A 1,4-Disubstituted Quinolizidine from a Madagascan Mantelline Frog (*Mantella*)

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A major alkaloid, **217A**, in skin extracts of a mantelline frog (*Mantella baroni*) was isolated by HPLC and the structure defined by ^{1}H-NMR spectral analysis as (1*R*,4*S*,10*S*)- or (1*R*,4*R*,10*R*)-1-methyl-4-(*Z*)-(1-pent-2-en-4-ynyl) quinolizidine (**1**). Four other alkaloids—**207I** (**2**), **231A** (**3**), **233A** (**4**), and **235E′** (**5**)—detected in frog skin extracts are proposed to be 1,4-disubstituted quinolizidines based on diagnostic mass and FTIR spectra.

The quinolizidine moiety is incorporated into an incredible array of complex plant alkaloids,[1] but relatively few quinolizidines (1-azabicyclo[4.4.0]decanes) *per se* have been found.[2] These few include, in addition to a number of 1-substituted or 1,3-disubstituted quinolizidines related in structure to lupinine (Papilionoideae), the 1-methylquinolizidin-3-ones myrtine and epimyrtine (Ericaceae); the 4,6-disubstituted quinolizidine porantherilidine (Euphorbiaceae); a variety of 1-aryl-3-hydroxyquinolizidines, such as lasubine (Lythraceae); 3,4-dehydro-3,4-diaryl quinolizidines, such as julandine (Urticaceae); and 1,7-dimethyl-4-furylquinolizidines (nuphar alkaloids), such as nupharidine (Nymphaceae). Castoramine, an alkaloid isolated from the scent gland of the Canadian beaver, *Castor fiber*,[3] is closely related in structure to the nupharidine class of plant alkaloids and may be of dietary origin.[2] Bisquinolizidine alkaloids occur in marine sponges.[2] Quinolizidine alkaloids also have been found in skin extracts of certain frogs.[4] One class, the homopumiliotoxins (typified by **223G**, whose 1-methyl-1-hydroxy-3-alkylidenequinolizidine structure has been defined by NMR spectral analysis),[5] is present as minor alkaloids in skin extracts of dendrobatid and mantelline frogs and bufonid toads.[4]

In addition, 1,4-disubstituted quinolizidines have been proposed as a class of amphibian skin alkaloids, based on GC−MS and GC−FTIR characterization only.[4,6,7] Such putative 1,4-disubstituted quinolizidines occur in dendrobatid frogs of the genera *Dendrobates*, *Minyobates*, and *Epipedobates*;[4] in mantelline frogs of genus *Mantella*,[6] and in bufonid toads of the genus *Melanophryniscus*.[7] 1,4-Disubstituted quinolizidines are analogous to the 5,8-disubstituted indolizidines, a major class of alkaloids in amphibian skin extracts, members of which were first characterized by NMR spectral analyses[5,8] and structures later confirmed by synthesis.[9−11] All of the so-called dendrobatid alkaloids detected in amphibian skin extracts[4] may prove to be of dietary origin.[12] Alkaloids from frog skin that in all likelihood have been sequestered from ant prey[12] include 2,5-disubstituted pyrrolidines; 2,6-disubstituted piperidines; 3,5-disubstituted pyrrolizidines, and 3,5-disubstituted indolizidines.

None of the proposed 1,4-dialkyl-substituted quinolizidines from amphibian skin extracts had been isolated previously in quantities sufficient for ^{1}H-NMR characterization. Thus, structures and stereochemistry were only inferred, not rigorously proven, for all of the alkaloids of this putative class. In 1993, about 20 frog-skin alkaloids were tentatively assigned to the quinolizidine class,[4] but it is now obvious that several will have to be reassigned to the indolizidine class (see below). Five alkaloids, namely **217A** (Figure 1, **1**), **207I**, **231A**, **233A**, and **235E′** (Figure 2, **2**−**5**), were characterized as 1,4-disubstituted quinolizidines by FTIR spectral analysis.[6,7] The FTIR spectra of **217A** and **235E′** have been published.[6,7] The (4,10-*Z*)-relationships for these alkaloids were proposed based upon the presence of a significant Bohlmann band in their FTIR spectra[6] that was usually broader and somewhat less intense than the Bohlmann band seen in analogous (5,9-*Z*)-5,8-disubstituted indolizidines. The configuration at C-1 remained unknown. The mass spectra of these five quinolizidines exhibited major fragment ions, due to α-cleavage at C-4 and a minor fragment ion at *m*/*z* 110 ($C_7H_{12}N^+$, 20−30% of the base peak intensity on an ion trap mass detector), analogous to the ion at *m*/*z* 96 ($C_6H_{10}N^+$) that is diagnostic for the 5,8-disubstituted indolizidines and is postulated to arise from a retro-Diels−Alder (RDA) rearrangement (see Scheme 1).

The 15 other alkaloids, tentatively placed in the 1,4-disubstituted quinolizidine class,[4] showed base peaks at *m*/*z* 152, 166, or 180, and in most cases, also exhibited a significant fragment ion (∼20%) at *m*/*z* 110. However, further FTIR analyses showed either a sharp Bohlmann band or no Bohlmann band for some of these alkaloids. Those showing a sharp Bohlmann band are probably 5,6,8-trisubstituted indolizidines with (5,9-*Z*)-configurations and with a methyl substituent at the 6-position. These include alkaloids **231B** and **273A**. The 6-methyl substituent would account for the presence of a *m*/*z* 110 fragment ion after RDA fragmentation (see Scheme 1). Alkaloid **223A**, previously tentatively assigned to the quinolizidine class,[4] has a sharp Bohlmann band and

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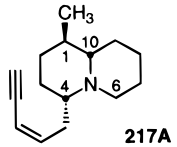

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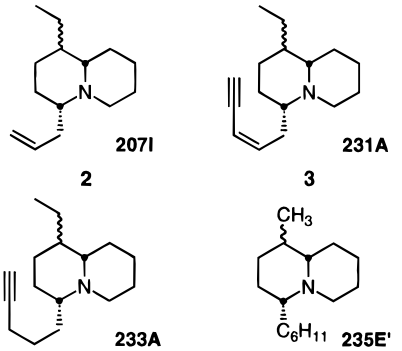
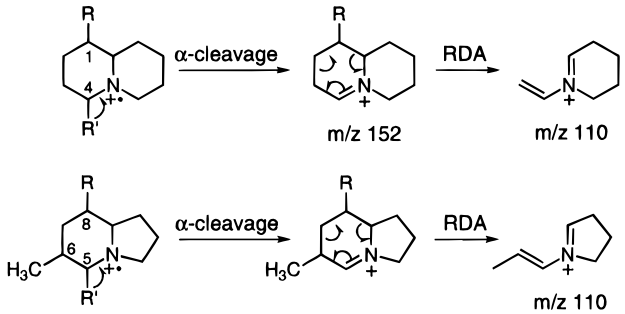
Figure 1. Structure of quinolizidine **217A**. Absolute stereochemistry unknown.



2 3 4 5

Figure 2. Tentative 1,4-disubstituted quinolizidine structures based on MS and FTIR spectra.

Scheme 1. Mass fragmentation pathways for 1,4-disubstituted quinolizidines and 6-methyl-5,8-disubstituted indolizidines



shows an ion derived by RDA fragmentation at *m*/*z* 124. It has now been shown to be a 6,8-diethyl-5-propyl indolizidine by NMR spectral analysis.[13] Alkaloids **249C** and **263A**, which show no significant Bohlmann bands, could belong either to the 1,4-disubstituted quinolizidine class or to the 5,6,8-trisubstituted indolizidine class with (4,10-*E*)- or (5,9-*E*)-configurations, respectively, and require further investigation. Alkaloids **275A**, **277A**, and **289A**, formerly tentatively assigned to the 1,4-disubstituted quinolizidine class,[4] but having weak Bohlmann bands and lacking the significant fragment ion at *m*/*z* 110 also require further investigation. FTIR spectra have not been obtained for the remaining eight alkaloids previously tentatively assigned to the 1,4-disubstituted quinolizidine class.[4]

One of the putative 1,4-disubstituted quinolizidines, namely **217A**, whose partial structure was based on mass spectrometry and FTIR spectroscopy,[6] has now been purified and its proposed structure and stereochemistry confirmed by NMR studies. In addition, a (1,10-*E*)-relationship of the hydrogens at C-1 and C-10 has been established as shown in **1**. The absolute configuration and optical rotation are unknown. The tentative structures of the four 1,4-disubstituted quinolizidines (**207I**, **231A**, **233A**, **235E′**) from amphibian skin, which are mentioned above, and whose relationship to **217A** is based on close similarities in their mass spectra and FTIR spectra, are also shown (**2**−**5**). The configuration at C-1 is unknown in these alkaloids. The position and configuration of the nonterminal double bond in **5** is unknown.

Alkaloid fractions from skin extracts of Madagascan mantelline frogs of the genus *Mantella* contain a wide range of alkaloids including pumiliotoxins, allopumiliotoxins, 3,5-disubstituted- and 5,8-disubstituted-indolizidines, and the putative 1,4-disubstituted quinolizidines.[6,14] All populations of one stream-side species, *Mantella baroni* Boulenger, 1888 (Ranidae) (*M. madagascariensis* autorum) had large amounts of the proposed quinolizidine **217A**.[14] An alkaloid fraction from skin extracts of one population of *Mantella baroni* showed, on GC−MS analysis, mainly quinolizidine **217A** along with a minor diastereomer and a variety of other alkaloids. Approximately 1 mg of alkaloid **217A** homogeneous by GC−MS, was purified by HPLC.

To remove small amounts of waxlike, nonvolatile, neutral material detected as impurities in a $CDCl_3$ ^{1}H-NMR spectrum, the $CDCl_3$ solution of **217A** was concentrated to dryness with N_2 and the ^{1}H-NMR spectrum tried in D_2O containing DCl. The ^{1}H-NMR of **217A**·DCl was now free of any major impurity; however, four signals at ca. δ 2.85 from the two H-12 allylic protons and two CHN protons overlapped. One of these (H-4) was critical to the structure elucidation of **217A**. These signals separated better when D_2O was replaced with Me_2CO-d_6, and consequently, all the ^{1}H-NMR spectral data reported here (Tables 1 and 2) for **217A**·DCl are reported in Me_2CO-d_6. Chemical shifts, assigned through a 2D-^{1}H−COSY spectrum, were further confirmed with 1D-decoupling experiments, which were also used to determine coupling constants reported in Table 1.

The signals at δ 6.32 (ddd, J = 10.8, 7.3, 7.0 Hz) and δ 5.64 (dddd ~ dq, J = 10.8, 2.4, 1.8, 1.5 Hz) were assigned to the olefinic protons H-13 and H-14, respectively. The coupling constant (10.8 Hz) between H-13 and H-14 indicated a *Z*-olefinic stereochemistry. H-14 showed long-range coupling with the two allylic protons at H-12. Cross peaks between the H-12 protons and H-14 were seen in RELAYH = 1 experiments. The signal for the conjugated acetylenic proton, H-16, appeared at δ 3.70 (d, 2.4 Hz). The chemical shift value for this signal seems anomalous, as it is generally seen at δ 3.10 in $CDCl_3$. The downfield shift of this signal may be due to the solvent effect of Me_2CO-d_6 on the DCl salt of **217A**. The H-16 signal integrated for less than one proton, since H-16 had partially exchanged with deuterium on exposure to D_2O−DCl. We had observed earlier for another frog skin alkaloid **275A**, of undetermined structure, but having a terminal triple bond, that it had completely exchanged the acetylenic hydrogen with deuterium when its DCl salt was left in D_2O for roughly one week. A cross peak indicating long-range coupling between H-16 and H-14 was seen clearly in the COSY spectrum of the DCl salt of **217A**. Irradiation of the H-14 signal changed the doublet assigned to H-16 to a sharp singlet.

The two allylic H-12 protons were seen at δ 3.05 (m) and δ 2.89 (dddd, J = 14.8, 7.5, 7.3, 1.5 Hz). The chemical shift for allylic protons has been reported at δ 2.38 for histrionicotoxins[15] and at δ 2.45 for gephyrotoxins[16] as bases in $CDCl_3$. The H-12 protons of **217A** (**1**) were coupled with H-13, but the coupling constants

Table 1. ^{1}H-NMR Parameters for **217A**·DCl (Me_2CO-d_6, 500 MHz)[a]

				irradiation at		
proton	δ (ppm)	multiplicity	J (Hz)	signal containing proton	affects	removes
H-1	2.14−2.32			H-1	H-11 H_{ax}-2 **H_{eq}-2**, H_{eq}-3, H_{eq}-7, H_{eq}-8	medium *J* to s
H_{eq}-2	1.74−1.88			H_{eq}-2	**H-1**, **H_{ax}-3**, H_{ax}-7 H_{ax}-2	
H_{ax}-2	1.31	qd	12.6, 3.5	H_{ax}-2	**H_{eq}-2**, **H_{eq}-3**, H_{eq}-7, H_{eq}-8 **H-1**, **H_{ax}-3**, H_{ax}-7	
H_{eq}-3	1.74−1.88			H_{eq}-3	H-1, **H_{ax}-3**, H_{ax}-7 H_{ax}-2	
H_{ax}-3	2.14−2.32			H_{ax}-3	**H-4**/H-12a **H_{eq}-2**, **H_{eq}-3**, H_{eq}-7, H_{eq}-8 H_{ax}-2	
H-4	3.05			H-4	H-1, **H_{ax}-3**, H_{ax}-7 H_{eq}-2, **H_{eq}-3**, H_{eq}-7, H_{eq}-8 H-12b	
H_{eq}-6	3.79	dtt	11.9, 4.0, 1.8	H_{eq}-6	**H_{ax}-6**, H-10 H-1, H_{ax}-3, **H_{ax}-7** H_{eq}-2, H_{eq}-3, **H_{eq}-7**, H_{eq}-8	
H_{ax}-6	2.69					
H_{eq}-7	1.74−1.88			H_{eq}-7	H_{ax}-8 H-1, H_{ax}-3, **H_{ax}-7** H-10, **H_{ax}-6** H_{eq}-6	
H_{ax}-7	2.14−2.32			H_{ax}-7	H_{eq}-6 H-10, **H_{ax}-6** H_{eq}-2, H_{eq}-3, **H_{eq}-7**, **H_{eq}-8** H_{ax}-8	
H_{eq}-8	1.74−1.88			H_{eq}-8	H_{ax}-8 H-1, H_{ax}-3, **H_{ax}-7**	
H_{ax}-8	1.48	tq	13.2, 4.0	H_{ax}-8	H_{eq}-2, H_{eq}-3, **H_{eq}-7**, **H_{eq}-8** H-1, H_{ax}-3, **H_{ax}-7**	
H_{eq}-9	1.88−2.0					
H_{ax}-9	2.0−2.14			H_{ax}-9	**H-10**, H_{ax}-6 H_{eq}-2, H_{eq}-3, H_{eq}-7, **H_{eq}-8** H_{ax}-8 H_{eq}-9	
H-10	2.69					
H-11	0.94	d	6.6	H-11	H-1	
H-12a	3.05			H-12a	H-12b H-13	 medium *J* to dd
H-12b	2.89	dddd	14.8, 7.5, 7.3, 1.5	H-12b	**H-12a**, **H-4** H-13 H-14	 medium *J* to dd
H-13	6.32	ddd	10.8, 7.3, 7.0	H-13	H-14 **H-12a**, H-4 H-12b	large *J* to br s medium *J* to ddd
H-14	5.64	dddd	10.8, 2.4, 1.8, 1.5	H-14	H-16 H-13 **H-12a**, H-4 H-12b	small *J* to s large *J* to t small *J* to dt
H-16	3.70	d	2.4	H-16	H-14	

[a] For overlapping signals, we propose the inferred, most likely coupling by bold face.

could not be measured because the signals for H-12 and H-4 overlapped at δ 3.05.

The four protons (H-4, H_{eq}-6, H_{ax}-6, H-10) on carbons adjacent to the deuteronated N appeared with the allylic protons in the region between δ 2.6 and δ 3.82. Protons on carbons adjacent to N in another quinolizidine, deoxynupharidine, are in this region.[17] The H_{eq}-6 signal was observed at δ 3.79 (dtt, J = 11.9, 4.0, 1.8 Hz). Irradiation of the H_{eq}-7 and H_{eq}-8 signals between δ 1.74 to 1.88 transformed the signal for H_{eq}-6 from dtt to dd, revealing a geminal $J_{(6eq-6ax)}$ of 11.9 Hz and a small vicinal $J_{(6eq-7ax)}$ of 4.0 Hz. Thus, the signal for H_{eq}-6 requires three additional couplings: a vicinal coupling of 4.0 Hz with H_{eq}-7, a W-coupling[18] of 1.8 Hz with H_{eq}-8, and another 1.8 Hz coupling not explained. Because the COSY spectrum indicated that H_{eq}-6 was coupled with a two-proton signal at δ 2.69, H_{ax}-6 was assigned as one of these two protons. Irradiation of the H_{eq}-6 signal affected the signal at δ 2.69, further confirming the assignment of H_{ax}-6. The H-12 protons showed no connectivity with the δ 2.69 signal, consequently H-10 was assigned as the second proton of this signal, instead of H-4. The signal at δ 3.05, which included one H-12 proton, integrated for two protons, strongly suggesting that the other CH−N (H-4) also be assigned to this signal. COSY spectra are ambiguous on this point, because the strong cross peak observed between the two H-12s could include an H-4, H-12 cross peak in addition to that from the geminal coupling. A cross peak between H-4 and H_{ax}-3 was also observed in a COSY spectrum, but the cross peak for the coupling between H-4 and H_{eq}-3 was missing. This cross peak did appear, however, in a RELAYH = 1 spectrum where longer-range connectivities were observed. Thus, further evidence from the ^{1}H-NMR spectra for the (4,10-*Z*)-configuration, assigned to **217A**, based on Bohlmann

Table 2. Observed Connectivities in **217A** [**1**] as Determined with the RELAYH Method[a]

^{1}H signal	RELAY = 0 (COSY)	RELAY = 1 (selected cross peaks)
H-1	H_{ax}-6/**H-10**, **H_{eq}-2**/H_{eq}-3/H_{eq}-7/H_{eq}-8, H_{ax}-2, H-11	
H_{eq}-2	**H-1**/**H_{ax}-3**/H_{ax}-7, **H_{eq}-3**/H_{eq}-7/H_{eq}-8, H_{ax}-2	
H_{ax}-2	**H-1**/**H_{ax}-3**/H_{ax}-7, **H_{eq}-2**/**H_{eq}-3**/H_{eq}-7/H_{eq}-8	**H-4**/H-12a, H_{ax}-6/**H-10**, H-11
H_{eq}-3	H-1/**H_{ax}-3**/H_{ax}-7, **H_{eq}-2**/H_{eq}-7/H_{eq}-8, H_{ax}-2	**H-4**/H-12a
H_{ax}-3	**H-4**/H12a, **H_{eq}-2**/**H_{eq}-3**/H_{eq}-7/H_{eq}-8, H_{ax}-2	H-11
H-4	H-12b, H-1/**H_{ax}-3**/H_{ax}-7	H_{eq}-2/**H_{eq}-3**/H_{eq}-7/H_{eq}-8, H_{ax}-2, H-10/**H_{ax}-6**, H-11
H_{eq}-6	**H_{ax}-6**/H-10, H-1/H_{ax}-3/**H_{ax}-7**, H_{eq}-2/H_{eq}-3/**H_{eq}-7**/H_{eq}-8	
H_{ax}-6	H_{eq}-6, H-1/H_{ax}-3/**H_{ax}-7**, H_{eq}-2/H_{eq}-3/**H_{eq}-7**/H_{eq}-8	**H-4**/H-12a
H_{eq}-7	H_{eq}-6, **H_{ax}-6**/H-10, H-1/H_{ax}-3/**H_{ax}-7**, H_{eq}-2/H_{eq}-3/**H_{eq}-8**, H_{ax}-8	
H_{ax}-7	H_{eq}-6, **H_{ax}-6**/H-10, H_{eq}-2/H_{eq}-3/**H_{eq}-7**/**H_{eq}-8**	H_{ax}-8
H_{eq}-8	H-1/H_{ax}-3/**H_{ax}-7**, H_{eq}-2/H_{eq}-3/**H_{eq}-7**, **H_{ax}-8**, H_{ax}-9, H_{eq}-9	
H_{ax}-8	H_{eq}-2/H_{eq}-3/**H_{eq}-7**/**H_{eq}-8**, H_{ax}-9, H_{eq}-9	H-1/H_{ax}-3/**H_{ax}-7**
H_{eq}-9	**H-10**/H_{ax}-6, H_{eq}-2/H_{eq}-3/H_{eq}-7/**H_{eq}-8**, H_{ax}-8	
H_{ax}-9	**H-10**/H_{ax}-6, H_{eq}-2/H_{eq}-3/H_{eq}-7/**H_{eq}-8**, H_{ax}-8	
H-10	**H-1**/H_{ax}-3/H_{eq}-7, H_{ax}-9, H_{eq}-9	H-11, H_{ax}-2
H-11	**H-1**/H_{ax}-3/H_{ax}-7	**H-10**/H_{ax}-6, H_{ax}-2, **H-4**/H-12a, H-1/**H_{ax}-3**/H_{ax}-7
H-12a	H-13, H-12b	H-14
H-12b	H-13, **H-12a**/**H-4**	H-1/**H_{ax}-3**/H_{ax}-7, H-14
H-13	H-14, **H-12a**/H-4, H-12b	
H-14	H-13, H-16	**H-12a**/H-4, H-12b
H-16	H-14	

[a] For overlapping signals as indicated by a slash, we propose the inferred, most likely coupling by bold face.

bands in the FTIR,[6] was not forthcoming, since the multiplicity for H-4 or H-10 could not be determined. However, H_{ax}-2 showed a long-range coupling with H-4 and H-10, supporting an axial configuration for both H-4 and H-10. A long-range coupling between H_{ax}-6 and H-4 was also seen. A ^{1}H NMR spectrum of **217A** in C_6H_6-d_6 also failed to separate the H-4 and H-10 signals.

The signal due to the methyl group (C-11), seen at δ 0.94 (d, J = 6.6 Hz), permitted H-1 to be assigned to the signal at δ 2.14−2.32 on the basis of coupling seen in the COSY spectrum.

The H_{eq}-2 was assigned to the region of δ 1.74−1.88. The H_{ax}-2 signal was located upfield and well separated at δ 1.31 (qd, J = 12.6, 3.5 Hz). H_{ax}-2 exhibited three large Js and one small J as a quartet of doublets signal, but also showed a long-range coupling with H-11 on a RELAYH = 1 experiment. These coupling constants measured for H_{ax}-2 permitted the relative configuration at C-1 to be assigned. Three Js were assigned as follows: $J_{(2ax-3eq)}$ (small), $J_{(2eq-2ax)}$ (large, geminal), $J_{(2ax-3ax)}$ (large, vicinal). The remaining large coupling of H_{ax}-2 can only be that with H_{ax}-1. Thus, the H_{ax}-2 multiplicity showed that H-1 is axial; that is, **217A** has a (1,10-*E*)-relationship and CH_3-11 has an equatorial configuration. The relative configuration of H-1 is analogous to that seen for H-8 in 5,8-disubstituted indolizidines.

The signals for H_{ax}-3 and H_{ax}-7 were assigned to the region δ 2.14−2.32. Signals for H_{eq}-3, H_{eq}-7, and H_{eq}-8 appeared in the region δ 1.74−1.88. H_{ax}-8 was well separated at δ 1.48 (qt, J = 13.2, 4.0 Hz) and showed three large couplings, one large geminal, $J_{(8eq-8ax)}$, and two large vicinal couplings, $J_{(8ax-9ax)}$ and $J_{(7ax-8ax)}$, and two small vicinal couplings, $J_{(8ax-9eq)}$ and $J_{(7eq-8ax)}$. The cross peak for the large vicinal coupling between H_{ax}-8 and H_{ax}-7 was not seen in the COSY spectrum, but was present in a RELAYH = 1 spectrum. The signal for H_{eq}-9 was assigned to the region δ 1.88−2.0, and the signal for H_{ax}-9, hidden by the Me_2CO-d_6, was assigned at δ 2.0−2.14, based on a coupling seen in the COSY spectrum. The geminal coupling between H_{ax}-9 and H_{eq}-9 was not seen because the cross peak was hidden beneath the solvent signal.

Experimental Section

General Experimental Procedures. GC−MS analysis used an RTX-5 fused silica-bonded capillary column (Restek, 30 m × 0.25 mm i.d.) in a Varian model 3400 gas chromatograph, programmed from 100 to 280 °C at a rate of 10°/min, and interfaced with a Finnigan ion trap Model 800 to obtain EIMS or CIMS with either NH_3 or ND_3 as reagent gas. GC−MS−FTIR spectra were obtained using a Hewlett-Packard Model 5890 gas chromatograph having a 25-m × 0.32-mm HP-5 (polymer of 5% diphenylsiloxane and 95% dimethylsiloxane) fused silica-bonded capillary column with the same program as used above for the GC−MS analysis, and interfaced with a Hewlett-Packard Model 5971 series mass selective detector and a Hewlett-Packard Model 5965B IR instrument with a narrow-band (4000−750 cm^{-1}) detector. A Hewlett-Packard MS/IR ChemStation (DOS-based) was used to generate the chromatograms and the EIMS and FTIR spectra of GC peaks. HRMS used a JEOL SX 102 instrument fitted with a 15-m × 0.20-mm HP-5 column. 1D ^{1}H-NMR and 2D ^{1}H-NMR−COSY spectra were measured with a Varian VXR-500 spectrometer.

Biological Material and Extraction. An alkaloid fraction was prepared in the usual manner[6] from MeOH extracts of 15 skins of the Madagascan frog, *Mantella baroni* obtained near the town of Andasibe in January 1993. Voucher specimens are in collections of the American Museum of Natural History, New York. On GC−MS, the alkaloid fraction showed mainly **217A** with a trace amount of a diastereomer at a slightly longer retention time. There were several minor alkaloids, including another quinolizidine, **231A**, as well as 3,5-disubstituted indolizidines, pumiliotoxins, and allopumiliotoxins. The alkaloid fraction was concentrated to approximately 125 μL, and five portions of 25 μL each were subjected to HPLC. A reversed-phase Beckman/Altex column (ultrasphere ODS, 80A, C-18 standard column with particle size of 5 μm, 4.6 mm i.d., and length 250 mm) was used with a linear gradient of $CH_3COOH-CH_3CN-H_2O$ from a ratio of 2:6:92 to a ratio of 2:68:30 programmed from 5 to 25 min. Fractions of 1 mL each were collected, concentrated, dissolved in

MeOH and subjected to GC−MS analysis. Fraction 14 showed nearly pure **217A** with a trace amount of the diastereomer. The fractions containing nearly pure **217A** from each of the five runs were pooled and used for the ^{1}H-NMR studies.

The properties of quinolizidine **217A** are as follows, with the molecular formula determined by HRMS, the EIMS with intensities relative to the base peak set equal to 100, the number of exchangeable hydrogens expressed as 0D, 1D, etc., the hydrogenation data as H_0, H_2, and so forth, derivatives and vapor-phase FTIR absorptions with intensities relative to the maximum absorbance set equal to 100. ^{1}H-NMR data are in Tables 1 and 2.

Quinolizidine 217A (**1**): $C_{15}H_{23}N$; EIMS *m*/*z* 217 (2), 152 (100), 110 (16); 0D; H_6 derivative; FTIR 3327 (19), 3039 (6), 2981 (23), 2937 (100), 2863 (29), 2788 (21), 2100 (2), 1451 (11), 1382 (7), 1339 (8), 1267 (8), 1209 (11), 1105 (11) cm^{-1}. The FTIR spectrum of quinolizidine **217A** has been reported.[6] A minor diastereomer emerged after **217A** (**1**) on GC and was characterized as follows: EIMS *m*/*z* 217 (2), 152 (100), 110 (18).

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