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CHROMANONES, BENZOFURANS AND OTHER CONSTITUENTS FROM *OPHRYOSPORUS LORENTZII*

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Key Word Index—*Ophryosporus lorentzii*; Compositae; Eupatorieae; chromanones; benzofuran derivatives; germacradienolide; mollisorin A; monoterpene; Z-8-hydroxylinalool.

Abstract—An extract of the aerial parts of *Ophryosporus lorentzii* afforded three new chromanones, a known chromene, a new prenylated benzofuran, three known benzofurans, the germacradienolide mollisorin A, Z-8-hydroxylinalool and the lignan mediaresinol, as well as some common plant constituents.

INTRODUCTION

In this article we continue our study of Argentine species of *Ophryosporus*, a South American genus of nearly 40 species, seven of which have been investigated previously [1–6]. Prenylated acetophenones, including tremetone derivatives and chromenes, are common, while diterpenes have been isolated from three species [2–4] and eudesmanolides from two species [4, 5]. The present report deals with *Ophryosporus lorentzii* Hieron., a species limited to Jujuy, Salta and Tucumán provinces of northwestern Argentina [7].

RESULTS AND DISCUSSION

The new chromanones **1a**, **1b** and **1c**, the chromene **2** [8], the benzofurans **3a** [9], **3b** [10] and **3c** [1], the new prenylated toxol derivative **4**, the germacradienolide mollisorin [11], Z-8-hydroxylinalool (**5**), the lignan mediaresinol, vomifoliol, isoscopoletin and 3-indolealdehyde were isolated from the aerial parts of *O. lorentzii*. The structures of **1a**, **1b** and **1c** were obvious from the ^{1}H NMR spectra which in each case exhibited the typical two proton signal of H-3a,b, the two singlets of the methyl groups on C-2, and the *meta*-coupled signals of H-5 and H-7. In the case of **1b** the methyl signal of the acetyl function on C-6 was replaced by –OH as evidenced by an –OH signal at δ 4.78 and the mass spectrum. The nature of the side chains on C-8 was also clear. In the case of **1a** and **1b** the frequencies of the vinylic protons indicated conjugation with the benzene ring and the coupling constants a *trans*-double bond, while in the case of **1c**, the situation was altered, with a secondary and benzylic hydroxyl group coupled to a vinylic proton which was allylically coupled to two vinylic methyls. On prolonged standing in $CDCl_3$ compound **1c** was completely converted to **1d** as shown by the ^{1}H NMR spectrum (see Experimental).

The structure of toxol derivative **4**, $C_{18}H_{22}O_5$, could also be inferred from the mass spectrum and the ^{1}H NMR spectrum. H-4, *meta*-coupled to H-6 as usual, was also allylically coupled to H-3, a broad doublet at δ 5.46, which in turn was vicinally coupled to the doublet of H-2 at δ 4.52. The two methyl singlets of the side chain attached to C-2 were easily differentiated from the vinylic methyls of the side chain on C-7 which were allylically coupled to vinylic H-2′. The magnitude of $J_{2,3}$ (4.5 Hz) indicated that the two groups on the furan ring were *trans*-orientated.

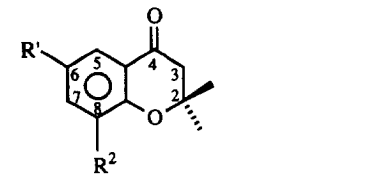
Z-8-Hydroxylinalool (**5**) was first reported, as was the *E*-isomer, as a hydrolysis product of the respective β-D-glucosides from *Betula alba* [12]. High resolution ^{1}H NMR data are given in the Experimental section. The *E*-isomer has most recently been reported from *Stevia breviaristata* [13].

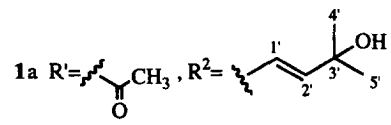
EXPERIMENTAL

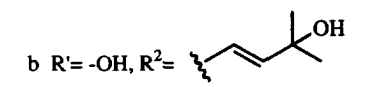
General. HPLC employed a differential refractometer and columns were (A) a Beckman Ultrasphere C18 (10 mm i.d. × 25 cm) and (B) a Phenomenex Maxsil 10C8 (10 mm i.d. × 50 cm). R_fs were measured from the solvent peak.

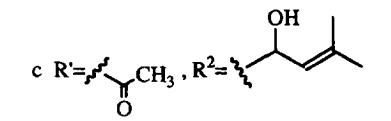
Plant material. Aerial parts of *Ophryosporus lorentzii* Hieron. were collected at the flowering stage on 15 June, 1994 at Apeadora General Muñoz, km 42, road No. 307, Tucumán Province. A voucher specimen (E. Sigstad, M. C. and A. S. #1) is on deposit in the herbarium of the Instituto Miguel Lillo, Tucumán.

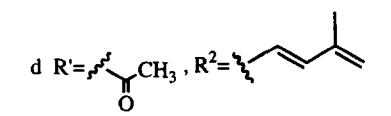
Extraction and isolation. Flowers and leaves (505 g) were extracted with $CHCl_3$ (3 × 5 l.) at room temp. for

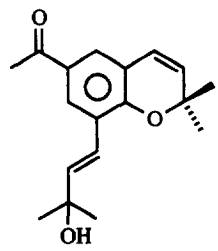


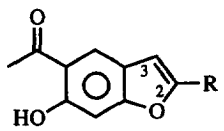


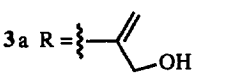


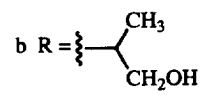


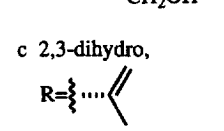


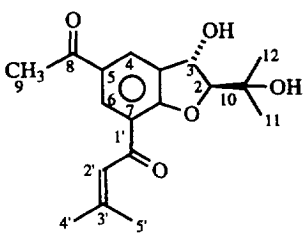


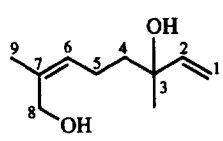












3 days to give 24.88 g (4.7%) of crude extract which was suspended in EtOH (300 ml) at 55°, diluted with H_2O (200 ml) and extracted successively with *n*-hexane (3 × 500 ml) and $CHCl_3$ (3 × 500 ml). The $CHCl_3$ extract on evapn at red. pres. furnished a residue (3.5 g) which was subjected to chromatography over silica gel (170 g) using $CHCl_3$ containing increasing amounts of EtOAc (0–100%), 152 fractions being collected which were monitored by TLC.

Frs 66–81 (265 mg) were combined and subjected to rechromatography over silica gel using $CHCl_3$ with increasing amounts of EtOAc (5–15%), 25 frs being collected. Frs 8–14 (64 mg) from the rechromatogram were combined and processed by RP-HPLC (column A, MeOH–H_2O 2:1, 2 ml min^{-1}) to give 1.4 mg of a mixture of **3a** (major component) and **3b** (minor component) (R_t 10.1 min), 1.6 mg of **1a** (R_t 13.5 min) and 4.0 mg of **2** (R_t 29.7 min). The first three fractions were rechromatographed separately (column B, MeOH–H_2O 2:1, 2 ml min^{-1}) to give 1.1 mg of isoscopoletin (R_t 4.2 min) and 1.8 mg of 3-indolealdehyde (R_t 5.0 min).

Frs 82–94 (524 mg) from the initial silica gel column were combined. A portion (111 mg) was subjected to HPLC (MeOH–H_2O 3:2, 2 ml min^{-1}, column A) to give 2.8 mg of **3c** (R_t 12.4 min), and 65 mg of a mixture from which 23 mg of solid **1a** separated on trituration with Et_2O. HPLC of the Et_2O-soluble material (MeOH–H_2O 3:2 ml min^{-1}, column A) furnished an additional 8.4 mg of **1a** (R_t 23.3 min) and a fraction (19 mg) of which 10 mg was reprocessed by HPLC (MeOH–H_2O 3:2, 2 ml min^{-1}, column B) to give 3.4 mg of **1c** (R_t 26.9 min) and 3.1 mg of **1a** (R_t 30.6 min).

Frs 105–117 (171 mg) from the mother column were combined and a portion (100 mg) was subjected to HPLC (MeOH–H_2O 4:3, 2 ml min^{-1}, column A) to give five peaks which were resubmitted to HPLC (from column A, MeOH–H_2O 2:1, 2 ml min^{-1}, column A) and (MeOH–H_2O 3:2, 2 ml min^{-1}, column A) to give

2.5 mg of mediaresinol (R_t 6.9 min), 0.7 mg of **5** (R_t 13.1 min) and 0.5 mg of a mixture, and from column B, 1.7 mg of **1b** (R_t 11.8 min) and 2.7 mg of mollisorin A (R_t 26.3 min). Frs 124–127 (60.5 mg) from the initial column were also combined and subjected to HPLC (MeOH–H_2O 1:1, 2 ml min^{-1}, column A) to give two fractions which were reprocessed by HPLC (MeOH–H_2O 4:3, 2 ml min^{-1}, column A) and (MeOH–H_2O 1:1, 2 ml min^{-1}, column B) to give from column B, 0.9 mg of vomifoliol (R_t 5.3 min) and from column A, 1.8 mg of **4** (R_t 17.2 min). Known compounds were identified by ^{1}H NMR (500 MHz) and mass spectrometry.

6-*Acetyl*-2,2-*dimethyl*-8-(3-*hydroxy*-3-*methyl*-1E-*butenyl*)-*chromanone* (**1a**). Solid, mp not taken; MS PCI (*i*-butane) *m/z* (rel. int.): 303 $[M+H]^+$, $[C_{18}H_{22}O_4+H]^+$ (86.9), 285 (100); ^{1}H NMR (500 MHz, $CDCl_3$); δ 8.34 (*d*, J = 2.5 Hz) and 8.24 (*d*, J = 2.5 Hz, H-5 and H-7), 6.87 (*d*, J = 16.5 Hz, H-3′), 6.53 (*d*, J = 16.5 Hz, H-2′), 2.78 (*br s*, 2H, H-3a,b), 2.61 (*s*, 3H, CH_3C=O), 1.52 and 1.45 (each *s* and (3H, C-2 and C-3′ methyls).

2,2-*Dimethyl*-6-*hydroxy*-8-(3-*hydroxy*-3-*methyl*-1-E-*butenyl*)-*chromanone* (**1b**). Gum; MS PCI (*i*-butane) *m/z* (rel. int.): 259 $[M+H-H_2O]^+$; ^{1}H NMR (500 MHz, $CDCl_3$): δ 7.20 (*br s*, 2H, H-5, H-7), 6.83 (*d*, J = 16.5 Hz, H-2′), 6.39 (*d*, J = 16.5 Hz, H-1′), 4.78 (*br s*, –OH), 2.70 (*s*, 2H, H-3a,b), 1.46 (*s*, 6H) and 1.37 (*s*, 6H, C-2 and C-3′ methyls).

6-*Acetyl*-2,2-*dimethyl*-8-(1-*hydroxy*-3-*methyl*-2-*butenyl*)-*chromanone* (**1c**). Gum; ^{1}H NMR (300 MHz, $CDCl_3$): δ 8.38 and 8.31, each *d*, 2 Hz, H-5 and H-7), 5.71 and 5.31 (each *d*, J = 8.5 Hz, H-1′ and H-2′), 2.78 (*s*, 2H, H-3a,b), 2.59 (*s*, 3H, CH_3C=O), 2.12 (*br*, OH) 1.83 and 1.74 (each *s* and 3H, H-4′ and H-5′), 1.51 and 1.46 (each *s* and 3H, C-2 methyls). After 2 weeks the ^{1}H NMR spectrum had changed to that of **3**, ^{1}H NMR signals (500 MHz) at δ 8.34 (*s*, 2H, H-5 and H-7), 7.04 and 6.77 (each *d*, J = 16 Hz, H-2′ and H-1′), 5.19 and 5.15 (each *br d*, J = 2, H-4′a,b), 2.79 (*br s*, 2H, H-3a,b), 2.61 (*s*, 3H, CH_3C=O), 2.00 (*br s*, H-5′ coupled to H-4′a,b), 1.52 and 1.45 (each *s* and 3H, C-2 methyls); MS PCI *m/z* (rel. int.): 285 $[M+H]^+$, $[C_{18}H_{20}O_3+H]^+$ (100).

5-*Acetyl*-trans-2-(*hydroxyisopropyl*)-3-*hydroxy*-7-*senecioylbenzofuran* (**4**). Solid, mp not taken; MS PCI (rel. int.): 319 $[M+H]^+$, $[C_{18}H_{22}O_5+H]^+$ (100); ^{1}H NMR (500 MHz, $CDCl_3$): δ 8.44 (*d*, J = 2 Hz, H-6), 8.16 (*br d*, J = 2 Hz, H-4), 5.46 (*br d*, J = 4.5 Hz, H-3), 4.52 (*d*, J = 4.5 Hz, H-2), 2.60 (*s*, 3H, CH_3C=O), 2.27 and 2.02 (each *br s* and 3H, H-4′ and H-5′), 1.41 and 1.37 (each *s* and 3H, C-2 methyls).

Z-8-*Hydroxylinalool* (**5**). Gum; MS PCI (*i*-butane) *m/z* (rel. int.): 153 $[M+H-H_2O]^+$ (40.0), 135 (100); ^{1}H NMR (500 MHz, $CDCl_3$): δ 5.91 (*dd*, J = 17.5, 10.5 Hz), 5.31 (*br t*, J = 7.5 Hz, H-6), 5.22 (*d*, J = 17.5 Hz, H-1_t), 5.07 (*d*, J = 10.5 Hz, H-1_c), 4.13 (*d*, J = 12 Hz, H-8a), 4.12 (*d*, J = 12 Hz, H-8b), 2.12 (*m*, 2H, H-5a,b), 1.79 (*br s*, 3H, H-9), 1.58 (*m*, 2H, H-4a,b), 1.29 (*s*, 3H, H-10).

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