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A NEW SESQUITERPENE ESTER FROM *FERULA TINGITANA*

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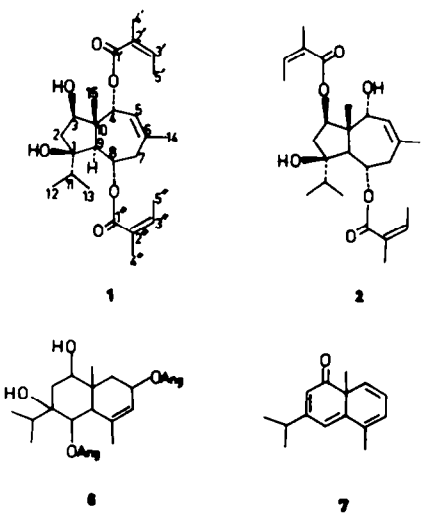
Abstract—A new sesquiterpene ester, tingitanol, isolated from *Ferula tingitana* L., is assigned as 1β,3β-dihydroxy-4α,8α-diangeloyloxydauc-5-ene on the basis of spectral, analytical, and X-ray data.

An investigation of the benzene extract of *Ferula tingitana* L. yielded a new sesquiterpene ester, tingitanol (**1**). The new ester was first thought to be a known compound, namely desoxodehydrolaserpitine, which was obtained from *Laserpitium latifolium* L. by Holub *et al.*[1] However, comparison with an authentic sample (TLC, ^{1}H NMR and ^{13}C NMR) showed that they were different. We report here that tingitanol (**1**) has the structure (1β,3β-dihydroxy-4α,8α-diangeloyloxydauc-5-ene) previously suggested for desoxodehydrolaserpitine, and that in the latter compound (**2**) one of the angeloyloxy moieties is at C_3 instead of C_4.

Tingitanol (**1**) has the composition $C_{25}H_{38}O_6$ on the basis of elemental analysis and MS (M^+ 434, 1%). Its IR clearly indicated the presence of hydroxyl (3470, 1075, 1030 cm^{-1}) and ester (1700, 1260, 1230 cm^{-1}) groups. The ^{1}H NMR spectrum showed the presence of two angeloyloxy moieties with typical signals at δ 6.12 (2H, br q, J = 7 and 10 Hz), 1.88 (3H, t, J = 1 Hz), 1.92 (3H, t, J = 1 Hz) and 2.03 (6H, tt, J = 1 and 7 Hz). The resonance at δ 5.35 (1H, dt, $J_{7\beta,8\beta}$ = 3 Hz, $J_{7\alpha,8\beta}$ = 10 Hz and $J_{8\beta,9\alpha}$ = 12 Hz) and examination of Dreiding models indicated that this hydrogen, geminal to one angeloyloxy moiety, should be β and situated at C_8 in order to give such a splitting pattern. Another peak at δ 5.07 (1H, d, $J_{4\beta,5}$ = 8 Hz) showed the other hydrogen geminal to the second angeloyloxy moiety was also β and could only be at the C_4 position. The vinylic ring proton peak was at δ 5.74 (1H, br d, J = 8 Hz, H-5) and other peaks for the sesquiterpene ring were as follows: δ 3.58 (1H, dd, J = 8 and 10 Hz, H_α-3), 2.72 (1H, br t, J = 13 Hz, H_β-7), 2.52 (1H, d, $J_{8\beta,9\alpha}$ = 10 Hz, H-9), 2.2 (2H, m, H_α-2, H_α-7), 1.55 (1H, dd, J = 10 and 12 Hz, H_β-2), 1.78 (3H, br s, C_6-Me), 1.14 (3H, s, C_{10}-Me), 0.92 (3H, d, J = 7 Hz) and 0.88 (3H, d, J = 7 Hz) (–CH(CH_3)$_2$). The ^{13}C NMR spectrum of tingitanol was consistent with the suggested structure (see Experimental).



1 **2**

6 **7**

In the ^{1}H NMR spectrum of desoxodehydrolaserpitine (**2**) the signals at δ 6.13 (2H, br q, J = 7 and 10 Hz), 1.88 (6H, t, J = 1 Hz) and 2.00 (6H, dt, J = 1 and 7 Hz) showed the presence of two angeloyloxy moieties. The signal at δ 5.88 (1H, dt, J = 3 and 10 Hz, H-8) showed that one of the angeloyloxy moieties was at C_8. This signal was similar to that of tingitanol, while the double doublet at 5.04 (1H, dd, J = 8 and 10 Hz, H-3) indicated that the second angeloyloxy moiety should be at C_3 instead of C_4 as in compound **1**. The signal at δ 3.7 (1H, d, J = 7 Hz, H-4) showed the hydrogen geminal to the hydroxyl group at C_4. The ^{13}C NMR spectrum was also in agreement with the revised structure of desoxodehydrolaserpitine (**2**) (see Experimental).

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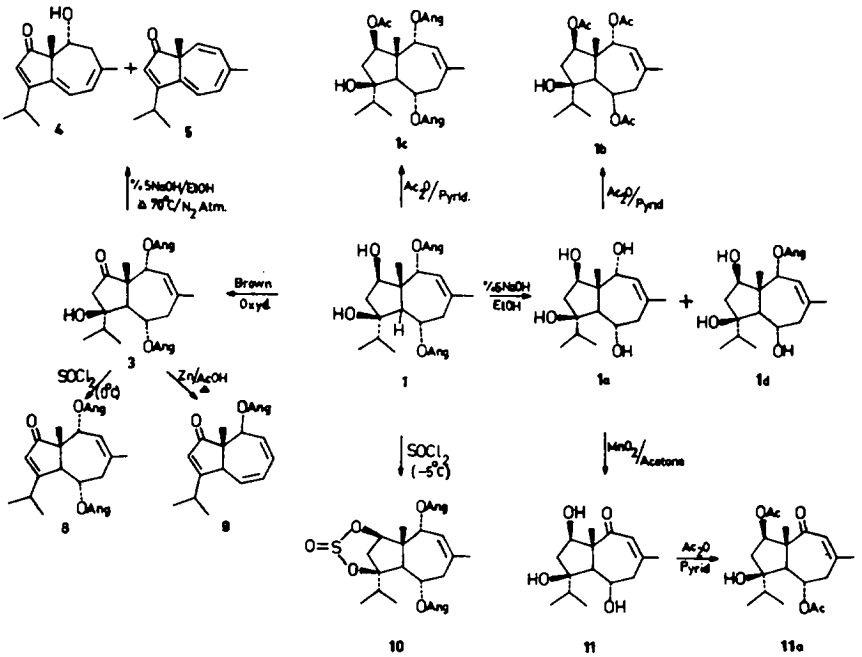
Hydrolysis of tingitanol with 5% NaOH in EtOH at room temperature yielded a tetrol (**1a**) with spectral data same as those of the hydrolysed product of **2**. Acetylation of **1a** yielded a triacetate (**1b**), the spectral data of which were as expected similar to those of the acetyl derivative of the tetrol obtained from compound **2**.

In order to prove the skeleton and the relative positions of hydroxyl groups, a series of chemical reactions were carried out (Scheme 1). Acetylation of **1** yielded a monoacetate (**1c**), in the IR spectrum of which the presence of a sharp peak at 3500 cm^{-1} indicated a tertiary hydroxyl group. Brown oxidation[2] of **1** yielded a ketone (**3**). Its IR spectrum showed a sharp hydroxyl peak at 3500 cm^{-1} and 5-membered ring ketone at 1730 cm^{-1} as well as α,β-unsaturated ester carbonyl bands at 1715 cm^{-1}. In the ^1H NMR spectrum of this product the one-proton double doublet at δ 3.58 which corresponded to H-3 disappeared, the H-4, H-5, H-8 and H-9 signals shifted downfield, while the angeloyloxy vinylic protons were resolved, giving two separate signals at δ 6.22 and 6.05. In order to remove the tertiary hydroxyl group and hydrolyse the angeloyloxy moieties, the ketone **3** was heated with 5% NaOH in EtOH under nitrogen at 70° for 2 hr,[3] yielding a mixture of two compounds. These were separated by TLC to yield compounds **4** and **5**. The UV spectrum of **4** showed extended conjugation by the peaks at 324 nm and 226 nm, indicating that the double bond at $\Delta^{5,6}$ had shifted to $\Delta^{6,7}$; its IR showing a broad hydroxyl band at 3430 cm^{-1} and a broad keto group at 1700 cm^{-1} which indicated conjugation in the five-membered ring as well as possible hydrogen bonding between the hydroxyl at C_4 and the keto group at C_3. A broad, not well resolved, triplet at δ 4.22 in the ^1H NMR spectrum showed the proton geminal to hydroxyl at C_4, while the lack of an H-9 doublet together with the UV data indicated the elimination of the C_8 hydroxyl group. Vinylic protons were found at δ 6.2 (1H, d, J = 8 Hz, H-8), 5.92 (1H, dt, J = 1 and 10 Hz, H-7) and 6.00 (1H, s, H-2). The UV spectrum of compound **5** showed additional conjugation, with peaks at 350 nm and 237 nm. Its IR spectrum showed no hydroxyl band, but the carbonyl band at 1695 cm^{-1} was much sharper. The ^1H NMR spectrum showed vinylic protons at δ 6.33 (1H, d, J = 8 Hz, H-8), 6.25 (1H, dt, J = 1 and 8 Hz, H-7), 5.98 (1H, d, J = 10 Hz, H-5†), 5.86 (1H, d, J = 9 Hz, H-4†) and 5.85 (1H, s, H-2). The UV and ^1H NMR data of compounds **4** and **5** indicated a daucane structure rather than a naphthalene structure; the only possible naphthalene structure would be **6** which should yield **7** in the above reaction; the latter should exhibit two narrow doublets (J ~ 2 Hz), two doublets (J ~ 8 Hz) and a triplet (J ~ 8 Hz) in the vinyl region of its ^1H NMR spectrum.

In order to prove the 1,3 positions of the two hydroxyl groups in the five-membered ring, a milder dehydration reaction was performed. Thionyl chloride was added to compound **3** at 0° to form compound **8**. Its UV spectrum had a maximum at 229 nm and its IR spectrum contained no hydroxyl groups. The sharp carbonyl band at 1705 cm^{-1} indicated the presence of an α,β-unsaturated five-membered ring ketone. The ^1H NMR showed the H-2 vinylic proton at δ 5.92. When the same dehydration was carried out with Zn dust in acetic acid, in addition to compound **8**, we obtained compound **9**. In this latter compound the hydroxyl at C_1 and the angeloyloxy moiety at C_8 were eliminated as well. Its ^1H NMR showed H-2 at δ 5.9 as a singlet, while the H-8 and H-7 vinylic protons were at δ 6.15 as a multiplet.

The formation of a cyclic sulfite compound (**10**) demonstrated that the hydroxyl group at C_1 and C_3

†Interchangeable.



Scheme 1.

were *cis* disposed.[4] Since the C_3 hydroxyl appeared to be β from Dreiding models, the C_1 hydroxyl should be β as well. This was confirmed by X-ray analysis of acetyltingitanol (**1c**). Finally the position of the last hydroxyl group at C_4 was further confirmed by the mild oxidation of tetrol **1a** with MnO_2 in acetone[5]; compound **11** was formed. Since this oxidation is only possible with an allylic hydroxyl group, the position of the C_4 hydroxyl was proven. Its IR spectrum showed a strong hydroxyl band at 3450 cm^{-1} and the α,β-unsaturated seven-membered ring ketone was at 1685 (sh) and 1630 cm^{-1}. Its ^1H NMR showed that the doublet for H-4 at δ 4.52 was missing and the doublet for H-5 became a singlet at 5.85. Acetylation of **11** yielded a diacetate **11a**.

X-ray analysis of the acetyltingitanol **1c** confirmed the suggested structure and the relative stereochemistry of compound **1** as shown in Fig. 1 which is an ORTEP[6] drawing of **1c**. The two rings are *trans*-fused with the five-membered ring in an envelope and the seven in a chair conformation.[7] The conformation of the five-membered ring results in steric interactions between the substituents, O(3)..C(15) = 2.768(7), O(3)..H(15a) = 2.43(4) and O(1)..C(15) = 3.171(7)Å. Each angeloyloxy moiety and the ring carbon to which it is attached is nearly planar. The two groups differ only in the orientation about the C—O bond with C(4) and O(41) being in a *cis* arrangement and O(8) and C(8) in a *trans* arrangement. The molecules are loosely packed in the crystal and the angeloyl groups exhibit high thermal motion. This is reflected in the shortened bond distances associated with these groups. No attempt was made to correct the side chain distances for thermal motion.

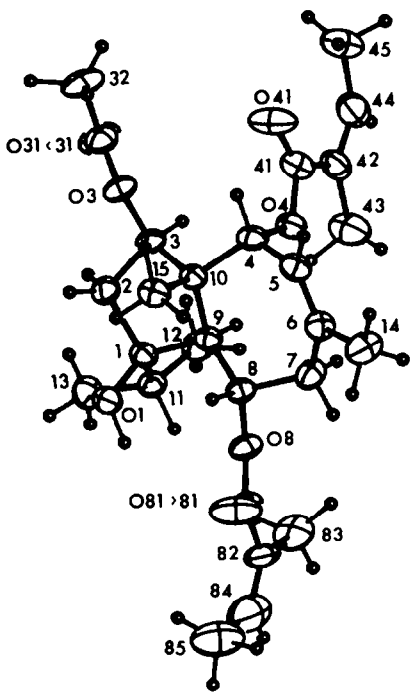


Fig. 1. Ortep drawing of compound **1**. The thermal ellipsoids of the side chains have been reduced in magnitude relative to the ring atoms.

EXPERIMENTAL

The plant material was collected from Aegean coast of Turkey (Kuşadası) in June 1982. A voucher specimen identified by Dr. E. Tuzlacı (Istanbul) was deposited in the Herbarium of the Faculty of Pharmacy, University of Istanbul (ISTE 48938).

The spectra were recorded on the following instruments: UV, Varian Techtron model 635; IR, Perkin–Elmer 577; ^1H NMR, FT-NT 200 MHz; ^{13}C NMR 22.6 MHz; MS, DuPont 21–491.

Isolation and identification of tingitanol (**1**).

Coarsely powdered roots of *Ferula tingitana* L. (Umbelliferae) (2.5 kg) were extracted with benzene in a Soxhlet. The benzene extract was concentrated *in vacuo* and chromatographed over a Sephadex LH-20 column (3 × 50 cm), eluting with ethanol. Tingitanol (**1**) was obtained from the first fractions and cleaned by passing through smaller Sephadex LH-20 columns a few times, yielding 30 g of pure tingitanol (yield 1.2%).

Tingitanol (**1**). Amorphous. IR (KBr) 3470, 2960, 2920, 2860, 1700, 1680, 1450, 1380, 1345, 1260, 1230, 1150, 1115, 1075, 1030, 950, 840, 750 cm^{-1}. ^1H NMR ($CDCl_3$): see text. ^{13}C NMR ($CDCl_3$): 168.1 (s) C_1', 167.9 (s) C_1'', 139.4 (d) C_5, 139.1 (d) C_3', 138.7 (d) C_3'', 127.7 (s) C_6, 127.6 (s) C_2', C_2'', 81.2 (s) C_1, 73.2 (d) C_3, 71.0 (d) C_8, 69.8 (d) C_4, 49.3 (d) C_9, 48.6 (s) C_{10}, 40.5 (t) C_2, 38.3 (t) C_7, 36.7 (d) C_{11}, 27.4 (q) C_{14}, 20.9 (q) C_5', 20.5 (q) C_5'', 18.3 (q) C_4', 17.2 (q) C_4'', 15.8 (q) C_{12}, C_{13}, 13.3 (q) C_{15}. MS: 70 eV (probe) (%), M^+ 434 (1), (M-18) 416 (2), (M-43) 391 (2), (M-Angeloyloxy) 334 (25), (M-Angeloyloxy-OH) 317 (12), (M-Angeloyloxy-43) 291 (60), (M-2 × Angeloyloxy-H_2O) 216 (75), 120 (100), (Angeloyl) 83 (85). (Found: C, 69.5; H, 8.8, $C_{25}H_{38}O_6$ requires C, 69.1; H, 8.8%.)

Acetyltingitanol (**1c**)

Ac_2O (1 ml) was added to tingitanol (100 mg) in pyridine (1 ml) and left at room temp for 16 hr. After work-up, the product (**1c**) crystallized from a mixture of ether:petrol (1:1), m.p. 141–143°, yield 105 mg. IR (KBr): 3510, 2960, 1730, 1710, 1650, 1460, 1440, 1375, 1360, 1260, 1230, 1150, 1095, 1085, 1040, 990 cm^{-1}. ^1H NMR ($CDCl_3$) δ 0.9 (3H, d, J = 7 Hz, Me-12), 0.94 (3H, d, J = 7 Hz, Me-13), 1.20 (3H, s, Me-15), 1.84 (3H, br s, Me-14), 1.9 (3H, t, J = 1 Hz, Me-4'), 1.95 (3H, t, J = 1 Hz, Me-4''), 2.02 (6H, dd, J = 1 and 7 Hz, Me-5' and Me-5''), 2.05 (3H, s, OAc), 6.12 (2H, tt, J = 1 and 8 Hz, H-3' and H-3''), 5.8 (1H, br d, J = 8 Hz, H-5), 5.38 (1H, dt, J = 2, 10 and 10 Hz, H-8), 4.82 (1H, br d, J = 8 Hz, H-4), 4.72 (1H, t, J = 9 Hz, H-3), 2.72 (1H, br t, J = 10 Hz, H_β-7), 2.70 (1H, d, J = 10 Hz, H-9), 2.42 (1H, dd, J = 8 and 14 Hz, H_α-2), 2.15 (1H, dd, J = 2 and 14 Hz, H_α-7), 1.55 (1H, dd, J = 10 and 14 Hz, H_β-2). (Found: C, 68.1; H, 8.4. $C_{27}H_{40}O_7$ requires C, 68.0; H, 8.4%.)

Hydrolysis of tingitanol

Tingitanol (100 mg) in 5% NaOH/EtOH (5 ml) was left overnight at room temp, then distilled under reduced pressure. Water was added to the residue, the aqueous solution was extracted with EtOAc, dried over anhyd. Na_2SO_4, then filtered and evaporated to dryness *in vacuo*. A mixture of two compounds was obtained; the tetrol **1a** precipitated from ether and crystallized from EtOH (yield 55 mg), while the triol **1d** was obtained by preparative TLC (using $CHCl_3$:EtOH 93:7) (yield 5 mg).

Tetrol (**1a**). M.p. 243–245° (lit.[1] 245°) (by sublimation). IR (KBr): 3440, 3380, 2950, 2840, 1670, 1500, 1470, 1430, 1380, 1330, 1300, 1250, 1145, 1130, 1120, 1060, 1015, 985, 930, 700, 600 cm^{-1}. ^1H NMR (C_5D_5N) δ 1.2 (3H, d, J = 7 Hz, Me-12), 1.22 (3H, d, J = 7 Hz, Me-13), 1.58 (3H, s, Me-15), 1.8 (3H, br s, Me-14), 6.00 (1H, br d, J = 8 Hz, H-5), 4.9 (1H, br t, J = 9 Hz, H-8), 4.7 (1H, br t, J = 8 Hz, H-3), 4.52 (1H, br d, J = 8 Hz, H-4), 3.2 (1H, d, J = 10 Hz, H-9), other peaks were between 2.8–2.2 ppm. (Found: C, 66.8; H, 9.8. $C_{15}H_{26}O_4$ requires: C, 66.6; H, 9.6%.)

Triacetate of tetrol **1b**—Tetrol (50 mg) was acetylated at room temp in the usual way (yield 60 mg), m.p. 122–124° (lit.[1] 124°). IR (KBr) 3540, 2960, 1730, 1665, 1460, 1430, 1365, 1250, 1135, 1080, 1015, 985, 790, 600 cm^{-1}. ^1H NMR ($CDCl_3$) δ 0.93 (3H, d, J = 6.5 Hz, Me-12), 0.98 (3H, d, J = 7 Hz, Me-13), 1.14 (3H, s, Me-15), 1.81 (3H, br s, Me-14), 2.04 (3H, s, OAc), 2.06 (6H, s, 2 × OAc), 5.72 (1H, br d, J = 8 Hz, H-5), 5.23 (1H, dt, J = 3, 10 and 10.5 Hz, H-8), 4.74 (1H, d, J = 8 Hz, H-4), 4.68 (1H, dd, J = 8 and 10 Hz, H-3), 2.65 (1H, d, J = 10 Hz, H-9), other peaks were between 2.5–1.5 ppm. MS 70 eV (probe) *m/z* (%) M^+ 396 (1), (M-43) 353 (3), (M-60) 336 (1), (M-43-60) 293 (35), (M-2 × 60) 276 (10), (M-2 × 60-43) 233 (70), (M-3 × 60) 216 (65), (M-3 × 60-43) 173 (95). (Found: C, 63.8; H, 8.1. $C_{21}H_{32}O_7$ requires C, 63.6; H, 8.1%.)

Triol **1d**. Amorphous. IR (KBr): 3450, 2960, 2870, 1695, 1640, 1450, 1380, 1230, 1160, 1140, 1120, 1075, 1040, 1000, 975, 930, 840 cm^{-1}. ^1H NMR ($CDCl_3$) δ 0.9 (3H, d, J = 7 Hz, Me-12), 0.96 (3H, d, J = 7 Hz, Me-13), 1.10 (3H, s, Me-15), 1.84 (3H, br s, Me-14), 1.92 (3H, t, J = 1 Hz, Me-4'), 2.02 (3H, dd, J = 1 and 7 Hz, Me-5'), 6.12 (1H, dq, J = 8 and 2 Hz, H-3'), 5.67 (1H, br d, J = 8 Hz, H-5), 5.05 (1H, d, J = 8 Hz, H-4), 4.18 (1H, dt, J = 3 and 10 Hz, H-8), other peaks were between 3.5–1.6 ppm (Found: C, 68.2; H, 9.1. $C_{20}H_{32}O_5$ requires C, 68.2; H, 91%.)

Oxidation of tingitanol

Tingitanol (200 mg) was dissolved in Et_2O, chromic acid solution (1 ml) was added and the solution was stirred at room temp for 2 hr. The ether layer was separated and washed with sat aqueous $NaHCO_3$, dried over anhyd. Na_2SO_4, filtered and evaporated, and the residue was crystallized from ether (yield 185 mg). The ketone (3) thus obtained had m.p. 116–118°. IR (KBr): 3500, 2970, 1730, 1715, 1640, 1460, 1380, 1230, 1150, 1040, 990, 970, 850, 750 cm^{-1}. ^1H NMR ($CDCl_3$): δ 0.94 (3H, d, J = 7 Hz, Me-12), 0.98 (3H, d, J = 7 Hz, Me-13), 1.34 (3H, s, Me-15), 1.60 (3H, br s, Me-14), 1.84 (3H, t, J = 1 Hz, Me-4'), 1.92 (3H, t, J = 1 Hz, Me-4''), 1.98 (3H, dd, J = 1 and 7 Hz, Me-5'), 2.07 (3H, dd, J = 1 and 7 Hz, Me-5''), 6.24 (1H, q, J = 7 Hz, H-3'), 6.05 (1H, q, J = 7 Hz, H-3''), 5.85 (1H, br d, J = 8 Hz, H-5), 5.5 (1H, dt, J = 5 and 10 Hz, H-8), 5.12 (1H, d, J = 7 Hz, H-4), 3.22 (1H, d, J = 10 Hz, H-9), other peaks were between 2.7–1.3 ppm. MS 70 eV (probe) *m/z* (%); no M^+ peak, (M-Angeloyl) 349 (8), (M-Angeloyloxy-H) 331 (10), (M-Angeloyloxy-Angeloyl) 249 (90), (M-2 × Angeloyloxy-H) 231 (100). (Found: C, 69.5; H, 6.4. $C_{25}H_{36}O_6$ requires C, 69.4; H, 6.3%.)

Basic dehydration of ketone

The ketone 3 (80 mg) was heated with 10 ml of 5% NaOH/EtOH to 70° for 2 hr under N_2. The reaction mixture was diluted with water and extracted with ether. The ether phase washed with dil HCl, then with water and dried over anhyd. Na_2SO_4, filtered and evaporated to dryness. A mixture of two compounds (**4** and **5**) was obtained and separated on preparative TLC plates (petrol:EtOAc 9:1) (R_f 0.3 for **4** and 0.7 for **5**).

Compound **4**. Amorphous, yield 8 mg, UV (ether): λ_{max} 324 nm (log ϵ 3.97), 226 (4.20). IR (KBr) 3430, 2980, 1700, 1600, 1550, 1450, 1380, 1260, 1150, 1075, 1040, 870, 840 cm^{-1}. ^1H NMR ($CDCl_3$) δ 0.98 (3H, s, Me-15), 1.25 (6H, t, J = 7 Hz, Me-12 and Me-13), 1.93 (3H, br s, Me-14), 6.2 (1H, d, J = 8 Hz, H-8), 5.92 (1H, dt, J = 1 and 10 Hz, H-7), 6.00 (1H, s, H-2), 4.22 (1H, br t, H-4), 2.9 (1H, septet, H-11), other peaks were between 3.5–2.0 ppm. MS 70 eV (probe) *m/z* (%) M^+ 232 (96), (M-18) 214 (20), (M-43) 189 (100), (M-43-18) 171 (60).

Compound **5**. Amorphous, yield 20 mg. UV (ether): λ_{max} 350 nm (log ϵ 3.60), 237 (4.30). IR (KBr): 2960, 2920, 1695, 1630, 1615, 1555, 1445, 1380, 1360, 1270, 1250, 1100, 850 cm^{-1}. ^1H NMR ($CDCl_3$): δ 1.02 (3H, s, Me-15), 1.22 (3H, d, J = 7 Hz, Me-12), 1.26 (3H, d, J = 7 Hz, Me-13), 2.06 (3H, br s, Me-14), 6.33 (1H, d, J = 8 Hz, H-8), 6.25 (1H, dt, J = 1 and 8 Hz, H-7), 5.98 (1H, d, J = 10 Hz, H-5), 5.86 (1H, d, J = 9 Hz, H-4), 5.85 (1H, s, H-2), 2.9 (1H, septet, J = 5 Hz, H-11). MS 70 eV (probe) *m/z* (%) M^+ 214 (80), (M-15) 199 (85), (M-43) 171 (100).

Dehydration of ketone with thionyl chloride

To the ketone 3 (20 mg) in pyridine (1 ml), $SOCl_2$ (0.3 ml) was added dropwise at 0°C. The reaction mixture was kept at 0°–(−5°) for 1 hr, then diluted with ice water and extracted with ether. The ether layer was washed with dil HCl, 5% $NaHCO_3$ and water, then dried over anhyd. Na_2SO_4 and evaporated to dryness. The residue was crystallized from ether, giving **8** (15 mg).

Compound **8**. M.p. 120–121°. UV (ether): λ_{max}: 229 nm (log ϵ 4.15). IR (KBr): 2960, 2920, 1705, 1600, 1450, 1380, 1350, 1250, 1230, 1155, 1080, 1030, 960, 880, 845, 750, 630, 600 cm^{-1}. ^1H NMR ($CDCl_3$): δ 1.15 (6H, d, J = 7 Hz, Me-12 and Me-13), 1.25 (3H, s, Me-15), 1.76 (3H, t, J = 1 Hz, Me-4'), 1.83 (3H, br s, Me-14), 1.90 (3H, dd, J = 1 and 7 Hz, Me-5'), 1.94 (3H, t, J = 1 Hz, Me-4''), 2.05 (3H, dd, J = 1 and 7 Hz, Me-5''), 6.15 (1H, q, J = 7 Hz, H-3'), 6.02 (1H, q, J = 7 Hz, H-3''), 5.92 (1H, s, H-2), 5.78 (1H, br d, J = 8 Hz, H-5), 5.5 (2H, m, H-4 and H-8). MS 70 eV: *m/z* (%) M^+ 414 (1), (M-Angeloyl) 331 (45), (M-Angeloyloxy) 231 (100), (Angeloyl) 83 (90).

Dehydration of ketone with Zn/AcOH

The ketone 3 (80 mg) was refluxed 5 hr with gl. AcOH and activated Zn dust (300 mg). The cooled mixture was filtered, and diluted with water, and extracted with ether. The ether phase was washed with water and dried over anhyd. Na_2SO_4, filtered and evaporated to dryness. The residue was separated on preparative TLC (petrol:EtOAc 7:3). The band R_f 0.60 was the main compound (**9**) (yield 20 mg); a small amount of compound **8** was also obtained.

Compound **9**. Amorphous. IR (KBr): 2960, 2930, 1710, 1640, 1600, 1510, 1460, 1380, 1260, 1225, 1150, 1070, 1040 cm^{-1}. ^1H NMR ($CDCl_3$): δ 1.12 (3H, d, J = 7 Hz, Me-12), 1.14 (3H, d, J = 7 Hz, Me-13), 1.28 (3H, s, Me-15), d, 1.92 (3H, s, Me-14), 1.94 (3H, t, J = 1 Hz, Me-4'), 2.04 (3H, dd, J = 1 and 7 Hz, Me-5'), 6.27 (1H, d, J = 11 Hz, H-8), 6.15 (1H, m, H-3'), 6.10 (1H, J = 10 Hz, H-7), 5.90 (1H, s, H-2), 5.05 (1H, d, J = 15 Hz, H-4). (Found: C, 76.5; H, 8.3. $C_{20}H_{26}O_3$ requires C, 76.4; H, 8.3%.)

Cyclic sulfite of tingitanol (**10**)

Tingitanol (50 ml) in pyridine (2 ml) was cooled to − 5°, $SOCl_2$ (0.3 ml) was added and the solution left in a refrigerator for 1 hr. Compound **10** was obtained for preparative TLC ($CHCl_3$: EtOH; 98:2) (yield 25 mg). IR (KBr): 2960, 1710, 1640, 1450, 1380, 1350, 1250, 1220, 1150, 1070, 1030, 980, 960, 920, 880, 850, 800, 740, 670 cm^{-1}. ^1H NMR ($CDCl_3$): δ 1.00 (3H, d, J = 7 Hz, Me-12), 1.07 (3H, d, J = 7 Hz, Me-13), 1.42 (3H, s, Me-15), 1.8 (3H, br s, Me-14), 1.89 (6H, t, J = 1 Hz, Me-5' and Me-5''), 2.01 (6H, tt, J = 1 and 7 Hz, Me-4' and Me-4''), 2.15 (1H, dd, J = 3 and 19 Hz, H_a-2), 2.26 (1H, septet, H-11), 2.67 (1H, d, J = 10.5 Hz, H-9), 3.1 (1H, dd, J = 7.5 and 18.5 Hz, H_s-2), 4.48 (1H, d, J = 4.5 Hz, H-4), 5.42 (1H, t, H_a-3), 5.44 (1H, d, J = 4.5 Hz, H-5), 5.54 (1H, ddd, J = 3, 7 and 10.5 Hz, H-8), 6.06 (1H, dq, J = 2 and 7 Hz, H-3') and 6.13 (1H, dq, J = 2 and 7 Hz, H-3''). (Found: C, 62.6; H, 7.5. $C_{25}H_{36}O_7S$ requires C, 62.5; H, 7.5%.)

Allylic oxidation of tetrol

To tetrol **1a** (50 mg) dried acetone (10 mg) activated MnO_2 (500 ml) was added and stirred for 5 hr at room temp. After filtration the acetone was evaporated and the residue separated by p.l.c. ($CHCl_3$:EtOH 9:1); compound **11** (25 mg) was obtained.

Compound **11**. Amorphous. IR (KBr): 3450, 2960, 2880, 1685 (sh), 1630, 1470, 1440, 1375, 1060, 910 cm^{-1}. ^1H NMR ($CDCl_3$): δ 0.9 (3H, d, J = 7 Hz, Me-12), 0.98 (3H, d, J = 7 Hz, Me-13), 1.32 (3H, s, Me-15), 2.00 (2H, br s,

Me-14), 5.85 (1H, br s, H-5), 4.58 (1H, dt, J = 5 and 10 Hz, H-8), 3.97 (1H, dd, J = 7 and 12 Hz, H-3), 2.12 (1H, d, J = 10 Hz, H-9), other signals were between 2.8–1.5 ppm. (Found: C, 67.3; H, 9.0. $C_{15}H_{24}O_4$ requires: C, 67.2; H, 0.9%.)

Diacetyl derivative of compound **11**

Compound **11** (10 mg) acetylated in the usual manner, yielded 12 mg **11a**, amorphous. IR (KBr): 3450, 2920, 1720, 1650, 1430, 1360, 1240, 1135, 1070, 1020, 950 cm^{-1}. ^1H NMR ($CDCl_3$): δ 0.88 (3H, d, J = 7 Hz, Me-12), 0.92 (3H, d, J = 7 Hz, Me-13), 1.42 (3H, s, Me-15), 1.96 (3H, br s, Me-14), 2.04 (3H, s, OAc), 2.08 (3H, s, OAc), 5.93 (1H, br s, H-5), 5.65 (1H, m, H-8), 4.92 (1H, t, J = 9 Hz, H-3), 2.4 (1H, d, J = 10 Hz, H-9). (Found: C, 64.8; H, 8.0. $C_{19}H_{28}O_6$ requires: C, 64.8; H, 8.0%.)

Compound **2**[1]. IR (KBr): 3470, 2960, 1690, 1640, 1450, 1380, 1350, 1250, 1230, 1170, 1080, 1040, 980, 950, 850, 750 cm^{-1}. ^1H NMR ($CDCl_3$): δ 0.92 (3H, d, J = 7 Hz, Me-12), 0.98 (3H, d, J = 7 Hz, Me-13), 1.20 (3H, s, Me-15), 1.82 (3H, br s, Me-14), 1.88 (6H, t, J = 1 Hz, Me-5′ and Me-5″), 2.00 (6H, dt, J = 1 and 7 Hz, Me-4′ and Me-4″), 6.13 (2H, br q, J = 7 and 10 Hz, H-3′ and H-3″), 5.7 (1H, br d, J = 8 Hz, H-5), 5.38 (1H, dt, J = 3 and 10 Hz, H-8), 5.04 (1H, dd, J = 8 and 10 Hz, H-3), 3.7 (1H, d, J = 7 Hz, H-4), other peaks were between 1.3–2.9 ppm. ^{13}C NMR ($CDCl_3$): 167.3 (s) C_1', 167.1 (s) C_1'', 137.7 (d) C_3', C_3'', 135.5 (d) C_5, 126.9 (s) C_2', C_2'', 125.6 (s) C_6, 80.9 (s) C_1, 73.7 (d) C_3, 69.3 (d) C_8, 67.8 (d) C_4, 48.5 (d) C_9, 46.3 (s) C_{10}, 39.1 (t) C_2, 35.9 (d) C_{11}, 35.5 (t) C_7, 26.4 (q) C_{14}, 19.6 C_5', 19.5 (q) C_5'', 17.4 (q) C_4', 16.2 (q) C_4'', 14.7 (q) C_{12}, C_{13}, 11.3 (q) C_{15}.

X-ray analysis of acetyltingitanol **1c**

A Syntex $P2_1$ diffractometer was used to collect data on an orthorhombic crystal of dimensions 0.41 × 0.37 × 0.26 mm belonging to space group $P2_12_12_1$ with a = 10.922(3), b = 23.074(4), c = 10.809(3)Å, V = 27.24(1)Å^3, Z = 4, dc = 1.162 Mg m^{-3}, and μ = 6.82 cm^{-1} (CuK_α). A total of 2183 independent reflections were collected by the $\theta:2\theta$ scan technique using CuK_α radiation (λ = 1.54178 Å) of which 2115 had intensities greater than $3\sigma(I)$. The structure was solved by direct methods.[8] Hydrogen atom positions were obtained from a difference Fourier map and least-squares refinement yielded a final R of 0.048. Atomic positional parameters (Table 1) and bond distances and valence angles (Table 2) are available from the Cambridge Crystallographic Data Centre.

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