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Synthesis of Thiadiazole Hemihexaporphyrazine Bearing Isopropyloxy Groups and its Trinuclear Ni^{II} Complex

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A thiadiazole derived expanded "hemihexaporphyrazine" of ABABAB-type has been prepared via cyclomerization reaction of 2,5-diamino-1,3,4-thiadiazole and 3,6-diisopropyloxyphthalonitrile in an extremely low 2% yield. Whereas a template condensation of the initial compounds in the presence of $Ni(OAc)_2 \cdot 4H_2O$ afforded a corresponding trinuclear Ni^{II} complex in a good yield.

Keywords: Macroheterocyclic compounds, hemihexaporphyrazines, thiadiazole, synthesis.

Introduction

Expanded conjugated macrocycles are of a deep interest for the last decades due to their specific spectral features.[1,2] These macromolecules evolve perfect models for the amplification of the Hückel rule of aromaticity[3] and computational studies[4] due of their structural variety, versatility and complicity, resulting in rich photophysics and electrochemistry.[5,6] From the functional viewpoint, expanded porphyrins possess exceptional coordination properties consisting in selective binding to certain metal ions with further homo- and heteropolynuclear complexes formation.[7] Thus, they are good candidates for application in catalysis, anion recognition, ion extraction and transport.[8-10]

Multiple trials to the modification of the tetraazaporphyrin structure have been undertaken in order to obtain other macrocycles structurally related to phthalocyanines and porphyrazines, but exhibiting nonconventional physicochemical features. Superphthalocyanine pentapyrrolic macrocycles have been remained the only reported example of expanded azaporphyrins for many years,[11] until different heterocyclic building blocks were incorporated into structures of azaporphyrins. That has fairly enriched synthetic sources toward the desirable structures and provided chemists with a big variety of objects for a further depth study. In the last decades, chemistry of azaporphyrins has been widely advanced due to the persistent work on this field.[12-14] Herein, the one problem for the rational design of expanded azaporphyrins, *i.e.* the spontaneous formation of macrocycles of the favorable structures and open-chain intermediates, has been overcome by the working out of some synthetic approaches.

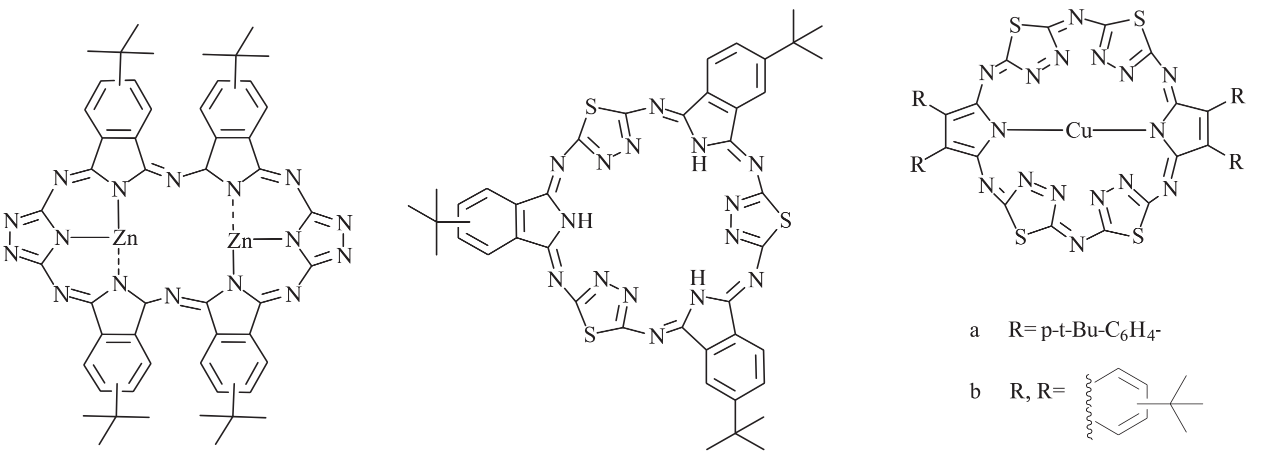
Following the stepwise procedure, the first example of an expanded 28 π-electron heteroazaporphyrinoid **1** of ABBABB-type, made up of four diiminoisoindoline (B) subunits and two face-to-face triazole (A) rings, was prepared.[15] (Figure 1). Its expanded macrocyclic cavity with two metal ions inside was constructed by the dimerization of metal complex of opened trimeric intermediate of two diiminoisoindoline and one triazole subunits (BAB). Later, another expanded metal-free 30 π-electron hemiporphyrazine **2** of ABABAB-type has been communicated[16] as a product of the crossover condensation of three 2,5-diamino-1,3,4-thiadiazole and three substituted diiminoisoindoline. This macrocycle is considered to be a hexaphyrin analogue where its subunits are bonded via six aza-bridges and three pyrrolic rings are replaced by three thiadiazoles. So, a term "hemihexaporphyrazine" that reproduces these features seems to be acceptable to define Mc of ABABAB-type. Recently, hemihexaporphyrazine has been unequivocally structurally characterized, and complete spectroscopic, redox, photophysical and thermal stability characterization newly was given.[17]

Furthermore, the copper(II) template crossover condensation was applied successfully to the preparation of the novel binuclear thiadiazole-derived azaporphyrin-like hexamer **3** of AABAAB-type, made up of four thiadiazole subunits, two face-to-face pyrrole rings and one metal ion.[18] However, authors noted that under those conditions corresponding ABABAB complexes have been also obtained.

Our previous attempts to prepare a metal free ABABAB heteroazaporphyrinoid bearing six strong electron-donating isopropyloxy substituents in *n*-pentanol were failed. Recently, we succeed in synthesis of compound **5** in an extremely low 2 % yield when isopropanol was used for the cyclomerization of precursors (Scheme 1). Complex **6** was prepared by crossover condensation in the presence of Ni^{II} salt as a template in 23% yield (Scheme 2). Thus, we report here the template condensation as a fitting method for the preparation of complexes of ABABAB hemiporphyrazines.

Experimental

UV-Vis spectra were recorded with a Hewlett-Packard 8453 instrument. IR spectra were collected with Bruker Vector 22 spectrophotometer. MALDI-TOF spectra were carried out with a



1 **2** **3**

Figure 1. Structures of expanded hemiporphyrazines.

Bruker Reflex III. NMR spectra were measured with a Bruker AC-300. Column chromatography was performed on silica gel Merck-60 (230-400 mesh, 60 Å). TLC was performed on aluminum sheets precoated with silica gel 60 F$_{254}$ (E. Merck).

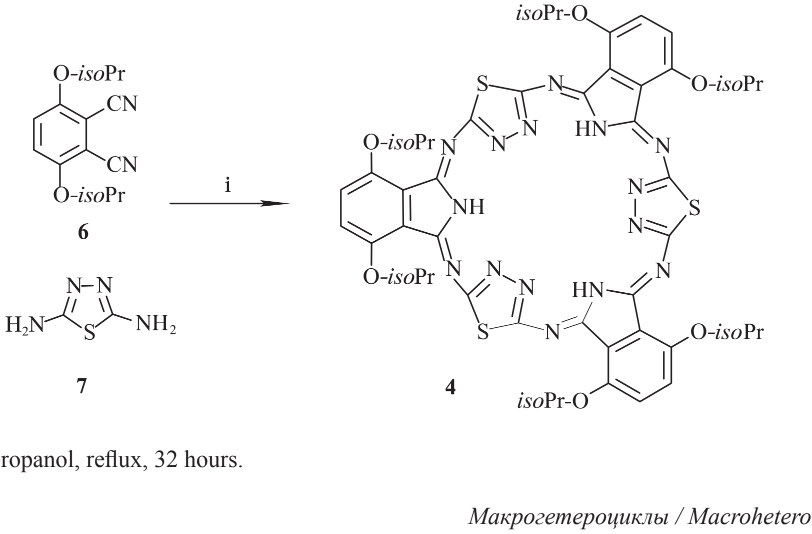
3,6-Diisopropoxyphthalonitrile[19] and 2,5-diamino-1,3,4-thiadiazole[20] were synthesized according to literature procedures. Chemicals were purchased from Aldrich Chemical Co. and used without further purification.

2,3,14,15,26,27-Hexa(isopropyloxy)-5,36:12,17:24,29-triimino-7,10:19,22:31,34-trithio-[f,p,z]-tribenzo-1,2,4,9,11,12,14,19,21,22,24,29-dodecaazacyclotriacontene-2,4,6,8,10,12,14,16,18,20,22,24,26,28,30-pentadecaen , ***4***. 3,6-Diisopropyloxyphthalonitrile (**6**, 244 mg, 1.0 mmol) and 2,5-diamino-1,3,4-thiadiazole, (**7**, 116 mg, 1.0 mmol) were dissolved in dry isopropanol (8 ml) at reflux. Sodium (12 mg, 0.5 mg-eq) was added and the reaction mixture was refluxed for 32 hours under argon. Afterwards, the isopropanol was rotary evaporated and the residue was suspended in methanol (10 ml), filtered and washed with water, acetone followed by hexane. The obtained solid was dissolved in chloroform and filtered through aluminum oxide. Purification by column chromatography on silica gel using chloroform-ethanol (50:1) mixture as eluent afforded 6.87 mg of **4** (2%) as a red solid. *m/z* (MALDI-TOF, dithranol): 1030 [M+H]$^+$. IR (KBr) ν_{max} cm^{-1}: 3223 (N-H), 2935, 2868 (C-H), 1616, 1508, 1468, 1400, 1427, 1373, 1283, 1256, 1188, 1121, 1068, 966, 918, 883, 837, 800, 735, 613. UV-vis (CHCl$_3$) λ_{max} (lgε) nm: 276 (4.71), 452 (4.88), 479 (4.69), 518 (4.34). ^{1}H NMR (CDCl$_3$, 300 MHz) δ_H ppm: 12.69 (s, 3H, NH), 7.15 (s, 6H, H arom), 4.72 (m, 6H, OCH$_2$), 1.48 (m, 36H, CH$_3$).

*Trihydroxy-1,4,13,16,25,28-hexa(isopropyloxy)-5,36:12,17:24,29-triimino-7,10:19,22:31,34-trithio-[f,p,z]-tribenzo-1,2,4,9,11,12,14,19,21,22,24,29-dodecaazacyclotriacontene-2,4,6,8,10,12,14,16,18,20,22,24,26,28,30-pentadecaenato(3$^-$)-N^8,N^{37},N^{33}:N^9,N^{38},N^{20}:N^{21},N^{39},N^{32}-trinickel(II), **5***. 3,6-Diisopropyloxyphthalonitrile (**6**, 205 mg, 2.05 mmol), 2,5-diamino-1,3,4-thiadiazole, (**7**, 204 mg, 2.05 mmol), nickel(II) acetate tetrahydrate (510 mg, 2.05 mmol) and 2-ethoxyethanol (30 ml) were stirred for 1 hour at 30°C and then refluxed for 20 hours. Afterwards, the 2-ethoxyethanol was evaporated and the residue was suspended in water (10 ml), filtered and washed with water-methanol (10:1) mixture, then dried. The obtained solid was washed by acetonitrile and purified by column chromatography on silica-gel using chloroform – methanol (4:1) mixture as eluent. After solvents evaporation, the solid was washed by methanol, hexane. Compound **5** (650 mg, 23%) was obtained as a dark red solid. Found: C 46.11, H 4.20, N 15.55, S 8.52 %. $C_{48}H_{48}N_{15}O_7S_3Ni_3 \cdot 3OH$ requires C 45.96, H 4.10, N 16.75, S 7.67. *m/z* (MALDI-TOF, dithranol) 1216 [M]$^+$. IR (KBr) ν_{max} cm^{-1}: 2923, 2852, 1600, 1539, 1099. UV-vis (CHCl$_3$) λ_{max} (lgε) nm: 527 (3.75), 570 (sh).

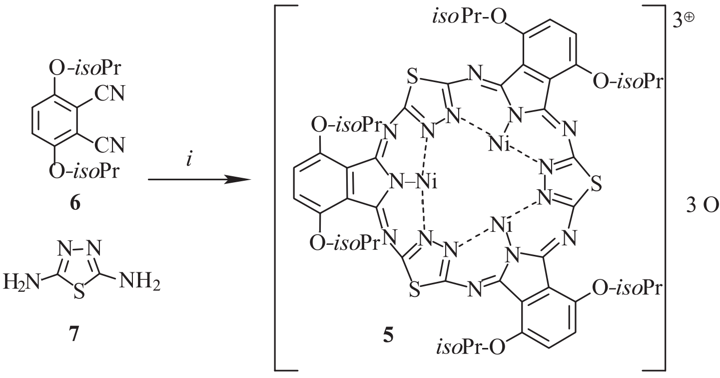
Results and Discussion

The compound **4** was obtained for the first time by the crossover condensation of 2,5-diamino-1,3,4-thiadiazole and 3,6-diisopropyloxyphthalonitrile in a presence of sodium isopropoxide in dry isopropanol in an extremely low 2 % yield (Scheme 1).



Scheme 1. i: *iso*-PrONa, isopropanol, reflux, 32 hours.

Choice of solvent is conditioned by a low solubility of 3,6-diisopropyloxyphthalonitrile in high-boiling alcohols. Moreover, using of other alcohols was avoided because of the competing *trans*-alkylations of *ortho*-alkoxy groups described for phthalocyanines.[21] The presence of two strong electron-donating and bulky substituents in 3,6-positions of initial phthalonitrile results in a high activation barrier of nucleophilic addition[22] reasoning the low yield of condensation in isopropanol. Preparation of complexes ABABAB consists in insertion of metal atoms into macrocyclic cavity by metallation reaction. Following this approach, trinuclear nickel(II) complexes have been characterized up to date.[16] In our case, usage of this route has been limited by the availability of free-base macrocycle. Whereas, nickel(II)-template condensation afforded macrocycle **5** in a good yield. The compounds obtained were characterized



Scheme 2. i: $Ni(OAc)_2 \cdot 4H_2O$, 2-ethoxyethanol, reflux, 24 hours.

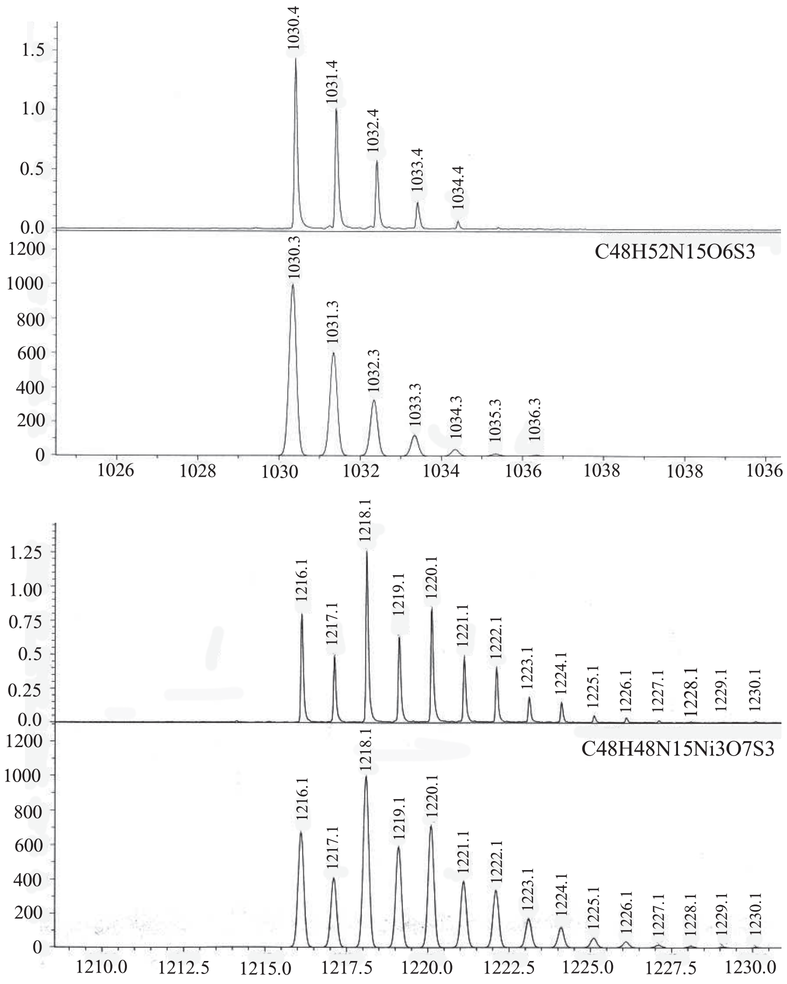


Figure 2. Isotopic patterns of molecular ions corresponding to **4** and **5.**

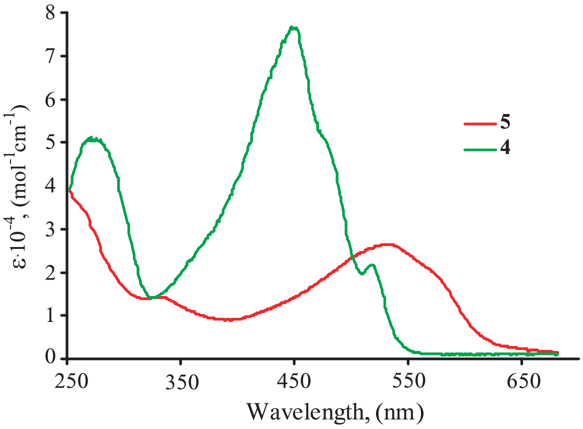


Figure 3. UV-Vis spectra of **4** and **5**.

by MALDI-MS, ^{1}H NMR, IR, UV-Vis spectroscopy and identified as thiadiazole-derived hemiporphyrazines. Signal at 1030 *m/z* in mass-spectrum of free-base **4** corresponds to $[M+H]^+$ molecular ion. MALDI-MS data for **5** indicate that it is the result of (3+3+3) template condensation (Scheme 2), and signal at 1216 *m/z* corresponds to $[3Ni+M+O]^+$ molecular ion. It seems that there is an elimination of OH groups during mass-spectrum experiment.

The ^{1}H NMR spectrum of **4** shows a singlet at 12.69 ppm of three H atoms of pyrrolic fragments. The signals of absorbing aromatic protons and those of isopropyl groups appear at 7.15 (s, 6H) and 4.72(m, 6H), 1.48 (d, 36H), ppm, respectively. UV-Vis spectrum of the compound **4** reveals strong absorption around 276 and 452 nm with a shoulders at 479, 518 nm assignable to π-π* transitions, in chloroform solution. Those bands are red-shifted to 80-90 nm (333, 532 nm) for **5** under nickel(II) complexation.

The band of pyrrolic *ν*(NH) located at 3211 cm^{-1} in infrared spectra of **4** disappears on going to complex compound **5**. Strong absorption at 1618 cm^{-1} caused by C=N stretching vibrations in spectrum of **4** are shifted negatively in the spectrum of complex **5** to the extent of 20 cm^{-1} due to the coordination of nitrogen. The absence of C=O stretching vibrations at 1670 cm^{-1} in the spectrum of **5** indicates that no acetate as a counter ion presents. Complexation mode of nickel(II) atoms within the ABABAB core is still under question and will be studied in a due course.

Conclusions

A new thiadiazole derived expanded "hemihexaporphyrazine" of ABABAB-type has been prepared via co-cyclohexamerization reaction of 2,5-diamino-1,3,4-thiadiazole and 3,6-diisopropyloxyphthalonitrile in an extremely low yield. A template condensation of the initial compounds in the presence of $Ni(OAc)_2 \cdot 4H_2O$ afforded its trinuclear Ni^{II} complex in a good yield and may be considered as a successful synthetic method.

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