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OCCURRENCE OF GERRARDINE IN *CASSIPOUREA GUIANENSIS*

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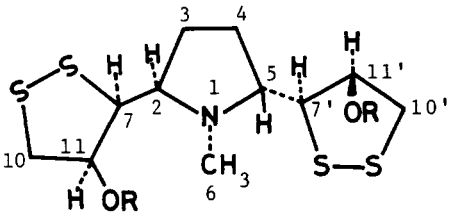
The bark of *Cassipourea guianensis* Aubl. (Rhizophoraceae) from South America yielded a *bis*-1,2-dithiolanyl pyrrolidine; its structure was identified as 1-methyl-2,5-*bis*(4-hydroxy-1,2-dithiolan-3-yl)pyrrolidine, or gerrardine (**1**) an alkaloid that has been previously isolated from *Cassipourea gerrardii* (1). This known alkaloid was thus isolated for the first time from this plant species, and pmr and cmr data of the compound are shown for the first time in this paper. Antimicrobial testing indicated some effects (MIC, 50 μg/ml) against *Candida albicans* TA., and a weak activity (MIC, 100 μg/ml) against three others (*Escherichia coli* NIHJ JC-2, *E. coli* 0-111, and *Klebsiella pneumoniae* DT).



1 R=H (gerrardine)
2 R=CONHCH$_3$

EXPERIMENTAL

GENERAL EXPERIMENTAL PROCEDURES.—Melting points were determined on a Yanagimoto apparatus and are uncorrected. Spectra were recorded with the following instruments: uv, Hitachi 124; ir, Hitachi 215; nmr, Varian XL-200 (200 MHz and 50 MHz for pmr and cmr, respectively); ms, Hitachi M-80. Optical rotation was measured on a Model DIP-181 Digital polarimeter from Japan Spectroscopic Co., Ltd.

PLANT MATERIAL.—The *C. guianensis* was collected at Belém Pará in Brazil. The botanical identification was determined by comparing with an authenticated specimen in the herbarium at the Musea Goldi Belém Pará in Brazil. The bark of the tree was collected and dried for the investigation.

EXTRACTION AND ISOLATION.—The dried bark of *C. guianensis* (2 kg) was extracted with petroleum ether and 80% MeOH. The concentrate from the 80% MeOH was extracted with 2% aqueous citric acid and partitioned with C_6H_6. The aqueous extract was basified with 10% Na_2CO_3 and extracted with $CHCl_3$; the $CHCl_3$ extract was dried over anhydrous Na_2SO_4, and the solvent was removed to give the crude alkaloids (4.5 g).

The crude basic substances on silica gel tlc [C_6H_6-Et_2O-$CHCl_3$-MeOH (10:10:3:3)] gave seven sulfur-containing alkaloidal spots (Dragendorff's reagent and 0.5% dilute HCl solution of $PdCl_2$ to indicate alkaloids and sulfur compounds, respectively). To isolate each alkaloid, the crude basic substances were chromatographed on a column of silica gel (same solvent system), and the first eluates furnished pale yellow crystals of **1** (200 mg; 0.01% yield), which were recrystallized from MeOH-$CHCl_3$, mp 180-181°, $[\alpha]^{24}D$ −131° (c=1.08, hydrochloride in MeOH).

IDENTIFICATION.—The compound (**1**) was identified as gerrardine, [mp 180°, $[\alpha]^{23}D$ −171° (c=1, hydrochloride in H_2O)] by uv, ir, ms, pmr and cmr, X-ray analysis, and comparison with similar data from an authentic sample (2,3). The pmr and cmr data of gerrardine have not been reported in previous papers. The pmr (200 MHz, $CDCl_3$, δ) shows the substituted *N*-methyl pyrrolidine (3.43, 2H, m, $H_{2,5}$; 2.83, 3H, s, H_6; 1.73-2.23, m, 4H, $H_{3,4}$) and the disubstituted dithiolanyl rings (4.60, 2H, m, $H_{11,11'}$; 3.52, 2H, dd, $H_{7,7'}$, J_1=2.5, J_2=10; 3.31, 2H, dd, $H_{10B,10B'}$, J_{AB}=11.5, J_{BX}=3; 3.26, 2H, dd, $H_{10A,10A'}$, J_{AX}=2, J_{AB}=11.5), which concur with cmr (50 MHz, d_5-pyridine, δ) absorption at 75.7 (2C, d, C-11, 11'); 65.23 (4C, d, C-2,5, C-7,7'); 47.16 (2C, t, C-10, 10'); 38.57 (1C, q, C-6) and 28.45 (2C, t, C-3,4).

The compound was converted into the *bis*-carbamate $C_{15}H_{25}O_4N_3S_4$ (**2**) by treatment with methyl isocyanate; mp 175-178°, pmr (200 MHz, $CDCl_3$, δ): 5.62 (2H, bs, $H_{11X,11X'}$); 5.0 (2H, m, -N*H*- x 2); 3.59 (2H, dd, $H_{7,7'}$, J_1=3.5, J_2=10.5); 3.50 (2H, dd, $H_{10B,10B'}$, J_{AB}=12.5, J_{BX}=4.5); 3.32 (2H, dd, $H_{10A,10A'}$, J_{AX}=2, J_{AB}=12.5); 3.24 (2H, m, $H_{2,5}$); 2.84 (6H, d, -NH-C*H*$_3$×2); 2.41 (3H, s, H_6). Cmr (50 MHz, $CDCl_3$, δ): 155.87 (2C, s, C=O×2); 64.14 and 63.94 (2C, d, C-2,5, C-7,7'); 44.78

(2C, t, C10,10'); 38.24 (1C, q, C-6); 28.45 (2C, t, C-3,4); 27.59 (2C, q, NH-CH_3×2).

ANTIMICROBIAL ACTIVITY TEST.—Each test organism was cultured in agar medium containing tri-sugar (sucrose, glucose, and lactose) at 37°. After 2 days, minimal inhibitory concentrations (MIC) were measured by the cup method.

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