Structure of Ajugarins

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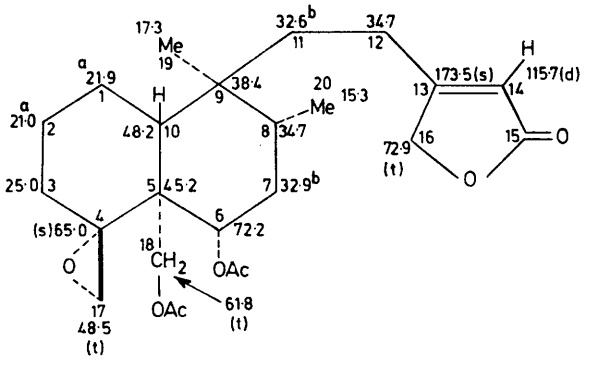
Summary The structure of three new *ent*-clerodanes, which are insect antifeedants, isolated from *Ajuga remota*, have been determined.

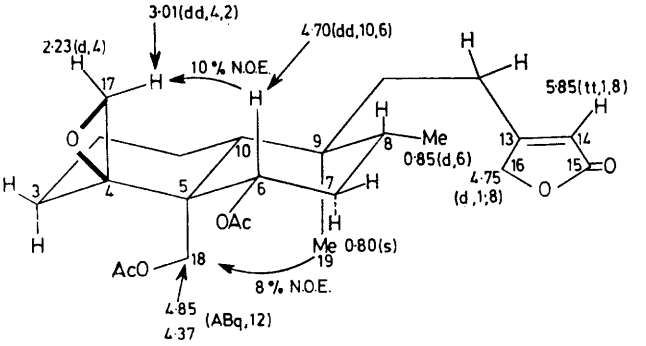
THE observation that *Ajuga remota* (Labiatae) leaves collected around Nairobi, Kenya, are not attacked by African army worms has led to the isolation of three moderately strong antifeedants: ajugarin-I (**1**), m.p. 155—157 °C, 0·05% yield from dry leaves, ajugarin-II (**2**), m.p. 188—189 °C, 0·002% yield, and ajugarin-III (**3**), m.p. 243—245 °C, 0·001% yield. The activity was followed by the host–plant leaf disc method using *Zea mays* (maize) for *Spodoptera exempta* (monophagous) and *Ricinus communis* for *S. littoralis* (polyphagous).‡



(**1**) Ajugarin-I; ^{13}C n.m.r. data (δ/p.p.m.) for $CDCl_3$ solutions. C=O resonances at 169·7, 169·9, and 170·7 p.p.m. a and b, assignments interchangeable. (**2**) Ajugarin-II; 6α-OH replaces 6α-OAc. (**3**) Ajugarin-III; 4α-OH, 4β-CH_2OH replaces epoxide.

We put forward the *ent*-clerodane structures (**1**)—(**3**) for these compounds. Ajugarin-I which is closely related to clerodin[1,2] has the following constants: $C_{24}H_{34}O_7$, *M* 434 by chemical ionisation mass spectrometry (c.i. m.s.) with isobutane and methane; *m/e* 404 by electron impact m.s. (*M* — CH_2O); λ_{max} (MeOH) 212 nm (ε 10,000); ν_{max} ($CHCl_3$) 1780 (conj. γ-lactone), 1750 and 1730 (acetate), and 1640 cm^{-1} (conj. double bond). The ^{13}C n.m.r. data for ajugarin-I, as summarized in structure (**1**), showed the presence of 2 Me, 2 Ac, 9 CH_2, 3 CH and 1 lactone carbonyl groups, together with 3 tetra-substituted and 2 olefinic carbon atoms; the results are based on a combination of proton-noise decoupling, off-resonance decoupling, Fourier transform, and Fourier transform off-resonance decoupling techniques.[3]

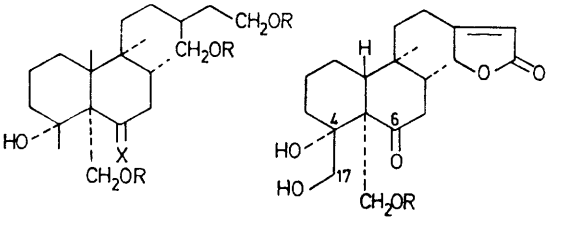
The pertinent ^1H n.m.r. data are shown in structure (**1a**); the presence of 3-*ax*-H and 7-methylene protons was apparent from the coupling pattern for 17-H (W coupling) and 6-H, respectively. The tt pattern of the 14-H signal (δ 5·85) showed that a methylene group was adjacent to the unsaturated γ-lactone ring. The 17-H (δ 2·23 and 3·01) signals were correlated with the δ 48·5 p.p.m. ^{13}C triplet by selective decoupling. The chemical shift of the C-4 (δ 65·0 p.p.m.) signal suggested that it was substituted by an oxygen function. However, since ajugarin-I contains no hydroxy-group, the data lead to an exocyclic epoxide ring, the presence of which was supported by the diagnostic *M* — 30 peak (*m/e* 404). The combined spectral data strongly suggested that ajugarin-I possessed a clerodane skeleton.[1,2,4] The N.O.E. data in structure (**1a**) are in full agreement with this deduction.



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

Ajugarin-II (**2**)§ contains a 6α-OH group instead of acetate as shown by the acetylation of (**2**) to yield (**1**).

Ajugarin-III (**3**),§ $C_{24}H_{36}O_8$, *M* 452 by c.i. m.s., had ^{13}C and ^1H n.m.r. spectra very similar to those of (**1**), except for the following: ^{13}C (C_5D_5N) C-4, δ 76·4 and C-17, δ 64·1 p.p.m.; ^1H (C_5D_5N) 17-H AB q at δ 4·25 (*J* 12 Hz). This leads to structure (**3**).



(**4**) R = H, X = α-OH, β-H
(**5**) R = Ac, X = O
(**6**) R = H
(**7**) R = Ac

The absolute configuration was determined by conversion into 6-oxo derivatives. Dihydroajugarin-I, obtained by hydrogenation of (**1**) over 10% Pd–C in ethanol, was

‡ The antifeedant levels are as follows (minimum concentration): 100 p.p.m. for ajugarins-I and-II against *S. exempta*, and 300 p.p.m. against *S. littoralis*. It was suspected that ajugarin had antiecdysone activity against army worms. However, topical and injection tests carried out by Dr. W. S. Bowers against looper larvae and milkweed bug nymphs showed that this was not the case.

§ Spectroscopic data for ajugarins-II and -III were consistent with the structures shown.

reduced with $LiAlH_4$ in dioxan at room temperature to yield the pentaol (**4**), which upon acetylation and Jones' oxidation gave the 6-oxo-triacetate (**5**), c.d. (MeOH) $\Delta\epsilon$ (298 nm) −3·41. The corresponding 6-ketone having an identical ring A–B unit (but different saturated side-chain) has been prepared by Hosozawa, *et al.*,[5] from clerodin[1] the absolute configuration of which has been established by *X*-ray crystallography;[2] the clerodin-derived 6-ketone has a positive c.d. (EtOH), $\Delta\epsilon$ (302 nm) + 3·51,[5] and hence the ajugarin configuration is antipodal to that of clerodin. Jones' oxidation of (**2**) gave the 6-oxo-diol (**6**), c.d. (MeOH) $\Delta\epsilon$ (298·5) − 2·98, which was acetylated to yield the 6-oxo-diacetate (**7**), c.d. (MeOH) $\Delta\epsilon$ (295 nm) −3·21.¶

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¶ The negative c.d.'s of (**5**), (**6**), and (**7**) show that changes in the 4-substitutents do not affect the sign of the Cotton effect for the 6-oxo group.

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