Alphabet Soup within a Porphyrinoid Cavity: Synthesis of Heterocarbaporphyrins with CNNO, CNOO, CNSO and CNSeO Cores from an Oxacarbatripyrrin

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The first examples of porphyrin analogues with four different core atoms have been synthesized from an oxacarbatripyrrin intermediate. Acid-catalyzed condensation of the tripyrrin analogue with pyrrole or furan dialdehydes gave 22-oxa- and 22,23-dioxacarbaporphyrins, while reactions with furan, thiophene or selenophene dicarbinols afforded diphenyl dioxa-, oxathia- and oxaselenacarbaporphyrins.

Carbaporphyrins are porphyrin analogues where one or more of the core nitrogen atoms have been replaced with carbons. Structures of this type have attracted a considerable amount of interest owing to their stability, aromatic properties, unusual reactivity and ability to generate organometallic derivatives. Furthermore, carbaporphyrin derivatives have shown some promise in the treatment of leishmaniasis. In addition, core modified porphyrins have found applications in the development of chemosensors and have proven to be adept at stabilizing transition metal ions in unusual oxidation states. True carbaporphyrins include the cyclopentadienyl analogue and benzo-fused structures such as.

The latter system has been particularly well studied due in part to its relative ease of synthesis. Carbaporphyrins such as act as trianionic ligands generating silver(iii), gold(iii), rhodium(iii) and iridium(iii) complexes, all of which retain highly diatropic characteristics. However, closely related 23-oxa- and 23-thiacarbaporphyrins have also been reported to give palladium(ii) complexes. N- and C-Alkylcarbaporphyrins also afford palladium(II) and nickel(II) complexes.

Recently, we reported a new route to carbaporphyrins using a novel carbatripyrrin intermediate. Reaction of indene with pyrrole-2-carbaldehyde and potassium hydroxide in refluxing ethanol generated fulvene and subsequent reduction with lithium aluminum hydride in refluxing THF afforded the related dihydrofulvene (Scheme 1). When 6 was condensed with pyrrole-2-carbaldehyde in refluxing KOH/ethanol under dilute conditions, mixtures of carbatripyrrene products 7a were formed. However, under more concentrated conditions, pure carbatripyrrene 8a precipitated from solution. It was speculated that 8a was present in equilibrium with intermediates such as 7 but under concentrated conditions precipitation of poorly soluble 8a drove the equilibrium towards the formation of this species. Carbatripyrrene 8a reacted with pyrrole dialdehydes in the presence of trifluoroacetic acid to give carbaporphyrins, while condensation with furan dialdehyde afforded oxacarbaporphyrin (Scheme 1). Furthermore, 8a reacted with furan, thiophene and selenophene dialcohols to produce diphenylheterocarbaporphyrins (Scheme 2). These diphenylporphyrinoids reacted with nickel(ii) or palladium(ii) acetate to give nickel(ii) and palladium(ii) complexes and also generated unique oxidation products. In total, this strategy provided access to porphyrin analogues with CNMN, CNON, CNSN and CNSeN coordination cores.

The generality of the carbatripyrrin strategy has not as yet been demonstrated as it relies on the poor solubility of carbatripyrrene 8a to generate this key intermediate. Alteration of the core atoms within the porphyrin macrocycle allows the
Thiophene is much less reactive again and this further decreases the chances that 8c could be used to generate porphyrinoid macrocycles. As it turned out, 8c failed to give porphyrin-like products under any of the reaction conditions that were explored. However, 8b proved to be a versatile precursor to heterocarbaporphyrins with CNNO, CNOO, CNSO and CNSeO cores.

Figure 1 UV-vis spectrum of 15b in 1% Et3N-CH2Cl2 (red line, free base) and 1% TFA-CH2Cl2 (blue line, cation 15bH+).

Reaction of 8b with pyrrole dialdehyde 9a in the presence of TFA in dichloromethane afforded 22-oxacarbaporphyrin 15a in 8% yield (Scheme 1). Similarly, 9b reacted with 8b to give the related diethylporphyrinoid 15b in 14% yield. These porphyrin analogues retain strongly aromatic characteristics and the proton NMR spectra for 15a and 15b showed the meso protons as four highly deshielded 1H singlets between 9.63 and 10.23 ppm. The pyrrolic and furan protons were similarly shifted downfield to give four 1H doublets between 9.10 and 9.55 ppm, while the internal CH appeared upfield between -5.4 and -5.8 ppm. The UV-vis spectra were also porphyrin-like and 15b gave rise to a Soret band at 430 nm and Q bands at 515, 547, 618 and 679 nm (Figure 1). Addition of trace amounts of TFA to solutions of 15a,b gave rise to the related monocations 15aH+ and 15bH+ (Scheme 3). The UV-vis spectra showed two Soret-like bands at 393 and 432 nm and two weaker absorptions at higher wavelengths. The UV-vis spectra were essentially unchanged in 50% TFA-CH2Cl2, indicating that the formation of diprotonated species such as

Figure 2 UV-vis spectrum of dioxacarbaporphyrin 12b in 1% Et3N-CH2Cl2 (red line, free base) and 1% TFA-CH2Cl2 (blue line, cation 12bH+).
In order to improve the solubility of the heterocarbaporphyrins, and provide access to additional core-modified structures, 8b was reacted with furan, thiophene and selenophene dicarbinols 13a-c in the presence of boron trifluoride ethereal (Scheme 2). Following oxidation with DDQ, diphenyl dioxacarba-oxathiacarba- and oxaselenacarba-porphyrins 16a-c were isolated in 9.5%, 16% and 9.6% yield, respectively. All three compounds exhibited global aromatic properties, although the proton NMR spectra indicate that 16b has the largest diamagnetic ring current while dioxacarba-porphyrin 16a has the smallest (Table 1). The meso-protons for 16b appeared as two 2H singlets 10.13 and 10.25 ppm, while the inner CH resonance showed up at c 11.00 giving a Δδ value of 14.25. This compares to Δδ values of 13.91 and 14.10 for 16a and 16c, respectively. The presence of an electronegative oxygen in 16a appears to slightly reduce the aromatic properties of these macrocycles compared to having a sulfur atom within the cavity, although the larger selenium atom present in 16c may reduce the planarity of the system. Addition of TFA to solutions of 16a-c afforded the corresponding monocations 16H+, all of which showed enhanced diatropic character compared to the free base forms. However, for the protonated species, 16a had the largest shifts (Δδ = 17.15 ppm), while 16b had an intermediary Δδ value of 16.45 ppm (Table 1). Protonation increases the ionic crowding within the porphyrinoid cavity and this issue is exacerbated by the presence of larger chalcogen atoms leading to a further decrease in the planarity of the macrocycle. This explains why the aromatic ring current decreases as the atomic number for the heteroatom at position 23 increases going from O to S to Se. Addition of d-TFA to solutions of 16a-c led to rapid deuterium exchange of the inner CH protons. Similar results were also obtained for oxacarba-porphyrins 15. These results contrast with experiments reported for carbaporphyrin 2 where slow deuterium exchange was noted at the meso-positions.10b The UV-vis spectra of 16a, 16b and 16c were porphyrin-like with strong Soret bands at 429, 436 and 439 nm, respectively, and a series of Q bands between 500 and 720 nm. The corresponding

15H2Z+ are not favoured for this system (Scheme 3). The proton NMR spectra for the monocations indicate that they have slightly enhanced diatropic properties and the meso-protons for 15b in TFA-CDCl3 gave rise to four 1H singlets at 10.33, 10.39, 10.43 and 10.47 ppm, while the internal CH showed up at -7.18 ppm. Hence the difference between the upfield and downfield resonances (Δδ), which is a useful measure for magnitude of global diatropic character, is 17.65 ppm.

Reactions of 8b with furan dialdehyde 11a in the presence of TFA gave a dioxacarba-porphyrin 12b in 37% yield. Even after prolonged vacuum drying, the sample retained one equivalent of chloroform and was therefore isolated as a chloroform so...
monocations 16H+ in 1% TFA-CH2Cl2 gave broadened Soret bands, and both the Soret and Q bands underwent substantial bathochromic shifts with increasing atomic number for the heteroatoms at position 23 (Figure 5).

Table 1  Selected proton NMR chemical shifts for heterocarboxaporphyrins 16a-c and the related monocations

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Figure 5  UV-vis spectra of heterocarboxaporphyrin monocations 16H+ in 1% TFA-CH2Cl2: 16H+ (red), 16bH+ (green), 16cH+ (blue)

Table 1  Selected proton NMR chemical shifts for heterocarboxaporphyrins 16a-c and the related monocations

In conclusion, syntheses of 22-oxa-, 22,23-dioxa-, 22-oxa-23-thia- and 22-oxa-23-selenacarboxaporphyrins have been accomplished using an oxacarboxaporphyrin as a key intermediate. Modification of the core atoms allows the spectroscopic properties of these porphyrin analogues to be fine-tuned. In addition, this strategy has allowed the first examples of porphyrin analogues with four different types of atoms within the macrocyclic core to be isolated and characterized. These modified porphyrinoids also have the potential to exhibit novel coordination chemistry complementing the results obtained for previously described carboxaporphyrin ligands.20

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Conflicts of interest
There are no conflicts to declare.

Notes and references
Alphabet Soup within a Porphyrinoid Cavity: Synthesis of Heterocarbaporphyrins with CNNO, CNOO, CNSO and CNSeO Cores from an Oxacarbatripyrrin

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The first examples of porphyrin analogues with four different core atoms have been synthesized from an oxacarbatripyrrin intermediate.