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A new α-methylene γ-lactone sesquiterpene from *Hedyosmum arborescens*

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Abstract

A new sesquiterpene lactone, 7α,10α-epoxy-1α(H),5α(H)-guaia-3,11(13)-dien-8α,12-olide, was isolated from the leaves of *Hedyosmum arborescens.* The structure of this unusual 7,10-epoxy-guaianolide was determined by spectroscopic methods, particularly one- and two-dimensional ^{1}H and ^{13}C NMR.

Keywords: Hedyosmum arborescens; α-Methylene-γ-lactone; Sesquiterpenoids; Guaianolide

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1. Introduction

Hedyosmum arborescens Swartz belongs to the Chloranthaceae, a small family with four genera and around 70 species occurring in tropical and subtropical areas (American and east Asian tropics, Polynesia, New Zealand and Madagascar) [1].This native plant grows in the elfin woodlands and wet mountain forests. In the West Indies, *H. arborescens* ranges from Cuba, Hispaniola, and Jamaica to Puerto Rico and the Lesser Antilles [2].

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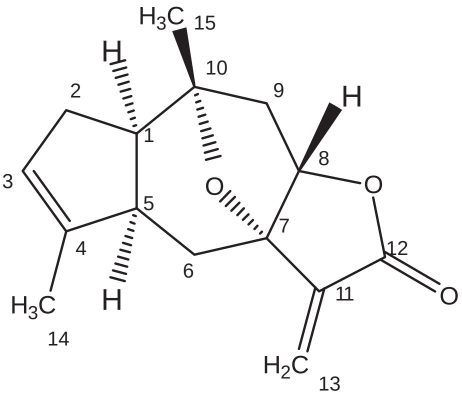

Fig. 1. 7,10 Epoxy-hedyosminolide (**1**).

H. arborescens is used in folk medicine in Jamaica as an antispasmodic, or for digestive and cold treatments [3].

Previous phytochemical investigations on this family have shown the presence of sesquiterpenoids and flavonoid glycosides [4–10]. To our knowledge, no phytochemical work on *H. arborescens* has been reported. The present communication describes the isolation and characterisation of a new guaianolide called hereafter 7,10-epoxy-hedyosminolide (**1**) (Fig. 1) from the petrol ether extract of aerial parts.

2. Experimental

2.1. General

Optical rotation: Perkin Elmer 341. IR: NICOLET Nexus 670 FTIR. NMR: Bruker DRX AVANCE 400 MHz. MS: FOCUS DFQ GC-MS Thermo Electron (EIMS) and MAT 95S Thermo Electron (HREIMS) spectrometers. UV: CARY 300 BIO UV-visible spectrometer.

2.2. Plant material

Leaves of *H. arborescens* were collected in the Soufrière forest in Basse Terre, Guadeloupe, French West Indies, in May 2001. The plant was identified by J. Fournet and a voucher specimen as FOURNET-1756 was deposited in the Herbarium of the National Institute of Agronomic Research (INRA-CRAAG), Guadeloupe, FWI.

2.3. Extraction and isolation

The powdered leaves (1.8 kg) were extracted with petrol ether (9 l) for one day at r. t. The combined extracts were evaporated in vacuo to yield 31.9 g of a gummy dark green residue. The petrol ether soluble part (8.6 g) of an aliquot of this extract (10.4 g) was Si-gel

Table 1
^{1}H and ^{13}C NMR data for **1** (400 and 125 MHz, $CDCl_3$+two drops of py-d_5, *J* in Hz and δ in ppm)

C	δ_C	δ_H	HMBC-correlations C→H
1	44.3 *d*	2.39[a]	1→15, 1→6
2	34.2 *t*	2β 1.85, *bd* (16.4) 2α 2.50, *bdd* (7.4, 16.4)	2→15
3	125.3 *d*	5.37, *br s*	3→14
4	140.7 *s*		4→6, 4→14
5	43.3 *d*	2.97[a]	5→6, 5→14
6	27.6 *t*	6β 1.91, *bd* (14.0) 6α 2.30, *dd* (8.7, 14.0)	
7	82.2 *s*		7→13, 7→9, 7→6
8	86.0 *d*	4.47, *dd* (3.2,7.4)	8→6, 8→15
9	41.0 *t*	9β 2.46,[a] *dd* (7.4, 13.7) 9α 1.66, *ddd* (1.2, 3.2, 13.7)	9→1, 9→15
10	85.8 *s*		
11	138.2 *s*		
12	169.6 *s*		12→13
13	125.0, *t*	13a 5.91 13b 6.40	
14	15.0 *q*	1.72[a]	
15	26.1 *q*	1.33, *d* (1.2)	

[a] Overlapping signals.

CC with petrol ether/EtOAc mixtures. One of the fractions eluted with petrol ether — EtOAc (75 : 25) was further subjected to CC on charcoal, then purified by PTLC using CH_2Cl_2/MeOH (95/5) to afford **1** (162 mg).

7,10-Epoxy-hedyosminolide [7α,10α-epoxy-1α(H),5α(H)-guaia-3,11(13)-dien-8α,12-olide] (**1**): light yellow oil; $[\alpha]_D^{20}$ +23.74° (c 0.02, MeOH); UVmax (MeOH): 198 (logε 5.36) nm; IR bands ($CDCl_3$): 1740 cm^{-1}; EIMS *m/z*: 246 [M^+](7%), 188 (6%), 91 (6%), 80 (100%), 43 (14); HREIMS *m/z* (relative intensity): 246.1250 [M]. Calc. for $C_{15}H_{18}O_3$ 246.1250.

^{1}H NMR and ^{13}C NMR data: see Table 1.

3. Results and discussion

7,10-Epoxy-hedyosminolide (**1**) was isolated as a light yellow oil. Its infrared spectrum exhibited a characteristic absorption of conjugated ethylenic γ lactone at 1740 cm^{-1}. HREIMS provided the molecular ion at *m/z* 246.1250 from which the molecular formula $C_{15}H_{18}O_3$ was calculated. The ^{13}C NMR spectrum indicated the presence of 15 carbon atoms. The presence of a conjugated lactone moiety was suggested by signals at δ 169.6, 125.0 and 138.2. The presence of an additional double bond was deduced from the ^{13}C NMR spectra which exhibited two other peaks at δ 125.3 and 140.7 Three peaks at δ 82.8, 86.0 and 85.8 could be assigned to three carbons bearing oxygen; seven other signals were assigned to methylene and methyl carbons. From the DEPT experiment, it was determined that this compound possessed two methyl groups, four methylene, four methines and three quaternary carbon including two carbon atoms bearing oxygen. Connectivity of some ^{13}C with relevant protons was deduced from HMBC experiments (Table 1). The HSQC spectrum was used to connect the protons to the relevant carbons.

The lack of multiplicity for the exocyclic methylene protons at δ 6.40 and δ 5.91 indicated that no hydrogen was connected to C-7. The double doublet at δ 4.47 (J 3.2 and 7.4 Hz) was assigned to the oxymethine proton H-8 coupled to H-9 methylenic protons. The presence of the 3,4 double bond was confirmed by the presence of a broad singlet at δ 5.37, which was assigned to H-3. The broad 3H singlet at δ 1.72 was assigned to a methyl on a double bond. The CH_3 doublet at δ 1.33 was assigned to 15-CH_3 according to a long range with 9α proton. The signal at δ 2.30 was assigned to equatorial proton at C-6α.

The HSQC spectrum allowed the assignment of signals at δ 2.50 and 2.46 to the protons at C-2α and C-9β, respectively. The TOCSY experiment performed on the signal at 4.47 ppm confirmed the assignment of C-9 equatorial proton. In the same range of the proton spectrum, the HSQC spectrum allowed to assign the signal at δ 2.39 to H-1.

Careful examination of the 1D NOE and 2D NOESY data was necessary to access to the relative configuration. The orientation of H-1, H-5, H-8 and C-10 methyl protons were determined as α, α, β and β, respectively, by cross-peaks between H-1 and H-5, H-1 and H-15 and the absence of cross-peak between H-1 and H-8. The NOE experiment showed that irradiation of H-8 enhanced the signal of 9β at δ 2.46 and with a minor magnitude, the signal of 6β at δ 1.91. The cross-peaks of the NOESY experiment showed that irradiation of the axial H-6 enhanced the equatorial H-6? but not the signal of H-5 at δ 2.97. Furthermore, irradiation of the axial H-6 signal enhanced the signal of the equatorial H-6 and H-1, while the irradiation of H-1 at δ 2.39 enhanced the methyl signal at δ 1.33 and the H-5 signal at δ 2.97. Furthermore, irradiation of H-6α enhanced the signal of H-6, H-5 and H-13a. Since no hydrogen was connected to C7, the NOE experiments did not allow to determine the *cis*- or *trans*-fused configuration of the cyclopentanone ring. Comparison of the 1D-NMR data with those previously reported for 7α,10α-epoxy-1,5,11α*H*,8β*H*-guaia-3-en-8,12-olide, synthesized in a seven step procedure [11] from santonin (a natural eudesmanolide), allowed to identify the structure of (**1**) to be 7α,10α-epoxy-1α(H),5α(H)-guaia-3,11(13)-dien-8α,12-olide. This compound is now named 7,10-epoxy-hedyosminolide.

To our knowledge, the 8,12 guaianolides have never been isolated from species of Chloranthaceae but have been reported, in species of several Asteraceae, Compositae or other families [12–26] and from species of marine origin [27,28].

Besides this new guaianolide, two other known compounds were identified on the basis of spectral evidences and comparison of physical data with literature values: spathulenol [29] and sitosterol [30].

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