CROATICA CHEMICA ACTA CCACAA **62** (2A) 115—128 (1989)

CCA-1846

YU ISSN 0011-1643
UDC 541.653
Original Scientific Paper

On the Optical Activity of Steroidal 5,7-Dienes

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Received October 18, 1988

Circular dichroism (CD) data are reported of a series of 9,10-stereoisomeric steroidal 5,7-dienes. In general the effects in the longest wavelength transition (270—280 nm) are large ($\Delta\varepsilon_{\max}$ 10—30) and consignate with respect to the diene helicity rule. The magnitude of the CD appears to vary markedly with the substituent at C-3 and at C-17, and with solvent. In the case of the 9α,10β-H dienes, variation of solvent and temperature can affect even the sign of the Cotton effect. This is explained from a change of geometry of the diene ring: solvation, substitution and temperature can affect the average geometry of the ring including the values of the angle of twist of the diene (ϕ (6—7)). The relevance of the observed chiroptical data for the theoretical description of the optical activity in the $S_0 \rightarrow S_1$ transition of homoannular cisoid dienes is discussed.

INTRODUCTION

Steroids, apart from being an important class of natural products, often serve as model systems in chemistry for the investigation of reactions, reaction mechanisms and spectroscopic properties. Part of their suitabity as such arises from the fact that the mode of junction of the 6- and 5-membered rings (usually *trans*) renders rigidity to the steroid skeleton — in particular when the rings contain sp^3-hybridized carbon atoms only — leading to well-defined conformations. Furthermore, with steroids optical purity is easily ensured and the absolute configuration is known. Introduction of trigonal carbon atoms in the skeleton introduces some flexibility, and it is of interest, then, to study molecular conformation, not in the least since flexibility is supposed to be related to biological activity.

In this paper we focus on the chiroptical properties of steroidal 5,7-dienes where the configuration at C-9 and C-10 is systematically varied. We also discuss some of the 10-demethyl analogues. The optical activity of conjugated dienes has been considered to arise from the chirality of the chromophore itself (»diene helicity rule«)[1] and from the influence of chirally disposed groups in the environment of the chromophore (*e. g.* »allylic chirality rule«)[2] but the description of the relationship between optical activity and molecular geometry is still evolving. The purpose of the present study is to present data which may be of help to a further study of this relationship for homoannular cisoid dienes.

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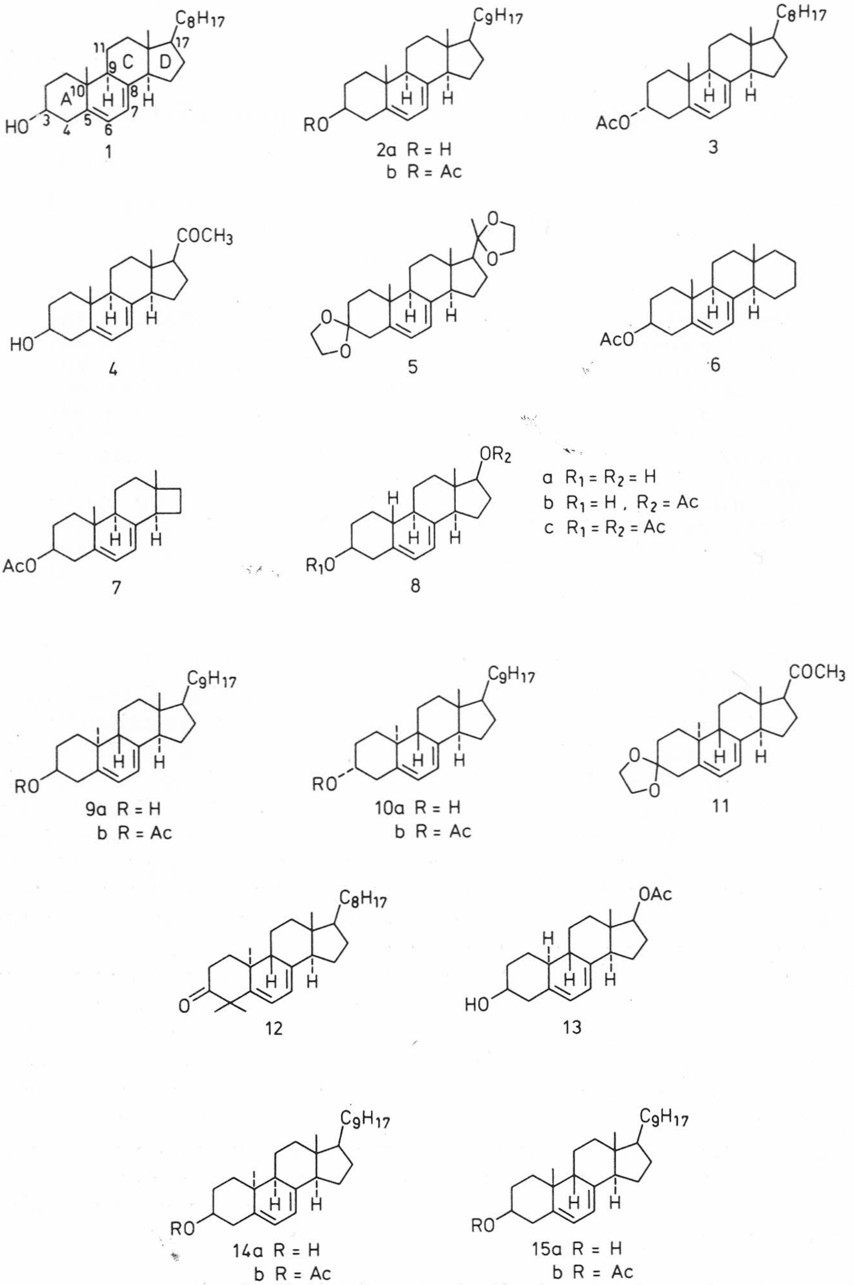
RESULTS

The 9,10-stereoisomeric steroid-5,7-dienes studied are shown in Scheme 1. Some representative CD spectra are pictured in Figure 1a. In Figure 1b the solvent effect on the CD is illustrated for the case of pyrocalciferol *(14a)*.



Scheme 1

TABLE I

CD data of steroidal 5,7-dienes: $\Delta\varepsilon_{max}$ (λ_{max} in nm) (room temperature unless otherwise indicated)

9α, 10β-configuration					*9β, 10α-configuration*				
1	— 18 (280)	— 19 (270)	MIP 1 : 1		*9a*		+ 14.9 (270)	O	
	— 25 (283)	— 21.5 (272)	MIP 1 : 1	a	*9b*		+ 12.9 (270)	M	
2a	— 14.2 (280)	— 15.1 (270)	M				+ 14.8 (269)	O	
	— 16.9 (280)	— 18.0 (269)	O		*10a*		+ 17.4 (270)	M	
2b	— 10.8 (280)	— 11.4 (270)	M				+ 17.8 (270)	O	
	— 13.8 (280)	— 14.6 (270)	O		*10b*		+ 14.9 (270)	M	
3	— 18.7 (281)	— 18.7 (270)	O				+ 15.6 (270)	O	
4	— 14.6 (280)	— 15.9 (270)	O : D 4 : 1	b	*11*	+ 10.6 (285)		O	c
5	— 9.9 (281)	— 9.9 (271)	M		*12*	+ 7.6 (282)	— 1.6 (314)	O	c
6	— 11.5 (280)	— 12.4 (270)	M		*13*		+ 13.2 (269)	MIP 1 : 1	d
7	— 9.6 (280)	— 10.4 (270)	M						
8a	+ 5.7 (283)	+ 5.0 (272)	M		*9α, 10α-configuration*				
8b	+ 4.7 (283)	+ 3.9 (273)	M		*14a*	+ 30.0 (284)	+ 31.0 (274)	M	
	+ 2.3 (283)	+ 1.4 (273)	P			+ 22.8 (283)	+ 23.0 (274)	O	
8c	+ 8.8 (282)	+ 8.1 (271)	M		*14b*	+ 27.6 (284)	+ 27.6 (274)	M	
	+ 5.5 (283)	+ 4.6 (272)	P			+ 28.8 (284)	+ 29.4 (274)	O	
9β, 10β-configuration									
15a	+ 24.5 (284)	+ 25.1 (273)	M		*15b*	+ 28.2 (282)	+ 29.4 (273)	M	
	+ 22.9 (284)	+ 24.7 (274)	O			+ 25.8 (282)	+ 27.2 (272)	O	

M: methanol; O: isooctane; P: *n*-pentane; MIP: methylcyclohexane/isopentane; D: dioxane.
a: at 110 K; b: additional extremum + 3.57 (303), due to the carbonyl n—π* transition; c: Cotton effect of the carbonyl n—π* transition is interfering; d: calculated with the assumption that the molar absorption coefficient at λ_{max} (272 nm) equals that of lumisterol$_2$ *9a*.

Numerical data are collected in Table I. They are arranged according to skeletal configuration. In the table only the principal CD maxima are listed.[3,4]

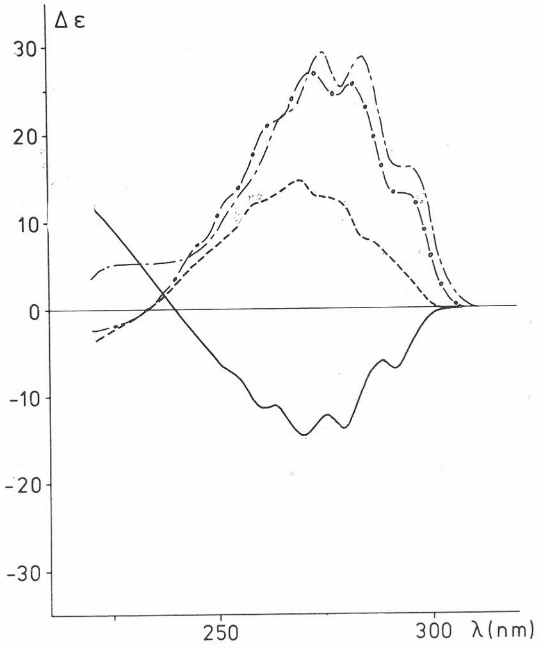
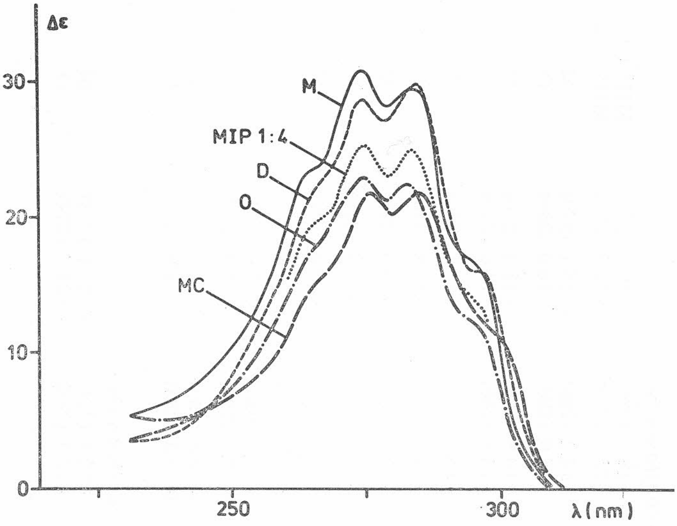


Figure 1. a) CD curves of ergosteryl acetate *2b* (————) and its 9,10-isomers *9b* (- - - - -), *14b* (— — —) and *15b* (— · —). Solvent: isooctane.



b) CD spectra of pyrocalciferol (*9a*) in various solvents at room temperature. M = methanol, D = dioxane, O = isooctane, MC = methylene chloride, MIP = methylcyclohexane/isopentane 1 : 4 (v/v).

From the data it appears that the choice of solvent has a marked influence on CD intensity. The latter is also sensitive to the nature (*e. g.* OH or OAc) and the orientation of the substituent at C-3, and it is affected by the substituent at C-17 and the size of ring D. One further observes that 5,7-dienes with »natural« (9α,10β) and those with 9β,10α-configuration display Cotton effects of about equal intensity but opposite sign; those of the 9α,10α- and 9β,10β-dienes are larger by a factor of 1.5 to 2 and both are positive. Replacement of the allylic hydrogen at C-10 by a methyl group does not influence the Cotton effect in the 9β,10α-series (*cf. 13* and *9a*); however, the same replacement in the 9α,10β structure results in reversal of sign (*1* and *8a,b,c*). Moreover, the 19-nor-9α,10β-5,7-dienes *8* appear to exhibit the largest (relative) change of CD with solvent (see *e. g.* entry *8b* of Table I). This, and the fact that 5,7-estradiene-3β,17β-diol *(8a)* has been cited as an exception to the diene helicity rule,[2] led us to extend the study into the dependence of CD of these compounds on solvent and temperature; Figures 2 and 3. It turns out that the choice of solvent markedly and similarly affects the CD amplitudes of *8b* and *8c*. The CD amplitude decreases in the order: methanol, diethyl ether = = ethanol = acetonitrile, tetrahydrofuran = *n*-pentane. Due to poor solubility of *8a* its CD was only measured in THF ($\Delta\varepsilon_{\max}$ + 2.3, 285 nm) and in methanol

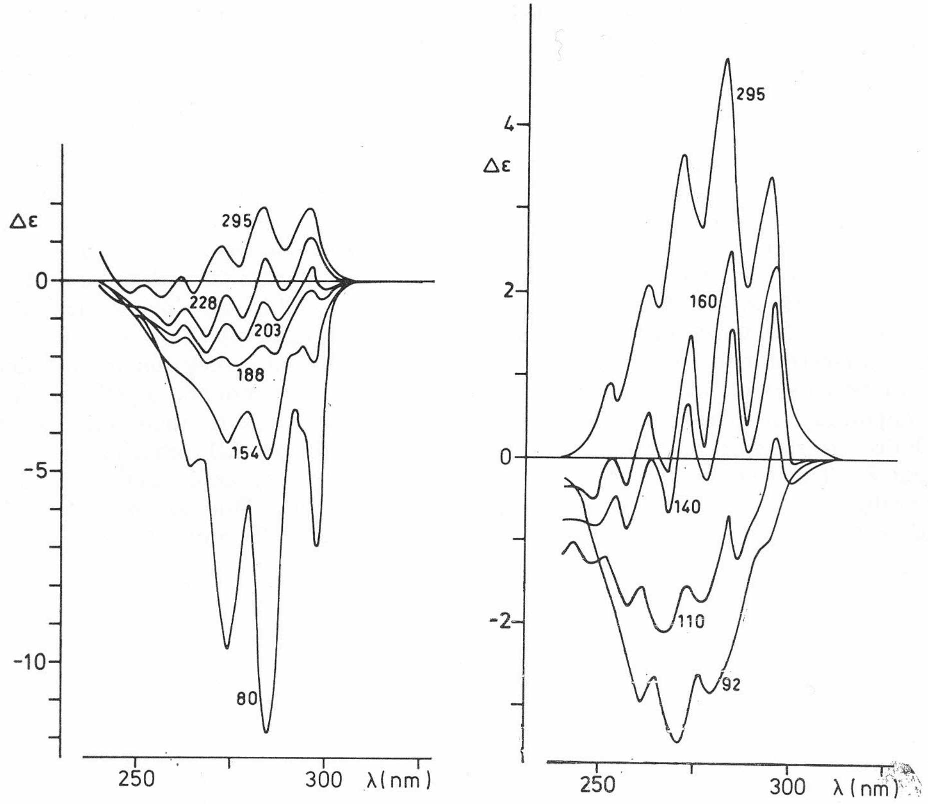


Figure 3. CD spectra of a) *8b* and b) *8c* in MIP at various temperatures. Temperature (K) is indicated in the figure. MIP = methylcyclohexane/isopentane 1 : 3 (v/v).

(see Table I). As evidenced from Figure 3 lowering the temperature affects the CD even more drastically. With *8b* the small positive Cotton effect at 295 K changes into a large negative one at 80 K; with *8c* the CD at room temperature is positive and of moderate intensity and — here too — sign inversion occurs upon cooling towards 92 K. This behaviour of the 19-nor-dienes *8* contrasts with that of the 10-methyl compound 7-dehydrocholesterol *1*: in MIP the integrated CD increases by only 13% upon cooling towards 110 K (the CD amplitude by 30% because of sharpening of the spectrum).

We also measured the CD of microcrystalline samples dispersed in KBr discs. In the case of *1* the CD in the solid phase is of the same sign as that in solution, but in *8a* the sign appears to be inverted. These experiments confirm the results reported by Dezentje.[5] We found that microcrystalline *8b* and *8c* also exhibit negative Cotton effects.

DISCUSSION

To facilitate discussion we summarize in Table II the maximum variation in the magnitude of the CD due to substitution and solvent for the various classes of 9,10-stereoisomers (*cf.* Table I). From the table it appears that the effect of solvent and that of substituent on CD is of the same order of magnitude.

TABLE II

Maximum variation of $|\Delta\varepsilon|$ *due to solvent (a) and substituent (b); mean value of* $|\Delta\varepsilon|$ *(c)*

Configuration	(a)	(b)	(c)
9α, 10β	3.0	4.6	12
9α, 10β—H	3.3	4.1	7
9β, 10α	1.9	4.5	15
9α, 10α	7.2	6.0	26
9β, 10β	2.4	3.7	27

If a change of solvent would produce no other effect than a change in refractive index of the medium, the CD amplitude in methanol would be expected to be slightly smaller than that in a paraffinic solvent. In most cases the Cotton effect in methanol is smaller indeed, but considerably more than is expected from the correction factor[6] $(n^2 + 2)/3$. The slight decrease of vibrational fine structure equally can not be held responsible for the often drastic influence of solvent on the Cotton effects, *cf.* Figure 1b.

Although other explanations cannot simply be ruled out,[7] we prefer an interpretation in conformational terms because it may provide a common *rationale* for all three effects. So we assume that the effects of solvent, substitution and temperature on CD are due either to a shift in an equilibrium of conformations with different angles of twist or to a change of the average geometry of the diene-ring.

Experimental[14,15] and theoretical studies[16] of the conformation of unsubstituted cyclohexadiene have shown that the molecule is not planar, but half-chair-like. The nonplanarity results from the balance between the tendency of the π-electron system to achieve maximal conjugation, and the minimization of bond angle strain, torsional strain and non-bonded interactions. If the double bonds are assumed to be planar the torsional angle between the ethylene groups is found[14,15,16a] to be 17—18 °; when deviation from planarity of the double bonds is allowed[16b,17] the torsion around the single bond is reduced to 11—12 °. The torsion angles in the saturated part of the ring are[14b] —32, 46 and —32 °.

The effect of incorporating cyclohexadiene in the steroid skeleton can be evaluated using the approach developed by Bucourt.[18] For example, in the case of 9α,10β-Me-5,7-dienes *1*—*7* the diene ring is connected to rings A and C *via* a transoid junction. According to the sum rule[18] an »undisturbed« cyclohexadiene ring would require the torsional angles ϕ_A (5—10) and ϕ_C (8—9) to close from their standard values[19] (—55.6 and —52.6 °, respectively) to about —30 °. Alternatively, the angles (5—10) and (8—9) in ring B have to close relative to unsubstituted cyclohexadiene. This would entail a general flattening of the diene ring, including closure of the torsional angle ϕ (6—7). The flattening is opposed by the concomitant increase of the endocyclic bond angles at the sp^3 carbon atoms 9 and 10, and in particular by the increased eclipsing of 10-CH_3 and CH_2-11. Possibly also the increased diaxial interactions between

10-CH_3 and 4β-H assist in putting a limit to the flattening of ring B. In actual fact a compromise between the conflicting demands will be reached.

Similar reasonings can be applied in considering the conformation of the cyclohexadiene ring in steroids with 9β,10α- *(9—13),* 9α,10α- *(14)* and 9β,10β-configuration *(15),* taking into account the geometrically necessary twist-boat conformation of ring C in 9β,10α- and 9β,10β-steroids. A detailed conformational analysis along these lines has been used in discussing the sign of the Cotton effects of 9,10,13-stereoisomeric 5,7-dienes.[3]

When, in the 9α,10β-steroids, the angular 10-methyl group is replaced by hydrogen (compounds *8*) the eclipsing and nonbonded interactions are considerably reduced, resulting in substantial weakening of the resistance against flattening of the cyclohexadiene ring.[20] This would imply that the potential well $V(\phi)$ of the 10-H structure is essentially broader than that of the 10-Me structure. In the 9β,10α-compounds, on the other hand, the twist-boat conformation of ring C provides the major resistance to flattening of ring B by opposing the decrease of torsional angle ϕ_B (8—9). Therefore, the absence of the angular methyl group in *13* is expected[21] to be of negligible influence on the puckering or flattening of ring B.

These conformational considerations are corroborated by X-ray data and force field calculations. For most basic configurations studied here, X-ray data on crystals at —180 °C have been reported. Characterizing the geometry of the compounds with the torional angles in the diene ring, the results are given in Table III. With respect to the sign and even the order of magnitude of the angle φ (6—7) the data agree with those predicted from the qualitative conformation-analytical arguments. The conformation of the diene-ring in the 9β,10α-skeleton approximately equals that of cyclohexadiene. In the 9α,10β-Me compounds the value of the torsional angle ϕ (6—7) has decreased due to torsions in the double bonds. The 9α,10β-H skeleton is considerably more planar, in agreement with the conformation-analytical prediction and with UV absorption data: removal of 10-Me in 7-dehydrocholesterol *1* results in a small bathochromic shift and a more pronounced vibrational fine structure.[21]

TABLE III

Experimental torsional angles in cyclohexadiene and in ring B of some steroidal 5,7-dienes

Configuration	(5—10)	(5—6)	(6—7)	(7—8)	(8—9)	(9—10)	Ref.
Cyclohexadiene	—32	0	18	0	—32	46	14b
9α, 10β—Me	33.5	—6.3	—11.4	—1.7	30.2	—44.0	22
9α, 10β—H	13.8	—0.7	— 6.5	—0.9	13.9	—19.5	20
9β, 10α—Me	—29.9	—0.4	15.5	4.0	—35.4	45.9	23a
9α, 10α—Me	—24.8	2.7	9.5	3.5	—25.7	34.5	23b
9β, 10β—Me	—16.4	—3.8	7.8	10.7	—30.9	32.1	23c

That removal of the angular methyl group does not appreciably affect the diene torsion angle in the 9β,10α-structure is also indicated by spectral data: the UV absorption spectra of lumisterol *(9a)* and its 10-demethyl analogue *13* are virtually identical.[21]

In general, the introduction of sp^2-hybridized carbon atoms in a ring of the steroid skeleton increases the flexibility of this ring. For example, from

X-ray data on steroidal 4-en-3-ones it appears that the enone twist angles differ in different crystal forms of the same molecule, and also in molecules which differ by a remote substituent.[19] This shows that in these compounds, which contain three trigonal carbon atoms in the steroidal A-ring, substituent and/or intermolecular interactions may considerably affect the average molecular geometry. It may be expected that a similar flexibility is exhibited by the homannular conjugated dienes which are discussed here.

For 5,7-dienes with $9\alpha,10\beta$ (—Me or —H)-configuration there is support for such flexibility from force-field calculations[24] where it is found that the most stable conformation of the 10-H steroid is characterized by torsional angles in the diene system ϕ(5—6), ϕ(6—7) and ϕ(7—8) of magnitude 0.8, —2.1 and —1.2°, respectively, and that of the 10-Me analogue by the angles —3.7, —10.3 and 2.1°. These torsion angles appear to deviate rather strongly from those found by X-ray diffraction (Table III). Constraining the torsion angles in the saturated part of the diene ring (bonds 5—10, 8—9 and 9—10) to the X-ray values, calculation led to improved agreement for the other geometrical quantities (—0.7, —6.6, —0.8° for the former and —5.5, —13.0 and —1.0° for the latter compound), but only to a slight increase in strain energy +0.27 kcal/mol and +0.69 kcal/mol, respectively.[24] This indicates that with the $9\alpha,10\beta$-Me and certainly with the $9\alpha,10\beta$-H structures, small intermolecular interactions or substituent effects can significantly affect equilibrium geometry. Although no quantitative knowledge on the potential wells of the other 9,10-stereoisomers is available, a similar torsional flexibility probably exists there as well.

Whereas — on an absolute scale — the substituent and solvent effects on CD at room temperature are not larger for the $9\alpha,10\beta$-H structures than for the others, the effect of lowering temperature is impressive and reminescent of a conformational equilibrium. If in a given system the temperature dependence of the CD arises from a shift in an equilibrium of two conformers (A and B), and if these conformers have equal entropies and exhibit rotational strengths that are intrinsically independent of temperature, the free-energy extrapolation method of Moscowitz, Wellman and Djerassi[25] may be used to obtain ΔG°. In this way we found ΔG° values of 2.5 and 1.0 kJ/mol for *8b* and *8c*, respectively. With $\Delta\varepsilon_A = -13$ (from the CD curve of *8b* at 80 K where conformer A is almost exclusively present), $\Delta\varepsilon_B$ is found to be +42 and +35 for *8b* and *8c*. For cisoid dienes such values seem extremely high, the more so since the angle of twist cannot be large.[26] That a good fit is obtained using the procedure of Moscowitz *et al.*[25] implies that the temperature dependence can (not necessarily: is to) be explained from an equilibrium between two (ideally behaving) species.

In fact we have a preference for an explanation of the substituent and solvent effects on the CD in terms of a shift of average geometry instead of a shift in a conformational equilibrium. On conformation-analytical grounds we do not see how in the potential energy curve of *8* a considerable barrier should arise. Moreover, if the solvent- and temperature-effects observed in the dienes are to be ascribed to a common origin, not *8* alone but most of the dienes studied should have a barrier separating two conformations — which is highly unlikely.[28] Further arguments against an equilibrium of two conformers derive from temperature dependent NMR experiments[29] on *8b* and from the fact that the fluorescence decay curves of *8a,b,c* appear to be monoexponential.[4] There is no indication for a second fluorescing species whereas according to the free-energy extrapolation method still 16% of conformer B should be present in the case of *8c* under the conditions of the lifetime experiment (MIP, 77K).

The suggestion that the bottom of $V(\phi)$ in the unperturbed (*i. e.* unsubstituted and unsolvated) $9\alpha,10\beta$-H-5,7-diene skeleton — and perhaps in the other structures as well — is rather broad, does not imply that it is devoid of all relief. On the contrary, it is hard to imagine that there are no shallow pits on this broad minimum. Small perturbations such as remote substitutents, solvation or even viscosity might then induce (or amplify) small barriers so that, while the effective amplitude of twisting motion is not large, its average value can be considerably shifted as a function of the chemical environment of the chromophore. That the range of realized conformations for $9\alpha,10\beta$-H is not much larger than that with the other classes of stereoisomers studied here, is suggested from the X-ray data: the values of the spread in the positions of the carbon atoms of the B-ring are of similar magnitude. Furthermore, the clear vibrational fine structure which is observed in the absorption spectra of *8b* (and 7-dehydrocholesterol *1*) would not be expected when the molecules were considerably non-rigid.

That there appears to be a relation between the helicity of the diene chromophore and the Cotton effect in the $S_o \rightarrow S_1$ transition has been realized long ago.[1,30] Moscowitz *et al.*[1] formulated the relation as follows: »... a strong positive Cotton effect... means the presence of (a) cisoid diene chromophore twisted in the sense of a righthanded helix. A strong negative effect is indicative of the lefthanded twist«. Although the authors explicitly restrict the rule to strong Cotton effects, *viz.* reduced rotational strength > 25 (*i. e.* $R > 23 \times 10^{-40}$ cgs corresponding[31] to $\Delta\varepsilon_{max}$ of about 8), the helicity rule has almost exclusively been used in the unrestricted sense. The validity of the helicity rule was questioned by Burgstahler *et al.*[2] who proposed that the long-wavelength CD of skewed 1,3-cyclohexadienes is determined primarily by chirality contributions of the homoannular allylic axial substituents and not by the helicity of the chromophore (allylic chirality rule). The authors illustrated this view with the CD data of three 5α-X,10β-Y steroidal 1,3-dienes, where X/Y is H/H, H/Me and Me/Me, which were assumed to have similar skew angles but showed different CD effects: $\Delta\varepsilon$ +3.8, —2.7 and —11.1, respectively. We remark, however, that the H/H compound only violates the unrestricted helicity rule, not the rule as originally formulated. Other exceptions to the unrestricted helicity rule have been reported.[32] Nonetheless it is evident that notably axial allylic substituents including alkyl groups can considerably contribute to the Cotton effect associated with the $S_0 \rightarrow S_1$ transition of 1,3-dienes. Recently, sector rules were proposed for cisoid dienes which take into account the effect of the inherent twist in the chromophore as well as that of extrachromophoric contributions.[11,33]

Whereas various quantum-chemical calculations on skewed butadiene yield the result that *P* helicity leads to a positive rotational strength *R* in the $S_0 \rightarrow S_1$ transition,[34a–e] calculations on (methyl substituted) 1,3-cyclohexadienes[34f–h] substantiate the idea that, with respect to the chiroptical properties, the entire molecule must be considered as the chromophore[5] and that allylic axial bonds are of prime importance.[34f–g] The fact that the $S_0 \rightarrow S_1$ transition in cisoid-butadiene is characterized by nearly perpendicular electric and magnetic transition dipole moments may explain that R is highly sensitive towards substituent effects[35a] and to details of the computational method.[35b]

The calculations in the random phase approximation (RPA) of Bouman and Hansen[36] are of special interest, the more so since the computed R can be decomposed into separate contributions due to various parts of the molecule, allowing to judge the importance of intrinsic bond contributions, of the electric dipole — magnetic dipole mechanism, and of the polarizability mechanisms. For methyl substituted 1,3-cyclohexadienes with a diene twist angle of 17°, the bond contributions have been estimated.[37] Theory works out fine for several dienes.

In this connection it is interesting to see whether our data reveal the prominent role of allylic axial C—H/C—Me bonds which is predicted from theory. A fruitful comparison can only be made for the pair 9β,10α-Me and 9β,10α-H since in these structures alone the twist angle approaches that used in the calculation. The angle for the 9β,10α-Me structure is known (see Table III) and, as argued above, removal of Me-10 will not appreciably affect the conformation of the B-ring. Calculation of the rotational strength from the bond contributions (see Figure 9 in ref. 37) yields $R = 37 \cdot 10^{-40}$ cgs for 9β,10α-Me and $R = 0$ for 9β,10α-H. To the extent that our conformational assignment of both structures is correct, this result is clearly at variance with experiment since the CD effects (+14.9 and +13.2, respectively) appear to be approximately equal. Obviously, our CD data equally do not confirm the prediction of Moriarty *et al.*[33] that the contribution to R of allylic hydrogen is larger than that of axial allylic methyl.

CONCLUSION

On the assumption that they are of similar origin, we have ascribed the large effects of remote substituents and solvent on the rotational strength of the $S_0 \rightarrow S_1$ transition of steroidal 5,7-dienes, as well as the temperature effect in the case of the 9α,10β-H compounds, to a shift of the average geometry of the species, rather than to a shift in a conformational equilibrium. We submit that the diene chromophore is rather flexible in the twisting modes (particularly that along ϕ (6—7)). This gives rise to a shift of the average geometry with environment. As compared to the 10-methyl analogue, the potential well of the 9α,10β-H species is broadened — which may account for the large sensitivity of R on temperature and environmental effects. To estimate the magnitude of these shifts, one should know the behaviour of R as a function of twist angles, *quod non.* If the variation of $\Delta\varepsilon$ with the angle ϕ (6—7) is roughly estimated to be in the order of 2 $\Delta\varepsilon$ units per degree (*cf.* Tables II and III), the variation of CD with environment should require shifts in the order of no more than 1—6°.

Our model is tentative and should be substantiated by additional force-field calculations. Moreover it would be worthwhile to study from X-ray analyses the effect of remote substitution, crystal form and temperature dependence on the conformation of the B-ring, the more so if also CD measurements on such crystals (*e. g.* in KBr discs) can be made. Our proposal that the change of solvent affects rotational strength by means of a conformational change and not directly, implies that with more rigid dienes (*e. g.* the 1,3-estradienes of ref. 2)[38] effects of solvent and temperature upon R will be considerably smaller — and it would be interesting to verify this prediction.

It would also be of interest to study from RPA-type calculations on methyl-substituted 1,3-cyclohexadienes the effect on rotational strength of twist in the double bonds and — *e. g.* by introducing ethyl groups in locked conformations — to see whether ring substituents can be adequately represented by methyl groups. Moreover, since the spatial orientation of the C5—C6 bond in cyclohexadiene and the allylic bonds with respect to the diene chromophore varies with twist in the chromophore, it would be helpful to have information on the development of the corresponding contributions to rotational strength as a function of skew angle.

EXPERIMENTAL

Compounds *1*, *2*, *4*, *5*, *9* and *11* have been obtained from Duphar B. V., Weesp (The Netherlands), through the courtesy of Dr. M. P. Rappoldt. All other compounds are from the collection of the Gorlaeus laboratories; their preparation has been described elsewhere.[4,39]

Solvents were purified to spectroscopic quality, or purchased as such.

CD spectra were taken with Jouan/Jobin-Yvon Dichrographs. Concentrations were approximately $5 \cdot 10^{-5}$ M. $\Delta\varepsilon$ values cited in this paper pertain to the extrema of the CD curves; their accuracy is estimated to be $\pm 5\%$.

Low temperature measurements were performed using an Oxford Instruments Ltd. cryostat (DN-704 modified). KBr discs were prepared by pulverizing the solid substrate and subsequently adding small portions of KBr while crushing. Under these conditions transparent discs were obtained after pressing, which turned out to give reproducible CD spectra.

Acknowledgement. — This research was supported by the Netherlands Foundation for Chemical Research (SON) with financial aid from the Netherlands Organization for the Advancement of Pure Research (ZWO).

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7. Other explanations include a) a direct effect of substituent or solvation upon rotational stength R without a change of skeleton conformation[8], b) an equilibrium between solvated and unsolvated species[9] and c) monomer-dimer equilibria.[10]
8. Substituent effects on R can be taken into account using the theory of Weigang.[11] The large magnitude of the effects which we observe makes such an explanation unlikely.
9. Solvent and temperature effects on CD have been ascribed to equilibria between solvated and unsolvated species.[12] In our case such an explanation seems not adequate because a) the magnitude of the observed solvent effects (*cf.* Figures 1b and 2) bears no obvious relation to the solvents complexing capacity (measured from quantities such as dielectric constant, polarizability *etc.*), b) the magnitude of the CD of a solvated species should be vastly different from that of the bare diene, which is highly unlikely, and c) in case

of solvation one expects vibrational fine structure in CD and absorption spectra to decrease[13] — whereas with *8b* we observe the opposite.

10. Even at the low concentrations used, one should be aware of the occurrence of molecular aggregation effects. Whereas it is unlikely that they occur at room temperature, they may interfere with the measurements at low temperatures. Indeed the low fluorescence yield[4] of *8b* as compared to *8c* (MIP 77 K) may be due to aggregation in the case of *8b*. Temperature-dependent CD spectra are, however, observed for *8b* and *8c*. Moreover, in the case of 7-dehydrocholesterol *1*, which also exhibits an anomalous fluorescence yield, strongly solvent and temperature-dependent CD spectra are not observed.[4]

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SAŽETAK

O optičkoj aktivnosti steroidnih 5,7-diena

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Izvještava se o cirkularno-dikroičkim podacima za niz 9,10-stereoizomernih steroidnih 5,7-diena. Općenito su efekti za prijelaze kod najvećih valnih duljina (270—280 nm) veliki ($|\Delta\varepsilon_{\max}| = 10—30$) i u skladu s dienskim helicitetnim pravilom. Zapaženo je veličina CD-efekta znatno varira sa supstituentom na C-3 i C-17, i otapalom. U slučaju $9\alpha,10\beta$-H diena varijacijom otapala i temperature bilo je moguće utjecati čak na predznak Cottonova efekta. To je objašnjeno promjenom geometrije dienskog prstena; solvatacija, supstitucija i temperatura mogu utjecati na prosječnu geometriju prstena, uključujući i vrijednost kuta zakrivljenja dienskog sustava (ΦC(6)—C(7)).

Raspravlja se o značenju zapaženih kiroptičkih podataka za teorijski opis optičke aktivnosti u području $S_0 \rightarrow S_1$ prijelaza homoanularnih cisoidnih diena.