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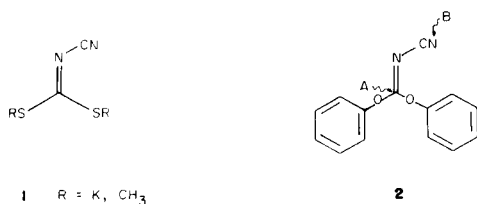
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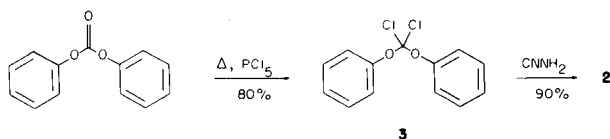
A simple high yield synthesis of diphenyl cyanocarbonimidate is reported. This synthon may be used to prepare functionalized benzimidazoles, benzoxazoles and triazoles in good yield under mild conditions.

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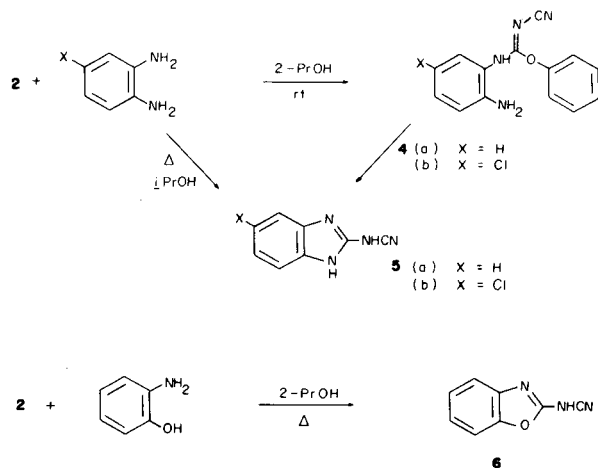
The general utility of the reagent *N*-cyanodithioimidocarbonate (**1**) for the synthesis of a wide variety of heterocycles has been well documented in the literature (1-5). We report here the synthesis of diphenyl cyanocarbonimidate (**2**) and a preliminary account of its versatility as a synthon of the preparation of a variety of heterocyclic systems.



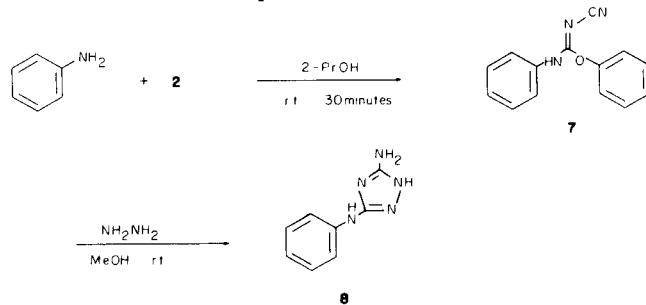
The synthetic method used to prepare **2** involves the formation of the dichloro intermediate **3** from diphenylcarbonate. By preheating the diphenylcarbonate and continuously removing the phosphorus oxychloride formed, the use of sealed tubes formerly used to prepare **3**, (6) is avoided. Condensation of **3** with cyanamide then affords **2** in high yield.



The phenoxy reagent **2** offers a number of advantages over **1**. The first advantage is that bifunctional nucleophiles such as diamines attack carbon atom A under extremely mild conditions allowing for the isolation of intermediates such as **4**. Slightly more vigorous conditions then lead to the fused heterocycles **5** and **6**. The reagent **1** produces the benzimidazoles **5** in low to moderate yield only when base is added to force the reaction and fails totally when the nucleophilicity of the diamine is decreased by adding electron withdrawing substituents (1). Intermediates such as **4** are not isolated with **1**. The formation of the benzoxazole **6** has not been reported previously.



The ease with which these transformations take place is presumably due in large part to the relative stability of the phenoxide ion as a leaving group and its weak nucleophilicity. Even poor nucleophiles such as aniline and *p*-chlorophenylenediamine condense with **2** in essentially quantitative yield simply on stirring with isopropanol at room temperature. In addition intermediates such as **7** are much more easily attacked by a second nucleophile than their *S*-methyl counterparts (7). After initial attack by a nucleophile, intermediates such as **7** can be cyclized to heterocycles by displacement of the second phenoxy group followed by attack on the nitrile. As an example **7** is converted instantaneously to the triazole **8** on treatment with one mole of hydrazine hydrate in methanol at room temperature.



An additional attraction of the phenoxy reagent **2** is that the formation of foul smelling methyl mercaptan and other sulphur containing impurities is avoided. By choice of

nucleophiles and step sequences a large variety of heterocycles should be amenable to preparation from **2** either by A-A or A-B fusion. We are currently investigating the scope and limitations of a number of these reactions.

EXPERIMENTAL

Melting points were determined using a Hoover capillary apparatus and are uncorrected. The ir and nmr spectra were recorded on Perkin Elmer 137 and R-24 spectrophotometers. Mass spectra were obtained using Hitachi-Perkin Elmer RMV-GE (ei) and Finnigan 3300 (CI) spectrometers. The gc separations were made using a Varian 3700 instrument.

1,1-Dichloro-1,1-diphenoxymethane (**3**).

Diphenyl carbonate (1.0 kg, 4.67 moles) was melted and heated to 150°. Phosphorus pentachloride (1.1 kg, 5.36 moles) was added in portions so that the pot temperature remained above 110°. The reaction was heated to 160° and held at this temperature for 24 hours while phosphorous oxychloride was distilled off. After 24 hours the pot temperature was raised to 200° and held for 15 minutes. The reaction was cooled and excess phosphorous oxychloride and pentachloride removed by distillation under aspirator vacuum. The remaining liquid was distilled bp 125-135/1 mm and yielded 1.2 kg (96%) of **3** which assayed 85% by gc. This material was pure enough for subsequent transformations. A sample was redistilled to give a white solid mp 42-44° identical in all respects to material prepared by the sealed tube method (6) (lit bp 183-185/12 mm; mp 42-44° (6)).

N-Cyanodiphenoxymethane (**2**).

A solution of cyanamide (165 g, 3.9 moles) in 600 ml of ethyl acetate was added to a solution of **3** (467 g, 1.75 moles) in ethyl acetate (600 ml) at such a rate the temperature did not rise above 80°. After stirring for 3½ hours at room temperature the precipitate was filtered and washed with ethyl acetate (200 ml). The solid was air dried overnight and slurried with 2 l of water. Solid sodium carbonate was added to adjust the pH to between 7.5 and 8.0 The suspension was filtered and washed with water. After vacuum drying 378 g of **2** (91%) mp 156-158° was obtained; ir (nujol): 2140 cm⁻¹ (C≡N), 1670 cm⁻¹ (C=N); ¹H nmr (deuteriochloroform); δ 7.0-7.6 (m, aromatics).

Anal. Calcd. for C₁₄H₁₀N₂O₂: C, 70.58; H, 4.23; N, 11.76; M⁺, 238. Found: C, 70.36; H, 4.23; N, 11.83; M⁺, 238.

N-(2-Aminophenyl)-N'-cyano-O-phenylisourea (**4a**).

Phenylenediamine (2.16 g, 0.02 mole) was dissolved in 2-propanol (40 ml) and **2** (4.76 g, 0.02 mole) added. After stirring at room temperature for 30 minutes the white precipitate was collected and washed with 15 ml of 2-propanol and dried to yield **4a** 4.42 g (88%) mp 234-235 dec; ir (nujol): 2200 cm⁻¹ (C≡N); ¹H nmr (DMSO-d₆): δ 6.5-7.5 (m, aromatics).

Anal. Calcd. for C₁₄H₁₂N₄O: C, 66.65; H, 4.79; N, 22.21; M⁺, 252. Found: C, 66.69; H, 4.71; N, 21.98; M⁺, 252.

2-Cyanoaminobenzimidazole **5a**.

A suspension of **2** (4.76 g, 0.02 mole) and phenylenediamine (2.16 g, 0.02 mole) in 2-propanol (40 ml) was refluxed for 1 hour. The volume was reduced to 10 ml by evaporation and the precipitate filtered, washed with cold 2-propanol (5 ml) and dried to yield **5a**, 2.90 g (92%), mp 278° (with decomposition and preliminary softening), (lit 275-285 (1)). Spectral characteristics were identical with those reported by Wittenbrook (1).

N-(2-amino-5-chlorophenyl)-N'-cyano-O-phenylisourea (**4b**).

4-chloro-*o*-phenylenediamine (2.86 g, 0.02 mole) was dissolved with 60 ml of 2-propanol and **2** (4.67 g, 0.02 mole) added with stirring. After stirring 12 hours the precipitate was filtered, washed with 2-propanol (10 ml) and dried yielding **4b** 2.3 g (80%) mp 265° dec; ir (nujol): 2200 cm⁻¹ (C≡N); ¹H nmr (DMSO-d₆): δ 7.0-7.45 (m, aromatics).

Anal. Calcd. for C₁₄H₁₁ClN₄O: C, 58.58; H, 3.86; N, 19.52; Cl, 12.35; M⁺, 287. Found: C, 58.65; H, 3.92; N, 19.45; Cl, 12.42; M⁺, 287.

2-Cyanoamino-5-chlorobenzimidazole (**5b**).

A mixture of **2** (4.76 g 0.02 mole) and 4-chloro-*o*-phenylene diamine (2.86 g, 0.02 mole) in 2-propanol (60 ml) was refluxed 15 hours. The volume was reduced to 20 ml and the precipitate collected, washed with acetone (10 ml), 2-propanol (10 ml) and dried to yield **5b** 3.4 g (88%) mp > 300°; (nujol): 2190 cm⁻¹ (C≡N). ¹H nmr (DMSO-d₆): δ 7.0-7.3 (m, aromatics).

Anal. Calcd. for C₈H₅ClN₄: C, 49.89; H, 2.62; N, 18.41; Cl, 29.09; M⁺, 192. Found: C, 49.65; H, 2.90; N, 18.25; Cl, 29.29; M⁺, 192.

2-Cyanoaminobenzoxazole (**6**).

A slurry of **2** (24.0 g, 0.01 mole) and *o*-aminophenol (11.0 g, 0.1 mole) in 2-propanol (150 ml) was stirred at room temperature for 1 hour. The solution was filtered and the filtrate refluxed for 10 minutes. The crystalline product which formed on cooling was filtered and dried to yield 11.8 g (74%) of **6** mp 175°. A sample was recrystallized from acetonitrile mp. 186-188°; ir (nujol): 2195 cm⁻¹ (C≡N); ¹H nmr.

Anal. Calcd. for C₈H₇N₃O: C, 60.38; H, 3.17; N, 26.40; M⁺, 159. Found: C, 60.14; H, 3.09; N, 26.65; M⁺, 159.

N-Phenyl-N'-cyano-O-phenylisourea (**7**).

Aniline (18.6 g, 0.2 mole) and **2** (47.2 g, 0.2 mole) was stirred in 2-propanol (400 ml) at room temperature for 2 hours. The white precipitate was filtered and washed with 30 ml of 2-propanol and dried to yield 44.5 g of **7** (98%) mp 190-192°; ir (nujol) 2200 cm⁻¹ (C≡N), 1640 cm⁻¹ (C=N); ¹H nmr (DMSO-d₆): δ 7.0-7.2 (m, aromatics).

Anal. Calcd. for C₁₄H₁₁N₃O: C, 70.87; H, 4.67; N, 17.71; M⁺, 237. Found: C, 70.94; H, 4.72; N, 17.55; M⁺, 237.

3-Amino-5-anilino-1,2,4-triazole (**8**).

To a slurry of **7** (2.37 g, 0.02 mole) in methanol (40 ml) was added hydrazine hydrate (0.5 g, 0.02 mole) all at once. The solution rapidly became homogeneous and exothermed slightly. After stirring at room temperature for 15 minutes the solution was concentrated to 15 ml and the white precipitate of **8** filtered, washed with 2-propanol (5 ml) and dried, yield 1.5 g, (86%) mp 160-161° (lit 163° (8); 157 (9)).

Anal. Calcd. for C₈H₈N₄: C, 54.85; H, 5.18; N, 39.97; M⁺, 175. Found: C, 54.90; H, 5.08; N, 39.81; M⁺, 175.

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