A Hydroperoxychroman with Insect Antifeedant Properties from an African Shrub. Characterization of Fully-substituted Aromatic Structures

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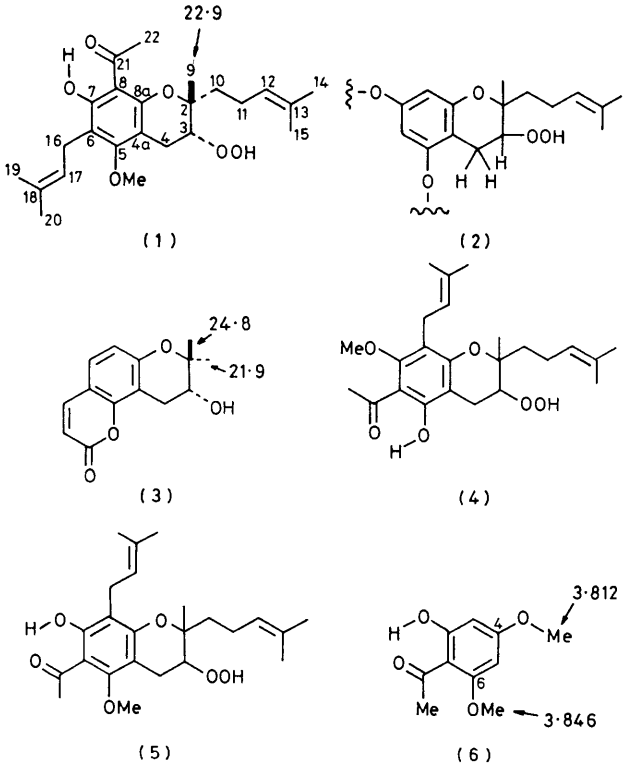
Summary The African shrub *Harrisonia abyssinica* (Simarubaceae) has yielded an army-worm antifeedant, the structure of which has been determined as 8-acetyl-3α-hydroperoxy-2α-isohex-3-enyl-6-isopent-2-enyl-5-methoxy-2β-methylchroman (**1**) (relative configuration).

THE shrub *Harrisonia abyssinica* Oliv. (Simarubaceae) is one of the most widely used folk medicinal plants in East Africa.[1,2] The ether extract of this plant has yielded the two limonoids harrisonin[3] and 12β-acetoxyharrisonin[4] which, besides exhibiting antifeedant activity against the African army-worm *Spodopetra exempta* and the Southern army-worm *S. eridania*, possess antibiotic and cytotoxic activities. The ether extract has yielded a third antifeedant compound effective against *S. eridania*, hydroperoxide-Ha, which has the unique hydroperoxychroman structure (**1**).

The chemical formula $C_{24}H_{34}O_6$ (calc. mass 418·23553) of (**1**) was determined by mass spectrometry which gave two prominent peaks at 418·23576 (M^+) and 402·24127 (M^+-16) (calc. for $C_{24}H_{34}O_5$, mass 402·24062). Since the loss of 16 (oxygen) and 34 (H_2O_2) mass units is characteristic of hydroperoxides,[5] the two sets of fragments found in the chemical ionization mass spectrum (methane carrier gas), namely 447 ($M^+ + 29$), 419 ($M^+ + 1$), 385 [$(M + 1)^+ - 34$], and 443 [$(M - 16)^+ + 41$], 431 [$(M - 16)^+ + 29$], 403 [$(M - 16)^+ + 1$], suggested the presence of a hydroperoxide moiety. This was supported by a positive iron(II) thiocyanate colour test[6] which is specific for hydroperoxides.

Pertinent physical data of hydroperoxide-Ha are as follows: ν_{max}(CHCl$_3$) 3420 (OO–H), 3030 (aromatic), 2700 (br., chelated OH), 1632 (chelated C=O), and 1380 cm^{-1} (doublet, *gem*-Me$_2$); λ_{max}(MeOH) 220 (sh), 282 (ε 15,500), and 357 (ε 2760) nm; c.d. (MeOH) 280 (Δε −0·23), 308 (Δε +0·03), and 352 (Δε −0·85) nm. The presence of the chelated hydroxy-function (i.r.) was supported by the red shift of the 282 nm band to 311 nm upon addition of $AlCl_3$.[7]



(1) (2) (3) (4) (5) (6)

The nature of the eight degrees of unsaturation derived from the molecular formula was clarified by ^{13}C n.m.r. analysis (in CDCl$_3$). Namely, a carbonyl group (δ 302·0 p.p.m., C-21), two trisubstituted double bonds (two singlets at 132·0 and 130·7 p.p.m., C-13 and C-18,† and two doublets

† The assignments are interchangeable.

at 124·1 and 123·3 p.p.m., C-12 and C-17),† and six aromatic signals characteristic of a 1,3,5-oxygenated system (161·5, 161·4, and 160·5 p.p.m., C-5, C-7, and C-8a† and 112·5, 105·8, and 103·2 p.p.m. C-6, C-8, and C-4a†) [8] which account for seven degrees of unsaturation were readily identified; the remaining unsaturation was assigned to a ring structure.

The 360 MHz ^{1}H n.m.r. spectrum (in $CDCl_3$) of (**1**) clarified the presence of the following moieties: (i) an ABX system δ 3·33 and 3·23 (both dd, *J* 14·4 and 8·8 Hz, benzylic 2 × 4-H) and 4·72 (t, *J* 8·8 Hz, 3-H); (ii) ArOMe, δ 3·93; (iii) Ar-Ac, δ 2·61 (21-Me); (iv) aliphatic Me, δ 1·34 (2-Me); (v) chelated OH, δ 13·1 (7-OH; disappears on D_2O addition); (vi) aromatic isopentenyl, δ 3·25 (br. d, *J* 6·3 Hz, benzylic 2 × 16-H), δ 5·17 (m, 17-H), and δ 1·76, 1·70 (2 × 18-Me);† and (vii) homoisopentenyl, δ 1·56 (m, 2 × 10-H), δ 2·15 (m, 2 × 11-H), δ 5·14 (m, 12-H), and δ 1·66, 1·64 (2 × 13-Me).†

The single aliphatic quaternary carbon appeared at δ 73·2 p.p.m. (C-2), a chemical shift typical for carbons linked to oxygen functions. In conjunction with the n.m.r. data given above and the presence of another ring, the 1,3,5-trioxygenated partial structure (**2**) was derived, the substituents on the aromatic ring being OH, OMe, COMe, and isopentenyl.

The ^{13}C n.m.r. peak at δ 90·1 p.p.m. (C-3) and the ^{1}H n.m.r. peak at δ 4·72 (3-H) are characteristic of aliphatic hydroperoxides.[9] The 2-Me and 3-OOH groups have been assigned a *trans*-configuration by comparison of ^{13}C n.m.r. data with those of the model compound lomatin (**3**).[10] Of the two Me signals at 21·9 and 24·8 p.p.m., the former is assignable to the α-Me due to the γ-effect; a longer α-oriented substituent would shift the β-Me 24·8 p.p.m. peak close to the 22·9 p.p.m. region of the 2-Me signal in (**1**) (γ-effect).

Three structures (**1**), (**4**), and (**5**) are conceivable for the aromatic substitution pattern of the title compound. The addition of trace amounts of [$^2H_5$]pyridine to the n.m.r. tube led to upfield shifts in only two ^{1}H n.m.r. signals, namely the aromatic isopentenyl CH_2 signal by 0·18 p.p.m. and the acetyl signal by 0·1 p.p.m.; the chemical shifts of all other signals, including that of the aromatic OMe, remained practically unchanged. The pyridine molecule would be expected to co-ordinate preferentially with the chelated moiety; the fact that only the methylene and acetyl signals underwent pyridine shifts[11] indicates that proton-containing groups other than these two are distal from the chelate ring. Hence structure (**4**) can be discarded. In order to differentiate between (**1**) and (**5**) a trace of [$^2H_5$]pyridine was added to synthetic dimethylphloroacetophenone (**6**), upon which the δ 3·846 *ortho*-OMe signal was shifted upfield (to δ 3·790).‡ Since the aromatic OMe signal in (**1**) remained unchanged when [$^2H_5$]pyridine was added, structure (**5**) can also be discarded. The structure of hydroperoxide-Ha is thus represented by (**1**) (relative configuration).

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‡ The δ 3·812 *para*-OMe signal remained practically unchanged; the two OMe signals can be differentiated by the peak heights, the *ortho*-OMe peak being slightly shorter.

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