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SCHISANLACTONE A, A NEW TYPE OF TRITERPENOID FROM A SCHISANDRA SP.

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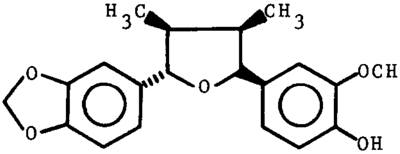
Abstract: Schisanlactone A, a triterpenoid isolated from a Schisandra sp., is shown to possess structure 2. The structure was assigned on the basis of spectroscopic studies and was confirmed by X-ray diffraction studies. Schisanlactone A represents a new structural type among the triterpenoids.

Recently, the structure of chicanine (1), the first tetrahydrofuran lignan isolated from the Schisandra genus, was reported.[1] Further separation of the crude extract of this unidentified Schisandra sp., collected in the Xiangfan district of the Hubei province of China, has provided a series of triterpene lactones named schisanlactone A, B, C, etc.[2] In this paper, we wish to report the structure of schisanlactone A, a new type of triterpenoid.

Schisanlactone A (2), $C_{30}H_{40}O_4$ (M^+ 464.2954), mp 227—229°C, $[\alpha]_D^{23}$ +365° (c 0.20, $CHCl_3$), displays two carbonyl bands (1725, 1685 cm^{-1}) but no hydroxyl absorption in the IR. The ^{13}C NMR spectrum reveals carbonyl carbons at δ 166.93 and 166.28 and oxygenated carbons at δ 80.37 (s) and 80.24 (d). Thus schisanlactone A possesses two lactone rings, one tertiary and one secondary. Since kadsuric acid (3) has been isolated from a plant of the same genus,[3] we considered that the lactone rings might arise from similarly located carboxyl groups. Indeed, ^1H-^1H selective decoupling experiments indicate the presence of a six membered α,β-unsaturated lactone ring. On irradiation of H-23A and H-23B, the signal of H-22 was decoupled to a doublet and the signal of H-24 to a quartet. On irradiation of H-22, the signal of H-24 was unaffected, whereas when the methyl protons (H-27) were irradiated, the signal for H-24 appeared as a double doublet. Thus, the side chain of schisanlactone A contains an α-methyl-α,β-unsaturated δ-lactone unsubstituted at the γ-position.

The ^{1}H NMR and ^{13}C NMR spectra show that schisanlactone A has only six methyl groups, one quaternary methyl less than kadsuric acid, and there is no evidence for the presence of a cyclopropane ring in the molecule. Furthermore, the UV spectrum, λ_{max}^{MeOH} nm (log ε): 334(4.25), 265(3.89), 212(4.11), indicates that the three remaining double bonds are conjugated with the other lactone carbonyl.[4] Thus schisanlactone A appeared to possess an A,B-*seco*-9,19-cyclolanostene skeleton, since only in this way, and with cleavage of the 9,10-bond, is it possible to construct the required extended system of conjugation to the A ring lactone. Structure **2**, derived in this manner is compatible with the remaining ^{1}H NMR and ^{13}C NMR data.[5] In order to verify the proposed structure, a single crystal X-ray diffraction study was carried out on schisanlactone A.



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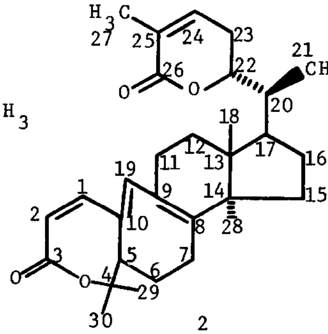

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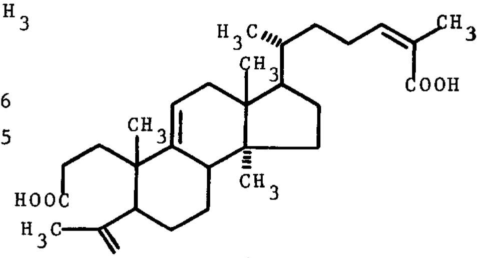

3

Clear, light yellow crystals of schisanlactone A were obtained from CH$_2$Cl$_2$: MeOH (3:1). The crystal system was monoclinic, lattice constants a = 12.101 (1), b = 14.195 (1), c = 7.8238 (5) Å, and β = 81.600 (6)°, space group P2$_1$ with one molecule forming the asymmetric unit. A phasing model was achieved using a direct methods phasing approach.[6] Hydrogens were located on a difference synthesis following partial refinement. Block-diagonal least squares refinement using anisotropic non-hydrogen atoms and isotropic hydrogens has converged to a standard crystallographic residual of 0.042 for the observed reflections.[7] A perspective view of the final X-ray model of schisanlactone A (**2**) less hydrogens is shown in Figure 1. The X-ray experiment did not define the absolute configuration and this is based on the CD measurements discussed below. The stereochemical designations are 5(*R*), 13(*R*), 14(*R*), 17(*S*), 20(*S*), and 22(*R*). The cyclopentane ring is in the half-chair (C$_2$) conformation and the cyclohexene ring is in the twist boat conformation. The A-ring is aligned at an approximate dihedral angle of 45° to the CD ring system. This twist is mediated by the twist boat conformation of the B-ring. The C8-C9-C19-C10 dihedral angle is approximately 40° so that the conjugation of the third double bond is diminished.

Schisanlactone A shows a strongly positive Cotton effect at 244 nm (Δ_ε +7.4), similar to ajugalactone[8] and jaborosalactone A[9] which have similar lactone moieties in the side chain, and thus C-22 is assigned the (*R*)-configuration.[10] To the best of our knowledge the carbon skeleton of schisanlactone A has not been previously observed among the triterpenoids.[11]

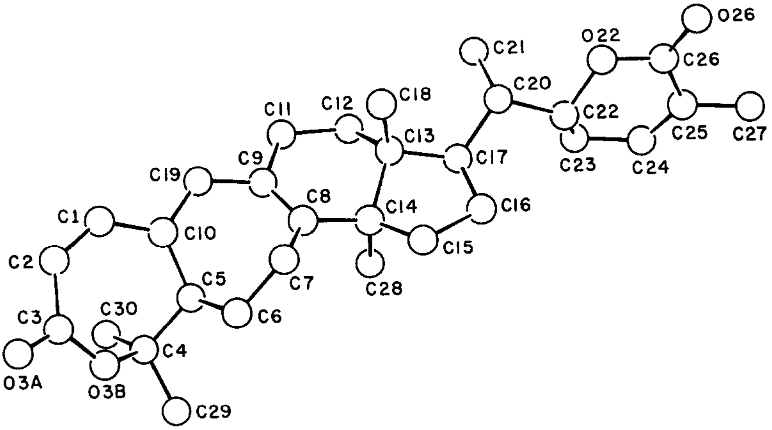

Figure 1. A computer generated perspective drawing the final X-ray model of schisanlactone A less hydrogens.

References and Notes

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3. Jia-Sen Liu, Mei-Fen Huang, and Yao-Liang Gao, *Acta Chim. Sin.*, **38**, 361 (1980).
4. A.I. Scott. Interpretation of the Ultraviolet Spectra of Natural Products. Pergamon Press, Oxford, 1964, p. 79.
5. Complete Table of ^{1}H NMR and ^{13}C NMR data are available from W.A.A.
6. All crystallographic calculations were done on a PRIME 850 computer, operated by the Cornell Chemistry Computing Facility. Principal programs employed were REDUCE and UNIQUE, data reduction programs: Leonowicz, M.E., Cornell University, 1978; MULTAN78, 'A System of Computer Programs for the Automatic Solution of Crystal Structures from X-ray Diffraction Data,' direct methods programs and Fast Fourier Transform routine (locally modified to perform all Fourier calculations including Patterson syntheses): Main, P.; Hull, S.E.; Lessinger, L.; Germain, G.; Declercq, J.-P.; Woolfson, M.M., University of York, England, 1978; NQEST, CYBER 173 version, negative quartets figure of

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11. This work was supported by the National Institutes of Health (J.C.) and the Natural Sciences and Engineering Research Council of Canada (W.A.A.).

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