

ALKALOIDS FROM *Bocconia frutescens* L.*

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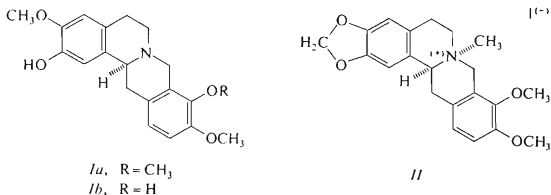
Received June 27th, 1979

Allocryptopine and protopine were isolated from the roots, stalks and leaves of *Bocconia frutescens* L. as the main alkaloids and chelerythrine, sanguinarine, chelirubine (not present in leaves), berberine and coptisine as the minor ones. In addition to this (–)-isocorypalmine and (–)-scoulerine were isolated from leaves and traces of rhoeadine were found in the leaves and stalks. From the quaternary fraction of all three parts of the plant columbamine and (–)- α -canadine methoxide were also isolated in the form of iodides.

The alkaloids from the South American shrub *Bocconia frutescens* L. of the *Papaveraceae* family have already been investigated several times (for literature survey see¹). Some years ago¹ we investigated the alkaloids from the leaves of this species and found allocryptopine, protopine and (–)-isocorypalmine as the main components, small amounts of chelerythrine, sanguinarine, rhoeadine, columbamine, berberine and coptisine, and traces of papaverrubine E and corysamine. This time we had the whole plant at our disposal, and we could investigate the alkaloids from the roots, stalks and leaves separately. It became evident that in the roots and stalks (1.44% or 0.74%, respectively, of total alkaloids) tertiary phenolic bases are completely lacking, in contrast to the leaves¹. Equally as in the leaves, the main alkaloids in roots and stalks are allocryptopine and protopine, while the other alkaloids form minor components only. From the "non-quaternary" fraction of the minor components we isolated chelerythrine, sanguinarine and also chelirubine, which could not be proved in the leaves. The highest content of the total alkaloids is in the leaves (2.05%). From the fraction of phenolic bases, obtained from the leaves, we isolated (–)-isocorypalmine (*Ia*) in agreement with paper¹, and (–)-scoulerine (*Ib*) as a further alkaloid which was found in this plant for the first time. In the stalks and the leaves we detected a small amount of rhoeadine, the isolation of which from the leaves has already been described¹. In the fraction of quaternary protoberberines from all parts of the plant we found a very small amount of berberine and coptisine. From the fraction of quaternary alkaloids, which are extractable with chloroform in the form of iodides, we separated columbamine iodide and as

* Part LXXI in the series Alkaloids of the *Papaveraceae*; Part LXX: This Journal 45, 914 (1980).

a further alkaloid also $(-)\text{-}\alpha\text{-canadine methiodide (II)}$. The presence of this alkaloid was also unknown in *B. frutescens* so far². Both mentioned quaternary alkaloids are present in all parts of the plant investigated; the highest content of $(-)\text{-}\alpha\text{-canadine methiodide (0.02\%)}$ was found in the leaves.



From the yields given in the experimental part it is evident that in no part of the plant could we find such a high content of chelerythrine or other quaternary benzophenanthridines as stated by other authors³⁻⁵. Since we studied young, two years old specimens, it cannot be excluded that only older plants accumulate a larger amount of quaternary benzophenanthridines, mainly in the bark^{3,5}, which in the *Bocconia* genus belong generally to dominant alkaloids.

EXPERIMENTAL

The melting points were determined on a Mettler FP 51 apparatus. The IR spectra (in KBr and in nujol) were measured on a Unicam SP 1000 Infrared Spectrophotometer and the UV spectra on a Unicam SP 1800 instrument. Thin-layer chromatography (TLC) was carried out both on Silica gel G (Merck) in cyclohexane-diethylamine 9 : 1 (S_1), cyclohexane-chloroform-diethylamine 7 : 2 : 1 (S_2), methanol-water-25% ammonia 15 : 3 : 1 (S_3) and ethanol-water-25% ammonia 15 : 9 : 1 (S_4), and on Silufol UV 254 (Kavalier) in benzene-methanol 9 : 1 (S_5) and methanol-diethylamine 4 : 1 (S_6). For paper chromatography (PC) Whatman No 1 paper was used in combination with the systems 1-butanol-acetic acid-water 10 : 1 : 3 (S_7) and ethanol-water 3 : 2 (S_8). The fluorescing alkaloids were detected under UV light, the other alkaloids with potassium iodoplatinate (TLC) or Dragendorff's reagent (PC).

Extraction and the Isolation of Alkaloids

The plants were cultivated in the Experimental Botanical Garden, Medical Faculty, Brno, from seeds obtained from the Botanical Garden, Zürich. After wintering in a greenhouse they were harvested in the second vegetation year on 27th September 1974. The harvested plants were divided into roots, stalks and leaves and dried at room temperature. Each of the plant parts was worked up separately, in a practically identical manner.

The dried and ground plant material (roots: 243 g, stalks: 910 g, leaves: 457 g) was extracted exhaustively in a Soxhlet extractor with methanol. This was then distilled off, the residue dissolved in cold 1% acetic acid and the undissolved material filtered off. The acid filtrate was ex

tracted with ether in order to eliminate non-basic lipid material (fraction L), alkalinized with sodium carbonate and extracted with ether (fraction A), then alkalinized with sodium hydroxide to pH > 13 and reextracted with ether (fraction B). The alkaline aqueous phase was then weakly acidified with acetic acid, alkalinized with ammonia and extracted with chloroform (fraction E). The aqueous layer was neutralized with acetic acid, a solution of potassium iodide was added and the mixture extracted four times with chloroform (fraction I). The remaining aqueous layer no longer reacted with Mayer's reagent.

Fractions L from all parts of the plant contained mainly lipid material in addition to a small amount of alkaloids, among which rhoeadine (in the stalks and the leaves) was identified by TLC in addition to further alkaloids present in fraction A.

In the further text the yields from the roots, stalks and leaves are given in brackets, in that order. Fraction A (3.43 g, 1.41%; 6.56 g, 0.72%; 9.08 g, 1.99%) — after evaporation of ether — was in all cases almost white and predominantly crystalline. Crystallizations from chloroform-ethanol and ethanol eliminated the main part of protopine (total yields: 1.41 g, 0.58%; 0.97 g, 0.11%; 2.25 g, 0.49%) and allocryptopine (total yields: 1.71 g, 0.70%; 4.56 g, 0.50%; 5.60 g, 1.23%). From the bases remaining in the mother liquor quaternary benzophenanthridines were separated in the form of non-basic pseudo-cyanides which were converted to chlorides in the conventional manner⁶. The bases prepared from chlorides were separated on an alumina column⁶ affording thus chelerythrine (18.0 mg, 0.0074%; 21.3 mg, 0.0023%; 12.3 mg, 0.0027%), sanguinarine (11.0 mg, 0.0045%; 15.3 mg, 0.0017%; 7.4 mg, 0.0016%) and chelirubine (1.5 mg, 0.0006%; 7.0 mg, 0.0008%; —, —); on TLC in system S₅ they gave the same R_F values as authentic specimens. The bases remaining in the filtrate after separation of pseudo-cyanides were separated⁷ to a fraction of hydrochlorides extractable with chloroform (AC) and unextractable with it (AD). The fraction AD was further separated to non-phenolic bases (AD₁) and phenolic ones (AD₂). In the fraction A from the roots and the stalks phenolic bases could not be detected. The fractions AC from the roots and stalks (0.02 g or 0.17 g respectively) contained merely allocryptopine or sometimes even protopine, which were obtained from them by crystallization from ether. In the amorphous residue of bases AC (0.05 g) from stalks the presence of an unidentified base with R_F 0.38 on TLC in S₂ was proved. From fraction AC from leaves (1.77 g) protopine (0.17 g), allocryptopine (0.25 g), isocorypalmine (0.12 g; total yield from leaves 0.25 g, 0.055%) and scoulerine (0.08 g; total yield from leaves 0.14 g, 0.031%) were obtained by systematic crystallizations of the bases from methanol. In the amorphous residue of the bases (0.12 g) two further substances were found with R_F values in S₂ 0.05 and 0.23 which are evidently oxidation products of scoulerine. From the fractions AD or AD₁ only a small amount of protopine and allocryptopine or of their mixture was obtained. Fraction AD₂ from leaves (0.74 g) was crystallized from ether and methanol affording isocorypalmine (0.13 g) and scoulerine (0.06 g). The remaining amorphous bases remained amorphous even after purification (0.18 g) and in addition to the two alkaloids mentioned they contained predominantly oxidation products of scoulerine.

In the fractions B (0.8 mg; 3.1 mg; 1.5 mg — after purification) berberine and coptisine were identified in systems S₆, S₇ and S₈. Amorphous fractions E (0.04 g; 0.19 g; 0.10 g) contained predominantly non-alkaloidal substances in addition to traces of alkaloids. Fractions I (0.14 g; 0.47 g; 0.36 g) afforded columbamine iodide (0.03 g, 0.012%; 0.09 g, 0.010%; 0.22 g, 0.048%) and (—)- α -canadine methiodide (0.04 g, 0.016%; 0.13 g, 0.014%; 0.09 g, 0.020%) on crystallizations from methanol.

Characterization of the Alkaloids Isolated

The isolated alkaloids were identified by melting points and mixed melting points, or also by specific rotation determination and UV and IR spectra and R_F values measurement, as well as by comparison of the spectra or R_F values with those of authentic samples.

Protopine: prisms, m.p. 207–208°C (chloroform–ethanol), R_F 0.36 (S_1), 0.66 (S_2).

Allocryptopine: prismatic needles, m.p. 162–163°C (ethanol), R_F 0.22 (S_1), 0.52 (S_2).

(–)-*Isocorypalmine*: prismatic needles, m.p. 230–232°C (methanol), $[\alpha]_D^{22} - 285^\circ \pm 5^\circ$ (c 0.11, methanol), R_F 0.10 (S_1), 0.32 (S_2).

(–)-*Scoulerine*: needles, m.p. 200–202°C (methanol), $[\alpha]_D^{22} - 349^\circ \pm 10^\circ$ (c 0.09, methanol), R_F 0.05 (S_1), 0.16 (S_2).

Columbamine iodide: yellow-orange needles, m.p. 221–222°C (methanol), R_F 0.36 (S_3) and 0.37 (S_4).

(–)- α -*Canadine methiodide*: needles from methanol, m.p. 160–163°C, the melt solidified at 173–176°C and remelted at 210–215°C, at about 220°C it again resolidified and remelted at 245°C (the authentic sample behaved in the same manner⁸), $[\alpha]_D^{22} - 117^\circ \pm 5^\circ$ (c 0.18, methanol), R_F 0.14 (S_3), 0.28 (S_4) and 0.72 (S_7); the β -form had R_F 0.45 in S_7 (cf.⁹).

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Translated by Ž. Procházka.