Table I. NMR Data for Hapalindole A (**1**) in $CDCl_3$

^{13}C $\delta^{a,b}$		^1H δ^c	^{13}C $\delta^{a,b}$		^1H δ^c
157.40 s[d]	20		63.59 d[d]	11	4.373 br d
142.99 d	21	6.100 dd	62.99 d	13	4.360 dd
137.52 s	8		44.39 d	15	2.317 ddd
133.17 s	4		43.86 s	12	
123.58 s	9		37.76 s	16	
123.21 d	6	7.190 m	36.80 d	10	3.875 br m
118.48 d	2	6.878 t	31.64 q	18	1.193 s
115.90 t	22	5.346 dd	30.82 t	14	2.142[e] dtd
		5.236 dd			1.472[f] q
113.65 d	5	6.969 m	24.07 q	17	1.553 s
110.14 s	3		18.60 q	23	0.878 s
108.33 d	7	7.199 m		1	8.085 br

$J_{H,H}$ (Hz): 1,2 = 2; 1,7 = ~0.5;[g] 2,6 = ~0.5;[g] 2,10 = 2; 5,6 = 7.2;[g,h] 5,7 = 0.6;[g,h] 6,7 = 8.2;[g,h] 10,11 = 1.6;[g] $10,14_{eq}$ = 1.2; 10,15 = 4.6; $13,14_{ax}$ = 12.4; $13,14_{eq}$ = 4.0; $14_{ax},14_{eq}$ = −13.5; 14_{ax},15 = 13.0; 14_{eq},15 = 3.8; trans 21,22 = 17.4; cis 21,22 = 10.9; gem 22,22 = 0.5

[a] 75 MHz; $CDCl_3$ as internal reference = 76.90. [b] ^1H–^{13}C connectivities determined using a phase-cycled 16-step heteronuclear chemical shift correlation map (CSCM) experiment.[9] [c] 300 MHz; residual $CHCl_3$ as internal reference = 7.25. [d] Broad 1:1:1 triplet in proton-noise-decoupled spectrum, $J_{^{13}C^{14}C}$ ~ 5 Hz. [e] Equatorial. [f] Axial. [g] Determined in benzene-d_6. [h] From simulation of ABX spectrum shown by protons on C-5, C-6, and C-7.

^{13}C NMR chemical shifts were comparable with those of skatole and 4-methylindole.[8] Futhermore, the ^1H–^1H coupling constants associated with the aromatic protons were consistent with this substitution pattern. The signal for the C-2 proton was a triplet, showing small vicinal coupling to the NH proton and allylic coupling to a methine (H on C-10) attached to C-3; in benzene-d_6 this signal was a broader triplet due to long-range zig-zag coupling to the proton on C-6. Two-dimensional spectra for determining the homonuclear ^1H (COSY/16) and heteronuclear ^1H–^{13}C connectivities (CSCM)[9] and selected proton spin–spin decoupling experiments strongly suggested that C-10 was in a X–$CH_{eq\,or\,ax}$–(C-10)H_{eq}–$CH_{ax}H_{eq}$–CH_{ax}–Y unit (where X and Y were CN and Cl, respectively) located in a six-membered ring. The ^{13}C signals for the C=NCH group were broad 1:1:1 triplets in the proton-noise-decoupled spectrum due to ^{13}C–^{14}N coupling. The ^1H signal for the C=NCH group was broad whereas the ^1H signal for the Cl–CH group was sharp.

Remaining for total assemblance of the structure were the placements of two quaternary carbon atoms along with three Me groups and a vinyl group which obviously had to be attached to the two quaternary carbons. One of the quaternary carbons was in the six-membered ring bearing the isocyano and chloro substituents.

The final structure, including relative stereochemistry, was decided from three ^1H–^1H NOE experiments. Irradiation of the Me signal at δ 0.878 produced strong NOE enhancements of the signals at δ 6.878 (C-2 H), 6.100 (C-21 H), 5.236 (C-22 H trans to C-21 H), 4.373 (C-11 H), and 1.472 (axial H on C-14). These NOEs indicated that (1) the irradiated Me group was on the C-12 quaternary carbon and axially disposed, (2) the H on C-11 was equatorial, (3) the vinyl group was on the same carbon as the irradiated methyl group, and (4) the remaining quaternary carbon with two Me groups had to bridge C-4 and the six-membered ring at C-15. The alkaloid therefore had to possess structure **1**. This was verified by irradiation of the Me signals at δ 1.193 [strong NOE enhancement of signals at δ 3.875 (C-10 H), 2.317 (C-15 H), and 1.553 (3H on C-17)] and δ 1.553 [strong NOE enhancement of signals at δ 6.969 (C-5 H), 2.317 (C-15 H), and 2.142 (equatorial H on C-14)].

Hapalindole A is accompanied by smaller amounts of several related compounds. One of these compounds is the corresponding isothiocyanate **2**[10] (EI MS: M^+ observed at m/z 370.1243).

The biogenesis of **1** apparently involves the fusion of tryptophan and monoterpene units. The origin of the isonitrile carbon, however, is unknown.[11] Recently glycine has been shown to serve as a satisfactory precursor of the *N*-formyl carbon in tuberin and possibly the isocyano carbons in xanthocillin X dimethyl ether from *Aspergillus clavatus*.[12]

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Registry No. 1, 92219-95-9; **2**, 92219-96-0.

Supplementary Material Available: 300-MHz ^1H NMR spectrum of **1** in dimethyl-d_6 sulfoxide and difference NOE spectra resulting from irradiation of the three quaternary methyl groups (1 page). Ordering information is given on any current masthead page.

(8) Stothers, J. B. "Carbon-13 NMR Spectroscopy"; Academic Press: New York, 1972.

(9) Bax, A. "Two-Dimensional Nuclear Magnetic Resonance in Liquids"; Delft University Press: Delft, Holland, 1982.

(10) Hapalindole B (**2**): Oil, $[\alpha]^{25}_D$ −194° (CH_2Cl_2, *c* 5.1), IR ($CHCl_3$) ν_{max} 2080, 2160 cm^{-1}; ^1H NMR ($CDCl_3$) δ 8.064 (br, NH), 7.197 (7, J = 7.2, 0.6 Hz, C-5 H), 7.183 (m, *J* = 8.2, 7.2 Hz, C-6 H), 6.961 (m, *J* = 8.2, 0.6 Hz, C-7 H), 6.882 (t, *J* = 2.0 Hz, C-2 H), 6.018 (dd, *J* = 17.4, 10.9 Hz, C-21 H), 5.322 (dd, *J* = 10.9, 0.5 Hz, C-22 H cis to C-21 H), 5.123 (dd, *J* = 17.4, 0.5 Hz, C-22 H trans to C-21 H), 4.534 (d, *J* = 2.3 Hz, C-11 H), 4.319 (dd, *J* = 12.6, 3.9 Hz, C-13 H), 3.867 (br m, C-10 H), 2.220 (ddd, *J* = 12.8, 4.6, and 3.6 Hz, C-15 H), 2.149 (dtd, *J* = −13.3, 3.9, 3.6, and 1.1 Hz, eq H on C-14), 1.555 (s, 3 H on C-17), 1.489 (q, *J* = −13.3, 12.8, and 12.6 Hz, ax H on C-14), 1.198 (s, 3 H on C-18), 0.870 (s, 3 H on C-23). Similar (to **1**) NOE are seen on irradiation of the Me signals at δ 0.870, 1.198, and 1.555. ^{13}C NMR ($CDCl_3$) δ 143.46 (C-21), 137.78 (C-8), 133.33 (C-4), 132.54 (C-20), 123.83 (C-9), 123.39 (C-6), 118.65 (C-2), 115.74 (C-22), 113.84 (C-7), 110.65 (C-3), 108.45 (C-5), 66.91 (C-11), 63.65 (C-13), 46.04 (C-12), 45.23 (C-15), 38.05 (C-16), 37.49 (C-10), 31.89 (C-18), 31.11 (C-14), 24.31 (C-17), 19.23 (C-23).

(11) Several isonitriles have been found in fungi and marine sponges. (a) Parry, R. J.; Buu, H. P. *Tetrahedron Lett.* **1982**, *23*, 1435. (b) Brewer, D.; Taylor, A. *J. Chem. Soc., Chem. Commun.* **1979**, 1061. (c) Marconi, G. G.; Molloy, B. B.; Nagarajan, R.; Martin, J. W.; Deeter, J. B.; Occolowitz, J. L. *J. Antibiot.* **1978**, *31*, 27. (d) Evans, R. J.; Napier, E. J.; Yates, P. *J. Antibiot.* **1976**, *29*, 850. (e) Nobuhara, M.; Tazima, H.; Shudo, K.; Itai, A.; Okamoto, T.; Iitaka, Y. *Chem. Pharm. Bull.* **1976**, *24*, 832. (f) Ando, K.; Tamura, G.; Arima, K. *J. Antibiot.* **1968**, *21*, 587. (g) Achenbach, H.; Grisebach, H. *Z. Naturforsch., Anorg. Chem., Org. Chem., Biochem., Biophys., Biol. B*: **1965**, *20*, 137. (h) Hagedorn, I.; Tönjes, H. *Pharmazie* **1957**, *12*, 567. (i) Hagadone, M. R.; Burreson, B. J.; Scheuer, P. J.; Finer, J. S.; Clardy, J. *Helv. Chim. Acta* **1979**, *62*, 2484 and references therein. (j) Hagadone, M. R.; Scheuer, P. J.; Holm, A. *J. Am. Chem. Soc.* **1984**, *106*, 2447.

(12) Herbert, R. B.; Mann, J. *J. Chem. Soc., Chem. Commun.* **1983**, 1008.

Models of Photosynthetic Chromophores. Molecular Structure and Aggregation of a Bacteriochlorin

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The recent crystallizations of reaction centers (RC's) containing bacteriochlorophyll *a* (BChl *a*, **1**)[1] and BChl *b*[2] (**2**) only emphasize the sparsity of structural information available for BChls.[3] The structure of a metal-free bacteriochlorin (**3**)[4] has been determined

(1) Allen, J. P.; Isaacson, R. A.; McPherson, A.; Feher, G. *Biophys. J.* **1984**, *45*, 256a.

(2) Michel, H. *J. Mol. Biol.* **1982**, *158*, 567–572. Zinth, W.; Kaiser, W.; Michel, H. *Biochim. Biophys. Acta* **1983**, *723*, 128–131. Gast, P.; Wasielewski, M. R.; Schiffer, M.; Norris, J. R. *Nature (London)* **1983**, *305*, 451–452.

(3) To date, only two structures of BChl derivatives have been reported. (a) A BChl *a* protein at 2.8 Å resolution (Matthews, B. W.; Fenna, R. E. *Acc. Chem. Res.* **1980**, *13*, 309–317) and (b) methylbacteriopheophorbide *a* (Barkigia, K. M.; Fajer, J.; Smith, K. M.; Williams, G. J. B. *J. Am. Chem. Soc.* **1981**, *103*, 5890–5893).

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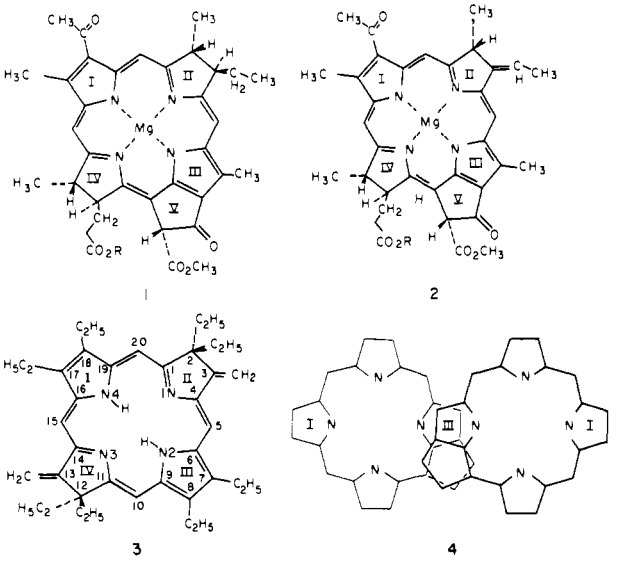
by X-ray diffraction in order to provide a simple model for the architecture of BChl derivatives and compare the molecular arrangements of synthetic analogues with those recently proposed for the structure of the oxidized primary donor (special pair) of bacterial RC's on the basis of ENDOR data, **4**.[6]



1 2 3 4

Crystals of **3** were obtained from hexane/dichloromethane and dichloromethane/chloroform.[7] The latter solvent mixture yields triclinic crystals in the space group $P\bar{1}$ whereas the first mixture gives monoclinic crystals that contain occluded solvent in space group $P2_1/n$. Because the two structures yield similar results and because the data for the $P2_1/n$ group were obtained at low temperature, the discussion that follows applies to that space group.

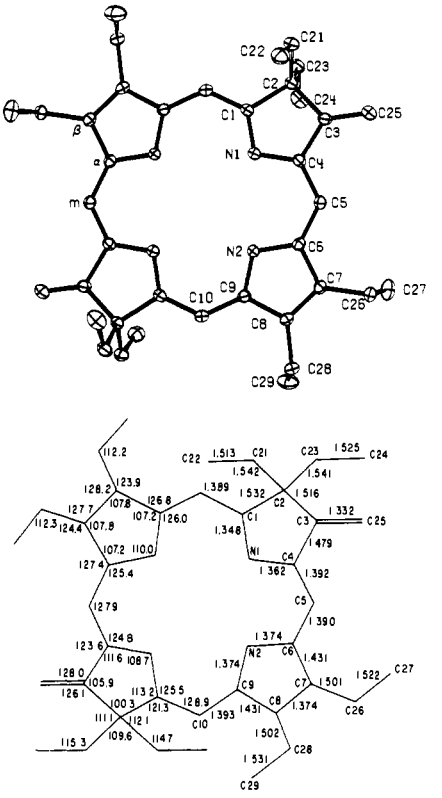


Figure 1. (Top) Structure of **3** and atom numbering scheme. The thermal ellipsoids are drawn to enclose 50% probability (space group $P2_1/n$, T = 140 K). (Bottom) Bond distances and angles. The estimated standard deviations are 0.003 Å for the core distances, 0.004 Å for the side chains, and 0.2° for the angles.

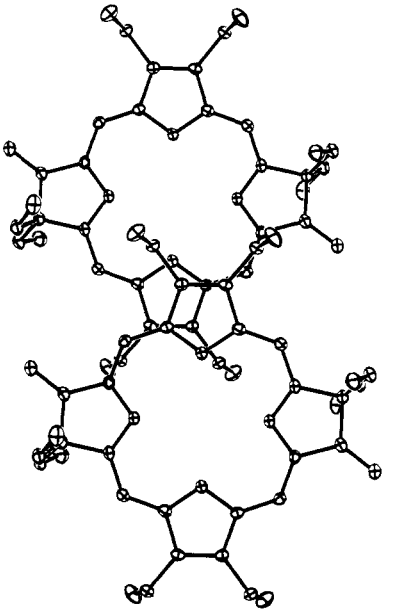


Figure 2. View of two adjacent molecules of **3** that illustrates the overlap of rings **I** and **III**. The separation between the rings is 3.59 Å.

The molecular structure of **3**, atom names, and bond distances and angles are presented in Figure 1. The bond differences in the saturated and unsaturated pyrroles are similar to those observed in other hydroporphyrins (chlorins, bacteriochlorins, and isobacteriochlorins).[8-10] A high symmetry in the bond distances

(4) 3,13-Dimethylene-2,2′,7,8,12,12′,17,18-octaethylporphyrin (**3**) was chosen to prevent the internal isomerization of the methylene double bond on the pyrroline ring to yield a pyrrole, a side reaction observed on oxidation of BChl *b* derivatives.[5] **3** was synthesized from the 3,13-diketo precursor by following the procedures developed for the syntheses of alkylchlorins and isobacteriochlorins (Chang, C. K. *Biochemistry* **1980**, *19*, 1971–1976). Thus, 3,13-dioxo-2,2′,7,8,12,12′,17,18-octaethylporphyrin was methylated with methyllithium to give a mixture of cis and trans diols which was treated with 15% HCl to effect dehydration. The product was purified on a silica gel column (20% hexane, CH_2Cl_2). NMR ($CDCl_3$) δ 0.35 (12 H, t, Et), 1.79 (12 H, m, Et), 2.25 (4 H, m, Et), 2.59 (4 H, m, Et), 3.87 (8 H, m, Et), 5.59 (2 H, s, methylene), 6.77 (2 H, s, methylene), 8.60 (2 H, s, meso), 9.27 (2 H, s, meso), −2.20 (2 H, s, NH). Optical spectra (CH_2Cl_2) λ_{max} (ϵ_M) 738 nm (123 000), 700 (10 000), 670 (5300), 520 (9500), 487 (15 900), 465 (3600), 407 (162 000), 384 (116 000). For comparison, the major peaks of bacteriopheophytin (BPheo) *b* occur at 782, 537, 401, and 366 nm.[5] The anion radical of **3** exhibits ESR and ENDOR parameters (Barkigia, K. M.; Chang, C. K.; Fujita, I.; Horning, T.; Fajer, J. *Biophys. J.* **1984**, *45*, 215) that further suggest that the compound is a useful model for BPheo and BChl *b*.[5]

(5) Davis, M. S.; Forman, A.; Hanson, L. K.; Thornber, J. P.; Fajer, J. *J. Phys. Chem.* **1979**, *83*, 3325–3332.

(6) Lubitz, W.; Lendzian, F.; Scheer, H.; Gottstein, J.; Plato, M.; Mobius, K. *Proc. Natl. Acad. Sci. U.S.A.* **1984**, *81*, 1401–1405.

(7) Compound **3**, $N_4C_{38}H_{50}$, crystallized from 1:1 mixtures of *n*-hexane and CH_2Cl_2 in the space group $P2_1/n$, in a unit cell of dimensions a = 11.244 (7) Å, b = 8.079 (4) Å c = 21.402 (7) Å, β = 96.54 (4)°, V = 1913.5 Å^3, and Z = 2. A total of 8724 reflections in the range $2° \le 2\theta \le 140°$ were collected at 140 K on an Enraf-Nonius CAD4 diffractometer equipped with Cu Kα radiation. Symmetry equivalents were averaged to give 3940 unique data and 3129 with $F_o \ge 3\sigma(F_o)$. All skeletal atoms were located from MULTAN. Subsequent difference Fourier maps indicated disordered solvent molecules which were included in the model as 0.80 hexane and 0.20 CH_2Cl_2. The identity of the solvates in the crystal was confirmed by mass spectral analysis. Positional and anisotropic thermal parameters for all non-hydrogen atoms were varied in a full-matrix least-squares refinement against the 3σ data until convergence at values of R_F and R_{wF} = 0.063 and 0.076. Hydrogen atoms (B = 4 Å^2) were positioned at idealized sites. Details of the determination are given in the supplementary material. Triclinic crystals of **3** were obtained from 1:1 mixtures of $CH_2Cl_2/CHCl_3$ in the space group $P\bar{1}$, in a unit cell of dimensions a = 8.655 (2) Å, b = 13.492 (4) Å, c = 7.856 (5) Å, α = 105.83 (4)°, β = 104.43 (4)°, γ = 97.23 (3)°, and Z = 1; 4005 reflections were collected by use of Mo Kα radiation in the range $2° < 2\theta < 42°$ at 300 K. Symmetry equivalents were averaged to give 1774 unique data and 1235 with $F_o > 3\sigma(F_o)$. The structure was solved and refined as above to R_F = 0.072 and R_{wF} = 0.070 (hydrogen atoms with B = Å^2). Details are available in the supplementary material.

(8) (a) Barkigia, K. M.; Fajer, J.; Chang, C. K.; Williams, G. J. B. *J. Am. Chem. Soc.* **1982**, *104*, 315–317. (b) Cruse, W. B. T.; Harrison, P. J.; Kennard, O. *J. Am. Chem. Soc.* **1982**, *104*, 2376–2380.

of the pyrroles and the bridges between them ($C\alpha$–C_{meso}) is evident and is most consistent with resonance forms of the tautomer in which the protons are localized on nitrogens N2 and N4 (protons at those positions are required for satisfactory refinements of both the $P2_1/n$ and $P\bar{1}$ structures).

The reduced rings II and IV bearing the exocyclic methylene group serve as synthetic analogues of rings II of BChl and BPheo *b*. The inductive effect of the double bond is reflected in the asymmetry of the ring: the C3–C4 bond is shorter than C1–C2 by 0.05 Å and 0.03 Å from the average of $C\alpha$–$C\beta$ bonds in several hydroporphyrins;[11] C1–N1 and C4–N1 also differ unlike the corresponding distances in pyrrole rings I and III. The C2–C3–C4 angle is stretched 5.6° relative to C1–C2–C3.

The enlarged cores observed in hydroporphyrins,[8-10] in which Ct–N distances to the reduced rings are longer than those to the pyrroles, are also evident in the present bacteriochlorin as well: Ct–N1 = 2.105 vs. Ct–N2 = 2.084 Å.

The macrocycle itself is effectively planar, with the largest deviations from the 24-atom core of −0.068 (2) and 0.066 Å at C2 and C3 and an out of plane displacement of 0.194 Å for C25. Individually, ring II is planar but slightly twisted as evidenced by a C1–C2–C3–C4 torsion angle of 5.3 (2)°. In comparison, ring III is flat, with atomic deviations of 0.00 Å and a value of 0.2 (2)° for the C6–C7–C8–C9 torsion angle. The planarity of the molecule is in sharp contrast to the distortions found in several hydroporphyrins where the torsional angles are as large as 48°.[9] The planarity of this synthetic model lends support to the suggestion advanced by Davis et al.[5] that BChl *b* is planar in *Rhodopseudomonas viridis* RC's.

The molecules of **3** pack in chains in which ring I of one molecule overlaps ring III of its neighbor with a vertical separation of 3.59 Å, indicative of π–π interactions. Significantly, the *same* overlap is observed in the $P\bar{1}$ and $P2_1/n$ crystal habits even though the latter includes molecules of solvation. The present results and those previously reported for a metal-free isobacteriochlorin,[8a] and for methyl-bacteriopheophorbide[3b] and -pheophorbide *a*,[12] suggest that π–π interactions alone can promote aggregation of these derivatives and thereby provide a mechanism for exciton migration in the crystal similar to those observed in vivo.[13] Indeed, although the synthetic bacteriochlorin (**3**) lacks the fifth ring, acetyl group, and magnesium atom of BChls *a* (**1**) or *b* (**2**), the packing of any two molecules of the model (Figure 2) mimics surprisingly well the overlapping structure **4** proposed[6] for the primary donors in bacterial reaction centers.[15]

Acknowledgment. This work was supported by the Division of Chemical Sciences, U.S. Department of Energy (Contract DE-AC02-76CH00016), at Brookhaven National Laboratory, and by the National Science Foundation (Grant CHE 7815285) and the U.S. Department of Agriculture (Grant 59-2261-0-1-437-0) at Michigan State University.

Note Added in Proof. The structure of *R. viridis* RC's at 3-Å resolution shows that rings I of the two BChls *b* of the special pair overlap with a vertical separation of ~3 Å and a Mg to Mg distance of ~7 Å to be compared with a separation of 3.6 Å and a center to center distance of 8.1 Å between overlapping molecules of **3**. (Deisenhofer, J.; Epp, O.; Miki, K.; Huber, R.; Michel, H. *J. Mol. Biol.*, in press. We thank these authors for communicating their results prior to publication.)

Supplementary Material Available: Experimental details, atom coordinates and anisotropic vibrational parameters for the nonhydrogen atoms, some least-squares planes, some intermolecular contacts, idealized positions for the hydrogen atoms, and a listing of the observed and calculated structure amplitudes for both crystal habits of **3** and a comparison of bond distances in several hydroporphyrins (41 pages). Ordering information is given on any current masthead page.

(9) Strauss, S. H.; Silver, M. E.; Ibers, J. A. *J. Am. Chem. Soc.* **1983**, *105*, 4108–4109. Gallucci, J. C.; Swepston, P. N.; Ibers, J. A. *Acta Crystallogr., Sect. B* **1982**, *B38*, 2134–2139.

(10) Barkigia, K. M.; Fajer, J.; Spaulding, L. D.; Williams, G. J. B. *J. Am. Chem. Soc.* **1981**, *103*, 176–181. Spaulding, L. D.; Andrews, L. C.; Williams, G. J. B. *J. Am. Chem. Soc.* **1977**, *99*, 6918–6923.

(11) See supplementary material for a comparison of bond distances and angles in several hydroporphyrins.

(12) Fischer, M. S.; Templeton, D. H.; Zalkin, A.; Calvin, M. *J. Am. Chem. Soc.* **1972**, *94*, 3613–3619. Chow, H. C.; Serlin, R.; Strouse, C. E. *J. Am. Chem. Soc.* **1975**, *97*, 7230–7237. Serlin, R.; Strouse, C. E. *J. Am. Chem. Soc.* **1975**, *97*, 7237–7242. Kratky, C.; Dunitz, J. D. *Acta Crystallogr., Sect. B* **1975**, *B31*, 1586–1589; **1977**, *B33*, 545–547; *J. Mol. Biol.* **1977**, *113*, 431–442.

(13) That such interactions in the crystal duplicate spectral features observed in vivo is evidenced by single crystals of methylbacteriopheophorbide *a*[14] and methyl- or ethylchlorophyllide *a*:[12] the first absorption bands are red shifted by 90 and 77 nm, respectively, relative to the spectra in solution.

(14) Hanson, L. K. *Proc. DOE Sol. Photochem. Conf., 7th, 1983* **1983**, LBL-16794, 135.

(15) One role of the magnesium and oxygen functional groups in vivo may well be to anchor the macrocycles in the protein so as to enhance the inherent tendency of the bacteriochlorin framework to form π–π aggregates.

Additions and Corrections

Nonvertical Triplet Excitation Transfer to *cis*- and *trans*-Stilbene [*J. Am. Chem. Soc.* **1984**, *106*, 3144]. JACK SALTIEL,* GARY R. MARCHAND, EWA KIRKOR-KAMINSKA, WILLIAM K. SMOTHERS, WARREN B. MUELLER, and JAMES L. CHARLTON

Page 3146, right column, 21st and 22nd lines: The sentence should read as follows—If $k_{-en} \ll k_{-dif}$ (case b′) then $k_{obsd} = K_{dif}k_{en}$, and if $k_{-en} \gg k_{-dif}$ (case b″) then $k_{obsd} = k_{dif}K_{en}$.