Circular Dichroism of Ketones at 185—195 nm

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Summary Many steroid ketones exhibit a strong Cotton effect in the region of 190 nm: α- and β-axial methyl or methylene groups appear to make large contributions, with signs determined by the Octant rule.

THE chiroptical properties of the $n \rightarrow \pi^*$ transition in saturated ketones (at *ca.* 290 nm) have been intensively studied, and are summarised in the familiar Octant rule,[1] with its more recent modifications.[2] Modern c.d. instruments, which can penetrate to about 184 nm, have made the shorter wavelength absorption band of ketones (*ca.* 190 nm, $\epsilon \sim 10{,}000$) accessible for measurement. This band has been attributed to the allowed $n \rightarrow \sigma^*$ transition in the carbonyl group.[3]

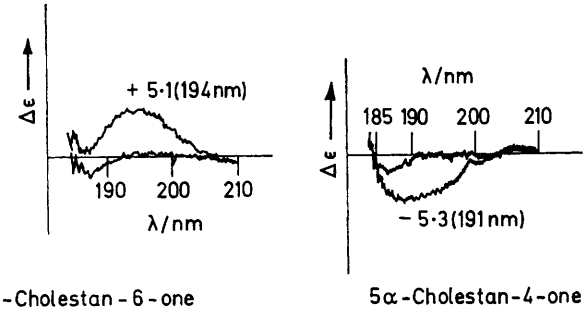

FIGURE 1. *Typical short wavelength c.d. curves for ketones. (Instrument base line also included.)*

We now report the observation of Cotton effects (c.d.) for a wide range of ketones in the steroid series, between 185 and 195 nm (Table); the $\Delta\epsilon$ values in this region are often large compared with those for the $n \rightarrow \pi^*$ transition. Typical curves are shown in Figure 1.

Our recent observation of Cotton effects near 190 nm for many steroidal alcohols[4] demands caution in studying hydroxy-ketones, although hydroxy-groups at C(3) showed negligible dichroism; acetoxy-groups at various positions do not interfere.[5]

TABLE

Circular dichroism of steroid ketones at 185—195 nm*

Class of compound	Found Δε	Predicted sign
Steroidal analogues of *trans*-decalones		
5α-1-one (1)	+3·7	(+)
19-nor-5α-2-one (1)	*ca.* 0	(small)
5α-2-one (2)	+3·7 to +5·2	(+)
5α-3-one (4)	*ca.* 0 to +0·5	(small)
5β,9β,10α-3-one (1)	*ca.* 0	(small)
19-nor-5α-3-one (3)	*ca.* 0 to +0·5	(small)
5α-4-one (3)	−4·8 to −5·6	(−)
19-nor-5α-6-one (1)[a]	−3·7	(small)
5α-6-one (4)	+4·4 to +5·5	(+)
5β,9β,10α-6-one (1)	*ca.* 0	(small)
5α-7-one (2)	*ca.* 0 to −2·6	b
D-homo-5α-7-one (1)	−4·3	b
5α or 5β-11-one (6)	+4·5 to +5·6	(+)
D-homo-5α-11-one (1)[a]	+3·6	(+)
5α or 5β-12-one (4)[c]	+4·3 to +10·5	(+)
D-homo-17a-one (2)	−5·3 to −6·1	(−)
Steroidal analogues of *cis*-decalones		
5β-2-one (1)	−8·7	(−)
19-nor-5β-3-one (1)	*ca.* 0	(small
5β-3-one (1)	+0·9	(small)
5-Methyl-5β-3-one (1)	−4·7	(−)
5β-4-one (1)	+15·9	(+)
5β-6-one (1)	+5·3	(?)
Steroidal analogues of *trans*-hexahydroindanones		
A-nor-19-nor-5α-2-one (1)	−5·6	(−)
A-nor-5α-2-one (1)	*ca.* 0	(small)
5-Methyl-A-nor-5α-2-one (1)	+2·8	(+)
5α-16-one	*ca.* 0	(small)
5α- or 5β-17-one (2)	−7·5 to −9·4	(−)

* Measurements with a Jouan Dichrographe (model CD 185) or Cary 6002 c.d. attachment, in hexane solution. Figures in parentheses indicate the number of compounds examined. Predicted signs are based upon Figure 2A or B.

[a] Prepared for the first time in these laboratories. [b] No prediction possible at present: may include Front Octant contribution. [c] 12-Oxo-steroids included pregnane, cholane, and cholestane side-chains, probably explaining the wide range of $\Delta\epsilon$ values.

Comparisons of data for key pairs of compounds in the Table (*e.g.* 5α-2-one *vs.* 19-nor-5α-2-one, or 5α-6-one *vs.* 19-nor-5α-6-one) show that β-axial methyl (or methylene) groups make a large contribution (*ca.* 5—6 units in the Octant rule sense) to the observed $\Delta\epsilon$ values. α-Axial methyl (or methylene) groups give Octant effects rather similar in magnitude to β-axial methyl (compare the 19-nor-4-oxo- and D-homo-17a-oxo-compounds). However, 2-decalones (*cis* or *trans*) without α- or β-axial substituents (*e.g.* 3-oxo-5α- or 5β- and 19-nor-2-oxo-5α-systems) generally give small or negligible $\Delta\epsilon$ values.

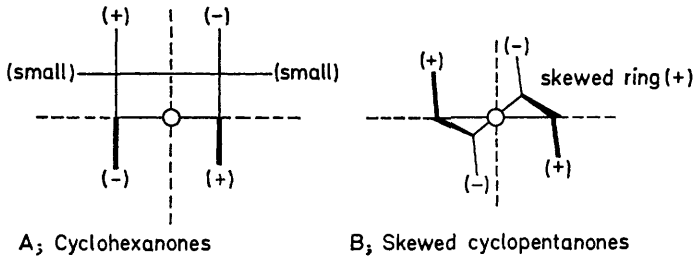

FIGURE 2. *Summary of short wavelength c.d. results. Octant-type projections showing signs for methyl and methylene substituents; rear octants only.*

The observed effects may be crudely rationalised with the hypothesis that α- or β-axial methyl or methylene substituents on a cyclohexanone ring make large contributions in the Octant sense to $\Delta\epsilon$ (Figure 2A), whereas α- or β-equatorial groups make relatively small contributions. There are, as yet, no clear indications of Front Octant effects, if these exist. Predicted signs, in the Table, are based upon dominance of the sign of $\Delta\epsilon$ by axial substituents.

We also suggest tentatively that $\Delta\epsilon$ values for *trans*-hexahydroindanones, with the oxo-group in the 5-membered ring, include a significant component decided by the chirality of the skewed cyclopentanone ring itself, the sign (Figure 2B, or its enantiomer), however, being the opposite of that associated with the $n \rightarrow \pi^*$ transition of chiral cyclopentanones.[6] (The sign may be controlled by Octant behaviour of the α-quasi-axial hydrogens when no substituent is present). Quasi-axial methyl groups again make quite large contributions to $\Delta\epsilon$ values, in the Octant sense.

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