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SPECIONIN AND SPECIOSIDES A AND B: NEW AROMATIC LACTONES FROM *ONONIS SPECIOSA*

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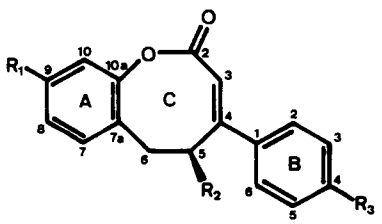
ABSTRACT.—Three new natural products **1–3** have been isolated from the EtOH extract of *Ononis speciosa*. The structures were established by chemical transformations and through their physical and spectroscopic features: uv, ir, ms, cd, and nmr.

Ononis speciosa Lag. is a vegetable species belonging to the Leguminosae and endemic to Andalucía (South of Spain). In a previous report (1), we described the isolation and identification of the major compounds (alkylresorcinols and flavonoids) from the $CHCl_3$ and EtOH extracts of the flowers. Herein we show three additional minor compounds **1–3**, possessing a skeleton which was recently proposed (2) for two glycosides isolated from *Pueraria lobata* Ohwi. on the basis of their uv, ir, ms, ^{1}H-nmr, and ^{13}C-nmr spectra. We have unambiguously extablished this molecular skeleton through 2D nmr techniques, chemical transformations, and cd curves.

Compounds **1–3** were isolated from the EtOH extract of the flowers of *O. speciosa*. Substance **1**, which we have named specionin, was recently described elsewhere as the hydrolysis product of a rhamnoside isolated from the roots of *P. lobata* (2). Speciosides A [**2**] and B [**3**] are also new natural products.

The structure of **1** had been assigned (2) on the basis of its spectral properties, although the relative positions of the substituents on the A ring and the absolute configuration at C-5 have remained uncertain until now. The first problem was solved through C-H correlation and C/H long range coupling experiments (Table 1). In the latter spectrum, the 3-bond C-H coupling between one hydrogen of C-6 and C-7, along with the large doublet coupling for H-7 with H-8, would only be consistent with the phenolic hydroxyl at C-9.

In order to determine the configuration at C-5, we attempted selective methylation of the phenolic hydroxyls of **1**. In this manner, only the C-5 hydroxyl would remain free; thus we planned es-



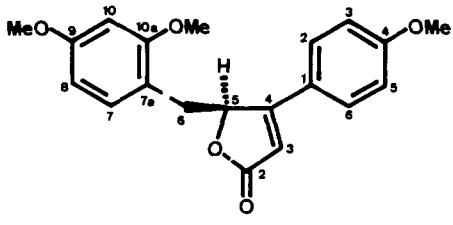
	R_1	R_2	R_3
1	OH	OH	OH
7	OAc	OAc	OAc
2	OH	OGlu	OH
8	OAc	OAcGlu	OAc
3	OGlu	OH	OH
9	OAcGlu	OAc	OAc
4	OMe	OH	OMe
5	OH	OMe	OMe

TABLE 1. Nmr C-H and C/H[a] Correlated Spectra of **1** (Me_2CO-d_6, 300 MHz).

δ	Proton	Carbon
173.79	H-5	C-2
113.33	H-3	C-3
158.84	H-6_a, -6_b	C-4
84.08	H-5, -3	C-5
39.70	H-6_a, -6_b	C-6
131.85	H-7, -6_b	C-7
109.02	H-8	C-8
104.02	H-10	C-10
156.95	H-10	C-10_a
131.42	H-2′, -6′	C-2′, -6′
115.60	H-3′, -5′	C-3′, -5′

[a]In the long range coupling (C/H), response of correlation resonance was optimized for $^nJ_{CH}$ values ranging between 3 and 10 Hz.

tablishment of the secondary alcohol configuration by Horeau's method (3). Unfortunately, when the reaction with Me_2SO_4 was performed in the presence of H_2O, **1** gave the lactone **6**. The formation of **6** was attributed to the hydrolysis of **1** with subsequent relactonization towards OH-5 and methylation of the phenolic hydroxyls.



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The structure of **6** was established through the uv, ir, ^{1}H-nmr (Table 2), ^{13}C-nmr (Table 3), ms, and cd spectra. The presence of the molecular ion at *m/z* 340 was in agreement with the formula $C_{20}H_{20}O_5$. The ^{1}H-nmr chemical shifts at 3.97, 3.90, and 3.73 ppm for the three methoxyl groups were consistent with aromatic methyl ethers. The ir spectrum was particularly significant, with a strong carbonyl absorption at 1742 cm^{-1}. The cd spectrum revealed a positive Cotton effect (4), which led us to propose the *S* configuration at C-5. As the transformation of **1** into **6** did not alter the configuration at C-5, the same *S*

TABLE 2. ^{1}H-nmr Spectra of **1**, **8**, **9** and **6** (performed at 300 MHz).

Position	Compound			
	1 (Me_2CO-d_6)	**8** ($CDCl_3$)	**9** ($CDCl_3$)	**6** (Me_2CO-d_6)
H-3	6.20 d (1.4)	6.10 d (1.4)	6.16 d (1.4)	6.17 d (1.4)
H-5	5.88 ddd (1.4,3.3,6.8)	5.84 ddd (1.4,4.0,6.4)	5.63 ddd (1.4,4.0,6.4)	5.86 ddd (1.4,3.5,6.6)
H-6_a	3.25 dd (3.3,14.5)	3.15 dd (4.0,14.2)	3.11 dd (4.0,14.2)	3.18 dd (3.5,14.6)
H-6_b	2.74 dd (6.8,14.5)	2.79 dd (6.4,14.2)	2.89 dd (6.4,14.2)	2.74 dd (6.6,14.6)
H-7	7.41 d (8.6)	7.24 d (8.1)	7.16 d (8.3)	7.52 d (8.6)
H-8	6.61 dd (2.4,8.6)	6.97–6.88 m	6.97–6.88 m	6.69 dd (2.4,8.6)
H-10	6.63 d (2.4)	6.97–6.88 m	6.97–6.88 m	6.73 d (2.4)
H-2',6'	6.94 d (8.5)	7.02 d (8.5)	7.04 d (8.6)	6.97 d (8.7)
H-3',5'	6.69 d (8.5)	6.97–6.88 m	6.97–6.88 m	6.77 d (8.7)
MeO				3.97 s
MeO				3.90 s
MeO				3.73 s
H-1"–4"		5.32–5.13 m	5.32–5.13 m	
H-6"		4.30–4.05 m	4.30–4.05 m	
H-5"		3.82 ddd (2.4,4.8,9.9)	3.94 ddd (2.4,4.8,9.9)	
9-OAc		2.33 s		
5-OAc			2.28 s	
4'-OAc		2.27 s	2.25 s	
Glu-OAc		2.08 s	2.07 s	
Glu-OAc		2.02 s	2.06 s	
Glu-OAc		2.02 s	2.05 s	
Glu-OAc		2.00 s	2.03 s	

TABLE 3. ^{13}C-nmr Spectra of **1**, **8**, **9**, and **6** (δ ppm, 75 MHz).

Carbon	Compound				
	1 (Me_2CO-d_6)	**8** ($CDCl_3$)	**9** ($CDCl_3$)	**6** (Me_2CO-d_6)	mult
C-2	173.79	172.29	173.24	173.32	C
C-3	113.33	110.93	114.27	115.00	CH
C-4	158.84	154.27	155.00	160.45	C
C-5	84.08	83.03	82.88	83.85	CH
C-6	39.70	38.34	38.68	39.42	CH_2
C-7	131.85	130.48	129.97	131.86	CH
C-8	109.02	118.37	118.50	106.96	CH
C-9	162.29	163.70	163.79	164.47	C
C-10	104.02	117.40	117.60	99.55	CH
C-10_a	156.95	153.45	153.60	159.48	C
C-7_a	110.61	119.84	118.30	113.13	C
C-1′	127.85	132.47	132.55	128.78	C
C-2′,-6′	131.42	130.73	130.95	131.44	CH
C-3′,-5′	115.60	121.49	121.60	114.18	CH
C-4′	165.89	167.83	168.40	165.06	C
MeO				56.06	Me
MeO				55.36	Me
MeO				49.74	Me
C-1″		98.69	98.36		CH
C-2″		71.32	71.07		CH
C-3″		72.31	71.85		CH
C-4″		67.86	68.10		CH
C-5″		72.59	72.40		CH
C-6″		61.51	61.94		CH_2
MeCOO		170.55	170.55		C
MeCOO		170.25	170.25		C
MeCOO		169.46	169.46		C
MeCOO		169.30	169.30		C
MeCOO		169.18	169.18		C
MeCOO		168.68	168.68		C
CH_3COO		21.25	21.25		Me
CH_3COO		21.18	21.18		Me
CH_3COO		20.71	20.71		Me
CH_3COO		20.62	20.62		Me
CH_3COO		20.62	20.62		Me
CH_3COO		20.53	20.53		Me

configuration was assigned to this carbon in **1**.

Compounds **2** and **3** were identified as glycosides of **1** through analysis of the spectroscopic features of their acetylated derivatives. The ^{1}H-nmr spectra contained, in addition to the signals corresponding to the specionin system, those due to a β-D-glucose unit, as revealed by a study of the ^{13}C-nmr spectra. The location of the β-D-glucosyl substituents at C-5 and C-9 for **2** and **3**, respectively, was established through chemical transformation into the corresponding peracetylated derivatives [**8** and **9**] and into **4** and **5** by methylation and subsequent hydrolysis of the resultant glycoside. The site of the sugar in the glycosides **2** and **3** was located through study of the ^{1}H-nmr spectra of the transformation products.

EXPERIMENTAL

PLANT MATERIAL AND EXTRACTION.—*O. speciosa* was collected in May 1987 in Izbor (Granada, Spain) and was identified by Professor F. Valle (Department of Botany, University of Granada). A voucher specimen (Reg. No. 3360)

is available at the herbarium of the Faculty of Sciences of the University of Granada. Air-dried flowers (2.5 kg) were extracted with $CHCl_3$, followed by EtOH in a Soxhlet apparatus. The EtOH extract, after removal of the solvent, was mixed with H_2O and extracted with $CHCl_3$ followed by EtOAc. The EtOAc extract was chromatographed on Si gel columns, eluting with mixtures of $CHCl_3$ and Me_2CO, to give specionin [**1**] (45 mg) and the mixture of the speciosides A [**2**] and B [**3**] (40 mg), together with the previously reported products (1).

TRIACETYL SPECIONIN [**7**].—Acetylation of **1** yielded **7**: ^{1}H-nmr ($CDCl_3$, 80 MHz) δ ppm 7.40–6.85 (7H, m, H-2′,-3′,-4′,-5′,-7,-8,-10), 6.19 (1H, d, J = 1.6 Hz, H-3), 5.66 (1H, ddd, J = 1.6 Hz, J = 4.0 Hz, J = 6.4 Hz, H-5), 3.19 (1H, dd, J = 4.0 Hz, J = 14.0 Hz, H_a-6), 2.85 (1H, dd, J = 6.4 Hz, J = 14 Hz, H_b-6), 2.33 (3H, s, OAc), 2.28 (3H, s, OAc), 2.25 (3H, s, OAc); ir ν (film) cm^{-1} 3079, 2928, 2853, 1761, 1618, 1505, 1431, 1369, 1195, 1112, 1075, 1016, 976, 908, 866, 848, 758, 665; uv λ max (MeOH) nm (log ε) 210 (4.20), 258 (3.97); $[\alpha]^{25}D$ −7.2 (c = 0.84 cg/ml, $CHCl_3$); ms (70 eV) *m/z* (rel. int.) 424 (1), 382 (2), 364 (1), 302 (7), 149 (57), 121 (61), 43 (100).

Acetylation of the mixture of **2** and **3** yielded a mixture of **8** and **9**: ir ν (film) cm^{-1} 3062, 2963, 2937, 2878, 2863, 1758, 1749, 1726, 1613, 1584, 1517, 1509, 1448, 1370, 1293, 1268, 1243, 1225, 1124, 1073, 1046, 990, 949, 908, 840, 814, 738, 704, 653, 628; uv λ max (MeOH) nm (log ε) 220 (4.4), 280 (4.3), 307 (4.2); $[\alpha]^{25}D$ −48.03 (c = 0.65 cg/ml, MeOH); ms *m/z* (rel. int.) 382 (1), 365 (1), 331 (23), 281 (1), 271 (8), 211 (3), 169 (100), 145 (5), 140 (1), 129 (18), 115 (3), 109 (48), 103 (3), 98 (1), 43 (51).

METHYLATION OF SPECIOSIDES A [**2**] AND B [**3**].—Methylation of the mixture of **2** and **3** with Me_2SO_4 and K_2CO_3 in Me_2CO for 2 h (reaction followed by tlc) and subsequent hydrolysis with refluxing 2N HCl for 24 h gave 4′,9-dimethoxyspecionin [**4**] and 4′,5-dimethoxyspecionin [**5**], which could not be separated: ir ν (film) cm^{-1} 3189, 3005, 2934, 2837, 1705, 1604, 1509, 1460, 1432, 1300, 1245, 1207, 1169, 1130, 1110, 1030, 985, 962, 829, 809, 756, 695, 609; ^{1}H nmr (80 MHz, Me_2CO-d_6) δ ppm (signals due to **4**) 7.49 (1H, d, J = 9 Hz, H-7), 6.21 (1H, d, J = 2 Hz, H-3), 3.85 (3H, s, 9-OMe), 3.75 (3H, s, 4′-OMe), (signals due to **5**) 7.43 (1H, d, J = 9 Hz, H-7), 6.14 (1H, d, J = 3 Hz, H-3), 3.94 (3H, s, 5-OMe), 3.75 (3H, s, 4′-OMe), (common signals) 7.10–6.50 (6H, m, H-8,-10,-2′,-3′,-5′,-6′), 5.75–6.00 (1H, m, H-5), 3.43–3.09 (2H, m, H-6); uv λ max (MeOH) nm (log ε) 218 (3.93), 280 (3.76), 316 (387); $[\alpha]^{25}D$ −8.79 (c = 1.06 cg/ml, $CHCl_3$); ms *m/z* (rel. int.) $[M]^+$ 326 (4), 269 (1), 268 (3), 267 (1), 177 (3), 151 (3), 149 (6), 148 (2), 147 (4), 121 (100).

(*S*)-5(2,4-DIMETHOXYBENZYL)-4(4-METHOXYPHENYL)-5*H*-FURAN-2-ONE [**6**].—Compound **1** (20 mg) was refluxed with Me_2SO_4 and K_2CO_3 in Me_2CO for 1 h; then H_2O (0.5 ml) was added, and the mixture was refluxed 1 h. After workup, **6** (21 mg, syrup at 25°) was obtained: ir ν (film) cm^{-1} 3467, 2928, 2841, 2596, 2328, 2056, 1742, 1607, 1565, 1509, 1463, 1301, 1286, 1248, 1211, 1162, 1028, 986, 941, 826, 756, 723, 687, 636; uv λ max (MeOH) nm (log ε) 219 (4.21), 280 (4.05), 316 (4.15); cd $\delta\epsilon_{335} = -0.02$, $\delta\epsilon_{301} = -0.21$, $\delta\epsilon_{257} = +0.201$; ms *m/z* (rel. int.) $[M]^+$ 340 (2), 249 (1), 205 (1), 191 (1), 167 (1), 163 (2), 161 (2), 149 (2), 137 (2), 135 (2), 133 (2), 123 (2), 122 (10), 121 (100).

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