Circular Dichroism of Saturated Chiral Alcohols

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Summary Chiral alcohols give significant Cotton effects between 185 and 198 nm.

COMPOUNDS containing hydroxy groups as the only substituent on a saturated hydrocarbon skeleton, show no absorption maximum above 200 nm, and consequently aliphatic alcohols have been used extensively as solvents for the study of o.r.d. and c.d. In addition, it has been possible to disregard the presence of hydroxy substituents in work with compounds containing other chromophores

such as carbonyl, carboxyl and aromatic groups, except for particular cases where there is interaction between a hydroxy group and a neighbouring chromophore *e.g.* α-hydroxy ketones.

Few absorption spectra have been reported for saturated alcohols. Methanol vapour has a maximum at 184 nm (ε 150)[1] and n-propyl alcohol shows a shoulder at 182 nm (ε 200);[2] secondary and tertiary alcohols would be expected to absorb at slightly longer wavelength.

We now report the existence of well-defined Cotton effects for saturated alcohols and related compounds in the region 185—198 nm (*e.g.* Figure 1). The Table gives examples of

TABLE

C.d. data[a] *for some monofunctional alcohols*

Compound	Prediction	Δε	λ (nm)
19-Nor-5α-cholestan-1β-ol ..	—	−0·25m	189
5α-Cholestan-2β-ol	+	+0·61m	198
5α-Cholestan-2α-ol	[b]	+0·50!	185
19-Nor-5α-cholestan-2α-ol ..	[b]	−0·51m	190
5α-Cholestan-3β-ol and four related compounds ..	[b]	−0·23m to −0·56m	187—189
5α-Cholestan-3α-ol and four related compounds ..	[b]	−0·12m to −0·75m	187—188
5α-Cholestan-4β-ol	—	−0·18m	202[c]
		+0·36!	191
5α-Cholestan-4α-ol	—	−0·38m	191
5α-Cholestan-5-ol	[b]	+1·47!	186
5α-Cholestan-6β-ol	+	+0·15m	196[c]
6α-Methyl-5α-cholestan-6β-ol	+	+1·02m	192[c]
5α-Cholestan-6α-ol	+	+0·51m	196
D-Homo-5α-androstan-6α-ol	+	+0·38m	193
5α-Cholestan-7β-ol	+	+0·62m	196[c]
5α-Androstan-11β-ol	+	+3·29m	188
D-Homo-5α-androstan-11β-ol	+	+2·86m	191
D-Homo-5α-androstan-11α-ol	—	−1·35m	193
5β-Cholan-12α-ol	[b]	+0·89m	203
		−1·22!	188
5α-Pregnan-16β-ol	[b]	−0·76!	187
5α-Androstan-17β-ol	—	−2·12m	191
5α-Pregnan-20β-ol	—	+0·79m	203
		−1·22m	193
5α-Pregnan-20α-ol	+	+0·26m	193
		+0·34!	185
5α-17βH-Pregnan-20β-ol ..	—	−4·19m	188
exo-(1*S*,3*S*)-Hydroxybornane (*epi*-isoborneol)	—	−2·32m	187
exo-(1*R*,2*R*)-Hydroxybornane (isoborneol)	+	+2·81m	189
(1*S*,3*S*)-Hydroxypinane .. (isopinocampheol)	[b]	+0·84m	187
(1*R*,2*R*)-Hydroxypinane ..	[b]	−1·92m	188
(1*R*,2*S*)-Hydroxypinane ..	[b]	−3·30!	186

[a] Measured in hexane solution on a Cary-60 with a model-6002 c.d. attachment; [b] no prediction made, no clear conformational preference, or contributions of opposing substituents appear to balance; [c] value obtained by resolution of experimental curve. m: maximum value; !: lowest wavelength measured.

results obtained for hydroxy steroids and terpenes, and Cotton effects have also been measured for chiral epoxides, ethers and cyclic ketals.[3] The c.d. curves for the steroid hydrocarbons 5α-androstane and 5α-cholestane each show the beginning of a positive Cotton effect below 190 nm but there is no maximum above 185 nm and the maxima recorded in the Table must therefore be due to the hydroxy group.

For many of the compounds listed in the Table it is possible to predict the preferred conformation of the hydroxy group (assuming staggering about the C–O bond, with O–H occupying the least hindered position), and then to consider the relationship between the molecular geometry and the sign of the observed Cotton effect. Figure 2

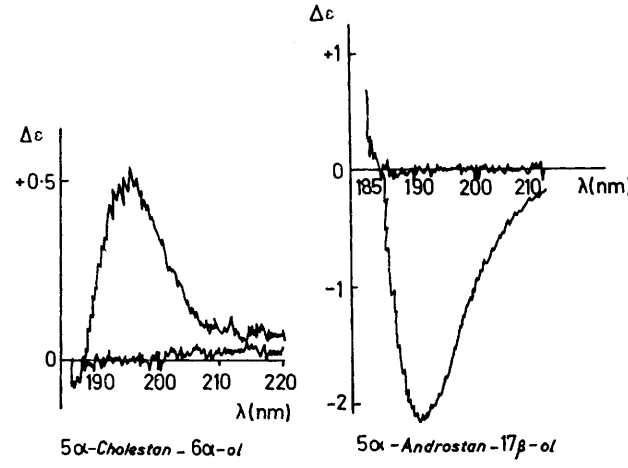

FIGURE 1. *Tracings of typical short wavelength c.d. curves for alcohols (the instrument base-line is included for comparison.)*

shows Newman projections of 5α-cholestan-7β-ol (**1**) and 5α-androstan-17β-ol (**2**) respectively, in which the molecule is viewed with the hydroxy group in the preferred conformation, and projected along the O–C bond. Those substituents which project forwards towards the lone pair orbitals of the oxygen atom, and which might be expected to make a large contribution to the Cotton effect, are shown in heavy type.

Since compounds (**1**) and (**2**) have positive and negative Cotton effects respectively, it appears that significant atoms to the right of the C–O–H plane (as defined in Figure 2)

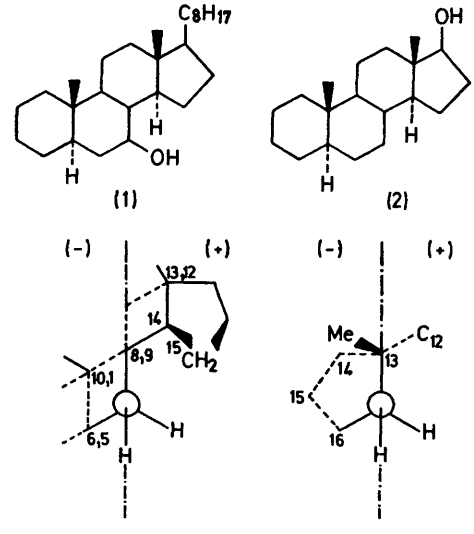

FIGURE 2

make a positive contribution to the Cotton effect, while atoms to the left make a negative contribution.

The Table shows the extent to which the sign of a hydroxy Cotton effect can be predicted on the basis of this possibly

oversimplified right–left rule. Where the preferred conformation of the hydroxy group cannot be defined unambiguously (*e.g.* 2α, 3α, 3β), Cotton effects are very small, as expected. For the great majority of compounds however, where a clearly preferred conformation is imposed by a sterically hindered environment, the observed sign agrees with the prediction. The possibility that more distant parts of the molecule may have a role in determing the magnitude of the Cotton effect is being examined.

Clearly hydroxy Cotton effects can no longer be ignored in c.d. studies of other chromophores such as olefins and ketones (short wavelength band[4]) which absorb below 200 nm.

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[1] S. F. Mason, *Quart. Revs.*, 1961, 287.
[2] J. R. Platt, I. Rusoff, and H. B. Klevens, *J. Chem. Phys.*, 1943, **11**, 535.
[3] F. Fernández, D. N. Kirk, and P. M. Scopes, unpublished observation.
[4] D. N. Kirk, W. Klyne, W. P. Mose, and E. Otto, *Chem. Comm.*, in the press.