

Synthesis of o-, m- and p-Deuterio-, [¹⁵N]- and mono[¹⁸O]Nitrobenzene

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For the determination of the complete substitution structure of nitrobenzene the microwave spectrum of the parent species ⁽¹⁾ and all different monoisotopically substituted nitrobenzenes ⁽²⁾ must be analysed. The synthesis of a statistical mixture of the four different mono[¹³C]nitrobenzenes has been described previously ⁽³⁾. This note reports the syntheses of [2-D]-, [3-D]-, [4-D]-, [¹⁵N]- and mono[¹⁸O]nitrobenzene.

[2-D]-, [3-D]- and [4-D]nitrobenzene was prepared according to the method described by Murray and Williams ⁽⁴⁾. 2.76 g (20 mmole) of the particular nitroaniline was dissolved in 8 ml HCl conc. and 10 ml D₂O. The solution was cooled and diazotised with 1.44 g NaNO₂ in 3.5 ml D₂O. Hypophosphorous acid was deuteriated by exchange with D₂O at room temperature. After exchanging three times, each time letting a mixture of equal volumes of H₃PO₂ and D₂O react for 72 hours, an NMR-spectrum showed that at least 90 % of all the protons had been eliminated from the hypophosphorous acid. The diazonium salt was reduced with 10 ml 50 vol % D₃PO₂ in D₂O, and the solution was neutralised with NaOH conc., extracted with ether and distilled on the vacuum line. The fraction 2.0-0.1 mm Hg was collected. The yields were 1.03 g, 0.89 g and 0.93 g (42 %, 36 % and 38 %) of [2-D]-, [3-D]- and [4-D]nitrobenzene, respectively. The mass spectra showed that the isotopic purity was ~50 % in each case.

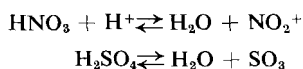
[¹⁵N]- and mono[¹⁸O]nitrobenzene were prepared by nitration of benzene with the corresponding nitric acid.

¹⁵N was available as NH₄Cl enriched to 33 %. The ammonium ion was oxydised to nitrate by potassium permanganate ^(5, 6). In order to avoid any complications from the oxydation of the chloride ion, NH₄Cl was transformed to (NH₄)₂SO₄.

0.537 g labelled NH₄Cl (~10 mmole) was dissolved in 0.5 ml 18 M sulfuric acid. When the reaction was terminated, 10 ml H₂O and 2 M NaOH was added until pH = 3. The solution was mixed with 4.35 g KMnO₄ in an autoclave and heated at 180° C for 20 hours. The MnO₂ formed was filtered off, washed, and the filtrate evaporated to dryness. 2 ml 18 M H₂SO₄ was added very slowly and the salts dissolved. 1.5 ml benzene was added at 50° C over ½ hour, and the solution then refluxed at 70° C for 1 hour. After cooling, 5 ml H₂O was added, the solution made alkaline with 2 M NaOH

and extracted with 4×10 ml ether. The ether was dried (CaCl_2) and distilled off. Yield of labelled nitrobenzene : $0.284 \text{ g} \sim 2.3 \text{ mmole} \sim 23 \%$. The mass spectrum confirmed that $[\text{^{15}N}]$ nitrobenzene was present in 33% .

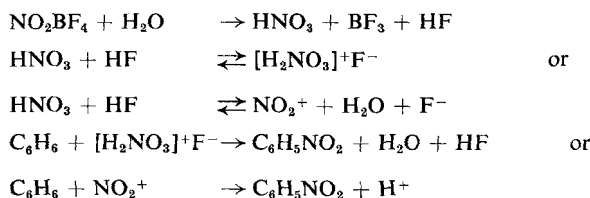
The synthesis of $[\text{^{18}O}]$ nitrobenzene *cannot* be performed by the usual nitration of benzene using conc. sulfuric acid and labelled nitric acid, since the ^{18}O -atoms via the equilibria :



will end up in the sulfuric acid molecules and thus altogether escape the actual nitration.

Pinchas *et al.* ⁽⁷⁾ suggested the use of a mixture of liquid hydrogen fluoride and labelled nitric acid. However, in order to avoid the slight inconvenience of handling liquid HF, the following very simple procedure was employed.

Reaction scheme :



It is not clear whether the nitronium or the nitracidium ion is the actual nitrating agent, since these ions probably are in equilibrium with each other ⁽⁷⁾.

Nitronium tetrafluoroborate NO_2BF_4 is commercially available from Schuchardt, Munich. $1.578 \text{ g NO}_2\text{BF}_4$ (11.8 mmole) was weighed off in a dry N_2 atmosphere and connected to the vacuum line. 0.212 g (11 mmole) ^{18}O labelled H_2O (32% enrichment) was slowly distilled onto the salt, and a quite violent formation of the gases HNO_3 , BF_3 and HF took place. The gases were in small portions distilled onto 1.5 ml dry benzene, and the nitration took place at room temperature. The benzene solution was stirred for 24 hours on the vacuum line and then heated to 60°C for 30 min. The solution was taken off the line, made alkaline with 2 M NaOH and extracted with $5 \times 3 \text{ ml}$ ether. The ether solution was dried (CaCl_2) and distilled. The yield of nitrobenzene was $0.534 \text{ g} \sim 4.4 \text{ mmole} \sim 40 \%$. The mass spectrum showed, that the isotopic purity was 20% , as expected, and that no detectable amount of $[\text{^{18}O}_2]$ nitrobenzene had been formed.

The method just described was found very simple and advantageous for small quantities, since the full synthesis could be carried out on the vacuum line as one process without isolation of any intermediate products. Further, this method is specific for mono $[\text{^{18}O}]$ nitrobenzene.

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