Article

J. Braz. Chem. Soc., Vol. 23, No. 11, 2021-2026, 2012.
Printed in Brazil - ©2012 Sociedade Brasileira de Química
0103 - 5053 $6.00+0.00

New Neolignans from *Krameria tomentosa* A. St.-Hil

Sara A. L. Madeiro,[a] Hellane F. S. de Lucena,[a] Caroline D. Siqueira,[a] Marcelo C. Duarte,[a] Raimundo Braz-Filho,[b] José M. Barbosa Filho,[a] Marcelo S. da Silva[a] and Josean F. Tavares*[*,a]

[a]Departamento de Ciências Farmacêuticas, Universidade Federal da Paraíba, CP 5009, 58051-970 João Pessoa-PB, Brazil

[b]Laboratório de Ciências Químicas, Universidade Estadual do Norte Fluminense, Campos dos Goytacazes, 28013-602 Rio de Janeiro-RJ, Brazil

A investigação fitoquímica das raízes de *Krameria tomentosa* A. St.-Hil. levou ao isolamento de cinco neolignanas, duas delas com estruturas inéditas [1,1'-(*E*)-propenil-4-metóxi-3,4'-oxineolignana (ottomentosa) e ácido 2-(2'-hidróxi-4',6'-dimetoxifenil) benzofurano-5-carboxílico (sobralina)], além de três compostos conhecidos [eupomatenoide 6, di-hidrocarinatidina e 2-(2',4'-di-hidroxifenil)-5-(*E*)-propenilbenzofurano]. A caracterização estrutural dos compostos isolados foi estabelecida com base na espectroscopia no infravermelho, espectrometria de massas, ressonância magnética nuclear uni e bidimensional, além de comparação com dados espectrais descritos na literatura.

A phytochemical investigation of the roots of *Krameria tomentosa* A. St.-Hil. led to the isolation of five neolignans, two of them with novel structures [1,1'-(*E*)-propenyl-4-methoxy-3,4'-oxyneolignan (ottomentosa) and 2-(2'-hydroxy-4',6'-dimethoxyphenyl)benzofuran-5-carboxylic acid (sobraline)] and three known compounds [eupomatenoid 6, dihydrocarinatidin and 2-(2',4'-dihydroxyphenyl)-5-(*E*)-propenylbenzofuran]. The structural characterization of the compounds isolated was established based on infrared spectroscopy, mass spectrometry, one- and two-dimensional nuclear magnetic resonance, along with comparison with spectral data described in the literature.

Keywords: *Krameria tomentosa*, Krameriaceae, neolignans, ottomentosa, sobraline

Introduction

The genus *Krameria* is the only member of the family Krameriaceae, and includes 18 herbaceous or shrub species that are predominantly represented in neotropical and ecologically restricted regions and arid or seasonally dry regions of the Americas.[1-3] The presence of neolignans and norneolignans is well documented for this genus.[4-9] *Krameria tomentosa* A. St.-Hil. (synonymy of *Krameria ovata* O. Berg) is popularly known as "rhatany" and as with other species of *Krameria*, its roots have been long used in popular medicine in the treatment of dysentery, stomatitis, diarrhea, vaginal discharges and afflictions of the mouth.[10-12] The alcoholic extract from *K. tomentosa* (root) showed toxicity to mice and fish.[13] Earlier studies have demonstrated that neolignans, norneolignans and steroids,[14,15] as well as the norlignan 2-(2'-hydroxy-4',6'-dimethoxyphenyl)-5-[(*E*)-propenyl]benzofuran, inhibit acetylcholine-induced relaxation in the aorta of rats.[16] In the present work, it is described the isolation and structural determination of two new neolignans, ottomentosa and sobraline (**1** and **2**), besides three known neolignans: eupomatenoid 6 (**3**), dihydrocarinatidin (**4**) and 2-(2',4'-dihydroxyphenyl)-5-(*E*)-propenylbenzofuran (**5**) (Figure 1).

Results and Discussion

Compound **1** was isolated in the form of a colorless oil. The high resolution mass spectrum (HS-ESI-MS) utilizing the ESI+ ionization mode showed the peak of the cationized molecule at *m/z* 303.1372 $[M + Na]^+$, compatible with the

*e-mail: josean@ltf.ufpb.br

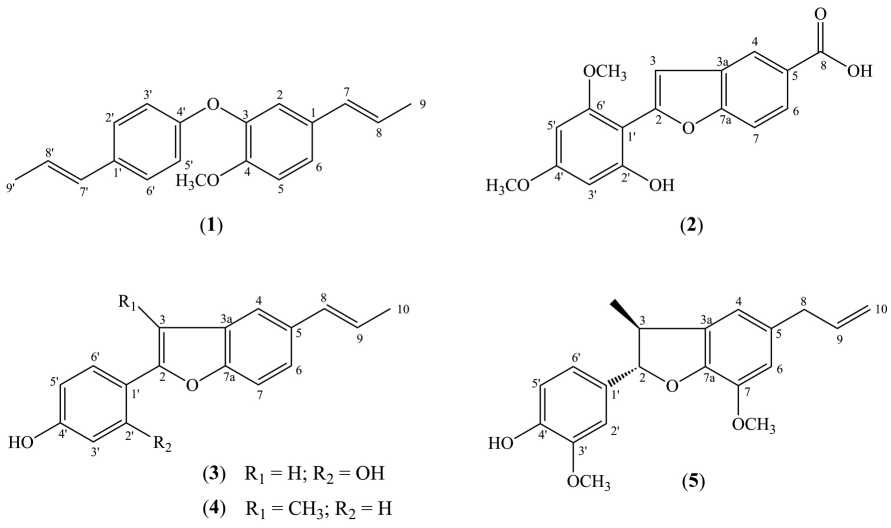

Figure 1. Neolignans isolated from the roots of *K. tomentosa.*

molecular formula $C_{19}H_{20}O_2Na$ (calc. 303.1356). The IR spectrum showed absorptions in the region of 1603-1441 cm^{-1}, characteristic of C=C stretching of the aromatic ring, as well as absorptions of 1269-982 cm^{-1}, characteristic of C–O stretching. The ^1H nuclear magnetic resonance (NMR) spectrum showed in the region of hydrogens in aromatic systems two connected doublets, one at δ_H 7.23 (*J* 9.0 Hz) and the other at δ_H 6.85 (*J* 9.0 Hz), compatible with the hydrogens of an AA'XX' system. In the same region, there was a doublet of doublets at δ_H 7.04 (*J* 2.5 and 8.5 Hz) coupled with the doublets at δ_H 6.95 (*J* 2.5 Hz) and at δ_H 6.89 (*J* 8.5 Hz), compatible with the hydrogens of an AMX system. The set of signals at δ_H 6.33, 6.10 and 1.84, as well as the set at δ_H 6.25, 6.00 and 1.80, characterized the hydrogens of two propenyl units. The ^{13}C APT NMR (attached-proton-test NMR) spectrum displayed 17 signals, corresponding to 19 carbon atoms. From these, 5 were assigned to non-hydrogenated carbons, from which 3 were oxygenated, 11 to methine carbons, 2 to methyl carbons and 1 to a methoxyl carbon. According to the data described, it was possible to suggest that the phenylpropanoid units of **1** were connected forming the skeleton of an oxyneolignan,[17,18] showing an oxygenated substitute, this being a methoxyl. The correlation of the hydrogens at δ_H 3.80 (OMe) with the hydrogen at δ_H 6.85 (H-3'/5'), observed in the NOESY (nuclear Overhauser effect spectroscopy) spectrum, made it possible to infer that the methoxy group was connected to C-4. In the heteronuclear multiple-quantum correlation (HMQC) spectrum, direct correlations can be seen between the hydrogens at δ_H 7.23 (d) and 6.85 (d) with the carbons at δ_C 126.9 and 117.3, assigning them to C-2'/C-6' and C-3'/C-5', respectively. Chemical shifts at δ_H 6.95 (d), 6.89 (d) and 7.04 (dd) showed correlations with the carbons at δ_C 117.9, 112.8 and 122.2, respectively, in which they were thereby assigned to carbons C-2, C-5 and C-6. In the heteronuclear multiple-bond correlation (HMBC) spectrum, correlations were observed between the hydrogens at δ_H 6.95 (H-2) and 1.80 (H-9) with the carbon at δ_C 129.9 (C-7), as well as the correlation between the hydrogen at δ_H 6.33 (H-7') with the carbon at δ_C 126.9 (C-2'/6'), confirming the insertion of the propenyl group more shielded in the ring of the AMX system and less shielded in the AA'XX' system. The shifts of the non-hydrogenated, non-oxygenated carbons were confirmed by the correlations between the signal at δ_H 7.04 (H-6) with the carbon at δ_C 150.3, assigned to C-4, and between the hydrogens at δ_H 7.23 (H-2'/H-6') and 6.85 (H-3'/H-5') with the carbon at δ_C 156.8, assigned to C-4'. Homonuclear correlation spectroscopy (COSY) showed correlations of the signal at δ_H 7.04 (H-6) with 6.95 (H-2) and 6.89 (H-5) and of the signal at δ_H 6.85 (H-3'/5') with 7.23 (H-2'/6'). Table 1 gives a compilation of the chemical shifts and correlations observed in the spectra of one- and two-dimensional ^1H and ^{13}C NMR for compound **1**. After the analysis of all the spectral data, this compound was determined to be 1,1'-(*E*)-propenyl-4-methoxy-3,4'-oxyneolignan, reported here for the first time and given the trivial name ottomentosa.

Compound **2** was isolated in the form of a white powder, with a melting point of 262-264 °C. The high resolution mass spectrum utilizing the ESI- ionization mode showed the peak of the deprotonated molecule at *m/z* 313.0708 $[M - H]^-$, compatible with the molecular formula $C_{17}H_{13}O_6$ (calc. 313.0706). The IR spectrum revealed the presence of a wide band between 3472 and 2650 cm^{-1} and a band at 1690 cm^{-1}, characteristic of O–H and C=O stretching of a carboxyl group, respectively. Absorption was also observed at 1624-1458 cm^{-1}, characteristic of C=C

Table 1. Data of one- and two-dimensional ^{1}H (500 MHz) and ^{13}C (125 MHz) NMR of compound **1** in $CDCl_3$ (δ in ppm, *J* in Hz)

	^{1}H-^{13}C HMQC		^{1}H-^{13}C HMBC		^{1}H-^{1}H COSY	^{1}H-^{1}H NOESY
	δ_C	δ_H	^{2}J	^{3}J		
C						
1	131.7		H-2	H-5		
3	145.2		H-2	H-5		
4	150.3		H-5	H-2; H-6; OMe		
1'	132.6			H-3'/H-5'		
4'	156.8		H-3'/H-5'	H-2'/H-6'		
CH						
2	117.9	6.95 (d, 1H, *J* 2.5)			H-6	
5	112.8	6.89 (d, 1H, *J* 8.5)			H-6	
6	122.2	7.04 (dd, 1H, *J* 2.5 and 8.5)	H-5	H-2		
7	129.9	6.25 (dd, 1H, *J* 1.5 and 16.0)		H-2; H-9	H-8	
8	124.3	6.00 (qd, 1H, *J* 6.5 and 16.0)	H-9		H-9	
2'/6'	126.9	7.23 (d, 1H, *J* 9.0)		H-7'		H-8'
3'/5'	117.3	6.85 (d, 1H, *J* 9.0)			H-2'/H-6'	
7'	130.3	6.33 (dd, 1H, *J* 1.5 and 16.0)		H-9'	H-8'	
8'	124.5	6.10 (qd, 1H, *J* 6.5 and 16.0)	H-9'		H-9'	
CH_3						
9	18.3	1.80 (dd, 3H, *J* 1.5 and 6.5)				
9'	18.4	1.84 (dd, 3H, *J* 1.5 and 6.5)				
OMe	56.1	3.80 (s, 1H)				H-3'/H-5'

stretching of an aromatic ring and between 1312-1107 cm^{-1} of C–O stretching. The ^{13}C APT NMR spectrum showed the presence of 17 signals, corresponding to 17 carbons. From these, 9 were assigned to non-hydrogenated carbons, 6 to methine carbons and 2 to methoxyl carbons. Based on comparison with ^{13}C NMR spectral data of the neolignans 2-(2'-hydroxy-4'-6'-dimethoxyphenyl)-5-(*E*)-propenylbenzofuran and krametosan, also isolated from *K. tomentosa*,[14] it was possible to make the following considerations: (*i*) the signals at δ_C 153.5, 107.5, 130.1 and 157.5 were assigned to carbons C-2, C-3, C-3a and C-7a, respectively, of the benzofuran ring; (*ii*) the signals at δ_C 100.6, 158.6, 95.1, 163.4, 91.6 and 160.8 were assigned to carbons C-1', C-2', C-3', C-4', C-5' and C-6', respectively; (*iii*) the absence of signals at approximately δ_C 131.0, 124.6 and 18.5 suggestive of a propenyl unit plus the presence of the signal at 168.0 (referring to a carbonyl) and the information obtained from the IR spectrum indicate that compound **2** is possibly the trinor-neolignan 2-(2'-hydroxy-4',6'-dimethoxyphenyl)benzofuran-5-carboxylic acid. The ^{1}H NMR spectrum of this compound indicated the presence of a signal at δ_H 7.03 (d, *J* 0.5 Hz) characteristic of H-3, as well as signals at δ_H 8.31 (d, *J* 1.7 Hz), 7.97 (dd, *J* 1.7 and 8.5 Hz) and 7.57 (d, *J* 8.5 Hz), assigned to the hydrogens H-4, H-6 and H-7, respectively, and signals at δ_H 6.23 (d, *J* 2.5) and 6.24 (d, *J* 2.5), corresponding to the hydrogens H-3' and H-5', respectively. It was also observed two singlets at δ_H 3.81 and 3.83, the first referring to the methoxyl at C-4' and the second to the methoxyl at C-6'. These assignments were confirmed by the direct correlations observed in the HMQC spectrum. The HMBC spectrum showed correlations between the hydrogens at δ_H 8.31 (H-4) and 7.97 (H-6) with the signal at δ_C 168.1, assigned to the carbon of the carbonyl, confirming its insertion at C-5. Correlations were observed between the hydrogen at δ_H 8.31 (H-4) and the signal at δ_C 107.5, assigned to C-3, and between the hydrogens at δ_H 7.03 (H-3), 8.31 (H-4) and 7.97 (H-6) and the signal at δ_C 157.4, assigned to C-7a. Table 2 gives a compilation of the chemical shifts and the correlations found in the spectra of one- and two-dimensional ^{1}H and ^{13}C NMR for this compound, which is reported here for the first time. This compound was given the trivial name sobraline.

Compound **3** (2-(2',4'-dihydroxyphenyl)-5-(*E*)-propenylbenzofuran) was isolated in the form of colorless crystals, showing a melting point of 181-184 °C. This substance has already been isolated from other species of the genus *Krameria*,[4-8] but this is the first report

Table 2. Data of one- and two-dimensional ^{1}H (500 MHz) and ^{13}C (125 MHz) NMR of compound **2** in CD_3COCD_3 (δ in ppm, J in Hz)

	^{1}H-^{13}C HMQC		^{1}H-^{13}C HMBC		^{1}H-^{1}H COSY	^{1}H-^{1}H NOESY
	δ_C	δ_H	^{2}J	^{3}J		
C						
2	153.5		H-3			
3a	130.1		H-3	H-7		
5	126.3					
7a	157.5			H-3/H4/H-6		
8	168.1			H4/H-6		
1’	100.6			H-3’/H-5’		
2’	158.6		H-3’			
4’	163.4		H-3’/H-5’			
6’	160.8		H-5’			
CH						
3	107.5	7.03 (d, 1H, *J* 0.5)		H-4		H-4
4	123.6	8.31 (d, 1H, *J* 1.7)		H-6	H-6	
6	126.1	7.97 (dd, 1H, *J* 1.7 and 8.5)	H-7	H-4	H-7	H-7
7	111.4	7.57 (d, 1H, *J* 8.5)				
3’	95.1	6.23 (d, 1H, *J* 2.5)		H-5’		
5’	91.6	6.24 (d, 1H, *J* 2.5)		H-3’		H-3’/H-5’
OMe-4’	55.7	3.81 (s, 3H)				
OMe-6’	56.2	3.83 (s, 3H)				

for the species *Krameria tomentosa*, besides being the first time that two-dimensional NMR data are described for compound **3**, confirming the values provided in the literature for carbons C-3, C-3’, C-7 and C-1’. The HMQC spectrum demonstrated the direct correlation between the hydrogen at δ_H 7.39 and the carbon at δ_C 111.1, assigning this shift to C-7, differentiating it from C-1’ at δ_C 110.6, which indicates a non-hydrogenated carbon. In the HMBC spectrum, correlations were observed between the hydrogens at δ_H 7.52 (H-4) and at δ_H 6.50 (H-5’) and the carbons at δ_C 104.0 and δ_C 103.9 assigned to C-3 and C-3’, respectively.

Compounds **4** (eupomatenoid 6) and **5** (dihydrocarinatidin) were identified based on direct comparison with NMR data described in the literature.[4,19]

Conclusions

Considering the wealth of neolignans in the species of the family Krameriaceae, this study comes to confirm the predominance of this class of secondary metabolites in the family and contributes to the expansion of their chemical knowledge with the isolation of two new neolignans.

Experimental

General experimental procedures

Melting points were obtained by the digital apparatus, model MQAPF-302 from Microchemical and were not corrected. IR spectra were recorded on a BOMEM-MB 100 spectrophotometer. One-dimensional (^{1}H and ^{13}C) and two-dimensional (gHMQC, gHMBC, gCOSY and gNOESY) NMR analyses were performed on a VARIAN-System spectrometer operating at 500 MHz (^{1}H) and 125 MHz (^{13}C). $CDCl_3$ or CD_3COCD_3 was used as the solvent with TMS as an internal standard. HR-ESI-MS was obtained using the microTOF-II system from Bruker. Conventional chromatographic methods were used for column chromatography (CC) (silica gel 60, Merck, 0.063-0.20 and 0.04-0.063 mm). Medium pressure liquid chromatography (MPLC) was performed using the Buchi system of binary gradient flash separation, in which the chromatograph was equipped with two pump modules (C-601 and C-605), controller module (C-615), Knauer UV detector and columns packed with silica gel (Merck, 0.063-0.20 and 0.04-0.063 mm).

Silica gel TLC (thin layer chromatographic) plates PF_{254} 7749 (Merck) stained with iodine and viewed under UV light (254/366 nm) were used to monitor chromatographic purification procedures.

Plant material

The botanical material utilized was collected in the municipality of Santa Rita, Paraíba State, Brazil, in June 2010. Its botanical identification was carried out by Prof. Dr. Maria de Fátima Agra and a dried specimen is deposited in the Herbário Professor Lauro Pires Xavier of UFPB under No. 3271.

Extraction and isolation

The roots of *K. tomentosa* (3.5 kg), dried and pulverized, were extracted with 95% EtOH at ambient temperature. The extract obtained was concentrated in a rotary evaporator under reduced pressure at 40 °C, yielding 685.0 g ethanolic extract. A portion (100.0 g) was suspended in MeOH:H_2O (7:3) and partitioned with hexane, CH_2Cl_2 and EtOAc to obtain the hexane (2.5 g), dichloromethane (5.4 g) and ethyl acetate (6.5 g) extracts. The hexane extract (2.5 g) was separated by CC, utilizing silica gel 60 (0.063-0.200 mm) and the eluents hexane and EtOAc and MeOH, pure or in binary mixtures, in increasing order of polarity, resulting in 67 fractions of 100 mL each, which were analyzed by analytical TLC. Fraction 14 yielded compound **4** (16.6 mg). Fractions 1-2 (168.3 mg) were submitted to another CC utilizing similar conditions as before, providing 25 subfractions of 10 mL each. Subfractions 10-15 gave the neolignan **1** (35.4 mg). Fractions 27-35 (99.3 mg) were rechromatographed as before, from which 55 subfractions of 10 mL each were collected. Subfractions 33-37 yielded compound **5** (26.2 mg).

The dichloromethane extract (5.0 g) was submitted to MPLC, with the column packed with silica gel 60 (0.063-0.200 mm), utilizing a flow rate of 30 mL min^{-1} and mobile phase of the solvents hexane and EtOAc and MeOH, pure or in binary mixtures, in increasing order of polarity. A total of 81 fractions of 100 mL each was collected, which were concentrated in rotary evaporator and combined, after analysis by analytical TLC, to form 24 groups. Fractions 42-45 provided compound **3** (22.7 mg). Fractions 67-81 (675.3 mg) were submitted to another MPLC, utilizing a column packed with silica gel 60 (0.04-0.063 mm) and flow rate of 30 mL min^{-1}. From this column, 53 subfractions of 100 mL each were collected, which were analyzed by analytical TLC and combined into 10 groups. Subfractions 5-6 yielded compound **2** (8.5 mg).

Characterization

1,1'-(*E*)-Propenyl-4-methoxy-3,4'-oxyneolignan (ottomentosa) (**1**)

Colorless oil; IR (KBr) ν_{max}/cm^{-1} 1603, 1505, 1441, 1269, 1227, 982; HR-ESI-MS at *m/z* 303.1372 $[M + Na]^+$, calcd. for $C_{19}H_{20}O_2Na$, 303.1356; ^1H and ^{13}C NMR (500 MHz and 125 MHz, $CDCl_3$), see Table 1.

2-(2'-Hydroxy-4',6'-dimethoxyphenyl)benzofuran-5-carboxylic acid (sobraline) (**2**)

Colorless crystals; mp 262-264 ºC; IR (KBr) ν_{max}/cm^{-1} 3472, 2650, 1690, 1624, 1589, 1458, 1312, 1207, 1107; HR-ESI-MS *m/z* 313.0708 $[M - H]^-$, calculated for $C_{17}H_{13}O_6$, 313.0706; ^1H and ^{13}C NMR (500 MHz and 125 MHz, CD_3COCD_3), see Table 2.

2-(2',4'-Dihydroxyphenyl)-5-(*E*)-propenylbenzofuran (**3**)

Colorless crystals; mp 181-184 ºC; IR (KBr) ν_{max}/cm^{-1} 3537, 3281, 1605, 1508, 1321, 1173; ^{13}C NMR (125 MHz, CD_3COCD_3) 110.6 (C-1'), 156.8 (C-2'), 103.9 (C-3'), 159.8 (C-4'), 108.4 (C-5'), 128.6 (C-6'), 154.8 (C-2), 104.0 (C-3), 131.3 (C-3a), 118.5 (C-4), 133.9 (C-5), 122.5 (C-6), 111.1 (C-7), 153.7 (C-7a), 132.3 (C-8), 124.4 (C-9), 18.5 (C-10); ^1H NMR (500 MHz, CD_3COCD_3) 6.57 (d, *J* 2.0, H-3'), 6.50 (dd, *J* 2.0 and 8.5, H-5'), 7.76 (d, *J* 8.5, H-6'), 7.20 (d, *J* 1.0, H-3), 7.52 (*d*, *J* 1.0, H-4), 7.26 (dd, *J* 1.0 and 8.5, H-6), 7.39 (*d*, *J* 8.5, H-7), 6.47 (d, *J* 1.5 and 13.0, H-8), 6.23 (dq, *J* 6.5 and 13.0, H-9), 1.84 (dd, *J* 1.5 and 6.5, H-10), 8.88 (s, OH).

Supplementary Information

Supplementary data associated with this work are available free of charge at http://jbcs.sbq.org.br as PDF file.

Acknowledgments

The authors thank CNPq (Conselho Nacional de Desenvolvimento Científico e Tecnológico), CAPES (Coordenação de Aperfeiçoamento de Pessoal de Nível Superior) and FAPESQ-PB (Fundação de Apoio à Pesquisa do Estado da Paraíba) for financial support and LMCA-Central Analitica of UFPB for providing the spectra. Dr. A. Leyva helped with the translation and editing of the manuscript.

References

1. Simpson, B. B.; Weeks, A.; Helfgott, D. M.; Larkin, L. L.; *Syst. Bot.* **2004**, *29*, 97.

2. Gimenes, M.; Lobão, C. S.; *Neotrop. Entomol.* **2006**, *35*, 440.
3. Giannini, T. C.; Takahasi, A.; Medeiros, M. C. M. P.; Saraiva, A. M.; dos Santos, I. A.; *J. Arid Environ.* **2011**, *75*, 870.
4. Achenbach, H.; Grob, J.; Dominguez, X. A.; Cano, G.; Star, J. V.; Brussolo, L. C.; Muñoz, G.; Salgado, F.; López, L.; *Phytochemistry* **1987**, *26*, 1159.
5. Achenbach, H.; Grob, J.; Bauereib, P.; Dominguez, X. A.; Vega, H. S.; Star, J. V.; Rombold, C.; *Phytochemistry* **1989**, *28*, 1959.
6. Achenbach, H.; Utz, W.; Dominguez, X. A.; *Phytochemistry* **1993**, *34*, 835.
7. Achenbach, H.; Utz, W.; Vega, H. S.; Touché, E. M. G.; Star, J. V.; Dominguez, X. A.; *Phytochemistry* **1995**, *39*, 413.
8. Dominguez, X. A.; Rombold, C.; Star, J. V.; Achenbach, H.; Grob, J.; *Phytochemistry* **1987**, *26*, 1821.
9. Dominguez, X. A.; Vega, H. S.; Espinoza, G. C.; Verde, J.; Achenbach, H.; Utz, W.; *Phytochemistry* **1990**, *29*, 2651.
10. Simpson, B. B.; *Krameriaceae: Flora Neotropica Monograph*; The New York Botanical Garden: New York, NY, USA, 1989.
11. Simpson, B. B.; *Econ. Bot.* **1991**, *45*, 397.
12. Corrêa, M. P.; *Dicionário das Plantas Úteis do Brasil e das Exóticas Cultivadas*; Ministério da Agricultura: Rio de Janeiro, RJ, Brasil, 1984.
13. Vieira, J. E. V.; Matos, F. J. A.; Barros, G. S. G.; Souza, M. P.; Medeiros, M. C.; Medeiros, M. J.; *Rev. Bras. Farm.* **1968**, *49*, 67.
14. Silva, S. A. S.; de Castro, J. C. M.; da Silva, T. G.; da Cunha, E. V. L.; Barbosa-Filho, J. M.; da Silva, M. S.; *Nat. Prod. Lett.* **2001**, *15*, 323.
15. Bulhões, G. C. C.; Silva, A. M.; *An. Fac. Farm. Univ. Fed. Pernambuco* **1976**, *15*, 45.
16. Castro, J. C.; da Silva, M. S.; Cortes, S. F.; Lemos, V. S.; *Planta Med.* **2006**, *72*, 78.
17. Ito, K.; Iida, T.; Ichino, K.; Tsunezuka, M.; Hattori, M.; Namba, T.; *Chem. Pharm. Bull.* **1982**, *30*, 3347.
18. Moss, G. P.; *Pure Appl. Chem.* **2000**, *72*, 1493.
19. Morais, S. K. R.; Teixeira, A. F.; Torres, Z. E. S.; Nunomura, S. M.; Yamashiro-Kanashiro, E. H.; Lindoso, J. A. L.; Yoshida, M.; *J. Braz. Chem. Soc.* **2009**, *20*, 1110.

Submitted: June 13, 2012
Published online: November 30, 2012