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SESQUITERPENES FROM *RZEDOWSKIA TOLANTONGUENSIS*

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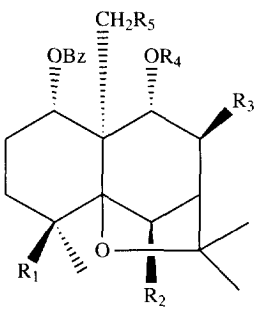
Key Word Index—*Rzedowskia tolantonguensis*; Celastraceae; dihydro-β-agarofuran sesquiterpenes.

Abstract—Six new dihydro-β-agarofuran-skeleton sesquiterpenes were isolated from the aerial part of *Rzedowskia tolantonguensis*. Their structures were elucidated by spectroscopic methods and chemical reactions.

INTRODUCTION

Celastraceae are widespread throughout the hot and hot-to-temperate regions of the world and have a long history of use at the folk level both for medicinal [1, 2] and agricultural purposes [3]. Species of Celastraceae frequently yield polyester dihydro-β-agarofuran sesquiterpenes, which are considered to be taxonomic indicators of this family [4]. The interest generated by polyester sesquiterpenes from this family has increased in line with the possibility of their application in the struggle against insect plagues as an alternative to the synthetic insectides [5].

Earlier papers on *Rzedowskia tolantonguensis*, a plant endemic to north-eastern Mexico, reported on the isolation and structural elucidation of bioactive metabolites with diverse structures [6–9]. This paper reports on the isolation and identification of six sesquiterpenes with a dihydro-β-agarofuran skeleton from *R. tolantonguensis*. Their structures were determined by spectroscopic methods and chemical correlations.



	R_1	R_2	R_3	R_4	R_5
1	OH	OAc	OAc	OBz	OAc
2	OH	OAc	OH	OBz	OAc
3	OH	ONic	OH	OBz	H
4	H	OAc	OAc	OBz	H
5	H	OH	OH	OBz	H
6	H	OAc	OH	OBz	H
7	OH	OAc	OAc	OAc	OAc

RESULTS AND DISCUSSION

After repeated chromatography of the methanol extract of the aerial part on silica gel, compounds **1**–**6** were obtained. Compound **1** was assigned the molecular formula $C_{35}H_{40}O_{12}$, based on its EI- and HREI-mass spectral data. Its IR spectra showed absorption bands for hydroxyl groups, and ester groups.

When acetylated at room temperature with acetic anhydride in pyridine, unaltered starting material was produced and the tertiary nature of the hydroxyl group was demonstrated. The mass spectrum showed fragments at *m/z* 105 and 597 [M−60$^+$] suggesting the presence of acetate and benzoate groups in the molecule. This was confirmed by the ^{1}H NMR spectrum (Table 1) which showed signals for three acetate methyls at δ 1.82, 2.16 and 2.42 as singlets with geminal protons at δ 5.65 as a double doublet (J = 3.2, 9.8 Hz), δ 6.58 as a singlet and an AB system as a double doublet centred at δ 4.88 (J = 12.7 Hz), respectively, signals for 10 aromatic protons between δ 6.91 and 7.60 with geminal protons at δ 5.62 as multiplets and δ 6.12 as a doublet (J = 9.9 Hz) and three angular methyls as singlets at δ 1.28, 1.38 and 1.73. The acetate groups were sited on C-6β, C-8β and

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Table 1. ^{1}H NMR (200 MHz) data (δ, $CDCl_3$) of compounds **1–6** (J are given in Hz in parentheses)

H	1	2	3	4	5	6
1	5.62 *m*	5.65 *dd* (4.0, 10.0)	5.52 *dd* (3.9, 11.4)	5.45 *m*	5.47 *dd* (4.1, 11.7)	5.48 *dd* (4.4, 11.8)
6	6.58 *s*	6.39 *s*	5.69 *s*	5.73 *s*	4.48 *s*	5.54 *s*
7	2.47 *d* (2.8)	2.42 *d* (4.0)	2.63 *d* (3.1)	2.46 *d* (3.0)	2.48 *s* (3.1)	2.44 *d* (3.2)
8	5.65 *dd* (3.2, 9.8)	4.40 *m*	4.32 *m*	5.34 *dd* (3.0, 9.7)	4.00 *dd* (3.1, 9.7)	4.20 *dd* (3.3, 9.4)
9	6.12 *d* (9.9)	5.98 *d* (9.0)	6.00 *d* (9.6)	6.00 *d* (9.9)	5.93 *d* (9.6)	5.92 *d* (9.6)
15	4.88 d_{AB} (12.7)	4.86 d_{AB} (14.0)				
Ac-6	2.16 *s*	2.12 *s*		2.15 *s*	2.17 *s*	
Ac-8	1.82 *s*			1.84 *s*		
Ac-15	2.42 *s*	2.32 *s*				

C-15 and the benzoates groups on C-1α and C-9α based on the coupling constants and chemical shifts of its geminal protons [10] and by double resonance studies. Comparison of the ^{1}H NMR data of **1** with those of 1α-benzoyloxy-6β,8β,9α,15-tetracetoxy-4β-hydroxydihydro-β-agarofuran (**7**) [11] showed that the main difference was the absence of the signal at δ 1.52 corresponding to the acetate methyl on C-9. This placed one of the benzoate groups of compound **1** at this position. All these data indicated **1** was 1α,9α-dibenzoyloxy-6β,8β,15-triacetoxy-4β-hydroxy-dihydro-β-agarofuran.

The data for compound **2** were very similar to those of **1** with the most notable differences being in its ^{1}H NMR spectrum (Table 1) i.e. the shift of the geminal proton on C-8 from δ 5.65 to δ 4.40 and the absence of the acetate methyl at δ 1.82. When **2** was acetylated under standard conditions, it afforded a product with physical and spectroscopic data superimposable on those of **1**. Compound **2** was therefore 6β-15-diacetoxy-1α,9α-dibenzoyloxy-4β,8β-dihydroxy-dihydro-β-agarofuran. The basic polyhydroxy skeleton of compounds **1** and **2** was 2,3,13-trideoxy-isoeuoniminol.

The molecular formula of compound **3** was assigned as $C_{35}H_{37}O_9N$ by EI- and HREI-mass spectral data. Its IR spectrum showed hydroxyl and ester group bands, and the mass spectrum suggested the presence of a nicotinate group with fragments at m/z 124 and 106 and a benzoate fragment at m/z 105. The ^{1}H NMR spectrum (Table 1) showed signals corresponding to the protons of a nicotinate group with the geminal proton at δ 5.69 as a singlet; two benzoate groups with the geminal protons at δ 5.52 as a double doublet (J = 3.9, 11.4 Hz) and δ 6.00 as a doublet (J = 9.6 Hz), respectively; the geminal proton to a hydroxyl group at δ 4.32 and four angular methyls as singlets at δ 1.39, 1.54, 1.62 and 1.77. These data characterized a polyester dihydro-β-agarofuran sesquiterpene, and placed the two benzoate groups at C-1α and C-9α, a nicotinate group at C-6β and a hydroxyl group at C-8β [10]. These assignments were later confirmed by double resonance experiments and comparison with other sesquiterpenes with the same substitution pattern [7]. These data allowed us to establish the structure of **3** as 1α,9α-dibenzoyloxy-4β,8β-dihydroxy-6β-nicotinoyloxy-dihydro-β-agarofuran, and its basic skeleton is 2,3,13,15-tetradeoxy-isoeuoniminol.

Compound **4** had the molecular formula $C_{33}H_{38}O_{10}$ and its IR spectrum showed absorption bands for ester groups. The mass spectrum showed fragments at m/z 105 and 534 $[M\text{-}60]^+$ suggesting that benzoate and acetate groups were present in the molecule. Its ^{1}H NMR spectrum (Table 1) showed signals for two methyl acetates at δ 1.84 and 2.15 with the geminal protons at δ 5.34 as a double doublet (J = 3.0, 9.7 Hz) and δ 5.73 as a singlet; 10 aromatic protons with geminal protons at δ 5.45 as multiplets and δ 6.00 as a doublet (J = 9.9 Hz) and four angular methyls, one of them as a doublet at δ 0.90 (J = 7.6 Hz). These data and the double resonance experiments indicated **4** was 6β,8β-diacetoxy-1α,9α-dibenzoyloxy-dihydro-β-agarofuran.

Compound **5** was identified as 1α,9α-dibenzoyloxy-6β,8β-dihydroxy-dihydro-β-agarofuran and **6** as 6β-acetoxy-1α,9α-dibenzoloxy-8β-hydroxy-dihydro-β-agarofuran from spectroscopic data and chemical correlation with **4**. Acetylation of **5** and **6** under normal conditions give both a product with identical spectroscopic data to those of **4**. Compounds **4**, **5** and **6** have a basic skeleton of 2,3,4,13,15-pentadeoxy-isoeuoniminol.

EXPERIMENTAL

General procedures. ^{1}H and ^{13}C NMR: 200 and 50 MHz, respectively; MS: VG Micromass LTD-ZAB-2F and/or on an HP 5930 A at 70 eV.

Isolation of metabolites. The plant was gathered in Jaumave, Tamaulipas (México), and a voucher specimen have been lodged with the Biology Department of the Instituto Tecnológico y de Estudios Superiores

de Monterrey, Mexico, no. 7853. The aerial part of the plant was extracted with MeOH. The extract (3.2 g) was subjected to repeated chromatography on silica gel with mixts of *n*-hexane–EtOAc as eluant affording the following products: **1** (5 mg), **2** (3 mg), **3** (6 mg), **4** (5 mg), **5** (4 mg) and **6** (5 mg).

1α,9α-*Dibenzoyloxy*-6β,8β,15-*triacetoxy*-4β-*hydroxy*-*dihydro*-β-*agarofuran* (**1**). IR $\nu_{max}^{CHCl_3}$ cm^{-1}: 3430, 2340, 1726, 1645, 1275, 1228, 1100; ^1H NMR ($CDCl_3$) δ: 1.28 (3H, *s*), 1.38 (3H, *s*), 1.73 (3H, *s*), 2.75 (1H, *s*, H-OH), 6.91 (2H, *t*), 7.12–7.60 (8H, *m*), for other signals see Table 1; EIMS *m/z* (rel. int.): 637 $[M-15]^+$ (1), 594 (1), 593 (3), 592 (7), 551 (2), 550 (5), 534 (1), 531 (2), 530 (6), 489 (2), 488 (5), 472 (2), 428 (2), 413 (3), 356 (2), 306 (3), 268 (4), 246 (10), 206 (5), 202 (8), 122 (2), 105 (100); HR-EIMS $[M-15]^+$ *m/z* at 637.2304 (calc. for $C_{34}H_{37}O_{12}$, 637.2306).

6β,15-*Diacetoxy*-1α,9α-*dibenzoyloxy*-4β,8β-*dihydroxy*-*dihydro*-β-*agarofuran* (**2**). ^1H NMR ($CDCl_3$) δ: 1.24 (3H, *s*), 1.38 (3H, *s*), 1.75 (3H, *s*), 2.76 (1H, *s*, H-OH), 6.85 (2H, *t*), 7.08 (2H, *t*), 7.35–7.65 (6H, *m*), for other signals see Table 1; EIMS *m/z*: 592 $[M-18]^+$ (1), 577 (0.4), 550 (2), 530 (0.4), 488 (2), 470 (1), 428 (1), 413 (1), 410 (1), 353 (1), 324 (1), 279 (3), 268 (2), 246 (4), 228 (2), 206 (3), 202 (7), 167 (14), 164 (12), 149 (47), 135 (5), 122 (3), 113 (6), 106 (11), 105 (100); HR-EIMS $[M-18]^+$ *m/z* at 592.2350 (calc. for $C_{33}H_{36}O_{10}$, 592.2346).

1α,9α-*Dibenzoyloxy*-4β,8β-*dihydroxy*-6β-*nicotinoyloxy*-*dihydro*-β-*agarofuran* (**3**). IR $\nu_{max}^{CHCl_3}$ cm^{-1}: 3471, 2944, 1721, 1592, 1234, 1045; ^1H NMR ($CDCl_3$) δ: 1.39 (3H, *s*), 1.54 (3H, *s*), 1.62 (3H, *s*), 1.77 (3H, *s*), 2.97 (1H, *s*, H-OH), 6.90 (1H, *t*). 7.17 (2H, *m*) 7.41–7.67 (8H, *m*), 8.53 (1H, *m*), 8.82 (1H, *dd*, *J* = 1.6, 4.8 Hz), 9.39 (1H, *br s*), for other signals see Table 1; EIMS *m/z*: 494 $[M-121]^+$ (1), 407 (2), 375 (3), 353 (1), 313 (1), 270 (6), 248 (3), 228 (9), 191 (4), 148 (10), 124 (27), 106, 105 (100); HR-EIMS *m/z* at 615.2543 (calc. for $C_{35}H_{37}O_9N$, 615.2536).

6β,8β-*Diacetoxy*-1α,9α-*dibenzoyloxy*-*dihydro*-β-*agarofuran* (**4**). IR $\nu_{max}^{CHCl_3}$ cm^{-1}: 3444, 2919, 1726, 1642, 1275, 1233, 1107, 1040, 703; ^1H NMR ($CDCl_3$) δ: 0.90 (3H, *d*, *J* = 7.6 Hz), 1.36 (3H, *s*), 1.55 (3H, *s*), 1.68 (3H, *s*), 6.90 (1H, *t*), 7.14 (1H, *t*), 7.35–7.60 (8H, *m*), for other signals see Table 1; EIMS *m/z*: 534 $[M-60]^+$ (2), 492 (2), 488 (1), 475 (1), 472 (3), 431 (1), 412 (1), 397 (1), 312 (1), 279 (8), 248 (4), 167 (19), 149 (54), 122 (3), 105 (100); HR-EIMS *m/z* at 594.2501 (calc. for $C_{33}H_{38}O_{10}$, 594.2497).

1α,9α-*Dibenzoyloxy*-6β,8β-*dihydroxy*-*dihydro*-β-*agarofuran* (**5**). ^1H NMR ($CDCl_3$) δ: 1.43 (3H, *s*) 1.57 (3H, *s*), 1.60 (3H, *s*), 1.72 (3H, *s*), 6.64–6.91 (2H, *t*), 7.14–7.65 (8H, *m*), for other signals see Table 1; EIMS *m/z* 495 $[M-15]^+$ (6), 492 (1), 477 (1), 388 (1), 370 (1), 355 (4), 248 (6), 233 (5), 143 (3), 122 (3), 109 (9), 105 (100).

6β-*Acetoxy*-1α,9α-*dibenzoyloxy*-8β-*hydroxy*-*dihydro*-β-*agarofuran* (**6**). ^1H NMR ($CDCl_3$) δ: 1.12 (3H, *d*, *J* = 7.8 Hz), 1.38 (3H, *s*), 1.55 (3H, *s*), 1.75 (3H, *s*), 6.89 (2H, *t*), 7.14 (8H, *m*), for other signals see Table 1.

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