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THE CHEMICAL AND PHYSICAL BEHAVIOR
OF PORPHYRIN COMPOUNDS
AND RELATED STRUCTURES



Editor
Alan D. Adler

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THE CHEMICAL AND PHYSICAL BEHAVIOR OF PORPHYRIN
COMPOUNDS AND RELATED STRUCTURES*

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STEREOCHEMISTRY AND CHIROPTIC PROPERTIES OF PHEOPHORBIDES AND RELATED COMPOUNDS*

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Chlorophylls and hemoproteins contain closely related chromophores which are derived from the aromatic tetrapyrrolic porphyrin nucleus. In both systems, the absorption bands correlated with the macrocyclic chromophore are optically active, i.e., they exhibit Cotton effects in the ORD spectra.^{1,2} Although in hemoproteins the heme Cotton effects are induced by interactions of the achiral chromophore with the chiral protein environment,³ the chromophoric systems of chlorophylls are themselves chiral.^{4,5} Therefore, optical activity is lost in hemes but preserved in chlorophylls, when they are isolated from the protein complex. In the following discussion, interest is focused on these chiral chromophores, especially on chlorophyll a and b and on pheophorbides derived from these compounds.

Fischer^{5,6} first determined an asymmetric center at C-10 in chlorophyll a and discussed the potential optical activity. A slight levorotation in the near infrared was

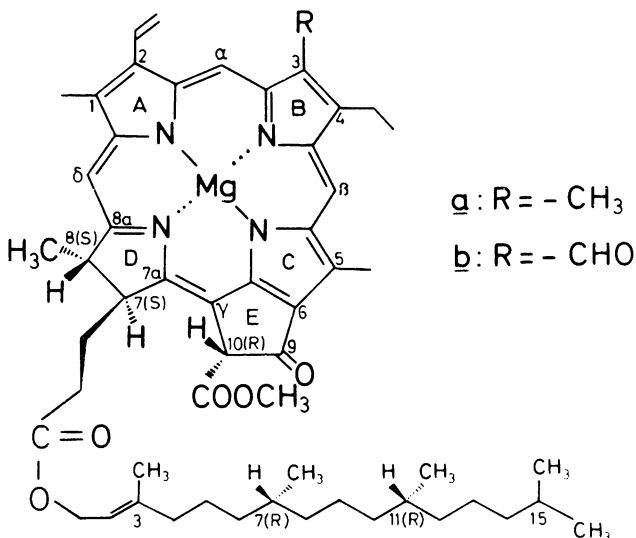


FIGURE 1. Chlorophyll a and b.

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observed by Stoll and Wiedemann⁷ and was confirmed by Fischer and Stern⁸ using a polarimeter with greater light intensity. Except for the dextrorotatory purpurins, they observed levorotation for a great number of chlorins. Although chlorins with achiral C-10 exhibit optical activity too, derived porphyrins are inactive. As a consequence, one or more additional asymmetric centers must be present. In the final structure presented by Fischer⁴ in 1940, chlorophyll *a* was proposed as a 7,8-dihydroporphyrin with the additional asymmetric centers at C-7 and C-8. This structure was proved by total synthesis⁹ twenty years later. The relative *trans*-configuration at C-7 and C-8 previously advanced by Fischer¹⁰ was verified by the isolation of *trans*-dihydrohematinic acid obtained by oxidative degradation¹¹ and by the determination of the 7H,8H spin-spin coupling constant.¹² The relative 7,10-*trans*-configuration was deduced from NMR and ORD measurements.¹³ Finally, the absolute (7S, 8S) configuration was determined by correlation with (-)- α -santonin¹⁴ and 2,3(S)-dimethyl-pentane.¹⁵

As early as 1935, Fischer and Stern⁸ observed that in certain reaction sequences optical activity was apparently lost and subsequently reappeared. Further studies¹⁶ revealed that in the vicinity of absorption bands the optical rotation strongly depends on the wavelength. The authors emphasized the need for ORD measurements, but instrumental difficulties were insurmountable at that time. After the development of sensitive spectropolarimeters and CD instruments, the preliminary investigations¹⁶ were resumed. The first genuine ORD spectrum of a chlorophyll *a* solution was published by Ke.² In the spectral range between 700 and 350 nm several Cotton effect (CE) curves of different sign and intensity were detected and correlated to the pertinent absorption bands.

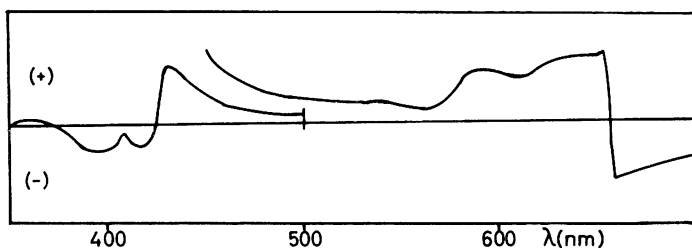


FIGURE 2. ORD spectrum of chlorophyll *a* in diethyl ether.²

A year later, the ORD spectra of chlorophyll holochromes isolated from chloroplasts and of various photosynthetic microorganisms were reported.^{17,18} Both absorption and ORD spectra of chlorophyll *a* and *b* in these preparations are superimposed on the transitions of the accompanying carotenoids in the blue region and of the proteins in the ultraviolet. Nevertheless, in several regions at longer wavelengths and in spectra from carotene-poor mutants, Cotton effects inherent in chlorophyll can be clearly seen. As compared with the free pigment spectra, the intensity and complexity of the ORD spectra are enhanced. Various degradation experiments with protein complexes¹⁷ and studies of concentration effects^{18,19} showed that this was due to chlorophyll-chlorophyll exciton interactions rather than to interactions with the proteins or carotenes.

Furthermore, the chiroptic properties of the chlorobium chlorophylls^{1,7}, bacteriochlorophyll a,^{18,20-22} as well as protochlorophyll^{23,24} and some C-10 disubstituted chiral porphyrins derived from chlorophyll a²⁵ were studied. Some theoretical work was done with protochlorophyll, chlorophyll a and bacteriochlorophyll a that gave the correct sign and relative intensities for the visible CD bands.^{22,23}

ORD and CD spectra of an extensive series of phytol-free methylpheophorbides and related compounds derived from chlorophyll a and b were reported by Wolf.^{1,3,25-28} In contrast to chlorophyll, the ORD and CD spectra of the pheophorbides are changed to some extent due to the loss of the central magnesium atom which lowers the molecular symmetry and, therefore, affects interactions between X- and Y-polarized transitions.²³ Since pheophorbides can be purified by simple chromatographic techniques, and can be handled and stored without decomposition, they are more suitable molecules than chlorophyll for structural modification. Thus, they lead the way to more general studies of their chiroptic properties as a function of the molecular structure of the chiral macrocycle.

*ORD and CD of 7,8-trans-Pheophorbides: Configurational
Assignment at C-10—the Influence of the Substitution
Pattern*

In the last two decades, experimental studies with pertinent physical methods such as electric birefringence and dichroism, fluorescence polarization, linear and magnetic dichroism, together with theoretical considerations (four-orbital model: Longuet-Higgins; Platt; Seely; Gouterman), led to a relatively good understanding of the absorption spectra of porphyrins.^{23,29,30} The results will be summarized briefly: all absorption bands are ascribed to $\pi-\pi^*$ transitions of the aromatic system isoconjugated to the [18]-annulene. In porphyrins of full D_{4h} symmetry such as porphyrin dianions, dications and metal complexes with uniform substitution patterns around the framework, both the highest occupied and the lowest unoccupied molecular orbitals are degenerate. The resulting electronic transition is split by configuration interaction and gives rise to one absorption band in the visible region (Q band) and one in the near ultraviolet region (B band). In derivatives of lower symmetry, such as porphyrin-free bases and chlorins, the degeneracy is lifted and both bands are split by polarization along the X (Q^x , B^x) and Y-axes (Q^y , B^y), and by vibronic transitions: ($0 \rightarrow 0$, $0 \rightarrow 1$, $0 \rightarrow 2$), although the B states remain more or less degenerate.

FIGURE 3 shows the absorption spectrum of pyromethylpheophorbide a (1), a typical chlorin spectrum with four well-resolved Q bands of lower intensity and the strongly allowed overlapping B-or Soret-band system around 400 nm. Further absorption bands are located in the UV region that have not yet been completely correlated with defined transitions.³¹ The absorption spectrum remains practically unaltered over the entire spectral region (700–200 nm) when a third chiral center is introduced as demonstrated by the epimeric 10(S)-methoxy-(4a) and 10(R)-methoxy-pyromethylpheophorbides a (4b) (FIGURE 4) whose absolute configuration at C-10 (relative to C-7) was determined by NMR spectroscopy.^{1,3,25}

On the other hand, the ORD and CD spectra^{1,3,25} (FIGURE 5) of both epimers show remarkable differences. Three of the four CE curves corresponding to the Q transitions are clearly discernable in the ORD spectra. Only the weak $Q^y_{0,1}$ -CE curve around 610 nm, which may be detected with the aid of the CD spectrum, is

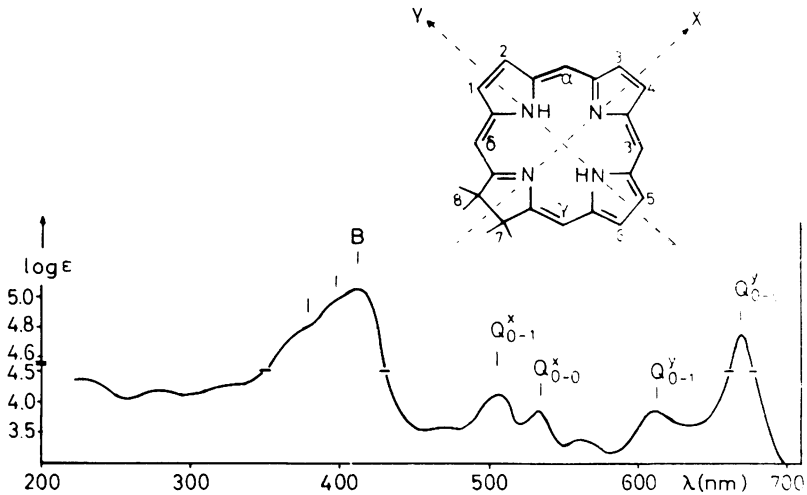


FIGURE 3. General formula of chlorins with X and Y polarization axes: absorption spectrum (dioxane) of pyromethylpheophorbide **a** (**1**).

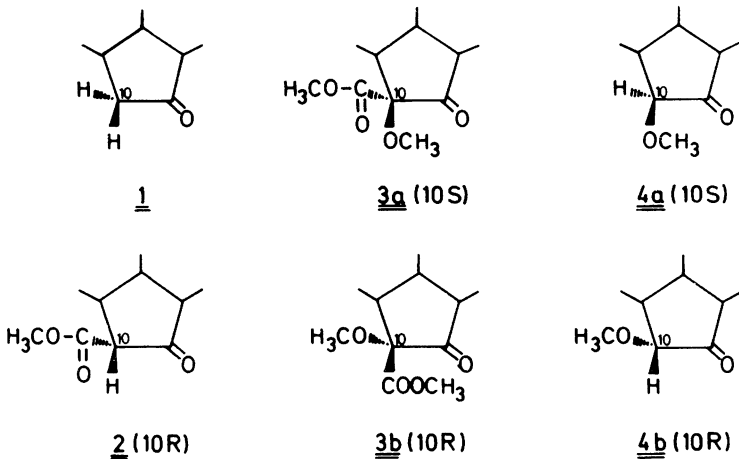


FIGURE 4. Partial structures (ring E) of the 7,8-*trans*-pheophorbides **a**.

hidden under the short wavelength tail of the strong Q_{0-0}^y -CE curve.† The Q_{0-0}^y band is strongly affected by the configuration at C-10; in the 10(S) epimer **4a**, the intensity is increased by a factor of three.

† The reduced intensity of the Q_{0-1} -CD bands as compared with the Q_{0-0} -CD bands is explained by mixing of the X and Y polarized components.²³

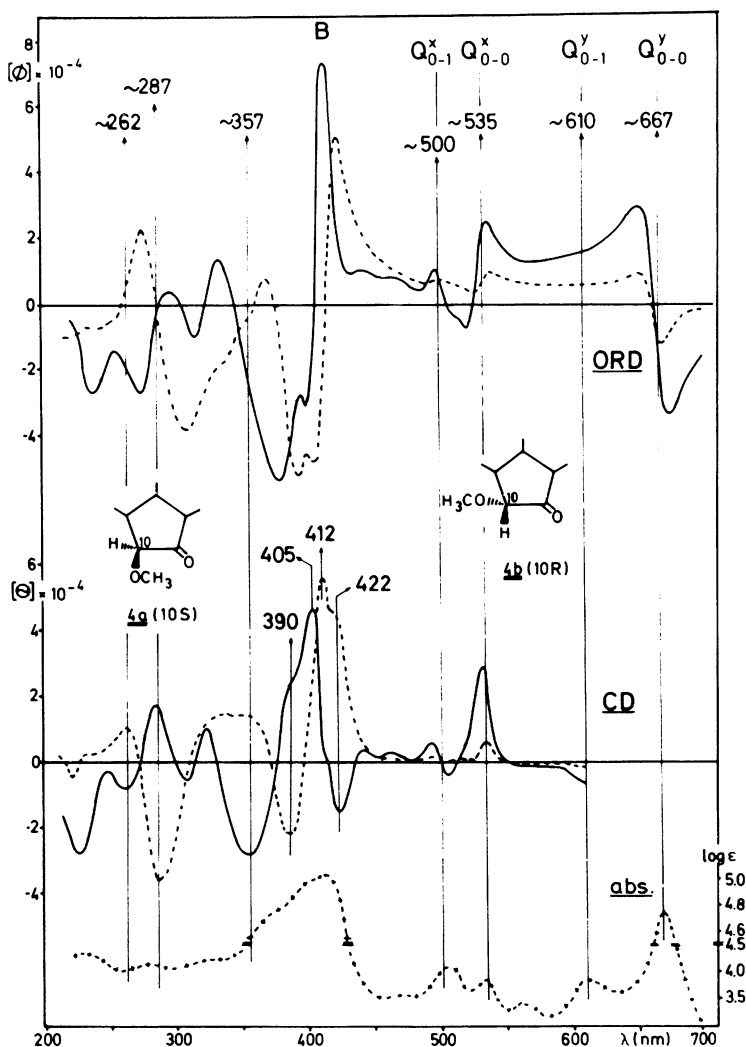


FIGURE 5. Absorption, ORD and CD spectra (dioxane) of the epimeric 10(S)-methoxy-(**4a**: —) and 10(R)-methoxy-(**4b**: ---) pyromethylpheophorbides a.

Two strongly overlapping CE curves appear in the Soret band region (450–370nm) of the ORD spectra, the one with long wavelength being positive for both epimers **4a** and **4b**, while in the CD spectra at least three bands can be detected corresponding to the different B^x and B^y transitions. The CD bands at 422 and 390 nm have different signs for both epimers. Another series of partially superimposed CE curves is located in the UV region (370–220 nm). Again, the CD spectra immediately demonstrate

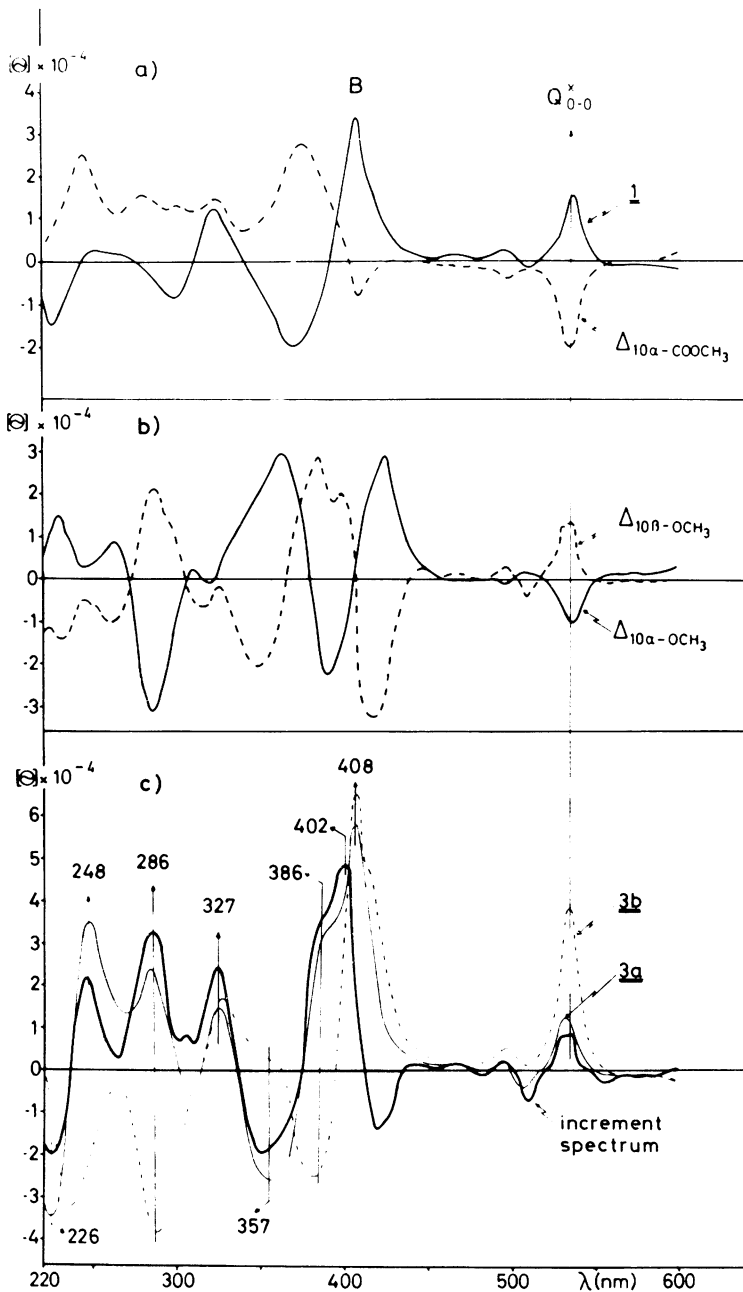


FIGURE 6. (a) CD spectrum of pyromethylpheophorbide **1** (—) and CD difference spectrum for the $10\alpha-COOCH_3$ substituent (**2a-1**: ---). (b) CD difference spectra for the $10\alpha-OCH_3$ (**4b-1**: —) and $10\beta-OCH_3$ (**4a-1**: ---) substituent. (c) CD spectra of $10(S)$ -methoxy (**3a**: —) and $10(R)$ -methoxy (**3b**: ----) methylpheophorbide **a** as compared to the increment spectrum of **3a**—(calculated from **1** + $\Delta_{10\alpha-COOCH_3}$ + $\Delta_{10\beta-OCH_3}$). All spectra were measured in dioxane.

that three of the four CD bands (at 262, 287 and 357 nm) have opposite signs for the epimers **4a** and **4b**.

The usefulness of chiroptic measurements for configurational assignments (by means of increment calculations of the C-10 substituents) in the series of pheophorbides may be demonstrated for the epimeric 10-methoxymethylpheophorbides **a** (**3a**, **3b**). For this purpose, ORD as well as CD spectra may be used.

FIGURE 6a shows the CD spectrum of pyromethylpheophorbide **a** (**1**) together with the CD increment spectrum for the 10α - \ddagger carbomethoxy substituent ($\Delta_{10\alpha\text{-COOCH}_3}$) obtained as difference spectrum from **2-1**. The CD increment spectra for the 10α - and 10β -methoxy group (FIGURE 6b) were derived in the same manner (**4b-1**; $\Delta_{10\alpha\text{-OCH}_3}$ and **4a-1**: $\Delta_{10\beta\text{-OCH}_3}$). It is noteworthy that the two increment spectra of the 10-OCH_3 group are almost perfect mirror images of each other over the entire spectral range, thus indicating a chiroptic contribution of equal magnitude for both configurations. Both the $10\alpha\text{-OCH}_3$ and the $10\alpha\text{-COOCH}_3$ group give a negative increment to the Q_{0-0}^y band (and a positive one to the rectangularly orientated Q_{0-0}^x transition as shown by ORD measurements § TABLE 1; FIGURES 5,6). The reverse is true for the $10\beta\text{-OCH}_3$ group of **4a**. This is in agreement with calculations using the Kirkwood polarizability approximation and point monopole transition moments.²²

TABLE 1
ORD AND CD DATA OF THE Q_{0-0} TRANSITIONS

Compound	Q_{0-0}^y -CE	Q_{0-0}^x -CE	Q_{0-0}^y -CD
1	$a^* \approx -280$	$a = +186$	$[\Theta]_{\max} \cdot 10^{-3} = +15.7$
2	$a \approx -80$	$a = -52$	$[\Theta]_{\max} \cdot 10^{-3} = -5.0$
4a	$a \approx -620$	$a = +315$	$[\Theta]_{\max} \cdot 10^{-3} = +28.7$
4b	$a \approx -210$	$a = +63$	$[\Theta]_{\max} \cdot 10^{-3} = +6.3$

$$* a = ([\phi]_{1\text{-extr.}} - [\phi]_{2\text{-extr.}}) \cdot 10^{-2}.$$

The CD spectrum of the $10(S)$ -methoxymethylpheophorbide **a** (**3a**) can now be calculated as the increment spectrum shown in FIGURE 6. It corresponds rather well to one of the experimental CD spectra except for minor deviations in the overlapping B-band region at about 400 nm (slight shift and a negative band at 425 nm). It is especially noteworthy that the CD bands at 226, 248, 286, 357 and 535 nm have the same sign and comparable intensities both for the experimental and the calculated spectra of **3a**.

The discussion so far has shown that the entire spectral range (from 600–220 nm) of the CD spectra of the pheophorbides may be used for configurational assignments at C-10. This has been done for an extensive number of epimeric 10-alkoxy methylpheophorbides of the *a* and *b* series.^{13,25,27} The results are fairly consistent and prove the validity of increment calculations. Modifications of the peripheral substitution pattern without affecting the chiral centers may, nevertheless, have a strong influence on distinct regions of the ORD/CD spectra.²⁷ Some pertinent examples concerning the substitution at positions C-3 and C-6, which are equivalent with respect to the X- and Y-polarization axes, are summarized in TABLE 2.

\ddagger α and β (as in terpene chemistry) mean below and above the molecular plane, respectively.

§ Due to instrumental limitations the Q_{0-0}^y -CD band could not be measured, and the α -value of the Q_{0-0}^y -CE curves are only of qualitative significance.

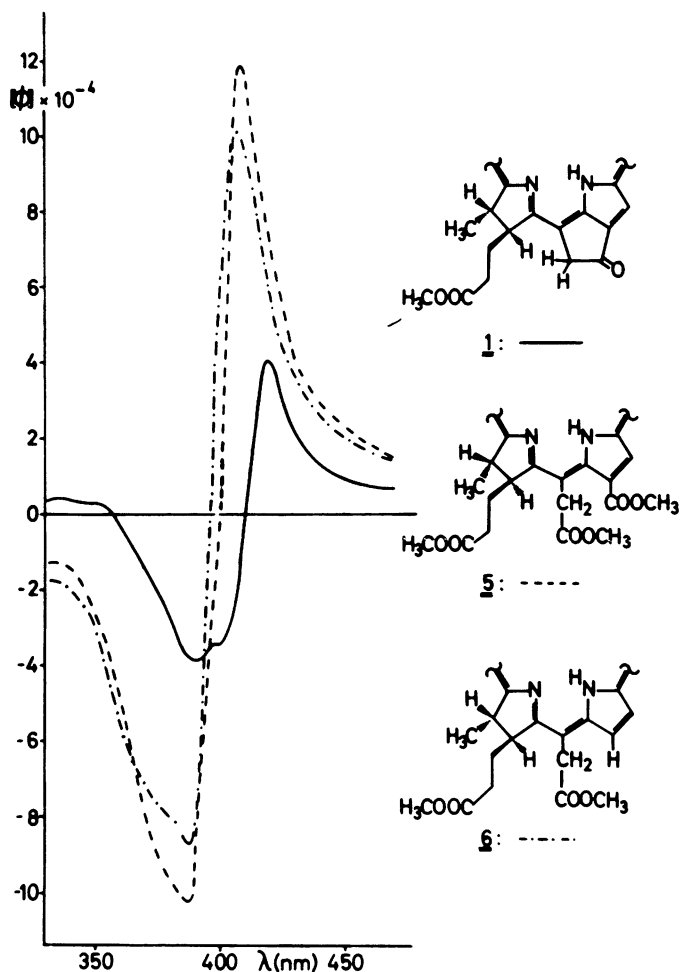


FIGURE 7. The effect of steric strain on the main CE curves (dioxane) in the Soret band region of γ -substituted chlorins.

leaves the ORD/CD spectra of the macrocyclic chromophore practically unaltered or has a minor influence (menthol, phytol.³² This may be expected, since these structural modifications are remote from the chromophoric system.

ORD and CD of 7,8-cis-Pheophorbides: Absolute Configuration—the Influence of C-7 and C-8

Pheophorbides of natural origin and those obtained by racemization¹⁰ or synthesis⁹ have the thermodynamically favored 7,8-*trans* configuration. The combined contributions of both asymmetric centers C-7 and C-8, substituted by different

groups, are therefore inherent to their chiroptic properties as analyzed by ORD and CD measurements. In order to be able to differentiate between the chiroptic effects of these two asymmetric centers, one must have at hand the corresponding 7,8-*cis*-pheophorbides. It is known that alkyl- or aryl-substituted porphyrins can be stereoselectively reduced to either the corresponding 7,8-*cis*-chlorins^{3,3} or to the racemic 7,8-*trans*-compounds.^{3,4}

We utilized the stereoselective reduction of suitable porphyrins in an indirect approach to *cis*-pheophorbides, using the following reaction sequence (FIGURE 8): *trans*-pheophorbides were dehydrogenated to the corresponding pheophorphyrins by HI isomerisation or treatment with Pd in glacial acetic acid. The pheophorphyrin zinc complexes were subsequently rehydrogenated by a Krasnovskii type photo-reduction with ascorbic acid and DABCO in ethanol.^{3,5} Since the 2-vinyl group was reduced in the first reaction step, this group was also catalytically hydrogenated in the reactant *trans*-chlorins used as reference compounds for configurational assignments.

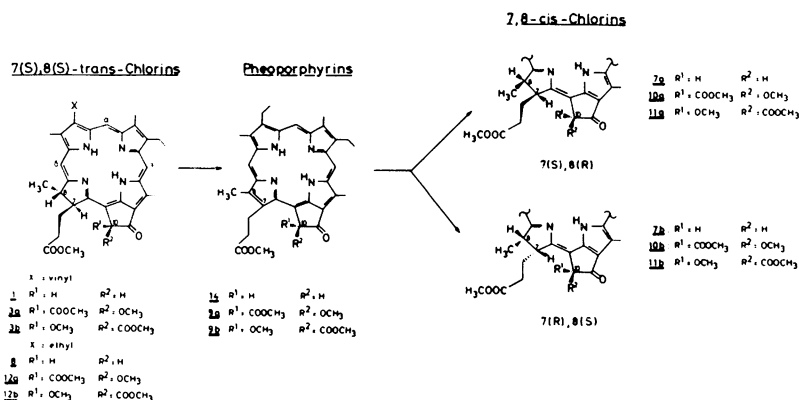


FIGURE 8. Reaction sequence for the preparation of 7,8-*cis* pheophorbides.

Starting with pyromethylpheophorbide **1**, racemic 7,8-*cis*]-mesopyromethylpheophorbide **a** (**7a**, **7b**) was obtained by this dehydrogenation-hydrogenation sequence (via phylloerythrin methyl ester **14**). **7a**, **7b** was free of the *trans* epimer within analytical error (less than 5% as measured by NMR). The racemate **7** was partially resolved by chromatography on acetylated cellulose. According to their "mirror image type" of ORD spectra, the enantiomers **7a** and **7b** have somewhat different enantiomeric purities.^{3,5}

In order to obtain optically pure 7,8-*cis*-pheophorbides, we started with reactants with an additional asymmetric center. The epimeric 10(S,R)-methoxy methylpheophorbides **a** (**3a/3b**) of known absolute configuration (see above) were best suited for

|| Evidence for the relative *cis* configuration was obtained from the absorption spectra (bathochromic shift of the visible bands), the NMR spectra (enhanced anisochrony of the 10-methylene protons) and the mass spectra (strong (M-2)⁺ peak.^{3,5}

this purpose since, under basic and slightly acidic conditions, they are configurationally stable at C-10.³² The 10(*S,R*)-methoxy pheoporphyrins **9a** and **9b** obtained by HI isomerization of **3a** and **3b** turned out to be optically pure enantiomers, as demonstrated by NMR data[¶] and their mirror image ORD spectra (FIGURE 9). Photoreduction of **9a** and **9b** resulted in the formation of two pairs of diastereomeric 7,8-*cis*-chlorins, **10a/10b** and **11a/11b**, respectively. As indicated by the schematic

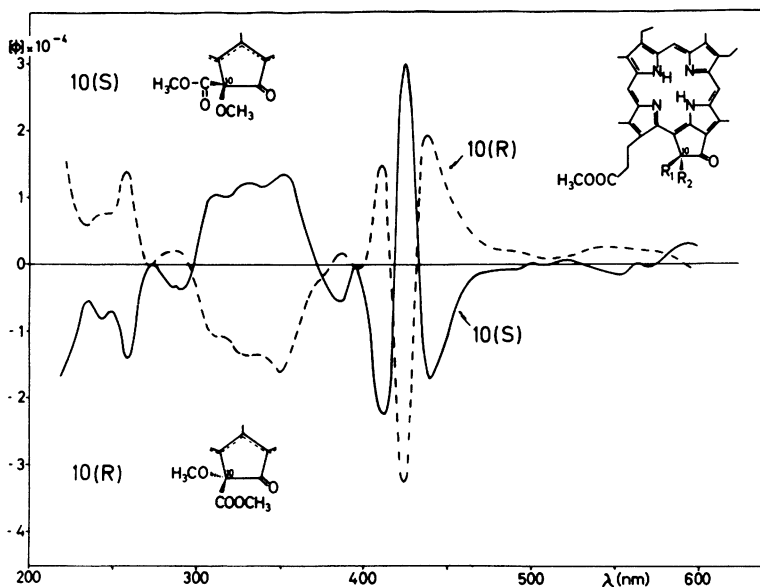


FIGURE 9. ORD spectra (dioxane) of the enantiomeric 10(*S*)- and 10(*R*)-methoxy pheoporphyrins **9a** and **9b**.

drawings (TABLE 3), these four diastereomeric *cis*-pheophorbides form two pairs of enantiomers (**10a/11b** and **10b/11a**). Their CD (FIGURE 10) as well as ORD spectra are, therefore, mirror images of each other.

The absolute configuration at C-7 (and consequently at C-8) could be determined (relative to C-10) by NMR spectroscopy; the C-7 proton *cis* to the 10-OCH₃ group is more strongly deshielded than that *cis* to the 10-COOCH₃ group, as shown for a series of 10-alkoxy methylpheophorbides a and b.^{13,25,27} Independent of the NMR data, the absolute configuration at C-7 could likewise be derived from the CD or ORD spectra in two different ways: as shown in FIGURE 11, the CD spectrum of the 7,8-*cis* pheophorbide **10a** is very similar to that of the 7,8-*trans* compound **12a**, except for the Q_b-band whose intensity is diminished to about one half of that in **12a**. The same is true for the CD spectra of the two 7,8-*cis/trans* compounds **10b** and

¶ In the enantiomers, the corresponding methine hydrogens (α , β and δ) become magnetically nonequivalent by addition of *l* as chiral shift reagent.³²

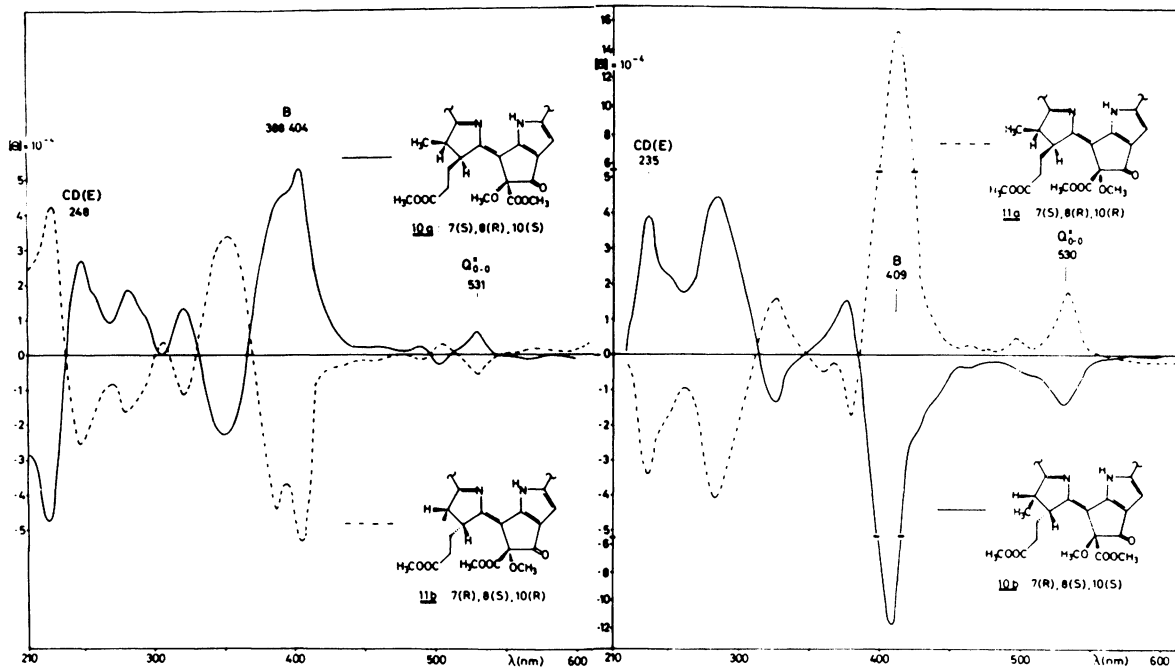


FIGURE 10. CD spectra (dioxane) of the two pairs of enantiomers **10a/11b** and **10b/11a** of 7,8-*cis*-10-methoxy mesomethylpheophorbides *a*.

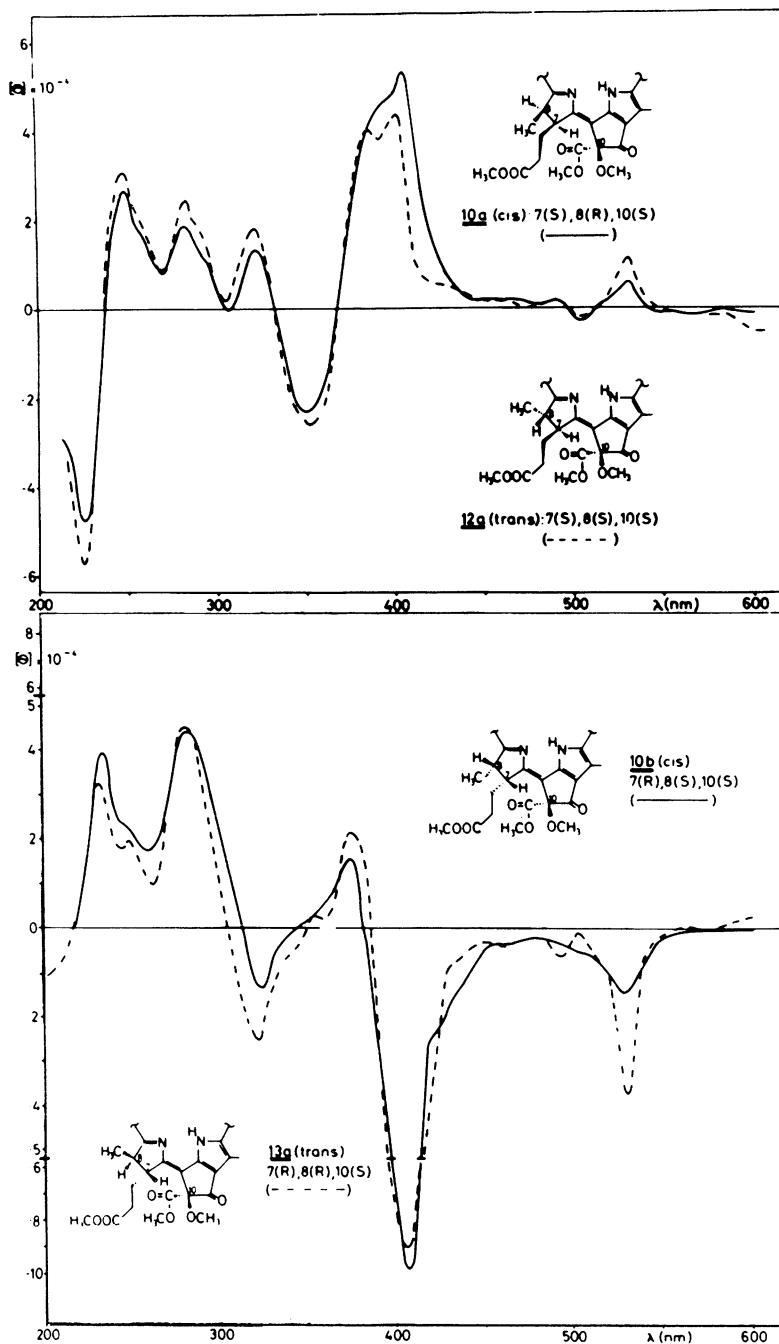
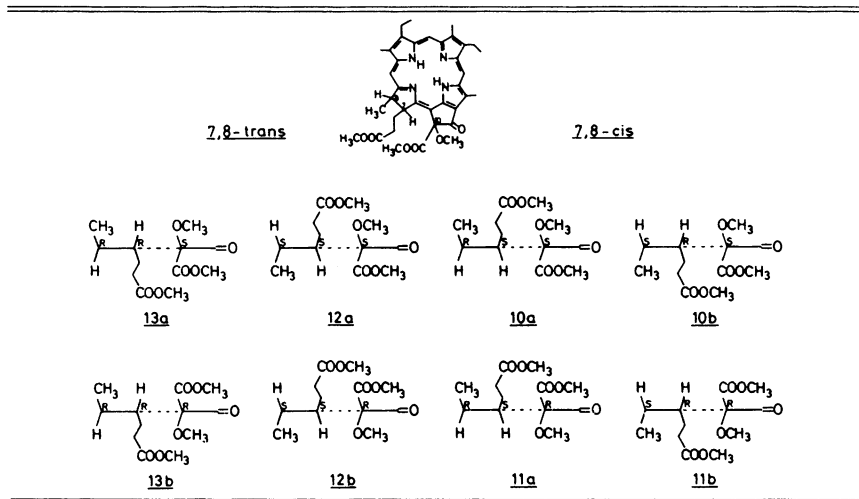


FIGURE 11. CD spectra (dioxane) of the 7,8-*cis*-10(S)-methoxy mesomethylpheophorbides a 10a and 10b as compared to the 7,8-*trans*-10(S)-methoxy mesomethylpheophorbides a 12a and 13a.

13a.** Since the C-10 configuration of all four compounds is known to be 10(S), only one of the two remaining asymmetric centers C-7 or C-8 determines the spectral characteristics of the molecule (signs of all CD bands as well as fine structure); the other asymmetric center merely affects the band intensities to a minor extent.

It appears reasonable to postulate that the more space-filling substituent determines the sign of the CD bands, i.e., the propionic methyl ester side chain at C-7 and not the C-8 methyl group. According to this argument, **10a** has a 7(S) configuration (as does **12a**) and **10b** has a 7(R) configuration (as does **13a**). Since both compounds **10a** and **10b** are *cis*-pheophorbides, their complete configurational assignment is 7(S)8(R)10(S), for **10a** and 7(R)8(S)10(S) for **10b**. Their enantiomers **11b** and **11a** must be denoted as shown in FIGURE 10 and TABLE 3.

TABLE 3
SCHEMATIC DRAWINGS OF THE EIGHT 10-METHOXY *meso*-METHYLPHEOPHORBIDES *a*
(LOWER PART OF THE MACROCYCLE VIEWED PARALLEL TO THE MOLECULAR PLANE).



There is yet another chiroptic argument for the configurational assignment of the *cis*-pheophorbides. FIGURE 12 shows the CD spectra in the uv region (340–220nm) of the 10(S) and 10(R)-methoxypyro compounds **4a/4b**, the 7,8-*trans* 10(S) and 10(R)-methoxy mesomethylpheophorbides **(12a, 12b)**, and of the two 7,8-*cis* pheophorbides **10a** and **11a** of known absolute configuration at C-10. The sign of the CD band at 285 nm is clearly determined by the configuration of the 10-methoxy group (negative in the 10(R) and positive in the 10(S) series, irrespective of the presence of the 10-carbomethoxy substituent). The shorter wavelength band indicated as CD(E) at 234 or 248 nm, respectively, must originate from the 10-carbomethoxy group since these CD(E) bands are absent in both 10-methoxypyro compounds

** **13a** and **13b** were not prepared; their CD spectra are the mirror images of the known **12b** and **12a**, respectively.

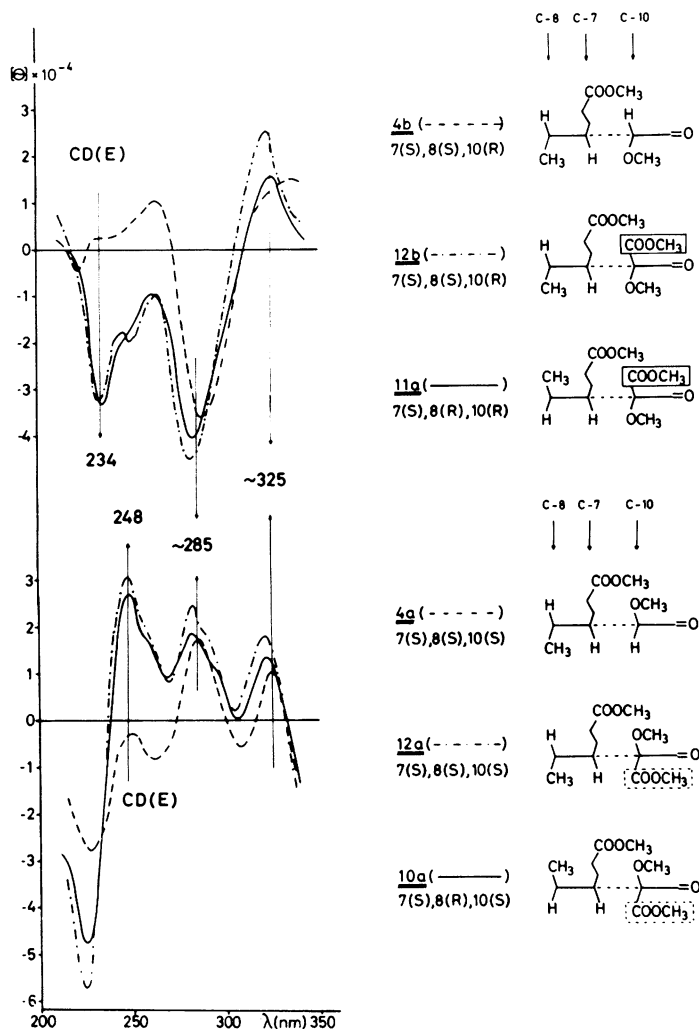


FIGURE 12. CD spectra in the UV region; assignment of the CD(E) band to the β,γ -unsaturated 10-carbomethoxy chromophore.

4a and **4b**. Spectral position and intensity of these CD bands suggest that they are due to an inherently dissymmetric chromophore $\dagger\dagger$ formed by the 10-ester carbonyl group and the C-7 α , C- γ double bond,^{13,25} as shown in FIGURE 13a and b. The 10(S)

$\dagger\dagger$ β,γ -unsaturated carbonyl compounds (ketones, aldehydes) form an inherently dissymmetric chromophore if the geometry of the two groups is such that their orbital system can overlap dissymmetrically³⁶; in pheophorbides this is only possible with the γ , 7 α -double bond. Further examples of β,γ -unsaturated carboxylic esters were published by Snatzke.³⁷

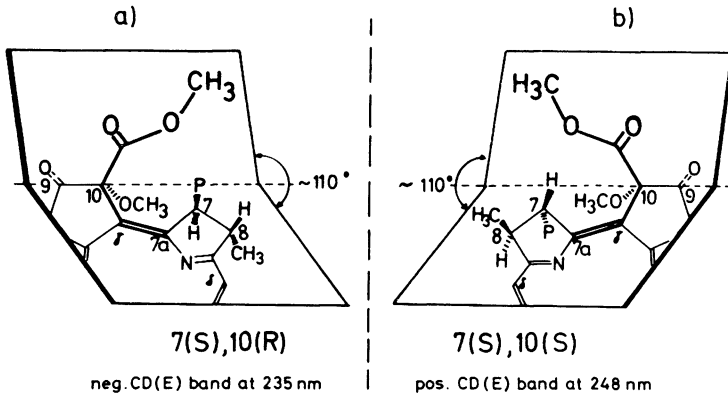


FIGURE 13. Mirror image geometry of the inherently dissymmetric β,γ -unsaturated 10-carbomethoxy chromophore.

configuration implies the geometry pictured in FIGURE 13b and, therefore, a positive CD band (248 nm); the 10(R) configuration indicates the mirror image geometry (FIGURE 13a) and, therefore, a negative CD band (234 nm). §§

The question arises of why these CD bands occur at different wavelengths (at 234 nm for both 7(S) and 10(R) epimers **12b/11a**, and at 248 nm for both 7(S) and 10(S) epimers **12a/10a**). The answer is that this must be due to deviations from the perfect mirror image geometry of both inherently dissymmetric chromophores. The equilibrium conformation of the 10-carbomethoxy group will certainly be determined by the configuration of the neighboring space-filling 7-propionic ester side chain, which can be orientated *cis* or *trans*. The spectral position of the CD(E) band then indicates the relative configuration between the 10-carbomethoxy group and the 7-propionic ester side chain. We therefore assign both *cis*-pheophorbides of FIGURE 12 the 7(S) configuration (cf. **11a/12b** and **10a/12a**). The configurations of the two other *cis*-pheophorbides **10b** and **11b** are deduced from their mirror image CD spectra (FIGURE 10). This configurational assignment is in agreement with the first one.

Conclusions

The results discussed so far indicate a dominant influence of the C-7 configuration, as compared to that of C-8, on the entire spectral range of the CD spectra of pheophorbides. The $Q_{y,0}$ band is the only strongly affected one (FIGURE 11). Recent calculations of Sauer²² predicted that C-7 and C-8 would make contributions of nearly equivalent magnitude to the rotational strength of both $Q_{0,0}$ transitions of chlorophyll a. The $Q_{y,0}$ -band is reduced to about one half in the CD spectra of the metal-free *cis*-pheophorbides as compared to the *trans* compounds (FIGURE 11),

§§ This correlation presents independent evidence for the absolute configuration of the 10-carbomethoxy group.

and the same is indicated for the Q_{0-0} CE from ORD measurements.¶¶¶ Nevertheless the chiroptic effect of C-8 on the Q bands is much weaker than that of C-7.

The strong influence of the C-7 configuration may be explained by some conformational details of the macrocycle which can be deduced from x-ray analyses. The macrocycle has been shown to be slightly nonplanar in various porphyrins.^{40,41} The atoms belonging to the aromatic system stick out of the least-squares plane by some hundredths of an angström and the double bonds are also distorted to some extent. However, the deviations from planarity are so small that the π -orbital overlap is kept at a maximum. Since the macrocycle behaves as a rigid system, local distortions caused by steric strain are transmitted over the entire macrocycle. Thus, the molecular geometry may be described as that of a shallow saucer.

Within the framework, the phylloerythrins (porphyrins with an additional ring E) investigated by Petterson⁴¹ behave normally. Ring D is completely included in the aromatic system and is planar in the above sense, although considerable steric strain is introduced by the γ -substituent (ring E). In contrast, ring D is strongly distorted in methylpheophorbide a (2).^{38,39} Flexibility is much enhanced by sp^3 hybridization of C-7 and C-8,¶¶¶ C-7 is bent up and C-10 is pushed down below the plane. These deviations are markedly greater than in porphyrins.

In 2, C-7 is located 0.29 Å above and C-10 0.14 Å below the least-squares plane, and the dihedral angle $C_{10} - C_7 - C_{7a} - C_7$ is 16°. The values for vanadyl deoxophylthioethioporphyrin are 0.11 Å, 0.05 Å and 5°, respectively.⁴⁰

The molecular geometry of γ -substituted chlorins may therefore be compared to one turn of a very flat coiled spring or helix, which takes on properties of an inherently dissymmetric chromophore. The configuration of the space filling 7-propionic ester side chain then determines whether C-7 is bent up or down. This induced chirality of the macrocycle determines the sign of the main CD band or CE curve, corresponding to the Soret band maximum at about 410 nm, as well as that of the longwave Q_{0-0} Cotton effect (footnote on the previous page). Therefore, only the 7(R) pheophorbides 10b, 11b, 13a, b have a negative main CD band FIGURES 10,11) whereas all pheophorbides investigated until now with natural 7(S) configuration, have a positive one, irrespective of the configurations at C-8, C-9, and C-10. In addition, this band is strongly enhanced by an increase of steric repulsion due to the opening of ring E, as shown by the γ -substituted chlorins 5 and 6 in FIGURE 7.²⁶

On the other hand, the sign of most CD bands in the uv region, and of some weaker B bands is determined by the C-10 configuration (compare 3a/3b, 4a/4b, 10a/10b, 11a/11b). The same is true for the Q_{0-0} band, if the C-10 substituent has a large perturbation effect (compare 1/2). However, the geometry of the macrocycle seems to remain unchanged by substitution or configurational inversion at C-10, as shown by the additivity of the CD increment spectra (FIGURE 6).

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¶¶¶ Semiquantitative results of the longwave Q_{0-0} transitions were obtained from the ORD spectra.³² The amplitude values are reduced to about one half in the *cis* pheophorbides as compared with the *trans* compounds. In the 7(S), 8(R) *cis* diastereomers 10a and 11a, the sign is negative as in all 7(S), 8(S) *trans* pheophorbides examined until now. In the 7(R), 8(S) diastereomers 10b and 11b, however, the sign of the long wavelength transitions is positive.

¶¶¶ In addition to the displacement of the 7,8-substituents out of plane,⁹ the enhancement of ring flexibility is an important factor for the release of steric strain.

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