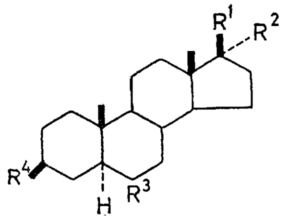
Use of Linear Dichroism for the Establishment of Rotameric Conformations of Acetyl Substituted Steroids

By Amnon Yogev,* Jacob Sagiv, and Yehuda Mazur*

(*Department of Organic Chemistry, The Weizmann Institute of Science, Rehovot, Israel*)

Summary The rotameric conformations of steroidal methylketones were established using linear dichroic spectroscopy in oriented polyethylene films.

We have recently shown that the short wavelength transition moment of the carbonyl chromophore (λ_{max} *ca.* 180 nm) is directed along the C=O bond axis.[1] Thus by establishing the relative direction of this transition the relative position of the C=O chromophore in a molecule will be obtained. We estimate the direction of electric transition moments from the linear dichroic spectra of compounds incorporated in stretched polyethylene films using the dichroic ratios, $d_0 = \epsilon_{\parallel}/\epsilon_{\perp}$, (the ratios of extinction coefficients for two orthogonal polarizations). The value of the dichroic ratio, which is unique for a chromophore in a compound, depends on: (a) the distribution of the molecules in the stretched film which is defined as f, the fraction of completely oriented molecules and (b) the angle α between the transition moment direction and the longitudinal axis of the molecule.[2]



	R1	R2	R3	R4
(1)	Ac	H	H	OAc
(2)	Ac	OH	H	OAc
(3)	OAc	H	---Ac	H
(4)	OAc	H	—Ac	H

We report the use of linear dichroic spectra of a number of steroidal methylketones for the establishment of the rotameric conformations of the acetyl group. These compounds and the respective dichroic ratios d_0 of the short wavelength transition of their C=O chromophores are listed in the Table.

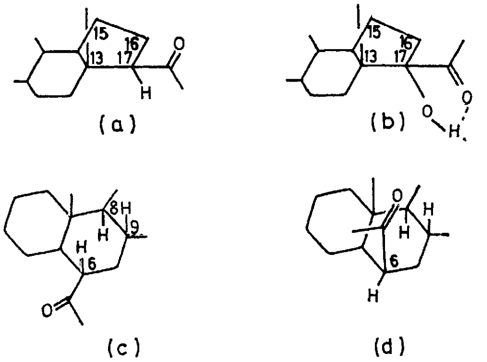
Compound	d^{a}	f^{b}	α^{c}
(**1**)	2·8—2·1	0·54	24—33
(**2**)	1·6—1·1	0·54	42—53
(**3**)	1·2—1·05	0·38	48—53
(**4**)	0·99—0·81	0·38	55—63

[a] Dichroic ratio. [b] Fraction of completely oriented molecules. [c] Angle between the transition moment vector and the longitudinal axis of the molecule.

Using the independently established values for the fraction of oriented molecules f in the androstane and pregnane series,† we have calculated the α values, representing angles between the direction of the C=O bond axis and the longitudinal axis which coincides in these compounds with their axis of inertia.[1] Since the dichroic ratios change slightly with the wavelength, probably due to the overlap with a shorter-wavelength transition, the calculated angles α, are within a 10° range.

In the pregnan-20-one derivative, [(**1**) Table] the direction of the C=O bond axis, compatible with the calculated angle α, is the one parallel to the plane passing through the C-16–C-17–C-20 carbon atoms (Figure a). This conformation is in accordance with X-ray structure determination of a derivative of pregnan-20-one.[3] The introduction of 17-OH α to the carbonyl group at C-20 [(**2**) Table] results in a decrease of dichroic ratio and in an increase of α, indicating a rotameric change of the position of the acetyl substituent‡ which now becomes eclipsed with the C-17-α-OH bond (Figure b). Internal hydrogen bonding observed previously in the i.r. spectrum of 17α-OH-pregnan-20-ones indicates also the existence of such conformation in solutions.[4]§

Of the two possible conformations of the 6α-acetyl derivative (**3**), in which the acetyl group forms an angle α with the longitudinal axis, the one having the C=O group eclipsed with the β-H at C-6 (Figure c) is the most probable, and the alternative one (C=O perpendicular to the C-6–β-H bond) may be disregarded for steric reasons.



FIGURE

There are four possible conformations of the acetyl group in the 6β-acetyl derivative (**4**) which accommodate the α values (Table): one in which the C=O chromophore points towards the C-8–C-9 bond (Figure d) and the other in which it points towards the C-4–C-4 bond; in the other two conformations the C=O bond is rotated by 180° from the former directions. However, the first conformation is more reasonable on steric grounds. The two rotameric conformations of the acetyl group at C-6 in (**3**) and (**4**) are similar to those proposed by us previously from the u.v. and c.d. measurements in the respective 6-acetyl derivatives having a double bond at C-4–C-5.[5]

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† Calculated from the l.d. spectra of αβ-unsaturated ketones belonging to these two series (*cf.* ref. 2).

‡ Similar dichroic ratios obtained by us for cholestan-6-one and its 5α-OH derivative, indicate that the substitution in α position by OH does not effect the transition moment direction of the C=O chromophore.

§ However, an X-ray analysis of 17α-hydroxyprogesterone shows an intermolecular H-bonding, and a rotameric conformation of the COMe group similar to that in (**1**) (J. P. Declerg, G. Germain, and M. Van Meersche, *Cryst. Struct. Comm.*, 1972, **1**, 9).

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