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5-Methyl coumarins and a new phenol from *Nassauvia pyramidalis* and *N. digitata*

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Abstract

The aerial parts of *Nassauvia pyramidalis* contain 5′epi-triptiliocoumarin and a new phenolic compound. *N. digitata* afforded the 5′-epi-triptiliocoumarin and triptiliocoumarin itself. © 1999 Elsevier Science Ltd. All rights reserved.

Keywords: Nassauvia pyramidalis; *N. digitata*; Asteraceae; 5′Epi-triptiliocoumarin; Triptiliocoumarin and 1-(2-hydroxy-6-methylphenyl)-3-ethenyl-3,7,11-trimethyl-6,7-dodecadienone

1. Introduction

The genus *Nassauvia* (family Asteraceae) is placed in the subtribe Nassauviinae and is represented by 37 species distributed in the Andes from S. Bolivia to Tierra del Fuego and the Malvinas Islands (Cabrera, 1982). In Chile there are 24 species, ten of which have been investigated chemically (Bittner, Jakupovic, Bohlmann, Grenz & Silva, 1988; Bittner, Jakupovic, Bohlmann & Silva, 1988, 1989; Bittner, Silva, Rozas, Papastergiou 1989; Bittner, Silva, Rozas, Papastergiou & Jakupovic, 1994; Pritschow, Jakupovic, Bohlmann, Bittner 1994; Pritschow, Jakupovic, Bohlmann, Bittner & Niemeyer, 1991; Zdero & Bohlmann, 1990; Zdero, Bohlmann, King & Robinson, 1986). As with many other genera of the tribe, they are characterized by the occurrence of isocedrenes and 4-hydroxy-5-methyl coumarins. Continuing with our studies of Chilean Asteraceae we have examined *Nassauvia pyramidalis* (Bittner et al., 1994) and *N. digitata* (Pritschow et al., 1991).

2. Results and discussion

The aerial parts of *Nassauvia pyramidalis* Meyen afforded the coumarin **1** and the phenolic compound **3**. The ^{1}H-NMR spectrum of **1** (Table 1) displayed a near identical signal pattern to that of triptiliocoumarin **2** (Bittner et al., 1988), first described as a constituent of *Triptilion benaventei* (Bittner et al., 1988). Small differences in chemical shifts of several signals indicated the possibility that **1** was a diastereomer of **2**. This assumption was confirmed by the analysis of NOE difference spectra. In particular the effects between the 1,4 positioned H-5′ and H-2′ required their *syn*-axial orientation, thus defining a 3′- or, more likely, 5′-epimer of triptiliocoumarin. The C-5′ epimers are more likely to be produced if the hetero bond formation of the pyran ring (between C-5′ and the oxygen at C-4) represents the last step during the biosynthesis of the pyranocoumarins. The precursor, a 3-3′ adduct between the linear sesquiterpene, nerolidol (Bates, Gale & Gruner, 1963), and 4-hydroxy-5-methylcoumarin, is presumably entering the subsequent steps (oxidation at C-5 and pyran formation) as a single enantiomer. However, as long as the absolute configurations of both compounds are unknown this problem remains unresolved.

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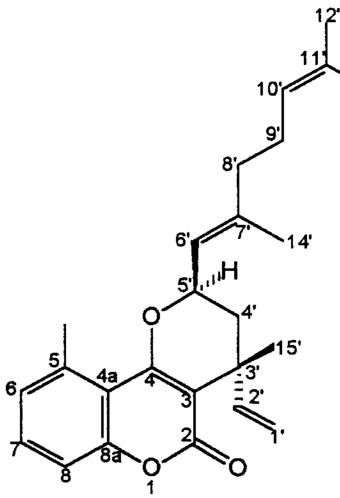
The aromatic signals in the ^{1}H-NMR spectrum of **3** (Table 2), likewise in the spectra of 5-methyl coumarins, indicated a 1,2,3-trisubstituted aromatic compound. In addition to an aromatic methyl group, a D_2O-exchangeable proton occurring as a singlet at δ 10.34 indicated a phenolic hydroxy group and thus excluded a coumarin base skeleton. Furthermore, the spectrum displayed a series of signals resembling those of nerolidol. Similar phenolic compounds derived by degradation of the pyrone ring and loss of C-2 from a coumarin-terpenoid precursor have already been isolated from the species of the tribe Mutisiae (Zdero, Bohlmann, King & Robinson, 1986). In fact, the spectrum was very similar to that of norbrachycoumarin (Zdero et al., 1986), a monoterpene-coumarin adduct. The molecular composition, $C_{24}H_{34}O_2$, determined by high resolution mass spectrum spectrocopy indicated a prenyl homologue of norbrachycoumarin. The structure was finally confirmed by spin decoupling NMR experiments.

N. digitata Wedd. also gave the isomer of triptiliocoumarin (**1**) and triptiliocoumarin (**2**) itself.

3. Experimental

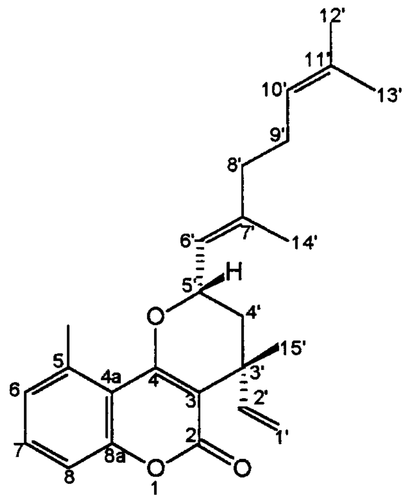
Leaves, stems and flowers of *N. pyramidalis* were collected on January 26, 1996, by German Duran and Patricio Peñailillo in Laguna del Maule, 10 km from Paso Pehuenche, 2220 m altitude, Chile; voucher No. 132470 was deposited in herbarium CONC, Concepción, Chile, whereas the leaves, stems and flowers of *N. digitata* were collected on January 29, 1996, by German Duran 1996, in Termas de Chillán, 1 km from the fumaroles, 2200 m altitude, Chile; voucher No. 132475 was deposited in herbarium CONC, Concepción, Chile.

250 g of air-dried *N. pyramidalis* was extracted at room temperature with a mixture of hexane–EtOAc–MeOH (1:1:1) to give 39 g of crude extract. After removal of waxy material by treatment with MeOH at −20°C the filtrate was evaporated and the residue (16 g) was separated by column chromatography (silica gel) to give 10 fractions: 1 (hexane), 2 (hexane/EtOAc, 11:1), 3 (hexane/EtOAc, 9:1), 4 (hexane/EtOAc, 3:1), 5 (hexane/EtOAc, 1:1), 6 (hexane/EtOAc, 1:3), 7



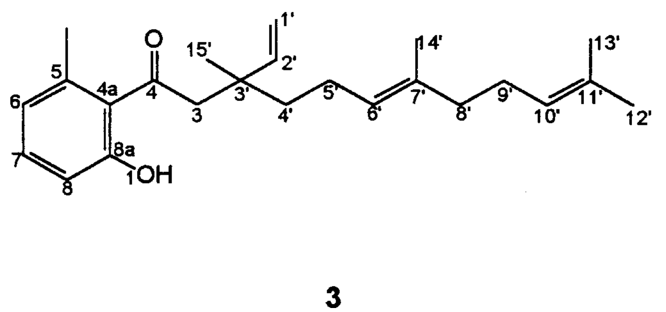
1

5′-epitriptiliocoumarin



2

triptiliocoumarin



3

Table 1
^{1}H-NMR spectral data, NOE results and ^{13}C-NMR spectral data for compound **1** (400 MHz and 100 MHz, $CDCl_3$)

H	**1**	NOE	C	**1**
6	7.00 brd		2	164.1 s
7	7.32 dd		3	104.8 s
8	7.14 brd		4	160.7 s
9	2.64 brs	H-6(10), H-6′(2), H-14′	4a	114.8 s
1′c	5.19 d		5	132.0 s
1′t	4.94 d		6	127.3 d
2′	6.00 dd		7	130.6 d
$4_1'$	1.87 dd		8	114.8 d
$4_2'$	1.79 dd		8a	153.9 s
5′	4.84 ddd	H-1′t(2), H-2′(2), H-14′	9	23.6 q
6′	5.37 brdq	H-9, H-8′	1′	114.3 t
8′	2.12 m		2′	144.4 d
9′	2.12 m		3′	37.8 s
10′	5.10 m		4′	42.2 t
12′	1.70 brs		5′	71.7 s
13′	1.62 brs		6′	122.4 d
14′	1.70 s	OH(5), $4_1'$(4)	7′	141.7 s
15′	1.58 s	H-1′t(5), H-2′(1), $4_1'$(3), $4_2'$(4)	8′	39.3 t
			9′	26.1 t
			10′	123.5 d
			11′	137.0 s
			12′	25.7 q
			13′	17.7 q
			14′	25.6 q
			15′	16.7 q

J (Hz): 6, 7 = 7, 8 = 8; 1′c, 1′t = 1; 1′c, 2′ = 10.5; 1′t, 2′ = 17.5; $4_1'$, $4_2'$ = 14; $4_1'$, 5′ = 2.5; $4_2'$, 5′ = 11.5; 5′, 6′ = 8.5; 6′, 14′ = 1.5

Table 2
^{1}H-NMR spectral data for **3** (400 MHz, $CDCl_3$, TMS as internal standard)[a]

H	**3**
3_1	3.00 d
3_2	2.94 d
6	6.71 brd
7	7.22 dd
8	6.79 brd
9	2.53 brs
1′c	4.98 dd
1′t	4.92 dd
2′	5.83 dd
4′	1.49 m
5′	1.89 m
6′	5.06 brd
8′	1.94 t
9′	2.04 dt
10′	5.07 m
12′	1.67 brs
13′	1.59 brs
14′	1.55 d
15′	1.15 s
OH	10.42 brs

[a] *J* (Hz):6, 7 = 7, 8 = 8; 1′c,2′ = 10.5; 1′t,2′ = 17.5;$3_1'$, $3_2'$ = 15.5; 6′, 14′ = 1; 8′, 9′ = 9′, 10′ = 7.5; 1t′, 1c′ = 1.

(EtOAc), 8 (EtOAc/MeOH, 11:1), 9 (EtOAc/MeOH, 9:1), 10 (MeOH). The fractions of interest were further purified by TLC on silica gel plates (silica gel 60 F 254). Preparative TLC on silica plates (hexane/EtOAc, 9:1) of fraction 4 gave 10 mg of 5′-epi-triptiliocoumarin (**1**) (R_f 0.16) and 2 mg (**3**) (R_f 0.45). The known compounds were identified by comparing the 400 MHz ^{1}H-NMR spectra with those of authentic material.

*3.1. 5′-Epi-triptiliocoumarin (**1**)*

MS: *m/z* (rel. int.) 378.219 $[M]^+$ (27) (calc. for $C_{25}H_{30}O_3$ 378.220), 363 $[M-Me]^+$ (5), 309 $[M-Prenyl]^+$ (40), 229 (100), 228 $[RDA]^+$ (60), 135 $[ArCO]^+$ (45) Ar = $C_6H_3(OH)(CH_3)$.

*3.2. Compound **3** (1(2-hydroxy-6-methylphenyl)-3-ethenyl-3,7,11-trimethyl-6,7-dodecadienone)*

MS: *m/z* (rel. int.) 354.256 $[M]^+$ (4) (calc. for $C_{24}H_{34}O_2$ 354.256), 339 $[M-Me]^+$ (8), 203 $[M-C_{11}H_{19}]^+$ (12), 135 $[ArCO]^+$ (100); 69 $[C_5H_9]^+$ (50); Ar = $C_6H_3(OH)(CH_3)$.

360 g of air-dried *N. digitata* was purified as described also or for *N. pyramidalis*, followed by HPLC (RP 18, MeOH/H_2O 9:1) to yield 6 mg triptiliocoumarin (**2**) and 5 mg 5′-epi-triptiliocoumarin (**1**). The known compounds were identified by comparing the 400 MHz ^{1}H-NMR spectra with those of authentic material.

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References

Bates, R. B., Gale, D. M., & Gruner, B. J. (1963). *Journal of Organic Chemistry*, *28*, 1086.

Bittner, M., Jakupovic, J., Bohlmann, F., Grenz, M., & Silva, M. (1988). *Phytochemistry*, *27*, 3263.

Bittner, M., Jakupovic, J., Bohlmann, F., & Silva, M. (1988). *Phytochemistry*, *27*, 3845.

Bittner, M., Jakupovic, J., Bohlmann, F., & Silva, M. (1989). *Phytochemistry*, *28*, 2867.

Bittner, M., Silva, M., Rozas, Z., Papastergiou, F., & Jakupovic, J. (1994). *Phytochemistry*, *36*, 695.

Cabrera, A. L. (1982). *Darwiniana*, *24*, 283.

Pritschow, P., Jakupovic, J., Bohlmann, F., Bittner, M., & Niemeyer, H. M. (1991). *Phytochemistry*, *30*, 893.

Zdero, C., Bohlmann, F., King, R. M., & Robinson, H. (1986). *Phytochemistry*, *25*, 509.

Zdero, C., Bohlmann, F., King, R. M., & Robinson, H. (1986). *Phytochemistry*, *25*, 2873.

Zdero, C., & Bohlmann, F. (1990). *Plant Systematics and Evolution*, *171*, 1.