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DRIMANE DERIVATIVES FROM *DRIMYS BRASILIENSIS*

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Key Word Index—*Drimys brasiliensis*; Winteraceae; drimane sesquiterpenes; confertifolin; 1β-*p*-coumaroyloxyvaldiviolide; 1β-*p*-coumaroyloxypolygodial.

Abstract—*Drimys brasiliensis* gave confertifolin and two new drimane derivatives identified as 1β-*p*-coumaroyloxypolygodial and 1β-*p*-coumaroyloxyvaldiviolide.

INTRODUCTION

Drimys sensu stricto is a small South American genus of four species, two of which have been investigated and provided the first examples of what are known as drimane sesquiterpenes [1–4]. We now report the isolation from *Drimys brasiliensis* Miers of confertifolin (1) and the new drimane derivatives 1β-*p*-coumaroyloxypolygodial (2) and 1β-*p*-coumaroyloxyvaldiviolide (3a).

RESULTS AND DISCUSSION

Confertifolin (1) has been isolated previously from *D. confertifolia* Phil. and in much better yield from *D. winteri* Forst. It also accompanies polygodial (4) in the pungent *Polygonum hydropiper* L. (Polygonaceae) [5–7]. Mp, IR and NMR data of our material compared well with those in the literature [2–4, 8].

Compound 2, $C_{28}H_{24}O_5$ (HRMS), was a *p*-coumarate derivative as evidenced by the typical signals of H-2′, H-3′, H-5′ and H-6′ in its ^{1}H NMR spectrum (Table 1), the signals of C-1′–C-7′ in its ^{13}C NMR spectrum (Table 2) and the loss of $C_9H_8O_3$ on EIMS. Partial structure A could also be deduced from the ^{1}H and ^{13}C NMR spectra. One of the two aldehyde functions (C-12) was α,β-unsaturated (H-12, *s*, δ9.32, C-12, *d*, δ193.21), the second (C-11) was normal (H-11, *d*, δ9.82, C-11, *d*, δ200.18) and adjacent to a methinyl group (H-9, *s* (*br*), δ3.34, C-9, *d*, δ60.35) whose proton was further allylically coupled to a vinylic proton (H-7 at δ7.09, C-7 at δ153.37) β to the α,β-unsaturated aldehyde. In turn H-7 and also a very shielded proton (H-5) appeared as a doublet of doublets at δ1.44 and were coupled to the protons (H-6) of a methylene group appearing as a complex multiplet centred at δ2.48.

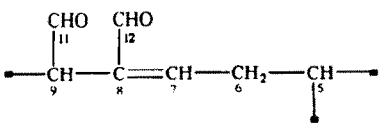
Partial structure A and the presence of three methyl singlets in the ^{1}H NMR spectrum indicated that 2 was a polygodial derivative. That the ester function was equatorial and located at C-1 or C-3 of the drimane skeleton was deduced from the magnitude (11 and 4 Hz) and number of the coupling constants involving the doublet of doublets at δ4.89. The NOE difference spectrum (Table 3) showed an appreciable interaction between H-1 and H-9 and located the coumarate at C-1. It also showed that H-1, H-5 and H-9 were all axial, thus establishing the complete stereochemistry of 2. That H-5 was axial and α was also shown by the coupling constants (11 and 6 Hz).

The ^{1}H NMR data for 2 compared well with those of polygodial (4) where applicable. The 250 MHz ^{1}H NMR spectrum of the latter has been reported recently [9]. The H-11 signal of 2 was considerably further downfield than in the case of polygodial and was more in keeping with that of 9-epipolygodial [10], but the NOEs and the value of $J_{9,11}$ ruled this out. Obviously H-11 of 2 was deshielded by the ester function on C-1.

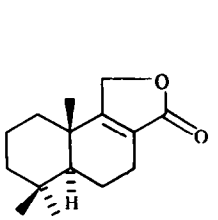
Comparison of the ^{1}H and ^{13}C NMR spectra (Tables 1 and 2) of the second new compound, $C_{28}H_{24}O_6$ (HRMS), with those of 2 permitted its formulation as the 1β-*p*-coumaroyloxy derivative 3a of valdiviolide (5). The latter is a minor constituent of *Drimys winteri* [4]. Oxidation of the α,β-unsaturated aldehyde of 2 to a carboxyl and lactal formation between C-11 and C-12 accounted for the extra oxygen atom of the empirical formula, the slight upfield shift of H-7 and the significant upfield shifts of C-11 (to δ116.77), C-12 (to δ170.17) and H-11 (to δ5.78). H-11 experiences a predictable paramagnetic shift to δ6.56 on conversion to the diacetate 3b. Since the coupling constants exhibited by 3a, b compare well in most respects with those of 2, the stereochemistry of 3a is the same as that of 2.

EXPERIMENTAL

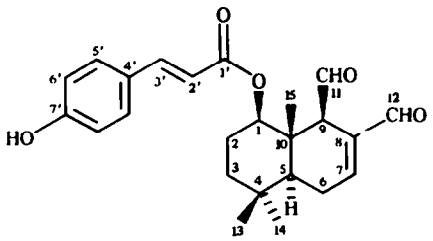
Extraction of Drimys brasiliensis. Aerial parts of *D. brasiliensis* Miers. (7.5 kg) were collected by Dr. Hermogenes de Freitas Leitão Filho in Campos do Jordão, São Paulo State, Brazil, in



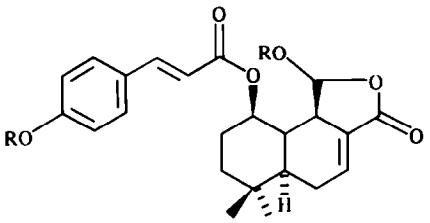
A



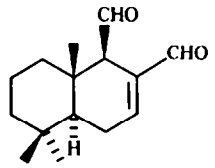
1



2



3a R = H
3b R = Ac



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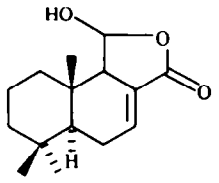

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March 1974. The pulverized plant was extracted with hexane–EtOAc (5:1) to give 37 g crude extract which was chromatographed over 276 g silica gel, 500 ml fractions being eluted as follows: 1–13 (hexane–EtOAc, 49:1), 14–28 (hexane–EtOAc, 24:1), 29–51 (hexane–EtOAc, 15.6:1), 52–81 (hexane–EtOAc, 11.5:1), 82–91 (hexane–EtOAc, 9:1), 92–104 (hexane–EtOAc, 7.3:1), 105–108 (hexane–EtOAc, 5.2:1), 109–114 (hexane–EtOAc, 4:1), 115–120 (hexane–EtOAc, 3:1), 121–126 (hexane–EtOAc, 2.5:1), 127–131 (hexane–EtOAc, 1.5:1), 132–138 (EtOAc) and 139–147 (EtOH). The crystals from fraction 39 were recrystallized from hexane–EtOAc (49:1) to give 30 mg **1**, 147–150°; IR ν_{max}^{KBr} cm^{-1}: 2902, 1760, 1740, 1670, 1430, 1000; IR $\nu_{max}^{CCl_4}$ cm^{-1}: 1755 (br), 1670 cm^{-1}; ^1H NMR: δ4.74 (*ddd*, J = 17.3, 3 Hz) and 4.66 (*ddd*, J = 17, 3.5, 1.8 Hz, AB system of H-11 allylically coupled to H-7), 2.40 *dd* (*br*), J = 17, 6 Hz) and 2.16 (*m*, AB system of H-7), 1.91 (*dd* (*br*), J = 13, 7 Hz, probably H-6a), 1.17, 0.95 and 0.92 (3 Me).

The solid material (12 g) from fr. 118–133 was rechromatographed on silica gel (84 g); the material eluted with hexane–EtOAc (2.3:1) gave 32 mg **3a**, mp 164–166°; IR ν_{max}^{KBr} cm^{-1}: 3450, 3320, 1710, 1690, 1630, 1605, 1590, 1510; MS *m/z* (rel. int.): 412 $[M]^+$ (1.4), 394 (2.2), 384 (3.9), 265 (2.1), 246 (3.2), 230 (9.0), 220 (26.0), 205 (13.9), 191 (11.0), 164 (18.8), 150 (5.0), 147 (100) [Calc. for $C_{28}H_{24}O_6$: M_r, 412.1884. Found: M_r (MS) 412.1874]. Other significant peaks in the HRMS were at *m/z* (composition, rel. int.): 394 ($C_{24}H_{26}O_5$, 0.4), 384 ($C_{23}H_{28}O_5$, 0.6), 366 ($C_{23}H_{26}O_4$, 0.2), 248 ($C_{15}H_{20}O_3$, 0.5), 220 ($C_{14}H_{20}O_2$, 11.9), 164 ($C_9H_8O_3$, 20.5), 150 ($C_9H_9O_2$, 9.2), 147 ($C_9H_7O_2$, 100). Acetylation in the usual fashion (Ac_2O–C_5H_5N) gave **3b**, MS *m/z* (rel. int.): 496 $[M]^+$ (2.9), 454 (14.2), 437 (2.7), 394 (6.0), 230 (74), 220 (11.8), 215 (10.6), 189 (17.8), 164 (14.4), 147 (100).

Fractions 126–127 gave 54 mg **2**, mp 201–204°; IR ν_{max}^{KBr} cm^{-1}: 3450 (br), 1725 (br), 1680 (br); MS *m/z* (rel. int.): 396 $[M]^+$ (0.6), 368 (1.3), 232 (0.8), 204 (23.5), 175 (4.2), 164 (10.6), 147 (100). [Calc. for $C_{24}H_{18}O_5$: M_r, 396.1937. Found: M_r (MS), 396.1941].

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

H	2	3a*	3b
1α	4.89 *dd* (11, 4)	4.74 *dd*	4.70 *dd*
2α	1.71 *dq* (4, 12)	1.68 *dq*	1.68 *dq*
2β	1.82 *dq* (12, 4)	1.88 *dq*	1.94 *dq*
3α, β†	1.58 *m*	1.58 *m*	1.58 *m*
5α	1.44 *dd* (11, 6)		1.5 *m*
6α	2.48 *m*	2.45 *ddt* (20, 5.5, 3.5)	2.52 *ddt*
6β		2.22 *ddd* (20, 12, 4, 3)	2.25 *m*
7	7.09 *br* ($W_{1/2}$ = 9 Hz)	6.86 (part obsc)	6.96 *q* (3.5)
9α	3.34 *br* ($W_{1/2}$ = 7 Hz)	2.59 *m*	2.86 *ddt* (5.5, 4, 3.5)
11	9.82 *d* (2.8)	5.78 *d* (5.5)	6.56 *d* (5.5)
12	9.35	—	—
13‡	1.09	1.00	1.04
14‡	1.03	0.97	0.94
15‡	0.98	0.94	0.96
2′	6.23 *d* (16)	6.28 *d*	6.26 *d*
3′	7.59 *d* (16)	7.42 *d*	7.65 *d*
5′†	6.87 *d* (8)	6.89 *d*	7.14 *d*
6′†	7.39 *d* (8)	7.42 *d*	7.55 *d*
Ac‡	§	‖	2.32 ¶, 1.88**

*Plus 2 drops DMSO.
†Intensity two protons.
‡Intensity three protons.
§In absence of D_2O, OH singlet at δ5.96.
‖In absence of D_2O, OH signals at δ9.16 and δ2.45, H-11 signal split into triplet.
¶On C-7′.
**On C-11.

Table 2. ^{13}C NMR spectra of compounds 2 and 3a (67.89 MHz)

C	2 (deutero-acetone)	3a (CD_3OD)
1	81.59 *d*	81.77 *d*
2	23.36 *t**	25.83 *t**
3	39.91 *t*	40.55 *t*
4	33.40 *s*	33.69 *s*
5	49.21 *d*	obsc. by solvent
6	24.99 *t**	25.18 *t**
7	153.37 *d*	137.26 *d*
8	140.92 *s*	129:71 *s*
9	60.55 *d*	59.41 *s*
10	42.33 *s*	39.70 *s*
11	200.18 *d*	116.77 *d*†
12	193.21 *d*	170.17 *s*
13	32.75 *q*	32.71 *q*
14	22.26 *q*	21.54 *q*
15	10.95 *q*	10.11 *q*
1′	166.54 *s*	168.73 *s*
2′	115.94 *d*	116.21 *d*
3′	145.62 *d*	145.96 *d*
4′	127.06 *s*	127.39 *s*
5′	131.04 *d*	131.19 *d*
6′	116.69 *d*	116.77 *d*†
7′	160.62 *s*	161.15 *s*

*Assignments interchangeable.
†Signals superimposed.

Table 3. ^{1}H NOE difference spectrum of 2a

Saturation	Observed NOE (%)
H-1α	H-5α (4.1)
	H-9α (10.6)
H-5α	H-1α (10.3)
	H-9α (8.6)
H-9α	H-1α (11.3)
	H-5α (7.3)

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