Phytochemistry, 1969, Vol. 8, pp. 1817 to 1819. Pergamon Press. Printed in England

SHORT COMMUNICATION

THE ISOLATION OF SALANNIN FROM *MELIA DUBIA*[1]

L. B. DE SILVA, W. STÖCKLIN and T. A. GEISSMAN

Department of Chemistry, University of California, Los Angeles 90024, U.S.A.

(*Received* 1 *April* 1969)

Abstract—The bitter principle in *Melia dubia* Cav. fruits is salannin, previously found in *Melia azadirachta* L.

INTRODUCTION

THE FAMILY Meliaceae has received intensive study in recent years,[2] and has yielded a large number of compounds of the general class described by the term "limonoid". *Melia azadirachta* L. (nim) has received particular attention; all parts of the tree—seeds, bark, root bark, blossoms and leaves—have been investigated. In addition to the principal bitter constituent, nimbin,[3] *M. azadirachata* has been found to contain the related principles, salannin,[4] azadirone, azadiradione and epoxyazadiradione,[5] melianone and melianol,[6] and meliantriol,[7] nimbolide,[8] and meldenin.[9] We have now examined the fruits of *M. dubia* Cav., a common tree of the wet forests of Ceylon, and found it to contain salannin (I) as the principal limonoid constituent.

RESULTS AND DISCUSSION

Chromatographic separation of the extracts of dried, mature fruits of *Melia dubia* yielded a crystalline compound which proved to be a hydrate. The anhydrous compound, m.p. 167–170°, had the composition $C_{34}H_{44}O_7$ and showed a molecular ion at m/e 596 in the mass spectrometer. Its composition and spectral properties corresponded with those reported for salannin (I), and the mass spectrum showed the expected fragments for this compound, with ions at m/e 513 (M-83), 496 (M-100), 83 (tigloyl) and 55 (C_4H_7). The identity of the compound with salannin was confirmed by its conversion into the following derivatives.

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[1] Contribution No. 2392 from the Department of Chemistry, U.C.L.A.

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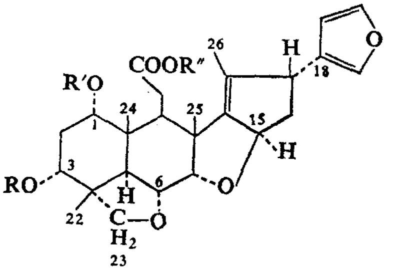

(I) R = CH_3CO; R′ = C_4H_7CO; R″ = CH_3
(II) R = R′ = R″ = H
(III) R = R′ = H′ R″ = CH_3
(IV) R = R′ = $CoCH_3$; R″ = CH_3

Alkaline hydrolysis gave the hitherto unreported dihydroxy acid, salannic acid (II), and tiglic acid. Methylation of II with diazomethane gave the known[4] ester (III), and acetylation of III yielded the known[4] diacetate (IV). The correspondence of the properties of I, III and IV with those reported, and the agreement of the 100 mc NMR spectrum of IV with the indicated structure left no doubt as to the identity of the compound.

EXPERIMENTAL

Isolation of Salannin from Melia dubia *Cav.*

The mature fruits of *Melia dubia* Cav. were collected near Colombo, Ceylon, in March 1968. The dried, finely powdered fruits (2 kg) were extracted in a Soxhlet with boiling petroleum ether (60–80°) during 18 hr. After the evaporation of the solvent, the residue was chromatographed on alumina (Merck, Activity I) and the column developed with petroleum ether (60–80°). The petroleum ether eluates were concentrated and extracted with 65 % aqueous methanol (3 × 500 ml). The aqueous methanolic solution on dilution with water slowly deposited a white solid (3 g) which was further purified by chromatography on silica gel and elution with $CHCl_3$. Recrystallization from ether–petroleum ether (20–40°) gave colorless prisms (2 g) with an indefinite m.p. which were homogeneous on TLC in four solvent systems; $[\alpha]_D^{25}$ +158·5 (*c*, 0·5 in $CHCl_3$) (reported +167 in $CHCl_3$).[4] U.v. λ_{max} 208 nm. (ϵ, 20,850); i.r. (CCl_4), 1707 (tiglate ester) 1741 (acetate and methyl esters) 1500 and 875 cm^{-1} (furan). Mass spectrum, *m/e* 596 (M^+), 513 (M-83), 496 (M-100), 83,55. Found: C, 67·71; H, 7·44 per cent. Calc. for $C_{34}H_{44}O_9$: 1/2 H_2O: C, 67·43; H, 7·33 per cent.)

Removal of the water of crystallization with absolute benzene gave anhydrous salannin (I), m.p. 167–170° (reported,[4] 167–170°); $[\alpha]_D^{25}$ +157° (*c*, 0·4 in $CHCl_3$). Found: C, 68·59; H, 7·44 per cent. Calc. for $C_{34}H_{44}O_7$: C, 68·43; H, 7·43 per cent.)

Hydrolysis of Salannin. Salannic Acid (II)

Salannin (I) (1·5 g) in methanol (150 ml) was hydrolyzed with 2 N NaOH (35 ml) by refluxing for 90 min to give the acid (II) (1 g) as prisms (from acetone–ether), m.p. 221°. M^+ 458; $[\alpha]_D^{25}$ +133·5 (*c*, 0·38 in $CHCl_3$). (Found: C, 68·22; H, 7·45 per cent. Calc. for $C_{26}H_{34}O_7$: C, 68·10; H, 7·47 per cent.) The mother liquor, after the crystallization of the acid (II), deposited tiglic acid as stout prisms, m.p. 64°. The m.p. was not depressed on admixture with an authentic specimen of tiglic acid, m.p. 63–64°.

Methyl Salanninate (III)

Methylation of the acid (II) with CH_2N_2 afforded the methyl ester (III), which crystallized in rosettes, m.p. 202–205° (reported,[4] m.p. 201–205°) from acetone–petroleum ether (20–40°); $[\alpha]_D^{25}$ +128° (*c*, 0·588 in $CHCl_3$) (reported,[4] $[\alpha]_D^{25}$ +135°); M^+ 472. (Found: C, 68·66; H, 7·85 per cent. Calc. for $C_{27}H_{36}O_7$; C, 68·62; H, 7·68 per cent.)

Methyl Salanninate Diacetate (IV)

Acetylation of the ester (III) with acetic anhydride and pyridine at room temperature during 7 days afforded the di-*O*-ester (IV) as colorless plates, m.p. 233–235° from acetone–petroleum ether (20–40°) (reported,[4] m.p. 232–234°); $[\alpha]_D^{25}$ +135·6° (*c*, 0·466 in $CHCl_3$) (reported,[4] $[\alpha]_D$ +126°), M^+ 556. (Found: C, 66·97;

H, 7·38 per cent. Calc. for $C_{31}H_{40}O_9$: C, 66·89; H, 7·24 per cent.). The 100 M.C. NMR spectrum of IV (in $CDCl_3$) showed the following signals: δ 0·93 (3H; 24-H); 1·18 s (3H; 22-H); 1·28 s (3H; 25-H) 1·64 d (J=1 cps) (3H; 26-H); 2·04 s (3H; CH_3COO—) 2·10 s (3H; CH_3COO); 2·74 d (J=12 cps) (1H; 5-H); *ca.* 2·74 m (1H; 9-H); 3·30 s (3H; OCH_3) 3·56 d (J=8 cps) (1H; 23-H); 3·69 d (J=8 cps) (1H; 23-H); *ca.* 3·60 m (1H; 17-H) 3·95 q (J_1=3 cps; J_2=12 cps) (1H; 6-H); 4·15 d (J=3 cps) (1H; H-7); 4·76 t (J=3 cps) (1H; 3-H); 4·92 t (J=3 cps) (1H; 1-H); 5·48 m (1H; 15-H); 6·31 d (J=2 cps) (1H; 20-H) 7·28 (2H, 19-H and 21-H). Chemical shifts are given in ppm on the δ scale, coupling constants in cps; s=singlet, d=doublet, t=triplet, m=multiplet, and q=quartet.

Acknowledgements—One of us (L. B. de Silva) is grateful for the award of a Fulbright Scholarship (1968–69). Part of the support of this study was provided by a U.S. Public Health Service Research Grant AI-07435, and part of the costs of the mass spectrometer and NMR spectrometer was provided by grants to the Department of Chemistry from E. I. du Pont de Nemours and Company, and by the National Science Foundation. Analyses are by Miss Heather King, UCLA.