A Convenient New Synthesis of 1-Cyanobenzotriazole and Its Use as a C-Cyanating Reagent

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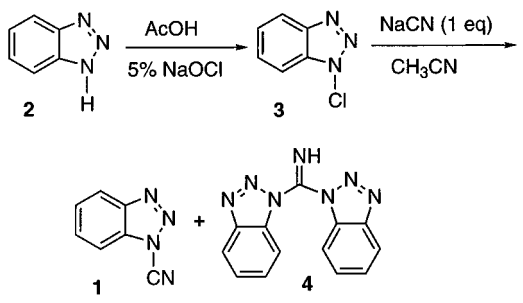
Introduction

The formation of a carbon−carbon bond by the introduction of a cyano group is a fundamental process in organic synthesis. Most often, this is accomplished by nucleophilic attack of a cyanide ion (CN^-) at an electrophilic carbon. A few reagents are known, however, that behave as cyano cation (CN^+) equivalents on treatment with a carbanion. These include tosyl cyanide,[1,2] 2-chlorobenzyl thiocyanate,[3] thiocyanogen,[4] and most important, cyanogen chloride.[5] In searching for additional CN^+ synthons, our attention focused upon the known 1-cyanobenzotriazole (**1**), which is already known to effect the cyanation of amines and thiols.[6,7] We now report a new and convenient synthesis of **1**, as well as the first examples of its use as a C-cyanation reagent.

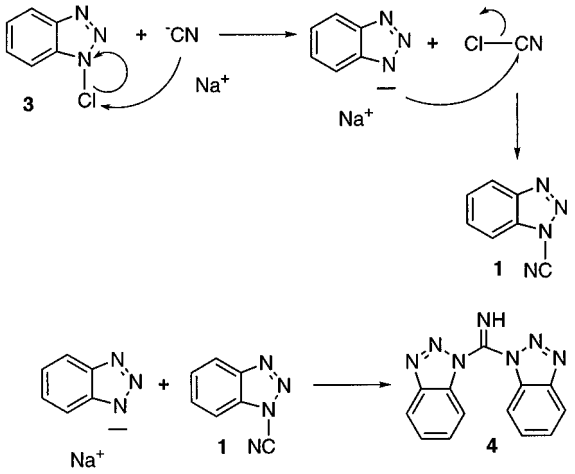
Results and Discussion

1-Cyanobenzotriazole (**1**) has been prepared previously only by the reaction of the benzotriazole anion with either cyanogen chloride or cyanogen bromide, both of which are highly toxic and irritating reagents.[6,8−10] We have now found that it may be conveniently prepared by a simple and safe two-step process. Thus, reaction of benzotriazole (**2**) with commercial 5% sodium hypochlorite affords 1-chlorobenzotriazole (**3**) in quantitative yield, as previously reported (Scheme 1).[11,12] Treatment of **3** with sodium cyanide in acetonitrile under mild conditions, followed by sublimation of the crude product, gave pure cyano compound **1** in 70% yield. Purification of the nonvolatile residue afforded the known imine **4**, which is a byproduct formed in the reaction of benzotriazole anion with BrCN.[6]

Scheme 1

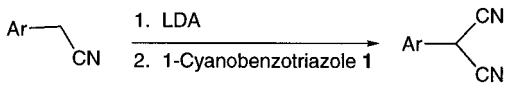


Scheme 2



The formation of **4** is consistent with the formation of the benzotriazole anion as an intermediate in our procedure. Consequently, the likely mechanism for the reaction is that shown in Scheme 2, in which ClCN is indeed formed as the other transient intermediate. The alternate possibility of a direct attack of CN^- at either N-1 or N-3 of **3** seems unlikely and, furthermore, would not explain the formation of **4**.

The utility of **1** as a cyanating reagent was tested by reacting it with a series of arylacetonitrile anions to give the corresponding arylmalonitriles in fair to good yields.



Experimental Section

General. Methods. Melting points are uncorrected. ^1H NMR were obtained at 360 MHz. Unless otherwise noted, materials were obtained from commercial suppliers and used without purification.

1-Chlorobenzotriazole (3). A 5% NaOCl solution (commercial bleach, 1280 mL, 0.96 mol) was added dropwise to a solution of benzotriazole (95.84 g, 0.80 mol) in 50% AcOH (384 mL) with stirring. After the addition was complete, the solution was stirred for 2 h and filtered, and the precipitate was washed with H_2O (∼3 L) until the washings were neutral. The solid was dried in vacuo to give 1-chlorobenzotriazole **3** (119.41 g, 97%) as white crystals: mp 103−105 °C (lit.[12] mp 104−106 °C); ^1H NMR ($CDCl_3$) δ 8.09 (d, 1H, J = 8.39 Hz), 7.62 (m, 2H), 7.46 (m, 1H).

1-Cyanobenzotriazole (1). A solution of NaCN (7.95 g, 160 mmol), 1-chlorobenzotriazole (24.56 g, 160 mmol), and CH_3CN (640 mL) was stirred for 3 h in an ice bath. The solution was

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Table 1. Arylmalononitriles from Arylacetonitriles

Ar	% yield	mp (°C)	lit.[3] mp °C
phenyl	66	67−68	68−69
4-bromophenyl	65	85−86	86−87
2-chlorophenyl	52	59−60	60−62
3,4-(methylenedioxy)phenyl	30	131−133	131−133
1-naphthyl	52	166−167	165−166

then allowed to slowly warm to rt and stirred for 24 h. The solvent was then removed and the resulting residue sublimed (70 °C, 2 mmHg) to give 1-cyanobenzotriazole (**1**) (16.08 g, 70%) as white crystals: mp = 73.4−74.8 °C (lit.[8] mp = 74−76 °C); ^{1}H NMR ($CDCl_3$) δ 8.22 (d, 1H, J = 8.32 Hz), 7.79 (m, 2H), 7.62 (m, 1H). Column chromatography of the nonvolatile residue on silica gel (hexane/EtOAc, 2:1) followed by crystallization (CH_2Cl_2/hexane) gave bis(benzotriazol-1-yl)methylimine (**4**) as white needles. The properties of **4** (mp, ^{1}H NMR, MS) were in accord with those previously reported.[6]

General Procedure for Arylacetonitrile Cyanation. To a solution of LDA (4.5 mmol) in THF (10 mL) at 0 °C under nitrogen was added the arylacetonitrile (3 mmol) in THF (5 mL), and the mixture was stirred for 15 min. This solution was syringed into a solution of 1-cyanobenzotriazole (0.86 g, 6.00 mmol) in THF (5 mL) at 0 °C under nitrogen, and the reaction mixture was stirred overnight. A solution of NH_4Cl (3 mL) was added, and the solvent was evaporated. The residue was dissolved in benzene (50 mL) and extracted with 10% NaOH (4 × 40 mL). The aqueous extracts were combined, cooled in an ice bath and acidified to pH 1 with concd HCl and extracted with CH_2Cl_2 (3 × 50 mL), and the combined extracts were dried over anhyd Na_2SO_4 and evaporated. The residue was purified via a short column (CH_2Cl_2) to give the corresponding arylmalononitrile (Table 1).

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