Synthesis of Aminobenzotriazoles

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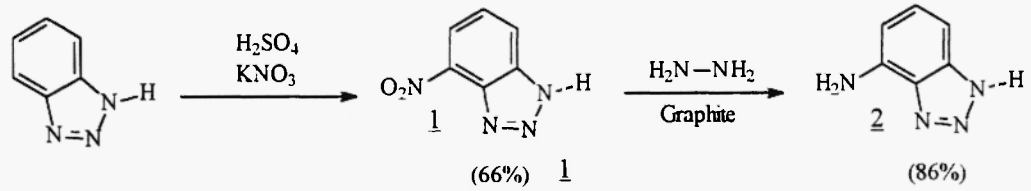
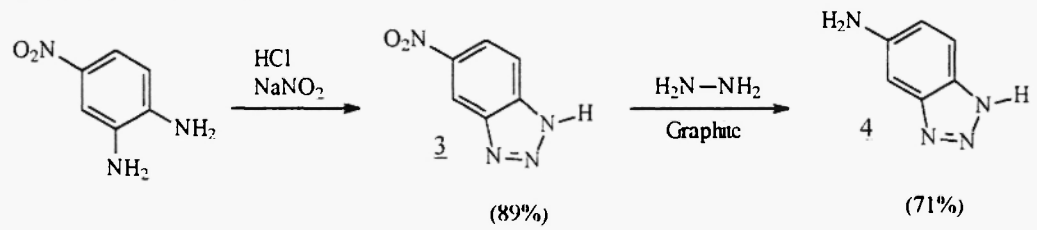
Abstract The synthesis of 4 and 5 aminobenzotriazole via reduction of a nitro group is described. Both routes include reduction at atmospheric pressure using hydrazine and graphite.

5-Aminobenzotriazole has recently become a much sought after item within our laboratory. The amine is widely used for formation of azo dyes (1) and is also of use synthetically as an amine moiety containing a metal complexing group. Demand for the compound lead to the commercially available stocks finishing and a waiting time of over one year for the 5-aminobenzotriazole. As such we decided to synthesise the compound ourselves from readily available starting materials. The previously reported methods of synthesis involved the formation of the nitro-benzotriazole followed by high pressure hydrogenation (2,3) which is not ideal due to the use of expensive metals and the extreme reaction conditions. Here we describe a methodology for obtaining both 4 and 5 aminobenzotriazole under standard laboratory conditions using readily available, cheap materials.

Synthesis of 4-aminobenzotriazole



Synthesis of 5-aminobenzotriazole



The starting material for 4-aminobenzotriazole was benzotriazole itself. Direct nitration of benzotriazole predominantly results in the formation of the 4-nitrobenzotriazole (4,5). In this case

we were able to directly nitrate the benzotriazole in 66% yield by the slow addition of potassium nitrate to benzotriazole dissolved in conc. sulfuric acid at 0 ^{0}C followed by heating to 60 ^{0}C for 3 hours (6). After pouring into ice water and filtering the crude solid, yellow microcrystals were obtained from methanol. The 4-nitrobenzotriazole 1 was then converted to the 4-aminobenzotriazole 2 by reduction using hydrazine hydrate and graphite. This method has previously been used for nitro reduction at atmospheric pressure under 'normal' laboratory conditions (7). The nitro was dissolved in methanol with hydrazine hydrate and graphite. After refluxing under nitrogen the suspension was filtered and the solvent removed. The pure amine was obtained by trituration from diethyl ether in 86% yield.

5-Aminobenzotriazole 4 was synthesised in a slightly different manner. As direct nitration predominantly gives the 4-nitrobenzotriazole the starting material was 4-nitrobenzene-1,2-diamine. The diamine was converted to the triazole by treatment with sodium nitrite and hydrochloric acid (8). Reduction of the 5-nitrobenzotriazole 3 was accomplished in the same manner as for the 4-aminobenzotriazole in 71% yield. Purification was achieved by trituration from ethyl acetate with hexane. In both cases the triazole function remained unaffected by the reduction process.

In summary we have developed a convenient route to both 4 and 5-aminobenzotriazole which starts with readily available, cheap compounds. The steps are easily conducted in any chemical laboratory without the need for extreme conditions or lengthy purification steps to produce the desired compounds in sufficient yield and purity for further reactions.

Experimental

Example of reduction by hydrazine hydrate to produce 4-Aminobenzotriazole 2. Compound 1 (4.0g, 24.4mmol) was dissolved in methanol (150ml) with hydrazine hydrate (2.36ml, 48.7mmol) and graphite powder (12g). After refluxing under nitrogen for six hours the suspension was filtered, the solvent removed and the product isolated by trituration from ethyl acetate with hexane to yield the product as a yellow powder in 86% yield. [2.806g, 20.3mmol; R_f (EtOAc/MeOH/NH_3 5:1:1) 0.31; δ_H [$(CD_3)_2CO$] 5.5 (2 H, s, NH_2) 6.5 (1 H, d, *J*7.5, 7H) 6.9 (1 H, d, *J*8.1, 6H) 7.2 (1 H, s, 4H) 14.6 (1 H, s, NH)].

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