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Justicidone, a Novel *p*-Quinone-Lignan Derivative from *Justicia hyssopifolia*

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An uncommon, previously unreported *p*-quinone-lignan compound called justicidone (4-(1,3-benzodioxol-5-yl)-6-methoxynaphtho[2,3-*c*]furan-1,5,8(3*H*)-trione) (2), along with the known savinin (1) were isolated from *Justicia hyssopifolia* (Acanthaceae). Their structures were determined by spectroscopic methods.

Key words *Justicia hyssopifolia*; justicidone; lignan

The family Acanthaceae consist of more than 2500 species distributed into 250 genera.[1] From species of this family a great amount of compounds with a variety of biological activities have been isolated. Lignans are very frequent among the components of species of this family and their activity against a series of diseases is well documented.[2]

In a previous paper[3] we reported on the isolation and structure elucidation of lignan derivatives of *Justicia hyssopifolia*, the only representative species of this family in the Macaronesia. Further studies on this plant, has yielded the known lignan savinin (**1**)[4] and justicidone (4-(1,3-benzodioxol-5-yl)-6-methoxynaphtho[2,3-*c*]furan-1,5,8(3*H*)-trione) (**2**), which we have called justicidone and is described for the first.

Compound **2** was isolated as a reddish powder with a molecular formula of $C_{20}H_{12}O_7$ by high resolution (HR)-MS. Its ^{1}H-NMR spectrum (Table 1), showed, in addition to the typical signals of piperonal moiety, shifts for a methylene group, a methoxy group and two singlets assignable to two aromatic protons. All these data suggested the compound to be a 6-methoxy-5,8-dihydroxy lignan derivative of the arylnaphthalene type. However, this hypothesis would give a molecular weight two units higher than that obtained by HR-MS, but could be explained if this moiety were a *para*-quinone derivative. This new hypothesis was supported by its ^{13}C-NMR spectrum with resonances at δ 169.2, 179.3 and 182.9, assigned to a lactonic carbonyl group and a *para*-quinone system respectively. Correlation of C-5 with H-7, and C-8 with H- 7 and H-9 in the heteronuclear multiple bond connectivity (HMBC) spectrum were in agreement with the presence of such a system. The carbonyl group at C-1 was assigned on the basis of HMBC and rotating frame Overhauser enhancement spectroscopy (ROESY) data. Thus, in the HMBC spectrum there were correlations from C-1 to H-9 and the protons of a methylene group, which was assigned to C-3. This was confirmed in its ROESY spectrum where correlations between the lactonic methylene group and the signals of H-4′ and H-6′ of the piperonal moiety were observed.

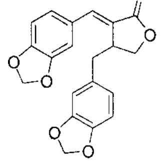
Table 1. ^{1}H-, ^{13}C-NMR, HMBC and ROESY Spectral Data for Justicidone (**2**) in $CDCl_3$

Position	^{1}H (δ)	^{13}C (δ)	HMBC	ROESY
1		169.2	3, 9	
3	α=5.17, d, J=16.4 β=5.06, d, J=16.4	69.7		4′, 6′
3a		151.4		
4		138.6	4′, 6′	
4a		129.1	3, 9	
5		179.3	7	
6		161.0	2″, 7	
7	8.72, s	109.2		2″
8		182.9	7, 9	
8a		135.1	7, 9	
9	6.26, s	123.9		
9a		131.7	3	
2′	6.05, d, J=10.8	101.5		
3′a		147.9	2′, 4′, 6′, 7′	
4′	6.61, s	120.3	6′	3
5′		129.8	7′	
6′	6.62, dd, J_1=8.4, J_2=1.6	107.9		7′, 3
7′	6.90, d, J=8.4	109.0	6′	6′
7′a		148.3	2′, 4′, 6′, 7′	
2″	3.86, s	56.7		7

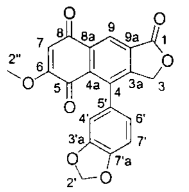
We consider compound **2** of interest since its structure has elements of both a lignan and a naphtoquinone, features that are often associated with compounds with antifungal, cytotoxic, antitumor, analgesic, *etc.* activities.[5—7] This structure is described for first time in the literature as a compound of natural origin and probably it is formed by enzymatic oxidation of **3**, the most abundant component from *J. hyssopifolia*.[3]

Experimental

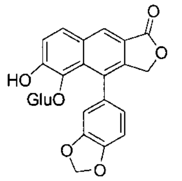
General Experimental Procedures Melting point was determined on a Büchi B-540 apparatus and is uncorrected. IR spectrum was recorded in $CHCl_3$ on a Bruker IFS 55 spectrophotometer. UV spectrum was obtained in



1



2



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absolute MeOH on a JASCO V-560 apparatus. ^{1}H-, ^{13}C- and two dimension spectra were taken in $CDCl_3$ on a Bruker Advance 400 NMR spectrometer. HR-MS was recorded on a Micromass Autospect spectrometer. Silica gel (particle size 40—63 μm, Merck) and Sephadex LH-20 (Pharmacia) were used for column chromatography. Kromasil 100 Si 5μ (25×1 cm) for HPLC.

Plant Material The aerial parts of *Justicia hyssopifolia* were collected in Punta Cangrejo, Adeje, Tenerife, in January 2002. A voucher specimen (HPJ-AO233) is deposited in the herbarium at the Instituto Universitario de Bioorganica “Antonio Gonzalez.”

Extraction and Isolation One thousand and five hundred grams of dried leaves of *J. hyssopifolia* were exhaustively extracted by refluxing with EtOH, giving about 200 g of dried extract. This extract was partitioned by decantation into the following soluble fractions: chloroform (85 g), ethyl acetate (8 g), butanol (24 g) and water.

The butanol soluble extract was taken to vacuum dryness and submitted to a silica gel flash chromatography, using ethyl acetate–methanol mixtures of increasing polarity as eluent. This gave 70 fractions, which were grouped after thin layer chromatography. From the group of fractions 31—70, eluted in ethyl acetate–methanol 50 : 50, was isolated and identified one compound (2 mg) that showed a reddish colouration both in solution and in solid state.

Justicidone (**2**): Red crystals (AcOEt–*n*-hexane): mp 114—115 °C; UV (MeOH) λ_{max} (log ε) 252 (4.92), 276 (4.69), 322 (4.29); IR (NaCl) ν_{max} 2924, 2852, 1772, 1688, 1651, 1619, 1504, 1455, 1223, 1064, 1012 cm^{-1}; ^{1}H-, ^{13}C-NMR, HMBC and ROESY NMR experiments (see Table 1); HR-MS *m/z* 364.0557 (Calcd for $C_{20}H_{12}O_7$, 364.0583).

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References

1) Kunkel G., “Flora y Vegetación del Archipiélago Canario. Tratado Florístico, 2^a Parte,” Las Palmas de Gran Canaria, Islas Canarias, 1991, p. 216.
2) Jyotishi S. G., Bagavant G., *Indian J. Nat. Prod.*, **8**, 3—19 (1992).
3) Trujillo J. M., Jorge E., Navarro E., Boada J., *Phytochemistry*, **29**, 2991—2993 (1990).
4) Shieh H.-L., Cordell G. A., Lankin D. C., Lotter H., *J. Org. Chem.*, **55**, 5139—5145 (1990).
5) Perry N. B., Blunt J. W., Munro M. H. G., *J. Nat. Prod.*, **54**, 978—985 (1991).
6) Papageorgiou V. P., Assimopoulou A. M., Couladouros E. A., Hepworth D., Nicolaou K. C., *Angew. Chem. Int. Ed.*, **38**, 271—300 (1999).
7) Khan R. M., Mlungwana S. M., *Phytochemistry*, **50**, 439—442 (1998).