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Project Title: Synthesis of Azaannulenes Related to the Porphyrins
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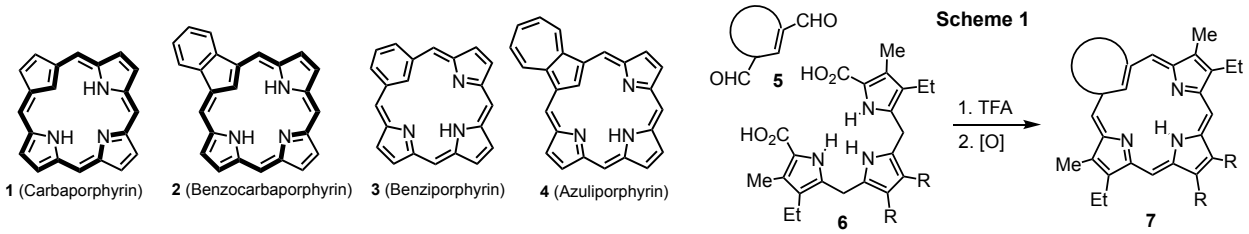
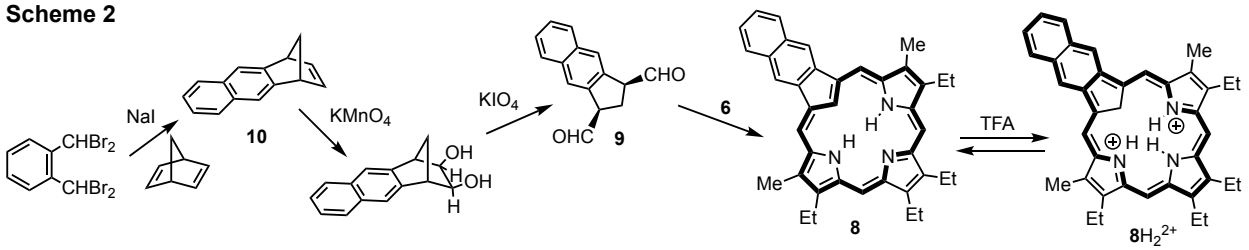
Porphyrins are macrocyclic systems built up from four pyrrolic subunits that possess global aromatic properties. We have investigated the synthesis of closely related porphyrin analogues where one or more of the usual pyrrolic subunits have been replaced by carbocyclic rings. Although many of these carbaporphyrinoids retain aromatic properties, some of these analogues are nonaromatic or even antiaromatic.[1,2] True carbaporphyrins such as **1** and **2** exhibit the strong diamagnetic ring currents associated with aromatic systems,[1,3] while benziporphyrins **3** are essentially nonaromatic[4] and azuliporphyrins **4** have intermediary properties.[5] These systems exhibit unusual reactivity, undergoing selective oxidation reactions and generating stable organometallic derivatives under mild conditions.[6] In addition, derivatives of benzocarbaporphyrins **2** have been shown to be effective agents in the treatment of leishmaniasis.[7] A "3 + 1" variant on the MacDonald reaction, where an aromatic dialdehyde **5** is condensed with a tripyrrane **6** in the presence of TFA, has commonly been used to prepare carbaporphyrinoid systems (Scheme 1).[8] This strategy has been very successful, and has provided straightforward access to carbaporphyrinoids such as **1**-**4**.[1,2] This methodology has recently been adapted to prepare new classes of carbaporphyrinoid systems.[9-11]



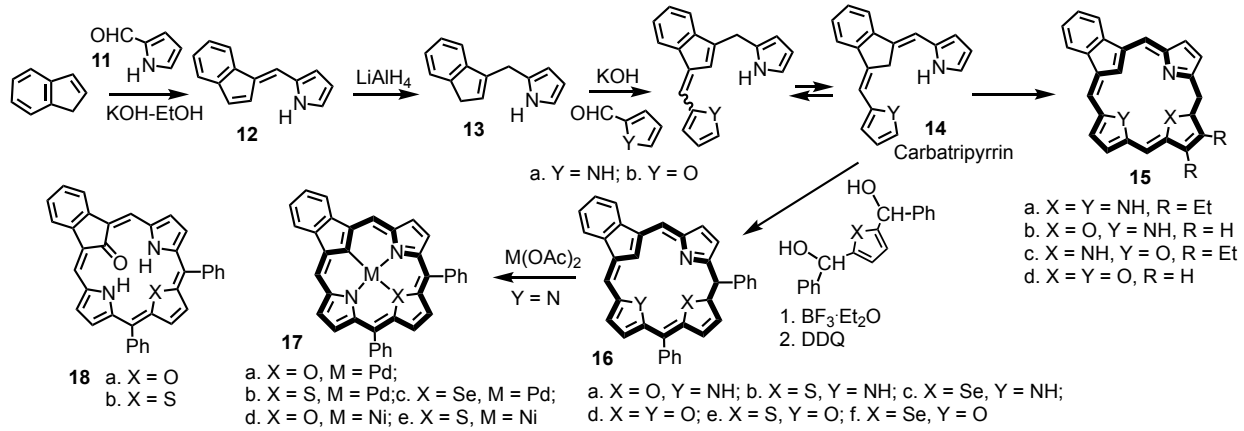
The "3 + 1" strategy was applied to the synthesis of a naphthalene-fused carbaporphyrin **8** (Scheme 2).[11] The required dialdehyde intermediate **9** was prepared in two steps from naphthonorbornadiene **10**. The presence of the fused conjugated ring led to only very small shifts in the UV-vis absorption spectrum.[11] Naphthocarbaporphyrin **8** was strongly aromatic but the fused arene unit is not significantly involved in the π-conjugation pathways. However, addition of excess TFA afforded a dicationic species $\mathbf{8}H_2^{2+}$ that showed large bathochromic shifts, and proton NMR spectroscopy, together with NICS and AICD calculations, indicated that the aromatic properties were now due, at least in part, to an extended 26 π-electron pathway. An internally methylated palladium(II) complex also exhibited similar conjugation through the fused naphthalene unit.[11]



An alternative route to carbaporphyrins from technical grade indene was developed recently (Scheme 3).[12] In this methodology, indene was reacted with pyrrole-2-carbaldehyde (**11**) and KOH in refluxing ethanol to give fulvene **12**. Reduction with $LiAlH_4$ gave dihydrofulvene **13** and further base-catalyzed condensation with **11** gave carbatripyrrin **14a**. Acid-catalyzed reaction with pyrrole dialdehydes or furan-2,5-dicarbaldehyde afforded carbaporphyrins **15a** and oxacarbaporphyrins **15b**. Furthermore, reactions with heterocyclic dialcohols gave a series of oxa-, thia- and selenacarbaporphyrins **16a-c**.[12] All three of these heterocarbaporphyrins afforded palladium(II) complexes **17a-c**, while the oxa- and thiacarbaporphyrins gave nickel(II) derivatives **17d,e**.[13] The latter underwent air oxidation to generate novel 21-oxycarbaporphyrins **18**.[13] This approach has been extended to introduce additional heteroatoms.[14] Hence, reaction of **13** with furfural gave an oxacarbatripyrrin **14b** and this reacted with

pyrrole or furan dialdehydes to give heterocarbaporphyrins **15c** and **15d**. Furthermore, reactions with heterocyclic dicarbinols yielded dioxacarba-, oxathiacarba- and selenacarbaporphyrins **16d-f**.[14] This is the first time that porphyrin analogues with four different atoms within the macrocyclic core have been synthesized.[14]

Scheme 3



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