8.84 p.p.m., until each has intensity representing one proton. The line due to *N*-methyl protons remains unaltered in shift or intensity. The appearance of two doublets is interpreted as the addition of methoxide at C(3) to give (III, R = R' = R'' = Me).



The large shift to high field of one resonance, towards the position expected for aliphatic protons, is also consistent with this formula.² Addition at C(1) is excluded, since in this formulation little variation would be expected in the shifts of the protons at C(3) and C(5).

As the ratio of methoxide to dimethylpicramide is increased from 1:1 to 2:1, the doublets gradually decrease in intensity and a new resonance, which is a single line, is observed at -6.05 p.p.m. By mole ratio 2:1 this new resonance has taken almost all the intensity of the ring-proton resonances. This change in spectrum is interpreted as indicating further methoxide addition, to give (IV; R = R' = R'' = Me). The occurrence of a single resonance due to ring protons is again inconsistent with addition at C(1).

The visible absorption spectra of dimethylpicramide were taken in methanolic dimethyl sulphoxide containing methoxide. For a low methoxide concentration the spectrum (λ_{max} 4000 Å) was very similar to that found by Gold and Rochester for dimethylpicramide in methanolic sodium methoxide and attributed by them to a 1:1 addition complex.⁸ Increase of the concentration of methoxide caused the absorption spectrum to change (λ_{max} 4230 Å) to a spectrum similar to that attributed by them to a 1:2 complex. These spectral analogies indicate that in the n.m.r. experiments the interaction being observed is between dimethylpicramide and methoxide without the incursion of chemical interaction with the solvent dimethyl sulphoxide.

Interaction of *NN*-Dimethylpicramide with Sodium Hydroxide (medium 40 moles-% water-60 moles-% dimethyl sulphoxide).—The n.m.r. spectral changes on addition of aqueous hydroxide to dimethylpicramide are similar to those found for methoxide and are similarly interpreted. In a solution equimolar in hydroxide and nitro-compound the ring-protons again show spin-coupling (*J* ~ 1.8 c./sec.) with chemical shifts of -6.13 and -8.38 p.p.m. As the proportion of hydroxide is increased a new single band due to a 1:2 complex appears at -6.00 p.p.m.

Interaction of Picramide with Sodium Methoxide (Figure 1, B).—The n.m.r. spectra of picramide in dimethyl sulphoxide containing methanolic sodium methoxide share some of the features shown by 2,4-dinitroaniline, exemplifying proton loss from the amino-group, and some of the features shown by *NN*-dimethylpicramide, exemplifying methoxide addition. This behaviour indicates that either proton loss or base addition can occur with this compound.

The spectrum of picramide itself consists of a sharp resonance at -9.07 p.p.m. due to ring protons, superimposed on a broader resonance at -9.0 p.p.m. due to the amino-protons. The addition of base results in the merging of the amine resonance with the hydroxyl resonance of the solvent into a broad band and the appearance of two doublets, *J* ~ 1.5 c./sec. at -8.61 and -6.14 p.p.m.

These are analogous to the resonances at -8.46 and -6.17 p.p.m. of dimethylpicramide in presence of base and are attributed to the protons at C(5) and C(3) of a methoxide adduct (III; $R' = \text{Me}$, $R = R'' = \text{H}$). As the amount of methoxide is increased, these new bands grow at the expense of the resonance attributed to the ring protons of picramide. The latter resonance, however, gradually shifts to high field until by a mole ratio methoxide : picramide of 1 : 1 it has a shift of -8.46 p.p.m. This behaviour is best explained by proton loss from the amino-group to give (I; $R = \text{H}$). The interconversion of picramide and the negative ion formed by proton loss is fast, giving a sharp time-averaged resonance for the ring proton of unchanged picramide and (I). The methoxide adduct, on the other hand, has a relatively long lifetime so that discrete resonances are observed for this species. Table 3 gives the chemical shifts of the combined peak due to the ring protons of picramide and species (I), together with the relative intensities of this peak and the doublets from the methoxide adduct. These results refer to a solvent composition of 50 moles-% methanol-50 moles-% dimethyl sulphoxide.

TABLE 3
Picramide-Sodium methoxide

| Mole ratio [OMe-] [Picramide] | Relative intensities of | | Chemical shift of combined peak | |
|-------------------------------------|-------------------------|---------------------|------------------------------------|---------|
| | Combined peak | Pair of doublets | Found | Calc.* |
| 0 | 1 | 0 | -9.07 | |
| 0.25 | 0.8 | 0.2 | -9.03 | -9.03 |
| 0.50 | 0.6 | 0.4 | -8.98 | -8.97 |
| 0.75 | 0.4 | 0.6 | -8.86 | -8.85 |
| 1.0 | 0.2 | 0.8 | -8.46 | |

* See text.

If the reasonable assumption is made that there is little free methoxide present in these mixtures then, when the mole ratio is 1 : 1, there will be no free picramide present and hence the ratio of concentrations of the methoxide adduct to the anions formed by proton loss is 4 : 1. Using this result we calculated the ratio of picramide to anion (IV) present in each solution and hence the expected shift of the combined peak. The agreement with the experimental values of the chemical shift confirms that *ca.* 80% of the picramide ionises by base addition.

The resonance due to the added methoxide group is not observed in these solutions since the solvent absorbs in the same region of the spectrum. However, the spectrum of the solid complex prepared from picramide and sodium methoxide shows in dimethyl sulphoxide a sharp band at -3.20 p.p.m. which is attributed to the added methoxide group.

The formulation of the major interaction between picramide and methoxide as base addition is in agreement with Farmer's interpretation.¹¹ However, these results indicate that addition occurs at C(3), whereas Farmer postulated addition at C(1), the carbon atom bearing the amino-group. Farmer's argument rested on the observation that the same complex could be obtained either by the reaction of picramide with sodium methoxide or by the reaction of trinitroanisole with ammonia plus a little base. In methanol we find that in the presence of ammonia the ultraviolet-visible absorption spectrum of trinitroanisole ($\lambda_{\text{max.}}$ 2200 Å) changes quickly to that of picramide ($\lambda_{\text{max.}}$ 2400, 3200, and 4100 Å). This indicates that trinitroanisole is converted into picramide in the presence of

ammonia and suggests that in each case the complex isolated by Farmer resulted from the attack of base on picramide.

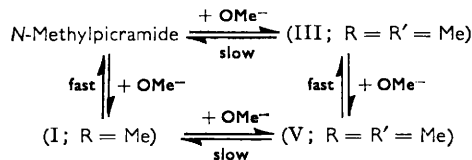
Interaction of Picramide with Sodium Ethoxide (medium 40 moles-% ethanol, 60% dimethyl sulphoxide).—The appearance of two new doublets with shifts of -8.61 and -6.19 p.p.m., and $J \sim 1.5$ c./sec., resembles the effect of addition of sodium methoxide but the upfield shift of the original resonance due to ring protons indicates that between 30 and 40% of the picramide ionises by proton loss while the remainder forms an ethoxide adduct.

*Interaction of Picramide with Potassium *t*-Butoxide* (medium 30 moles-% *t*-butyl alcohol, 70 moles-% dimethyl sulphoxide).—The addition of *t*-butoxide to picramide causes no new resonances due to ring protons of the nitro-compound. The original band at -9.07 p.p.m. moves uniformly to high field as the proportion of base is increased, having a shift of -8.46 p.p.m. at a mole ratio of 1 : 1. In this case, all the picramide is considered to ionise by proton loss. Broadening of the ring-proton resonance was observed in these solutions which is possibly due to the intermediate speed, by n.m.r. standards, of the interconversion of picramide and its anion.

Interaction of Picramide with Sodium Hydroxide.—On increase of the concentration of base in a medium containing equimolar amounts of water and dimethyl sulphoxide, new bands at -6.08 and -8.40 p.p.m. grew in intensity. They are attributed to a complex ion of formula (III; $R = R' = R'' = \text{H}$). Their intensities in a solution containing equimolar amounts of picramide and sodium hydroxide indicate that hydroxide addition is favoured over proton loss, approximately accounting for 70% of the product. In a solvent system containing only 30 moles-% of water similar observations were made, but proton loss was the major reaction. Quantitative measurements in these systems are restricted by the low solubility of picramide.

*Interaction of *N*-Methylpicramide with Methoxide*.—The n.m.r. spectrum of *N*-methylpicramide consists of three bands of relative intensity 1 : 2 : 3 assigned respectively to the amino-proton (-9.25 p.p.m., fairly broad), the ring protons (-8.93 p.p.m.), and the methyl protons (-2.90 p.p.m.). The addition of a trace of methoxide causes the amino-protons and hydroxylic protons of the solvent to give a broad combination band. Increasing the concentration of base causes the ring-proton resonance to move systematically to high field and in a solution of mole ratio base to picramide of 1 : 1 this resonance has a shift of -8.43 p.p.m. and is sharp. In addition, two small doublets ($J \sim 1.5$ c./sec.) are observed at -6.16 and -8.48 p.p.m. which increase in intensity as the methoxide concentration is increased and at equivalence account for *ca.* 20% of the ring-proton absorption. The shift to high field of the ring-proton resonance is taken to indicate fast exchange between the parent compound and an anion formed through proton loss from the amino-group (I; $R = \text{Me}$); the doublets result from methoxide addition at C(3) to give an adduct (III; $R = R' = \text{Me}$) of comparatively long life. Increasing the proportion of base beyond 1 : 1 causes the sharp band to broaden and decrease in intensity. The doublets increase in intensity until by a mole ratio of 2 : 1 methoxide : nitro-compound they each have intensity representing one proton. In addition, the low-field doublet shows a slight shift to lower field having a final value of -8.64 p.p.m. These observations are taken to represent formation of a 1 : 2 complex (V; $R = R' = \text{Me}$).

The fact that separate resonances due to the ring protons of (V) and (III) are not observed shows that these species must be in fast equilibrium. It is interesting that there is only a small shift in position for the ring protons of (V) and (III), complexes which carry different negative charges. Servis⁶ has found that in certain solutions the ring protons of species (I; R = Me) are non-equivalent and give a quartet pattern. We did not observe this fine structure although marked broadening of the resonance was found.



Interaction of N-Methylpicramide with Sodium Hydroxide (Medium 50 moles-% water, 50 moles-% dimethylsulphoxide).—As the content of sodium hydroxide increases in this system from zero to equimolar, the ring-proton resonance moves from -8.93 to -8.40 p.p.m. without change in appearance. This is attributed to the gradual conversion of N-methylpicramide into the anion (I; R = Me). An increase in the proportion of hydroxide to methylpicramide to 1.5 caused the ring-proton resonance to split into two doublets centred at -8.55 and -8.25 p.p.m., respectively, with a mutual coupling constant of 3 c./sec. As the proportion of sodium hydroxide is further increased to 2.5 the four lines decrease in intensity and, at their expense, two slightly split ($J = 1$ c./sec.) doublets at -8.59 and -6.22 p.p.m. increase in intensity. This pair of doublets is already present when the ratio hydroxide:methylpicramide is 1.5 and is attributed to the dianion analogous to (V; R = Me, R' = H). This behaviour and its interpretation are closely similar to the case of N-methylpicramide in the presence of excess of sodium methoxide in a medium consisting mainly of dimethyl sulphoxide.⁶ The splitting of the nuclear resonance of the ion (I; R = Me) into two mutually split doublets has been ascribed to the chemical non-equivalence of the ring protons owing to slow rotation about the partially double CN \equiv Me bond. This non-equivalence is not observed in less alkaline solutions (for example, when N-methylpicramide and sodium hydroxide are present in equimolar amounts) presumably because equilibration of the two forms by proton addition-abstraction involving the =NMe group and rotation about the C-NHMe bond is still rapid.

Interaction of 2,4,6-Trinitrodiphenylamine with Sodium Methoxide.—The spectrum in neutral solution consists of three bands of relative intensity 1:2:5 due to the amino-proton (-10.3 p.p.m.), the ring-protons of the nitro-substituted ring (-9.00 p.p.m.), and those of the unsubstituted ring (-7.29 p.p.m.). The addition of methoxide causes the resonance due to the two equivalent protons of the nitro-substituted ring to move to high field, the movement being proportional to the concentration of methoxide present up to a mole ratio of methoxide:nitro-compound of 1:1 when the chemical shift is -8.36 p.p.m. The change is consistent with loss of the amino-proton. The five phenyl protons in the second ring give a series of lines shifted to high field from the original unresolved resonance. Two major lines have shifts of -6.8 and -7.0 p.p.m. Increasing the proportion of methoxide beyond 1:1 causes a further change in spectrum. Three new resonances are

observed with shifts of -8.68 , -6.18 , and -7.00 p.p.m., and these grow at the expense of the resonance due to the ring protons of the mono-anion, as the concentration of methoxide is increased. These new resonances are attributed to the ring protons of a dianion (V; R = Ph, R' = Me). The resonances at -8.68 and -6.18 p.p.m. are of equal intensity and are attributed to the two non-equivalent protons of the nitro-substituted ring. The resonance at -7.00 p.p.m., which is fairly broad, is due to the N-phenyl protons. By contrast to the conjugate base of N-methylpicramide (I; R = Me) the aromatic protons of the nitro-substituted ring appear equivalent in the phenyl analogue (I; R = Ph).

Interaction of m-Dinitrobenzene with Sodium Methoxide.—The spectrum of m-dinitrobenzene in dimethyl sulphoxide-methanol is similar to the spectrum in deuteriochloroform, with a series of bands at ca. -8 p.p.m.¹⁶ Solutions containing sodium methoxide (0.5 or 1 mole per mole of dinitrobenzene) are coloured¹⁵ and showed initially no n.m.r. signal from the aromatic substrate. With increasing time a broad resonance (ca. -7 p.p.m.) was observed in each solution. After 24 hr. the less alkaline solution showed a series of fairly sharp bands centred at -7 p.p.m., together with a series of bands with positions and intensities characteristic of m-dinitrobenzene. The other solution showed only bands at ca. -7 p.p.m.; its acidification yielded a brownish solution and no dinitrobenzene was precipitated. No attempt has been made to identify the irreversible changes, and the reason for the absence of an initial spectrum,³ since confirmed by other workers,⁵ is not known with certainty.

Interaction of 2,4-Dinitroanisole with Sodium Methoxide.—The n.m.r. spectrum of 2,4-dinitroanisole consists of a sharp resonance at -4.10 p.p.m., attributed to the methoxy-protons, together with a series of bands at low field due to the ring protons (see Table 4, B).

In the presence of increasing concentrations of methoxide a new set of bands grows at the expense of those due to the parent compound until, by a mole ratio of 2.5 methoxide:1 nitro-compound, the change in spectrum is complete. The new spectrum consists of a resonance at -2.94 p.p.m. which has double the intensity of that previously attributed to methoxy-protons, and is attributed to the methoxy-protons in an addition complex. In addition, there is an AMX spectrum containing a doublet at -8.65 p.p.m. ($J = 3$ c./sec.), two pairs of lines centred at -7.25 p.p.m. ($J = 3$, $J = 9$ c./sec.), and a doublet at -5.18 p.p.m. ($J = 9$ c./sec.).

This spectrum is interpreted as indicating formation of a 1:1 methoxide adduct. The occurrence of a single methoxyl resonance in the spectrum of the complex argues strongly in favour of addition at C(1). The possibility of the addition at a position other than C(1) is rendered unlikely by the unchanged spin-coupling constants of the ring protons in the spectrum of the complex. The shifts to high field suffered by these protons are consistent with the greater screening in the complex relative to the parent compound.

There is also some evidence from infrared spectra that the solid alkali-metal methoxide adduct, which can be isolated, contains the C(OMe)₂ group.¹⁷

This interpretation³ has been confirmed by Foster and

¹⁶ R. Kaiser, *J. Chem. Phys.*, 1963, **39**, 2435.

¹⁷ S. Nagakura and S. Ohsawa, quoted by S. Nagakura, *Tetrahedron*, 1963, **19** (Suppl. 2), 361.

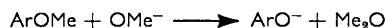
Fyfe⁵ whose results are in close agreement with the ones given above. However, they also report slow changes of the spectra at unspecified higher concentrations of base: these we have not observed. A possible explanation of the discrepancy is suggested by the study of 2,4-dinitrophenol.

Interaction of 2,4-Dinitrophenol with Sodium Methoxide.—The n.m.r. spectrum of 2,4-dinitrophenol in dimethyl sulphoxide shows a broad resonance at -7.76 p.p.m., ascribed to the phenolic proton and an AMX system (see Table 4, B).

In the presence of excess of sodium methoxide, the phenolic peak disappears: the chemical shifts of the aromatic protons of the phenoxide ion produced are slightly displaced (Table 4, B), but exhibit a splitting pattern corresponding to unaltered coupling constants.

In solutions containing less than one equivalent of sodium methoxide the ring protons give a series of sharp bands at positions intermediate between those of the dinitrophenol and the dinitrophenoxide ion. This shows that the two forms are in rapid equilibrium, as required by the interpretation.

The spectrum now assigned to the 2,4-dinitrophenoxide ion is identical with that reported by Foster and Fyfe⁵ for the product of the slow reaction of 2,4-dinitroanisole with methoxide at high concentrations. We therefore suggest that this slow reaction was the formation of 2,4-dinitrophenoxide, which did not occur in our media. The occurrence of the reaction in Foster and Fyfe's system may be due either to the presence of water,* or else to the reaction

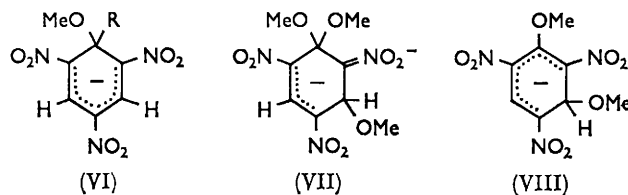


the analogue of which, it has been claimed, occurs with methyl picrate in methanolic sodium methoxide.¹⁸

Interaction of Methyl Picrate with Sodium Methoxide.—In the mixed solvent system containing equimolar amounts of methanol and dimethyl sulphoxide together with sodium methoxide (sodium methoxide:methyl picrate = 0.35–0.70) the resonances due to the aromatic protons of unchanged methyl picrate (at -9.07 p.p.m.) and of the Meisenheimer complex anion (VI; R = OMe) (at -8.70 p.p.m.) are observed. Even when the spectra were taken within $1\frac{1}{2}$ min. of mixing no additional lines were observed. The observed shift of the complex is in good agreement with our previously reported results on the methyl picrate-methoxide adduct¹ which referred to solutions of the potassium salt in pure dimethyl sulphoxide. However, in a solvent mixture of 30 moles-% methanol–70% dimethyl sulphoxide (sodium methoxide:methyl picrate = 0.2 or 0.6) two additional doublets (at -8.48 and -6.20 p.p.m.) with a mutual coupling constant of 1.5 c./sec. can be detected in freshly mixed solutions. These lines gradually disappear and the resonance due to (VI; R = OMe) increases in intensity. The half-life of the rearrangement is

* *Note added in proof.*—This interpretation is strengthened by a recent further publication by Foster and Fyfe (*Tetrahedron*, 1966, 22, 1831) in which it is stated that the resonance at -8.42 p.p.m. observed for solutions of the solid potassium methoxide adduct of trinitrobenzene in dimethyl sulphoxide is fairly rapidly replaced by a band at slightly higher field. We find that this change is very slow and does not occur in purified solvent at the rate stated by Foster and Fyfe, but that it is greatly accelerated by addition of water. However, there is a further and unexplained discrepancy between Foster and Fyfe's and our measurements in that we do not find a band at -5.56 p.p.m. which, according to Foster and Fyfe, appears along with the other spectral changes when such solutions are allowed to stand.

ca. 3 min. in the more dilute methoxide solution (ca. 0.16M) and between 30 and 50 sec. in 0.51M-sodium methoxide. Foster and Fyfe⁵ have observed these additional lines (at -8.36 and -6.06 p.p.m.; $J \sim 2$ c./sec.) in methanol–dimethyl sulphoxide mixtures containing sodium methoxide of unspecified composition and state that the absorptions increase as the concentration of methoxide is increased: they do not state whether the spectra changed with time. The lines were ascribed to a 1:2 adduct of structure (VII). This attribution is improbable, since the



spectra recorded in their paper show the resonance due to free methyl picrate, and it is our experience that higher complexes are not formed in solutions containing a molar deficit of sodium methoxide and hence free methyl picrate.

Servis⁶ also reported these resonances (at -8.42 and -6.17 p.p.m., $J \sim 1-2$ c./sec.) and first drew attention to their time-variation. From this fact and the position of the resonances he ascribed the resonances to structure (VIII), and the time variation to the rearrangement to the Meisenheimer complex (VI; R = OMe), which was stated to be catalysed by methanol. We concur with these conclusions, to which we add the observation that the reaction is also base-catalysed, which suggests that the rearrangement is likely to be intermolecular rather than intramolecular.

DISCUSSION

The results establish that the major interactions in the systems studied involve either addition of a basic group or loss of a side-chain proton. Electron transfer which occurs for many nitro-compounds in dimethyl sulphoxide–t-butyl alcohol containing potassium t-butoxide¹⁹ is ruled out as a major process in the systems studied by us on two grounds: (i) the systems are stable to atmospheric oxygen and yield the unchanged parent compounds on acidification, and (ii) the n.m.r. spectra are inconsistent with radical anions. These findings do not conflict with those of Russell and his collaborators¹⁹ who noted that for the two trinitro-compounds studied by them and for 4-nitrobenzyl cyanide, no radical (or only traces of radicals) could be detected. Similarly, our spectra are inconsistent with the transfer of ring protons as a major interaction in the systems studied.

Our results for the interactions of seven nitroanilines and *N*-substituted nitroanilines with base are of particular interest with regard to the use of these compounds as *H*₊ indicators in basic media. Anilines containing two nitro-groups ionise in the solvent systems studied by proton loss. However, for anilines containing three

¹⁸ V. A. Sokolenko, "Organic Reactivity," vol. II, Issue 1, Tartu, April 1965, p. 208.

¹⁹ G. A. Russell and E. G. Janzen, *J. Amer. Chem. Soc.*, 1962, 84, 4153; G. A. Russell, E. G. Janzen, and E. T. Strom, *ibid.*, 1964, 86, 1807.

nitro-groups the possibilities of base addition to the molecule and proton loss from the amino-group are fairly evenly balanced. This finding supports the reasoning by which a similar conclusion was reached from indicator measurements.⁸ For picramide the proportion of proton loss depends on the alkoxide used and the concentration of alcohol in the medium, as shown by Table 5. The dependence on the nature of the alkoxide

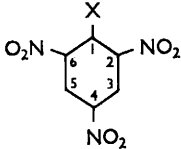
Similarly, an increase in the hydroxylic component of the solvent system causes a greater proportion of picramide to ionise by base addition.³ A similar effect has been noted for the ionisation of *N*-methylpicramide.⁶ This is attributed to the fact that the stoichiometric compositions of the anions formed through proton loss and base addition differ by one alcohol molecule.

Base addition in picramide and its *N*-substituted derivatives occurs at a ring carbon bearing a proton and not at the carbon atom bearing the amino-group, *i.e.*, the structure of the product is based on formula (III) and not on (II). This confirms the conclusions reached by Gold and Rochester⁸ on entirely different grounds.

In the light of the results on base addition it is possible to distinguish two main cases for nitro-compounds in which the nitro-groups are in *meta*-positions relative to each other: (a) addition to a position carrying hydrogen, (b) addition to a position carrying a substituent group. Under the heading (b) one need not at present consider the addition of base to a nuclear position carrying a nitro-group. Such complexes must be of low stability and have not been detected by n.m.r. spectroscopy. They do, however, represent labile intermediates in nucleophilic displacements, such as that of nitrite by methoxide.

The simplest example of category (a) is 1,3,5-trinitrobenzene, for which no alternative mode of addition is possible.¹ The simplest examples of case (b) are the complexes (VI; R = OMe) and (IX), in which the

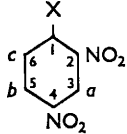
TABLE 4
Spectral parameters for nuclear hydrogen atoms of aromatic nitro-compounds and 1 : 1 methoxide adducts
(A) Picryl derivatives



| Parent molecule | Complex (a) * | | | Complex (b) † | |
|-------------------------------|-------------------------|--------------|--------------|--------------------------|-----------------|
| X | $-\delta_{3,5}$ | $-\delta_3$ | $-\delta_5$ | $ J_{3,5} $ (c./sec.) | $-\delta_{3,5}$ |
| H | 9.21 | 6.14 | 8.42 | ca. 1.5 | 8.42 |
| OH | 8.63 | — | — | — | — |
| OMe | 9.07 | 6.20 | 8.48 | ca. 1.5 | 8.7 |
| NH ₂ | 9.07 | 6.14 | 8.61 | ca. 1.5 | — |
| NMe ₂ | 8.84 | 6.17 (6.1) ‡ | 8.46 (8.4) ‡ | ca. 1.5 | — |
| | | | | (ca. 1.8) ‡ | |
| NHMe | 8.93 | 6.16 | 8.48 | ca. 1.5 | — |
| NHPh | 9.00 | — | — | — | — |
| O ⁻ | 8.69 (8.5) ‡ | — | — | — | — |
| NH ⁻ | 8.46 | — | — | — | — |
| NCH ₃ ⁻ | 8.43 (8.55), 8.25) ‡ | 6.10 (6.2) | 8.64 (8.6) | ca. 1.5 (1) ‡ | — |
| NPh ⁻ | 8.36 | 6.18 | 8.68 | — | — |

* Methoxide addition at position 3. † Methoxide addition at position 1. ‡ Values in parentheses relate to hydroxide adduct. (Chemical shifts, relative to internal tetramethylsilane are reliable to ca. ± 0.05 p.p.m.)

(B) *m*-Dinitrobenzene derivatives

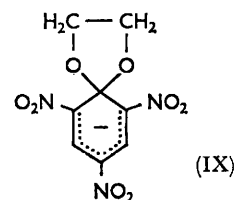


| X | $-\delta_a$ | $-\delta_b$ | $-\delta_c$ | $ J_{ab} $ | $ J_{bc} $ | $ J_{ac} $ |
|---------------------------------|-------------|-------------|-------------|------------|------------|------------|
| OH | 8.65 | 8.33 | 7.28 | 3 | 10 | <1 |
| OMe | 8.65 | 8.46 | 7.50 | 3 | 9 | <1 |
| NH ₂ | 8.71 | 8.11 | 7.05 | 2.5 | 10 | <1 |
| NHPh | 8.9 | 8.2 | 7.1 | 2.5 | 9 | <1 |
| O ⁻ | 8.81 | 7.94 | 6.53 | 3 | 10 | <1 |
| (OMe) ₂ ⁻ | 8.65 | 7.25 | 5.18 | 3 | 9 | <1 |
| NH ⁻ | 8.7 | 7.5 | 6.5 | 2.5 | 10 | <1 |
| NPh ⁻ | 8.7 | 7.5 | 6.4 | 2.5 | 9 | <1 |

TABLE 5

| Solvent system | Relative proportions of Base addition | Proton loss |
|--|--|-------------|
| 50 moles-% Methanol-50 moles-% D.M.S.O. | 80 | 20 |
| 15 moles-% Methanol-85 moles-% D.M.S.O. | 70 | 30 |
| 40 moles-% Ethanol-60 moles-% D.M.S.O. | 60 | 40 |
| 30 moles-% <i>t</i> -Butyl alcohol-70 moles-% D.M.S.O. | 0 | 100 |

is reasonably ascribed to the increasing steric hindrance in this series. Thus the bulky *t*-butoxide ion will not readily form an addition complex.



equivalence of the groups attached to the two ether oxygen atoms has been established by n.m.r. spectroscopy.^{1,4} The chemical shifts (and coupling constants) in these two types of complex are different and provide reference points for the identification of the structure of unknown complexes. In particular, the chemical shift of the hydrogen atom at the point of attachment of the base (ca. -6.2 p.p.m.) in (VI; R = H) can be taken to be characteristic of the complexes of type (a). Table 4 summarises the spectral parameters for some of the compounds and complexes now studied, the assignments being based on considerations detailed in the Results section.

Of the aromatic nitro-compounds studied for which methoxide addition occurs in methanol-dimethyl sulphoxide (mole ratio 1 : 1) only the two methyl ethers (2,4-dinitro- and 2,4,6-trinitro-anisole) form a complex in which the methoxide ion becomes attached to the aromatic ring at a position already carrying a substituent group. In 1,3,5-trinitrobenzene and the picramide compounds the attachment occurs at an unsubstituted nuclear position.

However, the contrast between the phenolic ethers and the amines need not be as profound as these remarks imply. It is found that even in methyl picrate the *first* change that is observed by n.m.r. spectroscopy when methoxide is added to methyl picrate, in a medium consisting mostly of dimethyl sulphoxide, is addition of methoxide to an unsubstituted position (VIII). This primary complex rearranges to give the thermodynamically more stable Meisenheimer complex (VI; $R = OMe$). This means that addition to an unsubstituted position to form the thermodynamically less stable product is more rapid than addition to a position carrying a methoxyl group to form the thermodynamically more stable product.

An analogous comparison was previously made concerning the relative rates of formation and stabilities of complexes (VI; $R = OMe$) and (VI; $R = H$) in methanol solution. Again it is the thermodynamically less stable complex (VI; $R = H$) which is formed more rapidly. The explanation offered for these observations was based on steric strain. It was suggested that complex (VI; $R = OMe$) was a less strained structure than methyl picrate, but that the transition state leading to the formation of (VI; $R = OMe$) was sterically more strained. By comparison, steric effects in the addition of methoxide to an unsubstituted position of 1,3,5-trinitrobenzene were considered unimportant. If this explanation is correct, steric effects should likewise be relatively unimportant in the formation of (VIII) from methyl picrate, and this model thus accounts qualitatively for the observed relative rates of formation and stabilities of (VIII) and (VI; $R = OMe$). The implied importance of these steric effects suggests that Meisenheimer complexes themselves are unlikely to be good models for the transition state of nucleophilic aromatic substitution reactions for systems containing *ortho*-substituents.

The same considerations may apply to *NN*-dimethylpicramide as a working hypothesis. We would suggest that the adduct (III; $R = R' = R'' = Me$) of type (a) is thermodynamically less stable than the type (b)

adduct (II; $R = R' = R'' = Me$), but that it is more rapidly formed owing to the steric hindrance in the transition state for the formation of (II). However, despite the greater thermodynamic stability of (II), this complex is not detected because it readily loses the dimethylamino-group.

The potential-energy diagram representing this hypothesis, the quantitative implications of which remain to be tested, is schematically given in Figure 2.

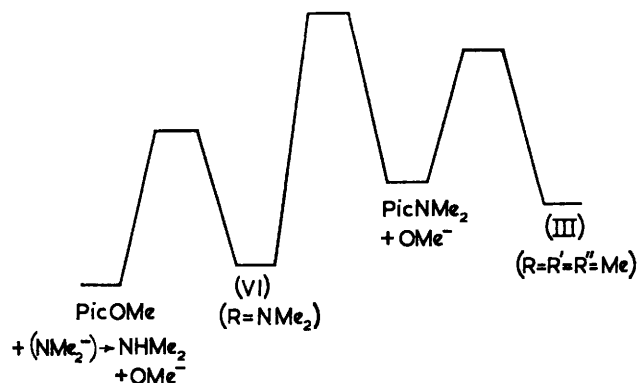


FIGURE 2 Suggested schematic potential energy profile for reaction between *NN*-dimethylpicramide and methoxide (Pic = 1,3,5-trinitrophenyl)

The chemical shifts summarised in Table 4 collate results for groups of structurally closely related molecules. They agree qualitatively with the polar characteristics of the changing substituent groups, but shielding constant of nuclear hydrogen atoms flanked by two nitro-groups are virtually constant.

Financial support by the Air Research and Development Command, U.S. Air Force, through its European Office, and by the U.K.A.E.A. is gratefully acknowledged. We thank Professor R. E. Richards, F.R.S., for encouragement and advice during the construction of the spectrometer.

DEPARTMENT OF CHEMISTRY,
KING'S COLLEGE, STRAND,
LONDON W.C.2. [6/301 Received, March 8th, 1966]