Synthesis of oxygen-containing heterocyclic *ortho*-dinitriles based on 4-bromo-5-nitrophthalonitrile

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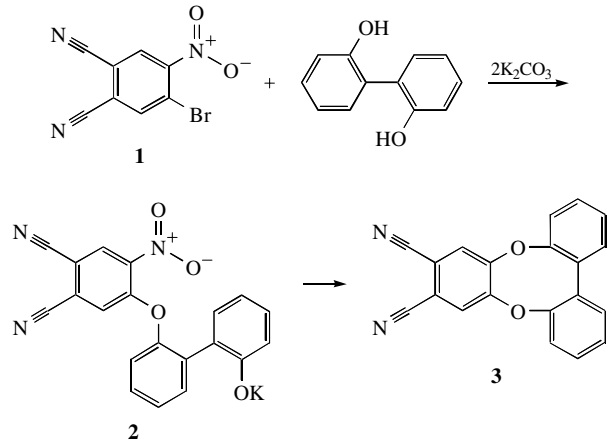
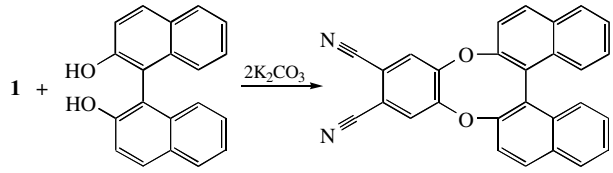
New dicyano derivatives of dioxin, dioxepin and dioxocine were prepared by the reactions of aromatic nucleophilic substitution for the bromine atom and the nitro group in 4-bromo-5-nitrophthalonitrile.

The reactions of activated aromatic nucleophilic substitution for the nitro group in 4-nitrophthalonitrile and for the bromine atom and the nitro group in 4-bromo-5-nitrophthalonitrile **1** are used for the synthesis of various new cyano-containing compounds,[1–3] which can be employed in the preparation of phthalocyanines, hexazocyclanes *etc*. A special feature of compound **1** is the presence of two mobile groups, *viz*., a bromine atom and a nitro group. The carbon atom bonded to the bromine atom is activated by the nitro group in the *ortho* position, and the presence of two cyano groups increases this effect and simultaneously activates the replacement of the nitro group. Thus, both of the nucleofuges can be readily replaced by various monofunctional O-, N- and S-nucleophiles (S_NAr reaction).[1–5] Here, we consider synthetic applications of compound **1** in reactions with bifunctional oxygen-containing nucleophiles. These reactions result in new cyano-containing six-, seven- and eight-membered heterocyclic compounds.



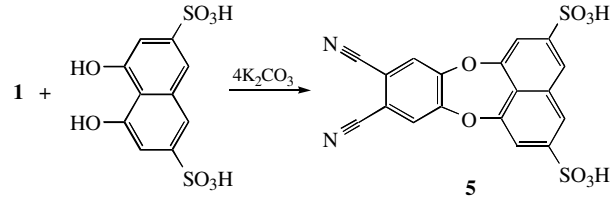
Scheme 1

The reaction of compound **1** with 2-(2-hydroxyphenyl)-phenol (Scheme 1) in the presence of a deprotonating agent afforded new tribenzo[*b*,*e*,*g*][1,4]dioxocine-7,8-dicarbonitrile **3**.† This heterophase reaction of nucleophilic substitution for a bromine atom proceeds *via* the *in situ* formation of potassium aryl oxide, which affords oxide **2** in a reaction with compound **1**. Previously,[1] we found that this reaction takes place even at room temperature. Substitution for the nitro group does not occur under these conditions. Resulting oxide **2** simultaneously bears an electrophilic centre and a nucleophilic centre, which are sufficiently activated for subsequent substitution. An increase in the temperature resulted in the interaction between these centres, *i.e.*, in intramolecular cyclisation. A similar reaction of compound **1** with 1-(2-hydroxynaphth-1-yl)naphth-2-ol resulted in benzo[*b*]dinaphtho[2,1-*e*:1,2-*g*][1,4]dioxocine-2,3-dicarbonitrile **4** (Scheme 2).



Scheme 2

New seven-membered oxygen-containing heterocyclic dicyano compound **5** from the dioxepin series was prepared by the interaction of compound **1** with 4,5-dihydroxynaphthalene-2,7-disulfonic acid (Scheme 3).‡ In this case, the nucleophile contained two sulfo groups in addition to two hydroxyl groups. In the presence of potassium carbonate, a salt insoluble in DMF is formed; therefore, the reaction became impossible. To perform this reaction successfully, a 75% aqueous DMF solution[1] was used under homophase conditions.



Scheme 3

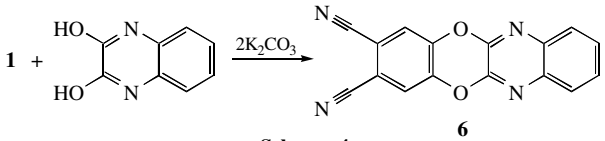
Compounds from the dioxin series were synthesised by nucleophilic substitution reactions with the use of pyrocatechol,[3,6] or by Smiles rearrangement with the use of substituted phenols.[7] However, there is no data on the use of quinoxaline-2,3-diol in reactions of this type. This fact can be explained by the presence of an electron-acceptor pyrazine ring in a starting reactant; consequently, the nucleophilicity of a salt of the hydroxy compound decreased. We pioneered the synthesis of benzo-[5,6][1,4]dioxino[2,3-*b*]quinoxaline-2,3-dicarbonitrile **6**§ by the reaction between compound **1**, which is highly reactive towards aromatic nucleophilic substitution, and quinoxaline-2,3-diol (Scheme 4).

The synthesised compounds were identified by NMR spectroscopy.¶

† *Tribenzo[*b,e,g*][1,4]dioxocine-7,8-dicarbonitrile* **3**. To 30 cm^3 of DMF 1.86 g (0.01 mol) of 2-(2-hydroxyphenyl)phenol, 2.8 g (0.02 mol) of K_2CO_3 and 2.52 g (0.01 mol) of 4-bromo-5-nitrophthalonitrile **1** were added. The resulting mixture was intensively stirred at 90 °C for 2 h. After cooling to room temperature, the reaction mixture was added to 100 cm^3 of water; the precipitate formed was filtered off, washed with 50 cm^3 of water and crystallised from DMF.

*Benzo[*b*]dinaphtho[2,1-*e*:1,2-*g*][1,4]dioxocine-2,3-dicarbonitrile* **4** was prepared in a similar manner with the use of 1-(2-hydroxynaphth-1-yl)-naphth-2-ol as a nucleophile.

‡ *9,10-Dicyanobenzo[*b*]naphtho[1,8-*ef*][1,4]dioxepin-2,5-disulfonic* acid **5**. To 40 cm^3 of a 75% aqueous DMF solution 3.20 g (0.01 mol) of 4,5-dihydroxynaphthalene-2,7-disulfonic acid, 5.6 g (0.04 mol) of K_2CO_3 and 2.52 g (0.01 mol) of 4-bromo-5-nitrophthalonitrile **1** were added. The resulting mixture was intensively stirred at 90 °C for 2 h. After cooling to room temperature, the reaction mixture was added to 50 cm^3 of water. To the resulting solution, 10 g of KCl was added, and pH 1 was adjusted by adding HCl. The precipitate formed was filtered off and washed with 50 cm^3 of diethyl ether.



Scheme 4

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§ *Benzo[5,6][1,4]dioxino[2,3-*b*]quinoxaline-2,3-dicarbonitrile* **6**. To 30 cm^3 of DMF 1.62 g (0.01 mol) of quinoxaline-2,3-diol, 2.8 g (0.02 mol) of K_2CO_3 and 2.52 g (0.01 mol) of 4-bromo-5-nitrophthalonitrile **1** were added. The resulting mixture was intensively stirred at 140 °C for 1 h. After cooling to room temperature, the reaction mixture was added to 100 cm^3 of water; the precipitate formed was filtered off, washed with 50 cm^3 of water and crystallised from DMF.

¶ ^{1}H NMR spectra of 5% solutions in [$^2H_6$]DMSO were measured on a Bruker AM-300 instrument using TMS as an internal standard.

For **3**: yield 79.1%, mp 205–206 °C. ^{1}H NMR, δ: 8.15 (s, 2H), 7.50–7.35 (m, 8H). Found (%): C, 77.28; H, 3.39; N, 8.94. Calc. for $C_{20}H_{10}N_2O_2$ (%): C, 77.41; H, 3.25; N, 9.03.

For **4**: yield 75%, mp > 300 °C. ^{1}H NMR, δ: 8.16 (s, 2H), 8.11 (d, 2H, *J* 8.3 Hz), 8.05 (dd, 2H, *J* 8.5 and 1.3 Hz), 7.60–7.50 (m, 4H), 7.45–7.38 (m, 4H). Found (%): C, 81.82; H, 3.52; N, 7.00. Calc. for $C_{28}H_{14}N_2O_2$ (%): C, 81.94; H, 3.44; N, 6.82.

For **5**: yield 63.8%, mp > 300 °C. ^{1}H NMR, δ: 8.38 (d, 2H, *J* 2.3 Hz), 8.04 (s, 2H), 7.70 (d, 2H, *J* 2.3 Hz). Found (%): C, 48.53; H, 1.82; N, 6.33; S, 14.45. Calc. for $C_{18}H_8N_2O_8S_2$ (%): C, 48.65; H, 1.81; N, 6.30; S, 14.43.

For **6**: yield 44.1%, mp > 300 °C. ^{1}H NMR, δ: 8.00 (s, 2H), 7.80 (dd, 2H, *J* 8.9 and 1.4 Hz), 7.65 (m, 2H). Found (%): C, 66.98; H, 2.13; N, 19.64. Calc. for $C_{16}H_6N_4O_2$ (%): C, 67.13; H, 2.11; N, 19.57.