Hydrolysis of Ethers of 2,4-Dinitrophenol. No Evidence for a Single Electron Transfer Mechanism

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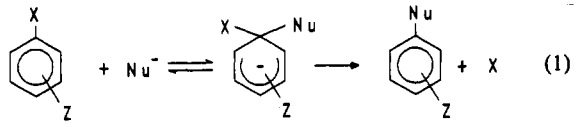
The reactions of 3-butenyl 2,4-dinitrophenyl ether (1), allyl 2,4-dinitrophenyl ether (5), and *n*-butyl 2,4-dinitrophenyl ether (6) with KOH in two DMSO–water mixtures (50% v/v and 70% v/v) were studied. In all cases, no evidence was found for a single electron transfer mechanism; 2,4-dinitrophenol was the only product formed. The reaction follows the classical S_NAr mechanism. The order of reactivity is **5** > **1** > **6** in both solvents, although the reactivities differ only by factors of 1.4 and 2 in 50 and 70% DMSO, respectively.

Introduction

The mechanism of the nucleophilic aromatic substitution reactions has been the object of many studies, especially kinetic studies[1] and those involving the isolation and identification of the intermediates.[2]

On the one hand, there is much evidence in favor of the mechanism described in eq 1[1–3] for nucleophilic substitution reactions of activated aromatic substrates, i.e., substrates with one or more electron-withdrawing groups.

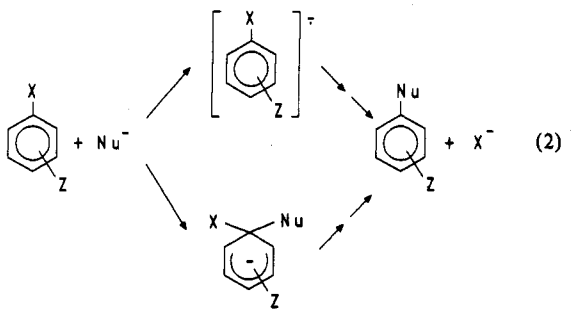


(1)

On the other hand, there is a growing awareness that single electron transfer may be the initial step in a wide range of chemical reactions.[4]

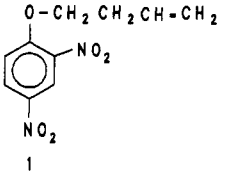
The ability of aromatic compounds carrying electron-withdrawing groups to act as electron acceptors in basic solutions has been demonstrated by Russell,[5] and radical anions are intermediates in $S_{RN}1$ reactions.[6] The $S_{RN}1$ mechanism is very well established for unactivated aromatic substrates. The participation of radical anions as intermediates in the reaction pathway to products was suggested for the hydrolyses of *o*- and *p*-dinitrobenzene in DMSO-rich mixtures; in these reactions, the rates of formation and decomposition of the intermediates were measured by means of the ESR technique.[7] Recently, a series of papers appeared in which the authors claimed to have evidence for the occurrence of one-electron transfer reactions prior to the formation of Meisenheimer complexes,[8] but some of the results could not be reproduced in another laboratory.[9]

We thought it important to find a compound that could serve to differentiate between the one-electron and two-electron transfer mechanisms (eq 2). 3-Butenyl 2,4-



(2)

dinitrophenyl ether (1) appeared to be a good candidate



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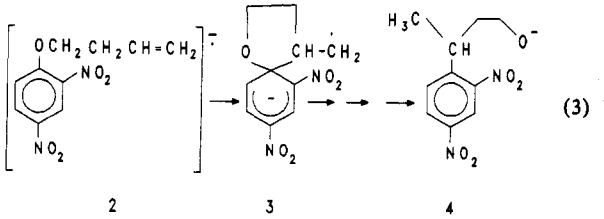
since, if a radical anion were formed, cyclization could lead to product 4, which is different from the product expected from intermolecular nucleophilic substitution by hydroxide ion, 2,4-dinitrophenol (eq 3).



(3)

2 3 4

Intramolecular rearrangements of this type usually occur at a very high rate and can compete with intermolecular reactions.[10] The formation of products derived from **3** could be clear proof of the involvement of radical anion

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Table I. Observed Rate Constants for the Hydrolysis of 3-Butenyl 2,4-Dinitrophenyl Ether (1) at 25 °C. Dependence on Hydroxide Ion Concentration

[KOH], M	$k_{obs} \times 10^4$, s^{-1}	[KOH], M	$k_{obs} \times 10^4$, s^{-1}
	50% DMSO–water[a]		
0.010	0.351	0.075	2.90
0.025	0.846	0.100	3.95
0.050	1.91 ± 0.01	0.125	5.08
0.050[b]	1.91 ● 0.01	0.150	6.4 ± 0.4
0.050[b,c]	2.02	0.175	7.14
0.050[b,d]	2.07	0.185	7.91
0.050[b,e]	1.84	0.200	8.8 ± 0.5
	70% DMSO–water[f]		
0.010	4.93	0.068	49.6 ± 0.9
0.020	8.6 ● 0.4	0.078	59.5 ± 0.3
0.030	10.8 ± 0.5	0.080	42 ± 2
0.040	18.6 ± 0.5	0.090	49 ± 2
0.050	25.3 ± 0.4	0.098	81 ● 2
0.060	44.0 ± 0.3		

[a] Ionic strength (μ) = 0.5 M unless otherwise indicated, $[1]_0 = 5 \times 10^{-5}$ M. [b] $[1]_0 = 3.36 \times 10^{-5}$ M. [c] $\mu = 0.05$ M. [d] $\mu = 0.2$ M. [e] $\mu = 0.35$ M. [f] $\mu = 0.1$ M, $[1]_0 = 5 \times 10^{-5}$ M.

2 in this reaction. However, the opposite, namely, the absence of such products, does not mean that 2 is not formed.

We report here a kinetic study of the reaction of 1, as well as the reactions of allyl 2,4-dinitrophenyl ether (5) and *n*-butyl 2,4-dinitrophenyl ether (6), with KOH in DMSO–water mixtures.

Results

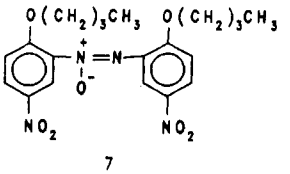
3-Butenyl 2,4-Dinitrophenyl Ether (1). The reaction of 1 was studied at different concentrations of KOH in two DMSO/water mixtures (50 and 70% v/v) (Table I). In all cases, 2,4-dinitrophenol was the only product, and a good isosbestic point was observed when the spectra of the solutions were taken at different reaction times (Figure 1).

In 50% DMSO, the effect of the ionic strength on k_{obs} was investigated, and it was found that the differences in the rates are within the experimental error.

The plot of k_{obs} vs [KOH] is linear with a zero intercept (Figure 2) and can be represented by eq 4.

$$k_{obs} = k_{OH}[HO^-] \quad (4)$$

In order to prove that the radical anion of 1 would lead to other products, we attempted to generate 2 by electron transfer from another radical anion. We first tried to generate 2 by electron transfer from the radical anion of benzophenone in anhydrous ethyl ether because the reduction potential of benzophenone is higher than that of *m*-dinitrobenzene.[11] This reaction led to a complex mixture of products from which we could isolate benzophenone, substrate, and adduct 7.



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Allyl 2,4-Dinitrophenyl Ether (5) and *n*-Butyl 2,4-Dinitrophenyl Ether (6). The reaction of 5 with KOH in 50 and 70% v/v DMSO/water led quantitatively to the formation of 2,4-dinitrophenol. Good isosbestic points were obtained when the spectra of the reaction solutions at different reaction times were plotted.

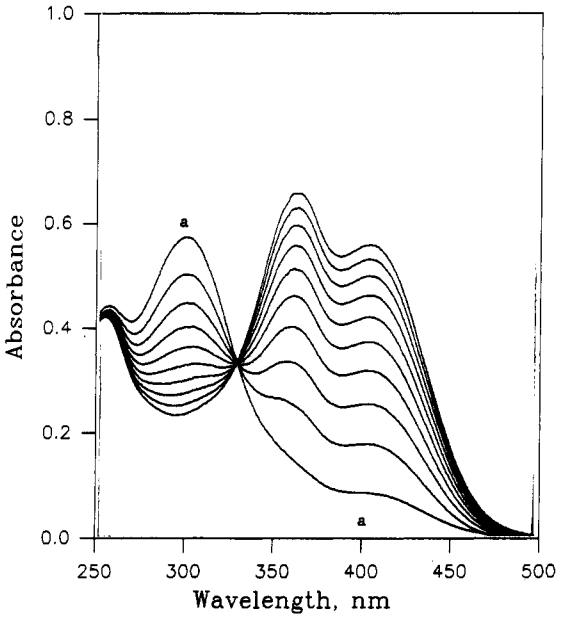

Figure 1. Absorbance of 1 in the presence of 0.2 M KOH at different reaction times in DMSO–water 50% v/v. $[1]_0 = 5.52 \times 10^{-5}$ M. First cycle (a) = 41 s. Intervals between cycles = 3 min.

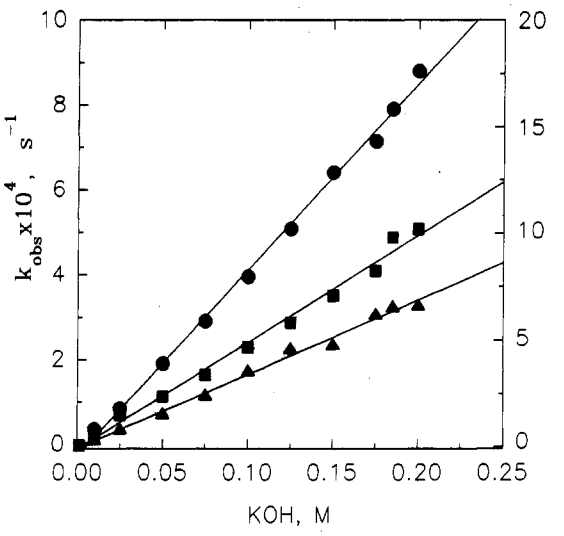

Figure 2. Plot of k_{obs} vs [HO⁻] for the formation of 2,4-dinitrophenol from 1 (·, left intercept), 4 (■, right intercept), and 5 (▲, right intercept) in DMSO–water 50% v/v at 25 °C (data from Tables I–III).

The observed rate constants at various KOH concentrations are collected in Table II. There is a linear dependence of k_{obs} on the KOH concentration (Figure 2).

The reactions of 6 with KOH in 50 and 70% v/v DMSO/water also gave 2,4-dinitrophenol as the only product, and the observed rate constants (Table III) show a linear dependence on the KOH concentration (Figure 2).

In Table IV, the values of k_{OH} for the three substrates in the two solvent mixtures are collected, and it should be noted that the reactivity order is 5 > 1 > 6.

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Table II. Observed Rate Constants for the Hydrolysis of Allyl 2,4-Dinitrophenyl Ether (5) at 25 °C. Dependence on Hydroxide Ion Concentration

[KOH], M	$k_{obs} \times 10^4$, s^{-1}	[KOH], M	$k_{obs} \times 10^4$, s^{-1}
	50% DMSO–water[a]		
0.001	0.0319	0.125	5.82
0.010	0.444	0.150	7.09
0.025	1.48	0.175	8.24
0.050	2.36	0.185	9.81
0.075	3.37	0.200	10.2
0.100	4.67		
	70% DMSO–water[b]		
0.010	10.3 ± 0.1	0.060	49.6 ± 0.1
0.020	17.1 ± 0.2	0.070	61 ● 2
0.030	27.3 ± 0.9	0.080	78 ± 4
0.040	32.8 ± 0.8	0.090	94 ± 4
0.050	43 ± 2	0.100	107 ● 7

[a] μ = 0.5 M, $[5]_0 = 5 \times 10^{-5}$ M. [b] μ = 0.1 M, $[5]_0 = 5.1 \times 10^{-5}$ M.

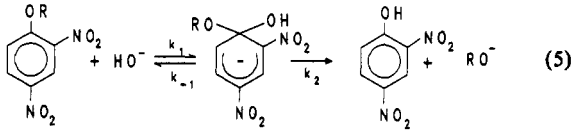
Table III. Observed Rate Constants for the Hydrolysis of n-Butyl 2,4-Dinitrophenyl Ether (6) at 25 °C. Dependence on Hydroxide Ion Concentration

[KOH], M	$k_{obs} \times 10^4$, s^{-1}	[KOH], M	$k_{obs} \times 10^4$, s^{-1}
	50% DMSO–water[a]		
0.010	0.289	0.125	4.57
0.025	0.787	0.150	4.77
0.050	1.51	0.175	6.19
0.075	2.39	0.185	6.53
0.100	3.54	0.200	6.60
	70% DMSO–water[b]		
0.010	3.85	0.074	39 ± 1
0.020	7.5 ± 0.3	0.074	37.4 ● 0.7
0.040	15.9 ± 0.3	0.080	43 ± 2
0.050	18.9 ± 0.05	0.086	45 ● 2
0.055	28 ± 1	0.090	46 ± 1
0.062	34 ± 2	0.098	49 ± 1
0.068	34 ● 2		

[a] μ = 0.5 M, $[6]_0 = 5 \times 10^{-5}$ M. [b] μ = 0.1 M; $[6]_0 = 5 \times 10^{-5}$ M.

Discussion

The formation of 2,4-dinitrophenol as the only product and the observation of good isosbestic points in all cases indicate that the hydrolyses of 1, 5, and 6 follow the classical S_NAr mechanism. This mechanism can be described in general terms by eq 5.



(5)

For the mechanism given in eq 5 the observed rate constant is given by eq 6. This equation predicts a linear

$$k_{obs} = \frac{k_1 k_2 [HO^-]}{k_{-1} + k_2} \quad (6)$$

dependence of k_{obs} on $[HO^-]$ independent of the ratios of k_2 and k_{-1}. If $k_2 \gg k_{-1}$, the addition of the nucleophile is rate determining, but if $k_{-1} \gg k_2$, the expulsion of the leaving group is rate determining.

The second-order rate constants for the three substrates are compared in Table IV, along with some data from the literature. The order of reactivity is **5** > **1** > **6** in both solvents, but the differences are greater in the less aqueous solvent.

The hydroxide ion is a very poor leaving group in protic solvents;[12] thus, $k_2 \gg k_{-1}$ for leaving groups such as alkoxide, phenoxide, and halogen anions, and the addition of the nucleophile to the aromatic ring is the rate-determining step.

Table IV. Second-Order Rate Constants for the Hydrolysis of Substrates

substrate	$k_{OH} \times 10^3$, M^{-1} s^{-1}	
	50% DMSO–water	70% DMSO–water
1	4.4 ± 0.2	77 ± 9
5	5.0 ± 0.2	106 ± 6
6	3.58 ± 0.01	54 ± 3
2,4-DNCB[a]		133[b]

[a] 2,4-DNCB = 2,4-dinitrochlorobenzene. [b] Value calculated from the slope of a plot of τ_3 vs $[HO^-]$ with data from ref 8c.

It is known that $-OCH_3$ in methanol and $-OCH_2CH_3$ in ethanol leave faster than $-OH$ in water from the corresponding Meisenheimer complexes of 1,3,5-trinitrobenzene.[12] So in protic solvents, the situation $k_2 > k_{-1}$ probably holds for the three substrates studied, but the fact that there are significant differences in the rates of the three substrates in 70% DMSO/water may indicate that there is some contribution of k_2 to the observed rate constant. The contribution of k_2 would indicate that the nonprotic solvent changes the relationship k_2/k_{-1} from a value higher than 1 to a value close to 1. This solvent effect is unlikely because it is expected that the rate of departure of RO^- and HO^- from Meisenheimer complexes would be affected in a similar way by a change in solvent composition.

It is well known that leaving group ability increases as the pK_a of the conjugated acid of the leaving group decreases.[13] The pK_a of allyl alcohol in water is 15.52[14] and that of RCH_2OH is approximately 16.[15] In the DMSO–water mixtures used, the pK_a of these alcohols is expected to increase,[16] but the difference between them should be the same as in pure water.

If the addition of the nucleophile is the rate-limiting step, a change in the leaving group should not have any major effect on the reaction rate provided that the steric and electronic effects of the three alcohols are about the same.[17] We believe that the conformation of the intermediates formed depends on the nature of the leaving group and that the transition state for the addition of the nucleophile in **5** is probably more stable than the others because of a favorable interaction between the developing negative charge and the double bond. This interaction should also be present in the reverse reaction, i.e., the addition of the unsaturated alcohol to the aromatic ring. For example, allyl alcohol is a better nucleophile than n-propyl alcohol in the reaction with picryl chloride.[18]

The fact that products derived from **3** could not be isolated from the reaction of **1** under conditions where its radical anion **2** should have been formed may be due either to the highly reducing medium used or to the fact that the reaction described in eq 3 does not compete with reduction of the nitro group.

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The formation of nitro reduction products such as adduct 7 was observed before in the reaction of monohalonitrobenzenes in 2-propanol solutions of potassium 2-propoxide under argon.[19] This nitro reduction was suggested to proceed via the nitroso derivative, which is formed from the radical anion of the halonitrobenzene.

Conclusions

The hydrolyses of substrates 1, 5, and 6 lead to 2,4-dinitrophenol as the only product, and the kinetic behavior is consistent with straightforward bimolecular aromatic nucleophilic substitution with addition of the nucleophile as the rate-determining step. The absence of other products in the reaction of 1 is considered good evidence that radical anions are not intermediates in these reactions, although they might be formed in the solvent cage but with much shorter lifetime than those reported in the literature for similar systems.[8c,20]

Experimental Section

Materials. 3-Butenyl 2,4-dinitrophenyl ether was prepared by the method of Whalley:[21] 3-buten-1-ol, 2,4-dinitrofluorobenzene, and triethylamine were stirred for 24 h at rt. Ether 1 was obtained as a yellow oil in 76% yield after purification by flash chromatography on silica gel. The compound was identified by ^{1}H-NMR, IR, and mass spectrometry. IR $\nu_{C=H}$ 3100 and 3086 cm^{-1}; $\nu_{C=C}$ 1640 cm^{-1}; ν_{ArOC} asim 1284 cm^{-1}; ν_{ArOC} sim 1050 cm^{-1}; ν_{ArH} 919 and 830 cm^{-1} (characteristic of 1,2,4-substituted benzenes); ^{1}H-NMR (90 MHz) (Cl_3CD) δ 2.65 (q, 2H, $-CH_2C=C$), 4.62 (t, 2H, OCH_2-), 5–6.17 (m, 3H, $-CH=CH_2$), 7.27 (d, 1H, aromatic proton), 8.34–8.48 (2d, 1H, aromatic proton), 8.72 (d, 1H, aromatic proton); MS 239 ($M^+ + 1$), 238 (M^+), 222 ($M^+ - O$), 192 ($M^+ - NO_2$), 167 ($M^+ - C_4H_7O$), 55 ($M^+ - 2,4\text{-}(NO_2)_2PhO$). Anal. Calcd for $C_{10}H_{10}N_2O_5$: C, 50.42; H, 4.20; N, 11.76. Found:[22] C, 50.09; H, 4.47; N, 11.58. The UV spectrum of 1 in 50% DMSO–water has an absorption band at 302 nm (ϵ = 11176).

Allyl 2,4-dinitrophenyl ether was synthesized by the same method[21] from allyl alcohol, 2,4-dinitrofluorobenzene, and triethylamine. The ether was isolated from the reaction mixture as pale yellow needles by flash chromatography, mp 43–44 °C (lit.[21] mp 45 °C). It was identified by ^{1}H-NMR and IR.

n-Butyl 2,4-dinitrophenyl ether was prepared from 2,4-dinitrochlorobenzene and *n*-butanol as described elsewhere[23] and isolated as a yellow oil from column chromatography on silica gel (lit.[23] mp 1.5–1.8 °C). It was identified by IR.

DMSO was dried over 4-Å molecular sieves and vacuum distilled. Solvent mixtures were made up from the desired number of volumes of DMSO in 100 volumes of solution. Water purified in a Millipore Milli-Q apparatus was used throughout. All of the inorganic reagents were of analytical reagent grade and were used without further purification.

UV spectra were recorded on a Shimadzu UV 260 spectrophotometer. IR spectra were scanned on a Nicolet 5SXC FTIR, the mass spectra on a Finnigan spectrometer, and the NMR spectra on a Bruker ACE 200.

Generation of Radical Anion 2. To a solution of benzophenone in anhydrous ethyl ether under N_2 was added metallic Li. The solution changed slowly from colorless to deep blue. After 5 h of reaction, a portion of this solution was poured over a solution of 1 in anhydrous ether under N_2. The color of this solution changed from yellow to brown. After 30 min, the reaction was stopped by the addition of water; the two phases were separated, and the ether portion was washed twice with water. A complex mixture of products, including benzophenone and 1, was obtained, and we could isolate one of the products by column chromatography on silica gel. All the others were formed in very small amounts: MS 432 (M^+), 359, 303, 224, 222, 208, 180, 168, 167, 165, 152, 151, 57, 56, 44, 41, 29, 28; ^{1}H-NMR (200 MHz) (Cl_3CD) δ 1 (t, 6H), 1.5 (sex., 4H), 1.85 (q, 4H), 4.15 (t, 2H), 4.25 (t, 2H), 7.1 (d, 1H), 7.2 (d, 1H), 8.25 (2d, 1H), 8.35 (2d, 1H), 8.52 (d, 1H), 8.55 (d, 1H); ^{13}C-NMR (200 MHz) (Cl_3CD) δ 13.708, 19.028, 19.134, 30.705, 30.948, 69.422, 70.173, 78.358, 78.995, 77.827, 111.884, 111.862, 113.353, 119.198, 119.358, 121.173, 121.328, 125.418, 127.100, 127.200, 140.701, 158.923. The spectral data are attributed to adduct 7.

Kinetic Procedures. Reactions were initiated by adding the substrate dissolved in DMSO to a solution containing all the other constituents. The total DMSO concentration was 50 or 70% v/v. The temperature was 25 °C, and the ionic strength was kept constant at 0.5 M in 50% DMSO and 0.1 M in 70% DMSO by adding KCl as a compensating electrolyte.

The observed rate constants, k_{obs}, were determined by following the appearance of 2,4-dinitrophenol. The change in optical density during a kinetic run was recorded on a Beckman 24 spectrophotometer for the slowest reactions or on a Shimadzu 260 recording spectrophotometer for the fastest reactions at the maximum absorption of the product (364 nm in 50% DMSO and 369 nm in 70% DMSO).

The kinetic measurements for the fastest reactions were made by rapidly injecting about 10 μL of the substrate solution in DMSO into the thermostated cell of the spectrophotometer and recording the increase in absorbance. The temperature inside the cell was maintained at 25 ± 0.5 °C.

All reactions were run under pseudo-first-order conditions, and they were followed up to 80–90% conversion. Good pseudo-first-order kinetic plots were obtained.

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