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Synthesis of aromatic dicarbaporphyrinoids from resorcinol and 2-methylresorcinol☆

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Abstract—23-Carba-oxybenziporphyrins, a new group of dicarbaporphyrinoids, are easily prepared by reacting tripyrrane analogues derived from resorcinol or 2-methylresorcinol with an indene dialdehyde under MacDonald '3+1' conditions.

Carbaporphyrinoids, porphyrin analogues with carbocyclic rings in place of one of the usual pyrrole subunits, were first reported in the mid-1990s.[1,2] Oxybenziporphyrin **1**, the first aromatic example of this type, retains strongly diatropic characteristics in its proton NMR spectrum, showing the internal CH upfield near −7 ppm, as well as a porphyrin-like UV–vis absorption spectrum.[3–5] Subsequently, many additional aromatic carbaporphyrinoids were reported, including benzocarbaporphyrins **2**.[6–9] These systems show varying degrees of aromatic character and give unusual chemistry, including the ability to generate stable organometallic derivatives under mild conditions.[10–13] In addition, ketals derivatives generated by the oxidation of carbaporphyrins with ferric chloride[14] have been shown to be active agents in the treatment of leishmaniasis.[15] However, little work has been conducted to date on dicarbaporphyrinoid systems, where two of the usual pyrrole rings are replaced by carbocyclic rings.[16,17] A dibenzodicarbaporphyrin **3** was prepared from 1,3-diformylindane and 3,4-diethylpyrrole in a one-pot procedure,[16] but this methodology does not have general application for the synthesis of related macrocycles. An example of a 23-carbaazuliporphyrin **4** was also obtained using a stepwise route via an azulene analogue of the tripyrranes.[17] In addition, two types of related doubly N-confused porphyrin systems, **5** and **6**, have also been reported.[18,19] Carbaporphyrins provide a link between the porphyrins and the annulenes,[1,2] but also show useful characteristics such as the ability to form complexes with higher oxidation levels for transition metal elements.[11–13] Oxybenziporphyrins easily afford silver(III) derivatives,[12] while benzocarbaporphyrins **2** form both silver(III) and gold(III) organometallic derivatives.[11] N-confused porphyrins,[20] and doubly N-confused porphyrins **5** and **6**, also share this ability giving silver(III) and copper(III) derivatives.[18–20] Hence, the development of syntheses for other families of dicarbaporphyrinoids has a considerable significance in this rapidly developing field.

Recently, we reported the synthesis of tripyrrane analogues **7** from resorcinol and 2-methylresorcinol.[21] The reaction of 2 equiv of acetoxymethylpyrrole **8** with the dihydroxybenzene in dichloromethane with *p*-toluenesulfonic acid and calcium chloride as cocatalysts gave 'benzitripyrranes' **7** in 30–33% yields (Scheme 1). Deprotection of the benzyl esters gave the related dicarboxylic acids **9**. These were reacted with indene dialdehyde **10**[22] in TFA–dichloromethane for 16 h. The solutions were washed with 0.1% ferric chloride solution to aid in the oxidation of the porphyrinoid products. Subsequent washing with aqueous sodium bicarbonate, followed by the evaporation of the solvents on a rotary evaporator, gave residues that were virtually insoluble in dichloromethane or chloroform and these poor solubility characteristics prevented us from purifying the products by column chromatography. The crude product derived from resorcinol tripyrrane **7a** was recrystallized from methanol to give brown crystals in a 40% yield. Further recrystallization from chloroform–methanol gave the

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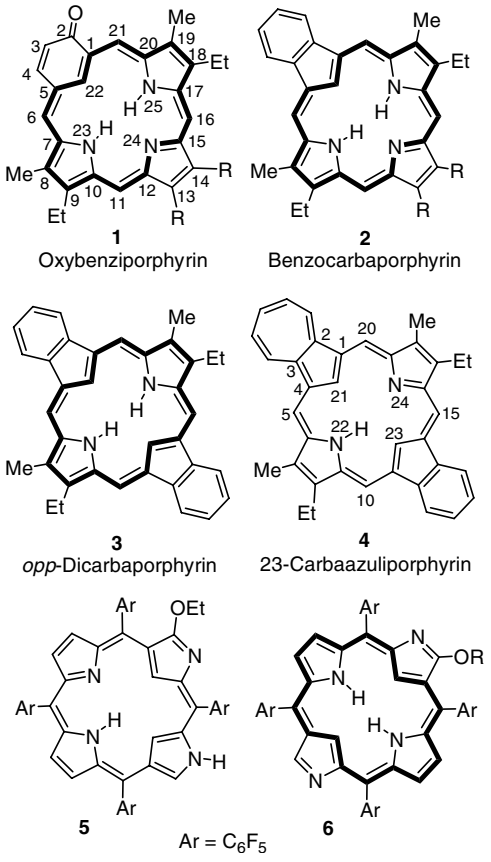
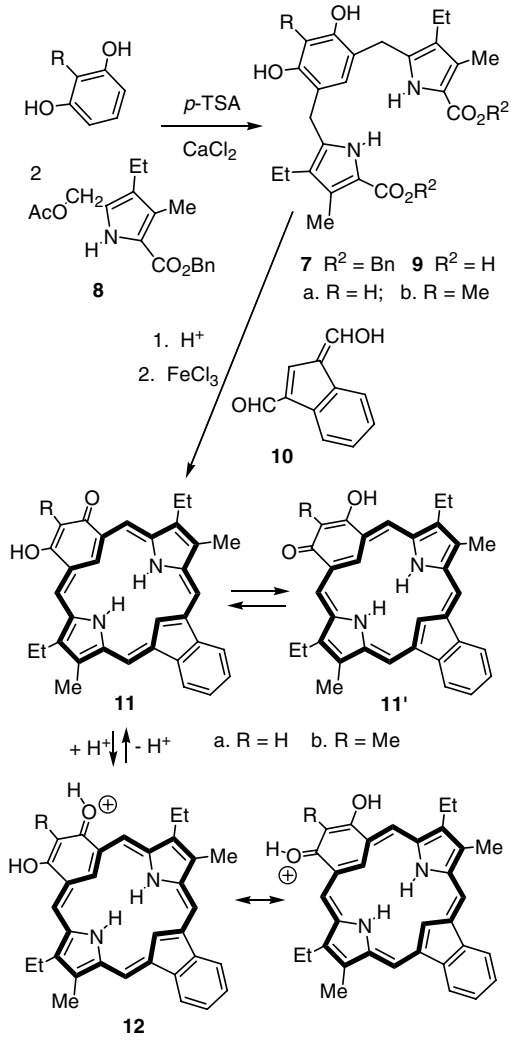


pure dicarbaporphyrinoid **11a** in a 25% yield.[23] The product derived from methylresorcinol tripyrrane **7b** was similarly crystallized from methanol and then chloroform methanol to give the related dicarbaporphyrinoid **11b** as a brown powder in an 18% yield.[23] Porphyrins and their analogues usually dissolve to a greater extent in chlorinated solvents such as $CHCl_3$ than other organic solvents, and in cases where they are sparingly soluble addition of TFA greatly improves the solubility by generating the corresponding dications. However, **11a** and **11b** were virtually insoluble in chloroform and the addition of TFA had no beneficial effect. It should be noted, however, that this system does not have the basic imine-type nitrogens found in porphyrins. Fortunately, porphyrinoids **11a** and **11b** are sparingly soluble in pyridine and to a slightly greater extent in DMSO, and this allowed us to acquire proton NMR data. DMSO is usually a poor solvent for porphyrinoid systems, but the observed solubility of **11** is presumably due to hydrogen bonding interactions to the resorcinol subunit (Fig. 1). The proton NMR spectrum of **11b** in DMSO-d_6 showed no plane of symmetry, indicating that the interconversion between the 2 equiv hydroxyoxybenziporphyrinoid tautomers **11b** and **11b′** is slow, and four resonances were observed for the *meso*-bridge protons at 9.56, 9.70, 9.98 and 10.02 ppm (Fig. 2A). An additional resonance was observed for the OH at 10.42 ppm, confirming the hydrogen bonding interaction depicted in Figure 1, while the 2-CH_3 was present at 2.44 ppm. The internal protons were all shifted upfield, giving two singlets for the CHs at −5.11 and −4.82 ppm, together with two NH resonances at



Scheme 1.

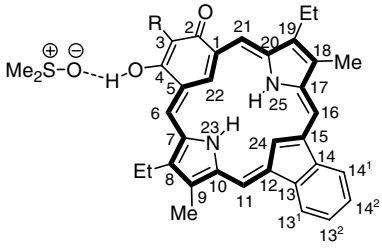


Figure 1. Structure of hydrogen bonded dicarbaporphyrinoids **11** in DMSO showing the numbering system for the porphyrinoid macrocycle.

−1.89 and −1.52 ppm. This highly diatropic character confirms that the carbaporphyrinoid system is aromatic. The addition of a drop of TFA to the NMR solution gave a similar but somewhat simplified proton NMR spectrum that showed a plane of symmetry and only two 2H resonances for the *meso*-protons (Fig. 2B). This indicates, as was expected, that the presence of acid increases the rate at which tautomers **11b** and **11b′** interconvert. However, the protonated species **12b** may also

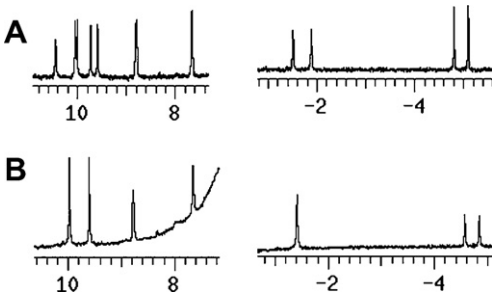


Figure 2. Partial 400 MHz proton NMR spectra of 24-carba-oxybenziporphyrin **11b** showing the upfield and downfield regions. (A) Spectrum in DMSO-d_6 showing the absence of a plane of symmetry in addition to the highly diatropic character of this porphyrinoid species. (B) Spectrum in TFA–DMSO-d_6 showing the apparent symmetrical nature of the structure under these rapid exchange conditions. The tail end of a broad peak centred on 6.8 ppm, that corresponds to the TFA, can also be seen.

be present as well (Scheme 1). The proton NMR spectrum of **11b** in pyridine-d_5 also showed only two 2H singlets for the *meso*-protons at 9.87 and 10.85 ppm, while the internal CHs appeared at −4.24 and −3.99 ppm and the NHs gave a 2H resonance at −1.50 ppm. These data also suggests that the tautomers interconvert more rapidly in the presence of a basic solvent, although anionic species may also be present in solution. A carbon-13 NMR spectrum of **11b** was obtained in TFA–DMSO-d_6 and this showed the carbonyl resonance at 175.3 ppm. Similar proton NMR data were obtained for **11a**, which also showed asymmetry in DMSO-d_6 but took on the appearance of a plane of symmetry in TFA–DMSO-d_6 or pyridine-d_5.

The IR spectra for **11a** and **11b** showed carbonyl stretching ($\nu_{C=O}$) at 1594 cm^{-1} and an OH absorption at approximately 3430 cm^{-1}. This compares to the values of 1611 ($\nu_{C=O}$) and 3440 cm^{-1} (ν_{OH}) for a related 3-hydroxyoxybenziporphyrin.[5] The UV–vis spectra of **11a** and **11b** were porphyrin-like, showing the presence of strong Soret bands near 450 nm, although there were significant variations depending upon the solvent used. In addition, the quality and intensity of the spectra varied due to aggregation in solution. For instance, the UV–vis spectrum of **11a** in chloroform gave a Soret band at 458 nm but in 50% methanol–chloroform the Soret band shifted to 451 nm and a clearer Q band was noted at 602 nm (Fig. 3). The addition of TFA resulted in a sharper Soret band that was blue shifted to 448 nm and a strong Q band was observed at 622 nm (these differences are consistent with the formation of a protonated species **12**). The UV–vis data for in pyridine were also similar, showing the Soret absorption at 455 nm and a Q band at 599 nm. Addition of 1% DBU to solutions of **11a** in methanol–chloroform also showed distinctive changes in the UV–vis spectrum with the Soret band shifting to 446 nm, suggesting the formation of the anionic species. Similar results were obtained for **11b**, although the spectra were generally of a lower quality due to aggregation effects.

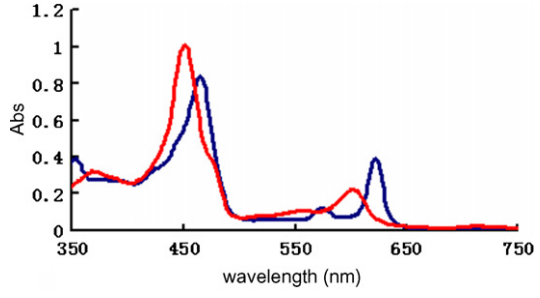


Figure 3. Electronic absorption spectra of **11a** in 50% methanol–chloroform (red line) or 1% TFA in 50/50 methanol–chloroform (blue line).

Dicarbaporphyrinoids **11a** and **11b** have very different solubility characteristics from any porphyrin analogue system that we have investigated previously. Although we have not as yet been able to metalate these structures, these unusual macrocyclic systems still show highly diatropic proton NMR spectra and porphyrin-like UV–vis spectra. This new group of dicarbaporphyrinoids demonstrates that highly modified benziporphyrins can retain aromatic character. However, it remains to be seen if related tri or tetracarbaporphyrinoids systems can be prepared or whether they will still retain porphyrin-like characteristics.

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Supplementary data

Supplementary data associated with this article can be found, in the online version, at doi:10.1016/j.tetlet.2006.10.053.

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23. *8,19-Diethyl-4-hydroxy-9,18-dimethyl-24-carbabenzo[m]oxybenziporphyrin* (**11a**). Resorcinol tripyrrane analogue **9a** (75.0 mg) was stirred under nitrogen with TFA (1 mL) in a 250 mL pear shaped flask for 2 min. Dichloromethane (200 mL) was added, followed immediately by diformyl indene **10** (29.3 mg), and the resulting mixture stirred in the dark under nitrogen for 16 h. The mixture was shaken with 0.1% w/v aqueous ferric chloride solution (200 mL) for 5 min, and then washed with water, sodium bicarbonate solution and water. The aqueous phases were back extracted with chloroform at each stage. The solvent was removed under reduced pressure and the resulting brown residue recrystallized from methanol and then chloroform–methanol to give the dicarbaporphyrin (20.3 mg, 25%) as a dark purple powder, mp >300 °C; UV–vis (50% MeOH–$CHCl_3$): λ_{max} ($\log_{10}\varepsilon$) 368 (4.41), 451 (4.91), 557 (3.95), 602 (4.26), 713 nm (3.29); UV–vis (5% Et_3N in 50/50 MeOH–$CHCl_3$): λ_{max} ($\log_{10}\varepsilon$) 376 (4.53), 450 (4.90), 544 (4.00), 593 nm (4.13); UV–vis (1% TFA in 50/50 MeOH–$CHCl_3$): λ_{max} ($\log_{10}\varepsilon$) 368 (4.35), 465 (4.83), 531 (3.71), 574 (4.00), 622 nm (4.51); IR (KBr): ν 3430 (ν_{OH}), 1594 cm^{-1} ($\nu_{C=O}$); ^1H NMR (DMSO-d_6): δ −5.13 (1H, s), −4.84 (1H, s), −1.92 (1H, s), −1.54 (1H, s), 1.58 (6H, m), 3.3 (6H, s, obscured by solvent), 3.78 (4H, m), 7.62 (2H, m), 7.9 (1H, br), 8.77 (2H, m), 9.56 (1H, s), 9.70 (1H, s), 9.98 (1H, s), 10.02 (1H, s), 10.42 (1H, s); ^1H NMR (TFA–DMSO-d_6): δ −4.92 (1H, s), −4.64 (1H, s), −1.49 (2H, s), 1.57 (6H, t, $J = 7.4$ Hz), 3.31 (6H, s), 3.76 (4H, q, $J = 7.2$ Hz), 7.62 (2H, m), 7.9 (1H, obscured by solvent), 8.75 (2H, m), 9.58 (2H, s), 9.96 (2H, s); ^1H NMR (pyridine-d_5): δ −4.26 (1H, s), −4.05 (1H, s), −1.65 (2H, s), 1.55 (6H, t, $J = 7.4$ Hz), 3.22 (6H, s), 3.75 (4H, q, $J = 7.6$ Hz), 7.82–7.85 (2H, m), 8.94–8.98 (2H, m), 9.90 (2H, s), 10.83 (2H, s); HRMS (FAB): Calcd for $C_{33}H_{30}N_2O_2$: 486.2307. Found 486.2306.
8,19-Diethyl-4-hydroxy-3,9,18-trimethyl-24-carbabenzo[m]-oxybenziporphyrin (**11b**). Using the foregoing procedure, methylresorcinol tripyrrane analogue **9b** (75.0 mg) was reacted with indene dialdehyde **10** (28.4 mg). Following evaporation of the solvent, the residue was recrystallized from methanol and then chloroform–methanol to give **11b** (14.8 mg; 18%) as a brown powder, mp>300 °C; UV–vis (DMSO): λ_{max} ($\log_{10}\varepsilon$) 377 (4.56), 451 (4.77), 523 (4.32), 595 (4.28), 719 (3.75), 778 nm (3.48); UV–vis (10% TFA–DMSO): λ_{max} ($\log_{10}\varepsilon$) 453 (4.70), 468 (4.70), 521 (4.27), 579 (4.20), 626 nm (4.37); IR (KBr): ν 3425 (ν_{OH}), 1595 cm^{-1} ($\nu_{C=O}$); ^1H NMR (DMSO-d_6): δ −5.11 (1H, s), −4.82 (1H, s), −1.89 (1H, s), −1.52 (1H, s), 1.60 (6H, m), 2.44 (3H, s), 3.31 (6H, s), 3.80 (4H, m), 7.63 (2H, m), 8.77 (2H, m), 9.56 (1H, s), 9.70 (1H, s), 9.98 (1H, s), 10.02 (1H, s), 10.42 (1H, s); ^1H NMR (TFA–DMSO-d_6): δ −4.89 (1H, s), −4.61 (1H, s), −1.46 (2H, s), 1.57 (6H, t, $J = 7.4$ Hz), 2.42 (3H, s), 3.31 (6H, s), 3.76 (4H, q, $J = 7.2$ Hz), 7.62 (2H, m), 8.75 (2H, m), 9.57 (2H, s), 9.95 (2H, s); ^1H NMR (pyridine-d_5): δ −4.24 (1H, s), −3.99 (1H, s), −1.50 (2H, s), 1.54 (6H, t, $J = 7.4$ Hz), 3.10 (3H, s), 3.23 (6H, s), 3.75 (4H, q, $J = 7.6$ Hz), 9.87 (2H, s), 10.85 (2H, s) (benzo-protons obscured by solvent); ^{13}C NMR (TFA–DMSO-d_6): δ 10.7, 11.4, 17.4, 19.7, 98.2, 104.6, 112.3, 113.5, 115.0, 120.7, 121.5, 127.4, 130.8, 134.5, 136.3, 141.6, 142.2, 175.3; HRMS (FAB): Calcd for $C_{34}H_{32}N_2O_2$: 500.2464. Found 500.2464.