

V. V. Kul'kova, K. Samikov,
R. Shakirov, and S. Yu. Yunusov

UDC 547.944/945

A new alkaloid kordiline has been isolated from the epigeal part of *Korolkowia sewerzowii*. On the basis of the results of a study of the IR, PMR, and mass spectra of kordiline and the products of its transformations, it has been established that kordiline has the structure and partial configuration of $3\alpha,11\beta$ -dihydroxy- Δ^8 -cevanine.

A new alkaloid — kordiline, $C_{27}H_{43}NO_2$ (I) — has been isolated from the epigeal part of *Korolkowia sewerzowii* Regel [1, 2] by the separation of the total chloroform-soluble alkaloids. The IR spectrum of (I) had absorption bands at (cm^{-1}) 3400, 1030 (OH); 2985–2835, 1470, 1440 ($-CH_3$; $-CH_2-$); and 2775 (trans-quinolizidine). The mass spectrum of (I) had the peaks of ions with m/z 98, 111, 112 (100%), 124, 125, 149, 150, 162, 164, 178, 180, 216, 342, 343, 356, 357, $(M - 29)^+$, $(M - 28)^+$, $(M - 18)^+$, $(M - 17)^+$, $(M - 15)^+$, $413 M^+$, which are characteristic for the C-nor-D-homosteroid alkaloids of the cevine group [3, 4]. The PMR spectrum of (I) contained a singlet at 1.20 ppm ($19-CH_3$), and doublets at 0.78 ppm ($21-CH_3$) and 0.85 ppm ($27-CH_3$). No signal was observed from an olefinic proton; nevertheless, in solutions made weakly acidic with sulfuric acid, kordiline instantaneously decolorized a solution of potassium permanganate, which indicated the presence of a double bond.

In kordiline, the oxygen atoms are present in the form of secondary hydroxy groups, as was confirmed by the production of diacetylkordiline (II). The IR spectrum of (II) showed absorption frequencies at 1737, 1250, and 1025 cm^{-1} (ester $C=O$) and lacked the absorption bands of hydroxy groups. The PMR spectrum of (II) showed a singlet at 0.96 ppm ($19-CH_3$), doublets at 0.78 and 0.84 ppm ($21-CH_3$ and $27-CH_3$, respectively), and signals from methyls of acetyl groups at 1.97 and 1.99 ppm and from protons geminal to acetoxy groups at 4.86 and 5.00 ppm.

On hydrogenation, (I) formed dihydrokordiline (III). The PMR spectrum of (III) contained a singlet at 1.18 ppm ($19-CH_3$) and doublets at 0.78 and 0.84 ppm ($21-CH_3$ and $27-CH_3$, respectively). The acetylation of dihydrokordiline with acetic anhydride in pyridine gave diacetyldihydrokordiline (IV). The IR spectrum of (IV) showed absorption bands at 1737, 1250, and 1030 cm^{-1} (ester $C=O$). The PMR spectrum of (IV) had a singlet at 0.93 ppm ($19-CH_3$), doublets at 0.81 and 0.81 ppm ($21-CH_3$ and $27-CH_3$), and signals from two methyls of acetyl groups at 1.98 and 2.00 ppm and from protons geminal to acetoxy groups at 4.87 and 5.06 ppm.

The oxidation of kordiline with chromium trioxide yielded monoketone (V) and a diketone (VI) derivative of kordiline. The IR spectrum of (V) showed absorption bands at 3400 cm^{-1} (OH) and 1710 cm^{-1} ($C=O$).

Thus, the results of a study of the physicochemical properties of kordiline and of the products of its transformations showed that kordiline is based on the heterocyclic skeleton of cevanine [4–10] with two secondary hydroxy groups and a tetrasubstituted double bond.

It can be seen from the mass spectra of (I–VI) that when the hydroxy group in (I) was replaced by an acetoxy group (II) or a keto group (V) the peaks of the ions with m/z 98, 111, 112, 124, 125, 149, 150, 162, 164, 178, and 179 that were formed from rings D, E, and F [3], remained unaffected. It followed from this that the secondary hydroxy groups in kordiline could be present only at carbon atoms of rings A, B, and C.

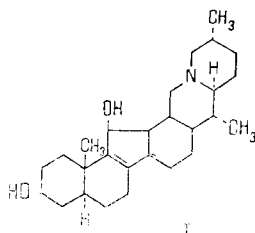
The IR spectra of (I) and (II) had bands at 1030 and 1025 cm^{-1} , respectively, showing the presence of an α -oriented hydroxy group at C_3 . This was confirmed by the presence of a multiplet at 5.00 ppm from $C-3\beta H$ in the PMR spectrum of diacetylkordiline [11, 12]. Consequently, the OH group at C_3 has the α -axial orientation. Kordiline was not oxidized by period-

ic acid, which showed the absence of adjacent hydroxyls and excluded the presence of the second hydroxy group at C₂ or C₄.

The upfield shift of the signals of the protons of the 19-CH₃ group in the PMR spectra of (II) and (IV) by 0.24 and 0.25 ppm in comparison with (I) and (III), respectively, showed that the second hydroxy group was located at C₁₁ in the β orientation [13, 14].

The presence in the mass spectra of (I-VI) of the peaks of ions with m/z 111, 112, 124, 125, 149, 150, 162, 164, and 178 [3] and the upfield shift of the resonance signals of the 19-CH₃ group in the PMR spectra of (II) and (IV) by 2 and 3 Hz, respectively, as compared with those in the PMR spectra of (I) and (III), showed that in (I) the tetrasubstituted double bond was probably located at C₈-C₉. Judging from the values of the chemical shifts of the protons of the 19-CH₃ group, rings A/B are trans-linked. It follows from the values of the chemical shifts of the 21-CH₃ and 27-CH₃ groups that they have α -equatorial orientations [8, 13].

According to the facts given kordiline has the most probable structure and partial configuration of 3 α ,11 β -dihydroxy- Δ^8 -cevanine (I).



EXPERIMENTAL

IR spectra (KBr) were taken on a UR-20 spectrometer, PMR spectra on a JNM-4H-100/100 MHz instrument ((I) in CDCl₃ + CD₃OD, and (II-IV) in CDCl₃) with HMDS as internal standard (the values are given in the δ scale), and mass spectra on an MKh-1310 instrument. For thin-layer chromatography (TLC) we used KSK silica gel in chloroform-methanol systems: 1) (10:0.5); 2) (10:1).

Isolation of Kordiline. The combined chloroform-soluble alkaloids of *Korelkwia sewerzowii* (20 g) were chromatographed on a column of alumina (activity grade II). The column was washed with chloroform and with chloroform-methanol (10:0.5; 10:1; and 10:2). Similar fractions, as judged by TLC, were combined. A total of 25 fractions was obtained, and the rechromatography of four of them (0.28 g) on silica gel (250 μ) with chloroform-methanol (10:0.5) as the eluent gave isolated kordiline with mp 286-288°C (acetone), R_f 0.24 (system 2), M⁺ 413.

Diacetylkordiline. A mixture consisting of 68 mg of kordiline, 2 ml of pyridine, and 3 ml of acetic anhydride was kept at room temperature for 3 days. After the elimination of the pyridine, the residue was dissolved in 5% sulfuric acid, the solution was made alkaline with ammonia, and the alkaloids were extracted with chloroform. This gave 60 mg of amorphous diacetylkordiline with R_f 0.48 (system 1).

Mass spectrum: m/z 98, 111, 112 (100%), 124, 125, 149, 162, 164, 178, 437, 438, 454, 468, 469, 482, 497 M⁺.

Dihydrokordiline. Kordiline (42 mg) was subjected to Adams hydrogenation in glacial acetic acid (0.4 g of PtO₂). After separation from the platinum black, the solution was diluted with water and made alkaline with ammonia, and the alkaloids were extracted with chloroform. This gave 34 mg of dihydrokordiline with mp 224-226°C (acetone), R_f 0.22 (system 2).

IR spectrum, ν_{\max} , cm⁻¹: 3360, 1035 (OH), 2780 (trans-quinolizidine). Mass spectrum: m/z 98, 111, 112, 124, 125, 149, 162, 164, 178, 179, (M - 29)⁺, (M - 28)⁺, (M - 18)⁺, (M - 17)⁺, (M - 15)⁺, 415 M⁺.

Diacetyldihydrokordiline. A mixture consisting of 30 mg of dihydrokordiline, 2 ml of pyridine, and 4 ml of acetic anhydride was treated in the same way as for the acetylation of kordiline. This gave 31 mg of amorphous diacetyldihydrokordiline with R_f 0.55 (system 1).

Mass spectrum: m/z 98, 111, 112, 124, 125, 149, 150, 162, 164, 178, 185, $(M - 60)^+$, $(M - 59)^+$, $(M - 56)^+$, $(M - 43)^+$, $(M - 42)^+$, $(M - 29)^+$, $(M - 28)^+$, $(M - 15)^+$, 499 M^+ .

Oxidation of Kordiline. A mixture of 20 mg of kordiline, 2 ml of pyridine, and 15 ml of chromium trioxide was kept at room temperature for 3 days. After the pyridine had been driven off, the residue was dissolved in 5% sulfuric acid, the solution was made alkaline with ammonia, and the alkaloids were extracted with chloroform. The solvent was distilled off and the residual mixture of mono- and diketones was separated on a column of alumina (with benzene-ethanol, 10:0.5) as eluent. This gave 5 mg of kordilinone (V) with R_f 0.42 and 1 mg of kordilinedione (VI) with R_f 0.60 (system 2).

IR spectrum of (V), ν_{\max} , cm^{-1} : 3400 (OH); 2780 (trans-quinolizidine); 1710 (C=O).

Mass spectrum of (V): m/z 98, 111, 112 (100%), 124, 125, 138, 149, 150, 162, 164, 178, 341, 342 $(M - 29)^+$, $(M - 28)^+$, $(M - 18)^+$, $(M - 17)^+$, $(M - 15)^+$, 411 M^+ .

Mass spectrum of (VI): m/z 98, 111, 112 (100%), 124, 125, 138, 139, 149, 150, 162, 164, 178, 380, 381, 394, 409 M^+ .

SUMMARY

1. A new alkaloid — kordiline — has been isolated from the epigeal part of *Korolkowia sewerzowii*.

2. It has been established on the basis of the results of a study of the IR, PMR, and mass spectra of kordiline and of the products of its transformations that kordiline has the most probable structure and partial configuration of $3\alpha,11\beta$ -dihydroxy- Δ^8 -cevanine.

LITERATURE CITED

1. K. Samikov, R. Shakirov, D. N. Safaeva, and S. Yu. Yunusov, Khim. Prir. Soedin., 780 (1976).
2. V. V. Kul'kova, K. Samikov, R. Shakirov, and S. Yu. Yunusov, Khim. Prir. Soedin., 72 (1983).
3. R. Shakirov and S. Yu. Yunusov, Khim. Prir. Soedin., 3 (1981).
4. H. Budzikiewicz, Tetrahedron, 20, 2264 (1964).
5. R. N. Jones and G. Roberts, J. Am. Chem. Soc., 80, 6121 (1958).
6. K. Samikov, R. Shakirov, and S. Yu. Yunusov, Khim. Prir. Soedin., 367 (1976).
7. F. Bohlmann, Ber., 91, 2157 (1958).
8. T. M. Moynehan, K. Schofield, R. A. V. Jones, and A. R. Katritzky, J. Chem. Soc., 2637 (1962).
9. F. Bohlmann, D. Schumann, and G. Arndt, Tetrahedron Lett., 31, 2705 (1965).
10. R. N. Nuriddinov, A. I. Saidkhodzhaev, M. R. Yagudaev, and S. Yu. Yunusov, Khim. Prir. Soedin., 333 (1968).
11. A. R. H. Cobe, R. N. Jones, and K. Dobriner, J. Am. Chem. Soc., 74, 5571 (1952).
12. I. Fried, P. Grabowich, E. F. Sabo, and A. I. Cohen, Tetrahedron, 20, 2297 (1964).
13. R. F. Zurcher, Helv. Chim. Acta, 46, 2054 (1963).
14. K. Samikov, R. Shakirov, and S. Yu. Yunusov, Khim. Prir. Soedin., 399 (1984).