

ON ALKALOIDS FROM THE LEAVES OF *Bocconia frutescens* L.

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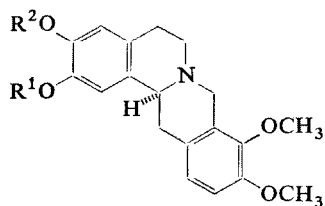
From the leaves of *Bocconia frutescens* L. allocryptopine, protopine and (–)-isocorypalmine were isolated as the main alkaloids, chelerythrine, sanguinarine, columbamine and rhoeadine were less abundant while berberine, coptisine, corysamine and one papaverrubine (probably papaverrubine E) were found in trace amounts only.

The genus *Bocconia* L. from the *Chelidoniae* tribe (*Papaveraceae*) comprises about 10 species native to tropical and subtropical areas of Central and South America. It is closely related to the East Asian genus *Macleaya* R. BR. (2 species) which is often connected with the *Bocconia* genus. The species *B. frutescens* L. is a shrub growing in Central and South America. The alkaloids of this species have already been investigated several times<sup>1-4</sup>. Earlier authors isolated protopine<sup>1-3</sup> (fumarine<sup>1,2</sup>), allocryptopine<sup>2,3</sup> (bocconine<sup>2</sup>,  $\alpha$ - and  $\beta$ -homochelidonine<sup>3</sup>), and also mentioned the presence of a considerable amount of an alkaloid which was considered to be probably identical with chelerythrine<sup>1-3</sup>. More recently Tani and Takao<sup>4</sup> isolated protopine, allocryptopine, chelerythrine, sanguinarine, and an unidentified alkaloid of the composition C<sub>20</sub>H<sub>17</sub>NO<sub>6</sub> from the whole plant.

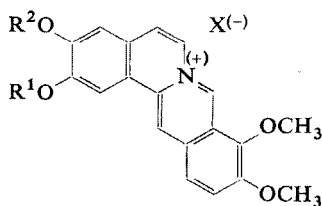
In this paper we present the results of a study of alkaloids from the leaves of *B. frutescens* L. which we obtained from two-year-old plants cultivated in Czechoslovakia. From the sum of the alkaloids isolated in an unusually high yield (3% of dry leaves) we isolated as the main alkaloids allocryptopine, protopine, and a phenolic base identical with (–)-isocorypalmine [(–)-tetrahydrocolumbamine, *Ia*]. The identity of the latter compound was proved by comparison with an authentic sample<sup>5</sup>, melting point and mixed melting point, optical rotation value, UV and IR spectra and *R<sub>F</sub>* values which were different from those of corypalmine (tetrahydrojatrorrhizine, *Ib*). On oxidation with mercuric(II)acetate a quaternary base was formed which was identical with columbamine (*IIa*) and not with jatrorrhizine (*IIb*; X is in both cases an anion). In contrast to the data from the authors mentioned<sup>1-4</sup> we were able to isolate from the leaves only a small amount of quaternary benzophenanthridines of

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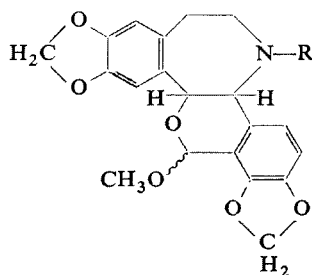
which only chelerythrine and sanguinarine could be separated by chromatography on alumina<sup>6</sup>.



*Ia*,  $R^1 = \text{H}$ ,  $R^2 = \text{CH}_3$   
*Ib*,  $R^1 = \text{CH}_3$ ,  $R^2 = \text{H}$



*IIa*,  $R^1 = \text{H}$ ,  $R^2 = \text{CH}_3$   
*IIb*,  $R^1 = \text{CH}_3$ ,  $R^2 = \text{H}$



*IIIa*,  $R = \text{CH}_3$   
*IIIb*,  $R = \text{H}$

The occurrence of rhoeadine (*IIIa*), which was isolated in a low yield only, is very surprising. It was identified by melting and mixed melting point, UV and IR spectra and  $R_F$  values, using an authentic sample isolated from *Papaver rhoeas* L.<sup>7</sup> for comparison. In the leaves of *B. frutescens* it is accompanied by trace amounts of a papaverrubine which is most probably identical with papaverrubine E (N-demethylrhoeadine, *IIIb*), as indicated by their  $R_F$  values. The alkaloids of rhoeadine type and corresponding N-demethyl derivatives (papaverrubines) were considered so far as being a specific biochemical character of the *Papaver* genus, because they have not yet been found anywhere else. Quite recently we also proved the presence of papaverrubines in several species of *Meconopsis* genus which is botanically close to the *Papaver* genus.

In the fraction of the quaternary non-phenolic protoberberines we detected and proved trace amounts of berberine, coptisine and corysamine. From the fraction of quaternary alkaloids which can be extracted with chloroform (fraction I) in the form of iodides we isolated columbamine iodide (*IIa*,  $X = \text{I}$ ). This represents the first finding of quaternary phenolic protoberberine in the *Papaveraceae* family. The

method mentioned is also suitable for the isolation of other quaternary phenolic protoberberines, for example jatrorrhizine<sup>8</sup>.

## EXPERIMENTAL

The melting points were determined (unless stated otherwise) on a Kofler block, and they were not corrected. The UV spectra were measured in methanol on a Unicam SP 1800 and the IR spectra on a UR 20, Zeiss, Jena, spectrophotometer. For thin-layer chromatography silica gel G (Merck) with gypsum (5 : 1) was used in combination with the systems cyclohexane–diethylamine 9 : 1 ( $S_1$ ) and cyclohexane–chloroform–diethylamine 7 : 2 : 1 ( $S_2$ ), 6 : 3 : 1 ( $S_3$ ) and 3 : 6 : 1 ( $S_4$ ), as well as Silufol UV 254 (Kavalier) in combination with the systems cyclohexane–methanol 3 : 1 ( $S_5$ ) and methanol–diethylamine 4 : 1 ( $S_6$ ). Paper chromatography was carried out on Whatman paper No 1, descending technique, in 1-butanol–acetic acid–water 10 : 1 : 3 ( $S_7$ ) and ethanol–water 2 : 1 ( $S_8$ ). The fluorescent spots were detected in UV light, other spots with potassium iodoplatinate or with Dragendorff's reagent.

### Extraction and Isolation of the Alkaloids

The plants were cultivated in the Experimental Botanical Garden of the Medical Faculty in Brno from the seeds obtained from the Botanical Garden in Zürich. They were hibernated in a hot-house. From the two-year-old plants the leaves were harvested on November 29th, 1972 and dried at room temperature. The dry, ground leaves (600 g) were extracted in a Soxhlet extractor with ethanol, the solvent was distilled off and the extract transferred into 1% sulfuric acid. From the aqueous extract alkaloidal fractions *A*, *B*, *E* and *I* were obtained in the conventional manner<sup>9,10</sup>. Fraction *A* (17.74 g) was further separated<sup>9</sup> to fraction *AC*, *AD*<sub>1</sub> and *AD*<sub>2</sub>. From the fraction *AC* allocryptopine (1.68 g), protopine (0.18 g), (–)-isocorypalmine (0.98 g; total yield 1.43 g, 0.24%) and rhoeadine (16 mg; 0.003%) were isolated both by direct crystallization from methanol and after separation of the fraction to non-phenolic (*AC*<sub>1</sub>) and phenolic (*AC*<sub>2</sub>) bases. Crystallizations of the fraction *AD*<sub>1</sub> from ethanol gave mainly mixed fractions of allocryptopine and protopine. From these mixed fractions allocryptopine (10.69 g; total yield 12.37 g, 2.06%) was isolated by crystallization from ethanol, m.p. 160–161°C (capillary), undepressed on admixture of an authentic sample.  $R_F$  values (0.23 in  $S_1$  and 0.70 in  $S_2$ ) and colour reactions were identical as in the case of the reference sample. Protopine (2.93 g; total yield 3.11 g, 0.52%) when crystallized from chloroform–ethanol had m.p. 207–208°C, undepressed with an authentic sample. The identity was confirmed by  $R_F$  values (0.40 in  $S_1$  and 0.79 in  $S_2$ ) and colour reactions. From fraction *AD*<sub>1</sub> a smaller amount of (–)-isocorypalmine (0.21 g) was obtained along with quaternary benzophenanthridines which were separated as non-basic pseudo-cyanides (0.03 g of bases; 0.005%). Their separation on a column of alumina (see<sup>6</sup>) afforded sanguinarine (9.2 mg), chloride as red needles of m.p. 279–281°C,  $R_F$  values 0.66 ( $S_5$ ) and 0.43 ( $S_7$ ), and chelerythrine (19.9 mg), chloride as yellow needles, m.p. 202–204°C,  $R_F$  values 0.40 ( $S_5$ ) and 0.53 ( $S_7$ ). The melting points of mixtures with authentic samples were undepressed, the  $R_F$  values were identical as in the case of reference samples. From fractions *AC*<sub>1</sub> and *AD*<sub>1</sub> there remained totally 0.13 g of amorphous bases which in addition to the residues of allocryptopine, protopine and isocorypalmine also contained (according to thin-layer chromatography) at least five additional alkaloids. From fraction *AC*<sub>2</sub> 0.03 g of amorphous bases remained. The phenolic fraction *AD*<sub>2</sub> gave on crystallization from methanol 0.24 g of isocorypalmine. The amorphous residue (0.06 g) contained according to thin-layer chromatography in addition to the residues of isocorypalmine a base as the main component the  $R_F$

value of which was 0.29 in  $S_3$  and 0.72 in  $S_4$ , and small amounts of three additional unidentified alkaloids. The fraction *B* consisted of 5 mg of yellow bases (0.001%) which contained mainly berberine ( $R_F$  0.19 in  $S_6$ , 0.59 in  $S_7$ , and 0.16 in  $S_8$ ) in addition to a small amount of coptisine ( $R_F$  0.44 in  $S_6$ , 0.45 in  $S_7$ , and 0.05 in  $S_8$ ) and traces of corysamine ( $R_F$  0.13 in  $S_6$ , 0.70 in  $S_7$  and 0.53 in  $S_8$ ). Fraction *E* (0.20 g) remained amorphous. Fraction *I* (0.55 g) gave on crystallization from chloroform 65 mg of columbamine iodide (0.011%). From the mother liquors 111 mg of a non-alkaloidal substance of m.p. 163–165°C crystallized out, which was not further investigated. The non-crystalline orange residue was reduced (zinc dust and dilute hydrochloric acid) to give 13.2 mg of ( $\pm$ )-tetrahydrocolumbamine, m.p. 204–205°C (methanol); it was identified by IR spectrophotometry (in chloroform) and chromatography, where the  $R_F$  values were identical to those of (–)-isocorypalmine.

(–)-*Isocorypalmine*: prisms of m.p. 231–232°C (chloroform–methanol), undepressed with a preparation isolated from *Glaucium fimbriigerum*<sup>5</sup>,  $[\alpha]_D - 285^\circ \pm 3^\circ$  ( $c$  0.33, chloroform). The identity was confirmed by UV and IR spectra (in chloroform) (see<sup>5,11</sup>) and  $R_F$  values, 0.41 in  $S_2$  (tetrahydrojatrorrhizine  $R_F$  0.34), 0.46 in  $S_3$  and 0.88 in  $S_4$ .

*Oxidation of (–)-isocorypalmine*: 100 mg of (–)-isocorypalmine were dissolved in 10 ml of 10% acetic acid, a solution of mercury(II)acetate (0.70 g) dissolved in 10 ml of 10% acetic acid was added and the mixture heated on a boiling water bath for one hour. The orange-yellow solution was filtered from the separated mercury(I)-acetate, excess sodium formate was added to the filtrate and the mixture heated on a boiling water bath for 10 minutes and the reduced precipitated mercury was filtered off. The filtrate was added with saturated potassium iodide solution to precipitate columbamine iodide which was crystallized from aqueous methanol; yield 126 mg (93%), orange needles, m.p. 230–231°C, well soluble in methanol and ethanol, very poorly soluble in water, even when boiling. The UV spectrum,  $\lambda_{\max}$  (log  $\epsilon$ ) 225 nm (4.64), 266 nm (4.50), 350 nm (4.46),  $\lambda_{\min}$  250 nm (4.36), 304 nm (3.94), as well as the IR spectrum (in nujol) are in good agreement with the literature<sup>11</sup> data.  $R_F$  values (for the sake of comparison the values for jatrorrhizine iodide are given in parentheses): 0.35 (0.48) in  $S_6$ , 0.47 (0.55) in  $S_7$ , and 0.12 (0.21) in  $S_8$ .

*Rhoeadine*: needles of m.p. 250–252°C (chloroform–methanol), undepressed on admixture of a preparation isolated from *Papaver rhoeas*<sup>7</sup>; the UV spectrum,  $\lambda_{\max}$  (log  $\epsilon$ ) 242 nm (4.03), 292 nm (3.94),  $\lambda_{\min}$  225 nm (3.86) and 263 nm (3.18), and the IR spectrum (in chloroform), as well as the  $R_F$  values (0.58 in  $S_1$  and 0.86 in  $S_2$ ) and the colour reactions were identical as in the reference sample. On heating with 3.5% hydrochloric acid to boiling point this preparation gave a light pink colour (papaverrubine reaction). Less pure fractions of rhoeadine obtained from the mother liquors gave a strongly positive papaverrubine reaction (purple colour). In  $S_1$  and  $S_2$  systems and detection with hydrochloric acid fumes (15 minutes) a single purple spot of  $R_F$  values 0.30 and 0.59, respectively, was demonstrated in these fractions, which was in agreement with the  $R_F$  values of papaverrubine *E* (papaverrubine A, i.e. N-demethylisorhoeadine also has very close  $R_F$  values in both systems.)

*Columbamine*: the iodide gives orange crystalline clusters m.p. 228–230°C (aqueous methanol), undepressed in admixture with a preparation prepared by oxidation of isocorypalmine (see above). The identity was confirmed by UV and IR spectra (in nujol) and  $R_F$  values in  $S_6$ ,  $S_7$  and  $S_8$ .

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