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TWO NEW CINNAMYL ISOVALERATE DERIVATIVES FROM *JUNIPERUS THURIFERA* LEAVES

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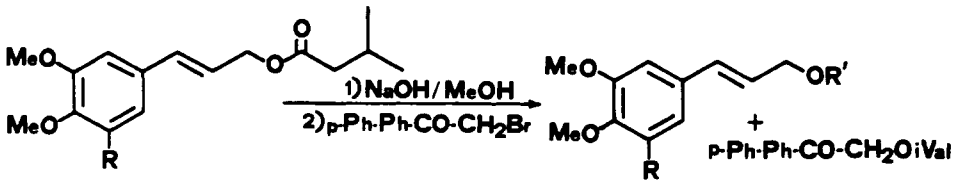
After our systematic research on the Spanish species of *Juniperus* (Cupressaceae) (1), we began the study of components from *Juniperus thurifera* L. leaves.

From the hexane extract, apart from some lignans and diterpenoids, we isolated two compounds related to linalool (2), and in the present paper we report the identification of two cinnamyl alcohol derivatives.

The hexane extract was cooled and the neutral fraction of the insoluble part chromatographed on Si gel. From the less polar fraction, two related compounds **1** and **2** were isolated.



1 R=H
2 R=OMe

3 R=H, R'=H
4 R=OMe, R'=H
5 R=OMe, R'=Ac

Compound **1** was an oily substance that absorbed in the uv at 266 and 212 nm. Its M^+ at m/z=278, together with the existence of sixteen carbon atoms in the ^{13}C-nmr spectrum, permitted us to deduce the molecular formula $C_{16}H_{22}O_4$. In the ir it displayed absorptions of ester, *trans*-double bond, and aromatic groups, that were also observed in its ^{13}C-nmr spectrum (Table 1), which showed, in addition, a carboxylic ester group, eight sp^2 carbons (aromatic and olefinic), one methylene and two methyls bonded to oxygen, one methine, one other methylene, and two identical methyls. The ^1H-nmr spectrum (Table 1) showed two aromatic methoxy groups, one 1,3,4-trisubstituted aromatic ring, a -CH=CH-CH_2-O-grouping, and signals corresponding to an isovalerate moiety.

The above data allowed us easily to deduce the structure 3',4'-dimethoxycinnamyl isovalerate (**1**) [3-(3',4'-dimethoxyphenyl)-prop-2-enyl isovalerate] for this substance; surprisingly, this compound has not been described in the literature either as a natural or as a synthetic compound.

The saponification of ester **1** followed by treatment with phenylphenacyl bromide afforded the alcohol **3** and one phenylphenacyl ester. The alcohol **3** was a crystalline compound that showed in the eims M^+ at m/z 194 ($C_{11}H_{14}O_3$) and uv absorptions at 260 and and 205 nm. Its ^1H-nmr and ^{13}C-nmr spectra agree with the structure of 3',4'-dimethoxycinnamyl alcohol (**3**) (3). The phenylphenacyl ester has physical and spectroscopic properties corresponding to those of phenylphenacyl isovalerate. The results obtained in the saponification of **1** confirm the proposed structure of 3',4'-dimethoxycinnamyl isovalerate for the natural product.

Compound **2** was also an oil and its spectroscopic data were similar to those

TABLE 1. ^{1}H-nmr (200 MHz) and ^{13}C-nmr (50.3 MHz) Spectra of Compounds **1** and **2**

H-atom	Compounds		C-atom	Compounds	
	1	**2**		**1**	**2**
1	4.73 dd (6.4; 1.5)[a]	4.72 dd (6.4; 1.5)	1	64.8	64.7
2	6.19 dt (15.7; 6.4)	6.21 dt (15.9; 6.4)	2	121.5	123.0
3	6.60 bd (15.7)	6.58 bd (15.9)	3	134.0	134.2
2′	6.96 s	6.62 s	1′	129.5	132.1
5′	6.80 d (8.4)	—	2′	111.5	104.2
6′	6.93 d (8.4)	6.62 s	3′	149.5	153.5
3′-OCH_3	3.85 s	3.87 s	3′	149.5	153.5
4′-OCH_3	3.88 s	3.84 s	4′	149.3	138.7
5′-OCH_3	—	3.87 s	5′	109.5	153.5
	(5.4)	(6.4)	6′	120.0	104.2
2″	2.25 d	2.24 d	3′-OCH_3	55.8	56.2
3″	2.20 m	2.19 m	4′-OCH_3	55.8	60.9
4″	1.00 d (6.7)	0.97 d (6.4)	5′-OCH_3	—	56.2
5″	1.00 d (6.7)	0.97 d (6.4)	1″	172.5	172.8
			2″	43.3	43.5
			3″	25.7	25.7
			4″	22.4	22.5
			5″	22.4	22.5

[a]*J* values, in Hz.

of compound **1**, especially its ir and uv spectra, but its eims has M^+ at *m/z* 308 ($C_{17}H_{24}O_5$). In the ^{1}H nmr (Table 1) the differences with compound **1** were the presence of three methoxy groups (two of them identical) and only one signal for aromatic protons, suggesting the existence of a symmetrical 1,3,4,5-tetrasubstitution in the aromatic ring, as is also revealed by the ^{13}C-nmr spectrum (Table 1).

These data agreed with a structure of 3′,4′,5′-trimethoxycinnamyl isovalerate for substance **2**, which was confirmed in the results obtained from its saponification. By a similar procedure, the saponification of ester **2** gave the alcohol **4** and phenylphenacyl isovalerate.

The alcohol **4** was a crystalline substance that showed in the eims M^+ at *m/z* 224 and uv absorptions at 260 and 214 nm. The ir, ^{1}H-nmr, and ^{13}C-nmr spectra were in accordance with the structure of 3′,4′,5′-trimethoxycinnamyl alcohol for **4**. Its spectroscopic properties agreed with those of 3′,4′,5′-trimethoxycinnamyl alcohol isolated from *Uvariodendron connivens* Benth. seeds (4).

Compound **2** has also not been described in the literature, and only the related 3′,4′,5′-trimethoxycinnamyl acetate has been obtained from Bergamot oil (*Citrus bergamia* Risso, Rutaceae) and fruits, and the spectroscopic properties agree with those of the acetylation product **5** of alcohol **4** (5).

The coexistence in the extract of *J. thurifera* leaves of several lignans and esters **1** and **2** of substituted cinnamyl alcohol would seem to suggest that compounds **3** and **4** were biogenetic precursors of lignans. However, this could not be the case because the precursors of lignans must contain a free phenolic group at C-4 (6). Thus, the existence could be postulated of an earlier intermediate which, by dimerization and methylation or methylenation, leads to lignans and, by esterification and methylation, to compounds **1** and **2**.

EXPERIMENTAL

GENERAL TECHNIQUES.—Uv were recorded

in EtOH on a Hitachi 100-60 spectrometer; ir spectra in film on a Beckman AcuLab VIII spectrophotometer, and ^{1}H-nmr (200 MHz) and ^{13}C-nmr (50.3 MHz) spectra in $CDCl_3$ (TMS internal standard) on a Bruker WP 200 SY spectrometer; eims were obtained on a Hewlett-Packard 5930 A at 70 eV. SiO_2 (Merck 9385) flash chromatographies were performed on a Eyela EF-10.

PLANT MATERIAL EXTRACTION AND ISOLATION.—Leaves of *J. thurifera* were collected in Prádena, Segovia, Spain, in September 1981. Voucher specimens are deposited in the Botany Department, Faculty of Biology, Salamanca, register no. SALA 7193.

J. thurifera leaves (15 kg) were extracted with hexane, and the resulting extract was cooled at 0° overnight to give 615 g (34.0%) of insoluble fraction, which was successively defatted with MeOH and a saturated solution of urea in MeOH and fractionated with 4% NaOH aqueous solution. The neutral part (130 g; 7.1%) was chromatographed over SiO_2. Flash chromatography of the fraction eluted with hexane-EtOAc (8:2) yielded the isovalerate esters **1** (668 mg; $CHCl_3$-EtOAc, 98:2) and **2** (407 mg; $CHCl_3$-EtOAc, 95:5), which were shown to be homogeneous by tlc.

3′,4′-DIMETHOXYCINNAMYL ISOVALERATE (**1**).—Colorless oil; uv λ max nm (ε) 266 (1400), 212 (1600); ir ν cm^{-1} 1730, 1670, 1615, 1600, 1275, 1040; eims *m/z* 278 (M^+).

3′,4′,5′-TRIMETHOXYCINNAMYL ISOVALERATE (**2**).—Colorless oil; uv λ max nm (ε) 266 (3300), 218 (4600); ir ν cm^{-1} 1720, 1660, 1580, 1290, 1230, 960; eims *m/z* 308 (M^+).

3′,4′-DIMETHOXYCINNAMYL ALCOHOL (**3**).—300 Mg of **1** were treated for 30 min with 8% NaOH in MeOH at room temperature. After neutralization with 2 N HCl to pH=7.2, 15 ml of EtOH and phenylphenacyl bromide (330 mg) were added and the reaction refluxed for 8 h. Flash chromatography of the reaction product produced 125 mg of phenylphenacyl isovalerate and 175 mg of **3**. Mp 89°; uv λ max nm (ε) 260 (22000), 205 (36200); ir ν cm^{-1} 3400, 1660, 1610, 1590, 1515, 1265; ^{1}H nmr δ ppm 3.87 (3H, s), 3.88 (3H, s), 4.29 (2H, dd, *J*=5.8 and 1.4 Hz), 6.23 (1H, dt, *J*=15.7 and 5.8 Hz), 6.54 (1H, bd, *J*=15.7 Hz), 6.80 (1H, d, *J*=8.0 Hz), 6.91 (1H, d, *J*=8.0 Hz), and 6.94 (1H, s); ^{13}C nmr δ ppm 56.1 (-OCH_3), 56.1 (-OCH_3), 63.7 (C-1), 109.7 (C-5′), 111.8 (C-2′), 119.8 (C-6′), 126.9 (C-2), 130.2 (C-1′), 131.2 (C-3), 149.5 (C-3′), 149.5 (C-4′); eims *m/z* 194 (M^+).

3′,4′,5′-TRIMETHOXYCINNAMYL ALCOHOL (**4**).—Compound **2** (200 mg) treated as above yielded 95 mg of phenylphenacyl isovalerate and 110 mg of **4**. Mp 106°; uv λ max nm (ε) 260 (10600), 214 (23000); ir ν cm^{-1} 3620, 3480, 1660, 1590, 1510, 1470, 1230, 915; ^{1}H nmr δ ppm 3.84 (3H, s), 3.85 (6H, s), 4.30 (2H, dd, *J*=5.6 and 1.4 Hz), 6.26 (1H, dt, *J*=15.8 and 5.6 Hz), 6.52 (1H, bd, *J*=15.8 Hz), 6.59 (2H, s); ^{13}C nmr δ ppm 56.1 (3′ and 5′-OCH_3), 60.8 (4′-OCH_3), 63.4 (C-1), 103.8 (C-2′ and 6′), 128.2 (C-2), 130.9 (C-3), 132.5 (C-1′), 138.1 (C-4′), 153.3 (C-3′ and 5′); eims *m/z* 224 (M^+).

3′,4′,5′-TRIMETHOXYCINNAMYL ACETATE (**5**).—Compound **4** (100 mg) with Ac_2O in pyridine, after usual work up, afforded 110 mg of **5**. Colorless oil; in ν cm^{-1} 1740, 1660, 1590, 1510, 1240, 1135, 970; ^{1}H nmr δ ppm 2.10 (AcO-), 3.84 (3H, s), 3.87 (6H, s), 4.72 (2H, dd, *J*=6.4 and 1.5 Hz), 6.20 (1H, dt, *J*=15.8 and 6.4 Hz), 6.58 (1H, bd, *J*=15.8 Hz), 6.62 (2H, s); ^{13}C nmr δ ppm 20.8 (*C*H_3-COO-), 56.2 (3′ and 5′-OCH_3), 60.8 (4′-OCH_3), 64.9 (C-1), 104.2 (C-2′ and 6′), 122.7 (C-2), 131.9 (C-1′), 134.8 (C-3), 138.7 (C-4′), 153.4 (C-3′ and 5′), 170.6 (CH_3-*C*OO-).

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