A Reliable Route to 1,2-Diamino-4,5-phthalodinitrile

Christian Burmester, Rüdiger Faust*

Institute for Chemistry and CINSaT - Center for Interdisciplinary Nanostructure Science and Technology, University of Kassel, Heinrich-Plett-Str. 40, 34132 Kassel, Germany
Fax +49(561)8044752; E-mail: r.faust@uni-kassel.de

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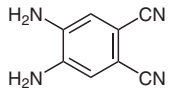
Abstract: Starting from *o*-phenylenediamine, we have developed a new and reliable route to 1,2-diamino-4,5-phthalodinitrile that is based on the reductive desulfurisation of 5,6-dicyano-2,1,3-benzothiadiazole with sodium borohydride. The reaction sequence uses only cheap reagents and relies on simple recrystallisations for the purification of all intermediates.

Key words: heterocycles, reduction, sulfur, boron, protecting groups

The juxtaposition of electron-donating and accepting groups across a delocalised organic framework is of continuing interest as this structural motif can be exploited to devise materials with unique electronic and/or optical properties.[1] A prototypical representative of this class of compounds is 1,2-diamino-4,5-phthalodinitrile (**1**; Figure 1), which, as a consequence, has emerged as a valuable building block inter alia for the construction of organic light-emitting diodes[2] and for chromophores with non-linear optical properties.[3] In addition, phthalodinitriles such as **1** serve as convenient starting materials for functionalised phthalocyanines and their nitrogen-rich congeners, the porphyrazines. Applications of these macrocyclic chromophores range from optical data storage, signal processing and optical limiting, to biological sensing and therapeutic applications.[4]

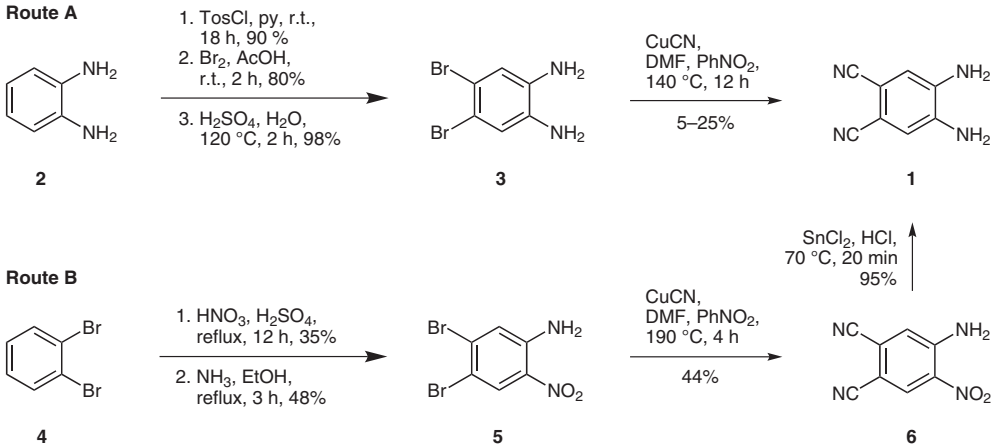
The significance of **1** in organic materials chemistry is contrasted by its synthetic availability. The reported



1

Figure 1

routes[5,6] for the synthesis of **1** are generally lengthy and expensive, require tedious work-up procedures and are notorious for their varying and often unsatisfactory low yields. Scheme 1 summarises two such syntheses and serves to illustrate these points. Whereas route A[5a] starts from 1,2-diaminobenzene (**2**), route B[5b–d] uses 1,2-dibromobenzene (**4**) as the starting material. In both cases, introduction of the cyano groups is achieved by an exchange of the vicinal bromine substituents in **3** and **5**, respectively, by Rosemund von Braun reactions with copper(I) cyanide. The yields of these reactions vary and range from 5–25% (route A) to optimised 44% (route B). Difficulties in the work-up of these reactions result largely from the need to remove residual copper salts from the chelating products. These problems are augmented in route B, where a subsequent reduction of the remaining nitro group in **6** with tin chloride leads to similar (if not worse) problems. In addition, the nitration of **4** as well as the substitution of one of the nitro groups with gaseous ammonia is hampered by low yields. Youngblood recently reported an alternative procedure for the synthesis of **1**,[6] relying on the



Scheme 1 Established routes to 1,2-diamino-4,5-phthalodinitrile

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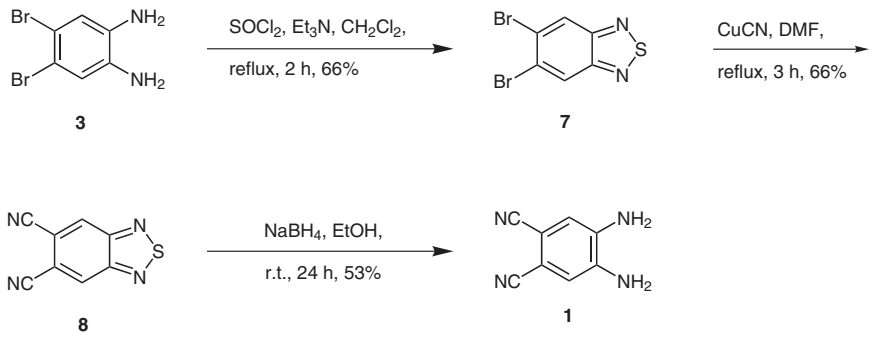

Scheme 2 The 2,1,3-benzothiadiazole route to **1**

diiodination of 1,2-dinitrobenzene followed by a reduction of the nitro groups with Fe/HCl and subsequent halide exchange with copper(I) cyanide. Again, problems with tedious work-up and low yields remain.

For an extensive study of quinoxalino-porphyrazines,[5a,7] we needed to prepare larger amounts of 1,2-diamino-4,5-phthalodinitrile (**1**) and were thus searching for a more reliable and more economical route to this valuable building block. We present here the results of our efforts, which capitalise on the successful reductive desulfurisation of a dicyanobenzothiadiazole (Scheme 2).

Our route to the title compound starts from 4,5-dibromophenylene-1,2-diamine (**3**),[8,9] whose synthesis could be significantly improved. Hence, *o*-phenylenediamine (**2**) was converted into *N*,*N*′-di(*p*-toluenesulfonyl)-*o*-phenylenediamine at room temperature according to Stetter[10] in 90% yield. Conducting the reaction at higher temperatures led to inferior yields, presumably due to the formation of *N*,*N*,*N*′-tri(*p*-toluenesulfonyl)-*o*-phenylenediamine.[11] Conversion of this intermediate into **3** was accomplished by its treatment with bromine in glacial acetic acid in the presence of anhydrous sodium acetate. Subsequent protodetosylation with dilute sulphuric acid at 120 °C gave 1,2-diamino-4,5-dibromobenzene (**3**) in an overall yield of 78%.[8]

Treatment of **3** with thionyl chloride in refluxing dichloromethane smoothly converted **3** into 5,6-dibromo-2,1,3-benzothiadiazole (**7**), which was obtained in 66% yield after recrystallisation from ethanol. As noted previously,[9] **7** is electronically predisposed to act as an efficient substrate in the Rosemund von Braun reaction with copper(I) cyanide. Moreover, and in contrast to the diamino-functionalised substrates **3** and **5**, problems arising from the chelation of copper ions are not to be expected. Therefore, under slightly modified conditions to those originally reported by Moerkved et al.[9] (omission of nitrobenzene, shorter reaction times), phthalodinitrile **8** could be isolated in 66% yield after recrystallisation from ethanol. The formation of 2,1,3-benzothiadiazole-5,6-dicarboximide, a side-product of the reaction,[9] was not observed in our case.

From **8**, the title compound **1** could be accessed by a reductive desulfurisation. Commonly used reagents for this transformation in general are sodium borohydride,[12] a combination of sodium borohydride and cobalt(II) chloride,[13] lithium aluminium hydride[14] or tin(II) chloride.[15] Lithium aluminium hydride can be readily discounted as a reducing agent in this particular case because of the reactive nitrile groups present in **8**. Consequently, an excess of sodium borohydride in ethanol at room temperature was used to furnish the desired target **1** in 53% yield. At higher temperatures (>40 °C), the reaction failed completely and an excess of reducing agent was needed to guarantee satisfactory yields. The use of alternative solvents was possible (47% yield in THF) as long as conditions were not strictly anhydrous. The reductive desulfurisation of **8** with a combination of cobalt(II) chloride and sodium borohydride[13] only gave minute amounts of diamine **1**. The capacity of tin chloride[15] to effect this transformation was also rather limited (27% yield).

The overall yield for the synthesis of **1** via the benzothiadiazole route is comparable to that of route A, but the reproducibility is higher and the handling of intermediates is more convenient. In comparison to route B, the benzothiadiazole route gives higher overall yields.

In summary, we have devised a reliable route to 1,2-diamino-4,5-phthalodinitrile (**1**), using cheap reagents and obviating the need for chromatographic purifications of intermediates. The synthesis delineated here is therefore suitable for a preparation of **1** on a large scale.

The ^{1}H and ^{13}C NMR spectra were recorded on a Varian Unity INOVA NMR spectrometer operating at 500 and 125 MHz, respectively, using residual solvent peaks ($CHCl_3$ at δ = 7.26 ppm and DMSO at δ = 2.50 ppm, for ^{1}H spectra, $CHCl_3$ at δ = 77.0 ppm and DMSO at δ = 39.5 ppm for ^{13}C spectra) as internal standards. IR spectra were obtained on a Bruker Vector 22 instrument in the 400–4000 cm^{-1} range. Melting points were determined on a Stuart SMP 10 hot-stage and are uncorrected. Reactions were monitored by analytical TLC on precoated plates (silica gel 60 F254). Compound **3** was prepared according to published procedures[8,9] using the improvements described in the text.

5,6-Dibromo-2,1,3-benzothiadiazole (7)[9]

To a solution of 1,2-diamino-4,5-dibromobenzene (**3**; 5.52 g, 20.7 mmol) and Et_3N (12 mL, 83 mmol) in CH_2Cl_2 (60 mL) was added, under reflux, a solution of thionyl chloride (2.27 mL, 31 mmol) in CH_2Cl_2 (10 mL). After addition was complete, the reaction mixture was stirred for 3 h under reflux. After cooling to r.t., H_2O (25 mL) was added and the phases were separated. The organic phase was washed with H_2O (2 × 25 mL), brine (25 mL) and dried ($MgSO_4$).

The solvent was removed under vacuum and the benzothiadiazole **7** was recrystallised from EtOH.

Yield: 4.00 g (66%); pale-yellow solid; mp 132–133 °C (Lit.[9] 131–135 °C)

IR (KBr): 3077, 3061, 1765, 1711, 1577, 1478, 1414, 1347, 1229, 1062, 951, 887, 859, 823, 686, 532 cm^{-1}.

^1H NMR (500 MHz, $CDCl_3$): δ = 8.38 (s, 2 H).

^{13}C NMR (125 MHz, $CDCl_3$): δ = 124.9, 127.2, 153.8.

5,6-Dicyano-2,1,3-benzothiadiazole (8)[9]

A suspension of 5,6-dibromobenzo-2,1,3-thiadiazole (2.87 g, 9.8 mmol) and CuCN (2.84 g, 32 mmol) in DMF (40 mL) was heated at reflux for 3 h under argon. After cooling to r.t., a solution of iron(III) chloride hexahydrate (13 g) in concd HCl (3.5 mL) and H_2O (20 mL) was added and the mixture was stirred at 70 °C for 30 min. The solution was extracted with CH_2Cl_2 (2 × 100 mL) and the combined organic phases were extracted with HCl (6M, 3 × 50 mL), H_2O (50 mL), brine (50 mL) and dried ($MgSO_4$). Solvent was removed under vacuum and the benzothiadiazole **8** was recrystallization from EtOH.

Yield: 1.20 g (66%); pale-yellow solid; mp 201 °C (Lit.[9] 205–208 °C).

IR (KBr): 3091, 3015, 2237 (s), 1814 (m), 1492, 1452, 1351, 1149, 911, 875, 829, 741 cm^{-1}.

^1H NMR (500 MHz, DMSO-d_6): δ = 9.18 (s, 2 H).

^{13}C NMR (125 MHz, DMSO-d_6): δ = 112.5, 115.6, 130.4, 153.6.

1,2-Diamino-4,5-dicyanobenzene (1)[5a]

To a solution of 5,6-dicyanobenzo-2,1,3-thiadiazole (**8**; 0.86 g, 4.6 mmol) in EtOH (80 mL) was added, portionwise, $NaBH_4$ (0.70 g, 18.5 mmol) under argon and the purple solution was stirred for 12 h. Sat. aq NH_4Cl (10 mL) was added and, after 30 min, the reaction mixture was extracted with CH_2Cl_2 (4 × 20 mL). The combined organic phases were extracted with H_2O (20 mL), brine (20 mL) and dried ($MgSO_4$). After removal of the solvent under vacuum the residue was purified by flash column chromatography on silica gel (CH_2Cl_2–EtOAc, 1:1) to give **1**.

Yield: 387 mg (53%); off-white solid; mp 262–264 °C (Lit.[5a] 272–275 °C).

The product was pure enough to be used in further reactions, however, additional purification steps (recrystallisation from H_2O–EtOH mixtures[5a]) can be undertaken if required. Conversion of 1.3 g starting material furnished the product in 43% yield.

IR (KBr): 3444, 3334, 2218 cm^{-1}.

^1H NMR (500 MHz, DMSO-d_6): δ = 5.86 (s, 4 H, NH), 6.86 (s, 2 H).

^{13}C NMR (125 MHz, DMSO-d_6): δ = 101.4, 115.5, 117.9, 139.1.

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