Table IV. Rotatory Strength of α-Phellandrene

	set I	set II	set III
20 °C calcd	−2.7	−11.31	−7.11
obsd[a] = −8.5			
−150 °C calcd	−2.7	−11.18	−4.88
obsd[b] = −2.0			

[a] This is the average of values obtained at this temperature from the data of ref 8-10. [b] From the data of ref 9.

perimental values.[10-12] One experimental value (+5.5) obtained by Snatzke et al.[12,13] in a rigid glass at −177 °C is not included in the table. Neither the optical rotation data of Ziffer et al.[10] done at temperatures of 82, 18, and 10 °C nor of Horseman and Emeis[11] at 20 and −150 °C extrapolate to positive values of the rotational strength at −177 °C. It is possible that the optical purity of the Snatzke et al. sample is slightly higher than that of the other two sets of investigators but optical artifacts in chiral measurements in rigid glasses are well known. The value (−10.3) that they obtained at room temperature is included in the data of Table IV. What is quite clear from the calculated values of [R] for the long-wavelength diene transitions is that the energy-minimized coordinates of set (III) result in far better agreement with experiment than sets (I) and (II). With set (I) the rotational strength is predicted to be independent of temperature because only one rotamer is stable. The temperature dependence of set (II) is also predicted to be very small, in this case, because of the very similar values of the rotamer rotational strengths. The restriction of the coordinates of the diene substituents at the carbon atoms of the diene moiety to prevent distortion of the double bond makes a very significant improvement in the agreement between experiment and theory. It appears highly likely that the generally accepted value of 26.2 kcal mol^{-1} rad^{-2} as the torsional constant about the double bond is too small when the double bond is part of a conjugated system.

Summary

The rotatory strength of the rotamers of the quasi-axial and quasi-equatorial conformers of α-phellandrene has been calculated by the CNDO/S method without configuration interaction using coordinates obtained by energy minimization' based on Westheimer concepts. This paper clearly demonstrates how sensitive the chiral activity of the allowed transition of a molecule is to its fine structure. Semiempirical potential energy calculations are shown to generate values of the structural parameters which produce excellent agreement with chiral measurements.

References and Notes

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A Quadrant Rule for the Prediction of Chiroptical Effects of Optically Active Homoannular Cisoid Dienes

Robert M. Moriarty,*[1a] Herbert E. Paaren,[1a] U. Weiss,[1b] and W. Basil Whalley[1c]

Contribution from the Department of Chemistry, University of Illinois at Chicago Circle, Chicago, Illinois 60680, the National Institute of Arthritis and Metabolic Diseases, National Institutes of Health, Bethesda, Maryland 20014, and The School of Pharmacy, London WC1N 1AX, England. *Received April 13, 1979*

Abstract: An empirical analysis for the chiroptical effects of cisoid homoannular dienes called the diene quadrant rule is presented. This regional rule uses a cubic space divided into quadrants in order to assign relative signs of the rotatory contribution of the diene and axial allylic substituents. The magnitude of the contribution of axial allylic substituents is estimated from their stereochemical relationship to the adjacent double bonds. Assumptions are made about the relative contributions of axial allylic hydrogen vs. methyl. The total $\Delta\epsilon$ is considered to consist of $\Delta\epsilon = \delta_{\text{diene}} - [\delta_{\text{X}} \sin^2 \omega + \delta_{\text{X}}' \sin^2 \omega]$, where δ_{diene} is the contribution of the diene, and δ_{X} and δ_{X}' are substituent contributions at torsional angle of ω to the adjacent olefinic unit. The algebraic sum derives from the orientation of the diene and axial allylic moieties inscribed within the cubic space. The diene quadrant rule is applied successfully to known exceptions to the original diene chirality rule.

In 1961 a rule was proposed for the relationship between the sign of the Cotton effect for the lowest energy $\pi \rightarrow \pi^*$ transition and the skew sense of a cisoid homoannular diene.[2a,b] A positive or negative Cotton effect results from a right- or left-handed diene, respectively. The chiroptical contribution of substituents in the vicinity of the diene was considered to be negligible compared to that associated with the inherent dissymmetry of diene chromophore. The original rule was based on HMO calculations on twisted butadiene[2c] and more elaborate calculations have confirmed the relationship between helical sense and chiroptical effect.[3a-g,4] The rule successfully predicted the sign of the CD for many compounds.[5] Unfortunately, a number of exceptions have come to light, and apparently the twist sense of the diene alone does not control the chiroptical effect.

Illustrative of such exceptions, which will be treated sub-

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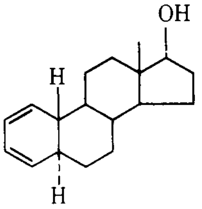
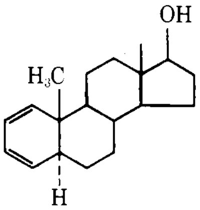
sequently in this paper, is the particularly egregious departure of prediction from observation in the case of the three steroids discussed recently by Burgstahler et al.,[6] namely, 5α-estra-1,3-dien-17β-ol (**1**), 5α-androsta-1,3-dien-17β-ol (**2**), and 5α-methylandrosta-1,3-dien-17β-ol (**3**).



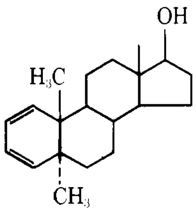
1

$\Delta\epsilon_{260}$ +3.8



2

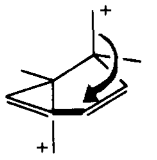
$\Delta\epsilon_{260}$ −2.7



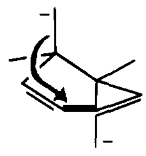
3

$\Delta\epsilon_{264}$ −11.1

All three possess left-handed chirality but a sign inversion occurs as one varies the *axial allylic substituents* throughout the series. This exemplifies the problem and is but one instance of a large number of perplexing exceptions to the original diene chirality rule[1a] in which the nature of the axial allylic substituent seems to play a role. As early as 1966, Beecham and Mathieson called attention to the possible role of adjacent asymmetry in influencing the CD of dienes.[7] Recently Rosenfield and Charney have calculated by CNDO/S and CNDO/2 methods the variation of rotatory strength of the diene as a function of allylic substituents.[4] They find that the contribution of the allylic substituents may be large and that axial allylic hydrogen makes a very strong contribution, comparable to that of the diene itself at a skew angle of 20°, while methyl increases the rotatory strength by a factor of about 2.[4] Prior to this calculation, some exceptions to the diene chirality rule were discussed in terms of the contribution of allylic chirality by Burgstahler et al., and the essential conclusion was that the chiroptical contribution of allylic substituents was the dominant factor in determining the CD of dienes.[6,8] However, the concept of "allylic chirality" applied by Burgstahler et al.[6,8] does not explain why exceptions should occur in the case of cisoid homoannular dienes since the chirality of the axial allylic substituent, regardless of its nature, must always have the same sign as the diene. Theoretical calculations show the possibility of a sign inversion in the CD of a related series but offer no predictive guides.[4] No current theory relates structure to the magnitude of $\Delta\epsilon$, even though trends have been indicated.[4]



P chirality

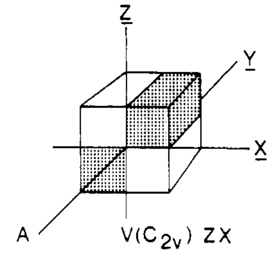


M chirality

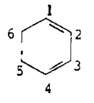
The present state of knowledge goes little beyond restatement of experimental observations; namely, in some cases, the effect of the allylic substituents may be large and even outweigh those of the diene contribution. Most importantly, with the finding[4,6,8] that axial allylic substituents play a role, there is absolutely no basis for predicting the sign of $\Delta\epsilon$.

The dilemma posed by this state of affairs appeared to us as an interesting problem in modern stereochemistry. We now present a concept called the *diene quadrant rule* which includes aspects lacking in other approaches, namely, rationalization of the sign of the chiroptical effect and estimation of the relative magnitude of the optical contribution of extrachromophoric groups which are allylic to the cisoid homoannular diene. The power of this rule lies in its simplicity and ability to incorporate and explain exceptions to the original diene chirality[2a,b] into a new model.

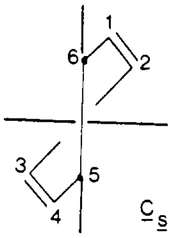
In order to understand the sign of the contribution of axial allylic groups in cisoid 1,3-dienes we employ a regional rule based on the cubic space, A, of a type used by Schellman in discussing chromophores of point group C_{2v} symmetry.[9] In A light and dark areas correspond to regions of opposite rotatory contribution. The nodal planes are areas of zero contribution to the rotatory power. This analysis gives only relative signs and does not deal with the relative magnitudes of contributions which will be treated in the second part of our formalism.



A V(C_{2v}) ZX

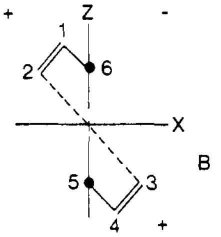


4

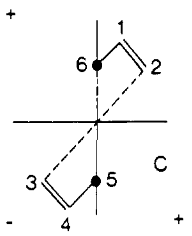


C_s

The skewed form of 1,3-cyclohexadiene (**4**) of approximate C_s symmetry is inscribed within the cubic regional diagram A. To conceptualize this operation we focus on the coordinate system upon which the regional space is structured. The center of the C_5–C_6 bond is placed at the origin, with this bond on the Z axis. This fixes the position of the diene chromophore within the space. Figure B represents a right-handed diene (P chirality) and figure C represents a left-handed diene (M chirality).

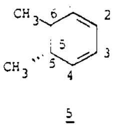


B

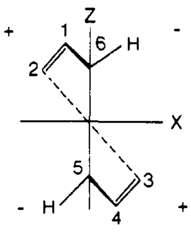


C

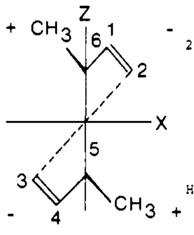
The C_2–C_3– is behind the ZX plane and its midpoint intersects the Y axis. The olefinic groups C_1C_2 and C_3C_4 fall into compartments of the same sign. Next we consider an allylically substituted diene such as *trans*-5,6-dimethylcyclohexadiene (5R, 6R) (**5**). Two diastereomeric conformational isomers may be considered for this configuration.



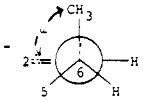
5



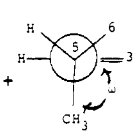
6



7



8



9

Conformational isomers **6** and **7** emphasize the C_2 diplanar structure; the former has the two allylic hydrogens quasi-axial and the two methyl groups quasi-equatorial. The quasi-equatorial allylic methyl groups have a small torsional angle (ca. 30°) with the adjacent olefinic group and the quasi-axial allylic hydrogen atoms have a 90° torsional angle with the adjacent double bond. Conformation **6**, which has P chirality, may ring flip to **7**, which has quasi-axial methyl groups and possesses left-handed helicity (M chirality). Structures **6** and **7** are placed in the quadrant diagram with C(5)–C(6) on the Z axis with its midpoint at the Z–Y origin and C(5)–C(6) and the axial allylic substituent approximately in the ZX plane; C(1), C(2), C(3), and C(4) lie behind this plane in compartments of different sign. The midpoint of the C(2)–C(3) bond intersects the *Y* axis but it is unnecessary in the present treatment to indicate this. Newman diagrams **8** and **9** show the torsional angle relationship at the allylic carbon atoms C(5) and C(6) in **7**.

The quadrant diagrams show two very important features. The first is the chiral sense of the diene. This is nontrivial since other formalisms do not indicate chiral sense as clearly. Second is the fact that the quasi-axial allylic substituents fall into quadrants of *opposite sign contributions* relative to the diene chromophore itself and might make opposite rotatory contributions.

While the quadrant analysis indicates that the sign of the contribution of the axial allylic substituents may be opposite to that of the diene itself, the magnitude of this contribution must be estimated. To this end we refer to the recent work of Kirk on the dominant "octant-dissignate" behavior of α-quasi-axial C–H bonds.[10,11] They consider a chiral four-center system of RC_{α}—C=O and chose a sine function:

$$\delta\Delta\epsilon = k \sin^2 \omega$$

to describe the dependence of $\Delta\epsilon$ on the orientation of the axial substituent, where ω is the torsional angle of the α substituent R with respect to the carbonyl group, k is a constant characteristic of the group R, and $\delta\Delta\epsilon$ is the contribution of R to the total Cotton effect, $\Delta\epsilon$. For the best fit with chiral cyclopentanones, the empirical values $k_C = 1.9$ and $k_H = 6.2$ were used.

We apply the same type approach in order to estimate the magnitude of contribution of allylic substituents. The following points summarize the approach:

(a) The diene has some inherent net contribution to the total Cotton effect $\Delta\epsilon$. The sign of the contribution is positive or negative depending upon the twist sense of the diene.[2a,b]

(b) The allylic substituents *make an opposite rotatory contribution* compared with the diene as indicated by the quadrant diagram.

(c) The magnitude of this contribution will depend upon (1) the orientation of the allylic substituent with respect to the adjacent double bond, which is maximal at ~90°, i.e., quasi-axial, and minimal at ~0–30°, i.e., quasi-equatorial (this is expressed by a sin ω relationship); (2) the two allylic groups of most concern (methyl and hydrogen) (*the contribution of axial allylic hydrogen is larger than that of axial allylic carbon*).

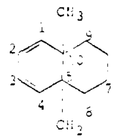
The relative rotatory contribution of axial allylic hydrogen vs. methyl is moot. Calculations by Rosenfield and Charney for two cisoid conformations of 1,3-hexadiene in which the C_5 carbon has successively an axial allylic hydrogen and an axial allylic methyl with a planar arrangement of the diene show that the rotatory strength of the axial allylic methyl structure is twice that of the axial allylic hydrogen array.[4] However, in Kirk's analysis of hexahydroindanones[12] and cyclopentanones,[10] the octant dissignate contribution of α-axial hydrogen was considered to be considerably larger than those of other common substituents (e.g., Me, Cl, Br, and I). Theoretical support also exists for the dominant contribution of α-axial hydrogen.[13-16]

Equation 1 gives the relationship between the observed total $\Delta\epsilon$ and the contribution from the diene and axial allylic substituents X at some torsional angle ω with the nodal plane of the adjacent ethylenic unit:

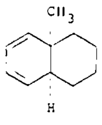
$$\Delta\epsilon = \delta_{\text{diene}}\Delta\epsilon - [\delta_X \sin^2 \omega + \delta_{X'} \sin^2 \omega] \qquad (1)$$

The contribution from the diene is a function of ω C(2)–C(3) and may be estimated from the work of Charney and Rosenfield[4] and experimental observation such as X-ray diffraction data.[25,28,33,34,43-46] Substituent contributions for the axial allylic substituents, δ_X, are empirical and may be derived from series of structurally related compounds of well-established structure.

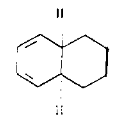
Application of the quadrant diene rule to various examples is presented below. At this point, however, it is useful to consider a hypothetical example for the purpose of illustration. For a series of *trans*-hexahydronaphthalenes **10–12**, the trans methyl groups are replaced successively by one and finally two hydrogen atoms.



10

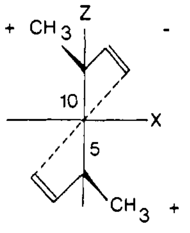


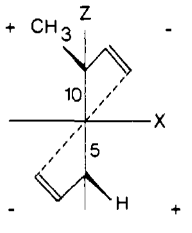
11

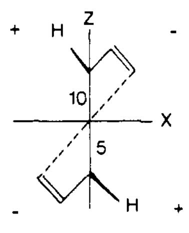


12

The quadrant representations for these three structures are the following.





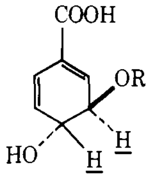


These systems possess rigid left-handed chirality with torsional angle C(1)(10)–C(5) (4) of ~30° as estimated from Dreiding models and this is invariant throughout the series. Also the axial allylic substituent has a torsional angle of 90° with the adjacent double bond. We may neglect the allylic equatorial carbon–carbon bonds because of the small torsional angles with the diene. From the relationship of the rotational strength, R, with α for small diene torsional angles and the equation $R = 43.956\Delta\epsilon(\Delta/\lambda)$ were Δ is the full bandwidth at half-height for a Gaussian CD band and $\lambda_{max} = 270$ nm, one calculates $\delta\Delta\epsilon$ of the diene of ~20.[18] In actual examples a more realistic estimate for $\delta\Delta\epsilon$ is 40 and we use it in this hypothetical example. A useful empirical group constant based on examples for axial allylic hydrogen is 25 and for methyl is 5. The calculated $\Delta\epsilon$ for **10, 11,** and **12,** would be $-40 + 10 = -30$, $-40 + 30 = -10$, and $-40 + 50 = +10$, respectively. The intent of this hypothetical example is to show that a sign change in $\Delta\epsilon$ for a closely related series of systems is perfectly reasonable. This is precisely the behavior which has been observed experimentally as shown above for **1–3**, even with respect to the pattern of substituent replacement, $CH_3 \rightarrow H$.[52]

Application of the Diene Quadrant Rule to Homoannular Cisoid Dienes

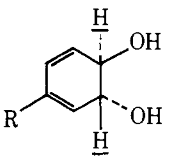
Now we may demonstrate the rule's application to certain compounds with particular attention to (a) the sign of the CD for unexplained exceptions to the original diene chirality rule[2a] and (b) variations in the magnitude of $\Delta\epsilon$ as a function of molecular structure, especially with respect to allylic substituents.

The feature common to all reported exceptions to the diene chirality rule for homoannular cisoid dienes is the presence of *two axial allylic hydrogen atoms.* In the case of some exceptions only the compound with axial allylic hydrogen is known. This is so for chorismic acid (**13**),[19a,b] the related diol (**13a**),[19a,23a] (−)-(1*R*,2*R*)-*trans*-1,2-dihydro-1,2-dihydroxybenzene (**14**),[23b] (−)-(1*R*,2*R*)-*trans*-1,2-dihydro-1,2-dihydroxy-4-chlorobenzene (**14a**),[23b] isochorismic acid (**14b**),[19a] and the related diol (**14c**)[19a] (the chirality (P = right-handed, M = left-handed) is that of the more stable quasi-diequatorial conformer), gliotoxin (**15**),[24] 3β-bromoacetoxy-16α-ethyl-



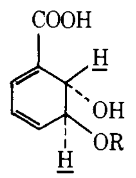
13, R = CCH_2COOH
$\Delta\epsilon_{270}$ −3.5
P chirality

13a, R = H
$\Delta\epsilon_{270}$ −4.5
P chirality



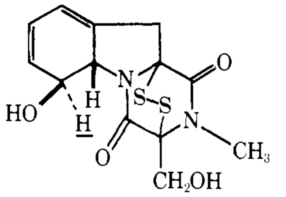
14, R = H
$\Delta\epsilon_{270}$ −5
P chirality

14a, R = Cl
$\Delta\epsilon_{270}$ −5
P chirality

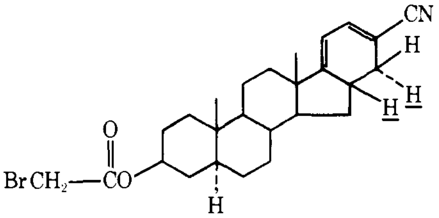


14b, R = CCH_2COOH
$\Delta\epsilon_{270}$ ~8
M chirality

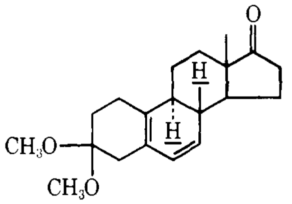
14c, R = H
$\Delta\epsilon_{270}$ ~8
M chirality



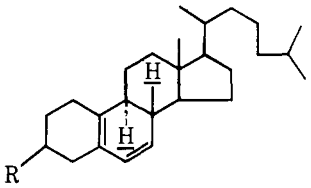
15
$\Delta\epsilon_{270}$ ~10
M chirality



16
$\Delta\epsilon_{297}$ −12.1
P chirality

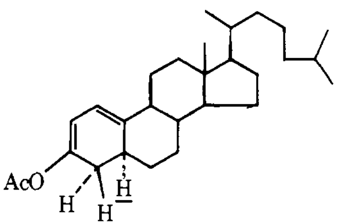


17
$\Delta\epsilon_{262}$ −5.50
P chirality



18, R = OAc
$\Delta\epsilon_{266}$ −5.70
P chirality

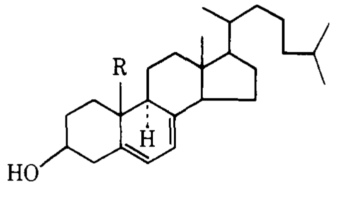
18a, R = H
$\Delta\epsilon_{266}$ −5.22
P chirality



19
$\Delta\epsilon_{297}$ −3.92
P chirality

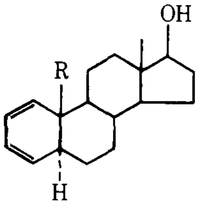
16^2-cyano-16^2-21-cyclo-5α-pregna-17,21-diene (**16**),[27] 3,3-dimethoxy-19-norandrosta-5(10),6-diene (**17**),[32] 3-acetoxy-19-norcholesta-5(10),6-diene (**18**)[34] and its 3-deoxy derivative (**18a**),[34] and 3-acetoxycholesta-1(10),3-diene (**19**).[37]

A second type of exception again conforms to the structural feature of two axial allylic hydrogens, but analogues in which a methyl group occurs in these positions obey the diene chirality rule. The trend observed is that the presence of two axial allylic methyl groups is associated with a strong positive or negative $\Delta\epsilon$. Replacement of one methyl by hydrogen reduces the intensity. Replacement of both methyl groups leads to an inversion in sign of $\Delta\epsilon$. This has been observed for trans diaxial allylic substituents; e.g., **1** vs. **2** and **20** vs. **21** follow this pattern. For example, 3-hydroxy-19-norcholesta-5,7-diene (**20**),[38] 273 nm, $\Delta\epsilon$ +5.6, M chirality, is considered an exception while 3β-hydroxycholesta-5,7-diene (**21**),[37] 270 nm, $\Delta\epsilon$ −11.4, M chirality, was considered in agreement with prediction. Similarly, 5α-estra-1,3-dien-17β-ol (**1**)[6] vs. 5α-androstane-1,3-dien-17β-ol (**2**)[6] show a sign inversion for the replacement of methyl by hydrogen. In the case of the A–B cis steroids (**22**)[39] compared with **23** a drop from $\Delta\epsilon$ 27.6 to 6.5[40] is observed by replacement of the axial allylic C_5 methyl group by hydrogen.[41]



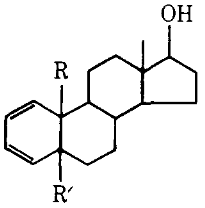
20, R = H
$\Delta\epsilon_{270}$ +5.6

21, R = CH_3
$\Delta\epsilon_{270}$ −11.4
M chirality



1, R = H
$\Delta\epsilon_{260}$ + 3.8

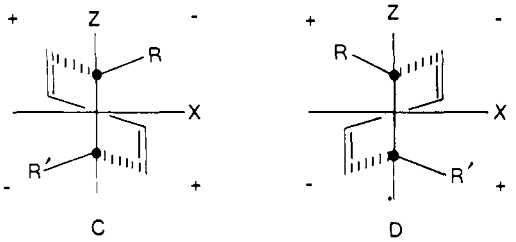
2, R = CH_3
$\Delta\epsilon_{260}$ −2.7
M chirality



22, R = R′ = CH_3
$\Delta\epsilon_{264}$ +27.6

23, R = CH_3; R′ = H
$\Delta\epsilon_{260}$ 6.5
P chirality

All the examples are explicable in terms of quadrant diagrams C or D.

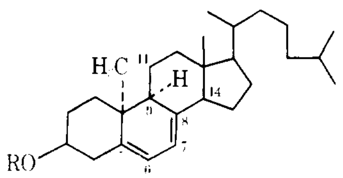


Thus, C describes a diene of P chirality and R, R′ refer to the axial allylic substituents. Compounds **13, 13a, 14, 14a, 16, 17, 18, 18c, 19, 22,** and **23** are accommodated by quadrant diagram C. Assuming that axial allylic hydrogen makes a dominant chiroptical contribution in cisoid homoannular dienes and since the axial allylic hydrogen atoms (R = R′ = H in C) fall into negative quadrants, their sign dominates the chiroptical effect. Compounds **1, 2, 3, 14b, 14c, 15, 20,** and **21** are explicable in terms of quadrant diagram D. Here the axial allylic hydrogen atoms (R = R′ = H in D) fall into positive quadrants and control the sign of the CD. Quadrant diagram D accommodates **20** in which the C(10) methyl and the C(5) hydrogen (R = CH_3; R′ = H) fall into positive quadrants. In

1 the C(10) methyl and C(9) hydrogen fall into positive quadrants (R = CH_3; R′ = H).

This essentially qualitative analysis satisfactorily explains the observed sign of the chiroptical effect for compounds **13–23** and **1–3**.

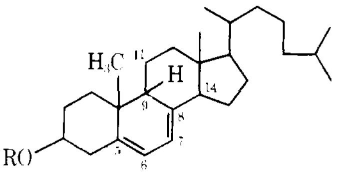
Rationalization of the sign and magnitude of $\Delta\epsilon$ for pyrocalciferol (**24**) and isopyrocalciferol (**25**) offers a strict test for any rule relating $\Delta\epsilon$ to stereochemistry. Indeed, in the original paper on the diene chirality rule,[2a] "an irreconcilable contradiction" was noted in that **24** and **25** are antipodal to each other at the allylic centers and both show strong positive Cotton effects. Both possess right-handed dienes. However, lumisterol (**26**) and ergosterol (**27**) are also antipodal at both C(9) and C(10) and have opposite Cotton effects in agreement with diene chirality. This led to the conclusion that the skew sense of the diene controlled the sign of the long-wavelength rotatory dispersion. Recently X-ray data have become available for **24**,[43] **25**,[44] **26**,[45] and **27**.[46]



24

R = 3,5-DNB

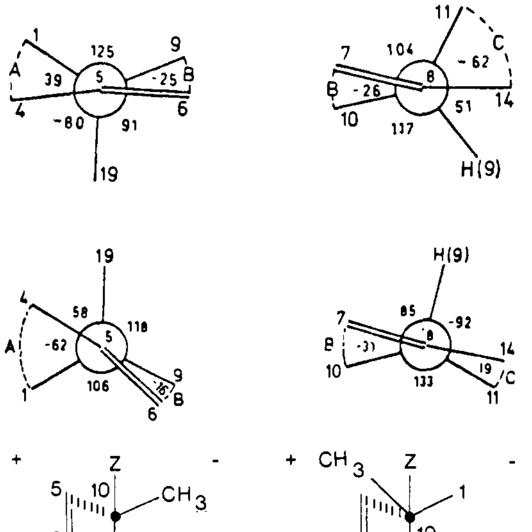
ω C(6)-C(7) = 9.5°
ω C(5)-C(6) = 2.7°
ω C(7)-C(8) = 3.5°

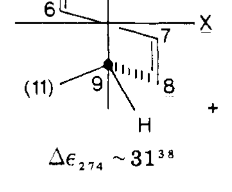


25

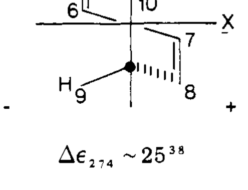
R = 3,5-DNB

ω C(6)-C(7) = 7.8°
ω C(5)-C(6) = −3.8°
ω C(7)-C(8) = 10.7°



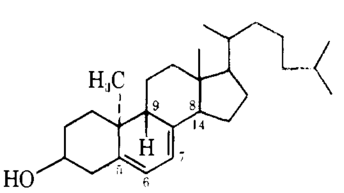


$\Delta\epsilon_{274} \sim 31^{38}$



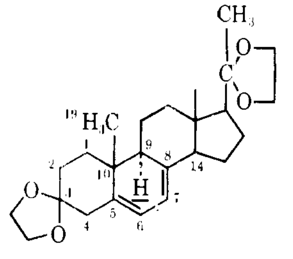
$\Delta\epsilon_{274} \sim 25^{38}$

First, we consider lumisterol (**26**) and the ergosterol analogue 3,20-bis(ethylenedioxy)pregna-5,7-diene (**27**). Except for the unexpectedly large olefinic torsional angle ω C(5)-C(6) = −6°, these two compounds have relatively ideal geometry for quadrant analysis. Assuming that the rotatory contribution of a diene of twist angle (ω C(6)-C(7)) ~ 19° is δ_{diene} 40,[48] δ CH_3 5, and δH = 23, then the $\Delta\epsilon$ for lumisterol (**26**) would be $\Delta\epsilon = 40 - [23 \sin^2 80° + 5 \sin^2 91°] = 15$ (observed $\Delta\epsilon$ = 14)[38] and that for ergosterol would be $\Delta\epsilon = -40 + [23 \sin^2 90° + 5 \sin^2 87°] = -12$ (observed $\Delta\epsilon$ = −11.4).[38] These empirical values also apply to 19-norcholesta-5,7-diene (**20**): $\Delta\epsilon = -40 + [23 \sin^2 90° + 23 \sin^2 90°] = +6$ (observed $\Delta\epsilon$ = 5.6).[38] Now considering **24** and **25** the situation is more complicated because of unusual torsional angles at the allylic carbon atoms. In constructing a quadrant diagram for **24** the situation at C(10) is normal (C(19)-C(5)-C(6) = 91°) but at C(9) the torsional angles are such that C(11) has ω 104° but the C(9) hydrogen atoms fall in the *same quadrant* as the C(7)-C(8) double bond with a torsional angle of 143° with respect to the adjacent double bond and by symmetry its contribution should have the same sign as the diene. The expression for $\Delta\epsilon$ for **24** is



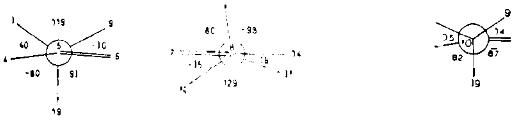
26

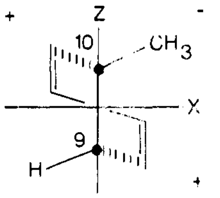
ω C(6)-C(7) = +15°
ω C(5)-C(6) = −0.4°
ω C(7)-C(8) = +4.0°



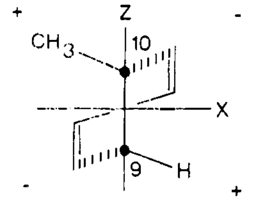
27

ω C(6)-C(7) = −11°
ω C(5)-C(6) = −6°
ω C(7)-C(8) = −2°





$\Delta\epsilon_{270} = 14^{38}$



$\Delta\epsilon_{270} = -11.4^{38}$

$$\Delta\epsilon = 40 + [23 \sin^2 143° - (5 \sin^2 90° + 5 \sin^2 104°)] = 38$$
$$(\text{observed } \Delta\epsilon = 31)^{38}$$

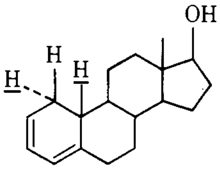
A similar situation exists for **25** in which the C(19) and C(1)-C(10) bonds fall into the same quadrant as the C(5)-C(6) double bond.

$$\Delta\epsilon = 40 + [5 \sin^2 134° - (23 \sin^2 85° + 5 \sin^2 106°)] = 15$$
$$(\text{observed } \Delta\epsilon = 25)^{38}$$

This is reasonably acceptable agreement in terms of assumptions about the value of δ_{diene}.

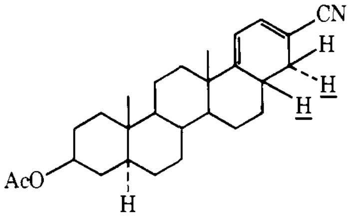
Results from trienes fit the quadrant rule very satisfactorily. Cholesta-2,4,6-triene (**28**), $\Delta\epsilon_{304}$ +4.2, and 3-acetoxycholesta-3,5,7-triene (**29**), $\Delta\epsilon_{315}$ −16.2,[49] may be inscribed into quadrant diagrams in a normal way, that is, the olefinic units fall into + or − sectors and the axial allylic groups make the expected quadrant contributions. In the case of 9(11)-dehydroergosterol acetate (**30**), $\Delta\epsilon_{323}$ +6.9, the helical sense of the diene is still negative but the p orbital at C(9) occupies a positive sector of the quadrant (the C(10) methyl is in the other positive sector). Although the sign of $\Delta\epsilon$ could not be predicted in advance, the quadrant treatment emphasizes the relationship of one quadrant having a p orbital in it rather than axial allylic substituents as in **30.**

Exceptions to the diene quadrant rule exist. For 2,4-estradien-17β-ol (**31**), which possesses a flexible dienic system, Lane and Allinger calculated by a field-force method that **31** should exist in a 92:8 ratio of extended:folded conformation with a calculated diene dihedral angle of +7.9°.[51] The observed $\Delta\epsilon$ of +2.1 does not agree with the prediction of a negative CD for this compound. Compound **32** also is an exception.



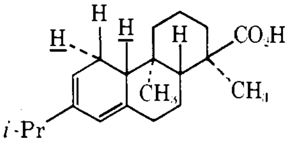
31

265 nm $\Delta\epsilon_{265} = 2.1^{37}$



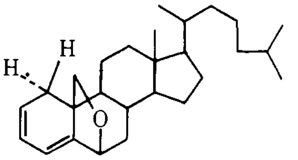
32

304 nm $\Delta\epsilon_{304} = 6.2^{29}$



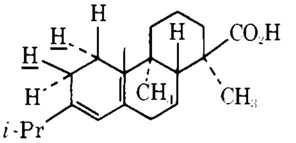
33

$\Delta\epsilon_{270} = -12.2$



34

$\Delta\epsilon_{270} = -12.6^{37}$



35

$\Delta\epsilon_{260} = 1.07^{37}$

Palustric acid (**35**) possesses a positive CD 260° (+1.07). The low-temperature dominant P-diene conformation[6] ought to show a negative CD according to the diene quadrant rule. Dreiding models indicate a considerable degree of conformational flexibility for this diene. Lacking more definitive structural information, palustric acid must be regarded tentatively as an exception.

Dienes **31** and **32** bear a structural resemblance to levopimaric acid (**33**), which adopts a folded conformation (M chirality, twist angle −9.1 and −11.8°), as demonstrated by X-ray diffraction.[50]

In the case of **34**, the 6β-oxide bridge twists the A-ring diene into a left-handed helix. Because of uncertainties in the conformational structures of **31** and **32** it is difficult to apply the diene quadrant rule with confidence. Interestingly, levopimaric acid in either M or P chiral forms obeys the diene quadrant rule.

In conclusion, the diene quadrant rule serves to explain on an empirical basis the exceptions to the original diene chirality rule. Particularly, the phenomenon of a sign inversion encountered in a series of related compounds with the same diene twist angle may be understood. The relative magnitude of rotatory contribution of components of the optical chromophore must be regarded as semiquantitative, but as new structures of known geometry become available the quantitative aspect of the diene quadrant rule should improve.

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(1) (a) University of Illinois at Chicago Circle; (b) National Institutes of Health; (c) The School of Pharmacy.

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(35) A related steroidal diene which is also an exception to the diene chirality rule is 3α,17β-dihydroxyestra-5(10)-6-diene.[33,36]

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(41) It should be noted that in the cis-AB series of 1,3-cholestadienes a very large difference exists in $\Delta\epsilon$ between **22** ($\Delta\epsilon$ = 27.6) and the $C_{5\alpha}$-methyl-$C_{10\alpha a}$-methyl analogue ($\Delta\epsilon$ 14.7). Both have P chirality; however, inspection of Dreiding models reveals a smaller diene twist angle for the latter compound. Without precise structural parameters from X-ray diffraction, further comment on this point appears unwarranted.

(42) Since the torsional angles about the double bonds in **26** and **27** have the same signs as ω C(6)–C(7) they may be added; accordingly the diene twist angle of **26** is 19° and 19° in **27.**

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(48) The assumed value is large compared to values used in calculations.[3a,4] Since, according to our theory, a measured $\Delta\epsilon$ must always be smaller than the contribution of the diene alone and considering $\Delta\epsilon$ can be as large as 31 with values around 25 being common, we believe $\delta_{\text{diene}} \sim 40$ is reasonable.

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Tunneling Corrections to Unimolecular Rate Constants, with Application to Formaldehyde

William H. Miller*

Contribution from the Department of Chemistry, and Materials and Molecular Research Division, Lawrence Berkeley Laboratory, University of California, Berkeley, California 94720. *Received January 22, 1979*

Abstract: Tunneling corrections to the rate constant for unimolecular reactions in an isolated molecule are treated within the standard transition state (i.e., RRKM) theory of such processes. The microcanonical distribution relevant to the unimolecular case causes tunneling effects to enter in a somewhat more complicated fashion than in the analogous transition-state theory for thermally averaged bimolecular rate constants; e.g., even within the separable approximation they do not enter as simply a multiplicative correction factor. Application of the theoretical expressions to some unimolecular processes ($H_2CO \rightarrow H_2 + CO$, *trans*-HCOH → H_2CO) of interest in the collisionless photochemistry of formaldehyde indicates that tunneling effects are quite significant for rates of 10^9 s^{-1} or slower. Isotope effects are also considered and seen to be quite interesting.

Much has been written over the years about tunneling corrections to transition-state theory[1] for thermal rate constants of bimolecular reactions, but there has been little discussion about the effect of tunneling in the analogous transition state (i.e., RRKM) theory[2] of *unimolecular* reactions. The purpose of this paper is to consider such effects and to illustrate them by application to some processes of current interest in the photochemistry of formaldehyde.

Brief Summary of the Standard Transition State (i.e., RRKM) Theory for Unimolecular Processes

To simplify the presentation, rotational degrees of freedom will be ignored here; the Appendix shows how the formulas are modified to take proper account of total angular momentum conservation and other aspects of the rotational degrees of freedom. With this proviso, the standard expression[2] for the unimolecular rate constant (units s^{-1}) of an isolated molecule with total energy E is

$$k(E) = \frac{N(E)}{2\pi\hbar N_0'(E)} \tag{1}$$

where $N(E)$ and $N_0(E)$ are the integral densities of states for the transition state and for the reactant molecule, respectively. Specifically

$$N(E) = \sum_{\mathbf{n}} h(E - \epsilon_{\mathbf{n}}^{\ddagger}) \tag{2a}$$

$$N_0(E) = \sum_{\mathbf{n}} h(E - \epsilon_{\mathbf{n}}) \tag{2b}$$

where $h(x)$ is the usual step-function

$$h(x) = \begin{cases} 0, & x < 0 \\ 1, & x > 0 \end{cases}$$

and $\epsilon_{\mathbf{n}}^{\ddagger}$ and $\epsilon_{\mathbf{n}}$ are the vibrational energy levels of the transition state and the reactant molecule. In practice the vibrational energy levels are almost always assumed to be given by a separable harmonic oscillator approximation, so that

$$\epsilon_{\mathbf{n}} = \sum_{i=1}^{s} \hbar\omega_i \left(n_i + \frac{1}{2}\right) \tag{3a}$$

$$\epsilon_{\mathbf{n}}^{\ddagger} = V_0 + \sum_{i=1}^{s-1} \hbar\omega_i^{\ddagger} \left(n_i + \frac{1}{2}\right) \tag{3b}$$

where s is the number of vibrational degrees of freedom of the stable molecule, $\{\omega_i\}$ and $\{\omega_i^{\ddagger}\}$ are the normal mode frequencies of the reactant molecule and transition state, and V_0 is the "bare" barrier height, i.e., the energy of the saddle point of the potential energy surface (i.e., the transition state) relative to the minimum of the potential energy surface which corresponds to the reactant molecule. The total energy E is also defined relative to the minimum of the potential-energy surface.

Because of the large sums involved in computing the densities of states, it is customary in practice to approximate them by closed-form expressions. The simplest such approximation is the classical expression[2] which gives

$$N_0(E) = \frac{E^s}{s! \prod_{i=1}^{s} (\hbar\omega_i)} \tag{4a}$$

$$N(E) = \frac{(E - V_0)^{s-1}}{(s-1)! \prod_{i=1}^{s-1} (\hbar\omega_i^{\ddagger})} \tag{4b}$$

With these approximations eq 1 gives the simple classical rate expression[2]

$$k(E) = A\left(\frac{E - V_0}{E}\right)^{s-1} \tag{5a}$$

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* Camille and Henry Dreyfus Teacher Scholar.

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