

XL.—*Metallic Derivatives of Alkaloids.*

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HAVING prepared the metallic derivatives of acid amides (T, 1913, 103, 1557) it was thought that the metallic derivatives of alkaloids could be obtained by a similar method. The sodium and potassium derivatives of codeine and narcotine and the sodium derivative of cotarnine were obtained by boiling the alkaloids with the respective metals in benzene, and the calcium derivative of morphine was isolated from the solution of morphine in lime-water or from its alcoholic solution, prepared by titrating morphine with an excess of slaked lime in alcohol. Of the metallic derivatives, those of narcotine require special mention; there is no hydroxyl group present in the molecule, and there is no hydrogen atom attached to the nitrogen that could be displaced by the metals, as is generally represented to be the case with basic or quasi-basic nitrogenous organic compounds.

*Sodium Codeine.*

A mixture of 200 c.c. of benzene, 5 grams of freshly cut sodium, and 10 grams of powdered anhydrous codeine was boiled under reflux. At the beginning of the experiment, a very faint ammoniacal odour was perceived at the open end of the condenser, and this continued until the end of the operation. Within ten minutes the benzene turned brownish-yellow, and after half an hour it became opaque. After the mixture had boiled for ten hours, the pieces of sodium were covered with a thin layer of a reddish-brown substance, and the boiling was discontinued. On cooling, the contents of the flask set to a viscous mass like brown jelly, which was collected, pressed between filter paper, and kept

over night in a desiccator over sulphuric acid, when it dried to a brownish-yellow powder:

0.3537 gave 0.0800  $\text{Na}_2\text{SO}_4$ .  $\text{Na} = 7.32$ .

$\text{C}_{18}\text{H}_{20}\text{O}_3\text{NNa}$  requires  $\text{Na} = 7.18$  per cent.

*Sodium codeine* is readily soluble in water, giving a brownish-yellow, turbid solution which does not become clear by filtration, but the turbidity disappears on the addition of dilute hydrochloric acid, and the colour is also considerably discharged. It is soluble in alcohol, but insoluble in ether, benzene, or chloroform, and is specifically lighter than the last solvent. The compound is slightly deliquescent; on exposure to the air, it absorbs moisture and becomes viscid, but when left in that condition for a long time it does not appear to change. Its aqueous solution does not give any precipitate with Mayer's reagent, but on acidifying the mixture, an immediate curdy, yellow precipitate is obtained.

#### *Potassium Codeine.*

Ten grams of dry powdered codeine were dissolved in 200 c.c. of benzene, and the solution was boiled with 10 grams of potassium as before. The potassium melted and formed smaller shining balls, around which a brisk evolution of gas took place. As in the former experiment, a faint ammoniacal odour was always perceived at the open end of the condenser. Within an hour the benzene gradually assumed a reddish-brown colour, and soon afterwards red crystals began to separate. The boiling was continued until a voluminous mass of crystals separated, which were collected, washed three times with boiling benzene, pressed between filter paper, and kept overnight in a desiccator over sulphuric acid. About 5 grams of the substance were powdered, added to 50 c.c. of benzene, and the mixture was gently boiled for five minutes. It was then filtered whilst hot, and the residue washed three times with boiling benzene to remove codeine, being finally pressed between filter paper and dried in a desiccator over sulphuric acid:

0.6000 gave 0.1590  $\text{K}_2\text{SO}_4$ .  $\text{K} = 11.88$ .

$\text{C}_{18}\text{H}_{20}\text{O}_3\text{NK}$  requires  $\text{K} = 11.59$  per cent.

*Potassium codeine* dissolves in water, giving a clear solution; it is soluble in alcohol, sparingly so in chloroform, and insoluble in ether or benzene.

#### *Sodium Narcotine.*

Five grams of narcotine were boiled with 200 c.c. of benzene and 5 grams of clean sodium; a faint ammoniacal odour was per-

ceived, and the colour of the liquid became brown. After boiling for three daily periods of five hours each, some crystals were deposited, which were collected, washed with hot benzene, pressed between filter paper, and kept overnight in a desiccator, when a reddish-yellow powder was obtained:

0.4110 gave 0.7400  $\text{Na}_2\text{SO}_4$ .  $\text{Na} = 5.82$ .

$\text{C}_{22}\text{H}_{22}\text{O}_7\text{NNa}$  requires  $\text{Na} = 5.41$  per cent.

*Sodium narcotine* is a non-deliquescent substance, readily soluble in water to a pale yellow, transparent solution, which does not produce any precipitate with Mayer's reagent, except on acidification. It is soluble in alcohol or chloroform, and almost insoluble in ether or benzene. Nothing could be extracted from its aqueous solution by benzene or ether. When the solution was boiled, however, a slight turbidity was observed, which increased on passing carbon dioxide; the precipitate was collected, washed, and dried, when it melted at  $175^\circ$ . Narcotine also separated in colourless, needle-shaped crystals when the solution was kept in an open flask for six or seven days, but the alkaloid was completely and readily recovered as a colourless, crystalline powder by dissolving the compound in ammonium chloride. It was collected, washed, dried, and recrystallised from benzene, when it melted at  $175^\circ$  and had all the properties of pure narcotine.

#### *Potassium Narcotine.*

In the preparation of other metallic derivatives, excess of the metals were used as a rule, but with the potassium derivative of narcotine considerable difficulty was experienced in obtaining the new compound free from unchanged metal. After a part of the reaction was completed, the molten potassium disintegrated into very small pieces, which were never completely separated from the derivative, but became entangled with the crystals of the new compound and did not settle down separately when cooled. To avoid this difficulty, excess of the alkaloid was employed, and the unchanged narcotine was removed by washing with benzene. Five grams of potassium and 40 grams of narcotine were boiled with 300 c.c. of benzene under reflux. Within an hour the potassium derivative began to be deposited as a brownish-yellow powder. The boiling was continued for twelve hours, during which period the usual faint ammoniacal odour was noticed; the mixture was filtered hot, and the precipitate washed five times with boiling benzene, care being taken to keep it covered with liquid, since the substance rapidly absorbs moisture, becoming nacreous,

and then cannot be filtered; the compound also undergoes slight decomposition. The washing with hot benzene, however, may be continued until the filtrate ceases to give any residue on evaporation. The substance was pressed between filter paper and dried in a desiccator over sulphuric acid:

0.1401 gave 0.0501  $K_2SO_4$ .  $K = 16.00$ .

$C_{22}H_{21}O_7NK_2$  requires  $K = 15.90$  per cent.

*Dipotassium narcotine* is a bright yellow, crystalline powder readily soluble in alcohol, giving a turbid solution; it dissolves in chloroform, is sparingly soluble in benzene, and insoluble in ether. On shaking its aqueous solution with benzene, only a very small quantity of the alkaloid was extracted by the solvent, but when the mixture was shaken with an excess of ammonium chloride, the benzene dissolved almost the whole of the alkaloid. The benzene solution was separated, washed, dried by potassium carbonate, and evaporated, when there remained a non-crystalline residue melting at  $160^\circ$ . Consequently, the substance thus recovered is not pure narcotine, as was the case with the sodium derivative.

#### *Sodium Cotarnine.*

Cotarnine was prepared by oxidising narcotine with dilute nitric acid, a slight modification of the method described by Anderson (*Annalen*, 1853, **86**, 187) being used. A mixture of 70 c.c. of nitric acid (D 1.4) and 200 c.c. of water was cooled to  $15^\circ$ , 25 grams of crystallised narcotine were added, and the whole was shaken continuously until the alkaloid was completely dissolved, the solution being kept in a cool place overnight. The white crystals of opianic acid which had settled at the bottom were collected, and the cotarnine was precipitated from the filtrate by means of potassium hydroxide. The alkaloid was well washed, dried in a desiccator over sulphuric acid, and recrystallised from benzene, when it weighed 6.1 grams.

Ten grams of cotarnine, 5 grams of sodium, and 200 c.c. of benzene were heated under reflux; after four hours crystals began to separate, and the boiling was continued for six hours, when the mixture was set aside overnight for the complete precipitation of crystals. These were collected, washed three times with hot benzene, pressed between filter paper, and dried in a desiccator:

0.0130 gave 0.0115  $Na_2SO_4$ .  $Na = 28.0$ .

$C_{12}H_{11}O_4NNa_4$  requires  $Na = 28.30$  per cent.

*Tetrasodium cotarnine* is a hygroscopic, bright yellow, crystalline powder, readily soluble in water, giving a clear solution, soluble

in alcohol or chloroform, sparingly so in ether, and practically insoluble in benzene. This compound showed a behaviour altogether different from that of the allied alkaloids in that its aqueous solution gave a precipitate with Mayer's reagent, the amount of which slightly increased on keeping the solution for a day or on acidifying the freshly prepared solution. When its saturated aqueous solution was treated with an excess of ammonium chloride, an immediate turbidity was observed, and on keeping overnight, a crystalline precipitate had formed. This was collected, washed, pressed between filter paper, and dried in a desiccator over sulphuric acid, when it melted at 132°.

#### *Calcium Morphinate.*

Morphine is well known to be soluble in lime-water, forming calcium morphinate, which was easily isolated by the following process. Thirty grams of pure morphine were triturated with 6 grams of pure calcium hydroxide, 100 c.c. of rectified spirit were added, the whole being well mixed for thirty minutes and then filtered. The pale brown filtrate was transferred to a shallow dish and kept in a desiccator over sulphuric acid; after two days, calcium morphinate separated as a shining, scaly, light powder. The product obtained by substituting water for alcohol was not so pure, and was much darker. The alcoholic product was completely dissolved by alcohol or water, whereas the other left a slight residue, and a clear solution was only obtained from it by filtration. Consequently, the alcoholic product was assumed to be pure:

0.2060 gave 0.0200 CaO. Ca = 6.93.

$(C_{17}H_{18}O_3N)_2Ca$  requires Ca = 6.58 per cent.

A quantity of the substance was dissolved in *N*/10-sulphuric acid, and the excess titrated with *N*/10-sodium carbonate, using methyl-orange as indicator.

0.5 required 32.6 c.c. of *N*/10-acid, whereas this weight of a compound of the above formula requires 33.11 c.c. of *N*/10-acid to neutralise both calcium and morphine.

*Calcium morphinate* is a brown, non-deliquescent powder readily soluble in water or alcohol, sparingly so in chloroform, and insoluble in ether or benzene. Its aqueous solution gives the usual precipitate of morphine with ammonium chloride, and with Mayer's solution it gives a precipitate only after acidification. It is readily decomposed by carbonic acid, calcium carbonate and morphine being precipitated.

The investigation is being extended to the metallic derivatives of other alkaloids and to the study of the constitution of the compounds described above.

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