Tetrahedron Letters No. 14, pp 1315 - 1318, 1972. Pergamon Press. Printed in Great Britain.

FRONT OCTANT EFFECTS IN THE CIRCULAR DICHROISM OF KETONES

D.N. Kirk,* W. Klyne, and W.P. Mose

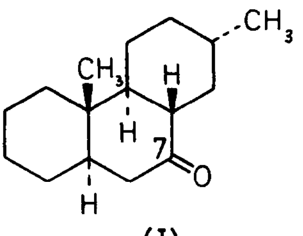
Chemistry Department, Westfield College, Hampstead, London, NW3 7ST

(Received in UK 9 February 1972; accepted for publication 24 February 1972)

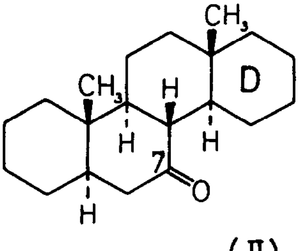
Chiroptical phenomena associated with the carbonyl $n \rightarrow \pi^*$ transition have been regarded for more than a decade as following the "Octant Rule",[1] although experimental evidence for the reversal of signs in the front octants has been so scanty as to be considered inconclusive by some workers.[2] Certainly no reliable data have existed to provide a quantitative indication of "front octant" effects;[3] our own and earlier attempts to assign numerical values to the c.d. contributions of structural features in rear octants have, however, met with partial success, especially for all-trans arrays of cyclohexane rings.[4]

We now report the preparation of the des-D-analogue (I) of 5α-androstan-7-one (the tricyclic compound, lacking ring D). With intact 7-oxo 5α-steroid structures available in 5α-androstan-7-one, 5α-cholestan-7-one, and also D-homo-5α-androstan-7-one (II),[5] it is now possible, by direct comparisons with the des-D compound, to assign numerical values to the c.d. contributions of ring D, most of which lies in the region generally designated as "front octant".[6]

The Table gives data both for the $n \rightarrow \pi^*$ transition (ca. 290-295 nm) and also for the shorter wavelength absorption band (ca. 190 nm, tentatively assigned to the $n \rightarrow \sigma^*$ transition), for which we have recently[7] reported observation of chiroptical properties.



(I)



(II)

Table. C.d. Data for 7-Oxo-5α-Steroids.[a]

Compound	290 nm ($n \rightarrow \pi^*$) transition				190 nm ($n \rightarrow \sigma^*$) transition	
	in MeOH		in hexane		in hexane	
	$\Delta\varepsilon$	$\Delta\Delta\varepsilon$[b]	$\Delta\varepsilon$	$\Delta\Delta\varepsilon$[b]	$\Delta\varepsilon$	$\Delta\Delta\varepsilon$[b]
Des-<u>D</u>-13β(H)-5α-androstan-7-one (I)	-0.85	-	-0.48	-	+1.0	-
5α-Androstan-7-one	-0.62	+0.23	-0.33	+0.15	-1.1	-2.1
5α-Cholestan-7-one	-0.64	+0.21	-0.48	0.00	-2.9	-3.9
<u>D</u>-Homo-5α-androstan-7-one (II)	+0.13[c]	+0.98	+0.17	+0.65	-4.3	-5.3

[a] Measurements made in this Department with a Jouan Dichrograph (model CD 185) in methanol) or with a Cary 6002 c.d. attachment (in hexane).

[b] $\Delta\Delta\varepsilon$ is the difference $\Delta\varepsilon$(tetracyclic structure) <u>minus</u> $\Delta\varepsilon$(tricyclic analogue (I)).

[c] Measurement in methanol-hexane (3:1), for reasons of solubility: the $\Delta\varepsilon$ value for 5α-cholestan-7-one in a similar mixture (-0.62) was not significantly different from that in methanol.

Comparison of data for the des-<u>D</u> and <u>D</u>-homo compounds reveals significant contributions to $\Delta\varepsilon$ from the <u>D</u> ring. The positive sign of this contribution ($\Delta\Delta\varepsilon$) for the $n \rightarrow \pi^*$ transition corresponds to the expected "front octant" behaviour, reversing the sign for the corresponding rear octant (see Figure). The value of $\Delta\Delta\varepsilon$ in methanol (+0.98) is notably greater than that in hexane (+0.65), the proportional difference (50%) being somewhat larger than we have observed previously for "<u>rear</u> octant" groups (values in methanol are generally 25-30% greater than in hexane[4]).

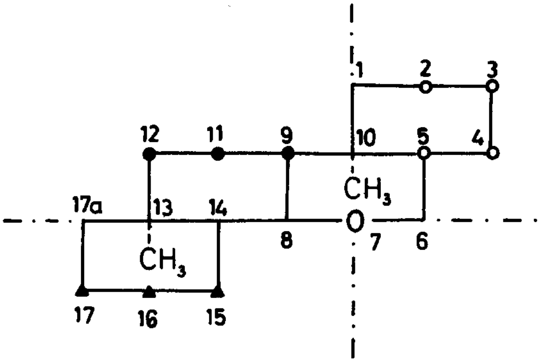


Figure. Octant projection of D-Homo-5α-androstan-7-one.

● = atoms in rear octant, positive contribution.

○ = atoms in rear octant, negative contribution.

▲ = atoms probably in front octant; these are missing in the des-*D*-analogue (I).

The "front octant" contributions of the *D* ring to observed $\Delta\varepsilon$ values are much smaller for 5α-androstan-7-one and 5α-cholestan-7-one, where only two carbon atoms of the five-membered ring *D* $\left[C_{(15)} \text{ and } C_{(16)}\right]$ can be considered to lie in the front octant. It is perhaps more significant that the $C_{(15)}$-methylene group is slightly further from the carbonyl oxygen than in the *D*-homo analogue, as a consequence of the strain in ring *D* (X-ray data[8] show that the valence angle $C_{(8)}-C_{(14)}-C_{(15)}$ is enlarged to nearly 120° in normal steroids). Apparently the contribution of a ring projecting into the front octant is considerable only when it approaches the carbonyl group very closely.

We have already commented[7] upon the major role of axial substituents in the short wavelength (*ca.* 190 nm) dichroism of cyclohexanone analogues, but were unable at that time to estimate the contributions of "front octant" groups. The negative values of $\Delta\Delta\varepsilon$ in the final column of the Table show there is no indication of "front octant" behaviour for this transition, the data being better accommodated by a quadrant rule covering the spatial regions so far explored. Signs for the quadrants correspond to those of the *rear* octants in the normal carbonyl Octant rule, with no reversal of sign in the front regions. Again the contribution is greater for the six-membered *D*-homo ring than for the normal five-membered ring, probably for the reasons discussed above.

The tricyclic ketone (I) was prepared by an unexceptional route from 3β-hydroxy-des-*D*-androst-5-en-14-one, the "Köster-Logemann" ketone (cf. ref. 5 for an analogous synthesis of the *D*-homo 7-ketone); its structure is supported by microanalytical and spectroscopic data.

We are indebted to the Science Research Council and the Medical Research Council for support, and to Dr. G. Anner, Ciba-Geigy A.G., Basel, for a generous supply of the "Köster-Logemann" ketone.

REFERENCES

1. W. Moffitt, R.B. Woodward, A. Moscowitz, W. Klyne, and C. Djerassi, J. Amer. Chem. Soc., 1961, 83, 4013.
2. J.A. Schellman, J. Chem. Phys., 1966, 44, 55; E.G. Höhn and O.E. Weigang, ibid., 1968, 48, 1127; G. Wagnière, J. Amer. Chem. Soc., 1966, 88, 3937.
3. C. Djerassi and W. Klyne, J. Chem. Soc., 1963, 2390. Early o.r.d. data for 1-oxo-5α-steroids suggested a "front octant" contribution from parts of rings C and D, but the interpretation was only qualitative: possible effects of the side-chain (at C-17), and of the strained ring D, still cannot be assessed.
4. D.N. Kirk, W. Klyne, and S.R. Wallis, J. Chem. Soc. (C), 1970, 350.
5. D.N. Kirk and M.A. Wilson, J. Chem. Soc. (C), 1971, 414.
6. For a recent proposal concerning the shape of the boundary surface between front and rear octants, see: C. Coulombeau and A. Rassat, Bull. Soc. chim. France, 1971, 516; see also Y.-H. Pao and D.P. Santry, J. Amer. Chem. Soc., 1966, 88, 4157.
7. D.N. Kirk, W.P. Mose, and P.M. Scopes, Chem. Comm., 1972, 81.
8. C. Altona, H.J. Geise, and C. Romers, Tetrahedron, 1968, 24, 13.