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Thiadiazole-Derived Expanded Heteroazaporphyrinoids

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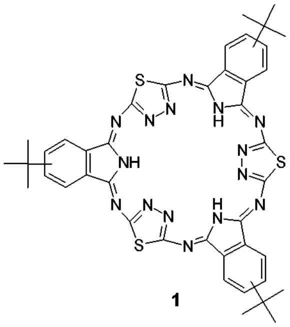
ABSTRACT



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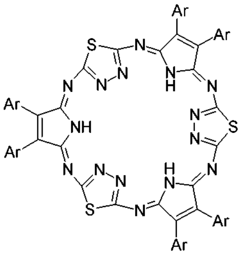

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Heteroannulenes 1 and 3 containing three subunits of isoindole or pyrrole, respectively, three 1,3,4-thiadiazole moieties, and six aza-bridges have been synthesized by reaction of the corresponding diiminoisoindoline or diiminopyrroline with 2,5-diamino-1,3,4-thiadiazole. These conjugated nonaromatic 30 π-electron macrocycles coordinate three metal ions within their central cavity and constitute one of the rare examples of expanded heteroazaporphyrinoids.

In recent years, legions of large porphyrinoid macrocycles have emerged as a result of the outstanding progress achieved in the field of expanded porphyrins.[1] Much of this interest is due to the fact that large pyrrole-containing macrocycles display particular properties such as anion-binding,[2] which are virtually inaccessible among tetrapyrrolic systems. Further attention derives from the interest in the elaboration of extended conjugated macrocycles able to absorb in the infrared region of the visible spectrum.[3]

On the contrary, the chemistry of expanded azaporphyrins lags far behind, perhaps owing to the difficulties encountered in the isolation of the corresponding intermediates and consequently the lack of controlled and stepwise procedures for the preparation of aza derivatives. Thus, superphthalocyanines, the synthesis of which was accomplished using a bulky *f*-block element, such as the uranyl cation, as template in the macrocyclization of diiminoisoindoline derivatives,[4]

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[1] (a) Jasat, A.; Dolphin, D. *Chem. Rev.* **1997**, *97*, 2267 and literature cited therein. (b) *The Porphyrin Handbook*; Kadish, K. M., Smith, K. M., Guilard, R., Eds.; Academic Press: San Diego, CA, 1999; Vol. 2.

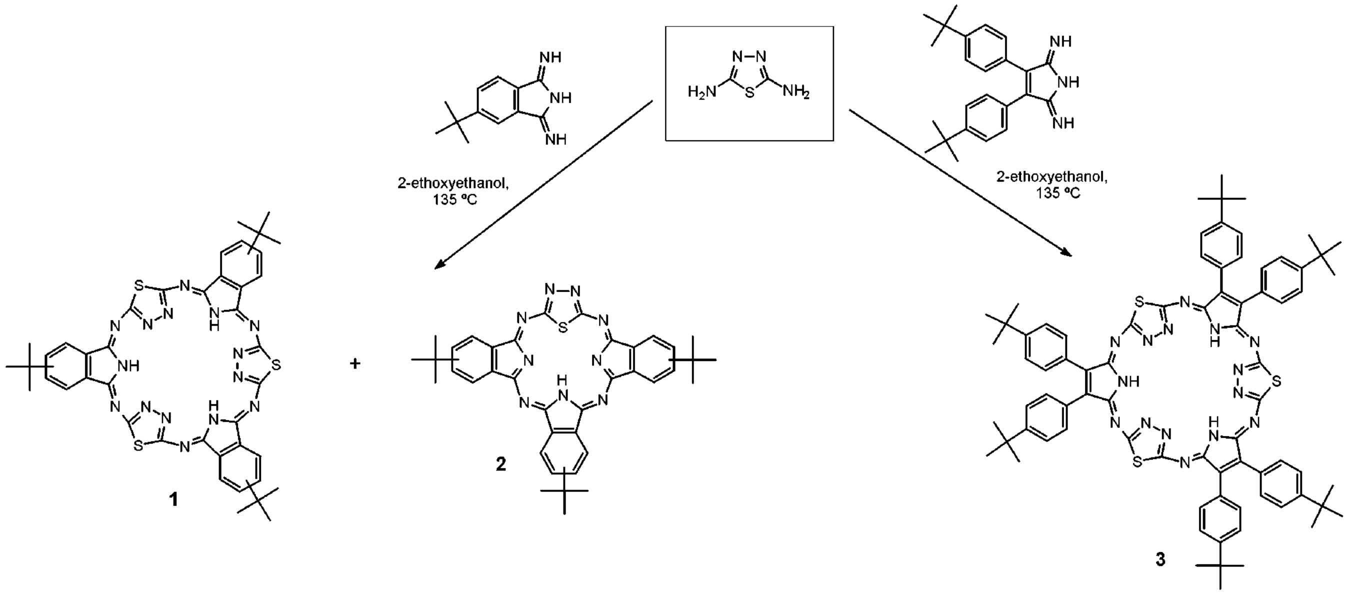
[2] See for example: (a) Sridevi, B.; Seenichamy, J. N.; Rao, R.; Chandrashekar, T. K. *Inorg. Chem.* **2000**, *39*, 3669. (b) Sessler, J. L. Weghorn, S. J. *Expanded, Contracted and Isomeric Porphyrins*; Elsevier: Oxford, 1997. (c) Allen, W. A.; Sessler, J. L. *Chem. Technol.* **1999**, *29*, 16.

[3] See for example: (a) Sessler, J. L.; Murai, T.; Hemmi, G. *Inorg. Chem.* **1989**, *28*, 3390. (b) Sessler, J. L.; Morishima, T.; Lynch, V. *Angew. Chem., Int. Ed. Engl.* **1991**, *30*, 977. (c) Mártire, D. O.; Jux, N.; Aramendía, P. F.; Negri, R. M.; Lex, J.; Braslavsky, S. E.; Schaffner, K.; Vogel, E. *J. Am. Chem. Soc.* **1992**, *114*, 9969. (d) Johnson, M. R.; Miller, D. C.; Bush, K.; Becker, J. J.; Ibers, J. A. *J. Org. Chem.* **1992**, *57*, 11763. (e) Bachmann, R.; Gerson, F.; Pütz, C.; Vogel, E. *J. Chem. Soc., Perkin Trans. 2* **1996**, 541.

[4] (a) Sessler, J. L.; Mody, T. D.; Lynch, V. *Inorg. Chem.* **1992**, *31*, 529. (b) Marks, T. J.; Stojakovic, D. R. *J. Am. Chem. Soc.* **1978**, *100*, 1695. (c) Day, V. W.; Marks, T. J.; Wachter, W. A. *J. Am. Chem. Soc.* **1975**, *97*, 4519.

10.1021/ol015924l CCC: $20.00

Scheme 1. Synthesis of Compounds **1**, **2**, and **3**



constituted for many years the only reported expanded azaporphyrins.

Recently, we developed studies on the synthesis of azaporphyrinic systems related to phthalocyanines[5] and hemiporphyrazines[6] with extended conjugation, mainly directed to the preparation of materials with unconventional physical properties.[7] To find new architectural possibilities and properties, we also focused our interest on the variation of the number of heterocyclic moieties that constitute the macrocycles,[8] and we prepared a second example of expanded azaporphyrinic derivatives using a stepwise sequence.[9]

Continuing our interest in expanded azaporphyrinic analogues, we report in this Letter the preparation of conjugated nonaromatic 30 π-electron heteroannulenes **1** and **3**, made up of three isoindole or pyrrole subunits, respectively, and three 1,3,4-thiadiazole moieties (Scheme 1). These "3 + 3" compounds, bearing a large cavity, represent an entry to expanded heteroazaporphyrinoids of interest in coordination chemistry as well as molecular recognition.[2]

The six-membered macrocycle **1**[10] was prepared in one step by condensation of 5-*tert*-butyl-1,3-diiminoisoindoline with 2,5-diamino-1,3,4-thiadiazole in a stoichiometric ratio, using 2-ethoxyethanol at reflux temperature as solvent (24 h). Under these conditions compound **2**[11,12] ("3 + 1") was also obtained. The crude was chromatographed on silica gel, using CH_2Cl_2 and then CH_2Cl_2/MeOH (10:1) as eluents, affording the "3 + 3" condensation product **1**, which was collected from the first fractions as an orange powder in 54% yield, and the "3 + 1" compound **2**, obtained from the last eluted fractions in 15% yield.

Likewise, macrocycle **3**[13] was obtained as an orange powder in 38% yield through condensation of 3,4-bis(4-*tert*-butylphenyl)pyrroline-2,5-diimine with 2,5-diamino-1,3,4-thiadiazole in a stoichiometric ratio.

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[5] For general overviews in this field see: (a) *Phthalocyanines, Properties and Applications*; Leznoff, C. C.. Lever, A. B. P., Eds.; VCH Publishers: Weinheim, 1989, 1993, 1996; Vols. 1−4. (b) Hanack, M.; Heckmann, H.; Polley, R. In *Methods of Organic Chemistry (Houben-Weyl)*; Schaumann, E., Ed.; Georg Thieme Verlag: Stuttgart, 1998; Vol. E 9d, p 717. For selected papers of our group see: (c) de la Torre, G.; Martínez-Díaz, M. V.; Ashton, P. R.; Torres, T.; *J. Org. Chem.* **1998**, *63*, 8888. (d) Maya, E. M.; Vázquez, P.; Torres, T.; Gobi, L.; Diederich, F.; Pyo, S.; Echegoyen, L. *J. Org. Chem.* **2000**, *65*, 823.

[6] Fernández-Lázaro, F.; Torres, T.; Hauschel, B.; Hanack, M. *Chem. Rev.* **1998**, *98*, 563.

[7] (a) de la Torre, G.; Nicolau, M.; Torres, T. Phthalocyanines: Synthesis, Supramolecular Organization and Physical Properties. In *Supramolecular Photosensitive and Electroactive Materials*; Nalwa, H. R., Ed.; Academic Press: New York, 2001; pp 1−111. (b) Gouloumis, A.; Liu, S-. G.; Sastre, A.; Vázquez, P. Echegoyen, L.; Torres, T. *Chem. Eur. J.* **2000**, *6*, 3600.

[8] (a) del Rey, B.; Keller, U.; Torres, T.; Rojo, G.; Agulló-López, F.; Nonell, S.; Martí, C.; Brasselet, S.; Ledoux, I.; Zyss, J. *J. Am. Chem. Soc.* **1998**, *120*, 12808. (b) Claessens, C. G.; Torres, T. *Chem. Eur. J.* **2000**, *6*, 2168.

[9] Rodríguez-Morgade, M. S.; Cabezón, B.; Esperanza, S.; Torres, T. *Chem. Eur. J. I*n press.

[10] Selected data for **1**: yield 54%;^{1}H NMR (200 MHz, $CDCl_3$) δ 12.35 (broad s, 3H, NH), 8.0−7.9 (m, 3H, arom.), 7.8−7.5 (m, 6H, arom.), 1.7−1.3 (broad s, 27H, CCH_3); IR (KBr) ν 3221 (N−H), 1646, 1618 cm^{-1} (C=C, C=N); LSIMS (*m*-NBA) *m/z* 850 [$(M + H)^+$], 982 [$(M + Cs)^+$], 1831 [$(2M + Cs)^+$]; UV/vis ($CHCl_3$) (log ϵ/dm^3 mol^{-1} cm^{-1}) λ_{max} 278 (4.71), 392 (4.88), 413 (4.89), 463 (4.25), 501 nm (4.10).

[11] Metal complexes [Zn(II) and Al(III)] of unsubstituted compound **2** have been described previously by one of us: Kudrik, E. V.; Islyaikin, M. K.; Smirnov, R. P. *Zh. Org. Chim.* **1997**, *33*, 1107. However, this is the first time that a free-base of this class of compounds, which we named thiadiazolephthalocyanines, is reported. Their electronic features are in good agreement with the 18 π-electron aromatic structure proposed for this system. The UV/vis spectrum of **2** (Figure 1) shows a group of bands in the visible range at 530, 564, and 615 nm, bathochromically shifted when compared with nonaromatic hemiporphyrazines. Therefore, compound **2** is electronically similar to the metalated complexes mentioned above and resembles its close relatives the triazolephthalocyanines: (a) Nicolau, M.; Cabezón, B.; Torres, T. *Coord. Chem. Rev.* **1999**, *190−192*, 231 and references therein. (b) Nicolau, M.; Cabezón, B.; Torres, T. *J. Org. Chem.* **2001**, *66*, 89.

[12] Selected data for **2**: yield 15%; ^{1}H NMR (200 MHz, DMSO-d_6) δ 8.0−7.3 (m, 9H, arom.), 1.37, 1.35, 1.22 (3s, 27H, CCH_3); IR (KBr) ν 3150, (N−H), 1614 cm^{-1} (C=C, C=N); MALDI-TOF-MS (dithranol) *m/z* 652 [$(M + H)^+$]; UV/vis (DMF) (log ϵ/dm^3 mol^{-1} cm^{-1}) λ_{max} 388 (3.73), 530 (sh), 564 (3.59), 615 nm (3.52).

Compounds **1** and **3** were characterized on the basis of spectroscopic evidences by LSIMS, IR, ^{1}H and ^{13}C NMR, UV, and analytical data.[14] Thus, they exhibit molecular ions at $m/z = 850$ $(M + H)^+$ and 1325 $(M + H)^+$, respectively. On the other hand, compounds **1** and **3** may be considered as 30 π-electron annulenes, and as such, should be aromatic according to the Hückel rule. However, no substantial diamagnetic ring current effects could be observed for the pyrrolic protons in the ^{1}H NMR spectra. Moreover, the spectra of **1** and **3** revealed a low-field resonance for the inner NH's at ca. $\delta = 12.5$.[15] This result is understandable under the assumption that these macrocycles exist in a nonplanar conformation and constitute nonaromatic compounds with delocalized π-systems.

The last hypothesis is also supported by their electronic features. Thus, the UV/vis spectrum of the expanded derivative **1** is dominated by two intense bands at 392 and 412 nm (Figure 1), along with two weaker absorptions at higher wavelengths (463 and 501 nm). Although these transitions are bathochromically shifted with respect to those typical of nonaromatic hemiporphyrazines,[6] the moderate red-shifting is diagnostic of the small increase in electronic delocalization on going from hemiporphyrazines to **1**, presumably due to a strong deviation in the planarity of the macrocyclic core in the last case.

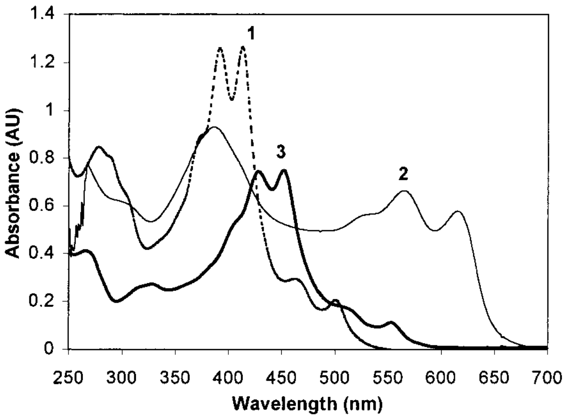

Figure 1. UV−vis spectra of compounds **1** ($CHCl_3$, 1.65×10^{-5} M), **2** (DMF, 1.99×10^{-5} M), and **3** ($CHCl_3$, 1.58×10^{-5} M).

A PLUTO model allows for visualization of the structure of the "3 + 3" compound **1** (Figure 2).[16]

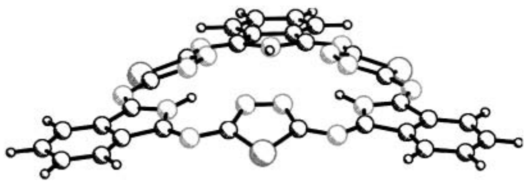

Figure 2. PLUTO model of compound **1** (side view). *tert*-Butyl groups have been omitted for clarity.

All bond lengths and angles are within the expected limits for porphyrins and related compounds. The most remarkable feature from the side view of macrocycle **1** is the inversion of the thiadiazole rings, whose sulfur atoms point outward, whereas the N−N unit is a part of the central cavity. The driving force for this preferred conformation would be the large size of the sulfur atom, but also a feasible intramolecular hydrogen bonding between the isoindolic NH and the thiadiazole nitrogens.[17] In the model, the thiadiazole rings are bent out of the plane defined by the nitrogen atoms at the *meso* positions, while the isoindole rings lie essentially on the plane. The extent of the distortion reflected by a dihedral angle HNC=N−C=N of approximately 17° would lead to perturbations in the p-orbital overlap of the extended π-framework, thus preventing the fully conjugated, reasonably planar $(4n + 2)\pi$ electronic pathway required for an aromatic system.

At first glance, the formation of compound **1** as the major product in the condensation of 2,5-diamino-1,3,4-thiadiazole with a 1,3-diiminoisoindoline derivative may appear quite out of the blue, taking into account the usual reactivity of these isoindolenines with aromatic diamines. Indeed, the condensation of 1,3-diiminoisoindolines with the structurally related 3,5-diamino-1,2,4-triazole (guanazole) under the same conditions is a reaction studied conscientiously by us and others[6] and yields exclusively the corresponding "2 + 2" triazolehemiporphyrazines. A detailed analysis of the geometry of these two diaminoheterocycles based on their X-ray structures[18,19] sheds light on their different reactivities.

First, the longer length observed for the C−S bond (ca. 1.75 Å) of the 1,3,4-thiadiazole with respect to the C−N(4)

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(13) Selected data for **3**: yield 38%; ^{1}H NMR (300 MHz, $CDCl_3$) δ 12.31 (broad s, 3H, NH), 7.50 (d, $J = 8.2$ Hz, 12H, arom.), 7.40 (d, $J = 8.2$ Hz, 12H, arom.), 1.36 (s, 54H, CCH_3); ^{13}C NMR (75 MHz, $CDCl_3$) δ 170.6 (*C*=N), 155.7 (*C*=N), 152.2 (C-4′), 139.7 (C-1′), 130.5 (C-3′), 127.0 (-*C*=C-), 125.2 (C-2′), 34.8 ($C(CH_3)$), 31.3 ($C(CH_3)$); IR (KBr) ν 3237 (N−H), 1602 cm^{-1} (C=C, C=N); LSIMS (*m*-NBA) m/z 1325 $[(M + H)^+]$, 1457 $[(M + Cs)^+]$; UV/vis ($CHCl_3$) (log ϵ/dm^3 mol^{-1} cm^{-1}) λ_{max} 265 (4.45), 328 (4.28), 428 (4.69), 452 (4.69), 515 (sh), 552 nm (3.73).

(14) Analytical data were in agreement with the proposed structures.

(15) The strong deshielding observed for the inner NH protons of **1** is noteworthy if compared with the chemical shifts exhibited by the corresponding pyrrolic protons of porphyrins and phthalocyanines. In these cases low-field shifts (−2 to −6 ppm) are observed owing to the diatropicity of the planar aromatic macrocycles. In contrast, values of ca. 14−15 ppm for the inner NH protons of nonplanar nonaromatic triazolehemiporphyrazines have been reported by us. See for example, ref 5c.

(16) Since structural assignments could not be carried out from X-ray diffraction analysis because it was not possible to obtain appropriate single crystals of **1**, a full optimization of the geometry was performed by a semiempirical quantum chemistry method (AM1). Dewar, M. J. S.; Zoebisch, E. G.; Healy, E. F.; Stewart, J. J. P. *J. Am. Chem. Soc.* **1985**, *107*, 3902.

(17) Intramolecular hydrogen bonding of the inner NH groups has been found responsible for the observed nonplanarity of several macrocycles together with other factors such as core size, peripheral substituents, or crystal packing. See for example: (a) Vangberg, T.; Ghosh, A. *J. Am. Chem. Soc.* **1999**, *121*, 12154. (b) Wondimagegn, T.; Ghosh, A. *J. Phys. Chem. A* **2000**, *104*, 4606. (c) Wondimagegn, T.; Ghosh, A. *J. Am. Chem. Soc.* **2000**, *122*, 6375. (d) Barkigia, K. M.; Chantranupong, L.; Smith, K. M.; Faker, J. *J. Am. Chem. Soc.* **1988**, *110*, 7566.

(18) Senda, H.; Maruha, J. *Acta Crystallogr.* **1987**, *43*, 347.

(19) Starova, G. L.; Frank-Kamenetskaya, O. V.; Makarskii, V. V.; Lopyrev, V. A. *Kristallografiya* **1980**, *25*, 1292.

bond (ca. 1.36 Å) of the 1,2,4-triazole, together with the larger size of the sulfur atom compared with the nitrogen, is in agreement with a higher tendency of the former heterocycle to render distorted and even thiadiazole-inverted macrocycles. 1,2,4-Triazole displays an angle of ca. 144° between the two $C-NH_2$ bonds (amino substituents),[19] while in the thiadiazole counterpart the corresponding angle should be broadened (ca. 156°)[18] in order to keep the sp^2 geometry. This fact by itself would not justify the different macrocycles obtained in each case. However, the larger size of the sulfur atom with two "bulky electron pairs" could play an important role both in the formation of an initial noncoplanar two-unit thiadiazole−isoindole compound and in its further reactivity. Accordingly, steric hindrance between the sulfur lone pairs of the thiadiazole and the NH group of the isoindole moiety could lead to the inversion of the thiadiazole ring already in the two-unit intermediate. As a consequence the angle between the two amino substituents to be considered should be the outer one, namely ca. 204°.[18] This geometry would be inappropriate for the effective "2 + 2" ring closure of an open tetramer, formed by condensation of two thiadiazole−isoindole moieties, and would propitiate further condensation of additional thiadiazole−isoindole subunits before closing to form the macrocycle. In fact, the corresponding "2 + 2" condensation compound in the thiadiazole series[20] was only observed by MS as a marginal component in the crude reaction mixture, along with "4 + 4", "5 + 5", and even "6 + 6" macrocycles.

Compound **3** appears to be electronically similar to **1** and displays a UV/vis spectrum characterized by two main bands at 428 and 452 nm (Figure 1) and two other weaker absorptions at 515 and 552 nm. In addition, the ^{13}C NMR spectrum of macrocycle **3** is in good agreement with the high degree of symmetry displayed by this compound. Thus, only three signals, at $\delta = 170.6$, 155.7, and 127.0 corresponding to the macrocyclic skeleton, together with a sole set of two signals for all *tert*-butyl groups, are discernible. Moreover, this compound shows in the ^1H NMR spectrum a unique kind of benzene ring with two different doublets centered at 7.50 and 7.40 ppm, respectively, together with the singlet at 12.3 ppm assignable to the NH protons.

Taking all these data into account, the same conclusions concerning the structure reached above for compound **1** can be drafted for its analogue **3**.

With a large, distorted nonadentate ligation core, one can anticipate a coordination chemistry for compounds **1** and **3** different from that exhibited by tetrapyrrolic systems. Thus, treating the free-base **1** with excess nickel(II) chloride in DMF at 100 °C, under argon during 5 h, the tris-nickel(II) chelate **4**[21] was obtained in 75% yield. The trinuclear nature of complex **4** was established by MALDI-TOF-MS, which reveals an intense isotopic cluster corresponding to $[MNi_3]^+$. Its IR spectrum shows the disappearance of the band at 3221 cm^{-1} characteristic of the N−H stretching in **1**. The model of **4** represented in Figure 3 shows that three nickel ions can be accommodated in the macrocyclic cavity and reveals that the molecule deviates from planarity to a lesser extent than its precursor **1**. Also in this case, the metalation of **3** with nickel(II) chloride afforded the trinuclear complex **5**,[22] which was also characterized by MALDI-TOF-MS and exhibited a broad band in UV−vis from 400 to 600 nm, with a maximum at 475 nm.

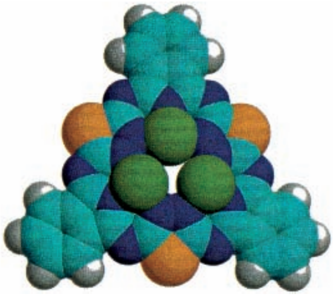

Figure 3. CPK model of trinuclear complex **4**. *tert*-Butyl substituents and chlorine counterions have been removed for clarity.

In summary, two rare examples of conjugated nonaromatic 30 π-electron expanded heteroazaporphyrinoids with a large cavity capable of accommodating three metal ions have been described. Their easy accessibility could play a stimulating role in the preparation of other expanded azaporphyrins and even giant molecules of practical and theoretical interest.

Acknowledgment. This work was supported by CICYT (Spain) through Grant MAT99/0180. We also acknowledge the MEC (Spain) for a sabbatical research fellowship (SAB 1999-0080) to M.K.I. and for a research contract to M.S.R.-M.

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[20] In analogy to other hemiporphyrazines, lower homologues of compound **1** (namely "2 + 2" thiadiazolehemiporphyrazines) have been described as nonaromatic 20 π-electron conjugated systems consisting of two alterning subunits of isoindole and two 1,3,4-thiadiazole moieties, bound to each other through aza-bridges: (a) Kolesnikov, N. A.; Borodkin, V. F. *Izv. Vyssh. Ucheb. Zaved., Khim., Khim. Tekhnol.* **1972**, *15*, 880. (b) Borodkin, V. F.; Kolesnikov, N. A.; *Izv. Vyssh. Ucheb. Zaved., Khim., Khim. Tekhnol.* **1970**, *13*, 738. (c) Danilova, E. A.; Islyaikin, M. K.; Smirnov, R. P. *Zh. Obshch. Khim.* **1997**, *67*, 1376. (d) Danilova, E. A.; Islyaikin, M. K.; Borodkin, V. F. *Izv. Vyssh. Ucheb. Zaved., Khim., Khim. Tekhnol.* **1990**, *33*, 18. However, in light of the present Letter some of the conclusions drafted therein should be revised. Large non-porphyrinic macrocycles based on 1,3,4-thiadiazole have been reported by one of us. (e) Kudrik, A. V.; Islyaikin, M. K.; Smirnov, R. P. *Zh. Obshch. Khim.* **1996**, *66*, 1564. (f) Kudrik, E. V.; Islyaikin, M. K.; Smirnov, R. P.; Kuzmitcenko, A. V. Russian Patent N 2134270.

[21] Selected data for **4**: yield 75%; IR (KBr) ν 3440 (broad, O−H), 1621, 1540 cm^{-1} (C=C, C=N); MALDI-TOF-MS (dithranol) *m/z* 1020−1029 $[M^+]$; UV/vis ($CHCl_3$) (log $\epsilon/dm^3\ mol^{-1}\ cm^{-1}$) λ_{max} 251 (4.73), 365 (sh), 442 nm (4.07).

[22] Selected data for **5**: yield 65%; IR (KBr) ν 3437, (O−H), 1625, 1578, 1531 cm^{-1} (C=C, C=N); MALDI-TOF-MS (dithranol) *m/z* 1494−1503 $[M^+]$; UV/vis ($CHCl_3$) (log $\epsilon/dm^3\ mol^{-1}\ cm^{-1}$) λ_{max} 348 (4.49), 413 (sh), 475 nm (4.59).