Pergamon

PII: S0031-9422(96)00245-2

Phytochemistry, Vol. 43, No. 2, pp. 457–459, 1996

0031-9422/96 $15.00 + 0.00

TRICHAVENSIN, A PRIEURIANIN DERIVATIVE FROM *TRICHILIA HAVANENSIS**

LYDIA RODRÍGUEZ-HAHN,† JORGE CÁRDENAS and CARLOS ARENAS

Instituto de Química, Universidad Nacional Autónoma de México, Circuito Exterior, Ciudad Universitaria, Coyoacán 04510, México, D.F.

(*Received in revised form* 15 *January* 1996)

Key Word Index—*Trichilia havanensis*; Meliaceae; seed; trichavensin, *seco*-limonoid.

Abstract—The *seco*-limonoid trichavensin, structurally related to prieurianin, was isolated from the mature seed material of *Trichilia havanensis*. Its structure was determined by spectroscopic studies. Copyright © 1996 Elsevier Science Ltd

INTRODUCTION

Trichilia havanensis (popular name 'xopiltetl' or 'tinajillo') has been used in popular medicine by the Totonac community of the Sierra de Puebla [1] and its seeds are used for corn protection. The study of the limonoid content of the unripened seeds of this plant led to the isolation of azaridone and havanensin derivatives [2]. The mature seeds contained havanensin triacetate (**1**), its hydroxybutenolide derivative (**2**) and a new limonoid whose structure was established as the prieurianin derivative, trichavensin (**3**).

RESULTS AND DISCUSSION

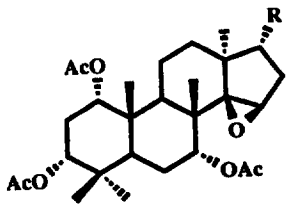
A hexane extract of the mature seeds was partitioned between hexane and aqueous methanol [3]. Chromatography of the ethyl acetate soluble fraction led to the isolation of havanensin triacetate (**1**), the hydroxybutenolide derivative **2** and a new *seco*-limonoid trichavensin, whose structure **3** was deduced from spectral data.

The high resolution FAB mass spectrum of **3** allowed the assignment of the molecular formula $C_{43}H_{60}O_{17}$. Its IR spectrum indicated the presence of hydroxyl (3500 cm^{-1}) and several ester groups in the molecule (broad absorption at 1720–1745 cm^{-1}).

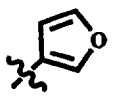
The ^1H and ^{13}C NMR spectra (Tables 1 and 2) helped to establish product **3** as an A,B-ring *seco*-limonoid structurally related to prieurianin [4]. It showed the usual β-furan proton resonances (δ 7.3, 7.12 and 6.22), the presence of a carbomethoxyl group (^1H δ 3.77, *s*, 3H; ^{13}C δ 52.9 *q*, 174.7 *s*) and an exocyclic methylene (^1H δ 5.60 *s* and 5.31 *s*; ^{13}C δ 122.1 *t* and 141.9 *s*). A carbonyl resonance at δ 168.6 and a singlet resonance at δ 83.5 assigned to C-4, indicated a seven-membered lactone A-ring with a similar type of substituent at C-4 as in prieurianin [5]. A second oxygen bound carbon singlet at δ 84.5 was attributed to C-14, which supported an hydroxyl group. A broad singlet at δ 7.9 was assigned to the formate ester; its carbonyl carbon resonated at δ 160.8 (d). The ^{13}C NMR spectrum of **3** showed four additional carbonyl resonances (δ 174.9, 175.8, 169.8 and 170.1) attributed to ester groups of which two were acetates as shown by the presence of two singlets (3H each) at δ 2.05 and 2.09. The other two ester groups were established as 2-hydroxy-2-methyl-valerate and 2-methyl butyrate by analysis of the resonance spectra and the mass spectral data (Tables 1 and 2 and Experimental). The assignment of the geminal protons of the ester groups was based on the analysis of their multiplicities, double NMR experiments and comparison with published data of structurally related products [6–8] (Table 1). Thus, a double doublet at δ 5.15 (J = 8 and 12 Hz) was assigned to H-11α and was shown to be coupled to H-12β (δ 6.02, *d*, J = 12 Hz) and to H-9 (δ 3.62, *d*, J = 8 Hz) by double irradiation experiments. Irradiation of the signal at δ 5.15 sharpened the broad singlet due to the formate proton, thus establishing the attachment of the formate group to C-11 as found in most structurally related limonoids [5–8]. A multiplet at δ 5.31 and a double doublet at 5.45 (J = 4 and 9 Hz) were attributed to the geminal protons of the ester groups bound to C-1α and to C-15β. An AB system (δ 4.12 and 4.47, J = 12 Hz) was ascribed to the C-29 methylene group. Three methyl singlets, two doublets and two triplets were also observed in the ^1H NMR spectrum (Table 1). The ^{13}C NMR data (Table 2) were in agreement with the presence of these functionalities in **3**. The assignments were based on the multiplicities found by SFORD and

*Contribution No. 1442 from the Instituto de Química, UNAM.

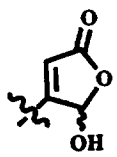
†Author to whom correspondence should be addressed.

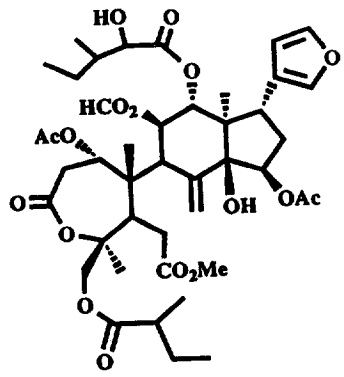


1 R=



2 R=





3

APT experiments and comparison with the data of similar structures [6–8].

The attachment of the different ester groups in the molecule was deduced by a careful analysis of the high resolution FAB mass spectrum and the CIMS. They showed ions at *m/z* 803.5 ($C_{42}H_{59}O_{15}$) and 743 ($C_{40}H_{55}O_{13}$) due to the successive loss of 1 mol of formic and acetic acids from the molecular ion. The formation of the fragmentation ions at *m/z* 167 ($C_9H_{11}O_3$) and 683 ($C_{34}H_{51}O_{14}$) was in agreement with the presence of an acetoxy group at C-15. The rupture of the C-9/C-10 bond produced the fragmentation ion at *m/z* 385 ($C_{19}H_{29}O_8$), which established the presence of an acetate and a 2-methylbutyrate bound to the A-ring of the molecule. The fragmentation ions at *m/z* 325 ($C_{17}H_{25}O_6$), 241 ($C_{12}H_{17}O_5$) and 211 ($C_{11}H_{15}O_4$) could be the result of successive loss of acetic acid, 2-methylbutyric acid and the C-29 hydroxymethylene group. Although this fragmentation pattern could not establish unequivocally the distribution of the ester groups in the A-ring of trichavensin, we propose that the acetoxy group is α-bound to C-1 as found in all the limonoids isolated so far from *Trichilia* species [6–8]. The 2-methylbutyrate must be bound to C-29. The fragmentation pattern established the substitution of the C- and D-rings of trichavensin to be the same as those found in limonoids isolated from *T. roka* [7], *T. hispida* [8] and *T. rubra* [6], among others.

The structure and substitution pattern of ring A in **3** is similar to that of prieurianin from which it differed in the presence of a 2-methylbutyric acid esterifying the C-29 hydroxy methylene group.

Table 1. ^{1}H NMR data for compound **3** (80 MHz, $CDCl_3$, TMS as internal standard)

1	5.31 *m*
9	3.62 *d* (8)
11	5.15 *dd* (12, 8)
12	6.02 *d* (12)
15	5.45 *dd* (9, 4)
17	3.89 *t* (9)
18	0.96 *s*
19	1.48 *s*
21	7.12 *dd* (2, 1)
22	6.22 *dd* (2, 1)
23	7.30 *t* (2)
28	1.34 *s*
29	4.12 *d* (12)
	4.47 *d* (12)
30	5.31 *s*
	5.60 *s*
OMe	3.77 *s*
OAc	2.05 *s*
OAc	2.09 *s*
5′	0.76 *t* (7)
6′	0.83 *d* (7)
4″	0.87 *t* (7)
5″	1.16 *d* (7)

EXPERIMENTAL

Mps: uncorr. ^{1}H and ^{13}C NMR were performed at 80 and 20 MHz, respectively, using TMS as int. standard. ^{13}C NMR assignments were made by SFORD and APT experiments. Plant material (seeds) was collected in the Sierra Norte, Xochitlan Puebla (México) and a voucher is deposited at the Herbarium of Colegio de Posgraduados, Chapingo.

Isolation of the limonoids from ripened seeds of Trichilia havanensis. Isolation of the limonoids was performed as previously described [2]. Product **3** was purified by chromatography (eluent EtOAc) and crystallized from Me_2CO–hexane to constant mp: 154–156°. $[\alpha]_D$ −31 (*c* 2.0 MeOH). UV λ_{max}^{MeOH}: 207 nm ($\varepsilon = 9022$). IR, ν_{max}^{nujol} cm^{-1}: 3500, 1745, 1730, 1720, 1240, 1165, 870. ^{1}H NMR: see Table 1; ^{13}C NMR: see Table 2. HRFABMS: observed *m/z* 849.3909 for $[MH]^+$ and 871.3728 for $[MNa]^+$; $C_{43}H_{61}O_{17}$ requires 849.383 and $C_{43}H_{60}O_{17}Na$ requires 871.3728. CIMS *m/z* (rel. int.): 803.5(1), 743(7), 683(4), 608(3), 508(8), 430(14), 385(7), 325(9), 283(11), 243(18),

Table 2. ^{13}C NMR data for compound **3** (20 MHz, $CDCl_3$, TMS as internal standard)

C	δ_c	C	δ_c	C	δ_c
1	71.9 *d*	16	36.7 *t*	$O\underline{C}OCH_3$	169.8 *s*
2	38.3 *t*	17	39.5 *d*	$H\underline{C}OO$	160.8 *d*
3	168.6 *s*	18	13.4 *q*	1′	174.9 *s*
4	83.5 *s*	19	13.5 *q*	2′	74.3 *d*
5	50.6 *d*	20	124.3 *s*	3′	38.5 *d*
6	33.3 *t*	21	140.3 *d*	4′	23.4 *t*
7	174.7 *s*	22	110.9 *d*	5′	11.6 *q*
8	141.9 *s*	23	142.8 *d*	6′	15.2 *q*
9	49.3 *d*	28	26.6 *q*	1″	175.8 *s*
10	49.0 *s*	29	66.8 *t*	2″	41.4 *d*
11	71.3 *d*	30	122.1 *t*	3″	26.6 *t*
12	74.7 *d*	OMe	52.9 *q*	4″	11.6 *q*
13	50.6 *s*	$OCOCH_3$	21.0 *q*	5″	16.5 *q*
14	84.5 *s*	$OCO\overline{C}H_3$	20.6 *q*		
15	72.8 *d*	$O\underline{C}O\overline{C}H_3$	170.1 *s*		

227.2(47), 209(47), 185(14), 167(14), 133(11), 115(13), 107(15), 85(30), 57(100).

Acknowledgements—We wish to express our gratitude to Dr C. Rodríguez (Colegio de Posgraduados, Chapingo) for the plant material collection and classification. We are also grateful to Messrs R. Villena, M. Torres, L. Velasco and R. Gaviño for technical assistance and to JEOL (U.S.A.) Inc., Peabody, MA, for the high resolution FAB mass spectrometry. This work was partially supported by the IOCD-CONACyT project (PVT/AI/NAL/86/3662).

REFERENCES

1. Martínez, M. A. (1984) *J. Ethnopharmacol.* **11**, 203.
2. Arenas, C. and Rodríguez-Hahn, L. (1990) *Phytochemistry* **29**, 2953.
3. Schroeder, D. R. and Nakanishi, K. (1987) *J. Nat. Prod.* **50**, 241.
4. Gullo, V. P., Miura, I., Nakanishi, K., Cameron, A. F., Conolly, J. D., Duncanson, F. D., Harding, A. E., McCrindle, R. and Taylor, D. A. H. (1975) *J. Chem. Soc., Chem. Commun.* 345.
5. Mac Lachlan, L. K. and Taylor, D. A. H. (1982) *Phytochemistry* **21**, 2426.
6. Musza, L. L., Killar, L. M., Speight, P., McElhiney, S., Barrow, C. J., Gillam, A. M. and Cooper, R. (1994) *Tetrahedron* **50**, 11369.
7. Nakatani, M., Okamoto, M., Iwashita, T., Mizukawa, K., Naoki, H. and Hase, T. (1984) *Heterocycles* **22**, 2335.
8. Jolad, S. D., Hoffmann, J. J., Schoam, K. H., Cole, J. R. Tempesta, M. S. and Bates, R. B. (1981) *J. Org. Chem.* **46**, 641.