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J. Braz. Chem. Soc., Vol. 23, No. 2, 301-305, 2012.
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0103 - 5053 $6.00+0.00

Furanoflavones and other Chemical Constituents of *Lonchocarpus obtusos*

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Dois novos furanoflavonoides, 5-hidróxi-2’’-isopropenil-3-metoxifurano-(2”,3”:7,8)-flavona e 5-hidróxi-2’’-(1-hidróxi-1-metiletil)-3-metoxifurano-(2”,3”:7,8)-flavona, juntamente com treze compostos conhecidos, foram isolados das cascas das raízes de *Lonchocarpus obtusos* (Leguminosae). As estruturas de todos os compostos isolados foram determinadas usando métodos espectrométricos tais como RMN 1D e 2D (COSY, HSQC e HMBC) e EMAR, além da comparação com dados espectrais descritos na literatura para compostos de estruturas semelhantes.

Two new furanoflavonoids, 5-hydroxy-2’’-isopropenyl-3-methoxyfurane-(2”,3”:7,8)-flavone and 5-hydroxy-2’’-(1-hydroxy-1-methylethyl)-3-methoxyfurane-(2”,3”:7,8)-flavone, along with thirteen other known compounds, were isolated from the root barks of *Lonchocarpus obtusus* (Leguminosae). The structures of all compounds were determined by spectrometric methods such as 1D and 2D NMR (COSY, HSQC and HMBC) and HREISMS beside comparison with spectral data for similar compounds.

Keywords: *Lonchocarpus obtusos*, Leguminosae, furanoflavonoids, flavones

Introduction

The flavonoids consist of a large group of low-molecular weight phenol compounds whose pharmacological and medicinal properties have been extensively investigated.[1,2] Several activities have been reported for these compounds, especially as antioxidant,[3] antiproliferative,[4] anti-inflammatory,[5] analgesic[6] and cytotoxic.[7]

The genus *Lonchocarpus* (Leguminosae, Papilionoideae), comprises approximately 135 species, twenty-four of which are native to Brazil.[7] *Lonchocarpus* is known as a prolific source of flavonoids (aurones, chalcones, flavones, flavonols, flavans, flavanones and stilbenes)[8] has been the subject of incessant investigations searching for compounds of chemical and biological interest. Activities such as gastroprotective,[9] trypanocidal and antimalarial,[10] cytotoxic,[11] anti-inflammatory and antimicrobial[12] have been reported for compounds isolated from *Lonchocarpus*.

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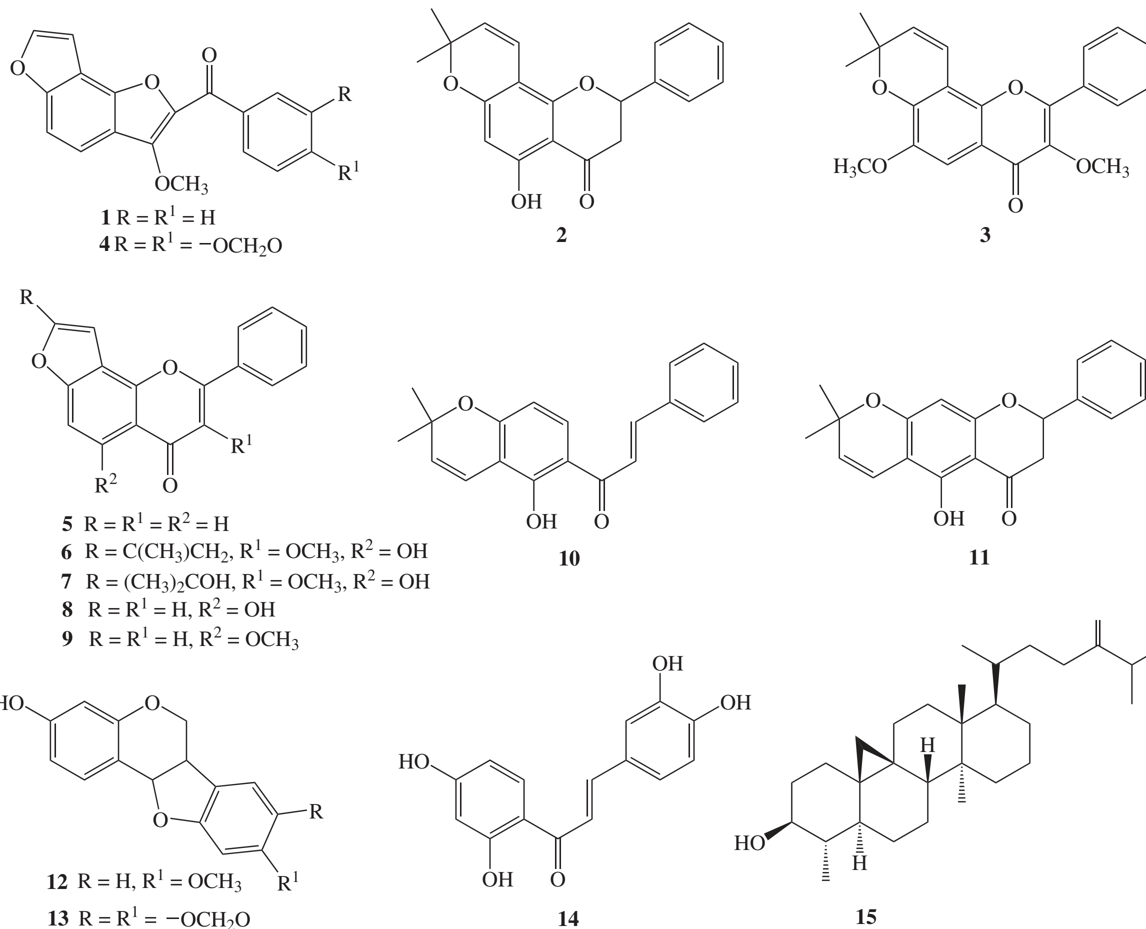
As part of an ongoing research for new secondary metabolites from plants of the northeastern Brazil flora we have investigated the extracts of *Lonchocarpus obtusus.* In the present work the isolation and characterization of two new flavonoids (**6** and **7**), from the roots of *L. obtusos* are described. Additionally, thirteen known flavonoids: derriobtusone A (**1**),[13] obovatin (**2**),[14] 3,6-dimethoxy-2”,2”-dimethylchromene-(3”,4”:7,8)-flavone (**3**),[15] derriobtusone B (**4**),[13] (2”,3”:7,8)-furanoflavone (**5**),[16] pongaglabol (**8**)[17] and its methyl ether (**9**),[17] lonchocarpin (**10**),[18] 5-hydroxy-2”,2”-dimethylchromene-(3”,4”:6:7)-flavone (**11**),[19] medicarpin (**12**),[21] maackiain (**13**),[22] butein (**14**)[23]and cycloeucalenol (**15**)[20] were isolated.

Results and Discussion

Compound **6** was isolated as a yellow resin. Its IR spectrum exhibited absorption bands at 3420 (hydroxyl), 1658 (carbonyl) and 1599 cm^{-1} (benzene ring) compatible with a flavonoid skeleton. Its HRESIMS spectrum, in the positive mode, revealed a peak at *m/z* 349.0941



[M + H]$^+$ indicating the molecular formula of $C_{21}H_{16}O_5$, corresponding to fourteen degrees of unsaturation. The ^{1}H NMR spectrum showed a signal at δ 12.64 (s) for a chelated hydroxyl group, two multiplets at δ 8.14 (m, H-2'/H-6') and 7.57 (m, H-3'/H-4'/H-5') appropriate for a monosubstituted benzene ring, two singlets at δ 6.88 (s, H-6) and 6.84 (s, H-3"), and a signal for one methoxyl group at δ 3.90 (3-OMe). In addition, the ^{1}H NMR spectrum showed characteristic signals for an isopropenyl moiety at δ 2.15 (s, 3H-5"), 5.79 (s, H-6a") and 5.21 (s, H-6b"). Apart from the signals typical of a flavonoidic skeleton, the ^{13}C NMR spectrum of **6** showed the signals at δ 132.3 (C-4"), 113.8 (C-6") and 19.4 (C-5"), which were inferred to the isopropenyl moiety already suggested by the ^{1}H NMR data. The signals at δ 156.8 (C-2") and 99.5 (C-3"), were associated with a furan ring while a signal at δ 60.6 with the methoxyl group located on C ring. The NMR spectral data (Table 1) of **6** combined with the molecular formula suggested a methoxy-furaneflavone.

In the HMBC spectrum, the correlations of the hydrogens at δ 6.84 (H-3"), 5.79/5.21 (2H-6") and 2.15 (3H-5") with the carbon at δ 156.8 (C-2") were in agreement with the presence of the isopropenyl moiety at C-2", while the long range correlation between the proton signal at δ 6.84 (H-3") with the carbon at δ 149.2 (C-9) confirmed the location of the furan ring at the C-7/C-8 position. In order to attend to the feature of a monosubstituted ring B in the structure of **6**, the methoxyl group was located in the C ring at the C-3 position in accordance with the carbon chemical shift at δ 140.7 (C-3) and the correlation between the signal at δ 3.90 (O-Me) with that carbon. Based on all spectroscopic evidences the structure of **6** was established as the 5-hydroxy-2''-isopropenyl-3-methoxyfurane-(2",3":7,8)-flavone.

Compound **7** was also isolated as a yellow resin. Its IR spectrum exhibited absorption bands at 3547 (hydroxyl), 1656 (carbonyl) and 1602 (benzene ring) compatible with the structure of a flavonoid. Its HRESIMS spectrum, in the positive mode, revealed the molecular peak at *m/z* 367.1064 [M + H]$^+$ indicating the molecular formula of $C_{21}H_{18}O_6$, corresponding to thirteen degrees of unsaturation. A detailed analysis of the 1D and 2D NMR spectral data of **7** revealed high structural similarity to flavonoid **6**. The main observed difference was related to an isopropyl alcohol moiety supported by the methyl signal at δ 1.89 (s), integrating to 6 hydrogen atoms (3H-5''/3-H-6'') and the

Table 1. ^{1}H (500 MHz) and ^{13}C (125 MHz) NMR spectral data of compounds **6** ($CDCl_3$) and **7** (C_5D_5N)

	6		7	
C	δ_C	δ_H	δ_C	δ_H
2	155.9	-	156.8	-
3	140.7	-	141.0	-
4	180.0	-	180.6	-
5	159.2	-	159.1	-
6	95.1	6.88 (s)	95.7	7.20 (s)
7	159.5	-	159.9	-
8	110.4	-	117.0	-
9	149.2	-	149.0	-
10	108.3	-	108.8	-
1’	130.8	-	131.4	-
2’	128.6	8.14 (m)	129.4	8.27 (m)
3’	129.4	7.57 (m)	129.7	7.58 (m)
4’	131.3	7.57 (m)	131.9	7.58 (m)
5’	129.4	7.57 (m)	129.7	7.58 (m)
6’	128.6	8.14 (m)	129.4	8.27 (m)
2”	156.8	-	166.0	-
3”	99.5	6.84 (s)	98.2	7.29 (s)
4”	132.3	-	68.9	-
6”	113.8	5.79 (s), 5.21 (s)	30.0	1.89 (s)
5”	19.4	2.15 (s)	30.0	1.89 (s)
MeO-3	60.6	3.90 (s)	60.8	3.96 (s)
HO-5	-	12.64 (s)	-	13.2 (s)

Chemical shifts (δ) in ppm. Deuterated solvent (0.6 mL).

carbon signals at δ 30.0 (C-5” and C-6”) and δ 68.9 (C-4”) (Table 1). The isopropyl alcohol moiety was positioned at C-2’’ through the HMBC correlations between the methyl signal at 1.89 (3H-5”/3-H-6”) and the carbon signal at 166.0 (C-2’’), in accordance with the hydration of the propenyl side chain of **6**. Additional long range correlations can be seen in Figure 1. Based on the aforementioned data the structure of **7** was established as 5-hydroxy-2’’-(1-hydroxy-1-methylethyl)-3-methoxyfurane-(2”,3”:7,8)-flavone, a new hydrated derivative of flavone **6**.

Previous phytochemicals studies have demonstrated that *Lonchocarpus* is a prolific source of flavonoids with furan or pyran substituent at ring A in an angular or linear position. Flavonoids **6** and **7** were previously unknown, while **8**, **9** and **14** are been reported for the first time in this genus.

Experimental

General experimental procedures

Melting points were measured on a digital Mettler Toledo FP90 apparatus and are uncorrected. IR spectra were recorded using a Perkin-Elmer FT-IR 1000 spectrometer. Electrospray ionization-high resolution mass spectra were run on a quadrupole LCMS-IT-TOF (Shimadzu) spectrometer equipped with an electrospray ionization source. 1D and 2D NMR experiments were performed on a Bruker Avance DRX-500 spectrometer (^{1}H 500 MHz, ^{13}C 125 MHz) equipped with a 5 mm inverse detection z-gradient probe. ^{1}H and ^{13}C NMR spectra were measured at 27 °C using $CDCl_3$ and pyridine as the solvent (0.6 mL). Open column chromatography was run using silica gel 60 (70-230 mesh, Vetec), while flash column chromatography was run on silica gel (230-400 mesh, Merck). TLC was performed on precoated silica gel polyester sheets (Kieselgel 60 F_{254}, 0.20 mm, Merck) by detection with a spraying reagent (vanillin/perchloric acid/EtOH solution) followed by heating at 100 °C.

Plant material

The roots of *Lonchocarpus obtusus* were collected, in April 2007, from Meruoca County (Ceará State, Brazil). The plant authentication was performed by Professor Afrânio Gomes Fernandes and a voucher specimen

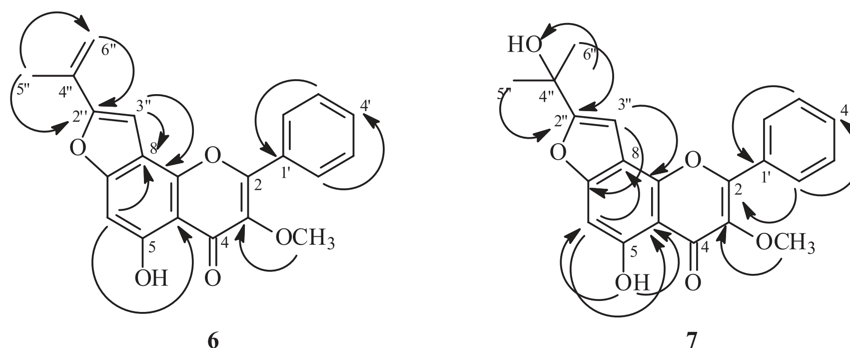


Figure 1. Key HMBC correlations for compounds **6** and **7.**

(No. 39550) has been deposited at the Herbário Prisco Bezerra (EAC) of the Departamento de Biologia, Universidade Federal do Ceará.

Extraction and isolation

Dried roots bark (720 g) and wood (750 g) of *L. obtusus* were separately, powdered and then extracted at room temperature with *n*-hexane (3 × 2.0 L) followed by ethanol (3 × 2.0 L). The solvents were distilled under reduced pressure to afford the crude *n*-hexane (root bark: 37.9 g; root wood: 56.1 g) and EtOH (root bark: 3.9 g; root wood: 20.5 g) extracts. During the distillation process of the *n*-hexane extract of the root bark was observed a yellowish precipitate which was filtrated and purified by crystallization in acetone to give **1** (21.3 mg). The *n*-hexane extract from the root bark (36.0 g) was subjected to silica gel column chromatography (36.6 g) by elution with *n*-hexane (800 mL), EtOAc (200 mL), $CHCl_3$ (500 mL) and MeOH (100 mL), yielding the following fractions, after solvent evaporation: *n*-hexane (9.8 g), $CHCl_3$ (23.0 g), EtOAc (643.0 mg) and MeOH (812.0 mg). The *n*-hexane fraction (9.8 g) was chomatographed over silica gel, eluting with *n*-hexane, *n*-hexane/EtOAc (9:1, 8:2, 7:3, 6:4, 1:1) and EtOAc to afford 7 fractions of 100 mL each (F_A1-F_A7). F_A3 (796.3 mg, *n*-hexane/EtOAc 8:2 mixture) was subjected to a silica gel flash column chromatography using *n*-hexane/EtOAc 9:1 mixture to yield **2** (5.6 mg).

The $CHCl_3$ fraction (23.0 g) was chromatographed over silica gel (81.3 g), eluting with *n*-hexane/$CHCl_3$ (6:4, 4:6, 2:8), $CHCl_3$, EtOAc and MeOH to afford 6 fractions of 200 mL each (F_B1-F_B6). F_B5 (7.1 g, EtOAc) was subjected to silica gel column chromatography using *n*-hexane/$CHCl_3$ (1:1, 2.5:7.5), $CHCl_3$, $CHCl_3$/EtOAc (9:1, 8:2, 7:3), EtOAc and MeOH, to afford 9 fractions of 125 mL each (F_C1-F_C9). F_C1 (3.0 g, *n*-hexane/$CHCl_3$ 1:1) was chromatographed over a silica gel column, using *n*-hexane with increasing amounts of $CHCl_3$ (9:1 to 1:9) as eluent to yield 102 fractions (10 mL each), that after TLC analysis yielded 9 fractions (F_D1-F_D9). F_D4 (1.4 g, *n*-hexane/$CHCl_3$ 1:1 and 4:6) was subjected to silica gel column chromatography using *n*-hexane/EtOAc gradient (9.5:0.5 to 0.5:9.5), EtOAc and MeOH to give 115 fractions, which after TLC analysis were combined into 7 fractions (F_E1-F_E7). F_E4 (60.6 mg, *n*-hexane/EtOAc 9.5:0.5 to 8:2) was rechromatographed using the same solvent system to afford **3** (34.1 mg) and **4** (16.4 mg). F_C2 (2.1 g, *n*-hexane/$CHCl_3$ 2.5:7.5) was subjected to silica gel column chromatography using *n*-hexane/EtOAc gradient (8:2, 7.5:2.5, 7:3) EtOAc, and MeOH. Fractions *n*-hexane/EtOAc 8:2 and 7.5:2.5 (364 mg) were combined and subjected to repeated silica gel column chromatography using *n*-hexane/EtOAC gradient to yield **5** (24.3 mg). F_C3 (1.1 g, $CHCl_3$) was chromatographed over a silica gel column, eluting with *n*-hexane/EtOAc gradient (8:2 to 2:8), EtOAc and MeOH, to give 119 fractions which after TLC analysis were combined into eight fractions (F_F1-F_F8). F_F3 (98.4 mg, *n*-hexane/EtOAc 8:2) was subjected to successive purifications using Sephadex LH-20 (CH_2Cl_2/MeOH 1:1) to yield **6** (6.5 mg) and **7** (3.0 mg). Chromatography of subfraction F_F7 (142.5 mg, EtOAc) over silica gel eluting with $CHCl_3$ yielded 8 (52.6 mg). The EtOH extract from the root bark (76.1 g) was subjected to silica gel column chromatography eluting with CH_2Cl_2, CH_2Cl_2/EtOAc (7.5:2.5, 1:1), EtOAc, EtOAc/MeOH (7.5:2.5) and MeOH (1000 mL of the each solvent), to afford the following fractions: CH_2Cl_2 I (2.0 g), CH_2Cl_2 II (8.8 g), CH_2Cl_2/EtOAc 7.5:2.5 (12.7 g), CH_2Cl_2/EtOAc 1:1 (4.2 g), EtOAc (2.6 g), EtOAc/MeOH 7.5:2.5 (9.5 g) and MeOH (7.7 g). CH_2Cl_2 I fraction (2.0 g) was subjected to repeated silica gel flash column chromatography using *n*-hexane/CH_2Cl_2 9:1 to afford compounds **9** (10.7 mg) and **10** (12.3 mg). The *n*-hexane extract from the root wood (3.9 g) was subjected to silica gel column chromatography eluting with *n*-hexane (920 mL), EtOAc (150 mL), $CHCl_3$ (450 mL) and MeOH (100 mL) to yield the fractions: *n*-hexane (0.8 g), $CHCl_3$ (2.5 g), EtOAc (0.3 g) and MeOH (0.02 g). $CHCl_3$ fraction (2.5 g) was fractioned over silica gel, eluting with *n*-hexane/EtOAc (9:1, 8:2, 7:3, 6:4, 1:1, 7.5:2.5), EtOAc and MeOH, to afford 100 fractions (10 mL each) which after TLC analysis were combined to 10 fractions (F_G1-F_G10). Fraction F_G3 (0.6 g, *n*-hexane/EtOAc 9:1 and 8:2) was subjected to successive silica gel column chromatography to yield compounds **1** (12.0 mg), **5** (6.2 mg) and **11** (7.2 mg). The EtOH extract from the root wood (15.9 g) was subjected to silica gel column chromatography eluted with CH_2Cl_2 (500 mL), CH_2Cl_2/EtOAc 1:1 (850 mL), EtOAc (600 mL), EtOAc/MeOH 1:1 (600 mL) and MeOH (800 mL), yielding the respective fractions: CH_2Cl_2 (2.9 g), CH_2Cl_2/EtOAc 1:1 (4.0 g), EtOAc (1.6 g), EtOAc/MeOH 1:1 (6.2 g) and MeOH (1.3 g). The CH_2Cl_2 fraction (2.9 g) was subjected to silica gel column chromatography using *n*-hexane/EtOAc gradient (95:0.5 to 1:1, 2.5:7.5), EtOAc and MeOH to give 103 fractions (10 mL) that after TLC analysis were pooled into 16 fractions (F_H1-F_H16). Fraction F_H7 (261.1 mg, *n*-hexane/EtOAc 8:2 and 7.5:2.5) yielded the mixture of compounds **12/13** (21.6 mg) and **3** (5.3 mg). Fraction CH_2Cl_2 III (0.7 g) was subjected to slica gel column chromatography using *n*-hexane/EtOAc (9:1, 8.5:1.5, 8:2, 7.5:2.5, 7:3, 4:6), EtOAc and MeOH resulting in 16 fractions (F_I1-F_I16), after TLC analysis. F_I5 (*n*-hexane/EtOAc 8:2, 130.5 mg) was fractionated on Sephadex LH-20 column using acetone/MeOH 1:1 to produce the mixture

of **13/14** (6.6 mg). Fraction CH_2Cl_2/EtOAc I (3.0 g) was chromatographed over silica gel, eluting with *n*-hexane/EtOAc (9:1, 8:2, 7:3, 1:1, 4:6), EtOAc and MeOH to afford 7 fractions (F1-F7, 100 mL each). F6 (*n*-hexane/EtOAc 1:1, 258.3 mg) after purification over Sephadex LH-20 (CH_2Cl_2/MeOH 1:9) yielded **15** (3.5 mg).

Supplementary Information

Supplementary data for compounds **6** and **7** are available free of charge at http://jbcs.sbq.org.br as PDF file.

Acknowledgments

The authors thank to Prof. Edilberto R. Silveira (UFC) for the plant material collection and for the providing the NMR facilities, and to CNPq/CAPES/FUNCAP and PRONEX for the financial support.

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Submitted: June 26, 2011
Published online: December 6, 2011