METELOIDINE: A NEW SOLANACEOUS ALKALOID. 2077

CCV.-Meteloidine: A New Solanaceous Alkaloid.

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Datura Meteloides is a small shrub closely resembling D. Metel, as its name implies. Botanically, it differs from the latter in several respects (Dunal in De Candolle, *Prod.*, xiii, 1, 554), having for instance smaller leaves and a pink flower, whereas the flower of D. Metel is white.

Schmidt (Arch. Pharm., 1905, **243**, 303) and Kircher (Arch. Pharm., 1905, **243**, 309) have shown that D. Metel contains about 0.5 per cent. of alkaloids, consisting mainly of hyoscine with a small amount of atropine and hyoscyamine. Datura Meteloides, however, does not appear to have been investigated chemically hitherto. It has now been found to contain 0.4 per cent. of total alkaloids, from which 0.13 per cent. of hyoscine, 0.03 per cent. of atropine, and 0.07 per cent. of a new alkaloid have been obtained; the latter has been designated meteloidine with reference to its source.

Meteloidine is a crystalline base of the empirical formula $C_{13}H_{21}O_4N$, and forms salts which crystallise readily; the hydrobromide,

 $C_{13}H_{21}O_4N, HBr, 2H_2O,$

aurichloride, $C_{13}H_{21}O_4N$, $HAuCl_{4,\frac{1}{2}}H_2O$, and *picrate* have been prepared. It is optically inactive, and has no marked physiological action.

When boiled with aqueous barium hydroxide, meteloidine is hydrolysed with formation of tiglic acid and a new base, which has been designated *teloidine*, according to the equation:

 $C_{13}H_{21}O_4N + H_2O = C_5H_8O_2 + C_8H_{15}O_8N.$

The formation of tiglic acid on hydrolysis of an alkaloid has been observed on only one previous occasion, when Wright and Luff (Trans., 1878, **33**, 347) obtained it from cevadine, one of the alkaloids of *Veratrum Sabadilla*.

The basic hydrolytic product, teloidine, crystallises from moist acetone with one molecule of water of crystallisation. It forms easily crystallisable salts, of which the hydrochloride, $C_8H_{15}O_3N$, HCl, hydrobromide, $C_8H_{15}O_3N$, HBr, and aurichloride, $C_8H_{15}O_3N$, HAuCl₄, $\frac{1}{2}H_2O$, have been characterised. Lack of material has prevented further investigation of this substance, but it may be pointed out that it has certain properties in common with tropine and oscine, and may conceivably be closely related to these bases. The three substances are all strongly basic, and each contains eight carbon atoms and a hydroxyl group in the molecule; they are all very soluble in water and alcohol, and are left as oily residues on the evaporation of these solvents; concentrated aqueous solutions of their salts give no precipitate with picric acid. It is interesting to note also that acyl derivatives of the three bases are found in D. Meteloides, atropine or tropyltropine, hyoscine or tropyloscine, and meteloidine or tiglylteloidine.

On the other hand, teloidine differs from tropine and oscine in that it cannot be distilled, and concentrated aqueous solutions of its salts do not give a precipitate with mercuric-potassium iodide solution.

EXPERIMENTAL.

Isolation of Meteloidine from Datura Meteloides.

The powdered herb was percolated with 95 per cent. alcohol, and the extract concentrated to a semi-solid mass, from which the alkaloids were removed by stirring with 1 per cent. aqueous hydrochloric acid. The aqueous liquor was rendered alkaline with ammonia, and shaken out with chloroform, and the latter fractionally extracted with successive quantities of dilute hydrobromic acid. The extracts were concentrated separately, and allowed to crystallise. Most, if not all, of the meteloidine was contained in the first fraction, and crystallised out on cooling as the hydrobromide. From the mother liquor of this and the later hydrobromic acid extracts, hyoscine and a mixture of hyoscyamine and atropine were separated in the usual manner.

Out of a yield of 0.40 per cent. of total alkaloids, 0.07 per cent. of meteloidine, 0.13 per cent. of hyoscine, and 0.03 per cent. of atropine were obtained.

Meteloidine, $CH_3 \cdot CH : C(CH_3) \cdot CO_2 \cdot C_8 H_{14}O_2 N$.

The base was prepared by adding sodium carbonate to an aqueous solution of the hydrobromide, extracting with chloroform, and crystallising the chloroform residue from benzene. It separated in tabular needles, which melted at $141-142^{\circ}$ (corr.). It is readily soluble in alcohol, acetone, or chloroform, and somewhat sparingly so in water, ether, ethyl acetate, or benzene :

0.1162 gave 0.2610 CO_2 and $0.0874 \text{ H}_2\text{O}$. C = 61.2; H = 8.4.

0.0702 , 3.4 c.c. N₂ at 19° and 764 mm. N = 5.6.

 $C_{13}H_{21}O_4N$ requires C = 61.1; H = 8.3; N = 5.5 per cent.

The hydrobromide crystallised from water in hard clusters of chiselshaped needles. It contains two molecules of water of crystallisation, and is readily soluble in water and absolute alcohol. After drying first at 40° and then at 100°, it melts and colours at 250° (corr.). It is optically inactive :

0.1858, air-dried, gave 0.2854 CO_2 and 0.1186 H_2O . C = 41.9; H = 7.2. 0.2726 , , lost 0.0258 at 100°. $H_2O = 9.5$. 0.1444, dried at 100°, gave 0.0804 AgBr. Br = 23.7. C₁₃H₂₁O₄N,HBr,2H₂O requires C = 41.9; H = 7.1; H₂O = 9.7 per cent. C₁₈H₂₁O₄N,HBr requires Br = 23.8 per cent.

The *aurichloride* crystallised on adding auric chloride to a solution of the hydrochloride. After recrystallisation from dilute alcohol, it formed short, yellow needles, which melted at $149-150^{\circ}$. It contains one-half of a molecular proportion of water of crystallisation, and is sparingly soluble in water, but readily so in alcohol:

0.0957, air-dried, lost 0.0017 at 100°. $H_0O = 1.8$.

0.0940, dried at 100°, gave 0.0315 Au. Au = 33.5.

 $C_{13}H_{21}O_4N$, $HAuCl_4, \frac{1}{2}H_2O$ requires $H_2O = 1.5$ per cent.

 $C_{13}H_{21}O_4N$, HAuCl₄ requires Au = 33.1 per cent.

The *picrate* separated in yellow, crystalline nodules on adding picric acid to a solution of the hydrobromide. After recrystallisation from alcohol, it formed yellow, hexagonal plates, which melted at 177—180° (corr.). It is sparingly soluble in water and cold alcohol.

Hydrolysis of Meteloidine by Barium Hydroxide. Formation of Tiglic Acid and Teloidine.

Twelve grams of meteloidine hydrobromide were converted into the free base, and this was dissolved in a warm solution of 10.2 grams of crystallised barium hydroxide in 150 c.c. of water and boiled for one hour. After cooling, the solution was extracted with chloroform, which removed 0.3 gram of unchanged meteloidine, boiled, acidified with 12 c.c. of 50 per cent. aqueous sulphuric acid, filtered from precipitated barium sulphate, and completely extracted with ether. The ethereal extract was dried, and on distillation gave 2.8 grams of a crystalline acid; on recrystallisation from water, it separated in long, flat needles, which melted at $64-64.5^{\circ}$ (corr.), and proved to be tiglic acid:

0.1456 gave 0.3174 CO₂ and 0.1050 H_2O . C=59.5; H=8.1. C₅H₈O₂ requires C=60.0; H=8.1 per cent.

For further proof of identity, the acid was converted into its dibromide, which separated from light petroleum in long, white needles, which melted at $87-88^{\circ}$ (corr.).

The yield of tiglic acid, based on the amount of meteloidine actually hydrolysed, is 91 per cent. of the theoretical.

The acid liquor remaining after the ether extraction was digested on the water-bath with barium carbonate and filtered, when it was found to be faintly alkaline. After neutralisation with a drop of dilute sulphuric acid, and evaporation to low bulk on the water-bath, it began to crystallise, and was then completely dried, first on the water-bath, then in a vacuum desiccator over sulphuric acid, and gave 6.2 grams of a dry, pale pink, crystalline powder. This proved to be teloidine hydrochloride mixed with a small proportion of sulphate, and the amount obtained represents 96 per cent. of the theoretical. The occurrence of the hydrochloric acid can only have been due to the decomposition of the chloroform used earlier in the process.

Teloidine, C₈H₁₅O₃N.

The free base cannot be extracted from an aqueous solution by shaking with the usual organic solvents. It was isolated in the following manner: The hydrochloride was dissolved in its own weight of water, mixed with a strong aqueous solution of one molecular proportion of potassium hydroxide, and diluted with absolute alcohol. After filtering from precipitated potassium chloride, the solution was evaporated to dryness under diminished pressure, and the residue again extracted with absolute alcohol, filtered, and evaporated to dryness, when the base was obtained as a viscid oil. This was dissolved by covering with about 10 volumes of boiling acetone and adding water drop by drop until nearly all had passed into solution. After filtering hot, the solution was allowed to stand, when the base separated in chisel-shaped needles, which contained one molecule of water of crystallisation. After drying at 120° , it melted at $168--169^\circ$ (corr.):

 $C_8H_{15}O_3N, H_2O$ requires C = 50.2; H = 9.0; N = 7.3; $H_2O = 9.4$ per cent. 0.1438, dried at 120°, gave 0.2906 CO_2 and 0.1142 H_2O . C = 55.1; H = 8.9.

 $C_8H_{15}O_8N$ requires C = 55.4; H = 8.7 per cent.

Teloidine is not deliquescent, nor does the anhydrous base take up water of crystallisation from moist air. It is very easily soluble in water or alcohol, and is left as an oil on the evaporation of these solvents; it is sparingly soluble in the other usual organic solvents when cold. It gives no precipitate with picric acid or mercuric potassium iodide even in concentrated solution. It cannot be distilled, but suffers decomposition.

The hydrochloride is obtained almost pure by the above method; after recrystallisation from absolute alcohol, it separates in well defined, monoclinic prisms with a macrodome, and does not melt at 300°. It is anhydrous, and is readily soluble in water, but sparingly so in boiling absolute alcohol:

0.1576 gave 0.2634 CO_2 and 0.1102 H_2O . C = 45.6; H = 7.8.

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0.1678 gave 9.6 c.c. N₂ at 21° and 766 mm. N = 6.6. 0.1803 , 0.1221 AgCl. Cl = 16.7.

 $\rm C_8H_{15}O_8N, HCl$ requires $\rm C=45.8$; $\rm H=7.7$; $\rm N=6.7$; $\rm Cl=16.9$ per cent.

The hydrobromide crystallised from absolute alcohol in hexagonal plates and needles, which melted and decomposed at 295° (corr.). It is anhydrous, and is readily soluble in water, but sparingly so in absolute alcohol:

0.1694 gave 0.2342 CO₂ and 0.0954 H_2O . C = 37.7; H = 6.3.

0.1776 , 0.1301 AgBr. Br = 31.2.

 $C_8H_{15}O_3N$, HBr requires C = 37.8; H = 6.4; Br = 31.5 per cent.

The *aurichloride* crystallised out on adding a concentrated solution of auric chloride to a strong solution of the hydrochloride. After recrystallisation from water, it separated in yellow, hexagonal plates, which melted and decomposed at 225° (corr.). It contains one-half of a molecular proportion of water of crystallisation, and is fairly easily soluble in water:

0.1919, air-dried, lost 0.0032 at 100°. $H_0O = 1.7$.

0.1887, dried at 100°, gave 0.0721 Au. Au = 38.2.

 $C_8H_{15}O_3N$, $HAuCl_4$, $\frac{1}{2}H_2O$ requires $H_2O = 1.7$ per cent.

 $C_8H_{15}O_3N$, $HAuCl_4$ requires Au = 38.4 per cent.

With the object of determining the number of hydroxy-groups in the molecule, teloidine has been subjected to the action of boiling acetic anhydride and benzoyl chloride in aqueous sodium hydroxide, but no crystalline derivatives were obtained from the small quantities employed.

It is proposed to investigate further the constitution of meteloidine when more material is available.

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