THE ALKALOIDS OF ISOPYRUM AND ISOPYROINE.[1]

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THE isopyrum, so far as can be ascertained, has only once been studied chemically. Hartsen,[2] in a brief examination of *isopyrum thalictroides,* reported the isolation of two new alkaloids. The one he named isopyrine and the other he called pseudoisopyrine. The following is a statement of the method which he used in obtaining these two substances: The root of the *thalictroides* was extracted with water and filtered. The filtrate was evaporated almost to dryness and treated with ammonia. The precipitate thus formed, consisted of aluminum hydroxide, tannic acid and the new base, isopyrine. To remove the latter, the precipitate was dried and extracted with ether. By filtering off and evaporating the ethereal solution, the alkaloid was obtained as an amorphous powder. Nothing further was done with the substance. No attempts were made to purify it or to study its properties and no salts of any kind were made.

Pseudoisopyrine, the other alkaloid, was obtained by treating the roots with alcohol, after they had been extracted with water. The alcoholic extract was condensed by evaporation and treated with ammonia as in the case of the aqueous extract. The precipitate formed by the ammonia, was filtered off, dried and extracted with ether. On removing the excess of ether, the alkaloid crystallized out in star-shaped crystals. As in the first case, no attempt was made to purify the substance and no salts were made. The author of the above paper, while applying the above names, suggested that, quite likely, these two substances were known substances, possibly mixtures of the aconite group.

The above paper was published twenty-eight years ago and nothing has been done since that time although the plant is quite abundant in certain localities. According to Gray, isopyrum is abundant throughout the central, northwestern and southwestern states. According to MacMillan,[3] it is widely distributed throughout Minnesota and Iowa.

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[1] Read before the American Association for the Advancement of Science, at Denver, 1901.

[2] *Chem. Centrbl.* (1872). p. 523.

[3] "Metaspermae of Minnesota," p. 231.

My attention was first called to the American species, *isopyrum biternatum,* by Professor MacDougal, of Bronx Park, New York, who, in studying the tubers botanically, observed certain reactions which gave evidence of the presence of a substance of unusual interest. A year later, with the assistance of students, enough material was obtained to make a preliminary examination and to prove beyond a doubt, the presence of an alkaloid. The work has been renewed recently, and enough material obtained to make a careful examination. Samples were collected at different times during the summer and examined. That gathered in the early spring contained only a small quantity of the alkaloid, while that gathered later in the summer contained a maximum amount of the alkaloid. In the early spring, the roots appear as fine fibers with only here and there a very small tuber; in midsummer, the tubers were very much larger and more abundant.

The first work done on the American species was to repeat the method given by Harsten on the *thalictroides.* The results, however, were unsatisfactory and other methods were tried and enough of the material was obtained for analysis.

METHOD OF EXTRACTION.

Many methods, including that of Harsten, were tried but with unsatisfactory results. The method which gave best results was as follows: The roots were cleaned, dried, and pulverized and the powder thus obtained, extracted with hydrochloric acid (1:250). The extraction was made first by heating on a water-bath for an hour and then allowing to stand for twelve hours. The acid solution was then filtered off and evaporated to about one-fifth of the original volume and refiltered. The almost clear filtrate was then treated with ammonia. The precipitate formed, which, according to Harsten should contain the alkaloid isopyrine, was saved, dried and extracted with ether. It proved to be only inorganic matter. The filtrate was then evaporated to dryness and extracted with alcohol. The alcoholic solution gave distinct alkaloidal reactions but all attempts to isolate the free base failed.

The roots were now extracted with alcohol in the presence of hydrochloric acid for several hours and filtered. The filtrate was then condensed by evaporation, treated with ammonia, and filtered. The precipitate thus obtained, was redissolved in hydrochloric acid, reprecipitated with ammonia, and filtered. This filtrate was added to the original filtrate, evaporated to dryness, and extracted with chloroform. The chloroform solution was treated with hydrochloric acid and allowed to stand for several days. At the end of that time, crystals had formed which proved to be the hydrochloride of the alkaloid.

These crystals were removed, purified by filtering through animal charcoal and again crystallized out of water. Thus obtained, the substance was a beautiful white felt-like mass of fine crystals. It is soluble in water and alcohol but almost insoluble in ether.

Under the microscope the crystals appear as long, fine, prismatic needles. The melting-point of the pure substance was found to be 255° to 257° C. The hydrochloride formed a well-crystallized platinum double salt. It is a bright yellow, granular substance, insoluble in water but slightly soluble in alcohol. It melts at 238° C.

THE FREE BASE, ISOPYROINE.

The hydrochloride was dissolved in a very small quantity of dilute alcohol, and sodium hydroxide cautiously added. The white flocculent precipitate formed was filtered off and dissolved in an excess of alcohol. On slowly evaporating the alcohol, the base was reprecipitated as a white, crystalline substance. These crystals had a sharp melting-point of 160° C. On drying at 100° C., the substance lost its crystalline nature and became a light gray powder. Analyses of the dried substance gave the following results:

I. 0.1230 gram of the dried substance gave 0.2814 gram CO_2; 0.0964 gram H_2O.

II. 0.2042 gram of the dried substance gave 0.4628 gram CO_2; 0.1599 gram H_2O.

	Calculated for the formula, $C_{28}H_{46}NO_9$.	Found. I.	II.
Carbon	62.22	62.22	61.81
Hydrogen	8.51	8.70	8.69
Nitrogen	2.54	....	....

In view of the fact that the alkaloid in hand differs widely from the isopyrine and pseudoisopyrine of Hartsen, the base has been called isopyroine.

ISOPYROINE METHYL IODIDE, $C_{28}H_{46}(CH_3)NO_9I$.

The powder was treated with methyl iodide for two hours on a water-bath with reflux condenser and at the end of that time, the substance, which at first dissolved, formed a yellow residue in the bottom of the flask. The iodide was removed and reprecipitated from an alcoholic solution with water. The substance thus formed was of a yellow color and almost insoluble in water, ether and chloroform. An iodine analysis gave the following numbers:

I. 0.2204 gram of the substance gave 0.0758 gram of silver iodide.

	Calculated for the formula, $C_{28}H_{46}(CH_3)NO_9I$.	Found.
Iodine.............	18.62	18.8

In addition to the iodide, the chloride and the platinum double salt have been made and are in process of analysis.

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