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Facile oxidation of a carbaporphyrin at the internal carbon atom: synthesis of novel benzo[18]annulene ketals†

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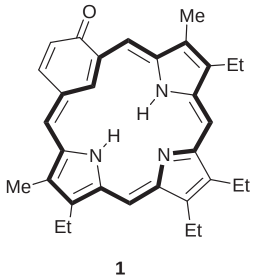
Treatment of benzocarbaporphyrin 2 with refluxing $FeCl_3$ in $CHCl_3$–alcohol mixtures leads to a remarkably selective oxidation at the interior carbon atom to produce dialkoxy products 5; these species show potentially valuable long wavelength absorptions in their UV–VIS spectra.

The unbounded potential for porphyrins and related macrocycles in novel technological[1] and medicinal applications[2] has lead to widespread interest in the synthesis of related systems such as expanded porphyrins[3] and porphyrin isomers.[4] The recent rediscovery of the '3 + 1' route for porphyrinoid synthesis[5] has allowed the preparation of novel aromatic species where a carbocyclic subunit replaces one of the pyrrolic moieties of the porphyrin macrocycle.[6–9] The first example of a 'carbaporphyrinoid',‡ oxybenzoporphyrin **1**, was first reported in 1995 and was obtained by the acid catalyzed condensation of a tripyrrane (2,5-bis[2-pyrrolylmethyl]pyrrole) with 4-hydroxyisophthalaldehyde.[6] Several related porphyrinoids were subsequently synthesized by the '3 + 1' approach.[7–9] Perhaps the most captivating of these new aromatic systems are the true carbaporphyrins[7,9] which incorporate a cyclopentadienyl unit instead of the usual pyrrole ring. Benzocarbaporphyrin **2** is particularly easy to synthesize by condensing a tripyrrane with 1,3-diformylindene[7] and thus provides a suitable 'work horse' molecule for further investigations.



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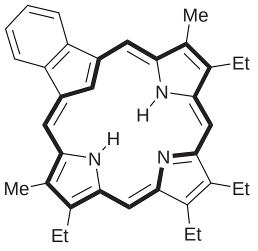
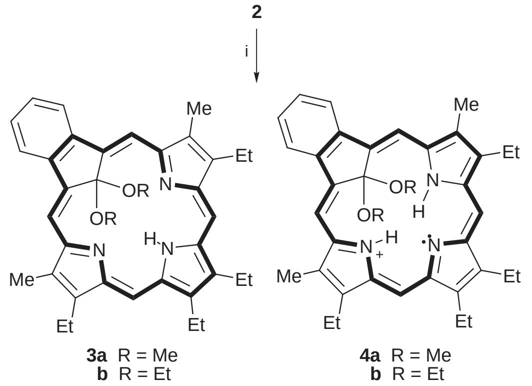


2

In our initial studies on the chemistry of **2**, the possibility of forming metal chelates was explored. However, attempts to isolate stable metal complexes by reacting **2** with various transition metal salts [$Zn(OAc)_2$, $Cu(OAc)_2$, $Ni(OAc)_2$, $FeCl_2$, $CrCl_3$, *etc.*] has so far been unsuccessful. On the other hand, when a solution of **2** in $CHCl_3$ was refluxed with saturated $FeCl_3$ in MeOH, the mixture rapidly turned from a deep brown to a bright green color and a polar green species could be isolated, following chromatography, in high yield.§ No reaction was observed in control experiments in the absence of $FeCl_3$. FAB MS gave an [M + H] ion at *m/z* 560 and confirmed that no Fe^{III} had been incorporated into the structure. The proton NMR spectrum for the green material (Fig. 1) showed an upfield 6H singlet at δ −1.32 while the *meso*-bridge protons were strongly deshielded appearing at δ 9.7 and 10.9. The data were consistent with a dimethyl ketal derivative **3** where the interior carbon atom has been regioselectively oxidized (Scheme 1). However, a closer examination of the ^1H NMR spectrum (Fig. 1) showed that a broad peak near δ 2.15 integrated for 2H and this was assigned to two strongly hydrogen bonded NHs, thereby implying that the isolated compound was in fact a monoprotonated species **4a**. Elemental analysis further confirmed that the isolated material corresponded to the monoHCl salt.§ Additional evidence for the ketal structure was provided by NOE difference proton NMR experiments, and it is particularly noteworthy that the internal NH resonance showed a strong NOE enhancement upon irradiation of the methoxy resonance at δ −1.32. The ^{13}C NMR spectrum for **4a** in $CDCl_3$ confirmed the symmetry of the macrocyclic structure, showing the 19 anticipated carbon resonances. DEPT demonstrated the presence of a quaternary carbon atom at δ 96.9, which is consistent with the presence of an allylic ketal moiety.



Scheme 1

We speculate that the regioselectivity for this chemistry may be due to the Fe^{III} being initially coordinated to the three pyrrolic nitrogens and thereby held in proximity to the inner carbon so that oxidation is directed towards this position. The aromaticity of this structure is maintained by reorganizing the 18π electron delocalization pathway through the fused benzene ring (pathway shown in bold) and in this respect **3a** can be

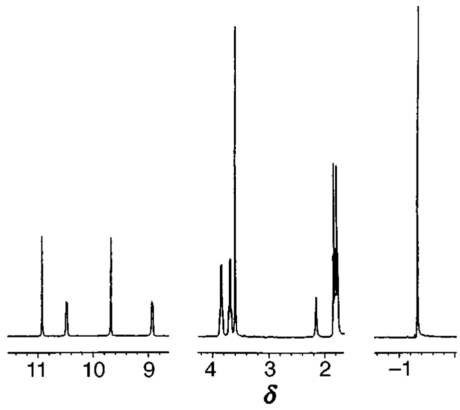


Fig. 1 400 MHz ^1H NMR spectrum of benzo[18]annulene **5a** in $CDCl_3$.

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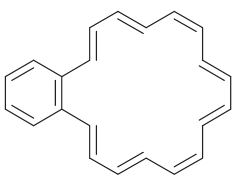
† Part 14 of the series 'Conjugated Macrocycles Related to the Porphyrins'. Part 13: T. D. Lash and D. T. Richter, *J. Am. Chem. Soc.*, 1998, **120**, 9965.

considered to be a benzo[18]annulene. Interestingly, benzo[18]annulene **5** has been shown[10] to have a much reduced diatropic ring current compared to [18]annulene itself (the difference in chemical shift between the inner and outer protons in **5** is <2 ppm), although this is clearly not the case for the porphyrinoid structure. Protonation is most likely highly favored due to the ability of the aromatic macrocycle to delocalize the positive charge and this factor may also explain the enhanced aromatic character of **4a** compared to benzo[18]annulene (**5**). The monocation was essentially uneffected by using [$^2H_5$]pyridine as a solvent, although addition of the stronger base Et_3N lead to decomposition possibly due to the instability of the free base **3a**. Reaction of carbaporphyrin **2** with $FeCl_3$ in refluxing EtOH–$CHCl_3$, although significantly slower than for MeOH, gave excellent yields of the diethoxy species **4b**.§



5

The UV–VIS spectra for **4a** and **4b** showed strong Soret bands near 423 nm, together with strong Q bands in the far red at 748 and 828 nm in the case of **4a** (Fig. 2). Addition of 5% TFA lead to the formation of a new species due to protonation of the remaining nitrogen where the longer wavelength bands underwent a hypsochromic shift (Fig. 2). Porphyrinoids with strong absorption bands in the far visible–near IR are of great current interest and have possible applications in the development of solid state optical devices[1] and as photosensitizers in photodynamic therapy.[2]

The discovery of a straightforward and highly selective method for derivatizing the inner carbon atom of the carbaporphyrin system has great potential for future studies and it should be possible to fine tune the physical properties of these novel chromophores by selecting other alcohols as reactants (*e.g.* long chain, dendritic). The versatility of this approach will also allow practical applications to be considered.

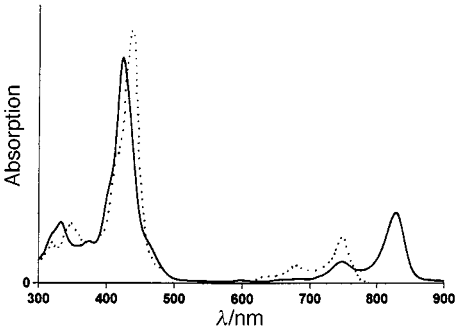


Fig. 2 Electronic absorption spectra of **5a** in $CHCl_3$ (bold line) and dication in 5% TFA–$CHCl_3$ (dotted line).

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Notes and references

‡ Carbaporphyrinoids are defined as fully aromatic systems where one or more of the pyrrolyl units of the porphyrin structure have been replaced by a carbocyclic ring.

§ *Selected data* for **5a**: mp 145–147 °C (decomp.); $\lambda_{max}(CHCl_3)$/nm ($\log_{10}\varepsilon$) 333 (4.55), 374 (4.40), 423 (5.12), 5.96 (3.28), 748 (4.10), 828 (4.61); λ_{max}(5% TFA–$CHCl_3$)/nm ($\log_{10}\varepsilon$) 323 (4.37), 348 (4.54), 435 (5.17), 682 (4.06), 748 (4.44); $\delta_H(CDCl_3)$ −1.32 (6H, s, 2 × OCH_3), 1.77 (6H, t), 1.82 (6H, t) (4 × CH_2CH_3), 2.15 (2H, br s, 2 × NH), 3.60 (6H, s, 2 × porphyrin-CH_3), 3.69 (4H, q), 3.84 (4H, q) (4 × porphyrin-CH_2), 8.93 (2H, m) and 10.48 (2H, m) (4 × benzo-H), 9.68 (2H, s) and 10.93 (2H, s) (4 × *meso*-H); $\delta_C(CDCl_3)$ 11.68, 17.29, 18.38, 19.50, 19.60, 47.95, 96.89, 107.37, 112.77, 124.62, 133.24, 135.28, 135.87, 138.63, 139.63, 143.82, 146.01, 147.08, 155.71; HRMS: calc. for $C_{37}H_{42}N_3O_2$ + H: 560.3277. Found: 560.3276. Calc. for $C_{37}H_{42}N_3O_2\cdot HCl\cdot 0.1CHCl_3$: C, 73.27; H, 6.98; N, 6.91. Found: C, 73.61; H, 7.02; N, 6.97%. This compound consistently analyzed as a partial $CHCl_3$ solvate even after prolonged drying in a vacuum oven. For **5b**: mp 149–151 °C (decomp.); $\lambda_{max}(CHCl_3)$/nm ($\log_{10}\varepsilon$) 332 (4.55), 373 (4.42), 423 (5.11), 594 (3.38), 747 (4.11), 827 (4.65); λ_{max}(5% TFA–$CHCl_3$)/nm ($\log_{10}\varepsilon$) 321 (4.36), 350 (4.54), 436 (5.17), 681 (4.06), 746 (4.43); $\delta_H(CDCl_3)$ −2.35 (6H, t, 2 × OCH_2CH_3), −1.36 (4H, q, 2 × OCH_2CH_3), 1.79 (6H, t), 1.83 (6H, t) (4 × porphyrin-CH_2CH_3), 2.41 (2H, br s, 2 × NH), 3.59 (6H, s, 2 × porphyrin-CH_3), 3.68 (4H, q) and 3.83 (4H, q) (4 × porphyrin-CH_2CH_3), 8.91 (2H, br) and 10.47 (2H, br) (4 × benzo-H), 9.64 (2H, s), 10.90 (2H, s) (4 × *meso*-H); $\delta_C(CDCl_3)$ 11.45, 11.66, 17.29, 18.27, 19.50, 19.58, 56.42, 95.28, 107.12, 112.60, 124.55, 133.11, 134.90, 135.54, 139.30, 139.82, 143.80, 145.74, 146.83, 155.72; HRMS: calc. for $C_{39}H_{46}N_3O_2$ + H: 588.3590. Found: 588.3592. Calc. for $C_{39}H_{46}N_3O_2\cdot HCl$: C, 75.04; H, 7.43; N, 6.73. Found: C, 74.80; H, 7.49; N, 6.60%.

1 J. Fabian, H. Nakazumi and M. Matsuoka, *Chem. Rev.*, 1992, **92**, 1197.
2 R. Bonnett, *Chem. Soc. Rev.*, 1995, **24**, 19; L. R. Milgrom and S. MacRobert, *Chem. Br.*, 1998, **34** (35), 45.
3 J. Ayub and D. Dolphin, *Chem. Rev.*, 1997, **97**, 2267.
4 E. Vogel, *J. Heterocycl. Chem.* 1996, **33**, 1461.
5 T. D. Lash, *Chem. Eur. J.*, 1996, **2**, 1197.
6 T. D. Lash, *Angew. Chem., Int. Ed. Engl.*, 1995, **34**, 2533. See also, T. D. Lash and S. T. Chaney, *Chem. Eur. J.*, 1996, **2**, 944.
7 T. D. Lash and M. J. Hayes, *Angew. Chem., Int. Ed. Engl.*, 1997, **36**, 840.
8 T. D. Lash and S. T. Chaney, *Tetrahedron Lett.*, 1996, **37**, 8825; T. D. Lash and S. T. Chaney, *Angew. Chem., Int. Ed. Engl.*, 1997, **36**, 839; M. J. Hayes and T. D. Lash, *Chem. Eur. J.*, 1998, **4**, 508.
9 K. Berlin, *Angew. Chem., Int. Ed. Engl.*, 1996, **35**, 1820.
10 U. E. Meissner, A. Gensler and H. A. Staab, *Tetrahedron Lett.*, 1977, **18**, 3.

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