Tetrahedron Letters No. 43, pp 3761 - 3764, 1974. Pergamon Press. Printed in Great Britain.

THE π-π* CIRCULAR DICHROISM OF αβ-UNSATURATED γ-LACTONES

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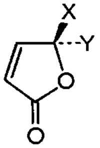
(Received in Japan 21 August 1974; received in UK for publication 18 September 1974)

Snatzke[1] and Beecham[2] proposed the rules relating the sign of the n-π* Cotton effect to the C=C-C=O chirality in endo-αβ-unsaturated lactones. These rules, however, in which sign and chirality have a contrary relationship, are ambiguous when applied to butenolides, because the ring atoms of most butenolides are coplanar. In fact, X-ray analysis of nine compounds containing variously substituted butenolide rings shows a maximum deviation of the C=C-C=O torsional angle from 180° of 3.9°.[3] Besides the n-π* Cotton effect, αβ-unsaturated γ-lactones usually show a Cotton effect associated with the π-π* transition in the region 205-235 nm. We have found that the chirality at the γ-carbon atom of the butenolide ring is the sign determining factor for the π-π* CD. Thus, in the diagram below, if the γ-carbon is assymmetrically substituted ($X \neq Y$), where neither substituent X nor Y can be in axial or equatorial orientation as the butenolide has planar conformation, the sign of the π-π* Cotton effect is negative when $X > Y$ in polarizability, and positive when $X < Y$.



Type A, $X > Y$, negative π-π* C.E.

Type B, $X < Y$, positive π-π* C.E.

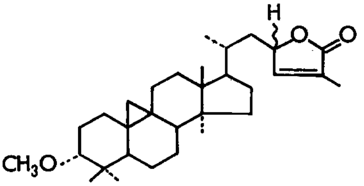
The results listed in the TABLE show that this new empirical rule can be applied to all compounds with the exception of linderenolide (IX) and its acetate (X) containing an allylic oxygen substituent. This rule can be understood as follows; in butenolides, the chromophore not only consists of the orbitals of the C=C-C(=O)-O moiety but also includes the σ-bond of the substituent on the γ-carbon atom. Consequently, the chirality of the part with (π-σ)-conjugation predominates over that of the part with (π-π)-conjugation, with the result that the chirality at γ-carbon atom contributes to the sign-determining factor for the π-π*

TABLE

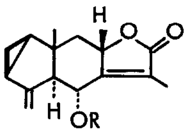
CD Data for αβ-Unsaturated γ-Lactones[a]

No.	Compounds	Type	Solv.*	λmax (Δε) n-π*	λmax (Δε) π-π*	Ref.
I	R(-)-2-Dodecyl-4-methylbut-2-enolide	A	D	245(+0.04)	210(-4.29)	7
II	Abieslactone	A	M	246(+0.12)	210(-13.6)	8
III	Cyclograndisolide	A	D	250(+0.11)	215(-13.3)	9
IV	Epicyclograndisolide	B	D	250(+0.52)	215(+11.9)	9
V	17β-Acetoxy-1-methyl-3-oxa-A-norestr-1(10)-en-2-one	A	M	274(+0.11)	235(-10.2)	10
VI	Lindestrenolide	B	D		215(+21.9)	11
VII	Hydroxylindestrenolide	B	D	248(+5.28)	210(+24.6)	11
VIII	Tetrahydrolindestrenolide	B	D	250(+1.22)	220(+11.2)	11
IX	Linderenolide	B	D	245(+3.03)	219(-24.1)	11
X	Linderenolide acetate	B	D	250(+1.40)	221(-16.0)	11
XI	Neolinderene	B	D	240(+3.23)	222(+ 9.9)	12
XII	Pseudoneolinderene	B	D	271(-0.39)	220(+15.2)	12
XIII	Tetrahydroelephantopin	A	M		223(- 5.4)	13
XIV	Anhydroginkgolide-A acetate	B	M	253(-5.67)	225(+12.0)	14
XV	3β-Acetoxy-16α-hydroxybisnor-5α-chol-17(20)-enic 22-16-lactone	A	M	249(+9.15)	218(-39.4)	15
XVI	Teucvin	B	D		233(+20.2)	16
XVII	Hexahydroteucvin	B	D	258(+0.35)	231(+15.5)	16
XVIII	Teucvidin	A	D		231(-13.9)	17
XIX	3β,17α-Dihydroxy-norchola-5,20(22)-dien-23,17-lacton	A	D	251(-1.28)[b]	225(-12.9)[b]	1
XX	Loliolide	A	M	268(+0.02)	219(-16.1)	18
XXI	16,21a-Epoxy-21-isopropyldigitoxigenin 3-acetate		M	252(-11.5)	225(+ 3.3)	19
XXII	16,21a-Epoxy-21-hydroxy-21-isopropyl-digitoxigenin 3-acetate		M	259(-12.9)	223(+ 8.8)	19

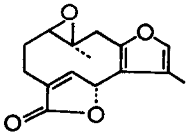
* D = dioxane, M = methanol; [a] C.d. curves were measured for ca. 0.1% solutions with a JASCO Model ORD/UV-6 spectropolarimeter. [b] Ref. 1.



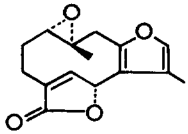
III 23R (---H)
IV 23S (—H)



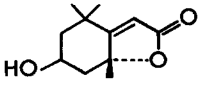
IX R = H
X R = Ac



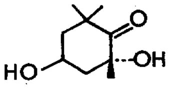
XI

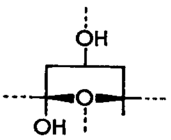


XII

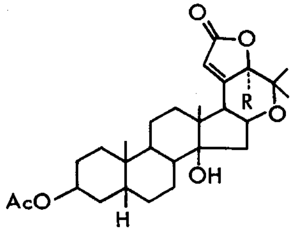


XX





XXIII



XXI R = H
XXII R = OH

CD. The abnormality exhibited by compounds IX and X can be explained on the basis of the overwhelming contribution of the left-handed chirality of the allylic oxygen substituent-double bond helix. The influence of allylic oxygen on the sign of the Cotton effect associated with the lowest frequency π-π^* transition in olefins,[4] dienes,[5,6] enones,[5,6] ene-acids,[6] and ene-lactones[2] has been described recently.

In contrast to the π-π^* Cotton effect, the sign of the n-π^* Cotton effect of butenolides is easily influenced by the contribution of the asymmetry external to the ring (III, IV and XI, XII). We therefore conclude that our rule for the π-π^* CD is better applicable than that for the n-π^* CD for determination of the absolute configuration of butenolides.

With the help of this rule, loliolide is assigned the absolute configuration shown in XX, which represents the antipode of that assigned by Snatzke[1] on the basis of the n-π^* CD. Ketol (XXIII) obtained by ozonolysis of loliolide exhibits the positive CD maximum ($\Delta\epsilon = +0.69$) at 308 nm in methanol, and it is possible to assign the absolute configuration to XXIII from the octant projection with an axial α-hydroxy group. This observation adds support to the absolute configuration XX of loliolide, which has been established chemically only recently.[20,21]

Also by the application of this rule, 16,21a-epoxy-21-isopropyl-digitoxigenin 3-acetate and its 21-hydroxy derivative belong to type B and are assigned formula XXI and XXII, respectively.

The authors are grateful to Professor S. M. Kupchan, University of Virginia, Dr. H. Irie, Kyoto University, Drs. Ken'ichi Takeda, T. Komeno, T. Sugasawa, K. Okabe, T. Wada and K. Aoyama, Shionogi Research Laboratory, for their generous gift of the samples used in this study and to Mr. T. Iwata for his cooperation in CD measurements.

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