

COUPLING OF NITROBENZIMIDAZOLES BY ZINC-AMMONIA REDUCTION

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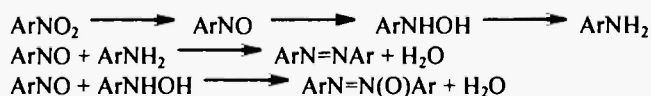
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Abstract: The couplings of 5-nitro-1*H*-benzimidazole and 5,6-dinitro-1*H*-benzimidazole to corresponding azo derivatives with zinc-ammonia reduction at room temperature were achieved. The structures of the new compounds were characterized by IR, MS and ¹H NMR spectroscopy.

Introduction

There are much many methods for the reduction of nitroarenes. Recently, metal mediate reactions have shown interest because of their simplicity and selectivity. (1-4). Catalytic reduction of nitro compounds, using metals such as zinc, tin, magnesium etc. is particularly important because it is a simple method for the synthesis of azo and azoxy compounds which have potent biological activities (5-8).

According to literature, the reduction of nitroarenes proceeds through nitroso and hydroxylamino intermediates. In addition to the formation of an amine, nitroso and amino groups can react to give azo compounds and the reaction of nitroso and hydroxylamino groups produces azoxy compounds (9, 10).



In this paper, the reductive coupling of nitrobenzimidazoles with zinc-ammonia-methanol system at room temperature is investigated. The preparation of 5-(1*H*-benzimidazol-5-yl diazenyl)-1*H*-benzimidazole and 6-amino-5-(6-amino-1*H*-benzimidazol-5-yl diazenyl)-1*H*-benzimidazole is reported.

Experimental

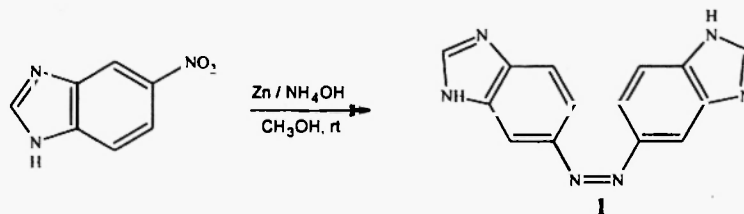
¹H NMR spectra were obtained in hexadeuteriodimethylsulfoxide with a Bruker DPX-400 spectrometer. Chemical shifts (δ) are reported in ppm and coupling constants (*J*) are reported in Hz. IR spectra in KBr discs were recorded on a Mattson 1000 FT-IR spectrophotometer and wavenumbers are given in cm⁻¹. Mass spectra were recorded on a Agilent GC-MSD spectrophotometer. Elemental analyses were performed with a LECO-932 C, H, N analyser. Melting points were determined on a Gallenkamp apparatus and are given uncorrected.

5-Nitro-1*H*-benzimidazole was purchased from Merck and 5,6-dinitro-1*H*-benzimidazole was prepared according to the literature procedure (11) (Scheme-1). Column chromatography purifications were carried out on Silica Gel (230-400 mesh).

Synthesis of 5-(1*H*-benzimidazol-5-yl diazenyl)-1*H*-benzimidazole **1**

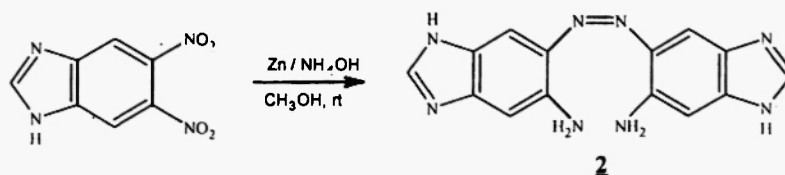
5-Nitro-1*H*-benzimidazole (1.63 g, 10 mmol) and methanol (10 ml) were placed in a 50 ml round-bottomed flask. NH₄OH (10 ml) was added to flask and the mixture was stirred at room temperature over 10 minutes to ensure complete dissolution. Zinc dust (1.30 g, 20 mmol) was added to the solution and stirring continued for 8h. The progress of the reaction was monitored by TLC. After completion, the reaction mixture was poured into water, extracted with diethylether (2 x 10 ml). The ether extract washed successively with water, 10% HCl and water, dried over anhydrous sodium sulfate and the solvent was removed. Further purification was achieved by column chromatography using chloroform:isopropanol (95:5) as eluent to give 5-(1*H*-benzimidazol-5-

ylidiazenyl)-1*H*-benzimidazole as yellow crystals in 70 % yield (mp 244-246^oC). MS; m/z: 262 [M⁺], 235, 180, 105. Anal. calc. for C₁₄H₁₀N₆: C, 64.12; H, 3.82; N, 32.06. Found: C, 64.08; H, 3.81; N, 32.01.



Scheme-1: Synthesis of 6-amino-5-(6-amino-1*H*-benzimidazol-5-ylidiazenyl)-1*H*-benzimidazole **1**

Similar reaction was carried out with 5,6-dinitro-1*H*-benzimidazole (0.3 g, 10 mmol) using NH₄OH (20 ml) and zinc dust (3.25 g, 50 mmol) and it was obtained 6-amino-5-(6-amino-1*H*-benzimidazol-5-ylidiazenyl)-1*H*-benzimidazole as brown powder, mp > 280 ^oC, (42 %). MS; m/z: 292 [M⁺], 260, 180, 105. Anal. calc. for C₁₄H₁₂N₈: C, 57.53; H, 4.11; N, 38.36. Found: C, 57.03; H, 4.00; N, 38.01.



Spectroscopic Properties

The structures of compounds **1** and **2** were examined by IR, MS and ¹H NMR spectroscopy. The elemental analysis results agreed with the structures determined.

The coupling was proved by the presence of a weak band in the region 1440 cm⁻¹ (-N=N- stretching vibration) in the IR spectra of the compounds **1** and **2**. Also, the IR spectrum of **2** indicated the characteristic absorption band of -NH₂ group at 3400-3500 cm⁻¹ (-NH₂ stretching vibration) showing that the reduction reaction 5,6-dinitro-1*H*-benzimidazole afforded an amino group in addition to the formation of azo bridge.

For ¹H NMR measurement, the samples were dissolved in hexadeuteriodimethyl sulfoxide. By comparison of ¹H NMR spectra of 5-nitro-1*H*-benzimidazole and their azo derivatives, the benzimidazole ring substituted with azo group could be easily detected. The chemical shifts of compound **1** displaced to upfield due to the less electron-withdrawing effect of azo group than that of nitro group. ¹H NMR δ of 5-nitro-1*H*-benzimidazole: 8.63 (d, *J* = 1.2 Hz, 1H), 8.37 (s, 1H), 8.25 (dd, *J* = 8.9, 2.2 Hz, 1H), 7.75 (d, *J* = 8.9 Hz, 1H). ¹H NMR δ of 5-(1*H*-benzimidazol-5-ylidiazenyl)-1*H*-benzimidazole **1**: 8.54 (d, *J* = 1.2 Hz, 1H), 8.45 (s, 1H), 8.23 (dd, *J* = 8.8, 1.9 Hz, 1H), 7.74 (d, *J* = 8.4 Hz, 1H).

The amino group on the benzimidazole ring caused upfield shifts the protons in the ortho- position for the compound **2**. ¹H NMR δ of 5,6-dinitro-1*H*-benzimidazole: 9.00 (s, 1H), 8.54 (s, 2H). ¹H NMR δ of 6-amino-5-(6-amino-1*H*-benzimidazol-5-ylidiazenyl)-1*H*-benzimidazole **2**: 8.85 (s, 2H), 8.72 (s, 2H), 7.61 (s, 2H).

The assignment observed at δ 12.80 proved the azo-hydrazone tautomerism in the solution for the compounds **1** and **2**(12). The appearance of a broad signal at δ 8.43 confirmed the presence of an amino group in compound **2**.

Results and Discussions

5-(1*H*-benzimidazol-5-yl-diazenyl)-1*H*-benzimidazole **1** and 6-amino-5-(6-amino-1*H*-benzimidazol-5-yl-diazenyl)-1*H*-benzimidazole **2** were prepared by a simple method based on the coupling of nitrobenzimidazoles. The reduction reaction can be accomplished at room temperature using commercial grade zinc dust-ammonia-methanol. This system reduced with ease nitrobenzimidazoles to corresponding azo derivatives. In previous papers, the reduction of dinitrobenzimidazoles using different reagents has been reported by author herself (2, 5). Here, in continuation of these investigations, zinc-ammonia reduction of 5-nitro-1*H*-benzimidazole and 5,6-dinitro-1*H*-benzimidazole is reported.

5-Nitro-1*H*-benzimidazole was reduced to 5-(1*H*-benzimidazol-5-yl-diazenyl)-1*H*-benzimidazole **1** by adding zinc dust to a solution of 5-nitro-1*H*-benzimidazole in methanol containing NH₄OH. It is remarkable that the reaction does not occur at room temperature when NH₄OH is replaced by NaOH and polymerisation occurs at elevated temperatures. As mechanistic studies showed, at the reduction reaction of nitroarenes, the coupling depends on the synchronous formation of two intermediate species either nitroso and hydroxylamino to give corresponding azoxy derivatives, or nitroso and amino to produce azo derivative. In the reaction conditions reported here, the formation of hydroxylamine was not observed. The coupling forming azo compound was detected by assignments of the ¹H NMR signals and the infrared spectroscopies.

Zinc-ammonia reduction of 5,6-dinitro-1*H*-benzimidazole gives 6-amino-5-(6-amino-1*H*-benzimidazol-5-yl-diazenyl)-1*H*-benzimidazole **2** as the major product. The condensation of nitroso and amino groups leads to the azo bridge formation. A detailed ¹H NMR and IR analysis described that the nitro group which could not give the reductive coupling reaction was reduced to corresponding amine. A second -N=N- bond formation can be hindered by a steric congestion which causes the reduction of the nitroso groups to be completed by the formation of amino group.

Conclusions

5-Nitro-1*H*-benzimidazole and 5,6-dinitro-1*H*-benzimidazole were reduced to 5-(1*H*-benzimidazol-5-yl-diazenyl)-1*H*-benzimidazole **1** and 6-amino-5-(6-amino-1*H*-benzimidazol-5-yl-diazenyl)-1*H*-benzimidazole **2** respectively by a simple method using zinc-ammonia system at room temperature.

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