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Carbaporphyrinoids

Towards True Carbaporphyrinoids: Synthesis of 21-Carba-23-thiaporphyrin**

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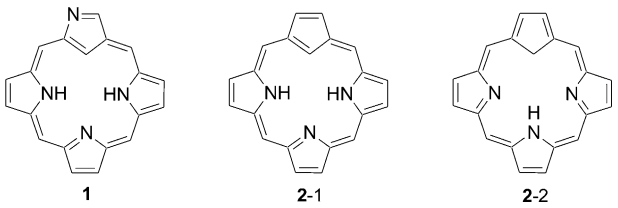
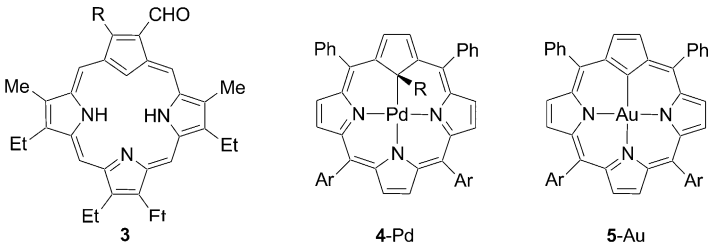
Abstract: *In the search for porphyrinoids with a built-in cyclopentadienyl moiety (true carbaporphyrins), a rational synthesis of carbathiaporphyrin, the synthons, has been elaborated. The donors (C,N,S,N) in the porphyrinic core of carbathiaporphyrinoids are potentially of fundamental importance for generating organometallic complexes, as exemplified through formation of the palladium(II) complex.*



Scheme 1. N-Confused porphyrin **1** and true carbaporphyrins **2**.



Scheme 2. True carbaporphyrins reported to date.

The formal permutation of a pyrroline nitrogen atom and a β-methine pyrrolic group of meso-tetraarylporphyrin resulted in the creation of 2-aza-21-carba-5,10,15,20-tetraarylporphyrin (N-confused porphyrin; **1**), which has fundamentally changed electronic and coordination properties compared to the parental macrocycle.[1,2] The synthesis of this molecule was achieved 20 years ago, although early suggestions about the structure of this peculiar porphyrin isomer were reported by Aronoff and Calvin in 1943[3] and Pauling in 1944.[4] The initial isolation of the N-confused porphyrin prompted intensive synthetic studies to generate a class of carbaporphyrinoids.[5–10]

The replacement of a single pyrrole unit in a porphyrin by a cyclopentadiene moiety seems at first to be a compelling strategy for creating true carbaporphyrins, which can be regarded as fundamental extensions of the classical porphyrinic motif.[11] In a retrospective approach,[12] this replacement corresponds to a substitution of an imine nitrogen atom of a pyrrole ring by a trigonally hybridized methine unit or of an amine NH group of a pyrrole by a tetrahedral methylene group to afford a tautomeric couple (**2**-1 and **2**-2; Scheme 1), which is a characteristic of all monocarbaporphyrinoids (monocarbaheteroporphyrinoids) including N-confused porphyrin **1**.

Originally the incorporation of a β-substituted cyclopentadiene moiety into a porphyrin frame to yield an aromatic carbaporphyrin **3** (Scheme 2), which is β-substituted at the pyrrole rings and mono- or disubstituted at the cyclopentadiene ring, was achieved by Berlin by a [3+1] condensation,[11] and subsequently clarified by Lash and Hayes.[13] To date the coordination chemistry of **3** has not been reported.

Recently we reported on 5,10,15,20-tetraaryl-21-carbaporphyrin—the first example of a true carbaporphyrin directly related to **2**-2—which was firmly stabilized through palladium(II) coordination (**4**-Pd).[14] Thus, the remarkable, facile palladium(II)-mediated contraction of *p*-phenylene to cyclopentadiene, embedded in palladium(II) *p*-benziporphyrin, produced palladium(II) complexes of 21-carbaporphyrins (**4**-Pd). The analogous gold(III)-promoted contraction of the *p*-phenylene group of *p*-benziporphyrin afforded the first representative of a 21-carbaporphyrin complex (**5**-Au) encompassing the frame of **2**-1.[15] Evidently the contraction route to provide complexes of true carbaporphyrins is far from being general and hitherto is, by our present understanding, limited to certain transition metals. Within this context, a different direction was probed to generate a free-base meso-substituted 21-carbaporphyrin, which would be potentially amenable to the insertion of a variety of metal cations. Inspired by the emerging chemistry of tetraaryl-21-carbaporphyrins, masked however by palladium(II) or gold(III) coordination, we have devoted our synthetic effort to the construction of a class of true carbaporphyrins or carbaheteroporphyrins related to **2**-1 and **2**-2.

Consequently, we report on the synthesis and characterization of meso-substituted true carbathiaporphyrinoid 10,15-dimesityl-21-carba-23-thiaporphyrin (**6**) and its reduced congener **7**. These carbaporphyrinoids can be formally con-

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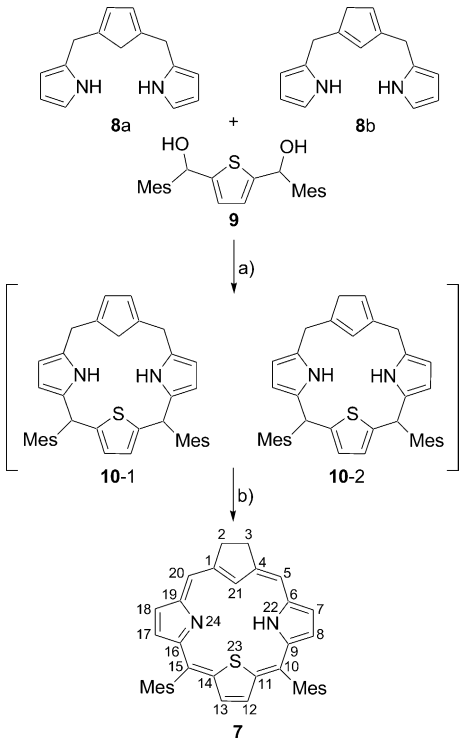
structed by replacement of a pyrrolidene fragment of 21-thiaporphyrin with a cyclopentadienylidene (**6**) or cyclopentenylidene (**7**) moiety with preservation of the general pattern of the parent skeleton.

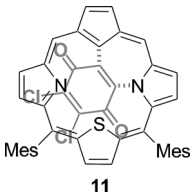
A key step in the synthesis of carbathiaporphyrinoids **6** and **7** is the construction of suitable synthons for introducing the cyclopentadiene ring into a porphyrin-like frame. We have taken advantage of the synthetic method of Seo et al. to produce a mixture of isomeric carba analogues of tripyrrane **8a** and **8b**, used previously as a suitable ligand to form *ansa*-cyclopentadienylpyrrolyltitanium complexes.[16]

The synthesis involves the one-pot reaction of 2,5-bis(mesitylhydroxymethyl)thiophene (**9**) with **8** in a 3% solution of ethanol in chloroform, catalyzed by $BF_3{\cdot}Et_2O$, followed by oxidation with *p*-chloranil (tetrachloro-1,4-benzoquinone; Scheme 3). The procedure follows the [3+1]



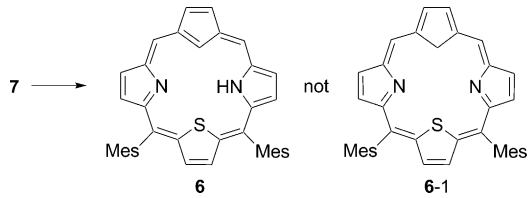
Scheme 3. Synthesis of **7**. Reaction conditions: a) $BF_3{\cdot}Et_2O$ (1 equiv), 3% EtOH in $CHCl_3$, RT, 1 h; b) triethylamine (1.2 equiv), *p*-chloranil (6 equiv), RT, 1 h. Mes = mesityl = 2,4,6-trimethylphenyl.

method previously utilized for the synthesis of heteroporphyrinoids and carbaporphyrinoids. Presumably two isomeric porphyrinogens **10**-1 and **10**-2 are formed on condensation that are differentiated by the orientation of the cyclopentadiene unit. After oxidation and chromatographic work up, the chlorin-like derivative **7** with the built-in cyclopentenyl moiety was isolated (yield 5.2%) instead of the targeted 21-carba-23-thiaporphyrin **6** or isomeric **6**-1.



The internally bridged 21-carba-23-thiaporphyrin **11**, where the C(21) and N(22) atoms of preformed **6** are covalently linked to a 4,5-dichloro-3,6-dioxocyclohexa-1,4-diene-1,2-diyl unit, was also identified as a macrocyclic side product. Evidently **11** was formed from **6** by substitution of two chloro substituents of *p*-chloranil by C(21) and N(22).

At this stage we realized that the proper oxidation conditions are particularly important. Eventually, the oxidation of carbathiachlorin **7** with one equivalent of DDQ (2,3-dichloro-5,6-dicyano-1,4-benzoquinone) afforded 21-carba-23-thiaporphyrin **6** (yield of oxidation 25%; Scheme 4). The progress of the conversion was monitored by ^{1}H NMR spectroscopy. An excess of DDQ or longer reaction time resulted in decomposition of **7**.



Scheme 4. Oxidation of **7**: [D]chloroform, DDQ (1 equiv) dissolved in [D_6]benzene, RT, 20 min.

The molecular structure of **7** reveals the bond-length pattern expected for aromatic carbaporphyrinoids and heteroporphyrinoids (Figure 1).[5,17–22] The bonds of the cyclopentene moiety not involved in the macrocyclic delocalization pathway are in the range typical for alkyl C–C bonds (1.515–1.537 Å).

Carbathiaporphyrinoids **6** and **7** give intense orange solutions in chlorinated solvents. The electronic absorption spectrum of **6** demonstrates a Soret band at 417 nm accom-

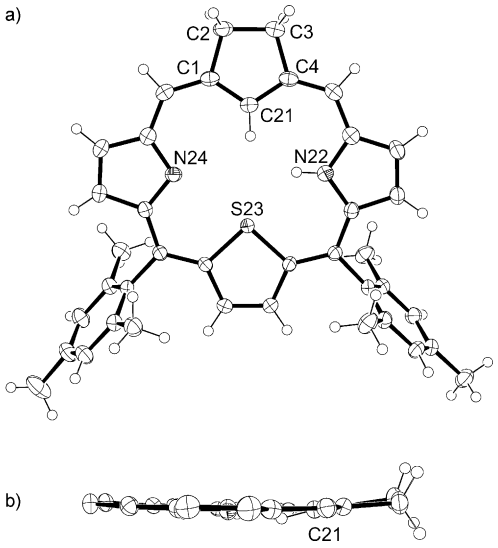


Figure 1. Molecular structure of carbathiachlorin **7**: a) perspective view and b) side view (mesityl groups and selected H atoms are omitted for clarity). The vibrational ellipsoids represent 50% probability. Selected bond lengths [Å]: C1-C2 1.515(3), C2-C3 1.536(3), C3-C4 1.524(3), C1-C21 1.403(3), C4-C21 1.404(3).

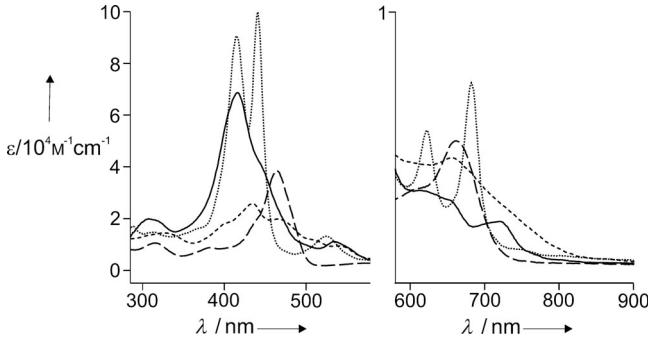


Figure 2. The electronic spectra of **6** (solid line), **7** (dotted line), **6**-Pd (short dashed line), and **7**-Pd (long dashed line) in dichloromethane.

panied by a set of four Q bands (Figure 2, solid line). The spectra can be related to the UV/Vis absorption spectrum of aromatic 21-thiaporphyrin, which is considered here to be an appropriate reference.[23] The electronic spectrum of carbathiachlorin **7** (Figure 2, dotted line) displays a split Soret band at 415 and 441 nm, and Q bands at 525, 621, and 682 nm, which are typical for aromatic, chlorine-like porphyrinoids.[24–26]

The ^{1}H NMR spectra of carbaporphyrinoids **6**, **7**, and **11** displayed resonances at positions consistent with an aromatic structure. All the macrocycles retain their macrocyclic aromaticity with an 18-π-electron delocalization pathway and show the basic features of aromatic carbaporphyrinoids (Figures 3 and 4).[5,18]

The ^{1}H NMR spectra of 21-carba-23-thiaporphyrin **6** (Figure 3a) and 21-carba-23-thiachlorin **7** (Figure 4a) measured at 300 K reflect the effective C_s symmetry, and show similar patterns, with remarkable deshielding of the meso-hydrogen atoms (**6**, 9.89 ppm; **7**, 9.49 ppm) and shielding of the internally located H(21) protons (**6**, −4.79 ppm; **7** −5.16 ppm). The cyclopentadienyl protons H(2) and H(3) of **6** give a doublet at 8.21 ppm. The NH protons are observed as highly broadened signals at −2.95 ppm for **6** and −3.70 ppm for **7**. The intensity ratio of the NH to H(21) signals is 1:1 for both **6** and **7**, which is consistent with the molecular structures. The alkyl hydrogen atoms H(2) and H(3) of the cyclopentene moiety of **7** result in a singlet in the region typical for dihydroporphyrins (4.91 ppm).[24,26] Significantly, the ^{13}C chemical shift determined for C(2) and C(3) of **7** ($\delta =$ 37.1 ppm) reflects their tetrahedral geometry.

21-Carba-23-thiapophyrin **6** and 21-carba-23-thiachlorin **7** tautomerize through a rapid exchange of the NH proton between two structurally equivalent nitrogen atoms (N(22) and N(23)). Significant spectral changes have been detected in variable-temperature ^{1}H NMR studies on **6** and **7** in [D$_8$]toluene. As the temperature gradually decreases, the skeleton resonances broaden. Eventually, at low temperature (180–200 K), the exchange process between the two principal tautomers is sufficiently slow on the ^{1}H NMR time scale and double the number of resonances is observed (Figures 3b and 4b for **6** and **7**, respectively). The scalar coupling detected between the inner NH and β protons of one pyrrole moiety unambiguously confirms the structure of **6** and **7**, with the NH proton specifically localized on a single pyrrole ring.

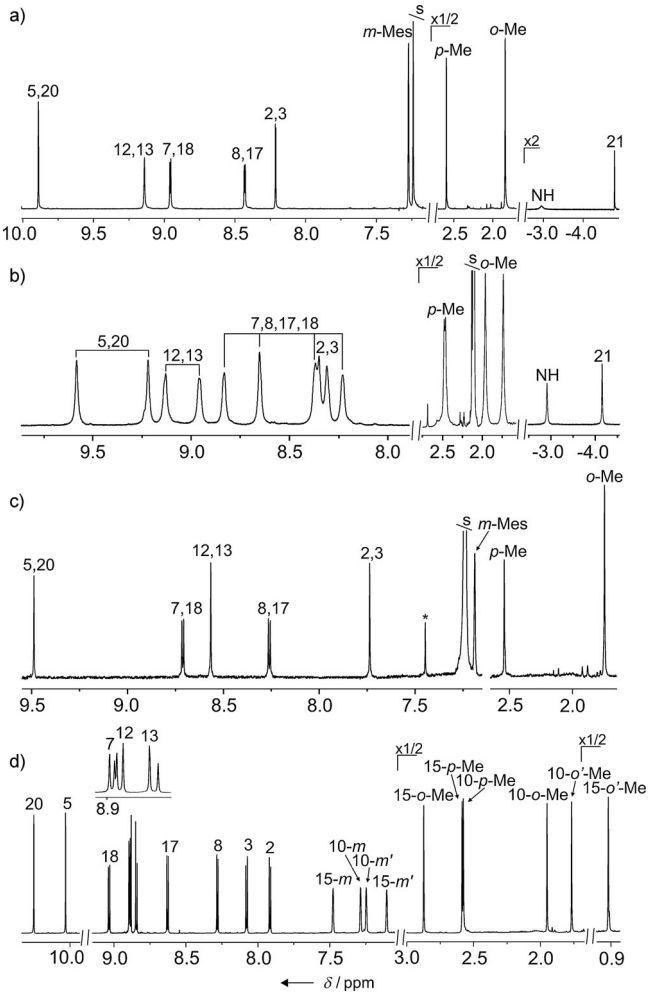


Figure 3. ^{1}H NMR spectra of a) **6** (300 K, [D]chloroform), b) **6** (190 K, [D$_8$]toluene), c) **6**-Pd (300 K, [D]chloroform), and d) **11** (300 K, [D$_2$]dichloromethane). Atom assignments correspond to the systematic position numbering or denote proton groups such as *o*-, *m*-, *p*-positions of the meso-mesityl groups.

In the presence of TFA, **6** and **7** readily generate green solutions of the cations, as confirmed by ^{1}H NMR (see Figures S1 and S2 in the Supporting Information) and UV/Vis spectroscopy (see Figures S7 and S8 in the Supporting Information).

The identity of **11** was unambiguously confirmed by high-resolution mass spectrometry ($m/z = 735.1611$ for $[M+H]^+$). The ^{1}H NMR spectrum of **11** shows it has a lower symmetry compared to **6**; however, the resonances are in the range found for other carbaporphyrins (Figure 3d). Furthermore, six additional signals from the benzoquinone ring were identified in the ^{13}C NMR spectrum of **11**, two of them ($\delta =$ 168.6 and 165.7 ppm) were assigned to carbonyl groups by analogy to the chemical shift of the C=O group in *p*-chloranil ($\delta = 168.2$ ppm).

Treatment of **6** and **7** with palladium(II) acetate in toluene resulted in the formation of palladium(II) carbathiaporphyrin **6**-Pd and palladium(II) carbathiachlorin **7**-Pd (Scheme 5), which was reflected by substantial changes in the UV/Vis electronic absorption spectra (Figure 2) and confirmed by

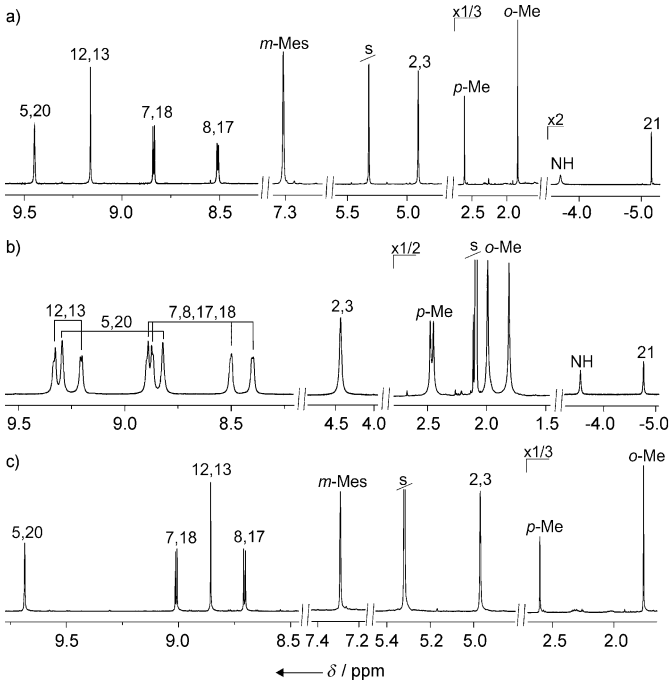
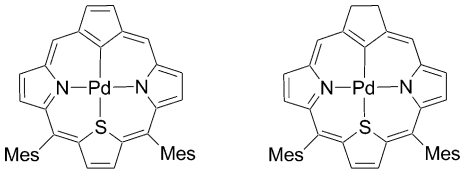


Figure 4. ^{1}H NMR spectra of a) **7** (300 K, [D_2]dichloromethane), b) **7** (190 K, [D_8]toluene) and c) **7**-Pd (300 K, [D_2]dichloromethane). Atom assignments correspond to the systematic position numbering or denote proton groups such as *o*-, *m*-, *p*-positions of the meso-mesityl groups.



6-Pd **7**-Pd

Scheme 5. Palladium(II) complexes of carbathiaporphyrin (**6**-Pd) and carbathiachlorin (**7**-Pd).

high-resolution mass spectrometry (**6**-Pd, $m/z = 666.1382$ for $[M]^+$; **7**-Pd, $m/z = 668.1477$ for $[M]^+$). Carbathiaporphyrin **6** and carbathiachlorin **7** distort to accommodate the palladium(II) cation, as shown in the DFT model of **6**-Pd and **7**-Pd (Figure 5 and see Figure S11 in the Supporting Information, respectively).

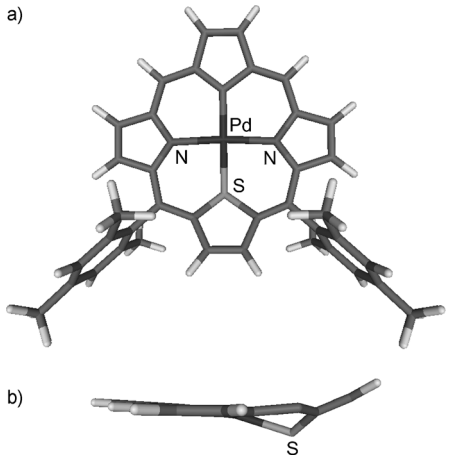
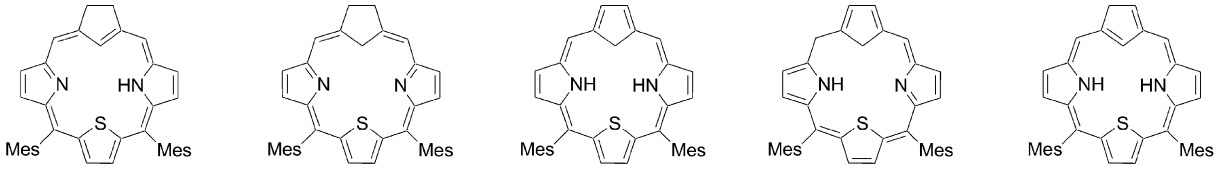


Figure 5. DFT-optimized structure of **6**-Pd: a) perspective view and b) side view (mesityl groups at the 10- and 15-positions are omitted for clarity). Selected bond lengths [Å]: Pd-C(21) 1.96, Pd-N(22) 2.09, Pd-N(24) 2.09, Pd-S(23) 2.32. The angle between the plane of the thiophene ring and the plane of four C_{meso} atoms is 30.0°.

Consequently, the thiophene ring is tilted with respect to the macrocyclic plane to allow the pyramidal side-on coordination of the palladium(II) ion, in a similar manner as detected for the reduced palladium(II) 21-thiaporphyrin[27] or palladium(II) thiaethyneporphyrin.[28] The ^{1}H NMR spectra of complexes **6**-Pd and **7**-Pd (Figures 3c and 4c, respectively) reveal similar spectroscopic patterns as those observed for the free ligands. In the ^{13}C NMR spectra, the inner C(21) atoms give resonances (**6**-Pd, 138.6 ppm; **7**-Pd, 146.8 ppm) that are significantly shifted downfield compared to those of the monocations (**6**-H^+, 113.6 ppm; **7**-H^+, 129.9 ppm), which is consistent with engagement of these carbon atoms in the coordination of palladium(II) and formation of organometallic complexes.

Several isomers of dihydro-10,15-dimesityl-21-carba-23-thiaporphyrin, including these which preserve the cyclopentadiene moiety, were subjected to DFT studies (see Scheme S5 and Table S3 in the Supporting Information). The isomers important for discussion alongside the experimental data are shown in Figure 6 and are ordered according to their total calculated energies (B3LYP/6-31G**). Evidently, the unique aromatic isomer **7** has the lowest energy, which accounts for the preference of **7** in solution and in the solid state. Nucleus-independent chemical shift (NICS) values of the central 16-membered ring (center ring) (Figure 6) were



	7	**7**-1	**7**-9	**7**-6	**7**-10
E	0	7.22	7.69	15.87	19.48
NICS	-14.56	-1.14	17.56	-2.17	5.93

Figure 6. Geometries, calculated energies (in kcal mol^{-1}), and NICS values (in ppm) of chosen dihydro-10,15-dimesityl-21-carba-23-thiaporphyrin isomers obtained by DFT optimization.

calculated for selected isomers of **7**, and readily indicates their macrocyclic aromaticity (**7**), antiaromaticity (**7**-9), and non-aromaticity (**7**-1, **7**-6, and **7**-10).[29]

An analogous approach to isomers of carbathiaporphyrin demonstrates a very small energy difference (1.62 kcal mol^{-1}) between isomers **6** and **6**-1, thus suggesting their simultaneous presence in equilibrium, even though only the less-stable **6** has been detected.

In conclusion we have presented a rational route to the synthesis of free-base 21-carba-23-thiaporphyrin, based on carba analogues of tripyrrane as synthons, which allow the incorporation of an unsubstituted cyclopentadiene moiety into the heteroporphyrin-like structure. This molecule and its chlorine-like derivative act as aromatic macrocyclic ligands, as shown by its reaction with palladium(II) ions, thus opening up alternatives to explore the coordination chemistry of true carbaporphyrins and true carbaheteroporphyrins. One can expect the true carbaporphyrins to prompt developments in carbaporphyrinoid and organometallic chemistry, building on the specific reactivity of the cyclopentadienyl moiety.

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[22] Crystal data for **7** are given in the Supporting Information. CCDC 976060 contains the supplementary crystallographic data for this paper. These data can be obtained free of charge from The Cambridge Crystallographic Data Centre via www.ccdc.cam.ac.uk/data_request/cif.
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