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Mendeleev Commun., 2010, **20**, 237–238
Mendeleev Communications

1,2-Dicyano-4,5-bis[2′-(2″-benzyloxyethoxy)ethoxy]benzene – precursor towards new functionalized phthalocyanines

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DOI: 10.1016/j.mencom.2010.06.019

1,2-Dicyano-4,5-bis[2′-(2″-benzyloxyethoxy)ethoxy]benzene can act as a precursor to new functionalized phthalocyanines with liquid crystal properties.

Tetrapyrrolic compounds modified with peripheral macrocyclic chelating groups capable of formation of heteronuclear assemblies are prominent molecular building blocks for novel functional materials.[1–4] Phthalocyanines condensed with macrocycles were reported previously. These molecules contain oligoethylene glycol chains linked with various bridges, *e.g.*, alkylated nitrogen atoms,[5] binaphtol[6,7] and benzene.[8,9] Generally, the synthesis of functionalized phthalocyanines is limited by the availability of the corresponding precursors, substituted phthalonitriles. Typically, phthalonitriles are prepared from corresponding *o*-dibromides *via* the Rosenmund–von Braun cyanation.[10] The harsh conditions of this heterogeneous reaction together with side reactions (reductive dehalogenation/decyanation)[11] usually lead to moderate yields (30–50%) of target compounds. In the case of macrocyclic precursors, it results in significant useless consumption of previously synthesized macrocyclic dibromide. Here, we report our attempt to synthesize open-ring phthalonitrile containing two diethylene glycol chains (Figure 1). This compound could be a universal precursor to various phthalonitriles and, therefore, phthalocyanines with lateral macrocyclic substituents incorporating chelating groups, *e.g.*, 1,10-phenanthrolines, as components of molecular assemblies with nontrivial topology (catenanes and rotaxanes).[3,4]

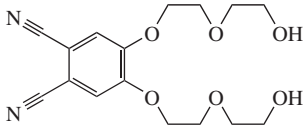


Figure 1 1,2-Dicyano-4,5-bis[2′-(2″-hydroxyethoxy)ethoxy]benzene.

The first attempt to make 1,2-dicyano-4,5-bis[2′-(2″-hydroxyethoxy)ethoxy]benzene was performed by Torres *et al.*[5] They synthesized 4,5-dibenzyloxyphthalonitrile, which underwent smooth Pd/C catalyzed debenzylation to give 4,5-dioxyphthalonitrile in 90% yield. However, its alkylation with 2-(2′-chloroethoxy)ethanol failed to produce any workable amount of target product because of the strong electron-withdrawing effect of the two cyano groups.

Here, we explored another strategy, which involved the synthesis of *o*-dibromobenzene bearing two diethylene glycol chains with terminal benzyl protecting groups followed by cyanation and, subsequently, cleavage of the benzyl protective groups to afford the desired compound.

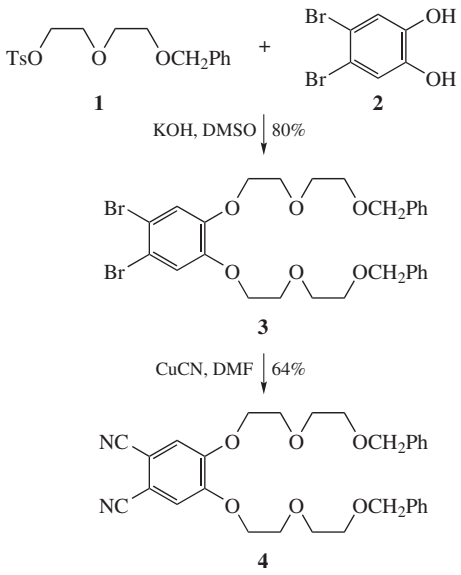
Reaction between stoichiometric amounts of previously synthesized O-tosylated 2-(2′-benzyloxyethoxy)ethanol **1**[12] with dibromocatechol **2**[13] in DMSO in the presence of KOH led to dialkylated dibromobenzene **3** in 80% yield. Further cyanation with CuCN afforded target dinitrile **4** in 64% yield (Scheme 1).† The chemical structure and purity of **3** and **4** were supported by IR, ^{1}H and ^{13}C NMR spectroscopy and elemental analysis.

The next step was the hydrogenolysis of compound **4** in the presence of 10% Pd/C as a catalyst. Unexpectedly, in contrast to 1,2-dicyano-4,5-dibenzyloxybenzene,[5] nitrile **4** did not undergo

† Tosylate **1**[12] and dibromocatechol **2**[13] were synthesized as reported elsewhere.

1,2-Dibromo-4,5-bis[2′-(2″-benzyloxyethoxy)ethoxy]benzene **3**: tosylate **1** (9.88 g, 28.2 mmol) together with a solution of dibromocatechol **2** (3.78 g, 14.1 mmol) in dry degassed DMSO (10 ml) were added *via* syringes to a degassed suspension of KOH (1.79 g, 31.9 mmol) in dry DMSO (20 ml). The mixture was stirred under argon for 36 h with TLC monitoring ($CHCl_3$ + 2% MeOH). After complete conversion of **2**, reaction mixture was poured into water, neutralized with HCl and extracted with $CHCl_3$ (3×50 ml). Combined organic extracts were washed with brine, dried over Na_2SO_4 and evaporated to produce dark viscous oil, which was purified by column chromatography on SiO_2 using pentane–EtOAc (7:3) as an eluent. Evaporation of solvent gave **3** as viscous turbid oil; yield, 7.05 g, 80%. ^{1}H NMR (300 MHz, CD_2Cl_2) δ: 7.34–7.27 (m, 10H, H_{Bn}), 7.16 (s, 2H, H_{Ar}), 4.53 (s, 4H, $OCH_{2\,Bn}$), 4.10, 3.81, 3.69, 3.64 (4m, 4×4H, OCH_2). ^{13}C NMR (75 MHz, CD_2Cl_2) δ: 148.8, 138.5, 128.3, 128.1, 127.7, 118.5, 114.9 (CBr), 73.1, 70.8, 69.7, 69.4, 69.2. IR (ν/cm^{-1}): 651 (C–Br). Found (%): C, 53.08; H, 5.19. Calc. for $C_{28}H_{32}Br_2O_6$ (%): C, 53.86; H, 5.17.

1,2-Dicyano-4,5-bis[2′-(2″-benzyloxyethoxy)ethoxy]benzene **4**: dibromide **3** (7.68 g, 12 mmol) was added to a suspension of CuCN (3.30 g, 36 mmol) in 70 ml of dry DMF, mixture was refluxed in slow argon flow with TLC monitoring (*n*-hexane–EtOAc, 1:1) for 9 h. After cooling, DMF was distilled off. Black oily residue was dissolved in $CHCl_3$ (50 ml), concentrated aqueous NH_3 (150 ml) was added and the resulting two-phase mixture was vigorously stirred overnight. Organic phase was separated and water layer was extracted with $CHCl_3$ (3×50 ml). Combined organic extracts were washed with brine, dried over Na_2SO_4 and evaporated to produce dark viscous oil, which was purified by column chromatography on SiO_2 using pentane–EtOAc (6.5:3.5) as an eluent. Evaporation of solvent gave **4** as viscous clear oil; yield, 4.10 g, 64%. ^{1}H NMR (300 MHz, CD_2Cl_2) δ: 7.31–7.27 (m, 10H, H_{Bn}), 7.23 (s, 2H, H_{Ar}), 4.51 (s, 4H, $CH_{2\,Bn}$), 4.20, 3.86, 3.70, 3.62 (4m, 4×4H, OCH_2). ^{13}C NMR (75 MHz, CD_2Cl_2) δ: 152.3, 138.4, 128.3, 127.6, 116.7, 115.9 (CN), 108.7 (*C*CN), 73.1, 70.9, 69.6, 69.4, 69.2. IR (ν/cm^{-1}): 2228 (C≡N). Found (%): C, 69.41; H, 6.38; N, 5.29. Calc. for $C_{30}H_{32}N_2O_6$ (%): C, 69.75; H, 6.24; N, 5.42.



Scheme 1

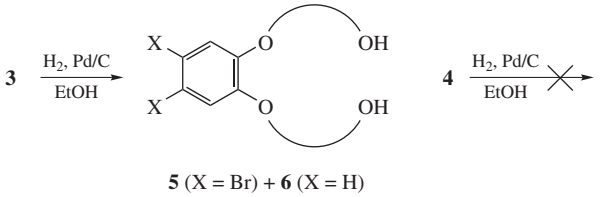
debenzylation (Scheme 2). Neither the variation of solvent (EtOAc or alcohols) and the addition of new catalyst portions, nor catalytic hydrogen transfer reaction (with cyclohexene as hydrogen donor)[14] and continuous reaction times (for several days) afforded cleavage of the protective group. In each case, the starting compound was recovered pure after the completion of the process.

In contrast, in the case of dibromide **3**, the very rapid absorption of hydrogen was observed. Even after 5 min, the formation of a new product was evidenced by TLC and complete conversion occurred in 1 h. ^{1}H NMR data showed that the resulting product is a mixture of two compounds: deprotected dibromide **5** and deprotected doubly dehalogenated derivative **6** in a ratio of 1.6:1 (Scheme 2). The observed reductive dehalogenation is a common side process in the debenzylation of halogenated substrates, which could be suppressed by the addition of acid in some cases, but this option was not explored in this study since the syntheses of both **5**[6] and **6**[8] have been described in the literature.

The high reactivity of dibromide **3** together with the inertness of phthalonitrile **4** under debenzylation conditions demonstrate that the phthalonitrile unit acts as a catalyst poison: its coordination to Pd inhibits further hydrogenolysis.

An analysis of published data evidences that the behavior of aromatic nitriles under hydrogenolysis conditions may be different from a compound to another. Depending on substrate, solvent or catalyst nature, the nitrile group can be either stable or partially reduced with the formation of an aminomethyl group. The latter process can be suppressed by addition of ethylenediamine (en), acting as a catalytic poison.[16] Therefore, the catalyst Pd/C(en) was proposed for the chemoselective hydrogenation of aromatic nitriles bearing other reducible groups (alkenes and alkynes) with retention of the CN group.

The O-benzyl protective group can be easily removed under Pd/C catalyzed hydrogenolysis, though Pd/C(en) can be used for chemoselective reduction of double and triple C–C bonds



5 (X = Br) + **6** (X = H)

Scheme 2

in benzylated substrates without debenzylation.[17] However, O-benzylated *p*-cyanophenol undergoes quantitative debenzylation even when a poisoned catalyst is used.[16] This is due to the electron-withdrawing effect of the cyano group, which facilitates hydrogenolysis even in the presence of less active catalysts. The same probably occurs in the case of 4,5-dibenzyloxyphthalonitrile.[5]

In the case of nitrile **4**, the O-benzyl groups are remote from the electron-withdrawing phthalonitrile fragment, resulting in lower reactivity and, in turn, higher sensitivity towards catalyst poisoning.

Notwithstanding the failure of catalytic deprotection of nitrile **4**, this compound can be used as a precursor of phthalocyanines bearing eight 2′-(2″-benzyloxyethoxy)ethoxy groups. Such compounds are expected to be discotic mesogens by analogy with previously described (2′-benzyloxyethoxy)-substituted phthalocyanines.[18] Langmuir–Blodgett layers of these compounds could be transferred on solid surfaces, and the resulting films demonstrated remarkable mechanical stability together with a highly ordered morphology.[19] Since nitrile **4** is an open-chained analogue of crown ethers (podand), phthalocyanines synthesized from this precursor can be prominent receptors for the binding of cations and small molecules resulting in formation of functional supramolecular assemblies.[20]

In conclusion, 1,2-dicyano-4,5-bis[2′-(2″-benzyloxyethoxy)-ethoxy]benzene was synthesized. This compound may act as a precursor of new functionalized phthalocyanines acting as discotic mesogens or supramolecular receptors.

This work was supported by ARCUS Alsace (a Russia/Ukraine project), the Russian Foundation for Basic Research (grant no. 09-03-93117), the CNRS and the Suprachem European Research Association.

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Received: 18th February 2010; Com. 10/3470