

ALKALOIDS OF THE *Papaveraceae*. I.\*  
 ON THE QUATERNARY ALKALOIDS  
 FROM *Argemone platyceras* LINK et OTTO

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*Dedicated to Prof. Dr. A. Okáč on the occasion of his 70th birthday.*

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Besides the already described alkaloids, the aerial parts of *Argemone platyceras* LINK et OTTO yielded the quaternary alkaloids (–)-platycerinemethohydroxide, (–)-argemoninemethohydroxide and (–)-stylopinemethohydroxide in form of perchlorates. Furthermore, the presence of a small amount of chelerythrine and corysamine could be demonstrated.

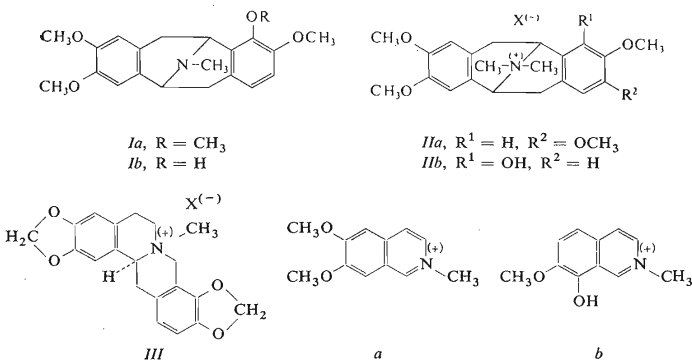
So far, the alkaloids of the species *Argemone platyceras* LINK et OTTO have been studied by two groups of authors<sup>1,2</sup>. The major alkaloid isolated from the aerial part of that plant is the phenolic pavine alkaloid platycerine<sup>2</sup> C<sub>20</sub>H<sub>23</sub>NO<sub>4</sub> which is isomeric with norargemonine. The partial structure<sup>3</sup> of platycerine was derived from the mass spectrum and from the identity of its O-methyl derivative with that of O,O-dimethylmunitagine<sup>4</sup> (*Ia*). The position of the phenolic hydroxyl was then resolved<sup>5</sup> by the assignment of the constitution *Ib*. Small quantities of platycerine were also found in the species *A. gracilentia* GREENE<sup>5</sup>. The other alkaloids isolated from *A. platyceras* were argemonine<sup>2</sup>, norargemonine<sup>1,2</sup>, allocryptopine<sup>1,2</sup>, protopine<sup>1,2</sup> and small quantities of the alkaloids sanguinarine, coptisine, and berberine<sup>2</sup>. In this paper, we have studied the polar water-soluble quaternary alkaloids whose presence has recently<sup>6</sup> been observed by us in the species *A. ochroleuca* SWEET.

After separation of the alkaloids, which on alkaline reaction can be extracted into ether or chloroform, we have isolated the quaternary bases in form of iodides by following the usual method<sup>7</sup>. After conversion of the iodides into perchlorates, two alkaloids could be separated by crystallization which were identical with (–)-argemoninemethoperchlorate (*IIa*, X = ClO<sub>4</sub>) and with (–)-stylopinemethoperchlorate (*III*, X = ClO<sub>4</sub>), yield 0.0002% and 0.0001%, respectively, of the dry aerial part. Evidence of the identity of these alkaloids was provided by comparison of the melting points and the mixed melting points of the perchlorates and iodides (*IIa*

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and *III*, respectively,  $X = I$ ), the ultraviolet and infrared spectra, the optical rotatory value, and the  $R_F$ -value with those of the methosalts prepared from  $(-)$ -argemonine or  $(-)$ -stylopine. Natural  $(-)$ -argemoninemethohydroxide was found for the first time in the species *A. gracilentia* GREENE<sup>5</sup>.  $(-)$ -Stylopinemethohydroxide has recently been isolated from *Glaucium corniculatum* CURT.<sup>8</sup> and from *A. ochroleuca* SWEET<sup>6</sup>. The major component of the quaternary portion was an amorphous perchlorate which was obtained in pure form by column chromatography and identified as  $(-)$ -platycerinemethoperchlorate (*IIb*,  $X = ClO_4$ ) (yield 0.0017% of the dry aerial part). On mass spectrometry of the iodide of this alkaloid (*IIb*,  $X = I$ ), the methyl iodide and iodine ( $m/e$  142 and 127) are pyrolytically split off. The rest of the spectrum displays peaks of a tertiary alkaloid ( $m/e$  341,  $M - CH_3I$ ) and characteristic peaks at  $m/e$  340, 204 ("a") and 190 ("b") which are identical with those observed in the spectrum of platycerine<sup>3</sup>. The identity of these alkaloids has been confirmed by comparison of the UV and IR spectra, the optical rotatory value and the  $R_F$ -value of the perchlorate with those of authentic  $(-)$ -platycerinemethoperchlorate prepared from  $(-)$ -platycerine<sup>2</sup>. This is the first observation of the occurrence of this alkaloid in nature.

In addition to these three alkaloids, we have isolated the crystalline perchlorate of another quaternary alkaloid, m.p. 221°C (alkaloid AP 1) whose m.p. and  $R_F$ -value resemble those of  $(-)$ -canadinemethoperchlorate, but the substances are not identical. The amount of the substance was, however, so small that it could not be studied in more detail. From the "non-quaternary" portion of the alkaloids, all the previously described<sup>2</sup> alkaloids were isolated and, moreover, the presence of small quantities of chelerythrine, corysamine and some other so far unidentified alkaloids could be demonstrated.



## EXPERIMENTAL

The melting points (uncorrected) were determined either in capillaries or on the Kofler block. The mass spectrum was measured on a mass spectrometer AEI-MS 902 at 70 eV, the UV spectra on a Unicam model SP 500 spectrophotometer and the IR spectra on an Infracan, Hilger and Watts spectrophotometer. Descending paper chromatography was carried out on Whatman paper No 1 with the solvent system *n*-butanol-acetic acid-water 10 : 1 : 3 ( $S_1$ ); the spots were detected in UV light. Thin-layer chromatography was carried out on silica gel G (5 : 1) by using the following solvent systems: cyclohexane-chloroform-diethylamine 7 : 2 : 1 ( $S_2$ ), and 3 : 6 : 1 ( $S_3$ ), and ethanol-water-25% ammonia 15 : 9 : 1 ( $S_4$ ). Spots were detected with potassium iodoplatinate. The previously isolated alkaloids of this plant were identified by comparison of the melting points and mixed melting points, the UV and IR spectra,  $R_F$ -values and colour reactions with those of authentic samples.

## Extraction and Isolation of Alkaloids

The plant material under investigation was cultivated in the Experimental Botanical Garden of the Medical Faculty in Brno and collected on September 26th, 1966, when the plant was flowering and the fruit was not mature. The dry aerial parts of the plant (9.89 kg) were ground and extracted with cold methanol (150 l). The extract was worked up and the alkaloids were isolated by adopting practically the same method as that described in paper<sup>2</sup>; there was, however, obtained an additional fraction *I* (ref.<sup>7</sup>). The yield of total alkaloids (without fraction *I*) amounted to 9.90 g (0.10%). The major alkaloid platycerine (4.63 g, 0.047%) was isolated from the fractions  $AC_2$  and  $AD_2$ , argemonine (1.44 g, 0.015%) from the fraction  $AC_1$ , protopine (1.34 g, 0.014%), allocryptopine (0.71 g, 0.007%), and the quaternary benzophenanthridine bases (0.12 g, 0.001%) from the fraction  $AD_1$ . Paper chromatography ( $S_1$ ) showed that the latter fraction consisted mainly of sanguinarine ( $R_F$  0.45) and a smaller quantity of chelerythrine ( $R_F$  0.54). Norargemonine (0.18 g, 0.002%) was obtained from the phenolic portions  $AC_2$ ,  $AD_2$  and from the fraction *E*. The fraction *B* (0.14 g, 0.001%) consisted mainly of coptisine and a smaller amount of berberine and corysamine ( $R_F$  ( $S_1$ ) 0.54, 0.66 and 0.75, respectively). In the amorphous nonphenolic fractions  $AC_1$  and  $AD_1$  (0.60 g), the presence of some unidentified bases of the  $R_F$ -values ( $S_2$ ) 0.24, 0.31, 0.63, and 0.73 could be demonstrated. The amorphous phenolic fractions  $AC_2$  and  $AD_2$  (0.35 g) gave the bases of  $R_F$  ( $S_2$ ) 0.29, 0.35, 0.45, and 0.51, and in the rest of the fraction *E* (0.39 g), bases of  $R_F$  ( $S_3$ ) 0.00, 0.13 (bisnorargemonine?), 0.33, 0.39, 0.51, and 0.79 were detected.

After separation of the fractions *A*, *B* and *E*, the fraction *I* was obtained from the remaining aqueous layer by acidification with hydrochloric acid, addition of a solution of potassium iodide, and repeated extraction into chloroform. The crude product (1.82 g) was dissolved in water and the present quaternary alkaloids were separated in form of almost insoluble perchlorates by precipitation with a 20% solution of sodium perchlorate. Fractionated crystallization of the perchlorates from methanol gave (–)-argemoninemethoperchlorate (22 mg) and (–)-stylopinemethoperchlorate (10 mg). The remaining amorphous residue (518 mg) was separated by column chromatography. The column was prepared with chloroform and aluminium oxide (60 g, Brockmann neutral, Reanal) which had been washed with 1% perchloric acid and dried at 250°C. The amorphous perchlorates were dissolved in chloroform and chromatographed. The column was washed with chloroform (100 ml) and with chloroform containing increasing amounts of methanol: 2.5% (250 ml), 5% (100 ml), 10% (200 ml), 20% (100 ml) and 50% (100 ml); collection of 50 ml fractions. The presence of the alkaloids in the individual fractions was detected by thin-layer chromatography ( $S_4$ ). The fractions 1 and 2 (71.5 mg) did not contain any alkaloids, the fractions 3–7 (60.3 mg) crystallized from methanol to yield 2.3 mg of a mixture of argemoninemethoperchlorate and stylopinemethoperchlorate. The mother liquors gave 3.6 mg of the perchlorate of the alkaloid AP I, after recrystallization from methanol m.p. 220–221°C,  $R_F$ -value 0.65; with authentic (–)-canadinemethoperchlorate<sup>9</sup> (m.p. 218–219°C,  $R_F$  0.65), strong depression of the melting point (185–194°C). Colour reaction with conc. sulphuric acid pink-violet,

with the Erdmann reagent olive green (canadinemethoperchlorate with these two reagents colourless). The main component of the amorphous residue was an unidentified alkaloid of  $R_F$ -value 0.49. The fractions 8–15 afforded pure (–)-platycerinemethoperchlorate (173 mg). The fractions 16–17 (10.0 mg) showed, in addition to the rest of platycerinemethoperchlorate, the presence of two other alkaloids of  $R_F$ -value 0.33 and 0.70 which could not be identified as yet.

#### Characterization of the Alkaloids

(–)-*Argemonimethohydroxide*. The iodide crystallizes from methanol in needles, m.p. 272 to 274°C (capillary), without depression with the authentic sample,  $[\alpha]_D^{25} -200^\circ \pm 6^\circ$  (c 0.14, methanol). UV spectrum (methanol), shoulder at 230 nm (log  $\epsilon$  4.42),  $\lambda_{\max}$  285 nm (log  $\epsilon$  3.90),  $\lambda_{\min}$  259 nm (log  $\epsilon$  3.26), the IR spectrum (KBr) and the  $R_F$  0.34 ( $S_4$ ) are identical with those of the authentic sample. The perchlorate crystallizes from methanol in long needles, m.p. 274 to 275°C (capillary) and 288–289°C (Kofler block), no depression with the authentic sample; it is very little soluble in methanol even on boiling. The authentic sample of (–)-argemonine-methiodide was prepared from (–)-argemonine (50 mg) by methylation with methyl iodide (0.5 ml) in a cold mixture of methanol (1 ml) and ether (4 ml). The precipitate crystallizes from methanol (57.5 mg), m.p. 273–274°C (capillary) which is consistent with the data given in the literature<sup>10,11</sup>, and  $[\alpha]_D^{25} -206^\circ \pm 2^\circ$  (c 0.28, methanol). From this sample, the perchlorate was prepared by dissolution in water, precipitation with a 20% solution of sodium perchlorate and crystallization from methanol; m.p. 275–276°C (capillary) and 288–290°C (Kofler block), respectively.

(–)-*Stylopinemethohydroxide*. The iodide crystallized from methanol in needles clustering to druses, m.p. 277–278°C (capillary) and 295–298°C (Kofler block), without depression with the authentic sample prepared from (–)-stylopine<sup>8</sup>. The IR spectrum (KBr), the  $R_F$  0.57 ( $S_4$ ) and the characteristic colour reactions are identical with those of the authentic sample. The perchlorate crystallizes from methanol, m.p. 336–338°C (Kofler block) without depression with the perchlorate (m.p. 338–340°C) which was prepared as described vide supra from authentic (–)-stylopinemethiodide.

(–)-*Platycerinemethohydroxide*. The iodide is amorphous, soluble in methanol, ethanol and chloroform, insoluble in ether, exposed to air it becomes yellow. The perchlorate is also amorphous; the product obtained by precipitation from a methanol solution with ether has m.p. 152–175°C,  $[\alpha]_D^{25} -257^\circ \pm 3^\circ$  (c 0.26, methanol). The UV spectrum (methanol),  $\lambda_{\max}$  234 nm (log  $\epsilon$  4.14),  $\lambda_{\max}$  284 nm (log  $\epsilon$  3.77),  $\lambda_{\min}$  227 nm (log  $\epsilon$  4.12),  $\lambda_{\min}$  260 nm (log  $\epsilon$  3.27), the IR spectrum (nujol),  $\nu(\text{OH})$  3380 and 3570  $\text{cm}^{-1}$ , and the  $R_F$  0.66 ( $S_4$ ) are identical with those of the authentic sample. This sample was prepared by methylation of (–)-platycerine (50 mg) with methyl iodide (0.5 ml) in a cold mixture of methanol and ether (1 : 4) to afford an amorphous product (in quantitative yield). The perchlorate prepared from it was precipitated from a methanol solution with ether, m.p. 158–173°C,  $[\alpha]_D^{23} -258^\circ \pm 2^\circ$  (c 0.50, methanol).

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