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SEMIEMPIRICAL RULES IN CIRCULAR DICHROISM OF NATURAL PRODUCTS

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Abstract - Qualitative MO-theory is applied to derive at nonempirical rules for the correlation of the sign of a Cotton effect with the stereochemistry of a molecule. For inherently chiral chromophores (examples: enol ethers, vinyl cyclopropanes) their absolute conformation gives this sign directly, for inherently (locally) achiral ones perturbation theory has to be used (examples: lactone acids from lichens, hemithioacetals of steroids). A generalization of sector rules is proposed.

INTRODUCTION AND BASIC THEORY

The determination of the optical rotation has played a great role in structure determination of organic compounds, and especially of natural products ever since its discovery at the beginning of the last century, but only few chemists have done more than routine measurements. It was the pioneering work of Prof. Carl Djerassi which initiated broad application of ORD and later on especially CD, and the great importance of empirical rules to determine absolute configurations or conformations has also several times been discussed in plenary lectures of these IUPAC Symposia.

The basic theory of optical activity is well developped (1), and theoretical predictions for relatively small chiral molecules can be done successfully, but in contrast to e.g. NMR spectroscopy, where we get from one spectrum many detailed informations about all sorts of, say, protons in a molecule, the Cotton effect is a property of the chromophoric system, which is determined either by its own absolute conformation or by the sum of interactions with many chirally arranged atoms or bonds. Thus in general only indirect informations are obtained about the neighbourhood of the chromophore, and if one does not very carefully choose the appropriate rule wrong results may be obtained. Furthermore nearly exclusively the use of CD was and is confined to discussion of the sign of the Cotton effects alone, but not of their magnitudes. The chance is thus quite good to get the right sign by a wrong reasoning, and such results will later often be cited as "proved". We have, therefore, tried to apply qualitative MO-theory to CD in order to rationalize the general facts, to explain experimental rules, to find out their scopes and limitations, and to predict new ones on a nonempirical basis for other chromophores, so that the natural products chemist may have better guidelines.

Let me first cite two striking examples from literature. (+)-O-Methylanhalonidine (1) and (-)-anhalonine (2) are closely related alkaloids which give optical rotations of opposite signs, and whose CD-spectra (Fig. 1) in the range of the α-band are enantiomorphous (2). It was, therefore, doubtful whether they have indeed the same absolute configuration or not. X-ray diffraction studies (2) showed that 1 and 2 are homochirally analogous, but in the crystalline state they have opposite helicities of their piperideine rings: the 1-methyl group of 1 is quasiaxially, that of 2 quasiequatorially disposed. As the sign of the CD is determined by the helicity of this chiral ring, obviously also in solution the same (enantiomeric) conformations prevail as in the crystals. This situation could hardly be predicted from molecular models and these examples nicely remind us of a fact which is very frequently overlooked: using only a single CD-argument, as e.g. the sign of a Cotton effect, gives us information only about the "absolute conformation" of a molecule (i.e. the sign of a torsion angle around a bond), but not about the absolute configuration! We need to have either a second
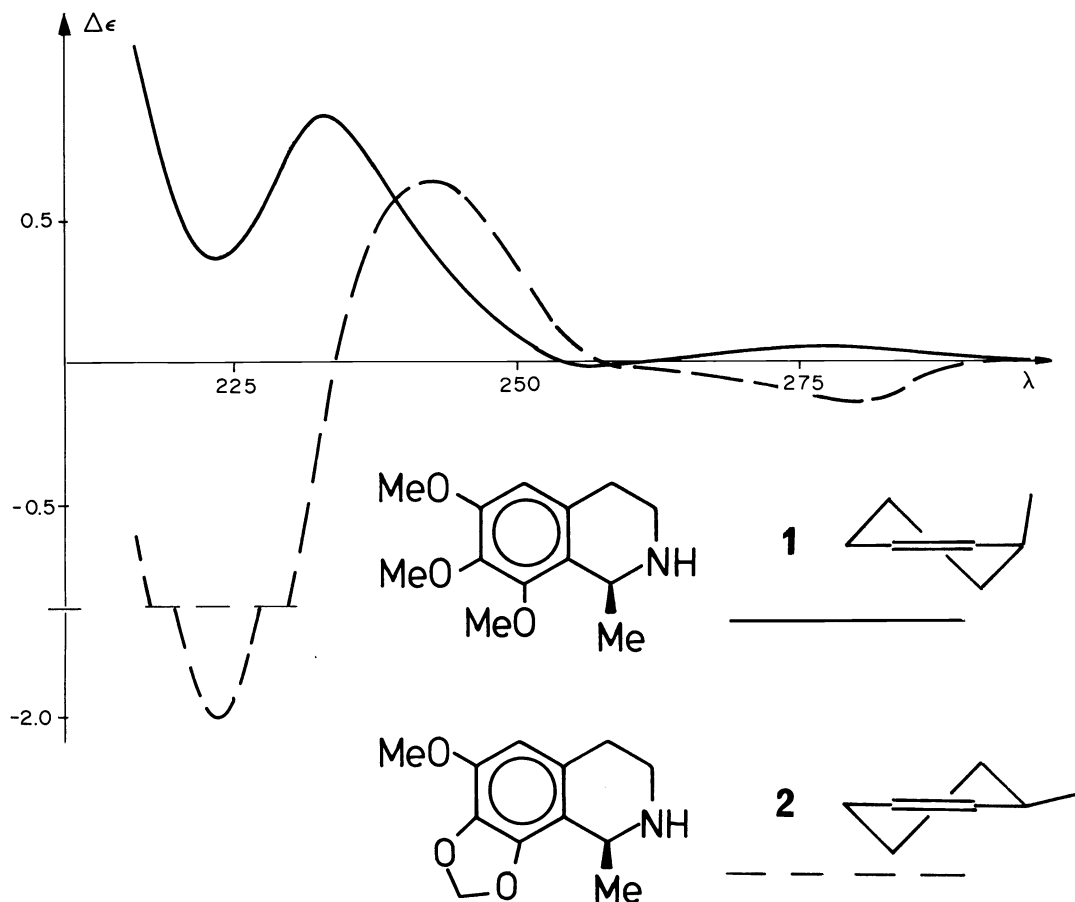
Fig. 1. CD curves and projections from the aromatic ring
towards the chiral piperideine ring of (+)-O-methyl anha-
lonidine (1) and (-)-anhalonine (2).

method (conformational analysis, NMR-, X-ray-data, etc.) or a second CD-
argument (e.g. magnitude, band positions etc.) to correlate the determined
absolute conformation with the wanted absolute configuration. Any such
"rule" as the one, that e.g. a positive CD around 280 nm proves (1S)-
configuration of a tetrahydroisoquinoline is thus only an "apparent" rule,
as can be seen from this example. That it nevertheless works often is only
due to the fact that in general the 1-substituent is present preferably in
the quasiaxial conformation.

The second warning example refers to the same type of chromophore. For
estradiol (3) and its 3-O-methyl ether (4) the CD around 270 nm is negative,
for its 3-O-acetate 5, however, positive, although here no change of confi-
guration or conformation is possible (Fig. 2). This clearly demonstrates
that on an aromatic chromophore an additional achiral substituent may have
a drastic influence, which can even lead to sign inversion of a Cotton
effect. Such achiral substituents must, therefore, not be neglected although
this is sometimes done (3).

Qualitative MO-theory, very successfully used in recent years to explain mo-
lecular properties (e.g. geometry (4), photoelectron spectra (5), or re-
activity (6)) can also help in better understanding CD-spectra, and in the
following a few examples are given.

Rotational strength, a substance property, which can be measured and is
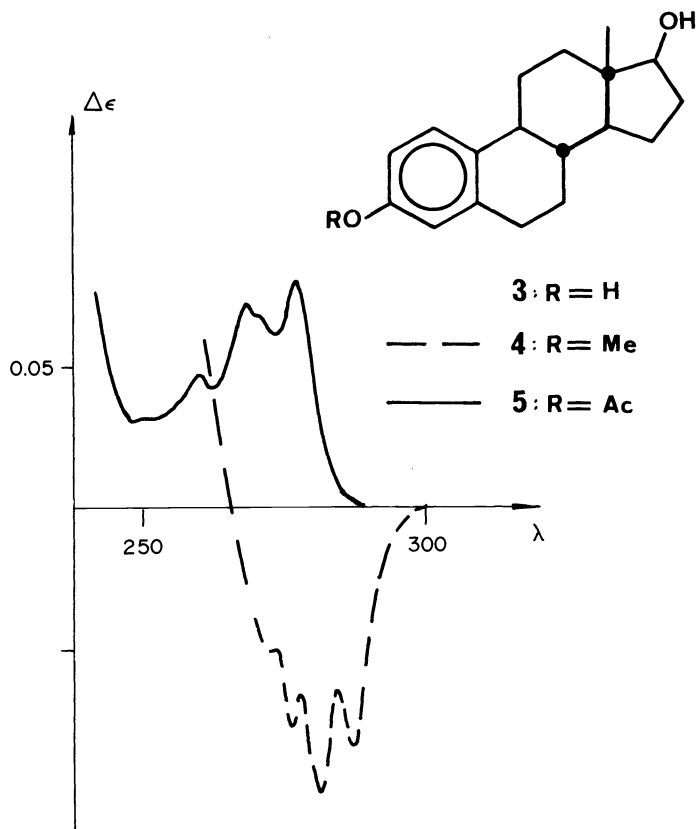defined as the (wavenumber-weighted) area under a CD-band, multiplied by a

Fig. 2. CD of estradiol 3-O-methyl ether (4) and 3-O-acetate (5) in range of α-band.

factor,

$$R = 0.229 \times 10^{-38} \int \frac{\Delta \epsilon}{\lambda} \, d\lambda \tag{1}$$

is theoretically given by the product

$$R = \mu . m . \cos(\vec{\mu}, \vec{m}) \tag{2}$$

where $\vec{\mu}$ is the electric, $\vec{m}$ the magnetic transition moment for the absorption in question. If light is absorbed by the electron cloud of a molecule, electron charge can be shifted along the direction of the electric field vector of the lightwave, and it may also be rotated. This first phenomenon corresponds to $\vec{\mu}$, the latter to $\vec{m}$. If we can identify the orbitals between which (mainly) the electron excitation occurs we can determine $\vec{\mu}$ and $\vec{m}$, and it follows from the cosine term of equation (2) that the CD is positive, if the angle between $\vec{\mu}$ and $\vec{m}$ is acute, and negative, if it is obtuse.
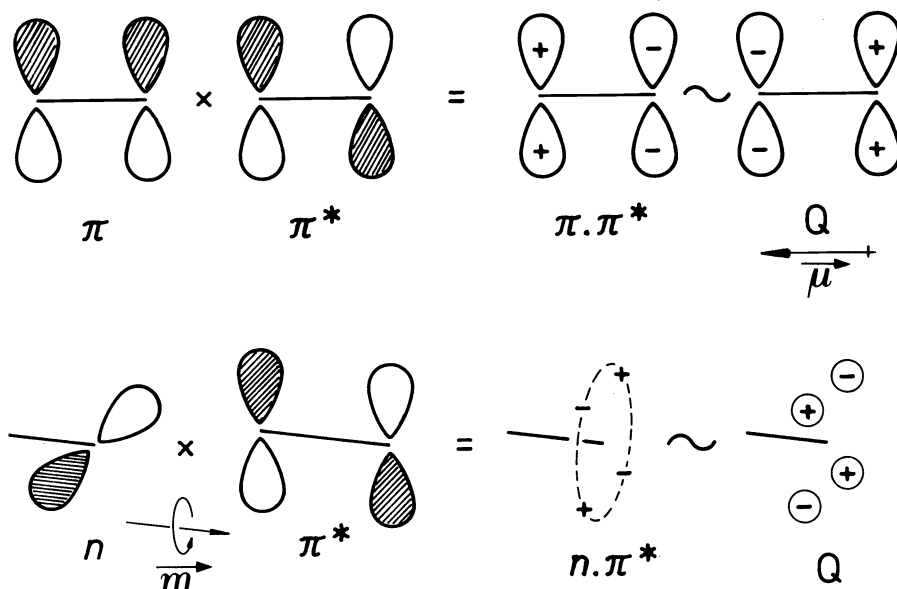
R–S—S–R′

6

7

8

9
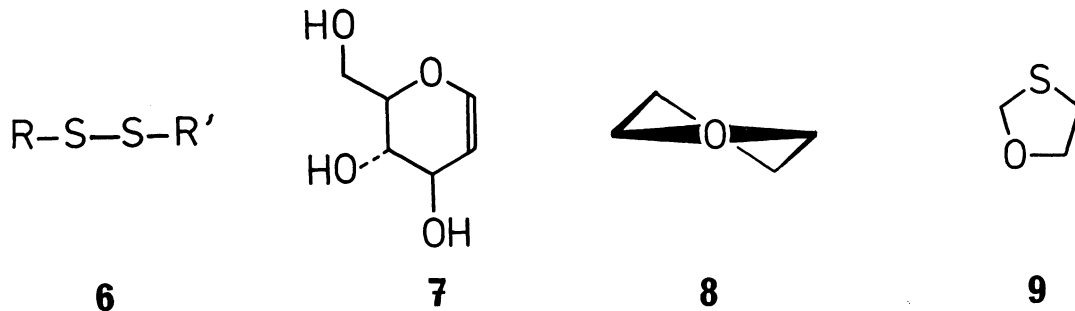
Fig. 3. Determination of electric ($\vec{\mu}$) and magnetic ($\vec{m}$) tran-
sition moments by formal orbital multiplication. TOP: $\pi \to \pi^*$-
transition (e.g. of ethylene or ketone), corresponding
quadrupole Q, and direction of developped electric transition
moment. BOTTOM: $n \to \pi^*$-transition (e.g. of a ketone), corres-
ponding quadrupole, and developped magnetic transition moment.

Moscowitz (7) has already pointed out that chiral molecules have to be
devided into two classes: 1) those which contain a chromophore which is lo-
cally chiral (typical example: disulfides, 6), and 2) those, whose chromopho-
res are locally achiral, but which are chirally perturbed by their neighbour-
hood. For theoretical reasons only in the first class $\vec{\mu}$ and $\vec{m}$ can have com-
ponents along the same line, and here it is often quite simple to correlate
the sign of the Cotton effect with the absolute conformation of the chromo-
phoric system. In the second class only one of the transition moments is
present, and the other has to be "stolen" from another transition. Perturba-
tion theory can help to find out how such a mechanism works, and leads thus
also to the determination of the angle between $\vec{\mu}$ and $\vec{m}$, the only important
property needed if we are interested just in the sign of a Cotton effect.

Qualitatively and even semiquantitatively we can determine $\vec{\mu}$ and $\vec{m}$ by multi-
plying together formally the two MOs between which the transition occurs, as
is shown in Fig. 3 for a $\pi \to \pi^*$ and an $n \to \pi^*$ transition. The physical meaning of
such a product $\Psi_1 \cdot \Psi_2$ is electron density (or probability, to find electron
charge in a given volume element), a positive sign of this product corres-
ponds thus to negative charge, a negative product is interpreted as a posi-
tive charge developped during the excitation $\Psi_1 \to \Psi_2$. In the simpler cases
$\Psi_1 \cdot \Psi_2$ represents a quadrupole Q. For a $\pi \to \pi^*$ transition (Fig. 3 top) these
four charges form a dipole along the bond, and this is the transition di-
pole $\vec{\mu}$. The UV/VIS-absorptions are correlated with these transition dipoles,
too, since the "dipole strength" D, defined as the (wavenumber weighted)
area under an isotropic absorption band multiplied by a factor,

$$D = 0.918 \times 10^{-38} \int \frac{\varepsilon}{\lambda} \, d\lambda \qquad (3)$$

is theoretically given by the square of μ,

$$D = \mu^2 \qquad (4)$$

The $\pi \to \pi^*$-bands, are, therefore, very intense ($\varepsilon \simeq 10^4$). No charge rotation is
produced by this transition.

On the other hand, the two partial dipoles which compose the quadrupole Q in case of an n→π* transition (Fig. 3, bottom) compensate each other exactly, μ = 0. Such a "forbidden" band is quite weak (ε ≃ 10^1), but during the excitation electron charge is rotated, and such a rotation (according to the right-hand-thumb-rule) can be characterized by the magnetic transition vector m̃.

The absolute directions of μ⃗ and m̃ depend on the arbitrary choice of the or-bital phases (hatched or not hatched in the Figures), and have no physical meaning, their relative orientation determines however, the sign of the CD. It should be remembered furthermore that there exists a one-to-one correla-tion between the direction of m̃ and the sign pattern within the corresponding quadrupole Q, as shown in Fig. 3 (bottom).

THE CHIRAL ENOL CHROMOPHORE

Let's apply this to a simple chromophore, the enol moiety, as is present _e.g._ in glycals and in many iridoids. Built into a ring system this chromophore deviates often from coplanarity and belongs then to Moscowitz's first class. The enol system is isoelectronic with the allyl anion, and the respective π-orbitals resemble each other, although the LCAO-coefficients are not identical. In a noncoplanar arrangement as given in Fig. 4 the formal multi-plication of the HOMO (π^0) with the LUMO (π^-) to first approximation gives a quadrupole whose four poles are not lying in one plane: the translation of electron charge (μ⃗) is combined with a rotation of charge (m̃), and whatever orbital phases we deliberately choose, the relative arrangement of μ⃗ to m̃ remains the same. In our example μ⃗ and m̃ are antiparallel (this corresponds to an electron excitation on a left handed screw), the CD of the respective band must thus be negative. This new rule was applied to glycals, as _e.g._ glucal (_7_), of which all _D_-derivatives give a strong negative CD around 205 nm, in accordance with the prediction, if the CH_2OH group (C-6) is positi-oned quasiequatorially (8).

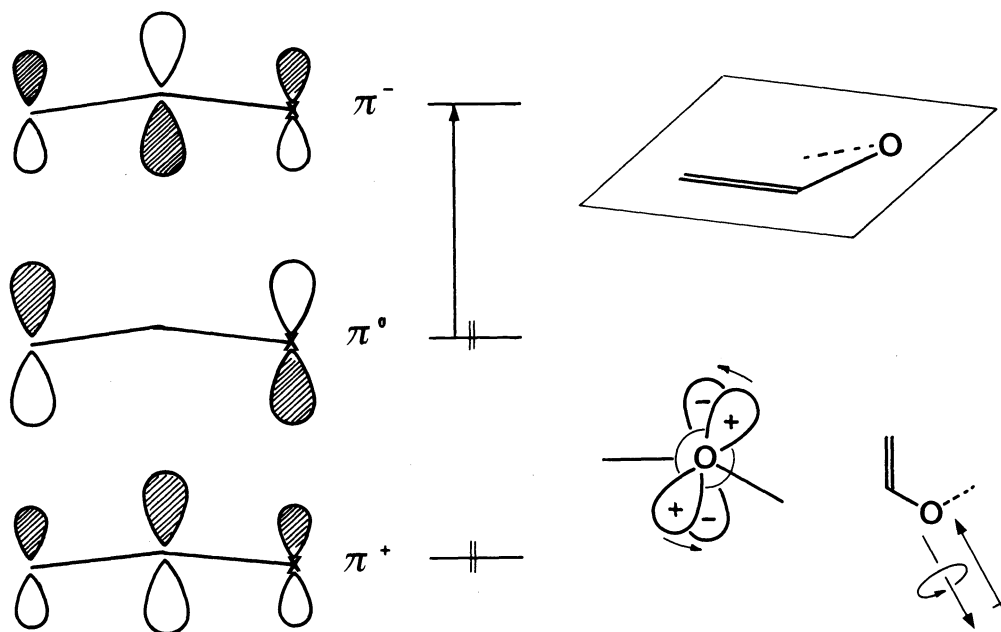The same rule can also be applied to the iridoids investigated by Sticher (9)

Fig. 4. Chiral enol ether chromophore. LEFT: MO of the isoelec-tronic allyl anion. RIGHT TOP: Absolute conformation chosen (negative torsion angle around (C-)O-C(=C) bond). RIGHT BOTTOM: Inherent helicity and transition moments for $\pi^0 \to \pi^-$-band.

(Fig. 5). For this cisfused system mainly two conformations are possible, A
and B, of which A is preferred because of the anomeric effect and the other
steric interactions. The main band in the CD-spectrum of glurosid (10) be-
longs to A, the small one around 213 nm to B. Introduction of the quasiaxial
(with respect to the dihydropyrane ring) angular OH-group stabilizes A be-
cause of the possible hydrogen bonding, thus in the spectrum of 6-deoxy
harpagide (11) and several of its substitution products (12-14) only the
short wavelength Cotton effect is discernible. On the other hand, acetyla-
tion of the angular hydrogen group (15) not only prevents such a stabili-
zation by hydroxyl bonding, but introduces also severe 1:3 diaxial inter-
action with the acetylated glucosyloxy moiety. The "characteristic" strong

10 $R^1 = R^2 = R^3 = R^4 = R^5 = H$

11 $R^1 = OH$, $R^2 = R^3 = R^4 = R^5 = H$

12 $R^1 = OH$, $R^2 = Ac$, $R^3 = R^4 = R^5 = H$

13 $R^1 = OH$, $R^2 = Ac$, $R^3 = R^5 = H$, $R^4 = OAc$

14 $R^1 = OH$, $R^2 = R^3 = Ac$, $R^4 = H$, $R^5 = OAc$
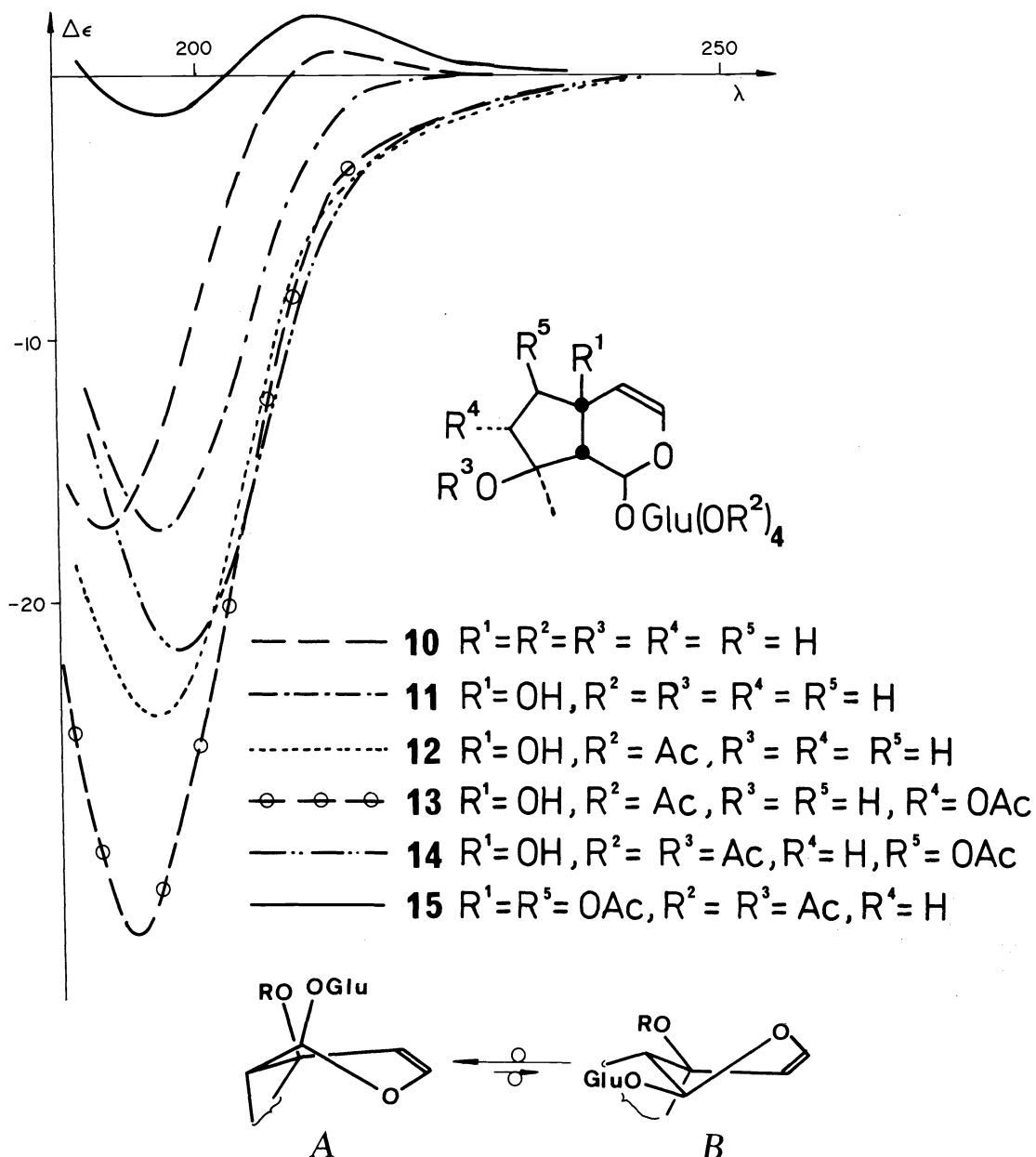
15 $R^1 = R^5 = OAc$, $R^2 = R^3 = Ac$, $R^4 = H$

Fig. 5. CD of gluroside (10) and some of its derivatives, and
the two main conformations A and B of their dihydropyrane ring.

negative CD-band has now nearly completely disappeared because of compensa-
tion by the CD of conformation B. The nonempirical CD-rule for enol ethers
proves thus independently the assigned absolute configuration which was
based on chemical and NMR-arguments.

In a similar way one can explain the strong negative Cotton effect obtained
for the methoxycarbonyl-dihydropyrane chromophore present in several indole
alkaloids (10). In Fig. 6 are drawn the full CD-spectra of the pentaacetates
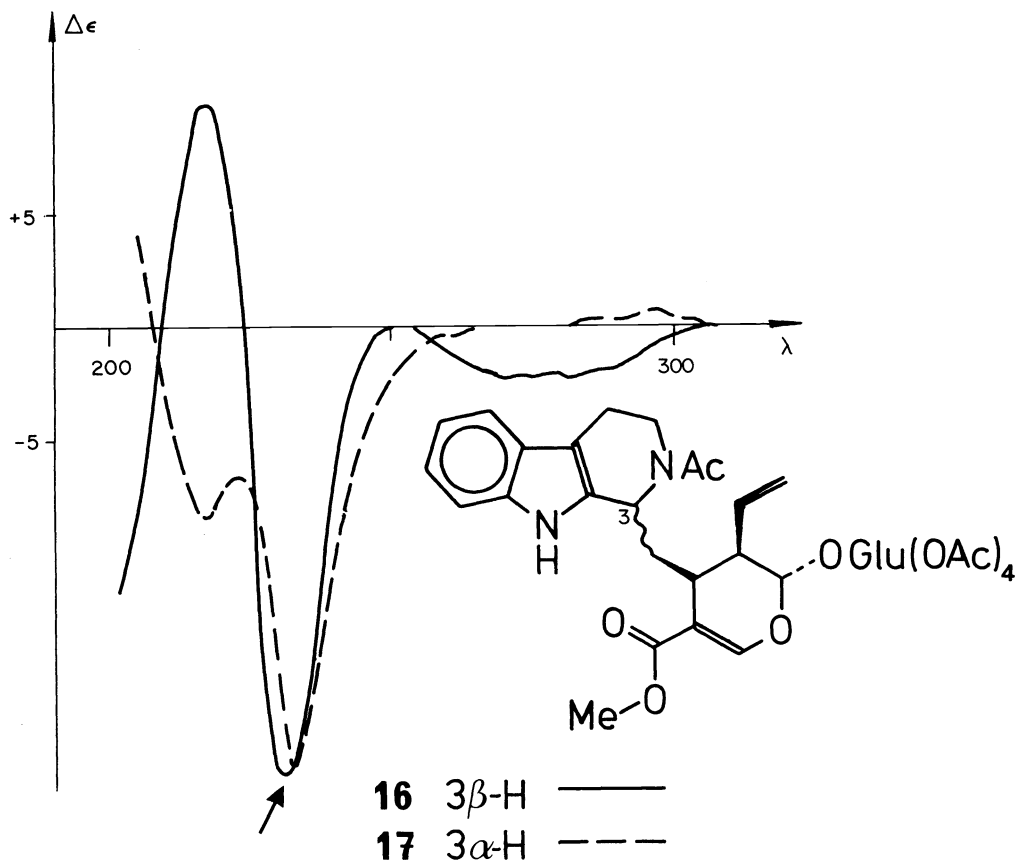

16 3β-H ——
17 3α-H - - -

Fig. 6. CD-spectra of diasteromeric pentaacetyl strictosides
16 and 17. Arrow points to Cotton effect of alkoxy acrylate
chromophore.

of the two diastereomeric (at C-3) strictosidines mentioned in lit. (11).
Those CD-bands which come from the indole chromophore have all opposite signs
for these two alkaloids, the CD around 230-235 nm (appr. -20) is, however,
the same. This Cotton effect corresponds to a strong UV-absorption, so it
must come from a $\pi \rightarrow \pi^*$-transition. In Fig. 7 are given the relevant molecular
orbitals, the products $\pi_3 . \pi_5^*$ and $\pi_4 . \pi_5^*$, and the torsion angles (C-)O-C(=C)
and (C=)C-C(=O); these latter are taken from X-ray data of such compounds
(12). For the $\pi_3 \rightarrow \pi_5^*$-transition the electric transition moment is localized
nearly exclusively in the "achiral" part of the chromophore, so this cannot
correspond to the strong Cotton effect measured, which must then come from
the $\pi_4 \rightarrow \pi_5^*$-transition. The greater part of the charge which is shifted from
the ether oxygen towards the other atoms (the direction "to" or "from" this
oxygen depends, of course, on the arbitrary choice of the orbital phases
and has no physical meaning) is transferred within the ring, and this is
again done on a lefthanded helical path for the absolute conformation present
in 16 and 17, in agreement with the negative sign of this Cotton effect
(Fig. 6). For additional remarks see the ADDENDUM after the references.
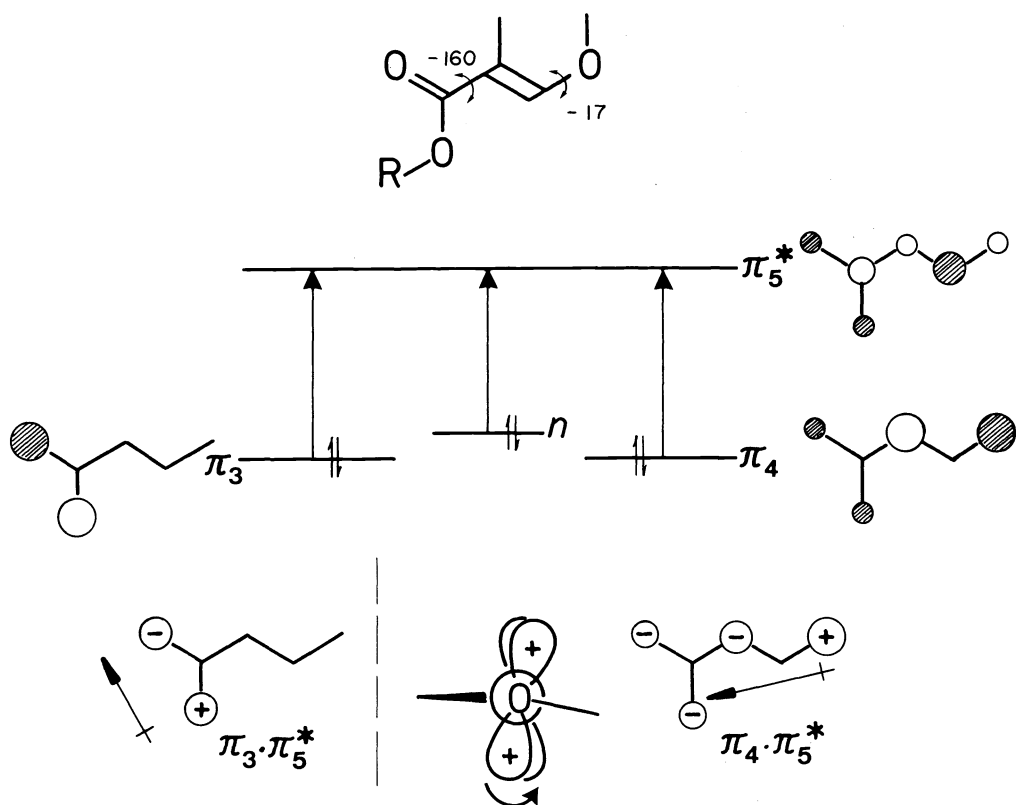
Fig. 7. Relevant orbitals of the chromophoric system of ß-
alkoxy acrylate, some of their formal products, and corres-
ponding transition moments. The torsion angles indicated on
top are average values from crystal structures.

THE CHIRAL VINYL CYCLOPROPANES

The vinyl cyclopropane chromophore is present in several terpenoids, and em-
pirical rules have been proposed for cisoid and transoid chiral arrangements
(13). These can easily be obtained from a similar qualitative MO-treatment
which also gives informations about scope and limitations of such rules.
Of each of the two degenerate Walsh-orbitals of the cyclopropane ring only
one has the right symmetry for a combination with the olefinic π- and π^*-
orbital, and Fig. 8 shows these which are relevant for the two achiral "bi-
sected" conformations, in which the torsion angle between the bisectrix of
the threemembered ring and the double bond is either $0°$ (cisoid) or $180°$
(transoid). HOMO and LUMO are drawn, however, only for the transoid confor-
mation. If this moiety is incorporated into a ring skeleton it may deviate
from these achiral conformations and the formal multiplication procedure
is shown in Fig. 9 for both the cisoid and transoid case for a positive
acute torsion angle. An inherent rotation of charge takes place only along
that bond connecting the threemembered ring with the double bond. For the
absolute conformation chosen this charge translation follows a righthanded
helical path, the CD is thus positive, in agreement with the experimental
findings. In a similar manner one obtains another rule if one starts from the
"perpendicular" conformation (torsion angle ± $90°$), for which one has to use
the other two of the degenerate Walsh-orbitals. The complete rule for this
first CD band of chiral vinyl cyclopropanes is then the one schematically
given in Fig. 10, together with one typical example, α-thujene(18). The
great advantage of such a qualitative MO-treatment is thus not only, that
one can predict correctly and nonempirically the sign of the CD, but one
derives also at the result that a sign inversion is expected when one approa-
ches the "perpendicular" conformation of such a vinyl cyclopropane.
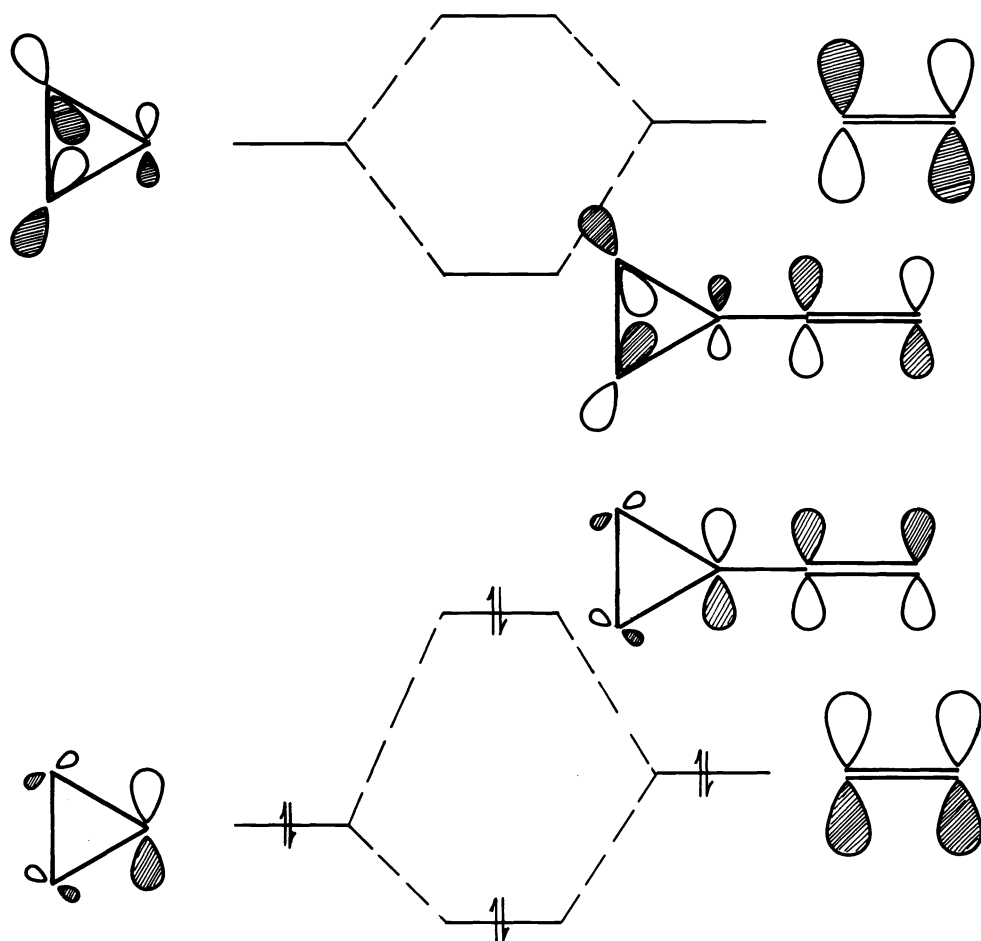
Fig. 8. Walsh orbitals of correct symmetry and their inter-
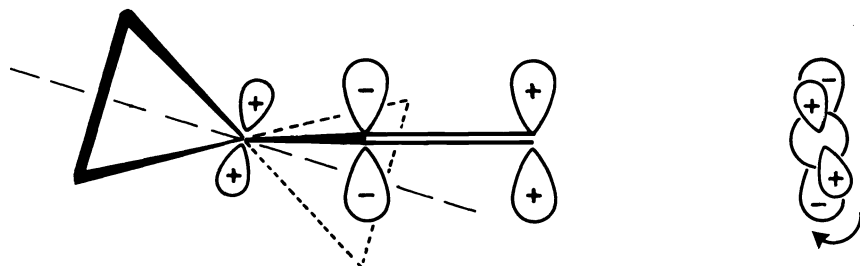action with ethylene orbitals in the "bisected" (transoid)
conformation.

Fig. 9. Transition multipole developped during excitation in
a chiral vinyl cyclopropane for an acute angle between bi-
sectrix and olefinic double bond. The transoid cyclopropane
ring is drawn with bold lines, the cisoid with broken lines
in the same figure. On the right the helical path of electron
excitation along the bond between the olefin and the cyclo-
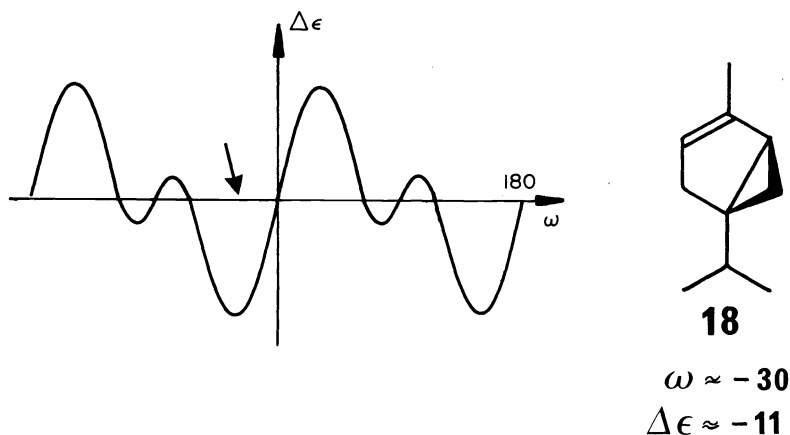propane ring is shown.

$$\omega \approx -30$$
$$\Delta\epsilon \approx -11$$

Fig. 10. Schematic representation of relation of torsion
angle ω between bisectrix of cyclopropane ring and double
bond in a chiral vinyl cyclopropane. The arrow indicates the
torsion angle for α-thujene (18).

In a similar way we have also explained the rules for chiral dienes (14),
enones (15), and even carotenoids (14), and many well established exciton
interactions (Nakanishi's dibenzoate rule (16), α-helix of polypeptides (1),
etc.) can be understood without calculations (15).

INHERENTLY ACHIRAL CHROMOPHORES: GENERAL CONSIDERATIONS

In the examples discussed hitherto both an electric and a magnetic transition
moment was present at the same time. In cases of inherently achiral chromo-
phores this is not so, but a few simple rules from perturbation theory (17)
allow us also to tackle this problem. From a practical point of view it is
convenient to subdivide this second class of Moscowitz into one category of
such molecules, where the ring, into which the chromophore might be incor-
porated, is chiral ("chirality of the second sphere"), and another one,
where this second sphere is also achiral ("chirality of the third sphere")
(18). The reason is, that the chiral perturbation in the first category comes
from bonds which are very close to the chromophore (e.g. cycloalkanones in
twist conformation, 8) so that it is mainly the helicity or chirality of
this ring which governs the whole CD, and we may neglect contributions from
all the other atoms as long as we are interested only in the sign of the
Cotton effects. Thus e.g. the CD around 300 nm of twisted alkanones of
absolute conformation 8 is always positive (19). Rules obtained in this way
can be classified as "chirality rules" or "helicity rules", similar as for
inherently chiral chromophores. In molecules with an achiral second sphere
(e.g. a hemithioacetal, 9) we have to take into consideration the chiral
perturbation (mainly through space; only if the perturbing bond is connected
to the chromophore by a coplanar zig-zag route perturbations through bonds
become important (20)) from many different atoms, and this is in general done
with the help of different sector rules. The theoretical treatment of these
two categories of molecules is, however, similar (15).

INHERENTLY ACHIRAL CHROMOPHORES: LICHEN-LACTONES

In order to show that the nonempirical correlation between chiroptical pro-
perties and stereochemistry is not restricted to very simple cases I should
like to apply it here to the determination of the absolute configuration of
acetyl isomurolic acid (19, Fig. 11), whose structure elucidation is dis-
cussed during the symposium by Dr. Huneck from another point of view (21).
The chromophore of 19 is essential that of fumaric acid derivatives (20),
and its 10π-system is isoelectronic with that of the dianion 21. Fig. 12
gives a qualitative picture of the relevant orbitals and their energies as
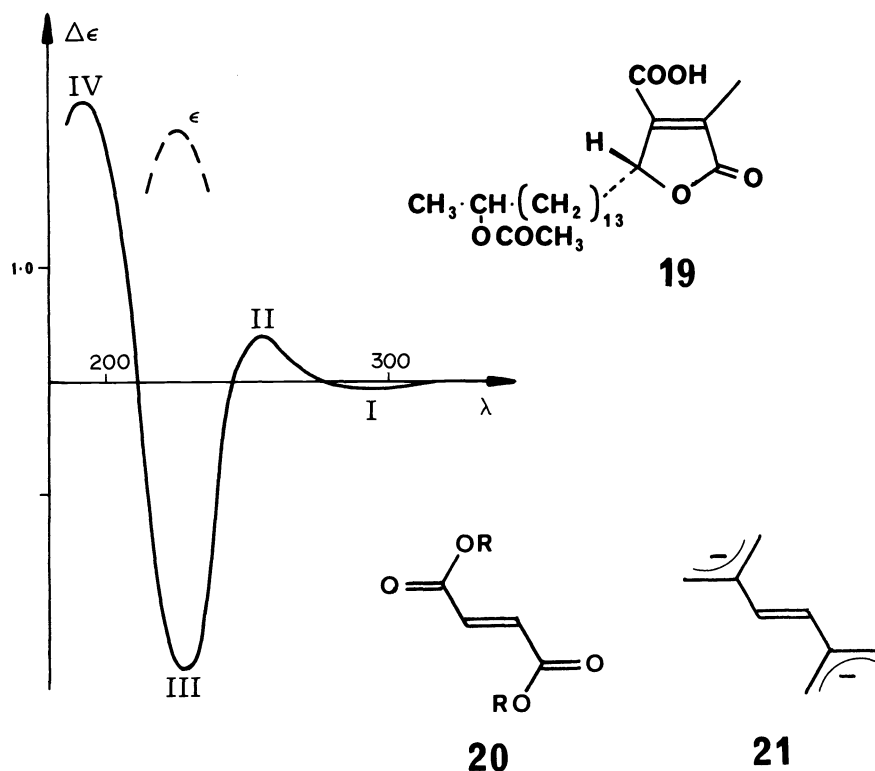estimated from simple HMO-theory. The orbitals are there also characterized

Fig. 11. CD and UV (ε = 7800) of acetyl isomurolic acid (19),
its chromophoric system (20), and the isoelectronic dianion 21.

by their symmetry properties (a: symmetric, b:antisymmetric with respect to
the C_2-axis; g (gerade): symmetric, u (ungerade): antisymmetric with respect
to the center of inversion), the possible transitions are numbered from ①
through ⑦ approximately according to their energy. The symmetry labels for
the different excited states are obtained from the well known rules: a.a =
b.b = A, a.b = B, g.g = u.u = g, g.u = u. Transitions ① and ②,③ and ④, as
well as ⑥ and ⑦ are approximately of same energy, resp., and the corres-
ponding electric and magnetic transition moments can be obtained by the same
formal multiplication procedure as above, although much easier with the help
of group theory. In Table 1 are summarized these data, the x- and y-
coordinates lie in the plane of the chromophore, the z-axis is perpendicular
to it. Transitions ① and ⑦ have formally nonvanishing z-components of $\vec{\mu}$,
but because of extremely weak overlap they are practically zero. As we can
read off Table 1 only the two $\pi \rightarrow \pi^*$-transitions ④ and ⑤ have thus a non-
vanishing electric transition moment and should be recognizable in the UV-
spectrum, transitions ① and ⑦ will neither be found in the UV- nor in the
CD-spectrum.

This simple picture can be improved by taking into account configurational
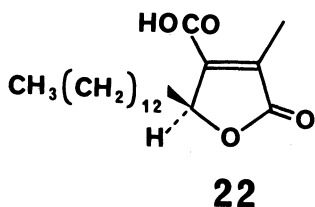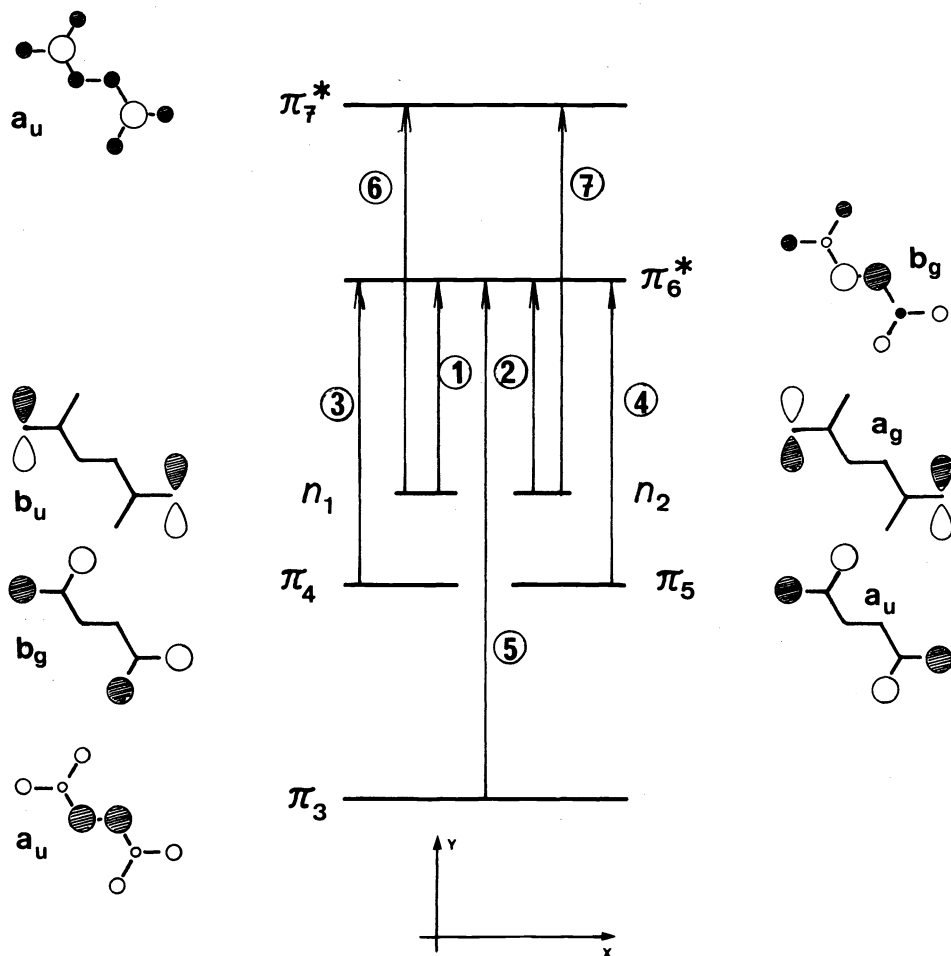interaction (CI), whose effect may be described as a mixing of states of same

TABLE 1.   Transitions of the fumarate chromophore.

Transition	Symmetry of Excited States	Type of Transition	Components of $\vec{\mu}$	$\vec{m}$
①	A_u	$n_1 \to \pi_o^*$	z ($\approx$ 0)	
②	B_g	$n_2 \to \pi_b^*$		x,y
③	A_g	$\pi_4 \to \pi_b^*$	z	
④	B_u	$\pi_5 \to \pi_6^*$	x,y	
⑤	B_u	$\pi_3 \to \pi_6^*$	x,y	
⑥	B_g	$n_1 \to \pi_7^*$		x,y
⑦	A_u	$n_2 \to \pi_7^*$	z ($\approx$ 0)	

Fig. 12. Some orbitals of the chromophore 21, together with their irreducible representations in point group C_{2v}, and possible transitions.
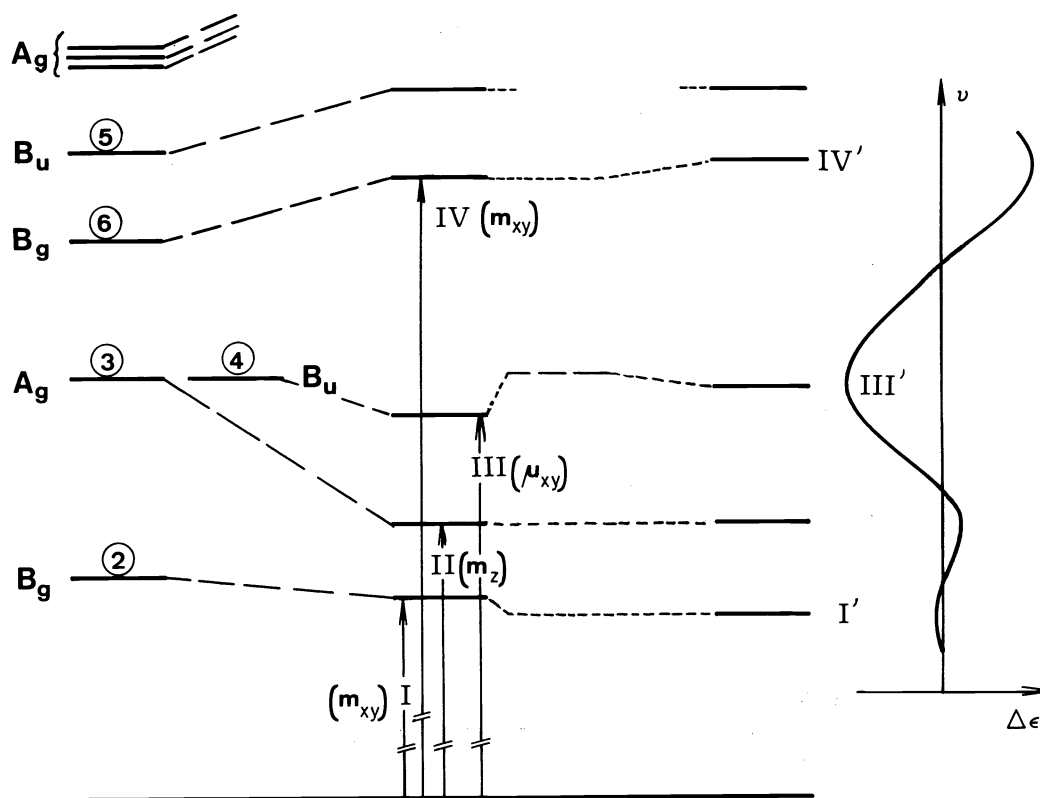
Fig. 13. Jabłoński diagram corresponding to the transitions
given in Fig. 12, taking qualitatively into consideration
configurational interaction. The energy levels at the right
side are drawn so as to correspond to the measured CD-maxima
of 19.

symmetry and a "repulsion" between their respective energy levels. Doubly
excited states have also to be considered in such a CI; they all have A_g-
symmetry as follows from the rules given above. This leads to the more rea-
listic Jabłoński diagramme of Fig. 13 (transitions ① and ⑦ already neglected),
which is drawn so as to correspond to the measured CD- and UV-spectrum; the
excited states are characterized by Roman numbers which correspond to the
bands in Fig. 11. Band III is the only one in the accessable wavelength
range with large absorption coefficient, so it must be associated with a
strong $\vec{\mu}$; bands I, II, and IV correspond to transitions with nonvanishing $\vec{m}$.
I and IV both have their magnetic transition moment in the plane of the
chromophore, they can steel the necessary electric transition moment best
from the nearest transition connected with a $\vec{\mu}_{x,y}$, and this is transition
III; the latter can in turn steel its magnetic transition moment from I and
IV. Mixing of the B_u- and B_g-states is caused by the chiral field around the
chromophore, and we can again apply the result of perturbation theory, that
interacting states "repel" each other obtaining thus slightly modified
molecular orbitals I', III', and IV'. Fig. 13 shows that I' corresponds to
the energetically favoured combination of I with III, IV' to the energe-
tically unfavoured combination of III with IV. To a first approximation
the chromophoric system of acetyl isomurolic acid (19) can be assumed to be
coplanar (if it were inherently chiral, larger rotational strengths would
have been expected), the first few methylene groups of the long side chain
being then the main perturber. As is generally accepted (1) the by their
electrons not fully screened positive residual charges of the nuclei can
electrostatically interact with the transition moments, and Fig. 14 summa-
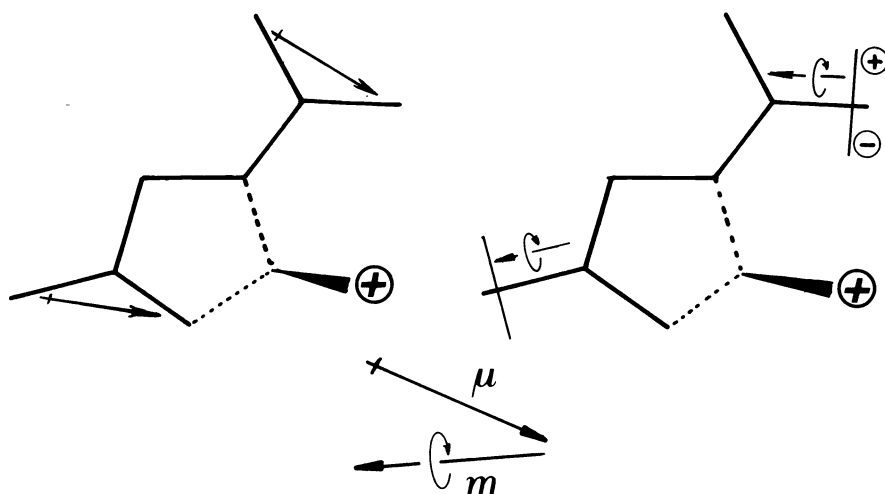rizes the result. The formal product $\pi_5 \cdot \pi_6^*$ shows that two partial dipoles

Fig. 14. Sign of Cotton effect of band I' of 19. Left $\pi_5.\pi_6^*$,
right $n_2.\pi_6^*$, and direction of electric and magnetic transition
moments as induced by a chirally arranged positive charge
(attractive interactions).

(each being actually the result of charge interaction within a quadrupole)
are localized within each COO-moiety. If we arbitrarily choose the energeti-
cally favoured interaction with the perturbing residual charge (more attrac-
ting forces than repulsive) the direction of $\vec{\mu}$ is that indicated in Fig. 14
(left).

The direct interaction between a charge and a magnetic moment is quite weak,
but we have learned that each magnetic moment is connected with a quadrupole.
By the multiplication procedure of $n_2.\pi_6^*$ (or $n_1.\pi_7^*$) two quadrupoles are
obtained, one around each carbonyl oxygen. One of these is rather symmetri-
cally disposed with respect to the perturbing charge and is therefore not
drawn, the signs of the charges of the other (nearer) one can, however, un-
equivocally be determined from the sign of the perturbing charge. As
mentioned above, we have to take again the energetically favoured inter-
action, which is that drawn in Fig. 14 (right), and from this we see that
the angle between $\vec{\mu}$ and $\vec{m}$ for the absolute configuration chosen is obtuse,
so the corresponding CD must be negative. According to Fig. 13 this type of
interaction corresponds to band I', which for acetyl isomurolic acid (19)
is indeed very weakly negative (Fig. 11 and 13). Within band III' we expect
then a similarly weak positive CD, as for this we have to take the
energetically unfavourable interaction, that means, that one of the two
transition moment vectors, $\vec{\mu}$ or $\vec{m}$, has to be inverted. Theory furthermore
predicts that these two corresponding Cotton effects should have equal
rotational strengths.

For the interaction between III and IV the same argumentation holds: for the
energetically lower transition (III') we expect a negative CD, for the
higher (IV') a positive one. The CD within IV' is indeed relatively
strong positive, and from this follows that within III' an equally strong
negative CD should be found. The sum of both contributions to the CD within
band III' is thus negative, and this result is in agreement with the
measured CD-spectrum (Fig. 11). Acetyl isomurolic acid has thus the absolute
configuration depicted in formula 19, which is identical with that obtained
from other reasoning (21). It should be mentioned that the absolute con-
figuration of (-)-lichesterinic acid (22). which is S, has several years
ago been assigned correctly by comparising the sign of the CD-band around
255 nm with that of chiral butenolides of known absolute configuration (22).
The influence of the second (conjugated) COOH group has, however, been com-
pletely neglected, assumed to be an "achiral" substituent. Although correct,
this result has thus been obtained only by good fortune because completely
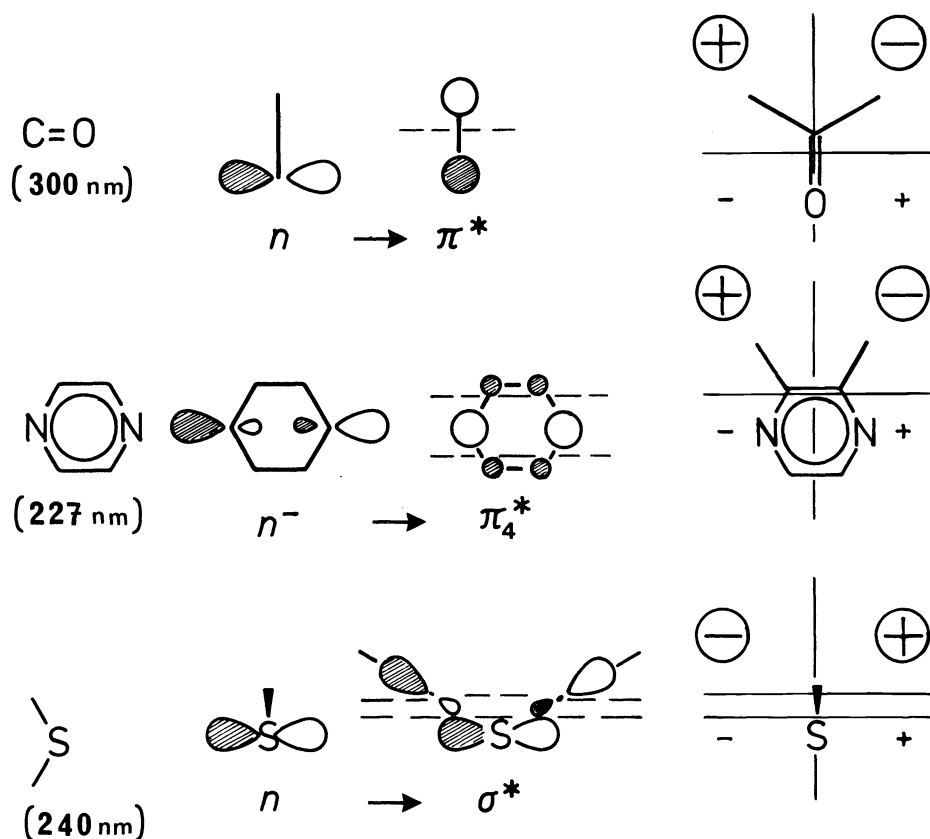different electronic transitions have been compared.

Fig. 15. Generalized Sector Rules in point group C_{2v} for transitions of similar parentage for ketone, 1.4-pyrazine, and sulfide chromophore. The signs of the sector rules on the right are for upper sectors (projection from top to bottom of molecule).

In a similar way as has been demonstrated in detail for this inherently achiral chromophore of fumaric acid one can also deduce the correlation between absolute conformation and signs of the contributions to the CD for several other chromophores (cf. 15,23). From such treatments and a survey of many experimental CD-data the following generalization emerged: If two chromophores 1) belong to the same point group, and 2) for analogous transitions $\Psi_a \rightarrow \Psi_b$ both orbitals Ψ_a and Ψ_b have same symmetry (belong to the same irreducible representation), resp., then the sign patterns for the two corresponding CD-rules (sector rules) are the same. If in spite of same symmetry the orbitals Ψ_a and/or Ψ_b differ in the number of nodal surfaces then one has to start with this assignment in that region where the respective orbitals are most similar to each other. In proceeding from there, each time one crosses a nodal surface one has to change the sign of the contribution to the CD. Fig. 15 illustrates this for three chromophores of C_{2v}-symmetry, viz. the carbonyl (24), the pyrazine (25), and the sulfide (hemithioacetal) group (23). The virtual orbitals are quite different for the corresponding transitions, the HOMO are, however, identical or rather similar in shape, so we build up the sign pattern around the latter in identical ways. Proceeding to back sectors we have once to change sign for the carbonyl ($n \rightarrow \pi^*$) and for the pyrazine ($n^- \rightarrow \pi_4^*$) sector rules, but twice for the sulfide ($n \rightarrow \sigma^*$) rule. The sign distribution in the back sectors is thus identical for the first two cases and inverted for the last one, in agreement with experimental experience.

With these few examples I wanted to show that the nonempirical treatment of chiroptical properties using qualitative MO-theory can successfully be under-

taken in just the same way as in other areas of chemistry. It is believed
that it can be applied also by those chemists who are mainly biased in
favour of isolation, structure elucidation or synthesis of organic
compounds, and that it can render them more critical when they apply the
different rules published to their own stereochemical problems.

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ADDENDUM: This correlation between the chirality of the dihydropyrane
ring and the CD around 235 nm is opposite to that proposed in the litera-
ture (10) and originally based on ORD-measurements (10a). Actually two
Cotton-effects can be recognized in this wavelength range in the CD-spec-
trum (e.g. 253 (+0.30) and 238 (-6.60) for ajmalicine). The first corre-
sponds to the indole ß-band and should be positive (26), the second is the
one in which we are interested. In the ORD-spectrum obviously these two
could not be separated and were thus described as a single positive Cotton-
effect. The Japanese authors (10b) have tested this original rule, but
with samples whose molecules lack conformational rigidity. Own results
with some iridoids indicate, however, that also the torsion angle around
the (C=)C-C(=OOR) - bond can be of prominent influence, as should be ex-
pected on the basis of the MO-treatment given here.