Strong Interactions in Covalently Stacked Trimeric Porphyrins

Gene M. Dubowchik and Andrew D. Hamilton*

Department of Chemistry, Princeton University, Princeton, New Jersey 08544, U.S.A.

The synthesis is reported of a closely stacked 'triple-decker' porphyrin which shows, by n.m.r., u.v.–visible, and fluorescence spectroscopy, strong interactions between the rings.

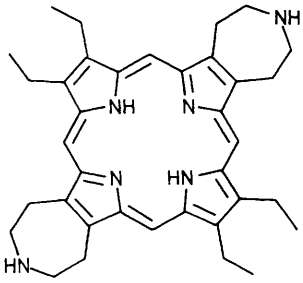
Specifically ordered aggregates of tetrapyrroles are found in many biochemical structures including tetrahaeme enzymes, haemoglobin and cytochrome c_3, and in multi-chlorophyll photosynthetic reaction centres. A key question concerns the nature and extent of interactions between the pigments and the unique properties imparted to the aggregate beyond those found in the monomeric unit.[1] The synthetic model approach has been particularly effective in probing this problem and a number of synthetic porphyrin aggregates have been reported.[2] As a result of our interests in multiple chromophoric molecules[3] we have developed[4] routes to covalently linked porphyrins in order to probe the relationship between aggregate structure and spectroscopic and electron transfer properties. In this paper we report the synthesis of a closely spaced porphyrin trimer which shows strong inter-porphyrin interactions.[5]

Our synthetic route employs a linear, stepwise sequence with the diaminoporphyrin (**1**)[4] in the two outer ring positions. The porphyrin (**1**) has D_{2h} symmetry and thus avoids the problems of diastereoisomerism encountered in this approach when porphyrins of C_{2h} symmetry are used.[5b] In addition the aza seven-membered rings ensure relatively close and rigid connections to a second porphyrin.

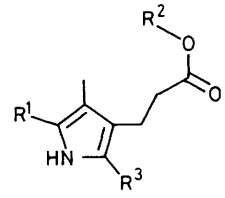
The central porphyrin derives from selectively protected coproporphyrin-II (**2**).[6] This was prepared by the following novel route. Reaction of the acetoxymethylpyrrole (**3**)[7] with the α-free pyrrole (**4**)[7] (CH_2Cl_2, *p*-$MeC_6H_4SO_3H$) gave the pyrromethane (**5**).† Acidic decarboxylation (CF_3CO_2H) and formylation [$(EtO)_3CH$] of (**5**) provided the formylpyrromethane (**6**)† which was smoothly debenzylated (H_2, Pd–C) to give the diacid (**7**)† in 75% overall yield from (**3**). The required diester diacid (**2**)†‡ was formed directly from (**7**) in 50% yield by treatment with acid (CF_3CO_2H, CH_2Cl_2).§

High dilution coupling (10^{-3} M, CH_2Cl_2, Et_3N) of the diamine (**1**) and diacid chloride (**8**) [formed from (**2**) and oxalyl chloride] provided the diester porphyrin dimer (**9**)† (M^+ 1207.6534, $C_{74}H_{82}N_{10}O_6$ requires 1207.6497) in 42% yield. The dimer (**9**) had u.v.–visible (Soret at 374 nm) and n.m.r. (δ_{NH} ~ −8) properties similar to those of the previously reported[4] unfunctionalised dimer. Mild base hydrolysis (KOH, EtOH–tetrahydrofuran) to give the diacid (**10**) followed by treatment with oxalyl chloride provided the diacid chloride (**11**).† The target trimer (**12**) (M^++H, *m/z* 1703.9532, $C_{108}H_{119}N_{16}O_4$ requires 1703.9599) was isolated in 20—30% yield by silica gel preparative layer chromatography (eluant CH_2Cl_2, MeOH) following a high dilution coupling (10^{-3} M, CH_2Cl_2, Et_3N) of (**11**) and a second equivalent of the diamine (**1**).

The ^{1}H n.m.r. spectrum of (**12**) shows two sets of NH signals, at δ −8.15 (4H) from the flanking porphyrins and at δ −10.55 (2H) from the central porphyrin. These large upfield shifts [relative to monomer (**1**), δ_{NH} −3.8] confirm the sandwich structure of (**12**), with the central ring coming under the influence of two anisotropic ring currents, and reflect the

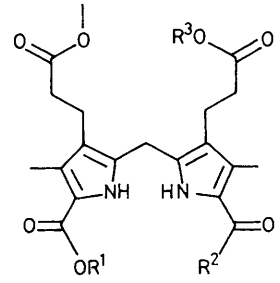


(**1**)



(**3**) $R^1 = CO_2Bu^t$, $R^2 = CH_2Ph$, $R^3 = CH_2OAc$

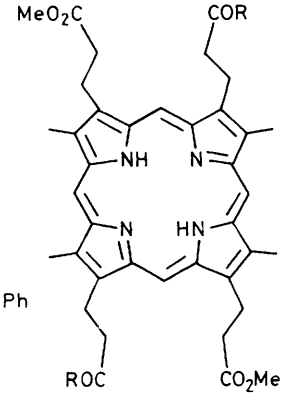
(**4**) $R^1 = CO_2CH_2Ph$, $R^2 = Me$, $R^3 = H$



(**5**) $R^1 = CH_2Ph$, $R^2 = OBu^t$, $R^3 = CH_2Ph$

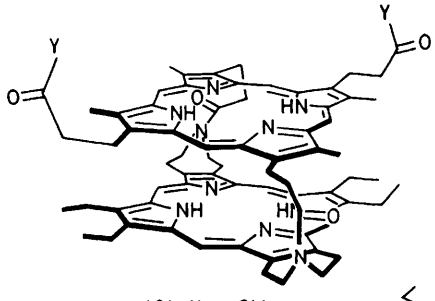
(**6**) $R^1 = CH_2Ph$, $R^2 = H$, $R^3 = CH_2Ph$

(**7**) $R^1 = R^2 = R^3 = H$



(**2**) R = OH

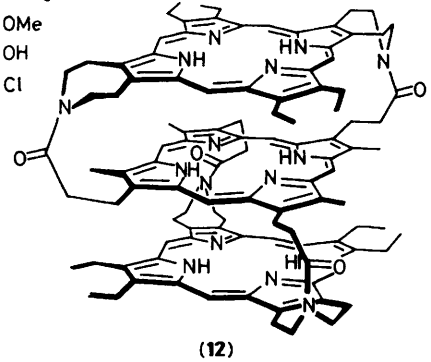
(**8**) R = Cl



(**9**) Y = OMe

(**10**) Y = OH

(**11**) Y = Cl



(**12**)

† All new compounds gave satisfactory spectroscopic, analytical, and/or mass spectral data.

‡ (**2**): ^{1}H n.m.r. in $(CD_3)_2SO$, δ 10.12, 10.05 (4H, 2 s, *meso*-H), 4.34 (8H, m, porp.CH_2), 3.64, 3.60 (12H, 2 s, porp.Me), 3.57 (6H, s, OMe), 3.21 (8H, m, $COCH_2$), and −3.98 (2H, s, NH).

§ For a related coupling see ref. 7, p. 177.

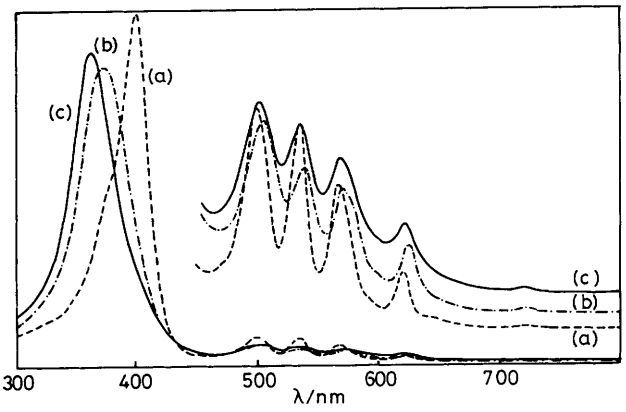


Figure 1. U.v.–visible spectrum of monomer (**1**) (a), dimer (**9**) (b), and trimer (**12**) (c) in CH_2Cl_2.

proximity of the stacked porphyrins (estimated at ~4 Å from Corey–Pauling–Koltun models). A simplified *meso* proton region containing 6 major peaks between δ 6.6 and 9.4 (each 2H) suggests that the trimer is predominantly in a double parallel conformation[4] with a cofacial orientation of the rings.

Further evidence for strong interaction between the rings comes from optical spectroscopy (Figure 1). The Soret band in (**12**) (at 364 nm) is blue-shifted 37 nm relative to the monomer (**1**) and 10 nm compared to the dimer (**9**) (see Table 1). These large shifts are presumably due to exciton coupling between the rings which results in excitation into a higher energy state in which all three transition dipoles are parallel and in phase.[8] The proximity of the rings also results in a strong quenching of fluorescence emission (see Table 1). With each additional ring there is a red shift in the emission wavelength (7—9 nm) and an increase in quenching to the point where the fluorescence emission of trimer (**12**) is reduced 450 fold relative to monomer (**1**).

Controlled metallation of (**12**) [*e.g.* $Zn(OAc)_2$, 2.2 equiv., CH_2Cl_2–MeOH] provides the symmetrical bis-metal derivative with zinc in the two outer porphyrins. More forcing conditions [excess of $Zn(OAc)_2$] lead to the tris-zinc system. We are continuing our characterization of (**12**) and its various metal derivatives and are extending our synthetic strategy to other oligomers with different orientations and compositions as models for biological multi-tetrapyrrole sites.

Table 1. U.v. data for the porphyrins.

Porphyrin	λ_{max}/nm (S = Soret)	$Q(00)$/nm[a]	Φ_F[a]
Monomer (**1**)	401(S), 499, 536, 566, 620	619	0.09
Dimer (**9**)	374(S), 505, 540, 571, 626	628	0.004
Trimer (**12**)	364(S), 504, 537, 570, 623	635	0.0002

[a] In degassed CH_2Cl_2 at 25 °C.

We thank the National Institutes of Health for financial support of this work.

Received, 2nd January 1986; Com. 005

References

1 See 'The Porphyrins,' ed. D. Dolphin, Academic Press, New York, 1978.
2 J. E. Baldwin and P. Perlmutter, *Top. Curr. Chem.*, 1984, **121**, 181; D. Dolphin, J. Hiom, and J. B. Paine, III, *Heterocycles*, 1981, **16**, 417.
3 A. D. Hamilton, H. D. Rubin, and A. B. Bocarsly, *J. Am. Chem. Soc.*, 1984, **106**, 7255.
4 G. M. Dubowchik and A. D. Hamilton, *J. Chem. Soc., Chem. Commun.*, 1985, 904.
5 Other related trimeric porphyrins with relatively weak interactions include (a) S. G. Boxer and R. R. Buck, *J. Am. Chem. Soc.*, 1979, **101**, 1883; (b) M. R. Wasielewski, M. P. Niemczk, and W. A. Svec, *Tetrahedron Lett.*, 1982, 3215; (c) I. Abdalmuhdi and C. K. Chang, *J. Org. Chem.*, 1985, **50**, 411.
6 For differentially-protected coproporphyrin-I derivatives see A. R. Battersby, S. G. Hartley, and M. D. Turnbull, *Tetrahedron Lett.*, 1978, 3169.
7 Prepared by standard methods; see J. B. Paine, III, in 'The Porphyrins,' ed. D. Dolphin, Academic Press, New York, 1978, Vol. I, p. 149.
8 M. Kasha, H. R. Rawls, and M. A. El-Bayoumi, *Pure Appl. Chem.*, 1965, **11**, 371.