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Article

The Reaction of 1,2-Dichloro-4,5-dinitrobenzene with Hydroxide Ion: Roles of Meisenheimer Complexes and Radical Pairs

Andrei Blaskó,[a] Clifford A. Bunton,[a] Nichollas D. Gillitt,[a] Radu Bacaloglu,[a] Santiago F. Yunes*,[b] and César Zucco*,[b]

[a]*Department of Chemistry and Biochemistry, University of California, Santa Barbara, 93106 California, USA*

[b]*Departamento de Química, Universidade Federal de Santa Catarina, 88090-400 Florianópolis-SC, Brazil*

A reação de 1,2-dicloro-4,5-dinitrobenzeno (DCDNB) com OH^- aquoso produz (após acidificação) 2-nitro-4,5-diclorofenol com perda de NO_2. No entanto, com $OH^- > 2$ mol L^{-1}, DCDNB foi recuperado devido à formação do complexo estável 3,6-di-hidroxi Meisenheimer (M^{2-}), e que em ácido, reverteu ao reagente inicial. A formação rápida do complexo mono-hidroxi Meisenheimer (M^{1-}) pode ser acompanhada em DMSO:H_2O 7:3 v/v e as constantes para sua interconversão com DCDNB e formação e retorno com M^{2-} foram estimadas, com evidência destas reações em DMSO:H_2O 1:1 v/v e H_2O. A troca rápida de hidrogênio em OD^-/D_2O limita o uso da técnica de ressonância magnética nuclear (NMR) de ^1H na identificação de intermediários. Sinais de RMN de ^1H e ^{13}C para o di-hidroxi Meisenheimer foram observados em DMSO-H_2O-KOH. Existe evidência da formação de radicais livres em DMSO:H_2O 4:1 v/v, e a cinética global em meio mais aquoso foi tratada considerando a existência transitória de pares de radicais aniônicos.

The reaction of 1,2-dichloro-4,5-dinitrobenzene (DCDNB) with aqueous OH^- produces (after acidification) 2-nitro-4,5-dichlorophenol with loss of NO_2. Nevertheless, with > 2 mol L^{-1} OH^-, only DCDNB was recovered due to the formation of the long-lived 3,6-dihydroxy Meisenheimer complex (M^{2-}), and that in acid, reverted to the starting material. Fast formation of monohydroxy Meisenheimer complex (M^{1-}) can be followed in DMSO:H_2O 7:3 v/v and rate constants for its interconversion with DCDNB and for formation and return with M^{2-} complex were estimated, with evidence for these reactions in DMSO:H_2O 1:1 v/v and H_2O. The rapid hydrogen exchange in OD^-/D_2O limits the use of ^1H nuclear magnetic resonance (NMR) spectroscopy in identifying intermediates. ^1H and ^{13}C NMR signals of M^{2-} complex were observed in DMSO-H_2O-KOH. There is evidence for the formation of free radicals in DMSO:H_2O 4:1 v/v, and overall kinetics in more aqueous medium were treated in terms of the transient existence of anionic radical pairs.

Keyword: aromatic nucleophilic substitution, Meisenheimer complexes

Introduction

Aromatic nucleophilic substitutions involve a variety of reaction paths, depending upon the reactant structure and the reaction medium.[1-5] In polar, hydroxylic, solvents reactions of hydroxide or alkoxide ions with halonitroarenes can be described in terms of formation of short lived *ipso*-Meisenheimer complexes, although unproductive Meisenheimer complexes can form and return to starting material,[1-8] and radicaloid species may be on the reaction path.[9,10] The formation of transient π-complexes has been postulated,[7,8,11] and demonstrated.[12] Arynes are intermediates in reactions with strong bases in apolar solvents,[13] the S_{RN1} (radical-nucleophilic aromatic substitution) reaction with, for example, potassium in liquid ammonia is a radical-chain process,[14] and there is evidence of radical reactions under other conditions.[9,15] Dediazonization is often described in terms of rate-limiting loss of N_2, and rapid trapping of a putative aryl cation,[16] although there is evidence of pre-association with a nucleophile.[17] These reactions are synthetically important, and the large scale decomposition

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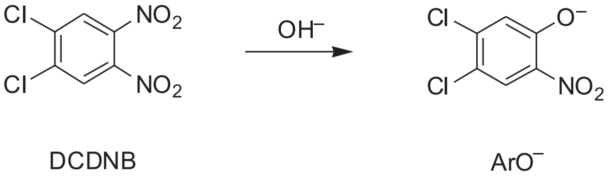
*e-mail: c.zucco@ufsc.br, santiago.yunes@ufsc.br of polynitroarenes in hot aqueous alkali is used in destruction of energetic materials.[18]

The reaction of OH^- and other nucleophiles with 1,2-dichloro-4,5-dinitrobenzene (DCDNB) shows some unusual features.[19,20] It involves the displacement of a nitro group, by either OH^-[19] (Scheme 1) or aliphatic amines,[20] although these reactions generally occur with loss of Cl^- assisted by electron withdrawal by a nitro group.

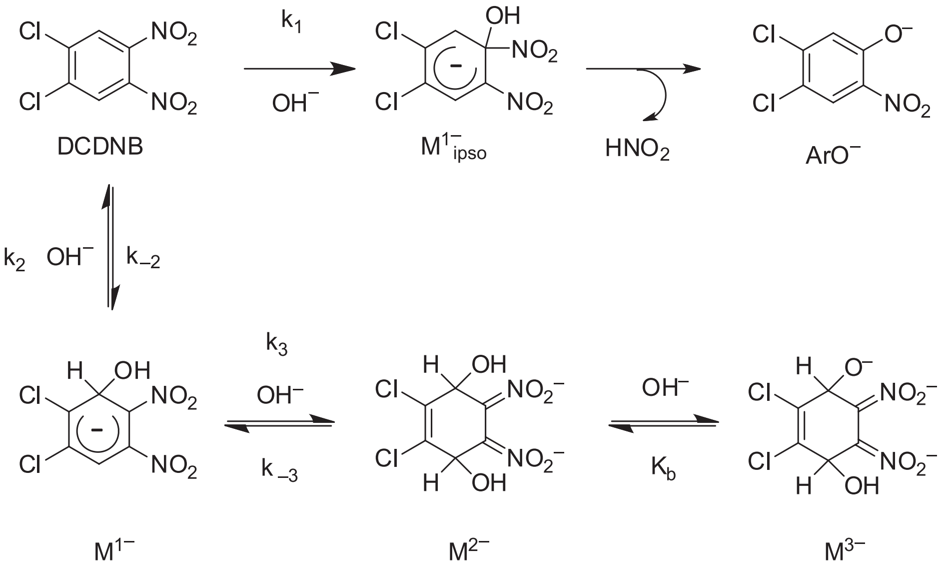


Scheme 1.

The scale and conditions of the original preparation were unspecified,[19] but when our group attempted on making the reaction under heterogeneous conditions in aqueous 2.5 mol L^{-1} NaOH and acidified the reaction mixture, only the starting material was obtained, and an experiment in homogeneous conditions in DMSO (dimethyl sulfoxide)-H_2O provided a similar result. A small-scale preparation in very dilute aqueous OH^-, and under reflux, gave the phenolic product described in the literature.[19]

In this qualitative exploratory work, the UV-Vis spectra typical of a nitro phenol in the reaction of DCDNB in dilute aqueous KOH and DMSO:H_2O were observed. The solubility of DCDNB is very low in water, and ^1H and ^{13}C nuclear magnetic resonance (NMR) spectra were examined in DMSO:H_2O because there is an isotopic exchange in DMSO:D_2O, and the technique in DMSO:H_2O was used to identify compounds formed in the course of reaction as described later, but under conditions very different from those subsequently used in the kinetic work. The simplest explanation for our failure in obtaining aryloxide ion (ArO^-) in reaction with moderately concentrated OH^- is that a relatively long-lived 3,6-dihydroxy Meisenheimer complex (M^{2-}) can form and return to DCDNB on acidification or over a long period of time. In dilute OH^-, an *ipso*-Meisenheimer complex (M^{1-}_{ipso}) could be reversibly, or irreversibly, formed in competition with a postulated unproductive monoanionic complex (M^{1-}), so that ArO^- should be the thermodynamically controlled product (Scheme 2).

The deprotonated dihydroxy Meisenheimer complex (M^{3-}) in this hypothetical scheme was included because there is evidence for deprotonation of unproductive Meisenheimer complexes.[1,4,6-8] These qualitative observations indicate that the unproductive Meisenheimer complexes have higher negative charges than the postulated *ipso* complex on the reaction path, irreversibly leading to the nitrodichlorophenoxide. This classical heterolytic reaction path (Scheme 2) does not explain the H/D exchange observed in the preliminary observations, and this weakness of the conventional mechanistic treatment is discussed later. The conversion of DCDNB into final products involves various reactions, some competing, other consecutive, and it is convenient to consider them as relaxations, which are well separated in time, and may involve several reactions, but can be simply analyzed, provided that the individual reactions follow first-order kinetics.[21] Relaxations did not need to be spectrophotometrically followed at wavelengths corresponding to λ_{max} of the reaction species, provided that Beer's law is obeyed, although it is best to select wavelengths giving significant changes in the absorbance. The rate measurements were made by UV-Vis spectroscopy with very



Scheme 2.

dilute DCDNB, but the products were isolated, or identified by NMR spectroscopy, at much higher concentrations. Some NMR measurements were made in the course of reaction, with short accumulation times and high substrate concentrations. The necessity of using reaction conditions for product identification very different from those used in the kinetic work is a major problem, but in considering the various reaction steps, which fit first-order kinetics, it was assumed that kinetic forms are independent of [DCDNB].

Experimental

Materials and preparation

1,2-Dichloro-4,5-dinitrobenzene (Aldrich) was converted into 2-nitro-4,5-dichlorophenol (ArOH) by heating 1.2 mg DCDNB with 100 mL of aqueous 0.1 mol L^{-1} NaOH, (two-fold excess), under reflux for 5 h, followed by acidification and separation of the crude phenol.[19] Details of the earlier preparation of the phenolic product are not given in reference 19. Recrystallization (aq. EtOH) produced yellow crystals, mp 66.5 °C (68 °C)[19,20] in 85% yield. ^1H NMR (DMSO-d_6) δ/ppm: 7.18, d, *J* 1.5 Hz; 7.93, d, *J* 1.5 Hz; ^{13}C NMR (DMSO-d_6) δ/ppm: 121.4, 122.51, 127.3, 136.0, 139.2, 152.3. For the phenoxide ion, ArO^-, NMR signals (DMSO-d_6) were, δ/ppm: 1H, 6.71, 7.80; ^{13}C, 113.0, 127.9, 128.2, 137.1, 139.1, 166.4, in D_2O and referred to sodium 3-(trimethylsilyl)tetrapropionate (TSP). The reaction in aqueous alkali was in heterogeneous conditions, but various preparative experiments in homogeneous conditions in KOH-H_2O-DMSO did not give the phenolic product and DCDNB was recovered after acidification, as for a reaction in aqueous 2.5 mol L^{-1} NaOH at room temperature. The ^1H NMR signal of DCDNB in DMSO-H_2O 7:3 v/v is a singlet at 8.39 ppm. DMSO was distilled in vacuum through a helix-packed column and stored under N_2. Solutions were made up with redistilled, deionized, CO_2-free water.

Instrumentation

Absorption spectra were obtained on HP 8450, 8451 or 8452A diode array and on Beckman DU-7 UV-Vis spectrophotometers at 25.0 ± 0.1 °C, and for the short-lived Meisenheimer complex (M^{1-}) on a Durrum stopped-flow spectrophotometer at 25.0 ± 0.1 °C. The NMR spectra were obtained on a Bruker 200F, or GN500 or Varian Unity (500 MHz for ^1H) instrument, at 25.0 ± 0.1 °C, generally with TSP as internal reference, although occasionally mesitoate ion was added as a chemically inert aromatic reference compound.[7,8] The NMR spectra were generally monitored with 0.05 or 0.1 mol L^{-1} substrate to avoid long accumulation times in the course of reaction, and therefore $[OH^-]$ decreased during the reaction.

Kinetics

The slower relaxations were followed on diode-array spectrophotometers at 25.0 ± 0.1 °C, and the rapid formation of a monohydroxy Meisenheimer complex was followed on the stopped-flow spectrophotometer. For the slower relaxations, DCDNB in 10^{-3} mL DMSO was added to 2 mL of the reaction solution to give 5×10^{-5} mol L^{-1} DCDNB in the reaction mixture. The reciprocal relaxation times (τ^{-1}) fitted the first-order equations for 3-5 half-lives.

In following the slowest-relaxation, the postulated return of M^{2-} and M^{3-} (Scheme 2), these complexes were prepared by the reaction of KOH with DCDNB in solution under conditions such that DCDNB had fully reacted without forming ArO^- and it was added the appropriate amount of this solution to the reaction mixture to give the desired $[OH^-]$, [DCDNB] and solvent composition. Under these conditions, OH^- was in considerable excess over the substrate, giving first-order kinetics in the relaxations.

Structural optimization

The structures were optimized with the HF/6-31G(d) or BP/6-31G(d) methods for neutral molecules and the HF/6-31+G(d) method for anions, with Spartan 04 software (Wavefunction, Inc.). The optimization considers species in vacuum, i.e., not solvated in the kinetic conditions.

Results

Formation of the alkoxide ion

The preparative reactions of DCDNB with dilute OH^- in water produced ArO^- in good yield (Experimental section and reference 19), but with higher $[OH^-]$, the absorbance of ArO^- was not observed. The reactions in water were heterogeneous, but the results were similar to 2.5 mol L^{-1} KOH in water and to DCDNB in solution in DMSO-H_2O. Under these conditions of high $[OH^-]$, regardless of the solvent composition, there was no indicative of formation of a phenoxide ion and only the substrate was recovered on acidification. The course of the reaction is not controlled by substrate solubility, but it involves the formation of compounds that do not give ArOH under acidification but revert to starting material, and ArO^- is formed only in dilute OH^- with the reaction mixture left for many hours at 25.0 ± 0.1 °C.

The phenolic product (ArO^-) was isolated from the reaction with dilute OH^- (Schemes 1 and 2 and reference 19), but for some reactions in DMSO-d_6-H_2O, minor ^1H NMR signals of what was probably a second aryloxide ion (designated $Ar'O^-$) were observed, as discussed later. This product could have been formed by the displacement of Cl^- by OH^- in the initial reaction of DCDNB, but alternative reactions can be considered. The concentration of DCDNB in H_2O is too low for the use of NMR spectroscopy in the course of reaction. The minor phenolic product in Schemes 1 and 2 were not shown.

Reactivities and characterization of intermediates

The absorption and NMR spectroscopies were used to identify compounds formed by the reaction of DCDNB with OH^-. Aqueous 10^{-4} mol L^{-1} DCDNB has λ_{max} at 275 nm, and in 3 mol L^{-1} OH^-, this signal disappeared and a broad signal (λ_{max} ca. 320 nm) appeared, plus, but only in very dilute OH^-, a very weak signal of ArO^- at > 400 nm. The signal at 320 nm disappeared on acidification and that of DCDNB reappeared, with little formation of phenolic product, in agreement with results in preparative experiments. However, in dilute OH^- (< 0.1 mol L^{-1}), it was observed, after some time, the signal of ArO^- and a weak signal at 320 nm.

Monohydroxy Meisenheimer complexes derived from polynitroarenes and OH^- absorb strongly at $\lambda > 500$ nm, and this absorption was observed when the absorbance in DMSO-H_2O 7:3 v/v was rapidly examined in a stopped-flow spectrophotometer, but the color soon disappeared and there was no formation of ArO^-. There was no indicative of formation of this complex in more aqueous media, but it is probably on the reaction path to longer lived Meisenheimer complexes, and mono- and dihydroxy complexes have been identified in other systems.[22] It was expected a M^{2-} complex, which is not aromatic, to be transparent in the visible region due to loss of conjugation of the nitro groups with the double bond.

The absorption spectra were repetitively scanned in alkaline H_2O, and DMSO:H_2O 1:1 v/v, and 7:3 v/v. On the basis of these spectra, and evidence for formation of a dihydroxy Meisenheimer complex, the absorbance over time at various wavelengths was followed, and the reciprocal relaxation times (τ^{-1}) were estimated for the processes following first-order kinetics. It was designated τ_1^{-1}, τ_2^{-1} and τ_3^{-1} from the shortest to the largest, and τ_1^{-1} was monitored only by stopped-flow spectroscopy in DMSO:H_2O 7:3 v/v. All reactions were at 25.0 ± 0.1 °C. The relaxations were followed at 275 nm, in which DCDNB absorbs, at 320 nm, in which M^{2-} absorbs, at 420 nm, in which ArO^- absorbs, and at 520-530 nm, in which M^{1-} absorbs.

The low solubility of DCDNB in water meant that it could not be examined by the NMR in H_2O. However, the incomplete reactions of DCDNB with KOD in DMSO-d_6-D_2O produced no ^1H signals of DCDNB or other compounds, showing that the isotopic hydrogen exchange is rapid under alkaline condition but there was no indicative of hydrogen exchange with ArO^-. The ^{13}C NMR spectra of the Meisenheimer complexes and phenolic products were observed in DMSO-d_6-D_2O and KOD, or the corresponding acidic media, with, or without, proton decoupling. Moreover, ^1H NMR signals of DCDNB, aryloxide ions and of what is probably a Meisenheimer complex in DMSO-d_6-H_2O and KOH, generally with suppression of the ^1H_2O signal, were observed. These observations are discussed in the context of the kinetic data, but were in experiments with [DCDNB] much higher than in the kinetic work (ca. 5×10^{-5} mol L^{-1}), which complicates the comparison of kinetic and NMR data. The ^1H NMR signals were also observed, probably of a second nitrophenoxide derivative, as discussed later.

Reactions in DMSO:H_2O 7:3 v/v

In this solvent, there is a rapid increase in absorbance at 520-530 nm ascribed to reversible formation of the short-lived monohydroxy Meisenheimer complex (Scheme 2), and no indicative of formation of a phenoxide ion. The variation of τ_1^{-1} with $[OH^-]$ fits equation 1 (Table 1), but the small value of the intercept at zero $[OH^-]$ leads to uncertainty in the values of k_{-2} and the related equilibrium constant given by the ratio of k_2 and k_{-2} for concentrations as in the course of reaction:

$$\tau_1^{-1} = k_2[OH^-] + k_{-2} \qquad (1)$$

The subsequent, much slower, relaxations were followed at various wavelengths in a conventional spectrophotometer and showed increase in the absorbance at 320 and 420 or 480 nm, and decreasing absorbance at 275 and 520 nm and the values of τ_2^{-1} are in Table 2. There was no indicative of build-up of an *ipso*-Meisenheimer complex (Scheme 2) and it was assumed that it would rapidly generate ArO^-, which is not evident to any significant extent in some of these conditions (Scheme 2). The second minor phenolic product is not shown in this scheme, and if it is formed directly from DCDBN, the rate constant would include a minor contribution from this reaction. The literature describes that similar nucleophilic aromatic substitutions may be stepwise or concerted.[23] The NMR evidence on phenolic products and Meisenheimer complexes was obtained with higher

Table 1. Initial formation of monohydroxy Meisenheimer complex[a]

$[OH^-]$ / (mol L^{-1})	0.013	0.032	0.047	0.064	0.10	0.15	0.20
τ_1^{-1} / s^{-1}, observed	0.15	0.35	0.52	0.66	1.00	1.40	1.70
τ_1^{-1} / s^{-1}, calculated	0.22	0.37	0.50	0.64	0.94	1.35	1.77

[a] In DMSO:H_2O 7:3 v/v at 25.0 ± 0.1 °C, calculated values are from data in Table 5.

Table 2. Formation of aryloxide ion and dihydroxy Meisenheimer complex

DMSO:H_2O 7:3 v/v										
$[OH^-]$ / (mol L^{-1})	0.025	0.048	0.093	0.190	0.270	0.320	0.370	0.400		
$\tau_2^{-1} \times 10^3$ / s^{-1}, observed	3.9[a]	8.0[c]	20.6[d]	41.9[c]	70.1[c]	92.7[d]	115[d]	137[c]		
$\tau_2^{-1} \times 10^3$ / s^{-1}, calculated[e]	4.1	8.3	17.9	44.6	72.8	93.3	116	131		
DMSO:H_2O 1:1 v/v										
$[OH^-]$ / (mol L^{-1})	0.013	0.032	0.047	0.064	0.100	0.150				
$\tau_2^{-1} \times 10^3$ / s^{-1}, observed	0.15[a]	0.35[a]	0.52[c]	0.66[c]	1.15[d]	1.95[d]				
$\tau_2^{-1} \times 10^3$ / s^{-1}, calculated[e]	0.12	0.31	0.48	0.68	1.18	2.00				
H_2O										
$[OH^-]$ / (mol L^{-1})	0.14	0.22	0.30	0.38	0.50	0.60	0.72	0.92	0.99	1.00
$\tau_2^{-1} \times 10^3$ / s^{-1}, observed	0.11[c]	0.25[c]	0.36[c]	0.51[c]	0.77[c]	1.12[c]	1.50[b]	2.41[b]	2.67[b]	2.71[b]
$\tau_2^{-1} \times 10^3$ / s^{-1}, calculated[e]	0.13	0.23	0.37	0.52	0.81	1.09	1.47	2.25	2.55	2.60

[a] At 275 nm; [b] at 320 nm; [c] at 420 nm; [d] at 520 nm; [e] calculated from data in Table 5.

substrate concentrations than the one used in the kinetic work which fitted the first-order kinetics.

The slowest relaxation, followed by the decreasing absorbance at 320 nm, or increasing absorbance at 480 nm (or 420 nm), involves the return of a dihydroxy Meisenheimer complex (and M^{3-}), which had been formed in high $[OH^-]$ and is long-lived under these conditions (Scheme 2). Its decomposition was induced by dilution to give the desired solvent composition (Table 3). This relaxation (τ_3) is much slower than the others, even in dilute KOH, and they are well separated. A few experiments were monitored at both 320 and 480 nm, and values of τ_3^{-1} were in good agreement, but the higher absorbance change at 320 nm made this wavelength the most convenient, and there is a slight tail in the absorbance spectrum of the Meisenheimer complex which interferes with the signal of ArO^- at 420 nm.

Reactions in DMSO:H_2O 1:1 v/v and in water

The examination of the UV-Vis spectra in the stopped-flow spectrophotometer gave no evidence of the absorbance at > 500 nm, and M^{1-} or an *ipso*-Meisenheimer

Table 3. Return of M^{2-} and M^{3-}

DMSO:H_2O 7:3 v/v											
$[OH^-] \times 10^3$ / (mol L^{-1})	0.5	2.0	4.7	8.6	35.0	76.0	95.0	143	270		
$\tau_3^{-1} \times 10^5$ / s^{-1}, observed	22.8	19.1	14.6	13.7	5.26	2.57	1.90	1.27	0.51		
$\tau_3^{-1} \times 10^5$ / s^{-1}, calculated	23.2	20.3	16.8	13.4	5.22	2.49	1.97	1.21	0.53		
DMSO:H_2O 1:1 v/v											
$[OH^-] \times 10^3$ / (mol L^{-1})	3.39	4.23	5.08	7.62	8.47	10.2	13.6	15.2	16.9	19.1	20.1
$\tau_3^{-1} \times 10^5$ / s^{-1}, observed	8.83	8.66	8.45	8.24	8.04	7.86	7.60	7.38	7.06	6.89	6.75
$\tau_3^{-1} \times 10^5$ / s^{-1}, calculated	8.84	8.69	8.50	8.14	8.04	7.84	7.43	7.26	7.08	6.87	6.78
H_2O											
$[OH^-] \times 10^4$ / (mol L^{-1})	0.169	0.170	0.394	0.402	1.31	1.47	3.20				
$\tau_3^{-1} \times 10^5$ / s^{-1}, observed	18.4	17.3	15.9	14.4	9.23	9.16	5.50				

[a] At 25.0 ± 0.1 °C, calculated values are from data in Table 5.

complex was not detected. The values of τ_2^{-1} for disappearance of DCDNB (and M^{1-}) and appearance of ArO^- and M^{2-}, depending on the conditions, were obtained at various wavelengths in a conventional spectrometer, for reactions in DMSO:H_2O 7:3 v/v (Table 2). Data for the slowest relaxation, τ_3^{-1}, followed at 320 nm, are in Table 3. This relaxation is inhibited by OH^- and is so slow in water that it was possible only to use very dilute OH^- which was not in significant excess over DCDNB.

The fastest relaxation (τ_1) in more aqueous solvents was not observed, and it was assumed that, in our experimental conditions, M^{1-} is then present in very low concentration and that its formation and return to DCDNB are considerably faster than the other relaxations.

Competitive formation of ArO^- and M^{2-}

The initial reaction of DCDNB with very dilute OH^- generates the thermodynamically stable aryloxide ion (ArO^-) probably via a transient *ipso* complex, and the "dead-end" dihydroxy Meisenheimer complexes (M^{2-} and M^{3-}) via the monohydroxy Meisenheimer complex (Scheme 2). These reactions compete, and the subsequent decomposition of the dihydroxy complex is so slow that the relative concentrations were spectrophotometrically estimated from the absorbance of ArO^- at 480 nm, under conditions such that [DCDNB] $\rightarrow 0$, $[M^{1-}] = 0$, and M^{2-} and M^{3-} are in equilibrium, and are transparent at 480 nm. The comparison was generally based on the concentration of ArO^- estimated by using solutions of known $[ArO^-]$. Values of $([M^{2-}] + [M^{3-}])/[ArO^-]$ as a function of $[OH^-]$ are in Table 4. The residual absorption of the double Meisenheimer complex near λ_{max} of the aryloxide ion at 420 nm was a complication when the Meisenheimer complex was dominant and it was expedient to use the higher wavelength.

NMR Spectroscopy

The loss of the ^1H NMR signals of DCDNB on addition to DMSO-D_2O and KOD is typical of reactions of polynitroarenes in which the hydrogen exchange is rapid.[1,7,8,24,25] It was not possible to use ^1H or ^{13}C NMR spectroscopy in H_2O because of the low solubility of DCDNB, and it was used short accumulation times because the composition changes with time. Therefore, the NMR spectra were examined only in DMSO-H_2O, generally 1:1 v/v, and usually with water signal suppression. The ^{13}C NMR spectrum of the dihydroxy Meisenheimer complexes (M^{2-} and M^{3-}) confirms the presence of only two equivalent hydrogens in the complex over a range of conditions. In one experiment after 40 min with 0.05 mol L^{-1} DCDNB and 2.0 mol L^{-1} KOH in DMSO-d_6:H_2O 1:1 v/v, with and without proton decoupling, the dihydroxy Meisenheimer complex was the dominant species and the splitting of the signal at 71.6 ppm (with proton coupling) and the observation of only three ^{13}C signals demonstrate the formation of a dihydroxy Meisenheimer complex and assignments are: C-1, C-2, 119.5, s; C-3, C-6, 71.6, J_{CH} 149 Hz; C-4, C-5, s, 133.5 ppm. With proton decoupling, the signal at 71.6 ppm was a singlet. These spectra were taken within 40 min of mixing, but did not change overnight. In this experiment, the ^{13}C NMR signals of ArO^- were not observed because almost no aryloxide ion is formed in high $[OH^-]$, however, with lower $[OH^-]$, signals of the aryloxide ions and dihydroxy Meisenheimer complex were observed. These observations show that the OH groups of the dihydroxy complex on C-3 and C-6 are

Table 4. Competitive formation of Meisenheimer complex and aryloxide ion[a]

DMSO:H_2O 7:3 v/v								
$[OH^-]$ / (mol L^{-1})	0.06	0.08	0.14	0.19	0.24	0.29		
$[M_T]/[ArO^-]$, observed	0.17	0.23	0.41	0.55	0.66	0.83		
$[M_T]/[ArO^-]$, calculated	0.17	0.23	0.40	0.54	0.69	0.83		
DMSO:H_2O 1:1 v/v								
$[OH^-]$ / (mol L^{-1})	0.21	0.43	0.60	0.75	1.00	1.10	1.20	1.40
$[M_T]/[ArO^-]$, observed	0.76	1.59	2.08	2.65	3.50	3.80	4.18	4.82
$[M_T]/[ArO^-]$, calculated	0.74	1.52	2.12	2.65	3.53	3.88	4.23	4.94
H_2O								
$[OH^-]$ / (mol L^{-1})	0.22	0.43	0.72	0.92	1.16	1.40		
$[M_T]/[ArO^-]$, observed	0.68	1.30	2.19	2.71	3.41	4.50		
$[M_T]/[ArO^-]$, calculated	0.69	1.34	2.25	2.87	3.62	4.37		

[a]At 25.0 ± 0.1 °C, calculated values are based on data in Table 2; M_T denotes $M^{2-} + M^{3-}$.

in identical positions, or that there is a rapid exchange between positions, which is improbable in view of kinetic data considered later.

In several experiments with relatively high [DCDNB], weak ^1H signals of ArO^- and weaker signals of a second product, δ ca. 6.7 and 8.1 ppm, were observed. The chemical shifts varied slightly depending upon concentrations and changes in the solvent composition. These signals, like those of ArO^-, were singlets and with chemical shifts typical of dinitrobenzene derivatives and the chemical shifts, and ratios of major and minor products varied slightly, probably depending on the conditions of the measurements. Our group considers possible sources of this second signal later. The addition of $NaNO_2$ at concentration similar to [DCDNB] did not affect the NMR signals.

All these NMR measurements were made with high reactant concentrations, relative to those used in the kinetic work. Usually with 0.1 mol L^{-1} DCDNB and 5-10 fold excess KOH in DMSO-d_6:H_2O, a sharp singlet at ca. 5.2 ppm was observed slightly depending on the conditions. This signal was on the side of the very broad signal of H_2O. With careful suppression of the ^1H_2O signal, a base line resolution between the signals was obtained. The signal at 5.2 ppm at ambient temperature with 0.1 mol L^{-1} DCDNB and 0.5 mol L^{-1} KOH in DMSO:H_2O 1:1 v/v disappeared after 3 days, but was still present in 1.0 mol L^{-1} KOH. This signal is upfield of nitroarene signals and it was assumed that it is from the dihydroxy Meisenheimer complex (M^{2-}) and, as it disappeared, signals in the nitrophenoxide region increased. It was observed a cross peak of this ^1H signal and the ^{13}C signal of the Meisenheimer complex at 71.6 ppm, consistent with this assignment.

^1H NMR Spectroscopy in DMSO:H_2O 4:1 v/v

Some ^1H NMR measurements were made in DMSO:H_2O 4:1 v/v with 0.1 mol L^{-1} DCDNB and 0.15 mol L^{-1} KOH, i.e., insufficient for complete reaction, and with suppression of the ^1H_2O signal, in the spectral region where the signals of DCDNB and the phenoxide ions were observed. The signal of DCDNB at 8.39 ppm disappeared on addition of KOH and new sharp aryloxide ion signals at 6.57 and 7.67 ppm (major signals) and 6.30 and 7.88 ppm (minor signals) appeared within 2 min of mixing, but with the decreasing [OH^-], a very strong broad signal of DCDNB reappeared within 6 min, sharpened after 10 min and became sharp after 15 min. Signals of the aryloxide ions and of mesitoate ion at 6.50 ppm, added as an inert marker, are sharp. Excess KOH (up to 0.22 mol L^{-1}) was then added and more aryloxide ion signals appeared, but there were no signals of DCDNB. The signals of the aryloxide ions, and the mesitoate ions at 6.50 ppm, were singlets, and long-range coupling was not observed, as with phenol (Experimental section).

These observations were confirmed in a subsequent experiment in the same conditions with 0.1 mol L^{-1} DCDNB and 0.15 mol L^{-1} KOH and no substrate signal was observed after 2 min, but it reappeared as a broad singlet at 8.39 ppm after 4 min. The sharp phenoxide signals were at 6.28, 6.55, 7.67 and 7.86. The pH was reduced to < 4 after further 30 min by addition of HCl and signals of phenols were then observed at 7.17, 7.27, 7.93 and 8.10 ppm. In all these experiments, the signals at 6.28 and 7.86 ppm, or at 7.17 and 8.10 ppm after acidification, were those of the minor aryloxide product.

The loss and return of the ^1H NMR signals of DCDNB could be ascribed to the rapid formation and subsequent decomposition of a dihydroxy Meisenheimer complex, but the forward reaction should be too slow to fit the results in the dilute KOH used here, and the transient existence of free radicals explains the reversible loss of the NMR signal. It seems that the formation of a radicaloid species of DCDNB markedly broadens its signals, but not those of phenoxide or mesitoate ions. Similar results had been obtained with other polynitroarenes in aqueous DMSO,[7,8] but not in more aqueous media. Because of the complexity of the system, kinetics in DMSO:H_2O 4:1 v/v was not examined, but the probable kinetic role of radicaloid species in the reactions in more aqueous media is discussed later, although there was no evidence from NMR spectroscopy for the evidence of free radicals in these more aqueous solutions.

Structural predictions

Coplanarity of the dinitro and phenyl groups is sterically unfavorable and a forced planar structure of DCDNB is predicted to be disfavored by 13.5 kcal mol^{-1}, relative to one with the nitro groups twisted out of plane by 40° or 38°, from calculations with the HF/6-31G(d) or BP/6-31G(d) methods, respectively. This lack of coplanarity is consistent with extensive evidence on nitroarenes,[26] and the well-established steric hindrance to resonance should affect the relative leaving group properties of Cl^- and NO_2^-. The predicted inter Cl distance of 3.22 Å is slightly less than the sum of the van der Waals radii,[27] and the subtended angles at C-1 and C-2 were predicted to increase slightly to 121°. The observed loss of NO_2^- by attack of OH^- is consistent with a high LUMO density adjacent to the nitro groups rather than at positions adjacent to the chloro substituents.

The dihydroxy Meisenheimer complex (M^{2-}) (Scheme 2) is a cyclohexene derivative, and has *syn*- or *anti*-3,6-hydroxy groups. The geometrical optimization with the HF/6-31+G(d) method indicates that the *syn*-isomer should be more stable than the *anti*- by 1.8 kcal mol^{-1}, but, when hydration (H_2O) is included at the semi-empirical SM 5.4 level,[28] the *anti*-isomer is predicted to be preferred by 8.6 kcal mol^{-1}. The estimated effect of solvation by water may not apply to the organic kinetic solvent mixtures.

Discussion

Kinetic data

The various relaxations are well separated and rate and product data (Tables 1-4) can be rationalized in terms of the reactions in Scheme 2, which are similar to those postulated in other reactions of polynitroarenes with oxide ions. It was not included the π-complexes in the kinetic scheme, although they may be transient species. There is rapid hydrogen exchange in DMSO-D_2O and KOD, as with other nitroarenes,[1,7,8,29] but no evidence for build-up of a carbanion of DCDNB, and this exchange does not perturb the kinetics, but requires consideration of the conventional reaction Scheme 2.

The interconversion of DCDNB and M^{1-} in DMSO:H_2O 7:3 v/v is so much faster than the other relaxations (Tables 1, 2 and 4) that in treating them in KOH it was assumed an equilibrium between DCDNB and M^{1-}, on the time scale of the other relaxations, with the equilibrium constant, $K_2 = k_2/k_{-2}$ in terms of the changing concentrations in the course of reaction. The inspection of a molecular model of a hypothetical *ipso* complex in the formation of ArO^- indicates that there should be hydrogen bonding between OH and NO_2 on the adjacent carbon. Values of k_2 and K_2 in DMSO:H_2O 7:3 v/v are in Table 5, together with other rate and equilibrium constants. The values of k_{-2} and K_2 depend on the intercept of a plot of τ_1^{-1} against $[OH^-]$ and are less reliable than the value of k_2 from the slope (equation 1). The predicted fit to experimental data in DMSO:H_2O 7:3 v/v is shown in Figure 1.

The formation of M^{2-} is reversible (Scheme 2), but except in very dilute OH^-, the reversion to M^{1-} and then to DCDNB and ArO^- is slow. Therefore, the conversion of DCDNB into M^{2-} and ArO^-, the second relaxation, fits equation 2 with the assumption that the postulated *ipso*-Meisenheimer complex (Scheme 2) goes rapidly to ArO^-. Except in very dilute OH^-, the formation of ArO^- is much slower than the formation of the nonproductive Meisenheimer complexes, so that the first term in equation 2 is relatively unimportant, but with time, there is return to DCDNB and irreversible formation of ArO^-. The relaxation in equation 2 is first-order with respect to the changing concentration of DCDNB, which on the time scale of this relaxation should be higher than that of M^{1-}, based on the disappearance of its color or its nonappearance in more aqueous solvents.

Table 5. Rate and equilibrium constants for reactions of DCDNB with OH^{-} [a]

Solvent	DMSO:H_2O 7:3	DMSO:H_2O 1:1	H_2O
k_1 / (L mol^{-1} s^{-1})	0.152	8.70×10^{-3}	6.31×10^{-4}
k_2 / (L mol^{-1} s^{-1})	8.33	(0.48)	(0.035)
k_{-2} / (L mol^{-1} s^{-1})	0.104	(0.1)	(0.1)
K_2 / (L mol^{-1} s^{-1})	80	(4.8)	(0.3)
k_3 / (L mol^{-1} s^{-1})	5.45×10^{-3}	(5×10^{-3})	(5×10^{-3})
K_2k_3 / (L^2 mol^{-2} s^{-2})	0.439	3.06×10^{-2}	1.97×10^{-3}
k_{-3} / s^{-1}	2.4×10^{-4}	1×10^{-4}	2×10^{-4}
K_3 / (L mol^{-1})	23	–	–
K_b / (mol L^{-1})	0.011	0.072	–
k_3K_2/k_1	2.9	3.7	3.1
k_3/k_{-2}	0.052		

[a]Values in parentheses are approximate and are estimated by comparison with values from reactions in DMSO:H_2O 7:3 v/v; see text.

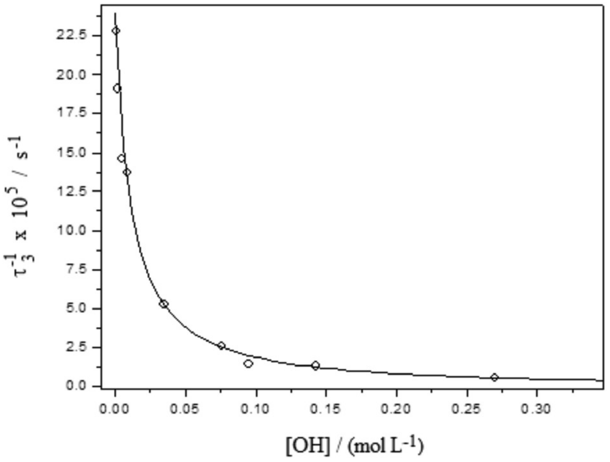


Figure 1. Predicted fit of kinetic data (equation 5) for DMSO:H_2O 7:3 v/v.

$$\tau_2^{-1} = k_1[OH^-] + k_3K_2[OH^-]^2 \qquad (2)$$

The relationship between τ_2^{-1} and $[OH^-]$ gives values of k_1 and k_3K_2. For reaction in DMSO:H_2O 7:3 v/v , the values of k_2 and k_{-2} (i.e., K_2) allow the estimate of k_3 (Table 5) with K_2 in terms of concentrations in the course of reaction.

This kinetic model is confirmed by the estimate of $[ArO^-]$ after approximately 10 half-lives of the second relaxation, in which only ArO^- and the dihydroxy Meisenheimer complexes ($M^{2-} + M^{3-}$) are present, and the concentrations are estimated by absorbance differences (equation 3):

$$\frac{[M^{2-}]+[M^{3-}]}{[ArO^{-}]}=\frac{k_2k_3}{k_1k_{-2}}[OH^{-}]=\frac{k_3K_2}{k_1}[OH^{-}] \qquad (3)$$

Under the conditions for which equation 3 is applicable, the low concentration of DCDNB can be neglected. The fits to the model are illustrated by comparison of observed and predicted values of τ_1^{-1} and τ_2^{-1} in Tables 1-3 and of ($[M^{2-}]$ + $[M^{3-}]$)/$[ArO^{-}]$ in Table 4.

Although all the rate and equilibrium constants in equations 1-3 can be estimated for reaction in DMSO:H_2O 7:3 v/v, it is not possible to estimate K_2 for interconversion of DCDNB and M^{1-} in the other solvents, and then, only k_3K_2 for formation of M^{2-} can be determined. The values of k_3K_2, like those of k_1, decrease with increasing water content of the solvent, as it is typical of rates of reactions with nucleophilic or basic anions.[30] Both k_3 and K_2 should be solvent sensitive, but most results in the literature are for nucleophilic reactions involving nonionic substrates. The separation of the constants is not experimentally feasible for the more aqueous solvents. In these cases, it was not observed the monohydroxy Meisenheimer complex, which can readily form the dianionic dihydroxy Meisenheimer complex (M^{2-}) under these conditions.

Return and deprotonation of the dihydroxy Meisenheimer complex

The third relaxation (τ_3) is relatively very slow, especially with high $[OH^{-}]$ which deprotonates M^{2-}, thereby inhibiting the return to M^{1-} and hence to DCDNB and there is little absorbance of M^{1-} at 520-530 cm^{-1} and on the time scale of τ_3, M^{1-} and DCDNB should produce largely ArO^{-}. Therefore, the extrapolation of τ_3^{-1} to zero $[OH^{-}]$ gives an approximate value of k_3.

In DMSO:H_2O 7:3 v/v, there is, after a short time, no absorbance of the monohydroxy Meisenheimer complex at 520-530 nm, i.e., both it and DCDNB behave as low concentration intermediates. The equilibrium constant (K_b) for the interconversion of M^{2-} and M^{3-} (equation 4) is given by the dependence of τ_3^{-1} upon $[OH^{-}]$ provided that

$$K_b=\frac{[M^{2-}][OH^{-}]}{[M^{3-}]} \qquad (4)$$

allowance is made for the return of M^{1-} to M^{2-} (Scheme 2). This calculation is not feasible for reaction in water where the relaxation is very slow, even in very dilute OH^{-} whose concentration is uncertain, because it may not be significantly greater than initial [DCDNB] (Table 3). In DMSO:H_2O 1:1 v/v, we have experimental values of only some of the rate constants involved in the return of the dihydroxy Meisenheimer complex.

The complete rate equation 5 includes K_b and some rate constants whose values are experimentally available only in DMSO:H_2O 7:3 v/v and the values of τ_3^{-1} in terms of k_{-3} and K_b with an extrapolated value of k_{-3} to zero $[OH^{-}]$ were fitted. The estimated values of k_{-3} and K_b are 2.4×10^{-4} s^{-1} and 0.011 mol L^{-1}, respectively. The extrapolated value of $k_{-3} = 10^{-4}$ s^{-1} in DMSO:H_2O 1:1 v/v is similar to that in the less aqueous solvent, but this extrapolation in water is uncertain, as noted earlier.

$$\tau_3^{-1}=\frac{k_1k_{-3}K_b}{(k_3K_2[OH^{-}]+k_1)(K_b+[OH^{-}])} \qquad (5)$$

Solvent effects upon the reactions

Kinetic solvent effects should be similar for reactions of OH^{-} and DCDNB, giving either ArO^{-} or M^{1-}, on the assumption that both involve formation of monoanionic Meisenheimer complexes from OH^{-} and a nonionic substrate. If k_1/k_2, which describes reactions of OH^{-} with DCDNB, is solvent independent it is possible to combine its value in DMSO:H_2O 7:3 v/v with those of k_1 in the three solvents (Table 5) to obtain k_2 ca. 0.48 and 0.035 L mol^{-1} s^{-1} in DMSO:H_2O 1:1 v/v and water, respectively. With these values and those of k_2k_3/k_{-2}, i.e., of k_3K_2 (Table 5), it was obtained values of k_3/k_{-2} equal to 0.064 and 0.056 mol^{-1} L in DMSO:H_2O 1:1 v/v and water, respectively, on the assumption that M^{1-} is on the reaction path, although it was not observed its absorption in these solvents. The directly estimated value of k_3/k_{-2} is 0.052 mol^{-1} L in DMSO:H_2O 7:3 v/v (Table 5), and the apparent similarities of these relative rate constants indicate that partitioning of M^{1-} between the return to DCDNB (+ OH^{-}) and the conversion into M^{2-} (Scheme 2), is not very sensitive to solvent composition.

The apparently similar values of k_3/k_{-2} in the three solvents are consistent with the forward and reverse reactions of M^{1-} involving no change of net charge, although they have different kinetic orders. Mole fractions of H_2O in the three solvent mixtures are not very different, and in the least aqueous solvent, DMSO:H_2O 7:3 v/v, the mole fraction of H_2O is ca. 0.61. It is possible that, except for the initial formation of M^{1-}, individual rate constants are not very sensitive to solvent composition and it is noted that the extrapolated values of k_{-3} for loss of OH^{-} from M^{2-} (Scheme 2) are not very different in DMSO:H_2O 7:3 v/v and DMSO:H_2O 1:1 v/v (Table 5). Based on this hypothesis, it appears that the addition of OH^{-} to an anionic Meisenheimer complex (M^{1-}) and the reverse reaction are not subject to large kinetic solvent effects, although they are typically large for the corresponding reactions involving nonionic substrates,[30] which should include DCDNB. If this speculation is correct, the decrease in experimentally estimated values of k_3K_2 in going to more aqueous solvents (Table 5) is due to a decrease in K_2 which describes the equilibrium for overall addition of hydrophilic OH^- to nonionic DCDNB, although it is possible only to estimate its value in DMSO:H_2O 7:3 v/v.

These qualitative generalizations accord with the Hughes-Ingold charge-type treatment of solvent effects upon nucleophilic substitutions, although it was developed for heterolytic reactions of nonionic and cationic aliphatic substrates.[31] In M^{1-} and M^{2-}, the negative charge is probably largely located on oxygens of the nitro groups and the generalizations may not apply to reactions of anionic substrates in which the charge is more delocalized.

Nucleophilic addition and substitution

Rate and equilibrium constants for the various reactions with dilute DCDNB (5×10^{-5} mol L^{-1}) are given with some estimated values in Table 5. Values in parentheses depend on the assumptions described earlier, or on extrapolations. Some aspects of the reaction of OH^- with DCDNB were unexpected, but they are consistent with the rate and equilibrium constants of the reactions in Scheme 2. The substitution of a nitro group by OH^-, or other anionic nucleophile, is not unusual, although many examples involve polarizable, low charge-density, nucleophiles.[19,20,32] In DCDNB, the displacement of Cl^- should be assisted by electron withdrawal by a nitro group, but the interference between the nitro groups reduces this resonance effect. The structural optimization indicates that the nitro groups are twisted out of plane (Results section), and this unfavorable interaction is relieved by loss of a nitro group. Steric hindrance to resonance is a well-studied phenomenon,[33] the loss of a nitro group should be sterically accelerated, and there is high LUMO density adjacent to the nitro groups (Results section).

The observed initial formation of ArO^- in very dilute OH^- is consistent with values of k_3K_2/k_1 (Tables 4 and 5), which indicate that partitioning of DCDNB is not very sensitive to solvent composition. The initial formation of unproductive Meisenheimer complexes is typical of arenes with strongly electron-withdrawing substituents in moderately concentrated OH^-.[1-5,7,8]

The formation of the unproductive Meisenheimer complexes is kinetically controlled, and in DMSO:H_2O 7:3 v/v k_2/k_1 ca. 55 which fits the slow formation of phenolic products (Table 5 and Scheme 2). It is generally assumed that in these conditions, *ipso*-complexes are very short-lived and do not return to the substrate,[1-6,22] or the reaction is concerted.[23]

Several factors contribute to build-up of the dihydroxy Meisenheimer complex (M^{2-} and M^{3-}) in > 0.3 mol L^{-1} OH^- (Tables 4 and 5 and reference 19). The return of M^{2-} is slow, especially in highly alkaline media, as shown by values of k_{-3} (Table 5), and in moderately concentrated OH^-, the formation of ArO^- does not compete strongly with addition of OH^- to DCDNB. As a result, the dihydroxy Meisenheimer complex (M^{2-}) slowly decomposes in dilute OH^-, and even more so with increasing $[OH^-]$ (Tables 3 and 5).

Stabilities of the dihydroxy Meisenheimer complexes

There are many examples of the formation of unproductive monohydroxy Meisenheimer complexes derived from di- and tri-nitroarenes,[1-8] and dihydroxy complexes typically form from moderately concentrated OH^- in solvents of relatively low water content. The rapid formation of M^{2-}, even in dilute aqueous OH^- (Tables 2 and 4), was therefore unexpected, and this behavior was not observed in reactions of OH^- with other chlorodinitrobenzenes,[8] although it is observed in reactions of 1,3,5-trinitrobenzene and its derivatives.[1-8] There is evidence for deprotonation of unproductive Meisenheimer complexes in strongly alkaline media,[1-2,4] but M^{2-} is apparently partially deprotonated in dilute OH^-. This dihydroxy complex is an aliphatic diol, but it is more acidic than expected from comparisons with acidities of alcohols with strongly electron-withdrawing substituents, e.g., the pK_b values in water are 1.5 and 0.45 for $CF_3CH_2O^-$ and $HC{\equiv}CCH_2O^-$, respectively,[34] and the classical pK_b for M^{3-} is 2.0 in DMSO:H_2O 7:3 (Table 5). The pK_b value cannot be estimated for M^{3-} in water, but the slow return of M^{2-} to M^{1-} in very dilute KOH (Table 3) indicates the deprotonation of M^{2-}. The negative charges in M^{2-} should be localized largely on nitro oxygens, favoring the deprotonation. Our kinetic data on formation of M^{1-} in DMSO:H_2O 7:3 v/v indicate that M^{1-} is not deprotonated in dilute OH^- and it therefore appears that the aliphatic M^{2-} is more acidic than M^{1-}. The inductive effect of one OH group in M^{2-} could increase the acidity of the other, but these groups are isolated and any effect should be small.[35] K_b was used in these comparisons rather than K_a because our data are in nonaqueous media and based on stoichiometric $[OH^-]$. Comparison with literature data for the alcohols is therefore qualitative.

The preferential formation of unproductive Meisenheimer complexes over ArO$^-$ is kinetically controlled, but the long lifetime of the dihydroxy Meisenheimer complex, in other than dilute OH$^-$, is, on the time scale of the first two relaxations, thermodynamically controlled. However, ArO$^-$ is the thermodynamically controlled product of the overall reaction, but is the kinetically controlled product in very dilute OH$^-$ (Experimental section and reference 19).

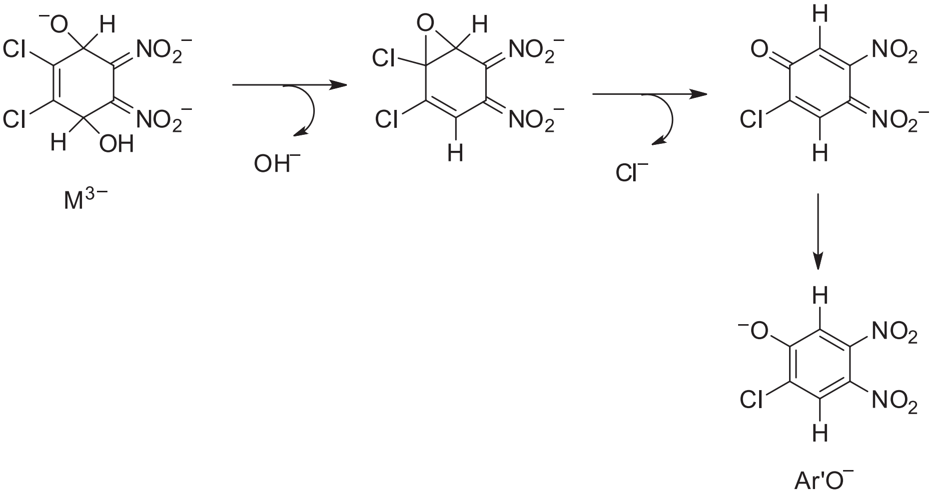
Phenolic products

The preparative work in water at ca. 100 °C (Experimental section and reference 19) and UV-Vis spectroscopy give evidence of only one phenolic product from loss of a nitro group in this heterogeneous system. However, the NMR data, with more concentrated DCDNB in DMSO-H_2O, indicate that a second phenolic product is formed, probably by loss of Cl$^-$. Such a dinitrophenoxide ion would not have been spectrophotometrically detected, but only in the NMR spectra in concentrated solutions very different from the kinetic conditions and may have been promoted by the change of solvent composition. The direct formation of both phenolic products with loss of NO_2^- or Cl$^-$ from DCDNB should be first-order in [DCDNB], and a minor phenolic product would not affect the kinetic form. Conditions for preparation of the phenolic product[19] and examination of the NMR spectra differ considerably in temperature, solvent and substrate concentration from those in the kinetic work and it is impracticable to monitor the NMR spectra during reaction with the very dilute DCDNB used in the kinetic work. However, the dihydroxy Meisenheimer complex, which in the NMR experiments is in relatively high concentration, could be the source of the minor phenoxide product rather than the different reaction conditions, although we know of no precedent for such a reaction. The dihydroxy Meisenheimer complex (M^{2-} or M^{3-}) might react nucleophilically in a classical aromatic nucleophilic substitution, displacing Cl$^-$ rather than the congested nitro group. On the basis of earlier work, such a first-formed dinitroaryl ether could react with OH$^-$.[3,4] It is difficult to test this speculation because in the kinetic experiments, with very dilute DCDNB, OH$^-$ is in very large excess over any other nucleophile. Another possible route, with M^{2-} and M^{3-} in relatively high concentration, involves stepwise decomposition of the dihydroxy complex (Scheme 3) with initial intramolecular nucleophilic addition forming a transient chlorohydrin, and loss of Cl$^-$ and aromatization giving Ar'O$^-$. A similar reaction could involve the base of M^{1-}, but such a reaction, or displacement of Cl$^-$ from the substrate, should not be very sensitive to the initial substrate concentration.

The formation of Ar'O$^-$ involves initial loss of two OH$^-$ groups, and aromatization (Scheme 3), as does formation of aryloxide ions, via return of M^{2-} to DCDNB in a conventional reaction (Scheme 2). These speculative individual reactions may be stepwise or concerted, with the possibility of reversible steps. However, other substitution routes fit the kinetic and preparative evidence and are consistent with earlier evidence.

Mechanism of substitution

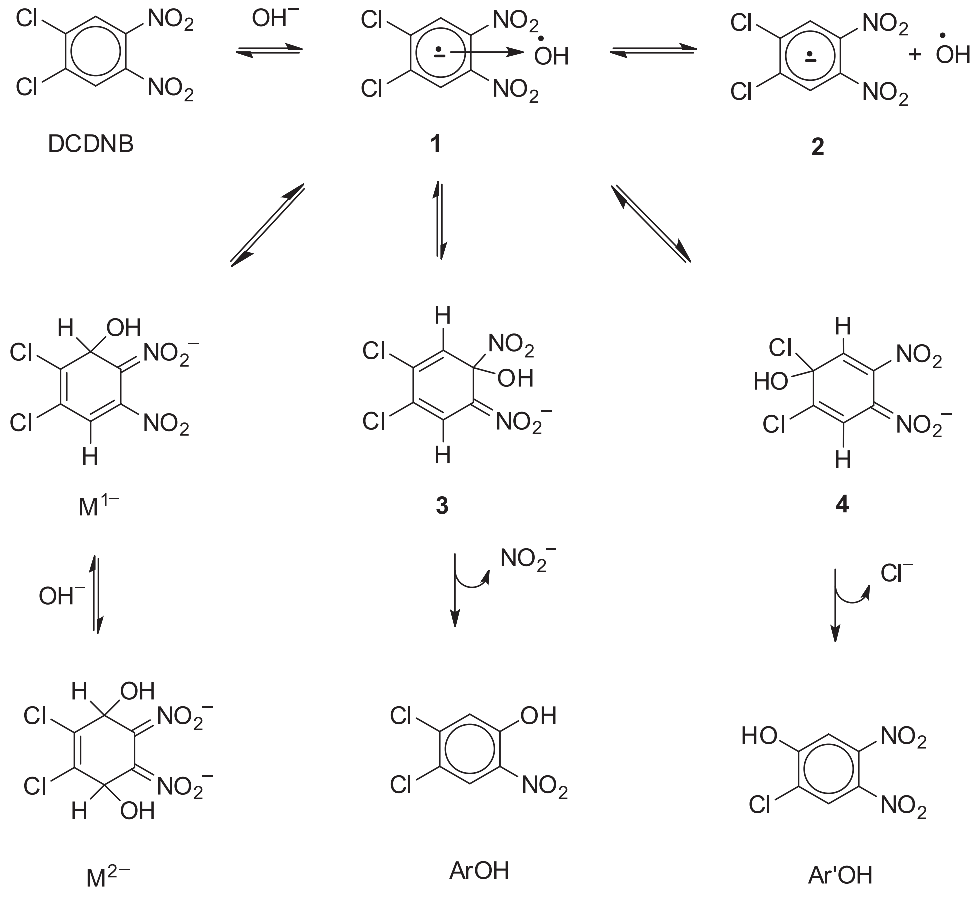
Descriptions of organic reaction mechanisms often involve the distinction between so-called "heterolytic" and "homolytic" reactions, which is descriptively convenient, and, for the former, nucleophilicity and leaving-group ability are often related to Brønsted basicity.[35] However, the avoided-crossing model of nucleophilic substitution indicates how "heterolytic" reactions can have radicaloid character.[36] Many aspects of aromatic nucleophilic



Scheme 3.

substitution by OH^- or alkoxide ions are characteristic of "heterolytic" reactions, especially in polar, protic, media,[1-6] but there is extensive evidence for the involvement of radical species in some substitutions, i.e., they have "homolytic" character.[7,8,36,37] There is probably not a sharp distinction between these limiting reaction paths, and a given reaction may exhibit both "ionic" and "radicaloid" characteristics. For example, the decomposition of trinitrotoluene in hot aqueous alkali generates formate and acetate ions[18] which are not products expected in a simple nucleophilic substitution, but could be formed by intervention of radicaloid species and oxidation.

The reaction path shown in Scheme 2 follows classical models of nucleophilic reactions with haloarenes, allowing the estimation of rate and equilibrium constants for individual steps, and the possible displacement of Cl^- is not shown because of the limited evidence for this reaction. The rapid H/D exchange in D_2O, or the radical induced line broadening in DMSO:H_2O 4:1 v/v, is not considered, and they could be ascribed to side reactions unrelated to the overall nucleophilic reaction, for example, by formation of a carbanion, although it is unlikely in dilute OD^- and D_2O-DMSO. However, these results, and the overall kinetics, can be explained in terms of reversible formation of tight anionic radical pairs, or charge-transfer complexes, e.g., **1**, on the reaction path, leading to long-lived, but unproductive, Meisenheimer complexes, and H/D exchange and displacement of NO_2^- or Cl^-, written as involving transient Meisenheimer complexes (Scheme 4). The initial pairs with the delocalized negative charge could rapidly exchange hydrogen with D_2O and their return would explain the rapid H/D exchange.[25,29] In less water content, e.g., DMSO:H_2O 4:1 v/v, the dissociation of **2** would form transient radicals giving the observed NMR line broadening and signal loss. In Scheme 4, which shows reactions involving radicaloid species, intermediates with finite lives, and products are numbered. Provided that these radical ion pairs do not dissociate to free radicals, the kinetic form in the higher water content media will be as for a classical heterolytic reaction (Scheme 2), and the rate constants in Tables 1-3 and 5 can be rewritten in terms of rate and equilibrium constants for the individual steps in Scheme 4. The initial rapid and reversible formation of a resonance stabilized anionic radical pair, **1**, from DCDNB allows formation of the productive and unproductive Meisenheimer complexes and H/D exchange



Scheme 4.

in DCDNB, and the observed Meisenheimer complexes and aryloxide products.

The partitioning between productive and unproductive Meisenheimer complexes involves the anionic radical pair, **2**, rather than DCDNB, but it was assumed that **2** and DCDNB are in rapid equilibrium on the time scale of the overall reaction (Scheme 4). The conversion of the unproductive monohydroxy Meisenheimer complex (M^{1-}) into M^{2-} (Scheme 2) could also involve an anionic radical pair, which is not shown to simplify Scheme 4, and the deprotonation of OH groups at high pH inhibits return of the dihydroxy Meisenheimer complex to the final phenolic products. The competitive losses of NO_2– or Cl^- depend on the abilities of the postulated *ipso* complexes, **3** and **4**, to lose either an anion or return to **1** and DCDNB (Scheme 4), and should be related to electron distributions in the complexes and, as noted earlier, to intramolecular hydrogen bonding in the postulated intermediate, **3**. In both aromatic substitution models, formations of *ipso*-Meisenheimer complexes are shown as reversible but are followed by irreversible loss of the leaving group, as in Scheme 2. The explanation of the observed H/D exchange in terms of a postulated radical pair, **1**, follows that earlier applied to exchange in nitroarenes,[25] with exchange being faster than nucleophilic substitution. However, we note that the NMR evidence for H/D exchange was obtained by NMR spectroscopy in nonkinetic conditions. In both mechanistic descriptions, intermediates are negatively charged and to those extent distinctions between Scheme 4 and the classical description (Scheme 2) depend on the postulated electron distributions and noncovalent interactions, as does the relative loss of NO_2^- or Cl^-. Unless free radical ions are detected, as in DMSO:H_2O 4:1 v/v, either model fits the rate data, but the reaction path in Scheme 4 is consistent with the overall kinetics, rapid H/D exchange and evidence for the formation of free radicals with extensive NMR line broadening in the less aqueous media. The loss of NO_2^-, rather than Cl^-, can be explained in either mechanistic model in terms of intramolecular hydrogen bonding involving NO_2 and OH and relief of steric strain.[38] Although in the mechanistic models, exchange and NMR line broadening are not necessarily on the overall reaction path, they can be explained in terms of reactions involving radicaloid species. The distinction between the reactions in Schemes 2 and 4 reflects limitations in graphical depictions of the organic chemical bond, for example as in single electron transfer in gas phase S_N2 reactions of quaternary ammonium salts.[39] The postulated initial formation of the anionic radical pair, **2**, is consistent with theoretical treatments and recent experimental evidence.[40]

Conclusions

The initial rapid reaction of OH^- with DCDNB in DMSO:H_2O 7:3 v/v gives an unproductive, short-lived monohydroxy Meisenheimer complex (M^{1-}) and very slow formation of aryloxide ion, largely with displacement of a nitro group, while M^{1-} forms a long-lived dihydroxy Meisenheimer complex (M^{2-}) which is deprotonated in alkali giving M^{3-}. The unproductive Meisenheimer complex (M^{1-}) is not observed in reactions in more aqueous media. The dihydroxy Meisenheimer complex has a lifetime long enough for identification by NMR spectroscopy in DMSO-H_2O-KOH. There is rapid exchange of arene hydrogens, even in dilute OD^-, which is not explained in terms of a classical heterolytic reaction scheme, even though it fits the chemical kinetics. Rate and equilibrium constants of all the individual reactions were determined in DMSO:H_2O 7:3 v/v and some could be estimated in more aqueous media. The preferential loss of a nitro group and ready formation of an unproductive dihydroxy Meisenheimer complex is probably related to intramolecular hydrogen bonding and repulsions between the nitro groups. The dihydroxy Meisenheimer complex (M^{2-}) slowly reverts to starting material and then to aryloxide ion, and in the concentrations required for examination of the NMR spectrum, weak signals of a second aryloxide ion are observed, and its formation probably involves loss of Cl^-. As an alternative to the classical model of nucleophilic substitution, the overall reactions, and the kinetics, can be described in terms of formation of tight anionic radical pairs, or charge-transfer complexes, which allow rapid H/D exchange and, in DMSO:H_2O 4:1 v/v, formation of free radicals. These results are consistent with evidence on the role of radicaloid species in other aromatic nucleophilic substitutions by ionic nucleophiles in aqueous-organic solutions.

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