Selective Synthesis of 1,3-Di(pyridylimino)-isoindolines from Tetracyanobenzene

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The synthesis of substituted 1,3-bis-(2-pyridylimino)isoindoline **4** from 1,2,4,5-tetracyanobenzene and 2,6-diaminopyridine under mild and dilute conditions constitutes a new approach to produce a functionalized compound **4**. The synthesis of an analogous compound **5** from 1,2,4,5-tetracyanobenzene and 2-amino-6-methylpyridine is also described.

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The selective functionalization of one out of several identical groups within the same molecule is challenging and often required for the synthesis of asymmetric polynucleating ligands in order to study the chemistry of the mixed metal systems. To the best of our knowledge, the only method available so far for synthesizing symmetric (tetrapyridylimino)isoindolines **2** is that reported by Siegl *et al.* [1] and subsequently we have prepared them from 1,2,4,5-tetracyanobenzene and 2-aminopyridines directly in a single step [2]. Also in previous papers [3,4] we have demonstrated that 1,2,4,5-tetracyanobenzene and ethylenediamine readily underwent catalytic (phosphorus pentasulfide) condensation to afford the polyhydroimidazole ligand **6**.

We describe here a mild and efficient method for the synthesis of partly functionalized tetracyanobenzenes of high purity in good yield and in a single step.

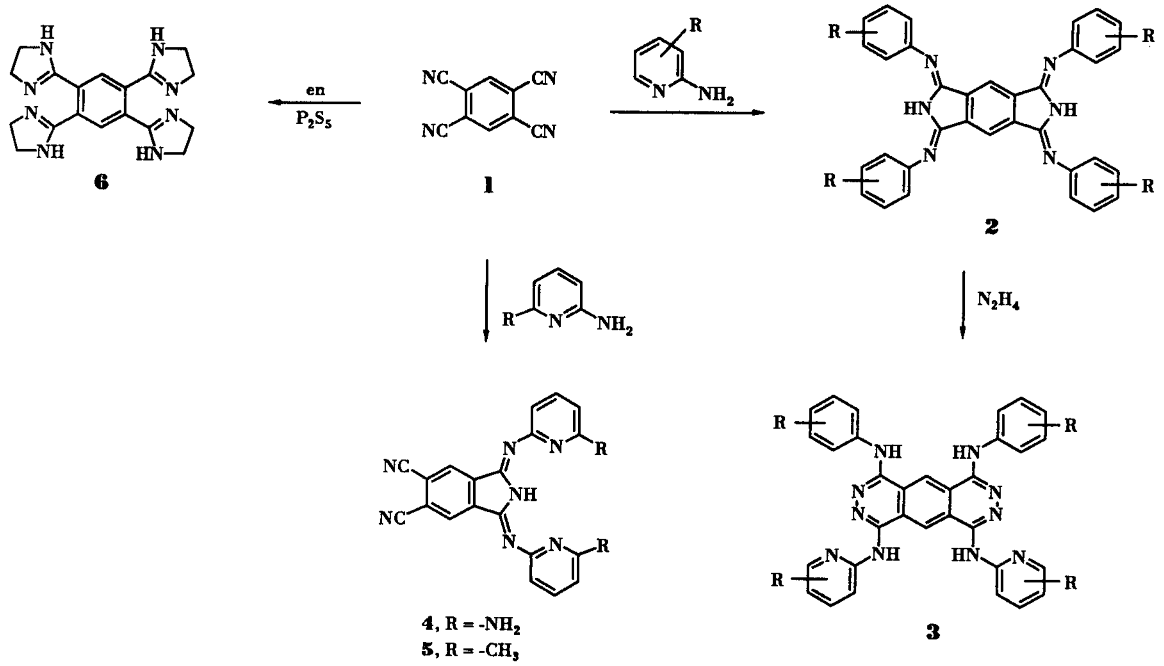
This procedure is general for a wide variety of pyridyl amines. Because of the mild conditions, the ease of experimental conditions and the relatively high yields to pure products, these reactions appear to be the method of choice for the synthesis of partly substituted isoindoline derivatives from 1,2,4,5-tetracyanobenzene.

The reaction of a mixture of one mole of 1,2,4,5-tetracyanobenzene and two moles of 2,6-diaminopyridine in refluxing methanol was found to give compound **4**, while compound **5** was prepared with 2-amino-6-methylpyridine using the general procedure in dioxane as shown in Scheme 1.

EXPERIMENTAL

Commercially available reagents were obtained from the Aldrich Chemical Co. Inc. and were used as such. Melting points determined on a Fisher-Johns melting point apparatus and are

Scheme 1



uncorrected. Proton nmr spectra were recorded with General Electric 300-NB spectrometer (TMS as the internal standard). Infrared spectra were obtained on a Perkin-Elmer Model 283 Spectrometer. Mass spectra were measured using a VG Micromass 7070 HS Mass Spectrometer. Microanalysis were carried out by the Canadian Microanalytical Service Limited.

5,6-Dicyano-1,3-bis(6'-amino-2'-pyridylimino)isoindoline (**4**).

2,6-Diaminopyridine (2.73 g, 0.025 mole) was dissolved in methanol (100 ml) and then filtered to remove the undissolved material. This solution was then added to the hot methanol solution (100 ml) of 1,2,4,5-tetracyanobenzene (2.23 g, 0.0125 mole). The resulting mixture was refluxed for 36 hours during which a red-brown product deposited. The product was filtered off, washed with methanol, which weighed 2.22 g (47%) of **4**. A portion of the compound was recrystallized from hot DMF for elemental analysis, mp >300°; ir: ν 3300 (NH, NH_2), 2240 (CN), 1640 cm^{-1} (C = N); ^1H nmr (DMSO-d_6): δ 13.39 (s, 1H, NH), 8.67 (s, 2H, benzene protons), 7.55 (t, 2H, pyridine protons H-4), 6.66 (d, 2H, pyridine protons H-3), 6.47 (d, 2H, pyridine protons H-5), 6.20 (s, 4H, NH_2); ms: m/z 379 (M^+, 100%).

Anal. Calcd. for $C_{20}H_{13}N_9$: C, 63.33; H, 3.45; N, 33.22. Found: C, 63.16; H, 3.14; N, 33.04.

5,6-Dicyano-1,3-bis(6'-methyl-2'-pyridylimino)isoindoline (**5**).

A mixture of 2-amino-6-methylpyridine (2.189 g, 0.02 mole) and 1,2,4,5-tetracyanobenzene (1.78 g, 0.01 mole) in dioxane (80 ml) was refluxed for 2 to 3 days. The mixture was cooled, and the product was collected by filtration, washed with ether and air dried. The mother liquor was concentrated to obtain more product. The combined product was chromatographed on an alumina column (chloroform as eluent) to give 1.80 g (50% yield) of **5**, and recrystallized from chloroform/methanol (50/50), mp 160-162°; ir: 3330 (NH), 2230 (CN), 1640 cm^{-1} (C = N); ^1H nmr (deuteriochloroform): δ 12.79 (s, 1H, NH), 8.44 (s, 2H, benzene protons), 7.71 (t, 2H, pyridine protons H-4), 7.26 (d, 2H, pyridine protons H-3), 7.06 (d, 2H, pyridine protons H-5), 2.61 (s, 6H, CH_3); ms: m/z 377 (M^+, 70%).

Anal. Calcd. for $C_{22}H_{15}N_7$: C, 70.02; H, 4.01; N, 25.99. Found: C, 69.81; H, 3.73; N, 25.83.

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