Pyriporphyrinone: A New 18-π Aromatic Porphyrinoid

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Dedicated to Professor Ernst Bayer, Tübingen, on the occasion of his 70th birthday

A pyriporphyrinone was synthesized by cyclocondensation of tripyrrane 2 with 2,6-diformyl-3-hydroxyxypyridine (1b). It was possible to identify 3b as the exclusively formed tautomer.

Because of many applications of porphyrins in medicine, as a catalyst, ligand and a chromophore,1 the search of new structural variants of porphyrins is reasonable. In recent years a number of porphyrin analogs, including compounds such as the isoporphyrins, heteroporphyrins, expanded porphyrins and vinylogous porphyrins2 have been synthesized.

Furuta et al.3 reported a porphyrin isomer containing an inverted pyrrole ring. A general concept for the preparation of new 18-π aromatic porphyrinoids with one pyrrole ring replaced by another carbo- or heterocyclic ring involves the condensation of a tripyrrane4 2 (Scheme) with a 1,3-dialdehyde. Subsequent oxidation affords the 18-π aromatic porphyrinoid, which displays the ring current, detected by a shielding of the inner (NH) protons and a deshielding of the peripheral meso protons in the 1H NMR spectrum. Following this concept, we synthesized carbaporphyrinoids by condensation of tripyrannes with cycloheptatriene-1,6-dicarboxaldehyde and azulene-1,3-dicarboxaldehyde.5 In the case of the azulene-1,3-dicarboxaldehyde, the new carbaporphyrinoid contained an indene unit instead of the expected azulene structure. The inner protons of the analogous porphyrin were observed at about δ = −7.0 to −8.5 and the meso protons ranged from δ = 9 to 11. Substitution of one pyrrole unit in the porphyrin ring by pyridine6 provided a pyriporphyrinogen which, upon oxidation, was converted into a dimer and an oxophenolin instead of the desired 18-π aromatic system. The corresponding cyclization with isophthalaldehyde also yielded the benzoid 6-π aromatic system.7 In both cases the aromaticity of the six-membered rings was not sacrificed in favor of the [18]annulenes. Recently, Lash8 reported the condensation of the 5-formylsalicylaldehyde (1a) (Scheme) with tripyrrane 2 to an oxybenzoporphyrin 3a 4a. This macrocycle indeed displayed the ring current in the NMR spectrum and an equilibrium between the two possible tautomers 3a and 4a was supposed because only one broad signal was observed for the two nonequivalent inner NH protons in the 1H NMR spectrum.

Obviously, oxidation of the phenolic OH function to the quinoid system promotes formation of the [18]annulene. Following this idea, tautomers 3b and 4b of a pyriporphyrinone should be obtainable by cyclization of 2,6-diformyl-3-hydroxyxypyridine (1b) with a tripyrrane 2. Our attempts to reproduce the only synthesis of 1b as an intermediate (without any documentation of spectroscopic and other physical data) reported in the literature9,10 via oxidation of the 2,6-bis(hydroxymethyl)-3-hydroxyxypyridine with manganese dioxide over seven days were not successful. We found selenium dioxide to be an appropriate oxidant within reasonable reaction time and the dialdehyde was isolated in moderate yield with matching NMR data.

The condensation of 2,6-diformyl-3-hydroxyxypyridine (1b) with tripyrrane-dicarboxylic acid, which is directly used after its preparation by hydrogenation of the corresponding dibenzyl ester and subsequent decarboxylation with trifluoroacetic acid, proceeds in dichloromethane at room temperature. After four hours the condensation of the reagents is complete, as monitored by thin layer chromatography. The reaction mixture is then neutralized with triethylamine and oxidized by 2,3-dichloro-5,6-dicyano-1,4-benzoquinone (DDQ). Upon column chromatography small dark violet crystals are isolated which give green solutions in methanol, ethanol and chloroform and were identified as the desired macrocycle by the correct high-resolved molecular mass and via NMR spectroscopy (complete assignment is given in the Figure). Because of the unsymmetric structure of the tautomers 3b and 4b, each carbon and proton of the...
molecule should display an individual signal in the \(^1\)H NMR and \(^{13}\)C NMR spectra. Indeed, six \(\text{CH}_2\) groups, four \(\text{CH}\), and fifteen quaternary carbon atoms can be detected by \(^{13}\)C NMR including DEPT experiments for multiplicity analysis; only two carbons overlap in one signal. Moreover, the interaction of the NH and CH protons as shown by the \(^2\)J\(_{\text{CH}}\) and \(^3\)J\(_{\text{CH}}\) couplings obtained from the gradient supported HMBC inverse CH correlation experiment (Figure) clarified that tautomer 3b had been formed exclusively. To the best of our knowledge this is the first precise identification of one porphyrin tautomer with two separated NH proton signals detectable at 500 MHz.

2.6-Diformyl-3-hydroxypyridine (1b): Bis(hydroxymethyl)-3-hydroxypyridine (4 g, 25.8 mol) was suspended in dioxane (150 mL) and made to dissolve by stirring and refluxing for 1 h. \(\text{Se}_2\) (5.73 g, 51.6 mmol) was added and the refluxing was continued for 20 h. The mixture was cooled to r.t., filtered, and the filtrate was evaporated to dryness. The crude dialdehyde 1b was chromatographed on silica gel [eluent: EtOAc/petroleum ether (bp 40–60°C) 1:1]; yield: 1.44 g, 9.3 mmol (36%), light yellow solid; mp 125°C.

HRMS: \(m/z = 155.083\) (calc. for \(\text{C}_9\text{H}_8\text{NO}_2\): 155.082).

\(^1\)H NMR (DMSO-\(d_6\)): \(\delta = 3.39\) (br, 1H, OH), 7.62 (d, 1H, \(J = 8.6\) Hz, 4-H), 8.06 (d, 1H, \(J = 8.6\) Hz, 5-H), 9.90 (s, 1H, 6-CHO), 10.22 (s, 1H, 2-CHO).

\(^{13}\)C NMR (DMSO-\(d_6\)): \(\delta = 127.06\) (C-4), 127.48 (C-5), 139.90 (C-2), 144.98 (C-6), 160.33 (C-3), 191.42 (CHO), 191.70 (CHO).

Pyriporphyrinone (3b): Tripyranedicarboxylic dibenz ester (1.27 g, 2.2 mmol) was dissolved in THF (150 mL) and charged with 10% Pd/C (400 mg) and Et\(_2\)N (0.2 mL). The well stirred suspension was hydrogenated at atmospheric pressure for 4 h. The catalyst was removed by filtration and washed with a small amount of THF. The solution was evaporated to dryness and the residue was stirred for 10 min with CF\(_3\)CO\(_2\)H (4 mL) under \(N_2\). To this solution 1b (0.31 g, 2 mmol) in \(\text{CH}_2\text{Cl}_2\) (80 mL) was added. The mixture was stirred under \(N_2\) for 4 h, then neutralized with Et\(_2\)N and oxidized with DDO (460 mg). After washing with H\(_2\)O, the solvent was evaporated and the residue first purified by column chromatography on silica gel (eluent: CH\(_2\)Cl\(_2\)/MeOH 20:1) and then with Sephadex LH 20 (same eluent); yield: 0.22 g (23% after chromatography); dark violet solid; mp >240°C (Lit.\(^{13}\) mp >300°C).

HRMS: \(m/z = 478.2728\) (calc. for \(\text{C}_{26}\text{H}_{16}\text{N}_{10}\text{O}_2\): 478.2733).

UV/vis (EtOH): \(\lambda_{\text{max}}\) (log e) = 331.0 (3.48), 395.0 (3.88), 418.0 (4.29), 437.0 (4.02), 548.0 (3.06), 587.0 (3.50), 601.0 (3.39), 609.0 nm (3.41).

IR (KBr): \(v = 3363.4 \, \text{cm}^{-1}\) (v\(_{\text{CO}}\)), 2963.1 \, \text{cm}^{-1}\) (v\(_{\text{CH}}\)), 2929.4 \, \text{cm}^{-1}\) (v\(_{\text{CH}}\)), 2867.7 \, \text{cm}^{-1}\) (v\(_{\text{CH}}\)), 1626.6 \, \text{cm}^{-1}\) (v\(_{\text{CO}}\)), 1449.0 \, \text{cm}^{-1}\) (v\(_{\text{CO}}\)).


\(\delta\)C: boldface; \(\delta\)H: italic

**Figure. NMR Data for 3b**

Proton shifts of the inner NH protons (\(\delta = -4.89\) and \(-5.07\)) and the four outer meso protons (\(\delta = 8.5\) to 10.54) clearly reflect the 18-\(\pi\) aromaticity of the pyriporphyrinone 3b in favor of which the 6-\(\pi\) aromaticity of the 3-hydroxopyrpyidine was sacrificed. The cone partial structure within the pyridine ring is also detectable in the IR spectrum (\(\nu_{\text{C}=\text{O}} = 1628 \, \text{cm}^{-1}\)) and the protons (\(\delta = 7.73\) and 8.68, doublets with \(J = 9.2\) Hz) of the double bond polarized by the electron withdrawing carbonyl function. Additionally, the UV/vis spectra are similar to those of porphyrins, including a strong Soret type absorption\(^{13}\) at \(\lambda = 418\) nm.

Melting points (uncorrected): SMP-20 (Büchi); UV/vis spectra: DU660 (Beckmann); IR spectra: Perkin-Elmer 1600; NMR spectra: Bruker DRX-500 (\(\text{H} = 500\) MHz; \(^{13}\)C: 125 MHz); HRMS (EI): MS 50 (A. E. I. Manchester).

THF was dried (Na\(_2\)SO\(_4\)) and distilled before use. \(\text{CH}_2\text{Cl}_2\) was dried (CaCl\(_2\)), distilled and stored over molecular sieves (4 Å). Et\(_2\)N (Riedel de\'Haën) was used as received. Pd/C was obtained from Merck (10\%, oxidic form).
(4) To simplify matters the trivial name tripyrane is used here instead of 2,5-bis[pyrrol-2-yl]methyl]pyrrole.
(9) Baldo, M. A.; Chessa, G.; Marangoni, G.; Pitteri, B. Synthesis 1987, 720.
(10) Result of searching in BEILSTEIN online [COPYRIGHT (C) 1995 Beilstein Informationsysteme GmbH] on 10 July 1996 and searching in REGISTRY online [COPYRIGHT (C) 1995 American Chemical Society (ACS)] on 04 December 1995.
(12) During the evaluation of this paper by the referees, the synthesis of the pyriporphyrinones 3 was published independently: Lash, T. D.; Chaney, S. T. Chem. Eur. J. 1996, 2, 944.
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