Tetrahedron Letters No. 14, pp 1229 - 1232, 1975. Pergamon Press. Printed in Great Britain.

STRUCTURE AND STEREOCHEMISTRY OF CAROLENALONE, A NEW SESQUITERPENE LACTONE FROM NORTH CAROLINA HELENIUM AUTUMNALE L.

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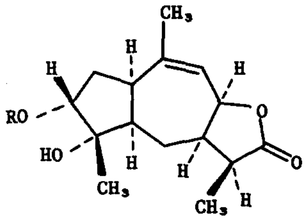
(Received in Japan 10 February 1975; received in UK for publication 28 February 1975)

We reported recently[1,2] on the isolation and structure determination of two new guaianolides, carolenalin(I) and carolenin(II), from North Carolina Helenium autumnale L. We now report on the isolation and characterization of an additional new sesquiterpene lactone, carolenalone(III), from this same plant. Carolenalone appears to represent the first recorded instance of a naturally-occurring guaianolide containing a cycloheptenone ring system.

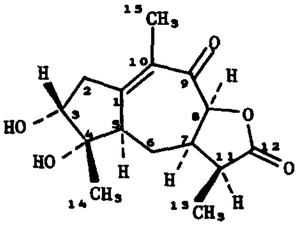
Carolenalone, a minor component, was isolated in the form of colorless needles from the mother liquor following the complete removal of carolenalin and carolenin by careful silica gel chromatography. Carolenalone(III), $C_{15}H_{20}O_5$, m.p. 245-247°, shows prominent mass spectral peaks at m/e 280(M+), 262(M-18), 237(M-43), 219(M-18-43), 208, 207, 191, and 189, and its ir spectrum (Nujol) discloses, in addition to the presence of two hydroxyl groups[3] (3560 and 3520 cm^{-1}) and a γ-lactone ring (1770 cm^{-1}), an α, β-unsaturated ketone (1670 cm^{-1}). The most conspicuous difference between the nmr spectrum

(in $CDCl_3$ and pyridine-d_5, 100-MHz) of carolenalone and that of carolenalin(I) is the presence of a low-field one proton doublet at δ 5.13 (J = 10.0 Hz) corresponding to the lactonic proton at C-8 in (III) instead of two multiplets at δ 5.o9 (1H, H-8) and 5.35 (1H, H-9) found in the spectrum of (I). Extensive nmr decoupling also led to the following assignment of protons which fitted into a carolenalone structure as depicted in (III) : δ 1.06 (3H, s, H-14), 1.11 (3H, d, J = 7.5 Hz, H-13), 1.80 (3H, m, H-15), and 3.94 (1H, dd, J = 2.0 and J = 4.0 Hz, H-3).



carolenalin(I), R = H

carolenin(II), R = Angelyl



carolenalone(III)

The entire molecular structure and relative stereochemistry of carolenalone were established by an X-ray single crystal analysis. Crystals from $CHCl_3$/hexane form as fine needles which belong to the orthorhombic system, space group $P\,2_12_12_1$, a = 7.31(1), b = 21.20(1), c = 9.21(1) Å, Z = 4. Three-dimensional intensity data were recorded on an Enraf-Nonius CAD 3 automated diffractometer using Ni-filtered Cu-K_α (λ = 1.542Å) radiation and the θ -2θ scanning technique as described eleswhere[4]. The structure was solved by direct phase-determining methods using MULTAN[5], and the atomic positional and thermal parameters (anisotropic C,O ; fixed H contributions) were refined by full-matrix least squares calculations to $\underset{\sim}{R}$ 0.078 over 476 statistically significant $[\underset{\sim}{I} > 2.0\sigma(\underset{\sim}{I})]$ reflections.

Bond lengths and valency angles all lie in the normal ranges; endocyclic torsion angles[6] are shown in the Figure. The cyclopentane and γ-lactone rings adopt envelope conformations with C-4 and C-7, respectively, being the out-of-plane atoms. The cycloheptenone ring conformation corresponds to a flattened twist-chair ($\underset{\sim}{C}_2$) form in which the approximate two-fold symmetry axis passes through C-7 and bisects the C-1═C-10 double bond. At the α,β-unsaturated ketone the C=C-C=O torsion angle of -157° indicates the distinct non-planarity of the atoms in this group due to the torsional strain introduced by the presence of the cis-fused γ-lactone ring.

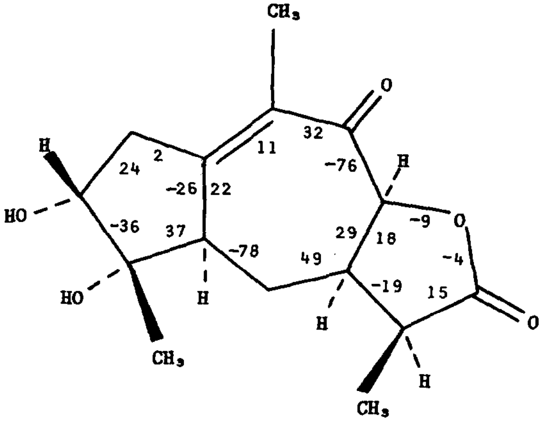
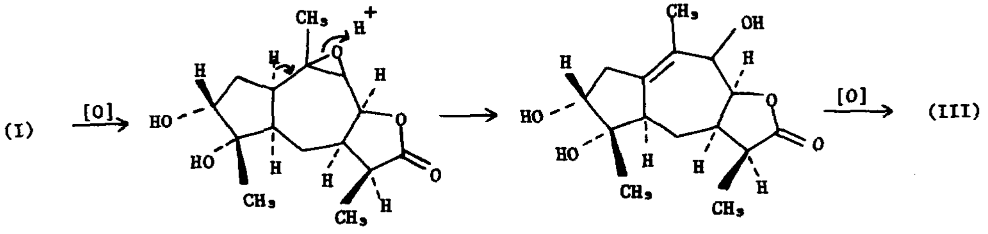


Figure. Endocyclic torsion angles (deg.) in (III)

The co-occurrence of (I), (II), and (III) in the single plant is strongly indicative of their biosynthetic interrelationship and the transformation of (I) ⟶ (III) may proceed through the sequence of mechanistically feasible steps shown below.



Acknowledgements

This investigation was supported in part by USPHS Grant No. CA-12360 from the National Cancer Institute to K. H. L. We thank the American Enka Company for a Graduate Fellowship (K. O.).

References and Footnotes

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