113597-92-5; Ru(C6-PBP)(CO)$_{out}$(THF)$_{in}$, 113585-10-7; Ru(C6-PBP)(CO)$_{out}$(pyr)$_{in}$, 113585-11-8; Ru(C8-PBP)(CO)$_{out}$(pyr)$_{in}$, 113585-12-9; Ru(PXY-PBP)(CO)$_{out}$(pyr)$_{in}$, 113585-13-0; Ru(C6-PBP)(1,5-DCI)$_{out}$, 113585-14-1; [Ru(C6-PBP)(1,5-DCI)$_{out}$(THF)$_{in}$]$^+$, 113585-24-3; [Ru(C6-PBP)(1,5-DCI)$_{out}$(PPh$_3$)$_{in}$]$^+$, 113585-25-4; [Ru(C6-PBP)-(1,5-DCI)$_{out}$(PCy$_3$)$_{in}$]$^+$, 113585-26-5; Ru(TPP)(pyr)$_2$, 34690-41-0.

Supplementary Material Available: Bond distances (Table 1S), bond angles (Table 2S), metric details on the toluene (Table 3S) and pyridine solvates (Table 4S), distances from pyridine inside the basket to basket atoms (Table 5S), positional and thermal parameters for the non-hydrogen atoms (Table 6S), dihedral angles (Table 7S), deviations from the mean porphyrin plane (Table 8S), hydrogen atom positional and thermal parameters (Table 9S) (14 pages); structure amplitudes (Table 10S) (49 pages). Ordering information is given on any current masthead page.

Proton Exchange and Nuclear Magnetic Resonance Line Broadening in Aromatic Nucleophilic Addition and Substitution

Radu Bacaloglu,* Clifford A. Bunton,* Giorgio Cerichelli,[1] and Francisco Ortega[2]

Contribution from the Department of Chemistry, University of California, Santa Barbara, California 93106. *Received June 5, 1987. Revised Manuscript Received December 22, 1987*

Abstract: Aromatic nucleophilic addition and substitution by OH$^-$ (OD$^-$) in DMSO-d_6–D$_2$O or D$_2$O are for many nitrobenzenes, naphthalenes, and activated azines accompanied by extensive hydrogen exchange. However, substrates that readily form Meisenheimer complexes or overall substitution products are the least readily exchanged. With some overall substitutions exchange is greater in products than in unreacted substrate, which shows that exchange involves an intermediate on the reaction path between substrate and product, and it has also been identified in overall addition. This intermediate is believed to be a charge-transfer complex between a radical anion and •OH or its anion, and it exchanges aromatic hydrogen with D$_2$O. Line broadening of the NMR proton signals of unreacted substrate can also be observed due to interaction between this complex and substrate. The complex slowly dissociates, giving very extensive line broadening, especially in less aqueous media, but in aqueous media it goes forward to products.

The generally accepted mechanism of aromatic nucleophilic substitution on activated arenes (**1**) in polar hydroxylic solvents involves rate-limiting ipso addition giving a σ or Meisenheimer complex (**2**), which rapidly forms **3** (Scheme I).[3]

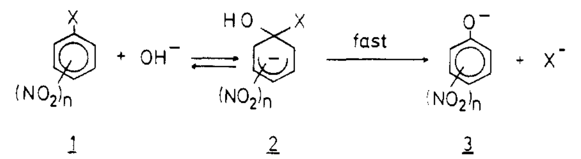
Reinvestigation of nucleophilic additions and substitutions involving nitroarenes, azines, and their halo and arenesulfonate derivatives shows that this simple mechanism is inadequate, even for solvents of high water content, under conditions in which the overall reaction is first order with respect to substrate.[4,5] Two intermediates were seen spectrophotometrically en route to the Meisenheimer complex, and the rate and equilibrium constants of the individual steps were calculated by using a general treatment based on relaxation theory.[4,5]

The postulated intermediates are a π-complex (**4**) and a charge-transfer complex of an anion radical and OH (**5**) (Scheme II). Scheme II is simplified because **5** can also react in its deprotonated form.[4,5]

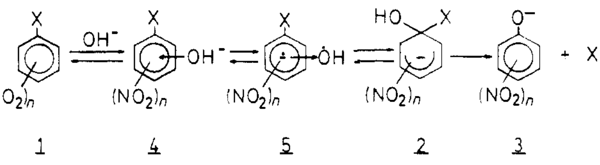
π-Complexes are possible intermediates in aromatic nucleophilic addition and substitution,[6] and anion radicals are formed by interaction of nitroarenes with bases, although usually in aprotic solvents of very low water content.[7] When we attempted to identify reaction intermediates by NMR spectroscopy, we saw loss of some aromatic proton signals, which was due both to exchange with D$_2$O of the solvent and to extensive line broadening,[4] and we therefore examined a number of nitroarenes and azines.

Aromatic compounds undergo base-catalyzed hydrogen exchange, and substrate deprotonation is postulated.[8] The position and rate of exchange can sometimes be correlated with inductive

Scheme I



Scheme II



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effects of substituents in arenes[9] and azines[10] and with the position of metalation,[11] but some workers have concluded that mesomeric effects are also important.[12] With 1,3-difluoro- and pentafluorobenzene in MeO^- (MeOH,D), hydrogen exchange is much faster than substitution, but there is no kinetic hydrogen isotope effect,[13] and these results do not fit slow substrate deprotonation.

Exchanges of 1,3-dinitrobenzene[14] or naphthalene[15] and 1,3,5-trinitrobenzene[14e,16] occur in mildly alkaline solution, competitively with formation of Meisenheimer complexes, which do not themselves undergo direct exchange.[14e,16c] We know of no evidence for proton exchange concurrent with overall aromatic nucleophilic substitution in polar, hydroxylic, media, but exchange[17] and a kinetic hydrogen isotope effect of ca. 5.7[17a] in an arynic overall substitution on haloarenes are consistent with formation of a free, intermediate, aryl anion. Formation of anion radicals[18-20] is sometimes accompanied by hydrogen exchange, because they are strong bases and can be protonated (deuteronated) by protic solvents.[21] Therefore hydrogen exchange, accompanying nucleophilic addition or substitution, does not necessarily involve aryl anions, although the mechanism may depend upon the solvent.

Line broadening in NMR spectra is evidence for interaction with a paramagnetic species.[22-24] We have noticed it earlier in the interaction of 1,3-dinitrobenzene with OD^- in DMSO-d_6–D_2O.[4]

Experimental Section

Materials. Most of the substrates were commercial samples and were purified by recrystallization or distillation. The following compounds were from Aldrich; nitrobenzene (6), 1,2- and 1,4-dinitrobenzene (**7** and **8**), 3,5-dinitrobenzonitrile (**9**), 2,6-dinitrotoluene (**10**), 4-nitrofluorobenzene (**11**), 2,4-dinitrofluorobenzene (**12**), 2,4- and 2,6-dinitrochlorobenzene (**13** and **14**), 2,3-dichloro-4,5-dinitrobenzene (**15**), 3,5-dinitro-4-chlorobenzonitrile (**16**), 3,5-dinitro-4-chlorobenzoic acid (**17**), 2-chloro-3,5-dinitrobenzoic acid (**18**), 1,3-dinitronaphthalene (**19**), 2-chloro-3,5-dinitropyridine (**20**), 2,6-dichloro-3-nitropyridine (**21**), 2,4-dichloropyrimidine (**22**), 4,6-dichloropyrimidine (**23**), 4,6-dichloro-5-nitropyrimidine (**24**), 2,6-dichloropyrazine (**25**), and quinazoline (**26**). The following compounds were from Eastman: 1,3-dinitrobenzene (**27**), 1,3,5-trinitrobenzene (**28**), 3-nitroacetophenone (**29**), and 2,4,6-trinitrobenzenesulfonic acid (**30**). Ethyl 3,5-dinitrobenzoate (**31**) and 3,5-dinitrobenzamide (**32**) were from Lancaster Synthesis Products, and 2,4,6-trinitrochlorobenzene (**33**) was from Matheson. The following derivatives of 2,4-dinitronaphthalene were prepared from 2,4-dinitronaphthol (Aldrich) by standard methods:[25] 1-chloro (**34**), 1-morpholinyl (**35**), 1-amino, 1-tosylate (**36**), and 1-methoxy (**37**). 1-Bromo-2,4-dinitronaphthalene (**38**) was prepared from 1-amino-2,4-dinitronaphthalene by the Sandmeyer reaction.[26] 1-Fluoro-2,4-dinitronaphthalene (**39**) was prepared from 5-fluoro-1,2,3,4-tetrahydronaphthalene,[27,28] and 4-chloroquinazoline (**40**) was prepared from 4-quinazoline.[29,30] DMSO-d_6 and D_2O were Aldrich products.

Table I. Hydrogen Exchange of Nitroarenes and Quinazoline[a]

	conditions			exchange, %		
substrate	DMSO-d_6, wt %	[S], M	time, s	2	4	6
1,3-$(NO_2)_2C_6H_4$ (**27**)	50	0.021	600	49	0	0
			2800	94	3	3
1-$COCH_3$-3-$NO_2C_6H_4$ (**29**)	72	0.032	1200	0	0	0
1,3,5-$(NO_2)_3C_6H_3$ (**28**)	70	0.026	600	60^b	58^b	58^b
				62^c	62^c	57^c
1-CN-3,5-$(NO_2)_2C_6H_3$ (**9**)	70	0.036	600	13^b	34^b	14^b
	50	0.014	600	51^b	94^b	47^b
1-CO_2Et-3,5-$(NO_2)_2C_6H_3$ (**31**)	80	0.015	600	0	100	0
			4000	11	100	11
1-$CONH_2$-3,5-$(NO_2)_2C_6H_3$ (**32**)	72	0.029	180	0	100	0
1,3-$(NO_2)_2C_{10}H_6$ (**19**)	70	0.034	600	16^d	6^d	
			10^4	50^d	23^d	
1,3-$C_8H_6N_2$ (**26**)	0^e	0.053	6000	15	15	

[a] At 25 °C, 0.2 M KOD, and exchange of substrate, unless specified. [b] In 2-monohydroxy Meisenheimer complex. [c] In 2,4-dihydroxy Meisenheimer complex. [d] In 4-monohydroxy Meisenheimer complex. [e] 2.5 M KOD.

NMR Spectra. NMR spectra were obtained with a 300-MHz Nicolet T300 spectrometer, with DSS as a chemical shift reference. The NMR spectra of the substrate and the standard, mesitoic acid (Aldrich) (**41**), were first measured and then KOD in D_2O was added. The first spectrum was obtained within 120–140 s. A large number of exploratory spectra were run in order to find satisfactory experimental conditions. Peak areas were calculated from the integrated areas calibrated with mesitoate ion.

Solutions of aqueous DMSO were made up by weight, and the quoted solvent compositions are weight percent DMSO. The highest D_2O content consistent with the solubility of the substrate was used, and $[OD^-]$ was chosen so that the overall reactions were not too fast for the NMR measurements. The molarity of OH^- (OD^-) is calculated in terms of the total solution volume. The variations in solvent compositions for experiments of different substrates were due to the problem of making up solutions with small amounts of deuteriated solvents. The countercation was K^+, because it allowed us to examine a wide range of solvent composition. Mesitoate ion is a convenient standard, because it has a sharp singlet at 6.73 ppm, which does not interfere with the other signals, and it does not interact with the other solutes. We verified that mesitoate ion and the phenols, naphthols, and hydroxyazines do not exchange hydrogen, except that 2,4,6-trinitrophenol undergoes a slow exchange at high $[OH^-]$. Where line broadening is discussed, we quote the width at half-height, and for multiplets the central peak is taken.

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The first-order rate constants of exchange were calculated from integrated peak areas. Some of the substrates equilibrated readily with mono- or dihydroxy Meisenheimer complexes, and in aqueous DMSO at high pH, equilibrium strongly favors these complexes. In these cases exchanges were followed by measuring the peak areas for the Meisenheimer complexes. The accuracy of these rate determinations is limited by the accuracy of the signal integration, which is ca. 10% under the conditions of our measurements.

Mass Spectra. Hydrogen exchange during reactions of 2,4-dinitro (**13**) and 2,4,6-trinitrochlorobenzene (**33**) was confirmed mass spectrometrically by use of a double-focusing mass spectrometer. Substrate (1 mmol) was allowed to react with 1 M OD^- in 66% DMSO-D_2O. After complete reaction the solution was acidified (HCl), and the nitrophenols were isolated after treatment with EtOH to normalize the hydroxyl hydrogen. 2,4,6-Trinitrophenol has a molecular ion at 231 mass units (mu), corresponding to doubly deuteriated material, and the other peaks were consistent with dideuteriation. A control experiment with 2,4,6-trinitrophenol confirmed that it undergoes slow hydrogen exchange and, from intensities of peaks at 229, 230, and 231 mu, we estimated 30% exchange of one hydrogen and 22% exchange of two hydrogens. It is also the only phenol for which formation of a Meisenheimer complex with OH^- has been reported.[31]

2,4-Dinitrophenol was obtained from 2,4-dinitrochlorobenzene (**13**) in a similar experiment, and it had a molecular ion at 185 mu corresponding to monodeuteriated material. The fragment ions were also consistent with monodeuteriation. 2,4-Dinitrophenol does not exchange arene hydrogens under the reaction conditions.

In other experiments under the same conditions, reaction at 25 °C was stopped after 30 s by adding HCl, and unreacted substrates were examined mass spectrometrically. The mass spectrum of 2,4,6-trinitrochlorobenzene (**33**) had peaks at 249 and 251 mu (intensities 3:1), corresponding to the formation of dideuteriated substrate, and there was also a small peak at 231 mu corresponding to dideuteriated product. The fragment ions also corresponded to the presence of dideuteriated materials. With 2,4-dinitrochlorobenzene (**31**) the mass spectrum of the isolated materials had peaks at 203 and 205 mu corresponding to monodeuteriation, and the fragment ions were consistent with this assignment.

Reaction of 1,3-dinitronaphthalene (**19**) with 2 M KOH was carried out in 50% DMSO containing 50% $H_2{}^{18}O$ for 30 min at 25 °C. The solution was acidified, and 1,3-dinitronaphthalene was isolated. Its mass spectrum was the same as that of authentic material: M^+, 218; M - OH^+, 201; M - $NO_2{}^+$, 172; M - NO_2 - NO^+, 142; M - $2NO_2{}^+$, 126; M - $2NO_2$ - C^+, 114 mu. There was no oxygen exchange between water and the nitro groups.

Kinetics. Reactions of 4-nitrofluorobenzene and 2,4-dinitrochlorobenzene (5×10^{-5} M) with 0.2 M KOH were followed spectrophotometrically at 25 °C at 400 and 360 nm, respectively. The solvent was 30 vol % H_2O plus DMSO and added inert solvent so that the final reaction contains 70 vol % of total organic solvent.

Results

Hydrogen Exchange. Mononitroarenes (e.g., **29** (Table I)) did not exchange in our relatively aqueous solvents, but 1,3-dinitroarenes rapidly exchanged at position 2 and sometimes slowly at the other positions (e.g., **9**, **19**, **27**, **28**, **31**, and **32** (Table I)). Diazines also exchange, but qualitatively more slowly than di- or trinitroarenes (e.g., **26**, Table I). Therefore nitro groups are not directly involved in exchange. Exchange of **26** was followed in D_2O, so DMSO is not directly involved.

Di- or trinitroarenes that readily give Meisenheimer complexes generally give *less* exchange than the less activated compounds that do not form these complexes, as shown by comparison of compounds **31** and **32** relative to **9** and **28** (Table I).

For compounds that do not give Meisenheimer complexes (**2**) in the experimental conditions, e.g., 1,3-dinitrobenzene (**27**), first-order rate constants of exchange vary linearly with [OD^-] and increase with increasing content of DMSO-d_6 (Table II). But when Meisenheimer complexes are formed, as with 3,5-dinitrobenzonitrile (**9**) or 1,3,5-trinitrobenzene (**28**), rate constants of exchange go through maxima with increasing [OD^-] and increasing content of DMSO-d_6 (Table II). These data are consistent with previous observations[14e,16c] that Meisenheimer complexes (**2**) do not exchange their hydrogens.

The hydrogens at positions 2 and 6 in 3,5-dinitrobenzonitrile (**9**) are not equivalent in its Meisenheimer complex with OD^-, but they exchange at the same rate (Table II), which is also inconsistent with direct exchange of the Meisenheimer complex (**2**). With 1,3,5-trinitrobenzene (**28**) two Meisenheimer complexes can form (with one or two OD^-), but again all the hydrogens of both complexes exchange at the same rate. Therefore exchange occurs either in the substrate or in an intermediate, other than the Meisenheimer complex, in which hydrogens are equivalent or can rapidly equilibrate.

Table II. Rate Constants of Hydrogen Exchange of Nitroarenes[a]

	conditions			
substrate	DMSO-d_6, wt	[KOD], M	[S], M	10^3k, s^{-1} at position noted
1,3-$(NO_2)_2C_6H_4$[b] (**27**)	50	0.05	0.028	0.20 (2)
	50	0.2	0.021	1.0 (2)
	50	0.3	0.019	1.7 (2)
	50	0.4	0.020	2.0 (2)
	70	0.05	0.032	3.0 (2)
1,3,5-$(NO_2)_3C_6H_3$ (**28**)	50	0.2	0.012	7.0 (2); 6.6 (4, 6)[c]
				5.9 (2, 4); 5.4 (6)[d]
	50	0.5	0.011	0.2 (2, 4); 0.2 (6)[d]
	70	0.2	0.026	2.2 (2); 2.2 (4, 6)[c]
				2.0 (2, 4); 2.1 (6)[d]
1-CN-3,5-$(NO_2)_2C_6H_3$ (**9**)	50	0.1	0.018	3.2 (4); 0.6 (2, 6)[c]
	50	0.2	0.014	5.2 (4); 0.8 (2, 6)[c]
	50	0.3	0.026	5.1 (4); 0.9 (2, 6)[c]
	50	0.4	0.028	2.2 (4); 0.4 (2, 6)[c]
	50	0.4	0.012	2.6 (4); 0.5 (2, 6)[c]
	70	0.2	0.036	0.7 (4); 0.1 (2, 6)[c]
1,3-$(NO_2)_2C_{10}H_6$ (**19**)	70	0.05	0.014	0.03 (2)[e]
	70	0.2	0.034	0.04 (2)[e]

[a] At 25 °C and from the NMR spectrum of the substrate unless specified. [b] Signals were broadened; see text. [c] Observation on the 2-monohydroxy Meisenheimer complex. [d] Observation on the 2,4-dihydroxy Meisenheimer complex. [e] Observation on the 4-monohydroxy Meisenheimer complex.

We could not distinguish between these possibilities for addition of OH^- (OD^-) and we therefore examined concurrent exchange and substitution of activated nitroarenes or azines with either halides or sulfite leaving groups (Tables III and IV). With some substrates there is extensive hydrogen exchange in the products (e.g., **13**, **15**, **16**, **18**, **30**, **33**, **34**, and **35** (Table III) and **23** (Table IV)), but little or no exchange with others (e.g., **8**, **11**, **14**, **17**, and **36** (Table III) and **22**, **24**, **25**, and **40** (Table IV)). The phenolic products did not exchange in our conditions, except for 2,4,6-trinitrophenol (Experimental Section). For compounds with similar activating, but different leaving groups (e.g., **12**, **13**, and **34**–**39** (Table III)) or the same group, but different activating groups (e.g., **23** and **24** (Table IV)), exchange decreases qualitatively as reactivity to substitution increases. These observations are again consistent with exchange of substrate or an intermediate.

Some overall substitutions were carried out with substrate in excess over OD^-, so that exchange of both unreacted substrate and product could be examined. With some compounds (e.g., **30**, **33**, and **34** (Table III) and **23** (Table IV)) both substrate and product were completely exchanged, and this result was confirmed mass spectrometrically with 2,4-dinitro- (**13**) and 2,4,6-trinitrochlorobenzene (**33**) (66% DMSO-d_6, 1 M OD^-) (Experimental Section). With 2,4,6-trinitrobenzenesulfonate ion (**30**) exchange is qualitatively similar in D_2O and D_2O–DMSO, confirming that DMSO is not required for exchange.

The key observation is that with some compounds the product is exchanged *more* than the unreacted substrate (e.g., **12**, **35**, **36**, and **37** (Table III)). Therefore an intermediate, on the reaction path, must be involved in these exchanges. This conclusion does not depend upon the precise mechanism of exchange. Reaction of 2,6-dichloro-3-nitropyridine with OD^- (**21** (Table IV)) gives both the 2- and 6-hydroxy derivatives, with exchange at position 4. Both products had exchanged to the same extent, which suggests that they are derived from a common precursor.

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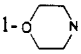
[31] Crampton, M. R.; El Ghariani, M. *J. Chem. Soc. B* **1969**, 330.

Table III. Hydrogen Exchange in Nitroarenes in the Course of Overall Substitution[a]

	conditions				extent of exchange,[b] %	
substrate	DMSO-d_6 %	[OD$^-$], M	[S], M	conv, %	substrate	product
1-F-4-$NO_2C_6H_4$ (**11**)	73	0.2	0.067	10–100	0	0
1,4-$(NO_2)_2C_6H_4$[c] (**8**)	77	0.2	0.058	10–100	0	0
1-F-2,4-$(NO_2)_2C_6H_3$ (**12**)	70	0.015	0.031	19	33 (3)	60 (3)
	70	0.05	0.106	20	33 (3)	53 (3)
1-Cl-2,4-$(NO_2)C_6H_3$ (**13**)	67	0.16	0.050	100		100 (3)
1-Cl-2,6-$(NO_2)_2C_6H_3$[c] (**14**)	70	0.10	0.060	65	29 (3, 5)	25 (3, 5)
1-CO_2^--2-Cl-3,5-$(NO_2)_2C_6H_2$ (**18**)	61	1.0	0.019	100		100 (4), 15 (6)
1-CO_2^--4-Cl-3,5-$(NO_2)_2C_6H_2$ (**17**)	51	1.0	0.039	72–100	0	0
1-CN-4-Cl-3,5-$(NO_2)_2C_6H_2$ (**16**)	69	0.10	0.014	100		100 (2, 6)
1,2-Cl_2-4,5-$(NO_2)_2C_6H_2$[d] (**15**)	72	0.20	0.038	100		100 (3, 6)
1-Cl-2,4,6-$(NO_2)_3C_6H_2$ (**33**)	75	0.20	0.25	80	98 (3, 5)	100 (3, 5)
1-SO_3^--2,4,6-$(NO_2)_3C_6H_2$ (**30**)	0	0.01	0.014	35		100 (3, 5)
	70	0.01	0.058	9	100 (3, 5)	100 (3, 5)
	70	0.10	0.06	100		100 (3, 5)
1-F-2,4-$(NO_2)C_{10}H_5$ (**29**)	70	0.01	0.02	50	50 (3)	45 (3)
	68	0.23	0.072	100		20 (3)
1-Cl-2,4-$(NO_2)_2C_{10}H_5$ (**34**)	83	0.015	0.015	40	100 (3)	100 (3)
	83	0.075	0.015	100		100 (3)
1-MeO-2,4-$(NO_2)_2C_{10}H_5$ (**37**)	78	0.017	0.017	37	36 (3)	46 (3)
	78	0.071	0.017	100		48 (3)
1-Tos-2,4-$(NO_2)_2C_{10}H_5$ (**36**)	77	0.016	0.016	54	12 (3)	20 (3)
	77	0.066	0.016	100		48 (3)
1-Br-2,4-$(NO_2)_2C_{10}H_5$ (**38**)	78	0.10	0.026	100		83 (3)
1--2,4-$(NO_2)_2C_{10}H_5$ (**35**)	85	0.007	0.010	75	75 (3)	100 (3)

[a] At 25 °C. [b] Extent of exchange at specified positions. [c] Signals of the substrate were broadened. [d] Product is 4,5-Cl_2-2-$NO_2C_6H_3OH$.

Table IV. Hydrogen Exchange in Chloroazines in the Course of Overall Substitution[a]

	conditions				extent of exchange,[c] %	
substrate	DMSO-d_6, %	[OD$^-$], M	[S], M	conv,[b] %	substrate	product
2-chloro-3,5-dinitropyridine (**20**)	66	0.72	0.069	100		62 (4), 57 (6)
2,6-dichloro-3-nitropyridine (**21**)	65	1.20	0.036	76 (2)		58 (4)
				24 (6)		55 (4)
	65	0.026	0.039	24 (2)	44 (4)	32 (4)
				12 (6)	44 (4)	33 (4)
	65	0.20	0.039	73 (2)		51 (4)
				27 (6)		51 (4)
2,4-dichloropyrimidine (**22**)	50	0.60	0.21	64 (4)		0
				36 (2)		0
4,6-dichloropyrimidine (**23**)	47	0.50	0.093	54	100 (2)	100 (2)
				100		100 (2)
4,6-dichloro-5-nitropyrimidine (**24**)	78	0.20	0.056	100		15 (2)
2,6-dichloropyrazine (**25**)	50	0.20	0.042	100		33 (3, 5)
4-chloroquinazoline (**40**)	60	0.10	0.040	100		28 (2)
		0.20	0.027	100		20 (2)

[a] At 25 °C. [b] Unless specified, substitution is at Cl; otherwise the position of substitution is specified in parentheses. [c] Position specified in parentheses.

Although these exchange experiments provided good evidence for the existence of an intermediate in the conversion of substrate into Meisenheimer complex (**2**) or phenolic products (**3**), we could not identify it by NMR spectrometry. However, a short-lived intermediate absorbing at 260–350 nm has been observed with many of our substrates, and we identify it with the intermediate responsible for the exchange.[4,5] Addition of OH^- (OD^-) to a nitro group could give intermediates with such UV spectra, but we exclude them because similar species are seen in reactions of azines, and also there is no exchange of oxygen between nitro groups and solvent (Experimental Section). Aryl anions cannot be on the reaction path because, in our conditions, their protonation (deuteriation) by water should be fast, and exchange should then *always* be faster than addition or substitution.

Line Broadening. NMR spectroscopy has been used extensively to study exchange reactions between diamagnetic (M) and paramagnetic (M$^•$) species, which may be written as[22]

$$M + M^\bullet \rightleftharpoons M^\bullet + M$$

The nuclei in a given molecule are interchanged between diamagnetic and paramagnetic sites as the reaction proceeds. A nucleus experiences only the external magnetic field while in the diamagnetic state, but when it is in the paramagnetic state, a field, due to the electron–nuclei hyperfine interaction, is added. The rapid interchange of the nuclei between these magnetic states results in a broadening of NMR signals arising from the diamagnetic molecules.

The extent of line broadening depends on the lifetimes of paramagnetic (t_P) and diamagnetic (t_D) states and the hyperfine coupling constant (A) of the nucleus being considered. The general equation, which accounts for the contribution of exchange reaction on the line width expressed as the transverse relaxation time (τ_2), may be written as[22a,b]

$$\tau_2^{-1} = A^2 t_P^2 / t_D(4 + A^2 t_P^2) \qquad (1)$$

If $At_P > 2$ the nucleus experiences a strong magnetic pulse while in the paramagnetic state, and eq 1 reduces to

$$\tau_2^{-1} = 1/t_D \qquad (2)$$

If this condition is not met, the nucleus experiences a relatively weak magnetic pulse. The lifetimes t_D and t_P of the diamagnetic and paramagnetic species are related to the rate constants of the electron exchange. The kinetics of a variety of transfer reactions of a single electron between diamagnetic and paramagnetic species have been studied. Examples include *N,N,N′,N′*-tetraalkyl-*p*-phenylenediamine cation radical,[22a,24a] semiquinone anion radi-

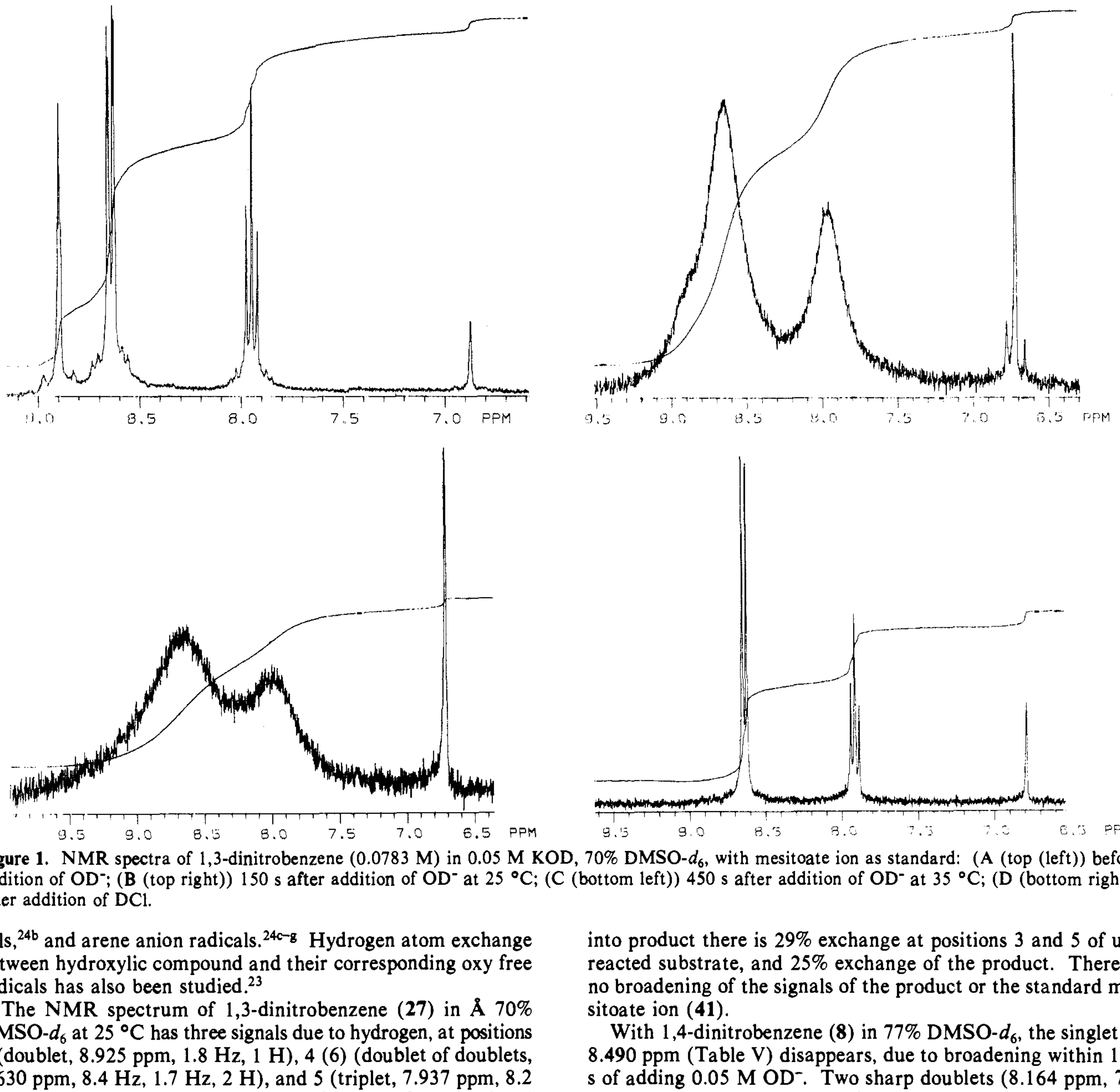


Figure 1. NMR spectra of 1,3-dinitrobenzene (0.0783 M) in 0.05 M KOD, 70% DMSO-d_6, with mesitoate ion as standard: (A (top (left)) before addition of OD^-; (B (top right)) 150 s after addition of OD^- at 25 °C; (C (bottom left)) 450 s after addition of OD^- at 35 °C; (D (bottom right)) after addition of DCl.

cals,[24b] and arene anion radicals.[24c-g] Hydrogen atom exchange between hydroxylic compound and their corresponding oxy free radicals has also been studied.[23]

The NMR spectrum of 1,3-dinitrobenzene (**27**) in Å 70% DMSO-d_6 at 25 °C has three signals due to hydrogen, at positions 2 (doublet, 8.925 ppm, 1.8 Hz, 1 H), 4 (6) (doublet of doublets, 8.630 ppm, 8.4 Hz, 1.7 Hz, 2 H), and 5 (triplet, 7.937 ppm, 8.2 Hz, 1 H) (Figure 1A). On addition of 0.05 M OD^- the signal at position 2 disappears due to exchange with D_2O, and signals at positions 4 (6) and 5 collapse to two broad singlets (8.65 and 7.95 ppm) (Figure 1B). These signals broaden, but do not shift, when the temperature is increased to 35 °C (Figure 1C), but they disappear at 45 °C due to extensive broadening. When the solution is cooled to 25 °C the signals reappear, and are similar to those shown in Figure 1B. Addition of DCl/D_2O gives the spectrum shown in Figure 1D. The doublet at 8.925 ppm does not reappear, but the doublet of doublets at 8.630 ppm reappears as a doublet with lower intensity, due to slight exchange, and the triplet at 7.937 ppm reappears unchanged. The singlet of mesitoate ion (**41**) at 6.985 ppm does not change in any of these spectra (Figure 1A–D).

The spectrum of 2,6-dinitrochlorobenzene (**14**), which gives overall substitution with OH^-, has a doublet (8.296 ppm, 8.4 Hz, 2 H (3 and 5)) and a triplet (7.824 ppm, 8.2 Hz, 1 H (4)) in 70% DMSO-d_6 at 25 °C (Figure 2A). After addition of 0.1 M OD^- (145 s) both signals collapse to two broad signals at 8.30 and 7.82 ppm, and two new sharp signals, a doublet (7.926 ppm, 8.1 Hz, 2 H) and a triplet (6.245 ppm, 8.1 Hz, 1 H), of 2,6-dinitrophenoxide ion, gradually appear (Figure 2B). After 540 s the substrate signals have weakened and sharpened. The signal of the product at 7.915 ppm is still a doublet, but that at 6.215 ppm is now an overlap of a triplet with a doublet, due to partial deuteriation at positions 3 and 5 (Figure 2C). At 65% conversion into product there is 29% exchange at positions 3 and 5 of unreacted substrate, and 25% exchange of the product. There is no broadening of the signals of the product or the standard mesitoate ion (**41**).

With 1,4-dinitrobenzene (**8**) in 77% DMSO-d_6, the singlet at 8.490 ppm (Table V) disappears, due to broadening within 120 s of adding 0.05 M OD^-. Two sharp doublets (8.164 ppm, 7.5 Hz and 7.003 ppm, 7.5 Hz) of 4-nitrophenoxide ion gradually appear, but the sharp singlet of the unreacted substrate reappears on addition of DCl.

With 1,2-dinitrobenzene (**7**) in 65% DMSO-d_6, the two doublet of doublets (8.151 ppm, 3.3 Hz, 5.7 Hz and 7.955 ppm, 3.4 Hz, 5.9 Hz) collapse to two broad signals on adding 0.2 M OD^- at 25 °C. Four sharp signals, two triplets (6.305 ppm, 8.2 Hz and 7.205 ppm, 8.1 Hz) and two doublets (6.675 ppm, 8.1 Hz and 7.775 ppm, 8.0 Hz), gradually appear with formation of 2-nitrophenoxide ion. Neither 1,2- nor 1,4-dinitrobenzene exchanges with D_2O in the above conditions.

The proton NMR signals of 1,3,5-trinitrobenzene (**28**) and 3,5-dinitrobenzonitrile (**9**) are broadened in dilute OD^- only if the substrate is in excess over OD^-, so that addition is not complete (Table V). In more concentrated OD^- the NMR signals of the Meisenheimer complexes are sharp: for addition of the first OD^- to 1,3,5-trinitrobenzene there are signals at 8.346 and 6.189 ppm, and with the second OD^- signals are at 8.455 and 5.915 ppm. For the Meisenheimer complex of 3,5-dinitrobenzonitrile (**9**) sharp signals are at 8.320, 7.557, and 5.523 ppm.

Mononitrobenzenes, e.g., **6** or **11**, also do not give broadened signals. Although in 73% DMSO-d_6 (0.2 M OD^-) 4-nitrofluorobenzene (**11**) reacts slowly with OD^- at 25 °C, its signals stay sharp (doublet of doublets, 8.350 ppm, 9.3 Hz, 4.5 Hz and a triplet, 7.493 ppm, 9.5 Hz).

Table V. Proton NMR Signal Broadening[a]

	conditions			signal			
					initial	final	
substrate	DMSO-d_6, %	[OD^-], M	[S], M	δ	$\Delta\nu_{1/2}$, Hz	time, s	$\Delta\nu_{1/2}$, Hz
$(NO_2)C_6H_5$ (6)	77	0.20	0.106	8.248 d (2, 6)	3.2	3400	3.2[b]
	80	0.20	0.106			1800	36.2[c]
1,2-$(NO_2)_2C_6H_4$ (**7**)	65	0.20	0.054	8.151 dd (3, 6)	6.1	220	47.8
						590	103.3
1,3-$(NO_2)_2C_6H_4$ (**27**)	70	0.20	0.034	7.937 t (5)	2.1	200	57.7
						670	70.3
						3700	br[d]
	70	0.05	0.040	7.937 t (5)	2.1	150	48.9
	70	0.10	0.040	7.937 t (5)		250	42.0
	70	0.16	0.040	7.937 t (5)		350	43.8
	70	0.27	0.040	7.937 t (5)		450	44.2
	70	0.05	0.078	7.937 t (5)	2.1	150	74.4
						450	187.5[e]
						750	br[d,f]
	61	0.05	0.035	7.937 t (5)	2.1	150	21.3
	77	0.20	0.040	7.937 t (5)	2.1	150	br[d,g]
1,4-$(NO_2)_2C_6H_4$ (**8**)	77	0.20	0.057	8.490 s	1.4	120	br[d]
1-COMe-3-$(NO_2)C_6H_4$ (**29**)	72	0.20	0.032	8.480 dd (5)	3.5	180	br[d]
1-Me-2,6-$(NO_2)_2C_6H_3$[h] (**10**)	72	0.20	0.031	7.694 t (4)	4.2	120	25.4
1-Cl-2,6-$(NO_2)_2C_6H_3$ (**14**)	72	0.20	0.035	8.278 d (3, 5)	1.2	145	83.6[i]
						415	42.0[j]
						800	29.4[k]
						5400	4.9[l]
1,3,5-$(NO_2)_3C_6H_3$[h] (**28**)	69	0.01	0.023	9.135 s (2, 4, 6)	1.2	200	27.3
	78	0.025	0.045	9.135 s (2, 4, 6)	1.2	300	6.81[m]
						900	26.7
						1200	63.2[f]
1-CN-3,5-$(NO_2)_2C_6H_3$[h] (**9**)	50	0.05	0.012	9.053 d (2, 6)	2.2	200	28.6
						400	br[d]
1-$CONH_2$-3,5-$(NO_2)_2C_6H_3$ (**32**)	72	0.20	0.029	9.020 s (2, 4, 6)	3.5	180	br[d]
1-CO_2Et-3,5-$(NO_2)_2C_6H_3$ (**31**)	72	0.20	0.031	9.082 t (2, 6)	0.8	1200	9.7
						4000	44.7
1,3-$(NO_2)_2C_{10}H_6$ (**19**)	79	0.20	0.040	8.178 d (4)	2.8	4800	38.6
	80	0.20	0.010	8.178 d (4)	2.8	420	25.0[n]
						690	49.0[n]
						1440	br[d,n]

[a] At 25 °C unless specified. The final signal is a singlet unless specified. The position of the hydrogens in the molecules is in parentheses. [b] Doublet. [c] With 0.162 M 1,3-$(NO_2)_2C_6H_4$ (**27**). [d] Broadening causes disappearance of the signal. [e] At 35 °C. [f] At 45 °C. [g] With 0.031 M 1,4-$(NO_2)_2C_6H_4$. [h] A Meisenheimer complex forms with OD^-. [i] 9.7% substitution. [j] 22% substitution. [k] 37% substitution. [l] 65% substitution. [m] At 0 °C. [n] With 0.033 M 1,3-$(NO_2)_2C_6H_4$.

The above experiments show that broadening of NMR signals in DMSO-D_2O appears only for species with significant electron-acceptor character due to the presence of at least two nitro groups. The signals of such anionic species as Meisenheimer complexes, mesitoate, or aryl oxide ions do not broaden in our conditions.

Signal broadening increases with increasing temperature and DMSO-d_6 content, but, except as noted, it is not very sensitive to [OD^-] (**27** and **28** (Table V)).

We examined the time dependence of the broadening of the signals of 1,3-dinitrobenzene (**27**). Broadening is almost constant for ca. 800 s but then rapidly increases, probably due to secondary reactions that generate radical species (Figure 3). The broadening of the signals of 2,6-dinitrochlorobenzene (**14**) decreases as it is converted into the phenoxide ion (Figure 2), and intermediate behavior was observed with 1,2-dinitrobenzene (**7**) (Figure 3).

Provided that at least one signal is not broadened, that of mesitoate ion, broadening is not due to thermal paramagnetic relaxation. The evidence discussed above implies that there is an exchange between a species with electron-acceptor character and a paramagnetic species with electron-donor character. The only species with both paramagnetic and electron-donor character, which can be formed in a reaction of a di- or trinitroarene with OD^- in DMSO-d_6–D_2O, is the corresponding radical anion, probably in a complex with $^{\bullet}OH$. This species may rapidly exchange an electron in a complex with the substrate.[24f,g]

Species with radical character formed from di- or trinitroarenes should be able to broaden the NMR signals of other aromatic systems whose signals do not broaden by direct interaction with OD^-. Although signals of nitrobenzene (**6**) do not broaden on addition of OD^-, they broaden on subsequent addition of 1,3-dinitrobenzene (**27**). Signals of 1,3-dinitronaphthalene (**19**) in OD^- also broaden on subsequent addition of 1,3-dinitrobenzene (**27**), and those of 1,3-dinitrobenzene (**27**) broaden on subsequent addition of 1,4-dinitrobenzene (**8**) (Table V).

Table VI. Solvent Effects upon Reactions of Halonitrobenzenes[a]

	rate constant for added solvent (vol %)			
substrate	none	dioxane (4.3)	anisole (5.4)	nitrobenzene (5)
4-nitrofluorobenzene	0.086	1.21	0.68	0.044
2,4-dinitrochlorobenzene	14.0	22.7	19.0	8.67

[a] Values of 10^3k (s^{-1}) at 25 °C with 0.2 M KOH and 70% organic solvent; values in parentheses are of volume percent of added organic solvent and correspond to 0.5 M.

If there is an interaction between an inert nitroarene and the intermediates in nucleophilic substitution, addition of an electron acceptor should slow the chemical reaction by interacting with complex **5** (Scheme II) and slowing its forward reaction. Addition of nitrobenzene, as predicted, slows the reactions of OH^- with both 4-nitrofluorobenzene (**11**) and 2,4-dinitrochlorobenzene (**13**) (Figure 4 and Experimental Section). This inhibition is apparently not due to a normal solvent effect because nucleophilic attack by OH^- is generally speeded by the addition of organic solvents to water, as shown by the effects of dioxane and anisole (Table VI). These experiments were carried out with equimolar nitrobenzene, anisole, and dioxane (0.5 M). The dielectric constants of those solvents are lower than that of DMSO, and simple solvent models

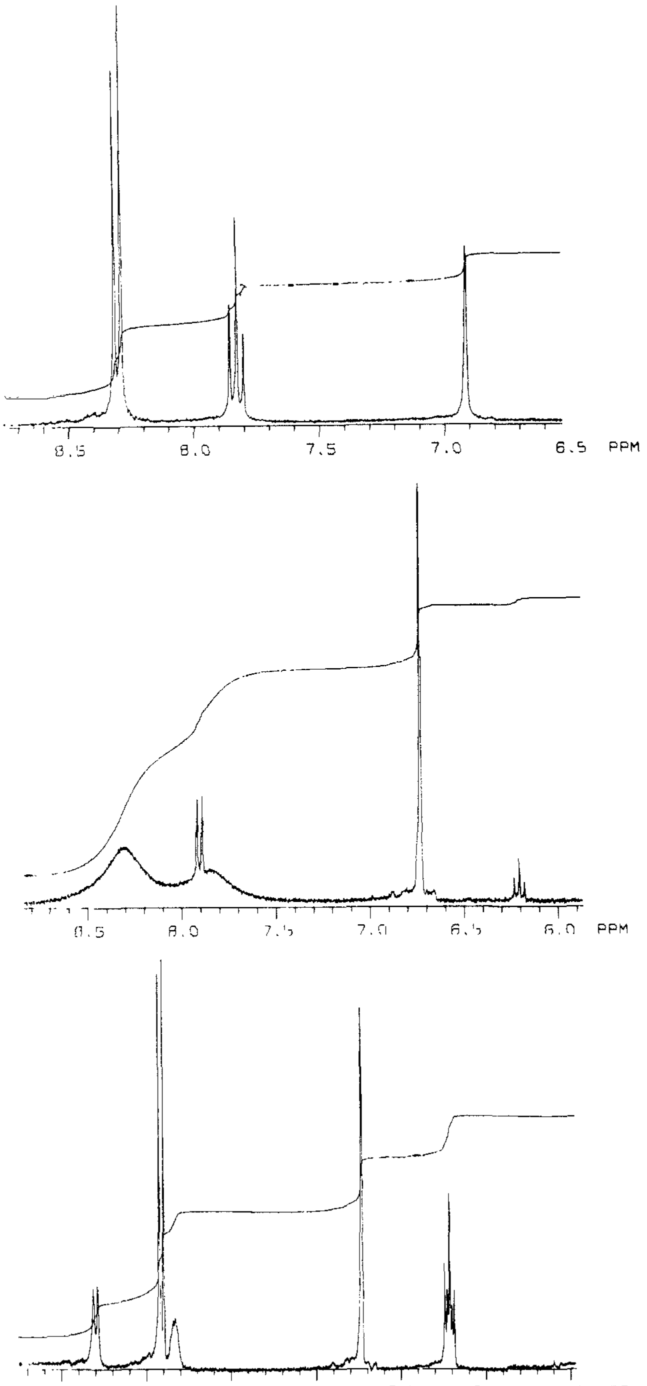


Figure 2. NMR spectra of 1-chloro-2,6-dinitrobenzene (0.06 M) and the phenolic product in 0.1 M KOD, 70% DMSO-d_6, with mesitoate ion as standard: (A (top)) before addition of OD^-; (B (middle)) and C (bottom)) 145 and 540 s after addition of OD^- at 25 °C.

predict that they should all speed the reaction.

Discussion

Our exchange and line-broadening results are consistent with the hypothesis that species with radical anion character are key intermediates in aromatic nucleophilic addition and substitution. Most of our NMR experiments were, of necessity, carried out in solutions of high DMSO-d_6 content, up to ca. 50 mol %, but some substrates were sufficiently water soluble to be examined in more aqueous media, and even in D_2O (**26** and **30** (Tables I and III)), so the general behavior is not restricted to solvents of very low water content.

The compounds studied in this work have a variety of structural elements so that species with radical anion character are possible intermediates in most, if not all, nucleophilic aromatic bimolecular reactions. Our mechanistic conclusions are consistent with earlier observations. Anion radicals have been observed by ESR spectroscopy with many nitroarenes in basic solutions.[32,33] But ESR signals were not seen with nitrobenzene (**6**) or 1,3,5-trinitrobenzene (**28**), because the former is not a good enough electron acceptor and the latter rapidly gives a Meiseheimer complex.[32] An ESR signal was observed with 2,4-dinitrochlorobenzene (**13**) in isopropyl alcohol–isopropoxide ion with crown ether.[34] Anion radicals, detected by their ESR spectra, have been postulated as intermediates in overall substitutions of nitroarenes in DMSO–alcohol mixtures or aqueous DMSO of very low water content.[7] Radi-

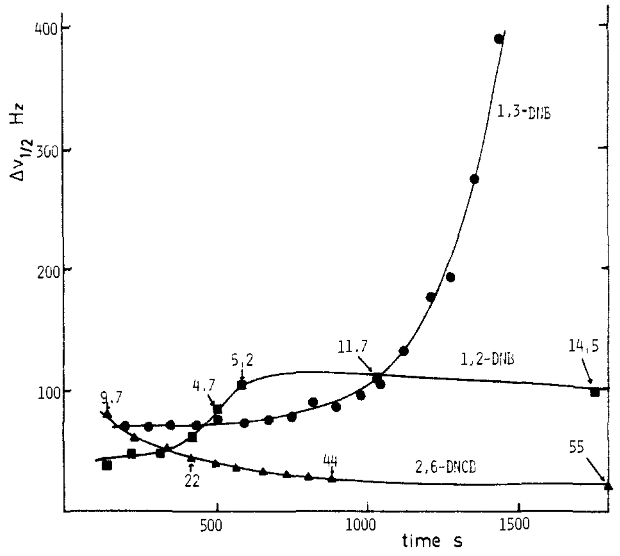


Figure 3. Time dependence of line broadening at 25 °C for 1,3-dinitrobenzene (1,3-DNB) (0.034 M, 0.2 M KOD, 70% DMSO-d_6), 1,2-dinitrobenzene (1,2-DNB) (0.054 M, 0.2 M KOD, 65% DMSO-d_6), and 1-chloro-2,6-dinitrobenzene (2,6-DNCB) (0.061 M, 0.1 M KOD, 70% DMSO-d_6). The numbers represent the extent of substitution percent in 2,6-DNCB and 1,2-DNB at the times specified.

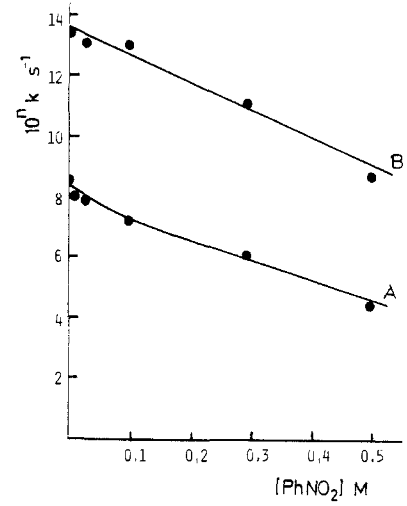


Figure 4. Influence of nitrobenzene on first-order rate constants of overall substitution with 0.2 M KOH in 30 vol % H_2O and 70% DMSO + nitrobenzene at 25 °C. (A) 4-nitrofluorobenzene, $n = 5$; (B) 2,4-dinitrochlorobenzene, $n = 3$. [substrate] = 5×10^{-5} M.

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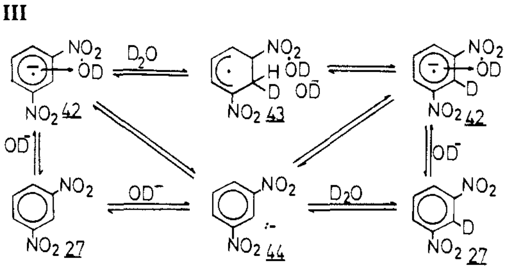
[32] (a) Russell, G. A.; Janzen, E. G. *J. Am. Chem. Soc.* **1962**, *84*, 4153. (b) Russell, G. A.; Janzen, E. G.; Storm, E. T. *Ibid.* **1964**, *86*, 1807. (c) Bellobono, I. R.; Gamba, A.; Sala, G.; Tampieri, M. *Ibid.* **1972**, *94*, 5781. (d) Buncel, E.; Menon, B. C. *Ibid.* **1980**, *102*, 3499.

[33] Fendler, E. J.; Fendler, J. H.; Arthur, N. L.; Griffin, C. E. *J. Org. Chem.* **1972**, *37*, 812.

[34] Mariano, C.; Modena, G.; Pizzo, G. P.; Scorrano, G. *J. Chem. Soc., Perkin Trans. 2* **1979**, 1187.

Scheme III



cal-derived products have been observed in reactions of nucleophiles with 1,3-dinitrobenzene (**27**) and other nitroarenes.[32,35] Although there is evidence for the presence of anion radicals under conditions that lead to overall addition or substitution, their role has not been clarified. In some cases overall reactions were much faster than radical formation, which suggested that radicals are involved only in some adventitious side reactions,[33] but in other cases radical anions were considered to be intermediates on the overall reaction path.[7]

On the basis of literature data and our NMR and kinetic evidence, we postulate that in relatively aqueous solvents charge-transfer complexes between radical anions and radicals of the nucleophiles (e.g., **5** (Scheme II)) rather than free radical anions are probable intermediates in nucleophilic aromatic addition and substitution. Their concentrations are probably low, but sufficient for observation of their UV spectra as well as their interaction with substrate, which is responsible for NMR line broadening.[4] The kinetic analysis of nucleophilic aromatic addition and substitution is consistent with this hypothesis.[5]

If substrates react slowly with nucleophiles or if they and the intermediates are in equilibrium with Meisenheimer complexes (**2**), the charge-transfer-complex intermediates **5** may, over time, dissociate, giving free radical anions. This is the probable situation in apolar, aprotic solvents. These radical anions may be identified by ESR spectroscopy[7,32,33] or be trapped by O_2[4] or by nitroxides.[36]

The charge-transfer complexes (e.g., **5** (Scheme II)) could pair with metal cations, just as has been seen with radical anions.[37] Crown ethers form complexes with cations and increase the lifetime of charge-transfer complexes (**5**), which may allow their dissociation to give radical species[34] or conversion into Meisenheimer complex.[36a]

Radical anions are more basic than the related anions,[21] and this should also be true of the charge-transfer complexes derived from them. Hydrogen exchange could occur by deuteronation of the complexes by D_2O, as shown for 1,3-dinitrobenzene (**27**) in Scheme III.

Observation of greater exchange in phenoxide product than in unreacted substrate (Table III) shows that substrate deprotonation cannot be the sole route of hydrogen exchange. This route involves the aryl anion (**44** (Scheme III); cf. ref 8–16), and we earlier suggested that it could be formed from **42**.[4] However, **44**, if formed, cannot be on the overall path for nucleophilic addition or substitution, because aryl anions are very strong bases and their rapid reaction with D_2O would make exchange much faster than overall addition or substitution. Therefore overall reaction should always be accompanied by very extensive exchange, but there is little or no exchange in the course of some reactions (Tables I–III).

Pross notes that radical anions, despite their high basicity,[38] are not always protonated very rapidly, and this could be the situation for a charge-transfer complex of a radical anion and a hydroxyl radical (**42**). It is useful to consider the position of exchange, because based on mesomeric effects of nitro groups, exchange in 1,3-dinitrobenzene (**8**), at position 2, is inconsistent with substrate deprotonation, which should occur most readily at positions 4 and 6, rather than 2. Protonation by water of anion radicals or of the related charge-transfer complexes should be at the positions of highest density of the unpaired electron, which are known from ESR coupling constants for various anion radicals. Coupling constants are high in the radical anions at positions 2, 4, and 6 of 1,3-dinitrobenzene (**27**)[32b,39] and at all positions of 1,3,5-trinitrobenzene (**28**)[40] and 3,5-dinitrobenzonitrile (**9**).[41] All of these compounds readily exchange their hydrogens (Table I). On the other hand, 1,2- (**7**) and 1,4-dinitrobenzene (**8**) form radical anions that have relatively small coupling constants,[7c,42] and they give little exchange (Table I). Radical anions of nitrobenzene (**6**)[40a] and 4-nitrofluorobenzene (**11**)[42] have fairly high coupling constants at positions 2 and 6, but we see no broadening of the NMR signals (Table V), which suggests that charge-transfer complexes of radical anions do not form, and as predicted, there is little hydrogen exchange (Table I).

Although we conclude that aryl anions are not intermediates in our reaction conditions, they are almost certainly involved in hydrogen exchange in strongly basic solutions of very low water content and in metalations.[11] However, they could form via π or charge-transfer complexes, rather than by a single-step substrate deprotonation. Anions are postulated intermediates in aryne reactions,[17] although the existence of anion radicals has been invoked to explain some reaction products.[43]

The energy barrier for electron transfer from the HOMO of nucleophiles to the LUMO of electrophiles is not necessarily very high.[5b,7c,44] Single-electron transfers have been postulated for a variety of nucleophilic and electrophilic reactions that had been written as two-electron transfers.[45–48]

The generation of anion radicals by dissociations of the complex, **5**, should be disfavored by solvents of high water content because the ordered water structure should help to keep the partners together and assist rearrangements to a Meisenheimer complex, e.g., **2**, with its high degree of charge delocalization.

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Single-Electron Transfer in Aromatic Nucleophilic Addition and Substitution in Aqueous Media

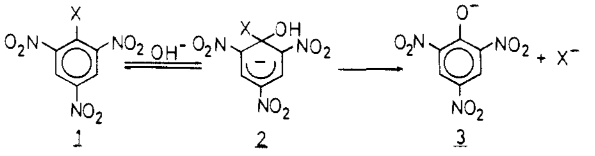
Radu Bacaloglu,* Clifford A. Bunton,* and Francisco Ortega

Contribution from the Department of Chemistry, University of California, Santa Barbara, California 93106. *Received June 5, 1987. Revised Manuscript Received December 22, 1987*

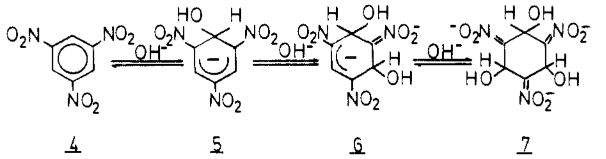
Abstract: Reactions of 1,3,5-trinitrobenzene, 2,4,6-trinitrochlorobenzene, and 2,4,6-trinitrobenzenesulfonate ion with OH^- in water and water-DMSO do not occur by a rate-limiting, single-step, addition of OH^- but involve very rapid formation of a π-complex of substrate and OH^-, which forms a charge-transfer complex of arene anion and hydroxyl radicals by single-electron transfer. In polar solvents the charge-transfer complexes rearrange to σ 1- or 3-complexes. The 1-complexes eliminate the leaving group to form the substitution product in a slow or fast step, and the 3-complexes can form long-lived dianionic σ-complexes or return to charge-transfer complexes. Rate and/or equilibrium constants of the individual steps can be calculated by computer simulation based on relaxation theory. Calculated overall equilibrium constants of addition or second-order rate constants of overall substitution in dilute OH^- agree with experimental values.

Aromatic nucleophilic substitutions and additions are strongly assisted by electron-withdrawing groups such as NO_2. The generally accepted aromatic nucleophilic substitution mechanism (S_NAr) involves rate-limiting formation of a σ or Meisenheimer complex, as in Scheme I.[1]

Scheme I



Scheme II



This mechanism is consistent with much experimental evidence. For example, Meisenheimer complexes (**2**) have been characterized,[2] and the frequently observed reactivity order for X of $F \gg Cl \simeq Br \simeq I$ has been ascribed to rate-limiting formation of **2**.[3] The reactivity sequence Br > Cl > F, which is occasionally observed, is explained in terms of a slow second step.[4] In some systems similar reactivities have been observed with X = SOPh, Br, Cl, I, SO_2Ph, and OPh as leaving groups, which is consistent with rate-limiting addition, but the very high reactivities observed with X = F, NO_2, and $ArSO_3$ are hard to explain solely in terms of an inductive effect of X.[3]

Substituent effects on overall substitution often follow the Hammett equation with σ^- parameters and high values of ρ,[1b] but there are exceptions.[5] Rates of nucleophilic aromatic substitution in aqueous or alcoholic solvents generally follow the N_+ scale, which is consistent with rate-limiting addition, and reactivity-selectivity relations do not apply.[6] General-base catalysis is often observed in aminolysis when X is a relatively poor leaving group, and its departure can be rate limiting.[1,7,8] However, in some reactions the order with respect to the nucleophile (or base) is larger than the predicted value of 2.[9,10]

Substrate-nucleophile π-complexes[9b,11,12] and anion radicals[13] appear to be intermediates in some aromatic substitutions, especially in aprotic solvents. Chain reaction involving radical anions has also been postulated.[13g] In some other cases anion radicals have been identified by ESR spectroscopy, but because of their slow formation, they were not considered to be reaction intermediates in polar hydroxylic solvents.[14] There is strong evidence

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