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RANKINIDINE, A NEW INDOLE ALKALOID FROM *GELSEMIUM RANKINII*

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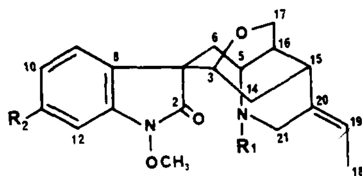
ABSTRACT.—A new oxindole alkaloid, rankinidine (**1**), has been isolated from the MeOH extract of the stem of *Gelsemium rankinii*. Its structure was elucidated by comparison with an analog, humantenirine (**3**), which also occurred in this plant.

Gelsemium rankinii Small (Loganiaceae) is a rare species native to the southeastern United States (1), which, until we recently reported (2) the isolation of a new oxindole alkaloid, 21-oxogelsevirine, was previously uninvestigated. Continued fractionation has led to the isolation and structure elucidation of another new oxindole alkaloid, rankinidine (**1**).

Rankinidine (**1**) was obtained as white needle crystals, $[\alpha]^{20°}D$ -126 (*c* 0.07, MeOH), decomposing quite rapidly to an orange brown amorphous gum, even at 5°. Its ir spectrum showed absorptions at 3300, 1722, 1716, 1698, 1466, and 753 cm^{-1}, and uv absorptions were noted at 217 and 256 nm revealing the characteristic oxindole alkaloid nucleus (3,4). The mass spectrum of compound **1** exhibited a molecular ion peak at 340, the facile loss of a methoxy group from the molecular ion, and an ion at *m/z* 164 ($M^{+\cdot}-176$), due to the loss of the aromatic portion. Such a fragmentation pattern was in agreement with that of humantenine (**2**), which exhibited an additional ion involving the loss of an *N*-methyl group.

Humantenirine (**3**) and humantenine (**2**) were both recently isolated from a Chinese *Gelsemium* species (*G. elegans*). They possess a different carbon framework than either gelsemine or gelsedine, and this was established for **2** through X-ray analysis (5,6).



	R_1	R_2
1	H	H
2	CH_3	H
3	H	OCH_3

Comparison of the ^{1}H-nmr spectrum of **1** with that reported for **2** indicated a close agreement but that **1** lacked an N-CH_3 group at 2.34 ppm. High resolution nmr (360 MHz), however, did provide an unambiguous assignment for H-21, H-6, H-14, and H-16 which were not identified in the original reports.

The high-field ^{1}H nmr of **3**, which is also present in *G. rankinii*, showed three aromatic protons at 7.30, 6.62, and 6.56 ppm for H-9, H-10, and H-12, respectively. A methoxy group at 3.83 ppm displayed the nOe with H-10 and H-12, establishing substitution at C-11 of the aromatic nucleus. From the homonuclear COSY spectrum, two H-21 protons at 3.87 and 3.32 ppm were correlated to H-19 and 5.23 ppm and H-18 at 1.59 ppm, respectively, and the signal at 3.32 ppm displayed a small coupling ($J=1.1$ Hz) in addition to geminal coupling ($J=16.8$ Hz). This proton was assigned to H-21α due to the long range coupling with the olefinic H-19 and a small **W** coupling

with H-15, as shown in the COSY spectrum. The assignments of H-17α at 4.29 ppm and H-17β at 4.02 ppm were in accordance with the observation that only H-17β was coupled with H-16 at 2.20 ppm. On the other hand, H-17α was the only proton exhibiting a nOe effect with H-6β at 2.30 ppm; consequently, the signal at 2.18 ppm was assigned to H-6α.

The limited sample of rankinidine available prevented an examination of its COSY spectrum. However, unambiguous assignment proton assignments could be made through a comparison with the assigned spectrum of humantenirine as shown in Table 1.

TABLE 1. ^{1}H-nmr Spectral Data of Rankinidine (**1**) and Humantenirine (**3**)[a]

Proton	Compounds	
	1[b]	**3**
3	3.56, d, 7.7	3.52, d, 8.4
5	3.84, m	3.68, m
6α	2.19, dd, 3.3, 15.3	2.18, dd, 3.3, 15.3
6β	2.30, dd, 3.3, 15.3	2.30, dd, 3.2, 15.6
9	7.42, d, 7.4	7.30, dd, 0.8, 8.4
10	7.14, t, 7.4	6.62, dd, 1.6, 8.4
11	7.41, t, 7.4	—
12	6.98, d, 7.4	6.56, d, 1.6
14α	2.38, dd, 7.0, 13.7	2.42, dd, 7.3, 15.6
14β	2.30, dd, 7.7, 13.7	2.30, dd, 8.4, 15.6
15	2.64, m	2.60, m
16	2.20, m	2.20, m
17α	4.33, d, 10.6	4.29, d, 10.5
17β	4.05, dd, 4.3, 10.6	4.03, dd, 4.2, 10.5
18	1.61, d, 6.8	1.59, d, 6.8
19	5.28, q, 6.8	5.23, q, 7.0
21α	3.37, dd, 2.7, 16.2	3.32, dd, 1.1, 16.8
21β	3.93, d, 16.2	3.87, d, 16.8
Ar-OCH_3	—	3.83, s
N-OCH_3	4.00, s	3.98, s

[a]Recorded at 360 MHz in $CDCl_3$.
[b]Chemical shift in ppm; multiplicity; *J* in Hz.

Humantenirine and humantenine were isolated from both American *Gelsemium* species, i.e., *G. sempervirens* and *G. rankinii*. Rankinidine was obtained from *G. rankinii*, but not from *G. sempervirens*. Because of the instability of both rankinidine and humantenirine, their ^{13}C-nmr spectra were not available for examination.

EXPERIMENTAL

GENERAL EXPERIMENTAL PROCEDURES.—The melting point was determined by means of a Kofler hotplate and is uncorrected. Uv spectra were obtained with a Beckman model DU-7 spectrophotometer. The ir spectrum was determined on a Nicolet MX-1 interferometer. ^{1}H-nmr spectra were recorded on a Nicolet NMC 360 (360 MHz) using $CDCl_3$ as a solvent and TMS as an internal standard. The mass spectra were obtained with a Finnigan/MAT 112S double focussing mass spectrometer operating at 70 eV. The optical rotation was measured with a Perkin-Elmer, Model 241 polarimeter. Silica gel for chromatography was purchased from E. Merck, Darmstadt, W. Germany, and preparative tlc plates were from Analtech, Newark, Delaware.

PLANT MATERIAL.—Dried stem matrial of *G. rankinii* was collected in the spring of 1984 and identified by Dr. M. Garland. Voucher specimens were deposited in the Field Museum of Natural History, Chicago, Illinois.

EXTRACTION AND PURIFICATION.—Chopped stems of *G. rankinii* (300 g) were percolated with MeOH at room temperature for 2 days, five times. The combined MeOH extracts were concentrated in vacuo at 30° to afford a thick dark syrup (ca. 35 g), which was dissolved in 2% citric acid and partitioned against Et_2O. After removal of the Et_2O extract, the acidic layer was basified with aqueous NH_3 to pH 8.0 and extracted extensively with EtOAc until a Dragendorff test was negative. The process was completed within the same day to avoid decomposition. The total alkaloid extract (2.5 g) was subjected to silica gel column chromatography eluting with mixtures of petroleum ether, EtOAc, and MeOH of increasing polarity.

ISOLATION OF RANKINIDINE (**1**).—The petroleum ether-EtOAc-MeOH (60:40:3) eluent (0.12 g) from the column chromatography was subjected to repeated preparative tlc using petroleum ether-C_6H_6-EtOAc-diethyl amine (25:10:10:4) as a solvent system, and a purple band under uv light at Rf 0.25 was eluted with Me_2CO to afford white needles of **1** (6 mg, became less than 2 mg after 2 weeks in cold room), mp 175-178° (Me_2CO); $[\alpha]^{20}D$ −126 (*c* 0.07, MeOH); uv λ max (MeOH) 217 (log ε 4.02) and 256 (3.75); ir ν max (AgCl) 3300, 1722, 1716, 1698, 1466, 753 cm^{-1}; ^1H nmr, see table 1; ms *m/z* (rel. int.) 340 (M^+, 26), 325 (5), 309 (20), 164 (29), 149 (21), 108 (100).

ISOLATION OF HUMANTENIRINE (**3**).—From the same eluent as compound **1** and the same preparative tlc process, compound **3** was isolated at Rf 0.20 as white needles (1 mg), mp 167-170° (Me_2CO); $[\alpha]^{20}D$ −135 (*c* 0.56, MeOH); uv λ max (MeOH) 226 (log ε 4.24, 261 (3.59); ir ν max (AgCl) 1722, 1717, 1632, 1622, 1467, 1462, 1221, 1215, 758 cm^{-1}; ^1H nmr, see table 1; ms *m/z* (rel. int.) 370 (M^+, 33), 355 (1), 339 (20), 164 (100), 108 (90). The ^1H nmr study was made possible through the availability of **3** from *G. sempervirens*.

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