Intebrinine (IV) – hydrochloride, mp 223-225°C, $C_{19}H_{21}NO_4 \cdot HCl$. Yield 76%.

Intebrimine (V) – hydrochloride, mp 171-172°C, $C_{20}H_{25}NO_4 \cdot HCl$. Yield 81%.

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UMBROFINE AND 6-ACETYLUMBROFINE – NEW C_{18}-DITERPENE ALKALOIDS FROM *Aconitum umbrosum*

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Two new alkaloids – umbrofine and 6-acetylumbrofine – have been isolated from *Aconitum umbrosum*, and their structures have been established on the basis of spectral characteristics.

Continuing a study of the alkaloids of the roots of *A. umbrosum* we have isolated, in addition to the known alkaloid lycaconitine [1, 2], two new bases: umbrofine (I), $C_{23}H_{37}NO_6$, mp 110-112°C and 6-acetylumbrofine (II), $C_{25}H_{39}NO_7$, mp 174-175°C (HRMS 465.2783).

The IR spectrum of (I) showed absorption bands of hydroxy groups at 3600 and 3400-3200 cm^{-1}.

The PMR spectrum of umbrofine contained signals from the protons of the following groups: the methyl of a N-ethyl group at (ppm) 1.08 (3H, t, J = 7.5 Hz) and three methoxy groups at 3.27, 3.37, and 3.44 (s, 3H, each); and one-proton signals at 3.64 (1H, t, J = 4.5 Hz) and 4.24 (1H, s).

In the mass spectrum of (I) the maximum peak was that of the $(M - 31)^+$ ion resulting from the ejection of a methoxy group at C-1 [3]. In the ^{13}C NMR spectrum of umbrofine there were 23 signals: 3 singlets, 10 doublets, 6 triplets, and 4 quartets.

The IR spectrum of 6-acetylumbrofine contained the absorption bands of hydroxy groups at (cm^{-1}) 3554 and 3460 and of an ester carbonyl at 1730 cm^{-1}.

IN the PMR spectrum of (II) signals of the protons of the following groups were observed: the methyl of a N-ethyl group at (ppm) 0.99 (3H, J = 7.5 Hz), an acetyl group at 1.99 (3H, s), and three methoxy groups at 3.22, 3.30, and 3.38 (s, 3H each); and one-proton signals at 3.68 (1H, t, J = 4.5 Hz) and 5.13 (1H, s).

In the mass spectrum of 6-acetylumbrofine the maximum peak was, as in that of (I), that of a $(M - 31)^+$ ion.

The ^{13}C NMR spectrum of (II) contained 25 signals; 4 singlets, 10 doublets, 6 triplets, and 5 quartets.

The alkaline hydrolysis of 6-acetylumbrofine gave an aminoalcohol $C_{23}H_{37}NO_6$, mp 110-112°C, which was identified by TLC, a mixed melting point, and mass, IR, and PMR spectra as umbrofine.

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TABLE 1. Chemical Shifts of the Carbon Atoms in the ^{13}C NMR Spectra of Umbrofine (I), 6-Acetylumbrofine (II), Vaginatine (IV), and Acosanine (V)

C	I	II	III	IV	V
1	86,1	86,0	86,7	85,0	84,3
2	26,3	26,1	26,2	25,1	25,8
3	30,8	30,7	30,1	32,1	32,0
4	36,4	35,9	36,4	38,8	38,5
5	46,2[a]	45,8[a]	45,6	46,4	44,1
6	80,3	79,4	29,0	80,2	80,8
7	89,7	88,5	46,1	88,0	87,5
8	76,4	76,1	73,2	76,9	78,7
9	47,5	47,1	47,2	45,0	54,4
10	37,8	38,0	45,9	37,4	37,3
11	48,7	48,2	48,8	47,9	48,3
12	29,3	30,1	27,8	27,7	29,0
13	45,9[a]	46,3[a]	38,1	46,0	45,8
14	84,8	84,2	75,7	75,4	84,3
15	35,2	35,1	39,2	34,0	36,3
16	82,5	81,9	82,9	82,1	82,4
17	63,2	63,6	63,3	65,9	65,8
18	—	—	—	78,9	79,2
19	50,3	50,1	50,4	54,0	53,6
N—CH_2	49,7	49,9	49,7	51,6	51,6
CH_3	13,6	13,9	13,7	14,4	14,6
C(1)′	56,1[b]	56,2[b]	56,4	55,8	55,7
C(14)′	57,9	57,8	—	—	57,8
C(16)′	56,3[b]	56,5[b]	56,5	56,4	56,3
C(18)′	—	—	—	59,5	59,5
C=O	—	169,5	—	—	—
CH_3	—	21,6	—	—	—

a and b in (I) and (II) – uncertain assignment of the signals.

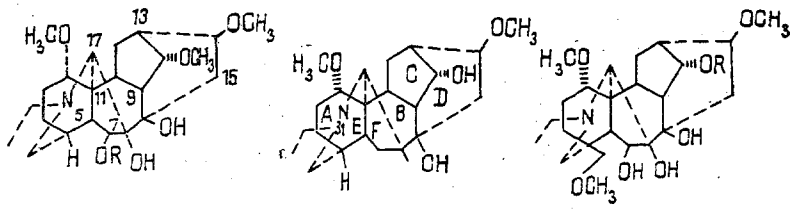
On the basis of an analysis of their spectral characteristics, umbrofine and 6-acetylumbrofine were assigned to the C_{18}-diterpene alkaloids.

The presence in the mass spectrum of each alkaloid of $(M - 31)^+$ as the maximum ion and also of one-proton signals at (ppm) 3.64 (I) and 3.68 (II) with SSCCs of 4.5 Hz (C-14 H-β) in the PMR spectra showed the presence of methoxy groups at C-1 and C-14 both in umbrofine and in 6-acetylumbrofine [3, 4].

In the PMR spectrum of (I) a broadened one-proton singlet was observed at 4.24 ppm, while in that of (II) the analogous signal appeared at 5.13 ppm. Consequently, there is an OH group at C-6 in umbrofine and an acetoxy group at C-6 in 6-acetylumbrofine [5].

In the ^{13}C NMR spectra of (I) and (II) the chemical shifts of the carbon atoms of rings A and E were the same as in the ^{13}C NMR spectra of alkaloids of the C_{18} series having a hydrogen atom at C-4: contortumine, delavaconine, aconosine (III), etc. [6].

On the basis of what has been said above and also of a comparison of the ^{13}C NMR spectra of umbrofine and 6-acetylumbrofine with the ^{13}C NMR spectra of vaginatine (IV) [7] and acosanine (V) [8], structures (I) and (II) have been established for the new alkaloids.



I. R=H; II. R=Ac III IV. R=H; V. R=CH_3

It must be mentioned that it was difficult to saponify the acetoxy group of (II). The reaction was monitored by TLC. Only after 2.4 h was 6-acetylumbrofine no longer detected in the reaction mixture.

Difficulty in saponifying an acetoxy group at C-1 in alkaloids with a lycoctonine skeleton has been shown previously [9].

At the present time, 36 diterpene alkaloids of the C_{18} series have been isolated. They are found mainly in Aconitum species growing in Central Asia, in the Far East, and in China. The majority of alkaloids of the C_{18} series have no oxygen-containing substituent at C-6, with the exception of five bases containing methoxy or keto groups: delbine, delboxine [10], taguaconitine [11], hispaconitine [12], and leuconine [13].

Umbrofine and 6-acetylumbrofine are the first diterpene alkaloids of the C_{18} series containing hydroxy and acetoxy groups, respectively, at C-6.

EXPERIMENTAL

IR spectra were taken on a UR-20 spectrometer; mass spectra on a MKh-1301 mass spectrometer fitted with a system for direct introduction into the ion source; and PMR spectra on JNM-4H-100/100 MHz and BS-567A (Tesla) instruments in deuterochloroform with HMDS as internal standard (values given on the δ scale). ^{13}C NMR spectra were recorded on a Bruker AM-300 spectrometer in deuterochloroform. Chemical shifts are given relative to the internal standard TMS.

For TLC we used: KSK silica gel (0-80 mesh) and alumina "for chromatography" (0-80 mesh). Systems: benzene-methanol (4:1), chloroform-ether-methanol (30:10:1), and petroleum ether-ether-methanol (30:10:1).

For column chromatography we used deactivated alumina "for chromatography" and KSKG silica gel.

Melting points are uncorrected.

Umbrofine (I). The acidic mother solution from the chloroform fraction of the total alkaloids (4.8 g) after the separation of lycaconitine perchlorate [2] was treated with chloroform (5 × 40 ml, fraction A). The insoluble residue amounted to 1.9 g (fraction B).

Fraction A was washed with sodium carbonate solution, and the alkaloids were extracted with 2% sulfuric acid (8 × 25 ml). The acid extracts were neutralized (pH 7) with $NaHCO_3$, and alkaloids were extracted with ether (3 × 70 ml, 0.43 g, fraction C). The mother solution was made alkaline (pH 10) with Na_2CO_3 and was extracted with ether (5 × 70 ml) (0.67 g, fraction D) and with chloroform (4 × 100 ml) (1.13 g, fraction E).

Fraction D (0.67 g) was deposited on a column of silica gel (1:100) and elution was performed with benzene and benzene-methanol (0.5-10% of methanol). A total of 110 25-ml fractions was collected. On treatment with acetone, fractions 25-34 (0.5% of methanol) deposited umbrofine (63 mg), mp 110-112°C [hexane-acetone (1:2)].

IR (KBr): 3600, 3400-3200, 1470, 1390, 1368, 1328, 1302, 1250, 1206, 1172, 1118, 1102, 1070, 1028, 998, 994, 968, 932, 887, 863, 753 cm^{-1}.

M^+ 423(11.3), 408(9.6), 406(9.4), 405(6), 392(100), 376(11.2), 374(5.0%).

6-Acetylumbrofine (II). The mother solution from the ether fraction of the alkaloids (7.96 g) after the separation of lyaconitine perchlorate and evaporation of the alcohol was dissolved in water (150 ml). Alkaloids were extracted from the acidic aqueous solution with chloroform (3 × 40 ml). The acidic chloroform extract was washed with 2% aqueous sodium solution and then with water, and it was dried over anhydrous sodium sulfate and the solvent was distilled off. The residue amounted to 2.34 g (fraction 1).

The acidic aqueous solution was made alkaline with sodium carbonate and was extracted successively with: petroleum ether (3 × 150 ml, fraction 2, 1.03 g); ether (3 × 100 ml, fraction 3, 2.63 g); and chloroform (4 × 100 ml, fraction 4, 1.73 g).

Fraction 2 was chromatographed on a column of alumina (1:50) with elution by benzene and benzene-methanol (0.5-10%). A total of ninety 15-ml fractions was collected.

Fractions 11-20 (0.5% of methanol, 0.37 g) were rechromatographed on a column of alumina (1:75) with elution by the same solvents. Fractions 6-10 yielded 6-acetylumbrofine, mp 174-175°C (0.16 g).

IR (KBr): 3554, 3460 (OH), 1730 (C=O), 1475, 1455, 1370, 1345, 1330, 1270, 1232, 1214, 1170, 1122, 1110, 1043, 1080, 1045, 1030, 1010, 994, 968, 934, 920, 887, 860, 814, 798, 764 cm^{-1}.

M^+ 465(17), 450(3.2), 434(100), 432(5.9), 422(2.5), 406(72), 390(12), 374(10), 362(5.9), 346(6.8).

Aminoalcohol from 6-Acetylumbrofine. A mixture of 0.04 g of 6-acetylumbrofine and 10 ml of 2% aqueous methanolic KOH was heated in the water bath for 2.5 h. The completion of the reaction was monitored by TLC. After the solvent had been distilled off, the residue was dissolved in water and extracted with ether (3 × 40 ml). This gave an aminoalcohol (0.025 g), mp 110-112°C, which was identified as umbrofine by a direct mixed melting point with an authentic sample, by TLC, and by a comparison of mass, IR, and PMR spectra.

IR (KBr): 3548, 3400-3200, 1471, 1392, 1368, 1326, 1302, 1250, 1205, 1170, 1118, 1100, 1068, 1028, 998, 995, 967, 932, 886, 863, 752 cm^{-1}.

M^+ 423(11.2), 408(9.7), 406(9.4), 405(5.9), 392(100), 376(11.0), 374(5.3).

PMR, ppm: $N-CH_2-CH_3-$ 1.06 (3H, t), J = 7.5 Hz; $3OCH_3$ groups at 3.28, 3.37, and 3.42 (3H each, s), β-H-C-14 at 3.65 (t, J = 4.5 Hz), α-H-C-6 at 4.23 (br.s).

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Berberis ALKALOIDS.

XXIII. STRUCTURE OF TURCBERINE

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Berberine, magnoflorine, palmatine, columbamine, jatrorhizine, epiberberine, berbamine, O-methylisothalicberine, armepavine, corypalline, glaucine, and corydine and the new alkaloid turcberine have been isolated from Berberis turcomanica Kar., and the structure of turcberine has been established. Apart from berberine, this is the first time that any of these alkaloids have been isolated from this species of barberry, while this is the first time that corydine and armepavine have been isolated from the genus Berberis.

We have investigated the alkaloid composition of the leaves and young shoots of Berberis turcomanica Kar. growing in Turkmenia (Kopet Dagh, environs of Bendeinsk) in the stage of incipient flowering.

The isolation of berberine from the roots of this plant has been reported previously [1].

Extraction of the leaves successively with chloroform and ethanol yielded 0.27% of total alkaloids, of which 0.07% consisted of berberine. By separating the total mixture so obtained on a column of silica gel we isolated glaucine, corydine, armepavine, and corypalline. The main alkaloid in the leaves was glaucine.

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