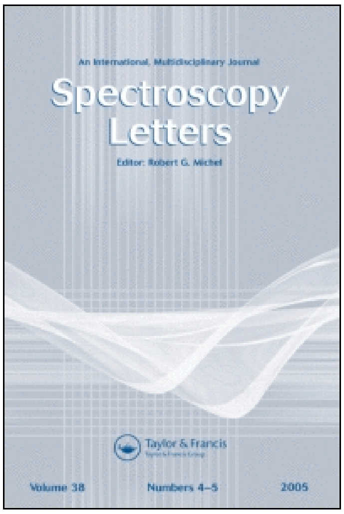
This article was downloaded by:
On: *30 January 2011*
Access details: *Access Details: Free Access*
Publisher *Taylor & Francis*
Informa Ltd Registered in England and Wales Registered Number: 1072954 Registered office: Mortimer House, 37-41 Mortimer Street, London W1T 3JH, UK



Spectroscopy Letters

Publication details, including instructions for authors and subscription information:
http://www.informaworld.com/smpp/title~content=t713597299

Ord And Cd Spectra Of 4,6,7-Trichloro-δ5-3-keto Steroids

V. Toome[a]; G. Reymond[a]
[a] Chemical Research Department, Hoffmann-La Roche Inc., Nutley, New Jersey

To cite this Article Toome, V. and Reymond, G.(1974) 'Ord And Cd Spectra Of 4,6,7-Trichloro-δ5-3-keto Steroids', Spectroscopy Letters, 7: 4, 229 — 234
To link to this Article: DOI: 10.1080/00387017408067241
URL: http://dx.doi.org/10.1080/00387017408067241

PLEASE SCROLL DOWN FOR ARTICLE

Full terms and conditions of use: http://www.informaworld.com/terms-and-conditions-of-access.pdf

This article may be used for research, teaching and private study purposes. Any substantial or systematic reproduction, re-distribution, re-selling, loan or sub-licensing, systematic supply or distribution in any form to anyone is expressly forbidden.

The publisher does not give any warranty express or implied or make any representation that the contents will be complete or accurate or up to date. The accuracy of any instructions, formulae and drug doses should be independently verified with primary sources. The publisher shall not be liable for any loss, actions, claims, proceedings, demand or costs or damages whatsoever or howsoever caused arising directly or indirectly in connection with or arising out of the use of this material.

SPECTROSCOPY LETTERS, 7(4&5), 229-234 (1974)

ORD AND CD SPECTRA OF 4,6,7-TRICHLORO-Δ^5-3-KETO STEROIDS

KEY WORDS: UV/ORD/CD spectra, conformation of ring A,
stereochemistry of Cl at C-4

V. Toome and G. Reymond

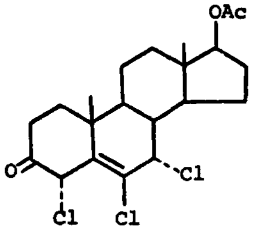
Chemical Research Department,
Hoffmann-La Roche Inc.,
Nutley, New Jersey 07110

Recently the synthesis of 4,6,7-trichloro-Δ^5-3-keto steroids has been described and the conformation of ring A ("skew" boat) and the stereochemistry of the three chloro substituents (4α-and 7α-chlorines axial) was established by the single crystal X-ray analysis of 4α,6,7α-trichloro-17α,21-dihydroxypregn-5-ene-3,11,20-trione 21-acetate III.[1] In order to correlate the solid state conformation with that in solution and also to demonstrate that the same conformation of ring A (and that of the 4-chloro substituents) is present when ring D is substituted differently, the ORD and CD spectra of III and 4α,6,7α-trichloro-5-androsten-3-one acetate I,4α,6,7α-trichloro-17α-hydroxypregn-5-ene-3,20-dione acetate II and 4α,6,7α-trichloro-21-hydroxy-16-methylpregn-5,16-diene-3,11,20-trione acetate IV[2] have been recorded in dioxane. The experimental results of the four compounds are in agreement with the boat conformation of ring A and the axial position of the 4-Cl substituent. The pertinent data is summarized in Table 1 and demonstrated in Figures 1 and 2.

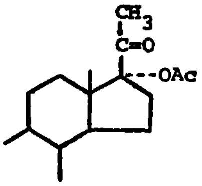
Before discussing the ORD and CD data, it should be mentioned that these compounds show an unusually strong UV absorption for

TABLE 1

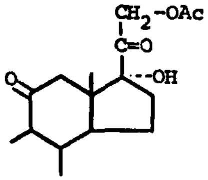
ORD and CD Spectral Data



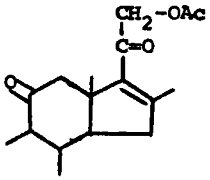
I



II



III



IV

Cpd.	ORD		CD	
	λ (nm)	[φ]	λ (nm)	[θ]
I	700	-403°	360	0
	589	-534°	310	+10,430
	338	0°pk	282	0
	261	-29,930°tr	242	-54,353
	229	+5,110°pk	227	-38,824
	217	-3,650°tr	210	-88,320last
II	700	-460°	360	0
	589	-644°	302	+18,240
	335	+713°pk	274	0
	261	-43,700°tr	242	-56,240
	227	-9,200°pk	226	-39,520
	218	-13,800°tr	208	-83,600last
III	700	-82°	352	0
	589	-94°	302	+23,100
	325	+8,700°pk	272	0
	260	-44,000tr	238	-48,840
	218	+7,200sh	220	-36,960
			204	-45,540last
IV	700	-279°	370	0
	589	-373°	312	+27,600
	343	+5,560°pk	276	0
	256	-48,650°tr	240	-90,000
	224	+25,715°pk	219	-42,320
	210	+18,070°last	210	-52,440last

(a) ORD and CD spectra recorded in dioxane on a JASCO Spectropolarimeter, Model ORD/CD/UV-5 at 23°C. Concentrations were 0.01 M.

(b) tr = trough; pk = peak; sh = shoulder.

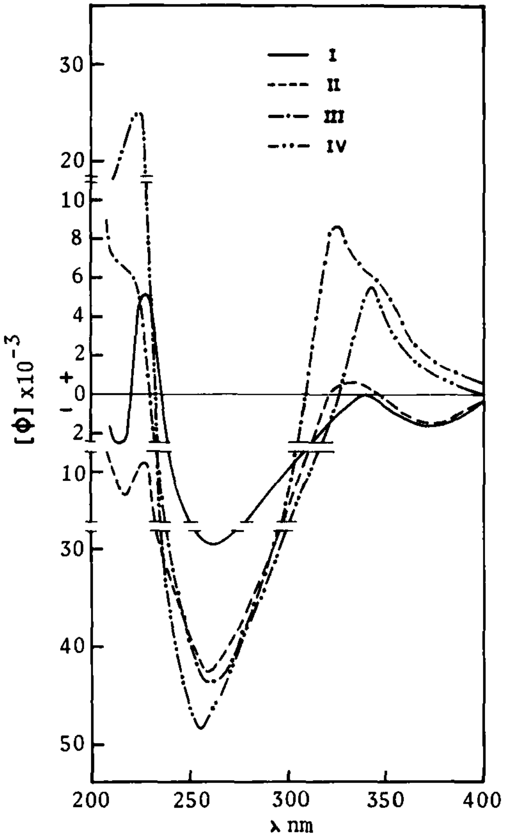


Figure 1. ORD SPECTRA IN DIOXANE

β,γ-unsaturated ketones (in ethanol λ max 240 nm, ε = 5400; shoulder 300 nm ε = 220). This may be explained by some overlap of the nonbonding p orbital of the oxygen atom and the π orbital of the chlorinated double bond.[3] On the other hand, the geometry of the orbital of the three chlorine substituents also seems to be of importance: after the reduction of the 3-keto group the UV maximum is still strong and undergoes a hypsochromic shift of only 10 nm (in ethanol λ max at 230 nm, ε = 7700) while the shoulder at 300 nm ($n \to \pi^*$ transition) has disappeared. This unusual UV absorption further motivated the analysis of ORD and CD spectral data of these compounds.

The ORD spectra of I-IV are shown in Figure 1. Because of the overlapping of the strong background rotation and the

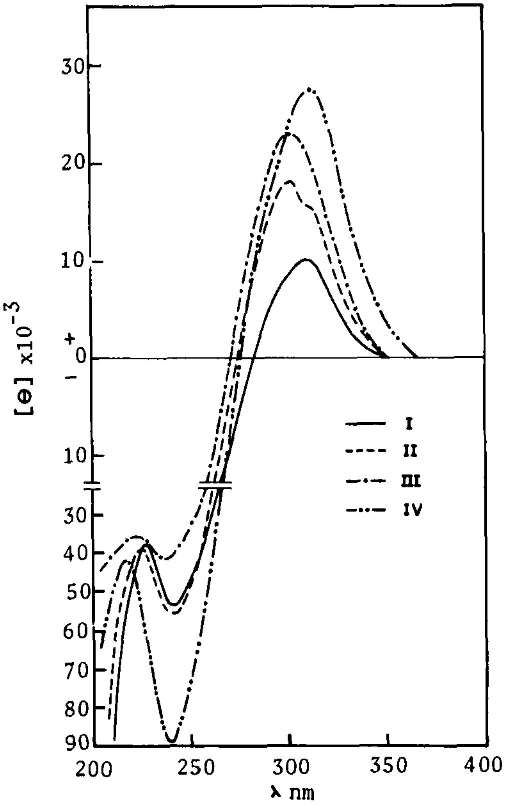


Figure 2. CD SPECTRA IN DIOXANE

Cotton effects, the ORD curves are less suitable for the quantitative determination of structure - spectral correlation. Therefore, only the CD spectra (Figure 2) are analyzed.

Compound I, which has only the Δ^5-3-keto chromophore, shows, as expected, two separate and distinct Cotten effects: a strong positive maximum at 310 nm, $[\theta] = 10{,}430$ ($n \rightarrow \pi^*$ transition of the keto group), and a very strong negative one at 242 nm, $\theta = -54{,}350$, corresponding to the observed UV maximum at 240 nm. Because the longer wavelength extrema usually can be measured more accurately, we will limit our discussion to the Cotton effects in the 300 - 320 nm region.

A Dreiding model of I, ring A in the chair conformation, reveals immediately that an axial chlorine at C-4 falls into a negative octant[4] and the result would be a strong negative Cotton effect. Although the chlorines at C-6 and C-7 would be in a positive octant, they are farther away from the carbonyl. Furthermore, it is known that 5α-halo and 5α,6α-dihalo-3-keto derivatives show abnormally low rotation.[5] As already mentioned, our experimental data shows a strong positive Cotton effect. Therefore, it is not in agreement with the chair form and an axial chlorine. Now, if the chlorine were equatorial, then the net result would be a weak Cotton effect, which contradicts the experimental data. On the other hand, if ring A is in the boat form and the chlorine in the axial position[1], one would expect a relatively strong positive Cotton effect in agreement with the experimental results.[6] The chlorines at C-6 and C-7 would now be in negative octants, but their influence would again be relatively small. The β,γ-unsaturated carbonyl system could also be treated as an inherently dissymmetric chromophore.[7]

Structure II has an additional chromophore, the 17β-acetyl group, which should also have a strong positive Cotton effect ($[\theta] \simeq +10{,}000 - 12{,}000$).[8] Both keto groups are situated in distant parts of the molecule, and it has been shown that the so-called "additivity rule" is applicable in those cases.[8] Therefore, the molar ellipticity should be approximately the arithmetic sum of the two Cotton effects. That is the case here, as seen in the experimental data.

In addition, structure III contains an 11-keto group which usually exhibits a mild Cotton effect ($[\theta] \simeq 1200$). An introduction of a C-5 double bond enhances this to ca 5300.[8] Again, as expected, the molecular ellipticity is in agreement with the experimental data [approximate arithmetic sum of the three Cotton effects due to the 3,11 and 20 keto groups[9]].

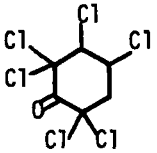
Finally, compound IV also has three asymmetrically perturbed chromophores present: 3-,11-and Δ^{16}-20-keto groups. The latter is expected to exhibit a positive circular dichroism maximum at ca 330 nm due to the $n \rightarrow \pi^*$ carbonyl transition ($[\theta] \simeq 8000$).[8] The sum of these three carbonyl Cotton effects should result in a strong positive circular dichroism maximum whose position should show a mild bathochromic shift. This is confirmed by the experimental data.

ACKNOWLEDGMENT

We thank Mrs. B. Wegrzynski for skillful experimental assistance.

REFERENCES

1. R. W. Kierstead, J. Blount, K. E. Fahrenholtz, A. Faraone, R. A. LeMahieu and P. Rosen, J. Org. Chem., 35, 4141 (1970).
2. Compounds kindly supplied by Dr. R. Kierstead, Chemical Research Department, Hoffmann-La Roche Inc., Nutley, New Jersey 07110.
3. A similar UV absorption of a β,γ-unsaturated ketone has been reported by H. Labhart and G. Wagniere, Helv. Chem. Acta, 42, 2219 (1959).



Its UV maximum at 235 nm (ε = 9000) is a good example of a strong nonclassical E. T. band of a β,γ-unsaturated ketone.
4. W. Moffitt, R. B. Woodward, A. Moscowitz, W. Klyne and C. Djerassi, J. Am. Chem. Soc., 83, 4013 (1961).
5. C. S. Barnes and C. Djerassi, Chem. and Ind., 177 (1962); J. Am. Chem. Soc., 84, 1962 (1962).
6. The octant rule[4] is deduced for the chair conformation and precaution must be taken in the case of different geometry.
7. K. Mislow, M. A. W. Glass, A. Moscowitz, and C. Djerassi, J. Am. Chem. Soc., 83, 2771 (1961).
8. P. Crabbé, Optical Rotatory Dispersion and Circular Dichroism in Organic Chemistry, Holden-Day, 1965 and references therein.
9. There is probably some electronic interaction between the three keto groups, so only a qualititive agreement is expected in most cases. The same is true for structure IV.

Received April 5, 1974

Accepted April 16, 1974