cursor: 28% overall yield from commercially available 1,5-hexadiyne (**3**) and 40% from 2-methylcyclopent-2-enone (**1**). In addition, the reported scheme should allow for considerable variation of the structure of the final product. We have previously demonstrated the extensive electrophilic substitution chemistry of *o*-bis(trimethylsilyl)arenes[2,11] as well as the scope of the A → B transformation (Scheme I). Easy access to a variety of steroids of the type **11** can thus be envisaged, in particular the unknown 7-azaestratriene derivatives, incorporating the tetrahydroisoquinoline moiety into the steroid nucleus, the unknown C norsteroids, and the synthetically useful 11-hydroxy[12] and A-ring aza analogues.[13]

Acknowledgments. We thank W. G. L. Aalbersberg for his help in obtaining ^{13}C NMR spectra. We are grateful for financial support of this work: National Science Foundation, National Institute of Health, and (in part) cancer research funds of the University of California.

References and Notes

(1) A. A. Akhrem and Y. A. Titov, "Total Steroid Synthesis", Plenum Press, New York, N.Y., 1970; K. Nakanishi in K. Nakanishi, T. Goto, S. Itô, S. Natori, and S. Nozoe, Ed., "Natural Products Chemistry", Vol. 1, Academic Press, New York, N.Y., 1974, Chapter 6.

(2) R. L. Funk and K. P. C. Vollhardt, *J. Am. Chem. Soc.*, **98**, 6755 (1976); see also W. G. L. Aalbersberg, A. J. Barkovich, R. L. Funk, R. L. Hillard III, and K. P. C. Vollhardt, *ibid.*, **97**, 5600 (1975); R. L. Hillard III and K. P. C. Vollhardt, *Angew. Chem.*, **87**, 744 (1975); *Angew. Chem., Int. Ed. Engl.*, **14**, 712 (1975); R. L. Funk and K. P. C. Vollhardt, *J. Chem. Soc., Chem. Commun.*, 833 (1976); R. L. Hillard III and K. P. C. Vollhardt, *J. Am. Chem. Soc.*, **99**, 4058 (1977); K. P. C. Vollhardt, *Acc. Chem. Res.*, **10**, 1 (1977).

(3) This conceptual scheme was first conceived in 1973 and publicly outlined at the 30th Annual Northwest Regional Meeting of the American Chemical Society, Honolulu, Hawaii, June 12–13, 1975.

(4) I. J. Rinkes, *Recl. Trav. Chim. Pays-Bas*, **57**, 176 (1938); A. M. Gaddis and L. W. Butz, *J. Am. Chem. Soc.*, **69**, 1203 (1947). **1** can also be prepared from 2-methylcyclopentane-1,3-dione via 3-ethoxy-2-methyl-2-cyclopentenone followed by reduction with diisobutylaluminum hydride and acidic workup, in a procedure adapted from W. F. Gannon and H. O. House, "Organic Syntheses", Collect. Vol. V, Wiley, New York, N.Y., 1973, p 294.

(5) All new compounds reported exhibited satisfactory spectral and/or analytical characteristics.

(6) **2:** colorless liquid; bp 48 °C (2.6 mm); *m/e* (rel intensity) 196 (M^+, 22), 73 (Me_3Si, 100); NMR (60 MHz) (CCl_4) δ 0.22 (s, 9 H) 1.47 (br s, 3 H), 1.4–2.5 (m, 4 H), 3.00 (m, 1 H), 4.93 (dd, $J = 9, 2.5$ Hz, 1 H), 5.00 (dd, $J = 17.5, 2.5$ Hz, 1 H), 5.70 (overlapping (5 lines) ddd, $J = 17.5, 10, 9$ Hz, 1 H). **5:** colorless liquid; bp 92 °C (6 mm); *m/e* (rel intensity) 232 (M^+, 0.3), 77 (100); NMR (60 MHz) (CCl_4) δ 1.9–3.1 (m, 5 H), 2.33 (t, $J = 2.5$ Hz, 1 H), 2.43 (d, $J = 2.5$ Hz, 1 H), 3.28 (dt, $J = 6, 1$ Hz, 2 H); IR (neat) $\nu_{C\equiv CH}$ 3310, 2145 cm^{-1}. **6:** colorless oil; *m/e* (rel intensity) 228 (M^+, 0.2), 124 (100); NMR (60 MHz) (CCl_4) δ 0.85, 1.03 (2s, 3 H), 1.2–2.8 (m, 14 H), 5.13 (dd, $J = 16, 2.5$ Hz, 1 H), 5.14 (dd, $J = 10, 2.5$ Hz, 1 H), 5.90 (m, 1 H); IR (neat) $\nu_{C\equiv CH}$ 3330, 2150 cm^{-1}, $\nu_{C=O}$ 1740 cm^{-1}. **7:** colorless crystals; mp 155–157 °C; *m/e* (rel intensity) 398 (M^+, 25), 383 (44), 73 (100); NMR (60 MHz) (CCl_4) δ 0.37 (s, 18 H), 0.93 (s, 3 H), 1.0–3.0 (m, 15 H), 7.27 (br s, 1 H), 7.52 (br s, 1 H); IR (neat) $\nu_{C=O}$ 1743 cm^{-1}.

(7) E. S. Binkley and C. H. Heathcock, *J. Org. Chem.*, **40**, 2156 (1975).

(8) The melting point of racemic **8** (107–109 °C) is somewhat lower than that of optically pure material (138–141 °C). We thank Dr. F. Li, Syntex Research, for a sample of authentic *d*-estra-1,3,5(10)-trien-17-one.

(9) See also T. A. Wittstruck and K. I. H. Williams, *J. Org. Chem.*, **38**, 1542 (1973).

(10) T. Kametani, H. Nemoto, H. Ishikawa, K. Shiroyama, H. Matsumoto, and K. Fukumoto, *J. Am. Chem. Soc.*, **99**, 3461 (1977); T. Kametani, Y. Hirai, F. Satoh, and K. Fukumoto, *J. Chem. Soc., Chem. Commun.*, 16 (1977); W. Oppolzer, *Angew. Chem.*, **89**, 10 (1977); *Angew. Chem., Int. Ed. Engl.*, **16**, 10 (1977).

(11) Oxygenated derivatives of the estrone type should be available via oxidative cleavage of the arylsilicon bond, as demonstrated for simple arylsilanes: J. R. Kalman, J. T. Pinhey, and S. Sternhell, *Tetrahedron Lett.*, 5369 (1972).

(12) See, for example, R. W. Freerksen, W. E. Pabst, M. L. Raggio, S. A. Sherman, R. R. Wroble, and D. S. Watt, *J. Am. Chem. Soc.*, **99**, 1536 (1977).

(13) S. Danishefsky and P. Cain, *J. Am. Chem. Soc.*, **98**, 4975 (1976); for a cobalt catalyzed route to annelated pyridines, see A. Naiman and K. P. C. Vollhardt, unpublished work.

(14) (a) Regents' Intern Fellow, 1975–1978; (b) Fellow of the Alfred P. Sloan Foundation, 1976–1978.

Raymond L. Funk,[14a] K. Peter C. Vollhardt*[14b]
Department of Chemistry, University of California
and the Materials and Molecular Research Division
Lawrence Berkeley Laboratory
Berkeley, California 94720

Received April 11, 1977

---

strati-Bisporphyrins. A Novel Cyclophane System

Sir:

The primary electron donor in bacterial photosynthesis is a dimer of bacteriochlorophyll molecules. The evidence for this assertion comes from ESR and ENDOR measurements on the cation resulting from the initial photoact.[1] Similar electron delocalization is known to occur in the radical-ion species of cyclophanes, triptycenes, and other intimate ring systems.[2] This delocalization is strongly dependent on the geometry of these multiring compounds. Linear and loosely stacked dimers of porphyrins have been synthesized,[3,4] but the ring-ring interactions appear to be minimal. In the cases of chlorophyll dimers held together by hydrogen-bonding nucleophiles and urea-linked binary prophyrins, substantial spectral alterations have been observed.[5,6] To evaluate the influence of distance and orientation parameters on the electron-transfer phenomena, we have begun the synthesis of well-defined dimeric systems in which transannular interactions can be observed. Recently, we reported the first member of a new class of macrocyclic cyclophanes, tetra-*meso*-[*p*,*p*′-(2-phenoxyethoxycarbonylphenyl)]-*strati*-bisporphyrin, III.[7,8] Now we present the proof of structure and some interesting spectral properties of this compound.

strati-Bisporphyrin III was synthesized by application of the tetraaldehyde modification[9] of the Adler-Longo porphyrin condensation procedure.[10] A suitable porphyrin tetraaldehyde, II, was derived from a porphyrin tetrahydroxide, I, by acylation with *p*-chlorocarbonylbenzaldehyde (Figure 1).

Tetra-*meso*-[*p*-(2-hydroxyethoxy)phenyl] porphyrin, I, was made by the reaction of pyrrole with *p*-2-hydroxyethoxybenzaldehyde[11] in refluxing acidified xylene (8 mM in trifluoroacetic acid).[12] The xylene precipitate was recrystallized from dimethylformamide yielding 14% I: mp >330 °C; ν_{max} (KBr) 1240, 1605 cm^{-1}; λ_{max} (pyridine) 426 nm (ϵ 471 000, 14-nm half-width), 521 (16 500), 558 (13 000), 595 (5090), 653 (7500).[13] Anal. Calcd for $C_{52}H_{46}N_4O_8$ (mol wt 854.9): C, 73.05; H, 5.42; N, 6.55; Found: C, 72.80; H, 5.36; N, 6.54. I was reacted with the thionyl chloride generated acid chloride of *p*-carboxybenzaldehyde in methylene chloride–pyridine–diisopropylethylamine (DIEA) (50:25:2). At completion, the solution was neutralized with aqueous base and the products were extracted into chloroform, concentrated, and precipitated with methanol. The precipitate was chromatographed with chloroform on deactivated alumina[14] and the first band was collected. Crystallization from $CHCl_3$–MeOH resulted in 40% yield of tetraaldehyde II: mp 225–228 °C; ν_{max} (KBr) 1240, 1275, 1605, 1705, 1725 cm^{-1}; λ_{max} (pyridine) 425 nm (ϵ 464 000, 14-nm half-width), 519 (17 400), 556 (12 700), 593 (5330), 651 (7170);[13] FT NMR (220 MHz, 1 mM in $CDCl_3$)[15] δ NH at −2.77 (2 H, s), CH_2O at 4.61 (8 H, t, $J = 4$ Hz), CO_2CH_2 at 4.89 (8 H, t, $J = 4$ Hz), C_6H_4O at 7.31 (8 H, d, $J = 8$ Hz), 8.12 (8 H, d, $J = 8$ Hz), $C_6H_4CO_2$ at 7.99 (8 H, d, $J = 8$ Hz), 8.32 (8 H, d, $J = 8$ Hz), β-pyrrole H at 8.83 (8 H, s), CHO at 10.11 ppm (4 H, s). Anal. Calcd for $C_{84}H_{62}N_4O_{16}$ (mol wt 1383.4): C, 72.93; H, 4.52; N, 4.05. Found: C, 71.72; H, 4.36; N, 4.05.[16a]

strati-Bisporphyrin III was made by the addition of II and pyrrole (4 equiv) to refluxing propionic acid–ethylbenzene (1:1) (0.4 mM in II). After 1.5 h, the solvent was removed by evaporation and the pyridine-soluble products were collected and fractionated on a Bio-Beads S-X1 exclusion gel.[17] After a long, diminishing band of polymeric porphyrins (*R* 0.5–1.0), III eluted as a narrow, isolated purple band (*R* 0.45) followed by a faint yellow band of pyrrole by-products.[18] This elution pattern is consistent with III being a compact, stacked dimer. On this same column the more extended and solvated porphyrins I and II migrated with *R*s of 0.61 and 0.67, respectively, while unsubstituted tetraphenylporphyrin eluted at *R*

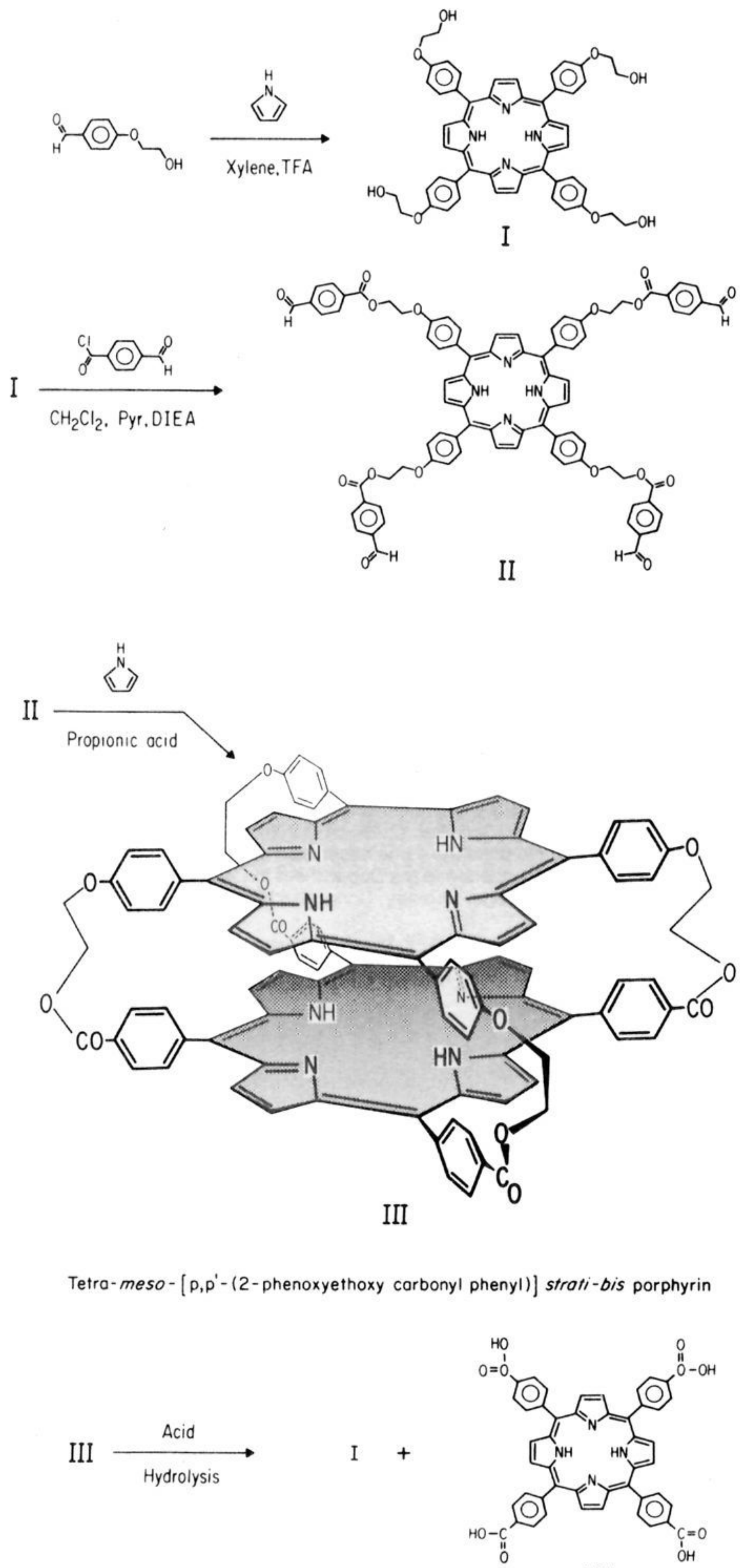

Figure 1. Synthetic scheme showing most probably H_4-dimer tautomer of III ($C_{100}H_{68}N_8O_{12}$, mol wt 1573.6) and proof of structure by acid hydrolysis.

0.44. Yields of III up to 6% in propionic acid and to 8% in propionic acid–ethylbenzene have been obtained.[16b]

Classical proof of structure III was obtained by identification of the products of acid hydrolysis.[19,20] Hydrolysis of III resulted in two distinct porphyrins, I and the de novo tetra-*meso*-[*p*-carboxyphenyl]porphyrin, IV, in a molar ratio of 1.05 ± 0.09. IV was unique to the dimer and was not obtained from any of the other fractions. Hydrolysates of the polymeric porphyrin fractions or II yielded the tetrahydroxide I as the sole porphyrin product. The equimolar presence of IV with I in the hydrolysis of III can be attributed only to the successful self-condensation of II with pyrrole to form a strati-bis structure.

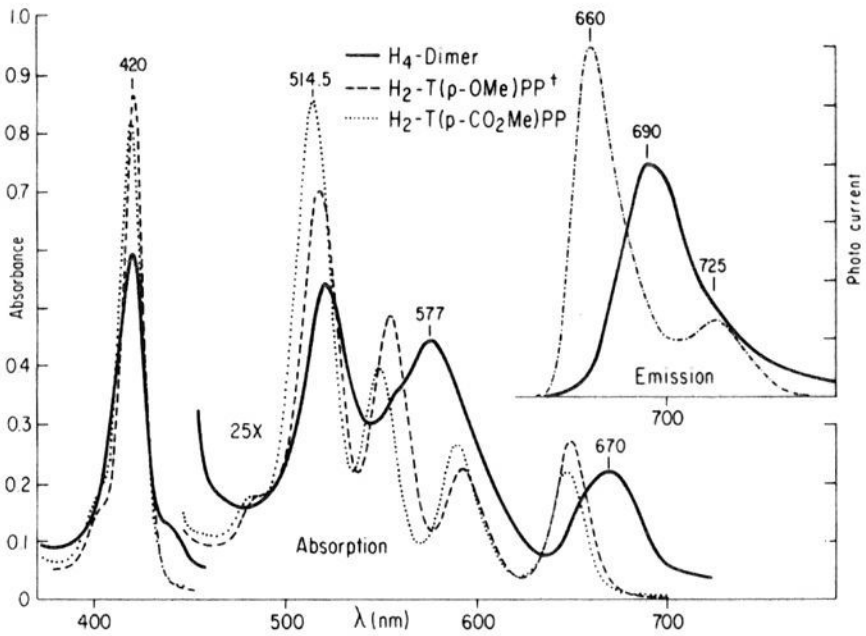

Figure 2. Absorption spectra of III (1.0 μM, 25.0 μM), T(p-OCH_3)PP† (†, contains trace of chlorin[13]) (1.6 μM, 40.8 μM), and T(p-CO_2CH_3)PP (1.7 μM, 42.2 μM) in CH_2Cl_2 and DIEA (0.1% v/v) and the uncorrected emission spectra of equally absorbant solutions at 420 nm of III and T(p-OCH_3)PP:T(p-CO_2CH_3)PP (1:1) excited at 420 nm. III was homogeneous by excitation–emission spectral analysis.

The IR spectrum of III was similar to that of II except for the loss of the 1705-cm^{-1} formyl carbonyl stretching frequency. The NMR spectrum was marred by extraneous peaks between 0.5 and 1.5 ppm due to impurities as well as by line broadening. Despite these imperfections, the NMR of III supported the proposed structure because (a) all resonances in the region above 2 ppm were assignable and suitably proportioned, (b) the A_2B_2 degeneracies of the phenoxy and the benzoyl ring protons were broken into AA′BB′ quadruplets due to distinguishable interior and exterior facing protons, and (c) the alkyl protons appeared as a nondegenerate AA′BB′ multiplet due to restricted rotation about the O–C–C–O bonds.[21]

Both the absorption and the emission of III showed evidence of interaction between the component porphyrins: λ_{max} (pyridine) 426 nm (ϵ 559 000, 18-nm half-width), 523 (19 600), 562 (sh), 584 (18 000), 677 (8650)[20] (Figure 2). The Soret band was significantly broadened (40% increased half-width) but was unmoved, while the visible absorptions were both broadened and red shifted (500 cm^{-1} for the red-most band). The fluorescence intensity also was red shifted (660-cm^{-1} peak shift) and broadened, but its quantum yield was relatively the same as those of its monomeric components.[22] The zinc chelate (λ_{max} (CH_2Cl_2) 422 nm (ϵ 750 000, 19-nm half-width), 562 (30 900), 606 (18 500))[20] (Figure 3) showed an unmoved but broadened Soret (60% increased half-width) and fully shifted visible bands. Its emission was greatly broadened and quenched by 50%.[23] Both III and its zinc chelate showed unusual low energy absorption shoulders to the red of the Soret rather than the usual high energy shoulders seen in monomeric porphyrins. The absorption properties of III were independent of concentration from 0.1 μM to 40.0 μM in CH_2Cl_2 and DIEA (0.1% v/v).

Similar spectral broadening and red shifting of visible bands have been seen upon porphyrin aggregation[24] and complexing with heterocycles.[25] A purely excitonic interaction would have shifted the Soret to the blue and would have affected the visible bands less.[26,27] We believe that the spectra of III and the zinc chelate can best be explained as due to weak incipient charge-transfer interactions.[25] The electron-withdrawing substituents on IV and the electron-donating substituents on I as components of III may enhance this effect.

In summary, we report a synthetic method for the preparation of well-defined, stacked porphyrins and the spectral characteristics of the first such *strati*-bisporphyrin. We an-

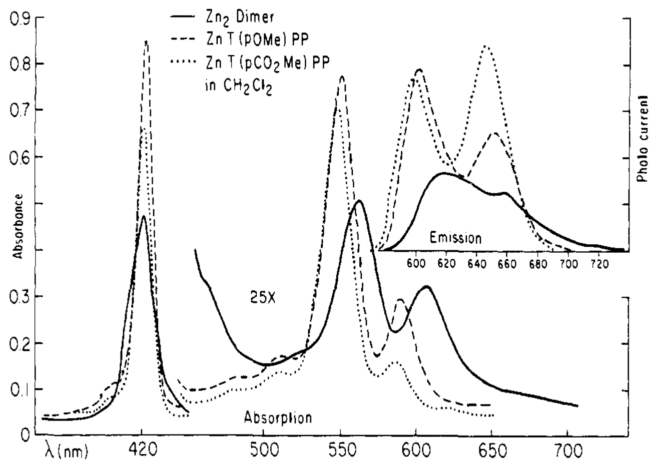

Figure 3. Absorption spectra of 1.2-μM and 30.0-μM solutions of the zinc metalloporphyrins in CH_2Cl_2 with the baseline offset from zero for clarity. Uncorrected emission spectra of equally absorbant solutions at 420 nm were excited at this wavelength. Homogeneity was verified by excitation-emission spectral analysis.

ticipate that the method will be general and that the correlation of structures with properties will significantly aid the interpretation of in vivo and in vitro porphyrin systems such as the photosynthetic chlorophyll dimers. The effects of systematic changes in ring separation, orientation, donor-acceptor substituents, metal and mixed-metal chelates, and intercalates can now be examined.

Acknowledgment. We gratefully acknowledge the funding of the Rockefeller University Graduate Program which supported this work. We thank Drs. D. Cowburn and T. H. Witherup for NMR spectra. Drs. A. D. Adler, P. S. Hines, and A. R. Mitchell have provided much vital discussion.

References and Notes

(1) Recent reviews: (a) P. A. Loach, *Prog. Bioorg. Chem.*, **4**, p. 89–192 (1976); (b) W. W. Parsons and R. J. Cogdell, *Biochem. Biophys. Acta*, **416**, 105 (1975).

(2) (a) M. Szwarc and J. Jagur-Grodzinski in "Ions and Ion Pairs in Organic Reactions", M. Szwarc, Ed., Wiley–Interscience, New York, N.Y., 1975, p 1–150; (b) T. Hayashi, N. Mataga, Y. Sakata, and S. Misumi, *Bull. Chem. Soc. Jpn*, **48**, 416 (1975).

(3) (a) F. P. Schwarz, M. Gouterman, Z. Muljiani, and D. H. Dolphin, *Bioinorg. Chem.*, **2**, 1 (1972); (b) J. A. Anton, J. Kwong, and P. A. Loach, *J. Heterocycl. Chem.*, **13**, 717 (1976).

(4) H. Ogoshi, S. Sugimoto, and Z. Yoshida, *Tetrahedron Lett.*, 169 (1977).

(5) (a) S. G. Boxer and G. L. Closs, *J. Am. Chem. Soc.*, **98**, 5406 (1976); (b) M. R. Wasielewski, M. H. Studier, and J. J. Katz, *Proc. Natl. Acad. Sci.*, **73**, 4282 (1976).

(6) J. P. Collman, C. M. Elliott, T. R. Halbert, and B. S. Tovrog, *Proc. Natl. Acad. Sci.*, **74**, 18 (1977).

(7) N. E. Kagan, *Brookhaven Symp. Biol.*, **28**, 371 (1976).

(8) As an alternative to the cyclophane nomenclature (originally designating carbon-linked, stacked aromatics), a new lexicon, strati, from the combining form of the Latin *stratum* for "covering", is introduced to denote any invarient overlaying of planar groups.

(9) J. Almog, J. E. Baldwin, and J. Huff, *J. Am. Chem. Soc.*, **97**, 226 (1975).

(10) A. D. Adler, F. R. Longo, L. D. Finarelli, J. Goldmacher, J. Assour, and L. Korsakoff, *J. Org. Chem.*, **32**, 476 (1967).

(11) J. Bernstein, H. L. Yale, K. Losee, M. Holsing, J. Martins, and W. A. Lott, *J. Am. Chem. Soc.*, **73**, 906 (1951).

(12) (a) Xylene–trifluoroacetic acid is used here rather than propionic acid to avoid propionylation of the free hydroxyl groups. (b) Optimum yield is critically dependent on acid and reactant concentrations and varies with differing aldehydes (unpublished work of A. D. Adler and V. Varadi).

(13) Contains traces of chlorin (Figure 2) which were not removed since final condensation to III would re-form chlorin in both old and new rings via autoxidation–reduction; cf. D. Dolphin, *J. Heterocycl. Chem.*, **7**, 275 (1970).

(14) Alumina was deactivated by saturation with ethyl acetate followed by drying at 115 °C for 1 h.

(15) Assignments are consistent with spectra of T(p-OCH_3)PP, T(p-CO_2CH_3)PP, and T(p-$CO_2CH_2CH_2OC_6H_5$)PP.

(16) (a) Low carbon analyses (here 1.2%) occur in large aromatic heterocycles such as big tetraarylporphyrins despite long burning (5′), high temperatures (975 °C), and added catalyst (V_2O_5). (b) Yields were determined spectroscopically after hydrolysis (*19,20*).

(17) This 1% cross-linked polystyrene support in pyridine was chosen to minimize adsorption of aromatic elutants. Standardization of the system with synthetic porphyrins and azulenes showed the retention constant (R, void volume/elution volume) to be proportional to species diffusional molecular size and not molecular weight; cf. T. C. Laurent and J. Killander, *J. Chromatogr.*, **14**, 317 (1964).

(18) (a) Alternately, III may be purified by chromatography of the $CHCl_3$-soluble fraction on deactivated alumina followed by silica gel TLC with CH_2Cl_2 and 1% EtOH. Treatment of III with dichlorodicyanobenzoquinone prior to TLC converts trace chlorins back to porphyrins; cf. G. H. Barrett, M. F. Hudson, and K. M. Smith, *Tetrahedron Lett.*, 2887 (1973).

(19) Samples were hydrolyzed in propionic acid–hydrochloric acid (12 N) (1:1) at 130 °C for 1 h in sealed evacuated ampules. Products were separated either by partitioning between aqueous base and 1-butanol, or by TLC on silica gel with 2,6-lutidine/water in NH_3 vapors; cf. J. Jensen, *J. Chromatogr.*, **10**, 236 (1963). Standards were recovered in 95% yields after workups. Products were identified by their comigration with authentic samples in two TLC solvent systems, similar acid–base partitioning, and absorption and emission spectra.

(20) Extinction coefficients for III and its zinc chelate were deduced from quantitative analysis of hydrolysis products I and IV based on their known ϵs. This procedure was verified by hydrolysis of I, II, T(p-CO_2CH_3)PP, and T(p-$CO_2CH_2CH_2OC_6H_5$)PP.

(21) The least strained CPK structures of III require interdigitation of the phenyl rings. This gives a slight twist to the molecule and results in a limited rotation-barrier chirality.

(22) Of the several possible H_4-dimer tautomers, III (Figure 1) with diagonally staggered inner hydrogens would be most probable. This would lead to minimal interaction of the orthogonal local dipoles.

(23) This partial quenching may be due to electron transfer and transition to the ground state limited by the large 6-Å ring–ring separation (gauged by CPK modeling).

(24) R. F. Pasternack, P. R. Huber, P. Boyd, G. Engasser, L. Francesconi, E. Gibbs, P. Fasella, G. C. Venturo, and L. Hinds, *J. Am. Chem. Soc.*, **94**, 4511 (1972).

(25) D. Mauzerall, *Biochemistry*, **4**, 1801 (1965).

(26) E. G. McRae and M. Kasha, *Phys. Proc. Rad. Biol.*, 23–42 (1964).

(27) (a) An example of a red-shifted Soret and minimally shifted visible bands in a porphyrin meso-substituted with cyanine dyes has been reported: F. J. Kampas, *J. Poly. Sci., Ser. C*, **29**, 81 (1970). (b) We have repeated this synthesis and obtained the same absorption spectrum.

(28) Address correspondence to the Department of Chemistry, Western Connecticut State College, Danbury, Conn. 06810.

Norman E. Kagan,*[28] **David Mauzerall, R. B. Merrifield**
The Rockefeller University, New York, New York 10021
Received March 14, 1977

Detection and Characterization of the Long-Postulated Fe-OO-Fe Intermediate in the Autoxidation of Ferrous Porphyrins

Sir:

Dioxygen bridged diiron complexes have been frequently proposed as important, although unstable, intermediates in the autoxidation of ferrous complexes.[1-3] Such bridged species have also been proposed to represent the oxygenated state of the respiratory pigment, hemerythryn.[4] In the development of strategies for the synthesis of low molecular weight models of myoglobins and hemoglobins, steric protection of the iron site has been deemed useful to prevent autoxidation via an Fe-OO-Fe intermediate.[5-8] Nevertheless, and in contrast to the situation with other metals, notably cobalt,[9,10] no Fe-OO-Fe complex has been unambiguously identified and none of its structural and electronic properties or chemical reactivity characterized. Only a few reports of O_2 uptake with a Fe:O_2 ratio of 2:1 have appeared which are suggestive of a Fe-OO-Fe species.[11,12] The proposed form for this bridged species has been variously described as Fe^{II}-O_2-Fe^{II} (dioxygen bridge[2,11]) or Fe^{III}-OO-Fe^{III} (peroxo bridge[2]), while others have anticipated rapid cleavage to two Fe-O monomers.[5] We report here on the ^{1}H NMR characterization of such a Fe-OO-Fe complex and show that the linkage involves the peroxo bridge.

As an initial step in elucidating the general mechanism of oxidation of ferrous porphyrins, we have investigated the reaction between unligated *meso*-tetra-(m-tolylporphyrin)-iron(II), designated PFe, and molecular oxygen in dry toluene-d_8. The final product is the expected μ-oxo dimer, PFeOFeP, and the proposed steps thought to account for the net reaction can be written