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SESQUITERPENE ESTERS, TRIPTOGELIN A-1–A-4, FROM *TRIPTERYGIUM WILFORDII* VAR. *REGELII*

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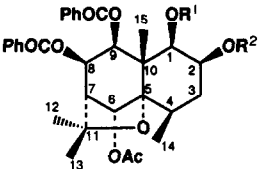
Key Word Index—*Tripterygium wilfordii*; Celastraceae; achenes; sesquiterpene; triptogelin.

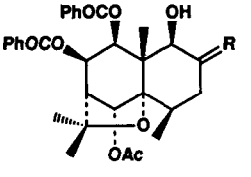
Abstract—New sesquiterpene esters, triptogelin A-1, A-2, A-3, A-4 and B-1, have been isolated from the achenes of *Tripterygium wilfordii* var. *regelii* and their structures established by chemical and spectroscopic means.

INTRODUCTION

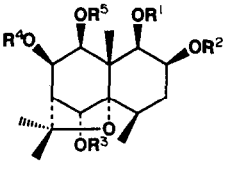
The sesquiterpene dihydroagarofuran derivatives are found in Nature in various oxygenated forms and these polyol esters mostly occur in members of the Celastraceae [1]. In continuation of previous interests in this area we describe here a group of esters which we named triptogelin A-1 (**1**), A-2 (**2**), A-3 (**3**), B-1 (**4**) and A-4 (**5**) isolated from the achenes of *T. wilfordii* Hook Fil. var. *regelii* [2–4].

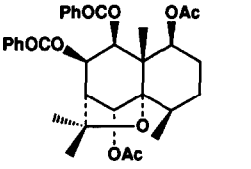


1 $R^1 = R^2 = COPh$
2 $R^1 = COPh$, $R^2 = H$
3 $R^1 = R^2 = H$



4 $R = H_2$
5 $R = O$





4a

1a $R^1 = R^2 = R^4 = R^5 = COPh$, $R^3 = H$
1b $R^1 = R^2 = R^3 = R^4 = R^5 = H$
3a $R^1 = R^3 = Ac$, $R^2 = H$, $R^4 = R^5 = COPh$
3b $R^1 = R^2 = R^3 = Ac$, $R^4 = R^5 = COPh$
3c $R^1 = R^2 = R^5 = H$, $R^3 = Ac$, $R^4 = COPh$
3d $R^1 = R^2 = R^4 = R^5 = H$, $R^3 = Ac$

RESULTS AND DISCUSSION

The methanolic extract of the achenes of *Tripterygium wilfordii* Hook fil. var. *regelii* Makino afforded, after extensive purification, triptogelin A-1 (**1**), A-2 (**2**), A-3 (**3**), B-1 (**4**) and A-4 (**5**).

Triptogelin A-1 (**1**) was obtained as needles, and showed an ester carbonyl band at 1720 cm^{-1} in the IR spectrum. The UV spectrum of **1** showed the presence of benzoate moieties. The ^1H NMR spectrum (Table 1) revealed the presence of one acetate group (δ2.16, *s*, 3H) and four benzoate groups (δ6.7–8.1, 20H), and the mass spectrum showed peaks due to the loss of acetic acid and benzoic acid units. The ^1H NMR spectrum of **1** showed the presence of three tertiary methyl groups at δ1.52–2.00 and one secondary methyl at δ1.41 (Table 1). The signals observed at δ5.76, 5.80, 5.80, 5.85 and 6.38 were assigned to the protons attached to the carbon atoms bearing the secondary ester groups. The ^{13}C NMR spectrum (Table 2) of **1** showed five ester carbonyl carbons at δ164.8–169.8, four methyls, three methines, five methines attached to an oxygen function, one quaternary carbon, and two quaternary carbons attached to an oxygen function. These facts agreed with a molecular formula of **1** as $C_{45}H_{44}O_{11}$, which was supported by means of high mass data. It was concluded that **1** was based on the dihydroagarofuran skeleton of the sesquiterpene polyol esters found in Celastraceae [1]. In the ^1H NMR spectrum, the signals of the methine protons at δ5.85 (*dd*) and 6.38 (*br s*) were assigned to 8-H and 6-H in the dihydroagarofuran skeleton as these signals collapsed to a doublet and singlet, respectively, on irradiation of the methine proton at δ2.67 (*br d*) assignable to 7-H [5]. Also, the signals at δ1.41 (*d*), 2.06 (*br d*) and 2.44 (*ddd*) were assigned to 14-H, 3-H_{eq} and 3-H_{ax}, respectively, from the spin decoupling experiments, and the signal at δ5.76 (*d*) was assigned to 9-H from the same coupling constant with 8-H. Assignments of another two methine protons attached to the carbon atoms bearing the secondary ester groups were very difficult due to the overlap of the signals. However, the coupling constants of 3-H showed the presence of one ester group on C-2, and the remaining ester linking site was assigned to C-1. The orientations of the ester groups on C-6, C-8 and C-9 were confirmed by NOE experiments. Thus, when the 14-H (Me) and 15-H (Me) methyl signals were irradiated, increases (20 and 6%, respectively) of the 6-H signal intensity occurred. On irradiation of the 12-H (Me) signal, the intensity of the 8-H and 9-H signals were increased. These results indicated that the orientations of the protons attached to oxygen-bearing carbon atoms were 6-H_{ax}, 8-H_{eq} and 9-H_{ax}.

Table 1. ^{1}H NMR data for compounds **1**–**5** and the derivatives **1b** and **3a**

H	1	1b	2	3	3a	4	5
1	5.80 *br s*	4.48 *d* (3.7)	5.62 *d* (3.7)	4.09 *d* (3.7)	5.36 *d* (3.4)	4.14 *dd* (10.7) (5.1)	4.72 *d* (3.7)
2	5.80 *br s*	4.56 *dd* (3.7) (2.9)	4.31 *ddd* (6.0) (3.7)	4.03 *dd* (6.2) (3.7)	4.17 *dd* (7.0) (3.4)	—	
3	2.06 *br d* (15.0) 2.44 *ddd* (15.0) (7.6) (3.6)	2.18 *br d* (14.4) 2.54 *ddd* (14.2) (6.1) (2.9)		1.88 *br d* (14.2)		—	2.32 *dd* (13.2) (1.5) 3.17 *dd* (13.2) (7.6)
6	6.38 *br s*	5.76 *d* (3.9)	6.32 *br s*	6.28 *br s*	6.28 *br s*	6.19 *br s*	6.25 *br s*
7	2.67 *br d* (4.2)	2.78 *br d* (3.9)	2.61 *br d* (4.2)	2.61 *br d* (4.2)	2.62 *br d* (4.4)	2.57 *br d* (3.7)	2.71 *br d* (4.4)
8	5.85 *dd* (5.4) (4.2)	4.62 *m*	5.84 *dd* (5.1) (4.2)	5.82 *dd* (5.1) (4.2)	5.87 *dd* (5.1) (4.4)	5.83 *dd* (5.1) (3.7)	5.84 *dd* (5.1) (4.4)
9	5.76 *d* (5.4)	4.62 *m*	5.71 *d* (5.1)	5.73 *d* (5.1)	5.58 *d* (5.1)	5.77 *d* (5.1)	6.09 *d* (5.1)
12	1.63 *s*	1.93 *s*	1.65 *s*	1.60 *s*	1.63 *s*	1.63 *s*	1.73 *s*
13	1.52 *s*	1.40 *s*	1.49 *s*	1.46 *s*	1.47 *s*	1.45 *s*	1.55 *s*
14	1.41 *d* (7.6)	2.02 *d* (7.6)	1.40 *d* (7.8)	1.32 *d* (7.3)	1.36 *d* (7.6)	1.06 *d* (7.3)	1.05 *d* (7.6)
15	2.00 *s*	2.08 *s*	1.91 *s*	1.65 *s*	1.78 *s*	1.44 *s*	1.31 *s*

Compound **1**: acetate [δ2.16 (3H, *s*)], benzoate [δ6.7–8.1 (20H)]; **2**: acetate [δ2.14 (3H, *s*)], benzoate [δ6.8–8.1 (15H)]; **3**: acetate [δ2.12 (3H, *s*)], benzoate [δ7.2–8.1 (10H)]; **3a**: acetate [δ1.51 and 2.13 (each 3H, *s*)], benzoate [δ7.2–8.1 (10H)]; **4**: acetate [δ2.13 (3H, *s*)], benzoate [δ7.2–8.1 (10H)]; **5**: acetate [δ2.13 (3H, *s*)], benzoate [δ7.2–8.1 (10H)].

Figures in parentheses are coupling constants in Hz, run at 200 MHz in chloroform-*d* (**1**–**3**, **3a**, **4** and **5**) and pyridine-d_5.

—The signals could not be assigned owing to overlapping.

The partial hydrolysis of **1** using K_2CO_3–methanol afforded **1a**. The ^{1}H NMR spectrum of **1a** showed the loss of one acetate group compared with **1**, the position of one acetate group in **1** was located at C-6 by the upfield shift of the signal due to 6-H (**1**; δ6.38, **1a**; δ5.22). The remaining four benzoyl ester groups were located on C-1, C-2, C-8 and C-9. The orientations of C-1 and C-2 were not assignable from the ^{1}H NMR spectra of **1** and **1a** and thus compound **1** was hydrolysed. The hydrolysis of **1** using NaOEt–methanol afforded the pentaol compound **1b**. In the NOE experiments of **1b**, irradiation of the 3-H_{ax} signal increased the intensity of the 1-H and 2-H signals *ca* 7 and 4%, respectively. From these results the structure of triptogelin A-1 was formulated as **1**.

Compound **2**, triptogelin A-2, $C_{38}H_{40}O_{10}$, contained one acetate and three benzoate residues (IR, UV, ^{1}H and ^{13}C NMR). The ^{13}C NMR spectra of **1** and **2** were very similar, except for the signals of the benzoate ester groups and methines attached to the ester function. The IR spectrum of **2** showed hydroxy absorption at 3500 cm^{-1}. In the ^{1}H NMR spectrum of **2** the methine protons attached to the carbon atoms bearing the secondary ester groups were well separated compared with those in **1**. The signals at δ5.62, 4.31, 6.32, 2.62, 5.84, and 5.71 were assigned to 1-H_{ax}, 2-H_{eq}, 6-H_{ax}, 7-H, 8-H_{eq}, and 9-H_{ax}, respectively (Table 1), from the spin decoupling experiments. The signal at δ4.31 (2-H_{ax}) in compound **2** showed a greater upfield shift than that of **1** indicating the hydroxy function in compound **2** was located on C-2. Comparison of chemical shifts of **1** and **2** in both the ^{1}H NMR spectra showed that the differing signals were 1-H and 2-H. It was concluded that structure **2** represents triptogelin A-2.

The absolute configuration of **2** was determined by the application of the dibenzoate chilality method [6]. The CD spectrum of **2** gave a split Cotton curve: $(\theta)_{235}$ $-87\,000$, $(\theta)_{219}$ $+54\,000$, thus corroborating the (8*R*,9*S*)-configuration.

Compound **3**, triptogelin A-3, $C_{31}H_{36}O_9$, contained one acetate and two benzoate residues (IR, UV, ^{1}H and ^{13}C NMR). The IR spectrum of **3** showed the hydroxy absorption at 3500 cm^{-1}. The ^{13}C NMR spectra of **3** was similar to that of **1** and **2** except for the benzoyl ester groups. The ^{1}H NMR spectrum of **3** was also similar to that of **2** except for the signal assignable to 1-H (**2**: δ5.62, **3**: δ4.09). This indicated that the structure of **3** was the C-1 debenzoate of compound **2**. The acetylation of compound **3** afforded a monoacetylated compound (**3a**) and a diacetylated compound (**3b**). The ^{1}H NMR spectra of **3a** and **3b** showed the unusual diamagnetic shifts of one of the acetate methyl signals at δ1.51 and 1.43, respectively. This phenomenon arises when an equatorially oriented acetate

Table 2. ^{13}C NMR data for the skeletal carbons of compounds **1–5** and derivative **1a**

C	1	1a	2	3	4	5
1	76.5 *d*	79.0 *d*	79.2 *d*	76.1 *d*	76.4 *d*	80.6 *d*
2	70.8 *d*	71.4 *d*	69.3 *d*	71.3 *d*	26.9 *t*	210.0 *s*
3	31.3 *t*	34.6 *t*	32.7 *t*	32.4 *t*	25.6 *t*	42.8 *t*
4	33.5 *d*	34.8 *d*	33.7 *d*	33.5 *d*	34.0 *d*	38.8 *d*
5	90.9 *s*	93.7 *s*	91.0 *s*	91.4 *s*	91.3 *s*	89.8 *s*
6	74.7 *d**	72.1 *d*	74.9 *d**	75.1 *d*	72.0 *d*	73.6 *d*
7	53.1 *d*	57.6 *d*	53.0 *d*	53.0 *d*	53.1 *d*	53.0 *d*
8	71.7 *d*	72.1 *d*	74.8 *d**	72.0 *d*	75.3 *d**	72.0 *d*
9	74.8 *d**	77.1 *d*	74.9 *d**	75.7 *d*	75.5 *d**	75.3 *d*
10	48.9 *s*	48.5 *s*	49.0 *s*	49.0 *s*	49.7 *s*	55.3 *s*
11	82.1 *s*	81.2 *s*	81.7 *s*	81.3 *s*	81.4 *s*	82.7 *s*
12	24.2 *q*	24.5 *q*	24.2 *q*	24.1 *q*	24.2 *q*	24.2 *q*
13	30.7 *q*	31.9 *q*	30.7 *q*	30.7 *q*	30.7 *q*	30.7 *q*
14	18.5 *q*	20.1 *q*	18.6 *q*	18.7 *q*	16.8 *q*	17.9 *q*
15	14.1 *q*	13.8 *q*	15.5 *q*	13.3 *q*	11.0 *q*	12.7 *q*
CO_2	164.8 *s*		164.9 *s*	165.6 *s*	165.5 *s*	165.4 *s*
	165.1 *s*		165.2 *s*	166.1 *s*	165.9 *s*	165.6 *s*
	165.3 *s*		165.4 *s*	169.1 *s*	169.8 *s*	165.6 *s*
	165.8 *s*		169.9 *s*			
	169.8 *s*					
Ac	21.4 *q*		21.2 *q*	21.2 *q*	21.2 *q*	21.2 *q*

*Assignment may be interchanged in each column.
Run at 50.1 MHz in chloroform-*d* (**1–5**) and pyridine-d_5 (**1a**).

ester on C-1 is shielded by an aromatic ester on C-9 [7, 8]. Consequently, the benzoate ester was placed on C-9 in compound **3**. Hydrolysis of **3** using K_2CO_3–methanol afforded compounds **3c** and **3d**, whose structures were determined as shown by comparison of ^{1}H NMR spectra of **1–3**. Compound **3d** had only one acetate ester signal and the ester could be placed at C-6 from the chemical shift of 6-H at δ6.76. The relative stereochemistry was determined by the NOE experiments on compound **3a**. From this physical and chemical evidence, the structure of triptogelin A-3 was formulated as **3**.

Compound **4**, triptogelin B-1, $C_{31}H_{36}O_8$, contained one hydroxy, one acetate and two benzoate groups as revealed by the NMR, UV, mass and IR spectra. The ^{13}C NMR spectrum of **4** was similar to that of **3** except that **4** had two methylenes and seven methines while **3** had one methylene and seven methines in the dihydroagarofuran skeleton. This indicated that one methine attached to an oxygen function in compound **3** was replaced with a methylene in compound **4**. In the ^{1}H NMR spectrum of **4** the chemical shifts and coupling pattern assignable to 6-H, 7-H, 8-H and 9-H were very similar to that of compound **3**, but the different points were due to 1-H and 2-H signals (Table 1). The signal at δ4.14 (*dd*, J=10.7 and 5.1 Hz) in compound **4** was assignable to 1-H and the coupling pattern was explained by the diaxial and axial–equatorial coupling with 2-H_2. Thus, the structure of **4** was indicated as the C-2 dehydroxy derivative of **3**. Thus, on irradiation of the 9-H signal the intensity of the 1-H signal was increased (6%). The acetylation of **4** afforded **4a**, in which the ^{1}H NMR signal of the acetyl methyl signal appeared at δ1.42. This fact established the presence of one benzoate ester group on C-9 in compound **4** [7, 8]. The absolute configuration of **4** was also determined by using the benzoate chirality method as the (8*R*,9*S*)-configuration.

Compound **5**, triptogelin A-4, $C_{31}H_{34}O_9$, contained one acetate and two benzoate groups as revealed by the NMR, UV, mass and IR spectra. The IR spectrum of compound **5** showed the absorptions of hydroxy and ketone functions at 3450 and 1715 cm^{-1}, respectively. The ^{13}C NMR spectrum of compound **5** also indicated the presence of a dihydroagarofuran skeleton in the molecule. In the ^{1}H NMR spectrum of compound **5**, the signals at δ1.05, 1.52, 1.68, 2.00, 5.84, 6.09 and 6.38 were assigned to 14-H_3, 12-H_3, 13-H_3, 15-H_3, 8-H, 9-H and 6-H, respectively, by comparison to the spectra of compounds **1–4**. The signal at δ4.72 (1H, *d*, J=3.7 Hz) was changed to a singlet with the addition of D_2O, which was assignable to a methine proton attached to a hydroxy function. From the comparison of the ^{13}C NMR data of **3** and **5**, the assignments from C-4 to C-15 in compound **5** were established as shown (Table 2). The remaining carbon signals were δ38.8, 42.8, 80.6 and 210.0, and the assignment of a carbonyl carbon signal was permitted for C-1, C-2 and C-3. In the ^{1}H NMR spectrum, the signals at δ3.17, 2.32, 2.84 and 1.05 were assigned to 3-H_{ax}, 3-H_{eq}, 4-H and 14-H_3, respectively, from the coupling patterns. The signals of 3-H_{ax} and 3-H_{eq} were shifted downfield *ca* 1 ppm compared with those of **1**. Therefore, it was concluded that a carbonyl carbon was located at C-2. The relative stereochemistry of compound **5** was confirmed by NOE experiments. On irradiation of 12-H_3 the intensity of the 8-H and 9-H signals were increased (10 and 14%). When the 9-H signal was irradiated, an increase intensity of the 1-H signal occurred (17%), demonstrating that the orientation of 1-H and 9-H were axial. The locations of one acetate and two benzoate groups were determined by comparison of the ^{1}H NMR spectra of compounds **1** and **5**. Thus, the chemical shifts of 6-H, 8-H and 9-H were very similar to those of compounds **1–4**, indicating that an acetate group was located on C-6 and benzoate groups

were located on C-8 and C-9. The absolute configuration of compound **5** was also determined by the above method to be (8*R*) and (9*S*). The structure of triptogelin A-4 was therefore formulated as **5**.

EXPERIMENTAL

Mps: uncorr. ^{1}H NMR: 200 MHz with TMS as int. standard; ^{13}C NMR: 50.1 MHz. CC: silica gel Merck 60 and Sephadex LH-20; HPLC: ODS (20 × 200 mm, Yamamura).

Isolation of triptogelin A-1 (**1**), *A*-2 (**2**), *A*-3 (**3**), *B*-1 (**4**) *and A*-4 (**5**). The dry achenes (2.75 kg) of *T. wilfordii* Hook fil var. *regelii* Makino were collected in September 1985 at Mt. Turugi (Tokushima Prefecture, Japan) and extracted with MeOH (15 l × 3) at 60°. The MeOH extracts were concd *in vacuo* to give a residue (682 g), which was partitioned between EtOAc and H_2O. The EtOAc layer was concd to give a residue (371 g), which was chromatographed on silica gel (1.5 kg). The column was eluted with solvents on increasing polarity (hexane–EtOAc, 4:1, EtOAc and MeOH) to give 14 fractions (frs 1–14). Fr. 2 (6.13 g) containing **1** and **2** was crystallized from hexane–EtOAc to give crude crystals (1.76 g) of the mixt. which was separated by HPLC (solv. MeOH–H_2O, 9:1) yielding **1** (438 mg). The mother liquor (4.37 g) of fr. 2 was chromatographed on a silica gel column with hexane–Me_2CO (4:1) to give a fraction (178 mg) containing **2**, which was chromatographed on Sephadex LH-20 (MeOH) and crystallized from MeOH yielding **2** (150 mg). Fr. 6 (5.8 g) containing **3** was chromatographed on silica gel with hexane–EtOAc (2:1) to give fr. 2–1 (1.0 g), which was separated by HPLC (MeOH–H_2O, 4:1) to yield **3** (500 mg). Fr. 4 (4.0 g) containing **4** and **5** was chromatographed on Sephadex LH-20 (MeOH) to give fr. 4–3 (0.8 g), which was chromatographed on a silica gel column with $CHCl_3$–Me_2CO (97:3) to give fr. 4-3-2 (252 mg). This fraction was sepd by HPLC (MeOH–H_2O, 9:1) to yield **4** (32 mg) and **5** (30 mg).

Triptogelin A-1 (**1**). Needles, mp 118–122°, $[\alpha]_D^{23}$ +24.0° (MeOH; *c* 1.0). IR ν_{max}^{KBr} cm^{-1}: 2960, 1720, 1600, 1580, 1170. UV λ_{max}^{MeOH} nm (ε): 228 (45 800), 272 (3400), 280 (2800). EIMS *m/z* (rel. int.): 760 $[M]^+$ (0.4), 745 $[M-Me]^+$ (0.3), 638 $[M-C_6H_5CO_2H]^+$ (0.6), 596 (0.8), 105 $[C_6H_5CO]^+$ (100), 43 $[Ac]^+$ (5.1). FABMS *m/z* 783 $[M+Na]^+$. HRMS *m/z* 760.2905 $[M]^+$. $C_{45}H_{44}O_{11}$ requires: 760.2884.

Triptogelin A-2 (**2**). Needles, mp 113–115°, $[\alpha]_D^{23}$ −52.3° (MeOH; *c* 0.9). IR ν_{max}^{KBr} cm^{-1}: 3500, 1720, 1280, 710 UV λ_{max}^{MeOH} nm (ε): 228 (35 600), 274 (4200), 282 (3600), EIMS *m/z* (rel. int.): 656 $[M]^+$ (0.4), 641 $[M-Me]^+$ (0.6), 613 $[M-Ac]^+$ (0.5), 534 $[M-C_6H_5CO_2H]^+$ (2.7), 491 (4.8), 412 $[M-C_6H_5CO_2H \times 2]^+$ (2.5), 105 $[C_6H_5CO]^+$ (12.3), 77 $[C_6H_5]^+$ (100). HRMS *m/z* 656.2638 $[M]^+$. $C_{38}H_{40}O_{10}$ requires: 656.2621. CD (EtOH; *c* 0.1): $[\theta]_{219}$ +54 000, $[\theta]_{235}$ −87 000.

Triptogelin A-3 (**3**). Amorphous powder, $[\alpha]_D^{23}$ −24.0° (MeOH; *c* 1.1). IR ν_{max}^{KBr} cm^{-1}: 3560, 1720, 1600, 1580, 1450, 800, 760. UV λ_{max}^{MeOH} nm (ε): 229 (3000), 273 (2400), 280 (200), EIMS *m/z* (rel. int.): 552 $[M]^+$ (0.2), 534 $[M-H_2O]^+$ (1.2), 509 $[M-Ac]^+$ (1.4), 492 $[M-MeCO_2H]^+$ (0.3), 440 $[M-C_6H_5CO_2H]^+$ (2.0), 105 $[C_6H_5CO]^+$ (100), 43 $[Ac]^+$ (6.3). HRMS *m/z* 552.2388 $[M]^+$. $C_{31}H_{36}O_9$ requires: 552.2359.

Triptogelin B-1 (**4**). Amorphous powder, $[\alpha]_D^{23}$ −29.0° (MeOH, *c* 1.0), IR ν_{max}^{KBr} cm^{-1}: 3420, 1720, 1280, 710. UV λ_{max}^{MeOH} nm (ε): 229 (30 300), 274 (2200), 280 (1800); EIMS *m/z* (rel. int.): 536 $[M]^+$ (0.1), 521 $[M-Me]^+$ (0.2), 518 $[M-H_2O]^+$ (0.3), 476 $[M-MeCO_2H]^+$ (1.8), 414 $[M-C_6H_5CO_2H]^+$ (1.6), 354 (4.0), 296 (10.0), 105 $[C_6H_5CO]^+$ (100), 43 $[Ac]^+$ (7.0); HRMS *m/z* 536.2438 $[M]^+$. $C_{31}H_{36}O_8$ requires: 536.2410.

Triptogelin A-4 (**5**). Amorphous powder, $[\alpha]_D^{23}$ −31.0° (MeOH; *c* 1.0). IR ν_{max}^{KBr} cm^{-1}: 3450, 1720, 1715, 1280, 710. UV λ_{max}^{MeOH} nm (ε): 230 (26 800), 275 (2900), 282 (2600); EIMS *m/z* 550 $[M]^+$ (0.2), 508 (0.1), 472 (0.2), 430 (26), 105 $[C_6H_5CO]^+$ (100), 43 $[Ac]^+$ (58); HRMS *m/z* 550.2211 $[M]^+$, $C_{31}H_{34}O_9$ requires 550.2203.

Partial hydrolysis of compound **1**. A soln of **1** (50 mg) in 0.02 M K_2CO_3–MeOH (2 ml) was stirred at room temp. for 7 hr, the reaction mixt. was neutralized with 1% HCl, concd to give a residue, which was chromatographed on a silica gel column (solv. $CHCl_3$–Me_2CO, 97:3) to afford **1a** (31 mg), amorphous powder, EIMS *m/z* (rel. int.): 718 $[M]^+$ (1.0), 703 $[M-Me]$ (0.6), 596 $[M-C_6H_5COOH]^+$ (3.2), 105 $[C_6H_5CO]$ (100); FABMS *m/z* 741 $[M+Na]^+$, HRMS *m/z* 718.2804 $[M]^+$, $C_{43}H_{42}O_{10}$ requires: 718.2778. ^{1}H NMR (pyridine-d_5): δ 1.59 (3H, *d*, *J* = 7.6 Hz, 14-H_3), 1.62 (3H, *s*, 13-H_3), 1.67 (3H, *s*, 12-H_3), 1.83 (1H, *d*, *J* = 3.9, 6-OH), 2.00 (3H, *s*, 15-H_3), 2.07 (1H, *quint* *J* = 7.6 Hz, 4-H), 2.52 (1H, *ddd*, *J* = 14.4, 7.6, 3.6 Hz, 3-H_{ax}), 2.63 (1H, *br d*, *J* = 4.2 Hz, 7-H), 5.22 (1H, *br d*, *J* = 3.9 Hz, 6-H), 5.75 (1H, *d*, *J* = 5.6 Hz, 9-H), 5.80 (2H, *br s*, 1-H and 2-H), 5.85 (1H, *dd*, *J* = 5.6, 4.2 Hz, 8-H), 6.7–8.1 (20H, aromatic H).

Hydrolysis of compound **1**. A soln of **1** (100 mg) in 0.2 M NaOEt–EtOH (10 ml) was stirred at room temp. for 29 hr, the reaction mixt. was neutralized with HOAc and concd to give a residue, which was chromatographed on a silica gel column (EtOAc) yielding **1b**, amorphous powder, $[\alpha]_D^{23}$ −18.0° (MeOH; *c* 1.0), EIMS *m/z* (rel. int.): 302 $[M]^+$ (0.4), 287 $[M-Me]^+$ (0.3), 284 $[M-H_2O]^+$ (0.6), 251 (6), 226 (31), 153 (42), 125 (51), 83 (100); HRMS *m/z* 302.0774 $[M]^+$, $C_{15}H_{14}O_6$ requires: 302.0774. ^{1}H NMR (pyridine-d_5): see Table 1.

Acetylation of compound **3**. A soln of **3** (50 mg) in pyridine (1 ml) and Ac_2O (1 ml) was stirred at room temp. for 18 hr. Usual work-up of the reaction mixt. gave a residue, which was separated by HPLC (solv. MeCN–H_2O, 4:1) to give **3a** (20 mg) and **3b** (15 mg). Compound **3a**, amorphous powder, EIMS *m/z* (rel. int.): 552 $[M]^+$ (0.4), 534 $[M-H_2O]$ (0.3), 492 $[M-MeCO_2H]^+$ (37), 430 $[M-C_6H_5CO_2H]^+$ (18), 412 (20), 105 $[C_6H_5CO]^+$ (100), 43 $[Ac]^+$ HRMS *m/z* 552.2403 $[M]^+$. $C_{31}H_{36}O_9$ requires: 552.2359. ^{1}H NMR δ ($CDCl_3$): Table 1. Compound **1b**, amorphous powder, EIMS *m/z* (rel. int.): 636 $[M]^+$ (0.5), 593 $[M-Ac]^+$ (10), 576 $[M-MeCO_2H]^+$ (3), 514 $[M-C_6H_5CO_2H]^+$ (1), 472 (2), 105 $[C_6H_5CO]^+$ (100), 77 (45), 43 $[Ac]^+$ (85); ^{1}H NMR δ ($CDCl_3$): δ 1.29 (3H, *d*, *J* = 7.6 Hz, 14-H_3), 1.43 (3H, *s*, 1-Ac), 1.47 (3H, *s*, 13-H_3), 1.59 (3H, *s*, 12-H_3), 1.73 (3H, *s*, 15-H_3), 2.03 (3H, *s*, 2-Ac), 2.14 (3H, *s*, 6-Ac), 2.62 (1H, *br d*, *J* = 4.2 Hz, 7-H), 5.37 (1H, *d*, *J* = 3.4 Hz, 1-H), 5.40 (1H, *dd*, *J* = 5.7, 3.4 Hz, 2-H), 5.61 (1H, *d*, *J* = 5.4 Hz, 9-H), 5.82 (1H, *dd*, *J* = 5.4, 4.2 Hz, 8-H), 6.28 (1H, *br s*, 6-H), 7.2–8.1 (10H, aromatic H).

Hydrolysis of compound **3**. A soln of **3** (50 mg) in 0.02 M K_2CO_3–MeOH (2 ml) was stirred at room temp. for 4 hr, the reaction mixt. was neutralized and concd to give a residue. This residue was separated by HPLC (solv. MeCN–H_2O, 6:4) to give **3c** (8 mg) and **3d** (20 mg). Compound **3c**, amorphous powder, EIMS *m/z* (rel. int.): 448 $[M]^+$ (0.5), 433 $[M-Me]^+$ (0.4), 405 $[M-Ac]^+$ (8), 388 $[M-MeCO_2H]^+$ (4), 326 $[M-C_6H_5CO_2H]^+$ (10), 105 $[C_6H_5]^+$ (100), 77 (40), 43 $[CH_3CO]^+$ (60), HRMS *m/z* 448.2076, $C_{24}H_{32}O_8$, requires 448.2097, ^{1}H NMR ($CDCl_3$): δ 1.29 (3H, *d*, *J* = 7.8 Hz, 14-H_3), 1.33 (3H, *s*), 1.42 (3H, *s*), 1.44 (3H, *s*), 1.96 (1H, *br d*, *J* = 14.2 Hz, 3-H_{eq}), 1.1–1.4 (2H, *m*, 3-H_{ax} and 4-H), 2.11 (3H, *s*, OAc), 2.50 (1H, *br d*, *J* = 4.4 Hz, 7-H), 4.04 (1H, *d*, *J* = 4.9 Hz, 9-H), 4.24 (2H, *m*, 1-H and 2-H) 5.48 (1H, *dd*, *J* = 4.6, 4.4 Hz, 8-H), 6.05 (*br s*, 6-H), 7.4–8.1 (5H, aromatic H). Compound **3d**, EIMS *m/z* (rel. int.): 344 $[M]^+$ (0.3), 329 $[M-Me]^+$ (0.3), 301 $[M-Ac]^+$ (10), 284 $[M-MeCO_2H]^+$ (6), 43 $[Ac]^+$ (100), HRMS *m/z* 344.1850, $C_{17}H_{28}O_7$ requires 344.1835, ^{1}H NMR (pyridine-d_5): δ 1.34 (3H, *s*), 1.54 (3H, *s*), 1.61 (3H, *d*, *J* = 7.8 Hz, 14-H_3), 2.06 (3H, *s*), 2.14 (3H, *s*, OAc), 2.2–2.5 (2H, *m*, 3-H_{ax} and 4-H), 2.74 (1H, *br d*, *J* = 3.9 Hz, 7-H), 4.41 (1H, *d*, *J* = 3.4 Hz, 1-H), 4.48 (1H, *d*, *J*

= 4.6 Hz, 9-H), 4.50 (1H, *m*, 2-H), 4.60 (1H, *dd*, J = 4.6, 3.9 Hz, 8-H), 6.76 (1H, *s*, 6-H).

Acetylation of compound **4**. A soln of **4** (10 mg) in pyridine (0.5 ml) and Ac_2O (0.5 ml) was stirred at room temp. for 24 hr, usual work-up of the reaction mixt. gave **4a** (10 mg). Compound **4a**, amorphous powder, ^{1}H NMR ($CDCl_3$): δ1.08 (3H, *d*, J = 7.3 Hz, 14-H_3), 1.42 (3H, *s*, 1-OAc), 1.46 (3H, *s*), 1.53 (3H, *s*), 1.63 (3H, *s*), 2.12 (3H, *s*, 6-OAc), 2.0–2.3 (2H, *m*, 3-H_{ax}, 4-H), 2.59 (1H, *br d*, J = 4.4 Hz, 7-H), 5.26 (1H, *dd*, J = 10.7, 5.4 Hz, 1-H), 5.67 (1H, *d*, J = 5.1 Hz, 9-H), 5.82 (1H, *dd*, J = 5.4, 4.4 Hz, 8-H), 6.20 (1H, *br s*, 6-H), 7.3–8.1 (10H, aromatic H).

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