π-π* CIRCULAR DICHROISM OF α-CYCLOPROPYL- AND α-EPOXY-KETONES

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Conjugated non-planer ketones have been considered as inherently dissymmetric chromophores, at least for the π-π* transition, and the helicity rule was advanced for correlating the chirality of the chromophore with the sign of the K band Cotton effect (1), while a "reverse octant rule" was found to apply for the R-band Cotton effect (2). Similarly, studies by Legrand (3), Djerassi (4) and Snatzke (5) on the optical activity of α-cyclopropyl- and α-epoxy-ketones also led to the proposal of a "reverse octant rule" (4). In these cases, the conjugative effect of the three-membered ring on the carbonyl group was considered to be responsible for the inversion (4).

In addition to the n-π* Cotton effect at 270-280 mμ, α-cyclopropyl and α-epoxy-ketones should be expected to exhibit a π-π* (6) Cotton effect near 200 mμ, the sign of which would be mainly governed by the chirality of the chromophores, as in the case of αβ-unsaturated ketones. We have measured the CD spectra of some twenty of these ketones, shown in the FIGURE, in the 200-400 mμ region and have observed the expected Cotton effect. Moreover, we have found a correlation between the chirality of the chromophores and both the sign of the π-π* Cotton effect and the molecular ellipticity [θ]. These correlations should find application in conformational and stereochemical studies.

The results listed in the TABLE disclosed that, without exception, the Cotton effects near 210 mμ showed solvent shifts similar to that observed for αβ-unsaturated ketones, in accord with the transition having a π-π* character.

n-π* COTTON EFFECT

Although the sign of the n-π* Cotton effect follows the "reverse octant rule"

I   VII   IX   X

XII   XIII   XIV   XIX   XX
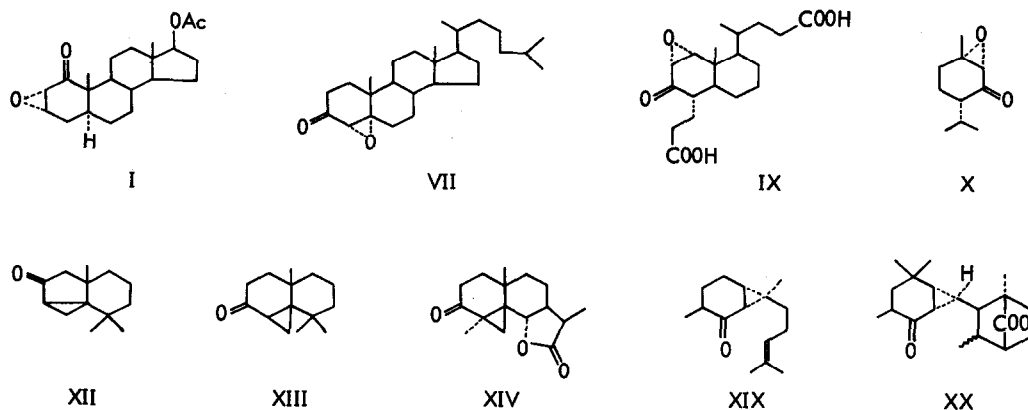
FIGURE

for many of the compounds examined in both the cyclopropyl and the epoxy series, the contribution of atoms and groups other than the three-membered ring can not be ignored. Thus, compounds II (8), V (8) and XVII (9) exhibit Cotton effects with signs opposite to that predicted by the rule. These anomalities can be explained on the basis of the overwhelming contribution of the remainder of the molecule (apart from the three-membered ring): The situation is clearly shown in the octant projections below.

II   V   XVII
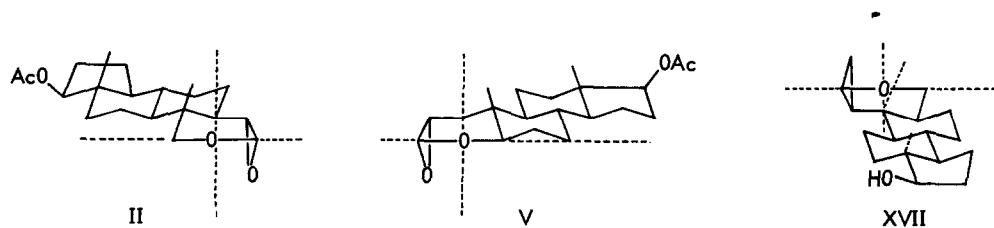
In the cyclopropyl series, another type of exception has already been observed for $n-\pi^*$ Cotton effects (4); (+) carone exhibited a positive Cotton effect, whereas a negative sign was predicted by the "reverse octant rule". Similar abnormalities were observed for the ketone XIX derived from sesquicarene (19) and the lactone (XX) obtained from anhydrotaxininol (20).

$\pi-\pi^*$ COTTON EFFECT   In contrast to the $n-\pi^*$ Cotton effect, the $\pi-\pi^*$ Cotton effect shows no such abnormalities within the same series (I-XI and XII-XX), and its sign depends on which octant the 3-membered rings appear in and is not affected by the remainder of the molecule. However, as explained below,

TABLE
CD Data of α-Epoxy- and α-Cyclopropyl-ketones

Formulae	Compounds	Solvent[†]	$[\theta]$ $(\lambda_{max}$ mμ)		Source[§] and ref.
			n-π* CE	π-π* CE	
I	2α,3α-Epoxy-17β-acetoxy-5α-androstan-1-one	M	−4080(321)	−9800(208)	T(8)
		H	−4110(325)	−12300(205)	
II	2α,3α-Epoxy-17β-acetoxy-5α-androstan-4-one	M	−3020(300)	+16000(200)!	T(8)
		H	−2720(310)	+15000(200)!	
III	1α,2α-Epoxy-17β-acetoxy-5α-androstan-3-one	M	+7940(305)	+20300(200)!	T(8)
		H	+7770(313)	+18300(200)!	
IV	1α,2α-Epoxy-7β-hydroxy-5α-cholestan-3-one	M	+5850(308)	+15400(200)	N(10)
		H	+6140(312)	+15900(200)!	
V	3α,4α-Epoxy-17β-acetoxy-5α-androstan-2-one	M	+3090(301)	−8890(205)	T(8)
		H	+1920(314)	−8840(203)	
VI	3β,4β-Epoxy-17β-acetoxy-5α-androstan-2-one	M	+9490(309)	+9030(206)	T(8)
		H	+9290(316)	+8600(200)!	
VII	4α,5-Epoxy-5α-cholestan-3-one	M	−15890(302)	+1000(223),−3000(205)	I(11)
		H	−14240(311)	+900(219),−[††]	
VIII	4β,5-Epoxy-5β-cholestan-3-one	M	+11250(307)	+2300(214),−2900(201)	I(12)
		H	+13950(314)	+5200(211),−4900(198)!	
IX	Epoxide from etianic acid	M	+12400(312)	+6870(205)!	H
X	(−)Epoxide from (+)piperitone	M	−6180(305)	−4470(210)!	K(13)
XI	Dihydrosantonin α-epoxide	M	−8240(303)	+13500(205)![b]	I(14)
		H	−9110(310)	+14700(195)![b]	
XII	Pyroketone from Thujopsene	M	+20100(283)	−25200(206)	I(15)
		H	+12300(289)	−22500(198)	
XIII	Dihydromayurone	M	+13340(287)	−29600(209)	I(15,16)
		H	+11600(299)	−27000(204)!	
XIV	4β,5-Methylene dihydro-santonin	M	+1710(290),+660(240)[a]	−18700(208)	I(17)
		M+NaOH	+2150(285)	−18200(212)	
		D	+1450(296),+1630(231)[a]	−18320(206)!	
XV	4β,5-Methylene 5β-cholestan-3-one	M	+8900(284)	−19200(212)	I(18)
		D	+8020(293)	−19200(210)	
		H	+7230(298)	−17600(202)	
XVI	4α,5-Methylene 5α-cholestan-3-one	M	−10010(280)	+16000(214)	I(18)
		D	−8130(288)	+6330(220)!	
		H	−7190(295)	+14800(203)	
XVII	1β,2β-Methylene 17β-hydroxy-5α-androstan-3-one	M	+8180(279)	+3750(225)!	W(9)
		H	+5070(288)	+2530(215)!	
XVIII	1β,2β-Methylene 17β-acetoxy-5β-androstan-3-one	M	−430(300),+1160(271)	+2210(225)!	W(9)
		H	−570(318),+910(280)	+320(226)	
XIX	Sesquicarene derivative	M	+7250(287)	+10000(217)[b]	O(19)
XX	Lactone from anhydrotaxininol	M	−350(318),+4250(282)	+8860(214)[b]	U(20)
		M+NaOH	−210(315),+4690(282)	+10800(210)	

† M = methanol; H = isooctane; D = dioxane   ! last reading

†† Although the sign of the Cotten effect was clearly defined from the curve, the absolute value could not be determined.
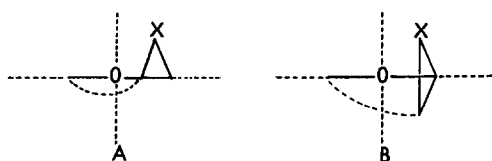
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a) Ascribed to n-π* Cotton effect due to γ-lactone.

b) n-π* Cotton effect due to the lactone appears as an inflection at around 230 mμ.

epoxy ketones and cyclopropyl ketones having the same absolute configuration show Cotton effects with

opposite sign, the "reverse octant rule" being applied to the formers and the "normal octant rule" to the

latters. The magnitude of the $[\theta]$ values is generally close to or greater than 10,000.

Cyclopropyl ketones   The sign of the $\pi-\pi^*$ Cotton effect follows the normal octant rule. Although the

magnitude of $[\theta]$ values usually exceeds 10,000, very small values have been observed for several com-

pounds. If the chirality of the chromophor is the predominant factor contributing to the $\pi-\pi^*$ Cotton effect,

the conformation of the chromophore would determine the magnitude of ellipticity as well as the sign of

the Cotton effect. Depending on the conformation of the ring containing the chromophore, the three

membered ring would tend to be either com-

pletely in one octant (as in A) or spread over

two octants (as in B). The conformation A, in

which one side of the three-membered ring is

on or near the plane of the carbonyl, would

contribute more asymmetrically to the $\pi-\pi^*$

X = CH$_2$ for cyclopropyl ketones
X = 0 for epoxyketones

transition than the conformation B, in which the plane of the carbonyl bisects the cyclopropyl ring. Hence

conformation A would result in larger $[\theta]$ values than conformation B. This assumption is supported by the

large $[\theta]$ values observed for compounds XII and XIV, the conformations of which are fixed as in A, and

the small values observed for compounds XVII and XVIII, both of which are assumed to be in conformation

B because of the release of the nonbonded interaction between 19 methyl and cyclopropyl methylene for

XVII and between 4a-H, 7a-H and 9a-H in XVIII. The relatively small $[\theta]$ values for XIX and XX can

be explained in terms of the conformational flexibility.

Epoxy-ketones   When the cyclopropane ring is replaced by an epoxide ring having the same absolute

configuration, the sign of the $\pi-\pi^*$ Cotton effect is reversed. This is explained as follows: The $\pi-\pi^*$

transition in the epoxy ketone can mix with the n-σ^* transition of the epoxy ring by direct overlap of the

lone-pair electrons on the epoxide oxygen with the π-orbital of the carbonyl. If the magnetic transition

moments (μ) due to the $\pi-\pi^*$ and the n-σ^* transitions have opposite sign, the rotational strength is de-

pendent on which of these two moments makes the predominant contribution. When the latter is larger

(this corresponds to conformation B), the sign of the $\pi-\pi^*$ Cotton effect is governed by the $\mu_{n-\sigma^*}$ and

always results in the sign being opposite to that of the cyclopropyl ketone with identical absolute con-

figuration and a large [θ] value. When the magnitude of both magnetic transition moments are com-

parable (this corresponds to the conformation A), the [θ] values are always small and their sign is

governed by whichever of the two moments predominates (21). Compounds VII, VIII and IX are typical

examples of this category, and the large values of the n→π* Cotton effect in these cases support this

conclusion. The small [θ] values of both the n→π* and the π→π* Cotton effect obtained in the case of

compound X can be attributed to conformational flexibility in the molecule. This discussion is only

applicable to ketones having no strongly perturbing group near the oxide oxygen. The presence of such

a group may change the whole situation as exemplified by the large positive [θ] value for XI, contrary

to the prediction of a negative value (22).

In addition to the expected maxima, additional maxima have been observed for both the n→π* (XVIII,

XX) and the π→π* (VII, VIII) Cotton effects. Although this might mean, in the first two cases, that the

compounds exist in conformational equilibrium in solution, the reason for the last two cases is not yet

clear.

Although the samples examined are limited both in number and in type, the result obtained can be

summarized as follows: In CYCLOPROPYL KETONES, i) the sign of the π→π* Cotton effect is

determined by the sign of the octant in which the methylene group lies, the "normal octant rule" being

applied; ii) the magnitude of the [θ] value reflects the conformation of the ring containing the

chromophore, conformation A producing a large [θ] value and conformation B a small value. In

EPOXY KETONES, i) the sign of the π→π* Cotton effect follows the "reverse octant rule" and is

determined by the sign of the octant in which the oxide oxygen is located; ii) the magnitude of the

[θ] value depends on the conformation of the ring containing the chromophore, thus conformation A

producing a small value and conformation B a large value. In both systems, however, the presence of

a strongly perturbing group in the vicinity of the oxygens may change the situation.

A compilation of data for other compounds is in progress in order to establish the generality and

limitation of this rule.

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21. In the cases examined, the μn-σ* seems always larger than μπ-π*, thus allowing the "reverse octant rule" applicable without exception.

22. ORD curves of the epimeric 3,4-dihydroxydihydroumbellulone (R. T. Gray and H. E. Smith, Tetrahedron, 23, 4229 (1967)) implies a strong negative π-π* Cotton effect, contrary to the predicted positive sign. An intramolecular hydrogen bonding may be responsible for the inversion of sign in α-cyclopropyl ketones.