

LVI.—*Corydaline*. Part II.

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SINCE the publication of our first paper on corydaline (Trans., 1892, 244), our attention has been directed to the work of F. Adermann on this subject (*Inaug. Dissert.*, Dorpat, 1890; *Chem. Centr.*, 1891, i, 978—979; Abstr., 1891, 1266). Adermann extracted the dried roots of *Corydalis cava** with alcohol, and obtained an acid solution from which he separated three bases by successive treatment with light petroleum, benzene, and chloroform.

The base obtained from the benzene solution, which Adermann designates A, is present in largest quantity, and is, unquestionably, identical with the corydaline which we are engaged in investigating, although Adermann assigns to it a formula differing from that proposed by us. The identity of the two substances will be apparent from the following comparison. Their behaviour towards solvents is identical. Both are dextrorotatory; a 1 per cent. alcoholic solution of Adermann's base A rotating the plane of polarised light $4^{\circ} 45'$, whilst a solution of corydaline of the same strength gives a rotation of $5^{\circ} 50'$. The influence of light and heat on both substances is the same, and Adermann has come to the conclusion, at which we also arrived, that the colouring matter formed by the action of light or heat is a decomposition product of the alkaloid. The melting point of Adermann's base A is 138° ; that of corydaline, 134.5° . The fol-

* *Corydalis cava* is the same species as that from which the alkaloid supplied to us by Schuchardt was extracted. We referred to it in our first paper under the synonym *C. tuberosa*.

lowing is a comparison of the analyses of the bases and their platino-chlorides with the numbers required by our formula:—

	Adermann's base A. Mean result of two analyses.*	Corydaline. Mean result of Dobbie and Lauder's analyses.	Theory for $C_{22}H_{29}NO_4$. Formula proposed by Dobbie and Lauder.
Carbon	= 71.28 p. c.	71.37 p. c.	71.16 p. c.
Hydrogen	= 7.07 „	7.76 „	7.81 „
Nitrogen	= 4.15 „	3.82 „	3.78 „
Oxygen	= 17.50 „	17.05 „	17.25 „
	<hr/> 100.00	<hr/> 100.00	<hr/> 100.00

Platinochloride.

	Adermann.	Dobbie and Lauder.	Theory for $C_{22}H_{29}NO_4, H_2PtCl_6$.
Platinum	= 17.75 p. c.	16.93 p. c.	16.93 p. c.

Further confirmation of the identity of the two substances is afforded by the difficulty of obtaining the common salts in the crystalline condition. Solutions of the chlorhydride and sulphate become gummy on evaporation, and crystals can only be obtained with great difficulty. Adermann's iodhydride and platinochloride resemble in all particulars the salts already described by us.

Whilst there cannot be any doubt as to the identity of our corydaline with Adermann's base A, we believe that Adermann is in error in identifying his alkaloid with hydroberberine, or even in supposing any close connection to exist between the two. Even taking into account the third determination of carbon and hydrogen given by Adermann, which we discarded in comparing the two alkaloids, the mean results of his analyses agree as well with our formula as with that of hydroberberine:

	Adermann. Mean of three analyses.	Theory for Hydroberberine.	Theory for $C_{22}H_{29}NO_4$.
Carbon	= 70.97 p. c.	70.38 p. c.	71.16 p. c.
Hydrogen	= 6.99 „	6.75 „	7.81 „
Nitrogen	= 4.15 „	4.11 „	3.78 „
Oxygen	= 17.89 „	18.76 „	17.25 „
	<hr/> 100.00	<hr/> 100.00	<hr/> 100.00

* Adermann gives three analyses of the base, but as the carbon in one of them differs by nearly 1 per cent. from the mean of the other two, we have left it out of account in making the comparison. The following are Adermann's results:—

I.	Carbon	= 71.13 per cent.	Hydrogen	= 7.12 per cent.
II.	„	= 71.43 „	„	= 7.03 „
III.	„	= 70.37 „	„	= 6.82 „

whilst if we omit the third analysis, Adermann's figures, as already shown, agree very closely with our own. We have carefully compared our corydaline with a sample of pure hydroberberine prepared for this purpose. We find that the melting point of hydroberberine is 165° , or 30° higher than that of corydaline; that whilst the solvents for the two bases are the same, hydroberberine requires for solution six to eight times as much absolute alcohol as corydaline; that hydroberberine is optically inactive; and that its sulphate crystallises without difficulty. If any further proof were needed that corydaline and hydroberberine are essentially distinct, it is to be found in the fact that, whereas berberine, which differs from hydroberberine by 4 atoms of hydrogen, contains only two methoxy-groups (Perkin, jun., Trans., 1889, 88), corydaline, as we shall presently show, contains four.

We have prepared some additional salts of corydaline, of which we shall now give an account.

Corydaline Hydrobromide.—This salt is easily obtained by adding potassium bromide to a solution of the hydrochloride in water. Like the corresponding hydriodide, it is pale yellow. It is almost insoluble in cold, but dissolves easily in hot water, from which it separates, on cooling, in crystals resembling those of the hydriodide. Analyses of this salt, dried at 100° , gave the following results:—

I. 0.3988 gram of the salt gave 0.1658 gram AgBr = 17.68 per cent. Br.

II. 0.3912 gram of the salt gave 0.1642 gram AgBr = 17.74 per cent. Br.

Found.	Theory for
(Mean of above numbers.)	$C_{22}H_{29}NO_4.HBr.*$
Bromine = 17.71 per cent.	17.69 per cent.

Corydaline Ethyl Sulphate.—This compound is easily prepared in a state of purity, and, unlike the other salts of corydaline, which are soluble in water, crystallises from its aqueous solution without difficulty. It can be obtained as a white, crystalline precipitate by mixing solutions of sodium ethyl sulphate and corydaline sulphate. It is, however, most easily prepared by adding sulphuric acid to an alcoholic solution of corydaline, evaporating to a syrupy consistency, and adding water, when the solution immediately sets to a crystalline mass. When this is dissolved in hot water and the solution allowed to cool slowly, beautiful, large, colourless, prismatic crystals, contain-

* In our first paper, the formula given for corydaline was $C_{22}H_{23}NO_4$, calculated directly from the results of analyses. The addition of an atom of hydrogen, which is necessary to bring the formula into conformity with the law of even numbers, makes no appreciable difference in the figures given in that paper.

ing 1 mol. H_2O , separate out. Corydaline ethyl sulphate dissolves easily in hot water, alcohol, and chloroform, but is only very sparingly soluble in cold water, and is insoluble in ether. The crystals melt at 152.5° to a clear, yellow liquid. The addition of ammonia or of potassium hydrate to their aqueous solution precipitates the corydaline. This salt is very stable, and it is only after long continued boiling of its aqueous solution that any precipitate of barium sulphate is obtained on the addition of barium chloride. Analyses of the ethyl sulphate, dried over concentrated sulphuric acid in a vacuum, gave the following results:—

- I. 0.2912 gram of the salt gave—
 0.1859 gram H_2O = 7.99 per cent. H.
 0.6014 „ CO_2 = 56.32 „ C.
 II. 0.3025 gram of the salt gave—
 0.1866 „ H_2O = 6.85 „ H.
 0.6200 „ CO_2 = 55.89 „ C.
 III. 0.4656 gram of the salt gave 0.0895 gram Pt = 2.77 per cent. N.
 IV. 0.4579 gram of the salt gave 0.0881 gram Pt = 2.77 per cent. N.
 V. 0.4036 gram of the salt gave 0.1968 gram BaSO_4 = 6.69 per cent. S.
 VI. 0.4294 gram of the salt gave 0.2100 gram BaSO_4 = 6.72 per cent. S.

	Found. (Mean of above analyses.)	Theory for $\text{C}_{22}\text{H}_{29}\text{NO}_4 \cdot \text{C}_2\text{H}_5\text{HSO}_4$ + H_2O .
Carbon	= 56.10 per cent.	55.92 per cent.
Hydrogen	= 6.97 „	7.18 „
Nitrogen	= 2.77 „	2.72 „
Sulphur	= 6.70 „	6.21 „
Oxygen	= 27.46 „	27.97 „
	<hr/> 100.00	<hr/> 100.00

The salt loses its water of crystallisation when dried at 100° :—

- I. 0.5906 gram of the salt lost 0.0213 gram H_2O = 3.60 per cent. H_2O .
 II. 0.2705 gram of the salt lost 0.0091 gram H_2O = 3.36 per cent. H_2O .

	Found. (Mean of above numbers.)	Theory for 1 mol. H_2O .
Water	= 3.48 per cent.	3.49 per cent.

The corydaline in the salt was determined by precipitation with ammonia:—

- | | Found. | Theory. |
|-----------------|-----------------|-----------------|
| I. Corydaline = | 74.49 per cent. | 74.64 per cent. |
| II. „ = | 70.94 „ | 72.03 „ |

I. 0.2314 gram of the	}	0.4158 gram CO_2 = 49.00 per cent. C.
salt gave—		0.0983 „ H_2O = 4.72 „ H.
II. 0.2401 gram of the	}	0.4307 „ CO_2 = 48.92 „ C.
salt gave—		0.1011 „ H_2O = 4.68 „ H.
III. 0.3180 gram of the salt gave	0.07055 gram Pt = 3.20 per cent. N.	
IV. 0.3376 gram of the salt gave	0.07475 gram Pt = 3.19 per cent. N.	
V. 0.3681 gram of the salt gave	0.1962 gram AgI = 28.79 per cent. I.	

VI. 0.3608 gram of the salt gave 0.1913 gram AgI = 28.65 per cent. I.

	Found. (Mean of above numbers.)	Theory. $C_{18}H_{21}NO_4.HI.$
Carbon	= 48.96 per cent.	48.77 per cent.
Hydrogen	= 4.70 „	4.96 „
Nitrogen	= 3.20 „	3.16 „
Iodine	= 28.72 „	28.64 „
Oxygen	= 14.42 „	14.47 „
	100.00	100.00

This salt appears, therefore, to be the iodhydride of a base derived from corydaline by the substitution of 4 atoms of hydrogen for four methyl groups, and bears the same relation to corydaline that papaveroline and berberoline bear to papaverine and berberine respectively. To preserve the analogy of nomenclature, the base ought, therefore, to be called "corydaloline," but we hesitate to perpetrate such a cacophony, and prefer for the present to call it apo-corydaline, until some more appropriate name is indicated by a fuller investigation of its relation to corydaline.

We have not yet succeeded in obtaining the free base in a form suitable for investigation. It can, however, be separated from the iodhydride by the cautious addition of dilute ammonia or of potassium hydrate. It dissolves in alcohol, forming a blood-red solution, but is insoluble in water and in all the other ordinary solvents. Its solution rapidly reduces silver salts in the cold, and, on evaporation, leaves a gummy residue which shows no tendency to crystallise. It is remarkable that the formula of the free base differs by only 2 atoms of hydrogen from Wicke's formula for corydaline ($C_{18}H_{19}NO_4$), and it is possible that the two substances may really be isomeric. The differences in their solubility and general behaviour show that they are not identical. For the direct determination of the number of methoxy-groups in corydaline, we made use of Zeisel's method, as described in the *Berichte*, 19, 143. The following results were given by pure corydaline, dried over concentrated sulphuric acid :—

- I. 0.2539 gram of corydaline gave 0.6338 gram AgI = 32.96 per cent. (CH_3O).
- II. 0.2920 gram of corydaline gave 0.7230 gram AgI = 32.7 per cent. (CH_3O).
- III. 0.2519 gram of corydaline gave 0.6320 gram AgI = 33.13 per cent. (CH_3O).

	Found. (Mean of above numbers.)	Theory for four (CH_3O) groups in $C_{22}H_{29}NO_4$.
(CH_3O)	= 32.93 per cent.	33.42 per cent.

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Corydaline, therefore, contains four methoxy-groups. The conclusion that all the oxygen in the alkaloïd is combined with methyl was confirmed by our failure to obtain any definite reaction with phenylhydrazine or phosphorus pentachloride.

We have not yet completed our experiments on the oxidation of the alkaloid with potassium permanganate, but we have already obtained evidence of the presence both of a pyridine and a benzene ring.

The physiological action of corydaline is being investigated in Professor McKendrick's laboratory in the University of Glasgow.
