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A 4-ARYLCOUMARIN FROM *COUTAREA HEXANDRA*

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Key Word Index—*Coutarea hexandra*; Rubiaceae; 4-arylcoumarins; ^{1}H and ^{13}C NMR, MS.

Abstract—From the methanolic extract of the stem of *Coutarea hexandra* we have isolated chromatographically a new natural product identified spectroscopically as 8,3′,4′-trihydroxy-5,7-dimethoxy-4-phenylcoumarin.

INTRODUCTION

Coutarea hexandra (Jacq.) Schum (Rubiaceae), a plant growing in north eastern Brazil and used in folk medicine as antimalarial and antidiabetic agent [1, 2], is an important source of 4-arylcoumarins [3–5] and 4-arylcoumarin glycosides [6]. Now, from the methanolic extract of the stem of this plant, we have isolated 8,3′,4′-trihydroxy-5,7-dimethoxy-4-phenylcoumarin (**1**), a new compound of the neoflavonoid series which is, with exostemin (**2**) [7], a quite rare example of a natural 8-oxygenated-4-arylcoumarin.

RESULTS AND DISCUSSION

Structure **1** was deduced from spectral data. The molecular formula was determined by means of high resolution MS (see Experimental). The ^{1}H NMR spectrum of this compound exhibited two peaks (both *s*, 1H) at δ6.57 and 5.90 due, respectively, to H-6 and H-3 of the tetrasubstituted coumarin and signals at δ6.66 (*dd*, J = 7.5 and 2 Hz, H-6′), 6.75 (*d*, J = 2 Hz, H-2′) and 6.81 (*d*, J = 7.5 Hz, H-5′) ascribable to the 3H ABX system of the 4-phenyl radical [3–6]. The two signals centred at δ3.98 (*s*, 3H) and δ3.50 (*s*, 3H) were assigned to the methoxyl groups placed, respectively, at C-7 and C-5. The methoxyl group at C-5 was strongly shielded (0.4 ppm) by the methoxyl group at C-7 due to the spatial orientation of the 4-phenyl residue placed perpendicularly to the plane of the coumarin nucleus.

The assignment to H-6 of the signal at δ6.57 and the 3′,4′-substitution have been established by means of NOEDS (NOE difference spectra) experiments. First, the peak at δ6.57 (H-6) showed a very clear enhancement when both methoxyl signals at δ3.50 and 3.98 were saturated. The irradiation at δ5.90 (H-3), moreover, led to the enhancement of the signals at δ6.75 (H-2′) and 6.66 (H-6′) indicating a spatial relationship for protons H-3, H-2′ and H-6′. According to structure **1**, the ^{13}C NMR spectrum of this compound, apart from the methoxyl peaks (at δ57.1 and 57.2), exhibited 15 signals, due to a 4-phenylcoumarin skeleton, divided by ^{13}C and DEPT ^{13}C NMR into five non-oxygenated CH groups (C-3, C-6, C-2′, C-5′ and C-6′) and ten quaternary carbons, seven of which are oxygenated (C-2, C-5, C-7, C-8, C-8a, C-3′ and C-4′) (6, 8). Thus, **1** is 8,3′,4′-trihydroxy-5,7-dimethoxy-4-phenylcoumarin.

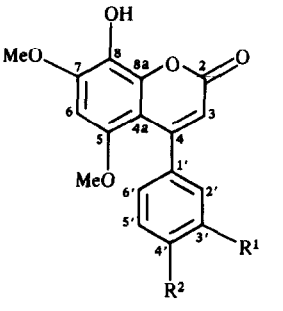
EXPERIMENTAL

MS was recorded by direct inlet at 70 eV. The NMR spectra were measured in CD_3OD solution at 250 MHz (^{1}H NMR) and at 69.5 MHz (^{13}C NMR) with TMS as internal standard. The DEPT experiment was performed using polarization transfer pulses of 90 and 135°, respectively, to obtain in the first case only CH groups and in the second positive signals for CH and CH_3 and negative ones for CH_2 groups. Polarization transfer delays were adjusted to an average CH coupling of 135 Hz. Determination of NOEDS experiments was performed on sample previously degassed by bubbling Ar through the solution for 40 min.

Biological materials. Stems of *C. hexandra* (Jacq.) Schum were collected in north eastern Brazil (Patacube, Fortaleza) and identified by José Elias de Paula (Universidade Federal de Brasilia).

Isolation. Methanolic extract (23 g) obtained from 1.5 kg of air-dried stem of *C. hexandra*, chromatographed on Sephadex LH-20 and later fractionated by means of HPLC (eluent MeOH–H_2O 40:60), as reported in our previous work [6], yield was 8 mg of **1** (R_t = 35 min).

8,3′,4′-Trihydroxy-5,7-dimethoxy-4-phenylcoumarin (**1**). UV λ_{max}^{MeOH} nm (log ε). 265 (2.81), 280 (2.98), 327 (3.6), 427 (2.48); ^{1}H NMR (CD_3OD): δ3.50 (3H, *s*, –OMe), 3.98 (3H, *s*, –OMe), 5.90 (1H, *s*, H-3), 6.57 (1H, *s*, H-6), 6.66 (1H, *dd*, J = 7.5 and 2 Hz, H-6′), 6.75 (1H, *d*, J = 2 Hz, H-2′), 6.81 (1H, *d*, J = 7.5 Hz, H-5′); ^{13}C NMR (CD_3OD) δ57.1 (–OMe), 57.2 (–OMe), 95.9 (C-6), 105.4 (C-4a), 112.6 (C-3), 115.6 (C-5′), 116.2 (C-2′), 120.4 (C-6′),



1 R^1 = R^2 = OH
2 R^1 = H, R^2 = OMe

129.6 (C-8), 133.1 (C-1'), 145.2 (C-8a), 145.5 (C-3'), 146.8 (C-4'), 152.5 (C-7 or C-5), 152.9 (C-5 or C-7), 158.7 (C-4), 162.8 (C-2); MS *m/z* (rel. int) 330 $[M]^+$ (100), 302 $[M-CO]^+$ (13), 287 $[M-MeCO]^+$ (21), 259 $[M-MeCO-CO]^+$ (7); high resolution MS *m/z* (M^+) 330.0824 (calc. for $C_{17}H_{14}O_7$ 330.0739).

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GANSCHISANDRINE, A LIGNAN FROM *SCHISANDRA SPHENANTHERA*

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Key Word Index—*Schisandra sphenanthera*; Schisandraceae, lignan, ganschisandrine, 2*S*,5*S*,-bis-(3,4-dimethoxyphenyl)-3*R*,4*S*-dimethyltetrahydrofuran

Abstract—The structure of ganschisandrine isolated from *Schisandra sphenanthera* was determined to be 2*S*,5*S*-bis(3,4-dimethoxyphenyl)-3*R*,4*S*-dimethyltetrahydrofuran.

INTRODUCTION

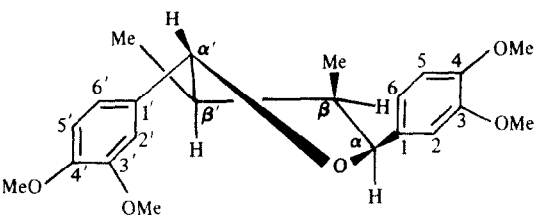
In continuing our study on the chemical ingredients of *Schisandra sphenanthera*, a Chinese medicinal plant [1, 2], collected from Wudu district in Gansu province of China, we have isolated a novel lignan, ganschisandrine. The present work describes the assignment of structure **1** to the new lignan from a study of its spectra (largely by NMR).

RESULTS AND DISCUSSION

From physical constants and spectral data (see Experimental), it is apparent that ganschisandrine (**1**) is a tetrahydrofuran derivative, a stereoisomer of galbelgin [3], galgravin and veraguensin [4, 5]. From the ^1H NMR (Table 1) and ^{13}C NMR (Table 2) data, magnetic non-equivalence of the α,α'-benzylic protons and β,β'-methyl protons of ganschisandrine suggests that one of the four substituents of the tetrahydrofuran ring is *trans* to the other three. The 2D NOESY spectrum of **1** showed correlations between the two methyl doublets (δ0.63 and 1.02) and Hα' signal (δ4.67); the 2D-COSY spectrum of **1** showed that the Hα (δ5.46) coupled with the Hβ (δ2.5) and the Hα' (δ4.67) coupled with the Hβ' (δ2.5), clearly indicating that two methyl groups have the *cis* configuration and Hα' is at the same side of the two methyl groups, Hα and Hβ protons are in *cis*-position, Hα' and Hβ' are in *trans*-position.

The proton coupling constants ($J=4.0$ and $J=9.0$ Hz) show that the dihedral angles between Hα and Hβ, Hα' and Hβ' should be *ca* 40 and 160°, respectively. Therefore, the tetrahydrofuran ring must be in 'twist envelope' conformation. It may be due to the mutual steric repulsion of three *cis*-substituents Ar-α, Me-β and Me-β'. The upfield shifted signal of Me-β is due to shielding effect of Ar-α and the downfield shifted signal of Hα is caused by deshielded effect of Ar-α

The ORD spectra of ganschisandrine (in MeOH, $[\phi]_{292}=+4130$pk, $[\phi]_{241}=+14310$pk) is similar to that of chicanine (in MeOH, $[\phi]_{296}=+5521$pk, $[\phi]_{245}=+19000$pk) [6]; both has a positive Cotton effect.



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