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OPTICAL ROTATORY DISPERSION AND CIRCULAR DICHROISM OF δ-LACTONES

DETERMINATION OF THE ABSOLUTE CONFIGURATION OF (+)5-DECANOLIDE AND (+)5-DODECANOLIDE

O. Korver
Unilever Research Laboratory, Vlaardingen, The Netherlands

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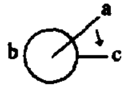
Abstract—ORD and CD measurements were made on (+)5-decanolide (tetrahydro-6-pentyl-2H-pyran-2-one) and (+)5-dodecanolide (tetrahydro-6-heptyl-2H-pyran-2-one). From the CD measurements, the absolute configuration of the asymmetric centre can be established as *RS*. From low-temperature CD measurements it is concluded that in 5-decanolide the half-chair conformation is more stable than the boat conformation.

The relation between the sign of the Cotton effect of optically active lactones and their absolute configuration has been discussed by several authors. Jennings *et al.*[1] formulated a sector rule, analogous to the octant rule, but more difficult to use. Wolf[2] related the sign of the Cotton effect of δ-lactones to the chiral character of the 6-membered ring. Legrand and Bucourt[3] simplified Wolf's rule and extended its use to 5-membered lactone rings.

We have used the approach of Legrand and Bucourt to determine the absolute configuration of the lactones of 5-hydroxy-decanoic and -dodecanoic acid (5-decanolide and 5-dodecanolide)*. These lactones occur, in optically active form, in numerous natural substances, such as fats,[4] but the relation between the sign of rotation and the absolute configuration has not been determined.

The following points of the rules of Legrand and Bucourt are important for our purpose:

(a) A dihedral angle formed by three bonds a, b and c is called positive (I) when in the Newman projection the front one (a) has to be rotated clockwise to place it on the back one (c). In the reverse case (II) the angle is called negative.



(I)

(II)

(b) The dihedral angles formed by the sides of a cyclic molecule have a characteristic sequence of signs for each conformation. This is demonstrated for the half-chair and the boat conformation in III and IV respectively (the antipodes have opposite signs).

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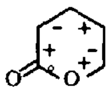
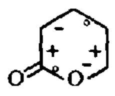
* The corresponding Chemical Abstracts names are tetrahydro-6-pentyl-2H-pyran-2-one and tetrahydro-6-heptyl-2H-pyran-2-one.

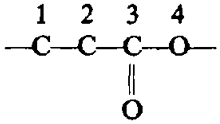


(III)



(IV)

(c) The sign of the Cotton effect of the lactone chromophore is opposite to that of the dihedral angle between $C_1C_2C_3$ and $C_2C_3O_4$ in the system:



$$-\overset{1}{C}-\overset{2}{C}-\underset{\underset{\displaystyle O}{\|}}{\overset{3}{C}}-\overset{4}{O}-$$

RESULTS

The UV spectrum of the lactones shows an absorption maximum at 221 nm ($\varepsilon = 50$) in hexane. According to Closson and Haug[5] this is a $n \rightarrow \pi^*$ transition. The CD spectrum, however, displays two bands (Fig. 1): a positive one at about 210 nm and a negative one at about 240 nm. Such a "double-humped" curve with a separation between the maxima of about 30 nm is the characteristic result obtained from two overlapping bands with opposite sign separated by a few nm.[6]

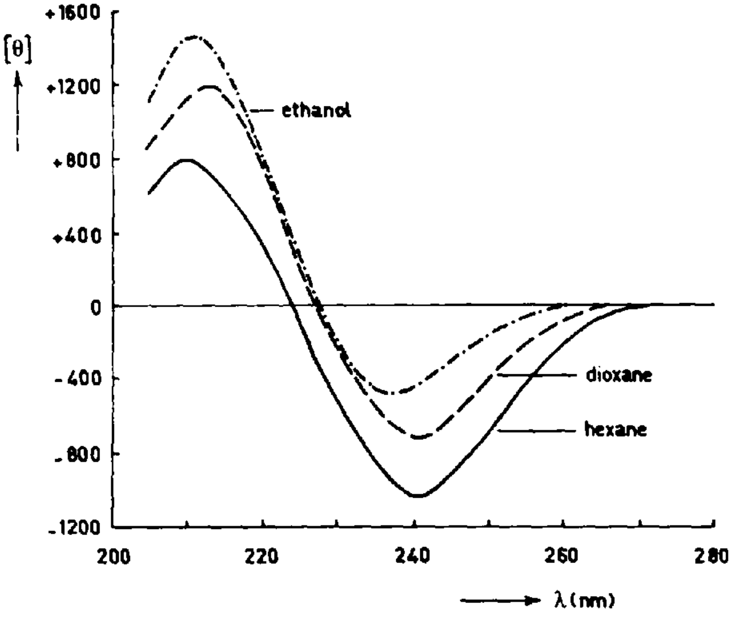


Fig 1. Circular dichroism spectrum of 5-decanolide in hexane, dioxane and ethanol

The two Cotton effects of the CD spectrum are both discernible in the ORD curve (Fig 2). The lactones used were dextrorotatory and of 100% optical purity with the following specific rotations: 5-decanolide: $[\alpha]_D = +57{\cdot}7°$ (pure substance) and $+53{\cdot}5°$ (1·4 g/100 ml EtOH); 5-dodecanolide: $[\alpha]_D = +48{\cdot}5°$ (pure substance) and $+46{\cdot}3°$ (1·4 g/100 ml EtOH). CD and ORD data are collected in Tables 1 and 2.

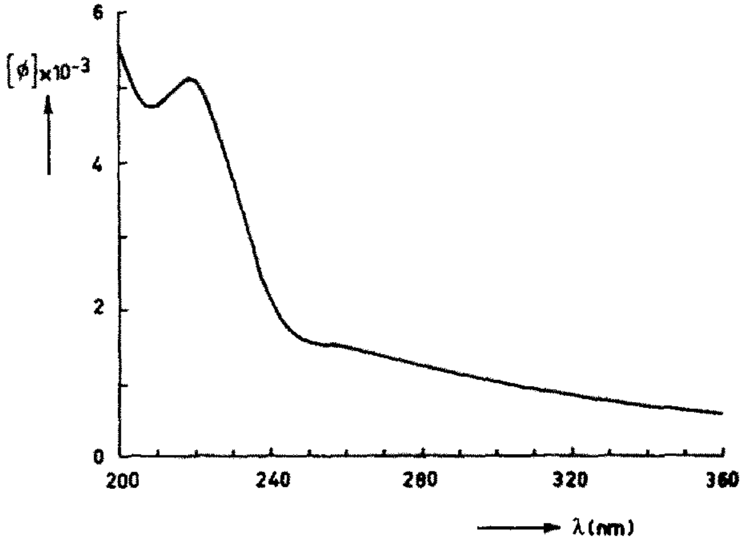
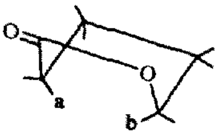


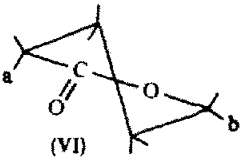
FIG 2. Optical rotatory dispersion curve of 5-decanolide in ethanol

DISCUSSION

The two bands in the CD-spectrum of a δ-lactone have been ascribed to the boat conformation ($\lambda < 225$ nm) and the half-chair conformation ($\lambda > 230$ nm)[2]. It has been assumed on the basis of X-ray analyses that a δ-lactone is normally in the boat conformation (V), with a planar lactone group (see Ref. 2 and references cited there).



(V)



(VI)

When the lactone is substituted in position a and/or b, 1,4-interactions that may force the molecule into the half-chair conformation (VI) arise.

The δ-lactones studied here have alkyl groups in the b position. The two bands in the CD spectrum of the lactones reflect the presence of both the boat and the half-chair conformation. The presence of this conformational equilibrium is confirmed by the solvent dependency of the CD spectrum (Table 1) and the low-temperature CD measurements (Fig 3).

Assuming the absolute configuration represented in VII, and using the rules of Legrand and Bucourt,[3] the sign of the Cotton effect of the bands can be predicted, as indicated in Table 3.

The experimental results (positive Cotton effect at 210 nm for the boat conformation, negative Cotton effect at 240 nm for the half-chair conformation) agree with the presence of b_I and C_I for the absolute configuration given in VII. For the antipodes all signs reverse and the presence of the antipodes of b_{II} and C_{II} would be in agreement with experiment. In these conformations the alkyl groups R are in an axial position,

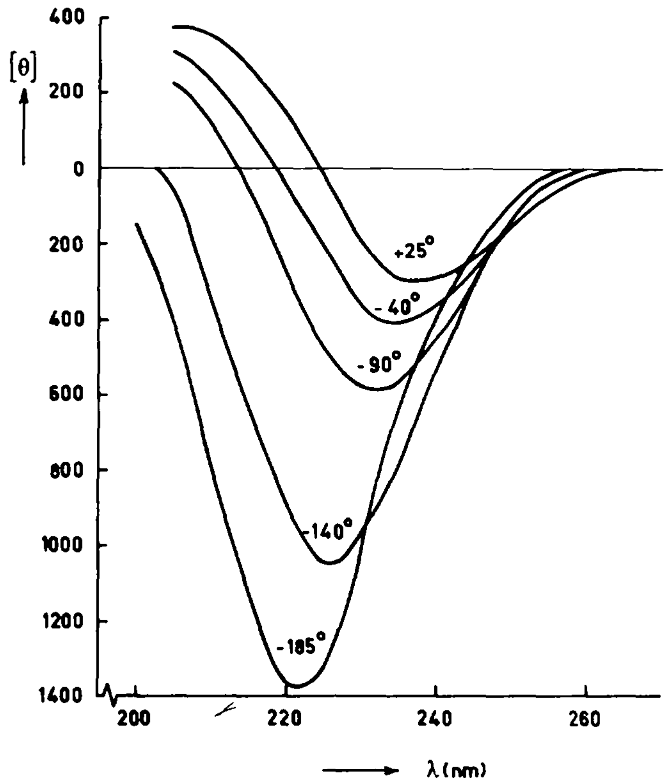
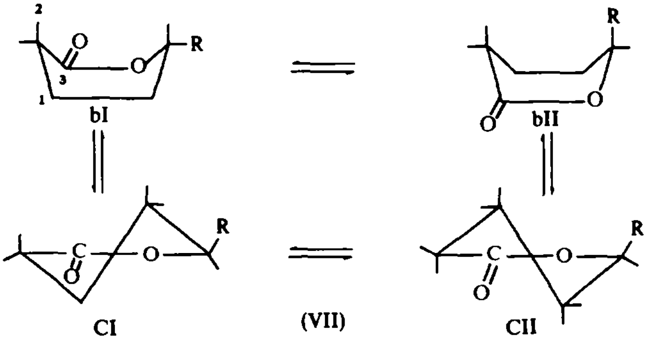


FIG 3. CD-spectra of 5-decanoide at different temperatures, measured in diethylether: isopentane: ethanol (5:5:2 v/v/v)



so that unfavourable 1,3 and 1,4 interactions arise. It may be assumed, therefore, that the lactones studied have the absolute configuration as given in VII. Following the sequence rule of Cahn *et al*[7] the asymmetric centre has the (*RS*) configuration. The systematic names of the lactones are therefore (*RS*)-tetrahydro-6-pentyl-2*H*-pyran-2-one and (*S*)-tetrahydro-6-heptyl-2*H*-pyran-2-one.

In agreement with the result obtained in this investigation is the fact that 5-hexanolide ((−)-dihydro parasorbic acid; (−)-tetrahydro-6-methyl-2*H*-pyran-2-one), the absolute configuration of which is known to be *SR*, has the following CD characteristics in isooctane.[8]

$$\lambda = 242, [\theta] = +725$$
$$\lambda = 213, [\theta] = -860$$

Interesting results have also been obtained by low-temperature CD measurements of 5-decanolide. The data in Fig 3 show that the intensity of the high wavelength band gradually increases with decreasing temperature. At the same time the wavelength of the negative maximum shifts from 238 at +25° to 222 nm at −185°. The latter wavelength is the wavelength of maximum UV absorption.

Two conclusions can be drawn from these data:

(a) The half-chair conformation is more stable than the boat conformation in 5-decanolide.

(b) At −185° the conformational equilibrium has shifted *completely* to the side of the half-chair conformation. The presence of the positive band of the boat conformation at slightly lower wavelength produces a red shift in the negative maximum at temperatures higher than −185°.

TABLE 1. MAXIMUM ELLIPTICITIES (θ) OF 5-DECANOLIDE AND 5-DODECANOLIDE IN DIFFERENT SOLVENTS

Sample	Hexane		Dioxane		Ethanol	
	λ	$[\theta]$	λ	$[\theta]$	λ	$[\theta]$
5-decanolide	241	−1040	240	− 720	237	− 490
	210	+ 780	213	+1180	210	+1450
5-dodecanolide	241	−1080	240	− 790	237	− 560
	209	+ 710	212	+1070	211	+1340

TABLE 2. MOLECULAR ROTATIONS OF 5-DECANOLIDE AND 5-DODECANOLIDE IN ETHANOL (CONC. = 1·4 G/100 ML) AT DIFFERENT λ

λ Sample	589	350	300	280	260	240	220	208	200
5-decanolide	91	570	965	1185	1425	2180	5105 p	4730 t	5650
5-dodecanolide	79	630	975	1200	1440	2255	5195 p	4795 t	5670

TABLE 3. RELATION BETWEEN DIHEDRAL ANGLE AND PREDICTED SIGN OF COTTON EFFECT FOR DIFFERENT CONFORMATIONS

	b_I	b_{II}	C_I	C_{II}
Dihedral angle in the system $C_1C_2C_3O$	<0	>0	>0	<0
Predicted sign of the Cotton effect	>0	<0	<0	>0

EXPERIMENTAL

The lactones were obtained by microbiological reduction of purified keto acids.[9] ORD and CD measurements were carried out on a FICA Spectropol I. Molecular rotations (ϕ) and ellipticities (θ) were calculated as:

$$\phi \text{ (or } \theta) = \frac{M \, . \, \alpha}{1 \, . \, c},$$

where M = mol wt, 1 = cell length (in dm), c = concentration (in g/100 ml) and α = measured rotation.

The UV spectra were measured on a Cary 14 spectrophotometer. The low-temp CD measurements were made on a Jouan Dichrograph in EPA solvent (diethylether:isopentane:ethanol, 5:5:2 v/v/v).

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