

Prenylflavonoids from *Flourensia fiebrigii*

María L. Uriburu ^{a,*}, Roberto R. Gil ^b, Virginia E. Sosa ^c, Juana R. de la Fuente ^a

^a Consejo de Investigación, Universidad Nacional de Salta, Avda. Bolivia 5150, 4400 Salta, Argentina

^b Department of Chemistry, Carnegie Mellon University, Pittsburgh, Fifth Avenue, PA 15213, USA

^c Facultad de Ciencias Químicas, Universidad Nacional de Córdoba, Instituto Multidisciplinario de Biología Vegetal (IMBIV-CONICET), Pabellón Argentina-Ala1, Córdoba, Argentina

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Abstract

Three compounds: (2*S*)-8-(3''-methylbut-2''-enyl)-7,3',4'-trihydroxyflavanone, (2*S*)-8-(3''-methyl-4''-hydroxy-but-2''-enyl)-7,3',4'-trihydroxyflavanone and (2*S*)-8-(3''-methyl-4''-hydroxy-but-2''-enyl)-5,3',4'-trihydroxy-7-methoxyflavanone, along with five previously known compounds, were isolated from the aerial parts of *Flourensia fiebrigii*. Their structures were elucidated by application of various spectroscopic methods, including 1D and 2D NMR techniques.

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1. Introduction

The genus *Flourensia*, Asteraceae, comprises 25 species distributed throughout America. This genus seems to be characterized by the occurrence of prenylflavonoids and benzofuran derivatives (Bohlmann and Grenz, 1977; Bohlmann and Jakupovic, 1979; Bohlmann et al., 1984). In previous articles, we have reported the isolation of several prenylflavonoids and benzofuran derivatives from both *Flourensia campestris* Wedd. and *Flourensia riparia* Griseb. (Uriburu et al., 2004, 2005).

As part of our continuing program aimed towards the study of *Flourensia* species present in Argentina, we herein report the isolation and structural characterization of three new prenylflavanones from *Flourensia fiebrigii* Blake, as well as the presence of five previously known compounds. Their structures were elucidated by application of various spectroscopic methods, including the use of 1D and 2D NMR spectroscopy.

2. Results and discussion

The Et₂O extract of the aerial parts of *F. fiebrigii* yielded three new compounds, the prenylflavonoids **1–3**, together with other known ones: tremetone (Zalkow et al., 1979), 6-methoxytremetone (Castañeda et al., 1996), 8-prenyl-eriodictyol (Fukai and Nomura, 1990), 2-isopropenyl-3-oxyangeloyl-5-acetyl-*cis*-2,3-dihydrobenzofuran (Bohlmann and Dutta, 1979) and 5,3'-dihydroxyisobavachin-7-*O*-methyl ether (Bohlmann and Jakupovic, 1979).

Compound **1** was obtained as an amorphous solid, and the molecular formula was determined to be C₂₀H₂₀O₅ from analysis of its HREIMS and NMR spectroscopic data. The UV, ¹H and ¹³C NMR spectra (Table 1) were consistent with a flavanone skeleton. In addition, both the lack of a downfield signal for a chelated phenolic group in the ¹H NMR spectrum and the absence of a bathochromic shift when the UV spectrum was recorded with the addition of AlCl₃/HCl were indicative of a 5-deoxyflavanone. This was confirmed by the appearance of two *ortho*-coupled doublets (*J* = 8.5 Hz) at δ 7.75 and 6.53, each integrating for one proton, assigned to H-5 and H-6, respectively. It also displayed a set of characteristic signals for a γ,γ-dimethylallyl moiety which was located at C-8, based on the HMBC

* Corresponding author. Tel./fax: +54 387 4255363.

E-mail address: luriburu@unsa.edu.ar (M.L. Uriburu).

Table 1
¹H (500 MHz, *J* in Hz) and ¹³C (125 MHz) spectroscopic data for compounds **1–3**

	1^a		2^b		3^b	
	δH	δC	δH	δC	δH	δC
2	5.35 <i>dd</i> (2.9, 13.1)	79.2 <i>d</i>	5.43 <i>dd</i> (3.2, 12.0)	80.0 <i>d</i>	5.44 <i>dd</i> (3.2, 11.5)	79.4 <i>d</i>
3 _{ax}	2.97 <i>dd</i> (2.9, 17.0)	44.0 <i>t</i>	2.96 <i>dd</i> (12.0, 16.6)	43.9 <i>t</i>	3.11 <i>dd</i> (11.5, 17.0)	43.3 <i>t</i>
3 _{eq}	2.81 <i>dd</i> (13.1, 17.0)		2.74 <i>dd</i> (3.2, 16.6)		2.84 <i>dd</i> (3.2, 17.0)	
4		191.5 <i>s</i>		191.0 <i>s</i>		198.5 <i>s</i>
5	7.75 <i>d</i> (8.5)	126.5 <i>d</i>	7.58 <i>d</i> (8.7)	126.0 <i>d</i>		163.9 <i>s</i>
6	6.53 <i>d</i> (8.5)	110.6 <i>d</i>	6.61 <i>d</i> (8.7)	110.2 <i>d</i>	6.13 <i>s</i>	92.8 <i>d</i>
7		161.5 <i>s</i>		162.2 <i>s</i>		166.8 <i>s</i>
8		114.7 <i>s</i>		116.0 <i>s</i>		109.2 <i>s</i>
9		160.3 <i>s</i>		162.1 <i>s</i>		160.1 <i>s</i>
10		114.0 <i>s</i>		116.2 <i>s</i>		103.9 <i>s</i>
1'		131.9 <i>s</i>		132.2 <i>s</i>		132.1 <i>s</i>
2'	7.00 <i>brs</i>	113.4 <i>d</i>	7.09 <i>d</i> (1.7)	114.4 <i>d</i>	7.07 <i>brs</i>	114.5 <i>d</i>
3'		143.5 <i>s</i>		146.2 <i>s</i>		146.6 <i>s</i>
4'		143.5 <i>s</i>		146.2 <i>s</i>		146.6 <i>s</i>
5'	6.90 <i>brs</i>	115.4 <i>d</i>	6.84 <i>d</i> (8.1)	115.8 <i>d</i>	6.85 <i>brs</i>	115.9 <i>d</i>
6'	6.90 <i>brs</i>	118.9 <i>d</i>	6.86 <i>dd</i> (1.7, 8.1)	118.5 <i>d</i>	6.85 <i>brs</i>	119.0 <i>d</i>
1''	3.43 <i>brd</i> (7.0)	22.2 <i>t</i>	3.40 <i>brd</i> (7.0)	22.0 <i>t</i>	3.26 <i>brd</i> (7.3)	21.5 <i>t</i>
2''	5.23 <i>brt</i> (7.0)	120.9 <i>d</i>	5.50 <i>brt</i> (7.0)	123.2 <i>d</i>	5.40 <i>brt</i> (7.3)	123.6 <i>d</i>
3''		135.4 <i>s</i>		136.3 <i>s</i>		136.1 <i>s</i>
4''	1.77 <i>brs</i>	25.8 <i>q</i>	3.93 <i>d</i> (5.5)	68.2 <i>t</i>	3.90 <i>brs</i>	68.5 <i>t</i>
5''	1.78 <i>brs</i>	18.0 <i>q</i>	1.70 <i>brs</i>	13.5 <i>q</i>	1.67 <i>brs</i>	13.8 <i>q</i>
OCH ₃					3.90 <i>s</i>	54.5 <i>s</i>
OH	5.97 <i>s</i>				8.15 <i>s</i>	
OH	5.59 <i>s</i>				7.91 <i>s</i>	
OH	5.40 <i>s</i>				12.21 <i>s</i>	
4''-OH			3.87 <i>t</i> (5.5)		5-OH	

Assignments aided with HH-COSY, HSQC and HMBC.

^a In CDCl₃.

^b In CD₃COCD₃.

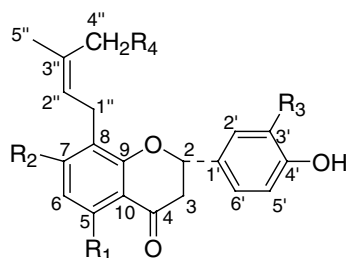
correlations from H-1'' through C-7, C-8, C-9. The aromatic signals of ring B also were evident as a two-proton singlet at δ 6.90 (H-5' and H-6') and an one-proton singlet at δ 7.00 (H-2') (Harborne, 1994); additionally three D₂O exchangeable signals were observed (Table 1) corresponding to three hydroxy phenolic groups. The 3',4' dihydroxy substitution was also evident from the HMBC correlations from H-2 through C-1', C-2', C-6', C-4, and from H-2' through C-1', C-6', C-2, respectively. In the CD spectrum, a negative Cotton effect at 301 nm (Δε −1.16), and a positive Cotton effect at 332 (Δε +6.35) indicated the *S*-configuration at C-2 (Inuma et al., 1994; Slade et al., 2005). Therefore, this new compound was characterized as (2*S*)-8-(3''-methylbut-2''-enyl)-7,3',4'-trihydroxyflavanone (**1**).

Compound **2** was isolated as a gum and was assigned the molecular formula C₂₀H₂₀O₆ from analysis of its

HRFABMS and NMR spectroscopic data. The UV spectrum in MeOH at 286 nm suggested a flavanone skeleton and the absorption maxima was also unaffected by addition of AlCl₃/HCl as for compound **1**. The ¹H NMR spectra was similar to that for **1** (Table 1), with the same substitution pattern, except for the presence of a 2H doublet at δ 3.93 (H-4'') attributable to a methylene carbinol allylic group. This allylic secondary hydroxyl group at δ 3.87, was unambiguously established to be at C-4'' by means of the COSY, HSQC and HMBC spectra. The attachment of the hydroxyprenyl moiety was determined to be at C-8 by the detection of HMBC correlations from H-1'' to C-7, C-8, C-9, C-3''. The absolute configuration at C-2 was considered to be *S* according to the results of the CD spectroscopic analysis (see Section 4). Consequently, the structure of **2** was concluded to be

(2*S*)-8-(3''-methyl-4''-hydroxy-but-2''-enyl)-7,3',4'-trihydroxyflavanone.

Compound **3** was isolated as a gum, and gave a molecular ion at m/z 387.1446 in the HRFABMS consistent with the molecular formula $C_{21}H_{22}O_7$. The UV spectrum showed a λ_{max} at 288 nm typical of a flavanone skeleton. The 1H NMR spectra was similar to that for **2** (Table 1), except for signals for a chelated phenolic group (δ 12.21) and a methoxyl group (δ 3.90) (Table 1). The phenolic group was confirmed to be at the C-5 position by the HMBC connectivities from the OH-5 through C-5, C-6, C-10. The methoxyl group was placed at C-7 on the basis of its HMBC correlation. The one proton singlet at δ 6.13 was assigned to H-6 due its HMBC connectivities with C-5, C-7, C-8, C-10. The 1H and ^{13}C NMR spectroscopic data of the B ring were similar to those of compounds **1** and **2**, suggesting the same substitution pattern (Table 1). The absolute configuration at C-2 was again concluded to be *S* according to the analysis of CD spectroscopic data (see Section 4). Consequently, the structure of compound **3** was established as (2*S*)-8-(3''-methyl-4''-hydroxy-but-2''-enyl)-5,3',4'-trihydroxy-7-methoxyflavanone.



	R ₁	R ₂	R ₃	R ₄
1	H	OH	OH	H
2	H	OH	OH	OH
3	OH	OMe	OH	OH

3. Concluding remarks

The chemical relationship of *Flourensia heterolepis* (Bohlmann and Jakupovic, 1979), *F. campestris*, *F. riparia* (Uriburu et al., 2004), and the results of this work in *F. fiebrigii*, suggest some chemotaxonomical relationships.

This is because several flavonoids found in these species exhibit an 8-prenylation at ring A. Therefore, this finding may support placing the genus *Flourensia* in the subtribe Ecliptinae (Bohlmann, 1990).

In the present study, identification of two 5-deoxyflavonoids is reported. This compound class represents a common feature in the family Leguminosae, with many being C-8 prenyl derivatives (Rodrigues Garcez et al., 1988; Rao et al., 1994; Inuma et al., 1995; Barron and Ibrahim, 1996; Magalhães et al., 1996). Until this study, the 5-deoxy-

flavanoids were only previously isolated from *F. heterolepis* (7-hydroxyflavanone and 7-methoxyflavanone) (Bohlmann and Jakupovic, 1979) and *F. campestris* (7,3',4'-trimethoxyflavone) (Uriburu M.L. Ph.D. Thesis, Salta University, 2002) in the Asteraceae. However, homologues of them have also been reported as present in the *Achillea* (Ahmad et al., 1995) and *Calea* (do Nascimento et al., 2002; do Nascimento and de Oliveira, 2004) plant families.

As far as we know through this is also the first report of 5-deoxy-C-8-prenylflavanones in the Asteraceae.

4. Experimental

4.1. General experimental procedures

NMR spectra were recorded using Bruker Avance 500 or Bruker AC 200 spectrometer. Whereas FABMS and HRFABMS were determined using a VG-ZAB spectrometer. Desorption EIMS (DEIMS) and HREIMS (HRDEIMS) were obtained using a VG-7070 spectrometer, with UV spectra being measured with a GBC 918 spectrophotometer. IR spectra were recorded as KBr disks, using an IR-FT Bruker model IFS-88 spectrometer, and CD spectra were obtained with a Jasco 715.

4.2. Plant material

F. fiebrigii was collected in March 1999, Parque Nacional Los Cardones, Salta Province, Argentina. A voucher specimen (No. 11244) is on deposit at the Museum of the Facultad de Ciencias Naturales, Universidad Nacional de Salta, Salta, Argentina.

4.3. Extraction and isolation

The dried aerial parts of *F. fiebrigii* (1.6 kg) were extracted with EtOH–H₂O (98:2) (3.5 l) at 35 °C, for 96 h. The resulting extract was conc. under reduced pressure and the residue was suspended in MeOH–H₂O 9:1 (250 ml). After 24 h, the resulting suspension was filtered, the MeOH–H₂O solution was washed with hexane (3 × 200 ml), and the MeOH was evaporated in vacuo. The remaining aq. solution was extracted with Et₂O. The resulting Et₂O extract (3 g) was next fractionated by reversed-phase silica gel vacuum liquid chromatography eluting with MeOH–H₂O 7:3 and MeOH, respectively. The MeOH–H₂O 7:3 eluent was then submitted to silica gel flash chromatography eluting with a gradient of hexane–EtOAc, to afford seven subfractions (F1 through F7).

Tremetone (22.0 mg) and 6-methoxy-tremetone (12.0 mg) were obtained from F1 (hexane–AcOEt 9:1). Fraction F2 (hexane–EtOAc 4:1) was purified by reversed-phase semiprep. TLC (MeOH–H₂O 4:1) to afford 2-isopropenyl-3-oxyangeloyl-5-acetyl-*cis*-2,3-dihydrobenzofuran (11.0 mg).

Fraction F3 (hexane–EtOAc 7:3) was purified on Sephadex LH-20, eluting with MeOH, to afford 5,3'-dihydroxyisobavachin-7-*O*-methyl ether (15 mg). Fraction F4 (hexane–EtOAc 3:2) and F5 (hexane–EtOAc 1:1) were reunited and submitted to silica gel flash chromatography (CHCl₃–MeOH 10:0.5) to yield 8-prenyleriodictyol (5.0 mg) and (2*S*)-8-(3''-methylbut-2''-enyl)-7,3',4'-trihydroxyflavanone (**1**, 13.0 mg). F6 (hexane–EtOAc 2:3) was subjected to silica gel flash chromatography using CHCl₃–MeOH followed by semiprep. TLC (CHCl₃–MeOH 5:1) (runs 3×), and finally purified by Sephadex LH-20 CC in MeOH to afford (2*S*)-8-(3''-methyl-4''-hydroxy-but-2''-enyl)-5,3',4'-trihydroxy-7-methoxyflavanone (**3**, 3 mg). Fraction F7 (hexane–AcOEt 1:9) was submitted to flash chromatography (hexane–EtOAc 1:1) to give (2*S*)-8-(3''-methyl-4''-hydroxy-but-2''-enyl)-7,3',4'-trihydroxyflavanone (**2**, 5 mg).

4.4. (2*S*)-8-(3''-methylbut-2''-enyl)-7,3',4'-trihydroxyflavanone (**1**)

Amorphous powder, CD (MeOH; *c* 0.175): ($\Delta\epsilon_{301}$ –11.16), ($\Delta\epsilon_{332}$ +6.35); UV $\lambda_{\max}^{\text{MeOH}}$ nm (log ϵ): 286 (4.31), 308 sh; $\lambda_{\max}^{\text{MeOH+AlCl}_3}$ nm: unchanged; $\lambda_{\max}^{\text{MeOH+NaOMe}}$ nm: 339; $\lambda_{\max}^{\text{MeOH+NaOAc}}$ nm: 336; IR ν_{\max}^{KBr} cm^{–1}: 3400, 2966, 2925, 1651, 1599, 1522, 1441, 1286. For ¹H (500 MHz, CDCl₃) and ¹³C (125 MHz) NMR spectroscopic data, see Table 1. DEIMS 70 eV *m/z* (rel. int.): 340 [M]⁺ (86), 325 [M–Me]⁺ (7), 297 [M–C₃H₇]⁺ (68), 205 [A₁+H]⁺ (30), 204 [A₁]⁺ (14), 189 [A₁–Me]⁺ (15), 176 (35), 161 [A₁–CO–Me]⁺ (53), 149 [A₁–C₄H₇]⁺ (97), 136 [B₁]⁺ (100); HRDE-IMS *m/z* 340.1300 [M]⁺ (Calcd. for C₂₀H₂₀O₅ 340.1310).

4.5. (2*S*)-8-(3''-methyl-4''-hydroxy-but-2''-enyl)-7,3',4'-trihydroxyflavanone (**2**)

Gum, CD (MeOH; *c* 0.045): ($\Delta\epsilon_{301}$ –10.06), ($\Delta\epsilon_{333}$ +6.00); UV $\lambda_{\max}^{\text{MeOH}}$ nm (log ϵ): 286 (4.31), 313 sh; $\lambda_{\max}^{\text{MeOH+AlCl}_3}$ nm: no change; $\lambda_{\max}^{\text{MeOH+NaOMe}}$ nm: 342, $\lambda_{\max}^{\text{MeOH+NaOAc}}$ nm: 337; IR ν_{\max}^{KBr} cm^{–1}: 3369, 2925, 1620, 1595, 1284. For ¹H (500 MHz, acetone-*d*₆) and ¹³C (125 MHz) NMR spectroscopic data, see Table 1. FABMS *m/z* (rel. int.): 379 [M+Na]⁺ (37), 357 [M+H]⁺ (50), 339 [(M+H)–H₂O]⁺ (24), 203 [(A₁+H)–H₂O]⁺ (100), 149 [(A₁)–C₄H₇O]⁺ (79); HRFABMS *m/z* 357.1334 from the [M+H]⁺ (Calcd. for C₂₀H₂₁O₆ 357.1338).

4.6. (2*S*)-8-(3''-methyl-4''-hydroxy-but-2''-enyl)-5,3',4'-trihydroxy-7-methoxyflavanone (**3**)

Gum, CD (MeOH; *c* 0.065): ($\Delta\epsilon_{293}$ –7.52), ($\Delta\epsilon_{335}$ +1.76); UV $\lambda_{\max}^{\text{MeOH}}$ nm (log ϵ): 283(4.21), 333 sh; $\lambda_{\max}^{\text{MeOH+AlCl}_3}$ nm: 312; $\lambda_{\max}^{\text{MeOH+AlCl}_3+\text{HCl}}$ nm: no change; $\lambda_{\max}^{\text{MeOH+NaOMe}}$ nm: no change; $\lambda_{\max}^{\text{MeOH+NaOAc}}$ nm: no change; IR ν_{\max}^{KBr} cm^{–1}: 3432, 2929, 1639, 1597, 1268. For ¹H (500 MHz, acetone-*d*₆) and ¹³C (125 MHz) NMR spectroscopic data, see Table 1. FABMS *m/z* (rel. int.): 387 [M+H]⁺ (100), 370 [(M+H)–HO]⁺ (15), 233 [(A₁+H)–

H₂O]⁺ (40), 179 [(A₁)–C₄H₇O]⁺ (20), 136 [B₁]⁺ (7); HRFABMS *m/z* 387.1446 from the [M+H]⁺ (Calcd. for C₂₁H₂₃O₇ 387.1443).

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References

- Ahmad, V.U., Khan, M.A., Baqai, F.T., Tareen, R.B., 1995. Santoflavone, a 5-deoxyflavonoid from *Achillea santolina*. *Phytochemistry* 38, 1305–1307.
- Barron, D., Ibrahim, R.K., 1996. Isoprenylated flavonoids – A survey. *Phytochemistry* 43, 921–982.
- Bohlmann, F., Grenz, M., 1977. Über Inhaltsstoffe der Gattung *Flourensia*. *Chem. Ber.* 110, 295–300.
- Bohlmann, F., Jakupovic, J., 1979. Neue sesquiterpene, triterpene, flavanone und andere Aromatische Verbindungen aus *Flourensia heterolepis*. *Phytochemistry* 18, 1189–1194.
- Bohlmann, F., Dutta, L., 1979. Ein Neues Heliangolid aus *Liatris platylepis*. *Phytochemistry* 18, 1228–1230.
- Bohlmann, F., Jakupovic, J., Schuster, A., King, R.M., Robinson, H., 1984. Eudesmanolides and costic acid derivatives from *Flourensia macrophylla*. *Phytochemistry* 23, 1445–1448.
- Bohlmann, F., 1990. Chemistry of the Heliantheae (Compositae). *Pl. Syst. Evol. (Suppl. 4)*, 67–75.
- Castañeda, P., Gómez, L., Mata, R., 1996. Phyto-growth-inhibitory and antifungal constituents of *Helianthella quinquenervis*. *J. Nat. Prod.* 59, 323–326.
- do Nascimento, A.M., Sousa e Silva, F., de Oliveira, D.C.R., 2002. Constituents of *Calea platylepis* Sch. Bip. ex Baker. *Biochem. Syst. Ecol.* 30, 993–996.
- do Nascimento, A.M., de Oliveira, D.C.R., 2004. A 5-deoxyflavone glycoside from *Calea uniflora* L. (Asteraceae). *Biochem. Syst. Ecol.* 32, 1079–1081.
- Fukai, T., Nomura, T., 1990. Structure of 6- or 8- isoprenoid substituted flavanone: chemical shift of the hydrogen-bonded hydroxyl group. *Heterocycles* 31, 1861–1872.
- Harborne, J.B., 1994. The Flavonoids. In: *Advances in Research Since 1986*. Chapman and Hall, New York, pp. 462.
- Iinuma, M., Yokoyama, J., Ohyama, M., Tanaka, T., Ruangrunsi, N., 1994. Eight phenolic compounds in root of *Sophora exigua*. *Phytochemistry* 35, 785–789.
- Iinuma, M., Ohyama, M., Tanaka, T., 1995. Six flavonostilbenes and a flavanone in roots of *Sophora alopecuroides*. *Phytochemistry* 38, 519–525.
- Magalhães, A.F., Azevedo Tozzi, A.M.G., Noronha Sales, B.H.L., Magalhães, E.G., 1996. Twenty-three flavonoids from *Lonchocarpus subglaucescens*. *Phytochemistry* 42, 1459–1471.
- Rao, E.V., Prasad, Y.R., Murthy, M.S.R., 1994. A prenylated flavanone from *Tephrosia maxima*. *Phytochemistry* 37, 111–112.
- Rodrigues Garcez, F., Scramin, S., do Nascimento, M.C., Mors, W.B., 1988. Prenylated flavonoids as evolutionary indicators in the genus *Dahlstedtia*. *Phytochemistry* 27, 1079–1083.

- Slade, D., Ferreira, D., Marais, J.P.J., 2005. Circular dichroism, a powerful tool for the assessment of absolute configuration of flavonoids. *Phytochemistry* 66, 2177–2215.
- Uriburu, M.L., de la Fuente, J.R., Palermo, J., Gil, R.R., Sosa, V.E., 2004. Constituents of two *Flourensia* species. *Phytochemistry* 65, 2039–2043.
- Uriburu, M.L., de la Fuente, J.R., Palermo, J., Sosa, V.E., 2005. A Chlorinated dihydrobenzofuran from *Flourensia riparia*. *J. Argent. Chem. Soc.* 93, 161–164.
- Zalkow, L.H., Ekpo, B.A., Gelbaum, L.T., Harris, R.N., Keinan III, E., Novak Jr., J.R., Ramming, C.T., Van Derveer, D., 1979. The benzofurans of *Isocoma wrightii* structure and stereochemistry. *J. Nat. Prod.* 42, 203–219.