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SALICIFOLIOL, A NEW FUROLACTONE-TYPE LIGNAN FROM *BUPLEURUM SALICIFOLIUM*

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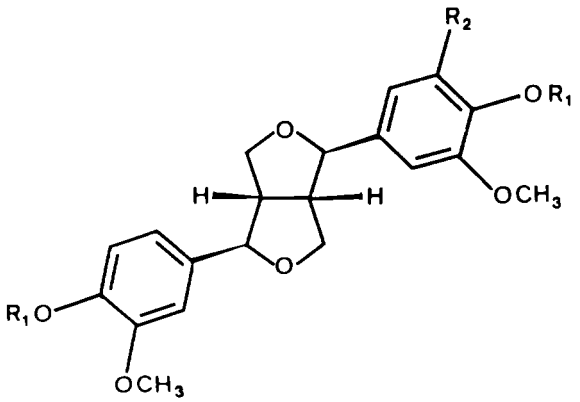
ABSTRACT.—Four lignans were obtained from the aerial part of *Bupleurum salicifolium*. Three 2,6-diaryl-3,7-dioxabicyclo-[3.3.0]-octane compounds were identified as eudesmin, pinoresinol, and medioresinol while a fourth, (1*R*,2*R*,5*S*)-6-(3′-methoxy-4′-hydroxyphenyl)-3,7-dioxa-6-oxobicyclo-[3.3.0]-octane, salicifoliol [**4**], is reported for the first time.

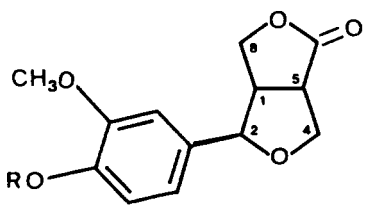
In a preliminary chemical assay of *Bupleurum salicifolium* Soland. (Umbelliferae), a species endemic to the Canary Islands (1), lignans were detected. As these compounds have interesting physiological properties (2), the plant was studied in depth, and stigmasterol, the bisepoxylignans eudesmin [**1**], pinoresinol [**2**], and medioresinol [**3**], and a new furolactone-type epoxylignan, salicifoliol [**4**], were obtained.

The petroleum ether and C_6H_6 extracts of the aerial parts of the plant were subjected to cc, and five substances were separated. Stigmasterol (3), pinoresinol [**2**] (4), and medioresinol [**3**] (5), their acetates, and eudesmin [**1**] (6) were identified by comparison of their spectral and physical data with those reported in the literature. The ir of the fifth substance showed the presence of a γ-lactone and phenolic OH. Its structure was determined as **4** on the basis of its physical and spectral properties and those of its acetyl derivative and by correlation with the data published for other lignans such as pluviatide (7), glaberide I (8), and acuminatolide (9) among others (10,11).

The ^{1}H-nmr spectrum of **4** showed signals for a 3-methoxy-4-hydroxyphenyl grouping; the H-5′ signals were shifted 1.4 ppm in the acetyl derivative



1 R_1=Me, R_2=H
2 R_1=R_2=H
3 R_1=H, R_2=OMe



4 R=H
5 R=Ac

(Table 1). Signals also appeared for the protons of a bicyclic [3.3.0]-octane system, with the bridgehead H-1 and H-5 at highest field. Two groups of signals for methylene groups were also observed; one was centered at δ 4.27 (2H) and the other 3 Hz further downfield, at δ 4.41 (2H). These latter signals were assigned to the lactone ring methylene (H-8), and this attribution was confirmed by COSY experiments that showed these signals coupled with the bridgehead H-1; the signals at δ 4.27, assigned to H-4, were coupled with H-5.

A doublet centered at δ 4.62 (6.7 Hz) was assigned to the benzylic proton H-2 both because it appeared furthest downfield and because COSY experiments coupled it only with the bridgehead H-1 and, at long distance, with the benzene proton H-2′. This means that the aryl substituent must be exo, as is the case in other bisepoxylignans obtained from *B. salicifolium*.

In the ^{13}C-nmr spectrum (Table 2), signals appeared at 86.30 ppm in **4** and 86.00 in **5** consistent with a C-2 carbon joined to an exo aryl grouping (12). The C-8 signals, just like the H-8 protons in the ^{1}H-nmr spectrum, were shifted further downfield than those of C-4 (Table 2) due to the paramagnetic shielding of the carbonyl.

The ^{1}H- and ^{13}C-nmr spectra of salicifoliol and salicifoliol acetate, taken in C_6D_6, ratified these conclusions (Tables 1 and 2), and the electronic fragmentation spectra are in agreement with the fragmentation pattern for structures such as **4** and **5** (13, 14).

EXPERIMENTAL

GENERAL.—Mp's were taken on a Kofler-type apparatus and are uncorrected. Tlc Si gel (type G Schleicher-Schüll F-1500/LS 254) plates were developed in $CHCl_3$–*n*-hexane (19:1 and 11:9), $CHCl_3$, and $CHCl_3$-EtOAc (9:1) and visualized with I_2 vapors or uv light or sprayed with H_2SO_4-HOAc-H_2O (80:16:4) and charred at 100°. The cc details varied with the compound involved and are given below. A Perkin-Elmer 681 spectrophotometer was used for ir spectra and a Perkin-Elmer 550 SE for uv with quartz cells of 1 and 5 mm and EtOH as solvent. The ms were collected on a VG-Micromass ZAB-2F spectrometer. ^{1}H- and ^{13}C-nmr spectra were taken on a Bruker WD-200 SY at 200 and 50 MHz, respec-

TABLE 1. ^{1}H-nmr Data of Salicifoliol [**4**] and Salicifoliol Acetate [**5**].[a]

Proton	Compound			
	4		**5**	
	In $CDCl_3$	In C_6D_6	In $CDCl_3$	In C_6D_6
H-1	3.12 dddd	2.19 dddd	3.07 dddd	2.19 dddd
H-5	3.42 ddd	2.56 ddd	3.38 ddd	2.49 ddd
H-4eq	4.18 dd	4.07 dd	4.17 dd	4.08 dd
H-8ax	4.32 dd	3.64 dd	4.29 dd	3.59 dd
H-4ax	4.36 dd	3.88 dd	4.31 dd	3.83 dd
H-8eq	4.50 dd	3.54 dd	4.46 dd	3.50 dd
H-2ax	4.62 d	4.15 d	4.63 d	4.14 d
H-6′	6.81 dd	6.42 dd	6.81 dd	6.42 dd
H-2′	6.89 d	6.68 d	6.92 d	6.68 d
H-5′	6.91 d	6.92 d	6.97 d	6.92 d
OMe	3.91 s	3.16 s	3.79 s	3.29 s
OH	5.67 s	5.47 s	—	—
MeCOO	—	—	2.26 s	1.89 s

[a]Chemical shifts in δ (ppm). Coupling constants (Hz), median values: $J_{1,2}=6.7$, $J_{1,5}=9.0$, $J_{1,8ax}=2.2$, $J_{1,8eq}=6.5$, $J_{4ax,4eq}=9.0$, $J_{4ax,5}=9.1$, $J_{4eq,5}=9.1$, $J_{8ax,8eq}=9.6$, $J_{2',6'}=2.0$, $J_{5',6'}=8.0$.

TABLE 2. ^{13}C-nmr Data for Salicifoliol [**4**] and Salicifoliol Acetate [**5**].[a]

Carbon	4		5	
	$CDCl_3$	C_6D_6	$CDCl_3$	C_6D_6
C-1	46.19	45.84	46.21	45.89
C-5	48.34	48.27	48.63	48.49
C-8	70.00	68.98	70.43	70.24
C-4	70.15	69.98	70.07	68.95
C-2	86.30	85.89	86.00	85.57
C-6	178.24	177.19	179.06	177.29
C-2′	108.69	108.86	109.99	110.16
C-5′	114.63	114.66	123.21	123.23
C-6′	119.27	119.27	118.16	117.96
C-1′	130.84	131.59	137.74	136.76
C-4′	146.07	146.37	140.05	141.40
C-3′	147.12	146.37	153.56	152.02
OMe	56.17	55.30	56.16	55.44
*C*OOMe	—	—	169.98	169.84
COO*Me*	—	—	20.81	20.20

[a]Chemical shifts are given in δ (ppm). Assignments based on DEPT experiments (15) and correlations with other substances.

tively, with $CDCl_3$ and C_6D_6 as solvents and TMS as internal reference.

PLANT MATERIAL.—Specimens of fully grown wild plants of *B. salicifolium* collected at the Barranco de Guayadeque, Gran Canaria, Canary Islands were used. A voucher specimen was lodged in the TFC File in the Dept of Biología Vegetal (Botánica) of the Universidad de La Laguna.

ISOLATION AND SEPARATION OF COMPOUNDS.—The aerial parts of *B. salicifolium* without leaves or flowers (5 kg) were cut and then ground and extracted in hot EtOH in a Soxhlet. The EtOH extract was reduced by in vacuo distillation of the solvent, leaving an oily-looking residue which was extracted by heating at reflux with petroleum ether (bp 50–70°) and C_6H_6.

The petroleum ether extract left a dark, oily residue (46.24 g) that was chromatographed on a column of 1000 g Al_2O_3, activity IV (with 10% H_2O) and then eluted repeatedly with *n*-hexane, solutions of *n*-hexane/C_6H_6 of increasing polarity, and C_6H_6; fractions of 500 ml were collected. With *n*-hexane–C_6H_6 (7:3) (1500 ml), a whitish substance (0.14 g) was separated and proved to be stigmasterol (^{1}H nmr, ms). The C_6H_6 fractions (1000 ml) yielded eudesmin (0.21 g), pinoresinol (^{1}H nmr, ms) (1.75 g), and medioresinol (^{1}H nmr, ms) (0.8 g), separated by thick layer chromatography.

The C_6H_6 extract (428 g) was chromatographed on a column of 3500 g Al_2O_3 and eluted with petroleum ether-C_6H_6 (4:1), petroleum ether/C_6H_6, C_6H_6, C_6H_6/EtOAc, and EtOAc in order of increasing polarity, and 1000-ml fractions were collected. From the C_6H_6-EtOAc (9:1) fractions (7 liters), pinoresinol (10.9 g) was separated; from the C_6H_6-EtOAc (4:1) (1 liter), medioresinol (2.5 g); and from the C_6H_6-EtOAc (2:3) (5 liters), salicifoliol [**4**] (0.12 g).

SALICIFOLIOL [**4**].—Crystallized from C_6H_6 with a few drops of petroleum ether as colorless needles, mp 102–103°. When irradiated with uv light, it shows a weak pale-blue fluorescence. Ir (Nujol) ν max cm^{-1} 3500, 3365 (broad), 1765, 1613, 1525, 1245, 1180, 1131, 1050, 1030, 990, 970; uv λ max nm 233, 282; ^{1}H nmr see Table 1; ^{13}C nmr see Table 2; eims *m/z* $[M]^+$ 250.0842 (100%), required for $C_{13}H_{14}O_5$, 250.0841, 233 (9), 235 (4), 191 (7), 165 (39), 152 (100); 151.0366 (10) (required for $C_8H_7O_3$, 151.0395), 137.0577 (100) (required 137.0603), 123 (18), 109 (19).

SALICIFOLIOL ACETATE [**5**].—Prepared by treating salicifoliol [**4**] with Ac_2O in pyridine at room temperature: mp 207–208°; ir ν max (Nujol) cm^{-1} 1760, 1742, 1615, 1520, 1220, 1124; ^{1}H nmr see Table 1; ^{13}C nmr see Table 2; eims *m/z* $[M]^+$ 292 (12%) ($C_{15}H_{16}O_6$), 250 (100), 218 (27), 165 (45), 151 (100), 152 (100), 137 (100), 135 (88), 91 (44), 79 (42), 77 (68), 43 (100).

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