Plant Antitumour Agents: Isolation and Structure of Samaderine A (*X*-Ray Analysis) and a New Antileukaemic Quassinoid Samaderine E from *Samadera indica*[1]

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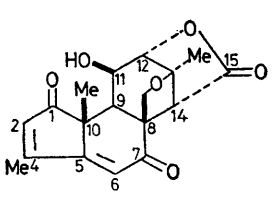
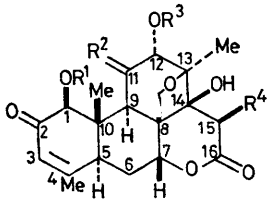
Summary Two quassinoids, samaderines A and E, have been isolated from *Samadera indica;* the structure of the former, a novel dienedione with a five-membered ring A, has been established by single-crystal *X*-ray analysis and that of the latter by spectral analysis.

THE partial characterization of samaderine A (**1**)† isolated from *Samadera indica* has been reported.[2] We now report on the complete structure of samaderine A and a new quassinoid, samaderine E (**2**), isolated from the same plant.

Fractionation of the alcoholic extract of the dried leaves of the plant, guided by assay in 9KB and P388 leukaemia systems,‡ showed that the antitumour activity was concentrated successively in the chloroform layer of a chloroform–water partition and the methanol layer of a 10% aqueous methanol–petroleum partition. The biological activity was further concentrated by a 10-tube countercurrent distribution procedure (CCl_4–$CHCl_3$–MeOH–H_2O 35:15:40:10). Chromatography (×2) on Sephadex LH-20 (MeOH) and silica gel ($CHCl_3$ with increasing amounts of MeOH) followed by preparative t.l.c. ($CHCl_3$–Me_2CO–MeOH 75:20:5) gave samaderine A (**1**) (0·004%) and samaderine E (**2**) (0·008%).



(1)

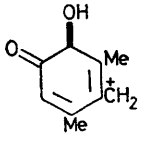


(2) $R^1 = R^3 = R^4 = H$, $R^2 = \beta$-OH, α-H

(3) $R^1 = R^3 = H$, $R^2 = \beta$-OH, α-H, $R^4 = OH$

(4) $R^1 = R^3 = Ac$, $R^2 = \beta$-OH, α-H, $R^4 = H$

(5) $R^1 = R^3 = Ac$, $R^2 = O$, $R^4 = H$



(6)

The molecular formula of (**1**) was found to be $C_{18}H_{18}O_6$, *m/e* 330·1109 (M^+); m.p. 253—255 °C (EtOAc); $[\alpha]_D^{25}$ −31·3° (*c* 0·259, pyridine; lit.[2] $[\alpha]_D$ −18·6, pyridine); ν_{max} ($CHCl_3$) 3500 (OH), 1800 (γ-lactone), 1780, 1720, and 1670 cm^{-1} (cross-conjugated dienedione); λ_{max} (MeOH) 288 nm (ϵ 13,400) (cross-conjugated dienedione]; δ ($CDCl_3$,Me_4Si) 1·58 (3H, s, 13-Me), 1·72 (3H, s, 10-Me), 2·22 (3H, s, 4-Me), 3·46 (1H, s, 14-H), 3·60 and 4·16 (each 1H, d, *J* 10 Hz, CH_2O), 4·31 (1H, d, *J* 3 Hz, 12-H), 4·85 (1H, d, *J* 8 Hz, 11-H), 6·02 (1H, s, 6-H), and 6·14 (1H, s, 2-H).

Because of the paucity of (**1**), its structure and stereochemistry were established by single-crystal *X*-ray analysis. Crystals of (**1**) belong to the monoclinic system, space group $P2_1$, with two molecules in a unit cell of dimensions a = 9·071(5), b = 11·279(5), c = 8·032(5) Å, β = 96·55(5)°. The crystal structure was solved by use of MULTAN,[3] and subsequent refinement of atomic positional and thermal (anisotropic C,O; isotropic H) parameters by full-matrix least-squares calculations led to an R of 0·047 over 1411 statistically significant [$I > 2{\cdot}0\sigma(I)$] reflections measured on an Enraf-Nonius CAD-3 diffractometer (θ–2θ scans; Ni-filtered Cu-K_α radiation). A view of the molecular conformation is shown in the Figure.§

The molecular composition of (**2**) was found to be $C_{20}H_{26}O_8$, *m/e* 394·1620 (M^+); m.p. 202—207 °C ($CHCl_3$–MeOH–EtOAc); $[\alpha]_D^{25}$ −11·7° (*c* 0·23, pyridine). The i.r. spectrum showed two carbonyl bands at 1670 ($\alpha\beta$-unsaturated ketone) and 1730 cm^{-1} (δ-lactone), and, in agreement with the formulation of ring A as in (**2**), the u.v. spectrum showed a maximum at 232 nm (ϵ 9300) and the mass spectrum showed a peak at *m/e* 151 (**6**).[4] The ^1H n.m.r. spectrum of (**2**) was very similar to that of brucein D (**3**)[5] and showed the characteristic singlets due to the three methyl groups at δ 1·04 (10-Me), 1·15 (13-Me), and 1·90 (4-Me), respectively. The broad triplet at δ 4·95 which was assigned to 7-H suggested the absence of a hydroxy-group at C-6.

Acetylation of (**2**) with acetic anhydride in pyridine gave the 1,12-diacetate (**4**), $C_{24}H_{30}O_{10}$; m.p. 267—270 °C; $[\alpha]_D^{24}$ +20·4° (*c* 0·27, pyridine); *m/e* 478·1845 (M^+). The

† The usual quassinoid numbering scheme is retained for atoms C-4 to C-15; the biogenetic relationships of C-1 and C-2 in (**1**) to C-1, C-2, and C-3 of the quassinoids remains to be established.

‡ Cytotoxicity and *in vivo* activity tests were carried out under the auspices of the National Cancer Institute by the procedures described in *Cancer Chemother. Reports,* 1962, **25**, 1. The quassinoid (**2**) showed moderate activity in 9KB and P388 systems while (**1**) was inactive.

§ The atomic co-ordinates for this work are available on request from the Director of the Cambridge Crystallographic Data Centre, University Chemical Laboratory, Lensfield Road, Cambridge CB2 1EW. Any request should be accompanied by the full literature citation for this communication.

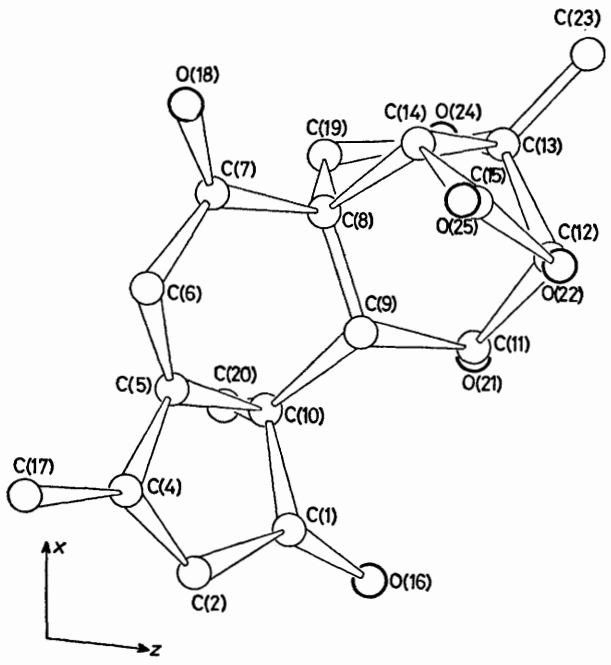


FIGURE. Molecular structure of samaderine A; darker circles denote oxygen atoms.

presence of the secondary hydroxy-group at C-11 and a tertiary hydroxy-group at C-14 was established by oxidation of (**4**) with chromium trioxide–pyridine in methylene chloride to produce the ketone (**5**), $C_{24}H_{28}O_{10}$; m.p. 230—233 °C; ν_{max} ($CHCl_3$) 3540 cm^{-1} (OH). In the ^1H n.m.r. spectrum of (**5**) 9- and 12-H appeared as singlets at δ 3·12 and 4·83, respectively. The doublets at δ 2·84 and 3·78 (J 17 Hz) were assigned to 15 β-H and 15 α-H, respectively, supporting the presence of the hydroxy-group at C-14; the low-field shift observed for 15α-H is in accord with the presence of a carbonyl group at C-11.[6] Because of the close similarity between the ^1H and ^{13}C n.m.r. spectra of (**2**) and its derivatives and (**3**) and its derivatives, it is reasonable to assume that the stereochemistries of the ring junctions and the configurations of the hydroxy-groups are as shown in (**2**).

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[1] For previous paper in this series see M. C. Wani, H. L. Taylor, M. E. Wall, A. T. McPhail, and K. D. Onan, *J. Amer. Chem. Soc.* 1975, **95**, 5955.
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