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MINOR POLYHYDROXYAGAROFURAN DERIVATIVES FROM *MORTONIA HIDALGENSIS*

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Key Word Index—*Mortonia hidalgensis*; Celastraceae; polyhydroxyagarofuran esters; sesquiterpenes.

Abstract—Two new β-dihydroagarofuran derivatives were isolated from *Mortonia hidalgensis*. One of them was shown to be the 6-dihydromortonol B. The structure of the second product was established as 1α,15-diacetoxy-9β-benzoyloxy-β-dihydroagarofuran, by X-ray crystallography.

INTRODUCTION

Mortonia is a small, mainly Mexican genus of the Celastraceae [1]. We have been studying the sesquiterpene constituents of this genus. The presence of mortonins 1–3, and mortonols **4a** and **b**, appears to be its distinctive feature [2–5].

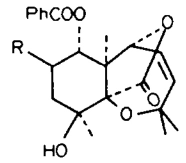
Recently we have described [5] the isolation of mortonins A (**1a**) and C (**2**), and of mortonol B (**4b**) from *Mortonia hidalgensis*. The isolation and structure elucidation of two new minor constituents of this plant with the β-dihydroagarofuran skeleton is the subject of this paper.

RESULTS AND DISCUSSION

Repeated chromatography of a polar fraction of the chloroform extract of *M. hidalgensis* yielded a crystalline product, mp 197–201°, which analysed for $C_{31}H_{36}O_9$ (M^+ at m/z 552). Its spectral data (see Experimental) indicated a close relationship of this new compound with mortonol B (**4b**). The absence of the 1760 cm^{-1} band [4, 5] in its IR spectrum, suggested that it was the 6-dihydro derivative of mortonol B (**5**).

The hydroxyl group at C-6 must be equatorial since H-6 was observed in the ^1H NMR of **5** as a broad singlet at δ4.5 due to a small coupling ($J = 1$ Hz) with the equatorial H-7 [7]. Treatment of **5** with Jones' reagent gave mortonol B (**4b**) proving the structure and stereochemistry proposed.

The second new product, compound **6**, was obtained by repeated chromatography of the less polar fractions of the chloroform extract of *M. hidalgensis*. It showed mp 160–163°, and $[M]^+$ at m/z 458 in the mass spectrum. Its IR spectrum did not show hydroxyl absorption but only ester carbonyl bands at 1710, 1730 and 1740 cm^{-1}. The presence of bands at 1605 and 1590 cm^{-1} suggested that it contained one or more benzoate groups and the mass spectrum showed peaks due to the loss of one benzoic and two acetic acid units.



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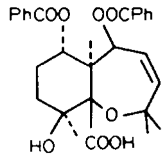
1b R = OAc



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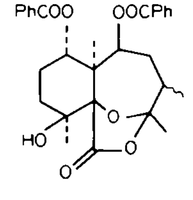

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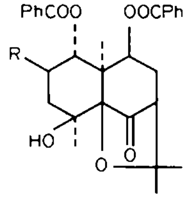

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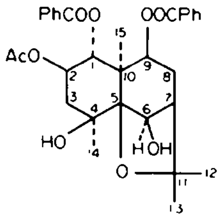
4b R = OAc



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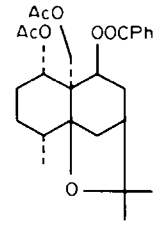

6

Its ^1H NMR spectrum confirmed that **6** contained one benzoate ester (5H, δ8.05 and 7.5, *m*). Two sharp singlets at δ2.17 and 1.59 (3H each) were assigned to the two acetate methyl groups. A double doubet observed at δ5.5 (1H, $J = 5$ and 10 Hz) was assigned to the axial methine proton at C-1 and a partially superimposed double doubet, centred at δ5.4 (1H, $J = 6$ and 3 Hz), to the equatorial methine proton at C-9, by comparison with related polyol esters of β-dihydroagarofuran [2–7]. An AB system at δ4.5 was attributed to the C-15 methylene bound to an ester function. The C-11 gem dimethyls were responsible for the singlets (3H each) observed at δ1.40 and 1.20. A doublet at δ1.1 (3H, $J = 7.5$ Hz) was assigned to the secondary methyl group at C-4 which is axial in all the products of this type so far described [6].

A strong upfield shift for one of the acetate methyl groups (δ 1.59) has been previously noted for compounds with a β-dihydroagarofuran skeleton in which an equatorial acetate at C-1 is shielded by an aromatic ester axially bound to C-9 [8]. It has been also observed in compounds with the ester group exchanged, i.e. with an equatorial benzoate at C-1 and an axial acetate at C-9 [7]. Observation of a Dreiding model revealed that this type of protection is possible in both cases. X-ray diffraction analysis of a single crystal of **6** showed that the equatorial acetate group is at C-1 and the axial benzoate is bound to C-9.

The molecular structure with numbering scheme is illustrated in Fig. 1. The A-ring exhibits a chair conformation. The average bond length and angle for the chair structure is 1.532 (6) Å and 111.2 (3)°, respectively, and agree with values obtained for cyclohexane [9]. The average value of the torsion angle is 55.2 (5)°. The substituents at C-1 and C-4 are in equatorial and axial positions respectively.

Examination of the B-ring shows it to be in highly strained chair conformation and distortion of bond angles is the key factor in strain relief. The substituent at C-9 is in the axial position. The ring junction between rings A and B is *trans*, with *trans* torsion angles of 50.9 (5) and -56.9 (4)°.

The conformation of the five-membered ring may be described by the parameters Δ and ϕ_m [10] with values of 17.4° and 48.2° respectively, indicating a conformation intermediate between half-chair and β-envelope.

The phenyl ring is planar and shows normal geometry, 1.379 (7) Å and 120.0 (5)° for the mean C_{sp^2}–C_{sp^2} bond distance and the mean internal angle. This mean bond distance is close to that given by Sutton [11] [1.395 (5) Å] and Brisse and Sygusch [12] (1.378 Å).

The acetate and benzoate groups and the furane ring are oriented to minimize transannular repulsions between their oxygen atoms [O-1 ... O-3 and O-2 ... O-3 distances are 2.90 (1) and 2.96 (1) Å]. In both acetate and benzoate groups the C=O groups are placed *syn* to the C-1–H and C-9–H bonds respectively [13, 14].

No significantly short intermolecular contacts can be observed and therefore the molecular arrangement of the molecules in the crystal appears to be determined by van der Waals interactions.

EXPERIMENTAL

Mps are uncorr. IR spectra were recorded in $CDCl_3$. ^{1}H NMR spectra were recorded in $CDCl_3$ unless otherwise stated. TMS was used as internal standard. Chemical shifts are given in δ values.

Isolation of sesquiterpenes from M. hidalgensis. Dried and ground leaves (4 kg) of the plant collected in Ixmiquilpan, Hidalgo (México) were extracted with MeOH under reflux and worked up in the usual manner [3–5]. A portion (66 g) of the total $CHCl_3$ soluble fraction (327 g) was chromatographed on silica gel. Mortonins A (**1b**) C (**2**), D (**3**) and mortonol B (**4b**) were isolated and identified by comparison with authentic samples. Repeated chromatography of the fraction eluted with hexane–EtOAc (7:3) gave **6** (100 mg) mp 160–163° (from MeOH) $[\alpha]_D^{25}$ +43.25° (*c* 0.4; MeOH). IR ν_{max} cm^{-1}: 1740, 1730, 1710, 1605, 1590. MS *m/z* (rel. int.): 458 $[M]^+$ (10), 398 (1), 337 (2), 277 (1), 217 (4), 137 (6), 124 (5), 105 (88.8), 77 (37), 43 (100); ($C_{26}H_{34}O_7$, requires $[M]^+$ at 458). ^{1}H NMR: δ8.05–7.45 (5H, *m*), 5.5 (1H, *dd*, $J = 5$ and 10 Hz), 5.4 (1H, *dd*, $J = 6$ and 3 Hz), 4.5 (2H, *s*), 2.17 (3H, *s*), 1.59 (3H, *s*), 1.4 (3H, *s*), 1.2 (3H, *s*) 1.10 (3H, *d*, $J = 7.5$ Hz).

Repeated chromatography of the fractions eluted with hexane–EtOAc (1:1) gave **5**, mp 197–201°. $[\alpha]_D^{25}$ +110.5° (*c* 0.20;

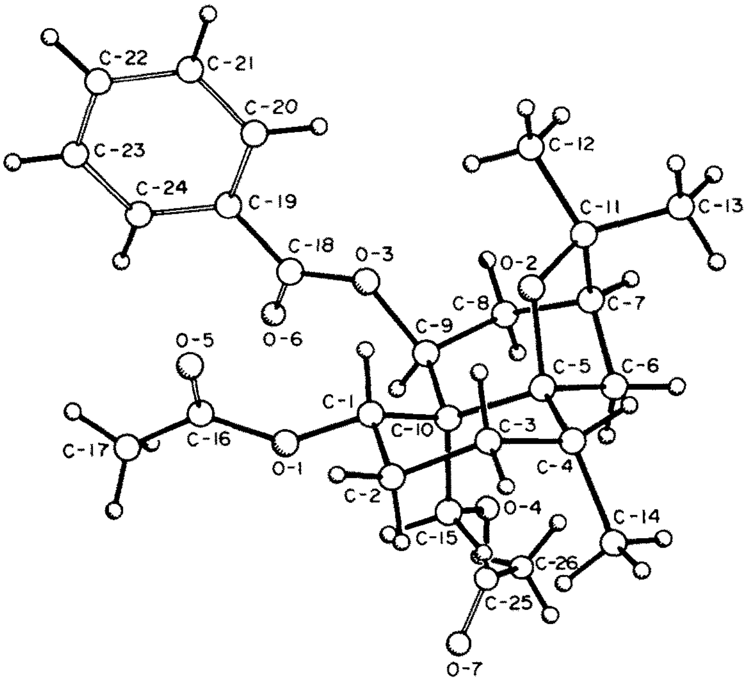

Fig. 1.

Table 1. Atomic co-ordinates ($\times 10^4$) and equivalent isotropic temperature factors ($Å^2 \times 10^3$) for 1α-15α-diacetoxy-9β-benzoyloxy-β- dihydroagarofurane

Atom	x	y	z	U_{eq}
O-1	2600 (3)	8719 (3)	1341 (1)	45 (1)
O-2	552 (3)	5574 (3)	553 (1)	39 (1)
O-3	−49 (3)	7145 (3)	1485 (1)	42 (1)
O-4	3759 (4)	5068 (3)	1790 (1)	54 (1)
O-5	1471 (5)	10410 (3)	927 (1)	74 (1)
O-6	142 (5)	7944 (4)	2275 (1)	96 (2)
O-7	6047 (5)	5483 (6)	1998 (2)	119 (2)
C-1	2286 (5)	7767 (4)	930 (1)	39 (1)
C-2	3360 (5)	7948 (5)	505 (1)	48 (2)
C-3	2973 (6)	6984 (4)	78 (2)	48 (2)
C-4	2982 (5)	5505 (4)	249 (2)	45 (1)
C-5	2026 (5)	5306 (4)	720 (1)	36 (1)
C-6	1969 (5)	3867 (4)	921 (2)	40 (1)
C-7	451 (5)	3846 (4)	1145 (2)	43 (2)
C-8	470 (5)	4719 (4)	1626 (2)	48 (2)
C-9	1121 (5)	6160 (4)	1576 (2)	40 (1)
C-10	2330 (4)	6329 (4)	1160 (1)	33 (1)
C-11	−410 (5)	4463 (4)	710 (2)	45 (1)
C-12	−1900 (5)	5050 (5)	848 (2)	59 (2)
C-13	−622 (6)	3460 (5)	279 (2)	63 (2)
C-14	4552 (5)	4946 (5)	273 (2)	63 (2)
C-15	3831 (5)	6136 (5)	1416 (2)	46 (1)
C-16	2104 (6)	10009 (4)	1285 (2)	50 (2)
C-17	2491 (6)	10822 (4)	1744 (2)	64 (2)
C-18	−398 (6)	8007 (5)	1858 (2)	53 (2)
C-19	−1419 (5)	9081 (4)	1696 (1)	47 (2)
C-20	−2344 (5)	8948 (5)	1284 (2)	56 (2)
C-21	−3260 (6)	9995 (5)	1148 (2)	64 (2)
C-22	−3225 (6)	11201 (6)	1406 (2)	66 (2)
C-23	−2310 (6)	11354 (5)	1815 (2)	64 (2)
C-24	−1420 (6)	10311 (5)	1960 (2)	55 (2)
C-25	4949 (5)	4834 (5)	2061 (2)	56 (2)
C-26	4759 (7)	3748 (5)	2441 (2)	69 (2)

$U_{eq} = (U_{11} \times U_{22} \times U_{33})^{1/3}$.

$CHCl_3$). IR ν_{max} cm^{-1}: 3510, 3550, 1740 (br), 1710 (s), 1605, 1590. MS m/z (rel. int.): 552 $[M]^+$ (1), 537 (0.5), 493 (1), 430 (0.5), 415 (10.6), 355 (3), 248 (2), 233 (3), 215 (1), 179 (5), 105 (100); ($C_{31}H_{36}O_9$ requires $[M]^+$ at 552). ^1H NMR ($CDCl_3$): δ7.9–7.25 (10H, *m*), 5.9 (1H, *d*, $J = 10$ Hz), 5.1 (2H, *m*), 4.5 (1H, *br*, *s*); 4.85 (1H, *s*), 3.45 (1H, *br s*, exchange with D_2O), 1.80 (3H, *s*), 1.75 (3H, *s*), 1.6 (3H, *s*), 1.57 (3H, *s*), 1.55 (3H, *s*).

Oxidation of 6-dihydromortonol B (**5**). 6-Dihydromortonol B, (**5**, 60 mg) in Me_2CO (2 ml) were treated with Jones' reagent at 5° for 15 min. Water was added and the reaction mixture extracted with EtOAc, washed with brine, dried and the solvent removed under vacuum. The solid product obtained (40 mg) was recrystallized from Me_2CO–hexane and was identified as mortonol B (**4b**) by comparison with an authentic sample.

X-ray structure determination. Preliminary characterization of the crystals using photographic techniques showed the mmm Lave symmetry and systematic absence in hOO with h = odd, OKO with k = odd and 001 with l = odd, thus uniquely defining the space group as $P2_12_12_1$. Unit cell dimensions were obtained by a least-squares fit to the angular settings of 25 centred reflections on a Nicolet R3m diffractometer equipped with a graphite monochromator crystal. Crystal data for 1α,15-diacetoxy-9β-benzyloxy-β-dihydroagarofuran: $C_{26}H_{34}O_7$, $M_r = 458.5$, $a = 9.137$ (4), $b = 9.844$ (4), $c = 26.502$ (10) Å, $V = 2384$ (1) $Å^3$, $d_{calc} = 1.28$ g/cm^3, $z = 4$, space group $P2_12_12_1$; μ(MoKα) = 1.00 xm^{-1}. The crystal chosen for intensity measurement had the dimensions 0.30 × 0.40 × 0.52 mm, and was mounted on a glass fibre. Intensity measurements were made with MoKα ($\lambda = 0.7107$ Å) radiation utilizing the ω-scan technique, the rate of scanning being varied from 4.0 to 29.3 deg/min^{-1}. Two reflections ($0\ 1\ \bar{1}$; $\bar{2}\ 1\ \bar{2}$) were routinely monitored at intervals of 50 measurements. All reflections in the hkl octant according to $3° < 2\theta < 45°$ with index range h 0/9, k 0/10 and l 0/28 were collected. The total number of data collected was 1840, of which 1518 reflections had $I > 2.5\sigma(I)$ and these formed the basis of the structural solution and refinement; these reflections were corrected for Lorentz and polarization effects; and numerical absorption correction was applied [15]. The crystal structure was solved by direct methods and partial structure expansion by iterative E-Fourier procedure using the program package SHELXTL [15]. The trial structure was refined by a blocked cascade least-squares procedure with anisotropic temperature factors for the non-H atoms and with a fixed isotropic temperature factor, U = 0.06 $Å^2$, for the H atoms bonded to C atoms. The function minimized was $\Sigma\omega\,(|Fo| - |Fc|)^2$ with a weighting scheme $\omega = [\sigma^2(Fo) + G\,(Fo)^2]^{-1}$, where σ is the standard deviation of the observed amplitudes, based on counting statistics, and G is a variable to be adjusted after each cycle, final $G = 0.001$; maximum shift of parameters in the last cycle was 0.06; no peaks > 0.25 e/Å^{-3}; scattering factors for the O, C and H atoms were from International Tables for X-ray Crystallography [16]; isotropic extinction parameter $X = 0.0019$; final $R = 0.046$, $R_w = 0.048$ ($R_w = \Sigma\omega^{1/2}(|Fo| - |Fc|)/\Sigma\omega^{1/2}|Fo|$).

All computations were performed in the laboratory on a Nova 4S computer and plots were drawn on a Tektronix plotter.

A list of the observed and calculated structure factors, anisotropic thermal parameters, interatomic distances and angles; and hydrogen atom positions have been deposited at the Cambridge Crystallographic Centre.

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