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ALKALOIDS OF THE *Papaveraceae*. XLVI.*

ALKALOIDS FROM *Glaucium fimbrilligerum* BOISS.

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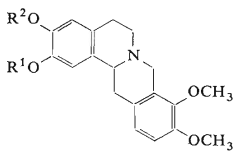
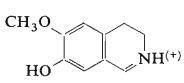
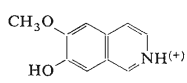
The species *Glaucium fimbrilligerum* BOISS. is an annual to biannual plant growing in Central Asia in the region of the Turkestan-highlands and Afghanistan. Alkaloids of this plant have been studied by Konovalova and coworkers[1] who isolated from its above-ground part corydine, allocryptopine and protopine, and from the root chelerythrine and sanguinarine.



Ia, $R^1 = H$, $R^2 = CH_3$
Ib, $R^1 = CH_3$, $R^2 = H$



a



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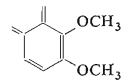

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From plants cultivated in Czechoslovakia we were able to isolate or identify five identified alkaloids in addition to the mentioned alkaloids. The main components of the aerial part are allocryptopine, corydine, and protopine (see Table I.). From the mother liquor after corydine we isolated a small amount of another phenolic base which according to its physical constants, UV and IR spectrum, coincided with (−)-isocorypalmine (tetrahydrocolumbamine) (*Ia*). Its mass spectrum with important peaks at *m/e* 341 (M), 178 (*a*), 176 (*b*), 164 (*c*; base peak) and 149 (*c*-15) is characteristic of fragmentation of tetrahydroprotoberberines and identical with the spectrum of (−)-isocorypalmine[2]. The identity was corroborated by the R_F value coinciding with that of (±)-tetrahydrocolumbamine and different from that of (±)-tetrahydrojatrorrhizine (*Ib*). The yellow quaternary base prepared on oxidation with mercuric acetate also was identical according to paper and thin-layer chromatography with columbamine, but not with jatrorrhizine.

From the fraction of quaternary protoberberines obtained from the aerial parts in negligible amount coptisine was isolated in the form of its crystalline chloride and the presence of berberine was also proved. In the fraction of other quaternary bases three alkaloids were found of which one was identified by thin-layer chromatography as magnoflorine. The main alkaloid of the roots is protopine, but they contain as minor components also corydine, sanguinarine, chelerythrine, chelirubine, coptisine and berberine. Allocryptopine is present only in trace amounts.

With its content of alkaloids *G. fimbrilligerum* is closely related to the species *G. elegans* FISCH. *et* MEY., *G. oxylobum* BOISS. *et* BUHSE, and *G. squamigerum* KAR. *et* KIR. In contrast to the botanically and biochemically closely related family *Fumariaceae* the presence of (−)-isocorypalmin in *G. fimbrilligerum* represents the second proved occurrence of this alkaloid in *Papaveraceae* family. Up to the present time it was isolated only from opium as a minor component[2,3].

EXPERIMENTAL

The melting points were determined both in capillaries and on a Kofler block and they were not corrected. Thin-layer chromatography was carried out on silica gel bound with gypsum (5 : 1) in cyclohexane–diethylamine 9 : 1 (S_1), cyclohexane–chloroform–diethylamine 7 : 2 : 1 (S_2), methanol–diethylamine 8 : 2 (S_3) and ethanol–water–25% ammonia 15 : 9 : 1 (S_4). The spots were detected with potassium iodoplatinate. The colours after detection are given in brackets. For paper chromatography Whatman paper No 1 and a mixture of n-butanol–acetic acid–water 10 : 1 : 3 (S_5) or ethanol–water 3 : 2 (S_6) were used. Detection was carried out under UV light (the colours of fluorescence are indicated in brackets).

Material

The plants were cultivated in the Experimental Botanical Garden, Faculty of Medicine, Brno, from seeds obtained from the Botanical garden of Minsk (USSR). They were harvested on the 26th June 1967 as two-year-old specimens during the period of flowering or early fruit maturation. The material was dried at room temperature.

Isolation of the Alkaloids from the Above-Ground Parts

The dry and ground above-ground parts (3 640 g) were extracted five times with cold methanol (total amount 100 l) and alkaloid fractions *A*, *B*, *E* and *J* were isolated from the extract in the usual manner[4,5].

Bases of the fraction *A* (11 g) were dissolved in dilute hydrochloric acid and partitioned with chloroform to give chloroform soluble fraction (*AC*) and chloroform insoluble fraction (*AD*). From bases obtained from fraction *AC* (4·80 g) a little soluble fraction of hydrochlorides was obtained on crystallisation from dilute hydrochloric acid. These were transformed to bases and crystallised from ether. Thus 3·12 g of (+)-corydine were obtained, m.p. 145—147°C (ether), undepressed on admixture of an authentic sample, $[\alpha]_D^{22} + 204° \pm 3°$ (*c* 0·5, chloroform), R_F

TABLE I

Content of Alkaloids in *Glaucium fimbrilligerum*

Alkaloid	Aerial parts %	Roots %
Allocryptopine	0·105	traces
(+)-Corydine	0·086	0·033
Protopine	0·028	0·222
(−)-Isocorypalmine	0·001	—
Coptisine	traces	0·002
Berberine	traces	0·002
Sanguinarine	—	0·019
Chelerythrine	—	0·009
Chelirubine	—	0·001
Amorphous residue of bases	0·017	0·026
Total	*0·237*	*0·312*

values 0·15 in S_1 and 0·48 in S_2 (blue-green spots). From the ethereal mother liquor after the crystallisation of corydine 40 mg of (−)-isocorypalmine were isolated. The bases regenerated from the mother liquors after the crystallisation of weakly soluble hydrochlorides gave on crystallisation from ether 0·34 g of allocryptopine.

The fraction *AD* was separated to a fraction of nonphenolic bases (AD_1) and phenolic bases (AD_2). Crystallisation of bases AD_1 (4·88 g) from ether, chloroform–ethanol, and ethanol gave 1·02 g of protopine, m.p. 207–208°C (chloroform–ethanol), undepressed on admixture of an authentic preparation, R_F values 0·34 in S_1 and 0·65 in S_2 (violet-brown spots) also identical with those of an authentic sample, and 3·46 g of allocryptopine, m.p. 160–161°C (ethanol), undepressed on admixture of an authentic sample, R_F values 0·23 in S_1 and 0·58 in S_2 (violet-brown spots), identical with those of an authentic specimen.

On crystallisation of fraction AD_2 from ether 10 mg of (−)-isocorypalmine were obtained. In the amorphous residue of bases the presence of two additional bases was proved in addition to the residues of corydine, isocorypalmine, protopine, and allocryptopine. The R_F values of the former two bases in S_2 were 0·07 (brown spot) and 0·12 (pink spot).

From the fraction *B* 5·3 mg of coptisine chloride were isolated on crystallisation from dilute hydrochloric acid. Its R_F value was 0·45 in S_5 (yellow fluorescence). On reduction with zinc in dilute hydrochloric acid it gave a tetrahydroderivative, m.p. 217–218°C (ethanol), mixture melting point with authentic (±)-tetrahydrocoptisine 219–220°C, with R_F value in S_1 0·59 (orange spot) also identical with that of the authentic sample. From the mother liquor after crystallisation of coptisine chloride 8·7 mg of yellow bases were isolated on alkalisation with sodium hydroxide and extraction with ether, which according to their R_F values in S_5, 0·45 (yellow fluorescence) and 0·59 (green-yellow fluorescence) consisted of a mixture of coptisine and berberine. On reduction the prepared tetrahydro derivatives gave spots of R_F values 0·53 (yellow spot) and 0·59 (orange spot) in S_1, identical with those of authentic tetrahydroberberine and tetrahydrocoptisine, respectively.

From fraction *E* (0·06 g) no crystalline compound has been obtained. Fraction *E* gave a white spot on thin layer, of R_F 0·24 in S_2.

Fraction *J* (1·07 g), containing predominantly non-alkaloid substances, was dissolved in water and precipitated with 20% sodium perchlorate. Amorphous perchlorates of quaternary bases were precipitated (0·15 g) which formed on thin layer and on paper three spots having the following R_F values: in S_4 0·27 (violet-brown spot), 0·37 (violet-blue spot), and 0·57 (violet-brown spot, blue fluorescence); in S_5 0·49 (blue fluorescence), 0·58, and 0·84; in S_6 0·41 (blue fluorescence), 0·48, and 0·75. Of these spots one conicided in all systems with authentic magnoflorine iodide (in S_4 0·57, in S_5 0·49, in S_6 0·41, blue fluorescence).

(−)-*Isocorypalmine* crystallised from methanol in small prisms, m.p. 231–232°C (open capillary and Kofler block), $[\alpha]_D^{22}$ −282° ± 5° (*c* 0·13, methanol). Literature gives m.p. 230 to 231°C (open capillary)[6] or 240–241°C (evacuated capillary)[6,7], and $[\alpha]_D^{27}$ −303° (chloroform)[6] or −255 ± 10° (chloroform)[2], respectively. Molecular weight 341 (by mass spectroscopy). UV spectrum (methanol), λ_{max} 284 nm (log ε 3·80), λ_{min} 254 nm (log ε 3·13), as well as the IR spectrum (chloroform), ν(OH) 3530 cm^{-1}, are in good agreement with the literature data[2,8]. R_F-Values 0·10 in S_1 and 0·38 in S_2 (yellow spots) are identical with the values of authentic (±)-isocorypalmine (tetrahydrocolumbamine) while (±)-corypalmine (tetrahydrojatrorrhizine) had different R_F values, *i.e.* 0·06 in S_1 and 0·30 in S_2 (orange spots). With conc. sulfuric acid the preparation did not assume any colour, with a mixture of sulfuric and nitric acids it turned yellow.

Oxidation of (−)-*isocorypalmine*: A small sample of the compound was heated with mercuric acetate in dilute acetic acid on a boiling water bath for 5 minutes. Sodium formate was then added and the reduced mercury was filtered off. The formed yellow oxidation product gave a spot (green-yellow fluorescence) of R_F values (thevalue for jatrorrhizine chloride is given in brackets) 0·71 (0·76) in S_3, 0·54 (0·59) in S_5, and 0·12 (0·25) in S_6, identical with those of authentic columbamine.

Isolation of Alkaloids from Roots

The ground root (189 g) was extracted with ethanol and further worked up as usual to give alkaloid fractions *AC*, AD_1, AD_2, and *B*.

From the fraction *AC* corydine (0·06 g) was isolated in the form of weakly soluble hydrochloride, from fraction AD_1 quaternary benzophenanthridine bases were isolated in the form of non-basic *ps*-cyanides, and the remaining bases gave on crystallisation from ether and chloroform–ethanol 0·42 g of protopine. In mother liquors the presence of a small amount of allocryptopine was proved by thin-layer chromatography. From the mixture of quaternary benzophenanthridines column chromatography on alumina gave under conventional conditions[9] 2·2 mg of chelirubine (R_F 0·53 in S_5, purple fluorescence; pseudo-cyanide m.p. 273–274°C), 36·4 mg of sanguinarine (R_F 0·43 in S_5, orange fluorescence; pseudo-cyanide m.p. 243–244°C), and 17·5 mg of chelerythrine (R_F 0·54 in S_5, yellow fluorescence, pseudo-cyanide m.p. 256–257°C). The identity was corroborated by mixture melting points of pseudo-cyanides with authentic samples and by coinciding R_F values of the latter.

From fraction *B* 3·1 mg of crystalline coptisine chloride and 1·0 mg of amorphous yellow bases were isolated. The latter consisted according to paper chromatography in S_5 of coptisine and berberine.

We greatly appreciate the donation by Professor M. Tomita, University of Kyoto, Japan, of the sample of magnoflorine iodide. Our thanks are also due to Dr L. Dolejš, Institute of Organic Chemistry and Biochemistry, Czechoslovak Academy of Sciences, Prague, for the measurement of the mass spectra on a MCh 1303 mass spectrophotometer, Dr. L. Hruban, Chemistry Department,

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STUDIES IN THE PYRIDINE SERIES. XXXIX.*

RING CLEAVAGE IN LITHIUM ALUMINUM HYDRIDE REDUCTIONS OF SOME DIALKYLPYRIDINE METHIODIDES

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It has been shown in one of the earlier papers[1] of this Series that the aluminum hydride (prepared *in situ* from lithium aluminum hydride and aluminum chloride) reductions of 2,5-dimethylpyridine methiodide and 2-methyl-5-ethylpyridine methiodide are accompanied by cleavage of the pyridine ring under the formation of 2-methylaminomethyl-2,4-hexadiene and 5-methylaminomethyl-2,4-heptadiene, respectively. It was of interest if a similar ring cleavage takes place also in reductions of some dialkylpyridine methiodides with the complex hydride alone. In the present paper we wish to report the lithium aluminum hydride reductions of the methiodides of 2,4-dimethylpyridine, 2,5-dimethylpyridine, 2-methyl-5-ethylpyridine, 2,6-dimethylpyridine, and 3-methyl-4-ethylpyridine.

Thus, reduction of 2,4-dimethylpyridine methiodide afforded a mixture containing both stereoisomeric 1,2,4-trimethylpiperidines, 1,2,4-trimethyl-3-piperideine, 1,4,6-trimethyl-3-piperi-

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