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5-METHOXY-1-OXO-TETRAHYDRO-β-CARBOLINE, AN ALKALOID FROM *ALSTONIA VENENATA*

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Key Word Index—*Alstonia venenata*; Apocyanaceae; alkaloid; root bark; 5-methoxy-1-oxo-tetrahydro-β-carboline.

Abstract—A new oxo-tetrahydro-β-carboline alkaloid has been isolated from the root bark of *Alstonia venenata*. It was identified as 5-methoxy-1-oxo-tetrahydro-β-carboline.

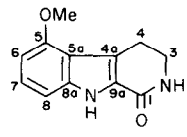
In continuation of our work on the alkaloidal constituents of *Alstonia venenata* [1–3] we isolated a new oxotetrahydro-β-carboline base. This paper reports the identification of this compound as 5-methoxy-1-oxo-tetrahydro-β-carboline. The isolation of the compound is significant as this unit has been found to be present in all the yohimbine alkaloids isolated from this plant.

5-Methoxy-1-oxo-tetrahydro-β-carboline (**1**) was obtained from the 2% methanol–chloroform eluate of the ethanolic extract of the root-bark of *A. venenata*. The new base, $C_{12}H_{12}N_2O_2$ (M^+ 216), mp 182–184° (MeOH) exhibited a UV spectrum characteristic of a β-carboline system viz. λ_{max}^{EtOH} 238, 258, 295 nm (log ε: 3.91, 2.57, 3.61). The presence of an amide function was evident from the IR spectrum (ν_{max}^{KBr} 3260 and 1660 cm^{-1}). The 80 MHz ^1H NMR (DMSO-d_6) showed the presence of an indole >NH δ 11.55 (1H, *s*) and an aromatic methoxyl δ 3.80 (3H, *s*). The C-3 and C-4 methylenes exhibited symmetrical triplets at δ 3.45 and 3.05, respectively, (2H each, $J_1 = J_2 = 6.0$ Hz) and the amide >NH appeared as a broad signal δ 7.45 (1H). The aromatic protons showed an ABC pattern, the signals appearing at δ 7.10 (1H, *d*), 6.95 (1H, *dd*) and 6.44 (1H, *dd*) with coupling constants $J_{AB} = 8.3$, $J_{AC} = 8.0$ and $J_{BC} = 2.0$ Hz. The only point which remained to be settled was the placement of the methoxyl group in the aromatic nucleus. This could be ascertained from an examination of the 20 MHz ^{13}C NMR spectrum (DMSO-d_6). The methoxyl group is placed at the C-5 position rather than at C-8 from a comparison of the chemical shifts of the C-5–C-8 carbons of **1** with those of the corresponding carbons, viz. C-9–C-12 in venenatine (**2**), alstovenine (**3**), 16-epivenenatine (**4**), 16-epialstovenine (**5**) [3] and scholarine (**6**) [4] (Table 1). The chemical shifts calculated on the basis of additivity relationships [5] agreed closely with those observed if the methoxyl group was placed at C-5. Hence the structure of the new base is undoubtedly 5-methoxy-1-oxo-tetrahydro-β-carboline **1**.

The most downfield peak at δ 161.82 was characteristic of the amide carbonyl carbon. The methoxyl carbon appeared at δ 55.01. As expected the C-3 carbon adjacent to the amide nitrogen resonated at a relatively high field (δ 41.27). The chemical shifts for all the carbons in **1** are given in Table 2.

Whilst examining the literature [6] we found that the assignments of the ^{13}CNMR signals of the C-4 and C-5 carbons in 7-methoxyindole (**7**) should be interchanged (Table 1). Compared to indole **8** the C-4 carbon in **7** would suffer a shielding effect by *ca.* δ 7 due to the presence of the methoxyl group at the C-7 position while the value of the C-5 carbon would remain unchanged as it does not undergo any change in electron density.

The mass spectrum of the compound was in agreement with the assigned structure **1** (Scheme 1). The fragment ion at *m/z* 187 was due to the retro Diels–Alder cleavage of ring C. Subsequent loss of carbonyl produced the fragment *m/z* 159. The peak at *m/z* 201 was produced by the loss of methyl from *m/z* 216 $[M]^+$.



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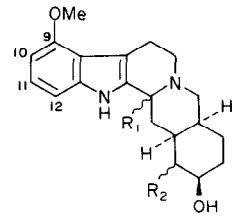
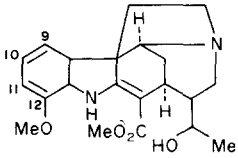


2 R_1 = β–H, R_2 = β–CO_2Me

3 R_1 = α–H, R_2 = β–CO_2Me

4 R_1 = β–H, R_2 = α–CO_2Me

5 R_1 = α–H, R_2 = α–CO_2Me



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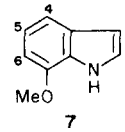

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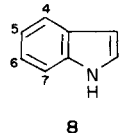

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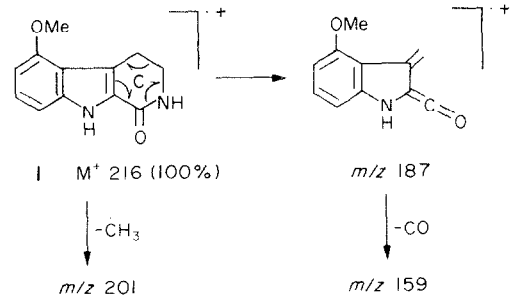
Table 1. Comparison of ^{13}C NMR shifts of compounds **1–8**

Carbon	1	Calc. values for 1	Carbon	2	3	4	5	6	Carbon	7(reported)	7(revised)	8
C-5	154.88	154.20	C-9	155.06	154.33	154.14	154.16	113.2	C-4	120.2	113.5	120.9
C-6	99.16	99.50	C-10	104.29	99.64	99.50	99.34	122.5	C-5	113.5	120.2	121.5
C-7	125.0	123.40	C-11	121.49	121.80	122.46	121.34	111.2	C-6	102.1	102.1	119.9
C-8	105.56	105.20	C-12	105.66	104.12	104.99	105.13	144.7	C-7	146.7	146.7	111.4

Table 2. ^{13}C NMR data on 5-methoxy-1-oxotetrahydro-β-carboline (**1**)

Carbon numbers	Chemical shifts δ-values (DMSO-d_6)	Multiplicity
C-1 (>C=O)	161.82	*s*
C-3	41.27	*t*
C-4	22.27	*t*
C-5	154.88	*s*
C-6	99.16	*d*
C-7	125.00	*d*
C-8	105.56	*d*
C-4a	115.51	*s*
C-5a	117.94	*s*
C-8a	138.44	*s*
C-9a	125.86	*s*
OCH_3	55.01	*q*



Scheme 1. Mass spectral fragmentation of 5-methoxy-1-oxotetrahydro-β-carboline.

EXPERIMENTAL

Plant material. The root-bark of *A. venenata* R. Br. was collected from Coimbatore. A voucher specimen (No. AV-x) has been preserved in our laboratory.

Isolation and properties of 5-methoxy-1-oxo-tetrahydro-β-carboline. The dried and powdered root-bark (10 kg) of *A. venenata* was extracted with EtOH (50 l.) for 30 days in a percolator at 25°. The EtOH extract was concd to *ca* 1 l., mixed with 6% citric acid soln (1 l.) for 24 hr. The resulting mixture was filtered through a bed of Celite, the filtrate made alkaline with NH_4OH soln at 0° and extracted with $CHCl_3$ (3 × 1 l.). The $CHCl_3$ extract was washed with H_2O, dried (Na_2SO_4), concd and then chromatographed over Brockmann Al_2O_3 (BDH, neutral). The 2% MeOH–$CHCl_3$ eluate afforded 5-methoxy-1-oxo-tetrahydro-β-carboline (yield: 20 mg, 0.0002%); $C_{12}H_{12}N_2O_2$, mp 182–184° (MeOH); IR ν_{max}^{KBr} cm^{-1}: 3260 (>NH), 2980, 2940 (C–H), 1660 (–NH–C(=O)–), 1620, 1590, 1555 (Ar–OMe), 1270 (Ar–O–C<), 780, 750 (1,2,3-trisubstituted benzene).

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TWO PYRROLIZIDINE ALKALOIDS FROM *GYNURA SCANDENS*

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Key Word Index—*Gynura scandens*; Asteraceae; pyrrolizidine alkaloids; gynuramine; acetylgynuramine.

Abstract—Two new pyrrolizidine alkaloids have been isolated from *Gynura scandens* and their structures analysed by spectroscopic methods. The names gynuramine and acetylgynuramine are proposed.

INTRODUCTION

Pyrrolizidine alkaloids are widely distributed in many plant families. Associations of Lepidoptera with *Gynura scandens* made it a likely source of such compounds [1]. These alkaloids are of great pharmaceutical interest, because they are hepatotoxic to man and domestic animals [2–7].

Gynura, a genus not previously examined for alkaloids, is closely related to *Senecio* and also belongs to the tribe Senecioneae, which is a major source of pyrrolizidine alkaloids. These considerations and its use as a medicinal herb in Africa [8, 9] caused me to investigate *G. scandens* with regard to its alkaloid content.

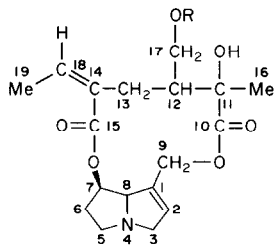
Two new pyrrolizidine alkaloids could be isolated after extraction and purification of plant material. Structural analysis was carried out by IR-, mass-, ^{1}H NMR-, and ^{13}C NMR spectroscopy. For these new alkaloids the names gynuramine and acetylgynuramine are proposed. Gynuramine was identified independently from insect sources [1].

RESULTS AND DISCUSSION

Methanolic extraction of plant material was followed by purification of the residue by distribution between aqueous ammonia and methylene chloride. The two new alkaloids were isolated by low pressure CC from the resulting alkaloid mixture. The IR data of the two substances are very similar. They only differ in showing two carbonyl bands and one hydroxyl band for alkaloid A, and one carbonyl band and two hydroxyl bands for alkaloid B.

The mass spectra proved the molecular formula $C_{20}H_{27}NO_7$ for alkaloid A, and $C_{18}H_{25}NO_6$ for alkaloid B. Typical fragmentations between *m/z* 140 and *m/z* 80 were characteristic of retronecine or its isomeric form. In addition, the other fragmentation shows, that A and B only differ in an acetyl group in alkaloid A. On account of this fact and with regard to the similarity of the IR spectra, alkaloid A must be the acetyl derivative of alkaloid B.

Important information for structure determination can be found from NMR analysis. The ^{1}H NMR spectroscopy data are given in Table 1, and that for ^{13}C NMR spectroscopy in Table 2. All peak-values were



1 R=H

2 R=C(=O)–Me