3. M. Shamma et al., J. Am. Chem. Soc., 89, 1739 (1967).
4. S. R. Johns and J. A. Lamberton, Tetrahedron Lett., 4883 (1966).
5. I. Ognyanov, B. Pyuskylev, et al., Tetrahedron, 24, 4641 (1968).
6. K. C. Chan, Phytochem., 8, 219 (1969).
7. M. R. Yagudaev, V. M. Malikov, and S. Yu. Yunusov, Khim. Prirodn. Soedin., 493 (1974).
8. A. D. Buckingham, Can. J. Chem., 38, 300 (1960); R. F. Zürcher, Progress in NMR, 2, 5 (1967).
9. D. J. Collins, J. J. Hobbs, and S. Sternhell, Aust. J. Chem., 16, 1030 (1963).
10. C. E. Johnson and F. A. Bovey, J. Chem. Phys., 29, 1012 (1958).

THE STRUCTURE OF KESSELRINGINE

M. K. Yusupov and A. S. Sadykov

UDC 547.944.6

We have previously reported the isolation from the epigeal parts of Colchicum kesselringii Rgl. of a new base kesselringine and its partial structure [1, 2]. From the nature of its UV spectrum, this compound differs considerably from the homoproaporphine and proaporphine bases with a dienone ring [3, 4]. Its IR spectrum (Fig. 1) shows the absorption bands of a hydroxy group (3530 cm^{-1}), a benzene ring (1600, 900-800 cm^{-1}), and methylene groups (1460 cm^{-1}).

The NMR spectrum of the alkaloid (Fig. 2) shows three-proton singlets at 2.32 and 3.32 ppm of N-methyl and O-methyl groups, respectively, and a one-proton singlet at 6.42 ppm corresponding to the C_3 proton of the benzene ring.

According to its mass spectrum, which has the peaks of the following main ions: m/e 331 (M^+, 42%), 330 $(M-1)^+$ (100%), 316, 288 $(M-43)^+$, 256, 244, 242, 238, 230, 228, 165, kesselringine is close to the proaporphine alkaloids of the type of amuramine [5], and probably has the basic skeleton I.

From the spectral characteristics and the elementary composition, it may be concluded that kesselringine is a homoproaporphine compound highly reduced in the dienone ring and is the first representative of substances with a spirocyclohexane ring.

Diazomethane methylates the phenolic hydroxy group of ring A of kesselringine with the formation of O-methylkesselringine (II, Scheme 1).

Judging from the value of its chemical shift (CS) in the PMR spectrum, the methoxy group of kesselringine is located in an alicyclic ring. The base is inert to the action of ammonia and alkalis, but it is readily hydrolyzed by heating in dilute acids, changing into norkesselringine (III). The hydrolysis of O-methylkesselringine forms O-methylnorkesselringine (IV), which is isomeric with kesselringine. These two compounds differ by the positions of the hydroxy and methoxy groups. The hydrolysis of the alicyclic methoxy group in the formation of O-methylnorkesselringine is shown by the absence of the corresponding CS (three-proton singlet at 3.32 ppm)

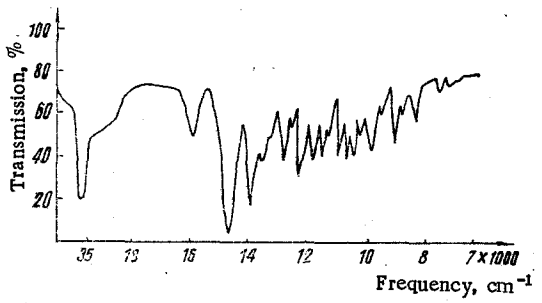


Fig. 1. IR spectrum of kesselringine (in paraffin oil).

V. I. Lenin Tashkent State University. Translated from Khimiya Prirodnykh Soedinenii, No. 3, pp. 350-354, May-June, 1976. Original article submitted October 13, 1975.

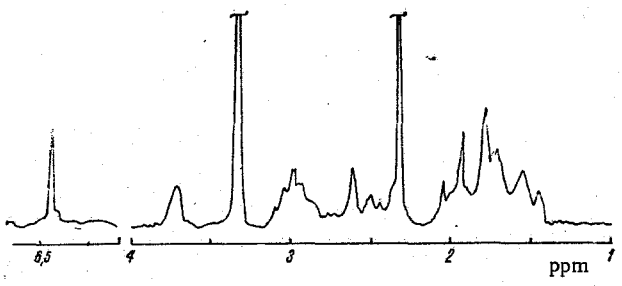
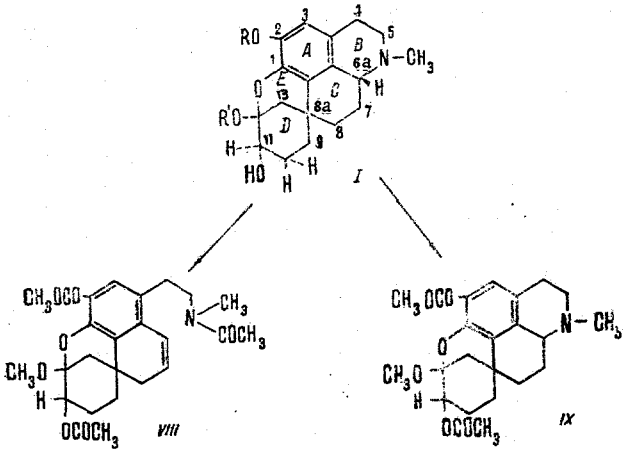


Fig. 2. NMR spectrum of kesselringine (in $CDCl_3$).

I. R = H; R′ = CH_3
II. R = R′ = CH_3
III. R = R′ = H
IV. R′ = CH_3; R′ = H
V. R′ = C_2H_5; R = H
VI. R′ = n-C_3H_7; R = H
VII. R′ = n-C_4H_9; R = H



Scheme 1. Structure and transformations of kesselringine.

from its PMR spectrum and by the appearance of an absorption band of a hydroxy group in the IR spectrum (ν_{max} 3650 cm^{-1}).

The base underwent no change when it was heated in solution in methanol containing hydrochloric acid. However, in ethanol, n-propanol, and n-butanol a transesterification reaction was observed with the formation of the corresponding alkylnorkesselringine (V-VII). In acid aqueous solutions, the latter are hydrolyzed to norkesselringine and on methanolysis they are converted into kesselringine.

The transformations of kesselringine reported above shows that its molecule contains a cyclic acetal grouping [6, 7]. Thus, the oxygen bridge and the methoxy group are attached to the same C atom of ring D. Since the formation of the ether bond in the homoproporphine is possible only at the C_1-C_{12} and C_1-C_{13} positions [8], the acetal group in ring D can be located at C_{12} or C_{13}. On studying the structure of the base with Dreiding models, we came to the conclusion that a six-membered ring E, i.e., with acetal group at C_{12}, is the most probable structure for it.

The acetylation of kesselringine with acetic anhydride in the presence of anhydrous sodium acetate led to a O,O,N-triacetyl derivative (VIII). This reaction, taking place with the opening of the nitrogen-containing heterocycle, confirms the presence of a tetrahydroisoquinoline fragment [9] in the molecule of the base. On acetylation with acetic anhydride in the presence of sulfuric acid, however, O,O-diacetylkesselringine (IX) was formed. These reactions show that the base contains, in addition to the phenolic hydroxyl of ring A, another, secondary, alcoholic hydroxy group. By analogy with related proaporphine and homoproaporphine alkaloids, the latter may be assigned to the C_{11} position. A comparative study of the CSs of a C_{11} proton in kesselringine and its acetyl derivatives shows that the actual and hydroxy groups in the spirocyclohexane ring are actually located on adjacent carbon atoms: in the PMR spectrum of the initial base the signal of this proton has a CS of 3.72 ppm, and in the products of acetylation, as is well known [10], it shifts downfield and appears at 5.13 ppm in the form of a broadened singlet with a half-width of 5.6 Hz. Consequently, the C_{12} position of the spirocyclohexane ring is occupied by the acetal group, and the proton at C_{11} has the equatorial orientation and interacts with only one of the protons of the methylene group at C_{10}.

On the basis of what has been said, kesselringine corresponds to the structure 2,11-dihydroxy-12-methoxyhexahydro-1,12-epoxyhomoproaporphine (I).

An analysis of the molecule of the base using Dreiding models shows that the linkage of rings E and D in it is possible only if the bonds at C_{8a} and C_{12} are both axial. Thus, the methoxy group at C_{12} is equatorial in ring D.

By analogy with other proaporphine and homoproaporphine alkaloids having a positive specific rotation, kesselringine is characterized by the R configuration at the C_{6a} atom.

EXPERIMENTAL

The chromatographic analysis of the reaction products was performed on Filtrak No. 1 paper in the following solvent systems: 1) n-butanol–hydrochloric acid–water (50:7.5:13.5); 2) n-butanol saturated with 5% acetic acid; 3) n-butanol saturated with water. The R_f values of the substances are given for system 2.

The UV spectra were taken in methanolic solution on an SF-4A spectrophotometer, the IR spectra on a UR-10 double-beam spectrometer, the PMR spectra on an XL-100 instrument, and the mass spectra on an MKh-1303 spectrometer.

O-Methylkesselringine (II). An excess of diazomethane in n-hexane was added repeatedly to a saturated solution of kesselringine in methanol. After the end of the reaction, the mixture of solvents was distilled off, and the residue was dissolved in chloroform. The chloroform solution was washed with water, and O-methylkesselringine with mp 200°C (from acetone), R_f 0.31, was isolated.

Mass spectrum: m/e 345 (M^+). NMR spectrum, ppm: 3.35 and 3.75 (2 OCH_3).

Norkesselringine (III). A mixture of 0.75 g of kesselringine and 15 ml of 3% sulfuric acid was heated at 100°C for 2 h. The solution was cooled and made alkaline with ammonia. Norkesselringine was isolated with the composition $C_{18}H_{23}O_4N \cdot H_2O$, mp 173-175°C and 236-237°C (from water), R_f 0.17.

Mass spectrum: m/e 317 (M^+). IR spectrum, cm^{-1}: 3590, 3420-3230 (3 OH).

O-Methylnorkesselringine (IV). A mixture of 0.5 g of O-methylkesselringine and 10 ml of 3% sulfuric acid was heated at 100°C for 1 h. The solution was made alkaline with ammonia and extracted with chloroform, giving O-methylnorkesselringine with mp 236-237°C (from acetone) and R_f 0.20.

Mass spectrum: m/e 331 (M^+). PMR spectrum: 3.75 ppm (arom. OCH_3).

O-Alkylnorkesselringines (V-VII). A solution of 0.1 g of kesselringine in the appropriate alcohol (ethanol, n-propanol, or n-butanol) containing 7% hydrochloric acid was heated for 50 min. The solvent was evaporated off, the residue was dissolved in water, and the solution was made alkaline with ammonia. The crystals that deposited were washed with water and with acetone. Faintly pink crystals of the O-alkylnorkesselringines were obtained: O-ethylnorkesselringine (V), mp 175-176°C, M^+ 345, R_f 0.50; O-n-propylnorkesselringine (VI), mp 156-157°C, M^+ 359, R_f 0.56- and O-n-butylnorkesselringine (VII), mp 96-98°C, M^+ 373, R_f 0.64.

Hydrolysis of the Alkylnorkesselringines to Norkesselringine. A mixture of 0.1 g of ethyl-, n-propyl-, or n-butylnorkesselringine and 10 ml of 3% sulfuric acid was heated at 100°C for 2 h. The reaction product–norkesselringine–was isolated in the manner described above. mp 174-175°C and 236-237°C, M^+ 317, R_f 0.17.

Methanolysis of the Alkylnorkesselringines. A solution of 0.1 g of n-propyl- or n-butylnorkesselringine in 10-15 ml of methanol containing 7% hydrochloric acid was boiled for 90 min, and the reaction product–kesselringine – was isolated in the manner described above. mp 194-196°C (from acetone), M^+ 331, R_f 0.26.

O,O,N-Triacetylkesselringine (VIII). A mixture of 0.2 g of kesselringine, 0.8 g of freshly fused sodium acetate, and 2 ml of acetic anhydride was heated at 40-50°C for 2 days. The excess of acetic anhydride was eliminated by the addition of methanol. The solvent was evaporated off, the dry residue was dissolved in water, and the reaction product was extracted with chloroform. After the solvent had been distilled off, amorphous triacetylkesselringine, having a neutral character and R_f 0.70, was obtained.

Mass spectrum: m/e 457 (M^+). IR spectrum, cm^{-1}: 1770, 1775, 1650 (2 $OCOCH_3$, $NCOCH_3$).

O,O-Diacetylkesselringine (IX). One drop of concentrated sulfuric acid was added to a solution of 0.2 g of kesselringine in 2 ml of acetic anhydride. After the end of the reaction, the excess of acetic anhydride was evaporated in vacuum, the residue was dissolved in water, the solution was made alkaline with ammonia, and the reaction product was extracted with chloroform. Diacetylkesselringine with mp 140-142°C (from acetone) and R_f 0.40 was isolated.

Mass spectrum: m/e 415 (M^+). IR spectrum, cm^{-1}: 1770, 1745 (2 $OCOCH_3$).

SUMMARY

On the basis of IR, PMR, and mass spectra and chemical transformations, the alkaloid kesselringine isolated from the epigeal parts of Colchicum kesselringii Rgl. has been shown to have the structure of 2,11-dihydroxy-12-methoxyhexahydro-1,12-epoxyhomoproaporphine with the R absolute configuration at the C_{6a} atom.

LITERATURE CITED

1. M. K. Yusupov and A. S. Sadykov, Uzb. Khim. Zh. No. 5, 49 (1961).
2. M. K. Yusupov, in: The Chemistry of Plant Substances [in Russian], Tashkent (1972), p. 19.
3. K. L. Stuart and M. P. Cava, Chem. Rev., 68, 321 (1968).
4. K. Bernauer and W. Hofheinz, Fortschritte der Chemie organischer Naturstoffe, 26, 245 (1968).
5. L. Dolejŝ, Collection Czech. Chem. Commun., 39, 571 (1974).
6. A. E. Chichibabin, Basic Principles of Organic Chemistry [in Russian], Vol. 1, Moscow (1963).
7. F. Santavy, Collection Czech. Chem. Commun., 30, 912 (1965).
8. T. Kametani, F. Satoh, H. Yagi, and K. Fukumoto, J. Chem. Soc., C, 1003 (1968).
9. A. P. Orekhov, The Chemistry of the Alkaloids [in Russian], Moscow (1955).
10. N. Bhacca and D. Williams, Applications of NMR Spectroscopy in Organic Chemistry, Holden-Day, San Francisco (1964).

THE STRUCTURE OF LUTEIDINE

N. L. Mukhamed'yarova, M. K. Yusupov, M. G. Levkovich, Kh. A. Aslanov, and A. S. Sadykov

UDC 547.944.6

The isolation from Colchicum luteum Baker. (yellow autumn crocus) of the nontropolone base luteidine (I) with the composition $C_{20}H_{25}O_4N$ (confirmed by the high-resolution mass spectrum), mp 231-232°C $[\alpha]_D$ −96° (in methanol) had been reported previously [1]. Its UV spectra has absorption maxima at 228 and 272 nm (log ε 3.89 and 4.05). Its IR spectrum contains absorption bands at 1677, 1667, 1617, 1600, and 3535 cm^{-1} showing the presence of an enone grouping [2], an aromatic ring, and a hydroxy group. A color reaction with ferric chloride and a bathochromic shift of the absorption maximum in the UV spectrum in an alkaline medium show the phenolic nature of the hydroxy group.

In the mass spectrum of luteidine, the strongest peak is that of the ion with m/e 244 $(M-99)^+$, and the molecular ion (M^+, 343) has an intensity of 38%. The $(M-1)^+$ ion that is characteristic for many isoquinoline alkaloids with the greatest intensity amounts to only 22%. The PMR spectrum of the base (Fig. 1) has the resonance signals of a N-methyl group (three-proton singlet at 2.37 ppm), two O-methyl groups, one of which is located in an aromatic ring (three-proton singlet at 3.78 ppm) and the other on an olefinic double bond (three-proton singlet at 3.51 ppm). In addition, in the weak-field region there are the singlets of one aromatic proton and one olefinic proton (at 6.46 and 5.79 ppm, respectively). The positive nuclear Overhauser effect (NOE) between the methoxy group (3.78 ppm) and a proton of the aromatic ring (27%) shows that they are in the ortho position with respect to one another. With the aid of an NEO we also showed the position of the other methoxy group and of the proton on the olefinic double bond.

On the basis of the spectral characteristics given, luteidine may belong to the group of alkaloids with the homoproaporphine or androcymbine skeleton [2-4]. The choice of the carbon–nitrogen skeleton for this base was made on the basis of the ^{13}C spectra at the natural content of the isotope. As was to be expected, with complete decoupling from protons the spectrum of luteidine (Fig. 2) consisted of 20 peaks. Below 100 ppm are located

V. I. Lenin Tashkent State University. Translated from Khimiya Prirodnykh Soedinenii, No. 3, pp. 354-359, May-June, 1976. Original article submitted October 13, 1975.