

Rationalization of the Chiroptical Properties of the Δ^4 -3-Oxo-steroids

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Summary The signs of the two lowest energy Cotton effects of the Δ^4 -3-oxo-steroids may be rationalized in terms of the contributions of the pseudoaxial bonds on the α' and γ carbon atoms.

transoid- $\beta\beta'$ -DISUBSTITUTED α,β -unsaturated ketones generally exhibit three optically active absorption bands between 200 and 350 nm, the lowest band being due to an $n \rightarrow \pi^*$ transition (ca. 320–350 nm), and the others to $\pi \rightarrow \pi^*$ transitions.^{1–3} Recently the sign of the Cotton effect of the highest energy band (200–220 nm) was correlated with the

equatorial hydrogen [R^3 in (XVI)–(XVII)] or change of the axial substituent on C-10 [R^1 ; Me \rightarrow H \rightarrow OH, (I)–(III)] does not (Table) suggesting that the chirality of this band is controlled solely by the γ -*transoid* substituent R^3 and its relative orientation to the α' axial hydrogen.

The effect of substitution of the axial hydrogen on C-6 [R^2 in (IV)–(XV)] on the sign of the Cotton effect $n \rightarrow \pi^*$ transition; (320–350 nm c.d. band) depends upon R^2 (Table). Those substituents that change the sign of the Cotton effect [Me in (VII), Cl in (IV), Br in (V), I in (XIV), SAc in (XIII)] also induce strong quadrant behaviour in α

C.d. and o.r.d. data for Δ^4 -3-oxosteroids

Compound	R^1	R^2	R^3	[θ] $\times 10^{-3}$		
				$n \rightarrow \pi^*$ (317–351 nm)	$\pi \rightarrow \pi^*$ (225–252 nm)	$\pi \rightarrow \pi^*$ (205–225 nm)
(I)	Me ^a	H	H	–38	+289	+316!
(II)	H ^a	H	H	–61	+260	
(III)	OH ^a	H	H	–55	+223	+181
(IV)	Me ^a	Cl	H	+25	–363	
(V)	Me ^a	Br	H	+71	–597	+312!
(VI)	H ^a	Br	H	+26	–345	+88!
(VII)	Me ^a	Me	H	+21	–148	+218
(VIII)	Me ^a	OH	H	–18	–132	+484
(IX)	H ^a	OH	H	–49	–170	+154
(X)	Me ^a	OAc	H	–43	–96	+443
(XI)	H ^a	OAc	H	–58	–115	+228
(XII)	H ^b	Me	H	–†		
(XIII)	Me ^b	SAc	H	+†		
(XIV)	Me ^b	I	H	+†		
(XV)	Me ^b	F	H	–†		
(XVI)	Me ^a	H	Br	–35	+395	+462!
(XVII)	Me ^a	H	OAc	–48	+123	+180
(XVIII)	Me ^c	H	Me	–†		
(XIX)	Me ^d	H	F	–†		
(XX)	Cl ^e	H	H	–†		

! Represents extremum.

† From o.r.d. data.

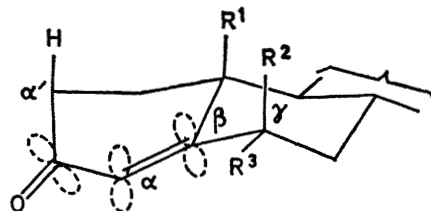
^a Ref. 3.^b Ref. 12, and references cited therein.^c C. Djerassi, O. Halpern, B. Halpern, and B. Riniker, *J. Amer. Chem. Soc.*, 1958, 80, 4001.^d C. Djerassi, J. Osiecki, R. Riniker, and B. Riniker, *J. Amer. Chem. Soc.*, 1958, 80, 1216.^e F. Mukawa, R. I. Dorfman, and H. J. Ringold, *Steroids*, 1963, 1, 9.

chirality contribution of the α' pseudoaxial bond,⁴ and we have rationalized⁵ the existing rules for the chirality of the $n \rightarrow \pi^*$ transition.⁶ The chirality of the medium energy band (230–250 nm) has not so far been correlated with molecular geometry. However, the signs of the Cotton effects of both low energy bands vary with substitution^{1,3} and this variation has been attributed to conformational changes in ring A;⁶ this has recently been criticised on the basis of n.m.r. evidence.⁷

We show that, with particular reference to Δ^4 -3-oxosteroids [(I)–(XX)], the chiralities of both low energy bands vary in a predictable manner that is related to the variation of the sign of the Cotton effect in α axially⁸ or β equatorially⁹ substituted cyclohexanones without postulation of conformational changes in ring A.¹⁰

Substitution of the axial hydrogen on C-6 [R^2 in (IV)–(XI)] changes the sign of the Cotton effect for the $\pi \rightarrow \pi^*$ transition (230–250 nm c.d. band) whereas substitution of the

axial⁸ or β equatorial⁹ substituted cyclohexanones but those which do not change the sign [OH in (VIII), OAc in (X), F in (XV)] induce only a very weak or anti-quadrant behaviour in such systems.^{9,11} The opposite effect is evident at C-2.¹²



The change of R^1 from Me to H in these Δ^4 -3-oxo systems leads to a negative increment in molar ellipticity ($\Delta[\theta]$ ca.

-28×10^2) of the $n \rightarrow \pi^*$ band, independent of R^2 suggesting that R^1 and R^2 are independently coupled to the enone chromophore.

Sterically the 6β axial bond is correctly positioned for efficient overlap with the π orbital of the enone system[†] whereas the 6α equatorial bond is not; substitution of the 6α equatorial hydrogen would not be expected to change the sign of the $n \rightarrow \pi^*$ Cotton effect [R^3 in (XVI)—(XIX)].

Study of the n.m.r. spectra of Δ^4 -3-oxo-steroids has

shown that whereas both axial protons at C-10 and C-6 are coupled with the C-4 olefinic proton, coupling of the equatorial proton at C-6 to the C-4 proton is negligible.¹³ The transmission of spin information from axial allylic protons¹⁴ and the transmission of chiral information may depend on a similar efficient overlap with the π system and σ electron framework.

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[†] The λ_{\max} changes can also be rationalized [J. Hudec, *Chem. Comm.*, 1970, 829, rules (i) and (ii)].

¹ L. Velluz, M. Legrand and R. Viennet, *Compt. rend.*, 1965, **261**, 1687.

² H. Ziffer and C. H. Robinson, *Tetrahedron*, 1968, **24**, 5803.

³ K. Kuriyama, M. Moriyama, T. Iwata, and K. Tori, *Tetrahedron Letters*, 1968, 1661.

⁴ A. W. Burgstahler and R. C. Barkhurst, *J. Amer. Chem. Soc.*, 1970, **92**, 7601.

⁵ G. H. Cooper and J. Hudec, in preparation.

⁶ G. Snatzke, "Optical Rotatory Dispersion and Circular Dichroism in Organic Chemistry", Heyden, London, 1967, ch. 13.

⁷ K. Tori, Y. Terui, M. Moriyama, and K. Kuriyama, *Tetrahedron Letters*, 1968, 1658.

⁸ C. Djerassi, "Optical Rotatory Dispersion," McGraw-Hill, New York, 1960.

⁹ G. Snatzke and G. Eckhardt, *Tetrahedron*, 1968, **24**, 4543.

¹⁰ E. M. Gopalakrishna, A. Cooper, and D. A. Norton, *Acta. Cryst.*, 1969, **25B**, 639; 1968, **24B**, 935; W. C. Duax, Y. Osawa, A. Cooper, and D. A. Norton, *Tetrahedron*, 1971, **27**, 331.

¹¹ L. Bartlett, D. N. Kirk, W. Klyne, and S. R. Wallis, *J. Chem. Soc. (C)*, 1970, 2678.

¹² G. Snatzke, *Tetrahedron*, 1965, **21**, 421.

¹³ T. A. Wittstruck, S. K. Malhotra, and H. J. Ringold, *J. Amer. Chem. Soc.*, 1963, **85**, 1699.

¹⁴ S. Sternhell, *Quart. Rev.*, 1969, **23**, 236.