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THE STRUCTURE OF ARTABSIN

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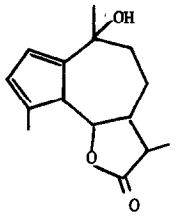
The sesquiterpene lactone artabsin, from Artemisia absinthium L., has been assigned the structure I on the basis of its relationship to isophotosantonic lactone and a degradation sequence which led to the placing of the double bonds as shown. (2,3)

We have examined a specimen of A. absinthium L. collected in Pullman, Washington, (4) the authenticity of which is supported by our isolation of artemetin (5-hydroxy-3,6,7,3′,4′-tetramethoxy flavone), which has been found in this species in several previous studies. (5) A sesquiterpene lactone, isolated in about 0.1% yield, had properties indicating that it was the artabsin described earlier (2) (and which was at that time also isolated in 0.1% yield). Our compound had the composition $C_{15}H_{20}O_3$, m.p. 131-133°, λ_{max} 248 mμ (log ε 3.49), $[\alpha]_D$ −38°; reported (2) for artabsin, m.p. 133-135°, λ_{max} 248 (3.65), $[\alpha]_D$ −49°. Our compound was unstable, tending to deteriorate on keeping, also a characteristic of the compound isolated earlier. (2) It is probable that our compound is the same as the one described by the Czech workers.

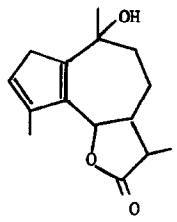
Artabsin does not, however, possess structure I, for the n.m.r. spectrum shows but one vinyl proton. In addition to signals for three methyl groups at δ 1.21 (3H, d, J = 6.5 cps), 1.57 (3H, s) and 2.16 (3H, d J = 1.5 cps), the spectrum contains but two protons in the low field region, at 5.35 (1H, mult.) and 6.05 (1H, broad triplet), corresponding, respectively, to the C-6 (lactone) proton and a vinyl proton at C-3 (II) or C-2 (III). The low field position of the vinyl methyl group (2.16 ppm) and the small splitting, are in accord with its attachment

at C-4 as in I, II or III, of which I is ruled out by the absence of a second proton in the vinyl region.

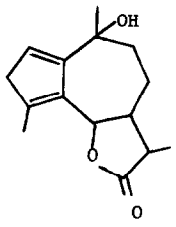
Artabsin is now shown to have the structure II by consideration of the n.m.r. spectrum of its Diels-Alder adduct with maleic anhydride (partial structures IV (from II) and V (from III)).



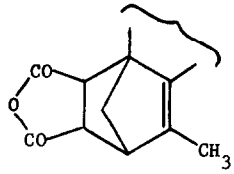
I



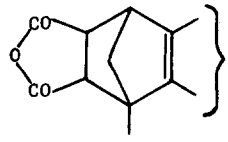
II



III



IV



V

The methyl group of adduct IV is vinylic and should be readily distinguishable from the methyl group of V by its n.m.r. signal. The adduct, which crystallized with a molecule of chloroform (found: C, 51.65; H, 5.15; calc. for $C_{19}H_{22}O_6 \cdot CHCl_3$: C, 51.55; H, 4.93) had m.p. 240° (dec.) after loss of solvent at 130°. The chloroform was readily identified in the mass spectrum, which also included peaks for the parent ion (m/e 346) and abundant ions corresponding to the loss of two separate molecules of CO, consistent with the expected behavior of this kind of compound. Appropriate metastable ions were observed for these fragmentations. The n.m.r. spectrum of the adduct showed the methyl group signals at C-10 and C-11 nearly unchanged from those of the original lactone; but the third methyl group appeared as a sharp singlet at δ 1.79, in complete accord with structure IV. The disappearance of the small coupling (J = 1.5 cps)

shown in the C-4 methyl signal in II, and the upfield shift, is consistent with the change II → IV. The spectrum of IV also lacks a vinylic proton signal but contains signals expected for the two protons at the junction of the anhydride ring.

A remarkable property of artabsin is its formation of an intense blue color with concentrated hydrochloric acid. (6) It was observed that in the course of the Diels-Alder reaction a t.l.c. spot corresponding to artabsin persisted even in the presence of excess maleic anhydride. This compound did not, however, give the blue color with acid and is probably a dihydroartabsin, for the mass spectrum of artabsin showed, besides the expected parent ion at m/e 248, an additional peak at m/e 250. This accompanying compound was present to a very small extent only, for the n.m.r. spectrum of the compound showed no discernable signals other than those expected for II; and recovery of the contaminant from the Diels-Alder reaction mixture gave only a very small amount of a substance which has not yet been completely characterized. (7)

A part of the experimental evidence advanced (2) for structure I was the formation of formic acid upon oxidation of a permanganate-hydroxylation product of artabsin. No such reaction can be formulated for II, and it seems probable that the formic acid found in the study was an artefact.

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References

1) Contribution No.2236 from the Department of Chemistry, U.C.L.A.

2) V. Herout and F. Šorm, Coll. Czech. Chem. Comm., 18, 854 (1953); 19, 792 (1954); V. Herout, L. Dolejš and F. Šorm, ibid., 22, 1914 (1957).

3) M. Suchy, V. Herout and F. Šorm, Coll. Czech. Chem. Comm., 29, 1829 (1964).

4) Collected by Dr. George H. Ward (Voucher No. 2313), to whom we express our thanks.

5) "Chemistry of Flavonoid Compounds," T. A. Geissman, Ed., Pergamon Press, Oxford, 1962; p. 428.

6) This color is not due to an azulene, for it changes to yellow in alkaline solution and is regenerated upon reacidification.

7) The A. absinthium used in this study contained another prominent constituent besides artabsin and the dihydrocompound. These components will be studied further when more plant material can be secured.