Phytochemistry, Vol. 30, No. 2, pp. 641–643, 1991
Printed in Great Britain.

0031-9422/91 $3.00+0.00

RESORCINOL DERIVATIVES FROM *ONONIS VISCOSA*

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(*Received in revised form* 7 *August* 1990)

Key Word Index—*Ononis viscosa*; Leguminosae; resorcinol derivatives.

Abstract—In the chloroform extract of the aerial parts of *Ononis viscosa* the three new compounds, (2′*R*,12′*S*)-6-(2,12-diacetoxy-tridecyl)-2,4-dihydroxybenzoic acid, (2′*R*,12′*S*)-6-(2-acetoxy-12-hydroxytridecyl)-2,4-dihydroxy-benzoic acid and (2′*R*,12′*S*)-5-(2-acetoxy-12-hydroxytridecyl) resorcinol were identified. The identification of all these substances was acheived by spectroscopic means.

INTRODUCTION

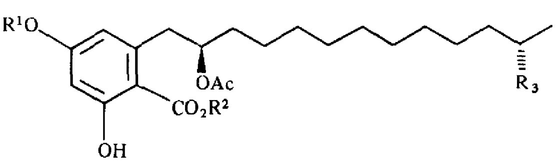
Ononis viscosa is a small annual plant of the Leguminosae family that grows in southern Spain. The high content of resorcinol derivatives found in *O. speciosa* [1], *O. natrix* L. subsp. *natrix* [2, 3] and *O. natrix* L. subsp. *hispanica* [4] led us to make a more extensive investigation on the chemical composition of the less polar extracts of other species of this genus, in order to find proper synthons to be used in the preparation of macrolides of the β-resorcilic acid series which would have antibiotic activity [5, 6] and also to extend our knowledge of the chemotaxonomy on *Ononis*.

RESULTS AND DISCUSSION

In the chloroform extract of the aerial parts of *Ononis viscosa* L. we found three new natural products with alkylresorcinol structures, (**1a**, **2a** and **3**). As the extract showed by TLC typical behaviour of acid substances, and its ^{1}H NMR spectrum showed no signals due to methoxyl groups, we treated it with a saturated ethereal solution of diazomethane in order to transform the carboxylic acids into their corresponding methyl esters, thus making their separation easier by usual chromatographic techniques. However, this process led to the partial formation of other methylated derivatives in addition to the expected esters, the methyl ester-monomethylethers that resulted from the methylation of phenolic hydroxyls.

The structure of the new natural product **1a** was established through the spectroscopic properties of its derivatives **1b** and **1c** and by comparison of these data with those previously reported for **4** [4]. Thus, **1b** showed a $[M]^+$ at m/z 466 (in agreement with $C_{25}H_{38}O_8$). Its IR spectrum exhibited absorption bands of an aromatic system (1618, 1588, 851 cm^{-1}), of free (1735, 1259 cm^{-1}) and hydrogen bonding linked (1703 cm^{-1}) acetoxyl groups as well as a linked aromatic ester (1654 cm^{-1}). An alkylbenzoic acid derivative structure was deduced from its ^{1}H NMR spectrum (Table 1) in which we can also see the presence of a signal due to a second acetoxyl group (2.02, *s*) attached to C-12′ from the presence of a *ddq* (δ4.88, *ddq*, $J_1 = J_2 = J_3 = 6.3$ Hz) coupled with a doublet ($\delta = 1.19$, *d*, $J = 6.3$ Hz). These data, together with the mass, UV and ^{13}C NMR spectra are in agreement with a structure of methyl(2′*R*,12′*S*)-6-(2,12-diacetoxy-tridecyl)-2,4-dihydroxybenzoate. The ^{13}C NMR spectrum (Table 2), in addition to other signals, showed those for two aliphatic oxygenated carbons bearing one hydrogen atom (74.79 CH and 71.54 CH), a benzylic methylene deshielded by the presence of an oxygenated vicinal group (41.35 CH$_2$), two more methylenes also deshielded (34.46 CH$_2$ and 35.91 CH$_2$) and the terminal methyl (20.0 Me). Similar spectroscopic features were exhibited by compound **1c**, which showed another singlet due to an aromatic methyl ether (3.78 *s*) as the most important feature in its ^{1}H NMR spectrum and in its IR absorptions due to a non hydrogen bonding linked acetoxyl group (1733, 1256 cm^{-1}). Thus, **1c** must be methyl(2′*R*,12′*S*)-6-(2,12-diacetoxytridecyl)-2-hydroxy-4-methoxybenzoate. The absolute configurations of the chiral atoms were fixed by comparison of the $[\alpha]_D$ for this compound and **4**. The change in the $[\alpha]_D$ value, was caused by the introduction of the new oxygenated function (from $[\alpha]_D - 15.2°$ for **4** to $[\alpha]_D - 5.52°$ for **1c**), led us, by comparison with similar situations [3] to propose a *S* absolute configuration for C-12′. Thus, we propose the structure of (2′*R*,12′*S*)-6-(2,12-diacetoxytridecyl)-2,4-dihydroxybenzoic acid for **1a**.

The derivatives of **2a** isolated by column chromatography of the methylated extract (**2b** and **2c**) showed similar spectroscopic features to those of **1b** and **1c**, respectively, the most significant difference being the presence in their ^{1}H NMR spectra of only one signal due to an acetoxyl group and the shielding of the H-12′, showing that it is bonded to a secondary hydroxyl group (3.82 *m* in **2b** and 3.77 *m* in **2c**). The ^{13}C NMR data (Table 2) also confirmed the location of the acetoxyl group on C-2′, as there is no significant change, when compared with those of **1b** and **1c**, in the value of the benzylic methylene (41.34 CH$_2$, **2b**) but there is a deshielding for C-11′ and C-13′ (39.21 CH$_2$ and 23.40 Me, respectively, **2b**). This, with the other spectroscopic properties and the values of $[\alpha]_D$ for **2b** and **2c** let us to propose the structure of (2′*R*,12′*S*)-6-(2-acetoxy-12-hydroxytridecyl)-2,4-dihydroxybenzoic acid for **2a**.



	R^1	R^2	R^3
1a	H	H	OAc
1b	H	Me	OAc
1c	Me	Me	OAc
2a	H	H	OH
2b	H	Me	OH
2c	Me	Me	OH
4	Me	Me	H

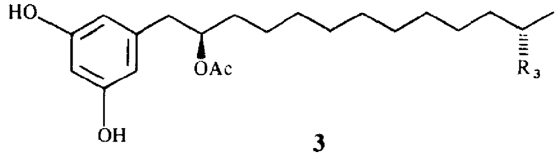


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Table 1. ^{1}H NMR data of compounds **1b**, **1c**, **2b**, **2c** and **3** (300 MHz, $CDCl_3$)

H	1b	1c	2b	2c
OH	11.66 *s*	11.68 *s*	11.66 *s*	11.67 *s*
3	6.28 *d* (2.5)	6.35 *d* (2.6)	6.28 *d* (2.5)	6.35 *d* (2.6)
5	6.21 *d* (2.5)	6.25 *d* (2.6)	6.21 *d* (2.5)	6.25 *d* (2.6)
2′	5.09 *dddd* (8.2, 4.8)	5.08 *dddd* (8.3, 4.8)	5.09 *dddd* (8.0, 5.2)	5.08 *dddd* (8.3, 4.8)
12′	4.88 *ddq* (6.3)	4.87 *ddq* (6.3)	3.82 *m*	3.77 *m*
CO_2Me	3.90 *s*	3.92 *s*	3.91 *s*	3.92 *s*
ArOMe	—	3.78 *s*	—	3.78 *s*
1′a	3.17 *dd* (13.3, 4.8)	3.19 *dd* (13.3, 4.8)	3.15 *dd* (13.3, 5.2)	3.19 *dd* (13.3, 4.8)
1′b	2.94 *dd* (13.3, 8.2)	2.96 *dd* (13.3, 8.3)	3.00 *dd* (13.3, 8.0)	2.97 *dd* (13.3, 8.3)
OAc-12′	2.02 *s*	2.01 *s*	—	—
OAc-2′	1.94 *s*	1.93 *s*	1.95 *s*	1.93 *s*
$(CH_2)_n$	1.23 *m*	1.24 *m*	1.23 *m*	1.24 *m*
Me-13′	1.19 *d* (6.3)	1.18 *d* (6.3)	1.19 *d* (6.2)	1.17 *d* (6.17)

The mass and ^{13}C NMR spectra for the new natural product **3** agreed with $C_{21}H_{34}H_5$ and in its IR spectrum signals of acetoxyl group (1736, 1266 cm^{-1}) and of aromatic ring (1603) appeared. Its ^{1}H NMR spectrum exhibited signals of hydrogens on a 1,3,5-trisubstituted aromatic ring (6.26 3H, *br s*) and of a chain bearing both an acetoxyl group in C-2′ and an hydroxyl group in C-12′. These considerations together with the spectroscopic data and the $[\alpha]_D$ value let us to propose the structure of (2′*R*,12′*S*)-5-(2-acetoxy-12-hydroxytridecyl) resorcinol for **3**.

EXPERIMENTAL

Ononis viscosa L. was collected in La Rábita (Granada, Spain) in May 1989. Plant material was identified by Professor F. Valle. A voucher specimen is deposited at the herbarium of the Faculty of Sciences of the University of Granada. Aerial parts (60 g) were air-dried, cut up and extracted with 200 ml $CHCl_3$ under reflux for 2 hr, yielding 3.2 g of extract (5.3% of dry wt). It was then methylated by treatment with a satd soln of CH_2N_2 in Et_2O and chromatographed over 50 g silica gel eluting with hexane–Et_2O mixts of increasing polarity. A mixt. of aliphatic compounds (400 mg, 11%) (hexane–Et_2O, 4:1) was obtained. The following CC frs yielded Me (2′*R*,12′*S*)-6-(2,12-diacetoxytridecyl)-2-hydroxy-4-methoxybenzoate (**1c**) (256 mg, 7%) (hexane–Et_2O, 7:3), Me (2′*R*,12′*S*)-6-(2,12-diacetoxytridecyl)-2,4-dihydroxybenzoate (**1b**) (965 mg, 30%) (hexane–Et_2O, 7:3), Me (2′*R*,12′*S*)-6-(2-acetoxy-12-hydroxytridecyl)-2-hydroxy-4-methoxybenzoate (**2c**) (376 mg, 12%) (hexane–Et_2O, 1:1), Me (2′*R*,12′*S*)-6-(2-acetoxy-12-hydroxytridecyl)-2,4-dihydroxybenzoate (**2b**) (496 mg, 15%) (hexane–Et_2O, 3:7), (2′*R*,12′S)-5-(2-acetoxy-12-hydroxytridecyl) resorcinol (**3**) (134 mg, 4%) (hexane–Et_2O, 1:4). All these compounds were purified by prep. TLC.

Methyl (2′R,12′S)-6-(2,12-diacetoxytridecyl)-2,4-dihydroxybenzoate (**1b**). Oily liquid. IR ν_{max}^{film} cm^{-1}: 3600–3100, 2930, 2854, 1735, 1654, 1618, 1588, 1524, 1444, 1375, 1321, 1259, 1172, 1107, 1023, 954, 851. UV λ_{max}^{MeOH} nm (log ε): 218 (4.13), 263 (4.01), 300 (3.65). $[\alpha]_D^{20}$ +11.9° ($CHCl_3$; *c* 1.198). MS *m/z* (rel. int.): 466 (10) $[M]^+$, 406 (11), 374 (12), 346 (25), 332 (6), 315 (26), 314 (100), 225 (1), 182 (61), 181 (12), 179 (9), 150 (60), 149 (7).

Methyl (2′R,12′S)-6-(2,12-diacetoxytridecyl)-2-hydroxy-4-methoxybenzoate (**1c**). Oily liquid. IR ν_{max}^{film} cm^{-1}: 3600–3100, 2929, 2855, 1733, 1653, 1615, 1576, 1508, 1434, 1372, 1329, 1305, 1256, 1204, 1160, 1111, 1045, 850, 764, 659. UV λ_{max}^{MeOH} nm (log ε): 219 (4.08), 255 (1.22), 295 (0.56). $[\alpha]_D^{20}$ −4.4° ($CHCl_3$; *c* 1.0). MS *m/z* (rel. int.): 480 (9) $[M]^+$, 420 (5), 388 (14), 360 (17), 346 (7), 329 (28), 328 (100), 225 (2), 196 (54), 195 (12), 193 (14), 182 (26), 165 (23), 164 (70), 163 (13).

Methyl (2′R,12′S)-6-(2-acetoxy-12-hydroxytridecyl)-2,4-dihydroxybenzoate (**2b**). Oily liquid. IR ν_{max}^{film} cm^{-1}: 3600–3100, 2928,

Table 2. ^{13}C NMR of compounds **1b**, **1c**, **2b** and **2c** (75 MHz, $CDCl_3$)

C	**1b**	**1c**	**2b**	**2c**	Mult.
1	105.04	105.12	104.98	105.14	C
2	142.83	142.28	142.80	142.28	C
3	112.66	112.50	112.67	112.49	CH
4	165.29	165.69	165.31	165.67	C
5	102.32	99.62	102.33	99.64	CH
6	161.06	163.75	161.22	163.76	C
1′	41.35	41.53	41.34	41.52	CH_2
2′	74.79	74.41	74.77	74.43	CH
3′	34.46	34.62	34.40	34.61	CH_2
4′	25.35[a]	25.44[a]	25.29[a]	25.41[a]	CH_2
	29.47	29.77	29.53	29.66	CH_2
5′–9′	29.44	29.58	29.48	29.60	CH_2
	29.37		29.35	29.56	CH_2
10′	25.41[a]	25.46[a]	25.71[a]	25.80[a]	CH_2
11′	35.91	35.99	39.21	39.41	CH_2
12′	71.51	71.17	68.64	68.27	CH
13′	19.99	20.03	23.40	23.54	CH_3
$\mathrm{Ar\underline{C}O_2Me}$	171.12[b]	170.51[b]	171.17[b]	170.53[b]	C
$\mathrm{ArCO_2\underline{Me}}$	52.08	52.10	52.07	52.09	Me
ArOMe	—	55.39	—	55.39	Me
$\mathrm{\underline{Me}CO_2\text{-}2'}$	21.18[c]	21.17[c]	21.21	21.15	Me
$\mathrm{Me\underline{C}O_2\text{-}2'}$	171.69[b]	171.70[b]	171.72[b]	171.69[b]	C
$\mathrm{\underline{Me}CO_2\text{-}12'}$	21.50[c]	21.46[c]	—	—	Me
$\mathrm{Me\underline{C}O_2\text{-}12'}$	171.54[b]	170.94[b]	—	—	C

[a–c] Interchangeable values.

2854, 1734, 1709, 1653, 1618, 1589, 1508, 1449, 1376, 1323, 1260, 1171, 1107, 1024, 952, 850, 805, 758, 719. UV λ_{max}^{MeOH} nm (log ε): 221 (4.02), 256 (3.99), 295 (3.68). $[\alpha]_D^{20}+8.2°$ ($CHCl_3$; *c* 1.166). MS *m/z* (rel. int.): 424 (13) $[M]^+$, 364 (27), 349 (12), 346 (27), 334 (3), 333 (12), 332 (33).

Methyl (2′R,12′S)-6-(2-*acetoxy*-12-*hydroxytridecyl*)-2-*hydroxy*-4-*methoxybenzoate* (**2c**). Oily liquid. IR ν_{max}^{film} cm^{-1}: 3600–3100, 2929, 2853, 1734, 1654, 1615, 1576, 1506, 1434, 1375, 1328, 1258, 1204, 1160, 1110, 1045, 1027, 956, 849, 834, 806, 717. UV λ_{max}^{MeOH} nm (log ε): 220 (4.10), 256 (4.08), 295 (3.75). $[\alpha]_D^{20}-5.5°$ ($CHCl_3$; *c* 1.015). MS *m/z* (rel. int.): 438 (5) $[M]^+$, 378 (8), 360 (16), 346 (34), 329 (11), 328 (44), 225 (1), 207 (26), 206 (31), 203 (37), 196 (62), 195 (16), 193 (19), 191 (28), 190 (46), 189 (18), 182 (19), 178 (25), 177 (26), 165 (30), 164 (100).

(2′R,12′S)-5-(2-*acetoxy*-12-*hydroxytridecyl*) *Resorcinol* (**3**). Oily liquid. IR ν_{max}^{film} cm^{-1}: 3600–3100, 2926, 2853, 1736, 1707, 1603, 1453, 1353, 1337, 1266, 1161, 1025, 945, 842, 706. ^{1}H NMR (300 MHz, $CDCl_3$): δ6.25 (3H, *s* H-2, H-4, H-6), 6.21 (1H, *m*, OH), 5.04 (1H, *dddd*, $J_1=J_2=J_3=J_4=6.6$ Hz, H-2′), 3.82 (1H, *ddq*, $J_1=J_2=J_3=6.2$ Hz, H-12′), 2.74 (1H, *dd*, $J_1=13.7$ Hz, $J_2=6.6$ Hz, H-1′a), 2.63 (1H, *dd*, $J_1=13.6$ Hz, $J_2=6.6$ Hz, H-1′b), 2.0 (3H, *s*, AcO-2′), 1.24 (18H, *br s*, H-3′ to H-11′), 1.18 (3H, *d*, $J=6.21$ Hz, H-13′), ^{13}C NMR (75 MHz, $CDCl_3$): δ171.50 (C, Me CO_2-2′), 157.09 (C, C-3, C-5), 140.47 (C, C-1), 108.81 (CH, C-2, C-6), 101.22 (CH, C-4), 74.97 (CH, C-2′), 68.54 (CH, C-12′), 40.68 (CH_2, C-1′), 39.20 (CH_2, C-11′), 33.34 (CH_2, C-3′), 29.78, 29.54, 29.39 (CH_2, C-5′ to C-9′), 25.65 (CH_2, C-10′), 25.14 (CH_2, C-4′), 23.51 (Me, C-13′), 21.37 (Me, Me–CO_2-2′). UV λ_{max}^{MeOH} nm (log ε): 208 (3.79), 278 (2.99). $[\alpha]_D^{20}+6.9°$ ($CHCl_3$; *c* 0.63). MS *m/z* (rel. int.): 366 (5) $[M]^+$, 306 (10), 288 (11), 163 (25), 161 (11), 150 (12), 149 (27), 137 (13), 136 (23), 125 (9), 24 (100), 123 (47).

Acknowledgements—We are grateful to Professor F. Valle for identification of plant material, and to the Junta de Andalucía and Ministerio de Educacion y Ciencia for financial support.

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