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STRUCTURE OF AJUGARIN-V

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The structure of a *neo*-clerodane diterpene, ajugarin-V isolated from *Ajuga remota* (Labiatae) has been established by means of spectroscopic and chemical data.

The ether extract of leaves of the East African medicinal plant, *Ajuga remota* (Labiatae) has recently yielded a series of *neo*-clerodane diterpenoids, ajugarin-I, -II and -III, and clerodin which have insect antifeedant activity against the African armyworm, *Spodoptera exempta*[1,2] with a leaf disk assay.[3] In addition to these antifeedant diterpenes, another *neo*-clerodane diterpenoid, ajugarin-IV has been identified as a moderate insecticide against silkworm, *Bombyx mori*[4] with an artificial diet feeding assay.[5] The structure-activity relationships among these diterpenes are of interest since ajugarin-IV exhibits insecticidal activity but not antifeedant property. The perhydro[2,3-*b*]furan ring in clerodin has been concluded as the active center of the molecule.[6] However, this can not explain the antifeedant activity of the ajugarins since they do not have this moiety. In these systems the antifeedant activity has been suggested in the *trans*-decalin portion of the molecule.[7] In order to investigate this structure-activity relationship, further purification of the ether extract has been carried out. This has now led to the isolation in trace amount of an additional new diterpene, ajugarin-V, which is colsely related to ajugarin-I.

Ajugarin-V, m.p. 217-218°C, $[\alpha]_D$ -13.5° (c, 0.18 in $CHCl_3$) has the following physical constants: $C_{22}H_{32}O_5$ (M^+ 376.2257; Calc. 376.2250); λ_{max} (EtOH) 210 nm (ε, 11000); ν_{max} ($CHCl_3$) 1780 and 1750 (conj. γ-lactone bearing α-H), 1725 (acetate) and 1638 cm^{-1} (conj. double bond). Both the ^1H n.m.r. and ^{13}C n.m.r. are similar to those of ajugarin-I except for the number of acetoxyl and methyl groups. Specifically, the ^1H n.m.r. shows only one acetoxyl signal at δ 1.96 ppm (3H, s) and dose not contain the typical AB doublets corresponding to $-CH_2OAc$ in the ajugarins. The ^{13}C n.m.r. shows the presence of three methyl groups at δ 14.6, 15.3 and 17.8 ppm, one of which is assigned to the secondary methyl group, this conclusion supported by the ^1H n.m.r. signals appearing at δ 0.79 ppm (3H, d, J= 6 Hz), and the others to the tertiary methyl groups at δ 0.77 (3H, s) and 1.24 ppm (3H, s). The comparison of the above mentioned spectra with those of ajugarin-I, together with the molecular formula indicated that ■-CH_2OAc group in ajugarin-I

was replaced by the CH_3 group in ajugarin-V.

The absolute configuration was determined by conversion of ajugarin-V into the 6-oxo derivative (2) by a procedure similar to that used for ajugarin-I, whose absolute configuration was established by x-ray crystallography.[2] The c.d. spectrum (in MeOH) of (2) $\Delta\varepsilon$(296 nm) -3.84 is almost identical with that of the corresponding 6-oxo derivative (3) of ajugarin-I. Therefore, the absolute configuration of ajugarin-V is that shown in (1).

Ajugarin-V is unique in lacking the C-18 oxygen substituent, and exhibits neither antifeedant nor insecticidal activity. This suggests that the *trans*-decalin portion of the molecule in the ajugarins, and also most likely in the clerodin, is involved in their antifeedant property.

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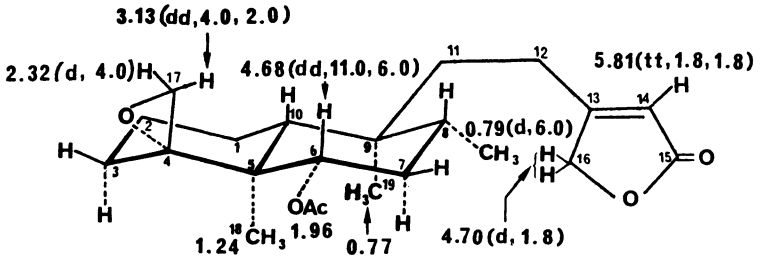
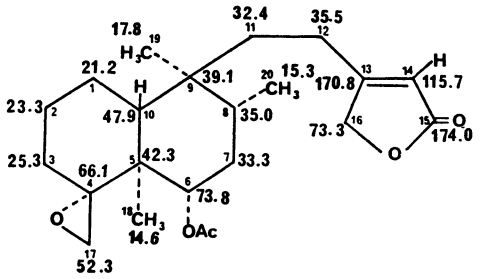
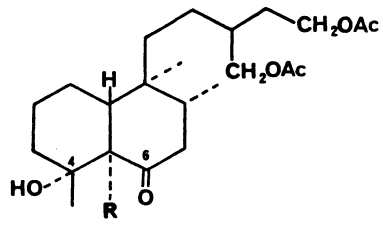


^1H n.m.r. data for ajugarin-V; $CDCl_3$ solution; δ values multiplicity and J values (in Hz) in parentheses.

(1) Ajugarin-V





(2) R = CH_3

(3) R = CH_2OAc

^{13}C n.m.r. data (δ/ppm) for $CDCl_3$ solution.

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