

## Minor Sesquiterpenes from *Maytenus magellanica*

Antonio G. Gonzalez, Mercedes P. Nuñez, Ignacio A. Jimenez, Angel G. Ravelo, and Isabel L. Bazzocchi

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MINOR SESQUITERPENES FROM *MAYTENUS MAGELLANICA*ANTONIO G. GONZALEZ,\* MERCEDES P. NUÑEZ, IGNACIO A. JIMENEZ,  
ANGEL G. RAVELO, and ISABEL L. BAZZOCCHIC.P.N.O. Antonio González, Instituto de Universitario de Bio-Organica, Universidad de La Laguna,  
Carretera La Esperanza 2, La Laguna, 38206 Tenerife, Canary Islands, Spain

ABSTRACT.—One known (**1**) and four new dihydro- $\beta$ -agarofuran sesquiterpenes (**2–5**) were isolated from *Maytenus magellanica*. Their structures were elucidated by means of  $^1\text{H}$ - and  $^{13}\text{C}$ -nmr spectroscopic studies, including  $^1\text{H}$ - $^{13}\text{C}$  heteronuclear correlation (HETCOR), long range correlation spectra with inverse detection (HMBC), and ROESY experiments. Their absolute configurations were determined by application of the cd exciton chirality method.

*Maytenus magellanica* Hook. (**1**), known locally as "black maytenus," is a species that grows in the phytogeographical region of the Antarctic forest (Argentina and Chile) and has shown moderate activity (LC<sub>50</sub> 650 ppm) in the brine shrimp lethality bioassay (**2**). Our earlier work on *M. magellanica*, in the context of an intensive study of bioactive metabolites from the Celastraceae, yielded eleven dihydro- $\beta$ -agarofuran sesquiterpenes that proved to have antifeedant activity against Egyptian cotton leafworm, *Spodoptera littoralis* (Bois.) (**3,4**), in an election test (**5,6**).

This paper reports the isolation and structural elucidation of five minor sesquiterpenes **1–5** with a dihydro- $\beta$ -agarofuran skeleton from the EtOH extract of *M. magellanica*. Except for **1**, which has already been isolated from another species of the Celastraceae (**7**), these sesquiterpenes are new to the literature. As they were minor constituents of the plant, they were not obtained in sufficient quantity to be assayed for biological activity.

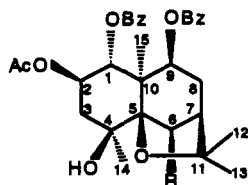
Their structures were determined by the combined use of spectroscopic techniques, and their absolute configurations were resolved by the dibenzoate chirality method, an extension of the circular dichroism exciton chirality method (**8,9**) as used earlier (**5,6**).

## RESULTS AND DISCUSSION

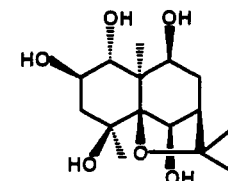
Repeated chromatography on Si gel and Sephadex LH-20 of the EtOH extract of the aerial part of *M. magellanica* gave five compounds, one of which, **1**, proved to be identical to 6 $\beta$ -acetoxydihydromortonol B, isolated earlier from the Celastraceae species *Schaefferia cuneifolia* L. (**7**).

Compound **2** had the molecular formula C<sub>38</sub>H<sub>40</sub>O<sub>10</sub> (hreims), and its ir showed absorption bands for hydroxy (3530 cm<sup>-1</sup>) and ester groups (1710 cm<sup>-1</sup>). The eims displayed sharp peaks at *m/z* 105 and [M-60]<sup>+</sup>, suggesting benzoate and acetate groups; this was confirmed by the  $^1\text{H}$ - and  $^{13}\text{C}$ -nmr spectroscopic data which included signals for 15 aromatic protons between  $\delta$  7.19 and 8.18, one acetate methyl as a singlet at  $\delta$  1.47, three carboxylic benzoate carbons at  $\delta$  165.2, 165.7, and 166.5, and one carboxylic acetate carbon at  $\delta$  170.8 (Tables 1 and 2). These data all indicated that **2** was a polyester sesquiterpene with a dihydro- $\beta$ -agarofuran skeleton (**10**).

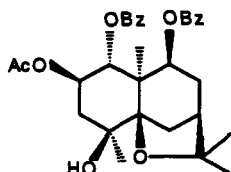
The substituent positions were determined as 1 $\alpha$ , 2 $\beta$ , 4 $\beta$ , 6 $\beta$ , and 9 $\beta$  from a careful study of the coupling constant (**10**) and double resonance experiments and were confirmed by a ROESY experiment (Figure 1). The regiosubstitution characteristics were determined by a long range correlation spectrum with inverse detection using the technique of heteronuclear multiple bond connectivity (HMBC) (**11**), which placed the benzoates at C-1, C-6, and C-9, the acetate group at C-2, and the hydroxy group at C-3, since H-1 ( $\delta$  5.88), H-6 ( $\delta$  5.63), and H-9 ( $\delta$  5.01) were clearly three-bond-coupled



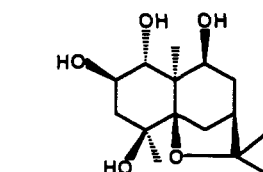
- 1 R=OAc  
2 R=OBz



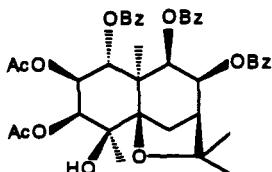
2β,4β-Dihydroxycelorbicol



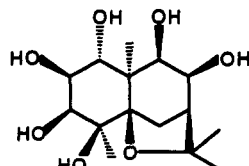
3



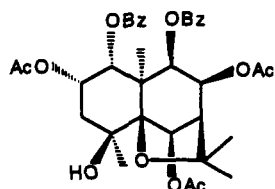
2β,4β-Dihydroxy-6-deoxycelorbicol



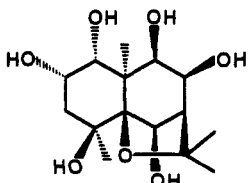
4



Isomagellanol



5

2α,4β-Dihydroxy-8-*epi*-celapanol

with the carboxylic carbons of three benzoates; H-2 ( $\delta$  5.08) exhibited coupling with the carboxylic carbon of an acetate. Three-bond and some two-bond coupling with other carbons was also observed. The absolute configuration of compound **2** was ascertained by studying the cd curve, which showed a split curve with a first positive Cotton effect at 237.8 nm ( $\Delta\epsilon = +20.6$ ) and a second negative effect at 220.3 nm ( $\Delta\epsilon = -6.5$ ). The absolute configuration of **2** was accordingly determined as (1*R*,2*R*,4*S*,5*S*,6*R*,7*R*,9*S*,10*R*)-2-acetoxy-1,6,9-tribenzoxy-4-hydroxy-dihydro- $\beta$ -agarofuran. Compounds **1** and **2** had the basic polyhydroxy skeleton of 2β,4β-dihydroxycelorbicol (12).

A detailed study of the spectroscopic data of compound **3** (Tables 1 and 2, Figure 2), which had the molecular formula  $C_{31}H_{36}O_8$  (hreims), showed it to be related to **2**, with the most notable differences being the existence of ten aromatic protons between  $\delta$  7.22 and 8.00 in the  $^1H$  nmr instead of fifteen as in **2** and the absence of the geminal proton at  $\delta$  5.63, thus establishing its regiosubstitution. The absolute configuration was resolved by studying the cd curve, which showed a split curve with the first Cotton effect at 236.0 nm ( $\Delta\epsilon = +24.4$ ) and the second at 221.7 nm ( $\Delta\epsilon = -7.9$ ); hence the absolute configuration of **3** was determined as (1*R*,2*R*,4*S*,5*R*,7*R*,9*S*,10*R*)-2-acetoxy-1,9-

TABLE 1.  $^1\text{H}$ -nmr (200 MHz) Data ( $\delta$ ,  $\text{CDCl}_3$ ) of Compounds 2-5.<sup>a</sup>

Proton	Compound			
	2	3	4	5
H-1	5.88 d (10.5)	5.92 d (10.5)	6.33 d (11.0)	5.71 <sup>b</sup>
H-2	5.08 m <sup>b</sup>	5.17 dt	5.32 dd <sup>b</sup> (3.0, 11.0)	5.71 <sup>b</sup>
H-3 $\alpha$	2.15 m	2.11 m <sup>b</sup>	5.30 d <sup>b</sup> (3.0)	2.03 dd (2.9, 15.1)
H-3 $\beta$				2.23 d (15.1)
H-6 $\alpha$	5.63 s	1.85 d (11.6)	2.12 d (12.8)	5.71 <sup>b</sup>
H-6 $\beta$		2.45 dd (2.7, 11.7)	2.65 dd (4.9, 12.8)	
H-7	2.40 m	2.11 m <sup>b</sup>	2.45 t	2.46 d (2.9)
H-8 $\alpha$	2.57 m	2.11 m <sup>b</sup>	5.71 dd (3.2, 5.8)	5.71 <sup>b</sup>
H-8 $\beta$	2.24 m	2.11 m <sup>b</sup>		
H-9	5.01 d (6.5)	5.03 d (6.4)	5.50 d (5.8)	5.36 d (6.3)
-OOC-Me				
2	1.74 s	1.79 s	1.74 s	1.99 s
3			2.31 s	
6				2.16 s
8				1.84 s

<sup>a</sup>J, in Hz, in parentheses.<sup>b</sup>Overlapping signals.TABLE 2.  $^{13}\text{C}$ -nmr (100 MHz) Data ( $\delta$ ,  $\text{CDCl}_3$ ) of 2-5.<sup>a</sup>

Carbon	Compound			
	2	3	4	5
C-1	73.24 d	73.00 d	68.01 d	68.21 d
C-2	69.15 d	69.24 d	69.27 d	70.60 d
C-3	45.03 t	42.80 t	76.02 d	42.12 t
C-4	71.67 s	70.65 s	70.33 s	69.94 s
C-5	91.52 s	90.04 s	89.82 s	91.27 s
C-6	80.77 d	31.65 t	33.10 t	77.18 d
C-7	49.38 d	43.48 d	48.03 d	53.97 d
C-8	32.16 t	31.03 t	71.03 d	68.80 d
C-9	73.42 d	73.73 d	72.42 d	72.11 d
C-10	52.48 s	48.49 s	48.95 s	50.34 s
C-11	85.47 s	84.11 s	84.67 s	85.04 s
C-12	26.37 q	24.48 q	25.92 q	26.41 q
C-13	30.10 q	29.99 q	31.35 q	30.19 q
C-14	25.31 q	24.99 q	24.32 q	25.28 q
C-15	21.12 q	20.06 q	20.40 q	21.63 q
CH <sub>3</sub> -COO-	21.30 q	20.90 q	20.91 q 21.43 q	20.63 q 21.07 q 21.48 q
CH <sub>3</sub> COO-	170.84 s	170.49 s	2×170.75 s	169.15 s 169.42 s 169.90 s
C <sub>6</sub> H <sub>5</sub> -COO-	128.42-133.94	127.91-132.85	128.31-133.47	127.94-133.20
C <sub>6</sub> H <sub>5</sub> -COO-	165.23 s 165.72 s 166.46 s	165.37 s 166.20 s	165.21 s 165.64 s 165.95 s	164.95 s 165.24 s

<sup>a</sup>Data are based on  $^1\text{H}$ - $^{13}\text{C}$  bidimensional experiments.

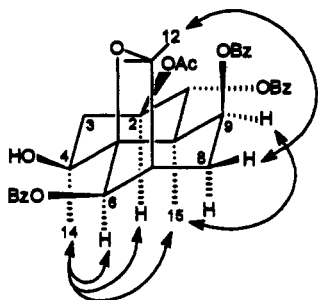


FIGURE 1. ROESY experiment of compound 2.

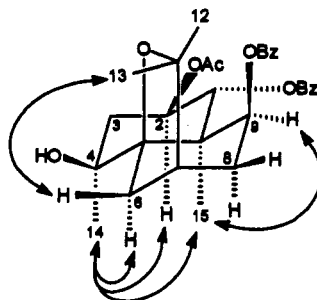


FIGURE 2. ROESY experiment of compound 3.

dibenzoyloxy-4-hydroxydihydro- $\beta$ -agarofuran. The basic polyhydroxy skeleton of **3** was that of 2 $\beta$ ,4 $\beta$ -dihydroxy-6-deoxycelorbicol (12).

The  $^1\text{H}$ -nmr (Table 1),  $^{13}\text{C}$ -nmr (Table 2), HMBC, and ROESY (Figure 3) experiments of compound **4** showed it to be a dihydro- $\beta$ -agarofuran sesquiterpene with one hydroxy group, two acetate groups, and three benzoate groups, which were assigned to positions C-1, C-2, C-3, C-8, and C-9 with the same sort of stereochemistry as isomagellanol (**4**). Its structure was established as 2 $\beta$ ,3 $\beta$ -diacetoxy-1 $\alpha$ ,8 $\beta$ ,9 $\beta$ -tribenzoyloxy-4 $\beta$ -hydroxy-dihydro- $\beta$ -agarofuran.

Compound **5** with the molecular formula,  $\text{C}_{27}\text{H}_{32}\text{O}_{11}$  (hreims) was shown, in a study of its ir,  $^1\text{H}$  nmr, and  $^{13}\text{C}$  nmr (Tables 1 and 2), to be a dihydro- $\beta$ -agarofuran sesquiterpene with three acetate groups, two benzoate groups, and one tertiary alcohol, positioned at 1 $\alpha$ , 2 $\alpha$ , 4 $\beta$ , 6 $\beta$ , 8 $\beta$ , and 9 $\beta$  by  $^1\text{H}$ - $^1\text{H}$  COSY and ROESY experiments (Figure 4). An HMBC experiment sited one of the benzoate groups at C-9, and the absence of an acetate methyl near  $\delta$  1.50, a characteristic signal of the acetate group on C-1 (13), placed the other benzoate group at C-1. This was confirmed by the cd curve, showing a split curve with a first positive Cotton effect at 237.6 nm ( $\Delta\epsilon = +22.7$ ) and a second negative Cotton effect at 222.6 nm ( $\Delta\epsilon = -11.9$ ) typical of benzoate groups at 1 $\alpha$ ,9 $\beta$ . Therefore the absolute configuration of **5** was determined to be (1*R*,2*S*,4*S*,5*S*,6*R*,7*R*,8*S*,9*R*,10*S*)-1,9-dibenzoyloxy-2,6,8-triacetoxy-4-hydroxy-dihydroxy- $\beta$ -agarofuran. The basic polyhydroxylated skeleton of **5** was that of 2 $\alpha$ ,4 $\beta$ -dihydroxy-8-*epi*-celapanol (14).

## EXPERIMENTAL

GENERAL EXPERIMENTAL PROCEDURES.—Ir spectra were taken on a PE 681 spectrophotometer and  $^1\text{H}$  and  $^{13}\text{C}$  nmr on a Bruker WP-200 SY in  $\text{CDCl}_3$  at 200 and 50 MHz, respectively, with TMS as the internal reference. The HMBC was run on a Bruker at 400 MHz. Optical rotations were measured on a PE 550-SE

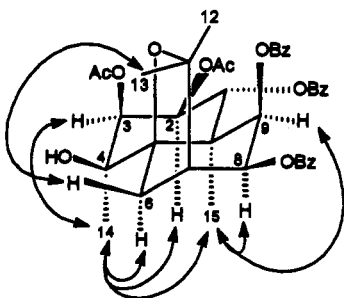


FIGURE 3. ROESY experiment of compound 4.

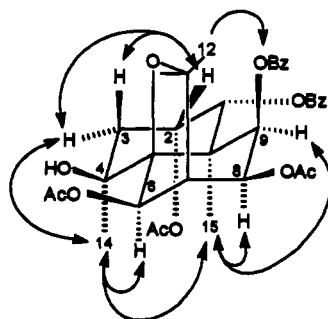


FIGURE 4. ROESY experiment of compound 5.

and cd spectra on a Jasco J-600 spectropolarimeter. Ms were recorded on a VG Micromass ZAF-2F and a Hewlett-Packard 5995. Uv spectra were obtained on a Perkin-Elmer model 550-SE.

PLANT COLLECTION.—*M. magellanica* plant material was gathered in January 1987 in the Novena region, province of Temuca, on the slopes of the volcano Osorno, in Chile, and a voucher specimen (no. 93-5341-C) is on file with the Facultad de Ciencias, Universidad de Chile, Santiago.

EXTRACTION AND ISOLATION.—The aerial part of the plant (4 kg) was extracted with EtOH (10 liters) at room temperature for a week. The extract (250 g) was repeatedly chromatographed on Sephadex LH-20 and Si gel using *n*-hexane-CHCl<sub>3</sub>-MeOH (2:1:1) and *n*-hexane-EtOAc, respectively, as solvents to afford the following products: **1** (6 mg), **2** (9 mg), **3** (7 mg), **4** (5 mg), and **5** (10 mg).

(1R,2R,4S,5S,6R,7R,9S,10R)-2-Acetoxy-1,6,9-tribenzoyloxy-4-hydroxy-dihydro-β-agarofuran [**2**].—Compound **2** was obtained as an oil: [α]<sub>D</sub><sup>20</sup> +64.5° (*c*=0.20, CHCl<sub>3</sub>); uv λ max nm (EtOH) 228, 271, 278; cd λ ext nm (MeCN) 237.8 (Δε=+20.6), 226.6 (Δε=0), 220.3 (Δε=-6.1); ir ν max cm<sup>-1</sup> (CHCl<sub>3</sub>) 3530, 3050, 2920, 2840, 1710, 1595, 1525, 1450, 1365, 1275, 1110, 1025, 710; eims *m/z* (rel. int. %) [M]<sup>+</sup> 656 (2), 641 (5), 596 (4), 578 (21), 563 (2), 534 (12), 519 (45), 474 (78), 459 (10), 353 (27), 230 (38), 105 (100); hrms *m/z* 656.2593 (calcd for C<sub>30</sub>H<sub>40</sub>O<sub>10</sub>, 656.2607); <sup>1</sup>H nmr (200 MHz) δ ppm 1.47 (6H, s), 1.51 (3H, s), 1.59 (3H, s), 3.24 (1H, s), 7.19–8.18 (15H, m), see Table 1 for additional data; <sup>13</sup>C nmr see Table 2.

(1R,2R,4S,5R,7R,9S,10R)-2-Acetoxy-1,9-dibenzoyloxy-4-hydroxydihydro-β-agarofuran [**3**].—Compound **3** was obtained as an oil: [α]<sub>D</sub><sup>20</sup> +110.8° (*c*=0.11, CHCl<sub>3</sub>); uv λ max nm (EtOH) 229, 272, 280; cd λ ext nm (MeCN) 236.0 (Δε=+24.4), 226.1 (Δε=0), 221.7 (Δε=-7.9); ir ν max cm<sup>-1</sup> (CHCl<sub>3</sub>) 3530, 3000, 2926, 1734, 1599, 1447, 1371, 1270, 1236, 1111, 1025, 710; eims *m/z* (rel. int. %) [M]<sup>+</sup> 536 (14), 521 (11), 494 (1), 476 (2), 431 (1), 414 (5), 399 (14), 372 (10), 354 (5), 339 (5), 235 (3), 217 (5), 105 (100); hrms *m/z* 536.2417 (calcd for C<sub>31</sub>H<sub>36</sub>O<sub>8</sub>, 536.2413); <sup>1</sup>H nmr (200 MHz) δ ppm 1.34 (3H, s), 1.42 (3H, s), 1.46 (3H, s), 1.49 (3H, s), 2.91 (1H, s), 7.22–8.00 (10H, m), see Table 1 for additional data; <sup>13</sup>C nmr see Table 2.

2β,3β-Diacetoxy-1α,8β,9β-tribenzoyloxy-4β-hydroxydihydro-β-agarofuran [**4**].—Compound **4** was obtained as an oil: [α]<sub>D</sub><sup>20</sup> +48.8° (*c*=0.09, CHCl<sub>3</sub>); uv λ max nm (EtOH) 230, 274, 282; ir ν max cm<sup>-1</sup> (CHCl<sub>3</sub>) 3522, 3066, 2965, 2923, 2855, 1732, 1597, 1445, 1108, 1066, 1023, 710; eims *m/z* (rel. int. %) [M-Me]<sup>+</sup> 699 (2), 577 (6), 517 (1), 457 (2), 413 (1), 371 (1), 293 (3), 105 (100); hrms *m/z* 714.2446 (calcd for C<sub>40</sub>H<sub>42</sub>O<sub>12</sub>, 714.2561); <sup>1</sup>H nmr (200 MHz) δ ppm 1.36 (3H, s), 1.56 (3H, s), 1.62 (3H, s), 1.71 (3H, s), 3.42 (1H, s), 7.18–7.97 (15H, m), see Table 1 for additional data; <sup>13</sup>C nmr see Table 2.

(1R,2S,4S,5S,6R,7R,8S,9R,10S)-1,9-Dibenzoyloxy-2,6,8-triacetoxy-4-hydroxydihydro-β-agarofuran [**5**].—Compound **5** was obtained as an oil: [α]<sub>D</sub><sup>20</sup> +48.4° (*c*=0.31, CHCl<sub>3</sub>) uv λ max nm (EtOH) 229, 273, 281; cd λ ext nm (MeCN) 237.6 (Δε=+22.7), 228.5 (Δε=0), 222.6 (Δε=-11.9); ir ν max cm<sup>-1</sup> (CHCl<sub>3</sub>) 3535, 3030, 3013, 2926, 2848, 1732, 1367, 1278, 1234, 1101; eims *m/z* (rel. int. %) [M-Me-C<sub>6</sub>H<sub>5</sub>CO]<sup>+</sup> 532 (1), 515 (1), 472 (1), 410 (1), 351 (1), 291 (1), 231 (4), 105 (100); hrms *m/z* 532.1976 (calcd for C<sub>27</sub>H<sub>32</sub>O<sub>11</sub>, 532.1960); <sup>1</sup>H nmr (200 MHz) δ ppm 1.53 (3H, s), 1.59 (3H, s), 1.68 (3H, s), 1.73 (3H, s), 7.25–7.83 (10H, m), see Table 1 for additional data; <sup>13</sup>C nmr see Table 2.

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#### LITERATURE CITED

1. A. Lourteig and C.A. O'Donnell, *Natura*, **1**, 181 (1955).
2. B.N. Meyer, N.R. Ferrigni, J.E. Putnam, L.B. Jacobsen, D.E. Nichols, and J.L. McLaughlin, *Planta Med.*, **45**, 31 (1982).
3. A.G. González, M.P. Núñez, A.G. Ravelo, J.G. Sazatornil, J.T. Vazquez, I.L. Bazzocchi, E.Q. Morales, and O.M. Muñoz, *J. Chem. Soc., Perkin Trans. 1*, 1437 (1992).
4. A.G. González, M.P. Núñez, I.L. Bazzocchi, A.G. Ravelo, and I.A. Jiménez, *Nat. Prod. Lett.*, **2**, 163 (1993).
5. X. Bellés, in "Insecticidas Biorracionales." Ed. by C.S.I.C., Raycar, S.A., Madrid, 1988, p. 355.
6. X. Bellés, F. Camps, J. Coll, and M.P. Piulachs, *J. Chem. Ecol.*, **10**, 314 (1985).
7. A.G. González, J.J. Mendoza, A.G. Ravelo, J.G. Luis, I.A. Jiménez, and J.T. Vázquez, *Rev. Latinoam. Quim.*, **20** (2), 91 (1989).
8. N. Harada and K. Nakanishi, *J. Am. Chem. Soc.*, **91**, 2989 (1979).
9. N. Harada and K. Nakanishi, in "Circular Dichroism Spectroscopy Exciton Coupling in Organic Stereochemistry." Ed. by University Science Books, Moll Valley, CA, 1983, p. 55.

10. R. Brüning and H. Wagner, *Phytochemistry*, **17**, 1821 (1978).
11. A. Bax and M.F. Sommers, *J. Am. Chem. Soc.*, **108**, 2093 (1986).
12. C.R. Smith, R.W. Miller, D. Wiesleder, W.K. Rohwedder, N. Eickman, and J. Clardy, *J. Org. Chem.*, **41**, 3264 (1976).
13. A.G. González, M.P. Núñez, A.G. Ravelo, J.G. Luis, I.A. Jiménez, J.T. Vázquez, and O.M. Muñoz, *Heterocycles*, **29**, 2287 (1989).
14. H. Wagner, E. Heckel, and J. Sonnenbichler, *Tetrahedron*, **31**, 1949 (1975).

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