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15-Hydroxyeremantholide B and derivatives from *Eremanthus arboreus*

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Abstract

Aerial parts of *Eremanthus arboreus* furnished two new eremantholides, a hydroxy acid related to them and 5,7-dihydroxy-3′,4′-dimethoxyflavone.

Keywords: *Eremanthus arboreus*; Asteraceae; Vernonieae; Eremantholides; Sesquiterpene lactones

1. Introduction

The genus *Eremanthus* Less. (Asteraceae, Vernonieae, Lychnophorinae) as revised by MacLeish (1987) comprises 18 species largely restricted to the Cerrado of the central plateau of Brazil and includes six members of the former genus *Vanillosmopsis* Sch. Bip. Characteristic constituents are sesquiterpene lactones with emphasis on lactones of the goyazensolide and eremantholide type (Baker et al., 1971; Vichnewski & Gilbert, 1972; Corbella, Gariboldi, Jommi, & Ferrari, 1974; Raffauf, Huang, LeQuesne, Levery, & Brennan, 1975; Vichnewski, Callegari Lopes, Santos Filho, & Herz, 1976; Vichnewski, Sarti, Gilbert, & Herz, 1976; Garcia, Da Silva, Baker, Gilbert, & Rabi, 1976; Vichnewski et al., 1977; LeQuesne, Levery, Menachery, Brennan, & Raffauf, 1978; Herz, Kumar, Vichnewski, & Blount, 1980; Bohlmann, Zdero, King, & Robinson, 1980; Bohlmann, Zdero, Robinson, & King, 1981b; Bohlmann, Gupta, Jakupovic, Robinson, & King, 1981; Bohlmann et al., 1982; Herz & Goedken, 1982; Barros et al., 1985; Lima, Garcia, & Rabi, 1985; Bannerjee et al., 1986; Vichnewski et al., 1989; Mauro, Nasi, Vichnewski, Díaz, & Herz, 1993; Vichnewski et al., 1995).

One of the six taxa transferred by MacLeish from *Vanillosmopsis* was *Eremanthus arboreus* (Gardner) MacLeish. Earlier work has dealt with the essential oil of this species (Craveiro, Alencar, Matos, Souza, & Machado, 1984; Matos, Souza, Matos, & Craveiro, 1988; Menezes, Almeida, Rao, & Matos, 1990). In the present article we describe isolation of two sesquiterpene lactones **1a** (15-acetoxyeremantholide B) and **1b** (15-hydroxyeremantholide B), the eremantholide B derivative **2** and 5,7-dihydroxy-3′,4′-dimethoxyflavone (ermanin) from the aerial parts of *E. arboreus*. Compounds **1a**,**b** and **2** are new and ermanin has not been reported previously from species in the tribe Vernonieae.

The ^{1}H NMR spectra of 15-acetoxyeremantholide B (**1a**), the main constituent, and the desacetyl derivative **1b** (Table 1) were almost identical, except for the downfield shift of the H-15a,b resonance caused by the presence of the acetoxy group in **1a** and were otherwise similar to the spectrum of eremantholide B (**1c**) from *Eremanthus elaeagnus* (LeQuesne et al., 1978) and *Eremanthus incanus* (Herz et al., 1980) which lacks the oxygen function on C-15. The ^{13}C NMR spectra of **1a** and **1b** (Table 2) also exhibited the expected

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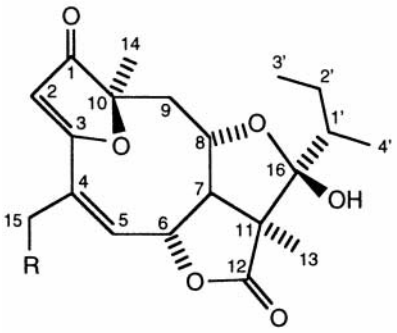
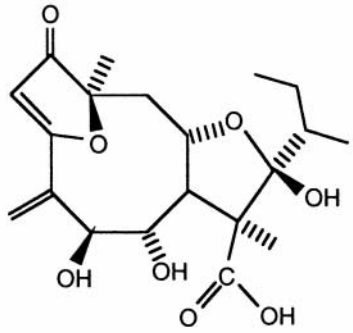


1 a R = OAc
b R = OH
c R = H



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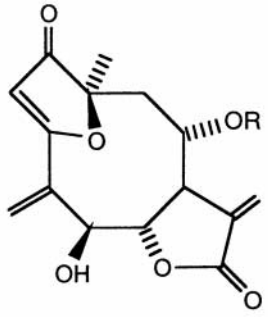

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chemical shifts compared with the ^{13}C NMR spectrum of **1c** (Herz et al., 1980). As for hydroxyacid **2** the magnitude of $J_{5,6}$ (9.6 Hz) indicated β-orientation of the hydroxyl group on C-5 as in compounds of type **3** (Vichnewski et al., 1995), with the hydroxyl on C-6 necessarily α as a result of opening of the lactone ring. Apparently the lactone ring opening did not significantly affect the conformation of the large alicyclic ring as $J_{7,8}$, $J_{8,9a}$ and $J_{8,9b}$ remained approximately the same. Hydroxyacid **2** could conceivably be an artifact,

Table 1
^{1}H NMR spectra of compounds **1a,b** and **2** (300 MHz, $CDCl_3$)

	1a	1b	2
H-2	5.87 s	5.72 s	5.83 s
H-5	6.30 td (1.5, 2.5)	6.32 td (1.6, 2.6)	4.62 td (2.3, 9.6)
H-6	5.00 dd (2.5, 7.5)	5.01 dd (2.6, 7.5)	4.24 dd (9.6, 7.5)
H-7	2.84 dd (7.5, 4)	2.86 dd (7.5, 4)	2.80 dd (7.5, 3.8)
H-8	4.00 ddd (4, 12, 2.6)	4.03 ddd (4, 12, 2.6)	3.89 ddd (3.8, 12, 2.6)
H-9α	2.05 dd (12, 13.6)	2.02 dd (12, 13.6)	2.02 dd (12, 13.4)
H-9β	2.33 dd (2.6, 13.6)	2.31 dd (2.6, 13.6)	2.32 dd (2.6, 13.4)
H-13[a]	1.21 s	1.31 s	1.33 s
H-14[a]	1.48 s	1.47 s	1.48 s
H-15	4.78 br s[b]	4.34 br s[b]	6.15 dd (2.3,1) 5.92 dd (2.3,1)
H-1′[c]	2.04 m	2.02 m	2.02 m
H-2′a	1.70 m	1.71 m	1.70 m
H-2′b[c]	0.97 m	0.96 m	0.97 m
H-3′[a]	0.95 t (7)	0.95 t (7)	0.89 t (7)
H-4′[a]	1.05 d (7)	1.04 d (7)	0.97 d (7)
OH	3.39 br s	3.39 br s	3.5 br s
OAc[a]	2.10 s		

In $CdCl_3$–MeOD. [a]Intensity three protons.[b]Intensity two protons. [c]Partially obscured.

Table 2
^{13}C NMR spectra of compounds **1a,b** and **2** (75 MHz, $CDCl_3$)

C	1a	1b	2
1	205.5 s	207.8 s	205.5 s
2	105.8 s	106.1 s	106.2 d
3	183.2 s	187.0 s	186.2 s
4	127.4 s	136.2 s	140.0 s
5	136.3 d	135.2 d	73.7 d
6	79.0 d	83.0 d	85.6 d
7	63.9 d	64.9 d	64.0 d
8	75.4 d	78.6 d	75.3 d
9	43.9 t	44.9 t	44.4 t
10	88.2 s	91.4 s	90.9 s
11	60.2 s	60.2 s	60.9 s
12	175.5 s	175.2 s	176.6 s
13	20.8 q	20.7 q	21.0 q
14	22.7 q	21.5 q	21.3 q
15	63.3 t	63.3 t	122.5 t
16	108.1 s	109.2 s	108.7 s
1′	39.4 d	40.7 d	39.8 d
2′	22.7 t	23.8 t	22.9 t
3′	12.0 q	12.1 q	12.3 q
4′	13.0 q	12.7 q	13.0 q
Ac	170.2 s 16.9 q		

although the lactone ring opening as a result of chromatography over silica gel has not previously been observed.

Eremantholides are characteristic constituents of Vernonieae subtribe Lychnophorinae (Robinson, Bohlmann, & King, 1980) which inter alia includes *Eremanthus* (Raffauf et al., 1975; Herz et al., 1980; Bohlmann et al., 1980, 1982; Barros et al., 1985), *Lychnophora* (Bohlmann, Müller, King, & Robinson, 1981; Bohlmann, Zdero, Robinson, & King, 1982; LeQuesne et al., 1982; Cunha, Callegari Lopes, Vichnewski, Herz, & Díaz, 1995; Borella, Callegari Lopes, Vichnewski, Cunha, & Herz, 1998) and *Piptolepis* (Bohlmann, Wallmeyer, King, & Robinson, 1982) and have also been found in *Proteopsis argentea* (Bohlmann, Zdero, Robinson, & King, 1981a) of subtribe Piptocarphinae (Robinson et al., 1980). In this connection we note that the literature dealing with *Eremanthus* species contains reports on the chemistry of four taxa, *E. bicolor* (DC.) Baker in C. Martius (Bohlmann et al., 1980; Bannerjee et al., 1986), *E. eriopus* (Sch. Bip.) Baker in C. Mart. (Vichnewski et al., 1995), *E. crotonoides* (DC.) Sch. Bip. (Bohlmann et al., 1982; Bannerjee et al., 1986) and *E. mollis* Sch. Bip. (Bohlmann et al., 1981; Herz & Goedken, 1982) which MacLeish (1987) has transferred to *Paralychnophora bicolor* (DC.) MacLeish, *Prestelia eriopus* Sch. Bip., *Vernonia crotonoides* (DC.) Sch. Bip. and *Vernonia pannosus* (Baker in C. Mart.) MacLeish, with *Prestelia* and *Paralychnophora* remaining in subtribe Lychnophorinae. However the chemistry of the two taxa transferred to *Vernonia* is essentially lychnophorine, with *E. crotonoides* in particular containing eremantholides, and quite uncharacteristic of neotropical Vernoniinae, thus raising doubts about the validity of these two transfers.

2. Experimental

2.1. General

NMR: 300 MHz (^1H), 75 MHz (^{13}C) with TMS as internal standard; Mp's uncorr.; IR: KBr or film; MS: Hewlett Packard Model 5995, direct inlet at 70 eV; Shimadzu LC-6^A liquid chromatograph; CG silica gel 60 (Merck 70-230 mesh; Si gel C_1, F_{254} (Merck); silica gel D (Riadel); HPLC: Shim-pack Prep-ODS (20 × 250 mm, 5 mm), with UV detector.

2.2. Plant material

E. arboreus (Gardner) MacLeish was collected at Conceiçao da Mata Dentro, Minas Gerais, Brazil, in July 1989 and identified by the late Dr. Hermógenes de Freitas Leitão Filho, Departamento de Botânica, Universidade de Campinas, SP. A voucher specimen (Vichnewski #303) is on deposit in the herbarium of UNICAMP.

2.3. Extraction and isolation

Dried and pulverized aerial parts (2.5 kg) were extracted with EtOAc to give 228.35 g of crude extract which was chromatographed over silica gel D under vacuum, using mixtures of hexane, EtOAc and MeOH of inceasing polarity. Frs 12–17 (hexane–EtOAc, 4:1, 13.58 g) furnished solid material which was recrystallized from benzene–Me_2CO to give 255.6 mg of 5,7-dihydroxy-3′,4′-dimethoxyflavone (ermanin) further characterized by acetylation in the usual manner to give the diacetate (91.8 from 100 mg of ermanin). Frs 23–26 (hexane–EtOAc, 3:1, 11.96 g) on recrystallization from EtOAc furnished 2.46 g of **1a**. Fr 37 (EtOAc, 88.8 g) was rechromatographed over silica gel 60 using hexane and increasing the polarity with EtOAc and MeOH. Solid material from subfr. 28 was recrystallized from hexane–EtOAc–MeOH (1:1:1) to give 281.4 mg of **2**. Frs 27–30 (hexane–EtOAc, 3:1) furnished a solid which on recrystallization from EtOAc gave 91.4 mg of **1b**.

2.4. 15-Acetoxyeremantholide B (*1a*)

Colorless crystals, mp 170–172°C (EtOAc). IR λ_{max} cm^{-1}; 3458 (–OH), 1765 (γ-lactone C = 0), 1750 (acetate C = 0), 1720 (ester C = 0, 1695 and 1585 (enone). GC–MS m/z (rel. int.): 363 (1[$M-C_4H_9$]$^+$),

320 (1[363-C_2H_2O]$^+$), 99 (23), 57 (76). ^{1}H and ^{13}C NMR spectra in Tables 1 and 2.

2.5. 15-Hydroxyeremantholide B (*1b*)

Colorless crystals, mp 132–136° (EtOAc). IR λ_{max} cm^{-1}: 3460 (–OH), 1775 (γ-lactone C = 0), 1710 (ester C = 0), 1680 and 1575 (enone). GC–MS m/z (rel. int.): 378 (23 [M–OH]$^+$), 361 (22), 333 (19), 293 (62), 276 (8), 85 (85), 57 (H); ^{1}H and ^{13}C NMR spectra in Tables 1 and 2.

2.6. Dihydroxyacid *2*

Colorless crystals, mp 270–272°C (EtOAc–MeOH). IR λ_{max} cm^{-1}: 3400 (–OH), 1738 (acid C = 0), 1695 and 1575 (enone); GC–MS *m/z* (rel. int.): 378 (23 [M–OH]$^+$), 361 (22), 333 (19), 293 (62), 276 (8), 85 (85), 57 (41). ^{1}H and ^{13}C NMR spectra in Tables 1 and 2.

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