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STEREOCHEMISTRY OF OLEFINS—IX*

CORRELATION OF MILLS' AND BREWSTER'S RULES WITH THE COTTON EFFECTS OF CYCLIC OLEFINS

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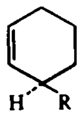
Abstract—The chiroptical properties of 74 substituted olefins are related to Mills' and Brewster's rules for optical activity *via* the olefin Octant rule. The latter rule provides a satisfactory solution for exceptional or difficult cases of distinction between epimers, and furthermore, can be used to derive the absolute configuration of a molecule without knowledge of the rotational properties of a diastereoisomer since a measurement of the *sign* of a Cotton effect rather than the relative magnitude of a rotation is involved for the majority of cases.

THE assignment of absolute configuration to epimeric pairs of endocyclic cycloalkenes has been possible in a large number of cases by application of the extremely useful set of parameters embodied in Brewster's refinement[1] of Mills' expirical rules.[2] For the purpose of the present discussion we consider first the enantiomeric 3-alkylcyclohexenes I and II. The configuration I is found to be more dextrorotatory than the enantiomer II, the $\Delta[M]_D$ values for a 3-methyl substituent being + 130° for I and − 130° for II with respect to the corresponding hydrocarbon (for poly substituted systems). Similarly it was shown[1] that an allylic hydroxyl group in configuration I (R = OH) contributes + 160° to the rotation of the parent cycloalkene. Thus an examination of the Cotton effects of allylically substituted chiral olefins is of considerable interest as an aid to understanding the basis for these successful correlations as well as the stated limitations of the applications of Mills' rule to heteroannular and other more complex olefins. Our studies reveal that in contrast to the sign of the D line rotation, the allylic alkyl system I (R = alkyl) shows a *negative* Cotton effect in the region of $\pi \rightarrow \pi^*$ absorption; yet the corresponding dextrorotatory alcohol (I; R = OH) displays a positive Cotton effect at the same wavelength.



I

II

A further complication appears to be the fact that for equatorial 4-alkyl-cyclohexenes (III and IV), the more dextrorotatory enantiomers (III) exhibit a positive

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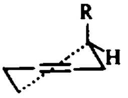
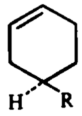
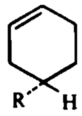


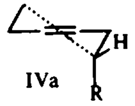
IIIa



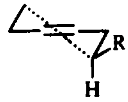
III



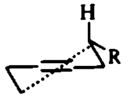
IV



IVa

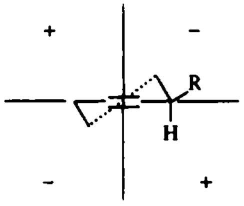


IIIc

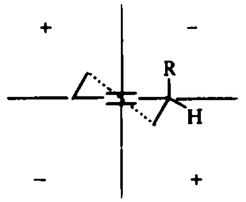


IVe

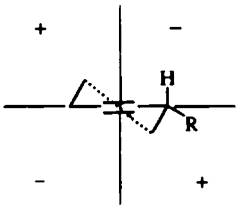
$\pi \rightarrow \pi^*$ Cotton effect, *i.e.* in contrast to cases I and II (R = alkyl) the D line rotation in 4-alkylcyclohexenes conserves the sign of the $\pi \rightarrow \pi^*$ circular dichroism. In order to clarify these effects, a detailed examination of the 185–210 nm region of the CD spectrum of a number of 3- and 4-substituted cyclohexenes has been made and the results collected in Table I. As pointed out by Brewster.[1] the *configuration* of an allylic alkyl cyclohexene is the main factor in determining its rotation while *conformational* effects dominate the observed rotations of the 4-substituted systems. In fact, these effects follow directly from construction of octant diagrams for the two sets I. II and III, IV. Thus the Mills-Brewster rule for (+)-3-methylcyclohexene assigns a *more positive* rotation to the 3 R enantiomer, regardless of its conformation Ie′ or Ia′.



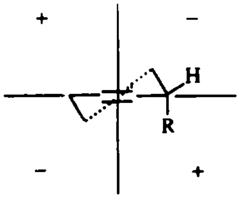
Ie′



Ia′



IIe′



IIa′

Either of these conformations (Ia′, Ie′) bears the methyl group in an upper *negative* octant.[3] Such an array predicts a *negative* $\pi \rightarrow \pi^*$ Cotton effect, *i.e.*, a Cotton effect opposite to the observed D line rotation. Measurement of the CD spectrum of (+)-(R)-3-methylcyclohexene[4] reveals that indeed a negative Cotton effect $[\theta]_{199\cdot5}$

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* In this paper the symbols e′ and a′ denote quasi-equatorial and quasi-axial cyclohexene substituents.

− 27,700 is present at the position associated with the $\pi_x \rightarrow \pi_x^*$ transition (Fig. 1), but that as noted for several olefins studied earlier,[3] a second, more intense transition with positive sign appears near 185 nm. The spectroscopic assignment for this higher energy band is still uncertain, but in our discussion we shall refer to this band as the $\pi_x \rightarrow \pi_y^*$ transition for reasons stated elsewhere.[4] In any event, the sign of rotation upon which the success of the Mills-Brewster rules depends is taken from this band rather than from the lowest energy $\pi_x \rightarrow \pi_x^*$ absorption in the case of 3-alkylcyclohexenes. Thus cyclohexenes with allylic alkyl substituents (which appear to dominate the chiroptical properties of the system) may be classified as type I or II, and where the Cotton effect has been measured (Table 1), both transitions are seen, the rotational shift (Δ[M]olefin-[M]saturated) having the same sign as the *higher* energy transition ($\pi_x \rightarrow \pi_y^*$), *i.e.*, opposite to the observed $\pi_x \rightarrow \pi_x^*$ Cotton effect.

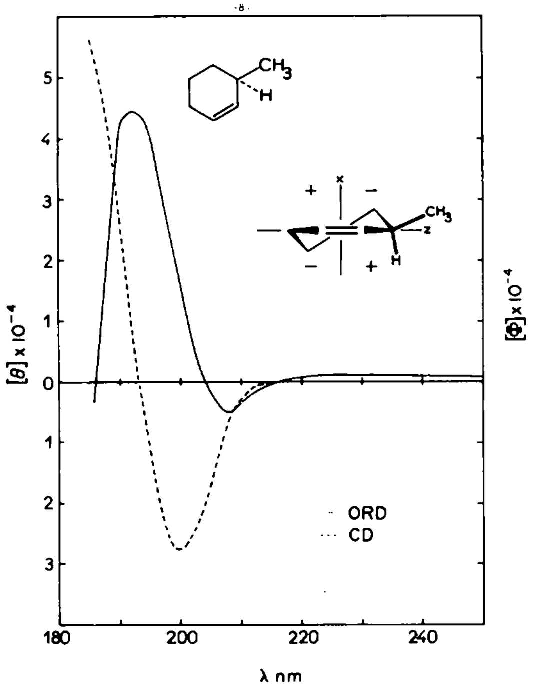


FIG 1. ORD (———) and CD (--------) spectra of (+) R 3-methylcyclohexene in cyclohexane

In the case of 4-substituted cyclohexenes (III, IV) Brewster[1] has pointed out that the rotations of these enantiomers will be dependent largely on their *conformations* IIIa, e and IVa, e. For application of the Octant rule to such a conformationally mobile system, it is of course necessary to know the configuration. Thus (+)-R-4-methylcyclohexene is assumed to have the conformation IIIe (equatorial CH_3) since it shows a positive Cotton effect at 198 nm (Table 1) in conformity with the Octant rule (Fig. 2). In this case, however, the relative intensities of the two Cotton effects ($\pi_x \rightarrow \pi_x^*$ and $\pi_x \rightarrow \pi_y^*$) are set so that the sign of the lowest energy CD maximum corresponds with that of $[M]_D$. The 25 olefins shown in Table 1 have been divided into 3-substituted (allylic) (Types I, II) and 4-substituted (Types III, IV)

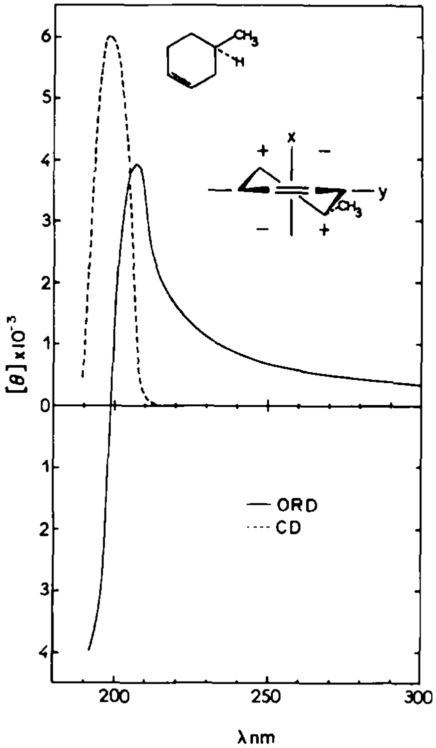


FIG 2. ORD (———) and CD (-----) spectra of (+) R 4-methylcyclohexene in cyclohexane

categories, their conformations illustrated and the expected $[M]_D$ and CD behavior compared with experimental results. In this way we can see the basis of the Mills-Brewster rules reflected in the relative intensities of the two oppositely signed Cotton effects and at the same time progress to correlation of absolute stereochemistry for several cases not strictly amenable to application of Mills' rule. With the establishment of these criteria it is no longer necessary to have epimeric pairs in order to assign absolute configuration; for a given relative configuration will display either a positive or negative Cotton effect whose sign follows in all cases from Octant rule considerations.

The data in Table 1 are fully consistent with this classification of the cycloalkenes. Types I and II are dominated by allylic substituents which confer positive and negative rotational shifts respectively, and generally the onset or appearance of the lower wavelength Cotton effect from which the D line is derived can be observed. The longest wavelength band carries the sign predicted by the Octant rule although in one case this is suppressed and only appears as a shoulder or inflexion (No. 13; see also Table 2, Nos 13, 14 and Fig 4). Several examples require analysis in terms of two or even three contributing effects. It has been assumed for this discussion that these are additive. In order to simplify the argument, we have also assumed that a double bond in a heteroannular position confers a symmetrical disposition of remote octant population (unless heavily substituted by axial substituents). Thus the conformations depicted in Column 2, Table 1, largely reflect the *local* cyclohexene environment. This is perhaps best illustrated with Nos 9. 10 and 11. 12 where the substitution of methyl by hydrogen at C_{10} inverts the sign of the Cotton effect in both sets. For several compounds CD data is not available (Nos 6, 14, 16) and predicted signs are given. The Δ^{16} case (No. 22) is treated as a modified "Ia" system.

We next examine Types I and II where R is a group of polarisability different from alkyl, in particular the allylic alcohols (R = OH). Mills' rules can be used to predict the relative signs of $[M]_D$ for the allylic alcohols of Types I and II (R = OH). Quantitative rigor was added to this argument by Brewster[1] who evolved parameters for calculation of $[M]_D$. In a large number of cases, excellent agreement was found, but again certain exceptions were noted. Examination of the Cotton effects of some 50 allylic alcohols and acetates reveals that the sign of the CD near 200 nm normally reflects the sign of the D line rotation. In this case an alcohol of Type I bears the allylic substituent with high polarisability in a *negative* octant, yet a *positive* Cotton effect (and $[M]_D$) is observed. As noted earlier,[3] a comparison with the ketone $n \to \pi^*$ Octant rule[5] suggests that substituents such as —OH, OAc, and —OCH_3 lead to an inverse or anti-Octant rule where the reference coordinate frame becomes right-handed as shown in Fig 3. Alkyl substituents and C—C bonds of course retain their original octant signs[3] and their contributions must be weighted accordingly.

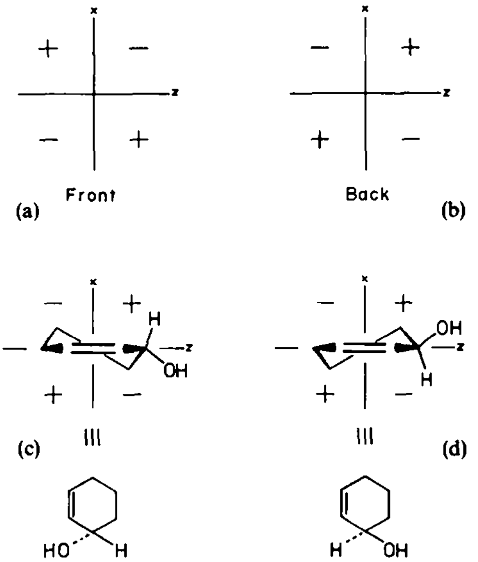


FIG 3. The inverse Octant rule for allylic oxygen substituents showing (a) front octants and (b) back octants viewed along the olefin y-axis. Inverse octant projections for (c) 3 S-hydroxycyclohexene and (d) 3 R-hydroxycyclohexene showing the OH in a pseudo-equatorial conformation.

The second, lower wavelength band is still optically active and of sign opposite to the $\pi_x \to \pi_x^*$ band, but in the case of an allylic oxygen function and in contrast to 3-alkylcyclohexenes, the sign at the D line corresponds to the *higher* wavelength $\pi_x \to \pi_x^*$ absorption. The data for 49 allylic alcohols, ethers, and acetates are given in Table II. Steroidal, terpenoid, and alkaloidal frameworks have been examined and several allocations of absolute stereochemistry are possible as a result of this survey.

Steroidal alcohols (Table II)

A change of configuration from 3β to 3α for oxygenated Δ^4 steroids inverts the sign of the $\pi_x \rightarrow \pi_x{}^*$ Cotton effect from negative to positive (Table 2; Nos 1–4) because in the 3β series, both the C_{10}—CH_3 and the C_3 substituent occupy allylic positions in negative octants, the latter group following the inverse rule (see Fig 3). Similarly, while the Δ^5-4β-hydroxy (No. 5) has a positive CD at 208 nm, the sign is inverted in 4α-hydroxycholest-5-ene (No. 6) where the hydroxyl group now occupies a negative (inverse) octant. Some conformational mobility apparently complicates the spectrum in this case as seen by the appearance of a positive Cotton effect at 198 nm. In examples 7 and 8, the use of methanol as solvent reveals that, as predicted by the inverse rule, the 12α-hydroxy-$\Delta^{9:10}$ system is much more positive than the 12β compound. These examples, however, require the availability of both epimers, and the effect was by no means reflected in cyclohexane solution. Compounds 9 and 10 are expected to show identical behaviour with that of Nos 5 and 6 respectively. We note that Compound 10 shows no evidence of sign inversion (*cf* the small but measurable positive maximum at 198 nm in No. 6).

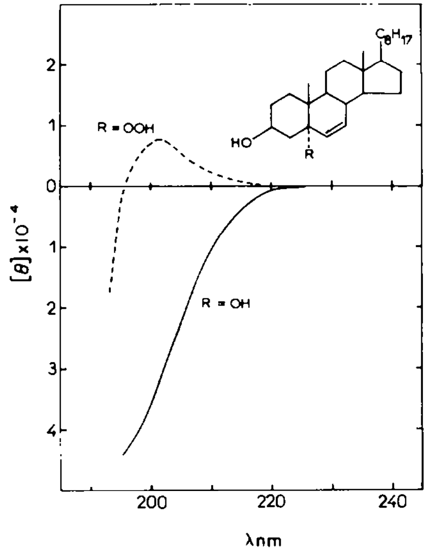


FIG 4. CD spectra of 3β,5α-dihydroxycholest-6-ene (———) and 3β hydroxy, 5α-hydroxycholest-6-ene (- - - - -) in methanol

For the Δ^6 series (Nos 13, 14), the predicted weak positive CD of the $\pi \rightarrow \pi^*$ band is only seen in No. 14, Fig. 4. The absence of a shoulder near 200 nm in the spectrum of No. 13 means that this transition is masked by the strongly negative $\pi_x \rightarrow \pi_y{}^*$ band at 193 nm. The same effect was noted earlier for Δ^6 steroids (where however a shoulder was observed) and the interpretation can be extended to the spectra of a range of exomethylene derivatives where the *lower* wavelength band of sign opposite to that predicted by the Octant rule dominates the $\pi \rightarrow \pi^*$ region. In all of these cases, however, recognition of the masked $\pi_x \rightarrow \pi_x{}^*$ absorption in the form of a shoulder or low intensity maximum provides a satisfactory basis for interpretation in terms of the Octant rule. The reasons for the variation of intensities (but not the energies) of the two olefinic transitions are not yet clear from structural analysis. Detailed vectorial analysis of the octant populations of these unusual (but not exceptional) cases and a study of their local symmetry properties may be helpful in arriving at an empirical classification of these effects for the purpose of predicting the relative intensities of the two observed transitions.

Terpenes

Turning now to some examples of oxygenated terpenes, it is found (Nos 15, 16) that the bicyclic allylic alcohols (+)-Sabinol and (+)-*trans*-pino carveol show the predicted Cotton effects at 210 and 195 nm respectively. These curves may conceal underlying complexities, e.g., small ring polarizability noted earlier,[3] and it is desirable to collect many more examples in this series.

Satisfactory agreement between the predicted and observed positive $\pi \rightarrow \pi^*$ CD of both hirsutic and gibberellic acids (Nos 18, 19) is found (Figs 5 and 6). The latter acid shows (Fig 6), in addition to the relatively weak ($[\theta]_{234}$ −2400) lactone contribution, a very powerful positive CD ($[\theta]_{203}$ + 62,700) due to superposition of *two* allylic alcohol arrays each occupying positive octants as defined by Fig. 3. The Cotton effect exhibited by the lactonic and carboxyl functions in this series is in the range $[\theta]_{215-230}$ 2000–3000 (see Nos 21–23). The 206 nm Cotton effect in Compounds 24–27 can thus be assigned to the olefinic chromophore and may be compared with the parent hydrocarbon, (−)-kaurene (No. 20; $[\theta]_{205}$ + 6000). As expected from the inverse or anti-octant rule, a 15β-hydroxyl group confers a strong positive CD by its contribution from an upper left octant (Fig 3). The configuration at C_{15} of deacetylxylopic acid (α—OH) (No. 24) and its epimer grandifloric acid (β—OH) (No. 25) are not reflected in the $[M]_D$ values of − 111° and − 114° respectively for these compounds. However, reference to Fig 7 confirms not only the epimeric C_{15} stereochemistry, but also the absolute configuration by application of the inverse rule for

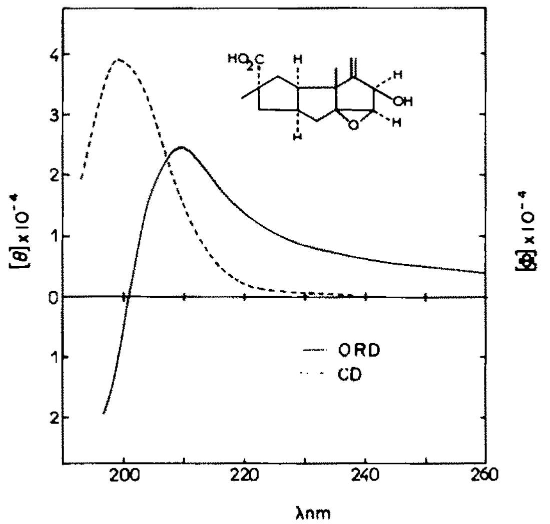


FIG 5. ORD (———) and (CD (- - - - -) of hirsutic acid C in methanol

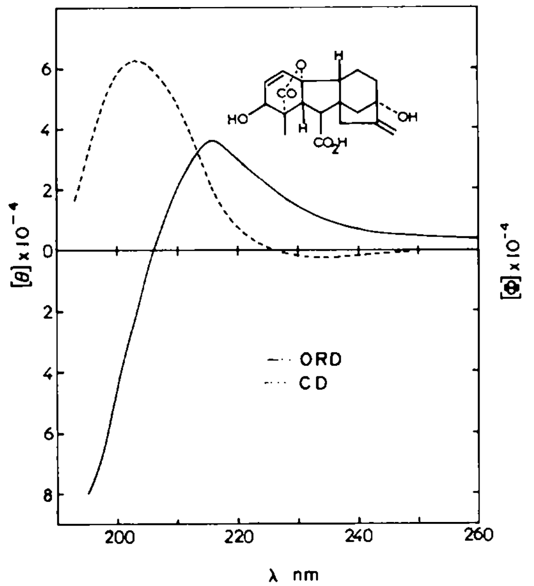


FIG 6. ORD (———) and CD (-----) of gibberellic acid in methanaol

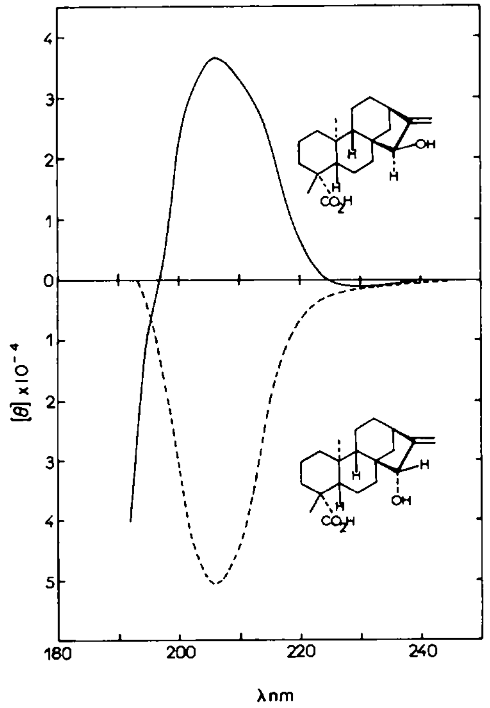


FIG 7. CD spectra of 15β-hydroxy-*ent*-kaur-16-en-19-oic acid (-----) and grandifloric acid (-----) in methanol

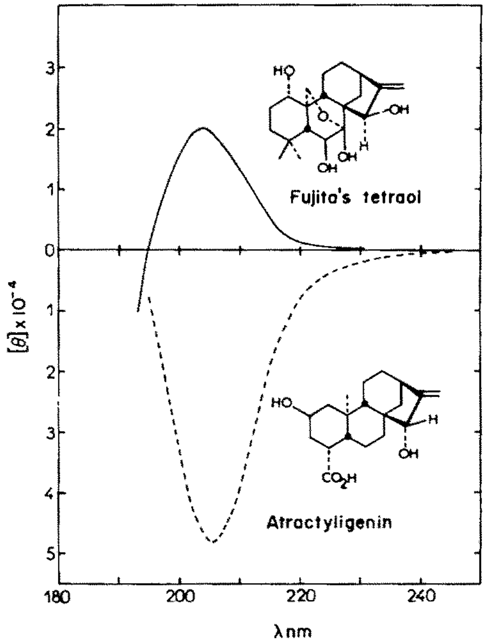


FIG 8. CD spectra of Fujita's tetraol (———) and atractyligenin (- - - - -) in methanol

allylic alcohols. A similar relationship is observed for Fujita's tetraol (No. 28) and atractyligenin (No. 26 Fig 8) in which 15β- and 15α-OH groups are placed in positive and negative octants (Fig 3) with respect to the exomethylene chromophore. Table II contains some 20 examples of the exomethylene chromophore which display $\pi_x \rightarrow \pi_x^*$ maxima at the expected wavelength. The only exceptional cases are those ethylidene or exomethylene steroids whose $\pi_x \rightarrow \pi_x^*$ absorption is masked by a lower lying $\pi_x \rightarrow \pi_y^*$ band. In these cases the CD spectrum contains a shoulder superimposed upon a strong background and the *sign* of the $\pi_x \rightarrow \pi_x^*$ can be inferred by assuming that the shoulder corresponds to a masked transition of opposite sign to the background absorption.[6]

Analysis of the spectra of some diterpene alkaloids is complicated by the appearance of several new bands in the spectra of compounds containing the grouping —N—CH_2—CH_2—O— in ionising solution. The effect is greatly reduced in cyclohexane solution where the maximum at 205 nm can be used to assign or confirm configuration, e.g., 15α in veatchine (Fig 9). From the data for Compounds 32–37, the 15-hydroxyl group in both isohypognavinol (No. 35) and ajaconine (No. 36) can be assigned the β-configuration (Figs 10, 11).

Compounds 38–40 represent a series of conformationally mobile systems which are recorded for correlative purposes as far as C_{13} stereochemistry is concerned. The remaining compounds (41–49) in Table II contain the allylic acetate moiety which exhibits the same inverse Octant rule behaviour. In several cases the n → π* band masks the expected π → π* transition. This is particularly pronounced in Nos 47 and 48 where the acetate n → π* transitions (213–222 nm) hide the predicted

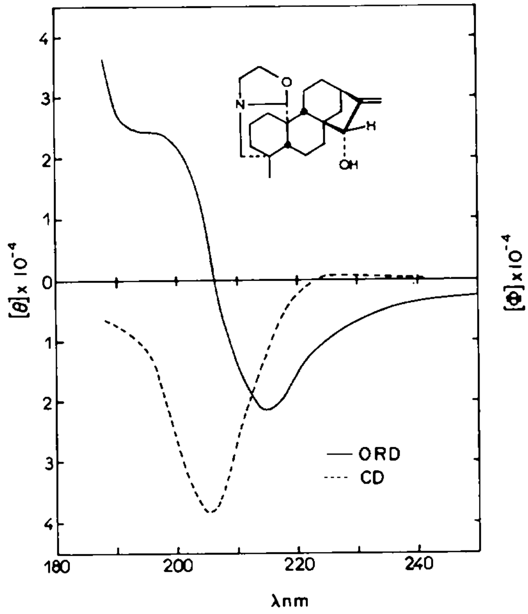


FIG 9. ORD (———) and CD (- - - - -) spectra of veatchine in cyclohexane

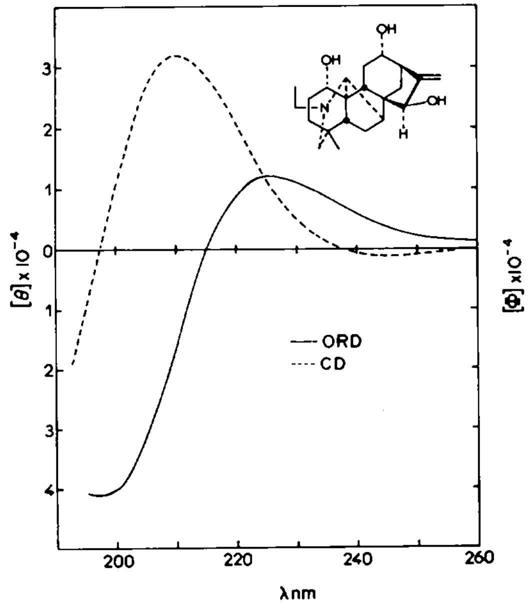


FIG 10. ORD (———) and CD (- - - - -) spectra of luciculine in methanol

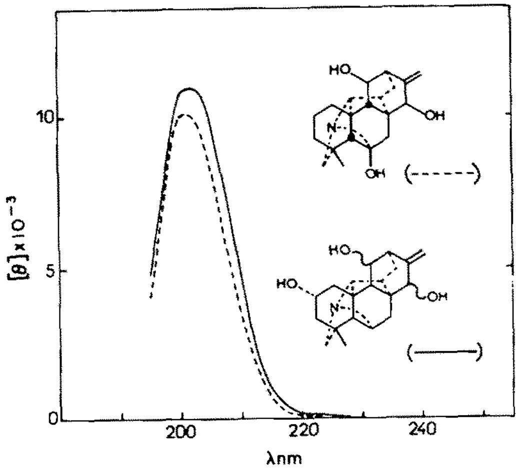


FIG 11. CD spectra of isohypognavinal (—— –) and pseudo-kobusine (-----) in methanol

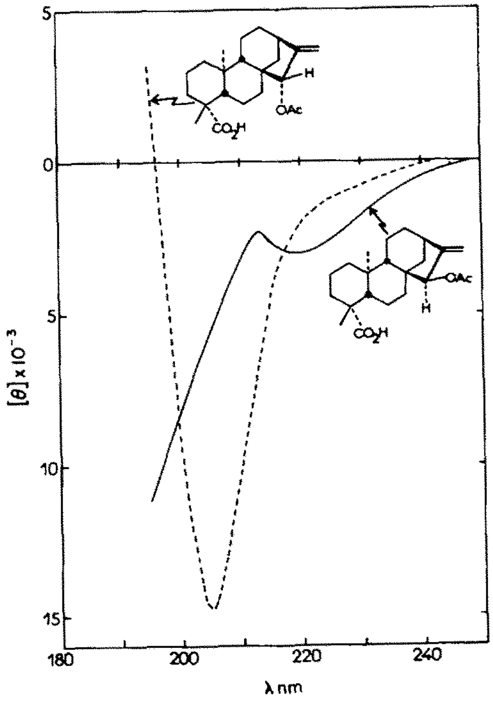


FIG 12. CD spectra of xylopic acid (———) and 15α-acetoxy-*ent*-kaur-16-en-19-oic acid) (-----) in methanol

TABLE 1

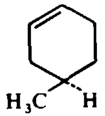
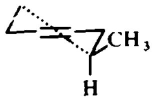
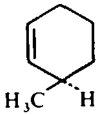
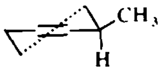
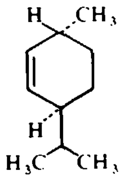
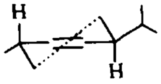
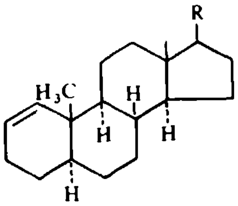
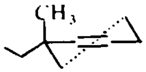
	Compound	Conformation	Type	Rotational shift[a]		Cotton effects in $\pi - \pi^*$ region			
						Predicted[b]		Observed[c,d]	
				Predicted	Observed	$\pi_x - \pi_x^*$	$\pi_x - \pi_y^*$	$\pi_x - \pi_x^*$	$\pi_x - \pi_y^*$
1			IIIe	+	+160°	+	−	+	−
2			Ie′	+	+130°	−	+	−	+
3			Ie′ + Ie′	+	+185°	−	+	−	+
4			Ie′ + IIa′	weak or zero	−41°	−	+	−	+

TABLE 1—*continued*

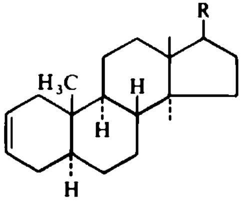
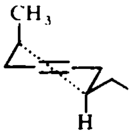
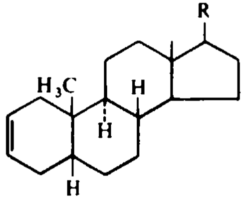
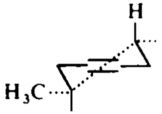
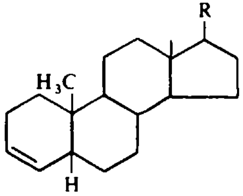
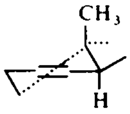
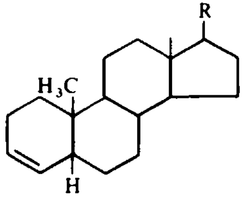
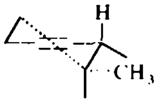
Compound		Conformation	Type	Rotational shift[a] Predicted	Rotational shift[a] Observed	Cotton effects in $\pi - \pi^*$ region Predicted[b] $\pi_x - \pi_x^*$	Cotton effects in $\pi - \pi^*$ region Predicted[b] $\pi_x - \pi_y^*$	Cotton effects in $\pi - \pi^*$ region Observed[c,d] $\pi_x - \pi_x^*$	Cotton effects in $\pi - \pi^*$ region Observed[c,d] $\pi_x - \pi_y^*$
5			IIIe + IVa	+	+170°	+	−	+	
6			2IVe + IIIe	−	−24°	−	+		
7			Ie′	+	+123°	−	+	−	+
8			IIe′	−	−44°	+	−	+	−

TABLE 1—*continued*

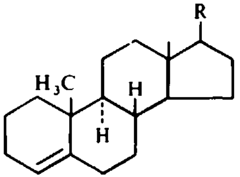
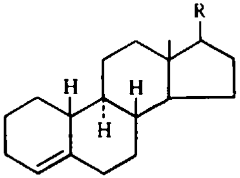
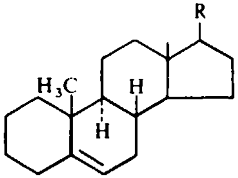
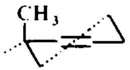
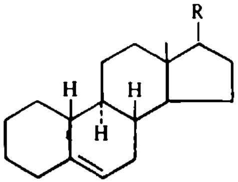
	Compound	Conformation	Type	Rotational shift[a] Predicted	Rotational shift[a] Observed	Cotton effects in $\pi - \pi^*$ region Predicted[b] $\pi_x - \pi_x^*$	Predicted[b] $\pi_x - \pi_y^*$	Observed[c,d] $\pi_x - \pi_x^*$	Observed[c,d] $\pi_x - \pi_y^*$
9			Ia′	+	+153°	−	+	−	+
10			IIIe	+		+	−	+	−
11			IIa′	−	−298°	+	−	+	(−)
12			IVe	−		−	+	−	(−)

TABLE 1-- *continued*

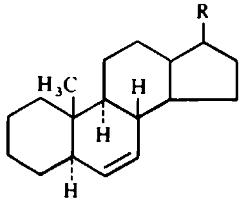
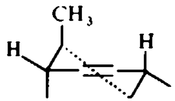
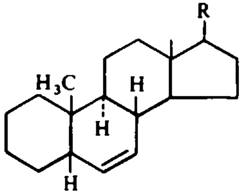
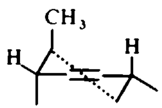
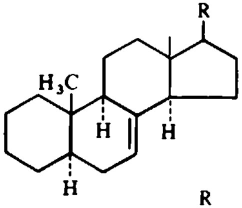
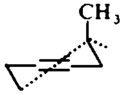
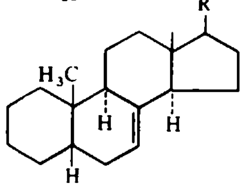
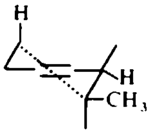
	Compound	Conformation	Type	Rotational shift[a] Predicted	Rotational shift[a] Observed	Cotton effects in $\pi - \pi^*$ region Predicted[b] $\pi_x - \pi_x^*$	Predicted[b] $\pi_x - \pi_y^*$	Observed[c,d] $\pi_x - \pi_x^*$	Observed[c,d] $\pi_x - \pi_y^*$
13			IIe' + IIe'	−	−402°	+	−	(+) inf.	−
14			Ia' + IIe' + IVa	weak	−110°	+	−		
15			IIIa	−	−66°	−		−	(+)
16			IIIe + IVa	+	+119°	+	−		

TABLE 1—*continued*

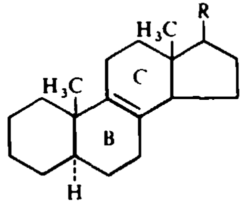
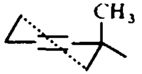
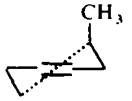
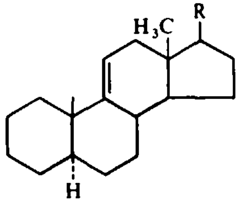
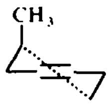
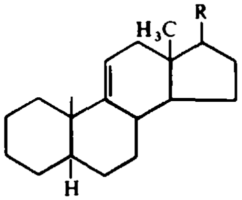
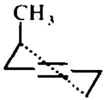
	Compound	Conformation		Type	Rotational shift[a]		Cotton effects in $\pi - \pi^*$ region			
					Predicted	Observed	Predicted[a]		Observed[c, d]	
							$\pi_x - \pi_x^*$	$\pi_x - \pi_y^*$	$\pi_x - \pi_x^*$	$\pi_x - \pi_y^*$
17		B		Ia′	+	+96°	−	+		
		C		IIIa	−		+	−	+	−
18				IVa	+	+109°	+	−	+	−
19				IVa	+	+49°	+	−	+	(−)

TABLE 1—*continued*

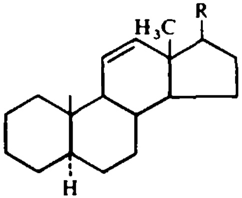
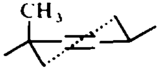
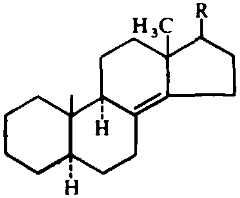
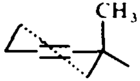
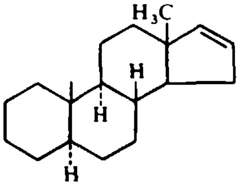
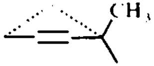
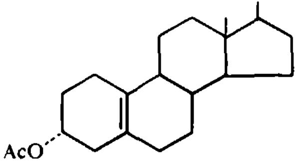
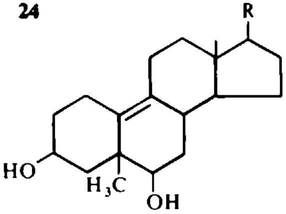
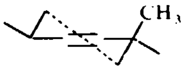
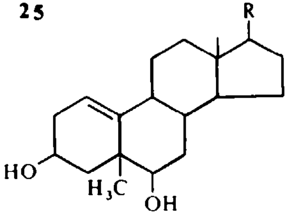
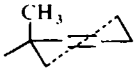
Compound		Conformation	Type	Rotational shift[a]		Cotton effects in $\pi - \pi^*$ region			
						Predicted[b]		Observed[c,d]	
				Predicted	Observed	$\pi_x - \pi_x^*$	$\pi_x - \pi_y^*$	$\pi_x - \pi_x^*$	$\pi_x - \pi_y^*$
20			2 × IIe′ + IIa′	+	+33°	−	+	−	(+)
21			Ia′	+	−16°	−	+	−	+
22			Ia′	+	+31°	−	+	−	+
23			IIe′	−		+	−	+	(−)

Table 1—*continued*

Compound	Conformation	Type	Rotational shift[a]		Cotton effects in $\pi - \pi^*$ region			
			Predicted	Observed	Predicted[b]		Observed[c,d]	
					$\pi_x - \pi_x^*$	$\pi_x - \pi_y^*$	$\pi_x - \pi_x^*$	$\pi_x - \pi_y^*$
24 		Ia' + 2 ×	−		+	−	+	(−)
25 		IIa'	−		+	−	+	(−)

[a] See Ref. 1

[b] See Ref. 3

[c] Experimental details of these measurements of CD spectra in this laboratory are given in Ref. 3

[d] Many of the samples listed in Tables 1 and 2 were kindly donated by the following colleagues: Drs. J. ApSimon. C. H. Brieskorn. J. A. Berson. C. Djerassi, O. E. Edwards, D. E. V. Ekong, E. Fujita, S. I. Goldberg, J. R. Hanson, P. R. Jefferies, G. D. Meakins, T. Okamoto, S. W. Pelletier, P. Crabbé, G. Snatzke, R. Stevenson and K. Wiesner

TABLE 2

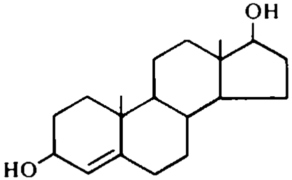
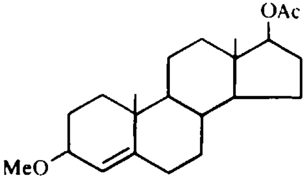
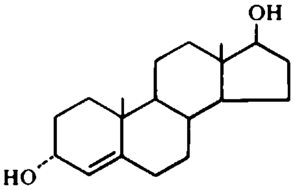
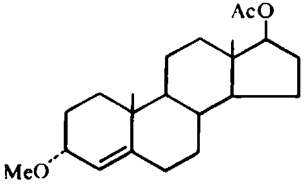
	Compound	Solvent	CD λ(nm)	CD [θ]	Predicted[a] sign	Comment[b]
1		EtOH	197	−33,000	−	Ref. 8
2		EtOH	197	−38,000	−	Ref. 8
3		MeOH	199	+13,400	+	Ref. 8
4		EtOH	202	+21,500	+	Ref. 8

TABLE 2– *continued*

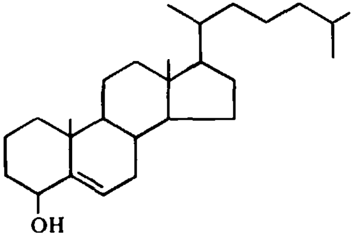
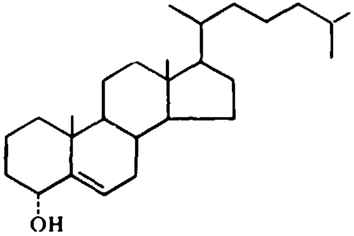
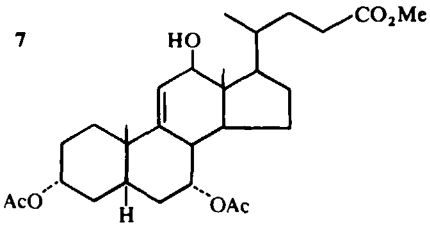
Compound		Solvent	CD λ(nm)	CD [θ]	Predicted[a] sign	Comment[b]
5		MeOH	208	+1,500	+	
			195*	−17,100		
		Cyclohexane	208	+2,300		
			185	−44,200		
6		Cyclohexane	208	−7,900		(+)10β-CH_3
			198	+3,300	±?	(−)4α-OH
			185*	−30,600		$\pi_x - \pi_y^*$
7		MeOH	202	+33,300	+ +	(+)10β, 18β-CH_3
					−	(−)12β-OH
		Cyclohexane	202	+57,600	+	$\pi_x - \pi_x^*$
			185*	−29,800	−	$\pi_x - \pi_y^*$

TABLE 2—*continued*

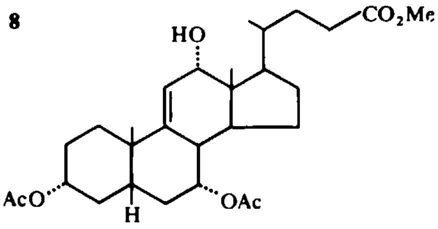
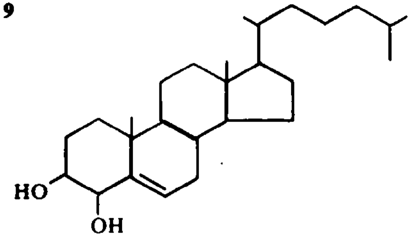
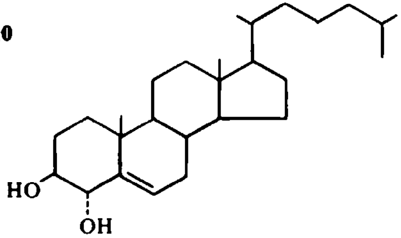
Compound		Solvent	CD		Predicted[a] sign	Comment[b]
			λ(nm)	$[\theta]$		
8		MeOH Cyclohexane	201·5 202·5	+81.600 +56.400	+ + +	(+)10β. 18β-CH_3 (+)12α-OH
9		MeOH	211 195*	+780 −39.600	+	
10		MeOH	205	−5.200	+ −	(+)10β-CH_3 (−)4α-OH

TABLE 2—*continued*

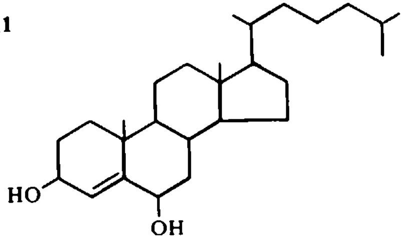
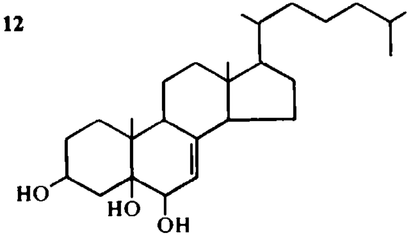
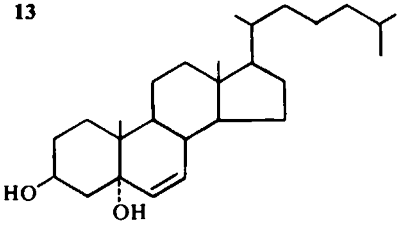
Compound	Solvent	CD λ(nm)	CD [θ]	Predicted[a] sign	Comment[b]
11 	MeOH	201	−43,100	−	(−)3β-OH, 6β-OH, 10β-CH_3
12 	MeOH	204	−27,400	−	
13 	Cyclohexane	193	−65,000	+ −	$\pi_x - \pi_x^*$ band not observed $\pi_x - \pi_y^*$

TABLE 2—*continued*

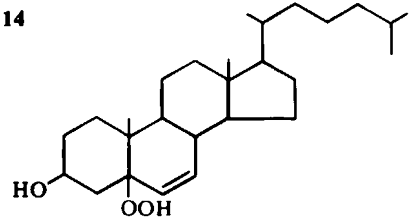
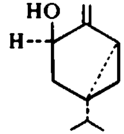
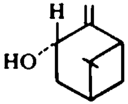
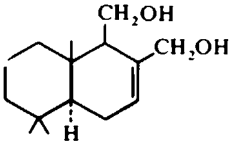
Compound		Solvent	CD λ(nm)	$[\theta]$	Predicted[a] sign	Comment[b]
14		MeOH	201·5 193	+7,700 −16,700	+ −	$\pi_x - \pi_x^*$ $\pi_x - \pi_y^*$
15		Cyclohexane	210 185*	−16,400 +4,700	− +	
16		MeOH	195	+39,700	+	
17		Cyclohexane	207·5	+19,700	?	

Table 2—*continued*

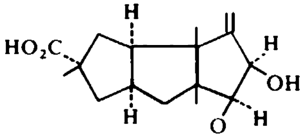
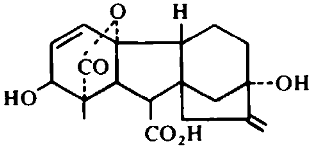
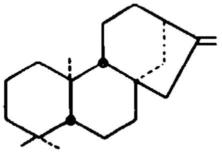
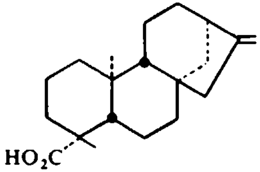
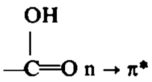
Compound	Solvent	CD λ(nm)	CD [θ]	Predicted[a] sign	Comment[b]
18  Hirsutic Acid C	MeOH	199	+38.500	+	Allylic OH (+) Allylic CH_3 (+)
19  Gibberellic Acid	MeOH	[234·5 203	−2.400] +62.700	+	2 × Allylic OH (+)
20  (−) Kaurene	MeOH Cyclohexane	206·5 205 185*	+7.900 +6,000 −21,800	+	
21  Ent-kaur-16-en-19-oic-Acid	MeOH	216*	−2,600		 $-\overset{\overset{OH}{\vert}}{C}=O$ n → π*

TABLE 2—*continued*

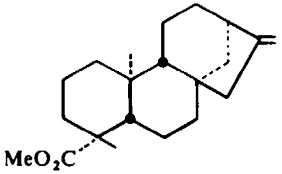
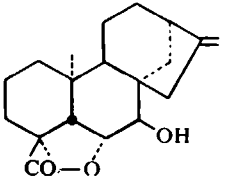
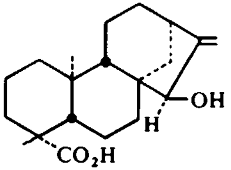
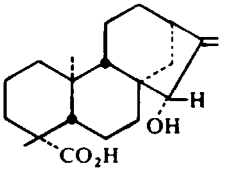
Compound		Solvent	CD λ(nm)	CD [θ]	Predicted[a] sign	Comment[b]
22		MeOH	216*	−2,500		$-\overset{\text{OMe}}{\overset{\vert}{C}}=O$ n → π*
23		MeOH	220 208 195*	+2,200 +2,900 −16,100	 + 	lactone
24	 15β-Hydroxy-ent-kaur-16-en-19-oic Acid (Deacetyl xylopic Acid)	MeOH	230 206 192*	−1,000 +36,500 −40,100	 + −	$-CO_2H$
		Cyclohexane	231 207 185*	−1,100 +39,200 −98,500	 + −	$-CO_2CH_3$ Data are for the methyl ester
25	 Grandifloric Acid	MeOH	206	−50,500	−	

Table 2—*continued*

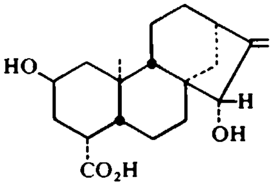
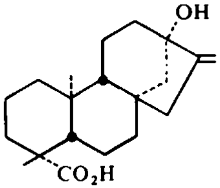
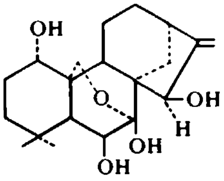
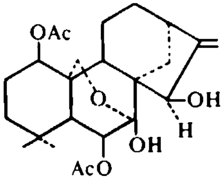
	Compound	Solvent	CD		Predicted[a] sign	Comment[b]
			λ(nm)	[θ]		
26	 Atractyligenin	MeOH Cyclohexane	205·5 206	−48,200 —	−	
27	 Steviol	Cyclohexane	202 185*	+29,600 −55,300		
28		MeOH	204	+20,000	+	
29		Cyclohexane	205 185	+28,100 −67,500	+	

TABLE 2—*continued*

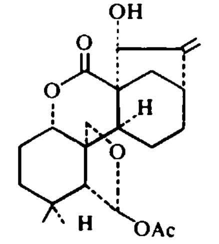
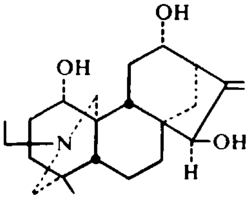
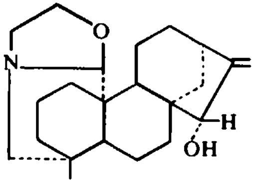
	Compound	Solvent	CD λ(nm)	CD [θ]	Predicted[a] sign	Comment[b]
30		MeOH	232 203	−960 +25.900	+	lactone, acetate C=O
31	 Luciculine	MeOH	246 210 193*	−1.300 +31.800 −18,300	+	
		N/10 HCl	207 195*	+42,300 −12.100	+	
32	 Veatchine	Cyclohexane	228 205	+640 −38.300	−	Origin of the 219–230 nm CD unknown. but is solvent dependent and requires the presence of | C - N | O
		MeOH	221·5 199·5	+25.600 −55.200	−	
		N/10 HCl	219 197	+30.800 −67.800	−	

Table 2—*continued*

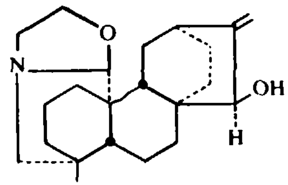
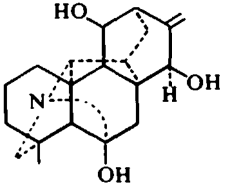
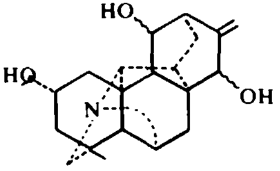
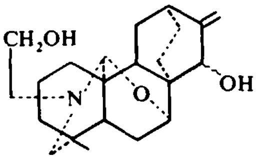
	Compound	Solvent	CD λ(nm)	 [θ]	Predicted[a] sign	Comment[b]
33	 Atisine	HCl^{de} in H_2O	215 187	+34,000 −24,500	+	λ is high *cf.* no. 32 β-OH assigned
34	 Pseudokobusine	MeOH N/10 HCl	210 199	+10,400 +10,300	+	
35	 Isohypognivinal	MeOH N/10 HCl	202·5 199	+10,900 +11,300		β-OH assigned
36	 Ajaconine	Cyclohexane	204 189	+ −		
		MeOH	260 218 202	−790 +9,500 +23,900		β-OH assigned
		N/10 HCl	259 211	−2,100 +42,400		

TABLE 2 *continued*

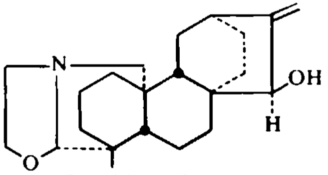
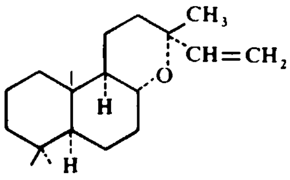
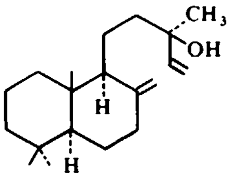
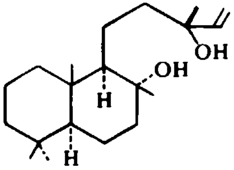
	Compound	Solvent	CD		Predicted[a] sign	Comment[b]
			λ(nm)	[θ]		
37	 Isoatisine HCl	H^2O	246 205	−2,800 +21.100		β-OH assigned
38	 (+) Manoyl Oxide	Cyclohexane MeOH	192 195	+13,400 +10.800		
39	 (+) Manoöl	Cyclohexane MeOH	200 200	−22,200 −16.800		
40	 Sclareol	Cyclohexane	190	−6.100		

Table 2—*continued*

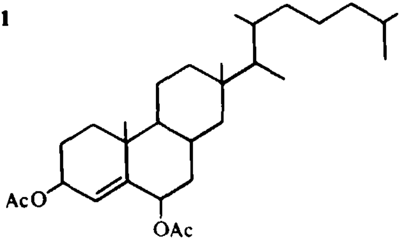
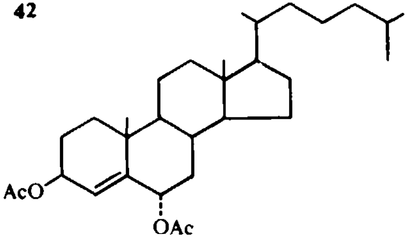
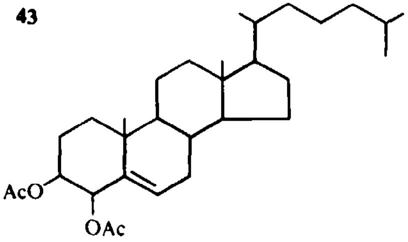
Compound	Solvent	CD		Predicted[a] sign	Comment[b]
		λ(nm)	[θ]		
41 	Cyclohexane	198·5	−56,500	−	
		185*	+22,700		
42 	Cyclohexane	190*	−48,100	±	$\pi_x - \pi_x^*$ band may be "missing"; 3βOAc(−) 6αOAc(+)
43 	Cyclohexane	220	−1,500		} OCOCH³
		212·5	−800	← +	
		185*	−83,600	−	$\pi_x - \pi_x^*$ positive band at 197 nm concealed by n → π* of OAc

TABLE 2—*continued*

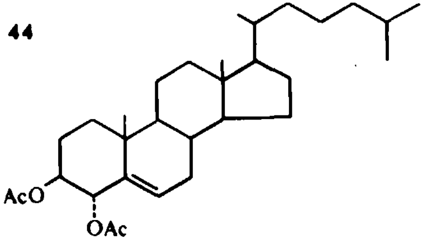
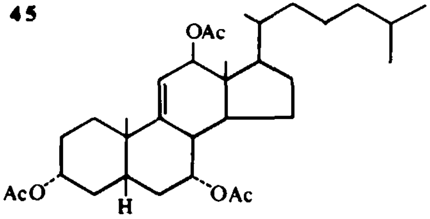
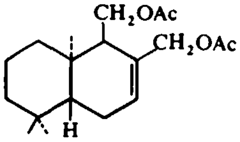
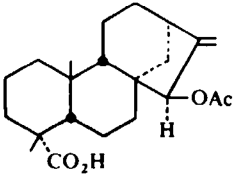
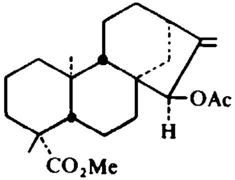
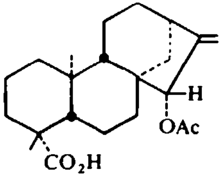
Compound	Solvent	CD		Predicted[a] sign	Comment[b]
		λ(nm)	[θ]		
44 	Cyclohexane	217 213 197	−1,300 −1,200 −12,00	 −	OAc OAc Cf. No. 43
45 	Cyclohexane	200 185*	+47,800 −71,600	±	(+) 10β, 18β-CH_3 (−) 12β-OAc
46 	Cyclohexane	258 244 238 199 185*	−4,300 −3,300 −3,600 +23,800 −9,700		} OAc

TABLE 2—*continued*

	Compound	Solvent	CD λ(nm)	CD [θ]	Predicted[a] sign	Comment [b]
47	 Xylopic Acid	MeOH	218·5 213 195*	−3,100 −2,300 −11,100	← +	{ Acetate CO$_2$H n → π* } Positive CD concealed by carbonyl; see No. 24. 48
48		Cyclohexane	222 213 185*	−2,900 −500 −95,800	← +	See No. 47
49		MeOH	205 195*	−14,800 +3,200		

[a] Using the Octant rule, Ref. 1.

[b] Other optically active chromophores (e.g. OAc, > C═O) and/or band overlapping observed in some cases. High octant populations also noted where appropriate.

$\pi_x \rightarrow \pi_x^*$ positive maximum at 205 nm. However, the 15α-acetoxy epimer (No. 49) displays the predicted negative CD at 205 nm (Fig 12).

In summary, the analysis of the 25 alkyl cycloalkenes (Table 1) and the 49 oxygenated cyclohexenes and methylene cyclohexanes (Table 2) provides a satisfactory correlation between the two oppositely signed $\pi \rightarrow \pi^*$ olefinic transitions and the resultant sign of D line rotation. In every case the olefin Octant rule (or its inverse for oxygen substitution) predicts the sign of the *longest* wavelength transition. In most, but not all cases, the $\Delta[M]_D$ values follow the Mills-Brewster rules. The correlation by the CD method, however, is found to be most useful in several examples which cannot be treated by molecular rotation differences and, for many of the examples studied, the availability of only one epimer does not preclude the prediction of absolute configuration.

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