

ISOLATION AND CHEMISTRY OF THE ALKALOIDS
FROM SOME PLANTS OF THE GENUS *Papaver*. LX.*

ISOLATION OF A SALT OF (—)-N-METHYLSTYLOPINIUM
FROM PLANTS OF THE GENUS *Papaver* L.

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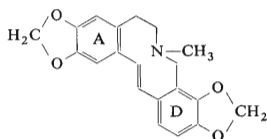
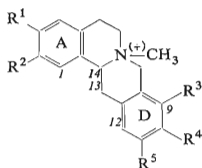
From the species *Papaver rhoeas* L., a salt of (—)-N-methylstylopinium (*I*), which is identical with the earlier described alkaloid R—D, has been isolated and its structure determined on the basis of mass and PMR spectroscopy. It has been found that alkalinization of the compound *I* in dimethyl sulphoxide leads to Hofmann degradation thus giving rise to the stilbene derivative *II*.

From the species *Papaver rhoeas* L. and *P. commutatum* FISCH. et MEY. (*Papavera-ceae*, genus *Papaver* L., Section *Orthorhoeades* FEDDE), the alkaloid R—D was isolated¹⁻⁴ by preparative chromatography on Al₂O₃ from an alkaline chloroform extract. Recently, an alkaloid in form of a salt (chloride) has been isolated⁵ from *P. rhoeas* L. Its quaternary nature was confirmed by reaction with silver oxide⁶. This alkaloid was extracted from alkaline medium (pH ~12) into chloroform and by preparative chromatography on Al₂O₃ it was eluted with a mixture of chloroform-methanol (98 : 2 up to 96 : 4). The alkaloid has been obtained in form of a chloride, which is accounted for by the fact that chloroform always contains traces of hydrochloric acid. The UV, CD and IR spectra are identical with those of the alkaloid R—D. The mass spectrum bears analogy to the spectrum of stylopine⁷. On the basis of the PMR spectrum (Table I), the isolated alkaloid is attributable structure *I*.

The PMR spectrum of the compound *I* in hexadeuteriodimethyl sulphoxide shows, after addition of sodium deuteriooxide, upfield shifts of the signals of the methyl group on nitrogen and of the methylene group (Ar—CH₂—N). The chemical

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shift of the methyl protons corresponds to that of the tertiary N—CH₃ group. The region of the aromatic protons exhibits additional signals of two protons attached to the double bond connecting two aromatic nuclei. The UV spectrum of the compound *I* in dimethyl sulphoxide (λ_{\max} nm (log ϵ) 291 (3.84)) differs from that recorded after addition of 10% sodium hydroxide (λ_{\max} nm (log ϵ) 292 (3.87), 318 sh (3.77)); the change is irreversible, acidification brings about a shift of the absorption band to 310 nm. This phenomenon was not observed in the UV spectra recorded in ethanolic or aqueous medium after alkalization. The PMR spectra of N-methyltetrahydroprotoberberinium and N-methyltetrahydropseudoprotoberberinium alkaloids *III*–*VI* (Table I) in hexadeuteriodimethyl sulphoxide did not change after alkalization. On the basis of the spectral data, we assume that on alkalization in dimethyl sulphoxide the compound *I* undergoes the Hofmann elimination to give rise to a stilbene derivative *II* (ref.^{8,9}).



- I*, R¹ + R² = R³ + R⁴ = OCH₂O, R⁵ = H
III, R¹ + R² = R⁴ + R⁵ = OCH₂O, R³ = H
IV, R¹ = R² = OCH₃, R⁴ + R⁵ = OCH₂O, R³ = H
V, R¹ + R² = OCH₂O, R³ = R⁴ = OCH₃, R⁵ = H
VI, R¹ = OH, R² = R³ = R⁴ = OCH₃, R⁵ = H

II

The isolated (–)-N-methylstylopinium chloride is the first quaternary tetrahydroprotoberberine alkaloid found in plants of the genus *Papaver*. In other natural material, such alkaloids were found already earlier^{10–13}; (–)-N-methylstylopinium iodide was isolated from *Glaucium corniculatum* CURT. (*Papaveraceae*) and described only recently⁷.

EXPERIMENTAL

The melting points have been determined on the Kofler block with an accuracy of $\pm 2^\circ\text{C}$ up to 200°C and are not corrected. For the measurements, the substances were dried for 1 hour at $100^\circ\text{C}/1$ Torr. The optical rotation was measured on a polarimeter Hilger, the CD curves on a Roussel-Jouan 185 instrument. The ultraviolet spectra were measured on a Unicam SP. 700 in 95% ethanol or in dimethyl sulphoxide; the solution (2.5 ml) was made alkaline with 10% sodium hydroxide (0.4 ml). The solutions of the substances (concentration $1 \cdot 10^{-4}\text{M}$) were measured in 1.00 or in 0.20 cm in silica cells. The infrared spectra were measured on an

TABLE I

PMR Spectra of N-Methyltetrahydroprotoberberinium and N-Methyltetrahydropseudoprotoberberinium Alkaloids

The coupling constants J are given in Hz; s singlet, bs broad singlet, d doublet, m multiplet. The chemical shifts of the protons of the Ar—CH₂—CH₂N⁽⁺⁾ fragment of the compounds *II*, *IV*–*VI* are in the region of 2.5–4.0 p.p.m. and have not been assigned.

Compound	CH ₃ —N ⁽⁺⁾ (CH ₃ —N)	Ar—CH ₂ —CH ₂ — —N ⁽⁺⁾ (Ar—CH ₂ —N ⁽⁺⁾)	—OCH ₂ O— (OCH ₃)	Aromatic protons
<i>I</i>	2.88 s	3.22 m, 4.02 m (4.88 bs)	6.12 s (A) 6.15 s (D) $J_{gem} = 1.0$	6.97 s (4-H), 7.17 s (1-H), 6.93 d, 7.10 d $J_{ortho} = 8.5$ (11,12-H)
<i>II</i>	(2.13 s)		6.03 s (A, D)	6.3–7.3 m (6 H)
<i>III</i>	2.83 s	3.17 m, 3.85 m (4.67 bs)	6.03 s (A, D)	6.87 s (4,9,12-H), 7.02 s (1-H)
<i>IV</i>	2.84 s	(4.73 bs)	6.05 s (D) (3.78 s, 3.82 s)	6.7–7.0 m (4 H)
<i>V</i>	2.85 s	(4.90 bs)	6.05 s (A) (3.80 s, 6 H)	6.88 s (4-H), 6.9–7.2 m (3 H)
<i>VI</i>	2.82 s	(4.82 bs)	(3.81 s, 9 H)	6.65 s (4-H), 6.95 s (1-H), 7.12 bs (11,12-H)

Infrascan H-900 in KBr tablets and the PMR spectra on a Varian T-60 in hexadeuteriodimethyl sulphoxide in 5% (w/v) concentration; the solution of the sample was treated with 50 μ l 10% NaOD. The chemical shifts are given in δ (p.p.m.) units to tetramethylsilane ($\delta = 0.00$) as internal standard. The mass spectrum was recorded on an AEI-MS 902 at 70 eV. For thin-layer chromatography and detection of the alkaloids see papers^{5,14,15}. The chromatograms were developed with the solvent systems cyclohexane–diethylamine 80:20 (S₁) or methanol–diethylamine 80:20 (S₂).

The isolated (–)-N-methylstylopinium chloride showed m.p. 275–280°C (decomp.; methanol-ether), $[\alpha]_D^{25} -142.8^\circ \pm 3^\circ$ (c 0.96 in methanol), hR_F values 0 (S₁), 12 (S₂). Colour reaction with conc. sulphuric acid blue-green changing into violet, λ_{max} nm (log ϵ) 241 (3.89), 291 (3.88), CD values in ethanol 241 nm ($\Delta\epsilon -2.70$) and 207 nm ($\Delta\epsilon -31$). For the alkaloid R–D, the authors^{1–4} reported m.p. 295–299°C (decomp.; methanol-ether), $[\alpha]_D^{22} +340^\circ \pm 5^\circ$ (c 0.57 in methanol–chloroform 1:1). The different melting points and the magnitude of rotation can be accounted for by the different degree of racemization¹⁶; in the papers^{1–4}, by error the sign of the optical rotatory value has been given as plus instead of minus.

For the preparation of (±)-N-methyltetrahydropseudoeipiberberinium iodide (*IV*) and (±)-N-methyltetrahydroberberinium iodide (*V*) and their melting points see ref.⁹; the preparation of (±)-N-methyltetrahydropseudocoptisinium iodide (*III*), m.p. >300°C (methanol) and (±)-N-methyltetrahydroiatrorrhizinium iodide (*VI*), m.p. 241–245°C (decomp.; methanol) was carried out in a similar manner.

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REFERENCES

1. Šantavý F., Němečková A., Potěšilová H.: *Acta Chim. Acad. Sci. Hung.* 18, 457 (1959).
2. Němečková A., Šantavý F.: *This Journal* 27, 1210 (1962).
3. Němečková A.: *Thesis*. Palacký University, Olomouc 1967.
4. Němečková A., Šantavý F., Walterová D.: *This Journal* 35, 1733 (1970).
5. Gašić O., Preininger V., Potěšilová H., Belia B., Šantavý F.: Unpublished results.
6. Veibel S.: *The Identification of Organic Compounds*, p. 222. Gad Publisher, Copenhagen 1961.
7. Novák V., Dolejš L., Slavík J.: *This Journal* 37, 3346 (1972).
8. Sallay I., Ayers R. H.: *Tetrahedron* 19, 1397 (1963).
9. Šimánek V., Preininger V., Sedmera P., Šantavý F.: *This Journal* 35, 1440 (1970).
10. Slavík J., Dolejš L., Sedmera P.: *This Journal* 35, 2597 (1970).
11. Jowett H. A. D., Pyman F. L.: *J. Chem. Soc.* 103, 290 (1913).
12. Kučková K. I., Terentjeva I. V., Lazurjevskij G. V.: *Chim. Prir. Sojedin.* 2, 141 (1967).
13. Calderwood J. M., Finkelstein W., Fish F., Partith R. T.: *Phytochemistry* 10, 682 (1971).
14. Preininger V., Šantavý F.: *Pharmazie* 25, 356 (1970).
15. Preininger V., Tošnarová V., Šantavý F.: *Planta Med.* 20, 70 (1971).
16. Pyman F. L.: *J. Chem. Soc.* 103, 817 (1913).

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