A Pyropheophorbide Dimer with Single Pyrrole π Overlap and a Low-Energy Q Absorption

Spencer Knapp,* Buwen Huang, Thomas J. Emge,
Suzie Sheng, Karsten Krogh-Jespersen,
Joseph A. Potenza,* and Harvey J. Schugar*

Department of Chemistry
Rutgers—The State University of New Jersey
New Brunswick, New Jersey 08854-8087

Plant P_{680} chlorophyll special pairs differ significantly from their structurally characterized bacterial counterparts [(BChl)₂].[1] Distinctive features of P_{680} special pairs include their 3−4-fold smaller inter-chromophoric electronic coupling (∼140 cm⁻¹)[2,3] and an oxidation potential[4] elevated by about 0.5 V from the value expected under the assumption that the P_{680} and (BChl)₂ are closely isostructural. The absence of a structure at atomic resolution for a plant photosynthetic reaction center has stimulated the study of model dimers to probe the structural dependence of spectroscopic and other features.[2,5−8] We report the characterization of a Zn(II) pyrochlorophyll *a* dimer **5** that shows (BChl)₂-like pyrrole-over-pyrrole overlap and electronic coupling in solution but forms a staircase polymer in the solid state.

Methyl pyropheophorbide *a* (**1**, Chart 1), prepared[9] from an extract of *Spirulina pacifica*, was oxidized[10] to the 2-carboxaldehyde, which was converted to its oxime derivative and further by zinc(II) insertion to the zinc(II) pyropheophorbide derivative **2**. In CHCl₃, **2** formed a mutually coordinated dimeric structure (**5**) according to spectroscopic and other evidence. Osmometric MW determination at 15.559 mg/3.000 mL of CHCl₃ gave 1235 Da (calcd for the dimer, $C_{66}H_{66}N_{10}O_8Zn_2$, 1257 Da).

The ¹H NMR spectrum of **5** in CDCl₃ (5 mg/mL) exhibits a single set of pyropheophorbide signals, some of which appear at unusually high field. Assignments are based on ROESY measurements and, for the oxime CH signal, the observation of ¹H−¹⁵N coupling ($J = 2.4$ Hz) in the ¹⁵N-labeled analogue **4**. Figure 1 illustrates the chemical shift differences (Δδ) between **5** and the monomeric zinc(II) pyropheophorbide formed by adding 2 equiv of 4-(*N*,*N*-dimethylamino)pyridine[11−13] (=**2·DMAP**). Protons in **5** are shielded according to their approximate distance from the oxime nitrogen, suggesting a ring current effect due to an overlying partner pyropheophorbide whose zinc is coordinated to the oxime. Cooling the CDCl₃ solution of **5** broadened all signals, whereas warming to 65 °C partially shifted the shielded signals closer to positions expected for monomeric pyropheophor-
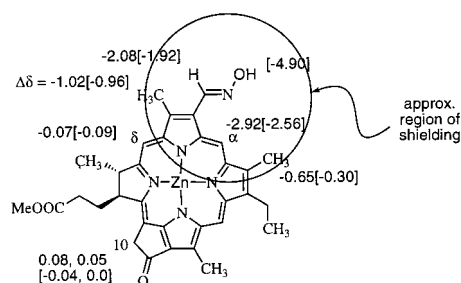
Figure 1. ¹H NMR shielding effects for pyropheophorbide dimer **5**: Δδ = δ(**5**) − δ(**2·DMAP**), and in brackets, [Δδ] = δ(**5**) − δ(free ligand).

## Chart 1
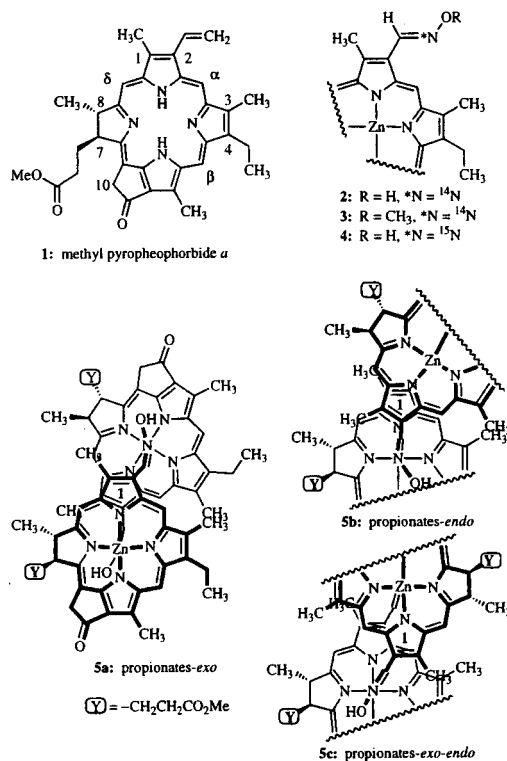
bide. Titration of the CDCl₃ solution of **5** with 2.5 equiv of pyridine-d_5 gradually shifted the signals to positions indicating monomeric **2·pyridine-d_5**. In particular, the (apparently nonacidified) oxime hydroxyl proton moves smoothly from its strongly shielded position in **5** at δ 3.9 to 8.8 in **2·pyridine-d_5**, suggesting that the zinc(II) is coordinated in **5** to the oxime N rather than O. Interestingly, the corresponding *O*-methyloxime zinc(II) pyropheophorbide (**4**) does not form a dimer in CDCl₃ solution according to NMR analysis, perhaps because of increased steric hindrance to zinc coordination at nitrogen.

The NMR experiments indicate that monomer−dimer exchange, which might have given rise to an additional set of signals,[14] is instead rapid on the NMR time scale. This reflects the weak ligating ability of oxime nitrogen toward zinc(II)[15] compared with the pyridine, imidazole, or amino nitrogen of related porphyrin dimers.[11−13,16] The NMR experiments are also consistent with any or all of three different pyropheophorbide facial contacts in **5**: propionates-*exo* (**5a**), propionates-*endo* (**5b**), and propionates-*exo−endo* (**5c**). Rapid equilibration among two or three of these could be occurring but cannot be discerned. Ab initio calculations at the HF/STO-3G//3G level indicate that the three isomeric possibilities for facial contact in the dimer (**5a−c**) lie within about 2 kcal/mol of one another. Semiempirical calculations

(1) Deisenhofer, J.; Michel, H. *Science* **1989**, *245*, 1463−73. Feher, G.; Allen, J. P.; Okamura, M. Y.; Rees, D. C. *Nature* **1989**, *339*, 111−6.

(2) Svensson, B.; Etchebest, C.; Tuffery, P.; van Kan, P.; Smith, J.; Styring, S. *Biochemistry* **1996**, *35*, 14486−502.

(3) Durrant, J. R.; Klug, D. R.; Kwa, S. L. S.; van Grondelle, R.; Porter, G.; Dekker: J. P. *Proc. Natl. Acad. Sci. U.S.A.* **1995**, *92*, 4798−802.

(4) Noguchi, T.; Tomo, T.; Inoue, Y. *Biochemistry* **1998**, *37*, 13614−25 and references therein.

(5) For reviews, see: Boxer, S. G. *Biochim. Biophys. Acta* **1983**, *726*, 265−92. Wasielewski, M. R. *Chem. Rev.* **1992**, *92*, 435−61.

(6) Chiefari, J.; Griebenow, K.; Greibenow, N.; Balaban, T. S.; Holzwarth, A. R.; Schaffner, H. J. *J. Phys. Chem.* **1995**, *99*, 1357−65.

(7) Jaquinod, L.; Senge, M. O.; Pandey, R. K.; Forsyth, T. P.; Smith, K. M. *Angew. Chem., Int. Ed. Engl.* **1996**, *35*, 1840−2.

(8) Boxer, S. G.; Closs, G. L. *J. Am. Chem. Soc.* **1976**, *98*, 5406−8. Bucks, R. R.; Boxer, S. G. *J. Am. Chem. Soc.* **1982**, *104*, 340−3.

(9) Mettath, S.; Shibata, M.; Alderfer, J. L.; Senge, M. O.; Smith, K. M.; Rein, R.; Dougherty, T. J.; Pandey, R. K. *J. Org. Chem.* **1998**, *63*, 1646−56 and references therein.

(10) Tamiaki, H.; Miyata, S.; Kureishi, Y.; Tanikaga, R. *Tetrahedron* **1996**, *52*, 12421−32.

(11) Stibrany, R. T.; Vasudevan, J.; Knapp, S.; Potenza, J. A.; Emge, T.; Schugar, H. J. *J. Am. Chem. Soc.* **1996**, *118*, 3980−1.

(12) Vasudevan, J.; Stibrany, R. T.; Bumby, J.; Knapp, S.; Potenza, J. A.; Emge, T. J.; Schugar, H. J. *J. Am. Chem. Soc.* **1996**, *118*, 11676−7.

(13) Knapp, S.; Vasudevan, J.; Emge, T. J.; Arison, B. H.; Potenza, J. A.; Schugar, H. J. *Angew. Chem., Int. Ed. Engl.* **1998**, *37*, 2368−70.
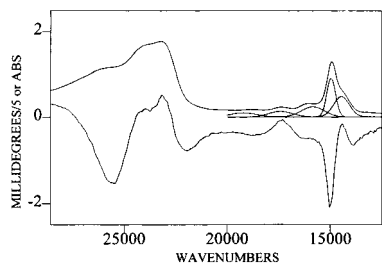
Figure 2. Upper trace: electronic spectrum of **5** (9.8 mg/mL) in CHCl$_3$ ($l = 0.0027$ cm). Lower trace: CD spectrum of **5** (5.2 mg/mL) in CHCl$_3$ ($l = 0.0058$ cm). Rotations are scaled to 20%.
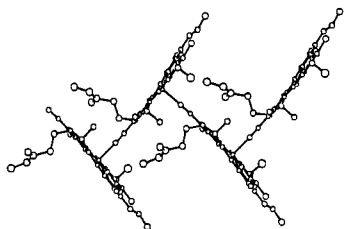
**Figure 3.** View of a polymeric chain in **2**·CHCl$_3$, showing the Zn—O(keto) linkage between the nearly perpendicular adjoining monomers.

(PM3) suggest somewhat higher energy (about 10 kcal/mol) for **5b** compared with that of **5a** and **5c**.

Electronic and CD spectra of dimer **5** taken at concentrations comparable to those used for the MW and NMR studies are presented in Figure 2. The most prominent Q$_y$ absorption, at 14 940 cm^{-1}, is little changed by either dilution to 0.098 mg/mL (14 940 cm^{-1}) or addition of 10 equiv of DMAP (14 850 cm^{-1}), conditions that should afford monomers with four- and five-coordinate zinc(II), respectively. A new low-energy Q absorption appears at 14 440 cm^{-1} in the spectra of solutions containing 1.63–15.7 mg/mL of **2** in dry, acid-free CHCl$_3$. This absorption, which is not seen in the spectra of the monomers, can be attributed to splitting of the Q$_y$ absorption for the dimer **5**. A second low-energy absorption, at 13 240 cm^{-1}, perhaps the result of a higher aggregate, appears in the spectrum of the most concentrated solution only. Deconvolution indicates that the Q$_y$ splitting is 500–550 cm^{-1}. The CD spectrum also reveals distinct electronic absorption to the red of the monomer Q$_y$ band.

Related edge-over-edge overlapped porphyrins show Soret absorptions split by ~1000 cm^{-1} with only minor changes in the Q$_y$ region,[11,13,14,16] whereas the special pair bacteriochlorophylls and chlorophylls in photosynthetic systems, overlapped in the region of pyrrole ring I, show Q$_y$ bands split by 400–600 and ≤140 cm^{-1}, respectively.[2,3] The smaller splitting reported for the plant special pairs has been attributed to greater separation, or suboptimal orientation, of the chlorophyll subunits or even deletion of one subunit.[3,4] A splitting of 418 cm^{-1} has been calculated[3] for the Q$_y$ absorption of a chlorophyll dimer fixed at the structure reported for the special pair of *R. viridis*, which is in harmony with the 500 cm^{-1} splitting of the Q$_y$ absorption observed for dimer **5**.

Dark green crystals of **2**·CHCl$_3$ were obtained upon slow evaporation of a CHCl$_3$ solution.[17] In contrast to the oxime-coordinated dimeric structure **5** found in solution, a polymeric staircase structure forms in the solid state (Figure 3). This coordination polymer superficially resembles those formed from [10,15,20-triphenyl-5-(4-pyridyl)porphyrinato]zinc(II)[21] and other metalloporphyrins[13] but has not been reported previously for structures containing the chlorin subunit. Each zinc atom is apically coordinated to the keto oxygen atom of an adjoining monomer, to afford a square-pyramidal zinc(II) geometry typical for five-co-
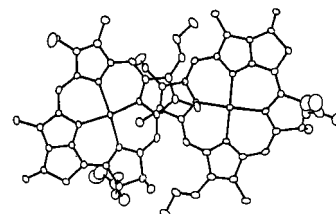
Figure 4. View of the overlapping monomeric units between adjacent polymeric chains. A β-carbon atom from pyrrole I of one monomer is nearly centered above pyrrole II of the adjacent monomer.

ordinate metalated porphyrin and chlorin systems.[22–24] Interestingly, the more basic oxime nitrogen does not coordinate to zinc in the solid state. A similar oligomeric structure with ketone–magnesium coordination has been proposed for chlorophylls in biological systems.[25] Structures for both keto[22] and isocyano[23] zinc-ligated cofacial chlorin dimers have been reported. In contrast to these and other cofacial dimers or stacks in which the chlorin subunits are approximately parallel and in varying degrees of π contact, the polymeric chains of **2**·CHCl$_3$ feature adjoining chlorin units that are nearly perpendicular. Interchain association brings pyrrole ring I in contact with ring II of a nearby chlorin, as shown in Figure 4. One carbon atom (C-1) is almost centered over ring II from an adjacent chain. Intermolecular distances [(C-1)···C-(pyrrole II) and (C-1)···N(pyrrole II)] range from 3.68 to 3.81 Å, indicating at least weak π contact. Adjacent chains appear to be linked further by an oxime-to-ester hydrogen bond [O···O = 2.85 Å], which taken with the other interactions may compensate for the absence of Zn—N(oxime) bonding in the solid-state structure.

Supporting Information Available: Experimental procedures for **2**–**5**, calculational methods for **5**, and crystallographic details for **2**·CHCl$_3$ (PDF). Crystallographic data, in CIF format, are also available. This material is available free of charge via the Internet at http://pubs.acs.org.

(17) A dark green crystal of **2**·CHCl$_3$ was mounted on the end of a glass fiber. Data were collected at 293(2) K (Enraf-Nonius CAD-4 diffractometer, Cu Kα radiation, $\lambda = 1.5418$ Å). Crystal data: C$_{33}$H$_{32}$N$_5$O$_4$Zn·CHCl$_3$; $M = 747.37$; orthorhombic, $P2_12_12_1$ (No. 19); $a = 11.791(1)$, $b = 12.405(1)$, and $c = 23.795(2)$ Å; $V = 3480.2$ Å^3; $Z = 4$; $\rho_{calc} = 1.426$ g/cm^3; 4088 unique reflections ($3 < \theta < 70°$) 3568 with $I > 2\sigma(I)$. Data were corrected for Lorentz, polarization, absorption (numerical, SHELX-76,[18] $0.57 < T < 0.72$), and decay (1.2%, linear) effects. The structure was solved by direct methods (SHELXS-97[19]) and refined anisotropically on F^2 by using all unique data with $I > 0$. H atoms were placed at calculated positions with fixed thermal parameters and were not refined. The chloroform solvate exhibited positional disorder and was modeled on two sites with occupancy factors of 0.62 and 0.38. C—Cl and Cl—Cl distances in these species were restrained with an esd of 0.02 Å (DFIX); relaxation of these restraints gave unrealistic geometries for the solvate species with little change in the pyropheophorbide parameters. Refinement (SHELXL-97,[20] 4088 data, 461 parameters, 60 restraints) gave $R_F = 0.065$ [$I > 4\sigma(I)$], $wR_F{}^2 = 0.166$ (all data), GOF = 1.02. A final difference map revealed excursions from −0.40 to 0.83 e$^-$/Å^3; the five largest residuals were within 1 Å of the Zn atom. Crystals of the pyropheophorbide **2** were also grown from ethyl formate solution. The resulting **2**·C$_3$H$_6$O$_2$, was found to be isostructural with the chloroform solvate, as confirmed by a subset of the data. Cell dimensions: $a = 11.668(2)$, $b = 12.379(4)$, and $c = 23.928$ Å; space group orthorhombic, $P2_12_12_1$ (No. 19).
(18) Sheldrick, G. M. *SHELX76. Program for Crystal Structure Determination;* University of Cambridge, England, 1976.
(19) Sheldrick, G. M. *SHELXS97. Program for the Solution of Crystal Structures;* University of Göttingen, Germany, 1997.
(20) Sheldrick, G. M. *SHELXL97. Program for Crystal Structure Refinement;* University of Göttingen, Germany, 1997.
(21) Fleischer, E. B.; Shachter, A. M. *Inorg. Chem.* **1991**, *30*, 3763–9.
(22) Senge, M. O.; Smith, K. M. *Acta Crystallogr.* **1997**, *C53*, 1022–4.
(23) Jaquinod, L.; Gros, C.; Olmstead, M. M.; Antolovich, M.; Smith, K. M. *Chem. Commun.* **1996**, 1475–6.
(24) Senge, M. O.; Ruhlandt-Senge, K.; Smith, K. M. *Z. Naturforsch.* **1995**, *50b*, 139–46. Kratky, C.; Dunitz, J. D. *Acta Crystallogr.* **1977**, *B33*, 545–7. Kratky, C.; Isenring, H. P.; Dunitz, J. D. *Acta Crystallogr.* **1977**, *B33*, 547–9. Chow, H.-C.; Serlin, R.; Strouse, C. E. *J. Am. Chem. Soc.* **1975**, *97*, 7230–7. Serlin, R.; Chow, H.-C.; Strouse, C. E. *J. Am. Chem. Soc.* **1975**, *97*, 7237–42. Spaulding, L. D.; Andrews, L. C.; Williams, G. J. B. *J. Am. Chem. Soc.* **1977**, *99*, 6918–23.
(25) Katz, J. J.; Shipman, L. L.; Cotton, T. M.; Janson, T. R. In *The Porphyrins*; Dolphin, D., Ed.; Academic Press: New York, 1978; Vol. V, pp 401–58. Tamiaki, H. *Coord. Chem. Rev.* **1996**, *148*, 183–97.

(14) Gerasimchuk, N. N.; Mokhir, A. A.; Rodgers, K. R. *Inorg. Chem.* **1998**, *37*, 5641–50.
(15) Smith, J. W. In *The Chemistry of the Carbon–Nitrogen Bond*; Patai, S., Ed.; Interscience Publishers: New York, 1970; pp 235–53.
(16) Kobuke, Y.; Miyaji, H. *J. Am. Chem. Soc.* **1994**, *116*, 4111–2.