Optical Rotatory Dispersion Studies on Aza-steroids

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WE report optical rotatory dispersion (o.r.d.) studies[1] on chromophoric systems for which no published data are yet available. These systems became available from our synthetic studies on aza-steroids[2-4] and consist of lactam, unsaturated lactam, and amide functions as part of the steroidal skeleton.

The o.r.d. measurements were carried out on a considerable number of 6-aza- and 11-aza-steroidal derivatives and the region, 380—200 mμ, which is of interest is discussed.

Studies in the 6-aza-series involve the parent lactam chromophore, and variants include the presence of double bonds in conjugation with this chromophore or different substitution of the nitrogen atom. The parent system is exemplified by the known 6-aza-7-oxo-compound in the cholestane series (I) which exhibits a positive Cotton effect with the peak at 258 mμ and the trough at 232 mμ (see Table). The effect of substitution was investigated for the *N*-benzyl series and in general, the overall effect was not

appreciable although some changes of the o.r.d. curve with concentration will be mentioned in the detailed paper.

The enol lactam (II) provides an example where a double bond is in conjugation with the lactam chromophore. Somewhat surprising is the finding that the positions of the extrema in the o.r.d. curve remain unaffected although a tremendous difference in the amplitude is noted (Table).

The presence of an additional double bond which extends the conjugation of the unsaturated lactam would be expected on the basis of its ultraviolet spectrum to have an appreciable influence on the position of the extremum in the o.r.d. curve. Indeed in the case of 17β-hydroxy-*N*-benzyl-6-aza-androsta-2,4-dien-7-one, (III), it is seen that the entire curve is shifted toward higher wavelength with the peak and trough at 311 mμ and 260 mμ respectively (Table).

TABLE

Optical rotatory dispersion data

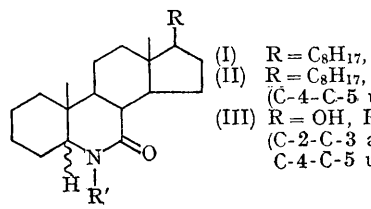
Cotton effects (pk = peak; tr = trough)

Compound	λ (mμ)	$[\Phi] \times 10^{-2}$
(I)	258 pk	+ 9
	232 tr	− 15
(II)	257 pk	+215
	228 tr	−314
(III)	311 pk	+118
	260 tr	−181
(IV)	285 pk	+ 36
	240 tr	−246
(V)	238 pk	+117
	215 tr	−126

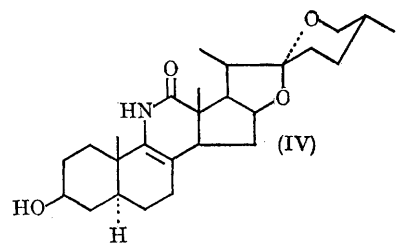
The extension of our investigations into the 11-aza-steroids provided further o.r.d. results on some novel chromophores. The enol lactam (IV) illustrates the effect of a double bond in conjugation with the lactam system when this linkage exists in the same ring as the lactam group. The ultraviolet spectrum of this chromophore suggests a shift of the o.r.d. curve to higher wavelength and this is indeed the case (Table).

Finally, o.r.d. measurements were made on 11-aza-steroid derivatives in which a carbonyl group was present as a substituent on the nitrogen atom. For this case the *N*-acetyl-11-aza-derivative (V) is cited as an example and it is noted that it shows an anomalous Cotton effect with the peak at 238 mμ and a trough at 215 mμ (Table).

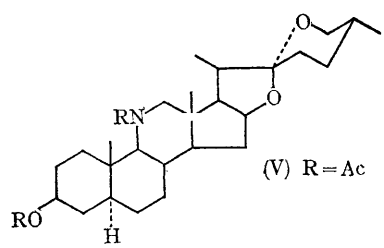
These results establish the utility of such substituents in extending the application of o.r.d. to the solution of stereochemical problems in instances where only limited information can be derived from plain curves. In particular the extension of this method to numerous stereochemical problems in alkaloid chemistry is now apparent



(I) R = C_8H_{17}, R′ = H
(II) R = C_8H_{17}, R′ = H (C-4–C-5 unsaturated)
(III) R = OH, R′ = Bz (C-2–C-3 and C-4–C-5 unsaturated)



(IV)



(V) R = Ac

since the conversion of the parent alkaloid into its *N*-acetate or -benzoate can often be achieved readily.

The application of the above results to problems in aza-steroids and interesting comparisons with the work of Klyne[5] and Wolf[6] will be published elsewhere.

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[1] The o.r.d. measurements were performed on a JASCO Model ORD/UV-5 instrument in methanol solution.
[2] J. P. Kutney, R. A. Johnson, and I. Vlattas, *Canad. J. Chem.*, 1963, **41**, 613.
[3] J. P. Kutney, I. Vlattas, and G. V. Rao, *Canad. J. Chem.*, 1963, **41**, 958.
[4] J. P. Kutney and I. J. Vlattas, *Steroids*, 1964, **4**, 595.
[5] J. P. Jennings, W. Klyne, and P. M. Scopes, *Proc. Chem. Soc.*, 1964, 412.
[6] H. Wolf, *Tetrahedron Letters*, 1965, 1075.