

Stacked Double-Macrocyclic Ligands II. Synthesis of Cofacial Diporphyrins (1-2)

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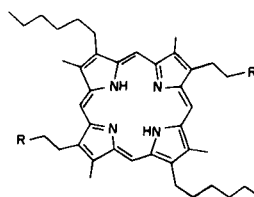
A new class of dimeric porphyrin ligands and their metal complexes have been prepared by an unambiguous and high-yield synthetic scheme.

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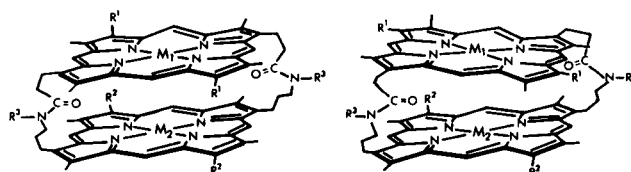
Sir:

Recent advances in bioinorganic chemistry have identified the need for well-defined binuclear metal complexes serving as models for a large number of metalloenzymes. We consider the dimetal complexes of two porphyrins constrained in a face-to-face conformation (hereafter termed "cofacial diporphyrins") to be particularly attractive in that they have the potential to convert light into redox potential and to catalyze specific redox reactions involving molecular oxygen (3-6). The synthesis of these composite dimers are currently under active pursuit and several groups have just reported their results (6-8). We wish to report here an unambiguous as well as esthetically pleasing synthetic scheme by which cofacial diporphyrins and their mixed metal complexes can be prepared in high yield.

Careful consideration of the chemistry of pyrroles and porphyrins led to a synthesis based on a number of premises: (a) A basic porphyrin monomer carrying diagonally functionalized side chains should be synthesized in large quantity. (b) The coupling of the two porphyrins should be in such a manner that the resultant dimer with dissimilar porphyrins and/or hetero metal ions can be obtained unambiguously. (c) The diporphyrins must have relatively high solubility so that a wide range of investigations can be carried out in solution. Recently, we have described a very efficient total synthesis using a modified pyrromethene route to provide 2,6-dihexylporphyrin II (1) in high yield (2). This porphyrin, for reason of its symmetry and high solubility in organic solvents, is an ideal building block for composite dimers. Thus the porphyrin ester 1 was reduced by lithium aluminum hydride in THF and converted to the mesylate 3 by treating with mesityl chloride in dichloromethane/triethylamine, which was then refluxed with *n*-butylamine to give the diamine 4 with almost quantitative yield from 1. The coupling of two porphyrins was effected using a high dilution, slow mixing procedure (2). Equimolar solutions (concentration *ca.* 5 mM) of the porphyrin diamine and the diacid chloride 2 in dichloromethane along with a third solution of triethylamine were injected simultaneously to 250 ml. refluxing dry dichloromethane/-



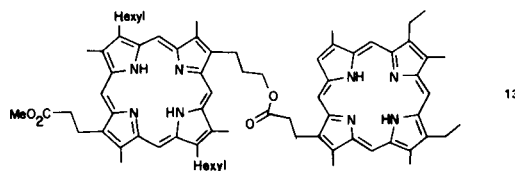
- 1 R = COOMe
- 2 R = COCl
- 3 R = CH₂OSO₂Me
- 4 R = CH₂NH(CH₂)₃CH₃
- 6 R = CH₂NHCH₂Ph



(a) SYN-

(b) ANTI-

- | | | | |
|--|----------------------------------|--|--------------------------------------|
| 6 R ¹ = <i>n</i> -hexyl | R ² = <i>n</i> -hexyl | R ³ = <i>n</i> -butyl | M ₁ = M ₂ = 2H |
| 7 R ¹ = methyl | R ² = <i>n</i> -hexyl | R ³ = CH ₂ Ph | M ₁ = M ₂ = 2H |
| 8 R ¹ = R ² = <i>n</i> -hexyl | R ³ = <i>n</i> -butyl | M ₁ = M ₂ = Fe ^{III} Cl | |
| 9 R ¹ = R ² = <i>n</i> -hexyl | R ³ = <i>n</i> -butyl | M ₁ = M ₂ = Cu ^I | |
| 10 R ¹ = R ² = <i>n</i> -hexyl | R ³ = <i>n</i> -butyl | M ₁ = M ₂ = Zn ^{II} | |
| 11 R ¹ = R ² = <i>n</i> -hexyl | R ³ = <i>n</i> -butyl | M ₁ = 2H | M ₂ = Cu ^I |
| 12 R ¹ = R ² = <i>n</i> -hexyl | R ³ = <i>n</i> -butyl | M ₁ = Fe ^{III} Cl | M ₂ = Cu ^I |



benzene mixture at a rate of 10 ml./hour *via* a syringe pump. The resulting dimeric porphyrin, being the only compound movable on silica gel using chloroform as the eluent, can be easily purified by chromatography (silica gel/chloroform). Typical yields of the diporphyrin from a 0.2 mmole batch were in the range of 55-65% based on the porphyrin diamine 4. (Example: 150 mg. each of 2 and 4 would provide ~ 160 mg. of the dimer.) We have tried

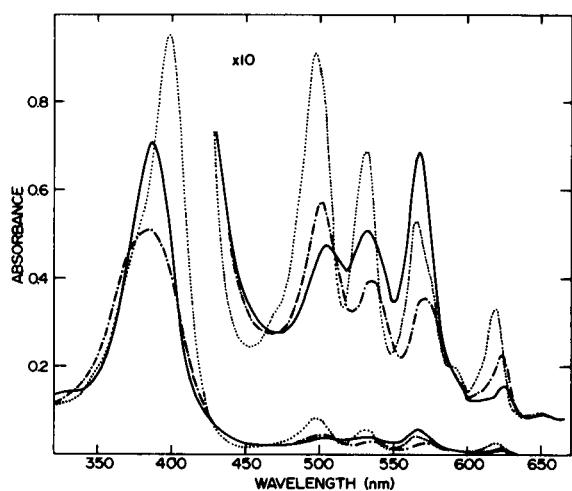


Figure 1. Visible absorption spectra of the parent porphyrin **1** (....), diporphyrin **6** (-.-), and the Cu-H₂ diporphyrin **11** (-.-), measured in dichloromethane at 24°. Concentrations: **1**, $5.62 \times 10^{-6}M$; **6**, $2.68 \times 10^{-6}M$; **11**, $2.88 \times 10^{-6}M$.

to couple the dialcohol of **1** with the acid chloride **2** by the same procedure but only obtained less than 3% of the diporphyrin with two ester linkages (**7**). In addition to

the apparent synthetic advantage, the amide linkages in our diporphyrins have proved to be very stable towards strong acids and bases.

The diporphyrins prepared by this route may give two isomers, designated as "syn" and "anti". Attempts to separate them on tlc plates have not been successful. The pmr spectrum of **6** in deuteriochloroform exhibited seven weak signals at 8.8-9.8 δ , belonging to the meso protons of the two isomers. It is noteworthy that the nitrogen protons were found at -6.3 δ . Since the inner NH signals are usually around -4 δ for monomeric alkyl porphyrins such as **1**, this large upfield shift indicates extensive ring current interactions in **6** (**9**). The pmr signals of the peripheral alkyl substituents all fell in the region of 4.3-0.5 δ and cannot be resolved because of the isomeric nature of the compound. The resolution was improved when the diporphyrin **7** was synthesized and examined by pmr (**10**). Here the sharp singlet of the six methyl protons of the parent 2,6-dimethyldeuterioporphyrin II (3.52 δ) was found to remain at 3.4 δ in the diporphyrin **7**. This is expected since the β -substituents of one porphyrin fall in the "blank region" of the anisotropic shielding effect of the second ring (**11**), if we assume the interplanar distance is close to 6.4 Å (**22**).

Table 1

Porphyrin Absorption Spectra and Fluorescence Intensities (a)

Compound	λ nm	Absorption (ϵ mM)				λ max	Fluorescence		Φ_F (d)
							Relative Intensity/ Concentration (b)	Relative Intensity/ O.D. (c)	
1 (H ₂)	398 (169.9)	497 (14.30)	532 (10.46)	566 (8.89)	618 (4.40)	619	1.147	1.045	0.094
6 (H ₂ -H ₂)	384 (191)	502 (17.74)	535 (11.70)	571 (10.29)	624 (5.54)	628	0.428	0.385	0.034
7 (H ₂ -H ₂)	382 (194)	504 (15.63)	537 (11.25)	572 (9.38)	625 (5.47)	628	0.347	0.319	0.029
11 (Cu-H ₂)	387 (246.5)	505 (14.06)	534 (15.24)	568 (21.49)	626 (2.95)	623	0.045	0.032	0.003
13 (H ₂ ,H ₂)	397 (205)	497 (20.5)	532 (14.06)	566 (11.65)	618 (6.02)	621	1.027	0.766	0.07
Etio I (H ₂)	397 (154)	497 (13.74)	530 (9.58)	565 (6.47)	617 (4.73)	619	1.000	1.000	0.09
10 (Zn-Zn)	388		538	570					
12 (Fe-Cu)	385	505	529	565	624-645				
8 (Fe-Fe) (e)	411		516	546					
9 (Cu-Cu)	386		531	562					

(a) In distilled dichloromethane, 24°. Absorption spectra were measured on a Cary 17 spectrophotometer. Fluorescence was measured with a Aminco-Bowman spectrophotofluorometer (λ excitation = 395 nm). Relative yields were measured according to standard procedures (15,16). Solutions at $5 \times 10^{-8} M$ were prepared using a Cahn electrobalance. (b) Relative integrated photon intensity divided by molar concentration. Etioporphyrin I was used as reference. (c) Relative integrated photon intensity divided by O.D. of the solution at excitation wavenlength. These data are proportional to the fluorescence quantum yields. (d) Fluorescence quantum yields assuming yield for etioporphyrin I = 0.09 (reference 16). (e) Reduced by dithionite in the presence of pyrazine or imidazole, presumably a bridged binuclear complex is formed.

While metal ions can be easily inserted into the diporphyrins to yield Fe-Fe (**8**), Cu-Cu (**9**), Zn-Zn (**10**) and other dimetal complexes (**12**), our synthetic approach has proved successful in preparing hetero metal complexes. Therefore, the Cu(II) complex of diamine **4** was condensed with the diacid chloride **2** to give the Cu(II)-H₂diporphyrin **11**. Insertion of iron to **11** by the standard ferrous sulfate/acetic acid method (**12**) afforded the Cu(II)-Fe(III)Cl complex **12**. The structure of all diporphyrins and metal complexes has been verified by mass spectra (**13**). Elemental analysis performed on **6** was also consistent with the indicated structure (**14**). The electronic absorption spectra are shown in Figure 1 and the absorption and luminescence data tabulated in Table 1.

A prominent feature of the diporphyrins revealed by these spectroscopic studies is a 14-16 nm blue shift of the Soret band accompanied by a quenching of fluorescence, with respect to that in the monomer. This strongly suggests the presence of exciton interaction (**17**). Under the conditions of exciton coupling, the electronic interaction between the chromophores is so strong that photon absorption results in the collective excitation of both chromophores. A splitting of energy levels occurs as the result of this coupling. Kasha, *et al.*, (**17**), have shown that with two parallel transition dipoles the exciton state is displaced upwards, thus, a blue shift may be produced. This blue shift of the Soret band has been seen by Collman, *et al.*, for the TPP systems (**6**), but was curiously absent in Ogoshi's compounds (**18**). The overall spectral difference in fact is related to two parameters, *i.e.*, the exciton shift factor which is proportional to the oscillator strength, and the environment factor which depends upon the polarizability of the environment (**19**). It has been suggested (**20**) that in porphyrin dimers while the exciton shift causes the absorption peak to move to the blue, the environment term causes a red-shift. The drastic difference in the oscillator strength between the Q bands (visible region) and the B band (Soret) may be responsible for the slight red-shift of the visible bands observed in the diporphyrins.

In addition to the doubly connected diporphyrins we have synthesized a singly connected dimeric porphyrin **13** (**21**). It is evident from Table I that the absorption spectrum of **13** is almost identical to that of monomeric porphyrins and its fluorescence intensity suggests that the two porphyrin moieties behave more like two separate chromophores. Clearly a single linkage is not sufficient to bring about a true cofacial conformation for the two rings.

Detailed study on metal-metal interactions and ligand binding properties of the diporphyrins are underway.

REFERENCES AND NOTES

(1) Acknowledgments are gratefully made for support of this

work by Research Corporation.

- (2) Paper I, C. K. Chang, *J. Am. Chem. Soc.*, **99**, 2819 (1976).
- (3) F. P. Schwarz, M. Gouterman, Z. Muljani, and D. Dolphin, *Bioorg. Chem.*, **2**, 1 (1972).
- (4) J.-H. Fuhrhop, *Angew. Chem., Int. Ed. Engl.*, **15**, 648 (1976).
- (5) J. A. Anton, J. Kwong, and P. A. Loach, *J. Heterocyclic Chem.*, **13**, 717 (1976).
- (6) J. P. Collman, C. M. Elliott, T. R. Halbert, and B. S. Tovrog, *Proc. Natl. Acad. Sci. USA*, **74**, 18 (1977).
- (7) H. Ogoshi, H. Sugimoto, and Z. Yoshida, *Tetrahedron Letters*, 169 (1977).
- (8) N. E. Kagan, D. Mauzerall, and R. B. Merrifield, Abstracts of Papers, 11th Middle Atlantic Regional Meeting of the American Chemical Society, Newark, Delaware (1977).
- (9) Concentration dependent upfield shifts are common for monomeric porphyrins, presumably caused by self-aggregation. See reference 11 for a general discussion. Similar shifts have been described, *c.f.* reference 6.
- (10) Diporphyrin **7** was synthesized by condensing **5** and 2,6-dimethyldeuteroporphyrin II diacid chloride. The latter porphyrin was prepared by self-condensation of 3,4,3',5'-tetramethyl-5-carboxyl-4'-(2-carbomethoxyethyl)dipyrromethene hydrobromide in formic acid with bromine (see reference 2).
- (11) H. Scheer and J. J. Katz in "Porphyrins and Metalloporphyrins", K. M. Smith, Ed., Elsevier, New York, N.Y., 1975, p. 402.
- (12) By the ferrous sulfate/acetic acid, the zinc acetate, and the cupric acetate methods, respectively. See J.-H. Fuhrhop and K. M. Smith in "Porphyrins and Metalloporphyrins", K. M. Smith, Ed., Elsevier, New York, N.Y., 1975, p. 757.
- (13) Mass spectral parent ions with correct mass units were obtained with a Varian MAT-CH5 mass spectrometer operating in the field desorption mode. The molecular ions can also be observed by direct electron impact when operated with a probe temperature at 310° and 70 eV.
- (14) Diporphyrin **6** (*Anal. Calcd.* for C₄₈H₃₂N₄: C, 79.19; H, 8.46; N, 10.04. *Found*: C, 79.08; H, 8.53; N, 10.11.) Elemental analyses of the metal complexes **8** and **9** yielded lower carbon contents, presumably caused by complexation of water and solvent molecules by the metal ions.
- (15) C. A. Parker and W. T. Rees, *Analyst*, **85**, 587 (1960).
- (16) P. G. Seybold and M. Gouterman, *J. Mol. Spectros.*, **31**, 1 (1969).
- (17) M. Kasha, H. R. Rawls, and M. A. El-Bayoumi, *Pure Appl. Chem.*, **11**, 371 (1965).
- (18) The Zn-Zn complex **10** as well as other metal derivatives of **6** all exhibit the pronounced blue shift. We have recently synthesized a series of diporphyrins with ring separations ranging from 4.2 Å to 6.4 Å and observed that the magnitude of the blue shift is indeed a function of the ring separation, the tighter the gap the more pronounced the shift. (*C.f.* reference 22).
- (19) J. B. Birks, "Photophysics of Aromatic Molecules," Wiley-Interscience, New York, N.Y., 1970, pp. 523-528.
- (20) M. Gouterman, private communication.
- (21) Prepared by condensation of the monoalcohol monoacid of **1** and pyrroporphyrin XV acid chloride. The former porphyrin was obtained by partial reduction of **1** by lithium aluminum hydride and the pyrroporphyrin was derived from chlorophyll (R. K. DiNello and C. K. Chang in "The Porphyrins," D. Dolphin, Ed., Vol. 1, Part A., Academic Press, New York, N.Y., in press).
- (22) The interplanar separation was estimated by epr studies of two interacting paramagnetic metal centers. (C. K. Chang, *J. Am. Chem. Soc.*, manuscript submitted).