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Synthesis and Characterization of Phenyl/4-Pyridyl *meso* Substituted Porphyrins

ABDULLAH SHAMIM, P. WORTHINGTON AND PETER HAMBRIGHT

Department of Chemistry, Howard University Washington, DC 20059 USA

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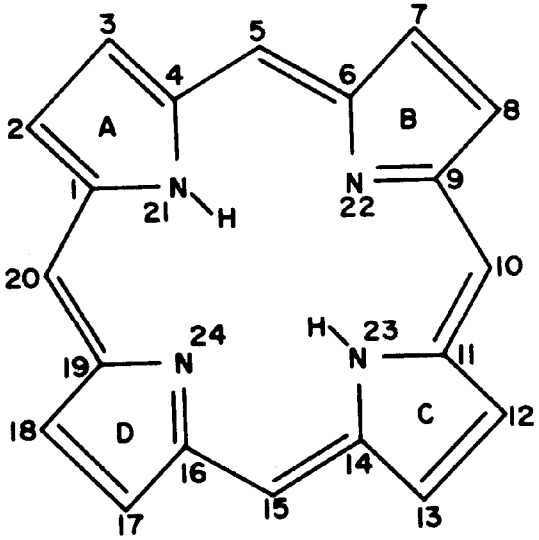
Summary: The complete series of the six phenyl/4-pyridyl *meso* substituted porphyrins were synthesized and characterized by analysis. The PMR spectra were consistent with the assigned structural representations. The new compounds, and others that can be made by similar procedures, will be useful both for kinetic and energy related surfactant studies.

Introduction

Porphyrins, which form the central core of many biologically important molecules, are highly conjugated macrocyclic pigments. Fig. 1 shows a typical representation of a porphyrin, where the positions numbered 2,3,7,8,12,13,17 and 18 are called the beta-pyrrole positions, while the 5, 10, 15 and 20 are termed the *meso* positions. Fisher's synthesis of prophin (all positions are hydrogens)[1], and Rothemund's synthesis[2] of 5,10,15,20-tetra (phenyl) prophyrin, H_2-TPP, (improved upon by Adler[3]) gave an impetus to research in porphyrin chemistry, which was hitherto limited to naturally occuring porphyrins and their derivatives. Fleisher[4] reported the synthesis of 5, 10, 15, 20-tetra (4-pyridyl) porphyrin, H_2-TPy (4)P, which was found to be water soluble below pH 2. Hambright[5] synthesized the 5, 10, 15, 20-tetra (N-methyl-4-pyridyl) porphyrin. H_2-TMTPy (4)P, which was found to be water soluble over the full pH range, as were the 3 and 2-N-methylated pyridyl prophyrin isomers[5]. These and other synthetic water soluble porphyrins have accelerated research in prophyrin chemistry, as such readily available compounds are found to mimic the features and properties of naturally occuring porphyrins.



(Numbering system of porphyrin molecules)

Most *meso* substituted porphyrins, synthesized by the condensation of an aldehyde and pyrrole[3] in acetic or propionic acid are symmetrically substituted in the sense that all of the four *meso* positions are occupied by the same substituent. Only two reports are found in the literature[6,7] where asymmetrical *meso* substituted prophyrins were synthesized. We report the synthesis and characterization of the complete set of the phenyl/4-pyridyl *meso* substituted porphyrins by a mixed-aldehyde procedure[6].

Experimental

Benzaldehyde (17 ml, 0.13 mole) and 47ml (0.48 mole) of 4-pyridinecarboxaldehyde were slowly added to 47ml (0.74 mole) of pyrrole refluxing in 1.7 liters of propionic acid. The heating was discontinued after thirty minutes, and the solution was allowed to cool. One liter of methanol was slowly added, whereupon the prophyrin precipitated. After filtration, the solid was dissolved in a minimum quantity of chloroform, and chromatographed on a dry alumnia column with chloroform as the elutant. The porphyrin fractions were collected, and recrystallized with hot methanol.

The recrystallized porphyrin mixture was again dissolved in a minimum amount of chloroform, and spotted on silica gel plates (Whatman PK 5, 1000μ thickness), and eluted with a 97.5% chloroform/2.5% methanol mixture. Six well separated bands were found. These fractions were removed from the plates with chloroform, and recrystallized with hot methanol. The fastest moving fraction, Fraction 1, R_f=0.97, was H_2-TPP, while the slowest band, Fraction 6, R_f=0.60, was identified as H_2-TPy(4)P. Since both compounds were well known[3,4], we focused our attention on the intermediate fractions 2 to 5.

The elemental analysis of the compounds were done by Schwarzkopf Microanalytical Labs (Woodside, NY). R_f values were determined in 97.5% $CHCl_3$/2.5% MeOH. The extinction coefficients in pyridine were measured on a Beckman Acta-III recording spectrophotometer. The ^{1}H NMR were run in deuterochlorform, with TMS as an internal standard, using a high resolution 200mHz Nicolet FT 200 spectrometer. The chemical shifts are reported in ppm.

Results

5-(4-pyridyl), 10, 15, 20-tri (phenyl) porphyrin. Fraction 2, R_f=0.94. Analysis: ($C_{43}H_{29}N_5$.½H_2O): Calc. C,82.7; H, 4.8; N,11.2;, Found C, 82.3; H,4.8; N,11.2. Extinction coefficients (Log ϵ, λ nm), (5.66, 419 nm), (4.27,514 nm), (3.87, 548 nm), (3.72,588 nm), (3.56,644 nm). NMR. 9.03 (*d*,2H,3,5 pyridyl protons); 8.21 (*m*,8H,2,6 pyridyl and o-phenyl protons); 8.40 (*d*,2H, beta pyrrole protons); 8.30 (*s*,4H, beta pyrrole protons); 8.20 (*d*,2H, beta pyrrole pro-) tons); 7.76, (*m*, 9H, m and p-phenyl protons).

Trans *5,15-di (phenyl), 10,20-di (4-pyridyl) prophyrin:* Fraction 3, R_f=0.86 ($C_{42}H_{28}N_6$); Calc, C,81.7: H,4.5: N,13.6. Found C,81.2; H,4.7; N,13.5%. Extinction coefficients, (5.62, 418 nm), (4.27, 512 nm), (3.91,547 nm), (3.72,588 nm), (3.47, 644 nm).

NMR. 9.039 (*d d*, 4H,3,5 pyridyl protons), 8.12 (*m*,8H,2,6 pyridyl and o-phenyl protons); 8.87 (*d*, 4H, beta pyrrole protons), 8.77 (*d*, 4H, beta pyrrole protons) 7.73 (*m*, 6H, m and p-phenyl protons).

cis *5,10-di (phenyl), 15,20-di (4-pyridyl) porphyrin:* Fraction 4, R_f=0.75 ($C_{42}H_{28}N_6$.½H_2O), Calc. C,80.6; H,4.6; N,13.4. Found C, 80.5; H,4.6; N,13.2% Extinction coefficients, (5.62,418 nm), (4.22,513 nm), (3.77, 548 nm), (3.67, 588 nm), 3.40,644 nm).

NMR. 9.042 (*dd*, 4H,3,5 pyridyl protons), 8.16 (*m*, 8H,2,6 pyridyl and o-phenyl protons), 7.77 (m, 6H,m and p-phenyl protons), 8.85 (sextet, 8H, beta pyrrole protons).

5-(phenyl), 10,15,20-tri (4-pyridyl) porphyrin: Fraction 5, R_f=0.66 ($C_{41}H_{27}N_7$.2.5 $H_2$0) Calc C,74.3; H, 4.8; N,14.7. Found, C,74.5; H,4.4, N,15.0) Extinction coefficients, (5.60,418 nm), (4.26,512 nm), 3.79, 546 nm), (3.74,582 nm), (3.43,643 nm).

NMR. 9.056 (*d*,6H,3,5 pyridyl protons), 8.166 (*m*,8H,2,6 pyridyl and o-phenyl protons), 7.78 (*m*, 3H, m and p-phenyl protons), 8.92 (*d*,2H, beta pyrrole protons), 8.85 (*s*, 4H, beta pyrrole protons), 8.82 (*d*,2H, beta pyrrole protons).

Discussion

As far as we know, this is the first time that a complete series of *meso* substituted asymmetrical prophyrins has been synthesized, The R_f values, as expected, varied with the number of pyridyl groups present: the greater the number of polar pyridyl groups, the less the R_f. The more symmetrical *trans* isomer moved faster than the *cis* form. In this series of compounds, the chemical shifts of the porphyrin protons were in the same ranges as found for H_2-TPy(4)P[8] and H_2-TPP[9]. The simultaneous presence of both phenyl and 4-pyridyl groups in the asymmetric porphyrins lead to characteristic splitting of the beta pyrrole protons, leading to the unambiguous assignment of structure.

All of our porphyrins were more soluble in pyridine than in other common solvents (C_6H_6,CH_3Cl, DMF,...), and thus pyridine was used for the extinction coefficient determinations. The solubility of these compounds decreases with an increase in the number of pyridly groups. For all of the compounds, the four banded Etio-type visible spectra and the Soret bands occur at about the same wavelengths, and all have similar extinction coefficients. H_2-TPP and H_2-TPy(4)P show similar spectral features[8].

The chloride, nitrate and tosylate (but not the iodide or perchlorates) salts of the tetrapositively charged H_2-TMTPy(4)P porphyrin are fully water soluble. We find that only the tripositive 5-(phenyl),

10,15,20-tri-(N-methyl-4-pyridyl) porphyrine is water soluble, and much less so than the tetra-N-methylated derivative. The porphyrins containing two or one positive charges due to N-methylation are insoluble above pH 1, in both their free base and copper complexed forms. The electrochemical reduction potentials of these asymmetric porphyrins, both in the methylated and unmethylated forms have been reported elsewhere[10,11] Kinetic and equilibrium studies have also been done on these and other water soluble porphyrins[10,12]

Calvin and co-workers[13] have recently synthesized surfactant porphyrins for energy studies by partially or fully alkylating H_2-TPy(4)P using various mole ratios of n-bromohexadecane. The low yields, and tedious purification and separation steps make their procedure difficult to apply. With our series of asymmetrical porphyrins, containing one to four pyridyl groups, one can selectively synthesize such surfactant porphyrins containing one to four long chain fragments, and the forementioned problems are avoided. Our mixed porphyrin procedure works well for many other substituted phenyl/pyridyl porphyrins types, and promises to furnish porphyrins with subtle structural and reactivity variations.

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