

XIX.—*Corydaline*. Part I.

By JAMES J. DOBBIE, M.A., D.Sc., and ALEXANDER LAUDER, University College of North Wales, Bangor.

THE rare alkaloid corydaline was discovered by Wackenroder in the year 1826 in the tubers of *Corydalis tuberosa* (*Kastner's Archiv*, 8, 423), and in the course of the next 40 years was investigated by numerous chemists, who failed, however, to arrive at a satisfactory conclusion with regard to its formula. In 1866, Wicke published in the *Annalen*, 137, 274, a more complete and careful account of the alkaloid than had hitherto appeared, accompanied by numerous analyses of the base and its compounds; from these he deduced the formula $C_{18}H_{19}NO_4$, which has since been accepted as representing correctly the composition of the alkaloid.

Before beginning an investigation of the decomposition products of corydaline, we subjected several samples to analysis, and came to the conclusion that Wicke's formula is incorrect. The corydaline with which we experimented was obtained from Schuchardt, of Görlitz, in different lots, prepared at different times from the dried roots of *C. tuberosa*, gathered partly in the Tyrol and partly in Thuringia. The various samples were examined and analysed separately with the view of establishing definitely the identity of the alkaloid obtained from different sources. After numerous experiments, we found that a mixture of absolute alcohol and ether, as recommended by Wicke, is the best solvent for corydaline. Such a solution rapidly assumes a yellow colour on exposure either to light or heat, and when employed for the crystallisation of the alkaloid, must be kept in a cool, dark chamber. This susceptibility of corydaline to the action of light and heat probably accounts for the difficulty which earlier experimenters experienced in purifying this alkaloid. The yellow resin with which they supposed it to be contaminated in the later stages of purification was no doubt an alteration product due to the action of light or heat, from which there is no evidence to show that they were careful to protect their solutions. In the paper already quoted, Wicke says: "The further purification of the crystals offered special difficulties, since the yellow colour could not be got rid of either by repeated crystallisation, or by treatment with freshly ignited animal charcoal." The former method of treatment would, in the presence of light, give rise to the production of the yellow matter from which it was intended to free the alkaloid, and the treatment with animal charcoal, if carried out in the usual way, would produce the same result.

When crystallised with the precautions described, corydaline forms perfectly colourless, flat, prismatic crystals, which sometimes measure an eighth of an inch in length, and are, like their solution, quickly coloured yellow by the action of light or heat. Pure corydaline, when heated, changes colour about 125°, softens about 133°, and melts finally at 134·5°. We were unable to detect any difference in the melting point of the various samples experimented with when they were examined under similar conditions. The melting point given by Wicke is 130°. Corydaline dissolves easily in ether, chloroform, carbon bisulphide, and benzene, but less readily in alcohol. It also dissolves in oil of turpentine, yielding a yellow solution. Corydaline is practically insoluble in cold water, and only very slightly soluble in boiling water. From a pure alcoholic solution, water precipitates it in the crystalline form. It is soluble in dilute hydrochloric and sulphuric acids. When heated with dilute nitric acid, nitrous fumes are evolved, and a small quantity of the alkaloid dissolves, forming a blood-red solution. Corydaline which has been coloured yellow by the action of light or heat is more easily soluble in alcohol or ether than the unaltered alkaloid. A small quantity of corydaline was heated on the water-bath for two hours at 80—90°. It became yellow, and on treatment with a mixture of ether and alcohol, the yellow portion dissolved easily to a yellow solution, leaving unaltered corydaline behind, which, when treated with the same solvent, dissolved yielding a colourless solution. We were able to make use of this in purifying the alkaloid, as we found it easy to remove a large part of the yellow substance by moistening with alcohol and ether and pressing between filter paper. Wicke has probably been misled by this difference between the solubility of altered and unaltered corydaline, when he states that alcohol dissolves pure corydaline with difficulty, although it dissolves corydaline which is mixed with resinous matter with great ease. We have further found that solutions of the purest corydaline rapidly become yellow on heating, although Wicke states that they remain colourless. The solution of corydaline in alcohol or ether has an alkaline reaction and a bitter taste.

The following are the results of the analysis of the pure alkaloid (dried over strong sulphuric acid) carried out in the usual way:—

I. 0·2389 gram coryd-	{	0·17005 gram H ₂ O =	7·90 p. c. H. (A.)
		0·6245 gram CO ₂ =	71·29 p. c. C. (A.)
II. 0·23325 " "	{	0·1656 gram H ₂ O =	7·88 p. c. H. (A.)
		0·6119 gram CO ₂ =	71·54 p. c. C. (A.)
III. 0·2504 " "	{	0·1740 gram H ₂ O =	7·72 p. c. H. (B.)
		0·6569 gram CO ₂ =	71·54 p. c. C. (B.)

IV.	0.2413	gram coryd- aline gave	0.1660	gram H ₂ O =	7.65 p. c. H. (B.)
V.	0.20805	„ „	0.5433	gram CO ₂ =	71.21 p. c. C. (C.)
VI.	0.2374	„ „	{ 0.1639	gram H ₂ O =	7.67 p. c. H. (D.)
			{ 0.62075	gram CO ₂ =	71.31 p. c. C. (D.)
VII.	0.4396	„ „	0.1156	gram Pt =	3.84 p. c. N. (A.)
VIII.	0.4549	„ „	0.1214	„ =	3.85 p. c. N. (B.)
IX.	0.4558	„ „	0.1230	„ =	3.89 p. c. N. (B.)
X.	0.4188	„ „	0.1206	„ =	3.68 p. c. N. (B.)
XI.	0.3802	„ „	0.1012	„ =	3.83 p. c. N. (C.)
XII.	0.4559	„ „	0.1212	„ =	3.83 p. c. N. (D.)

The mean of these numbers* is:—

Carbon	71.37 per cent.
Hydrogen	7.76 „
Nitrogen	3.82 „

from which we deduce the formula $C_{22}H_{28}NO_4$.

	Found.	Theory for $C_{22}H_{28}NO_4$.	Theory for Wicke's formula, $C_{18}H_{19}NO_4$.
Carbon	71.37 p. c.	71.36 p. c.	69.00 p. c.
Hydrogen ..	7.76 „	7.57 „	6.07 „
Nitrogen....	3.82 „	3.78 „	4.47 „
Oxygen	17.05 „	17.29 „	20.46 „
	100.00	100.00	100.00

Wicke's formula, $C_{18}H_{19}NO_4$, is only supported by two determinations of carbon and hydrogen and one of nitrogen, which agree, however, with his theoretical numbers.

Corydaline forms a large number of salts and derivatives, most of which can be prepared without difficulty. The hydrochloride and sulphate are difficult to crystallise on account of the tendency of their solutions to become gummy. For this reason, and because the hydrochloride contains water of crystallisation, we selected the hydriodide for analysis.

Corydaline Hydriodide.—This salt is very easily prepared by adding a solution of potassium iodide to a solution of the hydrochloride in water. The hydriodide separates out in pale-yellow flocks which redissolve readily in hot water, and crystallise out, on cooling, in clusters of lemon-yellow, short, prismatic crystals. The specimen used for analysis was purified by repeated recrystallisation from water, and dried at 100°. The results obtained are as follows:—

* The letters A, B, C, D, attached to the above analyses refer to the samples analysed.

I. 0.3017	gram salt gave	{ 0.1590 gram H_2O = 5.85 p. c. H.
		{ 0.5896 gram CO_2 = 53.29 p. c. C.
II. 0.3098	" "	{ 0.1625 gram H_2O = 5.82 p. c. H.
		{ 0.60525 gram CO_2 = 53.28 p. c. C.
III. 0.4832	" "	0.0924 gram Pt = 2.75 p. c. N.
IV. 0.3907	" "	0.0750 " Pt = 2.76 p. c. N.
V. 0.4799	" "	0.2279 gram AgI = 25.65 p. c. I.
VI. 0.4718	" "	0.2232 " AgI = 25.34 p. c. I.

	Found. (Mean of above analyses.)	Theory for $C_{22}H_{28}NO_4HI$.
Carbon....	53.28 per cent.	53.03 per cent.
Hydrogen .	5.83 "	5.80 "
Nitrogen ..	2.75 "	2.81 "
Iodine	25.49 "	25.47 "

The iodine, or other halogen, was determined in this and in other compounds containing them by heating the substance with pure lime and precipitation with nitrate of silver. The hydrobromide and hydrocyanide are prepared in the same way as the hydriodide, which they resemble in appearance and properties. Wicke analysed the hydrochloride and sulphate, but did not determine the carbon, hydrogen, and nitrogen in these salts. His determinations of chlorine agree well with his formula.*

Corydaline Platinochloride.—This salt is prepared in the pure state, suitable for exact analysis, by adding a solution of chloroplatinic acid, prepared by the action of chlorine and strong hydrochloric acid on

* Wicke describes two chlorides, one containing 5 mols. H_2O , one without water of crystallisation, and one sulphate without water of crystallisation. The results of his analyses of these salts are as follows:—

Hydrochloride (without water of crystallisation).

	Found.	Theory for $C_{18}H_{19}NO_4HCl$.
Corydaline	89.00 per cent.	89.53 per cent.
Hydrochloric acid	10.40 "	10.47 "
	99.40 "	100.00 "

Sulphate.

	Found.	Theory for $C_{18}H_{19}NO_4H_2SO_4$.
Corydaline	76.00 per cent.	76.15 per cent.
Sulphuric acid...	23.23 "	23.85 "
	99.23 "	100.00 "

The corydaline in both cases was determined by precipitation with ammonia.

pure spongy platinum, to a solution of pure corydaline in dilute hydrochloric acid. It has a pale buff-yellow colour, which deepens to orange-red on continued heating in the water-bath at 100° . It is soluble in hot water, from which it separates, on cooling, in brown crystals. The sample used for analysis, after precipitation, was washed with cold water until the washings were free from acid. The following are the results of the analysis of the salt dried at 100° :—

I.	0.2855	gram salt gave	{	0.1344 gram H_2O = 5.23 p. c. H.
			{	0.4853 gram CO_2 = 46.35 p. c. C.
II.	0.4332	„ „		0.0795 gram Pt = 2.64 p. c. N.
III.	0.4112	„ „		0.0739 „ Pt = 2.58 p. c. N.
IV.	0.2843	„ „		0.2084 gram $AgCl$ = 18.12 p. c. Cl.
V.	0.2368	„ „		0.1769 „ $AgCl$ = 18.45 p. c. Cl.
VI.	0.2433	„ „		0.0414 gram Pt = 17.01 p. c. Pt.
VII.	0.2919	„ „		0.0498 „ Pt = 17.06 p. c. Pt.
VIII.	0.2755	„ „		0.0465 „ Pt = 16.84 p. c. Pt.
IX.	0.3035	„ „		0.0511 „ Pt = 16.83 p. c. Pt.

	Found. (Mean of above analyses.)	Theory for $(C_{22}H_{28}NO_4)_2, H_2PtCl_6$.
Carbon	46.35 per cent.	45.92 per cent.
Hydrogen . .	5.23 „	5.04 „
Nitrogen ..	2.61 „	2.44 „
Platinum ..	16.93 „	16.94 „
Chlorine ..	18.28 „	18.52 „

Corydaline Methiodide.—This compound is obtained by dissolving corydaline in methyl iodide. The excess of methyl iodide employed must be removed by spontaneous evaporation, since distillation under the ordinary atmospheric pressure invariably decomposes the compound. Corydaline methiodide dissolves in absolute alcohol, from which it crystallises in radiating tufts of pure white, needle-shaped crystals. Analysis of this derivative, dried at 100° , yielded the following results:—

I.	0.3259	gram salt gave	0.1744 gram H_2O = 5.94 p. c. H.
II.	0.2777	„ „	{ 0.1486 gram H_2O = 5.95 p. c. H.
			{ 0.5441 gram CO_2 = 53.43 p. c. C.
III.	0.4427	„ „	0.0827 gram Pt = 2.91 p. c. N.
IV.	0.4368	„ „	0.0881 „ Pt = 2.89 p. c. N.
V.	0.4121	„ „	0.1892 gram AgI = 24.79 p. c. I.
VI.	0.4960	„ „	0.2261 „ AgI = 24.63 p. c. I.

	Found. (Mean of above analyses.)	Theory for $C_{22}H_{28}NO_4 \cdot CH_3I$.
Carbon	53.43 per cent.	53.92 per cent.
Hydrogen . .	5.95 „	6.05 „
Nitrogen . .	2.90 „	2.73 „
Iodine	24.71 „	24.79 „

The compound with allyl iodide was prepared in the same way as the methyl derivative. Like the methyl compound, it dissolves easily in absolute alcohol, from which it crystallises in beautiful, prismatic crystals of a brown colour.

When heated with hydrogen iodide, one formula weight of corydaline gives 4 mols. of methyl iodide, and yields the hydriodide of a base which apparently bears the same relation to corydaline that papaveroline bears to papaverine. On oxidation with potassium permanganate, corydaline yields a mixture of acids, which we are now engaged in investigating. We propose in a future paper to give the results of these experiments, together with fuller information as to the alkaloid.
