VII.—*The Alkaloids of Corydalis cava. Conversion of Corybulbine into Corydaline.*

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It has been shown in a previous paper (Trans., 1894, 65, 25) that the formula of corybulbine differs from that of corydaline by CH_2 , and that the former alkaloid contains only three methoxyl groups, whilst the latter contains four. Having regard to this relation between the formulæ of the two substances, and to the fact that corybulbine is readily soluble in caustic alkalis, in which corydaline is insoluble, and, as shown in this paper, forms an acetyl derivative, the two alkaloids would appear to be related to one another in the same manner as morphine, $\text{C}_{17}\text{H}_{17}\text{ON}(\text{OH})_2$, and codeine, $\text{C}_{17}\text{H}_{17}\text{ON}(\text{OH})\cdot\text{OCH}_3$, corydaline being the higher homologue of corybulbine.

The present paper contains an account of the experiments by which this supposed relation was established and the one alkaloid converted into the other.

When corydaline and corybulbine are treated with hydrogen iodide, the methoxyl groups which they contain are replaced by hydroxyl radicles. If corybulbine and corydaline are related to one another in the manner above suggested, the phenolic derivatives yielded by the two alkaloids should be identical. This was found to be the case.

The relation of the two alkaloids to one another having been thus established, the conversion of corybulbine into corydaline by the methods formerly employed in similar cases was next successfully attempted. In 1881, Grimaux converted morphine, $\text{C}_{17}\text{H}_{17}\text{ON}(\text{OH})_2$ into codeine, $\text{C}_{17}\text{H}_{17}\text{ON}(\text{OH})\cdot\text{OCH}_3$, by treating it with methyl iodide

in presence of potassium hydroxide (*Compt. rend.*, 1881, **92**, 1140, 1228 ; **93**, 67, 217) and ten years later, Grimaux and Arnaud converted cupreine, $C_{19}H_{22}N_2(OH)_2$, into quinine, $C_{19}H_{22}N_2(OH) \cdot OCH_3$, by the same method (*Compt. rend.*, 1891, **112**, 766, 1364 ; 1892, **114**, 548, 672). By similar treatment, corybulbine is converted without difficulty into corydaline. The yield, however, is much larger than that obtained by Grimaux in the case of quinine. The corydaline formed can be isolated without difficulty, since the solubility of corybulbine in sodium hydroxide affords a means of separating any unchanged corybulbine, and the methiodides of both alkaloids being unstable in hot solution, no complication in effecting the separation is caused by their presence. The corydaline thus prepared, and the salts which we have examined, agree in all respects with the natural alkaloid and its corresponding salts.

The position of the hydroxyl group in corybulbine has not yet been definitely ascertained, but the evidence, so far as it goes, points to its presence in the *isoquinoline* nucleus. When corydaline is oxidised with nitric acid, it readily yields corydic acid, $C_{14}H_9N(OCH_3)_2(CO_2H)_2 \cdot \frac{1}{2}H_2O$ (*Trans.*, 1897, **71**, 657), which contains an *isoquinoline* nucleus. This acid, on further oxidation, yields, amongst other products, *metahemipinic* acid, $[(CO_2H)_2 : (OCH_3)_2 = 1 : 2 : 4 : 5]$, but no *hemipinic* acid $[(CO_2H)_2 : (OCH_3)_2 = 1 : 2 : 3 : 4]$. Since corydaline on oxidation yields both *hemipinic* and *metahemipinic* acids, the benzene ring from which the former acid is derived must be the ring which is destroyed by the oxidation with nitric acid. If the hydroxyl group of corybulbine occurred in this ring, we should expect to obtain corydic acid on oxidising the alkaloid with nitric acid. All attempts, however, to obtain this acid from corybulbine have hitherto failed.

EXPERIMENTAL.

Action of Acetic Anhydride on Corybulbine.

Corybulbine was dissolved in a considerable excess of acetic anhydride, and the solution boiled for 4—5 hours under a reflux condenser. The greater part of the acetic anhydride was then distilled off under reduced pressure, and the concentrated solution set to crystallise in a desiccator. The product, which separated as a thick crystalline crust, was crystallised from carefully dried alcohol, from which it separated in tufts of slender, colourless needles melting at 160° . It was dried over sulphuric acid, and, on analysis, proved to be *acetylcorybulbine*, $C_{18}H_{15}N(OCH_3)_3 \cdot O \cdot C_2H_5O$.

0.2676 gave 0.6820 CO_2 and 0.1736 H_2O . C = 69.50 ; H = 7.20.

$C_{23}H_{27}O_5N$ requires C = 69.47 ; H = 6.87 per cent.

Action of Hydrogen Iodide on Corybulbine.

The corybulbine was boiled with a strong solution of hydrogen iodide under a reflux condenser until all the methyl iodide was expelled, 2 grams of corybulbine and 20 c.c. of hydrogen iodide being used for each operation. The crystalline solid which separated on cooling was collected by the aid of the pump, well pressed between filter paper, and then recrystallised several times from water. The fine yellow crystals thus obtained were exactly similar in appearance to those of the corresponding substance prepared from corydaline. Both substances behaved in precisely the same way when heated side by side in capillary tubes, melting at about 270° to a clear brown liquid; both dissolve easily in water or alcohol, but only sparingly in ether, and not at all in chloroform. The iodine in the hydriodide obtained from corybulbine was estimated by Carius' method in the substance dried at 100° .

0.2813 gave 0.1496 AgI. $I = 28.73$.

$C_{18}H_{15}N(OH)_4$. HI requires $I = 28.79$ per cent.

Conversion of Corybulbine into Corydaline.

The corybulbine used for this purpose was purified from traces of corydaline by dissolving in potassium hydroxide, in which corydaline is insoluble, and subsequently precipitating with carbon dioxide. It was afterwards repeatedly recrystallised from alcohol. The purified corybulbine, in quantities of 2.5 grams at each operation, was boiled under a reflux condenser for 15—20 hours with the equivalent quantity of methyl iodide and potassium hydroxide dissolved in methyl alcohol. After cooling, the contents of the flask were filtered. The residue was found to consist almost entirely of unaltered corybulbine, which is very sparingly soluble in cold alcohol. The filtrate, which contained corydaline mixed with a small quantity of corybulbine, was evaporated to dryness and dissolved in dilute hydrochloric acid. The corydaline was then precipitated from the acid solution with excess of potassium hydroxide and afterwards boiled repeatedly with the alkali, to get rid of the last traces of corybulbine. The crude corydaline was washed with water until free from alkali, and recrystallised repeatedly from alcohol. Under these conditions we found that from 25 to 30 per cent. of the corybulbine was converted into corydaline. The purified substance was dried at 100° and analysed, with the following results:

0.2515 gave 0.6586 CO_2 and 0.1740 H_2O . $C = 71.41$; $H = 7.68$.

0.4088 „ 0.1089 Pt. $N = 3.84$.

$C_{22}H_{27}O_4N$ requires $C = 71.54$; $H = 7.32$; $N = 3.79$ per cent.

The corydaline thus obtained was carefully compared with the natural alkaloid. Specimens of the two were heated side by side in capillary tubes, and were found to behave in exactly the same way, both of them melting at 135° . The solubilities of the two substances in alcohol, ether, chloroform, benzene, or carbon disulphide were compared, but no difference could be detected between them.

The specific rotatory power was determined, with the following result :

$$d\ 20^{\circ}/4^{\circ}, 0.7961; c, 0.7251; l, 2\text{ dcm.}; \alpha_D^{20} + 4.6^{\circ}; [\alpha]_D^{20} + 317.1^{\circ}.$$

Two determinations of the specific rotatory power of the natural alkaloid gave $[\alpha]_D^{20} = +311^{\circ}$ and $+309.5^{\circ}$ (Trans., 1895, 67, 17).

Platinichloride of synthetical Corydaline.—The platinichloride of synthetical corydaline was prepared by dissolving the alkaloid in dilute hydrochloric acid and precipitating with platinic chloride. The pale yellow precipitate was collected and washed with cold water till free from acid. It was dried at 100° for analysis :

0.3058 gave 0.0517 Pt. Pt = 16.90.

$(C_{22}H_{27}O_4N)_2, H_2PtCl_6$ requires Pt = 16.97 per cent.

The salt was exactly similar to corydaline platinichloride in appearance, and the behaviour of the two substances, when heated side by side in capillary tubes, was identical. Both softened at 194° , began to decompose at 203° , and were completely decomposed at 210° . The two salts were compared as regards their solubility in water, alcohol, and ether, and were found to agree in all respects.

Ethyl Sulphate of synthetical Corydaline.—This salt is easily prepared by adding a solution of potassium ethyl sulphate to a solution of the sulphate of synthetical corydaline. It forms large, colourless, prismatic crystals, and is identical in appearance with the corresponding salt of the natural alkaloid. The two salts, when heated side by side in capillary tubes, melt between 150° and 160° to a clear yellow liquid. No difference could be detected between the solubility of the two salts; both are easily soluble in hot water, alcohol, or chloroform, but only sparingly so in cold water, and insoluble in ether.

The hydriodides of the natural and artificial alkaloids were also compared and found to be identical.

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