

## Synthesis of [28]Heptaphyrin(1.0.0.1.0.0.0) and [32]Octaphyrin(1.0.0.0.1.0.0.0) via a Directed Oxidative Ring Closure: The First Expanded Porphyrins Containing a Quaterpyrrole Subunit

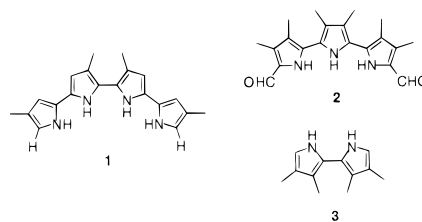
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In recent years, considerable effort has been devoted to the synthesis and study of expanded porphyrins, large porphyrin-like polypyrrolic macrocycles.<sup>1–3</sup> However, the number of synthetic methods that can be used to construct these kinds of macrocyclic structures remains quite limited. In fact, the vast majority of carbon-linked expanded porphyrins reported to date have been prepared using one of two generalized ring-forming procedures that involve, respectively, either (1) acid-catalyzed Rothmund-like<sup>1,2</sup> or MacDonald-like<sup>1,3</sup> condensations or (2) reductive McMurry-type couplings.<sup>1</sup> Although these methods are remarkably versatile, they are subject to limitations, as we discovered recently while trying unsuccessfully to convert quaterpyrrole **1**<sup>4</sup> into a range of macrocyclic products.<sup>5</sup> As we see it, therefore, there is thus a need for new expanded porphyrin-generating strategies. One attractive strategy involves the use of a directed oxidative pyrrole → bipyrrrole coupling procedure. While oxidative couplings are implicated in the formation of several bipyrrrole-containing macrocycles (e.g., corroles, sapphyrins, and rubeprins) under Rothmund-like conditions,<sup>6</sup> and have been used to prepare bipyrrrole itself,<sup>7</sup> their use as part of an explicit, expanded porphyrin-generating strategy remains relatively unexplored.<sup>8,9</sup> We now report that by using such a strategy it is possible to prepare

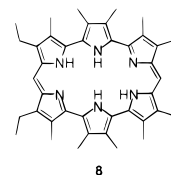
[28]heptaphyrin(1.0.0.1.0.0.0) (**5**) and [32]octaphyrin(1.0.0.0.1.0.0.0) (**6**); to the best of our knowledge, these systems constitute the first expanded porphyrins containing a quaterpyrrole fragment and the first higher order polypyrrolic macrocycles to be synthesized by using a directed oxidative pyrrole → bipyrrrole ring-closing procedure.



The synthesis of [28]heptaphyrin(1.0.0.1.0.0.0) (**5**), the first apparent heptaphyrin to be reported in the literature,<sup>1</sup> is summarized in Scheme 1. Briefly, the diformyl hexamethylterpyrrole precursor **2**<sup>10</sup> was condensed with 2.5 equiv of tetramethylbipyrrrole **3**<sup>11</sup> under conditions of acid catalysis to furnish the linear oligopyrrole **4**.<sup>12</sup> This latter intermediate, although apparently stable, was not isolated. Rather, it was treated immediately with aqueous Na<sub>2</sub>Cr<sub>2</sub>O<sub>7</sub> in TFA. Under these conditions, analogous to those used by Falk to produce bipyrrrole from pyrrole,<sup>7</sup> oxidative ring closure occurs spontaneously to afford **5** in 43% yield (2 steps). Treatment with sulfuric acid produced the corresponding sulfate salt, H<sub>2</sub>5<sup>2+</sup>·SO<sub>4</sub><sup>2-</sup>.

In some respects the synthesis of [32]octaphyrin(1.0.0.0.1.0.0.0) (**6**) proved even more straightforward. All that was required was exposure of the linear tetrapyrrolic precursor **7**<sup>13,14</sup> to Cr(VI) as above; this produced **6** in one step in 16% yield (Scheme 2).<sup>15</sup>

Macrocycles **5** and **6** are novel molecules and display some unique features. While not formally aromatic, they do contain extended  $\pi$ -electron conjugation pathways. Further, containing as they do quaterpyrrole subunits, they possess exceptionally high pyrrole to meso-like carbon ratios, namely 3.5 and 4.0 in the case of **5** and **6**, respectively. This makes them, along with amethyrin **8** (pyrrole to meso-like carbon ratio of 3),<sup>16</sup> the most “contracted” expanded porphyrins produced to date. Despite this, they appear quite stable under normal laboratory conditions in both their free-base and protonated forms.



The unique features of **5** and **6** are reflected in part in their spectroscopic properties. For instance, in the case of H<sub>2</sub>5<sup>2+</sup>·SO<sub>4</sub><sup>2-</sup>,

(10) Meyer, S.; Andrioletti, B.; Sessler, J. L.; Lynch V. *J. Org. Chem.* **1998**, *63*, 6752–6756.

(11) Sessler, J. L.; Hoehner, M. C. *Synlett* **1994**, 211–212.

(12) A derivative of **4** has recently been reported; see: Morosini, P.; Scherer, M.; Meyer, S.; Lynch V.; Sessler, J. L. *J. Org. Chem.* **1997**, *62*, 8848–8853.

(13) While, to the best of our knowledge, **7** is a new compound, unsubstituted tetrapyrroles of this type are known; see: Sepulveda-Boza, S.; Braitmaier, E. *Liebigs Ann. Chem.* **1983**, 894–896.

(14) The octaethyl-substituted form of **7** is also known; see: Bröring, M.; Jendry, J.; Zander, L.; Schmickler, H.; Lex, J.; Wu, Y.-D.; Nendel, M.; Chen, J.; Plattner, D. A.; Houk, K. N.; Vogel, E. *Angew. Chem., Int. Ed. Engl.* **1995**, *34*, 2515–2517.

(15) When DDQ or molecular oxygen were used as the oxidants, more complex product mixtures were obtained wherein **6** was still present, albeit in lower yield.

(16) Sessler, J. L.; Weghorn, S. J.; Hiseada, Y.; Lynch, V. *Chem. Eur. J.* **1995**, *1*, 56–67.

(1) (a) Sessler, J. L.; Weghorn, S. J. *Expanded, Contracted, and Isomeric Porphyrins*; Elsevier: Oxford, 1997. (b) Jasat, A.; Dolphin, D. *Chem. Rev.* **1997**, *97*, 2267–2340. (c) Sessler, J. L.; Gebauer, A.; Weghorn, S. J. In *The Porphyrin Handbook*; Kadish, K., Smith, K. M., Guillard, R., Eds.; Academic Press: San Diego, 1999, in press.

(2) For recent examples of expanded porphyrins prepared using Rothmund-like chemistry, see: (a) Neves, M. G. P. M. S.; Martins, R. M.; Tomé, A. C.; Silvestre, A. J. D.; Silva, A. M. S.; Félix, V.; Drew, M. G. B.; Cavaleiro, J. A. S. *Chem. Soc. Chem. Commun.* **1999**, 385–386. (b) Setsune, J.; Katakami, Y.; Iizuna, N. *J. Am. Chem. Soc.* **1999**, *121*, 8957–8958. See also ref 6.

(3) For recent examples of expanded porphyrins prepared using MacDonald-like chemistry, see: (a) Srinivasan, A.; Pushpan, S. K.; Ravikumar, M.; Chandrashekar, T. K.; Roy, R. *Tetrahedron* **1999**, *55*, 6671–6680. (b) Srinivasan, A.; Pushpan, S. K.; Kumar, M. R.; Mahajan, S.; Chandrashekar, T. K.; Roy, R.; Ramamurthy, P. *J. Chem. Soc., Perkin Trans. 2*, **1999**, 961–968. (c) Michels, M.; Zander, L.; Wytko, J. *Abstracts of the 24th International Symposium on Macrocyclic Chemistry* (Barcelona), July 1999.

(4) Ikeda, H.; Sessler, J. L. *J. Org. Chem.* **1993**, *58*, 2340–2342.

(5) Ikeda, H.; Hoehner, M.; Sessler, J. L., unpublished results.

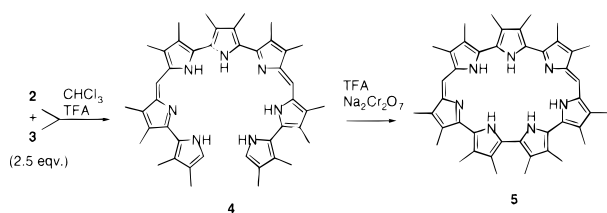
(6) For recent examples of Rothmund-like coupling procedures wherein oxidative couplings are implicated in the formation of expanded porphyrin products, see: (a) Rachlewicz, K.; Sprutta, N.; Chmielewski, P. J.; Latos-Grazynski, L. *J. Chem. Soc., Perkin Trans. 2*, **1998**, 969–975. (b) Narayanan, S. J.; Sridevi, B.; Chandrashekar, T. K.; Vij, A.; Roy, R. *Angew. Chem., Int. Ed.* **1998**, *37*, 3394–3397. (c) Gross, Z.; Galili, N.; Saltsman, I. *Angew. Chem., Int. Ed.* **1999**, *38*, 1427–1429. (d) Paolesse, R.; Jaquinod, L.; Nurco, D. J.; Mini, S.; Sagone, F.; Boschi, T.; Smith, K. M. *J. Chem. Soc., Chem. Commun.* **1999**, 1307–1308.

(7) Falk, H.; Flödl, H. *Monatsh. Chem.* **1988**, *119*, 247–252.

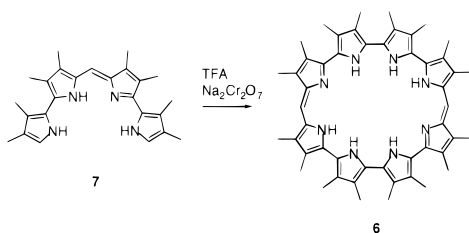
(8) The use of an oxidative coupling strategy to produce sapphyrin has recently been reported: Paolesse, R.; Licocchia, S.; Spagnoli, M.; Boschi, T.; Khoury, R. G.; Smith, K. M. *J. Org. Chem.* **1997**, *62*, 5133–5137.

(9) (a) While this manuscript was being prepared for publication, we became aware of a report wherein an oxidative coupling procedure was used to prepare heterosapphyrins; see: Narayanan, S. J.; Sridevi, B.; Chandrashekar, T. K.; Englich, U.; Ruhlandt-Senge, K. *Org. Lett.* **1999**, *1*, 587–590. (b) After this paper was submitted for publication and accepted subject to minor revisions, a report appeared detailing the use of an oxidative coupling to produce an expanded, tetrapyrrolic corrole: Paolesse, R.; Khoury, R. G.; Sala, F. D.; Natale, C. D.; Sagone, F.; Smith, K. *Angew. Chem., Int. Ed.* **1999**, *38*, 2577–2578.

## Scheme 1



## Scheme 2



as in the case of  $\text{H}_2\mathbf{8}^{2+}\cdot 2\text{Cl}^-$ , three sharp bands are seen in the electronic spectrum.<sup>17</sup> By contrast, in the case of  $\text{H}_2\mathbf{6}^{2+}\cdot 2\text{Cl}^-$ , perhaps as the result of deviations from planarity, these bands are more muted and appear in the form of shoulders. Still, even in this case, as for the free-base forms  $\mathbf{5}$  and  $\mathbf{6}$ , a spectral resemblance to amethyrin was seen, with the bands themselves being red-shifted.<sup>17</sup>

Proton NMR spectroscopic studies of both  $\mathbf{5}$  and  $\mathbf{6}$  were also carried out. In the case of the  $\text{C}_2$  symmetric system  $\text{H}_2\mathbf{5}^{2+}$ , one finds, as expected, four *NH* signals in an integral ratio of 2:2:2:1 in the 15.9–18.2 ppm spectral region. For  $\text{H}_2\mathbf{6}^{2+}\cdot 2\text{Cl}^-$  two pyrrolic *NH* signals are seen in a 1:1 ratio at 11.2 and 11.9 ppm, respectively, as would be expected based on considerations of symmetry. While the extent of downfield displacement is less in the case of  $\text{H}_2\mathbf{6}^{2+}\cdot 2\text{Cl}^-$  than  $\text{H}_2\mathbf{5}^{2+}\cdot \text{SO}_4^{2-}$ , the observation of inner *NH* signals at low field is, in itself, considered diagnostic of a nonaromatic expanded porphyrin; such signals are seen in a range of related systems, including  $\text{H}_2\mathbf{8}^{2+}$ .<sup>1,16</sup>

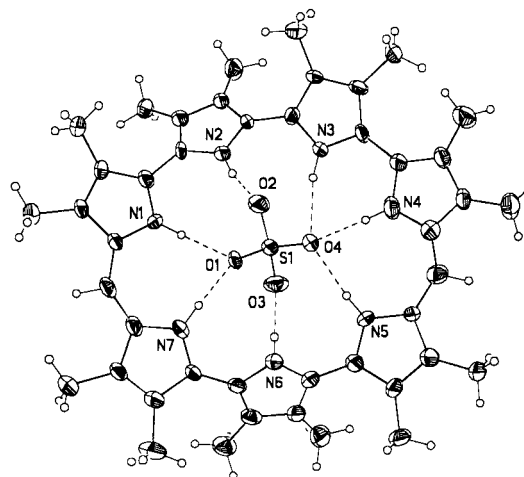
Definite proof of structure for compounds  $\mathbf{5}$  and  $\mathbf{6}$  came from single-crystal X-ray diffraction analyses of their diprotonated adducts,  $\text{H}_2\mathbf{5}^{2+}\cdot \text{SO}_4^{2-}$  and  $\text{H}_2\mathbf{6}^{2+}\cdot 2\text{Cl}^-$ .<sup>18</sup> In the case of  $\text{H}_2\mathbf{5}^{2+}\cdot \text{SO}_4^{2-}$  (Figure 1), the macrocycle was found to be fairly planar and to contain a large cavity into which the sulfate counterion is bound. Anion binding,<sup>19</sup> at least in the solid state, is also apparent in the X-ray diffraction structure of  $\text{H}_2\mathbf{6}^{2+}\cdot 2\text{Cl}^-$  (Figure 2). In this instance, however, the system is seen to deviate substantially from planarity. While this result is consistent with what was inferred from spectral studies (*vide supra*), the extent of this deviation is nonetheless far less than that which is observed in several other “less contracted” octapyrrolic macrocycles, including [32]octaphyrin(1.0.1.0.1.0.1.0),<sup>14</sup> [36]octaphyrin(2.1.0.1.2.1.0.1)<sup>20</sup> and [34]-

(17) For instance, the lowest-energy, Q-like transitions of  $\mathbf{8}$  and  $\text{H}_2\mathbf{8}^{2+}$  are observed at ( $\lambda_{\text{max}}$  ( $\epsilon$ )) 468 nm (45 600) and 597 nm (56 500), respectively,<sup>16</sup> whereas those of  $\mathbf{5}$ ,  $\text{H}_2\mathbf{5}^{2+}$ ,  $\mathbf{6}$ , and  $\text{H}_2\mathbf{6}^{2+}$  are observed at  $\lambda_{\text{max}}$  ( $\epsilon$ ) values of 507 nm (56 400), 613 nm (53 000), 526 nm (41 500), and  $\sim 660$  nm (sh), respectively. See the Supporting Information.

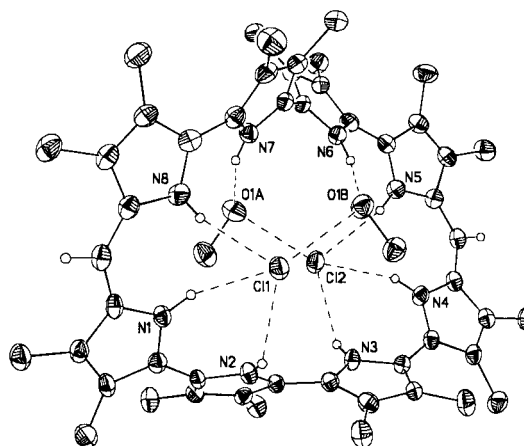
(18) For  $(\text{H}_2\mathbf{5}^{2+}\cdot \text{SO}_4^{2-})\cdot 2\text{CH}_2\text{Cl}_2$ , the structure was refined on  $F^2$  to an  $R_w = 0.210$ , with a conventional  $R = 0.082$ ; for  $(\text{H}_2\mathbf{6}^{2+}\cdot 2\text{Cl}^-)\cdot 2\text{CH}_3\text{OH}$ , the structure was refined on  $F^2$  to an  $R_w = 0.242$ , with a conventional  $R = 0.101$ . See Supporting Information for details.

(19) Anion binding in protonated expanded porphyrins is now well established; cf. Sessler, J. L.; Sansom, P. I.; Andrievsky, A.; Král, V. In *Supramolecular Chemistry of Anions*; Bianchi, A., Bowman-James, K., Garcia-España, E., Eds.; VCH Verlag: Weinheim, 1997; pp. 355–419. See also ref 1.

(20) Vogel, E.; Bröring, M.; Fink, J.; Rosen, D.; Schmickler, H.; Lex, J.; Chan, K. W. K.; Wu, Y.-D.; Plattner, D. A.; Nendel, M.; Houk, K. N. *Angew. Chem., Int. Ed. Eng.* **1995**, *34*, 2511–2514.



**Figure 1.** View of the  $\text{H}_2\mathbf{5}^{2+}\cdot \text{SO}_4^{2-}$  H-bonding complex showing a partial atom labeling scheme. The  $\text{N}\cdots\text{O}$  contacts range from 2.668(5) to 2.961(5) Å. The thermal ellipsoids are scaled to the 50% probability level.



**Figure 2.** View of  $\text{H}_2\mathbf{6}^{2+}\cdot 2\text{Cl}^-$  with a partial atom labeling scheme. Displacement ellipsoids are scaled to the 50% probability level. The macrocycle is H-bonded by two  $\text{Cl}^-$  ions and two molecules of methanol. The  $\text{Cl}^-$ – $\text{N}$  contacts range from 3.123(4) to 3.255(4) Å.

octaphyrin(1.1.1.0.1.1.1.0)<sup>20</sup> wherein “Figure 8” structures are observed. Presumably, this reflects the reduced number of pivot-like meso carbon atoms present in  $\text{H}_2\mathbf{6}^{2+}\cdot 2\text{Cl}^-$ .

In summary, the synthesis of two novel expanded porphyrin systems, prepared by a new directed oxidative coupling procedure, is described. This latter methodology is not only reasonably high-yielding and efficient in terms of the number of steps required to generate a macrocyclic product, it also appears to be quite versatile.<sup>21</sup> It could thus emerge as a quite useful synthetic tool.

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**Supporting Information Available:** Experimental details describing the syntheses and characterization of compounds  $\mathbf{5}$ ,  $\mathbf{6}$ , and  $\mathbf{7}$  as well as tables of positional and thermal parameters, bond lengths and angles, torsion angles, and thermal ellipsoid representations for  $(\text{H}_2\mathbf{5}^{2+}\cdot \text{SO}_4^{2-})$  and  $(\text{H}_2\mathbf{6}^{2+}\cdot 2\text{Cl}^-)$  (PDF). An X-ray crystallographic file (CIF). This material is available free of charge via the Internet at <http://pubs.acs.org>.

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(21) In addition to the [28]heptaphyrin(1.0.0.1.0.0.0) ( $\mathbf{5}$ ) and [32]octaphyrin(1.0.0.0.1.0.0.0) ( $\mathbf{6}$ ) products reported here, we have succeeded in preparing an alkyl-substituted [24]hexaphyrin(1.0.1.0.0.0) from an appropriate linear hexapyrrolic precursor.