The Optical Rotatory Dispersion of Steroid Acetates

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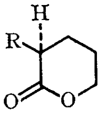
THE optical rotatory dispersion (o.r.d.) curves of compounds containing the carboxyl and related chromophores show Cotton effects with a first extremum at approx. 227 mμ corresponding to the absorption band centred at about 200—210 mμ. Several systematic studies of the o.r.d. of carboxylic acids[1] and of lactones[2] have appeared and correlations have been made between the sign of the carboxyl Cotton effect and the absolute stereochemistry of the compound.



(I)

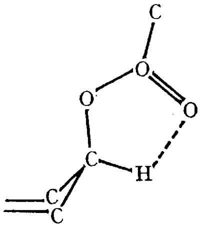
For lactones (I), the carboxyl chromophore is held in a more or less fixed conformation but for dissymmetric carboxylic acids and esters (II; RR'CH·CO$_2$R'', R''=H or alkyl), the existence of significant Cotton effects must indicate an appreciable degree of conformational preference, even though free rotation is formally possible about the bond C^{α}—CO$_2$R''.

We have now examined the o.r.d. curves of several types of esters (chiefly steroid acetates) in which the asymmetric centres are in the alkyl component (III; RCO$_2$CHR'R''), and have found that most of these show good Cotton effects.[4]

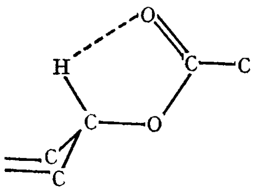
Mathieson[5] has recently analysed the available *X*-ray data on the conformations taken up by acyloxy-groups relative to saturated six-membered-ring systems; the evidence indicates that the preferred conformations of simple esters such as acetates will be as shown in (IV) and (V) for axial and equatorial esters respectively. Although this analysis refers strictly to compounds in the solid state, Mathieson suggests that the conformations (IV) and (V) will probably be dominant for the isolated molecule also.

We have now considered our o.r.d. data on steroid acetates in the light of the preferred conformations (IV) and (V), and have shown that the signs of the observed Cotton effects can be correlated with the stereochemical environment of the acetate groups by the *carboxyl sector rule*, as previously described for the more rigid lactones.[2]

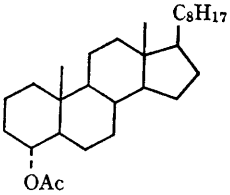
5α-Cholestan-4α-yl acetate (VI) gives a positive Cotton effect, [Φ], +1930 peak, at 227 mμ. The octant and sector projections (VIa) and (VIb) show the positions of the atoms relative to the acetate group, on the assumption that the preferred conformation is as in (V). When the molecule is viewed along the bisectrix of the carboxyl chromophore (octant projection; VIa) the contributions of atoms 2 and 3 cancel with those of 10 and 5; atoms 1 and 4 lie in a nodal plane (the plane of the carboxyl chromophore) and all the rest of the atoms lie in the front upper left sector of positive contribution. The sector projection perpendicular to the plane of the acetate group (VIb) shows that the significant atoms all fall within the sector of high positive contribution. The observed positive Cotton effect is thus in good agreement with the prediction of the sector rule.



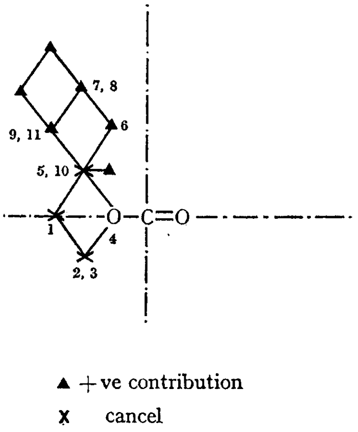
(IV)



(V)



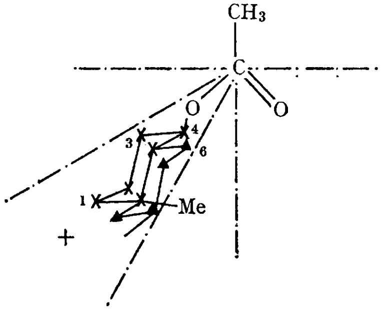
(VI)



▲ +ve contribution

X cancel

(VIa)



(VIb)

TABLE

O.r.d. curves of 5α-*steroid acetates*

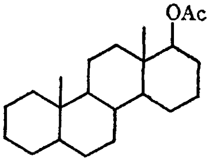
Position of substituent	Sign of Cotton effect		Position of substituent	Sign of Cotton effect	
	α	β		α	β
1	—	+	12	—	+
2	—		16	+	+
3	pl	pl	17	pl	pl
4	+		D-homo-series		
6	—	+	16	pl	+
7	+		17	pl	+
11		—	17a	+	—

pl = plain curve

It is important to note that all significant atoms in projections (VIa) and (VIb) lie in *front* sectors, with respect to the carboxyl group. The sector rule, as originally developed for lactones[2] referred only to the signs of contributions from atoms in back sectors, but it seems reasonable to assume that contributions from front sectors will be opposite in sign to those of back sectors (*cf.* ketone octant rule[6]).

D-Homo-5α-androstan-17aβ-yl acetate (VII) has an acetate group in a situation almost enantiomeric to that of (VI). The octant and sector diagrams show that all non-cancelling atoms fall in sectors of negative contribution and in accordance with this we observed a negative Cotton effect for compound (VII), $[\Phi]$ -855, trough at 232 mμ.

The two compounds (VI) and (VII) discussed above are both examples of *trans*-decalins with equatorial 1-acetoxy-groups. We have examined compounds of all the possible stereochemical types of *trans*-decalin and of *trans*-hexahydroindane acetates and have found that in the great majority of cases, their o.r.d. behaviour can be rationalised in terms of the carboxyl sector rule; similar arguments can be used to interpret the observed o.r.d. curves of the side-chain 5α-pregnan-20α- and -20β-yl acetates.[7] Signs of the observed Cotton effects for some (5α)-steroid acetates are shown in the Table.



(VII)

(*Received, July 14th,* 1966; *Com.* 499.)

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