CXXXVIII.—*Researches on Pseudo-bases. Part I. Some Condensation Reactions of Cotarnine, Hydrastinine, and isoQuinoline Methyl Hydroxide.*

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THE primary object of the authors in commencing this series of investigations was to extend the application of the method by means of which narcotine was synthesised (Perkin and Robinson, T., 1911, **99**, 777; Hope and Robinson, T., 1911, **99**, 1153, 2114; 1913, **103**, 361) to the production of bases belonging to the laudanosine and phenanthrene group of the *isoquinoline* alkaloids. The group which a substance should contain in order that it may be converted into a phenanthrene derivative by Pschorr's method is

and we accordingly made experiments with the object of preparing *isoquinoline* derivatives which contain such a group in their molecules.

Briefly we find that cotarnine and *isoquinoline* methyl hydroxide condense with 6-nitrohomoveratrole in the presence of sodium ethoxide in alcoholic solution to yield the bases I and II respec-

tively. Each of these substances is the object of further investigation, the former yielding a new laudanosine alkaloid by elimination of the nitro-group, and the latter an *iso-apomorphine* dimethyl ether* by a series of processes.

Cotarnine derivatives are, of course, useless for phenanthrene syntheses on account of the methoxyl group which replaces one of the hydrogen atoms essential to the condensation, but, on the other hand, hydrastinine should prove a fertile source of synthetical phenanthrene bases. Thus, for example, the condensation of hydrastinine with 6-nitrohomoveratrole, followed by reduction, diazotisation, and treatment with copper powder, should result in a synthesis of the alkaloid dicentrine. Unfortunately, however, we find that hydrastinine does not condense with mononitrotoluenes, owing to the fact that sodium ethoxide produces autocondensation of the hydrastinine. The product appears to be anhydrohydrastinine or, very much more probably, dianhydrodihydrastinine (III), and its properties are described in the experimental portion of the paper. The striking yellow colour of the salts of this base is somewhat difficult of explanation, even allowing that the probable formula of the hydrochloride is represented by the expression IV.

The decomposition of the acetate of the base into hydrastinine acetate may also receive some explanation if the above constitution for the salts is accepted.

Since we were unable to obtain *o*-nitrobenzylhydrohydrastinines, we next made attempts to produce *o*-nitrobenzylidene- or *o*-nitrobenzoyl-hydrohydrastinines, which would be equally useful for our purpose, and the investigation was first made with cotarnine. Nitrohomopiperonyl alcohol and cotarnine condense together to yield the base V, but hydrastinine undergoes a similar reaction only to a very small extent. Furthermore, all attempts to improve the yields were unsuccessful, and, for example, methyl 6-nitro-

* The publication of this research has been retarded by a disastrous fire which involved the destruction of all the specimens and starting material.

3:4-methylenedioxymandelate (VI) actually condenses less readily than nitrohomopiperonyl alcohol, although the former bears to the latter the relation that phenylacetic ester does to toluene.

Cotarnine also condenses with 6-nitropiperonal, and the product is undoubtedly 6-nitropiperonylhydrocotarnine (VII), and thus belongs to a new class of *isoquinoline* derivatives. We propose to continue the research mainly in this direction, especially since this reaction of cotarnine is shared by hydrastinine. 6-Nitropiperonylhydrocotarnine is a perfectly stable base, forming sparingly soluble pale yellow salts. It suffers decomposition on treatment with phenylhydrazine in acetic acid solution, and one of the products is the phenylhydrazone of nitropiperonal.

EXPERIMENTAL.

Anhydrocotarnine-6-nitroveratrole (I).

6-Nitroveratrole (10 grams) and cotarnine (10 grams) were added to ethyl alcohol (100 c.c.) containing sodium ethoxide (from 1 gram of sodium), and the mixture was allowed to remain at the temperature of the room during two weeks. A considerable amount of the nitro-compound gradually passed into solution during this period. Dilute hydrochloric acid was now added, and the solution filtered. The clear, yellow filtrate was basified with

ammonia, and the viscid mass which separated was washed with water, drained, and became at once crystalline in contact with methyl alcohol. The substance was collected and crystallised, first from ethyl alcohol, and then again from ethyl acetate. An alternative method of isolation is to add picric acid to the original reaction product in alcoholic solution, and then to extract the picrate, from which the supernatant liquid has been decanted, by boiling for half an hour with methyl alcohol. The picrate is very sparingly soluble, and remains as a yellow, crystalline powder. It may be decomposed by sodium hydroxide in the presence of ether, and the amount of the condensation product recovered from the ethereal solution was, in one experiment, 6.5 grams:

0.1132 gave 0.2508 CO_2 and 0.0594 H_2O . $\text{C}=60.4$; $\text{H}=5.8$.

$\text{C}_{21}\text{H}_{24}\text{O}_7\text{N}_2$ requires $\text{C}=60.6$; $\text{H}=5.8$ per cent.

This base resembles in its general properties anhydrocotarnine-*o*-nitrotoluene (Hope and Robinson, T., 1911, **99**, 2123), and is not decomposed on boiling with acetic acid. Its solution in dilute hydrochloric acid is yellow, and on the addition of a piece of zinc a colourless precipitate of zincchloride is first produced. On warming the liquid the precipitate disappears, and the solution now contains a diazotisable amine, which, by the addition of an excess of ammonia, was obtained as a colourless precipitate readily soluble in ether. The reduced base, in dilute hydrochloric acid solution, yields, with ferric chloride, a green coloration, which slowly changes to an intense indigo-blue, whilst with sodium nitrite a pale green diazo-solution was produced, from which, by the action of β -naphthol and sodium acetate, a crimson azo-dye was obtained. The latter dissolved in sulphuric acid to a purple-blue, dichroic solution.

1-(6-Nitrohomoveratryl)-2-methyl-1:2-dihydroisoquinoline (II).

This substance is the starting point for a synthesis of an isomeride of *apomorphine* dimethyl ether, which has now been successfully carried out, and on this account a large number of experiments have been made in order to find the best conditions for its preparation. The following method was finally adopted.

6-Nitrohomoveratrole (10 grams) and *isoquinoline* methiodide (7 grams) were added to a solution of sodium (2 grams) in ethyl alcohol (80 c.c.), and the mixture was heated to incipient ebullition and then allowed to cool. After remaining an hour, the solution was gently heated on the steam-bath during half an hour. About 2 grams of the garnet-red condensation product remained undissolved, and was separated by rapid filtration. The remainder of the base, together with the unchanged nitro-compound, crystal-

lised from the filtrate, which was cooled in ice-water. The mixed solids were collected and titrated with dilute hydrochloric acid in a mortar until no more of the red crystals could be seen.

The acid solution, after filtration and basification with ammonia, yielded a brick-red oil, which soon solidified, and was then collected and crystallised from ethyl alcohol. In this way 2.2 grams of pure substance were obtained, and a further 0.3 gram could be recovered from the alcoholic mother liquor, so that the total yield of condensation product amounted to 4.5 grams, or 51 per cent. of the amount that can theoretically be obtained from the *iso*-quinoline methiodide employed. The excess of the nitrohomoveratrole is recovered. The new substance is best crystallised from ethyl alcohol, in which it is sparingly soluble, and occurs in garnet-red needles of fine appearance, and melting at 145°. Its analysis was rendered difficult by its property of gently exploding, with production of flame, on being heated to a moderately high temperature in air :

0.1173 gave 0.2874 CO₂ and 0.0619 H₂O. C=66.8; H=5.9.

C₁₉H₂₀O₄N₂ requires C=67.1; H=5.9 per cent.

The base is more readily soluble in methyl alcohol than in ethyl alcohol; it is sparingly soluble in ether or light petroleum, readily so in chloroform or benzene. It dissolves readily in dilute hydrochloric acid, yielding a yellow solution, and when warmed with glacial acetic acid suffers decomposition, the yellow liquid rapidly becoming red. The further description of this interesting base and its derivatives is reserved for a future communication, which we hope in a short time to submit to the Society.

Dianhydrodihydrastinine (III).

As shown in the two preceding examples, pseudo-bases will condense with 6-nitrohomoveratrole in the presence of sodium ethoxide, but, under a variety of conditions, we were never successful in applying this reaction to hydrastinine, and the cause of the discrepancy was found to be the ease with which hydrastinine condenses with itself in alcoholic sodium ethoxide solution.

Hydrastinine (7 grams) was added to a solution of sodium (1 gram) in methyl alcohol (80 c.c.), and the mixture boiled during half an hour. Colourless needles separate from the liquid about five minutes after the reaction has commenced, and increase in amount, especially when the solution is afterwards allowed to remain in the ice-chest. The substance was collected, washed with alcohol, and dried at 100°:

0.1131 gave 0.2884 CO₂ and 0.0588 H₂O. C=69.5; H=5.8.

C₂₂H₂₂O₄N₂ requires C=69.8; H=5.9 per cent.

This base is very sparingly soluble, and recrystallisation is not a profitable process. It may, however, be crystallised in small quantities from ethyl acetate, from which it separates in colourless prisms, melting at 200° .

The most characteristic property it possesses is that of dissolving in dilute acids to yellow solutions. The solution of the base in dilute acetic acid is intensely yellow, and not fluorescent, but on warming it becomes pale yellow, and acquires the bluish-green fluorescence characteristic of hydrastinine salts. On the addition of sodium hydroxide, free hydrastinine separated, and was recognised by its conversion to anhydrohydrastinineneitromethane—colourless needles melting at 122° (Hope and Robinson, T., 1911, **99**, 2136).

It is noteworthy that this remarkable decomposition is not readily effected by strong acids such as hydrochloric and sulphuric or benzenesulphonic, and requires in these cases prolonged boiling of the solution, whilst on the other hand weak organic acids, as, for example, formic, acetic, propionic, tartaric, and benzoic acids are much more active agents for the change. There is parallelism here with the observations of Rabe (*Ber.*, 1912, **45**, 2927), who has shown that the cinchonine-cinchotoxine ring scission, and the very similar conversion of narcotine to nornarceine, are more readily accomplished by weak than by strong acids.

The addition of a solution of picric acid in acetone to a solution of the base in the same solvent produces at first an intense brick-red colour, probably indicating the monopicrate, which is much diminished by the addition of more picric acid. Three different kinds of crystals separate from the solution, namely, brick-red prisms, and yellow prisms and needles, but it was found impossible to obtain any one of these quite free from the others.

6-Nitropiperonylidenehydrocotarnine (V).

The nitration of homopiperonyl* alcohol in acetic acid solution leads to a variety of products, among which is undoubtedly 6-nitro-

* There has been some confusion in chemical literature as regards the use of the word piperonyl. This symbol has been used for the three radicles :

and of these the first is correctly termed piperonyl, the second is homopiperonyl and the third should be piperonyl. Thus the alcohol,

homopiperonyl alcohol, but this substance could not be obtained in a pure condition by crystallisation. In all probability, the crude substance, as obtained below, is mixed with nitrocatechol methylene ether.

Homopiperonyl alcohol (20 grams) was carefully added with constant cooling to a mixture of acetic acid (60 c.c.) and nitric acid (20 c.c., D 1.42). The nitro-compounds quickly crystallised from the solution, and after ten minutes the mixture was added to water, and the precipitate collected and washed. The dried product was treated with warm ethyl alcohol, when a very sparingly soluble substance, possibly a stilbene derivative, remained undissolved, and was collected.

The filtrate was diluted with water, and the precipitated nitro alcohol collected and dried. Many crystallisations of this product failed to yield a substance which had either the sharp melting point or the appearance of a pure compound. A solution of the crude nitrohomopiperonyl alcohol (8 grams) and cotarnine (10 grams) in ethyl alcohol (50 c.c.) was boiled for two hours under reflux, and then cooled and poured into excess of very dilute hydrochloric acid. When the liquid had become clear it was filtered and basified with ammonia. The precipitated base, which was viscid at first, but soon crystallised in contact with ice-water, was collected, crystallised from methyl alcohol, and so obtained in pale yellow prisms, melting at 112° :

0.1299 gave 0.2861 CO_2 and 0.0536 H_2O . $\text{C}=60.0$; $\text{H}=4.6$.

$\text{C}_{20}\text{H}_{18}\text{O}_7\text{N}_2$ requires $\text{C}=60.3$; $\text{H}=4.5$ per cent.

The base is readily soluble in hot methyl alcohol, cold benzene, ethyl acetate, or chloroform, sparingly so in cold methyl alcohol, ether, or light petroleum. It dissolves in dilute hydrochloric acid to a very pale yellow solution, from which the very sparingly soluble *hydrochloride* soon crystallises in colourless needles. The warm solution of the hydrochloride becomes colourless on the addition of zinc dust, and the filtered liquid, treated with a little sodium nitrite, and then added to alkaline β -naphthol, gives rise to a scarlet azo-dye. The *acid oxalate* of the base is sparingly soluble in cold water, and crystallises well in pale yellow needles. The canary-yellow *picrate* was obtained by mixing the base with picric acid in acetone solution and then adding alcohol. It crystallises in prisms, which melt sharply at 175° , and is sparingly soluble in alcohol.

usually called piperonyl alcohol is better described as homopiperonyl alcohol and the analogue of ethyl benzoylacetate in this series, which was named ethyl piperonylacetate, is in reality ethyl piperonylacetate.

Benzylidenehydrocotarnine, $\text{C}_8\text{H}_6\text{O}_3 \cdot \text{C} \cdot \text{CHPh}$
 $\text{C}_2\text{H}_4 \text{---} \text{NMe}$

An attempt was made to synthesise the foregoing 6-nitropiperonylidenehydrocotarnine by the nitration of piperonylidenehydrocotarnine, which it was thought might be prepared from magnesium homopiperonyl bromide and oxycotarnine. As a simpler case, the production of benzylidenehydrocotarnine by the action of magnesium benzyl chloride on oxycotarnine was first investigated and accomplished as follows. An ethereal solution of magnesium benzyl chloride, prepared in the usual manner from 10 grams of benzyl chloride, was added to a concentrated solution of oxycotarnine (5 grams) in benzene, when a vigorous reaction ensued and a solid separated. The ether was almost all removed by distillation, and the residue gently warmed during half an hour, a little more benzene being added if necessary to preserve fluidity. After the addition of water and ether, the ethereal solution was separated and several times extracted with small quantities of dilute hydrochloric acid. The combined extracts were boiled to expel ether, cooled, and basified with potassium hydroxide. The crystalline precipitate was collected and recrystallised from ethyl alcohol:

0.1204 gave 0.3259 CO_2 and 0.0659 H_2O . $\text{C} = 73.8$; $\text{H} = 6.1$.

$\text{C}_{19}\text{H}_{19}\text{O}_3\text{N}$ requires $\text{C} = 73.8$; $\text{H} = 6.1$ per cent.

This base crystallised in well-shaped quadratic prisms, melting at 135° ; it is sparingly soluble in alcohol or ether, readily so in chloroform or ethyl acetate.

Picrate.—A hot solution of the base in ethyl alcohol was mixed with a solution of picric acid in the same solvent. The derivative crystallised, on cooling the liquid, in canary-yellow prisms, melting and decomposing at 133° .

This bromide was prepared as already indicated, in order that the reaction between its magnesium derivative and oxycotarnine might be investigated. The ease with which the hydroxyl group of homopiperonyl alcohol is replaced by the bromine atom in the following experiment is quite remarkable. Aqueous hydrobromic acid (50 grams, saturated at 0°) was poured on homopiperonyl alcohol (10 grams), and the mixture vigorously shaken. The solid at once melted, but soon began to crystallise again, and, when this occurred, water was added, and the nodular mass collected, washed,

and dried by pressure between filter-paper. It is advisable that the shaking should be continued during the crystallisation of the substance, so that the lumps may be as small as possible, and consequently more rapidly and efficiently dried. For the purpose of analysis, a specimen was crystallised from light petroleum (b. p. 50—60°), and obtained in long, colourless needles, melting at 49°:

0.2060 gave 0.1789 AgBr. Br=37.0.

$C_8H_7O_2Br$ requires Br=37.2 per cent.

Homopiperonyl bromide has a faint but characteristic aromatic odour, and is readily soluble in organic solvents, with the exception of light petroleum. The bromine in this compound is in a labile condition, and the substance is slowly decomposed by water, yielding the original alcohol and hydrobromic acid; it also gives an immediate precipitate of silver bromide with alcoholic silver nitrate. The magnesium derivative of the bromide was found to be readily produced, and is no doubt of great service as a synthetical agent, but no satisfactory result was obtained in attempting its condensation with oxycotarnine.

The Action of Cotarnine on some Derivatives of Mandelic Acid.

Cotarnine and mandelonitrile in alcoholic solution yielded quantitatively cyanohydrocotarnine and benzaldehyde, and similar results were obtained with other cyanohydrins. We accordingly attempted to protect the cyanohydrin group, and prepared benzoyl-mandelonitrile by the method of Francis and Davis (T., 1909, 95, 1404). Benzoylmandelonitrile (11 grams) and cotarnine (12 grams) were dissolved in alcohol (70 c.c.), and the mixture allowed to remain during two days. A crystalline precipitate separated as the reaction proceeded, and this was collected and washed with dilute hydrochloric acid. This substance crystallised from methyl alcohol in colourless needles, melting at 125°, and was identified as benzoylbenzoin by direct comparison with a specimen of the substance obtained by the benzylation of benzoin, as well as by the fact that the melting point was unaltered when the products from the two sources were intimately mixed. The acid washings from the benzoylbenzoin were added to the original mother liquor, together with sufficient dilute hydrochloric acid to make the solution acid to Congo paper; the whole was then extracted with ether. The acid solution, on treatment with ammonia, deposited a crystalline base, which was recrystallised from methyl alcohol, and obtained in colourless prisms, melting at 87°. The melting point was not lowered when the substance was mixed with a specimen of cyanohydrocotarnine obtained by the action of potassium cyanide on an aqueous solution of cotarninium chloride, and,

moreover, the properties of the base were those of cyanohydrocotarnine.

The ethereal solution was washed with water, dried, and the ether removed by distillation. The residue was submitted to distillation in steam, and the portion remaining in the flask was identified as benzoylbenzoin. The oil volatile in steam was extracted with ether, dried, and distilled. The greater part distilled at about 210° , and consisted of ethyl benzoate, whilst a small fraction at about $300\text{--}320^{\circ}$ was identified by hydrolysis as benzyl benzoate. An alcoholic solution of sodium ethoxide was found to decompose benzoylmandelonitrile in a precisely similar manner.

We next investigated esters of mandelic acid, and found that cotarnine condenses with ethyl mandelate, but the product could not be crystallised or otherwise obtained in a pure condition.

Ethyl α -Benzoyloxyphenylacetate, $\text{OBz}\cdot\text{CHPh}\cdot\text{CO}_2\text{Et}$.

Benzoylmandelonitrile (20 grams) was dissolved in dry ether (100 c.c.) and ethyl alcohol (0.8 gram), cooled to 0° , saturated with hydrogen chloride, and allowed to remain overnight. The liquid was then mixed with alcohol, water, and ether, in the order indicated, and the ethereal layer washed with sodium carbonate solution, dried, and rapidly filtered. The solution soon began to deposit colourless crystals, the separation of which was assisted by cooling the liquid; these were collected and recrystallised from ethyl alcohol, being so obtained in colourless needles, melting at 164° . This substance consists of α -benzoyloxyphenylacetamide, since its melting point was not lowered by admixture with a specimen of this compound obtained as described below. The filtered ethereal solution was distilled, when, after removal of the solvent, the whole passed over at $227^{\circ}/20\text{ mm.}$:

0.1530 gave 0.4061 CO_2 and 0.0724 H_2O . $\text{C}=72.4$; $\text{H}=5.3$.

$\text{C}_{17}\text{H}_{16}\text{O}_4$ requires $\text{C}=71.8$; $\text{H}=5.6$ per cent.

The ester is a viscid oil, and is obtained by the above process in excellent yield. It does not condense with cotarnine or hydrastinine, probably on account of the heavy groups which surround the methine hydrogen atom.

α -Benzoyloxyphenylacetamide, $\text{OBz}\cdot\text{CHPh}\cdot\text{CO}\cdot\text{NH}_2$.

This amide is obtained in quantitative yield from benzoylmandelonitrile by dissolving the latter in concentrated sulphuric acid, and, after allowing to remain one minute, pouring the mixture into water. The solid was collected and crystallised from ethyl alcohol, in which it is sparingly soluble. It occurs in slender, colourless needles, which melt at 164° :

0.1116 gave 0.2878 CO₂ and 0.0523 H₂O. C=70.3; H=5.2.

C₁₅H₁₃O₃N requires C=70.6; H=5.1 per cent.

This substance condenses with cotarnine, but only as an amide, since the condensation product was found to be decomposed into the constituents from which it was obtained on treatment with dilute hydrochloric or acetic acids. In these circumstances it was not further investigated.

6-Nitro-3:4-methylenedioxymandelic Acid,

6-Nitropiperonal cyanohydrin (10 grams; see below) was boiled during ten minutes with concentrated hydrochloric acid (30 c.c.), the liquid then diluted with an equal volume of water, boiled with bone charcoal, and filtered. The cooled solution deposited the acid in greenish-yellow crystals, and a further quantity was recovered from the mother liquor, the total yield closely approaching that demanded by theory. The substance was several times recrystallised from water, in which it is sparingly soluble in the cold, and obtained in pale yellow needles, which on being heated darken at about 150°, and melt and decompose at 181–183°:

0.1238 gave 0.2032 CO₂ and 0.0324 H₂O. C=44.8; H=2.9.

C₉H₇O₇N requires C=44.8; H=2.9 per cent.

This acid can easily be prepared in large quantities, and on this account the many interesting reactions which it exhibits are being investigated. On boiling with aqueous potassium hydroxide, an intense, crimson solution is produced, and a bright, yellow crystalline solid precipitated; the crimson solution gives a brown precipitate on acidification. Most characteristic, however, is the behaviour of the acid on being boiled with glycerol, or, better still, nitrobenzene. The substance loses carbon dioxide, nitrogen, and water, and is converted into a chocolate-brown compound, which crystallises from the nitrobenzene. This compound is readily soluble in alkali carbonates, and a mere trace of it dissolved in sulphuric acid gives rise to a magnificent royal-blue solution. The investigation of this chocolate substance is not complete, and we prefer not to speculate regarding its constitution; its composition appears, however, to be C₃₂H₂₀O₁₆N₂ or C₃₂H₂₂O₁₆N₂.

6-Nitro-3:4-methylenedioxymandelonitrile (Nitropiperonal Cyanohydrin), CH₂:O₂:C₆H₂(NO₂)·CH(OH)·CN.

6-Nitropiperonal (20 grams) was dissolved by heating in glacial acetic acid (120 c.c.), and rapidly cooled while being vigorously

shaken. Powdered potassium cyanide (20 grams) was then added, and rise of temperature checked, after which the mixture was frequently stirred, and allowed to remain overnight. The nitropiperonal passed into solution, and a new, almost colourless substance separated, the quantity of which was very much increased by dilution of the solution with water. The solid was collected, washed, and dried in a vacuum, and weighed 18 grams. It was usually employed in this condition, but for purposes of analysis a portion was twice crystallised by solution in cold ethyl acetate, followed by addition of light petroleum. Almost colourless needles separated, but these in course of time were resolved into a powder of small, compact, very pale yellow prisms. The substance begins to decompose at 110° , and melts and decomposes at 119° :

0.1104 gave 0.1980 CO_2 and 0.0297 H_2O . $\text{C}=48.9$; $\text{H}=3.0$.

$\text{C}_9\text{H}_6\text{O}_5\text{N}_2$ requires $\text{C}=48.6$; $\text{H}=2.7$ per cent.

In solvents other than light petroleum this derivative is readily soluble.

Methyl 6-Nitro-3:4-methylenedioxy mandelate,

6-Nitropiperonal cyanohydrin (5.1 grams) was dissolved in dry ether (25 c.c.) and methyl alcohol (2 grams), and the solution, cooled in a freezing mixture, was saturated with hydrogen chloride. After remaining overnight, the imino-ether hydrochloride, which separated in colourless crystals, was collected, washed with ether, and decomposed with water. The ester was so obtained in a crystalline condition, and, after collection, was recrystallised from ethyl alcohol, from which it separated in very pale yellow leaflets, melting at 124° :

0.1194 gave 0.2069 CO_2 and 0.0395 H_2O . $\text{C}=47.2$; $\text{H}=3.6$.

$\text{C}_{10}\text{H}_9\text{O}_7\text{N}$ requires $\text{C}=47.1$; $\text{H}=3.5$ per cent.

On being heated with cotarnine in alcoholic solution, this ester yields a relatively small amount of a condensation product, which is doubtless the carbomethoxy-derivative of nitropiperonylidenehydrocotarnine. The reaction was not further investigated, since a better result was achieved by the use of the more simple nitrohomopiperonyl alcohol.

6-Nitropiperonylhydrocotarnine (VII).

The reaction between cotarnine and aldehydes has been under our observation for a considerable period, but unfortunately in most cases the products of condensation are difficult to crystallise or otherwise obtain in a pure condition; thus, for example,

cotarnine condenses with piperonal and benzaldehyde in alcoholic solution to form oily bases, and with the normal ester of opianic acid to an amorphous base, which we were unable to crystallise. Nitropiperonal, however, yields a crystalline condensation product with both cotarnine and hydrastinine, although in each case there are a number of by-products the investigation of which is not yet complete.

Cotarnine (20 grams) and 6-nitropiperonal (22 grams) were boiled together under reflux with ethyl alcohol (300 c.c.) during forty minutes. A greenish-yellow, sandy, crystalline precipitate separated from the solution as the reaction proceeded, and at the end was collected and washed with alcohol. The nature of the substances remaining in the filtrate is being investigated. After drying, the base, which is almost pure, weighed 9 grams. The substance is very sparingly soluble in almost all organic solvents, but could be crystallised by boiling with a large quantity of chloroform, and adding alcohol to the solution after concentration. It may also be crystallised, if the operation be conducted quickly, from a mixture of pyridine and alcohol. The substance was obtained as a yellow powder, consisting of small, compact prisms, and melting at 172° , after turning orange at 140° :

0.1345 gave 0.2727 CO_2 and 0.0492 H_2O . $\text{C}=55.3$; $\text{H}=4.1$.

$\text{C}_{20}\text{H}_{18}\text{O}_8\text{N}_2$ requires $\text{C}=55.3$; $\text{H}=4.1$ per cent.

This base forms sparingly soluble salts with mineral acids, so that it does not appear to dissolve in dilute hydrochloric acid. It is, however, readily soluble in acetic acid, and the solution gives no precipitate on dilution. The solution in either glacial or dilute acetic acid is unchanged on boiling, and when to the latter dilute nitric acid is added, there is an immediate precipitation of a sparingly soluble nitrate. Hydrochloric acid also causes a separation of a sparingly soluble *hydrochloride* when it is added to the solution of the base in dilute acetic acid, whilst with sulphuric acid, under similar conditions, no precipitation occurs at first, and then later the *sulphate* separates in gelatinous flocks, which slowly become crystalline. The *acid oxalate* crystallises from moderately concentrated solutions in slender needles, and, in common with the hydrochloride, sulphate, and nitrate, is pale yellow. The *picrate* will crystallise from a solution of the base and picric acid in glacial acetic acid, but it is more conveniently obtained by mixing this solution with acetone. It consists of bright yellow prisms and needles, melting and decomposing at $247\text{--}248^{\circ}$.

The suspension of the base in alcohol is unchanged by the addition of phenylhydrazine, even on boiling; a reaction between the two substances occurs, however, in the presence of a small propor-

tion of acetic acid. Nitropiperonylhydrocotarnine dissolved in dilute acetic acid was gently warmed with a solution of phenylhydrazine in the same solvent. A bright red substance separated in flocks, and was collected when the reaction appeared to be complete.

The compound crystallised from glacial acetic acid in bright red, prismatic needles, and melted at 218° . It was identified as the phenylhydrazone of nitropiperonal, a specimen of which was prepared for the purpose of comparison. A mixture of the compound obtained from the base with the substance obtained from the nitroaldehyde melted at 218° . Nitropiperonalphenylhydrazone has been prepared by Haber (*Ber.*, 1891, **24**, 625), who, however, describes it as needles, from aqueous alcohol, melting at 212° . Our substance is sparingly soluble in alcohol, and always crystallises in prisms.

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