Pergamon

0031-9422(95)00446-7

Phytochemistry, Vol. 40, No. 4, pp. 1327–1329, 1995

0031-9422/95 $9.50 + 0.00

THE PRINCIPAL ALKALOID OF *SENECIO SCHWEINFURTHII*

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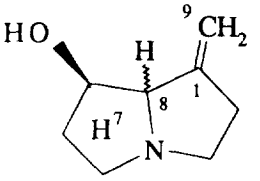
(*Received* 10 *April* 1995)

Key Word Index—*Senecio schweinfurthii*; Compositae; pyrrolizidine alkaloids; 7β-hydroxy-1-methylene-8α-pyrrolizidine *N*-oxide, 7β-hydroxy-1-methylene-8α-pyrrolizidine.

Abstract—Air-dried epigeal parts of *Senecio schweinfurthii*, collected from two sites in Kenya, yielded 7β-hydroxy-1-methylene-8α-pyrrolizidine *N*-oxide, as the predominant alkaloid.

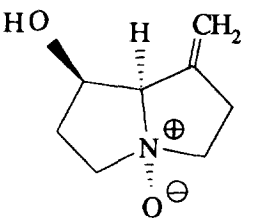
INTRODUCTION

In continuation of our studies of east African species of *Senecio* [1], we have examined the alkaloids of *S. schweinfurthii* O. Hoffm. (a plant which has extensive synonymy: *S. sera* Schweinf., *S. massaiensis* Muschl., *S. melanophyllus* Muschl., *S. theodori* K. Afzel., *S. roberti-friesii* K. Afzel., *S. roberti-friesii* var. *subcanescens* K. Afzel., *S. roberti-friesii* var. *kilimanjaricus* K. Afzel., and *S. sattimae* K. Afzel. [1]). Our material was first collected on Mt. Kenya and later in the Aberdare Mountains of Kenya.



1 8α-H

2 8β-H



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RESULTS AND DISCUSSION

Conventional processing of an ethanolic extract of air-dried and pulverized plant material from Mt. Kenya yielded an aqueous extract which gave a strong positive reaction when tested with Mayer's reagent. Most species of *Senecio* contain pyrrolizidine alkaloids [2–4] and these are usually preponderantly present as *N*-oxides [2–6]. Accordingly, the extract was partitioned between $CHCl_3$ and dilute aqueous sulphuric acid and a portion of the aqueous extract stirred with Zn dust. After basification and extraction with $CHCl_3$, this yielded alkaloidal material (*ca* 0.1%) as an oil which crystallized when it was stored at 0°. Both GC–mass spectrometry and NMR data for this product indicated that it was essentially a single substance which was recognized from its spectroscopic properties to be a 7-hydroxy-1-methylenepyrrolizidine. Both 7β-hydroxy-1-methylene-8α-and 8β-pyrrolizidines (**1** and **2**, respectively) have been described by Culvenor and Smith who isolated them from *Crotalaria goriensis* [7]. Distillation of our material gave a product whose $[\alpha]_D$ of −153° agreed with that reported for the 8α-isomer (−150°) and not the 8β-isomer (+36°). Additionally, our material had spectroscopic properties identical with those of **1** which we had recently prepared from retronecine [8]. Thus, the *S. schweinfurthii* base is **1**.

Culvenor and Smith showed that there was little difference in the amounts of alkaloid isolated from *C. goriensis* seeds with or without reductive work-up, i.e. that there was little *N*-oxide present. However in our case, omission of the reductive step resulted in a large drop in the yield of **1**. We therefore examined the unreduced extract for the presence of *N*-oxide and isolated material whose NMR–mass spectrometry data indicated that was **3**. Proof for this identification was provided by the oxidation of **1** to **3** which was identical to our isolate. Reductive processing of the *S. schweinfurthii* from our second collection site in the Aberdare Mountains revealed that it too contained **1** as the predominant base.

It is unusual, but precedented [1–4], to find a single pyrrolizidine base in an overwhelming amount; normally several such bases are present in comparable proportions. We also note that the 7-*O*-angelyl derivative of **3** was recently discovered in *S. chrysocoma*, another African species [9]. Together with our findings these appear

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to constitute the only reports of the occurrence of methylenepyrrolizidines in the genus *Senecio*.

EXPERIMENTAL

Plant material. A ref. specimen has been deposited in the Herbarium of the University of Calgary.

Extraction of alkaloids. Air-dried and pulverized plant material (810 g) was extracted in a Waring blender with 95% EtOH (4 × 2 l). The extracts were then concd under red. pres. to a syrup (128 g). This was partitioned between aq. H_2SO_4 (1 M, 200 ml) and $CHCl_3$ (350 ml) with centrifugation to separate the phases. The $CHCl_3$ layer was then re-extracted with aq. H_2SO_4 (2 × 75 ml) and the comb. aq. extracts filtered (Celite) and the filtrate (*ca* 300 ml), which gave a strongly positive reaction when tested with Mayer's reagent [10], was divided into two portions which were processed as follows. (a) *Reductively.* To a portion (*ca* 200 ml) of the aq. acidic soln was added Zn dust (5 g). The mixt. was stirred overnight at room temp. and then filtered (Celite). The filtrate was brought to pH *ca* 10 and extracted with $CHCl_3$ (4 × 75 ml), then EtOAC (1 × 100 ml), and finally with 1-BuOH (100 ml). These organic extracts were separately dried ($MgSO_4$) and the solvents removed under red. pres. The $CHCl_3$ extracts yielded an oil (1.4 g) which was redissolved in aq. H_2SO_4 (1 M, 100 ml) and this soln was washed with $CHCl_3$ (2 × 25 ml) before being rebasified to pH *ca* 10 with NH_4OH and then extracted with $CHCl_3$ (4 × 50 ml). The comb., dried ($MgSO_4$) $CHCl_3$ extracts were evapd to give a pale brown oil (610 mg) which crystallized when stored at 0°. TLC ($CHCl_3$–MeOH–NH_4OH, 4:1:0.1 and 5:1:0.1), as well as GC–MS, indicated that this material was essentially a single substance. Its ^1H and ^{13}C NMR spectra were essentially identical with those of the dist. material. Bulb-to-bulb distillation (80° at 1 mm) of this oil gave **1** as a colourless oil which crystallized when cooled to 0°. Mp 32–33°. $[\alpha]_D$ −153° (*c* 0.5, EtOH), lit. [7] for **1**, mp 35–36°, $[\alpha]_D$ −150° (EtOH). ^1H NMR (400 MHz, $CDCl_3$, ref. $CHCl_3$ δ_H 7.27) δ_H 5.16 and 4.86 (each 1H, *dt*, *J* = 2.1 Hz, H-9A and 9B), 3.89 (1H, *br s*, H-8), 4.14 (1H, *dt*, *J* = 4 and 2 Hz, H-7), 3.07 and 2.65 (each 1H, *m*, H-3A and 3B), 3.12 and 2.78 (each 1H, *m*, H-5A and 5B), 2.51 (2H, *m*, H-2) and 2.01 and 1.92 (each 1H, *m*, H-6A and 6B). ^{13}C NMR (100 MHz, $CHCl_3$, ref. 77.0) 149.0 (C-1), 107.4 (C-9), 73.9 (C-8), 72.2 (C-7), 55.0 (C-3), 52.9 (C-5), 35.6 (C-6) and 34.7 (C-2); these assignments were established by HXCORR spectra. (b) *Without reduction.* A portion of the aq. H_2SO_4 extract (50 ml) was basified first with Na_2CO_3, then NH_4OH to pH *ca* 10 and then extracted with $CHCl_3$ (4 × 50 ml) and then EtOAC (3 × 30 ml). These extracts were dried ($MgSO_4$) and the solvents removed under red. pres. to leave a small residue which was redissolved in aq. H_2SO_4, washed with $CHCl_3$ and then recovered by basification with NH_4OH to pH *ca* 10 and repeated extraction with $CHCl_3$. Removal of solvent from the comb., dried ($MgSO_4$) $CHCl_3$ extracts yielded a brownish oil (58 mg) whose NMR spectra were the same as those of the base obtained by reductive processing. (c) The remainder of the aq. H_2SO_4 extract (50 ml) was basified as before to pH *ca* 10 and then extracted with 1-BuOH (4 × 50 ml). The comb. BuOH extracts were dried (Na_2SO_4) and evapd *in vacuo* to a reddish-brown syrup. This was dild with H_2O and again evapd under red. pres., to remove traces of BuOH. The residual glass was largely insol. in $CDCl_3$ but sol. in MeOH. A ^1H NMR (CD_3OD) revealed, besides signals apparently due to glycosidic materials, relatively intense signals which were attributable to the *exo*-methylene functionality (δ_H 5.05 and 4.9 each 1H, *br s*), as well as others corresponding to H-7 and H-8 of a pyrolizidine alkaloid. A portion (88 mg) of the BuOH extract was subjected to vacuum short CC on silica gel 60 (3.3 cm × 3.5 cm) using 1-BuOH–EtOH–H_2O–NH_4OH (120:25:15:10) as eluant and collecting frs of 10 ml. After repeated re-evapn under red. pres. with H_2O added to remove BuOH, the individual frs were examined by ^1H NMR: frs 7 and 8 corresponded to pure **3**. These were comb. to afford the *N*-oxide as a near-colourless oil (20 mg). MS (FAB) *m/z* 156 $[M + 1]^+$. NMR δ_H (MeOH-d_4, δ_H 3.31 as ref.) 5.29 (1H, *q*, *J* = 2 Hz, H-9A), 5.12 (1H, *q*, *J* = 2 Hz, H-9B), 4.54 (1H, *dt*, *J* = 5.4 and 2 Hz, H-7), 4.32 (1H, *br dt*, *J* = 5.4, and 2 Hz, H-8), 3.97 (1H, *ddd*, *J* = 11.9, 9.7 and 7.1 Hz, H-5A), 3.91 (1H, *dt*, *J* = 11.2 and 8.2 Hz, H-3A), 3.64 (1H, *m*, H-5B), 3.59 (1H, *m*, H-3B), 2.99 (1H, *m*, H-2A), 2.80 (1H, *m*, H-2B), 2.73 (1H, *m*, H-6A) and 2.14 (1H, *m*, H-6B). δ_C (MeOH-d_4, δ_C 49.0 as ref.) 142.2 (*s*, C-1), 111.9 (*t*, C-9), 92.0 (*d*, C-8), 72.3 (*d*, C-7), 70.0 (*t*, C-3), 68.5 (*t*, C-5), 34.9 (*t*, C-6), 33.4 (*t*, C-2); δ_C (D_2O, TSP-d_4 δ_C 0 as ref.) 142.9 (*s*, C-1), 115.1 (*t*, C-9), 92.7 (*d*, C-8), 73.6 (*d*, C-7), 71.2 (*t*, C-3), 69.4 (*t*, C-5), 35.6 (*t*, C-6), 34.5 (*t*, C-2).

Preparation of **3** *by oxidation of* **1**. To a soln of **1** (10 mg) in D_2O (0.8 ml) was added 30% H_2O_2 (0.1 ml) and the reaction monitored by ^{13}C NMR. After 2 hr, the spectrum was identical with that of the product isolated from the unreduced *S. schweinfurthii* extract. The reaction mixt. was evapd to dryness under red. pres., taken up in MeOH and again evapd to leave **3** as a colourless glass (10 mg) with spectroscopic properties identical to those of the natural product.

Acknowledgements—The authors thank the Natural Sciences and Engineering Research Council of Canada for a grant in aid of research (to MHB) which helped support this work.

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