N-ACETYLSEPACONITINE — A NEW ALKALOID FROM Aconitum leucostomum

V. A. Tel'nov, M. S. Yunusov, N. D. Abdullaev,
and M. G. Zhamierashvili

UDC 547.944/945

The structure of the new alkaloid N-acetylsepaconitine, and also of a base (IV) formed from lycaconitine in the process of ethanolic extraction in an alkaline medium have been determined on the basis of spectral characteristics. Both bases were isolated from the epigeal part of Aconitum leucostomum.

We have previously [1] reported the isolation from the epigeal part of Aconitum leucostomum, collected in the budding and flowering phase, of an amorphous base (I) not described in the literature with the composition $C_{32}H_{44}N_2O_9$.

The IR spectrum of (I) had an absorption band at 1700 cm^{-1} (broadened band, ester carbonyl, amide carbonyl), and bands at 1600, 1280, 1250, and 750 cm^{-1} (1,2-substituted aromatic ring).

The PMR spectrum of the alkaloid contained the signals of the protons of the methyl part of an ethyl group at 1.11 ppm (3H, triplet, J = 7 Hz), of three methoxy groups at 3.25 and 3.35 ppm (singlets, 6H and 3H, respectively); and in the weak-field region at 6.92-8.52 ppm the signals of four aromatic protons were observed, together with the signal of the proton from Ar—N$\underline{H}$—COR at 10.77 ppm (1H, singlet).

The mass spectrum of (I) was characteristic for diterpene bases of the C-18 series esterified through a hydroxy group at C-4 (lappoconitine, sepaconitine, N-deacetyllappaconitine, etc.) where the maximum peak corresponds to the ejection of a molecule of acid from the molecular ion.

In the mass spectrum of (I), the peak of the $(M - 179)^+$ ion was the maximum peak and corresponded, as in the mass spectrum of lappaconitine (II), to the ejection of acetylanthranilic acid. The compositions of the alkaloids differed by the presence of an additional hydroxy group in (I).

In the ^{13}C NMR spectrum of the new base, 32 signals were observed, the assignment of which was made on the basis of the results of a comparative study of the ^{13}C NMR spectra taken under the conditions of complete and incomplete suppression of carbon—carbon interactions and a comparison of the results obtained with the ^{13}C NMR spectra of known diterpene alkaloids [2].

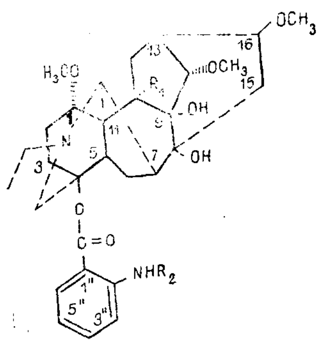
Our results proving the structure of the new alkaloid sepaconitine (III) isolated from the plants A. septentrionale and A. leucostomum have been published [3], and the ^{13}C NMR spectra of sepaconitine and other C-18 diterpene bases of similar structure have been analyzed in detail.

A similar analysis for (I) enabled its structure to be established as N-acetylsepaconitine (Table 1).

On continuing the separation of the mother liquors from the combined alkaloids of A. leucostomum, we isolated an amorphous base with the composition $C_{38}H_{54}N_2O_{11}$ (IV). The PMR spectrum of (IV) showed the signals of the following protons of the methyl part of an ethyl group at 1.02 ppm (3H, triplet, J = 7 Hz); of the methyl of an ethoxycarbonyl group at 1.19 ppm (3H, triplet, J = 7 Hz); of two methylene groups at 2.70 ppm (4H, singlet); of four methoxy groups at 3.22, 3.30, 3.34, and 3.36 ppm (singlets, 3H each); of a one-proton triplet at 3.58 ppm (J = 5 Hz) from H_β-14; a two-proton quartet at 4.10 ppm from a $COO\underline{CH_2}CH_3$ group; and four aromatic protons in the 7.04-8.61 ppm region.

Institute of the Chemistry of Plant Substances, Academy of Sciences of the Uzbek SSR, Tashkent. Translated from Khimiya Prirodnykh Soedinenii, No. 4, pp. 556-559, July-August, 1988. Original article submitted November 2, 1987.

0009-3130/88/2404-0472 $12.50



I. $R_1 = OH$; $R_2 = Ac$
II. $R_1 = H$; $R_2 = Ac$
III. $R_1 = OH$; $R_2 = Ac$

The mass spectrum of (IV) was characteristic for C-19 diterpene alkaloids, the maximum peak being that of the $(M - 31)^+$ ion due to the ejection of a methoxy group from C-1 [4].

The alkaline hydrolysis of (IV) yielded an amino alcohol which was identified by direct comparison with an authentic sample of lycoctonine.

The presence in the mass spectrum of (IV) of the peak of an ion with m/z 248, and also the features of its PMR spectrum showed that the acid residue in (IV) was the product of the ethanolysis of succinylanthranilic acid.

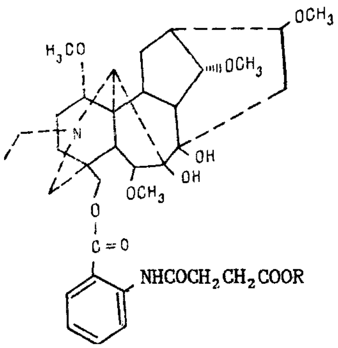
The facts given above showed structure (IV) for the base (see scheme on following page).

Alkaloid (IV) was isolated from the combined alkaloids of A. leucostomum obtained by the alcoholic extraction of the plant.

In view of the fact that we had previously isolated lycaconitine from the total alkaloids of the same plant obtained by chloroform extraction, it is possible to conclude that (IV) was of secondary origin, being formed in the process of ethanolic extraction from lycaconitine

TABLE 1. Chemical Shifts of the Carbon Atoms in the ^{13}C NMR Spectra of N-Acetylsepaconitine (I), Lappaconitine (II), and Sepaconitine (III)

C atom	I	II	III
1	77,8	84,2	78,1
2	26,5	26,2	26,7
3	31,6	31,9	31,9
4	84,7	84,7	83,1
5	44,3	43.6	44,7
6	24,5	26,8	24,5
7	46,9	47,6	47,1
8	74,6	75,6	74,8
9	78,9	78,6	79,8
10	79,6	49,0	79,1
11	56,4	51,0	56,4
12	37,5	24,2	37,6
13	34,7	36,4	34,8
14	87,9	90,0	88,0
15	44,8	44,9	44,9
16	82,8	82,9	83,0
17	61,5	61,5	61,6
18	—	—	—
19	55,6	55,5	55,9
$N-CH_2$	48,5	49,9	48,9
CH_3	13,4	13,5	13,5
1′	56,3	56,5	56,2
14′	58,0	57,9	58,1
16′	56,2	56,1	56,2
$NHC{=}O$	169,1	169,5	—
CH_3	25,5	25,6	—
$H_4C_6-C{=}O$	167,4	167,7	167,4
1″	115,8	115,9	112,1
2″	141,7	141,8	150,6
3″	120,3	120,4	116,3
4″	134,4	134,6	133,9
5″	122,8	122,6	116,9
6″	131,0	131,3	131,9



IV. $R = C_2H_5$
V. $R = CH_3$

[5, 6]. A methyl ester derivative of lycaconitine has been described in the literature — the alkaloid septentriodine (V), isolated from A. septentrionale [7].

EXPERIMENTAL

IR spectra were obtained on a UR-20 spectrophotometer, mass spectra on a MKh-1310 mass spectrometer fitted with a system for direct introduction into the ion source, PMR spectra on JNM-4H-100/100 MHz and BS-567A Tesla instruments in deuterochloroform with HMDS as internal standard (values given in the δ scale), and ^{13}C NMR spectra on a Varian CFT-20 spectrometer ($CDCl_3$, 0 – TMS).

Isolation of the Base (IV). The mother liquor from the combined alkaloids of A. leucostomum (100 g), after the separation of the lappaconitine [8], was dissolved in 1000 ml of chloroform, and the bases were extracted with 5% sulfuric acid (12 × 50 ml).

The chloroform solution after the extraction of the alkaloids was washed with 2% aqueous sodium carbonate and with water and was filtered and dried over anhydrous sodium sulfate. The solvent was distilled off. The residue (17 g) was dissolved in 5% aqueous sulfuric acid, and the resulting solution was washed with ether and was fractionally alkalinized with sodium carbonate to pH 6.5, 8.0, and 10.0, the alkaloids being extracted each time first with hexane—ether (1:1) and then with ether.

The ethereal extract obtained at pH 8 (2.5 g) was deposited on a column of deactivated alumina (1:60) and the alkaloids were eluted with ether. Fractions with a volume of 25 ml were collected.

Fractions 6-10 (0.19 g) were dissolved in 2% aqueous sulfuric acid and the solution was alkalinized fractionally with sodium carbonate solution to pH 6.0, 7.0, 8.0, and 10.0, the alkaloids being extracted each time with hexane. The hexane fraction obtained at pH 7 (90 mg) was chromatographed on a column of silica gel (KSK, 1:50) with elution by ether and the collection of 7-ml fractions. On treatment with hexane, fractions 4-7 yielded the amorphous base (IV) (60 mg).

Hydrolysis of (IV). The base (0.05 g) was heated in the water bath in 8 ml of a 2% aqueous methanolic solution of NaOH for 1.5 h. The solvent was distilled off, the residue was dissolved in water, and the solution was extracted with ether. After the solvent had been driven off, the residue was recrystallized from ethanol—ether. This gave lycoctonine with mp 135-138°C (0.02 g).

CONCLUSIONS

1. A new alkaloid, N-acetylsepaconitine, has been isolated from the epigeal part of Aconitum leucostomum, and its structure has been established.

2. The mother liquors from the combined alkaloids of the same plant have yielded a base (IV) formed in the process of ethanolic extraction from lycaconitine.

LITERATURE CITED

1. M. G. Zhamierashvili, V. A. Tel'nov, M. S. Yunusov, S. Yu. Yunusov, A. Nigmatullaev, and K. Taizhanov, Khim. Prir. Soedin., 658 (1980).
2. S. W. Pelletier, Alkaloids; Chemical and Biological Perspective, Vol. II, Wiley—Interscience, New York (1984), pp. 368, 406, 441.
3. S. K. Usmanova, V. A. Tel'nov, M. S. Yunusov, N. D. Abdullaev, A. I. Shreter, and G. B. Filippova, Khim. Prir. Soedin., 879 (1987).

4. M. S. Yunusov, Ya. V. Rashkes, V. A. Tel'nov, and S. Yu. Yunusov, Khim. Prir. Soedin., 515 (1969).
5. S. Yu. Yunusov and N. K. Abubakirov, Zh. Org. Khim., 24, 723 (1959).
6. S. W. Pelletier, F. W. Harraz, W. W. Badawi, Tantiraksachai Teng-peng Waug, and Szu-ying Chen, Heterocycles, 24, No. 7, 1853 (1986).
7. S. W. Pelletier and R. S. Sauhney, Heterocycles, No. 12, 377 (1979).
8. V. A. Tel'nov, M. S. Yunusov, and S. Yu. Yunusov, Khim. Prir. Soedin., 583 (1970).

ALKALOIDS OF *Papaver fugax*

V. A. Chelombut'ko and I. A. Israilov

UDC 517.943

Papaver fugax growing on the shore of Lake Kazenoi Am in the Checheno-Ingushskii ASSR at the boundary with the Dagestan ASSR has yielded 0.39% of alkaloids. Seven alkaloids have been isolated, of which cheilanthifoline, scoulerine, and reticuline have been detected in this species for the first time, while it is the first time that d-remeroline has been found in a plant of the *Papaver* genus.

Papaver fugax Poir. (*Papaver caucasicum* Bieb.) from the family Papaveraceae, *Meconidium* Spach (*Miltantha* Bernh.) section, is found in the USSR flora only in the Caucasus (Ciscuasia, Dagestan, East and South Transcaucasia [1, 2]) but it also grows in Turkey and Iran [3, 4].

Information on the alkaloid composition of *P. fugax* is fairly contradictory, which indicates a certain variability of the alkaloids present in it. Already, more than 23 alkaloids isolated from various samples of this species abroad [5-7] and also in our country [8] are known.

We have investigated *P. fugax* collected in the fruit-bearing period (September 1985) on the shore of the high-mountain lake Kazenoi Am in the Checheno-Ingushskii ASSR at the boundary with the Dagestan ASSR. Ethanolic extraction gave 0.39% of total alkaloids. From the nonphenolic fraction of the total, by chromatography on a column of silica gel, remerine and mecambrine were isolated, and from the phenolic fraction cheilanthifoline, scoulerine, armepavine, reticuline, and base (I). These alkaloids were identified by their spectral characteristics and also by the absence of depressions of the melting points of mixtures with authentic samples.

Base (I) was optically active. Its UV spectrum had absorption maxima at 222, 280, and 315 nm ($\log \varepsilon$ 4.25, 4.01, and 3.85). The mass spectrum showed the peaks of ions with m/z 295 (M^+), 280, 278, and 252, which are characteristic for the aporphine alkaloids [9]. The PMR spectrum contained the signals of the protons of a N-methyl group at 2.45 ppm and of a methylenedioxy group at 6.02 and 6.06 ppm in the form of one-proton doublets with $J \sim 1.5$ Hz. In the aromatic region of the spectrum there were a one-proton singlet at 6.61 ppm, a one-proton doublet at 7.98 ppm with $J = 9$ Hz, and a multiplet at 6.75-6.88 ppm corresponding to two protons. The spectral characteristics showed that base (I) belonged to the aporphine alkaloids with substituents in positions 1, 2, and 9. When the base was methylated with diazomethane, a O-methyl ether identical with isolaureline (II) was obtained [10]. Consequently, the base has structure (I) (see scheme on following page).

The alkaloid remeroline with structure (I) has previously been isolated from *Roemeria refracta* but its specific rotation was not determined. Thus, base (I) is d-remeroline.

Pyatigorsk Pharmaceutical Institute. Institute of the Chemistry of Plant Substances, Academy of Sciences of the Uzbek SSR, Tashkent. Translated from Khimiya Prirodnykh Soedinenii, No. 4, pp. 559-562, July-August, 1988. Original article submitted November 9, 1987; revision submitted February 4, 1988.