$\lambda<0.45$) calculated at this stage. Further refinement was carried out in the anisotropic approximation for the nonhydrogen atoms and in the isotropic approximation for the hydrogen atoms; the thermal parameters of the H atoms were not taken into account and were given as B = 4 Å^2. Finally (R = 0.054, R = 0.038).

The coordinates of the nonhydrogen atoms and their anisotropic temperature parameters B_{ij} are given in Table 3. Table 4 gives the coordinates of the hydrogen atoms and the distances to the atoms connected with them.

SUMMARY

A complete x-ray structural investigation of the spirobenzylisoquinoline alkaloid sibiricine in the form of the base has been carried out. The bond lengths and valence angles are the usual ones.

LITERATURE CITED

1. S.-M. Nasirov, A. A. Ibragimov, V. G. Andrianov, S. Kh. Maekh, Yu. T. Struchkov, and S. Yu. Yunusov, Khim. Prirodn. Soedin., 334 (1976).
2. R. H. F. Manske, Can. J. Res., 14B, 354 (1936).
3. R. H. F. Manske, R. Rodrigo, D. B. MacLean, D. E. Gracey, and J. K. Sannders, Can. J. Chem., 47, 3585 (1969).
4. B. C. Nalliah, D. B. MacLean, R. G. A. Rodrigo, and R. H. F. Manske, Can. J. Chem., 55, 922 (1977).
5. M. Mathew and G. J. Palenik, Acta Crystallogr., B31, 2899 (1975).
6. A. C. Macdonald and J. Trotter, J. Chem. Soc., B, 929 (1966).
7. K. S. Pitzer and W. E. Donath, J. Am. Chem. Soc., 81, 3213 (1959).
8. N. A. Aninger, J. Am. Chem. Soc., 81, 5727 (1959).
9. F. V. Brutcher and W. Baner, J. Am. Chem. Soc., 84, 2233 (1962).

ALKALOIDS OF *Haplophyllum latifolium*

THE STRUCTURE OF HAPLATINE

E. F. Nesmelova, I. A. Bessonova, and S. Yu. Yunusov

UDC 547.944/945

Continuing a study of the alkaloids of *Haplophyllum latifolium* Kar. et Kir. [1], we have investigated the epigeal part and roots of plants growing in the Chimkent oblast in the "Syrdar'ya" sovkhoz [communal farm] in the phase of vigorous flowering to the beginning of fruit bearing and the dying off of the epigeal part. The raw material was extracted with methanol. The evaporated extract was separated according to solubilities in organic solvents and then by the method described in a previous paper [1]. The amounts of alkaloids in the epigeal part and roots of *H. latifolium* were as follows (% of the weight of the dry raw material; the symbol + denotes alkaloids present in amounts of less than 0.005%):

Phase of development	Plant organ	Total alkaloids	Skimmianine	Evoxine	Haplopine	Glycoperine	7-Isopentenyloxy-γ-fagarine	Haplamine	Haplamide	Haplamidine
Flowering—beginning of fruit-bearing	Epigeal part	0,74	0,21	0,03	+	+	+	0,01		+
	Roots	0,17	0,02	0,01						
Withering of the epigeal part	Epigeal part	0,72	0,14	0,03	0,01	+		0,01	0,01	+
	Roots	0,06	+		+					

Institute of the Chemistry of Plant Substances, Academy of Sciences of the Uzbek SSR, Tashkent. Translated from Khimiya Prirodnykh Soedinenii, No. 6, pp. 758-764, November-December, 1978. Original article submitted July 20, 1978.

0009-3130/78/1406-0645$07.50

It can be seen from the figures given that alkaloids are present mainly in the epigeal part, their amount in the roots being considerably smaller. The dry died-off epigeal part is as rich in alkaloids as the green part, the alkaloids being localized mainly in the fruit and leaves (0.98%). The amount of alkaloids in the dry died-off stems is 0.23%. In the period of vegetation to the beginning of fruit-bearing alkaloids are present mainly in the buds, flowers, and fruit (1.35%) and in smaller amount in the leaves (0.6%).

The qualitative and quantitative compositions of the individual components in the epigeal part do not vary as considerably as in *H. perforatum* [2], but it may be mentioned that as the plant develops the amount of skimmianine falls, the 7-isopentenyloxy-γ-fagarine disappears, and haplamide appears. Only from *H. latifolium* growing in the Chimkent oblast did we isolate five known alkaloids — skimmianine, evoxine, haplopine, glycoperine, and 7-isopentenyloxy-γ-fagarine, which were identical with samples obtained from *H. perforatum* [2] — three new ones, called haplamide, haplamidine, and haplatine, and a neutral substance identified as β-sitosterol [3].

Haplamide and haplamidine have been shown to be putrescine derivatives [1]. For haplatine we have proposed the furanoquinoline structure (I) [4] on the basis of the spectral characteristics of the alkaloid and of its acetyl derivative (II) and also because the acid hydrolysis of (II) gives haplopine (III). In the present paper we give the results of a study of the isomerization and hydrogenation reactions of haplatine, confirming its structure.

Heating haplatine with methyl iodine in a sealed tube led to a mixture of substances from which we obtained compounds (IV), mp 165-166°C, mol. wt. 329 (mass spectrometry), and (V), mp 126-127°C, mol. wt. 343 (mass spectrometry). Their IR and UV spectra and also the dark crimson coloration of the crystals of (IV) ($CDCl_3$) had two pairs of doublets, at 1.83, 3.08 ppm (J = 10 Hz) and 2.73, 3.02 ppm (J = 2.5 Hz), representing the ortho protons of a benzene ring and the α,β-protons of a furan ring. Two three-proton singlets at 5.89 and 6.19 ppm are due to the protons of methoxy and N-methyl groups. Other signals in the spectrum of (IV) are observed at (ppm) 4.57 (1 H, triplet, J = 7 Hz, —CH=); 5.25 (2 H, doublet, J = 7 Hz, —O—CH_2—); 5.81 (2 H, singlet, —CH_2OH); and 8.16 (3 H, singlet, =C—CH_3) and represent the protons of the O-allyl side chain. These facts show that (IV) is isohaplatine (Scheme 1).

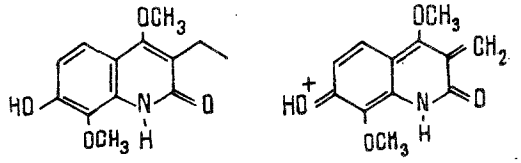
The strongest ion peaks in the mass spectrum of isohaplatine are the following, m/e (%): 329 (M^+, 45), 245 (70), 230 (100), 216 (14), 202 (24), and 201 (20). The ion with m/e 245 is formed by the detachment of the side chain from the M^+ ion with the migration of hydrogen, and the other ions by the breakdown of the fragment with m/e 245. The splitting out of a methyl radical and the subsequent elimination of carbon monoxide or a formyl radical gives the ions with m/e 230, 202, and 201, and the splitting out of a formyl radical the ion with m/e 216. Thus, the main difference between the spectrum of isohaplatine and that of haplatine itself [4] is that the ion with m/e 230 has the maximum intensity and there is no peak of an ion with m/e 227 as is present with a high intensity (91%) in the spectrum of haplatine.

According to its mass spectrum [m/e (%): 343 (M^+, 32), 246 (12), 245 (70), 244 (14), 230 (100), 216 (28), 202 (22), and 201 (38)], compound (V) is the O-methyl ether of isohaplatine. Consequently, the reaction of methyl iodine with haplatine leads to isomerization of the 4-methoxyfuranoquinoline nucleus into a N-methylfurano-4-quinolone nucleus and partial methylation of the primary alcohol group.

The results of a study of the hydrogenation of haplatine in the presence of a platinum catalyst showed that this led to two products; a hexahydro derivative (VI) with mol. wt. 335 (mass spectrometry) and a phenolic compound (VII), mol. wt. 249 (mass spectrometry) which was identified as tetrahydrohaplopine [6] (see Scheme). Consequently, in the catalytic hydrogenation of (I), in addition to the hydrogenolysis of the furan ring, on the one hand, the double bond of the side chain is hydrogenated and, on the other hand, the O-allyl ether bond undergoes hydrogenolysis. The results obtained show chemically the presence of a double bond in the allyl position to the ether oxygen of the side chain and confirm the structure of haplatine.

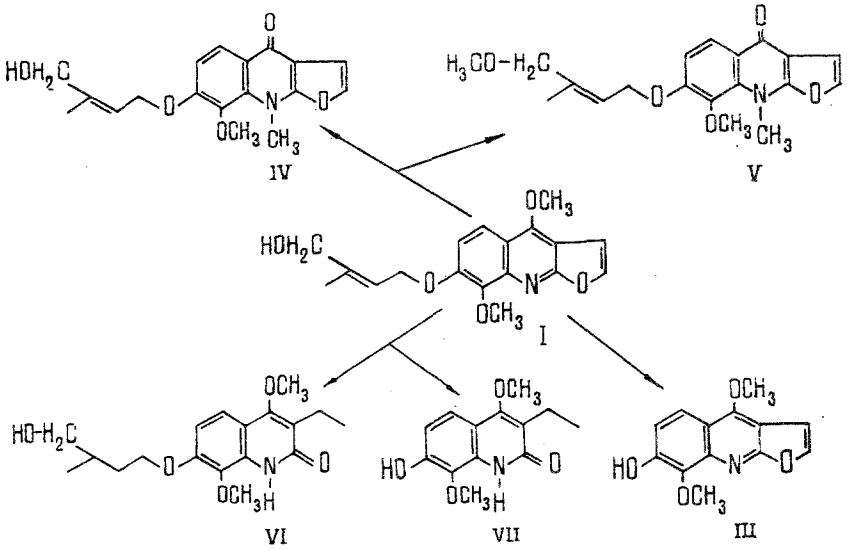
A characteristic feature of the mass spectra of (V) and (VII) is the presence of the peak of an ion with m/e 234 having the maximum intensity which is formed in the case of (VI) by the detachment of the side chain with migration of hydrogen to the oxygen atom and the

subsequent splitting out of the methyl radical. This process is favored by the stability of the fragment with m/e 234 due to a system of conjugated double bonds, which is possible only where the O-alkyl chain is present in position 7 [7]:



VI. M − 86 (97)
VII. M^+ (96)
M−86−15 (100)
M−15 (100)

On acid hydrolysis, haplatine formed haplopine (III). The facts given above show that haplatine has the structure (I).



Scheme 1. Transformations of haplatine.

We did not detect the new alkaloid haplatine and its analogs — 7-isopentenyloxy-γ-fagarine, evoxine, skimmianine, haplopine, and glycoperine — in the epigeal part of the plant growing in Kirghizia [1]. This indicates that the composition of the alkaloids in *H. latifolium* depends strongly on its growth site.

EXPERIMENTAL

The UV spectra were recorded on a Hitachi EPS-3T spectrophotometer (in C_2H_5OH), the IR spectra on a UR-20 instrument (in KBr), the mass spectra on an MKh-1303 instrument, and the PMR spectra of (I) and (IV) on a JNM-4H-100 MHz spectrophotometer and that of (II) on a JNM C-60 HL instrument (in $CDCl_3$, τ scale). For control and identification by TLC we used KSK silica gel with 5% of gypsum in the following systems: 1) toluene—ethyl acetate—formic acid (5:4:1); 2) benzene—methanol (4:1); 3) ether.

Isolation and Separation of the Combined Alkaloids. The dry comminuted epigeal part (14 kg) collected in the period of vigorous flowering to the beginning of fruit-bearing on May 13, 1974, was extracted with methanol. The black resin that deposited when the methanolic extract was evaporated (709 g, A) was separated off. The mother liquor was treated with ether. Chromatography of the ether-soluble fraction on alumina gave an oil (93 g) containing no alkaloids. The ether-insoluble fraction (135 g) was treated with chloroform. The chloroform solution (B) was shaken with 10% sulfuric acid, and then with 4% caustic soda solution.

The acid solution was made alkaline and the alkaloids were extracted with chloroform (86.32 g, main fraction). The alkaline solution contained no alkaloids. Distillation of the chloroform from solution B gave a neutral fraction (28 g) from which crystals of haplamidine (0.28 g) with mp 139-140°C (ethanol) were obtained by chromatography on silica gel. The mixture of alkaloids (86.32 g) was dissolved in chloroform and the solution was washed with 4% caustic soda (C). When the chloroform solution was concentrated, it deposited crystals of skimmianine with mp 176-177°C (methanol) (3.35 g).

Chromatography of the mother liquor on alumina followed by rechromatography of the individual fractions on silica gel gave skimmianine (20.25 g), evoxine (2.81 g) with mp 145-155°C (acetone), haplatine (0.68 g) with mp 139-140°C (benzene), 7-isopentenyloxy-γ-fagarine (0.06 g) with mp 105-106°C (ethyl acetate), and glycoperine (0.14 g) with mp 224-225°C (methanol). The alkaline solution C was saturated with ammonium chloride, and the phenolic alkaloids were extracted with ether and chloroform. On evaporation of the ether, crystals of haplopine deposited with mp 204-205°C (methanol) (0.12 g). Chromatography of the chloroform solution on alumina also gave haplopine (0.2 g).

Fraction A (709 g) was separated similarly into basic, acidic, and neutral fractions. Chromatography on alumina of the basic fraction (17.28 g gave skimmianine (5.9 g), evoxine (0.95 g), haplopine (0.21 g), and haplatine (0.14 g). The total amounts obtained from the epigeal part (14 kg) were 29.5 g of skimmianine, 3.76 g of evoxine, 0.53 g of haplopine, 0.82 g of haplatine, 0.06 g of 7-isopentenyloxy-γ-fagarine, and 0.28 g of haplamidine.

Methanol extraction of the dried roots (700 g) collected in the flowering to beginning of fruit-bearing period on May 13, 1974, gave a mixture of alkaloids (1.15 g) from which we isolated skimmianine (0.13 g) and evoxine (0.01 g).

Similarly, from the leaves (1000 g) we obtained 6.14 g of a mixture of bases from which we isolated skimmianine (3.1 g), evoxine (0.61 g), 7-isopentenyloxy-γ-fagarine (0.14 g), and haplatine (0.1 g), and from the dry buds, flowers, and unripe fruit (1410 g) we obtained 19 g of a mixture of bases including 7.34 g of skimmianine, 0.62 g of evoxine, and 0.1 g of haplamidine.

The dry died-off epigeal part (29 kg) collected on June 14, 1974 was extracted with 80% methanol. We separated the resin that had deposited (700 g, A) from the evaporated extract, and the aqueous mother liquor was extracted with ether (72 g, B), and chloroform (990 g, C). Residue A was treated with petroleum ether to eliminate the fatty fraction containing no alkaloids (150 g) and it was then dissolved in chloroform and was separated by the method described above into basic, acidic, and neutral fractions.

From the neutral fraction by gradient elution ethereal eluates yielded skimmianine (0.2 g) and β-sitosterol (20.1 g) with mp 140-141°C (acetone); from the main ethereal fraction (5.45 g) we obtained skimmianine (2.63 g), haplatine (0.41 g), and evoxine (0.05 g); and from the main chloroform fraction (2 g) we obtained haplopine (0.24 g). Ethereal fraction B (72 g) was treated with petroleum ether to eliminate a fatty fraction (50 g) and was chromatographed on alumina. The ethereal eluates gave skimmianine (10.67 g).

Rechromatography of the chloroform and chloroform–ethanolic eluates on alumina and silica gel gave haplamide (0.8 g), haplatine (0.63 g), and evoxine (1.91 g). After elimination of a fatty fraction (108 g) with petroleum ether, the chloroform fraction C (990 g) was dissolved in chloroform (1 liter) and extracted with 10% sulfuric acid, and then with 4% caustic soda solution. Distillation of the chloroform solution gave a neutral fraction (620 g), the rechromatography of which yielded skimmianine (0.6 g), haplatine (0.22 g), haplamide (0.56 g), and haplamidine (0.13 g).

The acid solution was made alkaline with ammonia and was extracted with ether (80.02 g) and chloroform (106.32 g).

The aqueous ammoniacal solution was evaporated to dryness and the residue was chromatographed on alumina. Chloroform eluates yielded haplamide (2.2 g). Treatment of the combined ether-soluble alkaloids (80.02 g) with acetone led to the isolation of skimmianine (10.03 g). Chromatography of the mother liquor gave skimmianine (5.84 g), haplatine (1.68 g), evoxine (7.97 g), and haplopine (0.87 g). The analogous treatment with chloroform of the combined alkaloids (106.32 g) gave skimmianine (13 g), haplatine (0.35 g), haplopine (0.78 g), and glycoperine (0.4 g).

In total, from the died-off epigeal part we isolated 42.97 g of skimmianine, 9.93 g of evoxine, 1.89 g of haplopine, 0.4 g of glycoperine, 3.29 g of haplatine, 3.56 g of haplamide, 0.13 g of haplamidine, and 20.1 g of β-sitosterol.

The methanolic extraction of the stems (400 g), roots (940 g), and leaves and fruit (550 g) collected in the period of the dying off of the epigeal part on June 14, 1974, gave a mixture of alkaloids. The mixture of bases from the roots (0.91 g) yielded skimmianine (0.06 g), those of the stems (0.6 g) skimmianine (0.03 g) and haplopine (0.01 g), and those of the leaves and fruit (5.4 g) skimmianine (0.79 g), evoxine (0.1 g), and haplopine (0.06 g).

Haplatine (I) formed colorless needles with mp 139-140°C (benzene). In UV light in system 1 it had a green fluorescence, and in system 2 and 3 blue. It was shown up by the Dragendorff reagent.

Acetylhaplatine (II) was obtained by heating haplatine (30 mg), acetic anhydride (0.5 ml), and pyridine (one drop) in the water bath for 1 h. It formed crystals with mp 87-88°C from a mixture of ether and acetone. Mass spectrum, m/e (%): 371 (M^+ 27), 245 (76), 244 (73), 230 (27), 227 (98), 216 (60), 127 (100). PMR spectrum, ppm: 2.10 and 2.91 (doublets, 1 H each, J_{ortho} = 10 Hz, H_5 and H_6); 2.48 and 3.04 (doublets, 1 H each, J = 3 Hz, H_α and H_β); 5.68 and 5.98 (singlets, 3 H each, 2 OCH_3); 4.30 (broadened triplet, 1 H, J = 6.5 Hz, =CH—); 5.24 (broadened doublet, 2 H, J = 6.5 Hz, —O—CH_2—); 5.40 (singlet, 2 H, —CH_2—OAc); 8.00 (singlet, 3 H, —$OCOCH_3$); 8.17 (doublet, 3 H, J = 1.5 Hz).

Hydrolysis of (II). A mixture of acetylhaplatine (0.01 g) with concentrated hydrochloric acid (0.2 ml) was heated on the water bath for 10 min, cooled, made alkaline with ammonia, and extracted with chloroform, and the extract was chromatographed. This gave crystals of (III) with mp 203-204°C, which were identified as haplopine from their melting point and IR spectrum.

Isomerization of (I). A mixture of haplatine (0.4 g) and freshly distilled methyl iodide (8 ml) in a sealed tube was heated in the boiling-water bath for 15 h. Repeated chromatography of the residue yielded (V) (0.01 g) from chloroform eluates and (IV) (0.29 g) from chloroform—methanolic eluates.

Isohaplatine (IV) formed dark crimson crystals with mp 165-166°C (acetone). It fluoresced dark crimson in UV light. IR spectrum, cm^{-1}: 3340, 3130, 3110, 1634, 1620, 1605, 1542, 1520. UV spectrum, nm: λ_{max} 238, 260, 333, 345 inflection (log ε 4.27, 4.56, 3.85, 3.73). In an acid medium, nm: λ_{max} 238 inflection, 257, 333, 345 inflection (log ε 4.27, 4.58, 3.85, 3.82).

The O-methyl ether of isohaplatine (V) formed dark crimson crystals with mp 126-127°C. It fluoresced dark crimson in UV light. IR spectrum, cm^{-1}: 3150, 3113, 1636, 1620, 1600, 1541, 1520 cm^{-1}.

Hydrogenation of (I). Over a platinum catalyst, 0.2 g of haplatine was hydrogenated in 10 ml of ethanol for 7 h. The catalyst was separated off and the ethanol was evaporated off, giving a residue which on chromatography yielded ethereal and ethereal—chloroformic eluates. Treatment of the ethereal eluates with hexane followed by rechromatography of the hexane-soluble fraction on silica gel yielded 0.02 g of (VI). The similar separation of the fraction soluble in ethyl acetate obtained from the ethereal—chloroformic eluates led to the isolation of (VII) (0.01 g).

Hexahydrohaplatine (VI) formed colorless needles with mp 119-120°C (hexane—ethyl acetate). It fluoresced pale blue in UV light. With the Dragendorff reagent it gave a pink coloration. IR spectrum, cm^{-1}: 1645. Mass spectrum, m/e (%): 335 (M^+, 50), 250 (34), 249 (97), 235 (31), 234 (100), 220 (22), 219 (25).

Tetrahydrohaplopine (VII) formed colorless crystals with mp 164-165°C (ethyl acetate). It fluoresced weakly in UV light and was not revealed with the Dragendorff reagent. It was revealed feebly with iodine vapor. It gave no depression of the melting point with an authentic sample of tetrahydrohaplopine. Their IR spectra were identical.

Hydrolysis of (I). Haplatine (0.05 g) was hydrolyzed under the conditions described for (II). This gave haplopine, mp 203-204°C (from methanol).

SUMMARY

The alkaloids skimmianine, evoxine, haplopine, glycoperine, 7-isopentenyloxy-γ-fagarine, haplamide, haplamidine, and haplatine have been isolated from the plant *Haplophyllum latifolium* Kar. et Kir. growing in the Chimkent oblast. It has been shown that haplatine has the structure of 7-(3'-hydroxymethylbut-2'-enyloxy)-4,8-dimethoxyfuranoquinoline.

It has been established that the qualitative and quantitative compositions of the alkaloids of the epigeal part of the plant change little from the period of flowering to the end of the vegetation season, but depend greatly on the growth site.

LITERATURE CITED

1. E. F. Nesmelova, I. A. Bessonova, and S. Yu. Yunusov, Khim. Prirodn. Soedin., 749 (1978), [in this issue].

2. Kh. A. Abdullaeva, I. A. Bessonova, and S. Yu. Yunusov, Khim. Prirodn. Soedin., 219 (1978).
3. E. F. Nesmelova and G.P. Sidyakin, Khim. Prirodn. Soedin., 376 (1971).
4. E. F. Nesmelova, I. A. Bessonova, and S. Yu. Yunusov, Khim. Prirodn. Soedin., 666 (1975).
5. F. N. Lahey, M. McCamish, and T. McEwan, Austr. J. Chem., 22, 447 (1969).
6. I. A. Bessonova, V. I. Akhmedzhanova, and S. Yu. Yunusov, Khim. Prirodn. Soedin., 677 (1974).
7. F. N. Lahey, I. Lauder, and M. McCamish, Austr. J. Chem., 22, 431 (1969).

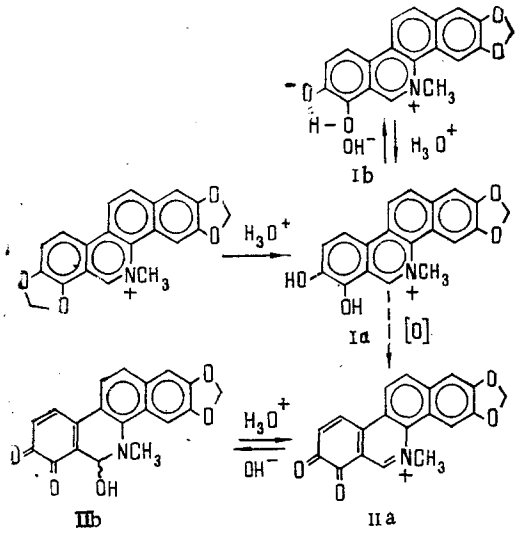
QUATERNARY BENZOPHENANTHRIDINE ALKALOIDS

9,10-DEMETHYLENE DERIVATIVES OF SANGUINARINE

O. E. Lasskaya and O. N. Tolkachev

UDC 547.944

In the process of isolating quaternary benzophenanthridine alkaloids from the herb *Macleaya cordata* Mil. R. Br. and *M. microcarpa* (Maxim.) Fedde, together with the acid sulfates of sanguinarine and chelerythrine (on chromatograms the spots are orange and yellow, respectively), we observed the presence in the mixture of two minor components, one of which on a thin layer of alumina appears in the form of a starting spot (compound B) colored violet, while on silica gel it is represented by a lilac or violet coloration (for the base). Compound A, which in chromatography on silica gel is about half as mobile as chelerythrine, appears in the form of an orange-yellow spot. The intensity of the starting spot increases when the bisulfates of the alkaloids are stored for a long time, but it has been found that the amount of this impurity does not exceed 1-2%.



In a comparative study of chromatograms of a series of samples of the alkaloids on prolonged storage, we observed a starting spot as impurity only in samples of sanguinarine bisulfate. This shows that compound B is a product of the transformation of the latter. Since the sanguinarine molecule differs from the chelerythrine molecule by the presence of a methylenedioxy group in the 9-10 position in place of two methoxy groups in the same positions, its transformation can be explained by the participation of just this group in the process.

In order to determine the nature of the impurity, the total acid sulfates of the alkaloids that had been stored for a long time were subjected to preparative chromatography in a thin layer or on a column of alumina. This led to the isolation of the two components mentioned above together with sanguinarine and chelerythrine. On the other hand, a mixture of sanguinarine and chelerythrine was subjected to saponification by heating with dilute sulfuric acid. In this case, a gradual decrease in the amount of sanguinarine in the reaction mixture was observed with the formation, after alkalinification, of an intensely violet-

All-Union Scientific-Research Institute of Medicinal Plants, Moscow. Translated from Khimiya Prirodnykh Soedinenii, No. 6, pp. 764-767, November-December, 1978. Original article submitted August 10, 1978.

 0009-3130/78/1406-0650$07.50