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SYNTHESIS OF HETEROCYCLIC SYSTEMS ON THE BASIS OF 4-BROMO-5-NITROPHTHALONITRILE

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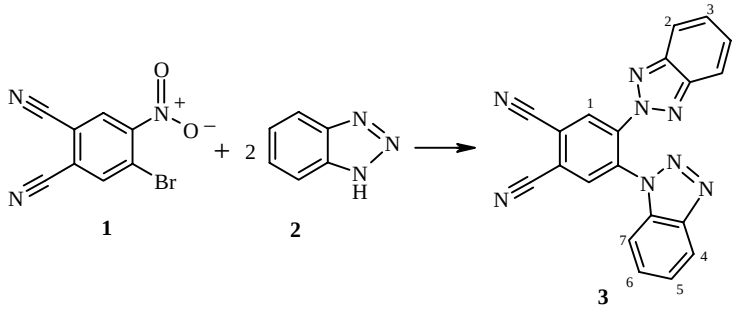
Reaction of 4-bromo-5-nitrophthalonitrile with aromatic and heterocyclic N- and O-nucleophiles in the presence of bases leads to the sequential substitution of the bromine atom and the nitro group to give the corresponding heterocyclic systems previously undescribed in the literature.

Keywords: benzotriazole, bifunctional nucleophiles, 4-bromo-5-nitrophthalonitrile, dioxin, nucleophilic substitution, oxazine, Smiles rearrangement.

The high activity of 4-bromo-5-nitrophthalonitrile (BNPN) (**1**) in S_NAr reactions with O- and N-nucleophiles [1] on the one hand and, on the other hand, the ability of heterocyclic systems to enter into analogous nucleophilic substitution reactions on being deprotonated [2] allowed us to synthesize a wide range of new nitrile-containing heterocyclic systems of different classes by the sequential substitution of both nucleofuges. Such classes included derivatives of benzotriazole, dioxin, oxazine, dioxocin, phenoxathiin, and thianthrene, which can be utilized to synthesize phthalocyanines, hexazocyclanes, and similar structures.

When benzotriazole **2** and compounds similar to it of "acid character" [2] are utilized as N-nucleophiles, the reaction under consideration only proceeds in the presence of a base by the heating in a dry aprotic dipolar solvent.



1 **2** **3**

Under these conditions, the substitution of the activated by nitro group and situated in the *ortho* position to it bromine atom in BNPN **1** takes place firstly. Two cyano groups of the substrate strengthen that influence, and then facilitate the substitution of the nitro group itself. We established that the sole product **3** in the reaction with benzotriazole has an unsymmetrical structure (Scheme 1).

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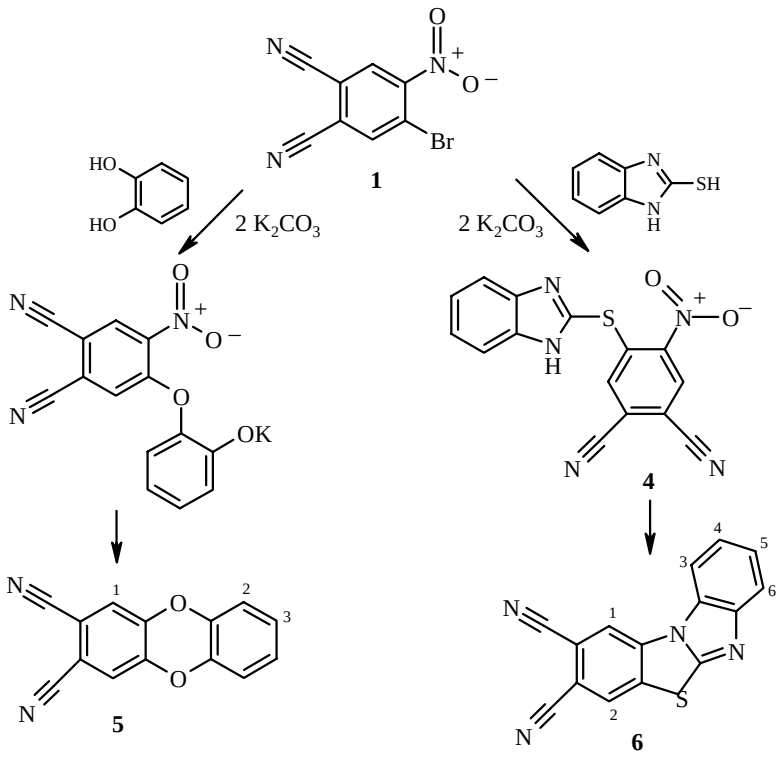
Scheme 1



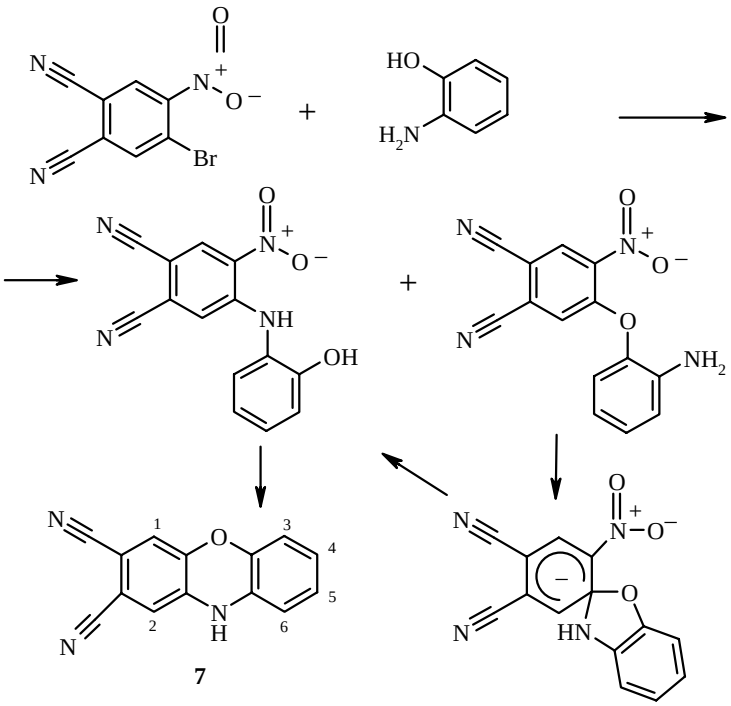
Another approach to the nucleophilic substitution reaction proceeding under the same conditions and leading to the formation of heterocycles is the reaction of compound **1** with bifunctional O-, N-, and S-nucleophiles. The heterophasic reaction of intermolecular nucleophilic substitution of the halogen atom begins with the *in situ* formation of the nucleophile, which reacts with the initial **1** to give the intermediate **4** containing both the nitro group and the nucleophilic center, sufficiently active for further substitution. The second nucleophile further enters into the intramolecular substitution of the nitro group situated in the same molecule which, in the case of pyrocatechol, leads to ring closure and the isolation of dibenzodioxin-2,3-dicarbonitrile **5**. When 2-mercaptobenzimidazole is utilized as a reagent under the same conditions, benzothiazolo[2,3-*b*]benzimidazole-2,3-dicarbonitrile (**6**) is formed. By analogy, the reaction of the initial **1** with 1,2-dimercaptobenzene and 2-mercaptophenol should proceed with the formation of the corresponding dinitrile derivatives of thianthrene and phenoxathiin [3]. The utilization of *o*-aminophenol instead of pyrocatechol in this reaction led to the isolation of dibenzo-1,4-oxazine-2,3-dicarbonitrile (**7**). Unreacted derivatives of diphenylamine and diphenyl oxide were identified together with the requisite product by means of ^{1}H NMR and mass spectroscopy. Diphenyl oxide undergoes intramolecular anionotropic Smiles rearrangement [3] under the reaction conditions with the preferred formation of diphenylamine derivatives (Scheme 2).

The synthesized heterocyclic dinitriles **3** and **5-7** are crystalline substances, the structure of which was confirmed by their spectral characteristics. Thus, the IR spectra of these compounds contain characteristic absorption bands of stretching vibrations of the –C≡N bond at 2240 cm^{-1}, the ether bond at 1260 cm^{-1}, the thioether bond at 650 cm^{-1}, and –NH– at 3130-3300 cm^{-1}. Characteristic absorption bands of the NO_2 group (1560 and 1340 cm^{-1}) are absent [4]. The ^{1}H NMR spectra contain signals of aromatic protons. The mass spectra of these compounds have strong peaks of the molecular ions M^+, and the character of the further fragmentation does not contradict the proposed structures.

TABLE 1. Characteristics of the Compounds Synthesized

Compound	Empirical formula	Found, % / Calculated, %				mp, °C	IR spectrum, ν, cm^{-1}	Mass spectrum, *m/z* (%)	^{1}H NMR spectrum, δ, ppm	Yield, %
		C	H	N	S					
3	$C_{20}H_{10}N_8$	66.08 / 66.29	2.84 / 2.78	31.05 / 30.39		291-293	2230 (–CN)	363 (30) [M^+], 334 (18), 305 (100), 280 (17), 90 (22), 63 (56), 50 (30), 39 (21)	8.90 (2H, s, H-1); 8.00 (2H, d, H-2, *J* = 9 Hz); 7.45-7.30 (6H, m, H-3, 4, 5, 6, 7, *J* = 30 Hz)	58
5	$C_{14}H_6N_2O_2$	71.64 / 71.79	2.67 / 2.59	11.99 / 11.96		>300	2225 (–CN) 1260 (–O–)	235 (15), 234 (100) [M^+], 178 (18), 151 (19), 121 (11), 117 (14), 63 (10)	7.70 (2H, s, H-1); 7.00 (4H, m, H-2,3, *J* = 25 Hz)	81
6	$C_{15}H_6N_4S$	65.67 / 65.70	2.25 / 2.21	20.47 / 20.42	11.79 / 11.68	305-306	2240 (–CN) 650 (–S–)	275 (19), 274 (100) [M^+], 137 (12), 63 (10), 39 (17)	9.11 (1H, s, H-2); 8.82 (1H, s, H-1); 8.55 (1H, d, H-6, *J* = 9 Hz); 7.75 (1H, d, H-3, *J* = 9 Hz); 7.45 (2H, m, H-4, H-5, *J* = 24 Hz)	59
7	$C_{14}H_7N_3O$	71.82 / 72.10	3.12 / 3.03	17.95 / 18.02		273-275	3130–3300 (–NH–) 2230 (–CN) 1260 (–O–)	234 (10), 233 (100) [M^+], 204 (29), 63 (24)	9.10 (1H, s, NH); 7.00 (1H, s, H-1); 6.75 (1H, s, H-2); 6.65-6.45 (4H, m, H-3, 4, 5, 6, *J* = 40 Hz)	57

Scheme 2



EXPERIMENTAL

4-Bromo-5-nitrophthalonitrile (1). This compound was synthesized by the method [1]. The ^{1}H NMR spectra were recorded on the Bruker AM-300 instrument utilizing the 5% solutions of the samples in DMSO-d_6 with TMS as the internal standard. The numbering of the protons in the spectra of the compounds **3** and **5-7** corresponds to the numbering of the protons in the schemes. The mass spectra were recorded on the MX-1321 spectrometer with direct input at 100-150°C and the accelerating voltage of 70 eV. The IR spectra were recorded on the IR-75 instrument utilizing the suspension in mineral oil.

1-(6-Benzotriazol-2-yl-3,4-dicyanophenyl)benzotriazole (3). To DMF (30 ml) benzotriazole **2** (2.4 g, 0.02 mol), anhydrous K_2CO_3 (2.8 g, 0.02 mol), and 4-bromo-5-nitrophthalonitrile **1** (2.5 g, 0.01 mol) were added sequentially with mixing. The resulting mixture was stirred strongly at 130-140°C for 2 h. After the cooling to room temperature, the reaction mass was poured into water (100 ml). The residue formed was filtered off, washed with water (50 ml), and crystallized from DMF.

By analogy, equimolar amounts of pyrocatechol, 2-mercaptobenzothiazole, and *o*-aminophenol afford dibenzo-1,4-dioxine-2,3-dicarbonitrile (**4**), benzothiazolo[2,3-*b*]benzimidazole-2,3-dicarbonitrile (**6**), and dibenzo-1,4-oxazine-2,3-dicarbonitrile (**7**) correspondingly.

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