Angewandte Chemie

DOI: 10.1002/ange.201303184

Porphyrinoids

Metal-Assisted Cyclomerization of N-Confused Dipyrrins into Expanded Norroles**

*Santosh C. Gadekar, Baddigam Kiran Reddy, and Venkataramanarao G. Anand**

Dedicated to Prof. K. N. Ganesh on the occasion of his 60th birthday

Porphyrinoids with N-confused pyrrole rings are widely studied for their unusual structural and chemical properties. The N-confused porphyrin[1] **1a** and N-confused corrole[2] **1b** are the simplest examples of N-confused porphyrinoids (Figure 1). It has been shown that one or more confused pyrrole rings can be accommodated in porphyrin and in its expanded derivatives.[3] Comparable ring inversions are known in expanded porphyrinoids too, and can transpire because of fluxional behavior as well.[4] Recently, Furuta and co-workers identified a rare nitrogen–carbon link between the adjacent pyrrole rings in a corrole framework. The norrole[2,5] **1c**, considered to be a structural isomer of corrole, has a C–N linked bipyrrole when synthesized through the neoconfused approach. Lash and co-workers have synthesized a porphyrin isomer, the neoconfused porphyrin[6] **1d** wherein the pyrrole nitrogen atom is covalently connected to the *meso* carbon atom of the porphyrin framework. In both **1c** and **1d** the pyrrole nitrogen atom is the key covalent N connector for the macrocyclic framework. Even though porphyrin and expanded porphyrins are known to accommodate multiple confused pyrrole rings,[7] similar reports are unknown to norrole chemistry so far. Herein, we report the first expanded norroles having six and eight pyrrole rings, as synthesized from 2,3-dipyrromethene (N-confused dipyrrin).

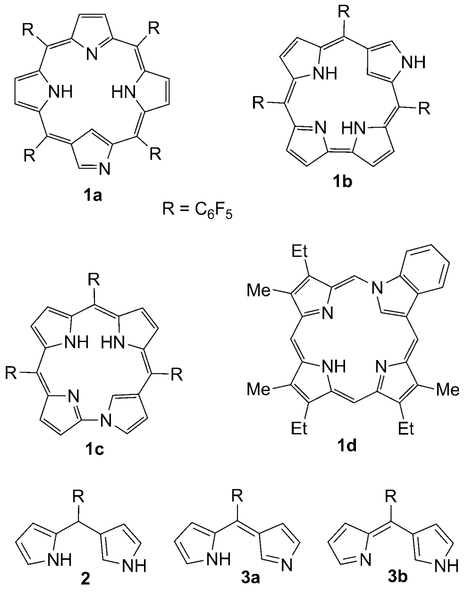


Figure 1. Structures of the N-confused porphyrin **1a**, N-confused corrole **1b**, norrole **1c**, and the neoconfused porphyrin **1d**, N-confused dipyrromethane **2**, and tautomers of N-confused dipyrrins **3a** and **3b**.

Short oligopyrroles are handy precursors for the synthesis of regular porphyrinoids. They are known to exist as dipyrrin, tripyrrin, or tetrapyrene,[8] depending on the number of pyrrole units in the chain. In general, they have attracted interest for their metal-binding properties, and dipyrrin in particular is known to be a versatile ligand for many metals and metalloids.[8] In spite of these reports on oligopyrroles, the ligation ability of 2,3-dipyrromethene has hardly been explored to date. We attempted to synthesize a metal complex from the N-confused dipyrrin by a process analogous to the synthesis of metal dipyrrin complexes. N-confused dipyrrin can be synthesized by the oxidation of the N-confused dipyrromethane **2** (Figure 1).[9] Unlike dipyrrin, the N-confused dipyrrin can have two possible tautomers, **3a** or **3b**, depending on the imine nitrogen atom in one of the pyrrole rings. In an attempt to synthesize a boron difluoride complex from phenyl N-confused dipyrrin (Scheme 1), we were able to isolate only its boron trifluoride complex (**4**). The composition of **4** was established from mass spectrometry and single-crystal X-ray diffraction studies (see the Supporting Information).

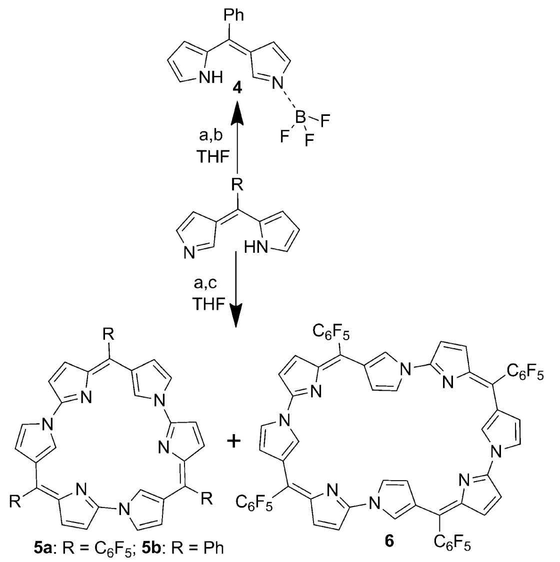
Since the imine nitrogen atom of **3a** coordinated to the boron alone, we expected a similar reactivity with metal salts too. In an identical procedure, anhydrous copper acetate was added to pentafluorophenyl N-confused dipyrrin and stirred overnight in dry tetrahydrofuran (Scheme 1). Interestingly, the MALDI-TOF mass spectrum of this reaction mixture indicated an *m*/*z* ratio equivalent to that for the cyclotrimer **5a** and the cyclotetramer **6**, of the dipyrrin. Addition of various other metal salts such as Co^{2+}, Zn^{2+}, Mn^{2+}, Fe^{2+}, Fe^{3+}, Ti^{4+}, and Sn^{2+}, to the dipyrrin, yielded the same products under identical reaction conditions. Apart from **5a** and **6**, the cyclodimer (equivalent of norcorrole)[10] and other larger macrocycles with *m*/*z* values corresponding to cyclopentamer and cyclohexamer units were also identified in the MALDI-

---

[*] S. C. Gadekar, B. K. Reddy, Prof. Dr. V. G. Anand
Department of Chemistry
Indian Institute of Science Education and Research (IISER)
Pune-411008, Maharashtra (India)
E-mail: vg.anand@iiserpune.ac.in

[**] We acknowledge the financial support from IISER Pune, India and Science and Engineering Research Board (SERB), DST, New Delhi (India).

Supporting information for this article is available on the WWW under http://dx.doi.org/10.1002/anie.201303184.



Scheme 1. Synthesis of expanded norroles **5** and **6**. a) Et_3N, b) $BF_3.OEt_2$, c) Cu^{2+}.

TOF mass spectrum. However they were formed in too low of a yield to be isolated for further characterization. Similar reaction with the phenyl derivative of the N-confused dipyrrin yielded the cyclotrimer **5b** as the major compound (see the Supporting Information).

Since α-α coupling of pyrrole/oligopyrroles is a well-known synthetic strategy to synthesize expanded porphyrinoids,[4] the detection of the cyclotrimer and cyclotetramer of the N-confused dipyrrin signified the possible formation of the N-confused rosarin **5R** and the N-confused octaphyrin **6O** (Figure 2). Rosarin (**7**), was isolated as a non-aromatic 24π macrocycle by the acid-catalyzed condensation of three bipyrrole units with an aryl aldehyde.[11] A recent communication has shown that planar rosarin is anti-aromatic in nature.[12] Since no other structural isomer of rosarin is known, to the best of our knowledge, we suspected the formation of the N-confused rosarin **5R**, by the coupling of three N-confused dipyrrin units. The ^{1}H NMR spectrum of **5a** exhibited multiplets at $\delta = 11.16$, 6.78, and 5.62 ppm, and two doublets at $\delta = 6.50$ and 6.48 ppm. The ^{1}H-^{1}H COSY spectrum shows strong correlation between the two doublets at $\delta = 6.50$ and 6.48 ppm while the other three signals were found to interact amongst themselves. This is possible only in the confused pyrrole with three different protons. Addition of D_2O did not change the spectral pattern, thus indicating the absence of any NH in the macrocycle. Five ^{13}C signals for the CH groups were observed in the DEPT-90 measurement. Four signals appeared between $\delta = 126$ and 112 ppm, while a solitary downfield signal appeared at $\delta = 136$ ppm. The downfield shift of a single carbon atom demonstrates the paratropic ring current effect on the inner CH group of the macrocycle. All these observations suggested the formation of an expanded norrole (**5a**) having three bipyrrole units bearing C–N bonds between the adjacent pyrrole rings. The upfield and downfield chemical shift values in the ^{1}H and ^{13}C NMR spectra emphasize its anti-aromatic character. The paratropic ring current effects also underline the delocalization of the π electrons by accommodating the lone pair of the electrons on the N-connectors of the confused pyrrole.

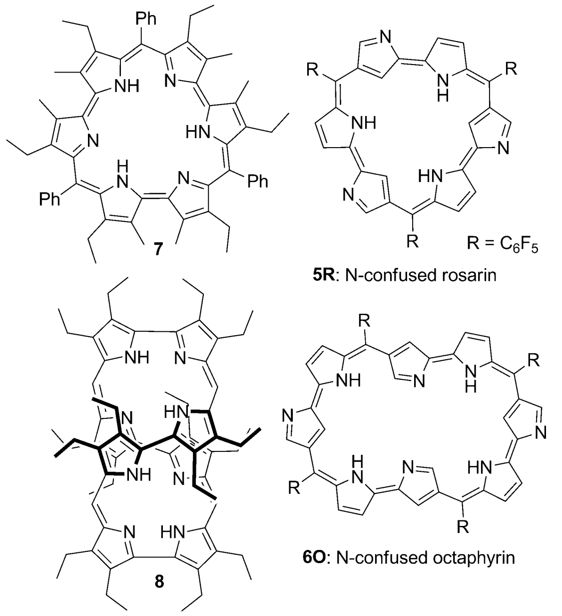


Figure 2. Possible structural isomer for the expanded norroles **5R** and **6O**, and their respective parent macrocycles rosarin (**7**) and the cyclooctapyrrole **8**.

The proton NMR spectrum of **6** displayed twice the number of signals observed for **5a** in the region between $\delta = 10.00$ and 6.00 ppm. Four well-resolved doublets between $\delta = 7.25$-6.97 ppm and six different multiplets were observed at $\delta = 9.97$, 8.69, 8.54, 7.64, 7.53, and 6.22 ppm. D_2O addition did not diminish the intensity of any peak, thus indicating the absence of any NH in the macrocycle. The ^{1}H-^{1}H COSY spectrum showed two different kinds of cross-correlations: a) two sets of correlations were observed for the four doublets and b) the rest of the six signals showed two sets of symmetrical correlations comprising three signals in each (see the Supporting Information). Similar correlations were observed for **5a**, and based on the above NMR analyses the (b) protons could be assigned to the confused pyrrole. DEPT-90 measurements showed eight ^{13}C signals for CH groups between $\delta = 127$ and 114 ppm while a downfield signal for two carbon atoms was observed at 138 ppm. The most deshielded signal at $\delta = 10.00$ ppm in the ^{1}H NMR spectrum and at $\delta = 138$ ppm in the DEPT-90 spectrum signified the paratropic ring current effects expected of anti-aromatic macrocycles. This observation clearly suggests there are two pairs of confused pyrrole units having dissimilar orientations in **6**. An earlier report of a the 32π octaphyrin **8**, with eight pyrrole subunits, was found to have a twisted conformation (Figure 2) and was hence characterized as non-aromatic in nature.[13] However, the shielding and deshielding of the protons in the ^{1}H NMR spectrum of **6** indicated a planar conformation for the 32π system and its anti-aromaticity.

Further confirmation for the structure of the expanded norroles **5a** and **6** came from the single-crystal X-ray diffraction studies (Figure 3). Good quality single crystals

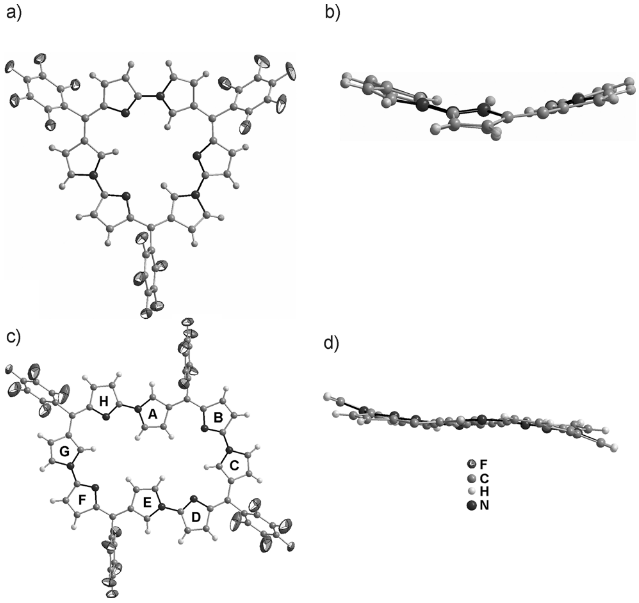


Figure 3. Molecular structures of expanded norroles determined from single-crystal X-ray diffraction studies. Top views of **5a** (a) and **6** (c), and side views of **5a** (b) and **6** (d).[16] Solvent molecules and the pentafluorophenyl rings (in the side view) are omitted for clarity. The C–N bond of bipyrrolic units are highlighted in black.

were grown by vapor diffusion of *n*-hexane into a chloroform solution of the macrocycles. The molecular structure confirmed the C–N bond between the adjacent pyrrole units in both the macrocycles. The hexapyrrolic expanded norrole **5a** displayed three C–N bonds in the three bipyrrolic units (Figure 3a). It clearly indicates a symmetrical head-to-tail connectivity between the three N-confused dipyrrins, thereby having an alternate arrangement of three regular and three N-linked pyrroles. One of the α-carbon atoms is inside the ring, while the other α- and ß-carbon atoms of the N-linked pyrrole are outside the core of the macrocycle. This observation is consistent with the signals observed in the NMR spectrum of **5a**. All the pyrrole rings are found to be coplanar, thus indicating a lone pair of electrons on the nitrogen atom in the N-linked pyrrole ring is delocalized throughout the π-electron circuit in the macrocycle. The dihedral angle between the two pyrroles, connected by a C–N bond, is found to be 16° and hence leads to deviation from perfect planarity (Figure 3b). The molecular structure of **6** revealed a near-planar structure with a rectangular shape in the solid state. Four N-confused dipyrrins are interconnected through C–N linked bipyrrolic units in a head-to-tail fashion, thus leading to an octapyrrole macrocycle. A near-planar structure is the most striking aspect of the expanded norrole **6**. Many macrocycles with eight pyrroles and four or more *meso* bridges are found to have a twisted conformation and are non-aromatic in nature.[4a,b] The expanded norrole **6** is the first example of a 32π cyclooctapyrrole with a nontwisted conformation. The second significant aspect of this structure lies in the two different types of N-linked pyrrole rings (Figure 3c). The apparent inversion along the C–N bond axis brings an α and ß CH of the N-linked pyrrole rings (A and E) inside the central cavity, while the other α C-H protrudes from the center. A distance of 7.0 Å between the nitrogen atom of the two pyrrole rings (B,H, and D,F) is sufficient enough to accommodate two carbon atoms. These two ring inversions reduce the symmetry of **6**, which is clearly marked by the two different signals for the N-linked pyrroles in its ^{1}H NMR spectrum. The shorter side, with only 5.0 Å between the nitrogen atom of the pyrrole rings (B,D, and F,H), is a constraint for the pyrrole to be inverted. The C–N linked pyrroles (A,H, and D,E) are coplanar, while the other two pairs (B,C, and F,G) form a dihedral angle of 18° between themselves. Interestingly, they are found to deviate unequally from the mean macrocyclic plane. The pair of pyrrole rings C,G and B,F make an angle of 17° and 4°, respectively, with the plane formed by the four *meso*-carbon atoms. This unsymmetrical deviation of the pyrrole rings prevents the macrocycle from adopting a perfect planar structure (Figure 3d). Besides, all the pyrrole rings are planar, thus indicating that the lone pair of the electrons on the nitrogen atom of N-linking pyrroles delocalizes throughout the macrocyclic π-electron cloud. The macrocyclic framework of C–C bonds in both **5** and **6** are found to have bond lengths inbetween that of single and double bond distances, thus suggestive of a π-delocalized network.

Further indication for their conjugated behavior came from the electronic absorption spectroscopy (see the Supporting Information). Because of their extensive conjugation, **5** and **6** form yellowish-green and red colored solutions in common organic solvents. The compound **5a** displays an absorption maximum at $\lambda = 402$ nm ($\varepsilon = 45\,000$) and a weak absorption at $\lambda = 526$ nm. The compound **6** was found to absorb at $\lambda = 423$ nm (152 000) and has two weak absorptions at $\lambda = 518$ and 550 nm. The weak absorptions are broad and typical of anti-aromatic systems. We also computed the nucleus independent chemical shift (NICS)[14] values for both the macrocycles, by employing Gaussian 03[15] for qualitative and quantitative estimation of π delocalization in macrocyclic systems. The computed values of NICS(0) for **5a**, **5b**, and **6** were found to be $\delta = 4.5$, 3.5, and 1.5 ppm, respectively. Even though these values are small, the positive values are suggestive of feeble anti-aromatic systems. This feature can be possibly attributed to the weak π delocalization because of the C–N linked bipyrrole systems.

In summary, N-confused dipyrrin does not show reactivity similar to that of dipyrrins with metal salts. Instead, it undergoes intermolecular cyclomerization, thus leading to the synthesis of the first examples of expanded norroles. They have multiple C–N bonds along the conjugated pathway of the macrocyclic framework. Their synthesis is simple and can be catalyzed by a variety of metal ions. The considerable upfield and downfield chemical-shift values signify π delocalization and anti-aromaticity. The compound **6** represents the first example of a 32π octaphyrin with a nontwisted conformation. These macrocycles also demonstrate the possibility of accommodating more than two neoconfused pyrrole moieties and represent a new class of stable, anti-aromatic expanded porphyrinoids with unusual π conjugation.

Received: April 16, 2013

Keywords: macrocycles · NMR spectroscopy · porphyrinoids · structure elucidation · template synthesis

[1] a) H. Furuta, T. Asano, T. Ogawa, *J. Am. Chem. Soc.* **1994**, *116*, 767 – 768; b) P. J. Chmielewski, L. Latos-Grazynski, K. Rachlewicz, T. Głowiak, *Angew. Chem.* **1994**, *106*, 805 – 808; *Angew. Chem. Int. Ed. Engl.* **1994**, *33*, 779 – 781.

[2] K. Fujino, Y. Hirata, Y. Kawabe, T. Morimoto, A. Srinivasan, M. Toganoh, Y. Miseki, A. Kudo, H. Furuta, *Angew. Chem.* **2011**, *123*, 6987 – 6991; *Angew. Chem. Int. Ed.* **2011**, *50*, 6855 – 6859.

[3] a) A. Srinivasan, H. Furuta, *Acc. Chem. Res.* **2005**, *38*, 10 – 20; b) M. Toganoh, H. Furuta, *Chem. Commun.* **2012**, *48*, 937 – 954.

[4] a) S. Saito, A. Osuka, *Angew. Chem.* **2011**, *123*, 4432 – 4464; *Angew. Chem. Int. Ed.* **2011**, *50*, 4342 – 4373; b) M. Stępień, N. Sprutta, L. Latos-Grazyński, *Angew. Chem.* **2011**, *123*, 4376 – 4430; *Angew. Chem. Int. Ed.* **2011**, *50*, 4288 – 4340; c) J. L. Sessler, D. Seidel, *Angew. Chem.* **2003**, *115*, 5292 – 5333; *Angew. Chem. Int. Ed.* **2003**, *42*, 5134 – 5175; d) T. K. Chandrashekar, S. Venkatraman, *Acc. Chem. Res.* **2003**, *36*, 676 – 691; e) T. D. Lash, *Angew. Chem.* **2000**, *112*, 1833 – 1837; *Angew. Chem. Int. Ed.* **2000**, *39*, 1763 – 1767.

[5] a) M. Toganoh, Y. Kawabe, H. Furuta, *J. Org. Chem.* **2011**, *76*, 7618 – 7622; b) M. Toganoh, Y. Kawabe, H. Uno, H. Furuta, *Angew. Chem.* **2012**, *124*, 8883 – 8886; *Angew. Chem. Int. Ed.* **2012**, *51*, 8753 – 8756.

[6] a) T. D. Lash, A. D. Lammer, G. M. Ferrence, *Angew. Chem.* **2011**, *123*, 9892 – 9895; *Angew. Chem. Int. Ed.* **2011**, *50*, 9718 – 9721; b) T. D. Lash, *J. Porphyrins Phthalocyanines* **2012**, *16*, 423 – 433.

[7] a) Y. S. Xie, K. Yamaguchi, M. Toganoh, H. Uno, M. Suzuki, S. Mori, S. Saito, A. Osuka, H. Furuta, *Angew. Chem.* **2009**, *121*, 5604 – 5607; *Angew. Chem. Int. Ed.* **2009**, *48*, 5496 – 5499; b) A. Srinivasan, T. Ishizuka, A. Osuka, H. Furuta, *J. Am. Chem. Soc.* **2003**, *125*, 878 – 879.

[8] T. E. Wood, A. Thompson, *Chem. Rev.* **2007**, *107*, 1831 – 1861, and references cited therein.

[9] H. Furuta, H. Maeda, A. Osuka, *J. Am. Chem. Soc.* **2000**, *122*, 803 – 807.

[10] a) M. Bröring, S. Kohler, C. Kleeberg, *Angew. Chem.* **2008**, *120*, 5740 – 5743; *Angew. Chem. Int. Ed.* **2008**, *47*, 5658 – 5660; b) T. Ito, Y. Hayashi, S. Shimizu, J.-Y. Shin, N. Kobayashi, H. Shinokubo, *Angew. Chem.* **2012**, *124*, 8670 – 8673; *Angew. Chem. Int. Ed.* **2012**, *51*, 8542 – 8545.

[11] J. L. Sessler, S. J. Weghorn, T. Morishima, M. Rosingana, V. Lynch, V. Lee, *J. Am. Chem. Soc.* **1992**, *114*, 8306 – 8307.

[12] M. Ishida, S. J. Kim, C. Preihs, K. Ohkubo, J. M. Lim, B. S. Lee, J. S. Park, V. M. Lynch, V. R. Roznyatovsky, T. Sarma, P. K. Panda, C. H. Lee, S. Fukuzumi, D. Kim, J. L. Sessler, *Nat. Chem.* **2013**, *5*, 15 – 20.

[13] E. Vogel, M. Broring, J. Fink, D. Rosen, H. Schmickler, J. Lex, K. W. K. Chan, Y.-D. Wu, D. A. Plattner, M. Nendeland, K. N. Houk, *Angew. Chem.* **1995**, *107*, 2705 – 2709; *Angew. Chem. Int. Ed. Engl.* **1995**, *34*, 2511 – 2514.

[14] P. von R. Schleyer, C. Maerker, A. Dransfeld, H. Jiao, N. J. R. v. E. Hommes, *J. Am. Chem. Soc.* **1996**, *118*, 6317.

[15] Gaussian 03 (Revision C.02), M. J. Frisch, et al., Gaussian, Inc., Wallingford, CT, **2004**. For full reference, see the Supporting Information.

[16] CCDC 933257 (**5a**) and CCDC 933258 (**6**) contain 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.