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CIRCULAR DICHROISM AND OPTICAL ROTATORY DISPERSION OF SESQUITERPENE LACTONES

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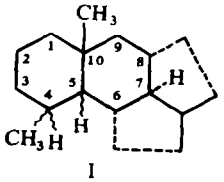
Abstract—The CD curves of a large number of sesquiterpene lactones together with a limited number of ORD curves have been measured. A simple correlation between the sign of the Cotton effect (CE) and the stereochemistry of the α-methylene-γ-lactone chromophore can be deduced from the resulting data. In addition the CE of several ketones (both saturated and unsaturated) and pyrazolines are reported.

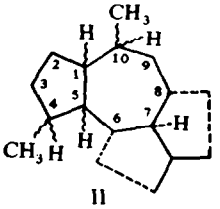
INTRODUCTION

SESQUITERPENE lactones[2–6] have been investigated extensively in recent years. These natural products occur most commonly in five different carbon skeletons (I–V) and possesses a γ-lactone group which occurs as a saturated γ-lactone (VI), as an α-methylene-γ-lactone (VII), or as an endocyclic α,β-unsaturated γ-lactone (VIII) (not yet found in nature). The application of modern spectroscopic methods has been of great value in the determination of the structures of these compounds. In particular, ORD and CD,[7–10] which have been used to solve stereochemical problems in compounds containing a saturated or an unsaturated keto group, have been applied to the study of the saturated γ-lactone chromophore,[11] but have not yet been used extensively for the determination of its stereochemistry. Very recently, Snatzke[12] and Suchy *et al.*[13] have reported investigations on pyrazoline derivatives (IX) which are readily available from VII.

Since a large number of sesquiterpene lactones contain the α-methylene-γ-lactone chromophore (VII) and since no correlation between Cotton effect (CE) and stereochemistry has been reported, we have measured the CD of fourty-four substances containing this chromophore. In a preliminary communication[14] we have described a simple correlation and report here in full our results. These studies also include other chromophores common in this class of natural products as well as earlier results obtained from ORD studies.



I
anolide



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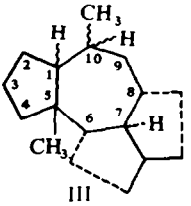

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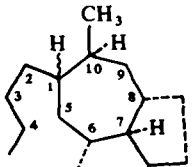

IV
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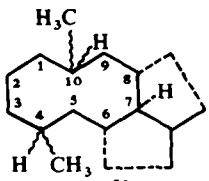
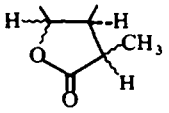
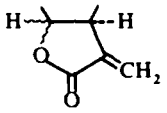


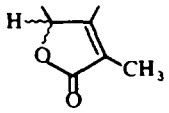
V
germacranolide



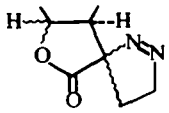
VI



VII



VIII



IX

RESULTS AND DISCUSSION

Our interest was mainly concerned with the n → π* transition of α,β-unsaturated lactones which give rise to an absorption at around 255 nm.[15, 16] In our investigation of the α-methylene-γ-lactone chromophore we have observed the maxima in the CD curves in the range 246–261 nm. Table 1 summarizes the correlation of the sign of the CE and the position and stereochemistry of the lactone ring fusion. A few compounds are not consistent with this rule and will be discussed later. It is important to note that the validity of this correlation is independent of the structural type of the lactone (I–V).

TABLE 1. SIGN OF THE COTTON EFFECT OF THE n → π* TRANSITION OF THE α-METHYLENE-γ-LACTONE CHROMOPHORE

Position \ Ring Fusion	*cis*	*trans*
C-6	+	−
C-8	−	+

Since the lactones *cis* (*trans*) fused at C-6 are pseudoenantiomeric to those *cis* (*trans*) fused at C-8, one expects opposite CE signs for the lactones *cis* (*trans*) fused at C-6 and C-8 respectively. This expectation assumes that the asymmetry of the chromophore or the asymmetry immediately surrounding the chromophore is responsible for the sign of the CE. Our results are in accordance with this assumption. Table 2 shows a very good agreement between the predicted and the observed CE sign. We have also included the data recently reported by Suchý *et al.*[13] who did not give any correlation for the α-methylene-γ-lactone chromophore. Although our rule does not rigorously prove stereochemistry it has been applied with much success to sesquiterpene lactones of all structural types (I–V) containing an α-methylene-γ-lactone chromophore. Furthermore, the inconsistencies occur, with the exception of the germacranolides chamissonin diacetate and heliangenol, only in *cis*-fused lactones closed at C-6.

TABLE 2. CD OF THE n → π* TRANSITION OF THE α-METHYLENE-γ-LACTONE CHROMOPHORE

Compound	Lactone	CE Predicted	CE Found λ_{max} (nm)	CE Found $[\theta]^a$
Santanolides				
Douglanine[17]	*trans*, C-6	−	250	−2780
Pinnatifidin[18]	*cis*, C-8	−	269	−2110 (ethanol)[13]
Artecalin[19]	*trans*, C-6	−	257	−1210
Dentatin diformate[20]	*trans*, C-6	−	258	−2800
Arbusculin A[21]	*trans*, C-6	−	253	−3620
Arbusculin C[21]	*trans*, C-6	−	249	−4040
Dehydrodentatin[20]	*trans*, C-6	−	255	−2440
Cyclized chamissonin diacetate[22]	*trans*, C-8	+	255	+1280
Guaianolides				
Cumambrin B[23]	*trans*, C-6	−	260	−2920
Dehydrocostuslactone[24]	*trans*, C-6	−	265	−830 (ethanol)[13]
Canin[25]	*trans*, C-6	−	250	−2870
Derivative of canin (XXVII)	*trans*, C-6	−	250	−2280
Rupin A[20]	*trans*, C-6	−	250	−2660
Rupin B[20]	*trans*, C-6	−	253	−2940
Pleniradin acetate[26]	*trans*, C-8	+	253	+5600
Ambrosanolides				
Neoambrosin (Fig 1)[27]	*cis*, C-6	+	255	+320
Damsin (Fig 1)[28]	*cis*, C-6	+	250	+496
Coronopilin (Fig 1)[29]	*cis*, C-6	+	246	+1785
			243	+2540 (ethanol)[13]
Deacetylconfertiflorin[30]	*cis*, C-6	+	250	+1620
Apoludin[31]	*cis*, C-6	+	255	−1080[b]
Ambrosiol[32]	*cis*, C-6	+	255	−1870[b]
Ambrosiol diacetate[32]	*cis*, C-6	+	248	−2370
Burrodin[31]	*cis*, C-8	−	254	−3400
Cumanin[33]	*cis*, C-8	−	256	−4360
Aromaticin[34]	*trans*, C-8	+	255	+1900[b]
Paucin[35]	*cis*, C-8	−	255	−4320
Bigelovin[36]	*trans*, C-8	+	255	+800[b]
Dihydrobigelovin[36]	*trans*, C-8	+	255	+274[b]
Ambrosin[37]	*cis*, C-6	+	not observed	
Helenalin[38]	*cis*, C-8	−	not observed	
Psilotropin (Fig 2)[39]	*cis*, C-8	−	254	−3460
Vermeerin (Fig 2)[40]	*trans*, C-8	+	254	+1685
Psilostachyin[41]	*cis*, C-6	+	255	−1550[b]
Psilostachyin C[42]	*cis*, C-6	+	254	−2370
Fastigilin C[43]	*cis*, C-8	−	not observed	
Xanthanolides				
Xanthumin (Fig 3)[44]	*cis*, C-8	−	256	−4730
Xanthinin (Fig 3)[44]	*trans*, C-8	+	255	+3280
Isoxanthanol[44]	*trans*, C-8	+	255	+3340
Xanthanol[44]	*trans*, C-8	+	255	+3150
Germacranolides				
Baileyin[45]	*trans*, C-8	+	255	+1550
Costunolide[46]	*trans*, C-6	−	261	−5460
			264	−4700 (ethanol)[13]
Parthenolide[47]	*trans*, C-6	−	250	−1400

TABLE 2—*continued*

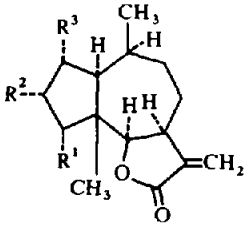
Compound	Lactone	CE Predicted	CE Found λ_{max} (nm)	CE Found $[\theta]^a$
Chamissonin diacetate[22]	*trans*, C-8	+	248	−3630
Jurineolide[13]	*trans*, C-6	−	263	−4900 (ethanol)[13]
Albicolide[48]	*trans*, C-6	−	263	−3400 (ethanol)[13]
Eupatolide[49]	*trans*, C-6	−	261	−5110
Ridentin[20]	*trans*, C-6	−	258	−5860
Heliangenol[50]	*trans*, C-6	−	249	+3910

[a] All values are given in molecular ellipticity. For better comparison the $\Delta\varepsilon_{max}$ values from the literature have been transformed by the equation $[\theta] = 3300 \cdot \Delta\varepsilon_{max}$

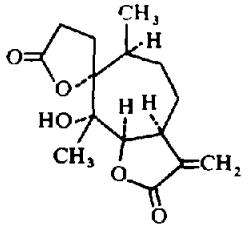
[b] No maximum detected; ellipticity taken at the given value.

Of the 41 sesquiterpene lactones measured whose structure and stereochemistry have been assigned without the aid of ORD and CD, only 7 show a CE sign opposite that predicted by our rule. In three others, helenalin, ambrosin, and fastigilin C, the CE of the $n \rightarrow \pi^*$ transition of the α-methylene-γ-lactone chromophore cannot be detected, possibly due to the cyclopentenone chromophore present in these molecules.

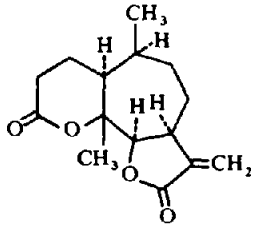
Five compounds of type II (apoludin (X); ambrosiol (XI); ambrosiol diacetate (XII); psilostachyin (XIII); and psilostachyin C (XIV)), all contain an oxygen function near the ring oxygen of a C-6, *cis*-fused γ-lactone and show a CE sign opposite to that expected. It is possible that this oxygen function is responsible for this anomaly.



X: $R^1 = R^3 = OH$
$R^2 = H$
XI: $R^1 = R^2 = OH$
$R^3 = H$
XII: $R^1 = R^2 = OAc$
$R^3 = H$



XIII



XIV

Since both ambrosiol (XI) and ambrosiol diacetate (XII) show the same deviation, H-bonding can be excluded as the cause. A similar inverted CE has been found in 17-oxo-steroids containing a 16β acetoxy group.[51] A second group of deviations contains two compounds (chamissonin diacetate and heliangenol) of the germacranolide type (V). The conformational flexibility of the $\Delta 10^{(1)}$, Δ^4-cyclodecadiene ring may be responsible for these exceptions. On the other hand it is to be noted that our rule predicts the sign of the CE of seven other germacranolides (see Table 2) whose lactone stereochemistry has been shown by other means.

A partial explanation for our rule has been offered by Snatzke, with whom these observations have been discussed. The CE of the R-band of an ene-lactone is governed by the same principles as that of an enone[16] and the sign is therefore determined by the chirality of the chromophore. If, on the other hand, the dissymmetry of the first sphere is very small, the dissymmetry of the second (or third) determines the sign of the CE. Models of *trans*-fused γ-lactones show that if the CE is determined by the first sphere, one can expect a negative value for lactones closed at C-6 and a positive value for those closed at C-8. If the CE is determined by the dissymmetry of the second sphere one can use Legrand's[52] or Beecham's[53] rule to determine the sign of the CE. In this case we would expect a positive CE for the *trans* lactones closed at C-6 and a negative CE for the *trans* lactones closed at C-8. The observed signs show that in *trans*-fused lactones the dissymmetry of the first sphere determines the sign of the CE. Since *cis*-fused γ-lactones are less rigid than their *trans*-fused isomers, models do not indicate whether the first or second sphere determines the sign of the CE. Therefore, from the theoretical point of view, it is surprising that our rule (Table 1) works so well for *cis*-fused lactones.

In this connection it seemed interesting to investigate the CD of the pyrazoline derivatives (IX) of some of the compounds which do not fit our rule. Application of the rule for corresponding ketones[54] to the pyrazoline adducts of α-methylene-γ-lactones allowed Snatzke[12] and Suchý *et al.*[13] to predict the sign of the CE for the azochromophore in *cis*-fused lactones. The results were in full agreement with the predictions. The pyrazoline adducts of lactones *cis*-fused to C-6 show a negative CE; those closed at C-8 show a positive value. No prediction could be made for the pyrazoline adducts of *trans*-fused lactones, but the only two measured (both closed at C-6) showed a positive CE. Each of the five pyrazoline derivatives (Table 3) measured in this study contained a *cis*-fused lactone and showed the expected sign of the CE.

In the pyrazoline derivative of ambrosin the values represent the sum of the contributions from the azochromophore and the cyclopentenone chromophore. The ellipticity at the maximum at 324 nm is mainly due to the n → π* transition of the azochromophore and only to a small extent (less than 10%, see Table 5) due to the cyclopentenone chromophore. However, both azochromophore and cyclopentenone chromophore contribute about the same amount to the maximum at 231 nm.

TABLE 3. THE COTTON EFFECT OF SOME PYRAZOLINE ADDUCTS

Pyrazoline adduct of	Lactone	CE Predicted	CE Found λ_{max} (nm)	CE Found $[\theta]^a$	CE Found λ_{max} (nm)	CE Found $[\theta]^a$
Ambrosiol[32, 55]	*cis*, C-6	–	319	−21400	229	−19700
Ambrosin[37]	*cis*, C-6	–	324	−40100	231	−35100
Psilostachyin[41, 55]	*cis*, C-6	–	323	−36900	233	−13650
Psilostachyin C[42, 55] (Fig 4)	*cis*, C-6	–	320	−25900	232	−17000
Psilotropin[39] (Fig 4)	*cis*, C-8	+	323	+37100	232	+11000

[a] All values are given in molecular ellipticity. For better comparison the $\Delta\varepsilon_{max}$ values from the literature have been transformed by the equation $[\theta] = 3300 \cdot \Delta\varepsilon_{max}$

Although our rule contains some inconsistencies—mostly in the C-6, *cis*-fused lactones of the ambrosanolides—it has been found valuable in solving stereochemical problems. This is best demonstrated by comparing the CD curves of vermeerin and xanthinin (C-8, *trans*) with those of psilotropin and xanthumin (C-8, *cis*) (Fig 2 and Fig 3).

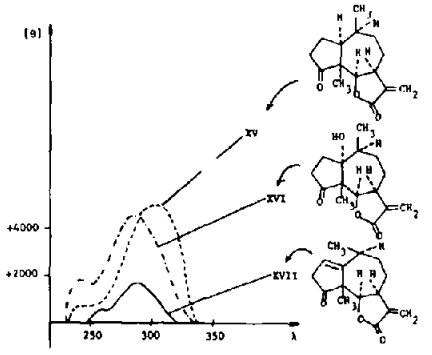


FIG 1. CD curves of damsin (XV) (– – –), coronopilin (XVI) (–·–·–), and neoambrosin (XVII) (———)

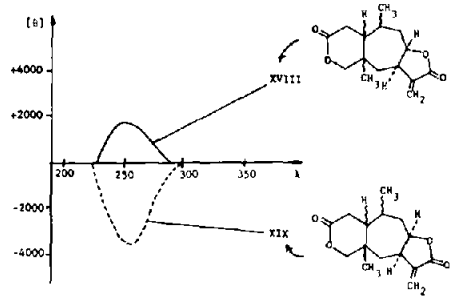
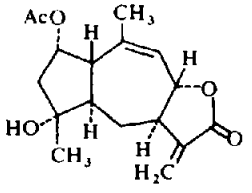


FIG 2. CD curves of vermeerin (XVIII) (———) and psilotropin (XIX) (– – –)

Based on our rule, the stereochemistry of psilotropin, vermeerin, and pleniradin acetate can be assigned as shown in structures XIX, XVIII, and XXIV, respectively. These findings show that the investigation of the CD of both the α-methylene-γ-lactone chromophore and of its pyrazoline derivative should be of value for the determination of the stereochemistry of the lactone ring fusion.



XXIV

In carrying out the study described above, a good deal of information was collected concerning the optical properties of other chromophores in this class of natural products. A common chromophore in these compounds is the ketonic CO group. Our results on saturated ketones are summarized in Table 4. Some similar compounds have been investigated by other groups.[41, 43, 55, 57, 58–60] The sign of the CE of saturated ketones can be predicted by the octant rule.[64] Its application to cyclopentanones[8, 65–67] together with examination of ORD curves of 17-oxosteroids[68] predicts for the investigated ambrosanolides a clear positive CE for the *trans*-fused cyclopentanones and a very weak (in steroids positive) CE for the *cis*-fused systems. Herz *et al.*[59] reported that in *trans*-fused systems the cyclopentanone ring is in a fixed conformation and 14α,17-oxosteroids can be used as models. On the contrary, in *cis*-fused systems, the cyclopentanone ring is flexible whereas in 14β,17-oxosteroids it is held in a rigid conformation. Neoambrosin (XXV), with a double bond

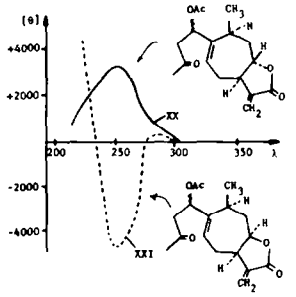


FIG 3. CD curves of xanthinin (XX) (— ——) and xanthumin (XXI) (- - - - -)

at the ring junction, shows a significantly lower (but still positive) ellipticity than do the *trans*-fused compounds. In the ORD curve of isoneoambrosin the CE of the ketone cannot be clearly detected. Herz, *et al.*[59] have measured the ORD of XXVI and have found a weak positive CE (a = +3·9). Δ^{14}-17-Oxosteroids also show a weaker CE than 14α,17-oxosteroids. Models of Δ^{1},4-oxoambrosanolides are not as rigid as those of Δ^{14},17-oxosteroids. The observed CE of the cyclohexanones are in accord with the octant rule. The difference in the amplitude between artecalin and γ-tetrahydrosantonin shows the effect of the stereochemistry of the 4-Me group on the

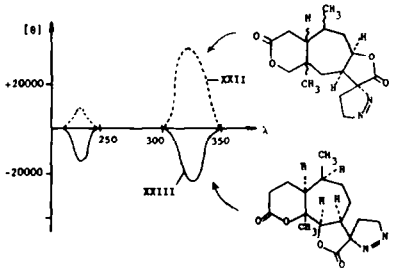


FIG 4. CD curves of the pyrazoline drivatives of psilotropin (XXII) (- - - -) and psilostachyin C (XXIII) (———)

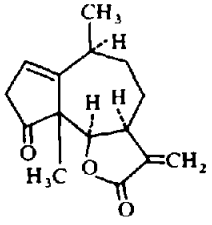
strength of the CE. Compounds containing a 4β-Me group (lying in a negative octant) show a smaller ellipticity than the corresponding 4α-methyl derivatives, where the equatorial 4α-Me group lies in the horizontal symmetry plane. The sign of the CE for the CO group in compound XXVII, which was obtained from canin by treatment with acetone and concentrated sulfuric acid, was not helpful in regard to stereochemistry since the cycloheptane ring is flexible. But together with the IR spectrum

TABLE 4. CD AND ORD OF SATURATED KETONES

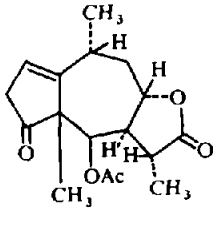
Compound	ORD 1st extremum λ(nm)	[Φ1]	2nd extremum λ(nm)	[Φ2]	amplitude	CD λmax (nm)	[θ]
Cyclopentanones							
Deacetylconfertiflorin[30]	323	+3770	282	−4480	+82·5	304	+6590
Damsin[28] (Fig 1)	—	—	—	—	—	310	+4800
Cornopilin[29] (Fig 1)	307	+2460	260	−3690	+61·5	300	+4290
Neoambrosin[27] (Fig 1)	—	—	—	—	—	292	+1759
Burrodin[31]	317	+3980	282	−1565	+55·4	298	+4100
Paucin[35]	315	+3720	279	−1664	+53·8	299	+3540
Tetrahydrohymenin[35]	—	—	—	—	ca. −2	—	—
Dihydrobigelovin[36]	—	—	—	—	—	295	+5800
Dihydroisoparthenin[61]	322	+525	285	−2620	+31·5	—	—
Isoneoambrosin[61]	322	−1750	not observable		—	—	—
13-Methoxydihydro-coronopilin[55]	—	—	—	—	—	292	+4420
Dihydrocoronopilin[27]	—	—	—	—	—	294	+4140
13-Dimethylaminodihydro-coronopilin[62]	—	—	—	—	—	293	+4100
13-Dimethylaminodihydro-coronopilin hydrochloride[62]	—	—	—	—	—	291	+3840
Paucin aglucone[35]	314	+2800	279	−290	+30·9		
Cyclohexanones	—	—	—	—	—	285	+2370
Dehydrodentatin[20]	—	—	—	—	—	298	+944
γ-Tetrahydrosantonin[63]	—	—	—	—	—	288	+718[a]
Cycloheptanones							
Derivative of Canin (XXVII)[25]	—	—	—	—	—	300	+3290[b]
Acyclic Ketones							
Xanthinin (Fig 3)[44]	—	—	—	—	—	290	+300
Xanthumin (Fig 3)[44]	—	—	—	—	—	290	+500

[a] The ORD of γ-tetrahydrosantonin has been reported by Djerassi *et al.*[56] Their values ($[\Phi_1]_{303} = +1251$; $[\Phi_2]_{276} = +712$; $a = +5{\cdot}4$) correspond well with ours.

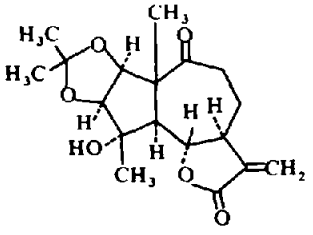
[b] Spectrum taken in methylene chloride.



XXV



XXVI

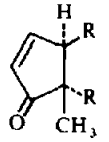


XXVII

(band at 1685 cm^{-1} in nujol) the CD curve clearly established the presence of a keto group.

Two compounds (xanthinin and xanthumin) contain an acyclic ketochromophore. The observed Cotton effects (weakly positive) indicate that the CO groups adopt a preferred conformation in solution. Since C-2 is the nearest asymmetric center the same sign of the CE in xanthinin and xanthumin may indicate that the stereochemistry of the acetoxy groups in these two substances is the same.

Table 5 summarizes the Cotton effects observed for α,β-unsaturated cyclopentenones, a chromophore relatively common in the ambrosanolides (III). The cyclopentenone ring of these natural products is always *trans*-fused to a cycloheptane ring. The ORD of several compounds of this type has been investigated by Djerassi *et al.*[57] Herz *et al.*[59] reported that *trans*-fused cyclopentenones (XXVIII) have a rigid conformation—i.e., a fixed chirality of the chromophore—independent of the conformation of the 7-membered ring. Thus, 14α,Δ^{15},17-oxosteroids can be used as



XXVIII

XXIX

models. But *cis*-fused cyclopentenones (XXIX) in ambrosanolides do not have the same rigidity as 14β,Δ^{15},17-oxosteroids and therefore the sign of the CE cannot be predicted by inspection of models. Snatzke[69] has correlated the sign of the CE and the chirality of the enone chromophore. The ambrosanolides of Table 5 all contain a *trans*-fused cyclopentenone ring and all display a negative CE for the R-band of the ketone. This corresponds to the chirality of the chromophore revealed by inspection of molecular models.

TABLE 5. CD OF α,β-UNSATURATED CYCLOPENTENONES (n → π* Transitions)

Compound	λ_{max} (nm)	$[\theta]$
Bigelovin[36]	326	−4940
Aromaticin[34]	330	−4300
Ambrosin[37]	330	−2600
Fastigilin C[43]	325	−6160[a]
Baileyolin[45]	325	−5640
Radiatin[26]	326	−5190
Plenolin[45]	322	−5210
Helenalin[38]	330	−2820[b]

[a] The ORD of fastigilin C has been reported by Herz *et al.*[59] Their values ($[\Phi_1]_{351} = -5740$; $[\Phi_2]_{306} = -354$; $a = -53{\cdot}9$) correspond well with ours.

[b] The ORD of helenalin has been reported by Djerassi *et al.*[57] Their values ($[\Phi_1]_{365} = -3360$; $[\Phi_2]_{320} = +1190$; $a = -45{\cdot}5$) correspond well with ours.

A few compounds containing a saturated γ-lactone ring have also been examined (Table 6). Several rules exist which correlate the sign of the CE and the stereochemistry[11, 70, 52, 53] of the lactone. However, the sign of the CE usually cannot be predicted in this class of compounds because of the uncertainty of the conformation of the γ-lactone ring. Only in santanolides (I) which have a relatively rigid decalin system can predictions be made. If the conformation can be determined by other means (e.g., NMR and IR[71]) CD is of great value in elucidating the absolute stereochemistry. It will be noted from an examination of the results shown in Table 6 that a bathochromic shift occurs for the maximum of the CD curve when a H atom of the 13-Me group is replaced by an atom containing unshared electrons. The observed shift for oxygen is 10–15 nm and for nitrogen about 20 nm.

TABLE 6. CD OF SATURATED γ-LACTONES

Compound	λ_{max} (nm)	$[\theta]$
Dihydrocoronopilin[27]	215	+3540
13-Methoxydihydrocoronopilin[55]	225	+1250
13-Dimethylaminodihydrocoronopilin[62]	236	+1305
13-Dimethylaminodihydrocoronopilin hydrochloride[62]	220	+2920
13-Methoxydihydropsilotropin[39]	231	−1328
γ-Tetrahydrosantonin[63]	217	+4450

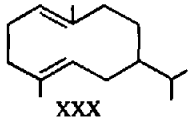
After protonation of the N atom the maximum is observed at the normal position, showing that the unshared electrons are responsible for the bathochromic shift. Despite this, the replacement of a hydrogen of the 13-Me group with oxygen or nitrogen causes very little or no change in the position of the lactone absorption in the IR spectrum.

Two sesquiterpene lactones containing an endocyclic α,β-unsaturated γ-lactone (VIII) have been examined. To our knowledge this type has not as yet been found in nature. These compounds are readily available by chemical means from a number of the corresponding α-methylene-γ-lactones (VII). The observed position CE (Table 7) is consistent with the chirality of the chromophore.[16]

TABLE 7. ORD OF ENDOCYCLIC α,β-UNSATURATED γ-LACTONES (n → π* transition)

Compound	First extremum		Second extremum		Amplitude
	λ(nm)	$[\Phi_1]$	λ(nm)	$[\Phi_2]$	
Dihydroisoparthenin[61]	250	+8050	not observed		—
Isoneoambrosin[61]	258	+8020	228	−39200	+472

Sesquiterpene lactones of the germacranolide type (V) often possess two non-conjugated double bonds ($\Delta^{10(1)}$ and Δ^{4}) (XXX). These two double bonds give rise to an absorption maximum in the UV around 210–230 nm (trans-annular conjugation).[2, 49] These and similar diene systems should show two strong Cotton effects



XXX

of opposite signs at a low wavelength.[7,2] These maxima have recently been observed by Snatzke[12] and by Suchý *et al.*[13] for some sesquiterpene lactones of this type. The only case observed in this study was 13-methoxydihydroeupatolide,[49] which shows a positive maximum at 232 nm ($[\theta] = +42200$). Germacranolides having the same stereochemistry at C-6 and C-7, and the same arrangement of double bonds show a CE of similar position, amplitude, and sign. The sign of the CE associated with this transition can be expected to be dependent on the chirality of the diene system.

EXPERIMENTAL

CD and ORD measurements. ORD and CD curves were measured on a Cary 60 recording spectropolarimeter using a CD accessory, model 6002. The solvent, unless otherwise specified, was methanol; l = 0·1 and 1 cm; c = 0·02 to 0·1%; t = 22°. The reported values of ellipticity and molecular rotation represent the maximum and extremum of each spectrum.

Pyrazoline derivative of psilostachyin. Psilostachyin (23 mg) was dissolved in 4 ml THF and diazomethane in ether was added until the soln remained yellow. After 18 hr at 22° the solvents were evaporated and the crystalline residue recrystallized once from methylene chloride-ether to give 17 mg of fine needles, m.p. m.p. 136–137°. (Found: C, 59·74; H, 6·78. Calc. for $C_{16}H_{22}O_5N_2$: C, 59·61; H, 6·88%).

Pyrazoline derivative of psilostachyin C. Psilostachyin C (52 mg) was dissolved in 4 ml of chloroform and diazomethane in ether was added until the soln remained yellow. After 3 hr at 22° the solvents were evaporated and the residue crystallized from acetone-ether. Recrystallization from the same solvents gave thick leaflets, m.p. 136–137°, showing different behavior on TLC [benzene-MeOH-(9:1)] from the above mentioned pyrazoline derivative of psilostachyin. The mass spectrum showed the following important peaks: *m/e* 306 (M, weak); 278 (M-28); 260; 139; 111.

Pyrazoline derivative of ambrosiol. Ambrosiol (23 mg) was dissolved in 4 ml of THF, cooled to 0° and diazomethane in ether added until the soln remained yellow. After 3 hr at 0° the solvents were evaporated. The residue crystallized from CH_2Cl_2-ether was recrystallized from acetone-ether to give 12 mg of fine needles, m.p. 153–154°. (Found: C, 62·52; H, 7·91: Calc. for $C_{16}H_{24}O_4N_2$: C, 62·31; H, 7·85%).

13-Methoxydihydrocoronopilin. One ml of a soln made by dissolving 93 mg Na in 10 ml abs MeOH was added to 167 mg coronopilin in 3 ml abs MeOH. After 4 days at 0° the formed crystals (125 mg) were filtered off and gave, after two recrystallizations from chloroform, 13-methoxydihydrocoronopilin, m.p. 235–236°. The NMR spectrum (60 Mc in $CDCl_3$; TMS internal standard) was as follows: δ 1.18 s (3H); δ 1·22 d (3H, J = 8 cps); 2·5 m (2H); δ 3·60 t (2H, J = 5 c/s); δ 4·98 d (1H, J = 8 c/s); δ 3·39 s (3H). (Found: C, 64·57; H, 7·93. Calc. for $C_{16}H_{24}O_5$: C, 64·84; H, 8·16%).

Tetrahydrohymenin. Hymenin (14 mg) in 1 ml 95% EtOH was hydrogenated over 20 mg PtO_2 at 22° and atm press. After 27 hr the soln was filtered and the filtrate evaporated to dryness. Crystallization of the residue from ether-hexane gave 6 mg of tetrahydrohymenin, m.p. 146–150°. The mass spectrum showed the molecular ion at *m/e* 266 and an intense peak at *m/e* 248 (M-H_2O). A peak at *m/e* 264 indicated an impurity in the sample (dihydrohymenin or dihydroisohymenin).

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