Pergamon

0031-9422(95)00520-X

Phytochemistry, Vol. 40, No. 5, pp. 1575–1576, 1995

0031-9422/95 $9.50 + 0.00

POLYODONINE, A PREFURANIC LABDANE DITERPENE FROM *MARRUBIUM POLYDON*

NATIQ A. R. HATAM, ANDREA PORZEL* and KARLHEINZ SEIFERT†

Al al-Byat University, Chemistry Department, Faculty of Arts and Science, Mafraq, Jordan; *Institute for Plant Biochemistry, Weinberg 3, D-6120 Halle/Saale, Germany; †University of Bayreuth, Organic Chemistry I/2, NW II, D-95440 Bayreuth, Germany

(*Received* 18 *May* 1995)

DEDICATED TO PROF. H. J. BESTMANN ON THE OCCASION OF HIS SEVENTIETH BIRTHDAY

Key Word Index—*Marrubium polydon*; Labiatae; prefuranic labdane diterpene; polyodonine.

Abstract—The new prefuranic labdane diterpene 9α,13*R*;15,16-diepoxy-12-oxo-labd-14-en-19,6β-olide (polyodonine) has been isolated from the aerial parts of *Marrubium polydon*. The known 3-*O*-(β-D-glucopyranosyl)-3β-hydroxystigmast-5-ene and the flavone glucosides 7-*O*-[β-D-(6-*O*-*p*-coumaroyl)-glucopyranosyl]-apigenin and 7-*O*-[β-D-(3,6-di-*O*-*p*-coumaroyl)-glucopyranosyl]-apigenin were also obtained from the same source. The structure of polydonine has been determined primarily on the basis of NMR spectroscopy.

INTRODUCTION

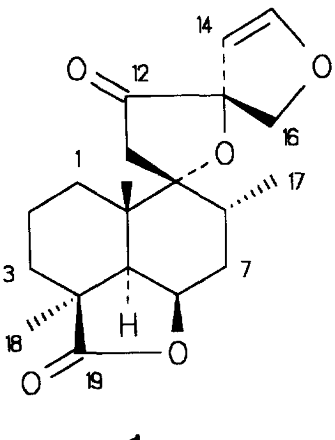
Marrubium polydon Boiss. grows wild in the Sulaimaniyah province in the north of Iraq. The sesquiterpene lactone and alkaloid fractions from this plant show antimicrobial activity [1]. The labdane diterpenes peregrinine and preperegrinine have been obtained from the aerial parts of *M. friwaldskyanum* Boiss. [2]. In this paper, we report on the isolation and structural elucidation of the new labdane diterpene polyodonine (**1**).

RESULTS AND DISCUSSION

The methanolic extract of the dried powdered aerial parts of *M. polydon* yielded **1**, 3-*O*-(β-D-glucopyranosyl)-3β-hydroxystigmast-5-ene (**2**) [3], 7-*O*-β-D-[(6-*O*-*p*-coumaroyl)-glucopyranosyl]-apigenin (**3**) [4] and 7-*O*-β-D-[(3,6-di-*O*-*p*-coumaroyl)-glucopyranosyl]-apigenin (**4**) [5].

The IR spectrum of **1** showed γ-lactone (1765 cm^{-1}), ketone (1745 cm^{-1}) and enol-ether (3090, 1600 cm^{-1}) absorptions. The HR mass spectrum gave a molecular ion peak at *m*/*z* 346.1781, indicating the molecular formula $C_{20}H_{26}O_5$. The ^{1}H NMR spectrum (500 MHz, $CDCl_3$) showed the presence of two tertiary methyl groups and one secondary methyl group characterized by the singlets at δ1.32 (H_3-18) and 1.07 (H_3-20), and the doublet at δ0.72 ($J_{8\beta,17\alpha} = 6.4$ Hz, H_3-17). Signals at δ2.37 and 2.80 ($J_{11A,11B} = 18.4$ Hz), and 4.33 (*d*, $J_{16A,16B} = 10.7$ Hz) and 4.47 (*dd*, $J_{16A,16B} = 10.7$ Hz, $J_{15,16B} = 0.5$ Hz) were attributed to the two AB systems H-11$_A$/H-11$_B$ and H-16$_A$/H-16$_B$. The signals of the olefinic and methine protons were observed at δ4.99 (*d*, $J_{14,15} = 2.5$ Hz, H-14) and 6.62 (*dd*, $J_{14,15} = 2.5$ Hz, $J_{15,16B} = 0.5$ Hz, H-15), and δ2.28 (*d*, $J_{5\alpha,6\alpha} = 4.4$ Hz, H-5) and 4.75 (*dd*, $J_{5\alpha,6\alpha} = 4.4$ Hz, $J_{6\alpha,7\alpha} = 6.0$ Hz, H-6).

After irradiation of H_3-17 in a one-dimensional NOE difference experiment, the NOEs to H-16$_A$ and H-16$_B$ could be detected, whereas no NOE was found to H-14. ROESY cross-peaks between H_3-17 and H-16$_A$ indicated the close spatial proximity of these protons. This behaviour clearly established [2, 6] the *R* configuration of the C-13 centre of **1**. Irradiation of H_3-20 and H_3-18 in two NOE difference experiments caused positive enhancements of H-11$_A$, H-11$_B$, H-8β, H-1$_\beta$ and H-5$_\alpha$, H-6$_\alpha$. The through-space connectivities of the protons H-11$_B$/H-1$_\beta$,



1

---

†Author to whom correspondence should be addressed.

Table 1. ^1H and ^{13}C NMR spectral data for polyodonine (**1**) in $CDCl_3$

C	δ_C	δ_H
		H_α/H_β
1	28.3	1.71/1.31
2	17.7	1.59/1.83
3	28.1	2.17/1.52
4	44.0	
5	44.3	2.28 (*d*, $J_{5\alpha,6\alpha} = 4.4$ Hz)
6	75.5	4.75 (*dd*, $J_{5\alpha,6\alpha} = 4.4$ Hz, $J_{6\alpha,7\alpha} = 6.0$ Hz)
7	31.1	1.73/2.23
8	31.3	2.15
9	84.6	
10	38.5	
11	40.0	A 2.37/B 2.80 (*d*, $J_{11A,11B} = 18.4$ Hz)
12	212.5	
13	92.7	
14	102.7	4.99 (*d*, $J_{14,15} = 2.5$ Hz)
15	151.4	6.62 (*dd*, $J_{14,15} = 2.5$ Hz, $J_{15,16B} = 0.5$ Hz)
16	77.9	A 4.33 (*d*, $J_{16A,16B} = 10.7$ Hz) B 4.47 (*d*, $J_{16A,16B} = 10.7$ Hz, $J_{15,16B} = 0.5$ Hz)
17	15.6	0.72 (*d*, $J_{8\beta,17\alpha} = 6.4$ Hz)
18	22.5	1.32 (*s*)
19	183.4	
20	23.7	1.07 (*s*)

H_3-18/H-5_α, H_3-18/H-6α, H-5α/H-6α and H-14/H-1α could be detected by ROESY cross-peaks.

The signals of the protonated carbons were assigned from the ^1H–^{13}C heteroscalar two-dimensional NMR spectrum (HMQC), and the quaternary carbon signals from the proton detected multiple-bond ^1H–^{13}C correlation spectrum (HMBC). All the data are consistent with the structure of 9α,13*R*;15,16-diepoxy-12-oxo-labd-14-en-19,6β-olide (polyodonine, **1**).

EXPERIMENTAL

General. NMR (Table 1): 500 MHz (^1H), 125 MHz (^{13}C), δ in ppm. CC: silica gel (0.063–0.2 mm) and Sephadex LH-20. TLC: silica gel (0.25 mm).

Isolation. Plants of *M. polydon* were collected from the Sulaimaniyah province in the north of Iraq in May 1987 and were identified by the Iraqui National Herbarium, Botany Directorate of Abu-Graib. Voucher specimens are kept in the Herbarium of the Biological Research Centre, Department of Pharmacognosy and Pharmacology, Baghdad. Dried powdered aerial parts (400 g) were extracted with MeOH (20°). The MeOH extract was evapd under red. pres., the residue successively partitioned between H_2O and C_6H_6–Et_2O (1:1) and the residue of the C_6H_6–Et_2O extract chromatographed on silica gel, eluting with CH_2Cl_2 and CH_2Cl_2–MeOH (19:1) to give **1** (25 mg) and **2** (20 mg). CC on Sephadex LH-20, eluting with MeOH, yielded **3** (31 mg) and **4** (4 mg).

Polyodonine (**1**). $C_{20}H_{26}O_5$, M_r 346.43. Mp 198–199°; $[\alpha]_D^{23}$ + 79° (*c* 0.1, $CHCl_3$); IR ν_{max}^{KBr} cm^{-1}: 3090 (enol-ether), 1765 (C=O, lactone), 1745 (C=O, ketone), 1600 (enol-ether); MS 70 eV *m/z* (rel. int.): 346.1781 (calc. for $C_{20}H_{26}O_5$ 346.1781) $[M]^+$ (16), 300 (4), 234 (34), 219 (16), 189 (22), 175 (29), 119 (25), 109 (100), 95 (37).

REFERENCES

1. Jawad, A. M., Jaffer, H. J., Al-Naib, A. and Naji, A. (1988) *Int. J. Drug Res.* **26**, 185.
2. Savona, G., Bruno, M. and Rodriguez, B. (1984) *Phytochemistry* **23**, 191.
3. Fang, J.-M., Wang, K.-C. and Cheng, Y. S. (1991) *Phytochemistry* **30**, 3383.
4. Rao, L. J. M., Kumari, G. N. K. and Rao, N. S. P. (1985) *J. Nat. Prod.* **48**, 150.
5. Rao, L. J. M., Kumari, G. N. K. and Rao, N. S. P. (1982) *Heterocycles* **19**, 1655.
6. Rodriguez, B. and Savona, G. (1980) *Phytochemistry* **19**, 1805.