CHII.—*The Constitution of Hydrastinine.*

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HYDRASTININE, $C_{11}H_{13}O_3N$, a derivative of the alkaloid hydrastine, is closely related to cotarnine, from which it differs only in being without the methoxyl group which is present in the benzene nucleus of the latter substance.

The main points in the constitution of these two substances have been satisfactorily determined by the study of their chemical reactions, but the data thus obtained are insufficient to allow of a decision being arrived at as to which of the formulæ proposed by different chemists should be assigned to the alkaloids in the solid state or in solution in any particular solvent.

In a former paper (Trans., 1903, 83, 598), evidence, drawn from an examination of the absorption spectra of cotarnine and its derivatives, was adduced in favour of the adoption of Decker's carbinol formula for this substance in the solid state and in solution in ether or chloroform. If this evidence is accepted as satisfactory in the case of cotarnine, it follows from the known relations of the two compounds that hydrastinine must be represented by a similar formula, but in view of the remarkable character of some of the results obtained

with cotarnine, it seemed to us desirable to make an entirely independent examination of hydrastinine.

Hydrastinine is a colourless, crystalline substance which is soluble in anhydrous, alcohol-free ether or chloroform to a colourless solution,* but with water or alcohol it yields a yellow, fluorescent solution. The absorption spectra of the colourless and coloured solutions are entirely different, the former being practically identical with those of hydrohydrastinine, a compound which is generally considered to have the constitution represented by formula (I), the latter with those of the hydrastinine salts. It may, therefore, be assumed that hydrastinine and hydrohydrastinine are constituted alike, and that the carbinol formula (II), which represents the former as being derived from the latter substance (I) by the replacement of an atom of hydrogen by hydroxyl, is to be preferred to Roser's open chain or aldehydic formula, which leaves the agreement between the spectra of the two substances unexplained. On the other hand, the identity of the absorption spectra of the aqueous or alcoholic solutions of hydrastinine with those of the hydrastinine salts shows that in these solvents hydrastinine possesses the quaternary ammonium form (III).

The spectra exhibited by solutions of hydrastinine and hydrastinine derivatives agree closely with those of the corresponding solutions of cotarnine and its derivatives.

1. The spectra of the colourless solutions have one band in the same position as the band of colourless solutions of cotarnine. The general absorption exhibited by these spectra is, however, slightly greater than that of the corresponding cotarnine spectra, the difference being nearly the same as between the spectra of the parent alkaloids, hydrastine and narcotine (Trans., 1903, 83, 605). Solutions of hydrastinine in ether or chloroform, hydrohydrastinine and its salts, cyanohydrohydrastinine in solution in ether or chloroform, cyano-hydrohydrastinine methiodide, and methoxyhydrohydrastinine methiodide possess spectra of this type.

All these substances are colourless, and can be represented, con-

* There is no reason to suppose that either ether or chloroform exercises any chemical action on hydrastinine, which can be recovered from these solvents without alteration. The absorption spectra of these solutions are therefore regarded as the absorption spectra of the solid substance.

sistently with their known reactions, by means of the carbinol formula.

2. The spectra of dilute aqueous or alcoholic solutions of hydrastinine* show, on the other hand, a large amount of general absorption, and possess three absorption bands. One of these corresponds in position with the band of cotarnine at the extreme ultra-violet end of the spectrum, whilst the other two together occupy the position of the cotarnine band which is nearest to the visible end of the spectrum. In other words, one of the cotarnine bands is represented in the hydrastinine spectra by two narrower bands. Apart from this difference, the agreement between the spectra of aqueous solutions of cotarnine and hydrastinine is very close. All the true salts of hydrastinine possess the same spectra as the aqueous or alcoholic solutions of hydrastinine. The solutions which give these spectra are all yellow and fluorescent, and the substances may be represented by the quaternary ammonium formula, in which the nitrogen atom is linked to an adjacent carbon atom by a double bond. It should be added that the spectra of a solution obtained by removing the chlorine from an aqueous solution of hydrastinine hydrochloride by means of silver oxide are identical with those of the chloride, whereas the spectra of a solution obtained by the addition of an excess of caustic soda to hydrastinine hydrochloride are identical with those of hydrastinine in ether.

* The absorption curve of hydrastinine in alcohol, given in a former paper (Trans., 1903, 83, 605), was drawn before it was known that the constitution of this substance is altered by solution in alcohol. The curve really represents the absorption caused by a mixture of the carbinol and quaternary ammonium forms.

As in the case of cotarnine, the argument in favour of assigning the carbinol formula to solid hydrastinine and its colourless solutions derives

Scale of oscillation-frequencies.

The curve of hydrastinine in water is coincident with the curve of hydrastinine hydrochloride except where indicated by the dotted line.

The numbers I, II, and III denote the positions of the absorption bands referred to in the text.

CURVE II.

confirmation from the study of the cyanide. By the interaction of hydrastinine hydrochloride and potassium cyanide in aqueous solution,

a colourless compound (m. p. 80—81°) is obtained, which differs in its slight solubility and other properties from the true salts of hydrastinine, and cannot, therefore, be represented by a similar formula. This substance, moreover, like cyanohydrocotarnine, forms a methiodide, the constitution of which can only be satisfactorily explained by regarding the cyanide as a derivative of hydrohydrastinine or of the carbinol form of hydrastinine (IV and V).

(IV) Cyanohydrohydrastinine.

(V) Cyanohydrohydrastinine methiodide.

As has already been pointed out, the spectra of both these substances are identical with those of the other colourless derivatives of hydrastinine. Cyanohydrohydrastinine, it should be mentioned, is less stable than cyanohydrocotarnine, for whilst the latter substance dissolves in alcohol as well as in ether or chloroform to a colourless solution, alcohol colours the former yellow, changing it partly into true hydrastinine cyanide.

Cyanohydrohydrastinine.

Hydrastinine cyanide.

The proportion of hydrastinine cyanide to cyanohydrohydrastinine is increased by the addition of more alcohol and diminished by the presence of an excess of potassium cyanide.

Alcohols act on solid hydrastinine or on an ethereal solution of hydrastinine in the same way as on cotarnine.

When hydrastinine is dissolved in a small quantity of alcohol, the solution, on being examined with the spectroscope, is seen to consist of a mixture of the carbinol and quaternary ammonium forms of the substance. By adding more alcohol or by raising the temperature, the proportion of the quaternary ammonium form is increased. The proportions of the two forms present under any given conditions can be ascertained with considerable accuracy by comparing the photographs of their spectra with a series of photographs of the spectra of solutions containing the two forms mixed in known proportions (Trans., 1903, 83, 598, Plate III). The action of methyl alcohol is similar to that of ethyl alcohol, but under the same conditions a given quantity of the former transforms a larger amount of the carbinol form into the ammonium base than an equivalent quantity of the latter. Under the influence of alkalis, the quaternary ammonium form of hydrastinine is changed into the carbinol modification. The amount of change depends principally on the amount of alkali, and is practically the same for molecular quantities of the fixed bases. The action of

bases on molecular quantities of hydrastinine and cotarnine effects a greater change in the former than in the latter case.

Thus a solution of cotarnine in $N/10$ caustic soda contains 90 per cent. of the carbinol form and 10 per cent. of the quaternary ammonium form, whilst an equivalent amount of hydrastinine dissolved in caustic soda of the same strength contains 95 per cent. of the carbinol form and 5 per cent. of the quaternary ammonium form. On the other hand, under the influence of alcohols, cotarnine changes more readily than hydrastinine from the carbinol to the quaternary ammonium form.

For example, a solution of cotarnine in methyl alcohol containing 1 mg. mol. in 500 c.c. contains 70 per cent. of the carbinol and 30 per cent. of the quaternary ammonium form, whilst a similar solution of hydrastinine contains 80 per cent. of the carbinol and 20 per cent. of the quaternary ammonium form.

Solutions of the ammonium form of hydrastinine are, as has been already stated, yellow, but the colour is less intense than that of the corresponding cotarnine solutions. They are, unlike the cotarnine solutions, strongly fluorescent. The fluorescence affords an excellent means of ascertaining whether or not a hydrastinine solution is free from the quaternary ammonium form, since it disappears at once when the conversion into the carbinol form is complete.

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