The Interaction of Aromatic Nitro-compounds with Bases

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1 Introduction

Aromatic nitro-compounds interact with a variety of Lewis and Brønsted bases to give, typically, brightly coloured solutions. The nature and the structure of the coloured species has been under investigation since before 1900[1] and during the intervening years several specific types of interaction have been recognised. For the present purpose the historical approach will not be taken; rather, the various interactions are treated according to the degree to which the base participates, through its unshared electron pair, with the nitro-compound.

A partial transfer (*e.g.*, through orbital overlap) of electronic charge from the base (Y: or Y^-) to the aromatic nucleus depleted of π-electron density owing to the electronegative nitro-substituents gives rise to π-complexes (1), known as donor–acceptor or charge-transfer complexes, after Mulliken.[2] A further degree of interaction may lead to an electron from Y^- becoming completely transferred to the nitro-compound, in which case a radical-anion (2) is produced.

In contrast to electron-transfer processes is the interaction by which the unshared electron pair of Y^- is used in formation of a covalent bond to an aromatic carbon atom. The resulting species (3) is then a σ-complex and will no longer have the benzenoid resonance intact. The best known of such σ-complexes is the red 'Meisenheimer adduct' (3; $Y = OCH_3$) formed from 2,4,6-trinitroanisole and methoxide ion in methanol.[3] If the aromatic nitro-compound contains a displaceable group (*e.g.*, halogen) then the base may act as a nucleophile and we enter the area of nucleophilic aromatic substitution. As a further possible interaction, the basic reagent may take part in proton-abstraction processes. This possibility arises owing to the powerful electron-withdrawing capability of nitro-groups which may cause a hydrogen atom of the aromatic nitro-compound to become sufficiently acidic. Abstraction of a nuclear hydrogen would yield an aryl carbanion (*e.g.*, 4), while abstraction of a hydrogen bound to an alpha carbon atom would give rise to a nitrobenzyl anion (*e.g.*, 5).

An enumeration of the various possible interactions is, however, only the first step in any consideration of these processes. From a practical viewpoint it would be important to know just which type of interaction would predominate in a given system and to have available definitive criteria for each interaction. One may ask some specific questions. (*a*) How is the nature of the species formed dependent on the number of nitro- (and other) substituents present? (*b*) For a given nitro-compound, does the base have any influence on the outcome (*e.g.*,

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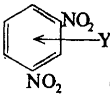
[1] C. A. Lobry de Bruyn, *Rec. Trav. chim.*, 1890, **9**, 208; 1901, **20**, 120; C. L. Jackson and W. F. Boos, *Amer. Chem. J.*, 1898, **20**, 444.
[2] R. S. Mulliken, *J. Amer. Chem. Soc.*, 1952, **74**, 811.
[3] J. Meisenheimer, *Annalen*, 1902, **323**, 205.



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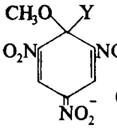

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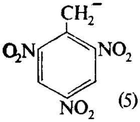

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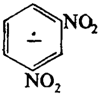

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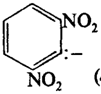

(4)

HO^-/H_2O as opposed to Bu^tO^-/Bu^tOH)? (*c*) Does the nature of the medium have any effect (*e.g.*, CH_3O^-/CH_3OH as opposed to $CH_3O^-/CH_3{\cdot}SO{\cdot}CH_3$)? (*d*) Is it possible for more than one species (1—5) to be present in a given system of a nitroaromatic compound and base? (*e*) What are the intimate mechanisms of the processes leading to the species (1)—(5)? (*f*) Is there any relationship between rate processes (*e.g.*, in nucleophilic aromatic substitution) and equilibrium processes [*e.g.*, in formation of adduct (3)]?

Another issue may be raised which has been a source of considerable confusion in the interpretation of these interactions. Paradoxically, the cause of this confusion has been the most characteristic aspect of the interactions, namely the colour of the resulting solutions. Colour formation has at various times been cited as evidence for the presence of *all* the species (1)—(5). A further point which needs critical examination is the relationship, if any, between the isolation and characterisation of a coloured adduct from the reaction of a nitro-compound with base, and any claim that that adduct was directly responsible for the colour of the solution. This point applies particularly to the situation where more than one species is present in a given system.

Evidence relating to various aspects of these interactions is discussed in this Review. The charge-transfer interaction is considered when there is evidence that it operates simultaneously with one of the other interactions, but is not treated as a separate topic. This is in part due to the fact that charge-transfer complexes have been treated in detail recently.[4] The first topic discussed is the formation of σ-complexes and the related evidence from electronic absorption and nuclear magnetic resonance spectroscopy, with some emphasis given to equilibrium constants and structural relationships. Proceeding to rate processes, we consider nucleophilic aromatic substitution, with emphasis on the evidence for σ-complex intermediates and reactivity relationships. Proton-transfer processes are considered next, and finally electron-transfer processes and the observation of radical anions by electron spin resonance spectroscopy.

2 Evidence from Ultraviolet–Visible Spectroscopy

A characteristic feature of the complexes formed in the initial, reversible interactions of aromatic nitro-compounds and a variety of bases is their absorption

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[4] (*a*) G. Briegleb, 'Elektronen-Donator-Acceptor Komplexe', Springer-Verlag, Berlin, 1961; (*b*) *Angew. Chem. Internat. Edn.*, 1964, **3**, 617; (*c*) J. N. Murrell, *Quart. Rev.*, 1961, **15**, 191; (*d*) L. J. Andrews and R. M. Keefer, 'Molecular Complexes in Organic Chemistry', Holden-Day, San Francisco, 1964; (*e*) E. M. Kosower, *Progr. Phys. Org. Chem.*, 1965, **3**, 81.

of light in the visible region. Among the systems investigated are: (i) 1,3,5-trinitrobenzene and aliphatic amines in chloroform, 1,4-dioxan, and ethanol;[5,6] (ii) 1,3,5-trinitrobenzene and a series of 1-X-2,4,6-trinitrobenzenes in liquid ammonia;[7] (iii) a series of 1-alkoxyl-2,4,6-trinitrobenzenes with alkoxide ions in a number of non-aqueous solvents;[8] (iv) 1,3-dinitrobenzene, a series of 1-X-2,4-dinitrobenzenes, and 1,3,5-trinitrobenzene with acetone in basic acetone–water solutions;[9–13] and (v) 1,3,5-trinitrobenzene with a variety of anions in different solvents. In this section, attention is focused upon the spectral properties and equilibrium constants associated with the formation of the latter group of complexes. Representative data in Table 1 refer to the initial 1:1 complexes formed at 25°. Similar spectral properties are displayed by the complexes formed in systems (i), (ii), and (iii).

Except for the spectra of the 1,3,5-trinitrobenzene–hydroxide ion and the 1,3,5-trinitrobenzene–sulphite ion complexes in aqueous solution which possess a single sharp maximum plus a shoulder on the long-wavelength side of this maximum, all the spectra display two distinct maxima in the 400—850 mμ region. The molar extinction coefficient (ϵ) of the high-energy band, typically a factor of from 1·3 to 2·5 times larger than that of the low-energy band, is characterised by a value in the range 2—4 × 10^4 l. mole^{-1} cm.$^{-1}$. These values of ϵ are much higher than those associated with the charge-transfer complexes of aromatic nitro-compounds with aromatic amines and hydrocarbons.[4a]

For a given 1,3,5-trinitrobenzene–anion complex the positions of maximum absorption, the energy separation of the absorption maxima, and the molar extinction coefficients at the positions of maximum absorption depend markedly on the solvent employed in studying the reaction. Unfortunately, few systematic investigations have been carried out in connection with these aspects of the equilibrium reactions. Foster and Fyfe[8] report that, in the alkoxide ion–picryl ether interactions, there is a bathochromic shift of the high-energy maximum and a hypsochromic shift of the low-energy band on altering the solvent from an ether to a more ionising solvent. The same effect has been noted in connection with the 1,3,5-trinitrobenzene–cyanide ion interaction[14a,b,c] although a simple relationship between the position of maximum absorption and a single solvent parameter such as its dielectric constant has not been observed. Much the same behaviour has been reported by Kimura, Kawata, and Nakadate[15] in connection with the acetonate ion complex of 1,3-dinitrobenzene in a variety of solvents,

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[5] R. Foster, *J. Chem. Soc.*, 1959, 3508.
[6] R. Foster and R. K. Mackie, *Tetrahedron*, 1961, **16**, 119.
[7] R. Foster and R. K. Mackie, *Tetrahedron*, 1962, **18**, 161.
[8] R. Foster and C. A. Fyfe, *Rev. Pure Appl. Chem.* (*Australia*), 1966, **16**, 61.
[9] T. Cänback, *Farm. Revy*, 1949, **48**, 217.
[10] M. J. Newlands and F. Wild, *J. Chem. Soc.*, 1956, 3686.
[11] S. S. Gitis and A. Ya. Kaminskii, *J. Gen. Chem.* (*U.S.S.R.*), 1960, **30**, 3771.
[12] R. Foster and R. K. Mackie, *Tetrahedron*, 1962, **18**, 1131.
[13] R. J. Pollitt and B. C. Saunders, *J. Chem. Soc.*, 1965, 4615.
[14] (*a*) A. R. Norris, *Canad. J. Chem.*, 1967, **45**, 2703; (*b*) Ph.D. thesis, Chicago, 1962; (*c*) A. R. Norris and W. Proudlock, unpublished results.
[15] M. Kimura, M. Kawata, and M. Nakadate, *Chem. and Ind.*, 1965, 2065.

Spectral properties and formation constants of some 1,3,5-*trinitrobenzene–anion complexes*

Anion	*Solvent*	λ_1 (mμ)	λ_2 (mμ)	ϵ_1 (l. mole^{-1} cm.$^{-1}$)	ϵ_2 (l. mole^{-1} cm.$^{-1}$)	K (l. mole^{-1})
HO^-	Water	450	475 (sh)	35,000	—	2·7[a]
CH_3O^-	Methanol	425	495	31,200	21,100	15·4[b]
$CH_3CH_2O^-$	Ethanol	424	497	33,900	22,800	2070[c]
$CH_3CH_2S^-$	Dimethylformamide	465	570	— (2·05)*	—	—[d]
$CH_3COCH_2^-$	Acetone	464	572	29,900	14,750	—[e]
$C_6H_5COCH_2^-$	Ethanol	464	565	23,100	10,800	—[f]
SO_3^{--}	Water	462	525 (sh)	23,500	12,050	267[g]
CN^-	Chloroform	437	555	39,900	22,500	33,500[h]
CH_3NH^-	Dimethyl sulphoxide	452	528	32,000	20,000	2,000[i]
$C_5H_{10}N^-$	Acetonitrile	444	521	33,000	—	0·05[j]

[a] T. Abe, *Bull. Chem. Soc. Japan*, 1960, **33**, 41; [b] V. Gold and C. H. Rochester, *J. Chem. Soc.*, 1964, 1692; [c] A. R. Norris, Ph.D. Thesis, Chicago, 1962; [d] R. J. Pollitt and B. C. Saunders, *J. Chem. Soc.*, 1965, 4615; [e] S. S. Gitis and A. Ya. Kaminskii, *J. Gen. Chem. U.S.S.R.*, 1963, **33**, 3226; [f] M. Kimura, M. Kawata, and M. Nakadate, *Chem. and Ind.*, 1965, 2065; [g] A. R. Norris, *Canad. J. Chem.*, 1967, **45**, 175; [h] A. R. Norris, *Canad. J. Chem.*, 1967, **45**, 2703; [i] M. R. Crampton and V. Gold, *J. Chem. Soc.* (*B*), 1967, 23; [j] G. Briegleb, W. Liptay, and M. Cantner, *Z. phys. Chem.* (*Frankfurt*), 1960, **26**, 55.

* Ratio of ϵ_1 to ϵ_2 at 25°c.

though these authors indicate that there exists no solvent effect on the position of maximum absorption in the case of the 1,3,5-trinitrobenzene–acetonate ion complex. Significantly, perhaps, the absorption maximum of the 2,4-dinitrophenylacetonate ion shifts very little on changing the solvent.[15]

Studies have been carried out on the effect of solvent on the equilibrium constant (K), the heat of formation, and the molar extinction coefficient (ϵ) of the resulting complex in the reaction of 1,3,5-trinitrobenzene with cyanide ion.[16] The solvent has a major effect upon the equilibrium constant; variations in K of 10^4 are noted on changing the medium from methanol to acetone or dimethyl sulphoxide. For the same solvents the variation in ϵ is less than two-fold, with ϵ being smaller in methanol. The equilibrium constant for formation of the 1,3,5-trinitrobenzene–methoxide ion complex is about 10^3 times greater in 1,4-dioxan and 1,2-dimethoxyethane than in methanol.[14b] Similar solvent effects have been noted in related studies on the 2,4- and 2,6-dinitroanisoles.[17]

The narrow range over which the absorption maxima for the 1,3,5-trinitrobenzene–anion complexes occur and the similarity in their band profiles and molar extinction coefficients have been taken as evidence that the absorbing species have, in all cases, an essentially identical structure.[14] One could argue perhaps that a similarity in the positions of absorption maxima might arise because all the anions had essentially the same ionisation potential. This seems unlikely in view of the widely varying contact-charge-transfer-to-solution bands exhibited by these anions.[18] The near-constancy of the absorption maxima and molar extinction coefficients of the 1,3,5-trinitrobenzene complexes with different anions is in marked contrast to the large variations in wavelengths of absorption maxima and molar extinction coefficients which occur in the 1,3,5-trinitrobenzene–aromatic hydrocarbon and 1,3,5-trinitrobenzene–aromatic amine complexes[4a] and suggests a different mode of complex formation in the two cases.

Because of the close correspondence in the visible absorption spectra of the 1,3,5-trinitrobenzene–ethoxide ion and the 2,4,6-trinitroanisole–ethoxide ion complexes in solution, the former was formulated as a σ-complex in which the ethoxide ion is covalently bonded to a ring carbon atom and the net negative charge is shared among the three nitro-groups.[19] This formulation has received strong support as a result of comparisons of the infrared spectra of the solid 1,3,5-trinitrobenzene–methoxide and the 2,4,6-trinitroanisole–methoxide addition products[20a,20b] and the nuclear magnetic resonance (n.m.r.) spectra of the same products dissolved in methanol[21,22] and in dimethyl sulphoxide.[23]

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[16] E. Buncel, A. R. Norris, W. Proudlock, and K. E. Russell, unpublished results.

[17] R. J. Pollitt and B. C. Saunders, *J. Chem. Soc.*, 1964, 1132.

[18] R. J. Marcus, *Science*, 1956, **123**, 399.

[19] R. Foster, *Nature*, 1959, **183**, 1042.

[20] (*a*) R. Foster and R. K. Mackie, *J. Chem. Soc.*, 1963, 3796; (*b*) R. Foster and D. Ll. Hammick, *ibid.*, 1954, 2153.

[21] M. R. Crampton and V. Gold, *J. Chem. Soc.*, 1964, 4293.

[22] M. R. Crampton and V. Gold, *Chem. Comm.*, 1965, 256.

[23] K. L. Servis, *J. Amer. Chem. Soc.*, 1965, **87**, 5495.

As a result of the close similarity in the absorption properties of the 1,3,5-trinitrobenzene–methoxide ion complex and other 1,3,5-trinitrobenzene–anion complexes, all the anions listed in the Table are thought to form σ-complexes. Support for this formulation has been advanced for the 1,3,5-trinitrobenzene–sulphite, the 1,3,5-trinitrobenzene–cyanide ion, and the 1,3,5-trinitrobenzene–acetonate ion complexes on the basis of infrared studies[14a,21–27] and for the 1,3,5-trinitrobenzene–piperidine anion complex on the basis of n.m.r. and conductivity measurements.[19] The n.m.r. spectrum of the 1,3,5-trinitrobenzene–sulphite complex is also in accord with this formulation.[14c]

Alternative structures of some of these 1,3,5-trinitrobenzene–anion complexes have, however, been advanced. Ainscough and Caldin,[28] for instance, formulated the 1,3,5-trinitrobenzene–ethoxide ion complex as a charge-transfer complex of unspecified geometry. Pollitt and Saunders[13] suggest that the complex between 1,3,5-trinitrobenzene and acetonate ion contains that ion situated above one of the ring carbon atoms and donating a lone pair on the methylene group to the lowest available π^* orbital of the benzene ring to form a dative σ bond. In this way, the hydrogen atom at the ring position concerned is still in or near its original position and the basic π-structure is not grossly disturbed. Gitis, Oksengendler, and Kaminskii[29] suggest that in the interaction of 1,3,5-trinitrobenzene with acetonate ion the absorption bands with maxima at 570, 462, and 518 mμ are associated with the mono-, di- and tri-salts of acetonate ion with 1,3,5-trinitrobenzene. This formulation certainly seems incorrect; Kimura, Kawata, and Nakadate[15] separated the 1:1 addition complex of 1,3,5-trinitrobenzene–acetonate ion and showed that it had, in ethanol, absorption maxima at 463 mμ (ϵ = 27,600) and 562 mμ (ϵ = 13,700). The complex resulting from the interaction of iodide ion and 1,3,5-trinitrobenzene has been formulated as a charge-transfer complex,[30,31] a 'Meisenheimer-like' adduct,[14b] and as an adduct involving co-ordination of the iodide ion with a nitrogen of the nitro-group.[32] In the case of iodide and possibly other anions, the solvent, in addition to influencing the values of K, ϵ, and $\lambda_{\max}$, may well determine whether σ- or π-complex formation is the predominant reaction.

For 1-substituted 2,4,6-trinitrobenzenes complex formation may occur at both the 1- and the 3-position either preferentially or simultaneously, and the absorption spectra of the two complexes may differ appreciably. In the interaction of 2,4,6-trinitroanisole with methoxide ion, attack occurs first at the 3-position[23] though the final product of the reaction contains methoxide ion

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[24] R. A. Henry, *J. Org. Chem.*, 1962, **27**, 2637.
[25] R. C. Farmer, *J. Chem. Soc.*, 1959, 3425,
[26] L. K. Dyall, *J. Chem. Soc.*, 1960, 5160.
[27] A. Ya. Kaminskii and S. S. Gitis, *J. Gen. Chem.* (*U.S.S.R.*), 1964, **34**, 3794.
[28] J. B. Ainscough and E. F. Caldin, *J. Chem. Soc.*, 1956, 2540.
[29] S. S. Gitis, G. M. Oksengendler, and A. Ya. Kaminskii, *J. Gen. Chem.* (*U.S.S.R.*), 1959, **29**, 2948.
[30] G. Briegleb, W. Liptay, and R. Fick, *Z. Elektrochem.*, 1962, **66**, 851.
[31] G. Briegleb, W. Liptay, and R. Fick, *Z. phys. Chem.* (*Frankfurt*), 1962, **33**, 181.
[32] A. B. Tronov, *J. Gen. Chem.* (*U.S.S.R.*), 1965, **35**, 1549.

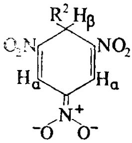
in the 1-position.[22,23] Unfortunately, visible absorption measurements corresponding to these two σ-complexes are not yet available. The observation that the cyanide complexes of 2,4,6-trinitrotoluene, picryl chloride, 2,4,6-trinitrobenzaldehyde, and 2,4,6-trinitroanisole have absorption maxima at wavelengths very little different from those of the 1,3,5-trinitrobenzene–cyanide ion complex may well indicate attack of cyanide ion at the 1-position in all cases.[33]

Consideration of the ultraviolet and visible absorption results so far reported for the interaction of aromatic nitro-compounds with both aliphatic amines and anions suggests that most of the data are associated with the formation of σ and Meisenheimer complexes. Few spectral data are available for aryl carbanion species, *e.g.*, (4), anion–nitroaromatic charge-transfer complexes (except 1,3,5-trinitrobenzene–iodide in certain solvents),[30,31] nitroaromatic radical anions, and nitrobenzyl anions. The spectral properties of the latter two classes of compound are referred to later.

3 Evidence from Nuclear Magnetic Resonance Spectroscopy

Application of the n.m.r. method to the problem of the interaction of aromatic nitro-compounds with bases has provided the most direct evidence on the structures of the species that are present in solution. While some of the resulting evidence has confirmed previous thinking, new facets to the problem have also been revealed.

The n.m.r. spectra of the species resulting from the interaction of 1,3,5-trinitrobenzene and a variety of anions and aliphatic amines, in a number of solvents,[21–23,34–37] can be rationalised in terms of the formation of σ-complexes of 1:1 stoicheiometry (6) but are not explicable on the basis of a π-complex formulation. The ring protons (H_α) absorb at low fields ($\delta = -8{\cdot}9$ to $-8{\cdot}7$ p.p.m., doublet, $J =$ *ca.* 1 c./sec.) while the hydrogen bonded to the carbon at which attack of the anion takes place (H_β) absorbs at higher fields ($\delta = -6{\cdot}10$ to $-6{\cdot}30$ p.p.m., broad, triplet, $J =$ *ca.* 1 c./sec.). The two resonances are of



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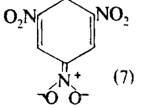

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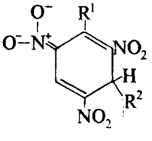

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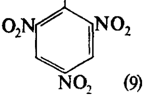

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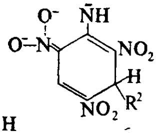

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[33] W. Depew and A. R. Norris, unpublished results.

[34] M. R. Crampton and V. Gold, *Chem. Comm.*, 1965, 549.

[35] R. Foster and C. A. Fyfe, *Tetrahedron*, 1965, **21**, 3363.

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

[37] R. Foster and C. A. Fyfe, *J. Chem. Soc.* (*B*), 1966, 53.

relative intensity 2:1. The positions of the resonance lines, particularly the resonance line of H_β, and the magnitudes of the spin–spin coupling constants of the ring protons seem to be solvent- and anion-dependent. For all the anion–1,3,5-trinitrobenzene interactions studied so far, n.m.r. spectra due to both species are observed in solutions containing both the complexed and uncomplexed 1,3,5-trinitrobenzene implying that anion exchange between different 1,3,5-trinitrobenzene units is not a rapid process. The shifts of the resonance lines upfield on going from the parent aromatic molecule ($\delta = -9{\cdot}2$ p.p.m.) to the complex are said to be due to larger screening of the protons in the anionic species.[21,36]

Only in the case of the interactions of 1,3,5-trinitrobenzene with aliphatic amines have simultaneous measurements of both n.m.r. and visible spectra been made as a function of the variation in the concentration of both components.[34,38] Despite this, the species in solution giving rise to the visible absorption is thought, in all cases, to be the same as that giving rise to the n.m.r. spectrum.

At ratios of anion to 1,3,5-trinitrobenzene greater than unity, the addition of a second anion may occur. This has been demonstrated only in the case of the interaction of methoxide with 1,3,5-trinitrobenzene.[35,39] Proton loss may be occurring simultaneously at these higher methoxide ion–1,3,5-trinitrobenzene ratios as the 1,3,5-trinitrobenzene resonance becomes broader with increasing concentration of base without corresponding broadening of the lines due to complex.[22]

The reaction of 1-substituted 2,4,6-trinitrobenzenes with bases is slightly more involved as either a σ-complex of the general type suggested by Meisenheimer (7) or a σ-complex formed by attack at C(3) (8) may be obtained. If, in addition, the substituent contains one or more acidic protons, ionisation to the conjugate base, *e.g.*, (9), may occur in competition with σ-complex formation and the conjugate base may itself undergo anion attack (10). Attack of the base at a carbon containing a nitro-group is not considered to be a likely process.

In the interaction of 2,4,6-trinitroanisole with methoxide ion in dimethyl sulphoxide, methoxide ion first adds at the 3-position of 2,4,6-trinitroanisole (8; $R^1{=}R^2{=}OCH_3$) but this anion is unstable and transforms into a complex with the methoxide ion attached at the 1-position (8).[35,36,40] Evidently, addition of methoxide ion 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. This is contrary to what would be expected on the basis of Miller's calculations.[41]

The stable 1:1 adducts formed by addition of methoxide ion to the 1-position of 2,4,6-trinitroanisole have also been reported in acetonitrile[23] and [$^2H_6$]-dimethyl sulphoxide.[42] Addition of dimethylamine, diethylamine, or azide ion

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[38] M. R. Crampton and V. Gold, *J. Chem. Soc.* (*B*), 1967, 23.

[39] K. L. Servis, *J. Amer. Chem. Soc.*, 1967, **89**, 1508.

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

[41] J. Miller, *J. Amer. Chem. Soc.*, 1963, **85**, 1628.

[42] P. Caveng, P. B. Fischer, E. Heilbronner, A. L. Miller, and H. Zollinger, *Helv. Chim. Acta*, 1967, **50**, 848.

to 2,4,6-trinitroanisole in dimethyl sulphoxide yields the 1-substituted Meisenheimer complexes with no evidence for preliminary complex formation at the 3-position.[39,43]

In picramide and *N*-alkylpicramides, ionisation to the conjugate base (9) occurs in competition with σ-complex formation at C(3) (10), the relative amounts depending on the structure of the reactant,[39] the alkoxide ion employed, and the concentration of alcohol in the medium.[22,36] In the series picramide, *N*-methylpicramide, and *N*-phenylpicramide the ratio of conjugate base to σ-complex increases in the order $-NH_2$, $-NH{\cdot}CH_3$, $-NH{\cdot}C_6H_5$ when interaction with methoxide ion is studied in dimethyl sulphoxide.[22,39] A second methoxide ion adds to the conjugate base of *N*-methylpicramide, at high methoxide to *N*-methylpicramide ratios.[39] In contrast, n.m.r. studies suggest that neither the picramide anion nor the picrate ion undergo addition of either methoxide or hydroxide ion even at high anion concentrations.[22] This observation may be peculiar to the anions and the solvent system used in this study.[44]

Addition of methoxide ion to *NN*-dimethyl- or *NN*-diethylpicramide yields the 3-substituted σ-complex while addition of the corresponding amines to 2,4,6-trinitroanisole yields the 1-substituted Meisenheimer complexes.[22,39] A 2:1 adduct with methoxide ion has been observed for *NN*-dimethylpicramide in dimethyl sulphoxide at high methoxide to dimethylpicramide ratios.[36] Hydroxide ion and acetonate ion behave similarly to methoxide ion in their interactions with *NN*-dimethylpicramide.[36,40]

On the basis of n.m.r. studies, the formation of benzyl-type anions from the interaction of methoxide ion and 2,4,6-trinitrotoluene in dimethyl sulphoxide–methanol mixtures is considered unlikely.[39] However, competing reactions at the high methoxide and 2,4,6-trinitrotoluene concentrations required in n.m.r. studies may prevent significant concentrations of 2,4,6-trinitrobenzylanion from being obtained. On the other hand, 4-nitrobenzyl cyanide[45] and anilines containing two nitro-groups, either in the 2,4- or the 2,6-position, ionise by proton loss when reacting with methoxide ion in dimethyl sulphoxide solution, and the anilines show no evidence of addition reactions.[22,36]

The interaction of methoxide ion with both 2,4-dinitroanisole or 2,6-dinitroanisole in dimethyl sulphoxide gives rise to a complex containing the added methoxide ion at the 1-position.[36,40] Addition of methoxide ion to 1,5-dimethoxy-2,4-dinitrobenzene in dimethyl sulphoxide yields a product in which attack of methoxide ion has occurred at the 1-position.[40] Addition of acetone gives rise to only a slight shift attributed to the effect of solvent. The similarity in the visible absorption spectra of this adduct and that formed as a result of the interaction of 1,5-diethoxy-2,4-dinitrobenzene and acetonate ion in acetone raises some question about Gitis and Kaminskii's formulation of the structure of the acetonate ion adduct[11] [attack at C(3)].

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[43] P. Caveng and H. Zollinger, *Helv. Chim. Acta*, 1967, **50**, 861.
[44] J. Murto, *Suomen Kem.*, 1961, *B*, **34**, 92.
[45] M. R. Crampton, *J. Chem. Soc.* (*B*), 1967, 85.

4 Janovsky Reaction

The interaction of aromatic nitro-compounds with ketones in basic ketone–water solutions, the Janovsky[46,47] reaction, has attracted the attention of chemists for some time. Cänback[48] reviewed the early literature and suggested that for the case of interactions of 1,3-dinitrobenzene the coloured species was the cyclohexadienide anion (σ-complex) formed by the attack of the conjugate base of the ketone on the 4-position of 1,3-dinitrobenzene.[49] On this interpretation this reaction is simply a special case of σ-complex formation in which the base is an anion of a ketone, usually the acetonate ion.[50]

Subsequent investigations[8,9,51] have offered considerable support for this formulation though questions have arisen concerning (*a*) the stoicheiometry of the coloured species, (*b*) whether an oxygen atom or a carbon atom in the conjugate base of the ketone is attached to the ring carbon atom,[52] (*c*) whether attachment occurs at both the 2- and the 4-position (in 1,3-dinitrobenzene) either simultaneously or consecutively,[26] (*d*) what effects ring substituents other than hydrogen have on the point of attachment of the ketonate ion[7,52] and on the absorption spectrum, and (*e*) whether a portion, or all, of the colour arises from a reduction product of the original complex.[53,54]

Despite a great deal of research in which the solid adducts of various ketonate ions and a number of di- and tri-nitro-compounds have been prepared and characterised according to composition,[52,55] decomposition temperature,[56] visible, infrared, and n.m.r. absorption characteristics[8,15,27,29,35,37,56] and chemical behaviour,[27,57] some of these questions remain unanswered. (Demonstration that the solid adduct which results from the 1,3-dinitrobenzene-acetonate ion interaction contains 1,3-dinitrobenzene and acetonate ion in a 1:1 mole ratio and is deeply coloured strongly suggests, but in no way proves, that the coloured species in solution is the result of 1,3-dinitrobenzene and acetonate ion interacting in a 1:1 mole ratio. Parallel infrared, n.m.r., and visible absorption studies of this complex in solution have not yet been carried out.)

In addition, the formulation of the Janovsky complex as a direct analogue of the Meisenheimer adducts has been questioned.[10,58] In the interaction of 1,3-dinitrobenzene with acetonate ion, Pollitt and Saunders[58] suggest that the colour in the system might arise owing to absorption by the conjugate base of 1,3-dinitrobenzene while, in the case of the 1,3,5-trinitrobenzene-acetonate ion interaction, the coloured species was formulated as a rather unusual σ-complex.[10]

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[46] J. V. Janovsky and L. Erb, *Ber.*, 1886, **19**, 2155.
[47] J. V. Janovsky, *Ber.*, 1891, **24**, 971.
[48] T. Cänback, *Svensk Farm. Tidskr.*, 1949, **53**, 151.
[49] T. Cänback, *Farm. Revy*, 1949, **48**, 153.
[50] R. Foster and R. K. Mackie, *Tetrahedron*, 1963, **19**, 691.
[51] T. Abe, *Bull. Chem. Soc. Japan*, 1959, **32**, 391.
[52] S. S. Gitis and A. Ya. Kaminskii, *Doklady Akad. Nauk S.S.S.R.*, 1962, **144**, 775.
[53] M. Ishidate and T. Sakaguchi, *J. Pharm. Soc. Japan*, 1950, **70**, 444.
[54] T. J. King and C. E. Newall, *J. Chem. Soc.*, 1962, 367.
[55] S. S. Gitis, *J. Gen. Chem.* (*U.S.S.R.*), 1957, **27**, 1956.
[56] S. S. Gitis and A. Ya. Kaminskii, *J. Gen. Chem.* (*U.S.S.R.*), 1963, **33**, 3226.
[57] T. Severin and R. Schmitz, *Angew. Chem. Internat. Edn.*, 1963, **2**, 266.
[58] R. J. Pollitt and B. C. Saunders, *Proc. Chem. Soc.*, 1962, 176.

The second formulation, based on qualitative observations concerning the magnitudes of the formation constants of acetonate and hydroxide ion adducts in dimethylformamide, the effect of blocking groups in ring positions, and differences in absorption spectra between what are considered to be two different types of complex, may well be correct. Reliable values of equilibrium constants, absorption maxima and molar extinction coefficients are required for both the ketonate ion complexes and other X^- complexes in a variety of solvents in order to support or refute such arguments.

It is possible that the solvent employed in such investigations may alter the mode of attachment of an ion to a nitro-compound or preferentially favour one reaction site over another. In addition a change in solvent may affect both the positions of maximum absorption and/or the molar extinction coefficients at these maxima or favour alternate reactions such as free-radical formation or aryl-carbanion formation.

In the conditions of di- or tri-nitroaromatic compound in excess over the ketone in basic ethanolic solution (the Zimmerman[59] reaction), solutions are produced whose spectral properties change rapidly with time and in which there is the eventual production of the corresponding dinitro- or trinitro-benzyl ketone.[13,52] The reaction products arising from the interaction of 1,3-dinitrobenzene with acetonate ion in the early stages of the Janovsky reaction and in the late stages of the Zimmerman reaction are two distinct species, as shown by differences in composition, decomposition temperature, infrared and visible absorption spectra, and chemical properties.[15,27]

5 Nucleophilic Aromatic Substitution

The present discussion is confined to benzenoid derivatives; for consideration of nucleophilic substitution in the heteroaromatic series the reader is referred to ref. 60.

A. 'Meisenheimer Structures' as Intermediates in Displacement Reactions.—Evidence was presented in the early 1950s[61,62] that nucleophilic displacement in nitro-, cyano-, etc., activated aryl halides does not proceed by a synchronous S_N2 mechanism [transition state (11)] analogous to aliphatic substitution, but that instead a two-stage mechanism obtains, with a discrete intermediate [a 'Meisenheimer structure', (12)] intervening between reactants and products. The carbon undergoing displacement is tetrahedral in (12) and the negative charge originating from the unshared electron-pair of nucleophile Y: is delocalised over the aromatic system. While the importance of charge delocalisation has generally been accepted, there has been discussion[63] as to whether the cyclohexadienide structure represents a minimum or a maximum on the potential-

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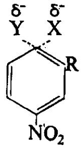
[59] W. Zimmerman, *Z. physiol. Chem.*, 1937, **245**, 47.
[60] G. Illuminati, *Adv. Heterocyclic Chem.*, 1964, **3**, 285.
[61] J. F. Bunnett and R. E. Zahler, *Chem. Rev.*, 1951, **49**, 273.
[62] J. Miller, *Rev. Pure Appl. Chem. (Australia)*, 1951, **1**, 171.
[63] R .E. Parker and T. O. Read, *J. Chem. Soc.*, 1962, 3149.



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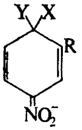

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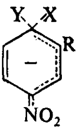

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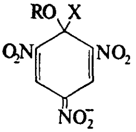

(14)

energy profile for reaction; in the latter case a synchronous mechanism would obtain and the configuration of the single transition state would be given by (13).

One of the focal points of discussion[64–67] on the mechanism of the aromatic displacement process has been the rôle of 'isolable intermediates', the stable Meisenheimer adducts formed between alkyl picryl ethers and alkali-metal alkoxides (14; X = OR where R = alkyl). Can species such as (14; X = Hal) be demonstrated to be present in a reacting solution of a picryl halide and alkoxide ion? One possible approach might be to detect (14) by the observation of colour. A rough estimate of the value of ϵ for a complex between picryl halide and methoxide ion is given by the corresponding value for the 1,3,5-trinitrobenzene–methoxide ion complex in methanol.[68b] If it is assumed that an absorbance value of 0·1 at 495 mμ would be detectable to the eye, the minimum visual detectable concentration of (14; R=CH_3, X = Hal) would be 5×10^{-6} mole $l.^{-1}$. In practice, coloured solutions are not observed in the course of reaction of picryl halides with base.[69] The formation of coloured solutions in equilibrium processes continues to be used as evidence in support of the intermediate complex mechanism in rate processes. A recent study[70] reports the following observations. 1-Fluoro-2,4-dinitrobenzene and ethyl malonate interact in presence of triethylamine to give a coloured product which is stable in dimethylformamide (λ_{max} = 397 and 510 mμ) but on addition of water is transformed into the 2,4-dinitrophenylmalonate ethyl ester. The coloured product is taken to be the triethylammonium salt of cyclohexadienide anion corresponding to (12; R = NO_2, X = F, Y = malonate)[70] (cf. also ref. 71).

The above discussion must be critically examined, however, for there is no absolute connection between the presence of a species in detectable concentration in a given reaction medium and the hypothesis that such a species is an intermediate along the reaction pathway of a particular rate process. That side equilibria are possible in suitable systems of aromatic nitro-compounds and bases is known;[67,72] such π-complexes of the charge-transfer type[2,4] are in

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[64] J. F. Bunnett, *Quart. Rev.*, 1958, **12**, 1.

[65] J. F. Bunnett, 'Theoretical Organic Chemistry', Butterworths, London, 1959, p. 144.

[66] J. Sauer and R. Huisgen, *Angew. Chem.*, 1960, **72**, 294.

[67] S. D. Ross, *Progr. Phys. Org. Chem.*, 1963, **1**, 31.

[68] V. Gold and C. H. Rochester, *J. Chem. Soc.*, 1964, (*a*) 1687, (*b*) 1692, (*c*) 1697, (*d*) 1710, (*e*) 1727.

[69] J. Murto, *Acta Chem. Scand.*, 1966, **20**, 303, 310.

[70] P. Baudet, *Helv. Chim. Acta*, 1966, **49**, 545.

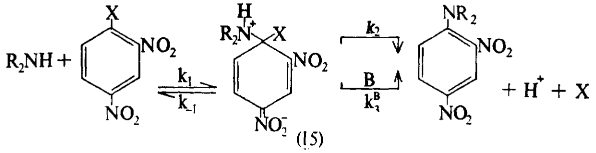
[71] R. Bolton, J. Miller, and A. J. Parker, *Chem. and Ind.*, 1960, 1026; 1963, 492.

[72] P. Caveng and H. Zollinger, *Helv. Chim. Acta*, 1967, **50**, 866.

contrast to the σ-bonded Meisenheimer structures. As an added consideration, the π-complexes themselves usually absorb in the visible region.

For these reasons, unequivocal evidence for a reaction intermediate such as (12) is sought through kinetic studies, by choosing a system in which the reactive intermediate can be partitioned along two or more reaction paths. This can sometimes be accomplished by the addition of reagents which will divert the intermediate in a predictable manner and thereby cause a change in the overall rate expression. Evidence of this nature has been presented for electrophilic aromatic substitution.[73–75]

B. Kinetic Evidence for a σ-Complex Intermediate.—In recent years the reaction system chosen for the kinetic demonstration of an intermediate in nucleophilic aromatic substitution is that between 2-nitro- or 2,4-dinitro-aryl derivatives and secondary amines (eqn. 1). Owing to the presence of a labile proton in (15) which may be removed by a Brønsted base (R_2NH, $CH_3{\cdot}CO_2^-$, OH^-, etc.) this system lends itself to studies of base catalysis. The removal of the N–H proton, which should itself be an easy process, provides an alternative pathway, of lower activation energy, for the conversion of intermediate into products. Since R_2N^- is a poorer leaving group than R_2NH, the reversion of intermediate into reactants will occur less readily when proton loss from (15) has been effected, and expulsion of X^- will correspondingly be more favoured.



(1)

There are two essential points to note about eqn. (1): (*a*) that conversion of intermediate (15) into products occurs by parallel, competing, paths and (*b*) that it implies some specific requirements with respect to the occurrence and the form of the base catalysis. The latter point is seen by examination of the kinetic expression (eqn. 2) derived on basis of the steady-state treatment.

$$\frac{\text{Rate}}{[\text{ArX}]\,[\text{R}_2\text{NH}]} = k = \frac{k_1k_2 + k_1k_3{}^{\text{B}}[\text{B}]}{k_{-1} + k_2 + k_3{}^{\text{B}}[\text{B}]} \tag{2}$$

In eqn. (2) the $k_3{}^{\text{B}}[\text{B}]$ term refers to any base effective in catalysis (including R_2NH; if more than one base is effective in a given system then additional such terms would be present). It is instructive to consider two limiting cases: (i) when

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[73] H. Zollinger, *Experientia*, 1956, **12**, 165.
[74] E. Grovenstein, jun., and N. S. Aprahamian, *J. Amer. Chem. Soc.*, 1962, **84**, 212.
[75] B. T. Baliga and A. N. Bourns, *Canad. J. Chem.*, 1966, **44**, 363, 379.

$k_{-1} \ll k_2 + k_3^B[B]$, then $k = k_1$, so that formation of the intermediate is rate-determining and base catalysis should not be observable; (ii) when $k_{-1} \gg k_2 + k_3^B[B]$, we have a pre-equilibrium condition in which the product-forming processes are rate-determining and base catalysis is expected. These conditions can now be related with physical systems. Since case (i) will be relatively favoured when k_2 is large, it follows that in related compounds base catalysis should be favoured for the one with the *poorer* leaving group (*e.g.*, ArF in favour of ArCl). Also, if $k_{-1} \approx k_2$ then base catalysis may be observed at low base concentration but will tend to diminish as [B] is increased; hence the sensitivity to base catalysis will decrease with increasing [B] and the overall rate constant will show a curvilinear dependence on [B]. These predictions, with respect to leaving-group and base-concentration dependence, thus become a test of the intermediate complex hypothesis.[76]

Base catalysis is in fact observed in reaction of 1-fluoro-2,4-dinitrobenzene with certain bases and it is much more effective than with 1-chloro-2,4-dinitrobenzene, in a particular system. Very marked catalysis by hydroxide and acetate ion is observed in the reaction of 1-fluoro-2,4-dinitrobenzene with *N*-methylaniline, but catalysis is barely detectable with the chloro-compound.[76] Similarly, the reactions of 4-nitrophenyl phosphate with dimethylamine and with piperidine are catalysed by hydroxide ion.[77] The reaction of 2,4-dinitrophenyl phenyl ether[78] with piperidine is catalysed by piperidine and by hydroxide ion but when the ease of removal of the leaving group is improved by nitro-substitution (in the 2- and 4-positions) base catalysis is no longer observed.[79] (The competing direct displacement of phenoxy- by hydroxide ion accounts for only 2% the total reaction in a medium of 40% dioxane–60% water. This is a result of the low nucleophilic reactivity of hydroxide ion in nucleophilic aromatic substitution.) Further, the 4-nitrophenyl phosphate and 2,4-dinitrophenyl phenyl ether processes show pronounced curvilinear dependence of rate on the concentration of the catalysing base. The observation by Hart and Bourns[80] of a variable kinetic oxygen (k^{16}/k^{18}) isotope effect as a function of hydroxide-ion concentration in the reaction of 2,4-dinitrophenyl phenyl ether with piperidine can only be accommodated by a two-stage intermediate complex mechanism.

C. Mechanism of Base Catalysis.—While the above observations are in full accord with the requirements of the two-step mechanism, it is not clear why some bases are effective in catalysis while others are not. For instance, the reaction of 1-fluoro-2,4-dinitrobenzene with aniline or with t-butylamine is not catalysed by hydroxide ion.[81] Also, the reaction of 4-nitrophenyl phosphate with dimethylamine is not catalysed by piperidine,[77] even though piperidine acts as a catalyst in the reaction of 2,4-dinitrophenyl phenyl ether with piperidine.[79]

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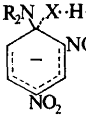
[76] J. F. Bunnett and J. J. Randall, *J. Amer. Chem. Soc.*, 1958, **80**, 6020.
[77] A. J. Kirby and W. P. Jencks, *J. Amer. Chem. Soc.*, 1965, **87**, 3217.
[78] J. F. Bunnett and R. H. Garst, *J. Amer. Chem. Soc.*, 1965, **87**, 3879.
[79] J. F. Bunnett and C. Bernasconi, *J. Amer. Chem. Soc.*, 1965, **87**, 5209.
[80] C. R. Hart and A. N. Bourns, *Tetrahedron Letters*, 1966, 2995.
[81] J. F. Bunnett and J. H. Beale, personal communication.

It is difficult to accept the suggestion[77] that proton abstraction from (15) should be subject to considerable steric effects. In certain systems[82] there appears to be a trend of a greater sensitivity for base catalysis with decreasing base strength of the reacting amine.

The timing of the proton-transfer step between intermediate (15) and base needs consideration. If proton removal were part of the rate-determining step then a kinetic hydrogen–deuterium isotope effect[83] should be observable. In practice the overall isotope effects are generally very close to unity (for a summary of earlier work see refs. 67 and 84) and may also take inverse values. For example, in the reactions of [*amino*-$^2H_2$]*p*-anisidine with 1-halogeno-2,4-dinitrobenzenes in benzene solution,[85] k_H/k_D varies between 0·80 and 0·94 for the chloro-compound and between 0·95 and 1·05 for the fluoro-compound, depending on base concentration and temperature. Isotope effects of this low magnitude generally signify 'secondary effects'[86] and their observation suggests that rupture of the N–H bond is not rate-determining. On the basis of theoretical considerations[87] the view would be taken that proton transfer from a nitrogen base should be a kinetically fast process for the cases considered here. However, from a study of the reaction 2,4-dinitrophenyl phenyl ether with [*N*-$^2H_2$]-piperidine in dioxan–D_2O catalysed by deuteroxide ion, it was deduced[80] that the rate constant ratio $k_3{}^H/k_3{}^D$ for conversion of intermediate into products is 1·80, which appears to be outside the range of secondary effects.



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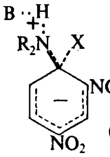

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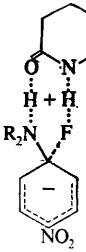

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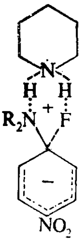

(19)

The mechanism of base catalysis now favoured by most workers[77,78,85] is an initial, equilibrium, proton transfer followed by rate-determining *general-acid-catalysed* removal of the leaving group by BH^+, as shown in transition state (16). This mechanism satisfies the requirements of the kinetic equation (2) but it raises certain questions, as discussed below. An alternative possibility therefore is (cf. also ref. 80) that removal of the N–H proton occurs simultaneously with weakening of the C–X bond as in transition state (17), which bears resemblance to that in bimolecular (*E*2) eliminations. This suggestion may better account for

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[82] G. Becker, C. F. Bernasconi, and H. Zollinger, *Helv. Chim. Acta*, 1967, **50**, 10.

[83] K. Wiberg, *Chem. Rev.*, 1955, **55**, 713.

[84] H. Zollinger, *Adv. Phys. Org. Chem.*, 1964, **2**, 163.

[85] C. Bernasconi and H. Zollinger, *Helv. Chim. Acta*, 1967, **50**, 3; 1966, **49**, 2570.

[86] E. A. Halevi, *Progr. Phys. Org. Chem.*, 1963, **1**, 180.

[87] M. Eigen, *Angew. Chem.*, 1963, **75**, 489.

a hydrogen–deuterium isotope effect of 1·80 with respect to N–H,[80] since hydrogen isotope effects in *E*2 processes are known to vary considerably in magnitude.[88,89] A further difficulty with the mechanism involving transition state (16) [and one which is perhaps met better by the *E*2 type transition state (17)], is that it would require that *electrophilic* catalysis (*e.g.*, by Ag^+) with respect to the leaving group be of fairly common occurrence in nucleophilic aromatic displacements. Whereas electrophilic catalysis in S_N2 displacement at saturated carbon is well established,[90] there appears to be only one report of metal-ion catalysis in the aromatic series: the reaction of 1-fluoro-2,4-dinitrobenzene with thiocyanate ion in methanol is accelerated by a factor of 2000 on the addition of thorium ions.[91] On the other hand, a case of bifunctional catalysis in the aromatic series has recently been reported. α-Pyridone (which has previously been shown to be effective in bifunctional catalysis[92]) strongly accelerates the reaction of 1-fluoro-2,4-dinitrobenzene with piperidine. Transition state (18) is suggested to account for this observation.[93] The possibility that piperidine itself may take part in bifunctional catalysis [transition state (19)] was suggested previously.[94]

The problem of the mechanism of nucleophilic aromatic substitution has also been approached through use of molecular orbital theory in the Hückel approximation.[95–97] A number of interesting correlations between molecular orbital quantities (π-electron density, localisation energy) and experimental quantities (rates, activation energies) are reported but basically the calculations do not allow a clear differentiation between the one-step, synchronous, and the two-step, intermediate complex, mechanisms.

In conclusion, the general evidence supports very strongly the two-stage mechanism of nucleophilic aromatic substitution but there are a number of anomalies which are not yet fully understood. Thus the structure of the rate-determining transition state is not known with certainty.

D. Quantitative Approach to Nucleophilic Aromatic Substitution.—A number of different approaches have been used in the quantitative correlation of reactivities in nucleophilic aromatic substitution processes. A thermochemical approach has been developed at length by Miller and his co-workers;[98–102]

[88] E. Buncel and A. N. Bourns, *Canad. J. Chem.*, 1960, **38**, 2457; A. N. Bourns and E. Buncel, *Ann. Rev. Phys. Chem.*, 1961, **12**, 1.

[89] J. F. Bunnett, *Angew. Chem. Internat. Edn.*, 1962, **1**, 225.

[90] C. K. Ingold, 'Structure and Mechanism in Organic Chemistry', Bell, London, 1953, p. 357.

[91] K. B. Lam and J. Miller, *Chem. Comm.*, 1966, 642.

[92] C. G. Swain and J. F. Brown, *J. Amer. Chem. Soc.*, 1952, **74**, 2538.

[93] F. Pietra and D. Vitali, *Tetrahedron Letters*, 1966, 5701.

[94] B. Capon and C. W. Rees, *Ann. Reports*, 1964, **61**, 278.

[95] C. Parkanyi and R. Zahradnik, *Coll. Czech. Chem. Comm.*, 1964, **29**, 973.

[96] J. Murto, *Suomen Kem.*, 1965, *B*, **38**, 246.

[97] S. Carra, M. Raimondi, and M. Simonetta, *Tetrahedron*, 1966, **22**, 2683.

[98] J. Miller, *J. Amer. Chem. Soc.*, 1963, **85**, 1628.

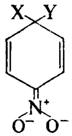
[99] J. Miller and K. W. Wong, *J. Chem. Soc.*, 1965, 5454.

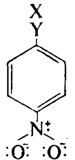
[100] J. Miller and K. W. Wong, *Austral. J. Chem.*, 1965, **18**, 117.

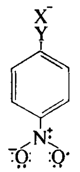
[101] D. L. Hill, K. C. Ho, and J. Miller, *J. Chem. Soc.* (*B*), 1966, 299.

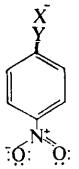
[102] K. C. Ho, J. Miller, and K. W. Wong, *J. Chem. Soc.* (*B*), 1966, 310.

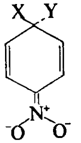
the method sets out to calculate activation energies on the basis of the intermediate complex mechanism. Transformation of the cyclohexadienide structure (20) into products (23) (or reactants) is considered in terms of stages (21) and (22) and the energies associated with these changes are then estimated. The energy levels of the initial and final states relative to that of the intermediate complex are thus obtained by taking into account terms due to changes in bonding, in electron affinity, in solvation, and in delocalisation energy. The energy levels of the two transition states, (24) and (25), for bond formation and bond rupture, are related to the intermediate complex by means of an unusual application of the Hammond hypothesis[103] and are further modified by the inclusion of the 'α-substituent effect' term. The latter useful concept is introduced on the basis that a strongly electronegative atom X already attached to the aromatic carbon atom would lower the energy of the transition state for attack by a nucleophile. The greater mobility of fluorine than iodine, amounting to 4 kcal./mole in activation-energy difference, is thus ascribed to an electronegativity effect alone.

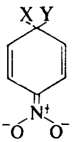

(20)


(21)


(22)


(23)


(24)


(25)

It is clear that this treatment[98] necessarily involves a number of assumptions and approximations since the required energy terms are not available for the actual processes under consideration and must be drawn from other systems. The solvation energy term being taken as an example, the data used are heats of hydration and it is assumed that the change to methanol medium would affect all the values equally. The solvation energy of the intermediate complex, for all cases of substitution, is equated to that of the picrate ion. In view of these and other assumptions used it is remarkable that agreement between calculated and experimental activation energies (where known) *is* in fact very good (generally within 1—2 kcal./mole). A general cancellation of errors is indicated. As with some other semi-empirical methods of calculation, one may take the view that the general applicability of the method to diverse processes is its own justification, despite any assumptions that may be used.

Some examples of Miller's method of calculation are given in the Figure: they are chosen to illustrate the changes in balance[104,105] between the situations where formation of the intermediate is rate-determining and where its decomposition is the slow step, and the influence upon this balance of factors such as

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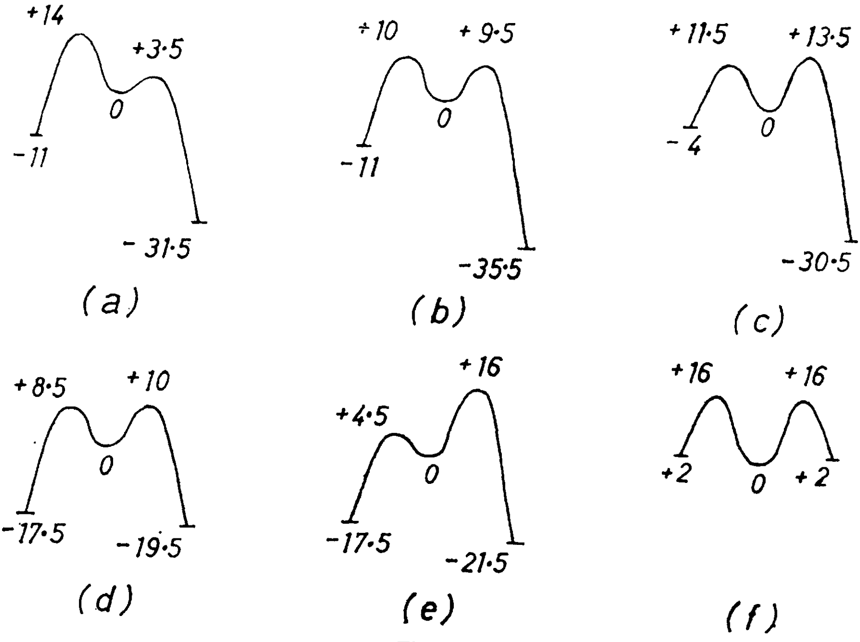
[103] G. S. Hammond, *J. Amer. Chem. Soc.*, 1955, **77**, 334.

[104] G. S. Hammond and L. R. Parks, *J. Amer. Chem. Soc.*, 1955, **77**, 340.

[105] J. F. Bunnett, E. W. Garbisch, jun., and K. M. Pruitt, *J. Amer. Chem. Soc.*, 1957, **79**, 385.



Figure

Potential energy–reaction co-ordinate diagrams for activated nucleophilic aromatic substitution (energies are shown in kcal. mole^{-1})
(*a*) 1-Iodo-4-nitrobenzene and CH_3O^-/CH_3OH
(*b*) 1-Fluoro-4-nitrobenzene and CH_3O^-/CH_3OH
(*c*) 1-Fluoro-4-nitrobenzene and CH_3S^-/CH_3OH
(*d*) 1-Bromo-2,4-dinitrobenzene and I^-/CH_3OH
(*e*) 1-Fluoro-2,4-dinitrobenzene and I^-/CH_3OH
(*f*) Methyl picryl ether and CH_3O^-/CH_3OH

nucleophile and leaving group. Comparison of (*a*) with (*b*) in the Figure shows the change from a 'typical' substitution in which bond formation is completely rate-determining[105] which results when the leaving group is changed. The approach to the second transition state becomes virtually rate-determining (Figure *c*) when additionally the nucleophile is changed to thiomethoxide.[100] This tendency of sulphur nucleophiles[106–108] to raise the energy barrier for bond rupture is predicted to be even more important with larger nucleophiles such as thiophenoxide.[101,102] The iodide–bromide exchange (Figure, *d*) is predicted to be a slow, reversible process; the very high activation energy calculated for iodide–fluoride exchange (Figure, *e*) is in accord with the observed preference for solvolysis in this system. The important case of a stable intermediate complex is shown in (*f*); the low calculated activation energy is noteworthy (cf. refs. 68a,

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[106] A. J. Parker, in 'Organic Sulfur Compounds', ed. N. Kharasch, Pergamon Press, Oxford, 1961, vol. 1, p. 103.

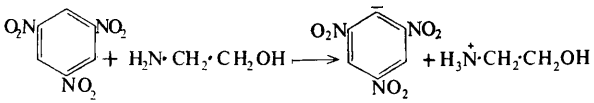
[107] J. F. Bunnett and J. D. Reinheimer, *J. Amer. Chem. Soc.*, 1962, **84**, 3284.

[108] R. F. Hudson and G. Klopman, *J. Chem. Soc.*, 1962, 1062.

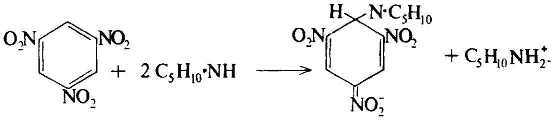
109—111). Miller's discussion of factors determining nucleophilic reactivity in these systems is related to the conclusions drawn from somewhat different points of view by Hudson,[112] Bunnett,[113] and Pearson.[114]

6 Proton-transfer Processes

A. Nuclear Hydrogen Abstraction.—The possibility of the occurrence of nuclear hydrogen abstraction in the interaction of aromatic nitro-compounds with bases first arose in connection with the observations that solutions of some aromatic nitro-compounds in amines, and in liquid ammonia, are conducting. The small conductance of 1,3,5-trinitrobenzene in pyridine was explained by Lewis and Seaborg[115] as being the result of partial proton transfer, while complete ionisation (eqn. 3) was postulated[116] to take place in 2-aminoethanol on the basis of conductance and cryoscopic data.



(3)



(4)

In contrast, it was concluded[117] from conductance and spectroscopic results that 1,3,5-trinitrobenzene interacts with piperidine in acetonitrile solution to give an adduct (eqn. 4). The intense colour and high conductivity of 1,3-dinitrobenzene in liquid ammonia was also explained on the basis of adduct formation;[118] this formulation received support from spectral examination in liquid ammonia of a series of polynitroaromatic compounds, including 1,3-dinitrobenzene and 1,3,5-trinitrobenzene.[7]

The use of isotopic exchange as a tool for the study of proton transfer in the nitroaromatic series was first reported on by Kharasch and his co-workers.[119] Treatment of 1,3,5-trinitrobenzene with 0·02M-sodium hydroxide in ethanol–D$_2$O at 110° for 68 hr. resulted in dilution of the deuterium of the medium to an extent equivalent to exchange of over 2 atoms of hydrogen from the trinitro-

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[109] T. Abe, T. Kumai, and H. Arai, *Bull. Chem. Soc. Japan*, 1965, **38**, 1526.
[110] J. Murto and E. Kohvakka, *Suomen Kem.*, 1966, *B*, **39**, 128.
[111] J. H. Fendler, *J. Amer. Chem. Soc.*, 1966, **88**, 1237.
[112] R. F. Hudson, *Chimia* (*Aarau*), 1962, **16**, 173.
[113] J. F. Bunnett, *Ann. Rev. Phys. Chem.*, 1963, **14**, 271.
[114] R. G. Pearson, *J. Amer. Chem. Soc.*, 1963, **85**, 3533; 1967, **89**, 1827.
[115] G. N. Lewis and G. T. Seaborg, *J. Amer. Chem. Soc.*, 1940, **62**, 2122.
[116] V. Baliah and V. Ramakrishnan, *Rec. Trav. chim.*, 1959, **78**, 783; 1960, **79**, 1150.
[117] G. Briegleb, W. Liptay, and M. Cantner, *Z. phys. Chem.* (*Frankfurt*), 1960, **26**, 55.
[118] J. D. Farr, C. C. Bard, and G. W. Wheland, *J. Amer. Chem. Soc.*, 1949, **71**, 2013.
[119] M. S. Kharasch, W. G. Brown, and J. McNab, *J. Org. Chem.*, 1937, **2**, 36.

benzene. It was pointed out recently,[120] however, that nucleophilic displacement of a nitro-group in 1,3,5-trinitrobenzene by alkoxide ion occurs[68d] under even milder conditions than in the exchange study[119] so that the observations of Kharasch cannot be taken at face value. No exchange of hydrogen occurred when 1,3,5-trinitrobenzene was treated with 8M-sodium hydroxide in D_2O[121] or with pyridine–D_2O.[122]

Whereas the conflicting results discussed above place the nuclear proton transfer process in question, other work is more conclusive. Shatenshtein[123] observed that 1,3-dinitrobenzene in liquid ND_3 undergoes significant exchange with the medium (at 50° and 24 hr. 0·3 atom hydrogen exchange). 1,3-Dinitrobenzene is also shown to undergo hydrogen exchange (in the 2-position as shown by n.m.r.[58,124]) with NaOD in dimethylformamide–D_2O,[58] methanol–D_2O,[125] dimethyl sulphoxide–D_2O,[124] and dimethoxyethane–D_2O.[124] Conclusive evidence was also given of hydrogen exchange in 1,3,5-trinitrobenzene by the action of sodium methoxide in tritiated methanol[120] and by NaOD (0·01M) in dimethylformamide–D_2O.[126] The observation of catalysis of hydrogen exchange in 1,3-dinitrobenzene[124] and in 1,3,5-trinitrobenzene[127] by a number of bases, both anionic and neutral, suggests that these aromatic hydrogen-abstraction processes are subject to Brønsted base catalysis.

While the feasibility of the proton-abstraction process in aromatic nitro-compounds can thus be considered as proven, there has been controversy about the relationship between colour and the proton abstraction process in these systems. Some workers have suggested[58,128] that colour development in the interaction of 1,3-dinitrobenzene with bases provides a quantitative measure of the formation of aryl carbanion. The problem was examined quantitatively by Crampton and Gold.[20] In tritium-labelled methanol and methanol–dimethyl sulphoxide mixtures containing sodium methoxide both the rate of exchange and the colour intensity ($\lambda_{\max}$ 430, 520 mμ) increase as the basicity of the medium (as measured by the H_- acidity function) increases, but beyond a certain basicity ($H_- \simeq 21$) both the rate and the absorbance level off. The development of colour appears to be instantaneous throughout the range of basicities. Even at the basicities corresponding to maximum absorbance the rate of tritium exchange still follows a first-order rate law so that the aryl carbanion cannot be present in significant concentration. The results are consistent, both qualitatively and quantitatively, with the reasoning that the coloured form is the predominant species present but is *unreactive* in the exchange process; the latter occurs by proton removal from 1,3-dinitrobenzene which has not been converted into the

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

[121] J. A. A. Ketelaar, A. Bier, and H. T. Vlaar, *Rec. Trav. chim.*, 1954, **73**, 37.

[122] R. E. Miller and W. F. K. Wynne-Jones, *J. Chem. Soc.*, 1959, 2375.

[123] A. I. Shatenshtein, N. M. Dykno, A. E. Izrailevich, L. N. Vasil'eva, and M. Faivush, *Doklady Akad. Nauk S.S.S.R.*, 1951, **79**, 479.

[124] E. Buncel and W. A. Zabel, *J. Amer. Chem. Soc.*, 1967, **89**, 3082.

[125] R. Foster and R. K. Mackie, *Tetrahedron*, 1963, **19**, 691.

[126] E. Buncel and E. A. Symons, *Canad. J. Chem.*, 1966, **44**, 771.

[127] E. Buncel and E. A. Symons, *Chem. Comm.*, 1967, 771.

[128] R. Schaal, *Compt. rend.*, 1954, **238**, 2156.

unreactive coloured form. From the characteristics of the visible absorption spectrum it is deduced that the coloured species is the Meisenheimer adduct [methoxyl at C(4)].[120]

The available evidence thus indicates that the dinitrophenyl anion, and by analogy the trinitrophenyl anion, is not formed in more than a very small concentration in the interaction of aromatic nitro-compounds with bases. The suggested mechanism[120,124] of the exchange process, for 1,3-dinitrobenzene and a base Y:, involves a rate-determining deprotonation to form the aryl carbanion (4) followed by rapid reaction of (4) with the solvent. The exchanging [C(2)] hydrogen is the most acidic one, owing to the adjacent electronegative nitro-groups. Evidence for the importance of the inductive effect in aromatic hydrogen abstraction has been presented.[129–131] Since, however, exchange in 1,3,5-trinitrobenzene is less easy than in 1,3-dinitrobenzene,[124,127] additional effects must be operative. One such effect is presumably a greater tendency for conversion of substrate into the (unreactive) Meisenheimer adduct in the case of 1,3,5-trinitrobenzene.

B. Formation of Nitrobenzyl Anions.—The introduction of nitro-groups into the aromatic ring of toluene and its derivatives increases their Brønsted acid strength and in sufficiently basic solution it is possible to remove a proton to produce substituted benzyl anions. 4-Nitrobenzyl cyanide (10^{-4}M), for example,[132] reacts with sodium ethoxide (10^{-3}M) in ethanol solution to give a red anion ($\lambda_{\max} = 560$ mμ, $\epsilon = 2{\cdot}6 \times 10^4$ l. mole^{-1} cm.$^{-1}$) by proton loss[45] and it is only at high hydroxyl-ion concentration in aqueous solution that another process, possibly formation of a σ-complex competes with the production of the anion.[133] Caldin and Long[134] have shown that under similar conditions 2,4,6-trinitrotoluene (TNT) gives a purple anion in the temperature range $-80°$ to $20°$; the anion has absorption maxima at 510 mμ ($\epsilon \approx 12{,}000$) and 370 m$\mu$ ($\epsilon \sim 7000$). They note that picrate ion in methanol has an absorption maximum close to 370 mμ and on the basis of this and other evidence conclude that the purple product is the 2,4,6-trinitrobenzyl anion (TNT$^-$). The reaction of ethoxide ion with TNT

$$\text{TNT} + \text{OEt}^- \rightleftharpoons \text{TNT}^- + \text{HOEt}$$

proceeds to an equilibrium position and the equilibrium constant increases from 60 l./mole at $-78{\cdot}5°$ to 2040 l./mole at 25°. The large positive entropy change, 27 cal. deg.$^{-1}$ mole^{-1}, in this reaction in ethanol solution is interpreted by Caldin as being due to the desolvation which occurs when the ethoxide ion, with its charge localised mainly on the oxygen, is replaced by the trinitrobenzyl anion in which the charge is delocalised. A significant part of this desolvation appears to occur in the formation of the transition state because the entropy of

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[129] A. I. Shatenshtein, *Adv. Phys. Org. Chem.*, 1963, **1**, 156.

[130] G. E. Hall, E. M. Libby, and E. L. James, *J. Org. Chem.*, 1963, **28**, 311.

[131] A. Streitweiser and J. H. Hammons, *Progr. Phys. Org. Chem.*, 1965, **3**, 41.

[132] E. F. Caldin and J. C. Harbron, *J. Chem. Soc.*, 1962, 2314.

[133] R. A. More O'Ferrall and J. H. Ridd, *J. Chem. Soc.*, 1963, 5030.

[134] E. F. Caldin and G. Long, *Proc. Roy. Soc.*, 1955, *A*, **228**, 263.

activation is positive (7 cal. deg.$^{-1}$ mole^{-1}). The activation energy for the forward reaction, 13·6 kcal./mole, is not much larger than that observed for association reactions of ethoxide ion with TNT and 1,3,5-trinitrobenzene in ethanol solution,[135] and Caldin suggests that the process of desolvation makes a considerable contribution to the activation energy.

The pK_a of TNT in ethanol at 25° can be estimated from the ethoxide–TNT studies[134] to be approximately 15·8 which is close to the value for phenol in ethanol.[136] Deuterium exchange with the methyl hydrogens should occur under relatively mild basic conditions but only 23% exchange was effected when TNT was allowed to stand for 2—3 weeks at 25° in pyridine–D_2O solution.[122] Exchange occurs rapidly however when catalysed by deuteroxide ion in dimethylformamide–D_2O mixtures.[137]

In view of the low pK_a of TNT it should be possible to produce the purple TNT$^-$ in ethanol solution by use of weaker bases than ethoxide ion. The reaction of TNT$^-$ with 3-methylphenol in ethanol yields a measurable equilibrium concentration of TNT$^-$,[138] inferring an attack by the 3-methylphenoxide ion on TNT, but direct studies in an aprotic solvent have not been reported.

In more strongly basic solutions a proton may be removed from 4-nitrotoluene or 2,4-dinitrotoluene.[139] With potassium t-butoxide in t-butyl alcohol (or dimethyl sulphoxide) in the absence of oxygen, the nitro- and dinitro-toluene yield their radical anions as shown by means of electron spin resonance spectroscopy. In the case of 2,4-dinitrotoluene significant amounts of radical anion are produced only when the solution is deficient in base. It is thought that the nitro- or dinitro-benzyl anion is first formed and that electron transfer occurs between this anion and the parent compound to produce the radical anion.[139] According to Miller and Pobiner[140] the concentration of 4-nitrobenzyl anion reached when potassium t-butoxide is added to a solution of 4-nitrobenzene in t-butyl alcohol is low and the anion has an absorption maximum at 362 mμ.

7 Formation of Radical Anions

Nitroaromatic compounds can be converted into radical anions by accepting a single electron from a strong base. 4-Nitrotoluene for example[139] has been observed to give a high concentration of radical anions when dissolved in t-butyl alcohol or t-butyl alcohol–dimethyl sulphoxide mixtures to which potassium t-butoxide has been added. Such experiments are performed in the absence of oxygen and the identification of the radical anion and the determination of its concentration are readily performed using electron spin resonance techniques. With t-butoxide ion in t-butyl alcohol, 1,3-dinitrobenzene is a better acceptor than nitrobenzene[141] and a small concentration of the dinitrobenzene anion

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[135] E. F. Caldin, *J. Chem. Soc.*, 1959, 3345.
[136] B. D. England and D. A. House, *J. Chem. Soc.*, 1962, 4421.
[137] E. Buncel and J. Wood, unpublished results.
[138] J. A. Blake, M. J. B. Evans, and K. E. Russell, *Canad. J. Chem.*, 1966, **44**, 119.
[139] G. A. Russell and E. G. Janzen, *J. Amer. Chem. Soc.*, 1962, **84**, 4153; 1967, **89**, 300.
[140] J. M. Miller and H. Pobiner, *Analyt. Chem.*, 1964, **36**, 238.
[141] G. A. Russell, E. G. Janzen, and E. T. Strom, *J. Amer. Chem. Soc.*, 1964, **86**, 1807.

radical is produced even when ethoxide ion is used as the donor in ethanol solution. However, 1,3,5-trinitrobenzene and t-butoxide give a very low concentration of radical anion and this is ascribed to the intervention of σ-complex formation between the two reactants. Many other bases can be used to produce the radical anion of nitrobenzene in t-butyl alcohol–dimethyl sulphoxide mixtures or of 1,3-dinitrobenzene in ethanol solution;[141] these include the conjugate bases of fluorene, indene, propiophenone, quinol and diethyl malonate. The ability of the basic anion to donate a single electron to the nitroaromatic compound is in part related to its base strength. The dithionite ion has also been successfully used to produce radical anions from a variety of nitroaromatic compounds.[142]

The rate of radical-anion formation is dependent on the solvent; the nitrobenzene radical anion is more rapidly formed from nitrobenzene and t-butoxide ion when the proportion of dimethyl sulphoxide in the solvent is increased.[141] Electron spin resonance studies show that radical anions of nitroaromatic compounds may interact strongly with the solvent particularly when a hydroxylic solvent such as ethanol which can form hydrogen bonds to the nitro-groups is used.[143] Interaction with the positive counter-ion is, however, usually weak except in solvents of low dielectric constant and solvating power.

Many of the radical anions of nitroaromatic compounds are reported to be coloured under the conditions used for study of their electron spin resonance spectra. For example, 1,3-dinitrobenzene gives a bright violet solution immediately after the start of electrolysis in dimethylformamide solution and 2,6-dinitrotoluene gives a bright red solution and it seems reasonable to associate the colours with the radical anions.[144] Ward[145] reports that the colours of solutions of 1,3-dinitrobenzene anion in 1,2-dimethoxyethane vary from a light yellow with the lithium counter-ion to a dark orange for the cæsium counter-ion. On the other hand, a purple colour observed in concentrated solutions of this anion has been ascribed to a decomposition product.[146] Miller and Wynne-Jones[147] suggested that there would be an electronic level in the 1,3,5-trinitrobenzene radical anion so situated as to produce absorption of light in the visible region and it is interesting that an unstable green complex is reportedly formed by the reaction of sodium with 1,3,5-trinitrobenzene in dioxan.[148]

There have been surprisingly few visible absorption studies of radical anions of nitroaromatic compounds. Kemula and Sioda[149] have reported that the radical anion of nitrobenzene generated electrochemically in dimethylformamide shows absorption maxima at 435 mμ ($\epsilon = 1{\cdot}5 \times 10^3$ l. mole^{-1} cm.$^{-1}$) and 465 mμ ($\epsilon = 1{\cdot}25 \times 10^3$ l. mole^{-1} cm.$^{-1}$). Chambers and Adams[150] also report

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[142] P. L. Kolker and W. A. Waters, *J. Chem. Soc.*, 1964, 1136.

[143] P. B. Ayscough, F. P. Sargent, and R. Wilson, *J. Chem. Soc.*, 1963, 5418.

[144] J. H. Freed and G. K. Fraenkel, *J. Chem. Phys.*, 1964, **41**, 699.

[145] R. L. Ward, *J. Chem. Phys.*, 1960, **32**, 410.

[146] M. J. Blandamer, T. E. Gough, J. M. Gross, and M. C. R. Symons, *J. Chem. Soc.*, 1964, 536.

[147] R. E. Miller and W. F. K. Wynne-Jones, *J. Chem. Soc.*, 1959, 2375.

[148] A. Mathias and E. Warhurst, *Trans. Faraday Soc.*, 1962, **58**, 942.

[149] W. Kemula and R. Sioda, *Bull. Acad. polon. Sci., Ser. Sci. chim.*, 1963, **11**, 395.

[150] J. Q. Chambers and R. N. Adams, *Mol. Phys.*, 1965, **9**, 413.

an absorption maximum for this species at 465 mμ in dimethylformamide. The position of maximum absorption is strongly solvent-dependent, shifting to lower wavelengths with increasing percentage of water in dimethylformamide-water mixtures. In 1,2-dimethoxyethane, the radical anion of nitrobenzene, generated through reaction of sodium with nitrobenzene, possesses an absorption maximum at 560 mμ and an ϵ estimated at *ca.* 1000.[151]

The extent to which radical anions are present under conditions which lead to significant concentrations of σ-complexes in solution is uncertain. Gold and Rochester[68b] observed no electron spin resonance spectrum of solutions of 1,3,5-trinitrobenzene in methanolic sodium methoxide or ethanolic sodium hydroxide solution and Russell, Janzen, and Strom[141] observed only a very low concentration of radical anions in t-butyl alcohol solutions of potassium t-butoxide. No electron spin resonance spectrum was given by a solution of 2,4,6, trinitroanisole in ethanolic sodium hydroxide.[68b] A spectrum was observed during the course of a slow reaction between 1,3,5-trinitrobenzene and diethylamine both in the presence and absence of acetone[68b,152] but the importance of this radical or radical anion in complex formation is uncertain.[6,7,68b] Similarly species having electron spin resonance spectra are generated in basic solutions of acetone and 1,3,5-trinitrobenzene,[68b,153] but whether these species are derived from the initially formed Meisenheimer complex and to what extent the radical is responsible for the colour of the resulting solutions is not known.

A further complicating factor in these studies is the possibility of a light-induced production of radical anions. Thus irradiation of solutions containing nitrobenzene and methoxide ion in ethanol[143] and 1,3,5-trinitrobenzene and cyanide ion in chloroform[153] gives rise to free-radical species. It is probable however that this is not a serious complication in the general studies of interactions of bases with aromatic nitro-compounds reported here.

[151] A. Ishitani, K. Kuwata, H. Tsubomura, and S. Nagakura, *Bull. Chem. Soc. Japan*, 1963, **36,** 1357.

[152] R. E. Miller and W. F. K. Wynne-Jones, *Nature*, 1960, **186,** 149.

[153] A. R. Norris, unpublished results.