"N-Confused Porphyrin": A New Isomer of Tetraphenylporphyrin

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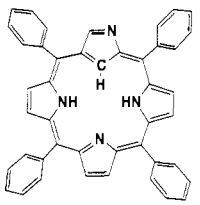
In recent years, a number of porphyrin analogs,[1] including compounds such as the isoporphyrins,[2] heteroporphyrins,[3] expanded porphyrins,[4] vinylogous porphyrins,[5] etc., have been synthesized. However, few examples are known that can be called true "isomers" of porphyrin.[6] One possible isomer could be a tetrapyrrole macrocycle, in which one pyrrole ring is linked through its α–β' axis instead of *via* a more normal α–α' linkage.[7] In this communication, we report the synthesis and the structural characterization of a phenyl-substituted derivative of a porphyrin isomer, **1**. To the best our knowledge, this new compound, to which we have assigned the trivial name "N-confused porphyrin; NC-P", is the first example of an isomeric porphyrin-like system in which the "starting" four methine bridges are still present.[8]



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The new compound, "N-confused tetraphenylporphyrin" (NC-TPP, **1**) was obtained using a modification of the well-known synthesis of TPP that involves the acid-catalyzed condensation between benzaldehyde and pyrrole.[9] However, in place of propionic acid, *t*-BuOH/CH_2Cl_2 (1:1) and concentrated HBr (1 equiv) were used.[10] More specifically, after addition of pyrrole and benzaldehyde to such a solvent mixture, and stirring for 2 days at room temperature in the dark, oxidation with 2 equiv of chloranil and standard workup gave a reaction mixture that could be purified by column chromatography on silica gel (eluent: 3% MeOH in CH_2Cl_2), followed by recrystallization from MeOH/CH_2Cl_2 to give **1** as a purple solid in yields of 5–7%. TPP was also obtained as the major product (~20% yields).

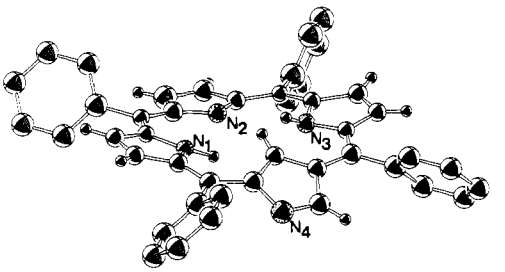

Figure 1. Molecular structure of NC-TPP (**1**). Hydrogen atoms at the phenyl rings have been removed for clarity. Thermal ellipsoids have been drawn at the 50% probability level.

The spectroscopic data obtained were consistent with the formulation of **1** as an isomer of TPP.[11] For example, the ^{1}H NMR spectrum of **1** revealed characteristic high-field shifts for the inner NH's and β-H of "confused pyrrole" (at –2.5 and –5.1 ppm, respectively), presumably as the result of the aromatic ring current. This latter β-H signal did not exchange rapidly upon the addition of D_2O, and it showed a cross peak with the pyrrole carbon at 99.2 ppm in the ^{13}C–^{1}H COSY spectrum. In addition, the "outside pointing" α-H in this same pyrrole appeared as a singlet at 8.68 ppm.

More direct evidence for the structural assignment came from a single-crystal X-ray diffraction analysis[12] (Figure 1). In contrast to TPP,[13] the structure obtained revealed that the molecule deviates from planarity. Among the four pyrrole rings in **1**, the "confused ring" is the most highly canted from the reference N_1–N_2–N_3 plane by 26.9°. The two adjacent pyrrole rings and that opposite to the "confused" one are tilted by 13.4°, 7.8°, and 5.8°, respectively.[14] Such ring distortions appear to result from the mutual repulsion of the three inner hydrogens (β-CH, N_1H, and N_3H), which in the absence of canting would necessarily be forced to reside in the same van der Waals sphere.

The Soret- and Q-type transitions of NC-TPP in CH_2Cl_2 were broadened and shifted to longer wavelengths (λ_{max} = 438 and 725 nm, respectively) as compared to those of TPP (419 and 647 nm) (Figure 2). These spectral red shifts and broadenings were also apparent when the compound was protonated. For instance, by adding excess (~1000 equiv) trifluoroacetic acid (TFA) to the solution, the monoprotonated (λ_{max} = 451 and 800 nm) and diprotonated forms (λ_{max} = 465 and 825 nm) of **1** could be prepared in turn. Since the corresponding shifts observed upon protonation of TPP to form $[H_2TPP]^{2+}$ are only on the order of 20–30 nm, the observed large spectral changes in the case of **1** are thought to be a reflection of the severe distortion from planarity.[15]

Changes due to protonation were also observed in the ^{1}H NMR spectrum. For instance, by increasing the amount of TFA present

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(1) For overviews of porphyrin analogs, see: (a) Johnson, A. W. *Porphyrins and Metalloporphyrins*; Smith, K. M., Ed.; Elsevier: Amsterdam, 1975; Chapter 18. (b) Grigg, R. *The Porphyrins*; Dolphin, D., Ed.; Academic Press, New York, 1978; Chapter 10.

(2) (a) Dolphin, D.; Felton, R. H.; Borg, D. C.; Fajer, J. *J. Am. Chem. Soc.* **1970**, *92*, 743–745. (b) Barkigia, K. M.; Renner, M. W.; Xie, H.; Smith, K. M.; Fajer, J. *J. Am. Chem. Soc.* **1993**, *115*, 7894–7895 and references cited therein.

(3) (a) Broadhurst, M. J.; Grigg, R.; Johnson, A. W. *J. Chem. Soc. C* **1971**, 3681. (b) Vogel E.; Haas, W.; Knipp, B.; Lex, J.; Schmickler, H. *Angew. Chem., Int. Ed. Engl.* **1988**, *27*, 406–409.

(4) Sessler, J. L.; Burrell, A. K. *Top. Curr. Chem.* **1991**, *161*, 177–273.

(5) (a) Gosmann, M.; Frank, B. *Angew. Chem., Int. Ed. Engl.* **1986**, *25*, 1100–1101. (b) Vogel, E. *Pure Appl. Chem.* **1993**, *65*, 143–152 and references cited therein.

(6) Porphycenes, bipyrrole and ethylene linked macrocycles ([2.0.2.0.] porphyrin), are the only known isomers of porphyrin. See: Vogel, E.; Köcher, M.; Schmickler, H.; Lex, J. *Angew. Chem., Int. Ed. Engl.* **1986**, *25*, 257–258. Recently, however, a new porphyrin isomer, [2.1.0.1] porphyrin, has been prepared jointly by the groups of Vogel and Sessler (private communication from J. L. Sessler).

(7) Macrocycles whose pyrroles are linked through α- and β'-positions are named "inverted porphyrins". See: Schumacher, K.-H.; Frank, B. *Angew. Chem., Int. Ed. Engl.* **1989**, *28*, 1243–1245.

(8) The IUPAC-recommended name for **1** is 5,10,15,20-tetraphenyl-2-aza-21-carbaporphyrin.

(9) (a) Adler, A. D.; Longo, F. R.; Shergalis, W. *J. Am. Chem. Soc.* **1964**, *86*, 3145–3149. (b) Adler, A. D.; Longo, F. R.; Finarelli, J. D.; Goldmacher, J.; Assour, J.; Korsakoff, L. *J. Org. Chem.* **1967**, *32*, 476.

(10) Hydrochloric acid was also found to be effective in giving **1**, albeit in modest yield.

(11) Satisfactory spectroscopic and analytical data were obtained for **1**; see supplementary material.

(12) The datum crystal was a violet prism obtained from a CH_2Cl_2/CH_3OH solution of **1**. Crystal data: $1{\cdot}CH_2Cl_2{\cdot}H_2O$, MW = 717.70, triclinic, space group $P\bar{1}$ (No. 2), with a = 14.14(1) Å, b = 14.43(1) Å, c = 9.525(4) Å, α = 102.15(5)°, β = 97.1(1)°, γ = 106.1(1)°, V = 1792(6) Å^3, Z = 2, ρ_{calcd} = 1.330 g/cm^3, $F(000)$ = 748. The data was collected at 300 K and the structure solved by direct methods. It refined to R = 0.097, R_w = 0.098 for 1141 reflections with $I > 3.0\sigma(I)$. See supplementary material. We would like to thank Dr. Vinny Lynch for initial help with the X-ray structural work.

(13) For X-ray structures of TPP, see: (a) Silvers, S. J.; Tulinsky, A. *J. Am. Chem. Soc.* **1967**, *89*, 3331–3337. (b) Stone, A.; Fleischer, E. B. *J. Am. Chem. Soc.* **1968**, *90*, 2735–2748.

(14) Similar tilting distortions of the pyrrole rings have been observed previously for N-substituted porphyrins. See: Lavallee, D. K.; Anderson, O. P. *J. Am. Chem. Soc.* **1982**, *104*, 4707–4708.

(15) Barkigia, K. M.; Berber, M. D.; Fajer, J.; Medforth, C. J.; Renner, M. W.; Smith, K. M. *J. Am. Chem. Soc.* **1990**, *112*, 8851–8857.

0002-7863/94/1516-0767$04.50/0

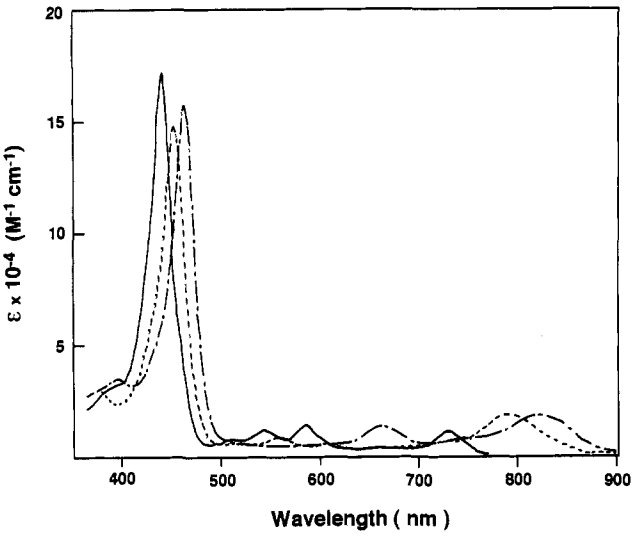

Figure 2. Absorption spectra recorded in CH_2Cl_2 for the various forms of NC-TPP (**1**): (—) free base; (- - -) monoprotonated **1**·$(TFA)_1$; (– – –) diprotonated **1**·$(TFA)_2$.

in a $CDCl_3$ solution of **1**, the inner β-H signal could be induced to shift from −5.1 to −1.4 ppm. Similarly, the initial broad signal at −2.5 ppm assigned to the inner NH could be transformed into three discrete peaks of ca. 1.3, 2.1, and 2.5 ppm. Finally, a signal at 11.3 ppm, assigned to an N_4H resonance, was observed at high TFA concentrations.

On the basis of the above spectroscopic studies, the protonation process is thought to be occurring in a stepwise manner. This, in turn, is considered to reflect the different geometries of the two imine-type nitrogens: protonation takes place, presumably, first at the inner N_2 and then, only subsequently, at the peripheral N_4 site.[16] In any case, the distortions from planarity that would result from double protonation lead us to predict that the loss in resonance stabilization should be substantial for the protonated forms of **1**.

At present, it is not clear why isomer **1** is formed under the present TPP-like condensation conditions. However, we consider it likely that the anions play a crucial templating role. Consistent with this supposition, we find, for instance, that NC-TPP was obtained in the presence of Br^- or Cl^- but not F^-, TFA^-, NO_3^-, and/or $H_2PO_4^-$. Thus, we postulate that if the various putative linear tetrapyrrole intermediates, known precursors to TPP,[17] could wrap around the spherical halide anions *and if such "wrapping around" served to destabilize the transition geometry required to cyclize on to TPP*, an alternative linking route, namely, the one required to obtain a precursor to **1**, could become partially favored. Such "anion template effects" are rare but are known in the literature.[18] In any case, since the present isomer of TPP and some of its derivatives are stable and easily prepared, we are tempted to predict that the "N-confused porphyrins" could serve as interesting porphyrin "substitutes" in the study of such normal porphyrin applications as metal ligation and photosensitization. In addition, the flexible structure and the strong basicity[16] of **1** could make it useful for various anion binding applications.[19]

Supplementary Material Available: ^1H, ^{13}C, and CH-COSY NMR spectra, pH titration curve, spectral data, and X-ray crystallographic details for **1** (34 pages); listing of observed and calculated structure factor for **1** (8 pages). This material is contained in many libraries on microfiche, immediately follows this article in the microfilm version of the journal, and can be ordered from the ACS; see any current masthead page for ordering information.

(16) Actually, separate pK_a values (pK_3 = 3.27 and pK_4 = 8.35) were obtained for **1** in aqueous 2.5% sodium dodecyl sulfate solution. See: Caughey, W. S.; Fujimoto, W. Y.; Johnson, B. P. *Biochemistry* **1966**, *5*, 3830–3843.

(17) Lindsey, J. S.: Wagner, R. W. *J. Org. Chem.* **1989**, *54*, 828–836.

(18) For recent examples for anion template mediated synthesis, see: (a) Sessler, J. L.; Mody, T. D.; Lynch, V. *J. Am. Chem. Soc.* **1993**, *115*, 3346–3347. (b) Yang, X.; Zheng, Z.; Knobler, C. B.; Hawthorne, M. F. *J. Am. Chem. Soc.* **1993**, *115*, 193–195.

(19) In the presence of tetrabutylammonium fluoride, the fluorescence spectrum of NC-TPP in CH_2Cl_2 (λ_{max} = 745 nm) showed ca. 40 nm blue shifts, which suggests the possibility of fluoride anion binding.