

A Novel Dioxano-annellated Benzofuroxan

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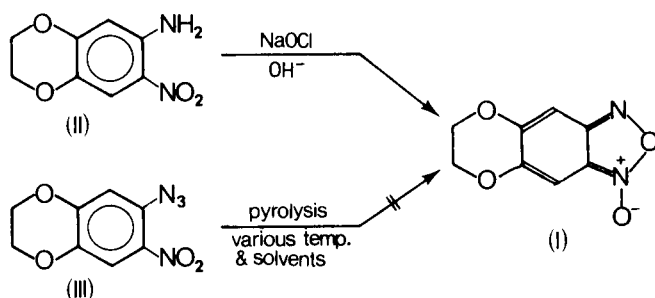
Oxidation of 6-amino-7-nitro-1,4-benzodioxane using alkaline hypochlorite affords 1,4-benzodioxano[6,7-c]furoxan in a very good yield. Pyrolysis of 6-azido-7-nitro-1,4-benzodioxane failed to give the same product. The structure of the new furoxan is confirmed by the spectra.

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Very few benzofuroxans with an heterocyclic ring annellated in the 5,6-positions of benzofuroxan have been described.

The synthesis of 1,4-benzodioxano[6,7-c]furoxan (I) is now reported with supporting evidence from spectral data (uv, ir, nmr and mass spectra).

This new furoxan (I) is prepared in a very good yield (67%) by oxidation of 6-amino-7-nitro-1,4-benzodioxane (II), using alkaline hypochlorite according to the method of Green and Rowe (1).



Many attempts to prepare 1,4-benzodioxano[6,7-c]-furoxan (I) by pyrolysis of 6-azido-7-nitro-1,4-benzodioxane (III), obtained according to the method of Bailey (2,3) from 6-bromo-7-nitro-1,4-benzodioxane (4), at various temperatures and using various solvents (ethanol, toluene, acetic acid, 1,2,3,4-tetrahydro-naphthalene, 1,3,5-trichlorobenzene) met with no success. Either the starting material was recovered unchanged or a charring with unidentifiable products was taking place.

Compound II was also diazotized by Schoutissen's method (5) and after dilution with ice-water, was converted into the azide (III) by addition of aqueous sodium azide; refluxing of the azide in acetic acid gave no furoxan, but it turned to a mixture of compounds which are now in the procedure of identification.

The uv spectrum (ethanol) of compound I gives two maxima at 218 and 350 nm. The ir spectrum gives the expected furoxan ring absorptions at 1635 and 1595 cm⁻¹, with no trace of the nitro or amino group.

The structure of I is further confirmed by its nmr and mass spectrum. The nmr spectrum (in deuteriochloroform) consists of two singlets; one at δ 6.8 (2H), averaged signal, and another at δ 4.36 (4H), at the normal temperature of the instrument.

However, low temperature nmr measurements showed clearly that the aromatic singlet, after passing the coalescence temperature, splits into two signals of almost equal height. From the coalescence temperature for the fusion of these two signals, the free energy of activation ΔG^* (for the isomerization of the two furoxan forms) was determined to be 13.1 kcal/mol⁻¹.

Compound I shows an intense molecular ion at m/e 194; the ms fragmentation pattern has several intense peaks among which the $M-161^+$ (loss of oxygen) and $M-601^+$ (loss of N₂O₂) are prominent, as is frequently observed in furoxans (6).

EXPERIMENTAL

Melting points were determined on a Gallenkamp melting point apparatus and are uncorrected. Uv spectra were taken with a Perkin-Elmer 137 spectrophotometer. Ir spectra (nujol mull) were obtained on a Perkin-Elmer 257 grating spectrophotometer. Nmr spectra were determined with a Varian Associates A-60A instrument using deuteriochloroform as a solvent and tetramethylsilane as internal standard. Mass spectra were recorded on a Hitachi Perkin-Elmer RMU-6L spectrometer with a direct inlet system operating at 70 ev. Microanalyses were performed by the Analytical Department of this University. Calcium sulfate was the drying agent used.

6-Amino-7-nitro-1,4-benzodioxane (II).

Compound II was prepared according to the method of Heertjes and Revallier (7) starting from 1,4-benzodioxane which was nitrated to give 6-nitro-1,4-benzodioxane; reduction of the latter compound gave 6-amino-1,4-benzodioxane which was isolated as the hydrochloride. Acetylation afforded 6-acetamido-1,4-benzodioxane which was again nitrated to give 6-acetamido-7-nitro-1,4-benzodioxane. Hydrolysis of the last compound gave II in 79% yield, red crystals, m.p. 151-152°, lit. (7) 151.8-152.6°; ir: ν 3460, 3340 cm^{-1} (NH_2); nmr: δ 7.73 (s, 1, aromatic H *ortho* to NO_2), 6.3 (s, 1, aromatic H *ortho* to NH_2), 4.3 (s, 4, OCH_2), 1,4-Benzodioxano[6,7-*c*]furoxan (I).

A mixture of 0.11 g. (2 mmoles) of potassium hydroxide and 4 ml. of 95% ethanol in a small flask was heated on a steam bath until the solid dissolved. 6-Amino-7-nitro-1,4-benzodioxane (II) (0.3 g., 1.5 mmoles) was dissolved in the warm alkaline solution. The resulting deep red solution was then cooled to 0°, and 3 ml. of sodium hypochlorite solution was added slowly with magnetic stirring over the course of 10 minutes. (The solution of sodium hypochlorite was prepared immediately before it was to be used, and was kept in the dark at 0° until needed. A mixture of 5 g. (0.125 mole) of sodium hydroxide and 20 ml. of water was swirled until the solid dissolved. The solution was cooled to 0°, and 10 g. of crushed ice was added. The flask was then placed in an ice bath, and chlorine gas from a gas cylinder was bubbled through the solution until 4.1 g. (0.058 mole) was absorbed. An excess of chlorine should be avoided). During the addition of the hypochlorite the solution turned intense violet and then became orange yellow. The flocculent yellow precipitate was collected on a sintered glass funnel, washed with 2 ml. of water, and air-dried.

Two recrystallizations (charcoal added) from 70% ethanol gave fine gold yellow needles of the furoxan I, yield, 0.2 g. (67%), m.p. 203-204° dec. Tlc using carbon tetrachloride/chloroform (1:3) as the eluent showed the product to be homogeneous; uv (95% ethanol): λ max 218 nm ($\log \epsilon = 4.25$), max 350 (3.7); ir (nujol mull): ν 1635, 1595 cm^{-1} (furoxan ring); nmr (deuteriochloroform): δ 6.8 (s, 2, aromatic H), 4.36 (s, 4, OCH_2); mass spectrum (relative abundance): m/e 194 (M^+ , 63), 178 (38), 134 (58), 78 (40), 69 (59), 64 (52), 53 (35), 50 (100), 41 (25), 30 (35).

Anal. Calcd. for $\text{C}_8\text{H}_6\text{N}_2\text{O}_4$: C, 49.49; H, 3.12; N, 14.43. Found: C, 49.78; H, 3.09; N, 14.25.

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