Behavior of Di- and Tetrahydroporphyrins under Alkaline Conditions. Direct Observation of the Chlorin–Phlorin Equilibrium[1]

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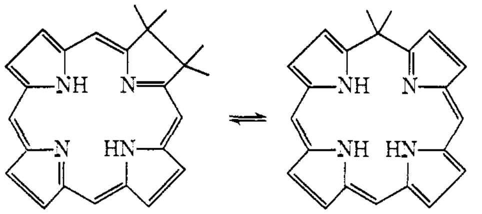
Abstract: The title phenomenon was investigated in *tert*-butoxide–*tert*-butyl alcohol-d_1 mixtures. A fast nonisomerizing H–D exchange is observed accompanied by a slower chlorin–phlorinide ion equilibration.

The kinetic and thermodynamic relationship between the two well characterized dihydroporphyrin ring systems, chlorins and phlorins, is not known (eq 1).



(1)

chlorin phlorin

While the chlorin structure is well documented historically, and indeed constitutes the basic nucleus of chlorophyll, phlorins are relatively new upon the chemical scene. Phlorins have been observed sporadically to arise on reduction of porphyrins and metalloporphyrins[2,3] and were involved as intermediates in Woodward's chlorophyll synthesis.[4,5] Although phlorins (or metallophlorinides) should be clearly less stable than chlorins (*e.g.*, ref 3), conditions necessary and sufficient to relate these two most interesting ring systems are to date unspecified. The chlorin–phlorin equilibrium is particularly intriguing in that if observed it affords a mechanism wherein the "saturation" of the chlorin might move about the great ring of the porphyrin.

In order to probe the above points, we have subjected the zinc complexes of *meso*-tetraphenylporphyrin (TPP), tetraphenylchlorin (TPC), tetraphenylbacteriochlorin (TPBC), and tetraphenylisobacteriochlorin (TP-*i*-BC) (Figure 1) to the action of potassium *tert*-butoxide in *tert*-butyl alcohol and *tert*-butyl alcohol-d_1.[6] In brief, we find that hydrogen–deuterium exchange at the saturated methylene groups of these porphyrin derivatives proceeds under mild conditions without the involvement of processes entailing movement of the sites of saturation about the great ring (*e.g.*, interconversion of bacterio- and isobacteriochlorin). Under harsher conditions there is observed in the case of zinc tetraphenylchlorin (ZnTPC) an exchange process involving *all* chlorin hydrogens, the mechanism of which most likely involves movement of the saturation about the porphyrin *via* chlorin–phlorin equilibration.

Results and Discussion

When allowed to stand at room temperature in 1 *M* base-*d*, ZnTPC is rapidly tetradeuterated (Table I).

Table I. Isotopic Distribution in ZnTPC, ZnTPBC, and ZnTP-*i*-BC on Equilibration with Base-*d* at 25° for 24 hr

Recovered porphyrin	% deuterium content[a] d_0	d_1	d_2	d_3	d_4	d_5	d_6	d_7	d_8	d_9	D/molecule
ZnTPC	1	1	5	20	69	4	0	0	0	0	3.67
ZnTBPC	0	0	0	0	1	1	5	30	56	6	6.91
ZnTP-*i*-BC	0	0	0	0	0	10	11	26	46	7	6.29

[a] Deuterium content was determined by mass spectral analysis of the free bases and rounded to the nearest per cent.

Localization of deuterium at the saturated carbons was shown by the nmr of the derived TPC-d_4. In the nmr spectrum of TPC (in deuteriochloroform), the phenyl hydrogens appear as a singlet at δ 7.6 (20 H), H1–H2 as a singlet at 4.10 (4 H), H3–H8 and H4–H7 as an AB quartet, δ_A 8.49, δ_B 8.10, J_{AB} = 4.5 Hz (4 H), and H5–H6 as a singlet at δ 8.34 (2 H). In TPC-d_4 the singlet at δ 4.10 had disappeared.

Under the above conditions the half-life for exchange of the saturated hydrogens is approximately 2 hr. This may be compared with a half-life for exchange of the benzylic proton in 2-phenylbutane in 0.41 *M* base-*d* at 215° of *ca.* 75 hr.[7] The saturated hydrogens of ZnTPC are accordingly rather acidic.

A similar situation holds for ZnTPBC and ZnTP-*i*-BC. These metal complexes rapidly afford the corresponding d_8 species under the above conditions (Table I) with a rate similar to that of ZnTPC. In both cases, nmr allows one to place the deuterium in the saturated methylene groups. Under these conditions, deuterium exchange of ZnTPBC and ZnTP-*i*-BC is not accompanied by interconversion of the two isomeric species. Accordingly, the cross-conjugated species **1** (Figure 2) which could arise from protonation of the conjugated bases of ZnTPBC and ZnTP-*i*-BC may be ruled out as an intermediate kinetically accessible from these isomers.

The above data, taken in conjunction with the ob-

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[2] (a) D. Mauzerall, *J. Amer. Chem. Soc.*, **84**, 2437 (1962); (b) H. H. Inhoffen, P. Jager, R. Mählhop, and C-D. Mengler, *Justus Liebigs Ann. Chem.*, 704, 188 (1972); (c) H. H. Inhoffen and P. Jager, *Tetrahedron Lett.*, 1317 (1964); (d) H. H. Inhoffen and P. Jager, *ibid.*, 3387 (1965).

[3] G. L. Closs and L. E. Closs, *J. Amer. Chem. Soc.*, **85**, 818 (1963).

[4] R. B. Woodward, *Ind. Chim. Belge*, **27**, 1293 (1962).

[5] R. B. Woodward, *Pure Appl. Chem.*, **2**, 383 (1961).

[6] Hereafter referred to as "base" and "base-*d*."

[7] D. J. Crum, C. A. Kingsbury, and B. Rickborn, *J. Amer. Chem. Soc.*, **83**, 3688 (1961).

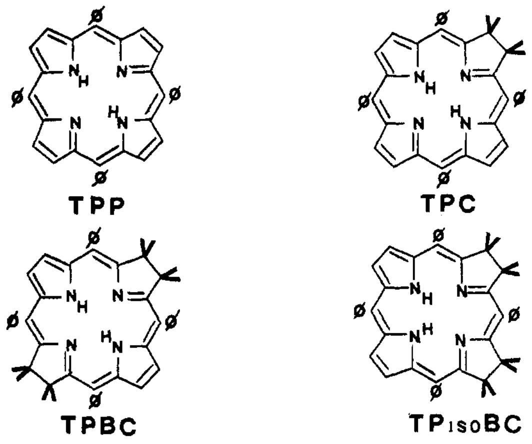

Figure 1.

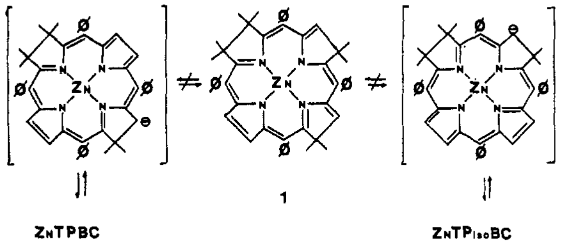

Figure 2.

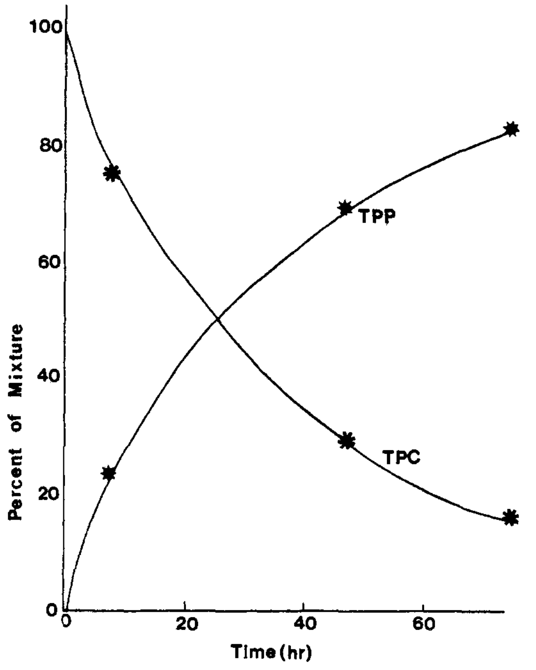

Figure 3. Decay of ZnTPC (isolated as TPC) on heating ZnTPP in 1 *M* base-*d* at 103°.

servation that ZnTPP is not deuterated under these conditions, are consistent with a mechanism involving simple deprotonation–protonation of the saturated methylene groups in the reduced porphyrin complexes.

When a degassed solution of ZnTPC in 1 *M* base-*d* is heated at 103° for extended periods of time, two further processes become apparent. Firstly, the chlorin complex is substantially consumed with concomitant isolation of TPP on aerobic aqueous acid work-up of the reaction mixture. A porphyrin:chlorin ratio of 6 is approached on extended periods of heating. The decay of ZnTPC with time is pictured in Figure 3. A similar phenomenon was observed with ZnTPBC and ZnTP-*i*-BC. Heating these in 1 *M* base led to their sequential dehydrogenation to ZnTPC and ZnTPP (Figures 4 and 5).

Secondly, heating ZnTPC in 1 *M* base-*d* leads to deuterium incorporation considerably in excess of 4 D/molecule of TPC and 2 D/molecule of the product TPP (Table II). The spectrum of ZnTPC in a degassed solution of potassium *tert*-butoxide in *tert*-butyl alcohol before and after heating at 130° is shown in Figure

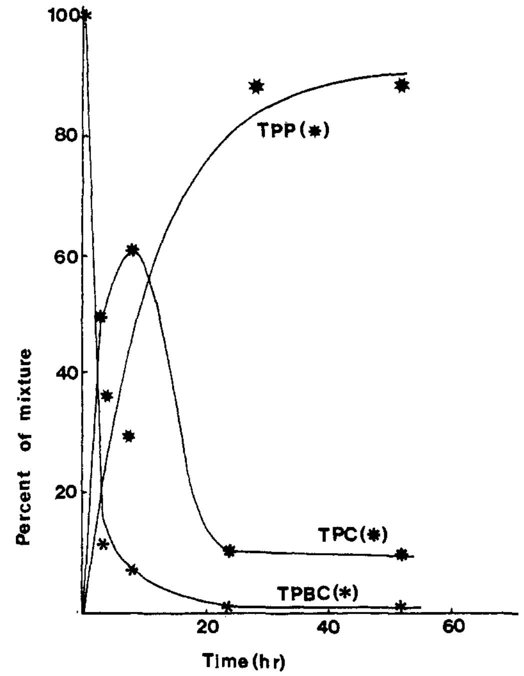

Figure 4. Disappearance of ZnTPBC on heating it in 1 *M* base. The zinc complexes were converted to free prophyrins before analysis.

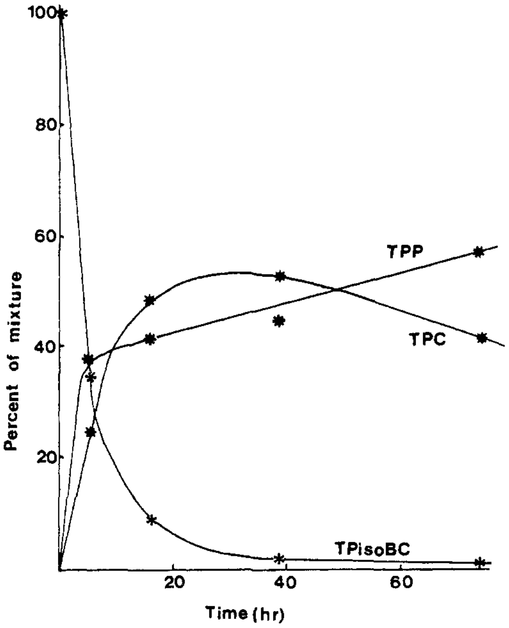

Figure 5. Time course arising from heating ZnTP-*i*-BC in base.

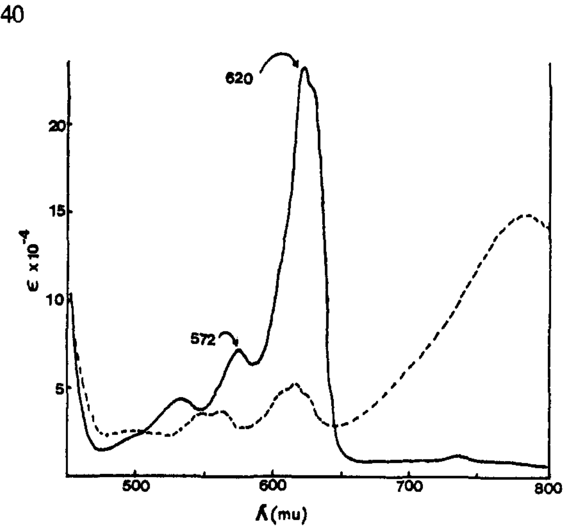

Figure 6. Spectra before (——) and after (-----) heating a solution of ZnTPC in potassium base at 130° for 37 hr.

Table II. Deuterium Incorporation in Recovered ZnTPC and ZnTPP Resulting from Equilibration of ZnTPC with Base-*d* at 103°

Product		% deuterium content[a]									D/molecule
	hr	d_0	d_1	d_2	d_3	d_4	d_5	d_6	d_7	d_8	
ZnTPP	20	5	15	70	3	2	1	4	1	0	2.08
	47	4	13	65	6	7	2	1	1	0	2.12
	75	3	10	53	8	12	3	4	3	3	2.72
	100	3	9	39	10	17	6	8	4	3	3.15
ZnTPC	20	4	1	5	18	62	4	5	0	1	3.71
	47	2	1	4	14	41	13	20	3	2	4.37
	75	1	1	3	8	26	17	30	7	6	4.97
	100	1	1	3	5	13	16	26	13	13	5.05

[a] Mass spectral analysis was performed on the free bases.

6. The development of an absorption maximum at *ca.* 790 mμ suggested that there was being produced an equilibrium mixture of ZnTPC and zinc tetraphenylphorinide anion. Preparation of potassium zinc tetraphenylphlorinide ($K^+ZnTPPhl^-$) by the procedure of Closs and Closs[3] afforded a product having an absorption maximum of 790 mμ (ε 1.9 × 10^4) essentially identical with that of the long-wavelength portion of the ZnTPC–base reaction mixture. Phlorins are known to suffer ready air oxidation to porphyrins[4] which accounts for isolation of a mixture of TPC and TPP on opening the reaction mixture to air and demetalation. That one was observing a chlorin–phlorin equilibrium

$$\mathrm{ZnTPC} + {}^-\mathrm{OC(CH_3)_3} \rightleftharpoons \mathrm{ZnTPPhl^-} + \mathrm{HOC(CH_3)_3}$$

was substantiated in two ways. Heating a solution of $K^+ZnTPPhl^-$ in 0.5 *M* base in 1:1 *tert*-butyl alcohol–tetrahydrofuran afforded a solution, analysis of which by its uv–vis spectrum indicated a $ZnTPPhl^-$:ZnTPC ratio of 6.8. Work-up afforded a TPP:TPC ratio of 5.6. Repetition of this experiment, starting with ZnTPC afforded a $ZnTPPhl^-$:ZnTPC ratio of 5.9 before work-up and a TPP:TPC ratio of 8.1. The expected proportionality between *tert*-butoxide ion concentration and $ZnTPPhl^-$:ZnTPC was observed. Starting from ZnTPC and using 0.4 *M* alcohol, a TPP:TPC ratio (after work-up) of 3.6 was observed. When 0.2 *M* base was used a TPP:TPC ratio of 2.1 was observed. An equilibrium constant ($K = [\mathrm{ZnTPPhl^-}]/[\mathrm{ZnTPC}][\mathrm{KO\text{-}Bu^+}]$) of approximately 10 M^{-1} may accordingly be calculated for the equilibration of chlorin and phlorinide anion in *tert*-butyl alcohol–*tert*-butoxide mixtures.

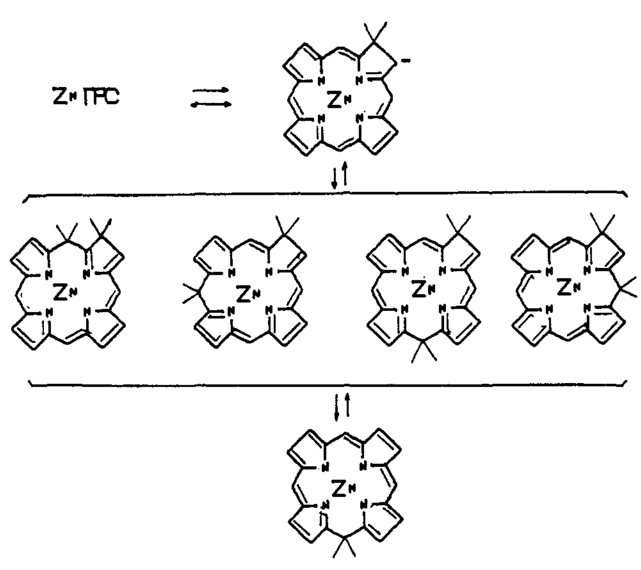

Figure 7.

Incorporation of solvent deuterons into recovered ZnTPC in excess of 4 D/molecule may now be explained in terms of the above demonstrated phlorin–chlorin equilibrium which effectively results in movement of the chlorin saturation about the porphyrin ring. An experimentally verifiable feature of this hypothesis is that incorporation of solvent deuterons in isolated TPC and TPP should occur in a pairwise fashion. Examination of Table II shows a tendency for this to occur.

To further probe this scheme, ZnTPC-*3,4*-d_2 and ZnTPC-*5,6*-d_2 were prepared from ZnTP-*i*-BC and ZnTPBC, respectively, by sequential: (1) deuteration at 25° to bacteriochlorin-d_8, (2) dehydrogenation with 1 equiv of chloranil to chlorin-d_6, and (3) treatment with potassium *tert*-butoxide–*tert*-butyl alcohol at 25° to chlorin-d_2. The two isomeric chlorin-d_2 species were subjected to base treatment at 130° (Table III). The results for isolated TPP indicate an essentially random loss of deuterium but ZnTPC-*5,6*-d_2 appears to lose its deuterons faster than ZnTPC-*3,4*-d_2.

Table III. Per Cent of Original Deuterium Remaining in TPP and TCC Isolated on Heating *trans*-ZnTPC-d_2 and *cis*-ZnTPC-d_2 in Base at 130°

Porphyrin	Precursor	% deuterium remaining		
		Time, hr		
		5	12	30
TPP	*trans*-ZnTPC-d_2	92	58	25
TPP	*cis*-ZnTPC-d_2	83	61	32
TPC	*trans*-ZnTPC-d_2	76	44	15
TPC	*cis*-ZnTPC-d_2	90	83	63

Conclusions

A somewhat speculative scheme to explain the zinc chlorin–zinc phlorinide equilibrium is presented in Figure 7. Which (if any) of the bracketed "isochlorins" should be invoked as intermediates cannot be said; one can only point out that they all predict a faster deuteron loss from ZnTPC-*3,4*-d_2 than from ZnTPC-*5,6*-d_2. With respect to the behavior of ZnTPBC and ZnTP-*i*-BC toward base, it is clear that the previously observed[1] differential behavior of TPC and its zinc complex toward diimide, the former being reduced to the bacteriochlorin TPBC and the latter to the zinc complex of the isobacteriochlorin (ZnTP-*i*-BC), is not due to a base catalyzed bacteriochlorin–isobacteriochlorin interconversion but reflects a fundamental difference in reactivity of the complexed and uncomplexed chlorin toward electrocyclic addition reactions.

Experimental Section[8]

Zinc Tetraphenylporphyrin (ZnTPP). A solution of 2.9 g (4.7 mmol) of tetraphenylporphyrin and 2.5 g of zinc acetate dihydrate in 200 ml of pyridine was stirred at 100° for 4 hr. The cooled reaction mixture was partitioned between benzene and water. Evaporation of the benzene layer followed by recrystallization of the residue from benzene afforded 2.3 g (65% yield) of the dipyridinate complex of ZnTPP. Heating of this for 10 hr (138° (0.01 mm)) afforded ZnTPP itself: uv $\lambda_{\max}^{C_6H_6}$ 421 mμ (5.2×10^5), 548 (2.3×10^4), 588 (3.7×10^4) [lit.[9] 422 mμ (5.9×10^5), 550 (2.2×10^4), 590 (3×10^4)].

Zinc tetraphenylchlorin (ZnTPC) was prepared in a similar manner under nitrogen, the heating period being 1 hr: uv $\lambda_{\max}^{C_6H_5N}$ 426 mμ (2.8×10^5), 530 (6×10^3), 575 (8.7×10^3), 601 (1.6×10^4), 627 (4.7×10^4) [lit.[9] $\lambda_{\max}^{C_6H_5N}$ 530 (6×10^3), 575 (10^4), 600 (1.6×10^4), 627 (4.7×10^4)]; nmr δ ($CDCl_3$) 4.18 (4 H, s), 7.7 (10 H, m), 7.90 (4 H, m), 8.10 (8 H, m), 8.40 (2 H, s), 8.55 (2 H, d, Δ_ν = 4.5 Hz).

Zinc tetraphenylbacteriochlorin (ZnTPBC) was prepared as above by heating a solution of 150 mg (0.25 mmol) of tetraphenylbacteriochlorin and 1.5 g of zinc acetate in 30 ml of pyridine in a sealed tube at 100° for 18 hr: uv $\lambda_{\max}^{C_5H_5N}$ 390 (10^5), 567 (4.4×10^4), 690 (1.1×10^4), 756 (1.3×10^4); nmr δ (C_5D_5N) 3.88 (8 H, s).

Zinc tetraphenylisobacteriochlorin (ZnTP-*i*-BC) was prepared as for ZnTPP, heating at 50° for 0.5 hr: $\lambda_{\max}^{C_6H_5N}$ 418 (1.5×10^5), 498 (1.1×10^4), 562 (1.5×10^4), 607 (5.7×10^4); δ (C_5D_5N) 3.21 (8 H, s).

Room Temperature Proton Exchange of Zinc Complexes. A solution of 30 mg (4.4×10^{-2} mmol) of the appropriate zinc complex in a mixture of 1 ml of 1.0 *M* base-*d* and 2 ml of dry tetrahydrofuran was placed in a vessel which was freeze–thaw degassed (10^{-5} mm), sealed, and allowed to stand at room temperature in the dark. After 24 hr (the exchange reactions had half-lives of *ca.* 2 hr), the vessel was opened and the solution was worked up by partitioning between benzene and water to afford the zinc complexes of the porphyrins. Demetalation of the zinc complexes was affected by brief shaking of the above benzene layer with 20% (v/v) hydrochloric acid. Analysis of the porphyrins and zinc porphyrins for deuterium content was done by nmr and mass spectrometry and is discussed in the text. Control experiments (comparing mass spectra of the porphyrins and their zinc complexes) showed that acid demetalation did not affect the deuterium content of the porphyrin.

High Temperature Proton Exchange of Zinc Complexes. A solution of 50 mg (7.8×10^{-2} mmol) of the appropriate zinc complex in a mixture of 3 ml of dry tetrahydrofuran and 3 ml of 0.1 *M* base-*d* was freeze–thaw degassed and sealed in a conventional vacuum line tree apparatus. That part of the tree containing the above mixture was immersed in an oil bath held at 130 ± 2°. Samples were removed periodically *via* tilting and sealing off the leaves of the tree. The sample removed was exposed to the atmosphere for 10 min and then partitioned between benzene and 10% hydrochloric acid. The benzene layer was then washed with water and sodium bicarbonate solution and dried. Analysis of the resulting solution for TPP, TPC, TPBC, and TP-*i*-BC was performed using the wavelengths 650, 740, 518, and 590 mμ, respectively. The results are discussed in the text. When the exchange behavior of ZnTPC was examined, the resulting TPP and TPC were separated for mass spectral analysis by extraction of the final benzene solution by 68% (w/w) phosphoric acid.[1]

Zinc Phlorin Anions. Sodium zinc tetraphenylphlorinide, as a solution in tetrahydrofuran, was prepared according to the procedure of Closs and Closs:[3] $\lambda_{\max}$ 800 mμ (2×10^4) (lit.[3] 2.1×10^4). A detailed discussion of the procedure and apparatus used is in ref 10. Repetition of this preparation, employing potassium naphthalenide rather than sodium naphthalenide, afforded a solution of potassium zinc tetraphenylphlorinide, $\lambda_{\max}$ 791 mμ (1.8×10^4).

Equilibration of Zinc Phlorinide Anion and Zinc Tetraphenylchlorin. (a) From Potassium Zinc Tetraphenylphlorinide. A degassed solution of potassium zinc phlorinide (from 36.0 mg of ZnTPP) in a mixture of 1.5 ml of dry tetrahydrofuran and 1.5 ml of 1.0 *M* base was prepared in an apparatus possessing a bulb (for heating), a 0.05-mm uv cell, and a single branch. After the solution was mixed, a sample was removed *via* the branch and analyzed after air oxidation for ZnTPP and ZnTPC. Only the former was observed. The bulb containing the solution was immersed in an oil bath held at 124° for 37 hr. At intervals of several hours, the reaction mixture was briefly cooled and its spectrum was determined.

(b) From Zinc Tetraphenylchlorin. The above procedure was repeated, using a solution of 24.5 mg of ZnTPC in a mixture of 1 ml of dry tetrahydrofuran and 1 ml of base. Before heating only ZnTPC was observed. Analysis of the above mixture at the end of 37 hr at 124° was performed by air oxidation to a mixture of ZnTPP and ZnTPC, demetalation of this to the TPP–TPC mixture and analysis of this as above. The results are presented in the text.

Effect of Base Concentration of the Zinc Chlorin–Zinc Phlorinide Equilibrium. A solution of 35.2 mg of ZnTPC in a mixture of 1 ml of dry tetrahydrofuran and 1 ml of 0.8 *M* base was prepared in an apparatus bearing a breakseal containing a mixture of 1 ml of tetrahydrofuran and 1 ml of *tert*-butyl alcohol. After the apparatus was freeze–thaw degassed and sealed, the reaction mixture was heated at 130° for 41 hr. The mixture was cooled and the additional tetrahydrofuran–*tert*-butyl alcohol mixture was added *via* the breakseal. An approximately 2-ml sample of the mixture was removed, opened to the atmosphere, and analyzed. A TPC:TPP ratio of 1:3.6 was found. The remainder of the mixture was heated at 130° for 18 hr, cooled, and worked up as above. Analysis afforded a TPC:TPP ratio of 1:2.1.

Isomeric Zinc Tetraphenylchlorin-d_2 Species from Zinc Tetraphenylbacteriochlorin. ZnTPBC-d_8 was prepared by allowing a mixture of 130 mg of ZnTPBC, 8 ml of tetrahydrofuran, and 4 ml of base-*d* to stand at room temperature for 48 hr. To a solution of the isolated bacteriochlorin in 15 ml of benzene was added 50 mg of *o*-chloranil. After standing at 25° for 45 min, the benzene solution was washed with a 10% solution of sodium bisulfite. The visible spectrum of the benzene layer was that of ZnTPC. The benzene was evaporated and a solution of the residual material in 10 ml of tetrahydrofuran and 5 ml of 0.8 *M* potassium *tert*-butoxide was allowed to stand at room temperature for 36 hr. Work-up then afforded after two recrystallizations from benzene 65 mg (50% yield) of ZnTPC-d_2: 10.2% d_0, 12.8 d_1, 70.9% d_2, 4.9% d_3, 1.7% d_4 by mass spectrometry. In its nmr spectrum the 2 H singlet at δ 8.4 was absent.

From ZnTP-*i*-BC. Repetition of the above sequence of operations afforded, from 225 mg of ZnTP-*i*-BC, 68 mg of ZnTPC-d_2: 32.6% d_0, 26.4% d_1, 35.7% d_2, 3.7% d_3, 1.1% d_4. The nmr of this substance possessed the 2 H singlet at δ 8.4 but lacked the 2 H doublet at δ 8.55.

Acknowledgment. Partial support of this work by the National Institutes of Health is acknowledged.

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[8] Nmr spectra were carried out on a Varian A-60A or HA-100 spectrometer. Deuterium analyses were performed at 7 eV nominal ionizing voltage on an AEI MS-902 instrument using experimentally determined P + 1, P + 2, and P + 3 intensities. These (except for Zn-*i*-TPBC) agreed well with theoretical values.

[9] G. D. Dorough, *J. Amer. Chem. Soc.*, 73, 4315 (1951).

[10] M. Y. Oester, Ph.D. Thesis, University of Wisconsin, 1970.