

POLAR ALKALOIDS FROM *Papaver orientale* L.*

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Received November 9, 1990

Accepted December 13, 1990

Corytuberine (*I*) and quaternary alkaloids N-methylthebainium hydroxide (*II*), N-methylisothebainium hydroxide (*III*), and magnofforine (*IV*) as iodides have been isolated for the first time from the fraction of strongly polar alkaloids obtained from aerial parts and roots of *Papaver orientale* L. The weakly polar fraction contains oripavine, thebaine, isothebaine, and alpinigenine as dominant components. Small amounts of bracteoline, isoboldine, scoulerine, papaverrubines G, A, B, D, and C, and traces of palmatine and coptisine have also been detected.

Papaver orientale L. is a perennial herb of *Macrantha* ELKAN (*Oxytona* BERNH.) section growing in Turkey, Iran, and transcaucasian U.S.S.R. (ref.¹). Until Goldblatt's botanical revision of the *Oxytona* section¹ in 1974, it was frequently confused with *P. pseudo-orientale* (FEDDE) MEDV. All papers published before this date (e.g. refs²⁻⁴), which gave isothebaine as the main alkaloid, started almost certainly from botanical misidentification¹ and obviously dealt with the species *P. pseudo-orientale*** . According to present knowledge, *P. orientale* involves five or six chemotypes (cf. e.g. refs⁶⁻⁹) differing in combinations of two to four dominant alkaloids. In most cases *P. orientale* contains oripavine as the main alkaloid^{1,6-9} accompanied most often by a larger or smaller amount of thebaine, isothebaine, or alpinigenine beside several minor alkaloids.

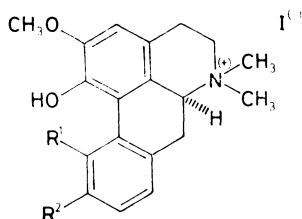
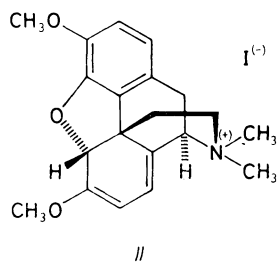
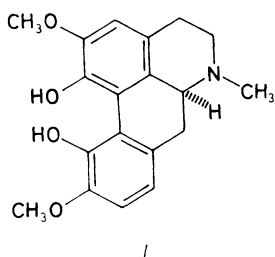
Although there are more than twenty papers dealing with the alkaloids of authentic species *P. orientale*, no attention has yet been paid to alkaloids of strongly polar nature whose presence could be expected since they were found in two closely related species, viz. *P. bracteatum* LINDL. and *P. pseudo-orientale* (FEDDE) MEDV.^{5,10-12} from the *Macrantha* section. It is known that in the acid-base isolation procedure usually adopted these alkaloids are not transferred into nonpolar solvents and remain (usually unnoticed) in the aqueous phase (cf. e.g. ref.¹³).

In the present work we have studied the alkaloids from two-years old plants cul-

* Part XCII in the series Alkaloids of the *Papaveraceae*; Part XCI: Collect. Czech. Chem. Commun. 56, 1116 (1991).

** The plant material used by the authors^{2,3} was identical with *P. pseudo-orientale* (see ref.⁵).

tivated in this country from seeds of a population originating from U.S.S.R. The alkaloids content in this plant material was relatively low (0.045% and 0.12% in the dry aerial parts and roots, respectively). Using the procedure described earlier^{11,13} we at first separated the fractions of weakly polar bases extractable with ether from alkaline medium, and then, after addition of potassium iodide, we obtained the fraction of iodides of strongly polar alkaloids by extraction with chloroform from slightly acidic medium. The main component of this fraction from roots was (+)-corytuberine (*I*) isolated as the hydriodide, the same compound being found only in a small amount in the aerial parts. This alkaloid was isolated earlier from *P. bracteatum* LINDL. (ref.¹¹) as well as from *P. pseudo-orientale*⁵. It seems to be a regular constituent in the species of the *Macrantha* section. The main quaternary alkaloid of the iodide fraction from both aerial parts and root of *P. orientale* was N-methylthebainium iodide (*II*) which was isolated earlier from *P. bracteatum*^{10,11}. The aerial parts gave small amounts of N-methylisothebainium iodide (*III*), which is known as the main quaternary alkaloid of the species *P. pseudo-orientale*^{5,12}, and, in addition, the root gave magnoflorine iodide (*IV*), which was also found in the two above-mentioned species of the *Macrantha* section^{5,11}. All four polar alkaloids mentioned were isolated from the *P. orientale* species for the first time. The mother liquors contain small amounts of an alkaloid (detected by chromatography) most probably identical with N-methyloripavinium iodide, which has not yet been reported as a natural product.



III, $R^1 = \text{OCH}_3$; $R^2 = \text{H}$
IV, $R^1 = \text{OH}$; $R^2 = \text{OCH}_3$

From the weakly polar fraction of nonquaternary bases obtained from the aerial parts we could isolate oripavine, thebaine, and isothebaine as dominant alkaloids beside a slight amount of alpinigenine. The main components of the same fraction from root included thebaine, isothebaine, and alpinigenine, whereas oripavine was present in a negligible amount only. The combination of all these four major tertiary alkaloids is known to be present in one of rather rare chemotypes (cf. refs⁷⁻⁹). In both the aerial parts and root we could detect small amounts of bracteoline, scoulerine and an unidentified alkaloid, isoboldine being present in addition in the root.

The mother liquors gave a positive test for papaverrubines (N-demethylrhoeadanes) whose presence in true *P. orientale* has not been reported yet. Chromatographical analysis of both aerial parts and root of our material showed that papaverrubine G (N-demethylalpinine) forms a strongly predominant component, its occurrence in nature being quite rare. Small amounts of papaverrubine A (N-demethylisoeadine), B (N-demethylglaudine), D (porphyroxine), and traces of papaverrubine C (epi-porphyroxine) were also detected. The fraction of nonphenolic protoberberines present in negligible amounts included palmatine and coptisine which were found also earlier in *P. bracteatum* as well as in *P. pseudo-orientale*^{5,11,12}. They were proved in *P. orientale* for the first time.

EXPERIMENTAL

The melting points were determined on a Mettler FP 51 apparatus and were not corrected. The IR spectra were measured in Nujol using a Specord 75 IR (Zeiss, Jena) spectrometer, and the UV spectra were measured in methanol using a Unicam SP 1800 instrument. The thin-layer chromatography (TLC) was carried out on Silica gel G (Merck): the weakly polar bases in the systems cyclohexane–diethylamine 9 : 1 (S1), cyclohexane–chloroform–diethylamine 7 : 2 : 1 (S2) and 6 : 3 : 1 (S3), benzene–methanol 4 : 1 (S4), and benzene–acetone–methanol 7 : 2 : 1 (S5); the quaternary alkaloids and corytuberine in the systems methanol–water–25% ammonia 15 : 3 : 1 (S6), ethanol–water–25% ammonia 15 : 9 : 1 (S7), and 1-propanol–water–85% formic acid 12 : 7 : 1 (S8). For quaternary protoberberines was also used Silufol UV 254 (Kavalier) with the systems methanol–diethylamine 4 : 1 (S9) and 1 : 1 (S10). The alkaloids were detected with potassium hexaiodoplatinate(IV) and (for alkaloids exhibiting fluorescence) in UV light. The papaverrubines were detected by 20 min exposition to vapours of concentrated hydrochloric acid (formation of purple spots). If not otherwise stated, the isolated alkaloids were identified by means of their melting points, mixed melting points, IR and UV spectra, and TLC with authentic standards.

Extraction and Isolation of the Alkaloids

The plants were grown in the Centre for the Cultivation of Medicinal Plants, Faculty of Medicine, Masaryk University, Brno, from seeds obtained from Botanic Garden of Moscow and were gathered in July 1989 in the second vegetation year in the phase of nonripe capsules. The herbarium specimen is deposited in our Department. The material was divided into aerial parts and roots and dried at room temperature.

The dried and ground plant material (270 g aerial parts or 100 g root) was extracted 8 times with cold methanol in a percolator. Then the methanol was distilled off and the sirupy residue was extracted several times with cold 1% acetic acid and the solution was filtered. The combined filtrates were alkalized with a sodium carbonate solution and extracted with ether several times (fraction *A*), whereupon 40% solution of sodium hydroxide was added to pH > 13 and the extraction with ether was repeated (fraction *B*). Then the aqueous layer was acidified to pH 5–6 with 20% sulfuric acid, a solution of potassium iodide was added, and the mixture was extracted with chloroform and/or chloroform with 20% ethanol several times (fraction *I*) until negative reaction with Mayer's reagent.

Aerial Part

The crude fraction *A* (0.23 g) was purified by repeating the usual acid-base procedure, and the bases obtained were separated into nonphenolic (A_1) and phenolic (A_2) fractions (cf. e.g. ref.¹¹). Crystallization of the concentrated ethereal solution of fraction A_1 gave thebain (9.5 mg; 0.0035%), m.p. 195–196°C, isothebain (4.2 mg; total yield 7.5 mg; 0.0028%), m.p. 205–206°C, and a slight amount of alpinigenine. The ether solution of fraction A_2 crystallized to produce oripavine (12.4 mg; 0.0046%), m.p. 204–205°C, and isothebaine (3.3 mg). The mother liquors A_1 (70.7 mg of bases) were submitted to TLC (S1, S2, S3, S4, S5) and beside the above-mentioned alkaloids papaverrubines G, A, and B were detected; similarly in A_2 (10.2 mg) papaverrubine D and traces of C, one unidentified alkaloid, and slight amounts of bracteoline and scoulerine were found. The fraction *B* contains (according to TLC in S6, S7, S9, S10) traces of palmatine and coptisine. The fraction *I* was divided¹⁴ into a nonphenolic (I_1) and a phenolic (I_2) parts. Crystallization of I_1 from a methanol–ethyl acetate mixture gave N-methylthebainium iodide (9.5 mg) and that of I_2 gave N-methylisothebainium iodide (3.0 mg). Beside the two alkaloids mentioned other alkaloids were found in mother liquors of both fractions (20.9 and 303. mg, respectively) by means of TLC in S6, S7, S8, namely small amounts of corytuberine, magnoflorine, and three nonidentified alkaloids, one of which is obviously identical with N-methyloripavinium iodide, whose authentic sample was prepared by methylation of oripavine with methyl iodide; the identity follows from the same R_F values and hue of the spots after detection.

Root

The crude fraction *A* (0.26 g) was purified and divided into nonphenolic (A_1) and phenolic (A_2) bases (vide supra). Crystallization of the bases A_1 from ether separated thebaine (21.5 mg; 0.022%), m.p. 195–196°C, and isothebaine (12.5 mg; total yield 18.6 mg; 0.019%), m.p. 205 to 206°C. The remaining bases were crystallized from methanol to give alpinigenine (7.6 mg; 0.008%), m.p. 184–185°C. Crystallization of the bases A_2 from ether gave isothebaine (6.1 mg) and oripavine (0.9 mg; 0.001%), m.p. 204–205°C. The amorphous bases from mother liquors A_1 (23.3 mg) and A_2 (19.6 mg) contain beside the alkaloids mentioned (detection in S1, S2, S3, S4, S5) also the papaverrubines G, A, B and D, C (traces), respectively, along with bracteoline, isoboldine, scoulerine, and an unidentified alkaloid. The fraction *B* (1.1 mg) contains (according to TLC in S6, S7, S9, S10) small amounts of palmatine and coptisine. The fraction *I* was crystallized from methanol and/or a methanol–ethyl acetate mixture to give corytuberine hydriodide (17.8 mg), N-methylthebainium iodide (10.1 mg), and magnoflorine iodide (1.1 mg). The mother liquors (81.9 mg of mostly non-alkaloid substances) were submitted to TLC (S6, S7, S8) and N-methylisothebainium iodide was found along with three nonidentified alkaloids (one of them is most probably identical with N-methyloripavinium iodide).

Characterization of Polar Alkaloids Isolated


Given in brackets is the yield from aerial parts or root as the percentage from the dry substance of the plant material. The presence of an alkaloid found only by TLC (S6, S7, S8) is denoted with + sign.

Corytuberine (I; +; hydriodide 0·018): hydriodide leaflets with nacreous lustre, m.p. 208–210°C (methanol–ether), no depression with the authentic sample, identification with UV and IR spectra¹¹ and by means of TLC.

N-Methylthebainium iodide (II; 0·0035; 0·010): large well-developed prisms from methanol, m.p. 228–229°C, identification by means of mixed m.p., UV and IR spectra¹¹ and TLC.

N-Methylisothebainium iodide (III; 0·0011; +): short needles in druses, m.p. 249–253°C (methanol), identification by means of mixed m.p. with a sample prepared by N-methylation of isothebaine with methyl iodide, UV and IR spectra^{5,12} and TLC.

Magnoflorine iodide (IV; +; 0·001): prisms m.p. 265–266°C, no depression with the authentic sample, the same R_f values in TLC (the spots show blue-violet fluorescence in UV light).

 The authors are indebted to J. Bochořáková from the same Department for the UV and IR spectral measurements.

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Translated by J. Panchartek.