The Conformation of Cholest-6-en-3-one: the Failure of the Octant Rule

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KLYNE, SONDHEIMER, SUMMERS, *et al.*, observed that cholest-6-en-3-one shows a very weak Cotton effect (which could be considered either positive or negative) superimposed on a strongly negative plain curve of cholest-6-ene, and thus they assigned a twisted boat conformation to ring A. Later Ourisson[2] reported a weakly positive double Cotton effect in the circular dichroism (c.d.) curve. As we had prepared the above mentioned compound and androst-6-en-3-one in connection with our studies on conformational transmissions,[3] we re-checked the spectroscopic data (Table 1) which agree with those of Klyne but not of Ourisson.

Examination of a model shows that the two π-systems are ideally aligned for coupling through the C-4–C-5 σ-bond if the ring is in a chair conformation. This results in four possible transitions, two allowed and two degenerate. One of the allowed transitions is observed normally at 220—250 nm.[5] The other possible transition,† as yet unobserved, arises from one of the linear combinations of the two degenerate transitions split by configuration interaction and its energy could be comparable to the $n \rightarrow \pi^*$ transition and overlap with it.

As the electric dipole transition moments are parallel in the new transition and the $n \rightarrow \pi^*$ but the magnetic dipole transition moments are opposite, the Cotton effects associated with the two transitions will have opposite sign;[6] the small negative $\Delta\epsilon$ being the resultant.

TABLE 1

	U.v.		C.d.					
Compound	λ_{max} (nm.)	ϵ	λ (nm.)	$\Delta\epsilon$	Solvent	O.r.d.	$a \times 10^{-2}$	Ref.
Cholest-6-en-3-one (m.p. 124°, $[\alpha]_D = -84°$)					MeOH	−380 (500 nm.) −2040 (308 nm.) −1650 (300 nm.) −3760 (260 nm.)	−4·0	1
			325 294	−0·04 +0·39	Dioxan			2
	282	27	307	−0·207	EtOH	−670 (400 nm.) −2015 (320 nm.) −1715 (299 nm.) −3800 (260 nm.)	−3·0	
	287	21	297	−0·465	n-Hexane			
Androst-6-en-3-one (m.p. 100—102°, $[\alpha]_D = -130°$)	281	30·5	309 279 257	−0·170 +0·017 −0·014	EtOH	−865 (400 nm.) −1900 (320 nm.) −1630 (299 nm.) −3670 (260 nm.)	−2·7	
	287	22·5	296	−0·41	n-Hexane			
			313	−0·21	$CHCl_3$			

The two maxima of opposite sign in the c.d. of androst-6-en-3-one at 279 and 309 nm. suggest that the ring A might exist as an equilibrium mixture of boat and chair conformations. However, this is discounted by the position of the signals due to C-19 methyl groups; if it were the case, the difference between the calculated and the observed chemical shifts would be expected to be much larger.[4] In fact, the n.m.r. spectrum indicates that the ring A is in a chair conformation which may be slightly distorted. Thus the discrepancy between the two physical methods used for conformational assignments must be sought in the unusual spectroscopic behaviour of $\gamma\delta$-unsaturated ketones.[5]

This work shows that the Octant Rule, which has been applied with outstanding success to a very large number of stereochemical problems,can break down in $\gamma\delta$-unsaturated ketones with the special geometry that exists in cholest-6-en-3-one, its 2α-methyl derivative,[1] and androst-6-en-3-one only when ring A is in a chair conformation. Thus 6-methylenecholestan-3-one‡ shows the expected positive curve and an inversion of ring A into a boat results in the expected amplitudes and the

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† The possibility of this transition has been pointed to us by Prof. R. Hoffmann.

‡ The spectral properties of other steroidal 3-ketones with unsaturation in rings B and C will be reported in a full paper.

TABLE 2

	Chem. shifts in c./sec. ($CDCl_3$)			
	C-19		C-18	
	obs.	calc.[4]	obs.	calc.[4]
Cholest-6-en-3-one	57·7	59·5	43·6	44·0
Androst-6-en-3-one	58·5	60·5	46·4	47·0

sign of the Cotton effect as is shown by 2β-methyl- and 2,2-dimethyl-cholest-6-en-3-ones.[1]

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