Articles

Facile Synthesis of *meso*-Tetraaryl Cofacial Diporphyrins

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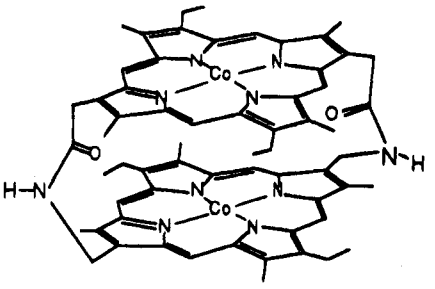
Metalated derivatives of cofacial diporphyrin ligands have been employed in the binding and catalytic multielectron redox transformations of small molecules. To date, the syntheses of these interesting molecules have been extremely cumbersome and low yielding. In addition, their synthetic methodologies have presented no convenient way to modify the electronic and structural properties of the constituent porphyrins. Here, we report a new method for the synthesis of a family of cofacial diporphyrin ligands in which the two porphyrins are attached via one rigid aromatic linker. The synthesis is considerably shorter—three steps from a suitable dialdehyde bridge—utilizes inexpensive, commercially available reagents, results in markedly increased yields, and allows for convenient variation of the constituent porphyrins. The method involves the monoprotection of a dialdehyde using 1,3-propanedithiol. The monoprotected aldehyde is then cocondensed under modified Lindsey conditions with pyrrole and the aromatic aldehyde of choice. The aldehyde of the resulting species is subsequently deprotected using DDQ and $BF_3{\cdot}O(Et)_2$—a new method for cleavage of dithiane protecting groups. A second Lindsey condensation results in formation of the cofacial diporphyrin ligand. Employing this method, we have synthesized a wide variety of cofacial hetero- and homodiporphyrin ligands, the metalated derivatives of which are currently under investigation in our laboratories.

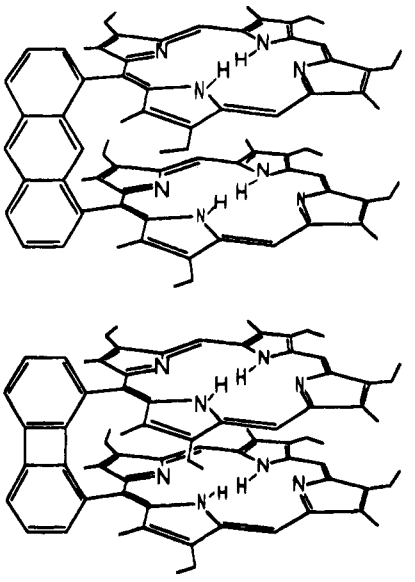
Introduction

Cofacial metallodiporphyrins have been used as molecular catalysts for the multielectron redox transformations of small molecules (e.g., O_2, N_2, and H_2).[1] The catalysts were designed to accommodate small substrates inside the cavity, thereby bridging the two metal centers. The first cofacial metallodiporphyrin to accomplish the catalytic four-electron reduction of dioxygen was Co_2FTF4 (**1a**) developed in 1979 by Collman *et al.*[2]



The two etio-type porphyrin structures are held together by amide linkages at the β-pyrrolic positions. Though the synthesis of these amide-linked porphyrins is versatile in that the interporphyrin distances can be varied by incorporating bridges of different lengths, it suffers from at least three disadvantages: (1) the amide linkages can be hydrolyzed or reduced; (2) a mixture of diastereomers is produced which are difficult to separate; and (3) the synthesis is quite long.[2]

Subsequently, two other cofacial diporphyrins were developed: the H_4DPA (**1b**) and H_4DPB (**1c**), first synthesized by Chang *et al.* in 1983.[3] Here the two porphyrin rings are bridged by a single, rigid, aromatic linker (anthracene for H_4DPA and biphenylene for H_4DPB).



In both cases the proximity of the two porphyrins allows for activation of small molecules between the metal centers. In particular, the cobalt derivatives of

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(1) Collman, J. P.; Wagenknecht, P. S.; Hutchison, J. E. *Angew. Chem., Int. Ed. Engl.* **1994,** *33,* 1537–1554 and references contained therein.

(2) (a) Collman, J. P.; Denisevich, P.; Konai, Y.; Marrocco, M.; Koval, C.; Anson, F. C. *J. Am. Chem. Soc.* **1980,** *102,* 6027–6036. (b) Durand, R. R., Jr.; Bencosme, C. S.; Collman, J. P.; Anson, F. C. *J. Am. Chem. Soc.* **1983,** *105,* 2710–2718.

(3) (a) Chang, C. K.; Abdalmuhdi, I. *J. Org. Chem.* **1983,** *48,* 5388–5390. (b) Chang, C. K.; Abdalmuhdi, I. *Angew. Chem., Int. Ed. Engl.* **1984,** *23,* 164–165. (c) Eaton, S. S.; Eaton, G. R.; Chang, C. K. *J. Am. Chem. Soc.* **1985,** *107,* 3177–3184.

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these molecules are potent four-electron dioxygen reduction catalysts.[4] These cofacial diporphyrins are chemically robust, and their final purification is straightforward.[5] Despite considerable effort to improve the original synthetic scheme, however, their syntheses remain formidable tasks: the most efficient synthesis to date requires 21 steps for H_4DPA (24 for H_4DPB).[6]

In spite of their difficult syntheses, extensive studies of these remarkable molecules have been rewarding. Significant examples include: dioxygen binding and efficient 4e$^-$ reduction to water by the bis-cobalt derivatives,[4a,6a] the microscopic reverse of dinitrogen fixation achieved with the bis-ruthenated species of **1c**,[7] and the isolation and characterization of a bridging dihydrogen adduct of the bis-ruthenated derivative of **1c**.[8]

The accomplishments of these past studies have spawned new questions regarding small molecule reactivity, particularly in the context of activation by two metals. Unfortunately, the cofacial diporphyrins developed to date are of limited use in further endeavors; the rigidity imposed by their arduous syntheses precludes any systematic variation of their electronic and structural properties. Four features of these molecules are worthy of mention at this time: (1) the electronic properties of the porphyrin significantly influence the redox properties of the metal; (2) the planar nature of the porphyrins allows intra- and intermolecular metal−metal bond formation;[9] (3) the two porphyrins are identical to each other; and (4) further chemical modification (e.g., for the purposes of covalent attachment to surfaces[10]) is impractical.

In 1986 a modification of the Rothemund porphyrin synthesis[11] was introduced by Lindsey.[12] The method involves condensation of pyrrole and benzaldehyde derivatives in the presence of an acid catalyst at room temperature. This results in formation of a porphyrinogen, which is subsequently oxidized in situ to yield the porphyrin. This pioneering method has made possible the synthesis of numerous new porphyrins.[13] Recently, a number of papers have appeared that describe the synthesis of *meso*-di- or -tetraarylporphyrin dimers linked by either an extended phenanthroline[14] or a phenyl bridge.[15,16] Some of these studies have utilized Lindsey preparations to synthesize their porphyrins. These molecules have been used mainly as models for the study of electron transfer in photosynthetic systems. No examples of multielectron catalysis have yet been reported.

In a similar fashion, we have applied the Lindsey method toward our own research needs. Thus, using modified Lindsey conditions[12] in the presence of biphenylene or anthracene dialdehydes has allowed the synthesis of a family of cofacial, *meso*-tetraarylporphyrin dimers. By judicious choice of the benzaldehyde derivative, we have a means of addressing all the issues mentioned above pertaining to the existing cofacial diporphyrins. Namely, we have developed a general, expedient method for cofacial diporphyrin synthesis which allows for systematic variation of the structural and electronic properties of these molecules.

In addition, during the course of this work we discovered a convenient and high yield method for the deprotection of dithiane derivatives. Details will be provided in the Results and Discussion.

Experimental Section

General. Reagent grade CH_2Cl_2 and $CHCl_3$ (ethanol stabilized) were purchased from Fisher and used as received. Flash silica was purchased from EM Science with particle size finer than 230 mesh ASTM. Activated neutral alumina, Brockman I standard grade (~150 mesh), was purchased from Aldrich. Doubly distilled boron trifluoride etherate (BF_3) was purchased from Aldrich and used as received. It was stored in an inert atmosphere N_2 box (O_2 < 1 ppm) during the interim. Pyrrole (Aldrich) was distilled under nitrogen and likewise stored under inert atmosphere. Benzaldehyde derivatives were either purchased from Aldrich or TCI and used as received or synthesized by published procedures. 2,3-Dichloro-5,6-dicyano-1,4-benzoquinone (DDQ) was purchased from Janssen Chimica and used as received. 1,8-Diformylbiphenylene[6a] and 1,8-diformylanthracene[6b] were synthesized according to literature procedures. All glassware and syringes were oven dried immediately prior to use. ^{1}H NMR spectra ($CDCl_3$ and C_6D_6) were obtained with a Nicolet NMC-300 MHz or a Varian XL-400 MHz spectrometer. UV−vis spectra were obtained with a Hewlett-Packard 8450A diode array spectrometer. Mass spectra were done by the Mass Spectrometry Facility at the University of California at San Francisco. Elemental analyses were performed by Midwest Microlab. Full characterization data will be presented for two representative cofacial dimers. Their syntheses are essentially identical, varying only in stoichiometry or choice of solvent. Thus, one general method will be described, with particular differences noted later. We emphasize that, thus far, we detect no reactivity differences between the two bridges and that methodology described for one particular bridge may be fully applicable to the other.

Synthesis. 1-(1,3-Dithiacyclohex-2-yl)-8-formylanthracene(3a). The protection of the dialdehyde was accomplished by modification of a procedure which used 1,2-ethanedithiol as the protecting group.[12a,17a] At room temperature, 2.00 g of 1,8-diformylanthracene[6b] (8.54 mmol) and 924 mg of 1,3-propanedithiol (8.54 mmol) were dissolved in 85 mL of dry CH_2Cl_2. To the yellow solution was added 200 μL of BF_3 (1.6 mmol) via syringe. A fine yellow-white precipitate was observed within 10 min. After being stirred at least 1 h, the reaction mixture was transferred to a separatory funnel and washed

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(5) All syntheses mentioned thus far rely on the stepwise synthesis of pyrrole and dipyrrylmethane subunits.

(6) (a) Collman, J. P.; Hutchison, J. E.; Lopez, M. A.; Tabard, A.; Guilard, R.; Seok, W. K.; Ibers, J. A.; L'Her, M. *J. Am. Chem. Soc.* **1992,** *114*, 9869−9877. (b) Guilard, R.; Lopez, M. A.; Tabard, A.; Richard, P.; Lecomte, C.; Brandes, S.; Hutchison, J. E.; Collman, J. P. *J. Am. Chem. Soc.* **1992,** *114*, 9877−9889.

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(9) Collman, J. P.; Kim, K.; Garner, J. M. *J. Chem. Soc., Chem. Commun.* **1986,** 1711−1713.

(10) Illustrative examples can be found in: *Molecular Design of Electrode Surfaces*; Murray, R., Ed.; Techniques of Chemistry; John Wiley & Sons, Inc.: New York, 1992; Vol. 22.

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(13) Lindsey, J. S. In *Metalloporphyrins Catalyzed Oxidations*; Montanari, F., Casella, L., Eds.; Kluwer Academic Publishers: Dordrecht, 1994; pp 49−86.

(14) Noblat, S.; Dietrich-Buchecker, C. O.; Sauvage, J. P. *Tetrahedron Lett.* **1987,** *47*, 5829−5832.

(15) Osuka, A.; Nakajima, S.; Nagata, T.; Maruyama, K.; Toriumi, K. *Angew. Chem., Int. Ed. Engl.* **1991,** *30*, 582−584.

(16) Meier, H.; Kobuke, Y.; Kugimiya, S. *J. Chem. Soc., Chem. Commun.* **1989,** 923−924.

(17) (a) Marshall, J. A.; Belletire, J. L. *Tetrahedron Lett.* **1971,** 871−874. (b) Greene, T. W.; Wats, P. G. M. *Protective Groups in Organic Synthesis*, 3rd ed.; John Wiley & Sons, Inc.: New York, 1991; Chapter 4, pp 198−207.

with 5% aqueous NaOH (1 × 100 mL) and water (2 × 100mL). The organic layer was collected and stripped of solvent, and the yellow residue was then chromatographed over flash silica (5 × 30 cm). The column was eluted with CH_2Cl_2/hexanes (9/1). The product was isolated as the second of three yellow bands (1.33 g, 48% yield): ^{1}H NMR ($CDCl_3$) δ 10.43 (s, 1H), 10.42 (s, 1H), 8.49 (s, 1H), 8.24 (d, 1H, J = 8.5 Hz), 8.00 (d, 1H, J = 6.8 Hz), 7.96 (d, 1H, J = 8.5 Hz), 7.87 (d, 1H, J = 7.0 Hz), 7.61 (dd, 1H, J_1 = 8.5 Hz, J_2 = 6.8 Hz), 7.52 (dd, 1H, J_1 = 8.5 Hz, J_2 = 7.0 Hz), 6.20 (s, 1H), 3.40 (m, 2H), 3.05 (m, 2H), 2.30 (m, 1H), 2.05 (m, 1H).

1-(1,3-Dithiacyclohex-2-yl)-8-formylbiphenylene (3b). The monoprotected biphenylene dialdehyde was synthesized from the dialdehyde[6a] under identical conditions as described above. Yields ranged from 45–48%: ^{1}H NMR ($CDCl_3$) δ 10.28 (s, 1 H), 7.14 (d, 1H, J = 8.3 Hz), 6.96 (d, 1H, J = 8.4 Hz), 6.86 (m, 2 H), 6.73 (d, 1H, J = 6.8 Hz), 6.61 (d, 1H, J = 6.7 Hz) 5.67 (s, 1H), 3.13 (m, 2H), 2.89 (m, 2H), 2.16 (m, 1H), 1.92 (m, 1H).

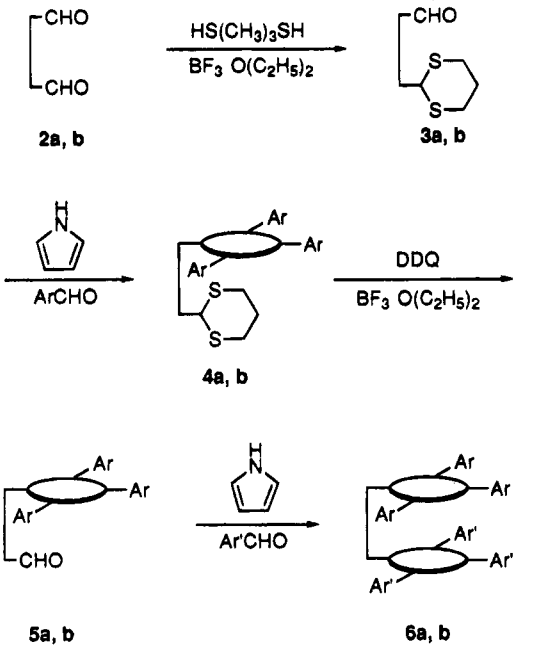
1-(5-Tris(10,15,20-(pentafluorophenyl)porphyrinyl))-8-formylbiphenylene (11). Three hundred mg (1 mmol) of the monoprotected biphenylene-dialdehyde was dissolved in 1.6 L of CH_2Cl_2 in a 3-L three-neck flask fitted with rubber septa and a condenser. The solution was purged continuously with a stream of nitrogen. To this was added 1.852 mL of pentafluorobenzaldeyde (15 mmol) and 1.11 mL of pyrrole (16 mmol), thus maintaining a 1:15:16 stoichiometry of aryl bridge: benzaldehyde:pyrrole. BF_3 (0.65 mL, 5.28 mmol) was then added via syringe. Its concentration is 3.3 × 10^{-3} M, thus maintaining recommended Lindsey conditions.[12] The reaction was stirred in the dark for 80 min. At this time DDQ (2.72 grams, 12 mmol) was added and the mixture was stirred for at least 1 h. The acid catalyst was neutralized with the addition of 0.81 mL (1.1 equiv) of triethylamine. The volume of the reaction was then reduced to approximately 300 mL (~20% of the original volume) by rotoevaporation and then loaded onto an alumina column (6 × 25 cm) packed in 1:1 hexanes:CH_2Cl_2 and eluted with CH_2Cl_2 until no more porphyrinic product was detected (approximately 1.5 L). This mixture was then concentrated to approximately 300 mL. To this was added 1 mL of BF_3 (8.13 mmol) and 1 g (4.4 mmol) of DDQ and the mixture stirred overnight in air. In 100 mL aliquots, the reaction mixture was washed 3× with 150 mL of 10% Na_2CO_3 to remove catechol. With deprotection of the monoporphyrin monoaldehyde accomplished, purification was achieved by silica chromatography (6 × 30 cm, 8:1 hexanes:CH_2Cl_2 → 1:1 hexanes:CH_2Cl_2): yield 220 mg (22% based on the bridge); mass spectrum m/e 985 (M^+); ^{1}H NMR ($CDCl_3$) δ 9.33 (d, 2H, J = 4.9 Hz), 8.93 (s, 4H), 8.90 (d, 2H, J = 4.8 Hz), 7.73 (d, 1H, J = 8.2 Hz), 7.34 (t, 1H, J = 7.6 Hz), 7.19 (d, 1H, J = 6.9 Hz), 6.99 (m, 1H), 6.85 (m, 2H), 6.66 (s, 1 H), −2.82 (s, 2H); UV/vis (CH_2Cl_2) λ_{max} (nm) 414 (Soret), 510, 540, 584, 640. Anal. Calcd for $C_{51}H_{17}F_{15}N_4O$: C, 62.08; H, 1.74; N, 5.68. Found: C, 61.99; H, 1.94; N, 5.42.

1-(5-Tris(10,15,20-mesitylporphyrinyl))-8-formylanthracene (7). The above procedures were used with the following exceptions. $CHCl_3$ was used as the solvent (3.5 L). The bridge:mesitaldehyde:pyrrole stoichiometry was 1:12:13. Following the alumina column, the mixture was chromatographed on silica (6 × 20 cm, 4:1 hexanes:CH_2Cl_2 → 2:1 hexanes:CH_2Cl_2): yield 570 mg (24% based on the bridge); mass spectrum m/e 868 (M^+); ^{1}H NMR ($CDCl_3$) δ 9.56 (s, 1H), 9.28 (s, 1H), 8.81 (s, 1H), 8.64 (d, 2H, J = 4.6 Hz), 8.62 (d, 2H, J = 4.6 Hz), 8.53 (d, 2H, J = 4.5 Hz), 8.49 (d, 2H, J = 4.5 Hz), 8.45 (d, 1H, J = 8.6 Hz), 8.32 (d, 1H, J = 8.6 Hz), 8.23 (d, 1H, J = 6.3 Hz), 7.90 (dd, 1H, J_1 = 8.6 Hz, J_2 = 6.2 Hz), 7.73 (d, 1H, J = 6.3 Hz), 7.51 (dd, 1H, J_1 = 8.6 Hz, J_2 = 6.3 Hz),7.29 (s, 1H), 7.26 (s, 1H), 7.23 (s, 2H), 7.21 (s, 2H), 2.62 (s, 3H), 2.57 (s, 6H), 1.97 (s, 3H), 1.86 (s, 6H), 1.84 (s, 6H), 1.82 (s, 3H), −2.34 (br s, 2H); UV/vis (CH_2Cl_2) λ_{max} (nm) 422 (Soret), 516, 550, 590, 646. Anal. Calcd for $C_{62}H_{52}N_4O$·1/2H_2O: C, 84.79; H, 6.09; N, 6.39. Found: C, 84.53; H, 6.25; N, 6.28.

1,8-Bis(5-tris(10,15,20-(pentafluorophenyl)porphyrinyl))biphenylene (20). The second Lindsey condensation proceeds identically to the first pentafluorobenzaldehyde condensation: 197 mg of porphyrin with formyl bridge **11** (0.20 mmol), 588 mg of pentafluorobenzaldehyde (3.0 mmol), 0.221 mL of pyrrole (3.19 mmol), 0.130 mL of BF_3 (1.06 mmol), 320 mL of CH_2Cl_2, and 1 g of DDQ. After normal workup and elution from the alumina column the product was purified by silica chromatography (5 × 25 cm, 8:1 hexanes:CH_2Cl_2 → 2:1 hexanes:CH_2Cl_2): yield 114 mg (32% based on the bridge porphyrin); mass spectrum m/e 1763 (M^+); ^{1}H NMR ($CDCl_3$) δ 8.66 (d, 2H, J = 4.7 Hz), 8.45 (d, 2H, J = 4.7 Hz), 8.07 (d, 2H, J = 4.6 Hz), 7.83 (m, 2H), 7.58 (m, 6H), 7.36 (t, 2H, J = 6.8 Hz), 7.14 (m, 4H), 6.48 (br d, 2H, J = 3.2 Hz), −5.40 (s, 4H); UV/vis (CH_2Cl_2) λ_{max} (nm) 402 (Soret), 514, 546, 590, 644. Anal. Calcd for $C_{88}N_8H_{24}F_{30}$: C, 59.88; H, 1.48; N, 6.35. Found: C, 59.81; H, 1.60; N, 6.12.

1,8-Bis(5-tris(10,15,20-mesitylporphyrinyl))anthracene (12). The second condensation proceeds identically to the first mesitaldehyde condensation: 570 mg of porphyrin with formyl bridge, **7** (0.66 mmol), 1.461 g of mesitaldehyde (10.5 mmol), 0.705 mg of pyrrole (9.86 mmol), 0.427 mL of BF_3 (3.47 mmol), 1.05 L of $CHCl_3$, 1.79 g of DDQ (7.92 mmol). Final purification was accomplished by silica chromatography (4 × 20 cm, 4:1 hexanes:CH_2Cl_2 → 2:1 hexanes:CH_2Cl_2): yield 130 mg (14% based on the bridged porphyrin); mass spectrum m/e 1504 (M^+ + 1); ^{1}H NMR (C_6D_6) δ 9.26 (s, 1H), 8.82 (s, 1H), 8.55 (d, 4H, J = 4.7 Hz), 8.42 (d, 4H, J = 4.7 Hz), 8.27 (d, 2H, J = 7.5 Hz), 8.19 (d, 4H, J = 4.7 Hz), 7.95 (d, 4H, J = 4.7 Hz), 7.35–7.4 (m, 4H), 7.08 (s, 2H), 6.98 (s, 4H), 6.92 (s, 4H), 6.64 (s, 4H), 2.36 (s, 6H), 2.35 (s, 12H), 1.90 (s, 6H), 1.62 (s, 12H), 1.59 (s, 6H), 0.21 (s, 12H), −2.72 (br s, 4H); UV/vis (CH_2Cl_2) λ_{max} (nm) 414 (Soret), 516, 550, 592, 646. Anal. Calcd for $C_{108}N_8H_{94}$·H_2O: C, 85.23; H, 6.36; N, 7.36. Found: C, 85.21; H, 6.48; N, 7.05.

Scheme 1

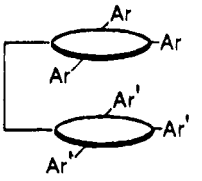


Results and Discussion

The general synthetic route is illustrated in Scheme 1. The dialdehyde bridge **2** (1,8-diformylbiphenylene or 1,8-diformylanthracene) is first monoprotected with 1 equiv of 1,3-propanedithiol. A mixture of three products (the diprotected, the monoprotected, and the unprotected dialdehyde) is produced, and these are separated on a silica column. The unreacted dialdehyde and the diprotected dialdehyde are isolated and recycled.

Lindsey porphyrin preparations are crucially dependent on solvent choice. We note that our mixed condensations sometimes involve benzaldehyde derivatives of differing reactivity. Thus, we expect the chosen solvent

Table 1. Free-Base *meso*-Tetraaryl Cofacial Diporphyrin



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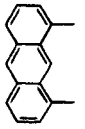
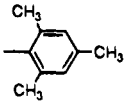
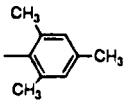
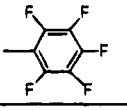
		(24)	7		(14) (24)[c]	12
					(18)	13
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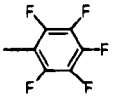
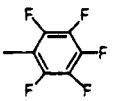
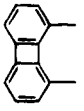
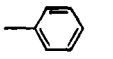
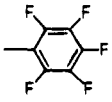
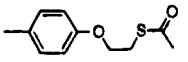
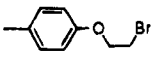
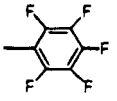
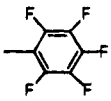
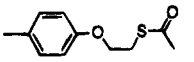
		(20)	9		(34)	15
		(33)	10		(30)	16
					(31)	17
					(6)	18
					(18)	19
		(22)	11		(32)	20
					(14)	21

[a] Isolated yield of monoporphyrin monoaldehyde, **5**. [b] Isolated yield of free-base cofacial diporphyrin, **6**. [c] Isolated yield of monometalated cofacial diporphyrin when the second condensation is done after the first porphyrin is metalated with zinc or nickel.

to reduce the overall yield in these cases. Tolerance of specific functional groups, steric limitations, and choice of acid catalyst (BF_3 or trifluoroacetic acid) are issues well-addressed by Lindsey.[12,13] We have found that fresh boron trifluoride etherate is essential to achieving good yields in these reactions.

The monoprotected monoaldehyde bridge **3** is then cyclized with pyrrole and the desired aryl aldehyde using the Lindsey procedure,[12] with modified stoichiometry, to give the protected monoporphyrin **4** in moderate yield. This is then deprotected in situ with BF_3 and DDQ to yield the monoporphyrin monoaldehyde **5** in >90% yield. Depending on the quantity of impurities present after the alumina column, more DDQ may be needed to complete the deprotection. (We sometimes deprotect prior to the alumina column, but this invariably requires excess DDQ and BF_3.) The alumina column typically allows isolation of essentially the desired product and the monomeric porphyrin (byproduct), and it is often possible to remove a large amount of the monomeric porphyrin at this stage. The deprotection is usually accomplished before final purification, because typically the free aldehyde is easier to separate from the monomeric porphyrin.

The final cofacial diporphyrin **6** is then obtained by

allowing **5** to react with pyrrole and the benzaldehyde of choice in another Lindsey condensation. Successful syntheses have been realized with stoichiometries varying from 1:12:13 to 1:31:32 (bridged-porphyrin:phenyl aldehyde:pyrrole). The desired product is cyclized in higher yields when higher reagent ratios are employed; however, at high ratios the yield of the monomeric porphyrin byproduct (usually the major component of the product mixture) is increased disproportionately. Thus, the choice of reagent ratio is a balance between higher cyclization yields and difficulty of purification. We note that the initial isolation and identification of the cofacial porphyrin is greatly aided by two distinct spectroscopic markers: the blue-shifted Soret in the UV/vis spectrum and the high field signals of the *N*-pyrrolic resonances in the ^{1}H NMR.

Through this general synthetic method, we are able to synthesize cofacial homoporphyrin dimers (the two porphyrin rings are identical), heteroporphyrin dimers (the two porphyrin rings are different), as well as heterometallic diporphyrins (two different metals in the cofacial diporphyrin; the two porphyrin rings can be identical or different).

Heterometallic species are synthesized conveniently by metallation[18] after the first porphyrin condensation. Depending on the reactivity of the first metal to be inserted (e.g., Ti), the monoporphyrin **4** may be isolated and purified prior to deprotection. For other metals (e.g., Ni, Zn) the aldehyde presence will not interfere with the metalation procedure and deprotection can be accomplished prior to metal insertion. After the final porphyrin condensation (performed under identical conditions as those described for unmetalated derivatives) the second metal can be inserted. For the mesitaldehyde condensations (e.g., **12**), the subsequent yield of the second porphyrin condensation is considerably increased (by roughly a factor of 2) when nickel or zinc has been inserted into the first porphyrin. Presumably, this is the result of improved cyclization; the monometalated derivative is not easier to isolate from the homoporphyrin than is the bis-free base. Table 1 shows some of the free-base cofacial diporphyrins that have been synthesized thus far.

The Lindsey conditions accommodate many different types of benzaldehydes[12] with varying results in yields. Lower yields are obviously a result of the inherent reactivity of the parent benzaldehyde derivative, but other factors play a role as well. Since these are mixed condensations, multiple porphyrin products are obtained and isolation of the desired product is correspondingly more difficult. Larger scale reactions tend to give lower yields—again, we believe this to result from the difficulty in purification. Poor solubility of the undesired monomeric porphyrin makes for difficult isolation of the desired porphyrin—invariably the symmetric monomeric porphyrin has a higher R_f (and lower solubility) than the bridged porphyrin; this monomer partially precipitates on top of the column and then leaches through continuously during the elution. This is a problem in particular with the phenyl and mesityl porphyrins. If the desired

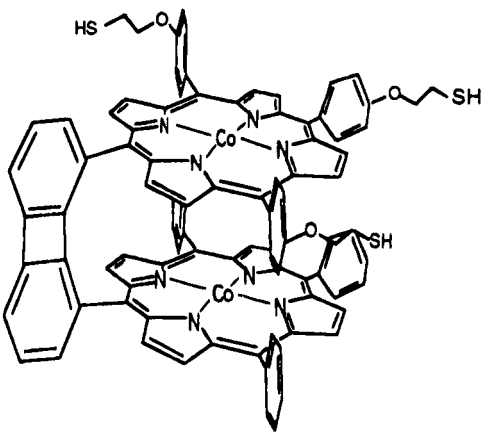


Figure 1.

porphyrin has low mobility on the silica (due to its constituent benzaldehyde derivative); in general, the isolated yield will be lower because of the preponderance of impurities with low R_f's.

Although these cofacial diporphyrins are easily made in four steps (starting from the bridge), they are not conveniently synthesized on a large scale (>1 g) because they are prepared under high dilution conditions and rely on silica chromatography as a means of purification. The cofacial homoporphyrin **12** or **15** can be synthesized in one step by allowing **2a** to react with pyrrole and the corresponding benzaldehyde. The yield of **12** or **15** in this case is comparable to the overall yield of the four step synthesis as shown in Scheme 1. The chromatographic separations are expectedly more difficult. We believe this result can be extended to other benzaldehydes.

We initially attempted deprotection of **4** using the various methods available for the deprotection of thioacetals and ketals,[17b] e.g., oxidation reactions[19] and alkylations.[20] These methods produced unsatisfactory yields and undesirable side products. Sankarama et al. recently reported that DDQ could effect photochemical deprotection of a variety of thioacetals.[21] Irradiation with a mercury lamp or reflux in acetonitrile was required. Lower yields were achieved when the reaction was carried out at room temperature.[22] In the course of our work, we have found that DDQ in the presence of an acid catalyst (BF_3 or CCl_3CO_2H) leads to clean deprotection of **4** in high yields (>90%). These reactions proceed at room temperature in CH_2Cl_2 or $CHCl_3$ in the presence of air (water is present as a byproduct of porphyrin condensations). The reaction is quite facile; indeed, care must be taken in order to isolate **4** under the reaction conditions. The reaction requires catalytic amounts of acid and stoichiometric amounts of DDQ. At higher concentrations (including that of BF_3) the deprotection is essentially instantaneous. Substituting *p*-chloranil for DDQ does not afford deprotection of the aldehyde (the $1e^-$ reduction potential of the former is 0.5 V less than that of DDQ).[23] The reactions are run in normal laboratory light; no cleavage was detected under identical conditions without the addition of an acid catalyst. This

(18) Metallation of free base porphyrins are performed according to published procedures. (a) Fuhrhop, J. H.; Smith, K. M. In *Porphyrins and Metalloporphyrins*; Smith, K. M., Ed.; Elsevier Scientific Publishing Co.: Amsterdam, 1975; Chapter 19, pp 795–804. (b) Buchler, J. W. In *The Porphyrins, Vol. 1, Structure and Synthesis, Part A*; Dolphin, D., Ed.; Academic Press, Inc.: New York, 1978; Chapter 10, pp 389–483.

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method allowed us to recycle the diprotected bridges in high yield.[24]

Conclusion

We have developed an expedient, efficient, and general method for cofacial diporphyrin synthesis which allows for the systematic variation of the structural and electronic characteristics of these molecules. We are employing cofacial metallodiporphyrins synthesized via this method in our current investigations of the binding and activation of small molecules.

The bis-cobalt derivatives of **18** and **21** (see Table 1) prove to be potent catalysts for the four electron reduction of dioxygen when adsorbed on edge plane pyrolytic graphite electrodes.[25] The bis-cobalt trimercaptan derivative of **18** has been investigated for its catalytic activity for dioxygen reduction when adsorbed on gold electrodes (Figure 1).[26]

Electronic and steric requirements for dioxygen reduction are also being investigated at this time. Iridium derivatives of **12** and **14** have been used in mechanistic studies on dioxygen reduction catalysis.[27]

In addition to dioxygen activation, these cofacial porphyrins are also being used to study the binding and activation of other small molecules. Preliminary data indicate that dinitrogen bridges the bis-ruthenium derivative of **14**.[28] Bis-ruthenated **12** catalyses the pairwise exchange of H_2/D_2, and we are employing it and its ruthenium–nickel mixed metal analog in our investigations concerning the mechanism of this fundamental reaction.[29] The activation of C–H bonds in methane and small aromatic hydrocarbons by the bis-rhodium derivatives of **12** are currently under examination in our laboratories. We believe the steric bulk of the constituent porphyrins combined with the relatively long anthracene bridge precludes the formation of both intramolecular and intermolecular metal–metal bonds involving 4d and 5d metals.[9,30,31] Thus, the ability to support two electron-poor metals in close proximity may account for the intriguing behavior of this molecule.

Acknowledgment. The support of the National Science Foundation is gratefully acknowledged. We thank the Mass Spectrometry Facility at the University of California at San Francicso, supported by NIH Division of Research Resources grant RR01614 and by NSF grant DIR8700766.

Supplementary Material Available: Characterization of **4a,b**, **7(Ni, Zn)**, **8–10**, **12(Ni, Zn)**, **13–19**, and **21** (4 pages). This material is contained in libraries on microfiche, immediately follows this article in the microfilm version of the journal, and can be ordered from the ACS; see any current masthead page for ordering information.

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