for 1 h, cooled, diluted with water, and extracted with ethyl ether. The solvent was evaporated, and the residue was then dissolved in methanol (25 mL); 20% sulfuric acid solution (15 mL) was added, and the reaction solution was stirred for 1 h at room temperature. After extraction, purification of the crude material by elution with a mixture of benzene and ethyl ether (7:3), on a column of silica gel, gave a semicrystalline yellow product (500 mg), which was recrystallized from water to give 373 mg (37%) of compound **1** as a stable white crystalline solid: mp 64–65 °C (lit.[8] mp 68.5 °C); IR (KBr) 3400, 1600, 1370, 1070, 1035, 990, 955 cm^{-1}; ^1H NMR ($CDCl_3$) δ 5.45 (s, 1 H), 4.3–3.6 (m, 1 H), 2.08 (s, 3 H), 1.67 (s, 3 H), 1.17 (s, 3 H), 1.05 (s, 3 H); ^{13}C NMR ($CDCl_3$) δ 193.5 (s), 189.3 (s), 137.5 (s), 130.1 (s), 103.4 (d), 64.1 (d), 47.9 (t), 41.1 (t), 36.3 (s), 29.6 (q), 28.9 (q), 25.7 (q), 20.9 (q). Anal. Calcd for $C_{13}H_{20}O_3$: C, 69.61; H, 8.99. Found: C, 69.71; H, 9.01.

e. 1-(2,6,6-Trimethyl-1,4-dihydroxycyclohexyl)-1-butyn-3-one (15). To a solution of pure isomer **2a** (250 mg, 1.2 mmol) in 85% formic acid (5 mL) was added a solution of mercuric sulfate[7] (12 mL). After 5 min of stirring at room temperature, the solution was refluxed for 2 h. After separation of the precipitated metallic mercury, the reaction mixture was extracted and hydrolyzed as above. The residue obtained was then purified by elution with *n*-hexane–ethyl acetate (1:1) on preparative TLC to give 176 mg (65%) of compound **15**: IR ($CHCl_3$) 3450, 2950, 2200, 1665, 1600, 1460, 1360, 1230, 1035, 965, 790 cm^{-1}; ^1H NMR ($CDCl_3$) δ 4.10 (m, 1 H), 2.38 (s, 3 H), 2.4–1.3 (m, 5 H), 1.25 (s, 3 H), 1.15 (s, 3 H), 1.10 (d, J = 7 Hz, 3 H); ^{13}C NMR ($CDCl_3$) δ 184.2 (s), 86.8 (s), 79.0 (s), 77.3 (s), 66.5 (d), 44.2 (t), 39.9 (t), 39.0 (s), 32.9 (d), 32.2 (q), 27.4 (q), 23.0 (q), 16.0 (q); mass spectrum, *m/e* (relative intensity) 224 (M^+, 1), 209 (1), 206 (6), 191 (5), 96 (61), 43 (100).

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Alkaloids from *Delphinium geyeri*. Three New C_{20}-Diterpenoid Alkaloids

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Three new C_{20}-diterpenoid alkaloids related to hetisinone were isolated from *Delphinium geyeri* (Ranunculaceae) and their structures determined by spectroscopic methods. The major new alkaloid, dubbed geyerine, was found to be 6-hydroxy-11-*O*-(2-methylbutanoyl)hetisinone. The two minor new alkaloids were 6-hydroxy-13-*O*-acetylhetisinone (geyeridine) and 3-acetoxy-6-hydroxy-11-*O*-(2-methylbutanoyl)hetisine (geyerinine). In addition to these substances, the known C_{19}-diterpenoid alkaloids dictyocarpine, glaucenine, delcosine, browniine, 14-acetyldelcosine, 14-acetylbrowniine, 14-dehydrobrowniine, and delphatine were isolated. The total alkaloid mixture was shown to have feeding deterrent activity against the migratory grasshopper, but results on some of the purified alkaloids were equivocal.

Delphinium geyeri, a Colorado larkspur, has been known for some time[1] to be toxic to range animals. Three alkaloids were isolated[1] as Hg complexes, but no structural characterizations were carried out. Considerable data are available[2,3] on the toxicity and biological activity of alkaloids from other Delphinium species. A grasshopper (*Melanoplus sanguinipes*) feeding deterrent screening[4] of 5-g range plant extracts showed the highest activity for *D. geyeri* and field observations[4,5] indicated little, if any, plant consumption by herbivorous insects. This research was undertaken to isolate and characterize the alkaloids of *D. geyeri* and to determine if they were responsible for the insect feeding deterrence.

Results and Discussion

A total of 11 alkaloids were isolated and characterized. Eight of these were known C_{19}-diterpenoid alkaloids, while three were C_{20}-diterpenoid alkaloids, all new. Table I lists the isolated alkaloids in an approximate order of decreasing concentration. Most of the known alkaloids were identified by spectral and TLC comparison with standard samples. Standards were not available for a few and the structures of these rest on spectral comparisons with the literature data. The new C_{20} alkaloids were identified as follows.

Table I. Relative Abundance of the Alkaloids Isolated from *D. geyeri*[a]

alkaloid	occurrence	type
browniine	major	C_{19}
14-acetylbrowniine	major	C_{19}
geyerine (1)	major	C_{20}
14-dehydrobrowniine	major	C_{19}
14-acetyldelcosine	moderate	C_{19}
delcosine	moderate	C_{19}
delphatine	minor	C_{19}
dictyocarpine	minor	C_{19}
geyeridine (2)	minor	C_{20}
geyerinine (3)	minor	C_{20}
glaucenine	minor	C_{19}

[a] Listed from top to bottom as most to least abundant.

The major new alkaloid, dubbed geyerine, was shown by HREIMS to have the molecular formula $C_{25}H_{33}NO_5$ (M_r

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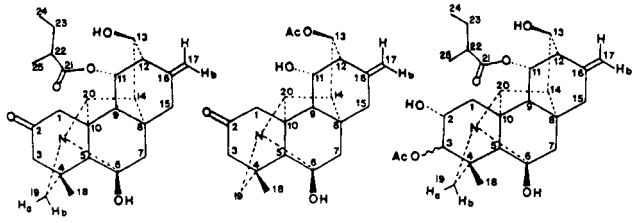
Table II. ^{13}C NMR Assignments for the C_{20}-Diterpene Alkaloids of *D. geyeri*



1 2 3

C	^{13}C NMR, ppm (mult)		
	geyerine (1)	geyeridine (2)	geyerinine (3)
1	44.39 (t)	43.19	31.64 (t)
2	211.21 (s)	209.96	67.44 (d)
3	51.55 (t)	51.39	77.36 (d)
4	45.82 (s)	45.91	51.53 (s)
5	60.34 (d)	59.23	63.36 (d)
6	99.19 (s)	100.25	96.88 (s)
7	33.13 (t)	32.93	33.64 (t)
8	42.87 (s)	42.84	44.92 (s)
9	53.67 (d)	52.17	54.32 (d)
10	56.12 (s)	55.74	57.82 (s)
11	74.01 (d)	69.80	75.14 (d)
12	48.12 (d)	48.57	48.69 (d)
13	72.13 (d)	75.26	73.55 (d)
14	48.43 (d)	49.71	49.36 (d)
15	43.83 (t)	42.94	44.71 (t)
16	143.55 (s)	143.18	144.34 (s)
17	109.78 (t)	109.94	109.24 (t)
18	30.30 (q)	30.13	26.79 (q)
19	61.21 (t)	59.89	77.40 (t)
20	69.19 (d)	68.39	67.69 (d)
21	176.02 (s)		175.88 (s)
22	40.92 (d)		41.37 (d)
23	26.53 (t)		26.52 (t)
24	11.71 (q)		11.62 (q)
25	16.75 (q)		16.80 (q)
OAc		170.64	170.24 (s)
OAc		21.34	21.07 (q)

427) and exhibited a base peak (m/z 326) corresponding to $C_{20}H_{24}NO_3$ or loss of a $C_5H_9O_2$ fragment from the molecular ion. The presence of an exo-methylene group was evidenced by two broad singlets in the ^1H NMR spectrum (4.98 and 4.80 ppm) and a singlet and triplet in the ^{13}C NMR spectrum (143.55 and 109.78 ppm, respectively). The ^{13}C NMR spectrum also showed a singlet at 99.19 ppm, indicative of a carbinolamine carbon. No signals characteristic of methoxy, acetyl, *N*-methyl, or *N*-ethyl groups (common in many diterpenoid alkaloids) were observed in the NMR spectra. The IR spectrum showed absorptions indicative of ester (1725 cm^{-1}), cyclic ketone (1705 cm^{-1}), and hydroxyl (3360 cm^{-1}) functions. Two minor alkaloids, geyeridine ($C_{22}H_{27}NO_5$, M_r 385, MS base peak m/z 326) and geyerinine ($C_{27}H_{37}NO_6$, M_r 471, MS base peak m/z 326) were also isolated and their ^1H and ^{13}C NMR, mass, and IR spectra suggested that they were close analogues of geyerine. Detailed analysis of the spectral data suggested that the three alkaloids could be assigned structures 1 (geyerine or 6-hydroxy-11-*O*-(2-methylbutanoyl)hetisinone), 2 (geyeridine or 6-hydroxy-13-*O*-acetylhetisinone), and 3 (geyerinine or 3-acetoxy-6-hydroxy-11-*O*-(2-methylbutanoyl)hetisine).

The basic carbon skeletons of 1 and 3 were established by off-resonance ^{13}C NMR, while that for the somewhat insoluble alkaloid 2 was assigned by proton noise decoupled ^{13}C NMR in comparison with that for 1. Table II presents these results. Proton multiplicities and relationships were established by 360-MHz ^1H NMR with extensive use of decoupling experiments, NOE difference spectroscopy and a 2D NMR COSY spectrum for 3. Full details and descriptions are available in theses,[5,6] the salient features of which are discussed in the following.

The loss of $C_5H_9O_2$ in the mass spectra of 1 and 3 suggested the presence of an alcohol esterified by a C-5 acid. The four isomeric C-5 acids are *n*-pentanoic, 2-methylbutanoic, 3-methylbutanoic, and 2,2-dimethylpropanoic acid. The ^1H NMR spectra of both 1 and 3 showed the presence of three *C*-Me groups represented by a singlet at 1.55 ppm, a doublet at 1.20 ppm, and a triplet at 0.96 ppm. The 1.55 ppm singlet is typical[7,8] of a ring C-18 quaternary methyl when a C-6 OH is present and hence the other two *C*-methyls could be assigned to the $C_5H_9O_2$ esterifying acid. Of the four possible isomers, only the 2-methylbutanoyl group would fit the multiplicities observed in the ^1H and ^{13}C NMR spectra. Assignment of the peaks for this acyl group was also facilitated by comparison of the NMR spectra of 1 and 3 with that of 2 where this group is absent.

Functionalities at the C-11, C-12, and C-13 positions of 1, 2, and 3 were determined by ^1H NMR experiments. For 1, irradiation of C-17 H_a (4.98 ppm) induced an 10% enhancement of the C-12 proton (2.50 ppm). Decoupling experiments showed that the C-12 proton was flanked on either side by downfield protons at C-11 (5.14 ppm) and C-13 (4.36 ppm). The C-11 proton showed a 9-Hz coupling to the C-9 proton, which appeared at 2.46 ppm. The dihedral angle between the C-9 and C-11 protons is proper for a 9-Hz coupling constant if the C-11 ester group has the indicated relative stereochemistry. This placement of functional groups in 1 could also be assigned beginning from the proton at C-20. It occurs as a singlet (2.88 ppm) since it is not coupled to the C-14 proton (90° dihedral angle). Irradiation at 2.88 ppm caused a 10% enhancement of a one proton doublet in a 2.23–2.34 ppm multiplet, which was assigned to the proton at C-14. This proton was in turn coupled (9 Hz) to the C-13 proton at 4.36 ppm. The C-13 proton showed a long-range coupling (1 Hz) to that at C-11, typical of two protons in a "*W*" relationship. This and the observed coupling (9 Hz) to the C-14 proton assured the relative stereochemistry at C-13. Virtually identical results for 3 indicated the same relationship of functionalities for the upper rings of geyerinine.

Geyeridine (2) lacked the 2-methylbutanoyl ^1H NMR resonances but showed an OAc methyl at 2.04 ppm. The carbonyl IR absorptions were at 1727 and 1709 cm^{-1}. Decoupling and NOE experiments[6] established a sequence of five contiguous methine protons (C-11 through C-20) as for 1. There was some difficulty in distinguishing the C-9 and C-14 protons since an unambiguous C-20 to C-14 NOE was not observed. The C-12 carbon was again assigned by an NOE from the C-17 H_a and was flanked by oxygen-bearing carbons, one of which was acetylated. In 1, the proton on the acyloxy-substituted carbon is coupled by a 3-Hz coupling to the C-12 proton, while in 2, it is the proton on the hydroxylated carbon which has this coupling constant. Additionally, the C-11 proton resonance is broad and that of C-13 sharp in 1, while the reverse is true for 2. Although the genesis of this effect is not clear, it is consistent with differing acylation patterns in 1 and 2.

Turning to functionalities in the lower two rings, the OH at C-6 was indicated by the carbinolamine carbon resonances at 99.19, 100.25, and 96.88 ppm respectively for 1, 2, and 3. This was confirmed for 1 by acetylation to form diacetylgeyerine as evidenced by its mass spectrum, ap-

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pearance of two acetyl methyls in the ^1H NMR spectrum, and shift of the C-13 proton resonance from 4.17 to 5.15 ppm. In addition, the C-18 methyl resonance was shifted from 1.48 to 1.19 ppm. In an analogous case,[7,8] the shift for a similar methyl upon acetylation was from 1.33 to 1.04 ppm. Placement of the ring carbonyl in **1** and **2** was achieved by analysis of their ^1H NMR spectra in comparison with that of the product obtained by $NaBH_4$ reduction of **1**. In **1**, one-proton doublets occurred at 3.54 (J = 15 Hz, C-1Hα) and 3.36 ppm (J = 12 Hz, C-3Hα), while in **2** they appeared at 3.34 (J = 13 Hz, C-1Hα) and 3.20 ppm (J = 12 Hz, C-3Hα). The chemical shifts are typical[9] for protons on carbons adjacent to a carbonyl and at a 0° vicinal angle with respect to the central axis of the carbonyl C–O bond. In **1** and **2**, these would be the α-oriented protons at C-1 and C-3. The methylenes were independent of each other, and the only location for a carbonyl which would separate the two methylenes would be at C-2. Reduction of **1** with $NaBH_4$ produced dihydrogeyerine, which no longer exhibited a carbonyl (IR) nor the doublet ^1H NMR signals at 3.54 and 3.36 ppm. (These were also absent in **3**.) The newly generated C-3 proton (presumably by hydride transfer from the top face) was a broad multiplet at 4.18 ppm. The C-20 proton singlet, whose resonance was at 2.88 ppm in **1**, now appeared at 3.73 ppm. (The same proton is at 3.76 ppm in **3**.) The C-19 protons of **1**, whose resonances were unassignable in the 2–2.75-ppm region of **1**, appeared as a clean AB quartet (3.15 and 3.03 ppm, J = 12 Hz) in dihydrogeyerine. All these changes are attributable to the anisotropic effect of the reduction-generated C-2 α-hydroxy substituent. This analysis is supported by data[10] on sanyonamine, a C_{20}-diterpene alkaloid with a C-2 hydroxy substituent, whose structure is known from X-ray analysis.

Geyerinine (**3**) did not show a molecular ion in the EI mass spectrum, but one was observed at m/z 488 [$(M + 1)^+$] in the NH_3 CIMS mode. Fragments were observed in the EIMS which suggested loss of acetoxy ($C_2H_3O_2$) and 2-methylbutanoyl ($C_5H_9O_2$) fragments, and these moieties could also be identified in the ^1H and ^{13}C NMR spectra. Functionality in the upper ring was discussed above. No ring carbonyl was evident in the IR or ^{13}C NMR spectra. The downfield portion of the ^1H NMR spectrum showed one proton resonances at 4.86 (C*H*OAc, d, J = 4 Hz) and 4.13 ppm (C*H*OH, br s) which were shown to be on adjacent carbons by a decoupling experiment. The 4.13-ppm resonance was further coupled to resonances appearing at 3.12 and 2.05 ppm (2 and 4 Hz, respectively). The latter two were themselves coupled (J = 15 Hz). The 3.12-ppm resonance could be assigned to C-1Hα, with the anomalous downfield position probably due to a steric interaction with the C-11 and C-13 oxygens. Dihydrogeyerine showed a similar relationship. This established the sequence CH(OAc)CH(OH)CH_2, and such a sequence can only be accommodated by the relative placement indicated in **3**. The chemical shifts and coupling constants for protons at C-1, C-2, and C-20 were closely analogous to those analyzed above for dihydrogeyerine and hence the stereochemistry should be the same at C-2. Neither the chemical shift for the C-3 proton nor its coupling to the C-2 proton (4 Hz) provided evidence for the stereochemistry of the C-3 acetoxy group. The C-18 methyl resonance was at a normal 1.4 ppm, and models indicated that an α-acetoxy group (but not a β-acetoxy) might be expected to shift the C-18 methyl upfield as does acetylation at C-6 (see above). This negative evidence suggests a C-3 β-acetoxy group. Recently, two C-2 and C-3 dioxygenated C_{20}-diterpenoid alkaloids, ignavine[11] and sadosine,[12] were reported but both lack a C-6 hydroxyl and structures were mainly determined by X-ray crystallography. Sufficient spectral data were not reported[11,12] so that these structures (both having 2α-benzoyl and 3β-hydroxyl groups) could be correlated with **3**.

We made numerous attempts to obtain suitable crystals of **1–3** or crystalline derivatives of **1**, but none met with success. The absolute configuration of the 2-methylbutanoyl group in **1** and **3** was not determined.

The spectrum of alkaloids obtained from *D. geyeri* is typical of a number of *Delphinium* species[13,14] and is perhaps most closely related to those of *D. cardinale*.[15] The C_{20} atisine-type structures exhibited by **1–3** are somewhat more common in *Aconitum* than *Delphinium*. Acylated hetisine or hetisinone derivatives have not previously been encountered.

For initial screening of feeding deterrence against the migratory grasshopper, four extracts were tested: the total MeOH extract, the total crude alkaloid mixture obtained by a differential pH extraction of the MeOH residue, an alkaloid mixture enriched in less polar bases (Et_2O extract of the mixture), and an alkaloid mixture enriched in the more polar bases ($CHCl_3$ extract of the mixture). All four showed deterrence at the level of 150 μg per feeding strip (see Experimental Section). None were active at the 15-μg level. The purified alkaloids geyerine, geyerinine, 14-acetylbrownine, and glaucenine were then tested at the 150 μg per strip level. In one experiment geyerine showed deterrence, while the other three were inactive. In a repeat experiment, glaucenine showed deterrence, while the others were inactive. Difficulty with grasshopper colony maintenance and/or natural collections prevented further testing.

The diterpenoid alkaloids clearly serve as feeding deterrents for *D. geyeri* against the omnivorous migratory grasshopper, as evidenced both by our field observations and part of the laboratory tests. The latter indicated that the activity may be due to the total mixture although sufficient data were not obtained to exclude the possibility that a single nontested alkaloid might exhibit especially strong activity. The alkaloids of *D. brownii*, some similar to those we have found in *D. geyeri*, were tested[16] and found to be toxic to a number of insect larvae and were particularly effective as stomach insecticides. In the case of the fall webworm, toxicity was similar to that of calcium arsenate.

Experimental Section

General Methods. ^1H NMR spectra were recorded on either Nicolet NT-360 or Bruker-IBM Model WP-270 spectrometers. ^{13}C NMR spectra were obtained on a JEOL FX-100 spectrometer at 25.0 MHz, a Bruker-IBM Model WP-270 instrument at 63 MHz, and a Nicolet NT 360 at 90 MHz. Chemical shifts are reported as parts per million downfield from Me_4Si. UV spectra were recorded on a Perkin-Elmer 320 UV–vis spectrometer. Electron impact (EIMS) and ammonia chemical ionization (NH_3

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CIMS) mass spectra were measured on a VG Micromass 16F spectrometer with a Systems Industries interface and a Digital PDP8-A computer. Exact mass spectra were obtained at the Midwest Center for Mass Spectroscopy, University of Nebraska, Lincoln, NE. IR spectra were recorded on a Perkin-Elmer 983 or 1420 infrared spectrometer. Optical rotations were measured on a Perkin-Elmer 241 polarimeter. Thin-layer (TLC) and preparatory layer chromatography (PLC) were accomplished on 0.25- and 2-mm precoated plates of silica gel 60 F-254 (Merck). Visualization was with ultraviolet light and iodoplatinic acid. Flash chromatography refers to the low-pressure system described by Still.[17] Medium-pressure liquid chromatography (MPLC) was accomplished on a system similar to that described by Meyers.[18] Products isolated by MPLC were detected with an ISCO Model UA-5 absorbance–fluorescence monitor at 254 nm.

Extraction and Isolation. *Delphinium geyeri* Greene (Ranunculaceae) was collected 12 mi north of Fort Collins, CO, on both sides of U.S. Highway 287 during the fourth week of June, 1983 (Colorado State University Herbarium voucher specimen 66047; identification by D. H. Wilkin).

Finely ground *D. geyeri* flowers, small stems, and leaves (1550 g) were extracted in 80% EtOH by percolation for 72 h. The solvent was removed in vacuo to yield 183 g of dry plant extract. This residue was dissolved in 1 M H_2SO_4, washed twice with $CHCl_3$, and basified with NH_4OH to pH 9. The basic aqueous layer was then washed four times with Et_2O to yield 1.0 g of alkaloidal material, followed by four washes with $CHCl_3$ to yield an additional 1.4 g of crude alkaloidal residue. A TLC comparison of the Et_2O and $CHCl_3$ washes indicated that the Et_2O layer was enriched in the more mobile and thus less polar alkaloids, while the $CHCl_3$ layer contained more of the polar bases.

The 1.0 g of Et_2O soluble residue was placed on a large silica gel flash column and a gradient elution carried out using EtOAc, with increasing amounts of MeOH. The four least polar alkaloids were mobile in EtOAc alone and were obtained in pure or nearly pure states directly from the column. The order of elution for these isolates was glaucenine (fractions 2–3), 14-dehydrobrowniine (fraction 4), and 14-acetylbrowniine (fraction 5–10), followed by browniine (fraction 12–19). The remaining bases eluted as multicomponent mixtures in fractions 20–45. Fraction 37 contained only one C_{19}-diterpene alkaloid (by ^1H NMR), along with a mixture of C_{20} bases. Filtering of this fraction through a short neutral alumina column (2:1 EtOAc/MeOH) purified the C_{19}-base delphatine.

The 1.4 g of $CHCl_3$ soluble residue was chromatographed on silica gel by flash chromatography with EtOAc/Et_2O (1:1) initially and then increasing amounts of a mixture of EtOH/NH_4OH (10:1). The early fractions (11–72) contained lesser amounts of the bases isolated from the Et_2O soluble residue. Fractions 73–97 contained a predominant compound, by ^1H NMR, that upon further purification by flash (3:1 EtOAc/$(CH_3)_2CO$) yielded 14-acetyldelcosine. Fractions 98–112 were a 1:1 mixture of geyerine (1) and several C_{19} alkaloids. Application of these fractions to another silica gel flash column (48:1:1 $CHCl_3$/EtOH/NH_4OH) led to the isolation of geyerine in the last fractions. Fractions 113–119 from the initial column were combined and further chromatographed by MPLC on neutral alumina, by using EtOAc with increasing amounts of EtOH. The midfractions furnished delcosine and then dictyocarpine. The latter fractions provided geyeridine (2) and geyerinine (3) as a mixture. These were separable by PLC on silica gel (12:2:1 Et_2O/EtOH/NH_4OH).

The relative amounts of each alkaloid (Table I) were estimated from pure isolates in combination with estimations from ^1H NMR data on mixture fractions.

Standard samples of browniine, delcosine, 14-acetyldelcosine, dicytocarpine, and glaucenine were available (S. W. Pelletier). Our isolates were identical with these by 360-MHz ^1H NMR and TLC and showed proper EIMS. Standards were not available for 14-acetylbrowniine, 14-dehydrobrowniine, or delphatine. The first two were identified by analysis of the EIMS and 360-MHz ^1H NMR spectra in comparison with that for browniine. In addition, ^{13}C NMR and ^1H NMR spectral comparisons were made with the literature values.[19] Delphatine showed a M_r of 481 by NH_3CIMS and five methoxy groups in the 270-MHz ^1H NMR spectrum at 3.41, 3.40, 3.34, 3.30, and 3.24 ppm. Of the only two known M_r 481 alkaloids with five methoxys, delphatine and deacetylambiguine, the resonances matched closest with those reported[19] for delphatine, and the remainder of the spectrum was also consistent with this assignment. Spectral data for all the above isolates are available.[5,6]

Geyerine (1) was isolated as a pure (TLC, 360-MHz ^1H NMR) glassy amorphous solid which turned translucent on standing but could not be crystallized: Silica gel TLC R_f 0.32 (10:1 $CHCl_3$/MeOH) and 0.67 (30:5:1 EtOAc/EtOH/NH_4OH); $[\alpha]^{23}_D$ +9.6° (*c* 0.36, EtOH); HREIMS, m/z (relative intensity, formula) 427.2341 (16, $C_{25}H_{33}NO_5$), 410.2331 (5, $C_{22}H_{32}NO_4$), 342.1701 (10, $C_{20}H_{24}NO_4$), 327.1781 (22, $^{12}C_{19}{}^{13}CH_{24}NO_3$), 326.1746 (100, $C_{20}H_{24}NO_3$), 325.1665 (20, $C_{20}H_{23}NO_3$), 298.1801 (25, $C_{19}H_{24}NO_2$), 269.1774 (7, $C_{18}H_{23}NO$); IR (thin film, cm^{-1}) 3360, 2930, 1725, 1705, 755; ^{13}C NMR ($CDCl_3$, 90.5 MHz) Table II; UV λ_{max} (EtOH) 252 sh, 297 sh; ^1H NMR ($CDCl_3$, 360 MHz) 5.14 (ddd, J = 1 Hz, J = 3 Hz, J = 10 Hz, C-11H), 4.98 (br s, C-17Hb), 4.80 (br s, C-17Ha), 4.36 (ddd, J = 1 Hz, J = 9 Hz, J = 1 Hz, C-13H), 3.54 (dd, J = 15 Hz, J = 2 Hz, C-1Hα), 3.36 (br d, J = 12 Hz, C-3Hα), 2.88 (s, C-20H), 2.65 (d, J = 14 Hz, C-1Hβ), 2.58 (m, J = 7 Hz, C-22H), 2.50 (dd, J = 1 Hz, J = 3 Hz, C-12H), 2.48–2.43 (m, 2 H), 2.34–2.23 (m, 4 H), 2.14–1.96 (m, 6 H), 1.78–1.70 (m, J = 7 Hz, C-23H?), 1.55 (s, C-18H_3), 1.53–1.49 (m, J = 7 Hz, C-23H?), 1.20 (d, J = 7 Hz, C-25H_3), 0.96 ppm (dd, J = 7 Hz, J = 7 Hz, C-24H_3). For decoupling and NOE data see ref 5.

Geyeridine (2) was isolated as a pure (TLC, ^1H NMR) gum: HREIMS, m/z 385.1889 (calcd for $C_{22}H_{27}NO_5$ *m/z* 385.1889); EIMS, *m/z* (relative intensity) 385 (35), 367 (7), 342 (17), 327 (23), 326 (100), 325 (22), 308 (14), 298 (15), 296 (18), 269 (16), 252 (9), 223 (10), 209 (8), 192 (9), 176 (16), 175 (25), 96 (35), 91 (21), 55 (24); UV λ_{max} (EtOH) 250 sh, 289 sh; IR (CH_2Cl_2, cm^{-1}) 3610, 3055, 2930, 1727, 1709, 1368, 1294, 1263, 1257, 1242, 1164, 1092, 1044, 863; ^1H NMR (360 MHz, $CDCl_3$) 5.14 (slightly broadened d, J = 9 Hz, J = 1 Hz, J < 1 Hz, C-13H), 4.94 (br s, C-17H_a), 4.79 (br s, C-17H_b), 4.17 (ddd, J = 9 Hz, J = 3 Hz, J = 1 Hz, C-11H), 3.34 (dd, J = 13 Hz, J = 2 Hz, C-1Hα), 3.20 (d, J = 12 Hz, C-3Hα), 2.98 (s, C-20H), 2.43–2.35 (m, 5 H), 2.28–2.17 (m, 6 H), 2.09 (br s, 1 H), 2.04 (s, 3 H, OAc), 2.00 (s, 1 H), 1.79 (d, J = 13 Hz, 1 H), 1.48 ppm (s, 3 H, C-18). A 2D NMR COSY spectrum is available.[6] For ^{13}C NMR (63 MHz, $CDCl_3$) data, see Table II.

Geyerinine (3) was isolated as a pure (TLC, ^1H NMR) gum: HRCIMS, *m/z* MH^+ = 488.2648 (calcd for $C_{27}H_{38}NO_7$ *m/z* 488.2615); NH_3 CIMS, *m/z* (relative intensity) 488 (48), 486 (16), 470 (12), 428 (57), 426 (33), 414 (42), 412 (25), 410 (22), 286 (84), 384 (78), 382 (30), 368 (22), 366 (16), 326 (100), 324 (61), 308 (37), 296 (19); EIMS, *m/z* (relative intensity) 428 (9), 427 (8), 386 (20), 385 (10), 368 (11), 356 (9), 342 (8), 326 (43), 325 (28), 308 (17), 298 (16), 297 (20), 296 (30), 268 (9), 176 (14), 132 (13), 105 (24), 91 (22), 74 (46), 57 (100); UV λ_{max} (EtOH) 230 sh, 257 sh, 285 sh; IR (CH_2Cl_2, cm^{-1}; 3595, 2910, 1727, 1360, 1225, 1065, 1040, 845; ^1H NMR (360 MHz, $CDCl_3$) 5.13 (dd, J = 9 Hz, J = 3 Hz, J = 1 Hz, C-11H), 4.94 (br s, C-17Ha), 4.86 (d, J = 4 Hz, C-3H), 4.78 (br s, C-17Hb), 4.32 (slightly broadened d, J = 9 Hz, J = 1 Hz, J < 1 Hz, C-13H), 4.13 (m, $W_{1/2}$ = 12 Hz, C-2Hβ), 3.76 (s, C-20H), 3.48 (d, J = 12 Hz, C-19Ha), 3.12 (dd, J = 15 Hz, J = 2 Hz, C-1Hα), 3.02 (d, J = 12 Hz, C = 19 Hb), 2.64 (m, 1 H), 2.50–2.20 (m, 4 H), 2.15 (s, 3 H), 2.10–1.82 (m, 6 H), 1.73 (m, 1 H), 1.60–1.48 (m, 2 H), 1.40 (s, 3 H, C-18), 1.32 (s, 1 H), 1.21 (d, J = 7 Hz, 3 H), 0.95 ppm (t, 3 H); ^{13}C NMR (25 MHz, $CDCl_3$) Table II.

Geyerine Diacetate. Geyerine (20 mg, .05 mmol) and 1 mL of a mixture of dry pyridine and acetic anhydride were added to a flask fitted with a drying tube and heated on a steam bath for 2 h. The solvent was removed in vacuo, and a ^1H NMR spectrum of the reaction mixture showed almost complete conversion to a diacetate and small amounts of the corresponding monoacetate derivatives. Purification was accomplished on an aluminum oxide PLC plate with EtOAc to yield 17 mg (0.03 mmol, 70% purified) of geyerine diacetate as a viscous oil: EIMS, *m/z* (relative intensity) 511 (6), 469 (18), 468 (31), 440 (2), 410 (3), 368 (3), 324

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(10), 111 (44), 109 (30), 97 (40), 95 (24), 85 (46), 83 (44), 71 (64), 69 (48), 57 (100); ^{1}H NMR (360 MHz, $CDCl_3$) 5.15 (d, J = 9.4 Hz, 2 H, exactly superimposed ester methines), 5.00 (s, 1 H), 4.83 (s, 1 H), 3.35 (d, J = 13.3 Hz, 1 H), 3.15 (d, J = 12.6 Hz, 1 H), 2.84 (s, 1 H), 2.69 (s, 1 H), 2.50–2.64 (m, 6 H), 2.10–2.48 (m, 7 H), 2.07 (s, 3 H), 2.02 (s, 3 H), 1.77 (m, 2 H), 1.55 (m, 1 H), 1.24 (d, J = 7 Hz, 3 H), 1.19 (s, 3 H), 0.97 ppm (t, 3 H).

Dihydrogeyerine. Geyerine (35 mg, 0.082 mmol) was added to a flask containing 20 mg of $NaBH_4$ (large excess) dissolved in 5 mL of 95% EtOH and 0.5 ml of H_2O. The solution was stirred at 25 °C for 25 min, at which time no starting material remained by TLC but with the appearance of one major, less polar spot. The excess $NaBH_4$ was decomposed with dilute H_2SO_4 and the solution made basic with 1 M NaOH and extracted twice with $CHCl_3$. The combined $CHCl_3$ washes were concentrated under reduced pressure. A ^{1}H NMR spectrum of the residue showed essentially one compound. Purification of the residue was achieved on a silica gel PLC plate (12:3:1 EtOAc/EtOH/NH_4OH) to yield 26 mg (0.06 mmol, 73% purified yield) of dihydrogeyerine as a viscous oil: UV λ_{max} (EtOH) 254 sh, 282 sh; ^{1}H NMR (250 MHz, $CDCl_3$) 5.17 (d, J = 9.9 Hz, 1 H), 4.95 (s, 1 H), 4.76 (s, 1 H), 4.32 (d, J = 9.0 Hz, 1 H), 4.18 (m, $W_{1/2}$ = 12 Hz, 1 H), 3.73 (s, 1 H), 3.15 (d, J = 11.9 Hz, 1 H), 3.03 (d, J = 11.9 Hz, 1 H), 2.93 (br d, J = 15.3 Hz, 1 H), 2.53–2.40 (m, 3 H), 2.37–2.25 (m, 4 H), 2.09 (s, 1 H), 2.08–2.00 (m, 3 H), 1.99 (s, 1 H), 1.87–1.60 (m, 6 H), 1.59 (s, 1 H), 1.58–1.38 (m, 3 H), 1.35 (s, 3 H), 1.19 (d, J = 7 Hz, 3 H), 0.91 ppm (t, 3 H).

Bioassays. Migratory grasshoppers, *Melanoplus sanguinipes* (Fabricius), were either obtained from a nondiapausing population kept by the Capinera research group or collected from local populations, sorted, and reared under the conditions described by Melman.[4]

Young male and female adult grasshoppers were offered a choice of filter paper strips impregnated with wheat extract only or wheat extract and diterpene alkaloid components from *D. geyeri*. After having been starved for 24 h, two grasshoppers were placed in a 500-mL plastic cup containing the filter paper strips inserted into a piece of florist's block. The cup was vented and water provided. For every experiment, 12 grasshoppers were used to evaluate each alkaloidal sample. Grasshopper consumption of filter paper strips was rated on scale of 0–4 as follows: 0, no consumption; 1, occasional nibbling around perimeter of strip; 2, nibbling around most of strip; 3, nibbling around most of perimeter with occasional areas of heavy consumption; 4, more than $^2/_3$ of the strip consumed. Deterrence was indicated by a significant difference in consumption level by Sign test ($P < 0.05$).

Wheat extract was prepared by macerating wheat sprouts (25 g) with methanol (150 mL). After 3 days the solution was filtered and the volume reduced to 50 mL. Of this solution 50 μL was delivered to each filter paper strip (1 × 4 cm). Alkaloid-containing strips were prepared by delivering 30 μL of a 5 mg/mL alkaloidal–methanolic solution to a filter paper already impregnated with wheat extract. In the case of the total plant extract, a 50 mg/mL solution was used due to the large amount of nonalkaloidal material present.

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Nitrogen Bridgehead Compounds. 62.[1] Conformational Analysis of 6,7,8,9-Tetrahydro-4*H*-pyrido[1,2-*a*]pyrimidin-4-ones and Their Methyl Derivatives by NMR Spectroscopy

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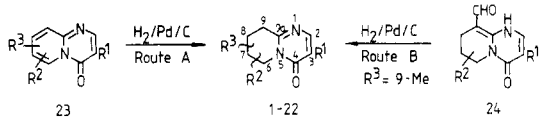
Proton and carbon-13 chemical shift data have been acquired for 2 6,7,8,9-tetrahydro-4*H*-pyrido[1,2-*a*]pyrimidin-4-ones and 20 methylated derivatives. Least-squares regression analysis has been undertaken on the aliphatic ring carbons of compounds with unequivocal conformations to determine the methyl substituent parameters for the four distinct aliphatic positions, and the results have been used to estimate the position of equilibrium of conformationally mobile compounds. It is concluded that at room temperature the 6-methyl derivatives predominantly adopt the conformation with a pseudoaxial methyl group and the 7- and 8-methyl derivatives that with an equatorial methyl group, but the 9-methyl derivatives exist in essentially equally populated conformers. Substituent parameters are compared with those previously determined for methylated tetralins.

6,7,8,9-Tetrahydro-4*H*-pyrido[1,2-*a*]pyrimidin-4-ones and their methyl-substituted derivatives have recently acquired much interest as intermediates in the synthesis of various pharmacologically active agents.[2]

So far, however, only the 6-methyl derivatives have been subjected to stereochemical investigation.[3-5] As concerns the conformation of the tetrahydropyridine ring in these derivatives, the half-chair conformer with a pseudoaxial methyl group has been shown to be energetically most

Scheme I



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