

CRYSTAL STRUCTURE OF CAROLENALIN MONOACETATE : REVISION OF THE STEREOCHEMISTRY OF
CAROLENALIN AND CAROLENIN

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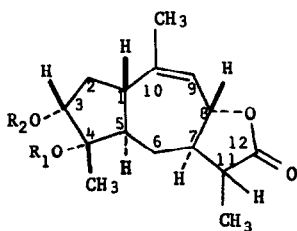
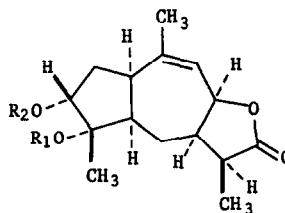
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Isolation of two new sesquiterpene lactones, carolenalin and carolenin, from North Carolina Helenium autumnale L. was reported recently¹, and the structure and stereochemistry of these guaianolides were deduced from extensive spectroscopic studies to be (I) and (II), respectively; the orientation of the C-11 methyl group was not determined. The assignment of stereochemistry to the ring junctions depended heavily on the value of the proton coupling constant $J_{7,8} = 7.2\text{Hz}$ and the result of nuclear Overhauser effect studies which produced enhancement of the H-8 proton signal when the H-1 proton was irradiated. These data were interpreted as being indicative of the presence of a trans-fused lactone. However, they are also compatible with a cis-fused geometry in which the central seven-membered ring adopts a boat conformation with H-1 and H-8 diaxially disposed, and therefore the stereochemical assignment could not be assumed to be unambiguously derived.

We have subjected carolenalin monoacetate, $C_{17}H_{24}O_5$, to single crystal X-ray analysis in order to establish unequivocally the stereochemistry. The crystals are orthorhombic, space group $P2_12_12_1$, $a = 16.21(2)$, $b = 16.59(2)$, $c = 6.14(1)$ Å, $Z = 4$. The structure was solved by direct phase-determining calculations using MULTAN² and 484 $|E|$ values > 1.0 . Molecular parameters were refined by full-matrix calculations to $R = 0.088$ over 1339 independent reflexions from photographic data³.

The X-ray analysis establishes structure (III), or its mirror image, for carolenalin monoacetate wherein both five-membered rings are cis-fused to the seven-membered ring. In addition, the C-11 methyl group is found to be β -oriented⁴. Moreover, the α H-7, β C₄-CH₃ relationship which had been assigned on the basis of biogenetic considerations is verified by this analysis. Thus, from the present result and the earlier spectroscopic studies, it follows that the structure of carolenalin must be modified to (IV) while that for carolenin is represented by (V). It is noteworthy that in the crystal the seven-membered ring adopts a very flattened chair conformation characterized by torsion angles $\theta_{1,5} = 44^\circ$, $\theta_{5,6} = -79^\circ$, $\theta_{6,7} = 77^\circ$, $\theta_{7,8} = -40^\circ$, $\theta_{8,9} = 7^\circ$, $\theta_{9,10} = 4^\circ$, $\theta_{1,10} = -15^\circ$, whereas the solution nmr spectral data can be accommodated only if this ring is in a boat conformation. Certainly, the latter appears to be preferred when molecular models are constructed and consequently crystal packing forces must be responsible for the different conformation found in the solid state.

(I) $R_1 = R_2 = H$ (II) $R_1 = H, R_2 = \text{Angelyl}$ (III) $R_1 = H, R_2 = \text{Acetyl}$ (IV) $R_1 = R_2 = H$ (V) $R_1 = H, R_2 = \text{Angelyl}$

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References

1. H. Furukawa, K. H. Lee, T. Shingu, R. Meck, and C. Piantadosi, J. Org. Chem., **38**, 1722 (1973).
2. G. Germain, P. Main, and M. M. Woolfson, Acta Cryst., **A27**, 368 (1971).
3. Full details of the crystal structure analysis will be reported elsewhere.
4. We assume that the C-7 hydrogen atom is α -oriented as in all other known naturally-occurring guaianolides.