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BASES DERIVED FROM TRYPTAMINE IN ARGENTINE *PIPTADENIA* SPECIES

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Abstract—The presence and distribution of indolic bases in the five Argentinian species of the genus *Piptadenia* (*Leguminosae*) are reported. *P. macrocarpa* Benth., has the highest alkaloid content, and 5-methoxy-N-methyltryptamine, bufotenine and N,N-dimethyl-tryptamine, have been isolated. *P. excelsa* (Gris.) Lillo contains bufotenine and N,N-dimethyltryptamine, but the other three species, *P. rigida* Benth., *P. paraguayensis* (Benth). Lindm. and *P. viridiflora* (Kunth.) Benth. do not contain tryptamine base.

INTRODUCTION

Piptadenia species have long been used by natives of several South American countries as a source of magical or medical drugs. In spite of this long tradition it was only recently that Stromberg[1] isolated bufotenine from seeds of *P. peregrina* (L.) Benth., a finding which explained most of the effects produced by the inhalation of the powdered material. Shortly afterwards, Fish, Johnson and Horning[2] studied the seeds and seed pods of *P. peregrina* (L.) Benth., *P. macrocarpa* Benth. and *P. paniculata* Benth. collected in several areas (Florida, U.S.A., Puerto Rico, Brazil) and showed that the first two species contained bufotenine, bufotenine oxide and N,N-dimethyltryptamine oxide in the seeds, and N,N-dimethyltryptamine in the seed pods. More recently, Legler and Tschesche[3] reported the isolation of N-methyltryptamine, 5-methoxy-N-methyltryptamine and 5-methoxy-N,N-dimethyltryptamine from the bark of *P. peregrina* collected in Brazil, and bufotenine was found in the seeds of another Brazilian species *P. colubrina* Benth.[4]

The indolic bases of the tryptamine type have a very wide distribution in the plant kingdom,[5] and in order to confirm previous work and to extend the knowledge of content and distribution of indolic bases in the genus *Piptadenia*, we have investigated the five species growing in the Argentine: *P. macrocarpa* Benth., *P. excelsa* (Gris.) Lillo, *P. rigida* (Benth.), *P. paraguayensis* (Benth.) Lindm. and *P. viridiflora* (Kunth.) Benth.†

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† The specimens of *P. macrocarpa* and *P. excelsa* were collected and identified by Dr. T. Meyer of the Instituto Miguel Lillo, Universidad Nacional de Tucumán, Tucumán, R. Argentina. The other three species were authenticated by Ing. R. Ratera of the Instituto de Botánica, Ministerio de Agricultura y Ganadería, Buenos Aires, R. Argentina.

[1] V. L. STROMBERG, *J. Amer. Chem. Soc.* **76**, 1707 (1954).

[2] M. S. FISH, N. M. JOHNSON and E. C. HORNING, *J. Amer. Chem. Soc.* **77**, 5892 (1955).

[3] G. LEGLER and R. TSCHESCHE, *Die Naturwiss.* **50**, 94 (1963).

[4] I. J. PACHTER, D. E. ZACHARIAS and O. RIBEIRO, *J. Org. Chem.* **24**, 1285 (1959).

[5] V. ERSPAMER, *Fortschr. Arzneim.* **3**, 151 (1961).

P. macrocarpa was by far the richest in total alkaloid content and in the number of bases present in different parts of the plant. Bufotenine and N,N-dimethyltryptamine were isolated both from seeds and seed pods, and when the remaining mother liquors were submitted to paper chromatography, bufotenine oxide, as well as traces of another unidentified 5-hydroxyindole derivative, were detected in the seeds. The bark yielded 0·1 % of 5-methoxy-N-methyltryptamine as a crystalline oxalate, but no bases were found in the wood. The latter compound was first discovered in *Phalaris arundinaceae* L. (*Gramineae*)[6] and was also recently reported in *Piptadenia peregrina*.[3]

The samples of *P. excelsa* which we examined contained alkaloids only in the seeds and seed pods. No bases could be detected in the bark, although Stucker and Paya[7] have reported the isolation of a quaternary alkaloid of unknown structure from this source. In the seeds, bufotenine and bufotenine oxide were identified by paper chromatography, and the former compound was also isolated, although in much lower yield than from the seeds of *P. macrocarpa*. From seed pods, N,N-dimethyltryptamine was isolated as its picrate, and paper chromatography showed that no other indole bases were present in this extract.

The three other species *P. paraguayensis* (bark, seed pods and seeds), *P. rigida* (seeds) and *P. viridiflora* (mixed seeds and pods) gave negative test for alkaloids except for the bark of *P. paraguayensis*, which yielded a faint positive reaction. Paper chromatography of the extract revealed only one compound which gave a positive reaction for alkaloids, but with the usual indole reagents only negative reactions were obtained. The extract was not further investigated.

EXPERIMENTAL

All the samples were extracted and worked up as described below for *P. macrocarpa*. Ascending paper chromatography was used on Whatmann No. 1 paper and the two mobile phases recommended by Fish *et al.*:[2] *n*-propanol–1 N ammonium hydroxide (5:1) (solvent 1), and *tert.*-butanol–formic acid–water (207:6:87) (solvent 2). The identification of crystalline compounds was by mixed m.p. determinations and by comparison of u.v. and i.r. spectra with authentic samples.

Extraction

The different parts of *P. macrocarpa* were ground, covered with 1 N HCl, stirred for 12 hr at room temperature, filtered and the extraction repeated three times more. The combined acid extracts were adjusted to pH 9 with solid Na_2CO_3 and the bases exhaustively extracted with ethyl acetate. The combined organic extracts were dried and evaporated, and the solid or semi-solid residues obtained worked up as follows.

Bark Extract

A solution in EtOH was treated with solid oxalic acid. After leaving overnight at 0°, the crystals formed were collected and recrystallized from EtOH to give pure 5-methoxy-N-methyl-tryptamine oxalate, m.p. 209–210°. (Found: C, 57·29; H, 6·38; N, 9·49; CH_3O, 10·46. Calc. for $C_{14}H_{18}O_5N_2$: C, 57·13; H, 6·16; N, 9·52; 1 CH_3O, 9·39 %.) From the oxalate was prepared the picrate, m.p. 221–222° (dec.). (Found: C, 49·96; H, 4·60; N, 16·00; mol. wt. (spectroph.) 431. Calc. for $C_{18}H_{19}O_8N_4$: C, 49·88; H, 4·41; N, 16·16 %; mol. wt. 433). The

[6] S. WILKINSON, *J. Chem. Soc.* **1958**, 2079.

[7] G. V. STUCKER and M. PAYÁ, *Investigaciones del Laboratorio de Quimica Biológica*. Tomo II, Facultad de Ciencias Médicas, Universidad Nacional de Córdoba (1938).

comparison of both compounds with synthetic samples showed no depression in m.p. and identical i.r. spectra.

Seed Extract

The crude solid residue was redissolved in ethyl acetate and the solution filtered through a small column of neutral alumina (activ. III). The solution was concentrated and left overnight at 0° yielding crystalline bufotenine, m.p. 123–124°, unchanged after further recrystallizations from the same solvent. (Found: C, 70·49; H, 7·95; N, 13·50. Calc. for $C_{12}H_{16}ON_2$: C, 70·56; H, 7·90; N, 13·72%.) The sample gave a series of derivatives, dipicrate m.p. 174–175°; N-Oxide m.p. 212–214° and methiodide m.p. 210°, identical in all respects with the same derivatives prepared from an authentic sample of bufotenine m.p. 146–147°, thus confirming its isomorphic nature. When the low melting form was dissolved in ethyl acetate and the hot solution seeded with bufotenine m.p. 146°, the higher melting point isomer was obtained. This was the more stable and could not be reconverted into the lower melting form. Both types of crystals gave bufotenine picrolonate m.p. 183–184°. (Found: N, 18·34. Calc. for $C_{22}H_{24}O_6N_6$: N, 17·94%), a value higher than that of m.p. 120–121° reported by Deulofeu and Berinzaghi.[8]

The mother liquors from the crystallization of bufotenine were evaporated to dryness, dissolved in $CHCl_3$ and fractionated on a column of neutral alumina (activ. III). From the eluates obtained with $CHCl_3$ N,N-dimethyltryptamine was isolated as the picrate, m.p. 168–169°. The eluate obtained with $CHCl_3$ containing 5% EtOH was submitted to 240 transfers in a countercurrent distribution apparatus using the solvent system *n*-butanol/phosphate buffer pH 3·4. Three peaks were observed using the absorptivity at 280 mμ of the upper phases as a guide. The middle peak (K = 0·10) contained bufotenine as shown both by paper chromatography and the isolation of the crystalline base, m.p. 144–145°. The material in the first peak (K = 0·05) had R_f values of 0·89 (solvent 1) and 0·40 (solvent 2) and the usual positive reactions for alkaloids and 5-hydroxyindole bases, but was not further examined. The third peak (K = 0·60) contained bufotenine oxide as shown by paper chromatography.

Seed Pods Extracts

The solid residue was dissolved in chloroform and subjected to a column chromatography on neutral alumina (activ. III), eluting first with $CHCl_3$ and then with $CHCl_3$ containing 1% and 5% EtOH. The $CHCl_3$ eluate gave a residue which, dissolved in EtOH and treated with picric acid, gave N,N-dimethyltryptamine picrate, m.p. 171–172°, alone or in admixture with an authentic sample. The eluate obtained with 5% EtOH in $CHCl_3$ when worked up in a similar way yielded bufotenine picrate, m.p. 174–175·5°.

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[8] V. DEULOFEU and B. BERINZAGHI, *J. Amer. Chem. Soc.* **68**, 1665 (1946).