

## Synthesis and Characterization of a Soluble Hemihexaphyrazine Derivative

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Dedicated to the member of Russian Academy of Sciences, Professor Aslan Tsvadze on the occasion of his Anniversary

*The symmetrically substituted hexakis(n-hexyl)hemihexaphyrazine was synthesized by condensation of 3,6-bis(n-hexyl)phthalonitrile and 2,5-diamino-1,3,4-thiadiazole in the presence of sodium pentanolate. The macrocycle was characterized by MALDI-TOF mass spectrometry, as well as IR, <sup>1</sup>H and <sup>13</sup>C NMR, UV-Vis absorption and fluorescence spectroscopies.*

**Keywords:** Expanded azaporphyrin, hemihexaphyrazine, 1,3,4-thiadiazole, hexaphyrin.

## Синтез и характеристика растворимого производного гемигексафиазина

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*Симметрично-замещенный гексакис(н-гексил)гемигексафиазин был синтезирован конденсацией 3,6-бис(н-гексил)фталонитрила и 2,5-диамино-1,3,4-тиадиазола в присутствии пентанолята натрия, взятых в стехиометрическом соотношении (1:1:0.5), в пентаноле. Целевое соединение было охарактеризовано с помощью масс-спектрометрии MALDI-TOF, данных ИК- и ЯМР-спектроскопии <sup>1</sup>H и <sup>13</sup>C, а также спектров поглощения и флуоресценции.*

**Ключевые слова:** Азапорфирин с увеличенной координационной полостью, гемигексафиазин, 1,3,4-тиадиазол, гексафиазин.

### Introduction

Expanded porphyrinoids display modified  $\pi$ -systems that alter the porphyrin aromatic character.<sup>[1-4]</sup> This translates into unusual optical, electrochemical and photophysical properties that render them promising building blocks

for the construction of new molecular materials at different technological fields.<sup>[5]</sup> In addition, their large, polydentate central cavities provide interesting coordination abilities, such as anion binding, or multimetallic complexation, which are virtually inaccessible within the corresponding tetramers.<sup>[6-8]</sup> Contrasting with the great assortment of ex-

panded porphyrins reported to date, examples of the corresponding expanded *meso*-aza-analogues are still very scarce. One prototypical example of the latter is constituted by the family of the hemihexaphyrazines, a kind of hexamer consisting of an expanded hemiporphyrazine that has been developed in our group.<sup>[9,10]</sup>

Hemihexaphyrazines are highly symmetrical macroheterocyclic compounds of ABABAB-type, made up of three alternated thiadiazole and pyrrole subunits interconnected by nitrogen atoms (see Scheme 2).<sup>[11]</sup> The macrocyclic backbone consists of a planar structure, displaying a 30  $\pi$ -electron electronic circuit, wherein the thiadiazole sulfur atoms point outside the macrocycle and the inner cavity contains 15 nitrogen atoms. The development of soluble, symmetric derivatives that are obtained as single regioisomers, is desirable from the preparative point of view, especially for many applications that involve the use large amounts of compounds. Alkyl substitution at the 3- and 6-positions of the isoindole fragments promotes self-organization of certain macrocycles, such as phthalocyanines, leading to molecular materials of interest for recording and storing information.<sup>[12]</sup> Inspired by these examples, we have developed in this work a soluble, processable hemihexaphyrazine derivative, hexafunctionalized at the isoindole 3,6-positions by linear hexyl chains.

## Experimental

MALDI-TOF spectra were recorded with a Bruker Reflex III. NMR spectra were recorded with a Bruker AC-300 and Bruker DRX-500 instruments. UV-vis spectra were recorded with a Hewlett-Packard 8453 instrument at the Interdepartmental Investigation Service (SIdI) of Universidad Autónoma de Madrid.

IR spectra were registered on an Avatar 360 FT-IR instrument. The study was carried out using the resources of the Center for collective use of scientific equipment of ISUCT.

The fluorescence quantum yield ( $\Phi_f$ ) was determined on FluoTime 300 (LDH-P-C-450) using an integration sphere. Time-resolved fluorescence measurements were carried out by means of a high performance fluorescence lifetime and a steady state spectrometer FluoTime 300 (PicoQuant, Germany) with a laser 450 nm, LDH-P-C-450 (PicoQuant, Germany) as an excitation source. The fluorescence decay curves were measured, and the fluorescence lifetimes were obtained by deconvolution of the decay curves using the EasyTau 2 software package (PicoQuant, Germany). This work was carried out with the help of the center of the scientific equipment collective use «The upper Volga region center of physico-chemical research».

**Hexylzinc iodide.** A suspension of zinc dust (7.5 g, 0.15 mol) was stirred and decanted twice in a 2% solution of HCl (20 mL) for 2 min. The resulting dust was sequentially stirred and decanted in water (3  $\times$  20 mL) and ethanol (2  $\times$  20 mL). The solid was washed with diethyl ether (20 mL). Finally, the activated zinc was dried under vacuum, purged with argon, flame dried under vacuum and again purged with argon. Under an argon atmosphere, 1,2-dibromoethane (0.35 mL, 0.80 g, 0.004 mol) was added *via* syringe to the freshly prepared activated zinc dust under stirring in anhydrous THF (20 mL), and the mixture was subsequently refluxed for *ca.* 20 min. After cooling to room temperature, trimethylsilyl chloride (0.50 mL, 0.45 g, 0.004 mol) was added, the mixture was refluxed once more and allowed to cool. Hexyl iodide (3.5 mL, 5 g, 0.024 mol) was added *via* syringe and the mixture was stirred for 16 h at 40 °C. The mixture was cooled to rt and the excess zinc was allowed to settle. The resultant grey solution was transferred to a Schlenk tube *via* cannula, and the remaining zinc powder was washed with THF (4 mL) and transferred to the Schlenk tube, to afford the title compound (24 mL, 0.90 M solution).

**3,6-Bis(*n*-hexyl)phthalonitrile (2).** In a flame-dried flask, bis(triphenylphosphine)nickel(II) dichloride (0.46 g, 0.70 mmol), triphenylphosphine (0.36 g, 1.35 mmol) and anhydrous THF (15 mL) were placed under argon. Addition of *n*-butyllithium (0.54 mL, 1.35 mmol, 2.5 M in hexanes) to the stirred mixture produced a blood red slurry. 3,6-Bis(trifluoromethanesulfonyloxy)phthalonitrile (2.90 g, 6.84 mmol) and KBr (2.45 g, 20.6 mmol) were added under argon and the resultant brown solution was cooled to -78 °C. Freshly prepared hexylzinc iodide (24 mL, 21.6 mmol, 0.90 M solution in THF) was added dropwise over a period of 1 h *via* cannula, the reaction mixture was allowed to warm to rt and stirred for a further 16 h. The reaction was quenched by careful addition of 10% HCl (25 mL) and the mixture was extracted with ethyl acetate (3  $\times$  25 mL). The combined organic extracts were successively washed with 10% HCl (25 mL), 5% NaOH (50 mL) and brine (50 mL). The solution was dried (MgSO<sub>4</sub>) and the solvent was evaporated at reduced pressure. The resultant solid was purified by column chromatography on silica gel using 5% EtOAc in hexane (v:v) as eluent. 3,6-Bis(*n*-hexyl)phthalonitrile was isolated as white solid (1.09 g, 54%).  $R_f$  = 0.34 (5% EtOAc in hexane). <sup>1</sup>H NMR (CDCl<sub>3</sub>, 300 MHz)  $\delta_H$  ppm: 7.46 (s, 2H, H<sub>arom</sub>), 2.87-2.82 (t, 4H, -CH<sub>2</sub>-), 1.70-1.60 (m, 4H, -CH<sub>2</sub>-), 1.29 (m, 12H, -CH<sub>2</sub>-), 0.89 (t, 6H, -CH<sub>3</sub>). <sup>13</sup>C NMR (CDCl<sub>3</sub>, 300 MHz)  $\delta_C$  ppm: 146.30 (C<sub>3</sub> and C<sub>6</sub>), 133.58 (C<sub>4</sub> and C<sub>5</sub>), 115.66 (C<sub>1</sub> and C<sub>2</sub>), 115.25 (CN), 34.49 (C<sub>4'</sub>), 31.52 (C<sub>2'</sub>), 30.75 (C<sub>3'</sub>), 28.89 (C<sub>1'</sub>), 22.56 (C<sub>5'</sub>), 14.08 (C<sub>6'</sub>). IR (KBr)  $\nu_{max}$  cm<sup>-1</sup>: 3414, 3064, 2925, 2854, 2228, 1618, 1559, 1464, 1382, 1280, 1230, 1173, 1114, 899, 850, 790, 759, 723, 647, 492, 463.

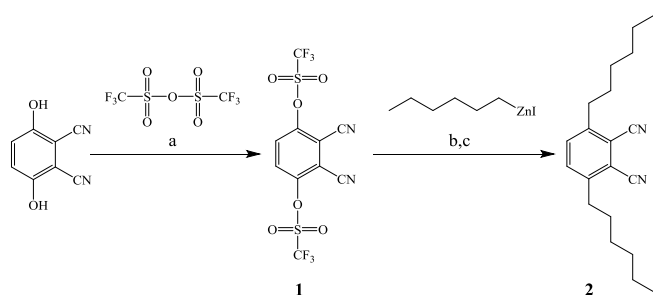
**1,4,13,16,25,28-Hexakis[*n*-hexyl]-5,36:12,17:24,29-triimino-7,10:19,22:31,34-trithio-*[f,p,z]*-tribenzo-1,2,4,9,11,12,14,19,21,22,24,29-dodecazacyclotriaconta-2,4,6,8,10,12,14,16,18,20,22,24,26,28,30-pentadecaene (4).** 3,6-Bis(*n*-hexyl)phthalonitrile (50 mg, 0.17 mmol) and 2,5-diamino-1,3,4-thiadiazole (20 mg, 0.17 mmol) were refluxed under argon in dry pentanol (4 mL) until the solution became homogeneous. Sodium (2 mg, 0.08 mmol) was added, and the reaction mixture was refluxed for 24 h under argon. Afterward, the pentanol was rotary evaporated, the residue was dissolved in THF (30 mL) and filtered through Celite. The solvent was evaporated and the residue was washed with methanol, ethyl acetate and hexane. Yield: 14 mg (21%). MS (MALDI-TOF, dithranol): 1186.6 [M+H]<sup>+</sup>, 1208.6 [M+Na]<sup>+</sup>, 1224.6 [M+K]<sup>+</sup>. <sup>1</sup>H NMR (CDCl<sub>3</sub>, 300 MHz)  $\delta_H$  ppm: 12.12 (s, 3H, NH), 7.14 (s, 6H, H<sub>arom</sub>), 2.87 (s, 12H, -CH<sub>2</sub>-), 1.61 (s, 12H, -CH<sub>2</sub>-), 1.39 (s, 36H, -CH<sub>2</sub>-), 0.96 (s, 18H, -CH<sub>3</sub>). <sup>13</sup>C NMR (CDCl<sub>3</sub>, 75.5 MHz)  $\delta_C$  ppm: 169.75, 153.48, 141.14, 133.76, 130.88, 31.92, 30.80, 30.47, 29.83, 22.94, 14.33. UV-Vis (CHCl<sub>3</sub>)  $\lambda_{max}$  nm (log  $\epsilon$ ): 280 (4.53), 400 (4.74), 420 (4.72), 465 (4.19), 505 (3.93). IR (KBr)  $\nu_{max}$  cm<sup>-1</sup>: 3211 ( $\nu_{N-H}$ ), 2955, 2924, 2853 ( $\nu_{C_{sp^3-H}}$ ), 1623 ( $\nu_{C=C}$ ), 1457, 1426, 1379 ( $\delta_{C_{sp^3-H}}$ ), 1254, 1191 ( $\nu_{C_{sp^3-C_{sp^3}}$ }), 1118, 1063, 833, 729 ( $\delta_{C_{sp^3-C_{sp^3}}$ }), 697 ( $\nu_{C-S}$ ).

## Results and Discussion

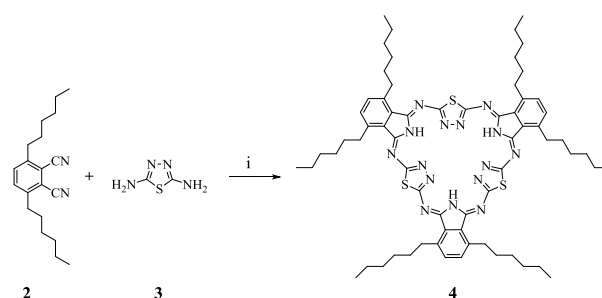
3,6-Bis(*n*-hexyl)phthalonitrile **2** was synthesized by reaction of the corresponding of 3,6-bis(triflate)phthalonitrile **1** and freshly prepared hexylzinc iodide (Scheme 1) following the methods described in literature.<sup>[13,14]</sup>

The preparation of hexakis(*n*-hexyl)hemihexaphyrazine **4** (Scheme 2) was carried out in 21 % yield by condensation of phthalonitrile **2** with 2,5-diamino-1,3,4-thiadiazole **3**<sup>[15]</sup> in stoichiometric 1:1 ratio, in the presence of sodium pentanoate in dry pentanol.

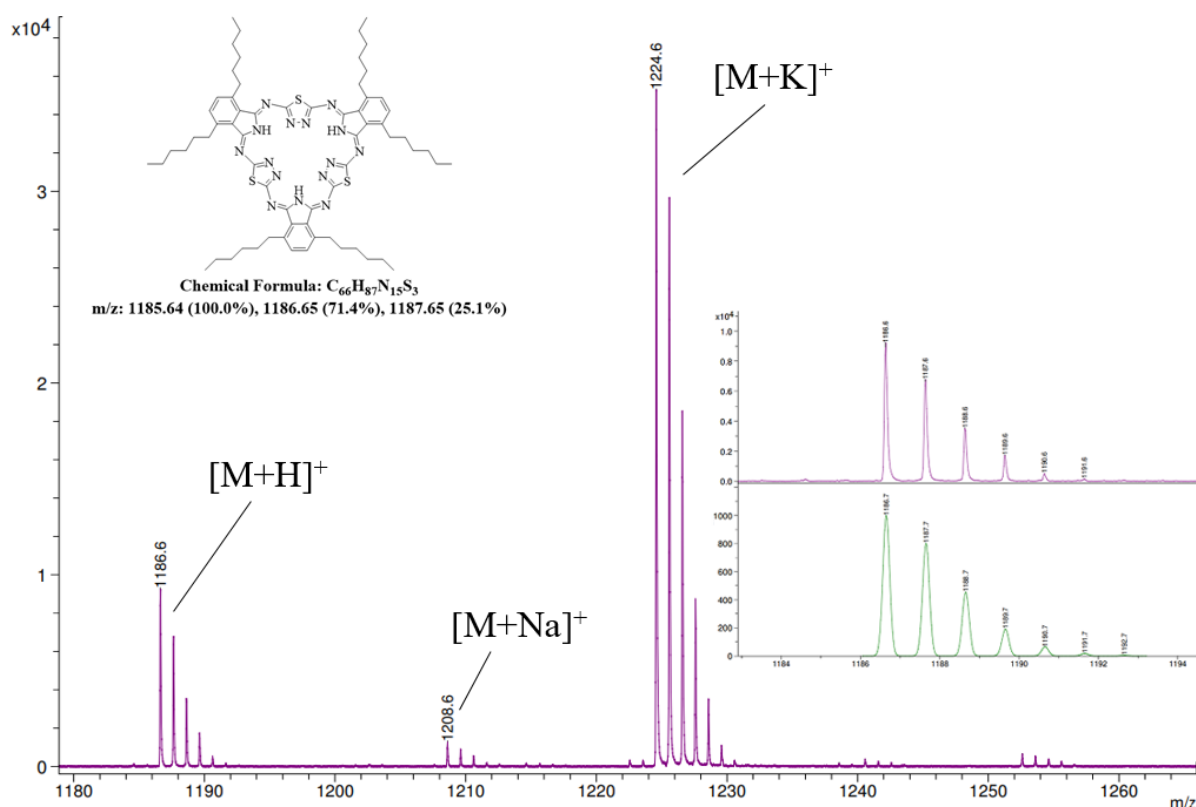
The characterization of macrocycle **4** was performed by <sup>1</sup>H and <sup>13</sup>C NMR, IR and UV-Vis spectroscopies, as well as MS. The MS spectrum (Figure 1) of **4** displays a peak at  $m/z$  = 1186.6 corresponding to the molecular ion [M + H]<sup>+</sup>, accompanied by peaks at  $m/z$  = 1208.6 and  $m/z$  = 1224.6, assigned to [M + Na]<sup>+</sup> and [M + K]<sup>+</sup>, respectively.



**Scheme 1.** Synthesis of 3,6-*bis*(*n*-hexyl)phthalonitrile **2**. a: Py, CH<sub>2</sub>Cl<sub>2</sub>, -78 °C to rt, 24 h, Ar; b: NiCl<sub>2</sub>(PPh<sub>3</sub>)<sub>2</sub>, PPh<sub>3</sub>, BuLi, KBr; c: -78 °C.



**Scheme 2.** Synthesis of hexakis(*n*-hexyl)hemihexaphyrazine **4**. i: C<sub>5</sub>H<sub>11</sub>ONa, C<sub>5</sub>H<sub>11</sub>OH, reflux, argon, 24 h.



**Figure 1.** MS spectrum (MALDI-TOF) of compound **4**. Insets: isotopic distributions of the main peak at 1186.6 Da (above); calculated isotopic pattern for [M+H]<sup>+</sup> (below).

<sup>1</sup>H NMR spectrum of hemihexaphyrazine **4** (Figure 2), reveals the aliphatic signals of the hexyl groups as four multiplets between 2.88–0.95 ppm, in addition to a singlet at 7.17 ppm corresponding to the benzene rings. A broad signal at 12.17 ppm characterizes the isoindolic NH protons, as a diagnostic of the non-aromatic character of **4**.

The <sup>13</sup>C NMR spectrum of **4** is shown in Figure 3. A signal at 169.75 ppm can be assigned to the 1,3,4-thiadiazole fragments, while four signals at 153.48, 141.14, 133.76 and 130.88 ppm account for the isoindole subunits.

The IR spectrum of **4** (Figure 4) shows a peak at 3211 cm<sup>-1</sup> corresponding to vibrations of the N–H bonds of the isoindole moiety.

Macrocycle **4** displays the typical optical attributes of

other hemihexaphyrazines.<sup>[9,10,16–19]</sup> Thus, a UV–Vis spectrum (Figure 5) that is dominated by two intense absorptions at 400 and 420 nm is obtained, in addition to weaker bands at 465 and 505 nm, the latter (log ε = 3.93) corresponding to the 0–\*0 energy gaps.

Light excitation in the range between 400 and 500 nm produces a broad fluorescence spectrum that maximizes at 580 nm, accompanied by weaker shoulders at 541 and 625 nm, which does not mirror image the absorption pattern (Figure 5). The fluorescence quantum yield (Φ<sub>F</sub>) of **4**, calculated using an integration sphere, was of 7 %. Actual pulsed light-source and sample response show the gradual decay of fluorescence intensity with time. A single-exponential fit gives a lifetime of 2 ns for the excited state of **4** (Figure 6).

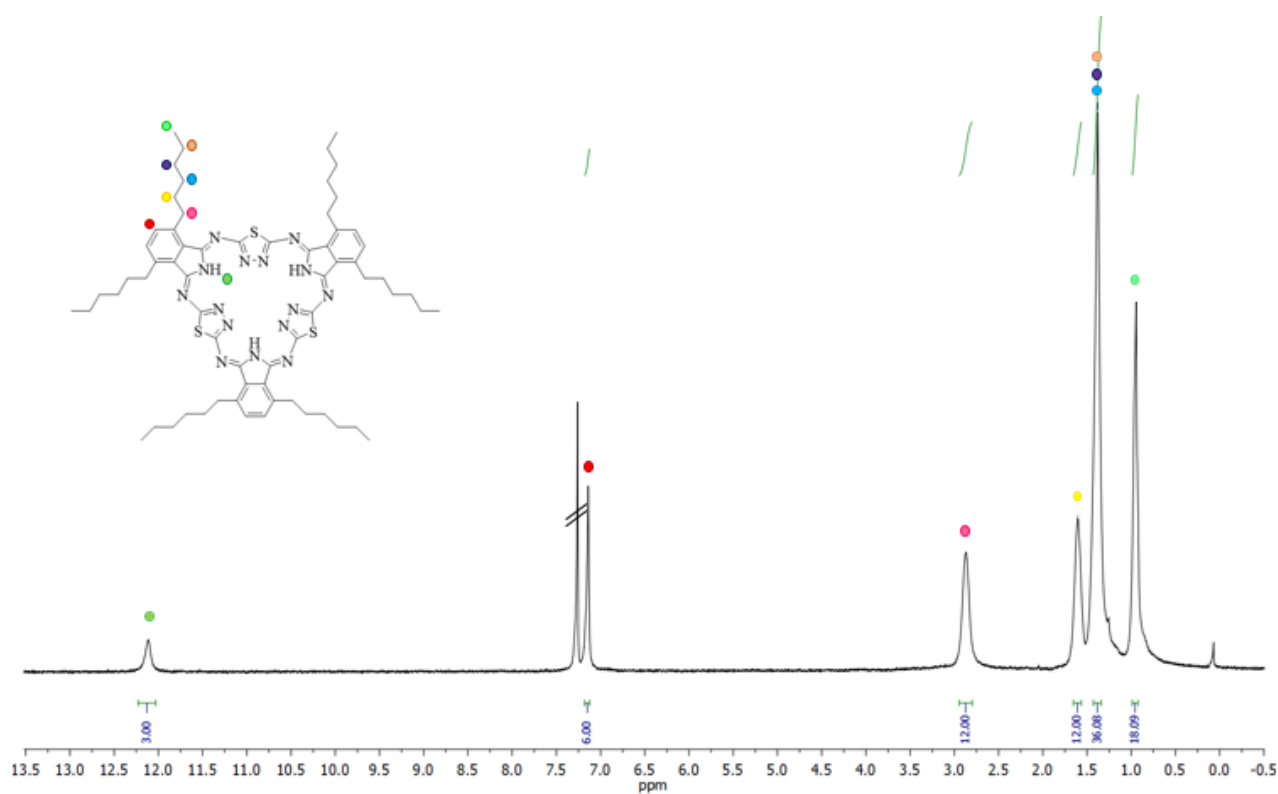


Figure 2.  $^1\text{H}$  NMR spectrum of compound 4 in  $\text{CDCl}_3$ .

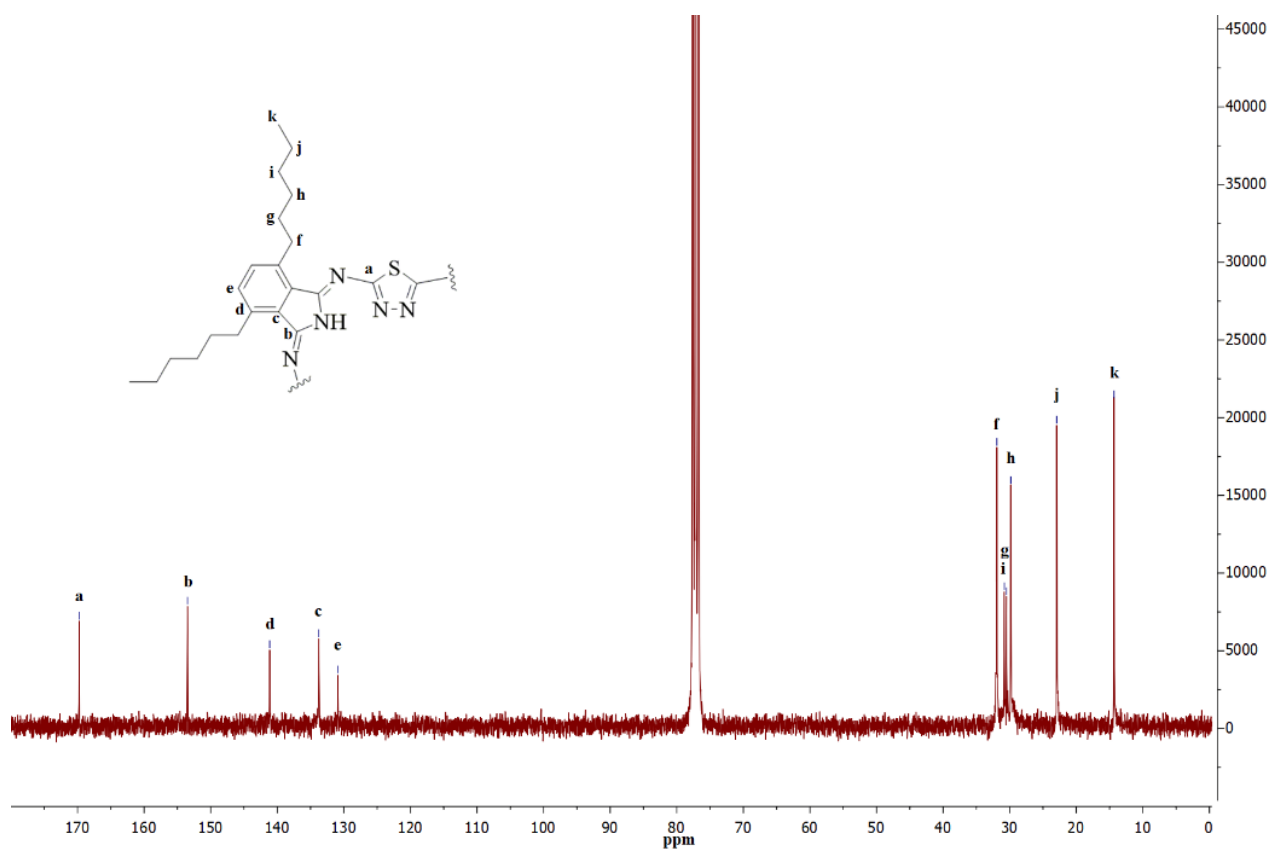
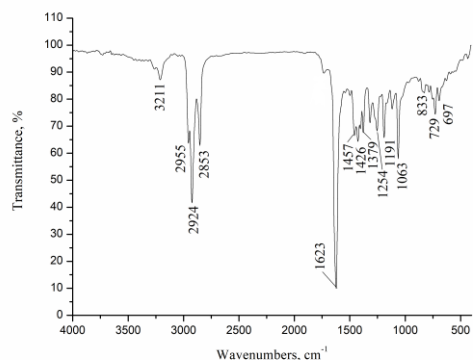
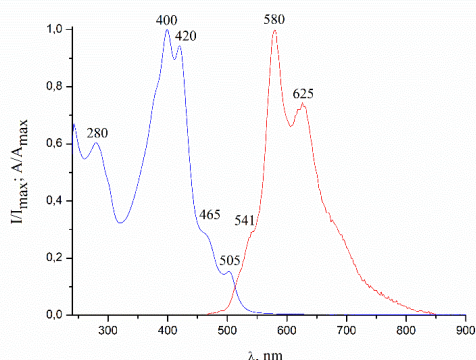


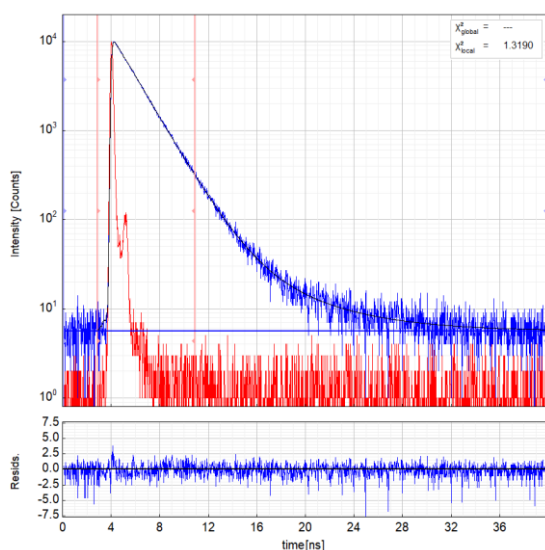
Figure 3.  $^{13}\text{C}$  NMR of compound 4 in  $\text{CDCl}_3$ .



**Figure 4.** IR spectrum (KBr) of **4**.



**Figure 5.** UV-Vis absorption (blue line) ( $C = 1.8 \cdot 10^{-5}$  mol/l) and fluorescence (red line) ( $C = 4.7 \cdot 10^{-6}$  mol/l) spectra in chloroform.



**Figure 6.** The intensity decay of the fluorescence of **4** (where red curve – LUDOX decay).

## Conclusions

A soluble hemihexaphyrazine hexasubstituted with hexyl chains was prepared by a reaction of 3,6-*bis*(*n*-hexyl)phthalonitrile and 2,5-diamino-1,3,4-thiadiazole. The product was characterized by MS,  $^1\text{H}$  and  $^{13}\text{C}$  NMR, IR, UV-Vis and fluorescence spectroscopies.

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