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ACETYLANONAMINE, A NEW SECOPYRROLIZIDINE ALKALOID FROM *SENECIO ANONYMUS*

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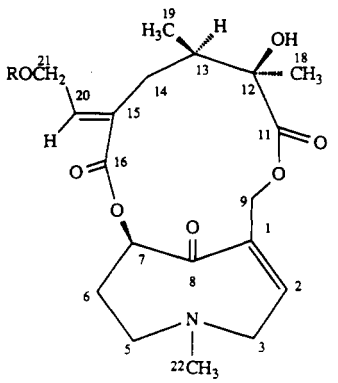
ABSTRACT.—A new secopyrrolizidine alkaloid, acetylanonamine [**1**], was isolated from *Senecio anonymus*. The structure was established by high resolution nmr (^{1}H-^{1}H COSY and ^{1}H-^{13}C HETCOR), ms, comparison of these spectral data with those of anonamine [**2**], and synthesis of **1** from **2**.

In an earlier article (1), we reported the isolation of four pyrrolizidine and six secopyrrolizidine alkaloids from *Senecio anonymus* Wood (Asteraceae). During the isolation of additional quantities of these alkaloids for further biological screening, we obtained a new alkaloid **1** related to the previously isolated anonamine [**2**] through the esterification of the hydroxyl group at C-21. This new alkaloid, named acetylanonamine, is a very minor component obtained from a plant extract which contained a significant amount of **2** and no hydroxysenkirkine. In this paper we report the isolation and structure elucidation of **1**.

Cc of a crude alkaloid mixture obtained by the usual zinc-acid reduction of the plant extract gave the following alkaloids, with relative compositions of the total crude alkaloids based on isolated yields: senkirkine (35.10), neosenkirkine (23.40), anonamine (12.54), otosenine (8.35), senecionine (7.95), retrorsine (6.88), integerrimine (3.99), acetylanonamine [**1**] (0.89), and usaramine (0.88).



1 R=$\overset{21}{C}H_3\overset{23}{C}O$
2 R=H

The ^{1}H-nmr spectrum of **1** showed three methyl singlets at δ 1.27, 2.01, and 2.04 assignable to Me-18, MeCO, and NMe, respectively. A doublet at δ 0.84 accounted for Me-19. Signals analogous to those of **2** were the triplet at δ 6.54 for CH-20 and the two sets of doublet-of-doublets at δ 4.60 and 4.71 due to the coupled CH_2-21 protons. The latter signals were downfield by 0.31–0.40 ppm compared to those in **2**, which is consistent with esterification of the hydroxyl group at C-21 (1). This is also borne out by the ^{13}C-nmr spectrum which shows a downfield shift of 1.09 ppm for C-21. The other signals are very similar to those of **2**. Complete assignments for the ^{1}H- and ^{13}C-nmr chemical shifts are given in the Experimental; they were determined by means of COSY and HETCOR spectra, respectively. The hrms gave an exact mass of *m/z* 423.1885 (calcd 423.1893), which is consistent with the formula $C_{21}H_{29}NO_8$.

Preparation of **1** was accomplished by coupling **2** with HOAc by the use of carbonyl diimidazole (CDI), giving a 62% isolated yield. The properties of natural **1** were identical to those of synthetic **1** by direct comparison (mp, tlc, H nmr, and ms).

Acetylanonamine [**1**] is a new addition to the list of over a dozen known acetyl derivatives of the otonecine-based pyrrolizidine alkaloids (2). Among

others in this list are ligularizine (3), florosenine (4), clivorine (5), acetylcrotaverrine (6), and acetylsenkirkine (7).

EXPERIMENTAL

GENERAL EXPERIMENTAL PROCEDURES.—Cc was performed using neutral, activity II, Al_2O_3 (70–230 mesh, ASTM). Tlc was performed on EM Al_2O_3 150F-254 plates developed in 2–5% MeOH in $CHCl_3$. Nmr spectra were run on a Varian XL-400 spectrometer operating at 399.934 MHz (^1H) and 100.575 MHz (^{13}C) in $CDCl_3$. Chemical shifts are reported relative to residual $CHCl_3$ (7.24 ppm) for ^1H and to $CDCl_3$ (77.0 ppm) for ^{13}C. HETCOR spectra were obtained as previously described (1). Mp's were taken on a Thomas Kofler micro hot stage and uncorrected. Optical rotations were measured on a JASCO DIP 360 polarimeter. Ir spectra were obtained on a Beckman 4240 IR spectrometer. The uv spectrum was measured on an HP 8451 A Diode Array Spectrophotometer.

PLANT MATERIAL.—*S. anonymus* was collected in May 1987 along the edges of a highway in North Atlanta, Georgia. A voucher specimen is on deposit at the Herbarium in the School of Chemistry and Biochemistry, Georgia Institute of Technology.

ISOLATION AND SEPARATION OF THE ALKALOID FRACTION.—Air-dried, finely cut, whole plant material (2.5 kg) was exhaustively extracted with 95% EtOH. The concentrated EtOH extract (400 g) was dissolved in 2 N H_2SO_4 and reduced with Zn overnight. Workup of the reaction mixture yielded 2.0 g of a crude alkaloid fraction. This was chromatographed on neutral Al_2O_3 (95 g, activity II) using 0–20% MeOH in $CHCl_3$ as eluent, collecting 10-ml fractions. Monitoring by tlc and ^1H-nmr analyses, the following alkaloids were obtained: from fractions 16–18 senecionine and integerrimine (100 mg, 2:1 ratio); from fractions 22–32 senkirkine and neosenkirkine (490 mg, 3:2 ratio), from fractions 33–35 otosenine (70 mg), from fractions 36–39 acetylanonamine, retrorsine, and usaramine (63 mg), from fractions 40–47 retrorsine and usaramine (20 mg, 19:1 ratio), and from fractions 48–67 anonamine (105 mg). A pool of fractions 36–39 was rechromatographed on Al_2O_3 (1.1 g, activity II, neutral) packed in hexane and eluting successively with 20 ml each of the following: 90% $CHCl_3$ in hexane, $CHCl_3$, 2% MeOH in $CHCl_3$, and 5% MeOH in $CHCl_3$. Fractions of 3.5 ml volume were collected. Fractions 4–7 gave acetylanonamine [**1**] (7.5 mg), while fractions 9–21 yielded a mixture of retrorsine and usaramine (45 mg; 6:1 ratio).

ACETYLANONAMINE.—Mp 124–125; $[\alpha]_D^{25.1}$ +17.99° (c = 0.91, $CHCl_3$); λ max 242 (log ε = 3.61); ir ($CHCl_3$, cm^{-1}) 3680 (w, free OH), 3600–3200 (b, hydrogen-bonded OH), 1745, 1725, 1605, 1450, 1262–1175, 1100, 1020; eims *m/e* (%) $[M]^+$ 423 (3.2), 324 (17.4), 308 (13.2), 307 (12.8), 249 (16.0), 248 (100), 169 (40.3), 168 (37), 59 (26.0), 151 (57.6), 123 (33.9), 122 (29), 110 (46.1); cims $[MH]^+$424 (100); exact mass calcd for $C_{21}H_{29}NO_8$, 423.1893, found 423.1885; ^1H nmr ($CDCl_3$, 400 MHz) δ 6.09 (1H, t, J = 2.3 Hz, H-2), 3.32 (1H, br d, J = 18 Hz, H-3α), 3.16 (1H, ddd, J = 18, 2.6, 2.3 Hz, H-3β), 2.76 (1H, ddd, J = 12.7, 5.7, 4.2 Hz, H-5α), 2.65 (1H, ddd, J = 12.7, 12.0, 4.2 Hz, H-5β), 2.46 (1H, dddd, J = 14.4, 12.0, 5.7, 3.2 Hz, H-6α), 2.28 (1H, dq, J = 14.4, 4.2 Hz, H-6β), 4.92 (1H, dd, J = 4.4, 3.2 Hz, H-7), 5.32 (1H, d, J = 11.4 Hz, H-9α), 4.38 (1H, br d, J = 11.4 Hz, H-9β), 1.76 (1H, ddq, J = 11.0, 2.5, 7.1 Hz, H-13), 2.12 (1H, dd, J = 14.0, 11.0 Hz, H-14α), 2.04 (1H, dd, J = 14.0, 2.5 Hz, H-14β), 1.27 (3H, s, H-18), 0.84 (3H, d, J = 7.1 Hz, H-19), 6.54 (1H, t, J = 6.8 Hz, H-20), 4.71 (1H, dd, J = 14.5, 6.8 Hz, H-21a), 4.60 (1H, dd, J = 14.5, 6.8 Hz, H-21b), 2.04 (3H, s, H-22), 2.01 (3H, s, H-24); ^{13}C nmr ($CDCl_3$, 100 MHz) δ134.44 (C-1), 137.35 (C-2), 57.89 (C-3), 52.72 (C-5), 34.76 (C-6), 79.04 (C-7), 64.47 (C-9), 177.58 (C-11), 76.09 (C-12), 38.53 (C-13), 29.91 (C-14), 133.91 (C-15), 166.53 (C-16), 24.51 (C-18), 11.27 (C-19), 135.23 (C-20), 60.37 (C-21), 40.58 (C-22), 20.41 (C-24).

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