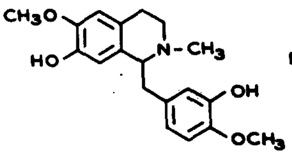
Tetrahedron Letters No.20, pp. 2261-2263, 1966. Pergamon Press Ltd.
Printed in Great Britain.

THE ISOLATION OF (-)-SCOULERINE FROM OPIUM

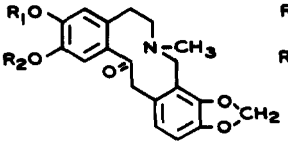
Einar Brochmann-Hanssen and Bendik Nielsen
Department of Pharmaceutical Chemistry
School of Pharmacy, University of California,
San Francisco, California

(Received 4 February 1966; in revised form 8 March 1966)

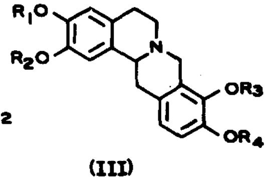
It has been shown that reticuline (I) is a precursor for berberine in Hydrastis canadensis (1) and for protopine (II, $R_1 + R_2 = CH_2$) in Dicentra spectabilis (1) and in Chelidonium majus (2), the C-8 carbon atom originating from the N-methyl group of the precursor. There is strong evidence that this transformation proceeds by way of the tetrahydroprotoberberine alkaloids scoulerine (III, $R_1 = R_4 = CH_3$, $R_2 = R_3 = H$) and stylopine (III, $R_1 + R_2 = CH_2$, $R_3 + R_4 = CH_2$) (2,3). The opium poppy contains reticuline as well as protopine (II, $R_1 + R_2 = CH_2$) and cryptopine (II, $R_1 = R_2 = CH_3$), and one may reasonably expect the same



(I)



(II)



(III)

biosynthetic pathway to be effective there. Support for this hypothesis is now presented by the isolation of scoulerine from opium.

The alkaloid was obtained from the mother liquor produced during the purification of morphine. A preliminary separation of groups of alkaloids was achieved as described in a previous communication (4). Extraction with chloroform at pH 1.5 gave the weak bases which contained the scoulerine fraction. Nonphenolic alkaloids were removed with chloroform at pH 13 - 14, and the phenolic bases separated by preparative thin-layer chromatography on silica gel. Scoulerine isolated from the plates was further purified by repeated crystallisation of the picrate and finally of the free base, m.p.197° (micro m.p. K) [Lit. (5) 195° and 204°] ; $[\alpha]^{26}_{D}$ - 318° (C = 0.41 in methanol); C, 70.17%, H, 6.15%, N, 4.28% (Calcd. for $C_{19}H_{21}NO_4$: C, 69.70%, H, 6.47%, N, 4.28%).

The purified alkaloid gave a single spot by thin-layer chromatography in different solvent systems (6). Mass spectrometry gave mass m/e 327. Major fragments appeared in the mass spectrum at m/e 135, 150, 176, 178 and 326, corresponding to the favoured cleavage of tetrahydroberberines (7). The N.M.R. spectrum revealed two O-methyl groups (singlet, τ 6.18), four aromatic protons in the region τ3.1 - 3.5 and the absence of an N-methyl group. The I.R. and U.V. spectra as well as the R_f values on silica gel and alumina plates were identical with those of authentic (-)-scoulerine.

Acknowledgement. The authors are indebted to Professor A.R. Battersby and to Dr. J.A. Martin for providing a sample of authentic scoulerine and for helpful suggestions and discussions during the structure elucidation.

This investigation was supported by a research grant MH-03487 from the National Institutes of Health, U.S. Public Health Service, Bethesda, Maryland.

REFERENCES

1. D.H.R. Barton, R.H. Hesse and G.W. Kirby, Proc. Chem. Soc., 1963, 267; J. Chem. Soc., 1965, 6379.
2. A.R. Battersby, R.J. Francis, E.A. Ruveda and J. Staunton, Chem. Comm., 1965, 89.
3. A.R. Battersby, personal communication.
4. E. Brochmann-Hanssen and T. Furuya, Planta Med., **12**, 328 (1964).
5. H.-G. Boit, "Ergebnisse der Alkaloid-Chemie bis 1960", Akademie-Verlag, Berlin 1961, p. 334.
6. N.Y. Mary and E. Brochmann-Hanssen, Lloydia, **26**, 223 (1963).
7. H. Budzikiewicz, C. Djerassi and D.H. Williams, "Structure Elucidation of Natural Products by Mass Spectrometry, Vol. I, Alkaloids", Holden-Day Inc., San Francisco, 1964, p. 181.