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TETRANORTRITERPENOIDS FROM *MELIA DUBIA*

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Key Word Index—*Melia dubia*, Meliaceae, tetranortriterpenoids, compositin (1,7-ditiglyl vilasinin), compositolide (photosalannin), salannin

Abstract—Two new tetranortriterpenoids, compositin and compositolide, have been isolated from leaves and seeds of *Melia dubia* The structures of the two new compounds were determined by spectroscopic methods and chemical reactions

INTRODUCTION

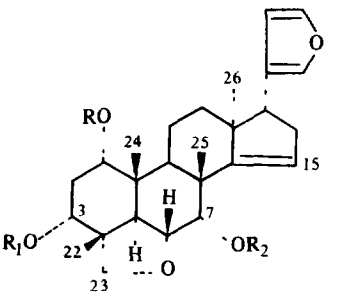
Tetranortriterpenoids salannin and vilasinin have been reported [1, 2] from seeds and leaves of *Melia azadirachta* syn to *A indica* [3] *Melia dubia* syn to *Melia composita* (Meliaceae) yielded two new tetranortriterpenoids, compositin and compositolide, closely related to vilasinin and salannin, respectively Their structures were determined by ^{1}H NMR spectroscopy and chemical reactions

RESULTS AND DISCUSSION

Compositin (**1**), mp 210°, $[\alpha]_D$ −40° ($CHCl_3$, *c* 0 5) The ^{1}H NMR spectra of **1** and vilasinin (**2**) [1] were very similar except for the presence of two tiglate ester groups in the case of **1** Proof for the two tiglate ester groups was the presence of four vinylic methyls at δ1 84 and two olefinic protons as a quartet at 6 94 (J = 7 5 Hz) Absorptions corresponding to the protons attached to the carbon atom carrying the tiglate groups were observed at δ5 03 and 5 72 The C<u>H</u> OH proton appeared at δ3 86 The molecular formula was fully in agreement with ditiglyl vilasinin The α-configuration of the tiglate group at C-7 followed from the doublet at δ5 72 (J = 3 Hz) It also accounted for the unusual shielding observed for the C-24 methyl at 0 64, as in the Dreiding model, this C-24 methyl is perpendicular to the plane of the tiglyl double bond

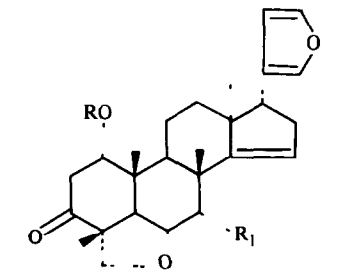
In order to confirm the placement of the tiglate group at C-1, compositin (**1**) was treated with Jones reagent The resulting ketone (**1a**) on alkaline hydrolysis yielded compound **1b**, $C_{26}H_{32}O_4$ The presence of an α,β-unsaturated ketone in ring A in **1b** was indicated by proton signals at δ7 08 (*d*, J = 10 Hz, 1-H) and 5 9 (*d*, J = 10 Hz, 2-H) If the keto group was in position C-1, the proton would have been observed at much higher field [4] Introduction of a carbonyl group at C-3 in this rigid system deshielded the C-24 methyl by 0 13 ppm, which was in agreement with the value of the C-24 methyl of salannin (**3**) and its 3-keto compound [2] (Table 1) In the 5α-steroids introduction of a Δ^1-3-keto group generally induces a 0 25 ppm downfield shift of the C-19 methyl group when compared with the corresponding hydrocarbon [5] The magnitude of the downfield shift of the C-24 methyl signal between **1** and **1b** was 0 2 ppm If the keto group was at C-1a much larger downfield shift should have been observed The structure of compositin is therefore 1,7-ditiglyl vilasinin (**1**) Compositin (**1**) on alkaline hydrolysis yielded vilasinin (**2**), which was identical in all respects with the naturally occurring compound **2**

Compositolide (**4**), mp 300°, $[\alpha]_D$ 160° ($CHCl_3$, *c* 1), was isolated together with salannin (**3**) from the seeds The ^{1}H NMR spectra of salannin (**3**) and compositolide (**4**) were very similar and they differed slightly from each other The signals corresponding to a β-substituted furan



1 R = R$_2$ = COC$_4$H$_7$, R$_1$ = H

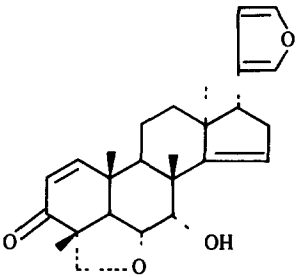
2 R = R$_1$ = R$_2$ = H



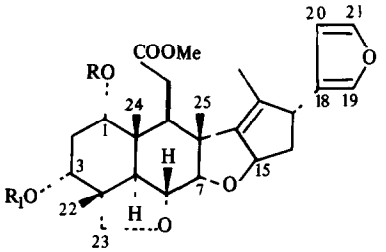
1a R$_1$ = R = COC$_4$H$_7$

Table 1 ^{1}H NMR spectral data for salannin (3), 3-keto salannin, compositin and compounds **1a** and **1b**

Methyl group	Salannin (3)	3-Keto salannin	Compositin	1a	1b
C-24	0 99	1 12	0 64	0 76	0 84
C 22	1 23	1 30	1 20	1 44	1 26
C-25	1 33	1 38	1 04	1 26	1 21



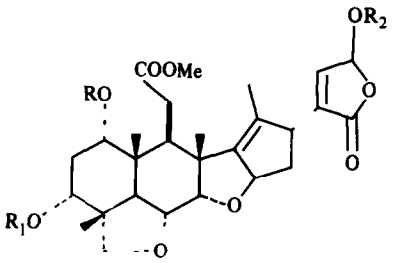
1b



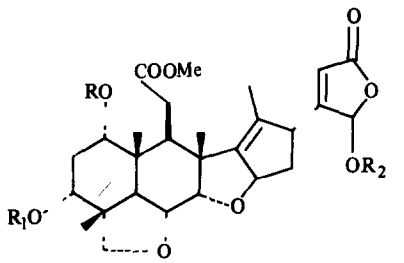
3 R = COC_4H_7, R_1 = COMe

which were present in the spectrum of compound **3** were absent in the spectrum of compound **4** Replacement of the β-substituted furan ring by the γ-hydroxybutenolide ring accounts for the molecular formula of compositolide Biogenetically this substitution is a normal pattern observed in certain members of the Meliaceae family

The γ-hydroxybutenolide is attached to the rest of the molecule through the carbon atom α to the carbonyl since the CHOH proton appeared as a broad singlet at δ6 06 and there was sharpening of the signal on D_2O exchange In the acetate (**4b**) it shifted to δ7 02 ($W_{1/2}$ = 3 Hz) In the alternate structure (**4a**) this proton should have been observed as a sharp singlet In order to confirm the structure of **4**, a solution of salannin (**3**) in benzene was irradiated with a Pyrex filtered UV light in a stream of oxygen until all the starting material had disappeared The reaction product upon chromatography yielded compositolide (**4**), which was identical in all respects with the naturally occurring compound Biogenetically compositolide (**4**) could be considered as the photo-oxygenation product of salannin (**3**)



4 R = COC_4H_7, R_1 = COMe, R_2 = H
4b R = COC_4H_7, R_1 = R_2 = COMe



4a R = COC_4H_7, R_1 = COMe, R_2 = H

EXPERIMENTAL

All mps are uncorr IR spectra were recorded as KBr pellets, ^{1}H NMR spectra were measured with 5–10% solns in $CDCl_3$ using TMS as int standard and the chemical shifts are expressed in δ ppm Silica gel (Acme's) 100–200 mesh was used for CC The separation was monitored by TLC (silica gel G)

Extraction and isolation procedure The leaves and seeds of *Melia dubia* were collected from the Yercaud hills of Salem district, Tamil Nadu, India at an altitute of 2000–3000 ft in June and November and immediately shade-dried The plant was collected and identified by Mrs P Brindha, Head, Department of Botany, of this Institute A specimen has been deposited at the herbarium of this Institute under the registry No 281 and is available for inspection

Isolation of compositin Coarsely powdered leaves (2 kg) were exhaustively extracted with *n*-hexane and $CHCl_3$ by cold percolation The two extracts were found to be similar by TLC (silica gel, C_6H_6–EtOAc, 4 1 or 1 1) and were combined The total extract (40 g) was chromatographed over silica gel (800 g) and eluted with *n*-hexane, C_6H_6, followed by a mixture of C_6H_6 with increasing quantities of EtOAc Fractions eluted with C_6H_6–EtOAc (9 1) were combined Repeated chromatography over silica gel gave compositin (**1**) (50 mg), crystallized from MeOH, mp 210°, $[\alpha]_D$ −40° ($CHCl_3$, *c* 1) (Found C, 72 88, H, 7 91 $C_{36}H_{48}O_7$ requires C, 72 98, H, 8 10%) IR ν_{max}^{KBr} cm^{-1} 3400, 2920, 1700, 1650, 1505, 1450, 1390, 1395, 1250, 1140, 1065, 875 MS *m/z* 592 $[M]^+$ ^{1}H NMR (100 MHz, $CDCl_3$) δ5 03 (1H, *t*, *J* = 3 Hz, 1-H) 3 86 (1H, *t*, *J* = 3 Hz, 3-H) 2 64 (1H, *d*, *J* = 12 Hz, 5-H), 4 3 and 4 18 (1H, *d*, *J* = 3 and 12 Hz, 6-H), 5 72 (1H, *d*, *J* = 3 Hz, 7-H), 5 5 (1H, *t*, *J* = 3 Hz, 15-H), 6 24 (1H, *s*, 20-H), 7 34 (2H, *m*, 19-H and 21-H), 1 84 (12H, *m*, 2 × Me of tiglate), 6 94 (2H, *q*, *J* = 7 5 Hz, olefinic H of tiglate), 3 92 and 3 58 (2H, *dd*, *J* = 8 Hz, 23-H), 0 64 (3H, *s*, 24-H) 1 04 (3H, *s*, 25-H), 1 2 (3H, *s*, 22-H), 1 12 (3H, *s*, 26-H)

Hydrolysis of composition Composition (1) (50 mg) was refluxed with methanolic KOH (5%) (5 ml) on a H_2O bath for 12 hr MeOH was removed *in vacuo* and the residue extracted with CH_2Cl_2 The product recovered from CH_2Cl_2 was subjected to CC over silica gel Elution with C_6H_6–EtOAc (1 1) yielded a compound (30 mg) which was identical in all respects with vilasinin (2)

Jones oxidation of composition Composition (1) (150 mg) in Me_2CO (10 ml) was treated with Jones reagent (2 ml) The soln was kept at 20° and shaken well for 1 hr Work-up in the usual way afforded a gum which was purified by chromatography over silica gel Elution with $CHCl_3$ gave 3-keto composition (**1a**) (100 mg) (Found C, 73 25, H, 7 75 $C_{36}H_{46}O_7$ requires C, 73 21, H, 7 79%) IR ν_{max}^{KBr} cm^{-1} 1710, 1720, 1495, 850 MS *m/z* 590 $[M]^+$ ^1H NMR ($CDCl_3$, 100 MHz) δ5 3 (1H, *t*, *J* = 3 Hz, 1-H), 4 42 and 4 3 (1H, *dd*, *J* = 12 and 3 Hz, 6-H), 2 6 (1H, *d*, *J* = 12 Hz, 5-H) 5 7 (1H, *d*, *J* = 3 Hz, 7-H), 5 58 (1H, *t*, *J* = 3 Hz, 15-H), 6 25 (1H, *s*, 20-H), 7 34 (2H, *m*, 19-H and 21-H), 1 8 (12H, *s*, 2 × Me of tiglate), 6 9 (2H, *q*, *J* = 7 5 Hz, olefinic H of tiglate), 0 76 (3H, *s*, 24-H), 1 26 (3H, *s*, 25-H), 1 3 (3H, *s*, 26-H), 1 44 (3H, *s*, 22-H)

Hydrolysis of 3-keto composition 3-Keto composition (**1a**) (100 mg) was refluxed with methanolic KOH (5%, 5 ml) on a H_2O bath for 24 hr MeOH was removed *in vacuo* and the residue was extracted with CH_2Cl_2 The gum left after removal of solvent gave **1b** (70 mg), mp 265° (from hexane–Et_2O) (Found C, 76 26, H, 7 75 $C_{26}H_{32}O_4$ requires C, 76 47, H, 7 84%) IR ν_{max}^{KBr} cm^{-1} 3450, 1660, 1500, 870 MS *m/z* 408 $[M]^+$ ^1H NMR ($CDCl_3$, 100 MHz) δ7 08 (1H, *d*, *J* = 10 Hz, 1-H), 5 9 (1H, *d*, *J* = 10 Hz, 2-H), 4 42 and 4 3 (1H, *dd*, *J* = 12 and 3 Hz, 6-H), 3 96 (1H, *d*, *J* = 3 Hz, 7-H), 2 82 (1H, *d*, *J* = 12 Hz, 5-H), 5 62 (1H, *t*, *J* = 3 Hz, 15-H), 6 34 (1H, *s*, 20-H), 7 41 (2H, *m*, 21-H and 19-H), 0 84 (3H, *s*, 24-H), 1 21 (3H, *s*, 25-H), 1 26 (3H, *s*, 22-H), 1 24 (3H, *s*, 26-H)

Isolation of salannin Coarsely powdered seeds (2 5 kg) were exhaustively extracted with *n*-hexane and $CHCl_3$ by cold percolation The two extracts were found to be similar by TLC (silica gel, C_6H_6–EtOAc, 4 1 or 1 1) and were combined The total extract (20 g) was chromatographed over a column of silica gel and the column was eluted with solvents of increasing polarity in the order hexane, C_6H_6, followed by a mixture of C_6H_6–EtOAc Waxy materials were removed by elution with hexane Fractions eluted with C_6H_6–EtOAc (9 1) on repeated chromatography over silica gel gave salannin (3) (250 mg) (crystallized from hexane–Et_2O), mp 150°, $[\alpha]_D$ 167° ($CHCl_3$, *c* 1) (Found C, 68 00, H, 7 45 $C_{34}H_{44}O_9$ requires C, 68 40; H, 7 38%) IR ν_{max}^{KBr} cm^{-1} 2950, 1750, 1735, 1710, 1650, 1500, 1270, 1150, 1050, 860 MS *m/z* 596 $[M]^+$ ^1H NMR ($CDCl_3$, 90 MHz) δ2 85 (1H, *d*, *J* = 12 Hz, 5-H), 3 9 and 4 02 (1H, *dd*, *J* = 12 and 3 Hz, 6-H), 4 15 (1H, *d*, *J* = 3 Hz, 7-H), 5 45 (1H, *m*, 15-H), 4 92 (1H, *t*, *J* = 3 Hz, 1-H), 4 75 (1H, *t*, *J* = 3 Hz, 3-H), 6 28 (1H, *s*, 20-H), 7 22 (2H, *m*, 20-H and 19-H), 6 92 (1H, *q*, *J* = 7 5 Hz, olefinic H of tiglate), 1 92 (6H, *m*, Me of tiglate), 0 93 (3H, *s*, 24-H), 1 18 (3H, *s*, 25-H), 1 26 (3H, *s*, 22-H), 1 63 (3H, *d*, 26-H), 1 9 (3H, *s*, OAc), 3 23 (*s*, 3H, OMe)

Isolation of compositolide C_6H_6–EtOAc (1 1) eluted a gum Repeated CC over silica gel yielded compositolide (4) (150 mg), mp 300°, $[\alpha]_D$ 160° ($CHCl_3$, *c* 1) (Found C, 64 50, H, 7 03 $C_{34}H_{44}O_{11}$ requires C, 64 90, H, 7 00%) IR ν_{max}^{KBr} cm^{-1} 3400, 2975, 2925, 1770, 1750, 1730, 1710, 1690, 1455, 1270, 1165, 1145, 1051 MS *m/z* 628 $[M]^+$ ^1H NMR ($CDCl_3$, 100 MHz), δ2 78 (1H, *d*, *J* = 12 Hz, 5-H) 4 24 (1H, *d*, *J* = 3 Hz, 7-H), 4 04 and 3 92 (1H, *dd*, *J* = 12 and 3 Hz, 6-H), 4 98 (1H, *t*, *J* = 3 Hz, 1-H), 5 42 (1H, *m*, 15-H), 4 88 (1H, *t*, *J* = 3 Hz, 3-H), 6 95 (1H, *q*, *J* = 7 5 Hz, olefinic H of tiglate), 1 9 (6H, *m*, Me of tiglate), 6 78 (1H, *s*, 20-H), 6 06 (1H, *br s*), $W_{1/2}$ = 3 Hz, 21-H), 0 94 (3H, *s*, 24-H), 1 33 (3H, *s*, 25-H), 1 23 (3H, *s*, 22-H), 1 8 (3H, *d*, 26-H), 2 (3H, *s*, OAc), 3 4 (3H, *s*, OMe)

Acetylation of compositolide Compositolide (4) (70 mg) in pyridine was treated with Ac_2O (3 ml) and the mixture heated on a H_2O bath for 3 hr Work-up in the usual way afforded the acetate (**4b**) (50 mg), mp 210° (from hexane–Et_2O) (Found C, 64 40; H, 6 82 $C_{36}H_{46}O_{12}$ requires C, 64 48, H, 6 86%) MS *m/z* 670 $[M]^+$ ^1H NMR ($CDCl_3$ 90 MHz) δ2 68 (1H, *d*, *J* = 12 Hz, 5-H), 4 03 and 3 92 (1H, *dd*, *J* = 12 and 3 Hz, 6-H), 4 2 (1H, *d*, *J* = 3 Hz, 7-H), 4 95 (1H, *t*, *J* = 3 Hz), 4 75 (1H, *t*, *J* = 3 Hz, 3-H), 5 32 (1H, *m*, 15-H), 6 95 (1H, *q*, *J* = 7 5 Hz, olefinic H of tiglate), 7 02 (1H, *br s*, $W_{1/2}$ = 3 Hz, 21-H), 6 82 (1H, *s*, 20-H), 0 93 (3H, *s*, 24-H), 1 18 (3H, *s*, 25-H), 1 25 (3H, *s*, 22-H), 1 8 (3H, *d*, 26-H), 2 05 (3H, *s*, OAc), 1 9 (6H, *m*, Me of tiglate), 3 42 (3H, *s*, OMe)

Photolytic oxidation of salannin A soln of salannin (500 mg) in dry C_6H_6 (75 ml) in a Pyrex flask and under a stream of O_2 was irradiated with a UV lamp (Hanovia 450 W) After disappearance of salannin (3 hr) as shown by TLC, the solvent was evapd and the residue subjected to chromatography over silica gel Elution with $CHCl_3$–C_6H_6 (1 1) gave 4 (150 ml), mp 297° (crystallized from hexane–Et_2O) It recorded an undepressed mp on admixture with 4 and was found to be identical in all respects with authentic 4 (mp, IR and ^1H NMR) (Found C, 64 55, H, 7 43 $C_{34}H_{44}O_{11}$ requires C, 64 90, H, 7 00%)

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