

X-Ray Crystal and Molecular Structure and the Circular Dichroism of 2-Aza- α -homo-5 α -cholestan-1-one

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Summary 2-Aza- α -homo-5 α -cholestan-1-one (**2**), which exhibits an $n \rightarrow \pi^*$ c.d. Cotton effect with the sign opposite to that predicted by Ogura's sign rule, is shown by X-ray diffraction to contain a quasi-chair seven-membered lactam ring with a mean C-7-NH-CO-C-3 dihedral angle of -20° indicating that the 'amide' chromophore is twisted in a way which is opposite to that of caprolactam (**1**).

CIRCULAR dichroism spectra of lactams exhibit a Cotton effect centred at 210–230 nm, which may be assigned to the $n \rightarrow \pi^*$ transition of the lactam chromophore.¹ The 7-membered ring carrying the lactam chromophore is itself chiral and recently Ogura proposed a sign rule for the $n \rightarrow \pi^*$ c.d. of seven-membered lactams, showing that the signs of the $n \rightarrow \pi^*$ Cotton effect observed for a series of seven-membered aza- α -homo steroidal lactams and lactams derived from tetrahydro- α -santonin and menthone depend solely on classification of these compounds into two types A and B² (Figure 1).

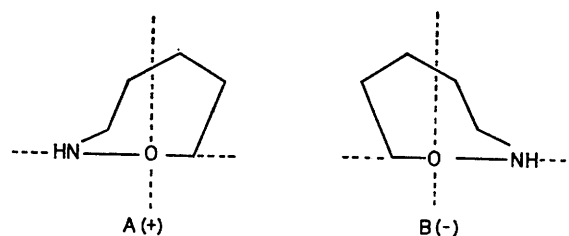
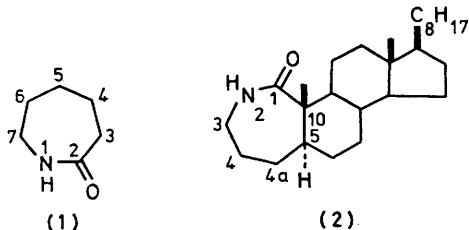


FIGURE 1

In the course of our investigation on the photo-Beckmann rearrangement of steroidal ketone oximes,³ we prepared several aza- α -homo steroidal lactams in which a second ring is adjacent to the amide chromophore, either at the 3,4-positions or at the 6,7-positions of caprolactam (**1**). It has been found that the rule fails to predict the sign of $\Delta\epsilon$ of several of these lactams. Thus, as a typical example, 2-aza-

$\Delta\epsilon$ value of -11.1 at λ_{\max} 230 nm in methanol whose sign is opposite of that predicted by Ogura's rule.

Since seven-membered monocyclic lactam rings appear to take up a quasi-chair conformation with the atoms of the C-NH-CO-C unit approximately coplanar^{4,5} and this geometry of lactams may be considered as the basis of Ogura's rule, we have determined the exact geometry of 2-aza- Δ -homo-5 α -cholestan-1-one (**2**) by X-ray crystallographic analysis.



Crystal data: C₂₇H₄₇NO, orthorhombic, space group C222₁, $a = 11.624(4)$, $b = 20.027(6)$, $c = 43.425(10)$ Å, $Z = 16$, $D_c = 1.056$ g cm⁻³. 3485 unique intensity data for $2\theta < 120^\circ$ were collected on an automatic, four-circle diffractometer with LiF-monochromated Cu- K_α radiation using the $\theta-2\theta$ scanning technique. The structure was solved by the Monte Carlo direct method using the 50 strongest reflections as a starting set.⁶ An E -map based on the 37th random phase set afforded 29 out of the 58 independent atoms. The remaining atoms were located in a second E -map and a difference Fourier map. The structure thus obtained was refined by the block-diagonal least-squares method with anisotropic temperature factors. After 76 hydrogen atoms had been located in a second difference Fourier map, several cycles of the least-squares refinement were carried out including these hydrogen atoms.

The final R value was 11.0%. The geometries of the two independent molecules are almost identical except that, in one molecule, the terminal methyl groups of the side chain are distributed statistically. A perspective view of the molecule having no disordered structure is given in Figure 2.

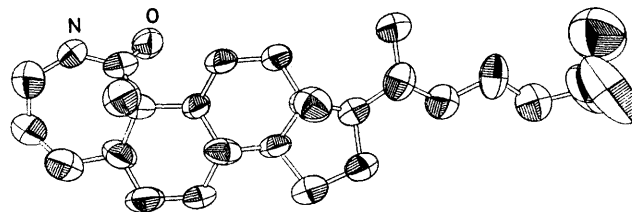


FIGURE 2. A perspective view of the 2-aza- Δ -homo-5 α -cholestan-1-one molecule (**2**).

The average values of the corresponding dihedral angles in the lactam rings are: C(1)-N(2), -20° ; N(2)-C(3), -51° ; C(3)-C(4), 77° ; C(4)-C(4a), -67° ; C(4a)-C(5), 63° ; C(5)-C(10), -73° ; and C(1)-C(10), 72° .[†]

Thus, although the conformation of the lactam ring of 2-aza- Δ -homo-5 α -cholestan-1-one (**2**) is a quasi chair, the mean C-7-NH-CO-C-3 torsion angle is -20° and the fusion of the second ring at the 3,4-position of caprolactam, in which the C-7-NH-CO-C-3 torsion angle is $+4.2^\circ$, twists the 'amide' chromophore in a way which is opposite to that of caprolactam (**1**).

The effect of the second adjacent ring in twisting the amide chromophore on $\Delta\epsilon$ values and the signs of c.d. Cotton effects of seven-membered lactams thus appears to be significant. Details of the assessment of these second-ring contributions and of the effects of substituents on $\Delta\epsilon$ values and the signs of the c.d. of a large number of steroidal seven-membered lactams and related lactones will be published shortly.⁷

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[†] The atomic co-ordinates for this work are available on request from the Director of the Cambridge Crystallographic Data Centre, University Chemical Laboratory, Lensfield Road, Cambridge CB2 1EW. Any request should be accompanied by the full literature citation for this communication.

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