

Porphine and pyrrole-substituted porphyrin from cyclocondensation of tripyrrane with mono-substituted pyrroles

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Abstract—The condensation of non-substituted tripyrrane with mono-substituted pyrroles did not lead to corrole, but to porphine and 5-pyrrolyl-porphyrin. Both compounds were fully characterized by a combination of spectroscopic methods and X-ray crystallography.

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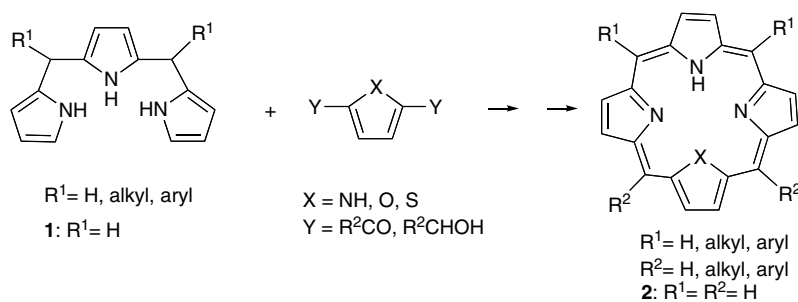
One of the most valuable routes for the synthesis of porphyrins and their analogues is the ‘3+1’ variant of the MacDonald reaction.¹ It relies on the condensation of the free α -pyrrole positions of tripyrranes with suitable substituents located on C $_{\alpha}$ of the other reactant and was first used almost 35 years ago by Johnson and co-workers for the synthesis of oxa- and thiaporphyrins (Scheme 1, X = O and S, respectively).² This approach regained popularity during the last decade, which may be attributed to the recent introduction of simple and high yielding syntheses of tripyrranes.³ The most relevant example for the current studies is that of Taniguchi and co-workers, who reported that the parent porphyrin (porphine, **2**) was obtained in 31% yield from the condensation of non-substituted tripyrrane **1** with 2,5-bis(hydroxymethyl)pyrrole (Scheme 1, R¹ = R² = H, X = NH, Y = CH₂OH).⁴

As a contribution to the increased interest in corrole chemistry,⁵ we decided to examine the condensation of **1**^{3a} with either 2-(hydroxymethyl)pyrrole **3**⁶ or 2-formylpyrrole **4** as a rational approach for the synthesis of the as yet unknown parent corrole **5** (Scheme 2). The hypothesis was that the initially formed condensation product could lead to **5** via oxidative C–C coupling of the free α -pyrrole carbon atoms that are present on both ends of a tetrapyrrolic intermediate.

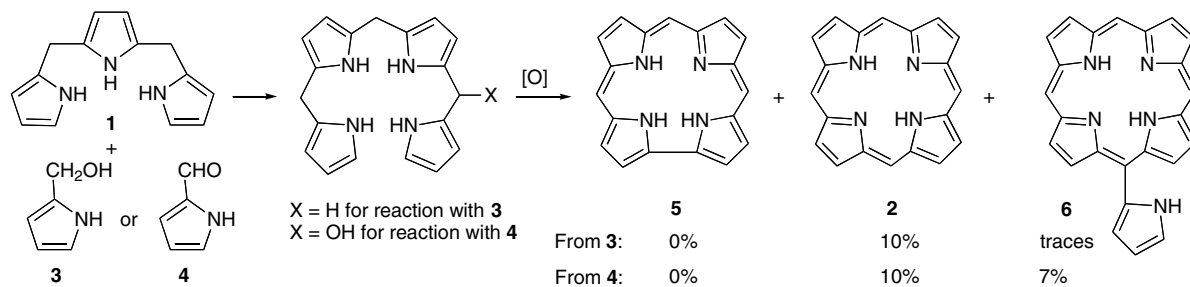
The condensation of equimolar amounts of **1** with **3** or **4** (Scheme 1) was carried out under high dilution reaction conditions (4.5 mM in dichloromethane of each reagent and 0.9 mM TFA), followed by chloranil oxidation.^{7,8} TLC examination of the reaction outcome focused on fluorescent products, the most distinctive property shared by porphyrins and corroles relative to other oligopyrroles.⁹ Surprisingly, the main such product (10% yield) was porphine **2**, accompanied by trace amounts of a new light pink compound **6**, but none of the targeted **5**. The same amount of **2** was obtained when **4** was used as substrate, but the yield of **6** increased to 7%. This allowed for the isolation of substantial amounts of both **6** and **2** and the subsequent full characterization of these compounds.

Figure 1 serves to demonstrate the very different ¹H NMR spectra obtained for **2** and **6**. The long known porphine displayed the distinctively simple spectrum with three singlets at 10.35, 9.52, and –2.97 ppm for the four *meso*-H, eight β -pyrrole-H and two NH atoms, respectively (Fig. 1a).⁸ On the other hand, the spectrum of compound **6** (Fig. 1b) seemed consistent with the C_{2v} symmetry that is classic for corroles (and expected for **5**):^{9b,10} two *meso*-H singlets in a 2:1 ratio at 9.94 and 9.83 ppm, respectively, and four β -pyrrole-H doublets (2H each) at 9.23, 9.15, 9.12, and 9.07 ppm. The HMQC spectrum (not shown) further revealed that the *meso*-H singlets are correlated with two tertiary ¹³C signals at 105.0 and 104.0 ppm at a 2:1 ratio (Fig. 1f). Nevertheless, several observations indicated that **6** was not a corrole (i.e., not compound **5**). First, all the β -pyrrole-H

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Scheme 1.



Scheme 2.

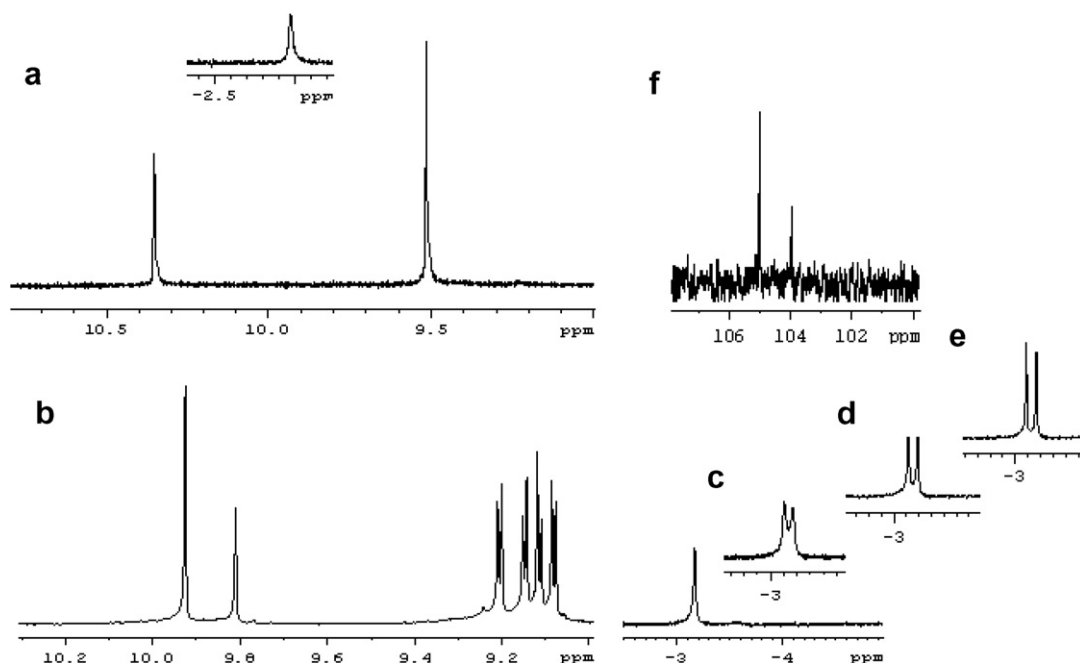


Figure 1. 500 MHz ^1H NMR spectra of (a) **2** (CDCl_3 , rt) and of (b) **6** ($\text{benzene-}d_6$, 300 K), as well as that of the NH protons of **6** ($\text{toluene-}d_8$) at (c) 263 K, (d) 253 K, (e) 220 K, and (f) the 125 MHz ^{13}C of **6** (*meso*-carbon atoms only).

J coupling constants in **6** were identical (4.5 Hz) rather than the corrole-characteristic division into large and small coupling constants.¹⁰ Secondly, the NH protons (at -3 ppm) appeared much sharper than in corroles and the integration was consistent with two rather than three hydrogen atoms. This high field signal was resolved into two singlets at low temperature, consistent with a low-symmetry macrocycle that has two magnetically different NH protons. Finally, the MS molecular ion at $m/z = 375$ was inconsistent with either **2** or **5**,

but rather corresponded to a compound that was larger by 65 and 77 mass units than these two options, respectively.

Fortunately, crystallization from dichloromethane and *n*-hexane afforded X-ray quality crystals of both **2**¹¹ and **6**.¹² Because of the importance of **2** as the parent porphyrin and of precise determination of its structural parameters, the ORTEP picture of the low temperature structure (at ca. 110 K) is provided in Figure 2 despite

the fact that ambient temperature data has been available for many years.¹³ The 24-membered porphine framework was found to be essentially planar, deviations of the individual atoms from the mean plane of the macrocycle not exceeding ± 0.03 Å. The inner H-atoms were found to be localized on two particular pyrrole nitrogen atoms, as opposed to their disordered location on all four nitrogen atoms at room temperature in earlier reported structures.¹³ In the crystal the porphine molecules are grouped in overlapping pairs (Fig. 2c), which are arranged in a herringbone manner in three-dimensional space. The flatness of the porphine molecules, their pairing at a close interplanar distance of 3.33 Å and a typical offset,¹⁴ reflect strong π – π interactions.

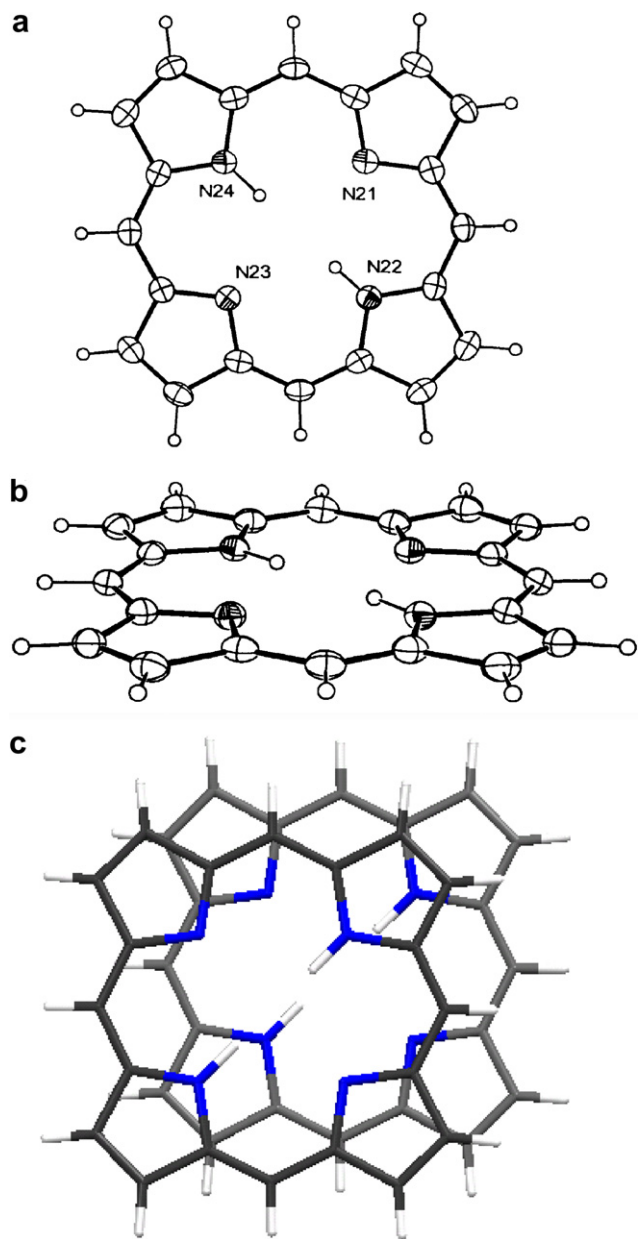


Figure 2. Structure of porphine **2** at ca. 110 K: two different views of the molecular structure (with 50%-probability thermal ellipsoids) are shown in (a) and (b) and the overlap within the π – π interacting pair of porphine molecules is shown in (c).

The ORTEP of **6** is shown in Figure 3, which revealed a porphyrin with one C_{α} -bound pyrrole bound to a C_{meso} atom. The molecular core is considerably more ruffled in this structure, possibly due to the pyrrole substitution, which breaks the square-planar symmetry of the macrocycle. The individual atoms of the 24-membered ring deviate from -0.16 to $+0.13$ Å from their mean plane. The dihedral angle between the plane of the pyrrole substituent and the plane of the four pyrrole nitrogen atoms is 54.5° . Despite these deformations the porphyrin units are paired in an offset-stacked manner in this structure also (Fig. 3c), in order to optimize the π – π attractions between adjacent molecules. The latter is also indicated by the close average interplanar distance between the overlapping fragments of 3.5 Å. The perpendicularly oriented pyrrole substituents are located outside of the overlapping region. In the crystal of **6** these molecular pairs are oriented in parallel-stacked columns.

The molecular structure of **6** is also fully consistent with the earlier discussed main features of its NMR

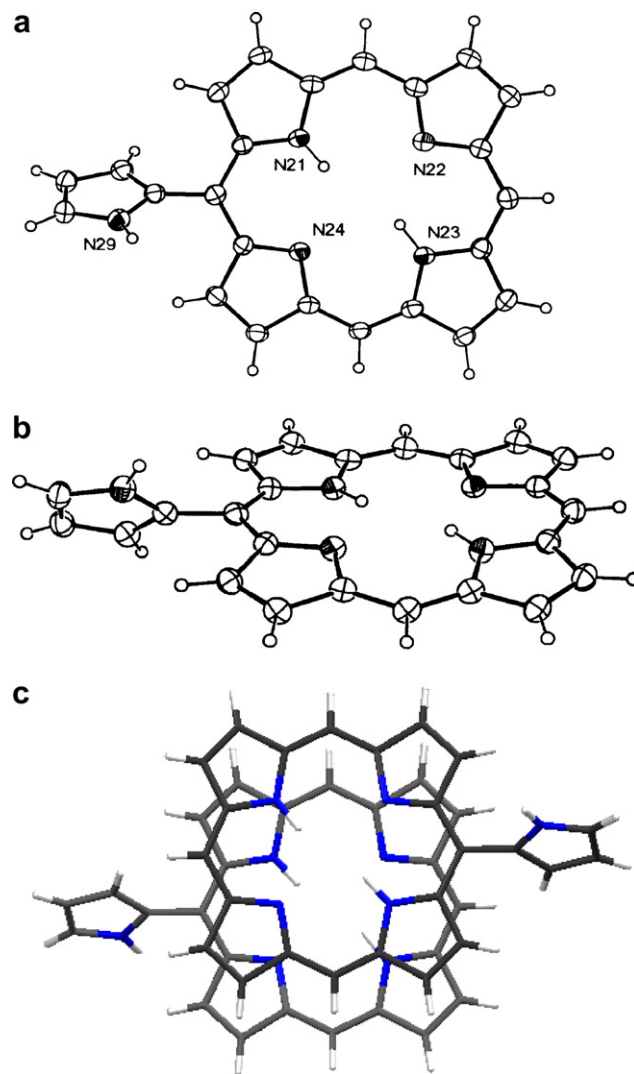


Figure 3. Structure of the pyrrole-substituted porphine **6**: two different views of the molecular structure are shown in (a) and (b) and the overlap within the π – π interacting pair of the substituted porphyrin molecules is shown in (c).

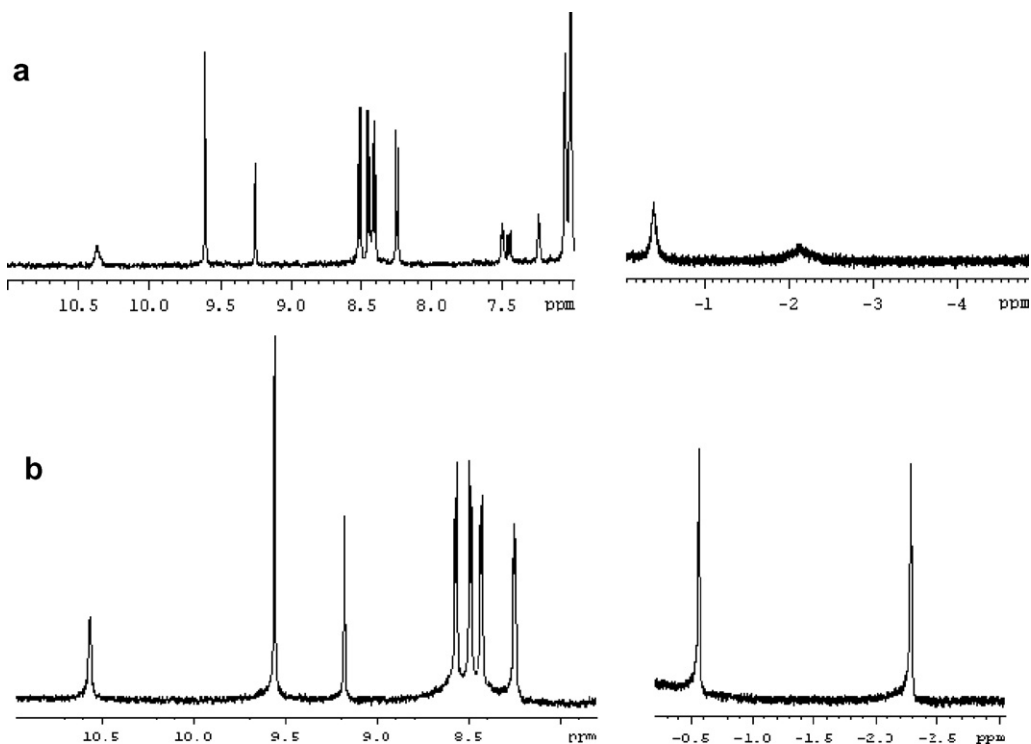
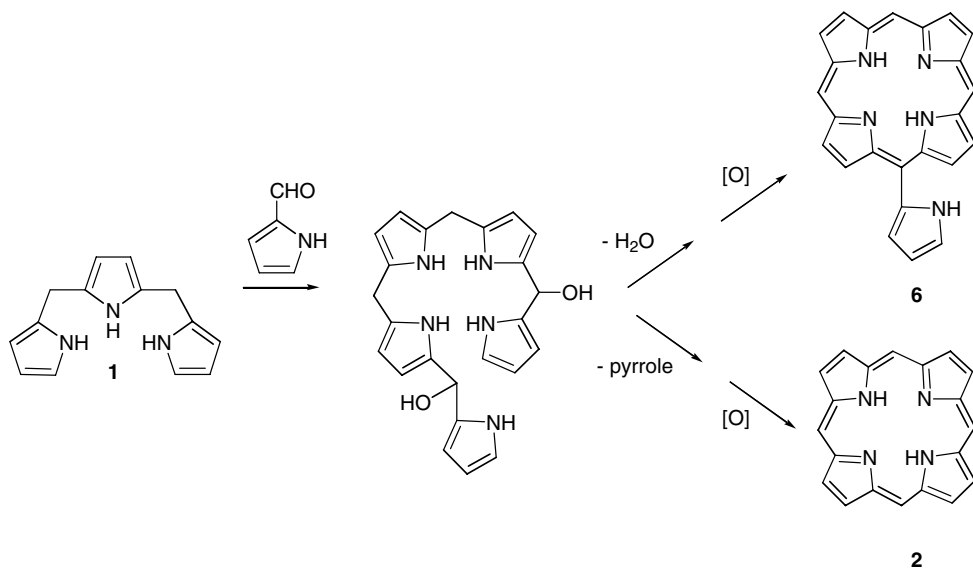


Figure 4. 500 MHz ^1H NMR spectra (toluene- d_6) of TFA-protonated **6** at rt (a) and at 253 K (b).

spectrum, regarding the C_{2v} symmetry and porphyrin-characteristic J -coupling constants and NH chemical shifts. Signals that were ignored in the initial analysis as belonging to non-important impurities are actually due to the *meso*-pyrrole substituent: three CH resonances at 7.4, 6.9, and 6.8 ppm and the broad NH signal at 8.0 ppm. This assignment was confirmed by recording the spectrum of protonated **6** (Fig. 4): in addition to the changes in chemical shifts and better resolution of all the CH protons, the NH proton of the pyrrole substituent shifted to 10.5 ppm. The total number of inner NH protons increased to four upon protonation and the

N–H correlation spectrum revealed that the signals at -0.3 and -2.1 ppm correspond to protons bound to magnetically different N atoms.

A reasonable mechanism that accounts for the production of both **2** and **6** from the reaction between **1** and **4** is shown in Scheme 3. The reaction apparently does not stop at the tetrapyrane stage (see Scheme 1), but rather continues by another condensation to the pentapyrane. This intermediate closes to an all *meso*-C bridged tetrapyrrolic macrocycle by expelling either water or pyrrole en route to compounds **6** and **2**, respec-



Scheme 3.

tively. The former option also exists when the condensation of **1** is performed with **3**, and accordingly, this could be the apparent source of compound **2** in that reaction.

In summary, the condensation of tripyrrane and 2-formylpyrrole did not lead to the desired parent corrole, the effective synthesis of which remains a considerable challenge, but rather to a mixture containing porphine and a new porphyrin substituted at one of its *meso*-carbon atoms by pyrrole. Both products were fully characterized by NMR spectroscopic methods and X-ray crystallography. The formation of pentapyrranes and their cyclization to substituted tetrapyrrolic rather than pentapyrrolic macrocycles appears to be quite general. Recent examples include the dipyrrole-substituted chlorins isolated by Gryko,¹⁵ Lee,¹⁶ and Callot¹⁷ and pyrrole-substituted porphyrins were also obtained by Maravin et al. from linear hexapyrrolic compounds.¹⁸ The isolation of the pyrrole-substituted porphyrin **6** from a synthesis devised for rational synthesis of corrole also possesses a historical perspective,¹⁹ as a similar structure was considered by Woodward and co-workers for the compound obtained during their attempted synthesis of corroles. This compound was later identified as being the first isolated member of the sapphyrin family,²⁰ which are nowadays best known for their anion binding capabilities.²¹

Crystallographic data of the structural analyses have been deposited with the Cambridge Crystallographic Data Centre, CCDC nos. 609953 and 609954 for **2** and **6**, respectively. Copies of this information can be obtained free of charge from The Director, CCDC, 12 Union Road, Cambridge, CB2 1EZ, UK (fax: +44 1223 336033; e-mail: deposit@ccdc.cam.ac.uk or web: <http://www.ccdc.cam.ac.uk>).

Acknowledgements

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 - Crystal data for 5-(pyrrole-2'-yl)-porphine (6) at 110(2) K*. C₂₄H₁₇N₅; *M_w* = 375.43, *a* = 7.7315(3), *b* = 11.3844(5), *c* = 11.4494(5) Å, α = 65.034(2)°, β = 76.394(3)°, γ = 76.414(2)°, *V* = 877.37(6) Å³, triclinic, space group *P-1*,

- $Z = 2$, $D_{\text{calc}} = 1.421 \text{ g cm}^{-3}$, $\mu(\text{Mo K}\alpha) = 0.09 \text{ mm}^{-1}$, 3912 unique reflections, $R = 0.056$ ($wR = 0.133$) for 2723 reflections with $F_o > 2\sigma(F_o)$, $R = 0.086$ ($wR = 0.153$) for all unique data.
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