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DI- AND TRITERPENOIDS FROM *TRIPTERYGIUM HYPOGLAUCUM*

HONGQUAN DUAN, KAZUYOSHI KAWAZOE, MASAHIKO BANDO*, MASARU KIDO* and YOSHIHISA TAKAISHI†

Faculty of Pharmaceutical Sciences, University of Tokushima, Shomachi 1-78, Tokushima, 770 Japan; *Otsuka Pharmaceutical Co., Ltd., Kagasuno, Tokushima 771-01, Japan

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Key Word Index—*Tripterygium hypoglaucum*; Celastraceae; triterpene; diterpene; celastolide; triptohypol; hypodiol.

Abstract—The methanol extract of dried root outer bark of *Tripterygium hypoglaucum* (Levl.) Hutch afforded five new triterpenes: 2,3-*seco*-2,24-epoxy-D:A-friedoolenane-2, 24-olide-29-oic acid named celastolide, 2,23-dihydroxy-3-methoxy-6-oxo-1,3,5(10), 8-tetraene-24-nor-D:A-friedoolenane-29-oic acid, 2-hydroxy-3-methoxy-6-oxo-1,3,5(10), 8-tetraene-24-nor-D:A-friedoolenane-29-oic acid, 2,3-dihydroxy-1,3,5(10), 8-tetraene-24-nor-D:A-friedoolenane-29-oic acid and 3β,11α-dihydroxy-13(18)-ene-oleanane named triptohypol A, B and C and hypodiol, and two new diterpenes: 3β,14,19-trihydroxy-abieta-8,11,13-triene and 7-oxo-11,13-dihydroxy-19(4-3)-*abeo*-abieta-3,8,11,13-tetraene-19,18-olide named triptobenzene J and K, and 18 known compounds. Their structures were established on the basis of chemical and spectroscopic studies. © 1997 Elsevier Science Ltd

INTRODUCTION

Plants of the Celastraceae have been the subject of continued and growing interest, due to the range of biological activities shown by many members of this family [1–3], with some having been used in folk medicine [4] or as a stimulant [5] from ancient times. In the course of our search for bioactive metabolites from plants, we have isolated active principles from *Tripterygium wilfordii* var. *regelii* [6–9]. In our previous paper, we reported the isolation of three new triterpenes, regeol A, B and C, with biological activities [10]. We have now investigated *T. hypoglaucum* (Levl.) Hutch, a plant from which a number of terpenoids have already been isolated [11–21]. In this paper we report on the isolation of five new triterpenes, celastolide (**1**), triptohypol A (**2**), B (**3**) and C (**4**) and hypodiol (**5**), respectively, and two new diterpenes, triptobenzene J (**6**) and K (**7**), and 18 known compounds (**8**–**25**) from the root outer bark of *T. hypoglaucum*. Compounds **8**–**12**, **14**–**20**, **22**, **24** and **25** have been isolated for the first time from this plant. This paper deals with the structural investigations of these compounds.

RESULTS AND DISCUSSION

Repeated column chromatography of the ethyl acetate-soluble fraction from the methanol extracts of root outer bark of *T. hypoglaucum* yielded celastolide (**1**), the new triterpenes triptohypol A–C (**2**–**4**) and hypodiol (**5**), the new diterpenes triptobenzene J (**6**) and K (**7**), and the known compounds **8**–**25**.

Compound **1** (celastolide) exhibited a molecular peak at *m/z* 486.3338 (HR-EIMS), indicating a molecular formula of $C_{30}H_{46}O_5$. It showed IR bands at 1794 and 1727 cm^{-1}, suggesting the presence of a γ-lactone and a carboxylic acid. The ^1H NMR spectrum of **1** revealed the presence of six methyls, one methine [δ 5.39 (1H, *s*)] and one methylene [δ 3.67 (1H, *m*), 3.86 (1H, *ddd*, J = 13.9, 11.9, 2.0 Hz)] attached to an oxygen function. The ^{13}C NMR spectrum of **1** showed two carbonyl signals at δ 178.6 and 184.6, one methylene and one methine attached to an oxygen function at δ 57.4 and 102.9, and six methyl, 10 methylene, four methine and six quaternary carbons (Table 1). Many types of triterpene have been isolated from Celastraceae plants [3, 22], and compound **1** was assumed to be the D:A-friedooleanan type of triterpene from the carbon number and the presence of six methyls and one carboxylic acid group. The ^{13}C NMR spectrum data of **1** were very similar to those of salaspermic acid (**16**) [23], except for the chemical shifts at C-1, 2, 3, 4, 5, 6, 10 and 23. This suggested that the B, C, D and E ring systems of **1** were the same as in salaspermic acid. The B–E ring systems accounted for five of the eight degrees of unsaturation (deduced from the molecular formula), and this left three degrees of unsaturation in ring A. The carbon signals which were still unassigned in compound **1** were δ 9.5 (CH_3), 18.3

† Author to whom correspondence should be addressed.

Table 1. ^{13}C NMR spectral data for compounds **1**–**5**, **12** and **16**

	1	2	3	4	5	12	16
1	18.3	111.7	111.7	109.8	41.1	109.4	20.6
2	57.4	153.8	155.0	140.7	27.6	142.8	39.1
3	178.6	144.9	146.0	142.7	78.6	144.5	106.7
4	41.1	134.8	133.7	121.4	39.3	122.9	57.3
5	42.1	122.8	122.4	124.2	55.7	125.1	47.1
6	31.5	188.2	186.9	28.3	18.2	28.8	34.1
7	17.5	125.2	126.6	118.4	35.9	19.1	19.6
8	49.2	175.2	170.7	149.9	41.9	45.0	50.2
9	37.7	40.9	40.4	37.1	56.2	37.1	37.6
10	45.9	156.2	155.3	145.1	38.9	142.7	53.9
11	34.7	34.0	34.5	35.1	70.3	34.6	34.8
12	29.5	29.7	30.1	30.7	37.6	29.5	29.5
13	39.1	39.4	39.4	38.2	132.4	39.4	39.6
14	39.0	45.3	44.6	44.0	44.3	39.6	39.3
15	29.8	28.8	29.0	29.4	26.4	30.7	29.6
16	36.1	36.5	36.8	37.3	39.2	37.4	36.7
17	30.1	30.6	30.8	30.9	34.5	30.5	30.5
18	44.0	44.4	44.8	44.8	134.3	44.7	44.8
19	30.2	31.0	31.2	31.2	38.7	31.1	30.9
20	40.4	40.3	40.6	40.6	33.4	40.6	40.7
21	29.4	29.8	30.5	30.5	35.3	30.4	30.5
22	36.9	34.8	35.5	35.5	36.6	36.7	37.4
23	9.5	63.3	14.8	12.2	28.3	12.2	8.6
24	102.9	—	—	—	15.6	—	73.1
25	18.6	37.6	37.7	34.8	16.5	27.8	16.9
26	17.9	20.9	21.1	23.1	19.0	17.8	16.7
27	17.0	19.2	18.9	18.8	21.0	16.5	18.1
28	31.9	31.7	31.7	31.8	23.7	32.1	32.1
29	184.6	182.6	181.0	181.1	32.4	181.3	181.4
30	31.2	32.6	33.2	33.3	24.0	32.1	32.4
OMe	—	56.9	60.0	—	—	—	—

1, **2**, **5**: $CDCl_3$; **3**, **4**, **12**, **16**: C_5D_5N

(CH_2), 57.4 (CH_2), 41.1 (CH), 45.9 (CH), 102.9 (CH), 42.1 (C) and 178.6 (C=O). The signal at δ 178.6 was assigned to a γ-lactone group, with the two remaining degrees of unsaturation were attributed to two rings. The ^{13}C NMR signal at δ 102.9 was assigned to a hemiacetal carbon from the chemical shift value. From the HMQC, ^1H–^1H COSY and HOHAHA spectra the partial structures I: [cgce]$CHCH_3$, II: –O–CH–O–, III: $-OCH_2CH_2CH$[cgcd] were obtained in relation to ring A (Fig. 1). In the HMBC spectrum, the proton signal at δ 1.12 (H_3-25) was correlated with the carbon signals at δ 34.7 (C-11), 37.7 (C-9), 49.2 (C-8) and 45.9, and the proton signal at δ 1.60 with the carbon signals at δ 34.7 (C-11), 18.3, 57.4 and 102.9. These facts indicated that the proton signal at δ 1.60 and the carbon signal at δ 45.9 were attributable to H-10 and C-10, respectively. The proton signal at δ 2.92 (in partial structure I) was correlated with the carbon signals at δ 9.5, 42.1, 45.9 (C-10), and 178.6, the proton signal at δ 5.39 (in partial structure II) with the carbon signals at δ 31.5 (C-6), 41.1, 178.6 and 57.4, the proton signal at δ 3.86 (in partial structure III) with the carbon signal at δ 102.9. From these facts the partial structures II and III were linked by an ether bond and the partial structures I and II were linked

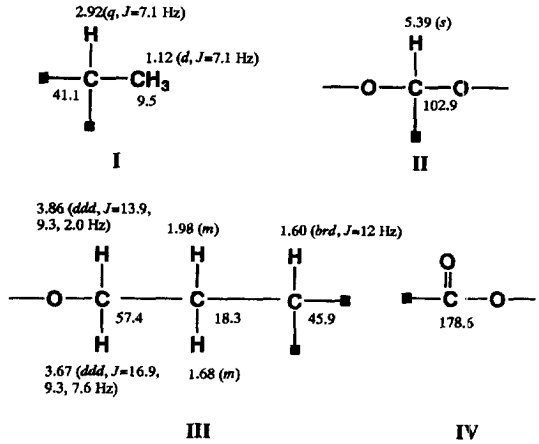


Fig. 1. Partial structures for ring A of compound **1**.

through a quaternary carbon (δ 42.1). The remaining carbonyl carbon (δ 178.6) was bound between partial structures I and II. Thus, the structure of ring A in compound **1** was 2,3-*seco*-2,24-epoxy-3,24-olide. The relative stereochemistry was determined from the NOESY spectrum. The proton signal at δ 0.98 (H_3-25) was correlated with the proton signals at δ 5.39 (H-24) and 3.86 (H_β-2), the proton signal at δ 5.39 (H-

24) with the proton signals at δ 3.86 (H_{β}-2), and the proton signal at δ 2.92 (H-4) with the proton signals at δ 1.60 (H-10) and 3.67 (H_{α}-2α).

In order to confirm the structure of **1**, the X-ray analysis of **1** was undertaken. The ORTEP drawing of the structure of **1** is shown in Fig. 2.

More than 100 triterpenes have been isolated from members of the Celastraceae or derived from congeners [22] but the only example of a compound related to celastolide is regelone [24] and celastrahydride [25] which are 2,3-*seco* types of 24-nor-D:A-friedooleanane. Regelone and celastranhydride are probably formed biogenetically from a quinonemethide precursor (ex: cerastrol **13**) as a result of ring A oxidation. But celastolide (**1**) is not a 24-nor type derivative and it is suggested that **1** is formed biogenetically from another precursor, for these reasons compound **1** is a unique triterpene.

Triptohypol A (**2**) was assigned the molecular formula $C_{30}H_{40}O_6$. The ^{1}H NMR spectrum revealed the presence of five methyls, one methoxy, one methylene attached to an oxygen function [δ 4.70, 4.93 (each 1H, *d*, J = 12.2 Hz)] and two olefinic protons [δ 6.35, 6.95 (each 1H, *s*)]. The ^{13}C NMR spectrum of **2** showed the presence of two carbonyls (δ 182.6, 188.2), five methyls, one methoxyl, four double bonds, one methylene attached to an oxygen function, seven methylenes, one methine and five quaternary carbons. From these facts, compound **2** was assumed to be 24-nor-D:A-friedooleanane triterpenoid. The ^{13}C NMR spectrum data were similar to those of wilforol A (**8**) [26] except for the methoxyl and one methylene attached to an oxygen function. From the HMQC and HMBC spectra of **2**, the C, D and E ring systems were confirmed to be the same as in **8**. With regard to rings A and B, in the HMBC spectrum the proton signal at δ 6.95 (H-1) showed correlation with the carbon signals at δ 144.9 (C-3), 122.8 (C-5), 156.2 (C-10), 153.8 and 188.2, but it was not possible to determine if the carbonyl carbon (δ 188.2) was C-2 or C-6. Methylation of **2** afforded dimethylate **2a**. In the NOESY spectrum of **2a**, the proton signal at δ 6.88 (H-1) was correlated with the methoxyl signal at δ 3.88. This clearly indicated that the hydroxy group could be placed at C-2 and the ketone at C-6 in compound **2**.

Triptohypol B (**3**) was assigned the molecular formula $C_{30}H_{40}O_5$. Its ^{13}C NMR spectrum data were very similar to those of **2** except for one methyl carbon (δ 14.8) in the case of compound **3** and one methylene carbon (δ 63.3) in compound **2**. It was assumed that the methylene (C-23) in compound **2** had been replaced by a methyl group in compound **3**. From the NOESY spectrum, the methoxyl signal at δ 3.71 was correlated with the methyl proton signal at δ 2.96 (3H, *s*), and this fact clearly showed that the methyl group was on C-4.

Triptohypol C (**4**), $C_{29}H_{40}O_4$, showed IR bands of hydroxy and carboxylic acid groups and UV absorption of an aromatic ring. The ^{13}C NMR spectrum of **4** showed the presence of an aromatic ring, a double bond and a carboxylic acid (Table 1). Its ^{13}C NMR spectral data were very similar to those of wilforic acid A (**12**) [27], except for the signals due to C-7, 8 and 25 (Table 1). Its ^{1}H NMR spectrum revealed the presence of two protons attached to double bonds at δ 5.86 (*d*, J = 5.6 Hz) and 7.15 (*s*), and methylene protons at δ 3.14 (1H, *d*, J = 20.7 Hz) and 3.37 (1H, *dd*, J = 20.7, 5.6 Hz), the signal at δ 7.15 was assigned to H-1 by comparison with the ^{1}H NMR data of **12**. The partial structure $-CH_2-CH=C-$ was estimated from the coupling constants of the remaining signals. This partial structure was attributed to C-6, 7 and 8 following a comparison of the ^{13}C NMR spectral data of compound **4** and **12** (Table 1). In order to confirm the structure of **4**, the reduction of celastol (**13**) [28] was undertaken. The ^{1}H and ^{13}C NMR spectral data for both compounds, establish that compound **4** was 2,3-dihydroxy-D:A-friedooleanan-1,3,5(10), 7-tetraene-29-oic acid. The monomethylate of compound **4**

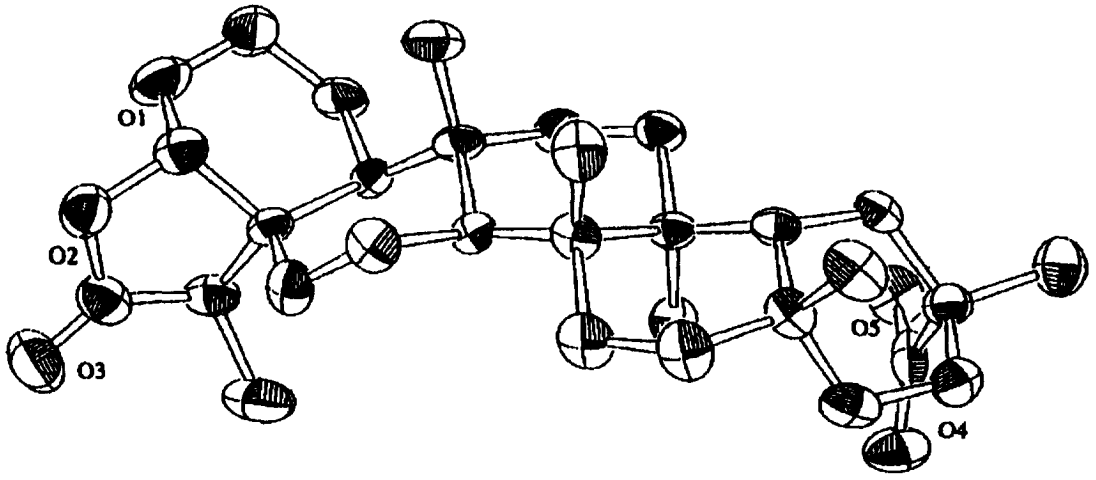
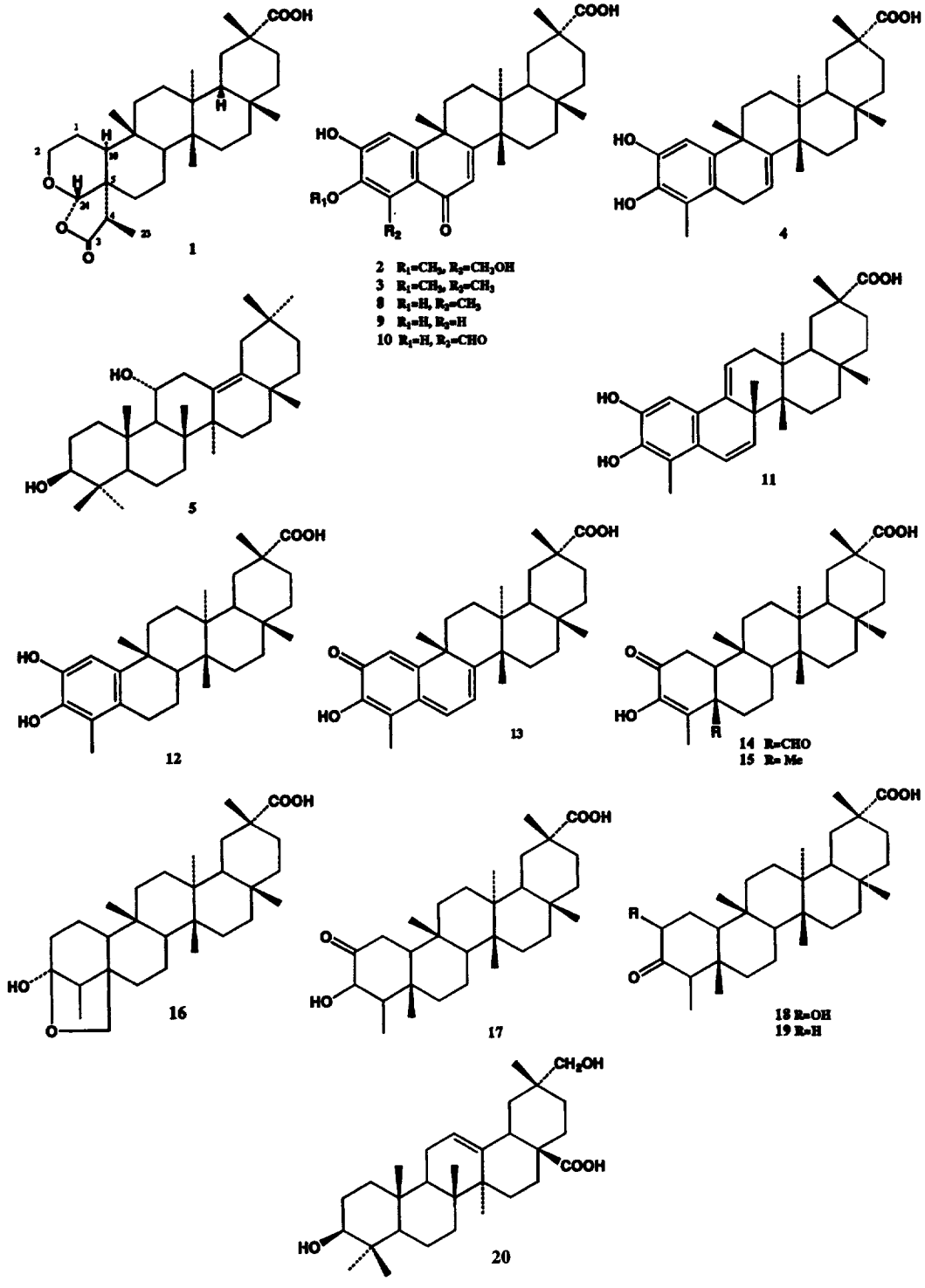
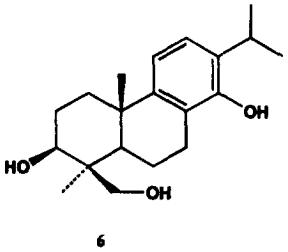


Fig. 2. ORTEP drawing of celaslide (**1**).



had already been synthesized [29], but this is the first reported isolation of this compound from a natural source.

Hypodiol (**5**) showed IR bands of hydroxyl groups. Its ^{1}H NMR spectrum showed the presence of eight methyl protons, and two methine protons attached to oxygen functions [δ 3.24 (1H, *dd*, J = 9.3, 7.3 Hz); 3.87 (1H, *ddd*, J = 10.7, 10.7, 5.9 Hz)], and also showed the signals of protons at allylic positions [δ 1.91 (1H, *ddd*, J = 14.2, 10.7, 2.9 Hz), 2.28 (1H, *dd*, J = 14.2, 2.4 Hz), 2.56 (1H, *ddd*, J = 13.2, 3.4, 3.4 Hz), 2.91 (1H, *dd*, J = 14.2, 5.9 Hz)]. These signals were very similar in chemical shift values and coupling constants to those reported for hirsudiol which has a double bond between C-13 and C-18 [30]. The ^{13}C NMR spectrum of **5** showed the presence of a double bond carbonyl



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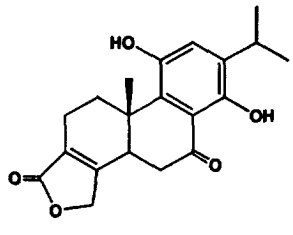

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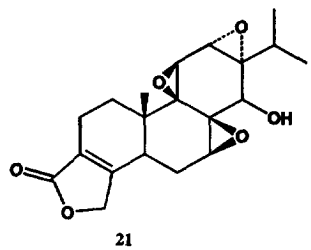

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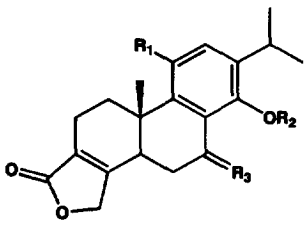
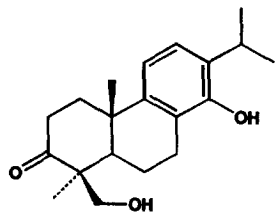


22 R_1= OH, R_2=Me, R_3=H_2
23 R_1= H, R_2=H, R_3=H_2
24 R_1= H, R_2=H, R_3=O



25

carbon [δ 132.4, 134.3], two methines attached to oxygen functions [δ 70.3, 78.6], eight methyl, ten methylene, two methine and six quaternary carbons (Table 1). These facts agreed with the molecular formula $C_{30}H_{50}O_2$. The positions of the two hydroxyl groups and the double bond were confirmed by the HMQC, ^{1}H-^{1}H COSY and HOHAHA spectra, which showed the presence of partial structures [cgce]CH–CH(OH)–CH_2– and –CH(OH)–CH_2–CH_2–. In the HMBC spectrum, the proton signal at δ 3.24 (H-3) was correlated with the carbon signal at δ 15.6 (C-24), and the proton signal at δ 0.80 (H_3-24) with the carbon signals at δ 39.3 (C-4), 55.7 (C-5) and 78.6 (C-3), and the proton signal at δ 2.91 (H-12) with the carbon signals at δ 56.2 (C-9), δ 44.3 (C-14) and δ 70.3 (C-11). These facts clearly indicated that the two hydroxy groups were placed at C-3 and C-11. In the same manner, the proton signal at δ 1.17 (H_3-27) was correlated with the carbon signals at δ 26.4 (C-15), 41.9 (C-8), 44.3 (C-14) and 132.4 (C-13), the proton signal at δ 0.99 (H_3-28) with the carbon signals at δ 34.5 (C-17) and 134.3 (C-18), and the proton signal at δ 1.91 (H-12) with the carbon signal at δ 134.3 (C-18). These findings clearly showed that the presence of double bond between C-13 and C-18. The relative stereochemistry of the hydroxyl groups at C-3 and C-11 were determined to be 3β and 11α. Thus in the NOESY spectrum, the proton signal at δ 3.24 (H-3) was correlated with the proton signals at δ 1.00 (H_3-23) and 0.76 (H-5), and the proton signal at δ 3.87 (H-11) with the proton signals δ 0.85 (H_3-26) and 1.07 (H_3-25). The coupling constants [H-3: *dd*, J = 7.3, 9.3 Hz, H-11: *ddd*, J = 10.7, 10.7, 5.9 Hz] of H-3 and H-11 showed the presence of axial protons.

Triptobenzene J (**6**) showed IR bands of hydroxyl groups and the UV absorption of an aromatic ring. The ^{1}H NMR spectrum revealed the presence of an isopropyl group [δ 1.22, 1.24 (each 3H, *d*, J = 6.8 Hz), 3.12 (1H, *sept.*, J = 6.8 Hz)], two methyl groups, [δ 1.16, 1.32 (each 3H, *s*)], a pair of methylene protons [δ 3.43, 4.32 (each 1H, *d*, J = 11.2 Hz)], one methine proton [δ 3.52 (1H, *dd*, J = 11.7, 4.4 Hz)], and a pair of methine protons [δ 6.82, 7.01 (each 1H, *d*, J = 8.3 Hz)] attached to double bond. Thus **6** ($C_{20}H_{30}O_3$) was deduced to have an abietane skeleton the same as the triptobenzenes A–G [31] isolated from *T. wilfordii* var. *regelii*. The ^{13}C NMR spectrum of **6** was very similar to that of triptobenzene B, except for the presence of one methylene attached to a hydroxy group in **6** and one methyl in triptobenzene B. It was reduced that the C-19 methyl in triptobenzene B was substituted by a hydroxy group in the structure of **6**. In the HMBC spectrum, the methylene proton at δ 4.32 (H-19) was correlated with the carbon signals at δ 80.6 (C-3), δ 22.8 (C-18), and the proton signal at δ 1.32 (H_3-18) with the carbon signals at δ 80.6 (C-3), 42.8 (C-4) and 50.1 (C-5). Thus, the hydroxy methylene carbon should be located on C-19. From the NOESY spectrum, the proton signal at δ 3.52 (H-3) was correlated with the proton signals at δ 1.43 (H-5) and 1.32 (H_3-18), and the proton signal at δ 4.32 (H-19) with the proton signal at 1.16 (H_3-20). This indicated that the relative stereochemistry in ring A of **6** was 3β-hydroxy, 19-hydroxy-methylene.

Triptobenzene K (**7**), $C_{20}H_{22}O_5$ showed the absorptions of hydroxyl groups and a conjugated ketone in its IR spectrum, and those of an aromatic ring in its UV spectrum. The ^{1}H NMR spectrum showed the presence of an isopropyl group, one methyl group, methylene protons [δ 4.72, 4.81 (each 1H, *ABq*, J = 19.5 Hz)], and one methine proton signal [δ 6.87 (1H, *s*)] attached to the double bond. The ^{13}C NMR spectrum was similar to that of triptonolide (**24**) [32] except for the signals due to C-9, 11, 12, 13 and 14. From these facts, the structure of **7** was assumed to be either 11-hydroxy or 12-hydroxy triptonolide.

Acetylation of 7 afforded the diacetate **7a**. In its NOESY spectrum, the methine proton signal at δ 7.12 (H-12) was correlated with the proton signals at δ 2.38 (OAc-11) and 1.22 (H_3-15 or H_3-16), and this clearly indicated that the hydroxy groups were located on C-11 and C-14.

The known triterpenoids wilforol A (**8**) [26], 23-nor-6-oxo-demethyl-pristimerol (**9**) [26], demthyl-zeylasteral (**10**) [26], wilforol B (**11**) [26], wilforic acid A (**12**) [27], celastrol (**13**) [28], cangoronine (**14**) [23], 3-hydroxy-D:A-friedoolean-3-en-2-on-29-oic acid (**15**) [33], salaspermic acid (**16**) [23], 3β-hydroxy-2-oxo-friedelan-29α-carboxylic acid (**17**) [34], wilforic acid C (**18**) [27], polpunonic acid (**19**) [23] and mesembryanthemoidigenic acid (**20**) [35], and the known diterpenoids triptolide (**21**) [36], neotriptophenolide (**22**) [37], hypolide (**23**) [37], triptonolide (**24**) [32] and triptobenzene A (**25**) [31] were identified from spectral data comparisons.

Compounds **8–12**, **14–20**, **22**, **24** and **25** were isolated by first time from this plant.

EXPERIMENTAL

General. Mps: uncorr.; ^{1}H NMR: 400 MHz with TMS as int. standard; ^{13}C NMR: 100 MHz; MS: JEOL JMSD-300 instrument; CC: silica gel, Sephadex LH-20, Toyopearl HW-40 (TOSOH); HPLC:GPC (Shodex packed column, GS-310, MeOH; Shodex H-2001, 2002, $CHCl_3$), silica gel (Si 60, Hibar RT 250-25).

Plant material. The root outer bark of *Tripterygium hypoglaucum* (Levl.) Hutch was purchased in 1995 from Kunming of Yunnan province in China.

Extraction and isolation. The root outer bark (15.3 kg) of *T. hypoglaucum* was crushed and extracted $\times$ 3 with MeOH (50 l each) at 60° for 6 hr. The MeOH extracts were concd. *in vacuo* to give a residue (860 g), which was partitioned between EtOAc and H_2O. The EtOAc layer was concd. to give a residue (314 g), which was chromatographed on silica gel (1.6 kg). The column was eluted with solvent of increasing polarity (hexane–EtOAc, EtOAc, EtOAc–MeOH and MeOH) to give 22 frs (fr. 1–22). Fr. 11+12 (21 g) on CC over silica gel ($CHCl_3$–MeOH, 19:1, 9:1, MeOH) gave 8 frs (11.1–11.8). Fr. 11.4 (9 g) on CC over LH-20 (MeOH) gave 7 frs (11.4.1–11.4.7); fr. 11.4.5 on CC over silica gel (CH_2Cl_2–Me_2CO, 9:1) gave 9 frs (11.4.5.1–11.4.5.9); fr. 11.4.5.4 on HPLC (GPC, MeOH) and crystallization gave **6** (7 mg), **13** (28 mg) and **14** (10 mg). Fr. 11.5 (5 g) on CC over silica gel (CH_2Cl_2–Me_2CO, 9:1) gave 12 frs (11.5.1–11.5.12), fr. 11.5.3 (26 mg) on HPLC (GPC, $CHCl_3$) yielded **20** (4.5 mg); fr. 11.5.7 (69 mg) by crystallization (MeOH) yielded **8** (38 mg). Fr. 11.8 (0.44 g) on CC over Sephadex LH-20 (MeOH) and crystallization yielded **2** (75 mg). Fr. 13 (13 g) on CC over silica gel (CH_2Cl_2–MeOH, 19:1, 9:1) gave 18 frs (13.1–13.18). Fr. 13.2 (1.1 g) on CC over LH-20 (MeOH) gave 7 frs (13.2.1–13.2.7), fr. 13.2.5 (0.15 g) on GPC ($CHCl_3$) and crystallization yielded **21** (20 mg). Fr. 13.8 (0.6 g) on CC over Toyopearl HW-40 ($CHCl_3$–MeOH, 2:1) gave 7 frs (13.8.1–13.8.7); fr. 13.8.4 (0.32 g) on LH-20 (MeOH) and prep. TLC ($CHCl_3$–MeOH, 9:1) yielded **10** (18 mg). Fr. 13.10 (0.8 g) on CC over Toyopearl HW-40 ($CHCl_3$–MeOH, 2:1) gave 7 frs (13.10.1–13.10.7); fr. 13.10.4 (0.16 g) on HPLC (GPC, MeOH) yielded **9** (77 mg). Fr. 9+10 (13 g) on CC over silica gel ($CHCl_3$–MeOH, 25:1, 19:1, 9:1, MeOH) gave 8 frs (9.1–9.8). Fr. 9.2 (1.5 g) on CC over Toyopearl HW-40 ($CHCl_3$–MeOH) gave 4 frs (9.2.1–9.2.4); fr. 9.2.3 (0.47 g) on LH-20 (MeOH) and HPLC (Si 60, hexane–EtOAc, 2:1) yielded **22** (15 mg) and **24** (3 mg). Fr. 9.3 (3.5 g) on CC over Toyopearl HW-40 ($CHCl_3$–MeOH, 2:1) gave 5 frs (9.3.1–9.3.5); fr. 9.3.4 (0.12 g) on HPLC (GPC, MeOH) yielded **7** (4 mg); fr. 9.3.3 (2.3 g) on CC over LH-20 (MeOH) gave 4 frs (9.3.3.1–9.3.3.4); fr. 9.3.3.1 (0.22 g) on HPLC (GPC, MeOH) and Si 60 (hexane–EtOAc, 2:1) yielded **5** (4.5 mg); fr. 9.3.3.2 (0.6 g) on CC over silica gel gave 6 frs (9.3.3.2.1–9.3.3.2.6); fr. 9.3.3.2.3 (0.12 g) on HPLC (GPC, MeOH) yielded **1** (7 mg). The remaining frs were sepd by prep. TLC (hexane–EtOAc, 1:1) to **19** (4 mg) and **25** (27 mg). Fr. 9.3.3.2.4 (0.16 g) on CC over HPLC (GPC, MeOH) gave 8 frs (9.3.3.2.4.1–9.3.3.2.4.8); fr. 9.3.3.2.4.5 (32 mg) by crystallization (MeOH) yielded **17** (6 mg); fr. 9.3.3.2.4.4 on prep. TLC ($CHCl_3$–MeOH, 19:1) yielded **3** (4 mg). Fr. 9.4 (0.6 g) by crystallization (MeOH) yielded **16** (200 mg) and mother liquor. HPLC (GPC, MeOH) of the latter yielded **11** (22 mg). Fr. 9.5 (1.7 g) on CC over Toyopearl HW-40 ($CHCl_3$–MeOH, 2:1) gave 9 frs (9.5.1–9.5.9); fr. 9.5.4 (0.7 g) on CC over LH-20 (MeOH) gave 6 frs (9.5.4.1–9.5.4.6); fr. 9.5.4.4 (59 mg) on prep. TLC ($CHCl_3$–MeOH, 9:1) yielded **15** (9.5 mg); fr. 9.5.4.6 on crystallization (MeOH) yielded **18** (27 mg); fr. 9.5.7 on HPLC (GPC, MeOH) yielded **4** (6 mg) and **12** (46 mg).

Celastolide (**1**). Needles (MeOH), mp. >300°, $[\alpha]_D^{25}$ −11.9° ($CHCl_3$ *c* 0.24). IR ν_{max}^{KBr} cm^{-1}: 3652, 3632, 3449, 1794, 1727, 1460, 1036; ^{1}H NMR: δ ($CDCl_3$): 0.91 (3H, *s*, H_3-26), 0.96 (3H, *s*, H_3-27), 0.98 (3H, *s*, H_3-25), 1.11 (3H, *s* H_3-28), 1.12 (3H, *d*, J = 7.1 Hz, H_3-23), 1.26 (3H, *s*, H_3-30), 1.60 (1H, *brd*, J = 12 Hz, H-10), 1.68 (1H, *m*, H-1), 1.98 (1H, *m*, H-1), 2.16 (1H, *brd*, J = 14.3 Hz, H-21), 2.30 (1H, *dd*, J = 18.7, 7.4 Hz, H-19), 2.92 (1H, *q*, J = 7.1 Hz, H-4), 3.67 (1H, *m*, Hα-2), 3.86 (1H, *ddd*, J = 13.9, 11.9, 2.0 Hz, Hβ-2), 5.39 (1H, *s*, H-24); ^{13}C NMR ($CDCl_3$): Table 1; EI-MS *m/z* (rel. int.): 486[M]$^+$(1), 471[M-CH_3]$^+$ (1.2), 474 [M-COO]$^+$ (5), 425 (4), 413 (4), 358 (10), 330 (9), 315 (17), 311 (12), 293 (11), 285 (19), 265 (10), 253 (10), 221 (20), 213 (18), 203 (17), 189 (38), 175 (25), 163 (32), 149 (33), 135 (42), 125 (33), 119 (37), 109 (100), 95 (83), 81 (58), 44 (75); HR-MS *m/z* 486.3338 [M]$^+$ $C_{30}H_{46}O_5$ required 486.3345.

Triptohypol A (**2**). Amorphous powder, $[\alpha]_D^{25}$ −41.5° (dioxane *c* 0.91). UV $\lambda_{max}^{dioxane}$ nm (log ε): 248 (4.11), 305 (3.95); IR ν_{max}^{KBr} cm^{-1}: 3632, 3434, 2944, 1702, 1636, 1578, 1460, 1317, 1271, 1203, 1030, 999,

876; ^{1}H NMR: δ ($CDCl_3$): 0.58 (3H, *s*, H_3-27), 1.08 (3H, *s*, H_3-28), 1.17 (3H, *s*, H_3-30), 1.26 (3H, *s*, H_3-26), 1.48 (3H, *s*, H_3-25), 3.88 (3H, *s*, $-OCH_3$), 4.70, 4.93 (each 1H, *ABq*, J = 12.2 Hz, H_2-23), 6.35 (1H, *s*, H-7), 6.95 (1H, *s*, H-1); ^{13}C NMR ($CDCl_3$): Table 1; EI-MS *m/z* (rel. int.): 496 $[M]^+$ (54), 481 (100), 463 (7), 313 (4), 245 (7), 231 (40), 203 (5), 121 (4), 109 (6), 95 (5), 69 (4), 55 (6), 41 (4); HR-MS *m/z* 496.2819 $[M]^+$ $C_{30}H_{40}O_6$ required 496.2825.

Methylation of **2**. Compound **2** (10 mg) was dissolved in MeOH–$CHCl_3$ (1:1, 10 ml) and treated with $(CH_3)_3SiCHN_2$ (0.8 ml) for 2 hr at room temp. The reaction mixt. was evapd under red. pres. and the residue was purified by silica gel CC to give **2a** (8.4 mg), amorphous powder, ^{1}H NMR: δ ($CDCl_3$): 0.51, 1.04, 1.11, 1.25, 1.51 (each 3H, *s*), 3.47, 3.79, 3.88 (each 3H, *s*, $-OCH_3$), 4.65 (1H, *dd*, J = 11.5, 4.9 Hz, –OH), 4.84 (1H, *dd*, J = 10.1, 4.9) 4.96 (1H, *dd*, J = 11.5, 10.1 Hz), 6.27 (1H, *s*, H-7), 6.88 (1H, *s*, H-1); ^{13}C NMR ($CDCl_3$): 107.9 (*d*, C-1), 155.2 (*s*, C-2), 146.6 (*s*, C-3), 135.6 (*s*, C-4), 123.7 (*s*, C-5), 187.9 (*s*, C-6), 125.7 (*d*, C-7), 173.7 (*s*, C-8), 41.0 (*s*, C-9), 156.7 (*s*, C-10), 34.4 (*t*, C-11), 29.9 (*t*, C-12), 39.4 (*s*, C-13), 45.2 (*s*, C-14), 28.8 (*t*, C-15), 36.5 (*t*, C-16), 30.7 (*s*, C-17), 44.5 (*d*, C-18), 31.1 (*t*, C-19), 40.7 (*s*, C-20), 30.0 (*t*, C-21), 35.0 (*t*, C-22), 56.8 (*t*, C-23), 37.6 (*q*, C-25), 20.9 (*q*, C-26), 18.5 (*q*, C-27), 31.8 (*q*, C-28), 179.0 (*s*, C-29), 33.0 (*q*, C-30), 51.7 (*q*, $-OCH_3$), 56.0 (*q*, $-OCH_3$), 62.2 (*q*, 2–OCH_3); HR-MS *m/z* 524.3123 $[M]^+$ $C_{32}H_{44}O_6$ required 524.3138.

Triptohypol B (**3**). Amorphous powder, $[\alpha]_D^{25}$ −67.5° (MeOH, *c* 0.31). UV λ_{max}^{MeOH} nm (log ε): 248 (3.99), 305 (3.84); IR ν_{max}^{KBr} cm^{-1}: 3570, 3431, 2927, 1720, 1703, 1639, 1572, 1460, 1317, 1062, 877, 802, 709. ^{1}H NMR: δ (C_5D_5N): 1.01, 1.06, 1.18, 1.35, 1.50 (each 3H, *s*), 2.96 (3H, *s*, H_3-23), 3.71 (3H, *s*, $-OCH_3$), 6.46 (1H, *s*, H-7), 8.51 (1H, *s*, H-1); ^{13}C NMR ($CDCl_3$): Table 1; EI-MS *m/z* (rel. int.): 480 $[M]^+$ (100), 436 (5), 355 (4), 289 (8), 248 (17), 232 (49), 217 (12), 203 (12), 155 (14), 149 (30), 121 (21), 109 (35), 95 (34), 81 (29), 55 (43), 43 (40); HR-MS *m/z* 480.2882 $[M]^+$ $C_{30}H_{40}O_5$ required 480.2876.

Triptohypol C (**4**). Amorphous powder, $[\alpha]_D^{25}$ −66.0° (MeOH, *c* 0.1), UV λ_{max}^{MeOH} nm (log ε): 245 (3.35), 280 (2.45), 430 (3.25); IR ν_{max}^{KBr} cm^{-1}: 3632, 3432, 2929, 1742, 1579, 1510, 1460, 1371, 1232, 1134, 603; ^{1}H NMR: δ (C_5D_5N): 1.13, 1.16, 1.28, 1.40, 2.39 (each 3H, *s*), 3.14 (1H, *d*, J = 20.7 Hz, Hα-6), 3.37 (1H, *dd*, J = 20.7, 5.6 Hz, Hβ-6), 5.86 (1H, *d*, J = 5.6 Hz, H-7), 7.15 (1H, *s*, H-1); ^{13}C NMR ($CDCl_3$): Table 1; EI-MS *m/z* (rel. int.): 452 $[M]^+$ (2), 437 $[M-CH_3]^+$ (8), 281 (6), 267 (7), 253 (21), 241 (25), 227 (34), 213 (10), 201 (54), 187 (100), 147 (10), 121 (10), 109 (12), 95 (15), 83 (12), 69 (18), 57 (23), 44 (31); FAB-HR-MS *m/z* 451.2859 $[M-H]^+$ $C_{29}H_{39}O_4$ required 451.2848.

Reduction of celastrol (**13**). Celastrol (10 mg) was dissolved in MeOH (10 ml) and treated with $NaBH_4$ (5 mg) for 1 hr at temp. The reaction mixt. on work up gave compound **4** (7 mg).

Hypodiol (**5**). Amorphous powder, $[\alpha]_D^{25}$ −12.5° (dioxane; *c* 0.14); IR ν_{max}^{KBr} cm^{-1}: 3652, 3451, 2927, 1720, 1639, 1459, 1385, 1264, 1137, 1030, 880, 806, 759; ^{1}H NMR: δ ($CDCl_3$): 0.71 (3H, *s*, H_3-30), 0.76 (1H, *m*, H-5), 0.80 (3H, *s*, H_3-24), 0.85 (3H, *s* H_3-26), 0.95 (3H, *s*, H_3-29), 0.99 (3H, *s*, H_3-28), 1.00 (3H, *s*, H_3-23), 1.07 (3H, *s*, H_3-25), 1.17 (3H, *s*, H_3-27), 1.91 (1H, *ddd*, J = 14.2, 10.7, 2.9 Hz, Hβ-12), 2.28 (1H, *dd*, J = 14.2, 2.4 Hz, Hα-19), 2.56 (1H, *ddd*, J = 13.2, 3.4, 3.4 Hz, Hα-1), 2.91 (1H, *dd*, J = 14.2, 5.9 Hz, Hα-12), 3.24 (1H, *dd*, J = 9.3, 7.3 Hz, H-3), 3.87 (1H, *ddd*, J = 10.7, 10.7, 5.9 Hz, H-11); ^{13}C NMR ($CDCl_3$): Table 1; EI-MS *m/z* (rel. int.): 442 $[M]^+$ (17), 424 (52), 409 (37), 322 (24), 270 (52), 255 (65), 237 (57), 234 (56), 229 (34), 223 (51), 219 (37), 206 (56), 191 (92), 151 (54), 135 (51), 121 (55), 109 (82), 95 (100), 83 (81); HR-MS *m/z* 442.3814 $[M]^+$ $C_{30}H_{50}O_2$ required 442.3811.

Triptobenzene J (**6**). Oil, $[\alpha]_D^{25}$ −28.9° (dioxane *c* 0.60). UV $\lambda_{max}^{dioxane}$ nm (log ε): 272 (3.16), 275 (3.15); IR ν_{max}^{KBr} cm^{-1}: 3420, 2960, 1720, 1626, 1571, 1458, 1422, 1382, 1301, 1265, 1136, 1084, 1039, 987, 913, 879, 735; ^{1}H NMR: δ ($CDCl_3$): 1.16 (3H, *s*, H_3-20), 1.22, 1.24 (each 3H, *d*, J = 6.8 Hz, 15, H_3-16), 1.32 (3H, *s*, H_3-18), 1.43 (1H, *dd*, J = 12.7, 1.9 Hz, H-5), 1.52 (1H, *ddd*, J = 13.7, 13.2, 3.4 Hz, Hα-1), 1.66 (1H, *dddd*, J = 18.6, 12.7, 11.2, 6.4 Hz, Hβ-6), 1.90 (1H, *dddd*, J = 13.2, 11.7, 4.4, 3.9 Hz, Hα-2), 1.98 (1H, *dddd*, J = 13.7, 11.7, 11.7, 3.4 Hz, Hβ-2), 2.05 (1H, *ddd*, J = 18.6, 7.3, 1.9 Hz, Hα-6), 2.32 (1H, *ddd*, J = 13.2, 3.4, 3.4 Hz, Hβ-1), 2.60 (1H, *ddd*, J = 16.6, 11.2, 7.3 Hz, Hα-7), 2.85 (1H, *dd*, J = 16.6, 6.4 Hz, Hβ-7), 3.12 (1H, *sept*. J = 6.8 Hz, H-15), 3.52 (1H, *dd*, J = 11.7, 4.4 Hz, H-3), 3.43, 4.32 (each 1H, *d*, J = 11.2 Hz, H_2-19), 6.82 (1H, *d*, J = 8.3 Hz, H-11), 7.01 (1H, *d*, J = 8.3 Hz, H-12); ^{13}C NMR ($CDCl_3$): 36.9 (*t*, C-1), 28.5 (*t*, C-2), 80.6 (*d*, C-3), 42.8 (*s*, C-4), 50.1 (*d*, C-5), 18.3 (*t*, C-6), 25.0 (*t*, C-7), 120.5 (*s*, C-8), 147.9 (*s*, C-9), 37.1 (*s*, C-10), 116.6 (*d*, C-11), 123.5 (*d*, C-12), 130.5 (*s*, C-13), 150.4 (*s*, C-14), 26.9 (*d*, C-15), 22.5 (*q*, C-16), 22.5 (*q*, C-17), 22.8 (*q*, C-18), 64.1 (*t*, C-19), 25.8 (*q*, C-20); EI-MS *m/z* (rel. int.): 318 $[M]^+$ (100), 303 $[M-CH_3]^+$ (17), 285 (36), 267 (31), 255 (20), 243 (16), 225 (36), 213 (31), 201 (23), 185 (20), 159 (20), 147 (16), 43 (17); HR-MS *m/z* 318.2174 $[M]^+$ $C_{20}H_{30}O_3$ required 318.2195.

Triptobenzene K (**7**). Amorphous powder, $[\alpha]_D^{25}$ +14.1° (MeOH *c* 0.19). UV λ_{max}^{MeOH} nm (log ε): 270 (3.36), 380 (2.88); IR ν_{max}^{KBr} cm^{-1}: 3413, 2926, 1742, 1630, 1510, 1460, 1368, 1233, 1159, 1096, 806; ^{1}H NMR: δ ($CDCl_3$): 1.21, 1.23 (each 3H, *d*, J = 6.8 Hz, H_3-15,16), 1.26 (3H, *s*, H_3-20), 2.66 (1H, *dd*, J = 17.1, 3.9 Hz, Hα-6), 2.82 (1H, *dd*, J = 17.1, 15.1 Hz, Hβ-6), 3.30 (1H, *br d*, J = 14.0 Hz), 3.72 (1H, *dd*, J = 14.2, 5.4 Hz, Hβ-1), 4.72, 4.81 (each 1H, *ABq*, J = 19.5 Hz, H_2-19), 6.87 (1H, *s*, H-12); ^{13}C NMR ($CDCl_3$): 30.6 (*t*, C-1), 18.2 (*t*, C-2), 126.4 (*s*, C-3), 159.9 (*s*, C-4), 41.4 (*d*, C-5), 36.1 (*t*, C-6), 202.7 (*s*, C-7), 115.5 (*s*, C-8), 156.7 (*s*, C-9), 37.7 (*s*, C-10), 137.3 (*d*, C-11), 124.5 (*d*, C-12), 130.9 (*s*, C-13), 144.8 (*s*, C-14), 26.1 (*d*, C-15), 22.1 (*q*, C-16), 22.2 (*q*, C-17), 173.7 (*s*, C-18), 70.1 (*t*,

C-19), 16.2 (*q*, C-20); EI-MS *m/z* (rel. int.): 342 $[M]^+$ (100), 327 $[M-CH_3]^+$ (50), 285 (5), 269 (3), 218 (5), 206 (4), 177 (5), 107 (4), 97 (6), 85 (6), 71 (8), 57 (12), 43 (8); HR-MS *m/z* 342.1457 $[M]^+$ $C_{20}H_{22}O_5$ required 342.1467.

Acetylation of **7**. Compound 7 (1.5 mg) was treated with Ac_2O (0.3 ml) and C_5H_5N (0.5 ml) at 45° for 12 hr. The reaction mixt. on work up gave diacetate **7a** (1 mg). **7a**: ^1H NMR: δ ($CDCl_3$): 1.17, 1.22 (each 3H, *d*, $J = 6.9$ Hz), 1.25 (3H, *s*, H_3-20), 2.38, 2.39 (each 3H, *s*, OAc), 3.05 (1H, *sept.* $J = 6.9$ Hz, H-15), 4.72 (2H, *ABq*, $J = 17.5$ Hz, H_2-19), 7.12 (1H, *s*, H-12).

X-ray crystallographic analysis of compound **1**. Crystal size $0.1 \times 0.50 \times 0.5$ mm. All data were obtained in a Rigaku AFC-5S automated four circle diffractometer with graphic-monochromated Mo$K\alpha$ radiation. Final lattice parameter were obtained from a least-squares refinement using 25 reflections. Crystal data: $C_{30}H_{46}O_5$, $M_r = 486.7$, triclinic space group $P2_1$, $a = 10.089$ (2) Å, $b = 11.855$ (4) Å, $c = 10.724$ (2) Å, $\beta = 94.45$ (2) Å, V = 1278.8 (5) Å^3, $Z = 2$, $Dx = 1.264$ g cm^{-3}, $f(000) = 532$, and μ(Mo$K\alpha$) = 0.78 cm^{-1}. The intensities were measured using $\omega/2\theta$ scan up to 45°. Three standard reflections were monitored every 150 measurements. The data were corrected for Lorentz and polarization factors. An absorption correction was applied which resulted in transmission factors ranging from 0.65 to 1.00. Of the 1787 unique reflections which were collected, 1284 reflections with $I > 3.0\,\sigma(I)$ were used for structure determination and refinement. The structure was solved by direct method using TEXSAN crystallographic software [38]. All non-H atoms were found in Fourier map. All H atoms except one attached to O atoms were calculated at geometrical positions. H atoms attached to O atoms were obtained from difference Fourier synthesis. The refinement of atomic parameters was carried out by the full matrix least-squares refinement, using anisotropically temp. factors for all non-H atoms. All H atoms were not refined. The final refinement converged with $R = 0.044$ and $R_w = 0.051$ for 315 parameters. The minimum and maximum peaks in the final difference. Fourier map were −0.18 and 0.19 e Å^{-3}. Atomic scattering factors were taken from ref. [39].

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