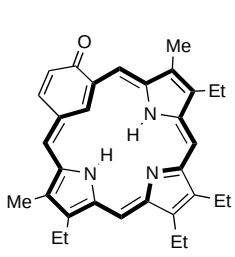
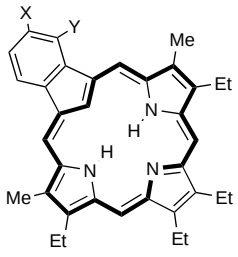
An Azulene Analogue of the Tripyrranes and Carbaporphyrinoids Therefrom**

Shelley R. Graham, Denise A. Colby, and Timothy D. Lash*

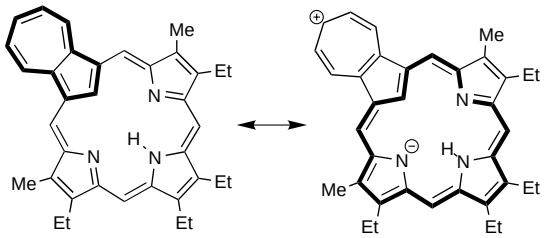
The "3+1" approach to porphyrinoid systems[2] provides an extraordinarily versatile methodology for the synthesis of novel conjugated structures related to the porphyrins.[1–5] The method relies upon the ready availability of tripyrranes[2, 6] and their ability to condense with various dialdehydes to give macrocycles that are built up from three pyrrole rings and a fourth, potentially dissimilar, subunit. This methodology has allowed the synthesis of carbaporphyrinoids with benzene (for example, **1**),[1, 5, 7] indene (for example, **2**),[8] azulene (for example, **3**),[9] or related subunits,[10] as components of the conjugated macrocycle. The methodology is less well suited to the synthesis of more functionalized macrocycles, because of the lack of availability of suitable precursors. Synthesis of an aromatic *opp*-dicarbaporphyrin **4** by the condensation of 1,3-indanedicarbaldehyde with 3,4-diethylpyrrole has been reported,[11] but this is a special case and does not provide the basis for synthesis of related macrocycles. There is currently a great deal of interest in the synthesis of modified porphyrinoids of this type,[3, 4] which include the related doubly N-confused porphyrins,[12] but rational approaches for the synthesis of highly modified porphyrinoid systems remain to be developed. We now report the synthesis of an azulene analogue of the tripyrranes and its utility in the synthesis of novel porphyrinoid systems.



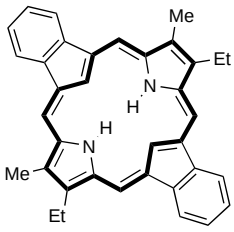
1 Oxybenziporphyrin



2 Carbaporphyrins
a) X = Y = H; b) X = CHO, Y = H; c) X = H, Y = CHO

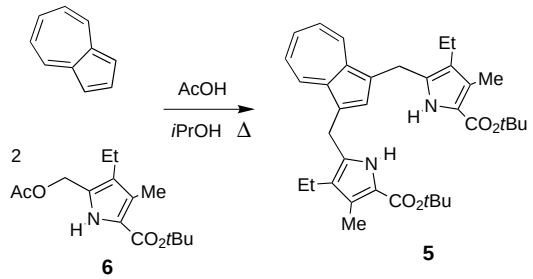


3 Azuliporphyrin **3a**



4
opp-Dicarbaporphyrin

Azulene (**3**) was prepared in good yields by condensing 1,3-azulenedicarbaldehyde with a tripyrrane under standard "3+1" conditions.[9] The macrocycle is cross-conjugated but nonetheless possesses a weak diatropic ring current as demonstrated by ^{1}H NMR spectroscopy, caused by zwitterionic resonance contributors, such as **3a**.[9] These aromatic characteristics dominate in the protonated species, in which porphyrinoid aromaticity is no longer undermined by charge separation.[9] Interestingly, oxidative rearrangements have been reported, in which ring contraction takes place to afford the benzocarbaporphyrins **2a**–**c**.[13] In our studies on the azuliporphyrins, we are investigating alternative routes to azulene-containing macrocycles. Azulene favors electrophilic substitution at the 1 and 3 positions, which are analogous to the α-positions on the pyrrole nucleus, and we speculated that this characteristic would allow the synthesis of novel tripyrrane analogues such as **5** (Scheme 1). This type of "carbatripyrrane" could act as a precursor to a series of porphyrin analogues with two modified subunits.



6 **5**

Scheme 1. Synthesis of an azulitripyrrane **5**.

The synthesis of carbatripyrrane **5** turned out to be remarkably straightforward. Condensation of azulene with two equivalents of acetoxymethylpyrrole **6** in refluxing acetic acid/isopropyl alcohol afforded the tripyrrane analogue in 59% yield, after column chromatography and recrystallization from toluene (Scheme 1). The system is stable compared with tripyrrolic tripyrranes and the simplicity of the synthesis may allow the preparation of many new macrocycles.

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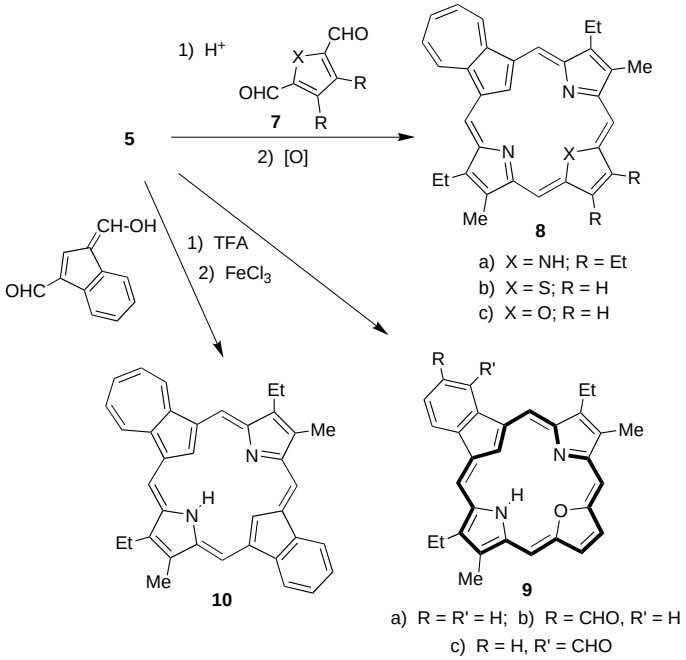
Tripyrrane **5** was treated with trifluoroacetic acid (TFA) to cleave the *tert*-butyl ester protective groups, and the resulting solution diluted with dichloromethane, treated with pyrrolealdehyde **7a**, and oxidized with 2,3-dichloro-5,6-dicyano-1,4-benzoquinone (DDQ) to give azuliporphyrin **8a** in 25% yield (Scheme 2). This method is a "back-to-front" synthesis



Scheme 2. "3+1" Syntheses of azuliporphyrin analogues.

of the azuliporphyrin system, and demonstrates the viability of this strategy. The resulting porphyrinoid **8a** only differs from **3** in the placement of the peripheral alkyl substituents and has very similar properties to the original porphyrinoid **3**.

Under the same conditions, **5** was condensed with 2,5-thiophenedicarbaldehyde (**7b**) to give the related thiaazuliporphyrin **8b** in 33% yield. This system also shows borderline aromatic properties and the UV/Vis spectrum in 5% Et_3N/CH_2Cl_2 had several moderate bands in the Soret band region at 372, 384, 448, and 477 nm, together with broad absorption bands between 500 and 800 nm that resemble the spectra of **3**.[9] Both the UV/Vis and ^{1}H NMR spectra for the protonated system show the manifestation of fully aromatic character (for example, the emergence of a Soret band at 468 nm and the presence of a diatropic ring current) as reported for **3**. Reaction of **5** with furandialdehyde **7c**, however, did not give the expected oxaazuliporphyrin **8c**, but instead a mixture of three oxacarbaporphyrins **9a–c** was isolated in a combined yield of 15% (Scheme 2). These compounds were presumably formed by ring contraction of the seven-membered ring, analogous to that of the parent system.[13] All three of the products, which represent a new macrocyclic system, were shown to be fully aromatic porphyrinoids by UV/Vis and NMR spectroscopy. The ^{1}H NMR spectra show the resonance signals of the internal CH units between $\delta = -6$ and -7, while the signals from the external *meso*-protons were observed downfield, between $\delta = 9.8$ and 10.9.

The success of these studies encouraged us to consider the first rational synthesis of a dicarbaporphyrin. Treatment of **5** with TFA, followed by reaction with diformylindene in CH_2Cl_2 and oxidation with $FeCl_3$, afforded the carbaazuliporphyrin **10** in 9.4% yield (Scheme 2). This new dicarbaporphyrinoid also appears to be weakly diatropic by ^{1}H NMR spectroscopy (Figure 1). The internal protons gave rise to three singlets in the upfield region at $\delta = 2.0$, 1.3, and 0.5, while the *meso*-protons appeared as two broadened singlets downfield between 8.4 and 8.7 ppm. The UV/Vis spectrum of **10** in chloroform has two broad bands at 494 and 675 nm (Figure 2). These results demonstrate that the system is nonaromatic, although dipolar contributors do allow for a weak diatropic ring current. Addition of trace amounts of TFA to the NMR solution gave rise to a monocation **11** and this shows a pronounced ring current with three upfield resonances at $\delta = -3.68$ (1H), -2.37 (1H), and -1.16 (2H). The signals arising from the *meso*-protons of **11** sharpened considerably and shifted downfield to $\delta = 8.87$ and 9.43. Further addition of TFA led to C protonation on the interior indene carbon, to afford the dication **12** (Scheme 3). C protonation of this type has previously been reported for mono- and dicarbaporphyrin systems,[8, 11] as well as for carbasapphyrins.[10d] However, it is notable that both **11** and **12** appear to be stabilized by charge delocalization caused by dipolar canonical forms such as **11a** and **12a**. In **12**, the 18-π-electron delocalization pathway is redirected through the fused benzene ring which causes the resonance signals from the benzo moieties to shift downfield from $\delta = 7.76$ and 8.25 in **11**, to $\delta = 8.40$ and 9.26 in **12**. The protons of the internal methylene group of **12** resonate at $\delta = -0.90$, while the resonance signal arising from the inner azulene proton is observed at $\delta = 1.49$ and the signals of the NH protons are evident at $\delta = 4.33$ ppm. In the UV/Vis spectrum, the addition of TFA to dilute solutions failed to show the formation of an intermediary monocationic species and the free-base spectrum evolved directly into the spectrum for the doubly-protonated species. Dication **12** gave a strong Soret-like band at 481 nm and weaker bands at 529, 623, and 670 nm (Figure 2).

In conclusion, we have demonstrated that an azulene-containing analogue of the tripyrranes can easily be synthesized by the electrophilic substitution of azulene. The synthesis of several new macrocyclic systems from this key intermediate demonstrates that this back-to-front "3+1" methodology can be utilized to construct porphyrinoids with two modified subunits. In addition, the method provides a convenient synthetic entry to dicarbaporphyrinoid macrocycles.

Experimental Section

5: Azulene (0.438 g) and **6** (2.140 g) were stirred and heated under reflux in acetic acid (10 mL) and 2-propanol (50 mL) under a nitrogen atmosphere for 16 h. The solvent was removed under reduced pressure and the residue chromatographed on a silica column eluting with CH_2Cl_2/hexanes (60/40). A major blue band was collected, the solvent evaporated, and the residue recrystallized from toluene to give the carbatripyrrane (1.027 g; 59%) as a pale blue powder. Selected physical and spectroscopic data for **5**: m.p. 150 °C (dec.), ^{1}H NMR (400 MHz, $CDCl_3$): $\delta = 1.07$ (6H, t, $J = 7.4$ Hz), 1.47

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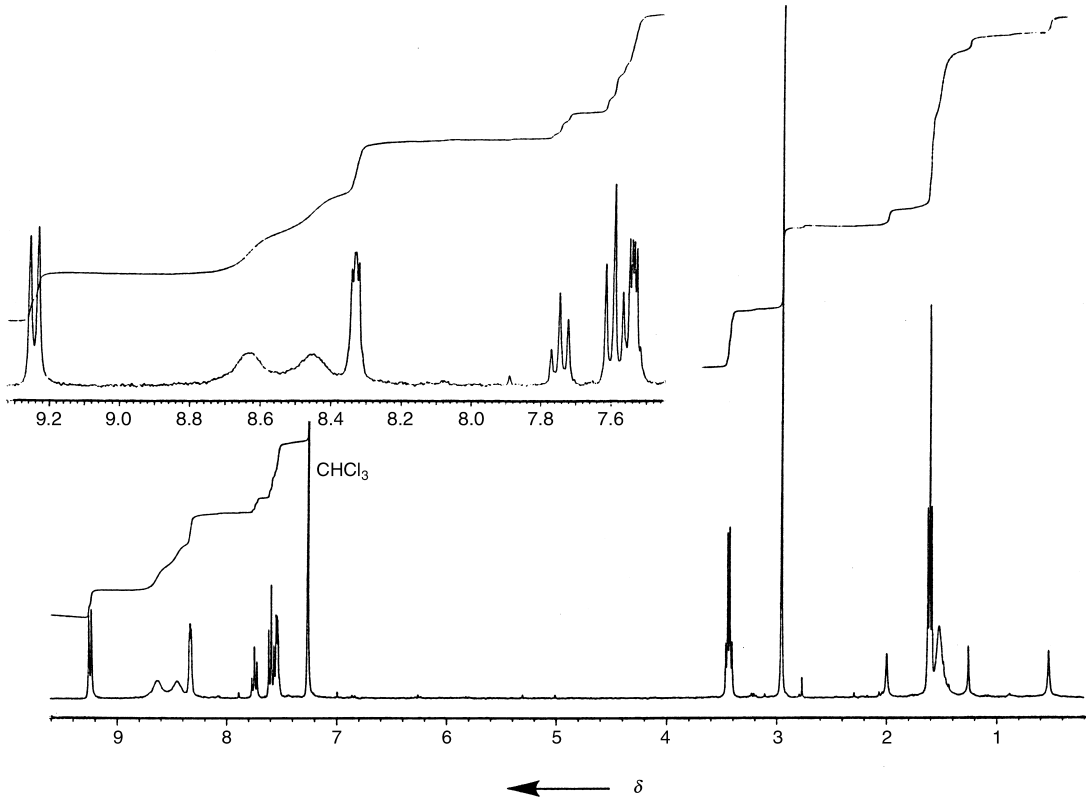


Figure 1. 400 MHz ^{1}H NMR spectrum of **10** in $CDCl_3$.

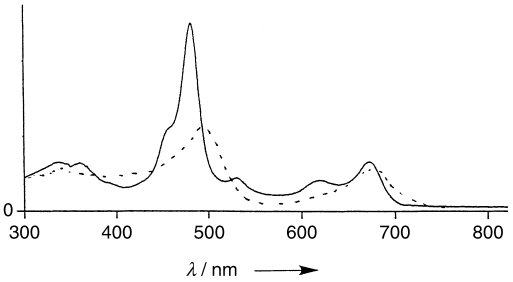
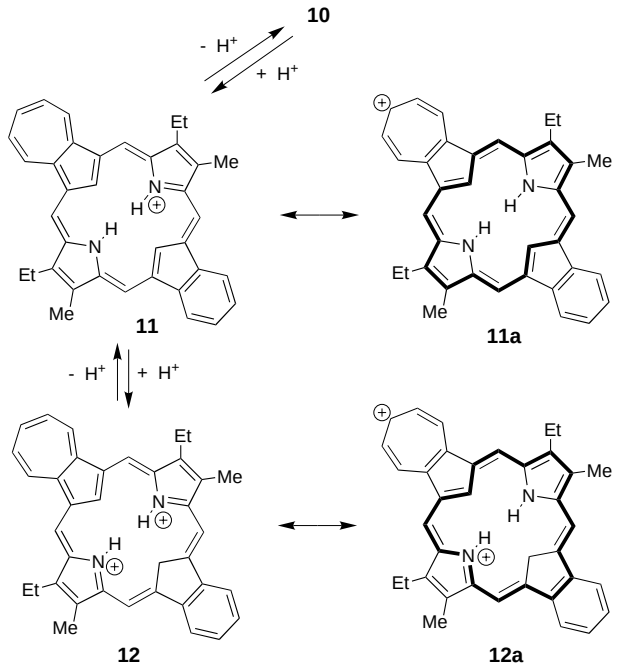


Figure 2. UV/Vis spectra of **10** in chloroform (----, free base) and 1% TFA/$CHCl_3$ (——, dication **12**).

(18H, s), 2.26 (6H, s), 2.48 (4H, q, $J = 7.4$ Hz), 4.31 (4H, s), 7.08 (1H, t, $J = 9.8$ Hz), 7.49 (1H, s), 7.56 (2H, t, $J = 9.8$ Hz), 8.11 (2H, br s), 8.18 (2H, d, $J = 10$ Hz); ^{13}C NMR (100 MHz, $CDCl_3$): $\delta = 10.74$, 15.74, 17.56, 24.31, 28.69, 80.23, 118.65, 122.42, 123.43, 124.66, 125.98, 131.59, 133.69, 137.04, 138.42, 138.67, 161.55; HRMS (EI): calculated for $C_{36}H_{46}N_2O_4$: *m*/*z* 570.3458; found: 570.3458; elemental analysis (%) calcd for $C_{36}H_{46}N_2O_4$: C 75.76, H 8.12, N 4.91; found: C 75.30, H 8.16, N 4.60.

10: Di-*tert*-butyl carbatripyrrane **5** (230 mg) was stirred with TFA (1 mL) under a nitrogen atmosphere for 10 min. Dichloromethane (49 mL) was added, followed immediately by addition of 1,3-diformylindene (72 mg) and the mixture was stirred under nitrogen for another 2 h. The mixture was diluted to 150 mL with chloroform and shaken with an aqueous ferric chloride solution (0.1%, 200 mL) for 5 min. The organic phase was separated and washed with water, 5% sodium bicarbonate solution, and water again. The combined organic solutions were dried over sodium sulfate and evaporated under reduced pressure. The brown residue was purified on a grade III alumina column eluting with 1% triethylamine/chloroform. The green product fraction was further purified on silica by flash chromatography eluting with 1% triethylamine/chloroform. A green fraction was collected, evaporated to dryness, and the residue recrystallized from chloroform/hexanes to give the dicarbaporphyrinoid (19.1 mg, 9.4%)



Scheme 3. Protonation of benzocarbaazuliporphyrin **11**.

as dark green crystals. Selected physical and spectroscopic data for **10**: m.p. 228–230 °C (dec.), UV/Vis ($CHCl_3$): λ_{max} (log ε) = 494 (4.74), 675 nm (4.44); UV/Vis (1% TFA/$CHCl_3$): λ_{max} (log ε) = 481 (5.08), 529(4.32), 623 (4.29), 670 nm (4.59); ^{1}H NMR (400 MHz, $CDCl_3$): $\delta = 0.52$ (1H, s), 1.25 (1H, s), 1.60 (6H, t, $J = 7.4$ Hz), 1.99 (1H, s), 2.95 (6H, s), 3.43 (4H, q, $J = 7.4$ Hz), 7.51–7.55 (2H, m), 7.59 (2H, t, $J = 9.6$ Hz), 7.75 (1H, t, $J = 9.6$ Hz), 8.31–8.35 (2H, m), 8.45 (2H, br s), 8.64 (2H, br s), 9.24 (2H, d, $J = 9.6$ Hz);

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^{1}H NMR (400 MHz, trace TFA/$CDCl_3$, monocation): $\delta = -3.68$ (1H, br s), -2.37 (1H, br s), -1.16 (2H, br s), 1.65 (6H, t, $J = 7$ Hz), 3.14 (6H, s), 3.72 (4H, br q), 7.51 – 7.55 (2H, br m), 8.25 (5H, br m), 8.87 (2H, s), 9.44 (2H, s), 9.75 (2H, br d, $J = 7.5$ Hz); ^{1}H NMR (400 MHz, TFA/$CDCl_3$, dication): $\delta = -0.90$ (2H, br s), 1.49 (1H, s), 1.58 (6H, t, $J = 7.4$ Hz), 3.04 (6H, s), 3.59 (4H, br q), 4.33 (2H, br s), 8.40 (2H, m), 8.51 (3H, m), 9.26 (2H, m), 9.42 (2H, s), 9.73 (2H, m), 9.79 (2H, s); ^{13}C NMR (100 MHz, TFA/$CDCl_3$): $\delta =$ 10.60, 16.10, 19.69, 35.82 (internal CH_2), 106.84, 118.18, 124.40, 127.49, 131.56, 134.01, 134.49, 139.48, 140.27, 140.67, 144.46, 146.71, 151.92, 152.02, 152.04, 154.99; HRMS (FAB): calculated for $C_{37}H_{32}N_2 + H$: m/z 505.2642; found: 505.2644; elemental analysis (%) calcd for $C_{37}H_{32}N_2 \cdot \frac{1}{2}H_2O$: C 86.51, H 6.47, N 5.45; found: C 86.26, H 6.24, N 5.66.

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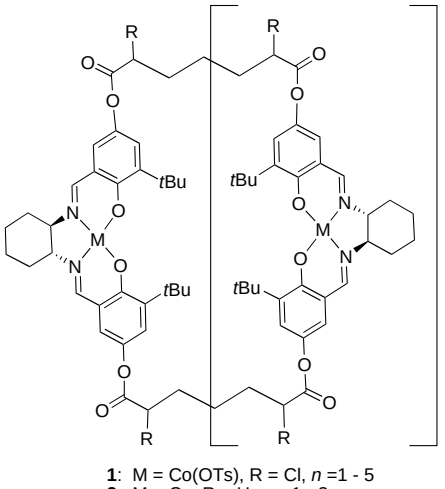
A Practical Oligomeric [(salen)Co] Catalyst for Asymmetric Epoxide Ring-Opening Reactions**

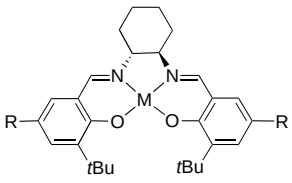
Joseph M. Ready and Eric N. Jacobsen*

The development of catalysts that are not only enantioselective and high yielding but also useful from a practical standpoint persists as a challenging goal in asymmetric synthesis. In the ideal case, a catalyst should be readily available or easily synthesized on any scale and should display both high reactivity (turnover frequency) and durability (turnover number). In this context, substantial progress has been made over the past several years in the discovery of chiral salen-metal-based catalysts (H_2salen = bis(salicylidene)ethylenediamine) for the asymmetric ring-opening of epoxides, and attention has focused recently on the development of these catalysts from a practical perspective.[1] We describe herein a significant advance in this regard, with the development of easily synthesized and highly active oligomeric [(salen)Co] catalysts for the asymmetric hydrolysis of *meso*-epoxides and kinetic resolution of terminal epoxides.

We reported recently the preparation of mixtures of cyclic oligomeric [(salen)Co] complexes (**1**), which were designed to enforce the cooperative bimetallic mechanism common to many epoxide ring-opening reactions.[2] Catalyst system **1** displayed substantial improvements in reactivity and enantioselectivity relative to monomeric analogues, with kinetic behavior consistent with cooperative reactivity within the



1: M = Co(OTs), R = Cl, n =1 - 5
2: M = Co, R = H, n = 1 - 3
3: M = Co(csa), R = H, n = 1 - 3
4: M = Co(nbs), R = H, n = 1 - 3



5: R = *t*Bu
6: R = OC(O) *t*Bu
7: R = OC(O)CH(Cl)CH_3
8: R = OC(O)$C(Cl)_2CH_3$

a: M = Co(OTs)
b: M = Co(csa)

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[**] This work was supported by the NIH (GM 43214). H_2salen = bis(salicylidene)ethylenediamine.

Supporting information for this article is available on the WWW under http://www.angewandte.com or from the author.

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