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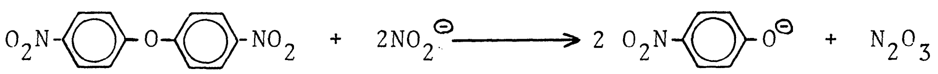
DEALKYLATION OF ALKYL ARYL ETHERS BY NITRITE ION

Tamio SAKAI, Nobuhisa YASUOKA, Hiroshi MINATO, and Michio KOBAYASHI
Department of Chemistry, Tokyo Metropolitan University, Fukazawa, Setagaya,
Tokyo 158

When an alkyl aryl ether possessing an electron-withdrawing substituent at its para position was heated with sodium nitrite in HMPA, it was dealkylated and the corresponding phenol was formed. This novel reaction was studied with various alkyl aryl ethers using oxygen-18 and an optically-active compound, and this ether cleavage was found to proceed by an S_N2 attack of nitrite on the alkyl carbon atom.

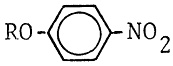
In aprotic polar solvents, nucleophilicity of nitrite ion is greatly enhanced, and various new reactions take place. We found that in a mixture with nitroarenes and HMPA(hexamethylphosphoric triamide) or DMSO, nitrite ion exchanges with the nitro group.[1] During the course of this study, we also found that 4,4'-dinitrophenyl ether is cleaved by nitrite ion in HMPA.



When this reaction was applied to alkyl aryl ethers, it was found that ethers with electron-withdrawing substituents at para positions (p-nitroanisole, p-methoxyacetophenone, p-cyanoanisole, and p-methoxyphenyl phenyl sulfone) were readily converted to the corresponding phenols when they were heated with nitrite ion in HMPA. m-Nitroanisole was demethylated in a similar manner. In the case of p-nitroanisole, the yield was more than 90%.

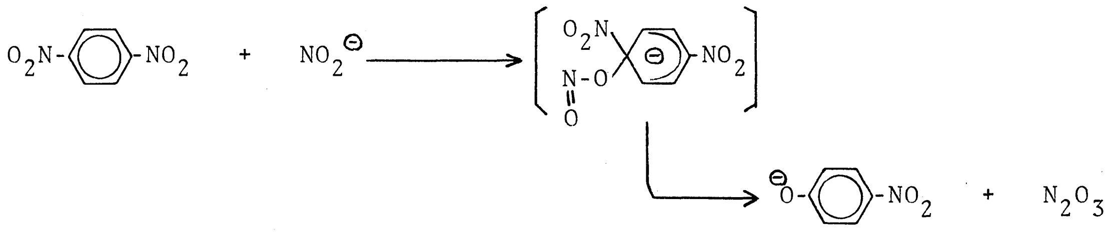
Various methodsfor cleaving ethers are reported, but most of them involve Lewis acids (HI, $AlCl_3$, BBr_3, etc).[2] 2,4,6-Trinitroanisole and 2,4-dinitroanisole were demethylated in refluxing pyridine, but m- or p-nitroanisole was not demethylated with pyridine.[3] The dealkylation with nitrite ion in HMPA described in this communication is the first example of cleaving m- and p-nitroanisole with a nucleophile.

The rates of dealkylation of various alkyl p-nitrophenyl ethers with nitrite ion in HMPA were determined. The dealkylation of primary and secondary alkyl ethers was of first order both in the substrate and in sodium nitrite. In t-butyl p-nitrophenyl ether, the reaction was of first order in the substrate alone. The results are shown in Table 1.

Table 1. Rate Constants of Dealkylation of  at 150°C

R	k_2 (l/mol·sec)	k_1 (sec^{-1})
Me	2.6×10^{-3}	
Et	2.5×10^{-4}	
i-Pr	0.35×10^{-4}	
t-Bu		2.4×10^{-5}
Benzyl	6.7×10^{-4}	
1-Methylheptyl	9.4×10^{-6}	
Neopentyl	no reaction	

In the cleavage of 4,4'-dinitrophenyl ether described above and in the formation of p-nitrophenol from p-dinitrobenzene, Meisenheimer-type intermediates are probably involved.

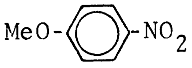
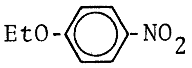
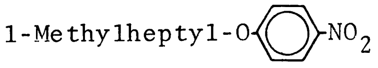
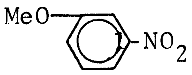
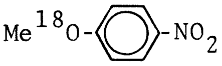
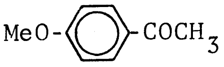


However, the rates of dealkylation shown in Table 1 were in the order of Me > Et > i-Pr > 1-methylheptyl >> neopentyl, and they are similar to those observed in S_N2 reactions of alkyl halides.

In order to determine whether or not this dealkylation proceeds via a Meisenheimer-type intermediate, various alkyl aryl ethers were dealkylated with $NaN^{18}O_2$. $Me^{18}O-C_6H_4NO_2$-p was also prepared and allowed to react with $NaNO_2$ in HMPA. The results are shown in Table 2.

Table 2 clearly shows that the ether oxygen of an alkyl aryl ether becomes the phenolic oxygen atom. It is clear that alkoxy groups are not displaced by nitrite ion, and Meisenheimer-type intermediates are not involved.

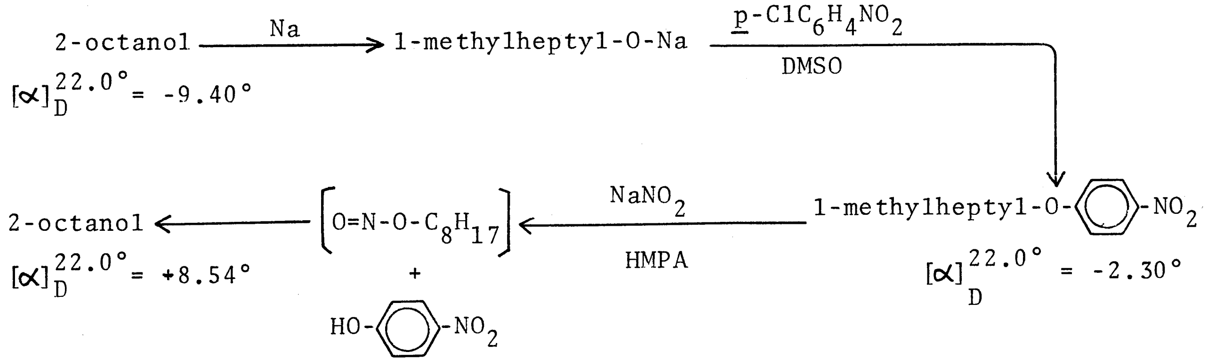
Table 2. Results of Reactions between R-O-Ar and $\mathrm{NaN^{18}O_2}$ and between $\mathrm{Me^{18}O\text{-}C_6H_4\text{-}NO_2}$-p and $\mathrm{NaNO_2}$[a]

Substrate	Nitrite	^{18}O Excess atom % in nitrite ion or in aryl ether	^{18}O Excess atom % in the phenol produced
	$\mathrm{NaN^{18}O_2}$	0.84 %	0.004 %
	$\mathrm{NaN^{18}O_2}$	1.11	0.008
	$\mathrm{NaN^{18}O_2}$	1.11	0.008
	$\mathrm{NaN^{18}O_2}$	1.11	0.002
	$\mathrm{NaNO_2}$	0.19[b]	0.18[b]
	$\mathrm{NaN^{18}O_2}$	0.84	0.009

[a] The reaction temperature was 150°C.

[b] The calculated value for the aryloxy oxygen is 3 times this figure.

When optically-active 1-methylheptyl p-nitrophenyl ether was allowed to react with sodium nitrite in HMPA, more than 90% of the 2-octanol produced was found to be of inverted configuration.[4]



These results show that dealkylation of primary and secondary alkyl aryl ethers with nitrite ion in HMPA is not a two-step reaction involving a Meisenheimer-type intermediate, but an S_N2-type reaction on the alkyl carbon atoms.

REFERENCES AND NOTES

1. M. Kobayashi, T. Sakai, and H. Minato, Chem. Lett., 1253 (1975).
2. L. F. Fieser and M. Fieser, "Advanced Organic Chemistry," Reinhold Publishing Co., New York, N. Y., 1961, p. 308.
3. R. S. Cahn, J. Chem. Soc., 1121 (1931).
4. It has been shown that the hydrolysis of (-)-1-methylheptyl nitrite proceeds with retention of configuration.[5]
5. A. D. Allen, J. Chem. Soc., 1968 (1954).

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