

A New Sesquiterpene Peroxide (Yingzhaosu C) and Sesquiterpenol (Yingzhaosu D) from *Artabotrys unciatus* (L.) Meer.

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The structures of the bisabolene derivatives yingzhaosu C (**3**) and D (**4**) have been determined by spectroscopic analysis in combination with chemical degradation.

The plant yingzhao *Artabotrys unciatus* (L.) Meer. is known as a folk medicine for treatment of malaria. Several years ago, Liang and his coworkers^{1,2} isolated yingzhaosu A (**1**) and B (**2**) from the root of this plant, but the stereochemistry of (**1**) and (**2**) was not completely solved. For this reason, we attempted to isolate (**1**) or (**2**) from the plant, but isolated instead another sesquiterpene peroxide (**3**), named yingzhaosu C, and sesquiterpenol (**4**), named yingzhaosu D. We now wish to report their structure determination.

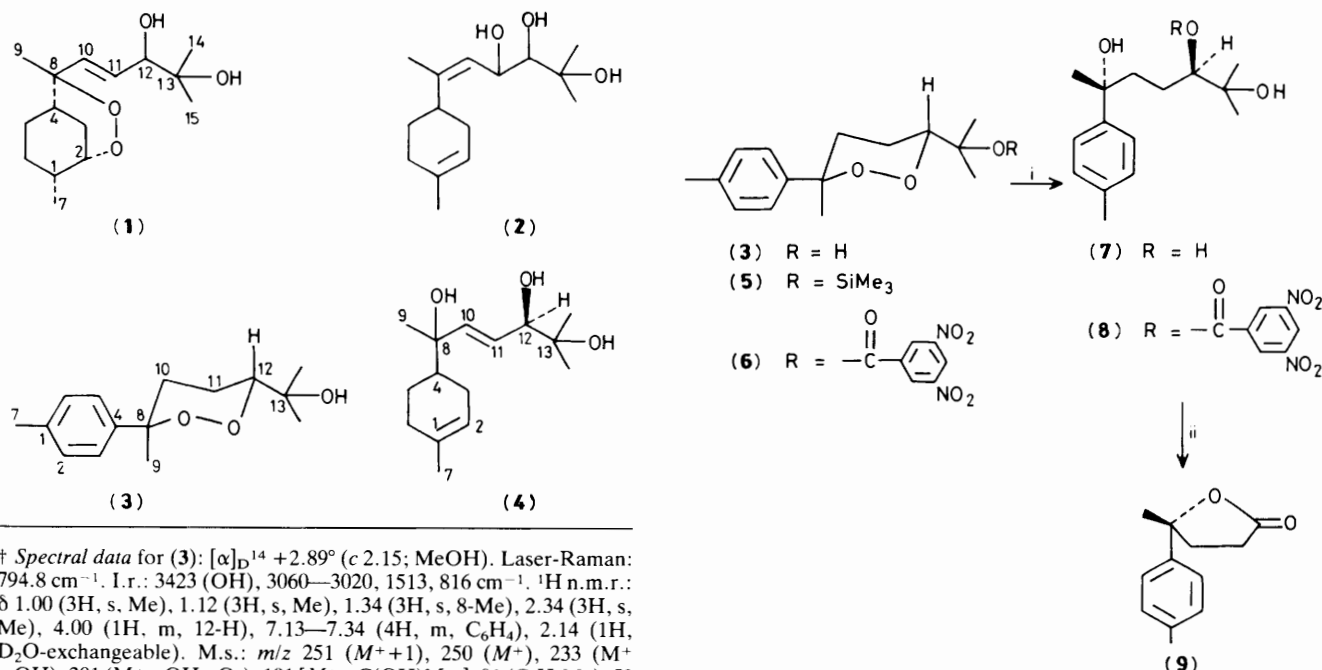
Yingzhaosu C (**3**) (C₁₅H₂₂O₃)[†] is a minor component in the plant and is an oily substance. The presence of a peroxide group is shown by the colour reaction with *p*-dimethylamino-aniline dihydrochloride³ and a distinct absorption at 794.8 cm⁻¹ in the laser-Raman spectrum.⁴ The i.r. spectrum showed benzene ring absorptions at 3060–3020, 1513, and 816 cm⁻¹ and a hydroxy group at 3423 cm⁻¹, which could not be acetylated under mild conditions, indicating it to be a tertiary hydroxy group. The mass spectrum of (**3**) shows, in addition to the molecular ion at *m/z* 250, a prominent peak at *m/z* 91 (PhCH₂ or MeC₆H₄) indicating an alkyl substituted benzene ring; and the base peak at *m/z* 59, which could be assigned as C(OH)Me₂. Compound (**3**) was silylated with CF₃SO₃-SiMe₃-EtNPr₂ (ref. 5) to give silylether (**5**) (Scheme 1). The i.r. spectrum shows no hydroxyl absorption and its m.s. has the base peak at *m/z* 131 [C(OSiMe₃)Me₂]. The ¹H n.m.r. spectrum of (**3**) indicates two methyl groups (δ 1.00 and 1.12) attached to a carbon bearing a hydroxy group and a methyl

group (δ 2.34) attached to a benzene ring. The splitting pattern of the aromatic protons at δ 7.13–7.34 (4H, m) indicates *p*-substitution.

The ¹H n.m.r. spectrum of (**3**) shows a single proton absorption at δ 4.00 which might be ascribed to a proton linked to a carbon bearing a peroxide oxygen. This was supported by the following observations. (**3**) furnished the trihydroxy compound (**7**) on catalytic hydrogenation over 5% Pd-CaCO₃ and the ¹H n.m.r. spectrum of (**7**) showed three D₂O-exchangeable protons at δ 2.86 p.p.m. Esterification of (**7**) with 3,5-dinitrobenzoyl chloride at room temperature gave monoester (**8**), indicating that there was only one secondary hydroxy group in (**7**). This led to the conclusion that the peroxide group linked a tertiary and a secondary carbon atom, respectively. By comparison with the structures of yingzhaosu A (**1**) and B (**2**), the structure (**3**) could be assigned to yingzhaosu C, this was confirmed by conversion into a known lactone (**9**).⁶

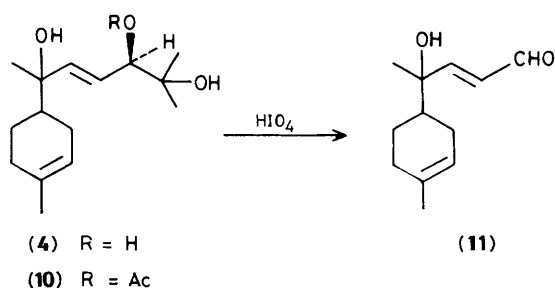
The ¹H n.m.r. spectrum of (**5**) exhibited a doublet of doublets for H-12, δ 3.88 (dd, *J*_{a,a} 10.8, *J*_{a,c} 2.7 Hz), so H-12 could be assigned as axial. Since (**7**) reacted with (±)-α-phenyl butyric anhydride (Horeau's method⁷) to give *S*(+)-α-phenyl butyric acid, the *R*-configuration could be assigned to C-12. Hence, the absolute configuration of C-12 in (**3**) could also be assigned as *R*. A molecular model of (**3**), showed that C-8 would have *R*-configuration, since the *S*-configuration would be unfavourable.

Yingzhaosu D (**4**) (C₁₅H₂₆O₃) is also a minor component and an oily substance. On comparison of the spectral data of



[†] Spectral data for (**3**): [α]_D¹⁴ +2.89° (c 2.15; MeOH). Laser-Raman: 794.8 cm⁻¹. I.r.: 3423 (OH), 3060–3020, 1513, 816 cm⁻¹. ¹H n.m.r.: δ 1.00 (3H, s, Me), 1.12 (3H, s, Me), 1.34 (3H, s, 8-Me), 2.34 (3H, s, Me), 4.00 (1H, m, 12-H), 7.13–7.34 (4H, m, C₆H₄), 2.14 (1H, D₂O-exchangeable). M.s.: *m/z* 251 (M⁺+1), 250 (M⁺), 233 (M⁺-OH), 201 (M⁺-OH-O₂), 191 [M⁺-C(OH)Me₂], 91 (C₆H₄Me), 59 [C(OH)Me₂]. H.r.m.s.: 234.1609 (C₁₅H₂₂O₂, M⁺+1-OH), 218.1664 (C₁₅H₂₂O, M⁺-O₂), 191.1052 [C₁₂H₁₅O₂, M⁺-C(OH)Me₂].

Scheme 1. Reagents: i, H₂, 5% Pd-CaCO₃; ii, HIO₄ then Jones' reagent.



Scheme 2

yingzhaosu D(4)[‡] with yingzhaosu B(2),² structure (4) could be assigned as yingzhaosu D. Compound (4) was acetylated with acetic anhydride and pyridine to give monoester (10), indicating that only one secondary hydroxy group is present in (4). An ABX system between the vinylic protons and H-12 [δ 5.11 (1H, d, J 7.2 Hz, H-12), 5.67 (1H, dd, J_1 7.2, J_2 15.7 Hz, H-11), 5.87 (1H, d, J 15.7 Hz, H-10)] indicates a *trans* double bond. (4) was oxidized with periodic acid (Scheme 2) to give

[‡] Spectral data for (4): $[\alpha]_D^{26} -39.5^\circ$ (c 0.73, CHCl₃). I.r.: 3400, 1670, 980 cm⁻¹. ¹H n.m.r.: δ 1.15 (3H, s, Me), 1.22 (3H, s, Me), 1.23 (3H, s, Me), 1.63 (3H, s, Me), 3.90 (1H, d, J 7.5 Hz, H-12), 5.37 (1H, br. s, H-2), 5.68–5.88 (2H, m, H-10, H-10). M.s.: 253 ($M^+ - 1$), 237 ($M^+ - OH$), 236 ($M^+ - H_2O$), 219 ($M^+ - H_2O - OH$), 95 (C₆H₈Me), 59 [C(OH)Me₂]. H.r.m.s.: 236.1856 (C₁₅H₂₄O₂, $M^+ - H_2O$), 218.1663 (C₁₅H₂₂O, $M^+ - 2 H_2O$).

an α,β -unsaturated aldehyde (11),[§] the structure of which was deduced from its spectral characteristics. Similarly to (3), the absolute configuration of C-12 in (4) was assigned as *R* using Horeau's method.⁷ The configuration of C-8 and C-4 are still to be determined. The antimalarial activity of (3) will be reported elsewhere.

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[§] Spectral data for (11): i.r.: 3450, 1680, 1630, 980 cm⁻¹. ¹H n.m.r.: 1.35 (3H, s, Me-8), 1.62 (3H, s, Me-1), 5.32 (1H, br. s, H-2), 6.20 (1H, dd, J_1 16, J_2 8 Hz, H-11), 6.80 (1H, d, J 16 Hz, H-10), 9.50 (1H, d, J 8 Hz, H-12). M.s.: 194 (M^+), 176 ($M^+ - H_2O$), 147 ($M^+ - H_2O - CHO$).