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OPTICAL ACTIVITY OF NON-PLANAR CONJUGATED DIENES—II

TRANSOID DIENES

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Abstract—Earlier work[1] has demonstrated that the sign of the Cotton effect associated with the longest wavelength electronic transition of a non-planar *cisoid* diene is determined by the helical sense of the diene system. The theoretical treatment has now been extended to non-planar *transoid* dienes and experimentally verified by determining the sign of the Cotton effect associated with a transoid diene (3-acetoxy-$\Delta^{8,14}$-cholestadiene) of unequivocal absolute configuration and skew sense. The optical rotatory dispersion of seven other transoid dienes has been determined and in all cases but one the sign of the measured Cotton effect agrees with the prediction.

A non-planar conjugated diene located in an asymmetric molecule is now known[1] to constitute by itself an element of dissymmetry such that its influence upon optical activity in the presently experimentally accessible spectral range may be about an order of magnitude or more greater than that of an adjacent asymmetric carbon atom.[2] Furthermore, the sign of the Cotton effect so produced depends upon the skew sense of the diene. In the case of the *cisoid* dienes, a test compound, (+)-*trans*-9-methyl-1,4,9,10-tetrahydronaphthalene, of unequivocal stereochemistry and high conformational stability was synthesized[3] and used to verify the prediction[1] that a *cisoid* diene chromophore twisted in the sense of a right-handed helix produces a strong positive Cotton effect, associated with the absorption band of lowest frequency (260–280 mμ in 1,3-cyclohexadienes).

The same theoretical considerations can now be extended to *transoid* conjugated dienes. In this case, the following rule results: if the diene is oriented in such a way that its carbon atoms 1, 2 and 3 define a plane in a right-handed coordinate system, with carbons 2 and 3 on the Y axis and carbon 1 in the negative X direction (Fig. 1), the sign of the Cotton effect associated with the UV absorption of lowest frequency is determined by the position of carbon 4 on the Z axis; it will be positive or negative, respectively, if the coordinate of C4 is positive or negative.

For convenience in use with models, the rule can be restated in the following way: if the model of the diene is held in such a way that its central single bond and the double bond to its left define a horizontal plane, the double bond pointing *away* from the observer, the sign of the Cotton effect will be positive or negative if the double bond on the right, pointing *towards* the observer, extends upwards or downwards, respectively.

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[1] A. Moscowitz, E. Charney, U. Weiss and H. Ziffer, *J. Amer. Chem. Soc.* **83**, 4661 (1961).

[2] H. Ziffer, E. Charney and U. Weiss, *J. Amer. Chem. Soc.* **84**, 2961 (1962).

[3] H. Ziffer and U. Weiss, *J. Org. Chem.* **27**, 2694 (1962).

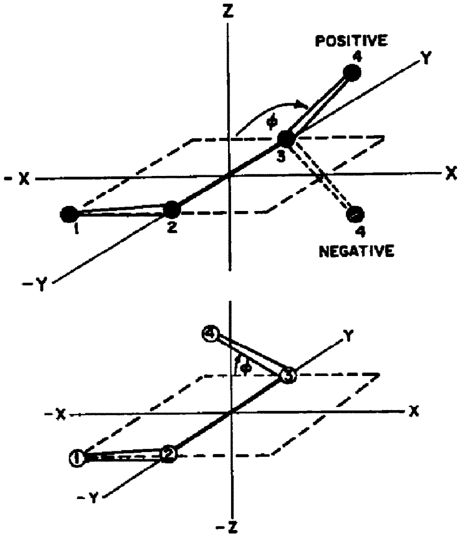

FIG. 1

The extension of the rule arises simply from the following considerations: it has been shown that the rotational contribution at a frequency ν of a particular electronic transition, ν_0, may be written[4]

$$[\alpha]_{oa} = K \frac{\nu^2}{\nu_0^{\,2} - \nu^2} R_{oa} \tag{1}$$

where the subscripts oa refer in this case to the longest wavelength singlet diene absorption band $^1B \leftarrow {}^1A$ (in this designation, the transition in *trans*-butadiene is $^1B_u \leftarrow {}^1A_g$ and in *cis* $^1B_1 \leftarrow {}^1A_1$). R_{oa} is the rotational strength associated with this band, and is given as the scalar product of the electric dipole transition moment, $\boldsymbol{\mu}_{oa}$, and the magnetic dipole transition moment, $\mathbf{m}_{oa}$,

$$R_{oa} = \boldsymbol{\mu}_{oa} \cdot \mathbf{m}_{oa} \tag{2}$$

($\mathbf{m}_{oa}$ is perpendicular to $\boldsymbol{\mu}_{oa}$ for a strictly planar diene, making R_{oa} and $[\alpha]_{oa} = 0$). It can be shown[5] that for the long wavelength, $^1B \leftarrow {}^1A$, transition

$$\boldsymbol{\mu}_{oa} = -4ab(\mathbf{j} \cos Y_{34} + \mathbf{k} \cos Z_{34})\langle\nabla_{34}\rangle + 2a^2\mathbf{j}\langle\nabla_{32}\rangle \tag{3}$$

and

$$\mathbf{m}_{oa} = -4ab[\mathbf{j}(Z_{34} \cos X_{34} - \bar{X}_{34} \cos Z_{34}) + \mathbf{k}(\bar{X}_{34} \cos Y_{34} - \bar{Y}_{34} \cos X_{34})]\langle\nabla_{34}\rangle \tag{4}$$

where a, b, $\langle\nabla_{34}\rangle$ and $\langle\nabla_{32}\rangle$ are all constants or parameters independent in sign of the configuration of the diene system. **i**, **j**, **k** are unit vectors along the x, y, z coordinates so that $\mathbf{i} \cdot \mathbf{j} = \mathbf{i} \cdot \mathbf{k} = \mathbf{j} \cdot \mathbf{k} = 0$ and $\mathbf{i} \cdot \mathbf{i} = \mathbf{j} \cdot \mathbf{j} = \mathbf{k} \cdot \mathbf{k} = 1$. The coordinates of the midpoints of the C_3–C_4 bond are given by $\bar{X}_{34}$, $\bar{Y}_{34}$, Z_{34} and the projection cosines of

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[4] See for example, H. Eyring, J. Walter and G. E. Kimball, *Quantum Chemistry* p. 345. J. Wiley, New York (1948).

[5] E. Charney, *Tetrahedron* **21**, 3127 (1965).

this bond in the direction of the transition moments are cos X_{34}, cos Y_{34}, cos Z_{34}. Φ is half the angle θ (Fig. 1) which the bond between carbons 3 and 4 makes with the plane of carbons 1, 2, and 3; thus rotation of θ by 180° or of Φ by 90° (see footnote*) transforms a *cisoid* diene into a *transoid* diene. θ is therefore located in a zone on either side of 0° for *cisoid* dienes and on either side of 180° for *transoid* dienes. Between $\theta = 0°$ and 180° ($\Phi = 0°$ and 90°), also between $\theta = 180°$ and 360°, i.e. in those quadrants in which carbon 4 remains on the same side of the plane formed by carbons 1, 2, and 3, the midpoints and projection cosines do not change sign, but the midpoint $\bar{X}_{34}$, and the cos X_{34} and consequently the factors (Z_{34} cos $X_{34} - \bar{X}_{34}$ cos Z_{34}) and ($\bar{X}_{34}$ cos $Y_{34} - \bar{Y}_{34}$ cos X_{34}), do change sign when carbon 4 crosses this plane.[5] Thus the sign of the electric dipole moment matrix element μ_{0a} is invariant to either the *cisoid* → *transoid* conformational change or the skew sense of the diene, but the magnetic moment matrix element $\mathbf{m}_{0a}$ does change sign when carbon 4 crosses the plane of the other three carbon atoms. Consequently, by Eq. (2), the rotational contribution of the singlet transition of lowest energy is negative or positive depending on the relative orientation of carbon 4 with respect to the plane of carbons 1, 2, and 3. It can then be seen from the figure that a *cisoid* diene having the skew sense of a right-handed helix (positive optical rotation) transforms to a *transoid* one having positive optical rotation when the C_3–C_4 bond remains on the same side of the plane of carbons 1, 2, and 3.

An experimental test of this rule required the investigation of the Cotton effect of a molecule with known absolute configuration and unequivocally defined sense of skewness of its diene system. Dreiding models of 3-acetoxy-$\Delta^{8,14}$-cholestadiene (I) indicate this substance to be suitable; while several conformations of rings C and D are possible, the diene system of all of them shows the sense of skewness that should produce a negative Cotton effect. A gas-chromatographically homogeneous sample of I (m.p. 99–100°) was prepared;[6] its optical rotatory dispersion (Fig. 2) exhibited the predicted negative Cotton effect, thus confirming the "*transoid* diene rule."

The negative rotations,[7] $[\alpha]_D = -23°$ and $-41°$, of two closely related compounds with the same chromophore: $\Delta^{8,14}$-cholestadiene and $\Delta^{8,14}$-cholestadiene-3β-ol, can be interpreted as giving additional support, keeping in mind the limited significance of $[\alpha]_D$ values.

As a further test of the theory, the optical rotatory dispersion of several other conjugated *transoid* dienes was investigated: they were 3,5-cholestadiene (II), 3-methylene-Δ^4-cholestene (III), abietic acid (IV), neoabietic acid (V), 5α-3,11,20-triacetoxy-$\Delta^{7,9}$-pregnadiene (VI), $\Delta^{6,8(14),22}$-ergostatriene-3β-ol acetate (VII), and

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* For reasons of symmetry it was preferable in deriving Eqs (3) and (4) to fix the skewed diene in the coordinate system symmetrically about the *XY* plane with a skew angle of 2Φ; that is, the orientation of the diene in the coordinate system is such as to place the bond between C_1 and C_2 at the angle $\theta/2$ below the plane and the bond between C_3 and C_4 at the same angle above the plane. Thus rotation of θ by 90° from the planar *cisoid* conformation transforms the diene to the planar *transoid* configuration. The projection cosines, cos X_{34}, cos Y_{34} and cos Z_{34} as well as the midpoints of the C_3–C_4 bond consequently do not change sign in making the cisoid → transoid transformation by rotating C_1 and C_4 about the y axis. For greater convenience in visualization, however, Fig. 1 shows the diene with carbon 1 fixed *in* the *XY* plane.

[6] L. F. Fieser and G. Ourisson, *J. Amer. Chem. Soc.* **75**, 4404 (1953).

[7] L. F. Fieser and M. Fieser, *The Steroids*, pp. 119, 265. Reinhold, New York (1959).

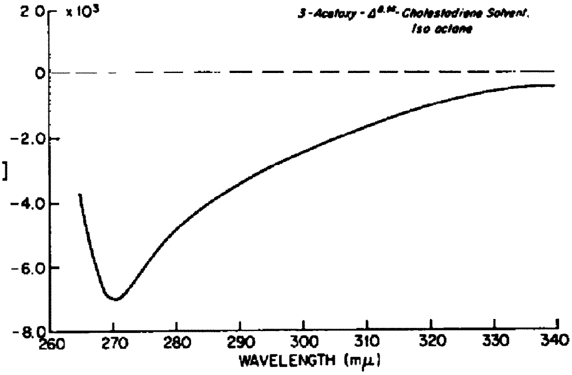
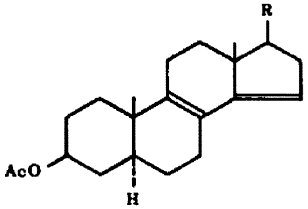
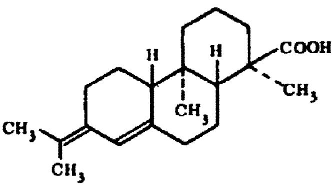
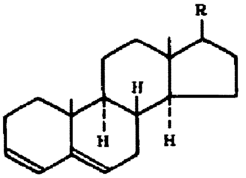
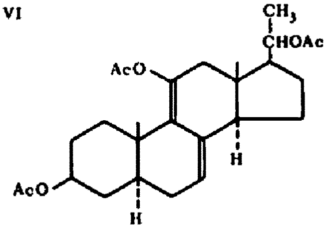
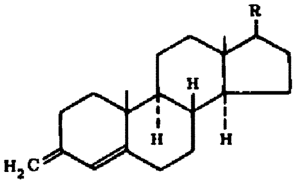
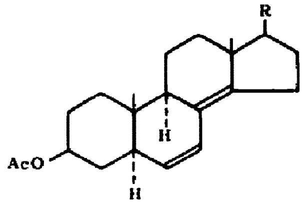
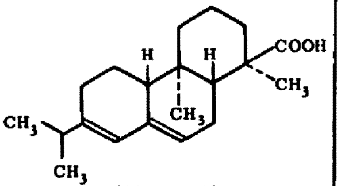
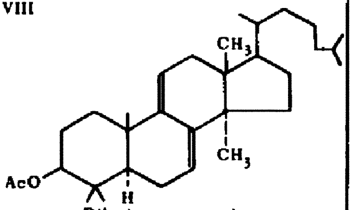


Fig. 2

dihydroagnosteryl acetate (VIII). Dreiding models of compounds III–V can exist with the conjugated system in more than one conformation, sometimes of opposite skewness; in several conformations the diene is almost planar. As a consequence, the sign of the Cotton effect of compounds III–V must be predicted from the skew sense of their diene in that conformation which is the most probable one on general principles (e.g. minimum number of non-bonded interactions, and of boat conformations). A model of III indicates that a change in the conformation of ring A can alter the skew sense of the diene system from positive to negative. However, the negative conformer appears to have additional repulsive interactions between the equatorial hydrogens at carbons 1 and 11, and on this basis the Cotton effect is predicted to be positive. IV can exist in two conformations in which the ring bearing the isopropyl group is either a semi-boat or a semi-chair ; in the first of these, the diene is planar, in the other skewed in the negative sense. On this somewhat tenuous basis, the Cotton effect, if present, is predicted to be negative. In V, two conformers of opposite sense of skew can be obtained from the model. The one in which the ring bearing the isopropyl group more nearly resembles a chair than a boat gives a positive skew sense to the diene, and the prediction is made on this basis. In the case of compounds II and VI, as in I, there are no ambiguities because VI, like I, appears to have only one skew sence, from which a positive Cotton effect is predicted; II can exist in several conformations, but these all show either a negatively skewed, or an almost planar diene. The same can be said for VIII, except that the conformations lead to a positively skewed or almost planar diene. As Table 1 shows, the predictions in all of these cases agree with the observations, thus providing additional evidence for the correctness of the rule.

In our investigation of the optical activity of *transoid* dienes, we have found one compound, $\Delta^{6,8(14),22}$-ergostatriene-3β-ol-acetate (VII), which exhibits a Cotton effect in the 260 mμ region *opposite* in sign to that predicted from Dreiding models on the basis of the chemical evidence for its structure. While we have no reason to suspect the validity of the chemical evidence, the excellent agreement between our theoretical treatment in both the *cisoid* and *transoid* cases with the bulk of the experimental evidence points either to an error in the chemically determined configuration or to the very real possibility that, in fact, inter-atomic repulsions in this molecule (in which the skew angle is small) force the conformation to take the opposite sense of skew

TABLE I

Compound	Sign of Cotton Effect		Compound	Sign of Cotton Effect	
	Pred.	Obs		Pred.	Obs
I  $\Delta^{8,14}$-cholestadiene-3-acetate	−	−	V  Neoabietic acid	+	+
II  3,5-cholestadiene	−	−	VI  5α-3,11,20-triacetoxy-$\Delta^{7,9}$-pregnadiene	+	+
III  3-methylene-Δ^{4}-cholestene	+	+	VII  $\Delta^{6,8(14),22}$ergostatriene-3β-ol-acetate	+	−
IV  Abietic acid	−	−	VIII  Dihydroagnosteryl acetate	+	+

from that exhibited by the Dreiding model. We do not rule out the possibility that our theoretical treatment is insufficiently complete to account for some anomalous behaviour, but additional theoretical and experimental considerations[5] argue in favor of the former possibilities.

The *transoid* diene rule can be applied to studies of configurational and conformational problems in the same way in which the *cisoid* diene rule has been. As is already apparent from Table I, in dienic compounds of *known configuration, conformational* behaviour can be deduced from rotatory dispersion. More detailed information can be obtained by investigating the rotation at different temperatures.

This has been done for the *cisoid* dienes, levopimaric acid,[8] 2,4-cholestadiene,[2] and (−)-α-phellandrene.[2] To the best of our knowledge, no other experimental approach to the study of the conformations of this class of compounds has been available thus far.

EXPERIMENTAL

Compounds II,[9] III[10] and VII[11] were prepared by known methods; III was kindly provided by A. W. Burgstahler, U. of Kansas, IV and V were samples supplied by R. V. Lawrence, Naval Stores Research Laboratory, Olustee, Florida; VI was a gift from E. R. H. Jones of Oxford University; VIII from J. Chanley, Mt. Sinai Hospital, New York. The optical rotatory dispersions were measured with a Rudolph recording spectropolarimeter at a spectral band width of 5 mμ. Compound VIII was measured with a Bendix Recording Spectropolarimeter. The observed [Φ] values are:

II	[Φ] 256 mμ = −7,400	C = 0·02 g/100 ml	Solvent: C_2H_5OH
III	[Φ] 256 mμ = 42,000	C = 0·0045 g/100 ml	CH_3CN
IV	[Φ] 260 mμ = −11,500	C = 0·0125 g/100 ml	C_2H_5OH
V	[Φ] 268 mμ = 49,000 (ave.)	C = 0·0037, 0·0018 g/100 ml	C_2H_5OH
VI	[Φ] 260 mμ = 7,200	C = 0·0140 g/100 ml	C_6H_{12}
VII	[Φ] 275 mμ = −8,800	C = 0·040 g/100 ml	iso-octane
VIII	[Φ] 250 mμ = 15,700	C = 0·026 g/100 ml	C_2H_5OH

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[8] U. Weiss, H. Ziffer and E. Charney, *Chem. & Ind.* 1286 (1962).

[9] H. E. Stavely and W. Bergmann, *J. Org. Chem.* **1**, 576 (1936).

[10] F. Sondheimer and R. Mechoulam, *J. Amer. Chem. Soc.* **79**, 5029 (1957).

[11] D. H. R. Barton and T. Bruun, *J. Chem. Soc.* 2728 (1951); G. D. Laubach, E. C. Schreiber, E. J. Agnello and K. J. Brunings, *J. Amer. Chem. Soc.* **78**, 4743 (1956).