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Conjugated Macrocycles Related to the Porphyrins. Part 7.[1] Tropiporphyrin: Tropylium versus Porphyrinoid Aromaticity

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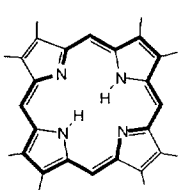
Abstract: *Acid catalyzed "3 + 1" condensation of 1,6-cycloheptatrienedicarboxaldehyde with a tripyrrane dicarboxylic acid, followed by neutralization with triethylamine and oxidation with DDQ, afforded the cycloheptatrienyl porphyrin analog "tropiporphyrin" in good yields; this system favors porphyrin-like 18π delocalization pathways for both the free base and the related monocation.* Copyright © 1996 Elsevier Science Ltd

Porphyrins (**1**) are in many respects the [18]annulenes of nature, possessing 18π electron delocalization pathways that contribute to the remarkable stability of these structures.[2] Although the [18]annulene model for porphyrins is an oversimplification, it nevertheless provides a useful conceptual framework and can be applied to many related systems, including porphyrin isomers[3] and expanded porphyrins.[4] Even though the porphyrin system is built up from four pyrrole subunits, the aromatic nature of these 6π electron building blocks is eclipsed by highly favored macrocyclic delocalization pathways. The replacement of one or more pyrrole unit with furan,[5,6] thiophene,[5,7,8] sellenophene[7,9] or tellurophene[10] affords analogous structures that retain macrocyclic aromaticity; on the other hand, insertion of a six-membered aromatic ring such as benzene or pyridine (structures **2a** and **3a**) disrupts overall π-delocalization.[11] In principle the arene or azine unit could tautomerize and thereby allow access to porphyrinoid aromaticity, but this would only be possible at the expense of loosing the resonance stabilization energy for the original subunit. Perhaps not too surprisingly, particularly in the case of benziporphyrin, the cost is too great and no macrocyclic ring current can be observed by proton NMR spectroscopy.[11b] However, the introduction of a hydroxyl moiety (structures **2b** and **3b**) allows a favorable "keto-enol" tautomerization to occur to give the fully aromatic macrocycles oxybenziporphyrin (**4**)[12] and oxypyriporphyrin (**5**).[1] These structures represent the first examples of porphyrin-like systems with benzene or pyridine subunits, and open the door to the construction of many new porphyrin/bridged annulene hybrid structures.



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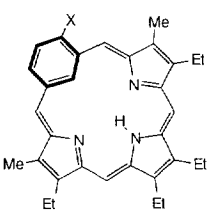
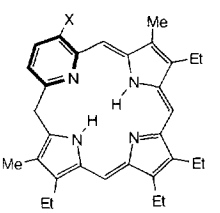
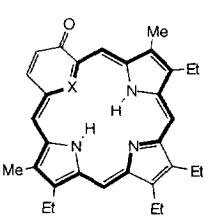


2 "Benziporphyrin"



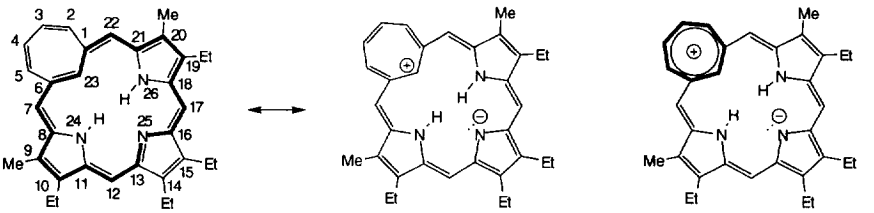
3 "Dihydropyriporphyrin"

a. X = H; b. X = OH



4 X = CH (Oxybenziporphyrin)
5 X = N (Oxypyriporphyrin)

Figure 1: Dipolar tropiporphyrin canonical forms have the potential for significant tropylium cation character.

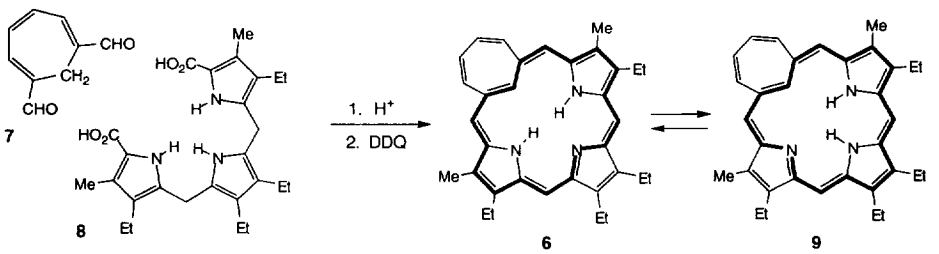


6a **6b** **6c**

These studies have now been extended to the synthesis of the cycloheptatrienyl porphyrin analog "tropiporphyrin" (**6**; Fig. 1). Although this proposed new porphyrinoid can potentially possess 18π electron delocalization pathways (structure **6a**), it is also possible to envision dipolar resonance contributors such as **6b** that could imbue the system with significant tropylium cation character (**6c**). Hence, at one extreme a porphyrin-like structure might be anticipated, while at the other a highly polarized system devoid of macrocyclic aromaticity could be imagined. Hence, it was clear that the spectroscopic and chemical properties of tropiporphyrin would provide valuable insights into the nature of porphyrinoid aromaticity.

The acid catalyzed condensation of tripyrranes with monocyclic dialdehydes (the "3 + 1" methodology[5]) has recently been shown to be a versatile route to porphyrinoid systems.[13] Condensation of 1,6-cycloheptatriene-dicarboxaldehyde **7**[14] with tripyrrane **8**[15] in the presence of trifluoroacetic acid in dichloromethane, followed by neutralization with triethylamine and dehydrogenation with DDQ, gave the desire macrocycle **6** (Scheme 1). Initially, poor and somewhat variable yields were obtained, and extensive decomposition occurred during workup. However, by using dilute reaction conditions and avoiding temperatures above 30°C, tropiporphyrin could be isolated as a dark microcrystalline solid in 23% yield.[16] This novel system gave deep orange-red solutions in dichloromethane and was reasonably stable in purified form.

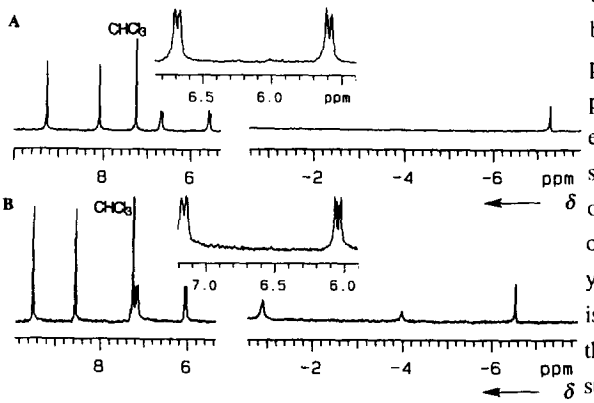
Scheme 1: "3 + 1" Synthesis of Tropiporphyrin.



7 **8** **6** **9**

The proton NMR spectrum of **6** in deuteriochloroform showed the presence of two distinct species, although it quickly became clear that one of these arose from monoprotonation. When the proton NMR spectrum was run in the presence of trace amounts of triethylamine (Fig. 2a), the data were consistent with a single structure corresponding to the anticipated macrocycle **6**. It should be noted that other tautomers such as **9** are possible, but these must interconvert rapidly with **6** at room temperature if they are present at all. Proton NMR spectroscopy provides overwhelming evidence for porphyrinoid aromaticity; the four *meso*-bridging protons appeared downfield as two 2H singlets at 8.1 and 9.3 ppm, while the internal CH was strongly deshielded producing a

Figure 2: Partial 300 MHz proton NMR spectra of tropiporphyrin: A. in $CDCl_3$-trace Et_3N (free base); B. in $CDCl_3$-trace TFA (monocation).



singlet at -7.3 ppm. The latter resonance is substantially further upfield than the signals corresponding to the inner protons of [18]annulene, although oxybenziporphyrin also shows a resonance near -7.2 ppm. On the face of it, this result suggests that tropiporphyrin has a stronger ring current than [18]annulene, although this is not entirely consistent with the smaller downfield shifts observed for the *meso*-protons. It is clear, however, that tropiporphyrin has little or no tropylium character and strongly favors porphyrinoid aromaticity. Carbon-13 NMR spectroscopy is fully consistent with structure **6**, and confirms that there is a plane of symmetry present in the 33 carbon structure (only 17 carbon resonances are observed, in accord with our expectations).

In the presence of trace amounts of trifluoroacetic acid, the bright green monocation was generated. The proton NMR spectrum (Fig. 2b) was entirely consistent with structure **10** (Fig. 3), where the positive charge can be delocalized over the whole ring system (**10a-c**). The slight downfield shift of both the internal and external CH's was consistent with the presence of a positive charge, and this species clearly retains a large diatropic ring current. The internal NH protons were observed at -0.89 (2H) and -3.98 (1H), although the NH's for the free base **6** were not observable (Fig. 2). These conditions might have promoted the formation of the tropylium species **11**, but our data indicates that this possibility cannot successfully compete with the porphyrinoid π-delocalization in **10**.

Figure 3: The tropiporphyrin cation also favors porphyrinoid aromaticity.

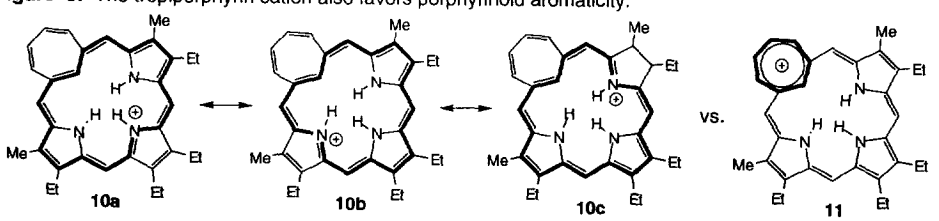
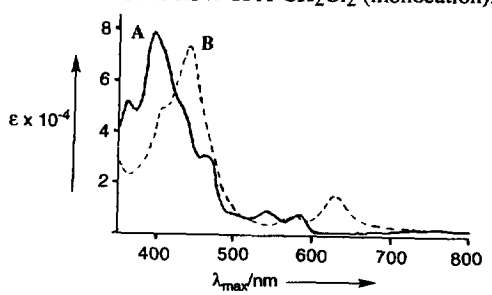


Figure 4: Electronic spectra of tropiporphyrin: A. in 1% Et_3N-CH_2Cl_2 (free base); B. in 0.5% TFA-CH_2Cl_2 (monocation).



The uv-vis spectrum for tropiporphyrin in dichloromethane showed a Soret band at 394 nm, together with several smaller "Q bands" in the visible region (Fig. 4a). The molar absorptivity for the Soret absorption was approximately 78,000, and this relatively low value was consistent with diminished aromaticity for this structure. In 0.5% TFA-CH_2Cl_2, a very different electronic spectrum was obtained (Fig. 4b), although the presence of a moderately strong absorption at 442 nm confirmed that the monocation **10** has a porphyrin-like electronic structure.

Part way through our investigations, an independent report on the synthesis of macrocycle **6** appeared in the literature.[17] The yield obtained for **6** in this case was very low (1 equiv. of DDQ failed to give any tropiporphyrin, dihydro species being isolated instead, and an excess of oxidant was needed to obtain a 0.4% yield of **6**), and some of the data reported contradicted our observations. The German group noted that **6** gave yellow-green solutions in dichloromethane, while our samples produced orange-red solutions, and these authors also noted a peak at 644 nm that was not evident in our spectroscopic investigations. The anomalies could be explained, in part, if these samples were contaminated with the corresponding monocation, although the low yields may have precluded complete purification of their samples. In any case, our methodology gives rise to a more than 50 fold increase in the yield of **6** and thus provides access to reasonable quantities of pure tropiporphyrin. This will allow the chemistry of this unusual porphyrinoid system to be explored in detail.

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REFERENCES AND NOTES

1. Part 6: Lash, T.D.; Chaney, S.T. *Chem. Eur. J.* **1996**, *2*, 944.
2. Crossley, M.J.; Harding, M.M.; Sternhell, S. *J. Am. Chem. Soc.* **1992**, *114*, 3266.
3. Vogel, E.; Kocher, M.; Schmickler, H.; Lex, J. *Angew. Chem. Int. Ed. Eng.* **1986**, *25*, 257; Sessler, J.L. *Angew. Chem. Int. Ed. Eng.* **1994**, *33*, 1348.
4. Sessler, J.L.; Burrell, A.K. *Top. Curr. Chem.* **1991**, *161*, 177-273. Franck, B.; Nonn, A. *Angew. Chem. Int. Ed. Eng.* **1995**, *34*, 1795.
5. Broadhurst, M.J.; Grigg, R.; Johnson, A.W. *J. Chem. Soc. (C)* **1971**, 3681.
6. Vogel, E.; Haas, W.; Knipp, B.; Lex, J.; Schmickler, H. *Angew. Chem. Int. Ed. Engl.* **1988**, *27*, 406; Lash, T.D. *J. Org. Chem.* **1992**, *57*, 4312.
7. Vogel, E.; Rohrig, P.; Sicken, M.; Knipp, B.; Herrmann, A.; Pohl, M.; Schmickler, H.; Lex, J. *Angew. Chem. Int. Ed. Engl.* **1989**, *28*, 1651.
8. Ulman, A.; Manassen, J. *J. Am. Chem. Soc.* **1975**, *97*, 6540; Ibid., *J. Chem. Soc. Perkin Trans. 1* **1979**, 1066
9. Ulman, A.; Manassen, J.; Frolow, F.; Rabinovich, D. *Tetrahedron Lett.* **1978**, 167.
10. Ulman, A.; Manassen, J.; Frolow, F.; Rabinovich, D. *Tetrahedron Lett.* **1978**, 1885; Latos-Grazynski, L.; Pacholska, E.; Chmielewski, P.J.; Olmstead, M.M.; Balch, A.L. *Angew. Chem. Int. Ed. Engl.* **1995**, *34*, 2252.
11. a. Berlin, K.; Breitmaier, E. *Angew. Chem. Int. Ed. Engl.* **1994**, *33*, 219; b. ibid. 1246.
12. Lash, T.D. *Angew. Chem. Int. Ed. Eng.* **1995**, *34*, 2533.
13. Lash, T.D. *Chem. Eur. J.* **1996**, in press.
14. Vogel, E.; Deger, H.M.; Sombroek, J.; Palm, J.; Wagner, A.; Lex, J. *Angew. Chem. Int. Ed. Engl.* **1980**, *19*, 41.
15. Sessler, J.L.; Johnson, M.R.; Lynch, V. *J. Org. Chem.* **1987**, *52*, 4394.
16. **Typical procedure**: Tripyrranedicarboxylic acid **8** (250 mg) was stirred with TFA (2.5 mL) under an atmosphere of nitrogen for 10 min. Dichloromethane (450 mL) was added, followed immediately by **7** (81 mg) and the mixture was stirred under nitrogen for a further 16 h. After neutralization by the dropwise addition of triethylamine, DDQ (130 mg) was added and the resulting solution was stirred in the dark for an additional 1 h. The mixture was washed with water, evaporated under reduced presssure (< 30°C) and chromatographed on Grade 3 alumina, eluting first with 1% Et_3N-dichloromethane. A reddish-green fraction was collected and rechromatographed on silica using 1% Et_3N-dichloromethane. The main red fraction was recrystallized from dichloromethane-hexane to give the tropiporphyrin (59 mg; 23%) as dark microcrystals, m.p. 248°C; UV/Vis (1% Et_3N-CH_2Cl_2): λ_{max} ($\log_{10}\varepsilon$) 360 (4.71), 394 (4.89), 464 (4.48), 498 (3.94), 542 (3.97), 584 (3.92), 740 nm (3.41); UV/Vis (0.5% TFA-$CHCl_3$; monocation): λ_{max} ($\log_{10}\varepsilon$) 404 (4.69), 442 (4.88), 574 (3.85), 624 (4.20), 754 nm (3.49); ^{1}H NMR (300 MHz, $CDCl_3$-trace Et_3N): δ -7.29 (1H, s, 23-H), 1.65-1.9 (12H, m, 4 x CH_2CH_3), 3.24 (6H, s, 2 x pyrrole-CH_3), 3.75 (6H, q, J = 7.8 Hz), 3.83 (6H, q, J = 7.8 Hz) (4 x CH_2CH_3), 5.58 (2H, m, 3,4-H), 6.69 (2H, d, J = 11.4 Hz, 2,5-H), 8.10 (2H, s), 9.27 (2H, s) (4 x *meso*-H); ^{1}H NMR (300 MHz, $CDCl_3$-trace TFA): δ -6.54 (1H, s, 23-H), - 3.98 (1H, br), -0.89 (2H, br) (3 x NH), 1.51 (6H, t, J = 7.8 Hz), 1.76 (6H, t, J = 7.8 Hz) (4 x CH_2CH_3), 3.16 (6H, s, 2 x pyrrole-CH_3), 3.80 (4H, q, J = 7.8 Hz), 3.89 (4H, q, J = 7.8 Hz) (4 x CH_2CH_3), 6.05 (2H, m, 2,3-H), 7.17 (2H, d, J = 11 Hz, 2,5-H), 8.56 (2H, s), 9.50 (2H, s) (4 x *meso*-H); ^{13}C NMR (75.46 MHz, $CDCl_3$-trace Et_3N): δ 11.45, 17.11, 18.40, 19.48, 19.68, 96.05, 104.88, 126.87, 130.77, 131.32, 133.39, 134.22, 137.02, 137.07, 142.38, 146.90, 150.47; ^{13}C NMR (75.46 MHz, $CDCl_3$-trace TFA): δ 11.69, 16.38, 17.61, 19.53, 19.85, 93.33, 109.01, 131.47, 133.36, 133.48, 135.79, 136.74, 138.17, 139.96, 140.40, 140.90, 146.06; HRMS (FAB): calculated for $C_{33}H_{37}N_3$ + H: m/z 476.30657; found: 476.3066.
17. Berlin, K.; Steinbeck, C.; Breitmaier, E. *Synthesis* **1996**, 336.

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