Manoyl Oxide α-Arabinopyranoside and Grindelic Acid Diterpenoids from *Grindelia integrifolia*

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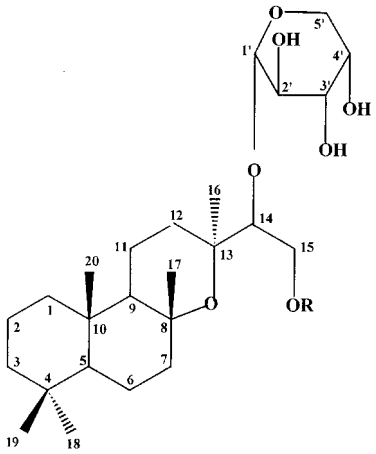
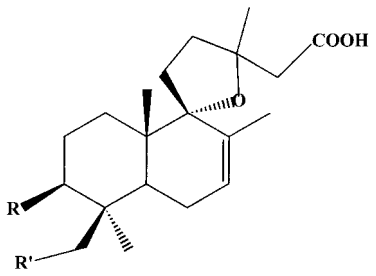
Two new manoyl oxide-α-arabinopyranoside diterpenoids, 15-hydroxy-13-*epi*-manoyl oxide-14-*O*-α-L-arabinopyranoside (tarapacol-14-*O*-α-L-arabinopyranoside) (**1**) and 15-acetoxy-13-*epi*-manoyl oxide-14-*O*-α-L-arabinopyranoside (tarapacol-15-acetate-14-*O*-α-L-arabinopyranoside) (**2**), as well as a new grindelic acid derivative, 19-hydroxygrindelic acid (**3**), together with five known diterpenoids (tarapacol, tarapacanol A, grindelic acid, methyl grindeloate, 3*β*-hydroxygrindelic acid, **4**) were isolated from the aerial parts of *Grindelia integrifolia*. The structures of **1**−**3** were elucidated by spectral data analysis.

The New World genus *Grindelia* (family Asteraceae, tribe Astereae, subtribe Soldiginae) is characterized by the abundant production of resinous exudates that cover the surfaces of the leaves, stems, and involucres of the flower head.[1] Earlier work on this genus revealed that diterpenoid acids of the labdane type, grindelic acid derivatives, are characteristic secondary metabolites.[2−9] Some manoyl oxide derivatives have been isolated from *G. tarapcana*.[10] Recently, we reported the isolation and characterization of three new grindelic and norgrindelic acid derivatives from *G. nana*.[11] In a continuation of our studies, we have now investigated the aerial parts of *G. integrifolia* DC., which has not been previously analyzed chemically. We report herein on the isolation and structure characterization of three new diterpenoids, including two manoyl oxide arabinopyranoside derivatives, 15-hydroxy-13-*epi*-manoyl oxide-14-*O*-α-L-arabinopyranoside (tarapacol-14-*O*-α-L-arabinopyranoside) (**1**) and 15-acetoxy-13-*epi*-manoyloxide-14-*O*-α-L-arabinopyranoside (tarapacol-15-acetate-14-*O*-α-L-arabinopyranoside) (**2**), and a new grindelic acid derivative, 19-hydroxygrindelic acid (**3**). The known compounds, tarapacol,[10] tarapacanol A,[10] grindelic acid,[2,12,13] methyl grindeloate,[2,12,13] and 3*β*-hydroxygrindelic acid (**4**),[8] were also isolated and identified by comparison of their MS and ^{1}H and ^{13}C NMR spectral data with those reported in the literature.



1 R = H

2 R = COCH$_3$



3 R = H, R' = OH

4 R = OH, R' = H

High-resolution CIMS provided a quasi-molecular ion peak $[M + H]^+$ at *m*/*z* 457.3165, corresponding to a molecular formula $C_{25}H_{45}O_7$, for compound **1**. The presence of an arabinosyl moiety in **1** was inferred from the CIMS fragment ion peak at *m*/*z* 325 $[M + H -$ arabinosyl$]^+$ and from the typical ^{1}H NMR signals which appeared at *δ* 4.24 (1H, d, *J* = 7.9 Hz, H-1′), 3.75 (1H, dd, *J* = 9.2, 7.9 Hz, H-2′), 3.66 (1H, dd, *J* = 9.2, 3.0 Hz, H-3′), 3.90 (1H, brs, H-4′), 4.08 (1H, dd, *J* = 14.0, 2.0 Hz, H-5a′), and 3.59 (1H, d, *J* = 14.0 Hz, H-5b′). These proton signals showed correlations in the ^{1}H−^{13}C COSY NMR spectrum with carbon resonances at *δ* 106.8 d (C-1′), 72.9 d (C-2′), 73.9 d (C-3′), 68.3 d (C-4′), and 66.5 t (C-5′), respectively, which are comparable to standard values reported in the literature.[14−16] The coupling constant of the anomeric proton (7.9 Hz) and the small couplings between the H-3′ and H-4′ (3.0 Hz) and the H-4′ and H-5a′ protons (2.0 Hz) indicated the α-configuration of an L-arabinopyranoside unit.[16,17] In agreement with the molecular formula, the ^{13}C NMR spectrum displayed, in addition to the five signals of the arabinosyl moiety, 20 other carbon signals, suggesting the presence of a diterpene core unit. DEPT experiments indicated that these 20 signals corresponded to five methyl groups, eight methylene groups, three methine groups, and four quaternary carbons (Table 1). The structure of the

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Table 1. ^{13}C NMR Spectral Data for Compounds **1**−**4** (125 MHz, $CDCl_3$, TMS)[a]

carbon	1	2	3	4
C-1	38.7 (t)	38.6 (t)	32.6 (t)	30.9 (t)
C-2	18.3 (t)	18.3 (t)	18.2 (t)	27.0 (t)
C-3	41.9 (t)	41.9 (t)	34.9 (t)	78.5 (d)
C-4	33.1 (s)	33.1 (s)	38.0 (s)	38.8 (s)
C-5	51.2 (d)	51.0 (d)	43.8 (d)	42.4 (d)
C-6	19.7 (t)	19.7 (t)	23.6 (t)	23.8 (t)
C-7	43.3 (t)	43.4 (t)	128.7 (d)	128.8 (d)
C-8	75.9 (s)	75.3 (s)	133.2 (s)	133.0 (s)
C-9	56.4 (d)	56.4 (d)	92.2 (s)	92.4 (s)
C-10	37.3 (s)	37.3 (s)	40.8 (s)	40.6 (s)
C-11	13.8 (t)	13.8 (t)	27.6 (t)	27.6 (t)
C-12	27.8 (t)	27.6 (t)	39.6 (t)	39.5 (t)
C-13	74.7 (s)	76.7 (s)	81.1 (s)	81.2 (s)
C-14	95.3 (d)	90.0 (d)	47.4 (t)	47.4 (t)
C-15	61.6 (t)	63.8 (t)	171.6 (s)	171.6 (s)
C-16	23.2 (q)	22.8 (q)	26.7 (q)	26.9 (q)
C-17	26.3 (q)	26.4 (q)	21.2 (q)	21.1 (q)
C-18	33.2 (q)	33.3 (q)	26.4 (q)	27.8 (q)
C-19	21.4 (q)	21.4 (q)	65.1 (q)	15.1 (q)
C-20	14.4 (q)	14.4 (q)	17.7 (q)	16.9 (q)
arabinose				
C-1′	106.8 (d)	107.0 (d)		
C-2′	72.9 (d)	73.0 (d)		
C-3′	73.9 (d)	74.1 (d)		
C-4′	68.3 (d)	68.3 (d)		
C-5′	66.5 (t)	66.3 (d)		
OAc		21.4 (q)		
		171.0 (s)		

[a] Assignments were confirmed by HMQC and HMBC spectra.

diterpene was elucidated in part by ^1H and ^{13}C NMR analysis (Table 1). These spectral data were quite similar to those exhibited by the major compound, tarapacol (14,15-dihydroxy-13-*epi*-manoyl oxide). In addition to the signals that were already assigned to the sugar component, the ^1H NMR spectrum contained five tertiary methyl signals at δ 0.78 (H-19), 0.79 (H-20). 0.84 (H-18), 1.17 (H-16), and 1.23 (H-17), integrating for three protons each within the manoyl oxide framework. Furthermore, an oxygenated proton at δ 3.45 (dd, J = 8.5, 3.0 Hz, H-14) showed correlations in the $^1H-^1H$ COSY NMR spectrum with methylene hydrogens of a primary alcohol at δ 3.39 (dd, J = 12.0, 8.5 Hz, H-15a) and 3.48 (dd, J = 12.0, 3.0 Hz, H-15b). The assignment of all protons in **1** and their connectivities to adjacent protons and carbons was established from the results of 2D $^1H-^1H$, $^1H-^{13}C$ COSY, and HMBC NMR experiments. Accordingly, compound **1** was an arabinopyranoside derivative of 14,15-dihydroxy-13-*epi*-manoyl oxide. To establish the location of the arabinosyl moiety on the manoyl oxide skeleton, the ^{13}C NMR data were compared between compound **1** and tarapacol, a manoyl oxide diterpene devoid of the sugar component. In tarapacol, C-14 and C-15 appeared at δ 75.8 and 63.6, respectively, while the values observed for **1** were 95.3 (d, C-14) and 61.6 (t, C-15), indicating that the arabinosyl moiety was attached to C-14. This was supported by the HMBC correlations (Table 2) of the anomeric proton H-1′ (δ 4.24) to C-14 of the manoyl oxide skeleton and H-14 (δ 3.45) to C-1′ of the sugar moiety. Finally, acid hydrolysis of **1** gave an aglycon having R_f and ^1H and ^{13}C NMR spectral data identical to those of tarapacol. The sugar fraction gave a positive optical rotation, +101° (c 0.12, H_2O), in accordance with L-arabinopyranoside. Thus, the structure of **1** was assigned as 15-hydroxy-13-*epi*-manoyl oxide-14-*O*-α-L-arabinopyranoside (tarapacol-14-*O*-α-L-arabinopyranoside).

Compound **2** showed an $[M + H]^+$ peak at m/z 499 and a molecular formula of $C_{27}H_{46}O_8$ as deduced by HRCIMS (m/z 499.3261). The ^1H NMR spectrum was very similar to that of tarapacol-14-*O*-α-L-arabinopyranoside (**1**). However, the methylene protons of the primary alcohol (H-15a and H-15b) were shifted downfield (δ 3.97 and 4.10, respectively) in **2** compared with those at δ 3.39 and 3.48 in **1**. In addition, the spectrum contained a new methyl signal (δ 2.06, s), corresponding to an acetyl group. The placement of the acetyl group at C-15 was deduced from HMBC measurements, which correlated H-15a (δ 3.97) with the acetyl carbonyl group (δ 171.0). The ^{13}C NMR spectrum was similar to **1** except for two new signals at δ 21.4 (q) and 171.0 (s), which were typical of an acetate group. The products of the acid hydrolysis of **2** were similar to those of **1**. Therefore, **2** was identified as 15-acetoxy-13-*epi*-manoyl oxide-14-*O*-α-L-arabinopyranoside (tarapacol-15-acetate-14-*O*-α-L-arabinopyranoside).

Table 2. HMBC Correlations for Compounds **1** and **2** (500 MHz, $CDCl_3$)

proton	1	2
H-14	C-13, C-15, C-16, C-1′	C-13, C-16, C-1′
H-15a	C-14	C-13, C-14, CO (AcO)
H-15b	C-14	C-14
H-16	C-12, C-13, C-14	C-12, C-14
H-17	C-7, C-8, C-9	C-7, C-9
H-18	C-3, C-4, C-5, C-19	C-4, C-5, C-19
H-19	C-3, C-4, C-5, C-18	C-4, C-5, C-18
H-20	C-1, C-5, C-9, C-10	C-5, C-10
H-1′	C-14	C-14
H-2′	C-1′, C-3′	C-1′, C-3′
H-3′	C-1′, C-2′	C-1′, C-2′
H-4′	C-2′, C-3′	C-5′
H-5a′	C-1′, C-3′	C-1′, C-4′
H-5b′	C-1′	C-1′

The HRCIMS of compound **3** exhibited a $[M + H]^+$ peak at m/z 337.2374 in accordance with the molecular formula $C_{20}H_{33}O_4$ (calcd m/z 337.2378). This molecular formula along with similarities in the ^1H and ^{13}C NMR spectra indicated that this compound might be a hydroxy derivative of grindelic acid.[8] However, differences included the replacement of the methyl group signal (Me-19) with a pair of doublets at δ 3.81 and 3.54 (d, J = 11.0 Hz) in **3**. Therefore, a hydroxyl group was placed at C-19. The proton signals at δ 3.81 and 3.54 (H-19a and H-19b) showed cross-peaks to C-3, C-4, and C-18, and the methine proton at δ 1.81 (H-5) showed cross-peaks to C-4, C-10, C-19, and C-20, confirming this observation in the HMBC spectrum. The relative stereochemistry at C-4 was given by the difference NOE NMR spectrum, which showed enhancements between H-19a and Me-20β, as well as between H-5α and Me-18. Therefore, **3** was assigned as 19-hydroxygrindelic acid. It is interesting to note that the structure of compound **3** has been reported from *Grindelia paludosa*.[8] However, 1D and 2D NMR measurements including ^{13}C NMR, $^1H-^{13}C$ COSY, and HMBC spectra, which have not been performed previously, were inconsistent with the previous data of this structure and may warrant revision of the earlier structure.

Experimental Section

General Experimental Procedures. Optical rotation measurements were made on a JASCO mode DIP 370 polarimeter. IR spectra (oily films) were taken on a Perkin-Elmer FT spectrometer. ^1H and ^{13}C NMR, DEPT, $^1H-^1H$ COSY, $^1H-^{13}C$ COSY, and HMBC (delay, 173.9 μs) spectra were measured on a JEOL JNM-GX-500 spectrometer, with TMS as an internal standard. Mass spectra were recorded with a JEOL JMS-D300 mass spectrometer using direct inlet electron impact ionization (70 eV). TLC: precoated silica gel 60F254

plates (Merck); preparative TLC: silica gel PF254 (Merck, 200 × 200 × 0.25 mm); column chromatography: silica gel type 60 (Merck, 200).

Plant Material. *G. integrifolia* was collected in July 1996 at Point Hudson, Port Townsend, WA. A voucher specimen (No. 187558) has been deposited at the Department of Forest Products, Oregon State University, Corvallis, OR.

Extraction and Isolation. The air-dried, powdered aerial parts of *G. integrifolia* (900 g) were extracted with CH_2Cl_2−MeOH (1:1) at room temperature, and the extract was concentrated to obtain 105 g of residue. The residue was prefractionated by column chromatography on Si gel eluting with petroleum ether (60−80 °C), followed by a gradient of petroleum ether−Et_2O, up to 100% Et_2O and Et_2O−MeOH, into five fractions: fraction 1 (petroleum ether−Et_2O, 3:1), fraction 2 (petroleum ether−Et_2O, 1:1), fraction 3 (petroleum ether−Et_2O 1:3), fraction 4 (Et_2O, 100%), and fraction 5 (Et_2O−MeOH, 9:1). Fractions 1 and 2 were separated on a Si gel column eluted with *n*-hexane−CH_2Cl_2 (2:1) to give fractions 1-A and 1-B. Fraction 1-A was further purified on a Sephadex LH-20 column eluted with *n*-hexane−CH_2Cl_2−MeOH (4:7:0.5) to afford methyl grindeloate[2,12,13] (200 mg). Fraction 1-B was repeatedly chromatographed on a Sephadex LH-20 column eluted with *n*-hexane−CH_2Cl_2−MeOH (4:7:0.5) to give grindelic acid[2,12,13] (500 mg). Fraction 3 was further purified on a Sephadex LH-20 column eluted with *n*-hexane−CH_2Cl_2−MeOH (4:7:0.5) to give tarapacol[10] (250 mg) and 3β-hydroxygrindelic acid (**4**)[8] (25 mg). One of these subfractions was further purified by preparative TLC (silica gel PF_{254}) eluted with petroleum ether−Et_2O (1:3) to give 19-hydoxygrandelic acid (**3**) (15 mg). Fractions 4 and 5 were purified on a Si gel column eluted with petroleum ether−Et_2O (4:1), then repeatedly chromatographed on a Sephadex LH-20 column eluted with *n*-hexane−CH_2Cl_2−MeOH (4:7:0.5), and finally purified by preparative TLC (silica gel GF_{254}) eluted with petroleum ether−Et_2O (1:3) and petroleum ether−Et_2O−MeOH (1:3:0.1) to give tarapacol 14-*O*-α-L-arabinopyranoside) (**1**) (15 mg), tarapacol-15-acetate-14-*O*-α-L-arabinopyranoside (**2**) (20 mg), and tarapacol A (13 mg). The known compounds were identified by ^1H and ^{13}C NMR analysis and by comparison with the literature data. The previously unreported ^{13}C NMR spectral data of **4** are listed in Table 1.

15-Hydroxy-13-*epi*-manoyloxide-14-*O*-α-L-arabinopyranoside (tarapacol-14-*O*-α-L-arabinopyranoside) (1): colorless oil, $[\alpha]^{25}_D$ +7.2° ($CHCl_3$, *c* 0.6); IR (NaCl) ν_{max} 3417, 2985, 2922, 1455, 1386 cm^{-1}; ^1H NMR spectral data ($CDCl_3$, 500 MHz) δ 4.24 (1H, d, J = 7.9 Hz, H-1′), 4.08 (1H, dd, J = 14.0, 2.0 Hz, H-5a′), 3.90 (1H, br s, H-4′), 3.75 (1H, dd, J = 9.2, 7.9 Hz, H-2′), 3.66 (1H, dd, J = 9.2, 3.0 Hz, H-3′), 3.59 (1H, d, J = 14.0 Hz, H-5b′), 3.48 (1H, dd, J = 12.0, 3.0 Hz, H-15b), 3.45 (1H dd, J = 8.5, 3.0 Hz, H-14), 3.39 (1H, dd, J = 12.0, 8.5 Hz, H-15a), 1.23 (3H, *s*, H-17), 1.17 (3H, *s*, H-16), 0.84 (3H, *s*, H-18), 0.79 (3H, *s*, H-20), 0.78 (3H, *s*, H-19); ^{13}C NMR spectral data, see Table 1; CIMS (positive ion) *m*/*z* 457 $[M + H]^+$, 325 $[M + H - arabinosyl]^+$ (30), 307 $[M + H - arabinosyl - H_2O]^+$ (100), 289 $[M + H - arabinosyl - 2H_2O]^+$, 271 (30), 263 (10), 191 (15); HRCIMS *m*/*z* 457.3165 (calcd for $C_{25}H_{45}O_7$, 457.3165).

15-Acetoxy-13-*epi*-manoyl oxide-14-*O*-α-L-arabinopyranoside (tarapacol-15-acetate-14-*O*-α-L-arabinopyranoside) (2): colorless oil; $[\alpha]^{25}_D$ +5° ($CHCl_3$, *c* 0.17); IR (NaCl) ν_{max} 3440, 2924, 2854, 1738, 1462 cm^{-1}; ^1H NMR spectral data ($CDCl_3$, 500 MHz) δ 4.29 (1H, d, J = 7.4 Hz, H-1′), 4.10 (1H, dd, J = 12.0, 3.0 Hz, H-15b), 4.02 (1H, dd, J = 13.1, 2.0 Hz, H-5a′), 3.97 (1H, dd, J = 12.0, 8.3 Hz, H-15a), 3.87 (1H, br s, H-4′), 3.70 (1H, dd, J = 9.1, 7.4 Hz, H-2′), 3.62 (1H, dd, J = 9.1, 3.0 Hz, H-3′), 3.60 (1H dd, J = 8.3, 3.0 Hz, H-14), 3.55 (1H, *d*, J = 13.1 Hz, H-5b′), 2.06 (3H, *s*, OAc), 1.25 (3H, *s*, H-17), 1.23 (3H, *s*, H-16), 0.84 (3H, *s*, H-18), 0.80 (3H, *s*, H-20), 0.79 (3H, *s*, H-19); ^{13}C NMR spectral data, see Table 1; CIMS (positive ion) *m*/*z* 499 $[M + H]^+$ (30), 367 $[M + H - arabinosyl]^+$ (28), 349 $[M + H - arabinosyl - H_2O]^+$ 331 (20), 307 (45), 289 (39), 271 (45), 263 (20), 191 (30); HRCIMS *m*/*z* 499.3261 (calcd for $C_{27}H_{45}O_8$, 499.3270).

19-Hydroxygrindelic acid (3): colorless oil; $[\alpha]^{25}_D$ −44° ($CHCl_3$, *c* 0.17); IR (NaCl) ν_{max} 3445, 2925, 1455, 1380 cm^{-1}; ^1H NMR spectral data ($CDCl_3$, 500 MHz) δ 5.60 (1H, br s, H-7), 3.81 (1H, d, J = 11.0 Hz, H-19a), 3.54 (1H, d, J = 11.0 Hz, H-19b), 2.69 (1H, d, J = 15.8 Hz, H-14a), 2.57 (1H, d, J = 15.8 Hz, H-14b), 1.81 (1H, m, H-5), 1.76 (3H, br s, H-17), 1.25 (3H, *s*, H-17), 1.49 (3H, *s*, H-16), 0.98 (3H, *s*, H-18), 0.81 (3H, *s*, H-20); HMBC H-5 (C-4, C-10, C-19, C-20), H-7 (C-8, C-5), H14a, H-14b (C-13, C-15, C-16), H-16 (C-12, C-13, C-14), H-17 (C-7, C-8, C-9), H-18 (C-4, C-8, C-19), H-19a and H-19b (C-3, C-4, C-18), H-20 (C-1, C-5, C-9, C-10); NOESY Me-18 (H-5α), H-19a (Me-20β), and Me-20β (H-19a); ^{13}C NMR spectral data, see Table 1; CIMS (positive ion) *m*/*z* 337 $[M + H]^+$ (80), 319 $[M + H - H_2O]^+$ (40), 288 $[M + H - CH_2OH - H_2O]^+$ (85), 223 (70), 177 (25), 153 (35), 135 (20); HRCIMS *m*/*z* 337.2374 (calcd for $C_{20}H_{33}O_4$, 337.2378).

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References and Notes

(1) Hoffmann, J. J.; Kingsolver, B. E.; McLaughlin, S. P.; Timmermann, B. N. *Rec. Adv. Phytochem*. **1984**, *18*, 251−271.
(2) Hoffmann, J. J.; Jolad, S. D.; Timmermann, B. N.; Bates, R. B.; Camou, F. A. *Phytochemistry* **1988**, *27*, 493−496.
(3) Timmermann, B. N.; Hoffmann, J. J.; Jolad, S. D.; Bates, R. B.; Siahaan, T. J. *Phytochemistry* **1987**, *26*, 467−470.
(4) Timmermann, B. N.; McLaughlin, S. P.; Hoffmann, J. J. *Biochem. Syst. Ecol.* **1987**, *15*, 401−404.
(5) Timmermann, B. N.; Hoffmann, J. J.; Jolad, S. D.; Schram, K. H. *Phytochemistry* **1985**, *24*, 1031−1034.
(6) Timmermann, B. N.; Luzbetak, D. J.; Hoffmann, J. J.; Jolad, S. D.; Schram, K. H.; Bates, B.; Klenck, R. E. *Phytochemistry* **1983**, *22*, 523−525.
(7) Jakupovic, J.; Baruah, R. N.; Zdero, C.; Eid, F.; Chau-Thi, T. V.; Bohlmann, F.; King, R. M.; Robinson, H. *Phytochemistry* **1986**, *25*, 1873−1881.
(8) Bohlmann, F.; Ahmed, M.; Borthakur, N.; Wallmeyer, M.; Jakupovic, J.; King, R. M.; Robinson, H. *Phytochemistry* **1982**, *21*, 167−172.
(9) Rose, A. F.; Jones, K. C.; Haddon, W. F.; Dreyer, D. L. *Phytochemistry* **1981**, *20*, 2249−2253.
(10) Zhou, L.; Fuentes, E. R.; Hoffmann, J. J.; Timmermann, B. N. *Phytochemistry* **1995**, *40*, 1201−1207.
(11) Mahmoud, A. A.; Ahmed, A. A.; Tanaka, T.; Iinuma, M. *J. Nat. Prod.* **2000**, *63*, 378−380.
(12) Sierra, M. G.; Colombo, M. I.; Zudenigo, M. E.; Ruveda, E. A. *Phytochemistry* **1984**, *23*, 1685−1688.
(13) Adinolfi, M.; Greca, M. D.; Mangoni, L. *Phytochemistry* **1988**, *27*, 1878−1988.
(14) Fullas, F.; Hussain, R. A.; Bordas, E.; Pezzuto, J. M.; Soejarto, D. D.; Kinghorn, A. D. *Tetrahedron* **1991**, *47*, 8515−8522.
(15) Gao, F.; Leidig, M.; Mabry, T. J. *Phytochemistry* **1986**, *25*, 1371−1376.
(16) Mizutani, K.; Kasai, R.; Tanaka, O. *Carbohydr. Res*. **1980**, *87*, 19−26.
(17) Bohlmann, F.; Misra, L. N.; Jakupovic, J.; King, R. M.; Robinson, H. *Phytochemistry* **1985**, *24*, 1315−1318.

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