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NUCLEOPHILIC RADICAL AROMATIC SUBSTITUTION WITH SUPEROXIDE ION

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The aliphatic nucleophilic substitution of halides and other leaving groups by O_2^- has been the subject of several reports.[1-8] Nevertheless, little has yet appeared on the interaction between O_2^- and aromatic compounds.

We observed that indeed nucleophilic displacement of halogen ion by O_2^- can occur at the aromatic ring activated by electron withdrawing substituents such as nitro groups. Thus halonitrobenzenes are efficiently converted to the corresponding nitrophenols by treatment with KO_2-crown ether complex in benzene.[9]

The results are summarized in the Table I.

In a typical experiment, 1-bromo-2,4-dinitrobenzene (247 mg, 1 mmole), KO_2 (284 mg, 4 mmole) and dicyclohexyl 18-crown-6 (744 mg, 2 mmole) in dry benzene (100 ml) were stirred in the dark for 3 hr. The solution was acidified with conc. HCl and the aqueous layer was washed several times with benzene.[10] The organic solution was dried over $MgSO_4$ and evaporated. The residue was chromatographed on silica gel to yield 2,4-dinitrophenol (174 mg). The reaction did not occur in the absence of crown ether.

The relative order of halogen displacement was determined by reacting competitively all four 1-halo-2,4-dinitrobenzenes with KO_2 and following the dissapearance of the starting material by GC in the initial stages of the reaction.[11] The order of reactivities was shown to be F > Br ∿ I > Cl in a ratio 6:4:1 respectively.

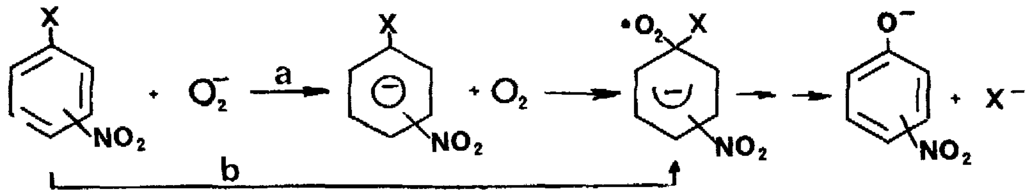
Table I

Substrate	Product (% yield)
1-fluoro-2,4-dinitrobenzene	2,4-dinitrophenol (95%)
1-chloro-2,4-dinitrobenzene	"
1-bromo-2,4-dinitrobenzene	"
1-iodo-2,4-dinitrobenzene	"
2-bromonitrobenzene	2-nitrophenol (55%)
4-bromonitrobenezene	4-nitrophenol (80%)
1,2-dinitrobenzene	2-nitrophenol (53%) + 2,4-dinitrophenol (4%)
1,3-dinitrobenzene	2,4-dinitrophenol (35%) + 3-nitrophenol (31%)
1,4-dinitrobenzene	4-nitrophenol (90%)

Furthermore, competition studies between 1-bromo-2,4-dinitrobenzene and 2-bromonitro benzene or 4-bromonitrobenzene indicated that the dinitro analog reacted at least 100 times faster than the latter. It was noted that no phenols resulting from the elimination of a nitro group rather than the halogen, could be detected in either reaction. However unsubstituted dinitrobenzenes react with O_2^- to give nitrophenols resulting from the displacement of one nitro group. The reaction of 1,2 and 1,3-dinitrobenzenes yielded in addition to the expected mono-nitrophenols, 2,4-dinitrophenol. For the 1,3-dinitrobenzene its formation can be explained by enhanced activation of the 4 position by the two nitro groups working in concert. The mechanism of formation of small amounts of this dinitrophenol from ortho analog is unclear.

The replacement of bromine by the second nitro group was found to increase the susceptibility of the compound to O_2^-. Thus 1,2-dinitrobenzene reacts at least 25 times faster than 2-bromonitrobenzene and 1,4-dinitrobenzene reacts 3 times faster than 4-bromonitrobenzene, as estimated in competitive reactions following the disapearance of the starting material.

Rapid electron transfer from superoxide ion to nitro substituted aromatic hydrocarbons to generate anion radical was reported by us.[12] Consequently it is possible that the present reaction involves as the first step a) an electron transfer from O_2^- to the substituted benzene to yield the anion radical which is subsequently scavenged by molecular oxygen,[13] or alternatively, b) the direct addition of O_2^- to the aromatic ring according to the general pattern of the nucleophilic aromatic substitution.[14]



Scheme I

In order to discriminate between these two possibilities the following experiment was performed. 1-Bromo-2,4-dinitrobenzene (12 mg) was reacted with ^{18}O-enriched KO_2[15] (86% ^{18}O,) (14 mg) - crown ether (37 mg) complex in an oxygen ^{16}O, saturated solution of 200 ml benzene. The mass spectrum of the resulting phenol revealed the presence of an ^{18}O-tag of less than 10%. *A control experiment performed with identical amounts of reactants in 10 ml air-saturate* benzene, led to a phenol carrying an ^{18}O tag of 72%. This result implies that the phenolic oxygen is incorporated, in large part after the equilibration with molecular oxygen dissolved in the solution according to reaction path a. This result contrasts the similar nucleophilic substitution by $O_2^{\cdot-}$ with aliphatic substrates which occurs with inversion of configuration and thus excludes a mechanism which involves a one-electron transfer process.[4,5,6,7]

Attempts were made to detect by ESR technique the paramagnetic specia, immediately following the mixing of the two reactants. Thus well resolved spectra of the corresponding radical anions could be recorded for 1,3-dinitrobenzene (a^N=4.6, a^H_2 = 3.1, $a^H_{4,6}$=4.2, a^H_5=1) and 1,4-dinitrobenzene (a^N=1.7, a^H=1.1). 3-Bromonitrobenzene was also easily reduced by KO_2 to the corresponding radical anion (a^N=8.7, $a^H_{2,6}$=3.0, a^H_4=4.0, a^H_5=1.2),but the usual work-up ended in the complete recovery of the starting material. A similar stability of the radical anion toward molecular oxygen was observed when nitrobenzene was reacted with KO_2.[12] The absence of detectable radical anions from the other compounds tested, is most probably due to their extensive sensitivity to molecular oxygen. Thus the corresponding radical anions prepared by electrochemical reduction in oxygen-free solutions were indeed very rapidly destroyed by the admittance of air into the cell.

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