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ISOCRYPTOLEPINE FROM *CRYPTOLEPIS SANGUINOLENTA*

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Key Word Index—*Cryptolepis sanguinolenta*; Asclepiadiaceae; indoloquinoline; alkaloid.

Abstract—A new alkaloid, 5-methyl, 5H-indolo-[3,2-c]-quinoline named isocryptolepine, has been isolated from the roots of *Cryptolepis sanguinolenta* and its structure determined from spectroscopic data, including IR, MS and NMR.

INTRODUCTION

Cryptolepis sanguinolenta (Lindl) Schlechter (Asclepiadiaceae), a shrub indigenous to tropical West Africa, has long been employed in the dyeing of textiles and leather [1]; it is also used in folk medicine as an antimalarial agent [2] and such bioactivities as antibacterial activity or action on vasodilation have been reported [3].

The first alkaloid isolated from *C. sanguinolenta* in 1951 by Gellert *et al.* [4] was cryptolepine (5-methyl, 5H-indolo-[3,2-b]-quinoline), previously extracted from *C. triangularis*. Later, the same alkaloid was re-isolated from *C. sanguinolenta* by Dwuma-Badu *et al.* [5], along with quindoline (norcryptolepine) and a non-characterized alkaloid (CSA-3). Recently, the spirononacyclic alkaloid cryptospirolepine was isolated from the same plant [3].

This paper reports the isolation of a new alkaloid **1** (5-methyl, 5H-indolo-[3,2-c]-quinoline) which is an isomer of cryptolepine **2**, and thus termed isocryptolepine.

RESULTS AND DISCUSSION

The EtOH extract of the defatted powdered roots of *C. sanguinolenta* was treated with aqueous HOAc, filtered, alkalinized with NH_4OH, and extracted repeatedly with CH_2Cl_2. The combined CH_2Cl_2 extracts were chromatographed over Al_2O_3 eluted with a CH_2Cl_2–MeOH gradient. Elution with CH_2Cl_2 gave a mixture of quindoline and isocryptolepine, and elution with CH_2Cl_2–MeOH (9 : 1) afforded cryptolepine. Quindoline and isocryptolepine (**1**) were separated by preparative silica gel thin-layer chromatography.

The EI mass spectrum of **1** showed the molecular ion at *m/z* 232 in agreement with the molecular formula $C_{16}H_{12}N_2$. The 16 carbon atoms were depicted in the ^{13}C NMR spectrum and distributed into 15 aromatic carbon atoms (9 CH and 6 quaternary sp^2 carbons) and one methyl group (Table 1). The ^1H NMR spectrum displayed resonances for 12 protons forming two four-spin systems assigned to two *ortho*-disubstituted benzene rings and a singlet at δ9.29. These spin systems were the same as those previously described for cryptolepine (**2**), but the chemical shifts were different, especially the aromatic singlet at δ8.91 in the spectrum of cryptolepine was shifted to lower field.

Analysis of the ^1H–^1H COSY, ^{13}C–^1H COSY and HMBC spectra allowed the assignment of one benzene ring in an indole substructure and the second in a quinoline substructure, as in the structure of cryptolepine. However, the assembling of the substructures was different for isocryptolepine, and was suggested to be as shown in structure **1**, due to the following long-range correlations observed in the HMBC. The quaternary carbon at δ152.1 (11a) was ^3J correlated to the proton at δ8.77 (H-1); the singlet proton at δ9.29 was ^3J correlated to carbon atoms at δ152.1 (C-11a), 137.5 (C-4a), 43.5 (*N*-Me) and ^2J to that of δ117.6 (C-6a), whereas the carbon atoms at 140.5 (C-6) and 137.5 (C-4a), gave strong correlations with the *N*-methyl protons. These data agreed with the position of the singlet methine α to the *N*-methyl group. The results led to structure **1** for isocryptolepine, which has thus an angular structure isomeric with cryptolepine for which the four rings are linear. Isocryptolepine could be the partially characterized alkaloid CSA-3 [5].

EXPERIMENTAL

General. ^1H 300.13 MHz and ^{13}C 75.47 MHz NMR spectra were performed on an AC 300 Bruker spectrometer. The HMBC spectrum was optimized for J_{C-H} 10 Hz. EIMS: obtained with a Nermag Sidar V 3.0 mass spectrometer.

Isolation. The roots of *Cryptolepis sanguinolenta* (Lindl) Schlechter (60 g) were air-dried, and ground to provide a fine powder. The powder was defatted with hexane for 12 hr and then extracted by percolation with EtOH (500 ml). After evapn of the solvent, the residue was

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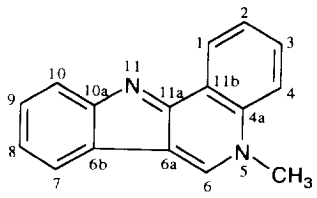

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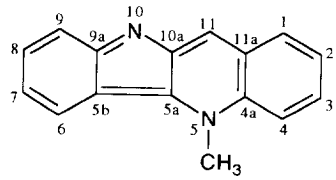

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Table 1. ^{13}C and ^{1}H NMR data for isocryptolepine (1) (CD_3OD)

C	1 δ_C	1 δ_H *m* *J*(Hz)	HMBC C correlated to H
1	125.4	8.77 *dd* 8.1, 1.4	3
2	127.5	7.78 *ddd* 8.4, 8.1, 0.9	4
3	131.7	7.92 *ddd* 8.4, 8.1, 1.4	1
4	118.8	8.12 *brd* 8.1	2
4a	137.5	—	1, 3, 6, *N*-Me
6	140.5	9.29 *s*	*N*-Me
6a	117.6	—	6,7
6b	125.7	—	8, 10
7	120.9	8.15 *dd* 8.1, 1.0	9
8	122.5	7.35 *ddd* 8.2, 8.2, 0.8.	10
9	127.8	7.53 *ddd* 8.1, 8.2, 1.0	7
10	117.6	7.81 *dd* 8.1, 0.8	8
10a	152.0	—	7, 9
11a	152.1	—	1, 6
11b	121.6	—	2, 4
N-Me	43.5	4.36 *s*	6

mixed with aq. HOAc (10%, 200 ml), and allowed to stand overnight. The mixt. was filtered, alkalinized with NH_4OH to pH 10, and extracted by CH_2Cl_2 (2 × 200 ml). The combined CH_2Cl_2 extracts were washed with H_2O, dried over Na_2SO_4, filtered and evapd to afford a dark alkaloidal residue (450 mg). This residue was dissolved in MeOH (2 ml) and chromatographed over Al_2O_3 (30 g). Elution with hexane, and then CH_2Cl_2 afforded a mixt. of quindoline and isocryptolepine (40 mg). Elution with CH_2Cl_2–MeOH (9:1) gave a violet residue of cryptolepine (400 mg). The mixt. of quindoline and isocryptolepine was further purified by prep. TLC (Kieselgel Merck 60) using toluene–Me_2CO–NH_4OH (50:50:2) as eluent yielding isocryptolepine (**1**, 5 mg, 0.08%, R_f 0.45) and quindoline (5 mg, R_f 0.80), which was identified by comparison with an authentic sample.

Isocryptolepine (**1**). $C_{16}H_{12}N_2$: (not crystallized); UV (EtOH) λ_{max} nm (log ε): 238 (4.18), 284 (4.26), 352 sh (3.64); IR (KBr) ν_{max} cm^{-1}: 1644, 1617, 1460, 1354, 1242, 1123, 762, 715, 617; EIMS (*m/z*) 232 $[M]^+$ (100%), 217 (16), 204 (4), 190 (10), 116 (12), 101 (5), 89 (6).

Cryptolepine (**2**). $C_{16}H_{12}N_2$; mp 167–168°, lit. 166–169° [4]; IR (KBr) ν_{max} cm^{-1}: 1644, 1615, 1466, 1354, 1308, 1242, 1031, 775, 715, 597; EIMS (*m/z*) 232 $[M]^+$ (100%), 217 (32), 190 (15), 116 (16), 102 (11), 94 (15), 89 (35). ^1H NMR (CD_3OD) δ ppm: 8.91 (*s*, H-11), 8.54 (*d*, 8.5, H-4), 8.50 (*d*, 9.1, H-6), 8.34 (*dd*, 7.8, 1.2, H-1), 8.05 (*ddd*, 8.5, 7.3, 1.2, H-3), 7.80 (*dd*, 7.8, 7.3, H-2), 7.74 (*dd*, 8.4, 1.3, H-9), 7.69 (*dd*, 8.4, 7.6, H-8), 7.34 (*ddd*, 9.1, 7.6, 1.3, H-7), 4.95 (*s*, *N*-Me).

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