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25,27-Dithiasapphyrin and Pyrrole-Inverted Isomer of 21,23-Dithiaporphyrin from Condensation of Pyrrole and 2,5-Bis(*p*-tolylhydroxymethyl)thiophene

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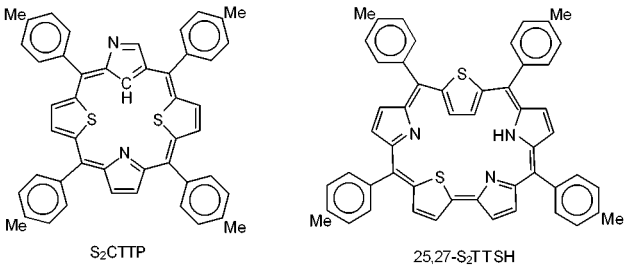
ABSTRACT



A novel aromatic isomer of 5,10,15,20-tetra(*p*-tolyl)-21,23-dithiaporphyrin (S_2TTP) with an inverted pyrrole ring, 5,10,15,20-tetra(*p*-tolyl)-2-aza-21-carba-22,24-dithiaporphyrin (S_2CTTP), and 5,10,15,20-tetra(*p*-tolyl)-25,27-dithiasapphyrin (25,27-S_2TTSH), have been obtained by a condensation of 2,5-bis((*p*-tolyl)hydroxymethyl)thiophene and pyrrole. A conformational equilibrium, unique in a sapphyrin class, between two S(27)-thiophene-flipped and planar structures of neutral 25,27-S_2TTSH was detected by ^{1}H NMR.

Reactions between 2,5-bis(arylhydroxymethyl)heterocyclopentadienes and pyrroles produced a variety of 5,10,15,-20-tetraphenyl-21,23-diheteroporphyrins in which the NH groups were replaced with oxygen, sulfur, or selenium atoms, respectively.[1−3] Once arylaldehyde was included in the condensation 5,10,15,20-tetraaryl-21-heteroporphyrins[3,4] were produced as well. The routine procedures, i.e., condensations of pyrrole, arylaldehyde, and 2,5-bis(arylhydroxymethyl)-furan or 2,5-bis(arylhydroxymethyl)thiophene, gave 5,10,-15,20-tetraaryl-26,28-dioxasapphyrin or 5,10,15,20-tetraaryl-26,28-dithiasapphyrin in addition to 5,10,15,20-tetraaryl-21-oxaporphyrin or 5,10,15,20-tetraaryl-21-thiaporphyrin.[5] The condensation of 5-(*p*-tolyl)dipyrromethane and furylpyrro-methanediol yielded 5,10,15-triaryl-21-oxacorrole in addition to the expected 5,10,15,20-tetraaryl-21-oxaporphyrin.[6] The novel 5,10,15,20-tetraaryl-2-aza-21-carba-22-selenaporphyrin with an inverted pyrrole ring has been produced in addition

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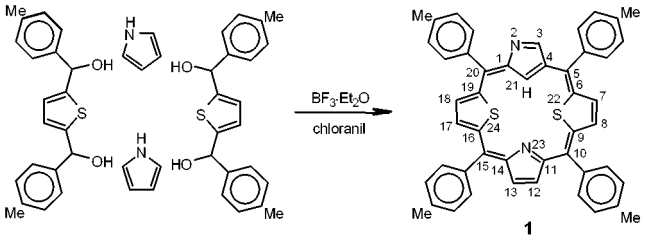
to the expected 5,10,15,20-tetraaryl-21-selenaporphyrin in a [3 + 1] condensation of bis(arylhydroxymethyl)selenophene and 5,10-ditolyltripyrrin.[7] All of these observations lead to anticipation that, in analogy to the formation of inverted tetraarylporphyrin,[8] diheteroporphyrins inverted on a pyrrole ring might be formed in the course of any typical synthesis used to produce 21,23-diheteroporphyrins.

Here we describe the synthesis and spectroscopic properties of 5,10,15,20-tetra(*p*-tolyl)-2-aza-21-carba-22,24-dithiaporphyrin S_2CTTP **1**, which is an isomer of 5,10,15,20-tetra(*p*-tolyl)-21,23-dithiaporphyrin **2**. S_2CTTP **1** can be formally constructed by the exchange of a nitrogen atom and a β-methine carbon atom of a pyrrole ring of **2** to create the porphyrin-like skeleton of 5,10,15,20-tetra(*p*-tolyl)-2-aza-21-carba-22,24-dithiaporphyrin. The synthesis involves the one-pot reaction of 2,5-bis(*p*-tolylhydroxymethyl)thiophene with pyrrole (1:1 molar ratio), carried out in dichloromethane, catalyzed by $BF_3{\cdot}Et_2O$ or CH_3SO_3H, which is followed by oxidation with *p*-chloranil.

The condensation process produces, in addition to 5,10,15,20-tetra(*p*-tolyl)-21,23-dithiaporphyrin S_2TTP **2**, its isomeric derivative 5,10,15,20-tetraaryl-2-aza-21-carba-22,24-dithiaporphyrin S_2CTTP **1** in reasonable yield (4.7%). In comparison to S_2TTP **2** the synthesis of S_2CTTP **1** requires one β-condensation step instead of the typical α-condensation at a single pyrrole moiety (Scheme 1).

Scheme 1



In addition to **1**, 5,10,15,20-tetra(*p*-tolyl)-25,27-dithiasapphyrin (25,27-S_2TTSH, **3**) has been obtained but only with CH_3SO_3H as a catalyst. 25,27-S_2TTSH **3** is isomeric to previously described 5,10,15,20-tetra(*p*-tolyl)-26,28-dithiasapphyrin 26,28-S_2TTSH **4** formed in the presence of either $BF_3{\cdot}Et_2O$ or CH_3SO_3H.[5,9] Related 5,10,15,20-tetraphenyl-25,29-dithiasapphyrin, 25,29-S_2TPSH was prepared by a different route.[10]

The rather minute yield of 25,27-S_2TTSH **3** was, however, sufficient for detailed spectroscopic characterization. The identities of S_2CTTP **1** and 25,27-S_2TTSH **3** have been confirmed by high-resolution mass spectrometry and ^{1}H NMR spectroscopy.[11] Dithiacarbaporphyrin **1** demonstrates spectroscopic properties typical for core-modified porphyrins and carbaporphyrinoids. The UV−vis spectrum of **1** is porphyrin-like, with the strong Soret band at 461 nm (Figure 1). The complete assignment of all ^{1}H NMR resonances

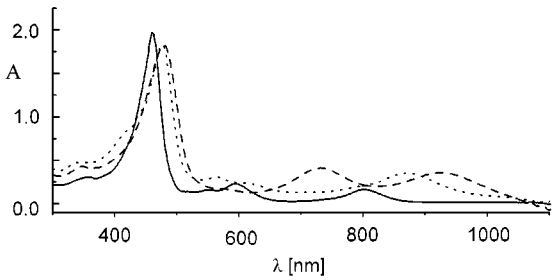


Figure 1. The electronic spectra of S_2CTTP (solid line), S_2CTTPH$^+$ (dotted line), and S_2CTTPH_2^{2+} (dashed line) in dichloromethane.

shown in Figure 2 has been obtained by means of 2D ^{1}H NMR COSY and NOESY. All outer perimeter thiophene [9.53, 9.27 (AB, $^3J_{AB}$ = 5.1 Hz, 7,8-H, th.), 9.51, 9.26 (AB, ^3J = 4.9 Hz, 17,18-H, th.)], pyrrole [8.40, 8.36 (AB, ^3J = 4.6 Hz, 12,13-H, pyrr.), 7.96 (s, inv. pyrr.)], and *meso*-(*p*-tolyl) resonances are downfield shifted as a result of the ring current effect. Essentially molecule **1** preserves the aroma-

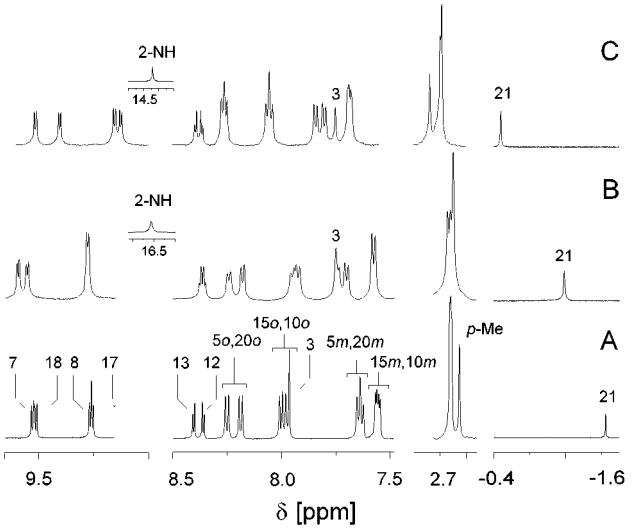


Figure 2. ^{1}H NMR spectra (selected downfield and upfield regions presented): (A) S_2CTTP, (chloroform-*d*, 298 K); (B) S_2CTTPH$^+$ (TFA/chloroform-*d*, 5:95 v/v, 228 K); (C) S_2CTTPH_2^{2+} (TFA/dichloromethane-d_2, 5:95 v/v, 298 K, inset 213 K). Peak labels follow systematic position numbering of the porphyrin ring or denote proton groups: *o*, *m*−*ortho*, *meta* positions of *meso*-*p*-tolyl (Tol) rings, respectively.

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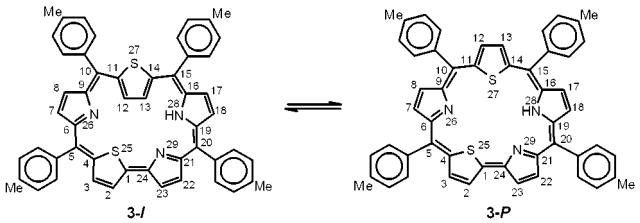
ticity of its parent isomer. The indicative shift difference of 9.6 ppm between the outer 3-H and inner 21-H pyrrole resonances reflects their location in the deshielding (3-H) and shielding (21-H) zones of the diatropic ring current similarly as determined for 2-aza-21-carbaporphyrin, 2-aza-21-carba-23-thiaporphyrin or 2-aza-21-carba-22-selenaporphyrin.[7,8,12]

The titration of a dichloromethane solution of **1** with TFA is accompanied by a distinct color change from green-yellow to dark yellow. The ^{1}H NMR spectroscopic titration with TFA carried out in dichloromethane-d_2 at 228 K demonstrated that the addition of the first proton takes place at the 2-N nitrogen atom, as documented by the position of the 2-NH resonance at 16.57 ppm for S_2CTTPH$^+$, and is followed by protonation at 23-N to form a dication S_2-CTTPH$_2^{2+}$. The macrocycle **1** has an unusual [S,(CH),S,N] coordination core combining the features of inverted porphyrin[8] and dithiaporphyrin.[1] The electronic spectrum of 5,-10,15,20-tetraphenyl-25,27-dithiasapphyrin 25,27-S_2TTSH **3** resembles those of the all-nitrogen 5,10,15,20-tetraphenylsapphyrin TPSH$_3$ and other tetraarylheterosapphyrins.[5,9,13]

To account for the ^{1}H NMR spectra of **3** and its protonation products we have considered an equilibrium between two aromatic flipped and planar structures dominated by the flipped form in the entire investigated (193−343 K) temperature range (Scheme 2).

Scheme 2



The assignments of the ^{1}H NMR resonances of 25,27-S_2-TTSH **3-*I*** (Figure 3), have been made on the basis of detailed two-dimensional studies (COSY, NOESY) carried out at 193 K in dichloromethane-d_2. The molar fraction of the inverted form equals 0.87 at 298 K.

The assignments for 25,27-S_2TTSH **3-*P*** have been readily obtained from the EXSY correlations between **3-*I*** and **3-*P*** in the NOESY maps. The ^{1}H NMR spectrum of **3-*I*** exhibits

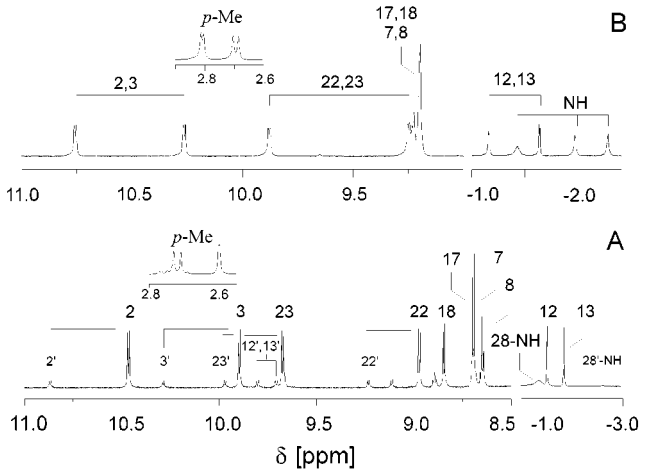


Figure 3. ^{1}H NMR spectra (selected downfield and upfield regions presented): (A) S_2TTSH, (chloroform-*d*, 298 K); (B) S_2TTSH$_3^{2+}$ (TFA/chloroform-*d*, 5:95 v/v, 230 K). Peak labels follow systematic position numbering of the dithiasapphyrin ring or denote proton groups: *o*, *m*−*ortho*, *meta* positions of *meso*-*p*-tolyl (Tol) rings, respectively.

five AB patterns reflecting the asymmetric structure of the compound. Accordingly the 12,13-H thiophene resonances have been identified at the very characteristic upfield positions −0.91 and −1.37 ppm that are diagnostic of the flipped structure. The considerable difference of the 2-H and 3-H thiophene chemical shifts (22-H, 23-H pyrrole chemical shifts) reflects the shielding effect of the 5-tolyl ring (20-tolyl) experienced by the 3-H (22-H) proton. The ^{1}H NMR spectrum of **3-*P*** form reveals features that can be fully accounted for by a planar macrocyclic structure, such as the 12,13-H AB system at 9.80, 9.71 ppm, which is similar to that found for thiophene resonances in other planar heterosapphyrins containing the thiophene moiety.[5,9,13] The detected differentiation of *ortho* and *meta* resonances for each *meso*-*p*-tolyl ring confirms the nonplanar flipped structure of **3-*I***. When the temperature is gradually raised from 193 to 293 K the 10-*ortho* (15-*ortho*) and 10-*meta* (15-*meta*) resonances broaden and coalesce in one practically nondetectable broad resonance. This behavior is characteristic for two unequivalent *ortho* (*meta*) positions exchanging through rotation.

In the same temperature range the 5-*p*-tolyl, and 20-*p*-tolyl resonances remain practically unchanged. The rotation barrier is lower for the 10- and 15-positions because the adjacent thiophene ring is flipped into the sapphyrin crevice. The dicationic form 25,27-S_2TTSH$_3^{2+}$ demonstrated the basic features of the flipped sapphyrin scaffold, verified by the upfield locations of the 12,13-H pyrrolic resonances (−1.16, −1.63 ppm) accompanied by three NH resonances (−1.43, −1.96, −2.27 ppm). Thus, in the whole class of tetraarylsapphyrins and tetraarylheterosapphyrins 5,10,15,20-tetra-

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(11) Aromatic 5,10,15,20,25-penta-(*p*-tolyl)-25,27,29-trithiahexaphyrin (1.1.1.1.1.0) with two flipped five-membered rings has been also detected. although only in NMR detectable quantities: δ = 10.0, 9.31 (AB, ^3J = 4.3 Hz); 9.24, 8.67 (AB, ^3J = 4.3 Hz); 8.34, 8.02 (AB, ^3J = 4.3 Hz); 8.16, 7.86 (AB, ^3J = 4.6 Hz); 1.52, 1.34 (AB, ^3J = 4.3 Hz); 0.70, 0.66 (AB, ^3J = 5.5 Hz); *m*/*z* = 954 found for [M + H]$^+$.

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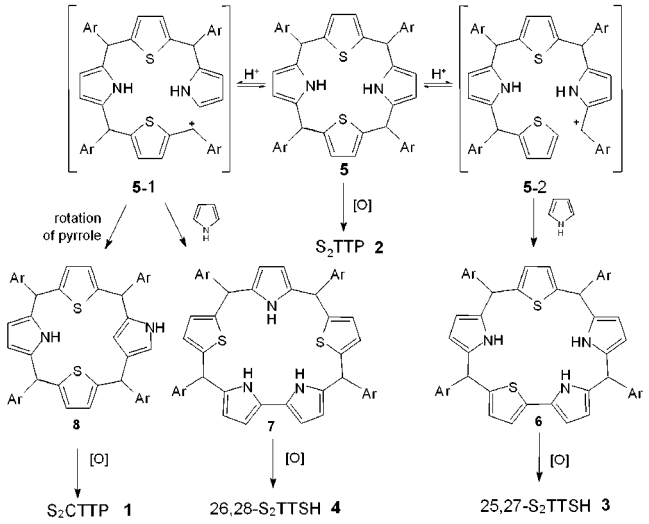
(*p*-tolyl)phenyl-25,27-dithiasapphyrin **3** provides a unique case conformational equilibrium between the flipped and planar structures that has been detected for the neutral form (Scheme 2). A related rearrangement was observed for tetraarylsapphyrin, but the process was triggered by protonation or reversible anion binding.[12] The temperature dependence of the conformational equilibrium constant $K = [\mathbf{3}\text{-}\boldsymbol{P}]/[\mathbf{3}\text{-}\boldsymbol{I}]$ has been examined by ^{1}H NMR in toluene-d_8. The corresponding values of $\Delta H°$ and $\Delta S°$ are 12.3 ± 0.3 kJ/mol and 25.6 ± 1.0 J/mol·K, respectively. Remarkably, $\Delta H°$ is in the range of energy differences between the flipped and planar structures for sapphyrin and 26,28-dioxasapphyrin estimated by DFT.[14]

The results of our investigations seem to be of importance for the mechanism of the acid-catalyzed condensation in the pyrrole−2,5-bis(phenylhydroxymethyl)thiophene system. Scheme 3 shows a simplified equilibrium that involves the

Scheme 3



21,23-dithiaporphyrinogen **5** and two open, presumably helical, transient forms: **5**-1 and **5**-2 (or the respective carbinols). Scrambling of tetraarylporphyrinogen fragments or fragmentation of tripyrranes in the presence of acids provides the precedence for such a reactivity.[9,15] It is important to notice that the ring opening of dithiaporphyrinogen is expected to take place alternatively at the C_α(pyrrole)−C_{meso} (**5**-1) or C_α(thiophene)−C_{meso} (**5**-2) locations. Similarly as for $TPSH_3$ and 26,28-S_2TPSH,[13] we suggest that the excess of pyrrole attacks **5**-1 or **5**-2, which preserves the preferred helical conformation of tetrapyrromethane.[16] The suitably prearranged helical geometry of the open intermediate provides the orientation required for the macrocyclic ring closure, through the sequence reaction between carbacation and the nucleophilic pyrrole or thiophene centers of **5**-1 or **5**-2. For the mechanism of dithiacarbaporphyrin **1** formation we propose that two helical conformations of **5**-1, differing only by a 180° rotation of the terminal pyrrole ring around the α-carbon−*meso*-carbon bond, give rise to the regular **5** or inverted dithiaporphyrinogen **8** ring closure. Subsequent oxidation of **5**, **6**, **7**, and **8** leads to the aromatic products.

In conclusion, the acid-catalyzed condensation of pyrrole and 2,5-bis(*p*-tolylhydroxymethyl)thiophene yields, apart from the well-known 21,23-dithiaporphyrin, the first diheroporphyrin with inverted pyrrole ring. Coordination properties of this inverted isomer are currently under considerations.

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Supporting Information Available: NMR spectra, detailed descriptions of experimental procedures, and a plot of ln *K* vs 1/*T*. This material is available free of charge via the Internet at http://pubs.acs.org.

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