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THE ALKALOIDS OF *LADENBERGIA HEXANDRA*

J. S. E. HOLKER, W. J. ROSS and W. B. WHALLEY*

The Robert Robinson Laboratories, The University, Liverpool

R. F. RAFFAUF

Smith Kline and French Laboratories, Philadelphia

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Abstract—The first isolation of a yohimbine type alkaloid from the genus *Ladenbergia* is reported.

INTRODUCTION

THE GENUS *Ladenbergia* is closely related to *Cinchona* (Family: Rubiaceae, Tribe: Cinchoneae); some botanists do not distinguish the two. From the chemotaxonomic standpoint, it is, therefore, not surprising that up to 2% of quinine had been reported present in the barks of *L. moritziana* and *L. macrocarpa*.[1] On the other hand, findings with respect to other species leave some questions concerning the nature of the alkaloids present in other members of the genus.[2] *L. hexandra* has been reported to contain no alkaloids.[1] Through the kindness of Dr. O. Ribeiro† we recently had the opportunity of investigating the bark of this plant.‡

The total alkaloid content was small and the principal constituent was identified as yohimbine, known to occur in other genera of the Rubiaceae closely related to *Ladenbergia* (e.g. *Corynanthe*). The minor component of the mixture was not identified but appeared to be of the yohimbine type.

As far as we are aware, this is the first record of the isolation of a yohimbine-type alkaloid from the genus *Ladenbergia*.

EXPERIMENTAL

The powdered bark (100 kg) of *L. hexandra* was exhaustively extracted with alcohol. Ammonium hydroxide (10 l. 5% solution) was added to the residue remaining after removal of the alcohol and the mixture was extracted with chloroform (50 l. in 7-l. portions). The chloroform was concentrated (7 l.) and washed with 2% aqueous tartaric acid (4 × 2 l.). The residual chloroform solution was evaporated and the syrup remaining dissolved in ether (3 l.) and re-extracted with the tartaric acid solution (5 × 1 l.). (Troublesome emulsions were formed during the various extraction stages.) The combined tartaric acid extracts were

* Present address: The School of Pharmacy, University of London, 29/39 Brunswick Square, London, W.C.1.

† Instituto de Quimica Agricola, Ministerio da Agricultura, Rio de Janeiro, Brazil.

‡ A voucher specimen of the plant used in this study has been deposited with Professor R. E. Schultes, Curator, Botanical Museum, Harvard University, Cambridge, Massachusetts.

[1] C. WEHMER, *Die Pflanzenstoffe*, Vol. II, pp. 1152, 1164, 1165, Fischer, Jena (1931).
[2] H. PITTIER, *Plantas Usuales de Venezuela*, pp. 353, 354, Caracas (1926).

basified with 5% ammonium hydroxide and extracted with ether. Saturation with gaseous HCl of the dried etheral extracts furnished a precipitate of crude alkaloid hydrochlorides (9 g) which was fractionally crystallized from methanol–acetone to yield three major crops, A, B, and C, totalling 8·4 g.

Preliminary investigations indicated that the three fractions were substantially similar, and paper-chromatography of the free-bases showed the presence of two components which were separated as follows.

The alkaloids (109 mg) from fractions A, B or C were chromatographed on Woelm alumina (Activity I) from benzene–chloroform (1:2) followed by elution with benzene–chloroform (4:1). The fraction eluted by this mixed solvent was purified from chloroform–light petroleum (b.p. 60–80°) to yield yohimbine (58 mg), m.p. and mixed m.p. 234–235°, $[a]_D^{20}+105°$ (*c.*, 1·25 in pyridine). (Found: C, 70·6; H, 7·4; N, 7·8. Calc. for $C_{21}H_{20}N_2O_3$: C, 71·2; H, 7·4; N, 7·9%). The i.r. and u.v. spectra were identical with those of an authentic specimen.

After removal of the yohimbine, elution with benzene–chloroform (7:3) furnished a product (21 mg) which separated from aqueous alcohol in pale yellow needles, m.p. 228–232°, $[a]_D^{20}-13°$ (*c.*, 0·99 in alcohol or pyridine). This compound decomposed easily in solution and exhibited i.r. and u.v. spectra very similar to those of the yohimbine-type alkaloids. It was not further investigated.

Hydrolysis of the mixture (from fractions A, B or C) of alkaloids (103 mg) with boiling *N*-methanolic potassium hydroxide (20 ml) during 4 hr or with acid gave yohimbic acid (73 mg), m.p. 256–260°, identical with an authentic specimen, and having the requisite i.r. and u.v. spectra. (Found: C, 66·9; H, 7·4; N, 7·8. Calc. for $C_{20}H_{24}N_2O_3.H_2O$: C, 67·0; H, 7·3; N, 7·8%.) $[a]_D^{20}+134°$ (*c.*, 1·1 in pyridine).

Infrared spectra were determined in Nujol mull using a Model 21 Perkin-Elmer Spectrophotometer.