NITRATION OF BENZOTRIAZOLE N-OXIDE

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The nitration of benzotriazole N-oxide with dilute nitric acid gives the 7-nitro derivative, whereas nitration with a mixture of nitric and acetic acids gives isomers with nitro groups in the 5 and 7 positions in a ratio of 1 : 9.

The conversion of heterocyclic bases to N-oxides increases their reactivities in electrophilic substitution reactions [1], and this makes it possible to prepare difficult-to-obtain nitro derivatives of heterocyclic compounds.

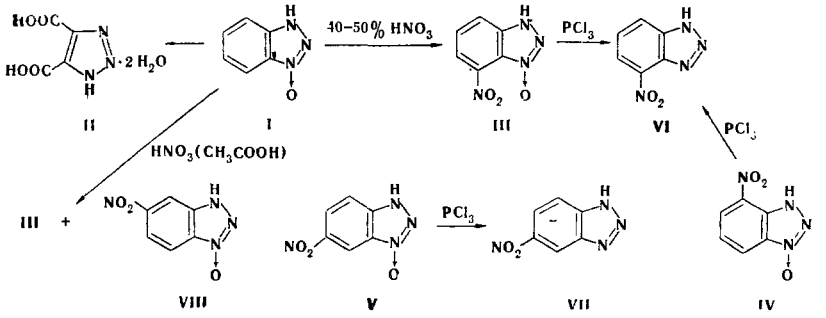
Benzotriazole is nitrated only under severe conditions to give a dinitro derivative [2]. The nitration of benzotriazole N-oxide (I) with a mixture of acetic and nitric acids leads to 6-nitrobenzotriazole N-oxide [3]; nitration with other nitrating agents has not been studied.

We have established that the reaction of I with nitrating agents depends to a considerable degree on their nature. Thus we were unable to bring about its nitration in sulfuric and nitric acid mixtures, probably because of protonation of the N-oxide and the formation of a cation having a low reactivity (pK_{BH^+} −0.95) [4]. In addition, oxidative destruction was observed under severe conditions, since 1,2,3-triazole-4,5-dicarboxylic acid (II) was isolated in small amounts.

Attempts to nitrate I in the free base form, for which nonacidic nitrating agents were used, were unsuccessful. Nitration with nitronium tetrafluoroborate in acetonitrile or ethyl acetate does not occur because of the limited solubility of I.

The nitration of I to give a mononitro derivative in 50% yield takes place in dilute nitric acid. From a comparison of the physicochemical characteristics [PMR spectra and thin-layer chromatography (TLC)] of product III and 4- and 6-nitrobenzotriazole N-oxides [5], it follows that structures IV and V of the 4- and 6-nitro isomers are excluded for III.

The same product — 4(7)-nitrobenzotriazoles (VI) — was isolated as a result of selective reduction of N-oxides IV and III. This is possible if the nitro group in III is in the 7 position. For comparison, we reduced the N-oxide group in 6-nitrobenzotriazole N-oxide V; the product was 5(6)-nitrobenzotriazole (VII).



The nitration of I with a mixture of acetic and nitric acid proceeds somewhat differently. According to the PMR spectra and the TLC data, in this case, despite the data in [3], a mixture of two nitro compounds is formed instead of an individual substance. The major portion (~90%) consists of III. We were unable to isolate the second nitro derivative in pure form, but judging from the results of an analysis of the mixture, it is also a

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mononitrobenzotriazole N-oxide. The character of its PMR spectra corresponds to 5-nitrobenzotriazole N-oxide (VIII).

Attempts to introduce a second nitro group in N-oxides III-V did not give positive results.

EXPERIMENTAL

The IR spectra of the compounds were recorded with a UR-20 spectrometer. The PMR spectra of DMSO solutions of the compounds were recorded with a Perkin–Elmer R-12 spectrometer (60 MHz) at 40° with hexamethyldisiloxane as the internal standard. Thin-layer chromatography (TLC) was carried out on LSL-254 5/40μ silica gel in an acetone–heptane system (2 : 1).

Nitration of Benzotriazole N-Oxide with a Mixture of Sulfuric and Nitric Acids. A total of 3.6 ml of a mixture prepared from 1.4 ml of HNO_3 (sp. gr. 1.51) and 2.2 ml of concentrated H_2SO_4 was added with stirring at 0-5° to a solution of 2.7 g of benzotriazole N-oxide in 20 ml of H_2SO_4 (sp. gr. 1.82) at 0-5°, after which the mixture was allowed to stand at 20° for 1 h. It was then poured over ice, and the precipitate was removed by filtration and washed with water to give 0.3 g (8%) of 1,2,3-triazole-4,5-dicarboxylic acid II with mp 198° (from water, mp 198° [6]). Found: C 24.6; H 1.8; N 21.4%. $C_4H_3N_3O_4 \cdot 2H_2O$. Calculated: C 24.8; H 1.5; N 21.7%. IR spectrum, cm^{-1}: 1730 (C=O) and 3300 (NH).

7-Nitrobenzotriazole N-Oxide (III). A) A 10-g (74 mmole) sample of N-oxide I was added with stirring at 20° to 45.5 ml of dilute HNO_3 (sp. gr. 1.25), after which the mixture was allowed to stand at 60° for 2 h. It was then cooled and poured over ice, and the product was removed by filtration and washed with water to give 6.6 g (50%) of a product with mp 187° (aqueous ethanol) and R_f 0.57. Found: C 39.4; H 2.6; N 30.8%; M 188 (potentiometrically). $C_6H_4N_4O_3$. Calculated: C 40.0; H 2.2; N 31.3%; M 180. IR spectrum, cm^{-1}: 1550 and 1355 (nitro group); 1255 (N→O). PMR spectrum: 8.55 q (6-H), 8.37 q (4H), 7.66 ppm q (5H); J_{4-6} 1.5, J_{5-6}, and J_{4-5} 8 Hz.

B) A 9.5-g (70 mmole) sample of I was dissolved in 19 ml of acetic acid, and 5.7 ml of HNO_3 (sp. gr. 1.51) was added slowly with stirring at 20°. The temperature of the reaction mixture rose spontaneously to 90°. It was then allowed to stand at 50° for 2 h, after which it was cooled, and the crystalline precipitate (2.6 g) was removed by filtration. Dilution of the mother liquor with water gave an additional 3.7 g of the nitro product for an overall yield of 6.3 g (50%) of a product with mp 178° (from aqueous ethanol). Found: C 39.5: H 2.4; N 31.0%. $C_6H_4N_4O_3$. Calculated: C 40.0; H 2.2; N 31.3%. IR spectrum, cm^{-1}: 1550 and 1355 (nitro group); 1265 (N→O).

The chromatogram of the product contained two spots: the first spot (R_f 0.57) was assigned to III, and the second spot (R_f 0.40) was assigned to VIII. The R_f values of N-oxides IV and V, which were found to be 0.34 and 0.50, respectively, were determined for comparison.

Signals at 9.08 (b), 8.69 (m), and 8.06 (m), in confirmity with the spectrum of VIII, were noted in the PMR spectrum of the mixture, along with a group of signals of product III.

Reduction of 7-Nitrobenzotriazole N-Oxide. A mixture of 1.5 g of III, 30 ml of phosphorus trichloride, and 100 ml of ethyl acetate was heated at 70° for 12 h, after which the solvent and phosphorus oxychloride were removed by vacuum distillation. The residue was treated carefully with ice water, and the precipitated VI was removed by filtration, washed with water, and purified by crystallization from ethanol to give a product with mp 233°. The melting point of a mixture of this product with 4(7)-nitrobenzotriazole [5] was 234-235°.

5(6)-Nitrobenzotriazole VII. This compound, with mp 202° (mp 205° [7]), was obtained by reduction of V under conditions similar to those in the synthesis of VI.

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