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Reduction and Substitution in the Reaction of 4-Chloronitrobenzene with Alkoxides

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Although the reduction of aromatic nitro derivatives in alkaline alcoholic media has been known for a long time,[1] the commonly reported reaction of chloronitrobenzenes with alkoxides is the nucleophilic aromatic substitution (S_NAr) leading to nitroaryl ethers.[2]

We have examined in detail the reaction of 4-chloronitrobenzene with potassium ethoxide, 2-propoxide, and *tert*-butoxide in the parent alcohols. Under air (Table I, first 3 entries) a substantial yield of the substitution product is obtained only in ethanol, whereas *p*,*p*'-dichloroazoxybenzene, *p*,*p*'-dichloroazobenzene, and *p*-chloroaniline are the main products in 2-propanol and *tert*-butyl alcohol.

A detailed study of the reaction in 2-propanol has revealed the impossibility of quantitative reproduction under air of the results reported in Table I. Good reproducibility is, however, obtained by carefully degassing the solution and running the reaction under helium. Under these conditions the reaction yields (Table I, entry 4) only *p*,*p*'-dichloroazoxybenzene and *p*-chloroaniline and is much faster (see Table I) than the one run under air (Figure 1, $k_1 = 9.77 \times 10^{-4}$ s^{-1} at 75 °C, [*i*-PrOK] = 0.24 M). On the contrary, a similar reaction run under oxygen yields *p*-nitrophenyl 2-propyl ether and *p*-nitrophenol with no trace of products deriving from reduction of the nitro group (Table I, entry 5).

The reaction of *p*-chloronitrobenzene with alkoxides may therefore take two different courses: reduction of the nitro group (to azoxy and aniline derivatives) and substitution of the chlorine, the reduction process becoming favored as the size of the alkoxide increases. It is, however, possible to force the reaction to follow only one of the two paths: reduction, by working under helium, or substitution, by working under oxygen, which can act as a scavenger for the radical ions involved in the reduction process.[1,3] It is clear that experiments run without careful control of the oxygen content in the solution are only of limited quantitative meaning.

The first step of the reaction between potassium 2-propoxide and *p*-chloronitrobenzene (**1**) is the formation of the radical anion of the aromatic[4] by electron transfer to **1** either from the potassium alkoxide or from an initial Meisenheimer-like complex.[5] The radical ion may either be protonated by the solvent or trapped by oxygen. In the first case, the reaction leads to reduction following the steps sketched in eq 1 and 2.

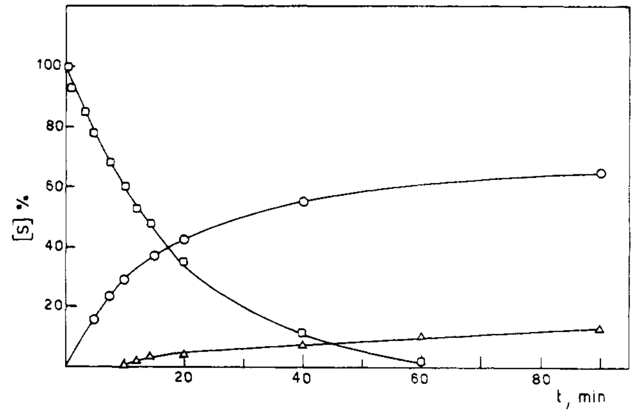
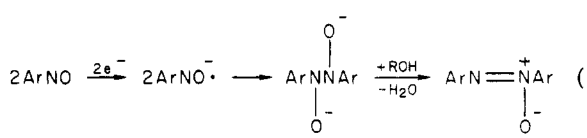


Figure 1. Reaction of *p*-chloronitrobenzene (0.03 M) with potassium 2-propoxide (0.24 M) in 2-propanol at 75 °C under helium: (□) *p*-chloronitrobenzene; (○) *p*,*p*'-dichloroazoxybenzene; (△) *p*-chloroaniline.

$$\mathrm{ArNO_2} \xrightarrow{e^-} \mathrm{ArNO_2^{-}\cdot} \xrightarrow{ROH} \mathrm{ArNO_2H\cdot} \xrightarrow{e^-} \mathrm{ArNO_2H^-} \xrightarrow{ROH} \mathrm{ArNO_2H_2} \xrightarrow{-H_2O} \mathrm{ArNO} \quad (1)$$



$$2\mathrm{ArNO} \xrightarrow{2e^-} 2\mathrm{ArNO^-\cdot} \longrightarrow \mathrm{Ar}\overset{\overset{O^-}{|}}{\mathrm{N}}\underset{\underset{O^-}{|}}{\mathrm{N}}\mathrm{Ar} \xrightarrow[-H_2O]{+ROH} \mathrm{ArN}{=}\underset{\underset{O^-}{|}}{\overset{+}{\mathrm{N}}}\mathrm{Ar} \quad (2)$$

The reduction to nitrosobenzene (eq 1) is depicted according to the accepted sequence for the chemical and electrochemical reduction of nitro aromatics.[3] Dimerization of nitrosobenzene to azoxybenzene (eq 2) is known to occur through the radical anion of the nitroso compound.[6] Under our conditions ([*i*-PrOK] = 0.24 M, 75 °C), *p*-chloronitrosobenzene is quantitatively dimerized to *p*,*p*'-dichloroazoxybenzene upon mixing. *p*,*p*'-Dichloroazoxybenzene is slowly reduced ($t_{1/2} > 20$ h) to *p*,*p*'-dichloroazobenzene which remains stable for more than 200 h. This explains why no trace of azo compound is observed under helium (fast reduction of the nitrobenzene) whereas up to 23% is formed when the reaction is run under air (partial quenching of the reduction by oxygen). The reduction of *p*-chloronitrobenzene to the nitroso derivative is accompanied by oxidation of the solvent (2-propanol) to acetone and formation of water. Condensation of acetone with nitrosobenzene and hydrolysis of the condensation product lead to *p*-chloroaniline. Details of these steps will be presented in a forthcoming paper.

If oxygen is present, the initial anion may be quenched, giving rise to the reaction sequence depicted in eq 3–5.

$$\mathrm{ArNO_2^{-}\cdot} + \mathrm{O_2} \rightarrow \mathrm{ArNO_2} + \mathrm{O_2^{-}\cdot} \quad (3)$$

$$\mathrm{O_2^{-}\cdot} + \mathrm{ArX} \rightarrow \ \rightarrow \mathrm{ArOH} \quad (4)$$

$$\mathrm{RO^-} + \mathrm{ArX} \rightarrow \mathrm{X^-} + \mathrm{ArOR} \quad (5)$$

The formation of superoxide by reaction of nitroaryl radical ions with oxygen (eq 3) is well documented.[7] Reaction of superoxide with chloronitrobenzenes yields nitrophenols (eq 4) as shown both in the gas phase[8] and in solution.[8,9] It is likely that in 2-propanol this reaction occurs through the hydroperoxide ion formed according to the equilibrium $2\mathrm{O_2^{-}\cdot} + \mathrm{ROH} \rightleftarrows \mathrm{O_2} + \mathrm{HO_2^-} + \mathrm{RO^-}$,

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Table I. Reaction of *p*-Chloronitrobenzene (0.03 M) with Potassium Alkoxides (0.24 M)[a]

ROH	atmosphere	t, h[b]	% ArOR[c]	% ArOH[c]	% azoxy[c]	% azo[c]	% amine[c]
EtOH	air	20	>95				
2-PrOH	air	20	9	5	33	23	28
t-BuOH	air	300		15	13	31	
2-PrOH	helium	1.3			65		13
2-PrOH	oxygen	45	40	12			

[a] At 75 °C, under the atmosphere described. [b] This is the time required for the disappearance of *p*-chloronitrobenzene. [c] The reaction products are the following: ArOR, *p*-nitrophenyl alkyl ether, where the alkyl group is ethyl or 2-propyl; ArOH, *p*-nitrophenol; azoxy, *p,p'*-dichloroazoxybenzene; azo, *p,p'*-dichloroazobenzene; amine, *p*-chloroaniline. The yields reported have been evaluated by gas chromatography.

whose constant has been shown to be greater than 10^8.[10]

Direct reaction of potassium alkoxide with *p*-chloronitrobenzene yields the aryl ether through the normal S_NAr mechanism (eq 5). In principle, the phenoxide could be formed via a base-catalyzed elimination from the aryl ether. Under our conditions ([*i*-PrOK] = 0.24 M, 75 °C, under oxygen), this reaction is, however, slower (only 5% of the starting ether reacted after 50 h) than the one leading to the phenol from chloronitrobenzene (12% formed after 50 h). Also, addition of water does not appreciably change the relative yields of ether and phenol.

The results presented call for caution in generalizing the behavior of nitro aromatics toward alkoxides and for a detailed reexamination of these reactions, now in progress in our laboratory.

Experimental Section

Materials and Solvents. Ethanol, 2-propanol, and *tert*-butyl alcohol were purified by distillation from magnesium turnings. *p*-Chloronitrobenzene, *p*-chloroaniline, and *p*-nitrophenol were commercial products recrystallized until pure by GLC. *p,p'*-Dichloroazoxybenzene, mp 154–155 °C,[11] *p,p'*-dichloroazobenzene, mp 186–187 °C,[12] *p*-chloronitrobenzene, mp 85–87 °C,[13] *p*-nitrophenyl ethyl ether, mp 59–60 °C,[14] *p*-nitrophenyl 2-propyl ether, mp 32–33 °C,[14] and *p*-nitrophenyl *tert*-butyl ether, bp 123–125 °C (0.5 mmHg),[15] were prepared according to published procedures.

General Reaction Procedures. Typical procedures for the reactions under helium or under oxygen were as follows:

Under Helium. Solutions of *p*-chloronitrobenzene (0.157 g) and tetracosane (0.053 g) in 2-propanol (20 mL) and of potassium 2-propoxide in 2-propanol (10 mL of a 0.72 M solution), in the side arms of an inverted Y-shaped tube, were carefully and repeatedly deaerated under helium by using the thaw–freeze procedure and thermostatted at 75 °C. At zero time the solutions were mixed by inverting the Y-tube. Aliquots were withdrawn at appropriate time intervals, diluted with a mixture of 95% ethanol and ethyl ether, quenched with solid CO_2, and analyzed by GLC and/or UV.

Under Oxygen. A solution of *p*-chloronitrobenzene (0.237 g) and tetracosane (0.075 g) in 2-propanol (25 mL) in a three-necked flask equipped with a reflux condenser, a gas inlet tube, and a rubber septum was deaerated by bubbling oxygen through for 15 min at 75 °C. A solution of potassium 2-propoxide in 2-propanol (25 mL of a 0.48 M solution) was injected at zero time and the reaction solution was kept in a thermostat at 75 °C under a continuous flow of oxygen. Aliquots withdrawn by a syringe at appropriate time intervals were analyzed by GLC (*p*-chloronitrobenzene and *p*-nitrophenyl 2-propyl ether) and UV (*p*-nitrophenol).

Analytical Procedures. GLC analyses were performed on a Varian 3700 gas chromatograph coupled to a Varian CDS 111 Digital Integrator with a 150 cm × 2 mm 10% UCW 982 on 80/100 Chromosorb WAW DMCS column. Concentrations were determined by calibration curves with tetracosane as internal standard. UV analyses were made on appropriate aliquots (2 mL) of the reacting solutions diluted with 2-propanol and examined at 416 nm on a Cary 219 instrument for the amount of potassium *p*-nitrophenoxide (ϵ 2.37 × 10^4 in 2-propanol at 416 nm and 25 °C).

Registry No. *p*-Chloronitrobenzene, 100-00-5; potassium ethoxide, 917-58-8; potassium isopropoxide, 6831-82-9; potassium *tert*-butoxide, 865-47-4; *p*-nitrophenyl ethyl ether, 100-29-8; *p*-nitrophenyl 2-propyl ether, 26455-31-2; *p*-nitrophenol, 100-02-7; *p,p'*-dichloroazoxybenzene, 614-26-6; *p,p'*-dichloroazobenzene, 1602-00-2; *p*-chloroaniline, 106-47-8.

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N-Nitroaziridines: Structure Confirmed[1a]

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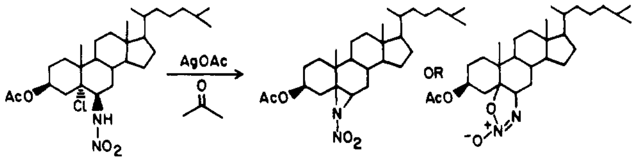
The first synthesis of *N*-nitroaziridine 2 was reported recently by Haire and Boswell.[2] The unique substitution of a nitro group on an aziridine nitrogen afforded a structure which was of interest both chemically and biologically. This class of compounds showed interesting thermal reactivity, reported earlier,[2] but none of the *N*-nitroaziridines tested have shown biological activity.



1 2 3

N-Nitrosoaziridines are known to decompose spontaneously at −15 °C.[3] Thus, it was surprising that the *N*-nitroaziridines appear to be quite stable at room temperature. In fact, rearrangement of 2 occurs at 180 °C. Support for structure 2 rested solely on spectroscopic and solvolytic data which were consistent but not conclusive for the *N*-nitroaziridine. The oxadiazole oxide structure 3 was suggested as an alternative to fit the experimental results.[4]

We now report on the X-ray crystal study which confirms the originally proposed structure 2. The important bond distances and angles are given in Table I (Supple-

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