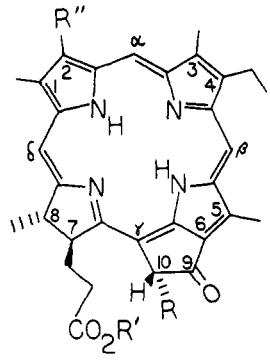
Bis(chlorophyll)cyclophanes. New Models of Special Pair Chlorophyll

Sir:

A key element in developing an understanding of the primary events of photosynthesis is the dependence of the optical and redox properties of chlorophyll special pairs on the orientation of the chlorophyll macrocycles relative to one another.[1] Dimeric chlorophyll derivatives in which the macrocycles are bound by a single covalent link exhibit several photochemical properties which mimic in vivo special pair chlorophyll.[2-4] Since the conformation responsible for the biomimetic properties of these dimers is both dynamic and highly solvent dependent, studies of special pair properties as a function of structure are somewhat restricted.

Recently, several workers have prepared bis(porphyrins) possessing cyclophane structures as models of multimetal redox enzymes.[5-8] Since these porphyrins do not possess the optical,[9] redox,[10] or donor-acceptor[11] properties unique to the chlorophylls, we have undertaken the synthesis of a series of bis(chlorophyll)cyclophanes to study the photochemical and redox properties of special pair models of well-defined structure compatible with a broad range of solvation conditions. We now report on the first member of this series, bis(chlorophyll)cyclophane **8**.

Pheophytin a (**1**) was converted to methyl pyropheophorbide a (**2**) in two well-known steps (90%).[12,13] The vinyl group of



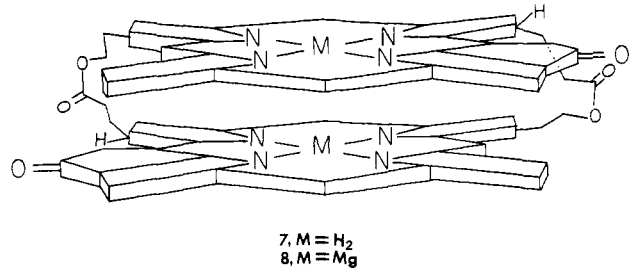
	R	R'	R"
1	CO_2CH_3	$C_{20}H_{39}$	$CH{=}CH_2$
2	H	CH_3	$CH{=}CH_2$
3	H	CH_3	$CH_2CH(OCH_3)_2$
4	H	CH_3	CH_2CHO
5	H	CH_3	CH_2CH_2OH
6	H	H	CH_2CH_2OH

2 was selectively oxidized with $Tl(NO_3)_3$ (2 × molar excess) in CH_2Cl_2–CH_3OH[14] (6:1 v/v, reflux 25 min) to the terminal dimethyl acetal **3** (63%; mass spectrum *m/e* 610 (M^+)). Following hydrolysis of acetal **3** to aldehyde **4** (THF–H_2O–HCl, 100:3:1 v/v; reflux 8 min; 98%; mass spectrum *m/e* 564 (M^+); ^1H NMR δ 10.07 (s, CHO)), aldehyde **4** was reduced to alcohol **5** (4 × molar excess $(C_4H_9)_4N^+BH_3CN^-$ in HMPA[15] containing 0.2 M H_2SO_4, 40 min, 25 °C; 51%; mass spectrum *m/e* 566 (M^+)). The methyl ester of **5** was hydrolyzed to yield hydroxy acid **6** (concentrated HCl under N_2, 25 °C, 1 h; mass spectrum *m/e* 552 (M^+)). Coupling of two molecules of **6** via double esterification was carried out with 2-chloro-*N*-methylpyridinium iodide (CMPI)[16] in the presence of Et_3N and a catalytic amount of 4-dimethylaminopyridine (DMAP) in refluxing butyronitrile to yield cyclophane **7** (10^{-3} M **6**, 10^{-2} M CMPI, 2 × 10^{-2} M Et_3N, 10^{-4} M DMAP, 115 °C, 20 min; 62%; mass spectrum *m/e* 1068 (M^+); vis λ_{max} (acetone) 390 nm (ϵ 135 000), 502 (13 400), 532 (11 100), 605 (10 000), 658 (48 500)). Magnesium insertion into both macrocycles of **7** was effected with iodomagnesium 2,6-di-*tert*-butyl 4-methylphenolate[17] in refluxing CH_2Cl_2 to yield bis(chlorophyll)cyclophane **8** (88%; vis λ_{max} (acetone) 422 nm (ϵ 100 000), 530 (4460), 578 (8840), 605 (15 200), 612 (15 700), 650 (84 200)).

Table I. Proton Magnetic Resonance Data

Position	Chemical shift, δ (ppm)			
	7[a]	**9**[a]	**8**[b]	**10**[b]
4b	1.27	1.64	1.47	1.59
8a	1.53	1.72	1.49	1.62
7a, 7b	1.6-2.3	1.6-2.3	1.8-2.4	1.8-2.4
1	3.05	3.18	2.87	3.05
3	3.10	3.22	3.23	3.07
4a	3.70	3.81	3.50	3.62
5	3.57	3.54	3.57	3.15
7d CO_2CH_3		3.59		3.67
$-CH_2CH_2O-$	3.75		3.76	
CH_2CH_2O-	3.90		3.86	
7	4.19	4.24	4.28	3.90
8	4.45	4.46	4.28	4.05
10	4.67	5.09	4.81	4.97
δ	7.97	8.38	8.38	8.27
$rka	8.79	9.13	8.90	9.29
β	9.22	9.40	9.62	9.73
NH	−2.42	−1.67		

[a] In chloroform-*d*. [b] In 10% pyridine-d_5 in benzene-d_6.



7, M = H_2
8, M = Mg

The ^1H NMR spectra of **7** and **8** indicate that both macrocycles in each cyclophane are equivalent and therefore support a symmetric structure. The protons at the periphery of the macrocycles in **7** and **8** experience small chemical-shift changes relative to monomeric *meso*-methyl pyropheophorbide a (**9**) and its magnesium complex (**10**), respectively (Table I). Since these shifts result from the influence of the ring current of the adjacent macrocycle,[18] their small magnitude suggests a structure for **7** and **8** in which the macrocycles are stacked approximately center to center. Moreover, the pyrrolic NH protons of **7** occur 0.75 ppm upfield of those in **9** consistent with the positioning of these protons directly above the π system of the adjacent macrocycle. The data do not preclude the possibility that there may be a small angle of tilt between the planes which the macrocycles occupy. Space-filling models indicate that the angle of twist between the ring I–ring III axes of the macrocycles may vary between 50 and 90°.

The Q_y transition in the optical spectra of **7** and **8** occurs at 658 and 650 nm, respectively. These transitions do not exhibit the solvent dependency characteristic of structural changes in the singly linked chlorophyll dimers.[2-4] Moreover, the optical spectra of **7** and **8** are virtually identical with those of their monomeric counterparts **9** and **10**, respectively. This result is consistent with the structure of **7** and **8** and the exciton description[19] of coupling between the Q_y transition dipoles of each macrocycle if the twist angle between these dipoles is on the average 90° at room temperature.

The fluorescence spectra of **7** and **8** are unchanged relative to monomeric **9** and **10** with maxima at 666 and 657 nm, respectively, in acetone. Despite the proximity (~4–6 Å) of the macrocycles in the cyclophane structure there is no evidence of exciton splitting.

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Table II. Redox Potentials vs. SCE

Compd	Oxidation[a,b] $E^1_{1/2}$	Oxidation[a,b] $E^2_{1/2}$	Reduction[b,c] $E^1_{1/2}$	Reduction[b,c] $E^2_{1/2}$
8	0.54	0.77	−1.29	−1.77
Chlorophyll a	0.61	0.84	−1.14	−1.61

[a] In $CH_3CH_2CH_2CN$. [b] 0.1 M tetra-*n*-butylammonium perchlorate supporting electrolyte. [c] In DMF.

Although optical spectroscopy of the singlet manifold at ambient temperatures reveals virtually no electronic interaction between the macrocycles, an examination of the doublet states as evidenced by the redox properties of **8** indicates quite the opposite. Cyclophane **8** undergoes photooxidation when irradiated with 650-nm light in the presence of electron acceptors, e.g., iodine, quinones, etc., and chemical oxidation by Zn $TPP^{+\cdot}$,[20] to yield a cation radical possessing a Gaussian EPR signal with 6.44-G line width. Based on the treatment of Norris et al.[21] the narrowing of this line width relative to the 9-G line width of monomeric chlorophyll a indicates that spin is shared *equally* by the two macrocycles analogous to special pair chlorophyll a in vivo.

Since the structure of **8** is not affected by polar solvents as is that of the singly linked chlorophyll dimers, we were able to determine the redox potentials of **8** by ac voltammetry (Table II). Cyclophane **8** undergoes reversible one-electron oxidation 70 mV more easily than chlorophyll a. This result is consistent with the delocalization of unpaired electron density over both macrocycles in the cation radical of **8**. Characteristically, chlorophyll special pairs in vivo are more readily oxidized than bulk chlorophyll in the organism.[1] The reversible one-electron reduction of **8** is more difficult than that of chlorophyll a by 150 mV. The possibility exists that the unpaired electron may be localized on one macrocycle in the radical anion of **8**. Electron spin resonance experiments have been initiated to clarify this point.

The only evidence that photoreaction center chlorophyll in both purple photosynthetic bacteria and in green plants consists of a *pair* of chlorophyll molecules is derived from magnetic resonance experiments. The line width of the EPR signal produced upon photooxidation of reaction centers is exchange narrowed relative to that exhibited by the corresponding monomeric chlorophyll cation radical in vitro.[21] Moreover, ENDOR experiments have shown that the proton hyperfine splittings of the species responsible for the EPR signal in vivo are one-half the magnitude of the splittings observed in vitro.[21] All known reaction center chlorophylls possess a long wavelength optical transition which is red shifted relative both to that of bulk antenna chlorophyll in the organism and to that of the corresponding monomeric chlorophyll in vitro.[1]

The results of this study support our earlier proposal[2] that special pair geometries exist which adequately account for both the redox and spin delocalization properties of chlorophyll special pairs in vivo, yet do not give rise to unusually red-shifted optical spectra. Thus, we have shown that the optical spectra exhibited by chlorophyll special pairs in vivo need not be exclusively an intrinsic property of the pair itself but may be influenced strongly both by the presence of additional chromophores and by important chlorophyll–protein interactions.

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Thermolysis of 2-Acetoxy-Δ^3-1,3,4-oxadiazolines. Evidence for Stepwise Homolysis of Cyclic Diazenes

Sir:

Mechanisms of thermal, homolytic decomposition of diazenes (azo compounds) continue to be of interest.[1] Various probes, including activation parameters,[2-4,7,8] stereochemistry,[2,4,8,9] isotope, and other substituent effects on rates,[3,8,10] and dependence of rates on viscosity[11] have been applied in attempts to distinguish between concerted and stepwise loss of nitrogen. The mechanistic pattern that has emerged is that symmetrical diazenes, with few exceptions,[12,13] adopt the concerted pathway and that unsymmetrical diazenes are more prone to homolysis by the stepwise mechanism.[2,9-11,13,14] More detailed structure-mechanism correlations for thermolysis of azo compounds must await further results, including the effects of heteroatom substituents. We now report studies of oxadiazolines **1d–j** which indicates that they undergo stepwise thermolysis through 1,5-diradical intermediates.

Thermolysis of oxadiazolines (**1a–c**) in solution had been reported[15] to yield acetoxyoxiranes (**2a–c**), which, in turn, decomposed to acetoxy ketones (**3a–c**). Compound **1c** had also been decomposed in the presence of olefinic dipolarophiles[16] which trapped an intermediate, probably the carbonyl ylide **6a**, by 1,3 cycloaddition.[16] Acetoxyoxirane **2c** was formed as a by-product.[16]

To our surprise, the analogues (**1f**, **1h**)[17,18] gave thermolysis products unrelated to **2** and **3**. In benzene, at 79 °C, decomposition of **1h** is first order ($k = 1.25 \times 10^{-5}$ s^{-1}) and the products are **4b** (87%) and small amounts of acetaldehyde, acetone, acetic acid, acetic anhydride, 1,1-diacetoxyethane,

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