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DITERPENOIDS FROM *GRINDELIA TARAPACANA*

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Key Word Index—*Grindelia tarapacana*; Asteraceae; Astereae; Solidagininae; isolation; characterization; diterpenoids; 13-epi-manoyloxide derivatives.

Abstract—Seven new and two known diterpenoids, as well as α-spinasterol, were isolated from *Grindelia tarapacana*. The new diterpenoids were fully characterized, on the basis of spectroscopic analysis and chemical evidence, as 14,15-dihydroxy-13-epi-manoyloxide (tarapacol), 15-acetoxy-14-hydroxy-13-epi-manoyloxide (tarapacol 15-acetate), 14,15-diacetoxy-13-epi-manoyloxide (tarapacol diacetate), 11α,14,15-trihydroxy-13-epi-manoyloxide (tarapacanol A), 14,15-diacetoxy-11α-hydroxy-13-epi-manoyloxide (tarapacanol A 14,15-diacetate), 14,15-dihydroxy-11-keto-13-epi-manoyloxide (tarapacanone) and 12α,14,15-trihydroxy-13-epi-manoyloxide (tarapacanol B). The known diterpenoids were identified as 13-epi-manoyloxide and 12α-hydroxy-13-epi-manoyloxide.

INTRODUCTION

Numerous arid-adapted taxa of the New World genus *Grindelia* are characterized by the abundant production of resinous exudates which cover the surfaces of the leaves, stems and involucres of the flower heads [1]. While the resin of several members of the genus have been investigated chemically in great detail, there is only one report on the exudate flavonoid aglycones of *G. tarapacana* [2]. In our previous phytochemical investigations of the resins of 22 species of *Grindelia* we found that while all species have distinct chemical patterns, they are all characterized by the presence of bicyclic diterpene acids of the labdane type [3–7].

In contrast to the other North American *Grindelia* species which produce grindelic acid, 17-hydroxy-grindelic acid and their derivatives as the main constituents, *G. havardii* Steyerm and the Argentinian *G. discoidea* Hook & Arn. are distinguished by labdanoids lacking the tetrahydrofuran ring characteristic of the grindelane-type diterpenoids [8–10].

Qualitative GC analysis of the neutral dichloromethane fraction of *G. tarapacana* gave a chromatogram which showed none of the typical grindelane-type terpenoids previously observed in the chromatograms of methyl ester mixtures of the previously investigated *Grindelia* species. This prompted us to extend our investigation to the resin constituents of *G. tarapacana*, which led to the isolation and structural elucidation of 10 compounds.

Grindelia tarapacana is native to the hyper-arid Atacama Desert in northern Chile where it is restricted to altitudes above 3000 m [11]. In contrast to the rest of the genus, *G. tarapacana* produces diterpenoids based on the manoyloxide skeleton with a glycol (–CHOR–CH_2OR) side chain. Seven are new natural products and they were identified as tarapacol diacetate (**1**), tarapacol (**2**), tarapacol 15-acetate (**3**), tarapacanol A 14,15-diacetate (**4**), tarapacanol A (**5**), tarapacanone (**6**) and tarapacanol B (**7**). The two known terpenoids were identified as 13-epi-manoyloxide (**8**) [12–14] and 12α-hydroxy-13-epi-manoyloxide (**9**) [15–17], and the steroid as α-spinasterol (**10**) [18–20].

For the new diterpenoids, we have proposed common names derived from the *Grindelia* species investigated in this study.

RESULTS AND DISCUSSION

Extraction of the dried and powdered aerial parts of *G. tarapacana* followed by solvent partitioning and column chromatography of the neutral phase on silica gel using increasing proportions of ethyl acetate in hexane followed by a methanol wash, afforded the seven new diterpenoids, namely, tarapacol diacetate (**1**), tarapacol (**2**), tarapacol 15-acetate (**3**), tarapacanol A 14,15-diacetate (**4**), tarapacanol A (**5**), tarapacanone (**6**) and tarapacanol B (**7**), as well as the two known diterpenoids 13-epi-manoyloxide (**8**) and 12α-hydroxy-13-epi-manoyloxide (**9**) and one known steroid, α-spinasterol (**10**).

The structures of known diterpenoids **8** [12–14] and **9** [15–17], as well as the known steroid **10** [18–20] were

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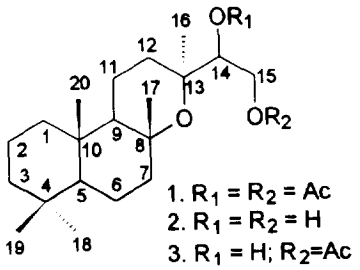

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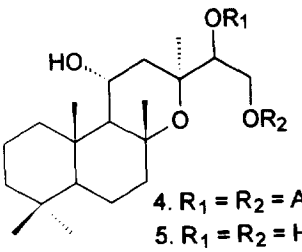
2. $R_1 = R_2 = H$
3. $R_1 = H$; $R_2 = Ac$



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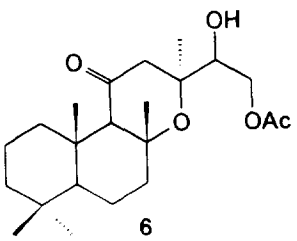
5. $R_1 = R_2 = H$



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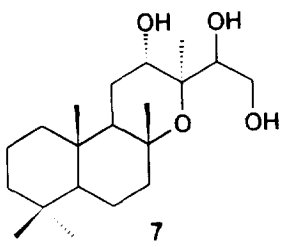

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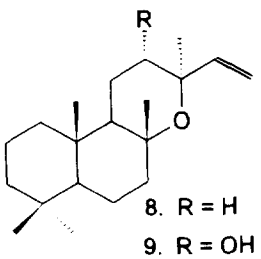
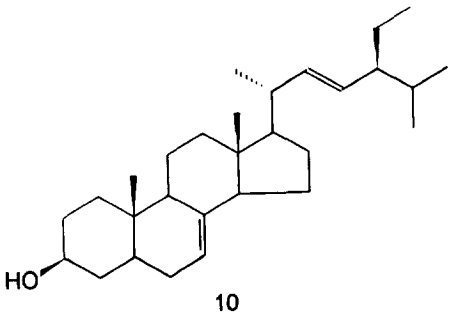


8. R = H
9. R = OH



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deduced from their CI mass spectrometry (MS), ^{1}H NMR and ^{13}C NMR spectra and by comparison of their physical and spectral data (mp, [α], IR, EIMS, ^{1}H NMR and ^{13}C NMR) with the reported literature values. These compounds are reported from the genus *Grindelia* for the first time.

In the EIMS, the molecular ion peaks for all the new diterpenoids (**1**–**7**) were negligible, therefore, their molecular weights were established by CIMS. The molecular formulae were determined by CIMS combined with ^{13}C NMR, DEPT and ^{1}H NMR data. The physical and spectral properties of **1**–**9** are reported in the Experimental section and Table 1. Since no CIMS data for **8** and **9** are available in the scientific literature, they are reported here for the first time.

Compound **1** was obtained as colourless crystals from acetone. The IR spectrum showed an ester band (1744 cm^{-1}), two strong acetate C–O bands (1273 and 1217 cm^{-1}), but lacked a band corresponding to an alcohol group. The ^{1}H NMR data (Experimental) showed signals assignable to five tertiary methyl groups at δ 0.789, 0.794, 0.86, 1.21 and 1.22 (3H each, *s*), two acetate methyl groups at δ 2.02 and 2.10 (3H each, *s*), a methine hydrogen of an acetylated secondary alcohol at δ 5.03 (1H, *dd*, J = 8.8, 2.6 Hz) and methylene hydrogens of a primary acetylated alcohol at δ 4.08 (1H, *dd*, J = 11.9, 8.8 Hz) and δ 4.45 (1H, *dd*, J = 11.9, 2.6 Hz). The coupling constants corresponded to a 1,2-glycol diacetate system (–CHOAcCH$_2$OAc), which was further suggested by the CIMS fragmentation ion (*m/z*) 263; [M – CHOAcCH$_2$OAc]$^+$). The ^{13}C NMR (Table 1) and DEPT spectra showed the presence of seven methyl groups, eight methylene groups, three methine groups and six quaternary carbons. The spectra also indicated the presence of six carbons linked to oxygen at δ 63.6, CH$_2$; 76.7, CH; 73.0, C; 75.0, CH; 170.7, C and 171.3, C. The NMR and CIMS (*m/z* 408; [M]$^+$) data indicated that the molecular formula for **1** was $C_{24}H_{40}O_5$, with an unsaturation index of five. On the basis of the absence of carbon–carbon double or triple bond signals in its spectra, the presence of two acetates and the C–O–C linkage, an oxo-tricyclic structure was proposed for this compound. The ^{1}H NMR and ^{13}C NMR (Table 1) spectral data were closely related to those for **8** [12, 21, 22]. Thus, the structure of **1** was assigned to 14,15-diacetoxy-13-epi-14, 15-dihydro manoyloxide (tarapacol diacetate).

Table 1. ^{13}C NMR spectral data for diterpenoids from *Grindelia tarapacana*

Carbon	8	1	2	3	4	5	6	7	9
1	39.4	38.9	39.0	39.0	40.1	40.1	39.7	38.7	39.0
2	18.6	18.5	18.5	18.5	18.4	18.4	18.3	18.3	18.5
3	42.2*	42.1	42.8	42.0	41.8	41.8	41.8	41.9*	42.1*
4	33.3	33.2	33.2	33.2	33.2	33.1	33.3	33.1	33.3
5	56.5	53.2	53.6	55.6	56.2	56.1	55.8	51.5	56.6
6	19.9	20.0	20.6	19.9	20.0	20.0	19.5	20.1	20.0
7	43.1*	43.7	43.9	43.5	43.7	44.0	43.3	43.7*	42.8*
8	76.1	75.0	75.7	73.7	74.0	74.5*	75.0	75.7	76.0†
9	58.5	56.6	56.6	56.4	61.5	60.9	67.6	56.4	49.8
10	36.9	37.2	37.2	37.0	37.9	37.9	37.3	37.2	36.4
11	15.9	14.4	14.4	14.8	63.7	63.6	206.3	21.4	23.6
12	34.9	28.6	29.3	31.9	37.2	37.9	46.8	64.4	69.2
13	73.3	73.0	76.7	76.0	72.7	75.3*	77.2	80.0	76.3†
14	147.7	76.7	75.8	73.8	77.2	77.9	75.9	73.1	147.2
15	109.5	63.6	63.6	66.1	63.1	62.7	64.8	63.2	110.6
16	32.7	26.4	25.4*	24.6*	26.9	27.4	27.1	26.9	26.9
17	23.9	25.4	25.3*	24.4*	26.5	25.2	26.3	24.6	24.3
18	33.3	33.4	33.3	33.3	33.3	33.3	33.5	33.3	33.3
19	21.3	21.4	21.4	21.3	21.4	21.3	21.5	21.4	21.2
20	15.9	14.9	15.1	15.4	16.3	16.3	15.5	14.7	15.8
MeCO		21.2		21.0	21.0		20.9		
		20.9			20.8				
MeCO		171.3		171.3	170.9		171.3		
		170.7			170.6				

*†Assignments may be interchangeable within the same column.

Compound **2** was obtained as colourless needles from methanol. Its spectral characteristics were close to those obtained for compound **1**, with the exception of a strong hydroxyl absorption at 3406 cm^{-1} and the absence of a carbonyl absorption in the IR spectrum. The major difference in the ^1H NMR spectrum (Experimental) was the shift of the signals for the 1,2-glycol group ($-CHOHCH_2OH$) to δ 3.49 (1H, *br s*, $W_{1/2}$ = 13 Hz), δ 3.61 (1H, *br d*, $W_{1/2}$ = 19 Hz) and δ 3.74 (1H, *dd*, J = 11.3, 5.7 Hz). The other principal difference between the ^1H NMR spectra of **1** and **2** was that the resonances corresponding to the two acetate methyl groups in **1** were replaced by two broad singlets, δ 2.80 (1H, *br s*) and 2.92 (1H, *br s*), suggesting the presence of two free hydroxyl groups in compound **2**. These data, together with the CIMS and ^{13}C NMR spectral data (Table 1), were consistent with **2** being 14,15-dihydroxy-13-epi-manoyloxide (tarapacol). Furthermore, the reduction of **1** with $LiAlH_4$ exclusively produced compound **2**.

Compound **3** crystallized from acetone as cubic crystals. The IR spectrum exhibited two strong bands at 3418 cm^{-1} (hydroxyl group) and 1738 cm^{-1} (ester carbonyl). By comparing the ^1H NMR, ^{13}C NMR and CIMS data for **3** with those obtained for **1** and **2**, it appeared to have the same skeleton as **1** and **2**, but with one primary acetate group. Reduction of **3** with $LiAlH_4$ gave only product **2**.

The position of the acetyl group in **3** was determined by comparison of its ^{13}C NMR data (Table 1) with those obtained for compounds **1** and **2**. The values for the side chain carbons for **1** were at δ 76.7 (C-14) and δ 63.6 (C-15), while those for **2** were at δ 75.8 (C-14) and δ 63.6 (C-15). In contrast, the values observed for **3** were at δ 73.8 (C-14) and 66.1 (C-15), indicating that the acetyl group was attached to C-15. The results are consistent with the structure of **3** as 15-acetoxy-14-hydroxy-13-epi-manoyloxide (tarapacol 15-acetate).

Compound **4** obtained as an amorphous powder, gave an apparent m/z 424 $[M]^+$, suggesting a molecular formula of $C_{24}H_{40}O_6$. The IR clearly showed the presence of one hydroxyl at 3472 cm^{-1} and two ester groups at 1742 and 1721 cm^{-1}. The ^1H NMR spectrum (Experimental) of **4** showed signals corresponding to five tertiary methyl groups at δ 0.81, 1.20 and 1.39 (3H each, *s*), as well as δ 0.87 (6H, *s*), two acetate methyl groups at δ 2.02 and 2.10 (3H each, *s*), a methine hydrogen of an acetylated secondary alcohol at δ 4.95 (1H, *dd*, J = 9.1, 2.5 Hz) and methylene hydrogens of a primary acetylated alcohol at δ 4.07 (1H, *dd*, J = 11.9, 9.1 Hz) and δ 4.45 (1H, *dd*, J = 11.9, 2.5 Hz). The coupling constants corresponding to the ester groups suggested the presence of a 1,2-glycol diacetate system ($-CHOAcCH_2OAc$), further evidence for this coming from its CIMS fragmentation ion (m/z 279 $[M - CHOAcCH_2OAc]^+$).

In the ^1H–^1H COSY spectrum, cross-peaks were obtained between H-11 and H-9, H-11 and H-12, as well as H-14 and H-15, revealing the partial structures $CH\text{-}CHOH\text{-}CH_2$ and $CHOAc\text{-}CH_2OAc$.

The NMR data indicated that **4** was a manoyloxide derivative containing a hydroxyl group in the ring system. According to the results obtained with the ^1H–^1H COSY spectrum, the hydroxyl group could be assigned to either the 11- or the 6-position. The application of CIMS gave fragmentation ions at *m/z* 203 $[M - H_2O - CH_2CMeOHCHOAcCH_2OAc]^+$ and 191 $[M - CHOHCH_2CMeOHCHOAcCH_2OAc]^+$, indicating that the free hydroxyl group was at C-11.

The ^1H–^{13}C HETCOR spectrum of **4** assisted in making the assignments for the ring carbon atoms and NOE experiments helped to determine the position of the five tertiary methyl groups. It was observed that: irradiation at δ0.81 (H-18) strongly enhanced the δ0.87 (H-19) signal; irradiation at δ0.87 (H-19) strongly enhanced the δ0.81 (H-18) and δ0.87 (H-20) signals; irradiation at δ0.87 (H-20) strongly enhanced the δ1.39 (H-17) and δ0.87 (H-19) signals; irradiation at δ1.39 (H-17) strongly enhanced the δ0.87 (H-20) signal. In contrast, irradiation at δ1.20 (H-16) did not noticeably enhance any other methyl hydrogen, leading to the conclusion that the protons at C-16 and C-17 were on opposite sides of the C-ring. These data indicated that **4** was a 13-epimer of manoyloxide.

The coupling constants obtained for the C-ring hydrogens of **4** [H-9 (*d*, J = 7.3 Hz); H-11 (*br t*, J = 7.0 Hz); H-12 (*dd*, J = 15.2, 0.6 Hz); H-12 (*dd*, J = 15.2, 6.4 Hz)] were abnormal. According to the vicinal Karplus correlation [23], we concluded that the conformation of the C-ring was of the twist boat type and not of the normal chair type.

The configurations of H-9 and H-11 were determined by their J values (7.3 and 7.0 Hz), which were higher than those corresponding to either Heq–Hax or Heq–Heq (J = 0–3 Hz). These data indicated that H-9 and H-11 were in a *trans* pseudodiaxial relationship. Therefore, the 11-hydroxyl must be pseudoequatorial (α-oriented). Thus, the structure of **4** was established as 14,15-diacetoxy-11α-hydroxy-13-epi-manoyloxide (tarapacanol A 14,15-diacetate).

Compound **5** was obtained as colourless crystals from acetone. The IR spectrum displayed a wide strong band at 3441 cm^{-1}, which corresponded to hydroxyl groups and the absence of any carbonyl bands. The ^1H NMR and ^{13}C NMR (Table 1) data for **5** although similar to those for **4**, showed the presence of three hydroxyl groups at δ2.34 (3H, *br*) and the absence of the acetyl signals of **4**. Comparison of the NMR and CIMS of **5** and **4** suggested that the structure of **5** was 11α,14,15-trihydroxy-13-epi-manoyloxide (tarapacanol A). This assignment was further confirmed by the fact that reduction of **4** with $LiAlH_4$ afforded exclusively **5** (see Experimental).

Compound **6** was obtained as needles from acetone, $C_{22}H_{36}O_5$ (*m/z* 380; $[M]^+$). The IR spectrum indicated the presence of one free hydroxyl group (at 3420 cm^{-1}), one acetyl (at 1740 cm^{-1}) and one keto group (at 1719 cm^{-1}). The ^1H NMR data (Experimental) showed signals discriminated into six tertiary methyl groups at δ0.81, 0.87, 1.01, 1.29, 1.30 and 2.10 (3H each, *s*), three keto α-hydrogens at δ2.42 (1H, *s*), δ2.32 (1H, *d*, J = 18.6 Hz) and δ2.85 (1H, *d*, J = 18.6 Hz), one secondary hydroxy group at δ3.59 (1H, *dd*, J = 8.1, 3.0 Hz), methylene hydrogens of a primary acetylated alcohol at δ4.03 (1H, *dd*, J = 11.7, 8.1 Hz), δ4.18 (1H, *dd*, J = 11.6, 3.0 Hz), and one hydroxylic proton at δ2.55 (1H, *br s*).

The ^{13}C NMR (Table 1) and DEPT data showed 22 carbon signals, indicating six methyl groups, seven methylene groups, three methine groups, two quaternary carbons, two tertiary carbons, one keto carbonyl group and one ester carbonyl group. Among these signals, six carbons were shown to be linked to at least one oxygen at δ67.6, CH_2; 75.9, CH; 75.0, C; 77.2, C; 171.3, C and 206.3, C.

The keto group at the 11-position and the acetyl group at the 15-position were determined by comparison of the ^1H NMR, ^{13}C NMR and DEPT signals for **6** with those obtained for **5** and **3**. Moreover, the assignment of the 11-keto functionality was further implied by the two strong CIMS fragmentation ions at *m/z* 219 $[M - CH_2CMeOHCHOHCH_2OAc]^+$ and 189 $[COCH_2CMeOHCHOHCH_2OAc]^+$. Compound **6** showed a large negative specific optical rotation value ($[\alpha]_D$ − 82°) which was consistent with the values reported for other 11-keto manoyloxide derivatives [24]. These results confirm the structure of **6** as 15-acetoxy-14-hydroxy-11-keto-13-epi-manoyloxide (tarapacanone).

Compound **7** was obtained as fine needles from acetone. The IR spectrum displayed a wide band, indicating the presence of hydroxyl groups at 3413 cm^{-1}. Comparison of the ^{13}C NMR data for **7** with those obtained for **2** and **9** (Table 1) indicated that **7** was a 12-hydroxyl derivative of **2**. This assignment was further confirmed by the CIMS fragmentation ion at *m/z* 205 $[M - CHOHCMeOHCHOHCH_2OH]^+$. The ^1H NMR spectrum showed one axial proton geminal to a hydroxyl group at δ4.46 (*br t*, J = 8.5 Hz). Both the coupling constant and signal shape are consistent with diterpenoids having the C ring with a twist boat conformation [23]. These data indicated that the hydroxy at C-12 should be α-oriented. This assignment was further supported by comparison of the ^{13}C NMR data for C-12 among 13-epi- **8** [21, 22], **9** [16, 22], 12β-hydroxy-13-epi-manoyloxide [25], **2** and **7** (Table 1). These results are in good agreement with the structure of **7** as 12α,14,15-trihydroxy-13-epi-manoyloxide (tarapacanol B).

Optical rotations were used to establish the absolute conformations of **1**–**9**. Compounds **8** and **9** showed positive rotations, the same as reported in the literature [12–15]. Positive rotations were also obtained for **2** and **7**. Compounds **1** and **3** showed negative rotations. After removal of the acetate groups, the resulting compounds showed positive rotations, identical to that obtained for **2**. These data clearly established that **1**–**3** and **7**–**9** were 13-epi-manoyloxide derivatives. Compounds **4**–**6** showed negative rotations which could be attributed to the presence of hydroxyl and keto groups at the 11-position. Based on biogenetic considerations, these compounds are assumed to be 13-epi-manoyloxide derivatives and not their 13-epimers.

EXPERIMENTAL

General. Mp: uncorr. CIMS: direct inlet. CH_4 as reagent gas. FTIR were determined in KBr pellets. ^1H (500 or 250 MHz) and ^{13}C NMR (126 or 63 MHz): $CDCl_3$ with TMS as int. standard. CC: silica gel 60 (Merck, 70–230 mesh). TLC: precoated plastic sheets (Polygram SIL G/UV 254). Spots were visualized by 2% $CeSO_4$ in H_2SO_4 after heating.

Plant material. Collected in northern Chile, Atacama Desert, region of Tarapaca, Tignamar, in March 1991. Voucher specimens have been deposited in the Herbarium of the Pontificia Universidad Catolica de Chile, Santiago, Chile. All plant material was air-dried, ground to 3 mm particle size and stored at 5° C prior to extraction.

Extraction and isolation. The milled above-ground parts of *G. tarapacana* (1.178 kg) were extracted (×3) with CH_2Cl_2 at room temp. to yield 157.7 g of crude extract, which was decolourized by activated charcoal in MeOH. After vacuum drying, the yellow extract was sepd into neutral (107.2 g) and acidic (7.7 g) frs. Neutral mixt. (107.2 g) was chromatographed on Silica gel 60 (2.5 kg) using eluents of increasing polarity from hexanes followed by hexanes–EtOAc (1:1) and finally increasing the polarity to MeOH. Frs of 200 ml were collected and those exhibiting similar TLC profiles were combined. A total of 1440 frs was collected. Compounds were purified by recrystallization. Elution with hexanes–EtOAc (49:1) afforded **8** (54 mg). Elution with hexanes–EtOAc (19:1) afforded **1** (1749 mg). Elution with hexanes EtOAc (47:3) **9** (87 mg). Elution with hexanes–EtOAc (93:7) afforded **10** (20 mg). Elution with hexanes–EtOAc (23:2) afforded **3** (3692 mg). Elution with hexanes EtOAc (22:3) afforded **4** (134 mg). Elution with hexanes–EtOAc (23:7) afforded **5** (13 mg). Elution with hexanes–EtOAc (4:1) afforded **2** (2262 mg). Elution with hexanes–EtOAc (11:9) afforded **5** (87 mg). Elution with hexanes–EtOAc (1:1) afforded **7** (155 mg).

Tarapacol diacetate (**1**). Crystalline solid from Me_2CO, mp 105–107°, $C_{24}H_{40}O_5$. $[\alpha]_D$ − 20° ($CHCl_3$; *c* 2.3). IR ν_{max} cm^{-1}: 2990, 2944, 2897, 1744, 1447, 1393, 1273, 1217, 1076, 1043. CIMS *m/z* (rel. int.): 409 $[M + H]^+$ (0.6), 408 $[M]^+$ (0.9), 407 $[M - H]^+$ (3), 391 $[M - OH]^+$ (8), 349 $[M - OAc]^+$ (3), 331 $[M - H_2O - OAc]^+$ (4), 289 $[M - HOAc - OAc]^+$ (8), 271 $[M - H_2O - HOAc - OAc]^+$ (44), 263 $[M - CHOAcCH_2OAc]^+$ (4.8), 245 $[M - H_2O - CHOAcCH_2OAc]^+$ (27), 205 $[M - CH_2CMeOH CHOAcCH_2OAc]^+$ (22), 191 $[M - CH_2CH_2CMeOH CHOAcCH_2OAc]^+$ (100), 177 (4), 163 (9), 149 (6), 137 (15), 123 (7), 109 (8), 95 (11), 81 (6). ^1H NMR (250 MHz, $CDCl_3$): δ 0.789 (3H, *s*, Me-19), 0.794 (3H, *s*, Me-20), 0.86 (3H, *s*, Me-18), 1.21 (3H, *s*, Me-16), 1.22 (3H, *s*, Me-17), 2.02 (3H, *s*, MeCO), 2.10 (3H, *s*, MeCO), 4.08 (1H, *dd*, J = 11.9, 8.8 Hz, H-15), 4.45 (1H, *dd*, J = 11.9, 2.6 Hz, H-15), 5.03 (1H, *dd*, J = 8.8, 2.6 Hz, H-14). ^{13}C NMR (126 MHz, $CDCl_3$): Table 1.

Tarapacol (**2**). Needles from MeOH, mp 77–79°, $C_{20}H_{36}O_3$. $[\alpha]_D$ + 21° ($CHCl_3$; *c* 2.23). IR ν_{max} cm^{-1}: 3406, 2990, 2938, 2870, 1456, 1377, 1248, 1156, 1129, 1096, 1074, 1024, 1007, 990. CIMS *m/z* (rel. int.): 325 $[M + H]^+$ (2), 324 $[M]^+$ (2), 323 $[M - H]^+$ (9), 307 $[M - OH]^+$ (62), 289 $[M - H_2O - OH]^+$ (44), 271 $[M - 2H_2O - OH]^+$ (35), 263 $[M - CHOHCH_2OH]^+$ (15), 245 $[M - H_2O - CHOHCH_2OH]^+$ (75), 219 $[M - CMeOHCHOHCH_2OH]^+$ (8), 205 $[M - CH_2CMeOH CHOHCH_2OH]^+$ (35), 191 $[M - CH_2CH_2CMeOH CHOHCH_2OH]^+$ (100), 177 (14), 163 (37), 149 (26), 137 (56), 123 (32), 109 (32), 95 (29), 81 (20). ^1H NMR (250 MHz, $CDCl_3$): δ 0.80 (6H, *s*, Me-19, 20), 0.86 (3H, *s*, Me-18), 1.12 (3H, *s*, Me-16), 1.28 (3H, *s*, Me-17), 2.80 (1H, *br s*, OH), 2.92 (1H, *br s*, OH) 3.49 (1H, *br s*, $W_{1/2}$ = 13 Hz, H-15), 3.61 (1H, *br d*, $W_{1/2}$ = 19 Hz, H-15), 3.74 (1H, *dd*, J = 11.3, 5.7 Hz, H-14). ^{13}C NMR (63 MHz, $CDCl_3$): Table 1.

$LiAlH_4$ reduction of tarapacol diacetate (**1**). A suspension of **1** (50 mg) and $LiAlH_4$ (50 mg) in dry Et_2O was refluxed for 24 hr with stirring. After cooling, the pH was adjusted to 2 with 10% HCl and then the phases were sepd. The organic phase was dried over Na_2SO_4 and evapd *in vacuo*. The IR, ^1H NMR and ^{13}C NMR spectra of the residue were identical to those of **2**: Table 1. $[\alpha]_D$ + 21° ($CHCl_3$; *c* 1.02).

Tarapacol 15-acetate (**3**). Cubes from Me_2CO, mp 112–114°, $C_{22}H_{38}O_4$ $[\alpha]_D$ − 15° ($CHCl_3$; *c* 3.05). IR ν_{max} cm^{-1}: 3418, 2994, 2945, 2867, 1738, 1458, 1388, 1246, 1074, 1049. CIMS *m/z* (rel. int.): 367 $[M + H]^+$ (2), 366 $[M]^+$ (1.6), 365 $[M - H]^+$ (6), 349 $[MH - H_2O]^+$ (53), 331 $[MH - 2H_2O]^+$ (8), 307 $[M - OAc]^+$ (2), 289 $[MH - H_2O - HOAc]^+$ (14), 271 $[MH - 2H_2O - HOAc]^+$ (57), 263 $[M - CHOHCH_2OAc]^+$ (17), 245 $[M - H_2O - CHOHCH_2OAc]^+$ (75), 219 $[M - CMeOHCHOHCH_2OAc]^+$ (4), 205 $[M - CH_2CMeOH CHOHCH_2OAc]^+$ (27), 191 $[M - CH_2CH_2CMeOH CHOHCH_2OAc]^+$ (100), 177 (7), 163 (18), 149 (15), 137 (37), 123 (19), 109 (17), 95 (19), 81 (11). ^1H NMR (250 MHz, $CDCl_3$): δ 0.78 (3H, *s*, Me-19), 0.79 (3H, *s*, Me-20), 0.86 (3H, *s*, Me-18), 1.07 (3H, *s*, Me-16), 1.31 (3H, *s*, Me-17), 2.11 (3H, *s*, MeCO), 3.00 (1H, *br s*, OH), 3.87 (2H, *m*, H-14, 15), 4.22 (1H, *dd*, J = 6.4, 2.8 Hz, H-15). ^{13}C NMR (63 MHz, $CDCl_3$): Table 1.

$LiAlH_4$ reduction of tarapacol 15-acetate (**3**). A suspension of **3** (100 mg) and $LiAlH_4$ (100 mg) in dry Et_2O was refluxed for 24 hr with stirring. After cooling, the pH was adjusted to 2 with 10% HCl and the two phases were sepd. The organic phase was dried over Na_2SO_4 and evapd *in vacuo*. The IR, ^1H NMR and ^{13}C NMR spectra of the residue were identical to those of **2**: Table 1. $[\alpha]_D$ + 21° ($CHCl_3$; *c* 1.02).

Tarapacanol A 14,15-diacetate (**4**). Amorphous powder from Me_2CO, mp 94–96°, $C_{24}H_{40}O_6$ $[\alpha]_D$ − 47° ($CHCl_3$; *c* 3.05). IR ν_{max} cm^{-1}: 3472, 2994, 2940, 2870, 1742, 1721, 1466, 1389, 1377, 1311, 1248, 1124, 1113, 1063, 1047, 1013, 995. CIMS *m/z* (rel. int.): 424 $[M]^+$ (0.3), 423 $[M - H]^+$ (0.9), 407 $[M - OH]^+$ (15), 389 $[M - H_2O - OH]^+$ (18), 365 $[M - OAc]^+$ (3), 347 $[M - H_2O - OAc]^+$ (17), 329 $[M - 2H_2O - OAc]^+$ (15), 287 $[M - H_2O - HOAc - OAc]^+$ (59), 279

$[M - CHOAcCH_2OAc]^+$ (8), 269 $[M - 2H_2O - HOAc - OAc]^+$ (100), 261 $[M - H_2O - CHOAcCH_2OAc]^+$ (24), 243 $[M - 2H_2O - CHOAcCH_2OAc]^+$ (15), 221 $[M - CH_2CMeOHCHOAcCH_2OAc]^+$ (11), 203 $[M - H_2O - CH_2CMeOHCHOAcCH_2OAc]^+$ (31), 191 $[M - CHOHCH_2CMeOHCHOAcCH_2OAc]^+$ (16), 177 (29), 163 (21), 149 (16), 137 (53), 123 (17), 109 (20), 95 (66), 81 (19). ^{1}H NMR (250 MHz, $CDCl_3$): δ 1.27 (1H, *ddd*, J = 12.7, 11.6, 3.6 Hz, H_{ax}-1), 1.64 (1H, *ddd*, J = 11.6, 6.9, 3.1 Hz, H_{eq}-1), 1.45 (2H, *m*, H-2), 1.17 (1H, *dt*, J = 13.6, 3.6 Hz, H_{ax}-3), 1.40 (1H, *ddd*, overlap, H_{eq}-3), 1.00 (1H, *dd*, J = 9.5, 2.3 Hz, H_{ax}-5), 1.33 (1H, *m*, overlap, H_{ax}-6), 1.66 (1H, *m*, overlap, H_{eq}-6), 1.37 (1H, *ddd*, overlap, H_{ax}-7), 1.72 (1H, *ddd*, J = 14.9, 5.9, 3.1 Hz, H_{eq}-7), 1.56 (1H, *d*, J = 7.3 Hz, H_{ax}-9), 4.15 (1H, *br t*, J = 7.0 Hz, H_{ax}-11), 1.58 (1H, *dd*, J = 15.2, 0.6 Hz, H_{eq}-12), 2.28 (1H, *dd*, J = 15.2, 6.4 Hz, H_{ax}-12), 4.95 (1H, *dd*, J = 9.1, 2.5 Hz, H-14), 4.07 (1H, *dd*, J = 11.9, 9.1 Hz, H-15), 4.45 (1H, *dd*, J = 11.9, 2.5 Hz, H-15), 1.20 (3H, *s*, Me-16), 1.39 (3H, *s*, Me-17), 0.81 (3H, *s*, Me-18), 0.87 (6H, *s*, Me-19, 20), 2.02 (3H, *s*, MeCO), 2.10 (3H, *s*, MeCO). ^{13}C NMR (63 MHz, $CDCl_3$): Table 1.

Tarapacanol A (**5**). Cubic from Et_2O, mp 85–87°, $C_{20}H_{36}O_4$, $[\alpha]_D$ − 14 ($CHCl_3$; *c* 0.41). IR ν_{max} cm^{-1}: 3441, 2942, 1458, 1386, 1365, 1323, 1294, 1219, 1182, 1155, 1116, 1080, 1045, 1018, 1001, 974. CIMS *m/z* (rel. int.): 341 $[M + H]^+$ (2.2), 339 $[M - H]^+$ (2.8), 323 $[M - OH]^+$ (34), 305 $[M - H_2O - OH]^+$ (84), 287 $[M - 2H_2O - OH]^+$ (54), 279 $[M - CHOHCH_2OH]^+$ (26), 269 $[M - 3H_2O - OH]^+$ (30), 261 $[M - H_2O - CHOHCH_2OH]^+$ (51), 243 $[M - 2H_2O - CHOHCH_2OH]^+$ (27), 217 $[M - H_2O - CMeOHCHOHCH_2OH]^+$ (48), 203 $[M - H_2O - CH_2CMeOHCHOHCH_2OH]^+$ (36), 191 $[M - CHOHCH_2COHMeCHOHCH_2OH]^+$ (17), 177 (36), 163 (31), 149 (21), 137 (58), 131 (100), 123 (20), 109 (26), 95 (37), 81 (19). ^{1}H NMR (250 MHz, $CDCl_3$): δ 0.82 (3H, *s*, Me-19), 0.88 (3H, *s*, Me-20), 0.89 (3H, *s*, Me-18), 1.23 (3H, *s*, Me-16), 1.34 (3H, *s*, Me-17), 1.01 (1H, *dd*, J = 11.8, 2.3 Hz, H-5), 2.34 (3H, *br s*, OH), 2.63 (1H, *dd*, J = 15.5, 6.4 Hz, H_{ax}-12), 3.25 (1H, *br s*, $W_{1/2}$ = 12.6 Hz, H-15), 3.61 (1H, *br s*, $W_{1/2}$ = 18.6 Hz, H-15), 3.88 (1H, *dd*, J = 11.5, 4.8 Hz, H-14), 4.18 (1H, *br t*, J = 7.0 Hz, H-11). ^{13}C NMR (63 MHz, $CDCl_3$): Table 1.

$LiAlH_4$ reduction of tarapacanol A 14,15-diacetate (**4**). A suspension of **4** (30 mg) and $LiAlH_4$ (30 mg) in dry Et_2O was refluxed for 17 hr with stirring. After cooling, the pH was adjusted to 2 with 10% HCl and then the phases were sepd. The organic phase was dried over Na_2SO_4 and evapd *in vacuo*. The IR, ^{1}H NMR and ^{13}C NMR spectra of the residue were identical to those of **5**: Table 1. $[\alpha]_D$ − 13° ($CHCl_3$; *c* 1.10).

Tarapacanone (**6**). Needles from Me_2CO, mp 103–105°, $C_{22}H_{36}O_5$, $[\alpha]_D$ − 82° ($CHCl_3$; *c* 1.63). IR ν_{max} cm^{-1}: 3420, 2959, 2921, 2869, 1740, 1719, 1462, 1458, 1379, 1393, 1372, 1314, 1252, 1213, 1169, 1101, 1090, 1053, 1040, 1026. CIMS *m/z* (rel. int.): 381 $[M + H]^+$ (2.5), 380 $[M]^+$ (1.3), 379 $[M - H]^+$ (4), 363 $[M - OH]^+$ (59), 345 $[M - H_2O - OH]^+$ (4), 321 $[M - OAc]^+$ (4), 303 $[M - H_2O - OAc]^+$ (15), 285 $[M - 2H_2O - OAc]^+$ (11), 277 $[M - CHOHCH_2OAc]^+$ (9), 263 $[M - H_2O - CHOHCH_2OAc]^+$ (4), 235 $[M - CH_2CMeHCHOHCH_2OAc]^+$ (12), 219 $[M - CH_2CMeOHCHOHCH_2OAc]^+$ (73), 191 $[M - C{:}OCH_2CMeOHCHOHCH_2OAc]^+$ (24), 189 $[C{:}OCH_2CMeOHCHOHCH_2OAc]^+$ (100), 177 (60), 163 (2), 147 (17), 137 (8), 129 (24), 123 (4), 111 (20), 95 (10), 81 (4). ^{1}H NMR (250 MHz, $CDCl_3$): δ 0.81 (3H, *s*, Me-19), 0.87 (3H, *s*, Me-20), 1.01 (3H, *s*, Me-18), 1.29 (3H, *s*, Me-16), 1.30 (3H, *s*, Me-17), 2.10 (3H, *s*, MeCO), 2.32 (1H, *d*, J = 18.6, H-12), 2.42 (1H, *s*, H-9), 2.55 (1H, *br d*, OH), 2.85 (1H, *d*, J = 18.6, H-12), 3.59 (1H, *dd*, J = 8.1, 3.0 Hz, H-14), 4.03 (1H, *dd*, J = 11.7, 8.1 Hz, H-15), 4.18 (1H, *dd*, J = 11.6, 3.0 Hz, H-15). ^{13}C NMR (63 MHz, $CDCl_3$): Table 1.

Tarapacanol B (**7**). Needles from Me_2CO, mp 143–145°; $C_{20}H_{36}O_4$ Mutarotation ($[\alpha]_D$ from + 10° to + 17°, $CHCl_3$; *c* 2.01). IR ν_{max} cm^{-1}: 3413, 2936, 2847, 1458, 1386, 1377, 1333, 1290, 1225, 1155, 1129, 1084, 1059, 1044, 1020, 972. CIMS *m/z* (rel. int.): 340 $[M]^+$ (0.6), 339 $[M - H]^+$ (3), 323 $[M - OH]^+$ (11), 305 $[M - H_2O - OH]^+$ (8), 287 $[M - 2H_2O - OH]^+$ (4), 279 $[M - CHOHCH_2OH]^+$ (5), 261 $[M - H_2O - CHOHCH_2OH]^+$ (3), 235 $[M - CMeOHCHOHCH_2OH]^+$ (6), 217 $[M - H_2O - CMeOHCHOHCH_2OH]^+$ (7), 205 $[M - CHOHCMeOHCHOHCH_2OH]^+$ (4), 191 $[M - CH_2CHOHCOHMeCHOHCH_2OH]^+$ (100), 177 (4), 163 (4), 137 (10), 131 (8), 123 (4), 109 (6), 95 (7), 81 (4). ^{1}H NMR (250 MHz, $CDCl_3$): δ 0.80 (3H, *s*, Me-19), 0.82 (3H, *s*, Me-20), 0.86 (3H, *s*, Me-18), 1.19 (3H, *s*, Me-16), 1.22 (3H, *s*, Me-17), 3.08 (1H, *br s*, OH), 3.11 (1H, *br s*, OH), 3.51 (1H, *br s*, H-15), 3.70 (1H, *dd*, J = 11.3, 3.5 Hz, H-15), 3.94 (1H, *dd*, J = 11.5, 3.6 Hz, H-14), 4.46 (1H, *br t*, J = 8.5 Hz, H-12). ^{13}C NMR (63 MHz, $CDCl_3$): Table 1.

13-Epi-manoyloxide (**8**). Crystalline from EtOAc–hexanes, mp 96–98°, $C_{20}H_{34}O$. $[\alpha]_D$ + 38° ($CHCl_3$; *c* 2.53). CIMS *m/z* (rel. int.): 289 $[M - H]^+$ (35), 275 $[M - Me]^+$ (36), 273 $[M - OH]^+$ (56), 257 $[M - H_2O - Me]^+$ (22), 191 $[M - CH_2CHCMeOHCH{:}CH_2]^+$ (27), 149 (45), 137 (60), 123 (37), 95 (43), 81 (100). ^{1}H NMR (500 MHz, $CDCl_3$): δ 0.72, 0.78, 0.85 (3H each, *s*, Me-18, Me-19, Me-20, resp.), 1.13 (3H, *s*, Me-16), 1.22 (3H, *s*, Me-17), 4.91 (1H, *dd*, J = 11.1, 0.9 Hz, H_t-15), 5.00 (1H, *dd*, J = 18.1, 0.9 Hz, H_c-15), 6.01 (1H, *dd*, J = 18.1, 11.1 Hz, H-14). ^{13}C NMR (126 MHz, $CDCl_3$): Table 1.

12α-Hydroxy-13-epi-manoyloxide (**9**). Microcrystalline powder from Me_2CO, mp 142–144°, $C_{24}H_{34}O_2$. $[\alpha]_D$ + 44° ($CHCl_3$; *c* 0.56). CIMS *m/z* (rel. int.): 306 $[M]^+$ (0.7), 305 $[M - H]^+$ (4), 289 $[M - OH]^+$ (10), 279 $[M - CH{:}CH_2]^+$ (0.6), 273 $[M - H_2O - Me]^+$ (7), 271 $[M - H_2O - OH]^+$ (10), 269 $[M - 2H_2O - H]^+$ (3), 235 $[M - CMeOHCH{:}CH_2]^+$ (2.3), 221 $[M - CHOHCHMeCH{:}CH_2]^+$ (3.6), 217 $[M - H_2O - CMeOHCH{:}CH_2]^+$ (4.2), 215 (2), 209 $[M - CH_2CHOHCHMeCH{:}CH_2]^+$ (2), 205 $[M - CHOHCMeOHCH{:}CH_2]^+$ (11), 191 $[M - CH_2CHOHCMeOHCH{:}CH_3]^+$ (100), 177 (16), 165 (7.9), 149 (7.9), 137 (26), 123 (14), 109 (16), 95 (18), 81 (11). ^{1}H NMR (250 MHz, $CDCl_3$): δ 0.75, 0.79, 0.86 (3H each, *s*, Me-18, Me-19, Me-20), 1.20 (3H, *s*, Me-16),

1.24 (3H, *s*, Me-17), 4.08 (1H, *br s*, H-12), 4.96 (1H, *d*, $J = 18.2$ Hz, H_e-15), 4.98 (1H, *d*, $J = 11.4$ Hz, H_t-15), 6.08 (1H, *dd*, $J = 18.2$, 11.4 Hz, H-14). ^{13}C NMR (126 MHz, $CDCl_3$): Table 1.

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