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Synthesis of 4,5-dihydroxyphthalonitrile

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4,5-Dihydroxyphthalonitrile was synthesized from pyrocatechol in a simple way. The compound obtained is a convenient starting reagent for the preparation of 4,5-dialkoxyphthalonitriles.

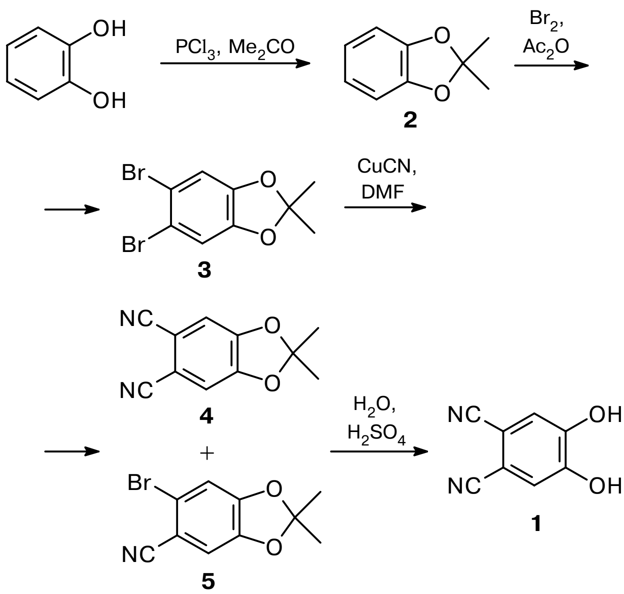
Key words: 4,5-dihydroxyphthalonitrile, 2,2-dimethyl-1,3-benzodioxole, bromination, cyanation.

4,5-Dialkoxyphthalonitriles could be synthesized by alkylating 4,5-dihydroxyphthalonitrile (**1**). In addition, this compound can be useful in the cases when direct introduction of cyano groups into the target molecule according to the Rosenmund—von Braun method is prevented by the low reactivity or instability of the starting dihalide. However, the synthesis of compound **1** has not been reported up to the present.

We synthesized 4,5-dihydroxyphthalonitrile (**1**) from pyrocatechol according to Scheme 1. The scheme includes benzodioxole protection of the hydroxy groups, bromination of the benzene ring, cyanation of the resulting dibromide **3**, and elimination of the protection group from symmetrical dinitrile **4**.

The preparation of 2,2-dimethyl-1,3-benzodioxole (**2**) was described in Ref. 1, but the target product is rather difficult to isolate in the presence of triethylamine used to bind HCl. The isolation was appreciably facilitated by using K_2CO_3 as a base, the yield of compound **2** remaining high (94%).

Scheme 1



Benzodioxole **2** is then brominated[2,3] to give 5,6-dibromo-2,2-dimethyl-1,3-benzodioxole (**3**) in high yield (92%). We preferred this method of preparing dibromide **3** because an alternative way, namely, bromination of pyrocatechol followed by the formation of the dioxolane ring, provides low yields of **3** (direct bromination of pyrocatechol[4] affords 4,5-dibromopyrocatechol only in ~30% yield).

Cyanation of dibromide **3** with copper(I) cyanide in the ratio of 1 : 5 in boiling DMF for 3.5 h gives dinitrile **4** in 36% yield. Another reaction product, 6-bromo-5-cyano-2,2-dimethyl-1,3-benzodioxole (**5**), is formed in 7—8% yield. Further heating is unsuitable since the reaction mixture turns green, and its UV-VIS spectrum shows a characteristic peak at 680 nm, indicating a cyclization of dinitrile **4** into copper 2,3,9,10,16,17,23,24-tetra(isopropylidenedioxy)phthalocyanine in the presence of an excess of the copper(I) salt.

The isopropylidene protection in dinitrile **4** is effectively removed under the action of conc. H_2SO_4 to give the target 4,5-dihydroxyphthalonitrile (**1**) in 90% yield. The use of HCl is less convenient, since the reaction duration is extended to two days, affording phthalonitrile **1** in only 80—83% yield.

The structure of compound **1** was proved by ^1H and ^{13}C NMR spectroscopy and mass spectrometry; its composition was confirmed by elemental analysis.

Thus, 4,5-dihydroxyphthalonitrile can be easily synthesized from pyrocatechol by closing a dioxolane ring to protect its hydroxy groups, brominating the benzene ring, and cyanating the resulting dibromide.

Experimental

^1H and ^{13}C NMR were recorded on Bruker AC-200 instrument (200 and 50.3 MHz, respectively) in $CDCl_3$ (for compounds **3**, **4**, and **5**) or in $(CD_3)_2CO$ (for dinitrile **1**); the

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chemical shifts (δ) are referred to tetramethylsilane. Mass spectra were recorded on a Finnigan MAT INCOS-50 instrument (EI, 70 eV, direct inlet). The compounds obtained were analyzed by TLC using Silufol UV-254 plates. Copper cyanide (Chemapol) was used without additional purification. Solvents were purified according to the conventional methods.[5]

2,2-Dimethyl-1,3-benzodioxole (2). Phosphorus trichloride (16.5 g, 0.12 mol) was added dropwise at 20 °C over 20 min to a stirred solution of pyrocatechol (33 g, 0.30 mol) and Me_2CO (23 g, 0.36 mol) in 120 mL of benzene. The reaction mixture was stirred until HCl ceased to evolve and then poured into K_2CO_3 (100 g). The organic layer was filtered, and the precipitate was washed with 50 mL of benzene. The benzene solution was washed with 10% NaOH and water and dried with anhydrous $CaCl_2$. Distillation gave benzodioxolane (**2**) (42 g, 94%). Its physicochemical characteristics correlate with the literature data.[1]

5,6-Dibromo-2,2-dimethyl-1,3-benzodioxole (3) was synthesized as described in Refs. 2 and 3. The yield of **3** was 42 g (92%); its characteristics are identical with the literature data.[2,3] ^{1}H NMR, δ: 1.67 (s, 6 H, C(2)Me_2); 6.98 (s, 2 H, Ar). ^{13}C NMR, δ: 24.9 (Me), 111.4 (C(4), C(7)), 114.0 (C(5), C(6)), 118.6 (C(2)), 145.3 (C(8), C(9)).

5,6-Dicyano-2,2-dimethyl-1,3-benzodioxole (4). A mixture of 5,6-dibromo-2,2-dimethyl-1,3-benzodioxolane (**3**) (2.5 g, 0.008 mol) and CuCN (3.63 g, 0.040 mol) was refluxed in 30 mL of freshly distilled DMF for 3.5 h. The reaction mixture was cooled to 20 °C and diluted with 75 mL of $CHCl_3$. The precipitate that formed was filtered off, and the filtrate was washed with water (5×100 mL) to remove DMF, dried with $CaCl_2$, and concentrated on a rotary evaporator. The residue was purified by column chromatography on silica gel in benzene. The yield of **4** was 50.59 g (36%), m.p. 167—168 °C. ^{1}H NMR, δ: 1.67 (s, 6 H, C(2)Me_2); 7.03, (s, 2 H, Ar.). ^{13}C NMR, δ: 26.1 (Me); 110.1 (C(5), C(6)); 112.5 (C(4), C(7)); 115.7 (CN); 123.1 (C(2)); 151.3 (C(8), C(9)). MS, *m/z*: 200 $[M]^+$. Found (%): C, 66.21; H, 4.28; N, 14.19. $C_{11}H_8N_2O_2$. Calculated (%): C, 66.00; H, 4.03; N, 13.99.

6-Bromo-5-cyano-2,2-dimethyl-1,3-benzodioxole (5) was isolated as a by-product while chromatographing the reaction mixture obtained by the cyanation of compound **3** (see the above experiment). The yield of **5** was 0.16 г (8%), m.p. 153—154 °C. ^{1}H NMR ($CDCl_3$), δ: 1.67 (s, 6 H, C(2)Me_2); 6.95, 7.03, (both s, each 1 H, Ar). ^{13}C NMR, δ: 26.0 (Me); 110.4 (C(6)); 111.7 (CN); 112.4 (C(7)); 113.3 (C(4)); 118.3 (C(2)); 121.6 (C(5)); 147.2 (C(9)); 152.1 (C(8)). MS, *m/z*: 253, 255 $[M]^+$. Found (%): C, 47.59; H, 3.40; N, 5.18. $C_{10}H_8BrNO_2$. Calculated (%): C, 47.27; H, 3.17; N, 5.51.

4,5-Dihydroxyphthalonitrile (1). A solution of 5,6-dicyano-2,2-dimethyl-1,3-benzodioxole (**4**) (1.5 g, 0.0075 mol) in 2.5 mL of conc. H_2SO_4 was poured into 10 mL of water. The precipitate that formed upon cooling was filtered off, washed with $CHCl_3$, and dried *in vacuo* to give compound **1** (1.08 g, 90%) as a colorless powder, m.p. 114—115 °C. ^{1}H NMR ($(CD_3)_2CO$), δ: 7.38 (s, 2 H, Ar); 9.96 (br.s, 2 H, OH). ^{13}C NMR, δ: 107.9 (C(1), C(2)); 116.8 (CN); 120.7 (C(3), C(6)); 150.7 (C(4), C(5)). MS, *m/z*: 160 $[M]^+$. Found (%): C, 59.64; H, 2.78; N, 17.15. $C_8H_4N_2O_2$. Calculated (%): C, 60.00; H, 2.52; N, 17.49.

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