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The Structure of Artabsin and Absinthin

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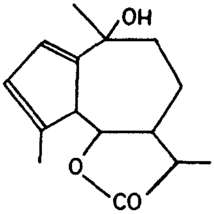
Lately we have reexamined the structures of the sesquiterpenic lactones artabsin (I) and absinthin (II), from Artemisia absinthium L., by means of n.m.r. spectroscopy and found that these compounds do not posses the structures I[1,2] and II[3] previously proposed for them.

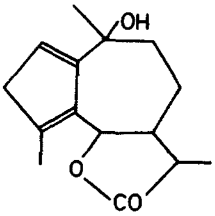
Artabsin is now shown to have the structure III on the basis of its n.m.r. spectrum ($CDCl_3$,HA-100). The vinyl proton H-2 forms a triplet at 3.97τ with $J_{2,3}$ = 1.6 Hz and $J_{2,15}$ = 0, the two H-3 protons form a complex multiplet at 7.17τ with $J_{3,2}$ = 1.6 Hz, $J_{3,6}$ = 2.1 Hz and $J_{3,15}$ = 0, the methylprotons H-15 form a sharp doublet at 7.86τ with $J_{15,6}$ = 1.7 Hz, and the H-6 proton appears as a complex doublet at 4.66τ with $J_{6,7}$ = 9.0 Hz, $J_{6,3}$ = 2.1 Hz and $J_{6,15}$ - 1.7 Hz. This assignment is based on frequency-swept decoupling experiments. The present long-range couplings clearly demonstrate that the alternative structure IV is out of consideration.

The structure IV was suggested by Geissman and Winters[4] on the basis of the n.m.r. spectrum of the Diels-Alder adduct of artabsin with maleic anhydride. We also prepared this adduct and obtained a crystalline product m.p. 210-228°C, but, as shown by its IR-spectrum (anhydride and OH bands absent; increased intensity of the lactonic band at 1775 cm^{-1} indicating the formation of a new five-membered lactone), this product is a dilactone-acid (found : C 66.21; H 6.52; H^+ 0.34; calc. for $C_{19}H_{22}O_6$: C 65.88; H 6.40; H^+ 0.28). The original adduct is unstable and rearranges into a dilactone-acid containing two five-membered lactones as we have clearly demonstrated by the time-dependence of the n.m.r. spectrum of a fresh solution of the adduct in hexadeuterobenzene, prepared by direct reaction of the components in this solvent. The structure of the dilactone-acid has not yet been elucidated in detail, the structure V is tentatively proposed. The reported chemical shifts for the methyl groups[4] are identical with our data for the dilactone-acid, and therefore, the adduct reported by Geissman and Winters[4] should be the same dilactone-acid.

Structure III of artabsin is further supported by the n.m.r. spectra of various derivatives (e.g. dihydroartabsin etc.), a detailed discussion and all experimental data are given in the full paper[5].



I



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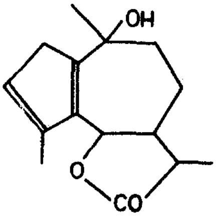
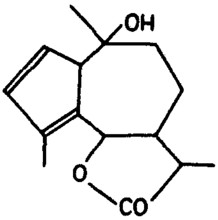
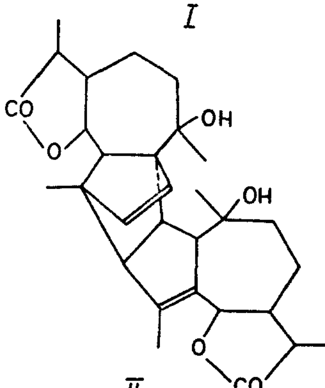


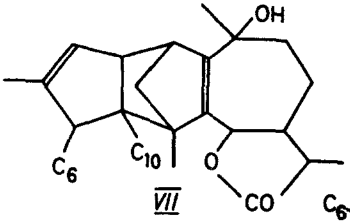
IV



VI



II



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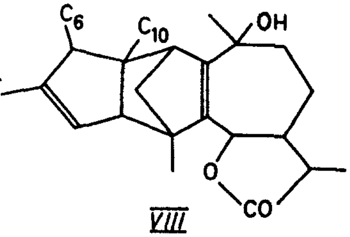

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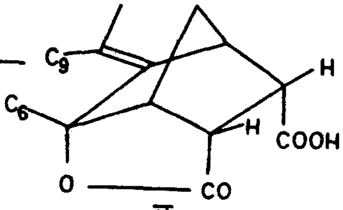

V

Absinthin, the bitter principle of Artemisia absinthium L., was considered[3] to be a Diels-Alder adduct of two guaianolide components I and VI. Therefore, the speculative structure II is ruled out by the new structure of artabsin. This finding is further supported by the presence of only one vinyl proton signal of the type $-CH=C(CH_3)-$ in the n.m.r. spectrum. The outcome of the alkaline degradation of absinthin[5] is in accordance with the view that this compound indeed arises by a Diels-Alder type condensation. Therefore, we tried to obtain the two true components forming absinthin by thermal dissociation. After refluxing of absinthin in decalin we isolated two monomeric lactones, one of which was identical according to n.m.r. spectrum with artabsin. The structure of the second, less polar, lactone was directly derived from its n.m.r. spectrum ($CDCl_3$,HA-100). In addition to signals for three methyl groups at 8.88τ (doublet, 3 H, J = 7.0 Hz), 8.46τ (sharp singlet, 3 H) and 7.92τ (doublet, 3 H, J = 1.35 Hz), a triplet at 4.95τ (1 H, J_1 = 9.8 Hz, J_2 = 8.7 Hz) and a complex multiplet at 3.95τ (2 H). As has been shown by the frequency-swept decoupling experiments, the assignment of the spectrum is clearly consistent with the structure I.

Assuming artabsin and the guaianolide I to be the true Diels-Alder components, the two alternative formulae VII and VIII may be now proposed for absinthin, in agreement with its n.m.r. spectrum.

The final proof of the structure of absinthin is in progress.

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