ON THE MINOR ALKALOIDS FROM *Argemone mexicana* L.*

K. HAISOVÁ and J. SLAVÍK

Institute of Medical Chemistry,
Purkyně University, 66243 Brno,

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Dedicated to Professor F. Šantavý on the occasion of his 60th birthday.

In addition to allocryptopine, protopine, berberine, coptisine, sanguinarine and chelerythrine the following additional alkaloids were isolated from *Argemone mexicana* L.: norsanguinarine, norchelerythrine, cryptopine, (−)-cheilanthifoline, (−)-β-scoulerine methohydroxide and (−)-α- and β-stylopine methohydroxide.

Alkaloids from *Argemone mexicana* L. have already been studied (for a review see[1]). So far allocryptopine[1-3], protopine[1-5] and berberine[1,4-6] have been isolated as main alkaloids from this plant, while sanguinarine[1,3,6], chelerythrine[1,3,6] and coptisine[1,6] were found in smaller amounts. Dihydrosanguinarine[1,7] and dihydrochelerythrine[1] were isolated from the seed oil or from the lipoid fractions of the plant. In this paper we concentrated on the study of minor alkaloids. In the conventional manner we had separated the alkaloids which were found[1] in this plant earlier, *i.e.* allocryptopine, protopine, berberine, coptisine, sanguinarine and chelerythrine. From the non-phenolic fraction norsanguinarine, norchelerythrine and cryptopine were isolated as further alkaloids. The occurence of the first two alkaloids in the *Argemone* species has been described recently[8,9]. The main fraction of phenolic bases consisted of (−)-cheilanthifoline. From the fraction of quaternary alkaloids (−)-β-scoulerine methohydroxide and (−)-stylopine methohydroxide were isolated in the form of iodides; the latter consisted mainly of the α-form with a small admixture of the β-form (see[10]).

From these findings it follows that the species *A. mexicana* is biochemically very closely related to the species *A. ochroleuca* SWEET (see[11]). Both species differ in minor alkaloids only, and the differences in the occurrence of quaternary alkaloids are especially remarkable. The presence of (−)-β-scoulerine methohydroxide in *A. mexicana* indicates a close relationship with the species *A. albiflora* HORNEM[8].

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EXPERIMENTAL

The melting points were determined on a Kofler block and they were not corrected. The IR spectra (in KBr) were measured on an Infrascan, Hilger and Watts, apparatus. For thin layer chromatography silica gel with gypsum (5 : 1) and the following solvent systems were employed: cyclohexane–diethylamine 9 : 1 (S_1), cyclohexane–chloroform–diethylamine 7 : 2 : 1 (S_2), 4 : 5 : 1 (S_3), and 3 : 6 : 1 (S_4), benzene–ethanol–25% ammonia 10 : 2 : 1 (S_5), benzene–ethyl acetate–diethylamine 5 : 4 : 1 (S_6), ethanol–water–25% ammonia 15 : 9 : 1 (S_7), 1-propanol–formic acid- water 12 : 1 : 7 (S_8), cyclohexane–methanol 1 : 1 (S_9). Paper chromatographies were carried out on paper Whatman No 1 in the descending manner, using 1-butanol–acetic acid–water 10 : 1 : 3 (S_{10}). Detection was carried out under the UV light or with Dragendorff reagent.

Isolation of Alkaloids

The plants were cultivated in the Experimental Botanical Garden Medical Faculty Brno, and they were collected at the stage of unripe fruits on September 1st, 1972 and then dried at room temperature. The dry, ground, whole plant (4165 g) was extracted seven times with cold methanol, totally 120 l. The extract was worked up in the same manner as in paper[8] and the fractions *A*, *B*, *E* and *I* were isolated from the extract. The yield of total alkaloids was 0·088%. The crude bases of the fraction *A* were separated to fractions *AC*, AD_1 and AD_2. From a solution of bases of the fraction *AC* in methanol 20·1 mg of norsanguinarine crystallized out (0·0005%), m.p. 285–287°C (chloroform–methanol), further 7·3 mg of norchelerythrine (0·0002%), m.p. 213–214°C (chloroform–methanol), both undepressed on admixture of authentic specimens (see[8]). These alkaloids were further identified by IR spectra, R_F values in S_2 and S_3 and colour reactions. From the mother liquor a smaller amount of allocryptopine was obtained on crystallization from ethanol, and a small amount of protopine by crystallization from chloroform–ethanol. Crystallization of the non-phenolic fraction AD_1 from ether afforded allocryptopine (total yield 1·77 g; 0·042%), m.p. 160–161°C (ethanol) and crystallization from chloroform–ethanol gave protopine (total yield 1·31 g; 0·031%), m.p. 206–207°C (chloroform–ethanol). From the mother liquors after the separation of these two alkaloids cryptopine was isolated by crystallization from methanol (14·2 mg; 0·0003%), m.p. 219–220°C (methanol), undepressed on admixture of an authentic sample. The identity was also confirmed by IR spectrum, R_F values in S_1 and S_2 and by colour reactions. From the remaining mother liquors quaternary benzophenanthridine alkaloids were then separated in the form of non-basic pseudo-cyanides which were converted to free bases in the usual manner (3·5 mg; 0·0001%) and identified as sanguinarine (R_F 0·86 in S_9, 0·46 in S_{10}, orange fluorescence) and chelerythrine (trace amount; R_F 0·71 in S_9, 0·55 in S_{10}; yellow fluorescence). In the amorphous residue of bases (22 mg) chromatography on thin layers proved only the presence of protopine. From the phenolic bases of the fraction AD_2 (–)-cheilanthifoline (11·5 mg; 0·0003%) was separated by crystallization from methanol, m.p. 183–184°C (methanol), undepressed on admixture of an authentic preparation (see[11]). The identity was confirmed by IR spectrum, R_F values in S_2, S_4 and S_6 and by colour reactions. In the amorphous residues of bases (20 mg) the residue of cheilanthifoline and traces of allocryptopine were demonstrated by thin-layer chromatography.

From fraction *B* berberine chloride was obtained by crystallization from dilute hydrochloric acid (total yield of berberine, calculated as base, was 0·50 g; 0·012%), R_F value 0·56 (S_{10}; green-yellow fluorescence), tetrahydro derivative had m.p. 163–165°C (ether), undepressed with an authentic sample. From the mother liquors after berberine chloride the residue of bases (54 mg) was obtained by alkalization with sodium hydroxide and extraction with ether. It consisted predominantly of berberine, in addition to a smaller amount of coptisine (R_F value 0·44 in S_{10}; in UV golden-yellow fluorescence). Fraction *E* was non-alkaloidal.

From the concentrated chloroform solution of fraction *I* (iodides of quaternary bases) 8·1 mg of (−)-β-scoulerine methiodide (0·0002%) crystallized out, m.p. 260−261°C (methanol), undepressed on admixture of an authentic sample (see[8]). Their identity was also confirmed by IR spectroscopy and R_F values in S_4, S_7, S_8 and S_{10}. From the mother liquor (−)-stylopine methiodide (2·4 mg; 0·00006%) was isolated by crystallization from methanol, which according to its melting point (278−280°C; undepressed on admixture of an authentic sample) and R_F values in S_7, S_8 and S_{10} represented the α-form with a small admixture of the β-form (see[10]). The rest of the fraction *I* was non-alkaloidal.

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REFERENCES

1. Slavíková L., Slavík J.: This Journal *21*, 211 (1956); Chem. listy *49*, 1546 (1955).
2. Čelombitko V. A., Muravjeva D. A., El Sawy J.: Chim. Prir. Soedin. *7*, 208 (1971).
3. Bori Thi Yu, Muravjeva D. A.: Rast. Resur. *9*, 200 (1973); Chem. Abstr. *79*, 15820 (1973).
4. Majumder B., Sarkar S. N., Dutta P. C.: J. Indian Chem. Soc. *33*, 351 (1956); Chem. Abstr. *51*, 1382 (1957).
5. Santra D. K., Saoji A. N.: Curr. Sci. *40*, 548 (1971).
6. Hakím S. A. E., Mijović V., Walker J.: Nature *189*, 198 (1961).
7. Roy A. C., Chaudhuri K. D., Achari G.: Patna J. Med. *28*, 269 (1954); Chem. Abstr. *50*, 11509 (1956).
8. Haisová K., Slavík J., Dolejš L.: This Journal *38*, 3312 (1973).
9. Haisová K., Slavík J.: This Journal *39*, 2491 (1974).
10. Slavík J., Slavíková L., Dolejš L.: This Journal *40*, 1095 (1975).
11. Haisová K., Slavík J.: This Journal *38*, 2307 (1973).

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