[DEPARTMENT OF EXPERIMENTAL THERAPEUTICS, LABORATORIO CUP]

Extraction of Reserpine and Other Alkaloids from Colombian *Rauwolfia hirsuta*

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Methods for the extraction and separation of reserpine, rauwolscine and alstonine from Colombian *Rauwolfia hirsuta* are described.

Rauwolfia hirsuta Jacq. or *Rauwolfia canescens* grows on the Atlantic coast and other regions of Colombia. Our preliminary work on that plant already has been published.[1,2]

The present paper describes the extraction from it of several alkaloids, the pharmacological properties of which have been studied by K. Mezey, and will be published elsewhere.

For the extraction of reserpine from *R. hirsuta*, it was not found necessary to separate and purify previously the "oleoresins," as it was done to obtain the alkaloid from other species.[3-5]

Experimental

Two kilograms of the finely powdered root of *R. hirsuta* were extracted with methanol until the solvent was alkaloid free. The extract was concentrated *in vacuo* to 2 l., diluted with an equal volume of water, and extracted with several 2-l. portions of chloroform. The combined chloroform solutions were chromatographed on a column with 200 g. of aluminum oxide, and the chromatogram eluted with 2 l. of chloroform. The eluate was evaporated to dryness *in vacuo*, and the residue recrystallized from methanol to give reserpine (1 g.).

The water–methanol solution left from the extraction of reserpine was concentrated *in vacuo* to remove the methanol, made slightly alkaline with ammonia (10%), and extracted several times with 2-l. portions of ether. The combined ether solutions were extracted with 2% tartaric acid, the tartaric acid solution was made alkaline with ammonia (10%), and the precipitated alkaloids filtered. From the ammoniacal filtrate a new portion of alkaloids was extracted with ether. The precipitated alkaloids were mixed with those obtained from the ethereal solution, dried and stirred several times with chloroform. The chloroform insoluble residue was filtered, washed with chloroform, redissolved in 2% tartaric acid, reprecipitated with ammonia, filtered and recrystallized from acetone, to give a small portion of an alkaloid which, according to its melting point and chemical behavior, seems to be sarpagine.

The chloroform solution was evaporated to dryness *in vacuo*, and the residue recrystallized from benzene, to give rauwolscine (10 g.).

The aqueous phase left from the extraction of the last two alkaloids was then made strongly alkaline with sodium hydroxide solution (10%), and extracted several times with ether to which 10% methanol was added; the combined organic phases were extracted with 10% acetic acid, the acetic acid solution alkalinized with sodium hydroxide solution (10%), and the precipitate filtered and recrystallized from ethyl alcohol, to give alstonine (1 g.).

The alkaloids were identified by their melting points and those of their derivatives. Equivalent weights were determined for rauwolscine and alstonine. All the experimental values compared well with those given in the literature.[3-9]

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[3] L. Dorfman, A. Furlenmeier and others, *Helv. Chim. Acta*, **37**, 59 (1954).

[4] N. Neuss, H. Boaz and J. W. Forbes, THIS JOURNAL, **76**, 2463 (1954).

[5] C. Djerassi, M. Gorman and A. L. Nussbaum, *ibid.*, **75**, 5446 (1953).

[6] A. Stoll and A. Hofmann, *Helv. Chim. Acta*, **36**, 1143 (1953).

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BOGOTÁ, COLOMBIA

[CONTRIBUTION FROM THE CHEMICAL RESEARCH LABORATORIES, THE LUBRIZOL CORPORATION]

Aromatic Phosphinic Acids and Derivatives. I. Diphenylphosphinodithoic Acid and Its Derivatives

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A modified Friedel–Crafts synthesis has been used for the preparation of diphenylphosphinodithioic acid. The acid was the precursor for the synthesis of diphenylphosphinothioic chloride and diphenylphosphinic chloride. Diphenylphosphinothioic acid was prepared by the reaction of the thioic chloride with sodium hydroxide and also by the reaction of the phosphinic chloride with sodium hydrosulfide.

No satisfactory method for the preparation of diphenylphosphinodithioic acid has been reported in the chemical literature. The method of Malatesta[1] employing the Grignard reagent and phosphorus pentasulfide is probably the best, but gave only a 24% yield.

Benzene reacts with phosphorus pentasulfide and anhydrous aluminum chloride to give the crude acid in 70–90% yields. When eight moles of aluminum chloride per mole of phosphorus pentasulfide (P_4S_{10}) are used, the best yields are obtained after about eight hours. When the aluminum chloride was decreased to four moles, the yields were halved.

Pure diphenylphosphinodithioic acid melted at 55–56°. The only melting point reported previously for this material was 25–30°.[1] Oxidation with dilute nitric acid formed diphenylphosphinic acid which melted at 190–192°. The acid obtained by Malatesta from a similar oxidation of his dithioic acid melted at 188–190°.

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[1] L. Malatesta, *Gazz. chim. ital.*, **76**, 167 (1947).