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Sesquiterpene Lactones and Flavonoids from *Eremanthus mattogrossensis* and *Eremanthus eriopus*

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Das partes aéreas de *Eremanthus mattogrossensis* foram isoladas as lactonas sesquiterpênicas goiazensolido e 5-epiisogoiazensolido, bem como a flavanona naringenina. Das partes aéreas de *Eremanthus eriopus* foram isoladas as lactonas sesquiterpênicas ereglomerulido e centraterina, bem como duas flavonas conhecidas.

The sesquiterpene lactones goyazensolide and 5-epiisogoyazensolide, as well as naringenin, were extracted from aerial parts of *Eremanthus mattogrossensis*. The sesquiterpene lactones ereglomerulide and centratherin and two known flavones were derived from aerial parts of *Eremanthus eriopus*.

Keywords: Eremanthus mattogrossensis; Eremanthus eriopus; *Vernonieae; Compositae; sesquiterpene lactones; flavonoids*

Introduction

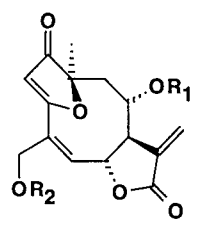
In the present work we continue our reports on the chemistry of the Brazilian genus *Eremanthus* (Compositae, Vernonieae)[1], the species of which produce a variety of sesquiterpene lactones, some of which are schistosomicidal[2].

Results and Discussion

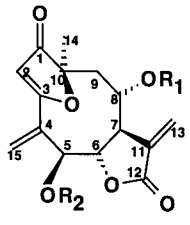
The primary constituent derived from the aerial parts of *Eremanthus mattogrossensis* Kuntze was the lactone goyazensolide (**1**a), first isolated from *Eremanthus goyazensis*[3,4], and subsequently from other species of the Vernonieae subtribes Lychnophorinae[2,5-10] and Centratherinae[11]. A secondary extraction of a sesquiterpene lactone was **2**a (5-epiisogoyazensolide), previously found[6] in *Eremanthus brasiliensis* (Gardn.) MacLeish and *E. pohlii* (Baker in C. Martius) MacLeish (old synonyms[1] *Vanillosmopsis brasiliensis* and *V. pohlii*, respectively). A third constituent was found the flavanone naringenin.

Aerial parts of *Eremanthus eriopus* Sch. Bip. ex Baker (syn. *Prestelia eriopus* Sch. Bip[1]) furnished centratherin (lychnophorolide A, **1**b), first isolated from *Centratherum punctatum*[12], and later from species of the subtribe Lychnophorinae[9,13-15], ereglomerulide (**4**), previously isolated from *Eremanthus glomerulatus*[8,17], and the known flavones **5**a and **5**b.

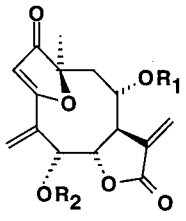
The ^{1}H-NMR spectrum of the minor lactone from *E. mattogrossensis* (Table 1) matched the data in the literature[6] for **2**a reported at a time when the lactone ring was erroneously assumed to be closed to C-8. As a result of the X-ray analysis of goyazensolide[4] the lactone ring closure to C-8 originally postulated for **1**b, **2**a and related compounds from Lychnophorinae[6,7,19-25] and Centratherinae had to be abandoned in favor of lactone ring closure to C-6. The ^{13}C-NMR spectrum (Table 2) was in agreement with the postulated structure **2**a, but otherwise the mp (162-164°) differed significantly from the reported[6] value of 226°. Since the mp's of sesquiterpene lactones in this series are frequently unreliable criteria for identification (*e.g.*



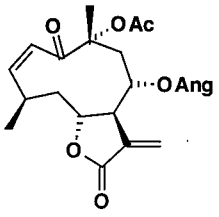
1 a R_1=MeAcr, R_2=H
b R_1=Ang, R_2=H
c R_1=MeAcr, R_2=Ac
d R_1=Ang, R_2=Ac



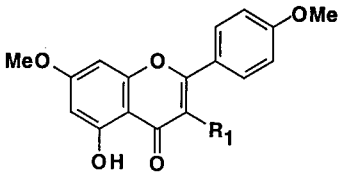
2 a R_1=MeAcr, R_2=H
b R_1=MeAcr, R_2=Ac
c R_1=Ang, R_2=H



3 a R_1=MeAcr, R_2=H
b R_1=MeAcr, R_2=Ac
c R_1=Ang, R_2=H
d R_1=Ang, R_2=Ac



4



5 a R_1=OMe
b R_1=H

centratherin [**1b**][12,13] and isocentratherin [**3c**][16,23,26]), our substance was converted to a monoacetate **2b**, mp 216-218°, whose ^{1}H- and ^{13}C-NMR spectra are also listed in Tables 1 and 2.

Acetylation of goyazensolide (**1a**), with a structure defined by X-ray analysis[4], was accompanied by an allylic rearrangement to isogoyazensolide acetate (**3b**)[3]. The stereochemistry assigned to C-5 of **3b** was based on the analysis of the coupling constants, and was subsequently confirmed by comparison with **3d**, the acetate of **3c** (isocentratherin), the latter a congener of centratherin in *Centratherum punctatum*[9,26], once the structures suggested earlier[4] for **3c** and **3d** had been confirmed by an X-ray analysis of **3c**[27]. Lactones of type **2**, with a β-oriented hydroxyl or ester function on C-5, can be differentiated from the very similar isomers of type **3** with an α-oriented hydroxyl or ester on C-5 by differences in the chemical shifts of H-7, H-15a and H-15b, approximately δ 4.2, 6.2 and 6.1 for type **3** *vs.* δ 3.6, 6.2 and 6.0 for type **2**, and by the values of $J_{5,6}$ = 8-10 Hz for type **2** *vs.* less than 1 Hz for type **3**. A comparison of the ^{1}H-NMR spectra from **2a** and **2b** with the previously reported data for **3b**[3] (Table 1) clearly shows that the hydroxy and acetoxy groups of the minor lactone from *E. mattogrossensis* and its acetate are β-oriented. Table 2 shows that acetylation of **2a** to **2b** produces, as expected, relatively small chemical shifts in the signals of C-3, C-4, C-6 and C-15. More significant is the comparison of **2b** with **3b** and **3d**[27] which shows that the change in stereochemistry at C-5 produces relatively small shifts in the signals of C-4, C-5, C-6 and C-8, but considerably larger shifts in the signals of C-7 (γ effect of the oxygen atom at C-5 of **3b**), and particularly C-15 (γ effect of the oxygen atom at C-5 of **2b**).

Experimental

Extraction of Eremanthus mattogrossensis

Aerial parts of *E. mattogrossensis* Kuntze (3 kg) were collected 50 km south of Ribeirão Preto, in the state of São Paulo, Brazil, in June 1987, and identified by Hermógenes de Freitas Leitão Filho of the Departamento de Botânica of Unicamp. The pulverized material was extracted with $CHCl_3$, and the extract was treated with celite-norit, filtered and evaporated at reduced pressure. The residue (160 g) was chromatographed on silica gel at reduced pressure, 600 mL fractions being collected as follows: Frs. 1-24 (hexane), 25-38, 39-70, 71-116, 117-146, 147-182, 183-198, 199-210, 211-226, 227-230, 231-252, 253-272, 273-280, 281-290 (hexane-EtOAc: 19:1, 9:1, 17:3, 4:1, 3:1, 8:3, 13:7, 3:2, 11:9, 1:1, 9:11, 2:3, 3:7, respectively), 291-302 (EtOAc), 303-322 (MeOH). Fr. 122 furnished **2a** (30 mg), mp 162-164°, the ^{1}H- and ^{13}C-NMR spectra of which are listed in Tables 1 and 2.

Frs. 116-121 and 123-133 were combined (2.28 g) and re-chromatographed over silica gel D at reduced pressure, using hexane containing increasing amounts of EtOAc, in 200 mL fractions. Re-chromatography of frs. 22-27 (409 mg), eluted with hexane-EtOAc, 3:1, over Si gel D at reduced pressure using hexane containing increasing amounts of EtOAc in 10 mL fractions, afforded 4',5,7-tri-

Table 1. ^{1}H-NMR spectra of compounds **2a**, **2b** and **3b** ($CDCl_3$, 270 MHz).

H	2a	2b	2a and 2b J(Hz)	3b*
2	5.96(s)	6.00(s)		5.86,s
5	4.67(ddd)	5.92(ddd)	(9.7,2.2,2.2)	5.93,br (0.8)
6	4.59(dd)	4.58(dd)	(9.7,5.9)	4.97,brd (5,0.8)
7	3.67(dddd)	3.75(dddd)	(5.9,1.8,3.6,3.1)	4.17,dddd (5,2.5,3.3,3)
8	4.38(ddd)	4.37(ddd)	(2,11.7,1.8)	4.31,ddd (12,2.5,2.5)
9a	2.51(dd)	2.59(dd)	(13.7,11.7)	2.53,dd (15,12)
9b	2.37(dd)	2.37(dd)	(13.7,1.8)	2.35,dd (15,2.5)
13a	6.20(d)	6.24(d)	(3.6)	6.23,d (3.3)
13b	5.57(d)	5.54(d)	(3.1)	5.53,d (3.0)
14	1.54(s)	1.55(s)		1.53,s
15a	6.25(dd)	6.24(dd)	(2.2,1)	6.17,m
15b	6.00(m)	5.96(m)		6.07,m
3'a	6.00(m)	5.96(m)		6.01,m (1.5)
3'b	5.56(brs)	5.54(brs)		5.54,m (1.5)
4'	1.83(brs)	1.81(brs)		1.81,brs
Ac		2.07(s)		2.07,s

* Taken from Ref. 3 (270 MHz).

hydroxiflavanone (naringenin, 31.5 mg) in Fr. 27, identified by MS and ^{1}H-NMR spectrometry and by conversion to the triacetate[18].

Frs. 134-170 of the original chromatogram were combined and furnished 7 g of crude goyazensolide (**1a**). Recrystallization produced material, mp 172-174°, which was identical (mp., ^{1}H - NMR spectrum) to an authentic sample.

(5S, 6S*, 7R*, 8S*, 10S*)-1-Oxo-5-acetoxy-3,10-epoxy-8-methacryloxy-2,4(15),11(13)-germacratrien-6,12-olide* (**2b**). Acetylation of **2a** (30 mg) with Ac_2O-pyridine and a work-up in the usual manner afforded 28 mg of **2b**, mp. 216-218, CIMS m/z (rel.int.): 403 (M^++H, 100); ^{1}H - NMR spectrum in Table 1, ^{13}C-NMR spectrum in Table 2.

Extraction of Eremanthus eriopus

Aerial parts of *E. eriopus* Sch. Bip. ex Baker were collected at the flowering stage in July 1989 near Diamantina, Minas Gerais, and identified by Dr. Hermógenes de Freitas Leitão Filho of the Departamento de Botânica of Unicamp. The pulverized material (2.2 kg) was extracted with $CHCl_3$. The crude extract (46.86 g) which showed molluscicidal activity against adults and embryonic forms of *Biomphalaria glabrata* was chromatographed over silica gel at reduced pressure, 1 L fractions being collected as follows: Frs. 1-10 (hexane), 11-21, 22-53, 54-77, 78-95, 96-101, 102-117, 118-127, 128-137, 138-145, 146-152 (hexane-EtOAc: 97:3, 47:3, 9:1, 17:3, 4:1, 7:3, 3:2, 1:1, 1:3, 1:9, respectively), 153-157 (EtOAc), 158-162 (MeOH).

Frs. 35-40 (0.52 g) were combined and re-chromatographed over silica gel 60, 50 mL frs. being eluted as follows: Frs. 1-14 (hexane), 15-27, 28-37, 38-41, 42-53, 54 and 55 (hexane-EtOAc, 97:3, 19:1, 9:1, 4:1, 1:1, repectively), 56 (EtOAc) and 57 (MeOH). Fractions 29-32 (yellow crystals, 16 mg), upon recrystallization from hexane-EtOAc (1:1), afforded **5a**, identified by MS and ^{1}H-NMR spectrometry[28].

Frs. 41-50 (0.58 g) were combined and re-chromatographed in the same manner, 70 mL frs. being eluted as follows: Frs. 1-3 (hexane), 4-13, 14-18, 19-24 (hexane-EtOAc: 9:1, 4:1, 17:3, respectively) and subsequent increases in the percentage of EtOAc. Frs. 16-21 (yellow crystals, 35 mg), upon recrystallization from Et_2O, furnished **5b**, identified by MS and ^{1}H-NMR spectrometry[29,30].

Frs. 78-91 (2.01 g) were re-chromatographed in the same manner, 50 mL fractions being eluted as follows: Frs. 1-21 (hexane), 22-39, 40-57, 58-75, 76-93, 94-111, 112-192 (hexane-EtOAc: 97:3, 19:1, 23:2, 9:1, 22:3, 17:3, respectively) and subsequent increases in the percentage of EtOAc. Frs. 139-171 (570 mg) were combined, and recrystallization from Et_2O-EtOAc furnished 90 mg of **4**, identified by MS, ^{1}H-NMR and ^{13}C-NMR spectrometry and by comparison with authentic material.

Frs. 128-136 (1.46 g) were re-chromatographed on silica gel 60 in the usual manner. Hexane-EtOAc (1:1) eluted 236 mg of crude **1b**. Recrystallization of a portion from Et_2O afforded centratherin (**1b**), mp. 167-171° [lit mp.

Table 2. ^{13}C-NMR spectra of compounds **2a**, b and **3b** ($CDCl_3$, 67.89 MHz).

C	2a*	2b	3b**
1	203.7(s)	203.9(s)	204.0(s)
2	106.5(d)	106.9(d)	107.0(d)
3	185.2(s)	183.7(s)	185.1(s)
4	137.3(s)	135.5(s)	134.0(s)
5	74.0(d)	73.1(d)	75.0(d)
6	85.0(d)	82.6(d)	83.8(d)
7	51.2(d)	51.6(d)	46.2(d)
8	70.6(d)	71.0(d)	72.1(d)
9	45.2(d)	45.0(d)	44.7(d)
10	90.2(s)	90.4(s)	90.4(s)
11	135.4(s)	135.2(s)	134.0(s)
12	167.6(s)	167.9(s)	168.2(s)
13	124.7(t)	124.6(t)	124.0(t)
14	21.2(q)	21.1(q)	21.1(q)
15	123.1(t)	121.4(t)	130.6(t)
1'	166.8(s)	166.7(s)	166.9(s)
2'	133.0(s)	132.5(s)	133.5(s)
3'	126.6(t)	126.6(t)	126.5(t)
4'	17.9(q)	17.9(q)	18.0(q)
1''		169.7(s)	169.5(s)
2''		20.6(s)	21.4(s)

* The multiplicity of the signals was deduced by comparative analysis of the proton noise-decoupled (PND) ^{13}C-NMR and DEPT (Distortionless Enhancement by Polarization Transfer) spectra.
** Taken from Ref. 3.

95-110°[12], 165-166°[13]]. The ^{1}H- and ^{13}C-NMR spectra matched the spectra recorded in the literature[12,13]. Acetylation with Ac_2O-Py in the manner described for **2a** and recrystallization from Et_2O-acetone (1:1) afforded **3d** (isocentratherin acetate). CIMS m/z: (rel. int.) 417 (M^+ + H, 100), 357 (34.3); ^{1}H- and ^{13}C-NMR spectra were identical with data in the literature[27].

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by the reaction of **3c** with acetic anhydride is incorrectly given as **1d** instead of **3d**. For the correct structure see Ref. 27. Authentic **1c** and **1d** have recently been isolated from *Lychnophora diamantinana*[9].

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