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PIPERDARDINE, A PIPERIDINE ALKALOID FROM *PIPER TUBERCULATUM**

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Key Word Index—*Piper tuberculatum*; Piperaceae; stem; piperidine alkaloid; (*E*,*E*)-1-[7-(1,3-benzodioxol-5-yl)-1-oxo-2,4-heptadienyl]piperidine; piperdardine; piperettine; piperine; NMR.

Abstract—A new piperidine alkaloid 1-[7-(1,3-benzodioxol-5-yl)-1-oxo-2, 4-heptadienyl]piperidine, piperdardine, was isolated from hexane and chloroform extracts of *Piper tuberculatum* var. *tuberculatum*. A combination of 1D and 2D NMR, together with other spectroscopic methods, led to the unambiguous assignments of all protons and carbons of the molecule. Copyright © 1997 Elsevier Science Ltd

INTRODUCTION

The genus *Piper* is well known for its use as a food flavouring agent and also for its various physiologically active principles [1, 2]. Herein, we describe the isolation and structural elucidation of 1-[7-(1,3-benzodioxol-5-yl)-1-oxo-2, 4-heptadienyl]piperidine, a new piperidine alkaloid, from hexane and chloroform extracts of the stem of *P. tuberculatum*, to which we have given the trivial name, piperdardine (**1**). The plant is used in the Brazilian state of Paraiba as a sedative and as an antidote for snake-bite and is locally known as 'pimenta d'arda' [3, 4]. We also give for the first time 2D NMR-based unambiguous assignments for all the protons and carbons of piperettine (**2**) [5] and piperine (**3**) [6].

RESULTS AND DISCUSSION

Powdered stems of *P. tuberculatum* were extracted successively with hexane, chloroform and ethanol. From the hexane and chloroform extracts, a mixture of various compounds was isolated. Using column chromatography and preparative TLC (continuous run for 5 hr), eluted with hexane–ethyl acetate (4:1), compound **1** was isolated. Compound **1** was a pale yellow oil and its IR spectrum showed bands at 2932, 2855, 1621, 1489, 1442 and 1247 cm^{-1}. HREI mass spectrometry gave the $[M]^+$ at *m/z* 313.1646, which is coherent with the proposed molecular formula of $C_{19}H_{23}NO_3$. Other important fragments observed were at *m/z* 84, which is indicative of the presence of a piperidine ($C_5H_{10}N$) moiety [7], 112, 135, 201 and 285. An NMR study using ^1H, ^{13}C HMBC (optimized for $J = 7$ Hz) and ^1H–^1H COSY 45 led to the unambiguous assignments of all protons and carbons (Table 1). The NMR data for **1**, showed signals typical of an acylpiperidine and were very similar to those of (**2**) (Table 2) except that one double bond was saturated. The methylene protons H_2-7′, the triplet at δ 2.66, showed long-range coupling in the HMBC spectrum with the carbons 4″, 5″ and 6″ of the piperonyl ring. This methylene also showed long-range coupling to C-6′ and C-5′ of the heptadienoyl chain. These data placed this methylene (δ_H 2.66/δ_C 35.2) at the benzylic position of the piperonyl group, and the ^1H–^1H COSY and HMBC correlations (Table 1) allowed unambiguous assignments of the structure as the new natural product 1-[7-(1,3-benzodioxol-5-yl)-1-oxo-2,4-heptadienyl]piperidine, to which we have given the trivial name, piperdardine (**1**).

The NMR data for the related acylpiperidine compounds piperettine (**2**) and piperine (**3**), based on 2D experiments, are included (Table 2) for comparative purposes; full NMR assignments of these compounds are given for the first time [8].

EXPERIMENTAL

CC was carried out on silica gel. Prep. and analyt. TLC (continuous run) were carried out on silica gel 60 PF_{254}. Spots were detected using UV light and also after spraying with H_2SO_4–vanillin or Dragendorff reagent. IR spectra was obtained in $CHCl_3$. HREIMS was obtained using a direct insertion probe at 70 eV. NMR data were obtained at 400 MHz for ^1H and

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

	H	^{1}J	^{2}J	^{3}J
2	3.48 2H *br s*	43.4	—	—
3	1.45–1.60 2H *m*	25.7	24.9	—
4	1.61–1.70 2H *m*	24.9	25.7, 26.9	43.4, 47.1
5	1.45–1.60 2H*m*	26.9	24.9	—
6	3.61 2 H *br s*	47.1	—	—
1′	—	165.8	—	—
2′	6.26 1H *d* (J = 14.8 Hz)	119.3	165.8	129.7
3′	7.21 1H *dd* (J = 10.8, 14.8 Hz)	142.7	119.3, 129.7	141.1, 165.8
4′	6.18 1H *dd* (J = 10.8, 15.1 Hz)	129.7	142.7	35.2, 119.3
5′	6.06 1H *dt* (J = 7.0, 15.1 Hz)	141.1	35.2	35.2, 142.7
6′	2.42 2H *dt* (J = 7.0, 7.3 Hz)	35.2	35.2	129.7, 135.4
7′	2.66 2H *t* (J = 7.3 Hz)	35.2	35.2, 135.4	109.0, 141.1, 121.4
2″	5.92 2H *s*	101.0	—	145.9, 147.8
3a″	—	147.8	—	—
4″	6.66 1H *d* (J = 1.5 Hz)	109.0	147.8	35.2, 121.4, 145.9
5″	—	135.4	—	—
6″	6.61 1H *dd* (J = 1.5, 7.9 Hz)	121.4	—	35.2, 109.0, 145.9
7″	6.70 1H *d* (J = 7.9 Hz)	108.4	145.9	135.4, 147.8
7a″	—	145.9	—	—

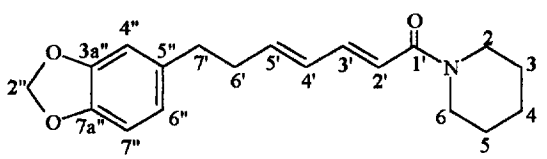
Table 2. ^{13}C and ^{1}H NMR ($CDCl_3$) data for piperettine (**2**) and piperine (**3**)

	Piperettine		Piperine	
	H	C	H	C
2	3.48 2H *br s*	43.4	3.48 2H *br s*	43.0
3	1.48–1.60 2H *m*	25.7	1.49 2H *m*	25.7
4	1.61–1.70 2H *m*	24.8	1.56 2H *m*	24.5
5	1.48–1.60 2H *m*	26.8	1.49 2H *m*	26.9
6	3.61 2H *br s*	47.0	3.48 2H *br s*	47.1
1′	—	165.5	—	165.2
2′	6.34 1H *d* (J = 14.6 Hz)	120.2	6.36 1H *d* (J = 14.6 Hz)	120.0
3′	7.33 1H *dd* (J = 11.4, 14.6 Hz)	142.4	7.31 1H *m*	142.3
4′	6.39 1H *dd* (J = 11.4, 14.0 Hz)	130.5	6.64 1H *m*	125.3
5′	6.62 1H *dt* (J = 14.0, 10.0 Hz)	139.2	6.65 1H *m*	138.0
6′	6.64 1H *dd* (J = 15.0, 10.0 Hz)	126.8	—	—
7′	6.57 1H *t* (J = 15.0 Hz)	135.4	—	—
2″	5.94 2H *s*	101.3	5.86 2H *s*	101.2
3a″	—	147.9	—	148.1
4″	6.94 1H *d* (J = 1.6 Hz)	105.6	6.88 1H *d* (J = 1.6 Hz)	105.5
5″	—	131.6	—	130.9
6″	6.84 1H *dd* (J = 1.6, 8.0 Hz)	122.1	6.79 1H *dd* (J = 1.6, 8.0 Hz)	122.3
7″	6.74 1H *d* (J = 8.0 Hz)	108.6	6.67 1H *d* (J = 8.0 Hz)	108.3
7a″	—	147.9	—	148.0

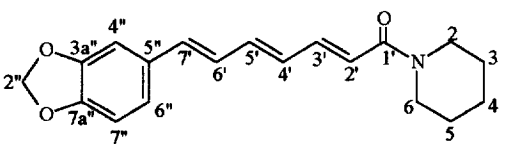
100 MHz for ^{13}C. Chemical shifts are reported in ppm relative to the solvent ($CDCl_3$) at 27°.

Plant material. Stems of *P. tuberculatum* Jacq. var. *tuberculatum* were collected at João Pessoa, Paraiba, Brazil, in September 1993. A voucher specimen (Agra et Locatelli 2405) has been deposited at the Herbarium of the Universidade Federal da Paraíba.

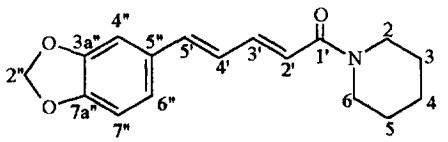
Extraction and isolation. Dried ground stems were extracted successively in a Soxhlet apparatus with hexane, $CHCl_3$ and EtOH. The hexane extract was



1



2



3

subjected to CC, eluting with hexane, hexane–EtOAc, EtOAc and EtOAc-MeOH; 247 frs were collected. Frs 151–164, eluted with hexane–EtOAc (4:1) were subjected to further CC using the same eluent conditions; 42 frs were collected. Frs 25–34, eluted with hexane–EtOAc (9:1), were subjected to a prep. TLC continuous run for 5 hr, eluting with hexane–EtOAc (4:1); fr. 4.1 was compound **1**. The $CHCl_3$ extract was subjected to CC, eluting with hexane, hexane–$CHCl_3$, $CHCl_3$ and $CHCl_3$–MeOH; 286 frs were collected. Frs 104–105, eluted with $CHCl_3$–MeOH (19:1) were subjected to a second CC, eluting with $CHCl_3$ and $CHCl_3$–MeOH, from which 52 frs were collected. Compound **1** was also obtained from this column (R_f 0.46 on silica gel: EtoAc).

Piperdardine (**1**). Pale yellow oil. IR ν_{max} cm^{-1}: 2932, 2855, 1621, 1489, 1442, 1247. Found $[M]^+$ *m/z* 313.1646. EIMS *m/z* (rel. int.): 84 (26), 112 (20), 135 (100), 201 (25), 285 (12), 313 (53). NMR: Table 1.

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