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Synthesis of expanded alkylphenoxythiadiazole macroheterocycles

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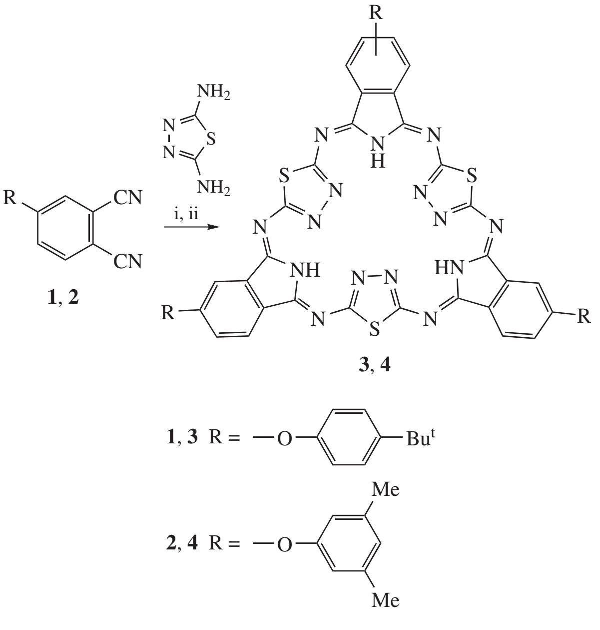
New substituted macroheterocyclic compounds of the ABABAB type were synthesised by condensation of 2,5-diamino-1,3,4-thiadiazole with the products of interaction of 4-(4-*tert*-butylphenoxy)- or 4-(3,5-dimethylphenoxy)phthalonitriles with sodium alkoxides in a butanol–methanol mixture.

Macroheterocyclic compounds of the ABABAB type consist of three 1,3,4-thiadiazole rings (A) and three isoindole subunits (B) connected to each other *via* aza bridges.[1–3] They belong to a new class of porphyrinoids having an expanded coordination cavity and can be considered as heteroanalogues of hexaphyrins.[4] At the same time, these compounds can be considered as expanded hemiporphyrazines,[5] more exactly, triazolehemiporphyrazines.[6,7] However, they are different from expanded ABBABB system discovered recently.[8] The coordinating properties and acid-basic behaviours of ABABAB-type compounds have been published recently.[9–11]

Here, we report on the synthesis and spectral characterization of new substituted macroheterocyclic compounds of the ABABAB type.

4-Aryloxyphthalonitriles **1**, **2** were synthesised using the S_NAr reaction of 4-nitrophthalonitrile with corresponding phenols in the presence of K_2CO_3 in aqueous DMF (75%). A substitution of the nitro group by [O$^-$]-nucleophiles, which have been generated *in situ* from corresponding phenols and potassium carbonate, took place. The synthesis of 4-(4-*tert*-butylphenoxy)phthalonitrile **1** and 4-(3,5-dimethylphenoxy)phthalonitrile **2** was described elsewhere.[12,†] 2,5-Diamino-1,3,4-thiadiazole was synthesised according to the procedure described previously.[13]



Scheme 1 *Reagents and conditions*: i, MeONa, BuONa, MeOH, BuOH, 7 h, 20–25 °C; ii, NH_4Cl, 3 h, 20–25 °C, 2,5-diamino-1,3,4-thiadiazole, 33 h, 120 °C.

Macroheterocyclic compounds **3**, **4** were synthesised by condensation of 2,5-diamino-1,3,4-thiadiazole with the products of interaction of 4-(4-*tert*-butyl)phthalonitrile **1** or 4-(3,5-dimethoxy)phthalonitrile **2** with sodium alkoxides in butanol–methanol (Scheme 1).[‡,§]

The reaction run has been monitored by TLC and UV-VIS spectroscopy. Compounds **3**, **4** were purified by column chromatography on aluminium oxide using dichloromethane as an eluent.

Compounds **3**, **4** were characterised by UV-VIS, IR and ^{1}H NMR spectroscopy, mass spectrometry and elemental analysis.[§]

[†] *4-(4-*tert*-Butylphenoxy)phthalonitrile* **1**. A solution of K_2CO_3 (1.56 g, 0.01 mol) in water (10 ml) was added under strong agitation into a solution containing 4-nitrophthalonitrile (1.73 g, 0.01 mol), 4-*tert*-butylphenol (1.50 g, 0.01 mol) and DMF (30 ml). The reaction mixture was very intensely agitated at 80–95 °C for 1 h. After cooling to room temperature, the reaction mixture was poured into water (100 ml), the precipitate was filtered, washed with water (50 ml) and recrystallised from propan-2-ol. The yield of compound **1** was 2.05 g (74%) as a white crystalline powder, mp 118–119 °C. ^{1}H NMR ([^{2}H$_6$]DMSO) δ: 8.03 (d, 1H, 6-H, *J* 8.8 Hz), 7.61 (d, 1H, 3-H, *J* 2.5 Hz), 7.48 (d, 2H, 3′-H, 5′-H, *J* 8.5 Hz), 7.32 (dd, 1H, 5-H, *J* 2.5 Hz, *J* 8.8 Hz), 7.05 (d, 2H, 2′-H, 6′-H, *J* 8.5 Hz), 1.33 (s, 9H, Bu^t). Found (%): C, 78.56; H, 5.91; N, 10.05. Calc. for $C_{18}H_{16}N_2O$ (%): C, 78.24; H, 5.84; N, 10.14.

4-(3,5-Dimethylphenoxy)phthalonitrile **2** was synthesised using equimolar quantity of 3,5-xylenol. The yield of compound **2** was 1.87 g (75%) as a white crystalline powder, mp 115–116 °C. ^{1}H NMR ([^{2}H$_6$]DMSO) δ: 8.02 (d, 1H, 6-H, *J* 8.8 Hz), 7.59 (d, 1H, 3-H, *J* 2.4 Hz), 7.32 (dd, 1H, 5-H, *J* 2.4 Hz, *J* 8.8 Hz), 6.92 (s, 1H, 4′-H), 6.73 (s, 2H, 2′-H, 6′-H), 2.31 (s, 6H, Me). Found (%): C, 77.65; H, 4.98; N, 11.11. Calc. for $C_{16}H_{12}N_2O$ (%): C, 77.40; H, 4.87; N, 11.28.

[‡] Compounds **3**, **4** were synthesised according to a general procedure: metallic sodium (0.267 mmol) was dissolved in a mixture of butanol (5 ml) and methanol (0.2 ml). Then dinitrile **1** or **2** (0.181 mmol) was added to this solution, and the reaction mixture was stirred for 7 h at room temperature. After addition of ammonium chloride (0.267 mmol), the reaction mass was stirred for 3 h. Finally, 2,5-diamino-1,3,4-thiadiazole (0.181 mmol) was added and the reaction mixture was stirred at 80 °C for 2 h and after that at reflux for 33 h. After the solvents were removed, a solid was treated with methanol and a precipitate was separated by filtration, washed with MeOH, and dried. Purification was made using column chromatography on aluminium oxide; eluent, dichloromethane. After solvent removal, the orange solid was washed with MeOH and dried in a vacuum.

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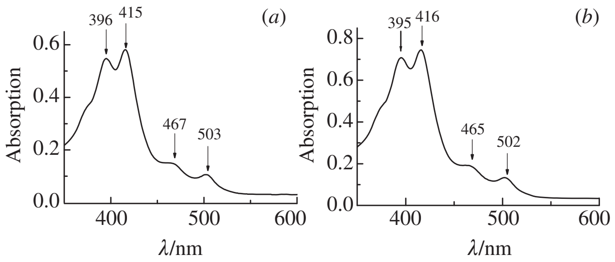

Figure 1 UV-VIS spectra of macroheterocycles in CH_2Cl_2: (*a*) **3** (C = = 3.30 mol dm^{-3}); (*b*) **4** (C = 3.80 mol dm^{-3}).

The IR spectra of compounds **3** and **4** are similar to each other. Thus, in the spectrum of compound **3**, a series of bands at 2959, 2918 and 2849 cm^{-1} characterises the C–H stretching vibrations of *tert*-butyl groups. The band at 3217 cm^{-1} is induced by N–H vibrations of imino groups. The strong bands at 2916 and 2848 cm^{-1} in the spectrum of **4** can be assigned to C–H vibrations of methyl groups. The absorption band corresponding to N–H stretching vibrations of imino groups is observed at 3212 cm^{-1}.

The UV-VIS spectra of compounds **3** and **4** shown in Figure 1 are similar. Thus, the strong absorbance bands at 396 and 415 nm (**3**) and at 395 and 416 nm (**4**) dominate in the spectra of both compounds while the bands of lower intensities are located at about 450–505 nm. These spectra are similar to the spectrum of *tert*-butyl-substituted macroheterocyclic compound of ABABAB type,[1,2] and it can evidence the similarity of their chromophore systems.

Mass spectra of compounds **3** and **4** are characterised by the presence of peaks corresponding to the molecular ions $[M + H]^+$. A perfect coincidence of molecular mass as well as the isotope distributions and calculated values proofs the structures of these compounds as macrocyclic systems of the ABABAB type containing three 1,3,4-thiadiazole rings and three substituted isoindole subunits.

^{1}H NMR spectra of compounds **3** and **4**, measured in $CDCl_3$, reveal the signals at 1.37 and 1.25 ppm, respectively, which can be assigned to the protons of alkyl groups. The multiplets at 7.79–7.02 (**3**) and 7.78–7.25 ppm (**4**) are due to the resonance of the protons of benzene rings, and the singlets at 12.27 (**3**) and 12.36 ppm (**4**) characterise the absorbance of the protons of imino groups. The presence of these signals in the low field highlights the non-aromatic character of ABABAB macrocycle.

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§ *2,14(15),26(27)-Tri(4-*tert*-butylphenoxy)-5,36:12,17:24,29-triimino-7,10:19,22:31,34-trithia-[*f,p,z*]-tribenzo-1,2,4,9,11,12,14,19,21,22,24,29-dodecazacyclotriaconta-2,4,6,8,10,12,14,16,18,20,22,24,26,28,30-pentadecaene* **3** was obtained following general procedure from 4-(4-*tert*-butylphenoxy)phthalonitrile (50 mg, 0.181 mmol) and 2,5-diamino-1,3,4-thiadiazole (21 mg, 0.181 mmol). Yield, 15 mg (22%). UV-VIS [CH_2Cl_2, λ_{max}/nm (log ε)]: 396 (4.92), 415 (4.94), 467 (sh), 503 (4.21). IR (thin film, ν/cm^{-1}): 3217, 2959, 2918, 2849, 1629, 1508, 1478, 1407, 1367, 1327, 1272, 1235, 1214, 1101, 1032, 928, 837, 716. ^{1}H NMR ($CDCl_3$) δ: 12.27 (s, NH), 7.79, 7.40, 7.13, 7.02 (m, H arom.), 1.37 (s, CMe). Found (%): C, 62.46; H, 4.31; N, 17.51; S, 7.59. Calc. for $C_{60}H_{51}N_{15}O_3S_3$ (%): C, 63.98; H, 4.56; N, 18.65; S, 8.54. MS (MALDI-TOF), *m/z*: 1126 $[M + H]^+$.

*2,14(15),26(27)-Tri(3,5-dimethylphenoxy)-5,36:12,17:24,29-triimino-7,10:19,22:31,34-trithia-[*f,p,z*]-tribenzo-1,2,4,9,11,12,14,19,21,22,24,29-dodecazacyclotriaconte-2,4,6,8,10,12,14,16,18,20,22,24,26,28,30-pentadecaene* **4** was obtained following general procedure from 4-(3,5-dimethylphenoxy)phthalonitrile (45 mg, 0.181 mmol) and 2,5-diamino-1,3,4-thiadiazole (21 mg, 0.181 mmol). Yield, 14 mg (20%). UV-VIS [CH_2Cl_2, λ_{max}/nm (log ε)]: 395 (4.95), 416 (4.97), 465 (sh), 502 (4.23). IR (thin film, ν/cm^{-1}): 3212, 2916, 2849, 1615, 1478, 1406, 1368, 1326, 1294, 1272, 1226, 1200, 1136, 1100, 1033, 950, 834, 741, 716. ^{1}H NMR ($CDCl_3$) δ: 12.36 (s, NH), 7.78, 7.39, 7.25 (m, H arom.), 1.25 (s, Me). Found (%): C, 62.06; H, 3.32; N, 18.42; S, 7.93. Calc. for $C_{54}H_{39}N_{15}O_3S_3$ (%): C, 62.23; H, 3.77; N, 20.16; S, 9.23. MS (MALDI-TOF), *m/z*: 1042 $[M + H]^+$.