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Sign Variation in the Magnetic Circular Dichroism Spectra of π-Substituted Porphyrins†

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Absorption spectroscopy with polarized light has long been used to obtain structural information about molecules. The application of circular dichroism (CD), the differential absorption of right and left circularly polarized light, to determine the absolute configuration of chiral compounds is an example familiar to chemists,[1] as is the dichroism for linearly polarized light exhibited by oriented samples such as single crystals and stretched films.[2] Another tool that is being increasingly used by chemists for structural studies is magnetic circular dichroism (MCD), the circular dichroism that is induced in any light-absorbing substance by a properly oriented magnetic field.[3] Chromophores to which MCD has been extensively applied include highly symmetrical inorganic complexes[4] and aromatic derivatives and heterocycles of relatively low symmetry,[5,6] such as porphyrin derivatives.

Because MCD has a different physical basis than natural CD, the structural information that it contains is of a different nature than that afforded by natural CD. MCD is closely related to the Zeeman effect of atomic spectroscopy, which corresponds classically to the asymmetry, with respect to handedness of rotation, of the energy of a circulating charge and its associated magnetic dipole in an applied magnetic field.[7] The form and intensity of MCD are strongly affected by degeneracies and near degeneracies in electronic energy levels associated with the degree of rotational symmetry experienced by the chromophoric electrons and, through spin–orbit coupling, by degeneracies due to spin. Therefore, MCD is sensitive to structural features that directly affect the electronic energy levels of the chromophore, in contrast to natural CD, which is sensitive to asymmetry in the spatial structure of the molecule or its environment. In samples that possess both natural and magnetic CD, the two techniques can thus provide complementary information. In hemoglobin, for example, the visible-band MCD reflects the coordination symmetry[8] and spin state[9] of the heme chromophore, whereas the natural CD of the heme bands reflects asymmetry in the protein structure around the heme.

Robert Goldbeck was born in 1950 in Evanston, IL. He completed his undergraduate work in chemistry at UC Berkeley and did his graduate work at UC Santa Cruz on the transient spectroscopy and quantum chemistry of polyene excited singlet states. He participated in studies of MCD sign variation in monosubstituted porphyrins as a postdoc in Carl Djerassi's group at Stanford, in collaboration with Gilda Loew of SRI International. He is now an assistant research chemist at UC Santa Cruz, where, with Dave Kliger's group, he is developing fast detection techniques for transient MCD spectroscopy.

† This paper is dedicated to the memory of Dr. Edward Bunnenberg.

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(2) Michl, J.; Thulstrup, E. W. *Spectroscopy with Polarized Light*; VCH: New York, 1986.

(3) An MCD spectrum is defined as the dispersion of $[\theta]_M$, the magnetically induced molar ellipticity per unit magnetic field:

$$[\theta]_M = 3300\Delta\epsilon/H \text{ (deg L mol}^{-1}\text{ m}^{-1}\text{ G}^{-1}\text{)}$$

where $\Delta\epsilon = \epsilon_{LC} - \epsilon_{RC}$ is the difference between the molar extinction coefficients for left and right circularly polarized light and H is the strength in gauss of a uniform magnetic field oriented along the propagation vector of the light beam. (Typical field strengths are 15 kG for electromagnets and 50 kG for superconducting magnets.)

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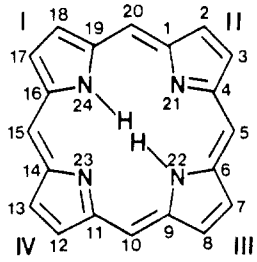
Interest in the MCD of the porphyrin chromophore began in the 1960s, when porphyrin-containing proteins were among the first organic compounds for which MCD spectra were measured.[10] The elegant symmetry



Porphine free base

of the large, conjugated ring results in an electronic structure that yields the large MCD extrema associated with the visible (Q band) and near-UV (Soret band) transitions. Porphyrin electronic structure is intimately connected with the central role played by the porphyrin macrocycle in energy collection and utilization by living organisms. Iron-substituted prophyrin derivatives are essential as prosthetic groups in the functioning of hemeproteins such as hemoglobin and myoglobin (protoheme) in dioxygen transport and storage,[11] cyotchrome oxidase (heme *a*) in oxidative metabolism,[12] cytochrome *c* (protoheme) in electron transfer,[13] and cytochrome P-450 (protoheme) in the hydroxylation of various substrates.[14] The reduced porphyrins chlorophyll *a* and *b* and bacteriochlorophyll are the primary harvesters of light energy for photosynthesis in green plants and bacteria.[15] Their biological importance and large MCD anisotropies have prompted studies of prophyrin derivatives containing a wide variety of peripheral and central substituents.[16-31]

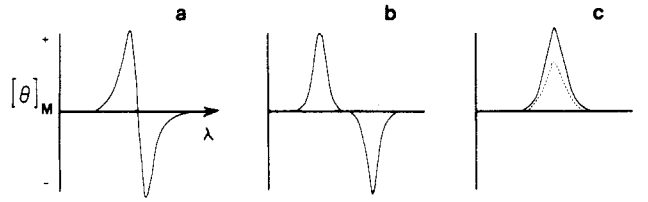


Figure 1. Schematic illustration of the three types of terms, *A*, *B*, and *C*, through which a transition between states can contribute to the magnetic molar ellipticity:

$$[\theta]_M = -21.3458[f_1A + f_2(B + C/kT)]$$

(a) An *A* term of positive sign. (b) *B* terms for two nearby final states. (c) A *C* term of negative sign at temperature T_1; the dashed line indicates the *C* term for the same transition at $T_2 = 1.5\ T_1$. The *A* term arises for transitions involving degenerate initial or final states and will occur in molecules with at least a threefold symmetry axis. The function f_1 resembles the derivative of an absorption line-shape function. A positive *A* term will contribute negative ellipticities at energies below the line center and positive ellipticity above. The *B* term contribution arises from magnetically induced mixing of nondegenerate states and is the only contribution seen in molecules of low symmetry. The function f_2 is a line-shape function which, in the absence of vibronic effects, is the same as the line-shape function of the corresponding absorption. A *C* term arises from transitions out of a degenerate initial state and is distinguished from a *B* term by its temperature dependence.

A recent series of studies focused on the variation in MCD signature induced by various π-perturbations to the porphyrin ring.[22-31] These studies found a sensitive and systematic correlation between the electronic Q-band MCD and structural variations that affect the porphyrin π-electron energies. Since this correlation between MCD spectra and structure is most easily understood in terms of the model due to Michl,[32] it is worthwhile to briefly consider the basis for this model before applying it to substituted porphyrins.

Perimeter Model of MCD Sign Variation

The types of extrema that can contribute to an MCD spectrum are illustrated schematically in Figure 1. We use the sign convention that the double-lobed *A*-term MCD is positive when the ellipticity of the low-energy lobe is negative and that a positive *B* term corresponds to negative ellipticity (*C* terms will not concern us).[33] The applied magnetic field and the propagation vector of the light are both taken to point in the positive *z* direction, and right and left circular polarization are referenced to an observer looking toward the light

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source. With these conventions in mind, we consider the perimeter model, a simple model for the MCD of ring-containing molecules with a delocalized electronic structure. This model for porphyrin MCD focuses on the nodal properties of the angular momentum wave functions of annulenes and is closely related to the free-electron and LCAO (linear combination of atomic orbitals) models. Angular momentum states form a natural basis for discussion of MCD because the magnetic moment is proportional to orbital angular momentum (we can neglect spin in discussing singlet spectra).[34]

The free-electron model is the most primitive of the perimeter approaches, and its prediction for MCD is very simple: a positive A term for each of the doubly degenerate transitions arising from the closed-shell ($4N + 2$ electron) ground state. The A terms are a consequence of excited-state degeneracy; they are positive because absorption of a left circularly polarized photon will always correspond in this model to an increase in orbital angular momentum of an electron (angular momentum aligned with the applied field is taken as positive). Because the electron charge is negative, this is an increase in magnetic moment aligned *against* the field. A magnetic moment aligned in opposition to the applied field will lie at higher energy than a moment aligned with the field; therefore, the left circularly (LC) polarized transition of the degenerate transition pair will be Zeeman shifted in energy above the RC-polarized component. The small shift of the absorption band for LC-polarized light relative to the band for RC-polarized light gives a net ellipticity with a "derivative" shape. The sign pattern of the ellipticity for a positive A term, − to + with increasing energy, is sometimes referred to as "normal", particularly in the context of the purely electronic MCD of the porphyrin visible bands.

The more realistic LCAO model introduces the possibility of "inverted" MCD (negative A term) for simple annulenes. This is because absorption of a LC-polarized photon (increase in orbital quantum number) can correspond in the LCAO model to a *decrease* in the orbital angular momentum of an electron, with the result that the LC-polarized component of a degenerate transition will be shifted in an applied field to lower energy than the RC component. This situation is most likely to occur when there are more electrons than orbitals, in other words, in annulenes of high net negative charge.

Of broader consequence as a mechanism for inducing MCD sign variation are perturbations that reduce the symmetry from the full D_{nh} symmetry of the unperturbed annulene. Whether a symmetry-lowering perturbation will give rise to sign inversion is determined by where lifting of the orbital degeneracy occurs: in the highest occupied MOs (HOMOs) or the lowest unoccupied MOs (LUMOs). If the perturbation splits the HOMOs, but leaves the LUMOs degenerate (as is the case for D_{4h} porphyrins), then a HOMO to LUMO orbital promotion will leave an electron with net angular momentum. In this case, as in the free-electron case, LC polarization is associated with positive angular momentum of an electron and MCD signature is normal. If, on the other hand, the perturbation splits the LUMOs and leaves the HOMOs degenerate, then electron promotion will leave a hole with net angular momentum. LC polarization is then associated with positive angular momentum of a (positively charged) hole, and the energy ordering of the polarized components in an applied field is inverted from the free-electron case.

A reduction in symmetry can also introduce B terms into the MCD spectrum. Indeed, in the MCD spectra of systems with less than a threefold symmetry axis there are only B terms left; all A terms have been split into pairs of B terms. The considerations outlined above for A terms act in higher order, in the sense of perturbation theory, to determine the signs of the corresponding B terms which result from the magnetically induced mixing of electronic wave functions. Both HOMOs and LUMOs can be nondegenerate in low-symmetry systems and the net effect on the sign of the MCD is determined by the relative magnitudes of the orbital splittings ΔHOMO and ΔLUMO.

If both ΔHOMO and ΔLUMO are nonzero and unequal, the major contribution to MCD is through the higher order analogue of the mechanism described just above for the A term of a perturbed annulene. There are two cases: If ΔHOMO is larger than ΔLUMO (classified as a "positive-hard" chromophore by Michl[32]), then the excitation is electron dominated and normal MCD signature is expected (positive B term for the lower energy transition of a nearly degenerate pair of transitions); if ΔLUMO is larger ("negative-hard" chromophore), then the excitation is hole dominated and inverted MCD signature is expected. When the magnitudes of the orbital splittings are equal, this contribution to MCD will vanish, leaving only a small contribution associated with the higher order analogue of the first MCD mechanism described above for the A term of a simple unperturbed annulene in the LCAO model. This last contribution is relatively insensitive to structural perturbations; although it can make a small contribution to MCD sign inversion in highly negatively charged systems, it usually provides a small background contribution of normal signature to the MCD of perturbed annulenes.

To summarize the conclusions of Michl's perimeter model of MCD, the sign of ΔHOMO − ΔLUMO will determine the sign of MCD observed for the low-energy electronic transitions, except in soft chromophores, where ΔHOMO ≈ ΔLUMO. The applicability of the perimeter model to molecules that can formally be regarded as perturbed, closed-shell annulenes has been reviewed by Michl.[6,32d] The four-orbital model of porphyrin electronic structure of Gouterman[35] combined with the perimeter model of MCD gives at least a qualitative accounting of the effect of substituents on porphyrin absorption and MCD spectra. Since the LUMOs of D_{4h} porphine dianion are degenerate by symmetry, while the HOMOs are nearly so, the frontier orbitals of porphine dianion (Figure 2) serve as the reference for a four-orbital model of MCD for $\pi\pi^*$ transitions in porphyrins that is closely analogous to the perimeter model of annulenes.[36]

(34) For simplicity, we will ignore the distinction between transitions among orbitals and transitions between states. This heuristic approach is adequate to show the physical basis of MCD sign variation in annulenes, although a proper treatment of the perimeter model of MCD (e.g., ref 32 and 36) necessarily uses many-electron configrations and allows them to interact.

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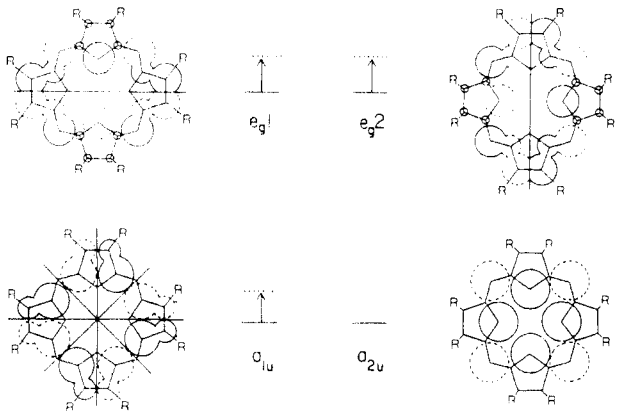

Figure 2. Effect of a symmetric perturbation, octaalkyl substitution, on MO energies (schematic). Symmetry labels refer to D_{4h} symmetry of the porphine ring. A substituent's perturbing effect on porphyrin MO energies is weighted by the square of the AO coefficient at the point of attachment. The sum of interactions is identical for the LUMO's, but different for the HOMO's; thus, the electron-donating alkyl groups raise the LUMO energies by identical amounts while splitting the HOMO energies.

Application to Porphyrins and Reduced Porphyrins

The key to understanding the influence of substituents on the sign and magnitude of porphyrin MCD, then, is to assess their effect on the relative sizes of ΔHOMO and ΔLUMO. Fortunately, this program can often be carried out by using only qualitative perturbation considerations familiar to organic chemists,[6,37] without recourse to explicit MO calculations. As an example, consider perturbations of the parent compound, porphine dianion, which preserve its D_{4h} symmetry: these can include alkyl substitution at the eight pyrrole carbons (C-2, -3, -7, -8, -12, -13, -17, -18), phenyl substitution at the four meso carbons (C-5, -10, -15, -20), the addition of central metals, or the addition of four N–H protons to form a dication. Such perturbations can split the energies of the HOMOs, while the LUMOs remain degenerate by symmetry (Figure 2). In accord with the prediction of the perimeter model, the electronic origins of the visible and Soret bands of the D_{4h} porphyrins typically do have positive *A* terms. The spectrum of zinc tetraphenylporphine (ZnTPP) (Figure 3) is an example of normal MCD. The few exceptions to this "golden rule" for perimeter symmetric and metalloporphyrins occur when ΔHOMO ≈ 0, and the electronic contribution to the Q-band MCD is weak. In this case, sign inversion may be accounted for by the lower symmetry of the porphyrin orbitals as compared to those of the annulene model,[36] although vibronic effects or small distortions of the ring in axially substituted metalloporphyrins may also be important.[26]

The porphyrin free bases present a perturbation of lower symmetry to the porphine ring that has important consequences for MCD. The large influence that tautomerism of the central protons has on MCD figures prominently in the discussion below of monosubstituted porphyrins. The addition of two (trans) protons to form free-base porphine lowers the molecular symmetry to D_{2h}; consequently, the LUMOs are no longer constrained to degeneracy. The size of the resulting

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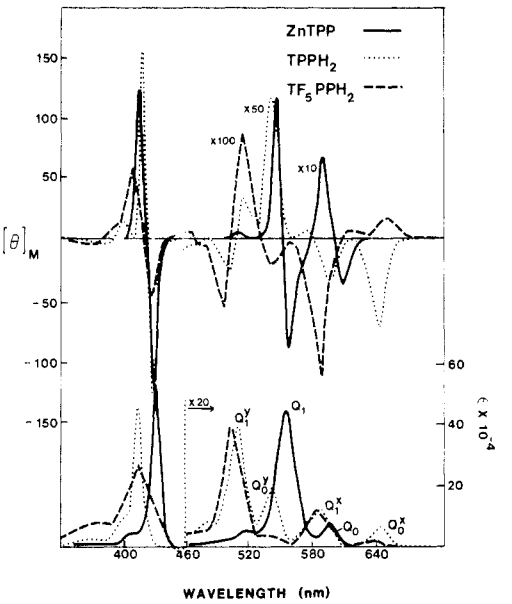

Figure 3. MCD and absorption spectra of tetraphenylporphine (TPP) and tetrakis(pentafluorophenyl)porphyrin (TF_5PP) free bases[24] and ZnTPP.[26]

ΔLUMO can again be estimated relative to ΔHOMO on qualitative grounds, by considering the relative sizes of the AO contributions indicated in Figure 2: because the nitrogen AOs have smaller coefficients in the e_g MOs than in the a_{2u} MO, the energy lowering engendered for one of the e_g MOs by protonation will be smaller than the lowering of the a_{2u} below the a_{1u} MO. The result is ΔHOMO greater than ΔLUMO, and the prediction of the perimeter model is again for normal MCD, which now appears in pairs of *B* terms for the visible and Soret bands. Normal MCD is found to hold as a general rule for many of the D_{2h} free-base porphyrins that can be derived from porphine, such as the octaalkyl- and tetraphenylporphyrins. The electron-donating character of an alkyl group results in an energy raising for the a_{1u} orbital which, when combined with the lowering of the a_{2u} orbital due to the free-base perturbation, is expected to give very strongly normal MCD, as is observed for free-base octaalkylporphyrins.[38]

When the effects of perturbations tend to oppose one another the outcome may not be predicted without a more quantitative model. The perimeter model is then useful as a protocol for extracting information about ΔHOMO and ΔLUMO from the observed MCD in order to form a basis for further predictions of MCD signature. This situation arises, for example, in tetraphenyl substitution of free-base porphine: electron donation from the phenyl groups to the meso carbons tends to raise the energy of the a_{2u} orbital, in opposition to the effect of the free-base perturbation. While the qualitative model makes no a priori prediction of sign, the observation that the MCD of tetraphenylporphine ($TPPH_2$, Figure 3) is in fact more strongly normal than that of porphine implies that the a_{2u} orbital has actually been raised in energy well above the a_{1u} by the domi-

(38) In the first-order spirit of the model, the effects of multiple perturbations, such as octaalkyl substitution on top of the free-base perturbation, are considered to be independent and additive. The first-order approach breaks down when considering multiple perturbations that change the extent of π-conjugation within the porphyrin ring, such as reduction of pyrrole double bonds or protonation of pyrrole nitrogens, because changes in the frontier orbital wave functions cannot be neglected.

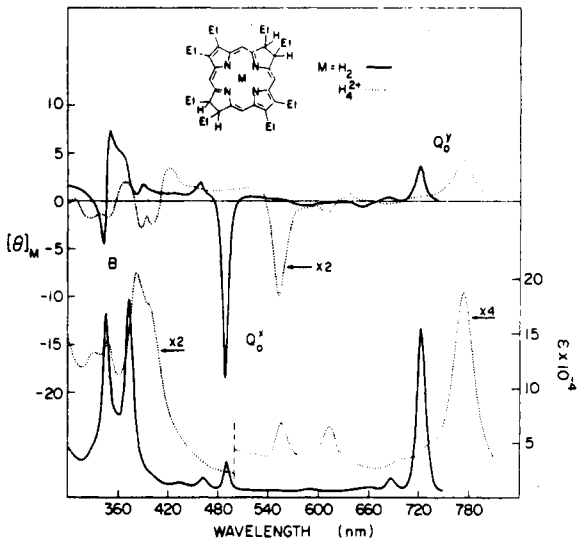

Figure 4. MCD and absorption spectra of octaethylbacteriochlorin free base ($OEBCH_2$) and dication ($OEBCH_4^{2+}$) (from ref 22).

nant tetraphenyl perturbation. From this inference follows the prediction that a modification of the phenyl groups that sufficiently diminishes their electron donation to the porphyrin ring, such that the free-base perturbation to the HOMOs is just offset, will result in the condition $\Delta HOMO \approx 0 < \Delta LUMO$, i.e., inverted MCD. Inverted MCD was in fact observed (Figure 3) for the visible bands of tetrakis(pentafluorophenyl)-porphyrin (TF_5PPH_2),[24] one of the few perimeter-symmetric free-base porphyrins found to exhibit MCD sign inversion.[39]

Most important as sources of MCD sign variation in porphyrins are the low-symmetry perturbations, such as reduction of a pyrrole double bond (the "chlorin" perturbation), or attachment of a single electron-withdrawing group to the porphyrin periphery. Such perturbations lead to sign inversion principally by increasing the size of ΔLUMO, although it is clear from the previous discussion that this statement becomes less certain as we consider derivatives further removed from porphine dianion. An electron-withdrawing group, such as a carbonyl, attached to porphine dianion at C-3 will simultaneously lower the energy of the a_{1u} and the e_{g1} orbitals, with the latter effect being dominant due to the larger C-3 AO coefficient in the e_{g1} orbital. A similar argument applies to reduction of the C2–C3 bond, with the affected orbitals being raised, rather than lowered, in energy.

The effect of the chlorin perturbation on the LUMO energies is sufficiently strong that inverted MCD is found to be typical for the reduced porphyrins. This is particularly true for the bacteriochlorins, where first-order considerations indicate that reduction of opposing pyrroles will give a doubled contribution to sign inversion. Sign inversion is indeed found to extend through the visible and into the UV bands for octaethylbacteriochlorin (OEBC) free base and dication (Figure 4) and tetraphenylbacteriochlorin free base, dication, and zinc derivatives.[22,23] In isobacteriochlorins, on the other hand, the saturated bonds are on adjacent

(39) This example also points out another feature of porphyrin MCD: sign inversion will often first appear in the Q band, before it becomes evident in the Soret.

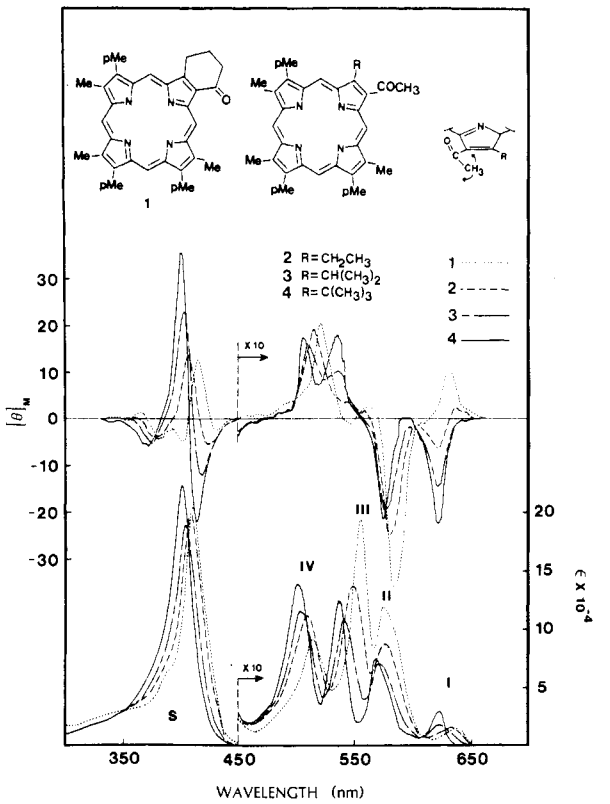

Figure 5. MCD and absorption spectra of sterically hindered acetylporphyrins 1–4.[31] Me = methyl; p = propionate.

pyrroles, and the chlorin perturbations cancel to first order in the LUMOs while remaining additive in the HOMOs. The normal MCD expected on this basis is found to be manifested in the free base, dication, and zinc derivatives of octaethylisobacteriochlorin,[22] although the corresponding derivatives for tetraphenylisobacteriochlorin continue to show inverted MCD, due to the opposing effects of the meso-tetraphenyl and chlorin perturbations on ΔHOMO, and a nonzero ΔLUMO arising from higher order effects.[38] Substituent effects similarly modulate the appearance of sign variation in the octaethylchlorin (OEC) derivatives: octaalkyl substitution acts with both the chlorin and zinc perturbations to increase ΔHOMO such that the chlorin perturbation to the LUMOs is overcome, and normal MCD is observed in ZnOEC. Remove the zinc, though, and inverted MCD reappears in the visible bands of OEC dianion, as the b_1 orbital (a_{2u} in D_{4h} symmetry) rises in energy to close the HOMO energy gap.

With the protocol described above, the signs of the electronic MCD bands of nearly 50 porphine and reduced porphyrin derivatives were systematically correlated in ref 23 by deriving an internally consistent set of perturbed orbital energies. The four-orbital model proved able to predict or rationalize in a simple way the substituent-induced sign variation in MCD throughout this varied set of porphyrin derivatives, without a proliferation of "rules" and exceptions.

With the correlation between MCD sign pattern and formal chemical structure well established using the qualitative four-orbital analysis, attention was focused on the access of more subtle aspects of porphyrin molecular structure through MCD spectroscopy. An intriguing indication along these lines is given by the MCD spectrum of an acetylporphyrin free base (com-

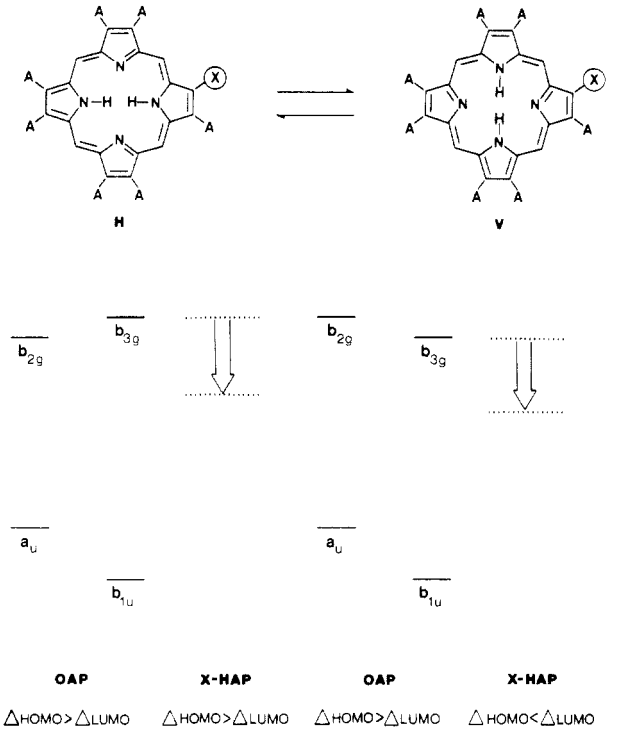

Figure 6. Equilibrium between vertical (V) and horizontal (H) tautomers in a monosubstituted heptaalkylporphyrin (X-HAP) free base. Symmetry labels refer to the D_{2h} symmetry of unsubstituted octaalkylporphyrin (OAP) free base. The b_{1u}, a_u, b_{2g}, and b_{3g} orbitals are descended from a_{2u}, a_{1u}, e_g, and e_{1g} MOs, respectively, in Figure 2.

pound **2** in Figure 5) whose lowest energy transition (Q_0^x band) exhibits an unusual superposition of oppositely signed *B* terms.[23] The bisignate *B* term seems to signal the presence of subpopulations of porphyrins conformers bearing oppositely signed Q_0^x band MCD at transition energies shifted by several hundred cm^{-1}. Possible sources of oppositely signed species suggested by the four-orbital model are tautomerism of the central protons with respect to the axis of the acetyl substituent and rotational conformerism of the acetyl itself (due to steric interaction with the adjacent alkyl group) with respect to the plane of the porphyrin ring. The studies of monosubstituted free-base porphyrins bearing finely graded electronic and steric perturbations[27,29-31] discussed below provide the quantitative determination of MCD spectra–structure correlation needed to assess these effects.

Sign Variation in Monosubstituted Porphyrins

The MCD of unsymmetrically substituted free-base porphyrins is significantly influenced by the location of the central protons. There is a 1:1 equilibrium in perimeter-symmetric free-base porphyrins between tautomers with nitrogens protonated on rings I;III ("V" tautomer) and on rings II;IV ("H" tautomer). The equilibrium is shifted toward the V tautomer when an electron-withdrawing group is substituted on rings II or IV.[40] This shift has consequences for MCD because the free-base perturbation will work with the π-substituent to enhance the LUMO splitting in the V tautomer, but the two effects will be opposed in the H tautomer (Figure 6). Thus, when sign inversion is contributed by the dominant V tautomer to the observed MCD of the Q_0^x band, it is offset somewhat by normally signed MCD from the H tautomer. Oppositely signed MCD for the two tautomers means that MCD spectroscopy will be sensitive to shifts in the tautomer equilibrium—shifts that are correlated with the donor–acceptor strengths of the perturbing substituents. An example of this effect is seen in the doubling of the Q_0^x-band MCD sign inversion that occurs when an alkyl group adjacent to the formyl group is removed from heptaalkylformylporphyrin:[30] nearly half of the increase is due to a shift in the tautomer equilibrium constant which decreases the ratio of H to V tautomers from 0.4 to 0.2.

The orientation of a planar π-substituent, such as a carbonyl group, with respect to the porphyrin ring can also have a dramatic effect on MCD. The electron-accepting ability of a carbonyl substituent is compromised by out-of-plane rotation about the single bond with the porphyrin ring; thus, the Q_0^x-band sign inversion observed (Figure 5) for cyclohexenone porphyrin **1**, with an in-plane carbonyl substituent, is reversed to normally signed MCD in the acetylporphyrins **2–4**, in which increasing steric interference forces the carbonyl out of plane.[31] This gives the acetylporphyrin with the bulkiest alkyl group, *tert*-butyl, the strongly normal MCD expected for a heptaalkylporphyrin. The simultaneous presence of in-plane and out-of-plane conformers is responsible for the bisignate pattern of the Q_0^x-band ellipticity observed in compound **2**, the acetylporphyrin with an intermediate amount of steric hindrance.[41]

Epilogue

MCD spectroscopy possesses a systematic sensitivity to structural variations that perturb the π-orbital energies of the porphyrin chromophore. This sensitivity is most dramatically displayed in the phenomenon of sign inversion, which can be induced in the electronic transitions of porphyrins by electron-withdrawing π-substituents, as well as by saturation of pyrrolic bonds. These symmetry-lowering perturbations induce hole-dominated MCD by interfering more strongly with the angular momentum of an electron promoted to a LUMO than they do with the angular momentum of the hole left in a HOMO. The way in which peripheral and central substituents modulate the appearance of sign inversion is explained by the perimeter model, which qualitatively correlates chemical structure with MCD spectra. MCD spectroscopy also yields more quantitative information about molecular structure, such as the conformational stereochemistry of π-substituents conjugated with the porphyrin ring and the extent of tautomer equilibria in free-base porphyrins.

The recent development of a technique for making very fast CD measurements[42] indicates that it should

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(41) Conformer contributions to the Q_0^x band MCD are resolved in this compound because a spectral red shift, as well as MCD sign inversion, accompanies increased conjugation of the acetyl with the porphyrin ring. This is in contrast to the small spectral shifts (<100 cm^{-1}) associated with tautomerism in these compounds.[30] The direction of spectral shift with respect to MCD sign is also opposite for the two effects conformerism and tautomerism: the V tautomer (with inverted MCD sign) is blue-shifted from the H (normally signed) tautomer.[40c]

soon be possible to perform kinetic measurements of MCD with a subnanosecond time resolution.[43] MCD could then be used to follow dynamic changes in porphyrin electronic structure induced by fast perturbations, such as a laser photolysis pulse. Examples of such applications might include the photolysis of axial ligands from metalloporphyrins[44] or from hemeproteins,[45] or the photochemical reduction of cytochrome proteins.[46] Recent advances in superconducting materials may lead to magnets for future MCD studies which could offer higher field strengths and lower operating costs than present superconducting magnets.[47]

A systematic understanding of porphyrin MCD spectroscopy in terms of porphyrin electronic structure and its variation with structural perturbations is emerging from studies of porphyrins at equilibrium. This understanding, while interesting in itself, will also be important to the application of MCD as a kinetic–spectroscopic probe of the role played by porphyrin structure in the chemical reactions of life.[48]

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Registry No. 1, 105230-15-7; 2, 112112-45-5; 3, 112087-43-1; 4, 112087-44-2; ZnTPP, 14074-80-7; $TPPH_2$, 2669-65-0; TF_5PPH_2, 25440-14-6; octaethylbacteriochlorin, 72260-12-9; octaethylbacteriochlorin dication, 73068-83-4.

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Mechanism of Oxygen Activation by Pteridine-Dependent Monooxygenases

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The mammalian aromatic amino acid hydroxylases (phenylalanine, tyrosine, and tryptophan hydroxylase; PAH, TH, and TPH, respectively) are a unique class of monooxygenases in their use of tetrahydropterins (Figure 1) as obligatory cofactors. These enzymes play important roles in mammalian metabolism: PAH initiates the detoxification of high levels of phenylalanine[1,2] while TH and TPH catalyze the committed steps in the biosynthesis of the neurotransmitters dihydroxyphenylalanine[3,4] and serotonin,[5,6] respectively; hence the latter are targets for therapeutic intervention. In addition, two other types of tetrahydropterin-dependent monooxygenases are known, a mammalian glyceryl ether cleavage enzyme[7,8] and a group of bacterial PAHs.[9,10] While the enzymes operate on different substrates, a commonality of substrate structure is apparent, and recent data have provided important sequence[11,12] and mechanistic[10,13] links between the different mammalian and bacterial hydroxylases. These enzymes are almost certainly descended from the same protein family,[14,15] with evolutionary divergences likely

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