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Isotope Effect in Oxidative Nucleophilic Substitution of Hydrogen in Nitroarenes

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Abstract: In a series of competitive experiments with labelled nitrobenzenes carried out in liquid ammonia at -70 °C it was shown that the rate of oxidative substitution of hydrogen with the carbanion of 2-phenylpropionitrile is *ca.* 9.8 times faster than the analogous substitution of deuterium in 4-D-nitrobenzene and perdeuterionitrobenzene. Thus $C_{arom.}$-H bond breaking is the rate limiting step of the oxidative process.

Keywords: Carbanions, nucleophilic aromatic substitution, oxidation, reaction mechanism

In our previous papers we have reported that addition of the carbanion of 2-phenylpropionitrile (1^-) to nitrobenzene proceeds quantitatively in liquid ammonia at -70 °C giving a relatively stable σ^H adduct. Subsequent treatment of this solution with $KMnO_4$ results in rapid oxidation of the σ^H adduct to 2-(4-nitrophenyl)-2-phenylpropionitrile (2)[1]. This oxidative nucleophilic substitution of hydrogen (ONSH) proceeds selectively in *para* position and is of general character in respect to nitroarenes which can contain a variety of substituents[2]. Nevertheless some substituents inhibit partially or totally the oxidation of the σ^H adducts. For example, although addition of 1^- to 3-fluoro-5-iodonitrobenzene and 3,5-dichloronitrobenzene and formation of the σ^H adducts proceeds quantitatively, they are oxidized to a negligible extent so the ONSH products are formed in 9 % and 1 % yield correspondingly.

ONSH in electrophilic arenes, including nitroarenes is a common process[3,4], nevertheless practically nothing is known about its mechanism and the rate limiting steps of the oxidation process of the intermediate σ^H adducts. Here we would like to report that in the permanganate oxidation of the σ^H adducts of 1^- to nitrobenzene the rate limiting step is $C_{arom.}$-H bond breaking. This information was obtained from measurement of kinetic isotope effect **kie** (k_H/k_D) of the oxidation process. The value of **kie** was measured in competitive experiments in which equimolar mixtures of σ^H and σ^D adducts of 1^- to nitrobenzene and 4-D-nitrobenzene[5], as well as perdeuterionitrobenzene were oxidized with small amounts of permanganate. We have pre-

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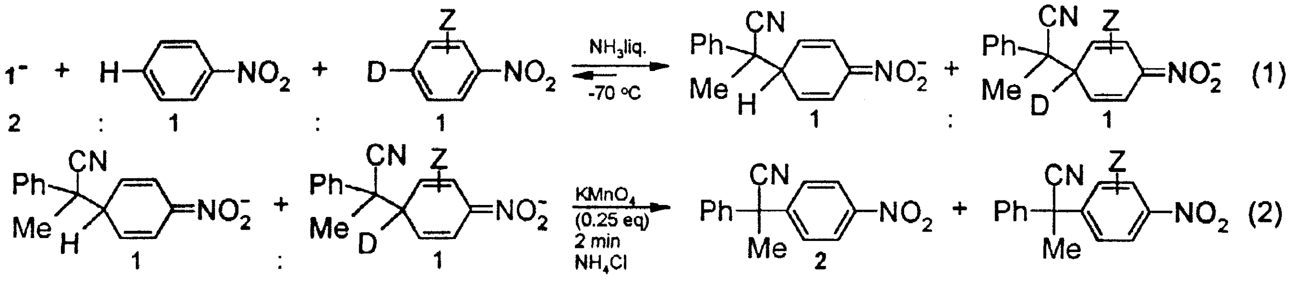
viously shown that **1**$^-$ adds to nitrobenzene quantitatively in liquid ammonia at -70 °C. The addition is also quantitative to 4-D-nitrobenzene and perdeuterionitrobenzene. Thus in the reaction (1) an equimolar mixture of σ^H and σ^D adducts is produced and then oxidized with potassium permanganate (2).



Z = H and Z = 2,3,5,6-D_4

After oxidation the mixture was analysed for the products and the recovered nitrobenzenes using MS and GC/MS. When Z=H the ONSH products of nitrobenzene and 4-D-nitrobenzene were identical and therefore the relative rates of σ^H and σ^D adduct oxidation had to be calculated from ratios of the recovered nitrobenzene and 4-D-nitrobenzene, giving k_H/k_D=9.79±0.50. For Z=D the relative rates could be calculated from ratios of the ONSH products[6] and also the recovered nitrobenzenes giving similar values of k_H/k_D=9.85±0.30. This good agreement confirms validity of the method and also the insignificant value of eventual effects of deuterium in vicinal and more remote positions. High values of kie indicate unambiguously that $C_{arom.}$-H bond breaking is the rate limiting step of ONSH.

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References and Footnotes:

[1] Mąkosza M, Staliński K, Klępka C. Chem. Commun. 1996;837-838.

[2] Mąkosza M, Staliński K. Eur. J. Chem. 1997;3:2025-2031.

[3] Terrier F. Nucleophilic Aromatic Displacement. Weiheim: Verlag Chemie, 1991.

[4] Chupakhin ON, Charushin VN, van der Plas HC. Nucleophilic Aromatic Substitution of Hydrogen. San Diego: Academic Press, 1994.

[5] Nitrobenzene-D_5 was a commercial product of 99 % purity from Dr. Glaser AG; 4-D-Nitrobenzene of 94 % isotopic purity was obtained by a modified procedure (Hoeg JH. J. Labelled Compd. 1971;7:179) in the following manner: to dry 4-nitrobenzenediazonium tetrafluoroborate (7 g) suspended in D_2O (100 mL) deuterated hypophosphorous acid (50 %, 11.2 g) was added. The mixture was vigorously stirred at room temperature for 30 min, the product was extracted with CH_2Cl_2 and purified by column chromatography on silica gel, yield 64 %.

[6] Spectral data of 2-(2,3,5,6-tetradeuterio-4-nitrophenyl)-2-phenylpropionitrile: M.p. 76-77 °C (EtOH); δ_H (acetone-d_6): 2.22 (3H, s, Me), 7.34-7.54 (5H, m, Ph); **MS** (EI), m/z (%): M^+ 256 (52), 241 (100), 210 (4), 195 (55), 182 (6), 167 (4), 130 (6), 103 (8), 77 (7), 51 (3); **IR** (KBr): 2236 (CN), 1513 and 1345 (NO_2); **Elementary Analysis**: calculated for $C_{15}H_8D_4N_2O_2$ (D=2H): C 70.29, H 4.68, N 10.93; found: C 70.30, H 4.42, N 10.85.